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DOTTORATO DI RICERCA IN
Scienze Chimiche

CICLO XXXVII

Visible – Light – Promoted Dearomative Cyclizations: New Routes to Complex Polycycles

Coordinatore: Chiar.mo Prof. Giovanni Maestri

Tutore: Chiar.mo Prof. Giovanni Maestri

Dottorando: Maurizio Chiminelli

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Chapter I

General Introduction

1.1: The sp^2 Bias

Modern organic chemistry is highly influenced by the use of metal-catalysed cross couplings. Since their discovery in early 80's, these methods showed numerous advantages in building complex molecular architectures. Indeed, Suzuki, Sonogashira, Heck couplings allow the formation of new $Csp^2 – Csp^2$ bonds with a relatively easy effort respect to other previously reported organic reactions. Low catalyst loadings, high TON, high yields, high functional group tolerance and robustness spread these methodologies in all synthetic laboratories, from the university to the fine chemical industry[1]. The reason is clear: if you adopt effective synthesis, you will lose less products or you will fail fewer synthetic steps. This sentence gains higher impact taking in consideration the pharmaceutical industry, because their products have a high value, and researchers do their best to reduce wastes. Moreover, university researchers have continued to optimize cross coupling, making them increasingly efficient and with low environmental impact. These motivations have pushed modern organic chemistry to always use the same classes of reactions. In 2010, Cooper *et al.*[2] highlighted that in medicinal chemistry 89% of the reactions fell into 10 reactions classes, in which palladium – catalysed couplings make the 22%. This attitude generated a problem in modern organic chemistry, named sp^2 bias, that brings to the synthesis and discovery of more and more highly unsaturated compounds in medicinal chemistry.

Lovering *et al.* described the need to interrupt this trend in two popular papers[3,4]. With a data analysis on the molecules involved in drug discovery, from early discovery to drug commercialization, they realised that complexity has a key role for a successful candidate. They defined molecular complexity as a sum of two parameters: Fsp^3 and the presence of stereocenters. The first is the ratio between the number of Csp^3 divided by the number of total carbons of the molecule. Authors noted that there is a positive correlation between the two factors and the probability of a molecule to become a commercialized drug (Figure 1).

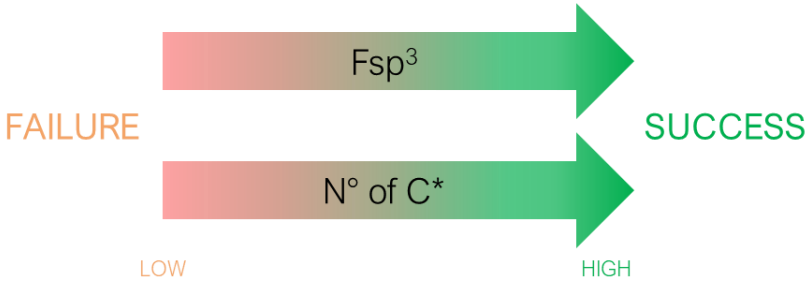


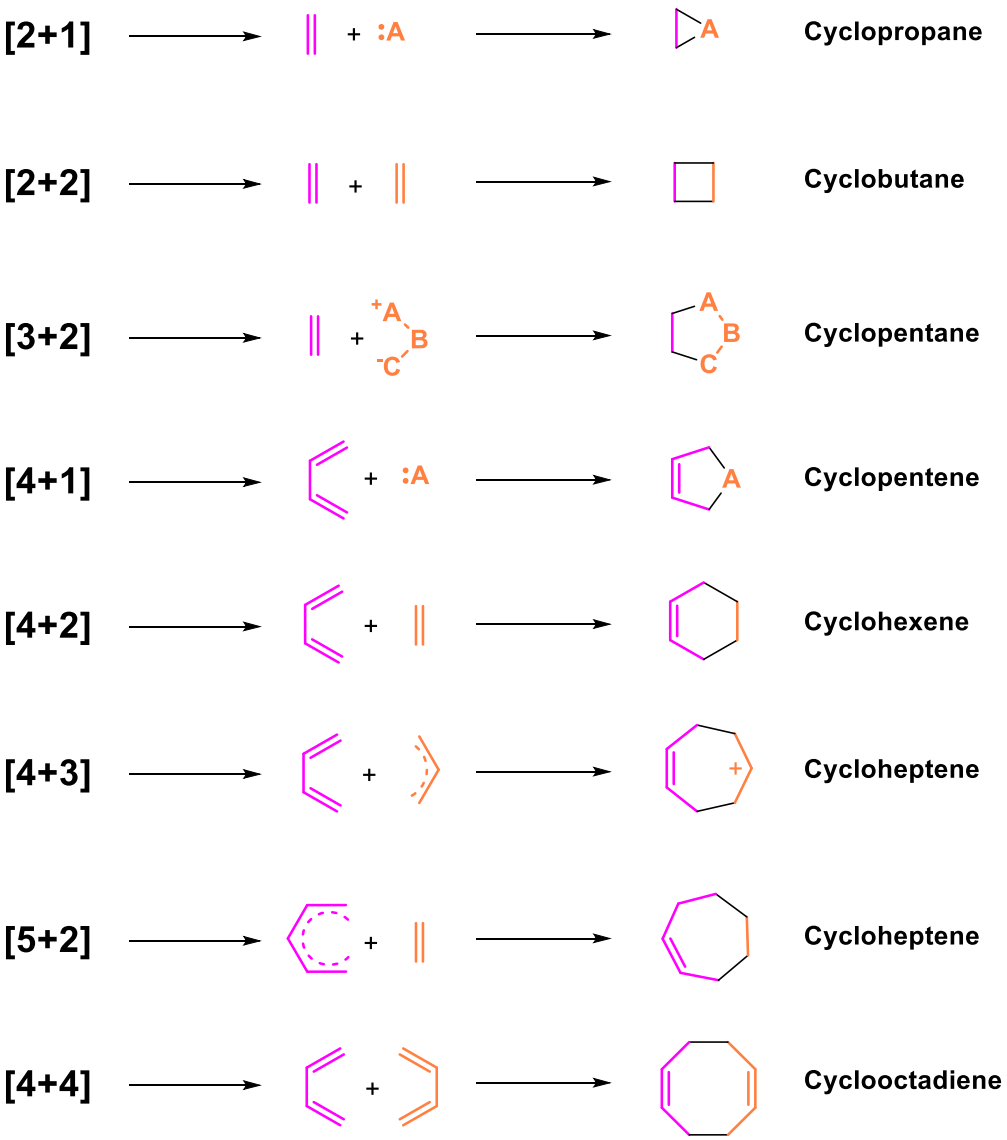
Figure 1: Probability of a molecule to become drug increases with complexity.

Indeed, saturation allows the synthesis of molecules with a higher architectural complexity, exploring a wider chemical space without a significative increment in molecular weight (MW). This is a key result, because there was the thought that higher MW corresponds to higher efficacy as drug[5]. Complexity can also influence important physical parameters, such as solubility and melting point, that are fundamental for drugs. To rationalize, molecules with a 3D scaffold tend to aggregate worse than flat ones, reducing π-π stacking and dispersion forces. Moreover, 3D architectures allow the formation of several interactions inside the active site of the protein, showing less off-target effects. In this way, drugs have improved potency and selectivity, resulting less promiscuous and toxic.

1.2: Cycloadditions

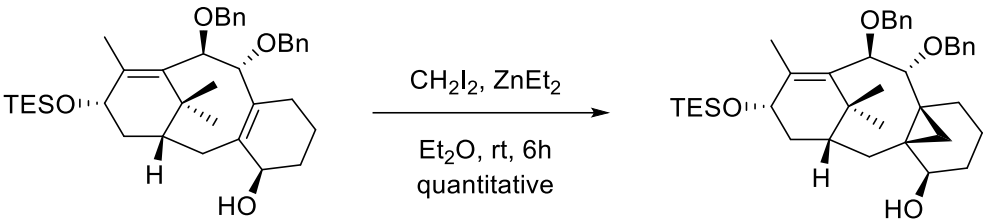
According to IUPAC[6], cycloaddition is "a reaction in which two or more unsaturated molecules (or parts of the same molecule) combine with the formation of a cyclic adduct in which there is a net reduction of the bond multiplicity". Thus, this type of chemical reaction is inherently one of the best strategies to increase bond's saturation in the product. With this approach, multiple C-C bonds are formed in only one synthetic step with complete atom economy[7]. This feature strongly reduces the amount of waste, one the most important principles of green chemistry[8]. Considering all these advantages, it's clear that several researchers in the world regard cycloadditions as one the most powerful reaction in organic synthesis. Furthermore, the intensive study of these methodologies has led us to effectively rationalize their mechanisms[9,10]. Many examples demonstrate precise control over regio- and diastereoselectivity, up to the applications of enantioselective cycloadditions for total synthesis[11–13].

Starting from the discovery of Otto Diels and Kurt Alder[14], several types of cycloadditions were developed (Scheme 1). The common system of notation involves the use of two square brackets that enclose two numbers separated by a plus, i.e. [X+Y]. X and Y represent the number of electrons in the interacting units that participate in the transformation of reagents to products. Interestingly, by adding the numbers inside the brackets you get the type of cycle that will be formed. For example, in a [2+2] cycloaddition you get a cyclobutane (4), or in a [4+2] you get a cyclohexene (6). Below are reported some examples of the most common cycloaddition reactions.



Scheme 1: List of most representative cycloaddition reactions.

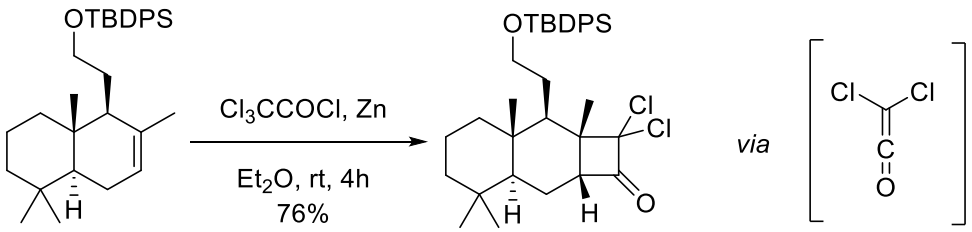
In 1996, Kuwajima *et.al.*[15] used the [2+1] cycloaddition in the synthesis of taxusin (Scheme 2). In this beautiful example, authors exploited the formation of a cyclopropane to install the methyl substituent of C19.



Scheme 2: Diastereoselective [2+1] cyclopropanation.

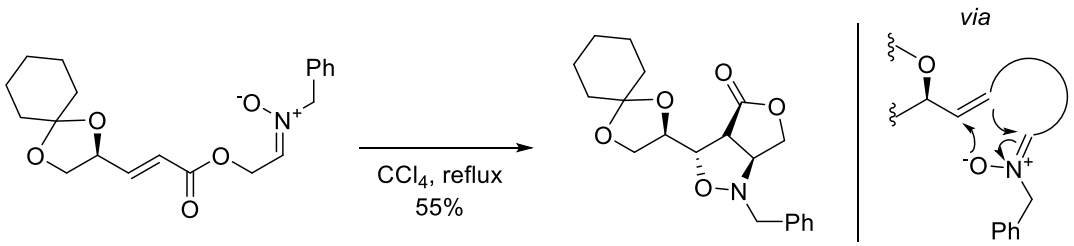
They formed the carbene with the common diiodomethane and they obtained a complete diastereoselective cyclopropanation due to the high structural rigidity of the starting material and the presence of the -OH substituent close to the double bond[16].

[2+2] cycloadditions are one of the most important reactions in modern organic chemistry, since cyclobutane rings can be found in several bioactive molecules[17]. In the total synthesis of (−)-isoscopariusin A[18], an immunosuppressive meroditerpenoid, Puno *et.al.* developed a thermal [2+2] between an alkene and a ketene to achieve a fundamental intermediate (Scheme 3). The reaction proceeds smoothly, with satisfactory yield and great diastereoselectivity.



Scheme 3: [2+2] cycloaddition promoted by dichloroketene.

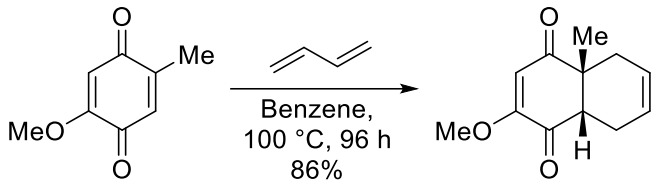
In 1998, Jørgensen et.al.[12] wrote a review of 1,3 dipolar cycloadditions (i.e. [3+2]), showing the importance of these methodologies in asymmetric synthesis. The reaction usually involves an alkene and a dipolar partner. The latter can vary from a nitrone to carbonyl and azomethine ylides, up to even being nitriles or azides. The necessary condition is that you need a 1,3 dipole, in other words a specie that has simultaneously a δ+ and a δ- in its three-terms-structure. Most of the time these dipoles are zwitterions, like the nitrone reported in Scheme 4 (right). Saito et.al.[19] described the use of a 4-alkenyl nitrone as substrate for a fascinating diastereoselective cycloaddition (Scheme 4, left).



Scheme 4: Bicyclic isoxazolidine formed with [3+2] cycloaddition.

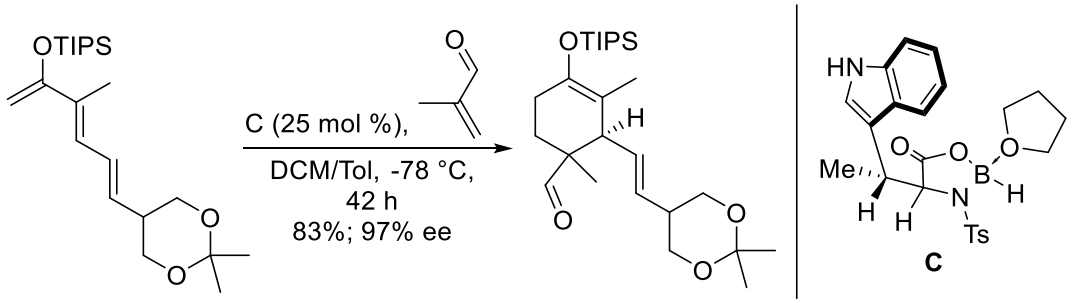
The resulting bicyclic isoxazolidine is obtained as a single isomer, because the exo-cyclic chiral center completely directs the selectivity of the process. However, there are several reports in literature where the diastereoselectivity is not controlled at all. A possible drawback of 1,3 dipolar cycloaddition is the forced formation of a heterocycle. Indeed, only with a recent discovery by Zhu et.al.[20] carbo-cyclopentane can be obtained with a formal [3+2] cycloaddition.

The last class of cycloadditions that needs to be highlighted is the [4+2], commonly known as Diels-Alder reaction[11]. Since the beginning, researchers recognized the potential of this methodology and applied it to total synthesis. Initially, the reactions proceeded through harsh conditions, with very high temperatures and often problems of tolerance to the functional groups. A brilliant example of the time is reported by Woodward *et. al.*[21] in the total synthesis of steroids (Scheme 5).



Scheme 5: Thermal Diels-Alder reaction with butadiene.

Benzoquinone is reacted with butadiene in autoclave at 100 °C for 96 hours. The product is predominantly obtained as *cis*-adduct in a high yield. This example shows the high diastereoselectivity induced by the Diels-Alder cycloaddition mechanism. Recent developments in [4+2] reactions have focused on the use of chiral partners, such as chiral Lewis acids or metal complexes, to obtain enantioselective transformations. In 1994, Corey and coworkers[22] demonstrated the utility of oxazaborolidine catalyst in the enantioselective synthesis of cassiol, a potent antiulcer substance (Scheme 6).



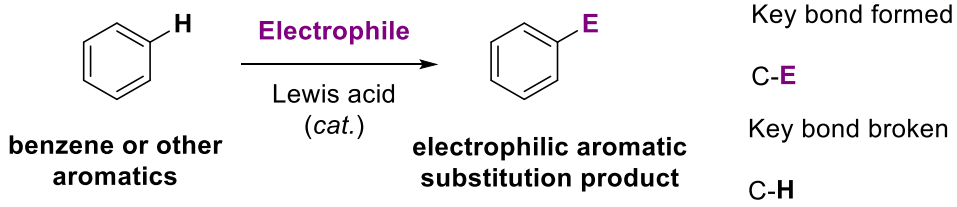
Scheme 6: Enantioselective [4+2] in the synthesis of cassiol.

With a reasonable amount of 25 mol%, the catalyst can direct the enantioselectivity of the reaction, achieving the complex intermediate with high yield and excellent enantiomeric excess. Then, after 4 simple steps, enantiopure cassiol is obtained.

Cycloadditions have thus proven to be extremely useful reactions in modern organic chemistry, with numerous applications in the total synthesis of bioactive molecules. Their main advantages consist of potentially excellent regio- and diastereoselectivity, complete atom economy and increased product's saturation (Fsp^3). The next step toward achieving even more remarkable results is to couple them with another very important reaction, which would lead to a further notable increase in Fsp^3: dearomatization.

1.3: Dearomatizations

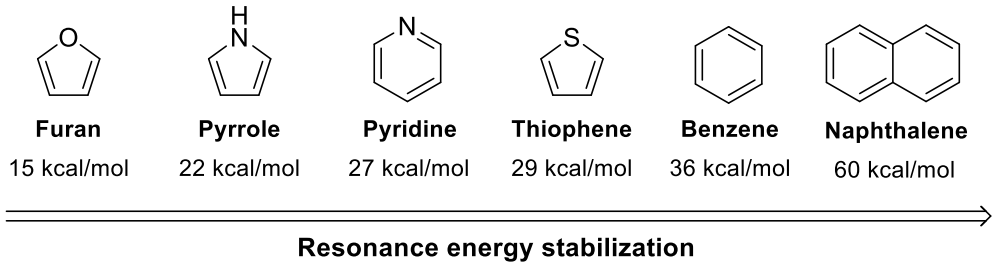
Aromatic compounds are one of the most available feedstocks in the world, with a production of around 100 million tons per year[23]. Although most are used for polymers, solvents and fuels, their enormous abundance has driven chemists to use them extensively as reagents for their synthetic transformations. Moreover, being chromophores, easy to install and relatively inert made them very present in all the laboratories of the world. The last peculiarity that made them so important is the commercial availability of a myriad of aromatics with different functional groups, often difficult to install in mild conditions. For these reasons, aromatics are crucial reagents in developing libraries of product for drug discovery. They can be added onto a molecular scaffold in several ways, from metal-catalysed couplings to reductive amination of aldehydes and nucleophilic substitution of benzyl halides. But aromatics can also face reactions on their scaffold, being the starting point of the synthesis. The most common reaction is electrophilic substitution (SeAr), which exchange one or more hydrogens with different functional groups, maintaining the aromaticity of the system (Scheme 7).



Scheme 7: Electrophilic aromatic substitution.

Poor chemoselectivity and functional group tolerance, along with harsh conditions and laborious purification steps made these methodologies less fascinating for modern organic chemistry. Essentially, the widespread use of aromatic rings, combined with synthetic methodologies that preserve their aromaticity, strongly increased the sp^2 bias.

Dearomatization is a brilliant strategy to significantly increasing the complexity of the system, moving from a planar 2D scaffold to an alicyclic 3D structure, starting from cheap and readily available feedstocks. Moreover, these methodologies often have a complete atom economy, one of the fundamental principles of green chemistry, producing drastically less waste than the aforementioned SeAr. Unfortunately, the chemical inertness of aromatics is precisely attributable to their high resonance stabilization[24] (Scheme 8).



Scheme 8: Resonance energy stabilization of principle aromatics.

Thus, dearomatization strategies often require to overcome high kinetic barriers, with the use of harsh reaction conditions. This results in low functional group tolerance and poor environmentally sustainable procedures. Moreover, generally low selectivity brings to the formation of inseparable mixtures of products. Nonetheless, research in this area is constantly growing, driven by the excellent results that can be obtained once the aromaticity obstacle has been overcome. As it shown in Figure 2, there is an exponential growth in the publications containing “dearomatization” in their text, with a significant rise in the last ten years. For example, in 2023 the number of papers was 415, while in 2013 it was only 134.

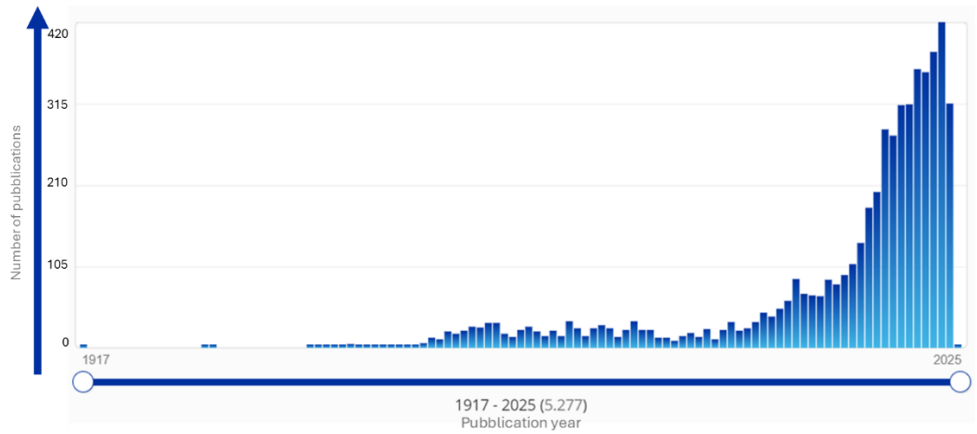
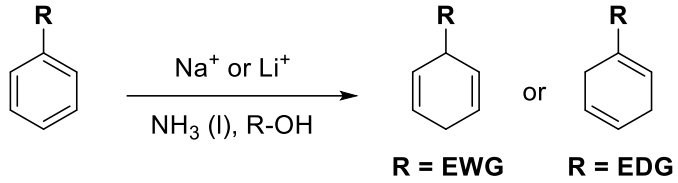


Figure 2: Recent growth of publications in the field of dearomatization. Form scifinder-n.cas.org.

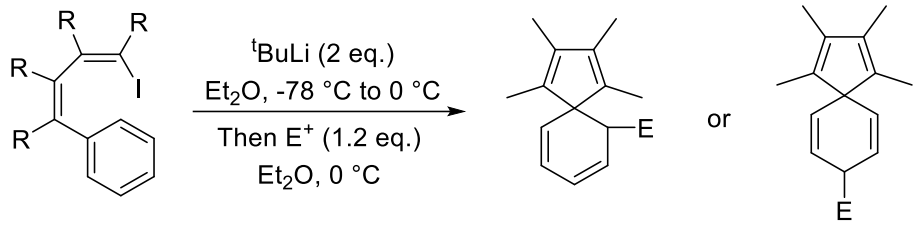
In 1944[25], Arthur J. Birch developed his famous reaction in which he reduced aromatic compounds into cyclohexadienes with liquid ammonia and alcohol in combination with an alkali metal (Scheme 9).



Scheme 9: Birch reduction and regiochemistry.

Electron withdrawing substituent (EWG) allows the synthesis of cyclohexadienes with disubstituted double bonds. On the other hand, with electron donating ones (EDG) is possible to obtain the opposite regioisomer, in which one of the double bonds is trisubstituted. Even if the conditions were very harsh and the scope was narrow, Birch reduction opened the way to dearomatizing methodologies in modern organic chemistry. Hydrogenation is one of the most important dearomatization strategies[26,27], but I will not discuss any examples related to this field, because it is far from the research works that I will discuss in the next chapters. Instead, I prefer to focus this introduction on the formation of new C-C bonds.

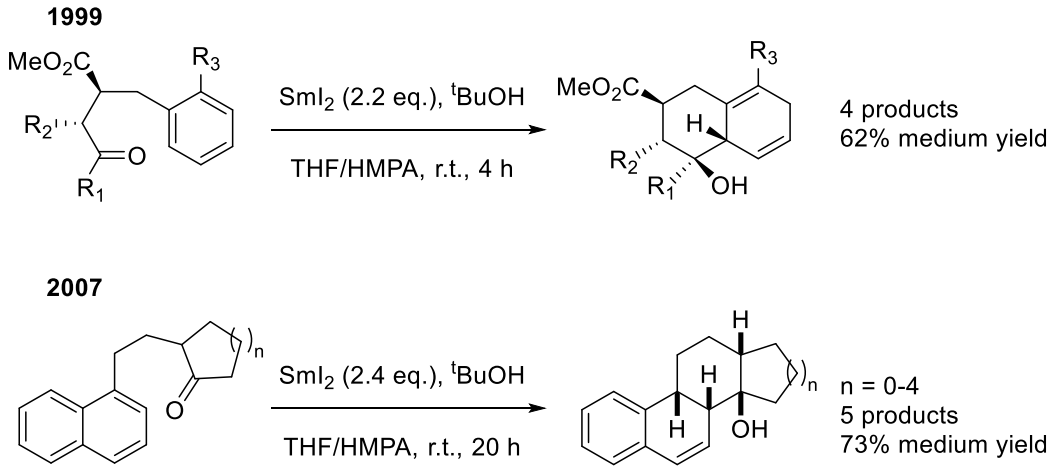
In 2007, Xi and coworkers[28] obtained an intramolecular dearomative addition of vinyl iodides into aromatic rings (Scheme 10).



Scheme 10: nucleophilic dearomatization.

The halogen-lithium exchange was performed at -78 °C, but it was necessary to increase the temperature up to 0 °C to induce the dearomatization. Then, the carbanion was trapped with an electrophile (usually an aldehyde or a ketone) to achieve the final product. Authors declare that the regiochemistry is dictated by the aromatic substrate and the nature of E^+. Xi was able to dearomatize simple benzene as well as naphthalene, the latter with higher yields due to the lower resonance energy of stabilization.

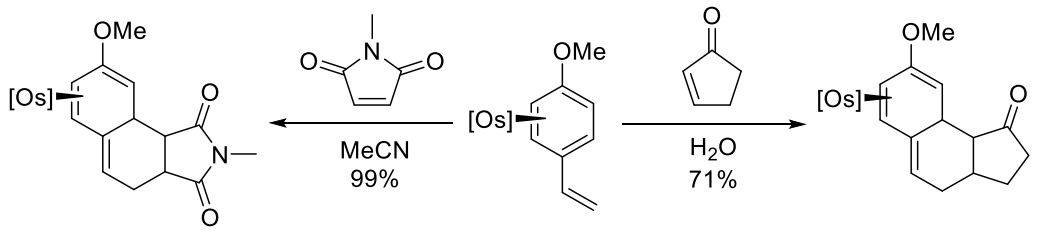
Samarium-mediated radical cyclization[29,30] of polynuclear arenes resulted in the formation of fused polycycles (Scheme 11).



Scheme 11: diastereoselective cyclization mediated by Samarium.

The diastereoselective cyclization step was highly dependent on the steric interactions between the alkoxysamarium and the arene motifs. Prof. Reissig *et.al.* were able to perform the reaction both onto benzyl and naphthalene with appreciable yields. The latter gave a library of products with a common structural motif that reminds human steroid-like cholesterol and estradiol.

Another interesting method to induce dearomatization involves using a transition metal to mediate the transformation[31]. Mn and Cr complexes can induce nucleophilic substitution on the arene, eventually trapping an electrophile to have a double substitution or a proton to re-aromatize. Os complexes prefer a η^2-coordination to the arene instead. Thus, they can increase the nucleophilicity of the system, enabling new electrophilic substitutions. Moreover, by coordinating to one double bond out of three, they also act as a "protecting agent" for that bond. In 1998, Harman et.al.[32] used this feature in a brilliant way (Scheme 12). Authors made an original Diels-Alder cyclization with electron poor dienophiles and the electron rich diene derived from the activation of benzene with Os complex. They obtained 8 products with high yields and mild reaction conditions, except for the use of toxic osmium itself.



Scheme 12: Application of Os mediated activation with Diels-Alder cyclization.

"The aromatic nucleus, known for its rigidity in the ground state, becomes an extremely flexible and extrovert acrobat when being doped with a light quantum"[33].

This statement by Havinga marks a turning point in the development of dearomative methodologies. Indeed, what we considered inert in its ground state can be activated with light. In 1964, the author could only think about UV-light (254 nm) to directly activate aromatic compounds, with a myriad of limitations concerning that powerful irradiation. However, the idea was brilliant and nowadays light is the most fascinating tool to induce dearomatization[34–36]. What is different is the source of light, because the old and extremely high energetic UV-Lamps were replaced by cheap and less energetic visible-light lamps. The advent of photocatalysis has therefore allowed the development of many efficient dearomatizing strategies.

1.4: Visible-Light Photocatalysis

In the last century, high reactive intermediates were generated upon excitation with UV-light[37]. However, UV is as powerful as unselective, often causing very low tolerance towards the functional groups and inseparable mixtures of compounds. The birth of modern visible – light promoted photocatalysis opened a new era in synthetic chemistry[38–40]. The main advantage of this strategy is accessing to fancy transformations with extremely mild conditions. Indeed, most of visible – light promoted reactions are conducted at room temperature, with great profits from an economical and environmental point of view. Unlike metal catalysts, which often require high temperatures, in photocatalysis there is easy access to very unstable intermediates, which have sufficient energy to push the reaction to completion. Furthermore, visible-light activation is very selective and relatively predictable, such as in HAT/XAT methodologies and energy transfer (EnT) processes.

The primordial examples of a reaction promoted by visible light date back to 1886, when Giacomo Ciamician attempted to conduct chemical reactions by leaving them on the roof of his university (Figure 3).

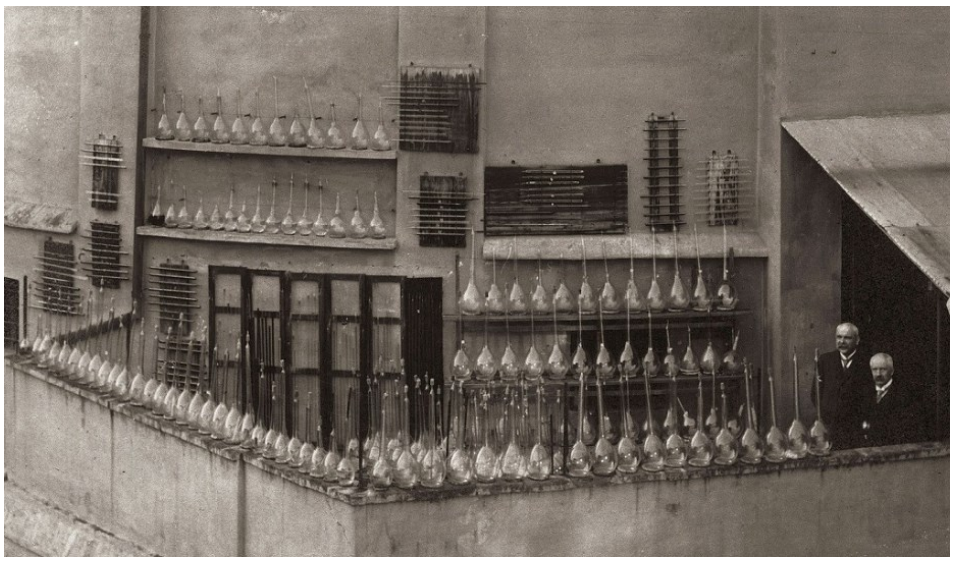
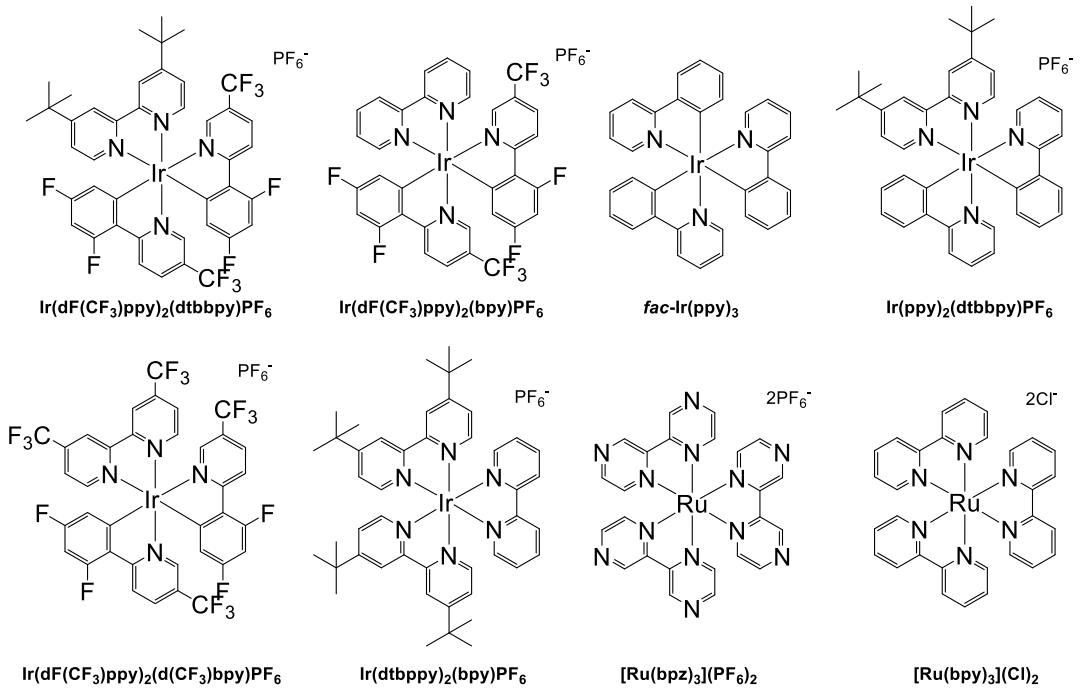


Figure 3: Ciamician and Silber in their rooftop laboratory in Bologna. From www.chemistry.unibo.it.

The idea was brilliant and Ciamician obtained sensational results that were unforeseeable according to the knowledge of the time[41,42]. However, even if interesting, reactions that need weeks or months to complete were not suitable for industrial applications. What was missing was proper catalyst to speed up the reaction times. Indeed, the topic of reactions promoted by visible light remained out of radar until the 2000s, when the pioneer articles on the use of metal catalysts to promote these reactions were reported[43,44]. Many of the most employed photocatalysts (PC) are polypyridyl complexes of ruthenium and iridium based catalysts (Scheme 13).



Scheme 13: Commonly employed metal photocatalysts.

These metal photocatalysts overcome all other candidates because their properties can be finely tuned, changing both bipyridyl and phenylpyridyl ligands[45]. Their catalytic mechanisms are all the same and the necessary condition is to absorb light in the visible region. When a photon is properly absorbed by the photocatalyst, it gets excited, causing one electron to move from the ground state to an excited state

(**^{1}PC***). Then, after intersystem crossing, the singlet becomes a triplet (**^{3}PC***), which has 2 unpaired electrons with the same spin. The relaxation from triplet to singlet is spin-forbidden, so it takes longer than usual to occur. Indeed, fluorescence decays occurs in the order of nanoseconds, while phosphorescence (from excited triplet to singlet) has times in the order of microseconds. This "temporal delay" allows the catalytic processes. Excited triplet has two unpaired electrons, now located in $SOMO_{-1}$ and SOMO (Figure 4).

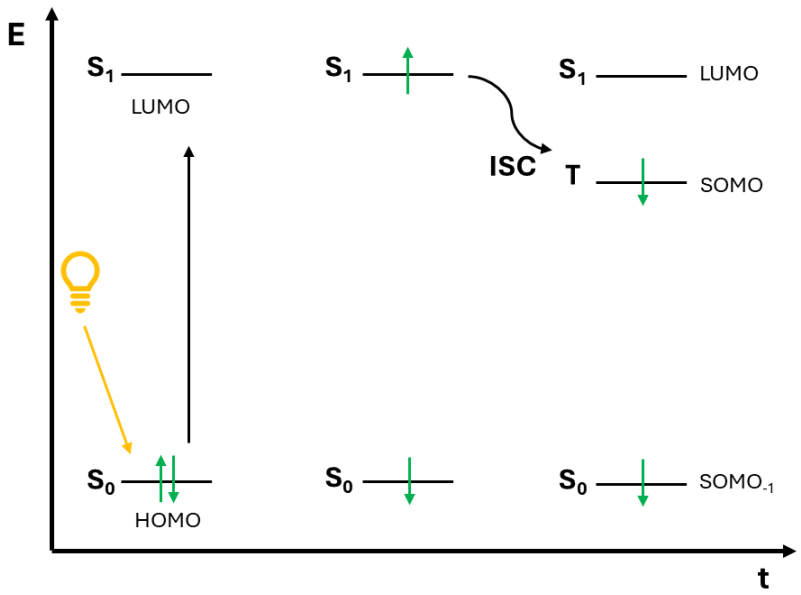
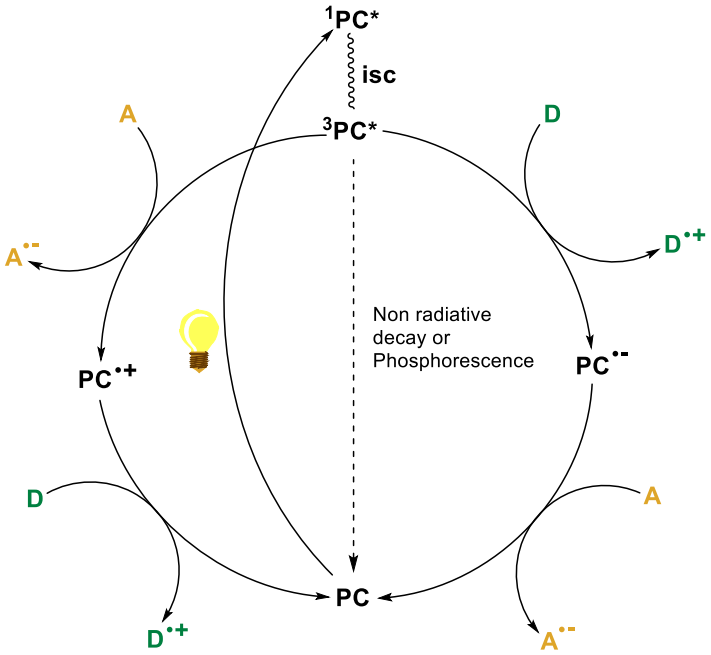


Figure 4: Semplified rappresentation of the activation of PC with visible light.

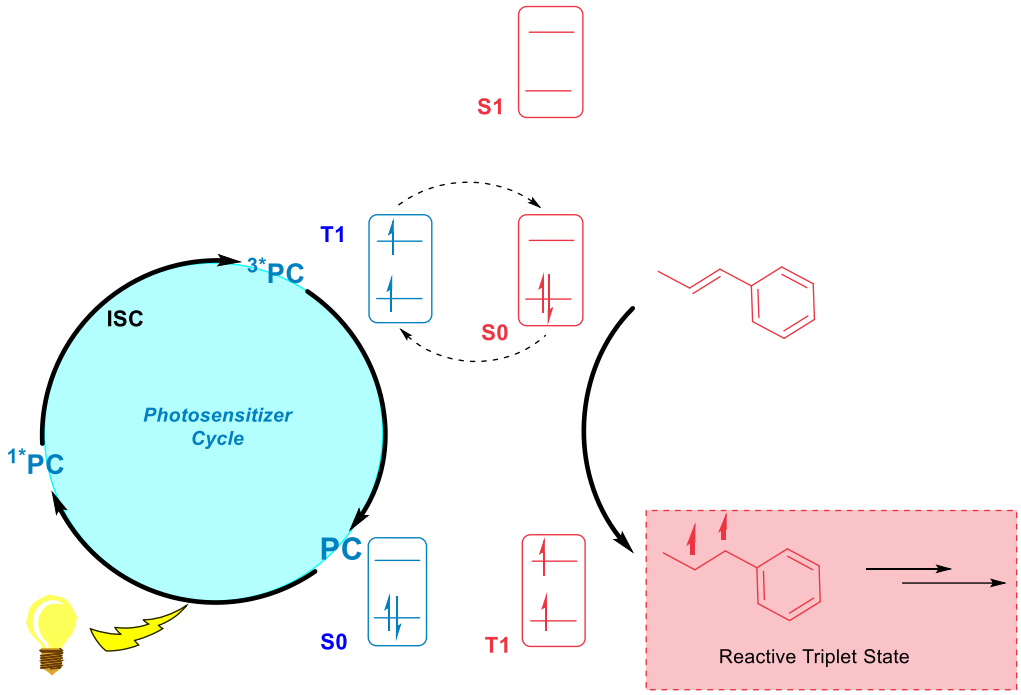
The former, wants to receive an electron to fill the orbital gap, while the latter wants to go away from that high energetic orbital. The photocatalyst becomes thus a strong oxidant and/or a strong reductant.

As it shown in Scheme 14, the photocatalyst can perform a reductive or oxidative quenching with an appropriate substrate, depending on their electronic potentials. This process is called Single Electron Transfer (SET).



Scheme 14: SET mechanism of photocatalysis.

On the other hand, **^{3}PC*** can evolve through an Energy Transfer process (EnT). There are two main mechanisms that rule this phenomenon, Forster and Dexter, but I will describe only the latter because it is the one involved in synthetic photocatalysis. Dexter type EnT is a process in which substrate and photocatalyst exchange two electrons simultaneously (Scheme 15).



Scheme 15: Dexter type EnT mechanism.

The resulting triplet on the substrate can then initiate organic reactions such as cyclizations or HATs. It is worth nothing that not all the unsaturation can be excited by EnT. Indeed, the substrate must have a triplet energy (E_T) lower than the one of the exciting photocatalyst. Moreover, even if the energy gap is satisfied, it is necessary to have a good overlap between the orbitals of both substrate and PC to enable a productive energy transfer. For each specific reaction under developing, is thus necessary screening several photocatalyst to find the one that matches better with the studied substrate. A general trick to lower the E_T is increase the conjugation of the double bond using auxiliary groups. Common substrates involved in EnT processes are cinnamyl, styrenes, enones etc.[46,47].

From a mechanistic perspective, several techniques have been developed to study these processes[48]. Among all, I believe it is appropriate to spend some words to describe the Stern-Volmer quenching studies (Figure 5).

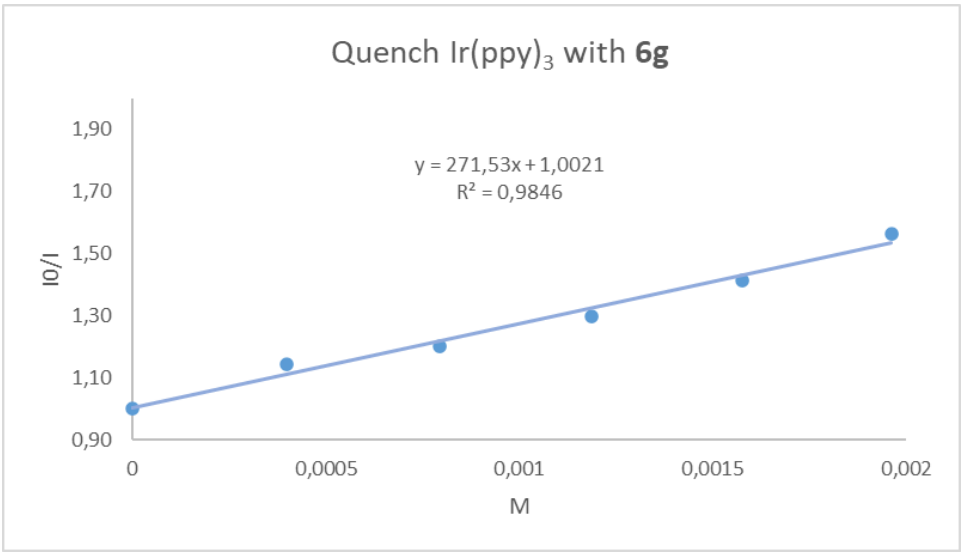


Figure 5: General appearance of a Stern-Volmer plot.

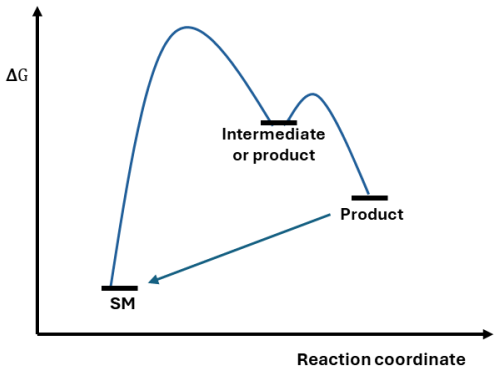
This methodology is very useful to understand and confirm if the photocatalyst is reacting with the substrate, regardless of whether it is via SET or EnT. From an experimental point of view, the analysis consists of measuring the emission of the excited photocatalyst (I_0) and successive additions of substrate (named quencher [Q]) are recorded (I), and spectra are eventually elaborated. A linear Stern – Volmer plot is obtained at varying concentrations of substrate, and K_{SV} constants are extracted according to the equation $I_0/I = 1 + K_{SV}[Q]$. When the intensity of emission decreases after each addition, the plot shows a straight line with a positive slope (i.e. K_{SV}) and you can assume that there is a productive interaction (i.e. a quench) between the photocatalyst and the substrate. Otherwise, when the straight line is flat, K_{SV} is close to zero and there are no interactions; in other words, the substrate doesn't quench the photocatalyst.

1.5: Dearomative Cycloadditions

Dearomative cycloadditions are a brilliant strategy to merge the advantages of cycloaddition and dearomatization transformations. With this approach it is possible to obtain very complex products starting from cheap and commercially available feedstocks. Moreover, the formation of the 3D-alicyclic scaffold occurs with the establishment of one or more stereocenters. The latters are often forced to assume only one configuration (due to the mechanism of the cyclization), resulting in diastereoselective reactions. Furthermore, these types of transformations proceed with a perfect atom economy, in accordance with the principles of green chemistry[8].

Synthetic chemists are thus interested in developing these methodologies but certain restrictions limit their use to specific examples[49,50]. The biggest issue regards the aromaticity. Indeed, aromatics don't want to lose their resonance stabilization and high energies are required to overcome this demand. Chemists solved this by adopting harsh conditions such as high temperatures or UV-activation[51] (Scheme 16; a, b), but this caused narrow reaction scopes most of time. In addition, some dearomatized products are less thermodynamically stable than substrates and they tend to go backwards, which is further enhanced by the harsh conditions. In this context, visible light photocatalysis can be an elegant solution to overcome the issues mentioned above[24,34–36] (Scheme 16; c). Indeed, with an appropriate photosensitizer (PS) you can activate via EnT the substrate, populating an excited triplet state. Now, the kinetic barrier becomes lower, and the reaction pathway is more accessible. Moreover, employing such mild conditions really improves the selectivity, yields and tolerance towards functional group. Finally, the trend to backwards is limited, because the system doesn't have the sufficient energy to overcome the kinetic barrier of the retro-cycloaddition.

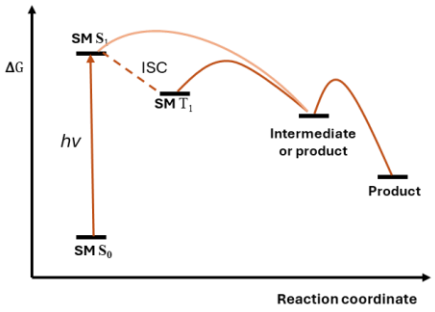
a)



THERMAL ACTIVATION

- Endergonic (ΔG > 0)
- High kinetic barrier
- Harsh reaction condition
- Reverse reaction favorable
- Low product yield

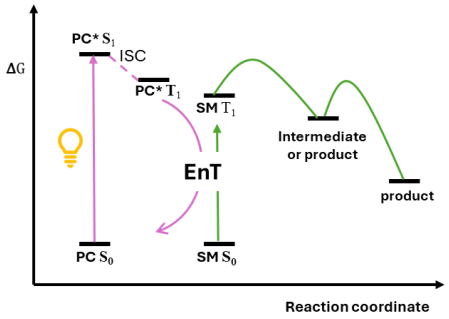
b)



UV ACTIVATION

- Endergonic (ΔG > 0)
- Low kinetic barrier
- High energy light source
- Reverse reaction prevented via selective excitation
- Uncontrolled side reactions (low yield and selectivity)

c)



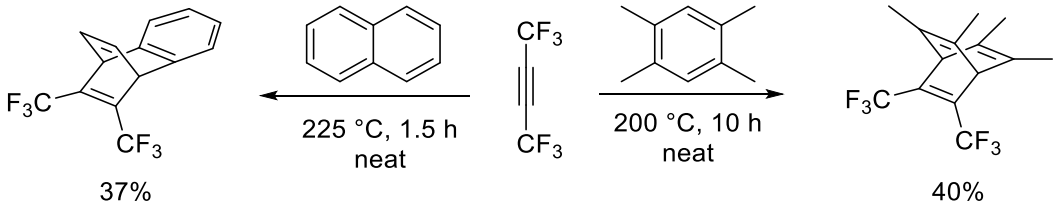
VISIBLE-LIGHT ACTIVATION

- Endergonic (ΔG > 0)
- Low kinetic barrier
- Mild reaction conditions
- Reverse reaction prevented via selective excitation
- High yield and selectivity

Scheme 16: Differences between dearomative cycloadditions strategies. a) thermal activation; b) UV activation; c) visible light activation.

In the next pages I reported examples of dearomative cycloaddition from the literature. They go from thermal activation to UV one, concluding with visible light activation (most examples). I will focus on [4+2] and [2+2] because these are the cycloadditions applied in the following chapters. Moreover, specific examples will be reported in the introduction of every chapter, to allow the reader to understand better the state of the art of every transformation that I will present in this thesis.

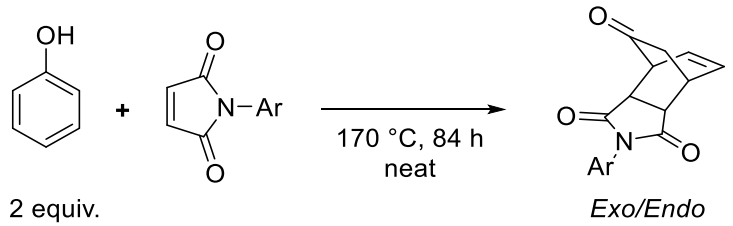
In 1961, Krespan and coworkers reported a pioneering work on the intermolecular dearomative cycloaddition of aromatics with bis-(polyfluoroalkyl)-acetylenes[52] (Scheme 17).



Scheme 17: Intermolecular cycloaddition between bis(trifluoromethyl)-acetylene and naphthalene (left) or durene (right).

They were able to dearomatize both naphthalene and durene (1,2,4,5-tetramethyl benzene) in an intermolecular fashion obtaining the corresponding [2.2.2] bicyclotrienes. However, yields were very low and there were no examples with susceptible functional groups. Moreover, they didn't observe reactivity with unbiased acetylene, and they had a complex mixture of 7 products performing the transformation with benzene instead of durene.

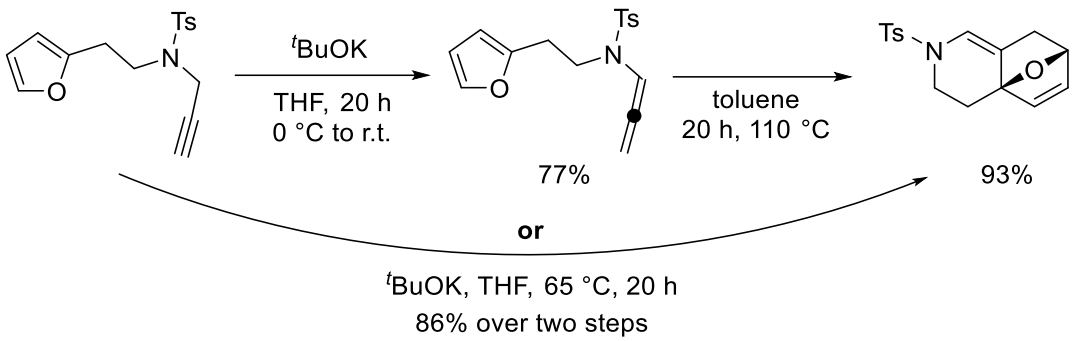
Another interesting examples of intermolecular [4+2] dearomative cycloaddition of a substituted maleimide on phenol was reported in 1987 by Bryce-Smith *et.al.*[53] (Scheme 18).



Scheme 18: Intermolecular cycloaddition between dihydric phenol and maleimide derivatives.

After 84 h at 170 °C the cyclic product was obtained as a mixture of *exo* and *endo* isomers. Authors reported only 8 examples, and yield goes from 9 to 37% with mostly polymerization side reaction.

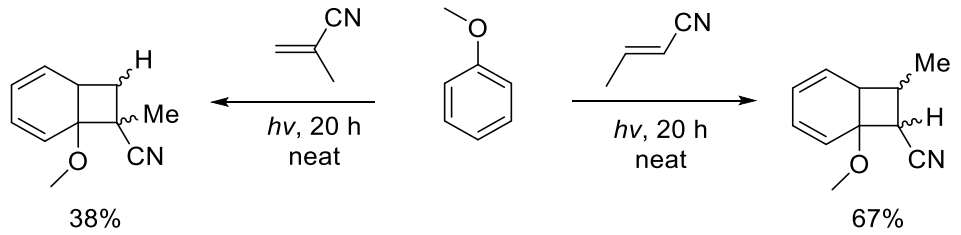
In 2009, Hsung *et.al.* reported an interesting stereoselective cyclization of allenamides on furane promoted by thermal activation[54](Scheme 19).



Scheme 19: Thermal dearomative [4+2] of allenamides on furane.

Starting from a propargyl amide, they obtained the corresponding sulfonyl-allenamide through isomerization with ^{t}BuOK. Then, the allene was reacted in toluene at 110 °C for 20 h giving the [4+2] adduct in 93% yield. Interestingly, they reported also the procedure to achieve the tandem isomerization-cyclization with no great loss in terms of yield.

Moving to UV-activated photocycloaddition, in 1977, Ohashi *et.al.* reported the intermolecular [2+2] cycloaddition between anisole and acrylonitrile derivatives[55] (Scheme 20).

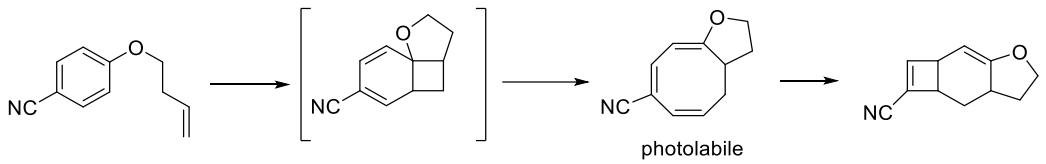


Scheme 20: Dearomative [2+2] between anisole and acylonitrile derivatives. with UV activation.

The cycloaddition with methacrylonitrile occurred with 38% yield, while it had a surprising 67% yield using crotoacrylonitrile. Both reactions were conducted with a low-pressure mercury arc for 20 hours. Authors tried also dimethoxy benzenes

(ortho, meta and para), but they always obtained undesirable products. The only example in which they had the cycloaddition, even with 32% yield, was by using *m*-dimethoxybenzene with crotoacrylonitrile.

In 1992, Gilbert and coworkers indirectly observed the [2+2] intramolecular cycloaddition of substituted anisoles with an alkene moiety[56] (Scheme 21).

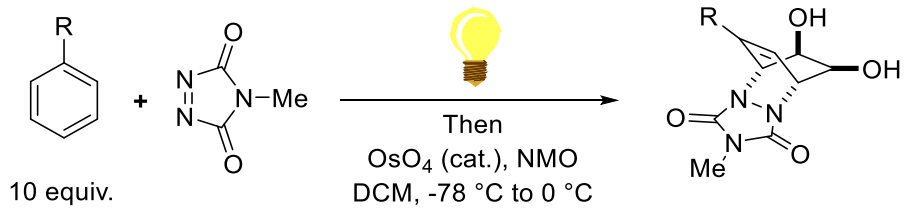


Scheme 21: intramolecular [2+2] of electron poor anisoles.

Authors studied the effect of electron withdrawing substituent in the cyclization of anisoles with enol ether. They tested both ciano and methoxycarbonyl groups, in *ortho*, *meta* and *para* positions. However, the resulting structure was a fascinating triene derived from a ring expansion that was photolabile and eventually convert to the tricycle reported in the scheme.

All these pioneering examples shows the potential of these strategies for the synthesis of very complex structures in a single step. However, these studies present too many limitations and conditions that are most often very harsh and economically disadvantageous.

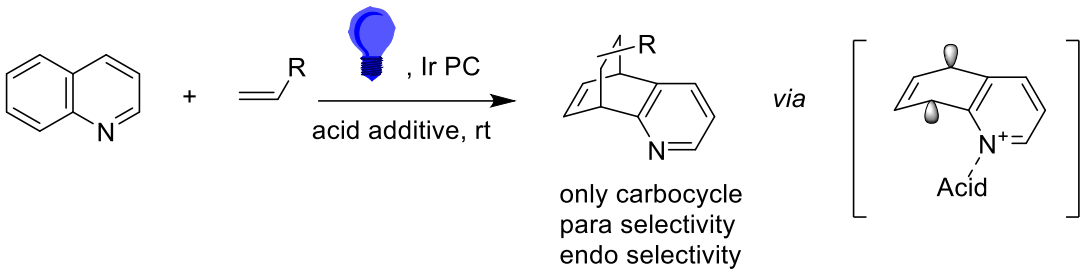
Moving forward to recent past, Sarlah *et.al.* presented a brilliant dearomative dihydroxylation with arenophiles in 2016[57] (Scheme 22).



Scheme 22: Sarlah's dearomatization with MTAD.

Upon irradiation with visible light, authors discovered the formation of an exciplex between the arene and the excited MTAD. This intermediate eventually brings to the cycloaddition product. The strategy is brilliant, and yields are good considering the complexity of the transformation. Moreover, Sarlah reported several derivatizations of its product, expanding the explorable chemical space for this type of scaffolds. However, they employ hard operative conditions (i.e. -78 °C) and a very toxic reagent such as OsO_4. Moreover, they don't evaluate so well the tolerance towards several functional groups, and, with this methodology, it is possible to achieve only bridged heterocycles.

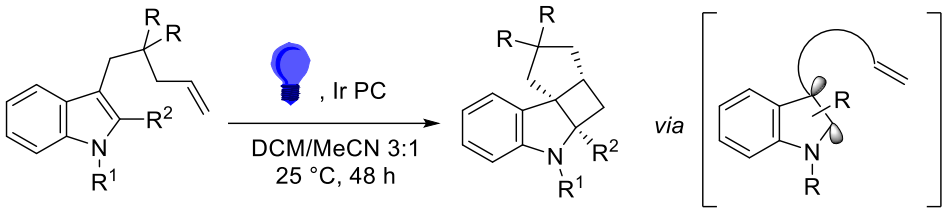
In 2021, Glorius and coworkers reported an innovative dearomatization of bicyclic azaarenes with alkenes[58] (Scheme 23).



Scheme 23: Glorius's intermolecular dearomatization of azaarenes.

Authors employed a different strategy in this case. With the addition of an acid additive, they formed in situ a quinolonium specie that has a low E_T. Then, upon activation via EnT, the biradical intermediate could attack the unbiased alkene partner and eventually seal the bicyclooctene 3D scaffold. The reaction is very selective, with the functionalization of only the carbocyclic ring of the heterocycle. Moreover, it has an excellent *para* and *endo* selectivity. Glorius reported an extremely wide scope, but he is limited to the use of sensitizable substrates. Indeed, this transformation occurs through the activation of the arene partner instead of arenophile. This approach is way more exploited in literature and several examples will be reported in next chapters.

To conclude, in 2019, You *et.al.* presented an intramolecular dearomative cycloaddition of indoles[59] (Scheme 24).



Scheme 24: Intramolecural dearomative [2+2] of indoles.

Authors obtained a complex cyclobutane – fused angular tetracyclic spiroindolines in very mild conditions. The reaction proceeds through the activation of indole's double bond and the cyclobutane is closed according to classical [2+2]. The reaction has a perfect atom economy and yields are very high, up to 99%, with tolerance towards several functional groups. However, You needed the presence of an auxochrome substituent, such as an aromatic ring or an acyl group, at the 2-position of the heterocycle to decrease the E_T of substrate. Thus, this requirement limits the reaction to decorated indoles

Chapter II

Visible – Light Promoted Intramolecular para-Cycloadditions on Simple Aromatics

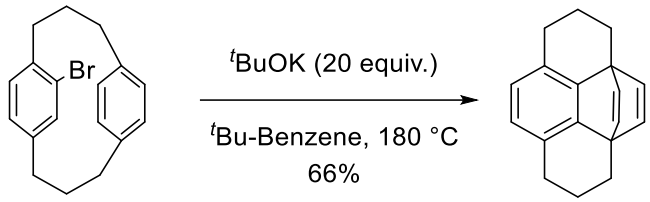
From this chapter:

M. Chiminelli, A. Serafino, D. Ruggeri, L. Marchiò, F. Bigi, R. Maggi, M. Malacria, G. Maestri. Visible-Light Promoted Intramolecular para-Cycloadditions on Simple Aromatics. *Angew. Chem. Int. Ed.* **2023**, *62*, e202216817. https://doi.org/10.1002/anie.202216817.

2.1: Intramolecular Dearomative Cycloadditions of Aromatics

The activation of benzene ring is the most difficult field in the chemistry of dearomative cycloadditions. Indeed, benzene has the highest aromaticity per ring, and it is known all over the world for its inertness. Because it is a monocyclic arene, the dearomatized product is endothermic, resulting in all the synthetic disadvantages that I mentioned before. The transformation is as difficult as it is challenging and promising, because the product is a very small 3D scaffold, with a high added value.

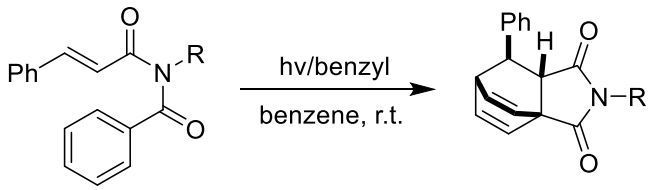
A pioneering example dates to 1976, when Longone and Gladysz reported their "bridged benzobarrelene formation by intramolecular trapping of a novel aryne"[60](Scheme 25).



Scheme 25: 1,4 intramolecular para-cycloaddition of benzyne on benzene.

With ^{t}BuOK and Δ the bromine eliminates to generate an active benzyne specie. Then, it attacks the other benzene ring performing a *para*-cycloaddition. The product shows a beautiful structure, and it is obtained in very high yields. However, such harsh conditions would not tolerate any functional groups onto the hydrocarbon scaffold.

In 1997, kishiwaka er.al. reported a beautiful “intramolecular photo [4+2] cycloaddition of an enone with a benzene ring”[61] (Scheme 26).

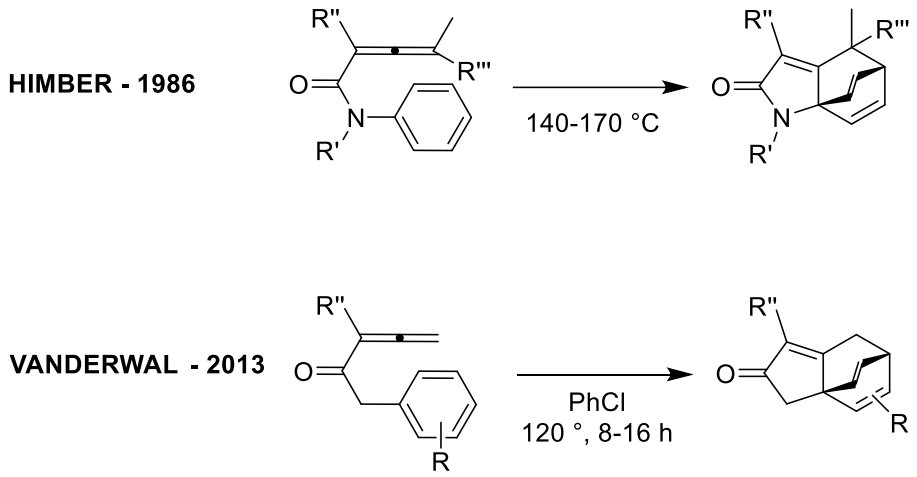


Scheme 26: UV promoted intramolecular dearomatization of benzene.

Authors prepared a highly conjugated system bearing an enone and a benzamide. Upon excitation with UV light, a stepwise cyclization occurred, and they obtained a bicyclooctadiene scaffold with excellent yields, up to 98%. The system, thanks to its high conjugation, is built to make cyclization more accessible, lowering the ΔG of the product. The strategy resulted brilliant, and authors achieved 16 products. However, some functional groups were not tolerated, such as -CN, -NO_2 and -OMe. In 2022, Yin and coworkers repeated this procedure using visible-light catalysis instead of UV and they expanded the scope of products, but without significant improvements for the chemical knowledge[62].

One of the first examples concerning the dearomative *para*-1,4 cycloaddition of an allene onto benzene is form Gilbert and coworkers[63], in 1972. According to their report, “irradiation (at 254 nm) of a 5% v/v solution of allene in benzene under nitrogen at 25 °C gave a very low yield of four 1:1 adducts in the approximate ratio 1:2:6:12”. The major product was determined as 1,4 cycloaddition, while the minor one corresponded to the *meta*-cycloaddition. Of course, this reaction was not applicable to an industrial process, but it showed the possibility to build complex 3D scaffold dearomatizing benzene with a *para*-cycloaddition.

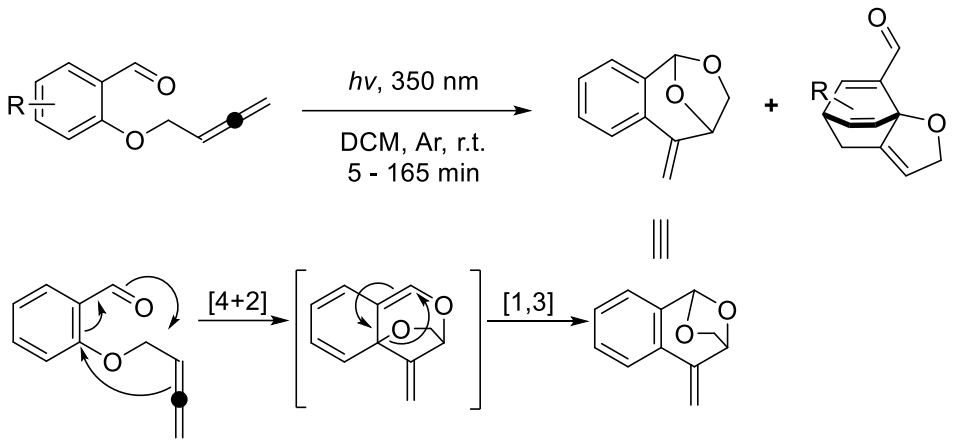
In 1982, Himbert et.al. reported the intramolecular cyclization of allene onto benzene[64] (Scheme 27; top).



Scheme 27: Studies on the arene/allene cycloaddition.

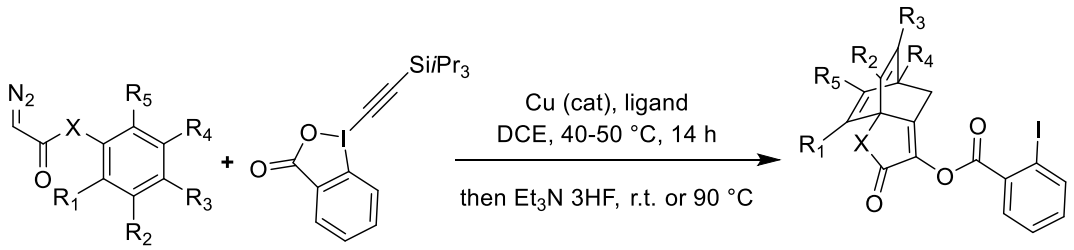
The discovery of Himbert had a great resonance among organic chemists. 30 years later, Vanderwal and Houk published a mechanistic study on this reaction and tried to expand the narrow scope of their predecessor[65](Scheme 27; bottom). They achieve full carbon polycycles, but the methodology had several limitations. They obtained only 7 products, most of time without complete conversion and with the formation of several undesirable side products. They had complete conversion only dearomatizing a naphthyl instead of benzyl, demonstrating, even with a modest 54%, how easier should be that reactivity.

In 2008, also Bochet and coworkers investigated the arene/allene cycloaddition, with an allenyl salicylaldehydes[66] (Scheme 28, top). After irradiation with UV lamp at 350 nm for mostly two hours, authors obtained 6 products as a mixture of two different isomers. The first is attributable to a sequence of intramolecular formal hetero Diels-Alder followed by an oxygen-to carbon formal 1,3-sigmatropic migration (Scheme 28, bottom), while the latter is derived from a *para*-cycloaddition of the allene onto the aromatic. Yields averaged between 0 to 44% for the first isomer and from 31 to 94% for the second.



Scheme 28: Case study of the arene/allene cycloaddition with allenyl salicylaldehydes.

Finally, Waser et.al. reported an exotic allene/arene para-cycloaddition at room temperature[67] (Scheme 29).



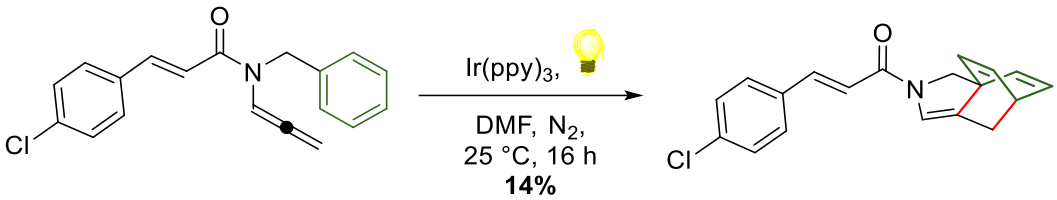
Scheme 29: room temperature allene/arene para-cycloaddition.

Authors obtained this fascinating transformation by reacting a diazo compound with a hypervalent iodine compound with copper catalyst at 40-50 °C for 14 h and a subsequent desilylation step with a highly corrosive reagent. They had decent yields and a quite big scope, but the dangerous and toxic compounds employed in the synthesis make it difficult to use this methodology in industry.

Allene/arene *para*-cycloaddition has been intensively studied among 60 years, but only few methodologies are reported, with several limitations ranging from narrow scopes to harsh conditions. It is thus necessary to develop a general and robust arene/allene *para*-cycloaddition which employs mild conditions and tolerance towards several functional groups.

2.2: Results and Discussion

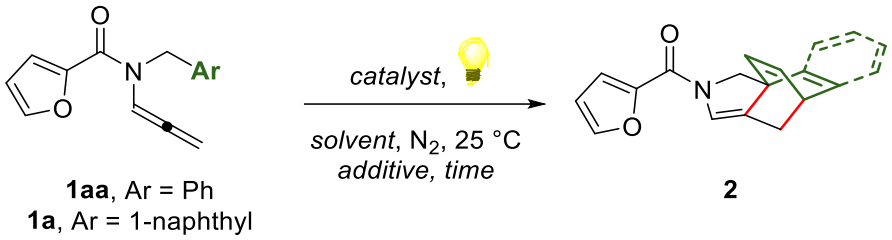
In this chapter I will present an unprecedent approach for the intramolecular dearomative *para*-cycloaddition on simple aromatics. In a previous paper[68] published in my research group, we reported the formation of an interesting byproduct (Scheme 30).



Scheme 30: Experimental observation of para-cycloaddition.

After NMR analysis and XRD-resolution, we understood that the byproduct was a cyclooctadiene derived from the intramolecular *para*-cycloaddition of allenamide on the benzyl substituent. Inspired by this original transformation, we decided to study the reaction. We did a great effort to increase the 14% yield and, after a long screening of substrates with different characteristics, we obtained 46% with **1aa** (Table 1; additional optimization experiments can be found in the experimental section). Mass balance could be accounted for substrate decomposition or deallenylation. Several different solvents, including binary mixtures, did not improve the outcome. A higher catalyst loading proved futile. Switching to different photosensitizers and photocatalyst, none proved better than Ir – complexes. These results suggested that we shelve the project. However, the model reaction was then carried out using **1a**. The rate of the reaction was ca. two orders of magnitude faster than that of **1aa** (entry 5). The product **2a** was isolated in 99 % yield upon three hours of irradiation. We thus added naphthalene (NP) to the reaction of **1aa**.

Table 1: Optimization of reaction conditions.



1aa, Ar = Ph
1a, Ar = 1-naphthyl

2

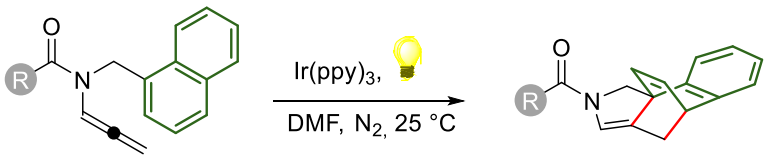
Entry[a]	Reagent	Sensitizer	Additive (equiv.)	T [h]	Yield of **2** [%]
1	**1aa**	$Ir(ppy)_3$	-	240	46
2[b]	**1aa**	$Ir(ppy)_3$	-	240	44
3[c]	**1aa**	TXT	-	240	-
4	**1aa**	$Ir(p\text{-}F\text{-}ppy)_3$	-	96	45
5	**1a**	$Ir(ppy)_3$	-	3	99
6	**1aa**	$Ir(ppy)_3$	$C_{10}H_8$ (10)	48	60
7	**1aa**	$Ir(ppy)_3$	$C_{10}H_8$ (20)	38	64
8	**1aa**	$Ir(ppy)_3$	1-Methoxy-naphthalene (10)	24	70
9	**1a/1aa**		-	96	-
10[d]	**1a/1aa**	$Ir(ppy)_3$	-	96	-

*[a] Reaction conditions: 0.15 mmol of **1** (0.1 M in DMF), 1 mol% sensitizer, in 5 mm NMR tube under N_2, isolated yields; [b] in toluene; [c] with 10 mol% of thioxanthone (TXT); [d] without light.*

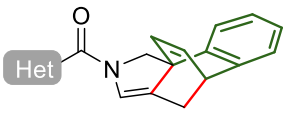
The additive proved beneficial, ensuring the full consumption of **1aa** in 38 hours. The use of 1-methoxynaphthalene gave a better result (entry 8). However, its higher cost and a more complicated recovery from the crude led us to prefer the conditions of entry 7. Finally, no reaction took place without either the sensitizer or light, using both **1a** and **1aa**.

With the best conditions in hand (entry 7), we then screened several substrates. Typically, a solution of the substrate, photosensitizer and additive (when necessary) is transferred to a 5 mm NMR tube to maximize the surface/volume ratio. Then it is degassed by freeze-pump-thaw, kept at 25 °C and irradiated with a 14 W – household LED strip with white light (400 – 750 nm). After full conversion, the solution was transferred to a round bottom flask and solvent was evaporated in vacuo with the Schlenk line. When NP was in the mixture, it was necessary to add

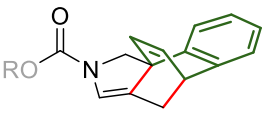
an additional trap to collect the sublimated additive. Finally, the crude was purified by chromatography on silica gel.



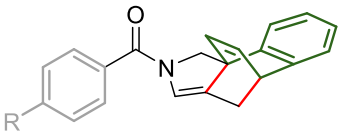
Naphthyl derivatives (*3-16 h,* ***no additive***)



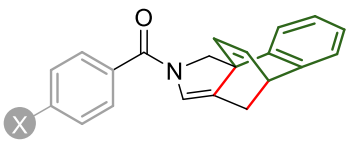
2a, Het = 2-furyl, 99%
2b, Het = 3-pyridyl, 90%
2c, Het = 2-thienyl, 99%



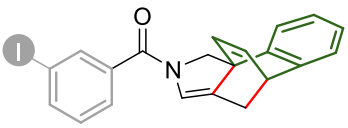
2d, R = Et, 93%
2e, R = Ph, 88%
2f, R = Bn, 93%
2g, R = ^{t}Bu, 92%



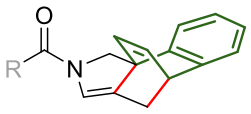
2h, R = H, 96%,
85% on 1 mmol
2i, R = OMe, 90%



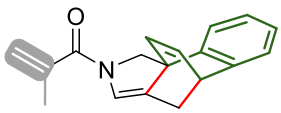
2j, X = 4-F, 89%
2k, X = 4-Cl, 86%
2l, X = 4-Br, 86%



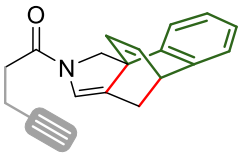
2m, 85%



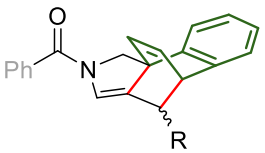
2n, R = Me, 90%
2o, R = cyclopropyl, 99%



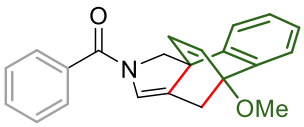
2p, 95%



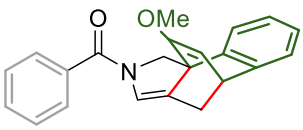
2q, 85%



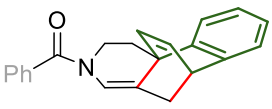
2r, R = Me, 88%, *dr* = 62:38
2s, R = Ph, 68%, *dr* = 64:36



2t, 89%



2u, 87%



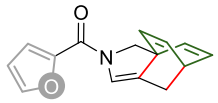
2v, 65%

Scheme 31: Scope of naphthyl derivatives.

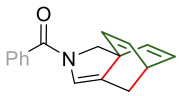
Pink box represents the scope of naphthyl derivatives (Scheme 31). Furans, thiophene and pyridine were tolerated by the method (**2a–c**). The amido group could be replaced by a carbamate one (**2d–g**). No major electronic effect was observed on the unreacted aryl ring of the substrate (**2h–m**). It is worth noting that halogens were fully compatible with the method, including bromides and iodides (**2l–m**). The R group could be further varied, allowing one to incorporate cyclopropyl, alkenes or alkynes into the final product (**2n–q**). Racemic disubstituted allenes afforded products in good yields. The naphthyl arm could be decorated without hampering the reaction (**2t–u**). Finally, a tetrahydropyridine ring could be sealed (**2v**). In all cases, the substrate was fully consumed in a few hours and overnight irradiation was required at most. The reaction could be scaled up to 1-mmol using a vial without a significant yield loss. The freeze-pump-thaw procedure is not crucial for **1a–v**, although full conversion is achieved faster by performing it (2–4 hours). The intramolecular dearomatization of naphthyls proved to be extremely efficient and tolerant towards various functional groups, with an excellent average yield of 89%. The reaction proceeds smoothly even without the use of the additive, reasonably due to the lower resonance energy of naphthalene.

Cyan box represents the scope of benzyl derivatives instead (Scheme 32). In this case, the reactions is more difficult and required longer reaction times. Several aryl amides, including perfluorinated rings and phenylacetylene ones, could be used, delivering products in moderate to good yields (**2aa–af**). The benzyl arm that underwent the dearomatization could be variously decorated at its *para* – position (**2ag–an**), affording products with an additional head bridging quaternary carbon. The series includes valuable functions such as amines, terminal vinyl groups, epoxides, pyridines and the formation of allylic bromides.

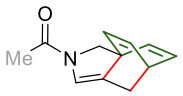
Simple arenes & pyridines (*24-96 h,* ***20 equiv. naphthalene***)



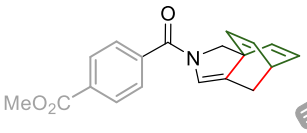
2aa, 65%



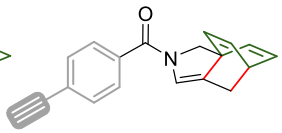
2ab, 75%,
62% on 2 mmol,
N.D. w/o $C_{10}H_8$



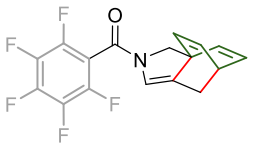
2ac, 56%



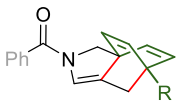
2ad, 51%



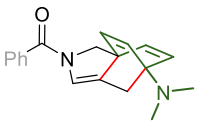
2ae, 49%



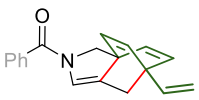
2af, 78%



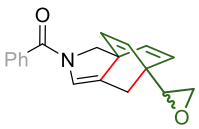
2ag, R = Me, 77%
2ah, R = OMe, 62%



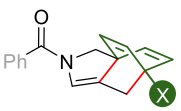
2ai, 54%



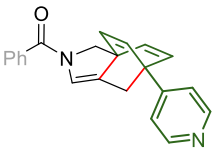
2aj, 41%



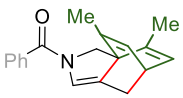
2ak, 76%, *dr* = 1:1



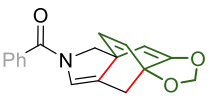
2al, X = F, 65%
2am, X = Br, 76%



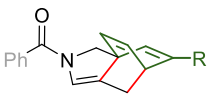
2an, 73%



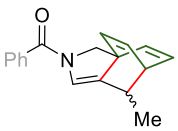
2ao, 18%



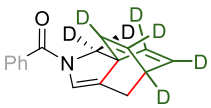
2ap, 44%



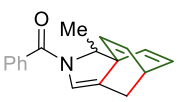
2aq, R = CF_3, 76%
2ar, R = OMe, 65%



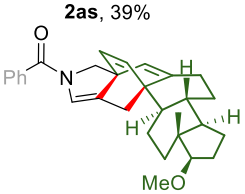
2as, 39%



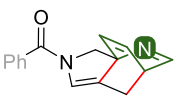
2at, 72%



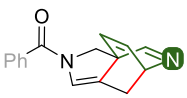
2au, 32%, *dr* = 88:12



2av, 55%, *dr* = 69:31



2aw, 61%

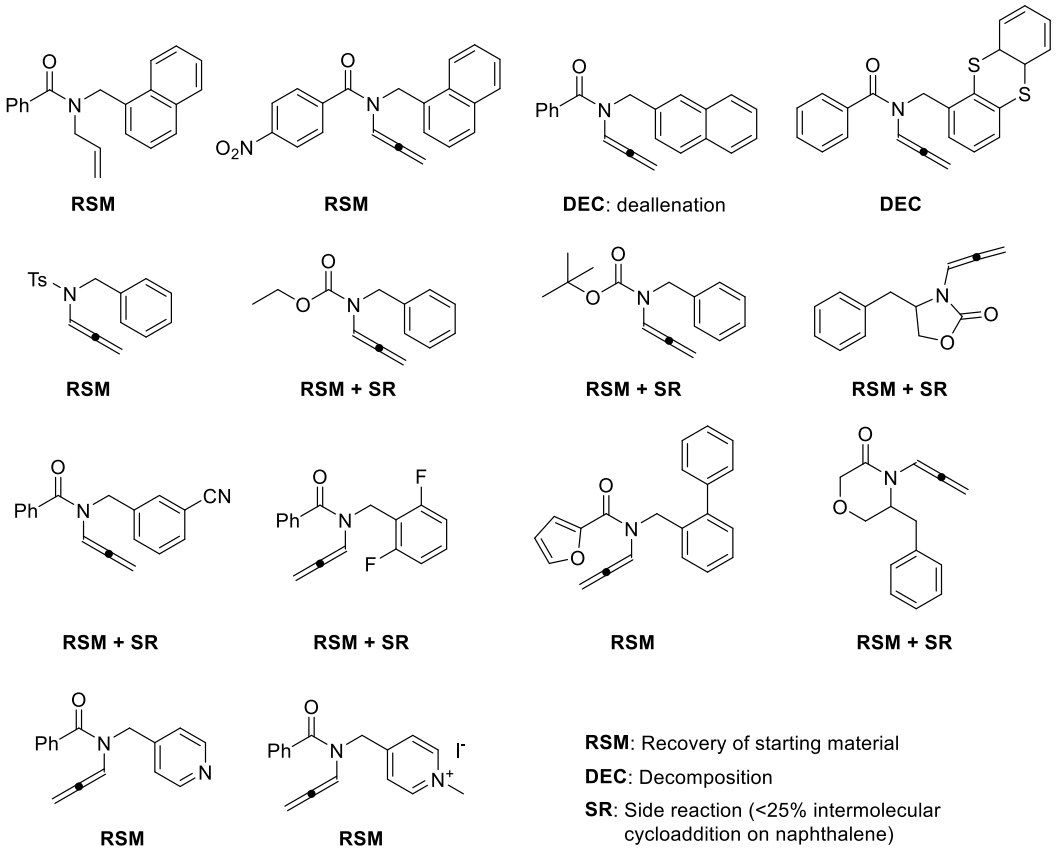


2ax, 56%

Scheme 32: Scope of benzyl derivatives.

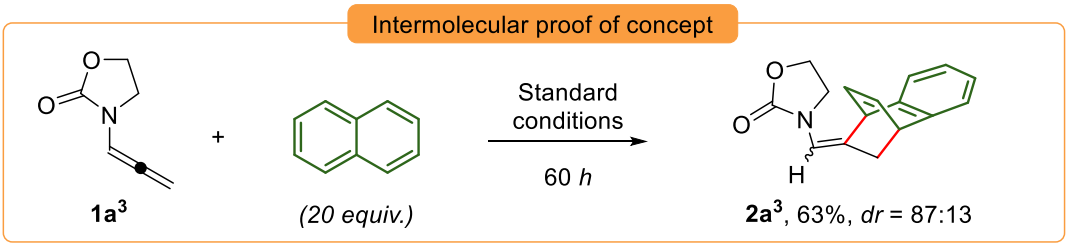
The dearomatization could occur on arenes functionalized in other positions, too (**2ao–ar**). The worst results were observed for 2,6 – disubstituted rings, while several other functionalities, such as protected acetals or trifluoromethyl groups, were tolerated regardless of their stereoelectronic demands. This experimental observation is consistent with our mechanistic hypothesis. Ortho substituents hinder the reaction with their steric demand because they prevent the formation of the first new C-C bond between the central carbon of the allene and the ipso substituted one of the benzyl (see later). Disubstituted allenes could be employed (**2as**) and the method allowed one to efficiently prepare d-labelled polycycles (**2at**). The yield was moderate using a reagent with a substituted benzylic position (**2au**). An estradiol-derived substrate gave congested hexacycle **2av** with good stereocontrol. Then, we attempted the cycloaddition on pyridines. 4-Pyridyl and 4-pyridinium groups were unreactive. On the contrary, both 2-and 3-pyridyl rings reacted smoothly, affording valuable imine-containing products (**2aw–ax**). These last two products, especially **2aw**, were unstable after isolation, so it was necessary to characterize them immediately. Furthermore, the reaction can be performed on a 2 mmol-scale with a limited yield loss. Considering the intrinsic difficulty of the transformation and the few reports in literature about benzyl derivatives[24,36], the reaction proceeded with satisfactory to excellent yields and high tolerance towards several functional groups.

Obviously, the methodology has some limitations (Scheme 33). 2-naphthyl substituents do not react, probably because the *meta*-cycloaddition would require a tailored optimization. Nitro and -CN group resulted not tolerated as well. Concerning the benzyl derivatives, carbamates and sulfonyl amides hinder reactivity, as does ortho substitution.



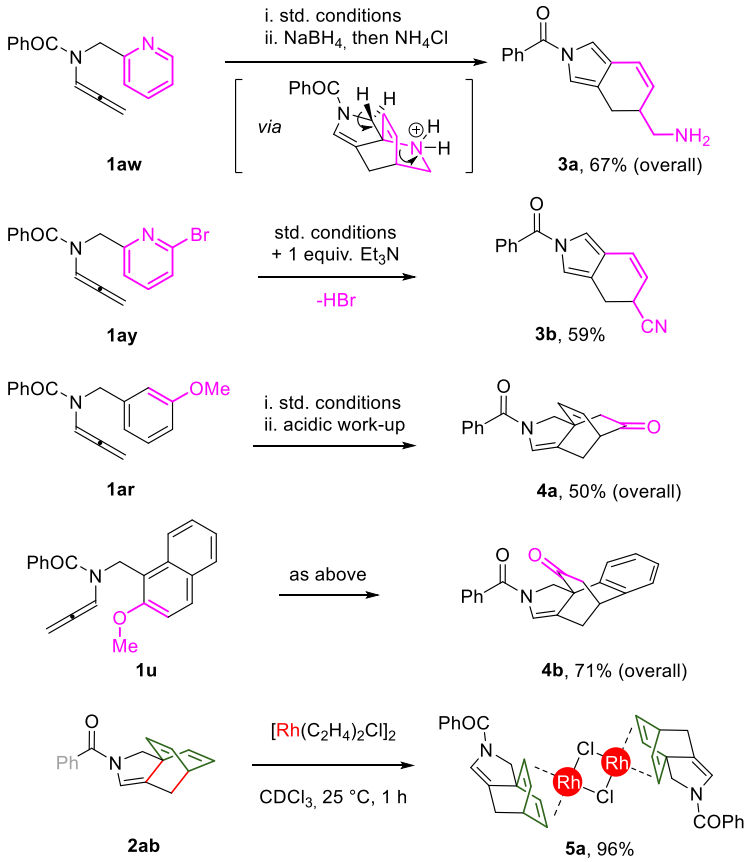
Scheme 33: Limitations.

Finally, an intermolecular reaction between **1a³** and NP delivered **2a³**, showing the potential of future developments that will be discussed in Chapter III (Scheme 34).



Scheme 34: Intermolecular para-cycloaddition on naphthalene.

We then designed some applications of products **2** to exploit the potential reactivity of the [2.2.2]-bicyclooctadiene that we obtained (Scheme 35). In this way, we aimed to expand the accessible chemical space of this approach. It is worth noting that this 3D alicyclic product would be very difficult to synthesize through other methodologies. By using our procedure, we got this useful scaffold in very mild conditions, high yields, complete atom economy and with cheap light source.

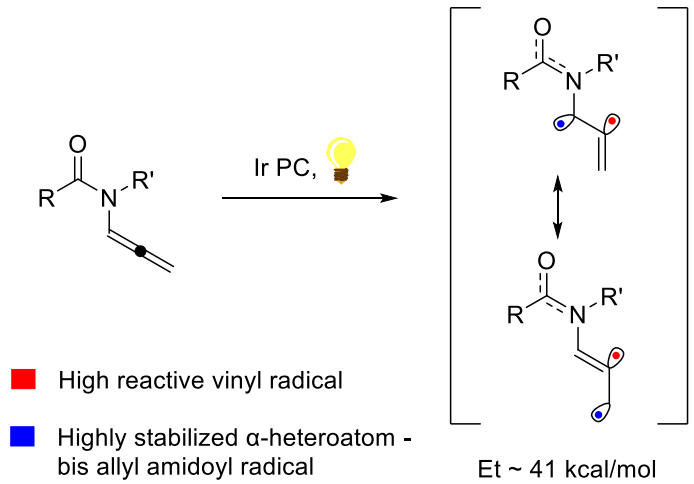


Scheme 35: Derivatization of products.

The reduction of the imine group of **2aw** followed by acidic work-up afforded isoindole **3a**, offering a concise route to this useful synthetic core[69]. On contrary, the dearomatization of **1ay** gave extensive decomposition. However, the addition of triethylamine led to the formation of **3b** in 59 % yield via formal elimination of

HBr. The dearomatization of methoxy-substituted aryls allowed one to access polycyclic 1,4-enones **4**. These cores have been used to trigger oxa-di-π-methane rearrangements and as precursors for oxy-Cope ones[70] but their assembly require long synthetic sequences. The 1,4-diene unit of **2** could act as a tunable bidentate ligand that is reminiscent of Carreira/Hayashi dienes[71,72]. For instance, Rh(I) dimer **5a** readily formed at room temperature and excellent yields.

