C-H Functionalization Hot Paper

How to cite: *Angew. Chem. Int. Ed.* **2023**, *62*, e202218928
International Edition: doi.org/10.1002/anie.202218928
German Edition: doi.org/10.1002/ange.202218928

Closing the Cycle as It Begins: Synthesis of *ortho*-Iodobiaryls via Catellani Reaction

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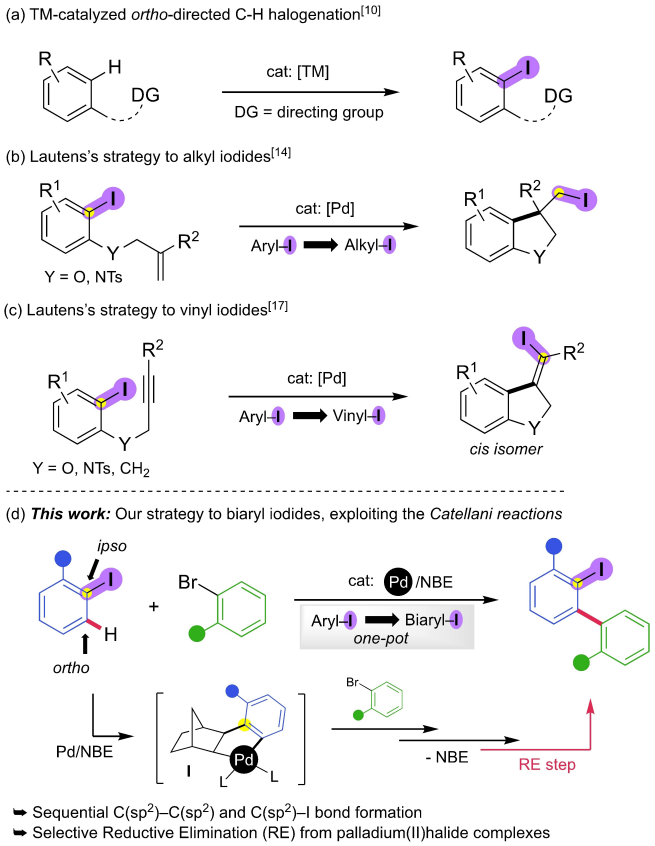
Dedicated to Professor Marta Catellani on the occasion of her 78th birthday

Abstract: Despite the advances in the field of carbon-halogen bond formation, the straightforward catalytic access to selectively functionalized iodoaryls remains a challenge. Here, we report a one-pot synthesis of *ortho*-iodobiaryls from aryl iodides and bromides by palladium/norbornene catalysis. This new example of Catellani reaction features the initial cleavage of a C(sp^2)–I bond, followed by the key formation of a palladacycle through *ortho* C–H activation, the oxidative addition of an aryl bromide and the ultimate restoration of the C(sp^2)–I bond. A large variety of valuable *o*-iodobiaryls has been synthesized in satisfactory to good yields and their derivatization have been described too. Beyond the synthetic utility of this transformation, a DFT study provides insights on the mechanism of the key reductive elimination step, which is driven by an original transmetallation between palladium(II)-halides complexes.

Introduction

Organic iodides are ubiquitous reagents for pivotal transformations that include transition-metal catalyzed cross-couplings (e.g. Mizoroki-Heck, Suzuki–Miyaura, Buchwald–Hartwig),[1] halogen exchange reactions,[2] radical pathways[3] and nucleophilic substitutions.[4] Furthermore, iodide-containing compounds are attractive targets in materials science,[5] molecular recognition[6] and medicinal chemistry.[7] Compared to analogous bromides and chlorides, aryl iodides represent privileged starting substrates due to their higher reactivity in many elegant catalytic sequences.[8] Traditional approaches to aryl iodides (e.g. Sandmeyer reaction, aromatic Finkelstein reaction) although largely in use, suffer from limited regioselectivity, low functional group tolerance and the production of stoichiometric co-products.[9] The widely investigated *ortho* C–H halogenation strategy (Scheme 1a) represents an atom- and step-economical alternative, further enhanced by high functional group tolerance and improved chemo-, regio- and stereoselectivity.[2,10] However, the increasing molecular complexity of synthetic targets[11] and the value of some halogenated compounds that are hardly accessible[12] have prompted synthetic chemists to further improve protocols in terms of atom and step



Scheme 1. Transition metal-catalyzed access to organic iodides: a) TM-catalyzed *ortho*-C–H halogenation; b) Lautens's strategy to alkyl iodides from aryl iodides; c) Lautens's strategy to vinyl iodides from aryl iodides; d) Strategy based on the *Catellani reactions* to access biaryl iodides from aryl iodides and bromides.

