Journal of Catalysis 427 (2023) 115101

Contents lists available at ScienceDirect

Journal of Catalysis

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

Synthesis of benzothienofuranones and dihydrobenzothienopyranones by palladium iodide-catalyzed carbonylative double cyclization

Ida Ziccarelli [a], Raffaella Mancuso [a,*], Domenico Santandrea [a], Angela Altomare [b], Diego Olivieri [c], Carla Carfagna [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] Institute of Crystallography, National Research Council, Via Amendola, 122/O, 70126 Bari, Italy
[c] Department of Biomolecular Sciences, University of Urbino "Carlo Bo", Piazza Rinascimento 6, 61029 Urbino (PU), Italy
[d] Department of Industrial Chemistry "T. Montanari", University of Bologna, Viale Risorgimento 4, 40136 Bologna, Italy

ARTICLE INFO

Keywords:
Carbonylation
Cyclization
Double cyclization
Heterocycles
Polycyclic heterocycles
Palladium

ABSTRACT

3-(2-(Methylthio)phenyl)prop-2-yn-1-ols have been successfully converted in one synthetic step into benzo[4,5]thieno[2,3-c]furan-1-ones by a PdI_2/KI-catalyzed oxidative carbonylative double cyclization process, performed in MeCN under relative mild conditions (1–10 mol % PdI_2, 7 equiv of KI, 80 °C, 60 atm of a 4:1 mixture CO–air). The process takes place through an ordered sequence of steps, involving 5-*endo-dig S*-cyclization, iodide-promoted demethylation of the ensuing sulfonium salt, CO insertion, a second cyclization (possibly, through the formation of a palladacycle intermediate followed by reductive elimination), and Pd(0) reoxidation by oxygen (from air) used as external benign oxidant. Under similar conditions, 4-(2-(methylthio)phenyl)but-3-yn-1-ols, bearing a butynol moiety *ortho* to the methylthio group, led to a mixture of double cyclization and dicarbonylation products, however, by slightly tuning the reaction conditions, dihydrobenzo[4,5]thieno[3,2-c]pyran-1-ones could be selectively obtained with no formation of the dicarbonylated byproduct. The structures of four representative products, including two tetracyclic derivatives, have been confirmed by XRD analysis.

1. Introduction

Palladium-catalyzed double cyclization processes represent a powerful method for the one-step synthesis of polycyclic heterocycles starting from readily available substrates [1]. When promoted by Pd(II) species, these reactions usually involve the use of a suitably substituted substrate bearing an unsaturated carbon–carbon bond [which becomes electrophilically activated by coordination to the Pd(II) center] and two nucleophilic moieties in appropriate positions [1].

Of particular interest are those reactions in which the palladium catalyst is also able to promote carbon monoxide incorporation into one of the two newly formed cycles, as in this case the double cyclization is accompanied by carbonylation [2], with direct formation of carbonyl-functionalized fused heterocycles [3]. Although several examples of carbonylative oxygen and/or nitrogen double cyclization have been reported [3], also in the most recent literature [4–6], processes involving *S*-cyclization are much less common (for recent examples of carbonylative *S*-cyclization reactions, see references [7–12]). In fact, to the best of our knowledge, the only example of Pd-catalyzed carbonylative *S*,*O* double cyclization has been recently disclosed by our research group [8]. The reaction, catalyzed by the PdI_2/KI catalytic system [13–16], took place under oxidative carbonylation conditions and led to the formation of 6,6a-dihydrothieno[3,2-*b*]furan-2(5*H*)-ones starting from 5-(methylthio)pent-1-yn-3-ols, resulting from an *S*-5-*exo-dig* cyclization – *O*-5-cyclocarbonylation process as shown in Scheme 1a [8].

In this work, we have studied the possibility to extend our oxidative carbonylation methodology to the use of 3-(2-(methylthio)phenyl)prop-2-yn-1-ols **1** and 4-(2-(methylthio)phenyl)but-3-yn-1-ols **3**, with the aim of realizing another example of carbonylative *S*,*O* double cyclization process leading to tricyclic heterocycles **2** and **4**, respectively (Scheme 1b). As in our previous oxidative carbonylative *S*-cyclizations [7,8,10], also in this case it was necessary to protect the sulfur atom of the substrates with a methyl group (readily removable under the reaction conditions), as a free sulfhydryl –SH group would have been unstable under the oxidative conditions employed. It is worth noting at this point

* Corresponding authors.
E-mail addresses: raffaella.mancuso@unical.it (R. Mancuso), bartolo.gabriele@unical.it (B. Gabriele).

https://doi.org/10.1016/j.jcat.2023.115101
Received 7 July 2023; Received in revised form 20 August 2023; Accepted 21 August 2023
Available online 22 August 2023

that we have previously reported that it is instead possible to employ substrates bearing a free phenolic group under basic conditions (in situ leading to the phenate anion) to trigger an *O*,*O* carbonylative double cyclization process, in the conversion of 2-(3-hydroxy-1-yn-1-yl)phenols into furobenzofuranone derivatives [17].

With substrates **1** and **3**, differently from the process leading to thienofuranones (Scheme 1a) [8], the initial *S*-cyclization should occur in a 5-*endo-dig* cyclization fashion, and would be followed by either *O*-5-cyclocarbonylation (in the case of substrates **1**, to give benzo[4,5]thieno[2,3-*c*]furan-1-ones **2**) or *O*-6-cyclocarbonylation (in the case of **3**, to give **4**). To the best of our knowledge, the only *S*-cyclization method reported so far for the preparation of benzo[4,5]thieno[2,3-*c*]furan-1-one derivatives (3 examples) was based on the reaction between tetronic acid and 2-iodothiophenols [18], while another method (not involving *S*-cyclization) was based on deprotonation of benzo[*b*]thiophene-3-carboxylic acid with LDA followed by reaction with ketones and lactonization with benzenesulfonyl chloride/pyridine (2 examples) [19]. On the other hand, no *S*-cyclization method has been reported so far for the preparation of 3,4-dihydrobenzo[4,5]thieno[2,3-*c*]pyran-1-ones. The only method reported in the literature for the preparation of these derivatives (2 examples) involved the reaction between 2-methylbenzo[*b*]thiophene-3-carbaldehyde and α-trifluoromethyl ketones [20] (for methods leading to related benzothienopyranone derivatives, see references [21–24]).

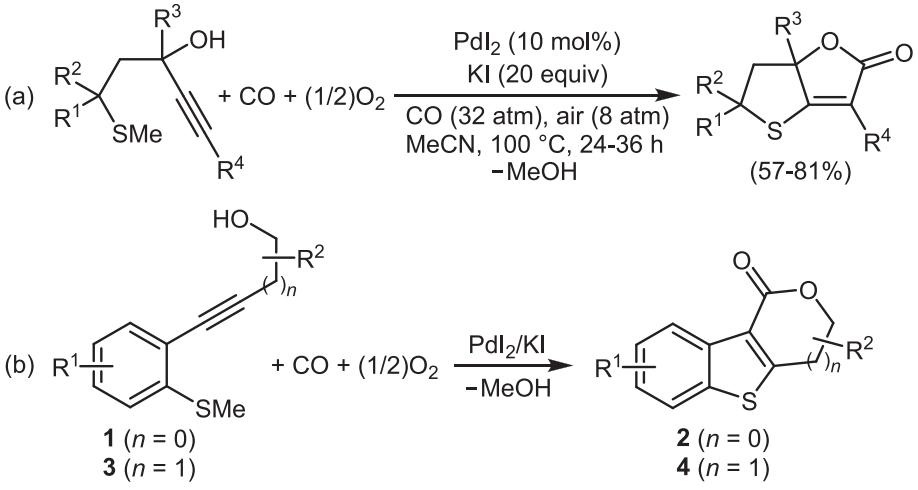
2. Results and discussion

To verify our work hypothesis, shown in Scheme 1b, we initially synthesized 4-(2-(methylthio)phenyl)but-3-yn-2-ol **1a** by Sonogashira coupling between 2 and iodo-1-methylthiobenzene and but-3-yn-2-ol (see the Supporting Information for details) and allowed it to react under conditions similar to those employed for 5-(methylthio)pent-1-yn-3-ols. With 10 mol% PdI_2 in conjunction with 10 equiv of KI, in MeCN as the solvent (0.02 mmol of starting **1a** per mL of MeCN) at 80 °C and under 40 atm (initial pressure) of a 4:1 mixture of CO-air, after 15 h substrate conversion was quantitative, and from the reaction mixture a carbonylated product was recovered that corresponded to the desired 3-methylbenzo[4,5]thieno[2,3-*c*]furan-1(3*H*)-one **2a** (63% yield; Table 1, entry 1). The structure of **2a** was confirmed by XRD analysis (Fig. 1; see the Supporting Information for full XRD data).

