Journal of Catalysis 459 (2026) 116918

Contents lists available at ScienceDirect

Journal of Catalysis

journal homepage: www.elsevier.com/locate/jcat

Palladium iodide – Catalyzed carbonylative double cyclization of (ω-hydroxyalkynyl)thiophenecarboxamides leading to new thiophene-fused heterocycles

Raffaella Mancuso [a,*], Patrizio Russo [a,1], Haritha Kumari Arram [a], Antonio Palumbo Piccionello [b], Nicola Della Ca' [c], Angela Altomare [d], Bartolo Gabriele [a,*]

[a] Laboratory of Industrial and Synthetic Organic Chemistry (LISOC), Department of Chemistry and Chemical Technologies, University of Calabria, Via Pietro Bucci 12/C, 87036 Arcavacata di Rende CS, Italy
[b] Department of Biological, Chemical and Pharmaceutical Science and Technology-STEBICEF, University of Palermo, Viale delle Scienze Ed.17, 90128 Palermo Italy
[c] SynCat Lab, Department of Chemistry, Life Sciences and Environmental Sustainability, University of Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy
[d] Institute of Crystallography, National Research Council, Via Amendola, 122/O, 70126 Bari, Italy

ARTICLE INFO

Keywords:
Carbonylation
Cyclization
Double cyclization
Fused heterocycles
Heterocycles
Thiophene-fused heterocycles
Palladium

ABSTRACT

The reactivity of (ω-hydroxyalkynyl)thiophenecarboxamides under PdI_2/KI-catalyzed oxidative carbonylation conditions has been studied. Under relatively mild conditions [1–5 mol% PdI_2, 10–50 mol% KI, in a 2:1 (*v*/*v*) HC$(OMe)_3$-MeCN mixture, under 40 bar of a 1:7 mixture CO-air, at 100 °C for 5–8 h], 3-(3-hydroxy-1-ynyl)thiophene-2-carboxamides were smoothly converted into previously unreported (*Z*)-5-imino-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-ones through a carbonylative double cyclization route, involving an initial 6-*endo*-*dig* *O*-cyclization followed by cyclocarbonylation. Under similar conditions, isomeric 4-imino-4,6-dihydro-8*H*-furo[3,4–*b*]thieno[2,3–*d*]pyran-8-ones were obtained from 2-(3-hydroxy-1-ynyl)thiophene-3-carboxamides. The *O*-cyclization – cyclocarbonylation process could be successfully extended to the higher homologues [3-(4-hydroxy-1-ynyl)thiophene-2-carboxamides, and 2-(4-hydroxy-1-ynyl)thiophene-3-carboxamides], with formation of the corresponding (*Z*)-6-imino-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-ones and (*Z*)-4-imino-6,7-dihydro-4*H*,9*H*-pyrano[4,3–*b*]thieno[2,3–*d*]pyran-9-ones, respectively. The structures of six representative products have been confirmed by XRD analysis.

1. Introduction

Polycyclic heterocycles are of primary importance in materials science (for reviews, see references [1,2]) as well as in the pharmaceutical and drug discovery field (for reviews and recent examples, see references [3–12]). Therefore, considerable efforts have been devoted to the development of efficient synthesis strategies for their preparation (for reviews, see reference [13–17]).

A particularly attractive approach to construct functionalized polycyclic heterocycles is based on catalytic one-step double cyclization of suitably functionalized precursors, bearing different functional groups in appropriate position [13–17]. In this field, we have recently reported several carbonylative (for a recent book on carbonylation, see reference [18]; for recent reviews, see reference [19–22]) double cyclization reactions [16] based on the use of our PdI_2/KI catalytic system (for reviews, see references [23–25]) under oxidative conditions (for reviews, see references [26–28]), which have allowed the direct synthesis of a various fused heterocyclic scaffolds (for recent examples, see references [29–34].

Among polycyclic heterocyclic derivatives, thiophene-fused heterocycles play a major role, for their significant applications in the development of new materials with special properties (for reviews, see references [35–37]) and of new bioactive principles [38–41]. For example, in a recent work some thiophene-fused γ-lactams were found to inhibit the SARS-CoV-2 main protease via a reversible covalent acylation mechanism [42]. Consequently, the implementation of synthetic strategies for the production of thiophene-fused heterocyclic derivatives, based, in particular, on cyclization of readily available

* Corresponding authors.
E-mail addresses: raffaella.mancuso@unical.it (R. Mancuso), bartolo.gabriele@unical.it (B. Gabriele).
[1] Co-first author.

https://doi.org/10.1016/j.jcat.2026.116918
Received 6 March 2026; Received in revised form 17 April 2026; Accepted 20 April 2026
Available online 26 April 2026
0021-9517/© 2026 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

precursors under catalytic conditions, is of primary importance in current organic synthesis (see, for example, references [43–45]). Our research group recently reported the synthesis of furothienopyran and pyranothienopyran derivatives by a sequential 6-*endo-dig* *O*-cyclization – *O*-cyclocarbonylation process, starting from thiophenecarboxylic acids bearing an ω-hydroxyalkynyl substituent in vicinal position (Scheme 1a) [31]. More recently, we have also found that 3-alkynylthiophene-2-carboxamides undergo iodocyclization in deep eutectic solvents (such as choline chloride/urea 1/2, mol/mol) to give 4-iodo-7*H*-thieno[2,3–*c*]pyran-7-imines, cyclization being in this case initiated from the amide nitrogen, as shown in Scheme 1b [46]. In this work, we have studied the reactivity of 3-(ω-hydroxyalkynyl)thiophene-2-carboxamides under our PdI_2/KI-catalyzed oxidative carbonylation conditions (Scheme 1c), in order to assess the possibility of synthesizing new thiophene-fused carbonylated heterocyclic scaffolds with potential applications in the pharmacological field.

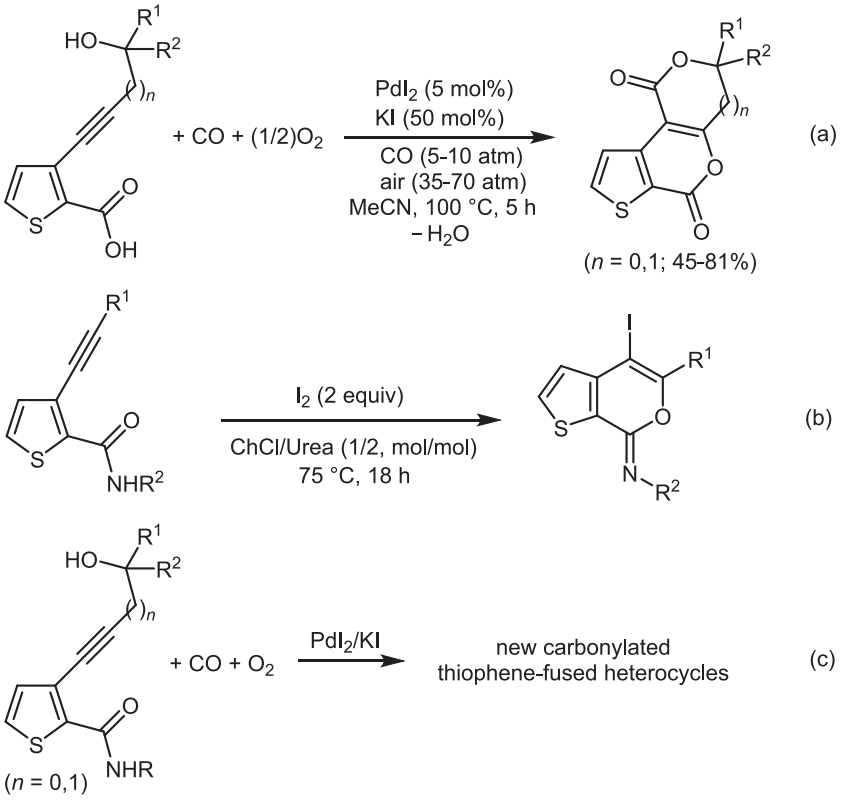
2. Results and discussion

2.1. PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 3-(3-hydroxy-1-ynyl)thiophene-2-carboxamides and 2-(3-hydroxy-1-ynyl) thiophene-3-carboxamides

The reactivity of *N*-butyl-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide **1a** under PdI_2/KI-catalyzed oxidative carbonylation conditions was initially assessed by allowing it to react with CO (5 bar) and O_2 (from air, 35 bar) in the presence of 5 mol % of PdI_2 and 50 mol% of KI, in MeCN as the solvent (**1a** initial concentration = 0.1 mmol per mL of MeCN) at 100 °C. After 5 h, substrate conversion was quantitative, and analysis of the reaction mixture revealed the formation of a product **2a** that was isolated in 60% yield and fully characterized by spectroscopic techniques and XRD analysis (Table 1, entry 1). The structure of **2a** corresponded to (*Z*)-5-(butylimino)-3,3-dimethyl-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-one (Fig. 1; see the Supporting Information for full XRD data), deriving from a 6-*endo-dig* *O*-cyclization – cyclocarbonylation process (Scheme 2).

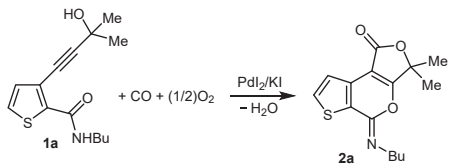
As shown in Scheme 2, the carbonylative double cyclization leading to **2a** starts with a 6-*endo-dig* intramolecular nucleophilic attack of the amido group to the triple bond activated by coordination to PdI_2 (anionic iodide ligands are omitted for clarity). In agreement to the fact that, under neutral conditions, amides are nucleophilic at the carbonyl oxygen rather than nitrogen [47], *O*-cyclization occurs selectively, leading to the corresponding vinylpalladium intermediate **I**. Carbon monoxide insertion then takes place to give acylpalladium complex **II**, from which the final product **2a** is formed by intramolecular nucleophilic displacement from the hydroxyl group. This step possibly occurs through the formation of palladacycle **III** followed by reductive elimination to Pd(0). The latter is then oxidized back to PdI_2 by oxidative addition of I_2, formed, in its turn, by oxidation with O_2 of the previously formed 2 mol of HI.

Having successfully verified the possibility to establish a catalytic route to previously unknown thiophene-fused heterocyclic derivatives based on carbonylative double cyclization, we next proceeded in changing some reaction parameters in order to optimize the product yield, and the results are shown in Table 1. In particular, the increase of initial substrate concentration to 0.2 mmol per mL of MeCN led to an augment of **2a** yield to 70% (Table 1, entry 3). The use of different CO and air partial pressures did not lead to improved results with respect to the parent experiment (Table 1, entries 4–7). Lower yields of **2a** were also observed when lowering the temperature to 80 °C (Table 1, entry 8) or the KI/PdI_2 molar ratio to 5 (Table 1, entry 9). On the other hand, an appreciable increase of product yield to 86% was obtained using a 2:1



Scheme 1. (a) PdI_2/KI-catalyzed oxidative carbonylative cyclization of thiophenecarboxylic acids bearing an ω-hydroxyalkynyl substituent in vicinal position to give furothienopyran and pyranothienopyran derivatives [31]. (b) Iodocyclization of 3-alkynylthiophene-2-carboxamides in choline chloride/urea (1/2, mol/mol) leading to 4-iodo-7*H*-thieno[2,3–*c*]pyran-7-imines [46]. (c) This work: PdI_2/KI-catalyzed oxidative carbonylation of 3-(ω-hydroxyalkynyl)thiophene-2-carboxamides for the synthesis of new thiophene-fused carbonylated heterocycles.

Table 1
PdI_2/KI – catalyzed oxidative carbonylation of *N*-butyl-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide **1a** under different conditions.



