

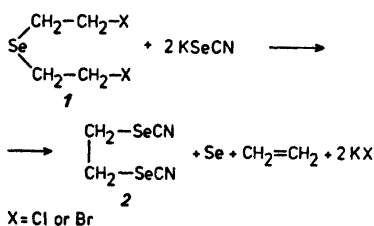
Synthesis of Aryl 2-Haloethyl Selenides and their Reactions with Potassium Selenocyanate

BJÖRN LINDGREN

Institute of Chemistry, University of Uppsala, Box 531, S-751 21 Uppsala, Sweden

A number of selenide dihalides, such as 2-bromoethyl phenyl selenide dibromide (3), 2-chloroethyl phenyl selenide dichloride (4) and 2-bromoethyl 4'-tolyl selenide dibromide (5), have been synthesized. Two of these dihalides (3 and 5) have been dehalogenated to give the corresponding selenides, 2-bromoethyl phenyl selenide (6) and 2-bromoethyl 4'-tolyl selenide (7), respectively. 2-Bromoethyl 2',4'-dinitrophenyl selenide (10) has also been prepared, but by another synthetic route. These 2-halogen substituted selenides have been allowed to react with potassium selenocyanate giving mixtures of normal and abnormal substitution products. A mechanism is presented for the reaction between aryl 2-haloethyl selenides and potassium selenocyanate.

The reaction of bis(2-bromoethyl) selenide (1; X=Br) and its chlorine analogue with potassium selenocyanate has been studied earlier (Scheme 1).¹



Scheme 1.

The question arose as to whether this reaction is specific for the bis(2-haloethyl) selenides (1), or if it could be generalized to systems of analogous structure. In order to investigate this a number of aryl 2-haloethyl selenides were synthesized and their reactions with potassium selenocyanate studied.

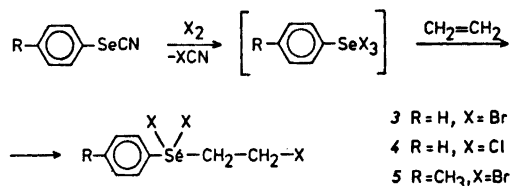
Alkyl or aryl 2-halogen substituted selenides are most conveniently synthesized by adding olefins to alkyl- or arylselenenyl halides.²⁻⁴ In all the cases mentioned above the selenenyl halides were synthesized in advance and then allowed to react with the olefin. The *in situ* generation of selenenyl bromides and addition of olefins to the reaction mixture, however, seemed to be a more rational method.⁵

RESULTS AND DISCUSSION

In accordance with the method mentioned above, efforts to generate selenenyl bromides *in situ* from a selenocyanate and bromine were made.⁶ The product isolated when ethylene was passed through the solution, however, consisted of a selenide dibromide and unreacted selenocyanate.

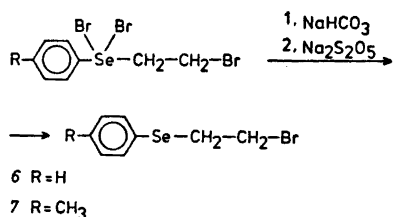
The direct preparation of aryl 2-haloethyl selenides according to the above method was thus not possible. On the other hand it was feasible to synthesize aryl 2-haloethyl selenide dihalides by the *in situ* generation of aryl-selenium trihalides and passing ethylene through the reaction mixture until completion of the reaction. 2-Bromoethyl phenyl selenide dibromide (3), 2-chloroethyl phenyl selenide dichloride (4) and 2-bromoethyl 4'-tolyl selenide dibromide (5) were prepared in this way (Scheme 2).

No reaction occurred when negatively substituted aryl selenocyanates, such as 2-nitrophenyl selenocyanate and 2,4-dinitrophenyl selenocyanate, were used as substrates.⁶ 2,4-Dinitrophenylselenium trichloride has, however, been found to add to other olefinic substrates.^{7,8}



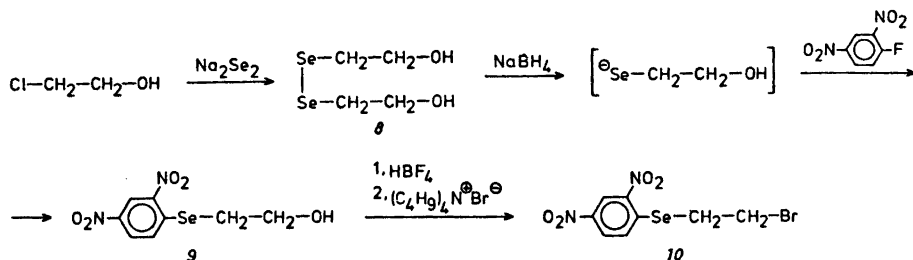
Scheme 2.

