Condensed Heterocycles; Part XII. Synthesis of [1,2,5]Thiadiazolo[3,4-*c*]quinolines and [1,2,5]Selenadiazolo[3,4-*c*]quinolines

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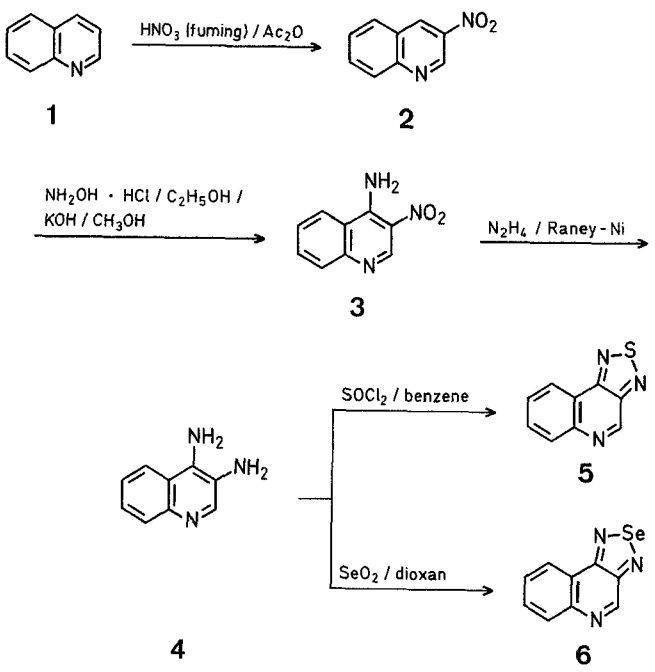
Quinoline[1], 1,2,5-thiadiazole[2], and 1,2,5-selenadiazole[3] moieties are associated with various kinds of biological activities. We have earlier reported the syntheses of [1,2,5]thia(selena)diazolo[3,4-*b*]- and [1,2,5]thia(selena)diazolo[3,4-*h*]quinolines[4]. In this communication, we describe the syntheses of [1,2,5]thia(selena)diazolo[3,4-*c*]quinolines.

Nitration of quinoline (**1**) with fuming nitric acid in acetic anhydride gives 3-nitroquinoline[5] in low yield (5.8%). Treatment of compound **2** with hydroxylamine hydrochloride in the presence of potassium hydroxide affords 4-amino-3-nitroquinoline[6] (**3**; 85%). Catalytic reduction of compound **3** using Raney nickel as catalyst and hydrazine hydrate as hydrogen donor and treatment of the resultant 3,4-diaminoquinoline (**4**) with thionyl chloride in dry benzene yields [1,2,5]thiadiazolo[3,4-*c*]quinoline (**5**; 26%). Analogous treatment of diamine **4** with selenium dioxide in dioxan yields [1,2,5]selenadiazolo[3,4-*c*]quinoline (**6**; 19%).



Thionyl chloride was purified by distillation from quinoline and a second distillation from linseed oil. The melting points are not corrected. I.R. spectra were recorded on a Beckman IR-20 spectrometer and the ^{1}H-N.M.R. spectra on a Perkin-Elmer R-32 90 MHz spectrometer.

3-Nitroquinoline (2):
Quinoline (**1**; 12.9 g, 0.01 mol) is nitrated with fuming nitric acid (12.6 g, 0.2 mol) in acetic anhydride (80 ml) according to Ref.[5]; yield: 1.0 g (5.8%); m.p. 127–128 °C (Ref.[5], m.p. 129–130 °C).

4-Amino-3-nitroquinoline (3):
3-Nitroquinoline[5] (**2**; 5.1 g, 0.03 mol) and hydroxylamine hydrochloride (6 g) are dissolved in hot 99% ethanol (90 ml). The solution is allowed to cool whilst being shaken so that the sparingly soluble 3-nitroquinoline separates in very small crystals. Then, methanolic 20% potassium hydroxide (30 ml) is added in one portion at room temperature. Potassium chloride separates out after brief shaking and 3-nitroquinoline dissolves imparting yellow coloration to the solution. The temperature rises by 20–30 °C and product **3** soon begins to separate as a crystalline mass. Luke warm water (200 ml) is added. The thus precipitated bright orange colored compound **3** is isolated by suction and dried; yield: 4.6 g (85%); m.p. 259–260 °C (Ref.[6], m.p. 260 °C).

