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Electrophilic Phenylselenenylation of Thiophenes. Synthesis of Poly(phenylseleno)thiophenes.

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Abstract: The phenylselenenyl sulfate, generated from the oxidation of diphenyl diselenide with ammonium persulfate, easily effects electrophilic aromatic substitution reactions on thiophene, 2- and 3-methylthiophenes and on 3-bromothiophene. The phenylseleno group activates the substrate to further substitution. Under controlled experimental conditions, it is thus possible to introduce the desired number of phenylseleno groups into the thiophene ring.

The reaction of diphenyl diselenide with ammonium persulfate in several solvents produces the strongly electrophilic phenylselenenyl sulfate[1, 2] which easily reacts with unsaturated compounds and, in the presence of several kinds of nucleophiles, affords the corresponding addition products. Starting from alkenes containing a nucleophilic substituent in the appropriate position, ring closure reactions can also be easily effected.[3-5]

Scheme 1

$$PhSeSePh + S_2O_8^{=} \rightleftharpoons 2\ PhSeOSO_3^{-} \rightleftharpoons (PhSe)_2SO_4 + SO_4^{=}$$

$$PhSeOSO_3^{-} + Ar\text{-}H \longrightarrow Ar(H)(SePh)^{+} + SO_4^{=} \longrightarrow Ar\text{-}SePh + HSO_4^{-}$$

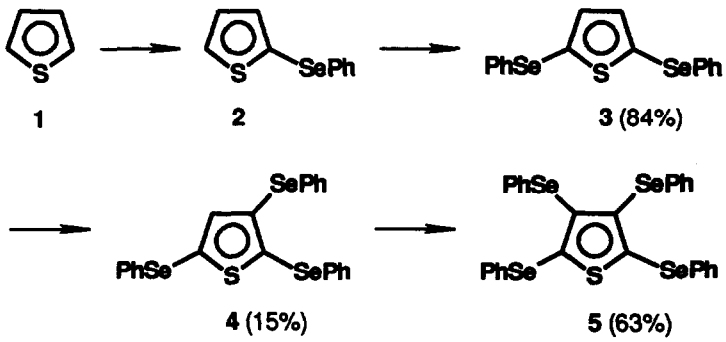
We now report that the same reagent can also be employed to effect efficient electrophilic aromatic substitution reactions under very simple experimental conditions (Scheme 1). The introduction of an aryl or an alkyl selenium group into an aromatic ring is usually carried out by nucleophilic substitution of activated halobenzenes,[6-8] halopyridines[9] or, using dipolar aprotic solvents, even unactivated halobenzenes.[10] Electrophilic substitutions by selenenyl groups have been scarcely reported in the literature. Benzeneselenenyl chloride did not give the expected products,[11] whereas the use of phenylselenenyl hexachlorophosphate[12] and dimethyl(phenylseleno)sulfonium tetrafluoborate[13] was limited to electron-rich aromatic compounds such as anilines, phenols and anisole.

These results indicate that in order to effect the substitution reactions on benzene derivatives it is necessary to use a strongly electrophilic selenenylating agent, *i. e.* a reagent in which the PhSe group is

linked to a non nucleophilic counterion. As a matter of fact it has recently been reported that not only the strongly activated benzenes but also toluene and even benzene can be selenenylated when the reactions are carried out with phenylselenenyl *m*-nitrobenzensulfonate.[14] This latter reagent can be prepared by oxidation of diphenyl diselenide with *m*-nitrobenzensulfonyl peroxide and directly used *in situ* to effect several addition reactions to alkenes also.[14, 15] The production and the reactivity of this selenenylating agent are similar to those described by us for the related phenylselenenyl sulfate.[1] Indeed we have now found that the reaction of phenylselenenyl sulfate with anisole proceeded smoothly to afford a 95:5 mixture of the 4- and 2-methoxyphenyl phenyl selenides in 97% yield. The use of this substitution reaction in the field of heteroaromatic compounds can give rise to selenides having interesting structures. We now report the results of an investigation carried out on thiophene, 2- and 3-methylthiophene and on 3-bromothiophene.

