Unexpected Disproportionation of 4,4'-Dialkylamino Substituted Diaryl Selenides and Tellurides

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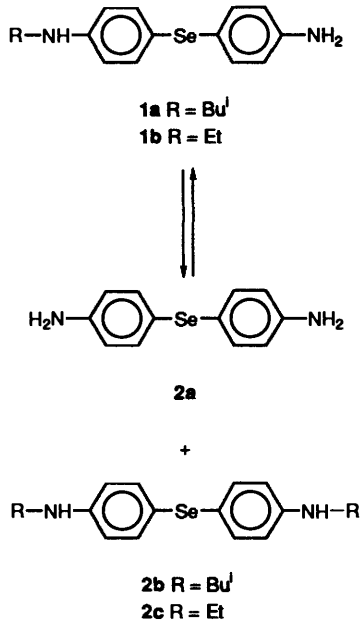
The unsymmetrical diaryl selenides **1a** and **b** disproportionate under acidic conditions, to produce the corresponding symmetrical analogues. Similarly, the aminosubstituted compounds **2b–d** and **2k** react with **2a** to establish an equilibrium mixture with high selectivity. Diaryl tellurides **5a** and **b** also exchange aryl groups, whereas aminosubstituted diaryl sulfides are stable under the reaction conditions. The process, which involves carbon–selenium/tellurium bond cleavage, may involve a free radical mechanism.

While organoselenium compounds are valuable tools in preparative organic chemistry,[1] their potential biological properties have remained essentially unexplored. The association of the importance of dietary selenium with the function of the glutathione peroxidase enzymes[2] has revived the interest in the pharmaceutical exploration of organoselenides.[3] The involvement of the glutathione peroxidases in the endogenous defence against prooxidants[4] suggests a role for organoselenium compounds in the control of conditions such as inflammation, atherosclerosis and ischemia/reperfusion injury. Indeed, the benzisoselenazolone Ebselen[5] and related derivatives,[6] as well as diselenides,[7] have been reported to show substantial glutathione peroxidase-like activity *in vitro*. Ebselen has also been extensively evaluated in animal studies.[8] The apparent toxicity of inorganic selenium compounds[9] suggests that reasonable stability of the carbon–selenium bonds would be desirable in potential organoselenium pharmaceuticals.

We recently required a series of substituted diaryl selenides to study their capacity as antioxidants in biological systems.[10] During the preparation of some unsymmetrical alkylamino substituted derivatives, we observed an unexpected disproportionation reaction which, to our knowledge, was unprecedented in the literature. Here, we report on our results from an extended study of this reaction.



Scheme 1

Results

During aqueous acidic work-up we observed that *N*-(2-methylpropyl)-4,4'-diamino-1,1'-selenobisbenzene (**1a**) underwent a disproportionation reaction to give a mixture of selenide **1a** and the symmetrical diaryl selenides **2a** and **b** according to Scheme 1. The identification of the disproportionation products was confirmed by LC–MS analyses and comparison with authentic samples. A representative chromatogram is given in Fig. 1, together with typical fragmentation patterns.

Since compound **1a** appeared to be stable towards disproportionation in organic solvents (*e.g.* trichloromethane, dichloromethane, acetonitrile) we undertook a study of the stability of this material at various pH values in a water–methanol–acetonitrile system. Solutions of compound **1a** with different pH values were allowed to stand either in the dark or exposed to sunlight. Only the two degradation products **2a** and **2b** were observed in acidic media under either conditions. The reaction products were always formed in equimolar amounts. Fig. 2 (●) shows the second order rate constants of disproportionation of compound **1a** as a function of pH in buffered solutions at constant ionic strength.

The reaction was found to be strongly pH dependent in a rather narrow range and with an optimum rate at pH 4. No disproportionation occurred above neutral pH. In addition, the product distribution at equilibrium (pH 3) indicated that compound **1a** delivered exclusively compounds **2a** and **b** in a statistical manner, *i.e.* 25% of each product, with 50% of **1a** remaining. We also confirmed that the same equilibrium mixture was obtained from an equimolar mixture of the symmetrical selenides **2a** and **b**. Similar results were obtained starting from *N*-ethyl-4,4'-diamino-1,1'-selenobisbenzene (**1b**), which provided selenide **2a** and the dialkylated product **2c**. The