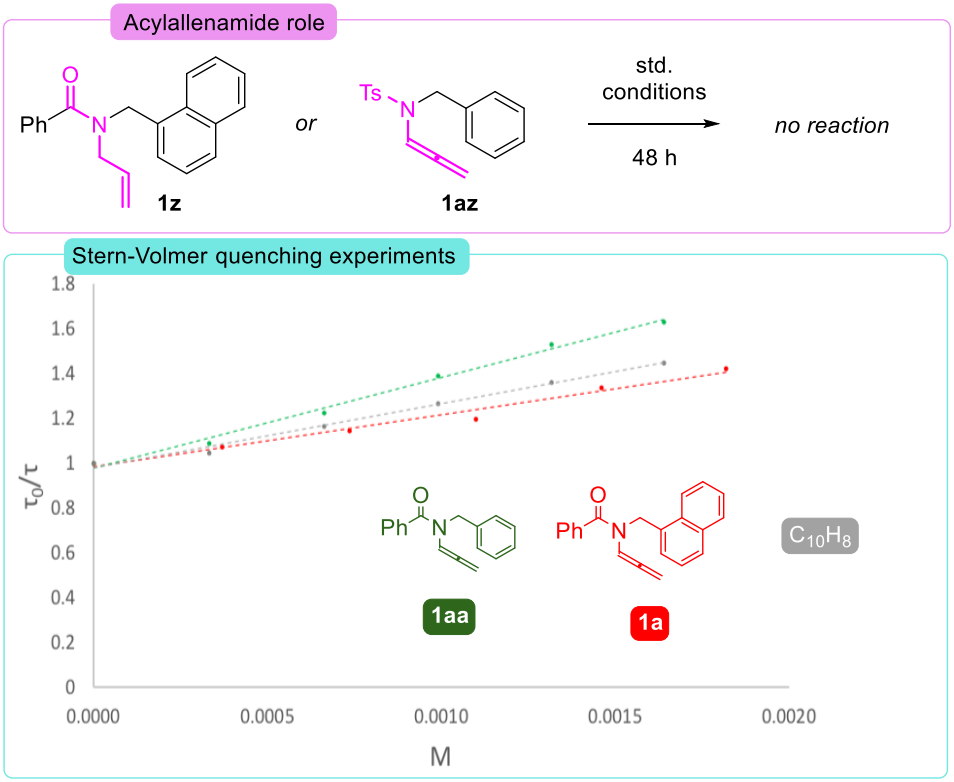
We finally focused on rationalize the mechanism of our synthetic transformation. Allenamides can be sensitized by common photocatalyst with an energy transfer process[68]. It results in a particular triplet made of two differently stabilized radicals (scheme 36).



Scheme 36: Resonance structures of allenamide's triplet.

The first is a high reactive vinyl radical, that can trigger cyclization or HAT processes. The latter is a highly stabilized α-heteroatom-bis allyl amidoyl radical, that make accessible the EnT, lowering the triplet energy to ca. 41 kcal/mol.

The crucial role of the acylallenamide unit was confirmed by testing substrates with either a tosyl-allenamide group or an allylamide one. Both failed to convert under optimized conditions (Scheme 37; Pink box).

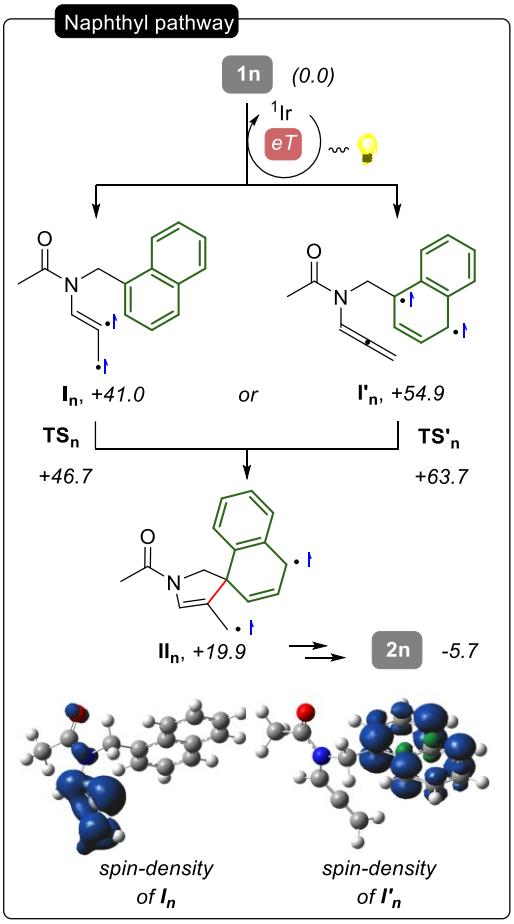


Scheme 37: Experimental proof of acylallenamide role (pink-box); Stern-Volmer quenching analysis (cian-box)

We then performed Stern–Volmer quenching experiments on **1a**, **1aa** and NP (Scheme 37; Cian box). Allenamide **1aa** is the best quencher and the efficiency of **1a** is lower than that of NP (K_{SV} are 404, 232 and 286 M^{-1} respectively; details in experimental section). No meaningful differences were observed using a mixture of **1aa** and NP. These analyses confirmed that our substrates could be sensitized with $Ir(ppy)_3$, but they couldn't yet explain why NP additive was so important for the cycloaddition on benzyl.

Calculations were carried out at the M06/Def2-TZVPlevel, using DMF as implicit solvent[73], to rationalize the role of NP. The redox potentials of $^3Ir(ppy)_3$ are unable to induce any single electron transfer on NP, **1ac** and **1n** (confirmed with CV; see experimental section). This is confirmed by the calculated ΔGs of these redox events. On the contrary, the E_T of $^3Ir(ppy)_3$, substrate **1ac**, **1n** and NP are compatible. Calculated values are very close to experimental ones[74], showing the reliability of the method.

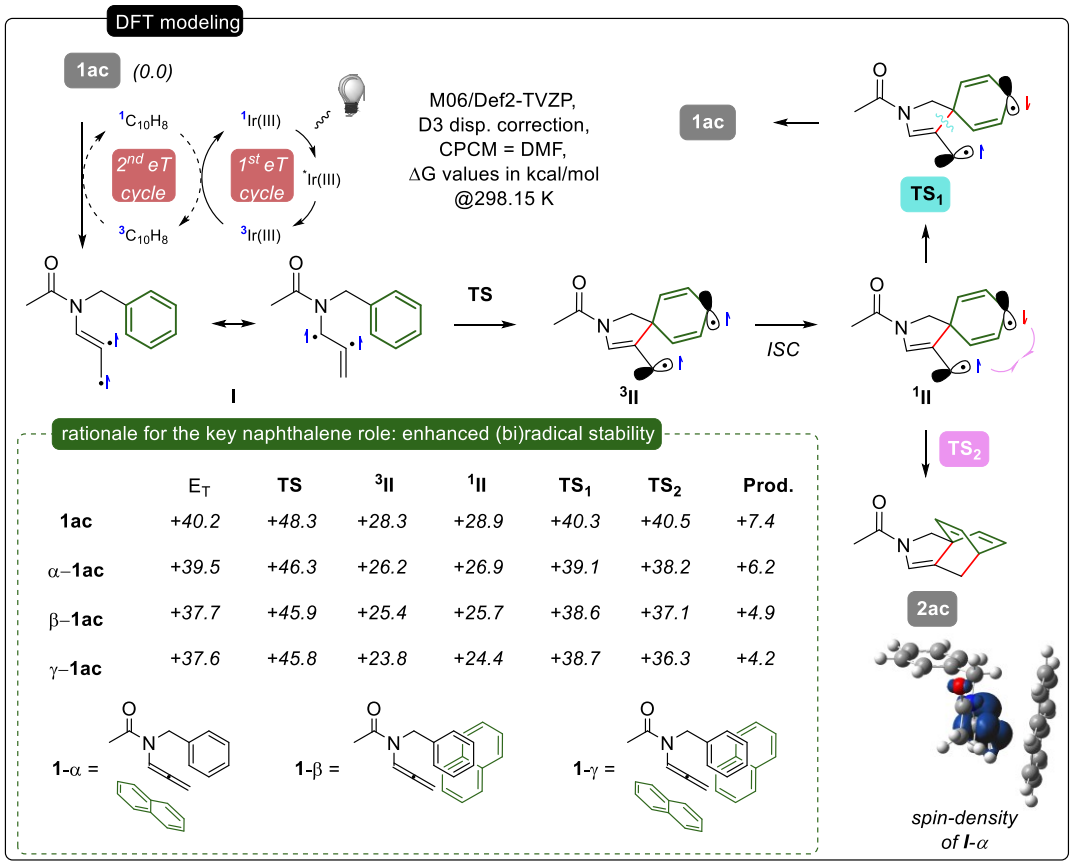
The reaction of **1n**, which has a naphthyl arm, can involve two pathways (Scheme 38).



Scheme 38: Calculated mechanism of naphthyl derivatives.

The triplet $\mathbf{I_n}$ has its spin density localized on the former allenyl arm. Its vinyl radical site could attack the aromatic ring through a low-barrier transition state (TS) and this step generates a spiro carbon. The triplet can relax via intersystem crossing (ISC) and the resulting singlet affords **2** upon radical recombination. The less stable triplet $\mathbf{I'_n}$ has the spin density spread over the naphthyl unit. This biradical might evolve into $\mathbf{I_n}$, or it could attack the central carbon atom of the allene, delivering $\mathbf{II_n}$. The $\mathbf{I'_n}$-pathway involves a less stable intermediate and a higher barrier for the TS (+2.1 kcal mol^{-1} in $\Delta\Delta G$). It is thus less favourable, in agreement with the lack of reactivity of **1z**.

The reaction of **1ac** has a more energy-costly TS and a less stable intermediate ^{3}**II** than that of **1n** (by +2.3 and +8.3 kcal mol^{-1} in $\Delta\Delta G$) (Scheme 39).



	E_T	TS	^{3}II	^{1}II	TS_1	TS_2	Prod.
1ac	+40.2	+48.3	+28.3	+28.9	+40.3	+40.5	+7.4
α–**1ac**	+39.5	+46.3	+26.2	+26.9	+39.1	+38.2	+6.2
β–**1ac**	+37.7	+45.9	+25.4	+25.7	+38.6	+37.1	+4.9
γ–**1ac**	+37.6	+45.8	+23.8	+24.4	+38.7	+36.3	+4.2

1-α = **1**-β = **1**-γ =

Scheme 39: Calculated mechanism of benzyl derivatives.

The two mono-occupied orbitals of ^{3}**II** are nearly perpendicular. This arrangement is kept in ^{1}**II**, which forms upon ISC. A rotation of the primary radical is necessary to allow the recombination. The rotation of the primary radical causes the loss of its allylic conjugation, resulting in an additional energy barrier. Two competing TSs were found for this rotation. The **TS$_2$** leads to **2ac** while the substrate **1ac** is reformed via **TS$_1$**, which is favoured by 0.2 kcal mol^{-1}. This route prevails because **2ac** is less stable than **1ac** (while **2n** is more stable than **1n**). Overall, the **TS$_1$** pathway is unproductive. This can explain the large reactivity gap between the two types of substrates. However, NP can likely stabilize radicals through its π-cloud[75]. Three reactions were modelled adding one NP molecule parallel to the allenyl arm of **1ac**, one stacked to its benzyl ring or two units flanking each arm of the reagent (α, β and γ, respectively). These systems were freely reoptimized considering dispersion interactions[76]. In all cases, the biradicals **I**, **TS** and **II** are more stable than the corresponding entry channel. The stabilization is smaller for **I** and **TS** (0.7–2.6 kcal mol^{-1}), and larger for intermediates **II** (2.1–4.5 kcal mol $^{-1}$). Moreover, **TS$_2$**s are slightly favoured over **TS$_1$**s (0.1–2.4 kcal mol^{-1}) and the NP-**2ac** adducts are less endergonic (1.2–3.2 kcal mol^{-1})[77]. Taken together, these effects could explain the enhanced reaction rate observed in the presence of NP because the additive reduces the odds that the sensitization of **1ac** is eventually unproductive.

It is worth noting that (bi)radical stabilization by π-clouds is original with respect to synthetic methods. This experimental and theoretical observation pushed us to better investigate the effect of naphthalene and derivatives in reactions involving triplets and we saw a general positive improvement in terms of yields and reactions rates[78]. I will briefly discuss the interesting aspects of this discovery in Chapter IV.

2.3: Conclusions

In summary, we have developed a new method to dearomatize benzyl and naphthyl moieties in an intramolecular fashion. As arenophile we used the peculiar triplet of allenamide. Indeed, its high reactive vinyl radical can trigger unusual cyclization that were impossible to achieve with other less energetic radicals. The transformation allows the synthesis of a [2.2.2]-bicyclooctene(diene) unit that have a potential biorelevant 3D alicyclic scaffold, starting from sp^2-rich compounds.

The reaction is performed in very mild conditions, with a cheap and simple setup. Moreover, it tolerates several functional groups and has complete atom economy. Naphthyl derivatives are converted to the product in few hours with an average yield of 89%; while benzyl derivatives, a true synthetic challenge, dearomatize with satisfactory yields up to 78%. We also demonstrated that is possible to explore new chemical space starting from our products, obtaining for example isoindoles.

Finally, we confirmed our mechanistic hypothesis with DFT calculations, Stern-Volmer quenching analyses and Cyclic Voltammetry. The reaction is a stepwise 1,4 *para*-cycloaddition that occurs through the formation of 2 new C-C bonds, the first due to the attack of the vinyl radical onto the ipso carbon of the arene moiety. We also saw an unusual stabilization of intermediate triplet biradicals by naphthalene, that had no precedent in literature.

This last observation opened the way to other studies performed in my research group.

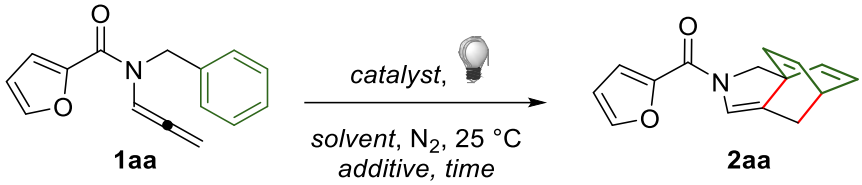
2.4: Experimental Section

General remarks

All chemicals those syntheses are not reported hereafter were purchased from commercial sources and used as received. Solvents were dried passing through alumina columns using an Inert® system and were stored under nitrogen. Present visible light promoted reactions did not required the use of dry solvents, but presence of molecular oxygen exerts a negative effect on their rate. Chromatographic purifications were performed under gradient using a Combiflash® system and prepacked disposable silica cartridges or through isocratic flash chromatography using commercial 60 Å silica gel. All reactions that required heating were performed with the use of high-vacuum grade silicon oil. Reactions promoted by visible light were performed into standard 5 mm NMR tubes, surrounded by a commercial strip of 300 RGB household leds (12V, 14W). These were put at a distance of ca 10 cm and irradiated with white light (model SMD5050-300 ip65). The tubes were inside an oil bath fitted with a thermometer to monitor the temperature. Cooling was ensured by two fans recovered by outdated PCs to avoid reproducibility issues. During summertime, solutions are kept at 25 °C through the addition of a rubber spire inside the silicon oil bath. The spire is linked to a chiller that keeps pumping a cooled water/ethylene glycol solution to maintain the desired temperature. ^{1}H and ^{13}C NMR spectra were recorded at 300 K on a Bruker 400 MHz or a Jeol 600 MHz spectrometers using residual non-deuterated solvents as internal standards (7.26 ppm for ^{1}H NMR and 77.00 ppm for ^{13}C-NMR for $CDCl_3$, 2.05 ppm for ^{1}H NMR and 29.84 ppm for ^{13}C NMR for acetone-*d6*). ^{19}F NMR spectra were recorded in $CDCl_3$ at 298 K on a Jeol 600 spectrometer fitted with a BBFO probehead at 564 MHz. The terms m, s, d, t, q and quint represent multiplet, singlet, doublet, triplet, quadruplet and quintuplet respectively, and the term brs means a broad signal. Reported assignments were based on decoupling, COSY, NOESY, HSQC and HMBC correlation experiments. Mass analyses were recorded on an Infusion Water Acquity Ultra Performance LC HO6UPS-823M instrument equipped with a SQ detector (Electrospray source); high-resolution mass analyses were recorded on a LTQ ORBITRAP XL Thermo Mass Spectrometer (Electrospray source). CCDC 2214197 and 2214197 contain the supplementary crystallographic data for compounds **2h** and **2av** (mayor diastereomer). Single crystal Data were collected with a Bruker D8 diffractometer equipped with PhotonII area detector, using a CuKα or a MoKα microfocus 4 radiation source. The data collection strategy covered the sphere of reciprocal space. Absorption corrections were applied using

the program SADABS. The structure was solved with the SHELXT code. Fourier analysis and refinement were performed by the full-matrix least-squares methods based on F2 using SHELXL-2014 as implemented in Olex2. All the nonH atoms were refined with anisotropic displacement parameters.

Additional optimization experiments



1aa **2aa**

Entry	Catalyst (1 mol%)	Solvent (0.1 M)	Additive	Time (h)	Conv. **1aa**[a]	Yield **2aa**[a]
1[b]	$Ir(ppy)_3$	DMF		312	>99 %	35%
2	$Ir(ppy)_3$	DMF		96	70 %	38%
3	$(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$	DMF		96	54 %	4%
4	$(Ir[dF(CF_3)ppy]_2(bpy))PF_6$	DMF		96	63 %	11%
5	$[Ir(dtbbpy)(ppy)_2]PF_6$	DMF		96	37 %	0%
6	$Ir(ppy)_3$	DMF-*d7*		240	91 %	52%
7	$Ir(ppy)_3$	DMSO-*d6*		240	96 %	51%
8	$Ir(ppy)_3$	Acetone-*d6*		240	88 %	29%
9	$Ir(ppy)_3$	MeCN-*d3*		240	82 %	29%
10	$Ir(ppy)_3$	Toluene-*d8*		240	90 %	50%
11[c,h]	-	DMF		72	>99 %	/
12[b]	$Ir(ppy)_3$	DMF	Naphthalene (1 eq.)	48	>99 %	38%
13[b]	$Ir(ppy)_3$	DMF	1-Methylnaphthalene (3 eq.)	48	>99 %	54%
14[b]	$Ir(ppy)_3$	DMF/Toluene 1:1	Naphthalene (20 eq.)	38	>99 %	63%
15[b]	$Ir(p\text{-}F\text{-}ppy)_3$	DMF	Naphthalene (20 eq.)	38	>99 %	61%
16[b,h]	Benzophenone[d]	DMF	Naphthalene (20 eq.)	96	32 %	/
17[b,h]	$Ru(bpy)_3Cl_2$	DMF	Naphthalene (20 eq.)	96	50 %	/
18[b,i]	2,4,6-Triphenylpyrylium tetrafluoroborate[e]	DMF	Naphthalene (20 eq.)	96	>99 %	/
19[b,h]	Eosin Y[e]	DMF	Naphthalene (20 eq.)	96	44 %	/
20[b,g]	$Ir(ppy)_3$	DMF	Naphthalene (20 eq.)	72	>99 %	61%

[a] ^1H NMR yield using 1,3,5-Trimethoxybenzene as internal standard, [b] isolated yield, [c] 45 °C, [d] 1 eq., [e] 10 mol%, [f] without light, [g] in presence of oxygen, [h] the product isolated derived from a [4+2] cycloaddition between furane and allene, [i] the product isolated was the secondary amide without allene.

Role of dioxygen

1a ⟶ **2a** **1ab** ⟶ **2ab**

conditions	yield (%)	time (h)	yield (%)	time (h)
std.	99	3	75	38
without freezing-thaw	95	5	63	72

Photoluminescence lifetimes

The measurements of photoluminescence lifetimes were carried out with a FLS1000 Edinburgh fluorometer using the MCS (multi-channel scaling) technique. Photoluminescence decays were collected by exciting the sample with an EPL picosecond pulsed diode laser at a repetition rate of 50 KHz; the exciting wavelength was set at 376 nm, corresponding to the maximum absorption of the $Ir(ppy)_3$ complex. The emission was collected at 525 nm. All the data were processed with the Fluorescence Analysis Software Technology (FAST) package supplied by Edinburgh Instruments. A quartz cuvette (optical path = 1 cm) capped with a rubber septum was used. The 10 µM stock solution of $Ir(ppy)_3$ employed for the measurements was degassed bubbling nitrogen in it immediately prior to use and then transferred into the capped cuvette by syringe. All the solutions of the three tested quenchers were similarly degassed by bubbling nitrogen into them immediately prior to use.

Each series of experimental points has been subject to a multi-valence 4-parameter regression performed via FAST. This provided the functions for the Stern-Volmer plot, from which the values of K_{SV} were obtained. The linear regression of the Stern-Volmer plot provides R^2 values > 0.98, indicating that a very good linear fit is present. **1aa**, which reacts slowly without NA is always the best quencher. The substrate **1a** and NA provide similar values.

Comprehensive table of Stern – Vollmer constants

QUENCHER	K_{SV}	R^2
1a	232.0 M^{-1}	0.98
1aa	404.5 M^{-1}	0.99
NP	286.5 M^{-1}	0.99

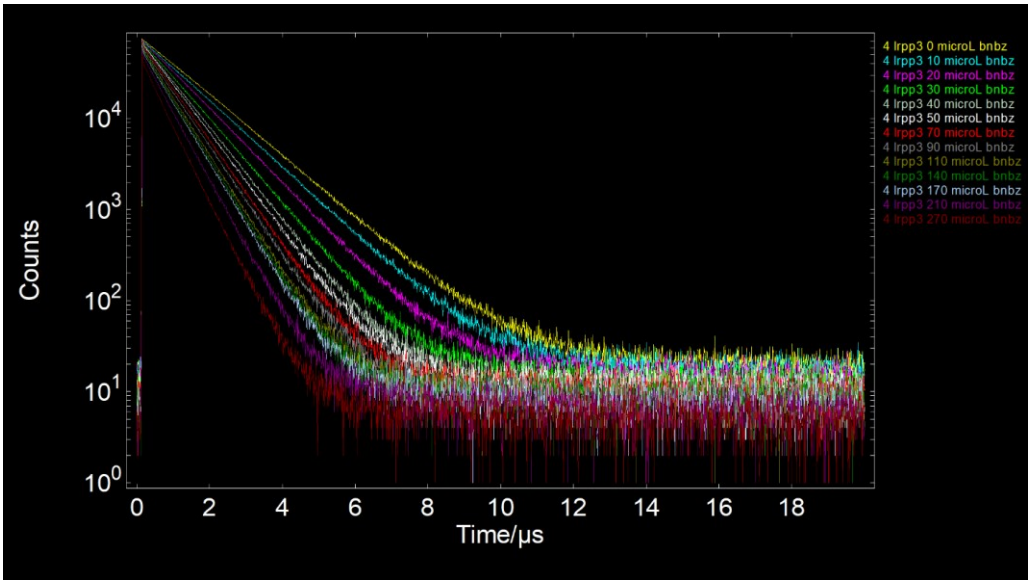


*Figure 6: Measured fluorescence decays for the quenching of $^3Ir(ppy)_3$ with substrate **1aa**.*

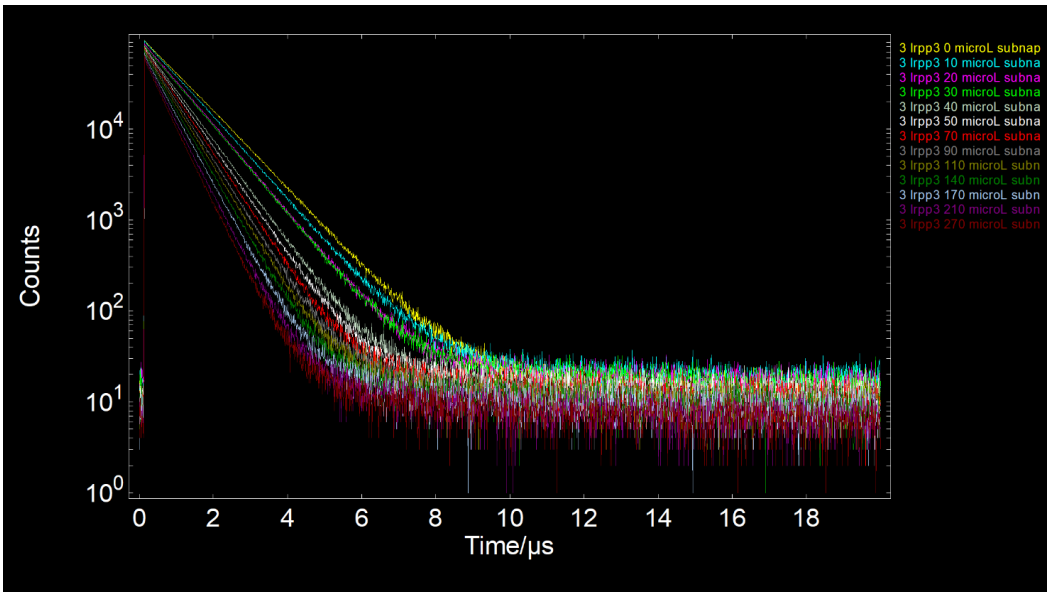


*Figure 7: Measured fluorescence decays for the quenching of $^3Ir(ppy)_3$ with substrate **1a**.*

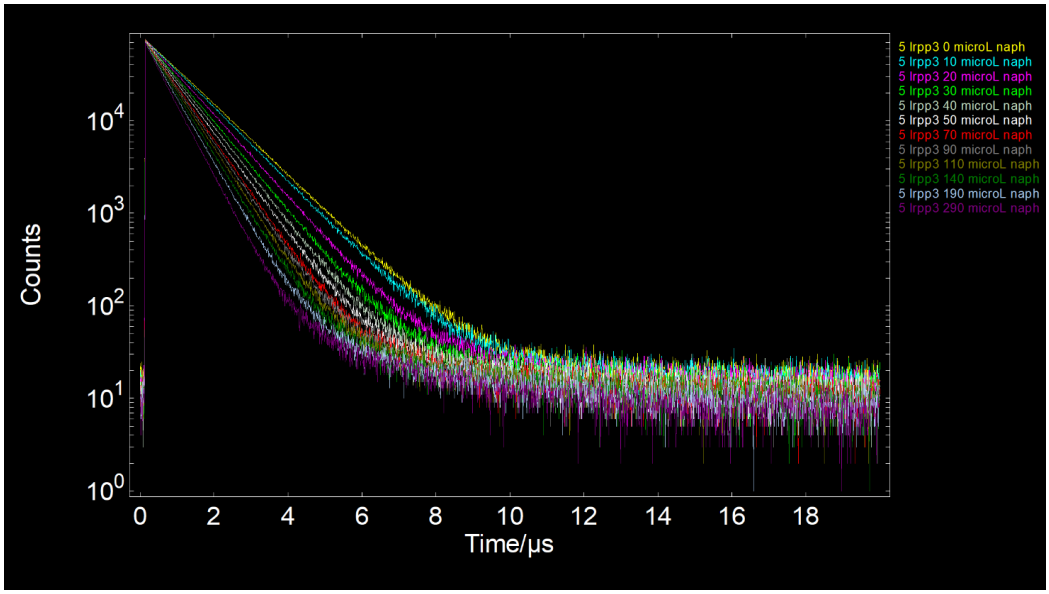
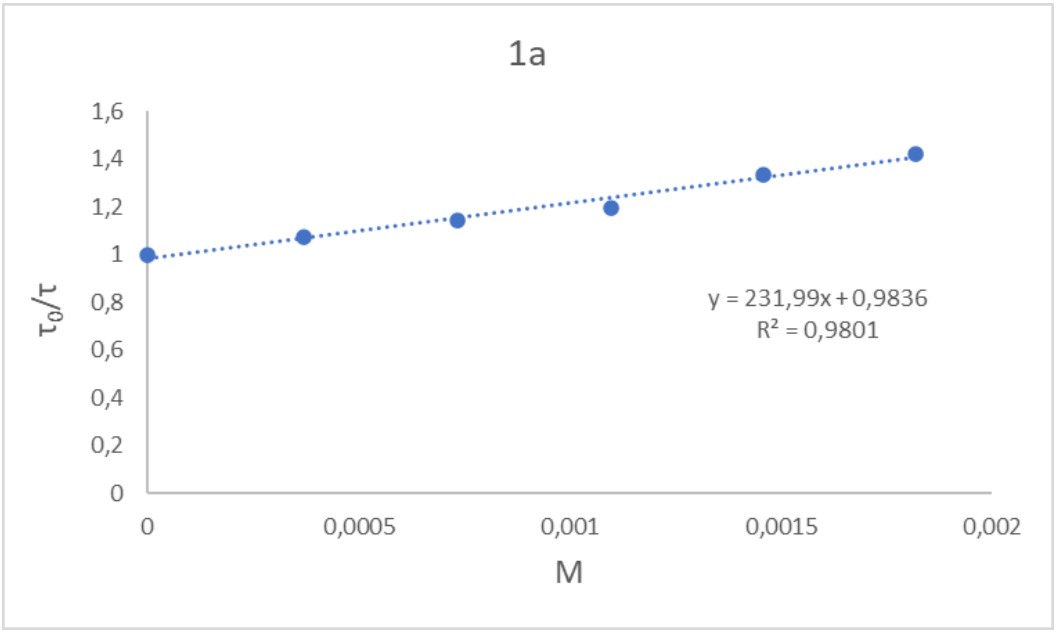
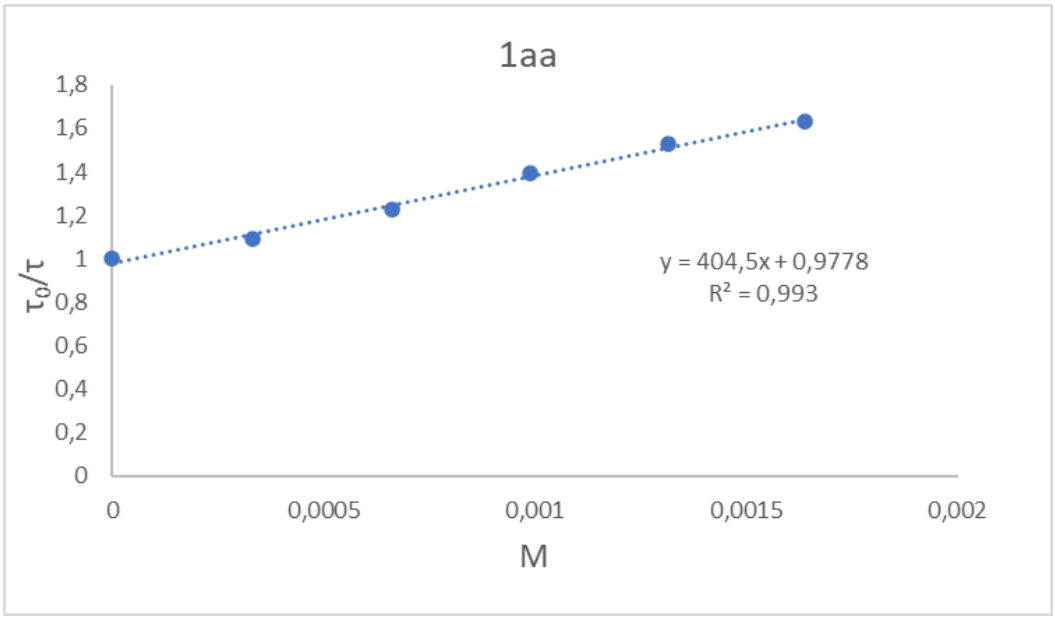
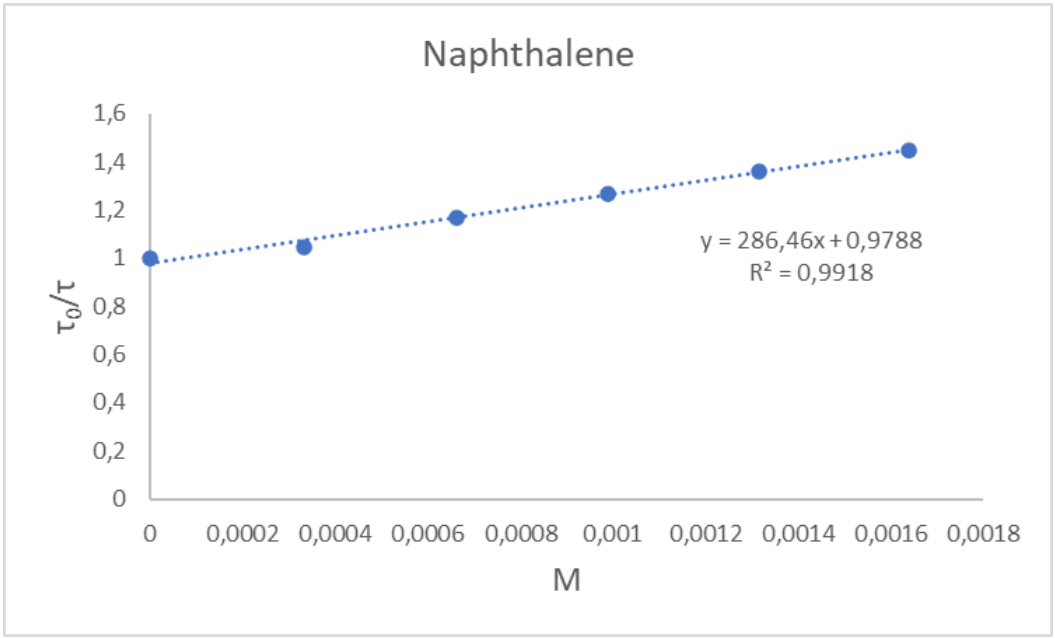


Figure 8: Measured fluorescence decays for the quenching of $^3Ir(ppy)_3$ with naphthalene.

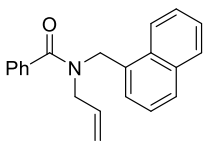



1aa
1,8
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
τ0/τ
y = 404,5x + 0,9778
R² = 0,993
0
0,0005
0,001
0,0015
0,002
M

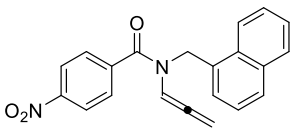

Naphthalene
1,6
1,4
1,2
1
0,8
0,6
0,4
0,2
0
τ0/τ
y = 286,46x + 0,9788
R² = 0,9918
0
0,0002
0,0004
0,0006
0,0008
0,001
0,0012
0,0014
0,0016
0,0018
M

Unsuccessful Substrates

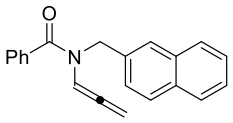
The following substrates did not afford the desired product **2**



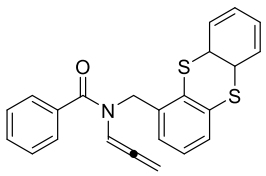
RSM



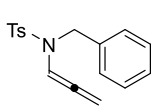
RSM



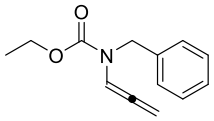
DEC: deallenation



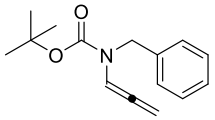
DEC



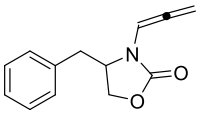
RSM



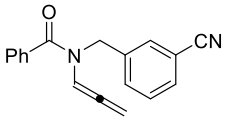
RSM + SR



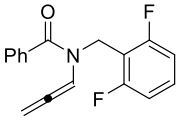
RSM + SR



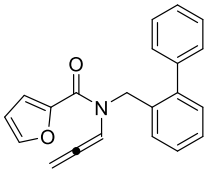
RSM + SR



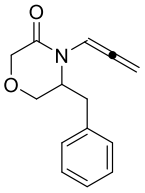
RSM + SR



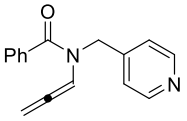
RSM + SR



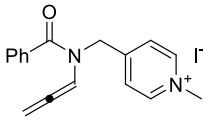
RSM



RSM + SR



RSM



RSM

RSM: Recovery of starting material

DEC: Decomposition

SR: Side reaction (<25% intermolecular cycloaddition on naphthalene)

Computational studies

Calculations were performed at the DFT level using Gaussian16[79]. The exchange/correlation hybrid M06 functional described by Zhao and Truhlar was used[80]. This broadly used functional already proved to afford reliable results in photochemical cascades and for the description of photoactive Ir complexes (see ref 12 and 15 of the main manuscript). Optimization were performed without any constraint using the Def2-SVP basis set described by Weigend and Ahlrichs[80]. Free optimization was then performed again using the Def2-TZVP basis set in order to achieve more precise results[80]. The two sets of results were comparable, differences remaining around or below 3 kcal/mol. Together with gas-phase geometries, solvated structures were then modeled using DMF as implicit solvent through the use of the CPCM method introduced by Barone and Cossi[81]. All values and geometries reported hereafter are those of freely optimized solvated structures, calculated at the M06/Def2-TZVP level. For the rationalization of the effect of naphthalene on rate, calculations on substrate-$C_{10}H_8$ adducts (α, β and γ of the main manuscript) were performed carrying out the free optimization of these systems using the above-mentioned model in combination with D3 corrections, as described by Grimme[81], in order to properly describe intermolecular dispersion interactions. To ascertain that this feature did not induce any bias on calculated data, the basic reaction was reoptimized also including D3 corrections. Gratifyingly, differences between the two sets of results remain below 0.2 kcal/mol. All intermediates, both in their ground and higher spin states were characterized by the absence of any imaginary frequency in their Hessian matrix. All transition states were characterized by the presence of a single imaginary frequency in their Hessian matrix, which corresponds to the molecular vibration connecting the reactant with the product.

Calculations on open-shell singlets were performed using the same computational model described above, performing analyses with the broken symmetry formalism. In contrast to higher-multiplicity spin states, it is worth noting that DFT modeling can provide less precise results on open-shell singlets compared to other computational approaches, most notably CASSCF ones. This approach is however not applicable to present large systems (63 atoms for the multimolecular γ reaction).

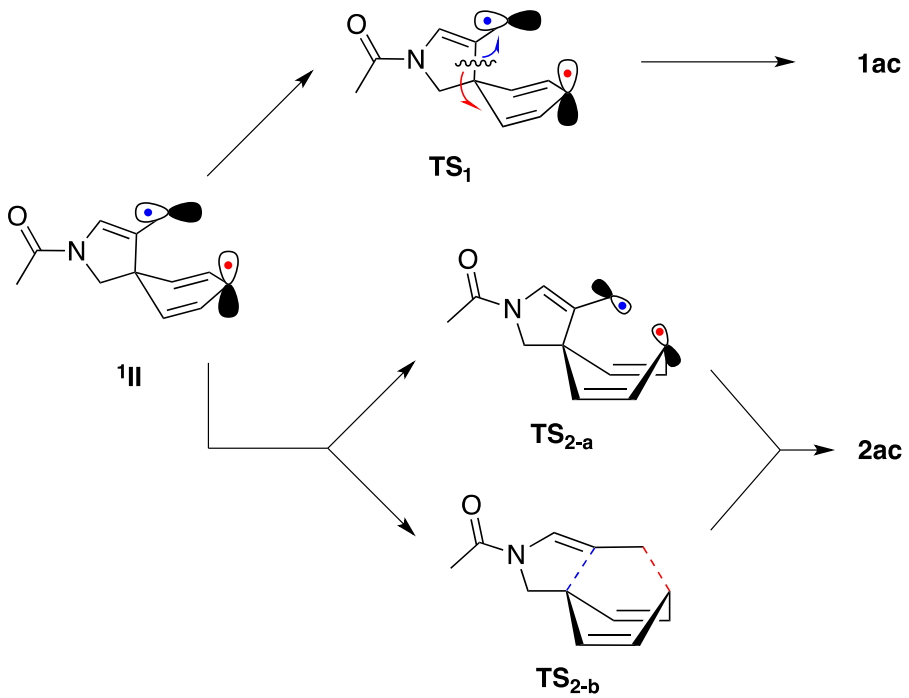


Figure 9: Calculated TSs for the biradical recombination.

The intermediate **^{3}II** can relax into the corresponding singlet biradical via ISC. The geometry of the two intermediates, and their population analyses, are essentially identical. Both have nearly perpendicular singly-occupied orbitals. That localized on the former allenyl arm cannot rotate freely because it has an allylic character and the steric congestion of the five-membered ring did not allow a simple rotation of the endocyclic double bond. As a result, a new barrier has to be overcome. The study of this step allowed to find transition states in which the new C-C bond initially formed is elongated as a result of the torsion. For TS_1, this elongation led directly to C-C cleavage, and the process eventually reforms the initial substrate. In the TS, the distance is between 1.95 and 2.05 Å, depending on the variously modeled systems.

For TS2, which allows instead to form the desired bridged polycycle **2**, two different processes have been found. The less stable one is labelled **$TS_{2\text{-}a}$**; it features a less elongated C-C bond (ca 1.65 Å), and has a very early character with respect to the C-C bond that is being formed (distances between 2.6 and 2.75 Å; for sake of comparison, usual C-C distances in TSs are between 1.9 and 2.2 Å, and can be ca 2.5 Å for Diels-Alder cycloadditions with a high degree of asynchronicity). The **$TS_{2\text{-}b}$** is more stable, by 2-4 kcal/mol among the different systems. Its shares an essentially identical geometry with respect to angles and nuclear distances, except for those between the four reacting carbons, which become very similar in this case (between

1.9 and 2.3 Å). The values obtained for the most stable **TS_2**s are presented in the main manuscript. In order to confirm modeling results on the putative redox event between the excited Ir complex and the allenamides reported in this work, we performed cyclic voltammetry studies on 1ab, which was used as representative example. According to the literature, the redox potentials of NA are well-beyond (>0.8 V) those of the excited Ir complex, in agreement with DFT calculated values[82]. The absence of redox events in present reactions is also suggested by the lack of clear electronic effects among the large considered scope; in particular, it would be expected that, if radical anions (or cations) are involved in these reactions, the presence of electron withdrawing (or donating) groups on the dearomatized ring would result in a significantly affected isolated yield of the final product. The absence of strong electronic effects is instead a usual feature on intramolecular radical processes.

Copies of CV spectra follow hereafter (conditions: 2 x 10^{-3} M solution of substrate, in dry and degassed MeCN, 0.1 M NBu_4PF_6; Pt working electrode, glassy carbon support electrode, Ag/AgCl as (pseudo)reference electrode). No oxidation or reduction wave have been observed (besides the reversible one due to the $Fe(CN)_4^{2-}$ ion used as internal reference) in the range of potential that are compatible with those of $^3Ir(ppy)_3$.

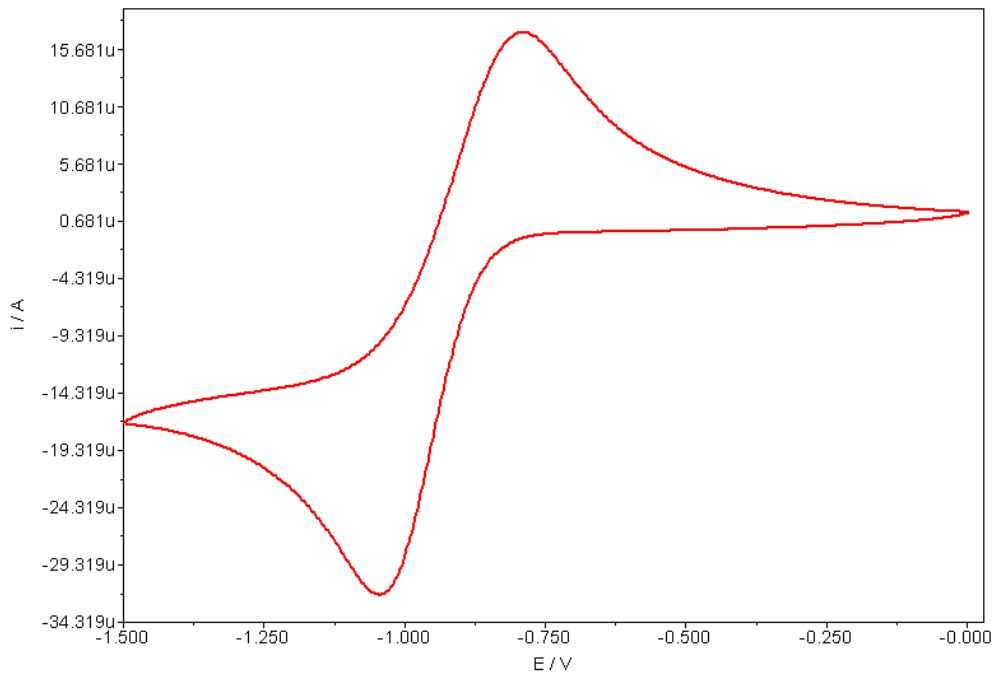


*Figure 10: Cyclic voltammetry of **1ab** (reduction range). Note the absence of any wave beside the reversible one of the internal ferrocyanide.*

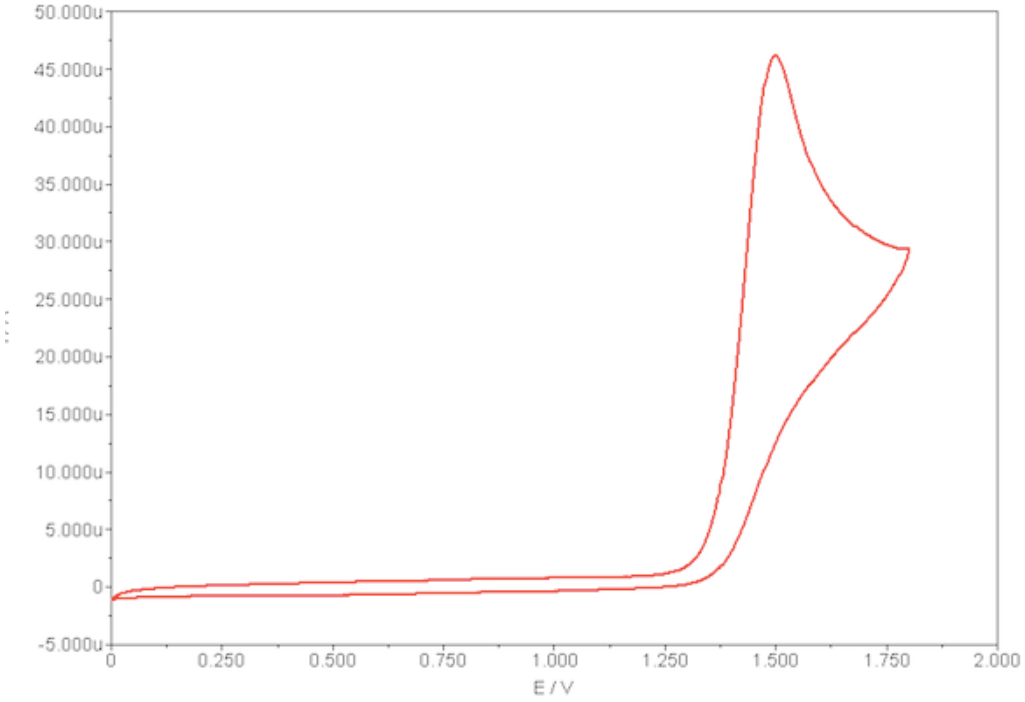


*Figure 11: Cyclic voltammetry of **1ab** (oxidation range). Note the absence of any wave.*

Synthesis and characterization of substrates

A) Synthesis of aldehydes

Synthesis of **6-bromopyridine-2-carbaldehyde**

To a three neck round bottom flask, *n*-BuLi (2.5 M in hexanes, 2.64 ml) was diluted by THF (7.1 ml), put under stirring and cooled to –75 °C. A solution of dibromopyridine (1.421g, 6 mmol) in THF (5 ml) was added dropwise using a dropping funnel to the mixture, maintaining a temperature at/or below –70 °C (~1.5 hours). Once the dropwise addition was complete, the resulting dark green solution) was stirred for 30 min at (–70 °C). Then over a 30 sec. period, excess anhydrous DMF (700 µl, 9 mmol) was added. Upon addition of the electrophile, the mixture was allowed to warm up to –40 °C, then cooled at –70 °C and eventually allowed to warm to 0 °C. The reaction was then quenched with MeOH (30 ml), providing a yellow solution. The crude was then extracted from an aqueous saturated $NaHCO_3$ solution with CH_2Cl_2 (3 x 15 ml). The organic fractions were combined, and the solvent was removed under reduced pressure. The crude aldehyde was purified using column chromatography (silica, CH_2Cl_2, Rf = 0.50) yielding 241.7 mg (22%) of the aldehyde product.

Representative procedure for the methylation of aldehydes

To a stirred mixture of aldehyde (1 equiv.) and K_2CO_3 (2 equiv.) in acetone (0.2 M) was added MeI (2 equiv.) and the reaction was refluxed for 18 h. The mixture was cooled down to room temperature, then it was filtered on celite and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 59-77%.

B) Synthesis of secondary amines

Representative procedure for the preparation of substituted benzyl propargylamine

One drop of AcOH was added to a solution of propargyl amine (1 equiv.) and aryl aldehyde (1.08 equiv.) in MeOH (0.6 M). The resulting mixture was then stirred for 18 h at room temperature. $NaBH_4$ (1.5 equiv.) was added at 0 °C and the solution was then stirred for 1 h prior to the evaporation of the solvent. The mixture was diluted with water, extracted with DCM (2 times), and the combined organic layers

were then washed with a 1 M HCl solution. Aqueous layers were neutralized, extracted with DCM (2 times), and the resulting organic phase was finally washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, and purified by chromatography on silica gel (DCM/EtOAc gradient). Yields between 28-98%.

Procedure for the preparation of **N-((2-methoxynaphthalen-1-yl)methyl)prop-2-yn-1-amine**

To a stirred solution of 2-methoxy-1-naphthaldehyde (1 equiv.) in THF (0.26 M) was added propargyl amine (1.1 equiv.). After 5 minutes, $Na(AcO)_3BH$ (2 equiv.) and AcOH (1 equiv.) were added subsequently and the resulting mixture was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the mixture was quenched with water and a saturated $NaHCO_3$ solution, and eventually extracted with Et_2O (3 times). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was used for the next step without purification (Yield = 99%).

Representative procedure for the preparation of benzyl alkynylamine

In a round bottom flask equipped with a magnetic stirring bar, alkynyl bromide (1 equiv.) was added at 0 °C to benzylamine (6 equiv.) and the resulting solution was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the mixture was quenched with a saturated $NaHCO_3$ solution and extracted with Et_2O (3 times). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 79-95%.

C) Synthesis of propargyl amides

Representative procedure for the preparation of propargyl amides (**GP-A**)

In a 25 mL round bottom flask equipped with a magnetic stirring bar, the desired acid was dissolved in DCM (0.6 M) and a catalytic amount of DMF (3 drops) was added. The solution was then cooled to 0 °C and oxalyl chloride (1.5 equiv) was added. The solution was stirred for 1 h at room temperature. Then, the mixture was concentrated under reduced pressure to afford the acyl chloride, that was added to a solution of DMAP (0.02 equiv.), TEA (1 equiv.) and the desired secondary amine (1 equiv.) in DCM (0.25 M) at 0 °C. The mixture was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the solution was

diluted with DCM and washed with either saturated NH_4Cl solution or water (for the precursors of **1ai, 1an, 1ax, 1ay**), followed by a saturated $NaHCO_3$ one. The aqueous layers were extracted with DCM (3 times), and the combined organic phase was finally washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 40-99%.
Alkynyl amides precursors of **1d, 1e, 1f, 1g, 1h, 1j, 1k, 1n, 1t, 1u, 1ab, 1ac, 1af, 1ah, 1ai, 1aj, 1an, 1ao, 1ap, 1aq, 1ar, 1as, 1ax, 1ay** were directly prepared from commercially available alkyl-, aryl-chlorides or chloroformate, BOC_2O was used for **1g**. The acid precursor of **1ae** was obtained after hydrolysis. **1a**[3] was obtained from the cyclic carbamate.

D) N-Derivatization of primary amines

Representative procedure for the preparation of primary benzamides

In a round bottom flask equipped with a magnetic stirring bar, primary amine (1 equiv.), DMAP (0.02 equiv.) and TEA (1 equiv.) were dissolved in DCM (0.25 M). The solution was cooled to 0 °C and benzoyl chloride (1 equiv.) was then added. The mixture was stirred at room temperature until completion, monitoring the process by TLC. The solution was then quenched with saturated NH_4Cl solution (or water for the precursor of **1aw**) and diluted with DCM. The organic phase was then washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 70-99%

Synthesis of ***d7*-Benzyl bromide**

$ZrCl_4$ (76 mg, 0.325 mmol, 0.05 equiv.) and *d8*-toluene (750 µL, 6.5 mmol, 1 equiv.) were subsequently added to a solution of N-bromosuccinimide (1.15 g, 6.5 mmol, 1 equiv.) in CH_2Cl_2 (50 mL) under a N_2 atmosphere. The resulting solution was stirred at room temperature for 24 h. After complete conversion as monitored by TLC, the reaction was quenched with a saturated $NaHCO_3$ solution and extracted twice with CH_2Cl_2. The combined organic layers were then washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to afford the desired product, that was used without purification for the further step (Yield = 93%).

Representative procedure for the synthesis of propargyl amides **(GP-B)**

To a solution of primary benzamide (1 equiv.) in DMF (0.6 M) at 0° C, NaH (60% in paraffine oil, 1.3 equiv.) was slowly added and the mixture was stirred for 1 h. The desired alkyl halide (1.5 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution (or water for the precursor of **1aw**) and extracted with EtOAc (3 x 15 mL). The combined organic layers were washed with a saturated LiCl solution (3 times), dried over over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 35-83%.

E) Preparation of propargyl amides precursors of 1r, 1s, 1ak, 1v, 1aw

Synthesis of **N-(but-2-yn-1-yl)-N-(naphthalen-1-ylmethyl)benzamide** (precursor of **1r**)

Propargyl amide (1.0 mmol, 1 equiv.) was dissolved in THF (0.21 M) into a Schlenk tube equipped with a magnetic stirring bar. The solution was cooled to –78 °C and KHMDS (1.2 equiv., 1 M in MTBE) was added slowly. The reaction was stirred at the same temperature for 30 minutes, prior to the addition of MeI (2.5 equiv.). Then, the solution was lifted from the cold bath, and it was kept under stirring for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (2 x 15 mL). The organic phase was then washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (yield = 92%).

Synthesis of **N-(naphthalen-1-ylmethyl)-N-(3-phenylprop-2-yn-1-yl)benzamide** (precursor of **1s**)

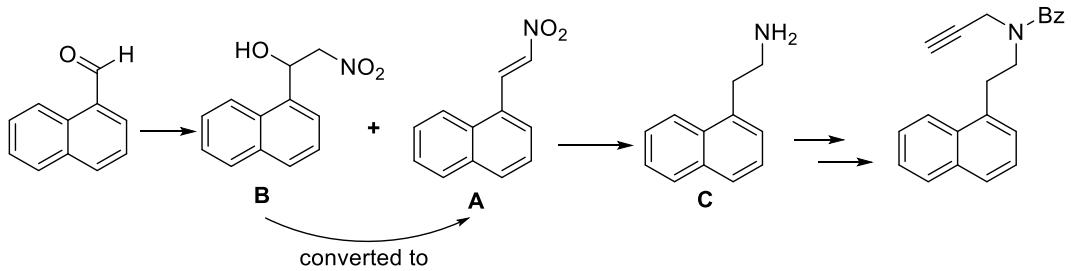
In a Schlenk tube equipped with a magnetic stirring bar were added $PdCl_2(PPh_3)_2$ (2 mol%), CuI (4 mol%), degassed TEA (2.5 equiv.) and iodobenzene (1.05 equiv.) in DMF (0.33 M). The reaction was stirred for 3 minutes under nitrogen, before the addition of a solution of propargyl amide (1 equiv.) in DMF (1 M). The mixture was stirred under N_2 for 2 h at room temperature. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 x 20 mL). The organic phase was then washed with brine

and a saturated solution of LiCl (2 times), dried over Na_2SO_4, and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (yield = 63%).

Synthesis of **N-(4-(oxiran-2-yl)benzyl)-N-(prop-2-yn-1-yl)benzamide** (precursor of **1ak**)

The propargyl amide (200 mg, 0.72 mmol) was diluted in DCM (40 mL) in a 100 mL round-bottom flask. The solution was cooled to 0 °C and *m*–CPBA (~70% wt/wt; 372 mg, 2.16 mmol, 3.0 equiv.) was added in one portion. The mixture is stirred while gradually warming up to room temperature over 2 h, and then kept under stirring overnight. Upon completion, as monitored by TLC, the solvent was evaporated under vacuum and the resulting crude was purified by flash chromatography (*n*-hexane/EtOAc gradient) to afford the desired compound (116 mg, 0.4 mmol, 55% yield) as a white solid.

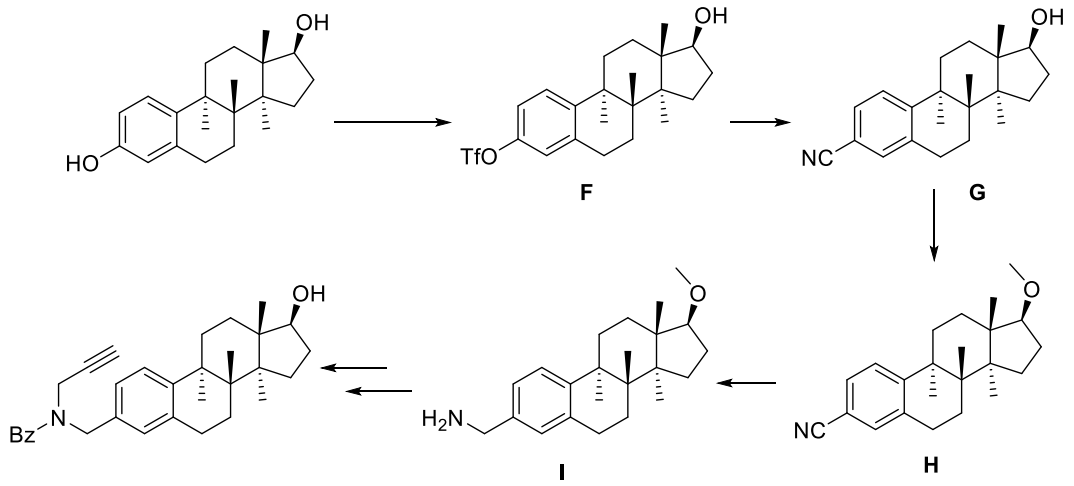
Synthetic route to afford **N-(2-(naphthalen-1-yl)ethyl)-N-(prop-2-yn-1-yl)benzamide** (precursor of **1v**)



To a solution of aldehyde (1 equiv.) and nitromethane (2.5 equiv.) in MeOH (0.3 M) at 0 °C was slowly added a solution of NaOH (2.5 equiv., 10 % w/w). The mixture was kept under stirring at 0 °C for 2 h. Keeping the same temperature and vigorous agitation, a 6M HCl solution was slowly added until the color of the mixture turned to an intense yellow. The mixture was then extracted with EtOAc (2 x 20 mL) and the combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **A** (yield = 15%) and a majority byproduct **B** (yield = 74%).
In a round bottom flask equipped with a magnetic stirring bar were added **B** (1 equiv.) and TEA (1.1 equiv.) in DCM (0.25 M). The solution was cooled to 0 °C before adding MsCl (1.1 equiv.) and the mixture was kept under stirring at room temperature for 18 h. The solution was diluted with DCM (20 mL) and washed with

water and brine. The organic phase was then dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **A** (yield = 69%).
A Schlenk-type flask was charged with BH_3-THF (4 equiv.) at 0 °C. Then, keeping cold the vessel, a solution of intermediate **A** (1 equiv., 4.78 mmol)) in THF (0.5 M) was added dropwise. The cold bath was finally removed and $NaBH_4$ (0.26 equiv.) was added to the reaction. The mixture was stirred at room temperature for 6 days. The reaction was then quenched with water (50 mL) and 1M HCl (24 mL), and eventually heated to reflux for 2 h, observing a color change from yellow to white. The mixture was washed with Et_2O, basified with $NaHCO_3$ and reextracted with Et_2O (3 x 30 mL). The organic phase was finally dried over Na_2SO_4 and concentrated under reduced pressure to afford product **C**, that was used without purification for the next step (yield = 62%). Benzoylation and propargylation was made follow the same procedures described above.

Synthetic route to afford **N-(((8R,9S,13S,14S,17S)-17-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)methyl)-N-(prop-2-yn-1-yl)benzamide** (precursor of **1av**)



In a round bottom flask equipped with a magnetic stirring bar were added Estradiol (1 equiv.), K_2CO_3 (2 equiv.) and 4-Nitrophenyl triflate (1.1 equiv.) in DMF (0.29 M). The mixture was stirred for 2 h at room temperature. The reaction was quenched with water, diluted with Et_2O and washed with 1M HCl, 1M NaOH (4 times) and brine. The organic phase was then dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **F** (yield = 98 %).

A Schlenk-type flask was charged with $Zn(CN)_2$ (2 equiv.) and **F** (1 equiv.) in degassed DMF (0.19 M) under nitrogen. $Pd(PPh_3)_4$ (8 mol%) was added and the mixture was stirred at 85 °C for 18 h. After complete conversion as monitored by TLC, the reaction was quenched with NH_4Cl and extracted with EtOAc (2 x 20 mL). The organic phase was then washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **G** (yield = 88%).

To a solution of **D** (1 equiv.) in THF (0.12 M) at 0° C, NaH (60% in paraffine oil, 2.5 equiv.) was slowly added and the mixture was stirred for 30 min. MeI (4.6 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, 1M NaOH was added, and the mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **H** (yield = 99%).

A Schlenk-type flask was charged with $LiAlH_4$ (2.3 equiv.) and $AlCl_3$ (2.3 equiv.) in Et_2O (0.23 M). The mixture was cooled to 0 °C before adding dropwise a solution of **H** (1 equiv.) in Et_2O (0.1 M). The resulting mixture was then stirred at room temperature for 9 h. After complete conversion as monitored by TLC, water and 1M NaOH were carefully added to the mixture and the reaction was then extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (DCM/MeOH gradient) to afford the desired product **I** (yield = 73%). Benzoylation and propargylation was made follow the same procedures described above.

General procedure for the synthesis of acyl allenamides **(GP-1A):**

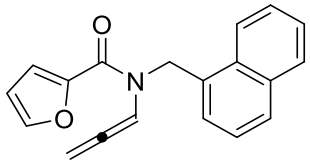
The desired propargyl amide (1 equiv.) and THF (0.20 M) were sequentially added to a Schlenk tube equipped with a magnetic stirring bar. The resulting mixture was stirred at room temperature for 10 minutes prior to the addition of ^{t}BuOK (0.2 equiv.). After complete conversion as monitored by TLC, 5 ml of a saturated NH_4Cl solution (or water for the preparation of **1b, 1an, 1aw, 1ax, 1ay**) were added. The mixture was extracted with EtOAc (3 x 15 ml), the organic layers separated and dried over Na_2SO_4. The solution was concentrated under reduced pressure and the crude purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the corresponding allene.

General procedure for the synthesis of acyl allenamides **(GP-1B):**

The desired propargyl amide (1 equiv.) and THF (0.20 M) were sequentially added to a Schlenk tube equipped with a magnetic stirring bar. The resulting mixture was stirred at room temperature for 10 minutes prior to the addition of KHMDS (0.5 equiv.). After 10 minutes, 5 ml of a saturated NH_4Cl solution (or water for the preparation of **1ai**) were added. The mixture was extracted with EtOAc (3 x 15 mL), the organic layers separated and dried over Na_2SO_4. The solution was concentrated under reduced pressure and the crude purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the corresponding allene.

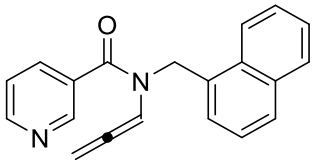
Characterization of substrates

N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)furan-2-carboxamide



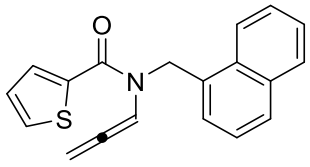
Allene **1a** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (231 mg, 0.8 mmol). Red viscous oil (159.1 mg, 69% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 – 7.30 (m, 10H RotA, 11H RotB), 6.58 – 6.23 (m, 1H RotA), 5.42 (s, 2H RotA, 2H RotB), 5.14 (d, J = 6.4 Hz, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.1, 158.5, 146.7, 145.0, 133.7, 131.8, 128.9, 127.6, 126.2, 125.7, 125.5, 122.4, 117.5, 111.5, 100.6, 87.4. **ESI-MS** calcd for $C_{19}H_{15}NNaO_2$ $[M+Na]^+$ 312.10, found 312.18. *(Partial decomposition during the acquisition of NMR spectra was observed)*

N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)nicotinamide



Allene **1b** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (210.3 mg, 0.7 mmol). Orange viscous oil (125.8 mg, 60% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.99 – 8.45 (m, 2H RotA, 2H RotB), 8.18 – 7.01 (m, 9H RotA, 10H RotB), 6.62 (brs, 1H RotA), 5.53 – 4.94 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.4, 201.4, 167.3, 151.3, 148.9, 147.7, 135.8, 134.3, 133.8, 131.4, 131.1, 128.9, 128.0, 126.3, 125.9, 125.4, 124.4, 123.3, 122.9, 121.8, 101.6, 99.1, 87.3, 49.4, 46.3. **ESI-MS** calcd for $C_{20}H_{17}N_2O$ $[M+H]^+$ 301.13, found 301.22.

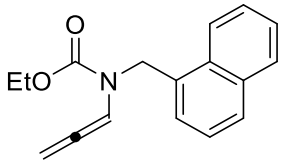
N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)thiophene-2-carboxamide



Allene **1c** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (238 mg, 0.8 mmol). Orange viscous oil (164.2 mg, 67% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR**

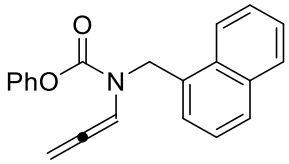
(400 MHz, $CDCl_3$) δ 8.03 – 7.30 (m, 10H RotA, 11H RotB), 6.94 (brs, 1H RotA), 5.40 (s, 2H RotA, 2H RotB), 5.13 (d, J = 6.3 Hz, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.2, 162.8, 137.1, 133.8, 131.7, 130.6, 129.0, 127.8, 127.2, 126.3, 125.8, 125.6, 123.5, 122.5, 101.0, 87.4, 48.7. **ESI-MS** calcd for $C_{19}H_{15}NNaOS$ $[M+Na]^+$ 328.08, found 328.16.

Ethyl (naphthalen-1-ylmethyl)(propa-1,2-dien-1-yl)carbamate



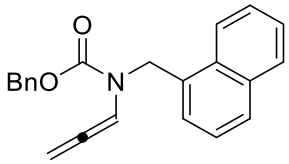
Allene **1d** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (192.5 mg, 0.72 mmol). Pale yellow viscous oil (98 mg, 51% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 – 7.71 (m, 3H RotA, 3H RotB), 7.61 – 7.13 (m, 5H RotA, 5H RotB), 5.22 – 5.03 (m, 4H RotA, 4H RotB), 4.39 – 4.13 (m, 2H RotA, 2H RotB), 1.46 – 1.06 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.4, 200.9, 154.3, 133.7, 132.3, 131.0, 130.7, 128.8, 127.4, 126.0, 125.6, 125.4, 123.5, 122.8, 122.5, 101.0, 100.2, 87.8, 87.2, 62.4, 46.3, 14.6. **ESI-MS** calcd for $C_{17}H_{18}NO_2$ $[M+H]^+$ 268.14, found 268.24.

Phenyl (naphthalen-1-ylmethyl)(propa-1,2-dien-1-yl)carbamate



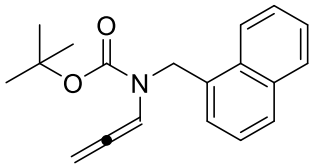
Allene **1e** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (252.3 mg, 0.8 mmol). White solid (148.8 mg, 59% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 – 7.76 (m, 3H RotA, 3H RotB), 7.63 – 6.92 (m, 10H RotA, 10H RotB), 5.54 – 5.16 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.5, 201.1, 152.8, 152.6, 151.2, 150.9, 133.84, 133.75, 132.1, 131.9, 131.1, 130.6, 129.4, 129.3, 128.9, 127.7, 127.6, 126.1, 126.0, 125.9, 125.7, 125.5, 125.3, 124.1, 122.9, 122.3, 121.6, 121.5, 101.0, 100.1, 88.3, 87.5, 48.4, 46.9. **ESI-MS** calcd for $C_{21}H_{17}NNaO_2$ $[M+Na]^+$ 338.12, found 338.20.

Benzyl (naphthalen-1-ylmethyl)(propa-1,2-dien-1-yl)carbamate



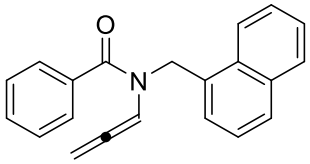
Allene **1f** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (230.6 mg, 0.7 mmol). Pale yellow oil (180.8 mg, 78% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 – 7.85 (m, 2H RotA, 2H RotB), 7.77 (d, J = 8.2 Hz, 1H RotA, 1H RotB), 7.57 – 7.07 (m, 10H RotA, 10H RotB), 5.37 – 5.05 (m, 6H RotA, 6H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.4, 200.9, 154.1, 136.1, 133.7, 132.2, 131.0, 130.7, 128.8, 128.5, 128.4, 128.3, 128.1, 127.9, 127.5, 126.0, 125.6, 125.4, 123.6, 122.8, 122.7, 122.4, 101.1, 100.1, 87.9, 87.3, 68.2, 67.9, 46.7, 46.3. **ESI-MS** calcd for $C_{22}H_{19}NNaO_2$ $[M+Na]^+$ 352.13, found 352.42.

Tert-butyl (naphthalen-1-ylmethyl)(propa-1,2-dien-1-yl)carbamate



Allene **1g** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (271.7 mg, 0.92 mmol). White solid (198.1 mg, 73% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 – 7.72 (m, 3H RotA, 3H RotB), 7.58 – 7.09 (m, 5H RotA, 5H RotB), 5.23 – 4.98 (m, 4H RotA, 4H RotB), 1.70 – 1.23 (m, 9H RotA, 9H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.5, 200.8, 153.2, 133.7, 132.9, 132.5, 130.8, 128.8, 127.3, 125.9, 125.5, 125.4, 123.3, 122.8, 122.6, 100.8, 87.5, 86.9, 81.4, 46.3, 46.0, 28.2, 28.1. **ESI-MS** calcd for $C_{19}H_{21}NNaO_2$ $[M+Na]^+$ 318.15, found 318.06.

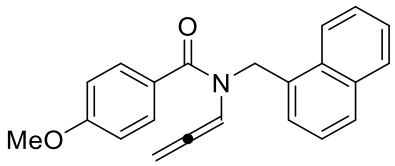
N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1h** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (209.5 mg, 0.7 mmol). Orange solid (152.2 mg, 73% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 – 7.14 (m, 12H RotA, 13H RotB), 6.79 (brs, 1H RotA), 5.52 – 4.97 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 200.5, 170.3,

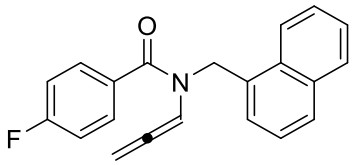
169.8, 135.0, 133.8, 131.9, 131.2, 130.4, 128.9, 128.6, 128.1, 127.7, 126.8, 126.1, 125.7, 125.4, 124.0, 123.0, 122.1, 102.4, 99.1, 87.2, 49.5, 45.8. **ESI-MS** calcd for $C_{21}H_{18}NO$ $[M+H]^+$ 300.14 found 300.04.

4-methoxy-N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



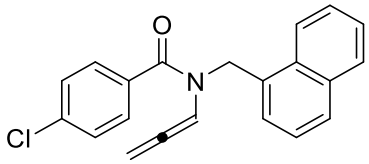
Allene **1i** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (250 mg, 0.76 mmol). Pale yellow oil (214.1 mg, 86% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 – 7.27 (m, 9H RotA, 10H RotB), 7.08 – 6.70 (m, 3H RotA, 2H RotB), 5.49 – 4.98 (m, 4H RotA, 4H RotB), 3.80 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.6, 169.8, 161.40, 161.37, 133.8, 132.1, 130.0, 128.9, 128.8, 127.6, 127.0, 126.1, 125.7, 125.4, 123.7, 122.7, 113.8, 102.7, 87.1, 55.4, 49.6, 46.2. **ESI-MS** calcd for $C_{22}H_{19}NNaO_2$ $[M+Na]^+$ 352.13, found 352.25. *(Partial decomposition during the acquisition of NMR spectra was observed)*.

4-fluoro-N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



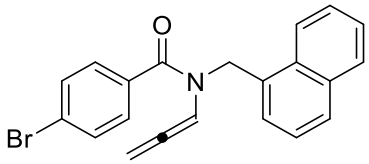
Allene **1j** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (190.4 mg, 0.6 mmol). Orange viscous oil (122.1 mg, 64% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 – 7.32 (m, 9H RotA, 10H RotB), 7.22 – 6.64 (m, 3H RotA, 2H RotB), 5.54 – 5.01 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 201.0, 169.0, 163.9 (d, *J* = 251.3 Hz), 133.8, 131.8, 131.1 (d, *J* = 3.5 Hz), 130.5 (d, *J* = 8.9 Hz), 128.9, 127.8, 126.2, 125.8, 125.4, 124.0, 122.9, 115.7 (d, *J* = 21.9 Hz), 102.2, 99.5, 87.2, 49.5, 46.2. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -108.43 – -109.13 (m). **ESI-MS** calcd for $C_{21}H_{17}FNO$ $[M+H]^+$ 318.13, found 318.21.

4-chloro-N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



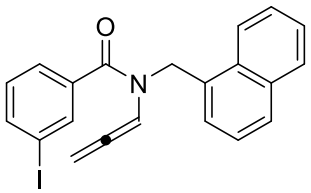
Allene **1k** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (263 mg, 0.79 mmol). Orange viscous oil (195.1 mg, 74% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 – 7.13 (m, 11H RotA, 12H RotB), 6.70 (s, 1H RotA), 5.45 – 5.03 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.8, 168.8, 136.6, 133.8, 133.4, 131.7, 129.7, 129.5, 128.9, 128.8, 128.3, 127.8, 126.2, 125.8, 125.4, 124.2, 122.9, 102.0, 99.2, 87.3, 49.4, 46.1. **ESI-MS** calcd for $C_{21}H_{17}ClNO$ $[M+H]^+$ 334.10, found 334.18.

4-bromo-N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1l** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (227 mg, 0.6 mmol). Orange viscous oil (179.9 mg, 79% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 – 7.24 (m, 11H RotA, 12H RotB), 6.70 (brs, 1H RotA), 5.46 – 5.00 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 200.9, 168.9, 133.84, 133.79, 131.8, 131.7, 129.8, 129.7, 128.9, 127.8, 126.3, 126.1, 125.8, 125.4, 125.3, 124.9, 124.2, 122.9, 122.0, 102.0, 99.2, 87.3, 49.5, 46.1. **ESI-MS** calcd for $C_{21}H_{16}BrNNaO$ $[M+Na]^+$ 400.03, found 400.13.

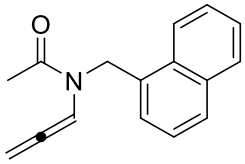
3-iodo-N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1m** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (235.5 mg, 0.55 mmol). Orange viscous oil (159.7 mg, 68% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 – 6.64 (m, 12H RotA, 12H RotB), 5.09 (d, J = 6.3 Hz, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 200.8, 168.4, 167.9, 139.4, 137.0, 136.7, 133.8, 131.6, 131.1, 130.1, 128.9, 127.9, 127.1, 126.3,

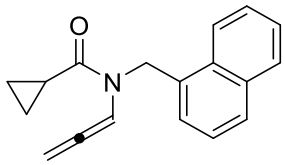
125.9, 125.8, 125.4, 124.1, 122.9, 122.0, 101.9, 99.2, 94.3, 87.4, 49.3, 46.0. **ESI-MS** calcd for $C_{21}H_{16}INNaO$ $[M+Na]^+$ 448.02, found 448.09.

N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)acetamide



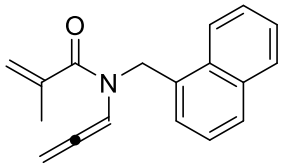
Allene **1n** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (142.4 mg, 0.6 mmol). Pale yellow oil (85.6 mg, 60% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.1 Hz, 1H RotB), 7.94 – 7.84 (m, 2H RotA, 2H RotB), 7.82 – 7.73 (m, 2H RotA), 7.61 – 7.37 (m, 3H RotA, 3H RotB), 7.23 (d, J = 7.1 Hz, 1H RotA, 1H RotB), 6.73 (t, J = 6.2 Hz, 1H RotB), 5.26 – 5.10 (m, 4H RotA, 4H RotB), 2.35 (s, 3H RotB), 2.11 (s, 3H RotA). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.84, 201.81, 169.6, 168.9, 133.8, 133.7, 132.1, 131.3, 131.2, 130.3, 129.1, 128.7, 127.8, 127.6, 126.4, 126.1, 126.0, 125.7, 125.6, 125.2, 124.2, 123.1, 121.95, 121.87, 100.7, 99.2, 87.5, 86.6, 47.8, 45.4, 22.1, 21.9. **ESI-MS** calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 238.13, found 238.25.

N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)cyclopropanecarboxamide



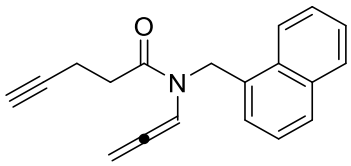
Allene **1o** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (180.5 mg, 0.69 mmol). Pale yellow solid (74 mg, 41% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 – 7.71 (m, 3H RotA, 3H RotB), 7.63 – 7.21 (m, 5H RotA, 4H RotB), 7.05 (t, J = 6.2 Hz, 1H RotB), 5.38 – 5.08 (m, 4H RotA, 4H RotB), 2.01 (brs, 1H RotB), 1.62 – 1.52 (m, 1H RotA), 1.19 – 1.04 (m, 2H RotA, 2H RotB), 0.97 – 0.86 (m, 2H RotB), 0.75 – 0.64 (m, 2H RotA). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 201.7, 172.8, 172.1, 133.7, 132.4, 131.7, 131.2, 130.3, 129.1, 128.7, 127.7, 127.6, 126.3, 126.0, 125.9, 125.8, 125.6, 125.3, 124.3, 123.2, 122.4, 121.9, 100.1, 99.9, 87.5, 86.3, 47.1, 46.1, 12.2, 12.1, 8.7, 8.2. **ESI-MS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$ 286.12, found 286.22.

N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)methacrylamide



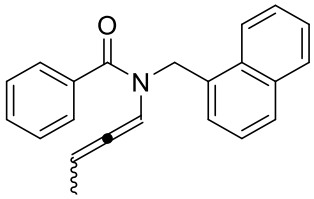
Allene **1p** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (158 mg, 0.6 mmol). Pale yellow viscous oil (112.5 mg, 71% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10 – 7.70 (m, 3H RotA, 4H RotB), 7.60 – 7.39 (m, 3H RotA, 3H RotB), 7.37 – 6.95 (m, 2H RotA, 1H RotB), 5.57 – 4.94 (m, 6H RotA, 6H RotB), 2.29 – 1.80 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, CDCl3) δ 202.3, 200.6, 170.9, 139.8, 133.8, 132.0, 130.9, 128.9, 127.6, 126.2, 125.7, 125.4, 123.6, 122.8, 118.0, 116.4, 101.6, 98.7, 87.2, 48.7, 45.0, 20.6. **ESI-MS** calcd for $C_{18}H_{18}NO$ $[M+H]^+$ 264.14, found 264.25.

N-(naphthalen-1-ylmethyl)-N-(propa-1,2-dien-1-yl)pent-4-ynamide



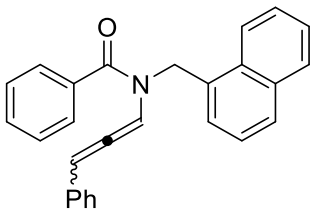
Allene **1q** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (218.3 mg, 0.8 mmol). Pale yellow oil (149.9 mg, 68% yield). Two rotamers are observed due to the dynamic rotation of the amido group. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 1H RotB), 7.96 – 7.73 (m, 4H RotA, 2H RotB), 7.63 – 7.36 (m, 3H RotA, 3H RotB), 7.27 – 7.17 (m, 1H RotA, 1H RotB), 6.72 (t, J = 6.2 Hz, 1H RotB), 5.27 – 5.11 (m, 4H RotA, 4H RotB), 2.84 (t, J = 7.5 Hz, 2H RotB), 2.71 – 2.50 (m, 4H RotA, 2H RotB), 2.03 (t, J = 2.7 Hz, 1H RotB), 1.94 – 1.90 (m, 1H RotA). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.2, 201.8, 170.0, 169.4, 133.8, 133.7, 132.0, 131.2, 131.0, 130.3, 129.1, 128.8, 127.9, 127.8, 126.5, 126.1, 126.0, 125.70, 125.67, 125.2, 124.5, 123.1, 121.9, 99.6, 99.3, 87.7, 86.6, 83.2, 83.1, 69.1, 69.0, 46.9, 45.9, 33.0, 32.6, 14.5, 14.4, 14.2. **ESI-MS** calcd for $C_{19}H_{17}NNaO$ $[M+Na]^+$ 298.12, found 298.20.

N-(buta-1,2-dien-1-yl)-N-(naphthalen-1-ylmethyl)benzamide



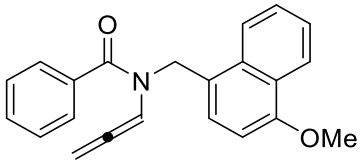
Allene **1r** was prepared following general procedure **GP-1B** from the corresponding propargyl amide (188.04 mg, 0.6 mmol). Brown viscous oil (48 mg, 25% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.19 – 7.16 (m, 12H RotA, 14H RotB), 6.66 (brs, 1H RotA), 5.66 – 4.83 (m, 3H RotA, 2H RotB), 1.37 – 1.01 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 197.5, 195.5, 170.4, 170.0, 135.3, 133.7, 132.1, 131.3, 130.3, 128.9, 128.5, 128.1, 127.5, 126.8, 126.1, 125.6, 125.4, 124.2, 123.0, 122.0, 101.4, 98.3, 49.4, 45.4, 15.4. **ESI-MS** calcd for $C_{22}H_{19}NNaO$ $[M+Na]^+$ 336.14 found 336.21.

N-(naphthalen-1-ylmethyl)-N-(3-phenylpropa-1,2-dien-1-yl)benzamide



Allene **1s** was prepared following general procedure **GP-1B** from the corresponding propargyl amide (469.3 mg, 1.25 mmol). Red viscous oil (168.5 mg, 36% yield). Note: the allene tends to decompose quickly, especially when it is concentrated. Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 – 6.85 (m, 18H RotA, 18H RotB), 6.42 (d, J = 6.1 Hz, 1H RotA, 1H RotB), 5.53 – 5.01 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 195.8, 170.1, 134.9, 133.7, 133.4, 131.8, 130.5, 128.8, 128.6, 128.5, 128.3, 127.7, 127.2, 126.0, 125.6, 125.3, 124.6, 123.0, 105.6, 45.6. **ESI-MS** calcd for $C_{27}H_{22}NO$ $[M+H]^+$ 376.17 found 376.41. *(Partial decomposition during the acquisition of NMR spectra was observed)*

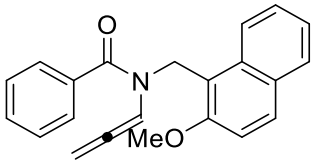
N-((4-methoxynaphthalen-1-yl)methyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1t** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (230.6 mg, 0.7 mmol). Viscous oil (197.3 mg, 86% yield). Two

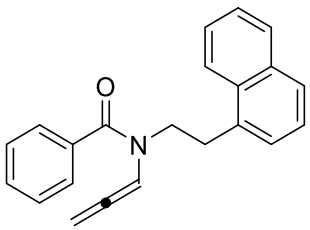
rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.37 – 8.29 (m, 1H RotA, 1H RotB), 8.15 – 7.13 (m, 10H RotA, 10H RotB), 6.88 – 6.65 (m, 1H RotA, 1H RotB), 5.41 – 4.94 (m, 4H RotA, 4H RotB), 4.01 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 200.9, 170.5, 169.9, 155.0, 135.1, 130.3, 128.5, 128.02, 127.98, 126.7, 125.9, 125.1, 123.6, 123.0, 122.7, 103.2, 102.2, 86.9, 55.5, 49.2, 45.7. **ESI-MS** calcd for $C_{22}H_{19}NNaO_2$ $[M+Na]^+$ 352.13 found 352.38.

N-((2-methoxynaphthalen-1-yl)methyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1u** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (329.4 mg, 1 mmol). Orange viscous oil (197.7 mg, 60% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.07 (s, 1H RotA), 7.90 – 7.70 (m, 2H RotA, 2H RotB), 7.58 – 7.08 (m, 8H RotA, 9H RotB), 6.45 – 6.18 (m, 1H RotA), 5.50 – 5.33 (m, 2H RotA, 2H RotB), 4.84 – 4.70 (m, 2H RotA, 2H RotB), 4.07 – 3.82 (m, 3H RotA, 3H RotB). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 202.5, 170.5, 156.3, 136.1, 133.3, 130.1, 130.0, 129.1, 128.6, 128.3, 128.0, 127.8, 127.7, 126.9, 123.6, 117.4, 112.9, 100.5, 85.0, 56.4, 39.7. **ESI-MS** calcd for $C_{22}H_{20}NO_2$ $[M+H]^+$ 330.15 found 330.33. *(Partial decomposition during the acquisition of NMR spectra was observed).*

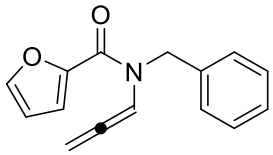
N-(2-(naphthalen-1-yl)ethyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1v** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (178.6 mg, 0.57 mmol). Pale yellow viscous oil (147.3 mg, 82% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.42 – 8.29 (m, 1H RotA), 7.92 – 7.07 (m, 11H RotA, 13H RotB), 6.72 – 6.61 (m, 1H RotA), 5.65 – 5.20 (m, 2H RotA, 2H RotB), 4.13 – 3.68 (m, 2H RotA, 2H RotB), 3.56 – 3.17 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 199.7, 170.0, 169.3, 135.3, 135.0, 133.8, 132.3, 130.4, 129.6, 128.7, 128.5, 128.1, 127.3, 127.1, 126.5, 126.1, 125.7, 125.5, 124.3, 123.0, 102.6, 98.4, 87.0, 48.3,

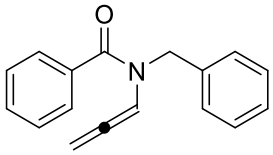
45.8, 31.8, 30.9. **ESI-MS** calcd for $C_{22}H_{19}NNaO$ $[M+Na]^+$ 336.14 found 336.25. *(Partial decomposition during the acquisition of NMR spectra was observed))*

N-benzyl-N-(propa-1,2-dien-1-yl)furan-2-carboxamide



Allene **1aa** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (291.8 mg, 1.22 mmol). Red solid (186.3 mg, 64% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 – 6.93 (m, 9H), 6.51 (s, 1H), 5.50 – 5.23 (m, 2H), 5.11 – 4.81 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.8, 158.2, 147.0, 144.9, 137.3, 128.5, 127.8, 127.2, 126.5, 117.8, 111.5, 101.3, 100.0, 87.5, 50.1, 48.6. **ESI-MS** calcd for $C_{15}H_{14}NO_2$ $[M+H]^+$ 240.10, found 240.22.

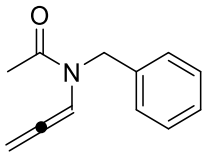
N-benzyl-N-(propa-1,2-dien-1-yl)benzamide



Allene **1ab** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (675.6 mg, 2.71 mmol). Orange solid (549.4 mg, 81% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.03 (m, 10H RotA, 11H RotB), 6.73 (s, 1H RotA), 5.38 – 5.16 (m, 2H RotA, 2H RotB), 4.94 (s, 2H RotA), 4.70 (s, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.1, 200.5, 170.2, 169.5, 137.5, 134.9, 130.4, 128.5, 128.0, 127.2, 126.9, 126.2, 102.5, 99.0, 87.4, 51.4, 47.7. **ESI-MS** calcd for $C_{17}H_{16}NO$ $[M+H]^+$ 250.12, found 250.25.

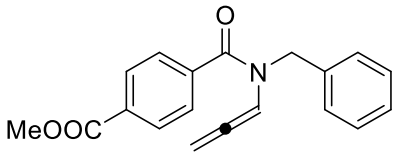
Coalescence of the two rotamers is observed warming a DMSO solution up to at least 80 °C. **^{1}H NMR** (400 MHz, DMSO, 353 K) δ 7.55 – 7.41 (m, 5H), 7.38 – 7.31 (m, 2H), 7.29 – 7.21 (m, 3H), 6.95 (bs, 1H), 5.31 (d, *J* = 6.3 Hz, 2H), 4.76 (s, 2H). **^{13}C NMR** (101 MHz, DMSO, 353 K) δ 201.5, 169.3, 137.9, 135.5, 130.6, 129.0, 128.8, 127.7, 127.41, 127.38, 101.5, 87.8, 48.9.

N-benzyl-N-(propa-1,2-dien-1-yl)acetamide



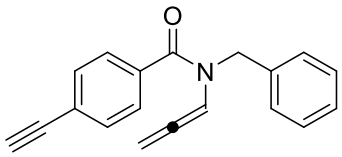
Allene **1ac** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (187.2 mg, 1 mmol). Pale yellow oil (161.1 mg, 86% yield). Two rotamers are observed due to the dynamic rotation of the amido group**.** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (t, *J* = 6.4 Hz, 1H RotB), 7.40 – 7.16 (m, 5H RotA, 5H RotB), 6.74 (t, *J* = 6.2 Hz, 1H RotA), 5.33 (d, *J* = 6.3 Hz, 2H RotA), 5.29 (d, *J* = 6.5 Hz, 2H RotB), 4.74 (s, 2H RotA), 4.67 (s, 2H RotB), 2.27 (s, 3H RotA), 2.14 (s, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.2, 201.4, 169.3, 168.6, 137.6, 136.8, 128.8, 128.3, 127.9, 127.4, 127.1, 126.0, 101.0, 99.4, 87.6, 87.1, 49.9, 47.1, 22.2, 21.9. **ESI-MS** calcd for $C_{12}H_{13}NNaO$ $[M+Na]^+$, 210.09 found 210.48.

