Structure of the Isomers of 1,4-Dinitro-2,3-butanediol

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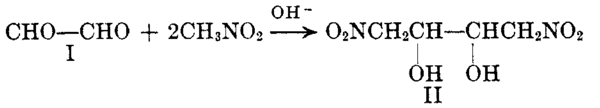
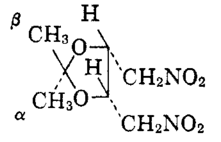
The preparation of the DL and *meso* isomers of 1,4-dinitro-2,3-butanediol is described. The assignment of isomers was obtained by chemically relating the isomers to DL- and *meso*-tartaric acid and by nmr spectral analysis of the acetonides of the isomers. The preparation and nmr spectrum of DL- and *meso*-dimethyl tartrate acetonides and DL- and *meso*-tartramide acetonides are also described.

Novikov, Korsakova, and Babievskii[1] obtained a 40% yield of 1,4-dinitro-2,3-butanediol (II) by condensing nitromethane with glyoxal (I) in the presence of sodium hydroxide.

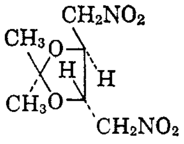


$$\underset{\text{I}}{\text{CHO—CHO}} + 2\text{CH}_3\text{NO}_2 \xrightarrow{\text{OH}^-} \underset{\text{II}}{\text{O}_2\text{NCH}_2\underset{\text{OH}}{\text{CH}}\text{—}\underset{\text{OH}}{\text{CH}}\text{CH}_2\text{NO}_2}$$

Two isomers of the diol were isolated in approximately equal amounts, but the authors gave no structural assignments to the isomers. We repeated this reaction, using potassium hydroxide as the base, and obtained 26.4% of an isomer melting at 135–135.5° and 10% of an isomer melting at 101–102°. The elemental analysis, infrared, and nmr spectra are consistent with the products being isomers of 1,4-dinitro-2,3-butanediol and are undoubtedly the same compounds isolated by Novikov, Korsakova, and Babievskii. *cis*- and *trans*-1,4-dinitro-2,3-butanediol acetonides (IIIa and IIIb) were prepared by refluxing the high-melting and low-melting 1,4-dinitro-2,3-butanediols, respectively, with acetone in the presence of anhydrous copper(II) sulfate. Evidence for the indicated isomer assignment of the acetonides was obtained by nmr spectroscopy. The *cis* isomer



IIIa



IIIb

IIIa, which has the methyl groups at position 2 of the 1,3-dioxolane ring in different environments, shows two methyl resonances, one at $\delta = 1.42$ ppm for β-CH_3 and the other at $\delta = 1.50$ ppm for α-CH_3. The β-CH_3 and α-CH_3 groups are, respectively, *cis* to H, H and $-CH_2NO_2$, $-CH_2NO_2$ at positions 4 and 5 of the 1,3-dioxolane ring. The α-CH_3 protons appear at lower field because of its closer proximity to the two $-CH_2NO_2$ groups, which effectively deshield α-CH_3 more than β-CH_3. The *trans* isomer IIIb, which has its methyl groups at position 2 of the 1,3-dioxolane ring in the same environment, shows only one methyl resonance at $\delta = 1.47$ ppm. Therefore, the high-melting diol is *meso*-1,4-dinitro-2,3-butanediol (IIa) and the low-melting isomer is DL-1,4-dinitro-2,3-butanediol (IIb).

Further evidence for the isomer assignments was obtained by catalytically reducing the DL- and *meso*-1,4-dinitro-2,3-butanediols to the corresponding 1,4-diamino-2,3-butanediols, isolated as their crystalline bissalicylaldehyde Schiff bases, and comparing their infrared spectra with the spectra of DL- and *meso*-1,4-diamino-2,3-butanediol bissalicylaldehyde Schiff bases prepared from DL- and *meso*-tartaric acid as shown in Chart I. The infrared spectrum of *meso*-1,4-diamino-2,3-butanediol bissalicylaldehyde Schiff base (IVa) prepared from *meso*-1,4-dinitro-2,3-butanediol (IIa) was identical with the spectrum of IVa prepared from *meso*-tartaric acid, and the infrared spectrum of the DL isomer IVb prepared from DL-1,4-dinitro-2,3-butanediol (IIb) was identical with the spectrum of IVb prepared from DL-tartaric acid. In addition, the infrared spectrum (KBr) of the DL isomer IVb is very similar to D-1,4-diamino-2,3-butanediol bissalicylaldehyde Schiff base,[2] whereas the *meso* isomer IVa shows some significant differences.

