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$FeCl_3$-Diorganyl Dichalcogenides Promoted Cyclization of 2-Alkynylanisoles to 3-Chalcogen Benzo[*b*]furans

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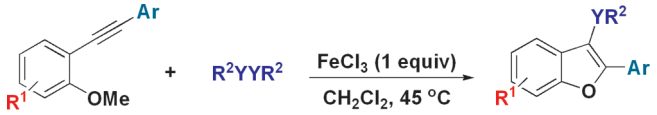

Y= Se, S, Te; R^1= H, Me, F; Ar= C_6H_5, *p*-Me(C_6H_4), *m*-CF_3(C_6H_4)

A general synthesis of 3-chalcogen benzo[*b*]furans from the readily available 2-alkynylanisoles, via $FeCl_3$/diorganyl dichalcogenides intramolecular cyclization, has been developed. Aryl and alkyl groups directly bonded to the chalcogen atom were used as cycling agents. The results revealed that the reaction significantly depends on the electronic effects of substituents in the aromatic ring bonded to the selenium atom of the diselenide species. We observed that the pathway of reaction was not sensitive to the nature of substituents in the aromatic ring of anisole since both the electron-donating and the electron-withdrawing groups delivered the products in similar yields. In addition, the obtained heterocycles were readily transformed to more complex products by using a chalcogen/lithium exchange reaction with *n*-BuLi followed by trapping of the lithium intermediate with aldehydes, furnishing the desired secondary alcohols in good yields.

Introduction

Substituted benzo[*b*]furans are structural units present in many natural products and pharmaceutical synthetic intermediates.[1] They were found to exhibit antiviral, antiparasitic, antifungal, and antidiabetic activities.[2] Therefore, significant efforts to prepare benzo[*b*]furans have been made in the past few years. In this context, palladium is probably the most versatile and widely used metal for the synthesis of these O-heterocycles.[3] For example, alkenes bearing a phenol at an appropriate distance from the carbon−carbon bond can readily undergo palladium(II)-catalyzed intramolecular cyclization to generate a wide variety of benzo[*b*]furans under mild reaction conditions.[4] The first report of the synthesis of benzofurans by such a cyclization appeared in 1973 when the sodium salts of phenols were cyclized to 2-substituted benzofurans with stoichiometric amounts of $PdCl_2$-$(PhCN)_2$.[5] Similarly, other palladium-based catalytic systems have also been successfully adopted in heterocyclic chemistry for the construction of furan derivatives.[6] Meanwhile, an efficient synthesis of 3-chalcogen benzo[*b*]furans

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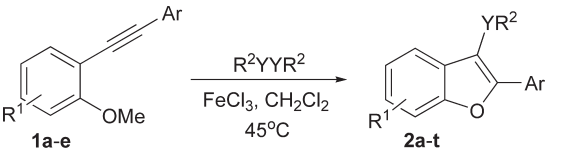
via palladium-promoted annulation reactions of 2-alkynylphenol derivatives with dichalcogenides and iodide has been developed.[7] More recently, significant advances have been made in the synthesis of benzo[*b*]furans by using the halocyclization reactions of the appropriate functional substituted aryl acetylenes.[8] Among them, the use of *o*-alkynylanisoles, as substrate in the electrophilic cyclization,[9] has some advantages in comparison to palladium cyclization, including the presence of halogen atoms which are suitable to suffer further transformations. For instance, the resulting halogenated heterocycles are particularly useful intermediates in many palladium-catalyzed processes, such as Sonogashira,[10] Suzuki,[11] Heck,[12] and carbonylation[13] cross-couplings, providing the corresponding coupling products in excellent yields. In addition, during the past years there has been an impressive increasing attention in the development of environmentally benign protocols and the great challenge for chemists is to apply cost-effective, green, mild, and alternative methodologies.[14] In this context, iron has appeared as a versatile alternative, due to its low price, nontoxicity, and environmentally benign properties. Considering these aspects, many findings concerning iron-mediated organic transformations have been reported. For example, iron trichloride was applied in the cross-coupling of Grignard reagents with several organic electrophiles,[15] iron-catalyzed C−N,[16] C−O,[17] and C−S[18] bond formation. Among these transformations iron salts have also emerged as alternative and promising catalysts or promoters for the cyclization process.[19] To date, cyclization of aryl ketones,[20] carbocyclization via $FeCl_3$-oxidative coupling reactions,[21] intramolecular Friedel−Crafts cyclization,[22] synthesis of benzoxazole derivatives,[23] and diastereoselective synthesis of substituted piperidines[24] are examples of a large number of methodologies which have successfully used $FeCl_3$ in the synthesis of interesting heterocycle or carbocycle compounds. Combining the knowledge that our group has accumulated in the synthesis of heterocycles containing a chalcogen[25] with the fact that iron-promoted cyclization of alkynylanisole derivatives remains unexplored, in this paper, we reported an inexpensive and environmentally friendly synthetic method for the synthesis of 3-chalcogen benzo[*b*]furans starting from 2-alkynylanisoles. Our idea is outlined in Scheme 1, which consists of treatment of 2-alkynylanisoles **1** with iron trichloride and diorganyl diselenides with the intention of the activation of both Y−Y and triple bonds, with concomitant cyclization to yield 3-chalcogen benzo[*b*]furans **2**. The synthesis of the starting material **1** was facile and scalable, starting from standard Sonogashira cross-coupling between 2-haloanisoles and terminal alkynes, in one step (Scheme 1).[26]

