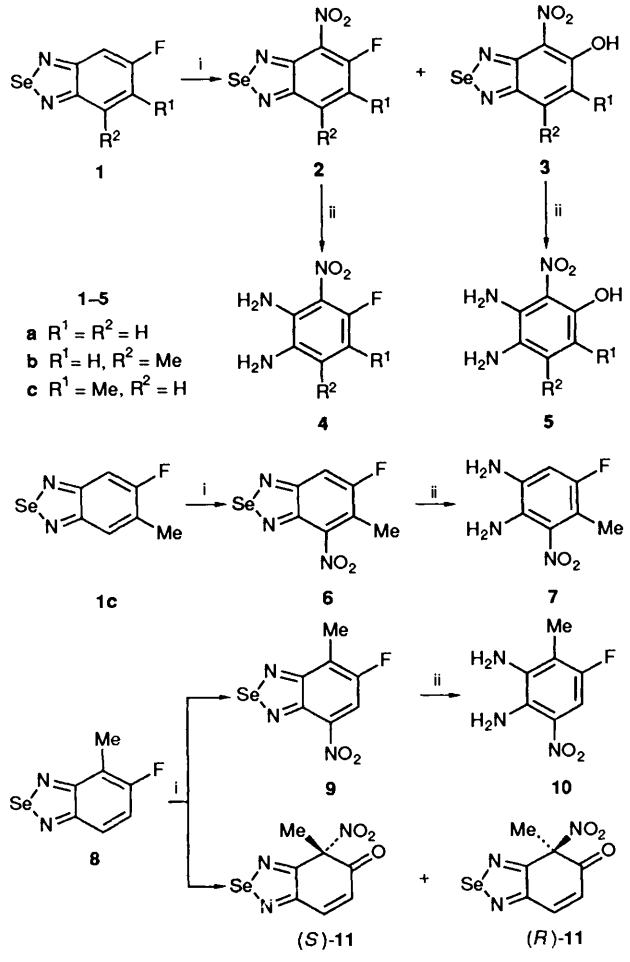
Nitration of 5-Fluoro-2,1,3-benzoselenadiazoles, and the Synthesis of 4-Fluoro-3-nitro-, 4-Fluoro-6-nitro-, 5-Fluoro-3-nitro-*o*-phenylenediamines and 3,4-Diamino-2-nitrophenols by Subsequent Deselenation

Wei Tian,† Spiros Grivas* and Kjell Olsson
Department of Chemistry, Swedish University of Agricultural Sciences, P.O. Box 7015, S-750 07 Uppsala, Sweden

Fuming nitric and concentrated sulfuric acids converted the title benzoselenadiazoles **1** and **8** into their 4- and/or 7-nitro derivatives. Unlike the *m*-fluoronitro substituted products **6** and **9**, the *o*-fluoronitro substituted products **2** were accompanied by the corresponding benzoselenadiazol-5-ols **3**. These were formed by hydrolysis in amounts increasing with the reaction time. *ipso*-Nitration of **8** was followed by instantaneous hydrolysis to benzoselenadiazol-5(4*H*)-one (*R,S*)-**11**. Reductive ring opening of the nitration products **2**, **6**, **9** and **3** with hydriodic acid yielded the corresponding novel fluoronitro-*o*-phenylenediamines **4**, **7**, **10** and *o*-nitrophenols **5** in 70–80% yield.

Recently, in connection with our synthetic work with 2,1,3-benzoselenadiazoles[1–5] we converted some 4-halogeno-*o*-phenylenediamines into their 3-nitro derivatives[6] by nitration of the appropriate 5-chloro- and 5-bromo-2,1,3-benzoselenadiazoles and subsequent deselenation. The present paper deals with the nitration of 5-fluoro-2,1,3-benzoselenadiazoles (**1a–c** and **8**, Scheme 1) and the selective reduction of the products **2**, **3**, **6** and **9** to the corresponding amines **4**, **7** and **10**, and phenols **5**.



Scheme 1 *Reagents and conditions:* i, fuming HNO_3, conc. H_2SO_4, 4 °C, 2 h; ii, 57% HI, 20 °C, 2 h

Results and Discussion

The title benzoselenadiazoles (**1** and **8**, Scheme 1) were obtained by condensation of selenium dioxide with the appropriate 4-fluoro 1,2-diamines, which were prepared by Raney nickel-catalysed hydrogenation of the corresponding 4-fluoro-2-nitroanilines. These were obtained from commercial 4-fluoro-2-nitroaniline and the requisite fluoronitrotoluenes according to, or in close analogy with, literature methods.

