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Preparation of unsymmetrical diaryl selenides in nucleophilic substitution reactions with activated aryl fluorides

Irina P. Beletskaya,*[a] Aleksandr S. Sigeev,[a] Aleksandr S. Peregudov[b] and Pavel V. Petrovskii[b]

[a] *Department of Chemistry, M. V. Lomonosov Moscow State University, 119899 Moscow, Russian Federation.*
Fax: +7 095 938 1844; e-mail: beletska@org.chem.msu.su
[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 117813 Moscow, Russian Federation*

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Activated aryl fluorides enter into nucleophilic substitution reactions with tributyltin phenyl selenide ($Bu_3SnSePh$) in the presence of catalytic amounts of fluoride ions to form corresponding unsymmetrical diaryl selenides in high yield.

Diaryl selenides are attractive as biologically active compounds[1] and conducting materials.[2] The introduction of perfluoroaromatic substituents into diaryl selenide molecules can be of considerable interest; however, such compounds are not easily accessible and almost unknown. The reaction between aryl selenyl bromides and perfluorophenyl lithium is the only method for the synthesis of these compounds.[3]

As an extension of studies concerning the use of $Bu_3SnSePh$, which can be easily prepared *in situ* upon irradiation of hexabutyldistannane and diphenyl diselenide,[4] as an effective phenylselenating agent,[5] we examined the reactions of this compound with fluoroaromatic compounds activated for a nucleophilic attack.

We found that tributyltin phenyl selenide **1** reacts with activated fluoroaromatic compounds in the presence of catalytic amounts of inorganic fluorides to give corresponding diaryl selenides in good yield according to reaction (1). Note that the nucleophilic effect of fluoride ions in reactions involving organotin compounds, in particular, tin selenides, is well known.[6]

$$\underset{\mathbf{1}}{Bu_3SnSePh} + \underset{\mathbf{2a{-}d}}{ArF} \longrightarrow \underset{\mathbf{3a{-}d}}{ArSePh} + Bu_3SnF \qquad (1)$$

a ArF = C_5F_5N **c** ArF = $4\text{-}FC_6H_4NO_2$
b ArF = $C_6F_5CF_3$ **d** ArF = C_6F_6

In a typical reaction procedure, $Bu_3SnSePh$ **1** (1 mmol) reacted with 1 equiv. of octafluorotoluene **2b** in chloroform (2 cm³) in the presence of catalytic amounts of CsF (10 mol%) and a phase-transfer catalyst (triethylbenzylammonium chloride, TEBACl, 10 mol%) at 61 °C for 12 h with the formation of aryl phenyl selenide **3b** in 81% yield (Table 1, entry 4).

Table 1 summarises the results of reactions between compound **1** and octafluorotoluene in the presence of various inorganic fluorides and phase-transfer catalysts. In the absence of fluoride ions, as well as in the absence of phase-transfer catalysts, aryl phenyl selenide **2b** was hardly formed (entries 1 and 2). In the presence of TEBACl or dibenzo-18-crown-6, the nature of the inorganic cation affected the yield of phenylselenation products only slightly, while the yield insignificantly decreased in the case of potassium fluoride (entries 3–6) . The reaction of **1** with octafluorotoluene in more polar dimethylformamide (DMF) did not require initiation by the addition of a fluoride catalyst and was complete in 2 h at room temperature to afford aryl phenyl selenide **2b** in almost quantitative yield.

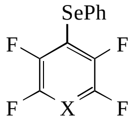
Under the specified conditions, compound **1** readily reacts with activated aryl fluorides. Table 2 summarises the results of reactions between $Bu_3SnSePh$ **1** and various aryl fluorides in the presence of fluoride ions in chloroform or DMF. The reaction of pentafluoropyridine with compound **1** in boiling chloroform proceeded at a higher rate and with a higher yield of phenylselenation product **2a** than in octafluorotoluene (entries 1 and 3). In DMF, the difference disappeared, and the yields of aryl phenyl selenides **2a** and **2b** became almost equal. The phenylselenaton of hexafluorobenzene under the specified conditions did not take place (entries 5 and 6). Thus, only traces of 2,3,4,5,6-pentafluorodiphenyl selenide **3d** were formed after heating in DMF for 15 h (entry 6). In the case of 1-fluoro-4-nitrobenzene **1c**, 4-nitrodiphenyl selenide **3c** was formed in low yield when the reaction was performed in chloroform (entry 7). In this case, diphenyl diselenide, an oxidation product of the $PhSe^-$ anion, was the main product. The yield of compound **3c** dramatically increased if the phenylselenation reaction was performed in DMF at 100 °C (entry 8). At the same time, aryl fluorides containing weaker electron-acceptor substituents, 4-fluoro-1-acetophenone and ethyl 4-fluorobenzoate, did not react with $Bu_3SnSePh$ **1** under the specified conditions.

Table 1 Catalysts and solvents in the reaction of $Bu_3SnSePh$ **1** with octafluorotoluene **2b** (reaction conditions: 1 mmol of **1**, 1 mmol of $C_6F_5CF_3$ and 2 cm³ of solvent).

