INTERACTION OF 1,2-BISHYROXYLAMINES WITH 1,2-DICARBONYL COMPOUNDS. ISOLATION AND PROPERTIES OF 2,3-DIHYDROPYRAZINE-1,4-DIOXIDES

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The condensation of 1,2-bishydroxylamines with 1,2-dicarbonyl compounds led to the isolation of derivatives of 2,3-dihydropyrazine-1,4-dioxide. The 2,3-bis(bromomethyl)-4a,5,6,7,8,8a-hexahydroquinoxaline reacts readily with O- and N-nucleophiles; condensed pyrazines are formed by interaction with o-phenylenediamine, phenylhydrazine, and tert-butylamine.

It is known that the interaction of 2,3-bishydroxyamino-2,3-dimethylbutane with 1,2-dicarbonyl compounds — glyoxal, methylglyoxal, and diacetyl — leads to 2,3-dihydropyrazine-1,4-dioxides [1, 2]. We recently accomplished the synthesis of aliphatic 1,2-bishydroxylamines (I) containing hydroxylamino groups on both the secondary and tertiary carbon atoms, as well as on both secondary carbon atoms [3]. With the object of synthesizing new 2,3-dihydropyrazine-1,4-dioxides, which may present interest as spin traps [4] and as initial compounds for the synthesis of derivatives of pyrazine-1,4-dioxide, the present work comprised a study of the reaction of 1,2-bishydroxylamines (I) with the glyoxals (IIa, f, *l*), the diketones (IIg, m, q), and dibromodiacetyl, and the consideration of some properties of the compounds obtained.*

The reaction of the 1,2-bishydroxylamines (Ia-e, p) with 1,2-dicarbonyl compounds — glyoxal (IIa), methylglyoxal (IIf), diacetyl (IIg), phenylglyoxal (II*l*), benzil (IIm), and the fural (IIq) — in water or alcohol leads to the derivatives of 2,3-dihydropyrazine-1,4-dioxide (IIIa-q). The reaction time and the yield of the compounds (IIIa-q) depend not only on the nature of the 1,2-dicarbonyl compound (II) and the 1,2-bishydroxyalmine (I), but also on the degree of substitution of the carbon atoms with the hydroxylamino groups in the 1,2-bishydroxylamines (I). Thus, the reactions of the compounds (Ia-e) with the glyoxals (IIa, f, *l*) and diacetyl (IIg) at room temperature are completed after 1-10 h, whereas the reaction of the 1,2-bishydroxyamino-cyclohexane (Ie) with the benzil (IIm) is completed after 10 days. The reaction of the sterically hindered 1,2-bishydroxyamino-2-methyl-1-phenylpropane (Ia) with benzil (IIm) is completed in the course of 1 month. The addition of catalytic amounts of acids (acetic acid, hydrochloric acid, or p-toluenesulfonic acid) or the substitution of the free base 1,2-bishydroxylamine (I) by its salt (the hydrochloride or the sulfate) speeds up the condensation reaction, but the yield of the 2,3-dihydropyrazine-1,4-dioxides (III) decreases in a series of cases. The monooxime of the 1,2-dicarbonyl compound is thereby formed as a reaction by-product. Thus, for example, the reaction of the hydrochloride of the 1,2-bishydroxylamine (Ib) with diacetyl (IIg) (at 20°C) and benzil (IIm) (by the boiling in alcohol) leads to the 2,3-dihydropyrazine-1,4-dioxides (IIIh) and (IIIn) with yields of 56% and 4% correspondingly. The monooximes of diacetyl and benzil are isolated together with the compounds (IIIh) and (IIIn).

*For previous communication, see [5].

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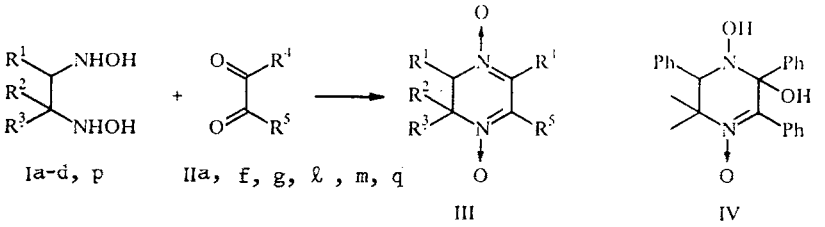
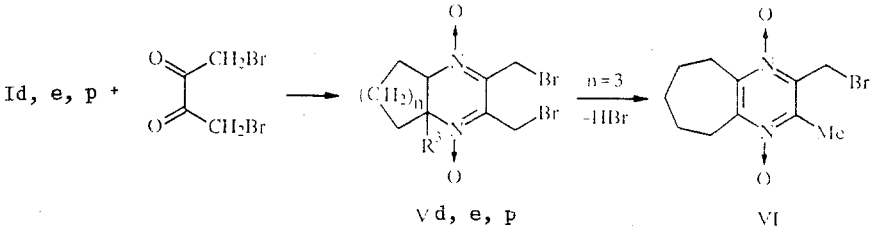


Ia-d, p IIa, f, g, ℓ, m, q III IV

a, g, m) R^1 = Ph; b, h, n) R^1 = Me; c, i) R^1 = Et; d-f, j-*l*, o, q) $R^1 + R^2 = (CH_2)_4$; p) $R^1 + R^2 = (CH_2)_5$; a-c, g-i, m, n) R^2 = Me; a-d, g-j, m, n) R^3 = Me; e, f, k, *l*, o-q) R^3 = H; a-e) R^4 = H; f-k) R^4 = Me; *l*-p) R^4 = Ph; q) R^4 = (2-furyl); a-f, *l*) R^5 = H; g-k) R^5 = Me; m-p) R^5 = Ph; q) R^5 = (2-furyl).