The nitration products **2**, **3**, **6**, **9** and **11** are depicted in Scheme 1. Their structures were established on the basis of spectral data and confirmed by elemental analyses. Additionally, the structure of **11** was also confirmed by X-ray crystallographic analysis in order to rule out the isomeric compund **17**, albeit a presumably difficult-to-isolate aromatic nitrate. The racemic nature of **11** was shown by the splitting of all its ^1H NMR signals in the presence of an optically active shift reagent.[7]

Table 1 shows the yields of products isolated without delay after nitration under the conditions indicated in Scheme 1. If the separation of the nitration products from the aqueous acid was postponed, the yields of benzoselenadiazol-5-ols **3** increased at the expense of the products **2**, which eventually disappeared completely. Such delay did not affect the yields of the other nitration products **6**, **9** and **11** materially. For comparison, the reported nitrations of 5-chloro-2,1,3-benzoselenadiazole **12**[8] and the 5-bromo analogue **13**[9] were repeated under the conditions used for the title fluoro compounds **1** and **8**. The yields of the promptly isolated products **3a**, **14** and **15** are included in Table 1.

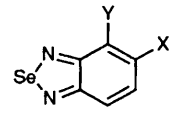
In the nitration of the fluorobenzoselenadiazoles **1**, benzoselenadiazolols **3** are probably formed *via* **2**, since the proportion of **3** to **2** increased with the reaction time. Accordingly, the isolated and purified *o*-fluoronitro substituted products **2** were slowly converted into **3** under acidic conditions. No such hydrolysis of the *m*-fluoronitro substituted products **6** and **9** was observed. It is, therefore, unlikely that fluoride ion will be displaced from **1** (by water or nitrate ion), until the *ortho*-position (4) has been nitrated. This should also apply to **8**, even though this position is occupied. Hence **11** is most likely not formed from **8** *via* the benzoselenadiazolol **16** or its nitrate **17** but rather *via* the cation **18** (only its *R*-form is shown).

In the cold, *o*- and *p*-fluoronitroarenes are generally resistant towards hydrolysis in acidic media. However, if the aromatic

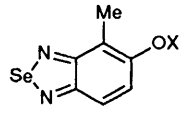
† Visiting scientist from the Harbin University of Science and Technology, China.

Table 1 Yields of promptly isolated products after nitration of 5-halogeno-2,1,3-benzoselenadiazoles under the conditions indicated in Scheme 1

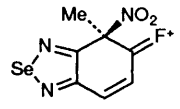
Substrate	Product yields (%)
1a	**2a** (37), **3a** (38)
1b	**2b** (55), **3b** (13)
1c	**2c** (16), **3c** (33), **6** (29)
8	**9** (25), **11** (50)
12[8]	**3a** (9), **14** (68)
13[9]	**3a** (4), **15** (72)



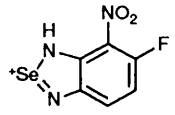
12 X = Cl, Y = H
13 X = Br, Y = H
14 X = Cl, Y = NO_2
15 X = Br, Y = NO_2



16 X = H
17 X = NO_2



(*R*)-**18**

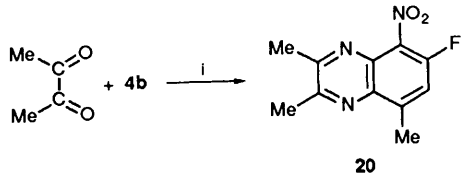


19

system contains nitrogen, such hydrolysis is possible.[10] The reason may be protonation of a ring nitrogen, which would convert **1** into the cationic species **19**. As to the activation of the fluorine atom towards nucleophilic displacement, the structure **19** could be compared to the Sanger's reagent, 2,4-dinitrofluorobenzene.

Reductive deselenation[8,11,12] of the readily obtainable benzoselenadiazole system offers a convenient way to substituted *o*-phenylenediamines.[5,6,13] Thus, removal of selenium from benzoselenadiazolols **3** with hydriodic acid[6,8] offered a simple and convenient method for the synthesis of 3,4-diamino-2-nitrophenols **5** (see Scheme 1). Similarly, the fluoronitro-*o*-phenylenediamines **4**, **7** and **10** were efficiently obtained by reductive cleavage of the respective fluoronitrobenzoselenadiazoles **2**, **6** and **9** by hydriodic acid.

The nature and pattern of the substituents in the deselenated products makes them useful synthetic intermediates in the synthesis of nitrogen and oxygen heterocycles. The randomly chosen 4-fluoro-6-methyl-3-nitro-*o*-phenylenediamine **4b** was allowed to react with butane-2,3-dione to yield 6-fluoro-2,3,8-trimethyl-5-nitroquinoxaline **20** (Scheme 2)—*cf.* ref. 6. For



20

Scheme 2 *Reagents and conditions:* i, MeOH, 20 °C, 30 min

example, the quinoxaline **20** can then be treated with methylamine, reduced and cyclized with cyanogen bromide to yield 2-amino-3,5,7,8-tetramethyl-1*H*-imidazo[4,5-*f*]quinoxaline (5,7,8-TriMeIQx),[14,15] a homologue of the broiled-food carcinogen 2-amino-3,8-dimethyl-1*H*-imidazo[4,5-*f*]quinoxaline (MeIQx).[16]

