Russian Journal of General Chemistry, Vol. 75, No. 3, 2005, pp. 457–460. Translated from Zhurnal Obshchei Khimii, Vol. 75, No. 3, 2005, pp. 493–496.

Synthesis of 1,2,5-Oxa-, -Thia-, and -Selenadiazole *N*-Oxides from Nitroso- and Isonitrosopyrimidines

A. A. Yavolovskii, V. D. Kishichenko, O. A. Oliinichenko, and E. I. Ivanov

Bogatskii Physicochemical Institute, National Academy of Sciences of Ukraine, Odessa, Ukraine

Received September 30, 2003

Abstract—The possibility of preparing 1,2,5-oxa-, -thia-, and -selenadiazole *N*-oxides from polyfunctional nitroso- and isonitrosopyrimidines and -pyridine was examined.

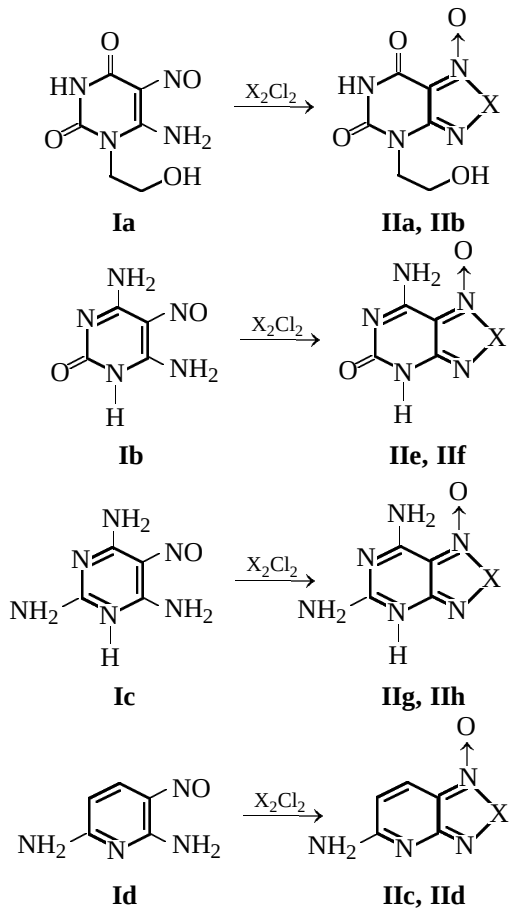
We found previously that the reactions of 6-amino-5-nitrosouracils with sulfur or selenium monochloride yield 1,2,5-chalcogenadiazolo[3,4-*d*]pyrimidines [1, 2]. In this study we examined the applicability of this reaction to *o*-amino nitroso compounds containing additional reaction centers such as hydroxy and amino groups. As starting compounds we used 5-nitroso derivatives of 1-hydroxyethyl-6-aminouracil (**Ia**) [3], 4,6-diamino-1,2-dihydropyrimidin-2-one (**Ib**) [4], and 2,4,6-triaminopyrimidine (**Ic**) [4], and also 3-nitroso-2,6-diaminopyridine **Id** [5]. Treatment of **Ia**–**Id** with sulfur or selenium monochloride under the conditions similar to those described in [1] resulted in formation of 1,2,5-chalcogenadiazole *N*-oxides **IIa**–**IIh** in good yields (Scheme 1).

The reactive functional groups present in the starting amino nitroso compounds, at equimolar ratio of the reactants, exert no appreciable effect on the course of cyclization with the formation of 1,2,5-thiadiazole *N*-oxides and their selenium analogs.

An alternative route to 1,2,5-oxa-, -thia-, and selenadiazoles, based on transformations of aliphatic and aromatic 1,2-dioximes [6–8], is limited by difficult availability of heterocyclic 1,2-dioximes.

With 6-amino-5-nitrosouracil **Ie** as example, we showed that the amino group in an acidic medium is readily replaced by hydroxylamine; the reaction product isomerizes into uracil 5,6-dioxime **IIIa** existing, according to single crystal X-ray diffraction data, in the form of the (4*Z*,5*E*) isomer [9]. The reactions between **Ib**–**Id** and excess hydroxylamine taken as a mixture of acetate and hydrochloride resulted in replacement of all the amino groups with the formation of tri- and tetraoxime derivatives of pyrimidine (**IIIb**, **IIIc**) and pyridine (**IIId**) (Scheme 2). The reactivity is apparently influenced by the steric factors: 1-Substituted 6-amino-5-nitrosouracils do not react with hydroxylamine under the similar conditions.

Scheme 1.