Entry	PdI_2/KI/**1a** molar ratio	Solvent	**1a** concn.[a]	P_{CO} (bar)	P_{air} (bar)	*T* (°C)	*t* (h)	Yield of **2a** (%)[b]
1	1/10/20	MeCN	0.1	5	35	100	5	60
2	1/10/20	MeCN	0.05	5	35	100	5	51
3	1/10/20	MeCN	0.2	5	35	100	5	70
4	1/10/20	MeCN	0.1	10	70	100	5	55
5	1/10/20	MeCN	0.1	16	4	100	5	43
6	1/10/20	MeCN	0.1	32	8	100	5	40
7	1/10/20	MeCN	0.1	48	12	100	5	30
8	1/10/20	MeCN	0.1	5	35	80	5	40
9	1/5/20	MeCN	0.1	5	35	100	5	24
10	1/10/20	$HC(OMe)_3$/MeCN (2:1, *v*/*v*)	0.2	5	35	100	5	86
11	1/10/50	$HC(OMe)_3$/MeCN (2:1, *v*/*v*)	0.2	5	35	100	5	26[c]
12	1/10/50	$HC(OMe)_3$/MeCN (2:1, *v*/*v*)	0.2	5	35	100	15	72
13	1/10/100	$HC(OMe)_3$/MeCN (2:1, *v*/*v*)	0.2	5	35	100	15	65

[a] Mmol of **1a** at start per mL of solvent.
[b] Isolated yield based on starting **1a**. Unless otherwise noted, substrate conversion was quantitative.
[c] Substrate conversion was 57% (determined by isolation of unreacted **1a** from the reaction mixture).

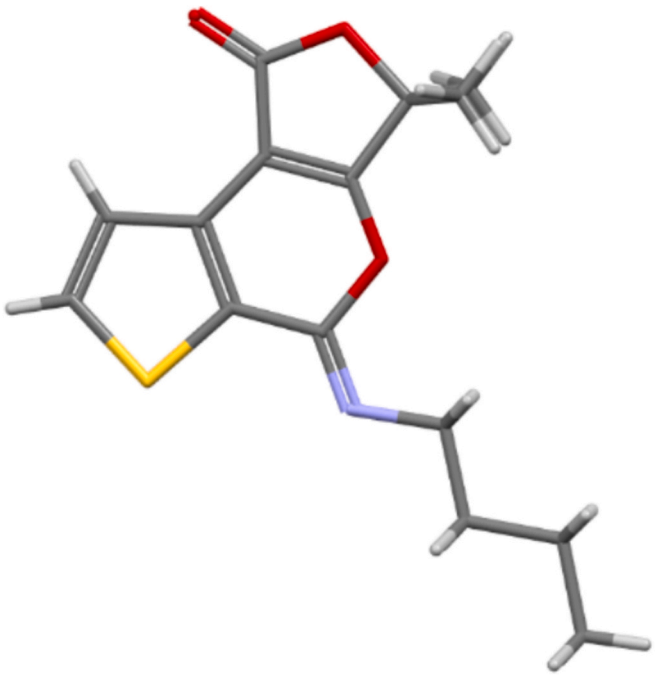


Fig. 1. X-ray molecular structure of (Z)-5-(butylimino)-3,3-dimethyl-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-one **2a**.

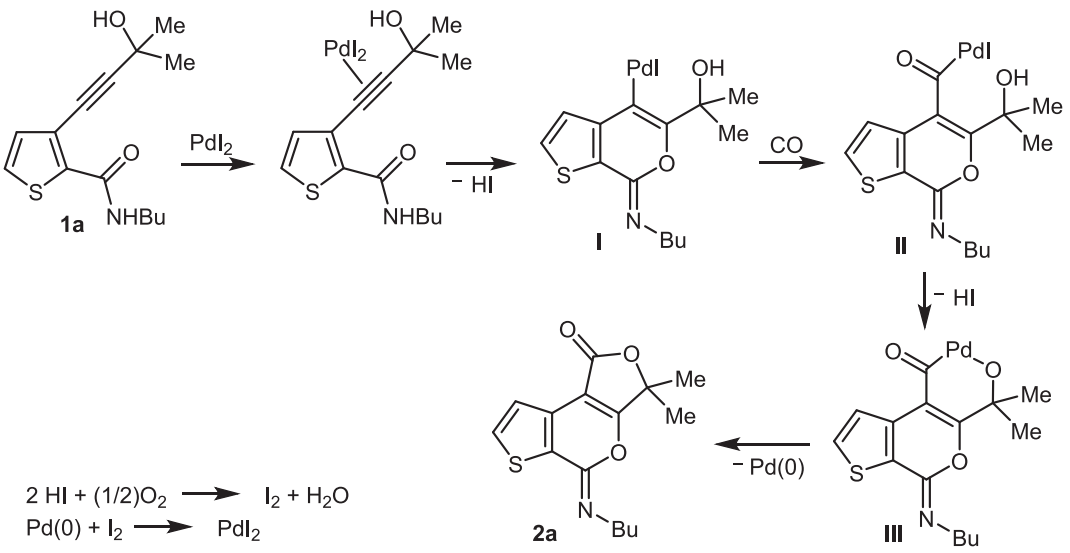
(*v*/*v*) mixture of $HC(OMe)_3$–MeCN as the reaction medium. This improvement was due to the dehydrating effect exerted by trimethyl orthoformate, which enhanced product stability, as it is known that imino groups can undergo degradation in the presence of water under heating [48]. We then tried to lower the catalyst loading under these optimized conditions. As shown in Table 1, entry 11, with 2 mol% PdI_2 substrate conversion was not complete after 5 h reaction time, so the process was performed overnight to achieve a good **2a** yield of 72% (Table 1, entry 12). With 1 mol% catalyst after 15 h product yield was lower, but still satisfactory (65%, Table 1, entry 13).

The process was then extended to various *N*-substituted 3-(3-hydroxy-1-ynyl)thiophene-2-carboxamides **1b-m**, bearing other tertiary as well as secondary or primary alcoholic groups and different substituents on nitrogen, including variously substituted aryl rings [49]. As can be seen from the results shown in Table 2, good to high yields of the corresponding iminofurothienopyranone derivatives **2** were generally obtained (up to 91%). A lower yield was instead obtained when the alcoholic group was primary (55%, Table 2, entries 12 and 13), probably due to a relative instability of the substrate and/or the product under the reaction conditions. The structure of (*Z*)-3,3-dimethyl-5-(phenylimino)-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-one **2f** was confirmed by XRD analysis (Fig. 2; see the Supporting Information for full XRD data).

Our method could be successfully extended to *N*-substituted 2-(3-hydroxy-1-ynyl)thiophene-3-carboxamides **3**, with inverted positions of the propargylic alcoholic and amido moieties with respect to **1**, to give 4-imino-4,6-dihydro-8*H*-furo[3,4–*b*]thieno[2,3–*d*]pyran-8-ones **4**, as shown in Scheme 3. The structure of a representative product, namely, (*Z*)-6,6-dimethyl-4-(phenylimino)-4,6-dihydro-8*H*-furo[3,4–*b*]thieno[2,3–*d*]pyran-8-one **4c**, has been confirmed by XRD analysis (Fig. 3; see the Supporting Information for full XRD data).

2.2. PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 3-(4-hydroxy-1-ynyl)thiophene-2-carboxamides

In spite of the higher degree of conformational mobility of a butynolic moiety with respect to a propynolic one, the reaction also worked nicely when applied to *N*-substituted 3-(4-hydroxy-1-ynyl)thiophene-2-carboxamides **5**. With these substrates, the best results in terms of product yield were obtained under conditions similar to those already optimized for substrates **1** (Table 2), but at 80 °C for 15 h and with an initial substrate concentration of 0.1 mmol per mL of solvent (Table 3, entries 1–5). Under these conditions, several differently substituted **5** were smoothly converted into the corresponding (*Z*)-6-imino-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-ones **6** in 50–90% isolated yields (Table 3, entries 5–13). The structures of (*Z*)-6-(butylimino)-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-one **6a**, (*Z*)-6-(phenylimino)-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-one **6c**, and (5a,8a-*cis*,*Z*)-10-(butylimino)-5a,6,7,8,8a,10-hexahydro-4*H*-cyclopenta[5,6]pyrano[4,3–*b*]thieno[3,2–*d*]pyran-4-one **6h** (and, in particular, the *cis* ring junction in **6h**) were unequivocally established by



Scheme 2. PdI_2/KI-catalyzed carbonylative double cyclization mechanism (6-*endo-dig O*-cyclization – cyclocarbonylation) leading to iminofurothienopyranone derivative **2a** from *N*-butyl-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide **1a**.

XRD analysis (Figs. 4-6; see the Supporting Information for full XRD data).

The reactivity of *N*-substituted 2-(4-hydroxy-1-ynyl)thiophene-3-carboxamides **7**, with the positions of the butynolic and amido groups inverted with respect to **5**, was finally tested. As can be seen from Scheme 4, the reaction led to the desired (*Z*)-4-imino-6,7-dihydro-4*H*,9*H*-pyrano[4,3–*b*]thieno[2,3–*d*]pyran-9-ones **8**, even though with generally lower yields compared to isomeric **6**.

3. Conclusions

In this work, we have studied the reactivity of 3-(ω-hydroxyalkynyl) thiophene-2-carboxamides and isomeric 2-(ω-hydroxyalkynyl)thiophene-3-carboxamides under PdI_2/KI-catalyzed oxidative carbonylation conditions, with the aim of synthesizing new thiophene-fused thiophene heterocyclic derivatives of pharmacological interest through a carbonylative double cyclization process. We have found that, with all substrates tested [3-(3-hydroxy-1-ynyl)thiophene-2-carboxamides, 2-(3-hydroxy-1-ynyl)thiophene-3-carboxamides, 3-(4-hydroxy-1-ynyl)thiophene-2-carboxamides, and 2-(4-hydroxy-1-ynyl)thiophene-3-carboxamides], the oxidative double carbonylation takes place under relatively mild conditions [1–5 mol% PdI_2, 10–50 mol% KI, in a 2:1 (*v*/*v*) HC$(OMe)_3$-MeCN mixture, under 40 bar of a 1:7 mixture CO-air, at 80–100 °C for 5–15 h], to afford the corresponding iminofurothienopyranone and iminopyranothienopyranone derivatives. The structures of six representative products have been confirmed by XRD analysis. Therefore, in all cases the process starts with a 6-*endo-dig* cyclization ensuing from the intramolecular nucleophilic attack of the oxygen of the amido group on coordinated triple bond. This is followed by a second cyclization with CO incorporation (cyclocarbonylation) with closure of a 5- or 6-membered ring depending on the length of the vicinal ω-hydroxyalkynyl substituent (propargylalcoholic or butynolic, respectively). Our method thus paves the way to the one-step catalytic preparation of previously unreported functionalized tricyclic heterocycles [50] starting from readily available substrates [the (ω-hydroxyalkynyl)thiophenecarboxamide, CO and O_2] in a multicomponent fashion.

4. Experimental section

4.1. General methods

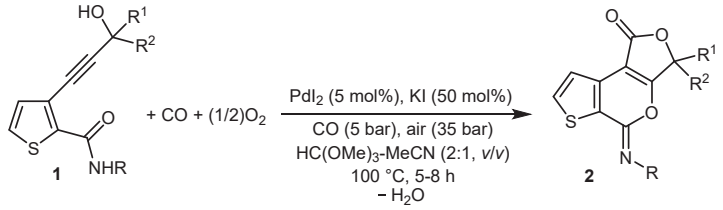
Solvent and chemicals were reagent grade and were used without further purification. All reactions were analyzed by TLC on silica gel 60 F254 and by GLC using capillary columns with polymethylsilicone + 5% phenylsilicone as the stationary phase. Column chromatography was performed on silica gel 60 (70–230 mesh) or neutral alumina (90–170). Evaporation refers to the removal of solvent under reduced pressure. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 25 °C on a 300 or 500 Spectrometer in $CDCl_3$ or DMSO-d_6 as the solvent with Me_4Si as internal standard. Chemical shifts (δ) and coupling constants (*J*) are given in ppm and in Hz, respectively. IR spectra were taken with an FT-IR spectrometer. Mass spectra were obtained using a GC–MS apparatus at 70 eV ionization voltage (normal resolution) and by electrospray ionization mass spectrometry (ESI-MS) (high resolution) with a UHD accurate-mass Q-TOF spectrometer equipped with a Dual AJS ESI source working in positive mode, and were recorded in the 150–1000 *m*/*z* range. The LC-MS experimental conditions were as follows: N_2 was employed as desolvation gas at 300 °C and a flow rate of 9 L/min. The nebulizer was set to 45 psig. The Sheat gas temperature was set at 350 °C and a flow of 12 L/min. A potential of 3.5 kV was used on the capillary for positive ion mode. The fragmentor was set to 175 V.

