Selenium Heterocycles. XLI [1]. Syntheses of Substituted Thiazolo, Selenazolo, 1,2,3-Thiadiazolo and 1,2,3-Selenadiazoloquinolines

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The reaction of thionyl chloride with the semicarbazone **2** gave 4,5-dihydro[1,2,3]thiadiazolo[4,5-*f*]quinoline. Selenium dioxide oxidaion of compound **2** gave 4,5-dihydro[1,2,3]selenadiazolo[4,5-*f*]quinoline (**4**) and the aromatic analog **5**. Thermolysis of compound **5** yielded [1,4]diselenino[2,3-*f*:5,6-*f'*]diquinoline (**6**). Reaction of selenourea with α-bromoketone **7** gave 2-amino-4,5-dihydroselenazolo[4,5-*f*]quinoline (**8**). Compounds **9** and **10** were prepared from the reaction of selenobenzamide and thiobenzamide with compound **7**.

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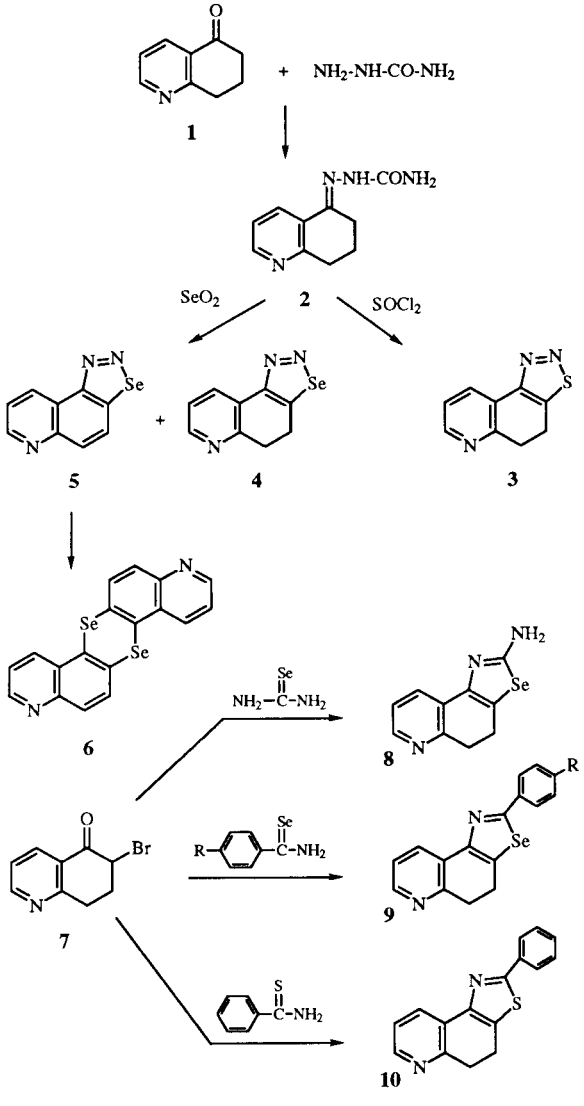
In view of the pentential biological activity of quinoline [2], 1,2,5-thiadiazole [3] and 1,2,3-selenadiazole [4], it was thought worthwhile to prepare the title compounds with the hope that these ring systems may prove to be biologically active.

Scheme 1



The title compounds were prepared according to Scheme 1.

The reaction of 7,8-dihydro-5(6*H*)quinolinone (**1**) [5] with semicarbazide hydrochloride afforded 7,8-dihydro-5-(6*H*)quinolinone semicarbazone (**2**). The reaction of compound **2** with thionyl chloride according to the method reported previously [6] gave 4,5-dihydro[1,2,3]thiadiazolo-[4,5-*f*]quinoline (**3**). Selenium dioxide oxidation of semicarbazone **2** gave in addition to the expected compound **4**, the oxidized compound **5**. The structure of compound **5** was confirmed by spectroscopic methods (nmr and ms) and chemical analysis (see Experimental). Heating of compound **5** at 210° for half an hour gave the dimer **6**.