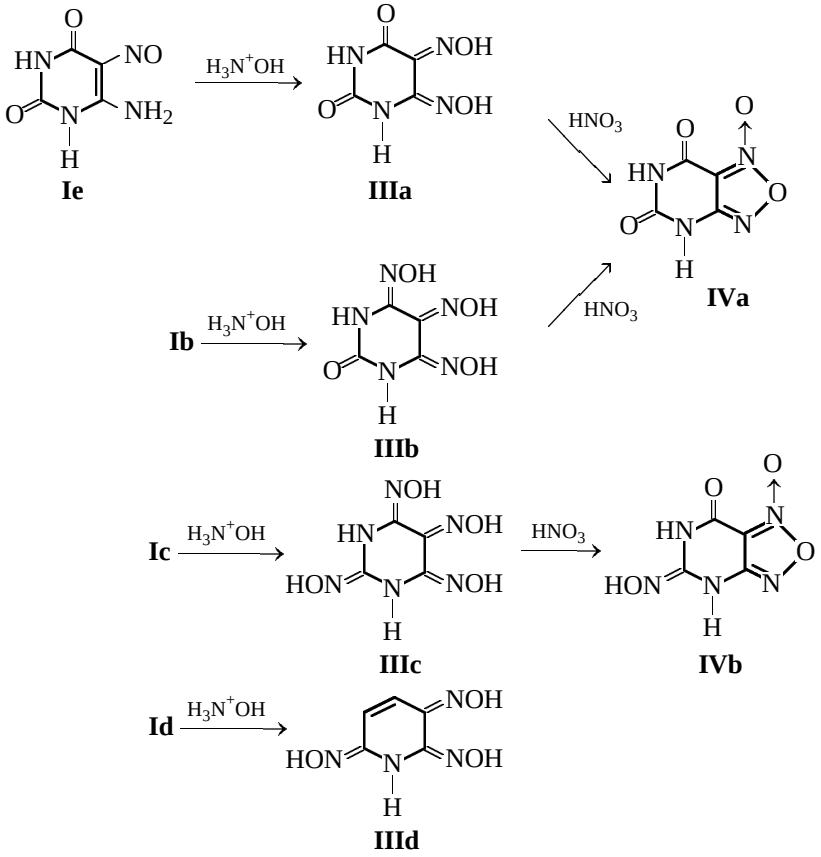


X = S (**IIa, IIc, IIe, IIg**), Se (**IIb, IId, IIf, IIh**).

Pyrimidine oximes **IIIa**–**IIIc** are oxidized with nitric acid to furoxanes **IVa** and **IVb**; in the case of **IIIb** and **IIIc**, the reaction is accompanied by the hydrolysis of the oxime group in the 4-position of the starting pyrimidine.

1070-3632/05/7503-0457

Scheme 2.



The compositions and structures of the products were determined by elemental analysis, mass spectrometry, and IR spectroscopy (Tables 1, 2).

In contrast to pyridine 2,3,6-trioxime **IIId** whose mass spectrum contains a strong molecular peak, in the mass spectra of **IIIa**–**IIIc** the molecular peaks are lacking, which is apparently due to low volatility of these compounds and their tendency to dehydration. The mass spectra of *N*-oxides **IIa**–**IIh**, **IVa**, and **IVb** contain strong and moderately intense peaks of molec-

Table 1. Properties of **IIa**–**IIh, IIIb**–**IIId**, and **IVb**

Comp. no.	Yield, %	mp, °C	Found, %			Formula	Calculated, %		
			C	H	N		C	H	N
IIa	75	250	31.30	2.60	24.35	$C_6H_6N_4O_4S$	31.30	2.61	24.35
IIb	65	>280 (decomp.)	25.90	2.20	20.15	$C_6H_6N_4O_4Se$	25.90	2.16	20.14
IIc	80	220	35.70	2.40	33.30	$C_5H_4N_4OS$	35.71	2.38	33.33
IId	75	260–280	32.40	1.85	25.90	$C_5H_4N_4OSe$	32.41	1.85	25.93
IIe	65	>300 (decomp.)	25.95	1.60	37.85	$C_4H_3N_5O_2Se$	25.95	1.62	37.84
IIf	60	>300 (decomp.)	20.60	1.30	30.00	$C_4H_4N_6OS$	20.60	1.29	30.04
IIg	85	>300 (decomp.)	26.10	2.20	45.60	$C_4H_4N_6OSe$	26.09	2.17	45.65
IIh	80	>340 (decomp.)	20.70	1.70	36.20	$C_4H_5N_5O_4$	20.69	1.72	36.21
IIIb	70	>260 (decomp.)	25.70	2.70	37.40	$C_4H_6N_6O_4$	25.67	2.67	37.43
IIIc	82	>260 (decomp.)	23.81	3.50	41.55	$C_4H_6N_6O_4$	23.76	2.97	41.58
IIId	85	270	35.30	2.95	32.90	$C_4H_6N_4O_3$	35.29	3.53	32.94
IVb	60	230–260	25.90	1.60	37.85	$C_4H_3N_5O_4$	25.95	1.62	37.84

