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Synthesis of Chalcogenophenes *via* Cyclization of 1,3-Diynes Promoted by Iron(III) Chloride and Dialkyl Dichalcogenides

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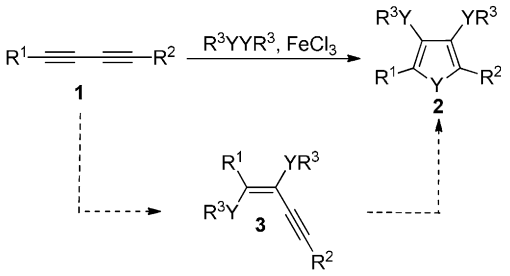
Abstract: In this paper, we report the iron(III) chloride and dibutyl diselenide-mediated cyclization of 1,3-diynes which leads to 3,4-bis(butylselanyl)selenophenes. The optimization studies showed that the reaction was best performed with equimolar amounts of iron(III) chloride and dibutyl diselenide in dichloromethane at 40 °C for 4 h. The method allows the synthesis of symmetrical and unsymmetrical selenophenes in moderate to good yields. A similar protocol was also extended to the synthesis of thiophene derivatives using dimethyl disulfide instead of dibutyl diselenide. The resulting selenophenes and thiophenes were further functionalized by selenium–halogen exchange reactions, Sonogashira cross-coupling reactions and electrophilic cyclizations.

Keywords: cyclization; diorganyl diselenides; iron; selenophenes; thiophenes

Introduction

The use of organoselenium compounds in organic synthesis has increased considerably because of their ability to construct new chemical bonds in a highly selective way, under mild reaction conditions,[1] and their promising pharmacological applications as therapeutic agents in the treatment of several diseases.[2] In this field, selenophenes can be considered as one of the most important classes of organoselenium compounds. Examples of selenophenes and their derivatives have shown biological activities as antidepressant,[3] antioxidant,[4] anticonvulsant,[5] antibacterial,[6] antitumoral,[7] antinociceptive[8] and anti-apoptotic agents.[9] Some of them exhibit an interesting profile of anti-inflammatory activity with a significant analgesic effect.[8] Apart from their biological activities, selenophenes have also been used in the preparation of materials that show potential as optical materials,[10] semiconductors,[11] solar cells,[12] film transistors[13] and energy storage applications.[14] Due to the growing importance and utility of these selenium heterocycles in organic synthesis, many new and remarkable findings and applications have been reported and considerable efforts have been made to develop new methodologies for their preparation. Traditional methods for the synthesis of selenophenes are based on the addition of either electrophilic or nucleophilic selenium reagents to active acyclic substrates to promote the intramolecular cyclization[15] or to apply suitable cyclization methodology to appropriate, previously prepared organoselenium substrates.[16] Many synthetic methods, including electrophilic (halogens source)[17] and transition metal-catalyzed reactions,[18] have been successfully employed in the cyclization of organoselenium substrates. Nowadays, the most user-friendly system for the production of selenophene derivatives by using environmentally friendly, cost effective, green and mild methodologies has undergone an impressive increase of attention by chemists.[19] The iron reagents have appeared as an attractive alternative to other transition metals due to their relative stability, abundance, low toxicity, economic and ecological advantages, and also excellent tolerance towards various functional groups.[20] It was shown that iron salts are useful to catalyze the cross-coupling reaction of Grignard reagents with organic electrophiles,[21] to create new carbon–carbon, carbon–heteroatom and heteroatom–heteroatom bonds[22] and recently they have been applied to the synthesis of heterocycles as well.[23] Our group and others have developed new approaches involving the use of the combination of iron salts and diorganyl diselenides, as cyclizing agents, in the preparation of heterocycles.[24] The main features of the use of diorganyl diselenide reagents in the cyclization reactions are their chemoselectivity and the



Scheme 1. General scheme.

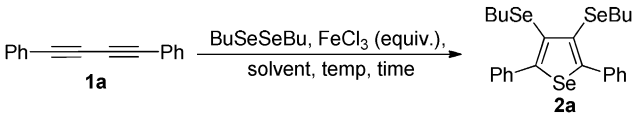
ability to incorporate both portions of diorganyl diselenides (2 PhSe) in the final product, thus providing a more useful and valuable method in terms of atom economy. Concerning the reaction with iron salts and diorganyl diselenides, a wide range of substrates were readily converted into naphthalenes,[25] benzoxazines,[26] indoles,[27] lactones,[28] isoxazoles,[29] chromenones[30] and cyclobutanes.[31] Although we have explored the electrophilic cyclization of homopropargylic selenides and selenoenynes for the preparation of selenophenes, both of these procedures are multistep, as they require the previous preparation of the starting materials.[32] The great versatility of the organoselenium moiety to construct new chemical bonds with defined stereo-, regio-, and chemoselectivity led us to explore if iron(III) chloride and diorganyl diselenides could be used to promote the one-step synthesis of selenophenes **2** from 1,3-diynes **1**, avoiding the previous preparation of selenoenynes **3** (Scheme 1).

