C. R. Chimie 20 (2017) 624–633

Contents lists available at ScienceDirect

Comptes Rendus Chimie

www.sciencedirect.com

Full paper/Mémoire

Comparative study on the reactivity of propargyl and alkynyl sulfides in palladium-catalyzed domino reactions

Étude comparative de la réactivité des thioéthers propargyliques et acétyléniques dans les réactions domino pallado-catalysées

Thomas Castanheiro, Angèle Schoenfelder, Jean Suffert, Morgan Donnard*, Mihaela Gulea**

Université de Strasbourg, CNRS, LIT UMR 7200, 67000 Strasbourg, France

ARTICLE INFO

Article history:
Received 20 October 2016
Accepted 20 December 2016
Available online 6 February 2017

Keywords:
Sulfur
Heterocycles
Domino
Thiacycle
Palladium
Carbopalladation
Catalysis

ABSTRACT

Three types of sulfides bearing a propargyl or an alkynyl moiety have been studied in cyclocarbopalladation/cross-coupling domino palladium-catalyzed sequences. The reactivity of different types of sulfured starting materials has been compared as well as the difference in behavior of these compounds depending on the type of cross coupling ending the domino sequence. It appeared that these cascades were constantly more efficient on the propargyl benzyl thioether. In addition, it has been demonstrated that domino sequences ending with Stille, Suzuki–Miyaura, or Mizoroki–Heck lead efficiently and selectively to the desired cyclized products. Notably, when the introduction of an alkyne is targeted at the end of the cascade, it appeared that the Sonogashira coupling leads every time to the desired cyclic product in the mixture with the product resulting from the direct coupling between the aryl moiety of the substrate and the alkyne used as partner. Finishing the domino sequence with a Stille coupling instead of a Sonogashira one allowed improving significantly the ratio of the mixture in favor of the desired cyclized compound.

Motsclés:
Soufre
hétérocycles
domino
thiacycle
palladium
carbopalladation
catalyse

RESUME

Divers substrats de type thioéther portant une partie propargylique ou acétylénique ont été étudiés dans des séquences domino pallado-catalysées de type cyclocarbopalladation/couplage croisé. La comparaison des différents types de composés soufrés en termes de réactivité a été réalisée ainsi que celle des comportements de ces mêmes substrats en fonction du type de couplage croisé terminant la séquence domino. Il est apparu que ces cascades réactionnelles sont systématiquement plus efficaces sur un précurseur de type benzyle propargyle thioether. De plus, il a été constaté que les réactions domino se terminant par un couplage de Stille, de Suzuki–Miyaura ou de Mizoroki–Heck conduisaient

* Corresponding author.
** Corresponding author.
E-mail addresses: donnard@unistra.fr (M. Donnard), gulea@unistra.fr (M. Gulea).

http://dx.doi.org/10.1016/j.crci.2016.12.007

toutes, de manière efficace et sélective, au composé cyclique soufré. De manière notable, lorsque l'objectif était d'introduire un alcyne en fin de séquence réactionnelle, il est apparu que le couplage de Sonogashira conduisait systématiquement à un mélange du produit cyclisé désiré avec le produit issu du couplage direct entre l'alcyne utilisé et la partie aromatique du substrat. En finissant la séquence domino avec un couplage de Stille, il a été possible d'améliorer de manière significative le ratio du mélange en faveur du produit cyclique désiré.

1. Introduction

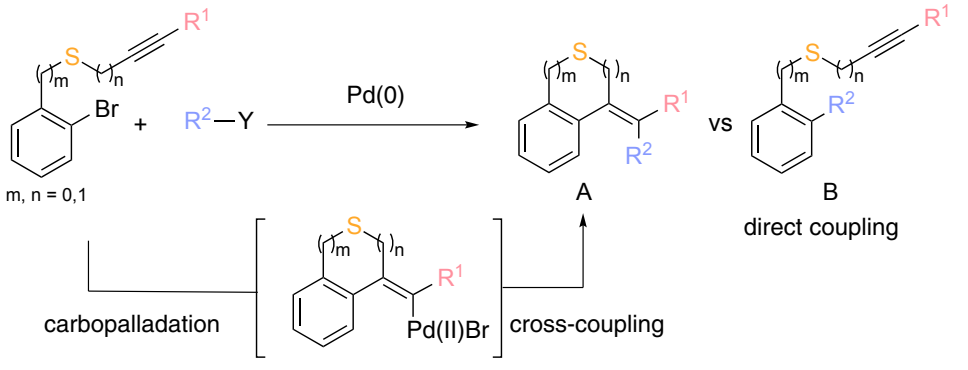
Among metal-catalyzed cascade reactions, those initiated by palladium-based catalysts are undoubtedly the ones that have been the most intensively studied for more than the last 40 years [1]. Efficient processes have been developed to quickly synthesize valuable molecular scaffolds bearing various heteroatoms mostly including nitrogen [2] and oxygen [3]. In contrast to this intensive work, transformations involving organosulfur substrates have been far less studied, certainly because of the poisoning of the catalyst caused by the thiophilicity of palladium. However, in recent years, the number of palladium-catalyzed processes involving substrates bearing a sulfur functionality has significantly increased and elegant methodologies have emerged insufflating a real interest to the synthetic chemist community [4]. During the course of our studies on metal-mediated transformations of sulfur-containing substrates [5], we have recently reported a domino palladium-catalyzed access to original thiacycles, which are compounds of outstanding importance in particular for the pharmaceutical industry, starting from propargylic or alkynyl sulfides [6]. This sequence involves an initial cyclizing carbopalladation step followed by a cross-coupling reaction between the resulting vinyl-palladium species and a coupling partner (stannylated or borylated) (Scheme 1).

However, in this preliminary report, only the most efficient cross-coupling reactions, namely the Stille and the Suzuki couplings, have been investigated and an additional effort had to be made to rationalize the behavior of such substrates under different palladium-catalyzed domino transformations. To do so, we are reporting here a complete study on the reactivity of three representative types of substrates (**1a**, **1b**, and **1c**) toward four distinct palladium-catalyzed domino reactions involving an initial cyclizing carbometalation step followed by the four most common cross-coupling reactions, respectively, the Stille reaction (organotin partner), the Suzuki–Miyaura reaction (organoboron partner), the Sonogashira reaction (alkyne partner), and the Mizoroki–Heck reaction (alkene partner) (Fig. 1).

2. Results and discussion

To rationalize the behavior of alkynyl and propargyl sulfides while submitted to these palladium-catalyzed domino transformations, we have first synthesized a set of three representative substrates namely propargyl aryl sulfide (**1a**), propargyl benzyl sulfide (**1b**), and alkynyl benzyl sulfide (**1c**). To access these three compounds, two different routes have been developed (Scheme 2).

The first route starts from 2-bromothiophenol and is based on a classical alkylation reaction using triethylamine as base and 3-(ethyl)propargyl bromide as an alkylating agent. After 4 h under reflux the desired aryl propargyl thioether **1a** was obtained almost quantitatively. The second route involves the in situ formation, by ethanolysis of a benzylic thioacetate, of a thiolate that can subsequently be alkylated. When 3-(ethyl)propargyl bromide is used as an alkylating agent, the thioether **1b** is obtained quantitatively. However, when propargyl bromide is used, the alkylation occurs to form the intermediary propargyl thioether that can then undergo a zip-type isomerization to reach the targeted ynethioether **1c** in a good 87% yield.



Scheme 1. General strategy of a palladium-catalyzed domino reaction of alkynyl and propargyl sulfides.

