Selenium Heterocycles XLIV [1]. Syntheses of 8,9-Dihydro-1,2,3-thiadiazolo[4,5-*a*]-4,7-dihydroxynaphthalene and 1,2,3-Selenadiazolo[4,5-*a*]-4,7-dimethoxynaphthalene

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The reaction of thionyl chloride with the semicarbazone **2** gave 4,5-dihydro-6,9-dihydroxynaphtho-[1,2-*d*][1,2,3]thiadiazole (**3**) instead of 4,5-dihydro-6,9-dimethyoxynaphtho[1,2-*d*][1,2,3]thiadiazole (**4**). Selenium dioxide oxidation of compound **2** gave 4,5-dihydro-6,9-dimethyoxynaphtho[1,2-*d*][1,2,3]selena-diazole (**5**). Oxidation of compound **5** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone afforded 6,9-dimethyoxynaphtho[1,2-*d*][1,2,3]selenadiazole (**6**).

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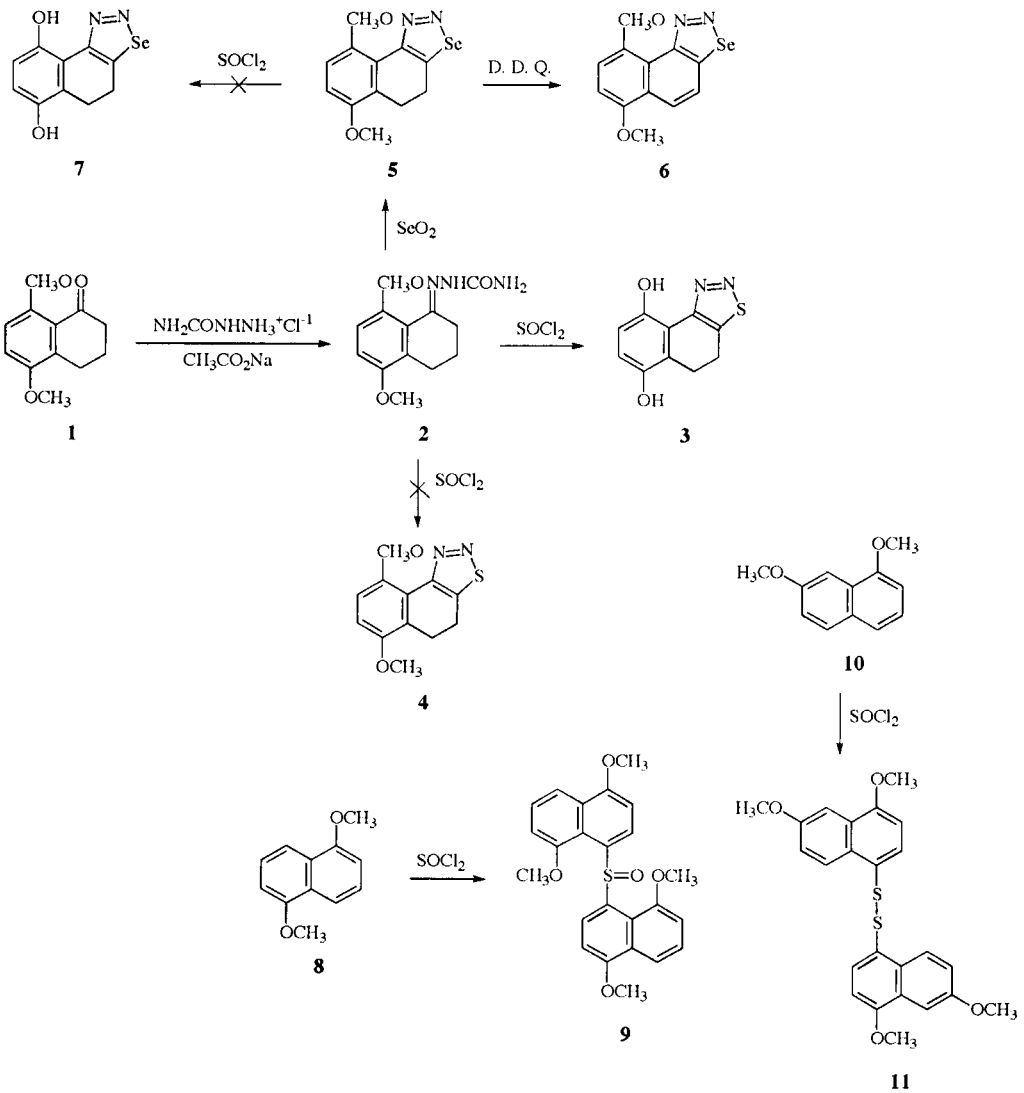
In continuation of the study on the chemisty of selenium heterocyclic compounds and as a part of a program designed to expand the chemistry of fused 1,2,3-thiadiazole, 1,2,3-selenadiazole heterocycles and in view of