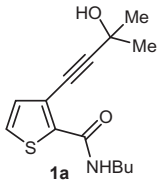
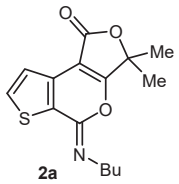
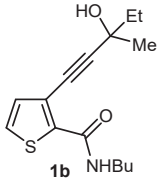
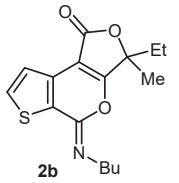
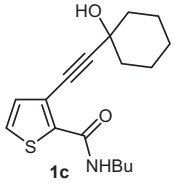
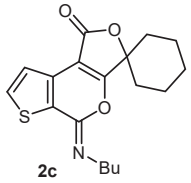
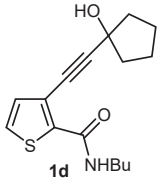
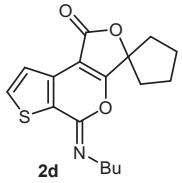
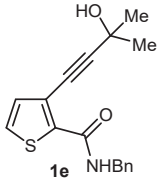
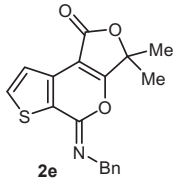
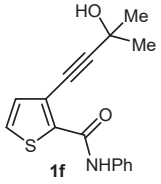
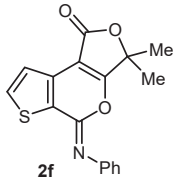
CCDC-2501712, CCDC-2499208, CCDC-2499200, CCDC-2499599, CCDC-2499670, CCDC-2505889 contain the supplementary crystallographic data for this paper for products **2a**, **2f**, **4c**, **6a**, **6c**, and **6h**, respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

4.2. General procedure for the synthesis of iminofurothienopyranone 2 and 4 from substrates 1 and 3 (Table 2 and Scheme 3, respectively)

A 50 mL stainless steel autoclave was charged in the presence of air with PdI_2 (7.2 mg, 2.0×10^{-2} mmol), KI (33.2 mg, 2.0×10^{-1} mmol) and a solution of **1** (0.40 mmol; **1a**, 107.0 mg; **1b**, 112.1 mg; **1c**, 123.0 mg; **1d**, 117.3 mg; **1e**, 120.0 mg; **1f**, 116.2 mg; **1g**, 138.1 mg; **1h**, 128.6 mg; **1i**, 101.5 mg; **1j**, 113.8 mg; **1k**, 109.0 mg; **1l**, 95.7 mg; **1m**, 109.3 mg) or **3** (0.40 mmol; **3a**, 107.3 mg; **3b**, 120.0 mg; **3c**, 115.2 mg) in a mixture $HC(OMe)_3$ (1.33 mL)–MeCN (0.67 mL). The autoclave was

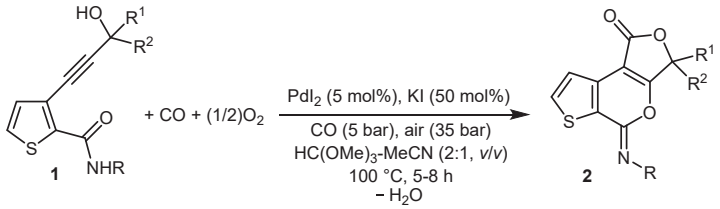
Table 2
Synthesis of *N*-substituted (*Z*)-5-imino-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-ones 2 from 3-(3-hydroxy-1-ynyl)thiophene-2-carboxamides 1 by PdI_2/KI-catalyzed oxidative carbonylative double cyclization.[a.]

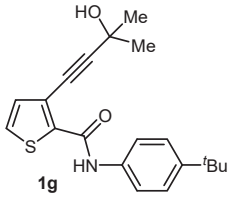
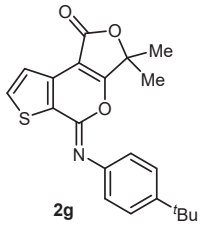
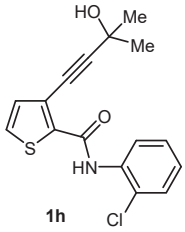
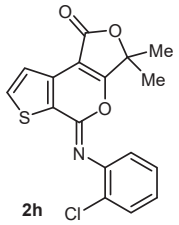
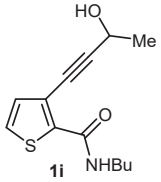
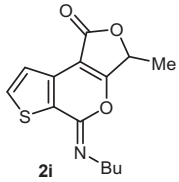
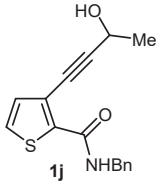
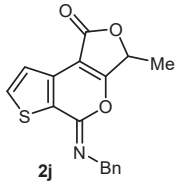
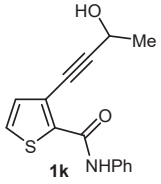
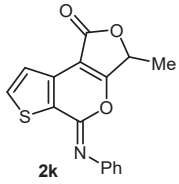
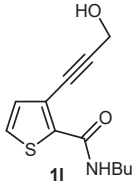
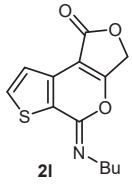
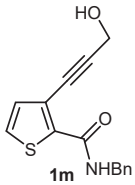
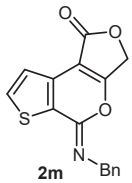


Entry	1	2	Yield of **2** (%)[b]
1	 **1a**	 **2a**	86
2	 **1b**	 **2b**	75
3	 **1c**	 **2c**	85
4	 **1d**	 **2d**	80
5	 **1e**	 **2e**	77
6	 **1f**	 **2f**	76

(*continued on next page*)

Table 2 (*continued*)



Entry	1	2	Yield of **2** (%)[b]
7	 **1g**	 **2g**	78
8	 **1h**	 **2h**	89
9	 **1i**	 **2i**	87
10	 **1j**	 **2j**	91
11	 **1k**	 **2k**	76
12[c]	 **1l**	 **2l**	55
13[c]	 **1m**	 **2m**	55

[a] Unless otherwise noted, all reactions were carried out at 100 °C for 5 h with 5 mol% of PdI_2 and 50 mol% of KI, under 40 bar of a 1:7 mixture CO–air, in $HC(OMe)_3$–MeCN (2:1, *v/v*) as the solvent with a substrate initial concentration of 0.2 mmol per mL of solvent.
[b] Isolated yield based on starting **1**.
[c] The reaction was carried out for 8 h.

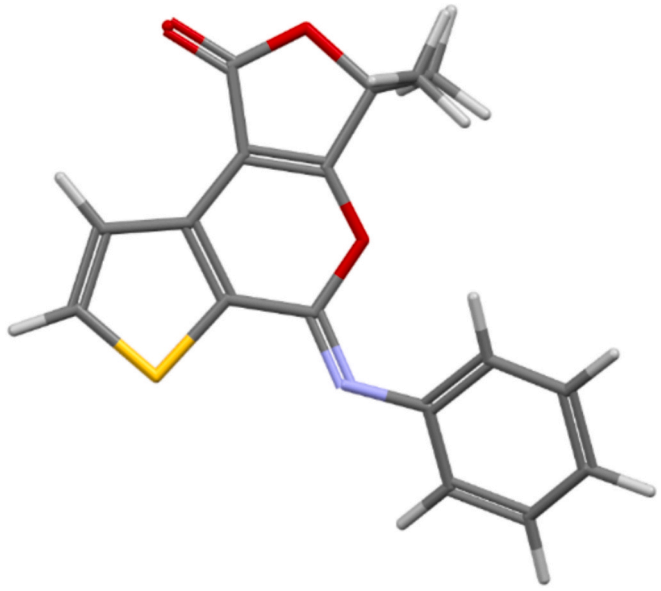


Fig. 2. X-ray molecular structure of (*Z*)-3,3-dimethyl-5-(phenylimino)-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-one **2f**.

sealed and, while the mixture was stirred, the autoclave was pressurized with CO (5 bar) and air (35 bar). After being stirred at 100 °C for 5 h (**1a-1k**, **3a-3c**) or 8 h (**1l**,**1m**), the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **2a-m** and **4a-c** were purified by column chromatography on silica gel using as eluent 90:10 hexane-AcOEt to 70:30 hexane-AcOEt.

4.2.1. (Z)-5-(Butylimino)-3,3-dimethyl-3,5-dihydro-1H-furo[3,4–b]thieno[3,2–d]pyran-1-one (2a)

Yield: 101.3 mg, starting from 107.0 mg of *N*-butyl-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide (**1a**) (86%; Table 2, entry 1). White solid, mp = 150–151 °C. IR (KBr): ν = 1759 (s), 1682 (s), 1443 (w), 1439 (m), 1369 (w), 1238 (w), 1196 (w), 1161 (m), 1061 (m), 914 (m), 787 (m), 764 (s), 725 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.58 (dist d, *J* = 4.9, 1H), 7.49 (dist d, *J* = 4.9, 1H), 3.57 (t, *J* = 7.0, 2H), 1.71–1.63 (m, 2H), 1.67 (s, 6H), 1.49–1.40 (m, 2H), 0.97 (t, *J* = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8, 166.2, 144.4, 132.7, 132.4, 127.3, 122.4, 100.4, 81.7, 46.1, 32.5, 24.5, 20.6, 13.9; GC–MS: *m/z* = 291 (M^+, 100), 274 (36), 248 (24), 235 (24), 217 (100), 205 (28), 192 (25), 177 (19), 121 (24); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for $(C_{15}H_{18}NO_3S)^+$: 292.1002; found, 292.1035.

4.2.2. (Z)-5-(Butylimino)-3-ethyl-3-methyl-3,5-dihydro-1H-furo[3,4–b]thieno[3,2–d]pyran-1-one (2b)

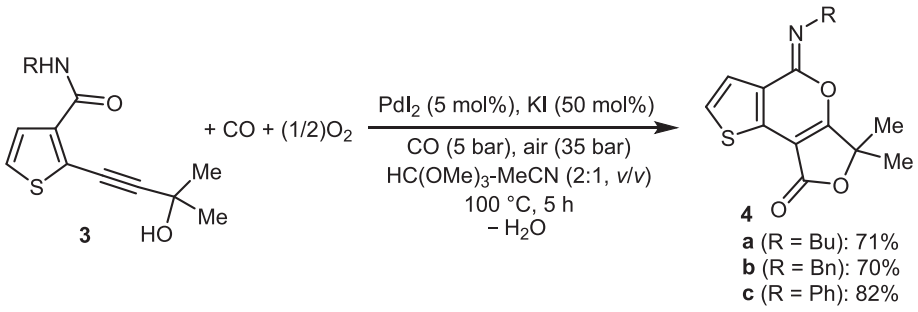
Yield: 92.2 mg, starting from 112.1 mg of *N*-butyl-3-(3-hydroxy-3-methylpent-1-yn-1-yl)thiophene-2-carboxamide (**1b**) (75%; Table 2, entry 2). Yellow solid, mp = 118–119 °C. IR (KBr): ν = 1759 (s), 1682 (s), 1543 (w), 1439 (m), 1343 (m), 1192 (w), 1146 (w), 1065 (w), 976 (w), 760 (m), 702 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.58 (dist d, *J* = 5.2, 1H), 7.48 (dist d, *J* = 5.2, 1H), 3.56 (t, *J* = 7.0, 2H), 2.07–1.90 (m, 2H), 1.70–1.63 (m, 2H), 1.65 (s, 3H), 1.48–1.39 (m, 2H), 0.97 (t, *J* = 7.4, 3H), 0.94 (t, *J* = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.9, 166.5, 144.4, 132.6, 132.4, 127.1, 122.4, 101.4, 84.4, 46.1, 32.5, 30.4, 22.8, 20.6, 13.9, 7.7; GC–MS: *m/z* = 305 (M^+, 57), 288 (30), 277 (47), 262 (40), 231 (100), 206 (38), 193 (17), 177 (19), 149 (41), 121 (32), 83 (45); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for $(C_{16}H_{20}NO_3S)^+$: 306.1158; found, 306.1193.