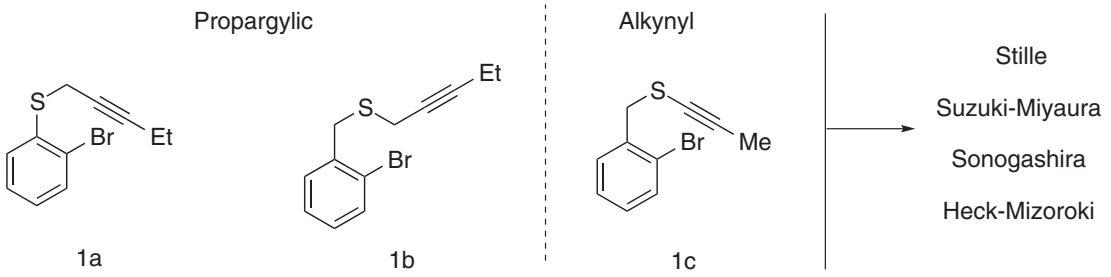
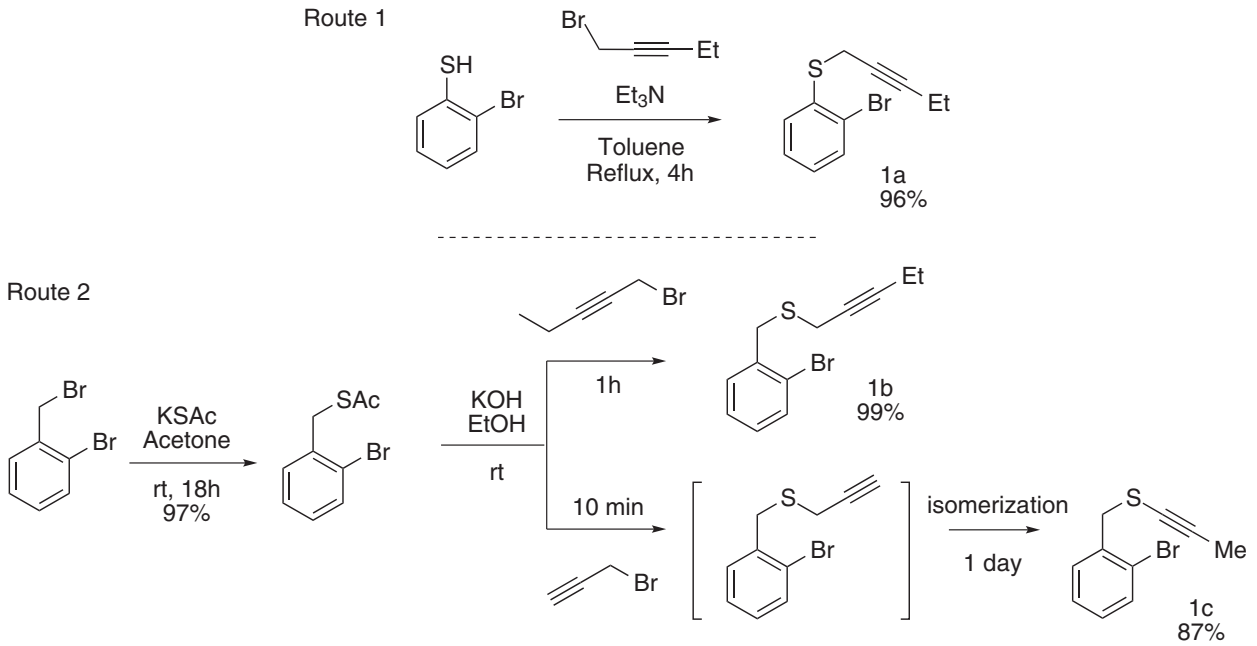


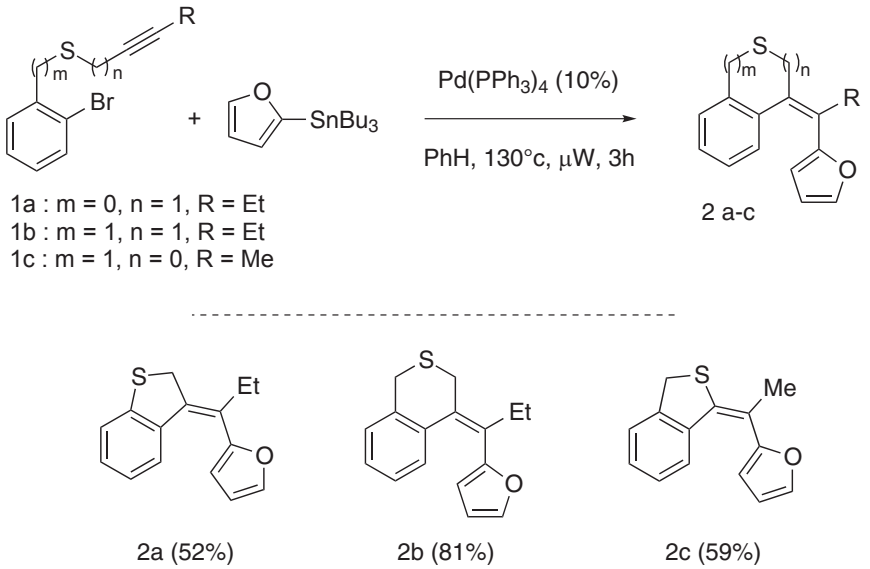
Fig. 1. The 3 substrates and the 4 ending couplings used for the study.



Scheme 2. Substrate syntheses.

With our substrates in hand, we have decided to first focus our interest on the sequences involving a cyclocarbopalladation/Stille coupling reactions. These reactions are usually highly efficient and their optimizations are classically easy and quick. Once optimized using the compound **1a** as substrate [7] and 2-furyl tributylstannane as coupling partner, it appeared that the best results were obtained with 10% of palladium tetrakis(-triphenylphosphine) with 1.5 equiv of stannane in benzene at 115 °C under microwave irradiation. After 3 h a complete conversion could be observed and the desired dihydro[*b*] benzothiophene derivative **2a** resulting from the cascade reaction was obtained in 52% yield. Notably, if the benzyl ynethioether **1c** led under the same conditions to the corresponding product dihydro[*c*]benzothiophene **2c** in a similar 59% yield, the substrate **1b** driving to a 6-membered heterocycle reacted in a better way and gave the targeted isothiochromane derivative **2b** in a good 81% yield. From these results it appeared that the 6-*exo*-dig/Stille coupling sequence was more efficient than the cascades involving a 5-*exo*-dig cyclization. However, the reaction seemed insensible to the mode of linkage of the sulfur atom to the alkyne moiety as the ynethioether **1c** and the propargyl thioether **1a** gave similar results (Scheme 3).

