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The diorgano dichalcogenides addition to benzyne under mild conditions[1]

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Abstract

The reaction between diorgano dichalcogenides and *o*-(trimethylsilyl)phenyl triflate in the presence of CsF at room temperature produced *o*-bis(organochalcogenide)benzenes in moderate to good yields.

Introduction

Benzyne is an important reactive intermediate in organic chemistry which has found application in mechanistic studies, total synthesis, and synthesis of functional materials.[2] Accordingly, benzyne has been generated by using several organic precursors.[2] However, we stand out *o*-(trimethylsilyl)phenyl triflate as a commercially available and bench stable reagent to generate benzyne under very mild reaction conditions.[3] In line with this, silylaryl triflates have emerged as outstanding reagents for generating arynes which have recently found use in a number of insertion reactions into σ bonds.[4]

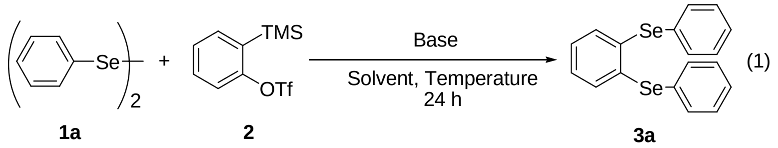
Although arynes generated under harsh conditions have reacted with diaryl dichalcogenides to give *o*-bis(arylchalcogenide)benzenes,[5,6] the published procedures are not general, and fail or give very low yields, when diphenyl dichalcogenides or eletron-poor diaryl dichalcogenides are employed.[5,6]

In the attempt to establish a more general procedure involving mild conditions for the insertion of benzyne into diorgano dichalcogenides, we decided to explore the reaction between dichalcogenides and *o*-(trimethylsilyl)phenyl triflate in the presence of a fluoride ion source.[3,4]

Results and Discussion

Initially, allowing diphenyl diselenide (**1a**) to react with 1.5 equiv of *o*-(trimethylsilyl)phenyl triflate (**2**) and 3 equiv of CsF in acetonitrile at room temperature, we obtained *o*-bis(phenylselenide)benzene (**3a**) in a 42% yield (Table 1, entry 1).

Table 1. Optimization of the synthesis of *o*-bis(phenylselenide)benzene (**3a**) (Eq 1).[a]



entry	**2** (equiv)	base (equiv)	solvent	temp (^{o}C)	% isolated yield
1	1.5	CsF (3)	MeCN	rt	42
2	1.5	CsF (3)	MeCN	80	47[b]
3	2	CsF (3)	MeCN	rt	53
4	**2**	**CsF (4)**	**MeCN**	**rt**	**76**
5	1.5	*n*-Bu_4NF (1.8)	THF	rt	16[c]
6	1.5	KF/[18]crown-6 (1.5/1.5)	THF	0 to rt	8
7	2		MeCN	rt	0

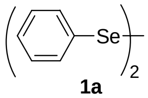
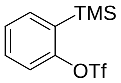
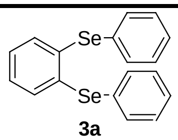
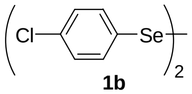
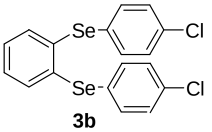
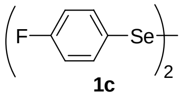
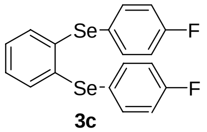
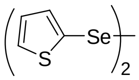
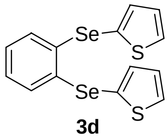
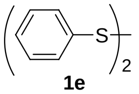
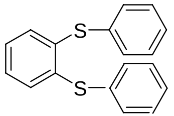
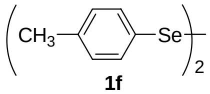
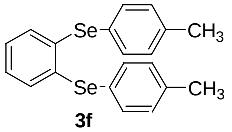
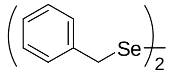
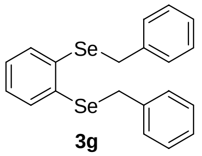
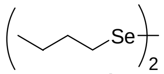
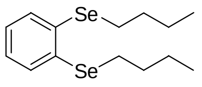
[a] Reaction conditions: 0.3 mmol of diphenyl diselenide (**1a**), the indicated amount of benzyne precursor **2**, the indicated amount of base, and 3 mL of solvent were stirred at the temperature shown for 24 h. [b] This reaction was stirred for 12 h. [c] This reaction was stirred for 3 h.