4.2.3. (Z)-5-(Butylimino)-1′H,5′H-spirocyclohexane-1,3′-furo[3,4–b]thieno[3,2–d]pyran-1′-one (2c)

Yield: 113.1 mg, starting from 123.0 mg of *N*-butyl-3-((1-hydroxycyclohexyl)ethynyl))thiophene-2-carboxamide (**1c**) (85%; Table 2, entry 3). White solid, mp = 130–132 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1539 (w), 1439 (m), 1373 (m), 1222 (m), 1150 (w), 1091 (w), 957 (w), 926 (m), 903 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.57 (dist d, *J* = 5.0, 1H), 7.49 (dist d, *J* = 5.0, 1H), 3.56 (t, *J* = 7.0, 2H), 1.97–1.87 (m, 2H), 1.87–1.77 (m, 6H), 1.71–1.63 (m, 2H), 1.50–1.38 (m, 3H), 1.26 (t, *J* = 7.1, 1H), 0.97 (t, *J* = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.8, 166.1, 144.0, 132.3, 131.8, 126.8, 121.9, 100.0, 82.9, 45.7, 33.1, 32.1, 23.8, 21.3, 20.1, 13.4; GC–MS: *m/z* = 331 (M^+, 96), 314 (58), 288 (90), 176 (92), 257 (97), 229 (49), 205 (63), 176 (44), 149 (63), 121 (85), 109 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for $(C_{18}H_{22}NO_3S)^+$: 332.1315; found, 332.1350.

4.2.4. (Z)-5-(Butylimino)-1′H,5′H-spirocyclopentane-1,3′-furo[3,4–b]thieno[3,2–d]pyran-1′-one (2d)

Yield: 102.8 mg, starting from 117.3 mg of *N*-butyl-3-((1-hydroxycyclohexyl)ethynyl))thiophene-2-carboxamide (**1d**) (80%; Table 2, entry 4). White solid, mp = 117–118 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1539 (w), 1435 (m), 1369 (m), 1335 (w), 1227 (w), 1184 (w), 1095 (w), 1057 (m), 980 (m), 937 (w), 841 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.57 (dist d, *J* = 5.1, 1H), 7.47 (dist d, *J* = 5.1, 1H), 3.55 (t, *J* = 7.0, 2H), 2.25–1.85 (m, 8H), 1.67 (quint, *J* = 7.3, 2H), 1.44 (sextet, *J* = 7.3, 2H), 0.97 (t, *J* = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.6, 166.5, 144.5, 132.8, 132.4, 127.2, 122.3, 101.4, 91.4, 46.1, 36.5, 32.6, 25.1, 20.6, 14.0; GC–MS: *m/z* = 317 (M^+, 73), 300 (69), 276 (77), 274 (55),



Scheme 3. Synthesis of 4-imino-4,6-dihydro-8*H*-furo[3,4–*b*]thieno[2,3–*d*]pyran-8-ones **4** by PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 2-(3-hydroxy-1-ynyl)thiophene-3-carboxamides **3**.

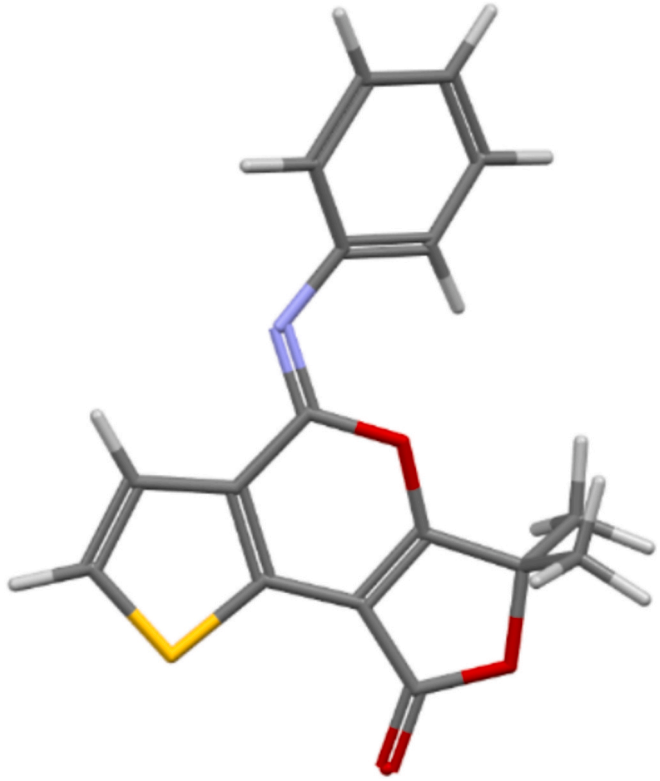


Fig. 3. X-ray molecular structure of (*Z*)-3,3-dimethyl-5-(phenylimino)-3,5-dihydro-1*H*-furo[3,4–*b*]thieno[3,2–*d*]pyran-1-one **4c**.

261 (11), 243 (100), 226 (22), 215 (61), 205 (52), 187 (25), 176 (28), 162 (16), 149 (48), 121 (52), 95 (98); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{20}NO_3S$)$^+$: 318.1158; found, 318.1187.

4.2.5. (Z)-5-(Benzylimino)-3,3-dimethyl-3,5-dihydro-1H-furo[3,4–b] thieno[3,2–d]pyran-1-one (2e)

Yield: 100.1 mg, starting from 120.0 mg of *N*-benzyl-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide (**1e**) (76%; Table 2, entry 5). White solid, mp = 139–140 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1543 (w), 1443 (m), 1358 (m), 1319 (w), 1188 (w), 1157 (m), 1042 (m), 926 (m), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.61 (dist d, J = 4.9, 1H), 7.50 (dist d, J = 4.9, 1H), 7.45–7.38 (m, 2H), 7.38–7.31 (m, 2H), 7.28–7.23 (m, 1H), 4.78 (s, 2H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.6, 166.0, 145.6, 139.4, 133.1, 133.0, 128.5, 127.6, 127.2, 126.9, 122.4, 100.7, 81.7, 50.2, 24.5; GC–MS: *m/z* = 325 (M$^+$, 13), 148 (2), 120 (2), 91 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{18}H_{16}NO_3S$)$^+$: 326.0845; found, 326.0866.

4.2.6. (Z)-3,3-Dimethyl-5-(phenylimino)-3,5-dihydro-1H-furo[3,4–b] thieno[3,2–d]pyran-1-one (2f)

Yield: 96.6 mg, starting from 116.2 mg of 3-(3-hydroxy-3-methylbut-1-yn-1-yl)-*N*-phenylthiophene-2-carboxamide (**1f**) (76%; Table 2, entry 6). Pale yellow solid, mp = 187–188 °C. IR (KBr): ν = 1767 (s), 1678 (s), 1593 (m), 1539 (w), 1485 (w), 1423 (m), 1358 (m), 1157 (m), 1042 (w), 930 (m), 772 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, J = 4.5, 1H), 7.56 (dist d, J = 4.5, 1H), 7.42–7.34 (m, 2H), 7.28–7.12 (m, 3H), 1.64 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.4, 165.8, 144.02, 143.96, 136.3, 134.4, 134.3, 128.9, 124.9, 123.0, 122.6, 101.1, 81.8, 24.5; GC–MS: *m/z* = 311 (M$^+$, 73), 296 (17), 225 (100), 196 (37), 152 (19), 77 (34); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{14}NO_3S$)$^+$: 312.0689; found, 312.0718.

4.2.7. (Z)-5-((4-(tert-Butyl)phenyl)imino)-3,3-dimethyl-3,5-dihydro-1H-furo[3,4–b]thieno[3,2–d]pyran-1-one (2g)

Yield: 116.4 mg, starting from 138.1 mg of *N*-(4-(*tert*-butyl)phenyl)-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide (**1g**) (78%; Table 2, entry 7). White solid, mp = 232–233 °C. IR (KBr): ν = 1767 (s), 1678 (s), 1651 (m), 1543 (w), 1504 (w), 1427 (m), 1358 (m), 1269 (w), 1196 (m), 1042 (m), 926 (m), 833 (w) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (dist d, J = 5.0, 1H), 7.54 (dist d, J = 5.0, 1H), 7.39 (dist d, J = 8.3, 2H), 7.24 (dist d, J = 8.3, 2H), 1.64 (s, 6H), 1.35 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.5, 165.9, 148.1, 143.3, 140.9, 134.1, 128.0, 126.6, 125.7, 123.3, 122.6, 101.1, 81.8, 34.5, 34.4, 24.6; GC–MS: *m/z* = 367 (M$^+$, 47), 352 (100), 324 (2), 281 (9), 266 (13), 238 (7), 225 (5), 119 (8); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{21}H_{22}NO_3S$)$^+$: 368.1315; found, 368.1324.

4.2.8. (Z)-5-((2-Chlorophenyl)imino)-3,3-dimethyl-3,5-dihydro-1H-furo [3,4–b]thieno[3,2–d]pyran-1-one (2h)

Yield: 124.3 mg, starting from 128.6 mg of *N*-(2-chlorophenyl)-3-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-2-carboxamide (**1h**) (89%; Table 2, entry 8). Yellow solid, mp = 160–162 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1651 (m), 1582 (w), 1535 (w), 1466 (w), 1435 (m), 1358 (w), 1188 (m), 1157 (m), 1042 (m), 934 (m), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (dist d, J = 4.5, 1H), 7.59 (d, J = 4.5, 1H), 7.44 (d, J = 7.9, 1H), 7.31–7.22 (m, 1H), 7.17–7.05 (m, 2H), 1.56 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 176.3, 165.7, 145.7, 142.3, 135.1, 129.8, 127.3, 126.2, 125.2, 123.1, 122.6, 101.3, 81.9, 24.4; GC–MS: *m/z* = 347 [(M + 2)$^+$, 31], 345 (M$^+$, 79), 330 (15), 310 (15), 259 (100), 219 (8), 196 (50), 186 (25), 143 (11), 111 (16); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{13}ClNO_3S$)$^+$: 346.0299; found, 346.0304.

4.2.9. (Z)-5-(Butylimino)-3-methyl-3,5-dihydro-1H-furo[3,4–b]thieno [3,2–d]pyran-1-one (2i)

Yield: 97.0 mg, starting from 101.5 mg of *N*-butyl-3-(3-hydroxybut-1-yn-1-yl)thiophene-2-carboxamide (**1i**) (87%; Table 2, entry 9). White solid, mp = 80–81 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1643 (m), 1543 (m), 1435 (m), 1366 (m), 1327 (w), 1096 (m), 1042 (m), 918 (m), 779 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 (dist d, J = 5.2, 1H), 7.49 (d, J = 5.2, 1H), 5.23 (q, J = 6.8, 1H), 3.59–3.52 (m, 2H), 1.71–1.63 (m, 2H), 1.65 (d, J = 6.8, 3H), 1.44 (sextet, J = 7.4, 2H), 0.97 (t, J = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.4, 166.8, 144.1, 132.4, 127.5, 122.3, 101.7, 74.1, 46.2, 32.6, 20.6, 17.8, 13.9; GC–MS: *m/z* = 277 (M$^+$, 20), 260 (35), 234 (14), 221 (32), 205 (12), 178 (100), 149 (28), 121 (20); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{14}H_{16}NO_3S$)$^+$: 278.0845; found, 278.0862.