The dihalides were dehalogenated by dissolving them in an aqueous sodium hydrogen carbonate solution and reducing the generated selenoxides with sodium pyrosulfite.^{9,10} 2-Bromoethyl phenyl selenide (6) and 2-bromoethyl 4'-tolyl selenide (7) were prepared in this way (Scheme 3).



Scheme 3.

The negatively substituted selenide 2-bromoethyl 2',4'-dinitrophenyl selenide (10) was synthesized by a reaction sequence starting from 2-chloroethanol and 1-fluoro-2,4-dinitrobenzene. Bis(2-hydroxyethyl) diselenide (8) was prepared from 2-chloroethanol and sodium diselenide. The diselenide was reduced with sodium borohydride in ethanol and to this reaction mixture, 1-fluoro-2,4-dinitrobenzene was added. 2-Hydroxyethyl 2',4'-dinitrophenyl selenide (9) was isolated. The alcohol was treated with fluoboric acid and then allowed to react with tetrabutylammonium bromide in dry chloroform to give 2-bromoethyl 2',4'-dinitrophenyl selenide (10) (Scheme 4).

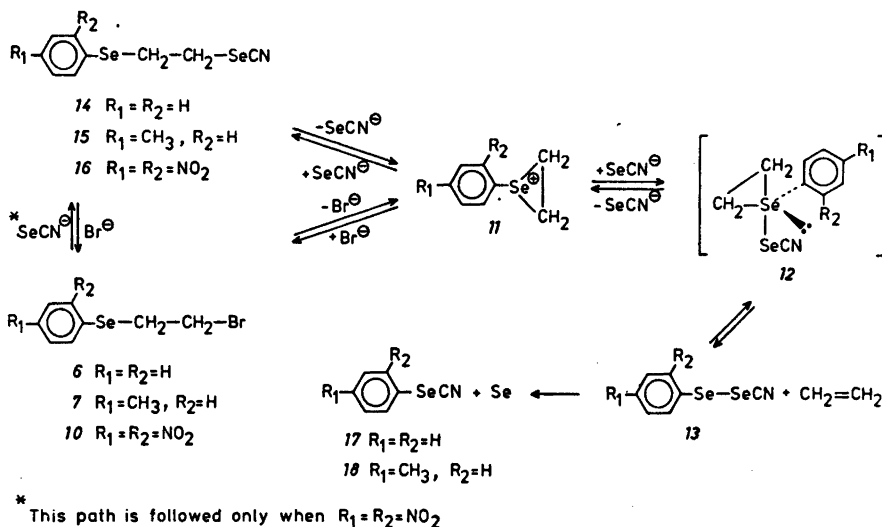


Scheme 4.

When 2-bromoethyl phenyl selenide (6) and 2-bromoethyl 4'-tolyl selenide (7) were allowed to react with potassium selenocyanate, using acetone as solvent, phenyl selenocyanate (54 %) and 4-tolyl selenocyanate (69 %), respectively, were isolated. The reaction between 6 and potassium selenocyanate was followed by ¹H NMR spectroscopy using acetone-*d*₆ as solvent. The original A₂B₂ spectrum, centred around a δ value of 3.48 and corresponding to the two methylene groups of the starting material, rapidly disappeared when potassium selenocyanate was added to the NMR tube. Two singlets at δ 5.33 and 3.41 were formed during the reaction. The singlet at δ 5.33 corresponded to ethylene.

The crude product from the reaction between 6 and potassium selenocyanate was also studied by mass spectroscopy. A peak was obtained at *m/e* 183 corresponding to phenyl selenocyanate as well as a peak at *m/e* 291 originating from the molecular ion of the normal substitution product phenyl 2-selenocyanatoethyl selenide (14).

The ¹H NMR spectrum of 14 should give rise to an A₂B₂ spectrum corresponding to the two non-equivalent methylene groups. From investigations on A₂B₂ spectra, however, it is possible that these can appear as singlets in certain solvents.¹¹ The singlet at δ 3.41 might thus originate from the two methylene groups of the normal substitution product. Alternatively, the singlet at δ 3.41 could correspond to the two methylene groups of the episelenurane (12) (Scheme 5), which may be proposed as an intermediate when a selenocyanate ion attacks the positive selenonium ion (11).^{4,12} During the reaction the intensity of the singlet increased but on completion its intensity remained unchanged. From this and the fact that phenyl seleno-



Scheme 5.

cyanate was isolated as the end product, the peak could not correspond to an intermediately formed episelenurane (12). From the ¹H NMR spectrum of the raw product it was obvious that the formation of the normal substitution product could not constitute more than 30 % of the complete reaction.

