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Chalcogenoalkynes: Precursors for the Regioselective Preparation of 2-Chalcogeno-1-halonaphthalenes through [4+2] Cycloaddition

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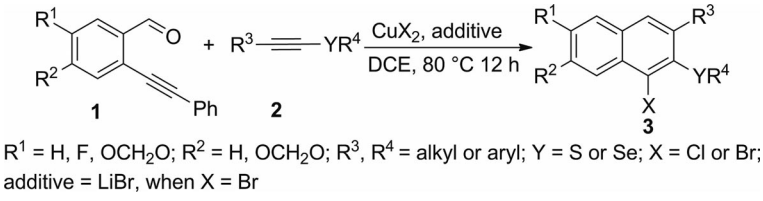
Chalcogenoalkynes and *o*-alkynylbenzaldehydes reacted in the presence of copper(II) salt to give the [4+2] cycloadducts 2-chalcogeno-1-halonaphthalenes in good yields (46–89 %) and high regioselectivities. The methodology was carried out by using $CuCl_2$ or $CuCl_2$/LiBr in 1,2-dichloroethane (DCE) at 80 °C. The potential and generality of this system was evaluated by using a variety of chalcogenoalkynes including aromatic, substituted aromatic, and aliphatic substrates having both sulfur and selenium atoms. In this sequence, due to the ability of the chalcogen atoms to stabilize charges, these substituents exert regiocontrol that guides the selectivity.

Introduction

Polycyclic aromatic compounds with fused benzene rings have received much attention because of their interesting physical and chemical properties.[1] In particular, polycyclic π-conjugated structures have recently become increasingly important in the area of organic electronics.[2] The construction of a fused benzene ring can be achieved by derivatization of naphthalenes through electrophilic or nucleophilic substitution or by functional-group transformation and annulation methods from open-chain precursors. The annulation approach has significant advantages over conventional linear substitution reactions, in particular for the preparation of highly substituted naphthalenes.[3] One advantage is that annulation reactions generally avoid the regioselectivity problems, the restricted scope, and the low yields associated with aromatic substitution reactions.[4] Likewise, in contrast to naphthalenes, preparative methods that can be used to access halogenated naphthalenes are rare. The transition-metal-catalyzed annulation strategy has been shown to be a versatile approach to the regioselective construction of such compounds.[5] However, the preparation of naphthalene derivatives in which C-1 and C-2 contain a halogen and chalcogen atom, respectively, has, to the best of our knowledge, not been reported in the literature. In addition, the introduction of chalcogen groups into organic molecules has found wide utility because of their effects on an extraordinary number of very different reactions.[6] There are several reasons for this: (i) they have a widely varied synthetic organochemical potential, (ii) the chalcogen atom exercises a stabilizing effect on neighboring positive as well as negative charges, (iii) the latter effect makes the carbon atom directly bonded to the chalcogen atom responsive towards both nucleophilic and electrophilic attack, which can allow control of regioselectivity. Considering that the chemical behavior of the halogen atom is distinctly different to that of a chalcogen atom, this class of compounds has become valuable in synthesis, particularly when one considers that there are many ways to transform the resulting halogen and chalcogen functionalities into other substituents. Keeping in mind the capacity of chalcogen atoms to stabilize positive as well as negative charges, we decided to study the influence of such atoms in the re-



Scheme 1. Copper(II)-mediated cyclization of *o*-alkynylbenzaldehydes **1** and chalcogenoalkynes **2**.

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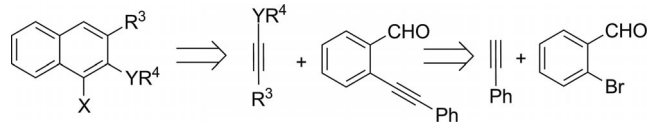
gioselectivity of the cycloaddition reactions of chalcogenoalkynes towards *o*-alkynylbenzaldehydes in the preparation of 2-chalcogeno-1-halonaphthalenes (Scheme 1).



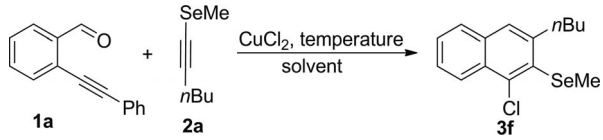
Scheme 2. Retrosynthetic analysis.