Methyl 4-(benzyl(propa-1,2-dien-1-yl)carbamoyl)benzoate



Allene **1ad** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (215 mg, 0.7 mmol). Pale yellow oil (73.1 mg, 34% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.6 Hz, 2H RotA), 8.02 (s, 2H RotB), 7.75 (s, 1H RotB), 7.64 (d, *J* = 7.5 Hz, 2H RotA), 7.50 – 7.21 (m, 5H RotA, 5H RotB), 7.10 (s, 2H RotB), 6.65 – 6.54 (m, 1H RotA), 5.35 – 5.21 (m, 2H RotA, 2H RotB), 4.92 (s, 2H RotA), 4.68 – 4.56 (m, 2H RotB), 3.96 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.0, 200.6, 168.5, 166.2, 139.4, 139.1, 137.2, 136.8, 131.7, 129.8, 128.5, 128.04, 127.95, 127.3, 126.9, 126.0, 102.0, 98.9, 87.6, 52.4, 51.2, 47.7. **ESI-MS** calcd for $C_{19}H_{18}NO_3$ $[M+H]^+$, 308.12 found 308.00.

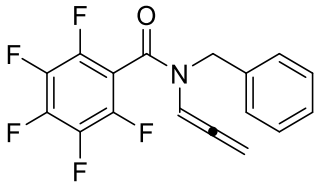
N-benzyl-4-ethynyl-N-(propa-1,2-dien-1-yl)benzamide



Allene **1ae** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (319.8 mg, 1.17 mmol). Orange viscous oil (224.1 mg, 71% yield). Two rotamers are observed due to the dynamic rotation of the amido group**.** **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 – 7.01 (m, 9H RotA, 10H RotB), 6.65

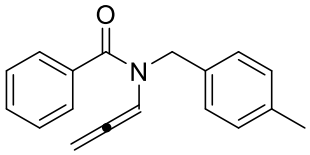
(s, 1H RotA), 5.30 (brs, 2H RotA, 2H RotB), 5.00 – 4.54 (m, 2H RotA, 2H RotB), 3.19 (s, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.0, 200.6, 169.2, 168.7, 137.3, 135.0, 132.2, 128.5, 128.1, 127.3, 126.1, 124.3, 102.2, 99.1, 87.5, 82.7, 79.1, 51.3, 47.8. **ESI-MS** calcd for $C_{19}H_{16}NO$ $[M+H]^+$, 274.12 found 274.23.

N-benzyl-2,3,4,5,6-pentafluoro-N-(propa-1,2-dien-1-yl)benzamide



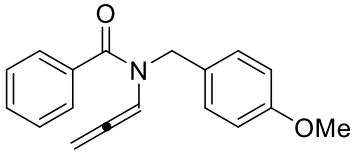
Allene **1af** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (251 mg, 0.74 mmol). Red viscous oil (113.0 mg, 45% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (t, *J* = 6.5 Hz, 1H RotB), 7.44 – 7.22 (m, 4H RotA, 5H RotB), 7.05 (d, *J* = 6.7 Hz, 1H RotA), 6.38 (t, *J* = 6.2 Hz, 1H RotA), 5.36 (d, *J* = 6.5 Hz, 2H RotB), 5.31 (d, *J* = 6.3 Hz, 2H RotA), 4.95 (s, 2H RotA), 4.61 (s, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 202.8, 201.7, 157.3, 157.1, 144.52 – 143.95 (m), 143.81 – 143.32 (m), 141.98 – 141.45 (m), 141.28 – 140.63 (m), 139.38 – 138.54 (m), 136.86 – 136.18 (m), 135.6, 128.7, 128.6, 128.5, 127.8, 127.7, 127.6, 127.6, 126.1, 99.7, 98.6, 88.4, 87.9, 50.8, 48.1. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -139.47 – -139.72 (m, 2F RotA, 2F RotB), -150.61 (t, *J* = 20.6 Hz, 1F RotA), -150.93 (t, *J* = 20.7 Hz, 1F RotB), -159.27 (tt, *J* = 20.6, 5.9 Hz, 2F RotA), -159.41 (tt, *J* = 20.6, 5.9 Hz, 2F RotB). **ESI-MS** calcd for $C_{17}H_{11}F_5NO$ $[M+H]^+$, 340.08 found 339.93.

N-(4-methylbenzyl)-N-(propa-1,2-dien-1-yl)benzamide



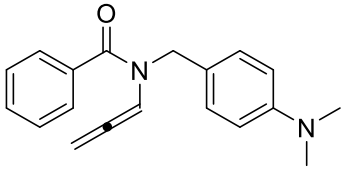
Allene **1ag** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (210 mg, 0.8 mmol). Pale yellow oil (94.8 mg, 45% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 6.94 (m, 9H RotA, 10H RotB), 6.70 (s, 1H RotA), 5.38 – 5.19 (m, 2H RotA, 2H RotB), 4.88 (s, 2H RotA), 4.64 (s, 2H RotB), 2.36 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 203.2, 200.5, 169.5, 136.8, 135.0, 134.5, 130.3, 129.1, 128.8, 128.5, 128.0, 126.9, 126.1, 102.5, 99.0, 87.3, 51.1, 47.4, 21.1. **ESI-MS** calcd for $C_{18}H_{18}NO$ $[M+H]^+$, 264.14 found 264.26.

N-(4-methoxybenzyl)-N-(propa-1,2-dien-1-yl)benzamide



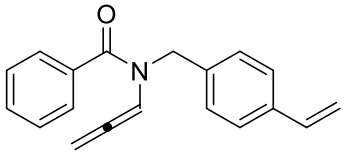
Allene **1ah** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (223.9 mg, 0.8 mmol). Pale yellow oil (195 mg, 87% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.23 (m, 7H RotA, 7H RotB), 7.09 – 6.97 (m, 1H RotB), 6.88 (d, *J* = 7.8 Hz, 2H RotA, 2H RotB), 6.68 (brs, 1H RotA), 5.31 (brs, 2H RotA, 2H RotB), 4.73 (d, *J* = 87.5 Hz, 2H RotA, 2H RotB), 3.82 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.2, 200.5, 169.4, 158.8, 135.0, 130.3, 129.6, 128.5, 128.0, 113.8, 113.4, 102.4, 98.9, 87.2, 55.2, 47.3, 47.1. **ESI-MS** calcd for $C_{18}H_{17}NNaO_2$ $[M+Na]^+$, 302.11 found 302.19.

N-(4-(dimethylamino)benzyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1ai** was prepared following general procedure **GP-1B** from the corresponding propargyl amide (283.6 mg, 0.97 mmol). Orange viscous oil (98.5 mg, 35% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.32 (m, 7H RotA, 8H RotB), 6.77 – 6.60 (m, 3H RotA, 2H RotB), 5.37 – 5.31 (m, 2H RotA, 2H RotB), 4.94 – 4.49 (m, 2H RotA, 2H RotB), 2.97 (s, 6H RotA, 6H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.3, 200.7, 169.4, 149.9, 135.2, 130.2, 129.6, 128.4, 128.0, 127.3, 125.3, 112.5, 102.4, 98.9, 87.1, 50.8, 47.1, 40.6. **ESI-MS** calcd for $C_{19}H_{20}N_2NaO$ $[M+Na]^+$, 315.15 found 315.28.

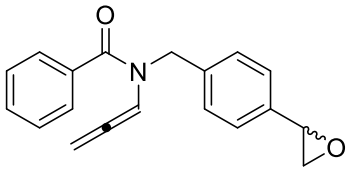
N-(propa-1,2-dien-1-yl)-N-(4-vinylbenzyl)benzamide



Allene **1aj** was obtained as coproduct following general procedure **GP-B** from the corresponding primary benzamide (334 mg, 2.1 mmol). Pale yellow oil (173.5 mg, 30% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.03 (m, 9H RotA, 10H RotB), 6.73 (dd, *J* = 17.6, 10.9 Hz, 2H RotA, 1H RotB), 5.76 (d, *J* = 17.6 Hz, 1H RotA, 1H RotB), 5.37 –

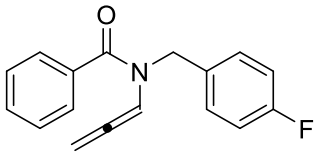
5.20 (m, 3H RotA, 3H RotB), 4.98 – 4.56 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.1, 200.5, 169.5, 137.1, 136.6, 134.9, 130.4, 128.5, 128.2, 128.0, 126.9, 126.3, 113.7, 102.5, 99.0, 87.3, 51.2, 47.4. **ESI-MS** calcd for $C_{19}H_{17}NNaO$ $[M+Na]^+$, 298.12 found 298.21.

N-(4-(oxiran-2-yl)benzyl)-N-(propa-1,2-dien-1-yl)benzamide



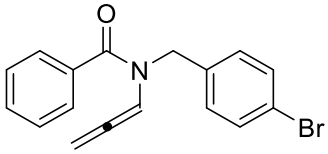
Allene **1ak** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (116 mg, 0.4 mmol). Pale yellow viscous oil (67 mg, 58% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 6.99 (m, 9H RotA, 10H RotB), 6.71 (s, 1H RotA), 5.36 – 5.16 (m, 2H RotA, 2H RotB), 4.91 (s, 1H RotA), 4.67 (s, 1H RotB), 3.88 (dd, *J* = 3.8, 2.7 Hz, 1H RotA, 1H RotB), 3.17 (dd, *J* = 5.3, 4.2 Hz, 1H RotA, 1H RotB), 2.83 (dd, *J* = 5.4, 2.5 Hz, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.4, 170.2, 169.5, 137.6, 136.5, 134.7, 130.5, 128.5, 128.2, 128.0, 126.9, 126.3, 125.2, 102.5, 99.0, 87.4, 52.2, 51.2, 47.4. **ESI-MS** calcd for $C_{19}H_{17}NNaO_2$ $[M+Na]^+$, 314.11 found 314.22.

N-(4-fluorobenzyl)-N-(propa-1,2-dien-1-yl)benzamide



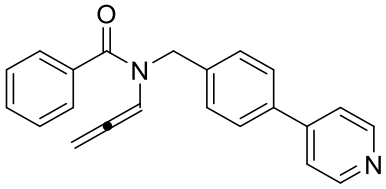
Allene **1al** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (213.8 mg, 0.8 mmol). Pale yellow oil (95 mg, 44% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.17 (m, 7H RotA, 8H RotB), 7.01 (t, *J* = 8.6 Hz, 2H RotA, 2H RotB), 6.68 (brs, 1H RotA), 5.29 (brs, 2H RotA, 2H RotB), 4.94 – 4.50 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.4, 169.5, 163.2, 160.8, 134.7, 132.6, 130.5, 129.9, 128.5, 127.3, 126.1, 115.4, 115.2, 102.4, 99.0, 87.4, 51.3, 47.0. **^{19}F NMR** (565 MHz, $CDCl_3$) δ = -115.62. **ESI-MS** calcd for $C_{17}H_{14}FNNaO$ $[M+Na]^+$, 209.09 found 290.03.

N-(4-bromobenzyl)-N-(propa-1,2-dien-1-yl)benzamide



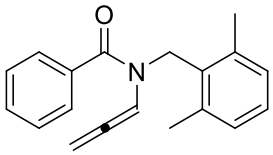
Allene **1am** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (262.6 mg, 0.8 mmol). Pale yellow oil (209.1 mg, 80% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 – 6.87 (m, 9H RotA, 10H RotB), 6.72 (s, 1H RotA), 5.35 – 5.25 (m, 2H RotA, 2H RotB), 4.86 (s, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.3, 169.5, 136.6, 134.6, 131.6, 130.6, 129.8, 128.6, 128.0, 126.8, 121.1, 102.4, 98.9, 87.6, 50.8, 47.1. **ESI-MS** calcd for $C_{17}H_{15}BrNO$ $[M+H]^+$, 328.03 found 328.11.

N-(propa-1,2-dien-1-yl)-N-(4-(pyridin-4-yl)benzyl)benzamide



Allene **1an** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (228.5 mg, 0.7 mmol). Red oil (177.4 mg, 78% yield). Two rotamers are observed due to the dynamic rotation of the amido group.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.67 (d, *J* = 6.0 Hz, 2H RotA, 2H RotB), 7.96 – 7.11 (m, 11H RotA, 12H RotB), 6.77 (s, 1H RotA), 5.45 – 5.16 (m, 2H RotA, 2H RotB), 4.97 (s, 2H RotA), 4.74 (s, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.4, 200.3, 169.5, 150.2, 148.0, 138.7, 137.0, 134.6, 130.6, 130.3, 128.7, 128.6, 128.6, 128.1, 127.4, 127.1, 127.0, 121.5, 102.6, 98.9, 87.6, 51.1, 47.4. **ESI-MS** calcd for $C_{22}H_{19}N_2O$ $[M+H]^+$, 327.15 found 327.37.

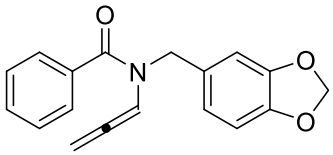
N-(2,6-dimethylbenzyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1ao** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (258.2 mg, 0.93 mmol). Orange viscous oil (141.1 mg, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.46 (m, 2H), 7.49 – 7.38 (m, 3H), 7.15 – 7.07 (m, 1H), 7.02 (d, *J* = 7.5 Hz, 2H), 6.39 (brs, 1H), 4.97 (s, 2H), 4.88 (d, *J* = 6.3 Hz, 2H), 2.42 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 170.1, 137.8, 135.6,

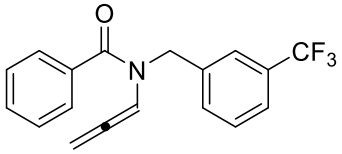
132.8, 130.2, 128.5, 128.3, 128.0, 127.5, 100.1, 85.0, 44.3, 20.5. **ESI-MS** calcd for $C_{19}H_{20}NO$ $[M+H]^+$, 278.15 found 278.27.

N-(benzo[d][1,3]dioxol-5-ylmethyl)-N-(propa-1,2-dien-1-yl)benzamide



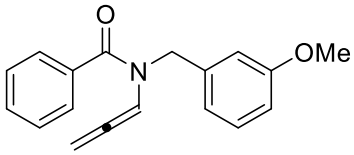
Allene **1ap** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (234.6 mg, 0.8 mmol). Pale yellow oil (71.4 mg, 30% yield). Two rotamers are observed due to the dynamic rotation of the amido group.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 – 7.33 (m, 5H RotA, 5H RotB), 6.99 – 6.49 (m, 3H RotA, 3H RotB), 6.03 – 5.89 (m, 2H RotA, 2H RotB), 5.39 – 5.21 (m, 2H RotA, 2H RotB), 4.87 – 4.47 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.3, 200.4, 171.0, 169.1, 148.1, 147.7, 147.3, 146.7, 135.4, 134.8, 131.3, 130.4, 130.1, 128.6, 128.5, 128.0, 127.0, 121.7, 108.7, 108.1, 102.4, 101.2, 101.0, 87.4, 51.1, 47.4. **ESI-MS** calcd for $C_{18}H_{15}NNaO_3$ $[M+Na]^+$, 316.09 found 316.22.

N-(propa-1,2-dien-1-yl)-N-(3-(trifluoromethyl)benzyl)benzamide



Allene **1aq** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (415.7 mg, 1.31 mmol). Yellow viscous oil (309.7 mg, 75% yield). Two rotamers are observed due to the dynamic rotation of the amido group.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 – 7.20 (m, 9H RotA, 10H RotB), 6.72 (s, 1H RotA), 5.32 – 5.26 (m, 2H RotA, 2H RotB), 4.94 (s, 2H RotA), 4.71 (s, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 200.3, 169.6, 138.5, 134.4 (brs), 131.4 (brs), 130.9, 130.6 (brs), 129.0, 128.6, 128.0 (brs), 126.8 (brs), 124.9 (brs), 124.12 (q, *J* = 3.8 Hz), 124.11 (q, *J* = 271.42 Hz), 102.4, 98.9, 87.7, 51.0, 47.3. **^{19}F NMR** (565 MHz, $CDCl_3$) δ = -62.48, -62.55. **ESI-MS** calcd for $C_{18}H_{15}F_3NO$ $[M+H]^+$, 318.11 found 318.00.

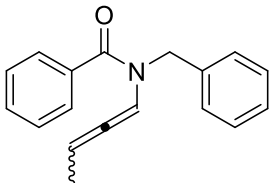
N-(3-methoxybenzyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1ar** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (195.5 mg, 0.7 mmol). Yellow viscous oil (140.8 mg,

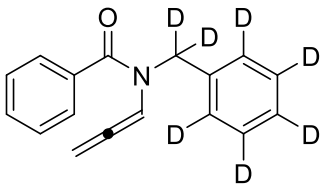
72% yield). Two rotamers are observed due to the dynamic rotation of the amido group.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.15 (m, 6H RotA, 7H RotB), 7.03 – 6.57 (m, 4H RotA, 3H RotB), 5.27 (brs, 2H RotA, 2H RotB), 4.87 (brs, 2H RotA), 4.62 (brs, 2H RotB), 3.80 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.0, 200.4, 170.0, 169.5, 159.7, 138.6, 134.8, 130.4, 129.4, 128.5, 128.0, 127.0, 120.3, 118.4, 113.6, 112.5, 102.5, 99.1, 87.4, 55.2, 51.3, 47.6. **ESI-MS** calcd for $C_{18}H_{17}NNaO_2$ $[M+Na]^+$, 302.11 found 302.23.

N-benzyl-N-(buta-1,2-dien-1-yl)benzamide



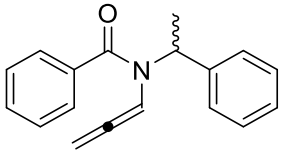
Allene **1as** was prepared following general procedure **GP-1B** from the corresponding propargyl amide (324 mg, 1.1 mmol). Yellow viscous oil (138 mg, 43% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 – 7.07 (m, 10H RotA, 11H RotB), 6.62 (s, 1H RotA), 5.67 – 5.58 (m, 1H RotA, 1H RotB), 5.20 – 4.98 (m, 1H RotA), 4.87 – 4.49 (m, 1H RotA, 2H RotB), 1.64 – 1.32 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 214.8, 197.9, 195.3, 170.3, 169.7, 137.6, 135.2, 130.2, 128.5, 128.4, 128.0, 127.9, 127.0, 126.2, 101.5, 98.3, 51.4, 47.6, 15.8, 15.3. **ESI-MS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$, 286.12 found 286.22.

N-((phenyl-d5)methyl-d2)-N-(propa-1,2-dien-1-yl)benzamide



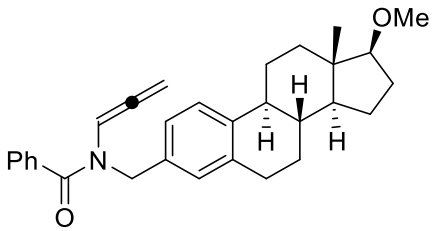
Allene **1at** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (184.8 mg, 0.72 mmol). White viscous oil (136.4 mg, 74% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82 – 7.22 (m, 5H RotA, 6H RotB), 6.70 (s, 1H RotA), 5.35 – 5.14 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.1, 200.5, 170.2, 169.5, 137.2, 137.0, 135.2, 134.9, 130.4, 128.5, 128.2, 128.0, 127.7, 127.4, 126.9, 126.7, 126.5, 102.4, 99.0, 87.3, 47.5 - 46.7 (m). **ESI-MS** calcd for $C_{17}H_9D_7NO$ $[M+H]^+$ 257.17 found 257.43.

N-(1-phenylethyl)-N-(propa-1,2-dien-1-yl)benzamide



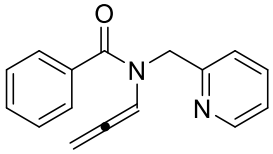
Allene **1au** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (197.5 mg, 0.75 mmol). Yellow viscous oil (88.1 mg, 45% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.54 – 7.51 (m, 2H RotA, 2H RotB), 7.43 – 7.32 (m, 7H RotA, 7H RotB), 7.28 – 7.24 (m, 1H RotA, 1H RotB), 6.49 – 5.69 (m, 1H RotA, 1H RotB), 4.89 – 4.71 (m, 3H RotA, 3H RotB), 1.76 (d, J = 7.0 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 204.3, 170.3, 140.4, 136.1, 130.1, 128.4, 128.3, 127.3, 127.2, 84.4, 16.7. **ESI-MS** calcd for $C_{18}H_{18}NO$ $[M+H]^+$ 264.14 found 264.34.

N-(((8R,9S,13S,14S,17S)-17-methoxy-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)methyl)-N-(propa-1,2-dien-1-yl)benzamide



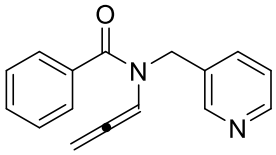
Allene **1av** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (432.7 mg, 0.98 mmol). Pale yellow viscous oil (347.3 mg, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 – 7.05 (m, 8H RotA, 8H RotB), 6.94 – 6.63 (m, 1H RotA, 1H RotB), 5.38 – 5.15 (m, 2H RotA, 2H RotB), 4.90 – 4.51 (m, 2H RotA, 2H RotB), 3.42 – 3.28 (m, 4H RotA, 4H RotB), 2.85 (s, 2H RotA, 2H RotB), 2.36 – 2.18 (m, 2H RotA, 2H RotB), 2.14 – 2.01 (m, 2H RotA, 2H RotB), 1.94 – 1.84 (m, 1H RotA, 1H RotB), 1.78 – 1.64 (m, 1H RotA, 1H RotB), 1.61 – 1.16 (m, 7H RotA, 7H RotB), 0.80 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.2, 200.5, 170.3, 169.4, 139.3, 136.8, 135.0, 134.6, 130.3, 128.8, 128.5, 128.0, 127.0, 125.4, 123.5, 102.7, 99.0, 90.8, 87.4, 57.9, 51.0, 50.5, 47.3, 44.3, 43.2, 38.4, 38.1, 29.6, 27.8, 27.2, 26.2, 23.1, 11.6. **ESI-MS** calcd for $C_{30}H_{36}NO_2$ $[M+H]^+$ 442.27 found 442.09.

N-(propa-1,2-dien-1-yl)-N-(pyridin-2-ylmethyl)benzamide



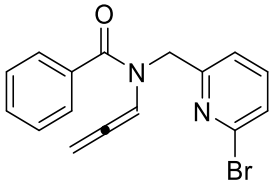
Allene **1aw** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (308 mg, 1.23 mmol). Yellow viscous oil (186.9 mg, 61% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.56 (s, 1H RotA, 1H RotB), 7.90 – 7.08 (m, 8H RotA, 9H RotB), 6.80 (s, 1H RotA), 5.22 – 4.68 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.2, 170.3, 169.6, 157.1, 149.4, 136.6, 134.6, 130.5, 130.3, 128.5, 128.1, 126.9, 122.0, 120.7, 102.5, 98.9, 87.4, 53.3, 49.7. **ESI-MS** calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$, 251.12 found 251.26.

N-(propa-1,2-dien-1-yl)-N-(pyridin-3-ylmethyl)benzamide



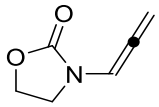
Allene **1ax** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (250.3 mg, 1 mmol). Yellow viscous oil (148 mg, 59% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.66 – 8.47 (m, 2H), 7.81 – 7.23 (m, 9H), 6.70 (s, 1H), 5.39 – 5.22 (m, 2H), 4.96 – 4.50 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.2, 169.6, 149.7, 148.7, 136.0, 134.3, 133.1, 130.7, 128.6, 128.1, 123.5, 102.3, 87.8, 45.3. **ESI-MS** calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$, 251.12 found 251.26.

N-((6-bromopyridin-2-yl)methyl)-N-(propa-1,2-dien-1-yl)benzamide



Allene **1ay** was prepared following general procedure **GP-1A** from the corresponding propargyl amide (253.3 mg, 0.77 mmol). Yellow viscous oil (176.7 mg, 70% yield). Two rotamers are observed due to the dynamic rotation of the amido group. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 – 7.13 (m, 8H RotA, 9H RotB), 6.79 (s, 1H RotA), 5.23 (d, *J* = 6.1 Hz, 2H RotA, 2H RotB), 5.03 (s, 2H RotA), 4.73 (s, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 200.0, 169.6, 158.6, 141.6, 139.0, 134.4, 130.7, 128.6, 128.1, 126.8, 126.4, 119.4, 102.4, 98.8, 87.8, 52.7, 49.2. **ESI-MS** calcd for $C_{16}H_{13}BrN_2NaO$ $[M+Na]^+$, 351.01 found 351.05.

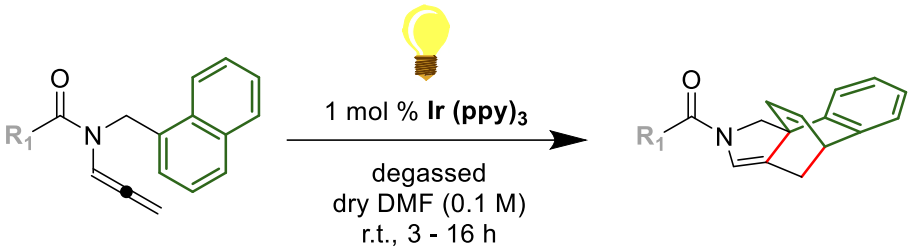
3-(propa-1,2-dien-1-yl)oxazolidin-2-one



Allene **1a**[3] was prepared following general procedure **GP-1A** from the corresponding propargyl amide (179.0 mg, 1.43 mmol). White solid (108.4 mg, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 (t, *J* = 6.4 Hz, 1H), 5.42 (d, *J* = 6.3 Hz, 2H), 4.45 – 4.37 (m, 2H), 3.63 – 3.56 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.4, 155.3, 97.0, 87.9, 62.3, 43.1. **ESI-MS** calcd for $C_6H_7NNaO_2$ $[M+Na]^+$, 148.04 found 148.16..

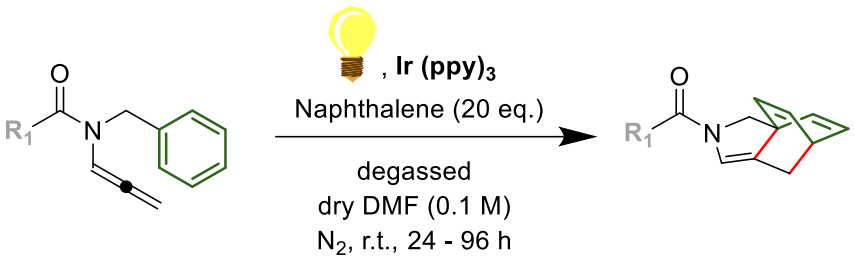
Characterization of products

Photocatalytic reactions [GP-2A]:



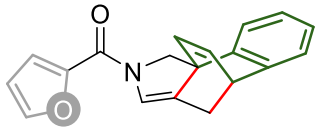
To a vial charged with substrate **1** (1 equiv., 0.2 mmol, pink box of figure 1) and **Ir(ppy)$_3$** (1 mol%), dry and degassed DMF (0.1 M) was added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum, and the tube was placed in an oil bath kept at 25 °C by means of a chiller. The tube was irradiated with a white (RGB) 14W-household LED strip for 3-16 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel; the catalyst was removed using toluene as eluent prior to the separation of desired products (*n*-hexane/EtOAc, under gradient).

Photocatalytic reactions [GP-2B]:



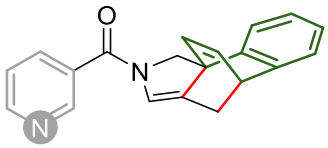
To a vial charged with substrate **1** (1 equiv., 0.15 mmol, cyan box of figure 1), **Ir(ppy)$_3$** (1 mol%), and naphthalene (20 equiv.), dry DMF (0.1 M) was added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum, degassed by freeze-pump-thaw (3 times) and the tube was placed in an oil bath kept at 25 °C by means of a chiller. The tube was irradiated with a white (RGB) 14W-household LED strip for 24-96 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo with an additional trap to collect sublimated naphthalene. The residue was purified by chromatography on silica gel; the catalyst and the excess of naphthalene were removed using toluene as eluent prior to the separation of desired products (*n*-hexane/EtOAc, under gradient).

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(furan-2-yl)methanone



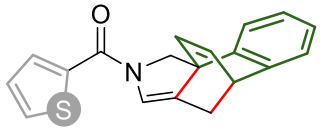
Product **2a** was prepared following general procedure **GP-2A** from the corresponding allene (58 mg, 0.2 mmol). Pale yellow solid (57.6 mg, 99% yield). Two rotamers are observed due to the dynamic rotation of the amido group (74:26 mixture of rotamers). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (s, 1H RotB), 7.49 (s, 1H RotA), 7.35 – 7.24 (m, 2H Rot A, 2H Rot B), 7.24 – 7.09 (m, 4H RotA, 4H RotB), 6.83 (s, 1H RotB), 6.64 – 6.55 (m, 1H RotA, 1H RotB), 6.54 – 6.44 (m, 2H RotA, 1H RotB), 5.35 (d, *J* = 12.3 Hz, 1H RotB), 5.13 (d, *J* = 13.6 Hz, 1H RotA), 4.60 (d, *J* = 12.3 Hz, 1H RotB), 4.35 (d, *J* = 13.6 Hz, 1H RotA), 4.22 (brs, 1H RotA, 1H RotB), 2.44 (dt, *J* = 15.4, 2.4 Hz, 1H RotA, 1H RotB), 2.34 (dt, *J* = 15.5, 2.3 Hz, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 154.7, 148.5, 148.3, 144.5, 144.0, 143.0, 142.9, 142.0, 138.9, 138.7, 135.1, 129.8, 128.4, 125.7, 125.5, 123.6, 123.5, 119.1, 119.0, 118.8, 117.2, 116.6, 111.9, 111.6, 58.2, 54.6, 50.5, 49.7, 42.4, 28.9, 28.7. **ESI-HRMS** calcd for $C_{19}H_{16}NO_2$ $[M+H]^+$ 290.1176, found 290.1180.

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(pyridin-3-yl)methanone



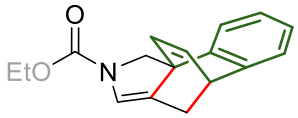
Product **2b** was prepared following general procedure **GP-2A** from the corresponding allene (60.8 mg, 0.2 mmol). White solid (54.5 mg, 90% yield). Two rotamers are observed due to the dynamic rotation of the amido group (76:24 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 8.97 (s, 1H RotB), 8.78 – 8.62 (m, 2H RotA, 1H RotB), 8.16 (d, *J* = 8.0 Hz, 1H RotB), 7.87 (dt, *J* = 7.9, 2.0 Hz, 1H RotA), 7.58 – 7.50 (m, 1H RotB), 7.47 – 7.37 (m, 2H RotA), 7.35 – 7.23 (m, 1H RotA, 1H RotB), 7.24 – 7.08 (m, 2H RotA, 3H RotB), 6.74 (s, 1H RotB), 6.58 (t, *J* = 5.7 Hz, 2H RotA, 2H RotB), 6.24 (t, *J* = 2.0 Hz, 1H RotA), 5.07 (d, *J* = 13.5 Hz, 1H RotA), 4.94 (d, *J* = 11.7 Hz, 1H RotB), 4.42 (d, *J* = 11.6 Hz, 1H RotB), 4.34 (d, *J* = 13.5 Hz, 1H RotA), 4.26 – 4.22 (m, 1H RotA, 1H RotB), 2.43 (d, *J* = 15.8 Hz, 1H RotB), 2.39 – 2.24 (m, 1H RotA, 1H RotB), 2.19 (dt, *J* = 15.6, 2.3 Hz, 1H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 163.6, 151.0, 148.5, 143.4, 143.2, 142.4, 142.2, 139.0, 138.6, 135.1, 135.0, 134.9, 132.5, 132.1, 128.8, 125.4, 125.32, 125.28, 123.5, 123.3, 119.3, 119.0, 118.9, 118.7, 58.1, 55.8, 50.9, 48.7, 42.2, 28.5, 28.4. **ESI-HRMS** calcd for $C_{20}H_{17}N_2O$ $[M+H]^+$ 301.1335, found 301.1330.

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(thiophen-2-yl)methanone



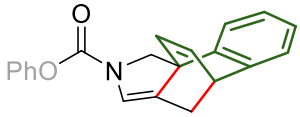
Product **2c** was prepared following general procedure **GP-2A** from the corresponding allene (61.3 mg, 0.2 mmol). Pale yellow oil (60.6 mg, 99% yield). Two rotamers are observed due to the dynamic rotation of the amido group (60:40 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.99 (brs, 1H RotB), 7.83 – 7.63 (m, 1H RotA, 1H RotB), 7.56 – 7.07 (m, 6H RotA, 5H RotB), 6.79 – 6.71 (m, 1H RotA, 1H RotB), 6.66 – 6.53 (m, 2H RotA, 2H RotB), 5.40 – 4.97 (m, 1H RotA, 1H RotB), 4.70 (brs, 1H RotB), 4.39 – 4.23 (m, 2H RotA, 1H RotB), 2.50 – 2.19 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 158.6, 157.9, 143.3, 142.3, 138.9, 138.5, 135.0, 130.6, 129.7, 129.5, 129.2, 128.8, 128.2, 127.7, 127.1, 125.4, 125.3, 123.5, 119.5, 119.1, 118.9, 58.6, 55.3, 50.9, 49.3, 42.2. **ESI-HRMS** calcd for $C_{19}H_{15}NNaOS$ $[M+Na]^+$ 328.0767, found 328.0761.

Ethyl (5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindole-2(1H)-carboxylate



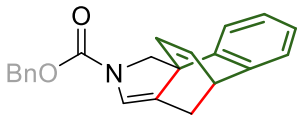
Product **2d** was prepared following general procedure **GP-2A** from the corresponding allene (54.1 mg, 0.2 mmol). White solid (50.2 mg, 93% yield). Two rotamers are observed due to the dynamic rotation of the amido group (57:43 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.32 – 7.25 (m, 2H RotA, 2H RotB), 7.18 – 7.06 (m, 2H RotA, 2H RotB), 6.56 – 6.46 (m, 2H RotA, 2H RotB), 6.25 – 6.17 (m, 1H RotA, 1H RotB), 4.85 – 4.75 (m, 1H RotA, 1H RotB), 4.24 – 4.01 (m, 4H RotA, 4H RotB), 2.32 (d, *J* = 15.4 Hz, 1H RotA, 1H RotB), 2.18 (d, *J* = 15.6 Hz, 1H RotA, 1H RotB), 1.32 (t, *J* = 7.2 Hz, 3H RotB), 1.22 (t, *J* = 7.3 Hz, 3H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 152.3, 151.8, 143.3, 142.7, 139.1, 134.7, 134.6, 125.3, 125.1, 125.0, 124.8, 123.5, 118.7, 118.6, 118.5, 118.2, 60.8, 57.5, 56.2, 48.4, 48.2, 42.2, 28.1, 14.3, 14.2. **ESI-HRMS** calcd for $C_{17}H_{18}NO_2$ $[M+H]^+$ 268.1332, found 268.1332.

Phenyl (5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindole-2(1H)-carboxylate



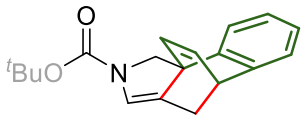
Product **2e** was prepared following general procedure **GP-2A** from the corresponding allene (63.6 mg, 0.2 mmol). White solid (56.1 mg, 88% yield). Two rotamers are observed due to the dynamic rotation of the amido group (56:44 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.46 – 7.12 (m, 9H RotA, 9H RotB), 6.64 – 6.53 (m, 2H RotA, 2H RotB), 6.44 (t, *J* = 2.0 Hz, 1H RotA), 6.30 (t, *J* = 2.0 Hz, 1H RotB), 5.10 (d, *J* = 12.1 Hz, 1H RotB), 4.90 (d, *J* = 12.4 Hz, 1H RotA), 4.37 (d, *J* = 12.1 Hz, 1H RotB), 4.28 – 4.22 (m, 1H RotA, 1H RotB), 4.19 (d, *J* = 12.4 Hz, 1H RotA), 2.42 (t, *J* = 2.4 Hz, 1H RotB), 2.38 (t, *J* = 2.4 Hz, 1H RotA), 2.27 (t, *J* = 2.3 Hz, 1H RotA), 2.23 (t, *J* = 2.4 Hz, 1H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 151.58, 151.56, 150.4, 149.7, 143.31, 143.29, 142.5, 142.4, 139.03, 138.98, 134.9, 134.8, 129.2, 126.6, 126.5, 125.4, 125.32, 125.28, 125.2, 125.1, 123.5, 121.9, 121.7, 118.8, 118.2, 118.1, 57.6, 56.3, 48.74, 48.67, 42.2, 28.31, 28.28. **ESI-HRMS** calcd for $C_{21}H_{18}NO_2$ $[M+H]^+$ 316.1332, found 316.1335.

Benzyl (5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindole-2(1H)-carboxylate



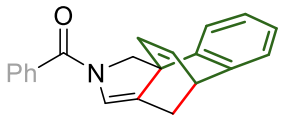
Product **2f** was prepared following general procedure **GP-2A** from the corresponding allene (66.8 mg, 0.2 mmol). White viscous oil (62.1 mg, 93% yield). Two rotamers are observed due to the dynamic rotation of the amido group (56:44 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.57 – 7.25 (m, 7H RotA, 7H RotB), 7.19 – 7.07 (m, 2H RotA, 2H RotB), 6.58 – 6.47 (m, 2H RotA, 2H RotB), 6.26 (s, 1H RotA, 1H RotB), 5.30 – 5.14 (m, 2H RotA, 2H RotB), 4.92 – 4.80 (m, 1H RotA, 1H RotB), 4.23 – 4.07 (m, 2H RotA, 2H RotB), 2.39 – 2.28 (m, 1H RotA, 1H RotB), 2.24 – 2.14 (m, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 152.1, 151.6, 143.29, 143.27, 142.61, 142.58, 139.1, 137.3, 137.2, 134.7, 134.6, 128.5, 128.4, 127.90, 127.87, 125.4, 125.3, 125.24, 125.16, 123.5, 118.72, 118.66, 118.5, 118.1, 66.5, 57.5, 56.3, 48.5, 48.3, 42.2, 28.2. **ESI-HRMS** calcd for $C_{22}H_{19}NNaO_2$ $[M+Na]^+$ 352.1308, found 352.1305.

Tert-butyl(5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindole-2(1H)-carboxylate



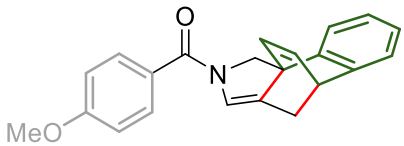
Product **2g** was prepared following general procedure **GP-2A** from the corresponding allene (59.2 mg, 0.2 mmol). White solid (54.7 mg, 92% yield). Two rotamers are observed due to the dynamic rotation of the amido group (61:39 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.29 (dd, *J* = 6.9, 1.8 Hz, 2H RotA, 2H RotB), 7.17 – 7.04 (m, 2H RotA, 2H RotB), 6.54 – 6.47 (m, 2H RotA, 2H RotB), 6.19 (s, 1H RotB), 6.14 (t, *J* = 2.0 Hz, 1H RotA), 4.69 (d, *J* = 12.2 Hz, 1H RotA, 1H RotB), 4.20 – 4.15 (m, 1H RotA, 1H RotB), 4.03 (dd, *J* = 12.3, 4.2 Hz, 1H RotA, 1H RotB), 2.25 (dd, *J* = 15.6, 2.6 Hz, 1H RotA, 1H RotB), 2.10 (dd, *J* = 15.3, 2.6 Hz, 1H RotA, 1H RotB), 1.51 (s, 9H RotB), 1.43 (s, 9H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 151.7, 151.2, 143.5, 142.9, 142.8, 139.5, 134.93, 134.89, 125.6, 125.5, 124.7, 124.6, 123.88, 123.85, 119.2, 119.1, 118.8, 79.9, 79.8, 57.5, 56.4, 48.5, 48.2, 42.0, 28.6, 28.5. **ESI-HRMS** calcd for $C_{19}H_{21}NNaO_2$ $[M+Na]^+$ 318.1465, found 318.1466.

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(phenyl)methanone



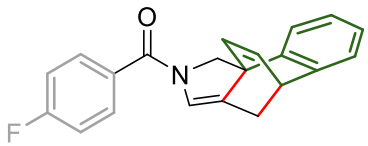
Product **2h** was prepared following general procedure **GP-2A** from the corresponding allene (29.9 mg, 0.1 mmol; 299.9 mg, 1 mmol). White solid (28.8 mg, 96% yield; 253.6 mg, 85% yield). Two rotamers are observed due to the dynamic rotation of the amido group (80:20 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.77 – 7.71 (m, 2H RotB), 7.59 – 7.37 (m, 6H RotA, 5H RotB), 7.34 – 7.29 (m, 1H RotA, 1H RotB), 7.22 – 7.07 (m, 2H RotA, 1H RotB), 6.68 (brs, 1H RotB), 6.62 – 6.51 (m, 2H RotA, 2H RotB), 6.18 – 6.15 (m, 1H RotA), 4.98 (d, J = 13.5 Hz, 1H RotA), 4.75 (d, J = 11.9 Hz, 1H RotB), 4.32 (d, J = 13.6 Hz, 1H RotA, 1H RotB), 4.24 – 4.19 (m, 1H RotA, 1H RotB), 2.39 – 2.05 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 166.0, 143.6, 143.3, 142.6, 142.4, 139.4, 138.9, 136.5, 136.2, 135.3, 135.2, 130.7, 130.6, 129.0, 128.8, 128.4, 127.9, 127.8, 125.74, 125.66, 123.9, 120.0, 119.5, 119.3, 119.2, 58.1, 55.9, 51.0, 48.8, 41.9, 28.84, 28.78. **ESI-HRMS** calcd for $C_{21}H_{18}NO$ $[M+H]^+$ 300.1383, found 300.1379.

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(4-methoxyphenyl)methanone



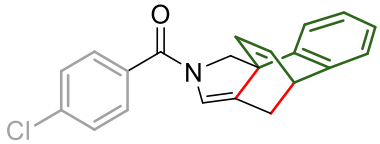
Product **2i** was prepared following general procedure **GP-2A** from the corresponding allene (65.0 mg, 0.2 mmol). White solid (58.6 mg, 90% yield). Two rotamers are observed due to the dynamic rotation of the amido group (82:18 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.80 – 7.72 (m, 2H RotB), 7.49 – 7.27 (m, 4H RotA, 2H RotB), 7.25 – 6.91 (m, 4H RotA, 4H RotB), 6.66 (brs, 1H RotB), 6.61 – 6.51 (m, 2H RotA, 2H RotB), 6.25 (s, 1H RotA), 5.01 – 4.78 (m, 1H RotA, 1H RotB), 4.42 – 4.25 (m, 1H RotA, 1H RotB), 4.23 – 4.18 (m, 1H RotA, 1H RotB), 3.89 – 3.74 (m, 3H RotA, 3H RotB), 2.38 – 2.06 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.8, 161.2, 161.1, 143.6, 143.4, 142.7, 142.6, 139.4, 139.0, 135.2, 130.0, 129.9, 128.3, 127.9, 125.7, 125.6, 123.9, 120.3, 119.5, 119.3, 114.2, 58.2, 55.82, 55.76, 51.3, 48.9, 41.9, 28.8. **ESI-HRMS** calcd for $C_{22}H_{20}NO_2$ $[M+H]^+$ 330.1489, found 330.1492.

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(4-fluorophenyl)methanone



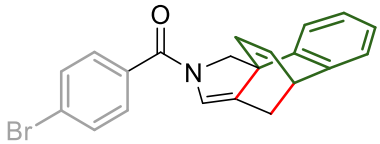
Product **2j** was prepared following general procedure **GP-2A** from the corresponding allene (63.3 mg, 0.2 mmol). White solid (56.3 mg, 89% yield). Two rotamers are observed due to the dynamic rotation of the amido group (78:22 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.88 – 7.80 (m, 2H RotB), 7.58 – 7.48 (m, 2H RotA), 7.42 – 7.06 (m, 6H RotA, 6H RotB), 6.67 (brs, 1H RotB), 6.62 – 6.50 (m, 2H RotA, 2H RotB), 6.19 (s, 1H RotA), 4.98 (d, J = 13.5 Hz, 1H RotA), 4.79 (d, J = 11.8 Hz, 1H RotB), 4.38 – 4.28 (m, 1H RotA, 1H RotB), 4.25 – 4.18 (m, 1H RotA, 1H RotB), 2.39 – 2.06 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.1, 163.5 (d, *J* = 246.8 Hz), 163.3 (d, *J* = 247.4 Hz), 143.5, 143.3, 142.6, 142.4, 139.4, 138.9, 135.3, 135.2, 132.9, 132.7 (d, *J* = 3.2 Hz), 130.5 (d, *J* = 8.7 Hz), 128.9, 128.6, 128.5, 125.73, 125.67, 125.6, 123.9, 120.0, 119.5, 119.4, 119.2, 115.9 (d, *J* = 21.8 Hz), 58.1, 55.9, 51.1, 48.9, 41.9, 28.8. **^{19}F NMR** (565 MHz, DMSO-*d*6) δ -110.01 – -110.15 (m). **ESI-HRMS** calcd for $C_{21}H_{17}FNO$ $[M+H]^+$ 318.1289, found 318.1283.

(4-chlorophenyl)((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)methanone



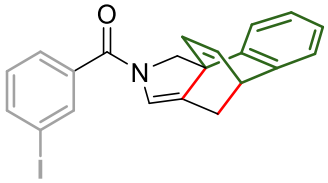
Product **2k** was prepared following general procedure **GP-2A** from the corresponding allene (66.0 mg, 0.2 mmol). White solid (56.6 mg, 86% yield). Two rotamers are observed due to the dynamic rotation of the amido group (81:19 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.83 – 7.76 (m, 2H RotB), 7.61 – 7.44 (m, 4H RotA, 2H RotB), 7.41 – 7.28 (m, 2H RotA, 2H RotB), 7.26 – 7.08 (m, 2H RotA, 2H RotB), 6.71 (brs, 1H RotB), 6.62 – 6.48 (m, 2H RotA, 2H RotB), 6.22 (t, J = 2.0 Hz, 1H RotA), 5.04 (d, J = 13.4 Hz, 1H RotA), 4.91 (d, J = 11.7 Hz, 1H RotB), 4.39 – 4.21 (m, 2H RotA, 2H RotB), 2.46 – 2.14 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 164.74, 164.70, 143.3, 143.2, 142.4, 142.3, 139.0, 138.6, 135.4, 135.1, 135.0, 129.5, 129.4, 128.5, 128.3, 125.4, 125.3, 123.5, 119.6, 118.9, 118.7, 58.0, 55.8, 51.1, 48.7, 42.2, 28.45, 28.42. **ESI-HRMS** calcd for $C_{21}H_{17}ClNO$ $[M+H]^+$ 334.0993, found 334.0998.

(4-bromophenyl)((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)methanone



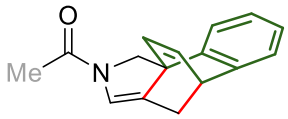
Product **2l** was prepared following general procedure **GP-2A** from the corresponding allene (75.1 mg, 0.2 mmol). White solid (64.4 mg, 86% yield). Two rotamers are observed due to the dynamic rotation of the amido group (78:22 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.78 – 7.60 (m, 2H RotA, 4H RotB), 7.45 – 7.36 (m, 3H RotA), 7.34 – 7.28 (m, 1H RotA, 1H RotB), 7.26 – 7.21 (m, 1H Rot B), 7.19 – 7.07 (m, 2H RotA, 2H RotB), 6.67 (s, 1H RotB), 6.62 – 6.49 (m, 2H RotA, 2H RotB), 6.19 (s, 1H RotA), 4.97 (d, J = 13.4 Hz, 1H RotA), 4.77 (d, J = 11.8 Hz, 1H RotB), 4.36 – 4.27 (m, 1H RotA, 1H RotB), 4.25 – 4.19 (m, 1H RotA, 1H RotB), 2.39 – 2.05 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.0, 143.5, 143.3, 142.5, 142.4, 139.3, 138.9, 135.6, 135.32, 135.26, 132.0, 130.15, 130.09, 129.2, 128.8, 125.74, 125.68, 125.6, 124.2, 124.1, 123.9, 119.9, 119.5, 119.4, 119.1, 58.1, 55.9, 51.0, 48.8, 41.9, 28.8. **ESI-HRMS** calcd for $C_{21}H_{17}{}^{79}BrNO$ $[M+H]^+$ 378.0488, found 378.0494.

((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(3-iodophenyl)methanone



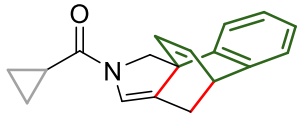
Product **2m** was prepared following general procedure **GP-2A** from the corresponding allene (64.5 mg, 0.15 mmol). White solid (54.6 mg, 85% yield). Two rotamers are observed due to the dynamic rotation of the amido group (79:21 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 8.03 (s, 1H RotB), 7.93 (d, J = 7.9 Hz, 1H RotB), 7.87 – 7.75 (m, 2H RotA, 1H RotB), 7.46 (d, J = 7.8 Hz, 1H RotA), 7.41 – 7.29 (m, 2H RotA, 2H RotB), 7.27 – 7.21 (m, 1H RotA, 1H RotB), 7.19 – 7.07 (m, 2H RotA, 2H RotB), 6.66 (s, 1H RotB), 6.61 – 6.53 (m, 2H RotA, 2H RotB), 6.15 (s, 1H RotA), 4.96 (d, J = 13.5 Hz, 1H RotA), 4.75 (d, J = 11.7 Hz, 1H RotB), 4.37 – 4.27 (m, 1H RotA, 1H RotB), 4.25 – 4.19 (m, 1H RotA, 1H RotB), 2.39 – 2.06 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 164.3, 143.6, 143.3, 142.5, 142.3, 139.3, 139.2, 138.9, 138.6, 138.4, 136.3, 136.1, 135.3, 135.2, 131.1, 129.4, 128.9, 127.1, 125.74, 125.69, 125.6, 123.9, 119.8, 119.6, 119.5, 119.0, 95.4, 95.3, 58.1, 55.9, 50.9, 48.8, 41.92, 41.86, 28.8. **ESI-HRMS** calcd for $C_{21}H_{17}INO$ $[M+H]^+$ 426.0349, found 426.0355.

1-((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)ethan-1-one



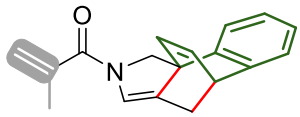
Product **2n** was prepared following general procedure **GP-2A** from the corresponding allene (48.0 mg, 0.2 mmol). Yellow solid (43.1 mg, 90% yield). Two rotamers are observed due to the dynamic rotation of the amido group (66:34 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.44 (d, *J* = 5.9 Hz, 1H RotB), 7.33 – 7.25 (m, 2H RotA, 1H RotB), 7.17 – 7.06 (m, 2H RotA, 2H RotB), 6.57 – 6.47 (m, 2H RotA, 3H RotB), 6.44 (t, *J* = 1.95 Hz, 1H RotA), 4.93 (d, *J* = 11.7 Hz, 1H RotB), 4.77 (d, *J* = 13.2 Hz, 1H RotA), 4.27 – 4.18 (m, 1H RotA, 2H RotB), 4.05 (d, *J* = 13.2 Hz, 1H RotA), 2.33 – 2.25 (m, 1H RotA, 1H RotB), 2.19 – 2.11 (m, 1H RotA, 4H RotB), 2.02 (s, 3H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.9, 165.7, 143.5, 143.4, 142.8, 142.7, 139.5, 139.3, 135.1, 127.1, 127.0, 125.64, 125.59, 125.5, 123.9, 120.1, 119.5, 119.3, 118.3, 58.0, 56.0, 49.2, 48.1, 42.0, 28.7, 28.6, 22.6, 22.1. **ESI-HRMS** calcd for $C_{16}H_{15}NNaO$ $[M+Na]^+$ 260.1046, found 260.1040.

Cyclopropyl((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)methanone



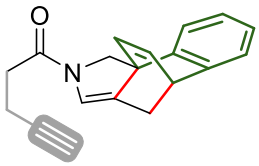
Product **2o** was prepared following general procedure **GP-2A** from the corresponding allene (52.3 mg, 0.2 mmol). Green viscous oil (52.2 mg, 99% yield). Two rotamers are observed due to the dynamic rotation of the amido group (63:37 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.43 – 7.24 (m, 2H RotA, 2H RotB), 7.21 – 7.08 (m, 2H RotA, 2H RotB), 6.70 (s, 1H RotA), 6.61 – 6.44 (m, 2H RotA, 3H RotB), 5.22 (d, J = 11.5 Hz, 1H RotB), 4.88 (d, J = 13.2 Hz, 1H RotA), 4.44 (d, J = 11.5 Hz, 1H RotB), 4.27 – 4.19 (m, 1H RotA, 1H RotB), 4.09 (d, J = 13.3 Hz, 1H RotA), 2.44 – 2.32 (m, 1H RotA, 1H RotB), 2.28 – 2.18 (m, 1H RotA, 1H RotB), 2.09 – 1.98 (m, 1H RotB), 1.93 – 1.84 (m, 1H RotA), 0.97 – 0.82 (m, 4H RotA), 0.80 – 0.68 (m, 4H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 168.5, 168.4, 143.4, 143.3, 142.71, 142.66, 139.2, 139.1, 134.8, 134.7, 127.0, 126.1, 125.3, 125.24, 125.20, 125.1, 123.50, 123.45, 118.8, 118.73, 118.70, 118.5, 57.7, 55.5, 48.7, 48.4, 42.2, 28.4, 28.2, 11.9, 11.5, 7.0, 6.9, 6.7, 6.5. **ESI-HRMS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$ 286.1202, found 286.1200.

1-((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)-2-methylprop-2-en-1-one



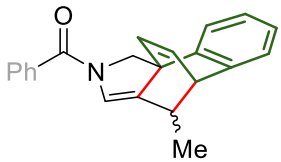
Product **2p** was prepared following general procedure **GP-2A** from the corresponding allene (53.4 mg, 0.2 mmol). White solid (50.8 mg, 95% yield). Two rotamers are observed due to the dynamic rotation of the amido group (84:16 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.33 – 7.27 (m, 2H RotA, 2H RotB), 7.19 – 7.08 (m, 2H RotA, 2H RotB), 6.59 – 6.49 (m, 2H RotA, 2H RotB), 6.38 (t, *J* = 2.0 Hz, 1H RotA, 1H RotB), 5.43 (s, 2H RotB), 5.29 (s, 1H RotA), 5.06 (s, 1H RotA), 4.97 (d, *J* = 11.6 Hz, 1H RotB), 4.88 (d, *J* = 13.4 Hz, 1H RotA), 4.33 (d, *J* = 12.3 Hz, 1H RotB), 4.24 – 4.19 (m, 1H RotA, 1H RotB), 4.13 (d, *J* = 13.5 Hz, 1H RotA), 2.34 (d, *J* = 15.4, 1H RotA, 1H RotB), 2.18 (d, *J* = 15.6, 1H RotA, 1H RotB), 2.02 (s, 3H RotB), 1.90 (s, 3H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 166.8, 143.4, 142.6, 141.4, 141.2, 139.1, 138.6, 134.8, 128.1, 127.1, 125.3, 125.2, 123.5, 119.9, 118.8, 118.4, 116.4, 116.0, 57.7, 55.7, 50.5, 48.0, 42.2, 28.4, 19.4, 19.3. **ESI-HRMS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$ 286.1202, found 286.1206.

1-((5R,9bR)-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)pent-4-yn-1-one



Product **2q** was prepared following general procedure **GP-2A** from the corresponding allene (55.9 mg, 0.2 mmol). Green viscous oil (47.5 mg, 85% yield). Two rotamers are observed due to the dynamic rotation of the amido group (61:39 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.44 (d, *J* = 7.3 Hz, 1H RotB), 7.33 – 7.25 (m, 2H RotA, 1H RotB), 7.17 – 7.06 (m, 2H RotA, 2H RotB), 6.59 – 6.48 (m, 3H RotA, 3H RotB), 4.96 (d, *J* = 11.7 Hz, 1H RotB), 4.78 (d, *J* = 13.2 Hz, 1H RotA), 4.29 – 4.17 (m, 1H RotA, 2H RotB), 4.08 (d, *J* = 13.2 Hz, 1H RotA), 2.90 – 2.77 (m, 2H RotB), 2.75 (t, *J* = 2.6 Hz, 1H RotA), 2.72 – 2.36 (m, 4H RotA, 3H RotB), 2.29 (dq, *J* = 15.8, 2.7 Hz, 1H RotA, 1H RotB), 2.14 (dt, *J* = 15.5, 2.3 Hz, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 166.7, 166.5, 143.5, 143.4, 142.8, 142.7, 139.4, 139.3, 135.2, 135.1, 127.5, 127.4, 125.7, 125.61, 125.58, 125.55, 123.89, 123.87, 119.6, 119.3, 119.2, 118.2, 84.6, 84.4, 71.8, 71.7, 58.0, 55.7, 48.5, 48.3, 42.0, 33.0, 32.6, 28.8, 28.7, 14.03, 13.96. **ESI-HRMS** calcd for $C_{19}H_{17}NNaO$ $[M+Na]^+$ 298.1202, found 298.1205.

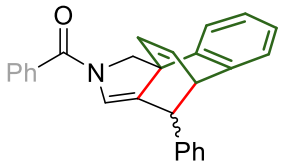
((5S,9bS)-4-methyl-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(phenyl)methanone



Product **2r** was obtained as a mixture of two diasteroisomers (dr 64:36) following general procedure **GP-2A** from the corresponding allene (31.4 mg, 0.1 mmol). Pale yellow solid (27.5 mg, 88% yield). Two rotamers are observed due to the dynamic rotation of the amido group (Dia1, 72:28 mixture of rotamers; Dia2, 76:24 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.82 – 7.04 (m, Dia1, 9H RotA, 9H RotB; Dia2, 9H RotA, 9H RotB), 6.78 – 6.37 (m, Dia1, 2H RotA, 3H RotB; Dia2, 2H RotA, 3H RotB), 6.23 – 6.14 (m, Dia1, 1H RotA; Dia2, 1H RotA), 5.05 – 4.88 (m, Dia1, 1H RotA; Dia2, 1H RotA), 4.79 – 4.65 (m, Dia1 1H RotB, Dia2 1H RotB), 4.39 – 4.23 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 4.02 – 3.81 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 2.64 – 2.29 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 1.17 – 0.98 (m, Dia2, 3H RotA, 3H RotB), 0.83 – 0.63 (m, Dia1, 3H RotA, 3H RotB). 13C NMR (101 MHz, DMSO-*d*6) δ 166.11, 166.08, 144.4, 144.3, 142.5, 142.2, 142.1, 141.9, 141.0, 140.7, 139.6, 139.4, 138.6, 137.9, 136.6, 136.4,

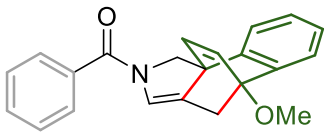
136.2, 134.6, 134.41, 134.35, 133.3, 133.0, 130.6, 129.0, 127.90, 127.86, 127.8, 126.2, 126.1, 126.0, 125.9, 125.8, 125.70, 125.67, 125.6, 125.4, 123.9, 120.4, 119.8, 119.7, 119.1, 118.8, 58.5, 58.0, 56.3, 55.9, 51.2, 51.0, 49.0, 48.93, 48.86, 48.7, 35.8, 34.5, 34.3, 21.6, 20.21, 20.18. **ESI-HRMS** calcd for $C_{22}H_{19}NNaO$ $[M+Na]^+$ 336.1359, found 336.1355.

Phenyl((5S,9bS)-4-phenyl-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)methanone



Product **2s** was obtained as a mixture of two diasteroisomers (dr 62:38) following general procedure **GP-2A** from the corresponding allene (75.1 mg, 0.2 mmol). Pale yellow solid (51.2 mg, 68% yield). Two rotamers are observed due to the dynamic rotation of the amido group (Dia major, 76:24 mixture of rotamers; Dia minor, 78:22 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 8.00 – 6.46 (m, Dia1, 16H RotA, 17H RotB; Dia2, 15H RotA, 16H RotB), 6.29 – 6.21 (m, Dia2, 1H RotA, 1H RotB), 6.09 – 6.04 (m, Dia2, 1H RotA), 5.99 – 5.93 (m, Dia1, 1H RotA), 5.16 – 5.00 (m, Dia1, 1H RotA; Dia2, 1H RotA), 4.91 – 4.80 (m, Dia1 1H RotB, Dia2 1H RotB), 4.51 – 4.36 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 4.30 – 4.19 (m, Dia2, 1H RotA, 1H RotB), 4.05 – 3.99 (m, Dia1, 1H RotA, 1H RotB), 3.95 – 3.84 (m, Dia1, 1H RotA, 1H RotB), 3.77 – 3.64 (m, Dia2, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 166.25, 166.23, 144.0, 143.8, 143.3, 143.2, 142.7, 142.5, 142.4, 142.3, 140.2, 140.0, 139.8, 139.7, 139.5, 139.1, 136.4, 136.03, 135.98, 135.95, 133.1, 133.0, 132.4, 132.0, 131.6, 130.8, 130.73, 130.70, 129.0, 128.6, 128.54, 128.50, 128.2, 128.1, 127.92, 127.89, 127.8, 127.5, 127.1, 126.9, 126.8, 126.2, 126.1, 126.0, 125.8, 125.4, 124.1, 122.4, 122.0, 121.5, 121.2, 119.9, 119.3, 119.0, 58.7, 58.5, 56.6, 56.3, 51.3, 51.1, 50.9, 50.6, 49.1, 48.8, 46.2, 46.1, 46.0. **ESI-HRMS** calcd for $C_{27}H_{22}NO$ $[M+H]^+$ 376.1696, found 376.1693.

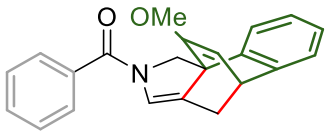
((5S,9bR)-5-methoxy-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(phenyl)methanone



Product **2t** was prepared following general procedure **GP-2A** from the corresponding allene (65.9 mg, 0.2 mmol). Pale yellow viscous oil (58.7 mg, 89% yield). Two rotamers are observed due to the dynamic rotation of the amido group

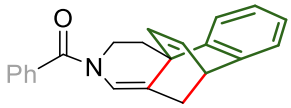
(80:20 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.78 – 7.71 (m, 2H RotB), 7.58 – 7.53 (m, 3H RotB), 7.50 – 7.36 (m, 7H RotA, 2H RotB), 7.24 – 7.12 (m, 2H RotA, 2H RotB), 6.75 – 6.67 (m, 1H RotA, 2H RotB), 6.62 (d, J = 8.2 Hz, 1H RotA), 6.55 (d, J = 8.2 Hz, 1H RotB), 6.16 (s, 1H RotA), 4.97 (d, J = 13.5 Hz, 1H RotA), 4.74 (d, J = 11.9 Hz, 1H RotB), 4.34 (d, J = 13.5 Hz, 1H RotA, 1H RotB), 3.68 – 3.61 (m, 3H RotA, 3H RotB), 2.79 – 2.57 (m, 1H RotA, 1H RotB), 2.20 – 2.00 (m, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 166.2, 143.5, 143.3, 140.2, 140.0, 137.8, 137.4, 136.4, 136.1, 134.9, 130.8, 130.7, 129.0, 127.9, 127.4, 127.0, 126.1, 126.0, 125.6, 120.7, 120.6, 120.1, 119.4, 119.2, 119.1, 83.4, 83.3, 57.2, 55.1, 53.3, 50.8, 48.6, 32.65, 32.59. **ESI-HRMS** calcd for $C_{22}H_{20}NO_2$ $[M+H]^+$ 330.1489, found 330.1485.

((5R,9bS)-10-methoxy-4,5-dihydro-5,9b-ethenobenzo[e]isoindol-2(1H)-yl)(phenyl)methanone



Product **2u** was prepared following general procedure **GP-2A** from the corresponding allene (65.6 mg, 0.2 mmol). *Note: it was necessary add 1% TEA to the eluent to prevent the degradation of product during the separation.* White viscous oil (57.3 mg, 87% yield). Two rotamers are observed due to the dynamic rotation of the amido group (83:17 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.95 – 7.88 (m, 1H RotB), 7.79 – 7.71 (m, 2H RotB), 7.59 – 7.34 (m, 6H RotA, 3H RotB), 7.31 – 7.26 (m, 1H RotA, 1H RotB), 7.22 – 7.08 (m, 2H RotA, 2H RotB), 6.74 (brs, 1H RotB), 6.22 – 6.18 (m, 1H RotA), 5.32 – 5.24 (m, 1H RotA, 1H RotB), 4.76 – 4.57 (m, 2H RotA, 2H RotB), 4.14 – 4.08 (m, 1H RotA, 1H RotB), 3.58 – 3.47 (m, 3H RotA, 3H RotB), 2.56 – 2.17 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.9, 163.3, 163.2, 145.7, 145.5, 141.7, 141.4, 136.8, 136.4, 130.0, 128.5, 128.4, 127.8, 127.6, 127.5, 127.4, 125.8, 125.6, 125.2, 125.1, 122.8, 120.2, 119.5, 119.1, 118.9, 97.3, 97.2, 59.2, 57.1, 55.4, 44.8, 42.2, 40.0, 29.63, 29.58. **ESI-HRMS** calcd for $C_{22}H_{20}NO_2$ $[M+H]^+$ 330.1489, found 330.1492.

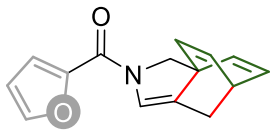
Phenyl((6R,10bS)-1,2,5,6-tetrahydro-3H-6,10b-ethenobenzo[f]isoquinolin-3-yl)methanone



Product **2v** was prepared following general procedure **GP-2A** from the corresponding allene (60.2 mg, 0.19 mmol). The reaction required 24 h of

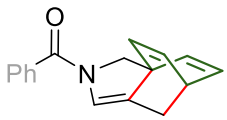
irradiation to fully consume the starting material. White solid (38.9 mg, 65% yield). Two rotamers are observed due to the dynamic rotation of the amido group (63:37 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.62 – 6.95 (m, 9H RotA, 10H RotB), 6.70 – 6.57 (m, 1H RotA, 1H RotB), 6.41 – 6.17 (m, 2H RotA, 1H RotB), 4.18 – 3.67 (m, 3H RotA, 3H RotB), 3.13 – 2.89 (m, 1H RotA, 1H RotB), 2.57 – 2.19 (m, 3H RotA, 2H RotB), 2.16 – 2.10 (m, 1H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 167.6, 167.0, 145.0, 143.5, 138.6, 138.4, 136.2, 136.0, 135.6, 130.1, 129.7, 128.3, 128.2, 127.4, 125.3, 125.0, 123.1, 121.0, 120.8, 119.8, 118.5, 50.1, 44.5, 43.9, 40.9, 38.5, 32.9, 27.7. **ESI-HRMS** calcd for $C_{22}H_{20}NO$ $[M+H]^+$ 314.1539, found 314.1543.

((3ar,6r)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(furan-2-yl)methanone



Product **2aa** was prepared following general procedure **GP-2B** from the corresponding allene (23.9 mg, 0.1 mmol). Pale yellow solid (15.5 mg, 65% yield). The reaction required 38 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (59:41 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.80 (s, 1H RotB), 7.73 (s, 1H RotA), 7.23 – 7.16 (m, 1H RotB), 7.09 (d, *J* = 3.2 Hz, 1H RotA, 1H RotB), 6.77 – 6.55 (m, 1H RotA, 2H RotB), 6.54 – 6.26 (m, 4H RotA, 4H RotB), 4.74 (s, 1H RotB), 4.38 (s, 1H RotA), 4.01 – 3.89 (m, 1H RotA, 1H RotB), 2.15 – 2.09 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 154.0, 148.7, 144.8, 144.4, 138.3, 133.8, 133.6, 129.9, 128.7, 117.2, 117.1, 116.0, 115.7, 111.5, 111.4, 58.6, 55.0, 54.7, 54.1, 40.0, 27.8, 27.7. **ESI-HRMS** calcd for $C_{15}H_{14}NO_2$ $[M+H]^+$ 240.1019, found 240.1015.

((3ar,6r)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone

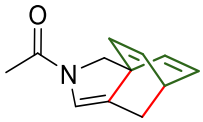


Product **2ab** was prepared following general procedure **GP-2B** from the corresponding allene (24.9 mg, 0.1 mmol; 498 mg, 2 mmol). White solid (18.7 mg, 75% yield; 309 mg, 62%). The reaction required 28 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (79:21 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.71 – 7.61 (m, 2H RotB), 7.55 – 7.39 (m, 5H RotA, 3H RotB), 6.69 (s, 1H RotB), 6.45 – 6.26 (m, 4H RotA, 4H RotB), 6.16 (s, 1H RotA), 4.38 (s, 2H RotA), 4.33 (s, 2H RotB), 3.96 – 3.87 (m, 1H RotA, 1H RotB), 2.12 (brs, 2H RotB), 2.03 – 2.00 (m, 2H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.7, 165.5, 138.4, 138.2, 136.8, 133.7, 133.5,

129.9, 128.5, 128.3, 127.5, 127.3, 118.1, 117,3, 55.9, 53.5, 39.9, 27.6. **ESI-HRMS** calcd for $C_{17}H_{15}NNaO$ $[M+Na]^+$, 272.1046 found 272.1040.

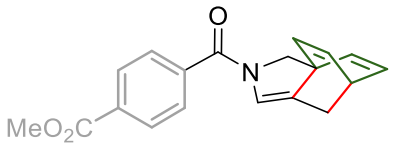
Coalescence of the two rotamers is observed warming a DMSO solution up to at least 80 °C. **^{1}H NMR** (400 MHz, DMSO, 353 K) δ 7.69 – 7.29 (m, 5H), 6.42 (d, *J* = 7.2 Hz, 2H), 6.32 (t, *J* = 6.6 Hz, 2H), 6.11 (bs, 1H), 4.36 (bs, 2H), 3.94 – 3.85 (m, 1H), 1.99 (bs, 2H).

1-((3as,6s)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)ethan-1-one



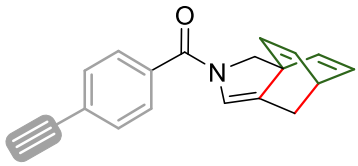
Product **2ac** was prepared following general procedure **GP-2B** from the corresponding allene (28.5 mg, 0.15 mmol). White solid (16.1 mg, 56% yield). The reaction required 40 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (66:34 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 6.51 (t, *J* = 1.9 Hz, 1H RotB), 6.40 – 6.27 (m, 5H RotA, 4H RotB), 4.34 (s, 2H RotB), 4.16 (s, 2H RotA), 3.95 – 3.88 (m, 1H RotA, 1H RotB), 2.09 – 2.01 (m, 5H RotA, 5H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 164.8, 164.7, 138.6, 138.4, 133.5, 133.4, 127.7, 127.0, 117.7, 116.5, 58.1, 56.0, 54.2, 52.9, 39.9, 27.6, 27.4, 21.2, 20.9. **ESI-HRMS** calcd for $C_{12}H_{14}NO$ $[M+H]^+$ 188.1070, found 188.1068.

Methyl 4-((3ar,6r)-2,3,6,7-tetrahydro-3a,6-ethenoisoindole-2-carbonyl)benzoate



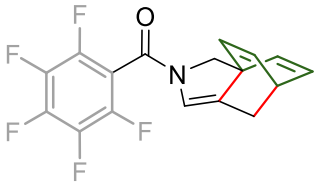
Product **2ad** was prepared following general procedure **GP-2B** from the corresponding allene (45.8 mg, 0.15 mmol). Pale yellow oil (23.5 mg, 51% yield). The reaction required 96 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 8.21 – 7.97 (m, 2H RotA, 2H RotB), 7.80 (d, *J* = 8.3 Hz, 2H RotB), 7.59 (d, *J* = 8.3 Hz, 2H RotA), 6.65 (s, 1H RotB), 6.50 – 6.25 (m, 4H RotA, 4H RotB), 6.09 (s, 1H RotA), 4.39 (s, 2H RotA), 4.29 (s, 2H RotB), 3.92 – 3.84 (m, 4H RotA, 4H RotB), 2.05 (s, 2H RoB), 1.94 (s, 2H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 166.2, 166.1, 164.70, 164.66, 141.0, 140.7, 138.6, 138.5, 134.1, 134.0, 131.22, 131.19, 130.0, 129.8, 129.7, 128.2, 118.0, 117.2, 58.3, 56.1, 55.5, 53.6, 52.9, 52.8, 39.9, 28.22, 28.17. **ESI-HRMS** calcd for $C_{19}H_{18}NO_3$ $[M+H]^+$, 308.1281 found 308.1277.

((3ar,6r)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(4-ethynylphenyl)methanone



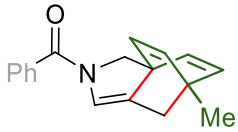
Product **2ae** was prepared following general procedure **GP-2B** from the corresponding allene (41.3 mg, 0.15 mmol). White solid (20.2 mg, 49% yield, 75% conversion). The reaction was irradiated for 60 h. Two rotamers are observed due to the dynamic rotation of the amido group (74:26 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.68 (d, *J* = 8.1 Hz, 2H RotB), 7.62 – 7.52 (m, 2H RotA, 2H RotB), 7.46 (d, *J* = 8.2 Hz, 2H RotA), 6.63 (s, 1H RotB), 6.48 – 6.25 (m, 4H RotA, 4H RotB), 6.13 (s, 1H RotA), 4.39 – 4.28 (m, 3H RotA, 3H RotB), 3.93 – 3.84 (m, 1H RotA, 1H RotB), 2.05 (s, 2H RotB), 1.94 (s, 2H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 164.9, 164.8, 138.7, 138.5, 136.9, 136.6, 134.1, 133.9, 132.3, 132.1, 130.0, 129.8, 128.2, 128.2, 123.8, 123.8, 118.2, 117.4, 83.4, 83.3, 82.8, 58.4, 56.1, 55.5, 53.6, 39.9, 28.2. **ESI-HRMS** calcd for $C_{19}H_{16}NO$ $[M+H]^+$, 274.1226 found 274.1225.

((3ar,6r)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(perfluorophenyl)methanone



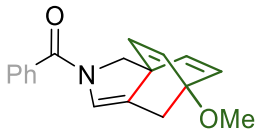
Product **2af** was prepared following general procedure **GP-2B** from the corresponding allene (51.6 mg, 0.15 mmol). White solid (40.4 mg, 78% yield). The reaction required 48 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (79:21 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 6.67 (t, *J* = 1.9 Hz, 1H RotB), 6.45 (dd, *J* = 7.1, 1.5 Hz, 2H RotA), 6.41 – 6.32 (m, 2H RotA, 4H RotB), 6.14 (p, *J* = 1.7 Hz, 1H RotA), 4.46 (s, 2H RotA), 4.28 (s, 2H RotB), 4.03 – 3.90 (m, 1H RotA, 1H RotB), 2.18 – 2.13 (m, 2H RotB), 2.05 – 1.99 (m, 2H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 152.4, 144.76 – 144.20 (m), 143.44 – 143.12 (m), 142.61 – 141.55 (m), 141.23 – 140.48 (m), 139.40 – 138.90 (m), 137.8, 137.5, 137.0 – 136.38 (m), 134.2, 134.0, 132.2, 131.6, 116.5, 115.7, 57.3, 56.3, 54.0, 53.4, 39.8, 27.8, 27.7. **^{19}F NMR** (565 MHz, Acetone-*d*6) δ -143.21 – -143.31 (m, 2F RotB), -143.37 – -143.48 (m, 2F RotA), -155.27 (t, *J* = 20.2 Hz, 1F RotB), -155.37 (t, *J* = 20.2 Hz, 1F RotA), -162.31 (dd, *J* = 20.4, 14.3 Hz, 2F RotB), -162.60 – -162.72 (m, 2F RotA). **ESI-HRMS** calcd for $C_{17}H_{11}F_5NO$ $[M+H]^+$, 340.0755 found 340.0759.

((3ar,6r)-6-methyl-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



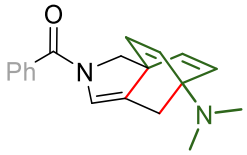
Product **2ag** was prepared following general procedure **GP-2B** from the corresponding allene (41 mg, 0.16 mmol). White solid (31.7 mg, 77% yield). The reaction required 55 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.69 – 7.61 (m, 2H RotB), 7.54 – 7.41 (m, 5H RotA, 3H RotB), 6.61 (s, 1H RotB), 6.42 (d, *J* = 7.1 Hz, 2H RotA), 6.37 (d, *J* = 7.1 Hz, 2H RotB), 6.10 – 5.99 (m, 3H RotA, 2H RotB), 4.36 (s, 2H RotA), 4.29 (s, 2H RotB), 1.95 (s, 2H RotB), 1.84 (d, *J* = 1.3 Hz, 2H RotA), 1.58 – 1.52 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.8, 165.7, 139.3, 139.1, 138.5, 138.4, 136.7, 136.5, 131.3, 131.1, 130.5, 130.5, 129.0, 128.8, 127.8, 127.8, 117.8, 116.9, 58.9, 56.7, 55.5, 53.3, 45.6, 35.8, 35.8, 22.0. **ESI-HRMS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$, 286.1202 found 286.1202.

((3as,6s)-6-methoxy-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



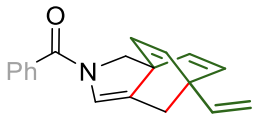
Product **2ah** was prepared following general procedure **GP-2B** from the corresponding allene (56.9 mg, 0.2 mmol). White solid (35.5 mg, 62% yield). The reaction required 44 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (79:21 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.66 (s, 2H RotB), 7.54 – 7.41 (m, 5H RotA, 3H RotB), 6.70 (s, 1H RotB), 6.50 – 6.29 (m, 4H RotA, 4H RotB), 6.18 (s, 1H RotA), 4.39 (s, 2H RotA), 4.33 (s, 2H RotB), 3.57 (s, 3H RotA, 3H RotB), 2.30 (s, 2H RotB), 2.20 (d, *J* = 1.5 Hz, 2H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.8, 165.6, 136.6, 136.2, 136.0, 134.9, 134.8, 130.0, 128.3, 127.5, 127.4, 126.9, 118.4, 117.5, 86.3, 55.5, 55.4, 53.1, 52.7, 32.5. **ESI-HRMS** calcd for $C_{18}H_{17}NNaO_2$ $[M+Na]^+$, 302.1151 found 302.1152.

((3as,6s)-6-(dimethylamino)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



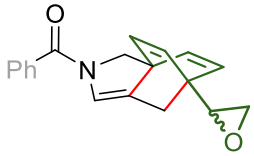
Product **2ai** was prepared following general procedure **GP-2B** from the corresponding allene (59.2 mg, 0.2 mmol). The crude was purified by chromatography on silica gel (EtOAc/MeOH gradient) to afford the corresponding product. Pale yellow solid (32.2 mg, 54% yield). The reaction required 96 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.70 – 7.62 (m, 2H RotB), 7.56 – 7.39 (m, 5H RotA, 3H RotB), 6.62 (s, 1H RotB), 6.48 – 6.35 (m, 4H RotA, 4H RotB), 6.09 (s, 1H RotA), 4.35 (s, 2H RotA), 4.29 (s, 2H RotB), 2.46 – 2.39 (m, 6H RotA, 6H RotB), 2.17 (s, 2H RotB), 2.07 (s, 2H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.7, 137.5, 137.4, 136.7, 136.4, 134.5, 134.3, 130.5, 130.1, 129.9, 129.0, 128.8, 127.8, 117.9, 117.1, 112.7, 72.0, 57.5, 55.3, 53.3, 41.0, 31.4, 31.3. **ESI-HRMS** calcd for $C_{19}H_{21}N_2O$ $[M+H]^+$, 293.1648 found 293.1652.

Phenyl((3as,6s)-6-vinyl-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)methanone



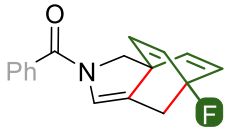
Product **2aj** was prepared following general procedure **GP-2B** from the corresponding allene (40.5 mg, 0.15 mmol). Pale yellow oil (16.7 mg, 41% yield). The reaction required 120 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.69 – 7.64 (m, 2H RotB), 7.53 – 7.43 (m, 5H RotA, 3H RotB), 6.66 (brs, 1H RotB), 6.52 – 6.38 (m, 3H RotA, 3H RotB), 6.26 – 6.19 (m, 2H RotA, 2H RotB), 6.13 (t, J = 1.8 Hz, 1H RotA), 5.49 – 5.40 (m, 1H RotA, 1H RotB), 5.33 – 5.27 (m, 1H RotA, 1H RotB), 4.39 (s, 2H RotA), 4.33 (s, 2H RotB), 2.09 (s, 2H RotB), 1.98 (s, 2H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.9, 165.8, 141.4, 138.6, 138.5, 136.6, 136.42, 136.41, 136.2, 130.6, 130.5, 130.0, 129.7, 129.0, 128.8, 127.82, 127.79, 118.3, 117.5, 115.2, 59.3, 57.1, 55.4, 53.3, 51.55, 51.52, 34.84, 34.78. **ESI-HRMS** calcd for $C_{19}H_{17}NNaO$ $[M+Na]^+$ 298.1202, found 298.1197.

((3as,6s)-6-(oxiran-2-yl)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



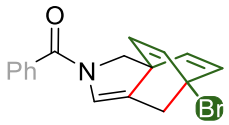
Product **2ak** was prepared following general procedure **GP-2B** from the corresponding allene (43.7 mg, 0.15 mmol). White solid (33.3 mg, 76% yield, dr 1:1). The reaction required 48 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.70 – 7.63 (m, 2H RotB), 7.56 – 7.41 (m, 5H RotA, 3H RotB), 6.67 (s, 1H RotB), 6.50 (dd, *J* = 7.4, 3.6 Hz, 2H RotA), 6.45 (dd, *J* = 7.3, 2.6 Hz, 2H RotB), 6.18 – 6.06 (m, 3H RotA, 2H RotB), 4.38 (s, 2H RotA), 4.32 (s, 2H RotB), 3.55 – 3.47 (m, 1H RotA, 1H RotB), 2.93 – 2.81 (m, 2H RotA, 2H RotB), 2.16 – 1.88 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.8, 139.1, 139.1, 139.0, 138.9, 136.6, 136.4, 133.4, 133.3, 133.2, 133.2, 130.6, 129.4, 129.1, 129.0, 128.8, 127.8, 118.6, 117.7, 59.4, 57.2, 55.3, 53.9, 53.2, 50.1, 50.0, 44.4, 31.5. **ESI-HRMS** calcd for $C_{19}H_{17}NNaO_2$ $[M+Na]^+$, 314.1151 found 314.1148.

((3as,6s)-6-fluoro-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



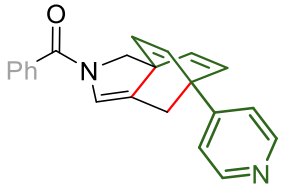
Product **2al** was prepared following general procedure **GP-2B** from the corresponding allene (40.9 mg, 0.15 mmol). White solid (26.6 mg, 65% yield). The reaction required 48 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (78:22 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.70 – 7.64 (m, 2H RotB), 7.57 – 7.42 (m, 5H RotA, 3H RotB), 6.76 (s, 1H RotB), 6.51 – 6.35 (m, 4H RotA, 4H RotB), 6.26 (s, 1H RotA), 4.52 – 4.35 (m, 2H RotA, 2H RotB), 2.50 (brs, 2H RotB), 2.40 (dd, *J* = 3.6, 1.7 Hz, 2H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.9, 165.7, 136.7, 136.4, 135.67 (d, *J* = 10.5 Hz), 135.48 (d, *J* = 10.8 Hz), 134.04 (d, *J* = 26.3 Hz), 133.87 (d, *J* = 26.2 Hz), 130.1, 128.4, 128.3, 127.5, 127.4, 124.08 (d, *J* = 11.8 Hz), 119.23 (d, *J* = 3.8 Hz), 118.3, 99.57 (d, *J* = 191.6 Hz), 58.1, 55.87 (d, *J* = 2.4 Hz), 55.1, 52.8, 33.19 (d, *J* = 24.7 Hz). **^{19}F NMR** (565 MHz, Acetone-*d*6) δ -172.81 – -175.77 (m). **ESI-HRMS** calcd for $C_{17}H_{14}FNNaO$ $[M+Na]^+$, 290.0952 found 290.0946.

((3as,6s)-6-bromo-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



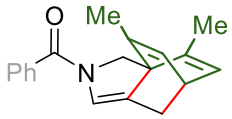
Product **2am** was prepared following general procedure **GP-2B** from the corresponding allene (49.7 mg, 0.15 mmol). White viscous oil (37.7 mg, 76% yield). The reaction required 46 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (78:22 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.67 (s, 2H RotB), 7.56 – 7.40 (m, 5H RotA, 3H RotB), 6.74 (s, 1H RotB), 6.55 – 6.38 (m, 4H RotA, 4H RotB), 6.25 (s, 1H RotA), 4.43 (s, 2H RotA), 4.39 (s, 2H RotB), 2.68 (s, 1H RotB), 2.58 (d, *J* = 1.4 Hz, 1H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.8, 138.3, 138.1, 137.9, 136.3, 130.1, 128.4, 128.3, 127.6, 126.7, 118.5, 117.6, 57.7, 55.2, 52.8, 40.1. **ESI-HRMS** calcd for $C_{17}H_{15}{}^{79}BrNO$ $[M+H]^+$, 328.0332 found 328.0330.

Phenyl((3as,6s)-6-(pyridin-4-yl)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)methanone



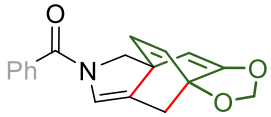
Product **2an** was prepared following general procedure **GP-2B** from the corresponding allene (49.1 mg, 0.15 mmol). Pale yellow solid (31.3 mg, 73% yield). The crude was purified by chromatography on silica gel (EtOAc) to afford the corresponding product. The reaction required 72 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (74:26 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 8.67 – 8.57 (m, 2H RotA, 2H RotB), 7.74 – 7.64 (m, 2H RotB), 7.62 – 7.44 (m, 5H RotA, 3H RotB), 6.73 (s, 1H RotB), 6.65 (d, *J* = 7.2 Hz, 2H RotA), 6.60 (d, *J* = 7.2 Hz, 2H RotB), 6.41 (d, *J* = 7.1 Hz, 2H RotA), 6.37 (d, *J* = 7.2 Hz, 2H RotB), 6.20 (s, 1H RotA), 4.47 (s, 2H RotA), 4.40 (s, 2H RotB), 2.41 (s, 2H RotB), 2.29 (d, *J* = 1.4 Hz, 2H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 166.0, 165.9, 153.22, 153.15, 150.5, 139.3, 139.1, 136.6, 136.4, 136.3, 130.6, 129.3, 129.04, 129.0, 128.9, 127.9, 127.8, 122.8, 118.7, 117.9, 59.5, 57.2, 55.3, 53.24, 53.21, 34.8, 34.5. **ESI-HRMS** calcd for $C_{22}H_{19}N_2O$ $[M+H]^+$ 327.1492, found 327.1488.

((3ar,6r)-4,9-dimethyl-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



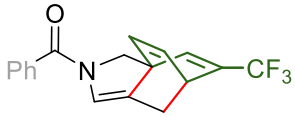
Product **2ao** was prepared following general procedure **GP-2B** from the corresponding allene (41.8 mg, 0.15 mmol). White solid (7.7 mg, 18% yield). The reaction required 120 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (81:19 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.69 – 7.62 (m, 2H RotB), 7.56 – 7.40 (m, 5H RotA, 3H RotB), 6.66 (s, 1H RotB), 6.13 (s, 1H RotA), 6.03 – 5.92 (m, 2H RotA, 2H RotB), 4.42 (s, 2H RotA), 4.31 (s, 2H RotB), 3.57 (tt, *J* = 6.0, 2.7 Hz, 1H RotA, 1H RotB), 2.17 – 2.12 (m, 2H RotB), 2.06 – 2.03 (m, 2H RotA), 1.89 (d, *J* = 1.3 Hz, 6H RotA), 1.80 (s, 6H RotB). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.5, 143.6, 136.7, 129.9, 129.2, 128.8, 128.7, 128.4, 128.3, 127.6, 127.1, 118.1, 117.3, 60.4, 46.0, 37.9, 28.6, 16.3. **ESI-HRMS** calcd for $C_{19}H_{20}NO$ $[M+H]^+$, 278.1539 found 278.1545.

((3aS,7aR)-4H-3a,7a-etheno[1,3]dioxolo[4,5-f]isoindol-6(7H)-yl)(phenyl)methanone



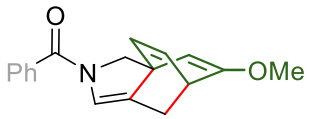
Product **2ap** was prepared following general procedure **GP-2B** from the corresponding allene (44 mg, 0.15 mmol). White solid (19.4 mg, 44% yield). The reaction required 48 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (76:24 mixture of rotamers). Note: slow decomposition occurred during the acquisition of NMR spectrum. **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.67 – 7.63 (m, 2H RotB), 7.53 – 7.43 (m, 5H RotA, 3H RotB), 6.67 (s, 1H RotB), 6.55 (d, *J* = 7.6 Hz, 1H RotA), 6.51 (d, *J* = 7.7 Hz, 1H RotB), 6.39 (d, *J* = 7.6 Hz, 1H RotA, 1H RotB), 6.15 (t, *J* = 1.7 Hz, 1H RotA), 5.67 – 5.64 (m, 1H RotA, 1H RotB), 5.55 (s, 1H RotB), 5.53 (s, 1H RotA), 5.27 (s, 1H RotA), 5.22 (s, 1H RotB), 4.37 (d, *J* = 13.2 Hz, 1H RotA), 4.34 – 4.25 (m, 1H RotA,1H RotB), 4.20 (d, *J* = 11.4 Hz, 1H RotB), 2.57 – 2.51 (m, 1H RotB), 2.43 (dd, *J* = 14.2, 1.5 Hz, 1H RotA), 2.35 (d, *J* = 15.4 Hz, 1H RotB), 2.25 (dd, *J* = 14.3, 1.6 Hz, 1H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.8, 165.7, 160.4, 160.3, 139.9, 136.5, 136.3, 132.5, 132.3, 130.6, 129.0, 128.8, 127.84, 127.80, 118.5, 117.6, 100.5, 97.2, 97.1, 86.82, 86.75, 57.3, 55.4, 55.1, 53.2, 30.9. **ESI-HRMS** calcd for $C_{18}H_{16}NO_3$ $[M+H]^+$ 294.1125, found 294.1129.

