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FORMATION OF 1,1,4,4-TETRAMETHOXY-2,3,5,6-TETRAHYDROXIMINOCYCLOHEXANE BY THE INTERACTION OF TRINITROSOPHLOROGLUCINOL WITH HYDROXYLAMINE HYDROCHLORIDE IN METHANOL

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1,1,4,4-Tetramethoxy-2,3,5,6-tetrahydroximinocyclohexane was obtained by the treatment of trinitrosophloroglucinol with hydroxylamine hydrochloride in methanol. Oxidation of the product with an alkaline solution of potassium hexacyanoferrrate(III) gave a mixture of the isomers 4,4,8,8-tetramethoxy-4H,8H-benzo[1,2-c:4,5-c']bis[1.2.5]oxadiazole-1,5-dioxide and 4,4,8,8-tetramethoxy-4H,8H-benzo[1,2-c:4,5-c']bis-[1.2.5]oxadiazole-1,7-dioxide. Removal of the N-oxide groups from these compounds with triethyl phosphite followed by hydrolysis of the diketal groups gave 4,8-dioxo-4H,8H-benzo[1,2-c:4,5-c']bis[1.2.5]-dioxazole. Reaction with malonodinitrile gave 4,8-di(dicyanomethylene)-4H,8H-benzo[1,2-c:4,5-c']bis[1.2.5]-oxadiazole which is an analog of known electron acceptors.

Since nitrosophenols in solution are in equilibrium with their quinone oxime tautomers and react with hydroxylamine hydrochloride to give quinone dioximes [1, 2] it might be expected that trinitrosophloroglucinol (I) [3] would give triquinoyl hexaoxime under similar conditions. However as a result of keeping a methanolic solution of I with hydroxylamine hydrochloride at room temperature for a month a colorless crystalline precipitate separated which was poorly soluble in most organic solvents and water, but which dissolved well in aqueous alkali. The ^{1}H NMR spectrum of the product consisted of two singlets for OMe groups at 3.15 and 3.40 ppm and a singlet for oxime protons at 11.51 ppm. The ^{12}C NMR spectrum contained signals at 50.3 and 51.2 ppm corresponding to carbon atoms of OMe groups, at 99.7 corresponding to sp^3 hybridized carbon atoms, and at 144.6 ppm corresponding to carbon atoms of the oxime group. The compound was recrystallized from dimethylsulfoxide to give a product with the elemental analysis corresponding to the formula $C_{10}H_{16}N_4O_8 \cdot 2Me_2SO$. On the basis of these results the compound was ascribed the structure of 1,1,4,4-tetramethoxy-2,3,5,6-tetrahydroximinocyclohexane (II). The high yield (70%) of (II) may be explained since it is the least soluble in methanol of all the many products which can be obtained from the interaction of compound (I) with hydroxylamine in methanol.

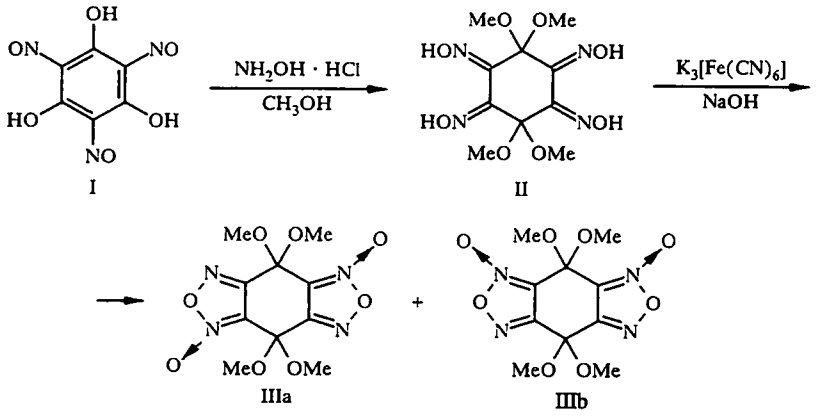

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TABLE 1. Characteristics of the Compounds Synthesized