These experiments were carried out by stirring a mixture of diphenyl diselenide, ammonium persulfate and the thiophene derivative in refluxing acetonitrile. Preliminary experiments showed that, in order to obtain the monosubstituted products, an excess of the thiophene derivative (20 mol. eqv.) was necessary. In these cases therefore reaction yields were calculated on the amount of the PhSeSePh employed (1 mol. eqv.). The molar ratios of thiophene derivatives/diphenyl diselenide were 1/1.5 (1/0.5 in the case of the 3-methylthiophene) for the reactions carried out to obtain the products of partial substitution and 1/3 in the cases in which complete substitution was desired. Ammonium persulfate was always employed in equimolecular amount in respect to the PhSeSePh. The progress of the reactions was easily monitored by TLC or GC-MS. The reaction times ranged from 2 to 7 hours.

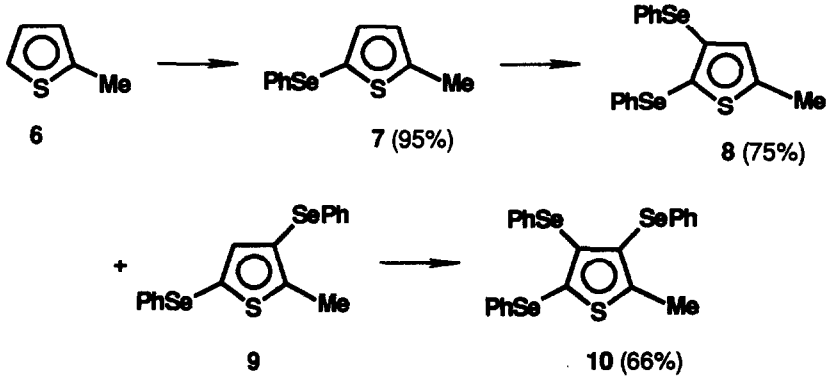
Scheme 2



The course of the reaction of thiophene **1** is illustrated in Scheme 2. In this case the monosubstituted product **2** could not be obtained. Even at the early reaction stages the only product present in the reaction mixture was the 2,5-bis(phenylseleno)thiophene **3**. Difficulties were also encountered in the case of the synthesis of **4**. This product was in fact obtained in low yield (15%), the major reaction product being **5** (52%). Compounds **3** and **5** were instead easily obtained in 84% and 63% yield, respectively, using the molar ratios indicated above. It can be argued from these results that the phenylseleno group activates the thiophene ring to further electrophilic substitution.

The three reactions of 2-methylthiophene **6** (Scheme 3) gave cleanly the monosubstituted, the disubstituted and the trisubstituted products, **7** (95%), **8** (75%) and **10** (66%), in good yields. The 2-methyl-4,5-bis(phenylseleno)thiophene **8** was accompanied by the isomeric 2-methyl-3,5-bis(phenylseleno)thiophene **9**, which was present in minute amounts and which could be only detected by GC-MS. Structural attributions were easily made by proton NMR.

Scheme 3

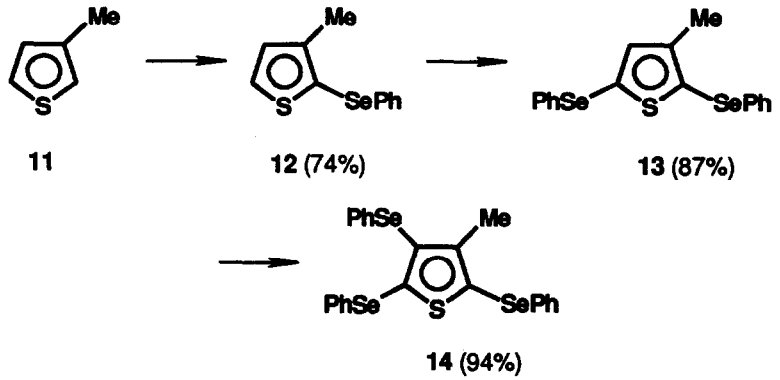


6 **7** (95%) **8** (75%)

9 **10** (66%)

Similarly, compounds **12** (74%), **13** (87%) and **14** (94%) were easily obtained from the reactions of the 3-methylthiophene **11** (Scheme 4).