Results and Discussion

The retrosynthetic analysis of this cyclization suggested the use of 2-bromobenzaldehyde, terminal alkynes, and chalcogenoalkynes as the starting materials and copper salts as cyclizing agents (Scheme 2). The required precursors *o*-alkynylbenzaldehydes **1a**–**c** were synthesized in good yields by the reaction of appropriate 2-bromobenzaldehydes with terminal alkynes under Sonogashira conditions.[7] For the preparation of chalcogenoalkynes, we first generated the lithium acetylide intermediate by reaction of terminal alkynes with 1 equiv. of *n*BuLi, in tetrahydrofuran (THF) at –78 °C for 1 h, then treated the lithiated intermediate with an electrophilic chalcogen species.[8] Based on our recent report on the cyclization of (*Z*)-chalcogenoenynes to afford 3-halochalcogenophenes mediated by copper(II) salts,[9] the cyclization reaction was initially investigated by treating *o*-alkynylbenzaldehyde **1a** (1 equiv.), chalcogenoalkyne **2a** (1 equiv.), and $CuCl_2$ (2 equiv.) in 1,2-dichloroethane (DCE) (3 mL) under argon at room temperature for 12 h. The use of these reaction conditions, however, did not generate the desired product **3a** in an acceptable yield (Table 1, Entry 1). In view of this disappointing result, we further investigated the reaction with different solvents, temperatures and amounts of copper salt, aiming to improve the protocol. The outcome of these studies and an investigation of other reaction parameters is summarized in Table 1. As listed in Table 1, by increasing the temperature to either 50 °C or to reflux temperature, we observed a significant improvement in the reaction, and the product was formed in good yields (Table 1, Entries 2 and 3). However, the best result was obtained at 80 °C, which gave the desired product **3a** in 82% yield (Table 1, Entry 4). Next, the amount of $CuCl_2$ was investigated (from 1.0 to 2.5 equiv.); however, no improvement in the yield was observed (Table 1, Entries 5–7). We assume that the use of 2.0 equiv. $CuCl_2$ is necessary in this reaction, because $CuCl_2$ acts not only as a triple-bond activator but also as a chlorine source and as a Cu^0 oxidizing reagent (see Scheme 4). Regarding the influence of the solvent, the best results were achieved by using DCE as solvent. We observed that dioxane, MeCN, $MeNO_2$, CH_2Cl_2 and THF were less effective, because the product **3a** was obtained in poor yields with these solvents (Table 1, Entries 8–12). Poor yields of **3a** were found when the reaction was performed in DCE at 80 °C by using either larger amounts of *o*-alkynylbenzaldehyde (3.0 mmol) or lower amounts (0.2 mmol) of chalcogenoalkyne (Table 1, Entries 13 and 14).

To examine the effect on the yield of the substituents on the chalcogen alkynes, we next tested the optimized reaction conditions summarized in Table 1, Entry 4 [Method: **1** (0.25 mmol), **2** (0.25 mmol), $CuCl_2$ (0.5 mmol), DCE (3 mL), 80 °C] with other *o*-alkynylbenzaldehydes (Table 2).

Table 1. Optimization of cyclization conditions.[a]



1a **2a** **3f**

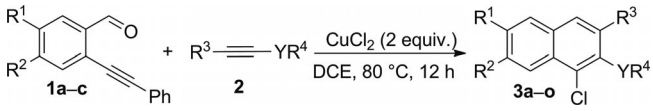
Entry	Solvent	Temperature [°C]	$CuCl_2$ [equiv.]	Yield [%][b]
1	DCE	25	2	30
2	DCE	50	2	76
3	DCE	reflux	2	63
4	DCE	80	2	82
5	DCE	80	1	49
6	DCE	80	1.5	55
7	DCE	80	2.5	60
8	dioxane	80	2	31
9	MeCN	80	2	33
10	$MeNO_2$	80	2	44
11	CH_2Cl_2	reflux	2	69
12	THF	reflux	2	24
13[c]	DCE	80	2	68
14[d]	DCE	80	2	54

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), solvent (3 mL). [b] GC yield. [c] Reaction performed by using 0.3 mmol of **2a**. [d] Reaction performed by using 0.2 mmol of **2a**.

The results indicated that the reaction seems to be sensitive to electronic effects of the substituents in the aromatic ring directly bonded to the alkyne. For example, chalcogenoalkynes with –F and –Cl groups gave lower yields than those with a methyl group (Table 2, Entries 2–4). The results demonstrated that the cyclization efficiency was also significantly influenced by the steric effects of the alkyl group bonded to the selenium atom in the chalcogenoalkynes, because the cyclization reaction gave lower yields with a butyl group than with a methyl or ethyl group (Table 2, Entries 5–8). Cyclization with chalcogenoalkynes containing a substituted aromatic ring directly bonded to the selenium atom smoothly gave the expected cyclized products in good yields (Table 2, Entries 9 and 10). Compared with the selenium derivatives, the reaction employing sulfur was similar, giving the cyclized products equally in good yields (Table 2, Entries 12–16). It should be noted that the yield for substituted *o*-alkynylbenzaldehydes **1b** and **1c** (Table 2, Entries 17–19) was lower than for unsubstituted *o*-alkynylbenzaldehyde **1a**. This is probably due to the slower copper triple-bond activation step (Scheme 4, Step 1) in the reaction course, resulting in a decrease in the alkyne electrophilicity. Meanwhile, to evaluate the possibility of introducing further functionality at C-1 of the naphthalene ring, we tested the behavior of this cyclization reaction using $CuBr_2$ as a bromine source. Unfortunately, all conditions tested were found to be ineffective, and $CuBr_2$ did not produce

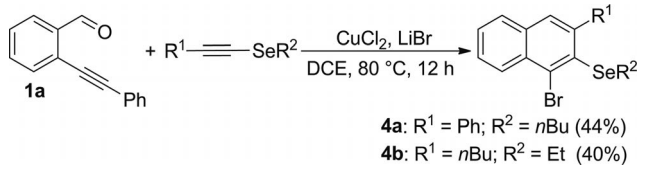
the desired cyclized product. Rudrawar reported that a mixture of copper(II) bromide and LiBr provides quantitative access to nucleophilic bromine species.[10] Gratifyingly, we found that the addition of LiBr (1 equiv.) to the optimized reaction conditions described in Table 1 (Entry 4) gave 1-bromo-2-chalcogenonaphthalenes **4a** and **4b** in 44 and 40% yield, respectively (Scheme 3).