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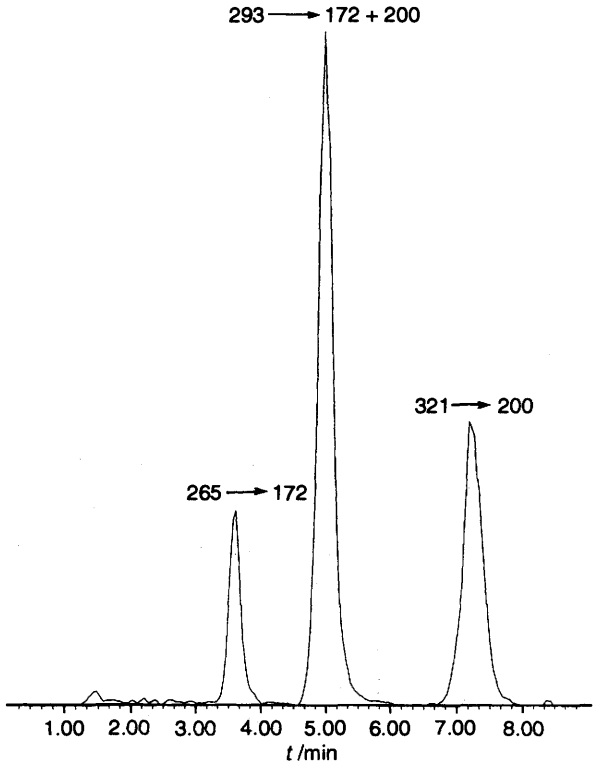
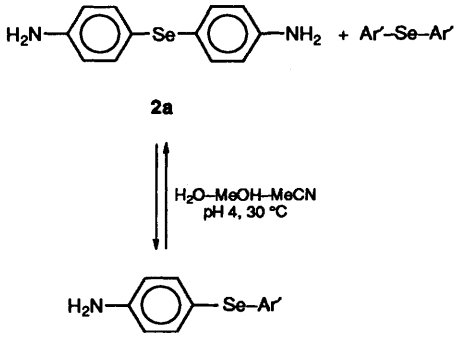


Fig. 1 HPLC/MS total ion chromatogram of the reaction mixture according to Scheme 3. The identity of **2a** (3.7 min), **2k** (7.3 min) and the disproportionation product (**1c**, 5.0 min) was supported by the fragments formed as depicted.

observed second order rate constant (pH 4; 30 °C) for both reactions was 140 $dm^3\ mol^{-1}\ h^{-1}$.

To investigate the generality of the process we synthesised and treated a series of symmetrical *para*-substituted diaryl selenides **2c–k** with an equimolar amount of compound **2a** according to Scheme 2. The results, summarised in Table 1,



Scheme 2

indicated that the presence of an amino-function was crucial for the disproportionation to occur. The performance of the dimethylamino derivative **2d** demonstrated that an NH-functionality was not necessary for the reaction to occur, and, since no traces of *N*-monomethyl analogues could be detected, that the methyl–nitrogen bonds had remained intact in the process. Furthermore, the ring-alkylated 3,3′,5,5′-tetramethyl-4,4′-diamino-1,1′-selenobisbenzene (**2k**) afforded the expected unsymmetrical product **1c** when mixed with selenide **2a** (Scheme 3).

Analogous experiments utilising diaryl sulfides failed to produce disproportionation products. Thus, *N*,*N*′-diethyl-4,4′-diamino-1,1′-thiobisbenzene (**3b**) reacted with neither its diamino analogue **3a** nor with compound **2a**. On the other

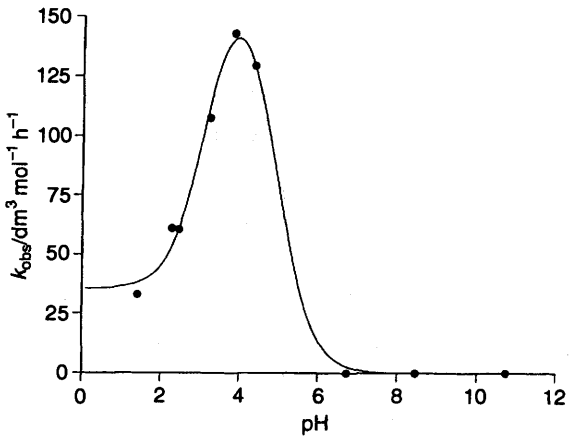
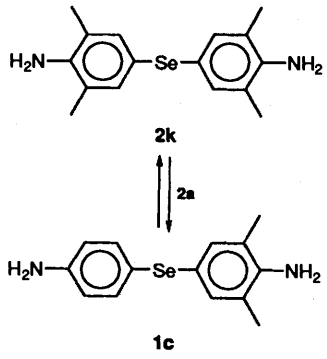


Fig. 2 pH Dependence of the second order rate constant for the disproportionation of **1a**. Experimental values (●), and values calculated according to eqn. (2).