Results and Discussion

The starting 1,3-diynes **1** were readily available by using the process of homo- and cross-coupling of alkynes and haloalkynes.[33] Firstly, we added the 1,4-diphenylbuta-1,3-diyne **1a** (0.25 mmol) to a mixture of $FeCl_3$ (2 equiv.) and dibutyl diselenide (2 equiv.) under an argon atmosphere with different reaction parameters to determine the best reaction conditions (Table 1). For the reaction to take place in dichloromethane (3 mL) at room temperature, 10 h reaction time was necessary to provide selenophene **2a** in 58% yield (Table 1, entry 1). When the reaction was carried out under aerobic conditions and the reaction temperature was increased to 40 °C for 4 h, the yield did improve (Table 2, entry 2). Although we carried out many experiments using a catalytic amount of $FeCl_3$ under aerobic conditions, to determine if the oxygen atom could be the mediator for catalyst regeneration, an improvement in the reaction efficiency was only obtained under an argon atmosphere (Table 1, entry 3). Even though different solvents including CH_3CN, CH_3NO_2, DCE, $CHCl_3$ and THF were rather effective, the reaction conducted in dichloromethane gave the best result in the formation of selenophene **2a** (Table 1, entries 4–9). The reaction yields were not improved either by the use of larger quantities of $FeCl_3$ or catalytic amounts, even in the presence of DMSO which could restore the catalytic activity (Table 1, entries 10–12).[34] We propose that to obtain the products in maximum yields, the 1,3-diynes **1a**:dibutyl diselenide mol ratio should be 1:2. The use of two equiv. of dibutyl diselenide gives four equiv. of reactive BuSe; we postulate that three equiv. are incorporated in the final product and one equiv. acts as a nucleophile in an S_N2 reaction to remove the butyl group directly bonded to the selenium atom. To confirm this assumption, we carried out the reaction using 1.5 equiv. of dibutyl diselenide (Table 1, entry 13). The fact that the yield of the product decreased indicates that the reaction requires more than 1.5 equiv. In addition, in all reactions which have product formation, we detected the presence of BuSeBu as a side-product. These two experiments confirm that one BuSe anion acts as a nucleophile in the cyclization.

We further investigated the compatibility of a variety of 1,3-diynes **1** with dibutyl diselenide in the preparation of several selenophenes **2**. All reactions were carried out following the optimized procedure de-

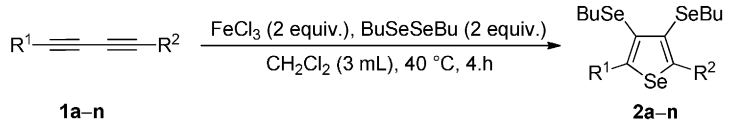
Table 1. Effect of different reaction parameters on the preparation of selenophene **2a**.[a]