Table 2. $CuCl_2$-promoted cycloaddition of 2-alkynylbenzaldehydes and chalcogenoalkynes.[a]



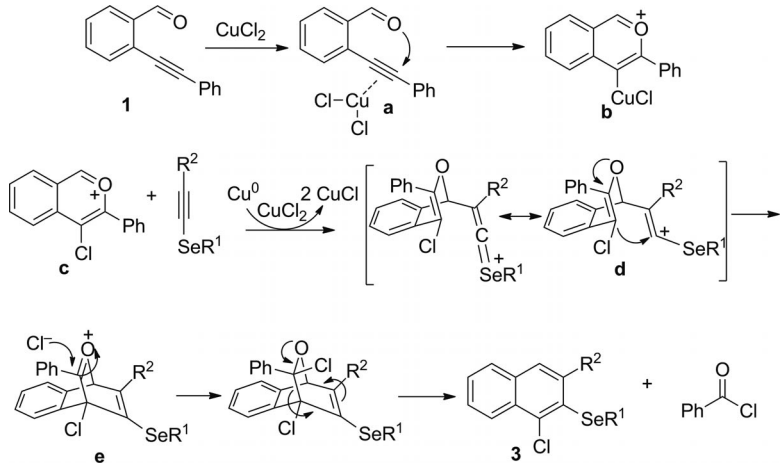
Entry	Aldehyde	R^3	R^4	Y	Product	Yield [%][b]
1	**1a**	Ph	*n*Bu	Se	**3a**	75
2	**1a**	*p*-MeC_6H_4	*n*Bu	Se	**3b**	89
3	**1a**	*p*-FC_6H_4	*n*Bu	Se	**3c**	66
4	**1a**	*p*-ClC_6H_4	*n*Bu	Se	**3d**	78
5	**1a**	Ph	Me	Se	**3e**	76
6	**1a**	*n*Bu	Me	Se	**3f**	82
7	**1a**	*n*Bu	Et	Se	**3g**	60
8	**1a**	*n*Bu	*n*Bu	Se	**3h**	56
9	**1a**	*n*Bu	Ph	Se	**3i**	62
10	**1a**	Ph	*p*-MeC_6H_4	Se	**3j**	72
11	**1a**	*p*-ClC_6H_4	Et	Se	**3k**	78
12	**1a**	Ph	Me	S	**3l**	74
13	**1a**	*p*-FC_6H_4	*n*Bu	S	**3m**	66
14	**1a**	Ph	Ph	S	**3n**	84
15	**1c**	Ph	*n*Bu	S	**3o**	63
16	**1a**	*n*Bu	*n*Bu	S	**3p**	63
17	**1b**	*n*Bu	Et	Se	**3q**	68
18	**1b**	Ph	*n*Bu	S	**3r**	46
19	**1c**	*n*Bu	Et	Se	**3s**	56

[a] Reaction conditions: **1** (0.25 mmol), **2** (0.25 mmol), $CuCl_2$ (0.5 mmol), DCE (3 mL), 80 °C. [b] Isolated yield.



Scheme 3. Preparation of 1-bromo-2-chalcogenonaphthalenes **4**.

The [4+2] benzannulation of *o*-alkynylbenzaldehydes and unsymmetrical alkynes promoted by Lewis acids could gave a mixture of regioisomers.[11] The results have shown that the regiochemical outcome of the reaction is strongly dependent on the electronic (relative nucleophilicity of the functional groups, polarization of the carbon–carbon triple bond, and cationic nature of the intermediate) and steric effects (hindrance and geometrical alignment of the functional groups), as well as on the nature of the transition-metal source. In this context, our cyclization methodology showed high regioselectivity, providing the desired 2-chalcogeno-1-halonaphthalenes **3** as unique regioisomers; this result was confirmed by X-ray diffraction analysis (Figure 1). This high selectivity is probably due to the presence of the chalcogen atom directly bonded to the carbon atom of the triple bond. The selenium atom exerts a significant stabilization of the positive charge at C-1 of the selenonium intermediate **d** (Scheme 2), forcing subsequent attack at this carbon atom. Considering that the chalcogenoalkynes used are unsymmetrical alkynes, which could give a mixture of regioisomers, and based on an understanding that the chalcogen atom exerts a high stabilization of the positive charge at the α-position, we propose a plausible mechanism to support the current Cu^{II} cyclization, as illustrated in Scheme 4. Thus, (i) coordination of the carbon–carbon triple bond to the Cu^{II} species generates intermediate **a**; (ii) *anti* attack of the carbonyl group on the activated triple bond of intermediate **a** produces salt **b**, and (iii) copper reductive elimination provides heterodiene **c** and Cu^0. The formed Cu^0 can be oxidized by $CuCl_2$ to produce CuCl, which makes sense given the need for 2 equiv. of $CuCl_2$ for this reaction;[12] (iv) the [4+2] cycloaddition between **c** and the chalcogenoalkyne results in the creation of cycloadduct **e**, via intermediates **d**. There is a stabilization of a positive charge on C-1 of the intermediary **d**, which is attacked by π-electrons from the double bond to give **e**, and (iv) chlorine attack on the carbonyl group followed by a retro-Diels–Alder reasction



Scheme 4. Proposed mechanism for the copper(II)-mediated cyclization of *o*-alkynylbenzaldehydes **1** and chalcogenoalkynes **2**.

produces the desired naphthalenes as product and benzoyl chloride as side-product.