Scheme 4

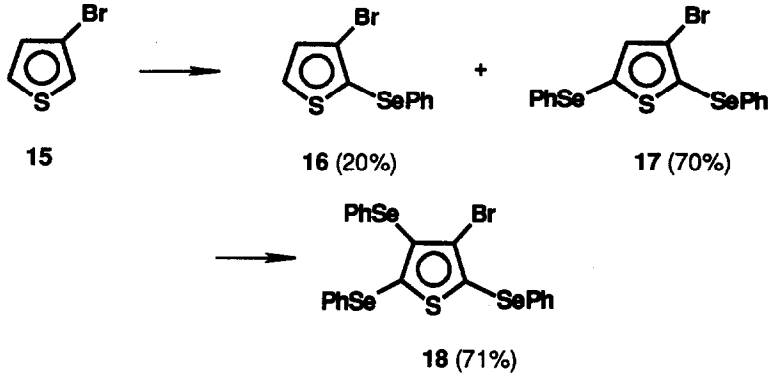


11 **12** (74%) **13** (87%)

14 (94%)

The reaction of the 3-bromothiophene **15** (Scheme 5) with phenylselenenyl sulfate could not be stopped at the stage of the monosubstituted product **16**. In fact, from the experiment carried out with a large excess of **15**, the 3-bromo-2-(phenylseleno)thiophene **16** was isolated in 20% yield, the main reaction product (70%) being the 3-bromo-2,5-bis(phenylseleno)thiophene **17**. Good yield (71%) of the 3-bromo-2,4,5-tris(phenylseleno)thiophene **18** was obtained from the reaction carried out with an excess of phenylselenenyl sulfate.

Scheme 5



In conclusion the results presented in this paper indicate that phenylselenenyl sulfate, easily produced from commercially available diphenyl diselenide and ammonium persulfate, can be conveniently used to effect electrophilic phenylselenenylation reactions with considerable advantages over the previously described methods. The phenylseleno group activates the substrate to further substitution. Thus, under controlled experimental conditions, it is possible to introduce the desired number of phenylseleno groups and to obtain several interesting selenium substituted thiophene derivatives.

EXPERIMENTAL

GLC analyses and MS spectra were carried out with an HP 5890 gaschromatograph (dimethyl silicone column, 12.5 m) equipped with an HP 5971 Mass Selective Detector. Proton and carbon-13 NMR spectra were recorded at 200 and 50.32 MHz, respectively, on a Bruker AC 200 instrument; $CDCl_3$ was used as solvent and TMS as standard. Elemental analyses were carried out on a Carlo Erba 1106 Elemental Analyzer. Compounds **1**, **6**, **11** and **15** were commercially available and were used without further purification. All new compounds were fully characterized by MS, ^1H, and ^{13}C-NMR spectroscopy.

Electrophilic Phenylselenenylation of Thiophenes. General Procedure. A mixture of diphenyl diselenide, thiophene derivative (0.01 mol) and ammonium persulfate, in the ratios indicated above, was stirred in refluxing acetonitrile (30 ml). The progress of the reactions was easily monitored by TLC or GC-MS. The reaction times ranged from 2 to 7 hours. The reaction mixture was poured on water and extracted with chloroform. The organic layer was washed with water, dried and evaporated. The reaction products were isolated in pure form after column chromatography on silica gel using mixtures of light petroleum and ether or chloroform as eluant. Reaction yields are reported in the Schemes. Physical and spectral data of reaction products are reported below. In the mass spectra, in the case of the ions containing from one to four selenium atoms or from one to three selenium atoms and one bromine atom, only the most prominent peaks are reported. These peaks are due to the ions containing the isotopes ^{80}Se, $^{80}Se^{80}Se$, $^{80}Se^{80}Se^{78}Se$, $^{80}Se^{80}Se^{80}Se^{78}Se$, or $^{80}Se^{79}Br$ and $^{78}Se^{81}Br$, $^{80}Se^{80}Se^{79}Br$ and $^{80}Se^{78}Se^{81}Br$,

$^{80}Se^{80}Se^{80}Se^{79}Br$ and $^{80}Se^{80}Se^{78}Se^{81}Br$, respectively. In all cases the patterns of the various peaks were in perfect agreement with those of simulated spectra.