Experimental

All reactions and purifications were monitored by TLC with UV detection on aluminium sheets coated with silica gel 60 F_{254} (Merck). Flash liquid chromatography (FC) was performed on silica gel (230–400 mesh ASTM, Merck). M.p.s (uncorrected) were determined on a Mettler FP5 instrument. The mass spectra were obtained on a Finnigan 4021 instrument with direct insertion, electron impact ionisation (70 eV) and an ion source temperature of 250 °C. Ions containing isotopes other than ^{80}Se are not listed. The NMR spectra were obtained on a Varian VXR-400 spectrometer at 25 °C, and referenced to the solvent deuteriochloroform ($CHCl_3$, δ 7.26), unless otherwise indicated. The IR spectra were obtained on a Perkin-Elmer FT-IR 1760X spectrometer.

Materials.—All organic solvents were either freshly distilled or of p.a. quality. Solvent mixtures are given in ratios by volume (v/v). Petroleum means light petroleum (b.p. 40–60 °C). 4-Fluoro-2-nitroaniline was commercially obtained. 4-Fluoro-2-methyl-6-nitroaniline and 4-fluoro-3-methyl-2-nitroaniline were prepared in the same fashion as 4-fluoro-5-methyl-2-nitroaniline[17] from commercially available 5-fluoro-2-nitrotoluene and 2-fluoro-5-nitrotoluene, respectively.

4-Fluoro-2-methyl-6-nitroaniline. M.p. 103–105 °C (Found: C, 48.7; H, 4.1; N, 16.4. $C_7H_7FN_2O_2$ requires C, 49.4; H, 4.15; N, 16.5%); δ_H 2.26 (3 H, s, 2-Me), 6.1 (2 H, br s, NH_2), 7.12 (1 H, dd, *J* 7.9 and 2.5, 3-H) and 7.75 (1 H, dd, *J* 8.8 and 2.9, 5-H); *m/z* 170 (M^+, 34%), 153 (2), 140 (3), 134 (2) and 77 (100).

4-Fluoro-3-methyl-2-nitroaniline. M.p. 83–85 °C (Found: C, 49.2; H, 4.1; N, 16.1. $C_7H_7FN_2O_2$ requires C, 49.4; H, 4.15; N, 16.5%); δ_H 2.35 (3 H, d, *J* 2.6, 3-Me), 4.9 (2 H, br s, NH_2), 6.62 (1 H, dd, *J* 9.0 and 4.9, 6-H) and 7.04 (1 H, t, *J* 8.9, 5-H); *m/z* 170 (M^+, 40%), 154 (3), 153 (52), 124 (14) and 84 (100).

Preparation of 5-Fluoro-2,1,3-benzoselenadiazoles **1** *and* **8**.—*General procedure.* A solution of 4-fluoro-2-nitroaniline (1.56 g, 10 mmol) or its methyl derivatives (1.70 g, 10 mmol) in ethanol (50 cm^3) were hydrogenated with Raney nickel under ambient conditions (TLC solvents: CH_2Cl_2–EtOAc, 10:1). The catalyst was filtered off. To the filtrate was added 10% selenium dioxide (14 cm^3, 13 mmol) with stirring. Pure 5-fluoro-2,1,3-benzoselenadiazole or its methyl derivatives were obtained by filtration and recrystallization (ethanol).

5-Fluoro-2,1,3-benzoselenadiazole **1a**. Yield 1.72 g (85%), m.p. 105–107 °C (lit.,[18] 104–106 °C).

6-Fluoro-4-methyl-2,1,3-benzoselenadiazole **1b**. Yield 1.62 g (75%), m.p. 150–151 °C (Found: C, 38.8; H, 2.3; N, 12.9. $C_7H_5FN_2Se$ requires C, 39.1; H, 2.3, N, 13.0%); δ_H 2.70 (3 H, s, 4-Me), 7.13 (1 H, br dd, *J* 9.1, 2.5 and 1.3, 5-H) and 7.28 (1 H, br dd, *J* 9.3 and 2.4, 7-H); *m/z* 216 (M^+, 24%), 189 (8), 186 (2), 176 (1) and 80 (100).

5-Fluoro-6-methyl-2,1,3-benzoselenadiazole **1c**. Yield 1.68 g (78%), m.p. 110–111 °C (Found: C, 39.0; H, 2.3; N, 12.9. $C_7H_5FN_2Se$ requires C, 39.1; H, 2.3; N, 13.0%); δ_H 2.42 (3 H, dd, *J* 2.4 and 1.3, 6-Me), 7.39 (1 H, d, *J* 10.3, 4-H) and 7.63 (1 H, ddd, *J* 7.1, 1.5 and 0.3, 7-H); *m/z* 216 (M^+, 79%), 189 (23), 186 (5), 162 (7) and 80 (100).