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economy, sustainability and molecular sophistication achieved in a single-pot reaction.[13] A breakthrough in the field has been achieved by Lautens,[14] who has developed a palladium-catalyzed carboiodination of alkenes with aryl iodides, that involves the formation of a alkyl C(sp^3)–I bond starting from an aryl C(sp^2)–I one (Scheme 1b). The presence of a proper R^2 group in *beta* precludes the common Heck pathway in favor of a C–I reductive elimination step. A wide variety of iodinated alkyl heterocycles has been synthesized following this innovative strategy with both palladium[15] and nickel[16] catalytic systems. Taking advantage of the steric effect between ligand and substrate, Lautens's group developed an unprecedented intramolecular palladium-catalyzed alkyne carbohalogenation sequence that forms alkenyl C(sp^2)–I bonds (Scheme 1c).[17] The intermolecular version starting from aryl iodides and internal alkynes has been later disclosed by Kurahashi and Matsubara[18] exploiting radical nickel(III) species and Morandi[19] under palladium catalysis.

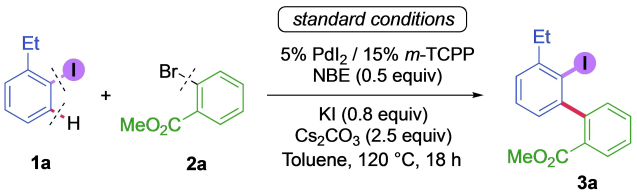
A different conceptual approach could be conceived starting from an easily accessible aryl iodide, which, after a stage of *ortho* C–H arylation, may give rise to a new aryl C(sp^2)–I bond at the *ipso* position of the initial reagent (Scheme 1d). Since their discovery, Catellani reactions have become a widespread popular strategy for the multi functionalization of aromatic compounds.[20] In one specific aspect, Catellani reactions can give access to a large variety of biaryl-containing compounds starting from differently substituted aryl halides (or aryl boronic acid derivatives) and a long series of terminating agents, including olefins, alkynes and heterocycles.[21] Taking advantage of the alkyl aromatic palladacycle **I**, originated from the reaction of an *ortho*-substituted aryl iodide, Pd^0 and norbornene, the selective formation of a biaryl unit can be achieved. The presence of an *ortho* substituent on the aryl iodide is essential to generate the Pd^{IV} intermediate that directs the sequence to the selective formation of a C(sp^2)–C(sp^2) bond.[22a] Otherwise, transmetallation between Pd^{II} species could take place,[22c] and the C(sp^2)–C(sp^3) coupling becomes a competitive pathway. In this work, for the first time, we have tackled the highly demanding task of directing the cascade toward the selective formation of a C(sp^2)–I bond as termination step. To implement this, some inherent challenges have been faced. For instance, while the starting C(sp^2)–I must be reactive, the newly installed C(sp^2)–I bond needs to remain unaffected under the reaction conditions. At this point, we assume that the relative steric hindrance of the iodinated species has to play a crucial role in preventing the formation of polyaryl byproducts. Furthermore, the reductive elimination (RE) that forms the envisaged C-(sp^2)–I bond has to take place under the same reaction conditions that are supposed to promote the oxidative addition (OA) of the starting aryl iodide. Likely, the choice of the ligand is essential to struck a clean balance between these two competitive elementary steps.

Herein, we report the first palladium/norbornene-catalyzed one-pot synthesis of *ortho*-iodo biaryl compounds starting from readily available *o*-substituted aryl iodides and bromides (Scheme 1d, *this work*). The original termination can be triggered thanks to a suitable transmetallation step between Pd^{II}-halide intermediates, which marks a remarkable come-back for this reactivity in Catellani-type reactions.[20,22]

Results and Discussion

At the outset, we investigated the optimal conditions for the Catellani-type cross-coupling of 1-ethyl-2-iodobenzene **1a** and methyl 2-bromobenzoate **2a**, selected as model substrates (Table 1). An extensive investigation of the reaction parameters (Table S1, Supporting Information) revealed that the expected biaryl product **3a** was obtained in synthetically useful yield (Table 1, entry 1, 61 %) when PdI_2 (5 mol %), tris-(3-chlorophenyl)phosphine (*m*-TCPP, 15 mol %) and norbornene (NBE, 0.5 equiv)[23] were used as a catalytic system, in the presence of KI (0.8 equiv) as additional source of iodide anions and Cs_2CO_3 as base (2.5 equiv).[24] The presence of an almost stoichiometric amount of KI appears to be beneficial for the reaction (entry 2) while an excess of iodide anions reduces the rate of the process. Among all the tested palladium precursors, only $PdCl_2$ approaches the PdI_2 performance level, highlighting the relevance of the palladium counteranions in this transformation (entries 3–5). An even more important role in the catalyst efficiency is played by the ligand. Product **3a** was not detected when the reaction was performed in the absence of ligands (entry 6). The investigation on different type of phosphines (Table S1, Supporting Information)