Scheme 3

hand, aminosubstituted diaryl tellurides were shown to behave analogously to the selenides. Thus, at pH 4, the symmetrical tellurides **5a** and **b** afforded an equilibrium mixture containing the disproportionation product **6**.

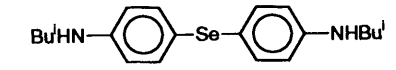
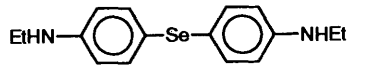
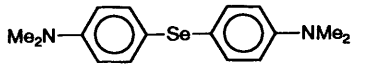
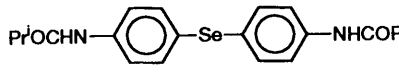
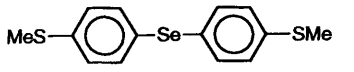
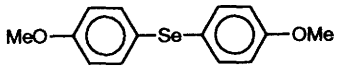
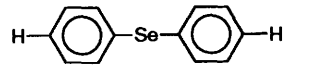
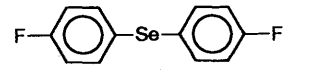
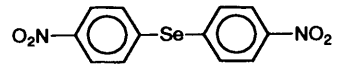
We also briefly assessed the influence of metal ions, chelating agents and antioxidants on the disproportionation process. The presence of small amounts of copper(II) ions (1–5 ppm) was found to accelerate the disproportionation of selenides **1a** and **b**, indicating a role for the transition metal as initiator. A pH profile obtained for the reaction of **1a** in the presence of 5 ppm copper(II) was, however, identical to that obtained in the absence of added copper.

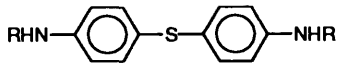
The presence of EDTA (0.01%) in the reaction medium suppressed, but did not inhibit the disproportionation of **1a** or **b**. Some thiol chelators, displayed a profound influence on the disproportionation of compound **1a**. Thus, the presence of 1% (relative to **1a**) of cysteamine, *N*,*N*-dimethylcysteamine or thiosalicylic acid inhibited the reaction, whereas thioglycolic acid and cysteine were virtually ineffective. The antioxidants BHA and hydroquinone at the same concentration showed only a marginal attenuating influence on the disproportionation reaction, whereas, at equimolar amounts, the latter suppressed the reaction completely. In addition, the dinitro compound **2j** not only failed to undergo disproportionation with selenide **2a**, but indeed completely inhibited the disproportionation of compound **1a** when present in equimolar quantities.

Discussion

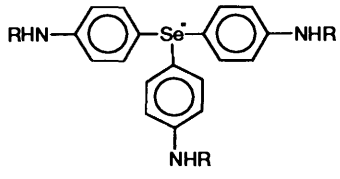
The above results reveal an unexpected lability of amino substituted diaryl selenides and tellurides under acidic condi-

Table 1 Rates of disproportionation between compound **2a** and various diaryl selenides according to Scheme 2

Compound		Rate constant k_{obs}/dm^3 mol^{-1} h^{-1}
	**2b**	7.1
	**2c**	10.3
	**2d**	7.8
	**2e**	—
	**2f**	—
	**2g**	—
	**2h**	—
	**2i**	—
	**2j**	—



3a R = H
3b R = Et



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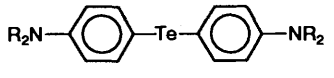
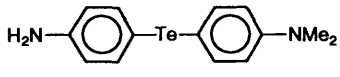


5a R = H
5b R = Me



6

tions. Although we initially suspected that a trans-alkylation pathway was involved in the disproportionation process, the experiments with the tetramethyl compounds **2d** and **k** ruled out this possibility. Also the fact that the sulfide analogues **3a** and **b** were completely stable under the conditions seems to disfavour such a reaction mechanism.

Only a rather narrow pH range allowed disproportionation. The optimum reaction rate was observed at the pH where the monoprotonated species would be expected to predominate. We estimated the pK_{a_1} and pK_{a_2} values for the unsymmetrical derivative **1a** to 3.1 and 4.9 respectively from experimental data, in reasonable agreement with the corresponding values for 1,4-diaminobenzene (2.8 and 5.0). By assuming that each individual protolyte contributes uniquely to the overall reaction rate, *i.e.* using eqn. (1) we arrive at eqn. (2).

$$k_{obs} = k_1[MH_2^{2+}] + k_2[MH^+] + k_3[M] \quad (1)$$

$$k_{obs} = k_1[H^+]^2 + k_2K_{a_1}[H^+] + k_3K_{a_1}K_{a_2})/(K_{a_1}K_{a_2} + K_{a_1}[H^+] + [H^+]^2) \quad (2)$$

This equation [Fig. 2, (——)], which nicely describes the pH dependence of the reaction gives the individual rate constants k_1 = 23.8, k_2 = 163.2 and k_3 = 0 dm^3 mol^{-1} h^{-1}, indicating that the unprotonated species does not participate in the reaction at all while the diprotonated species shows some reactivity.