This encouraging preliminary result prompted us to carry out a brief optimization study in order to possibly improve the product yield (Table 1, entries 2–8). A higher **2a** yield was observed by decreasing the amount of KI to 7 equiv (70%; Table 1, entry 2) or by increasing the total pressure to 60 atm (68%; Table 1, entry 3). On the other hand, the product yield decreased when further decreasing the amount of KI to 5 equiv (**2a** yield, 52%; Table 1, entry 4), by performing the process under 20 atm total pressure (**2a** yield, 49%; Table 1, entry 5), starting with a higher substrate concentration (0.05 mmol/mL of MeCN; **2a** yield, 50%; Table 1, entry 6), changing the solvent to 1,2-dimethoxyethane (DME; **2a** yield, 40%; Table 1, entry 7), or raising the reaction temperature to 100 °C (Table 1, entry 8; **2a** yield, 55%). Accordingly, the optimized conditions corresponded to the use of 10 mol% PdI_2 in conjunction with 7 equiv of KI, in MeCN as the solvent (0.02 mmol of starting **1a** per mL of MeCN) at 80 °C and under 60 atm (initial pressure) of a 4:1 mixture of CO-air for 15 h. Under these conditions, the benzothienofuranone product **2a** was obtained in 77% isolated yield (Table 2, entry 1).

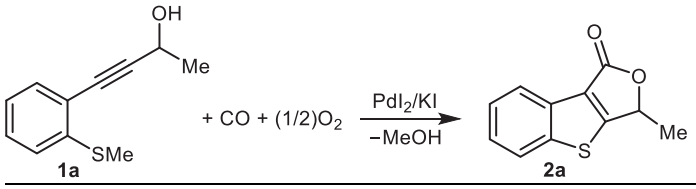
We then assessed the reaction scope by applying the optimized conditions to different 3-(2-(methylthio)phenyl)prop-2-yn-1-ols **1b-1 k**, bearing various substituent of the aromatic ring as well as α to the hydroxyl group, and the results obtained are shown in Table 2, entries 2–11. As can be seen from Table 2, fair to good product yields were obtained in all cases, including the synthesis of spiro derivatives **2g** and **2h** (obtained in 61% and 69% yields, entries 7 and 8). Only the α,α-diphenyl substituted substrate **1j** led to a modest yield of the corresponding benzothienofuranone **2j** (40%; Table 2, entry 10), probably for steric reasons.

Mechanistically, according to our previous studies [7–10], the process starts with a 5-*endo-dig* nucleophilic attack of sulfur to the triple bond coordinated to the Pd(II) center to give the sulfonium salt **I** (Scheme 2; anionic iodide ligands are omitted for clarity). This is followed by sulfur demethylation by the iodide anion, with formation of a vinylpalladium intermediate **II** and methyl iodide. The latter is attacked by water (initially present in the reaction mixture as an impurity, and then also formed in the palladium reoxidation process) to give MeOH and one mole of HI. On the other hand, intermediate **II** undergoes carbon monoxide insertion followed by intramolecular nucleophilic displacement by the hydroxyl group (possibly through the formation of palladacycle intermediate **III**) to give a second mol of HI, product **2** and Pd(0). Finally, Pd(0) is oxidized back to PdI_2 by the action of I_2, formed in its turn by oxidation of 2 mol of HI with oxygen (Scheme 2). It is worth noting that we recently reported that substrates bearing a simple alkyl or aryl group on the triple bond (2-(methylthio)phenylacetylenes), for which a second cyclization is clearly impossible, underwent *S*-cyclization followed by CO insertion and intramolecular nucleophilic displacement by an alcohol as external nucleophile, to give



Scheme 1. PdI_2-catalyzed carbonylative *S*,*O* double cyclization of: (a) 5-(methylthio)pent-1-yn-3-ols leading to 6,6a-dihydrothieno[3,2-*b*]furan-2(5*H*)-ones [8] and (b) *This work:* 3-(2-(methylthio)phenyl)prop-2-yn-1-ols **1** and 4-(2-(methylthio)phenyl)but-3-yn-1-ols **3** to give benzo[4,5]thieno[2,3-*c*]furan-1-ones **2** and 3,4-dihydrobenzo[4,5]thieno[3,2-*c*]pyran-1-ones **4**, respectively.

Table 1
PdI_2/KI-catalyzed oxidative carbonylation of 4-(2-(methylthio)phenyl)but-3-yn-2-ol **1a** under different conditions.[a]



Entry	PdI_2/**1a**/KI molar ratio	Solvent	T [°C]	P_{CO} (atm)	P_{air} (atm)	Concn. of **1a**[b]	Yield of **2a** (%)[c]
1	1:10:100	MeCN	80	32	8	0.02	63
2	1:10:70	MeCN	80	32	8	0.02	70
3	1:10:100	MeCN	80	48	12	0.02	68
4	1:10:50	MeCN	80	32	8	0.02	52
5	1:10:100	MeCN	80	16	4	0.02	49
6	1:10:100	MeCN	80	32	8	0.05	50
7	1:10:100	DME	80	32	8	0.02	40
8	1:10:100	MeCN	100	32	8	0.02	55

[a] All reactions were carried out for 15 h.
[b] Mmol of **1a** at start per mL of MeCN.
[c] Isolated yield based on starting **1a**. Substrate conversion was quantitative in all cases.

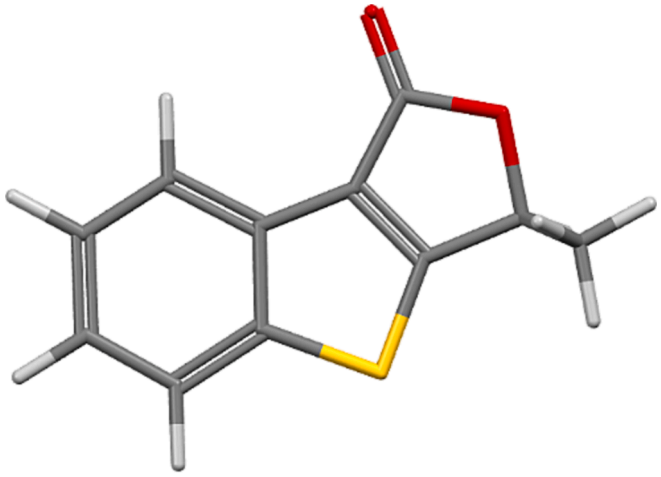


Fig. 1. X-ray molecular structure of 3-methylbenzo[4,5]thieno[2,3-*c*]furan-1(3*H*)-one **2a**.

benzothiophene-3-carboxylic esters [7].

We then moved to assess the reactivity of the higher homologues of **1**, namely, 4-(2-(methylthio)phenyl)but-3-yn-1-ols **3**, bearing a butynol moiety *ortho* to the methylthio group. With these substrates, we expected the double cyclization to be more difficult with respect to **1**, owing to the higher degrees of freedom of the butynol moiety compared to the propargylalcoholic one. We began our investigation by allowing to react 4-(2-(methylthio)phenyl)but-3-yn-1-ol **3a** under the conditions optimized for substrates **1** [10 mol% PdI_2 in conjunction with 7 equiv of KI, in MeCN as the solvent (0.02 mmol of **3a** per mL of MeCN) at 80 °C, under 60 atm of a 4:1 mixture of CO-air]. After 15 h, the reaction led to the formation of two carbonylated products, namely, the desired 3,4-dihydro-1*H*-benzo[4,5]thieno[3,2-*c*]pyran-1-one **4a** (41% yield) and methyl (*Z*)-2-(2-(methylthio)phenyl)-2-(2-oxodihydrofuran-3(2*H*)-ylidene)acetate **5a** (10% yield) (Table 3, entry 1). The structure of **4a** was confirmed by XRD analysis (Fig. 2; see the Supporting Information for full XRD data).

Dicarbonylated product **5a** derived from a competitive oxidative dicarbonylation of the triple bond, according to a known reactivity [13–16] (Scheme 3, pathway *b*). The MeOH incorporated into the estereal function of **5a** clearly ensued from the double cyclization process leading to **4a**, occurring in a similar manner as seen for the formation of products **2** (Scheme 3, pathway *a*).

Interestingly, the process turned out to be selective toward the formation of the desired double cyclization product **4a** when carried out under more concentrate conditions (0.10 mmol of **3a** per mL of MeCN): after 3 h, substrate conversion was complete with formation of **4a** in 78% isolated yields and only traces of **5a** (Table 3, entry 2). Moreover, the reaction could also be successfully performed with a lower catalyst loading (1–2 mol%) with a reaction time of 15 h, still with excellent results (Table 3, entries 3 and 4).

Under the conditions optimized for **3a**, other differently substituted 4-(2-(methylthio)phenyl)but-3-yn-1-ols **3b-l**, were selectively converted into the corresponding benzo[4,5]thieno[3,2-*c*]pyran-1-ones **4b-l** in 55–79 % yields (Table 3, entries 5–15). As can be seen from Table 3, the method worked nicely with substrates bearing a primary, secondary, tertiary, or benzylic alcoholic group (substrates **3b-j**) and also in the case of 2-cyclohexanol and 2-cyclopentanol moieties bonded to the triple bond (substrates **3k** and **3l**, respectively). In the latter two cases, fused tetracyclic compounds **4k** and **4l** were obtained, and the *trans* junction between the C and D rings in both compounds was confirmed by XRD analysis (Fig. 3; see the Supporting Information for full XRD data).