Table 1: Screening of optimal reaction conditions.[a]



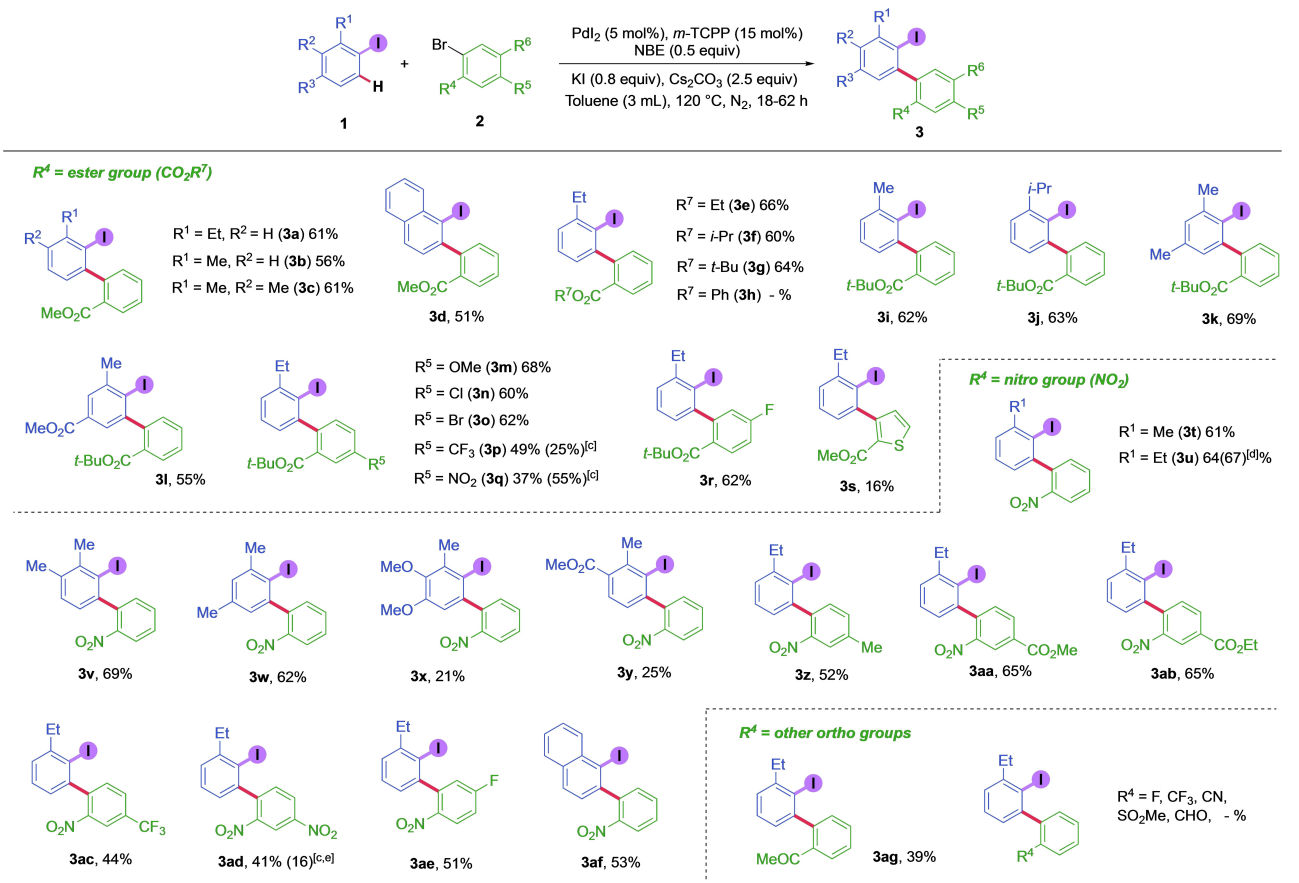
Entry	Variation from standard conditions	Yield [%][b]
1	none	61
2	without KI	40
3	$PdCl_2$ instead of PdI_2	54
4	$Pd(OAc)_2$ instead of PdI_2	21
5	$Pd(TFA)_2$ instead of PdI_2	20
6	without *m*-TCPP	–
7	*p*-TCPP instead of *m*-TCPP	16
8	*p*-TFPP instead of *m*-TCPP	18
9	TPP instead of *m*-TCPP	3
10	TFP instead of *m*-TCPP	15
11	KOAc instead of Cs_2CO_3	25

