FORMATION OF FUROXANS AND 1,2-DIAZETINE 1,2-DIOXIDES BY OXIDATION OF α-HYDROXYLAMINO OXIMES

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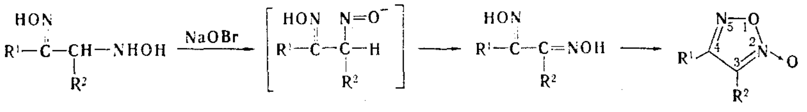
The oxidation of secondary and tertiary α-hydroxylamino oximes with sodium hypobromite gives, respectively, furoxans and 3-bromo-1,2-diazetine 1,2-dioxides. The intermediate oxidation products, which confirm the proposed reaction mechanism, were isolated. When 3-bromo-1,2-diazetine 1,2-dioxides are heated in benzene, the ring opens with the evolution of nitrogen oxides and the formation of halo olefins.

It has been shown that α-hydroxylamino oximes have a number of peculiarities associated with the vicinal orientation of two reactive groups, and this leads to their ability to form different compounds with the two nitrogen atoms in the ring [1]. This ability is also manifested in oxidation reactions of α-hydroxylamino oximes, and the structures of the resulting products depend substantially on the nature of the starting α-hydroxylamino oximes.

Furoxans II are formed in high yields in the oxidation of secondary α-hydroxylamino oximes (I) with sodium hypobromite. As in the case of α-diketone dioximes [2, 3], the configuration of the oxime group does not affect the structure of furoxan II.



I a-c III IV a II a-c

a $R^1=C_6H_5$, $R^2=CH_3$; b $R^1+R^2=(CH_2)_4$; c $R^1+R^2=(CH_2)_5$

The reaction apparently commences with oxidation of the hydroxylamino group to give nitroso oxime III, which is isomerized to dioxime IV, the subsequent oxidation of which gives furoxans II [2, 4]. Indicative of the probability of this sort of reaction is the fact that methylphenylglyoxime (IVa) is formed in 93% yield when an alkaline solution of α-hydroxylamino oxime Ia is allowed to stand in air for 6 days [2].

The oxidation of tertiary α-hydroxylamino oximes with sodium hypobromite gives different results [5]. Thus colorless crystalline compounds of the composition $C_{10}H_{11}BrN_2O_2$ (VIa) and $C_5H_9BrN_2O_2$ (VIb) are formed in 80 and 50% yields, respectively, when aqueous alkali solutions of N-(1-oximino-1-phenyl-2-methyl-2-propyl)- and N-(3-oximino-2-methyl-2-butyl)hydroxylamines (Va, b) are treated with excess sodium hypobromite. The action of hydrazine hydrate on VIa, b does not lead to halogen removal, and this indicates the absence of an N—Br bond. Compounds VIa, b have similar UV spectra with λ_{max} 270-273 nm (log ε 3.9), and this constitutes evidence that the benzene ring does not participate in conjugation in the case of VIa and indicates the presence in VIa, b of an identical chromophore system similar to the chromophore system of cis-dimeric nitroso compounds with λ_{max} 270 nm (log ε 4.0) [6]. The IR spectra of VIa, b contain a characteristic intense double band at 1450-1480 cm^{-1} and an intense band at 1560 cm^{-1}, which can be assigned to the stretching vibrations of the N—O group [7]. In addition to signals of the substituent in