5-Fluoro-4-methyl-2,1,3-benzoselenadiazole **8**. Yield 1.53 g (71%), m.p. 144–145 °C (Found: C, 39.0; H, 2.2; N, 12.8. $C_7H_5FN_2Se$ requires C, 39.1; H, 2.3; N, 13.0%); δ_H 2.59 (3 H, d, *J* 2.5, 4-Me), 7.35 (1 H, t, *J* 9.3, 6-H) and 7.64 (1 H, ddq, *J* 8.7, 5.4 and 0.7, 7-H); *m/z* 216 (M^+, 60%), 189 (11), 186 (3), 176 (1) and 57 (100).

Nitration of 5-Fluoro-2,1,3-benzoselenadiazoles **1** *and* **8**.—*General procedure.* To a cold solution of **1** or **8** (5 mmol) in 97% sulfuric acid (5 cm^3) was added dropwise a cold mixture of 100% nitric acid (0.63 g, 10 mmol) and 97% sulfuric acid (2 cm^3) with

stirring in an ice–water bath. After 2 h at 4 °C (TLC solvents: CH_2Cl_2–EtOAc, 10:1), the mixture was poured onto ice (10 g). The precipitate was filtered off and washed with cold water to ensure the absence of acid. The dried crude product was subjected to FC. A mixture of CH_2Cl_2–EtOAc (10:1) was used to elute the 5-fluoro-2,1,3-benzoselenadiazoles and MeOH–CH_2Cl_2 (30:1) to obtain the corresponding 2,1,3-benzoselenadiazol-5-ols. Pure products were obtained by recrystallization (toluene). The yields are listed in Table 1. If the precipitated nitration products were stirred with the aqueous acid for 24 h at 20 °C before being processed, no **2** was obtained, and the yield of **3** approached the combined yield of promptly isolated **2** and **3**.

5-*Fluoro*-4-*nitro*-2,1,3-*benzoselenadiazole* **2a**. M.p. 150–151 °C (Found: C, 29.8; H, 1.0; N, 16.6. $C_6H_2FN_3O_2Se$ requires C, 29.3; H, 0.8; N, 17.1%); δ_H ([$^2H_6$]-DMSO) 7.86 (1 H, t, *J* 10.1, 6-H) and 8.24 (1 H, dd, *J* 9.9 and 5.2, 7-H); *m/z* 247 (M^+, 100%), 217 (78), 201 (16), 189 (50) and 121 (91).

4-*Nitro*-2,1,3-*benzoselenadiazol*-5-*ol* **3a**. M.p. 213–215 °C (Found: C, 29.1; H, 1.2; N, 16.8. $C_6H_3N_3O_3Se$ requires C, 29.5; H, 1.2; N, 17.2%); δ_H 7.48 and 8.08 (1 H each, d, *J* 9.7, 6-and 7-H) and 13.06 (1 H, s, OH); *m/z* 245 (M^+, 37%), 215 (10), 185 (5), 160 (5) and 80 (100).

5-*Fluoro*-7-*methyl*-4-*nitro*-2,1,3-*benzoselenadiazole* **2b**. M.p. 182–183 °C (Found; C, 32.5; H, 1.5; N, 15.9. $C_7H_4FN_3O_2Se$ requires C, 32.3; H, 1.55; N, 16.2%); δ_H 2.78 (3 H, d, *J* 1.2, 7-Me) and 7.31 (1 H, dq, *J* 10.8 and 1.2, 6-H); *m/z* 261 (M^+, 15%), 231, (36), 204 (2), 188 (10) and 108 (100).

7-*Methyl*-4-*nitro*-2,1,3-*benzoselenadiazol*-5-*ol* **3b**. M.p. 198–200 °C (Found: C, 32.5; H, 1.9; N, 15.9. $C_7H_5N_3O_3Se$ requires C, 32.6; H, 1.95; N, 16.3%); δ_H 2.75 (3 H, d, *J* 1.2, 7-Me), 7.25 (1 H, q, *J* 1.2, 6-H) and 13.24 (1 H, s, OH); *m/z* 259 (M^+, 44%), 243 (2), 229 (17), 201 (3) and 94 (100).

5-*Fluoro*-6-*methyl*-4-*nitro*-2,1,3-*benzoselenadiazole* **2c**. This compound was separated from its isomer **6** by FC (CH_2Cl_2–EtOAc, 15:1); R_f 0.15, m.p. 236–238 °C (Found: C, 32.3; H, 1.6; N, 15.8. $C_7H_4FN_3O_2Se$ requires C, 32.3; H, 1.55; N, 16.2%); δ_H 2.53 (3 H, dd, *J* 2.7 and 1.4, 6-Me) and 7.89 (1 H, dq, *J* 7.1 and 1.3, 7-H); *m/z* 261 (M^+, 52%), 244 (4), 231 (39), 213 (3) and 108 (100).