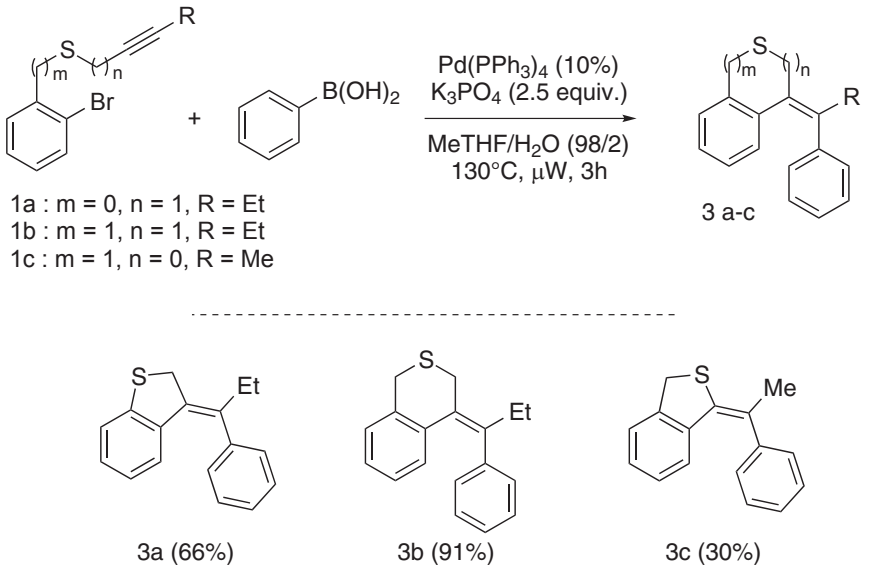
Then, we have been interested in comparing the reactivity of our three representative substrates in the case of a cascade ending with a Suzuki–Miyaura cross coupling after the initial cyclizing carbopalladation step. In that case a greater effort had to be made to optimize the reaction to obtain the cyclized molecules as sole products versus those coming from the direct coupling. When performing the reaction with **1a** as a starting material and phenylboronic acid as a coupling partner, after having screened several reaction conditions, the best results were obtained with 10% of $Pd(PPh_3)_4$ and K_3PO_4 as a base in a mixture of 2-MeTHF and water (98/2) at 130 °C under microwave irradiation. Under these conditions, after 3 h, the substrate **1a** reached the targeted compound **3a** in a 66% yield. Remarkably, no trace of the



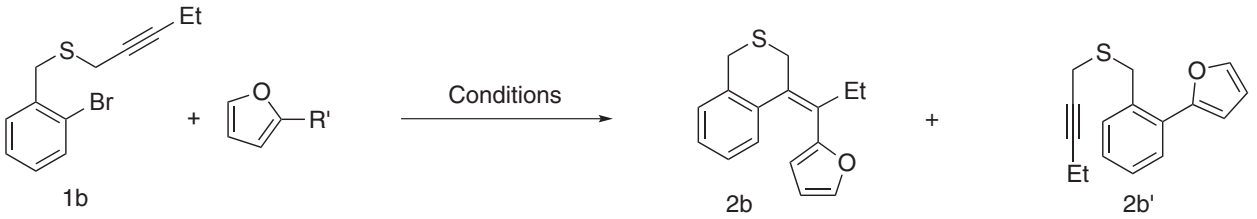
Scheme 3. Results for the cyclocarbopalladation/Stille coupling domino reactions.

corresponding product coming from a direct coupling has been detected. Then, the starting material **1c**, having the sulfur atom directly linked to the alkyne has been investigated. Notably, in this case the reactivity appeared similar but the desired product **3c** has been only obtained in a modest 30% yield mainly because of its instability. The benzyl propargyl thioether substrate **1b** gave better results and led to the desired isothiochromane derivative **3b** in a very good 91% yield. Once again the sequence involving a 6-*exo*-dig cyclizing step seemed to be more effective than the one based on a 5-*exo*-dig cyclization (Scheme 4).

Then, to compare the efficiency of the sequence involving a Stille or a Suzuki final step, 2-furylboronic acid was reacted with the best substrate in both transformations, namely the compound **1b**. Surprisingly in that case, our optimized conditions led only to the product resulting from the direct coupling **2b′**, whereas the Stille coupling gave only the targeted compound **2b**. By substituting the $Pd(PPh_3)_4$ catalyst by $PdCl_2$ as a metal source and 2-Dicyclohexylphosphino-2′,6′-dimethoxybiphenyl (SPHOS) as a ligand, we obtained our best results consisting in an equimolar mixture of the desired cyclized product **2b** and the direct coupling compound **2b′** (Scheme 5).



Scheme 4. Results for the cyclocarbopalladation/Suzuki–Miyaura coupling domino reactions.

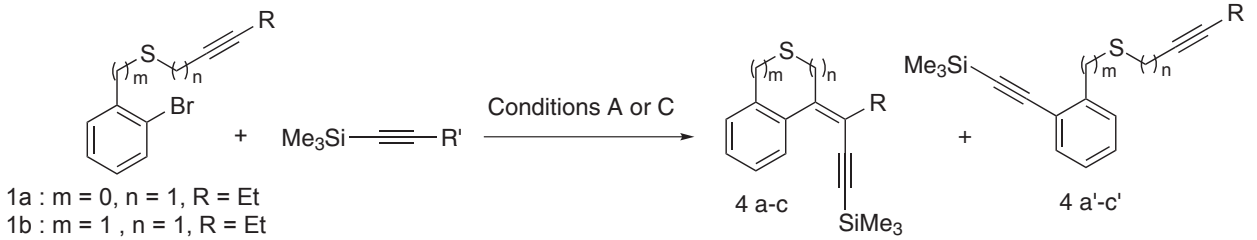


Conditions A: $Pd(PPh_3)_4$ 10 mol%, PhH, 130 °C, 3 h
Conditions B: $Pd(PPh_3)_4$ 10 mol%, MeTHF/H_2O, K_3PO_4, 130 °C, 3 h
Conditions B': $PdCl_2$ (10 mol%) / SPHOS (20 mol%), MeTHF/H_2O, K_3PO_4, 130 °C, 3 h

Entry	R'	Conditions	Conv. % (Yield %)	Ratio **2b**/**2b'**
1	$B(OH)_2$	**B**	100 (65)	0:1
2	$B(OH)_2$	**B'**	100 (60)	1:1
3	$SnBu_3$	**A**	100 (81)	1:0

Scheme 5. Comparison between the sequences ending with a Stille or a Suzuki–Miyaura coupling.

Then we attempted to introduce after the cyclocarbopalladation an alkynyl substituent via a Stille or a Sonogashira cross-coupling reaction with 1-trimethylsilyl alkynyl tributylstannane (method A) or with trimethylsilylacetylene (method C), respectively (Scheme 6) [8]. In the case of **1a** (Scheme 6 table, entries 1 and 2), both of the methods gave disappointing results, with a low conversion (20%) and a **4a**/**4a**′ ratio of 3/2 using Sonogashira coupling, and with a **4a**/**4a**′ ratio of 5/1, but a low isolated yield because of the degradation of the products during purification, when Stille coupling was involved. When **1b** was reacted in conditions C, the conversion was total and product **4b**′ resulting from the direct cross-coupling Sonogashira reaction was obtained with almost total selectively (Scheme 6, entry 3). In contrast, under conditions A, sulfide **1b** led to an inseparable mixture of products **4b** and **4b**′ in a ratio of 2/1 (Scheme 6, entry 4). Ynethioether **1c** was then involved in the same two types of processes (Scheme 6 table, entries 5 and 6). The best selectivity in favor of the cyclic product **4c** was obtained via the Stille reaction (ratio **4c**/**4c**′, 3/1). Because of the inconvenient presence of stannane derivatives, it was not