The disproportionation apparently involves cleavage of carbon–selenium bonds. Considering that the *para*-amino substituted diaryl selenides are readily oxidised, we were speculating that a selenoxide, which is the sole product from electrochemical oxidation of *e.g.* compound **2a**,[11] was an intermediate. The addition of the crude oxide of **2a**, prepared by hydrogen peroxide treatment of the selenide, to a solution containing selenides **2a** and **2b** did not, however, enhance the rate but rather suppressed the reaction severely.

As the present disproportionation reaction was sensitive to a variety of chelators as well as to hydroquinone and also was inhibited by the nitro compound **2j**, a free radical mechanism seems probable. We speculate that an aryl radical is formed, capable of producing a triarylselenium radical[12] as the chain carrying species (*e.g.* **4**, or a protonated form thereof). This radical would be highly stabilised through conjugatory effects similar to those observed in the triphenylmethyl radical; an amino group further stabilises a radical species by conjugative electron delocalisation of the semi-occupied molecular orbital.[13] Subsequent delivery of one of the aryl groups to another diaryl selenide would propagate a radical chain process. This type of mechanism is supported by the fact that trialkyltellurium radicals have been suggested to be involved in the modulation of free radical processes by tellurides.[14] In this process alkyl radical exchange was observed. Also, radical displacement reactions at sulfur centres have been suggested to involve tricoordinate, hypervalent sulfuranyl radical intermediates,[15] although the existence of true radical intermediates or merely transition states appears to be a matter of controversy[16] in free radical substitution at chalcogens.

The disproportionation process displays several interesting features; the strong substituent effects, the apparent dependency on copper ions and the profound influence of pH. With regard to substituent effects, we have found that the diamino derivatives are by far the most easily oxidised in the series.[17] The presence of copper ions, or other adventitious transition metals, may be important in the initiation step. It is a possibility that radical generation can be derived from traces of contaminating diselenides, but seems improbable that only the diamino derivatives should suffer such contamination. At the present time, it is difficult to rationalise the pH dependency of the process. The fact that this disproportionation process is highly selective suggests the involvement of comparatively stable intermediates.

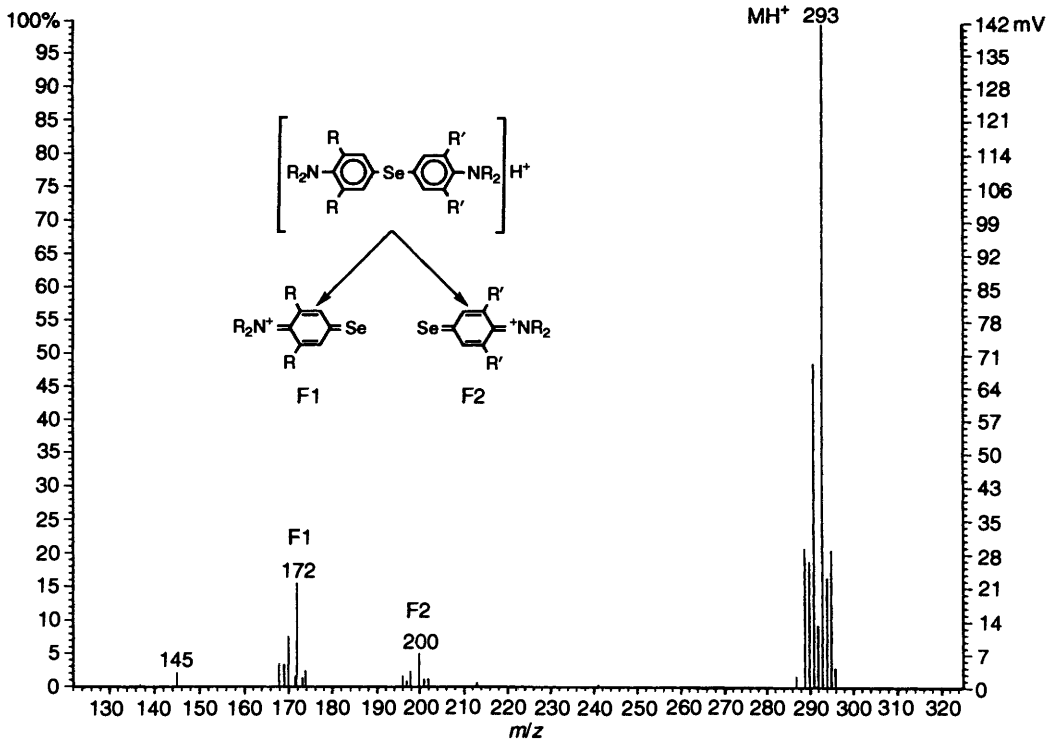


Fig. 3 Schematic representation of the TSP–HPLC/MS fragmentation of the diaryl selenides and the TSP mass spectrum of the product in Scheme 3, with MH^+ and the fragments corresponding to F1 and F2