Strong bands at 1530-1570 cm^{-1} and 1440-1470 cm^{-1}, corresponding with the stretching vibrations of conjugated nitrone groups [2, 6], are observed in the IR spectra of the 2,3-dihydropyrazine-1,4-dioxides (IIIa-q). The UV spectra have the common maximum in the region of 345-370 nm, indicating the chromophoric system of dinitrone [2, 6, 7]. The reduction of the time of the reaction of the 1,2-bishydroxylamine (Ia) with benzil (IIm) led to the isolation of the intermediate compound (IV) which, according to the data of the elemental analysis and the ^1H and ^{13}C NMR, has the structure of 1,6-dihydroxy-3,3-dimethyl-2,5,6-triphenyl-1,2,3,6-tetrahydropyrazine-4-oxide. Thus, in the ^{13}C NMR spectrum of the compound (IV), the signals of the carbon atoms C^3 and C^2, connected with the nitrogen atoms of the nitrone and hydroxylamino groups (taking their multiplicity into account), are observed at 68.7 and 73.2 ppm correspondingly. Such an assignment was made on the basis of the comparison with the chemical shifts of the carbon atoms in 1-hydroxy-6,6-dimethyl-2-oxo-5-phenyl-1,2,5,6-tetrahydropyrazine-4-oxide [8] (in DMSO-D_6), in which the corresponding carbon atoms are observed at 82.8 ppm (CHPh) and 60.9 ppm [$C(CH_3)_2$].

Dibromodiacetyl reacts with the 1,2-bishydroxylamine (Ie) as a 1,2-dicarbonyl compound when the reaction is performed in glacial acetic acid with the quantitative formation of 2,3-(bisbromomethyl)-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (Ve). The reaction of the 1,2-bishydroxylamine (Id) with dibromodiacetyl also leads to the 2,3-(bisbromomethyl)hexahydroquinoxaline (Vd), but with a low yield. The final product of the reaction of 1,2-bishydroxyaminocycloheptane (Ip) with dibromodiacetyl is 2-bromomethyl-3-methyl-5,6-pentamethylenepyrazine-1,4-dioxide (VI). The initially formed 2,3-(bisbromomethyl)dihydropyrazine (Vp) probably undergoes the cleavage of the HBr molecule in the process of isolation, and is converted to the compound (VI).