3. Conclusion

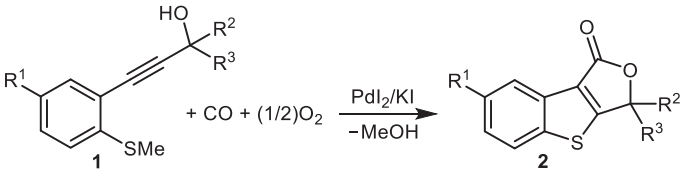
In conclusion, we have studied the reactivity of 3-(2-(methylthio)phenyl)prop-2-yn-1-ols and 4-(2-(methylthio)phenyl)but-3-yn-1-ols under PdI_2/KI-catalyzed oxidative carbonylation conditions, and found appropriate conditions for selectively achieving a carbonylative double cyclization process leading to fused heterocyclic derivatives in one step. The reaction represents the first example of carbonylative *S*-cyclization leading to benzo[4,5]thieno[3,2-*c*]furan-1-ones and 3,4-dihydrobenzo[4,5]thieno[3,2-*c*]pyran-1-ones, and takes place through an ordered sequence of mechanistic steps. In particular, an initial *S*-cyclization [from intramolecular 5-*endo-dig* attack of the methylthio group to the triple bond coordinated to Pd(II] is followed by iodide-promoted demethylation, carbon monoxide insertion, a second cyclization (via intramolecular nucleophilic displacement), and Pd(0) reoxidation (with O_2 from air as benign external oxidant). The structures of four representative products, including two tetracyclic derivatives, have been confirmed by XRD analysis.

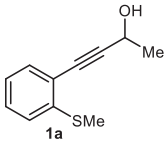
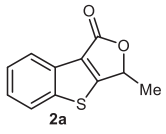
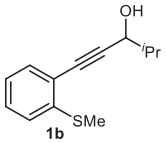
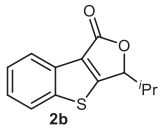
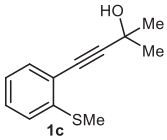
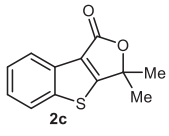
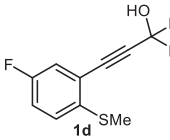
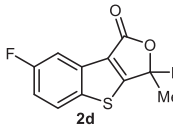
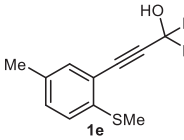
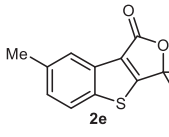
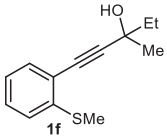
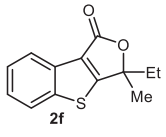
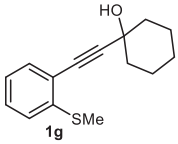
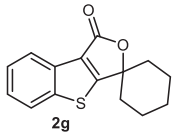
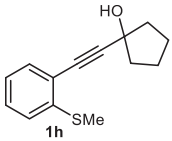
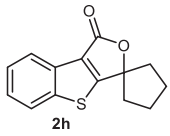
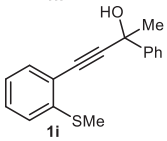
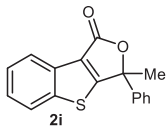
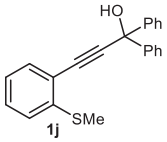
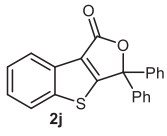
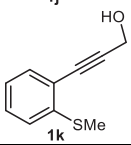
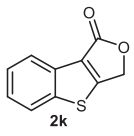
4. Experimental section

4.1. General methods

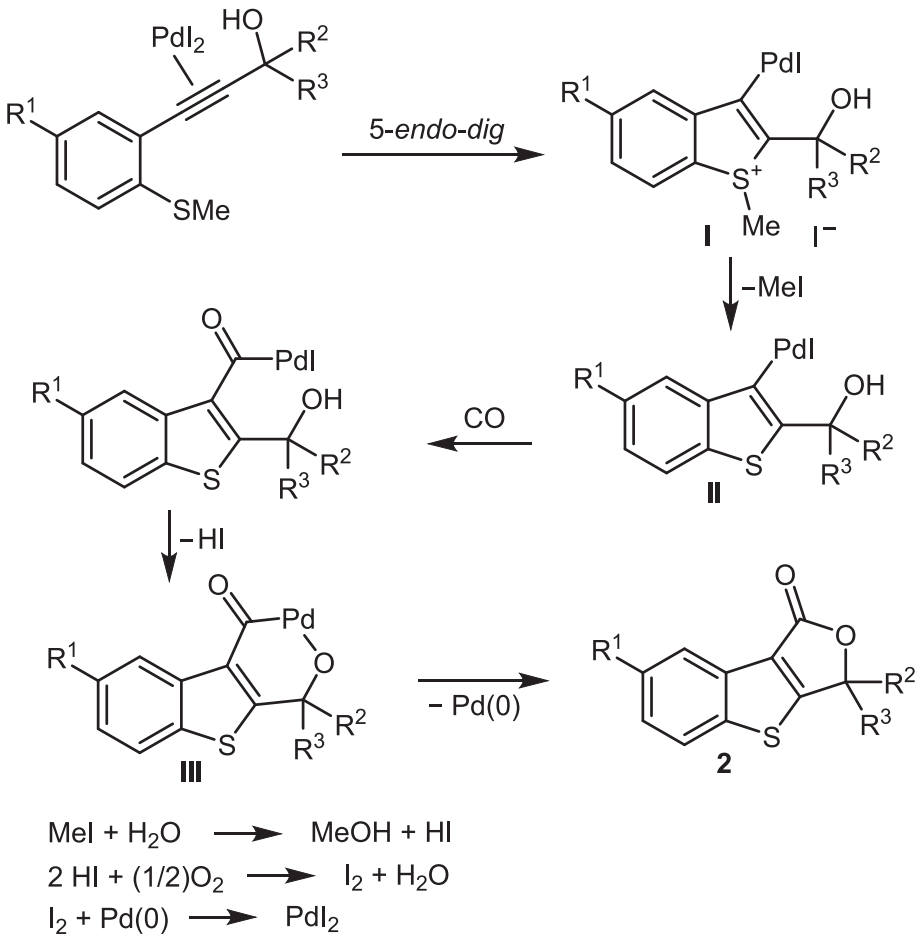
Solvent and chemicals were reagent grade and were used without further purification. All reactions were analyzed by TLC on silica gel 60

Table 2
Synthesis of benzo[4,5]thieno[2,3-*c*]furan-1-ones **2** by PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 3-(2-(methylthio)phenyl)prop-2-yn-1-ols **1**.[a]



Entry	1	2	Yield of **2** (%)[b]
1	 **1a**	 **2a**	77
2	 **1b**	 **2b**	64
3	 **1c**	 **2c**	79
4	 **1d**	 **2d**	83
5	 **1e**	 **2e**	74
6	 **1f**	 **2f**	76
7	 **1g**	 **2g**	61
8	 **1h**	 **2h**	69
9	 **1i**	 **2i**	52
10	 **1j**	 **2j**	40
11	 **1k**	 **2k**	55

[a] All reactions were carried out at 80 °C for 15 h in MeCN (0.02 mmol of **1** per mL of MeCN) under 60 atm of a 4:1 mixture of CO–air, in the presence of 10 mol% of PdI_2 and 7 equiv of KI.
[b] Isolated yield based on starting **1**.



Scheme 2. Mechanistic hypothesis leading to benzo[4,5]thieno[2,3-*c*]furan-1-ones **2**.

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)). 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 $CDCl_3$ 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.

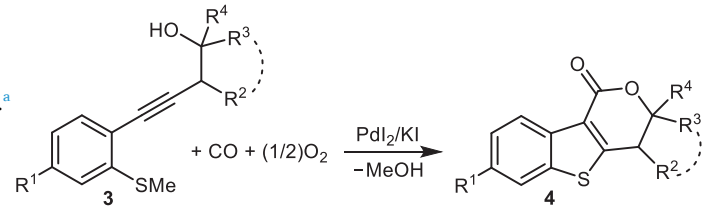
4.2. General procedure for the synthesis of benzo[4,5]thieno[2,3-c]furan-1-ones 2 from 3-(2-(methylthio)phenyl)prop-2-yn-1-ols 1 (Table 2)

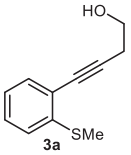
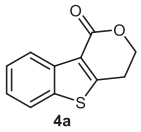
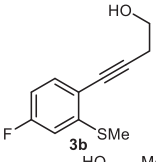
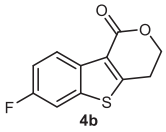
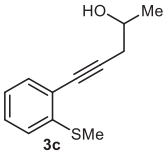
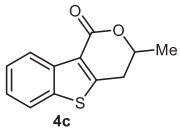
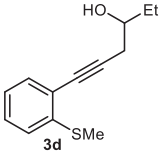
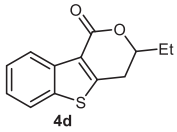
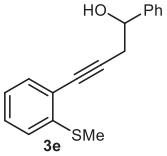
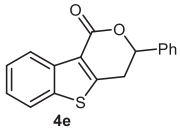
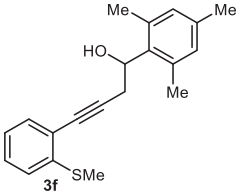
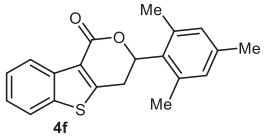
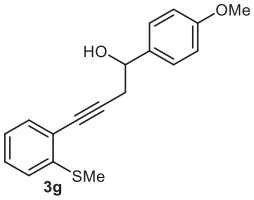
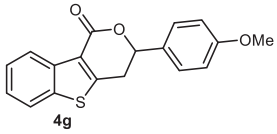
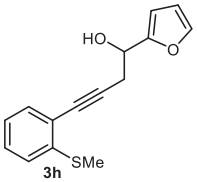
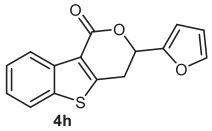
A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (12.0 mg, 3.33×10^{-2} mmol), KI (387 mg, 2.33 mmol) and a solution of **1** (0.33 mmol; **1a**, 63.7 mg; **1b**, 72.5 mg; **1c**, 68.9 mg; **1d**, 74.4 mg; **1e**, 73.1 mg; **1f**, 72.9 mg; **1g**, 82.2 mg; **1h**, 77.6 mg; **1i**, 89.0 mg; **1j**, 110.2 mg; **1k**, 59.5 mg) in MeCN (16.5 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (48 atm) and air (12 atm). After being stirred at 80 °C for 15 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **2a-k** were purified by column chromatography on silica gel using as eluent hexane–AcOEt from 100:0 to 90:10 (for **2a**, **2c**, **2e**, and **2 h**); hexane–AcOEt from 100:0 to 99:1 for **2b**, **2g**, **2i,** and **2j**; hexane–AcOEt from 100:0 to 95:5 (for **2d** and **2f**); hexane–AcOEt from 100:0 to 80:20 (for **2k**).