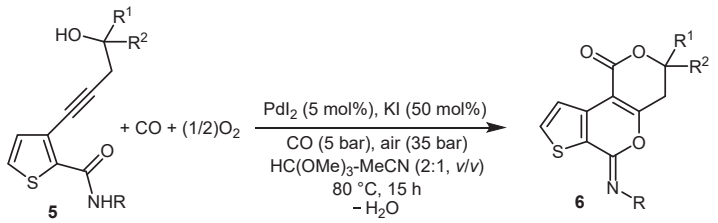
4.2.10. (Z)-5-(Benzylimino)-3-methyl-3,5-dihydro-1H-furo[3,4–b]thieno [3,2–d]pyran-1-one (2j)

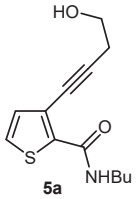
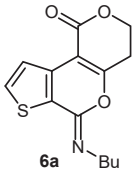
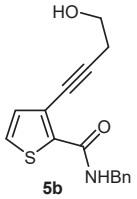
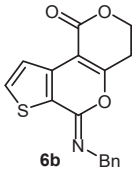
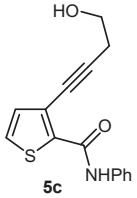
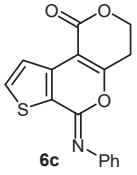
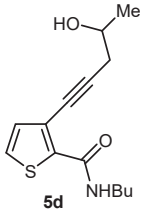
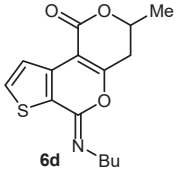
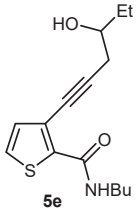
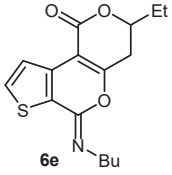
Yield: 113.5 mg, starting from 113.8 mg of *N*-benzyl-3-(3-hydroxybut-1-yn-1-yl)thiophene-2-carboxamide (**1j**) (91%; Table 2, entry 10). Yellow solid, mp = 120–121 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1543 (w), 1443 (m), 1366 (m), 1327 (w), 1234 (w), 1096 (m), 1042 (m), 926 (m), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.61 (dist d, J = 5.0, 1H), 7.50 (dist d, J = 5.0, 1H), 7.46–7.42 (m, 2H), 7.40–7.34 (m, 2H), 7.30–7.25 (m, 2H), 5.24 (q, J = 6.8, 1H), 4.77 (s, 2H), 1.62 (d, J = 6.8, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.2, 166.7, 145.3, 139.3, 133.0, 128.9, 128.4, 127.9, 127.5, 126.9, 122.2, 101.9, 74.2, 50.0, 17.7; GC–MS: *m/z* = 311 (M$^+$, 6), 120 (4), 91 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{14}NO_3S$)$^+$: 312.0689; found, 312.0699.

4.2.11. (Z)-3-Methyl-5-(phenylimino)-3,5-dihydro-1H-furo[3,4–b]thieno [3,2–d]pyran-1-one (2k)

Yield: 90.5 mg, starting from 109.0 mg of 3-(3-hydroxybut-1-yn-1-yl)-*N*-phenylthiophene-2-carboxamide (**1k**) (76%; Table 2, entry 11). Yellow solid, mp = 142–143 °C. IR (KBr): ν = 1767 (s), 1674 (s), 1589 (m), 1535 (w), 1489 (w), 1443 (m), 1366 (w), 1327 (w), 1250 (w), 1188 (w), 1096 (m), 1042 (m), 941 (m), 756 (m) cm^{-1}; ^{1}H NMR (500 MHz,

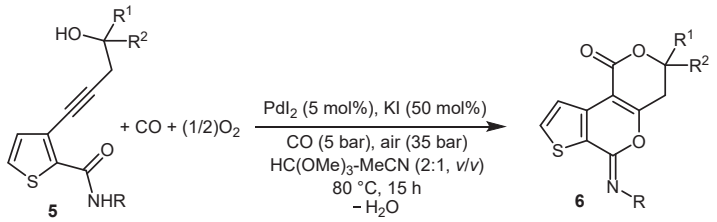
Table 3
Synthesis of *N*-substituted (*Z*)-6-imino-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-ones 6 from 3-(4-hydroxy-1-ynyl)thiophene-2-carboxamides 5 by PdI_2/KI-catalyzed oxidative carbonylative double cyclization.[a.]

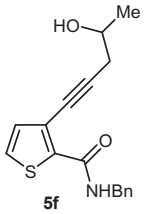
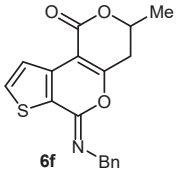
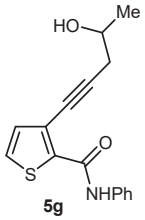
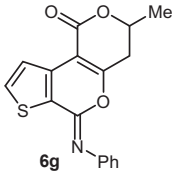
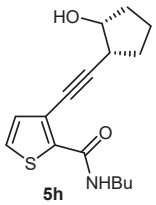
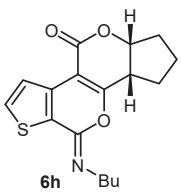
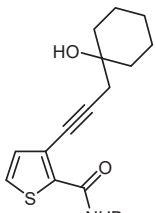
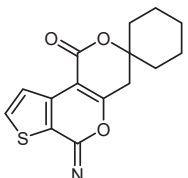


Entry	5	6	Yield of **6** (%)[b]
1[c]	 **5a**	 **6a**	55
2[d]	**5a**	**6a**	72
3[e]	**5a**	**6a**	64
4[f]	**5a**	**6a**	63
5	**5a**	**6a**	90
6	 **5b**	 **6b**	78
7	 **5c**	 **6c**	68
8	 **5d**	 **6d**	82
9	 **5e**	 **6e**	82

(*continued on next page*)

Table 3 (*continued*)



Entry	5	6	Yield of **6** (%)[b]
10	 **5f**	 **6f**	85
11	 **5g**	 **6g**	63
12	 **5h**	 **6h**	61
13	 **5i**	 **6i**	50

[a] Unless otherwise noted, all reactions were carried out at 80 °C for 15 h with 5 mol% of PdI_2 and 50 mol% of KI, under 40 bar of a 1:7 mixture CO–air, in $HC(OMe)_3$–MeCN (2:1, *v/v*) as the solvent with a substrate initial concentration of 0.1 mmol per mL of solvent.
[b] Isolated yield based on starting 5. Substrate **5h** and product **6h** were in racemic form.
[c] The reaction was carried out at 100 °C for 5 h with an initial substrate concentration of 0.2 mmol per mL of solvent.
[d] The reaction was carried out at 80 °C for 8 h with an initial substrate concentration of 0.2 mmol per mL of solvent.
[e] The reaction was carried out at 100 °C for 5 h with an initial substrate concentration of 0.1 mmol per mL of solvent.
[f] The reaction was carried out at 100 °C for 5 h with an initial substrate concentration of 0.05 mmol per mL of solvent.

$CDCl_3$): $\delta = 7.72$ (dist d, $J = 5.1$, 1H), 7.55 (dist d, $J = 5.1$, 1H), 7.36 (t, $J = 7.7$, 2H), 7.21 (dist d, $J = 7.7$, 2H), 7.16 (dist t, $J = 7.3$, 1H), 5.18 (q, $J = 6.7$, 1H), 1.58 (d, $J = 6.7$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 173.9$, 166.5, 144.0, 134.4, 134.0, 128.9, 127.6, 124.8, 122.9, 122.5, 102.4, 74.2, 17.8; GC–MS: $m/z = 297$ (M^+, 84), 254 (4), 225 (100), 196 (39), 170 (7), 152 (21), 120 (8), 77 (55); HRMS-ESI (m/z): $[(M + H)^+]$ calcd for $(C_{16}H_{12}NO_3S)^+$: 298.0532; found, 298.0539.

4.2.12. (Z)-5-(Butylimino)- 3,5-dihydro-1H-furo[3,4–b]thieno[3,2–d] pyran-1-one (2l)

Yield: 58.7 mg, starting from 95.7 mg of *N*-butyl-3-(3-hydroxyprop-1-yn-1-yl)thiophene-2-carboxamide (**1l**) (55%; Table 2, entry 12). Yellow solid, mp = 127–128 °C. IR (KBr): $\nu = 1759$ (s), 1682 (s), 1543 (w), 1443 (m), 1373 (w), 1335 (w), 1026 (m), 910 (m), 772 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.57$ (dist d, $J = 5.1$, 1H), 7.46 (dist d, $J = 5.1$, 1H), 5.00 (s, 2H), 3.54 (t, $J = 7.1$, 2H), 1.69–1.62 (m, 2H), 1.44 (sextet, $J = 7.4$, 2H), 0.96 (t, $J = 7.4$, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.4$, 167.6, 144.0, 132.4, 132.2, 127.5, 122.1, 102.3, 66.3, 46.3, 32.6, 20.6, 13.9; GC–MS: $m/z = 263$ (M^+, 26), 246 (63), 220 (15), 207 (100), 178 (92), 149 (20), 121 (22); HRMS-ESI (m/z): $[(M + H)^+]$ calcd for $(C_{13}H_{14}NO_3S)^+$: 264.0689; found, 264.0693.

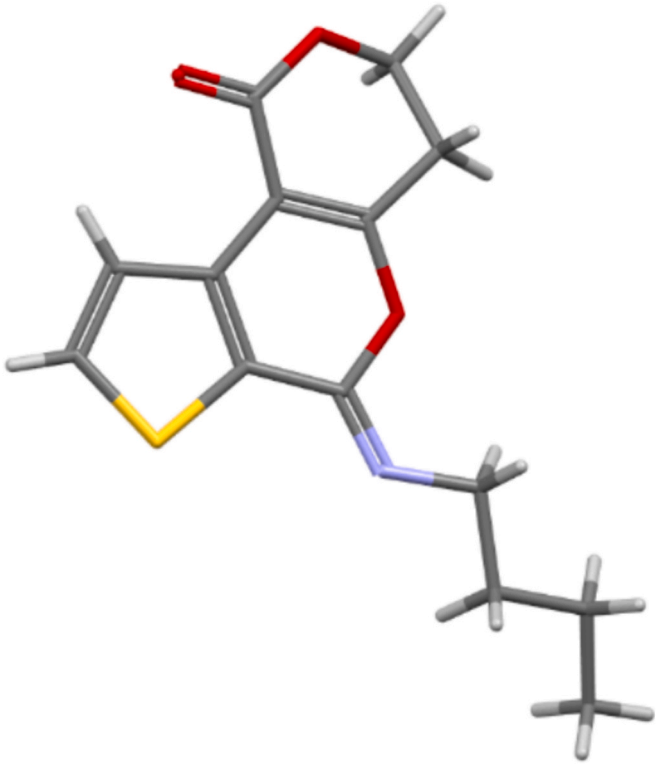


Fig. 4. X-ray molecular structure of (*Z*)-6-(butylimino)-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-one **6a**.

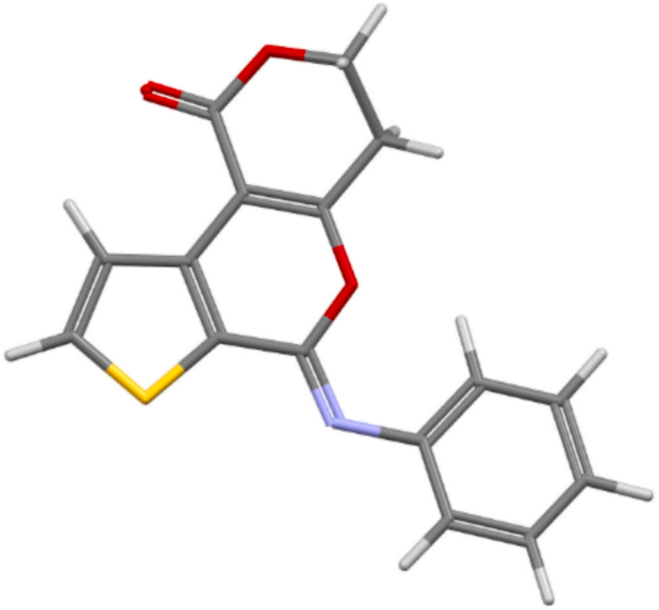


Fig. 5. X-ray molecular structure of (*Z*)-6-(phenylimino)-4,6-dihydro-1*H*,3*H*-pyrano[4,3–*b*]thieno[3,2–*d*]pyran-1-one **6c**.

4.2.13. (Z)-5-(Benzylimino)-3,5-dihydro-1H-furo[3,4–b]thieno[3,2–d]pyran-1-one (2m)

Yield: 65.8 mg, starting from 109.3 mg of *N*-benzyl-3-(3-hydroxyprop-1-yn-1-yl)thiophene-2-carboxamide (**1m**) (55%; Table 2, entry 13). Yellow solid, mp = 92–93 °C. IR (KBr): ν = 1769 (s), 1642 (w), 1427 (m), 1331 (m), 1022 (m), 870 (m), 754 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.62 (dist d, J = 5.1, 1H), 7.51 (d, J = 5.1, 1H), 7.45–7.38 (m, 2H), 7.38–7.30 (m, 2H), 7.29–7.21 (m, 1H), 5.03 (s, 2H), 4.79 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.1, 167.5, 145.1, 139.3, 133.0, 132.6, 128.5, 127.5, 126.9, 122.2, 102.7, 66.3, 50.0; GC–MS: *m/z* = 297 (M^+, 9), 120 (3), 91 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for $(C_{16}H_{12}NO_3S)^+$: 298.0532; found, 298.0531.