The preparation of *meso*- and DL-1,4-diamino-2,3-butanediol bissalicylaldehyde Schiff bases (IVa and IVb) from *meso*- and DL-tartaric acid warrants further comment. Initially, we attempted to prepare IVa and IVb by the lithium aluminum hydride reduction of *meso*- and DL-tartramide. The complexes formed between the tartramides and lithium aluminum hydride were apparently so insoluble in ether or tetrahydrofuran that no reduction took place. *meso*- and DL-tartramide acetonides (VIIIa and VIIIb), however, were smoothly reduced with lithium aluminum hydride in ether to the corresponding 1,4-diamino-2,3-butanediol acetonides. The acetonides, without isolation, were converted by acid hydrolysis of the isopropylidine group to the 1,4-diamino-2,3-butanediols, isolated as their yellow, crystalline bissalicylaldehyde Schiff bases, IVa and IVb.

The chemical shifts observed in the nmr spectra of the isomeric pairs of acetonides reported in this paper are shown in Table I. A significant aspect of the spectra is the appearance of two methyl resonances in each of the *cis* isomers, whereas the corresponding *trans* isomers show only one methyl resonance. Similar results were obtained by Anet[3] for *cis*- and *trans*-2,2,4,5-tetramethyldioxolane and by Baggett, *et al.*,[4] for some isopropylidine derivatives of polyhydric alcohols. This is a result of the *trans* isomers having their isopropylidine methyl groups in the same environment, whereas the corresponding *cis* isomers have their methyl groups in different environments. The *cis* isomers have one methyl *cis* to nonprotonic substituents at position 4 and 5 of the dioxolane ring, and, because of increased deshielding, its signal appears