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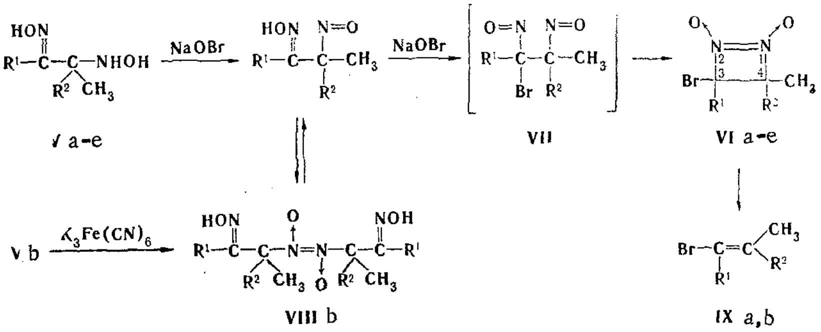
the 3 position, signals of two nonequivalent methyl groups are observed in the PMR spectra of VIa, b (Table 1). These data enabled us to assign 3-bromo-3-phenyl- (VIa) and 3-bromo-3-methyl-4,4-dimethyl-1,2-diazetine 1,2-dioxide (VIb) structures to the compounds obtained. The spectral characteristics of VIa, b are close to the spectral characteristics of the recently described 3,3,4,4-tetramethyl-1,2-diazetine 1,2-dioxide [7, 8]. 3-Bromo-1,2-diazetine 1,2-dioxides (VIc-e) were similarly obtained. Thus, it was shown that the formation of 1,2-diazetine 1,2-dioxides VI from tertiary α-hydroxylamino oximes is a quite general reaction.

The formation of 3-bromo-1,2-diazetine 1,2-dioxides from tertiary α-hydroxylamino oximes V can be represented by a scheme in which the reaction commences with oxidation of the hydroxylamino group to a nitroso group with subsequent action of halogen on the ketoxime group to give vicinal dinitroso compound VII. Vicinal dinitroso compounds are postulated during the formation or isomerization of benzofuroxans [6], for example, in the pyrolytic isomerization of unsymmetrical furoxan IIa to its isomer [2, 6]. However in our case the possibility of the formation of a furoxan ring from dinitroso derivative VII is not realized, and as in the dimerization of nitroso compounds, the intramolecular reaction of the vicinal nitroso groups gives 3-bromo-1,2-diazetine 1,2-dioxides (VI) (see [6]).



V, VI, IX a $R^1=C_6H_5$, $R^2=CH_3$; V, VI, VIII, IX b $R^1=R^2=CH_3$; V, VI c $R^1=C_2H_5$, $R^2=CH_3$; d $R^1+R^2=(CH_2)_4$; e $R^1+R^2=(CH_2)_3$

A confirmation of this reaction mechanism is the fact that when α-hydroxylamino oxime Vb was treated with an equimolecular amount of sodium hypobromite, dimeric 2-nitroso-3-oximino-2-methylbutane (VIIIb) was isolated from the reaction mixture along with 1,2-diazetine 1,2-dioxide VIb. Dimer VIIIb is formed in 54% yield in the oxidation of α-hydroxylamino oxime Vb with potassium ferricyanide. An absorption band is observed at 293 nm (log ε 3.95) in the UV spectrum of VIIIb, and an intense band at 1285 cm^{-1} is observed in its IR spectrum; this is characteristic for trans-dimeric nitroso compounds [6]. Dimer VIIIb is only slightly soluble in water, alcohols, and organic solvents, and when it is heated in them it gives a characteristic blue coloration of the monomeric nitroso compound [6]. Treatment of nitroso oxime VIIIb with sodium hypobromite gives 3-bromo-1,2-diazetine 1,2-dioxide (VIb).

The 3-bromo-1,2-diazetine 1,2-dioxides (VIa-e) are stable compounds and can be stored for a long time without decomposition. They are resistant to heating in acetic and hydrochloric acids. However, when VIa, b are refluxed in benzene, nitrogen oxides are evolved and 1-bromo-1-phenyl-2-methylpropene (IXa) and 2-bromo-3-methyl-2-butene (IXb) [9, 10], respectively, are formed. Two signals of gemiral methyl groups at 1.71 and 2.02 ppm and a signal of five aromatic hydrogen atoms at 7.22 ppm are observed in the PMR spectrum of IXa. The results of elementary analysis and the IR and UV spectra are in agreement with α-bromostyrene structure IXa. It should be noted that the desctruction of the ring of 1,2-diazetine 1,2-dioxide in benzene is complete in 30-40 min, whereas refluxing for 4-5 h is required for this in chloroform or alcohol.