3-Methylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2a**). Yield: 52.4 mg, starting from 63.7 mg of 4-(2-(methylthio)phenyl)but-3-yn-2-ol **1a** (77%; Table 2, entry 1). Yellow solid, mp = 68–69 °C. IR (KBr): ν = 1751 (s) 1567 (w), 1470 (m), 1435 (m), 1377 (w), 1304 (w), 1142 (m), 1042 (m), 976 (m), 910 (w), 783 (m), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.0, 1H, H-8), 7.85 (d, *J* = 8.1, 1H, H-5), 7.53–7.47 (m, 1H, H-6 or H-7), 7.47–7.41 (m, 1H, H-7 or H-6), 5.69 (q, *J* = 6.8, 1H, C*H*CH$_3$), 1.72 (d, *J* = 6.8, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.4, 165.2, 145.2, 130.9, 128.4, 126.2, 126.0, 123.5, 122.9, 76.5, 21.1; GC–MS: *m/z* = 204 (M^+, 26), 189 (16), 161 (100), 133 (23), 115 (8), 89 (31); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{11}H_9O_2S$)$^+$: 205.0318; found, 205.0310.

3-Isopropylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2b**). Yield: 49.2 mg, starting from 72.5 mg of 4-methyl-1-(2-(methylthio)phenyl)pent-1-yn-3-ol **1b** (64%; Table 2, entry 2). White solid, mp = 117–118 °C. IR

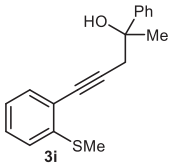
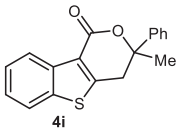
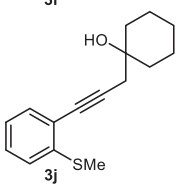
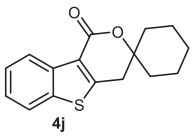
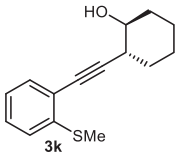
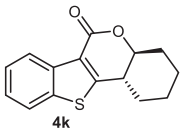
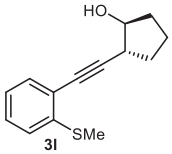
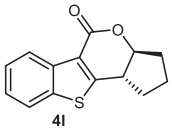
Table 3
Synthesis of 3,4-dihydrobenzo[4,5]thieno[3,2-*c*]pyran-1-ones **4** by PdI_2/KI-catalyzed oxidative carbonylative double cyclization of 4-(2-(methylthio)phenyl)but-3-yn-1-ols **3**.[a]



Entry	3	4	Yield of **4** (%)[b]
1[c]	 **3a**	 **4a**	41[d]
2	**3a**	**4a**	78
3[e]	**3a**	**4a**	77
4[f]	**3a**	**4a**	80
5	 **3b**	 **4b**	55
6	 **3c**	 **4c**	73
7	 **3d**	 **4d**	70
8	 **3e**	 **4e**	79
9[g]	 **3f**	 **4f**	74
10	 **3g**	 **4g**	70
11	 **3h**	 **4h**	60

(*continued on next page*)

Table 3 (*continued*)

Entry	3	4	Yield of **4** (%)[b]
12[h]			79
13[h]			63
14			76
15			66

[a] Unless otherwised noted, all reactions were carried out at 80 °C for 3 h in MeCN (0.10 mmol of **3** per mL of MeCN) under 60 atm of a 4:1 mixture of CO–air, in the presence of 10 mol% of PdI_2 and 7 equiv of KI.
[b] Isolated yield based on starting **3**.
[c] The reaction was carried out for 15 h with a substrate concentration of 0.02 mmol per mL of MeCN.
[d] The reaction also led to the formation of methyl (*Z*)-2-(2-(methylthio)phenyl)-2-(2-oxodihydrofuran-3(2*H*)-ylidene)acetate **5a** in 10% isolated yield.
[e] The reaction was carried out for 15 h with a PdI_2/KI/**3a** molar ratio of 1:350:50.
[f] The reaction was carried out for 15 h with a PdI_2/KI/**3a** molar ratio of 1:700:100.
[g] The reaction was carried out for 5 h.
[h] The reaction was carried out for 15 h.

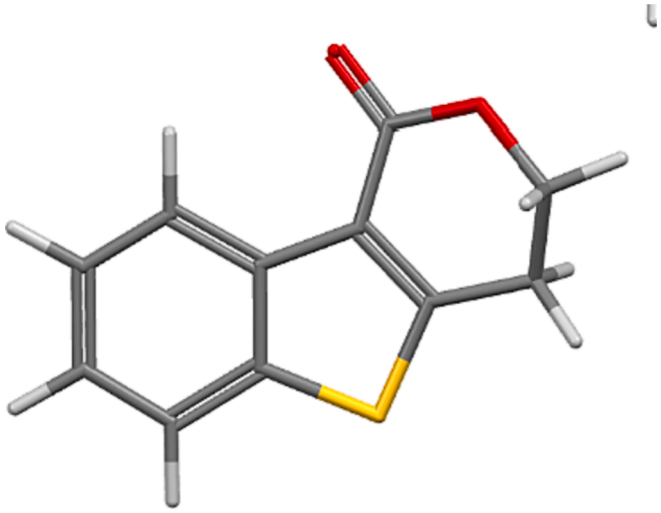


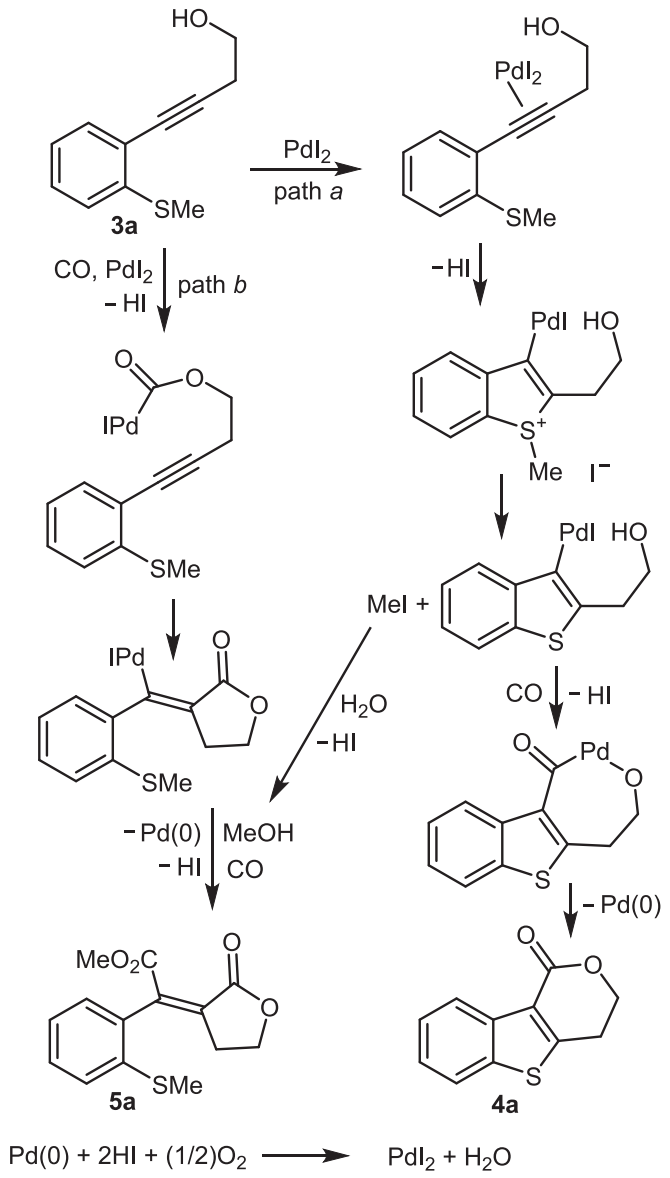
Fig. 2. X-ray molecular structure of 3,4-dihydro-1*H*-benzo[4,5]thieno[3,2-*c*]pyran-1-one **4a**.

