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Separation and NMR Spectra of *meso*- and DL-Forms of Pentanediols

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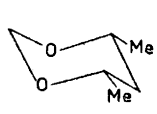
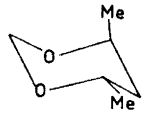
meso- and DL-2,4-Pentanediols and their 3-methyl derivatives were separated after converting them into cyclic formaldehyde or acetaldehyde acetals. The structures of these diastereomeric diols were elucidated by means of their NMR spectra. The ABX_3 spectrum given by *meso*-2,4-pentanediol is fully analyzed by an abx subspectrum.

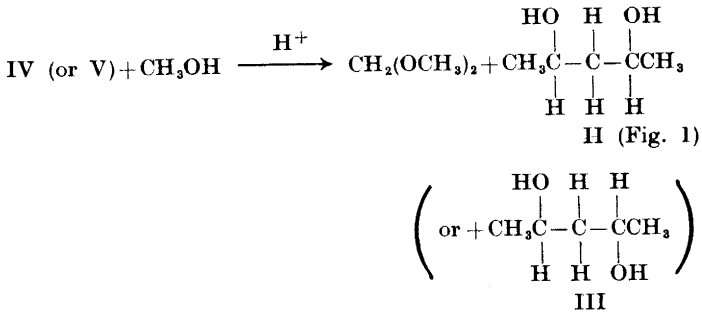
Pritchard and Vollmer [1] have reported the separation of the isomeric 2,4-pentanediols *via* their cyclic sulfite esters. They recorded the NMR spectra of these diols in deuterium oxide. The diastereomeric 3-methyl-2,4-pentanediols have not been resolved earlier. 3-Methyl-2,4-pentanediol has two *meso* forms and one DL form, the cyclic acetals of which have been prepared earlier.[2] *meso*-2,4,5,6-Tetramethyl-1,3-dioxanes cannot be separated,[3] but they can easily be separated from the DL-2,4,5,6-tetramethyl-1,3-dioxanes.

GENERAL

The following direct stereoselective route to the diastereomeric 2,4-pentanediols was used:

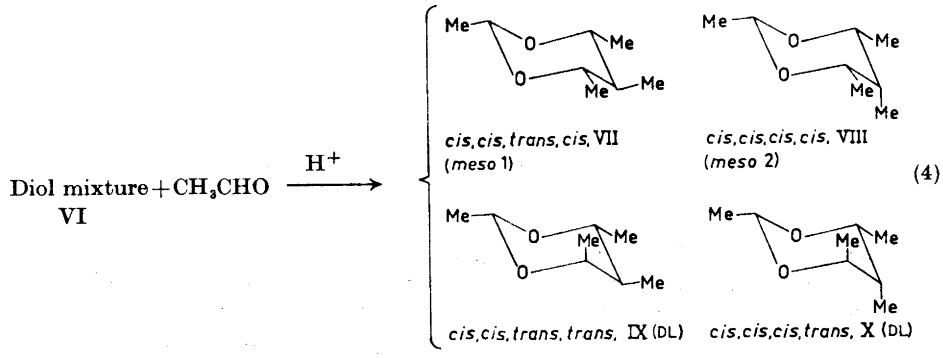
$$\underset{\text{I}}{CH_3COCH_2COCH_3} \xrightarrow[\text{Raney Ni}]{H_2,\ \text{EtOH}} CH_3CHOHCH_2CHOHCH_3 \quad \text{about 1:1 mixture of } \textit{meso}\text{- (II) and DL-2,4-pentanediols (III)} \qquad (1)$$

$$\text{II } (+\text{III}) + CH_2O \xrightarrow{H^+} \underset{\textit{cis}\ (\textit{meso})\ \text{IV}}{\text{  }} + \underset{\textit{trans}\ (\text{DL})\ \text{V}}{\text{  }} \qquad (2)$$



(3)

The diastereomeric 3-methyl-2,4-pentanediols were synthesized *via* their cyclic acetaldehyde acetals:



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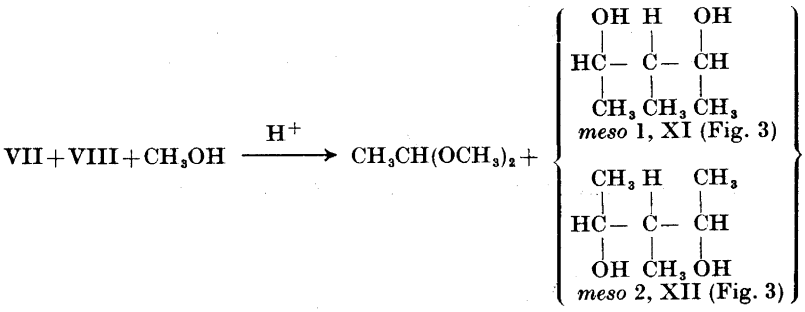

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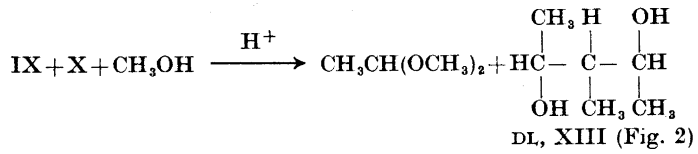

(6)

EXPERIMENTAL

The approximately equimolar mixture of diastereomeric 2,4-pentanediols was prepared from 2,4-pentanedione by catalytic reduction in the presence of Raney nickel (100 atm, 125°C, EtOH).[1,2] B.p. 100°/7 mm Hg, n_D^{20} 1.4330. The yield was 80 %.

The mixture of diastereomeric 3-methyl-2,4-pentanediols was obtained from Fluka AG.

The isomeric 4,6-dimethyl-1,3-dioxanes and 2,4,5,6-tetramethyl-1,3-dioxanes were prepared from the diol mixture as described elsewhere.[2]

meso-2,4-Pentanediol (II) was prepared from *cis*-4,6-dimethyl-1,3-dioxane (IV) by methanolysis. IV (0.895 mole) and methanol (8.95 moles) were added to a flask which contained 6.1 g of *p*-toluenesulfonic acid. The flask was equipped with an efficient column. The mixture was boiled gently so that the dimethoxymethane formed (b.p. 42°C) was slowly distilled off. After the evolution of dimethoxymethane had ceased, the reaction mixture was neutralized with diethylamine and the excess methanol was evaporated off. On fractionation, the remaining syrup yielded 53.4 g (57.3 %) of II. B.p. 109–111°C/18 mm Hg, n_D^{20} 1.4332, d_4^{20} 0.9542. Pritchard and Vollmer [1] reported b.p. 73°/3 mm Hg, n_D^{20} 1.4327. The over-all yield from 2,4-pentanedione was about 18 % (Ref. 1; 30 %). Rerunning the reaction with the recovered IV improves the yield.

DL-2,4-Pentanediol was prepared similarly from *trans*-4,6-dimethyl-1,3-dioxane (V, 0.68 mole). The yield was 68.8 g (97 %). B.p. 110°/18 mm Hg, m.p. 47.5–48.5°C. Pritchard and Vollmer [1] reported b.p. 74°/3 mm Hg, m.p. 48–49°C. The over-all yield from 2,4-pentanedione was about 27 % (Ref. 1; 17 %).

meso-3-Methyl-2,4-pentanediols (XI+XII) were prepared from an unresolvable mixture [3] of *cis*-2,*cis*-4,*trans*-5,*cis*-6- (VII) and *cis*-2,*cis*-4,*cis*-5,*cis*-6-tetramethyl-1,3-dioxanes (VIII) by methanolysis. The method differed from the above procedure in that the boiling point of the formed 1,1-dimethoxymethane is only a few degrees lower than that of methanol and thus the preliminary fractionation was carried out more slowly. The yield was 48 %. B.p. 121–122°/30 mm Hg, n_D^{20} 1.4431, d_4^{20} 0.9571. The proportion of XI was about 30 % according to the NMR spectrum.

DL-3-Methyl-2,4-pentanediol (XIII) was prepared similarly from a mixture of *cis*-2,*cis*-4,*trans*-5,*trans*-6- (IX) and *cis*-2,*cis*-4,*cis*-5,*trans*-6-tetramethyl-1,3-dioxanes (X). The yield was 91 %. B.p. 112°/15 mm Hg, n_D^{20} 1.4421, d_4^{20} 0.9557.

The NMR spectra were recorded on a 60 MHz Perkin-Elmer NMR spectroscope M R 10 at 33.5°C. The solvents were carbon tetrachloride, benzene and pyridine (80 v-%) and tetramethylsilane was used as internal standard.