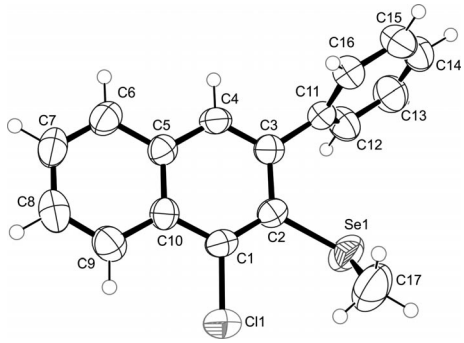


Figure 1. ORTEP representation of the molecular structure of **3e**.

Conclusions

The presented work allowed us to study the reactivity of readily available chalcogenoalkynes and *o*-alkynylbenzaldehydes toward 2-chalcogeno-1-halonaphthalenes. As a result, we have found that the [4+2] cycloaddition reactions of chalcogenoalkynes and *o*-alkynylbenzaldehydes promoted by $CuCl_2$ led to the exclusive formation of 2-chalcogeno-1-halonaphthalenes in good yields. It has been shown that the protocol is not only a facile method but is also applicable to a large substrate range; both electron-rich and electron-poor chalcogenoalkynes, having a sulfur or selenium atom, cyclized with *o*-alkynylbenzaldehydes in the presence of $CuCl_2$. Another feature of this protocol is that the organochalcogen used as substrate serves as a regiocontrolling agent that guides the selectivity. Our process could, therefore, provide an efficient protocol for the preparation of molecules that have two independent reactive centers. It should prove quite useful in synthesis, particularly when one considers that there are many ways to transform the resulting halogen and chalcogen functionalities into other substituents. It is also important to point out that both chalcogenoalkynes and 2-chalcogenonaphthalenes are either solids or oils, they are completely odorless, very stable, and can be purified and stored in the laboratory in a simple flask for more than 1 month.

Experimental Section

General Remarks: ^{1}H NMR spectra were obtained at 200 MHz with a DPX-200 NMR spectrometer or at 400 MHz with a DPX-400 NMR spectrometer; spectra were recorded in $CDCl_3$ solutions. ^{13}C NMR spectra were obtained either at 50 MHz with a DPX-200 NMR spectrometer or at 100 MHz with a DPX-400 NMR spectrometer; spectra were recorded in $CDCl_3$ solutions. Column chromatography was performed by using Merck silica gel (230–400 mesh). Thin layer chromatography (TLC) was performed by using Merck silica gel GF254 (0.25 mm thickness); for visualization, TLC plates were either placed under UV light, or stained with iodine vapor, or acidic vanillin. Most reactions were monitored by TLC for disappearance of starting material. Mass spectra were recorded with a Shimadzu GC–MS-2010P. Elemental analyses were performed with a Vario EL III elemental analysis instrument. HR mass spectra were recorded with a Shimadzu LC-MS-IT-TOF spectrometer.

General Procedure for the $CuCl_2$-Mediated Cycloaddition: Into a two-necked round-bottomed flask equipped with a reflux condenser, under argon, containing a solution of $CuCl_2$ (0.067 g, 0.5 mmol) in 1,2-dichloroethane (3 mL), was added 2-(phenylethynyl)benzaldehyde (0.051 g, 0.25 mmol) and the alkynyl chalcogenide (0.25 mmol). The reaction mixture was stirred at 80 °C for 12 h, then the mixture was diluted with dichloromethane (20 mL) and washed with saturated NH_4Cl (20 mL). The organic phase was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane.

2-(Butylseleno)-1-chloro-3-phenylnaphthalene (3a): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.37–8.32 (m, 1 H, ArH), 7.83–7.78 (m, 1 H, ArH), 7.68 (s, 1 H, ArH), 7.64–7.49 (m, 2 H, ArH), 7.46–7.48 (m, 5 H, ArH), 2.58 (t, J = 7.4 Hz, 2 H, CH_2CH_2), 1.44–1.09 [m, 4 H, 2× ($CH_2CH_2CH_3$)], 0.74 (t, J = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.4, 142.8, 137.8, 133.4, 130.4, 130.5, 129.5, 128.4, 128.0, 127.6, 127.6, 127.4, 127.3, 127.1, 125.3, 32.0, 29.1, 22.6, 13.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 374 (76), 318 (62), 282 (69), 238 (100), 202 (63), 57 (7). $C_{20}H_{19}ClSe$ (373.78): calcd. C 64.27, H 5.12; found C 64.40, H 5.19.

2-(Butylseleno)-1-chloro-3-(*p*-tolyl)naphthalene (3b): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.33 (d, J = 8.6 Hz, 1 H, ArH), 7.78 (d, J = 7.3 Hz, 1 H, ArH), 7.66 (s, 1 H, ArH), 6.61 (quint, J = 7.6 Hz, 2 H, ArH), 7.33 (d, J = 8.0 Hz, 2 H, ArH), 7.23 (d, J = 7.9 Hz, 2 H, ArH), 2.61 (t, J = 7.4 Hz, 2 H, CH_2CH_2), 2.43 (s, 3 H, CH_3), 1.44–1.10 [m, 4 H, 2× ($CH_2CH_2CH_3$)], 0.74 (t, J = 7.2 Hz, 3 H,CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.7, 140.0, 137.7, 137.0, 133.4, 130.4, 129.4, 128.4, 127.9, 127.6, 127.2, 127.0, 125.3, 32.0, 29.2, 22.7, 21.2, 13.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 332 (67), 296 (78), 252 (100), 215 (70), 189 (11), 73 (11). HRMS: calcd. for $C_{21}H_{21}ClSe$ 388.0497; found: 388.0518.

