salts from methanolic solution, or by their direct crystallization from aqueous solution. It seems probable that the aqueous reaction conditions will be particularly applicable for the preparation of those higher-carbon deoxynitroalditols that, like 1-deoxy-1-nitro-D-*glycero*-D-*gala*-heptitol and 1-deoxy-1-nitro-D-*erythro*-L-*manno*-octitol, are sparingly soluble in water.

Experimental

1-Deoxy-1-nitro-D-arabitol.—D-Erythrose (0.7 g.), prepared by the method of Perlin and Brice,[3] was dissolved in 2 equivalents of 2 *N* sodium hydroxide containing 2 equivalents of nitromethane. After 30 minutes at room temperature, the reaction mixture was acidified with 8% hydrochloric acid, deionized, and concentrated at reduced pressure to a sirup (0.8 g.). The latter was dissolved in 2 ml. of absolute ethanol and the solution was seeded with 1-deoxy-1-nitro-D-arabitol to yield 78 mg. of the deoxynitropentitol, m.p. 144–145°.[4]

1-Deoxy-1-nitro-D-mannitol.—Five grams of D-arabinose was dissolved in 2 equivalents of 2 *N* sodium hydroxide containing 2 equivalents of nitromethane. After 25 minutes at room temperature, the reaction mixture was acidified with dilute hydrochloric acid, deionized, and concentrated at reduced pressure to a sirup. Fractional crystallization of the latter from 95% ethanol yielded 1.23 g. (17.5%) of crude 1-deoxy-1-nitro-D-mannitol, m.p. 120–130°; 2.0 g. (40%) of crude D-arabinose, m.p. 145–155°; and a few mg. of 1-deoxy-1-nitro-D-glucitol, m.p. 106–107°. Recrystallization of the crude 1-deoxy-1-nitro-D-mannitol from 95% ethanol yielded the pure deoxynitrohexitol,[5] m.p. 132–133°, $[\alpha]^{24}\text{D}$ −6.4° in water, *c* 6.

Wide variations in the reaction conditions with regard to concentration and reaction time did not improve the above yield of 1-deoxy-1-nitro-D-mannitol.

1-Deoxy-1-nitro-D-*glycero*-D-*gala*-heptitol.—A large number of condensations of D-mannose with nitromethane were performed employing from 5 to 10 equivalents of nitromethane, from 0.25 to 2 equivalents of sodium hydroxide (0.08 to 5 *N*), reaction temperatures from 0° to room temperature, and reaction times from 30 minutes to 28 days. The best results were obtained in the following experiment. Five grams of D-mannose was dissolved at room temperature in a mixture containing 1.5 equivalents of 5 *N* sodium hydroxide and 10 equivalents of nitromethane. After 30 minutes, the reaction mixture was cooled to 0° and maintained at this temperature for 15 hours. The mixture then was neutralized with dilute hydrochloric acid and filtered. The product was recrystallized from water, after decolorization, to give 0.73 g. of 1-deoxy-1-nitro-D-*glycero*-D-*gala*-heptitol, m.p. 190–198°. An additional 0.62 g. (total yield, 20%), m.p. 190–198°, was obtained from the combined filtrates by deionization and concentration. Recrystallized from water, the deoxynitroheptitol[6] showed m.p. 197–198° and $[\alpha]^{20}\text{D}$ +2.1° in water, *c* 0.9.

The combined filtrates from the preparation of the deoxynitroheptitol, on treatment with phenylhydrazine and acetic acid, yielded 3.37 g. (45% recovery) of D-mannose phenylhydrazone, m.p. 188–189° dec.

1-Deoxy-1-nitro-D-*erythro*-L-*manno*-octitol.—One gram of D-*glycero*-D-*gala*-heptose in 5 equivalents of nitromethane and 2 equivalents of 5 *N* sodium hydroxide was allowed to stand at room temperature for 48 hours. Filtration then yielded 0.324 g. of crude 1-deoxy-1-nitro-D-*erythro*-L-*manno*-octitol, m.p. 185–195°. Acidification of the filtrate with dilute hydrochloric acid, followed by deionization and concentration, provided an additional 0.217 g. of the deoxynitroöctitol, m.p. 195–200°, for a total, crude yield of 42%. Recrystallization from water raised the m.p. to 202–203°.[7]

Reaction times of 2 or 3 hours at room temperature, with the same concentrations of reactants as above, gave lower yields (*ca.* 30%) of the deoxynitroöctitol.

---

(3) A. S. Perlin and C. Brice, *Can. J. Chem.*, **33**, 1216 (1955).

(4) J. C. Sowden, THIS JOURNAL, **72**, 808 (1950).

(5) J. C. Sowden and H. O. L. Fischer, *ibid.*, **69**, 1963 (1947).

(6) J. C. Sowden and R. Schaffer, *ibid.*, **73**, 4662 (1951).

(7) J. V. Karabinos and C. S. Hudson, *ibid.*, **75**, 4324 (1953), record the m.p. of this substance as 191–192°. However, preparations in this Laboratory using either aqueous sodium hydroxide or sodium methoxide in methanol have all shown the higher m.p. On one occasion, after several recrystallizations from water, we obtained material with m.p. 209–210°. The deoxynitroöctitol apparently is polymorphous, since our product of m.p. 202–203° showed the correct analysis and gave D-*erythro*-L-*manno*-octose in normal fashion and yield when subjected to hydrolysis according to the directions of Karabinos and Hudson.