SCHEME 1



R^1= H, Me, F, Ar= *m*-F_3C-C_6H_5, *p*-Me-C_6H_5; Y = S, Se, Te

Results and Discussion

We have investigated the procedure with respect to four key variables: (1) solvent, (2) diorganyl diselenide loading, (3) iron trichloride loading, and (4) temperature. We employed the reaction of alkynylanisole **1a** and diphenyl diselenide as a model to study the key variables. Thus, a mixture of diphenyl diselenide (0.5 mmol) and $FeCl_3$ (0.5 mmol), using methanol as solvent, was reacted with **1a** (0.5 mmol) under heating of 65 °C for 12 h. As shown in Table 1, using this reaction condition the desired product **2a** was obtained in 60% yield. To identify the solvent potentially suitable for the cyclization we initially chose CH_3CN, toluene, THF, DMSO, and CH_2Cl_2. The use of CH_3CN, toluene, and THF instead of MeOH delivered moderate to low yields (Table 1, entries 6−8), whereas DMSO did not give the cyclized product (Table 1, entry 9). The use of CH_2Cl_2 gave the best yield of the desired product (Table 1, entry 10). Concerning the amount of $FeCl_3$ a good yield of desired product was obtained in the presence of 1.0 equiv of $FeCl_3$. Intending to carry out the cyclization in a catalytic system we reduced the amount of $FeCl_3$ to 0.2 and 0.5 equiv. These reaction conditions gave the cyclized product in inacceptable 20% and 42% yields, respectively, even with oxygen atmosphere or different ligands

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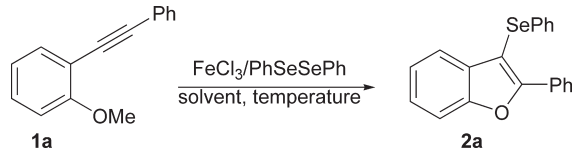
TABLE 1. Influence of Reaction Conditions in the $FeCl_3$/PhSeSePh Cyclization of 2-Alkynylanisoles 1a



1a 2a

entry	$FeCl_3$ (equiv)	$PhSe)_2$ (equiv)	solvent	temp (°C)	yield (%)[a]
1	1.0	1.0	MeOH	65	60
2	0.2	1.0	MeOH	65	20
3	0.5	1.0	MeOH	65	42
4	1.0	0.5	MeOH	65	48
5	1.0		MeOH	65	
6	1.0	1.0	CH_3CN	82	40
7	1.0	1.0	toluene	110	50
8	1.0	1.0	THF	65	17
9	1.0	1.0	DMSO	100	
10	1.0	1.0	CH_2Cl_2	45	71
11	1.0	1.0	CH_2Cl_2	rt	55
12	1.5	1.0	CH_2Cl_2	45	65
13	2.0	1.0	CH_2Cl_2	45	45
14	0.1	1.0	CH_2Cl_2	45	20[b]
15	1.0	1.0	CH_2Cl_2	45	68[c]

[a]Yields are given by GC analysis. [b]Reaction performed under air atmosphere. [c]This reaction was carried out with 1 equiv of methanol.