In an attempt to improve the yield, subsequent work focused on optimization of these reaction conditions (Table 1). When the transformation was performed at 80^{o}C, compound **3a** was obtained in a slightly better yield of 47% (entry 2). By using 2 equiv of the benzyne precursor **2** at room temperature, we isolated **3a** in a 53% yield (entry 3).

Treatment of diphenyl diselenide (**1a**) with 2 equiv of *o*-(trimethylsilyl)phenyl triflate (**2**) and 4 equiv of CsF in acetonitrile at room temperature gave *o*-bis(phenylselenide)benzene (**3a**) in a 76% yield (Table 1, entry 4). In order to explore the effect of the fluoride source on the reaction, 1.8 equiv of tetrabutylammonium fluoride (TBAF) was added to a mixture of diphenyl diselenide (**1a**) and 1.5 equiv of *o*-(trimethylsilyl)phenyl triflate (**2**) in THF at room temperature. After 3 h, compound **3a** was obtained in a 16% isolated yield (entry 5). In line of this, diphenyl diselenide (**1a**) was treated with 1.5 equiv of *o*-(trimethylsilyl)phenyl triflate (**2**), 1.5 equiv of KF and 1.5 equiv of [18]crown-6 in THF initially at 0^{o}C with slow increase to room temperature, producing the *o*-bis(phenylselenide)benzene (**3a**) in an 8% isolated yield (entry 6). As can be seen in Table 1, entry 7, the product **3a** was not obtained and the starting materials **1a** and **2** were recovered when the reaction was carried out in the absence of CsF. This experiment clearly shows that the success of the reaction depends on the presence of a fluoride ion source.

Employing the optimal conditions shown in Table 1, entry 4, we examined the scope of this process using some diorgano dichalcogenides (Table 2). The reaction using the electron-poor diaryl dichalcogenide **1b** with the benzyne precursor **2**, gave the *o*-bis(*p*-chlorophenylselenide)benzene (**3b**) in a 35% isolated yield (entry 2). The same yield was obtained for **3c**, when the reaction was carried out using the diaryl diselenide **1c**, bearing fluoro groups (entry 3). When dithienyl diselenide (**1d**) was allowed to react with **2**, the product was isolated in a 43% yield (entry 4). Allowing diphenyl disulfide (**1e**) to react with 2 equiv of the benzyne precursor **2** and 4 equiv of CsF in acetonitrile at room temperature for 24 h, we obtained *o*-bis(phenylsulfide)benzene (**3e**) in a 27% isolated yield. Increasing the reaction time to 48 h, the product **3e** was formed in a similar yield of 29% (entry 5). For our surprise, when the electron-rich diaryl dichalcogenide **1f** was subjected to the reaction with *o*-(trimethylsilyl)phenyl triflate (**2**), *o*-bis(*p*-tolylselenide)benzene (**3f**) was obtained in a very low yield of 15%. In the attempt to increase this yield, the same reaction was performed at 50^{o}C, and compound **3f** was isolated in a good yield of 74% (Table 2, entry 6). When dibenzyl diselenide (**1g**) was allowed to react with the benzyne precursor **2** in the presence of CsF in acetonitrile at room temperature for 24 h, traces of the product **3g** were obtained along with some by-products. The starting materials were completely consumed, and no attempts were made to identify the by-products. On the other hand, when dibutyl diselenide (**1h**) was submitted to the same reaction conditions, it was almost completely recovered after 24 h.