2-(Butylseleno)-1-chloro-3-(4-fluorophenyl)naphthalene (3c): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.33 (d, J = 8.3 Hz, 1 H, ArH), 7.79 (d, J = 8.3 Hz, 1 H, ArH), 7.65 (s, 1 H, ArH), 7.64–7.50 (m, 2 H, ArH), 7.46–7.36 (m, 2 H, ArH), 7.10 (t, J = 8.8 Hz, 2 H, ArH), 2.60 (t, J = 7.0 Hz, 2 H, CH_2CH_2), 1.45–1.11 [m, 4 H, 2× ($CH_2CH_2CH_3$)], 0.75 (t, J = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.2 (d, J = 246 Hz), 143.6, 138.8, 137.6 (d, J = 3.6 Hz), 133.4, 131.6, 131.4 (d, J = 8.0 Hz), 130.6, 128.0, 127.7, 127.5, 127.2, 125.4, 114.6 (d, J = 22 Hz), 32.0, 29.2, 22.6, 13.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 392 (53), 336 (49), 300 (43), 256 (100), 220 (47), 207 (19), 57 (10). HRMS: calcd. for $C_{20}H_{18}ClFSe$ 392.0246; found 392.0253.

2-(Butylseleno)-1-chloro-3-(4-chlorophenyl)naphthalene (3d): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.32 (d, J = 8.3 Hz, 1 H, ArH), 7.77 (d, J = 8.3 Hz, 1 H, ArH), 7.63 (s, 1 H, ArH), 7.59–7.47 (m, 2 H, ArH), 7.37 (s, 4 H, ArH), 2.61 (t, J = 7.3 Hz, 2 H, CH_2CH_2), 1.39 (quint, J = 7.2 Hz, 2 H, $CH_2CH_2CH_2$), 1.20 (sext, J = 7.0 Hz, 2 H, $CH_2CH_2CH_3$), 0.75 (t, J = 7.0 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.6, 141.3, 138.3, 133.5, 131.0, 130.8, 128.3, 128.0, 127.9, 127.6, 127.2, 125.5, 32.0, 29.4, 22.6, 13.3 ppm. MS (EI, 70 eV): *m*/*z* (%) = 408 (80), 352 (77), 316 (72), 272 (100), 200 (44), 73 (18), 57 (22). HRMS: calcd. for $C_{20}H_{18}Cl_2Se$ 407.9951; found 407.9946.

1-Chloro-3-phenyl-2-(methylseleno)naphthalene (3e): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.33 (d, J = 8.2 Hz, 1 H, ArH), 7.80 (d, J

= 7.3 Hz, 1 H, ArH), 7.68 (s, 1 H, ArH), 7.63–7.24 (m, 7 H, ArH), 2.04 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.1, 142.6, 137.1, 133.3, 130.5, 129.4, 128.0, 127.8, 127.7, 127.4, 127.4, 127.1, 125.1, 10.0 ppm. MS (EI, 70 eV): *m/z* (%) = 331(0.15), 283 (83), 233 (100), 189 (16), 94 (8). $C_{17}H_{13}ClSe$ (331.70): calcd. C 61.56, H 3.95; found C 61.68, H 4.01.

3-Butyl-1-chloro-2-(methylseleno)naphthalene (3f): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.30–8.25 (m, 1 H, ArH), 7.77–7.72 (m, 1 H, ArH), 7.60 (s, 1 H, ArH), 7.55–7.45 (m, 2 H, ArH), 3.07 (t, *J* = 7.3 Hz, 2 H, CH_2CH_2), 2.35 (s, 3 H, CH_3), 1.71–1.60 (m, 2 H, $CH_2CH_2CH_2$), 1.43 (sext, *J* = 7.44 Hz, 2 H, $CH_2CH_2CH_3$), 0.97 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 144.4, 134.0, 129.9, 127.4, 127.0, 126.5, 126.0, 125.3, 38.3, 34.1, 22.5, 14.0, 9.7 ppm. MS (EI, 70 eV): *m/z* (%) = 311 (51), 309 (25), 270 (23), 175 (100), 152 (23), 139 (24). HRMS: calcd. for $C_{15}H_{17}ClSe$ 312.0184; found 312.0194.

3-Butyl-1-chloro-2-(ethylseleno)naphthalene (3g): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.31–8.26 (m, 1 H, ArH), 7.77–7.72 (m, 1 H, ArH), 7.61 (s, 1 H, ArH), 7.55–4.45 (m, 2 H, ArH), 3.11–2.94 [m, 4 H, 2× (CH_2CH_2)], 1.71–1.59 (m, 2 H, $CH_2CH_2CH_2$), 1.52–1.41 (m, 2 H, $CH_2CH_2CH_3$), 1.33 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 0.96 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 144.9, 138.7, 129.0, 129.9, 129.4, 127.4, 126.9, 126.5, 125.9, 125.4, 38.3, 33.9, 23.0, 22.5, 15.4, 14.0 ppm. MS (EI, 70 eV): *m/z* (%) = 326 (76), 220 (29), 201 (11), 175 (100), 165 (36), 139 (39), 55 (4). $C_{16}H_{19}ClSe$ (325.74): calcd. C 59.00, H 5.88; found C 59.21, H 5.91.