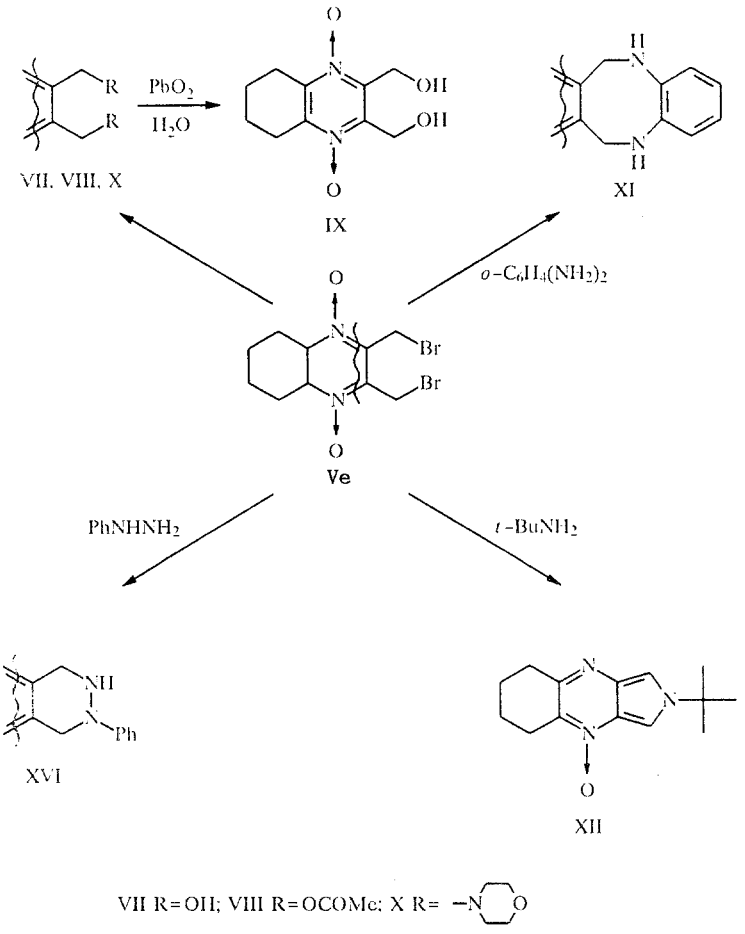


Id, e, p Vd, e, p VI

d) R^3 = Me, n = 2; e) R^3 = H, n = 2; p) R^3 = H, n = 3

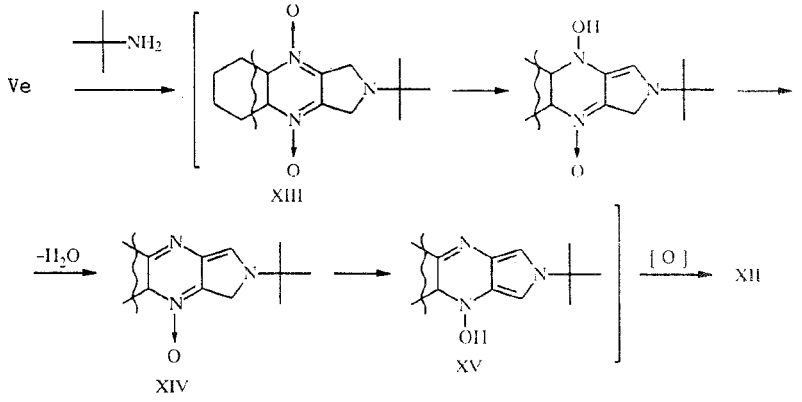
The study of the properties of bis(bromomethyl)hexahydroquinoxaline (Ve) showed that the atoms of bromine readily enter into the nucleophilic substitution reaction (cf. [9]). Thus, the brief boiling of the compound (Ve) in water in the presence of calcium carbonate leads to bis(hydroxymethyl)hexahydroquinoxaline (VII) with a high yield, and the reaction of the compound (Ve) with sodium acetate in the presence of crown ether leads to bis(acetoxymethyl)hexahydroquinoxaline (VIII). The tetrahydroquinoxaline (IX) is formed by the oxidation of the hexahydroquinoxaline (VIII) by lead dioxide in water (see scheme on top of following page).

The reaction of bis(bromomethyl)hexahydroquinoxaline (Ve) with morpholine leads to bis(morpholinomethyl)hexahydroquinoxaline (X). In the reaction of the compound (Ve) with o-phenylenediamine, both amino groups of the reagent participate in the substitution of the bromine atoms, and the quinoxalino-[2,3-c][1,6]benzodiazocine (XI) is formed. The reaction of the bis(bromomethyl)hexahydroquinoxaline (Ve) with tert-butylamine — a sterically hindered primary aliphatic amine — led to the pyrrolo[3,4-b]quinoxaline-mono-N-oxide (XII). The most characteristic feature in the PMR spectrum of the compound (XII) is the quadruplet of protons of the pyrrole ring (the AB-system) determined by their different steric environment. Several schemes can be proposed to explain the formation of the compound (XII), which may proceed as the result of a series of sequential



VII R=OH; VIII R=OCOMe; X R=

reactions. For example, it can be proposed that the resulting pyrrolo[3,4-b]octahydroquinoxaline (XIII) undergoes isomerization and, after dehydration, gives the hexahydro derivative (XIV), the subsequent isomerization of which the oxidation of the hydroxylamino group in the compound (XV) leads to the pyrrolo[3,4-b]quinoxaline (XII (cf. [10]).



The reaction of the compound (Ve) with phenylhydrazine led to the pyridazino[4,5-b]quinoxaline (XVI).

EXPERIMENTAL

The IR spectra were recorded on the UR-20 spectrometer and on the Specord M-80 using tablets of KBr (the concentration 0.25%, l = 1 mm). The UV spectra were taken on the Specord UV-Vis spectrometer in alcohol and KBr. The PMR spectra were taken on the Varian A-56-60A (60 MHz) and Bruker WP-200SY (200.2 MHz) instruments for the 10-15% solutions; the internal standard was HMDS (0.04 ppm from TMS). The ^{13}C NMR spectra were taken on the Bruker AC-200

(50.3 MHz) instrument using the regimes of broad-band and extra-resonance decouplings from ^1H. The molecular mass of the compound (XI) was determined by the method of vapor phase osmometry using the Knauer instrument. The monitoring of the course of the reactions was accomplished by the method of TLC using plates of Silufol UV-254 and Silufol UV-254+366; the eluent was the 15:1 mixture of chloroform–methanol. The development of the compounds (Ia-e, p) was performed with iodine vapor, and the development of the remaining compounds was performed using UV light. The yields, melting points, empirical formulas, and the IR and UV spectra of the compounds obtained are presented in Table 1; the data of the PMR spectra are presented in the Tables 2 and 3.

The data of the elemental analysis of the compounds obtained for C, H, Br, and N correspond with the calculated data.

2,2-Dimethyl-3-phenyl-2,3-dihydropyrazine-1,4-dioxide (IIIa). To the solution of 1.90 g (13 mmoles) of the 40% aqueous glyoxal (IIa) in 10 ml of water is added, with mixing in the course of 2 h, the solution of 1.96 g (10 mmoles) of the 1,2-bishydroxylamine (Ia) in 13 ml of the 3% solution of HCl; the mixture is held for 10 h. The reaction mixture is filtered, and to the filtrate is added $KHCO_3$ to the pH ~ 7. The mixture is saturated with the NaCl suspension; the precipitated residue is filtered off and washed with cold water and dried prior to the isolation of 1.40 g of the dihydropyrazine (IIIa). The extraction of the aqueous filtrate with chloroform leads to the additional isolation of 0.24 g of the compound (IIIa).

2,2,3-Trimethyl-2,3-dihydropyrazine-1,4-dioxide (IIIb). This compound is obtained by analogy with the compound (IIIa) from the hydrochloride of the 1,2-bishydroxylamine (Ib). After the holding of the reaction mixture for 3 h, it is neutralized with $NaHCO_3$ and concentrated. The chromatography of the residue on a column with silica gel, using the 20:1 mixture of chloroform–methanol as the eluent, leads to the isolation of the compound (IIIb).