6-*Methyl*-4-*nitro*-2,1,3-*benzoselenadiazol*-5-*ol* **3c**. M.p. 216–218 °C (Found: C, 32.2; H, 2.0; N, 15.8. $C_7H_5N_3O_3Se$ requires C, 32.6; H, 1.95; N, 16.3%); δ_H 2.49 (3 H, d, *J* 1.1, 6-Me), 7.94 (1 H, s, 7-H) and 13.73 (1 H, s, OH); *m/z* 259 (M^+, 37%), 241 (11), 227 (2), 213 (28) and 66 (100).

6-*Fluoro*-5-*methyl*-4-*nitro*-2,1,3-*benzoselenadiazole* **6**. R_f 0.30, m.p. 193 °C (decomp.) (Found: C, 32.3; H, 1.5; N, 15.8. $C_7H_4FN_3O_2Se$ requires C, 32.3; H, 1.55; N, 16.2%); δ_H 2.46 (3 H, d, *J* 2.5, 5-Me) and 7.64 (1 H, br dd, *J* 9.5 and 0.5, 7-H); *m/z* 261 (M^+, 13%), 244 (13), 231 (6), 216 (2) and 108 (100).

5-*Fluoro*-4-*methyl*-7-*nitro*-2,1,3-*benzoselenadiazole* **9**. This compound was separated from compound **11** by FC (CH_2Cl_2–EtOAc, 15:1), R_f 0.50, m.p. 198–200 °C (Found: C, 32.3; H, 1.5; N, 16.0. $C_7H_4FN_3O_2Se$ requires C, 32.3; H, 1.55; N, 16.2%); δ_H 2.72 (3 H, d, *J* 2.7, 4-Me) and 8.39 (1 H, d, *J* 9.0, 6-H); *m/z* 261 (M^+, 15%), 245 (1), 231 (15), 213 (1) and 57 (100).

(±)-4-*Methyl*-4-*nitro*-2,1,3-*benzoselenadiazol*-5(4H)-*one* (*R,S*)-**11**. R_f 0.30, m.p. 115–117 °C (Found: C, 32.3; H, 1.9; N, 16.2. $C_7H_5N_3O_3Se$ requires C, 32.6; H, 1.95; N, 16.3%); $\nu_{max}(CHCl_3)/cm^{-1}$ 1684 (CO) and 1562 (NO_2); δ_H 2.14 (3 H, s, 4-Me), 6.62 and 7.84 (2 H each, d, *J* 10.3, 6- and 7-H); $\delta_C(CDCl_3/Me_4Si)$ 22.42 (Me), 92.72 (C-4), 127.73 and 139.36 (C-6 and C-7), 155.73, 160.55 (C-3a and C-7a) and 189.99 (C-5); *m/z* (CI, iso-C_4H_{10}) 260 (M + 1, 28%); (EI) 213 (60), 185 (10), 158 (12), 133 (25) and 80 (100).

Reductive Ring-opening of 2,1,3-*Benzoselenadiazoles* **2**, **3**, **6** *and* **9**.—*General procedure*. A mixture of compound **2** (or **3**, **6** and **9**) (0.5 mmol) and 57% hydriodic acid (3 cm^3) was stirred for 2 h at room temperature (TLC solvents: petroleum–EtOAc, 5:1), Aqueous sodium bisulfite (10%) was then added dropwise until the formed iodine was completely reduced. The mixture was carefully neutralized with concentrated ammonia to pH 6 and extracted with chloroform. The organic phase was evaporated and the residue subjected to FC. The pure diamines or phenols were obtained by recrystallization (methanol).

4-*Fluoro*-3-*nitro*-o-*phenylenediamine* **4a**. Yield 60 mg (70%), m.p. 137–139 °C (Found: C, 42.2; H, 3.5; N, 23.6. $C_6H_6FN_3O_2$ requires C, 42.1; H, 3.5; N, 24.6%); δ_H 3.2 and 5.6 (2 H each, br s, 1- and 2-NH_2), 6.42 (1 H, dd, *J* 11.3 and 8.5, 5-H) and 6.82 (1 H, dd *J* 8.5 and 4.6, 6-H); *m/z* 171 (M^+, 100%), 154 (30), 153 (45), 125 (25) and 123 (52).

4-*Fluoro*-6-*methyl*-3-*nitro*-o-*phenylenediamine* **4b**. Yield 70 mg (75%), m.p. 158–160 °C (Found: C, 45.9; H, 4.5; N, 22.7. $C_7H_8FN_3O$ requires C, 45.4; H, 4.4; N, 22.7%); δ_H 2.25 (3 H, s, 6-Me), 3.1 and 5.6 (2 H, each, br s, 1- and 2-NH_2) and 6.37 (1 H, d, *J* 12.3, 5-H); *m/z* 185 (M^+, 100%), 168 (29), 167 (54), 150 (10) and 138 (54).