Scheme 1

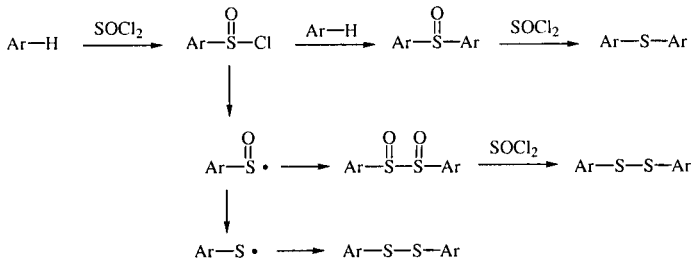


potential biological activity of 1,2,3-thiadiazole [2] and 1,2,3-selenadiazole [3], it was thought worthwhile to prepare the title compounds with the hope that these ring systems may prove to be biologically active.

The title compounds were prepared according to Scheme 1.

The reaction of 5,8-dimethoxy-α-tetralone (**1**) [4] with semicarbazide hydrochloride afforded 5,8-dimethoxy-α-tetralone semicarbazone (**2**). The reaction of compound **2** with thionyl chloride according to the method reported previously [5] gave 4,5-dihydro-6,9-dihydroxynaphtho[1,2-*d*][1,2,3]thiadiazole (**3**). In this reaction the expected compound, namely 4,5-dihydro-6,9-dimethyoxynaphtho[1,2-*d*][1,2,3]thiadiazole (**4**) was not obtained. We could presume that the reaction of thionyl chloride with compound **2** gave initially the expected product **4**. However, compound **4** under experimental condition gave compound **3**. In order to investigate whether thionyl chloride would demethylate other aromatic methyl ethers we undertook the following experiment.

It has been reported that aromatic methyl ethers and thionyl chloride gives initially aromatic sulfinyl chloride which could further lead to diaryl sulfoxide, diaryl sulfide and diaryl disulfide [6,7] and the reaction of 1,4-dimethoxynaphthalene with thionyl chloride gives 2-chloro-1,4-dimethoxy-naphthalene and bis-(1,4-dimethoxy-2-naphthyl)sulfide [6]. We have observed that methoxybenzene and 1,4-dimethoxybenzene with thionyl chloride under our experimental condition (50°) were unreactive and 1,5-dimethoxynaphthalene gave bis-(4,8-dimethoxy-1-naphthyl)sulfoxide (**9**). The reaction of 1,7-dimethoxynaphthalene with thionyl chloride afforded bis-(4,6-dimethoxy-1-naphthyl)disulfide (**11**). A possible mechanism for the formation of compounds **9** and **11** is shown below:



In the above experiments we did not observe the demethylation of methyl ether. Therefore we concluded that demethylation of compound **4** is not general.

Selenium dioxide oxidation of semicarbazone **2** gave 4,5-dihydro-6,9-dimethyoxynaphtho[1,2-*d*][1,2,3]selenadiazole (**5**). Reaction of thionyl chloride with compound **5** afforded mixture of compounds and 4,5-dihydro-6,9-dihydroxynaphtho[1,2-*d*][1,2,3]selenadiazole (**7**) was not obtained. Reaction of compound **5** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone in dichloromethane at room temperature gave the desired 6,9-dimethyoxynaphtho-[1,2-*d*][1,2,3]selenadiazole (**6**).

The structure of all compounds were confirmed by elemental analysis, ir, nmr and mass spectroscopy.