[a] Standard conditions: 2-iodoethyl benzene **1a** (0.24 mmol, 1.5 equiv), methyl 2-bromobenzoate **2a** (0.16 mmol, 1.0 equiv), PdI_2 (5 mol %), TCPP (15 mol %), NBE (0.5 equiv), KI (0.8 equiv), Cs_2CO_3 (2.5 equiv), and Toluene (3 mL) at 120 °C under N_2 atmosphere for 18 h. [b] Isolated yields. TFA = trifluoroacetate; *m*-TCPP = tris (3-chlorophenyl)phosphine; *p*-TCPP = tris (4-chlorophenyl)phosphine; *p*-TFPP = tris (4-fluorophenyl)phosphine; TPP = triphenylphosphine; TFP = tri(2-furyl)phosphine.

allowed to identify *m*-TCPP as the ligand of choice (entry 1). Changing the nature of the ligand was found to be detrimental to the reaction outcome. For example, *p*-TCPP and *p*-TFPP gave only 16 and 18 % of **3a**, respectively (entries 7 and 8), and TPP was highly inefficient under the reported conditions (entry 9). An electron rich phosphine with reduced cone angle, such as TFP, gave only poor results (entry 10). A series of inorganic bases was tested, and Cs_2CO_3 turned out to be the best one, with KOAc much less efficient (entry 11). Lastly, the solvent was also a crucial variant, since only anisole and toluene (Table S1, Supporting Information), allowed to efficiently achieve **3a**.

With the optimized reaction conditions in hand, the scope of the reaction was examined (Table 2). We anticipate that, as expected, the presence of an *ortho* substituent on the starting aryl iodide is essential for the formation of a biaryl unit.[22] However, the present transformation relies also on a second "*ortho effect*" on the bromide coupling partner. The presence of an ester or a nitro group as R^4 at the *ortho* position of the aryl bromide was found to be crucial for the formation of the target compound. Variously substituted aryl iodides, including 1-iodonaphtalene, were successfully coupled with the commercially available methyl 2-bromobenzoate leading to the corresponding biaryl iodides in satisfactory yields (**3a–d**). Similar good results were obtained starting from more hindered ester moieties, such as CO_2Et, CO_2i-Pr and CO_2t-Bu (**3e–g**), while phenyl 2-bromobenzoate was unreactive under these conditions. To our delight, a wide number of electron donating and electron-withdrawing functionalities (OMe, Me, CO_2Me, Cl, Br, F, CF_3, NO_2) were well tolerated affording the desired products in satisfactory to good yields (**3i–r**). Biaryl **3s**, featuring the thiophene ring, was obtained albeit with a low yield (16 %). 2-Bromo nitrobenzene was also a viable coupling partner in this cascade reaction because it provided the biaryl iodide scaffold with good yields (**3t–w**) together with aryl iodides bearing alkyl substituents in various positions. However, additional methoxy and methyl ester functional groups on the aryl iodide were less tolerated (**3x**, R^2, R^3 = OMe and **3y**, R^2 = CO_2Me). This is likely due to a reactivity mismatch between the aryl iodide and the bromide, showing that a good balance between the electronic properties of the two coupling partners is the key for a satisfactory reaction outcome. A series of R^5 groups on the 2-nitro substituted arylbromide **2**, such as Me, CO_2Me, CO_2Et and CF_3, were well tolerated under the optimal

Table 2: Scope of aryl iodides and bromides.[a,b]