3-Butyl-2-(butylseleno)-1-chloronaphthalene (3h): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.30–8.25 (m, 1 H, ArH), 7.76–7.71 (m, 1 H, ArH), 7.60 (s, 1 H, ArH), 7.54–7.44 (m, 2 H, ArH), 3.07 (t, *J* = 7.4 Hz, 2 H, CH_2CH_2), 2.97 (t, *J* = 7.2 Hz, 2 H, CH_2CH_2), 1.71–1.25 [m, 8 H, 4× ($CH_2CH_2CH_3$)], 0.96 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.86 (t, *J* = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.8, 138.6, 164.0, 129.9, 127.4, 126.9, 126.4, 125.9, 125.3, 38.3, 34.0, 32.3, 29.4, 22.9, 22.5, 14.0, 13.5 ppm. MS (EI, 70 eV): *m/z* (%) = 354 (100), 300 (30), 218 (49), 177 (41), 175 (98), 139 (22), 57 (17). $C_{18}H_{23}ClSe$ (353.79): calcd. C 6.11, H 6.55; found C 61.27, H 6.59.

3-Butyl-1-chloro-2-(phenylseleno)naphthalene (3i): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.32–8.26 (m, 1 H, ArH), 7.84–7.79 (m, 1 H, ArH), 7.69 (s, 1 H, ArH), 7.63–7.52 (m, 2 H, ArH), 7.16 (s, 5 H, ArH), 3.01 (t, *J* = 7.4 Hz, 2 H, CH_2CH_2), 1.68–1.53 (m, 2 H, $CH_2CH_2CH_2$), 1.46–1.21 (m, 2 H, $CH_2CH_2CH_3$), 0.90 (t, *J* = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.8, 139.5, 134.6, 133.0, 131.5, 130.1, 129.2, 129.1, 127.7, 127.5, 127.4, 126.7, 126.6, 126.0, 125.9, 38.0, 33.7, 22.5, 13.9 ppm. MS (EI, 70 eV): *m/z* (%) = 374 (100), 283 (35), 215 (93), 177 (32), 139 (32), 91 (71). $C_{22}H_{15}ClSe$ (393.77): calcd. C 67.10, H 3.84; found C 67.33, H 3.90.

1-Chloro-3-phenyl-2-(*p*-tolylseleno)naphthalene (3j): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.34 (d, *J* = 8.3 Hz, 1 H, ArH), 7.87–7.82 (m, 1 H, ArH), 8.74 (s, 1 H, ArH), 7.64–7.44 (m, 2 H, ArH), 7.31–7.20 (m, 5 H, ArH), 7.94–7.83 (m, 4 H, ArH), 2.23 (s, 3 H, CH_3) ppm. ^{13}C ($CDCl_3$, 100 MHz): δ = 144.9, 142.6, 138.4, 136.3, 136.1, 133.8, 130.9, 130.6, 129.6, 129.3, 129.0, 128.3, 128.1, 128.0, 127.5, 127.4, 127.1, 125.7, 21.0. MS (EI, 70 eV): *m/z* (%) = 408 (100), 372 (33), 357 (21), 292 (53), 278 (30), 202 (57), 91 (213). $C_{23}H_{17}ClSe$ (407.80): calcd. C 67.74, H 4.20; found C 67.92, H 4.37.

1-Chloro-3-(4-chlorophenyl)-2-(ethylseleno)naphthalene (3k): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.33 (d, *J* = 9.0 Hz, 1 H, ArH), 7.82–7.77 (m, 1 H, ArH), 7.65 (s, 1 H, ArH), 7.61–7.50 (m, 2 H, ArH), 7.38 (s, 4 H, ArH), 7.63 (q, *J* = 7.4 Hz, 2 H, ArH), 2.63 (q, *J* = 7.4 Hz, 2 H, CH_2CH_3), 1.14 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.6, 141.3, 138.3, 133.5, 133.4, 130.9, 130.7, 128.0, 127.9, 127.7, 127.6, 127.6, 127.3, 125.4, 23.1, 15.2 ppm. MS (EI, 70 eV): *m/z* (%) = 380 (57), 341 (31), 316 (93), 281 (51), 207 (100), 73 (73). HRMS: calcd. for $C_{18}H_{14}Cl_2NaSe$ 402.9535; found 402.9581.

1-Chloro-2-(methylthio)-3-phenylnaphthalene (3l): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.33 (d, *J* = 8.4 Hz, 1 H, ArH), 7.78 (d, *J* = 7.7 Hz, 1 H, ArH), 7.68 (s, 1 H, ArH), 7.60–7.37 (m, 7 H, ArH), 2.15 (s, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.7, 141.5, 137.5, 133.3, 132.7, 130.7, 129.4, 128.2, 127.9, 127.8, 127.4, 127.3, 127.2, 125.1, 18.9 ppm. MS (EI, 70 eV): *m/z* (%) = 284 (93), 234 (100), 202 (15), 189 (16), 117 (35), 104 (4), 94 (8). $C_{17}H_{13}ClSe$ (331.70): calcd. C 61.56, H 3.95; found C 61.68, H 4.01.