The reaction of the α-bromoketone **7** with selenourea afforded 2-amino-4,5-dihydroselenazolo[4,5-*f*]quinoline (**8**).

2-Aryl-4,5-dihydroselenazolo[4,5-*f*]quinoline (**9**) was prepared from the reaction of compound **7** with substituted-selenobenzamide. Compound **10** was prepared similarly from the reaction of compound **7** with thiobenzamide.

The physical constants of compounds **8-10** are summarized in Table 1.

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

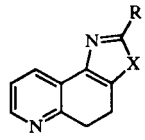
EXPERIMENTAL

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 spectrometer and chemical shifts (δ) are in ppm relative to internal tetramethylsilane. The mass spectra were run on a Varian Model MAT MS-311 spectrometer at 70 eV.

7,8-Dihydro-5(6*H*)-quinolinone Semicarbazone (**2**).

A solution of 7,8-dihydro-5(6*H*)-quinolinone (**1**) [5] (1.47 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

Table 1



Compound No.	R	X	Solvent for preparation	Mp, °C [a]	Yield	Formula	Calcd./Found C%		Calcd./Found H%		Calcd./Found N%	
8	NH_2	Se	water	205-207° [b]	36	$C_{10}H_9N_3Se$	48.00	48.18	3.60	3.48	16.80	16.95
9a	C_6H_5	Se	acetone	96-97°	23	$C_{16}H_{12}N_2Se$	61.74	61.86	3.86	3.93	9.00	8.91
9b	*p*-$CH_3C_6H_5$	Se	acetone	115-117°	24	$C_{17}H_{14}N_2Se$	62.77	62.61	4.31	4.45	8.62	8.49
10	C_6H_5	S	water	88-90°	23	$C_{16}H_{12}N_2S$	72.73	72.59	4.55	4.41	10.61	10.78

[a] Unless otherwise mentioned the compound was crystallized from ether-petroleum ether. [b] This compound was crystallized from chloroform.

stirred for 15 minutes. After cooling the mixture was made alkaline with 5% ammonia and the precipitate was filtered to give 1.94 g (95%) of 2, mp 225-228°; ms: m/z 204 (M^+).

Anal. Calcd. for $C_{10}H_{12}N_4O$: C, 58.82; H, 5.88; N, 27.45. Found: C, 58.71; H, 5.93; N, 27.56.

4,5-Dihydro[1,2,3]thiadiazolo[4,5-*f*]quinoline (**3**).

A mixture of compound **2** (204 mg, 1 mmole) and thionyl chloride (4 ml) was heated on a steam bath for half an hour. After cooling chloroform (10 ml) was added and the mixture was neutralized with 10% sodium carbonate solution. 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 the eluent. The desired compound was crystallized from petroleum ether to give compound **3** (85 mg, 45%), mp 76-77°; ^{1}H-nmr (deuteriochloroform): 8.55-8.4 (m, 2H, $H_{7,9}$), 7.40-7.20 (q, 1H, H_8) and 3.36 ppm (s, 4H, $H_{4,5}$); ms: m/z (%) 189 (M^+, 49), 161 [(M^+-N_2), 100], 160 (50), 117 (88), 116 (17), 90 (15), 89 (16) and 63 (12).

Anal. Calcd. for $C_9H_7N_3S$: C, 57.14; H, 3.70; N, 22.22. Found: C, 57.01; H, 3.60; N, 22.06.

Selenium Dioxide Oxidation of Compound **2**.

To a stirring mixture of compound **2** (204 mg, 1 mmole) in dioxane (4 ml) and water (8 drops) powder selenium dioxide (222 mg, 2 mmoles) was added. The mixture was refluxed in a hot water bath for 3 hours. The mixture was cooled and filtered. The solvent was evaporated and the residue was purified by preparative tlc on silica gel using chloroform-methanol (30:1) as eluent.