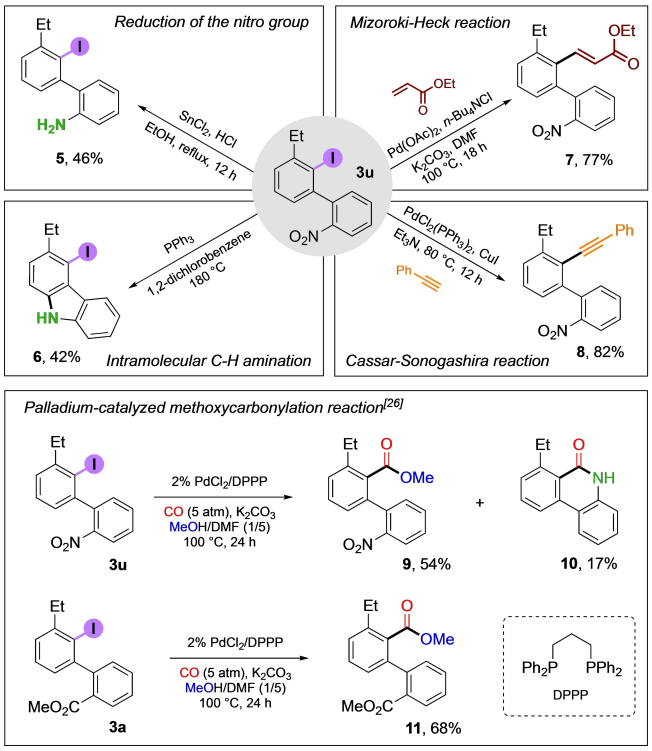
[a] Reaction conditions: **1** (0.24 mmol, 1.5 equiv), **2** (0.16 mmol, 1.0 equiv), PdI_2 (5 mol %), TCPP (15 mol %), NBE (0.5 equiv), KI (0.8 equiv), Cs_2CO_3 (2.5 equiv), and Toluene (3 mL) at 120 °C under N_2 atmosphere for 18–62 h. [b] Isolated yields. [c] Starting material **2** recovered. [d] Gram scale synthesis. [e] From 2,4-dinitrochlorobenzene as starting material.

reaction conditions (**3z**–**3ac**). Notably, product **3ad**, displaying two nitro groups on the same aromatic ring, was obtained coupling 1-ethyl-2-iodobenzene **1a** with an activated aryl chloride. The extensive screening of several other potentially coordinating groups in *ortho* on the aryl bromide allowed to identify another useful substituent, the COMe group, which exhibits some sort of compatibility under the optimized conditions (**3ag**).

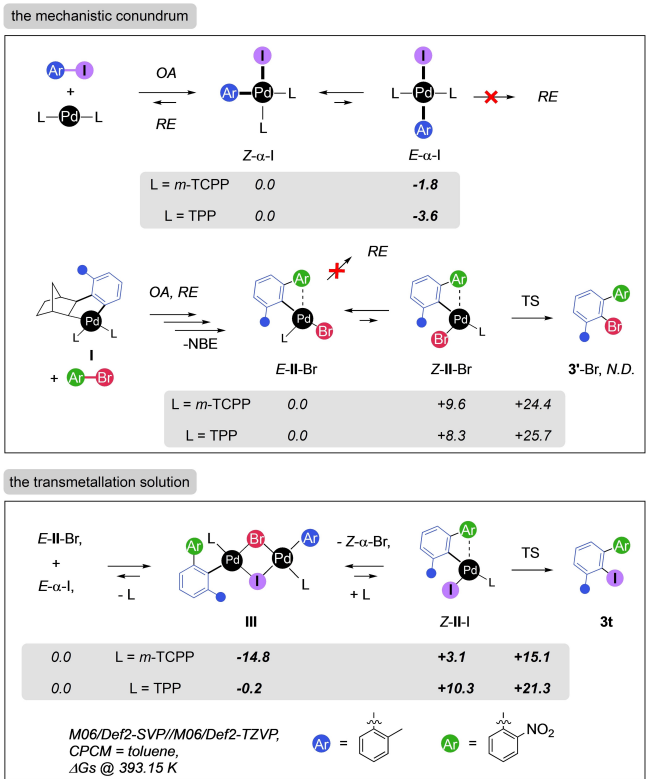
The present methodology offers a straightforward synthesis of biaryl iodides **3** which can be valuable building blocks for further derivatization reactions, as depicted in Scheme 2. Selectively iodinated 2-aminobiaryl and carbazole derivatives **5** and **6** have been synthesized in moderate yields using standard procedures,[23] respectively by reduction and intramolecular C–H amination of **3u**. We consider these results notable, as no specific optimization study has been carried out for these transformations, and the products **5** and **6** are difficult to access with alternative step-economical synthetic protocols. Under typical reaction conditions,[25] Mizoroki-Heck and Cassar-Sonogashira reactions have been performed starting from **3u** with ethyl acrylate and phenylacetylene, respectively, achieving high yields of the corresponding coupling products **7** and **8** (Scheme 2). Furthermore, a palladium-catalyzed alkoxycarbonylation protocol,[26] featuring the bidentate ligand DPPP (1,3-Bis(diphenylphosphino)propane), has been successfully applied to **3u** and **3a**, leading to the corresponding methoxycarbonylated compounds **9** and **11** that are not typically accessible through the Catellani reactions.