Compound	Molecular formula	(Found, %) / (Calculated, %) C	H	N	mp, °C*	(Found†) / (Calculated)	IR spectrum ν, cm^{-1}	UV spectrum, λ_{max} (lgε)	Yield, %
II	$C_{10}H_{16}N_4O_8$	37,45 37,50	5,00 5,04	17,40 17,50	238 (decomp.)			235(3,95)	70
IIa‡	$C_{18}H_{40}N_4O_{12}S_4$	33,95 34,18	6,30 6,33	8,79 8,86	270...272				
IIIa, b	$C_{10}H_{12}N_4O_8$	37,76 37,98	3,80 3,83	17,63 17,72	149...151	316,0655 316,0697	2850 (OMe)	275(4,00)	96
IVa, b	$C_6N_4O_6$	32,10 32,14	—	24,90 25,00	129...130	223,9813 223,9818	1720 (C=O)	222(4,00), 278(3,68)	62
V	$C_{10}H_{12}N_4O_6$	42,15 42,25	4,15 4,26	19,70 19,71	101...103		2850 (OMe)	222(4,05)	94
VI	$C_6N_4O_4$	37,28 37,50	—	28,92 29,17	170...173		1750 (C=O)	305(3,64)	77,5
VIIa, b	$C_6H_2N_6O_4$	32,39 32,43	0,80 0,90	37,89 37,84	290 (decomp.)			268(4,37)	81
VIII	$C_{12}N_8O_2$	50,15 50,00	—	38,70 38,89	Over 360	228,0142 228,0145	2210, 2215 (C≡N)	310(3,98), 388(4,03), 490(3,50), 660(2,60)	40

*Compounds were recrystallized from ethanol (II, IVa, IVb, VIIa, VIIb), chloroform (IIIa, IIIb, V, VI) and acetic anhydride (VIII).

†High resolution mass spectral data (mol. mass).

‡S: found 20.10%, calculated 20.25%.

TABLE 2. ^{13}C NMR and Mass Spectra of the Compounds Synthesized

Compound	^{13}C NMR spectra, ppm*	Mass spectrum, m/z (I_{rel}, %)†
II	50,3 and 51,2 (OCH_3); 99,7 [>C(OMe)$_2$]; 144,6 (C=NOH)	
IIIa,b	52,4, 53,1and 53,6 (OCH_3); 92,2, 93,3 and 94,4 [>C(OMe)$_2$]; 108,5 and 108,8 (C=N — O), 152,6 and 153,0 (C=N)	316 M^+(30), 285(40), 218(20), 158(60), 128(70), 105(100)
IVa,b	109,4 and 110,1 (C=N — O), 150,4, 151,0 (C=N), 161,6, 163,7, 165,8 (C=O)	224 M^+ (10), 140(40), 88(15)
V	52,2 (OCH_3), 92,6 [>C(OMe)$_2$], 151,0 (C=N)	284 M^+(10), 253(100), 222(10), 194(10), 100(15), 74(20)
VI	153,1(C=N), 166,6 (C=O)	192 M^+(40), 96(40), 70(100), 54(50)
VIIa,b	130,3, 130,6, 144,10, 149,0 (C=N)	222 M^+(100), 205(10), 175(10), 137(20), 122(20), 70(20)
VIII	150,0 (C=N), 139,5 (C=C), 111,6 (C=C), 90,9 (C ≡ N)	288 M^+ (60), 258(100), 130(30), 114(20)

*Spectra of compounds II, IVa, IVb, VIIa, VIIb, and VIII were recorded in $(CD_3)_2SO$, and of compounds IIIa, IIIb, V, and VI in $CDCl_3$.