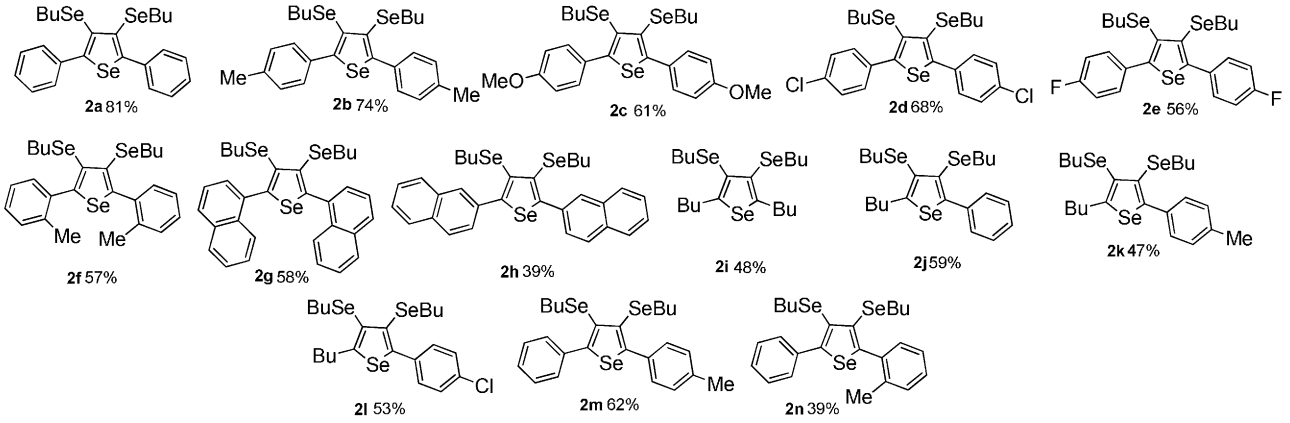
Entry	$FeCl_3$ (equiv.)	Solvent	Temp. [°C]	Time [h]	Yield [%]
1	2	DCM	25	10	58
2	2	DCM	40	4	62[b]
3	2	DCM	40	4	81
4	2	CH_3CN	25	72	–
5	2	CH_3CN	80	36	38
6	2	CH_3NO_2	100	4	59
7	2	DCE	80	4	40
8	2	$CHCl_3$	60	2	64
9	2	THF	60	12	–
10	3	DCM	40	4	56
11	1.5	DCM	40	16	48
12	0.2	DMSO	110	24	–
13	2	DCM	40	4	65[c]

[a] The reaction was performed by the addition of BuSeSeBu to a solution of $FeCl_3$ in CH_2Cl_2 (3 mL), at room temperature, under an argon atmosphere. After 15 min, at this temperature, the 1,3-diyne **1a** (0.25 mmol) was added. The resulting mixture was heated at 40 °C for 4 h.
[b] The reaction was carried out under the ambient atmosphere.
[c] The reaction was performed with 1.5 equiv. of BuSeSeBu.

Table 2. Synthesis of selenophenes **2**.[a,b]



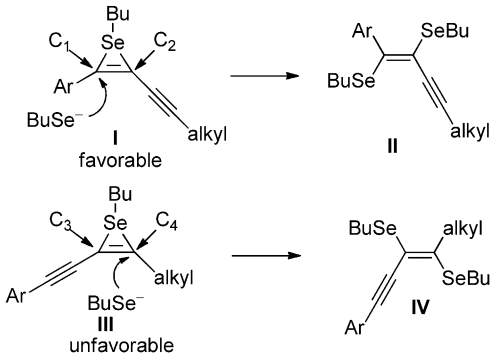
1a–n **2a–n**



[a] The reaction was performed by the addition of BuSeSeBu (2 equiv.) to a solution of $FeCl_3$ (2 equiv.) in CH_2Cl_2 (3 mL), at room temperature, under an argon atmosphere. After 15 min the 1,3-diyne **1** (0.25 mmol) was added. The resulting mixture was heated to 40 °C for 4 h.

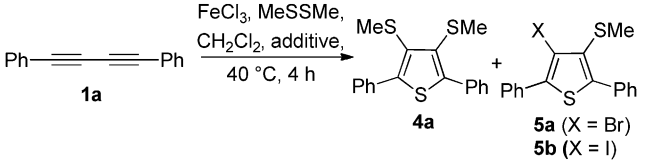
[b] Yields of purified products.

scribed in Table 1 entry 3: addition of ditubyl diselenide to a solution of iron(III) chloride in dichloromethane, at room temperature, under an argon atmosphere. After 15 min the 1,3-diynes **1** were added. The progress of the reaction of each substrate was monitored by TLC to determine the necessary reaction time for complete consumption of the starting material. We observed that 4 h was the required time for the reactions to be completed. According to the results shown in Table 2, the optimized conditions were compatible with a variety of symmetrical 1,3-diynes **1** possessing either electron-donating or electron-withdrawing groups in the aromatic ring (Table 2, **2a–e**). When the reaction was carried out using the *ortho*-methylaryl and naphthyl groups the selenophenes **2f–h** were obtained in moderate yields, presumably due to the steric congestion around the triple bonds (Table 2, **2f–h**). Although the substrate 1,3-diyne **1i** has a deactivated alkyl group, it reacted under the optimized reactions to give the corresponding selenophene (Table 2, **2i**). Besides, we examined the reactivity of unsymmetrical 1,3-diyne derivatives that have the bifunctional alkyl and aryl groups directly bonded to the triple bond. The cyclization of unsymmetrical 1,3-diynes **1j–n** afforded the corresponding selenophenes **2j–n** in 39–62% yields (Table 2, **2j–n**). In the cyclization of unsymmetrical 1,3-diynes **1j–n** two possible regioisomers could be obtained, but it is not possible to determine them by final product analysis. However, as indicated in Scheme 2, the first step of the cyclization of unsymmetrical 1,3-diynes possesses two key intermediates which could be helpful to determine the exact position of each selenium atom as well as which selenium atom is responsible for the cyclization. One way of cyclization is the nucleophilic *anti*-attack of the selenolate species at the C-1 of seleniranium ion **I** giving the selenoenynes **II**, while the second anti-attack way takes place at the C-4 of seleniranium ion **III** to give the selenoenynes **IV** (Scheme 2). The positive influence of the π bonds, from the aromatic rings next to the alkyne, is much stronger than the ones found in an alkyl chain. The aromatic ring increases the electron density in the carbon–carbon bond inducing the seleniranium ion **I** formation. Because of this effect, the nucleophilic attack of the BuSe group is di-