Table 2. Spectral characteristics of **IIa**–**IIh, IIIb**–**IIId**, and **IVb**

Comp. no.	Mass spectrum, *m/z* (I_{rel}, %)	IR spectrum, ν, cm^{-1}
IIa	230 (21), 214 (3), 200 (4), 187 (100), 171 (43), 156 (25), 140 (44)	3400–3000, 1720, 1690, 1680, 1640, 1610, 1550–1480
IIb	278 (10), 262 (3), 240 (2), 235 (84), 219 (26), 204 (18) 188 (18), 170 (13), 157 (100)	3400–3050, 1710, 1680, 1610, 1540–1490
IIc	168 (38), 152 (13), 138 (100), 108 (25), 90 (26), 79 (32)	3200–3000, 1670, 1650, 1610, 1590, 1570, 1560, 1540, 1520
IId	216 (32), 200 (10), 138 (27), 122 (46), 104 (7), 93 (9), 79 (100)	3320–3010, 1680, 1630, 1580, 1550, 1500
IIe	185 (100), 169 (72), 155 (7), 141 (12), 126 (22), 109 (14), 105 (8)	3400–3000, 1720, 1690, 1650, 1630–1500
IIf	233 (6), 217 (14), 201 (28), 157 (22), 155 (25), 153 (6) 105 (6)	3350–3000, 1700, 1680, 1650, 1640, 1600–1500
IIg	184 (48), 168 (16), 154 (57), 136 (8), 96 (15), 82 (18), 68 (23)	3350–3050, 1650, 1610, 1550, 1540–1500
IIh	232 (24), 216 (5), 154 (47), 138 (36), 95 (24), 82 (27), 68 (33)	3400–3050, 1650, 1610, 1550–1500
IIIb	169 (84) $[M - H_2O]^+$, 154 (100), 152 (12), 139 (35), 111 (26)	3530–3100, 1710, 1700, 1680, 1650, 1630, 1600–1500
IIIc	184 (22) $[M - H_2O]^+$, 168 (19), 154 (12), 152 (14), 138 (20), 122 (26)	3400–3100, 1630, 1620, 1600, 1580, 1560, 1550
IIId	170 (55), 152 (42), 140 (8), 122 (32), 106 (13), 95 (34), 93 (16), 79 (57), 64 (31), 52 (100)	3360–3050, 1640, 1620, 1600, 1580, 1570, 1540
IVb	185 (11), 169 (19), 155 (6), 154 (10), 153 (14), 138 (12), 123 (29), 82 (12), 69 (18), 53 (41)	3600–3000, 1710, 1660, 1650, 1640, 1610, 1600–1550

ular ions; these ions show consistent fragmentation pattern [1, 10, 11].

EXPERIMENTAL

The mass spectra were recorded on a Varian MAT-112 device at the ionizing electron energy of 70 eV and ion source temperature of 220°C. The IR spectra were taken on a Specord-80 spectrometer (mulls in mineral oil). The purity of the substances was checked by TLC on Silufol UV-254 plates.

4-(2-Hydroxyethyl)-4,5,6,7-tetrahydro[1,2,5]thiadiazolo[3,4-*d*]pyrimidine-5,7-dione N^1-oxide IIa. A 0.2-ml portion of sulfur monochloride was added with cooling and vigorous stirring to a suspension of 0.4 g of **Ia** in anhydrous DMF. The mixture was diluted with anhydrous chloroform until the reaction product fully precipitated. The product was recrystallized from water avoiding prolonged heating. Yield 0.35 g.

5-Amino[1,2,5]thiadiazolo[3,4-*b*]pyridine N^1-oxide IIc. A suspension of 0.3 g of **Id** in anhydrous DMF was cooled on an ice bath, and 0.2 ml of sulfur monochloride was carefully added. The precipitate was immediately filtered off, washed with anhydrous chloroform, and recrystallized from water. Yield 0.3 g.

7-Amino-4,5-dihydro[1,2,5]thiadiazolo[3,4-*d*]pyrimidin-5-one N^1-oxide IIe. A 0.2-ml portion of sulfur monochloride was added with vigorous stirring to a suspension of 0.3 g of **Ib** in anhydrous DMF. The precipitate was filtered off, washed with anhydrous chloroform, and dried in air. Then the product was dissolved in a minimal amount of hot water, and the solution was filtered. A saturated sodium acetate solution was added to the filtrate until a precipitate formed, which was filtered off and dried in air. Yield 0.23 g.