EXPERIMENTAL METHOD

The IR spectra of KBr pellets of the compounds (0.25% concentration) and CCl_4 solutions (5%) were recorded with a UR-20 spectrometer. The UV spectra of alcohol solutions were recorded with a Specord spectrophotometer. The PMR spectra of 5-7% solutions in $CDCl_3$ were recorded with Varian A-56-60A and Varian HA-100 spectrometers with hexamethyldisiloxane as the internal standard.

TABLE 1. Data from the PMR Spectra of 3-Bromo-1,2-diazetine 1,2-Dioxides

Compound	δ, ppm		
	CH_3	R^2	R^1
VIa	1,24	1,98	7,53
VIb	1,69	1,74	2,27
VIc	1,70	1,81	CH_3 1,26 tr. (J=7,5 Hz) CH_AH_B 2,27 and 2,52 (J=15Hz)[a]
VId	1,79	1,5—2,8[b]	
VIe	1,77	1,5—3,1[b]	

a) The assignment of the chemical shifts and the constants were obtained from an analysis of the spectra by the double-magnetic-resonance method. b) Superimposition of the signals of alicyclic protons.

N-(3-Oximino-2-methyl-2-pentyl)- (Vc), N-(1-oximino-2-methyl-2-cyclohexyl)- (Vd), and N-(1-oximino-2-methyl-2-cyclopentyl)hydroxylamines (Ve) were obtained from dimeric olefin nitrosochlorides by the methods in [11, 12].

3-Methyl-4-phenylfuroxan (IIa). An alkaline solution of 0.54 g (3 mmole) of anti- or syn-N-(1-oximino-1-phenyl-2-propyl)hydroxyamine (Ia) [13] was added carefully dropwise with stirring to a cooled (to −5 to 0°) solution of 1.45 g (9 mmole) of bromine in 7 ml of 10% sodium hydroxide solution, and the resulting precipitate was removed by filtration and washed with water and petroleum ether to give 0.39 g (74%) of a product with mp 94-95° (mp 95.2-95.8° [2]). The IR spectrum of the product was identical to the IR spectrum presented in [14].

Tetramethylenefuroxan (IIb). Oxidation of N-(1-oximino-2-cyclohexyl)hydroxylamine (Ib) [11] under the above-indicated conditions gave an oily product, which was extracted with chloroform. The extract was dried with magnesium sulfate, the solvent was evaporated, the residue was treated with petroleum ether, and the solid was removed by filtration to give a product with mp 43-44° (mp 43-45° [14]) in 82% yield. UV spectrum: λ_{max} 263 nm (log ε 3.84).

Pentamethylenefuroxan (IIc). This compound was obtained by the method in the preceding experiment from N-(1-oximino-2-cycloheptyl)hydroxylamine (Ic) [11]. The resulting oil was purified by chromatography on silica gel with elution by ether—petroleum ether (1:10). UV spectrum: λ_{max} 259 nm (log ε 3.82). IR spectrum, ν, cm^{-1}: 1615, 1445-1475 (doublet), 1110, and 1010.

Methylphenylglyoxime (IV). A solution of 1.5 g (8 mmole) of Ia in 15 ml of 10% sodium hydroxide solution was allowed to stand with access to air oxygen for 6 days at room temperature, after which it was neutralized with 5% hydrochloric acid, and the resulting precipitate was removed by filtration to give 1.37 g (93%) of a product with mp 236-237° (from alcohol) (mp 237.5-238.2° [2]).

3-Bromo-3-phenyl-4,4-dimethyl-1,2-diazetine 1,2-Dioxide (VIa). This compound was formed from N-(1-oximino-1-phenyl-2-methyl-2-propyl)hydroxylamine (Va) [13] under the conditions used to synthesize IIa.

3-Bromo-1,2-diazetine 1,2-Dioxides (VIb-e). An aqueous solution of 5 mmole of the appropriate tertiary α-hydroxylamino oxime (Vb-e) was added carefully dropwise with stirring to a cooled (to −5 to 0°) solution of 3.2 g (20 mmole) of bromine in 18 ml of 10% sodium hydroxide, and the resulting precipitate was removed by filtration and washed with water and petroleum ether. Compound VIe was isolated by chromatography of the reaction mixture on silica gel with elution with ether—petroleum ether (1:2). Data on the compounds obtained are presented in Table 2.