Phenyl((3aR,6R)-5-(trifluoromethyl)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)methanone



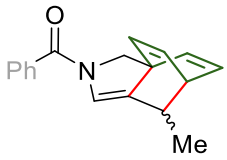
Product **2aq** was prepared following general procedure **GP-2B** from the corresponding allene (47.3 mg, 0.15 mmol). Pale yellow oil (36 mg, 76% yield). The reaction required 72 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (78:22 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.69 (d, *J* = 6.1 Hz, 2H RotB), 7.57 – 7.41 (m, 5H RotA, 3H RotB), 7.18 – 6.99 (m, 1H RotA, 1H RotB), 6.83 (s, 1H RotB), 6.64 – 6.42 (m, 2H RotA, 2H RotB), 6.33 (s, 1H RotA), 4.60 – 4.38 (m, 2H RotA, 2H RotB), 4.13 (ddt, *J* = 6.1, 4.4, 2.4 Hz, 1H RotA, 1H RotB), 2.26 (s, 2H RotB), 2.16 (s, 2H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.9, 165.7, 141.89 (q, *J* = 5.6 Hz), 138.7, 138.5, 136.7, 136.4, 135.02 (q, *J* = 32.7 Hz)., 132.8, 132.7, 130.1, 128.4, 128.3, 127.6, 127.4, 125.6, 125.37 (q, *J* = 1.5 Hz), 123.38 (q, *J* = 268.9 Hz), 120.2, 119.3, 56.5, 55.1, 52.8, 38.6, 38.6, 27.6. **^{19}F NMR** (565 MHz, Acetone-*d*6) δ -67.13 – -67.15 (m), -67.17. **ESI-HRMS** calcd for $C_{18}H_{15}F_3NO$ $[M+H]^+$, 318.1100 found 318.1103.

((3aR,6R)-5-methoxy-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



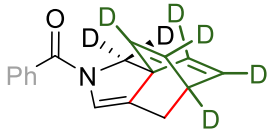
Product **2ar** was prepared following general procedure **GP-2B** from the corresponding allene (42.0 mg, 0.15 mmol). *Note: it was necessary add 1% TEA to the eluent to prevent the degradation of product during the separation.* White solid (27.2 mg, 65% yield). The reaction required 68 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.69 – 7.63 (m, 2H RotB), 7.56 – 7.41 (m, 5H RotA, 3H RotB), 6.68 (s, 1H RotB), 6.52 (d, *J* = 7.2 Hz, 1H RotA), 6.47 (d, *J* = 7.1 Hz, 1H RotB), 6.37 – 6.26 (m, 1H RotA, 1H RotB), 6.16 (t, *J* = 1.7 Hz, 1H RotA), 5.10 – 5.01 (m, 1H RotA, 1H RotB), 4.42 – 4.17 (m, 2H RotA, 2H RotB), 3.63 – 3.54 (m, 1H RotA, 1H RotB), 3.50 (s, 3H RotA), 3.46 (s, 3H RotB), 2.35 (d, *J* = 15.3 Hz, 1H RotB), 2.25 (dt, *J* = 15.1, 2.1 Hz, 1H RotA), 2.13 (d, *J* = 15.0 Hz, 1H RotB), 2.05 – 1.99 (m, 1H RotA). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 165.41, 165.38, 141.4, 141.1, 137.1, 136.8, 132.1, 131.9, 130.0, 129.9, 128.31, 128.25, 127.5, 127.3, 117.4, 116.6, 101.2, 56.3, 55.2, 54.6, 53.9, 43.2, 27.6. **ESI-HRMS** calcd for $C_{18}H_{18}NO_2$ $[M+H]^+$, 280.1332 found 280.1328.

((3ar,6r)-7-methyl-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone



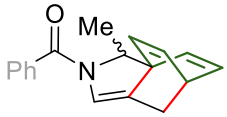
Product **2as** was prepared following general procedure **GP-2B** from the corresponding allene (58.7 mg, 0.2 mmol). Pale yellow solid (22.8 mg, 39% yield, 84% conversion). The reaction was irradiated for 96 h. Two rotamers are observed due to the dynamic rotation of the amido group (71:29 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.69 – 7.61 (m, 2H RotB), 7.54 – 7.40 (m, 5H RotA, 3H RotB), 6.66 (d, *J* = 1.8 Hz, 1H RotB), 6.52 – 6.29 (m, 3H RotA, 3H RotB), 6.27 – 6.06 (m, 2H RotA, 1H RotB), 4.48 – 4.23 (m, 2H RotA, 2H RotB), 3.65 – 3.56 (m, 1H RotA, 1H RotB), 2.31 (q, *J* = 6.6, 5.8 Hz, 1H RotB), 2.23 (q, *J* = 6.8 Hz, 1H RotA), 1.02 (d, *J* = 6.8 Hz, 3H RotB), 0.91 (d, *J* = 6.8 Hz, 3H RotA). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 165.8, 165.7, 139.0, 138.9, 138.1, 137.9, 136.7, 136.4, 135.2, 135.1, 132.1, 131.7, 130.5, 129.0, 128.8, 128.7, 127.8, 127.71, 127.66, 118.8, 118.1, 58.7, 56.5, 55.7, 53.6, 46.9, 46.8, 35.4, 21.6, 21.5. **ESI-HRMS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$, 286.1202 found 286.1197.

((3ar,6r)-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl-3,3,4,5,6,8,9-d7)(phenyl)methanone



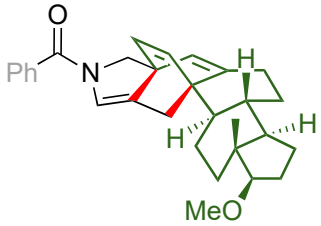
Product **2at** was prepared following general procedure **GP-2B** from the corresponding allene (38.5 mg, 0.15 mmol). White solid (27.8 mg, 72% yield). The reaction required 62 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (73:27 mixture of rotamers). **^{1}H NMR** (600 MHz, DMSO-*d*6) δ 7.64 – 7.60 (m, 2H RotB), 7.48 – 7.39 (m, 5H RotA, 3H RotB), 6.61 – 6.59 (m, 1H RotB), 6.06 (t, J = 1.8 Hz, 1H RotA), 2.00 – 1.98 (m, 2H RotB), 1.90 – 1.87 (m, 2H RotA). **^{13}C NMR** (151 MHz, DMSO-*d*6) δ 165.8, 138.3 (t, *J* = 25.5 Hz), 136.8, 136.6, 133.7 (t, *J* = 25.5 Hz), 130.6, 130.5, 129.7, 129.5, 129.0, 128.9, 127.9, 127.8, 118.4, 117.5, 58.1, 55.8, 40.6, 39.3 (t, *J* = 20.9 Hz), 28.2, 28.1. **ESI-HRMS** calcd for $C_{17}H_9D_7NO$ $[M+H]^+$ 257.1666, found 257.1664.

((3R,3aR,6R)-3-methyl-6,7-dihydro-3a,6-ethenoisoindol-2(3H)-yl)(phenyl)methanone 2at



Product **2au** was isolated as a mixture of diastereomers (dr = 88:12) following general procedure **GP-2B** from the corresponding allene (39.1 mg, 0.15 mmol). Pale yellow solid (12.7 mg, 32% yield). The reaction required 120 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.55 – 7.23 (m, $5H_{anti}$, $5H_{syn}$), 6.65 – 6.21 (m, $4H_{anti}$, $5H_{syn}$), 6.03 (s, $1H_{anti}$), 5.33 (q, *J* = 7.2 Hz, $1H_{syn}$), 4.87 (q, *J* = 6.6 Hz, $1H_{anti}$), 4.08 – 3.97 (m, $1H_{syn}$), 3.91 – 3.81 (m, $1H_{anti}$), 2.10 (t, *J* = 2.2 Hz, $1H_{syn}$), 2.02 – 1.85 (m, $2H_{anti}$), 1.63 (d, *J* = 6.4 Hz, $3H_{anti}$), 1.56 (d, *J* = 7.2 Hz, $3H_{syn}$). ^{13}C NMR (101 MHz, DMSO-*d*6) δ 176.6, 166.0, 142.2, 140.4, 136.8, 135.9, 135.7, 135.0, 133.4, 132.4, 131.2, 131.1, 130.5, 129.0, 128.9, 127.8, 127.7, 127.6, 126.8, 123.2, 118.6, 118.0, 61.9, 59.8, 58.6, 49.5, 40.5 (from HSQC), 39.7 (from HSQC), 29.4, 28.0, 19.4, 16.6. **ESI-HRMS** calcd for $C_{18}H_{17}NNaO$ $[M+Na]^+$ 286.1202 found 286.1200.

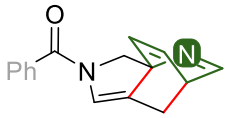
((1R,3aR,3bS,6aS,10aR,10bR,12aR)-1-methoxy-12a-methyl-2,3,3a,3b,4,5,10b,11,12,12a-decahydro-1H,7H-6a,10a-ethenocyclopenta[5,6]naphtho[1,2-f]isoindol-8(10H)-yl)(phenyl)methanone



Product **2av** was obtained as a mixture of two diasteroisomers (dr 69:31) following general procedure **GP-2B** from the corresponding allene (67.3 mg, 0.15 mmol). White solid (36.8 mg, 55% yield, 93% conversion). The reaction was irradiated for 96 h. Two rotamers are observed due to the dynamic rotation of the amido group (Dia1, 86:14 mixture of rotamers; Dia2, 84:16 mixture of rotamers). Crystals suitable for X-ray diffraction were obtained by slow evaporation from a CD_2Cl_2 solution; NMR analysis on crystals showed that they are composed of the mayor diastereoisomer of the product. **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 7.64 – 7.40 (m, Dia1, 5H RotA, 5H RotB; Dia2, 5H RotA, 5H RotB), 6.69 (brs, Dia1, 1H RotB; Dia2, 1H RotB), 6.49 – 6.25 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 6.15 – 6.07 (m, Dia1, 2H RotA, 1H RotB; Dia2, 2H RotA, 1H RotB), 5.99 – 5.93 (m, Dia1, 1H RotA; Dia2, 1H RotA), 5.87 (brs, Dia1, 1H RotB; Dia2, 1H RotB), 4.40 – 4.10 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 3.40 – 3.26 (m, Dia1, 4H RotA, 4H RotB;

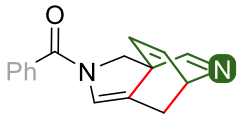
Dia2, 4H RotA, 4H RotB), 2.58 – 0.74 (m, Dia1, 20H RotA, 20H RotB; Dia2, 20H RotA, 20H RotB). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 166.1, 166.0, 165.9, 149.5, 149.3, 145.5, 145.4, 139.4, 138.9, 138.8, 138.1, 137.5, 136.8, 136.54, 136.52, 134.3, 134.1, 131.8, 131.5, 131.44, 131.38, 131.0, 129.92, 129.88, 129.5, 128.4, 128.3, 127.5, 127.2, 117.24, 117.16, 116.33, 116.26, 90.5, 90.4, 57.5, 56.43, 56.38, 55.7, 55.6, 53.7, 52.3, 51.3, 51.2, 51.1, 46.5, 43.2, 43.1, 41.9, 41.8, 38.0, 37.5, 35.8, 34.2, 31.9, 31.8, 29.7, 27.8, 27.7, 27.5, 27.4, 26.7, 26.3, 23.9, 23.8, 23.4, 22.7, 22.6, 11.4, 11.3. **ESI-HRMS** calcd for $C_{30}H_{36}NO_2$ $[M+H]^+$, 442.2741 found 441.2744.

((3aR,6R)-6,7-dihydro-3a,6-(azenometheno)isoindol-2(3H)-yl)(phenyl)methanone



Product **2aw** was prepared following general procedure **GP-2B** from the corresponding allene (37.5 mg, 0.15 mmol). The crude was purified by chromatography on silica gel (*n*-hexane/DCM/EtOAc/TEA; 3:1.5:5.4:0.1) to afford the corresponding product. Yellow oil (23 mg, 61% yield). The reaction required 36 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (75:25 mixture of rotamers). *Note: this compound has proved to be very unstable, especially after concentration. For this reason, the NMR spectra were registered after few minutes upon the isolation of the compound.* **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 8.11 (d, *J* = 3.3 Hz, 1H RotA), 8.08 (d, *J* = 3.0 Hz, 1H RotB), 7.70 – 7.42 (m, 5H RotA, 5H RotB), 6.78 (s, 1H RotB), 6.59 (d, *J* = 7.1 Hz, 1H RotA), 6.53 (d, *J* = 7.1 Hz, 1H RotB), 6.37 – 6.21 (m, 2H RotA, 1H RotB), 4.66 – 4.44 (m, 2H RotA, 2H RotB), 4.25 – 4.17 (m, 1H RotA, 1H RotB), 2.05 – 1.78 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 167.6, 167.5, 165.5, 162.3, 136.3, 135.7, 130.2, 129.6, 128.53, 128.45, 127.4, 127.3, 125.0, 124.7, 120.2, 119.2, 77.2, 75.0, 56.9, 54.5, 42.7, 30.8, 24.3. **ESI-HRMS** calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$, 251.1179 found 251.1184.

((5R,7aR)-4,5-dihydro-5,7a-(azenometheno)isoindol-2(1H)-yl)(phenyl)methanone



Product **2ax** was prepared following general procedure **GP-2B** from the corresponding allene (37.5 mg, 0.15 mmol). The crude was purified by chromatography on silica gel (*n*-hexane/DCM/EtOAc/TEA; 3:1.5:5.4:0.1) to afford the corresponding product. Yellow oil (20.9 mg, 56% yield). The reaction required

80 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amido group (85:15 mixture of rotamers). **^{1}H NMR** (400 MHz, CD_2Cl_2) δ 8.12 (s, 1H RotA), 8.04 (s, 1H RotB), 7.67 – 7.60 (m, 2H RotB), 7.58 – 7.39 (m, 5H RotA, 3H RotB), 6.47 – 6.30 (m, 2H RotA, 2H RotB), 6.29 – 6.21 (m, 1H RotA, 1H RotB), 5.57 – 5.49 (m, 1H RotA, 1H RotB), 4.64 (d, *J* = 13.4 Hz, 1H RotA), 4.50 (d, *J* = 13.4 Hz, 1H RotA, 1H RotB), 4.27 (d, *J* = 11.7 Hz, 1H RotB), 2.26 – 2.06 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, CD_2Cl_2) δ 169.0, 166.4, 135.9, 133.5, 132.1, 130.2, 128.4, 127.5, 122.8, 120.3, 62.2, 58.8, 51.1, 26.7. **ESI-HRMS** calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$, 251.1179 found 251.1182.

3-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)oxazolidin-2-one

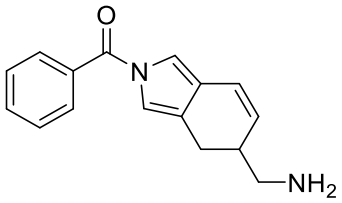
Dia1 (E) **Dia2 (Z)**

Product **2a^3** was obtained as a mixture of two diasteroisomers (87:13) following general procedure **GP-2B** from the corresponding allene **1a^3** (19.3 mg, 0.15 mmol). White solid (20.5 mg, 53% yield). The reaction required 72 h of irradiation to fully consume the starting material.

Product **2a^3** was further purified to obtain diasteroisomer ***E***. The relative structure was confirmed with selective NOE experiments. **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.28 – 7.20 (m, 2H), 7.12 – 7.04 (m, 2H), 6.66 – 6.54 (m, 2H), 6.46 (t, *J* = 2.4 Hz, 1H), 4.45 – 4.41 (m, 1H), 4.36 – 4.25 (m, 2H), 4.17 – 4.12 (m, 1H), 3.96 – 3.83 (m, 2H), 2.51 (dt, *J* = 15.2, 2.6 Hz, 1H), 2.33 (dt, *J* = 15.2, 2.5 Hz, 1H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 156.2, 143.7, 143.0, 135.2, 134.5, 125.3, 125.1, 123.1, 122.7, 122.6, 117.5, 62.0, 49.0, 44.5, 41.0, 31.7. **ESI-HRMS** calcd for $C_{16}H_{15}NO_2$ $[M+H]^+$ 253.1098, found 253.1095.

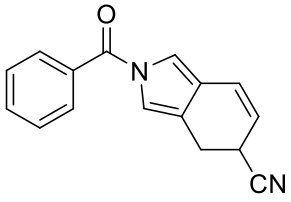
Derivatizations of products

(2-benzoyl-4,5-dihydro-2H-isoindol-5-yl)methanaminium formate-d 3a



The crude from **2aw** (37.5 mg, 0.15 mmol) was transferred in a separatory funnel and 5 mL of methanol were added. The mixture was washed with cold (-40° C) hexane (3 x 15 mL) in order to remove the excess of naphthalene. The methanol solution was then transferred in a 25 mL round bottom flask equipped with a magnetic stirring bar. The solution was cooled to 0° C and $NaBH_4$ (2 equiv.) was added in one portion. The reaction mixture was stirred for 1 hour at the same temperature and then solvent was removed under reduced pressure. The crude mixture was dissolved in DCM and treated with 1 M HCl. The aqueous layers were neutralized and extracted with DCM (3 x 10 mL). The resulting organic phase was finally washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure affording **3a** (25.2 mg, 67%), that was quickly dissolved in DMSO-*d*6 adding one drop of deuterated formic acid, which is able to prevent the otherwise rapid degradation of the product.
^{1}H NMR (400 MHz, DMSO-*d*6) δ 8.03 – 7.26 (m, 7H), 7.10 (d, *J* = 1.8 Hz, 1H), 7.04 (s, 1H), 6.60 – 6.46 (m, 1H), 5.81 (dd, *J* = 9.8, 3.5 Hz, 1H), 2.95 – 2.61 (m, 4H), 2.49 – 2.39 (m, 1H). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 167.1, 133.2, 132.5, 129.3, 128.8, 127.8, 123.3, 122.2, 121.9, 117.3, 116.0, 42.8, 33.2, 23.1. **ESI-HRMS** calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$, 253.1335 found 253.1340.

2-benzoyl-4,5-dihydro-2H-isoindole-5-carbonitrile 3b

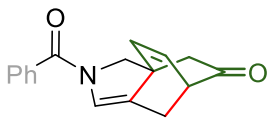


To a vial charged with substrate **1ay** (1 equiv., 49.3 mg, 0.15 mmol), $Ir(ppy)_3$ (1 mol%), TEA (1.5 equiv.), H_2O (3 equiv.) and naphthalene (20 equiv.) in dry DMF (0.1

M) were added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum and it was then degassed through three freeze-pump cycles. The tube was finally placed in an oil bath kept at 25 °C and irradiated with LED stripes for 44 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo with an additional trap to collect sublimated naphthalene. The residue was purified by chromatography on silica gel; the catalyst and the excess of naphthalene were removed using toluene as eluent prior to the separation of desired products (*n*-hexane/EtOAc, under gradient). **3b**: Pale yellow oil, 22 mg, 59%.

^{1}H NMR (400 MHz, Acetone-*d*6) δ 7.83 – 7.75 (m, 2H), 7.75 – 7.66 (m, 1H), 7.66 – 7.57 (m, 2H), 7.26 (d, *J* = 1.9 Hz, 1H), 7.21 – 7.19 (m, 1H), 6.80 – 6.72 (m, 1H), 5.90 (dd, *J* = 9.5, 4.6 Hz, 1H), 3.83 (tdd, *J* = 6.6, 4.6, 1.8 Hz, 1H), 3.04 (qdd, *J* = 15.7, 6.8, 1.2 Hz, 2H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 166.9, 133.3, 132.2, 129.2, 128.6, 123.7, 122.1, 121.2, 120.6, 119.9, 117.5, 116.8, 25.7, 24.0. **ESI-HRMS** calcd for $C_{16}H_{12}N_2NaO$ $[M+Na]^+$, 271.0842 found 271.0839.

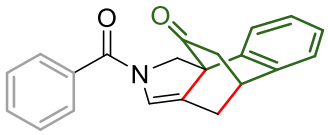
(3aR,6R)-2-benzoyl-2,3,6,7-tetrahydro-3a,6-ethanoisoindol-8-one 4a



To a solution of product **2ar** (1 equiv., 20.6 mg, 0.074 mmol) in MeOH (0.1 M) was added a 1M HCl solution (10 equiv.) and the reaction was stirred at room temperature for 6 h. After complete conversion as monitored by TLC, the solution was concentrated and was then diluted with 10 mL of EtOAc. The organic phase was washed with brine (2 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product. **4a:** white solid, 15.1 mg, 77%.

Two rotamers are observed due to the dynamic rotation of the amido group (77:23 mixture of rotamers). **^{1}H NMR** (600 MHz, Acetone-*d*6) δ 7.59 (s, 2H RotB), 7.52 – 7.40 (m, 5H RotA, 3H RotB), 6.80 (s, 1H RotB), 6.56 (d, *J* = 8.0 Hz, 1H RotA), 6.50 (d, *J* = 7.5 Hz, 1H RotB), 6.33 – 6.19 (m,2H RotA, 1H RotB), 4.14 – 4.02 (m, 2H RotA, 1H RotB), 3.95 (d, *J* = 11.2 Hz, 1H RotB), 3.26 – 3.21 (m, 1H RotA, 1H RotB), 2.73 (d, *J* = 17.9 Hz, 1H RotB), 2.63 (d, *J* = 17.2 Hz, 1H RotA), 2.38 (d, *J* = 17.9 Hz, 1H RotB), 2.34 – 2.17 (m, 3H RotA, 2H RotB). **^{13}C NMR** (151 MHz, Acetone-*d*6) δ 209.0, 165.7, 140.7, 136.4, 130.1, 128.4, 127.8, 127.7, 127.4, 125.6, 120.7, 119.9, 53.3, 50.5, 50.2, 45.2, 45.0, 24.8. **ESI-HRMS** calcd for $C_{17}H_{16}NO_2$ $[M+H]^+$, 266.1176 found 266.1181.

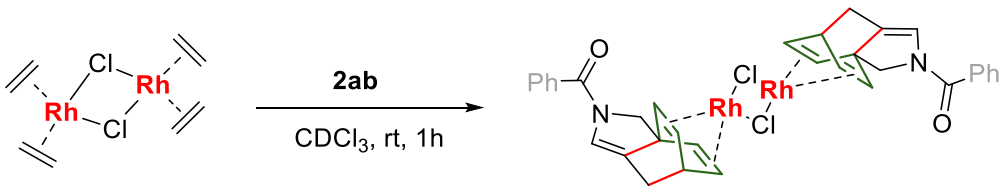
(5R,9bR)-2-benzoyl-1,2,4,5-tetrahydro-5,9b-ethanobenzo[e]isoindol-10-one 4b



To a solution of product **2u** (1 equiv., 48.6 mg, 0.148 mmol) in MeOH (0.1 M) was added a 1M HCl solution (10 equiv.) and the reaction was stirred at room temperature for 6 h. After complete conversion as monitored by TLC, the solution was concentrated and then diluted with 10 mL of EtOAc. The organic phase was washed with brine (2 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product. **4b:** white solid, 38.4 mg, 82%.

Two rotamers are observed due to the dynamic rotation of the amido group (81:19 mixture of rotamers). **^{1}H NMR** (400 MHz, DMSO-*d*6) δ 7.80 – 7.21 (m, 9H RotA, 9H RotB), 6.88 (brs, 1H RotB), 6.35 (s, 1H RotA), 4.71 (d, J = 13.2 Hz, 1H RotA), 4.46 (d, J = 13.2 Hz, 1H RotA, 2H RotB), 3.71 – 3.62 (m, 1H RotA, 1H RotB), 2.91 – 2.66 (m, 1H RotA, 1H RotB), 2.59 – 2.47 (m, 1H RotA, 1H RotB), 2.44 – 2.19 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, DMSO-*d*6) δ 203.7, 203.3, 166.4, 143.0, 142.9, 136.0, 135.7, 134.9, 134.4, 131.0, 130.8, 129.0, 127.9, 127.6, 127.5, 125.2, 123.9, 123.2, 122.0, 121.3, 66.3, 64.5, 44.9, 42.3, 40.6, 36.1, 27.8. **ESI-HRMS** calcd for $C_{21}H_{18}NO_2$ $[M+H]^+$, 316.1332 found 316.1339.

Rh complex 5[14]



5a

$[RhCl(C_2H_4)_2]_2$ (19.0 mg, 0.048 mmol, 1 eq) and **2ab** (23.7 mg, 0.095 mmol, 2 eq) were dissolved in $CDCl_3$ (3 mL), which had been neutralized over K_2CO_3 overnight. The solution was stirred for 1 h at room temperature under an inert atmosphere. Then, the solution was concentrated evaporating part of the solvent with a flow of

nitrogen and NMR characterization was directly performed without any purification. **5a:** bright orange solid, 35 mg, 96% yield.
Two rotamers are observed due to the dynamic rotation of the amido group (82:18 mixture of rotamers). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (m, 2H RotB), 7.57 – 7.48 (m, 2H RotA, 3H RotB), 7.47 – 7.37 (m, 3H RotA), 6.68 (s, 1H RotB), 6.03 (s, 1H RotA), 4.77 (s, 2H RotA), 4.53 (s, 2H RotB), 4.48 (brs, 1H RotA, 1H RotB), 3.66-3.40 (m, 4H RotA, 4H RotB), 1.98 (s, 2H RotB), 1.87 (s, 2H RotA). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.4, 135.6, 130.4, 128.5, 127.7, 118.5, 57.2, 56.8, 53.4, 51.5, 41.9, 28.4. **ESI-HRMS** calcd for $C_{19}H_{18}N_2ORh$ [Rh-**2ab**+CH_3CN]$^+$ 393.2635, found 393.2639.

Comprehensive tables in AU

M06/Def2-TZVP, CPCM = DMF	H (Hartrees)	S (cal/K*mol)	imaginary frequency (cm^{-1})
^{1}Ir(III)(ppy)$_3$	-1539.635775	191.664	
^{3}Ir(III)(ppy)$_3$	-1539.545823	196.190	
^{2}Ir(II)(ppy)$_3^-$	-1539.713463	194.086	
^{2}Ir(IV)(ppy)$_3^+$	-1539.443413	192.542	
^{1}C$_{10}$H$_8$	-385.570898	82.014	
^{3}C$_{10}$H$_8$	-385.477708	86.554	
^{2}C$_{10}$H$_8^+$	-385.349574	84.334	
^{2}C$_{10}$H$_8^-$	-385.640218	85.080	
^{2}1ac$^+$	-594.382208	117.724	
^{2}1ac$^-$	-594.665389	120.396	
^{2}1n$^+$	-747.911791	129.621	
^{2}1n$^-$	-748.202700	132.230	
1ac	-594.604204	117.656	
Iac	-594.539052	119.596	
TS I-IIac	-594.529221	113.484	-502.9758
IIac	-594.560992	114.054	
2ac	-594.598844	104.477	
1n	-748.132518	129.515	
In	-748.066122	131.744	
TS I-IIn	-748.059310	126.985	-455.8166
IIn	-748.102242	126.662	
2n	-748.147351	117.640	
I'n	-748.041388	137.299	
TS I-II'n	-748.030631	130.141	
IIn	-748.102242	126.662	
^{1}C$_{10}$H$_8$ D3	-385.572698	82.02	
1ac D3	-594.608534	117.423	
Iac D3	-594.543317	119.935	
TS I-IIac D3	-594.533452	113.469	-504.3453

IIac D3	-594.565062	113.994	
[1]IIac D3	-594.565142	111.646	
TS1 (II-1)ac D3	-594.546888	111.832	-777.9511
TS2 (II-2)ac D3	-594.546969	111.117	-600.8229
2ac D3	-594.602802	104.518	
α (D3, $C_{10}H_8$ side-on allene)			
1ac D3	-980.195456	161.519	
I D3	-980.129886	166.927	
TS I-II D3	-980.122423	159.78	-498.0253
II D3	-980.154283	160.175	
[1]II D3	-980.154359	157.596	
TS1 (II-1) D3	-980.135433	156.605	-789.7457
TS2 (II-2) D3	-980.140419	149.455	-594.7379
α-**2ac** D3	-980.190849	150.514	
β (D3, $C_{10}H_8$ stacking phenyl)			
1ac D3	-980.192565	160.342	
I D3	-980.12904	167.687	
TS I-II D3	-980.120091	158.831	-498.3169
II D3	-980.151345	161.971	
[1]II D3	-980.151497	160.501	
TS1 (II-1) D3	-980.131697	158.838	-706.7389
TS2 (II-2) D3	-980.136705	153.525	-594.4898
β-**2ac** D3	-980.187867	153.867	
γ (D3, 2 * $C_{10}H_8$)			
1ac D3	-1365.784765	197.721	
I D3	-1365.720804	206.065	
TS I-II D3	-1365.709234	202.882	-491.9475
II D3	-1365.745287	201.004	
[1]II D3	-1365.746093	197.182	
TS1 (II-1) D3	-1365.727965	187.381	-391.149200
TS2 (II-2) D3	-1365.729571	192.147	-588.0708
γ-**2ac** D3	-1365.779974	193.727	

B3LYP/Def2-TZVP, CPCM = DMF			
w/o NA (D3)			
1ac D3	-595.072368	118.082	
Iac D3	-595.005906	120.025	
TS I-IIac D3	-594.997864	113.695	-379.9318

IIac D3	-595.026914	114.036	
2ac	-595.056506	104.083	
α (D3, NA side-on allene)			
1ac D3	-980.984464	166.688	
I D3	-980.917120	172.276	
TS I-II D3	-980.910322	161.884	-375.8963
II D3	-980.938623	161.981	
β (D3, NA stacking phenyl)			
1ac D3	-980.981769	161.313	
I D3	-980.915529	169.402	
TS I-II D3	-980.908943	161.502	-373.7245
II D3	-980.936143	165.457	
β **2ac**	-980.965974	153.13	
γ (D3, 2 NA)			
1aa D3	-1366.896190	211.845	
I D3	-1366.829941	214.717	
TS I-II D3	-1366.821814	210.357	-368.8569
II D3	-1366.851800	208.217	
B97D3/Def2-TZVP, CPCM = DMF			
w/o NA (D3)			
1ac D3	-594.625406	119.018	
Iac D3	-594.562003	121.741	
TS I-IIac D3	-594.556110	114.773	-323.4956
IIac D3	-594.579485	115.313	
2ac	-594.604864	105.037	
α (D3, NA side-on allene)			
1ac D3	-980.226606	167.216	
I D3	-980.162183	170.095	
TS I-II D3	-980.157856	163.15	-314.9669
II D3	-980.180798	158.356	
α-**2ac**	-980.203614	154.84	
β (D3, NA stacking phenyl)			
1ac D3	-980.224323	168.507	
I D3	-980.161128	171.097	
TS I-II D3	-980.156498	164.343	-315.4484
II D3	-980.178288	170.074	
β **2ac**	-980.203614	154.84	

M06-2X/Def2-TZVP, CPCM = DMF			
w/o NA (D3)			
1ac D3	-594.787875	118.496	
Iac D3	-594.714467	118.522	
TS I-IIac D3	-594.702764	113.302	-461.9569
IIac D3	-594.736616	113.564	
2ac	-594.784804	103.787	
α (D3, NA side-on allene)			
1ac D3	-980.515967	162.166	
I D3	-980.442021	163.426	
TS I-II D3	-980.430447	157.93	-462.0475
II D3	-980.464399	157.177	
β (D3, NA stacking phenyl)			
1ac D3	-980.513022	161.226	
I D3	-980.440030	163.998	
TS I-II D3	-980.428803	159.211	-458.027
II D3	-980.461564	162.188	
β **2ac**	-980.509806	151.638	
γ (D3, 2 NA)			
1aa D3	-1366.242990	203.703	
I D3	-1366.171172	206.652	
TS I-II D3	-1366.157114	204.055	-459.2461
II D3	-1366.193650	198.457	

M06/Def2-SVP, CPCM = DMF			
α (D3, $C_{10}H_8$ side-on allene)			
1ac D3	-979.133149	161.519	
I D3	-979.070680	159.403	
TS I-II D3	-979.062383	159.676	-491.4067
II D3	-979.095237	158.272	
^{1}**II** D3	-979.095344	155.987	
TS1 (II-1) D3	-979.075610	154.535	-761.4902
TS2 (II-2) D3	-979.081593	150.736	-586.3685
α-**2ac** D3	-979.135129	149.523	
β (D3, $C_{10}H_8$ stacking phenyl)			
1ac D3	-979.131536	159.906	
I D3	-979.068149	166.068	

TS I-II D3	-979.060358	157.37	-487.6404
II D3	-979.092753	158.835	
^{1}II D3	-979.092868	156.549	
TS1 (II-1) D3	-979.072324	157.151	-766.3687
TS2 (II-2) D3	-979.077489	153.872	-582.3653
β-**2ac** D3	-979.131205	151.791	
γ (D3, 2 * $C_{10}H_8$)			
1ac D3	-1364.311754	204.521	
I D3	-1364.249199	208.368	
TS I-II D3	-1364.238929	203.748	-483.2832
II D3	-1364.274883	199.358	
^{1}II D3	-1364.274682	198.976	
TS1 (II-1) D3	-1364.252305	199.235	-777.7248
TS2 (II-2) D3	-1364.259257	192.956	-578.8789
γ-**2ac** D3	-1364.313977	190.749	
w/o NA			
1ac D3	-593.957001	116.815	
Iac D3	-593.893628	120.541	
TS I-IIac D3	-593.884435	113.418	-495.6222
IIac D3	-593.917334	113.711	
^{1}IIac D3	-593.917417	111.502	
TS1 (II-1)ac D3	-593.898085	110.693	-761.3648
TS2 (II-2)ac D3	-593.900104	108.143	-590.0264
2ac D3	-593.957926	104.44	
M06L/Def2-TZVP, CPCM = DMF			
α (D3, $C_{10}H_8$ side-on allene)			
1ac D3	-980.794533	164.781	
I D3	-980.730354	168.888	
TS I-II D3	-980.720863	158.013	-494.7892
II D3	-980.747555	153.995	
^{1}II D3	-980.747472	157.829	
TS1 (II-1) D3	-980.731468	153.601	-313.0716
TS2 (II-2) D3	-980.735306	150.396	-537.3357
α-**2ac** D3	-980.779682	148.277	
β (D3, $C_{10}H_8$ stacking phenyl)			
1ac D3	-980.792416	160.869	
I D3	-980.729803	165.39	
TS I-II D3	-980.719171	160.505	-494.6108

II D3	-980.744847	163.176	
[1]II D3	-980.745458	162.198	
TS1 (II-1) D3	-980.730024	157.723	-715.1725
TS2 (II-2) D3	-980.732802	154.207	-561.7131
β-**2ac** D3	-980.777176	153.948	
γ (D3, 2 * $C_{10}H_8$)			
1ac D3	-1366.632593	205.611	
I D3	-1366.570647	209.012	
TS I-II D3	-1366.557404	206.625	-492.6589
II D3	-1366.586990	201.963	
[1]II D3	-1366.587034	199.419	
TS1 (II-1) D3	-1366.570492	193.279	-442.8099
TS2 (II-2) D3	-1366.573647	197.282	-541.7155
γ-**2ac** D3	-1366.617354	194.729	
w/o NA			
1ac D3	-594.957237	118.251	
Iac D3	-594.894112	119.72	
TS I-IIac D3	-594.883378	113.714	-498.4587
IIac D3	-594.909373	114.326	
[1]IIac D3	-594.909571	112.196	
TS1 (II-1)ac D3	-594.895795	111.03	-708.0609
TS2 (II-2)ac D3	-594.894245	107.094	-372.8576
2ac D3	-594.942397	104.055	

Chapter III

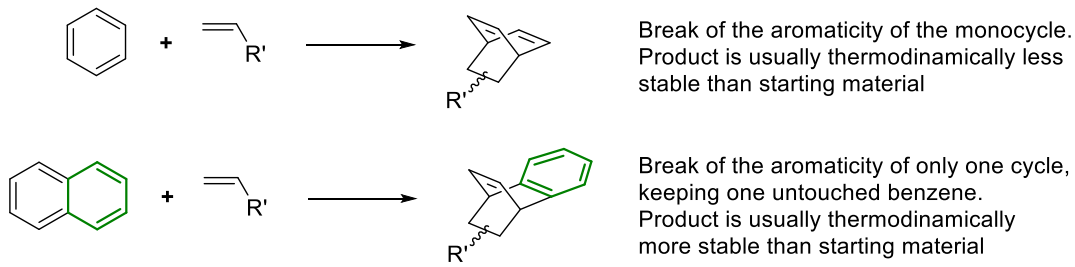
Visible – Light – Promoted Intermolecular para-Cycloadditions of Allenamides on Naphthalene

From this chapter:

M. Chiminelli, G. Scarica, D. Balestri, L. Marchiò, N. Della Ca', G. Maestri. The visible-light-promoted intermolecular para-cycloadditions of allenamides on naphthalene. *Tetrahedron Chem* **2023**, *8*, 100053. DOI:10.1016/j.tchem.2023.100053.

3.1: Intermolecular Dearomative Cycloadditions on Naphthalene

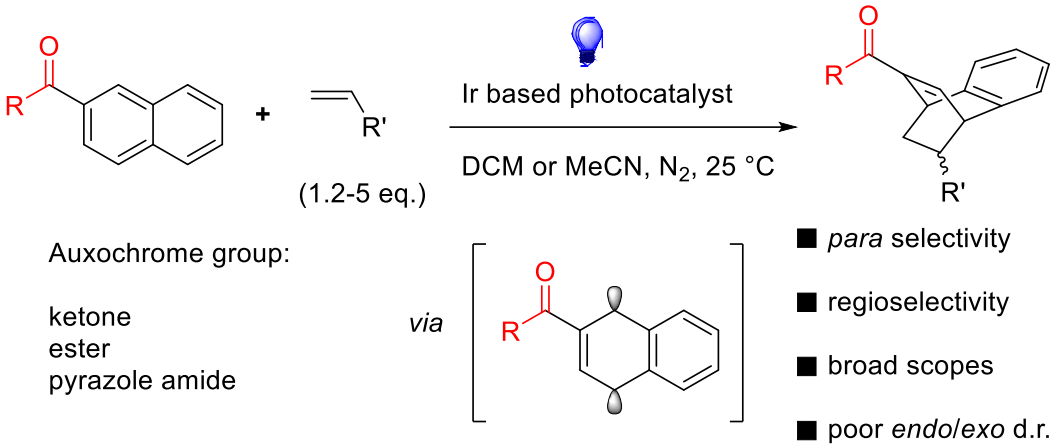
In chapter II (paragraph 2.1) I presented several examples of the allene/arene cycloaddition. The same strategy can be used to dearomatize naphthalene. This bicycle has a lower aromatic stabilization than benzene, in fact the energy loss corresponding to the dearomatization of one ring is ≈ 25 kcal/mol. The value is 2/3 of the one of benzene because the aromaticity corresponds to 10 π electrons shared among two rings. Breaking the stabilization of one ring, means keep a benzene in the second ring, that stabilizes the product formed (Scheme 40).



Scheme 40: representative structure for the intermolecular para-cycloaddition on naphthalene and benzene.

This is why dearomatization of naphthalene is more developed than benzene one. For the same reason, only recent examples will be mentioned, focused on visible – light – promoted methodologies for the intermolecular *para*-cycloaddition on naphthalene derivatives.

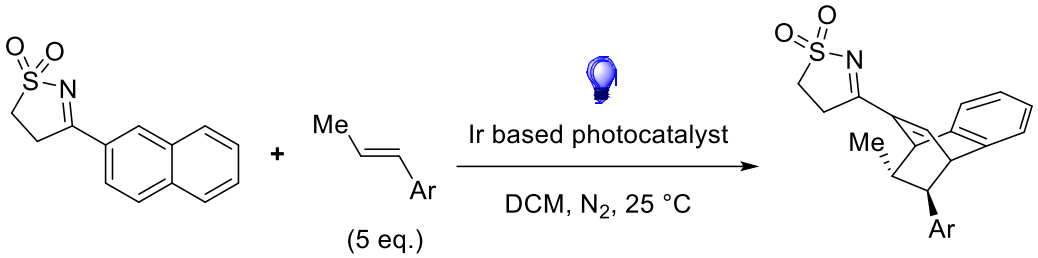
In 2022, Brown and Maji reported two independent works on the dearomative para-cycloaddition of alkenes on naphthalene derivatives[83,84] (Scheme 41).



Scheme 41: Intermolecular dearomative para-cycloaddition on naphthalene derivatives.

The two works have strong analogies with Glorius's dearomatization of quinolines (see Chapter I, 1.5). Indeed, the reaction starts with the sensitization of naphthalene by EnT to form a biradical intermediate. Then, it can trap an alkene to seal the 3D-bicyclooctene scaffold. The auxochrome moiety (in red) is a substituent that increase the conjugation of the system, lowering E_T of the naphthalene derivative, and enabling the energy transfer process. With this methodology the two authors synthesized two broad scopes of products, with exclusive *para* selectivity and excellent regioselectivity. However, they obtained the products as a mixture of two diastereomers (i.e. *endo* and *exo*) with poor diastereoselectivity (no more than 4:1).

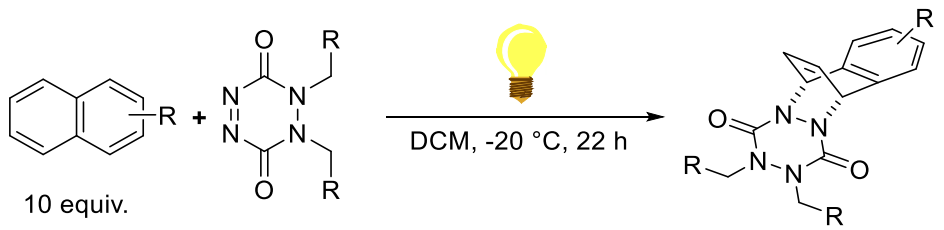
In 2023, Brown et.al. overcome the above limitation building a new and more efficient intermolecular *para*-cycloaddition on a diverse naphthalene derivative (Scheme 42)[85].



Scheme 42: intermolecular para-cycloaddition on naphthalene derivatives with endo diastereoselectivity.

Brown designed its new substrate employing a sulfonylimine as auxochrome group. He showed that this big substituent prevents one of the two possible attacks to the alkene for its steric hindrance, resulting in a diastereoselective reaction with *endo*/*exo* dr > 20:1. However, Brown is limited to the use of disubstituted styrenes, otherwise the most favourable reaction is the [2+2] cycloaddition between the imine and the alkene (i.e. aza-Paternò-Buchi).

In 2023, Matsunaga and coworkers adopted a different approach to dearomatize substituted naphthalenes and benzenes[86] (Scheme 43).



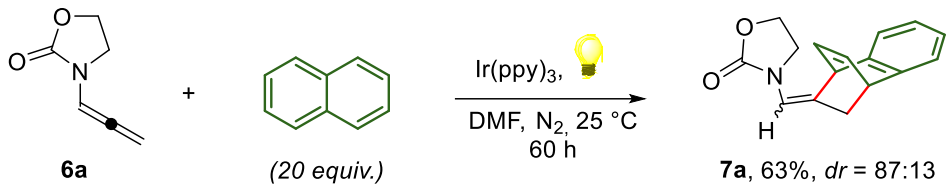
Scheme 43: Intermolecular dearomatization with TETRAD.

This methodology is similar to that of Sarlah (see Chapter I, 1.5), but the authors declare that their arenophile forms much more stable cycloadducts, even managing to isolate and crystallize them. They synthesized a broad number of products, including benzenes (even if with lower yields), successfully dearomatizing naphthalenes that are not susceptible to energy transfer activation.

Indeed, it is clear from the literature that there is a gap in the intermolecular dearomatization methodologies of naphthalenes that cannot be activated via energy transfer. New arenophiles must be found, and the development of a general approach for the synthesis of unsubstituted bicyclooctene seems to provide an answer to this demand.

3.2: Results and Discussion

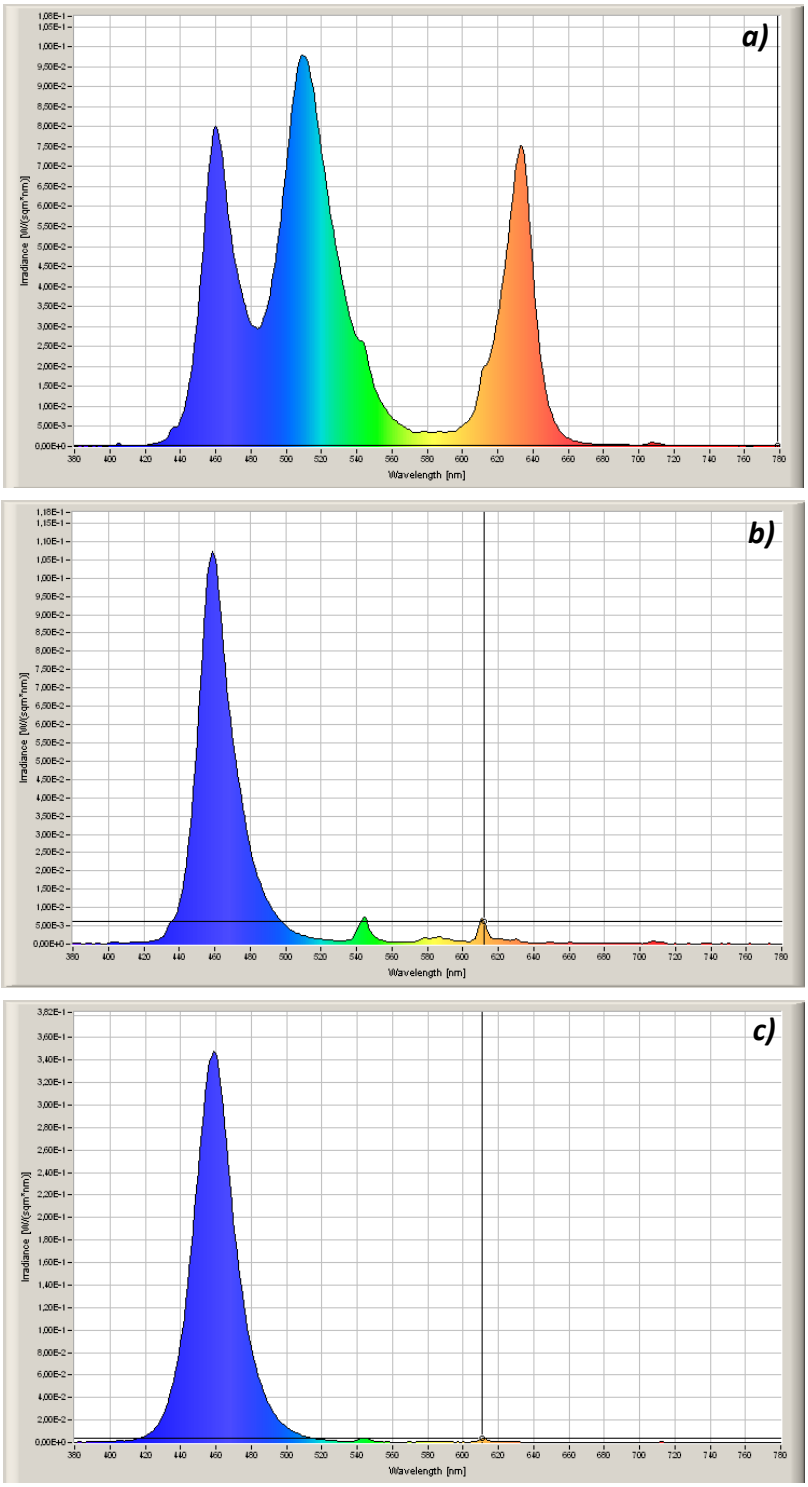
In this chapter I will present an unprecedent approach for the intermolecular dearomative *para*-cycloaddition of allenamides on naphthalene (NP). In the previous chapter, we demonstrated the potency of allenamides as arenophiles also for intermolecular dearomatizations[87] (Scheme 44).



Scheme 44: Intermolecular dearomatization of NP.

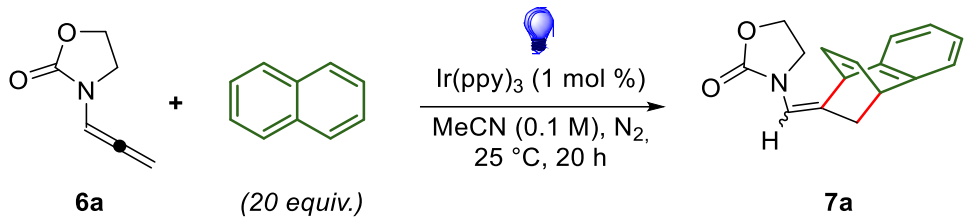
The product is [2.2.2]-bicyclooctene that has higher Fsp^3 than the starting materials. Moreover, this alicyclic 3D scaffold is difficult to achieve with other synthetic procedures. Looking at the literature (see 3.1) we understood that the "standard" dearomative approach for naphthalene derivatives involves their sensitization through EnT, by tailoring NP with auxochrome substituent that lowers the E_T. On the contrary, our method allows the functionalization of simple naphthalene with various allenamides partners.

We soon realized that the reaction worked well but it was too slow compared to the intramolecular version. We tested several catalysts, but we didn't get any better results. Thanks to experiments carried on by my colleague Davide Ruggeri[88], we saw a significant difference in the intensity emission at 456 nm of our light sources, which is the one absorbed by our PC (Scheme 45). Indeed, the intensity of white LEDs at 456 nm was lower than the one of blue LEDs in the same region (3.5 times more). We therefore decided to change our light setup, hoping that Ir-PC would be excited more times. As a result, we increased the reaction rate by three times, achieving complete conversion after less than 24 hours with more than 80% yield.



Scheme 45: Intensity of emission for different setups. a) white light with blue, green and red LEDs on b) white light with only blue LEDs on c) blue LEDs.

Table 2: Optimization of reaction conditions.



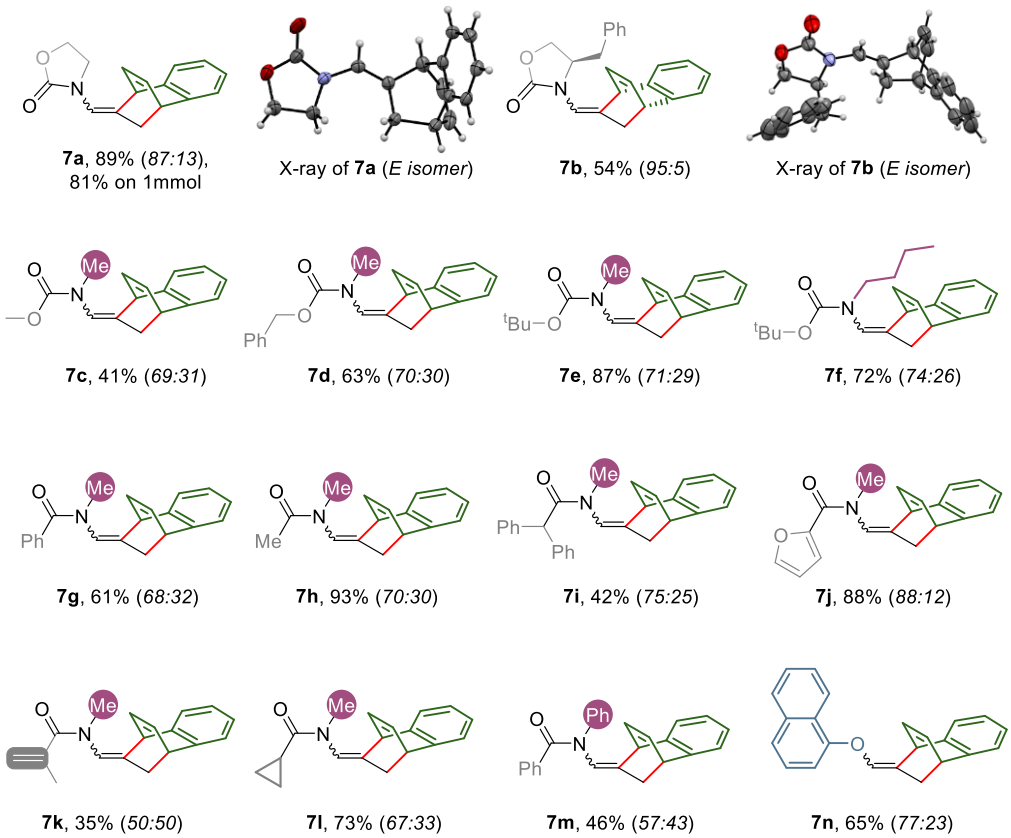
6a *(20 equiv.)* **7a**

Entry[a]	Deviation from optimal	Conversion of **6a** [%][b]	Yield of **7a** [%][b]
1	-	>99	87
2	in DMF	>99	79
3	in acetone	>99	78
4	in DCM	>99	58
5	in toluene	>99	79
6	with Ir(p-F-ppy)$_3$	>99	75
7	with Ir(p-CF$_3$-ppy)$_3$	>99	78
8	using 10 equiv. of NP	93	69
9	using 5 equiv. of NP	80	60
10	using 2 equiv. of NP	65	47
11	w/o sensitizer	0	0
12	w/o light	0	0

*[a] Reaction conditions: 0.15 mmol of **6a** (0.1 M in MeCN), 3 mmol of NP, 1 mol% sensitizer, irradiated for 20 h with blue LEDs at 25 °C; [b] ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard.*

In Table 2 I summarised some of the optimization experiments (additional optimization experiments can be found in the experimental section). The best outcome was achieved mixing **6a** (0.15 mmol, 0.1 M in acetonitrile) with 20 equiv. of NP in the presence of 1 mol% of Ir(ppy)$_3$. The solution was transferred to a standard 4-mm NMR tube to optimize the surface/volume ratio, degassed via freeze-pump-thaw, placed in a thermostated silicon-oil bath at 25 °C, and then irradiated with blue LEDs for 20 hours. Full conversion of the substrate was achieved, and the desired product **7a** was obtained with an 87% yield, as determined by ^{1}H NMR (entry 1). Slightly lower results were obtained with other solvents, with their polarity having minimal impact on process efficiency, except for chlorinated solvents, which were less effective (entries 2–5). Various Ir-based

photosensitizers could be used, but none outperformed the simple $Ir(ppy)_3$ (entries 6–7). The molar excess of the arene could be reduced, although this led to a slight decrease in yield, which remained synthetically useful even with just 2 equiv. of NP (entries 8–10). Finally, routine control experiments highlighted the crucial roles of both the Ir-complex and light in the model reaction (entries 11–12). Product **7a** was obtained a mixture of two diastereomers depending on the orientation of the enamine respect to the dearomatized naphthalene. The major one (Dia1) has the double bond in the *E* configuration. Although the diastereoselectivity should be improved, the two isomers could be separated with chromatography on silica gel. The main advantages of this dearomatization are the perfect atom economy and very mild operative conditions, characteristic historically unusual for these reactions. With the best conditions in hand, we then evaluated the generality of the method (Scheme 46).

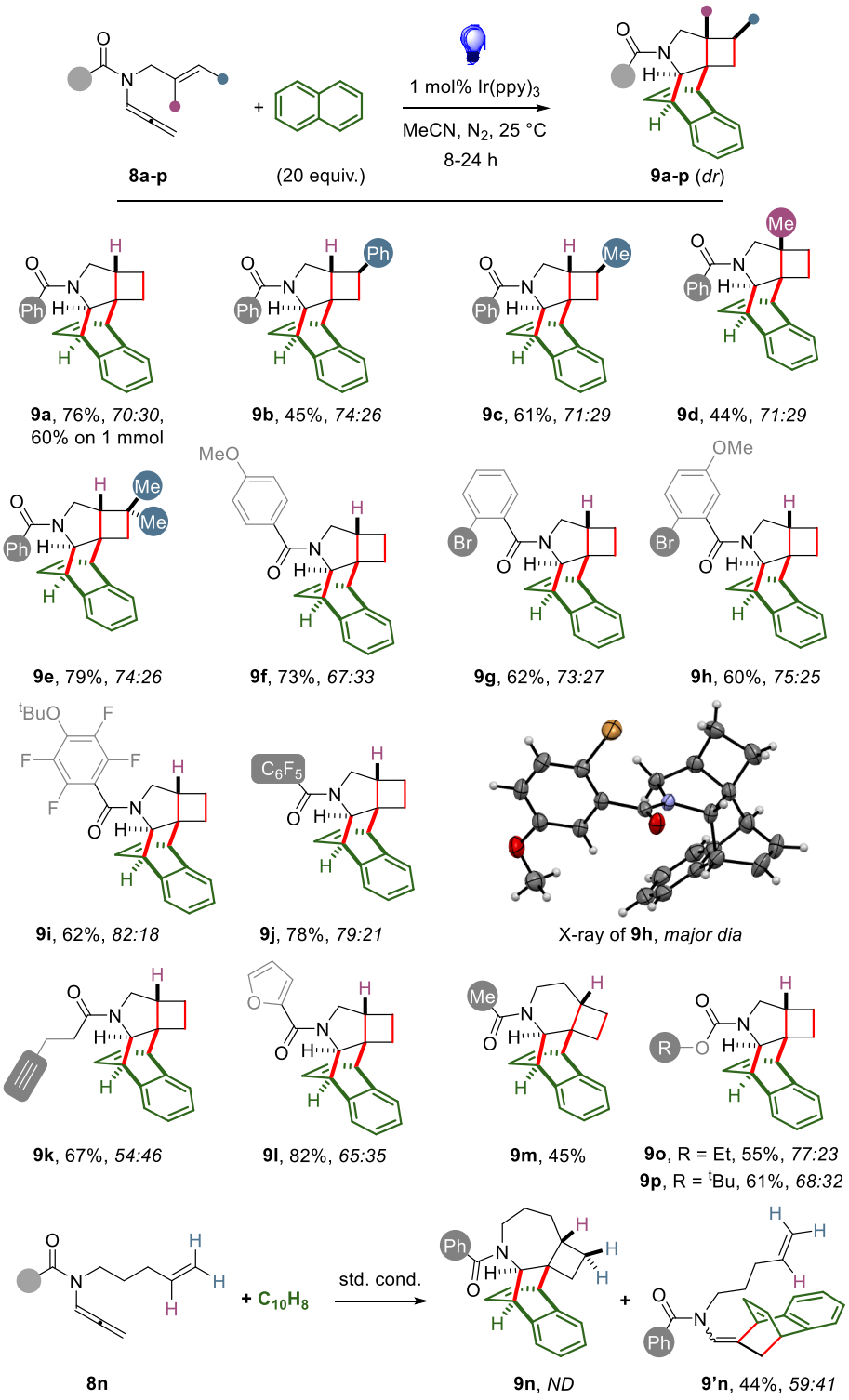


Scheme 46: Scope of simple allenamides.

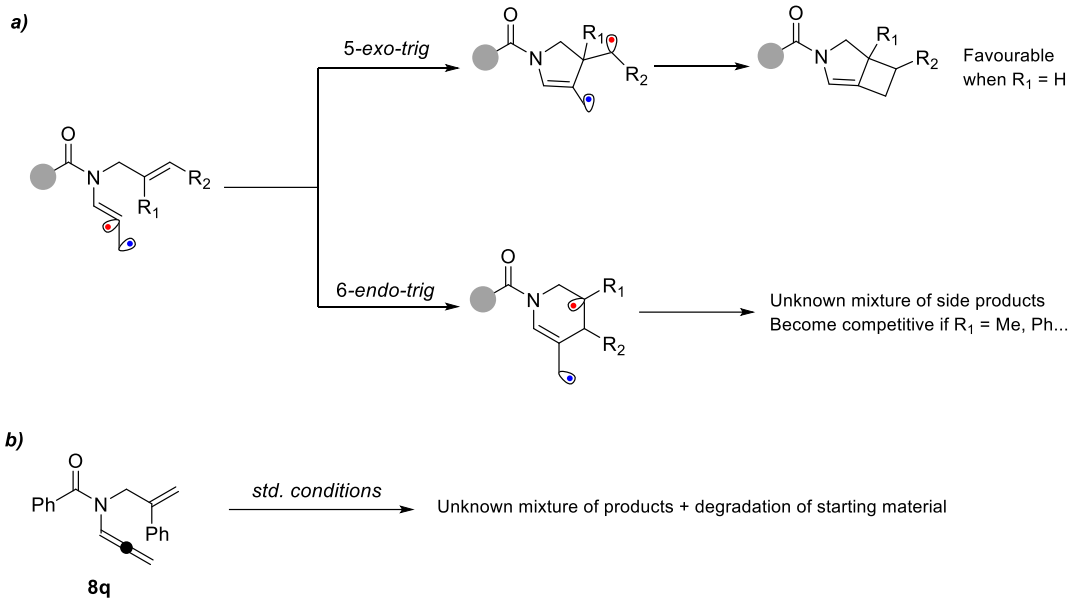
The model reaction can be scaled up to 1 mmol without a significant efficiency loss. The cyclic carbamate unit of the model substrate can be decorated by additional groups, as witnessed by product **7b** that was derived from L-phenylalanine. The product was retrieved in a lower yield compared to the model but as a single diastereomer, indicating that the chiral information of the substrate can be efficiently transferred to the stereocenters generated by the NP dearomatization. Various linear carbonates can be converted into the corresponding products (**7c-f**), and the best result was achieved using a BOC-protected derivative. The alkyl substituent of the nitrogen atom can be varied, and linear alkyl chains are well tolerated. N-alkyl amides, too, are tolerated by the method (**7g-m**). The worst results were achieved employing substrates that present relatively acidic protons (**7i**) and in the presence of an additional terminal C–C double bond (**7k**), owing to the formation of a complex mixture of byproducts. On the contrary, excellent yields were observed using an acyl- and a furoyl-protected allenamide (**7h** and **7j**, respectively). Finally, the allenamide unit of the substrate could be replaced by an arylallenylether, allowing one to access the corresponding dearomatized enol ether (**7n**). This last product is very interesting because there are few reports in literature regarding the sensitization of allenols. This result can open the way for further studies on this topic, focused on the exploitation of another high reactive vinyl radical, but with slightly different electronics properties. Regarding the limitations of the method, efforts to activate sulfonyl allenamides and allenoates were at present fruitless. With respect to the arene partner, the method is at present unsuitable for the dearomatization of monocyclic (hetero)arenes and bicyclic heteroarenes such as benzofurans and indoles. The attempted dearomatization of (iso)quinolines led to a complex mixture of in which both the carbo- and the hetero-cyclic ring were unselectively difunctionalized by the allenamide partner (see experimental section for full details).

We then decided to prepare a 1,6-enallene **8a** wondering whether if it would have been possible to selectively trigger an additional cyclization within the same sequence. We obtained a new unknown product, without NMR signals of the alkene, that had a molecular weight in accordance with an intermolecular

dearomatization of naphthalene. The reaction proceeded smoothly in only 8 hours, with complete conversion and an isolated yield of 76%. After NMR analyses and XRD-resolution we understood the structure of the new product. The outcome of the reaction is a congested, fused/bridged tetracycle **9**, which was established with the formation of 4 new C-C bonds in one step. Moreover, this new 3D-scaffold has a very high Fsp^3 compared to the starting materials, building up to 6 contiguous stereocenters. Furthermore, the reaction has a great diastereoselectivity considering that product **9** is obtained as a mixture of only two diastereomers out of the 32 possible ones. The two isomers differ for the relative configuration of the residual benzo-group with respect to the fused [3.2.0] bicyclic unit. The cascade led also to the direct conversion of the central sp carbon of the allene into a synthetically challenging, doubly spiro carbon that is shared among three different rings. Intrigued by this original sequence, we tested its scope by first examining the substitution of the alkenyl arm of **8** (Scheme 47). Gratifyingly, various substituted olefins were well tolerated, affording the corresponding products **9** in moderate to good yields (**9b-e**, 44–79 %). The best results were achieved with the tri-substituted olefin partner of **9e**, while the worst one was observed using a substrate with a terminal disubstituted olefin (**9d**). These results let us think that the enallene, upon the initial sensitization of its cumulated double-bond system, undergoes a fast intramolecular 5-*exo*-*trig* cyclization with the alkene partner[89]. This step would become more favourable employing **3e** because it would give a tertiary radical. On the contrary, the corresponding 6-*endo*-*trig* cyclization can become competitive in the presence of terminal disubstituted alkenes as radical acceptors (Scheme 48, a)[90]. This hypothesis was supported by testing a related substrate bearing an α-styrene arm (**8q**) (Scheme 48, b). A complex mixture of products that contained just traces of the desired polycycle **9** was retrieved, likely because the corresponding radical 6-*endo*-*trig* became too fast in this case.



Scheme 47: Scope of enallenes.



*Scheme 48: a) Representation of the two possible reactive pathways of substrates **8**. b) Substrate **8q** did not give the desired polycycle **9q**.*

We next investigated the substitution of the acyl group. Various aryl rings, regardless of their stereo-electronic properties, were well tolerated by the method (**9f-l**, 60–82 %). The series includes the presence of C (sp^2)-Br groups, which can be useful synthetic handles for further derivatization, as well as heterocycles such as furans and a terminal alkyne unit. The method allows one to seal a piperidine central ring in a synthetically useful yield (**9m**). However, further elongation of the tether between the insaturation of **8** hindered the intramolecular cyclization (**9'n**), likely because of the relative slower rate of the radical 7-*exo-trig* annulation[89]. Finally, the amido group of the substrate can be replaced by a carbamate one (**9o-p**). Regarding the limitations of the process, no traces of polycycle **4** were observed testing the corresponding sulfonylallenamides, and these reactions led to the formation of complex, inseparable mixtures. This could be due to a competitive sulfonyl β-scission upon the initial sensitization[91], which would then hinder the desired process.

We then investigated the mechanism of our transformation. We performed Stern-Volmer analyses (Figure 12), and we confirmed that both substrates **6** and **8**

are activated by Ir-PC, with K_{SVs} consistent with other allenamides (271.5 and 426.6 M^{-1} respectively).

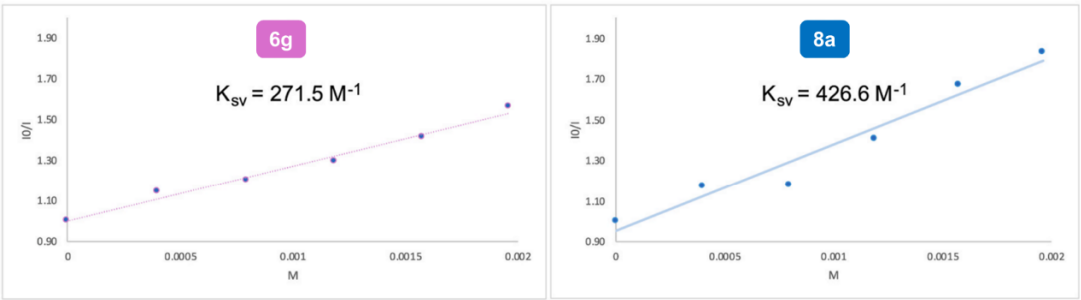
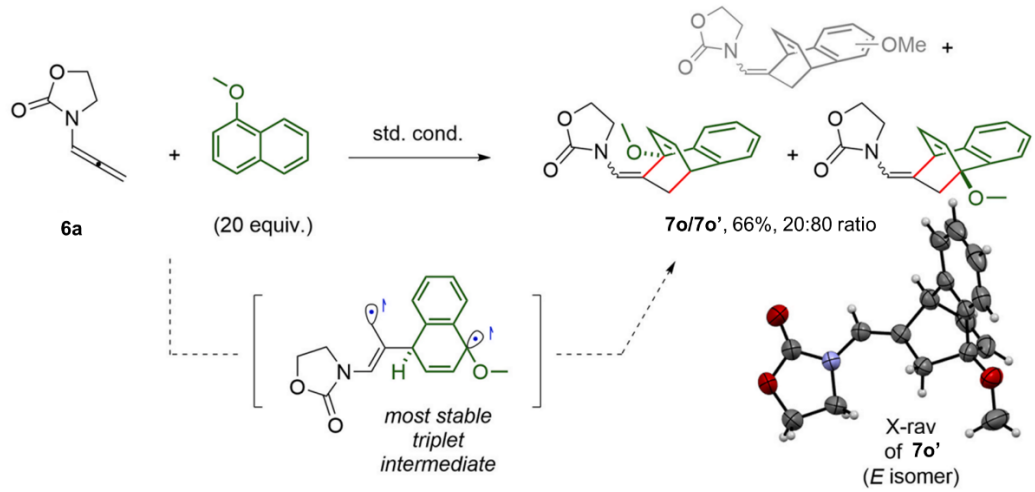


*Figure 12: Stern-Volmer analyses on **6g** and **8a**.*

Substrates **6g** and **8a** were freely optimized by DFT at the M06/Def2-TZVP level, using acetonitrile as implicit solvent. The triplet energies of the two substrates were calculated (+40.9 and + 39.5 kcal/mol, respectively), and that of **8a** proved lower in ΔG by − 1.4 kcal/mol. This is due to a radical-π stacking-like interaction between the sensitized allene arm and the tethered alkene group, which cannot take place in substrates **6**. The relatively more stable triplet of **8a** compared to that of **6g** could be the reason of the higher measured Ksv of the former. The higher quenching efficiency of **8a** compared to **6g** could possibly explain the shorter reaction time observed in the synthesis of **9** compared to that of **7**. The triplet energy of NP is higher than that of the excited photocatalyst according to literature data, and this prevents an efficient EnT step between these species. Taken together, these results strongly suggest that these sequences are initiated by the sensitization of the allenamide (as in Chapter II). The initial EnT on the cumulated arm is also consistent with the observed limitations of present methods. Indeed, no conversion was observed by testing reagents with isolated allenyl arms, which have triplet energies that are inaccessible by Ir-based complexes.

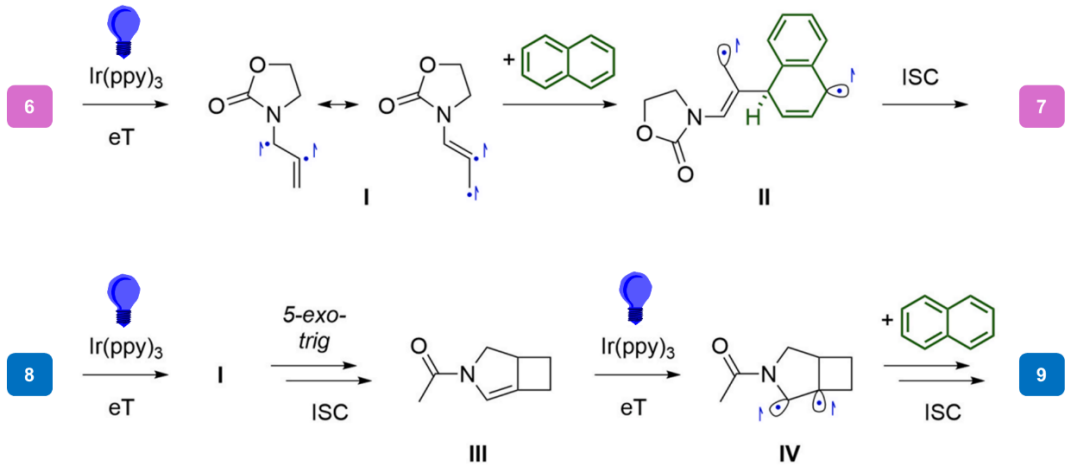
To further investigate the initial step of these sequences, we tested the model reaction of **6a** in the presence of 1-methoxynaphthalene (Scheme 49).



Scheme 49: Mechanistic hypothesis for dearomative cycloaddition of NP with simple allenamides.

The control of the selectivity of the process is highly challenging because the reaction could in principle lead to several isomers. However, we hypothesized that the dearomatization of the substituted aryl ring should be favoured, despite its higher steric hindrance, because it would yield a more stable, substituted radical intermediate. The reaction afforded a mixture of dearomatized products in 85 % combined yields. Their separation by prep-TLC allowed us to isolate **7o** and **7o'** in 66% yield (20:80 ratio), and the structure of the latter was unambiguously assigned by XRD-resolution. Although these results show that a complete control of the selectivity using substituted NPs is still an open issue, they nonetheless further support that present reactions involve the initial activation of the cumulated partner.

Scheme 50 shows a plausible mechanism for these cascades.



Scheme 50: Mechanistic hypothesis for the cyclizations.

The first step features the generation of biradical **I** via EnT from the excited photocatalyst. The triplet **I** could then attack naphthalene, forming **II**. The loss of the aromatic stabilization in the latter species is partially compensated by the allylic/benzylic resonance stabilization of its two mono-occupied molecular orbitals. Upon intersystem crossing, radical recombination is favored on the terminal carbon of the former allenyl arm because of a reduced steric hindrance compared to the nucleus alfa to the nitrogen atom. This step eventually affords the product **7**. Upon the sensitization of **8**, it could be proposed that an intramolecular radical cyclization would lead to the intermediate [3.2.0] bicyclic enamine **III** upon intersystem crossing (ISC), in analogy with related enallene photocycloadditions[91,92]. This group may then undergo a second EnT[93], providing **IV** and paving the way for the intermolecular dearomatization of NP that eventually affords **9**, following a stepwise process like the one described above.

Further studies are ongoing to proof this hypothesis. It is worth nothing that the use of cyclic enamine similar to **III** as substrate for new EnT promoted reactions can expand the current known chemical space in the field of radical methodologies.

3.3: Conclusions

In summary, we have developed a new method to dearomatize naphthalene in an intermolecular fashion, using allenamide as arenophile. The reaction allows the synthesis of a [2.2.2]-bicyclooctene unit that have a potential biorelevant 3D alicyclic scaffold, starting from sp^2-rich compounds. Moreover, with enallenamides, we obtained a complex congested fused/bridged tetracycle with the formation of 4 new C-C bonds in one step. With this cascade we established up to six contiguous stereocenters, increasing significantly the Fsp^3 of product **9** respect to the starting materials.

The reactions are both performed in very mild conditions, with a cheap and simple setup. Moreover, they tolerate several functional groups and have complete atom economy. Simple allenamides are converted to product **7** in 24 hours with satisfactory yields. Enallenes gave product **9** with excellent selectivity, indeed we obtained **9** as a mixture of only two diastereomers out of the 32 possible ones.

Finally, we confirmed our mechanistic hypothesis with DFT calculations and Stern-Volmer quenching analyses and Cyclic Voltammetry. With simple allenamides, the reaction is a stepwise 1,4 *para*-cycloaddition that occurs through the formation of 2 new C-C bonds, the first due to the attack of the vinyl radical onto the ipso carbon of the arene moiety. On the other hand, product **9** is probably formed after a first [2+2] cyclization of enallenes to give an intermediate enamine, that, after a second EnT process, dearomatize naphthalene.

This last observation opens the way to other possible studies in the field of EnT promoted reations and their applications for unusual cyclization.

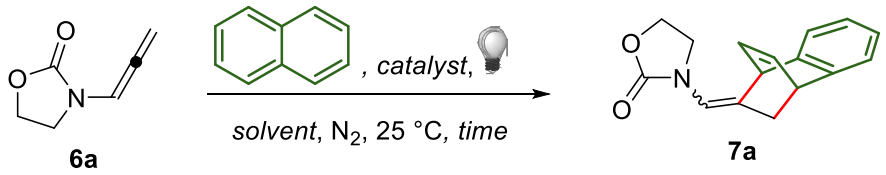
3.4: Experimental Section

General remarks

All chemicals those synthesis are not reported hereafter were purchased from commercial sources and used as received. Solvents were dried passing through alumina columns using an Inert® system and were stored under nitrogen. Present visible-light promoted reactions did not require the use of dry solvents but the presence of molecular oxygen exerts a negative effect on their rate. Chromatographic purifications were performed under gradient using a Combiflash® system and prepacked disposable silica cartridges or through isocratic flash chromatography using commercial 60 Å silica gel. All reactions that required heating were performed with the use of high-vacuum grade silicon oil. Reactions promoted by visible light were performed into standard 5 mm NMR tubes, surrounded by a commercial strip of 300 household leds (12V, 17W). These were put at a distance of ca 10 cm and irradiated with blue light (chip SMD5630-300 ip65). The tubes were inside an oil bath fitted with a thermometer to monitor the temperature. Cooling was ensured by two fans recovered by outdated PCs to avoid reproducibility issues. During summertime, solutions are kept at 25 °C through the addition of a transparent rubber spire inside the silicon oil bath. The spire is linked to a chiller that keeps pumping a cooled water/ethylene glycol solution to maintain the desired temperature. ^{1}H and ^{13}C NMR spectra were recorded at 300 K on a Bruker 400 MHz or a Jeol 600 MHz spectrometers using residual non-deuterated solvents as internal standards (7.26 ppm for ^{1}H NMR and 77.00 ppm for ^{13}C-NMR for $CDCl_3$, 2.05 ppm for ^{1}H NMR and 29.84 ppm for ^{13}C NMR for acetone-d6). ^{19}F-NMR spectra were recorded in $CDCl_3$ at 298 K on a Jeol 600 spectrometer fitted with a BBFO probehead at 564 MHz. The terms m, s, d, t, q and quint represent multiplet, singlet, doublet, triplet, quadruplet and quintuplet respectively, and the term brs means a broad signal. Reported assignments were based on decoupling, COSY, NOESY, HSQC and HMBC correlation experiments. Mass analyses were recorded on an Infusion Water Acquity Ultra Performance LC HO6UPS-823M instrument equipped with a SQ detector (Electrospray source); high-resolution mass analyses were recorded on a LTQ ORBITRAP XL Thermo Mass Spectrometer (Electrospray source). CCDC 2297940-2297943 contain the supplementary crystallographic data for compounds **7a**, **7b**, **9h** and **7o'**, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif. Single crystal Data were collected with a Bruker D8 diffractometer equipped with PhotonII area detector, using a CuKα or a MoKα microfocus 4 radiation source. The data collection strategy

covered the sphere of reciprocal space. Absorption corrections were applied using the program SADABS. The structure was solved with the SHELXT code. Fourier analysis and refinement were performed by the full-matrix least-squares methods based on F2 using SHELXL-2014 as implemented in Olex2. All the nonH atoms were refined with anisotropic displacement parameters

Optimization experiments

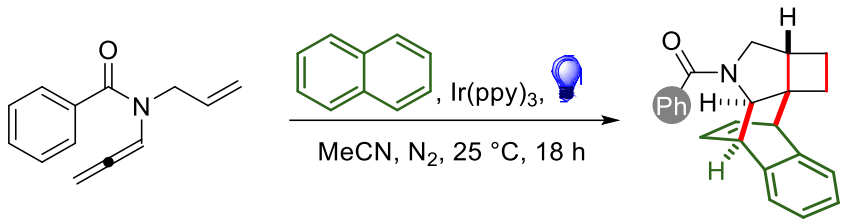


6a **7a**

Entry	Catalyst (1 mol %)	Solvent (0.1 M)	Naphthalene (eq.)	Time (h)	Conversion of **6a**[a] [%]	Selectivity[a] [%]
WHITE LEDS						
1	$Ir(ppy)_3$	DMF	20	40	76	58
2	$Ru(bpy)_3Cl_2$	DMF	20	40	19	0
3	$(Ir[dF(CF_3)ppy]_2(bpy))PF_6$	DMF	20	40	39	19
4	$(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$	DMF	20	40	63	43
5	$Ir(p\text{-}F\text{-}ppy)_3$	DMF	20	40	93	70
6	$[Ir(dtbbpy)(ppy)_2]PF_6$	DMF	20	40	25	0
7	$Ir(p\text{-}CF_3\text{-}ppy)_3$	DMF	20	40	86	65
8	$Ir(p\text{-}tBu\text{-}ppy)_3$	DMF	20	40	59	35
9	2,4,6-Triphenylpyrylium tetrafluoroborate[c]	DMF	20	40	>99	0[f]
10	Thioxanthen-9-one[c]	DMF	20	40	21	0
11	Eosin Y[c]	DMF	20	40	20	0
12	Ir(ppy)3[b]	DMF	20	40	>99	77
BLUE LEDS						
13	$Ir(ppy)_3$	DMF	20	20	>99	79
14	$Ir(p\text{-}F\text{-}ppy)_3$	DMF	20	20	>99	75
15	$Ir(p\text{-}CF_3\text{-}ppy)_3$	DMF	20	20	>99	78
16	$Ir(ppy)_3$	DCM	20	20	>99	58
17	$Ir(ppy)_3$	MeOH	20	20	NP is insoluble	
18	$Ir(ppy)_3$	Acetone	20	20	>99	78
19	$Ir(ppy)_3$	MeCN	20	20	>99	87
20	$Ir(ppy)_3$	Toluene	20	20	>99	79
21	$Ir(ppy)_3$	Toluene	-	20	0	0
22	$Ir(ppy)_3$	THF	20	20	>99	70
23	$Ir(ppy)_3$	MeCN-Tol 1:1	20	20	>99	81
24	$Ir(ppy)_3$	MeCN	10	20	93	69
25	$Ir(ppy)_3$	MeCN	5	20	80	60
26	$Ir(ppy)_3$	MeCN	2	20	65	47
27	$Ir(ppy)_3$	MeCN	20	20	37	29
28	-	MeCN	20	20	0	0
29[d]	$Ir(ppy)_3$	MeCN	20	20	0	0

[a] ^1H NMR yield using 1,3,5-Trimethoxybenzene as internal standard, [b] blue LEDs, [c] 10 mol%, [d] without light, [e] 0.1 mol%, [f] degradation of starting material.

Best conditions



8a **9a**

Entry	Naphthalene (eq.)	Conversion of **8a** [%]	Isolated yield [%]
1	20	>99	76
2	10	>99	63
3	5	>99	56
4	2	>99	35

Stern-Volmer quenching studies

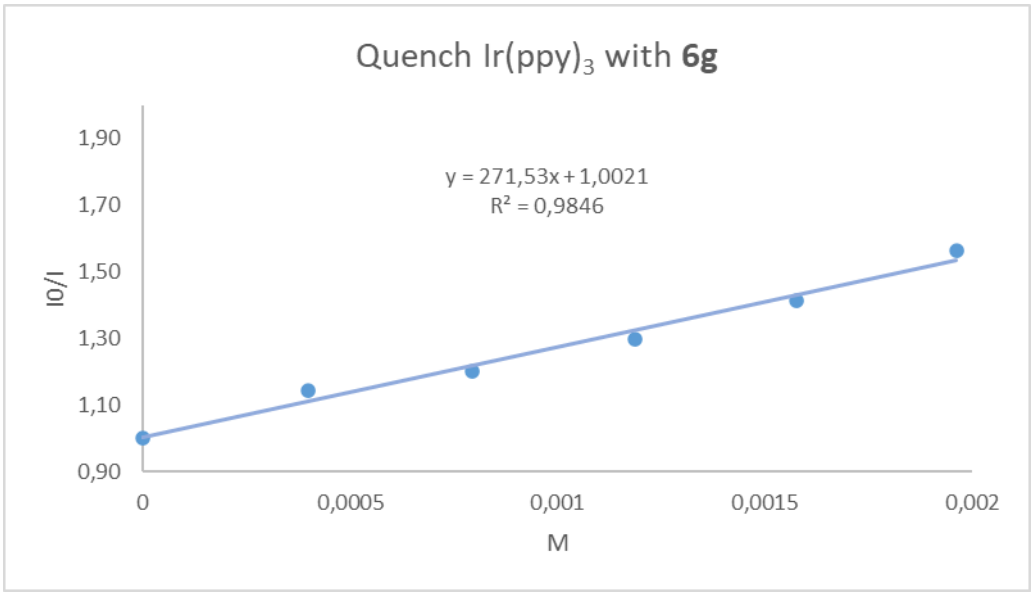
The measurements of fluorescence emissions were carried out with a FLS1000 Edinburgh fluorometer, equipped with automatic polarizers. Emissions have been collected by exciting samples with a Xenon lamp at 375 nm and the luminescence was measured at 527 nm. Fluorescence spectra are corrected for the excitation intensity and detector sensitivity.

Stern – Vollmer quenching studies were carried out using a $5*10^{-5}$ M solution of $Ir(ppy)_3$ [**PC1**] in acetonitrile and variable concentrations of both **6g** and **8a** from 0 to 2 mM. 2.5 mL of PC1's solution was transferred in a 3.5 mL quartz cuvette and degassed twice for 5 minutes (with a 30 second break in between) before collecting the first spectra. Then, after each addition of quenching, the samples were degassed for 3 minutes and spectra were quickly recorded. *Note: $Ir(ppy)_3$ emission is highly sensitive to the presence of oxygen, more than other common photocatalysts.*

A linear Stern – Vollmer plot was obtained at varying concentrations of both **6g** and **8a**, and K_{SV} constants were extracted according to the equation $I_0/I = 1 + K_{SV}[Q]$. There are slight differences between the values of the two constants, that are consistent with previous data collected in our group with similar allenamides[87]. However, these values are not sufficient to explain such a large difference in reaction rate, which is more reasonably imputable to the fast intramolecular step involved in the cyclization of enallenes **8**.

Comprehensive table of Stern – Vollmer constants

QUENCHER	K_{SV}	R^2
6g	271,5 M^{-1}	0.98
8a	427.6 M^{-1}	0.95



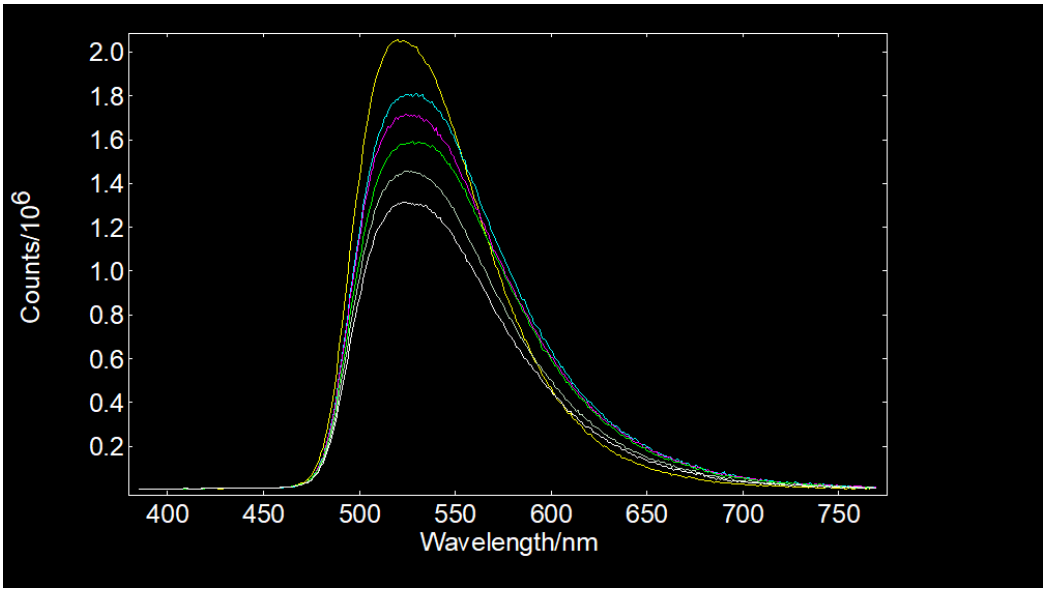
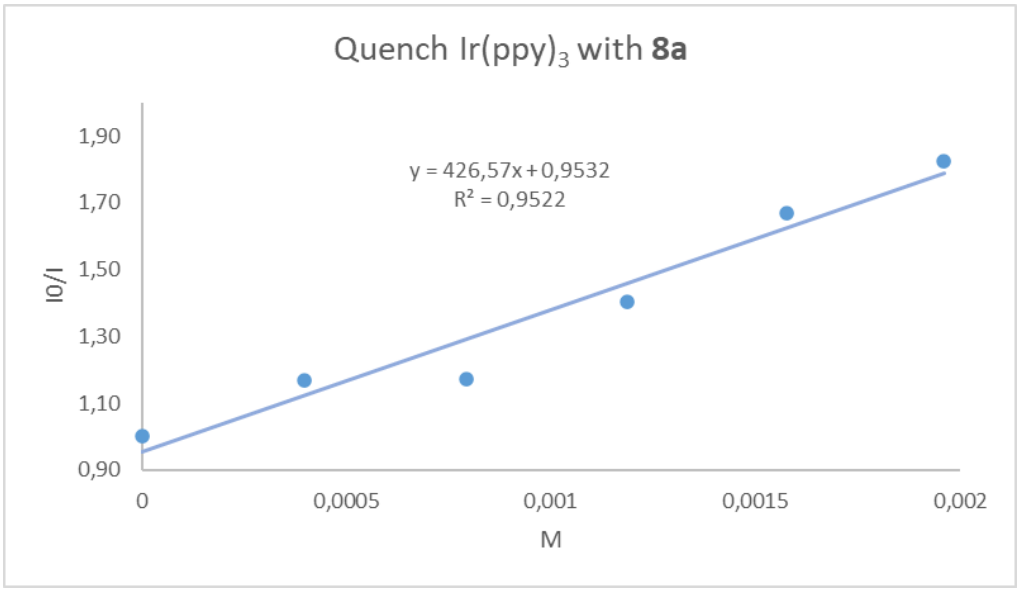


*Figure 13: Measured emissions for quench of $Ir(ppy)_3$ with **6g**.*



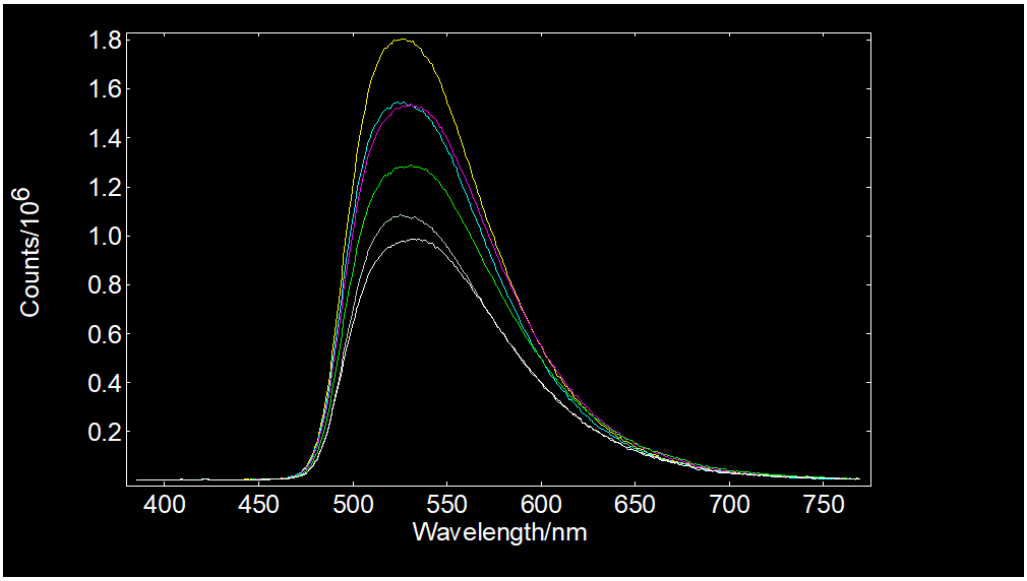
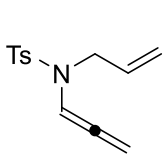


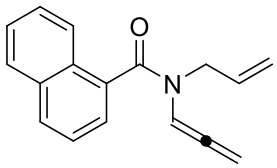
*Figure 14: Measured emissions for quench of $Ir(ppy)_3$ with **8a**.*

Unsuccessful substrates

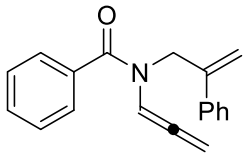
The following substrates did not afford the desired products **7** and **9**. Moreover, the aromatic compounds at the bottom were not able to dearomatize with model allene **6a**.