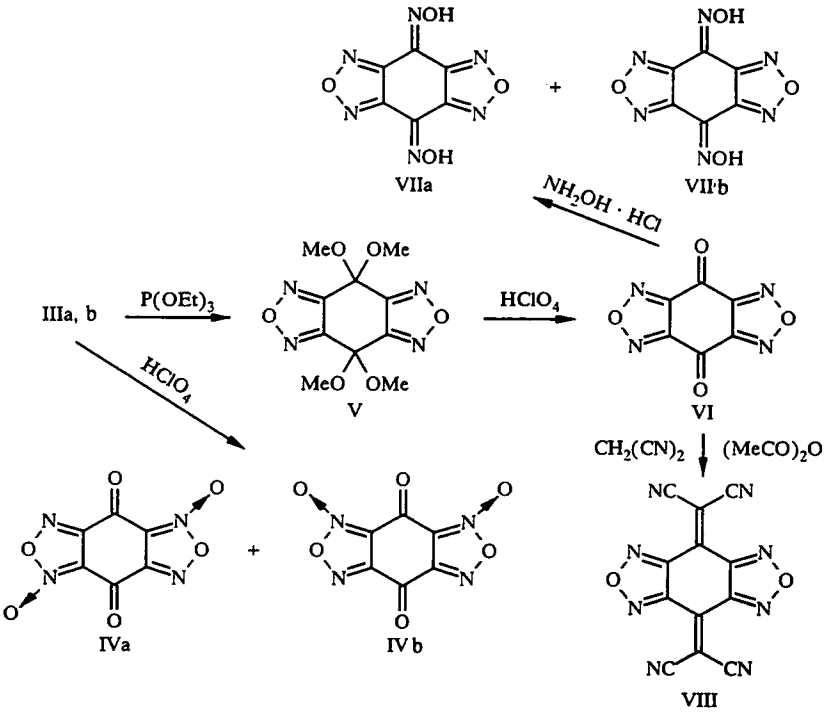
†Molecular ion peaks and peaks with intensities greater than 10% are cited.

Oxidation of the tetraoxime II with potassium hexacyanoferrate(III) in alkaline medium gave a quantitative yield of a compound, the ^1H NMR spectrum of which contained three signals for hydrogens of an OMe group at 3.41, 3.57, and 3.68 ppm with 1:2:1 integrated intensities. The ^{13}C NMR spectrum contained signal of carbons of the furoxane ring at 153.0 and 152.6 (C=N) and 108.8 and 108.5 (C=N→O) (see [4]), three signals for sp^3 hybridized carbon atoms at 94.4, 93.3 and 92.3, and also signal for the carbons of OMe groups at 52.6, 53.1 and 52.4 ppm. That the product is a 1:1 mixture of two

isomers which differ in the position of the N-oxide oxygen atoms is consistent with these data: 4,4,8,8-tetramethoxy-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,5-dioxide (IIIa) and 4,4,8,8-tetramethoxy-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,7-dioxide (IIIb). Treatment of IIIa and IIIb with perchloric acid caused ready hydrolysis of the diketal groups to give a product, the ^{13}C NMR spectrum of which showed two sets of signals corresponding to a mixture of the two isomers 4,8-dioxo-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,5-dioxide (IVa) and 4,8-dioxo-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,7-dioxide (IVb).

Treatment of the mixture of IIIa and IIIb with triethyl phosphite gave 4,4,8,8-tetramethoxy-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]dioxazole (V). Its ^1H NMR spectrum contains a singlet corresponding to OMe protons at 3.64 ppm while the ^{13}C NMR spectrum contains signals for the OMe carbon at 52.2, for sp^3 hybridized carbon at 92.6 and for carbon atoms of the C=N group at 150.0 ppm. Hydrolysis of the diketal groups of V with perchloric acid gave 4,8-dioxo-4H,8H-benzo[1,2-*c*:4,5-*c*']oxadiazole (VI) which reacted with hydroxylamine hydrochloride to give the dioxime (VII). The ^{13}C NMR spectrum of VII showed two sets of signals indicating that it was a mixture of isomers VIIa and VIIb which differ in the configuration of the oxime groups. Treatment of compound VI with malonodinitrile gave 4,8-di(dicyanomethylene)-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole (VIII) the structure of which was confirmed by physicochemical methods of analysis (see Tables 1 and 2).

It should be noted that compound VIII is an analog of the known electron acceptor, 4,8-di(dicyanomethylene)-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]thiadiazole [5].