5,7-Amino[1,2,5]thiadiazolo[3,4-*d*]pyrimidine N^1-oxide IIg. A 0.2-ml portion of sulfur monochloride was added with vigorous stirring and cooling to a suspension of 0.3 g of **Ic** in anhydrous DMF. The precipitate was filtered off, washed with anhydrous chloroform, and dried in air, after which it was dissolved

in hot water, and the solution was neutralized with a saturated sodium carbonate solution. The precipitate that formed upon neutralization was filtered off, washed with a small amount of cold water, and dried in air. Yield of **IIg** 0.3 g.

Selena derivatives **IIb**, **IId**, **IIf**, **IIh** were prepared similarly.

4,5,6-Tris(hydroximino)hexahydropyrimidin-2-one IIIb. A mixture of 1.0 g of **Ib**, 7.0 g of hydroxylamine hydrochloride, and 4.0 g of sodium acetate in 25 ml of water was heated with stirring at 65–70°C until the mixture decolorized. The precipitate was filtered off, washed with cold water and alcohol, and dried in air. Yield 0.85 g.

2,4,5,6-Tetrakis(hydroximino)hexahydropyrimidine IIIc. To 1.5 g of **Ic** in 50 ml of water we added 6.3 g of hydroxylamine hydrochloride and 3.3 g of sodium acetate. On heating to 60°C, the starting compound dissolved to form a yellow solution, from which the product gradually precipitated. After cooling, the precipitate was filtered off, washed with water and alcohol, and dried in air. Yield 1.6 g.

2,3,6-Tris(hydroximino)-1,2,3,6-tetrahydropyridine IIId. To 1.4 g of **Id** in 50 ml of water we added 4.2 g of hydroxylamine hydrochloride and 2.5 g of sodium acetate. The mixture was heated to 60°C. The red solution became yellow, and a precipitate formed, which was filtered off after cooling, washed with water and alcohol, and dried in air. Yield 1.47 g.

5-Hydroximino-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*d*]pyrimidin-7-one N^1-oxide IVb. A 2.0-g portion of **IIIc** was carefully dissolved in 10 ml of nitric acid and 1 ml of sulfuric acid on heating to 40°C. Then the mixture was cooled and neutralized with aqueous ammonia. The precipitate was filtered off and recrystallized from aqueous alcohol. Yield 0.9 g.

4,5,6,7-Tetrahydro[1,2,5]oxadiazolo[3,4-*d*]pyrimidine-5,7-dione N^1-oxide IVa was prepared similarly from **IIa** and **IIIb**. The product is identical to that described in [10, 11].

REFERENCES

1. Yavolovskii, A.A., Kuklenko, E.A., and Ivanov, E.I., *Khim. Geterotsikl. Soedin.*, 1996, no. 7, p. 997.
2. Yavolovskii, A.A., Timofeev, O.S., and Ivanov, E.I., *Khim. Geterotsikl. Soedin.*, 1998, no. 8, p. 1130.
3. Krutovskikh, G.N., Rusanov, A.M., Gornaeva, G.F., Vartanyan, L.P., Kolesova, M.B., Muravin-Aleksandr, Kh.L., Smirnova, N.V., and Cherkazova, S.S., *Khim.-Farm. Zh.*, 1977, vol. 11, no. 2, p. 82.
4. Taylor, E.C., Vogl, O., and Cheng, C.C., *J. Am. Chem. Soc.*, 1959, vol. 81, no. 10, p. 2442.
5. Chichibabin, A.E. and Zeide, O.A., *Zh. Russk. Fiz.-Khim. O–va.*, 1920, vol. 50, p. 522.
6. Smith, L.J., *Chem. Rev.*, 1938, vol. 23, p. 193.
7. Pilgram, K., *J. Org. Chem.*, 1970, vol. 35, no. 4, p. 1165.
8. Pedersen, C.L., *Acta Chem. Scand.*, 1976, vol. 30, no. 7, p. 675.
9. Simonov, Yu.A., Fonari, M.S., Lipkowski, J., Yavolovskii, A.A., and Ganin, E.V., *J. Inclus. Phenom. Macrocyclic Chem.*, 2003, vol. 46, nos. 1–2, p. 27.
10. Temple, C., Kussner, C.L., and Montgomery, J.A., *J. Org. Chem.*, 1968, vol. 33, no. 5, p. 2086.
11. Sako, M., Oda, S., Ohara, S., Hirota, K., and Maki, I., *J. Org. Chem.*, 1998, vol. 63, no. 20, p. 6947.