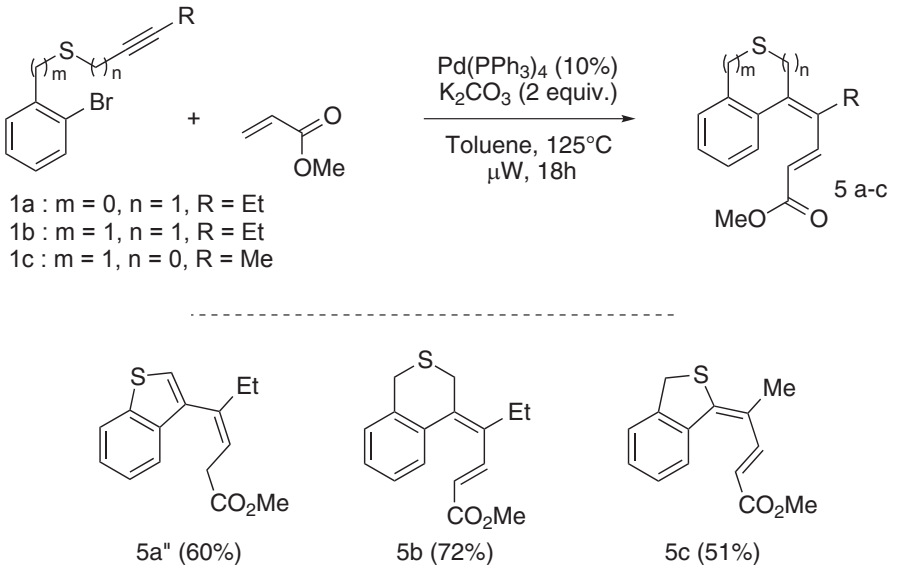
1a : m = 0, n = 1, R = Et
1b : m = 1 , n = 1, R = Et
1c : m = 1, n = 0, R = Me

Conditions A: $Pd(PPh_3)_4$, 10 mol%, PhH, 130 °C, 3 h
Conditions C: $Pd(OAc)_2$ 5 mol% / PPh_3 10 mol%, CuI 10 mol%, iPr_2NH (3 mL), MW, 120 °C, 30 min

Entry	Substrate	R'	Conditions	Product	Conv.% (Yield %)	Ratio **4**/**4'**
1	**1a**	H	**C**	**4a** + **4a'**	20 (nd*)	3:2
2	**1a**	$SnBu_3$	**A**	**4a** + **4a'**	100 (37)	5:1
3	**1b**	H	**C**	**4b** + **4b'**	100 (96)	1:20
4	**1b**	$SnBu_3$	**A**	**4b** + **4b'**	100 (92)	2:1
5	**1c**	H	**C**	**4c** + **4c'**	100 (41)	2:1
6	**1c**	$SnBu_3$	**A**	**4c** + **4c'**	100 (nd*)	3:1

* not determined

Scheme 6. Comparison between the sequences ending with Sonogashira (C) or Stille (A) coupling.



Scheme 7. Results for the cyclocarbopalladation/Mizoroki–Heck coupling domino reactions.

possible to isolate the products; however, we were able to characterize the compounds from their mixture resulting from the Sonogashira reaction (ratio **4c/4c′**, 2/1; 41% yield).

To complete this comparative study, the Mizoroki–Heck coupling was investigated as a final step of the domino sequence. We started by exploring the reactivity of the aryl propargyl thioether substrate **1a**. After optimization, we have determined that the best reaction conditions, when using methyl acrylate as a coupling partner, are 10% of $Pd(PPh_3)_4$ as a catalyst and potassium carbonate as a base in toluene for 18 h at 125 °C under classical heating (sealed tube). In that case the benzothiophene **5a″**, from the isomerization of the targeted product **5a**, was obtained in a 60% yield as an exclusive product. Pleasingly, no trace of the compound resulting from the direct coupling was detected. Nonetheless the ynethioether **1c** was subjected to the same reaction conditions and gave the desired product **5c** in a lowest 51% yield whereas the benzyl propargyl thioether led to the isothiochromane **5b** in a 72% yield. It is interesting to note that in the case of this cyclocarbopalladation/Mizoroki–Heck domino sequence, the size of the newly formed cycle does not impact the efficiency of the overall process as substrates **1a** and **1b** gave similar results in terms of yields. However, it appeared clearly that a significant difference in reactivity exists between the substrate bearing an alkynyl or a propargyl thioether as the yield of the reaction decreases by 10% when the sulfur atom is directly linked to the alkyne moiety (Scheme 7).

3. Conclusions

This study demonstrates that palladium-catalyzed domino sequences are an efficient tool for the synthesis of valuable heterocycles containing a sulfur atom. We have been able to observe the behavior of three representative substrates when submitted to four distinct cyclocarbopalladation/cross-coupling domino reactions. During the course of this study, it clearly appeared that the domino sequences applied to the substrate driving to a 6-*exo*-dig initial cyclocarbopalladation reaction were constantly more efficient than the same transformations done on 5-*exo*-dig precursors. The sequences ending by Stille, Suzuki–Miyaura, or Mizoroki–Heck coupling have been shown to be efficient and highly selective to the cyclized products. Notably, when the introduction of an alkyne was targeted at the end of the cascade, it appeared that the Sonogashira coupling led every time to a mixture of the desired cyclic product with the product resulting from the direct coupling between the aryl moiety of the substrate and the alkyne used as partner. Finishing the domino sequence with a Stille coupling instead of a Sonogashira coupling allowed improving significantly the ratio of the mixture in favor of the desired cyclized compound.

4. Materials and methods

4.1. General consideration

All reagents, chemicals, and dry solvents were purchased from commercial sources and used without purification. Reactions were monitored by thin-layer silica gel chromatography using Merck silica gel 60 F254 on aluminum sheets. Thin-layer silica gel chromatography plates were visualized under UV light and revealed with acidic *p*-anisaldehyde stain or $KMnO_4$ stain. Crude products were purified by flash column chromatography on Merck silica gel Si 60 (40–63 μm). All NMR spectra were recorded in $CDCl_3$, C_6D_6, or CD_2Cl_2 on a Bruker Avance III 400 MHz $BBFO^+$ probe spectrometer for ^1H NMR and 100 MHz for ^{13}C NMR, and a Bruker Avance 300 MHz dual probe spectrometer for ^1H NMR. Proton chemical shifts are

reported in ppm (δ), relatively to residual solvent. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublet (dd), triplet (t), quartet (q), broad signal (br s), and multiplet (m). Coupling constant values J are given in hertz. Carbon chemical shifts are reported in parts per million with the respective solvent resonance as the internal standard. ^{1}H NMR and ^{13}C NMR signals were assigned mostly on the basis of distortionless enhancement by polarization transfer (DEPT) and 2D-NMR (correlation spectroscopy (COSY), heteronuclear multiple-bond correlation spectroscopy (HMBC), and heteronuclear single-quantum correlation spectroscopy (HSQC)) experiments. High-resolution mass spectral analysis (HRMS) was performed using an Agilent 1200 rapid resolution liquid chromatography (RRLC) high performance liquid chromatography (HPLC) chain and an Agilent 6520 Accurate mass Quadrupole Time-of-Flight (QToF). Microwave irradiation was carried out with a microwave reactor from BIOTAGE using pressurized vials. Infrared (IR) spectra were recorded on a FT IR Thermo Nicollet ATR 380 Diamond Spectrometer. Microwave irradiations have been performed using a BIOTAGE Smith Creator apparatus.