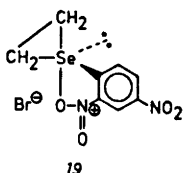
The mechanistic interpretations of the above results are all in accordance with the proposed mechanism for the reaction between bis(2-bromoethyl) selenide (1; X = Br) and potassium selenocyanate (Scheme 5).¹

The reaction between 2-bromoethyl 4'-tolyl selenide (7) and potassium selenocyanate was also studied by ¹H NMR spectroscopy using acetone-*d*₆ as solvent. It was found that 7 behaved similarly to 6. The aliphatic region of the ¹H NMR spectrum of 7 consisted of an A₂B₂ spectrum centred around a value of δ 3.43 and a singlet at δ 2.29 corresponding to the methyl group. When potassium selenocyanate was added to the NMR tube containing the starting material, immediate formation of ethylene was observed. A singlet at δ 3.38 was obtained, corresponding to the A₂B₂ spectrum of the methylene groups of the normal substitution product 2-selenocyanatoethyl 4'-tolyl selenide (15). The appearance of the A₂B₂ spectrum as a singlet could be explained as above for compound 14. Two singlets corresponding to methyl groups were also obtained.

The singlet at δ 2.36 corresponds to the methyl group of 4-tolyl selenocyanate (18) and the singlet at δ 2.31 originates from the methyl group of the normal substitution product 15.

2-Bromoethyl 2',4'-dinitrophenyl selenide (10) was also used as starting material for the reaction with potassium selenocyanate. The reason for choosing 10 for this reaction was that intermediate 13, corresponding to 2,4-dinitrobenzeneselenenyl selenocyanate, would be stable if formed.¹³ The motive for this experiment, was therefore that any attack on the positive selenium atom of the cyclic selenonium ion 11 would give 13 as the product and not the corresponding selenocyanate as in earlier reactions. The reaction between 10 and potassium selenocyanate was studied by ¹H NMR spectroscopy using acetone-*d*₆ as solvent. No ethylene was formed during the reaction. It was, however, obvious that a reaction took place from changes of the ¹H NMR spectrum. The product had an elemental composition corresponding to the normal substitution product 16. An ¹H NMR spectrum of the product in acetone-*d*₆ showed a singlet at δ 3.71. By similar reasoning as before, this singlet could be attributed to an A₂B₂ spectrum. Furthermore, an episelenurane structure (12) for the product in the reaction between 10 and potassium selenocyanate could not be excluded. From a mechanistic point of view the forma-

tion of an episelenurane is, however, not very likely since the destabilizing effect of the two nitro groups on the episelenonium ion *11* makes preliminary formation of such a cyclic selenonium ion improbable. The most likely explanation is that starting material *10* is attacked on the β -carbon giving the normal substitution product 2',4'-dinitrophenyl 2-selenoethoxyethyl selenide (*16*) without preliminary formation of *11*. Alternatively, intermediate *11*, by interaction with the nitro group in the *ortho* position, may be represented as *19*, as has been proposed for analogous sulfur compounds.¹⁴



The possibility of a nucleophilic attack on the selenium atom of *19* and the formation of an episelenurane is thereby reduced. The reactions of the bis(2-haloethyl) or aryl 2-haloethyl selenides mentioned here and potassium selenocyanate have thus been shown to give analogous products and the reactions most probably proceed *via* the same mechanism except for 2-bromoethyl 2',4'-dinitrophenyl selenide (*10*). When *10* is used as starting material, it is obvious that the introduction of nitro groups in the aromatic part of the molecule may exclude the formation of an episelenonium ion or change its appearance, which is accompanied by exclusive formation of the normal substitution product *16*.

EXPERIMENTAL

The selenium analyses were performed by a microanalytical method developed by Bengtsson¹⁵ and very similar to that of Gould.¹⁶ The melting points are uncorrected.

2-Bromoethyl phenyl selenide dibromide (3). To a solution of 36.4 g (0.2 mol) of phenyl selenocyanate in 80 ml of carbon tetrachloride 64 g (0.4 mol) of bromine in 80 ml of carbon tetrachloride was added dropwise. The reaction mixture was kept at room temperature for 30 min with stirring. Ethylene was passed into the reaction mixture until the solution had turned pale yellow and the evolution of heat had ceased. Evaporation of the reaction mixture left a yellow residue, which was washed

with ether and recrystallized from carbon tetrachloride. Yield 74.0 g (87%), m.p. 110–111.5 °C. (Found: C 22.66; H 2.07; Br 56.58; Se 18.65. Calc. for C₆H₅Br₂Se: C 22.67; H 2.14; Br 56.56; Se 18.63).