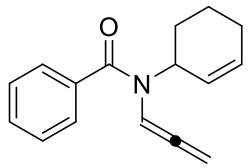
DEC



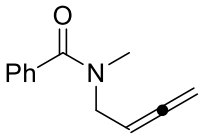
DEC + SR



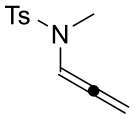
DEC + SR



SR



RSM



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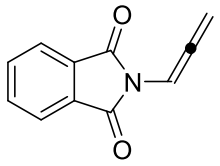
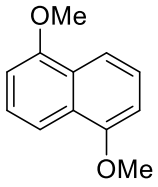
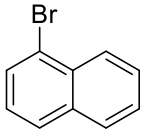


RSM

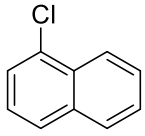
RSM: recovery of starting material
DEC: decomposition
SR: side reaction, intramolecular cyclization



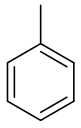
INSOLUBLE



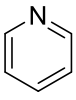
DEC



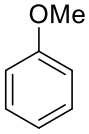
RSM + DEC



RSM



RSM



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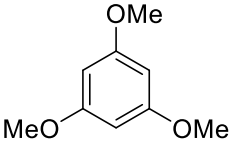
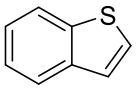


RSM



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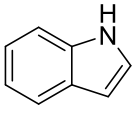


RSM

Synthesis of substrates

A) Synthesis of secondary amines

Synthesis of **N-(prop-2-yn-1-yl)butan-1-amine**

In a round bottom flask equipped with a magnetic stirring bar, propargyl bromide (1 equiv.) was added at 0 °C to *n*-butylamine (6 equiv.) and the resulting solution was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the mixture was quenched with a saturated $NaHCO_3$ solution and extracted with Et_2O (3 times). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (Yield = 50%).

Synthesis of **N-(prop-2-yn-1-yl)prop-2-en-1-amine**

In a round bottom flask equipped with a magnetic stirring bar, propargyl bromide (1 equiv.) was added at 0 °C to allylamine (6 equiv.) and the resulting solution was stirred for 4 h at room temperature. When the solution turns red, it was quenched with a saturated $NaHCO_3$ solution and extracted with Et_2O (3 times). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The vacuum was kept at 500 psi and the bath was at 35 °C. The crude was used for the next step without purification, with a slight excess of amine.

Synthesis of **N-(prop-2-yn-1-yl)but-3-en-1-amine**

In a round bottom flask equipped with a magnetic stirring bar, omoallyl bromide (1 equiv.) was added at 0 °C to propargylamine (6 equiv.) and the resulting solution was stirred for 4 h at room temperature. When the solution turns to red, it was quenched with a saturated $NaHCO_3$ solution and extracted with Et_2O (3 times). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The vacuum was kept at 500 psi and the bath was at 35 °C. The crude was used for the next step without purification, with a slight excess of amine.

B) N-Derivatization of primary amines

Representative procedure for the preparation of primary benzamides/carbamates
In a round bottom flask equipped with a magnetic stirring bar, primary amine (1 equiv.), DMAP (0.02 equiv.) and TEA (1 equiv.) were dissolved in DCM (0.25 M). The solution was cooled to 0 °C and chloride (1 equiv.) was then added. The mixture was stirred at room temperature until completion, monitoring the process by TLC. The solution was then quenched with saturated NH_4Cl solution and diluted with DCM. The organic phase was then washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 95-99%.
BOC_2O was used for **6e**.

C) Synthesis of propargyl amides/carbamates

Representative procedure for the preparation of propargyl amides/carbamates *via* secondary amines

In a 25 mL round bottom flask equipped with a magnetic stirring bar, the desired acid was dissolved in DCM (0.6 M) and a catalytic amount of DMF (3 drops) was added. The solution was then cooled to 0 °C and oxalyl chloride (1.5 equiv) was added. The solution was stirred for 1 h at room temperature. Then, the mixture was concentrated under reduced pressure to afford the acyl chloride, that was added to a solution of DMAP (0.02 equiv.), TEA (1 equiv.) and the desired secondary amine (1 equiv.) in DCM (0.25 M) at 0 °C. The mixture was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the solution was diluted with DCM and washed with saturated NH_4Cl solution, followed by a saturated $NaHCO_3$ one. The aqueous layers were extracted with DCM (3 times), and the combined organic phase was finally washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 45-99%.
Alkynyl amides precursors of **6f, 8g, 8i, 8m, 8o** were directly prepared from commercially available alkyl-, aryl-chlorides or chloroformate, BOC_2O was used for **8p**.

Representative procedure for the preparation of propargyl amides/carbamates *via* nucleophilic substitution **(GP-1)**

To a solution of primary amide/carbamate (1 equiv.) in DMF (0.6 M) at 0° C, NaH (60% in paraffine oil, 1.3 equiv.) was slowly added and the mixture was stirred for 1 h. The desired alkyl halide (1.5 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 48-98%.

Synthesis of **3-(prop-2-yn-1-yl)oxazolidin-2-one**

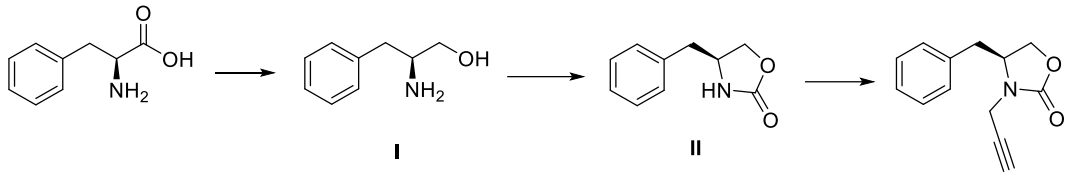
To a solution of oxazolidin-2-one (1 equiv.) in DMF (0.6 M) at 0° C, NaH (60% in paraffine oil, 1.3 equiv.) was slowly added and the mixture was stirred for 1 h. Propargyl bromide (1.5 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (Yield = 77%).

Representative procedure for the propargylation of amides *via* nucleophilic substitution

To a solution of primary amide (1 equiv.) in DMF (0.6 M) at 0° C, NaH (60% in paraffine oil, 1.3 equiv.) was slowly added and the mixture was stirred for 1 h. Propargyl bromide (1.5 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product. Yields between 87-99%.

D) Preparation of precursors of 6b, 6n

Synthetic route to afford **(S)-4-benzyl-3-(propa-1,2-dien-1-yl)oxazolidin-2-one**



I II

A Schlenk-type flask under nitrogen was charged with $LiAlH_4$ (2 equiv.) in THF (0.33 M). L-Phenylalanine (1 equiv.) was added at 0 °C to the mixture, that was stirred for 1 h at the same temperature. Then, the reaction was refluxed for 18 h. After complete conversion as monitored by TLC, the temperature decreased to 0 °C and the reaction was quenched with NaOH (2M). After filtration on Celite®, the solution was diluted with EtOAc and washed twice with brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (DCM/MeOH gradient) to afford the desired aminoalcohol **I** (Yield = 74%).

A distillation apparatus was charged with aminoalcohol **I** (1 equiv.), diethyl carbonate (2 equiv.) and dry K_2CO_3 (0.9 equiv.). The mixture was heated to 145 °C and stirred. Meanwhile, co product ethanol was collected in another flask and was used to monitor the reaction. After 2 h, when ethanol stopped collecting, the mixture was cooled to room temperature and potassium carbonate was filtered off. The solution was then diluted with DCM and washed twice with brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford (S)-4-benzyloxazolidin-2-one **II** (Yield = 90%).

To a solution of (S)-4-benzyloxazolidin-2-one **II** (1 equiv.) in DMF (0.6 M) at 0° C, NaH (60% in paraffine oil, 1.5 equiv.) was slowly added and the mixture was stirred for 1 h. Propargyl bromide (4 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford (S)-4-benzyl-3-(propa-1,2-dien-1-yl)oxazolidin-2-one **6b**(Yield = 78%).

Synthesis of **1-(prop-2-yn-1-yloxy)naphthalene**

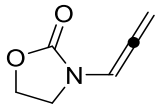
In a round bottom flask were added 1-naphthol (1.2 equiv.) and potassium carbonate (1.6 equiv.) in DMF (0.66 M). The mixture was stirred at room temperature for 1 h, then propargyl bromide (1 equiv.) was slowly added and the mixture was reacted for 18 h. After complete conversion as monitored by TLC, potassium carbonate was filtered off and the solution was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **6n** (Yield = 95%).

General procedure for the synthesis of allenamides **(GP-2)**

The desired propargyl amide/carbamate (1 equiv.) and THF (0.20 M) were sequentially added to a Schlenk tube equipped with a magnetic stirring bar. ^{t}BuOK (0.2 equiv.) was added and the resulting mixture was stirred at room temperature for 10 minutes. After complete conversion as monitored by TLC, 5 ml of a saturated NH_4Cl solution were added. The mixture was extracted with EtOAc (3 x 15 ml), the organic layers separated and dried over Na_2SO_4. The solution was concentrated under reduced pressure and the crude purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the corresponding allene.
Note: sometimes the isomerization is not quantitative with 0.2 equiv. of ^{t}BuOK. Other portions of base were added.

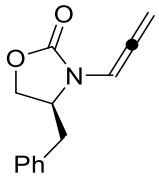
Characterization of substrates

3-(propa-1,2-dien-1-yl)oxazolidin-2-one



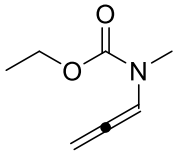
Allene **6a** was prepared following general procedure **GP-2** from the corresponding propargyl carbamate (179.0 mg, 1.43 mmol). White solid (108.4 mg, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 (t, *J* = 6.4 Hz, 1H), 5.42 (d, *J* = 6.3 Hz, 2H), 4.45 – 4.37 (m, 2H), 3.63 – 3.56 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.4, 155.3, 97.0, 87.9, 62.3, 43.1. **ESI-MS** calcd for $C_6H_7NNaO_2$ $[M+Na]^+$, 148.04 found 148.16.

(S)-4-benzyl-3-(propa-1,2-dien-1-yl)oxazolidin-2-one



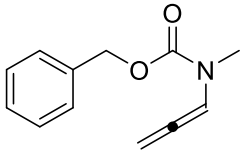
Allene **6b** was prepared following general procedure **GP-2** from the corresponding propargyl carbamate (215.2 mg, 1 mmol). Pale yellow oil (194.4 mg, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.26 (m, 3H), 7.22 – 7.15 (m, 2H), 6.93 (t, *J* = 6.5 Hz, 1H), 5.63 – 5.49 (m, 2H), 4.29 – 4.23 (m, 1H), 4.20 – 4.09 (m, 2H), 3.28 (dd, *J* = 13.7, 3.2 Hz, 1H), 2.76 (dd, *J* = 13.7, 8.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.7, 155.0, 135.4, 129.3, 128.9, 127.3, 96.0, 87.9, 66.7, 55.6, 37.2. **ESI-MS** calcd for $C_{13}H_{13}NNaO_2$ $[M+Na]^+$ 238.24, found 238.59.

Ethyl methyl(propa-1,2-dien-1-yl)carbamate



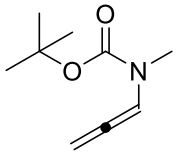
Allene **6c** was prepared following general procedure **GP-2** from the corresponding propargyl carbamate (114.4 mg, 0.81 mmol). *Note: it was necessary add 1% TEA to the eluent to prevent the degradation of the product during the separation.* Pale yellow oil (59.7 mg, 52% yield). Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.02 (m, 1H RotA, 1H RotB), 5.36 (s, 2H RotA, 2H RotB), 4.19 (q, *J* = 7.1 Hz, 2H RotA, 2H RotB), 3.00 – 2.88 (m, 3H RotA, 3H RotB), 1.28 (t, *J* = 7.1 Hz, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.7, 200.7, 154.1, 101.6, 101.0, 87.3, 86.7, 62.12, 62.05, 31.8, 31.6, 14.6. **ESI-MS** calcd for $C_7H_{12}NO_2$ $[M+H]^+$ 142.18, found 142.35.

Benzyl methyl(propa-1,2-dien-1-yl)carbamate



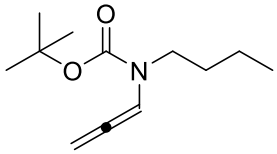
Allene **6d** was prepared following general procedure **GP-2** from the corresponding propargyl carbamate (168.2 mg, 0.83 mmol). Pale yellow oil (140.0 mg, 83% yield). Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.30 (m, 5H RotA, 5H RotB), 7.27 – 7.21 (m, 1H RotB), 7.12 (t, *J* = 6.4 Hz, 1H RotA), 5.42 – 5.34 (m, 2H RotA, 2H RotB), 5.20 (s, 2H RotA, 2H RotB), 3.01 – 2.94 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.7, 200.8, 154.0, 153.9, 136.3, 136.2, 128.6, 128.2, 128.1, 101.6, 101.0, 87.5, 86.9, 67.8, 67.7, 32.1, 31.8. **ESI-MS** calcd for $C_{12}H_{13}KNO_2$ $[M+K]^+$ 242.34, found 242.42.

Tert-butyl methyl(propa-1,2-dien-1-yl)carbamate



Allene **6e** was prepared following general procedure **GP-2** from the corresponding propargyl carbamate (165.0 mg, 0.98 mmol). *Note: it was necessary add 1% TEA to the eluent to prevent the degradation of the product during the separation.* Yellow oil (135.4 mg, 81% yield). Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (s, 1H RotB), 7.02 (s, 1H RotA), 5.33 (s, 2H RotA, 2H RotB), 2.88 (s, 3H RotA, 3H RotB), 1.47 (s, 9H RotA, 9H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.8, 200.7, 153.1, 153.0, 101.5, 101.4, 87.0, 86.4, 80.9, 80.8, 31.9, 31.3, 28.3. **ESI-MS** calcd for $C_9H_{16}NO_2$ $[M+H]^+$ 170.22, found 169.98.

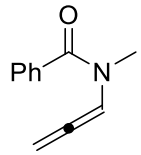
Tert-butyl butyl(propa-1,2-dien-1-yl)carbamate



Allene **6f** was prepared following general procedure **GP-2** from the corresponding propargyl carbamate (190.3 mg, 0.9 mmol). Pale yellow oil (98.3 mg, 52% yield). Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.11 (s, 1H RotA), 6.95 (s, 1H RotB), 5.29 (d, *J* = 5.7 Hz, 2H RotA, 2H RotB), 3.37 – 3.24 (m, 2H RotA, 2H RotB), 1.53 – 1.39 (m, 11H RotA, 11H RotB), 1.27 (h, *J* = 7.4 Hz, 2H RotA, 2H RotB), 0.88 (t, *J* = 7.4 Hz, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.7, 200.5, 153.0, 152.6, 100.4, 100.3, 86.6, 86.0, 80.7, 80.6,

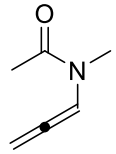
44.7, 44.4, 30.0, 29.6, 28.3, 19.9, 19.8, 13.9. **ESI-MS** calcd for $C_{12}H_{22}NO_2$ $[M+H]^+$ 212.16, found 212.88.

N-methyl-N-(propa-1,2-dien-1-yl)benzamide



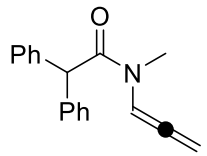
Allene **6g** was prepared following general procedure **GP-2** from the corresponding propargyl amide (173.7 mg, 1 mmol). Pale yellow oil (104.2 mg, 60% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (brs, 1H RotB), 7.54 – 7.40 (m, 5H RotA, 5H RotB), 6.76 (brs, 1H RotA), 5.49 – 5.34 (m, 2H RotA, 2H RotB), 3.24 – 2.95 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 200.0, 169.6, 164.4, 135.3, 134.9, 130.2, 128.5, 127.9, 127.4, 103.4, 100.0, 87.0, 35.8, 31.4. **ESI-MS** calcd for $C_{11}H_{12}NO$ $[M+H]^+$ 174.23, found 174.48. *(Partial decomposition was observed during the acquisition of NMR spectra).*

N-methyl-N-(propa-1,2-dien-1-yl)acetamide



Allene **6h** was prepared following general procedure **GP-2** from the corresponding propargyl amide (182.3 mg, 1.64 mmol). Pale yellow oil (97.1 mg, 53% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (t, *J* = 6.4 Hz, 1H RotB), 6.76 (t, *J* = 6.2 Hz, 1H RotA), 5.39 – 5.36 (m, 2H RotA, 2H RotB), 3.02 (s, 3H RotA), 2.96 (s, 3H RotB), 2.19 – 2.15 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.3, 200.9, 168.8, 168.5, 102.0, 99.5, 87.1, 86.7, 33.6, 30.7, 22.2, 21.5. **ESI-MS** calcd for $C_6H_{10}NO$ $[M+H]^+$ 112.15, found 112.39.

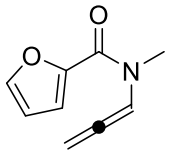
N-methyl-2,2-diphenyl-N-(propa-1,2-dien-1-yl)acetamide



Allene **6i** was prepared following general procedure **GP-2** from the corresponding propargyl amide (269.3 mg, 1 mmol). White solid (152.9 mg, 57% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (t, *J* = 6.4 Hz, 1H RotA), 7.37 – 7.26 (m, 10H RotA, 10H RotB),

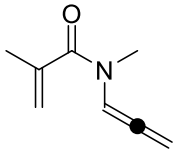
6.90 (t, *J* = 6.2 Hz, 1H RotB), 5.41 – 5.31 (m, 3H RotA, 3H RotB), 3.07 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 201.2, 170.1, 170.0, 139.0, 138.9, 129.0, 128.7, 127.2, 101.3, 100.2, 87.3, 86.6, 55.6, 55.1, 33.2, 31.8. **ESI-MS** calcd for $C_{18}H_{18}NO$ $[M+H]^+$ 264.14, found 264.21.

N-methyl-N-(propa-1,2-dien-1-yl)furan-2-carboxamide



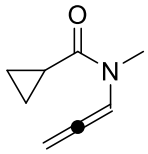
Allene **6j** was prepared following general procedure **GP-2** from the corresponding propargyl amide (163.1 mg, 1 mmol). Yellow pale oil (144.7 mg, 88% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 1.7 Hz, 1H), 7.47 – 7.45 (m, 1H), 7.06 (d, *J* = 3.5 Hz, 1H), 6.49 (dd, *J* = 3.5, 1.8 Hz, 1H), 5.42 (d, *J* = 6.3 Hz, 2H), 3.19 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 201.1, 158.1, 147.2, 144.6, 117.5, 111.4, 102.2, 100.7, 87.2, 34.1, 32.1. **ESI-MS** calcd for $C_9H_{10}NO_2$ $[M+H]^+$ 164.07, found 164.17.

N-methyl-N-(propa-1,2-dien-1-yl)methacrylamide



Enallene **6k** was prepared following general procedure **GP-2** from the corresponding enyne (159.1 mg, 1.16 mmol). Pale yellow liquid (75.2 mg, 47% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (s, 1H RotB), 7.01 (s, 1H RotA), 5.39 (d, *J* = 6.3 Hz, 2H RotA, 2H RotB), 5.31 (d, *J* = 6.5 Hz, 1H RotA, 1H RotB), 5.15 (s, 1H RotA, 1H RotB), 3.03 (s, 3H RotA, 3H RotB), 1.98 (t, *J* = 1.4 Hz, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 200.1, 170.5, 139.7, 117.7, 116.8, 102.7, 99.3, 86.7, 34.7, 30.5, 20.3. **ESI-MS** calcd for $C_8H_{12}NO$ $[M+H]^+$ 138.09, found 138.55.

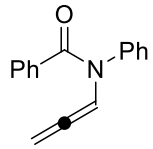
N-methyl-N-(propa-1,2-dien-1-yl)cyclopropanecarboxamide



Allene **6l** was prepared following general procedure **GP-2** from the corresponding propargyl amide (148.3 mg, 1.08 mmol). Yellow oil (74.8 mg, 51% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (t, *J* = 6.4 Hz, 1H RotA), 7.17 (t, *J* = 6.2 Hz, 1H RotB), 5.55 – 5.23 (m, 2H RotA, 2H RotB), 3.21 (s, 3H RotA), 3.01 (s, 3H RotB), 1.84 (tt, *J* = 8.2, 4.8 Hz,

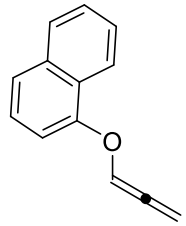
1H RotA, 1H RotB), 1.05 (h, *J* = 4.2 Hz, 2H RotA, 2H RotB), 0.85 (dt, *J* = 8.0, 3.4 Hz, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.2, 201.5, 171.9, 171.8, 101.5, 100.2, 87.0, 86.6, 32.9, 31.5, 11.9, 11.5, 8.3, 7.9. **ESI-MS** calcd for $C_8H_{12}NO$ $[M+H]^+$ 138.09, found 138.00.

N-phenyl-N-(propa-1,2-dien-1-yl)benzamide



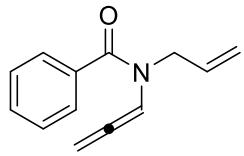
Allene **6m** was prepared following general procedure **GP-2** from the corresponding propargyl amide (235.3 mg, 1 mmol). Pale orange solid (108.4 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (t, *J* = 6.4 Hz, 1H), 7.44 – 7.32 (m, 2H), 7.38 – 7.10 (m, 6H), 7.11 (dd, *J* = 7.4, 1.8 Hz, 2H), 5.10 (d, *J* = 6.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 168.5, 140.3, 135.1, 130.0, 128.85, 128.82, 128.5, 127.8, 127.5, 102.0, 86.8. **ESI-MS** calcd for $C_{16}H_{14}NO$ $[M+H]^+$ 236.11, found 236.23.

1-(propa-1,2-dien-1-yloxy)naphthalene



Allene **6n** was prepared following general procedure **GP-2** from the corresponding propargyl naphthol (182.2 mg, 1 mmol). Pale yellow solid (111.7 mg, 61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.35 – 8.28 (m, 1H), 7.89 – 7.83 (m, 1H), 7.61 – 7.50 (m, 3H), 7.43 (t, *J* = 7.9 Hz, 1H), 7.14 (d, *J* = 6.6 Hz, 1H), 7.05 (t, *J* = 5.9 Hz, 1H), 5.52 (d, *J* = 5.9 Hz, 2H). Spectroscopic data are consistent with those reported in literature[94].

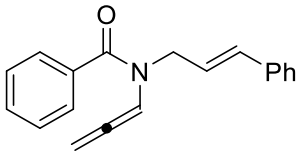
N-allyl-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8a** was prepared following general procedure **GP-2** from the corresponding enyne (199.3 mg, 1 mmol). Pale yellow oil (143.6 mg, 72% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.31 (m, 5H RotA, 6H RotB), 6.65 (s, 1H RotA), 5.94 – 5.65 (m, 1H RotA, 1H RotB), 5.39 – 5.03 (m, 4H RotA, 4H RotB), 4.34 – 3.88 (m, 2H RotA, 2H

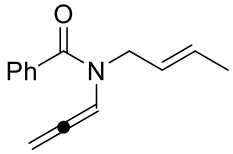
RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.3, 169.9, 169.1, 135.3, 134.9, 132.8, 132.5, 130.3, 128.4, 128.0, 126.8, 117.2, 102.2, 98.5, 87.0, 49.9, 46.5. **ESI-MS** calcd for $C_{13}H_{14}NO$ $[M+H]^+$ 200.11, found 200.43.

N-cinnamyl-N-(propa-1,2-dien-1-yl)benzamide



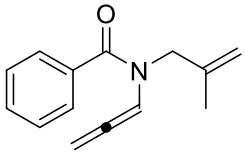
Enallene **8b** was prepared following general procedure **GP-2** from the corresponding enyne (319 mg, 1.16 mmol). Yellow viscous oil (216.6 mg, 68% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78 – 7.11 (m, 10H RotA, 11H RotB), 6.79 – 6.05 (m, 3H RotA, 2H RotB), 5.48 – 5.36 (m, 2H RotA, 2H RotB), 4.56 – 4.11 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.0, 200.4, 170.0, 169.2, 136.8, 135.4, 134.8, 133.4, 132.3, 130.4, 128.6, 128.5, 128.1, 127.7, 127.0, 126.5, 126.4, 124.1, 102.2, 98.6, 87.1, 49.7, 46.3. **ESI-MS** calcd for $C_{19}H_{17}NNaO$ $[M+Na]^+$ 298.12, found 297.82.

(E)-N-(but-2-en-1-yl)-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8c** was prepared following general procedure **GP-2** from the corresponding enyne (255.4 mg, 1 mmol). Yellow oil (178.0 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.37 (m, 5H), 6.63 (s, 1H), 5.70 – 5.32 (m, 4H), 4.06 (m, 2H), 1.69 (d, *J* = 6.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.1, 200.4, 169.7, 169.0, 135.0, 130.2, 129.2, 128.4, 128.4, 128.0, 126.9, 125.2, 102.1, 98.4, 86.8, 49.4, 46.0, 17.8. **ESI-MS** calcd for $C_{14}H_{16}NO$ $[M+H]^+$ 214.12, found 213.97.

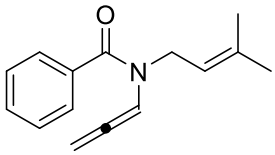
N-(2-methylallyl)-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8d** was prepared following general procedure **GP-2** from the corresponding enyne (170.6 mg, 0.8 mmol). Pale yellow oil (140.3 mg, 82% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 7.31 (m, 5H RotA, 6H RotB), 6.67 (brs, 1H RotA), 5.30 (s, 2H RotA, 2H RotB), 4.96 – 4.78 (m, 2H RotA, 2H RotB), 4.24 (s, 2H RotA), 3.86 (s, 2H

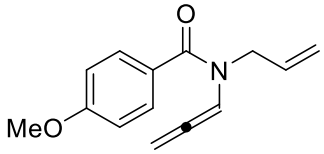
RotB), 1.84 – 1.51 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.4, 170.0, 169.2, 139.9, 135.3, 135.0, 130.2, 128.5, 128.4, 127.9, 126.7, 111.0, 102.3, 98.8, 86.8, 53.1, 49.4, 20.2. **ESI-MS** calcd for $C_{14}H_{16}NO$ $[M+H]^+$ 214.12, found 214.06. *(Partial decomposition was observed during the acquisition of NMR spectra).*

N-(3-methylbut-2-en-1-yl)-N-(propa-1,2-dien-1-yl)benzamide



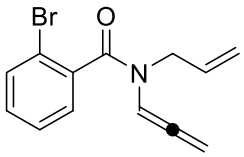
Enallene **8e** was prepared following general procedure **GP-2** from the corresponding enyne (181.8 mg, 0.8 mmol). Orange oil (103 mg, 57% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 – 7.31 (m, 5H RotA, 6H RotB), 6.62 (s, 1H RotA), 5.41 – 5.07 (m, 3H RotA, 3H RotB), 4.35 – 3.83 (m, 2H RotA, 2H RotB), 1.89 – 1.12 (m, 6H RotA, 6H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 200.1, 169.7, 169.1, 135.5, 135.2, 134.7, 130.1, 128.4, 128.0, 127.0, 119.7, 102.2, 98.5, 86.5, 46.3, 42.7, 25.8, 18.2. **ESI-MS** calcd for $C_{15}H_{18}NO$ $[M+H]^+$ 228.14, found 228.66.

N-allyl-4-methoxy-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8f** was prepared following general procedure **GP-2** from the corresponding enyne (183.4 mg, 0.8 mmol). Pale yellow oil (127.6 mg, 87% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.6 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.87 – 6.64 (m, 1H), 5.84 (brs, 1H), 5.34 (d, *J* = 6.3 Hz, 2H), 5.26 – 5.14 (m, 2H), 4.20 (brs, 2H), 3.83 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.5, 161.3, 132.8, 130.0, 117.1, 113.7, 102.4, 86.9, 55.4, 46.9. **ESI-MS** calcd for $C_{14}H_{16}NO_2$ $[M+H]^+$ 230.12, found 229.84.

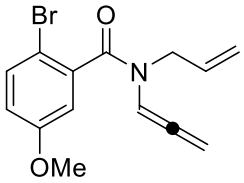
N-allyl-2-bromo-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8g** was prepared following general procedure **GP-2** from the corresponding enyne (236.4 mg, 0.85 mmol). Pale yellow viscous oil (149.1 mg, 63% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 – 7.58 (m, 1H RotA, 2H RotB), 7.44 – 7.25 (m, 3H RotA,

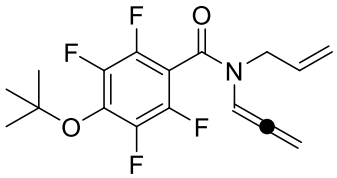
3H RotB), 6.34 (t, J = 6.3 Hz, 1H RotA), 5.98 – 5.85 (m, 1H RotA), 5.73 – 5.62 (m, 1H RotB), 5.46 – 5.22 (m, 4H RotA, 2H RotB), 5.16 – 5.09 (m, 1H RotB), 5.03 – 4.95 (m, 1H RotB), 4.46 – 4.17 (m, 2H RotA), 3.99 – 3.77 (m, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.6, 167.3, 166.8, 137.3, 137.0, 133.0, 132.8, 132.2, 132.0, 130.8, 130.6, 128.4, 128.0, 127.8, 127.4, 119.5, 119.2, 117.6, 117.4, 100.9, 97.8, 87.4, 87.2, 49.4, 46.0. **ESI-MS** calcd for $C_{13}H_{13}BrNO$ $[M+H]^+$ 278.02, found 277.80.

N-allyl-2-bromo-5-methoxy-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8h** was prepared following general procedure **GP-2** from the corresponding enyne (277.4 mg, 0.9 mmol). Pale yellow viscous oil (185.6 mg, 67% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (t, *J* = 6.5 Hz, 1H RotB), 7.49 – 7.41 (m, 1H RotA, 1H RotB), 6.86 – 6.75 (m, 2H RotA, 2H RotB), 6.35 (t, *J* = 6.3 Hz, 1H RotA), 5.96 – 5.82 (m, 1H RotA), 5.75 – 5.61 (m, 1H RotB), 5.43 – 5.26 (m, 3H RotA, 2H RotB), 5.25 – 5.19 (m, 1H RotA), 5.14 – 5.09 (m, 1H RotB), 5.03 – 4.96 (m, 1H RotB), 4.43 – 4.15 (m, 2H RotA), 3.99 – 3.72 (m, 3H RotA, 5H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 200.6, 167.1, 166.6, 159.2, 158.8, 137.9, 137.6, 133.8, 133.7, 132.4, 132.0, 117.7, 117.3, 117.2, 117.0, 113.4, 113.3, 109.6, 109.3, 100.9, 97.7, 87.4, 87.3, 55.7, 55.6, 49.5, 45.9. **ESI-MS** calcd for $C_{14}H_{15}BrNO_2$ $[M+H]^+$ 308.03, found 307.85.

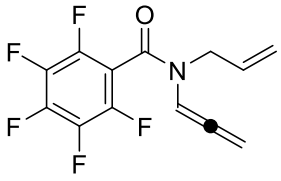
N-allyl-4-(tert-butoxy)-2,3,5,6-tetrafluoro-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8i** was prepared following general procedure **GP-2** from the corresponding enyne (289.2 mg, 1 mmol). *Note: The correspondent allene was obtained in mixture with allene **3j** as a consequence of the base excess performing the isomerization.* Yellow pale oil (128.8 mg, 45% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.53 (t, *J* = 6.5 Hz, 1H RotB), 6.39 (t, *J* = 6.3 Hz, 1H RotA), 5.82 (ddt, *J* = 17.3, 10.5, 5.3 Hz, 1H RotA), 5.67 – 5.52 (m, 1H RotB), 5.43 (d, *J* = 6.5 Hz, 2H RotB), 5.34 (d, *J* = 6.3 Hz, 2H RotA), 5.24 (t, *J* = 1.6 Hz, 1H RotA), 5.24 – 5.20 (m, 1H RotA), 5.10 (dq, *J* = 10.3, 1.4 Hz, 1H RotB), 4.95 (d, *J* = 17.2 Hz, 1H RotB), 4.30 (dd, *J* = 5.4, 1.7 Hz, 2H RotA), 3.93 (d, *J* = 5.3 Hz, 2H RotB), 1.40 (s, 9H RotA), 1.39 (s, 9H RotB). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 202.8,

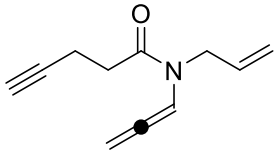
201.3, 158.0, 157.6, 144.8 – 144.2 (m), 144.1 – 143.6 (m), 143.1 – 142.3 (m), 142.5 – 141.8 (m), 136.0 (t, *J* = 13.5 Hz), 135.8 (t, *J* = 13.5 Hz), 131.7, 131.3, 117.8, 117.5, 110.5 (t, *J* = 21.3 Hz), 110.1 (t, *J* = 21.0 Hz), 100.0, 98.0, 88.1, 87.6, 86.2, 49.7, 46.8, 28.5. **^{19}F NMR** (565 MHz, CDCl3) δ -142.2 (dp, *J* = 18.2, 5.8 Hz, 2F RotA, 2F RotB), -146.4 – -151.4 (m, 2F RotA, 2F RotB). **ESI-MS** calcd for $C_{17}H_{17}F_4NNaO_2$ $[M+Na]^+$ 365.90, found 366.10.

N-allyl-2,3,4,5,6-pentafluoro-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8j** was prepared following general procedure **GP-2** from the corresponding enyne (289.2 mg, 1 mmol). *Note: The correspondent allene was obtained in mixture with allene **3i**.* Yellow pale oil (122.2 mg, 42% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.52 – 7.50 (m, 1H RotB), 6.33 (t, *J* = 6.3 Hz, 1H RotA), 5.81 (ddt, *J* = 17.5, 10.6, 5.4 Hz, 1H RotA), 5.64 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H RotB), 5.44 (d, *J* = 6.5 Hz, 2H RotB), 5.35 (d, *J* = 6.2 Hz, 2H RotA), 5.23 (dt, *J* = 3.7, 1.4 Hz, 1H RotA), 5.22 – 5.20 (m, 1H RotA), 5.13 (dq, *J* = 10.5, 1.4 Hz, 1H RotB), 5.00 (dt, *J* = 17.2, 1.8 Hz, 1H RotB), 4.29 (dt, *J* = 5.4, 1.7 Hz, 2H RotA), 3.93 – 3.92 (m, 2H RotB). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 202.7, 201.5, 156.9, 156.5, 144.3 – 143.7 (m), 143.5 – 142.9 (m), 142.6 – 142.0 (m), 141.8 – 140.9 (m), 139.0 – 138.3 (m), 137.7 – 136.8 (m), 131.5, 131.1, 117.9, 117.7, 112.5 – 109.3 (m), 99.6, 97.9, 88.2, 87.7, 49.6, 47.0. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -135.1 – -142.1 (m, 2F RotA, 2F RotB), -150.9 (tt, *J* = 20.6, 3.0 Hz, 1F RotA), -151.2 (tt, *J* = 20.6, 2.7 Hz, 1F RotB), -159.5 (dddd, *J* = 26.0, 20.6, 11.6, 5.1 Hz, 2F RotA, 2F RotB). **ESI-MS** calcd for $C_{13}H_9F_5NO$ $[M+H]^+$ 290.05, found 289.05.

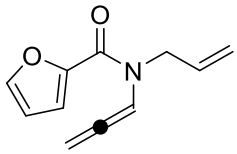
N-allyl-N-(propa-1,2-dien-1-yl)pent-4-ynamide



Enallene **8k** was prepared following general procedure **GP-2** from the corresponding enyne (196.3 mg, 1.12 mmol). Yellow oil (61,9 mg, 32% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (t, *J* = 6.4 Hz, 1H Rot A), 6.72 (t, *J* = 6.3 Hz, 1H Rot B), 5.77 (dddd, *J* = 19.2, 11.1, 9.6, 5.2 Hz, 1H RotA, 1H RotB), 5.38 (dd, *J* = 6.4, 1.9 Hz, 2H RotA, 2H RotB), 5.23 – 5.11 (m, 2H RotA, 2H RotB), 4.15 – 4.04 (m, 2H RotA, 2H RotB), 2.73 –

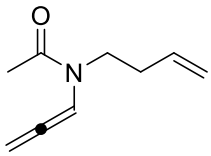
2.54 (m, 4H RotA, 4H RotB), 1.99 (dt, *J* = 4.9, 2.6 Hz, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.1, 201.5, 169.3, 168.6, 132.5, 132.0, 117.1, 116.5, 99.6, 98.7, 87.3, 86.8, 83.2, 68.9, 68.9, 47.7, 46.6, 32.7, 32.6, 14.3. **ESI-MS** calcd for $C_{11}H_{14}NO$ $[M+H]^+$ 176.11, found 176.43.

N-allyl-N-(propa-1,2-dien-1-yl)furan-2-carboxamide



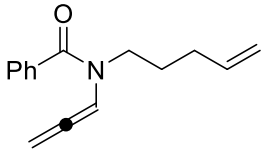
Enallene **8l** was prepared following general procedure **GP-2** from the corresponding enyne (189.2 mg, 1 mmol). Orange oil (104.8 mg, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.31 (m, 2H), 7.11 (dd, *J* = 3.5, 0.8 Hz, 1H), 6.49 (dd, *J* = 3.5, 1.8 Hz, 1H), 5.87 (ddt, *J* = 17.1, 10.4, 5.2 Hz, 1H), 5.39 (d, *J* = 6.4 Hz, 2H), 5.22 – 5.17 (m, 1H), 5.17 (t, *J* = 1.7 Hz, 1H), 4.30 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 201.6, 157.8, 147.0, 144.71, 132.7, 117.5, 117.1, 111.5, 100.8, 99.7, 87.2, 48.5, 47.8. **ESI-MS** calcd for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.09, found 189.95.

N-(but-3-en-1-yl)-N-(propa-1,2-dien-1-yl)acetamide



Enallene **8m** was prepared following general procedure **GP-2** from the corresponding enyne (158.6 mg, 1.05 mmol). Pale yellow oil (78.9 mg, 50% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (t, *J* = 6.5 Hz, 1H RotB), 6.69 (t, *J* = 6.2 Hz, 1H RotA), 5.82 – 5.70 (m, 1H RotA, 1H RotB), 5.41 – 5.37 (m, 2H RotA, 2H RotB), 5.16 – 4.97 (m, 2H RotA, 2H RotB), 3.59 – 3.54 (m, 2H RotA), 3.50 – 3.44 (m, 2H RotB), 2.39 – 2.23 (m, 2H RotA, 2H RotB), 2.21 – 2.16 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.1, 200.9, 168.5, 168.2, 135.2, 134.0, 117.6, 116.5, 100.9, 98.0, 86.8, 86.5, 46.1, 43.1, 32.5, 31.7, 21.9, 21.8. **ESI-MS** calcd for $C_9H_{14}NO$ $[M+H]^+$ 152.11, found 151.78.

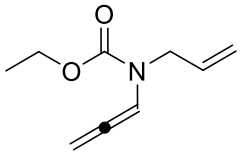
N-(pent-4-en-1-yl)-N-(propa-1,2-dien-1-yl)benzamide



Enallene **8n** was directly obtained following general procedure **GP-1** from the corresponding propargyl amide (478.1 mg, 3 mmol). *Note: It is well known in*

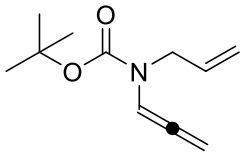
literature that sometimes, performing the alkylation reaction with NaH, you can directly obtain allene in mixture with the correspondent enyne. Pale yellow oil (235.2 mg, 34% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.34 (m, 5H RotA, 5H RotB), 6.62 (s, 1H RotA, 1H RotB), 5.81 (ddt, *J* = 16.6, 10.4, 6.2 Hz, 1H RotA, 1H RotB), 5.31 (d, *J* = 6.2 Hz, 2H RotA. 2H RotB), 5.06 – 4.80 (m, 2H RotA, 2H RotB), 3.65 (t, *J* = 7.6 Hz, 2H Rot A), 3.34 – 3.32 (m, 2H Rot B), 2.21 – 1.60 (m, 4H RotA, 4H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.5, 199.9, 169.6, 169.1, 137.9, 137.1, 135.6, 135.2, 130.2, 129.8, 128.5, 127.9, 126.7, 115.3, 115.0, 102.4, 98.3, 86.7, 47.2, 44.0, 31.1, 30.7, 27.3, 26.4. **ESI-MS** calcd for $C_{15}H_{18}NO$ $[M+H]^+$ 228.13, found 228.24.

Ethyl allyl(propa-1,2-dien-1-yl)carbamate



Enallene **8o** was prepared following general procedure **GP-2** from the corresponding enyne (142.1 mg, 0.85 mmol). Yellow pale oil (115.6 mg, 81% yield). Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.14 (t, *J* = 6.2 Hz, 1H RotA), 6.98 (t, *J* = 6.5 Hz, 1H RotB), 5.74 – 5.71 (m, 1H RotA, 1H RotB), 5.30 (s, 2H RotA, 1H RotB), 5.09 (s, 2H RotA, 2H RotB), 4.17 (q, *J* = 7.1 Hz, 2H RotA, 2H RotB), 3.99 – 3.92 (m, 2H RotA, 2H RotB), 1.25 (dt, *J* = 12.9, 6.8 Hz, 3H RotA, 3H RotB). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 201.8, 200.9, 153.9, 153.7, 132.9, 116.8, 116.5, 100.4, 99.9, 87.4, 86.9, 62.2, 47.1, 14.6. **ESI-MS** calcd for $C_9H_{14}NO_2$ $[M+H]^+$ 168.14, found 168.10.

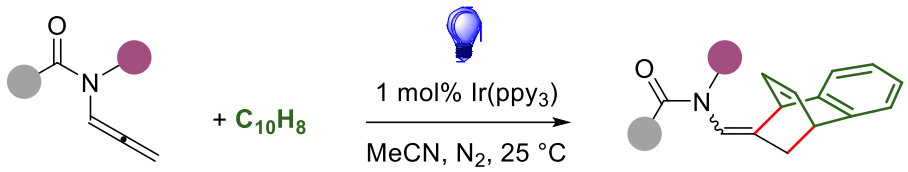
Tert-butyl allyl(propa-1,2-dien-1-yl)carbamate



Enallene **8p** was prepared following general procedure **GP-2** from the corresponding enyne (128.9 mg, 0.66 mmol). White liquid (73.9 mg, 57% yield). Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 – 6.94 (m, 1H RotA, 1H RotB), 5.85 – 5.71 (m, 1H RotA, 1H RotB), 5.39 – 5.28 (m, 2H RotA, 2H RotB), 5.19 – 5.07 (m, 2H RotA, 2H RotB), 4.04 – 3.88 (m, 2H RotA, 2H RotB), 1.50 (s, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.7, 200.8, 152.8, 133.1, 116.2, 100.2, 87.1, 86.6, 81.0, 47.4, 46.8, 28.3. **ESI-MS** calcd for $C_{11}H_{18}NO_2$ $[M+H]^+$ 196.13, found 195.87. *(Partial decomposition was observed during the acquisition of NMR spectra).*

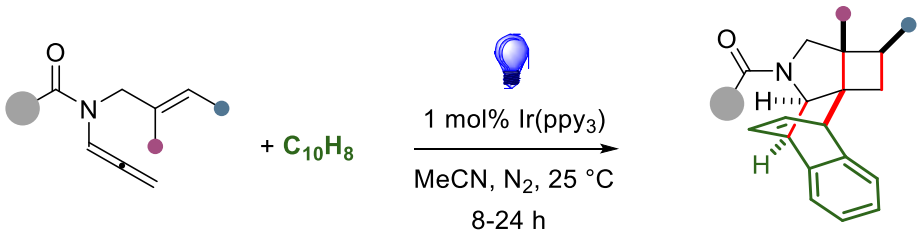
Synthesis and characterization of products

Photocatalytic reactions [GP-3A]:



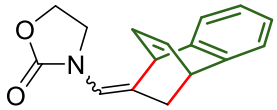
A vial was charged with substrate **6** (1 equiv., 0.15 mmol), **Ir(ppy)$_3$** (1 mol%), naphthalene (20 equiv.), and dry ACN (0.1 M). The solution was transferred into an NMR tube capped with a rubber septum, degassed by freeze-pump-thaw (3 times) and the tube was placed in an oil bath kept at 25 °C by means of a chiller. The tube was irradiated with a blue LED strip for 20 – 72 h. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel; the catalyst and the excess of naphthalene were removed, and could be recovered, using toluene as eluent prior to the separation of desired products (*n*-hexane/EtOAc, under gradient).

Photocatalytic reactions [GP-3B]:



A vial was charged with substrate **8** (1 equiv., 0.15 mmol), **Ir(ppy)$_3$** (1 mol%), naphthalene (20 equiv.), and dry ACN (0.1 M). The solution was transferred into an NMR tube capped with a rubber septum, degassed by freeze-pump-thaw (3 times) and the tube was placed in an oil bath kept at 25 °C by means of a chiller. The tube was irradiated with a blue LED strip for 8-24 h. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel; the catalyst and the excess of naphthalene were removed, and could be recovered, using toluene as eluent prior to the separation of desired products (*n*-hexane/EtOAc, under gradient).

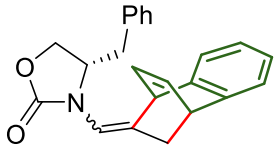
3-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)oxazolidin-2-one



Product **7a** was obtained as a mixture of diastereomers (87:13) following general procedure **GP3-A** from the corresponding allene (18.8 mg, 0.15 mmol; 150.0 mg, 1.2 mmol). White solid (34 mg, 89% yield; 245.2 mg, 81%). The reaction required 20 h of irradiation to fully consume the starting material.

Product **7a** was further purified by crystallization to obtain single crystals of the *E*-isomer. The relative structure was confirmed with selective NOE experiments. **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.28 – 7.20 (m, 2H), 7.12 – 7.04 (m, 2H), 6.66 – 6.54 (m, 2H), 6.46 (t, *J* = 2.4 Hz, 1H), 4.45 – 4.41 (m, 1H), 4.36 – 4.25 (m, 2H), 4.17 – 4.12 (m, 1H), 3.96 – 3.83 (m, 2H), 2.51 (dt, *J* = 15.2, 2.6 Hz, 1H), 2.33 (dt, *J* = 15.2, 2.5 Hz, 1H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 156.2, 143.7, 143.0, 135.2, 134.5, 125.3, 125.1, 123.1, 122.7, 122.6, 117.5, 62.0, 49.0, 44.5, 41.0, 31.7. **ESI-HRMS** calcd for $C_{16}H_{16}NO_2$ $[M+H]^+$ 254.1176, found 254.1180.

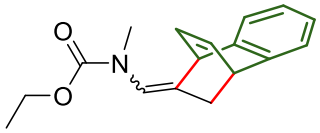
(4S)-4-benzyl-3-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)oxazolidin-2-one



Product **7b** was obtained as a mixture of diastereomers (95:5) following general procedure **GP-3A** from the corresponding allene (32.4 mg, 0.15 mmol). White solid (35.6 mg, 54% yield). The reaction required 40 h of irradiation to fully consume the starting material.

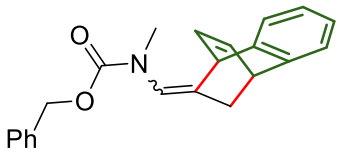
Product **7b** was further purified by crystallization to obtain single crystals of the *E*-isomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.21 (m, 5H), 7.17 – 7.10 (m, 2H), 7.02 – 6.96 (m, 2H), 6.69 – 6.57 (m, 2H), 6.30 (t, *J* = 2.3 Hz, 1H), 4.46 (dd, *J* = 5.9, 1.7 Hz, 1H), 4.23 – 4.06 (m, 4H), 2.81 (dd, *J* = 13.8, 3.2 Hz, 1H), 2.52 (dd, *J* = 13.8, 8.7 Hz, 1H), 2.43 (dt, *J* = 15.3, 2.6 Hz, 1H), 2.23 (dt, *J* = 15.4, 2.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.0, 143.8, 141.8, 135.3, 134.7, 131.7, 129.1, 128.9, 127.2, 125.7, 125.6, 123.0, 122.8, 115.1, 66.2, 57.1, 49.0, 41.1, 37.8, 33.2. **ESI-HRMS** calcd for $C_{23}H_{22}NO_2$ $[M+H]^+$ 344.1645, found 344.1652.

Ethyl ((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)(methyl)carbamate



Product **7c** was obtained as a mixture of diastereomers (69:31) following general procedure **GP-3A** from the corresponding allene (21.2 mg, 0.15 mmol). Pale yellow solid (16.4 mg, 41% yield). The reaction required 20 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** was taken at 273K to decrease the dynamic rotation and increase spectral resolution. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.05 (m, Dia1, 4H RotA, 4H RotB; Dia2, 4H RotA, 4H RotB), 6.67 – 6.48 (m, Dia1, 2H RotA, 3H RotB; Dia2, 2H RotA, 2H RotB), 6.38 (s, Dia1, 1H RotA), 5.93 (s, Dia2, 1H RotB), 5.82 (s, Dia2, 1H RotA), 4.68 – 4.64 (m, Dia2, 1H RotA, 1H RotB), 4.38 – 4.30 (m, Dia1, 1H RotA, 1H RotB), 4.24 – 4.01 (m, Dia1, 3H RotA, 3H RotB; Dia2, 3H RotA, 3H RotB), 3.12 (s, Dia2, 3H RotA, 3H RotB), 2.96 (s, Dia1, 3H RotA, 3H RotB), 2.42 – 2.28 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 2.25 – 2.13 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 1.36 – 1.15 (m, Dia1, 3H RotA, 3H RotB; Dia2, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.3, 155.4, 144.1, 143.8, 142.5, 141.3, 136.4, 135.5, 134.4, 133.3, 130.1, 125.6, 125.5, 125.4, 123.1, 123.0, 122.8, 122.7, 121.7, 120.6, 61.7, 61.6, 48.9, 44.0, 41.2, 40.8, 37.5, 34.9, 33.0, 32.5, 14.8, 14.6. **ESI-HRMS** calcd for $C_{17}H_{20}NO_2$ $[M+H]^+$ 270.1489, found 270.1486.

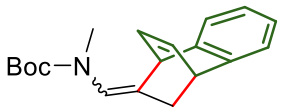
Benzyl((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)(methyl)carbamate



Product **7d** was obtained as a mixture of diastereomers (70:30) following general procedure **GP-3A** from the corresponding allene (30.5 mg, 0.15 mmol). Transparent oil (31.3 mg, 63% yield). The reaction required 24 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.10 (m, Dia1, 9H RotA, 9H RotB; Dia2 9H RotA, 9H RotB), 6.68 – 6.32 (m, Dia1, 3H RotA, 3H RotB; Dia2, 2H RotA, 2H RotB), 5.92 – 5.86 (m, Dia2, 1H RotA, 1H RotB), 5.39 – 5.11 (m, Dia1, 2H RotA, 2H RotB), 4.69 (dd, Dia2, *J* = 6.1, 1.4 Hz, 1H RotA, 1H RotB), 4.42 – 4.34 (m, Dia1, 1H RotA, 1H RotB), 4.12 – 4.06 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 3.19 (s, Dia2, 3H RotA, 3H RotA), 3.16 (s, Dia1, 3H RotB), 3.02 (s, Dia1, 3H RotA), 2.48 – 2.12 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.8, 156.1, 155.3, 144.1, 142.3, 141.2, 136.9, 136.6, 136.4, 135.7, 134.3, 133.3, 132.5, 128.8, 128.5, 127.9, 127.6, 125.7, 125.6, 125.5, 123.2, 123.0, 122.9,

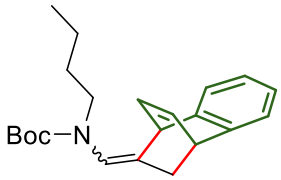
122.8, 122.5, 121.5, 120.5, 68.9, 67.2, 49.0, 48.6, 44.0, 41.1, 40.8, 37.6, 35.2, 33.0, 32.4. **ESI-HRMS** calcd for $C_{22}H_{22}NO_2$ $[M+H]^+$ 332.1651, found 332.1646.

Tert-butyl((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)(methyl)carbamate



Product **7e** was obtained as a mixture of diastereomers (71:29) following general procedure **GP-3A** from the corresponding allene (24.5 mg, 0.15 mmol). Pale yellow solid (38.8 mg, 87% yield). The reaction required 24 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** was taken at 273K to decrease the dynamic rotation and increase spectral resolution. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 – 7.04 (m, Dia1, 4H RotA, 4H RotB; Dia2, 4H RotA, 4H RotB), 6.66 – 6.49 (m, Dia1, 2H RotA, 3H RotB; Dia2, 2H RotA, 2H RotB), 6.27 (s, Dia1, 1H RotA), 5.92 (s, Dia2, 1H RotB), 5.81 (s, Dia2, 1H RotA), 4.71 – 4.61 (m, Dia2, 1H RotA, 1H RotB), 4.36 – 4.27 (m, Dia1, 1H RotA, 1H RotB), 4.12 – 4.00 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 3.08 (s, Dia2, 3H RotA, 3H RotB), 2.91 (s, Dia1, 3H RotA, 3H RotB), 2.41 – 2.11 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 1.57 – 1.29 (m, Dia1, 9H RotA, 9H RotB; Dia2, 9H RotA, 9H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.5, 154.4, 144.2, 143.8, 142.6, 141.5, 136.3, 135.4, 134.3, 133.4, 130.1, 125.6, 125.5, 125.3, 123.1, 123.0, 122.8, 122.7, 122.2, 121.4, 80.0, 79.9, 48.9, 44.0, 41.2, 40.8, 36.9, 34.9, 34.4, 33.0, 32.4, 29.7, 28.4, 28.3. **ESI-HRMS** calcd for $C_{19}H_{23}NNaO_2$ $[M+Na]^+$ 320.1621, found 320.1620.

Tert-butylbutyl((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)carbamate

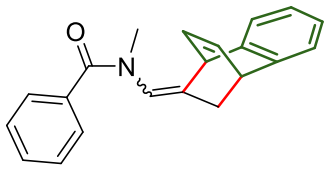


Product **7f** was obtained as a mixture of diastereomers (74:26) following general procedure **GP-3A** from the corresponding allene (31.7 mg, 0.15 mmol). Pale yellow solid (36.5 mg, 72% yield). The reaction required 24 h of irradiation to fully consume the starting material.

Product **7f** was further purified to obtain diastereomers **E**. Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** was taken at 273K to decrease the dynamic rotation and increase spectral resolution. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.23 – 7.05 (m, 4H RotA, 4H RotB), 6.57 (s, 2H RotA, 2H RotB), 6.26

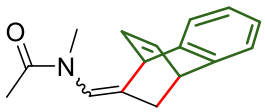
(s, 1H RotB), 5.98 (s, 1H RotA), 4.35 – 4.32 (m, 1H RotA, 1H RotB), 4.10 – 4.04 (m, 1H RotA, 1H RotB), 3.30 – 3.14 (m, 2H RotA, 2H RotB), 2.31 – 2.04 (m, 2H RotA, 2H RotB), 1.47 – 1.15 (m, 13H RotA, 13H RotB), 0.84 (t, *J* = 7.3 Hz, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.2, 143.9, 142.5, 135.6, 134.0, 125.4, 125.3, 122.8, 122.6, 120.4, 79.5, 48.8, 46.9, 41.2, 32.6, 29.72, 29.68, 28.5, 28.2, 19.9, 13.8. **ESI-HRMS** calcd for $C_{22}H_{30}NO_2$ $[M+H]^+$ 340.2271, found 340.2276.

N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-methylbenzamide



Product **7g** was obtained as a mixture of diastereomers (68:32) following general procedure **GP-3A** from the corresponding allene (26.1 mg, 0.15 mmol). White solid (27.6 mg, 61% yield). *Note: **7g** was isolated with traces of a third inseparable product.* The reaction required 40 h of irradiation to fully consume the starting material. **^{1}H NMR** was taken at 273K to decrease the dynamic rotation and increase spectral resolution. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.1 Hz, 1H Dia1), 7.46 – 7.04 (m, 8H Dia1, 9H Dia2), 6.58 – 6.43 (m, 2H Dia1, 2H Dia2), 6.19 (s, 1H Dia1), 5.89 (s, 1H Dia2), 4.61 (d, *J* = 6.1 Hz, 1H Dia2), 4.23 (d, *J* = 6.0 Hz, 1H Dia1), 4.10 – 4.05 (m, 1H Dia1), 4.01 – 3.96 (m, 1H Dia2), 3.27 (s, 3H Dia2), 3.13 (s, 3H Dia1), 2.26 – 2.01 (m, 2H Dia1, 2H Dia2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 170.5, 143.8, 143.3, 141.2, 140.6, 136.9, 136.7, 136.1, 136.0, 135.8, 133.3, 130.0, 129.9, 128.6, 128.1, 127.7, 127.6, 125.8, 125.7, 125.6, 125.5, 124.6, 123.2, 123.03, 123.00, 122.92, 122.88, 48.2, 43.8, 40.8, 40.6, 36.9, 34.8, 33.3, 32.7. **ESI-HRMS** calcd for $C_{21}H_{20}NO$ $[M+H]^+$ 302.1539, found 302.1544.

N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-methylacetamide

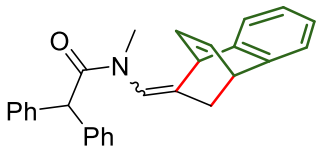


Product **7h** was obtained as a mixture of diastereomers (70:30) following general procedure **GP-3A** from the corresponding allene (22.2 mg, 0.2 mmol). White viscous oil (44.6 mg, 93% yield). The reaction required 44 h of irradiation to fully consume the starting material.

Product **7h** was further purified to obtain diastereomer **E**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.09 (m, 4H), 6.67 – 6.56 (m, 2H), 6.25 (s, 1H), 4.42 – 4.38 (m, 1H), 4.15 – 4.09 (m, 1H), 2.91 (s, 3H), 2.26 (dt, *J* = 16.0, 2.6 Hz, 1H), 2.13 – 2.06 (m, 1H), 1.89 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.8, 143.6, 141.4, 139.2, 136.3, 133.6, 125.8,

125.7, 123.0, 122.97, 122.9, 48.1, 40.8, 33.9, 32.4, 21.8. **ESI-HRMS** calcd for $C_{16}H_{17}NNaO$ $[M+Na]^+$ 262.1202, found 262.1207.

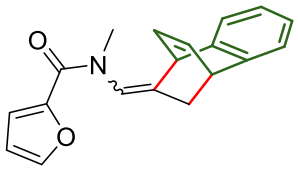
N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-methyl-2,2-diphenylacetamide



Product **7i** was obtained as a mixture of diastereomers (75:25) following general procedure **GP-3A** from the corresponding allene (40.4 mg, 0.15 mmol). Colorless oil (25.0 mg, 42% yield). The reaction required 24 h of irradiation to fully consume the starting material.

Product **7i** was further purified to obtain diastereomer **E**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.07 (m, 12H), 6.98 – 6.93 (m, 2H), 6.61 (dq, *J* = 7.6, 5.8 Hz, 2H), 6.23 (t, *J* = 2.4 Hz, 1H), 4.98 (s, 1H), 4.42 (dd, *J* = 5.6, 1.9 Hz, 1H), 4.01 (dd, *J* = 5.5, 2.6 Hz, 1H), 2.96 (s, 3H), 2.05 (dt, *J* = 16.1, 2.6 Hz, 1H), 1.78 (dt, *J* = 16.1, 2.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.1, 143.6, 142.1, 141.2, 139.7, 139.1, 136.6, 133.2, 128.8, 128.4, 126.8, 126.7, 125.9, 125.8, 123.2, 123.0, 122.4, 54.7, 47.9, 40.7, 34.3, 32.1. **ESI-HRMS** calcd for $C_{28}H_{26}NO$ $[M+H]^+$ 392.2014, found 392.2020.

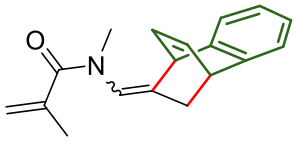
N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-methylfuran-2-carboxamide



Product **7j** was obtained as a mixture of diastereomers (88:12) following general procedure **GP-3A** from the corresponding allene (24.5 mg, 0.15 mmol). Yellow oil (38.5 mg, 88% yield). The reaction required 48 h of irradiation to fully consume the starting material.

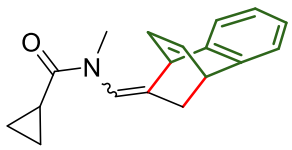
Product **7j** was further purified to obtain diastereomer **E**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.23 (d, *J* = 7.1 Hz, 1H), 7.13 (ddd, *J* = 7.2, 5.0, 3.7 Hz, 1H), 7.07 (d, *J* = 4.4 Hz, 3H), 6.70 – 6.69 (m, 1H), 6.63 (ddd, *J* = 7.4, 6.0, 1.3 Hz, 2H), 6.32 (dd, *J* = 8.3, 5.2 Hz, 3H), 6.07 (t, *J* = 2.0 Hz, 1H), 4.66 (dd, *J* = 6.1, 1.3 Hz, 1H), 4.09 (dq, *J* = 6.0, 2.4 Hz, 2H), 2.39 (dt, *J* = 15.3, 2.4 Hz, 2H), 2.25 (dt, *J* = 15.3, 2.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.9, 147.3, 144.4, 143.7, 140.5, 139.1, 136.7, 132.8, 125.8, 125.7, 123.3, 123.0, 122.0, 116.6, 111.0, 43.8, 40.7, 37.0, 33.3. **ESI-HRMS** calcd for $C_{19}H_{18}NO_2$ $[M+H]^+$ 292.1338, found 292.1342.

N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl) methylmethacrylamide



Product **7k** was obtained as a mixture of diastereomers (50:50) following general procedure **GP-3A** from the corresponding allene (20.5 mg, 0.15 mmol). Transparent oil (14.6 mg, 35% yield). The reaction required 56 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.27 – 7.06 (m, Dia1, 4H; Dia2, 4H), 6.69 – 6.47 (m, Dia1, 2H; Dia2, 2H), 6.32 (s, Dia1, 1H), 5.93 (t, Dia2, *J* = 1.9 Hz, 1H), 5.18 (d, Dia1, *J* = 4.3 Hz, 1H; d, Dia2, *J* = 4.3 Hz, 1H), 5.10 (d, Dia1, *J* = 3.4 Hz, 1H), 5.01 (s, Dia2, 1H), 4.64 (d, Dia1, *J* = 6.1 Hz, 1H), 4.34 (d, Dia2, *J* = 5.7 Hz, 1H), 4.18 – 4.03 (m, Dia1, 1H; m, Dia2, 1H), 3.17 (s, Dia1, 3H), 3.00 (s, Dia2, 3H), 2.37 – 2.25 (m, Dia1, 1H ; m, Dia2, 1H), 2.25 – 2.11 (m, Dia1, 1H; m, Dia2, 1H), 1.90 (s, Dia1, 3H), 1.79 (s, Dia2, 3H) **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.5, 171.9, 143.9, 143.5, 141.6, 141.0, 140.7, 137.4, 137.0, 136.0, 134.8, 133.6, 132.7, 125.9, 125.7, 125.6, 123.7, 123.2, 123.1, 122.9, 122.4, 118.4, 117.8, 48.4, 43.8, 41.0, 40.7, 36.5, 34.2, 33.2, 32.6, 20.1, 19.8. **ESI-HRMS** calcd for $C_{18}H_{20}NO$ $[M+H]^+$ 266.1545, found 266.1544.

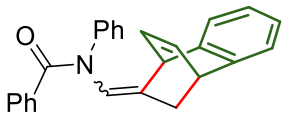
N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-methylcyclopropanecarboxamide



Product **7l** was obtained as a mixture of diastereomers (67:33) following general procedure **GP-3A** from the corresponding allene (20.6 mg, 0.15 mmol). Yellow oil (29.1 mg, 73% yield). The reaction required 48 h of irradiation to fully consume the starting material. Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, Acetone-*d6*) δ 7.31 – 7.21 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 7.15 – 7.06 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 6.73 – 6.57 (m, Dia 1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 6.44 (t, Dia1, *J* = 2.4 Hz, 1H RotA, 1H RotB), 6.06 (t, Dia2, *J* = 1.9 Hz, 1H RotA, 1H RotB), 4.72 (dd, Dia2, *J* = 6.0, 1.4 Hz, 1H RotA, 1H RotB), 4.58 (dd, Dia1, *J* = 5.9, 1.7 Hz, 1H RotA, 1H RotB), 4.19 – 4.14 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 2.99 (s, Dia2, 3H RotA, 3H RotB), 2.83 (s, Dia1, 3H RotA; Dia2, 3H RotA), 2.44 (t, Dia2, *J* = 2.4 Hz, 1H RotB), 2.40 (t, Dia2, *J* = 2.4 Hz, 1H RotA), 2.36 (t, Dia1, *J* = 2.7 Hz, 1H RotB), 2.32 (t, Dia1, *J* = 2.7 Hz, 1H RotA), 2.24 (t, Dia2, *J* = 2.4 Hz, 1H RotA), 2.20 (t, Dia2, *J* = 2.3 Hz, 1H RotB), 2.15 (t, Dia1, *J* = 2.6 Hz, 1H RotA), 2.12 – 2.10 (m, Dia1, 1H RotB), 1.76 (tt, Dia2, *J* = 7.9, 4.6 Hz, 1H RotA, 1H RotB), 1.65 (tt, Dia1, *J* = 7.9, 4.7 Hz, 1H

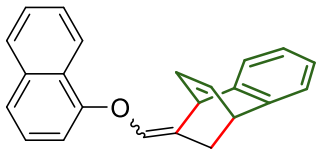
RotA, 1H RotB), 1.11 – 0.99 (m, Dia2 2H RotA), 0.94 – 0.51 (m, Dia1, 3H RotA, 3H RotB; Dia2, 2HRotA, 4H RotB), 0.49 – 0.38 (m, Dia1, 1H RotA, 1H RotB) **^{13}C NMR** (101 MHz, Acetone-*d6*) δ 172.6, 172.0, 144.3, 144.0, 142.0, 141.1, 140.0, 139.7, 136.9, 136.2, 133.6, 133.0, 125.6, 125.4, 123.3, 123.0, 122.9, 122.6, 121.5, 47.8, 43.8, 40.7, 40.6, 34.6, 33.0, 32.2, 11.3, 11.0, 8.6, 7.3, 7.2, 6.7. **ESI-HRMS** calcd for $C_{18}H_{20}NO$ $[M+H]^+$ 266.1545, found 266.1547.

N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-phenylbenzamide



Product **7m** was obtained as a mixture of diastereomers (57:43) following general procedure **GP-3A** from the corresponding allene (35.3 mg, 0.15 mmol). White solid (25.4 mg, 46% yield, 73% conversion). The reaction was irradiated for 72h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 6.2, 2.6 Hz, Dia1, 1H; Dia 2, 1H), 7.37 – 7.00 (m, Dia1, 12H; Dia2, 12H), 6.69 (d, *J* = 7.1 Hz, Dia1, 1H; Dia2, 1H), 6.56 – 6.50 (m, Dia 1, 2H; Dia2, 2H), 6.17 – 6.16 (m, Dia1, 1H; Dia2, 1H), 4.50 (dd, *J* = 6.1, 1.3 Hz, Dia 2, 1H), 4.42 (d, *J* = 5.8 Hz, Dia1, 1H), 4.01 (dq, *J* = 6.8, 2.3 Hz, Dia2 1H), 3.91 – 3.90 (m, Dia 1 1H), 2.45 – 2.30 (m, Dia2, 1H), 2.25 – 2.20 (m, Dia 1, 1H), 1.69 – 1.63 (m, Dia1, 1H; Dia2, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4, 169.6, 144.0, 143.6, 143.2, 141.8, 141.7, 140.2, 136.6, 136.0, 136.0, 135.9, 133.5, 132.6, 130.3, 130.0, 129.1, 129.0, 128.8, 128.8, 127.9, 127.7, 127.1, 127.0, 126.4, 126.4, 126.2, 126.0, 125.6, 125.5, 125.4, 125.4, 123.6, 123.0, 122.8, 122.7, 121.6, 48.9, 43.8, 41.0, 40.6, 33.8, 32.9. **ESI-HRMS** calcd for $C_{26}H_{22}NO$ $[M+H]^+$ 364.1736, found 364.1744.

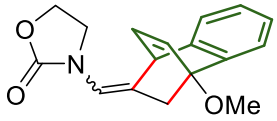
9-((naphthalen-1-yloxy)methylene)-1,4-dihydro-1,4-ethanonaphthalene



Product **7n** was obtained as a mixture of diastereomers (77:23) following general procedure **GP-3A** from the corresponding allene (27.3 mg, 0.15 mmol). *Note: it was necessary add 1% TEA to the eluent to prevent the degradation of the product during the separation.* White solid (30 mg, 65% yield). The reaction required 28 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 8.44 – 8.38 (m, 1H Dia2), 8.22 – 8.16 (m, 1H Dia1), 7.95 – 7.84 (m, 1H Dia1, 1H Dia2), 7.63 – 7.46 (m, 3H Dia1, 3H Dia2), 7.39 (t, *J* = 8.0 Hz, 1H Dia1, 1H Dia2), 7.31 – 7.23 (m, 2H Dia1, 2H Dia2), 7.15 – 7.06 (m, 2H Dia1, 2H Dia2), 7.01 – 6.91 (m, 2H Dia1, 1H Dia2), 6.71 – 6.62 (m, 2H Dia1, 2H Dia2), 6.56 – 6.53 (m, 1H Dia2), 5.22 – 5.18 (m, 1H Dia2), 4.63 – 4.55 (m, 1H Dia1), 4.24 – 4.15 (m, 1H Dia1, 1H Dia2), 2.55

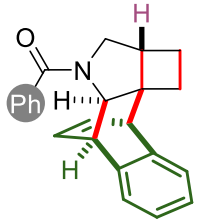
– 2.42 (m, 1H Dia1, 1H Dia2), 2.38 – 2.24 (m, 1H Dia1, 1H Dia2). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 153.5, 153.1, 144.4, 144.2, 143.0, 142.3, 136.2, 136.1, 134.83, 134.76, 134.3, 134.1, 133.8, 133.1, 127.6, 127.5, 126.6, 126.5, 125.93, 125.86, 125.6, 125.5, 125.34, 125.32, 125.2, 124.4, 123.9, 123.0, 122.9, 122.6, 121.7, 121.6, 121.54, 121.53, 107.7, 107.6, 44.9, 41.7, 40.8, 40.7, 31.2, 31.0. **ESI-HRMS** calcd for $C_{23}H_{18}NaO$ $[M+Na]^+$ 333.1250, found 333.1252.

3-((1-methoxy-1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)oxazolidin-2-one



Product **7o'** was obtained as a mixture of diastereomers (91:9) following a modified general procedure **GP-3A** from the corresponding allene (19.4 mg, 0.15 mmol). *Note: O_2 was removed by bubbling N_2 in the solution because freeze-pump-thaw broke the NMR tube.* White solid (22.9 mg, 53% yield). The reaction required 42 h of irradiation to fully consume the starting material.
Product **7o'** was further purified by crystallization to obtain single crystals of the *E*-isomer. **^{1}H NMR** (400 MHz, CDCl*3*) δ 7.41 (d, *J* = 8.6 Hz, 1H), 7.22 – 7.10 (m, 3H), 6.68 (d, *J* = 8.2 Hz, 1H), 6.62 – 6.57 (m, 1H), 6.50 – 6.47 (m, 1H), 4.37 – 4.22 (m, 3H), 3.91 – 3.65 (m, 5H), 2.70 (dd, *J* = 14.0, 2.2 Hz, 1H), 2.32 (dd, *J* = 14.0, 2.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.5, 142.9, 140.2, 134.3, 133.1, 126.0, 125.5, 122.5, 122.3, 119.8, 117.3, 82.9, 62.1, 53.6, 48.7, 44.7, 36.8. **ESI-HRMS** calcd for $C_{17}H_{18}NO_3$ $[M+H]^+$ 284.1281, found 284.1290.

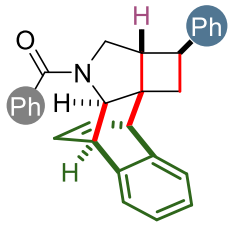
(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)(phenyl)methanone



Product **9a** was obtained as a mixture of diastereomers (70:30) following general procedure **GP-3B** from the corresponding enallene (29.6 mg, 0.15 mmol; 239.3 mg). White oil (37.4 mg, 76% yield; 235.4 mg, 60%). Two rotamers are observed due to the dynamic rotation of the amide. *Note: For model product **4a**, assignments of B rotamer resonances were made with a series of selective NOE experiments.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 – 6.95 (m, Dia1, 9H RotA, 9H RotB; Dia2, 9H RotA, 9H RotB), 6.70 – 6.54 (m, Dia1, 2H RotA; Dia2, 2H RotA; 1H RotB), 6.53 – 6.48 (m, 1H RotB),

6.36 (t, *J* = 6.8 Hz, 1H RotB), 6.15 (t, *J* = 6.3 Hz, 1H RotB), 4.75 – 4.70 (m, Dia2, 1H RotA), 4.66 – 4.58 (m, Dia1, 2H RotA), 4.43 (d, *J* = 3.2 Hz, Dia2, 1H RotA), 4.09 (d, *J* = 3.3 Hz, Dia1, RotB), 3.92 – 3.81 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 3H RotB), 3.67 (dd, *J* = 10.9, 5.8 Hz, Dia2, 1H RotA), 3.60 – 3.52 (m, Dia1, 1H RotB; Dia2, 2H RotB), 3.47 (d, *J* = 12.3 Hz, Dia1, 1H RotB), 3.26 (d, *J* = 10.9 Hz, Dia2, 1H RotA), 2.77 (d, *J* = 11.0 Hz, Dia1, 1H RotA; Dia2, 1H RotB), 2.66 (q, *J* = 7.2 Hz, Dia2, 1H RotA), 2.36 – 1.71 (m, Dia1, 5H RotA, 5H RotB; Dia2, 2H RotA, 2H RotB), 1.65 – 1.47 (m, Dia1, 1H RotA, 1H RotB; Dia2, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 170.8, 170.0, 169.7, 141.5, 141.2, 141.1, 140.7, 140.5, 140.3, 138.6, 138.0, 137.4, 137.3, 136.1, 135.3, 134.8, 134.6, 134.3, 134.1, 133.9, 133.3, 132.1, 129.8, 129.7, 128.8, 128.7, 128.25, 128.15, 127.2, 127.0, 126.7, 126.6, 126.4, 126.04, 125.96, 125.89, 125.73, 125.67, 125.61, 125.57, 125.48, 124.8, 124.7, 124.5, 123.94, 123.89, 123.7, 123.5, 122.9, 122.8, 73.3, 72.2, 71.5, 70.0, 58.6, 57.5, 56.8, 56.7, 55.9, 55.6, 55.1, 53.8, 51.1, 51.0, 50.7, 46.6, 46.4, 44.29, 44.27, 42.7, 42.0, 41.0, 40.5, 31.9, 31.0, 21.6, 21.1, 21.0, 20.4. **ESI-HRMS** calcd for $C_{23}H_{22}NO$ $[M+H]^+$ 328.1696, found 328.1690.

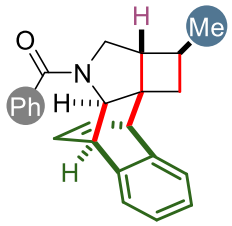
Phenyl(2-phenyl-1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)methanone



Product **9b** was obtained as a mixture of diastereomers (74:26) following general procedure **GP-3B** from the corresponding enallene (41.9 mg, 0.15 mmol). White solid (27.3 mg, 45% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 – 6.98 (m, Dia1, 14H RotA, 14H RotB; Dia2, 14H RotA, 14H RotB), 6.74 – 6.55 (m, Dia1, 2H RotA; Dia2, 2H RotA; 2H RotB), 6.42 (t, *J* = 6.7 Hz, 1H RotB), 6.24 – 6.18 (m, 1H RotB), 4.82 – 4.76 (m, Dia2, 1H RotA), 4.74 – 4.65 (m, Dia1, 2H RotA), 4.53 (d, *J* = 3.2 Hz, Dia2, 1H RotA), 4.20 (d, *J* = 3.3 Hz, 1H RotB), 4.13 (d, *J* = 12.4 Hz, Dia2, 1H RotB), 4.02 (d, *J* = 3.1 Hz, 1H RotB), 3.97 – 3.84 (m, Dia1, 1H RotA; Dia2, 1H RotA; 2H RotB), 3.80 (dd, *J* = 11.0, 5.6 Hz, Dia2, 1H RotA), 3.74 – 3.58 (m, 4H RotB), 3.48 (d, *J* = 11.0 Hz, Dia2, 1H RotA), 3.33 – 3.21 (m, 2H RotB), 3.14 – 2.95 (m, Dia1, 2H RotA; Dia2, 1H RotA), 2.85 – 2.72 (m, Dia2, 1H RotA, 1H RotB), 2.64 – 2.50 (m, Dia1, 1H RotA; 1H RotB), 2.44 – 2.07 (m, Dia1, 2H RotA; Dia2, 2H RotA; 4H RotB), 1.93 (dd, *J* = 11.1, 5.4 Hz, Dia1, 1H RotA), 1.85 (dd, *J* = 12.5, 5.6 Hz, Dia1, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 170.8, 170.0, 169.7, 144.1, 143.9, 141.4, 141.0, 140.9, 140.4, 140.3, 138.6, 137.8, 137.2, 137.1,

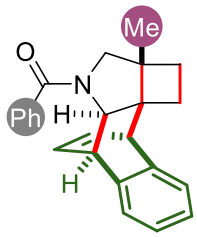
135.1, 134.9, 134.5, 134.3, 134.2, 133.4, 132.5, 130.0, 129.9, 128.9, 128.8, 128.6, 128.5, 128.45, 128.42, 128.3, 128.24, 128.16, 127.2, 127.0, 126.7, 126.6, 126.4, 126.32, 126.29, 126.26, 126.22, 126.16, 126.1, 126.0, 125.9, 125.8, 125.7, 124.9, 124.8, 124.7, 124.01, 123.96, 123.8, 123.7, 72.8, 71.7, 71.2, 69.6, 58.2, 56.4, 55.2, 53.9, 53.5, 53.1, 52.1, 51.3, 51.02, 50.98, 50.8, 50.64, 50.61, 50.2, 49.7, 49.2, 46.6, 46.3, 44.28, 44.27, 39.5, 38.9, 38.8, 38.7, 38.4, 38.1. **ESI-HRMS** calcd for $C_{29}H_{26}NO$ $[M+H]^+$ 404.2009, found 404.2004.

(2-methyl-1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)(phenyl)methanone



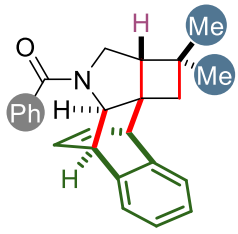
Product **9c** was obtained as a mixture of diastereomers (71:29) following general procedure **GP-3B** from the corresponding allene (38.3 mg, 0.15 mmol). Yellow oil (35.3 mg, 61% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.04 (m, Dia1, 9H RotA, 9H RotB; Dia2, 9H RotA, 9H RotB), 6.75 – 6.49 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 1H RotB), 6.24 (t, Dia2, *J* = 1.7 Hz, 1H RotB), 4.73 – 4.70 (m, Dia2, 1H RotA, 1H RotB), 4.63 – 4.60 (m, Dia1, 1H RotA, 1H RotB), 4.53 – 4.52 (m, Dia1, 1H RotA, 1H RotB), 4.36 – 4.32 (m, Dia2, 1H RotA, 1H RotB), 3.93 – 3.79 (m, Dia1, 1H RotA, 1H RotB; Dia2,1H RotA, 1H RotB), 3.67 (dd, Dia2, *J* = 10.9, 5.8 Hz, 1H RotB), 3.38 (d, Dia2, *J* = 11.4 Hz, 1H RotB), 3.29 (d, Dia2, *J* = 10.8 Hz, 1H RotA), 2.91 (d, Dia1, *J* = 11.6 Hz, 1H RotB), 2.80 (d, Dia1, *J* = 10.9 Hz, 1H RotA), 2.47 – 2.13 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 1.93 – 1.54 (m, Dia1, 5H RotA, 4H RotB; Dia2, 3H RotA, 3H RotB), 1.02 (d, Dia1, *J* = 6.5 Hz, 3H RotB), 0.98 (d, Dia2, *J* = 6.6 Hz, 3H RotA), 0.87 (dd, Dia2, *J* = 7.3, 1.4 Hz, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 169.6, 169.3, 166.2, 141.7, 141.2, 141.0, 140.4, 140.2, 138.2, 137.6, 137.5, 137.3, 134.6, 134.4, 134.4, 134.2, 134.0, 133.9, 133.6, 133.3, 130.2, 129.8, 129.7, 129.6, 128.8, 128.7, 128.4, 128.2, 128.2, 128.1, 127.7, 127.2, 127.0, 126.8, 126.6, 125.9, 125.8, 125.8, 125.6, 125.5, 125.4, 124.8, 124.6, 124.5, 123.9, 123.9, 123.7, 116.6, 73.1, 71.6, 71.3, 69.7, 58.0, 56.2, 54.4, 54.3, 52.9, 52.9, 52.0, 51.9, 52.0, 51.3, 51.1, 50.7, 50.7, 50.1, 44.4, 44.2, 44.0, 43.2, 39.5, 38.6, 38.4, 29.0, 24.8, 24.5, 21.2, 21.0, 15.4, 15.1, 12.0. **ESI-HRMS** calcd for $C_{24}H_{24}NO$ $[M+H]^+$ 342.1858, found 342.1861.

(2a-methyl-1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH) yl)(phenyl)methanone



Product **9d** was obtained as a mixture of diastereomers (71:29) following general procedure **GP-3B** from the corresponding enallene (32.0 mg, 0.15 mmol). White solid (22.3 mg, 44% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 – 6.93 (m, Dia1, 9H RotA, 9H RotB; Dia2, 9H RotA, 9H RotB), 6.70 – 6.50 (m, Dia1, 2H RotA, 1H RotB; Dia2, 2H RotA, 1H RotB), 6.33 (t, *J* = 6.8 Hz, Dia1, 1H RotB), 6.18 – 6.10 (m, Dia2, 1H RotB), 4.78 – 4.63 (m, Dia1, 1H RotA; Dia2, 2H RotA), 4.51 – 4.46 (m, Dia1, 1H RotA), 4.20 (brs, Dia2, 1H RotB), 3.98 (brs, Dia1, 1H RotB), 3.93 – 3.85 (m, Dia1, 1H RotB; Dia2, 1H RotA), 3.83 – 3.74 (m, Dia1, 1H RotA, 1H RotB), 3.58 – 3.48 (m, Dia1, 1H RotB), 3.34 (d, *J* = 10.6 Hz, Dia1, 1H RotA), 3.30 – 3.18 (m, Dia1, 1H RotA, 1H RotB), 2.83 (d, *J* = 10.8 Hz, Dia2, 1H RotA), 2.15 (q, *J* = 10.2 Hz, Dia2, 1H RotA), 2.03 – 1.64 (m, Dia1, 2H RotA, 2H RotB; Dia2, 4H RotA, 4H RotB), 1.58 – 1.20 (m, Dia1, 5H RotA, 5H RotB; Dia2, 3H RotB), 1.07 (s, Dia2, 3H RotA). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 169.7, 169.6, 141.7, 141.3, 141.2, 141.1, 140.9, 137.6, 137.4, 137.3, 134.8, 134.7, 134.4, 134.2, 133.9, 132.1, 129.8, 129.7, 128.8, 128.7, 128.24, 128.15, 127.2, 127.0, 126.7, 126.6, 125.8, 125.7, 125.6, 125.53, 125.49, 124.9, 124.8, 124.6, 123.9, 123.7, 123.6, 74.4, 72.9, 71.4, 64.3, 62.7, 61.1, 58.8, 57.0, 55.2, 47.9, 47.8, 47.0, 46.90, 46.86, 46.6, 45.5, 44.4, 44.0, 29.6, 28.9, 27.89, 27.86, 27.3, 19.1, 18.7, 16.7. **ESI-HRMS** calcd for $C_{24}H_{24}NO$ $[M+H]^+$ 342.1852, found 342.1860.

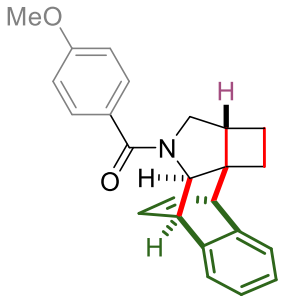
(2,2-dimethyl-1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH) yl)(phenyl)methanone



Product **9e** was obtained as a mixture of diastereomers (74:26) following general procedure **GP-3B** from the corresponding enallene (34.5 mg, 0.15 mmol). Pale yellow viscous oil (42.0 mg, 79% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 – 6.95 (m, Dia1,

9H RotA, 9H RotB; Dia2, 9H RotA, 9H RotB), 6.73 – 6.49 (m, Dia1, 2H RotA; Dia2, 2H RotA; 2H RotB), 6.35 (t, *J* = 6.8 Hz, 1H RotB), 6.14 (t, *J* = 7.0 Hz, 1H RotB), 4.70 (brs, Dia2, 1H RotA), 4.62 (q, *J* = 3.4 Hz, Dia1, 1H RotA), 4.49 (d, *J* = 3.3 Hz, Dia1, 1H RotA), 4.33 – 4.28 (m, Dia2, 1H RotA), 4.05 – 3.99 (m, 2H RotB), 3.89 – 3.76 (m, Dia1, 1H RotA; Dia2, 1H RotA; 1H RotB), 3.65 – 3.47 (m, Dia2, 1H RotA; 3H RotB), 3.38 (d, *J* = 11.5 Hz, Dia2, 1H RotA), 2.91 (d, *J* = 11.4 Hz, Dia1, 1H RotA), 2.36 (d, *J* = 7.4 Hz, 1H RotB), 2.26 (d, *J* = 7.0 Hz, Dia2, 1H RotA), 2.05 – 1.70 (m, Dia1, 4H RotA; Dia2, 1H RotA), 1.57 – 1.48 (m, Dia2, 1H RotA; 2H RotB), 1.23 (s, 3H RotB), 1.18 (s, 3H RotB), 1.12 – 1.01 (m, Dia1, 3H RotA; Dia2, 6H RotA), 0.85 (s, Dia1, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.1, 169.74, 169.67, 169.3, 141.6, 141.4, 141.24, 141.19, 141.15, 140.7, 140.2, 138.5, 138.0, 137.7, 137.6, 136.1, 135.9, 135.2, 134.9, 134.30, 134.27, 133.7, 133.5, 131.8, 129.73, 129.69, 129.6, 128.8, 128.7, 128.3, 128.2, 126.8, 126.6, 126.5, 126.45, 126.39, 125.9, 125.75, 125.71, 125.65, 125.59, 125.5, 125.4, 124.85, 124.76, 124.5, 124.05, 123.97, 123.8, 123.5, 122.84, 122.76, 74.3, 73.3, 72.7, 71.2, 54.6, 53.1, 51.9, 51.55, 51.52, 51.47, 50.94, 50.88, 50.2, 49.8, 49.7, 49.1, 46.5, 46.35, 46.28, 46.0, 45.8, 45.6, 44.3, 32.5, 32.44, 32.38, 31.3, 31.1, 30.9, 30.8, 23.5, 23.2, 22.8, 22.6. **ESI-HRMS** calcd for $C_{25}H_{26}NO$ $[M+H]^+$ 356.2009, found 356.2010.

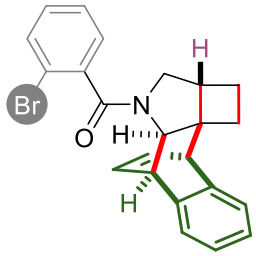
(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)(4-methoxyphenyl)methanone



Product **9f** was obtained as a mixture of diastereomers (67:33) following general procedure **GP-3B** from the corresponding enallene (34.6 mg, 0.15 mmol). White solid (39.2 mg, 73% yield). Two rotamers are observed due to the dynamic rotation of the amide. *Note: small traces of resonances due to the minor rotamers of products are not assigned.* **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 – 7.49 (m, Dia2, 2H RotA; 2H RotB), 7.37 – 6.89 (m, Dia1, 6H RotA; Dia2, 6H RotA; 6H RotB), 6.83 (d, *J* = 8.7 Hz, Dia1, 2H RotA), 6.67 – 6.52 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 4.70 – 4.61 (m, Dia1, 1H RotA; Dia2, 1H RotA), 4.57 (q, *J* = 3.4 Hz, Dia1, 1H RotA), 4.48 – 4.43 (m, Dia2, 1H RotA), 3.93 – 3.77 (m, Dia1, 4H RotA, 3H RotB; Dia2, 4H RotA, 3H RotB), 3.72 (dd, *J* = 10.7, 5.9 Hz, Dia2, 1H RotA), 3.34 (d, *J* = 10.8 Hz, Dia2, 1H RotA), 2.84 (d, *J* = 10.9 Hz, Dia1, 1H RotA), 2.67 (q, *J* = 6.8 Hz, Dia2, 1H

RotA), 2.31 – 2.21 (m, Dia1, 1H RotA), 2.19 – 1.81 (m, Dia1, 4H RotA; Dia2, 2H RotA), 1.63 – 1.47 (m, Dia1, 1H RotA, 1H RotB; Dia2, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 169.6, 169.4, 160.8, 160.7, 141.5, 141.2, 141.1, 140.4, 135.2, 134.9, 134.5, 134.2, 134.1, 134.0, 133.3, 129.6, 129.5, 129.3, 129.1, 128.5, 126.4, 125.9, 125.8, 125.6, 125.5, 124.8, 124.7, 124.5, 123.9, 123.7, 114.0, 113.9, 113.4, 113.3, 72.3, 71.6, 70.0, 58.7, 56.9, 56.8, 55.7, 55.4, 55.3, 54.9, 54.1, 51.1, 50.7, 46.3, 44.4, 42.8, 42.2, 40.4, 31.1, 21.1, 20.4. **ESI-HRMS** calcd for $C_{24}H_{24}NO_2$ $[M+H]^+$ 358.1802, found 358.1808.

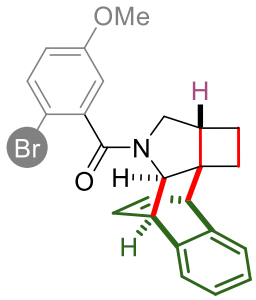
(2-bromophenyl)(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)methanone



Product **9g** was obtained as a mixture of diastereomers (73:27) following general procedure **GP-3B** from the corresponding enallene (42.2 mg, 0.15 mmol). White solid (37.9 mg, 62% yield). Two rotamers are observed due to the dynamic rotation of the amide.

Product **9g** was further purified to obtain major diastereomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 – 7.43 (m, 1H RotA, 2H RotB), 7.38 – 6.87 (m, 7H RotA, 6H RotB), 6.65 – 6.43 (m, 2H RotA, 1H RotB), 6.18 – 6.11 (m, 1H RotB), 4.80 – 4.64 (m, 1H RotA), 4.54 – 4.47 (m, 1H RotA), 3.89 – 3.73 (m, 1H RotA, 2H RotB), 3.68 – 3.57 (m, 2H RotB), 2.61 – 2.47 (m, 1H RotA), 2.36 – 1.40 (m, 6H RotA, 6H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 168.0, 167.6, 141.2, 140.0, 139.5, 134.8, 134.4, 133.9, 132.7, 130.4, 130.0, 127.7, 127.6, 127.4, 126.3, 126.1, 125.9, 124.7, 123.9, 69.8, 56.1, 55.7, 50.6, 43.8, 41.4, 40.7, 30.9, 20.9, 20.4. **ESI-HRMS** calcd for $C_{23}H_{21}BrNO$ $[M+H]^+$ 406.0801, found 406.0805.