2-(Butylthio)-1-chloro-3-(4-fluorophenyl)naphthalene (3m): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.33 (d, *J* = 8.3 Hz, 1 H, ArH), 7.79 (d, *J* = 8.3 Hz, 1 H, ArH), 7.66 (s, 1 H, ArH), 7.64–7.50 (m, 2 H, ArH), 7.48–7.38 (m, 2 H, ArH), 7.11 (t, *J* = 8.6 Hz, 2 H, ArH), 2.35 (t, *J* = 7.0 Hz, 2 H, CH_2CH_2), 1.36–1.08 [m, 4 H, 2× ($CH_2CH_2CH_3$)], 0.73 (t, *J* = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.3 (d, *J* = 246 Hz), 143.3, 138.2, 137.6 (d, *J* = 3.6 Hz), 133.4, 131.6, 131.4 (d, *J* = 8.0 Hz), 130.9, 128.1, 128.0, 127.4, 127.3, 125.4, 114.6 (d, *J* = 22 Hz), 35.4, 31.4, 21.6, 13.3 ppm. MS (EI, 70 eV): *m/z* (%) = 344 (72), 288 (100), 252 (91), 233 (20), 220 (20), 207 (36), 73 (13). $C_{20}H_{18}ClFS$ (344.87): calcd. C 69.65, H 5.26; found C 69.77, H 5.31.

1-Chloro-3-phenyl-2-(phenylthio)naphthalene (3n): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.36 (d, *J* = 8.5 Hz, 1 H, ArH), 7.84 (m, 1 H, ArH), 7.76 (s, 1 H, ArH), 7.61 (m, 2 H, ArH), 7.28 (s, 5 H, ArH), 7.13–7.02 (m, 3 H, ArH), 6.90–6.85 (m, 2 H, ArH) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.4, 141.1, 138.9, 137.2, 133.9, 130.8, 129.5, 129.3, 128.6, 128.1, 127.8, 127.5, 127.2, 125.6, 125.3 ppm. MS (EI, 70 eV): *m/z* (%) = 346 (73), 311 (100), 234 (30), 207 (23), 190 (10), 73 (15). $C_{22}H_{15}ClS$ (346.87): calcd. C 76.18, H 4.36; found C 76.37, H 4.41.

6-(Butylthio)-5-chloro-7-phenylnaphtho[2,3-*d*][1,3]dioxole (3o): ^1H NMR ($CDCl_3$, 200 MHz): δ = 7.92 (d, *J* = 9.0 Hz, 1 H, ArH), 7.66 (s, 1 H, ArH), 7.50–7.37 (m, 5 H, ArH), 7.27–7.23 (m, 1 H, ArH), 6.16 (s, 2 H, ArH), 2.50 (t, *J* = 7.0 Hz, 2 H, CH_2CH_2), 1.34–1.07 [m, 4 H, 2× ($CH_2CH_2CH_2$)], 0.72 (t, *J* = 7.2 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.7, 144.4, 141.6, 141.5, 138.7, 129.6, 129.3, 127.6, 127.3, 127.0, 119.8, 119.7, 119.6, 111.3, 102.2, 35.3, 31.3, 21.6, 13.4 ppm. MS (EI, 70 eV): *m/z* (%) = 370 (60), 314 (47), 281 (46), 253 (31), 207 (100), 147 (21), 73 (67). $C_{21}H_{19}ClO_2S$ (370.89): calcd. C 68.00, H 5.16; found C 68.20, H 5.19.

3-Butyl-2-(butylthio)-1-chloronaphthalene (3p): ^1H NMR ($CDCl_3$, 200 MHz): δ = 8.30–8.25 (m, 1 H, ArH), 7.75–7.71 (m, 1 H, ArH), 7.59 (s, 1 H, ArH), 7.54–7.44 (m, 2 H, ArH), 3.06 (t, *J* = 7.4 Hz, 2 H, CH_2CH_2), 2.91 (t, *J* = 7.3 Hz, 2 H, CH_2CH_2), 1.74–1.32 [m, 8 H, 4× ($CH_2CH_2CH_3$)], 0.97 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.88 (t, *J* = 7.2 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.5, 138.4, 133.9, 132.6, 130.2, 127.4, 126.9, 126.4, 126.3, 125.1, 35.9, 33.7, 31.7, 22.6, 22.0, 13.9, 13.6 ppm. MS (EI, 70 eV): *m/z* (%) = 306 (94), 250 (66), 207 (100), 172 (75), 139 (15), 73 (12). HRMS: calcd. for $C_{18}H_{23}ClS$ 306.1209; found 306.1215.

3-Butyl-1-chloro-6-fluoro-2-(ethylseleno)naphthalene (3q): ^1H NMR ($CDCl_3$, 400 MHz): δ = 8.31–8.24 (m, 1 H, ArH), 7.53 (s, 1 H, ArH), 7.28–7.31 (m, 2 H, ArH), 3.09 [m, 4 H, 2× (CH_2CH_2)], 1.70–1.41 [m, 4 H, 2× ($CH_2CH_2CH_3$)], 1.33 (t, *J* = 7.3 Hz, 3 H, CH_3), 0.96 (t, *J* = 7.3 Hz, 3 H, CH_3) ppm. ^{13}C NMR ($CDCl_3$,

100 MHz): δ = 161.4 (d, J = 248.8 Hz), 146.4, 139.0, 135.1 (d, J = 9.1 Hz), 128.9, 128.4 (d, J = 8.7 Hz), 127.2, 125.3 (d, J = 5.1 Hz), 116.7 (d, J = 24.8 Hz), 110.4 (d, J = 20.4 Hz), 38.3, 33.8, 23.1, 22.5 ppm. MS (EI, 70 eV): m/z (%) = 344 (84), 238 (29), 193 (100), 183 (31), 170 (33), 157 (40), 55 (5). HRMS: calcd. for $C_{20}H_{18}ClFSe$ 392.0246; found 392.0253.