2,2-Dimethyl-3-ethyl-2,3-dihydropyrazine-1,4-dioxide (IIIc). This compound is obtained by analogy with compound (IIIb) from the hydrochloride of the 1,2-bishydroxylamine (Ic). The reaction mixture is maintained in the course of 10 h.

4a-Methyl-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (IIId). This compound is obtained by analogy with the compound (IIIc) from the sulfate of the 1,2-bishydroxylamine (Id).

4a,5,6,7,8,8a-Hexahydroquinoxaline-1,4-dioxide (IIIe). This compound is obtained by analogy with the compound (IIIb) from the hydrochloride of the 1,2-bishydroxylamine (Ie). After the neutralization and concentration, the residue is treated with abs. alcohol. The residue of NaCl is filtered off, and the filtrate is evaporated. The residue is treated with acetone; the residue is filtered off prior to the isolation of the dihydropyrazine (IIIe).

2-Methyl-4a,5,6,7,8,8a-1,4-dioxide (IIIf). The warm solution of 1.46 g (10 mmoles) of the compound (Ie) in 30 ml of water is added in the course of 10 min to the solution of 1.60 g (11.1 mmoles) of the 50% aqueous methylglyoxal (IIf) in 5 ml of water; the mixture is held for 10 h. The mixture is filtered, and the filtrate is evaporated. The residue is treated with the 1:1 mixture of ether–acetone; the residue is filtered off prior to the isolation of 0.64 g of the compound (IIIf).

5,6-Dimethyl-2,3-dihydropyrazine-1,4-dioxides (IIIg-k). To the solution of 0.90 g (10.5 mmoles) of the diacetyl (IIg) in 10 ml of alcohol is added, with stirring in the course of 5 min, the solution of 10 mmoles of the 1,2-bishydroxylamine (Ib-d) in 10 ml of alcohol [the compounds (Ia, e) are added in portions]. The solution is held for 1-3 h with the monitoring by TLC; the solution is evaporated, and the residue is treated with the 1:1 mixture of ether–hexane. The residue of the dihydropyrazine (IIIg, h, k) is filtered off. For the isolation of the compounds (IIIi, j), the residue is chromatographed on a column with silica gel using the 20:1 mixture of chloroform–methanol as the eluent.

2-Phenyl-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (IIIl). To the solution of 1.52 g (10 mmoles) of the phenylglyoxal hydrate (IIl) in 20 ml of alcohol are added, with stirring, 1.46 g (10 mmoles) of the 1,2-bishydroxylamine (Ie). The reaction mixture is held in the course of 10 h; the residue is filtered off prior to the isolation of 2.30 g of the dihydropyrazine (IIIl).

2,2-Dimethyl-3,5,6-triphenyl-2,3-dihydropyrazine-1,4-dioxide (IIIm). **A.** The mixture of 0.20 g (1.0 mmole) of the 1,2-bishydroxylamine (Ia) and 0.21 g (1.0 mmole) of (IIm) in 5 ml of methanol is stirred until the solution is effected; it is held at room temperature for 1 month. The methanol is evaporated, and the residue is treated with ether; the residue is filtered off prior to the isolation of 0.23 g of the compound (IIIm).

B. To the suspension of 4.20 g (20 mmoles) of the benzil (IIm) in 30 ml of alcohol is added the warm solution of 3.92 g (20 mmoles) of the 1,2-bishydroxylamine (Ia) in 20 ml of alcohol; mixing is performed until the solution is effected. After 3 days, the reaction mixture is heated at 70°C with stirring for 2 h, and is then cooled at −10°C for 1 day. The residue is filtered off and washed with cold alcohol and repeatedly with ether. The yield of 2.08 g (28%) of the dihydropyrazine (IIIm) is obtained. The additional 0.90 g (12%) of the compound (IIIm) is obtained from the filtrate by the evaporation of the solvent and the chromatography of the residue on a column with silica gel with chloroform as the eluent.