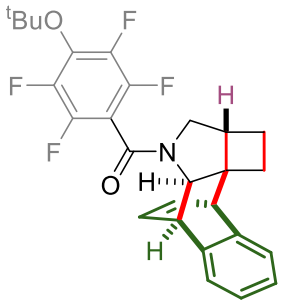
(2-bromo-5-methoxyphenyl)(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)methanone



Product **9h** was obtained as a mixture of diastereomers (75:25) following general procedure **GP-3B** from the corresponding enallene (46.3 mg, 0.15 mmol). White solid (39 mg, 60% yield). Two rotamers are observed due to the dynamic rotation of the amide.

Product **4h** was further purified by crystallization to obtain single crystals of the major isomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.52 (brs, 1H RotB), 7.38 – 7.05 (m, 5H RotA, 4H RotB), 6.89 (dd, *J* = 8.9, 3.0 Hz, 1H RotB), 6.70 (dd, *J* = 8.8, 3.0 Hz, 1H RotA), 6.64 – 6.44 (m, 3H RotA, 2H RotB), 6.18 (t, *J* = 6.9 Hz, 1H RotB), 4.75 (s, 1H RotA, 1H RotB), 4.53 – 4.45 (m, 1H RotA), 3.95 – 3.71 (m, 4H RotA, 6H RotB), 2.63 – 2.49 (m, 1H RotA), 2.35 – 1.40 (m, 6H RotA, 6H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 167.7, 167.4, 159.1, 158.9, 141.2, 140.9, 140.2, 134.8, 134.5, 133.8, 133.5, 126.3, 126.1, 125.9, 125.7, 124.6, 124.0, 116.2, 112.7, 69.6, 56.1, 55.8, 55.5, 50.6, 43.7, 41.4, 30.8, 20.9, 20.4. **ESI-HRMS** calcd for $C_{24}H_{23}BrNO_2$ $[M+H]^+$ 436.0907, found 436.0902.

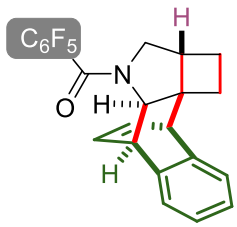
(4-(tert-butoxy)-2,3,5,6-tetrafluorophenyl)(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)methanone



Product **9i** was obtained as a mixture of diastereomers (82:18) following general procedure **GP-3B** from the corresponding allene (51.5 mg, 0.15 mmol). White solid (43.5 mg, 62% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.35 (m, Dia2, 1H RotA, 1H RotB), 7.27 – 7.27 (m, Dia 1, 1H RotA, 1H RotB), 7.21 – 7.13 (m, Dia 1, 3H RotA, 3H RotB;

Dia2, 3H RotA, 3H RotB), 6.61 (qt, Dia 1, *J* = 7.8, 3.9 Hz, 2H RotA, 1H RotB; Dia2, *J* = 7.8, 3.9 Hz, 1H RotA, 1H RotB), 6.55 – 6.50 (m, Dia2, 1H RotA), 6.35 (ddd, Dia2 *J* = 7.5, 6.0, 1.5 Hz, 1H RotB), 6.25 (ddd, Dia 1 *J* = 7.7, 6.2, 1.4 Hz, 1H RotB), 4.83 (ddd, Dia2, *J* = 5.4, 3.1, 1.6 Hz, 1H RotA, 1H RotB), 4.68 (ddd, Dia 1, *J* = 5.5, 3.2, 1.8 Hz, 1H RotA, 1H RotB), 4.51 (d, Dia 1, *J* = 3.3 Hz, 1H RotA), 4.31 (d, Dia1 *J* = 3.2 Hz, 1H RotB), 3.88 (ddd, Dia1, *J* = 11.0, 5.8, 1.8 Hz, 1H RotA, 1H RotB), 3.77 (d, Dia2, *J* = 3.3 Hz, 1H RotA), 3.69 (t, Dia2, *J* = 4.1 Hz, 1H RotB), 3.65 – 3.62 (m, Dia2, 1H RotA), 3.59 – 3.52 (m, Dia2, 1HRotA, 3H RotB), 3.15 (d, Dia2 *J* = 10.6 Hz, 1H RotA), 2.79 (q, Dia2, *J* = 7.5 Hz, 1H RotB), 2.69 (m, Dia1 ,1H RotA, 1H RotB; Dia2 ,1H RotA), 2.38 – 2.31 (m, Dia1, 1H RotB), 2.26 (td, Dia1, *J* = 8.4, 5.6 Hz, 1H RotA), 2.20 – 2.15 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 2.10 – 1.96 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 1.72 – 1.58 (m, Dia1, 2H RotA, 2H RotB; Dia2, 1H RotA, 1H RotB), 1.49 (s, Dia2, 9H RotA), 1.44 (s, Dia 1, 9H RotB), 1.40 (s, Dia1, 9H RotA), 1.37 (s, Dia2, 9H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.4, 158.1, 145.0 – 144.5 (m), 144.3 – 143.9 (m), 143.7 – 143.3 (m), 142.8, 142.5 – 142.0 (m), 141.9 – 141.4 (m), 141.3, 140.8, 140.6, 140.5, 139.2, 138.0, 136.5, 135.2, 134.6, 133.9, 133.6, 132.8, 132.7, 126.6, 126.1, 125.9, 125.3, 125.2, 124.2, 124.0, 123.8, 123.7, 112.7 (t, *J* = 21.4 Hz), 86.1, 85.8, 85.7, 85.4, 73.0, 72.0, 71.5, 70.5, 56.9, 56.5, 55.6, 55.3, 53.6, 50.8, 50.5, 50.4, 43.7, 43.5, 41.7, 41.1, 40.8, 40.5, 30.9, 30.8, 28.4, 28.4, 21.3, 21.2, 20.6, 20.4. **^{19}F NMR** (565 MHz, CDCl3) δ -142.4 (ddd, *J* = 23.5, 9.6, 5.1 Hz), -142.6 (ddd, *J* = 23.6, 9.8, 5.3 Hz), -143.0 (ddd, *J* = 23.5, 10.2, 4.8 Hz), -143.1 (ddd, *J* = 23.7, 9.4, 5.0 Hz), -143.3 (ddd, *J* = 23.6, 9.9, 4.8 Hz), -143.6 (ddd, *J* = 23.6, 9.8, 4.9 Hz), -143.8 (ddd, *J* = 24.1, 9.7, 5.2 Hz), -144.5 (ddd, *J* = 23.5, 9.8, 4.9 Hz), -148.5 (dd, *J* = 23.3, 9.7 Hz), -149.3 (dd, *J* = 23.9, 9.6 Hz), -149.5 (dd, *J* = 23.4, 9.6 Hz), -149.8 (dt, *J* = 23.2, 11.3 Hz), -150.0 (dd, *J* = 23.7, 9.9 Hz), -151.0 (dd, *J* = 23.9, 9.1 Hz). **ESI-HRMS** calcd for $C_{27}H_{25}F_4NO_2$ $[M+H]^+$ 472.1900, found 472.1904.

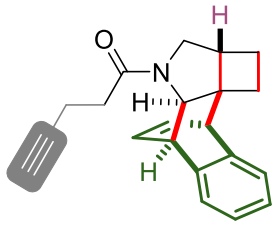
(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)(perfluorophenyl)methanone



Product **9j** was obtained as a mixture of diastereomers (79:21) following general procedure **GP-3B** from the corresponding allene (43.4 mg, 0.15 mmol). White solid (48.8 mg, 78% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.34 (m, Dia2, 1H RotA, 1H RotB), 7.27 – 7.25 (m, Dia1 1H RotA, 1H RotB), 7.22 – 710 (m, Dia 1, 3H RotA, 3H RotB;

Dia2 3H RotA, 3H RotB), 6.65 – 6.57 (m, Dia1, 2H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 6.51 (dd, Dia2 *J* = 7.7, 5.8 Hz, 1H RotA), 6.43 (ddd, Dia 2, *J* = 7.6, 6.0, 1.6 Hz, 1H RotB), 6.30 (ddd, Dia1 *J* = 7.7, 6.1, 1.4 Hz, 1H RotB), 4.81 (ddd, Dia2 *J* = 5.4, 3.2, 1.6 Hz, 1H RotA, 1H RotB), 4.67 (ddd, Dia1 *J* = 5.6, 3.4, 1.5 Hz, 1H RotA, 1H RotB), 4.50 (d, Dia 1, *J* = 3.2 Hz, 1H RotA), 4.30 (d, Dia1, *J* = 3.2 Hz, 1H RotB), 3.89 (ddd, Dia 1 *J* = 11.6, 5.9, 1.6 Hz, 1H RotA, 1H RotB), 3.74 (d, Dia2 *J* = 3.3 Hz, 1H RotA), 3.68 – 3.66 (m, Dia2, 1H RotB), 3.65 – 3.62 (m, Dia2, 1H RotA), 3.56 – 3519 (m, Dia 2, 1H RotA, 3H RotB), 3.12 (d, Dia2, *J* = 10.5 Hz, 1H RotA), 2.82 – 2.77 (m, Dia2, 1H RotB), 2.72 – 2.64 (m, Dia1 ,1H RotA, 1H RotB; Dia2 ,1H RotA), 2.36 (td, Dia1, *J* = 8.1, 5.5 Hz, 1H RotB), 2.27 (td, Dia 1, *J* = 8.5, 5.6 Hz, 1H RotA), 2.22 – 2.16 (m, Dia1, 1H RotA, 1H RotB; Dia2, 1H RotA, 1H RotB), 2.10 – 1.92 (m, Dia1, 2H RotA, 2H RotB; Dia2, 2H RotA, 2H RotB), 1.70 – 1.58 (m, Dia1, 2H RotA, 2H RotB; Dia2, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.2, 157.0, 144.5 – 142.4 (m), 141.9 – 141.4 (m), 141.2, 140.7, 140.4, 139.1, 139.0 – 138.5 (m), 137.8, 136.8, 136.7 – 136.1 (m), 135.3, 134.7, 133.8, 133.5, 132.7, 132.2, 131.9, 131.6, 126.7, 126.4, 126.0, 125.9, 125.8, 125.2, 125.2, 124.6, 124.2, 124.0, 123.8, 123.7, 113.2 – 111.8 (m), 73.1, 72.0, 71.6, 70.6, 56.9, 56.6, 55.6, 55.3, 50.4, 47.4, 47.1, 43.6, 43.5, 41.0, 31.6, 30.9, 30.8, 29.7, 21.2, 20.5, 20.4. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -140.0 (dt, *J* = 23.9, 6.7 Hz), -140.1 – -140.2 (m), -140.5 (d, *J* = 25.1 Hz), -140.7 (ddd, *J* = 23.6, 8.9, 4.5 Hz), -141.0 (ddd, *J* = 23.1, 9.1, 4.5 Hz), -141.2 (ddd, *J* = 23.3, 9.1, 4.7 Hz), -141.5 (ddd, *J* = 23.5, 9.0, 4.9 Hz), -141.8 (dt, *J* = 23.5, 7.0 Hz), -142.3 (ddd, *J* = 23.6, 9.1, 4.6 Hz), -151.2 (t, *J* = 21.4 Hz), -151.5 (t, *J* = 20.7 Hz), -152.2 (t, *J* = 20.5 Hz), -152.5 (t, *J* = 20.5 Hz), -158.5 (ddd, *J* = 23.1, 20.6, 8.9 Hz), -159.1 (ddd, *J* = 23.7, 20.7, 8.7 Hz), -159.5 (ddd, *J* = 23.3, 20.4, 8.9 Hz), -159.7 (td, *J* = 22.0, 8.3 Hz), -159.7 – -160.0 (m), -161.4 (ddd, *J* = 24.0, 21.4, 8.2 Hz). **ESI-HRMS** calcd for $C_{23}H_{16}F_5NO$ $[M+H]^+$ 418.1230, found 418.1235.

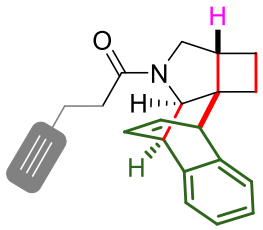
1-(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)pent-4-yn-1-one (Dia 1)



Product **9k** (Dia 1) was obtained as a single diastereomer following general procedure **GB-3B** from the corresponding allene (26.3 mg, 0.15 mmol). Transparent oil (16.5 mg, 36% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.26 – 7.04 (m, 4H RotA, 4H RotB), 6.61 (ddd, *J* = 7.7, 6.1, 1.5 Hz, 1H RotB), 6.53 (ddd, *J* = 7.7, 6.1, 1.6 Hz, 1H RotA), 6.38 – 6.35 (m, 1H RotA, 1H RotB), 4.67 (ddd, *J* = 5.5, 3.1, 1.6 Hz, 1H RotA), 4.17 (ddd, *J* =

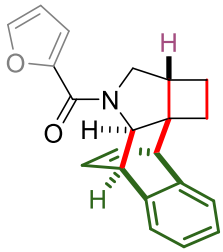
5.9, 3.0, 1.5 Hz, 1H RotB), 4.09 (d, *J* = 3.1 Hz, 1H RotA), 3.88 (dd, *J* = 6.1, 1.4 Hz, 1H RotB), 3.85 – 3.82 (m, 1H RotA, 2H RotB), 3.49 (dd, *J* = 10.2, 6.0 Hz, 1H RotA), 3.40 (d, *J* = 10.2 Hz, 1H RotA), 3.31 (dd, *J* = 12.0, 6.0 Hz, 1H RotB), 2.76 – 2.42 (m, 5H RotA, 5H RotB), 2.09 – 1.94 (m, 3H RotA, 3H RotB), 1.60 – 1.50 (m, 2H RotA, 2H RotB). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.9, 141.5, 141.2, 135.6, 134.4, 133.8, 132.2, 126.1, 125.9, 125.8, 125.6, 124.5, 124.2, 123.8, 83.7, 72.2, 71.8, 69.0, 68.7, 56.0, 51.1, 47.2, 43.9, 42.0, 41.1, 34.3, 33.3, 30.8, 21.6, 21.4, 15.0, 14.4. **ESI-HRMS** calcd for $C_{21}H_{21}NNaO$ $[M+Na]^+$ 326.1521, found 326.1523.

1-(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)pent-4-yn-1-one (Dia 2)



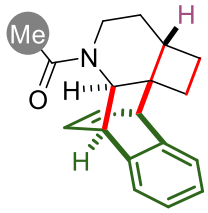
Product **9k'** (Dia 2) was obtained as a single diastereomer following general procedure **GP-3B** from the corresponding allene (26.3 mg, 0.15 mmol). Transparent oil (14.7 mg, 31% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.16 – 7.05 (m, 4H RotA, 4H RotB), 6.60 – 6.47 (m, 2H RotA, RotB), 4.56 (ddd, *J* = 6.2, 3.3, 1.4 Hz, 1H RotA), 4.28 (d, *J* = 3.2 Hz, 1H RotA), 4.08 (ddd, *J* = 6.2, 3.2, 1.2 Hz, 1H RotB), 4.03 (d, *J* = 3.1 Hz, 1H RotB), 3.83 (dd, *J* = 6.0, 1.4 Hz, 1H RotB), 3.79 (dd, *J* = 5.8, 1.5 Hz, 1H RotA), 3.41 (d, *J* = 12.2 Hz, 1H RotB), 2.94 (d, *J* = 10.3 Hz, 1H RotA), 2.81 – 2.62 (m, 4H RotB), 2.55 – 2.45 (m, 2H RotA), 2.35 (ddd, *J* = 15.3, 8.3, 6.8 Hz, 1H RotA), 2.25 (td, *J* = 8.1, 5.5 Hz, 1H RotA), 2.20 – 2.07 (m, 2H RotA, Rot B), 2.03 (t, *J* = 2.6 Hz, 1H RotB), 1.99 – 1.93 (m, 3H RotA, 2H RotB), 1.68 (dd, *J* = 10.4, 5.7 Hz, 1H RotA, 1H RotB), 1.56 – 1.48 (m, 1H RotA, 1H RotB). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 169.7, 141.0, 140.0, 135.1, 134.3, 134.1, 133.4, 126.4, 126.2, 126.0, 125.7, 125.1, 124.8, 124.0, 123.8, 83.7, 71.3, 70.6, 69.0, 68.7, 54.9, 54.3, 50.8, 43.7, 41.4, 40.5, 34.0, 33.3, 30.9, 20.9, 20.7, 15.0, 14.3. **ESI-HRMS** calcd for $C_{21}H_{21}NNaO$ $[M+Na]^+$ 326.1521, found 326.1523.

Furan-2-yl(1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indol-4(4aH)-yl)methanone



Product **9l** was obtained as a mixture of diastereomers (65:35) following general procedure **GP-3B** from the corresponding allene (28.4 mg, 0.15 mmol). Pale yellow oil (39.0 mg, 82% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 2H RotB), 7.53 (t, Dia2, *J* = 1.2 Hz, 1H RotA), 7.43 (d, Dia2, *J* = 1.6 Hz, 1H RotA), 7.34 – 7.08 (m, Dia1, 5H RotA, 6HRotB; Dia2 5H RotA, 5H RotB), 6.81 (d, Dia 1, *J* = 3.4 Hz, 1H RotA), 6.62 – 6.42 (m, Dia1, 3H RotA, 3H RotB; Dia2, 3H RotA, 3H RotB), 4.75 (d, Dia 2, *J* = 3.1 Hz, 1H RotB), 4.72 (ddd, Dia2 = 5.4, 3.2, 1.6 Hz, 1H RotA), 4.62 – 4.58 (m, Dia1, 2H RotA, 2H RotB; Dia2, 1H RotB), 4.42 (d, Dia2 *J* = 3.1 Hz, 1H RotA), 4.07 – 4.02 (m, 1H RotB), 3.99 – 3.96 (m, 1H RotB), 3.91 – 3.84 (m, Dia 1, 1H RotA; Dia2, 3H RotA; 1H RotB), 3.56 (dd, *J* = 12.5, 6.1 Hz, 1H RotB), 3.49 (d, *J* = 12.5 Hz, 1H RotB), 3.42 (d, Dia1, *J* = 11.1 Hz, 1H RotA), 2.82 – 2.68 (m, Dia2, 1H RotA, 1H RotB), 2.38 – 2.33 (m, Dia 1, 1H RotA, 1H RotB), 2.27 – 1.94 (m, Dia 1, 3H RotA, 2H RotB; Dia2, 1H RotA, 1H RotB), 1.77 – 1.71 (m, 1H RotB), 1.68 – 1.55 (m, Dia2, 1H RotA, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.5, 158.3, 149.1, 148.9, 148.4, 144.1, 144.1, 144.0, 143.8, 141.6, 141.4, 141.0, 140.0, 135.4, 134.9, 134.4, 134.1, 133.9, 133.6, 132.3, 126.3, 126.0, 125.7, 125.6, 125.0, 124.9, 124.6, 124.1, 123.8, 123.7, 123.6, 117.1, 116.9, 116.1, 115.6, 111.8, 111.7, 111.4, 111.1, 72.5, 71.9, 71.2, 57.8, 57.0, 56.9, 56.3, 55.4, 54.7, 54.6, 53.9, 51.0, 50.8, 50.7, 47.5, 43.9, 43.9, 42.7, 42.0, 40.1, 39.6, 31.2, 31.0, 30.9, 30.8, 21.5, 21.4, 20.8, 20.7. **ESI-HRMS** calcd for $C_{21}H_{20}NO_2$ $[M+H]^+$ 356.1053, found 356.1058.

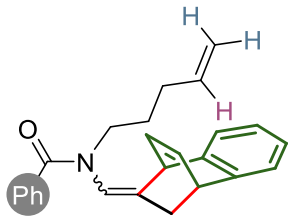
1-(2,2a,3,4,6,11-hexahydro-1H-6,11-ethenobenzo[g]cyclobuta[d]quinolin-5(5aH)-yl)ethan-1-one



Product **9m** was obtained as a single diastereomer following general procedure **GP-3B** from the corresponding enallene (23.0 mg, 0.15 mmol). White solid (18.8 mg,

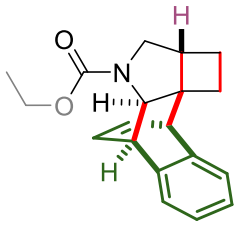
45% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.04 (m, 4H RotA, 4H RotB), 6.65 – 6.55 (m, 2H RotA, 2H RotB), 4.24 – 4.11 (m, 1H RotA, 1H RotB), 4.04 – 3.93 (m, 2H RotA, 1H RotB), 3.86 – 3.79 (m, 1H RotB), 3.47 (s, 1H RotB), 3.22 – 3.13 (m, 1H RotA), 2.46 – 2.24 (m, 1H RotA, 4H RotB), 2.19 – 2.04 (m, 4H RotA, 1H RotB), 1.98 – 1.82 (m, 2H RotA, 2H RotB), 1.61 – 1.45 (m, 2H RotA, 2H RotB), 1.25 – 0.97 (m, 2H RotA, 1H RotB), 0.70 – 0.59 (m, 1H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.4, 169.9, 142.6, 142.2, 141.0, 139.5, 135.5, 134.9, 133.8, 133.2, 125.9, 125.6, 125.2, 125.1, 124.88, 124.85, 124.5, 64.9, 61.2, 50.4, 50.2, 48.9, 46.0, 42.2, 41.2, 40.9, 38.4, 38.2, 36.4, 31.9, 31.7, 29.1, 28.4, 23.4, 23.2, 22.9, 21.8. **ESI-HRMS** calcd for $C_{19}H_{22}NO$ $[M+H]^+$ 280.1696, found 280.1700.

N-((1,4-dihydro-1,4-ethanonaphthalen-9-ylidene)methyl)-N-(pent-4-en-1-yl)benzamide



Product **9'n** was obtained as a mixture of diastereomers (59:41) following general procedure **GP-3B** from the corresponding allene (34.0 mg, 0.15 mmol). Pale yellow oil (23.5 mg, 44% yield). The reaction required 72 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 – 7.55 (m, Dia1, 1H; m, Dia2, 1H), 7.31 (d, Dia1, *J* = 8.4 Hz, 2H; d, Dia2, *J* = 8.4 Hz, 2H), 7.24 – 7.03 (m, Dia1, 6H; m, Dia2, 6H), 6.51 – 6.32 (m, Dia1, 2H; m, Dia2, 2H), 6.12 (s, Dia1, 1H), 5.89 – 5.75 (m, Dia1, 1H; m, Dia2, 1H), 5.70 (t, Dia2, *J* = 6.7 Hz, 1H), 5.11 – 4.92 (m, Dia1, 2H; m, Dia2, 2H), 4.44 (d, Dia2, *J* = 6.0 Hz, 1H), 4.23 (d, Dia1, *J* = 5.9 Hz, 1H), 3.94 (d, Dia1, *J* = 16.5 Hz, 1H; d, Dia2, *J* = 16.5 Hz, 1H), 3.86 – 3.75 (m, Dia2, 1H), 3.59 – 3.39 (m, Dia1, 2H; Dia2, 1H), 2.20 – 1.96 (m, Dia1, 4H; m, Dia2, 4H), 1.91 – 1.56 (m, Dia1, 2H; m, Dia2, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.2, 170.0, 143.9, 143.2, 140.5, 138.1, 137.9, 136.4, 136.2, 136.1, 135.8, 135.0, 133.1, 132.0, 130.0, 129.7, 128.8, 128.6, 127.9, 127.6, 125.7, 125.5, 125.5, 125.5, 123.4, 122.9, 122.8, 121.2, 115.0, 48.4, 48.3, 46.8, 43.7, 40.7, 40.5, 33.5, 32.9, 31.3, 31.2, 26.7, 26.6. **ESI-HRMS** calcd for $C_{25}H_{26}NO$ $[M+H]^+$ 356.2014, found 356.2020.

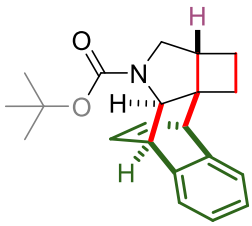
Ethyl 1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indole-4(4aH)-carboxylate



Product **9o** was obtained as a mixture of diastereomers (77:23) following general procedure **GP-3B** from the corresponding allene (25.1 mg, 0.15 mmol). White solid (24.5 mg, 55% yield).

Product **9o** was further purified to obtain diastereomer **E**. Two rotamers are observed due to the dynamic rotation of the carbamate. **^{1}H NMR** (600 MHz, Acetone-*d6*) δ 7.25 – 7.22 (m, 1H RotA, 1H RotB), 7.14 – 7.07 (m, 3H RotA, 3H RotB), 6.60 (ddd, *J* = 7.5, 5.8, 1.4 Hz, 1H RotA, 1H RotB), 6.50 (ddd, *J* = 7.7, 6.1, 1.5 Hz, 1H RotA, 1H RotB), 4.46 (ddd, *J* = 6.2, 3.3, 1.4 Hz, 1H RotA), 4.35 – 4.24 (m, 2H RotB), 4.13 – 3.99 (m, 3H RotA, 2H RotB), 3.94 (dt, *J* = 5.8, 1.7 Hz, 1H RotA, RotB), 3.02 (dd, *J* = 14.8, 10.9 Hz, 1H RotA, 1H RotB), 2.27 – 2.17 (m, 2H RotA, 2H RotB), 2.00 – 1.94 (m, 2H RotA, 2H RotB), 1.61 – 1.54 (m, 2H RotA, 2H RotB), 1.36 (t, *J* = 7.1 Hz, 3H RotB), 1.17 (t, *J* = 7.1 Hz, 3H RotA). **^{13}C NMR** (151 MHz, Acetone-*d6*) δ 154.3, 154.1, 141.2, 141.2, 140.1, 139.9, 134.7, 134.6, 133.6, 133.6, 125.7, 125.6, 125.5, 125.5, 124.7, 124.6, 123.9, 70.8, 70.1, 60.3, 60.0, 56.4, 55.2, 53.6, 53.3, 50.5, 45.8, 44.3, 41.3, 40.6, 30.5, 20.7, 20.6, 14.4, 14.2. **ESI-HRMS** calcd for $C_{19}H_{21}NO_2$ $[M+H]^+$ 296.1651, found 296.1657.

Tert-butyl 1,2,2a,3,5,10-hexahydro-5,10-ethenobenzo[f]cyclobuta[c]indole-4(4aH)-carboxylate



Product **9p** was obtained as a mixture of diastereomers (68:32) following general procedure **GP-3B** from the corresponding enallene (29.9 mg, 0.15 mmol). White viscous oil (29.8 mg, 61% yield). Two rotamers are observed due to the dynamic rotation of the carbamate.

Product **9p** was further purified to obtain major diastereomer. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 – 7.05 (m, 4H RotA, 4H RotB), 6.58 – 6.51 (m, 2H RotA), 6.49 – 6.43 (m, 2H RotB), 4.56 – 4.52 (m, 1H RotA), 4.30 – 4.26 (m, 1H RotB), 4.04 (d, *J* = 3.3 Hz,

1H RotA), 3.91 (d, *J* = 3.2 Hz, 1H RotB), 3.80 – 3.76 (m, 1H RotA, 1H RotB), 3.06 (d, *J* = 11.2 Hz, 1H RotB), 2.94 (d, *J* = 11.1 Hz, 1H RotA), 2.22 – 1.91 (m, 4H RotA, 4H RotB), 1.64 – 1.53 (m, 2H RotA, 11H RotB), 1.43 (s, 9H RotA). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.6, 154.2, 141.1, 140.8, 140.2, 139.6, 134.7, 134.3, 134.1, 133.7, 126.1, 125.8, 125.7, 125.5, 124.9, 124.8, 123.75, 123.68, 79.4, 79.0, 70.4, 70.3, 56.4, 55.4, 53.9, 53.5, 50.9, 45.8, 44.2, 41.3, 40.7, 31.0, 30.9, 28.8, 28.5, 21.0, 20.9. **ESI-HRMS** calcd for $C_{21}H_{25}NNaO_2$ $[M+Na]^+$ 346.1778, found 346.1771.

Chapter IV

Visible – Light – Promoted Dearomative [2+2] Cycloaddition of Cinnamyls on (Benzo) Heteroaromatics.

Manuscript in preparation.

4.1: Dearomative [2+2] Cycloadditions of Heteroaromatics

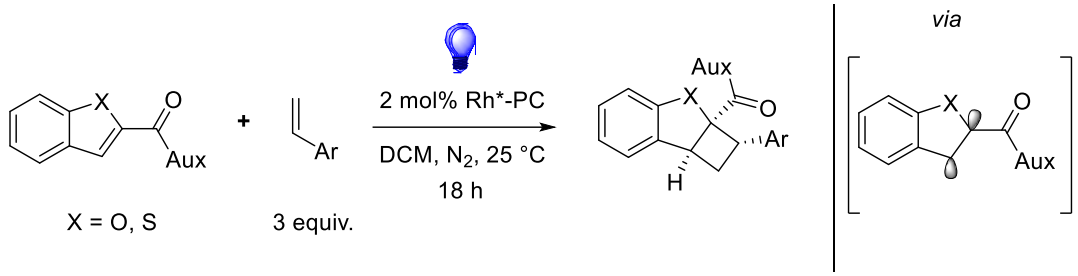
The dearomative [2+2] cycloaddition of heteroaromatics is a strategy well exploited in literature. Indole is the most reported heterocycle in this field[95], with fascinating examples of both intra- and intermolecular reactions. This is probably because this heterocycle is very present in the scaffolds of biologically active molecules and there has always been intense research on the methods of synthesis and transformation of indoles. Unlike benzothiophene and benzofuran, indole has 3 functionalizable sites in the 5-member ring (N, C2 and C3). This feature opens the possibilities to design way more substrates than in the above-mentioned benzo heterocycles. However, benzofuran and benzothiophene are very important scaffolds as well. For example, most benzofuran compounds show relevant antitumor, antibacterial and antioxidant properties[96].

The most used approach for inducing the dearomative cycloaddition is activating the benzoheterocycles via EnT and then, the resultant triplet can attack one unsaturation in an inter- or intramolecular fashion. This strategy is relatively easy for benzoheterocycles because they have an E_T around 65 kcal/mol. It is however necessary to decorate the aromatic with auxochrome substituents to lower this E_T and make them accessible to common photocatalysts, with a consequent synthetic and economic effort. The complementary approach is activating an appropriate arenophile that attacks the heteroaromatic. This strategy has some reported examples regarding the dearomatization of benzoheterocycles, because they have a lower resonance energy per ring. This results in endergonic and favourable processes that proceeds smoothly when the substrate is well designed. However, there are few reports regarding the dearomative [2+2] cycloaddition of simple heteroaromatics like furan, thiophene and pyrrole. Firstly, because their high E_T make them inaccessible to EnT processes. Moreover, monocyclic heteroarenes could give rise both the [2+2] and [4+2] product, especially in stepwise cyclizations. Finally, since there is only one ring, the processes are mostly endergonic. This result in low reaction rates, conversions and yields.

Nonetheless, achieve the dearomative cycloaddition on simple heteroaromatics would increase the molecular complexity keeping low molecular weight, developing interesting new scaffolds for the drug discovery. Moreover, the dearomatized heterocycle is characterized by having a synthetic useful double bond in its molecule, that can be used for a myriad of further functionalizations.

In the next pages, I will present some examples of dearomative [2+2] cycloaddition of benzo- or simple heteroaromatics, focusing on the recent examples developed with visible light promoted reactions both in inter- or intramolecular fashion.

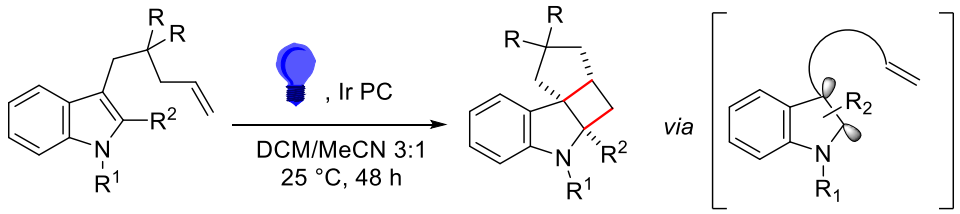
In 2018, Meggers *et. al.*[97] developed an asymmetric intermolecular dearomative cycloaddition of substituted benzofurans and benzothiophenes with alkenes (Scheme 51).



Scheme 51: Asymmetric [2+2] between benzoheteroaromatics and stryrenes.

In this example, authors designed a benzoheterocycle substituted with an auxochrome group (i.e. acyl-pyrazole or imidazole) to lower the E_T of substrate. Then, thanks to a chiral Rh-based photocatalyst they could achieve an asymmetric [2+2] cycloaddition between the triplet biradical and a styrene. They synthesized a broad scope of products, with ees up to 99% and high yields. Notably, they also had appreciable diastereo- and regioselectivities, explained with DFT calculations on the stability of their intermediates.

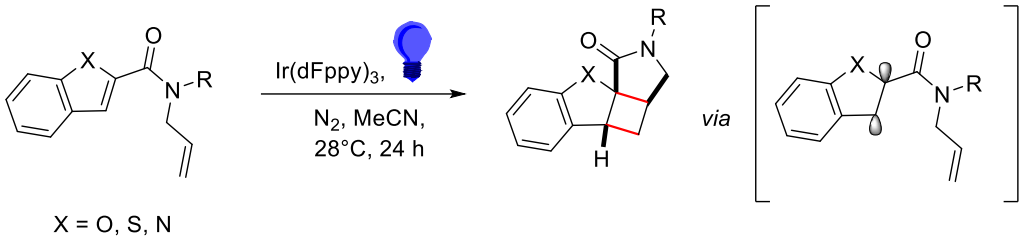
One year later, You and coworkers[98] reported an intramolecular dearomatization of substituted indoles (Scheme 52).



Scheme 52: Intramolecular dearomative [2+2] of activated indoles.

As Meggers, they lower the E_T of their substrate with -Ph or -acyl substituents. The reaction occurs upon activation via EnT with an Ir-PC, and several products are obtained. Notably, authors reported that with unsubstituted or electron rich indoles the reaction didn't occur, because of their too high E_T.

Similarly, in 2020 Dhar[99] obtained complex cyclobutane-fused tetracyclic scaffolds starting from benzofuran, benzothiophene and indoles as well (Scheme 53).



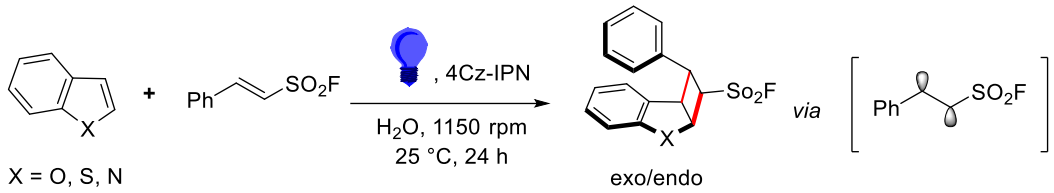
Scheme 53: Dearomative [2+2] cycloaddition for the construction of cyclobutane-fused tetracyclic scaffolds.

Also in this example, authors reported several substrates designed to have low E_T and be sensitized by Ir-PC. They achieved a broad scope of products, with notably yields up to 99% and perfect diastereoselectivity.

However, the limitations of these similar approaches are clear. You need substrates with low E_T, otherwise the reaction didn't occur. This could result in synthetic efforts in the substrate design, with the increase of dimensions and molecular weight of products, that is not always useful for medicinal chemistry. Moreover, even if you can access the sensitization of benzoheteroaromatics, activating simple/unbiased heterocycles like furan, thiophene and pyrrole results impossible because their ET are too high (≈ 70-75 kcal/mol[100]).

Researchers, started to develop methodologies that face the activation of an appropriate arenophile, that can react with the heteroaromatic in an inter- or intramolecular fashion.

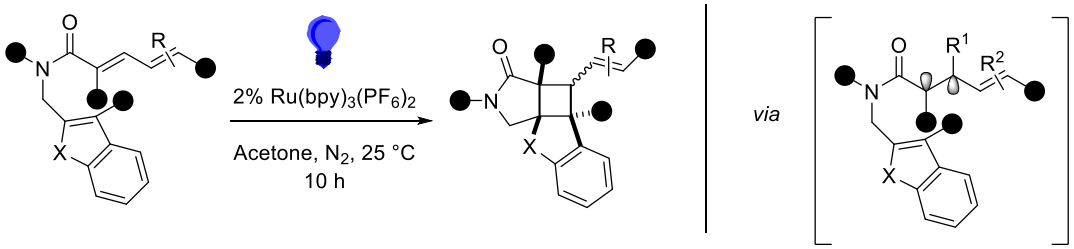
A recent example is reported by Bae et.al.[101], in which they achieved a fascinating intermolecular dearomatization of unbiased benzoheterocycles activating a SuFEx precursor (Scheme 54).



Scheme 54: Intermolecular [2+2] of benzo and simple heteroaromatics.

Authors reported an innovative methodology in which the dearomative cycloaddition occur in aqueous media. Using the heteroaromatic as reactant/solvent and a vigorous stirring, they make a myriad of small droplets inside the reactor. This media can maximize the interaction between the organic reagents and force them to efficiently react together. Author reported that the same reactivity was suppressed in standard organic solvents. Notably, they also reported the dearomatization of simple furan, even with moderate yields (44%).

In 2022, Xu and coworkers[102] presented an intramolecular [2+2] cycloaddition on benzo heteroaromatics that involves the activation via EnT of a dienone as arenophile (Scheme 55).

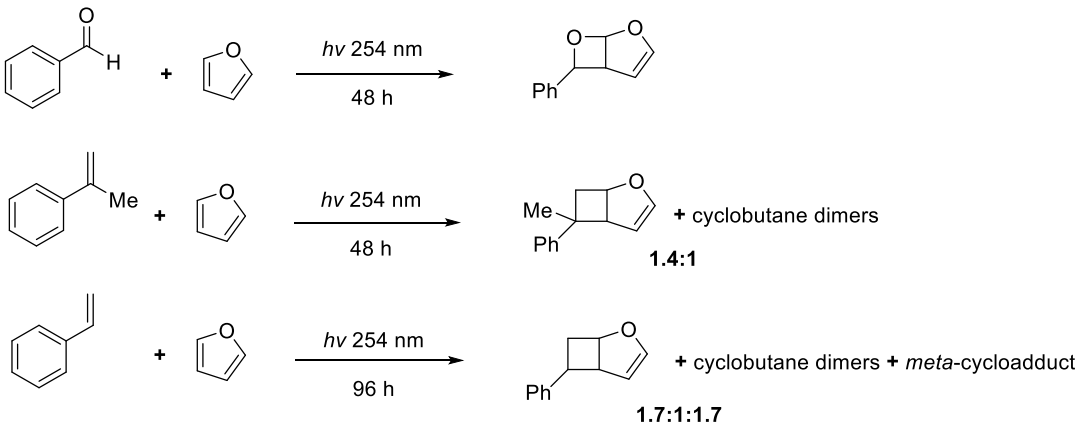


Scheme 55: Intramolecular [2+2] between benzoheterocycles and activated dienone.

They designed a particular dienamide that have a very low E_T and can be sensitized with Ru-PC upon irradiation with blue LEDs. With this transformation, they achieved complex products in high yields, with the formation of up to 4 contiguous quaternary carbon stereocenters in an appreciable diastereolective manner. Also in this paper, authors reported two examples where they dearomatized furan (45%) and thiophene (80%). It is worth saying that single, sporadic examples are not sufficient to understand the true feasibility of the above-

mentioned methodologies in a general approach for the dearomative [2+2] cycloaddition of simple heteroaromatics.

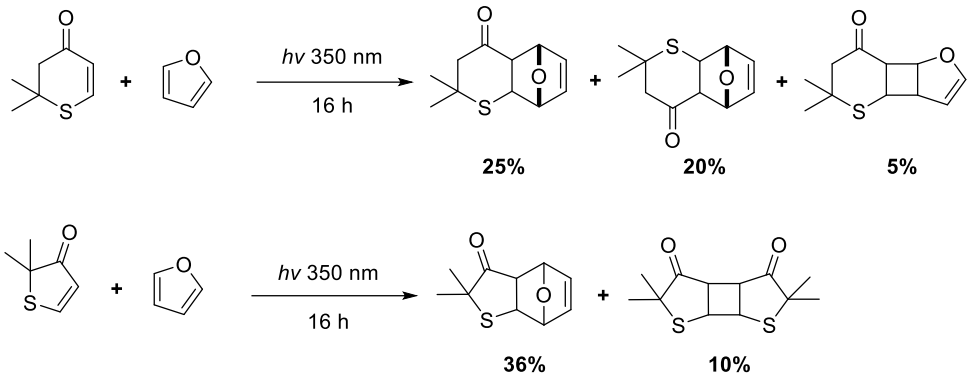
Pioneering examples for the [2+2] dearomative cycloaddition of furan are attributable to Gilbert and coworkers[103,104] (Scheme 56).



Scheme 56: pioneering examples of dearomative [2+2] cycloaddition of furan.

In these studies, authors showed that furan can undergo to [2+2] cycloaddition with benzaldehyde, 2-phenyl propene and styrene upon excitation with UV-lamp at 254 nm. However, the desired products are obtained as complex mixtures together with the *meta*-cycloadduct and the dimers derived from the [2+2] between two styrenes. Although with few examples, this proof demonstrates that furan can dearomatize by forming [2+2 cycloadducts] with an appropriate arenophile (i.e. the excited arene).

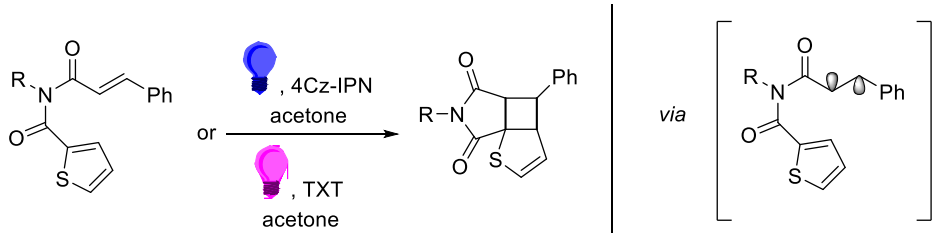
Another early work was reported by Margaretha et.al.[105], in 1992 (Scheme 57).



Scheme 57: UV-induced reactivity of furan with cycloalkenones.

Authors described the light-induced reactivity of furan with particular cycloalkenones. The two reactivities are not selective, achieving mixtures of compounds with mainly [4+2] cycloadduct products. Indeed, when the substrate was the cyclohexenone only 5% of [2+2] cycloadduct was recovered, while when a cyclopentenone was reacted no traces of [2+2] products were isolated.

To the best of my knowledge, from the literature emerges the lack of efficient methodologies that involves the dearomatization of simple heterocycles. Only recently, Yin and coworkers[106] reported a general procedure for the visible-light-promoted dearomative [2+2] cycloaddition of simple thiophenes (Scheme 58).



Scheme 58: Efficient [2+2] cycloaddition of thiophenes.

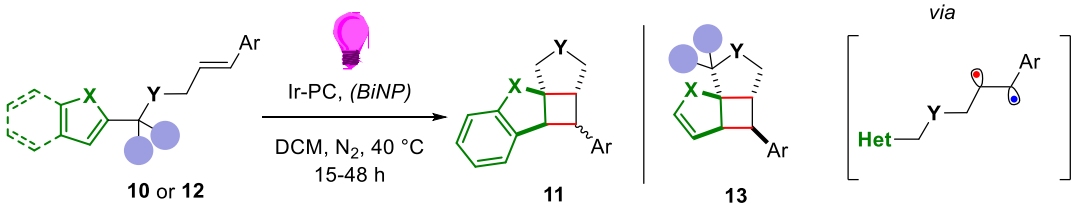
Upon EnT activation of the styrene, the triplet can attack the heterocycle (mainly thiophene) in an intramolecular fashion. The process is favoured by the

succinimide-like cycle that stabilizes the structure of the product[102]. They also reported the dearomatization of an indole, a benzofuran and a benzothiophene with high yields and diastereoselectivity. However, yield dropped down replacing thiophene with furan (27-54%) because the reaction was not selective, isolating the undesired [4+2] cycloadduct in a 1:0.7 ratio between [2+2] and [4+2].

From the reported examples, it is worth nothing that a methodology that bring to a general and selective dearomative [2+2] cycloaddition of benzo and simple heteroaromatic (in particular furan) would increase the accessible chemical space in this field and can contribute to the discovery of new potential biological active species with high molecular complexity and saturation, by keeping low molecular weights.

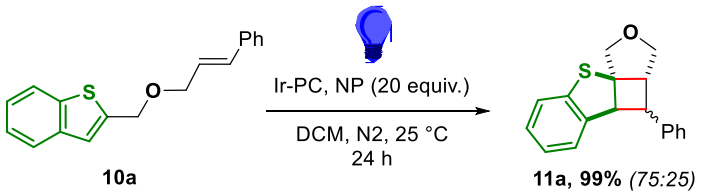
4.2: Results and Discussion

In this chapter I will present an unprecedent approach for the visible light promoted intramolecular dearomative [2+2] cycloaddition of cinnamyls on (benzo)heteroaromatics (Scheme 59).



Scheme 59: New intramolecular dearomative [2+2] cycloaddition on (benzo)heteroaromatics.

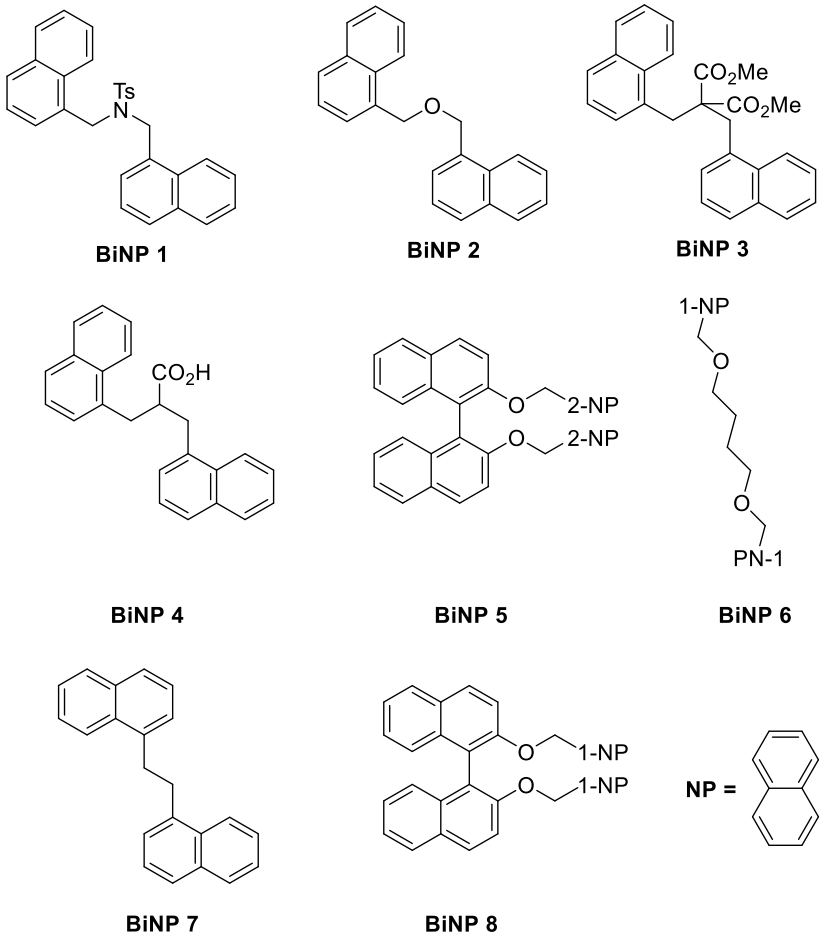
We designed a substrate that contain a simple- or benzoheterocycle as arene and a substituted cinnamyl moiety as arenophile. It is well known in literature that cinnamyl derivative can be activated via EnT upon sensitization with an Ir-PC[107]. Wondering if the resulting triplet can trigger the dearomative [2+2] cycloaddition with heteroaromatics, we synthesized substrate **10a** bearing a benzothiophene as aromatic and an ether linker (Scheme 60).



Scheme 60: First hit of the dearomatization of benzothiophene.

Mixing substrate **10a**, $Ir(ppy)_3$ and NP in DCM we achieved product **11a** with 99% yield and good diastereoselectivity upon 24 hours of irradiation with blue LEDs. Inspired by this great preliminary result, we decided to investigate the intramolecular dearomatization of simple heterocycles, which are known to be much less susceptible to this reactivity. We envisioned **12a** (Table 3, top) as good

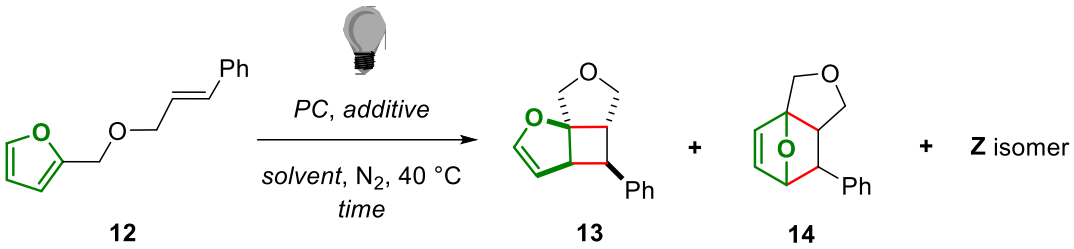
model substrate, because furan has the lowest resonance stabilization energy among all the heterocycles[24] and the synthesis of the starting material proceeded through only one step, by alkylating the commercially available furfuryl alcohol with cinnamyl bromide. Unfortunately, the reaction didn't proceed as good as that of benzothiophene, recovering mixtures of three products and unreacted starting material (Table 3). Since the reaction had probably an endergonic pathway, we wondered if the addition of NP and BiNP derivatives (Scheme 61) could be beneficial for isolating the desired product in high yields.



Scheme 61: BiNP derivatives tested in this project.

In two recent papers published in our research group[78,108], we demonstrated that NP and its BiNP derivatives have a positive effect in promoting reactions that involves the formation of triplet biradicals, by stabilizing all the intermediates that belong to the reaction pathway. In table 3 I summarized some of the main optimization studies that we performed (for other optimization experiments, see the experimental section).

Table 3: Optimization of reaction conditions.

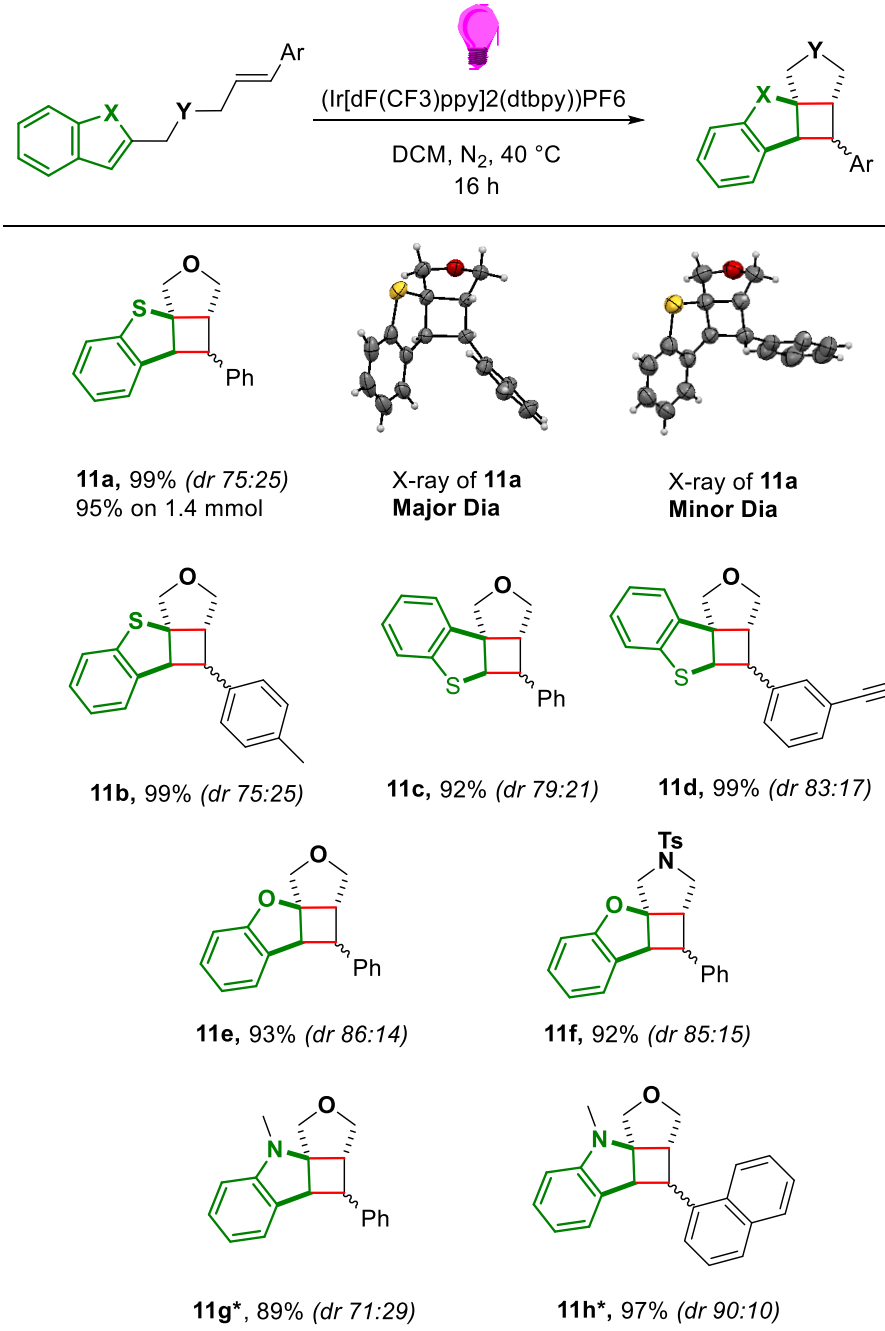


Entry[a]	Sensitizer	Additive (equiv.)	t [h]	Selectivity
BLUE LEDS (λ = 456 nm)				
1	$Ir(ppy)_3$	BiNP 1 (30 mol%)	48	38% **13**; 9% **14**; 17% **Z**; 8% **SM**
2	$Ir(ppy)_3$	BiNP 4 (30 mol%)	48	14% **13**; 4% **14**; 49% **Z**; 15% **SM**
3	$Ir(ppy)_3$	BiNP 7 (30 mol%)	48	45% **13**; 14% **14**; 12% **Z**; 5% **SM**
PURPLE LEDS (λ = 390 nm)				
4[b]	MTH161	-	48	37% **13**; 14% **14**; 23% **Z**; 7% **SM**
5	MTH161	BiNP 7 (30 mol%)	48	77% **13**
6	PC4	BiNP 7 (30 mol%)	48	85% **13**
7[c]	PC4	BiNP 7 (30 mol%)	48	71% **13**
8	PC3	BiNP 7 (30 mol%)	48	65% **13**; 3% **14**; 9% **Z**; 9% **SM**
9[d]	PC4	BiNP 7 (30 mol%)	48	82% **13**
10[e]	PC4	BiNP 7 (30 mol%)	48	41% **13**; 17% **14**; 5% **Z**
11[f]	PC4	BiNP 7 (30 mol%)	48	82% **13**
12[g]	PC4	BiNP 7 (30 mol%)	48	13% **13** + decomposition
13	w/o PC or light		120	-

*[a] Reaction conditions: 0.15 mmol of **12** (0.1 M in DCM), 1 mol% PC, 30 mol% BiNP in 5 mm-NMR tube under N_2, yields was determined using 1,3,5 trimethoxybenzene as internal standard; [b] in MeCN (0.1 M); [c] without freeze-pump-thaw; [d] in DMF (0.1 M); [e] in $CHCl_3$ (0.1 M); [f] with 2 mol% cat; [g] with Kessil Lamp (λ = 390 nm). MTH161 = $(Ir[dF(CF_3)ppy]_2(Me_4phen))PF_6$; PC4 = $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$; PC3 = $(Ir[dF(CF_3)ppy]_2(bpy))PF_6$*

We screened 8 BiNPs in the preliminary tests and BiNP 7, bearing an ethane linker, revealed as the best to promote the desired reactivity (Table 3, entries 1-3). However, the reaction was not selective, isolating desired product **13a** with the [4+2] cycloadduct **14a**, the isomer **Z** and the starting material. We then tested a PC that works better with purple light, and we obtained a surprising result, because even without additive the reaction was similar to the previous tests (entry 4). We thus decided to repeat the experiment adding BiNP 7 and we increase the yield of **13a** to 77% (entry 5). MTH161 is an heteroleptic Ir-based PC that have a tetramethyl phenantroline instead of the common bipyridyl unit. We thus tested a similar PC, the commercial $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$ (PC4) and we got 85% yield (entry 6). We then screened other catalysts and solvents, but no one allowed us to achieve better results (entries 8-10). Furthermore, any variation in the amount of PC and BiNP turned out to be useless for increasing the yield (entry 11). Because the output of the reaction was influenced by light source, we tried to use Kessil lamp (λ = 390 nm), but we observed high decomposition, probably due to the high power of the light source (entry 12). Finally, we confirmed that the removal of O_2 with freeze-pump-thaw is beneficial for the yield and that there is no reaction without light or PC (entries 7, 13). It is worth noting that the T = 40 °C is crucial in the presented reactivity. Indeed, by-product **14** is metastable and tends to comeback to starting material **12** also at room temperature (in days). We believe that the higher temperature can significantly speed up the retro [4+2], reducing the amount of **14** and increasing that of **13** (that is thermally more stable). Typically, a solution of the substrate, photosensitizer and additive (when necessary) is transferred to a 5 mm NMR tube to maximize the surface/volume ratio. Then it is degassed by freeze-pump-thaw and irradiated with a 14 W – household LED strip with purple light. After fully conversion monitored by TLC, the solution is transferred to a round bottom flask, solvent is evaporated in vacuo and the crude is purified through chromatography on silica gel.

With the best conditions in hand (entry 6), we screened several substrates (Scheme 62 and Scheme 63).

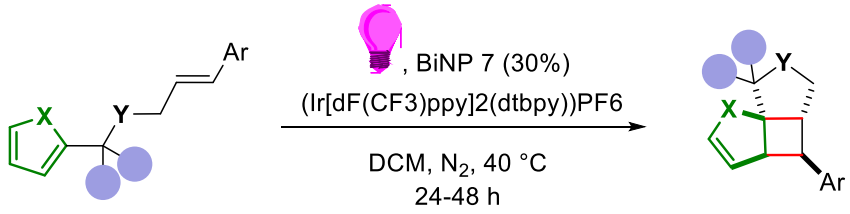


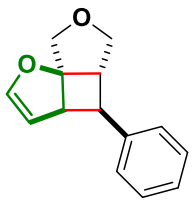
Scheme 62: Scope of benzoheterocycles.

The reaction with benzo-heterocycles proceeded smoothly, allowing us to generally isolate product **11** with excellent yields in less than 16 hours without the

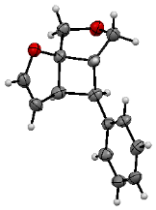
use of any BiNP additive. The product was isolated as a mixture of two diastereomers with good diastereoselectivty. The two isomers can be separated, and we could confirm their relative configuration through XRD analysis. In the major diastereomer, the phenyl of cinnamyl moiety and the benzene ring of the heteroaromatic are stacked, while in the minor the two have an anti-configuration. When the reaction was scaled up to 1.4 mmol, the surface/volume ratio decreased and we needed more irradiation time to achieve the full conversion of **10a**, but without significative loss in the yield (95%). A *para*-methyl cinnamyl is tolerated, isolating **11b** with the same yield as **11a**. The benzothiophene can be linked in position 2 or 3 without differences in the reactivity and diastereoselection (**11c-d**). A synthetically useful terminal alkyne is well tolerated (**11d**) and it can be the starting point for further derivatizations. Moreover, benzofurans react well, isolating two products with high yields (**11e-f**). Notably, the O- linker can be replaced with a Ts-N one without significative differences. Finally, we achieved the successful dearomatization of two electron rich indoles with excellent yields (**11g-h**). Because of their electronic properties, it was necessary to replace the highly oxidant PC4 with $Ir(ppy)_3$ to access the desired reactivity. It is worth noting that, the indoles of these two last substrates can't be activated by EnT because their E_T would be too high. Thus, it would be impossible to achieve these products following the other dearomative approach, activating the arene instead of the arenophile.

We then moved to the scope of simple heterocycles (Scheme 63). As I mentioned before, the reaction is way more challenging because the process is endergonic. This normally result in very yields and longer reaction time, but after the optimization we isolated product **13a** with 82% yield in a reasonable irradiation time (48 h). Also in this case, the scaled-up reaction needed more time of irradiation to fully consume the starting material, allowing us to isolate it with a satisfactory 65% yield. Notably, product **13** is recovered as a single isomer, with the phenyl ring and the dearomatized heterocycle directed in the same way.

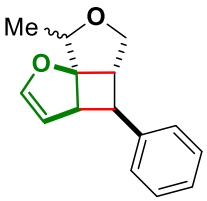




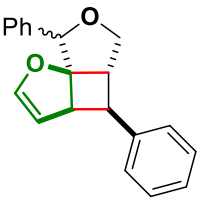
13a, 82%
65% on 1.6 mmol



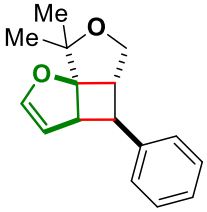
X-ray of **13a**



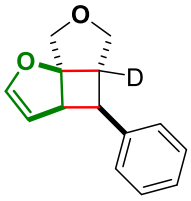
13b, 55% *(dr 58:42)*



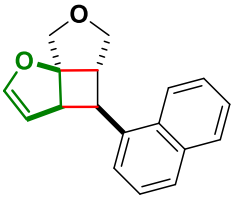
13c, 70% *(dr 57:43)*



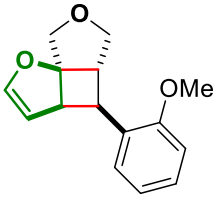
13d*, 59%



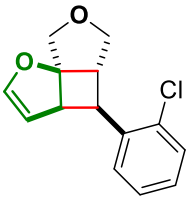
13e, 71%



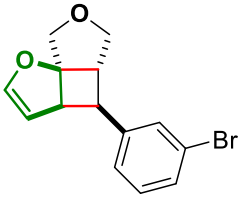
13f, 53%



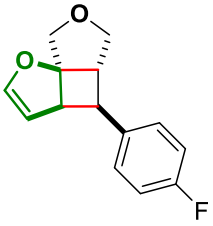
13g, 62%



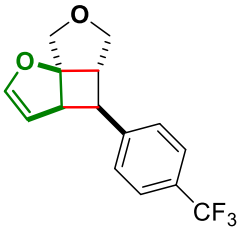
13h, 88%



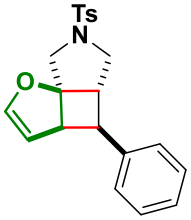
13i, 84%



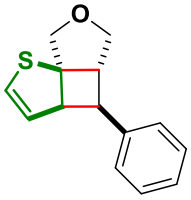
13j, 70%



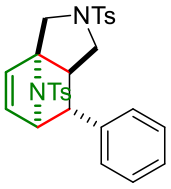
13k, 75%



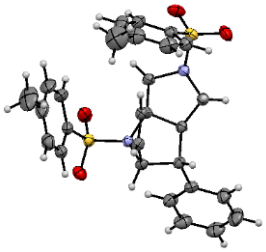
13l, 56%



13m*, 35%



14n, 55%



X-ray of **14a**

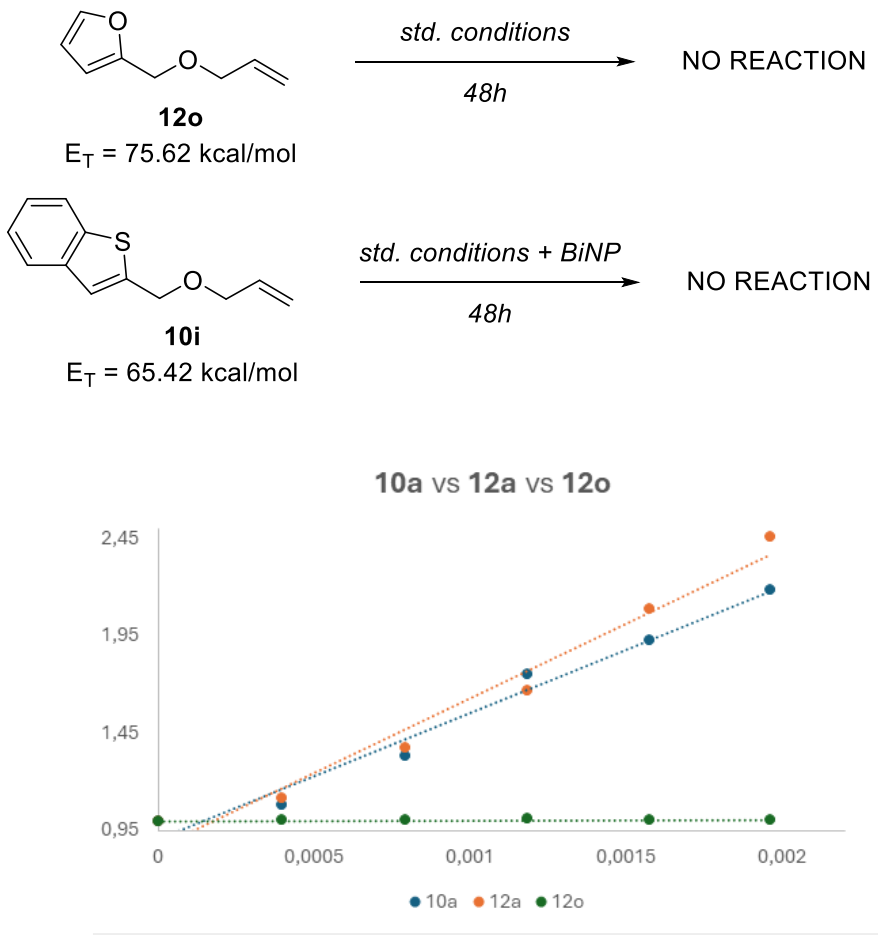
Scheme 63: Scope of simple heterocycles.

We then evaluated substitution in α position respect to the furan, wondering if Thorpe-Ingold effect could speed up the reaction. Indeed, products **13b-d** had faster reaction rates (around 36 h) but the yield decreases. We observed that these substrates are sensitive to reaction conditions, and they are very prone to degradation if the temperature increases too much. Moreover, product **13d** was obtained upon replacing PC4 with $Ir(ppy)_3$, probably for the same electronic reason as above. The deuterated substrate **12e** reacted well and was useful to identify the structure of the product, that was eventually confirmed by XRD analysis. Then, we tested several substituted cinnamyls (**13f-k**). Notably, electron withdrawing group seems to favour the reactivity more than electron donating one, allowing us to isolate product **13h** with the best yield of the scope (88%) upon only 24 hours of irradiation. Halogens are well tolerated (**13h-j**), except iodine, that gave only the isomerized starting material (for a complete scheme of limitation see the experimental section). Finally, we changed the O- linker with Ts-N one (**13l**) with a slightly decrease of yield (56%). Unfortunately, N-Boc and N-Ac linker didn't react well, isolating only traces of the desired product. We tested also substituted furans in C5-position, but the outputs of the reaction were complex and from the NMR analysis there were only traces of the desired products. Further studies are ongoing to understand the reason of these observations. Then we successfully dearomatize a thiophene (**13m**), that has a higher resonance stabilization energy with satisfactory yield (35%). Indeed, with a derivatization, it should be possible to induce a diastereoselective oxidation to form synthetically useful sulfones.

The reaction with an electron-rich pyrrole didn't go well, resulting in the degradation of starting material. We then synthesized the electron-poor **12n**, with two Ts_s in the molecule and we isolated a product with 55% yield. However, from NMR analysis the resonances were unusual, and, thanks to the XRD resolution, we confirmed that product **14n** is the [4+2] cycloadduct and not the desired [2+2]. In our opinion, the increased steric hindrance of the two Ts groups, especially the one on the pyrrole prevent the formation of the [2+2] product and favoured the [4+2] cycloadduct. Nonetheless, this last example could be a potential starting point for

the development of a new dearomative strategy of pyrroles to access [4+2] products.

Finally, we performed some mechanistic experiments to understand better if the reaction starts with the activation of the cinnamyl moiety (Scheme 64).

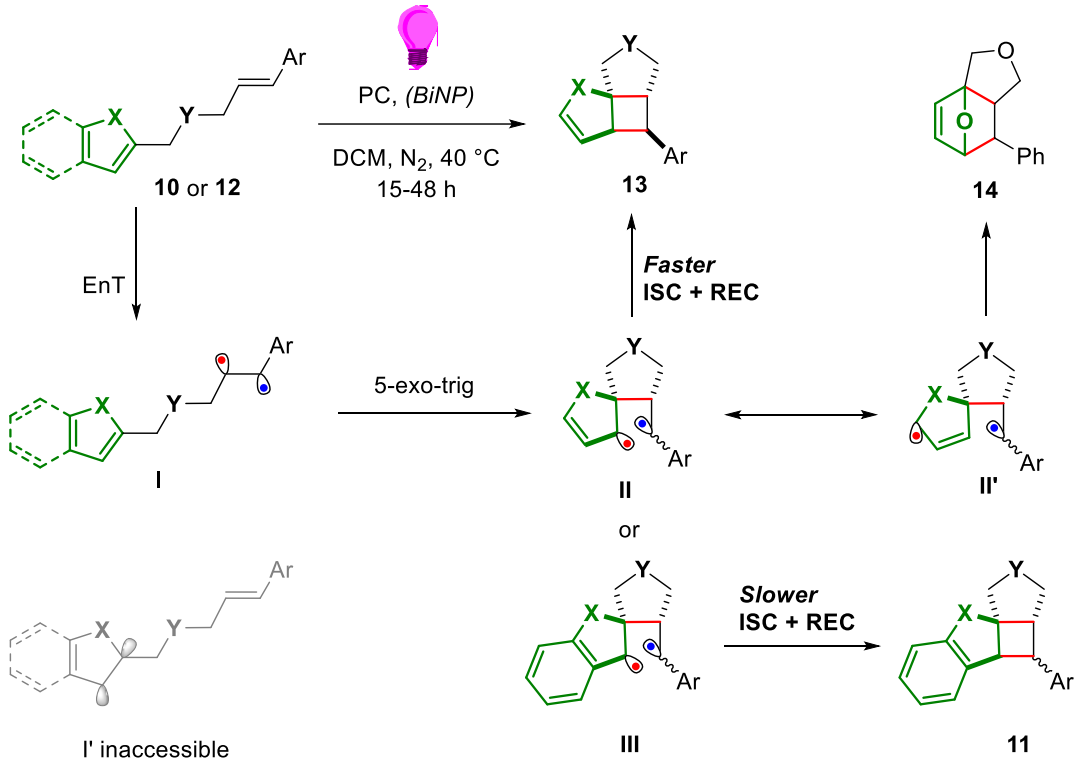


Scheme 64: mechanistic experiments.

Substrates **12o** and **10i** didn't react in the optimized conditions. Only starting material was recovered, confirming that the cinnamyl moiety is necessary to access the reactivity. Both have E_T too high to be activated via EnT. This was further confirmed by Stern-Volmer analyses. Indeed, both **10a** and **12a** quench the Ir-PC

with a high Ksv (648 M^{-1} and 766 M^{-1}respectively, full details in experimental section), while substrate **12o** didn't interact with PC4.

In Scheme 65 is reported the hypothesized mechanism that we are assuming.



Scheme 65: Hypothesized mechanism.

First, Substrate **12** is activated via EnT upon sensitization with Ir-PC. According to Stern-Volmer studies, the only accessible triplet is **I**, that can then perform a 5-*exo-trig* cyclization obtaining intermediate **II**, that is characterized by a spiro quaternary carbon. Probably, the rigidity of this atom imposes the diastereselectivity of the reaction. Indeed, with intermediate **II** the process is fast, and we achieved only one isomer. In the case of benzoheterocycles, intermediate **III** has a longer lifetime and the system can assume two configurations, even if with an unbalanced diastereoselection. Finally, intermediate **II** can seal product **13** after ISC and radical recombination. Products **14** are obtained in the same stepwise

pathway, but the ISC and recombination involve the allyl radical centred on C5 instead of C3.

4.3: Conclusions

In this chapter I showed a new intramolecular dearomatization of benzo- and simple heterocaromatics using a cinnamyl moiety as arenophile. We achieved a broad scope of 22 products with good to excellent yield. Moreover, the dearomatization of simple heterocycles, the most difficult one, is accessed with complete diastereoselectivity and exclusive [2+2] regiochemistry. To the best of my knowledge, this is the first example of a general and reliable dearomative [2+2] cycloaddition of simple furans.

We demonstrated our hypothesized mechanism with experimental proofs, and DFT calculations are ongoing to confirm the origin of the unusual diastereoselectivity.

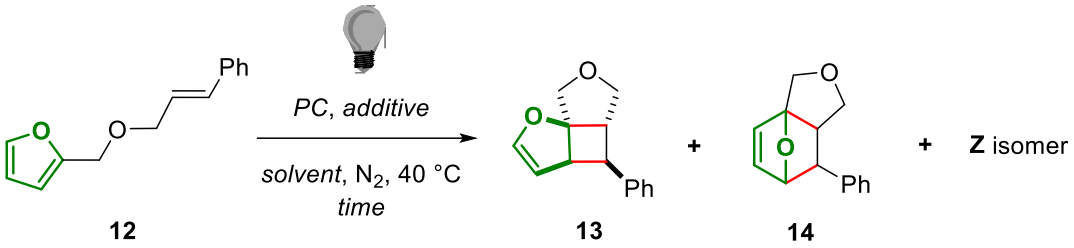
Furthermore, we isolated the [4+2] cycloadduct of pyrrole with good yield considering that this is the result of an unoptimized reaction. This example can open a possible new project in our research group.

4.4: Experimental Section

General remarks

All chemicals those synthesis are not reported hereafter were purchased from commercial sources and used as received. Solvents were dried passing through alumina columns using an Inert® system and were stored under nitrogen. Present visible-light promoted reactions did not require the use of dry solvents but the presence of molecular oxygen exerts a negative effect on their rate. Chromatographic purifications were performed under gradient using a Combiflash® system and prepacked disposable silica cartridges or through isocratic flash chromatography using commercial 60 Å silica gel. All reactions that required heating were performed with the use of high-vacuum grade silicon oil. Reactions promoted by visible light were performed into standard 5 mm NMR tubes, surrounded by a commercial strip of 300 household leds (12V, 17W). These were put at a distance of ca 10 cm and irradiated with blue light or purple light (chip SMD5630-300 ip65). ^{1}H and ^{13}C NMR spectra were recorded at 300 K on a Bruker 400 MHz or a Jeol 600 MHz spectrometers using residual non-deuterated solvents as internal standards (7.26 ppm for ^{1}H NMR and 77.00 ppm for ^{13}C-NMR for $CDCl_3$, 2.05 ppm for ^{1}H NMR and 29.84 ppm for ^{13}C NMR for acetone-d6). ^{19}F-NMR spectra were recorded in $CDCl_3$ at 298 K on a Jeol 600 spectrometer fitted with a BBFO probehead at 564 MHz. The terms m, s, d, t, q and quint represent multiplet, singlet, doublet, triplet, quadruplet and quintuplet respectively, and the term brs means a broad signal. Reported assignments were based on decoupling, COSY, NOESY, HSQC and HMBC correlation experiments. Mass analyses were recorded on an Infusion Water Acquity Ultra Performance LC HO6UPS-823M instrument equipped with a SQ detector (Electrospray source); high-resolution mass analyses were recorded on a LTQ ORBITRAP XL Thermo Mass Spectrometer (Electrospray source). Single crystal Data were collected with a Bruker D8 diffractometer equipped with PhotonII area detector, using a CuKα or a MoKα microfocus 4 radiation source. The data collection strategy covered the sphere of reciprocal space. Absorption corrections were applied using the program SADABS. The structure was solved with the SHELXT code. Fourier analysis and refinement were performed by the full-matrix least-squares methods based on F2 using SHELXL-2014 as implemented in Olex2. All the nonH atoms were refined with anisotropic displacement parameters.

Additional optimization experiments



12 13 14

Entry	Catalyst	Solvent	Additive	Time (h)	Conversion of **12a**[a]	Selectivity[a]
BLUE LEDS (λ = 456 nm)						
1	$Ir(ppy)_3$	DCM	NP (5eq)	40	99%	44% **13**; 14% **14**
2	$Ir(ppy)_3$	DCM	NP (20eq)	24	99%	56% **13**; 23% **14**
3	$Ir(ppy)_3$	DCM	BiNP 2	48	93%	43% **13**; 10% **14**; 10% **Z**
4	$Ir(ppy)_3$	DCM	BiNP 3	48	97%	41% **13**; 10% **14**; 7% **Z**
5	$Ir(ppy)_3$	DCM	BiNP 5	48	95%	49% **13**; 11% **14**; 13% **Z**
6	$Ir(ppy)_3$	DCM	-	96	90%	14% **13**; 2% **14**; 46% **Z**
7	$Ir(ppy)_3$	DCM	BiNP 2 (1eq)	48	93%	33% **13**; 9% **14**; 16% **Z**
8	$Ir(ppy)_3$	DCM	BiNP 3 (1eq)	48	94%	31% **13**; 8% **14**; 8% **Z**
9	$Ir(ppy)_3$	DCM	BiNP 6 (1eq)	48	91%	32% **13**; 8% **14**; 23% **Z**
10	$Ir(ppy)_3$	DCM	BiNP 7 (1eq)	48	96%	50% **13**; 14% **14**; 3% **Z**
11	$Ir(ppy)_3$	DCM	BiNP 8 (1eq)	48	84%	16% **13**; 6% **14**; 52% **Z**
12	$Ir(ppy)_3$	DCM	NP (20eq)	48	99%	63% **13**
PURPLE LEDS (λ = 390 nm)						
13	$Ir(ppy)_3$	DCM	BiNP 7	48	90%	40% **13**; 23% **Z**
14	TXT(10%)	DCM	BiNP 7	48	99%	78% **13**
15	BP (10%)	DCM	BiNP 7	48	62%	56% **Z**

16	PC4	DCM	BiNP 7	48	99%	61% **13**; 23% **14**
17	PC4	MeCN/DCM 3:1	BiNP 7	48	99%	61% **13**
18	PC4	Toluene	BiNP 7	48	93%	70% **13**; 3% **14**; 9% **Z**
19	PC4	EtOAc	BiNP 7	48	99%	83% **13**
20	PC4	DCE	BiNP 7	48	99%	82% **13**
21	PC4	DCM (0.05M)	BiNP 7	48	99%	80% **13**
22	PC4	DCM	BiNP 7 (1 eq.)	48	99%	66% **13**
23	PC4 (2%)	DCM	BiNP 7 (1 eq.)	48	99%	76% **13**
24	PC4	DCM (0.2M)	BiNP 7	48	83%	51% **13**; 26% **Z**
25	PC4	DCM	BiNP 7 (10%)	48	99%	81% **13**
26	PC4	DCM	BiNP 7 (50%)	48	99%	74% **13**
27	PC4	DCM	NP (20eq)	48	99%	67% **13**
28	PC4	DCM	BiNP 7	24	99%	35% **13**; 12% **14**; 23% Z
29	PC4	DCM	-	48	99%	50% **13**; 12% **14**

*[a] Reaction conditions: 0.15 mmol of **12** (0.1 M in DCM), 1 mol% PC, 30 mol% BiNP in 5 mm-NMR tube under N_2, yields was determined using 1,3,5 trimethoxybenzene as internal standard. TXT = thioxanthone, BP = benzophenone, PC4 = $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$.*

Stern-Volmer quenching studies

The measurements of fluorescence emissions were carried out with a FLS1000 Edinburgh fluorometer, equipped with automatic polarizers. Emissions have been collected by exciting the sample with a Xenon lamp at 380 nm and the luminescence was measured at 480 nm. Fluorescence spectra are corrected for the excitation intensity and detector sensitivity.

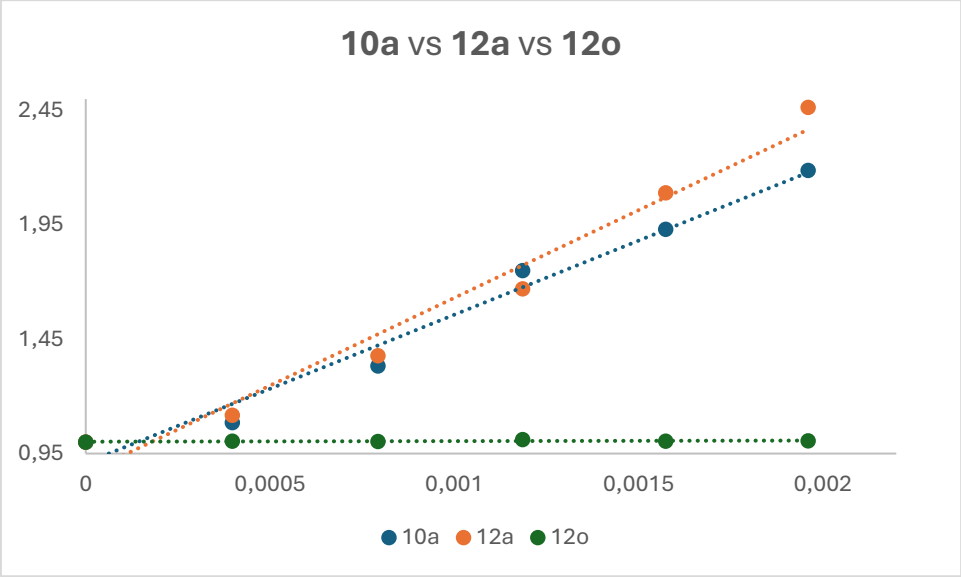
Stern – Volmer quenching studies were carried out using a 10^{-5} M solution of $(Ir[dF(CF_3)ppy]_2(dtbpy))PF_6$ [**PC4**] in DMF and variable concentrations of **10a**, **12a** and **12o** from 0 to 2 mM. 2.5 mL of **PC4**'s solution was transferred in a 3.5 mL quartz cuvette and degassed twice for 5 minutes (with a 30 second break in between) before collecting the first spectra. Then, after each addition of quencher, the samples were degassed for 3 minutes and spectra were quickly recorded.

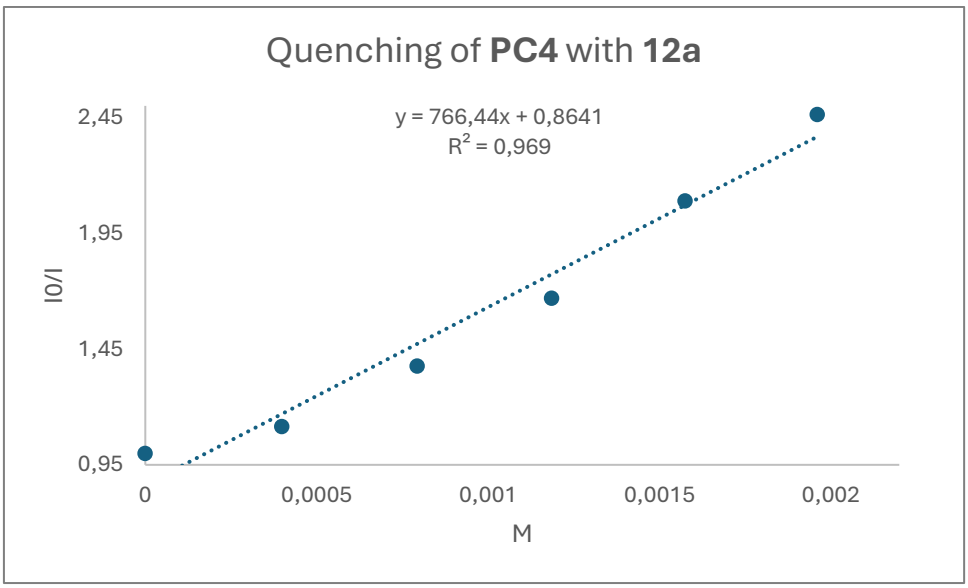
Linear Stern – Volmer plots were obtained at varying concentrations of the three substrates, and K_{SV} constants were extracted according to the equation $I_0/I = 1 + K_{SV}[Q]$. **10a** and **12a** clearly quench **PC4**, with high Ksv and without significant differences. On the other hand, **12o** doesn't quench **PC4**, with only 2.5 as Ksv. This result is consistent with experimental observations. Indeed, when **12o** was tested with optimized reaction conditions it showed no reactivity (recover of starting material), reasonably because its triplet energy is too high (≈ 75 Kcal/mol[100]).