Experimental

General.—Melting points are uncorrected, and were determined by using a Mettler FP 90 automatic device, equipped with an FP-82 cell. ^1H NMR spectra were recorded on Varian VXR 300 and Unity Plus 500 (compound **6**) instruments. Tetramethylsilane was used as internal standard. Elemental analyses were obtained from Mikrokemi AB, Uppsala, Sweden.

Liquid chromatography. The chromatographic system consisted of a Waters M600 gradient pump, a Spectra Physics SP8780 autoinjector and an Applied Biosystems 783 variable UV-detector set at 260 nm. The column was a Merck RP Select B C-8 (125 × 4.0 mm) with a particle size of 5 μm. The mobile phase contained acetonitrile and ammonium acetate (pH 7, 50 mmol dm^{-3}). The ratio between organic and aqueous eluent was varied in the range 40:60 to 60:40 (*v*/*v*) depending on the type of compound analysed. The concentrations of the test compounds and the reaction products were determined by external standard methodology.

Mass spectrometry. The identities of the reaction products were determined by HPLC/MS, using a VG Trio-2 quadrupole mass spectrometer equipped with a thermospray interface. The ion source was kept at 200 °C, and the capillary temperature was typically between 260 and 280 °C. The chromatographic system was identical to that described above except for a change of pH to 5 in the eluting buffer. The thermospray spectra of diaryl selenides typically gave an abundant protonated molecular ion, together with diagnostic selenoquinone iminium ion fragments, resulting from cleavage of the carbon–selenium bonds. A representative spectrum is given in Fig. 3.

Kinetic measurements. The experiments were carried out in buffered, aqueous solutions (50 mmol dm^{-3} of phosphate, acetate or carbonate) containing 30% (*v*/*v*) of methanol and 10% (*v*/*v*) of acetonitrile (the organic modifiers were added in order to increase the solubility of the test compounds). The ionic strength was maintained constant at 0.5 mol dm^{-3} by the addition of an appropriate amount of potassium chloride. The glass vessel containing the reaction medium (10 cm^3) was thermostatted at the appropriate temperature, normally 30 °C, for 1 h before the experiment was started by the addition of the test compound(s) dissolved in methanol (1 cm^3). The initial concentration was typically 0.5 mmol dm^{-3}. Samples were periodically withdrawn from the reaction solution and analysed by liquid chromatography and mass spectroscopy. The observed reaction rate constant was elucidated from a concentration profile assuming second order kinetics with regard to the starting material. Reactions starting from two symmetrical selenides were assessed by determining the initial rate of disappearance of one of the reactants. The pH profile given in Fig. 2 was produced iteratively by using the MINSQ software (MicroMath Scientific Software, Salt Lake City, USA).

Synthetic Procedures.—The symmetrical diaryl selenides **2a**,[18] **2d**,[19] **2f**,[20] **2g**,[21] **2h**,[22] **2i**[23] and **2j**[24] and tellurides **5a**[17] and **5b**[17] were synthesised according to literature procedures. The sulfide **3a** is commercially available. The monoalkylated derivates **1a** and **b** were obtained through monoacylation [treatment with 1.0 equiv. of the appropriate acid chloride in tetrahydrofuran (THF) in the presence of triethylamine] and reduction ($LiAlH_4$ in THF) protocols starting from **2a**. The selenides **2b**, **c** and sulfide **3b** were prepared similarly, but applying an excess of the acylating agent. The selenide **2k** was obtained from 3,5-dimethyl-4-nitroaniline by diazotisation and reaction with disodium selenide followed by reduction. Detailed experimental data for new compounds are given below. All other chemicals and solvents were of analytical grade. Water for kinetic measurements was deionised and purified in a MilliQ water purification system.