The fast moving fraction (R_f = 0.5) was crystallized from petroleum ether to give 1,2,3-selenadiazolo[4,5-*f*]quinoline (**5**, 26 mg, 11%), mp 123-124°; ^{1}H-nmr (deuteriochloroform): 9.45 (q, 1H, H_9, $J_{8,9}$ = 8.3 Hz, $J_{7,9}$ = 1.7 Hz), 9.09 (q, 1H, H_7, $J_{7,8}$ = 4.4 Hz), 8.36 (s, 2H, $H_{4,5}$) and 7.70 ppm (q, 1H, H_8, $J_{7,8}$ = 4.4 Hz, $J_{8,9}$ = 8.3 Hz); ms: m/z (%) 235 (M^+, 2), 207 [(M^+-N_2), 20], 127 (100), 117 (27), 75 (13) and 63 (11).

Anal. Calcd. for $C_9H_5N_3Se$: C, 46.15; H, 2.14; N, 17.95. Found: C, 46.23; H, 2.01; N, 17.79.

The slow moving fraction (R_f = 0.4) was crystallized from petroleum ether to give 4,5-dihydro-1,2,3-selenadiazolo[4,5-*f*]-quinoline (**4**) (47 mg, 20%), mp 82-83°; ^{1}H-nmr (deuteriochloroform): 8.55-8.40 (m, 2H, $H_{7,9}$), 7.40-7.20 (q, 1H, H_8) and 3.36 ppm (s, 4H, $H_{4,5}$); ms: m/z (%) 237 (M^+, 8), 209 [(M^+-N_2), 36]. 129 (100), 128 (29), 117 (20), 102 (21) and 63 (12).

Anal. Calcd. for $C_9H_7N_3Se$: C, 45.76; H, 2.97; N, 17.80. Found: C, 45.83; H, 3.01; N, 17.95.

[1,4]Diselinino[2,3-*f*:5,6-*f*']diquinoline (**6**).

Compound **5** (23.4 mg, 0.1 mmole) was heated at 210° for half an hour. The residue was purified by preparative tlc on silica gel using chloroform-methanol (30:1) as eluent to give 12.4 mg (60%) of **6**, mp 248-249° (ether-petroleum ether); ms: m/z (%) 414 (M^+, 100), 336 (40), 254 [(M^+-2Se), 32], 190 (19), 154 (12), 64 (26) and 45 (14).

Anal. Calcd. for $C_{18}H_{10}N_2Se_2$: C, 52.43; H, 2.43; N, 6.80. Found: C, 52.57; H, 2.61; N, 6.91.

2-Amino-4,5-dihydroselenazolo[4,5-*f*]quinoline (**8**).

A stirring solution of 6-bromo-7,8-dihydro-5(6*H*)-quinolinone hydrobromide (**7**, 307 mg, 1 mmole) and selenourea (246 mg, 2 mmoles) in water (10 ml) was refluxed for 45 minutes. After cooling, it was neutralized with 5% ammonia and extracted with chloroform. The solvent was concentrated and the crystals were filtered to give 100 mg (40%) of **8**, mp 205-207°; ir (potassium bromide): 3280 and 3110 (NH_2), 1640 (NH_2), 1550 and 1440 cm^{-1} (aromatic); ^{1}H-nmr (deuteriochloroform): 8.31 (q, 1H, H_7, $J_{7,9}$ = 1.6 Hz; $J_{7,8}$ = 4.9 Hz), 7.95 (q, 1H, H_9, $J_{8,9}$ = 7.7 Hz, $J_{7,9}$ = 1.6 Hz), 7.16 (q, 1H, H_8) and 3.14 ppm (m, 4H, $H_{4,5}$); ms: m/z (%) 251 (M^+, 82), 170 (100), 143 (13), 128 (37), 102 (12), 89 (10) and 63 (10).

Compounds **9** and **10** were prepared similarly. For the preparation of compound **9** the salt of compound **7** was neutralized with 5% ammonia before reaction (see Table 1).

REFERENCES AND NOTES

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