2-(Butylthio)-1-chloro-6-fluoro-3-phenylnaphthalene (3r): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.38–8.31 (m, 1 H, ArH), 7.62 (s, 1 H, ArH), 7.47–7.30 (m, 7 H, ArH), 2.51 (t, J = 7.20 Hz, 2 H, CH_2CH_2), 1.36–1.07 [m, 4H 2× (CH_2CH_2)], 0.73 (t, J = 7.35 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.59 (d, J = 249.55 Hz), 145.67, 141.43, 138.24, 134.45 (d, J = 9.51 Hz), 129.69, 128.38 (d, J = 8.78 Hz), 128.01, 127.178, 127.52, 127.38 (d, J = 5.12 Hz), 117.57 (d, J = 25.61 Hz), 111.13 (d, J = 20.49 Hz), 35.46, 31.46, 21.64, 13.39 ppm. MS (EI, 70 eV): m/z (%) = 344 (89), 287 (100), 251 (80), 223 (18), 206 (13). $C_{20}H_{18}ClFS$ (344.87): calcd. C 69.65, H 5.26; found C 69.80, H 5.30.

7-Butyl-5-chloro-6-(ethylseleno)naphtho[2,3-*d*][1,3]dioxole (3s): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.88 (d, J = 8.9 Hz, 1 H, ArH), 7.57 (s, 1 H, ArH), 7.20 (t, J = 8.9 Hz, 1 H, ArH), 6.17 (s, 2 H, ArH), 3.09–2.91 [m, 4 H, 2× (CH_2CH_2)], 1.71–1.41 [m, 4 H, 2× ($CH_2CH_2CH_2$)], 1.33 (t, J = 7.3 Hz, 3 H, CH_2CH_3), 0.96 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 145.3, 144.3, 140.8, 139.5, 127.5, 126.4, 120.4, 119.9, 117.3, 110.5, 102.0, 38.5, 33.7, 23.1, 22.5, 15.3, 13.9 ppm. MS (EI, 70 eV): m/z (%) = 370 (42), 341 (33), 253 (29), 208 (22), 207 (100), 147 (20), 73 (68). $C_{17}H_{19}ClO_2Se$ (369.75): calcd. C 55.22, H 5.18; found C 55.34, H 5.22.

General Procedure for the $CuCl_2$/LiBr-Mediated Cycloaddition: Into a two-necked round-bottomed flask equipped with a reflux condenser, under argon, containing a solution of $CuCl_2$ (0.067 g, 0.5 mmol) and LiBr (0.087 g, 1 mmol) in 1,2-dichloroethane (3 mL), was added 2-(2-phenylethynyl)benzaldehyde (0.051 g, 0.25 mmol) and the alkynyl chalcogenide (0.25 mmol). The reaction mixture was stirred for the desired time at 80 °C, then the mixture was diluted with dichloromethane (20 mL) and washed with saturated aqueous NH_4Cl solution (20 mL). The organic phase was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane.

1-Bromo-2-(butylseleno)-3-phenylnaphthalene (4a): ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 8.37–8.33 (m, 1 H, ArH), 7.78 (t, J = 8.4 Hz, 1 H, ArH), 7.69 (d, J = 12.8 Hz, 1 H, ArH), 7.61–7.50 (m, 2 H, ArH), 7.46–7.37 (m, 5 H, ArH), 2.60–2.53 (m, 2 H, CH_2CH_2), 1.47–1.33 (m, 2 H, $CH_2CH_2CH_2$), 1.24–1.14 (m, 2 H, $CH_2CH_2CH_3$), 0.74 (t, J = 7.3 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 144.8, 143.1, 137.8, 133.4, 132.2, 131.5, 130.5, 129.5, 128.6, 127.9, 127.6, 127.2, 127.0, 125.3, 32.0, 29.1, 22.6, 13.3 ppm. MS (EI, 70 eV): m/z (%) = 419 (42), 417 (52), 361 (37), 281 (100), 279 (46), 202 (63), 57 (6). HRMS: calcd. for $C_{20}H_{20}BrSe$ 417.9835; found 417.9846.

Supporting Information (see footnote on the first page of this article): Experimental procedures, additional experimental details for the preparation of all compounds and ^{1}H and ^{13}C NMR spectra for all reaction products.

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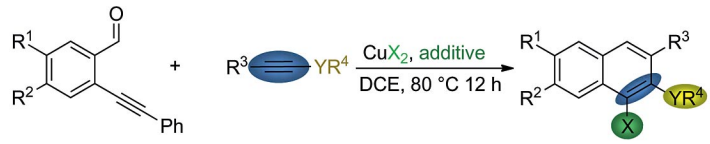

R^1 = H, F, OCH_2O; R^2 = H, OCH_2O; R^3, R^4 = alkyl or aryl; Y = S or Se; X = Cl or Br; additive = LiBr, when X = Br

Chalcogeoalkynes and *o*-alkynylbenzaldehydes reacted in the presence of $CuCl_2$ to furnish the [4+2] cycloadducts 2-chalcogeno-1-halonaphthalenes in good yields (46–89%) and high regioselectivities. The methodology was carried out by using $CuCl_2$ or $CuCl_2$/LiBr in dichloroethane (DCE) at 80 °C.

Keywords: Alkynes / Selenium / Sulfur / Regioselectivity / Cycloaddition