Scheme 2. Key intermediates for the cyclization of unsymmetrical 1,3-diynes.

Table 3. Effect of different reaction parameters on the preparation of thiophene **4a**.[a]



Entry	MeSSMe (equiv.)	Additive (equiv.)	$FeCl_3$ (equiv.)	Yield of **4/5** [%][b]
1	2	NBS (2)	2	13/31
2[c]	2	NBS (2)	2	5/30
3	2	NBS (0.5)	2	24/trace
4	4	NBS (0.5)	2	63/trace
5	4	NBS (1.25)	2	73/8
6	4	NBS (4)	2	–/44
7	4	NBS (1.25)	1.5	78/13
8	4	I_2 (1.25)	1.5	77/–
9	4	I_2 (0.5)	1.5	76/–
10	4	I_2 (0.2)	1.5	77/–

[a] The reaction was performed by the addition of the additive to a solution of MeSSMe in CH_2Cl_2 (3 mL), at room temperature, under an argon atmosphere. After 10 min, the $FeCl_3$ was added and the solution was stirred for 15 min at room temperature and then 1,3-diyne **1a** (0.25 mmol) was added. The resulting mixture was heated at 40 °C for 3 h.

[b] Yields were determined by GC analysis.

[c] The reaction was carried out at room temperature.

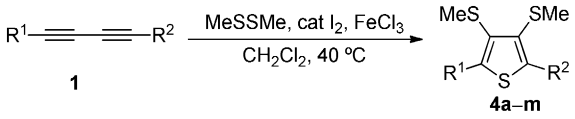
rected to C-1 in the seleniranium ion **I**, next to the aromatic ring, leading to selenoenynes **II**. Consequently, the selenium butyl group bonded to C-1 of the selenoenynes **II** will promote the selenophene closure (Scheme 2). We also studied the effect of dimethyl and dibenzyl diselenides in this cyclization. When dimethyl diselenide was used, there was no product obtained. The reaction worked well with dibenzyl diselenide; however, the product was lost by decomposition during the purification stage.

In the sequence, our attention was focused on the application of the optimized reaction conditions found in Table 1, entry 3 to the cyclization of 1,3-diynes by using dimethyl disulfide and dibutyl ditelluride aiming to prepare thiophenes and tellurophenes, respectively. In contrast to the dibutyl diselenide case, the iron-mediated cyclization of 1,3-diynes **1a** in the presence of dibutyl ditelluride failed to give the tellurophene, while the reaction with dimethyl disulfide gave only 31% yield of the thiophene **4a**. Because of the low yield obtained in the synthesis of thiophenes, we decided to review our early conditions to improve the yield of desired product **4a**. As previously observed, the combination of the stronger sulfur–sulfur bond with the energy of the iron–sulfur bond could hamper the complex formation between iron and diorganyl disulfides.[31] In this case, the addition of a halogen source could be useful in the dissolution of $FeCl_3$ and breaking the polymeric $FeCl_3$ to single molecular form. Thus, we decide to test the influence of the halogen source in the reaction medium. In our case, when the reaction of 1,3-diynes **1a** was conducted in the presence of NBS (2 equiv.), as additive, using the previously optimized reaction conditions, a mixture of thiophene product **4a** with 4-bromothiophene **5a** was obtained (Table 3, entries 1 and 2). In the case where 0.5 equiv. of NBS was used the yields of thiophene **4a** increased up to 63% and only trace of **5a** was obtained (Table 3, entries 3 and 4). The change of the NBS and $FeCl_3$ amount showed no significant improvement in the selectivity (Table 3, entries 5–7). However, the change in the halogen source from NBS to I_2 (1.25 equiv.) and the use of $FeCl_3$ (1.5 equiv.) provided the thiophene **4a** product in 77% yields in the complete absence of 4-iodothiophene **5b** (Table 3, entry 8). Furthermore, the reaction also proceeded smoothly by reducing the quantity of I_2 to a catalytic amount affording good yields of the desired thiophene **4a** (Table 3, entries 9 and 10). After the analysis of the above results, we selected the reaction conditions described in Table 3, entry 10 as the most consistent to extend the protocol to the preparation of other thiophenes **4** (Table 3).