as the oxidizing agent (Table 1, entries 2 and 3). Iron trichloride in the amount of 1.5 and 2.0 equiv was also found to be insufficient to improve the yields (Table 1, entries 12 and 13). Regarding the influence of the diselenide loading, optimal results were achieved by using 1.0 equiv of diselenide (Table 1, entry 10), while 0.5 equiv was less effective (Table 1, entry 4). Remarkably, in the absence of diselenide the reaction failed to give the unsubstituted benzofuran (Table 1, entry 5). In fact, complete recovery of the starting material, even under forcing conditions, led to the conclusion that the amount of diselenide was critical for the success of this cyclization reaction.

The application of the above standardized conditions to other anisoles with different diorganyl diselenides was studied, and the results are summarized in Table 2. Both hindered and unhindered diaryl diselenides gave the desired benzo[*b*]furans in good yields (Table 2, entries 1 and 7). The reaction seems to be sensitive to electronic effects of the substituents in the aromatic ring of dichalcogenides. For example, diaryl diselenides with $-CF_3$ and Cl groups gave worst yields than a methyl group (Table 2, entries 2, 4, and 5). Gratifyingly, dialkyl diselenide or dibenzyl diselenide were also suitable for the reaction, which gave the desired products in 80% and 64% yields, respectively (Table 2, entries 3 and 6). It is worth mentioning that, through our methodology it was possible to prepare highly functionalized benzo[*b*]furans, using not only diorganyl diselenides but also diorganyl ditelluride and disulfide (Table 2, entries 8 and 9). The introduction of the organotellurium moiety in the structure of benzo[*b*]furans is significant since many classes of organotellurium compounds have been prepared and studied to date. Moreover, the structures having a $C(sp^2)-Te$ bond are certainly the most useful and promising of these compounds in view of their usefulness in organic synthesis, including palladium cross-coupling reactions[27] and synthesis of natural products.[28] In an attempt to broaden the scope of our methodology, the possibility of performing the reaction with other 2-alkynylanisole derivatives, which have Me **1b** and F **1c** groups in the aromatic ring, was also investigated. Both the electron-donating (Me) and the electron-withdrawing (F) groups delivered products with good yields (Table 2, entries 10−16). We have also investigated the possibility of carrying out double cyclizations, which might be quite useful for the quick assembly of systems with extended conjugation. Alkynyl-anisole **1f** underwent Fe/PhSeSePh condition to afford double cyclization product in 78% yield (Table 2, entry 19).

The 3-chalcogen benzo[*b*]furans obtained appear highly promising as intermediates for the preparation of more highly substituted benzo[*b*]furans. To further prove the utility of our methodology, we have carried out the selenium−lithium exchange reaction of products **2** with *n*-butyllithium. The selenium−lithium exchange is a very attractive transformation of selenides, since it affords the corresponding organolithium species,[29] which could react with a wide range of electrophiles generating directly polyfunctionalized molecules.[30] The generation of the organolithium reagent from selenide **2a** was attempted under a variety of reaction conditions by changing the medium, temperature, and amount of *n*-BuLi. On the basis of these experiments we have concluded that the best condition for the Se/Li exchange reaction was as follows: *n*-Butyllithium (1.0 equiv) was added to a solution of 3-phenylselanylbenzo[*b*]furans **2a** (1.0 equiv) and THF (2 mL), at −78 °C. The resulting solution was stirred for 10 min at −78 °C and quenched by H_2O, producing the corresponding hydrogenated product in almost quantitative yield. After standardizing the conditions of the Se/Li exchange reaction, the reaction of the lithium intermediate with aldehydes was screened in order to determine the scope and limitations of our method.

As demonstrated in Table 3, many functional groups were compatible with the reaction conditions. In general, all the reactions proceeded smoothly with good results. The experiments showed that the reaction of the lithium intermediate with aldehydes having an aromatic ring was not sensitive to the electronic effects of the substituents. For example, the aromatic ring having either neutral, electron-donating, or electron-withdrawing substituents gave the cyclized products in very similar yields, although the presence of halogen in the aromatic ring led to a little reduced yield of **3** (Table 3, entries 7 and 8). In addition to aromatic aldehydes, the reaction with alkyl aldehydes also led to the formation of the desired products in a comparable yield to that obtained for aromatic aldehydes (Table 3, entry 5).