(KBr): ν = 1748 (s), 1470 (m), 1435 (w), 1292 (w), 1142 (w), 1007 (m), 934 (m), 760 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.22 (d, J = 7.3, 1H, H-8), 7.87 (d, J = 7.7, 1H, H-5), 7.60–7.40 (m, 2H, H-6 + H-7), 5.46–5.37 (m, 1H, C*H*^{i}Pr), 2.36–2.22 (m, 1H, C*H*Me_2), 1.17–1.00 (m, 6H, CH*Me*$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5, 163.1, 145.2, 130.9, 129.5, 126.2, 126.0, 123.3, 123.0, 84.9, 32.4, 17.13, 17.10; GC–MS: m/z = 232 (M^+, 32), 189 (100), 161 (39), 133 (19), 89 (32); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{13}H_{13}O_2S)^+$: 233.0631; found, 233.0629.

3,3-Dimethylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2c**). Yield: 57.4 mg, starting from 68.9 mg of 2-methyl-4-(2-(methylthio)phenyl) but-3-yn-2-ol **1c** (79%; Table 2, entry 3). Yellow solid, mp = 100–102 °C. IR (KBr): ν = 1755 (s), 1470 (m), 1435 (w), 1385 (w), 1288 (m), 1188 (m), 1146 (w), 1045 (m), 991 (m), 891 (m), 783 (m), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.20–8.13 (m, 1H, H-8), 7.86 (dist d, J = 7.8, 1H, H-5), 7.55–7.40 (m, 2H, H-6 + H-7), 1.77 (m, 6H, 2 Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2, 164.6, 145.0, 131.0, 127.7, 126.2, 125.9, 123.5, 122.9, 84.4, 27.8; GC–MS: m/z = 218 (M^+, 58), 203 (100), 174 (74), 161 (44), 133 (21), 115 (16), 89 (28); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{12}H_{11}O_2S)^+$: 219.0474; found, 219.0462.

7-Fluoro-3,3-dimethylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2d**). Yield: 65.4 mg, starting from 74.4 mg of 4-(5-fluoro-2-(methylthio) phenyl)-2-methylbut-3-yn-2-ol **1d** (83%; Table 2, entry 4). White solid, mp = 139–141 °C. IR (KBr): ν = 1753 (s), 1578 (w), 1439 (m), 1366 (w), 1288 (m), 1254 (m), 1206 (m), 1179 (w), 1121 (w), 1043 (m), 995 (m), 903 (m), 887 (m), 856 (m), 799 (m), 777 (w) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.82 (dd, J = 8.8, 2.6, H-8), 7.79 (dd, J = 8.8, 4.6, 1H, H-5), 7.20 (td, J = 8.8, 2.6, 1H, H-6), 1.78 (s, 6H, 2 Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.2, 164.2, 161.8 (d, J = 245.4), 140.2, 132.3 (d, J = 13.2), 127.4, 124.7 (d, J = 9.5), 114.7 (d, J = 27.3), 109.2 (d, J = 24.5), 84.5, 27.8; GC–MS: m/z = 236 (M^+, 51), 221 (100), 193 (56), 179 (45), 151 (13), 133 (9), 107 (20); HRMS-ESI (m/z): [$(M+H)^+$] calcd for $(C_{12}H_{10}FO_2S)^+$: 237.0380; found, 237.0392.

3,3,7-Trimethylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2e**). Yield: 57.3 mg, starting from 73.1 mg of 2-methyl-4-(5-methyl-2-(methylthio) phenyl)but-3-yn-2-ol **1e** (74%; Table 2, entry 5). White solid, mp = 136–137 °C. IR (KBr): ν = 1748 (s), 1458 (m), 1364 (w), 1287 (m), 1269



Scheme 3. Divergent mechanistic pathways leading to products **4a** and **5a**.

(m), 1211 (m), 1179 (w), 1128 (m), 1059 (m), 991 (m), 881 (m), 797 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.97$ (s, 1H, H-8), 7.72 (d, $J =$ 8.3, 1H, H-5), 7.26 (d, J = 8.3, 1H, H-6), 2.49 (s, 3H, Me at C-7), 1.76 (m, 6H, 2 Me at C-3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 170.4$, 164.7, 142.2, 136.4, 131.3, 127.6, 123.1, 123.0, 84.3, 27.8, 21.3; GC–MS: $m/z = 232$ (M^+, 54), 217 (100), 189 (62), 175 (31), 161 (7), 147 (14); HRMS-ESI (m/z): $[(M+H)^+]$ calcd for $(C_{13}H_{13}O_2S)^+$: 233.0631; found, 233.0639.

3-Ethyl-3-methylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2f**). Yield: 58.2 mg, starting from 72.9 mg of 3-methyl-1-(2-(methylthio)phenyl) pent-1-yn-3-ol **1f** (76%; Table 2, entry 6). Yellow oil. IR (film): $\nu =$ 1755 (s), 1570 (w), 1470 (m), 1435 (w), 1385 (w), 1304 (w), 1184 (m), 1053 (w), 988 (m), 895 (m), 783 (m), 748 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.17$ (d, $J = 7.9$, 1H, H-8), 7.86 (d, $J = 8.2$, 1H, H-5), 7.53–7.49 (m, 1H, H-6 or H-7), 7.46–7.41 (m, 1H, H-7 or H-6), 2.14–2.05 (m, 1H, C*H*HCH$_3$), 2.05–1.96 (m, 1H, CH*H*CH$_3$), 1.74 (s, 3H, Me at C-3), 0.91 (t, $J = 7.4$, 3H, CH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 168.7, 164.9, 145.1, 131.0, 128.4, 126.2, 125.9, 123.5, 122.9, 87.3, 33.2, 26.1, 8.0; GC–MS: $m/z = 232$ (M^+, 29), 203 (100), 189 (16), 161 (29), 133 (13), 89 (13); HRMS-ESI (m/z): $[(M+H)^+]$ calcd for $(C_{13}H_{13}O_2S)^+$: 233.0631; found, 233.0633.

1H-Spiro[benzo[4,5]thieno[2,3-c]furan-3,1′-cyclohexan]-1-one (**2g**). Yield: 52.8 mg, starting from 82.2 mg of 1-((2-(methylthio)phenyl) ethynyl)cyclohexan-1-ol **1g** (61%; Table 2, entry 7). Yellow solid, mp = 92–93 °C. IR (KBr): $\nu = 1755$ (s), 1470 (m), 1435 (m), 1389 (w), 1177 (m), 1111 (w), 995 (w), 910 (m), 779 (w), 748 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.18$ (d, $J = 7.1$, 1H, H-8), 7.84 (d, $J = 7.6$, 1H, H-5), 7.57–7.36 (m, 2H, H-6 + H-7), 2.10–1.85 (m, 6H, aliphatic), 1.85–1.70 (m, 2H, aliphatic), 1.70–1.52 (m, 2H, aliphatic); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.1$, 164.9, 144.6, 130.9, 127.4, 126.2, 125.8, 123.3, 122.9, 86.9, 36.7, 30.9, 24.4, 22.8; GC–MS: $m/z = 258$ (M^+, 81), 230 (38), 215 (28), 202 (39), 187 (100), 160 (30), 146 (34), 132 (40), 115 (30), 102 (21), 89 (33); HRMS-ESI (m/z): $[(M+H)^+]$ calcd for $(C_{15}H_{15}O_2S)^+$: 259.0787; found, 259.0798.

1H-Spiro[benzo[4,5]thieno[2,3-c]furan-3,1′-cyclopentan]-1-one (**2h**). Yield: 56.5 mg, starting from 77.6 mg of 1-((2-(methylthio)phenyl) ethynyl)cyclopentan-1-ol **1h** (69%; Table 2, entry 8). White solid, mp = 102–103 °C. IR (KBr): $\nu = 1755$ (s), 1570 (w), 1470 (m), 1435 (m), 1385 (w), 1261 (w), 1188 (w), 1142 (m), 1115 (m), 1057 (m), 988 (m), 941 (m), 748 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 8.15$ (d, $J = 7.2$, 1H, H-8), 7.84 (d, $J = 7.7$, 1H, H-5), 7.56–7.35 (m, 2H, H-6 + H-7), 2.35–2.22 (m, 2H, aliphatic), 2.22–2.05 (m, 4H, aliphatic), 2.05–1.90 (m, 2H, aliphatic); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 168.0$, 164.7, 145.1, 131.2, 128.3, 126.2, 125.9, 123.5, 123.0, 93.9, 24.8; GC–MS: $m/z = 244$ (M^+, 100), 216 (72), 187 (84), 160 (65), 147 (30), 132 (32), 115 (23); HRMS-ESI (m/z): $[(M+H)^+]$ calcd for $(C_{14}H_{13}O_2S)^+$: 245.0631; found, 245.0626.