2,5-Bis(phenylseleno)thiophene (3): mp 47-48 °C; ^1H NMR δ 7.37 - 7.28 (m, 4 H), 7.22 - 7.18 (m, 8 H); ^{13}C NMR δ 136.9, 132.5, 130.5, 129.4, 129.1, 127.0; MS *m/z* (relative intensity) 316 (3), 239 (100) 158 (56), 115 (39), 77 (42), 51 (30). Anal. Calcd for $C_{16}H_{12}SSe_2$: C, 48.74; H, 3.07. Found: C, 48.60; H, 3.16.

2,3,5-Tris(phenylseleno)thiophene (4): mp 77-78 °C; ^1H NMR δ 7.5 - 7.05 (m, 15 H), 7.01 (s, 1 H). ^{13}C NMR δ 140.6, 132.8, 132.6, 132.2, 130.8, 129.3, 129.2, 127.7, 127.4, 127.2. MS *m/z* (relative intensity) 550 (4), 314 (21), 238 (87), 234 (66), 158 (100). 154 (89), 117 (22), 114 (38), 77 (61), 51 (42). Anal. Calcd for $C_{22}H_{16}SSe_3$: C, 48.10; H, 2.94. Found: C,47.70; H, 3.02.

2,3,4,5-Tetrakis(phenylseleno)thiophene (5): mp 105-108 °C; ^1H NMR δ 7-49 - 7.38 (m, 4 H), 7.23 - 7.1 (m, 10 H), 7.09 - 6.98 (m, 6 H). ^{13}C NMR δ 138.6, 133.5, 132.3, 130.7, 130.2, 129.3, 128.9, 128.2, 126.4. Anal. Calcd for $C_{28}H_{20}SSe_4$: C, 47.75; H, 2.86. Found: C, 48.00; H, 3.06.

2-Methyl-5-(phenylseleno)thiophene (7): oil;^1H NMR δ 7.35 - 7-08 (m, 5 H), 7.12 (d, 1 H, J = 3.5 Hz), 6.67 (dq, 1 H, J = 3.5 and 1.0 Hz), 2.5 (d, 3 H, J = 1.0 Hz). ^{13}C NMR δ 146.8, 137.3, 133.8, 131.7, 128.8, 128.1, 126.5, 15.3; MS *m/z* (relative intensity) 254 (32), 174 (100), 141 (10), 115 (6), 97 (14), 77 (10), 51 (15). Anal. Calcd for $C_{11}H_{10}SSe$: C, 52.18; H, 3.98. Found: C, 52.24; H, 4.05.

2-Methyl-4,5-bis(phenylseleno)thiophene (8): oil; ^1H NMR δ 7.42 - 7.28 (m, 4 H), 7.23 - 7.08 (m, 6 H), 6.48 (q, 1 H, J = 1.0 Hz), 2.34 (d, 3 H, J = 1.0 Hz). ^{13}C NMR δ 145.6, 132.8, 132.4, 131.0, 130.8, 129.1, 127.2, 126.9, 15.3. MS *m/z* (relative intensity) 410 (32), 253 (100), 238 (78), 172 (41), 128 (23), 115 (20), 77 (44), 59 (41), 51 (39). Anal. Calcd for $C_{17}H_{14}SSe_2$: C, 50.01; H, 3.46. Found: C, 50.10; H, 3.51.

2-Methyl-3,4,5-tris(phenylseleno)thiophene (10): oil;^1H NMR δ 7.5 - 7.4 (m, 2 H), 7.27 - 7.11 (m, 5 H), 7.1 - 6.98 (m, 8 H), 2.41 (s, 3 H). ^{13}C NMR δ 148.6, 133.2, 132.6, 130.6, 129.5, 129.2, 128.8, 127.9, 126.2, 125.9, 17.0. MS *m/z* (relative intensity) 564 (9), 331 (13), 252 (100), 171 (34), 139 (41), 115 (16), 77 (57), 51 (34). Anal. Calcd for $C_{23}H_{18}SSe_3$: C, 49.04; H, 3.22. Found: C, 48.97; H, 3.31.