N-Ethyl-4,4′-diamino-1,1′-selenobisbenzene (**1b**). $LiAlH_4$ (1.4 g, 36 mmol) in THF (50 cm^3) was stirred at ambient temperature. Crude *N*-acetyl-4,4′-diamino-1,1′-selenobisbenzene[17] (2.2 g) in THF (50 cm^3) was added with caution. The mixture was refluxed for 2 h. Quenching with water, filtration from inorganic salts and evaporation afforded a yellow oil (1.85 g), which was purified by flash chromatography (SiO_2; EtOAc–light petroleum) to give a solid. Recrystallisation of

0.27 g from Et_2O–heptane gave 0.12 g (39%) of pure **1b**, m.p. 72.5–74 °C (Found: C, 57.9; H, 5.5; N, 9.5. $C_{14}H_{16}N_2Se$ requires C, 57.73; H, 5.54; N, 9.62%); δ_H(300 MHz, $CDCl_3$), 1.24 (t, 3 H), 3.13 (q, 2 H), 3.62 (bs, 2 H), 6.50 (m, 2 H), 6.57 (m, 2 H), 7.25 (m, 2 H) and 7.31 (m, 2 H).

N-(2-*Methylpropyl*)-4,4′-*diamino*-1,1′-*selenobisbenzene* (**1a**). Isobutyryl chloride (1.05 cm^3, 10 mmol) in THF (25 cm^3) was added dropwise at 0 °C to a solution of 4,4′-diamino-1,1′-selenobisbenzene[18] (2.63 g, 10 mmol) and triethylamine (3 cm^3, 20 mmol) in THF (50 cm^3). After stirring for 0.5 h the solvent was evaporated and the solid residue was washed with water and dried *in vacuo* to give 3.35 g of crude material, containing the monoacylated, diacylated and non-acylated compounds in a molar ratio of 3:1:1. Part of the crude material (0.5 g) was reduced with $LiAlH_4$ (0.38 g) using the procedure described for **1b**. Flash chromatography and recrystallization from Et_2O–heptane afforded pure **1a** (0.3 g, 63%) as an off-white solid, m.p. 51.4–53.2 °C (Found: C, 60.4; H, 6.3; N, 8.8. $C_{16}H_{20}N_2Se$ requires C, 60.18; H, 6.31; N, 8.77%); δ_H(300 MHz, $CDCl_3$) 0.97 (d, 6 H), 1.85 (p, 1 H), 2.89 (d, 2 H), 3.62 (bs, 1 H), 3.74 (bs, 1 H), 6.48 (m, 2 H), 6.55 (m, 2 H), 7.24 (m, 2 H) and 7.30 (m, 2 H).

N,N′-*Diethyl*-4,4′-*diamino*-1,1′-*selenobisbenzene* (**2c**). The compound was prepared from *N,N′*-diacetyl-4,4′-diamino-1,1′-selenobisbenzene[18] (0.62 g) and $LiAlH_4$ (1.4 g) in analogy with the procedure described for the preparation of **1b**, with the exception that the selenide was added as a solid. Purification by flash chromatography afforded pure **2c** as an oil (0.40 g, 70%) (Found: C, 59.9; H, 6.3; N, 8.6. $C_{16}H_{20}N_2Se$ requires C, 60.18; H, 6.31; N, 8.77%); δ_H(300 MHz, $CDCl_3$) 1.23 (t, 6 H), 3.11 (q, 4 H), 3.57 (s, 2 H), 6.47 (m, 4 H) and 7.29 (m, 4 H).

N,N′-*Di*(2-*methylpropyl*)-4,4′-*diamino*-1,1′-*selenobisbenzene* (**2b**). The compound was prepared from **2e** (1.3 g) and $LiAlH_4$ (1.5 g) in analogy with the procedure described for the preparation of **1b**, with the exception that the selenide was added as a solid. After work-up a yellow solid was obtained (1.3 g), which was recrystallized from petroleum ether to give 0.8 g (66%) of pure compound **2b**, m.p. 57–59 °C (Found: C, 64.4; H, 7.4; N, 7.3. $C_{20}H_{28}N_2Se$ requires C, 63.99; H, 7.52; N, 7.46%); δ_H(300 MHz, $CDCl_3$) 0.96 (d, 12 H), 1.86 (hept, 2 H), 2.89 (d, 4 H), 3.72 (bs, 2 H), 6.48 (m, 4 H) and 7.29 (m, 4 H).

N,N′-*Di*(2-*methylpropanoyl*)-4,4′-*diamino*-1,1′-*selenobisbenzene* (**2e**). Isobutyryl chloride (2.7 cm^3, 25 mmol) in THF (10 cm^3) was added slowly to a stirred solution of 4,4′-diamino-1,1′-selenobisbenzene[18] (2.63 g, 10 mmol) and triethylamine (4 cm^3, 30 mmol) in THF (50 cm^3) at ambient temperature. After stirring for 5–10 min the white precipitate was filtered from the solution and washed with THF and water and dried to give 2.3 g (57%) of crude compound **2e** of sufficient purity, m.p. 264.9–266.4 °C (Found: C, 59.7; H, 6.2; N, 6.9. $C_{20}H_{24}N_2O_2Se$ requires C, 59.55; H, 6.00; N, 6.94%; δ_H(300 MHz, [$^2H_6$]DMSO) 1.10 (d, 12 H), 2.58 (hept, 2 H), 7.37 (m, 4 H), 7.59 (m, 4 H) and 9.94 (s, 2 H).