ST. LOUIS, MISSOURI

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AT THE UNIVERSITY OF OTTAWA AND QUEEN'S UNIVERSITY]

The Configurations of the 3-Methoxycyclohexene Oxides. A Novel Application of Proton Magnetic Resonance Spectroscopy to the Determination of Structure and Configuration[1]

BY R. U. LEMIEUX, R. K. KULLNIG[2] AND R. Y. MOIR

RECEIVED DECEMBER 16, 1957

It was found possible to assign the structures and configurations to two of the diastereoisomeric 1,3-dimethoxy-2-acetoxycyclohexanes on the basis of their proton magnetic resonance spectra and thereby assign configurations to the parent diastereoisomeric 3-methoxycyclohexene oxides. The conclusions thus reached were substantiated by a variety of chemical means.

McRae, Moir and co-workers[3] have reported the diastereoisomeric D,L-3-methoxycyclohexene oxides, but did not provide evidence for their configurations. Methanolysis of the so-called α-oxide with sodium methoxide produced essentially only one product which on treatment with hydriodic acid gave 1α,2β,3α-cyclohexanetriol.[4] Thus, the product of methanolysis appeared to be either Ia or IIa. Similar experiments with the so-called β-oxide[3] produced 1α,2α,3β-cyclohexanetriol and it could be concluded that the product of methanolysis was either IIIa or IVa.

---

(1) Presented in part at the Miami Meeting of the American Chemical Society, April 7–12, 1957.

(2) A portion of this work is to be submitted by R. K. K. as part of a thesis in partial fulfillment of the requirements for the Ph.D. degree at the University of Ottawa.

(3) J. A. McRae, R. Y. Moir, J. W. Haynes and L. G. Ripley, *J. Org. Chem.*, **17**, 1621 (1952).

(4) The system of nomenclature used herein to describe a variety of *meso* and racemic compounds is adopted from the field of steroid chemistry and is similar to that proposed by L. F. Fieser [THIS JOURNAL, **72**, 623 (1950)] for the carbohydrates. The names give no information on absolute configuration since the orientations of the molecules are not specified. The use of the symbol α is given preference over β.

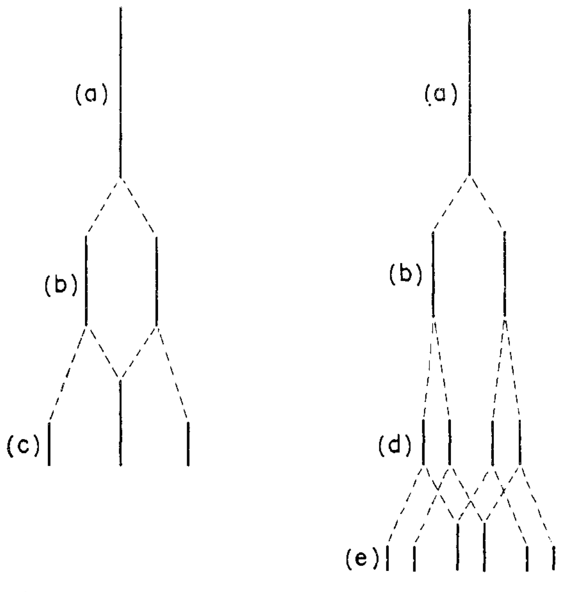
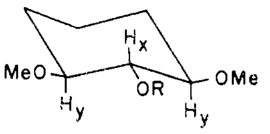


Fig. 1.—Simple graphical approximation (first-approximation perturbation theory) of the type of NMR signals produced by the H_x atoms in compounds Ib, IIb, IIIb and IVb. This procedure yields useful information when the chemical shifts for the coupled hydrogens are large as compared to the coupling constants[6]: (a) signal of H_x if not coupled with other hydrogen atoms; (b) signal of H_x if coupled with H_y only; (c) signal of H_x coupled with two H_y atoms as in Ib; (d) signal of H_x coupled either with H_y and H_z atoms as in IIIb or with H_y and H_b as in IIb and IVb; (e) signal of H_x coupled with H_y, H_b and H_a as in IIb and IVb.

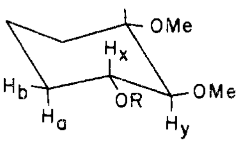
It occurred to us that the structures and configurations of these compounds could be established by application of the configurational effects on proton magnetic resonance (NMR) spectra recently discovered by Lemieux, Kullnig, Bernstein and Schneider.[5] This expectation has been completely fulfilled, so that the work described in this communication is the first example of a new method of determining points of configuration which should gain widespread application in the field of organic chemistry.

Bernstein, Pople and Schneider[6] have recently published the results of a quantum mechanical treatment of the effect of spin–spin coupling interactions on the signals of hydrogen atoms in simple systems. The information provided in this article allows calculations of the structure to be expected for the signals of the H_x atoms in compounds Ib and IIIb. These calculations have been made and the number of resolvable bands in the signals together with their separation and relative intensities were in remarkable agreement with the experimental results. However, the anticipation of the structures of these signals on the basis of the method described in Fig. 1 is sufficient for the present purposes. The more exact treatment of the problem is reserved for the future communication where other problems of the type will be dealt with.