Present sequence is the first example of a Catellani reaction terminated by C-halogen bond formation. DFT modeling was carried out to rationalize the mechanistic issues of this original reactivity (Scheme 3).

The most stable isomer of Ar–Pd^{II}-X species with ancillary phosphines that have relatively limited steric demands is the *trans*-one.[27] However, the C–X forming reductive elimination (RE) from Pd^{II} complexes occurs if coupling partners are in a *cis*-arrangement.[28] Biaryl-Pd^{II}-X intermediates of Catellani couplings invariably feature the more thermodynamically stable *trans*-isomer, hindering a straightforward RE.[20–22] Its isomerization via associative mechanism is disfavored by entropic factors, especially for reactions performed at 120 °C. Similarly, the dissociation of the halide seems unlikely because the so-formed cationic complex would be poorly stabilized by the apolar solvent (Table 1). The solution of these conundrums comes from the involvement of a key transmetallation step. This concept has been put forward to in the past,[22c] but was later proved to be less favorable than the competing Pd^{IV} manifold.[21,22a,b] Herein, we observed that the concept is nonetheless highly relevant, being at the origin of present cascade. The halide bridged Pd^{II} dimer **III** is indeed in equilibrium with the two corresponding monomers. The dimer is reluctant to undergo a RE step,[29] and could revert back to the two starting complexes. However, the most energetically favored route involves the formation of the two halide-scrambled monomers, which paves the way for a convenient C(sp^2)–I RE step thanks to the newly established *cis*- arrangement between reacting partners. This rationale is consistent with the positive effect on the yield of **3** observed using a molar excess of the Ar–I partner, which would serve to keep in



Scheme 2. Examples of derivatization of the biaryl iodides **3u** and **3a**.



Scheme 3. Proposed mechanistic rationale.

solution a relatively steady concentration of the corresponding Ar–Pd^{II}–I intermediate. The proposed rationale is furthermore coherent with the experimentally observed difference between TPP and *m*-TCPP ligands. The calculated pathway using the former is indeed much less favorable. The *E*- isomers of α- and **II**- Pd^{II}–I intermediates are significantly more stable than their *Z*- peers. This could be due to a lower *trans*- influence coupled with a higher back-donating acceptor character of the chlorinated phosphine. These features would play a stabilizing effect when the ligand is *trans*- to the strongly donating Ar group. The relatively diminished donating properties of *m*-TCPP compared to TPP are likely convenient to favor the dissociation of one L fragment from Pd^{II} species, which is required to form the transmetallation intermediate **III**. Moreover, as a result of these effects on the energies of Pd^{II} complexes, the intermediate **III** is more likely to fragment into the desired *Z*-**II–I** complex rather than revert back to the *E*- monomers in the presence of *m*-TCPP. Similarly, the calculated C–I RE barriers show that the process is more favorable with the less electron rich phosphine (additional computational results and details in Supporting Information).

Conclusion

In conclusion, we have reported the first example of formal *ortho* C–H arylation of *ortho*-substituted aryl iodides by palladium and norbornene cooperative catalysis (Catellani reactions). The C–I bond is cleaved and reinstalled at the same position of the original arene (*ipso* position), with formation of richly decorated *ortho*-iodobiaryls. A transmetallation pathway is likely at work in the reductive elimination step to the new formed C–I bond.

Acknowledgements

This work was supported by MSCA-IF "METACYL" (grant No. 894026) and UniPR (Grant PHOTO-CO-PY). This work has benefited from the equipment and framework of the COMP-HUB Initiative, funded by the "Departments of Excellence" program of the Italian Ministry for Education, University and Research (MIUR, 2018–2022). We thank CIM (Interdepartmental Measurements Centre) for NMR facilities. Use of modeling facilities was provided by the HPC center of UniPR. Open Access funding provided by Università degli Studi di Parma within the CRUI-CARE Agreement.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the Supporting Information of this article.

Keywords: Aryl Iodides · C–H Arylation · Catellani Reactions · Palladium · Reductive Elimination