3-Methyl-3-phenylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2i**). Yield 48.2 mg, starting from 89.0 mg of 4-(2-(methylthio)phenyl)2-phenyl-but-3-yn-2-ol **1i** (52%; Table 2, entry 9). White solid, mp = 89–91 °C. IR (KBr): $\nu = 1755$ (s), 1570 (w), 1539 (w), 1470 (m), 1435 (m), 1389 (w), 1258 (m), 1173 (m), 1157 (m), 1076 (w), 984 (m), 922 (w), 880 (w), 779 (m), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.19$ (d, $J = 7.8$, 1H, H-8), 7.83 (d, $J = 8.0$, 1H, H-5), 7.61–7.28 (m, 7H, H-6 + H-7 + Ph), 2.11 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 169.4$, 164.5, 145.2, 139.7, 130.7, 128.9, 128.7, 127.3, 126.3, 126.1, 124.8, 123.4, 123.1, 86.9, 28.8; GC–MS: $m/z = 280$ (M^+, 45), 265 (100), 237 (88), 221 (19),

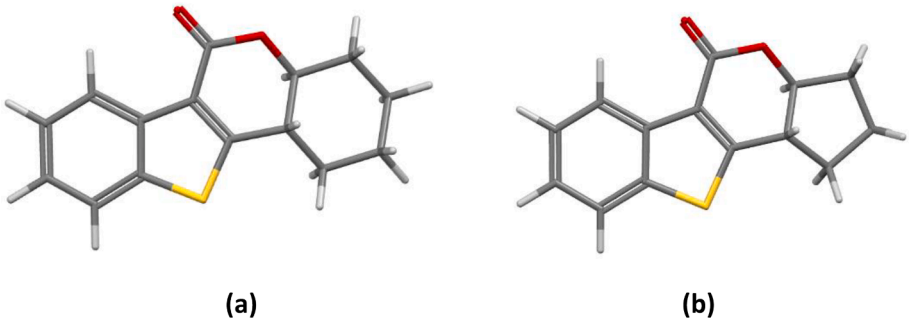


Fig. 3. X-ray molecular structures of (a) (4a*RS*,11b*RS*)-1,2,3,4,4a,11b-hexahydro-6*H*-benzo[4,5]thieno[3,2-*c*]chromen-6-one **4k** and (b) (3a*RS*,10b*RS*)-2,3,3a,10b-tetrahydrobenzo[4,5]thieno[2,3-*d*]cyclopenta[b]pyran-5(1*H*)-one **4l**.

175 (19), 165 (15), 105 (14), 77 (20); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{17}H_{13}O_2S)^+$: 281.0631; found, 281.0633.

3,3-Diphenylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2j**). Yield: 46.1 mg, starting from 110.2 mg of 3-(2-(methylthio)phenyl)-1,1-diphenylprop-2-yn-1-ol **1j** (40%; Table 2, entry 10). White yellow solid, mp = 228–230 °C. IR (KBr): ν = 1767 (s), 1493 (w), 1470 (m), 1450 (m), 1389 (w), 1277 (m), 1153 (w), 991 (m), 779 (w), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 7.8, 1H, H-8), 7.83 (d, *J* = 8.1, 1H, H-5), 7.56–7.27 (m, 12H, H-6 + H-7 + 2 Ph); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.7, 164.3, 145.9, 140.1, 130.7, 128.9, 128.8, 128.2, 126.9, 126.4, 126.3, 123.37, 123.36; GC–MS: *m/z* = 342 (M^+, 14), 297 (25), 265 (18), 237 (100), 221 (16), 165 (12), 105 (9), 77 (13); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{22}H_{15}O_2S)^+$: 343.0787; found, 343.0784.

Benzo[4,5]thieno[2,3-c]furan-1(3H)-one (**2k**). Yield: 35.2 mg, starting from 59.5 mg of 3-(2-(methylthio)phenyl)prop-2-yn-1-ol **1k** (55%; Table 2, entry 11). Pale yellow solid, mp = 107–109 °C. IR (KBr): ν = 1748 (s), 1470 (m), 1435 (m), 1342 (w), 1204 (w), 1103 (m), 1053 (m), 1003 (m), 964 (m), 899 (w), 776 (s), 748 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 7.8, 1H, H-8), 7.87 (d, *J* = 7.8, 1H, H-5), 7.60–7.40 (m, 2H, H-6 + H-7), 5.45 (s, 2H, OCH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9, 161.5, 145.2, 130.7, 128.5, 126.12, 126.05, 123.4, 122.7, 68.5; GC–MS: *m/z* = 190 (M^+, 47), 161 (100), 133 (25), 102 (5), 89 (32); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{10}H_7O_2S)^+$: 191.0161; found, 190.0154. The spectroscopic data agreed with those reported [18].

4.3. Procedure for the synthesis of 3-methylbenzo[4,5]thieno[2,3-c]furan-1(3H)-one *2a* from 4-(2-(methylthio)phenyl)but-3-yn-2-ol *1a* in larger scale

A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (60 mg, 0.17 mmol), KI (1.94 g, 11.7 mmol) and a solution of **1a** (318.5 mg, 1.66 mmol) in MeOH (82.5 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (48 atm) and air (12 atm). After being stirred at 80 °C for 15 h, 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 hexane–AcOEt from 100:0 to 90:10 (251 mg, 74 %).

4.4. General procedure for the synthesis of benzo[4,5]thieno[3,2-c]pyran-1-ones *4* from 4-(2-(methylthio)phenyl)but-3-yn-1-ols *3* (Table 3)

A 50 mL stainless steel autoclave was charged in the presence of air with PdI_2 (25.0 mg, 6.9 × 10^{-2} mmol), KI (802 mg, 4.83 mmol) and a solution of **3** (0.69 mmol; **3a**, 133 mg; **3b**, 145 mg; **3c**, 143 mg; **3d**, 152 mg; **3e**, 186 mg; **3f**, 215 mg; **3g**, 206 mg; **3h**, 178 mg; **3i**, 195 mg; **3j**, 180 mg; **3k**, 170 mg; **3l**, 160 mg) in MeCN (6.9 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (48 atm) and air (12 atm). After being stirred at 80 °C for 3 h (**3a-e**, **3g**, **3h**, **3k**, and **3l**), 5 h (**3f**) or 15 h (**3i** and **3j**), the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **4a-l** were purified by column chromatography on silica gel using as eluent 98:2 hexane-AcOEt to 9:1 hexane-AcOEt for **4a-4i**, **4k**, and **4l**; 98:2 hexane-AcOEt to 95:5 hexane-AcOEt for **4j**.

3,4-Dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4a**). Yield: 110 mg, starting from 133 mg of 4-(2-(methylthio)phenyl)but-3-yn-1-ol **3a** (78%; Table 3, entry 2). Pale yellow solid, mp = 103–105 °C. IR (KBr): ν = 1713 (s), 1466 (m), 1404 (w), 1273 (w), 1196 (m), 1119 (m), 1065 (w), 1042 (w), 949 (w), 903 (w), 787 (m), 706 (m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 8.50 (d, *J* = 8.0, 1H, H-8), 7.80 (d, *J* = 8.0, 1H, H-5), 7.51–7.45 (m, 1H, H-6 or H-7), 7.42–7.36 (m, 1H, H-7 or H-6), 4.63 (t, *J* = 6.1, 2H, OCH_2), 3.24 (t, *J* = 6.1, 2H, OCH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.8, 152.8, 137.6, 136.5, 126.0, 125.5, 124.5, 122.1, 121.6, 67.1, 25.4; GC–MS: *m/z* = 204 (M^+, 67), 174 (77), 146 (100), 102 (62); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{11}H_9O_2S)^+$: 205.0317; found, 205.0326.

7-Fluoro-3,4-Dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4b**). Yield: 85 mg, starting from 145 mg of 4-(4-fluoro-2-(methylthio)phenyl) but-3-yn-1-ol **3b** (55%; Table 3, entry 5). Pale yellow solid, mp = 176–178 °C. IR (KBr): ν = 1707 (s), 1535 (w), 1481 (m), 1341 (w), 1267 (m), 1184 (m), 1064 (m), 995 (w), 822 (m), 772 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.46 (dd, *J* = 8.9, 5.3, H-8), 7.49 (dd, *J* = 8.6, 2.3, 1H, H-5), 7.23 (td, *J* = 8.9, 2.3, 1H, H-7), 4.66 (t, *J* = 6.2, 2H, OCH_2), 3.25 (t, *J* = 6.2, 2H, OCH_2CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.9 (d, *J* = 246.4), 160.7, 152.2 (d, *J* = 2.8), 138.6 (d, *J* = 10.2), 132.9, 125.8 (d, *J* = 8.9), 121.2, 114.9 (d, *J* = 23.6), 108.5 (d, *J* = 25.7), 67.2, 25.4; GC–MS: *m/z* = 222 (M^+, 94), 192 (67), 164 (100), 133 (9), 120 (53), 96 (24); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{11}H_8FO_2S)^+$: 223.0224; found, 223.0234.

3-Methyl-3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4c**). Yield: 111 mg, starting from 143 mg of 5-(2-(methylthio)phenyl)pent-4-yn-2-ol **3c** (73%; Table 3, entry 6). White solid, mp = 144–145 °C. IR (KBr): ν = 1713 (s), 1528 (w), 1466 (m), 1389 (m), 1211 (s), 1119 (w), 1057 (w), 1003 (w), 926 (w), 787 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.51 (d, *J* = 8.1, 1H, H-8), 7.79 (d, *J* = 8.1, 1H, H-5), 7.47 (dist t, *J* = 7.6, 1H, H-6 or H-7), 7.38 (dist t, *J* = 7.6, 1H, H-7 or H-6), 4.85–4.76 (m, 1H, $OCHCH_3$), 3.14 (dist dd, *J* = 17.1, 4.0, 1H, $CHHCHCH_3$), 3.07 (dist dd, *J* = 17.1, 11.1, 1H, $CHHCHCH_3$), 1.58 (d, *J* = 6.4, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.2, 152.5, 137.8, 136.4, 125.9, 125.4, 124.5, 122.1, 121.3, 75.3, 32.1, 20.7; GC–MS: *m/z* = 218 (M^+, 60), 174 (100), 146 (99), 102 (40); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{12}H_{11}O_2S)^+$: 219.0474; found, 219.0476.