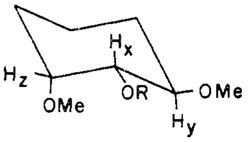
The axial H_x atom of Ib is *strongly* coupled only with the two axial H_y atoms on the neighboring carbon atoms (H_x $(H_y)_2$ systems). Therefore, as shown in Fig. 1, the signal for this atom should appear as a triplet with the intensity of the central band double that of the two side bands. Since these bands should be separated by 6–8 c.p.s.[5] they could be expected to be resolved readily by the high resolution Varian spectrometer at our disposal. In the case of the compound IIIb, the H_x atom is coupled with an axial hydrogen (H_y) and an equatorial hydrogen (H_z) ($H_xH_yH_z$ system). Since the coupling of H_x with H_z is considerably weaker (approximately 3 c.p.s.)[5] than that with H_y, the signal for H_x could be anticipated to be a quartet of bands as shown in Fig. 1. The H_x atoms of compounds IIb and IVb are, however, part of a much more complex system ($H_xH_yH_bH_a$ system). As shown in Fig. 1, the signals for these atoms should be in the form of at least six bands and, therefore, should at best appear as a broad and complex series of low intensity bands. Thus it could be anticipated that the dimethoxyacetoxycyclohexanes Ib and IIIb could be distinguished and these from the isomeric compounds IIb and IVb on the basis of the structure of the signals for the H_x atoms. The fact that an axial methoxy group could be expected[5] to produce a signal at different field than an equatorial methoxy group in the same molecule also could be expected to be useful in these configurational assignments. That is, compounds Ib and IIb could be expected to have a single sharp signal for the hydrogens in the methoxy groups, whereas these hydrogens should produce two more or less resolvable signals in the case of compounds IIIb and IVb.



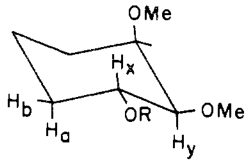
Ia, R = H
Ib, R = Ac



D,L-mixture
IIa, R = H
IIb, R = Ac



D,L-mixture
IIIa, R = H
IIIb, R = Ac



D,L-mixture
IVa, R = H
IVb, R = Ac

The spectra as obtained for the two dimethoxyacetoxycyclohexanes are shown in Figs. 2 and 3. Obviously, the compound obtained from the α-oxide is represented by formula Ib and that obtained from the β-oxide by the formula IIIb. It is to be noted that the signal for the methoxy group hydrogens (175 c.p.s.) of the latter compound is in the form of a doublet as was expected for structure IIIb. These conclusions are consistent with the

---

(5) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein and W. G. Schneider, THIS JOURNAL, **79**, 1005 (1957).

(6) H. J. Bernstein, J. A. Pople and W. G. Schneider, *Can. J. Chem.*, **35**, 65 (1957).

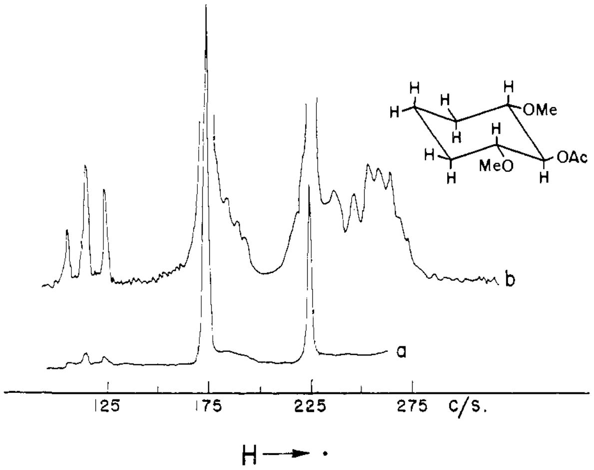


Fig. 2.—Proton magnetic resonance spectrum of 1α,3α-dimethoxy-2β-acetoxycyclohexane (Ib). The upper spectrum was determined at high gain to better demonstrate the signal for the H_x atom at 115 c.p.s.

earlier, indecisive results,[3] mentioned above, of converting the products of the methanolyses of the oxides to known cyclohexanetriols.

Since the opening of an oxide ring by methoxide ion must invert the reacting carbon center, the formation of Ia from the α-oxide requires this epoxide to be D,L-2-*exo*-methoxy-7-oxa-bicyclo[4.1.0]heptane (V) and referred to hereon as the *exo*-oxide. The β-oxide would then have the structure XI as required by the fact that it gave IIIa on methanolysis, and being the *endo* isomer of V will hereon be referred to as the *endo*-oxide.

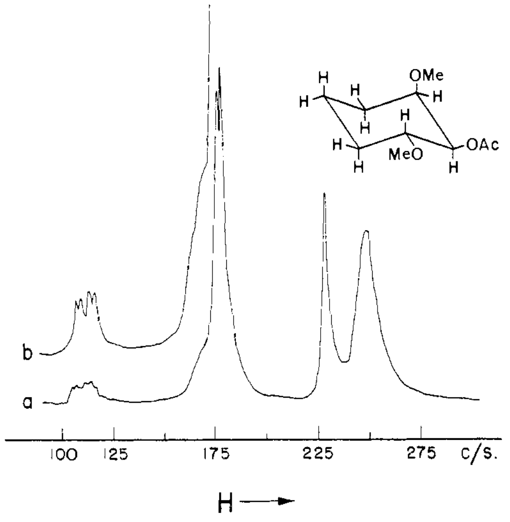


Fig. 3.—Proton magnetic resonance spectrum of 1α,3β-dimethoxy-2α-acetoxycyclohexane (IIIb). The upper spectrum was determined at high gain to better demonstrate the signal for the H_x atom at 112 c.p.s.