[1] a) A. Biffis, P. Centomo, A. Del Zotto, M. Zecca, *Chem. Rev.* **2018**, *118*, 2249–2295; b) *Metal-Catalyzed Cross-Coupling Reactions and More* (Eds.: A. de Meijere, S. Bräse, M. Oestreich), Wiley-VCH, Weinheim, **2014**.
[2] a) A. D. Marchese, T. Adrianov, M. Lautens, *Angew. Chem. Int. Ed.* **2021**, *60*, 16750–16762; *Angew. Chem.* **2021**, *133*, 16888–16900; b) D. A. Petrone, J. Ye, M. Lautens, *Chem. Rev.* **2016**, *116*, 8003–8104.
[3] a) N. Kvasovs, V. Gevorgyan, *Chem. Soc. Rev.* **2021**, *50*, 2244–2259; b) I. Ghosh, L. Marzo, A. Das, R. Shaikh, B. König, *Acc. Chem. Res.* **2016**, *49*, 1566–1577.
[4] M. Smith, J. March, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, Wiley, Hoboken, **2020**.
[5] M. L. Tang, Z. Bao, *Chem. Mater.* **2011**, *23*, 446–455.
[6] T. M. Beale, M. G. Chudzinski, M. G. Sarwar, M. S. Taylor, *Chem. Soc. Rev.* **2013**, *42*, 1667–1680.
[7] a) R. Wilcken, M. O. Zimmermann, A. Lange, A. C. Joerger, F. M. Boeckler, *J. Med. Chem.* **2013**, *56*, 1363–1388; b) S. Boldon, I. Stenhagen, J. Moore, S. Luthra, V. Gouverneur, *Synthesis* **2011**, *2011*, 3929–3953.
[8] a) E. S. Isbrandt, A. Nasim, K. Zhao, S. G. Newman, *J. Am. Chem. Soc.* **2021**, *143*, 14646–14656; b) S. Cuesta-Galisteo, J. Schörgenhumer, X. Wei, E. Merino, C. Nevado, *Angew. Chem. Int. Ed.* **2021**, *60*, 1605–1609; *Angew. Chem.* **2021**, *133*, 1629–1633; c) M. De La Higuera Macias, B. A. Arndtsen, *J. Am. Chem. Soc.* **2018**, *140*, 10140–10144.
[9] a) P. B. D. De la Mare, *Electrophilic Halogenation: Reaction Pathways Involving Attack by Electrophilic Halogens on Unsaturated Compounds*, Cambridge University Press, Cambridge, **1976**; b) F. Mo, D. Qiu, Y. Zhang, J. Wang, *Acc. Chem. Res.* **2018**, *51*, 496–506; c) G. Evano, A. Nitelet, P. Thilmany, D. F. Dewez, *Front. Chem.* **2018**, *6*, 114.
[10] D. J. Jones, M. Lautens, G. P. McGlacken, *Nat. Catal.* **2019**, *2*, 843–851.
[11] S. Caille, S. Cui, M. M. Faul, S. M. Mennen, J. S. Tedrow, S. D. Walker, *J. Org. Chem.* **2019**, *84*, 4583–4603. K. C. Nicolaou, C. R. H. Hale, C. Nilewski, H. A. Ioannidou, *Chem. Soc. Rev.* **2012**, *41*, 5185.
[12] a) M. Hernandes, S. M. Cavalcanti, D. R. Moreira, W. de Azevedo Junior, A. C. Leite, *Curr. Drug Targets* **2010**, *11*, 303–314; b) "Halogenated Heterocycles as Pharmaceuticals": T. Kosjek, E. Heath in *Halogenated Heterocycles: Synthesis, Application and Environment* (Ed.: J. Iskra), Springer, New York, **2012**.
[13] S. Kar, H. Sanderson, K. Roy, E. Benfenati, J. Leszczynski, *Chem. Rev.* **2022**, *122*, 3637–3710.
[14] S. G. Newman, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 1778–1780.
[15] For selected palladium-catalyzed sequences to iodoalkyl compounds, see: a) X. Chen, J. Zhao, M. Dong, N. Yang, J. Wang, Y. Zhang, K. Liu, X. Tong, *J. Am. Chem. Soc.* **2021**, *143*, 1924–1931; b) D. A. Petrone, H. Yoon, H. Weinstabl, M. Lautens, *Angew. Chem. Int. Ed.* **2014**, *53*, 7908–7912; *Angew. Chem.* **2014**, *126*, 8042–8046; c) D. A. Petrone, M. Lischka, M. Lautens, *Angew. Chem. Int. Ed.* **2013**, *52*, 10635–10638; *Angew. Chem.* **2013**, *125*, 10829–10832; d) H. Liu, C. Li, D. Qiu, X. Tong, *J. Am. Chem. Soc.* **2011**, *133*, 6187–6193; e) S. G.