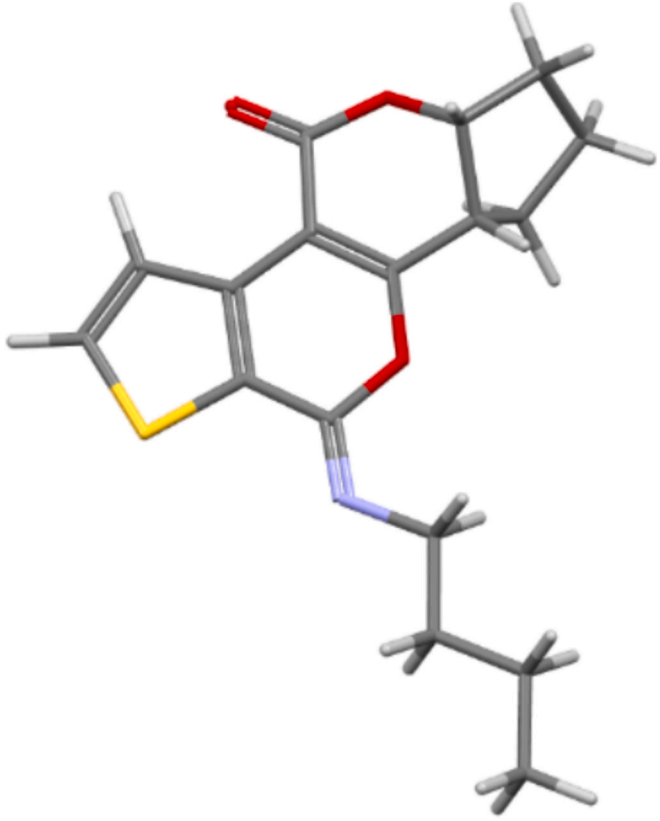


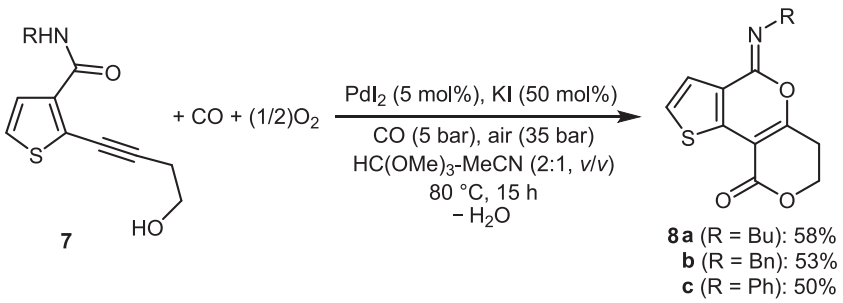
Fig. 6. X-ray molecular structure of (5a,8a-*cis*,*Z*)-10-(butylimino)-5a,6,7,8,8a,10-hexahydro-4*H*-cyclopenta[5,6]pyrano[4,3–*b*]thieno[3,2–*d*]pyran-4-one **6h**.

4.2.14. (Z)-4-(Butylimino)-6,6-dimethyl-4,6-dihydro-8H-furo[3,4–b]thieno[3,2–d]pyran-8-one (4a)

Yield: 84.0 mg, starting from 107.3 mg of *N*-butyl-2-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-3-carboxamide (**3a**) (71%; Scheme 3). Yellow solid, mp = 166–168 °C. IR (KBr): ν = 1759 (s), 1682 (s), 1528 (w), 1458 (m), 1373 (m), 1335 (w), 1188 (m), 995 (m), 926 (w), 756 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.49 (dist d, J = 5.3, 1H), 7.35 (dist d, J = 5.1, 1H), 3.56 (t, J = 7.3, 2H), 1.67 (quint, J = 7.3, 2H), 1.67 (s, 6H), 1.45 (sextet, J = 7.3, 2H), 0.97 (t, J = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.3, 165.8, 144.8, 132.2, 126.7, 126.4, 125.5, 100.1, 82.3, 46.0, 32.6, 24.5, 20.6, 13.9; GC–MS: *m/z* = 291 (M^+, 94), 274 (12), 248 (9), 235 (96), 217 (100), 190 (95), 149 (61), 121 (44), 69 (58); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for $(C_{15}H_{18}NO_3S)^+$: 292.1002; found, 292.1008.

4.2.15. (Z)-4-(Benzylimino)-6,6-dimethyl-4,6-dihydro-8H-furo[3,4–b]thieno[3,2–d]pyran-8-one (4b)

Yield 91.0 mg, starting from 120.0 mg of *N*-benzyl-2-(3-hydroxy-3-methylbut-1-yn-1-yl)thiophene-3-carboxamide (**3b**) (70%; Scheme 3). Yellow solid, mp = 96–97 °C. IR (KBr): ν = 1767 (s), 1682 (s), 1643 (m), 1458 (m), 1366 (m), 1342 (m), 1188 (m), 995 (w), 926 (w), 748 (m), 702 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.56 (dist d, J = 5.1, 1H), 7.45–7.41 (m, 2H), 7.37–7.32 (m, 3H), 7.28–7.24 (m, 1H), 4.77 (s, 2H), 1.65 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.0, 165.6, 145.9, 139.5, 132.6, 128.5, 127.6, 126.9, 126.7, 125.6, 100.4, 82.3, 50.1, 24.4; GC–MS: *m/z* = 325 (M^+, 12), 148 (3), 120 (5), 91 (100); HRMS-ESI (*m/*



Scheme 4. Synthesis of (*Z*)-4-imino-6,7-dihydro-4*H*,9*H*-pyrano[4,3–*b*]thieno[2,3–*d*]pyran-9-ones **8** by PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 2-(4-hydroxy-1-ynyl)thiophene-3-carboxamides **7**.

z): [(M + H)$^+$] calcd for ($C_{18}H_{16}NO_3S$)$^+$: 326.0845; found, 326.0841.

4.2.16. (Z)-6,6-Dimethyl-4-(phenylimino)-4,6-dihydro-8H-furo[3,4–b] thieno[3,2–d]pyran-8-one (4c)

Yield: 103.2 mg, starting from 115.2 mg of 2-(3-hydroxy-3-methyl-but-1-yn-1-yl)-*N*-phenylthiophene-3-carboxamide (**3c**) (82%; Scheme 3). Yellow solid, mp = 195–196 °C. IR (KBr): ν = 1767 (s), 1674 (s), 1589 (w), 1528 (w), 1481 (w), 1458 (w), 1373 (w), 1335 (w), 1188 (m), 1049 (w), 995 (m), 926 (m), 764 (m), 694 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 4.5, 1H), 7.45 (d, *J* = 4.5, 1H), 7.40–7.33 (m, 2H), 7.22–7.12 (m, 3H), 1.59 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.7, 165.3, 144.3, 134.1, 128.9, 127.0, 126.9, 125.8, 124.7, 124.4, 122.5, 100.8, 82.4, 24.5; GC–MS: *m/z* = 311 (M$^+$, 85), 296 (19), 225 (100), 196 (44), 153 (18), 94 (14), 77 (50); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{14}NO_3S$)$^+$: 312.0689; found, 312.0695.

4.3. Procedure for the synthesis of (Z)-5-(butylimino)-3,3-dimethyl-3,5-dihydro-1H-furo[3,4–b]thieno[3,2–d]pyran-1-one (2a) in larger scale

A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (30.6 mg, 0.085 mmol), KI (141 mg, 0.85 mmol) and a solution of **1a** (450 mg, 1.70 mmol) in a mixture $HC(OMe)_3$ (5.7 mL)–MeCN (2.8 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (5 bar) and air (35 bar). After being stirred at 100 °C for, the autoclave was cooled, degassed and opened. The solvent was evaporated, and product **2a** was purified by column chromatography on silica gel using as eluent 90:10 hexane-AcOEt to 70:30 hexane-AcOEt (360 mg, 73%).

4.4. General procedure for the synthesis of iminopyranothienopyranone 6 and 8 from substrates 5 and 7 (Table 3 and Scheme 4, respectively)

A 50 mL stainless steel autoclave was charged in the presence of air with PdI_2 (7.2 mg, 2.0 × 10^{-2} mmol), KI (33.2 mg, 2.0 × 10^{-1} mmol) and a solution of **5** (0.40 mmol; **5a**, 101.5 mg; **5b**, 115.2 mg; **5c**, 109.0 mg; **5d**, 107.2 mg; **5e**, 112.8 mg; **5f**, 120.3 mg; **5 g**, 115.0 mg; **5h**, 117.0 mg; **5i**, 128.2 mg) or **7** (0.40 mmol; **7a**, 101.0 mg; **7b**, 115.3 mg; **7c**, 109.2 mg) in a mixture $HC(OMe)_3$ (2.65 mL)–MeCN (1.35 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (5 bar) and air (35 bar). After being stirred at 80 °C for 15 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **6a-i** and **8a-c** were purified by column chromatography on silica gel using as eluent 90:10 hexane-AcOEt to 70:30 hexane-AcOEt.

4.4.1. (Z)-6-(Butylimino)-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno [3,2–d]pyran-1-one (6a)

Yield: 100.5 mg, starting from 101.5 mg of *N*-butyl-3-(4-hydroxybut-1-yn-1-yl)thiophene-2-carboxamide (**5a**) (90%; Table 3, entry 5). White solid, mp = 114–116 °C IR (KBr): ν = 1721 (s), 1682 (s), 1535 (w), 1466 (w), 1420 (m), 1366 (m), 1320 (m), 1227 (m), 1188 (w), 1111 (m), 1080 (w), 980 (w), 949 (m), 779 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 5.0, 1H), 7.49 (d, *J* = 5.0, 1H), 4.52 (t, *J* = 6.2, 2H), 3.51 (t, *J* = 7.3, 2H), 2.93 (t, *J* = 6.2, 2H), 1.65 (quint, *J* = 7.3, 2H), 1.43 (sextet, *J* = 7.3, 2H), 0.96 (t, *J* = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.6, 163.1, 144.1, 135.2, 131.1, 127.4, 125.5, 103.0, 64.0, 46.0, 32.7, 26.5, 20.7, 14.0; GC–MS: *m/z* = 277 (M$^+$, 16), 260 (100), 234 (76), 221 (17), 193 (35), 149 (35), 121 (25); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{14}H_{16}NO_3S$)$^+$: 278.0845; found, 278.0875.

4.4.2. (Z)-6-(Benzylimino)-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno [3,2–d]pyran-1-one (6b)

Yield: 98.5 mg, starting from 115.2 mg of *N*-benzyl-3-(4-hydroxybut-1-yn-1-yl)thiophene-2-carboxamide (**5b**) (78%; Table 3, entry 6). White solid, mp = 114–115 °C. IR (KBr): ν = 1722 (s), 1651 (s), 1531 (w), 1452 (w), 1437 (w), 1416 (m), 1366 (m), 1317 (m), 1233 (m), 1190 (w), 1115 (m), 1082 (w), 1030 (w), 962 (m), 847 (w), 730 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 5.1, 1H), 7.49 (d, *J* = 5.1, 1H), 7.43–7.38 (m, 2H), 7.36–7.30 (m, 2H), 7.27–7.21 (m, 1H), 4.72 (s, 2H), 4.48 (t, *J* = 6.3, 2H), 2.90 (t, *J* = 6.3, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.4, 163.0, 145.2, 139.8, 135.5, 131.6, 128.4, 127.6, 126.7, 125.4, 103.1, 64.0, 49.9, 26.4; GC–MS: *m/z* = 311 (M$^+$, 22), 233 (2), 91 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{14}NO_3S$)$^+$: 312.0689; found, 312.0698.