EXPERIMENTAL

Melting points were taken on a Kofler hot stage apparatus and are uncorrected. The uv spectra were recorded using a Perkin-Elmer Model 550 SE. The ir spectra were obtained using a Perkin-Elmer Model 781 spectrograph (potassium bromide disks). The ^{1}H nmr spectra were recorded on a Bruker FT-80 or Varian 400 Unity plus spectrometer and chemical shifts (δ) are in ppm relative to internal tetramethylsilane. The mass spectra were run on Finnigan TSQ 70 Mass spectrometer at 70 eV.

5,8-Dimethoxy-α-tetralone semicarbazone (**2**).

A solution of 5,8-dimethoxy-α-tetralone (**1**) [4] (2.06 g, 0.01 mole), semicarbazide hydrochloride (1.11 g, 0.01 mole) and sodium acetate (1.64 g, 0.02 mole) in water (20 ml) was stirred for 15 minutes. After warming the mixture for several minutes, the precipitate was filtered to give 2.16 g (82%) of compound **2**, mp 130-132°; ms: m/z (%): 263 (M^+, 60), 245 (25), 189 (55), 116 (90), 109 (30), 72 (100), 57 (90) and 44 (58).

Anal. Calcd. for $C_{13}H_{17}N_3O_3$: C, 59.32; H, 6.46; N, 15.97. Found: C, 59.11; H, 6.24; N, 15.74.

4,5-Dihydro-6,9-dihydroxynaphtho[1,2-*d*][1,2,3]thiadiazole (**3**).

A mixture of compound **2** (263 mg, 1 mmole) and thionyl chloride (4 ml) was heated on a steam bath for half an hour. After cooling, water was added and the mixture was neutralized with 10% sodium carbonate solution, and extracted with chloroform. The organic layer was separated and the aqueous layer was extracted with chloroform (2 x 10 ml). The combined organic extract was washed with water (5 ml), dried (sodium sulfate) and filtered. The solvent was removed under reduced pressure. The residue was purified by preparative tlc on silica gel using chloroform-methanol (30:1) as eluent. The desired compound was crystallized from petroleum ether to give 104 mg (47%) of compound **3**, mp 53-55°; uv (methanol): λmax 254 (log ε 3.5); ^{1}H nmr (deuteriochloroform); δ 7.65 (AB q, 2H, aromatic), 2.51 (t, 2H,CH_2) and 2.38 ppm (t, 2H, CH_2); ms: m/z 220 (M^+).

Anal. Calcd. for $C_{10}H_8N_2O_2S$: C, 54.55; H, 3.64; N, 12.73. Found: C, 54.73; H, 3.85; N, 12.95.

4,5-Dihydro-6,9-dimethoxynaphtho[1,2-*d*][1,2,3]selenadiazole (**5**).

To a stirring mixture of compound **2** (1.05 g, 4 mmoles) in glacial acetic acid selenium dioxide (888 mg, 8 mmoles) was added. The mixture was refluxed in a hot water bath for 2 hours. The mixture was cooled, filtered and water (10 ml) was added to the filtrate. The filtrate was extracted with chloroform (3 x 10 ml), dried (sodium sulfate) and the solvent was evaporated. The residue was purified by preparative tlc on silica gel using chloroform-methanol (30:1) as eluent. The fast moving fraction (R_f =

0.75) was crystallized from petroleum ether to give 244 mg (21%) of compound **5**, mp 82-85°; uv (methanol): λmax 255 nm (log ε 3.41); ^{1}H nmr (deuteriochloroform): δ 6.91 (AB q, 2H, aromatic), 3.94 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.16 (t, 2H, CH_2) and 3.01 ppm (t, 2H, CH_2).

*Anal.*Calcd. for $C_{12}H_{12}N_2O_2Se$: C, 48.81; H, 4.07; N, 9.49. Found: C,48.98; H, 3.87; N, 9.28.

6,9-Dimethoxynaphtho[1,2-*d*][1,2,3]selenadiazole (**6**).

To a stirring solution of compound **5** (240 mg, 0.8 mmole) in dichloromethane, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (189 mg, 0.8 mmole) was added in one portion. After two hours the solvent was removed under reduced pressure. The residue was dissolved in methanol and purified by preparative tlc on silica gel using chloroform-methanol (9:1) as eluent. The fast moving fraction (R_f = 0.8) was crystallized from methanol to give 134 mg (55%) of compound **6**, mp 118-120°; uv (methanol): λmax (log ε), 255 (3.53), 308 nm (2.6); ^{1}H nmr (deuteriochloroform): δ 7.65 (AB q , 2H, aromatic), 7.1 (AB q, 2H, aromatic), 4.17 (s, 3H, OCH_3) and 4.05 (s, 3H, OCH_3).