RESULTS AND DISCUSSION

Separation of the isomeric diols (except the two *meso* forms of 3-methyl-2,4-pentanediol) by fractional distillation of their cyclic formaldehyde or acetaldehyde acetals followed by methanolysis was successful. The conversion of the diol mixtures to cyclic acetal mixtures requires only a simple water-entrainment unit.[2] The *meso* and racemic cyclic acetals can be separated easily (b.p. difference $\geq$10°C) in a Todd precise fractionation assembly. The conversion of these acetals to the isomeric diols by methanolysis is known to occur without change in configuration.[1,2] The over-all yield of pure *meso*- and DL-2,4-pentanediols were 18 and 27 % (30 and 17 % in Ref. 1), respectively.

Pritchard and Vollmer [1] recorded the NMR spectra of isomeric 2,4-pentanediols at 60 MHz in deuterium oxide. Their spectrum for the racemic diol is consistent with our spectrum (Table 1) although we recorded the spectrum using a mixture of benzene and pyridine as solvent. Our spectrum for II differs appreciably from that reported by Pritchard and Vollmer [1] since the *meso* diol gives a fully resolvable ABX_2-type spectrum in pyridine.[4] We have analyzed this spectrum as an (ABX)X system and then calculated

Table 1. The chemical shifts and coupling constants (cps) of DL-2,4-pentanediol (III) and DL-3-methyl-2,4-pentanediol (XIII, Fig. 2).

	ν_{OH}	ν_{2Me}	ν_{3Me}	ν_{4Me}	ν_A	ν_Y	ν_X	J_{XMe}	J_{YMe}	J_{AX}	J_{AY}	Solvent
III[a]	274.8	78.3	—	78.3	100.1	261.2	261.2	6.4	6.4	6.1	6.1	C_6H_6+ C_5H_5N
XIII[b]	343.1 358.4	77.2	58.4	78.2	83.0	245.6	260.5	6.4	6.2	3.0	7.6	C_5H_5N
XIII	—	69.7	50.0	67.7	99.7	224.0	241.5	6.3	6.1	2.8	7.6	CCl_4

[a] Averaged spectrum of two pairs of equivalent conformations.
[b] Average coupling constants due to two rapidly interconverting conformations. $\nu_{TMS}=0$.

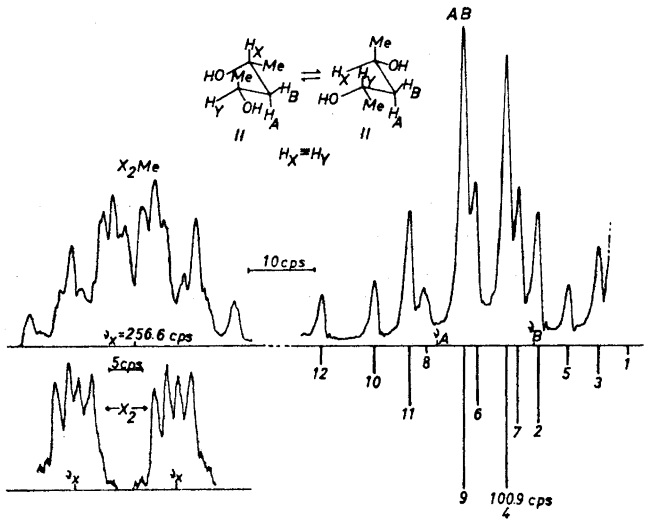

Fig. 1. The calculated and found AB part of the NMR spectrum of *meso*-2,4-pentanediol (II). Also the X_2 part shown before (X_2Me) and after decoupling (X_2).

the theoretical ABX_2 spectrum which is in close agreement with the observed spectrum (Fig. 1 and Table 2). The decoupling of the X_2 or AB part of this spectrum revealed that the coupling constants did not remain constant after and before decoupling (Fig. 1) in accordance with a similar conclusion of Anet *et al.*[5]

The racemic 2,4-pentanediol exists in two pairs of equivalent conformations and consequently its NMR spectrum is an average one (Table 1, and Fig. 1 in Ref. 1). The spectrum of DL-3-methyl-2,4-pentanediol can be fully analyzed although this isomer is also a mixture of two conformations (ab. 1:2) and thus the coupling constants are also averaged (Fig. 2 and Table 1).