EXPERIMENTAL

IR spectra of KBr discs (0.25% concentration) were recorded on a UR-20 spectrometer, UV spectra of ethanol solutions with a Specord UV-VIS spectrometer. ^1H NMR and ^{13}C NMR spectra were measured with a Bruker AC-200 instrument and mass spectra with a Finnigan MS 8200 instrument with an ionizing voltage of 70 eV.

Characteristics of the compounds synthesized are given in Table 1 and their ^{13}C NMR and mass spectra in Table 2.

1,1,4,4-Tetramethoxy-2,3,5,6-tetrahydroximinocyclohexane (II). Hydroxylamine hydrochloride (30 g, 435 mmol) was added to a solution of trinitrosophloroglucinol hydrate (100 g, 434 mmol) in methanol (800 ml) and the mixture was kept at room temperature for 30 day. The precipitate was filtered off, washed with water and methanol and dried to give II (98 g). ^1H NMR spectrum (Me_2SO): 3.15 (6H, s, OCH_3), 3.40 (6H, s, OCH_3), 11.51 ppm (4H, s, NOH). The solvate $C_{10}H_{16}N_4O_8 \cdot 4Me_2SO$ (IIa) was formed when compound II was recrystallized from dimethylsulfoxide.

4,4,8,8-Tetramethoxy-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,5-dioxide (IIIa) and 4,4,8,8-Tetramethoxy-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,7-dioxide (IIIb). Potassium hexacyanoferrate(III) (3 g, 9.1 mmol) in water 10 ml) was added dropwise with stirring to a solution of tetraoxime II (1 g, 1.58 mmol) in 10 ml 10% aqueous sodium hydroxide (10 ml). The mixture was kept at room temperature for 30 min, the precipitate was filtered off, washed with water, and dried to give a mixture of IIIa and IIIb (0.48 g). ^{1}H NMR spectrum ($CDCl_3$): 3.41 (6H, s OCH_3), 3.56 (12H, s, OCH_3), 3.67 ppm (6H, s, OCH_3).

4,8-Dioxo-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,5-dioxide (IVa) and 4,8-Dioxo-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole-1,7-dioxide (IVb). A mixture of compounds IIIa and IIIb (2.0 g, 63.2 mmol) was added to perchloric acid (20 ml) and the mixture was stirred at 20°C for 30 min. The mixture was cooled, added to water (200 ml) and extracted with ethyl acetate (4 × 50 cm^3). The extract was washed with saturated sodium chloride solution, dried over magnesium sulfate and evaporated. The residue was suspended in chloroform and the precipitate filtered off to give a mixture of IVa and IVb (0.9 g).

4,4,8,8-Tetramethoxy-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole (V). Triethyl phosphite (8 cm^3) was added to a mixture of the difuroxanes IIIa and IIIb (1.0 g, 31.6 mmol), the mixture was carefully heated to boiling and then boiled for 5 min. The mixture was then cooled and added to 10% hydrochloric acid (20 ml). The precipitate was filtered off after 1 h, washed with water and dried to give compound V (0.82 g). ^{1}H NMR spectrum ($CDCl_3$): 3.63 ppm (12H, s, OCH_3).

4,8-Dioxo-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole (VI) was obtained as described for compounds IVa and IVb.

4,8-Dihydroximino-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazoles (VIIa, b). Hydroxylamine hydrochloride (1.4 g, 20 mmol) in water (10 ml) was added to a solution of diketone VI (1.92 g, 10 mmol) in methanol (50 ml) and the mixture was kept at room temperature for 24 h. The precipitate was filtered off, washed with water, and dried to give a mixture of the dioximes VIIa and VIIb (1.8 g).

4,8-Di(dicyanomethylene)-4H,8H-benzo[1,2-*c*:4,5-*c*']bis[1.2.5]oxadiazole (VIII). Malonodinitrile (1.4 g, 21.2 mmol) was added to a solution of diketone VI (1.92 g, 10 mmol) in acetic anhydride (20 ml) and the mixture was boiled under reflux for 15 min. The reaction mixture was cooled, the precipitate filtered off, washed with acetic anhydride, then with ether, and dried to give compound VIII (1.12 g).

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