Anal. Calcd. for $C_{12}H_{10}N_2O_2Se$: C, 49.15; H, 3.41; N, 9.56. Found: C, 48.96; H, 3.32; N, 9.37.

Bis-(4,8-dimethoxy-1-naphthyl)sulfoxide (**9**).

A mixture of compound **8** (188 mg, 1 mmole) and thionyl chloride (10 ml) was heated at 50° for 2 hours. Thionyl chloride was removed under reduced pressure. The residue was purified by preparative tlc on silica gel using chloroform-ethanol (16:1) as eluent. The desired compound (R_f = 0.4) was crystallized from ethanol to give 132 mg (63%) of compound **9**, mp 220-222°; uv (methanol): λmax (log ε) 244 (4.67), 319 (4.58), 332 nm (4.61); ir (potassium bromide): ν 1060 cm^{-1} (SO); ^{1}H nmr (deuteriochloroform): δ 3.68, 3.95 (12H, 2s, OCH_3), 6.79 (2H, d, J = 8 Hz, HC-7 and HC-7'), 6.88 (2H, d, J = 8 Hz, HC-3 and HC-3'), 7.39 (2H, t, J = 8 Hz, HC-6 and HC-6'), 7.74 (2H, d, J = 8 Hz, HC-5 and HC-5'), 7.90 (2H, d, J = 8 Hz, HC-2 and HC-2'); ^{13}C nmr (deuteriochloroform): δ 57.36 (C of OCH_3), 104.00 (C-7 and C-7'), 107.46 (C-3 and C-3'), 115.11 (C-5 and C-5'), 123.50 (C-1 and C-1'), 125.83 (C-6 and C-6'), 126.74 (C-2 and C-2'), 127.42 (C-4a, 4'a and C-8a, 8'a) 155.69 (C-8 and C-8'), 156.74 (C-4 and C-4'); ms: m/z (%) 422 (M^+, 14), 406 (14), 235 (14), 219 (56), 203 (100), 189 (30), 175 (36).

Anal. Calcd. for $C_{24}H_{22}O_5S$: C, 68.25; H, 5.21. Found: C, 68.06; H, 5.43.

Bis-(4,6-dimethoxy-1-naphthyl)disulfide (**11**).

A mixture of compound **10** (188 mg, 1 mmole) and thionyl chloride (10 ml) was heated at 50° for 2 hours. Thionyl chloride was removed under reduced pressure. The residue was purified by preparative tlc on silica gel using chloroform as eluent. The desired compound (R_f = 0.75) was crystallized from ether to give 116 mg (53%) of compound **11**, mp 161-162°; uv (methanol): λmax (log ε) 248 (4.98), 300 (4.52), 340 nm (4.46); ^{1}H nmr (deuteriochloroform): δ 3.95 (6H, s, OCH_3), 4.00 (6H, s, OCH_3), 6.64 (2H, d, J = 8 Hz, HC-3 and HC-3'), 7.10 (2H, d, J = 8 Hz, HC-2 and HC-2'), 7.18 (2H, dd, J = 8.8 and 2.8 Hz, HC-7 and HC-7'), 7.56 (2H, d, J = 2.8 Hz, HC-5 and HC-5'), 8.27 (2H, d, J = 8.8 Hz, HC-8 and HC-8'); ^{13}C nmr (deuteriochloroform): δ 55.18 (C of OCH_3), 55.30 (C of OCH_3), 100.60 (C-7 and C-7'), 104.53 (C-3 and C-3'), 119.40 (C-5 and C-5'), 123.57 (C-1 and C-1'), 126.73 (C-2 and C-2'), 127.16 (C-4a and C-4'a), 127.70 (C-8 and C-8'), 128.54 (C-8a and C-8'a), 154.22 (C-6 and C-6'), 157.48 (C-4 and C-4'); ms: m/z (%): 438 (M^+, 60), 425 (29), 406 (100), 391 (31), 188 (31).

Anal. Calcd. for $C_{24}H_{22}O_4S_2$: C, 65.75; H, 5.02. Found: C, 65.96; H, 5.23.

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