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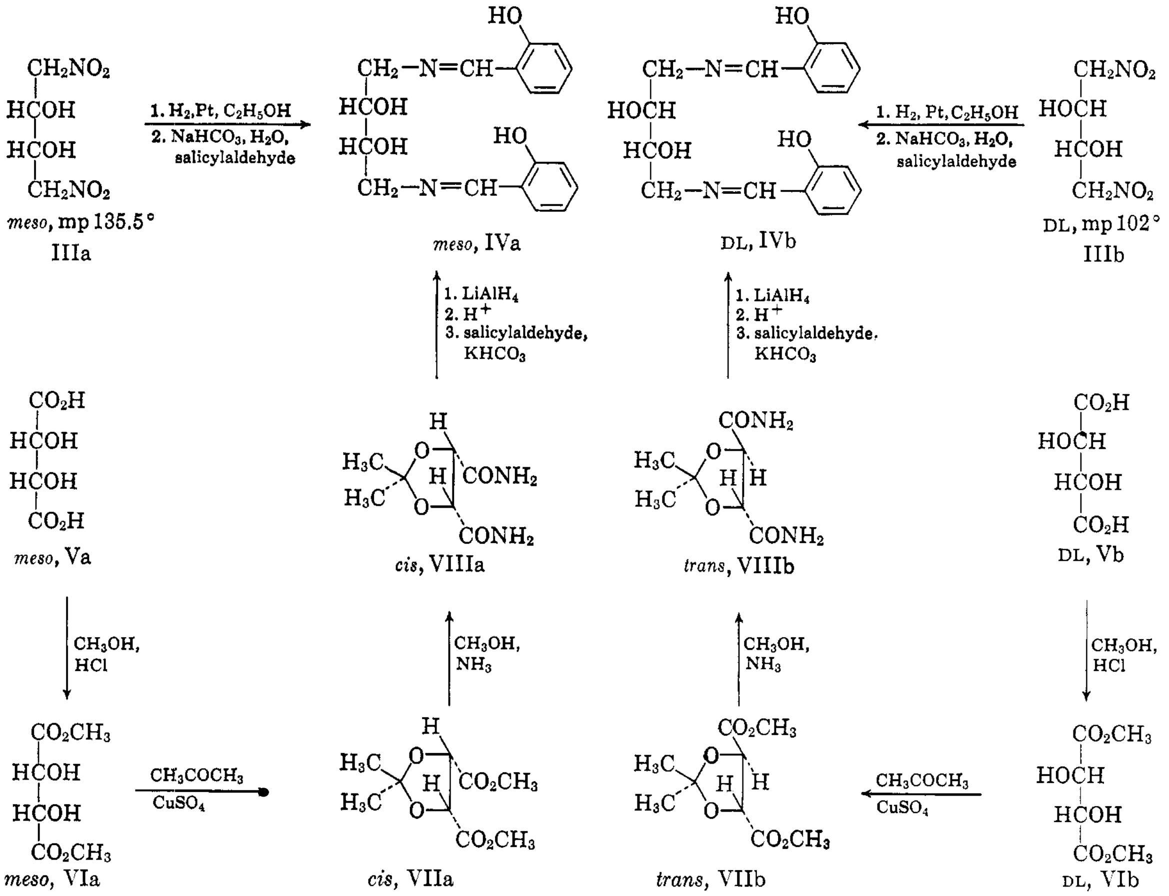
[1] S. S. Novikov, I. S. Korsakova, and K. K. Babievskii, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 882 (1960).

[2] The author is indebted to Dr. M. L. Wolfrom, The Ohio State University, for providing a sample of the optically active isomer. See M. L. Wolfrom, F. Shafizadeh, J. O. Wehrmüller, and R. K. Armstrong, *J. Org. Chem.*, **23**, 571 (1958), for the preparation of this isomer.

[3] F. A. L. Anet, *J. Am. Chem. Soc.*, **84**, 747 (1962).

[4] N. Baggett, K. W. Buck, A. B. Foster, R. Jefferies, B. H. Rees, and J. M. Webber, *J. Chem. Soc.*, 3382 (1965).

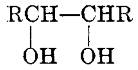
Chart I



at lower field than that for the other methyl which is *cis* to H, H.

The ring-hydrogen methine resonance of the *trans* isomers are shifted to lower field relative to the *cis* isomers. This can be attributed to increased substituent-ring-hydrogen deshielding in the *trans* isomer. The differences between δ_{cis} and δ_{trans} are included in Table I.

The above results appear to be general in nature and should be helpful in assigning structures to *cis* and *trans* acetonides of 1,2-glycols (IX).



$$\underset{\mathrm{OH}}{\mathrm{RCH}}-\underset{\mathrm{OH}}{\mathrm{CHR}}$$

IX

Experimental Section[5]

Preparation of 1,4-Dinitro-2,3-butanediol (II).—Employing a procedure similar to that reported by Novikov, Korsakova, and Babievskii,[1] 145 g (1.0 mole) of 40% glyoxal and 129 g of potassium hydroxide in 120 ml of water were added simultaneously from separate funnels to an ice-cooled mixture of 700 ml of nitromethane and 700 ml of methanol. After dilution with 500 ml of water and acidification with sulfur dioxide gas, the organic layer was separated from the aqueous layer. The aqueous layer was extracted with benzene in a continuous liquid–liquid extractor. All the organic layers were combined, dried over anhydrous sodium sulfate, and concentrated under vacuum. The remaining residue was recrystallized from nitromethane with treatment with Norit to give 47.46 g (26.4%) of *meso*-1,4-dinitro-2,3-butanediol (IIa), mp 133–135°. Recrystallization from nitromethane gave crystals: mp 135–135.5° (lit.[1] mp 134°); ν_{max}^{KBr} 3480 (–OH), 3030, 2975, 2925, 2860 (C–H), 1560, and 1390 cm^{-1} (NO$_2$).