The above conclusions regarding the structures of the oxides V and XI have been fully substantiated by independent chemical means as outlined in Fig. 4. The proofs of structure which involve the solvolyses of the acetoxy tosylates VI and XII are based on the observations made by Winstein and Buckles[7] that in the presence of water the intermediate acetoxonium ions (such as VII) lead to orthoacids. Thus, the solvolyses led eventually to the *cis*-glycols VIII and XIII which must have the hydroxyl groups on the same side of the cyclohexane ring as that occupied by the acetoxy groups in the acetoxy tosylates VI and XII. The structure of the acetoxy tosylate VI was established by converting the compound (using the reactions VI → IX → X shown in Fig. 4) to 1α,2β,3α-trimethoxycyclohexane (X). The configuration of the latter compound X was established through its formation on the methylation of Ia. The second acetoxy tosylate XII must have the configuration shown in view of the facts that aqueous acetolysis converted the substance to the methoxydiol XIII and reductive hydrolysis produced a new methoxydiol XIV which is isomeric to the other three possible methoxydiols VIII, IX and XIII. The presence of an α-glycol group in each of compounds VIII, IX, XIII and XIV was confirmed by periodate oxidation.

Both the 3-methoxycyclohexene oxides (V and XI) showed marked preference to undergo ring opening at position 1 when treated with either sodium methoxide or sodium hydroxide. The infrared spectrum of the product obtained on the lithium aluminum hydride reduction of the *exo*-oxide V showed that position 1 was also preferentially attacked by this reagent. Examination of the products formed on the alkaline hydrolyses of the oxides by paper chromatography showed that both the *trans*-glycols IX and XIV were formed in each case. Quantitative analyses based on chromatographic separation of the glycols indicated that these were formed in about 87% yield from the *exo*-oxide V with the α,β,α-isomer IX being formed 10 to 12 times more rapidly than the β,α,α-form XIV. The yield of the glycols was about 75% in the case of the *endo*-oxide XI with attack at position 1 to form the β,α,α-glycol XIV being preferred by a factor of four. The preference shown in these nucleophilic attacks is, in all probability, mainly an electronic effect of the presence of the electronegative methoxy group on carbon-3. If so, it is another example supporting the idea that ease of developing carbonium-ion character in the transition state[8a] is more important in S_N2 reactions than is *polar* facilitation of reagent approach.[8b] Dominance of steric effects in determining the relative reactivities of positions 1 and 2 of the oxides V and XI seems less likely, since different effects would have to be postulated for each oxide. Nevertheless it seems probable that the reaction of the *exo*-oxide V also was influenced by the methoxy group through steric repulsion by this group of the entering methoxide ion when attacking at carbon-2, since this steric effect has been observed in related compounds. Lemieux and Brice[9] have observed a strong *cis* effect in reactions of sugar acetates which they attributed to steric interaction of the C3-acetoxy group with the five-membered ring in acetoxonium ions of the type XVIII. The fact that the hydroxylation of the

---

[7] S. Winstein and R. E. Buckles, This Journal, **64**, 2787 (1942).

[8] (a) A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956); (b) R. G. Kadesch, This Journal, **68**, 41 (1946).

[9] R. U. Lemieux and Carol Brice, *Can. J. Chem.*, **34**, 1006 (1956).