4-*Fluoro*-5-*methyl*-3-*nitro*-o-*phenylenediamine* **4c**. Yield 67 mg (72%), m.p. 145–147 °C (Found, 45.5; H, 4.4; N, 22.6. $C_7H_8FN_3O_2$ requires C, 45.4; H, 4.4; N, 22.7%); δ_H 2.17 (3 H, br dd, *J* 2.5, 5-Me), 3.2 and 5.2 (2 H each two br s, 1- and 2-NH_2) and 6.70 (1 H, d, *J* 6.7, 6-H); *m/z* 185 (M^+, 100%), 168 (25), 167 (18), 151 (4) and 138 (53).

3,4-*Diamino*-2-*nitrophenol* **5a**. Yield 70 mg (83%), m.p. 176 °C (decomp.) (Found: C, 41.8; H, 4.1; N, 24.5. $C_6H_7N_3O_3$ requires C, 42.6; H, 4.2; N, 24.85%); δ_H 2.9 and 6.5 (2 H each, br s, 3- and 4-NH_2), 6.22 and 6.94 (1 H each, d, *J* 8.4) and 10.86 (1 H, s, OH); *m/z* 169 (M^+, 81%), 152 (12), 151 (67), 134 (30) and 44 (100).

3,4-*Diamino*-5-*methyl*-2-*nitrophenol* **5b**. Yield 71 mg (77%), m.p. 165–168 °C (Found: C, 45.8; H, 5.0; N, 22.1. $C_7H_9N_3O_3$ requires C, 45.9; H, 4.95; N, 22.9%); δ_H 2.24 (3 H, s, 5-Me), 2.7 and 6.6 (4 H, two br s, 3- and 4-NH_2), 6.17 (1 H, s, 6-H) and 10.97 (1 H, s, OH); *m/z* 183 (M^+, 100%), 166 (12), 165 (95), 148 (28) and 138 (15).

3,4-*Diamino*-6-*methyl*-2-*nitrophenol* **5c**. Yield 67 mg (73%), m.p. 163–166 °C (Found: C, 45.8; H, 4.9; N, 22.4. $C_7H_9N_3O_3$ requires C, 45.9; H, 4.95; N, 22.9%); δ_H 2.14 (3 H, s, 6-Me), 2.9 and 6.2 (2 H each, br s, 3- and 4-NH_2), 6.87 (1 H, s, 5-H) and 11.09 (1 H, s, OH); *m/z* 183 (M^+, 96%), 166 (13), 165 (100), 148 (40) and 136 (10).

5-*Fluoro*-4-*methyl*-3-*nitro*-o-*phenylenediamine* **7**. Yield 73 mg (78%), m.p. 107–109 °C (Found: C, 45.7; H, 4.5; N, 22.5. $C_7H_8FN_3O_2$ requires C, 45.4; H, 4.4; N, 22.7%); δ_H 2.25 (3 H, d, *J* 2.3, 4-Me), 3.6 and 4.5 (2 H each, two br s, 1- and 2-NH_2) and 6.63 (1 H, d, *J* 10.0 6-H); *m/z* 185 (M^+, 100%), 168 (62), 166 (14), 150 (8) and 137 (73).

4-*Fluoro*-3-*methyl*-6-*nitro*-o-*phenylenediamine* **10**. Yield 68 mg (73%), m.p. 149–150 °C (Found: C, 44.8; H, 4.3; N, 22.4. $C_7H_8FN_3O_2$ requires C, 45.4; H, 4.4; N, 22.7%); δ_H 2.19 (3 H, d, *J* 1.7, 3-Me), 3.6 and 5.7 (2 H each, br s, 1-and 2-NH_2) and 7.43 (1 H, d, *J* 10.2, 5-H); *m/z* 185 (M^+, 100%), 168 (29), 167 (16), 150 (15) and 138 (44).

6-*Fluoro*-2,3,8-*trimethyl*-5-*nitroquinoxaline* **20**.—To a solution of **4b** (93 mg, 0.5 mmol) in methanol (5 cm^3) was added butane-2,3-dione (60 mg, 0.7 mmol). The mixture was stirred for 30 min at ambient conditions (TLC: petroleum–EtOAc, 5:1). The product precipitated when water (3 cm^3) was added. Filtration followed by recrystallization (methanol) furnished pure **20** as white crystals (105 mg, 89%), m.p. 122–123 °C (Found: C, 56.0; H, 4.3; N, 17.6. $C_{11}H_{10}FN_3O_2$ requires C, 56.2; H, 4.3; N, 17.9%); δ_H 2.74, 2.75 and 2.81 (3 H each, three s, 2-, 3- and 8-Me) and 7.39 (1 H, d, *J* 10.1, 7-H); *m/z* (M^+, 76%), 219 (6), 205 (22), 189 (9) and 43 (100).