Table 2. Synthesis of *o*-bis(organochalcogenide)benzenes (**3**) by the reaction of diorgano dichalcogenides (**1**) and *o*-(trimethylsilyl)phenyl triflate (**2**) in the presence of CsF.[a]

entry	diorgano dichalcogenide	benzyne precursor	product	% isolated yield
1	 **1a**	 **2**	 **3a**	76
2	 **1b**	**2**	 **3b**	35
3	 **1c**	**2**	 **3c**	35
4	 **1d**	**2**	 **3d**	43
5	 **1e**	**2**	 **3e**	29[b]
6	 **1f**	**2**	 **3f**	74[c]
7	 **1g**	**2**	 **3g**	traces
8	 **1h**	**2**	 **3h**	traces

[a] Reaction conditions: 0.3 mmol of diorgano dichalcogenide (**1**), 0.6 mmol of *o*-(trimethylsilyl)phenyl triflate **2**, 1.2 mmol of CsF, and 3 mL of MeCN were stirred at room temperature for 24 h. [b] This reaction was stirred for 48 h. [c] This reaction was carried out at 50°C.

The structures of compounds **3a-f** were assigned according to its LRMS, IR, ^{1}H, and ^{13}C NMR spectra. All new componds (**3b-d, f**) provided elemetal analyses or HRMS (ESI) that agree with the proposed structures.

In summary, a simple and more general procedure involving mild conditions for the insertion of benzyne into diorgano dichalcogenides has been developed, and *o*-bis(organochalcogenide)benzenes were prepared in moderate to good yields.

Experimental procedures

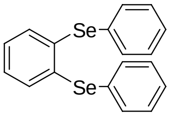
General Methods

The ^{1}H and the ^{13}C NMR spectra were recorded on a spectrometer operating at 300 MHz and 75 MHz respectively. The ^{1}H NMR spectra were taken in $CDCl_3$ and the chemical shifts are given in ppm with respect to tetramethylsilane (TMS) used as an internal standard. The ^{13}C NMR spectra were taken in $CDCl_3$ and the central peak of the solvent was ajusted to 77.000 ppm and used as a reference. The infrared spectra were obtained using a FTIR spectrometer. The mass spectra were obtained using a low resolution mass spectrometer. All melting point values are uncorrected. Elemental and HRMS (ESI) analyses were performed at the Microanalytical Laboratory of the Institute of Chemistry, at the University of São Paulo. CsF was used as obtained commercially. Acetonitrile was distilled from CaH_2 prior to use. The products were purified by preparative thin layer chromatography using silica gel and hexane as eluent.

Procedure for preparation of compounds 3a-f

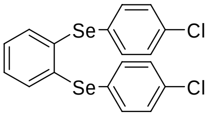
To a vial (20 mL) were added the appropriate diorgano dichalcogenide **1a-h** (0.3 mmol), *o*-(trimethylsilyl)phenyl triflate (**2**) (178.8 mg, 0.6 mmol), acetonitrile (3 mL) and CsF (182.4 mg, 1.2 mmol). The vial was sealed using a cap and the mixture was stirred for 24 h at room temperature unless otherwise indicated. Afterwards, brine (30 mL) was added to the mixture, which was extracted with ethyl acetate (3 x 30 mL). The organic phase was dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure. The residue was purified by preparative thin layer chromatography using silica gel and hexane as eluent, affording the desired products **3a-f**.

Characterization data for compounds 3a-f



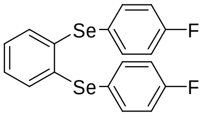
3a

***o*-bis(phenylselenide)benzene (3a) [CAS Registry Number 90454-87-8]:** yield 88.5 mg (76%); colorless liquid; ^{1}H NMR (200 MHz, CDCl$_3$) δ (ppm) 7.53-7.50 (m, 4H), 7.33-7.30 (m, 6H), 7.24-7.16 (m, 2H), 7.10-7.04 (m, 2H); ^{13}C NMR (50 MHz, CDCl$_3$) δ (ppm) 135.8, 133.9, 132.9, 130.5, 129.5, 127.9, 127.8; IR (film, cm^{-1}) 3053, 2925, 1577, 1476, 1437, 1016, 738, 690; LRMS (*m*/*z*, %) 390 (58), 232 (100), 152 (90), 77 (52).