2-Bromoethyl 4'-tolyl selenide dibromide (5). The synthetic procedure was similar to that used for *3* described above, starting from a solution of 19.6 g (0.1 mol) of 4-tolyl selenocyanate in 40 ml of carbon tetrachloride. The crude product was recrystallized from carbon tetrachloride. Yield 21.2 g (48%), m.p. 112–114.5 °C. (Found: C 24.67; H 2.54; Br 54.87; Se 18.08. Calc. for C₉H₁₁Br₂Se: C 24.68; H 2.54; Br 54.75; Se 18.03).

2-Chloroethyl phenyl selenide dichloride (4). A solution of 4.55 g (0.025 mol) of phenyl selenocyanate in 10 ml of chloroform was prepared. Chlorine was passed into the solution with stirring at room temperature. Evolution of heat occurred and a yellowish precipitate was obtained. After some minutes the reaction was complete. Ethylene was passed through the reaction mixture, heat was developed and the solid product slowly dissolved. When the evolution of heat had ceased, the reaction was considered complete and the solvent was evaporated giving a solid residue, which was washed with ether and recrystallized from carbon tetrachloride. Yield 4.3 g (59%), m.p. 89–90.5 °C. (Found: C 32.87; H 3.18; Cl 36.50; Se 26.93. Calc. for C₆H₅Cl₂Se: C 33.08; H 3.13; Cl 36.61; Se 27.18).

2-Bromoethyl phenyl selenide (6). To a solution, heated to 40–50 °C, of 9.25 g (0.11 mol) of sodium hydrogen carbonate in 250 ml of water, 21.2 g (0.05 mol) of 2-bromoethyl phenyl selenide dibromide (*3*) was added. The substance dissolved with evolution of carbon dioxide. The reaction mixture was cooled to 0 °C and poured into a separatory funnel containing 75–100 g of ice. To this solution was added 250 ml of ice cold ether and a cold solution of 5.75 g (0.03 mol) of sodium pyrosulfite in 125 ml of water. When the pyrosulfite solution was added an instantaneous reaction took place. The ether layer was separated and the extraction was repeated. The combined extracts were washed with water and dried. The dried solvent was evaporated at reduced pressure and at a low temperature giving 12.1 g (92%) of raw product. The product was recrystallized at –50 °C from light petroleum, m.p. 18–19 °C. (Found: C 36.34; H 3.41; Br 30.46; Se 29.97. Calc. for C₈H₉BrSe: C 36.39; H 3.44; Br 30.26; Se 29.90).

2-Bromoethyl 4'-tolyl selenide (7). The synthetic procedure was similar to that of *6* described above, starting from 21.9 g (0.05 mol) of 2-bromoethyl 4'-tolyl selenide dibromide (*5*). Yield 9.0 g (65%) of raw product, which was recrystallized from light petroleum, m.p. 41–42 °C. (Found: C 38.89; H 4.01; Br 28.89; Se 28.43. Calc. for C₉H₁₁BrSe: C 38.87; H 4.00; Br 28.74; Se 28.40).

The reaction between 2-bromoethyl phenyl selenide (6) and potassium selenocyanate. To a solution of 5.2 g (0.02 mol) of 6 in 100 ml of acetone 3.2 g (0.022 mol) of potassium selenocyanate dissolved in 30 ml of acetone was added. The reaction mixture was refluxed for 2 h with stirring.

After filtering the mixture the solvent was evaporated leaving a residue. Distillation of the residue gave 1.95 g (54 %) of phenyl selenocyanate, b.p. 96–98°C/3.0 mmHg, $n_D^{17.5}$ 1.6043 (verified by IR spectroscopy). Elemental selenium (0.8 g) was regained from the reaction mixture.

The reaction between 2-bromoethyl 4'-tolyl selenide (7) and potassium selenocyanate. To a solution of 2.8 g (0.01 mol) of 7 in 50 ml of acetone 1.6 g (0.011 mol) of potassium selenocyanate dissolved in 15 ml of acetone was added. After refluxing the mixture for 2 h, filtration and evaporation of the solvent, the residual product was recrystallized from light petroleum giving 1.35 g (69 %) of 4-tolyl selenocyanate, verified by ^1H NMR and IR spectroscopy. Elemental selenium (0.5 g) was regained from the reaction mixture.