I.R. (KBr): ν = 3420, 3340 (NH_2, stretching); 1620 (NH, bending); 1530, 1370 cm^{-1} (NO_2).

3,4-Diaminoquinoline (4):
To a boiling solution of 4-amino-3-nitroquinoline (**3**; 9.4 g, 0.05 mol) in ethanol (100 ml), Raney-Nickel (1.0 g out of a total of 2.5 g) and 98% hydrazine hydrate (3 ml out of a total of 7.5 ml) are added whereupon a vigorous reaction ensues. After the reaction has subsided another portion each of Raney nickel (0.5 g) and hydrazine hydrate (1.5 ml) is added. The procedure is repeated until the additions are complete and refluxing is continued until the yellow color has disappeared. The mixture is filtered hot and the solvent removed to give crude **4** as a dark brown residue (8.0 g) which is used as such for next step.

[1,2,5]Thiadiazolo[3,4-*c*]quinoline (5):
Purified thionyl chloride (5 ml) is gradually added to a stirred, cooled solution of 3,4-diaminoquinoline (**4**; 3.9 g, 0.025 mol) in benzene (100 ml). The mixture is then refluxed on a water bath for 10 h. Excess thionyl chloride and benzene are removed, water (100 ml) is added to the residue, and the solution is basified with aqueous ammonia. The organic material is extracted with chloroform (1 × 100 ml, 2 × 50 ml). The combined chloroform extracts are washed with water (2 × 100 ml) and dried with magnesium sulfate. The solvent is distilled off and the residual product column-chromatographed on silica gel using petroleum ether (60–80 °C)/benzene (1/1) as eluent. Removal of the solvent gives the colorless product **5**; yield: 1.2 g (26%); m.p. 118–119 °C.

$C_9H_5N_3S$	calc.	C 57.57	H 2.67	N 22.46
(187.2)	found	57.34	2.72	22.34

^{1}H-N.M.R. ($CDCl_3$/TMS_{int}): δ = 9.42 (s, 1H, 4-H); 8.62 (dd, 1H, 9-H); 8.18 (dd, 1H, 6-H); 7.72–7.80 ppm (sextet, 2H, 7-H and 8-H); $J_{8,9}$ = 9.0 Hz; $J_{7,9}$ = 2.5 Hz; $J_{6,7}$ = 9.0 Hz.

[1,2,5]Selenadiazolo[3,4-*c*]quinoline (6):
Selenium dioxide (11.0 g, 0.05 mol) is added to a solution of 3,4-diaminoquinoline (**4**; 7.9 g, 0.05 mol) in dioxan (100 ml) and the mixture is refluxed for 8 h. Thereafter it is poured into water (150 ml) and extracted with chloroform (3 × 100 ml). The combined chloroform extracts are washed with water (2 × 100 ml) and dried with magnesium sulfate. The solvent is removed and the residue column-chromatographed on silica gel using petroleum ether (60–80 °C)/benzene (1/1) as eluent. Removal of the solvent gives light yellow colored product **6**; yield: 2.2 g (19%); dec. 214–215 °C.

$C_9H_5N_3Se$	calc.	C 46.36	H 2.16	N 18.02
(234.1)	found	46.29	2.08	17.87

^{1}H-N.M.R. (DMSO-d_6/TMS_{int}): δ = 9.20 (s, 1H, 4-H); 8.47 (dd, 1H, 9-H); 7.95 (dd, 1H, 6-H); 7.65–7.70 ppm (sextet, 2H, 7-H and 8-H); $J_{8,9} = J_{6,7}$ = 9 Hz; $J_{7,9} = J_{6,8}$ = 2.5 Hz.

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