4.2. Procedures and characterizations

4.2.1. (2-Bromophenyl)(pent-2-yn-1-yl)sulfide (**1a**)

To a solution of 2-bromobenzenethiol (1.5 g, 8 mmol, 1 equiv) in toluene (80 mL), triethylamine (1.2 mL, 8.3 mmol, 1.03 equiv) and then 3-(ethyl)propargyl bromide (1.84 g, 12.5 mmol, 1.5 equiv) were added. The reaction mixture was heated under reflux for 4 h. After filtration of the triethylammonium hydrobromide, the filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (eluent: pentane 100%, then pentane/ethyl acetate 95/5) to afford 1.96 g of sulfide **1a** (7.7 mmol, 96%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (t, J = 7.5 Hz, 3H, CH_3), 2.13–2.20 (m, 2H, CH_2), 3.65 (t, J = 2.3 Hz, 2H, SCH_2), 7.06 (td, J = 7.7, 1.6 Hz, 1H), 7.30 (td, J = 7.7, 1.5 Hz, 1H), 7.42 (dd, J = 7.9, 1.6 Hz, 1H), 7.55 (dd, J = 7.9, 1.5 Hz, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 12.5 (CH_3), 13.7 (CH_2), 22.1 (SCH_2), 73.9 ($CH_2C{\equiv}C$), 85.8 ($CH_2C{\equiv}C$), 123.5 (Cq), 127.0 (CH), 128.6 (CH), 130.7 (CH), 133.2 (CH), 137.2 (Cq). HRMS (ESI, 120 eV) calculated for $C_{11}H_{11}BrS$ $[M]^+$ 253.9763, found 253.9764.

4.2.2. S-(2-Bromobenzyl)ethanethioate (precursor of **1b** and **1c**)

To a solution of 2-bromobenzyl bromide (3.5 g, 15 mmol, 1 equiv) in acetone (100 mL), potassium thioacetate (2.05 g, 18 mmol, 1.2 equiv) was added. The reaction mixture was stirred at room temperature overnight. After filtration of the potassium bromide, the filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel to afford 3.5 g of product (97% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H, CH_3), 4.24 (s, 2H, SCH_2), 7.11 (td, J = 7.7, 1.6 Hz, 1H), 7.25 (td, J = 7.7, 1.4 Hz, 1H), 7.45 (dd, J = 7.5, 1.5 Hz, 1H), 7.54 (dd, J = 8.0, 1.4 Hz, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 30.5 (CH_3), 34.2 (CH_2), 124.7 (Cq), 127.8 (CH), 129.2(CH), 131.4 (CH), 133.0 (CH), 137.3 (Cq), 195.1 (CO).

4.2.3. (2-Bromobenzyl)(pent-2-yn-1-yl)sulfide (**1b**)

To a solution of KOH (336 mg, 6 mmol, 1.5 equiv) in ethanol (60 mL), *S*-(2-bromobenzyl)ethanethioate (980 mg, 4 mmol, 1 equiv) and then 3-(ethyl)propargyl bromide (882 mg, 6 mmol, 1.5 equiv) were added. The reaction mixture was stirred at room temperature for 1 h. After evaporation of the solvent, hydrolysis by water, and extraction with ether, the organic phases were separated, dried ($MgSO_4$), and the solution was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (pentane/Et_2O 9/1) to afford 1.06 g of sulfide **1b** (99% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, J = 7.5 Hz, 3H, CH_3), 2.21–2.28 (m, 2H, CH_2), 3.15 (t, J = 2.3 Hz, 2H, SCH_2), 3.98 (s, 2H, SCH_2), 7.12 (td, J = 7.7, 1.8 Hz, 1H), 7.26 (td, J = 7.5, 1.4 Hz, 1H), 7.38 (dd, J = 7.6, 1.8 Hz, 1H), 7.57 (dd, J = 7.9, 1.4 Hz, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 12.7 (CH_3), 14.2 (CH_2), 19.7 (SCH_2), 35.9 (SCH_2), 75.0 (C≡), 85.7 (≡C), 124.8 (Cq), 127.5 (CH), 128.8 (CH), 130.9 (CH), 133.4 (CH), 137.4 (Cq). HRMS (ESI, 120 eV) calculated for $C_{12}H_{13}BrS$ $[M]^+$ 267.9938, found 267.9921.

4.2.4. (2-Bromobenzyl)(prop-1-yn-1-yl)sulfide (**1c**)

To a solution of *S*-(2-bromobenzyl)ethanethioate (980 mg, 4 mmol, 1 equiv) in ethanol (60 mL), KOH (448 mg, 8 mmol, 2 equiv) and then propargyl bromide (1.2 g of 80% solution in toluene, 12.5 mmol, 1.5 equiv) were added. The reaction mixture was stirred at room temperature for 24 h. After filtration of the potassium bromide, the filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel (pentane 100%) to afford 835 mg of sulfide **1c** (87% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92 (s, 3H, CH_3), 4.00 (s, 2H, SCH_2), 7.15 (dt, J = 7.4, 1.0 Hz, 1H, H^4), 7.29 (dt, J = 7.7, 1.8 Hz, 1H, H^5), 7.37 (dd, J = 7.5, 1.8 Hz, 1H, H^6), 7.58 (dd, J = 8.0, 1.1 Hz, 1H, H^3). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 5.0 (CH_3), 40.2 (SCH_2), 66.8 (SC≡), 91.8 (≡$\underline{C}$Me), 124.5 (CBr), 127.3 (C^5), 129.2 (C^6), 131.1 (C^4), 133.1 (C^3), 136.3 (C^1). HRMS (ESI, 120 eV) calculated for $C_{10}H_9BrS$ $[M]^+$ 239.9595, found 239.9608.

4.2.5. General procedure A (cyclocarbopalladation/Stille domino reaction)

In a 2–5 mL microwave vial were added a solution of sulfide **1** (0.4 mmol, 1 equiv) and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv) in benzene (3 mL). The vial was sealed with a Teflon cap and the 2-furyl tributylstannane (0.6 mmol, 1.5 equiv) was added, then the mixture was irradiated in the microwave for 3 h at 115 °C. The reaction mixture was then filtered through Celite to eliminate the metal traces and then concentrated under reduced pressure. The product was purified by flash column chromatography on silica gel (eluent: heptane 100%).

4.2.6. General procedure B (cyclocarbopalladation/Suzuki–Miyaura domino reaction)

In a 10–20 mL microwave vial were added a solution of sulfide **1** (0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), K_3PO_4 (212 mg, 1 mmol, 2.5 equiv), and boronic acid (0.6 mmol, 1.5 equiv) in a mixture of 2-methyltetrahydrofurane (5 mL) and water (0.1 mL). The

vial was sealed with a Teflon cap and the mixture was irradiated in the microwave for 3 h at 130 °C. The reaction mixture was then evaporated and heptane was added to dissolve the product. The liquid phase was filtered through silica gel (previously treated by triethylamine) to eliminate the metal traces and then concentrated under reduced pressure. The ratio **A**/**B** was measured in the crude mixture by ^{1}H NMR. The product was purified by flash column chromatography on silica gel (eluent: heptane 100%, then heptane/diethyl ether 99/1).

4.2.7. General procedure C (cyclocarbopalladation/Sonogashira domino reaction)

In a 2–5 mL microwave vial were added sulfide **1** (1 equiv, 0.166 mmol), $Pd(OAc)_2$ (0.05 equiv), copper iodide (0.1 equiv), and PPh_3 (0.1 equiv). The vial was sealed with a Teflon cap and the reaction mixture was then dissolved in distilled diisopropylamine (3 mL). The reaction mixture was placed under argon, freezed in liquid nitrogen, and put under vacuum. The O_2 liberation proceeds when the temperature rises back to ambient. The operation was repeated two times. Then, the trimethylsilylacetylene (1.5 equiv) was added to the reaction mixture. The vial was irradiated in the microwave for 30 min at 120 °C. The reaction mixture is then filtered through Celite to eliminate the metal traces and then concentrated under reduced pressure. The product was purified by flash column chromatography (eluent: heptane 100%).