Bis(2-hydroxyethyl) diselenide (8).¹⁷ In a 1 l three-necked flask, equipped with a dropping funnel, reflux condenser and a gas inlet, 16 g (0.4 mol) of sodium hydroxide and 25 g (0.162 mol) of sodium formaldehydesulfoxylate were dissolved in 250 ml of water. To the solution 32 g (0.4 mol) of elemental selenium was added. The reaction was performed in a nitrogen atmosphere. When the selenium was completely reduced, 32.2 g (0.4 mol) of 2-chloroethanol was added. The reaction mixture was left at room temperature for 5 h with stirring. A heavy oil containing some elemental selenium was obtained. The oil was separated and dissolved in acetone. The water phase was extracted with chloroform and the extracts were combined with the acetone solution. After drying the obtained solution, the solvents were evaporated giving an orange-coloured oil. Distillation gave 19.5 g (39 %) of bis(2-hydroxyethyl) diselenide (8), b.p. 169–179°C/1.6–4.0 mmHg, n_D^{25} 1.6412. Some decomposition of the product was obtained during the distillation, but the purity of the product was acceptable for further synthetic use.

2-Hydroxyethyl 2',4'-dinitrophenyl selenide (9). To an alcoholic solution of 12.4 g (0.05 mol) of bis(2-hydroxyethyl) diselenide (8) was added 1.0 g (0.025 mol) of sodium borohydride or sufficient so that the colour of the solution disappeared. Large excess of borohydride should be avoided. The reaction was performed in a nitrogen atmosphere. When the reaction had terminated, 20.0 g (0.105 mol) of 1-fluoro-2,4-dinitrobenzene in the least possible amount of ethanol was added to the mixture containing the reduced diselenide. The reaction mixture was allowed to stand at room temperature under stirring and in a nitrogen atmosphere

overnight. After filtration the solvent was evaporated, and 16.2 g of a solid residue was obtained. The raw product was recrystallized from ethyl acetate/light petroleum. Yield 12.5 g (43 %), m.p. 104–105.5°C. (Found: C 33.02; H 2.74; Se 27.35. Calc. for $\text{C}_8\text{H}_9\text{N}_2\text{O}_5\text{Se}$: C 33.00; H 2.78; Se 27.12).

2-Bromoethyl 2',4'-dinitrophenyl selenide (10). A suspension of 4.0 g (0.014 mol) of dry 2-hydroxyethyl 2',4'-dinitrophenyl selenide (9) in dry chloroform was prepared. The suspension was cooled to –40°C and 15.0 g (0.09 mol) of a solution of fluoboric acid in ether (54 %) was added. A cooled solution of 5.3 g (0.016 mol) of tetrabutylammonium bromide in dry chloroform was added and the temperature of the reaction mixture was allowed to rise to room temperature. The reaction mixture was refluxed for 1 1/2 h and washed with an aqueous sodium hydrogen carbonate solution. The organic solution was dried over magnesium sulfate. The dry solvent was evaporated to give an oily residue which was extracted with ether. The ether extract was dried over magnesium sulfate and the solvent evaporated. A solid product was obtained which was recrystallized from ethyl acetate/light petroleum. Yield 1.8 g (36 %), m.p. 110.5–111.5°C. (Found: C 27.34; H 1.99; Br 22.54; Se 22.34. Calc. for $\text{C}_8\text{H}_9\text{BrN}_2\text{O}_4\text{Se}$: C 27.14; H 2.00; Br 22.57; Se 22.30).

The reaction between 2-bromoethyl 2',4'-dinitrophenyl selenide (10) and potassium selenocyanate. To a solution of 1.05 g (0.003 mol) of 10 in 30 ml of acetone 0.48 g (0.0033 mol) of potassium selenocyanate dissolved in 15 ml of acetone was added. The reaction mixture was refluxed for 4 h and then filtered. The solvent was evaporated and a residue was obtained. The raw product was recrystallized from benzene/light petroleum. Yield 0.95 g (83 %), m.p. 123–125°C. (Found: C 28.59; H 1.86; Se 41.65. Calc. for $\text{C}_8\text{H}_9\text{N}_2\text{O}_4\text{Se}_2$: C 28.51; H 1.86; Se 41.66). ^1H NMR (60 MHz, acetone- d_6): δ 3.71 (4 H, s), 8.17 (1 H, d, J 9.0), 8.49 (1 H, dd, J 9.0 and 2.5), 9.07 (1 H, d, J 2.5).

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