3-Ethyl-3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4d**). Yield: 112 mg, starting from 152 mg of 6-(2-(methylthio)phenyl)hex-5-yn-3-ol **3d** (70%; Table 3, entry 7). White solid, mp = 139–140 °C. IR (KBr): ν = 1713 (s), 1528 (w), 1466 (m), 1396 (m), 1204 (s), 1111 (m), 1065 (w), 972 (w), 787 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.52 (d, *J* = 8.0, 1H, H-8), 7.79 (d, *J* = 8.1, 1H, H-5), 7.51–7.45 (m, 1H, H-6 or H-7), 7.43–7.35 (m, 1H, H-7 or H-6), 4.63–4.56 (m, 1H, $OCHCH_2$), 3.14 (dist dd, *J* = 17.1, 4.9, 1H, $CHHCHEt$), 3.09 (dist dd, *J* = 17.1, 10.5, 1H, $CHHCHEt$), 2.03–1.92 (m, 1H, $CHHCH_3$), 1.90–1.80 (m, 1H, $CHHCH_3$), 1.12 (t, *J* = 7.5, 3H, CH_2CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.3, 152.6, 137.8, 136.4, 125.9, 125.4, 124.5, 122.1, 121.5, 80.0, 30.0, 27.9, 9.5; GC–MS: *m/z* = 232 (M^+, 54), 203 (5), 174 (100), 146 (68), 102 (30); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{13}H_{13}O_2S)^+$: 233.0630; found, 233.0615.

3-Phenyl-3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4e**). Yield: 154 mg, starting from 186 mg of 4-(2-(methylthio)phenyl)-1-phenylbut-3-yn-1-ol **3e** (79%; Table 3, entry 8). Pale yellow solid, mp = 167–168 °C. IR (KBr): ν = 1713 (s), 1466 (w), 1381 (m), 1265 (w), 1204 (m), 1119 (w), 1057 (w), 772 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 7.9, 1H, H-8), 7.81 (d, *J* = 8.0, 1H, H-5), 7.56–7.45 (m, 3H, aromatic), 7.45–7.34 (m, 4H, aromatic), 5.66 (dd, *J* = 11.5, 4.0, 1H, $CHPh$), 3.42 (dist dd, *J* = 17.2, 11.5, 1H, $CHHCHPh$), 3.34 (dist dd, *J* = 17.2, 4.0, 1H, $CHHPh$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.7, 152.4, 138.0, 137.8, 136.3, 128.83, 128.76, 126.2, 126.0, 125.5. 124.5, 122.1, 121.6, 80.0, 32.7; GC–MS: *m/z* = 280 (M^+, 18), 234 (6), 174 (100), 146 (70), 102 (31); HRMS-ESI (*m/z*): $[(M+H)^+]$ calcd for $(C_{17}H_{13}O_2S)^+$: 281.0630; found, 281.0647.

3-Mesityl-3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4f**). Yield: 166 mg, starting from 215 mg of 1-mesityl-4-(2-(methylthio) phenyl)but-3-yn-1-ol **3f** (74%; Table 3, entry 9). Pale yellow solid, mp = 195–196 °C. IR (KBr): ν = 1713 (s), 1466 (w), 1435 (m), 1381 (w), 1265 (w), 1204 (m), 1119 (m), 1057 (m), 1003 (w), 856 (w), 756 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.60 (d, *J* = 8.0, 1H, H-8), 7.83 (d, *J* = 8.0, 1H, H-5), 7.51 (dist t, *J* = 7.6, 1H, H-6 or H-7), 7.42 (dist t, *J* = 7.6, 1H, H-7 or H-6), 6.89 (s, 2H, mesityl ring), 6.10 (dd, *J* = 13.3, 4.1, 1H, OCH), 3.70 (dist dd, *J* = 17.8, 13.3, 1H, $OCHCHH$), 3.14 (dist dd, *J* = 17.8, 4.1, 1H, $OCHCHH$), 2.43 (s, 6H, 2 Me), 2.29 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.2, 152.8, 138.3, 137.8, 136.5, 136.3, 130.4, 126.0, 125.6. 124.7, 122.1, 121.5, 77.4, 29.8, 20.9; GC–MS: *m/z* = 322 (M^+, 15), 174 (100), 146 (35), 102 (13); HRMS-ESI (*m/z*):

[(M+H)$^+$] calcd for ($C_{20}H_{19}O_2S$)$^+$: 323.1100; found, 323.1102.

3-(4-Methoxyphenyl)-3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4g**). Yield: 150 mg, starting from 206 mg of 1-(4-methoxyphenyl)-4-(2-(methylthio)phenyl)but-3-yn-1-ol **3g** (70%; Table 3, entry 10). Pale yellow solid, mp = 157–158 °C. IR (KBr): ν = 1713 (s), 1512 (m), 1466 (m), 1381 (m), 1250 (m), 1204 (m), 1119 (m), 1057 (w), 1034 (w), 833 (w), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.55 (d, J = 7.9, 1H, H-8), 7.81 (d, J = 8.0, 1H, H-5), 7.54–7.45 (m, 1H, H-6 or H-7), 7.45–7.35 (m, 1H, H-7 or H-6 + 2H on aryl ring), 6.93 (d, J = 8.4, 2H, aryl ring), 5.62 (dd, J = 11.9, 3.3, 1H, OCH), 3.82 (s, 3H, OMe), 3.44 (dist dd, J = 17.2, 11.9, 1H, OCHCH*H*), 3.31 (dist dd, J = 17.2, 3.3, 1H, OCHCH*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.0, 160.0, 152.5, 137.9, 136.4, 130.1, 127.8, 126.0, 125.5, 124.5, 122.2, 121.7, 114.1, 80.0, 55.4, 32.6; GC–MS: *m/z* = 310 (M$^+$, 13), 221 (7), 174 (100), 146 (54), 102 (25); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{18}H_{15}O_3S$)$^+$: 311.0736; found, 311.0745.

3-(Furan-2-yl)-3,4-dihydro-1H-benzothieno[3,2-c]pyran-1-one (**4h**). Yield: 112 mg, starting from 178 mg of 1-(furan-2-yl)-4-(2-(methylthio)phenyl)but-3-yn-1-ol **3h** (60%; Table 3, entry 11). Pale yellow solid, mp = 140–142 °C. IR (KBr): ν = 1713 (s), 1466 (w), 1381 (m), 1265 (w), 1196 (m), 1119 (m), 1057 (w), 1003 (w), 980 (w), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.45 (d, J = 7.9, 1H, H-8), 7.82 (d, J = 7.9, 1H, H-5), 7.56–7.39 (m, 3H, H-6 + H-7 + H-5′ on furyl ring), 6.52–6.46 (m, 1H, furyl ring), 6.43–6.36 (m, 1H, furyl ring), 5.73 (dd, J = 10.8, 4.0, 1H, OCH), 3.71 (dd, J = 17.2, 10.8, 1H, OCHCH*H*), 3.43 (dist dd, J = 17.2, 4.0, 1H, OCHCH*H*); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.2, 152.0, 150.1, 143.3, 137.8, 136.3, 126.1, 125.6, 124.6, 122.1, 121.4, 110.7, 109.4, 73.1, 29.0; GC–MS: *m/z* = 270 (M$^+$, 34), 174 (100), 146 (14), 102 (21); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{15}H_{11}O_3S$)$^+$: 271.0423; found, 271.0421.

3-Methyl-3-phenyl-3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one (**4i**). Yield: 161 mg, starting from 195 mg of 5-(2-(methylthio)phenyl)-2-phenylpent-4-yn-2-ol **3i** (79%; Table 3, entry 12). White solid, mp = 137–138 °C. IR (KBr): ν = 1711 (s), 1466 (m), 1433 (w), 1383 (m), 1267 (w), 1219 (m), 1115 (m), 1063 (w), 993 (m), 766 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.48 (d, J = 8.0, 1H, H-8), 7.73 (d, J = 7.9, 1H, H-5), 7.49–7.39 (m, 3H, aromatic), 7.36–7.26 (m, 3H, aromatic), 7.23–7.17 (m, 1H), 3.70 (dist d, J = 17.2, 1H, C*H*H), 3.52 (dist d, J = 17.2, 4.0, 1H, CH*H*Ph), 1.81 (s, 3H, Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.6, 151.6, 143.4, 137.6, 136.3, 128.7, 127.7, 125.8, 125.3, 124.43. 124.36, 122.0, 121.5, 84.3, 36.1, 30.0; GC–MS: *m/z* = 294 (M$^+$, 14), 249 (2), 234 (5), 174 (100), 146 (51), 102 (21), 77 (16); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{18}H_{15}O_2S$)$^+$: 295.0787; found, 295.0797.