Table 2 Crystal data for compound **11**

Formula	$C_7H_5N_3O_3Se$
M	258.09
Crystal system	Monoclinic
Space group	$C2/c$
a	15.751(8) Å
b	10.02(3) Å
c	12.70(1) Å
β	113.37(5) °
V	1842 Å^3
Z	8
D_c	1.861 g cm^{-3}

Table 3 Atomic parameters for compound **11** with esds in parentheses

Atom	x	y	z
Se	0.875 60(3)	0.220 58(4)	0.130 59(3)
O(1)	0.615 6(2)	0.092 5(3)	0.374 6(2)
O(2)	0.654 9(2)	0.366 1(3)	0.276 5(3)
O(3)	0.552 1(2)	0.292 4(4)	0.121 8(3)
N(1)	0.756 5(2)	0.204 3(3)	0.113 4(2)
N(2)	0.918 2(2)	0.179 9(3)	0.282 2(2)
N(3)	0.617 9(2)	0.279 8(4)	0.205 9(3)
C(1)	0.844 5(2)	0.158 3(3)	0.304 8(3)
C(2)	0.757 0(2)	0.169 8(3)	0.213 4(2)
C(3)	0.667 7(2)	0.141 5(3)	0.226 7(2)
C(4)	0.682 3(3)	0.108 7(3)	0.352 6(3)
C(5)	0.775 0(3)	0.095 1(4)	0.438 4(3)
C(6)	0.852 1(3)	0.118 1(3)	0.419 9(3)
C(7)	0.610 9(4)	0.039 1(6)	0.144 8(4)
H(2)	0.774(2)	0.055(3)	0.498(3)
H(3)	0.918(3)	0.121(3)	0.483(3)
H(4)	0.638(1)	−0.038(2)	0.162(2)
H(5)	0.564(3)	0.032(5)	0.126(3)

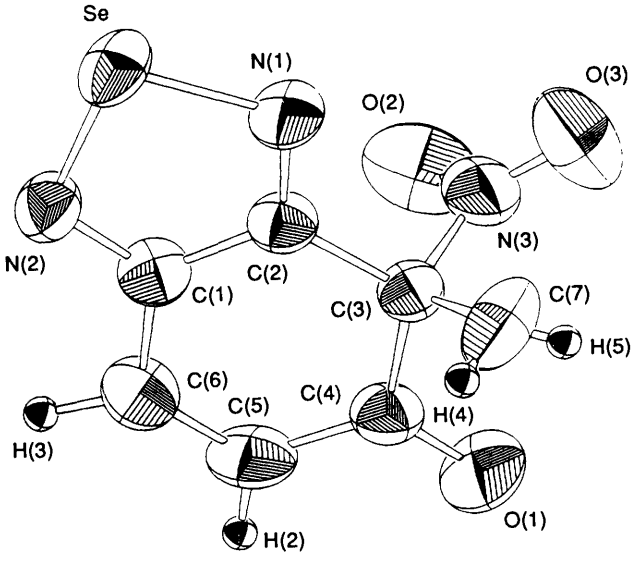


Fig. 1 Molecular structure of compound **11**

Crystal Structure Analysis of Compound **11**.—Yellow diamond-shaped crystals were obtained by recrystallization from petroleum. A single crystal of dimensions 0.24 × 0.35 × 0.40 mm was used for data collection on a Rigaku AFC6R diffractometer with molybdenum radiation (λ = 0.71073 Å). The lattice parameters given in Table 2 were determined from a least-squares fit of the setting angles of 21 reflections in the 2θ range 43.7–47.2. Correction for crystal degradation (−24%) was applied to the 6901 reflections measured with ω-2θ scans. The crystal structure was solved with direct methods and refined with least-squares methods. All atoms except one methyl-hydrogen were successfully included in the refinement. All programmes used were included in the TEXSAN software package.[19] 6726 Reflections with $I > 0$ were used in the final refinement of 143 variables to give the atomic parameters listed in Table 3. The final values of R and R_w were 0.127 and 0.123, respectively. The highest and lowest peaks in the final difference electron density map were 1.55 and −1.72 e Å^{-3}, respectively. Intramolecular distances and angles are given in Table 4. Atomic scattering factors were taken from ref. 20, and anomalous dispersion factors from ref. 21. Hydrogen coordinates, thermal parameters and full lists of bond lengths and angles have been deposited at the CCDC.*

Table 4 Intramolecular distances (Å) and angles (°) of compound **11** with esds in parentheses