Considering what little we have known about the reaction of diorganyl diselenides with $FeCl_3$,[31] our working mechanism for the $FeCl_3$/RYYR conversion of alkynylanisole to

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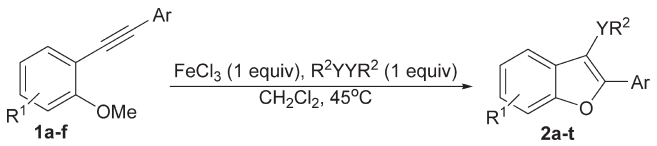
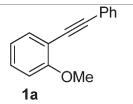
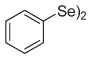
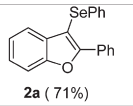
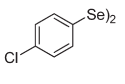
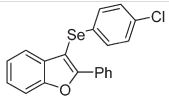
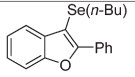
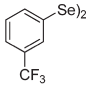
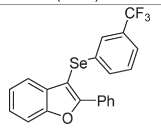
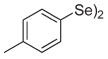
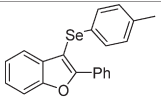
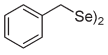
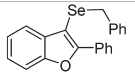
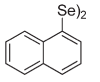
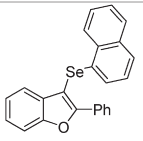
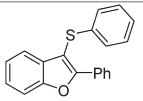
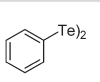
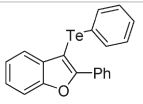
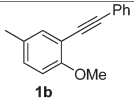
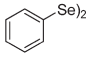
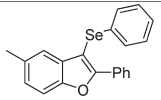
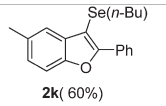
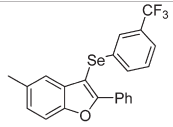
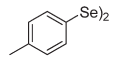
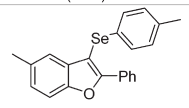
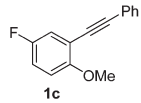
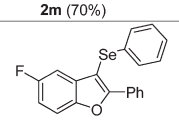
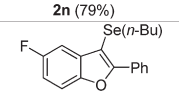
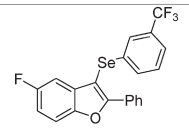
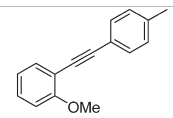
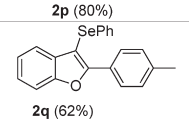
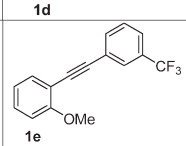
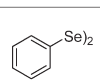
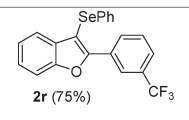
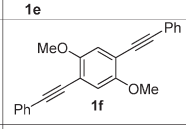
TABLE 2. Synthesis of 3-Chalcogen Benzo[*b*]furan Derivatives 3 via $FeCl_3/R^2YYR^2$ Cyclization of 2-Alkynylanisoles

