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Starting from the readily available 4-bromomethyl-5-benzoyl-1,2,3-thiadiazole and 5-bromomethyl-4-benzoyl-1,2,3-thiadiazole; thieno[3,4-*d*][1,2,3]thiadiazole, selenolo[3,4-*d*][1,2,3]-thiadiazole and pyrrolo[3,4-*d*][1,2,3]thiadiazole were synthesized in good yield.

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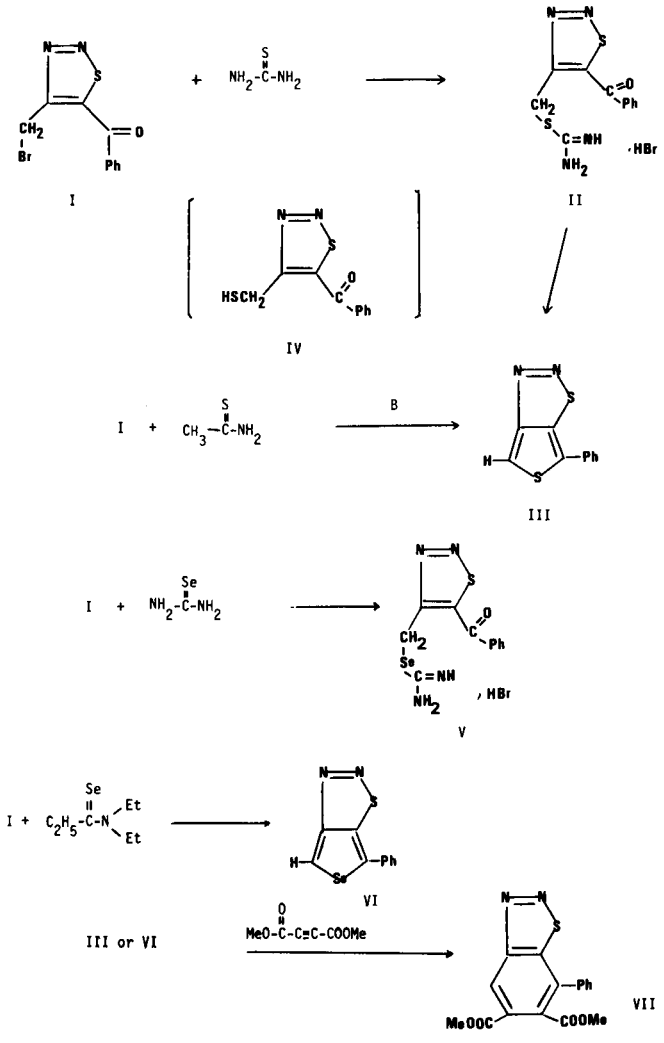
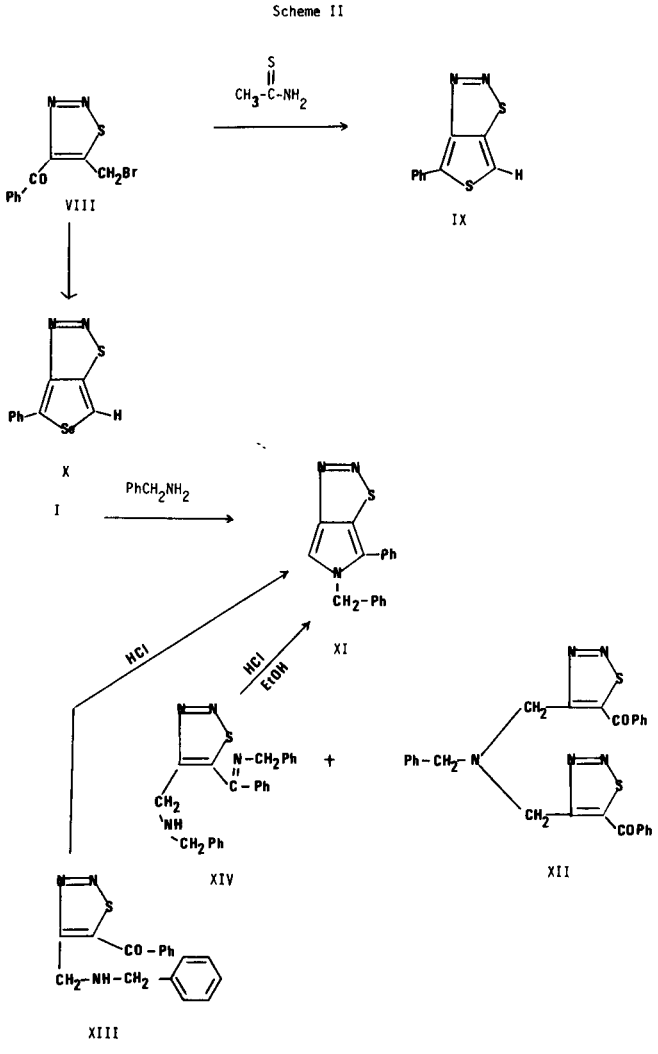
In continuation of the study on the chemistry of selenium heterocyclic compounds (2-5), and as a part of a program designed to expand the chemistry of 1,2,3-thiadiazole (6), the synthesis of the title compounds are reported.