4.4.3. (Z)-6-(Phenylimino)-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno [3,2–d]pyran-1-one (6c)

Yield: 81.8 mg, starting from 109.0 mg of 3-(4-hydroxybut-1-yn-1-yl)-*N*-phenylthiophene-2-carboxamide (**5c**) (68%; Table 3, entry 7). Yellow solid, mp = 178–179 °C. IR (KBr): ν = 1721 (s), 1667 (vs), 1589 (m), 1535 (w), 1489 (w), 1420 (m), 1366 (w), 1319 (m), 1196 (m), 1111 (w), 980 (m), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.89 (dist d, *J* = 5.1, 1H), 7.64 (d, *J* = 5.1, 1H), 7.40–7.30 (m, 2H), 7.22–7.16 (m, 2H), 7.16–7.08 (m, 1H), 4.49 (t, *J* = 6.2, 2H), 2.87 (t, *J* = 6.2, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.3, 162.7, 144.7, 143.8, 136.9, 135.0, 133.1, 128.8, 125.6, 124.4, 122.9, 103.7, 64.1, 26.4; GC–MS: *m/z* = 397 (M$^+$, 100), 269 (6), 225 (47), 196 (19), 152 (11), 77 (20); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{16}H_{12}NO_3S$)$^+$: 298.0532; found, 298.0561.

4.4.4. (Z)-6-(Butylimino)-3-methyl-4,6-dihydro-1H,3H-pyrano[4,3–b] thieno[3,2–d]pyran-1-one (6d)

Yield: 96.8 mg, starting from 107.2 mg of *N*-butyl-3-(4-hydroxypent-1-yn-1-yl)thiophene-2-carboxamide (**5d**) (82%; Table 3, entry 8). Yellow solid, mp = 98–99 °C. IR (KBr): ν = 1721 (s), 1682 (s), 1534 (w), 1410 (m), 1391 (m), 1338 (w), 1235 (w), 1119 (m), 1103 (w), 982 (w), 941 (m), 862 (w), 780 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.84 (dist d, *J* = 5.1, 1H), 7.49 (d, *J* = 5.1, 1H), 4.76–4.67 (m, 1H), 3.49 (t, *J* = 7.2, 2H), 2.85 (dist dd, *J* = 17.6, 11.5, 1H), 2.76 (dist dd, *J* = 17.6, 4.0, 1H), 1.68–1.59 (m, 2H), 1.54 (d, *J* = 6.3, 3H), 1.47–1.37 (m, 2H), 0.96 (t, *J* = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.6, 163.3, 144.3, 135.2, 133.1, 127.2, 125.4, 102.5, 72.2, 46.0, 33.4, 32.7, 20.7, 14.0; GC–MS: *m/z* = 397 (M$^+$, 14), 274 (100), 248 (80), 206 (11), 193 (31),

149 (36), 121 (30); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{15}H_{18}NO_3S$)$^+$: 292.1002; found, 292.1003.

4.4.5. (Z)-6-(Butylimino)-3-ethyl-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno[3,2–d]pyran-1-one (6e)

Yield: 101.6 mg, starting from 112.8 mg of *N*-butyl-3-(4-hydroxyhex-1-yn-1-yl)thiophene-2-carboxamide (**5e**) (82%; Table 3, entry 9). Yellow solid, mp = 110–111 °C. IR (KBr): ν = 1721 (s), 1682 (vs), 1533 (w), 1458 (m), 1437 (m), 1389 (m), 1234 (w), 1217 (w), 1107 (m), 1072 (m), 974 (m), 951 (m), 777 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.83 (d, J = 5.2, 1H), 7.48 (d, J = 5.2, 1H), 4.55–4.41 (m, 1H), 3.49 (t, J = 7.1, 2H), 2.86 (dist dd, J = 17.5, 11.9, 1H), 2.73 (dist dd, J = 17.5, 3.9, 1H), 1.97–1.86 (m, 1H), 1.86–1.75 (m, 1H), 1.69–1.58 (m, 2H), 1.47–1.37 (m, 2H), 1.09 (t, J = 7.4, 3H), 0.96 (t, J = 7.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.6, 163.5, 144.3, 135.2, 131.0, 127.2, 125.4, 102.6, 76.9, 46.0, 32.7, 31.3, 27.8, 20.7, 14.0, 9.2; GC–MS: *m/z* = 305 (M$^+$, 13), 288 (100), 262 (76), 232 (14), 206 (15), 176 (16), 149 (21), 121 (17); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{16}H_{20}NO_3S$)$^+$: 306.1158; found, 306.1164.

4.4.6. (Z)-6-(Benzylimino)-3-methyl-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno[3,2–d]pyran-1-one (6f)

Yield: 111.3 mg, starting from 120.3 mg of *N*-benzyl-3-(4-hydroxypent-1-yn-1-yl)thiophene-2-carboxamide (**5f**) (85%; Table 3, entry 10). Yellow solid, mp = 125–127 °C. IR (KBr): ν = 1721 (s), 1679 (s), 1621 (w), 1495 (w), 1410 (m), 1390 (m), 1337 (m), 1236 (m), 1119 (m), 1072 (w), 946 (m), 862 (w), 780 (m), 736 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.82 (dist d, J = 5.1, 1H), 7.48 (d, J = 5.1, 1H), 7.43–7.38 (m, 2H), 7.36–7.30 (m, 2H), 7.27–7.22 (m, 1H), 4.72 (s, 2H), 4.72–4.65 (m, 1H), 2.38 (dist dd, J = 17.6, 11.5, 1H), 2.74 (dist dd, J = 17.6, 4.1, 1H), 1.51 (d, J = 6.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.9, 162.7, 144.9, 139.2, 135.0, 131.1, 127.9, 127.1, 126.6, 126.2, 124.9, 102.3, 71.7, 49.4, 32.8, 21.1; GC–MS: *m/z* = 325 (M$^+$, 13), 207 (1), 91 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{18}H_{16}NO_3S$)$^+$: 326.0845; found, 326.0864.

4.4.7. (Z)-3-Methyl-6-(phenylimino)-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno[3,2–d]pyran-1-one (6g)

Yield: 79.4 mg, starting from 115.0 mg of 3-(4-hydroxypent-1-yn-1-yl)-*N*-phenylthiophene-2-carboxamide (**5g**) (63%; Table 3, entry 11). Yellow solid, mp = 188–189 °C. IR (KBr): ν = 1721 (s), 1666 (vs), 1590 (m), 1448 (w), 1485 (m), 1412 (w), 1336 (w), 1204 (m), 1070 (w), 951 (m), 862 (w), 781 (w), 749 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.87 (dist d, J = 5.1, 1H), 7.60 (d, J = 5.1, 1H), 7.36–7.28 (m, 2H), 7.23–7.16 (m, 2H), 7.14–7.07 (m, 1H), 4.72–4.61 (m, 1H), 2.78 (dist dd, J = 17.6, 11.7, 1H), 2.67 (dist dd, J = 17.6, 3.6, 1H), 1.48 (d, J = 6.3, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 163.1, 144.7, 144.0, 136.9, 135.0, 133.1, 128.8, 125.5, 124.3, 122.9, 103.2, 72.3, 33.2, 20.6; GC–MS: *m/z* = 311 (M$^+$, 81), 259 (19), 225 (100), 196 (30), 152 (20), 77 (82); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{14}NO_3S$)$^+$: 312.0689; found, 312.0671.

4.4.8. (5a,8a-cis,Z)-10-(Butylimino)-5a,6,7,8,8a,10-hexahydro-4H-cyclopenta[5,6]pyrano[4,3–b]thieno[3,2–d]pyran-4-one (racemic) (6h)

Yield: 78.2 mg, starting from 117.0 mg of *N*-butyl-3-((2-hydroxycyclopentyl)ethynyl)thiophene-2-carboxamide (**5h**) (61%; Table 3, entry 12). Yellow solid, mp = 80–81 °C. IR (KBr): ν = 1713 (s), 1678 (s), 1531 (w), 1413 (m), 1377 (w), 1234 (w), 1114 (m), 1075 (m), 980 (m), 957 (w), 783 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.91 (d, J = 5.2, 1H), 7.49 (dist d, J = 5.2, 1H), 5.05–5.01 (m, 1H), 3.55–3.45 (m, 2H), 2.96 (td, J = 9.0, 5.3, 1H), 2.37–2.27 (m, 1H), 2.25–2.15 (m, 1H), 2.12–2.01 (m, 2H), 1.98–1.80 (m, 2H), 1.65 (quint, J = 7.4, 2H), 1.42 (sextet, J = 7.4, 2H), 0.96 (t, J = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9, 162.8, 144.6, 135.3, 131.9, 127.2, 125.8, 100.8, 81.6, 46.0, 40.6, 33.3, 32.7, 30.3, 23.4, 20.7, 14.0; GC–MS: *m/z* = 317 (M$^+$, 15), 300 (96), 274 (100), 261 (9), 232 (25), 206 (17), 176 (18), 149 (27), 121 (29); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{20}NO_3S$)$^+$: 318.1158; found, 318.1143.

4.4.9. (Z)-6′-(Butylimino)-4′,6′-dihydro-1′H-spiro[cyclohexane-1,3′-pyrano[4,3–b]thieno[3,2–d]pyran]-1′-one (6i)

Yield: 69.8 mg, starting from 128.2 mg of *N*-butyl-3-(3-(1-hydroxycyclohexyl)prop-1-yn-1-yl)thiophene-2-carboxamide (**5i**) (50%; Table 3, entry 13). White solid, mp = 81–82 °C. IR (KBr): ν = 1713 (s), 1682 (s), 1533 (w), 1437 (m), 1412 (m), 1375 (m), 1362 (m), 1323 (w), 1234 (m), 1105 (m), 1070 (m), 984 (m), 939 (m), 853 (w), 777 (w), 754 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.87 (d, J = 5.1, 1H), 7.48 (dist d, J = 5.1, 1H), 3.50 (t, J = 7.1, 2H), 2.84 (s, 2H), 2.08–1.99 (m, 2H), 1.87–1.76 (m, 2H), 1.69–1.57 (m, 5H), 1.57–1.47 (m, 2H), 1.47–1.35 (m, 3H), 0.96 (t, J = 7.4, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.8, 162.2, 144.6, 135.3, 131.0, 127.1, 125.5, 102.2, 79.6, 46.0, 36.7, 36.4, 32.7, 25.1, 21.6, 20.6, 13.9; GC–MS: *m/z* = 345 (M$^+$, 21), 328 (100), 302 (53), 284 (49), 250 (19), 232 (37), 206 (42), 194 (29), 149 (21), 121 (21), 176 (36); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{19}H_{24}NO_3S$)$^+$: 346.1471; found, 346.1480.

4.4.10. (Z)-4-(Butylimino)-6,7-dihydro-4H,9H-pyrano[4,3–b]thieno[2,3–d]pyran]-9-one (8a)

Yield: 65.0 mg, starting from 101.0 mg of *N*-butyl-3-(3-(1-hydroxycyclohexyl)prop-1-yn-1-yl)thiophene-2-carboxamide (**7a**) (58%; Scheme 4). Yellow solid, mp = 189–190 °C. IR (KBr): ν = 1721 (s), 1682 (vs), 1620 (w), 1531 (w), 1456 (m), 1402 (w), 1360 (m), 1342 (w), 1281 (w), 1215 (m), 1194 (w), 1111 (m), 1082 (m), 993 (m), 922 (w), 748 (w) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.44 (dist d, J = 5.2, 1H), 7.34 (dist d, J = 5.2, 1H), 4.56 (t, J = 6.4, 2H), 3.51 (t, J = 7.2, 2H), 2.94 (t, J = 6.3, 2H), 1.65 (quint, J = 7.2, 2H), 1.44 (sextet, J = 7.2, 2H), 0.96 (t, J = 7.2, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.3, 162.2, 144.8, 136.8, 127.8, 125.2, 124.4, 102.7, 64.4, 45.9, 32.7, 26.2, 20.7, 13.9; GC–MS: *m/z* = 277 (M$^+$, 19), 260 (100), 234 (41), 221 (34), 193 (51), 149 (42), 121 (35); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{14}H_{16}NO_3S$)$^+$: 277.0845; found, 278.0862.