3b

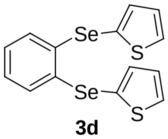
***o*-bis(*p*-chlorophenylselenide)benzene (3b):** yield 48.0 mg (35%); light yellow solid; mp 97-100 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.44-7.40 (m, 4H), 7.30-7.24 (m, 4H), 7.21-7.17 (m, 2H), 7.13-7.09 (m, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm) 135.6, 135.1, 134.2, 133.2, 129.7, 128.7, 128.3; IR (KBr, cm^{-1}) 3070, 3046, 1559, 1469, 1438, 1088, 1009, 817, 745; LRMS (*m*/*z*, %) 422 (29), 232 (78), 152 (72), 40 (100); Anal. Calcd for $C_{18}H_{12}Cl_2Se_2$: C, 47.30; H, 2.65. Found: C, 47.32; H, 2.81.



3c

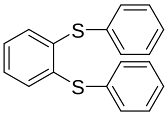
***o*-bis(*p*-fluorophenylselenide)benzene (3c):** yield 44.5 mg (35%); white solid; mp 102-103 ºC; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm) 7.54-7.91 (m, 4H), 7.16-7.12 (m, 2H), 7.10-7.00 (m, 6H); ^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm) 162.8 (d, *J* = 264,7 Hz), 136.3 (d, *J* = 7.9 Hz), 135.8, 132.6, 128.0, 124.9 (d, *J* = 3.3 Hz), 116.8 (d, *J* = 21.5 Hz); IR (KBr, cm^{-1})

3088, 3055, 1559, 1482, 1438, 1085, 1008, 828, 746, 685; LRMS (*m/z*, %) 426 (7), 251 (26), 250 (39), 175 (18), 170 (100), 95 (52); Anal. Calcd. for $C_{18}H_{12}F_2Se_2$: C, 50.96; H, 2.85. Found: C, 50.69; H, 2.95.



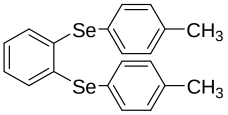
3d

***o*-bis(thiophen-2-ylselenide)benzene (3d):** yield 51.6 mg (43%); light yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.47 (dd, J = 5.4 Hz, J = 1.2 Hz, 2H); 7.37 (dd, J = 3.3 Hz, J = 0.9 Hz, 2H), 7.16-6.97 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 137.1, 135.7, 132.2, 131.5, 128.4, 128.0, 132.6; IR (film, cm^{-1}) 3098, 3049, 1561, 1433, 1397, 1014, 842, 745, 698; LRMS (*m/z*, %) 402 (13), 400 (12), 238 (35), 236 (26), 166 (100), 163 (12), 83 (6); Anal. Calcd. for $C_{14}H_{10}S_2Se_2$: C, 42.01; H, 2.52. Found: C, 42.20; H, 2.77.



3e

***o*-bis(phenylsulfide)benzene (3e) [CAS Registry Number 3379-36-0]:** The reaction to obtain **3e** was stirred for 48h; yield 25.9 mg (29%); light yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.39-7.21 (m, 10H), 7.16-7.08 (m, 4H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm) 137.4, 134.5, 131.8, 131.4, 129.3, 127.5; IR (film, cm^{-1}) 3055, 1577, 1476, 1441, 1030, 745, 692; LRMS (*m/z*, %) 294 (99), 184 (100), 152 (17), 77 (14).



3f

***o*-bis(*p*-methylphenylselenide)benzene (3f):** The reaction to obtain **3f** was carried out at 50^oC; yield 92.3 mg (74%); white solid; mp 91-92 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm) 7.44 (d, J = 8.1 Hz, 4H), 7.15-7.12 (m, 6H), 7.05-7.00 (m, 2H), 2.35 (s, 6H); ^{13}C NMR (75

MHz, $CDCl_3$) δ (ppm) 138.0, 136.0, 134.4, 132.4, 130.4, 127.6, 126.7, 21.2; IR (KBr, cm^{-1}) 3042, 2917, 2856, 1437, 1009, 802, 741; LRMS (*m/z*, %) 418 (6), 246 (11), 232 (19), 165 (50), 152 (40), 91 (100), 65 (96), 40 (61); HRMS (ESI) calcd for $C_{20}H_{18}Se_2Na$ $[M+Na]^+$ 440.9637, found 440.9638.

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