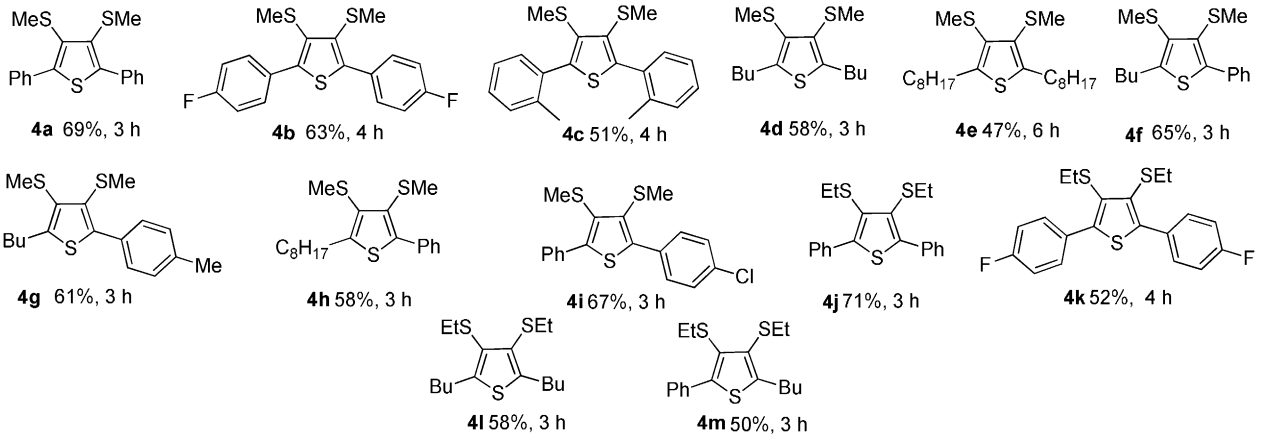
The optimized reaction conditions shown in Table 1, entry 10 proved to be efficient and general when applied to different 1,3-diynes. The results obtained with the variations of 1,3-diynes are presented in Table 4. The reaction allows the conversion of both symmetrical aryl and alkyl 1,3-diynes to give the thiophene derivatives **4a**–**e** in good yields; however, hindered *ortho*-methylphenyl and deactivated alkyl groups, directly bonded to the carbon–carbon triple bond, gave moderate yields. We carried out the cyclization of unsymmetrical 1,3-diynes and found that the expected thiophenes **4f**–**i** were obtained in similar yields. We also investigated the effect of different disulfides on the course of the cyclization. The reaction worked well with diethyl disulfides for both symmetrical and unsymmetrical 1,3-diynes (**4k**–**m**).

Organoselenium substrates, which have a Csp^2–Se bond, were recognized as attractive starting materials for diverse transformations due to their region- and stereoselectivity, mild reaction conditions and tolerance to many functional groups avoiding protection group chemistry.[7] The selenophenes prepared by our methodology offer the possibility to introduce a halogen atom at C-3 and C-4 to the selenophene ring, *via* selenium–halogen exchange reactions.[36] For this propose, we carried out the reaction of selenophene **2a** with bromine (4 equiv.) in $CHCl_3$ (5 mL) and after 4 h under reflux the 3,4-dibromoselenophene **6** was obtained in 65% yield (Scheme 3). The potential application of such derivatives is unquestionable because,

Table 4. Synthesis of thiophenes **4**.[a]