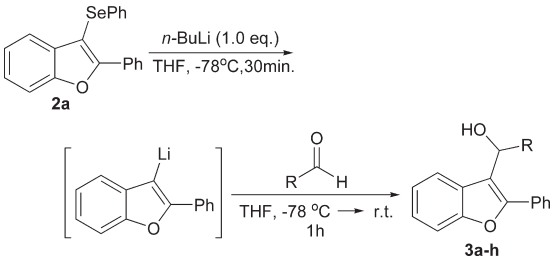


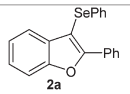
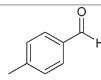
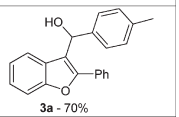
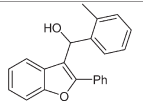
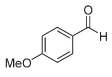
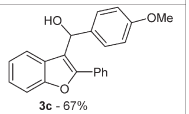
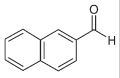
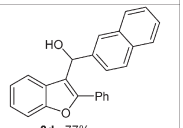
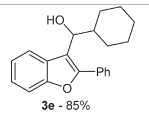
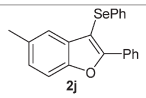
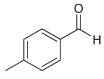
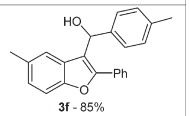
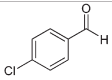
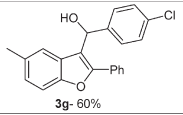
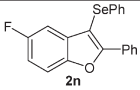
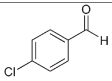
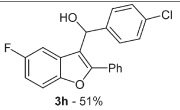
entry	alkynylanisole	R^2YYR^2	product (yield)
1	 **1a**		 **2a** (71%)
2	**1a**		 **2b** (62%)
3	**1a**	*n*-BuSe)$_2$	 **2c** (80%)
4	**1a**		 **2d** (51%)
5	**1a**		 **2e** (90%)
6	**1a**		 **2f** (64%)
7	**1a**		 **2g** (84%)
8	**1a**		 **2h** (60%)
9	**1a**		 **2i** (36%)
10	 **1b**		 **2j**(60%)

entry	alkynylanisole	R^2YYR^2	product (yield)
11	**1b**	*n*-BuSe)$_2$	 **2k**(60%)
12	**1b**		 **2l** (50%)
13	**1b**		 **2m** (70%)
14	 **1c**		 **2n** (79%)
15	**1c**	*n*-BuSe)$_2$	 **2o** (71%)
16	**1c**		 **2p** (80%)
17	 **1d**		 **2q** (62%)
18	 **1e**		 **2r** (75%)
19	 **1f**		**2s** (78%)

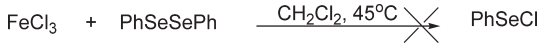
3-chalcogen benzo[*b*]furans is based on the following experimental data obtained in this study: (1) In all reactions, we isolated the RYMe as byproduct. This indicates that a chalcogenolate anion (RY^-) is acting as a nucleophile agent to remove the methyl group from methoxyl. (2) The reaction did not work with $FeCl_3$ in the absence of diorganyl dichalcogen. (3) When we reacted $FeCl_3$ with PhSeSePh, in the same reaction condition used to obtain the cyclized products, in the absence of the substrate anisole, no PhSeCl was formed (Scheme 2). This indicates that the pathway does not follow the typical electrophilic cyclization, where the electrophilic source is PhSeCl (Scheme 3).[9] (4) The decrease in the yields to 48%, when we used 0.5 equiv of PhSeSePh, supports the hypothesis that one-half of diselenide is incorporated in the structure of benzo[*b*]furan, whereas the other one acts as nucleophile. (5) $FeCl_3$ did not work as catalyst (Table 1, entry 2). Then, with these data in mind the working mechanism could involve the following: (a) Fe(III) could

TABLE 3. Reactions of Intermediate 3-Lithio Benzo[b]furan with Aldehydes



entry	3-chalcogen-benzo[*b*]furan	aldehyde	product (yield)
1	 **2a**		 **3a** - 70%
2	**2a**		 **3b** - 80%
3	**2a**		 **3c** - 67%
4	**2a**		 **3d** - 77%
5	**2a**		 **3e** - 85%
6	 **2j**		 **3f** - 85%
7	**2j**		 **3g**- 60%
8	 **2n**		 **3h** - 51%