The synthesis of 6-phenylthieno[3,4-*d*][1,2,3]thiadiazole (III) was achieved through the reaction of thiourea with 4-bromomethyl-5-benzoyl-1,2,3-thiadiazole (I) (6), and subsequent cyclization of the intermediate II with hydrochloric acid. The intermediate in the latter cyclization could be 4-mercaptomethyl-5-benzoyl-1,2,3-thiadiazole (IV); therefore, theoretically it seemed possible to obtain the desired compound III from the reaction of hydrogen sulfide with compound I. However, we could not obtain compound III through the reaction of hydrogen sulfide with I under different experimental conditions. Even, the reaction of sodium hydrogen sulfide or hydrogen sulfide with compound I failed to give III. Finally, compound III could be synthesized in high yield through the reaction of thioacetamide wiht compound I (See Scheme I).

Scheme I



Scheme II



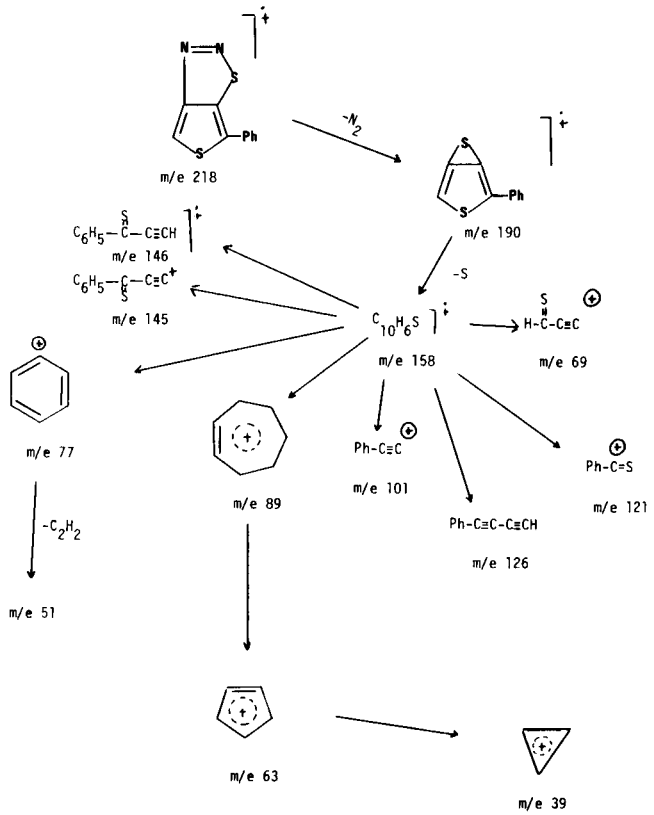
The selenium analog of II, namely V, could not be cyclized, since the compound decomposed under the experimental conditions and selenium was deposited. However, the desired compound, 6-phenyl-selenolo[3,4-*d*]-[1,2,3]thiadiazole (VI) could be obtained through the reaction of *N,N*-diethylselenopropionamide (7) with I (See Scheme I).