3,3′,5,5′-*Tetramethyl*-4,4′-*dinitro*-1,1′-*selenobisbenzene*. 3,5-Dimethyl-4-nitroaniline[25] (3.3 g, 20 mmol) was diazotized in THF (10 cm^3)–H_2O/(50 cm^3) with $NaNO_2$ (1.5 g, 22 mmol) in water (15 cm^3) and 37% hydrochloric acid (5 cm^3, 60 mmol) at 0–5 °C. The solution was neutralized with solid $NaHCO_3$ (1.5 g, 18 mmol) and was kept at 0–5 °C. A stirred suspension of black selenium (1.15 g, 15 mmol) in water (25 cm^3) was reduced with $NaBH_4$ (1.15 g, 30 mmol in 25 cm^3 of water) dropwise. A colourless solution was obtained, to which the diazotized solution was added to yield an oily brown precipitate. After stirring for 1 h the oil was separated and dissolved in acetone which was filtered to remove some black selenium. Evaporation afforded a red oil which was triturated with ethanol and dried to give 1.1 g (29%) of crude title compound as a yellow solid, m.p. 150 °C; δ_H(300 MHz, $CDCl_3$) 2.3 (s, 12 H) and 7.22 (s, 4 H); *m/z* 380 (100%).

4,4′-*Diamino*-3,3′,5,5′-*tetramethyl*-1,1′-*selenobisbenzene* (**2k**). 3,3′,5,5′-Tetramethyl-4,4′-dinitro-1,1′-selenobisbenzene (0.76 g, 2 mmol) was dissolved in hot glacial acetic acid (25 cm^3). $SnCl_2$, $2H_2O$ (3.16 g, 14 mmol) in 37% hydrochloric acid (3 cm^3) was added. The mixture was allowed to cool and was stirred overnight. After evaporation, aqueous NaOH was added to *ca.* pH 10 and the clear solution was extracted with $CHCl_3$. Following drying and evaporation of the organic phase, flash chromatography (SiO_2; EtOAc–light petroleum) gave almost pure **2k**, which was recrystallized from ethanol (10 cm^3) to give 0.23 g (36%) of pure compound, m.p. 161.9–163.6 °C (Found: C, 60.3; H, 6.5; N, 8.7. $C_{16}H_{20}N_2Se$ requires C, 60.18; H, 6.31; N, 8.77%); δ_H(300 MHz, $CDCl_3$) 2.12 (s, 12 H), 3.58 (bs, 4 H) and 7.11 (s, 4 H); *m/z* 320, 240 (100%).

N,N′-*Diethyl*-4,4′-*diamino*-1,1′-*thiobisbenzene* (**3b**). The compound was prepared in analogy with **2b** from *N,N′*-diacetyl-4,4′-diamino-1,1′-thiobisbenzene[26] (2.16 g) and $LiAlH_4$ (1.05 g) in THF. After work-up an oil was obtained (1.8 g), which (1.7 g) was purified by flash chromatography (SiO_2; EtOAc–heptane) to give an oil (1.2 g, 65%) (Found: C, 70.5; H, 7.6; N, 10.3. $C_{16}H_{20}N_2S$ requires C, 70.55; H, 7.40; N, 10.28%); δ_H(300 MHz, [$^2H_6$]DMSO) 1.15 (s, 6 H), 3.00 (pent, 4 H), 5.72 (t, 2 H), 6.50 (m, 4 H) and 7.07 (m, 4 H).

N,N′-*Dimethyl*-4,4′-*diamino*-1,1′-*tellurobisbenzene* (**6**). This compound was isolated from a disproportionation experiment (MeOH–MeCN–acetate buffer, 9:1:9) starting from an equimolar mixture of **5a** (2.1 mg) and **5b** (2.5 mg). The TLC (CH_2Cl_2–MeOH, 50:1) showed three spots at R_f 0.69, 0.48 and 0.26. Flash chromatography (CH_2Cl_2–MeOH, 100:1) allowed the isolation of the compound of intermediate polarity (**6**) contaminated by a minor amount of **5b**; δ_H(500 MHz, $CDCl_3$) 2.93 (s, 6 H), 3.67 (bs, 2 H), 6.54 (m, 2 H), 6.57 (m, 2 H), 7.48 (m, 2 H) and 7.60 (m, 2 H); *m/z* (FAB–MS) 342 (MH^+]. Linked scan (B/E): *m/z* 250 [MH^+ – $C_6H_4(NH_2)$], 240 [$(CH_3)_2NC_6H_4C_6H_4N(CH_3)_2$], 212 [$MH^+$ – Te].