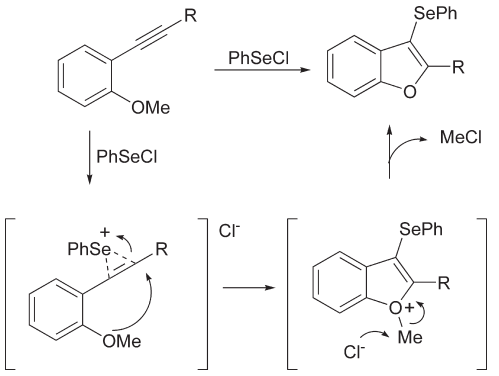
SCHEME 2



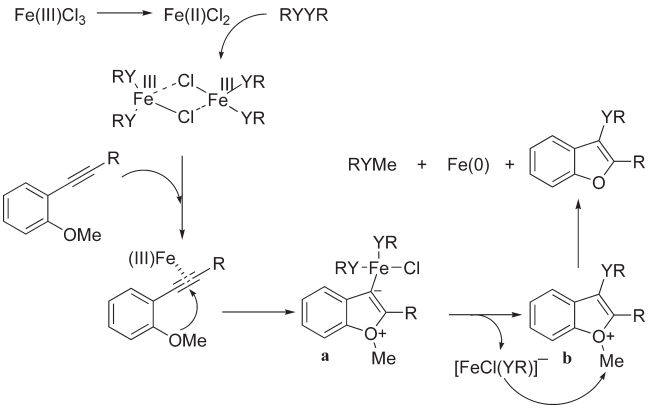
be first reduced to Fe(II);[31a] (b) Fe(III) tetracoordinated square-planar selenolate is formed from diphenyl diselenide and Fe(II), via an oxidation addition with displacement of chlorine; (c) alkyne coordination to the metal center gives the cationic organo-Fe(III) complex; (d) antiattack of the oxygen atom on the activated triple bond produces the intermediate **a**; (e) a coupling reaction[32] produces the salt **b** and the Fe(II) anionic complex $[FeCl(SePh)]^-$; and (f) nucleophilic attack of selenolate anion on the methyl group bonded to the oxygen atom affords the product (Scheme 4).

(32) Hatakeyama, T.; Yoshimoto, Y.; Gabriel, T.; Nakamura, M. *Org. Lett.* **2008**, *10*, 5341.

SCHEME 3



SCHEME 4



Conclusion

We have shown the synthesis of 3-chalcogen benzo[*b*]furans using inexpensive and environmentally friendly $FeCl_3$-promoted cyclization and readily available diorganyl dichalcogenides and 2-alkynylanisoles as the starting materials, and no additional ligand or additive was required. Aryl and alkyl groups directly bonded to the chalcogen atom were used as cycling agents. The results revealed that the reaction significantly depends on the electronic effects of substituents in the aromatic ring bonded to the selenium atom of the diselenide species. We observed that the pathway of reaction was not sensitive to the nature of substituents in the aromatic ring of anisole since both the electron-donating and the electron-withdrawing groups delivered the products with good yields. We have also investigated the possibility of carrying out double cyclizations, which might be quite useful for the quick assembly of systems with extended conjugation. The benzo[*b*]furans obtained in the current protocol appear highly promising and attractive intermediates for the synthesis of more highly substituted benzo[*b*]furans. For instance, 3-chalcogen benzo[*b*]furans were treated under selenium/lithium exchange conditions with *n*-BuLi, and trapping the lithium intermediates with aldehydes provided the corresponding secondary alcohols in good yields. We believe that this approach to benzo[*b*]furans should prove quite useful in synthesis, particularly when one considers that there are

many ways to transform the resulting chalcogen functionalities into other substituents.[33]

Experimental Section

General Procedure for Iron-Promoted Cyclization of 2-Alkynylanisole and Diorganoyl Dichalcogenides. To a two-necked round-bottomed flask equipped with a reflux condenser, under argon, containing a solution of $FeCl_3$ (0.081 g, 0.5 mmol) in CH_2Cl_2 (3 mL) was added 2-alkynylanisole **1a**−**e** (0.5 mmol) in CH_2Cl_2 (2 mL). The reaction mixture was stirred for the desired time at 45 °C. After this, the mixture was diluted with dichlorometane (20 mL) and washed with a saturated solution of NH_4Cl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with hexane.

2-Phenyl-3-(phenylselanyl)benzofuran (2a): yield 0.123 g (71%); white solid, mp 41 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.20 (d, J = 7.8 Hz, 2H), 7.53−7.49 (m, 2H), 7.43−7.40 (m, 2H), 7.37−7.26 (m, 4H), 7.22−7.18 (m, 2H), 7.12−7.09 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.2, 154.0, 131.8, 131.4, 131.3, 129.2, 129.1, 128.4, 127.7, 127.6, 126.2, 125.2, 123.4, 121.1, 111.1, 99.6; ^{77}Se NMR ($CDCl_3$, 400 MHz) δ (ppm) 221.8; MS (EI, 70 eV) m/z (rel intensity) 349 (36), 270 (100), 255 (7), 241 (16), 165 (42). Anal. Calcd for $C_{20}H_{14}OSe$: C 68.77, H 4.04. Found: C 68.85, H 4.26.