TABLE 1. Characteristics of the Compounds Synthesized

Compound	Empirical formula	mp, °C*	UV spectrum (EtOH), λ_{max}, nm (log ε)	IR spectrum, ν, cm^{-1}	Yield, %
IIIa	$C_{12}H_{14}N_2O_2$	184...186	359 (4,29)	1570, 1460	75
IIIb	$C_7H_{12}N_2O_2$	119...121	222 (3,68); 357 (4,11)	1560, 1455	56
IIIc	$C_8H_{14}N_2O_2$	137...138	219 sh (3,51); 359 (4,14)	1555, 1510, 1460	34
IIId	$C_9H_{14}N_2O_2 \cdot H_2O$	130...138	222 (3,71); 359 (4,24)	1640, 1560, 1515, 1455	12
IIIe	$C_8H_{12}N_2O_2$	156...158	218 (3,84); 358 (4,22)	1565, 1530, 1455	72
IIIf	$C_9H_{14}N_2O_2$	169...170	219 (3,93); 357 (4,19)	1570, 1515, 1455	35
IIIg	$C_{14}H_{18}N_2O_2$	180...183	213 (3,91); 354 (4,09)	1570, 1510, 1470	60
IIIh	$C_9H_{16}N_2O_2$	100...102	221 (3,86); 347 (4,19)	1565, 1500, 1445	88
IIIi	$C_{10}H_{18}N_2O_2$	88...90	220 (3,88); 350 (4,20)	1555, 1500, 1460	48
IIIj	$C_{11}H_{18}N_2O_2$	100...112	220 (3,90); 348 (4,17)	1555, 1490, 1450, 1440	30
IIIk	$C_{10}H_{16}N_2O_2$	154...156	217 (4,02); 346 (4,18)	1570, 1510, 1450, 1435	96
IIIℓ	$C_{14}H_{16}N_2O_2$	212...214	272 (4,30); 366 (4,05)	1555, 1500, 1450	95
IIIm	$C_{24}H_{22}N_2O_2$	207...209	253 (4,04); 290 (4,19); 371 (3,96)	1540, 1505, 1445	62
IIIn	$C_{19}H_{20}N_2O_2$	133...135	253 (4,04); 285 (4,18); 363 (4,01)	1535, 1500, 1445	57
IIIo	$C_{20}H_{20}N_2O_2$	196...198	253 (4,11); 285 (4,21); 365 (4,05)	1535, 1500, 1450	66
IIIp	$C_{21}H_{22}N_2O_2$	188...189	286 (3,83); 353 (4,06)	1535, 1490, 1440	41
IIIs	$C_{16}H_{16}N_2O_4$	185...187	238 (4,00); 303 (4,53); 373 (3,91); 387 sh (3,89)	1535, 1500, 1490, 1450	36
IV	$C_{24}H_{24}N_2O_3$	decom. > 80	261**	3440, 1550	36
Vd	$C_{11}H_{16}Br_2N_2O_2$	115...119	217 (3,90); 267 (4,00); 368 (4,01)	1530, 1495, 1445	17
Ve	$C_{10}H_{14}Br_2N_2O_2$	122...124	218 (4,05); 267 (4,13); 368 (4,07)	1530, 1495	98
VI	$C_{11}H_{15}BrN_2O_2$	151...153	216 (4,11); 253 (4,43); 313 (4,28)	1460, 1340, 1325	32
VII	$C_{10}H_{16}N_2O_4$	149...152	232 (4,01); 354 (4,13)	3380, 3180, 1570, 1510, 1450, 1430	69
VIII	$C_{14}H_{20}N_2O_6$	94...95	235 (4,06); 358 (4,08)	1755, 1745, 1550, 1495	60
IX	$C_{10}H_{14}N_2O_4$	144...146	244 (4,44); 312 (4,29)	1450, 1425, 1355, 1330	34
X	$C_{15}H_{30}N_4O_4$	175...178	233 (3,88); 353 (4,01)	1555, 1510, 1465	66
XI	$C_{16}H_{20}N_4O_2$	195...197	223 (4,58); 248 sh (3,88); 307 sh (3,88); 345 (4,09)	3375, 3350, 1600, 1565, 1505, 1470	32
XII	$C_{14}H_{10}N_2O$	164...165	243 (4,70); 291 (4,14); 314 (4,16); 327 (4,13); 400 (3,60)	1540, 1505, 1460	25
XVI	$C_{16}H_{20}N_4O_2$	147...149	242 (4,26); 351 (4,21)	3220, 1605, 1580, 1505, 1450	50

*The compounds (IIIb-d, g, h, i-k, n, q), (Vd), and (VIII) were crystallized from hexane–ethyl acetate. The compounds (IIIa) and (XI) were crystallized from ethyl acetate. The compound (IIIℓ) was crystallized from dioxane; (IX) was crystallized from benzene, and (VI) was crystallized from ethyl acetate–ethanol. The compounds (IIIe, f, m, o, p) and (XVI) were crystallized from ethanol; (Ve) and (VII) were crystallized from acetonitrile. The compound (X) was crystallized from methanol, and the compound (XII) was purified by sublimation.

**The UV spectrum of the compound (IV) was recorded in KBr.

2,2,3-Trimethyl-5,6-diphenyl-2,3-dihydropyrazine-1,4-dioxide (IIIn). To the suspension of 2.10 g (10 mmoles) of the benzil (IIm) in 30 ml of methanol is added the solution of 1.34 g (10 mmoles) of the 1,2-bishydroxylamine (Ib) in 20 ml of methanol; the mixture is stirred for 1 h. After 4 days, the alcohol is evaporated, and the residue is chromatographed on a column with silica gel using the 1:1 mixture of ethyl acetate–hexane as the eluent prior to the isolation of 1.76 g of the compound (IIIn).

2,3-Diphenyl-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (IIIo). **A.** The suspension of 0.15 g (1.0 mmole) of the 1,2-bishydroxylamine (Ie) and 0.23 g (1.1 mmoles) of the benzil (IIm) in 5 ml of methanol is mixed until the solution is effected. After 10 days, the precipitated residue is filtered off prior to the isolation of 0.21 g of the dihydropyrazine (IIIo).

B. To the suspension of 0.36 g (2.0 mmoles) of the hydrochloride of the 1,2-bishydroxylamine (Ie) in 5 ml of methanol is added, with stirring, the solution of 0.46 g (2.2 mmoles) of the benzil (IIm) in 5 ml of methanol; the mixture is held for 20 h. The solvent is evaporated, and the residue is dissolved in 20 ml of chloroform and washed with 5 ml of water. The chloroform solution is dried with $MgSO_4$ and evaporated. The residue is triturated in ether; the residue is filtered off prior to the isolation of 0.40 g (63%) of the compound (IIIo).