The reaction of compound III and VI with dimethyl acetylenedicarboxylate afforded dimethyl 7-phenylbenzothiadiazole-5,6-dicarboxylate (VII) in support of the structure III and VI.

4-Phenylthieno[3,4-*d*][1,2,3]thiadiazole (IX) and its selenium analog X could be prepared through the reaction of 5-bromomethyl-4-benzoyl-1,2,3-thiadiazole (VIII) (6) with thioacetamide or *N,N*-diethylselenopropionamide, respectively (See Scheme II).

The mass spectra fragmentation pattern of compound III is summarized in Scheme III is in good agreement with the suggested structure. A part of this fragmentation is similar to the one reported previously (8,9). The spectra of compounds VI, IX and X were also very similar to compound III (See Experimental).

Scheme III



The nmr spectrum of compound VI was also in agreement with the suggested structure. In the nmr spectrum of this compound the proton which is geminal to the selenium appears as a strong singlet and a weak doublet, centered around the singlet, this doublet is assigned to the splitting caused by the presence of the selenium isotiop ^{77}Se with a natural abundance of 7.5%. The selenium splitting constant was found to be 44 cps. This splitting was close to the one reported for selenophene (48 Hz) (10).

Finally, the reaction of benzylamine with I was also studied. The reaction of one mole of benzylamine with one mole of compound I gave 5-benzyl-6-phenylpyrrolo-[3,4-*d*][1,2,3]thiadiazole (XI) in low yield. In the latter reaction, in addition to small amount of starting material, compound XII was also isolated as the major product. The reaction of four moles of benzylamine with one mole of compound I gave in addition to XI and XIII compound XIV as a major product; both compounds XIII and XIV could be converted to XI in the presence of acid (See Scheme II).

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope and are uncorrected. Nmr spectra were determined using Varian T60A spectrometer and chemical shifts (δ) are in ppm relative to tetramethylsilane. Mass spectra were run on a Varian MAT MS-311 instrument at 70 eV.

Reaction of Thiourea with 4-Bromomethyl-5-benzoyl-1,2,3-thiadiazole (I).

A solution of I (283 mg., 1 mmole) and thiourea (76 mg., 1 mmole) in 20 ml. of ethanol was refluxed for five hours. After evaporation of the solvent the residue was crystallized from ethanol to give 323 mg. (90%) of compound II; m.p. 222-223°; ms: m/e (relative intensity): 237 [M^+-(NH_2-C=NH, HBr), 61], 236 (59), 76 (32), 59 (54), 58 (98) and 42 (100).

Anal. Calcd. for $C_{11}H_{11}BrN_4OS_2$: C, 36.77; H, 3.06; N, 15.60. Found: C, 36.91; H, 3.25; N, 15.45.

6-Phenylthieno[3,4-*d*][1,2,3]thiadiazole (III).

Method A.

A mixture of II (359 mg., 1 mmole) and 30 ml. of concentrated hydrochloric acid was refluxed for 48 hours. After cooling, the mixture was extracted with chloroform. The chloroform was dried, filtered and evaporated. The residue was crystallized from ethanol to give 131 mg. (60%) of III; m.p. 115-116°; nmr (deuteriochloroform): 7.96 (s, 1H, H_4) and 7.28 ppm (m, 5H, aromatic); ms: m/e (relative intensity): 218 (30), 191 (12), 190 (81), 158 (8), 146 (19), 145 (26), 126 (37) 121 (100), 114 (18), 95 (10), 69 (29), 63 (5), 43 (29), 39 (11).

Anal. Calcd. for $C_{10}H_6N_2S_2$: C, 55.04; H, 2.75; N, 12.84. Found: C, 55.19; H, 2.67; N, 12.71.

Method B.

A solution of I (283 mg., 1 mmole) (6) and thioacetamide (82.5 mg., 1.1 mmoles) in 10 ml. of ethanol was refluxed for 7 hours. The solvent was evaporated and the residue was crystallized from ethanol to give 201 mg. (92%) of III; m.p. 115-116°.