Dimeric 2-Nitroso-3-oximino-2-methylbutane (VIIIb). A solution of 1.32 g (10 mmole) of Vb in 8 ml of 5% sodium hydroxide solution was added dropwise with stirring at 0° to an aqueous solution of 4.78 g (20 mmole) of potassium ferricyanide, after which the mixture was allowed to stand for 15 min. It was neutralized with 10% hydrochloric acid, and the resulting precipitate was removed by filtration and washed with water and petroleum ether. UV spectrum: λ_{max} 293 nm (log ε 3.95). IR spectrum, ν, cm^{-1}: 1455, 1285, and 955.

TABLE 2. Synthesized Compounds

Compound	mp, °C	Empirical formula	Found, %				Calculated, %				Yield, %
			C	H	Br	N	C	H	Br	N	
IIc	13—15[a]	$C_7H_{10}N_2O_2$	54,8	6,2		18,3	54,5	6,5		18,2	78
VIa	110—112[c]	$C_{10}H_{11}BrN_2O_2$[c]	44,0	4,0	29,5	10,3	44,3	4,1	29,5	10,0	82
VIb	125—127[b]	$C_5H_9BrN_2O_2$[c]	28,7	4,4	37,9	13,1	28,7	4,3	38,2	13,4	53
VIc	94—96[b]	$C_6H_{11}BrN_2O_2$[c]	32,5	5,0	35,9	12,7	32,3	4,9	35,9	12,5	51
VId	118—120[b]	$C_7H_{11}BrN_2O_2$	35,4	4,7	33,8	11,6	35,7	4,7	34,0	11,9	40
VIe	123—125[a]	$C_6H_9BrN_2O_2$	32,7	4,2	35,9	12,9	32,5	4,1	36,2	12,7	10
VIIIb	105—106[d]	$C_{10}H_{20}N_2O_2$	46,4	7,6	—	21,4	46,2	7,8	—	21,5	54
IXa	Oil[a]	$C_{10}H_{11}Br$	56,7	4,9	37,9	—	56,8	5,2	37,9	—	95

a) This compound was purified by chromatography. b) From alcohol. c) The molecular weight was found by the isothermal distillation method. Found: VIa 274, VIb 214, and VIc 227. Calculated: VIa 271, VIb 209, and VIc 223. d) From dioxane—petroleum ether.

Treatment of Dimer VIIIb with Sodium Hypobromite. A solution of 0.26 g (1 mmole) of VIIIb in dioxane was added dropwise with stirring at 0° to a threefold excess of alkaline solution of sodium hypobromite at 0°, and the precipitated oily product was extracted with chloroform. The extract was dried with magnesium sulfate, the solvent was evaporated, and the residue began to crystallize on treatment with diethyl ether. The yield of 1,2-diazetine 1,2-dioxide VIb was 0.06 g (14%).

Treatment of α-Hydroxylamino Oxime Vb with an Equimolecular Amount of Sodium Hypobromite. An equimolecular amount of a cold solution of sodium hypobromite was added dropwise with stirring at 0° to an aqueous solution of 0.66 g (5 mmole) of Vb, and the resulting precipitated mixture of VIb and VIIIb was removed by filtration and washed with water and petroleum ether to give 0.18 g of product. The product was triturated with chloroform, and undissolved VIIIb [0.1 g (16%)] was removed by filtration. Evaporation of the solvent gave 0.06 g (6%) of VIb.

1-Bromo-1-phenyl-2-methyl-1-propene (IXa). A solution of 0.55 g (2 mmole) of VIa in 5 ml of benzene was refluxed for 30 min until nitrogen oxide evolution ceased. The solvent was then evaporated, and the residual oil was purified by chromatography on silica gel with elution by petroleum ether to give IXa with n_D^{20} 1.5685. UV spectrum, λ_{max}, nm (log ε): 220 (4.06) and 268 (3.52). PMR spectrum (CCl_4), ppm: 7.22 (5H), 2.02 (3H), and 1.71 (3H).

3-Bromo-3-methyl-2-butene (IXb), which was identical to the compound obtained in [9, 10], was formed under similar conditions from VIb.

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