Entry	Additive	Solvent	*T*/°C	*t*/h	Yield[a] (%)
1	—	$CHCl_3$	61	8	0
2	10% KF	$CHCl_3$	61	14	10
3	10% KF + 10% TEBACl	$CHCl_3$	61	12	78
4	10% CsF + 10% TEBACl	$CHCl_3$	61	12	81 (75)
5	10% KF + 10% Dibenzo-18-crown-6	$CHCl_3$	61	12	79
6	10% CsF + 10% Dibenzo-18-crown-6	$CHCl_3$	61	12	82
7	—	DMF	25	2	97 (95)

[a]The yields were determined using ^{19}F NMR spectroscopy (isolated yields are given in parentheses).

The phenylselenation reaction of perfluoroaromatic compounds is highly selective, and only fluorine at the 4-position with respect to a substituent is replaced in the product. The structure of the products and the regioselectivity of the reaction were confirmed by ^{19}F and ^{77}Se NMR spectroscopy.† The replacement of two or more fluorine atoms did not occur with the use of an excess of phenylselenating agent **1**.



X = N, C–CF$_3$

The reaction was followed by ^{19}F NMR spectroscopy (the disappearance of signals from the starting aryl fluoride was de-

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† ^{19}F NMR spectra were measured on Bruker WP-200 SY and Bruker AMX-400 instruments (188.3 and 376.5 MHZ, respectively) in chloroform or DMF solutions. ^{77}Se NMR spectra were recorded on a Bruker WP-200 SY instrument at 38.19 MHz in chloroform solutions. The resonance conditions were stabilised with the use of external D_2O. The ^{19}F and ^{77}Se chemical shifts were measured with reference to trifluoroacetic acid and diphenyl diselenide as external standards, respectively.

For 4-(PhSe)C_5F_4N: ^1H NMR ($CHCl_3$) δ: 7.35 (m, 3H), 7.65 (m, 2H). ^{19}F NMR ($CHCl_3$) δ: –1 3.25 (m, 2F, 3,5-F), –5 3.8 (m, 2F, 2,6-F). ^{77}Se NMR ($CHCl_3$) δ: –126. MS for $C_{11}H_5F_4N^{80}Se$, *m/z*: 307 [M⁺].

For 4-(PhSe)$C_6F_4CF_3$: ^1H NMR ($CHCl_3$) δ: 7.32 (m, 3H), 7.52 (m, 2H). ^{19}F NMR ($CHCl_3$) δ: 21.10 (t, 3F, CF_3, *J* 22 Hz), –48.69 (m, 2F), –6 2.91 (m, 2F). ^{77}Se NMR ($CHCl_3$) δ: –158. MS f or $C_{13}H_5F_7{}^{80}Se$, *m/z*: 374 [M⁺].

For PhSeC_6F_5: ^{19}F NMR (DMF) δ: –85.8 (t, 2F, 3,5-F, *J* 18.3 Hz), –7 7.5 (t, 1F, 4-F, *J* 18.3 Hz), –5 1.1 (d, 2F, 2,6-F, *J* 18.3 Hz).

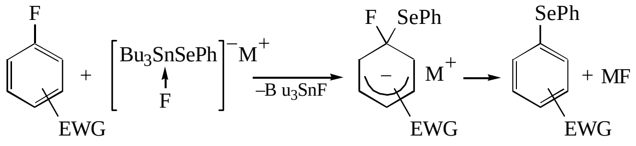
For 4-$NO_2C_6H_4$SePh: ^{77}Se NMR ($CHCl_3$) δ: –2 7.

Table 2 Reactions of $Bu_3SnSePh$ **1** with aryl fluorides (reaction conditions: 1 mmol of ArF, 1 mmol of $Bu_3SnSePh$ **1**, and 2 cm^3 of solvent).

Entry	ArF	ArSePh†	Method[a]	*t*/h	Yield[b] (%)
1	C_5F_5N	4-(PhSe)C_5F_4N	A	5	98 (95)
2			B	2	97 (92)
3	$C_6F_5CF_3$	4-(PhSe)$C_6F_4CF_3$	A	12	82 (75)
4			B	2	97 (95)
5	C_6F_6	$PhSeC_6F_5$[3]	A	10	0
6			C	15	7
7	4-$FC_6H_4NO_2$	4-$NO_2C_6H_4SePh$[5(a)]	A	10	20
8			C	5	98 (92)
9	4-FC_6H_4COMe	4-$MeCOC_6H_4SePh$	C	12	0
10	4-$FC_6H_4CO_2Et$	4-$EtO_2CC_6H_4SePh$	C	12	0

[a]Method A: 10% CsF + 10% TEBACl, $CHCl_3$, 61 °C; Method B: DMF, 25 °C; Method C: 10% CsF, DMF, 100 °C. [b]The yields were determined using ^{19}F NMR spectroscopy (isolated yields are given in parentheses).

tected). In the case of monofluoroarenes, fluorobenzene was added as an internal standard to the reaction mixture. The reaction was performed until the disappearance of signals from the starting fluoroarene. The purity of the products was monitored by ^{77}Se NMR spectroscopy.



EWG = F_5, 2,3,5,6-F_4-4-CF_3, 4-NO_2, 2,3,5,6-F_4-4-N

Scheme 1

Although we did not examine the reaction mechanism in detail, classical aromatic substitution with the participation of fluoride ions seems most reasonable (Scheme 1).

A solvent effect was observed in DMF in the absence of fluoride additives.

In summary, the reaction of $Bu_3SnSePh$ with activated aryl fluorides in the presence of catalytic amounts of fluoride ions or in DMF efficiently proceeds to form aryl phenyl selenides in high yield.

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