Reaction of Selenourea with 4-Bromomethyl-5-benzoyl-1,2,3-thiadiazole (I).

A solution of I (283 mg., 1 mmole) and selenourea (123 mg., 1 mmole) in 10 ml. of ethanol was refluxed for 5 hours. The solvent was evaporated and residue was crystallized from ethanol to give 325 mg. (80%) of V; m.p. 212-214°; ms: (relative

intensity): m/e 284 [M-(N≡C-NH_2, HBr), 5], 175 (9), 106 (8), 105 (100), 82 (15), 80 (15), 79 (6), and 77 (42).

Anal. Calcd. for $C_{11}H_{11}BrN_4OSSe$: C, 32.51; H, 2.71; N, 13.79. Found: C, 32.34; H, 2.60; N, 13.64.

6-Phenylselenolo[3,4-*d*][1,2,3]thiadiazole (VI).

A solution of I (283 mg., 1 mmole) and *N,N*-diethylselenopropionamide (211 mg., 1.1 mmoles) in 10 ml. of ethanol was refluxed for 4 hours. The solvent was evaporated and the residue was purified by tlc (silica gel, chloroform:methanol; 1:1) to give 252 mg. (95%) of VI; m.p. 105-106° (ethanol); nmr (deuteriochloroform): 8.83 (s, 1H, H_4), 7.73 ppm (m, 5H, phenyl), H_4 was split into a doublet with J = 44 Hz (^{77}Se coupling); ms: m/e (relative intensity): 266 (M^+, 13), 238 (23), 236 (12), 158 (44), 126 (100), 114 (6), 89 (13), 77 (5), 69 (6), 63 (7), and 51 (5).

Anal. Calcd. for $C_{10}H_6N_2SSe$: C, 45.28; H, 2.26; N, 10.57. Found: C, 45.39; H, 2.42; N, 10.73.

Dimethyl 7-Phenylbenzothiadiazole-5,6-dicarboxylate (VII).

A solution of III (218 mg., 1 mmole) and dimethyl acetylenedicarboxylate (142 mg., 1 mmole) in 10 ml. of toluene was refluxed for 24 hours. The solvent was evaporated and the residue was purified by tlc (silica gel, chloroform:methanol; 1:1) to give 65.6 mg. (20%) of VII; m.p. 65-67° (ether-petroleum ether); nmr (deuteriochloroform): 9.26 (s, 1H, H_4), 7.46 (s, 5H, phenyl), 4.0 (s, 3H, OCH_3) and 3.70 ppm (s, 3H, OCH_3); ms: m/e (relative intensity): 328 (M^+, 7), 297 (38), 270 (34), 269 (98), 268 (100), 253 (22), 237 (27), 210 (27), 183 (24), 182 (43), 139 (28), 138 (35) and 126 (21).

Anal. Calcd. for $C_{16}H_{12}N_2O_4S$: C, 58.54; H, 3.66; N, 8.54. Found: C, 58.63; H, 3.50; N, 8.39.

4-Phenylthieno[3,4-*d*][1,2,3]thiadiazole (IX).

This compound was prepared similar to its 6-phenyl analog (III, method B) in 90% yield; m.p. 108-110° (ethanol); nmr (deuteriochloroform): 8.38-8.15 (m, 2H, aromatic), 7.73-7.45 (m, 3H, aromatic), and 7.22 ppm (s, 1H, H_6); ms: m/e (relative intensity) 218 (M^+, 70), 190 (49), 147 (14), 146 (29), 145 (100), 127 (12), 126 (99), 121 (31), 114 (17), 101 (16), 93 (16), 89 (11), 77 (12), 75 (13), 69 (14), 63 (12), and 51 (19).

4-Phenylselenolo[3,4-*d*][1,2,3]thiadiazole (X).