4.4.11. (Z)-4-(Benzylimino)-6,7-dihydro-4H,9H-pyrano[4,3–b]thieno[2,3–d]pyran]-9-one (8b)

Yield: 67.0 mg, starting from 115.3 mg of *N*-benzyl-2-(4-hydroxybut-1-yn-1-yl)thiophene-3-carboxamide (**7b**) (53%; Scheme 4). Yellow solid, mp = 102–104 °C. IR (KBr): ν = 1749 (s), 1706 (s), 1684 (s), 1457 (w), 1362 (w), 1229 (w), 1203 (m), 1115 (m), 996 (m), 759 (w), 692 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51 (d, J = 5.3, 1H), 7.45–7.40 (m, 2H), 7.37–7.32 (m, 3H), 7.28–7.23 (m, 1H), 4.73 (s, 2H), 4.56 (t, J = 6.3, 2H), 2.95 (t, J = 6.3, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.1, 162.0, 145.6, 140.0, 135.7, 129.0, 128.4, 127.9, 127.6, 126.7, 124.6, 103.1, 64.4, 49.9, 26.2; GC–MS: *m/z* = 311 (M$^+$, 12), 207 (5), 91 (100); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{17}H_{14}NO_3S$)$^+$: 312.0689; found, 312.0682.

4.4.12. (Z)-4-(Phenylimino)-6,7-dihydro-4H,9H-pyrano[4,3–b]thieno[2,3–d]pyran]-9-one (8c)

Yield: 60.3 mg, starting from 109.2 mg of 2-(4-hydroxybut-1-yn-1-yl)-*N*-phenylthiophene-3-carboxamide (**7c**) (50%; Scheme 4). Yellow solid, mp = 158–160 °C. IR (KBr): ν = 1720 (m), 1712 (m), 1659 (s), 1588 (m), 1529 (m), 1483 (m), 1462 (w), 1364 (w), 1227 (w), 1077 (w), 1002 (m), 770 (m), 689 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.60 (d, J = 5.1, 1H), 7.45 (dist d, J = 5.1, 1H), 7.41–7.31 (m, 2H), 7.22–7.07 (m, 3H), 4.54 (t, J = 6.3, 2H), 2.88 (t, J = 6.3, 2H); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.0, 161.9, 145.0, 140.2, 137.3, 129.4, 128.9, 128.5, 124.8, 124.2, 122.4, 103.5, 64.4, 26.1; GC–MS: *m/z* = 297 (M$^+$, 100), 225 (53), 196 (29), 153 (3), 136 (10), 120 (9), 77 (60); HRMS-ESI (*m/z*): [(M + H)$^+$] calcd for ($C_{16}H_{12}NO_3S$)$^+$: 298.0532; found, 198.0531.

4.5. Procedure for the synthesis of (Z)-6-(butylimino)-4,6-dihydro-1H,3H-pyrano[4,3–b]thieno[3,2–d]pyran-1-one (6a) in larger scale

A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (30.6 mg, 0.085 mmol), KI (142 mg, 085 mmol) and a solution of **5a** (427 mg, 1.70 mmol) in a mixture $HC(OMe)_3$ (11.4 mL)−MeCN (5.6 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (5 bar) and air (35 bar). After being stirred 80 °C for 15 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and product **6a** was purified by column chromatography on silica gel using as eluent 90:10 hexane-AcOEt to 70:30 hexane-AcOEt (378 mg, 73%).

CRediT authorship contribution statement

Raffaella Mancuso: Validation, Methodology, Investigation, Conceptualization. **Patrizio Russo:** Validation, Methodology, Investigation, Conceptualization. **Haritha Kumari Arram:** Validation, Methodology, Investigation. **Antonio Palumbo Piccionello:** Investigation. **Nicola Della Ca':** Validation, Methodology. **Angela Altomare:** Validation, Investigation. **Bartolo Gabriele:** Writing – review & editing, Writing – original draft, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The research leading to these results received funding from the Ministero dell'Università e della Ricerca (MUR, Italy), PRIN Project COXSECAT, grant no 20223B4JWC 'Valorization of carbon oxides by sequential catalysis: Combining the reverse water gas shift reaction with catalytic carbonylation for the synthesis of high value added compounds' (B.G.).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcat.2026.116918.

Data availability

Data will be made available on request.

References

[1] A. Borissov, Y.K. Maurya, L. Moshniaha, W.-S. Wong, M. Żyła-Karwowska, M. Stępień, Chem. Rev. 122 (2022) 565–788.
[2] M. Stępień, E. Gońka, M. Żyła, N. Sprutta, Chem. Rev. 117 (2017) 3479–3716.
[3] I. Kadi, G. Şekerci, H. Boulebd, Z. Zebbiche, S. Tekin, H. Küçükbay, F. Küçükbay, T. Boumoud, J. Mol. Struct. 1271 (2023) 134054.
[4] E. Kabir, M. Uzzaman, Results Chem. 4 (2022) 100606.
[5] K. Aknin, A. Bontemps, A. Farce, E. Merlet, P. Belmont, P. Helissey, P. Chavatte, M.-A. Sari, S. Giorgi-Renault, S. Desbène-Finck, J. Enzyme Inhib. Med. Chem. 37 (2021) 252–268.
[6] F. Salehian, H. Nadri, L. Jalili-Baleh, L. Youseftabar-Miri, S.N.A. Bukhari, A. Foroumadi, T.T. Küçükkilinç, M. Sharifzadeh, M. Khoobi, Eur. J. Med. Chem. 212 (2021) 113034.
[7] A. Ghosh, R.G. Carter, Angew. Chem. Int. Ed. 58 (2019) 681–694.
[8] K. Passador, S. Thorimbert, C. Botuha, Synthesis 51 (2019) 384–398.
[9] I.K. Hyland, R.F. O'Toole, J.A. Smith, A.C. Bissember, ChemMedChem 13 (2018) 1873-1884.
[10] F. Hemmerling, F. Hahn, Beilstein J. Org. Chem. 12 (2016) 1512–1550.
[11] E.A. Shokova, V.V. Kovalev, Pharm. Chem. J. 50 (2016) 63–75.
[12] M. Fizer, M. Slivka, Chem. Heterocycl. Compd. 52 (2016) 155–157.
[13] A. Molnár, Coord. Chem. Rev. 504 (2024) 215668.
[14] Z. Jin, G. Shen, X. Lv, Chin. J. Chem . 41 (2023) 3751–3771.
[15] X. Tang, L. Song, E.V. Van der Eycken, Chem. Rec. 23 (2023) e202300095.
[16] B. Gabriele, R. Mancuso, L. Veltri, I. Ziccarelli, N. Della Ca', Catalysts 13 (2023) 1025.
[17] B. Gabriele, R. Mancuso, L. Veltri, I. Ziccarelli, N. Della Ca', Eur. J. Org. Chem. 2019 (2019) 5073–5092.
[18] B. Gabriele (Ed.), Carbon Monoxide in Organic Synthesis – Carbonylation Chemistry, Wiley-VCH, Weinheim, 2022.
[19] J.-B. Peng, H.-Q. Geng, X.-F. Wu, Chem 5 (2018) 526–552.
[20] M. Novello, R. Mancuso, B. Gabriele, X.-F. Wu, Chem. Commun. 62 (2026) 5625–5650.
[21] Y. Yuan, C.-S. Kuai, X.-F. Wu, Chem. Commun. 62 (2026) 1440–1458.
[22] H. Yang, X.-F. Wu, Chem. Commun. 61 (2025) 18327–18339.
[23] R. Mancuso, N. Della Ca', L. Veltri, I. Ziccarelli, B. Gabriele, Catalysts 9 (2019) 610.
[24] B. Gabriele, Targets Heterocycl Syst. 22 (2018) 41–55.
[25] B. Gabriele, G. Salerno, PdI_2, in: D. Crich (Ed.), *e*-EROS (electronic Encyclopedia of Reagents for Organic Synthesis), Wiley-Interscience, New York, 2006.
[26] B. Gabriele, Tetrahedron Chem 12 (2024) 100107.
[27] B. Gabriele, R. Mancuso, G. Salerno, Eur. J. Org. Chem. 2012 (2012) 6825–6839.
[28] B. Gabriele, G. Salerno, M. Costa, Top. Organomet. Chem. 18 (2006) 239–272.
[29] R. Mancuso, P. Russo, A. De Salvo, H.K. Arram, S. Tropiano, C. Cuocci, D. Olivieri, C. Carfagna, N. Della Ca', B. Gabriele, J. Catal. 452 (2025) 116437.
[30] I. Ziccarelli, R. Mancuso, D. Santandrea, A. Altomare, D. Olivieri, C. Carfagna, B. Gabriele, J. Catal. 427 (2023) 115101.
[31] R. Mancuso, A. De Salvo, P. Russo, A. Falcicchio, N. Della Ca', L. Pantoja Munoz, B. Gabriele, Chin. J. Chem . 41 (2023) 2801–2809.
[32] R. Mancuso, P. Russo, M. Lettieri, D. Santandrea, C. Cuocci, B. Gabriele, Adv. Synth. Catal. 364 (2022) 3917–3926.
[33] R. Mancuso, P. Russo, R. Miliè, M. Dell'Aera, F. Grande, N. Della Ca', B. Gabriele, Catal. Today 397-399 (2022) 631-638.
[34] F. Pancrazzi, N. Sarti, P.P. Mazzeo, A. Bacchi, C. Carfagna, R. Mancuso, B. Gabriele, M. Costa, A. Stirling, N. Della Ca', Org. Lett. 22 (2020) 1569-1574.
[35] R. Ali, R. Siddiqui, RSC Adv. 12 (2022) 36073–36102.
[36] A. Ishii, N. Nakata, J. Synth. Org. Chem Jpn. 76 (2018) 1042–1054.
[37] I.F. Perepichka, D.F. Perepichka, Handbook of Thiophene-based Materials: applications in Organic Electronics and Photonics, Wiley-VCH, Weinheim, 2009.
[38] A.E. Kassab, E.M. Gedawy, A.S. Sayed, Int. J. Biol. Macromol. 265 (2024) 131018.
[39] S. Pandey, S. Aggarwal, R. Choudhary, S.K. Awashti, RSC Adv. 12 (2022) 15787–15813.
[40] M.A. Gouda, A.A. Abu-Hashem, A.A.M. Abdelgawad, Mini-Rev. Org. Chem. 19 (2022) 629–653.
[41] C. Yang, L.P. Slavětínská, M. Fleuti, B. Klepetářová, M. Tichý, S. Gurská, P. Pavliš, P. Džubák, M. Hajdúch, M. Hocek, J. Am. Chem. Soc. 144 (2022) 19437.
[42] L. Gayatri, L. Brewitz, E. Ibbotson, S. Salah, H. Basak, C.J. Choudhry, Schofield, Chem. Sci. 15 (2024) 7667–7678.
[43] S. Liu, G.-J. Deng, H. Huang, Synlett 32 (2021) 142–158.
[44] J. Dong, Y. Lv, Y. Li, K. Xu, X. Cui, C.-Y. Guo, B. Li, J. Org. Chem. 90 (2025) 5845–5855.
[45] A. Acharya, V. Gautam, H. Ila, J. Org. Chem. 82 (2017) 7920.
[46] R. Mancuso, P. Russo, I. Ziccarelli, M. Lettieri, A. Altomare, M. Tiecco, E. Mosconi, T. Moretti, B. Gabriele, Chem Eur J 31 (2025) e202500081.
[47] F.A. Carey, R.J. Sundberg, *Advanced Organic Chemistry, Part B: Reactions and Synthesis*, 5th Ed., Springer, New York, 2007, p. 230.
[48] N. T. Subasi (Ed.), *Overview of Schiff Bases*, IntechOpen, 2023 (DOI: 10.5772/intechopen.104134).
[49] We also tried to synthesize a substrate bearing a primary amido group, by allowing to react 3-bromothiophene-2-carboxamide with 2-methylbut-3-yn-2-ol under the same Sonogashira coupling conditions used for the preparation of substrates **1**. However, only small amounts of the desired product could be isolated at the pure state from the reaction mixture.
[50] We are currently testing our products as possible antitumor agents, in particular against breast cancer cells, with promising results. The derivative that has so far shown the best activity is (*Z*)-5-(butylimino)-1'*H*,5'*H*-spirocyclopentane-1,3'-furo[3,4-*b*]thieno[3,2-*d*]pyran-1'-one (**2d**). Full details on biological data will be reported in due course.