Anal. Calcd for $C_4H_8N_2O_6$: C, 26.67; H, 4.48; N, 15.56. Found: C, 26.94; H, 4.47; N, 15.70.

The nitromethane filtrate was cooled in a Dry Ice–acetone bath to precipitate 22.1 g of solid, mp 80–96.5°. Recrystallization from 1-butanol gave 18.0 g (10%) of DL-1,4-dinitro-2,3-butanediol (IIb), mp 97–101°. An analytical sample, prepared by further recrystallization from the same solvent, had mp 101–102° (lit.[1] mp 89.5–90°); ν_{max}^{KBr} 3460, 3320 (–O–H), 3050, 2995, 2977, 2930 (C–H), 1570 and 1395 cm^{-1} (-NO$_2$).

Anal. Calcd for $C_4H_8N_2O_6$: C, 26.67; H, 4.48; N, 15.56. Found: C, 26.99; H, 4.43; N, 15.44.

Preparation of *cis*-1,4-Dinitro-2,3-butanediol Acetonide (IIIa).—A stirred mixture of 2 g (11.1 mmoles) of *meso*-1,4-dinitro-2,3-butanediol, 6 g of anhydrous copper(II) sulfate, and 30 ml of acetone was heated at reflux for 4 days. The copper(II) sulfate was separated by filtration and washed with acetone. Concentration of the acetone solution afforded 2.20 g of an oily solid. A thin layer chromatogram (benzene–ethyl acetate, 80:20) showed two spots. (The R_f of one was identical with starting diol while the other had a much higher R_f value.) Benzene (20 ml) was added to the oily solid and then cooled. After 2 hr 0.45 g of starting diol was separated by filtration. The benzene filtrate was washed with three 10-ml portions of water, dried over anhydrous sodium sulfate, and concentrated *in vacuo* to give 1.75 g of crystals. Recrystallization from carbon tetrachloride afforded 1.59 g (65.2%) of *cis*-1,4-dinitro-2,3-butanediol acetonide (IIIa), mp 82–84°. An analytical sample prepared by further recrystallization from the same solvent had mp 83–83.5°; ν_{max}^{KBr} 1570, 1390 (NO$_2$), 1180, and 1105 cm^{-1} (C–O).

Anal. Calcd for $C_7H_{12}N_2O_6$: C, 38.18; H, 5.50. Found: C, 38.20; H, 5.43.

Preparation of *trans*-1,4-Dinitro-2,3-butanediol Acetonide (IIIb).—Using the same procedure as described for the preparation of *cis*-1,4-dinitro-2,3-butanediol acetonide, a 30% yield of *trans*-1,4-dinitro-2,3-butanediol acetonide (IIIb) was obtained: mp 87.5–90.5°. The analytical sample was recrystallized from

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(5) The melting points were obtained on a Kofler hot stage and are corrected. The boiling points are uncorrected. The infrared spectra were obtained using a Perkin-Elmer Model 221 spectrophotometer. Thin layer chromatograms were obtained, using silica gel HF. Microanalyses were by Micro-Tech Laboratories, Inc., Skokie, Ill., and Triangle Chemical Laboratories, Inc., Chapel Hill, N. C.

TABLE I

SPECTRA OF SOME ISOPROPYLIDINE DERIVATIVES

Compd	State	Chemical shifts, δ CH$_3$	Chemical shifts, δ CH	$\delta_{cis} - \delta_{trans}$
cis-1,4-Dinitro-2,3-butanediol acetonide[a]	$CDCl_3$	1.42, 1.50	4.96[b]	0.28
trans-1,4-Dinitro-2,3-butanediol acetonide[a]	$CDCl_3$	1.47	4.67[c]	
cis-Dimethyl tartrate acetonide[a]	$CDCl_3$	1.42, 1.65	4.87	0.05
trans-Dimethyl tartrate acetonide[a]	$CDCl_3$	1.50	4.82	
cis-Tartramide acetonide[d]	D_2O	1.45, 1.67	4.90	0.20
trans-Tartramide acetonide[d]	D_2O	1.54	4.70	
cis-2,2,4,5-Tetramethyldioxolane[e]	Neat	1.22, 1.33	4.15	0.77
trans-2,2,4,5-Tetramethyldioxolane[e]	Neat	1.28	3.38	