Newman, J. K. Howell, N. Nicolaus, M. Lautens, *J. Am. Chem. Soc.* **2011**, *133*, 14916–14919.
[16] For selected nickel-catalyzed reactions to iodoalkyl compounds, see: a) A. D. Marchese, T. Adrianov, M. F. Köllen, B. Mirabi, M. Lautens, *ACS Catal.* **2021**, *11*, 925–931; b) A. D. Marchese, F. Lind, Á. E. Mahon, H. Yoon, M. Lautens, *Angew. Chem. Int. Ed.* **2019**, *58*, 5095–5099; *Angew. Chem.* **2019**, *131*, 5149–5153; c) H. Yoon, A. D. Marchese, M. Lautens, *J. Am. Chem. Soc.* **2018**, *140*, 10950–10954.
[17] C. M. Le, P. J. C. Menzies, D. A. Petrone, M. Lautens, *Angew. Chem. Int. Ed.* **2015**, *54*, 254–257; *Angew. Chem.* **2015**, *127*, 256–259.
[18] T. Takahashi, D. Kuroda, T. Kuwano, Y. Yoshida, T. Kurahashi, S. Matsubara, *Chem. Commun.* **2018**, *54*, 12750–12753.
[19] Y. H. Lee, B. Morandi, *Angew. Chem. Int. Ed.* **2019**, *58*, 6444–6448; *Angew. Chem.* **2019**, *131*, 6510–6515.
[20] a) M. Catellani, F. Frignani, A. Rangoni, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 119–122; *Angew. Chem.* **1997**, *109*, 142–145; b) J. Wang, G. Dong, *Chem. Rev.* **2019**, *119*, 7478–7528; c) N. Della Ca', M. Fontana, E. Motti, M. Catellani, *Acc. Chem. Res.* **2016**, *49*, 1389–1400; d) J. Ye, M. Lautens, *Nat. Chem.* **2015**, *7*, 863–870; e) M. Catellani, E. Motti, N. Della Ca', *Acc. Chem. Res.* **2008**, *41*, 1512–1522.
[21] a) Q. Gao, C. Wu, S. Deng, L. Li, Z.-S. Liu, Y. Hua, J. Ye, C. Liu, H.-G. Cheng, H. Cong, Y. Jiao, Q. Zhou, *J. Am. Chem. Soc.* **2021**, *143*, 7253–7260; b) Z.-S. Liu, Y. Hua, Q. Gao, Y. Ma, H. Tang, Y. Shang, H.-G. Cheng, Q. Zhou, *Nat. Catal.* **2020**, *3*, 727–733; c) P. Wang, S. Chen, Z. Zhou, H.-G. Cheng, Q. Zhou, *Org. Lett.* **2019**, *21*, 3323–3327; d) A. Casnati, M. Fontana, E. Motti, N. Della Ca', *Org. Biomol. Chem.* **2019**, *17*, 6165–6173; e) Q. Zhao, W. C. Fu, F. Y. Kwong, *Angew. Chem. Int. Ed.* **2018**, *57*, 3381–3385; *Angew. Chem.* **2018**, *130*, 3439–3443; f) N. Della Ca', G. Maestri, M. Catellani, *Chem. Eur. J.* **2009**, *15*, 7850–7853; g) F. Faccini, E. Motti, M. Catellani, *J. Am. Chem. Soc.* **2004**, *126*, 78–79.
[22] a) G. Maestri, E. Motti, N. Della Ca', M. Malacria, E. Derat, M. Catellani, *J. Am. Chem. Soc.* **2011**, *133*, 8574–8585; b) M. Catellani, E. Motti, *New J. Chem.* **1998**, *22*, 759–761; c) D. J. Cárdenas, B. Martín-Matute, A. M. Echavarren, *J. Am. Chem. Soc.* **2006**, *128*, 5033–5040.
[23] Substituted norbornenes used in place of norbornene gave less satisfactory results (see Table S1 in Supporting Information for details).
[24] The main byproduct (< 15 %) is 1-ethyl-9*H*-fluoren-9-one **4a**, that can be obtained by intramolecular ring-closure of biarylpalladium intermediate **II**.
[25] See Supporting Information for details.
[26] C. F. J. Barnard, *Org. Process Res. Dev.* **2008**, *12*, 566–574.
[27] E. Galardon, S. Ramdeehul, J. M. Brown, A. Cowley, K. K. Hii, A. Jutand, *Angew. Chem. Int. Ed.* **2002**, *41*, 1760–1763; *Angew. Chem.* **2002**, *114*, 1838–1841.
[28] T. Sperger, C. M. Le, M. Lautens, F. Schoenebeck, *Chem. Sci.* **2017**, *8*, 2914–2922.
[29] F. Barrios-Landeros, B. P. Carrow, J. F. Hartwig, *J. Am. Chem. Soc.* **2009**, *131*, 8141–8154.

Manuscript received: December 22, 2022
Accepted manuscript online: March 8, 2023
Version of record online: March 27, 2023