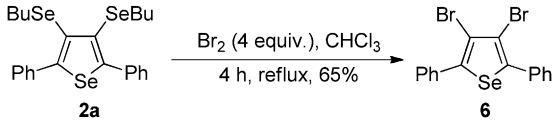
1 → 4a–m



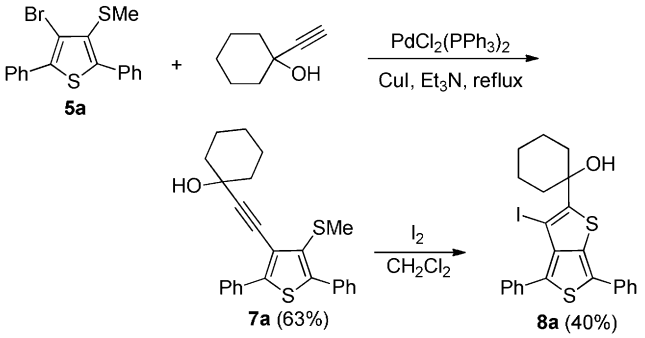
[a] The reaction was performed by the addition of I_2 (20 mmol%) to a solution of MeSSMe (1 mmol) in CH_2Cl_2 (3 mL), at room temperature, under an argon atmosphere. After 10 min, $FeCl_3$ (0.375 mmol) was added and the solution was stirred for 15 min at room temperature and then 1,3-diyne **1a** (0.25 mmol) was added. The resulting mixture was heated at 40 °C for the time indicated.

[b] Yields of purified products.

[c] EtSSEt (1 mmol) was used.



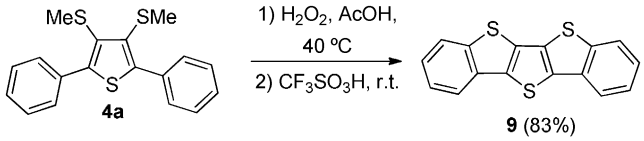
Scheme 3. Preparation of 3,4-dibromoselenophene **6**.



Scheme 4. Preparation of 3-alkynylthiophene **7a** and thieno[3,4-*b*]thiophene **8a**.

as the Csp^2–halogen bond finds applications in the transition metal-catalyzed cross-coupling reactions with nucleophilic compounds allowing the introduction of various functional groups to the selenophene ring. After proving the synthetic utility of the Csp^2–Se bond from selenophene **2**, we planned the preparation of the thieno[3,4-*b*]thiophenes **8** aiming to test the application of the thiophenes prepared. Thieno[3,4-*b*]thiophene-based polymers have emerged as attractive materials for both thin film transistors and solar cell devices.[37] Our exploration begun with a sequential palladium cross-coupling and cyclization reaction using 3-bromo-4-(methylthio)thiophene **5a**, as starting material obtained under the optimized reaction conditions (Table 3, entry 6). The Sonogashira cross-coupling reaction of 3-bromo-4-(methylthio)thiophene **5a** with propargyl alcohol, afforded the 3-alkynylthiophene **7a** in 63% yield (Scheme 4).[38] Afterward, the cyclization step was achieved by the reaction of **7a** with iodine in CH_2Cl_2 at room temperature, which afforded the thieno[3,4-*b*]thiophene **8a** in 40% yield (Scheme 4).[39]

In a final attempt to illustrate the potential application of the chalcogenophenes prepared, we decided to use the thiophene **4a** as staring material in the preparation of dibenzo[*d,d'*]thieno[3,2-*b*;4,5-*b'*]-dithiophene (DBTDT) **9**, which has been recently proposed for high-performance organic film-effect transistors and for their high ionization potential and photostability.[40] Thus, DBTDT **9** was prepared in 83% overall yield *via* oxidation of thiophene **4a** to the sulfoxide derivative followed by its cyclization promoted by CF_3SO_3H (Scheme 5).[41]



Scheme 5. Preparation of dibenzo[*d,d'*]thieno[3,2-*b*;4,5-*b'*]-dithiophene (DBTDT) **9**.