2-Phenyl-3-(p-tolylselanyl)benzofuran (2e): yield 0.162 g (90%); yellow solid, mp 77 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.21 (dt, J = 7.3 Hz and J = 1.5 Hz, 2H), 7.52 (t, J = 8.8 Hz, 2H), 7.46−7.36 (m, 3H), 7.31 (td, J = 7.1 Hz and J = 1.5 Hz, 1H), 7.23−7.19 (m, 3H), 6.97 (d, J = 8.3 Hz, 2H), 2.23 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.0, 136.2, 131.9, 130.2, 130.0, 129.5, 129.2, 128.4, 127.7, 127.4, 125.1, 123.3, 121.2, 111.1, 100.1, 20.9; MS (EI, 70 eV) m/z (rel intensity) 363 (32), 284 (100), 269 (12), 255 (9), 241 (12), 165 (31). Anal. Calcd for $C_{21}H_{16}OSe$: C 69.42, H 4.44. Found: C 69.60, H 4.58.

3-(Naphthalen-1-ylselanyl)-2-phenylbenzofuran (2g): yield 0.168 g (84%); yellow solid, mp 86 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.23 (d, J = 7.3 Hz, 1H), 8.10−8.00 (m, 1H), 7.73−7.66 (m, 4H), 7.58−7.26 (m, 9H), 7.20−7.15 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.3, 154.1, 133.9, 131.8, 130.3, 129.3, 128.7, 128.6, 128.4, 127.7, 127.6, 127.3, 127.0, 126.9, 126.5, 126.4, 126.1, 125.6, 125.2, 123.4, 121.1, 111.1; MS (EI, 70 eV) m/z (rel intensity) 399 (62), 320 (100), 291 (32), 165 (52), 115 (30); HRMS calcd for $C_{24}H_{16}OSe$ 400.0366, found 400.0360.

2-Phenyl-3-(phenylthio)benzofuran[7] (2h): yield 0.096 g (60%); white solid, mp 76 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.24−8.21 (m, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.48−7.28 (m, 6H), 7.23−7.18 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.5, 153.9, 136.1, 131.6, 129.7, 129.3, 129.0, 128.5, 127.3, 126.5, 125.5, 125.2, 123.4, 111.3, 104.6; MS (EI, 70 eV) m/z (rel intensity) 302 (100), 241 (13), 225 (27), 197 (27), 165 (33), 105 (20). Anal. Calcd for $C_{20}H_{14}OS$: C 79.44, H 4.67. Found: C 79.66, H 4.73.

2-Phenyl-3-(phenyltellanyl)benzofuran (2i): yield 0.071 g (36%); yellow solid, mp 80 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.13−8.11 (m, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.46−7.43 (m, 4H), 7.41−7.31 (m, 2H), 7.26−7.22 (m, 1H), 7.17−7.07 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 159.2, 154.7, 134.9, 134.3, 130.6, 129.5, 129.3, 128.5, 128.3, 127.2, 125.2, 123.3, 123.1, 114.8, 111.0, 82.6; MS (EI, 70 eV) m/z (rel intensity) 397 (15), 270 (100), 241 (18), 165 (82), 139 (14), 77 (16). Anal. Calcd for $C_{20}H_{14}OTe$: C 60.37; H 3.55. Found: C 60.42, H 3.63.

5-Methyl-2-phenyl-3-(phenylselanyl)benzofuran[7] (2j): yield 0.108 g (60%); yellow solid, mp 47 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.17 (d, J = 7.8 Hz, 2H), 7.40−7.36 (m, 3H), 7.33−7.26 (m, 4H), 7.12−7.08 (m, 4H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.5, 152.6, 133.0, 132.1, 131.6, 130.3, 129.2, 129.1, 129.0, 128.3, 127.7, 126.5, 126.2, 120.9, 110.6, 99.5, 21.3; MS (EI, 70 eV) m/z (rel intensity) 364 (32), 284 (100), 255 (8), 178 (40), 152 (9). Anal. Calcd for $C_{21}H_{16}OSe$: C 69.42, H 4.44. Found: C 69.35, H 4.68.