Comprehensive table of Stern – Volmer constants

QUENCHER	K_{SV}	R^2
10a	648	0.98
12a	766	0.97
12o	2.5	0.22*

**From a quantitative point of view, the difference between the values of residues is very low. The quality of the plot, in particular the low R^2 should be attributed to statistical experimental and instrumental errors.*





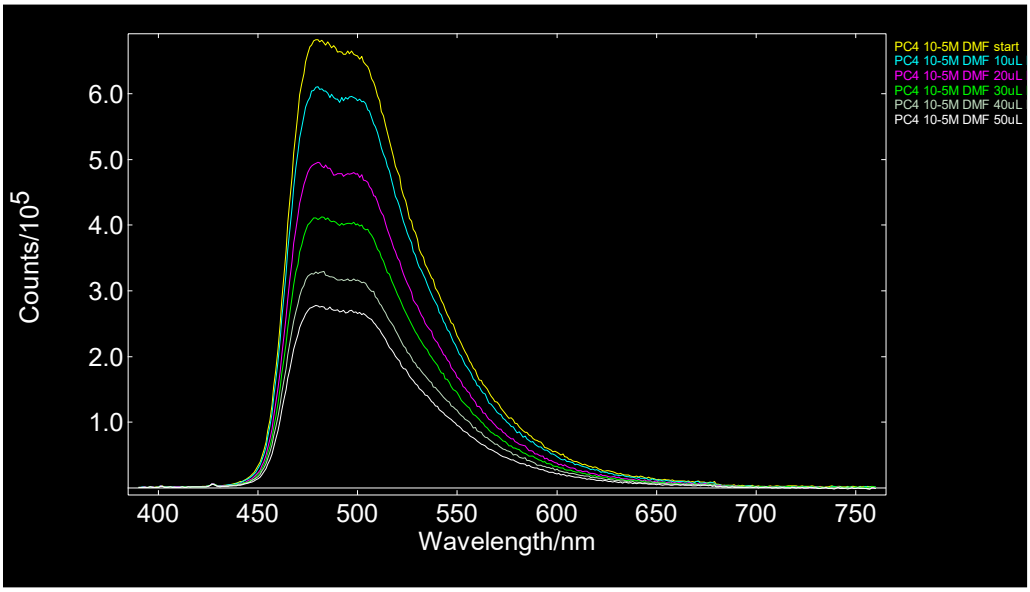
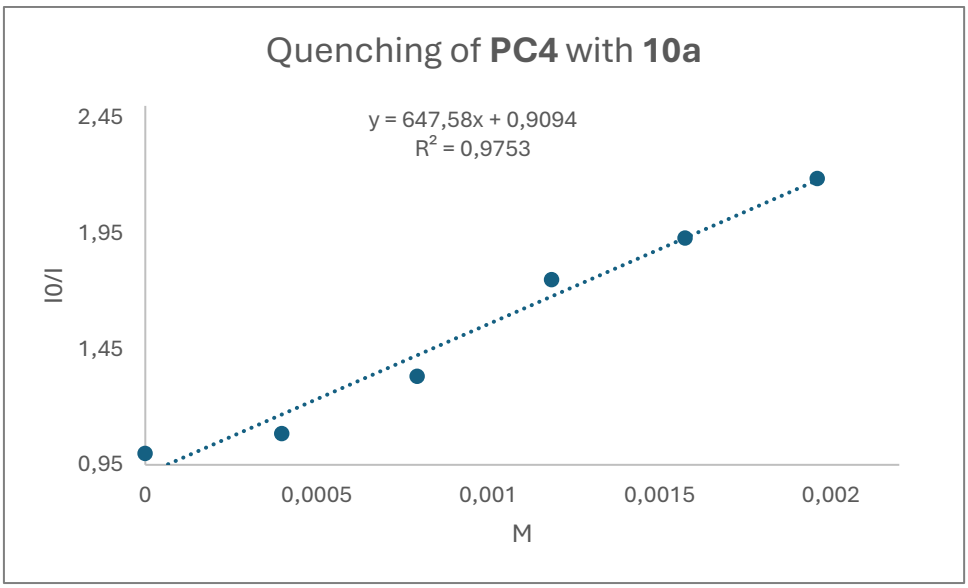


*Figure 15: Measured emissions for the quenching of **PC4** with **12a.***



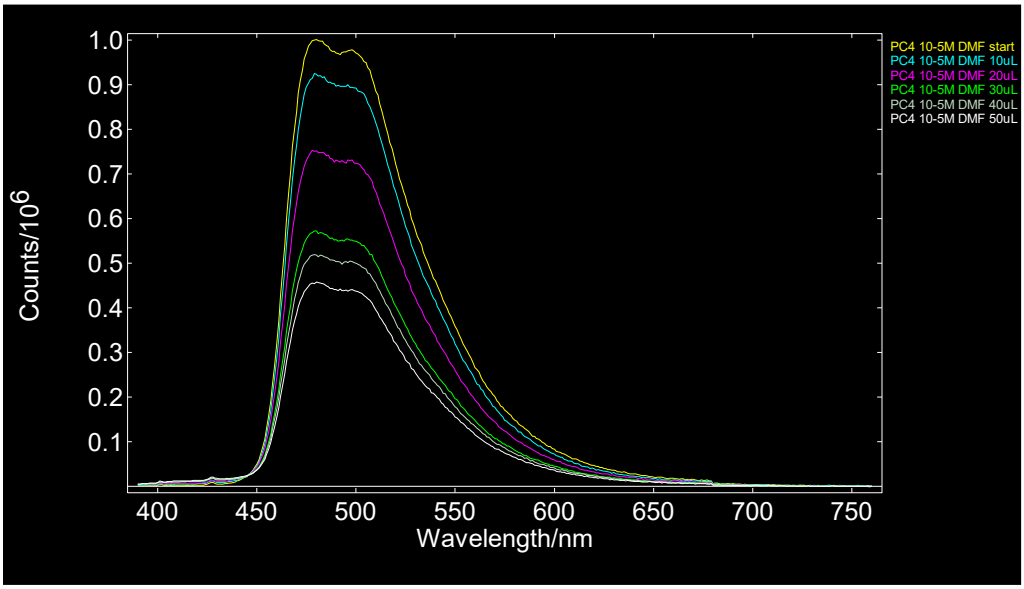
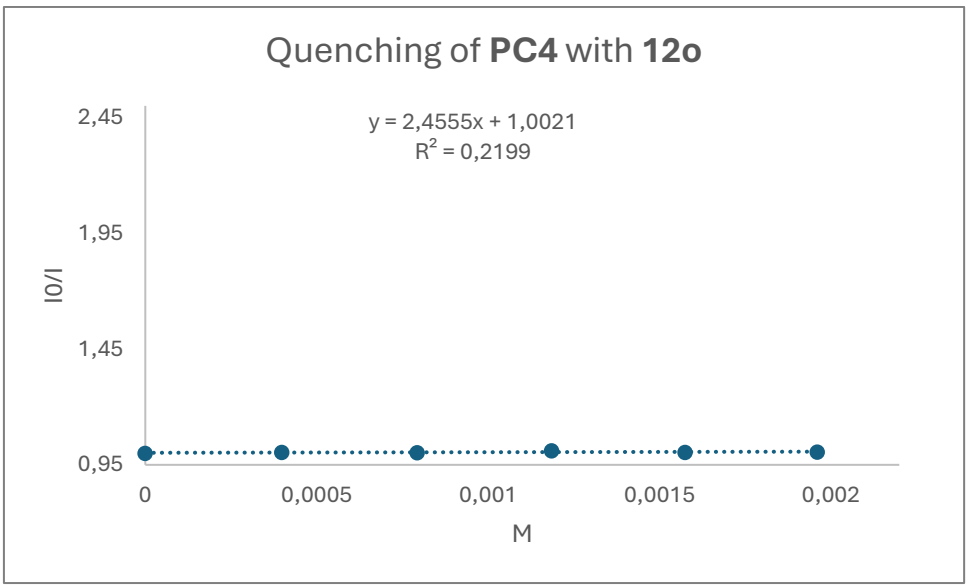


*Figure 16: Measured emissions for the quenching of **PC4** with **10a.***



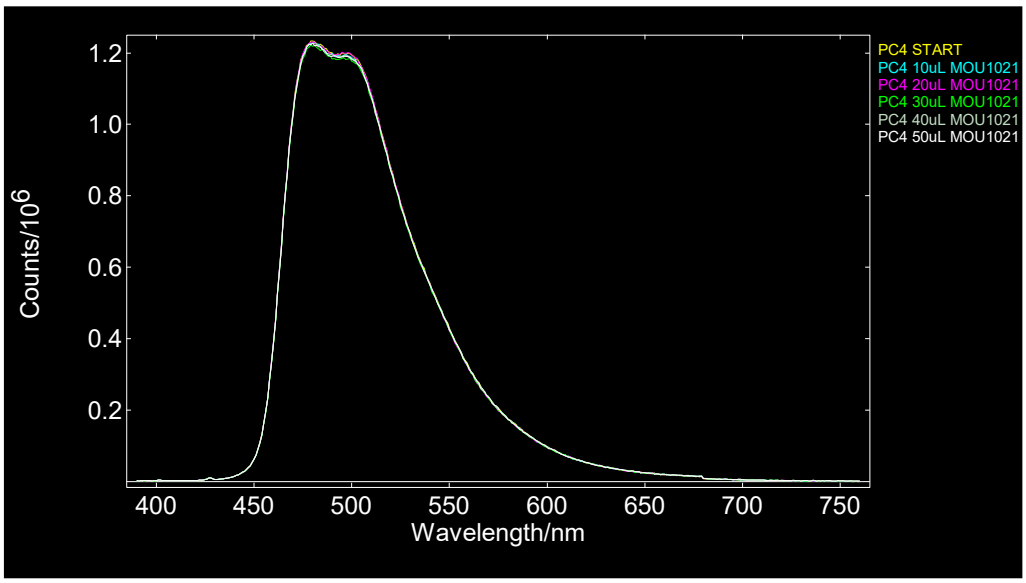
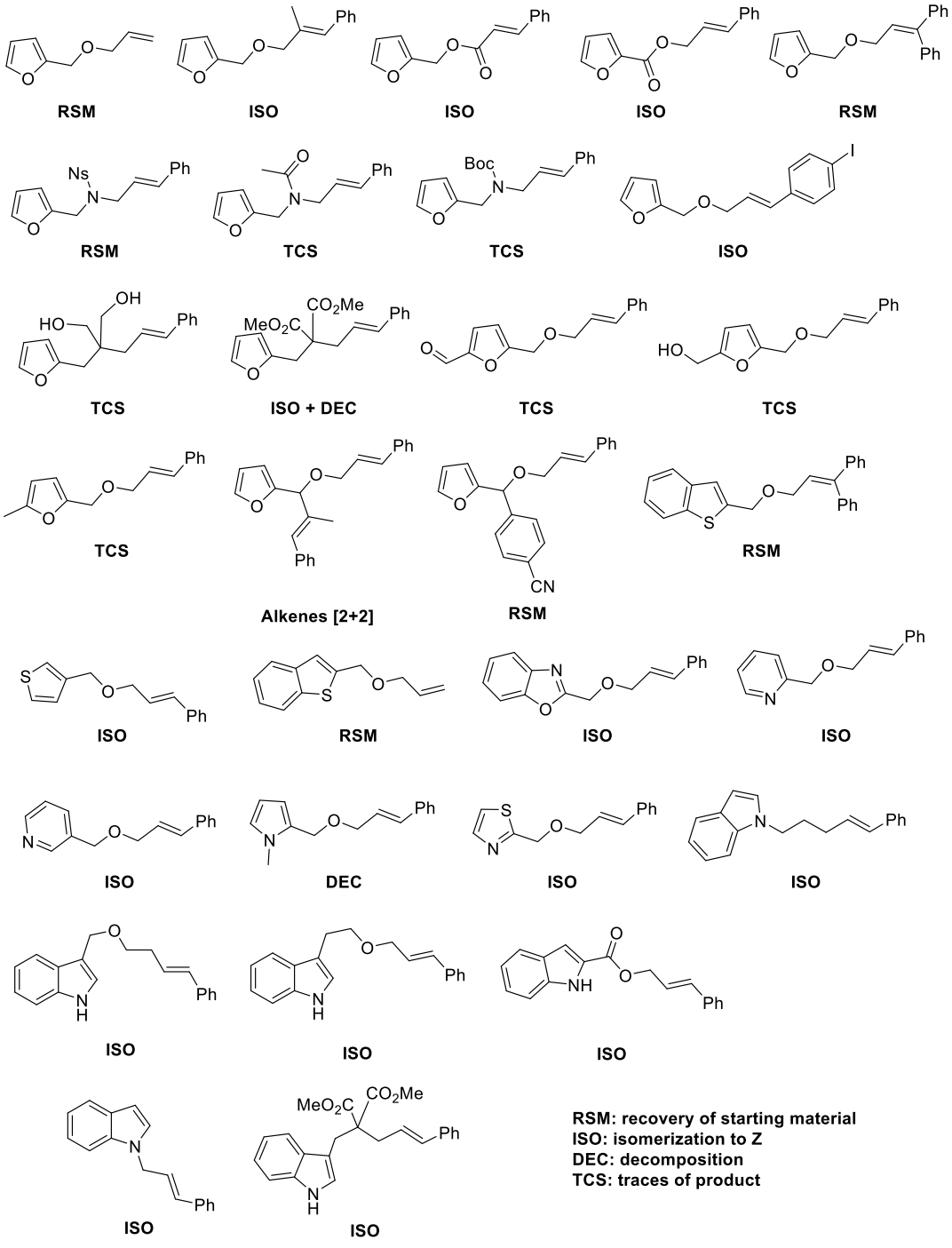


*Figure 17: Measured emissions for the quenching of **PC4** with **12o.***

Unsuccessful substrates

The following substrates did not afford the desired products **11** or **13**.



Synthesis of substrates

A) Synthesis of aldehydes

Synthesis of **1-methyl-1H-indole-2-carbaldehyde**

To a solution of 1-methyl-1H-indole (1 equiv.) in Et_2O (0.7 M) at 0° C, *n*-BuLi (2.5 M in hexane, 1.1 equiv.) was slowly added, and the mixture was refluxed for 3 hours. The reaction was cooled down to room temperature, then DMF (1.5 equiv.) was added, and the solution was refluxed for 5 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (Yield = 63%).

B) Synthesis of alcohols

Representative procedure for the reduction of aldehydes/ketones

A solution of aldehyde/ketone (1 equiv.) in MeOH (0.2M) was cooled to 0 °C and $NaBH_4$ (1.5 equiv.) was then added in three portions. The mixture was stirred at room temperature until completion, monitoring the process by TLC. The solution was then quenched with saturated NH_4Cl solution and solvent was evaporated. Then, the product was extracted with EtOAc. The organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The resulting crude was used without further purification for the next step.

Synthesis of **furan-2-yl(phenyl)methanol**

PhMgBr (1.2 M in THF, 1.25 equiv.) was slowly added to a solution of furfural (1 equiv.) in THF (0.5M) at 0 °C. The mixture was stirred at room temperature for 18 hours. After complete conversion as monitored by TLC, the solution was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic phase was then washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (n-hexane/EtOAc gradient) to afford the desired product. (Yield = 95%).

Synthesis of **2-(furan-2-yl)propan-2-ol**

n-BuLi (2.5 M in hexane, 1.2 equiv.) was slowly added to a solution of furan (1 equiv.) in THF (1M) at -10 °C. The mixture was stirred at the same temperature for 2 hours, before adding dry acetone (1.2 equiv.). After complete conversion as monitored by TLC, the solution was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic phase was then washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (n-hexane/EtOAc gradient) to afford the desired product. (Yield = 56%).

C) Synthesis of primary Ts-amine

Synthesis of Ts-amines *via* reductive amination

To a solution of aldehyde (1 equiv.), Ts-NH_2 (1 equiv.) and TEA (5 equiv.) in DCM (0.04 M) was slowly added $TiCl_4$ (1M in DCM, 0.5 equiv.) at 0 °C and the mixture was then stirred at room temperature for 18 hours. The reaction was then quenched with water and extracted with DCM. The combined organic phase was washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude was later dissolved in MeOH (0.1 M) and $NaBH_4$ (1.25 equiv.) was added portion wise at 0 °C. After 2 hours of stirring at room temperature, the solvent was evaporated, and then diluted with EtOAc. The combined organic phase was then washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (n-hexane/EtOAc gradient) to afford the desired product. Yields between 63-90%.

Tosylation of primary amines

To a solution of primary amine (1.05 equiv.) and TEA (1.05 equiv.) in DCM (0.4 M) was slowly added TsCl (1 equiv.) at 0 °C, and the reaction was stirred at room temperature for 18 hours. After complete conversion as monitored by TLC, the solution was quenched with water, extracted with DCM and the organic phase was washed with water and brine. Then, the organic phase was dried over with Na_2SO_4, filtered and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (n-hexane/EtOAc gradient) to afford the desired product. Yields between 85-95%.

D) Synthesis of cinnamic-2-*d* acid

In a round bottom flask equipped with a magnetic stirring bar and a condenser a solution of malonic acid (1 equiv.), piperidine (0.35 equiv.) and D_2O (14 equiv.) in pyridine (1.5 M) were refluxed for 2 hours; benzaldehyde (1 equiv.) was then added, and the mixture was stirred for an additional 3 hours. The resulting mixture was poured in a HCl solution (10% m/V), the precipitate was filtered, washed with water and dried under vacuo affording the corresponding carboxylic acid (Yield = 53%; deuterium incorporation: 84%).

E) Synthesis of esters

Synthesis of esters *via* Fisher's esterification

In a schlenk equipped with a magnetic stirring bar, were dissolved cinnamyl acid (1 equiv.) and sulfuric acid (cat.) in methanol (0.5M). The reaction was refluxed for 18 hours. After complete conversion as monitored by TLC, the solution was quenched with water, extracted with EtOAc and the organic phase was washed with water and brine. Finally, the organic phase was dried over with Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude was used without further purification for the next step.

Synthesis of esters *via* Heck's coupling

In a Schlenk tube equipped with a magnetic stirring bar under nitrogen atmosphere, were added $Pd(OAc)_2$ (0.02 equiv.), P(*o*-tol)$_3$ (0.04 equiv.), TEA (1.5 equiv.), acrylate (1.3 equiv.) and the aryl halide (1 equiv.) in DMF (1 M). The resulting mixture was stirred at 120 °C for 18 h. After complete conversion as monitored by TLC, the mixture was diluted with EtOAc, washed twice with water and a saturated LiCl solution, dried with Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 40-92%.

Synthesis of esters *via* Wittig olefination

To a solution of phosphonium ylide (1.08 equiv.) in MeCN (0.12 M) the desired aldehyde (1 equiv.) was added. The resulting mixture was refluxed for 45 min under stirring. After complete conversion monitored by TLC, the mixture was concentrated under reduced pressure and purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 70-96%.

F) Reduction of esters with DIBAL

To a solution of ester (1 equiv.) in THF (0.25M) at -78 °C was slowly added DIBAL (1M in toluene, 2.3 equiv.) and the mixture was stirred at -78° C for 2 hours. The reaction was then warmed to 0 °C before adding saturated NH_4Cl solution and Rochell's salt. The mixture was then extracted with EtOAc, and the organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 60-90%.

G) Bromination of substituted cinnamyl alcohols with PBr_3

To a stirred solution of alcohol (1 equiv.) in dry Et_2O (0.8 M) under nitrogen was added PBr_3 (1.05 equiv.) at 0°C. The resulting mixture was stirred at 0 °C for 30 minutes. The solution was quenched with saturated $NaHCO_3$ solution and extracted with DCM. The combined organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude was used without further purification for the next step.

General procedure for the synthesis of unbiased starting materials (**10a-f**; **12a**, **12e-m**) [**GP-1S**]

In a schlenk-type flask containing TBAI (5 mol%) and the desired alcohol (1 equiv.) in THF (0.5 M) was added NaH (60% wt, 1.15 equiv.) at 0 °C under nitrogen atmosphere. The reaction was stirred for 30 minutes at 0 °C, and bromide (1.15 equiv.) was slowly added. The resulting mixture was stirred for 18 hours at room temperature. After complete conversion monitored by TLC, the mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude was purified by chromatography on silica gel (n-hexane/EtOAc gradient).

General procedure for the synthesis of starting materials with N-linker (**10f, 12l, 12n**) [**GP-2S**]

A mixture of sulfonyl amide (1 equiv.), cinnamyl chloride (1.3 equiv.) and K_2CO_3 (1.5 equiv.) in acetone (0.33 M) was refluxed for 18 hours. After complete conversion monitored by TLC, the mixture was quenched with saturated NH_4Cl solution and filtered on Celite®. Acetone was evaporated, and the mixture was diluted with EtOAc. The combined organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude was purified by chromatography on silica gel (n-hexane/EtOAc gradient).

General procedure for the synthesis of indole-derivative starting materials (**10g, 10h**) [**GP-3S**]

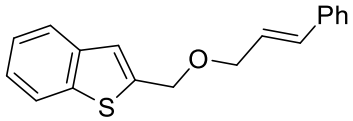
To a stirred suspension of NaH (60% wt, 1.5 equiv.) in THF (0.13 M) at 0 °C, **(1-methyl-1H-indol-2-yl)methanol** (1 equiv.) was slowly added, and the mixture was stirred at the same temperature. After 2 hours, bromide (2 equiv.) was added, and the reaction was stirred for 18 hours at room temperature. After complete conversion monitored by TLC, the mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude was purified by chromatography on silica gel (n-hexane/EtOAc gradient).

General procedure for the synthesis of biased starting materials (**12b-d**) [**GP-4S**]

To a stirred suspension of NaH (60% wt, 1.1 equiv.) in DMF (0.32 M) at 0 °C, the unbiased alcohol (1 equiv.) was slowly added, and the mixture was stirred at the same temperature. After 30 minutes, bromide (1.1 equiv.) was added, and the reaction was stirred for 18 hours at room temperature. After complete conversion monitored by TLC, the mixture was quenched with saturated NH_4Cl solution and extracted with EtOAc. The combined organic phase was washed with water and brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The resulting crude was purified by chromatography on silica gel (n-hexane/EtOAc gradient).

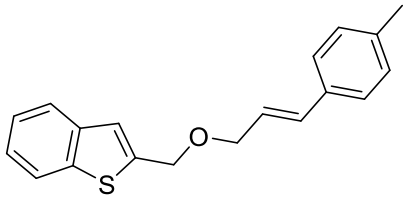
Characterization of substrates

2-((cinnamyloxy)methyl)benzo[b]thiophene



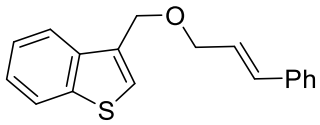
Alkene **10a** was prepared following general procedure **GP-1S** from the corresponding alcohol (410.55 mg, 2.5 mmol). Pale yellow solid (630.9 mg, 90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89 – 7.83 (m, 1H), 7.80 – 7.74 (m, 1H), 7.47 – 7.24 (m, 8H), 6.68 (d, *J* = 15.9 Hz, 1H), 6.36 (dt, *J* = 15.9, 6.1 Hz, 1H), 4.86 (d, *J* = 1.0 Hz, 2H), 4.28 (dd, *J* = 6.1, 1.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.2, 140.3, 139.5, 136.6, 133.1, 128.6, 127.8, 126.6, 125.6, 124.29, 124.27, 123.5, 122.6, 122.5, 70.6, 67.2. **ESI-MS** calcd for $C_{18}H_{17}OS$ $[M+H]^+$ 281.10 found 281.23.

(E)-2-(((3-(p-tolyl)allyl)oxy)methyl)benzo[b]thiophene



Alkene **10b** was prepared following general procedure **GP-1S** from the corresponding alcohol (121.5 mg, 0.74 mmol). Pale yellow oil (146.0 mg, 67% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86 – 7.82 (m, 1H), 7.77 – 7.72 (m, 1H), 7.38 – 7.28 (m, 4H), 7.24 (brs, 1H), 7.15 (d, *J* = 7.9 Hz, 2H), 6.63 (d, *J* = 16.0 Hz, 1H), 6.29 (dt, *J* = 15.9, 6.2 Hz, 1H), 4.83 (s, 2H), 4.25 (dd, *J* = 6.2, 1.4 Hz, 2H), 2.36 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.3, 140.3, 139.5, 137.7, 133.8, 133.1, 129.3, 126.5, 124.5, 124.3, 123.5, 122.6, 122.5, 70.7, 67.1, 21.3. **ESI-MS** calcd for $C_{19}H_{19}OS$ $[M+H]^+$ 295.12 found 294.97.

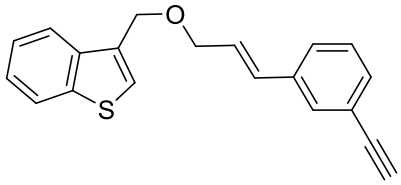
3-((cinnamyloxy)methyl)benzo[b]thiophene



Alkene **10c** was prepared following general procedure **GP-1S** from the corresponding alcohol (328.4 mg, 2 mmol). Yellow solid (417.4 mg, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.88 (m, 2H), 7.49 – 7.23 (m, 8H), 6.68 (d, *J* = 16.0 Hz, 1H), 6.43 – 6.32 (m, 1H), 4.86 (s, 2H), 4.31 – 4.25 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.7, 138.2, 136.7, 133.3, 132.8, 128.6, 127.8, 126.5, 125.9, 124.8, 124.5,

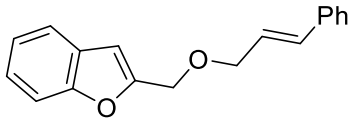
124.2, 122.8, 122.3, 70.8, 66.4. **ESI-MS** calcd for $C_{18}H_{17}OS$ $[M+H]^+$ 281.10 found 281.45.

(E)-3-(((3-(3-ethynylphenyl)allyl)oxy)methyl)benzo[b]thiophene



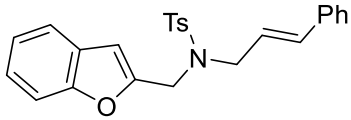
Alkene **10d** was prepared following general procedure **GP-1S** from the corresponding alcohol (228.3 mg, 1.39 mmol). Yellow solid (287.9 mg, 68% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 – 7.87 (m, 2H), 7.55 – 7.52 (m, 1H), 7.46 – 7.36 (m, 5H), 7.33 – 7.26 (m, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 6.37 (dt, *J* = 16.0, 5.9 Hz, 1H), 4.88 – 4.82 (m, 2H), 4.26 (dd, *J* = 5.9, 1.5 Hz, 2H), 3.10 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 140.7, 138.2, 136.9, 133.2, 131.5, 131.3, 130.2, 128.6, 127.1, 126.9, 124.8, 124.6, 124.2, 122.8, 122.4, 122.3, 83.5, 70.5, 66.6. **ESI-MS** calcd for $C_{20}H_{17}OS$ $[M+H]^+$ 305.10 found 305.33.

2-((cinnamyloxy)methyl)benzofuran



Alkene **10e** was prepared following general procedure **GP-1S** from the corresponding alcohol (133.3 mg, 0.9 mmol). Yellow solid (226.3 mg, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.5 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 1H), 7.46 – 7.40 (m, 2H), 7.39 – 7.22 (m, 5H), 6.77 – 6.65 (m, 2H), 6.36 (dt, *J* = 15.9, 6.1 Hz, 1H), 4.71 (s, 2H), 4.33 – 4.27 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.3, 154.3, 136.6, 133.3, 128.6, 128.1, 127.8, 126.6, 125.5, 124.4, 122.8, 121.1, 111.4, 105.8, 71.0, 64.4. **ESI-MS** calcd for $C_{18}H_{17}O_2$ $[M+H]^+$ 265.12 found 264.95.

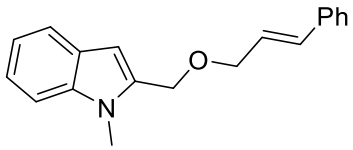
N-(benzofuran-2-ylmethyl)-N-cinnamyl-4-methylbenzenesulfonamide



Alkene **10f** was prepared following general procedure **GP-2S** from the corresponding tosyl amide (473.4 mg, 1.57 mmol). Yellow solid (426.1 mg, 65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 – 7.70 (m, 2H), 7.51 – 7.47 (m, 1H), 7.33 – 7.17 (m, 10H), 6.56 – 6.54 (m, 1H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.03 (dt, *J* = 15.8, 6.7 Hz, 1H), 4.59 (s, 2H), 4.07 – 4.02 (m, 2H), 2.38 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.9, 152.5, 143.3, 137.2, 136.1, 134.6, 129.5, 128.6, 128.0, 127.9, 127.4, 126.5,

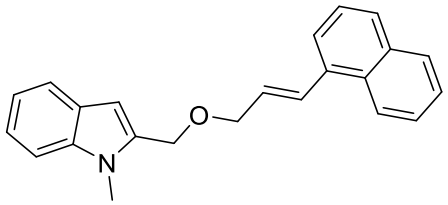
124.3, 123.6, 122.8, 121.0, 111.1, 106.2, 49.6, 43.3, 21.5. **ESI-MS** calcd for $C_{25}H_{24}NO_3S$ $[M+H]^+$ 418.15 found 418.26.

2-((cinnamyloxy)methyl)-1-methyl-1H-indole



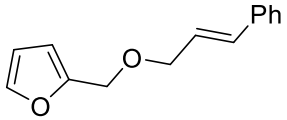
Alkene **10g** was prepared following general procedure **GP-3S** from the corresponding alcohol (161.2 mg, 1 mmol). Yellow solid (208.4 mg, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.8 Hz, 1H), 7.43 – 7.23 (m, 7H), 7.17 – 7.10 (m, 1H), 6.65 (d, *J* = 15.9 Hz, 1H), 6.53 (s, 1H), 6.32 (dt, *J* = 16.0, 6.1 Hz, 1H), 4.76 (s, 2H), 4.19 (dd, *J* = 6.1, 1.4 Hz, 2H), 3.84 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.2, 136.7, 135.7, 132.9, 128.6, 127.8, 127.2, 126.5, 125.7, 121.9, 120.8, 119.5, 109.2, 103.1, 69.8, 64.0, 30.0. **ESI-MS** calcd for $C_{19}H_{19}NNaO$ $[M+Na]^+$ 300.14 found 300.33.

(E)-1-methyl-2-(((3-(naphthalen-1-yl)allyl)oxy)methyl)-1H-indole



Alkene **10h** was prepared following general procedure **GP-3S** from the corresponding alcohol (178.6 mg, 1.11 mmol). Yellow solid (261.7 mg, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 – 8.08 (m, 1H), 7.89 – 7.84 (m, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.66 – 7.57 (m, 2H), 7.55 – 7.32 (m, 5H), 7.29 – 7.23 (m, 1H), 7.17 – 7.10 (m, 1H), 6.56 (s, 1H), 6.34 (dt, *J* = 15.6, 6.0 Hz, 1H), 4.81 (s, 2H), 4.28 (dd, *J* = 6.0, 1.6 Hz, 2H), 3.85 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 138.2, 135.8, 134.4, 133.6, 131.2, 130.0, 129.0, 128.6, 128.1, 127.2, 126.1, 125.8, 125.6, 124.0, 123.8, 121.9, 120.8, 119.5, 109.2, 103.1, 70.0, 64.1, 30.0. **ESI-MS** calcd for $C_{23}H_{22}NO$ $[M+H]^+$ 328.17 found 328.00.

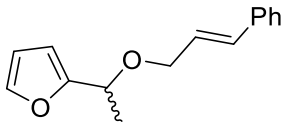
2-((cinnamyloxy)methyl)furan



Alkene **12a** was prepared following general procedure **GP-1S** from the corresponding alcohol (197.0 mg, 2 mmol). Pale yellow liquid (330.2 mg, 77% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 3H), 7.38 – 7.32 (m, 2H), 7.31 – 7.25 (m, 1H), 6.67 (d, *J* = 15.9 Hz, 1H), 6.41 – 6.29 (m, 3H), 4.55 (s, 2H), 4.23 (dd, *J* = 6.2, 1.4

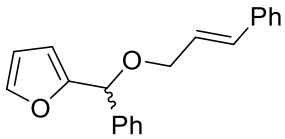
Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.8, 142.9, 136.7, 133.0, 128.6, 127.8, 126.5, 125.7, 110.3, 109.4, 70.6, 63.9. **ESI-MS** calcd for $C_{14}H_{15}O_2$ $[M+H]^+$ 215.11 found 215.33.

2-(1-(cinnamyloxy)ethyl)furan



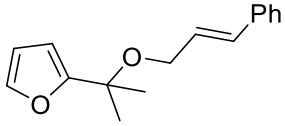
Alkene **12b** was prepared following general procedure **GP-4S** from the corresponding alcohol (134.2 mg, 1.2 mmol). Pale yellow oil (150.7 mg, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.22 (m, 6H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.40 – 6.24 (m, 3H), 4.61 (q, *J* = 6.6 Hz, 1H), 4.21 – 4.05 (m, 2H), 1.58 (d, *J* = 6.5 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.6, 142.2, 136.8, 132.4, 128.5, 127.6, 126.5, 126.2, 110.0, 107.0, 69.8, 69.0, 19.9. **ESI-MS** calcd for $C_{15}H_{17}O_2$ $[M+H]^+$ 229.12 found 229.24.

2-((cinnamyloxy)(phenyl)methyl)furan



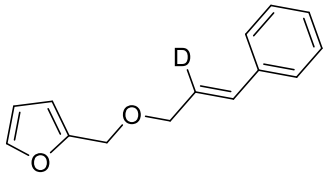
Alkene **12c** was prepared following general procedure **GP-4S** from the corresponding alcohol (209.04 mg, 1.2 mmol). Yellow liquid (271.8 mg, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.44 (m, 2H), 7.43 – 7.28 (m, 8H), 7.27 – 7.21 (m, 1H), 6.61 (d, *J* = 16.0 Hz, 1H), 6.38 – 6.28 (m, 2H), 6.16 – 6.13 (m, 1H), 5.52 (s, 1H), 4.24 – 4.17 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.5, 142.8, 139.2, 136.7, 132.8, 128.6, 128.5, 128.1, 127.7, 127.3, 126.5, 125.8, 110.1, 108.6, 76.2, 69.5. **ESI-MS** calcd for $C_{20}H_{19}O_2$ $[M+H]^+$ 291.14 found 291.28.

2-(2-(cinnamyloxy)propan-2-yl)furan



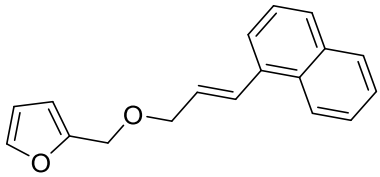
Alkene **12d** was prepared following general procedure **GP-4S** from the corresponding alcohol (126.2 mg, 1 mmol). Pale yellow liquid (126.5 mg, 52% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.18 (m, 6H), 6.55 (d, *J* = 15.9 Hz, 1H), 6.37 – 6.34 (m, 1H), 6.32 – 6.29 (m, 1H), 6.27 – 6.19 (m, 1H), 3.93 – 3.88 (m, 2H), 1.63 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.6, 142.0, 137.0, 131.5, 128.4, 127.4, 127.0, 126.5, 109.8, 106.9, 73.1, 64.3, 25.9. **ESI-MS** calcd for $C_{16}H_{18}NaO_2$ $[M+Na]^+$ 265.12 found 264.93.

(E)-2-(((3-phenylallyl-2-d)oxy)methyl)furan



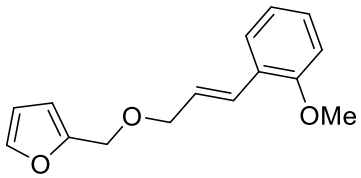
Alkene **12e** was prepared following general procedure **GP-1S** from the corresponding alcohol (132.2 mg, 1.35 mmol). Yellow liquid (148.2 mg, 51% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.23 (m, 6H), 6.70 – 6.62 (m, 1H, 1H non-deuterated 1x), 6.41 – 6.28 (m, 2H, 1H non-deuterated 1x), 4.55 (s, 2H), 4.22 (s, 2H). **^{13}C NMR** (101 MHz, CDCl3) δ 151.8, 142.9, 136.7, 128.6, 127.7, 126.5, 125.7 (non-deuterated 1x), 125.4 (t, *J* = 23.2 Hz), 110.3, 109.4, 70.6 (non-deuterated 1x), 70.5, 63.9. **ESI-MS** calcd for $C_{14}H_{14}DO_2$ $[M+H]^+$ 216.11 found 215.88.

(E)-2-(((3-(naphthalen-1-yl)allyl)oxy)methyl)furan



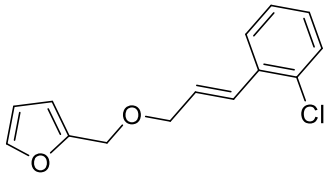
Alkene **12f** was prepared following general procedure **GP-1S** from the corresponding alcohol (66.8 mg, 0.68 mmol). Yellow viscous oil (114.8 mg, 64% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.16 – 8.11 (m, 1H), 7.89 – 7.84 (m, 1H), 7.79 (d, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 7.1 Hz, 1H), 7.56 – 7.37 (m, 5H), 6.42 – 6.30 (m, 3H), 4.60 (s, 2H), 4.32 (dd, *J* = 6.0, 1.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.8, 142.9, 134.5, 133.6, 131.2, 130.0, 129.0, 128.6, 128.1, 126.1, 125.8, 125.6, 124.0, 123.8, 110.4, 109.5, 70.8, 64.0. **ESI-MS** calcd for $C_{18}H_{17}O_2$ $[M+H]^+$ 265.12 found 265.23.

(E)-2-(((3-(2-methoxyphenyl)allyl)oxy)methyl)furan



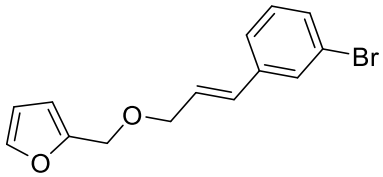
Alkene **12g** was prepared following general procedure **GP-1S** from the corresponding alcohol (98.1 mg, 1 mmol). Yellow oil (139.1 mg, 57% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48 – 7.37 (m, 2H), 7.29 – 7.20 (m, 1H), 6.99 – 6.85 (m, 3H), 6.38 – 6.27 (m, 3H), 4.51 (s, 2H), 4.23 – 4.18 (m, 2H), 3.85 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.8, 151.9, 142.8, 128.8, 128.2, 127.1, 126.3, 125.7, 120.7, 110.8, 110.3, 110.2, 109.3, 71.2, 63.7, 55.5. **ESI-MS** calcd for $C_{15}H_{17}O_3$ $[M+H]^+$ 245.12 found 244.91.

(E)-2-(((3-(2-chlorophenyl)allyl)oxy)methyl)furan



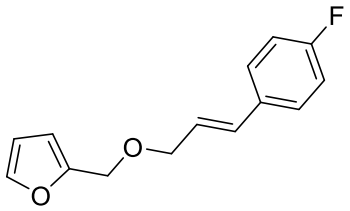
Alkene **12h** was prepared following general procedure **GP-1S** from the corresponding alcohol (84.4 mg, 0.86 mmol). Pale orange oil (166.8 mg, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.35 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.25 – 7.15 (m, 2H), 7.02 (d, *J* = 15.9 Hz, 1H), 6.38 – 6.34 (m, 2H), 6.28 (dt, *J* = 15.9, 6.1 Hz, 1H), 4.53 (s, 2H), 4.23 (dd, *J* = 6.1, 1.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.6, 142.9, 134.8, 133.1, 129.7, 129.1, 128.7, 128.6, 127.0, 126.9, 110.3, 109.5, 70.5, 63.9. **ESI-MS** calcd for $C_{14}H_{14}ClO_2$ $[M+H]^+$ 249.07 found 249.35.

(E)-2-(((3-(3-bromophenyl)allyl)oxy)methyl)furan



Alkene **12i** was prepared following general procedure **GP-1S** from the corresponding alcohol (98.1 mg, 1 mmol). Yellow oil (193.7 mg, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.51 (m, 1H), 7.43 (s, 1H), 7.39 – 7.33 (m, 1H), 7.32 – 7.27 (m, 1H), 7.18 (t, *J* = 7.8 Hz, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 6.38 – 6.24 (m, 3H), 4.51 (s, 2H), 4.22 – 4.15 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.6, 142.9, 138.9, 131.1, 130.6, 130.1, 129.4, 127.4, 125.1, 122.8, 110.3, 109.5, 70.2, 64.1. **ESI-MS** calcd for $C_{14}H_{14}BrO_2$ $[M+H]^+$ 293.02 found 293.13.

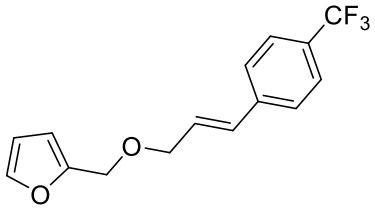
(E)-2-(((3-(4-fluorophenyl)allyl)oxy)methyl)furan



Alkene **12j** was prepared following general procedure **GP-1S** from the corresponding alcohol (91.7 mg, 0.93 mmol). Pale yellow oil (151.2 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.41 (m, 1H), 7.38 – 7.32 (m, 2H), 7.04 – 6.97 (m, 2H), 6.59 (d, *J* = 15.9 Hz, 1H), 6.38 – 6.33 (m, 2H), 6.21 (dt, *J* = 15.9, 6.1 Hz, 1H), 4.51 (s, 2H), 4.20 – 4.15 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4 (d, *J* = 246.8 Hz),

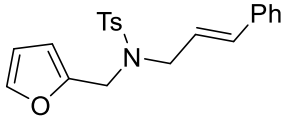
151.7, 142.9, 132.8 (d, *J* = 3.4 Hz), 131.7, 128.0 (d, *J* = 8.0 Hz), 125.4 (d, *J* = 2.3 Hz), 115.5 (d, *J* = 21.7 Hz), 110.3, 109.4, 70.5, 64.0. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -114.16 – -114.22 (m). **ESI-MS** calcd for $C_{14}H_{14}FO_2$ $[M+H]^+$ 233.10 found 233.27.

(E)-2-(((3-(4-(trifluoromethyl)phenyl)allyl)oxy)methyl)furan



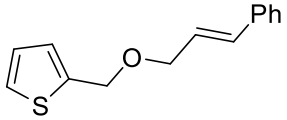
Alkene **12k** was prepared following general procedure **GP-1S** from the corresponding alcohol (128.9 mg, 1.3 mmol). Yellow liquid (154.1 mg, 42% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 2H), 7.51 – 7.45 (m, 3H), 6.69 (d, *J* = 15.9 Hz, 1H), 6.45 – 6.37 (m, 3H), 4.55 (s, 2H), 4.24 (dd, *J* = 5.8, 1.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.6, 143.0, 140.19, 140.18, 131.0, 129.9, 129.6, 129.3, 128.6, 126.6, 125.5 (q, *J* = 3.9 Hz), 122.8, 110.3, 109.5, 70.2, 64.2. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -62.4. **ESI-MS** calcd for $C_{15}H_{14}F_3O_2$ $[M+H]^+$ 283.09 found 283.25.

N-cinnamyl-N-(furan-2-ylmethyl)-4-methylbenzenesulfonamide



Alkene **12l** was prepared following general procedure **GP-2S** from the corresponding tosyl amide (251.3 mg, 1 mmol). Yellow solid (305.2 mg, 83% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.24 (m, 8H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.31 – 6.28 (m, 1H), 6.21 – 6.18 (m, 1H), 6.03 – 5.94 (m, 1H), 4.46 (s, 2H), 3.96 (d, *J* = 6.7 Hz, 2H), 2.44 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.8, 143.2, 142.5, 137.3, 136.3, 134.2, 129.6, 128.6, 127.9, 127.3, 126.5, 123.7, 110.4, 109.5, 49.3, 42.8, 21.5. **ESI-MS** calcd for $C_{21}H_{22}NO_3S$ $[M+H]^+$ 368.13 found 367.83.

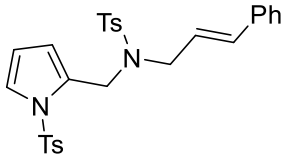
2-((cinnamyloxy)methyl)thiophene



Alkene **12m** was prepared following general procedure **GP-1S** from the corresponding alcohol (114.2 mg, 1 mmol). Pale yellow oil (165.8 mg, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.40 (m, 2H), 7.39 – 7.32 (m, 3H), 7.31 – 7.25 (m, 1H), 7.08 – 7.05 (m, 1H), 7.04 – 7.01 (m, 1H), 6.67 (d, *J* = 15.9 Hz, 1H), 6.35 (dt, *J* = 15.9, 6.1 Hz, 1H), 4.77 (d, *J* = 0.8 Hz, 2H), 4.25 (dd, *J* = 6.1, 1.5 Hz, 2H). **^{13}C NMR** (101

MHz, $CDCl_3$) δ 141.0, 136.7, 132.9, 128.6, 127.8, 126.7, 126.5, 125.9, 125.8, 70.4, 66.5. **ESI-MS** calcd for $C_{14}H_{15}OS$ $[M+H]^+$ 231.08 found 230.94.

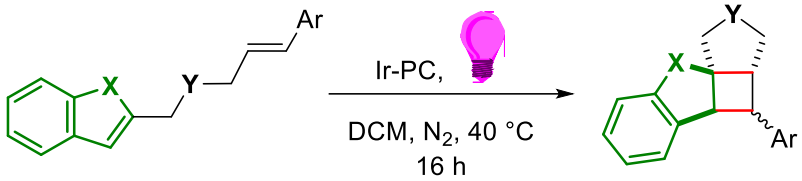
N-cinnamyl-4-methyl-N-((1-tosyl-1H-pyrrol-2-yl)methyl)benzenesulfonamide



Alkene **12n** was prepared following general procedure **GP-2S** from the corresponding tosyl amide (635.5 mg, 1.57 mmol). Yellow viscous oil (572.0 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.32 – 7.20 (m, 6H), 7.16 – 7.06 (m, 4H), 6.26 – 6.11 (m, 3H), 5.75 – 5.65 (m, 1H), 4.55 (s, 2H), 3.90 – 3.84 (m, 2H), 2.43 (s, 3H), 2.31 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.1, 143.5, 136.9, 136.3, 135.9, 134.0, 130.0, 129.8, 128.5, 127.9, 127.4, 126.7, 126.5, 123.40, 123.35, 115.0, 111.9, 50.0, 44.2, 21.6, 21.5. **ESI-MS** calcd for $C_{28}H_{28}N_2NaO_4S_2$ $[M+Na]^+$ 543.14 found 543.33.

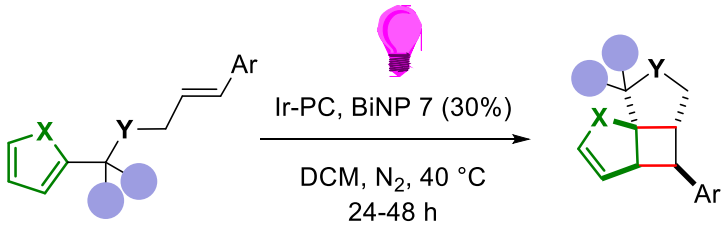
Synthesis and characterization of products

Photocatalytic reaction [GP-1P]:



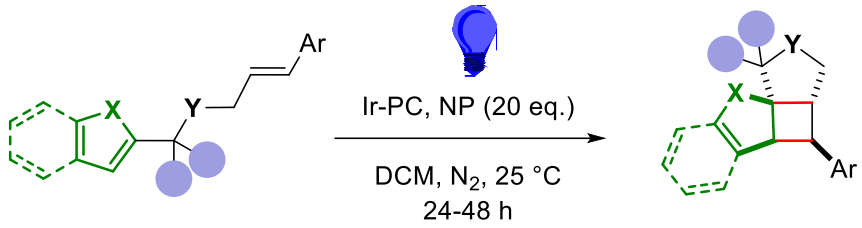
To a vial charged with substrate **10** (1 equiv., 0.15 mmol) and **(Ir[dF(CF$_3$)ppy]$_2$(dtbpy))PF$_6$** (1 mol%), dry and degassed DCM (0.1 M) was added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum, degassed by freeze-pump-thaw (2 times) and the tube was irradiated with purple household LEDs strip for 16 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc, under gradient).

Photocatalytic reaction [GP-2P]:



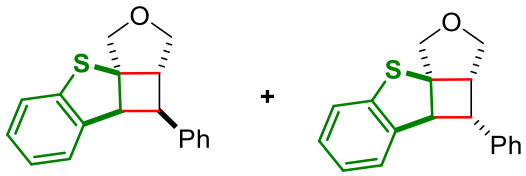
To a vial charged with substrate **12** (1 equiv., 0.15 mmol), **BiNP 7** (30 mol%) and **(Ir[dF(CF$_3$)ppy]$_2$(dtbpy))PF$_6$** (1 mol%), dry and degassed DCM (0.1 M) was added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum, degassed by freeze-pump-thaw (2 times) and the tube was irradiated with purple household LEDs strip for 24 – 48 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc, under gradient).

Photocatalytic reaction [GP-3P]:



To a vial charged with substrate **10** or **12** (1 equiv., 0.15 mmol), **naphthalene** (20 equiv.) and **Ir(ppy)$_3$**((1 mol%), dry and degassed DCM (0.1 M) was added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum, degassed by freeze-pump-thaw (2 times) and the tube was irradiated with blue household LEDs strip for 24 – 48 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel (*n*-hexane/EtOAc, under gradient).

4-phenyl-3,3a,4,4a-tetrahydro-1H-benzo[4',5']thieno[2',3':1,4]cyclobuta[1,2-c]furan



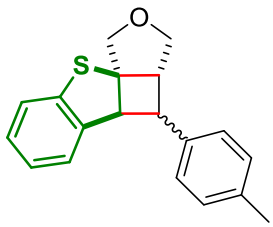
DIA 1 DIA 2

Product **11a** was obtained as a mixture of diastereomers (75:25) following general procedure **GP-1P** from the corresponding alkene (42.1 mg, 0.15 mmol; 392.5 mg, 1.4 mmol). White solid (41.6 mg, 99% yield; 372.9 mg, 95%). The millimolar scale required 50 h of irradiation to fully consume the starting material. The two diastereomers were then separated and crystallized to obtain their relative configurations.

DIA 1: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 – 7.09 (m, 4H), 7.06 – 6.95 (m, 3H), 6.70 – 6.64 (m, 1H), 6.18 (d, *J* = 7.7 Hz, 1H), 4.41 (d, *J* = 9.2 Hz, 1H), 4.34 (d, *J* = 10.0 Hz, 1H), 3.99 (d, *J* = 9.7 Hz, 1H), 3.89 – 3.82 (m, 2H), 3.69 (d, *J* = 10.0 Hz, 1H), 3.42 – 3.36 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.2, 139.2, 138.5, 128.5, 127.9, 127.7, 126.9, 126.6, 124.1, 121.7, 74.7, 74.0, 60.4, 57.9, 56.0, 49.1. **ESI-HRMS** calcd for $C_{18}H_{16}NaOS$ $[M+Na]^+$ 303.0814 found 303.0816.

DIA 2: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.14 (m, 7H), 7.06 – 7.00 (m, 2H), 4.44 (d, *J* = 7.6 Hz, 1H), 4.17 (d, *J* = 9.6 Hz, 1H), 3.92 (dd, *J* = 9.4, 7.6 Hz, 1H), 3.83 – 3.70 (m, 2H), 3.58 (d, *J* = 9.6 Hz, 1H), 3.47 – 3.40 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.4, 141.9, 138.3, 128.6, 128.04, 128.01, 126.8, 124.8, 124.2, 122.0, 75.1, 69.3, 60.4, 56.9, 53.0, 48.0. **ESI-HRMS** calcd for $C_{18}H_{16}NaOS$ $[M+Na]^+$ 303.0814 found 303.0817.

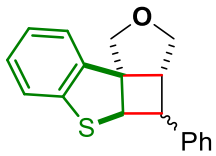
4-(p-tolyl)-3,3a,4,4a-tetrahydro-1H-benzo[4',5']thieno[2',3':1,4]cyclobuta[1,2-c]furan



Product **11b** was obtained as a mixture of diastereomers (75:25) following general procedure **GP-1P** from the corresponding alkene (44.2 mg, 0.15 mmol). Pale yellow solid (43.7 mg, 99% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.15 (m, 1H Dia1, 6H Dia2), 7.10 – 6.94 (m, 3H Dia1, 2H Dia2), 6.91 – 6.85 (m, 2H Dia1), 6.73 (t, *J* = 7.4 Hz, 1H Dia1), 6.24 (d, *J* = 7.6 Hz, 1H Dia1), 4.44 – 4.33 (m, 2H Dia1, 1H Dia2), 4.17 (d, *J* = 9.6 Hz, 1H Dia2), 4.00 (d, *J* = 9.7 Hz, 1H Dia1), 3.91 – 3.78 (m, 2H Dia1, 2H Dia2), 3.75 – 3.68 (m, 1H Dia1, 1H Dia2), 3.57 (d, *J* = 9.6 Hz, 1H Dia2), 3.44 – 3.35 (m, 1H Dia1,

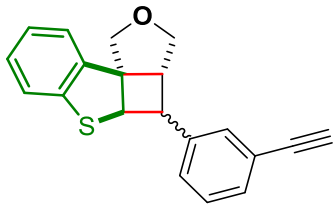
1H Dia2), 2.40 (s, 3H Dia2), 2.28 (s, 3H Dia1). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.4, 142.1, 142.0, 138.7, 136.4, 136.2, 136.1, 135.3, 129.3, 128.6, 128.4, 128.0, 127.9, 127.7, 127.0, 124.8, 124.1, 121.9, 121.7, 75.1, 74.7, 73.9, 69.3, 60.4, 57.9, 57.1, 56.4, 53.0, 48.8, 47.7, 21.1, 21.0. **ESI-HRMS** calcd for $C_{19}H_{19}OS$ $[M+H]^+$ 295.1151 found 295.1154.

4-phenyl-3,3a,4,4a-tetrahydro-1H-benzo[4',5']thieno[3',2':1,4]cyclobuta[1,2-c]furan



Product **11c** was obtained as a mixture of diastereomers (79:21) following general procedure **GP-1P** from the corresponding alkene (42.0 mg, 0.15 mmol). White solid (38.8 mg, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.07 (m, 9H Dia1, 9H Dia2), 4.71 (d, *J* = 8.4 Hz, 1H Dia1), 4.47 (d, *J* = 7.8 Hz, 1H Dia2), 4.39 (d, *J* = 10.0 Hz, 1H Dia1), 4.26 (d, *J* = 9.6 Hz, 1H Dia2), 4.11 – 4.00 (m, 1H Dia1, 1H Dia2), 3.97 – 3.83 (m, 3H Dia1, 1H Dia2), 3.82 – 3.75 (m, 1H Dia2), 3.69 (d, *J* = 9.7 Hz, 1H Dia2), 3.51 – 3.45 (m, 1H Dia2), 3.36 (t, *J* = 5.5 Hz, 1H Dia1). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.4, 144.3, 139.8, 139.2, 138.1, 138.0, 128.9, 128.6, 128.50, 128.47, 128.1, 127.9, 126.9, 126.8, 124.7, 124.4, 124.1, 123.1, 122.8, 121.9, 76.0, 75.4, 74.2, 69.1, 64.6, 63.6, 55.4, 55.1, 54.9, 52.2, 50.8, 48.1. **ESI-HRMS** calcd for $C_{18}H_{17}OS$ $[M+H]^+$ 281.0995 found 281.0993.

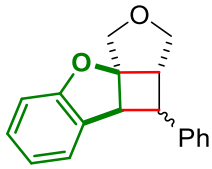
4-(3-ethynylphenyl)-3,3a,4,4a-tetrahydro-1H-benzo[4',5']thieno[3',2':1,4]cyclobuta[1,2-c]furan



Product **11d** was obtained as a mixture of diastereomers (83:17) following general procedure **GP-1P** from the corresponding alkene (45.7 mg, 0.15 mmol). White solid (45.3 mg, 99% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.32 (m, 1H Dia1, 3H Dia2), 7.31 – 7.21 (m, 3H Dia1, 3H Dia2), 7.21 – 7.05 (m, 4H Dia1, 2H Dia2), 4.68 (d, *J* = 8.4 Hz, 1H Dia1), 4.43 (d, *J* = 7.8 Hz, 1H Dia2), 4.38 (d, *J* = 10.0 Hz, 1H Dia1), 4.25 (d, *J* = 9.7 Hz, 1H Dia2), 4.06 (d, *J* = 9.7 Hz, 1H Dia1), 4.02 – 3.96 (m, 1H Dia2), 3.95 – 3.88 (m, 2H Dia1), 3.86 – 3.75 (m, 1H Dia1, 2H Dia2), 3.67 (d, *J* = 9.7 Hz, 1H Dia2), 3.49 – 3.43 (m, 1H Dia2), 3.33 (t, *J* = 5.5 Hz, 1H Dia1), 3.11 (s, 1H Dia2), 3.06 (s, 1H Dia1). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.1, 144.2, 140.0, 139.0, 138.4, 137.8, 132.1, 131.5,

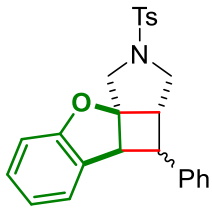
130.6, 130.5, 129.0, 128.9, 128.7, 128.5, 128.3, 128.1, 124.7, 124.5, 124.1, 123.1, 122.8, 122.4, 121.9, 121.8, 83.7, 77.3, 77.1, 75.9, 75.3, 74.1, 69.0, 64.6, 63.6, 55.2, 54.8, 54.7, 51.9, 50.3, 47.7. **ESI-HRMS** calcd for $C_{20}H_{17}OS$ $[M+H]^+$ 305.0955 found 305.0953.

4-phenyl-3a,4,4a,5-tetrahydro-1Hbenzo[4',5']cyclobuta[1,2-b:1,4-c']difuran



Product **11e** was obtained as a mixture of diastereomers (86:14) following general procedure **GP-1P** from the corresponding alkene (38.1 mg, 0.144 mmol). Yellow solid (35.2 mg, 93% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 – 7.67 (m, 1H Dia2), 7.53 – 7.46 (m, 1H Dia2), 7.45 – 7.08 (m, 4H Dia1, 5H Dia2), 7.04 – 6.85 (m, 3H Dia1, 2H Dia2), 6.72 – 6.64 (m, 1H Dia1), 6.43 (d, *J* = 7.4 Hz, 1H Dia1), 4.34 (d, *J* = 10.0 Hz, 1H Dia1), 4.28 – 4.18 (m, 1H Dia1, 2H Dia2), 4.03 – 3.91 (m, 3H Dia1), 3.86 – 3.68 (m, 1H Dia1, 3H Dia2), 3.62 (d, *J* = 10.3 Hz, 1H Dia2), 3.46 – 3.39 (m, 1H Dia2), 3.38 – 3.31 (m, 1H Dia1). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.6, 160.5, 138.9, 138.4, 132.2, 132.1, 131.4, 128.7, 128.53, 128.51, 128.3, 128.1, 128.0, 127.8, 127.4, 126.8, 126.6, 125.0, 121.6, 120.9, 110.3, 110.2, 94.2, 92.6, 72.9, 71.7, 71.5, 69.2, 50.9, 50.5, 49.1, 48.8, 46.5, 44.0. **ESI-HRMS** calcd for $C_{18}H_{17}O_2$ $[M+H]^+$ 265.1223 found 265.1222.

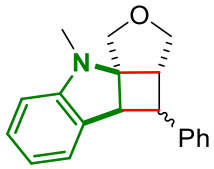
4-phenyl-2-tosyl-1,2,3,3a,4,4a-hexahydrobenzofuro[2',3':1,4]cyclobuta[1,2-c]pyrrole



Product **11f** was obtained as a mixture of diastereomers (85:15) following general procedure **GP-1P** from the corresponding alkene (62.7 mg, 0.15 mmol). White solid (57.7 mg, 92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H Dia1), 7.64 (d, *J* = 8.3 Hz, 2H Dia2), 7.45 – 7.29 (m, 2H Dia1, 6H Dia2), 7.23 – 7.12 (m, 3H Dia1, 3H Dia2), 7.11 – 7.04 (m, 1H Dia1), 6.94 – 6.85 (m, 2H Dia1, 1H Dia2), 6.82 (d, *J* = 8.0 Hz, 1H Dia2), 6.76 (d, *J* = 8.0 Hz, 1H Dia1), 6.68 – 6.61 (m, 1H Dia1), 6.39 (d, *J* = 7.4 Hz, 1H Dia1), 4.36 – 4.27 (m, 1H Dia1, 1H Dia2), 4.04 (d, *J* = 10.3 Hz, 1H Dia1), 3.90 – 3.72 (m, 1H Dia1, 2H Dia2), 3.56 (d, *J* = 10.0 Hz, 1H Dia1), 3.30 – 3.23 (m, 1H Dia2), 3.22 – 3.15 (m, 1H Dia1), 3.10 (d, *J* = 10.5 Hz, 1H Dia2), 3.05 (d, *J* = 10.3 Hz, 1H Dia1), 2.99 – 2.91 (m, 1H Dia1, 1H Dia2), 2.80 – 2.74 (m, 1H Dia2), 2.52 – 2.43 (m, 3H Dia1,

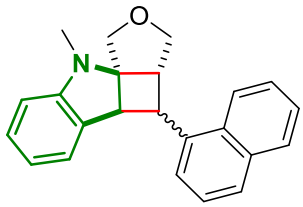
3H Dia2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.3, 159.9, 144.2, 144.0, 138.2, 137.1, 131.2, 130.9, 129.9, 129.7, 128.72, 128.66, 128.4, 128.2, 128.14, 128.05, 127.8, 127.3, 126.84, 126.79, 124.9, 121.8, 121.2, 110.2, 110.0, 92.3, 90.9, 53.6, 53.0, 52.8, 51.3, 49.2, 49.1, 48.6, 47.8, 46.9, 44.1, 21.63, 21.59. **ESI-HRMS** calcd for $C_{25}H_{24}NO_3S$ $[M+H]^+$ 418.1471 found 418.1474.

9-methyl-4-phenyl-3a,4,4a,9-tetrahydro-1H,3H-furo[3',4':1,4]cyclobuta[1,2-b]indole



Product **11g** was obtained as a mixture of diastereomers (71:29) following general procedure **GP-3P** from the corresponding alkene (42.0 mg, 0.15 mmol). Pale yellow solid (37.4 mg, 89% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 1H Dia2), 7.55 – 7.49 (m, 1H Dia2), 7.45 – 6.90 (m, 6H Dia1, 5H Dia2), 6.72 – 6.66 (m, 1H Dia2), 6.59 – 6.50 (m, 1H Dia1, 1H Dia2), 6.49 – 6.42 (m, 1H Dia1), 6.20 (dt, *J* = 7.4, 1.3 Hz, 1H Dia1), 4.20 (d, *J* = 10.1 Hz, 1H Dia1), 4.11 – 4.05 (m, 1H Dia1, 1H Dia2), 4.04 – 3.98 (m, 2H Dia2), 3.94 (d, *J* = 9.6 Hz, 1H Dia1), 3.89 – 3.80 (m, 2H Dia1), 3.78 – 3.72 (m, 1H Dia1), 3.71 – 3.65 (m, 3H Dia2), 3.49 – 3.42 (m, 1H Dia2), 3.39 – 3.32 (m, 1H Dia1), 2.92 – 2.81 (m, 3H Dia1, 3H Dia2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.3, 153.5, 139.3, 138.9, 133.4, 128.9, 128.8, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.0, 126.5, 126.4, 125.9, 123.9, 118.5, 118.1, 108.3, 107.3, 75.5, 75.0, 74.0, 71.1, 71.0, 69.9, 50.2, 48.8, 47.3, 45.1, 44.2, 44.1, 30.5, 30.0. **ESI-HRMS** calcd for $C_{19}H_{20}NO$ $[M+H]^+$ 278.1539 found 278.1541.

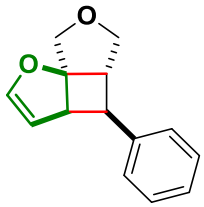
9-methyl-4-(naphthalen-1-yl)-3a,4,4a,9-tetrahydro-1H,3H-furo[3',4':1,4]cyclobuta[1,2-b]indole



Product **11h** was obtained as a mixture of diastereomers (90:10) following general procedure **GP-3P** from the corresponding alkene (49.1 mg, 0.15 mmol). Yellow solid (47.8 mg, 97% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 7.9 Hz, 1H Dia2), 7.95 – 7.87 (m, 1H Dia1, 1H Dia2), 7.85 – 7.76 (m, 2H Dia1), 7.74 – 7.55 (m, 2H Dia1, 3H Dia2), 7.54 – 7.42 (m, 2H Dia1, 2H Dia2), 7.31 – 7.25 (m, 1H Dia2), 7.24 – 7.16 (m, 1H Dia1), 7.05 (d, *J* = 7.2 Hz, 1H Dia1, 1H Dia2), 6.95 (t, *J* = 7.7 Hz, 1H Dia2), 6.75 –

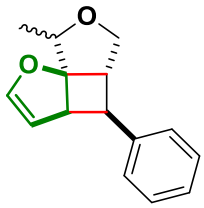
6.67 (m, 1H Dia1), 6.59 (d, *J* = 7.9 Hz, 1H Dia1), 5.64 (d, *J* = 7.3 Hz, 1H Dia2), 4.47 – 4.38 (m, 1H Dia1, 2H Dia2), 4.37 – 4.29 (m, 1H Dia1, 1H Dia2), 4.03 – 3.96 (m, 1H Dia1, 2H Dia2), 3.78 – 3.65 (m, 2H Dia1, 2H Dia2), 3.60 – 3.53 (m, 1H Dia1), 3.17 (d, *J* = 10.2 Hz, 1H Dia1), 2.95 (s, 3H Dia1), 2.88 (s, 3H Dia2). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.6, 134.1, 133.8, 133.7, 133.6, 131.9, 131.6, 129.0, 128.9, 128.3, 128.0, 127.2, 126.9, 126.2, 126.0, 125.9, 125.7, 125.58, 125.56, 125.2, 124.5, 124.1, 123.9, 123.7, 123.5, 118.4, 107.5, 75.5, 75.4, 74.1, 70.9, 70.1, 50.3, 46.5, 44.8, 44.2, 41.5, 30.3. **ESI-HRMS** calcd for $C_{23}H_{21}NNaO$ $[M+Na]^+$ 350.1515 found 350.1511.

4-phenyl-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13a** was obtained following general procedure **GP-2P** from the corresponding alkene (31.9 mg, 0.15 mmol, 342.8 mg, 1.6 mmol). White solid (26.2 mg, 82% yield, 228.8 mg, 65% yield). The millimolar scale was irradiated for 120 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.21 (m, 5H), 6.42 – 6.36 (m, 1H), 4.91 – 4.85 (m, 1H), 4.25 (d, *J* = 9.9 Hz, 1H), 3.99 – 3.89 (m, 2H), 3.86 – 3.77 (m, 2H), 3.56 (t, *J* = 7.3 Hz, 1H), 3.41 – 3.35 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.3, 140.1, 128.2, 127.6, 126.4, 104.6, 91.6, 72.9, 71.3, 51.0, 51.0, 44.0. **ESI-HRMS** calcd for $C_{14}H_{15}O_2$ $[M+H]^+$ 215.1067 found 215.1070.

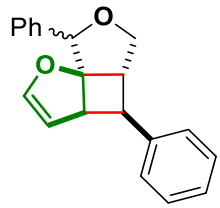
7-methyl-4-phenyl-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13b** was obtained as a mixture of diastereomers (58:42) following general procedure **GP-2P** from the corresponding alkene (34.4 mg, 0.15 mmol). Transparent viscous oil (18.9 mg, 55% yield). The reaction required 36 h of irradiation to fully consume the starting material. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 2H Dia1, 2H Dia2), 7.26 – 7.17 (m, 3H Dia1, 3H Dia2), 6.38 – 6.33 (m, 1H Dia1, 1H Dia2), 4.83 – 4.77 (m, 1H Dia1, 1H Dia2), 4.36 (q, *J* = 6.7 Hz, 1H Dia2), 4.08 (dd, *J* = 9.6, 5.3 Hz, 1H Dia2), 3.96 – 3.90 (m, 2H Dia1), 3.86 – 3.79 (m, 2H Dia1), 3.77 – 3.74 (m, 1H Dia2), 3.71 (d, *J* = 9.6 Hz, 1H Dia2), 3.51 (t, *J* = 7.3 Hz, 1H Dia2), 3.43 (t, *J* = 7.3 Hz, 1H

Dia1), 3.34 – 3.29 (m, 1H Dia1, 1H Dia2), 1.38 (d, *J* = 6.2 Hz, 3H Dia1), 1.24 (d, *J* = 6.7 Hz, 3H Dia2). **ESI-HRMS** calcd for $C_{15}H_{17}O_2$ $[M+H]^+$ 229.1223 found 229.1225.

4,7-diphenyl-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran

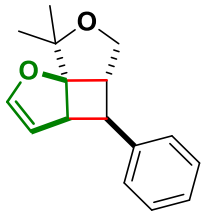


Product **13c** was obtained as a mixture of diastereomers (57:43) following general procedure **GP-2P** from the corresponding alkene (43.4 mg, 0.15 mmol). White solids. The reaction required 40 h of irradiation to fully consume the starting material.

DIA 1 (17.3 mg; 40% yield): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 – 7.18 (m, 10H), 6.40 – 6.36 (m, 1H), 5.02 (s, 1H), 4.76 – 4.70 (m, 1H), 4.19 (dd, *J* = 9.7, 4.8 Hz, 1H), 4.07 (d, *J* = 9.7 Hz, 1H), 3.56 – 3.45 (m, 2H), 3.39 – 3.33 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.0, 140.1, 137.8, 128.4, 128.2, 127.5, 126.3, 125.7, 104.6, 94.4, 80.6, 71.7, 51.2, 47.4, 43.9. **ESI-HRMS** calcd for $C_{20}H_{19}O_2$ $[M+H]^+$ 291.1380 found 291.1378.

DIA 2 (12.7 mg; 30% yield): **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 – 7.24 (m, 10H), 6.35 – 6.31 (m, 1H), 5.28 (s, 1H), 4.86 (t, *J* = 2.8 Hz, 1H), 4.44 (dd, *J* = 9.5, 6.0 Hz, 1H), 4.05 – 4.00 (m, 1H), 3.95 (dd, *J* = 9.6, 1.9 Hz, 1H), 3.71 (t, *J* = 7.3 Hz, 1H), 3.59 – 3.52 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.6, 139.9, 137.7, 128.2, 128.1, 127.7, 127.6, 127.3, 126.5, 103.7, 92.7, 83.8, 72.3, 51.9, 51.6, 45.4. **ESI-HRMS** calcd for $C_{20}H_{19}O_2$ $[M+H]^+$ 291.1380 found 291.1381.

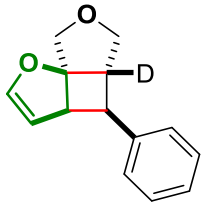
7,7-dimethyl-4-phenyl-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13d** was obtained following general procedure **GP-3P** from the corresponding alkene (36.5 mg, 0.15 mmol). Transparent viscous oil (21.6 mg, 59% yield). The reaction required 38 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.29 – 7.21 (m, 3H), 6.39 – 6.35 (m, 1H), 4.79 (t, *J* = 2.9 Hz, 1H), 4.05 (dd, *J* = 9.7, 5.0 Hz, 1H), 3.94 – 3.88 (m, 1H), 3.70 (d, *J* = 9.7 Hz, 1H), 3.48 (t, *J* = 7.2 Hz, 1H), 3.33 (t, *J* = 5.8 Hz, 1H), 1.43 (s, 3H), 1.29 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.1, 140.3, 128.1, 127.7, 126.3,

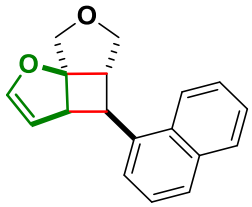
103.9, 95.3, 78.6, 68.7, 50.9, 47.6, 44.8, 23.2, 21.1. **ESI-HRMS** calcd for $C_{16}H_{19}O_2$ $[M+H]^+$ 243.3255 found 243.3254.

4-phenyl-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran-4a-d



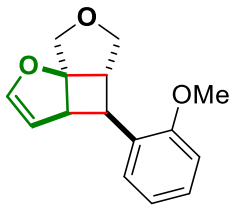
Product **13e** was obtained following general procedure **GP-2P** from the corresponding alkene (32.3 mg, 0.15 mmol). Transparent viscous oil (22.8 mg, 71% yield). The reaction required 72 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.22 (m, 5H), 6.41 – 6.36 (m, 1H), 4.90 – 4.85 (m, 1H), 4.24 (d, *J* = 10.0 Hz, 1H), 3.98 – 3.89 (m, 2H), 3.86 – 3.78 (m, 2H), 3.59 – 3.53 (m, 1H), 3.40 – 3.35 (m, 1H non-deuterated 2x). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.3, 140.1, 128.2, 127.5, 126.4, 104.6, 91.63 (non-deuterated 2x), 91.56, 72.92 (non-deuterated 2x), 72.86, 71.3, 51.0 (non-deuterated 2x), 50.9, 50.6 (t, *J* = 21.9 Hz), 43.9. **ESI-HRMS** calcd for $C_{14}H_{14}DO_2$ $[M+H]^+$ 216.1129 found 216.1131.

4-(naphthalen-1-yl)-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



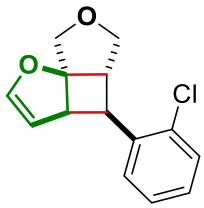
Product **13f** was obtained following general procedure **GP-2P** from the corresponding alkene (39.9 mg, 0.15 mmol). White solid (21.0 mg, 53% yield). The reaction required 24 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.84 (m, 2H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.54 – 7.44 (m, 3H), 7.40 (d, *J* = 7.0 Hz, 1H), 6.29 – 6.25 (m, 1H), 4.41 (brs, 1H), 4.31 (d, *J* = 9.9 Hz, 1H), 4.16 – 4.12 (m, 2H), 4.05 (dd, *J* = 9.6, 5.1 Hz, 1H), 3.93 (d, *J* = 9.6 Hz, 1H), 3.85 (d, *J* = 9.9 Hz, 1H), 3.68 – 3.62 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.4, 135.5, 133.8, 131.8, 128.9, 127.1, 126.1, 125.7, 125.2, 123.8, 123.7, 104.1, 91.7, 73.2, 71.4, 51.8, 48.7, 42.0. **ESI-HRMS** calcd for $C_{18}H_{17}O_2$ $[M+H]^+$ 265.1223 found 265.1220.

4-(2-methoxyphenyl)-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



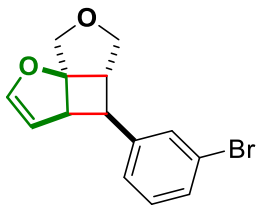
Product **13g** was obtained following general procedure **GP-2P** from the corresponding alkene (35.1 mg, 0.144 mmol). Transparent viscous oil (21.9 mg, 62% yield). The reaction required 46 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.21 (m, 2H), 7.00 – 6.94 (m, 1H), 6.87 (d, *J* = 7.4 Hz, 1H), 6.33 – 6.29 (m, 1H), 4.80 – 4.75 (m, 1H), 4.24 (d, *J* = 9.9 Hz, 1H), 3.98 (dd, *J* = 9.4, 5.0 Hz, 1H), 3.93 – 3.77 (m, 6H), 3.69 (t, *J* = 7.4 Hz, 1H), 3.39 – 3.35 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.5, 147.0, 128.4, 127.4, 127.3, 120.0, 109.9, 105.0, 91.9, 73.1, 71.4, 55.2, 50.5, 49.6, 39.6. **ESI-HRMS** calcd for $C_{15}H_{17}O_3$ $[M+H]^+$ 245.1172 found 245.1170.

4-(2-chlorophenyl)-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13h** was obtained following general procedure **GP-2P** from the corresponding alkene (37.1 mg, 0.15 mmol). White solid (32.7 mg, 88% yield). The reaction required 24 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 – 7.15 (m, 4H), 6.36 – 6.29 (m, 1H), 4.75 – 4.68 (m, 1H), 4.25 (d, *J* = 9.9 Hz, 1H), 4.05 – 3.95 (m, 2H), 3.90 (d, *J* = 9.6 Hz, 1H), 3.83 – 3.74 (m, 2H), 3.43 (t, *J* = 6.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.5, 137.5, 134.1, 129.5, 128.0, 127.7, 126.4, 104.3, 91.3, 72.9, 71.2, 50.7, 48.8, 42.6. **ESI-HRMS** calcd for $C_{14}H_{14}ClO_2$ $[M+H]^+$ 249.0677 found 249.0673.

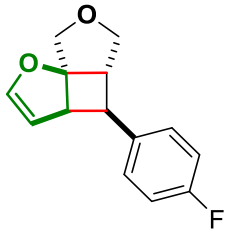
4-(3-bromophenyl)-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13i** was obtained following general procedure **GP-2P** from the corresponding alkene (42.9 mg, 0.146 mmol). White solid (37.1 mg, 84% yield). The

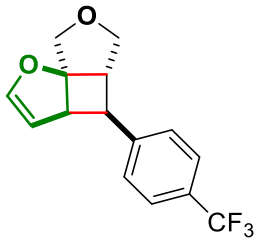
reaction required 48 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 2H), 7.24 – 7.15 (m, 2H), 6.42 – 6.38 (m, 1H), 4.88 – 4.83 (m, 1H), 4.23 (d, *J* = 9.9 Hz, 1H), 3.96 – 3.87 (m, 2H), 3.84 – 3.76 (m, 2H), 3.51 (t, *J* = 7.3 Hz, 1H), 3.36 – 3.28 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.6, 142.6, 130.6, 129.8, 129.5, 126.2, 122.4, 104.1, 91.6, 72.8, 71.2, 43.7. **ESI-HRMS** calcd for $C_{14}H_{14}BrO_2$ $[M+H]^+$ 293.0172 found 293.0170.

4-(4-fluorophenyl)-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13j** was obtained following general procedure **GP-2P** from the corresponding alkene (34.3 mg, 0.15 mmol). Pale yellow liquid (24.0 mg, 70% yield). The reaction required 40 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 – 7.15 (m, 2H), 7.04 – 6.96 (m, 2H), 6.40 – 6.35 (m, 1H), 4.83 – 4.78 (m, 1H), 4.20 (d, *J* = 9.9 Hz, 1H), 3.94 – 3.84 (m, 2H), 3.81 – 3.73 (m, 2H), 3.49 (t, *J* = 7.3 Hz, 1H), 3.32 – 3.25 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.6 (d, *J* = 244.5 Hz), 147.5, 135.8 (d, *J* = 3.3 Hz), 129.0 (d, *J* = 7.8 Hz), 115.0 (d, *J* = 21.2 Hz), 104.3, 91.5, 72.8, 71.2, 51.3, 51.1, 43.4. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -116.57 – -116.68 (m). **ESI-HRMS** calcd for $C_{14}H_{14}FO_2$ $[M+H]^+$ 233.0972 found 233.0970.

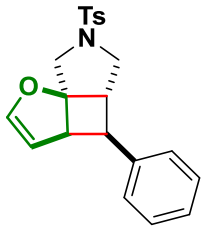
4-(4-(trifluoromethyl)phenyl)-3a,4,4a,5-tetrahydro-7H-cyclobuta[1,2-b:1,4-c']difuran



Product **13k** was obtained following general procedure **GP-2P** from the corresponding alkene (42.3 mg, 0.15 mmol). Transparent viscous oil (31.7 mg, 75% yield). The reaction required 32 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.40 – 6.35 (m, 1H), 4.83 – 4.77 (m, 1H), 4.22 (d, *J* = 10.0 Hz, 1H), 3.96 – 3.75 (m, 4H), 3.57 (t, *J* = 7.3 Hz, 1H), 3.37 – 3.31 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 147.7, 144.2, 128.8, 128.5, 127.8, 125.6, 125.1 (q, *J* = 3.9 Hz), 122.9, 104.0, 91.6, 72.8, 71.2,

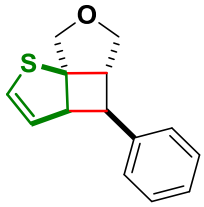
50.9, 50.8, 43.9. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -62.3. **ESI-HRMS** calcd for $C_{15}H_{14}F_3O_2$ $[M+H]^+$ 283.0940 found 283.0943.

4-phenyl-6-tosyl-3a,4,4a,5,6,7-hexahydrofuro[2',3':1,4]cyclobuta[1,2-c]pyrrole



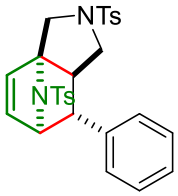
Product **13l** was obtained following general procedure **GP-2P** from the corresponding alkene (55.0 mg, 0.15 mmol). White solid (30.8 mg, 56% yield). The reaction required 60 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.3 Hz, 2H), 7.42 – 7.19 (m, 7H), 6.30 – 6.26 (m, 1H), 4.84 (t, *J* = 2.9 Hz, 1H), 3.96 (d, *J* = 10.2 Hz, 1H), 3.92 – 3.87 (m, 1H), 3.67 (t, *J* = 7.4 Hz, 1H), 3.54 (d, *J* = 9.9 Hz, 1H), 3.26 – 3.20 (m, 1H), 2.98 – 2.91 (m, 2H), 2.48 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 146.7, 144.1, 139.4, 131.4, 129.8, 128.2, 128.1, 127.5, 126.5, 104.5, 89.9, 52.9, 52.8, 51.4, 49.6, 44.2, 21.6. **ESI-HRMS** calcd for $C_{21}H_{21}NNaO_3S$ $[M+Na]^+$ 390.4522 found 390.4525.

4-phenyl-3a,4,4a,5-tetrahydro-7H-thieno[2',3':1,4]cyclobuta[1,2-c]furan



Product **13m** was obtained following general procedure **GP-3P** from the corresponding alkene (34.3 mg, 0.15 mmol). White solid (11.5 mg, 35% yield). The reaction was irradiated for 48 h. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.22 (m, 5H), 6.11 (dd, *J* = 6.1, 1.8 Hz, 1H), 5.09 – 5.04 (m, 1H), 4.31 (d, *J* = 10.0 Hz, 1H), 4.06 – 4.00 (m, 1H), 3.92 (d, *J* = 9.6 Hz, 1H), 3.86 – 3.77 (m, 2H), 3.67 (d, *J* = 10.0 Hz, 1H), 3.50 – 3.44 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.6, 128.2, 128.1, 127.1, 126.5, 123.9, 74.2, 73.7, 61.1, 58.5, 55.7, 49.2. **ESI-HRMS** calcd for $C_{14}H_{14}NaOS$ $[M+Na]^+$ 253.0658 found 253.0655.

7-phenyl-2,8-ditosyl-1,2,3,6,7,7a-hexahydro-3a,6-epiminoisoindole



Product **14n** was obtained following general procedure **GP-1P** from the corresponding alkene (78.1 mg, 0.15 mmol). White solid (42.9 mg, 55% yield). The reaction required 36 h of irradiation to fully consume the starting material. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 – 7.72 (m, 2H), 7.60 – 7.55 (m, 2H), 7.37 – 7.22 (m, 9H), 6.30 – 6.26 (m, 1H), 5.42 – 5.39 (m, 1H), 4.72 – 4.69 (m, 1H), 4.12 (d, *J* = 9.3 Hz, 1H), 3.71 (d, *J* = 9.4 Hz, 1H), 3.51 – 3.44 (m, 1H), 2.70 – 2.61 (m, 1H), 2.48 – 2.37 (m, 8H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.1, 143.9, 141.3, 139.3, 136.2, 134.8, 132.1, 130.0, 129.9, 128.9, 128.1, 127.2, 127.1, 127.0, 75.7, 75.2, 58.4, 48.4, 48.1, 47.9, 21.64, 21.57. **ESI-HRMS** calcd for $C_{28}H_{29}N_2O_4S_2$ $[M+H]^+$ 521.1563 found 521.1565.

Chapter V

Visible – Light – Promoted Tandem Skeletal Rearrangement/Dearomatization of Heteroaryl Enallenes

From this chapter:

M. Chiminelli, G. Scarica, A. Serafino, L. Marchiò, R. Viscardi, G. Maestri. Visible-Light-Promoted Tandem Skeletal Rearrangement/Dearomatization of Heteroaryl Enallenes. *Molecules* **2024**, *29*, 595. https://doi.org/10.3390/molecules29030595.

5.1: Retro-Cycloaddition as Synthetic Tool to Access Unexpected Products

In the previous chapters I showed how useful can be the dearomative cycloaddition, with a myriad of beautiful example reported in literature. Although most of the time the target product is the cycloadduct, sometimes the latter can be the starting point for new transformations that are difficult to access. This is the case of the retro-cycloadditions, in which the product of a cycloaddition is the starting material for a new reaction, that broke it into diverse partner respect to the two that made the cycloadduct. This phenomenon can occur when the breaking of one or more bonds leads to the formation of a more stable structure (Figure 18, right) than the one that generated the cycloaddition intermediate (Figure 18, left).

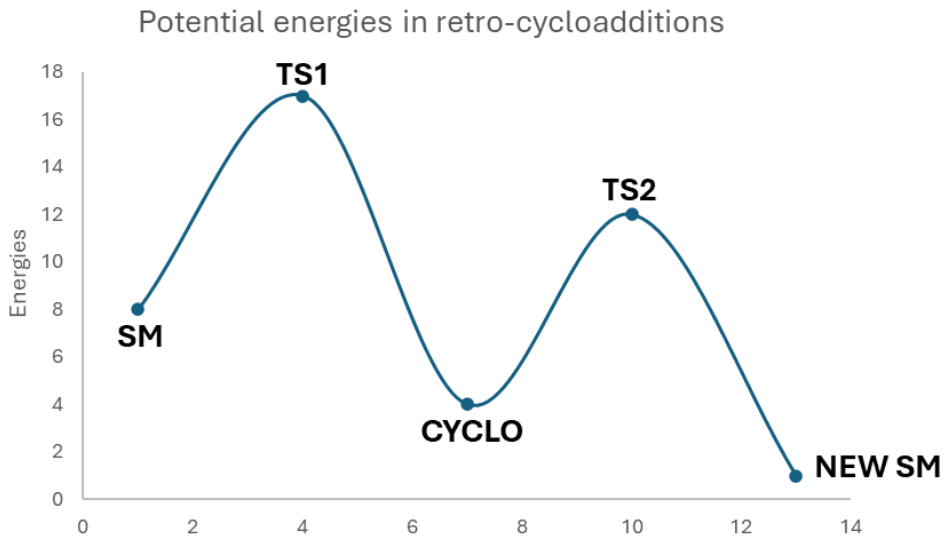
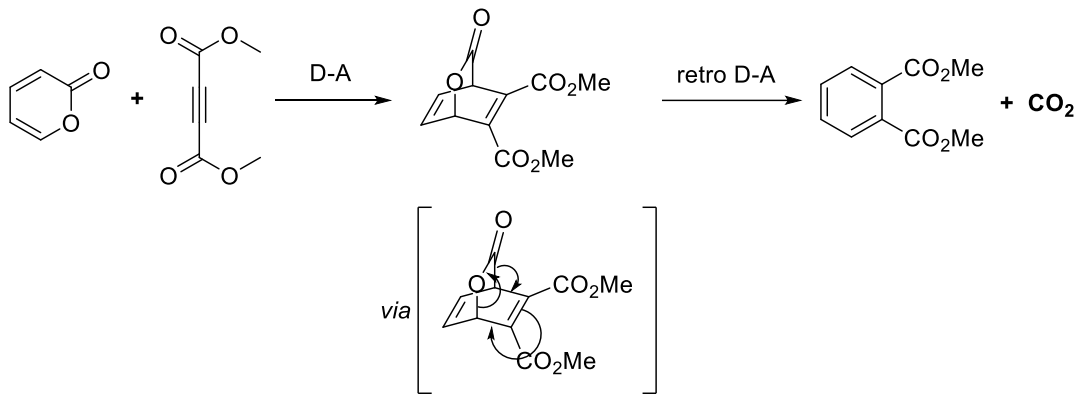


Figure 18: Graphical rappresentation of the potential energies for a retro-cycloaddition mechanism.

The transformation can be promoted by temperature, light, mechanical stress or can occur spontaneously within synthetic processes. In the next pages will be reported some interesting examples of this strategy.

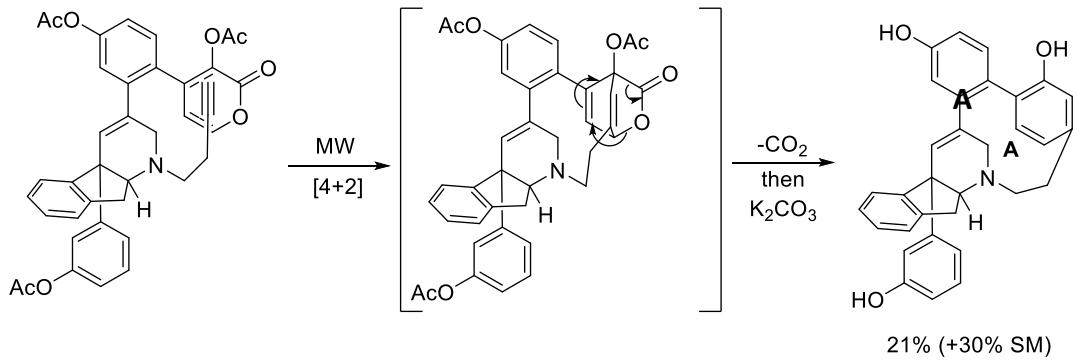
One seminal example of this concept is the Diels-Alder cycloaddition of 2-pyrone with acetylenes, reported by Stille *et.al.*[109] in 1969 (Scheme 66).



Scheme 66: Seminal example of retro-cycloaddition.

When heated, the product of this reaction can undergo to a reverse cycloaddition that bring to two partners different from the original ones. In particular, the formation of an aromatic ring is trigger by the release of CO_2. The two new products are more stable than the starting one and the reaction is irreversible, indeed CO2 is a poor dienophile, and the aromatic is a low reactive diene.

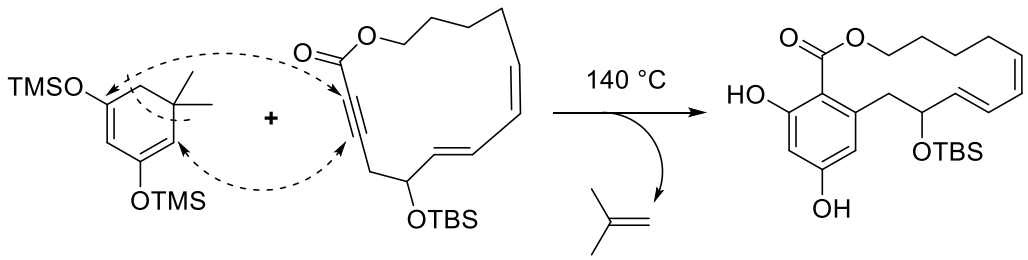
In 2006, Baran and coworkers applied this concept in the final step of the total synthesis of (±)-Haouamine A[110] (Scheme 67).



Scheme 67: Application of retro D-A in the final step of a total synthesis.

In their retrosynthetic approach, authors envisioned the formation of the 12-member ring **A** as result of a retro Diels-Alder cyclization. They synthesized the substrate bearing a terminal alkyne in the right position respect to the substituted pyrone ring and they reacted it at 250 °C in the microwave. The reaction worked quite well, and they achieved the final product in 21% yield with the recovery of a percentage of starting material (30%). This was a brilliant idea to seal this synthetically challenging macrocycle.

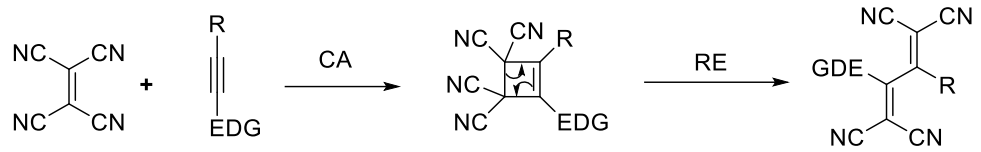
Another fancy application of retro-cycloaddition was provided by Danishefsky *et.al.* in their route to benzofused macrolactones (Scheme 68)[111].



Scheme 68: Application of retro D-A in the synthesis of cycloproparadicicol.

Authors used this strategy to seal a benzofused macrolactone. The transformation proceeds through an intermolecular D-A cycloaddition between an electron rich diene and an electron poor alkyne. Then, upon heating at 140 °C the retro-cycloaddition is triggered by the release of gaseous isobutene and the formation of a thermodynamically stable benzene, achieving the final product with an appreciable 60% yield.

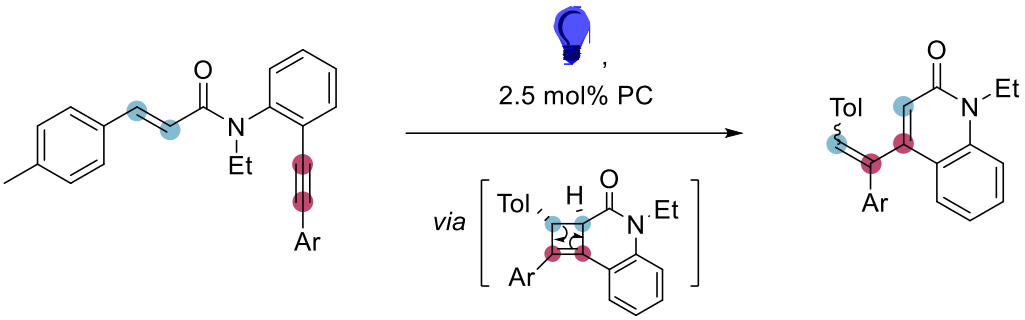
Also cyclobutane/-ene can undergo to retro cycloaddition. A famous example is the [2+2] cycloaddition – retro electrocyclization[112,113] (CA-RE), a click-like methodology for the synthesis of donor-acceptor chromophores from an electron rich alkyne and tetracyanoethylene (Scheme 69).



Scheme 69: General rappresentation for CA-RE reation.

The reaction was discovered in 1981 in the group of Prof. Bruce, and proceeds through a "classical" [2+2] cycloaddition, that undergo a favourable cyclobutene ring-rearrangement that bring to the diene represented in the scheme. In the above-mentioned examples, the release of a gaseous molecule was crucial to access an efficient retro-cycloaddition. However, the breakdown of cyclobutene is promoted by the release of steric strain, another important phenomenon that can give rise to these interesting transformations.

In 2020, Park et.al.[114] developed the visible light synthesis of conjugated diene as a result of a retro-[2+2] cycloaddition between an alkyne and an akene (Scheme 70).



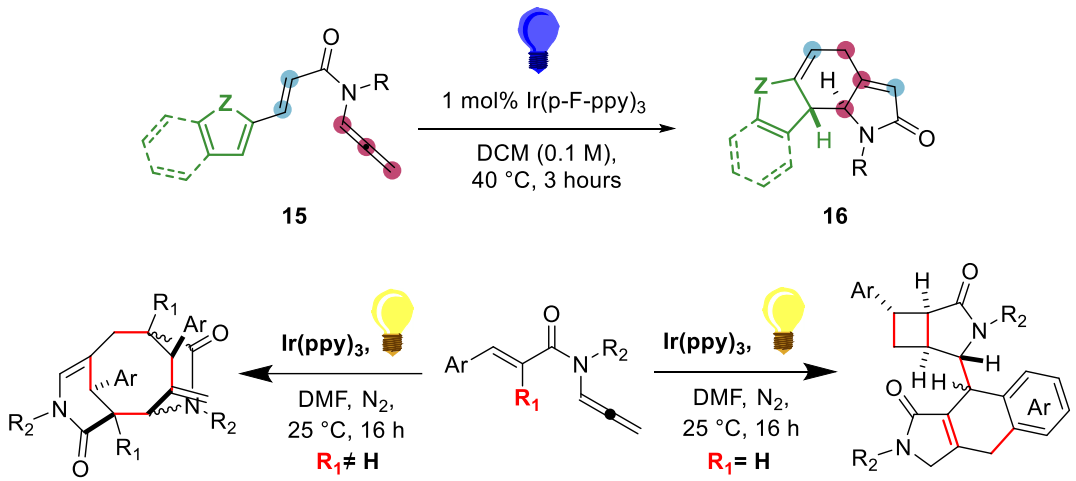
Scheme 70: Park's synthesis of dienes through retro-cycloaddition.

According to his experimental and computational studies, the reaction of 1,7-enynes leads to the intermediate formation of a strained bicyclic compound, which then undergoes a selective retro-[2+2] that eventually affords in the desired product a 1,3-conjugated diene unit.

Inspired by these literature examples, we envisioned a new dearomative cycliazation that proceeds with a fancy [2+2]/retro-[2+2] rearrangement.

5.2: Results and Discussion

In this chapter, I will present a new intramolecular dearomative cyclization of heteroaromatic enallenes that we developed in our research group (Scheme 71, top).



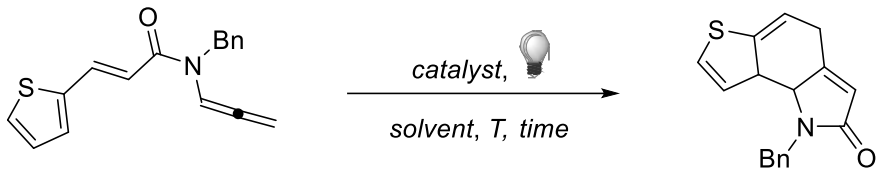
Scheme 71: Visible-light-promoted intramolecular dearomative cyclization with heteroaromatic enallenes.