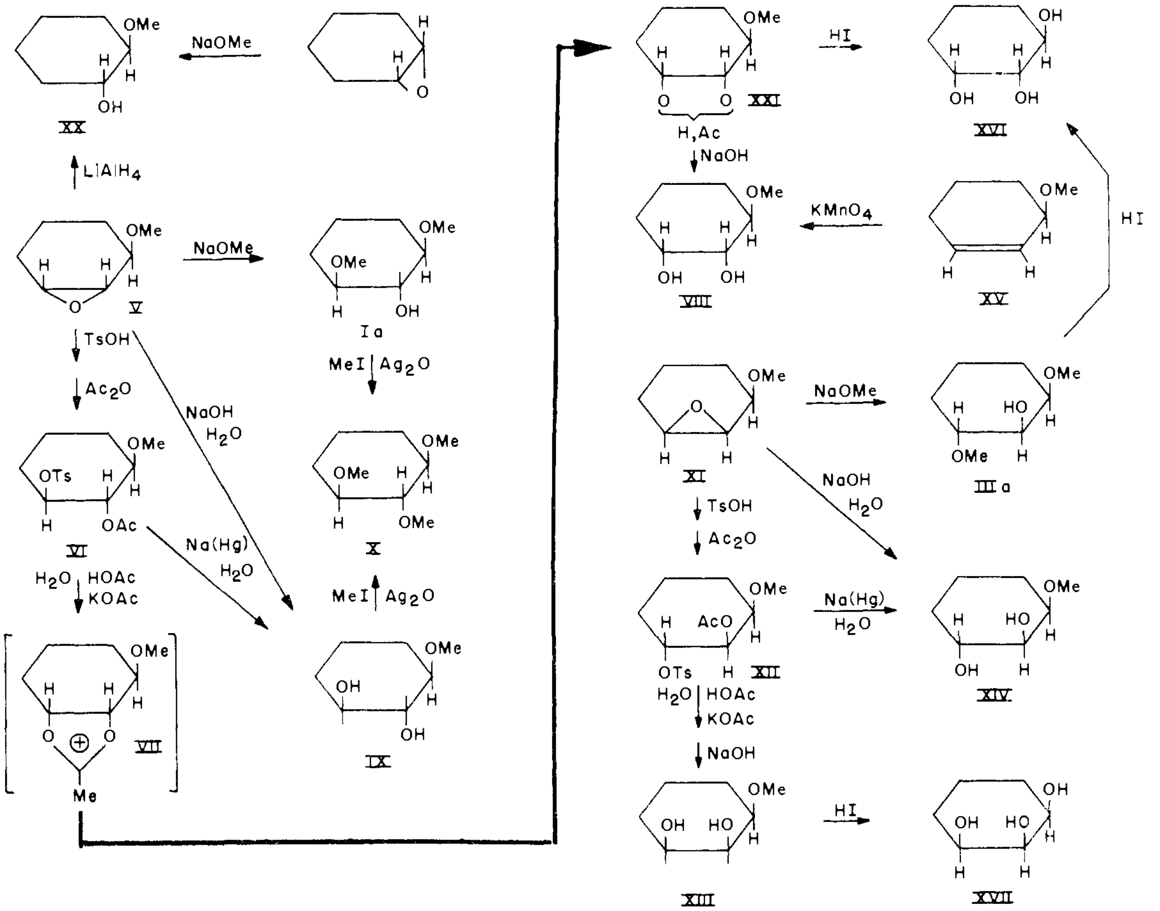
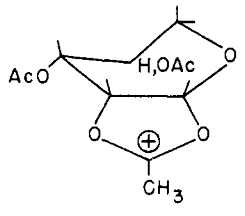
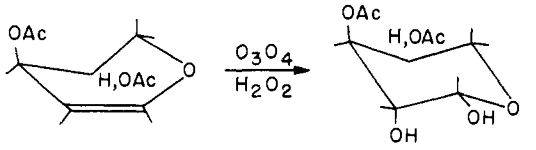


Fig. 4.—The transformations used to establish the configurations of the racemic 3-methoxycyclohexene oxides (V and XI) and related compounds.

acetylated glycals XIX with osmium tetroxide leads to 2,3-*trans*-sugars[10] is believed to arise for the same reason. Thus it was anticipated that the hydroxylation of 3-methoxycylohexene (XV) with permanganate would show a strong preference for the formation of 3β-methoxy-1α,2α-cyclohexanediol (VIII), as did occur. Brunel[11] had provided some evidence that this was the preferred reaction in the hydroxylation of 3-ethoxycyclohexene with permanganate. It seems likely that the *cis*-glycol prepared by Mousseron[12] by the permanganate hydroxylation of 3-methylcyclohexene will prove to have the methyl group and the *cis*-hydroxyl groups in *trans* relationship. Recently Henbest and Wilson[13] have shown the *cis* effect to operate in the epoxidation of 3-alkoxycyclohexenes with perbenzoic acid. The effect is receiving further study in these laboratories.



XVIII



XIX

The demethylation with hydriodic acid of the methoxydiols VIII and XIII in high yields to the corresponding triols XVI and XVII together with the previous experience[3] in the demethylation of the dimethoxy alcohols Ia and IIIa provides experimental support to the previous assumption[3] that demethylation occurs with retention of the configurations of the secondary carbon centers.

Acknowledgments.—The authors wish to thank Drs. H. J. Bernstein and W. G. Schneider of the National Research Council of Canada for the use of their nuclear magnetic resonance spectrometer. The authors gratefully acknowledge grants in aid of the research from the National Research Council of Canada to R. U. L. and from the R. S. McLaughlin Science Research Fund to R. Y. M.

(10) R. C. Hockett, A. C. Sapp and S. R. Millman, This Journal, **63**, 2051 (1941).

(11) L. Brunel, *Compt. rend.*, **150**, 986 (1910).

(12) M. Mousseron, F. Winternitz and G. Combes, *ibid.*, **223**, 909 (1946).

(13) H. B. Henbest and R. A. L. Wilson, *Chemistry & Industry*, 659 (1956).

A few preliminary experiments were performed by R. Y. M. in the laboratories of Drs. C. B. Purves and J. A. McRae.

Experimental

The proton magnetic resonance spectra were all determined on nearly saturated solutions of the compounds in chloroform contained in 5-mm. spinning tubes at room temperature using a Varian V-4300 NMR spectrometer, equipped with a field stabilizer, and operating at a fixed frequency of 40 Mc./sec. The signal for the hydrogen of the chloroform was used as a reference signal to fix the positions of the signals in the field, using the usual side-band technique.