Conclusions

We have developed in this work a two-step, one-pot protocol for the direct cyclization of 1,3-diynes into selenophenes. This was promoted by iron(III) chloride and dibutyldiselenide avoiding the prior preparation of selenoenyne substrates or unstable and air-sensitive selenolate anions. The essential role of equimolar amounts of iron(III) chloride and dibutyl diselenide to the cyclization was described. In this regard, the results of the optimization process indicated that the use of the mole rati 1:2 of 1,3-diynes:dibutyl diselenide was required for the reactions in order to achieve the maximum yields. Considering that two equiv. of dibutyl diselenide give four portions of the reactive species BuSe, we concluded that three portions were incorporated in the final product and one portion acted as a nucleophile in an S_N2 reaction to remove the butyl group directly bonded to the selenium atom. Our cyclization methodology was stereoselective, providing exclusively the desired *E*-selenoenynes as intermediates, which form the selenophene *via* an intramolecular 5-*endo*-dig cyclization. The positive influence of the π bonds, from the aromatic rings next to the alkyne, increases the electron density in the carbon–carbon bond inducing the stereoselectivity in the cyclization. The versatility of these chalcogenophenes was also studied for the selenium–halogen exchange reaction, Sonogashira cross-coupling reaction and electrophilic cyclization reaction. In addition the selenenophene prepared was also applied as starting material in the preparation of a thin film transistor device structure. Furthermore, another feature of this protocol is the fact that the reactions were carried out using iron salts, which are readily commercially available, less expensive and relatively less toxic.

Experimental Section

General Procedure for Iron-Promoted Cyclization of Diynes and Dibutyl Diselenides

To a Schlenk tube, under an argon atmosphere, containing $FeCl_3$ (2 equiv.) in dry CH_2Cl_2 (3 mL) was added the dibutyl diselenide (2 equiv.). The resulting solution was stirred for 10 min at room temperature. After this the appropriate diyne (0.25 mmol) was added in CH_2Cl_2 (1 mL) and the resulting solution was stirred for 4 h at 40 °C. The mixture was cooled to room temperature, dissolved in ethyl acetate and, washed with a saturated solution of NH_4Cl, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography over silica gel, using hexane as eluent to provide the 3,4-bis(butylselanyl)-selenophenes **2**.

3,4-Bis(butylselanyl)-2,5-diphenylselenophene (2a): Obtained as a yellow oil; yield: 0.111 g (81%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ?7.61–7.56 (m, 4H), 7.45–7.33 (m, 6H), 2.63 (t, J=7.2 Hz, 4H), 1.43 (quint, J=7.8 Hz, 4H), 1.19 (sex, J=7.48 Hz, 4H), 0.76 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ=136.8, 129.7, 128.9, 128.1, 127.9, 31.7, 29.5, 22.6, 13.5; MS (EI, 70 eV): *m/z* (relative intensity)= 554 [M+1] (23), 360 (53), 282 (100), 202 (99), 57(16); HR-MS (ESI-TOF): *m/z*=556.9771, calcd. for $C_{24}H_{29}Se_3$ (M+H^+): 556.9765.

3,4-Bis(butylselanyl)-2,5-di-*para*-tolylselenophene (2b): Obtained as a yellow oil; yield: 0.107 g (74%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ=7.49 (d, J=8.0 Hz, 4H), 7.23 (d, J=7.8 Hz, 4H), 2.67 (t, J=7.2 Hz, 4H), 2.41 (s, 6H), 1.47 (quint, J=7.6 Hz, 4H), 1.24 (sex, J=7.4 Hz, 4H), 0.8 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ=149.9, 137.8, 137.7, 134.1, 129.6, 128.8, 128.6, 31.9, 29.6, 22.8, 21.3, 13.5; MS (EI, 70 eV): *m/z* (relative intensity)=582 [M+1] (20), 389 (34), 310 (100), 230 (30), 206 (12); HR-MS (ESI-TOF): *m/z*=585.0083, calcd. for $C_{26}H_{33}Se_3$ (M+H^+): 585.0078.

3,4-Bis(butylselanyl)-2,5-bis(4-methoxyphenyl)selenophene (2c): Obtained as a yellow oil; yield: 0.093 g (61%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ=7.51 (d, J=8.8 Hz, 2H), 6.96 (d, J=8.8 Hz, 2H), 3.85 (s, 6H), 2.64 (t, J=7.2 Hz, 4H), 1.45 (quint, J=7.1 Hz, 4H), 1.21 (sex, J=7.9 Hz, 4H), 0.78 (t, J=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ= 136.8, 129.7, 128.9, 128.1, 127.9, 31.7, 29.5, 22.6, 13.5; MS (EI, 70 eV): *m/z* (relative intensity)=554 [M+1] (23), 360 (53), 282 (100), 202 (99), 57(16); HR-MS (ESI-TOF): *m/z*= 556.9771, calcd. for $C_{26}H_{33}O_2Se_3$ (M+H^+): 556.9765.