[a] Measured at 60 Mc, using tetramethylsilane as internal standard. [b] Taken as the midpoint of a distorted triplet. [c] The $-CH_2CO_2$ and ring-hydrogen resonances appeared together as a sharp singlet at $\delta = 4.67$ ppm. [d] Measured at 60 Mc, using 3-trimethylsilyl-1-propanesulfonic acid sodium salt as internal standard. [e] Reference 3.

ethanol: mp 90–92°; $\nu_{\max}^{\text{KBr}}$ 1555, 1398 (NO_2), 1175, and 1120 cm^{-1} (C–O).

Anal. Calcd for $C_7H_{12}N_2O_6$: C, 38.18; H, 5.50. Found: C, 38.41; H, 5.77.

Preparation of *trans*-Dimethyl Tartrate Acetonide (VIIb).—A stirred mixture of 20 g (0.112 mole) of DL-dimethyl tartrate,[6] 33.2 g of anhydrous copper(II) sulfate, and 130 ml of dry acetone was refluxed for 3 days. The copper(II) sulfate was separated by filtration and washed well with acetone. The filtrate and washings were combined and concentrated under vacuum. The liquid obtained was distilled to give 14.6 g (59.5%) of *trans*-dimethyl tartrate acetonide (VIIb): bp 139° (16 mm); $n^{20}\text{D}$ 1.4386; $\nu_{\max}^{CH_2Cl_2}$ 3000, 2965, (C–H), 1760 (C=O), 1387, 1397 ($C-CH_3$), 1220, and 1120 cm^{-1} (C–O).

Anal. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.32; H, 6.35.

Preparation of *cis*-Dimethyl Tartrate Acetonide (VIIa).—The conditions employed for the preparation of *cis*-dimethyl tartrate acetonide were identical with those used for the preparation of *trans*-dimethyl tartrate acetonide. A 58.6% yield of VIIa was obtained: bp 149–150° (18 mm); $n^{20}\text{D}$ 1.4414; $\nu_{\max}^{CH_2Cl_2}$ 2995, 2960 (C–H), 1767 (C=O), 1217, and 1112 cm^{-1} (C–O).

Anal. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47. Found: C, 49.63; H, 6.40.

Preparation of *trans*-Tartramide Acetonide (VIIIb).—A solution of 2.25 g (10.3 mmoles) of *trans*-dimethyl tartrate acetonide was cooled in an ice bath and saturated with dry ammonia gas. The mixture was then stored at 0° overnight. Concentration of the mixture *in vacuo* gave a white solid. Recrystallization from ethanol afforded 1.75 g (90.3%) of VIIIb: mp 178–180°; $\nu_{\max}^{\text{KBr}}$ 3440, 3300, 3200 (NH), 1680, and 1613 cm^{-1} (amide I and II bands).

Anal. Calcd for $C_7H_{12}N_2O_4$: C, 44.67; H, 6.43. Found: C, 44.67; H, 6.48.

Preparation of *cis*-Tartramide Acetonide Hemihydrate (VIIIa).—*cis*-Tartramide acetonide was prepared in the same manner as described for the preparation of *trans*-tartramide acetonide. In order to obtain a good yield, however, a longer reaction time was required. If the reaction mixture was kept at 0° overnight, a 48.7% yield was obtained. If kept at 0° for 7 days, a 98% yield of hemihydrate VIIIa was obtained: mp 162–164° from 95% ethanol; $\nu_{\max}^{\text{KBr}}$ 3370, 3230 (NH_2), 1710, 1605 cm^{-1} (amide I and II bands).