C. The mixture of 1.46 g (10 mmoles) of the 1,2-bishydroxylamine (Ie), 2.30 g (11 mmoles) of the benzil (IIm), and 1 ml of acetic acid in 15 ml of alcohol is boiled for 2.5 h. The solution is cooled to 5°C, and the precipitated residue is filtered off. Chromatography of the residue on a column with silica gel using chloroform as the eluent leads to the isolation of 1.67 g (52%) of the compound (IIIo).

2,3-Pentamethylene-5,6-diphenyl-2,3-dihydropyrazine-1,4-dioxide (IIIp). This compound is obtained from the 1,2-bishydroxylamine (Ip) by analogy with the compound (IIIo) (according to the method C) without the addition of acetic acid. After the cooling of the reaction mixture at −10°C for 3 days, the residue of the dihydropyrazine (IIIp) is filtered off and washed with cold alcohol and ether.

2,3-Bis(2-furyl)-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (IIIq). The mixture of 1.83 g (10 mmoles) of the hydrochloride of the 1,2-bishydroxylamine (Ie) and 1.90 g (10 mmoles) of the furil (IIq) in 30 ml of methanol is boiled for 3.5 h. The solvent is evaporated, and the residue is chromatographed on a column with silica gel using chloroform as the eluent prior to the isolation of 1.07 g of the dihydropyrazine (IIIq).

1,6-Dihydroxy-3,3-dimethyl-2,5,6-triphenyl-1,2,3,6-tetrahydropyrazine-4-oxide (IV). To the solution of 0.21 g (1.0 mmole) of the benzil (IIm) in 4 ml of methanol is added the solution of 0.20 g (1.0 mmole) of the 1,2-bishydroxylamine (Ia) in 2 ml of methanol. After 2-3 days, following the onset of the precipitation of the residue of the compound (IV), the mixture is cooled at −10°C for 24 h. The residue is filtered off and washed with methanol and chloroform prior to the isolation of 0.14 g of the compound (IV). The PMR spectrum in DMSO-D_6 was as follows: 1.31 ppm (3H, s, CH_3), 1.53 ppm (3H, s, CH_3), 4.89 ppm (1H, s, H^2), 6.67 ppm (1H, s, OH), 7.05-7.50 and 7.65-7.80 ppm (15H, m, arom. protons), and 7.72 ppm (1H, s, NOH). The ^{13}C NMR spectrum in DMSO-D_6 was as follows:* 22.38 ppm (q, CH_3), 23.69 ppm (q, CH_3), 68.67 ppm (s, C^3), 73.18 ppm (d, C^2), 89.69 ppm (s, C^6), 126.67 ppm, 127.10 ppm, 127.23 ppm, 127.49 ppm, 129.50 ppm, 130.69 ppm, 133.19 ppm, 137.30 ppm, 141.16 ppm, and 142.61 ppm (arom. atoms of carbon and C^5).

Condensation of the 1,2-Bishydroxylamines (Ia, e, p) with Dibromoacetyl. To the solution of 4.88 g (20 mmoles) of dibromodiacetyl in 75 ml of glacial acetic acid is added, with stirring in the course of 15-25 min, the solution of 20 mmoles of the 1,2-bishydroxylamine (Ie, p) in 35 ml of CH_3COOH [in the case of the compound (Id), the aqueous solution of its sulfate salt (20 mmoles) is cautiously neutralized with 14.4 ml (40 mmoles) of 10% aqueous NaOH and acidified with 20 ml of CH_3COOH]. The reaction mixture is held for 4-5 h [for 2 days in the case of the 1,2-bishydroxylamine (Id)]; the solvent is evaporated, and the residue is triturated in ether. The residue of the hexahydroquinoxaline (Ve) is filtered off. The compounds (Vd, p) are isolated by the chromatography of the residue on a column with silica gel with the 15:1 mixture of chloroform–methanol as the eluent. After its isolation, the dihydropyrazine (Vp) darkens rapidly in air and is converted into a viscous oily mass, from which the pyrazine (VI) is isolated by chromatography on a column with silica gel using the 15:1 mixture of chloroform–methanol as the eluent.

2,3-Bis(hydroxymethyl)-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (VII). To the boiling suspension of 2.10 g (21 mmoles) of calcium carbonate in 100 ml of water are added 1.06 g (3.0 mmoles) of the hexahydroquinoxaline (Ve), and the mixture is boiled for 15 min and cooled to room temperature. The mixture is brought to the pH ~ 7 with a saturated

*The signals of the second diastereomer are absent from the PMR spectra of the compound (IV).