Table 2. Chemical shifts and coupling constants (cps) of *meso*-2,4-pentanediol (II) and the calculated and observed frequencies in the AB part of its NMR spectrum. Solvent 80 vol. % C_5H_5N (+some drops of D_2O). See also Fig. 1.

ν_A 111.4, ν_B 96.8, ν_X 256.6, ν_{Me} 77.9.
J_{XMe} 6.2, J_{AB} −13.6, J_{AX} 8.77, J_{BX} 3.83.

The AB part of the spectrum:

Band No.	H	ν_H, calc. cps	ν_H, found cps	Relative intensity
1	B	82.6	— [a]	1.0
2	B	96.2	96.2	10.1
3	B	87.3	87.2	3.6
4	B	100.9	100.9	18.7
5	B	91.85	91.8	2.4
6	B	105.25	105.4	7.9
7	A	99.3	99.3	10.1
8	A	112.9	113.0	1.0
9	A	107.2	107.3	18.7
10	A	120.8	120.8	3.6
11	A	115.45	115.5	7.9
12	A	129.0	128.9	2.4

[a] Obscured by alkyl peaks. $\nu_{TMS}=0$.

Table 3. Chemical shifts and coupling constants of *meso*-3-methyl-2,4-pentanediols (XI and XII, Fig. 3).

	ν_A	ν_X	ν_M [a]	ν_{B_3} [b]	ν_{OH}	J_{XB}	J_{AM}	J_{AX}	Solvent (80 vol.%)
XI	221.3	80	67.5	45.2	292.2	6.7	6.2	7.8±0.2	CCl_4
XI	244.0	90	75.7	53.5	—	6.7	6.2	7.8±0.2	C_5H_5N
XI	227.4	80	72.2	41.4	—	6.7	6.2	7.8±0.2	C_6H_6
XII	239.7	65	67.5	50	292.2	6.7	6.2	2.6±0.2	CCl_4
XII	253.2	85	75.7	65	—	6.7	6.2	2.6±0.2	C_5H_5N
XII	241.5	70	70.7	55	—	6.7	6.2	2.6±0.2	C_6H_6

[a] M means the end methyl groups. [b] B_3 means the 3-methyl group. All values in cps. $\nu_{TMS}=0$.

The spectrum of the approximately 3:7 mixture of XI and XII is shown in Fig. 3. The spectrum of XI is easily analyzed, but that of XII contains an "AB_3" part which is due to the coupling of the protons of the 3-methyl group (B_3) and 3-hydrogen atom (X), since the chemical shifts of the X proton and the B_3 protons differ only about $2J_{XB}$.[4] However, the part A of this spectrum (Fig. 3) can be analyzed by first-order analysis since $J_{AB}=0$ (Table 3).

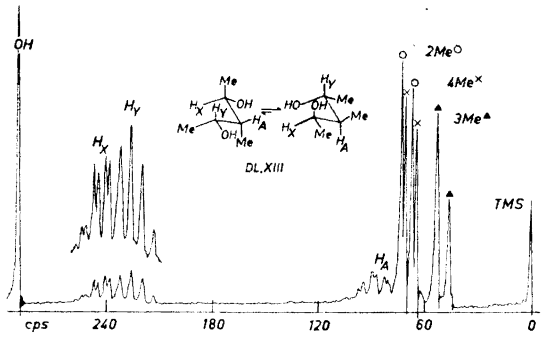

Fig. 2. The NMR spectrum of DL-3-methyl-2,4-pentanediol in CCl_4 (1:4, v/v).

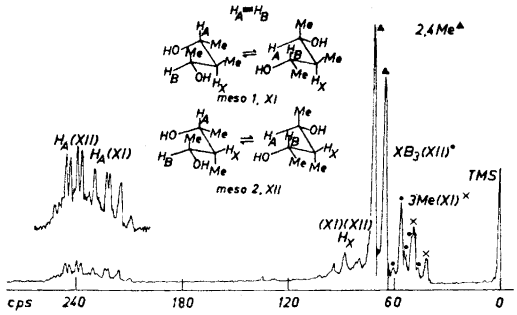

Fig. 3. The NMR spectrum of the approximately 3:7 mixture of *meso*-3-methyl-2,4-pentanediols (XI and XII) in CCl_4 (1:4, v/v).

The recorded spectra are fully consistent with the known configurations of the studied diastereomers and we consider this analysis to provide adequate identification of the isomeric diols.

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