Melting points are corrected except as noted. The demethylations were performed substantially as previously described.[3]

1α,3α-Dimethoxy-2β-acetoxycyclohexane (Ib).—The product [now known to be 1α,3α-dimethoxy-2β-cyclohexanol (Ia)], n^{20}_{D} 1.4590, of the methanolysis of the *exo*-oxide[3] V was acetylated in boiling acetic anhydride containing sodium acetate. The acetate, isolated in the usual way, was completely crystalline. Recrystallization from ligroin gave pure material, m.p. 65.5–66.5°, which possessed the saponification equivalent, 202, expected for the compound Ib.

3α-Methoxy-1α,2β-cyclohexanediol (IX).—The *exo*-oxide V, approximately 100 mg., was treated at 100° for 24 hours in a sealed tube with 0.2 ml. of 10% aqueous sodium hydroxide solution. The reaction mixture was absorbed on 1.2 parts by weight of dry Celite and the resulting powder, packed as a column, was extracted with chloroform.[14] Evaporation of the chloroform left a sirupy residue which was examined by paper chromatography using the xylene–methyl ethyl ketone–water (1:1:1) system and the ammoniacal silver nitrate spray described by Henbest and Wilson.[15] It was observed that the sprayed chromatogram can be kept for record purposes if it is washed with aqueous ammonium hydroxide immediately after the spots have appeared. The R_f values obtained at room temperature for the variety of glycols prepared in this work are listed in Table I. The chromatogram showed the presence of the 1α,2β,3α-compound IX contaminated with a small amount of the 1β,2α,3α-isomer XIV. The same solvent system as was used in the paper chromatography was employed for quantitative separation of the compounds by partition chromatography on Celite.[16] The amounts of the glycols in the zones were determined by titration using sodium metaperiodate.[17] The method was established using known mixtures of the 1,2-cyclohexanediols and was found reliable to ±1%. It was necessary to remove completely the organic solvents prior to the periodate titration. It is noteworthy that considerable losses of the glycols occurred in the *in vacuo* evaporation of the solvents if a large excess of water (40 ml.) was not added. The purity of the compound in each fraction was tested by paper chromatography. These experiments indicated that the yield of 1α,2β,3α-compound IX was 80% and that of the 1β,2α,3α-isomer XIV was 7%.

TABLE I

PAPER CHROMATOGRAPHY OF SOME α-GLYCOLS USING XYLENE–METHYL ETHYL KETONE–WATER (1:1:1)[15]

Compound	R_f
1α,2α-Cyclohexanediol	0.33
1α,2β-Cyclohexanediol	.20
3β-Methoxy-1α,2α-cyclohexanediol (VIII)	.28
3α-Methoxy-1β,2α-cyclohexanediol (XIV)	.22
3α-Methoxy-1α,2α-cyclohexanediol (XIII)	.18
3α-Methoxy-1α,2β-cyclohexanediol (IX)	.15

A sample of the 1α,2β,3α-methoxydiol IX, purified by chromatography, was converted to the di-*O*-*p*-nitrobenzoyl derivative. The derivative, purified by recrystallization from ethyl acetate, melted at 134.0–134.5° (uncor.).

Anal. Calcd. for $C_{21}H_{20}N_2O_9$: C, 56.76; H, 4.54. Found: C, 56.78; H, 4.56.

1α,2β,3α-Trimethoxycyclohexane (X).—The 1α,3α-dimethoxy-2β-cyclohexanol (Ia) (purified by way of the crystalline acetate) was methylated with methyl iodide and silver oxide in the usual manner. The distilled product, n^{25}_{D} 1.4393, possessed no hydroxyl group (infrared) and had the nuclear magnetic resonance spectrum expected for the trimethyl ether X. The number of methoxy groups in the compound was indicated clearly by the presence in the NMR spectrum of two signals for methoxy group hydrogens of relative intensity 1 to 2. A compound of identical infrared spectrum was obtained by methylation of 3α-methoxy-1α,2β-cyclohexanediol (IX) (purified by way of the dibenzoate, m.p. 121.5–122.5° (uncor.)).

Reduction of the *exo*-Oxide V.—The *exo*-oxide,[3] 1.5 g., was allowed to react with 1 g. of lithium aluminum hydride in ethereal solution at the boiling point for about 16 hours. The mixture was acidified and extracted in the usual manner to yield a product which was distilled *in vacuo*. The yield, 400 mg., is not significant due to the accidental loss of about half the material during the isolation. The substance, n^{20}_{D} 1.4626, possessed an infrared spectrum which could be interpreted to mean that it was mainly 2β-methoxy-1α-cyclohexanol (XX). The material gave a 3,5-dinitrobenzoate derivative, m.p. 101.5–103°, which was identical (mixed m.p. and infrared spectra) with that (m.p. 102–104°)[18] prepared from authentic 2β-methoxy-1α-cyclohexanol.

1α-Tosyloxy-2β-acetoxy-3α-methoxycyclohexane (VI).—The dried monohydrate of *p*-toluenesulfonic acid, 16.2 g., was added in portions to a stirred solution of 10.9 g. of the *exo*-oxide V in 100 ml. of dry ether. Crystallization of the product began after 5 hours. The partially crystalline precipitate, after 18 hours, was subjected to a series of fractional crystallizations from ether, ethyl acetate and benzene-petroleum ether to give 7.5 g., 29% yield, of crude crystals melting above 124° as well as a large amount of an uncrystallizable, neutral sirup. The analytical sample had a melting point of 127.5–129° (uncor.) with some decomposition.