This project born during the scope of a previous one, in which we reported the first visible light promoted dimerization of enallenamides (Scheme 71, bottom)[68]. Depending on substituent R_1 onto the cinnamoyl moiety, the output of the reaction was different. When R_1 was an alkyl or alkynyl group, we formed a polycycle with a central cyclooctane decorated with two bridged lactams. On the other hand, when R_1 was a hydrogen, we got the formation of a [3.2.0] bicyclic unit tethered with a fused tricycle. In the first case both aromatic and heteroaromatic enallenes reacted well, while in the latter we didn't achieve the desired product with substrate **15a**, that has a thiophene instead of benzene. The reaction worked, but the product had completely different NMR signals and we struggled a lot to understand its structure. Thanks to XRD resolution we confirmed the formation of a fused tricyclic scaffold, in which the heterocycle was dearomatized.

In a typical experiment (Table 4, entry 1), 0.2 mmol of substrate **15a** (0.1 M in DCM) and 1 mol% of an Iridium – based photosensitizer were put in a standard 5-mm NMR tube, in order to maximize the surface/volume ratio of the solution. The tube was immerged in a silicon-oil bath thermostated at 40 °C and surrounded at ca. 10 cm by a 14 W blue LEDs strip, which has its maximum emission band centered at 455 nm. The solution is irradiated for three hours, and the complete conversion of the starting material was monitored by TLC. The reaction led to the formation of the desired tricycle **2a** in 66% yield according to ^{1}H NMR using an internal standard as reference. From the crude NMR spectrum, no significant additional resonances were observed, suggesting that mass balance could be accounted for by partial substrate decomposition, likely by oligomerization/polymerization as observed in related cascades. The reaction did not require the use of degassed solvents.

Several optimization tests were performed, and a summary of the main trend observed is provided in Table 4, while the complete list of performed essays is provided in the experimental section.

Table 4: Optimization experiments.



15a **16a**

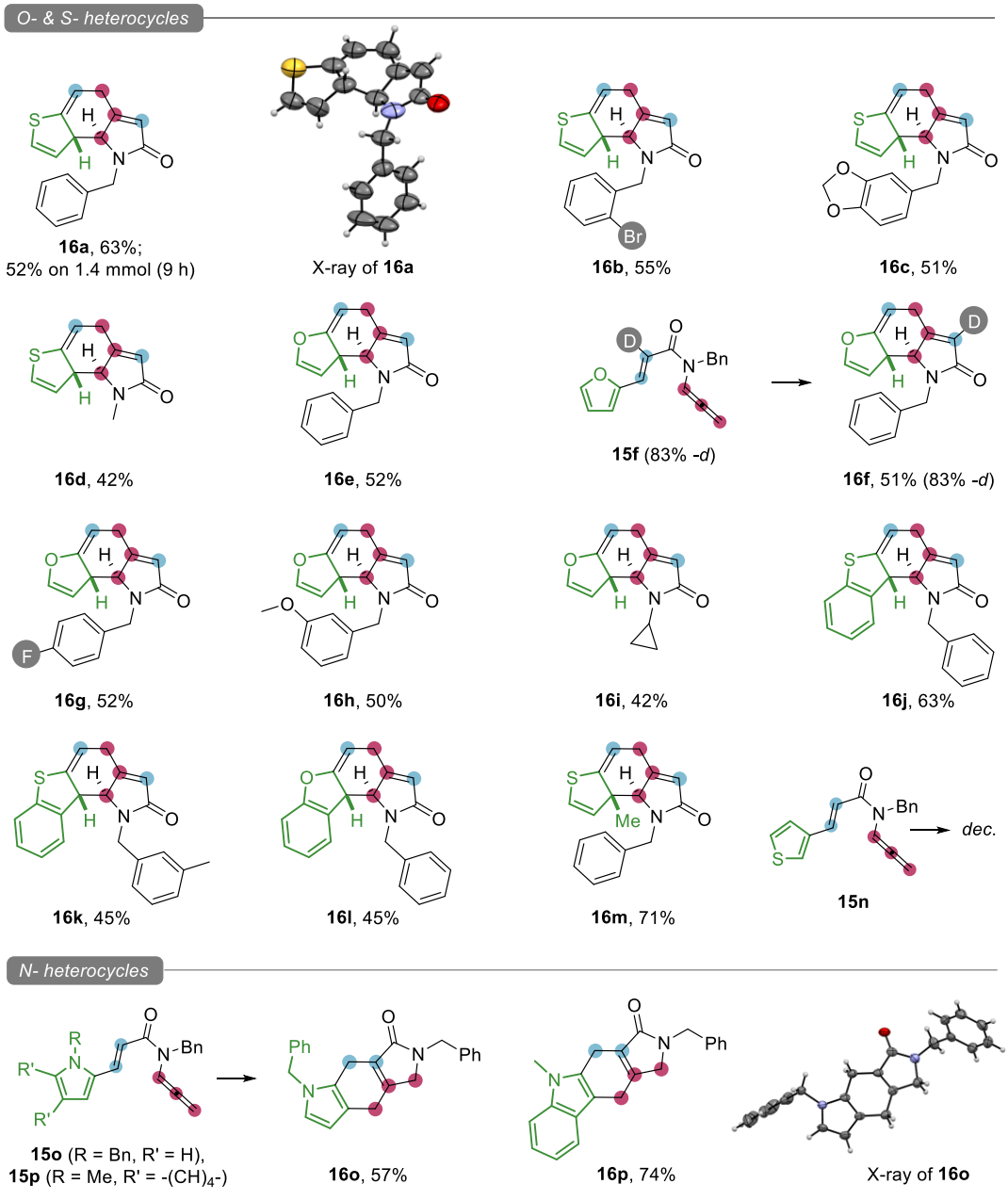
Entry[a]	Deviation from optimal	Yield of **16a** [%][b]
1	-	66
2	0.2 M on **15a**	39
3	at 25 °C	60
4	DCE, at 25 °C	35
5	THF, at 25 °C	24
6	toluene, at 25 °C	26
7	DMF, at 25 °C	37
8	$Ru(bpy)_3Cl_2$ as PC, DMF, at 25 °C	24
9	$Ir(ppy)_3$ as PC, DMF, at 25 °C	32
10[c]	10 mol% TXT as PC, DMF, at 25 °C	14
11	w/o light or PC	0

*[a] Reaction conditions: 0.2 mmol of **15a** (0.1 M in DCM), in a 5 mm NMR tube thermostated at 40 °C and irradiated with blue LEDs strip, full conversion of the starting material monitored by TLC; [b] ^1H NMR yield using 2,2'-bipyridyl as internal standard; [c] using purple LEDs (λ_{max} = 395 nm), TXT = thioxanthene-9-one.*

The adopted dilution of **15a** proved optimal, and lower yields were measured either using a more diluted solution, which might erode the yield because a lower rate of the photocatalytic process would increase the impact of the spontaneous substrate decomposition, or increasing the concentration (entry 2), which might favour the formation of dimeric/oligomeric species. The experiment performed at room temperature provided **16a** in a slightly diminished yield (entry 3). Various solvents were tested (entries 4-7), and no clear correlation between their polarity and the yield of the desired product emerged. The choice of the photocatalyst

proved crucial to steer the selectivity of the reaction (entries 8-10). In general, various Ir(III) photosensitizers proved competent for the desired transformation, while other popular organic and organometallic derivatives gave worst results. Among Iridium complexes, the best result was achieved with the fluorinated derivative used in entry 1, which has the highest triplet energy of the series. Finally, no reaction occurred without either the sensitizer or light (entry 11) or performing the reaction at 10 °C.

With the optimized reaction conditions in hand, we then tested the generality of our methodologies, preparing 20 enallenes with various functional groups (Scheme 72). The reaction on the model substrate **15a** led to the isolation of **16a** in 63% yield. The model reaction could be scaled up to 1.4 mmol, without a significant erosion of the yield. The use of a 15 mL sealed-tube, which has a lower surface/volume ration compared to an NMR tube, required however to irradiate the reacting solution for a longer period (9 hours). We next tested the effect of substituents on the benzyl group on the nitrogen atom. Gratifyingly, both electron-donating and electron-withdrawing groups were tolerated by the method (**16b-c**), which is thus suitable to treat acetals-protected diols and arylbromides that can be useful synthetic tools for further derivatizations. A slightly diminished yield was observed using an N-methyl substrate (**16d**). The replacement of the thienyl ring with a furyl one did not alter the outcome of the sequence (**16e**). The deuterium labelling of the C(sp2)-H group α- to the carbonyl unit led to the recovery of the corresponding product **16f**, in which the deuterium group was retrieved exclusively on the carbon atom bound to the carbonyl motif. Additional attempts to label with *d*- nuclei the carbon atoms of the allenyl unit were however at present fruitless. Furan- based substrates can tolerate various functionalities on the benzyl protecting group, such as fluorides and ethers (**16g-h**). Interestingly, an N-cyclopropyl derivative could be prepared in a synthetically useful yield (**16i**). Benzothiophene groups can be reacted, leading to the formation of the corresponding fused tetracyclic derivatives with good efficiency (**16j**). The presence of *meta*- substituents on the N- protecting group had a negative effect on the yield in this case (**16k**), possibly because of a negative steric clash with the heteroarene.



Scheme 72: Scope of the reaction.

The benzofurane scaffold is similarly tolerated (**16l**). The installation on the model substrate of an additional substituent on the C3 position of the heterocycle led to the recovery of the corresponding product that features a challenging quaternary carbon at one head bridging position. Remarkably, the product **16m** was

recovered with the highest yield of the series, suggesting that the bis allylic nature of the corresponding tertiary C-H group of products **16** might have been the cause of a partial yield loss because of their reduced bond dissociation energy[115]. Finally, we prepared enallene **15n**, in which the heterocycle is bound to the alkene through its C3 position rather than the C2 one. However, no traces of the corresponding product were observed, and extensive substrate decomposition occurred in this case.

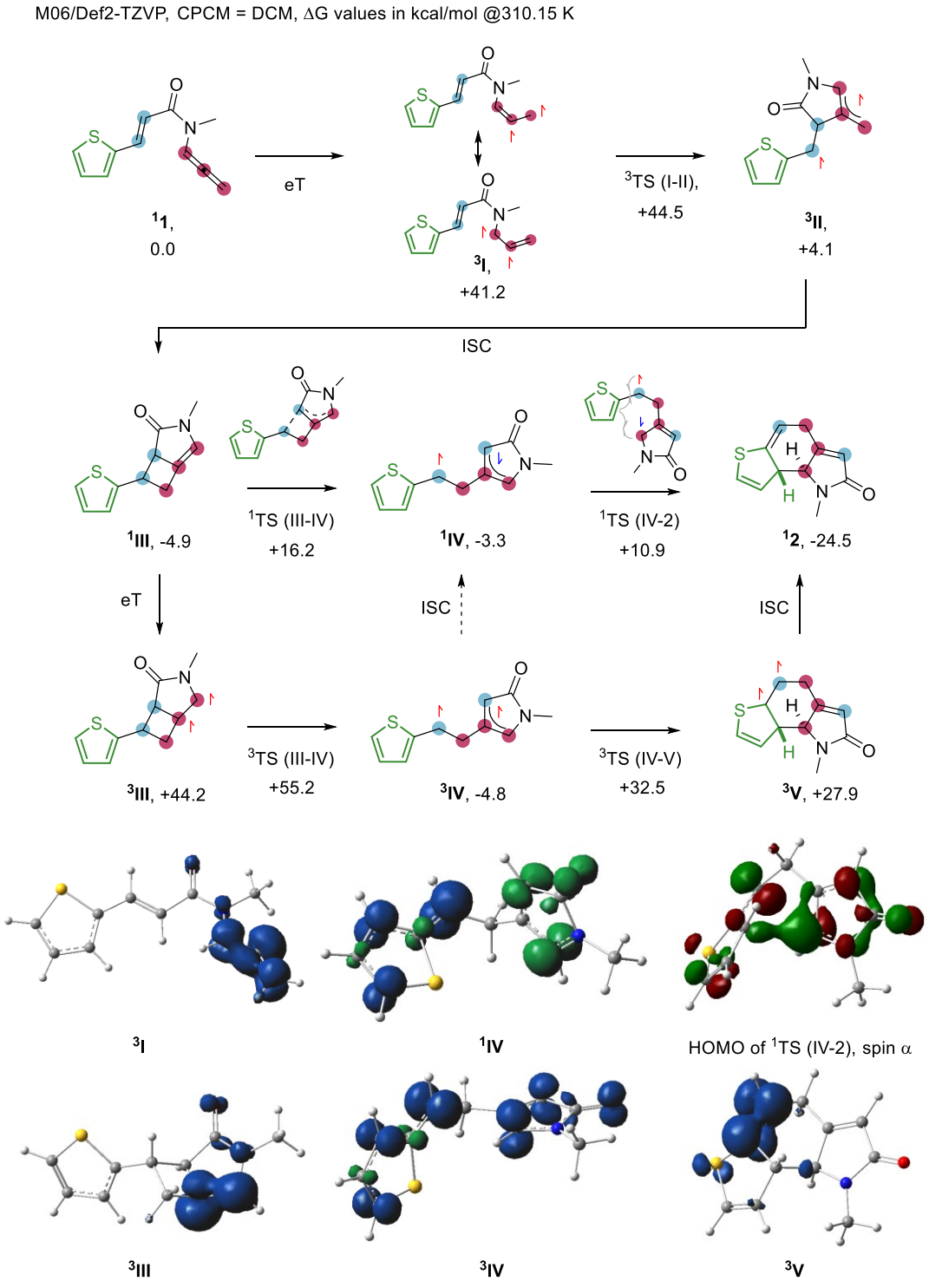
The preparation of substrates **15** in which a second electron withdrawing group, such as a BOC or a tosyl one, was bound to the nitrogen atom of the amide was limited by the reduced tendency of the corresponding alkyne precursors to undergo the final isomerization. Upon several failed attempts, a substrate in which the benzyl group of **15a** was replaced by a BOC one could be isolated. However, under the optimized photocatalytic conditions, no traces of **16** were observed and the substrate underwent extensive decomposition. These results suggest that the present method is not suitable to react enallenes in which the allenamide arm is substituted by two electron withdrawing groups.

We then attempted the dearomatization of nitrogen-containing heterocycles. The reaction of pyrrole-derived substrate **15o** led to the formation of tricycle **16o**, which was established in a clear-cut fashion via XRD analysis. This result showed that the cascade observed for S- and O- heterocycles is not accessible with N-derivatives. Because these classes of derivatives have similar aromatic stabilization energies[116], we assume that the divergent behaviour of N- heterocycles might be due to steric factors stemming from the presence of the substituent on the heteroatom. The outcome observed with the pyrrole- based reagent was confirmed by reacting the corresponding indole derivative. The fused tetracycle **16p** was recovered in good yield, confirming that the reactivity of 5-membered N-heteroaryls bound to the alkene partner gave preferentially a product that is similar to those previously observed in the visible light promoted dimerization of enallenamides[68].

We obtained a good library of products, however, the mechanism that bring to these fused polycycles was not clear. In particular, it seemed that one between the allene or the cinnamoyl moieties was broken following a particular skeletal rearrangement. In our previous works we demonstrated that allenamides can be sensitized with Ir – based PCs, so we decided to avoid any Stern-Volmer quenching studies. Since, the model allene is yellow, we thus preferred check if it has a significant absorption in the blue region (the same of LEDs). It doesn't (see experimental section), so we can exclude mechanisms that involves the direct activation of the substrate.

Thanks to DFT calculations, we hypothesized a mechanism that involves an original [2+2]/retro [2+2] rearrangement (Scheme 73). Calculations were performed at the M06/def2-TZVP level[80], which proved a reliable method to assess the pathways of related photochemical cascades, using dichloromethane as an implicit solvent[81]. According to the literature, both the allenamide and the cinnamamide groups of enallenes **15** are redox neutral in the range of potentials of common photocatalysts, including the Ir(III) complexes used in present study. The substrate **15** can be activated by the excited Iridium photosensitizer by energy transfer (EnT), forming intermediate **I** (+41.2 kcal/mol in ΔG). The triplet can evolve via 5-*exo*-*trig* cyclization. This step occurs through the low-barrier **TS (I-II)** and affords intermediate **II**, in which the two radicals are in an allylic and benzylic resonance form, respectively. The stabilization of these two mono-occupied orbitals is responsible for the relatively low energy of the triplet, making this step largely exergonic. Spin-relaxation by intersystem crossing (ISC) gives closed-shell intermediate **III**, which lies slightly below the entry channel (-4.9 kcal/mol in ΔG).

In agreement with our previous studies on related aryl-enallenes, the localization of the two spins on the former alkenyl carbon atoms would provide triplet **I'**, which is less stable than **I** (by +4.4 kcal/mol in ΔG). This suggests that the initial activation of the allenyl arm is more favorable.



Scheme 73: Hypothesized mechanism (top) and calculated spin densities of intermediates and TSs (bottom).

It is worth noting that if the energy transfer step could cause the population of triplet **I'**, this species would still evolve into intermediate **II** via radical 5-*exo*-*dig* cyclization, eventually following the proposed pathway for the skeletal rearrangement cascade. The [3.2.0] bicyclic core of **III** is characterized by a significant steric strain, which is due to the presence of the endocyclic double bond that is bound to the cyclobutane ring. This strain explains the relatively high energy of **III** compared to **15**, considering than two π- bonds of the latter become σ- ones in the former. Indeed, similar alkene-allene [2+2] photocycloadditions in which products are less congested are invariably much more exergonic. The intermediate **III** could then evolve through two different manifolds. The enamine group can be activated by EnT in the presence of a photoexcited Ir species, in analogy to similar reactivities reported in the literature[93]. The triplet energy of ^{3}**III** is +49.1 kcal/mol in ΔG. The value is higher than that observed for substrate **15** but still accessible by the Iridium photosensitizer. The cyclobutane ring can then undergo ring-opening because of the presence of a radical at its α- position. The process occurs through the low-barrier **TS (III-IV)** and affords intermediate **IV**, in which the two mono-occupied molecular orbitals are stabilized by an allylic and a benzylic-like conjugation, respectively. The former could then attack the aryl ring via 6-*endo/exo*-*trig* cyclization, delivering endergonic triplet **V**. This step occurs through **TS (IV-V)** (ΔG = +32.5 kcal/mol), which represents a relatively high barrier for a process that occurs at 40 °C. In intermediate **V**, the two mono-occupied molecular orbitals are arranged in a nearly perpendicular fashion in order to minimize spin repulsion. This species could then afford the desired product **16** via ISC. Because this pathway would involve a relatively high-energy transition state, we tried to model more feasible alternatives. The closed shell intermediate **III** might undergo a C-C cleavage affording the biradical singlet ^{1}**IV**. The process occurs via ^{1}**TS (III-IV)**, which has a ΔG of +16.2 kcal/mol. Although this step is more energy demanding than the corresponding one that occurs at the triplet state, the barrier is still remarkably low for the cleavage of a σ C-C bond. It is worth noting that the geometry of ^{1}**IV** and ^{3}**IV** are nearly superposable. Moreover, the localization of their two mono-occupied molecular orbitals is nearly identical, too. As a results, it can be

also conceived that the formation of ^{1}**IV** might occur via ISC from ^{3}**IV**. The former biradical singlet intermediate could then directly afford the desired product **16** through **TS (IV-2)**. This step has a relatively low barrier for the dearomative cyclization (ΔG = +10.9 kcal/mol), which makes it much more energetically convenient than the above-mentioned triplet alternative. By analyzing the population of the optimized **TS (IV-2)**, it can be observed that the singlet biradical character is essentially lost in the **TS**. Indeed, the two HOMOs of its α and β electrons are superposable, and, together, they represent the electronic reorganization typical of a radical recombination process, which eventually affords the final product **16**.

The final product features a carbon skeleton that has underwent a reorganization compared to the starting material because of the ring-opening of an intermediate cyclobutane ring, which was favoured by the release of its steric strain. The process leads to a skipped 1,4,7- triene motif thanks to the tandem dearomatization of the heteroaryl partner.

Attempts to locate a concerted transition state for the conversion of **III** into **16** via 3,3- sigmatropic rearrangement were fruitless, likely because of the rigidity of **III** that prevents the required frontier orbital overlap for this concerted process.

The reaction of substrates featuring an N- heterocycle (**15o**, **15p**) led to the formation of a product that did not undergo any skeletal rearrangement. The structure of these tricyclic compounds is identical to that of the minor byproduct that was observed in our previous study[68]. This suggests that the formation of **16o** and **16p** could result from the same mechanism described for related aryl-enallenes. Alternatively, it can be conceived that intermediate ^{3}**II** might undergo a radical 6-*endo/exo-trig* cyclization on the N- heterocycle, and the subsequent rearomatization would form the products. Finally, we cannot exclude that a similar scenario might occur upon the formation of intermediate **III**, which could undergo a strain-release-driven C-C cleavage reforming either ^{3}**II** or the corresponding biradical singlet. In both cases, the allyl radical arm would then attack the heterocyclic ring and eventually afford the final product via rearomatization.

5.3: Conclusions

The cascades reported herein affords complex molecular architectures in a concise fashion and with complete atom economy. These structures can be of interest because they present a 1,4,7- triene motif, which might be further used to increase their molecular complexity.

The rationalization of the skeletal rearrangement observed in present reactions showed that the dearomatization of the heteroaryl ring is triggered by the ring-opening of an intermediate fused bicycle, which is driven by the release of its steric congestion. A similar manifold holds for vast future development because it represents an additional tool for dearomative processes. Indeed, while light-promoted strategies are based on the direct activation of an arenophile or of a sufficiently conjugated arene, the present approach relies on the use of light to build up steric strain as a form of chemical energy into an intermediate species, eventually using its release to unleash the final functionalization of an arene partner.

It is worth noting that, at present, a similar approach is however limited to the dearomatization of derivatives with a relatively limited aromatic stabilization. Therefore, further development will likely aim to overcome these limitations and extend the concept to more challenging arenes.

5.4: Experimental Section

General remarks

All chemicals were purchased from commercial sources and used as received. Solvents were dried passing through alumina columns using an Inert® system and were stored under nitrogen. Chromatographic purifications were performed under gradient or an isocratic regime using mesh 60 silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded at 300 K on a Bruker 400 MHz spectrometer using the solvent as internal standard (7.26 ppm for ^{1}H NMR and 77.00 ppm for ^{13}C NMR for $CDCl_3$). Reported assignments are based on decoupling, COSY, NOESY, HSQC, and HMBC correlation experiments. The terms m, s, d, t, q, and quint represent multiplet, singlet, doublet, triplet, quadruplet, and quintuplet, respectively, and the term br means a broad signal. MS analyses were recorded on an Agilent Mass Spectrometer and exact masses were recorded on an LTQ ORBITRAP XL Thermo Mass Spectrometer (electrospray sources).

Calculations were performed using the Gaussian16 package, using the model described in the previous paragraph. The geometry of all intermediates and transition states was optimized without any constraint. The approximate starting geometry of TSs was located through relaxed scans of the corresponding putative reaction coordinate. Intermediates were characterized by the absence of imaginary frequencies in their Hessian matrix. TSs were characterized by the presence of a single imaginary frequency in their Hessian matrix, which corresponded to the vibration connecting the reagent with the product. Biradical singlets were modelled through the broken-symmetry formalism in combination with the use of an unrestricted DFT functional. The actual biradical character of the resulting species was then assessed by population analyses.

Details on the experimental setup

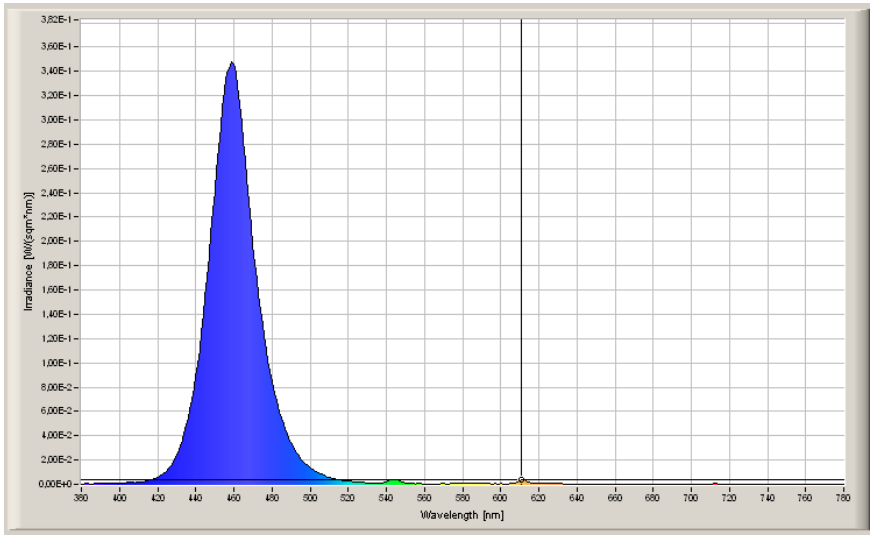


Figure 19: Measured emission of LED strips (above) and experimental setup (below).

UV-VIS ABSORPTION OF 1a AND SILICON OIL

Substrate **15a** and silicon oil were dissolved in MeCN to a dilution of 10^{-3} M. Then, both solutions were diluted to 10^{-5} M and UV-vis absorption spectra were recorded using a Lambda 750 spectrophotometer (Perkin Elmer).

Substrate **15a** starts absorbing below 370 nm, far from the emission of the LED strip. This is consistent with the absence of detection of the desired product performing the reaction without the photocatalyst. On the other hand, silicon oil has no significant absorption below 300 nm, so it does not interfere with the emission of blue LEDs.

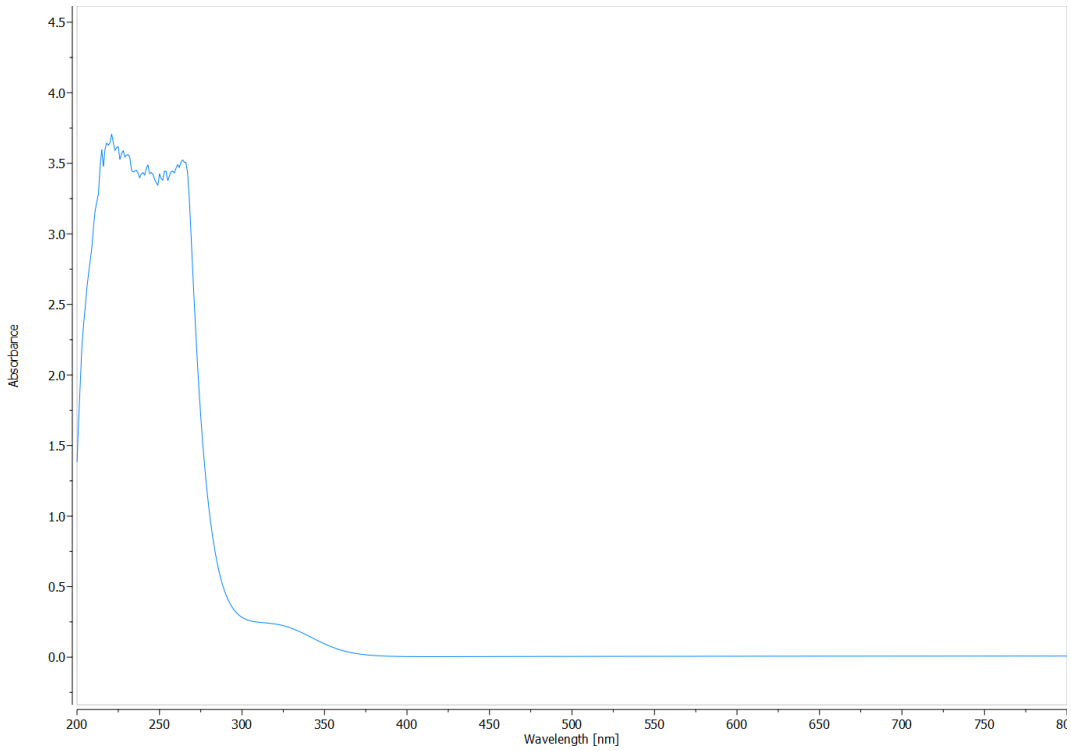


*Figure 20: UV Spectra of **15a**.*

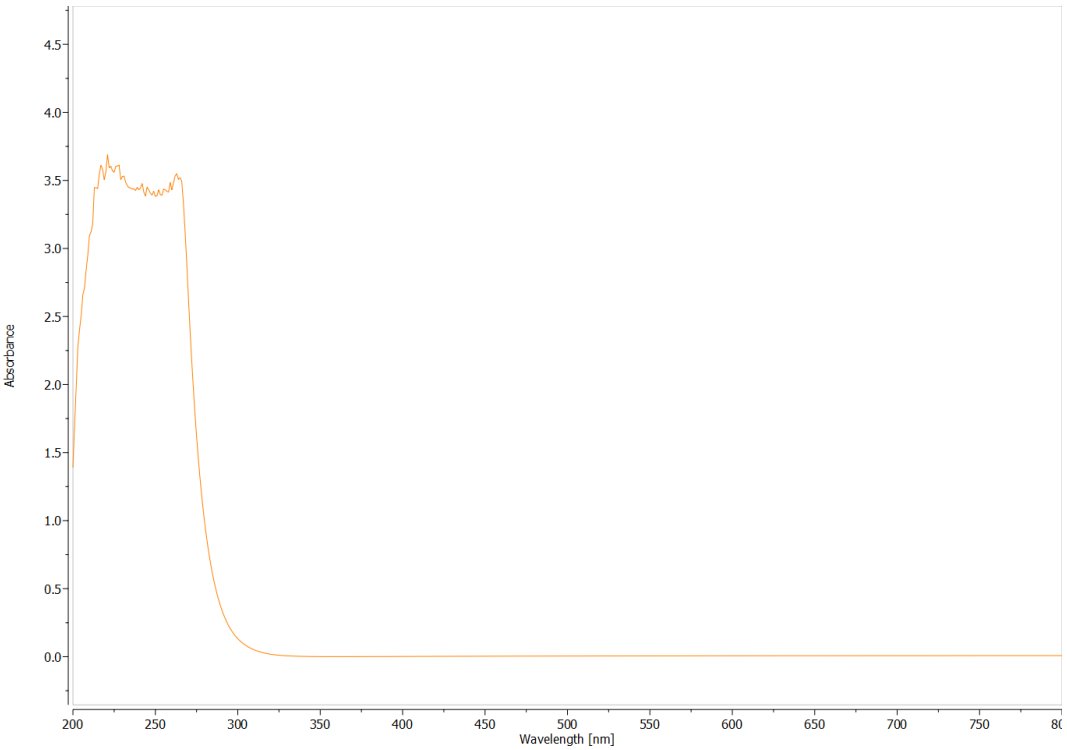
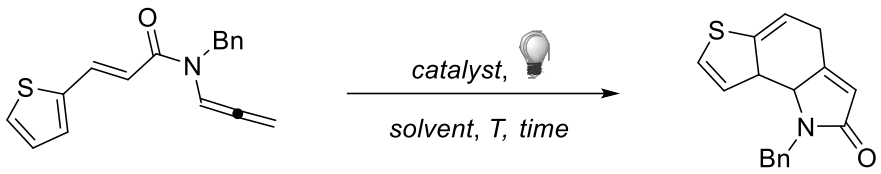


Figure 21: UV Spectra of silicon oil.

Optimization experiments



15a **16a**

Entry	Catalyst (1 mol %)	Solvent (0.1 M)	Temperature	Time (h)	Yield of **16a**[a] [%]
1[b]	$Ir(ppy)_3$	DMF	25	3	31
2	$Ir(ppy)_3$	DMF	25	3	32
3	$Ir(ppy)_3$	DMF	25	18	32
4	$Ru(bpy)_3Cl_2$	DMF	25	18	24
5	$Ir(p\text{-}F\text{-}ppy)_3$	DMF	25	18	37
6	$(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$	DMF	25	18	19
7	Thioxanthen-9-one[c,e]	DMF	25	18	14
8	Benzophenone[c,e]	DMF	25	18	11
9	$Ir(p\text{-}F\text{-}ppy)_3$	Toluene	25	18	26
10	$Ir(p\text{-}F\text{-}ppy)_3$	Toluene/DCM 1:1	25	18	50
11	$Ir(p\text{-}F\text{-}ppy)_3$	DCM	25	18	60
12	$Ir(p\text{-}F\text{-}ppy)_3$	MeCN	25	18	0[f]
13	$Ir(p\text{-}F\text{-}ppy)_3$	MeCN/$CHCl_3$ 7:3	25	18	24
14	$Ir(p\text{-}F\text{-}ppy)_3$	Chlorobenzene	25	18	40
15	$Ir(p\text{-}F\text{-}ppy)_3$	THF	25	18	24
16	$Ir(p\text{-}F\text{-}ppy)_3$	$CHCl_3$	25	18	33
17	$Ir(p\text{-}F\text{-}ppy)_3$	DCE	25	18	35
18	$Ir(p\text{-}F\text{-}ppy)_3$	DCM [0.05 M]	25	18	53
19	$Ir(p\text{-}F\text{-}ppy)_3$	DCM [0.01 M]	25	18	5
20	$Ir(p\text{-}F\text{-}ppy)_3$[e]	DCM	25	18	58
21	$(Ir[dF(CF_3)ppy]_2(bpy))PF_6$[e]	DCM	25	18	40
22	$(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$[e]	DCM	25	18	37
23	$Ir(p\text{-}F\text{-}ppy)_3$	DCM	10	9	0[f]
24	$Ir(p\text{-}F\text{-}ppy)_3$	DCM	40	3	66
25	$Ir(p\text{-}F\text{-}ppy)_3$	DCM [0.2 M]	40	3	39
26	-	DCM	25	120	0[f]
27[d]	$Ir(p\text{-}F\text{-}ppy)_3$	DCM	25	120	0

[a] ^1H NMR yield using 2,2'-Bipyridtl as internal standard, [b] with freeze-pump-thaw for removing O_2, [c] 10 mol%, [d] without light, [e] purple light, [f] degradation of starting material.

Best conditions

Synthesis of substrates

A) Synthesis of secondary amines

Synthesis of secondary amines *via* nucleophilic substitution (precursor of **15a, 15e, 15f, 15i, 15j, 15l, 15m, 15n, 15o, 15p**)

In a round bottom flask equipped with a magnetic stirring bar, propargyl bromide (1 equiv.) was added at 0 °C to primary amine (6 equiv.) and the resulting solution was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the mixture was quenched with a saturated $NaHCO_3$ solution and extracted with Et_2O (3 times). The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (Yield = 95%) or used without purifications for the synthesis of **15i**.

Synthesis of secondary amines *via* reductive amination (precursor of **15b, 15c, 15g, 15h, 15k**)

One drop of AcOH was added to a solution of propargyl amine (1 equiv.) and aryl aldehyde (1.08 equiv.) in MeOH (0.6 M). The resulting mixture was then stirred for 18 h at room temperature. $NaBH_4$ (1.5 equiv.) was added at 0 °C and the solution was then stirred for 1 h prior to the evaporation of the solvent. The mixture was diluted with water, extracted with DCM (2 times), and the combined organic layers were then washed with a 1 M HCl solution. Aqueous layers were neutralized, extracted with DCM (2 times), and the resulting organic phase was finally washed with brine, dried over Na_2SO_4, concentrated under reduced pressure, and purified by chromatography on silica gel (DCM/EtOAc gradient).

B) Synthesis of Esters

Synthesis of esters *via* Heck coupling (precursor of **15a-d**, **15m**, **15n**)

In a Schlenk tube equipped with a magnetic stirring bar under nitrogen atmosphere, were added $Pd(OAc)_2$ (0.02 equiv.), P(*o*-tol)$_3$ (0.04 equiv.), TEA (1.5 equiv.), acrylate (1.3 equiv.) and the aryl halide (1 equiv.) in DMF (1 M). The resulting mixture was stirred at 120 °C for 18 h. After complete conversion as monitored by TLC, the mixture was diluted with EtOAc, washed twice with water and a saturated LiCl

solution, dried with Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 40-92%.

Synthesis of esters *via* Wittig olefination (precursor of **15e**, **15g**-**l**)

To a solution of phosphonium ylide (1.08 equiv.) in MeCN (0.12 M) the desired aldehyde (1 equiv.) was added. The resulting mixture was refluxed for 45 min under stirring. After complete conversion of reagents, the mixture was concentrated under reduced pressure and purified by chromatography on silica gel (*n*-hexane/EtOAc gradient). Yields between 70-96%.

C) Synthesis of carboxylic acids

Hydrolysis of esters (precursor of **15a-e**, **15g-n**)

In a round bottom flask equipped with a stir bar were added the desired ester (1 equiv.), EtOH (0.15 M) and a 1 M solution of KOH (2.5 equiv.). The resulting mixture was stirred 18 h at 45 °C. After complete conversion as monitored by TLC, the mixture was concentrated under reduced pressure and acidified to pH = 1 with a 1 M HCl solution. During the process, the formation of a precipitate was observed. The solid was filtered, washed with water, and dried under high vacuum to afford the corresponding carboxylic acid. Yields between 70-91%.

Synthesis of (E)-3-(furan-2-yl)acrylic-2-d acid (precursor of **15f**)

In a round bottom flask equipped with a magnetic stirring bar and a condenser a solution of malonic acid (1 equiv.), piperidine (0.35 equiv.) and D_2O (14 equiv.) in pyridine (1.5 M) were refluxed for 2 hours; furfural (1 equiv.) was then added, and the mixture was stirred for an additional 3 hours. The resulting mixture was poured in a HCl solution (10% m/V), the precipitate was filtered, washed with water and dried under vacuo affording the corresponding carboxylic acid (Yield = 74%; deuterium incorporation: 80%).

D) Synthesis of amides

Synthesis of amides *via* coupling with acyl chlorides (precursor of **15a-c**, **15e-n**)

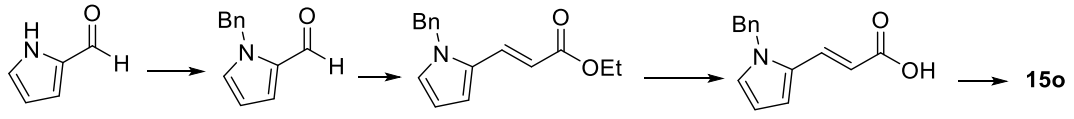
In a 25 mL round bottom flask equipped with a magnetic stirring bar, the desired acid was dissolved in DCM (0.6 M) and a catalytic amount of DMF (3 drops) was added. The solution was then cooled to 0 °C and oxalyl chloride (1.5 equiv) was added. The solution was stirred for 1 h at room temperature. Then, the mixture was concentrated under reduced pressure to afford the acyl chloride, that was added to a solution of DMAP (0.02 equiv.), TEA (1 equiv.) and the desired amine (1 equiv.) in DCM (0.25 M) at 0 °C. The mixture was stirred for 18 h at room temperature. After complete conversion as monitored by TLC, the solution was diluted with DCM and washed with saturated NH_4Cl solution, followed by a saturated $NaHCO_3$ one. The aqueous layers were extracted with DCM (3 times), and the combined organic phase was finally washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The crude was finally purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired products. Yields between 41-98%.

Synthesis of amides *via* nucleophilic substitution (precursor of **15d**)

To a solution of primary amide (1 equiv.) in DMF (0.6 M) at 0° C, NaH (60% in paraffine oil, 1.3 equiv.) was slowly added and the mixture was stirred for 1 h. The desired alkyl halide (1.5 equiv.) was then slowly added, and the reaction was stirred at room temperature for 18 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product (Yield = 53%).

E) Synthesis of precursors of 15o and 15p

Synthesis of **(E)-N-benzyl-3-(1-benzyl-1H-pyrrol-2-yl)-N-(prop-2-yn-1-yl)acrylamide** (precursor of **15o**)



I **II** **III**

To a solution of pyrrole-2-carboxaldehyde (1 equiv.) in DMF (0.5 M) at 0° C, NaH (60% in paraffine oil, 1.5 equiv.) was slowly added and the mixture was stirred for 1 h. Benzyl bromide (1.2 equiv.) was then slowly added, and the reaction was stirred at room temperature overnight. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc 85:15) to afford 1-benzyl-1H-pyrrole-2-carbaldehyde (**I**). (Yield 73%)

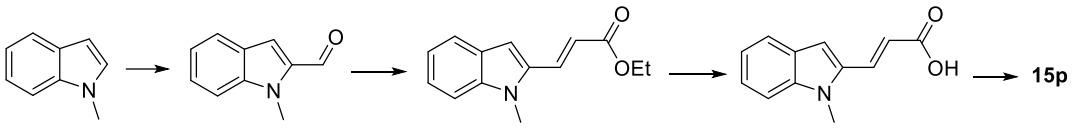
To a solution of phosphonium ylide (1.5 equiv.) in THF (0.5 M) the 1-benzyl-1H-pyrrole-2-carbaldehyde (1 equiv.) was added. The resulting mixture was refluxed 6 hours under stirring. After that the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/MTBE 88:12) to afford (E)-ethyl 3-(1-benzyl-1H-pyrrol-2-yl)acrylate (**II**). (Yield 59%)

In a round bottom flask equipped with a stir bar were added (E)-ethyl 3-(1-benzyl-1H-pyrrol-2-yl)acrylate, MeOH (0.6M) and a 10M solution of NaOH (2 equiv.). The resulting mixture was stirred for 1 hour at 45°C. After complete conversion as monitored by TLC, the mixture was concentrated under reduced pressure and acidified to pH=1 with a 1M HCl solution. During the process, the formation of a precipitate was observed. The following solid was filtered, washed with water and finally dried under high vacuum to afford (E)-3-(1-benzyl-1H-pyrrol-2-yl)acrylic acid (**III**). (Yield 56%)

In a round bottom flask were added N-benzylprop-2-yn-1-amine (1 equiv.), 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCl) (1.3 equiv.) and Et_3N (1.3 equiv.) in DCM (0.1 M). The mixture was stirred at room temperature for 15 minutes, then a solution of (E)-3-(1-benzyl-1H-pyrrol-2-yl)acrylic acid (1 equiv.) and DCM was slowly added at 0°C and the mixture was reacted overnight. After complete conversion as monitored by TLC, the solution was quenched with a saturated NH_4Cl solution and

extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc 7:3) to afford (E)-N-benzyl-3-(1-benzyl-1H-pyrrol-2-yl)-N-(prop-2-yn-1-yl)acrylamide (**15o**). (Yield 47%)

Synthesis of **(E)-N-benzyl-3-(1-methyl-1H-indol-2-yl)-N-(prop-2-yn-1-yl)acrylamide** (precursor of **15p**)



I **II** **III**

To a solution of 1-methyl-1H-indole (1 equiv.) in Et_2O (0.7 M) at 0° C, *n*-Buli (2.5 M in hexane, 1.1 equiv.) was slowly added, and the mixture was refluxed for 3 hours. The reaction was cooled down to room temperature, then DMF (1.5 equiv.) was added, and the solution was refluxed for 5 h. After complete conversion as monitored by TLC, the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc gradient) to afford the desired product **I** (Yield = 63%).

To a solution of phosphonium ylide (1.5 equiv.) in THF (0.5 M) the 1-benzyl-1H-pyrrole-2-carbaldehyde (1 equiv.) was added. The resulting mixture was refluxed 6 hours under stirring. After that the mixture was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc 85:15) to afford (E)-ethyl 3-(1-methyl-1H-indol-2-yl)acrylate (**II**). (Yield 81%).

In a round bottom flask equipped with a stir bar were added (E)-ethyl 3-(1-methyl-1H-indol-2-yl)acrylate, MeOH (0.6M) and a 10M solution of NaOH (2 equiv.). The resulting mixture was stirred for 1 hour at 45°C. After complete conversion as monitored by TLC, the mixture was concentrated under reduced pressure and acidified to pH=1 with a 1M HCl solution. During the process, the formation of a precipitate was observed. The following solid was filtered, washed with water and finally dried under high vacuum to afford (E)-3-(1-methyl-1H-indol-2-yl)acrylic acid (**III**). (Yield 89%).

In a round bottom flask were added N-benzylprop-2-yn-1-amine (1 equiv.), 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCl) (1.3 equiv.) and Et_3N (1.3 equiv.) in

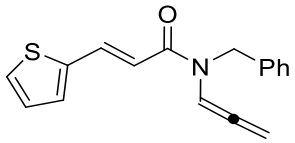
DCM (0.1 M). The mixture was stirred at room temperature for 15 minutes, then a solution of (E)-3-(1-benzyl-1H-pyrrol-2-yl)acrylic acid (1 equiv.) and DCM was slowly added at 0°C and the mixture was reacted overnight. After complete conversion as monitored by TLC, the solution was quenched with a saturated NH_4Cl solution and extracted with EtOAc (3 times). The combined organic layers were washed with brine (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by chromatography on silica gel (*n*-hexane/EtOAc 72:28) to afford (E)-N-benzyl-3-(1-methyl-1H-indol-2-yl)-N-(prop-2-yn-1-yl)acrylamide (**15p**). (Yield 58%).

General procedure for the alkyne isomerization leading to enallenes **15** (**GP-1**)

The desired enyne (1 equiv.) and THF (0.20 M) were sequentially added to a Schlenk tube equipped with a magnetic stirring bar. tBuOK (0.2 equiv.) was added and the resulting mixture was stirred at room temperature for 10 minutes. After complete conversion as monitored by TLC, 5 ml of a saturated NH4Cl solution were added. The mixture was extracted with EtOAc (3 x 15 ml), the organic layers separated and dried over Na2SO4. The solution was concentrated under reduced pressure and the crude purified by chromatography on silica gel (n-hexane/EtOAc gradient) to afford the corresponding enallene.

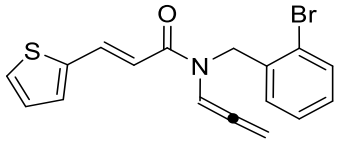
Characterization of substrates

(E)-N-benzyl-N-(propa-1,2-dien-1-yl)-3-(thiophen-2-yl)acrylamide



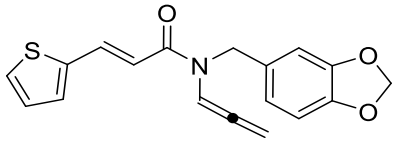
Enallene **15a** was prepared following general procedure **GP-1** from the corresponding enyne (436.3 mg, 1.55 mmol). Yellow solid (292.7 mg, 67% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 15.0 Hz, 1H RotA, 1H RotB), 7.81 (t, *J* = 6.5 Hz, 1H RotA), 7.41 – 7.20 (m, 7H RotA, 7H RotB), 7.10 – 7.00 (m, 1H RotA, 1H RotB), 6.94 – 6.78 (m, 2H RotB), 6.62 (d, *J* = 14.9 Hz, 1H RotA), 5.36 (d, *J* = 6.3 Hz, 2H RotA, 2H RotB), 4.88 – 4.78 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 202.6, 164.8, 164.7, 140.2, 137.6, 137.2, 137.1, 136.6, 130.8, 128.9, 128.4, 128.1, 128.0, 127.9, 127.5, 127.1, 126.2, 115.7, 115.6, 100.1, 87.7, 86.8, 49.3, 48.3. **ESI-MS** calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, 282.09 found 282.41.

€-N-(2-bromobenzyl)-N-(propa-1,2-dien-1-yl)-3-(thiophen-2-yl)acrylamide



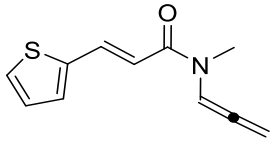
Enallene **15b** was prepared following general procedure **GP-1** from the corresponding enyne (432.3 mg, 1.2 mmol). Yellow solid (309.8 mg, 72% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 – 7.87 (m, 1H RotA, 1H RotB), 7.83 (t, *J* = 6.4 Hz, 1H RotA), 7.65 – 7.52 (m, 1H RotA, 1H RotB), 7.45 – 6.85 (m, 6H RotA, 8H RotB), 6.44 (d, *J* = 15.0 Hz, 1H 1H RotA), 5.38 – 5.22 (m, 2H RotA, 2H RotB), 4.96 – 4.80 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.2, 165.0, 164.7, 140.2, 140.1, 137.6, 137.0, 135.9, 132.8, 132.7, 131.0, 130.9, 129.0, 128.4, 128.2, 128.1, 128.0, 127.4, 127.2, 121.9, 115.1, 100.0, 87.9, 86.8, 49.5, 48.9. **ESI-MS** calcd for $C_{17}H_{15}BrNOS$ $[M+H]^+$, 360.01 found 360.46

(E)-N-(benzo[d][1,3]dioxol-5-ylmethyl)-N-(propa-1,2-dien-1-yl)-3-(thiophen-2 yl)acrylamide



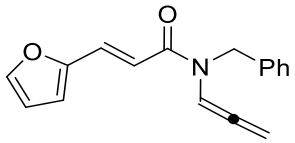
Enallene **15c** was prepared following general procedure **GP-1** from the corresponding enyne (292.8 mg, 0.9 mmol). Orange viscous oil (188.5 mg, 64% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 15.0 Hz, 1H RotA, 1H RotB), 7.79 – 7.71 (m, 1H RotA), 7.37 – 7.17 (m, 2H RotA, 2H RotB), 7.07 – 6.98 (m, 1H RotA, 1H RotB), 6.87 – 6.55 (m, 4H RotA, 5H RotB), 5.98 – 5.87 (m, 2H RotA, 2H RotB), 5.37 (d, *J* = 6.3 Hz, 2H RotA, 2H RotB), 4.74 – 4.64 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.6, 202.5, 164.7, 164.6, 148.2, 147.7, 147.0, 146.7, 140.2, 137.1, 136.6, 131.4, 131.1, 130.8, 128.1, 127.9, 121.6, 119.5, 115.7, 115.6, 108.8, 108.5, 108.0, 106.8, 101.2, 100.9, 100.0, 87.8, 86.8, 49.0, 48.0. **ESI-MS** calcd for $C_{18}H_{16}NO_3S$ $[M+H]^+$, 326.08 found 326.56.

(E)-N-methyl-N-(propa-1,2-dien-1-yl)-3-(thiophen-2-yl)acrylamide



Enallene **15d** was prepared following general procedure **GP-1** from the corresponding enyne (153.9 mg, 0.75 mmol). Orange viscous oil (87.1 mg, 57% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 – 7.78 (m, 1H RotA, 1H RotB), 7.73 – 7.64 (m, 1H RotA), 7.38 – 7.20 (m, 2H RotA, 2H RotB), 7.09 – 6.93 (m, 1H RotA, 2H RotB), 6.79 – 6.65 (m, 1H RotA, 1H RotB), 5.49 – 5.36 (m, 2H RotA, 2H RotB), 3.25 – 3.02 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 201.7, 164.8, 164.3, 140.3, 136.8, 136.1, 130.9, 130.7, 128.1, 127.8, 127.7, 115.4, 101.3, 100.3, 87.3, 86.7, 33.0, 31.8. **ESI-MS** calcd for $C_{11}H_{12}NOS$ $[M+H]^+$, 206.06 found 206.13.

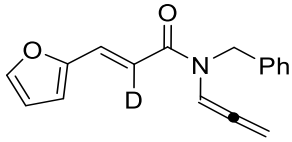
(E)-N-benzyl-3-(furan-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide



Enallene **15e** was prepared following general procedure **GP-1** from the corresponding enyne (185.6 mg, 0.7 mmol). Orange solid (140.9 mg, 76% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400

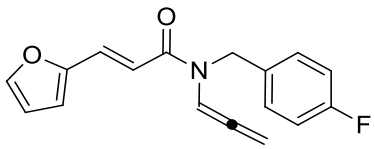
MHz, $CDCl_3$) δ 7.80 (t, *J* = 6.5 Hz, 1H RotA), 7.63 – 7.19 (m, 7H RotA, 7H RotB), 6.99 – 6.89 (m, 2H RotB), 6.73 (d, *J* = 15.0 Hz, 1H RotA), 6.64 – 6.56 (m, 1H RotA, 1H RotB), 6.53 – 6.42 (m, 1H RotA, 1H RotB), 5.39 – 5.29 (m, 2H RotA, 2H RotB), 4.90 – 4.79 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 202.4, 164.9, 151.5, 144.3, 137.6, 137.1, 131.1, 130.5, 128.8, 128.7, 128.4, 128.1, 128.0, 127.4, 127.1, 126.2, 114.8, 114.6, 114.3, 112.3, 100.2, 99.9, 87.6, 86.8, 49.2, 48.2. **ESI-MS** calcd for $C_{17}H_{16}NO_2$ $[M+H]^+$, 266.11 found 265.72.

(E)-N-benzyl-3-(furan-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide-2-d



Enallene **15f** was prepared following general procedure **GP-1** from the corresponding enyne (234.4 mg, 0.88 mmol). Orange solid (155.9 mg, 67% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 (t, *J* = 6.4 Hz, 1H RotA), 7.61 – 7.53 (m, 1H RotA, 1H RotB, 7.52 – 7.17 (m, 6H RotA, 6H RotB), 6.98 – 6.91 (m, 1H RotB, 1H RotB non-deuterated 1f), 6.73 (d, *J* = 15.1 Hz, 1H RotA non-deuterated 1f), 6.64 – 6.55 (m, 1H RotA, 1H RotB), 6.51 – 6.42 (m, 1H RotA, 1H RotB), 5.39 – 5.27 (m, 2H RotA, 2H RotB), 4.88 – 4.79 (m, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 202.4, 164.9, 151.5, 151.4, 144.3, 137.6, 137.1, 131.1, 131.0, 130.5, 130.4, 128.8, 128.4, 128.0, 127.4, 127.1, 126.2, 114.8, 114.6, 114.3, 114.2, 114.0 (t, *J* = 24.1 Hz), 112.3, 100.2, 99.9, 87.6, 86.8, 49.2, 48.1. **ESI-MS** calcd for $C_{17}H_{15}DNO_2$ $[M+H]^+$, 267.12 found 266.96.

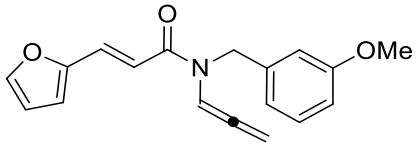
(E)-N-(4-fluorobenzyl)-3-(furan-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide



Enallene **15g** was prepared following general procedure **GP-1** from the corresponding enyne (311.6 mg, 1.1 mmol). Orange solid (189.6 mg, 61% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (t, *J* = 6.4 Hz, 1H RotA), 7.60 – 7.52 (m, 1H RotA, 1H RotB), 7.45 (d, *J* = 22.8 Hz, 1H RotA, 1H RotB), 7.34 – 7.18 (m, 2H RotA, 2H RotB), 7.09 – 6.88 (m, 2H RotA, 4H RotB), 6.70 (d, *J* = 15.0 Hz, 1H RotA), 6.62 – 6.59 (m, 1H RotA, 1H RotB), 6.49 – 6.45 (m, 1H RotA, 1H RotB), 5.37 – 5.33 (m, 2H RotA, 2H RotB), 4.79 (s, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 202.3, 164.9, 164.8, 163.3 (d, *J* = 8.3 Hz), 160.8 (d, *J* = 8.5 Hz), 151.5, 151.4, 144.4, 133.4, 132.8, 131.3, 130.6, 129.8, 129.7, 127.9, 127.8, 115.8, 115.6, 115.2, ,115.1, 115.0, 114.7, 114.1, 114.0,

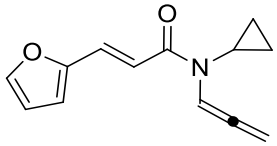
112.4, 100.1, 99.8, 87.7, 86.9, 48.5, 47.4. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -115.02 (q, *J* = 7.2 Hz, 1F RotA), -115.52 (q, *J* = 7.1 Hz, 1F RotB). **ESI-MS** calcd for $C_{17}H_{15}FNO_2$ $[M+H]^+$, 284.11 found 284.06.

(E)-3-(furan-2-yl)-N-(3-methoxybenzyl)-N-(propa-1,2-dien-1-yl)acrylamide



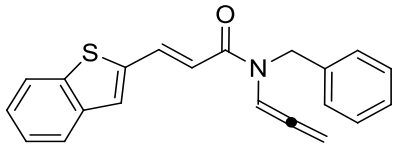
Enallene **15h** was prepared following general procedure **GP-1** from the corresponding enyne (295.3 mg, 1.0 mmol). Orange solid (222.6 mg, 75% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (t, *J* = 6.4 Hz, 1H RotA), 7.56 (dd, *J* = 15.1, 3.7 Hz, 1H RotA, 1H RotB), 7.48 (s, 1H RotB), 7.41 (s, 1H RotA), 7.30 – 7.21 (m, 1H RotA, 1H RotB), 6.97 – 6.69 (m, 4H RotA, 5H RotB), 6.64 – 6.55 (m, 1H RotA, 1H RotB), 6.51 – 6.42 (m, 1H RotA, 1H RotB), 5.35 (d, *J* = 9.0 Hz, 2H RotA, 2H RotB), 4.81 (d, *J* = 9.0 Hz, 2H RotA, 2H RotB), 3.80 (s, 3H RotA, 3H RotB).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 202.4, 164.9, 160.0, 159.7, 151.5, 144.3, 139.2, 138.8, 131.1, 130.5, 129.9, 129.3, 120.3, 118.4, 114.8, 114.6, 114.3, 113.6, 112.6, 112.5, 112.3, 112.0, 100.3, 99.9, 87.7, 86.8, 55.2, 49.1, 48.1. **ESI-MS** calcd for $C_{18}H_{18}NO_3$ $[M+H]^+$, 296.13 found 296.07.

(E)-N-cyclopropyl-3-(furan-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide



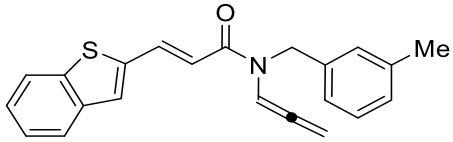
Enallene **15i** was prepared following general procedure **GP-1** from the corresponding enyne (129.2 mg, 0.6 mmol). Brown oil (86.1 mg, 66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 – 7.46 (m, 3H), 7.18 (d, *J* = 15.3 Hz, 1H), 6.60 (d, *J* = 3.4 Hz, 1H), 6.48 (dd, *J* = 3.4, 1.8 Hz, 1H), 5.36 (d, *J* = 6.5 Hz, 2H), 2.74 (tt, *J* = 7.0, 3.8 Hz, 1H), 1.05 – 1.00 (m, 2H), 0.88 – 0.84 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 203.6, 166.2, 151.7, 144.2, 129.7, 115.8, 114.5, 112.3, 99.6, 85.5, 28.0, 10.1. **ESI-MS** calcd for $C_{13}H_{14}NO_2$ $[M+H]^+$, 216.10 found 216.04.

(E)-3-(benzo[b]thiophen-2-yl)-N-benzyl-N-(propa-1,2-dien-1-yl)acrylamide



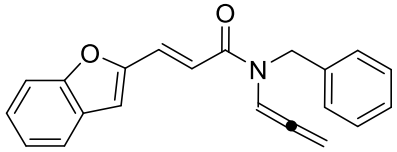
Enallene **15j** was prepared following general procedure **GP-1** from the corresponding enyne (334.4 mg, 1.0 mmol). Brown solid (128.5 mg, 38% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 15.1, 3.2 Hz, 1H RotA, 1H RotB), 7.84 – 7.74 (m, 3H RotA, 2H RotB), 7.54 – 7.23 (m, 8H RotA, 8H RotB), 6.91 – 6.88 (m, 1H RotA, 1H RotB), 6.68 (d, *J* = 14.9 Hz, 1H RotB), 5.39 (d, *J* = 6.3 Hz, 2H RotA, 2H RotB), 4.85 (d, *J* = 14.5 Hz, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 164.5, 164.4, 140.1, 139.9, 139.7, 137.6, 137.5, 137.14, 137.06, 128.9, 128.6, 128.4, 128.1, 127.6, 127.2, 126.3, 126.1, 124.9, 124.44, 122.37, 122.4, 118.3, 118.2, 100.1, 87.9, 86.8, 49.3, 48.4. **ESI-MS** calcd for $C_{21}H_{18}NOS$ $[M+H]^+$, 332.11 found 332.08.

(E)-3-(benzo[b]thiophen-2-yl)-N-(3-methylbenzyl)-N-(propa-1,2-dien-1-yl)acrylamide



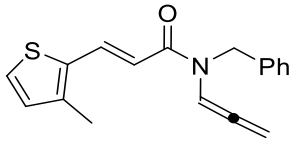
Enallene **15k** was prepared following general procedure **GP-1** from the corresponding enyne (390.37 mg, 1.13 mmol). Yellow solid (226.3 mg, 58% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 – 7.95 (m, 1H RotA, 1H RotB), 7.86 – 7.71 (m, 3H RotA, 2H RotB), 7.50 – 7.06 (m, 7H RotA, 7H RotB), 6.94 – 6.86 (m, 2H RotB), 6.68 (d, *J* = 14.9 Hz, 1H RotA), 5.40 (d, *J* = 6.4 Hz, 2H RotA, 2H RotB), 4.86 – 4.76 (m, 2H RotA, 2H RotB), 2.41 – 2.33 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 202.7, 164.5, 164.4, 140.2, 139.9, 139.7, 138.7, 138.1, 137.5, 137.3, 137.1, 137.0, 128.84, 128.81, 128.7, 128.6, 128.51, 128.47, 128.4, 128.3, 128.0, 126.9, 126.1, 125.2, 125.1, 125.0, 124.9, 124.4, 123.4, 122.43, 122.36, 118.4, 118.2, 100.2, 87.8, 86.8, 49.3, 48.4, 21.5, 21.4. **ESI-MS** calcd for $C_{22}H_{20}NOS$ $[M+H]^+$, 346.13 found 345.88. *(Partial decomposition was observed during the acquisition of NMR spectra)*

(E)-3-(benzofuran-2-yl)-N-benzyl-N-(propa-1,2-dien-1-yl)acrylamide



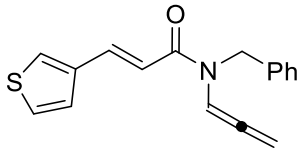
Enallene **15l** was prepared following general procedure **GP-1** from the corresponding enyne (414.4 mg, 1.2 mmol). Pale yellow solid (248.8 mg, 60% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (t, *J* = 6.4 Hz, 1H RotA), 7.69 (dd, *J* = 15.0, 8.2 Hz, 1H RotA, 1H RotB), 7.60 (dd, *J* = 11.4, 7.7 Hz, 1H RotA, 1H RotB), 7.57 – 7.19 (m, 8H RotA, 8H RotB), 7.03 – 6.99 (m, 1H RotA, 2H RotB), 6.94 (d, *J* = 10.2 Hz, 1H RotA, 1H RotB), 5.39 – 5.34 (m, 2H RotA, 2H RotB), 4.89 (s, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.9, 202.5, 164.5, 155.4, 153.0, 152.9, 137.5, 137.0, 131.4, 130.7, 128.8, 128.5, 128.4, 128.0, 127.5, 127.2, 126.32, 126.28, 123.3, 121.8, 117.3, 117.2, 111.3, 111.2, 110.9, 100.2, 99.8, 87.7, 86.9, 49.3, 48.3. **ESI-MS** calcd for $C_{21}H_{17}NNaO_2$ $[M+Na]^+$, 338.12 found 338.52.

(E)-N-benzyl-3-(3-methylthiophen-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide



Enallene **15m** was prepared following general procedure **GP-1** from the corresponding enyne (295.4 mg, 1 mmol). Brown solid (236.3 mg, 80% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 – 7.93 (m, 1H RotA, 1H RotB), 7.82 (t, *J* = 6.4 Hz, 1H RotA), 7.41 – 7.17 (m, 6H RotA, 6H RotB), 6.94 – 6.83 (m, 1H RotA, 2H RotB), 6.76 (d, *J* = 15.0 Hz, 1H RotB), 6.55 (d, *J* = 14.9 Hz, 1H RotA), 5.37 (d, *J* = 6.3 Hz, 2H RotA, 2H RotB), 4.88 – 4.77 (m, 2H RotA, 2H RotB), 2.40 – 2.30 (m, 3H RotA, 3H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 202.6, 165.05, 164.95, 141.2, 137.7, 137.3, 135.5, 135.1, 134.3, 131.3, 128.8, 128.4, 128.0, 127.5, 127.1, 126.4, 126.3, 114.8, 114.5, 100.2, 87.7, 86.8, 49.3, 48.3, 14.2. **ESI-MS** calcd for $C_{17}H_{18}NOS$ $[M+H]^+$, 296.11 found 295.67.

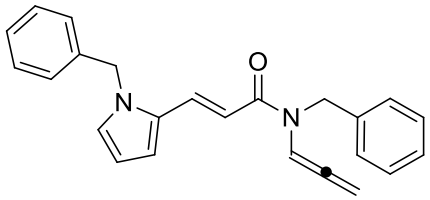
(E)-N-benzyl-N-(propa-1,2-dien-1-yl)-3-(thiophen-3-yl)acrylamide



Enallene **15n** was prepared following general procedure **GP-1** from the corresponding enyne (281.4 mg, 1 mmol). Orange oil (202.6 mg, 72% yield). Two

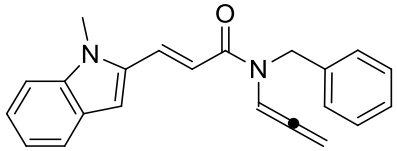
rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, $CDCl_3$) δ .83 – 7.77 (m, 2H RotA, 1H RotB), 7.52 – 7.26 (m, 7H RotA, 8H RotB), 7.16 (d, *J* = 5.2 Hz, 1H RotA), 6.93 – 6.83 (m, 2H RotB), 6.62 (d, *J* = 15.2 Hz, 1H RotA), 5.35 (d, *J* = 6.4 Hz, 2H RotA, 2H RotB), 4.84 (d, *J* = 12.0 Hz, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.7, 202.4, 165.3, 165.2, 138.2, 138.1, 137.6, 137.3, 128.9, 128.4, 128.0, 127.9, 127.7, 127.5, 127.1, 126.9, 126.8, 126.1, 125.1, 116.6, 116.5, 100.2, 100.1, 87.7, 86.8, 49.3, 48.2. **ESI-MS** calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, 282.09 found 281.63.

(E)-N-benzyl-3-(1-benzyl-1H-pyrrol-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide



Enallene **15o** was prepared following general procedure **GP-1** from the corresponding enyne (212.6 mg, 0.6 mmol). Orange oil (98.2 mg, 46% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, Acetone-*d6*) δ 7.72 – 7.64 (m, 2H RotA, 2H RotB), 7.34 – 7.26 (m, 9H RotA, 9H RotB), 7.13 – 7.06 (m, 3H RotA, 3H RotB), 7.00 – 6.94 (m, 1H RotA), 6.75 – 6.67 (m, 1H RotA, 2H RotB), 6.25 – 6.19 (m, 1H RotA, 1H RotB), 5.40 – 5.31 (m, 4H RotA, 4H RotB), 4.83 – 4.77 (m, *J* = 8.6 Hz, 2H RotA, 2H RotB). **^{13}C NMR** (101 MHz, Acetone-*d6*) δ 202.7, 202.1, 164.5, 138.5, 138.1, 132.0, 129.5, 128.7, 128.5, 128.3, 127.6, 127.4, 127.1, 126.7, 126.6, 126.3, 121.4, 111.9, 111.8, 109.3, 100.4, 99.6, 86.8, 85.9, 50.2, 49.7, 48.3, 47.3. **ESI-MS** calcd for $C_{24}H_{23}N_2O$ $[M+H]^+$, 355.18 found 355.10. *(Partial decomposition was observed during the acquisition of NMR spectra).*

(E)-N-benzyl-3-(1-methyl-1H-indol-2-yl)-N-(propa-1,2-dien-1-yl)acrylamide

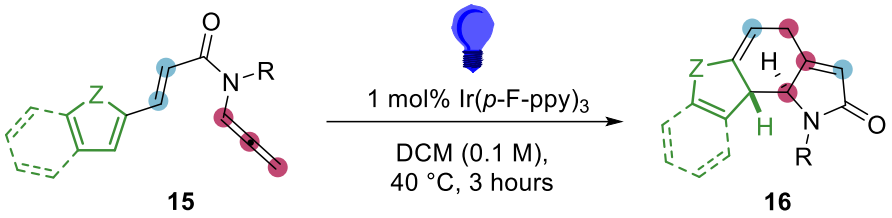


Enallene **15p** was prepared following general procedure **GP-1** from the corresponding enyne (164.2 mg, 0.5 mmol). Orange solid (79.4 mg, 48% yield). Two rotamers are observed due to the dynamic rotation of the amide. **^{1}H NMR** (400 MHz, Acetone-*d6*) δ 7.93 – 7.81 (m, *J* = 19.8, 10.0 Hz, 1H RotA, 2H RotB), 7.58 – 6.96 (m, 12H RotA, 11H RotB), 5.39 (d, *J* = 6.4 Hz, 2H RotA, 2H RotB), 4.91 (d, *J* = 43.3 Hz, 2H RotA, 2H RotB), 3.89 (s, 3H RotB), 3.80 (s, 3H RotA). **^{13}C NMR** (101 MHz, Acetone-*d6*) δ 207.9, 207.4, 169.2, 144.3, 143.4, 140.9, 137.2, 136.9, 133.9, 133.8, 133.4, 133.0, 133.0, 132.8, 132.5, 132.4, 131.5, 128.3, 126.1, 125.3, 122.6, 122.4, 115.1,

114.1, 108.2, 105.6, 104.9, 92.3, 91.3, 53.7, 52.7, 34.5. **ESI-MS** calcd for $C_{22}H_{21}N_2O$ $[M+H]^+$, 329.17 found 329.60. *(Partial decomposition was observed during the acquisition of NMR spectra).*

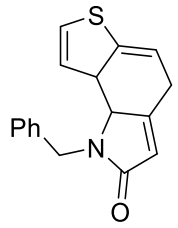
Synthesis and characterization of products

Photocatalytic reactions [GP-2]



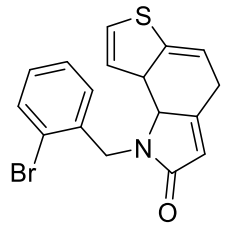
To a vial charged with substrate **15** (1 equiv., 0.2 mmol) and Ir(p-F-ppy)$_3$ (1 mol%), dry DCM (0.1 M) was added through a syringe. The solution was transferred into an NMR tube capped with a rubber septum and it was placed in an oil bath kept at 40 °C and irradiated with LED stripes for 3 hours. Conversion was monitored by TLC and the mixture was then concentrated in vacuo. The residue was purified by chromatography on silica gel; the catalyst was removed using toluene as eluent prior to the separation of desired products (n-hexane/EtOAc, under gradient).

1-benzyl-1,4,8a,8b-tetrahydro-2H-thieno[2,3-g]indol-2-one



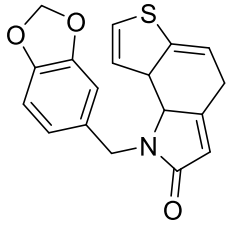
Product **16a** was prepared following general procedure **GP-2** from the corresponding enallene (56.7 mg, 0.2 mmol; 392.1 mg, 1.39 mmol). White solid (35.7 mg, 63% yield; 205.9 mg, 52%, 9 hours of irradiation). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.19 (m, 5H), 6.33 (dd, *J* = 6.4, 2.6 Hz, 1H), 6.07 (s, 1H), 5.76 (dd, *J* = 6.4, 1.4 Hz, 1H), 5.67 (q, *J* = 3.4 Hz, 1H), 5.15 (d, *J* = 15.8 Hz, 1H), 4.48 (d, *J* = 15.8 Hz, 1H), 3.91 (d, *J* = 10.3 Hz, 1H), 3.63 – 3.55 (m, 1H), 3.46 – 3.27 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.3, 157.3, 137.6, 137.5, 128.9, 127.5, 127.4, 127.3, 121.2, 121.1, 115.6, 62.4, 56.1, 45.4, 28.8. **ESI-HRMS** calcd for $C_{17}H_{16}NOS$ $[M+H]^+$, 282.0948 found 282.0955.

1-(2-bromobenzyl)-1,4,8a,8b-tetrahydro-2H-thieno[2,3-g]indol-2-one



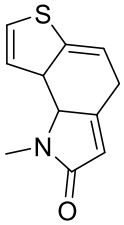
Product **16b** was prepared following general procedure **GP-2** from the corresponding enallene (71.6 mg, 0.2 mmol). White solid (39.4 mg, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.32 – 7.24 (m, 1H), 7.19 – 7.08 (m, 2H), 6.29 (dd, *J* = 6.4, 2.6 Hz, 1H), 6.11 (s, 1H), 5.70 (q, *J* = 3.5 Hz, 1H), 5.58 – 5.53 (m, 1H), 4.93 (d, *J* = 17.0 Hz, 1H), 4.81 (d, *J* = 17.0 Hz, 1H), 4.02 (d, *J* = 10.3 Hz, 1H), 3.64 – 3.56 (m, 1H), 3.49 – 3.33 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4, 157.7, 137.6, 136.3, 133.0, 128.9, 128.2, 127.9, 127.4, 122.3, 121.1, 115.5, 63.6, 56.0, 45.8, 28.8. **ESI-HRMS** calcd for $C_{17}H_{15}BrNOS$ $[M+H]^+$, 360.0053 found 360.0051.

1-(benzo[d][1,3]dioxol-5-ylmethyl)-1,4,8a,8b-tetrahydro-2H-thieno[2,3-g]indol-2-one



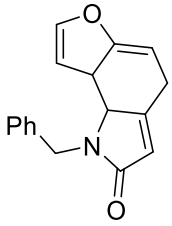
Product **16c** was prepared following general procedure **GP-2** from the corresponding enallene (65.7 mg, 0.2 mmol). White solid (33.3 mg, 51% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 6.74 (d, *J* = 7.8 Hz, 1H), 6.69 – 6.64 (m, 2H), 6.33 (dd, *J* = 6.3, 2.6 Hz, 1H), 6.02 (s, 1H), 5.93 (s, 2H), 5.77 (dd, *J* = 6.4, 1.4 Hz, 1H), 5.65 (q, *J* = 3.9 Hz, 1H), 5.03 (d, *J* = 15.6 Hz, 1H), 4.34 (d, *J* = 15.6 Hz, 1H), 3.88 (d, *J* = 10.3 Hz, 1H), 3.58 – 3.52 (m, 1H), 3.38 (dt, *J* = 22.1, 4.1 Hz, 1H), 3.30 (dq, *J* = 22.0, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.3, 157.4, 148.2, 147.0, 137.6, 131.3, 127.4, 121.2, 121.1, 120.6, 115.6, 108.4, 107.9, 101.1, 62.3, 56.1, 45.2, 28.7. **ESI-HRMS** calcd for $C_{18}H_{16}NO_3S$ $[M+H]^+$, 326.0846 found 326.0851.

1-methyl-1,4,8a,8b-tetrahydro-2H-thieno[2,3-g]indol-2-one



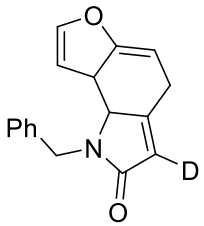
Product **16d** was prepared following general procedure **GP-2** from the corresponding enallene (40.5 mg, 0.2 mmol). White solid (16.9 mg, 42% yield). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 6.58 (dd, *J* = 6.4, 2.6 Hz, 1H), 6.11 – 6.07 (m, 1H), 5.90 (q, *J* = 1.6 Hz, 1H), 5.76 – 5.72 (m, 1H), 3.94 (d, *J* = 10.3 Hz, 1H), 3.56 – 3.48 (m, 1H), 3.41 – 3.36 (m, 2H), 3.08 (s, 3H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 170.7, 156.7, 137.3, 126.8, 121.8, 120.8, 115.9, 64.3, 56.5, 28.14, 28.06. **ESI-HRMS** calcd for $C_{11}H_{12}NOS$ $[M+H]^+$, 206.0635 found 206.0639.

1-benzyl-1,4,8a,8b-tetrahydro-2H-furo[2,3-g]indol-2-one



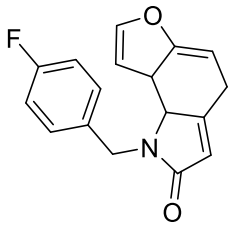
Product **16e** was prepared following general procedure **GP-2** from the corresponding enallene (53.0 mg, 0.2 mmol). White solid (27.6 mg, 52% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.20 (m, 5H), 6.53 – 6.49 (m, 1H), 6.09 – 6.05 (m, 1H), 5.23 – 5.18 (m, 2H), 5.03 (d, *J* = 15.6 Hz, 1H), 4.47 (d, *J* = 15.6 Hz, 1H), 3.85 (d, *J* = 9.4 Hz, 1H), 3.44 – 3.34 (m, 2H), 3.32 – 3.21 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.1, 157.6, 154.7, 147.4, 137.6, 128.8, 127.53, 127.47, 121.5, 103.3, 94.8, 63.6, 47.8, 45.0, 25.2. **ESI-HRMS** calcd for $C_{17}H_{16}NO_2$ $[M+H]^+$, 266.1176 found 266.1170. *(Partial decomposition was observed during the acquisition of NMR spectra).*

1-benzyl-1,4,8a,8b-tetrahydro-2H-furo[2,3-g]indol-2-one-3-d



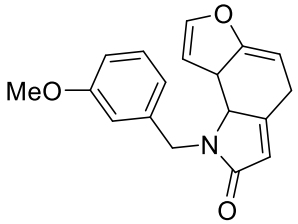
Product **16f** was prepared following general procedure **GP-2** from the corresponding enallene (53.3 mg, 0.2 mmol). White solid (27.2 mg, 51% yield). **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.34 – 7.17 (m, 5H), 6.49 – 6.46 (m, 1H), 6.03 (brs, 1H non-deuterated 2f), 5.19 – 5.15 (m, 2H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.43 (d, *J* = 15.6 Hz, 1H), 3.81 (d, *J* = 9.8 Hz, 1H), 3.39 – 3.31 (m, 2H), 3.27 – 3.19 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.1, 157.6 (non-deuterated 2f), 157.4, 154.7, 147.3, 137.7, 128.8, 127.52, 127.46, 121.5 (non-deuterated 2f), 103.3, 94.8, 63.59 (non-deuterated 2f), 63.56, 47.8, 45.0, 25.22 (non-deuterated 2f), 25.19. **ESI-HRMS** calcd for $C_{17}H_{15}DNO_2$ $[M+H]^+$, 267.1239 found 267.1243. *(Partial decomposition was observed during the acquisition of NMR spectra)*

1-(4-fluorobenzyl)-8a,8b-dihydro-1H-furo[2,3-g]indol-2(4H)-one



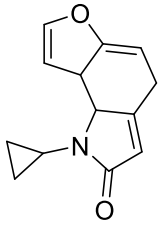
Product **16g** was prepared following general procedure **GP-2** from the corresponding enallene (56.7 mg, 0.2 mmol). Pale yellow solid (29.4 mg, 52% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.24 – 7.21 (m, 2H), 7.05 – 7.00 (m, 2H), 6.53 (dd, *J* = 3.0, 2.1 Hz, 1H), 6.06 (dt, *J* = 2.3, 1.2 Hz, 1H), 5.23 – 5.19 (m, 2H), 4.98 (d, *J* = 15.5 Hz, 1H), 4.43 (d, *J* = 15.6 Hz, 1H), 3.82 (d, *J* = 9.3 Hz, 1H), 3.42 – 3.34 (m, 2H), 3.31 – 3.22 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.1, 163.4, 161.0, 157.7, 154.6, 147.6, 133.5, 133.4, 129.2, 121.5, 115.8, 115.6, 103.2, 94.9, 63.6, 47.7, 44.3, 25.2. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -114.78 (td, *J* = 8.7, 4.4 Hz). **ESI-HRMS** calcd for $C_{17}H_{15}FNO_2$ $[M+H]^+$, 284.1082 found 284.1081.

1-(3-methoxybenzyl)-8a,8b-dihydro-1H-furo[2,3-g]indol-2(4H)-one



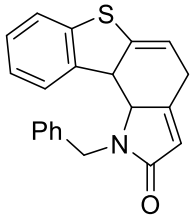
Product **16h** was prepared following general procedure **GP-2** from the corresponding enallene (59.1 mg, 0.2 mmol). White solid (29.3 mg, 50% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.8 Hz, 1H), 6.84 – 6.78 (m, 3H), 6.52 (dd, *J* = 3.0, 2.1 Hz, 1H), 6.06 (dt, *J* = 2.3, 1.2 Hz, 1H), 5.23 – 5.20 (m, 2H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.44 (d, *J* = 15.6 Hz, 1H), 3.86 (dd, *J* = 9.3, 1.4 Hz, 1H), 3.80 (s, 3H), 3.43 – 3.35 (m, 2H), 3.30 – 3.21 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.0, 160.0, 157.6, 154.7, 147.4, 139.3, 129.8, 121.5, 119.7, 113.1, 112.8, 103.4, 94.8, 63.6, 55.3, 47.8, 44.9, 25.2. **ESI-HRMS** calcd for $C_{18}H_{18}NO_3$ $[M+H]^+$, 296.1282 found 296.1288.

1-cyclopropyl-8a,8b-dihydro-1H-furo[2,3-g]indol-2(4H)-one



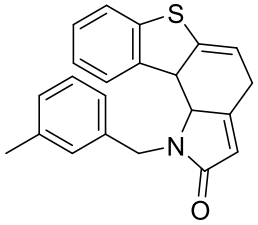
Product **16i** was prepared following general procedure **GP-2** from the corresponding enallene (43.1 mg, 0.2 mmol). Ocher solid (19.3 mg, 44% yield). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 6.76 (dd, *J* = 3.0, 2.3 Hz, 1H), 5.80 (dt, *J* = 2.4, 1.3 Hz, 1H), 5.77 (ddd, *J* = 3.2, 2.2, 1.1 Hz, 1H), 5.20 (dddd, *J* = 4.8, 3.8, 2.8, 1.2 Hz, 1H), 3.90 (dd, *J* = 9.9, 1.3 Hz, 1H), 3.47 – 3.39 (m, 1H), 3.37 – 3.22 (m, 2H), 2.65 – 2.59 (m, 1H), 0.94 – 0.87 (m, 1H), 0.82 – 0.74 (m, 3H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 170.9, 157.0, 155.1, 146.8, 121.5, 104.6, 94.8, 64.3, 48.0, 24.7, 23.0, 7.7, 4.6. **ESI-HRMS** calcd for $C_{13}H_{14}NO_2$ $[M+H]^+$, 216.1020 found 216.1013.

1-benzyl-10b,10c-dihydro-1H-benzo[4,5]thieno[2,3-g]indol-2(4H)-one



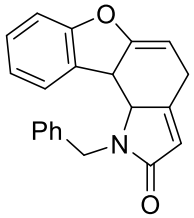
Product **16j** was prepared following general procedure **GP-2** from the corresponding enallene (66.3 mg, 0.2 mmol). Pale brown solid (42.1 mg, 63% yield). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.51 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.31 – 7.23 (m, 5H), 7.16 – 7.08 (m, 3H), 6.11 (dt, *J* = 2.2, 1.1 Hz, 1H), 5.83 (dt, *J* = 5.0, 3.1 Hz, 1H), 5.31 (d, *J* = 15.9 Hz, 1H), 4.59 (d, *J* = 15.9 Hz, 1H), 4.23 – 4.18 (m, 2H), 3.56 – 3.49 (m, 1H), 3.44 – 3.35 (m, 1H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 173.9, 160.2, 139.9, 138.0, 136.9, 136.8, 128.7, 128.6, 127.3, 127.1, 126.4, 124.6, 121.9, 120.8, 115.8, 63.5, 56.0, 47.0. **ESI-HRMS** calcd for $C_{21}H_{18}NOS$ $[M+H]^+$, 332.1104 found 332.1102.

1-(3-methylbenzyl)-1,4,10b,10c-tetrahydro-2H-benzo[4,5]thieno[2,3-g]indol-2-one



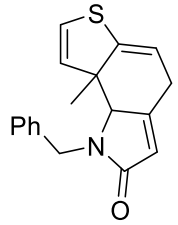
Product **16k** was prepared following general procedure **GP-2** from the corresponding enallene (45.6 mg, 0.13 mmol). White solid (20.3 mg, 45% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.7 Hz, 1H), 7.30 – 7.20 (m, 2H), 7.18 – 7.10 (m, 2H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.86 – 6.79 (m, 2H), 6.13 (s, 1H), 5.76 – 5.73 (m, 1H), 5.40 (d, *J* = 15.5 Hz, 1H), 4.47 (d, *J* = 15.6 Hz, 1H), 4.16 – 4.11 (m, 2H), 3.54 – 3.45 (m, 1H), 3.39 – 3.29 (m, 1H), 2.28 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.9, 160.2, 140.0, 138.5, 137.6, 137.1, 136.3, 128.8, 128.6, 128.3, 128.2, 126.5, 124.6, 122.1, 121.3, 114.8, 63.7, 56.0, 47.4, 28.9, 21.4. **ESI-HRMS** calcd for $C_{22}H_{20}NOS$ $[M+H]^+$, 346.1261 found 346.1266.

1-benzyl-10b,10c-dihydro-1H-benzofuro[2,3-g]indol-2(4H)-one



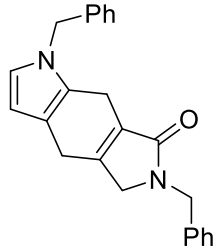
Product **16l** was prepared following general procedure **GP-2** from the corresponding enallene (63.1 mg, 0.2 mmol). Pale orange solid (28.0 mg, 45% yield). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.52 (d, *J* = 7.4 Hz, 1H), 7.33 – 7.21 (m, 6H), 7.00 (td, *J* = 7.6, 1.1 Hz, 1H), 6.95 (dd, *J* = 8.1, 1.0 Hz, 1H), 6.13 (dt, *J* = 2.4, 1.2 Hz, 1H), 5.38 (dt, *J* = 5.6, 2.9 Hz, 1H), 5.26 (d, *J* = 16.1 Hz, 1H), 4.76 (d, *J* = 16.1 Hz, 1H), 4.19 (dd, *J* = 9.9, 1.2 Hz, 1H), 4.13 – 4.09 (m, 1H), 3.50 (dddd, *J* = 21.3, 4.4, 2.0, 0.9 Hz, 1H), 3.39 – 3.31 (m, 1H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 172.8, 159.2, 158.6, 154.3, 138.2, 129.3, 128.6, 127.2, 127.1, 126.5, 125.6, 122.1, 121.5, 109.8, 95.3, 63.2, 48.4, 45.9, 24.8. **ESI-HRMS** calcd for $C_{21}H_{18}NO_2$ $[M+H]^+$, 316.1333 found 316.1337.

1-benzyl-8a-methyl-8a,8b-dihydro-1H-thieno[2,3-g]indol-2(4H)-one



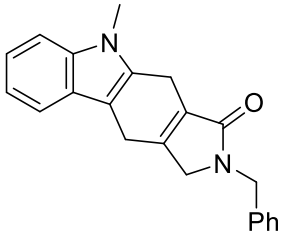
Product **16m** was prepared following general procedure **GP-2** from the corresponding enallene (59.1 mg, 0.2 mmol). Pale yellow solid (42.2 mg, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.21 (m, 5H), 6.27 (d, *J* = 6.3 Hz, 1H), 6.10 (dt, *J* = 2.5, 1.3 Hz, 1H), 5.85 (dd, *J* = 6.4, 1.0 Hz, 1H), 5.64 – 5.62 (m, 1H), 5.29 (d, *J* = 15.6 Hz, 1H), 4.21 (d, *J* = 15.6 Hz, 1H), 4.07 (s, 1H), 3.42 – 3.32 (m, 1H), 3.33 – 3.25 (m 1H), 0.93 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.0, 156.3, 143.3, 137.2, 128.8, 127.7, 127.6, 127.4, 124.6, 121.8, 115.2, 65.0, 55.7, 45.2, 28.1, 18.4. **ESI-HRMS** calcd for $C_{18}H_{18}NOS$ $[M+H]^+$, 296.1104 found 296.1101.

1,6-dibenzyl-4,5,6,8-tetrahydropyrrolo[3,4-f]indol-7(1H)-one



Product **16o** was prepared following general procedure **GP-2** from the corresponding enallene (70.9 mg, 0.2 mmol). White solid (40.4 mg, 57% yield). **^{1}H NMR** (400 MHz, Acetone-*d*6) δ 7.36 – 7.25 (m, 8H), 7.13 – 7.10 (m, 2H), 6.84 (d, *J* = 2.8 Hz, 1H), 5.99 (d, *J* = 2.8 Hz, 1H), 5.18 (s, 2H), 4.62 (s, 2H), 3.88 (t, *J* = 2.2 Hz, 2H), 3.47 (t, *J* = 6.8 Hz, 2H), 3.27 – 3.20 (m, 2H). **^{13}C NMR** (101 MHz, Acetone-*d*6) δ 170.3, 149.6, 139.1, 138.5, 128.6, 128.4, 127.8, 127.1, 126.6, 124.4, 121.4, 113.9, 105.7, 52.0, 49.9, 45.3, 24.5, 19.6. **ESI-HRMS** calcd for $C_{24}H_{23}N_2O$ $[M+H]^+$, 355.1805 found 355.1804.

2-benzyl-5-methyl-1,2,5,10-tetrahydropyrrolo[3,4-b]carbazol-3(4H)-one



Product **16p** was prepared following general procedure **GP-2** from the corresponding enallene (49.3 mg, 0.15 mmol). White solid (36.3 mg, 74% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.8 Hz, 1H), 7.40 – 7.22 (m, 7H), 7.15 – 7.11 (m, 1H), 4.74 (s, 2H), 3.92 (d, *J* = 8.4 Hz, 2H), 3.74 (s, 3H), 3.67 (s, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.1, 149.1, 137.5, 132.8, 128.84, 128.80, 128.1, 127.6, 126.1, 121.3, 119.1, 117.8, 108.9, 105.0, 52.6, 46.2, 29.5, 23.4, 20.4. **ESI-HRMS** calcd for $C_{22}H_{21}N_2O$ $[M+H]^+$, 329.1649 found 329.1646

Comprehensive Table in AU

M06/def2-TZVP CPCM = DCM	H (hartrees)	S (cal/K*mol)	imag. freq. (1/cm)
1	-953.497142	124.563	
I (triplet on allene)	-953.430997	125.497	
I' (triplet on alkene)	-953.422908	127.675	
TS (I-II)	-953.428770	119.348	-231.0468
II	-953.492264	121.253	
^{1} III	-953.510536	113.431	
^{3} III	-953.429974	117.888	
^{1} TS (III-IV)	-953.477120	112.755	-558.0511
^{3} TS (III-IV)	-953.413271	116.322	-840.5435
^{1} IV	-953.504603	120.285	
^{3} IV	-953.505037	123.948	
TS (IV-V)	-953.451373	112.324	-530.2581
V	-953.459504	110.672	
TS (IV-2)	-953.487623	108.639	-78.5296
2	-953.544601	107.556	

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