3-Methyl-2-(phenylseleno)thiophene (12): oil; ^1H NMR δ 7.38 (d, 1 H, J = 5.3 Hz), 7.28 - 7.1 (m, 5 H), 6.97 (d, 1 H, J = 5.3 Hz), 2.31 (s, 3 H). ^{13}C NMR δ 144.5, 133.3, 130.0, 129.9, 129.1, 126.3, 15.7. MS *m/z* (relative intensity) 254 (40), 174 (100), 141 (9), 129 (6), 97 (34), 77 (12), 51 (15). Anal. Calcd for $C_{11}H_{10}SSe$: C, 52.18; H, 3.98. Found: C, 52.10; H, 3.92.

3-Methyl-2,5-bis(phenylseleno)thiophene (13): oil; ^1H NMR δ 7.48 - 7.37 (m, 2 H), 7.28 - 7.08 (m, 8 H), 7.1 (s, 1 H), 2.28 (s, 3 H). ^{13}C NMR δ 145.3, 138.5, 131.0, 129.7, 129.2, 127.1, 126.6, 15.7. MS *m/z* (relative intensity) 410 (25), 253 (100), 179 (66), 128 (23), 96 (25), 77 (29), 51 (27). Anal. Calcd for $C_{17}H_{14}SSe_2$: C, 50.01; H, 3.46. Found: C, 49.93; H, 3.52.

3-Methyl-2,4,5-tris(phenylseleno)thiophene (14): mp 51-53 °C; ^1H NMR δ 7.59 - 7.51 (m, 2 H), 7.28 - 7.18 (m, 2 H), 7.18 - 7.08 (m, 11 H), 2.25 (s, 3 H). ^{13}C NMR δ 148.5, 134.1, 132.6, 132.0, 129.5, 129.4, 129.2, 128.4, 126.6, 126.2, 17.2. MS *m/z* (relative intensity) 564 (10), 329 (15), 252 (100), 172 (47), 154 (61), 128 (44), 77 (44), 51 (37). Anal. Calcd for $C_{23}H_{18}SSe_3$: C, 49.04; H, 3.22. Found: C, 49.12; H, 3.18.

3-Bromo-2-(phenylseleno)thiophene (16): oil; ^1H NMR δ 7.43 - 7.37 (m, 2 H), 7.4 (d, 1 H, J = 5.5 Hz), 7.29 - 7.21 (m, 3 H), 7.05 (d, 1 H, J = 5.5 Hz). MS *m/z* (relative intensity) 318 (70), 238 (100), 195 (20),

158 (32), 115 (46), 77 (50), 51 (68). Anal. Calcd for $C_{10}H_7BrSSe$: C, 37.76; H, 2.22. Found: C, 37.66; H, 2.16.

3-Bromo-2,5-bis(phenylseleno)thiophene (17): oil; ^1H NMR δ 7.46 - 7.38 (m, 4 H), 7.26 - 7.17 (m, 6 H), 7.15 (s, 1 H). ^{13}C NMR δ 138.2, 138.1, 132.0, 131.5, 129.4, 127.8, 127.7, 118.8. MS *m/z* (relative intensity) 474 (34), 317 (93), 238 (63), 193 (8), 158 (100), 102 (7), 77 (52), 51 (48). Anal. Calcd for $C_{16}H_{11}BrSSe_2$: C, 40.62; H, 2.34. Found: C, 40.54; H, 2.41.

3-Bromo-2,4,5-tris(phenylseleno)thiophene (18): oil; ^1H NMR δ 7.56 - 7.48 (m, 2 H), 7.42 - 7.14 (m, 13 H). ^{13}C NMR δ 134.3, 132.0, 130.8, 129.6, 129.5, 129.2, 128.8, 127.8, 126.9. MS *m/z* (relative intensity) 392 (11), 314 (62), 237 (48), 193 (41), 157 (87), 145 (100), 113 (22), 77 (89), 51 (57). Anal. Calcd for $C_{22}H_{15}BrSSe_3$: C, 42.06; H, 2.41. Found: C, 42.13; H, 2.49.

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