5-Methyl-2-phenyl-3-(3-(trifluoromethyl)phenylselanyl)benzofuran (2l): yield 0.107 g (50%); yellow solid, mp 63 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 8.15−8.13 (m, 2H), 7.60 (s, 1H), 7.44−7.30 (m, 7H), 7.20 (t, J = 7.8 Hz, 1H), 7.14 (dd, J = 7.3 Hz and J = 1.2 Hz, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 157.8, 152.6, 133.3, 132.9, 129.6 (q, J = 32 Hz), 128.5, 128.4, 126.5 (q, J = 272 Hz), 127.6, 126.7, 125.4 (q, J = 3.6 Hz), 124.8, 122.9 (q, J = 3.6 Hz), 120.7, 120.5, 110.8, 110.6, 101.0, 98.2, 21.3; MS (EI, 70 eV) m/z (rel intensity) 432 (29), 352 (100), 178 (43), 152 (9); HRMS calcd for $C_{22}H_{15}F_3OSe$ 432.0240, found 432.0234.

General Procedure for the Reaction of Intermediate 2-Phenyl-3-lithiobenzo[*b*]furan with Aldehydes. To a two-necked round-bottomed flask, under argon, containing a solution of **2a** (0.5 mmol) in THF (4 mL) at −78 °C was added *n*-BuLi (0.5 mmol, of a 2.5 M solution in hexane) in one portion. The reaction mixture was stirred for 30 min, and then a solution of the appropriated aldehyde (0.5 mmol) in THF (2 mL) at −78 °C was added. The reaction mixture was allowed to stir at room temperature for 1 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with a saturated solution of NH_4Cl (20 mL). The organic phase was separated, dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography and eluted with ethyl acetate/hexane.

(2-Phenylbenzofuran-3-yl)(*p*-tolyl)methanol (3a): yield 0.109 g (70%); colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.72 (d, J = 7.6 Hz, 2H), 7.50−7.36 (m, 6H), 7.27−7.21 (m, 2H), 7.17−7.09 (m, 3H), 6.28 (s, 1H), 2.40 (s, 1H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.4, 152.6, 139.0, 137.2, 130.3, 129.2, 128.9, 128.9, 128.7, 127.8, 126.9, 126.3, 124.4, 122.6, 121.9, 117.6, 111.1, 68.6, 21.0; MS (EI, 70 eV) m/z (rel intensity) 314 (100), 298 (49), 221 (63), 205 (27), 165 (88), 119 (98); HRMS calcd for $C_{22}H_{18}O_2$ 314.1307, found 314.1311.

(2-Phenylbenzofuran-3-yl)(*o*-tolyl)methanol (3b): yield 0.125 g (80%); white solid, mp 129 °C dec; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.73−7.69 (m, 3H), 7.48−7.39 (m, 4H), 7.30 (d, J = 7.8 Hz, 1H), 7.24−7.19 (m, 3H), 7.12−7.10 (m, 1H), 7.06 (td, J = 7.1 Hz and J = 1.0 Hz, 1H), 6.26 (s, 1H), 2.41 (s, 1H), 2.08 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.2, 153.0, 139.7, 135.8, 130.7, 130.2, 128.9, 128.7, 128.0, 127.8, 127.7, 126.2, 125.9, 124.3, 122.7, 121.6, 116.5, 111.1, 67.2, 19.0; MS (EI, 70 eV) m/z (rel intensity) 314 (91), 298 (22), 223 (33), 165 (79), 119 (100). Anal. Calcd for $C_{22}H_{18}O_2$: C 84.05, H 5.77. Found: C 84.29, H 5.83.

Naphthalen-1-yl(2-phenylbenzofuran-3-yl)methanol (3d): yield 0.134 g (77%); colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 7.98 (s, 1H), 7.76−7.71 (m, 5H), 7.47 (d, J = 8.4 Hz, 2H), 7.42−7.36 (m, 5H), 7.31 (d, J = 7.9 Hz, 1H), 7.19 (t, J = 8.2 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 6.41 (s, 1H), 2.62 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 154.3, 152.9, 139.3, 133.1, 132.7, 130.2, 129.0, 128.7, 128.2, 128.1, 127.7, 127.6, 127.5, 126.0, 125.8, 124.6, 124.5, 122.7, 121.7, 117.2, 111.1, 68.7; MS (EI, 70 eV) m/z (rel intensity) 350 (99), 334 (89), 221 (100), 165 (85), 127 (72); HRMS calcd for $C_{25}H_{18}O_2$ 350.1307, found 350.1311.

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Supporting Information Available: Experimental procedures, additional experimental details for the preparation of all compounds, and ^{1}H and ^{13}C NMR spectra for all reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

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