Anal. Calcd for $C_7H_{12}N_2O_4 \cdot 0.5H_2O$: C, 42.63; H, 6.64; N, 14.20. Found: C, 42.74; H, 6.71; N, 14.46.

Preparation of DL-1,4-Diamino-2,3-butanediol Bissalicylaldehyde Schiff Base (IVb) from *trans*-Tartramide Acetonide.—To an ice-cooled suspension–solution of 0.400 g of lithium aluminum hydride in 20 ml of dry ether[7] was added in small portions 0.400 g (2.12 mmoles) of *trans*-tartramide acetonide. After the addition was completed, the reaction mixture was heated at reflux for 3 hr. Ether (30 ml) was added and the excess lithium aluminum hydride was cautiously decomposed by the addition of water. The aqueous layer was separated from the ether layer, saturated with potassium sodium tartrate, and extracted with four 25-ml portions of chloroform. After the addition of 0.1 ml of concentrated hydrochloric acid to the extracts, the chloroform solution was evaporated to dryness on a steam bath. The residue was taken up in 25 ml of water and made alkaline with solid potassium bicarbonate. Salicylaldehyde (0.2 ml) was added and the mixture was heated on the steam bath for 5 min, whereupon a yellow solid formed. When the mixture was cooled overnight, 0.340 g (49%) of DL-1,4-diamino-2,3-butanediol bissalicylaldehyde Schiff base (IVb) was obtained: mp 213–215°. The analytical sample was recrystallized from methanol: mp 214–215°.

Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.82; H, 6.02; N, 8.81.

Preparation of *meso*-1,4-Diamino-2,3-butanediol Bissalicylaldehyde Schiff Base (IVa) from *cis*-Tartramide Acetonide.—Reduction of *cis*-tartramide acetonide hemihydrate with lithium aluminum hydride in the same manner as described for the reduction of *trans*-tartramide acetonide afforded a 34.2% yield of IVa, mp 224–226°. The analytical sample was recrystallized from methanol: mp 229–230°.

Anal. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found: C, 65.65; H, 6.40; N, 8.59.

Preparation of *meso*-1,4-Diamino-2,3-butanediol Bissalicylaldehyde Schiff Base (IVa) from *meso*-1,4-Dinitro-2,3-butanediol.—*meso*-1,4-Dinitro-2,3-butanediol (0.180 g, 0.001 mole) in 3 ml of ethanol was added to a suspension of 0.050 g of prereduced platinum oxide in 10 ml of ethanol. The mixture was hydrogenated at atmospheric pressure until hydrogen ceased to be taken up. The catalyst was separated by filtration, and the filtrate was concentrated to dryness under vacuum. The residue was dissolved in 10 ml of water, and 0.100 g of sodium bicarbonate was added. Then 0.22 ml of salicylaldehyde was added, whereupon a yellow precipitate formed. The mixture was warmed on the steam bath for 5 min and cooled overnight in the refrigerator. Filtration afforded 0.21 g (64%) of IVa, mp 223–225°. Recrystallization from methanol gave yellow crystals, mp 229–230°. A mixture melting point with the *meso* Schiff base obtained from *meso*-tartramide acetonide occurred at 229–230°. The infrared spectrum of the two products were identical.

Preparation of DL-1,4-Diamino-2,3-butanediol Bissalicylaldehyde Schiff Base (IVb) from DL-1,4-Dinitro-2,3-butanediol.—Catalytic reduction of DL-1,4-dinitro-2,3-butanediol as described for *meso*-1,4-dinitro-2,3-butanediol above afforded 0.23 g (70.2%) of IVb, mp 208–211°. Recrystallization from methanol gave yellow crystals, mp 214–215°. A mixture melting point with the DL Schiff base obtained from DL-tartramide acetonide occurred at 215–217°. The infrared spectra of the two products were identical.

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(6) A. Skrabol and L. Hermann, *Monatsch.*, **43**, 633 (1923).

(7) The ether was dried over sodium ribbon.