Se–N(1)	1.803(3)	C(1)–C(2)	1.411(4)
Se–N(2)	1.817(3)	C(1)–C(6)	1.477(4)
O(1)–C(4)	1.199(4)	C(2)–C(3)	1.510(4)
O(2)–N(3)	1.216(4)	C(3)–C(4)	1.559(4)
O(3)–N(3)	1.164(4)	C(3)–C(7)	1.483(6)
N(1)–C(2)	1.314(4)	C(4)–C(5)	1.441(5)
N(2)–C(1)	1.319(4)	C(5)–C(6)	1.344(5)
N(3)–C(3)	1.563(6)		
N(1)–Se–N(2)	92.1(1)	C(2)–C(3)–C(4)	113.0(3)
Se–N(1)–C(2)	107.4(2)	C(2)–C(3)–C(7)	112.5(3)
Se–N(2)–C(1)	106.3(2)	C(4)–C(3)–C(7)	112.1(3)
O(2)–N(3)–O(3)	126.3(4)	O(1)–C(4)–C(3)	118.7(3)
O(2)–N(3)–C(3)	116.4(3)	O(1)–C(4)–C(5)	122.0(3)
O(3)–N(3)–C(3)	117.1(4)	C(3)–C(4)–C(5)	119.2(3)
N(2)–C(1)–C(2)	117.7(3)	C(4)–C(5)–C(6)	124.5(3)
N(2)–C(1)–C(6)	121.9(3)	C(4)–C(5)–H(2)	110(2)
C(2)–C(1)–C(6)	120.4(3)	C(6)–C(5)–H(2)	125(2)
N(1)–C(2)–C(1)	116.5(3)	C(1)–C(6)–C(5)	119.8(4)
N(1)–C(2)–C(3)	120.6(3)	C(1)–C(6)–H(3)	115(2)
C(1)–C(2)–C(3)	122.9(3)	C(5)–C(6)–H(3)	125(2)
N(3)–C(3)–C(2)	104.0(3)	C(3)–C(7)–H(4)	110(2)
N(3)–C(3)–C(4)	102.7(2)	C(3)–C(7)–H(5)	126(4)
N(3)–C(3)–C(7)	111.9(4)		

Acknowledgements

We thank Drs. T. Gustafsson and H. Karlsson (Uppsala University) for performing the X-ray crystallographic analysis, and Mrs. R. Andersson, S. Gohil and B. Malmensten for their valuable help with the NMR, mass and IR spectra. Grants from the Swedish Council for Forestry and Agricultural Research and from the Foundation for Promotion of Cancer Research (Japan), and a Swedish Institute scholarship to Wei Tian are gratefully acknowledged.

* For details of the Cambridge Crystallographic Data Centre deposition scheme, see 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1993, Issue 1.

References

1 S. Grivas, *Acta Chem. Scand., Ser. B*, 1986, **40**, 404; this letter was printed again and included in the November issue of volume **40**.
2 T. Nyhammar and S. Grivas, *Acta Chem. Scand., Ser. B*, 1986, **40**, 583.
3 S. Grivas, W. Tian and R. Andersson, *J. Chem. Res.*, 1992, (*S*), 328; (*M*), 2701.
4 W. Tian and S. Grivas, *Synthesis*, in the press.
5 S. Grivas and W. Tian, *Acta Chem. Scand.*, in the press.
6 W. Tian and S. Grivas, *J. Heterocycl. Chem.*, 1992, **29**, 1305.
7 G. R. Sullivan, *Top. Stereochem.*, 1978, **10**, 287.

8 C. W. Bird, G. W. H. Cheeseman and A. A. Sarsfield, *J. Chem. Soc.*, 1963, 4767.
9 V. G. Pesin, S. A. Dyachenko and A. M. Khaletskii, *J. Gen. Chem. USSR* (*Engl. Transl.*), 1964, **34**, 3807.
10 E. Forche, in *Houben-Weyl*, Georg Thieme Verlag, Stuttgart, 1962, vol. 5/3, p. 415.
11 C. Brizzi, D. Dal Monte and E. Sandri, *Ann. Chim.* (*Rome*), 1964, **54**, 476.
12 E. Sawicki and A. Carr, *J. Org. Chem.*, 1957, **22**, 503.
13 J. A. Elvidge, G. T. Newbold, A. Percival and I. R. Senciall, *J. Chem. Soc.*, 1965, 5119.
14 F. T. Hatch, M. G. Knize and J. S. Felton, *Environ. Mol. Mutagen.*, 1991, **17**, 4.
15 S. Grivas, W. Tian, S. Lindström, E. Ronne and K. Olsson, *Acta Chem. Scand.*, in the press.
16 H. Kasai, T. Shiomi, T. Sugimura and S. Nishimura, *Chem. Lett.*, 1981, 675.
17 S. Grivas, *Acta Chem. Scand., Ser. B*, 1985, **39**, 213.
18 A. F. Al-Attar and G. Nickless, *Analyst*, 1990, **115**, 1441.
19 TEXSAN–TEXRAY Structure Analysis Package, Molecular Structure Corporation (1985).
20 D. T. Cromer and J. T. Waber, International Tables for X-Ray Crystallography, The Kynoch Press, Birmingham, England, 1974, vol. IV, p. 72.
21 D. T. Cromer, International Tables for X-Ray Crystallography, The Kynoch Press, Birmingham, England, 1974, vol. IV, p. 149.

Paper 2/04497H
Received 20*th August* 1992
Accepted 22*nd September* 1992