This compound was prepared similar to its 6-phenyl analog (VI) in 50% yield; m.p. 119-120° (ethanol); nmr (deuteriochloroform): 8.33-8.05 (m, 2H, aromatic), 7.85 (s, 1H, H_6) and 7.70-7.37 ppm (m, 3H, aromatic); ms: m/e (relative intensity): 266 (M^+, 11), 238 (16), 236 (8), 158 (20), 145 (18), 127 (12), 126 (100), 114 (9), 101 (6) and 89 (9).

Anal. Calcd. for $C_{10}H_6N_2SSe$: C, 45.28; H, 2.26; N, 10.57. Found: C, 45.09; H, 2.12; N, 10.69.

Reaction of Benzylamine with 4-Bromomethyl-5-benzoyl-1,2,3-thiadiazole (I).

Method A.

A solution of I (283 mg., 1 mmole) and benzylamine (107 mg., 1 mmole) in 10 ml. of ethanol was refluxed for 2 hours. The solvent was evaporated and the residue was chromatographed (tlc, silica gel, chloroform:methanol; 1:1). The following compounds were isolated according to their increasing polarity. Compound XI (29 mg., 10%), m.p. 67-68° (ether-petroleum ether); nmr (deuteriochloroform): 7.75 (s, 1H, H_4), 7.55-7.16 (m, 10H, phenyl) and 5.50 ppm (s, 2H, CH_2); ms: (relative intensity): 291 (M^+, 5), 263 [(M^+-N_2), 10], 106 (24), 105 (44), 91 (100), 78 (10), 77 (47), 65 (21) and 51 (22).

Anal. Calcd. for $C_{17}H_{13}N_3S$: C, 70.10; H, 4.47; N, 14.43. Found: C, 70.25; H, 4.65; N, 14.61.

The second fraction was compound I (57 mg., 20%). The third fraction was compound XII; nmr (deuteriochloroform): 8.0-7.33 (m, 10H, phenyl), 7.11 (s, 5H, phenyl), 4.30 (s, 4H, CH_2) and 3.83 ppm (s, 2H, Ph-CH_2-N).

Anal. Calcd. for $C_{27}H_{21}N_5O_2S_2$: C, 63.40; H, 4.11; N, 13.70. Found: C, 63.59; H, 4.31; N, 13.52.

Method B.

A solution of I (283 mg., 1 mmole) and benzylamine (428 mg., 4 mmoles) in 10 ml. of ethanol was refluxed for 2 hours. The solvent was evaporated and the residue was chromatographed (tlc, silica gel, chloroform:methanol; 1:1). The following compounds were isolated according to their increasing polarity.

Compound XI (43 mg., 15%), m.p. 67-68° (ether-petroleum ether) was obtained.

Compound XIII was obtained as an oil, (46 mg., 15%); nmr (deuteriochloroform): 7.93-7.26 (m, 5H, C_6H_5CO), 7.23 (s, 5H, C_6H_5), 4.33 (s, 2H, CH_2), 3.76 (s, 2H, Ph-CH_2) and 2.33 ppm (broad s, 1H, NH), the latter was exchangeable by deuterium oxide.

Anal. Calcd. for $C_{17}H_{15}N_3OS$: C, 66.02; H, 4.85; N, 13.59. Found: C, 66.21; H, 4.98; N, 13.76.

Compound XIV was an oil (154 mg., 40%); nmr (deuteriochloroform): 8.0-7.10 (m, 15H, phenyl), 5.46 (s, 2H, Ph-CH_2-N=), 4.36 (s, 2H, CH_2), 3.80 (s, 2H, Ph-CH_2-NH) and 2.46 ppm (broad s, 1H, NH), the latter was exchangeable by deuterium oxide.

Anal. Calcd. for $C_{24}H_{22}N_4S$: C, 72.36; H, 5.53; N, 14.25. Found: C, 72.21; H, 5.34; N, 14.26.

Method C.

A solution of 1 mmole of I and 4 mmoles of benzylamine in 10 ml. of ethanol was refluxed for 2 hours. The reaction mixture was acidified with hydrochloric acid and refluxed for 15 minutes. The solvent was evaporated and the residue was purified by tlc giving XIV (185 mg., 60%). (See above).

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