Spiro[benzo[4,5]thieno[3,2-c]pyran-3,1′-cyclohexan]-1(4H)-one (**4j**). Yield: 119 mg, starting from 180 mg of 1-(3-(2-(methylthio)phenyl) prop-2-yn-1-yl)cyclohexan-1-ol **3j** (63%; Table 3, entry 13). White solid, mp = 140–141 °C. IR (KBr): ν = 1703 (s), 1537 (m), 1466 (w), 1433 (m), 1384 (w), 1269 (m), 1159 (m), 1063 (m), 962 (m), 762 (w), 748 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.54 (d, J = 7.8, 1H, H-8), 7.80 (d, J = 7.8, 1H, H-5), 7.47 (dist t, J = 7.3, 1H, H-6 or H-7), 7.38 (dist t, J = 7.2, 1H, H-7 or H-6), 3.18 (s, 2H, $OCCH_2$), 2.12–1.97 (m, 2H, aliphatic), 1.90–1.72 (m, 2H, aliphatic), 1.71–1,57 (s, 3H, aliphatic), 1.57–1.45 (m, 2H, aliphatic), 1.45–1.32 (m, 1H, aliphatic); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 160.5, 151.3, 137.7, 136.5, 125.8, 125.2, 124.5, 122.0, 120.9, 92.6, 36.2, 35.4, 25.3, 21.7; GC–MS: *m/z* = 272 (M$^+$, 20), 216 (6), 174 (100), 146 (39), 102 (15); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{16}H_{17}O_2S$)$^+$: 273.0944; found, 273.0950.

(4aRS, 11bRS)-1,2,3,4,4a,11b-Hexahydro-6H-benzo[4,5]thieno[3,2-c]chromen-6-one (**4k**). Yield: 136 mg, starting from 170 mg of *trans*-2-((2-(methylthio)phenyl)ethynyl)cyclohexan-1-ol **3k** (76%; Table 3, entry 14). White solid, mp = 168–170 °C. IR (KBr): ν = 1713 (s), 1458 (w), 1389 (m), 1265 (w), 1219 (m), 1196 (m), 1119 (w), 1049 (m), 772 (s) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.50 (d, J = 8.0, 1H, H-8), 7.80 (d, J = 8.0, 1H, H-5), 7.46 (dist t, J = 7.6, 1H, H-6 or H-7), 7.37 (dist t, J = 7.6, 1H, H-7 or H-6), 4.17 (td, J = 11.4, 4.0, 1H, OCH), 3.00 (td, J = 11.4, 3.7, 1H, OCHC*H*), 2.37–1.19 (m, 2H, aliphatic), 2.01–1.83 (m, 2H, aliphatic), 1.81–1.68 (m, 1H, aliphatic), 1.54–1.36 (m, 3H, aliphatic); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 161.2, 158.9, 137.8, 136.8, 125.9, 125.2, 124.3, 122.2, 121.2, 82.3, 40.8, 31.1, 29.0, 25.0, 24.0; GC–MS: *m/z* = 258 (M$^+$, 87), 230 (19), 187 (100), 163 (12), 147 (4), 115 (37); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{15}H_{15}O_2S$)$^+$: 259.0787; found, 259.0789.

(3aRS, 10bRS)-2,3,3a,10b-Tetrahydrobenzo[4,5]thieno[3,2-d]cyclopenta[b]pyran-5(1H)-one (**4l**). Yield: 111 mg, starting from 160 mg of *trans*-2-((2-(methylthio)phenyl)ethynyl)cyclopentan-1-ol **3l** (66%; Table 3, entry 16). White solid, mp = 175–176 °C. IR (KBr): ν = 1709 (s), 1462 (m), 1431 (w), 1393 (m), 1354 (m), 1263 (w), 1211 (m), 1180 (w), 1159 (m), 1059 (m), 978 (w), 949 (w), 870 (w), 793 (m), 766 (m) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.52 (d, J = 8.0, 1H, H-8), 7.80 (d, J = 7.8, 1H, H-5), 7.42 (t, J = 7.4, 1H, H-6 or H-7), 7.36 (dist t, J = 7.2, 1H, H-7 or H-6), 4.40–4.24 (m, 1H, OCH), 3.29–3.11 (m, 1H, OCHC*H*), 2.35–1.24 (m, 1H, aliphatic), 2.24–2.13 (m, 1H, aliphatic), 2.12–1.86 (m, 3H, aliphatic), 1.70–1.56 (m, 1H, aliphatic); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 162.5, 157.5, 137.9, 136.8, 126.0, 125.2, 124.1, 122.3, 121.4, 84.2, 42.0, 27.3, 23.8, 19.8; GC–MS: *m/z* = 244 (M$^+$, 79), 216 (44), 187 (100), 160 (28), 147 (21), 115 (79); HRMS-ESI (*m/z*): [(M+H)$^+$] calcd for ($C_{14}H_{13}O_2S$)$^+$: 245.0631; found, 245.0643.

4.5. Procedure for the synthesis of 3,4-dihydro-1H-benzo[4,5]thieno[3,2-c]pyran-1-one *4a* from 4-(2-(methylthio)phenyl)but-3-yn-1-ol *3a* in larger scale

A 250 mL stainless steel autoclave was charged in the presence of air with PdI_2 (80 mg, 0.22 mmol), KI (2.58 g, 15.5 mmol) and a solution of **3a** (427 mg, 2.22 mmol) in MeCN (22.2 mL). The autoclave was sealed and, while the mixture was stirred, the autoclave was pressurized with CO (48 atm) and air (12 atm). After being stirred at 80 °C for 3 h, the autoclave was cooled, degassed and opened. The solvent was evaporated, and products **4a** was purified by column chromatography on silica gel using as eluent 98:2 hexane-AcOEt to 9:1 hexane-AcOEt (75%, 340 mg).

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.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcat.2023.115101.

References

[1] For a recent review, see: B. Gabriele, R. Mancuso, L. Veltri, I. Ziccarelli, N. Della Ca', Eur. J. Chem. 2019 (2019) 5073-5092.
[2] For a recent book on carbonylation chemistry, see: B. Gabriele (Ed.), Carbon Monoxide in Organic Synthesis - Carbonylation Chemistry, Wiley-VCH, Weinheim, Germany, 2021 (ISBN: 978-3527347957).
[3] For a very recent review on carbonylative double cyclization processes, see: B. Gabriele, R. Mancuso, N. Della Ca', L. Veltri, I. Ziccarelli, Catalysts 13 (2023) 1025.
[4] R. Mancuso, A De Salvo, P. Russo, A. Falcicchio, N. Della Ca', L. Pantoja Munoz, B. Gabriele, Chin. J. Chem. 41 (2023) 2801–2809.
[5] R. Mancuso, P. Russo, M. Lettieri, D. Santandrea, C. Cuocci, B. Gabriele, Adv. Synth. Catal. 364 (2022) 3917–3926.
[6] L. Shi, M. Wen, F. Li, Chin. J. Chem . 39 (2021) 317–322.
[7] R. Mancuso, S. Cuglietta, R. Strangis, B. Gabriele, J. Org. Chem. 88 (2023) 5180–5186.
[8] R. Mancuso, P. Russo, R. Miliè, M. Dell'Aera, F. Grande, B. Gabriele, Catal. Today 397–399 (2022) 631–638.

[9] R. Mancuso, M. Lettieri, I. Ziccarelli, P. Russo, A. Palumbo Piccionello, B. Gabriele, Adv. Synth. Catal. 363 (2021) 4612–4620.
[10] R. Mancuso, R. Strangis, I. Ziccarelli, N. Della Ca', B. Gabriele, J. Catal. 393 (2021) 335–343.
[11] Y. Hu, Z. Yin, T. Werner, A. Spannenberg, X.-F. Wu, Eur. J. Org. Chem. 2018 (2018) 1174–1280.
[12] J. Ying, H. Wang, X. Qi, J.-B. Peng, X.-F. Wu, Eur. J. Org. Chem. 2018 (2018) 688–692.
[13] R. Mancuso, N. Della Ca', L. Veltri, I. Ziccarelli, B. Gabriele, Catalysts 9 (2019) 610.
[14] B. Gabriele, Targets Heterocycl. Syst. 22 (2018) 41–55.
[15] B. Gabriele, PdI_2, in: D. Crich (Ed.), *e*-EROS (electronic Encyclopedia of Reagents for Organic Synthesis), Wiley-Interscience, 2006.
[16] B. Gabriele, M. Costa, G. Salerno, G.P. Chiusoli, J. Chem. Soc. Perkin Trans. 1 (1994) (1994) 83–87.
[17] R. Mancuso, R. Miliè, A. Palumbo Piccionello, D. Olivieri, N. Della Ca', C. Carfagna, B. Gabriele, J. Org. Chem. 84 (2019) 7303–7311.
[18] M.A. Waseem, Shireen, K. Ansari, F. Ibad, A. Ibad, J. Singh, I.R. Siddiqui, Tetrahedron Lett. 58 (2017) 4169–4173.
[19] G.A. Molander, D.J. St. Jean Jr., J. Org. Chem. 67 (2002) 3861–3865.
[20] X. Chen, S. Yang, B.-A. Song, Y.R. Chi, Angew. Chem. Int. Ed. 52 (2013) 11134–11137.
[21] Q. Deng, A. Yu, S. Zhang, X. Meng, Org. Chem. Front. 8 (2021) 936–940.
[22] M.-J.-R.-P. Queiroz, R.C. Calhelha, L.A. Vale-Silva, E. Pinto, M.-S.-J. Nascimento, Eur. J. Med. Chem. 44 (2009) 1893–1899.
[23] T.-K. Pradhan, A. De, J. Mortier, Tetrahedron 61 (2005) 9007–9017.
[24] T.-K. Pradhan, A. De, Tetrahedron Lett. 46 (2005) 1493–1495.