4.2.8. General procedure D (cyclocarbopalladation/Mizoroki–Heck domino reaction)

In a sealed tube (or a microwave vial) were added a solution of sulfide **1** (0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), potassium carbonate (110 mg, 0.8 mmol, 2 equiv), and then methyl acrylate (69 mg, 0.8 mmol, 2 equiv) in toluene (3 mL). The vial was sealed with a Teflon cap and the mixture was stirred at 130 °C for 7–18 h. The reaction mixture was then evaporated and heptane was added to dissolve the product. Afterward, the reaction mixture was allowed to cool to room temperature and filtered through a pad of Celite. The solvent was evaporated under reduced pressure and the residue was purified by flash column chromatography on silica gel (eluent: heptane 100%, then heptane/diethyl ether 95/5).

*4.2.9. (E)-2-(1-(Benzo[b]thiophen-3(2H)-ylidene)propyl)furan (**2a**)*

The general procedure A was followed using sulfide **1a** (102 mg, 0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), and 2-furyl tributylstannane (0.6 mmol, 1.5 equiv). Product **2a** was isolated as a yellow oil (50 mg, 52% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (t, J = 7.5 Hz, 3H, CH_3), 2.44 (q, J = 7.5 Hz, 2H, CH_2), 4.16 (s, 2H, SCH_2), 6.28 (dd, J = 3.3, 0.7 Hz, 1H), 6.43 (m, 1H), 6.46 (m, 1H), 6.80 (m, 1H), 7.05 (dt, J = 7.5 Hz, 1.2 Hz, 1H), 7.18 (m, 1H), 7.43 (dd, J = 1.9, 0.8 Hz, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 12.2 (CH_3), 29.2 (CH_2), 36.4 (SCH_2), 108.3 (CH), 111.3 (CH), 122.8 (CH), 123.8 (CH), 125.7 (CH), 127.2 (Cq), 128.5 (CH), 136.3 (Cq), 139.0 (Cq), 141.5 (CH), 145.6 (Cq), 153.2 (Cq). HRMS (ESI, 120 eV) calculated for $C_{15}H_{14}OS$ $[M]^+$ 242.0765, found 242.0768.

*4.2.10. (E)-2-(1-(Isothiochroman-4-ylidene)propyl)furan (**2b**)*

Stille coupling: procedure A was followed using sulfide **1b** (107 mg, 0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), and 2-furyl tributylstannane (0.6 mmol, 1.5 equiv). Product **2b** was isolated as a yellow oil (82 mg, 81% yield).

Suzuki coupling: procedure B was modified as following: sulfide **1b** (107 mg, 0.4 mmol, 1 equiv), $PdCl_2$ (7 mg, 0.04 mmol, 0.1 equiv), SPHOS (32 mg, 0.08 mmol, 0.2 equiv), potassium phosphate (212 mg, 1 mmol, 2.5 equiv), and 2-furylboronic acid (67 mg, 0.6 mmol, 1.5 equiv). The yield was 60%. Compounds **2b** and **2b′** were obtained as an inseparable equimolar mixture.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.5 Hz, 3H, CH_3), 2.64 (q, J = 7.5 Hz, 2H, CH_2), 3.59 (s, 2H, SCH_2), 3.67 (s, 2H, SCH_2), 5.78 (d, J = 3.3 Hz, 1H), 6.19 (dd, J = 3.6, 1.8 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 7.10 (m, 1H), 7.20 (m, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 14.1, 24.9, 29.1, 29.4, 109.5, 110.9, 126.5, 126.7, 127.3, 128.6, 129.6, 130.7, 137.4, 140.5, 141.2, 154.2. HRMS (ESI, 120 eV) calculated for $C_{16}H_{16}OS$ $[M]^+$ 256.0917, found 256.0921.

*4.2.11. (E)-2-(1-(Benzo[c]thiophen-1(3H)-ylidene)ethyl)furan (**2c**)*

The general procedure A was followed using sulfide **1c** (96 mg, 0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), and 2-furyl tributylstannane (0.6 mmol, 1.5 equiv). Product **2c** was isolated as a yellow oil (53 mg, 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.93 (s, 3H, CH_3), 4.10 (s, 2H, SCH_2), 6.03 (dd, J = 3.3, 0.8 Hz, 1H), 6.21 (m, 1H), 6.54 (d, J = 8.1 Hz, 1H), 6.80 (m, 1H), 6.91 (dt, J = 7.4, 1.1 Hz, 1H), 7.16 (dd, J = 1.9, 0.7 Hz, 1H), 7.21 (m, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 24.4 (CH_3), 36.5 (SCH_2), 107.7 (CH), 111.4 (CH), 124.6 (CH), 125.4 (CH), 126.8 (CH), 127.6 (CH), 140.9 (CH), 128.6 (Cq), 137.8 (Cq), 142.2 (Cq), 143.4 (Cq), 154.2 (Cq). IR (neat) ν (cm^{-1}): 2919, 1619, 1485, 1469, 1153, 1004, 905, 759, 736, 595. HRMS (ESI, 120 eV) calculated for $C_{14}H_{12}OS$ $[M]^+$ 228.0628, found 228.068.

*4.2.12. (E)-3-(1-Phenylpropylidene)-2,3-dihydrobenzo[b]thiophene (**3a**)*

The general procedure B was followed using sulfide **1a** (102 mg, 0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), potassium phosphate (212 mg, 1 mmol, 2.5 equiv), and phenylboronic acid (73 mg, 0.6 mmol, 1.5 equiv). The product was isolated as a yellow oil (66 mg, 66% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (t, J = 7.5 Hz, 3H, CH_3), 2.46 (q, J = 7.5 Hz, 2H, CH_2), 4.21 (s, 2H, SCH_2), 6.15 (d, J = 8.0 Hz, 1H), 6.58 (t, J = 7.8 Hz, 1H), 6.95 (t, J = 7.5 Hz, 1H), 7.13–7.18 (m, 3H), 7.32–7.42 (m, 3H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 11.6 (CH_3), 31.1 (CH_2), 35.8 (SCH_2), 122.7 (CH), 123.5 (CH), 126.0 (CH), 127.3 (CH), 127.8 (CH), 128.6 (2CH), 129.2 (2CH), 134.1 (Cq), 136.8 (Cq), 139.2 (Cq), 142.1 (Cq), 145.1 (Cq). IR (cm^{-1}): 2963, 2927, 1577, 1486, 1370, 1455, 1438, 1274, 1161, 1134, 1065, 750, 727, 702, 687. HRMS (ESI, 120 eV) calculated for $C_{17}H_{16}S$ $[M]^+$ 252.0973, found 252.0984.

*4.2.13. (E)-4-(1-Phenylpropylidene)isothiochroman (**3b**)*

The general procedure B was followed using sulfide **1b** (107 mg, 0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), potassium phosphate (212 mg, 1 mmol,

2.5 equiv), and phenylboronic acid (73 mg, 0.6 mmol, 1.5 equiv). The product was isolated as a yellow oil (98 mg, 91% yield).