Anal. Calcd. for $C_{14}H_{20}O_5S$: C, 56.00; H, 6.67. Found: C, 56.15; H, 6.69.

Acetylation[7] with acetic anhydride and a trace of sulfuric acid gave the crude product, m.p. 86.5–88°, in 96% yield. The pure compound VI, obtained by recrystallization from ether, melted at 88.0–88.8° (uncor.).

Anal. Calcd. for $C_{16}H_{22}O_6S$: C, 56.14; H, 6.43. Found: C, 55.88; H, 6.47.

Reduction of the Tosylate VI.—The tosylate, 410 mg., was dissolved in 20 ml. of 80% aqueous ethanol. Five grams of 5% sodium amalgam[19] was added in small portions to the solution kept at 0°. After standing overnight at about 4° and a further 24 hours at room temperature, the aqueous phase was neutralized with carbon dioxide and evaporated to near dryness. The residue was absorbed on Celite for extraction with chloroform.[14] Evaporation of the chloroform and distillation of the residue at 0.08 mm. pressure gave 65 mg., 38% yield, of an oily substance which possessed an infrared spectrum identical to that of 3α-methoxy-1α,2β-cyclohexanediol (IX). The methoxydiols VIII, IX, XIII and XIV were found to be clearly distinguishable by means of their infrared spectra.

3β-Methoxy-1α,2α-cyclohexanediol (VIII).—(a) The tosylate VI, prepared from the *exo*-oxide V, 2.80 g., was heated under reflux for 6 hours with 1.5 ml. of water, 10 ml. of glacial acetic acid and 1.14 g. of potassium acetate. The mixture was evaporated to a small volume and extracted with chloroform to give a liquid product which was purified by distillation *in vacuo*. Assuming that the product was the monoacetate XXI, the yield was 75%. A sample was converted in 57% yield to the crystalline 1α,2α,3β-triol XVI by treatment with hydriodic acid.[3] The triol was characterized as its tribenzoate, m.p. 183.8–184.6°, and mixed m.p. with an authentic sample.[3]

A second portion of the monoacetate XXI was deacetylated with aqueous sodium hydroxide in the usual manner. Distillation *in vacuo* of the product gave a colorless sirup

---

[14] R. U. Lemieux and R. Charanduk, *Can. J. Chem.*, **29**, 759 (1951).

[15] H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1958 (1957).

[16] R. U. Lemieux, C. T. Bishop and G. E. Pelletier, *Can. J. Chem.*, **34**, 1365 (1956).

[17] P. Fleury and J. Lange, *J. pharm. chim.*, [8] **17**, 107 (1933).

[18] S. Winstein and R. B. Henderson, THIS JOURNAL, **65**, 2196 (1943).

[19] K. Freudenberg and F. Brauns, *Ber.*, **55**, 3233 (1922).

in 83% yield which was converted to the bis-*p*-nitrobenzoate, m.p. 165.2–166.2°, in about 85% yield.

Anal. Calcd. for $C_{21}H_{20}O_9N_2$: C, 56.75; H, 4.54. Found: C, 56.58; H, 4.40.

(b) A solution of 6.55 g. of 3-methoxycyclohexene (XV) in 300 ml. of 66% aqueous ethanol containing 1 ml. of 10% aqueous sodium hydroxide solution was cooled to −60° and a solution of 18.5 g. of potassium permanganate in 300 ml. of water was added at once with stirring. After 90 seconds, an acidified solution of 60 g. of sodium bisulfite in 150 ml. of water was added and the resulting clear solution extracted continuously with ether. Solvent removal gave 4.0 g. of viscous oil (47% yield) which exhibited a positive dinitrophenylhydrazone test for ketones. It is probable that this was due to ketol impurities formed in the permanganate oxidation.[20] Acylation of the oil in pyridine with *p*-nitrobenzoyl chloride gave a 67% yield of the bis-*p*-nitrobenzoate of the 1α,2α,3β-methoxydiol (VIII), m.p. 164.4–165.3°, after three recrystallizations from ethanol. The compound was identical with the *p*-nitrobenzoate described in part (a), as shown by mixed-melting point determination and infrared spectra. Saponification of the *p*-nitrobenzoate gave a substance with the type of physical properties (low melting, highly hygroscopic white needles) reported for the compound VIII by Christian, Gogek and Purves.[21]

1α,3β-Dimethoxy-2α-acetoxycyclohexane (IIIb).—Acetylation as described above of the product [now known to be 1α,3β-dimethoxy-2α-cyclohexanol (IIIa)], $n^{20}D$ 1.4588, obtained without special purification from the methanolysis of the *endo*-oxide[3] XI, gave a liquid, $n^{24.5}D$ 1.4485, which resisted crystallization. The material gave a saponification equivalent, 199, in good agreement with that expected for IIIb. The NMR spectrum of this compound (IIIb), Fig. 3, is a good criterion for assuming that it and the starting material IIIa were reasonably pure compounds, and this assumption was checked as follows. The same direct methanolysis product IIIa, 12.40 g., was converted to its *p*-nitrobenzoate in pyridine in the usual way (45% yield after one recrystallization). After seven crystallizations, the material was pure, m.p. 79.3–80.5°.

Anal. Calcd. for $C_{15}H_{19}O_6N$: C, 58.24; H, 6.19. Found: C, 58.08; H, 6.39.