TABLE 2. PMR Spectra of the 2,3-Dihydropyrazine-1,4-dioxides (IIIa-q)

Compound	δ, ppm, SSCC, J, Hz*					
	CHR^1	R^1	R^2	R^3	R^4	R^5
IIIa	4,77 s	7,35 s (Ph)	1,25s (CH_3)	1,70 s (CH_3)	7,24s (H)	7,24 s (H)
IIIb	3,90 q J = 7	1,49 d J = 7 (CH_3)	1,39 s (CH_3)	1,55 s (CH_3)	7,10 s (H)	7,10 s (H)
IIIc	3,70 t J = 6	1,13t, J = 7 (CH_3); 1,63...2,12 m (CH_2)	1,44 s (CH_3)	1,57 s (CH_3)	7,10 s (H)	7,10 (H)
IIId	3,65 d.d.d $^3J_{8-A}$ = 12, $^3J_{8-B}$ = 4,5, $^4J_2$ = 1	1,05...1,87; 2,16...2,38; 2,60...2,73 m ($(CH_2)_4$)		1,38 s (CH_3)	6,97 m J_{AB} = 5, $^4J_{8a}$ = 1; (HA)	7,04m, J_{AB} = 5 (HB)
IIIe	4,35...4,65 m	1,35...2,65 m ($(CH_2)_4$)		4,35...4,65 m (H)	7,53 s (H)	7,53s (H)
IIIf	4,20...4,70 m	1,30...2,50 m ($(CH_2)_4$)		4,20...4,60 m (H)	2,17 s (CH_3)	7,64 s (H)
IIIg	4,79 s	7,15...7,55 m (Ph)	1,27 s (CH_3)	1,62 s (CH_3)	2,32 s (CH_3)	2,32 s (CH_3)
IIIh	3,82 q J = 7,5	1,35 d, J = 7,5 (CH_3)	1,32 s (CH_3)	1,41 s (CH_3)	2,15 s (CH_3)	2,15 s (CH_3)
IIIi	3,72 d.d J = 5 and 8	1,00 t, J = 7 (CH_3); 1,72 m, (CH_2)	1,44 s (CH_3)	1,44 s (CH_3)	2,18 s (CH_3)	2,23 s (CH_3)
IIIj	3,57 d.d J_1 = 4, J_2 = 12	0,93...1,70; 1,88...2,12; 2,51...2,70 m ($(CH_2)_4$)		1,16 s (CH_3)	2,01s (CH_3)	2,01 s (CH_3)
IIIk	3,93...4,39 m	1,32...2,57 m ($(CH_2)_4$)		3,93...4,39 m (H)	2,22s (CH_3)	2,22 s (CH_3)
IIIl	4,37...4,55 m	1,37...2,69 m ($(CH_2)_4$)		4,37...4,55m (H)	7,40...7,50; 7,85...7,95 m (Ph)	7,77 s(H)
IIIm	4,98 s	7,50 m (Ph)	1,40 s (OCH_3)	1,90 s (CH_3)	7,10...7,50 m (Ph)	7,10...7,50 m (Ph)
IIIn	4,10 q J = 6	1,64 d J = 6 (CH_3)	1,50s (CH_3)	1,71 s (CH_3)	7,10...7,40 m (Ph)	7,10...7,40 m (Ph)
IIIo	4,30...4,60m	1,10...2,80 m ($(CH_2)_4$)		4,30...4,60 m (H)	7,22 m (Ph)	7,22 (Ph)
IIIp	4,50...4,60m	1,50...2,15; 2,40...2,60 m ($(CH_2)_5$)		4,50...4,609 m (H)	7,12...7,31 m (Ph)	7,12...7,31 m (Ph)
IIIq	4,20...4,60m	1,35...2,70 m ($(CH_2)_4$)		4,20...4,60 m (H)	6,57 d.d, J = 1,5 J = 3,5; 7,29 d, J = 1,5; 7,78 d J = 3,5 furyl	6,57 d.d, J = 1,5 and J = 3,5; 7,29 d J = 1,5; 7,78 d J = 3,5 (furyl)

*The PMR spectra of the compounds (IIIa-d, g, i-k, m-q) were recorded in $CDCl_3$. The PMR spectra of (IIIe, f) were recorded in D_2O, and that of (IIIh) was recorded in CCl_4. The PMR spectrum of (IIIl) was recorded in DMSO-D_6. In the recording of the spectra of the compounds (IIIe, f), tert-butanol was utilized as the internal standard.

TABLE 3. PMR Spectra of the Compounds (V)-(XII) and (XVI)

Compound	δ, ppm, SSCC, J, Hz*			
	$-(CH_2)_4-$	$-CH_2-C=N-O$	aromatic protons	other signals
Vd	1,11...2,25 m 2,66...2,80 m	4,39 m	—	1,30 s (CH_3); 3,78 dd $^3J_{8\text{-}A}$ = 12, $^3J_{8\text{-}B}$ = 4 (CH)
Ve	1,35...2,60 m	4,50 s	—	4,15...4,45 m (2CH)
VI	1,63...1,96 m 3,24...3,38 m**	4,71 s	—	2,54 s (CH_3)
VII	1,15...2,40 m	4,49 s	—	4,15...4,40 m (2CH); 4,40...5,50 br.s (2OH)
VIII	1,30...2,65 m	5,03 s	—	2,05 s ($2COCH_3$); 4,05...4,40 m (2CH)
IX	1,73...2,11 m 2,78...3,14 m	5,04 s	—	4,75 br.s (2OH)
X	1,40...2,60 m	3,80 s	—	2,35...2,70 m ($4CH_2N$); 3,50...3,80 m ($4CH_2O$); 4,10...4,35 m (2CH)
XI	1,28...2,35 m	4,17 s	6,58...6,74 m (C_6H_4)	4,17 sym (2CH); 4,90 t J = 6 (2NH)
XII	1,75...2,10 m 2,85...3,20 m	—	7,39 m J_{AB} = 2,5; 7,54 m J_{AB} = 2,5 (H^1 and H^3)	1,67 s ($C(CH_3)_3$)
XVI	1,39...2,00 m 2,19...2,47 m	4,09 d J = 8; 4,27 s	6,85...6,97 m 7,13...7,35 m (Ph)	3,11 t, J = 8 (NH); 4,17...4,31 (2CH)

*The spectra of the compounds (V), (VI), (IX), (X), (XII), and (XVI) were recorded in $CDCl_3$. The spectra of (VIII), (VII), and (XI) were recorded in CCl_4, DMSO-D_6, and the mixture of $CDCl_3$ and DMSO-D_6, correspondingly.