^{1}H NMR (400 MHz, CD_2Cl_2) δ 0.93 (t, $J = 7.5$ Hz, 3H, CH_3), 2.52 (q, $J = 7.50$ Hz, 2H, CH_2), 3.50 (s, 2H, SCH_2), 3.59 (s, 2H, $PhSCH_2$), 6.53 (d, $J = 8.0$ Hz, 1H), 6.72 (t, $J = 7.5$ Hz, 1H), 6.86 (dd, $J = 7.1$ Hz, 1.7 Hz, 2H), 6.93 (t, $J = 7.5$ Hz, 1H), 6.98–7.01 (m, 4H). **^{13}C NMR** (100.6 MHz, CD_2Cl_2) δ 13.0 (CH_3), 27.8 (CH_2), 28.6 (SCH_2), 28.9 (SCH_2), 125.9 (CH), 126.0 (CH), 126.3 (CH), 126.4 (CH), 127.67 (2CH), 129.3 (2CH, Cq), 129.7 (CH), 138.1 (Cq), 139.9 (Cq), 140.9 (Cq), 142.8 (Cq). IR (cm^{-1}): 2963, 2928, 1478, 1451, 1441, 1372, 1192, 1054, 907, 754, 697. HRMS (ESI, 120 eV) calculated for $C_{18}H_{18}S$ $[M]^+$ 266.1129, found 230.1124.

4.2.14. (E)-1-(1-Phenylethylidene)-1,3-dihydrobenzo[c] thiophene (**3c**)

The general procedure B was followed using sulfide **1c** (96 mg, 0.4 mmol, 1 equiv), $Pd(PPh_3)_4$ (46 mg, 0.04 mmol, 0.1 equiv), potassium phosphate (212 mg, 1 mmol, 2.5 equiv), and phenylboronic acid (73 mg, 0.6 mmol, 1.5 equiv). The product was isolated as a yellow oil (29 mg, 30% yield).

^{1}H NMR (400 MHz, C_6D_6) δ 2.27 (s, 3H, CH_3), 3.93 (s, 2H, SCH_2), 6.66 (dd, $J = 6.6$, 7.84 Hz, 1H), 6.76–6.82 (m, 3H), 7.06–7.15 (m, 5H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 27.3 (CH_3), 36.0 (SCH_2), 125.4 (CH), 125.9 (CH), 126.5 (Cq), 126.8 (CH), 127.3 (CH), 127.5 (CH), 129.0 (2CH), 129.6 (2CH), 137.7 (Cq), 138.9 (Cq), 143.7 (Cq), 144.5 (Cq). IR (cm^{-1}): 2922, 2850, 1688, 1593, 1489, 1471, 1454, 1440, 1264, 1026, 903, 757, 734, 698. HRMS (ESI, 120 eV) calculated for $C_{16}H_{14}S$ $[M]^+$ 238.0816, found 238.0824.

4.2.15. (E)-(3-(Benzo[b]thiophen-3(2H)-ylidene)pent-1-yn-1-yl)trimethylsilane (**4a**)

A small amount of the pure titled compound was isolated from the crude mixture obtained by method A (eluent: 100% heptane) and characterized by NMR spectroscopy.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.33 (s, 9H, $SiMe_3$), 1.25 (t, $J = 7.3$ Hz, 3H, CH_3), 2.30–2.35 (m, 3H, CH_2), 4.16 (s, 2H, SCH_2), 7.08–7.31 (m, 3H, H), 8.71 (d, $J = 8.0$, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 0.02 ($SiMe_3$), 12.2 (CH_3), 28.6 (CH_2), 35.8 (SCH_2), 102.8 (C≡$\underline{C}$Si), 105.2 (C≡CSi), 117.5 (Cq), 122.4 (CH), 123.6 (CH), 125.8 (CH), 129.2 (CH), 136.3 (Cq), 144.1 (Cq), 146.0 (Cq).

Trimethyl((2-(pent-2-yn-1-ylthio)phenyl)ethynyl) silane (**4a′**). The titled compound was not isolated, as it was obtained by method C (via Sonogashira) or A (via Stille) only in a lesser amount, in mixture with compound **4a**. One signal at $\delta = 3.69$ (SCH_2) was assigned to this compound in ^{1}H NMR ($CDCl_3$).

4.2.16. (E)-(3-(Isothiochroman-4-ylidene)pent-1-yn-1-yl) trimethylsilane (**4b**)

We were unable to isolate a pure sample of the titled compound; however, it was characterized from its mixture with compound **4b′** (obtained by method A).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.10 (s, 9H, $SiMe_3$), 1.17 (t, $J = 7.5$ Hz, 3H, CH_3), 2.34–2.40 (m, 3H, CH_2), 3.57 (s, 2H, SCH_2), 3.64 (s, 2H, SCH_2), 7.13–7.26 (m, 3H, H), 7.86 (d, $J = 7.2$, 1H, H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 0.05 ($SiMe_3$), 13.7 (CH_3), 26.3 (CH_2), 28.4 (SCH_2), 29.5 (SCH_2), 97.9 (C≡$\underline{C}$Si), 106.2 (*C*≡CSi), 121.2 (Cq), 125.9 (CH), 126.4 (CH), 127.7 (CH), 129.8 (CH), 136.9 (Cq), 137.2 (Cq), 138.6 (Cq).

4.2.17. Trimethyl((2-((pent-2-yn-1-ylthio)methyl)phenyl) ethynyl)silane (**4b′**)

The pure titled compound was isolated from the crude mixture obtained by method C (eluent: heptane/ethyl ether 99:1) and characterized by NMR spectroscopy.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.26 (s, 9H, $SiMe_3$), 1.15 (t, $J = 7.5$ Hz, 3H, CH_3), 2.20–2.26 (m, 2H, CH_2), 3.15 (s, 2H, SCH_2), 4.00 (s, 2H, SCH_2Ar), 7.18 (t, $J = 7.7$ Hz, 1H, H), 7.25–7.34 (m, 2H, H), 7.47 (d, $J = 7.7$, 1H, H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 0.08 ($SiMe_3$), 12.7 (CH_3), 14.2 (CH_2), 19.6 (SCH_2), 34.1 (SCH_2Ar), 75.1 (*C*≡CEt), 85.2 (C≡$\underline{C}$Et), 100.1 (C≡$\underline{C}$Si), 102.8 (*C*≡CSi), 122.9 (Cq), 126.9 (CH), 128.5 (CH), 129.0 (CH), 132.8 (CH), 140.6 (Cq).

4.2.18. (E)-(3-(Benzo[c]thiophen-1(3H)-ylidene)but-1-yn-1-yl) trimethylsilane (**4c**)

We were unable to isolate a pure sample of the titled compound; however, it was characterized from its mixture with compound **4c′** (obtained by method C).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.26 (s, 9H, $SiMe_3$), 2.05 (s, 3H, CH_3), 4.31 (s, 2H, SCH_2), 7.25–7.29 (m, 2H, H), 7.29 (dd, $J = 4.6$, 1.8 Hz, 1H, H), 8.78 (dd, $J = 4.4$, 4.8 Hz, 1H, H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 0.2 ($SiMe_3$), 24.2 (CH_3), 36.5 (SCH_2), 99.9 (*C*$SiMe_3$), 103.7 (C=*C*Me), 106.9 (*CC*$SiMe_3$), 124.8 (CH), 125.7 (CH), 126.8 (CH), 128.2 (CH), 138.2 (Cq), 143.2 (Cq), 149.5 (*C*C=C).

