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NEW EXAMPLES OF THE USE OF SULFUR AND SELENIUM MONOCHLORIDES IN THE SYNTHESIS OF AZOLES

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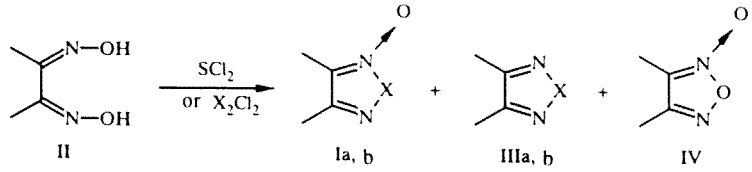
Sulfur and selenium monochlorides can be used in the synthesis of new heterocyclic systems: 1,2,5-thiadiazolo- and 1,2,5-selenodiazolo-[3,4-d]pyrimidine-5,7-(4H,7H)dione N-oxides and isothiazolo- and isoselenoazolo[4,3-e]-5,6-dihydro-4H-1,4-diazepines.

Although 1,2,5-oxadiazolo-N-oxides (furoxanes) have been known for a long time and have been studied extensively, the first report on the structure of 1,2,5-thiadiazole N-oxides (Ia) only appeared in 1970 [1]. 1,2,5-Thiadiazole N-oxides were obtained in low yield by the reaction of 1,2-diketone dioximes (II) wih an excess of sulfur dichloride in benzene or sulfur ıonochloride in DMF [2]; the main reaction products were the corresponding 1,2,5-thiadiazoles (IIIa) [1]:

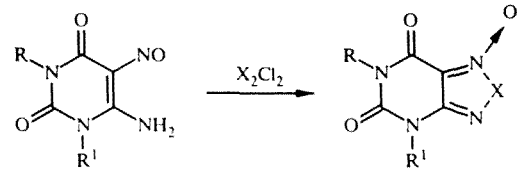


II Ia, b IIIa, b IV

a X = S, b X = Se

Among the products from the reaction of dioxime II with selenium monochloride [3, 4], apart from the N-oxide (Ib), were considerable amounts of the selenodiazole (IIIb) and the furoxane (IV). Unfortunately, there has been no further study of this interesting class of heterocycle.

We have found that 1,2,5-thiadiazole and 1,2,5-selenodiazole N-oxides can be obtained from heterocyclic *o*-nitrosoamines with the help of sulfur and selenium monochlorides. We have used as model compounds the 5-nitroso-6-aminouracils (Va-c), which are widely used in the Traube synthesis of purines [5-7]:



Va-c VIa-f

Va $R = R^1 = H$, b $R = H, R^1 = Me$, c $R = R^1 = Me$; VIa $R = R^1 = H, X = S$, b $R = R^1 = H, X = Se$, c $R = H, R^1 = Me, X = S$, d $R = H, R^1 = Me, X = Se$, e $R = R^1 = Me, X = S$, f $R = R^1 = Me, X = Se$

Treatment of Va-c with sulfur or selenium monochlorides in DMF at temperatures of 40-60°C gave the 1,2,5-thiadiazolo- or 1,2,5-selenodiazolo[3,4-*d*]pyrimidin-5,7-(4H,6H) dione N-oxides (VIa-f), which are high-melting (with decomposition) compounds which dissolve poorly in water or organic solvents. The most characteristic feature of the mass spectra of these compounds is that the molecular ion has the highest intensity. Other features are the loss of oxygen from the molecular

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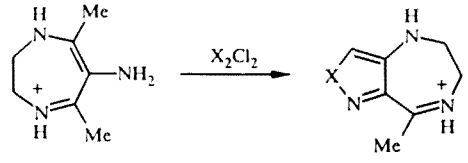
TABLE 1. Characteristics of the Compounds Synthesized

Compound	Molecular formula	Found, %			Calculated, %		
		C	H	N	C	H	N
VIa	$C_4H_2N_4O_3S$	25,70	1,10	30,18	25,81	1,08	30,11
VIб	$C_4H_2N_4O_3Se$	20,41	0,83	24,1	25,51	0,85	23,93
VIc	$C_5H_4N_4O_3S$	30,16	1,84	27,80	30,00	2,00	28,00
VId	$C_5H_4N_4O_3Se$	23,92	1,59	22,61	24,19	1,61	22,58
VIe	$C_6H_6N_4O_3S$	33,59	2,78	26,20	33,64	2,80	26,17
VIf	$C_6H_6N_4O_3Se$	27,42	2,34	21,35	27,48	2,29	21,37
VIIIa	$C_7H_9N_3S$	50,19	5,40	25,10	50,30	5,39	25,15
VIIIб	$C_7H_9N_3Se$	39,00	4,24	19,56	39,07	4,19	19,53

ion radical and the elimination of RNCO. The IR spectra show intense N–O stretching frequencies at 1260-1220 cm^{-1}. We have obtained 1,2-thiazoles and 1,2-selenodiazoles from 6-amino-2,3-dihydro-5,7-dimethyl-1,4-diazepin (VII) [8] using sulfur and selenium monochlorides:



VII VIIIa, b

VIII a X = S, b X = Se

Annelated isothiazoles and isoselenoazoles have been obtained previously by the reaction of aromatic or heteroaromatic *o*-methylanilines with N-sulfinylmethanesulfonamides [9, 11] or thionyl chloride and selenious acid in dioxane [12].