**The chemical shift of the $(CH_2)_5$ fragment is presented.

solution of $NaHCO_3$, and the residue is filtered off. The aqueous filtrate is extracted with chloroform. After evaporation, the residue is dissolved in methanol and chromatographed on a column with silica gel using the 10:1 mixture of chloroform–methanol as the eluent for the isolation of 0.47 g of the compound (VII).

2,3-Bis(acetoxymethyl)-4a,5,6,7,8,8a-hexahydroquinoxaline-1,4-dioxide (VIII). To the solution of 0.35 g (1.5 mmoles) of 15-crown-5 in 70 ml of dry acetonitrile are added 4.92 g (60 mmoles) of fused sodium acetate. The mixture is stirred for 10 min prior to the addition of 3.54 g (10 mmoles) of the compound (Ve). The mixture is stirred for 4 days. The residue is filtered off, and the filtrate is evaporated. The residue is dissolved in 100 ml of chloroform and washed with water, and the chloroform solution is dried with $MgSO_4$; it is then evaporated. The residue is chromatographed on a column with silica gel using the 50:1 mixture of chloroform–methanol as the eluent prior to the isolation of 1.87 g of the hexahydroquinoxaline (VIII) in the form of a bright yellow oil, which is crystallized on prolonged storage in a refrigerator.

2,3-Bis(hydroxymethyl)-5,6,7,8-tetrahydroquinoxaline-1,4-dioxide (IX). To the solution of 1.50 g (6.6 mmoles) of the hexahydroquinoxaline (VIII) in 80 ml of water are added 15.77 g (66 mmoles) of PbO_2, and the mixture is stirred for 90 h with the addition of 6.0 g (25 mmoles) portions of fresh lead dioxide after each 30 h. The mixture is centrifuged. The aqueous layer is decanted and subjected to continuous extraction with chloroform for 30 h for the isolation of 0.51 g of the compound (IX).

2,3-Bis(morpholinomethyl)-4a,5,6,7,8,8-hexahydroquinoxaline-1,4-dioxide (X). To the solution of 3.57 g (41 mmoles) of morpholine in 40 ml of methanol are added, with stirring in the course of 20 min, 3.54 g (10 mmoles) of the compound (Ve). The reaction mixture is held at 0°C for 10 h. The residue of the hexahydroquinoxaline (X) is filtered off and washed with alcohol prior to the isolation of 2.40 g of the compound (X).

1,2,3,4,4a,6,7,12,13,14a-Decahydroquinoxalino[2,3-c][1,6]benzodiazocine-5,14-dioxide (XI). To the suspension of 3.54 g (10 mmoles) of the hexahydroquinoxaline (Ve) in 150 ml of alcohol is added, with stirring in the course of 10 min, the solution of 2.25 g (20.8 mmoles) of o-phenylenediamine in 30 ml of alcohol; the mixture is held for 10 h. The alcohol is evaporated, and the residue is chromatographed on a column with silica gel using the 40:1 mixture of chloroform–methanol as the eluent prior to the isolation of 0.96 g of the compound (XI). The molecular mass was as follows: Found 302, 304, and

calculated 300. The ^{13}C NMR spectrum in DMSO-D_6 + $CDCl_3$ was as follows: 21.72 ppm (t, C^2 and C^3), 23.68 ppm (t, C^1 and C^4), 43.21 ppm (t, C^6 and C^{13}), 64.63 ppm (d, C^{4a} and C^{14a}), 119.21 ppm, 120.14 ppm (d, C^8, C^{11}, C^9, and C^{10}), 140.11 ppm, and 140.71 ppm (s, C^{5a}, C^{13a}, C^{7a}, and C^{11a}).

2-Tert-butyl-5,6,7,8-tetrahydropyrrolo[3,4-b]quinoxaline-4-oxide (XII). To the solution of 0.45 ml (4 mmoles) of tert-butylamine in 10 ml of dry acetonitrile is added, with stirring in the course of 5 min, 0.35 g (1.0 mmole) of the compound (Ve). After 1 h, the solution is filtered off, and the filtrate is evaporated. The residue is chromatographed on a column with silica gel using the 40:1 mixture of chloroform–methanol as the eluent prior to the isolation of 0.06 g of the compound (XII).

2-Phenyl-1,2,3,4,5a,6,7,8,9,9a-decahydropyridazino[4,5-b]quinoxaline-5,10-dioxide (XVI). To the solution of 0.92 g (8.5 mmoles) of phenylhydrazine in 10 ml of methanol is added, with stirring in the course of 20 min, 0.71 g (2.0 mmoles) of the hexahydroquinoxaline (Ve). The reaction mixture is maintained for 30 min. The precipitated residue is filtered off and washed with methanol prior to the isolation of 0.29 g of the compound (XVI).

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