3,4-Bis(butylselanyl)-2,5-bis(4-chlorophenyl)selenophene (2d): Obtained as a brown solid; yield: 0.108 g (68%); mp 40–42 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ=7.54–7.51 (m, 4H), 7.40–7.37 (m, 4H), 2.67 (t, J=7.2 Hz, 4H), 1.46 (quint, J=7.5 Hz, 4H), 1.24 (sex, J=7.4 Hz, 4H), 0.80 (t, J=7.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ=148.8, 135.2, 134.1, 131.1, 128.4, 31.9, 29.9, 22.9, 13.3; MS (EI, 70 eV): *m/z* (relative intensity)=624 [M+1] (15), 429 (55), 350 (100), 270 (64), 200 (58), 57 (50); HR-MS (ESI-TOF): *m/z*= 624.8987, calcd. for $C_{24}H_{27}Cl_2Se_3$ (M+H^+): 624.8985.

General Procedure for Iron-Promoted Cyclization of Diynes and Diorganoyl Disulfide

To a Schlenk tube, under an argon atmosphere, containing the appropriate diorganoyl disulfide (4 equiv.) in dry CH_2Cl_2 (3 mL) was added iodine or NBS (20 mol%). The resulting solution was stirred for 5 min at room temperature. After this time, $FeCl_3$ (1.5 equiv.) was added and the resulting mixture was stirred for additional 15 min. To this solution was added the appropriate diyne (0.25 mmol) in CH_2Cl_2 (1 mL) and resulting solution was stirred under 40 °C for the time indicated in Table 4. The mixture was cooled to room temperature, dissolved in ethyl acetate and, washed with a saturated solution of NH_4Cl, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by column chro-

matography over silica gel, using hexane as eluent to provide the 3,4-bis(methylthio)-thiophenes **4**.

3,4-Bis(methylthio)-2,5-diphenylthiophene (4a): Obtained as a brown solid; yield: 0.056 g (69%); mp 83–85 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.76–7.74 (m, 4H), 7.51–7.41 (m, 6H), 2.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 144.1, 133.9, 133.1, 129.4 128.5, 128.3, 132.3, 19.9; MS (EI, 70 eV): *m/z* (relative intensity) = 328 [M+1] (100), 265 (51), 233 (13), 77 (4); HR-MS (ESI-TOF): *m/z* = 329.0499, calcd. for $C_{18}H_{25}S_3$ ($M+H^+$): 328.0417.

2,5-Bis(4-fluorophenyl)-3,4-bis(methylthio)thiophene (4b): Obtained as a brown solid; yield: 0.057 g (63%); mp 106–108 °C. ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.66–7.63 (m, 4H), 7.15–7.11 (m, 4H) 2.29 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 162.8 (d, J = 248.7 Hz), 142.9, 133.3, 131.1 (d, J = 8.3 Hz), 129.7 (d, J = 3.2 Hz), 115.5 (d, J = 21.7 Hz); MS (EI, 70 eV): *m/z* (relative intensity) = 364 [M+1] (100), 302 (78), 270 (34), 138 (49), 73 (16); HR-MS (ESI-TOF): *m/z* = 365.0307, calcd. for $C_{18}H_{15}F_2S_3$ ($M+H^+$): 365.0304.

3,4-Bis(methylthio)-2,5-di-*ortho*-tolylthiophene (4c): Obtained as a brown oil; yield: 0.045 g (51%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.35–7.23 (m, 8H), 2.30 (s, 6H), 2.20 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 142.9, 137.8, 133.3, 133.3, 132.9, 131.1, 130.1, 128.8, 125.4, 29.6; MS (EI, 70 eV): *m/z* (relative intensity) = 356 [M+1] (25), 324 (100), 309 (44), 243 (21), 130 (10); HR-MS (ESI-TOF): *m/z* = 357.0807, calcd. for $C_{20}H_{21}S_3$ ($M+H^+$): 357.0805.

2,5-Dibutyl-3,4-bis(methylthio)thiophene (4d): Obtained as a yellow oil; yield: 0.041 g (58). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 2.94 (t, J = 7.8 Hz, 4H), 2.32 (s, 6H), 1.61 (quint, J = 7.2 Hz, 4H), 1.40 (sex, J = 7.2 Hz, 4H), 0.94 (t, J = 7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 145.8, 131.2, 33.8, 29.2, 22.3, 20.2, 13.8; MS (EI, 70 eV): *m/z* (relative intensity) = 288 [M+1] (100), 245 (77), 202 (33), 187 (20); HR-MS (ESI-TOF): *m/z* = 289.1122, calcd. for $C_{14}H_{25}S_3$ ($M+H^+$): 289.1118.

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