We also obtained compound VIIIa by treatment of VII with thionyl chloride in THF but no positive results were obtained when selenious acid was used in an attempt to make VIIIb. The mass spectra of compounds VIII a and b contain intense molecular ions. The ^1H NMR spectra are characterized by signals of the aromatic proton of the isothiazolo and isoselenoazolo rings at 7.90 and 8.20 ppm respectively, by multiplets of the ethylene fragment of the diazepin ring at 3.30 ppm (VIIIa) and 3.50 ppm (VIIIb), and by singlets of the exocyclic methyl groups at 1.90 ppm (VIIIa) and 2.40 ppm (VIIIb).

EXPERIMENTAL

Purity of the products was monitored by TLC on Silufol UV 254-vis strips. Mass spectra were recorded with a Varian MAT-112 with direct inlet and an ionizing energy of 70 eV. IR spectra of thin films in Nujol were recorded with a Specord-80 spectrometer, and ^1H NMR spectra of CF_3CO_2D solutions were recorded with a Tesla BS-497 (100 MHz) machine.

1,2,5-Thiadiazolo[3,4-*d*]pyrimidin-5,7-(4H,6H)dione N-oxides (VI: a — $C_4H_2N_4O_3S$; c — $C_5H_4N_4O_3S$; e — $C_6H_6N_4O_3S$). Sulfur monochloride (10 cm^3, 0.125 mole) was added with intense stirring to a solution of a 5-nitroso-6-aminouracil (0.1 mole) in dry DMF (50 cm^3) at such a rate that the precipitate did not exceed 60°C. The precipitate was filtered off and purified either by precipitation from basic solution with hydrochloric acid or by recrystallization from DMF to give VIa (7.9 g, 43%), mp > 300°C, M^+ 186, IR spectrum 3560-3000, 1720, 1650, 1610, 1520, 1260 cm^{-1}, or VIc (15 g, 75%), mp > 300°C, M^+ 200, IR spectrum 3140-3000, 1730, 1690, 1530, 1510, 1240 cm^{-1}, or VIe (10 g, 47%), mp > 300°C, M^+ 214, IR spectrum 1700, 1660, 1520, 1240 cm^{-1}.

1,2,5-Selenodiazolo[3,4-*d*]pyrimidin-5,7-(4H,6H)dione N-oxides (VI: b — $C_4H_2N_4O_3Se$; d — $C_5H_4N_4O_3Se$; f — $C_6H_6N_4O_3Se$). Selenium monochloride (10 cm^3, 0.125 mole) was added with intense stirring to a solution of a 5-nitroso-6-aminouracil (0.1 mole) in dry DMF (50 cm^3) at such a rate that the precipitate did not exceed 40°C. The precipitate was recrystallized from DMF to give VIb (8.6 g, 37%), mp >300°C, M^+ 234, IR spectrum 3550-3000, 1700, 1600, 1560, 1500, 1240 cm^{-1}, or VId (8.0 g, 32%), mp >300°C, M^+ 248, IR spectrum 3140-3000, 1710, 1680, 1510, 1230 cm^{-1}, or VIf (10 g, 38%), mp >300°C, M^+ 262, IR spectrum 1690, 1650, 1520, 1230 cm^{-1}.

8-Methylisothiazolo[4,3-*e*]-5,6-dihydro(4H)-1,4-diazepin Perchlorate (VIIIa, $C_7H_9N_3S \cdot HClO_4$). Sulfur monochloride (2 cm^3, 0.02 mole) was added to 6-amino-2,3-dihydro-5,7-dimethyl(1H)-1,4-diazepin (VIII) (2.39 g, 0.01 mole) in dry

DMF (50 cm^3). The mixture heated up spontaneously. The solvent was decanted from the oily product which was dissolved in hot ethanol. The solution was boiled with charcoal and filtered. The crystals which separated were recrystallized from 2:3 ethanol–acetone to give VIIIa (1.70 g, 64%), mp 270°C, M^+ 167 (for the free base). ^1H NMR spectrum: 1.9 (3H, s, CH_3), 3.0 (4H, m, C_2H_4), 7.9 ppm (1H, s, 3-H). IR spectrum: 3185-3100, 1730, 1700, 1670, 1600 and 1560 cm^{-1}.

8-Methylisoselenoazolo[4,3-*e*]-5,6-dihydro(4H)-1,4-diazepin perchlorate (VIIIb, $C_7H_9N_3Se \cdot HClO_4$) was prepared analogously to VIIIa (yield 34%), mp 275°C, M^+ 215 (for the free base). ^1H NMR spectrum: 2.4 (3H, s, CH_3), 3.5 (4H, m, C_2H_4), 8.2 (1H, s, 3-H). IR spectrum: 3230-3100, 1670, 1610, 1580, 1550 and 1510 cm^{-1}.

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