Saponification of the purified *p*-nitrobenzoate, 3.69 g., gave an oily distillate in a yield of 81.2%. The distillate was then acetylated as above to give the **sterically pure acetate IIIb** as a colorless oil in a yield (after one distillation) of 84.8%.

Anal. Calcd. for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97. Found: C, 59.59; H, 8.89.

The infrared spectrum of the sterically pure acetate was identical with that of the acetate made from the crude product of the methanolysis described above. Part of the sterically pure acetate IIIb, 0.19 g., was demethylated and deacetylated with hydriodic acid to give an 81% yield of distilled crude triol XVI. The melting point, 182.1–184.2°, of the tribenzoyl derivative, after two recrystallizations from ethanol, was undepressed by admixture with an authentic sample of 1α,2α,3β-tribenzoxycyclohexane, previously known as β-pyrogallitol tribenzoate.[3] Together with the previous work,[3] this section shows that the methanolysis of the *endo*-oxide occurred overwhelmingly at the position remote from the methoxyl group.

3α-Methoxy-1β,2α-cyclohexanediol (XIV).—The *endo*-oxide XI, approximately 150 mg., was hydrolyzed with aqueous sodium hydroxide and the product was isolated in the same manner as described above for the *exo*-isomer. Partition chromatography on Celite with subsequent periodate titration of the isolated fractions showed the product to contain the 3α,1β,2α-methoxydiol XIV, 60% yield, and the 3α,1α,2β-methoxydiol IX, 15% yield. A sample of the 3α,1β,2α-methoxydiol XIV was isolated by preparative partition chromatography.[16] On distillation, *in vacuo*, the compound crystallized, m.p. 50.5–52°. The substance possessed an infrared spectrum clearly different from those of its isomers (VIII, IX and XIII) and consumed the expected amount of sodium periodate. The bis-*p*-nitrobenzoate melted at 142.5–143.5° (uncor.).

Anal. Calcd. for $C_{21}H_{20}N_2O_9$: C, 56.76; H, 4.54. Found: C, 56.53; H, 4.58.

1β-Tosyloxy-2α-acetoxy-3α-methoxycyclohexane (XII).—Finely ground and dried *p*-toluenesulfonic acid monohydrate, 13.0 g., was added to a cooled solution of 10.2 g. of the *endo*-oxide XI in 59 ml. of dry ether. The solution was kept at 0° for 41 hours. Removal of the ether followed by acetylation with 33 ml. of acetic anhydride and a trace of sulfuric acid, led to the isolation of 15.4 g. (56.6% yield) of crystalline solid, as well as 7.2 g. of an uncrystallizable sirup. Two recrystallizations from ether gave pure XII, 11.5 g., m.p. 81.5–82.6°.

Anal. Calcd. for $C_{16}H_{22}O_6S$: C, 56.12; H, 6.48. Found: C, 56.31, 56.13; H, 6.45, 6.36.

Reduction of the Tosylate XII.—The tosylate, 368 mg., was converted using sodium amalgam, as described above for the reduction of the isomeric tosylate VI, in 49% yield to a substance identical (infrared spectra) to the 3α 1β,2α-methoxydiol XIV.

3α-Methoxy-1α,2α-cyclohexanediol (XIII).—The tosylate XII, prepared from the *endo*-oxide XI, 2.05 g., was heated under reflux for 6.5 hours with 1.6 ml. of water, 9 ml. of acetic acid and 0.83 g. of potassium acetate. The distilled product, a colorless oil, isolated in the manner described above, weighed 1.00 g., a yield of 89% assuming that it was a monoacetate of XIII. A portion of the product, 0.795 g., was saponified to give an 85% yield of distilled glycol. Part of the glycol was recrystallized to give 0.317 g. of colorless crystals, m.p. 67.8–70.4°. Two more recrystallizations, first from acetone and then from ligroin, raised the melting point to 69.2–70.6°. The material did not depress the melting point of an authentic sample of XIII made from pyrogallol.[21] The remainder of the crude glycol, 114 mg., was converted to the bis-*p*-nitrobenzoyl derivative, m.p. 205.7–207.0°, in 83.3% yield after one recrystallization from ethanol. A second recrystallization gave the pure material, m.p. 205.8–206.5°.

Anal. Calcd. for $C_{21}H_{20}O_9N_2$: C, 56.75; H, 4.54. Found: C, 56.96; H, 4.54.

The bis-*p*-nitrobenzoate of an authentic sample of XIII and the above compound were identical (mixed melting point and infrared spectra).

The above described monoacetate (?) of XIII was demethylated and deacetylated with hydriodic acid to yield 1α,2α,3α-cyclohexanetriol (XVII), m.p. 146.2–147.0°, in 84% yield. The triol and its tribenzoyl derivative, m.p. 138.7–139.7°, were identified by mixture melting point determinations with authentic samples.[21–23]

OTTAWA 1, ONTARIO
KINGSTON, ONTARIO

---

[20] R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955).

[21] W. R. Christian, C. J. Gogek and C. B. Purves, *ibid.*, **29**, 911 (1951).

[22] H. Lindemann and A. de Lange, *Ann.*, **483**, 31 (1930).

[23] T. Posternak and F. Ravenna, *Helv. Chim. Acta*, **30**, 441 (1947).