4.2.19. Trimethyl((2-((prop-1-yn-1-ylthio)methyl)phenyl) ethynyl)silane (**4c′**)

A small amount of the titled compound was isolated from the crude mixture obtained by method C (eluent: 100% heptane) and characterized by NMR spectroscopy.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.24 (s, 9H, $SiMe_3$), 1.89 (s, 3H, CH_3), 4.02 (s, 2H, SCH_2), 7.22 (dt, $J = 6.6$, 1.6 Hz, 1H, H), 7.27 (dt, $J = 7.3$, 1.8 Hz, 1H, H), 7.33 (dd, $J = 6.8$, 1.8 Hz, 1H, H), 7.47 (dd, $J = 7.3$, 1.6 Hz, 1H, H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 0.1 ($SiMe_3$), 5.3 (CH_3), 39.0 (SCH_2), 67.5 (SC), 91.7 (CMe), 100.3 (*C*$SiMe_3$), 102.8 (*CC*$SiMe_3$), 123.3 (Cq), 127.5 (CH), 128.6 (CH), 129.4 (CH), 132.7 (CH), 139.6 (Cq).

4.2.20. Methyl (Z)-4-(benzo[b]thiophen-3-yl)hex-3-enoate (**5a″**)

The general procedure D was followed starting from sulfide **1a** (102 mg, 0.4 mmol, 1 equiv). The entitled product was isolated as a yellow oil (63 mg, 60% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, $J = 8$ Hz, 3H, CH_3), 2.51 (q, $J = 8$ Hz, 2H, CH_2), 3.37 (d, $J = 8$ Hz, 2H, CH_2), 3.78 (s, 3H, OCH_3), 5.86 (t, $J = 8$ Hz, 1H), 7.36–7.43 (m, 3H), 7.88–7.92 (m, 2H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 13.3, 25.2, 33.7, 52.1, 121.1122.4, 122.9, 123.3, 124.2, 124.4, 138.6, 139.1, 140.0, 140.5, 172.4. IR (cm^{-1}): 2965, 1735, 1455, 1169, 761, 735. HRMS (ESI, 120 eV) calculated for $C_{15}H_{16}O_2S$ $[M]^+$ 260.0871, found 260.0883.

*4.2.21. Methyl (E)-4-((E)-isothiochroman-4-ylidene)hex-2-enoate (**5b**)*

The general procedure D was followed starting from sulfide **1b** (107 mg, 0.4 mmol, 1 equiv). The entitled product was isolated as a yellow oil (69 mg, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.15 (t, $J = 8$ Hz, 3H, CH_3), 2.51 (q, $J = 8$ Hz, 2H, CH_2), 3.60 (s, 2H, SCH_2), 3.62 (s, 2H, SCH_2), 3.70 (s, 3H, OCH_3), 6.01 (d, $J = 16$ Hz, 1H), 7.12 (m, 1H), 7.21 (m, 1H), 7.28–7.32 (m, 2H), 7.54 (d, $J = 16$ Hz, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 13.8, 21.9, 29.1, 29.4, 51.7, 117.8126.94, 126.98, 128.7, 130.4, 135.1, 137.8, 137.9, 140.6, 144.5, 168.1. IR (cm^{-1}): 2962, 1708, 1603, 1464, 1434, 1249, 1163, 1048, 815. HRMS (ESI, 120 eV) calculated for $C_{16}H_{18}O_2S$ $[M]^+$ 274.1028, found 274.1038.

*4.2.22. Methyl (2E)-4-(benzo[c]thiophen-1(3H)-ylidene)pent-2-enoate (**5c**)*

The general procedure D was followed starting from sulfide **1c** (91 mg, 0.4 mmol, 1 equiv). The entitled product was isolated as a yellow oil (40 mg, 51% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (s, 3H, CH_3), 3.79 (s, 3H, OCH_3), 4.36 (s, 2H, SCH_2), 5.90 (d, $J = 16$ Hz, 1H), 7.31–7.37 (m, 3H), 7.87 (d, $J = 8$ Hz, 1H), 8.35 (d, $J = 16$ Hz, 1H). **^{13}C NMR** (100.6 MHz, $CDCl_3$) δ 20.0, 36.9, 51.7, 115.2, 125.9, 126.5, 127.7, 128.4, 137.9, 142.0, 144.4, 146.5, 150.5, 168.7. IR (neat) ν (cm^{-1}) 2359, 2341, 1710, 1600, 1455, 1293, 1260, 1166, 759. HRMS (ESI, 120 eV) calculated for $C_{14}H_{14}O_2S$ $[M]^+$ 246.0715, found 246.0700.

Acknowledgments

This project was supported by the “Université de Strasbourg” (IDEX grant for T.C.) and the “Centre national de la recherche scientifique (CNRS)”.

References

[1] For recent reviews on palladium-catalyzed cascade processes, see (a) A. Düfert, D. Werz, Chem. Eur. J. 22 (2016) 16718–16732; (b) H. Ohno, Asian J. Org. Chem. 2 (2013) 18–28; (c) T. Vlaar, E. Ruiter, R.V.A. Orru, Adv. Synth. Catal. 353 (2011) 809–841.

[2] (a) J. Schönhaber, W. Frank, T.J.J. Müller, Org. Lett. 12 (2010) 4122–4125; (b) S.B.J. Kan, E.A. Anderson, Org. Lett. 10 (2008) 2323–2326; (c) S. Couty, B. Liegault, C. Meyer, J. Cossy, Org. Lett. 6 (2004) 2511–2514.

[3] (a) A. Arcadi, F. Blesi, S. Cacchi, G. Fabrizi, A. Goggiamani, F. Marinelli, J. Org. Chem. 78 (2013) 4490–4498; (b) H. Yu, R.N. Richey, M.W. Carson, M.J. Coghlan, Org. Lett. 8 (2006) 1685–1688; (c) F. Teply, I.G. Stara, I. Stary, A. Kollarovic, D. Saman, P. Fiedler, Tetrahedron 58 (2002) 9007–9018; (d) R. Grigg, V. Savic, Tetrahedron Lett. 37 (1996) 6565–6568; (e) J. Wallbaum, R. Neufeld, D. Stalke, D.B. Werz, Angew. Chem., Int. Ed. 52 (2013) 13243–13246.

[4] For recent reviews, see (a) N. Kaur, Catal. Rev. 57 (2015) 478–564; (b) I.P. Beletskaya, V.P. Ananikov, Chem. Rev. 111 (2011) 1596–1636; (c) F. Alonso, I.P. Beletskaya, M. Yus, Chem. Rev. 104 (2004) 3079–3160; (d) I. Nakamura, Y. Yamamoto, Chem. Rev. 104 (2004) 2127–2198.

[5] (a) T. Castanheiro, M. Gulea, M. Donnard, J. Suffert, Eur. J. Org. Chem. 2014 (2014) 7814–7817; (b) T. Castanheiro, J. Suffert, M. Gulea, M. Donnard, Org. Lett. 18 (2016) 2588–2591; (c) T. Castanheiro, J. Suffert, M. Donnard, M. Gulea, Chem. Soc. Rev. 45 (2016) 494–505.

[6] T. Castanheiro, M. Donnard, M. Gulea, J. Suffert, Org. Lett. 16 (2014) 3060–3063.

[7] The complete optimization study is available free of charge in the supporting material of ref 6.

[8] For a study comparing Stille vs Sonogashira coupling, see: M. Charpenay, A. Boudhar, A. Siby, S. Schigand, G. Blond, J. Suffert Adv. Synth. Catal. 353 (2011) 3151–3156.