N,N-*Dimethyl*-4,4′-*diamino*-1,1′-*selenobisbenzene*. TSP–MS: *m/z* (relative intensity) 293 (100) MH^+, 278 (10) $MH^+ - CH_3$, 213 (10) MH^+ – Se, 198 (15) MH^+ – Se–CH_3.

References

1 *Organoselenium Chemistry*, ed. D. Liotta, John Wiley & Sons, New York, 1987; C. Paulmier, *Selenium Reagents and Intermediates in Organic Synthesis*, Pergamon, Oxford, 1986.
2 R. J. Shamberger, Biochemistry of Selenium, Plenum, New York, 1983.
3 M. J. Parnham and E. Graf, *Prog. Drug. Res.*, 1991, **36**, 9.
4 B. Halliwell and J. M. C. Gutteridge, *Free Radicals in Biology and Medicine*, 2nd edn., Clarendon, Oxford, 1989, ch. 3.
5 H. Sies, *Free Rad. Biol. Med.*, 1993, **14**, 313; M. J. Parnham and E. Graf, *Biochem. Pharmacol.*, 1987, **36**, 3095.
6 H. J. Reich and C. P. Jasperse, *J. Am. Chem. Soc.*, 1987, **109**, 5549.
7 S. R. Wilson, P. A. Zucker, R. C. Huang and A. Spector, *J. Am. Chem. Soc.*, 1989, **111**, 5936.
8 M. J. Parnham, E. Graf, P. Kuhl and S. Leyck, *Adv. Infl. Res.*, 1988, **12**, 257.
9 *Organic Selenium Compounds: Their Chemistry and Biology*, eds. D. L. Klayman and W. H. H. Günther, John Wiley & Sons, New York, 1973.
10 C.-M. Andersson, A. Hallberg, M. Linden, R. Brattsand, P. Moldeus and I. A. Cotgreave, *Free Rad. Biol. Med.*, 1994, **16**, 17.
11 We confirmed this by cyclovoltammetry. For the electrochemical oxidation of selenobisbenzene: see: R. Seeber, P. Cinquantini, P. Zanello and G. A. Mazzocchin, *Electroanal. Chem.*, 1978, **88**, 137.
12 M. Hori, T. Kataoka, H. Shimizu and K. Tsutsumi, *Tetrahedron Lett.*, 1989, **30**, 981; Phenyl and phenylselenyl radicals were observed upon photolysis of selenobisbenzene, see: R. Franzi and M. Geoffroy, *J. Organomet. Chem.*, 1981, **218**, 321. For additional selenium free radical chemistry, see ref. 1.

13 S. Dinctürk and R. A. Jackson, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1127.
14 D. H. R. Barton, N. Ozbalik and J. C. Sarma, *Tetrahedron Lett.*, 1988, **29**, 6581.
15 K. M. Ferris, J. A. Franz, C. Sosa and R. J. Bartlett, *J. Org. Chem.*, 1992, **57**, 777.
16 D. P. Curran, A. A. Martin-Esker, S.-B. Ko and M. Newcomb, *J. Org. Chem.*, 1993, **58**, 4691; J. E. Lyons, C. H. Schiesser and K. Sutej, *J. Org. Chem.*, 1993, **58**, 5632; J. E. Lyons and C. H. Schiesser, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1655.
17 L. Engman, J. Persson, C.-M. Andersson and M. Berglund, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1309.
18 J. Matti, *Bull. Soc. Chim. Fr.*, 1940, 617.
19 O. Behagel and K. Hofmann, *Ber. Dtsch. Chem. Ges.*, 1939, **72**, 582.
20 S. Gronowitz, A. Konar and A.-B. Hörnfeldt, *Org. Magn. Reson.*, 1977, **9**, 213.
21 H. Rheinboldt in *Methoden der Organischen Chemie*, Houben-Weyl, band IX, ed. E. Müller, Georg Thieme-Verlag, Stuttgart, 1955, p. 992.
22 H. M. Leicester, *Org. Synth., Coll. Vol. II*, 1943, 238.
23 J. D. McCullough and B. A. Eckerson, *J. Am. Chem. Soc.*, 1945, **67**, 707.
24 Ref. 21, p. 993.
25 K. Ibbotson and J. Kenner, *J. Chem. Soc. Trans.*, 1923, **123**, 1260.
26 V. Merz and W. Weith, *Ber. Deutsch. Chem. Ges.*, 1871, 384.

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