81. *Alicyclic Glycols. Part X.** *1 : 4-Bishydroxymethyl*cyclo*hexane.*

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The configurations of the stereoisomers of this diol have been confirmed by preparation of the *cis*-isomer by reduction of dimethyl *cis*-hexahydroterephthalate with lithium aluminium hydride. Some reactions of the methanesulphonates and toluene-*p*-sulphonates are described. Attempts to prepare an intramolecular anhydride, analogous to those obtained from the 1 : 2- and 1 : 3-isomers (Parts VIII and IX *) were unsuccessful. Alkaline hydrolysis of the *cis*- or *trans*-dimethanesulphonate, although resulting chiefly in substitution, also gives rise to some elimination, to yield 4-methylene*cyclo*hexylmethanol.

The 1 : 4-bishydroxymethyl*cyclo*hexanes (I) were first prepared by Malachowski, Wasowska, Jóźkiewcz, Adamiczka, and Zimmerman-Pasternak (*Ber.*, 1938, **71**, 759) by reduction of diethyl hexahydroterephthalate with sodium and alcohol. From either the *cis*- or the *trans*-hexahydro-ester they obtained a stereoisomeric mixture of diols, which were separated by fractional crystallisation of the dibenzoates and hydrolysis of these to give the *cis*- and the *trans*-diol, m. p. 43° and 67°, respectively. The configurations were related to those of the corresponding diamines, which in turn were rigorously correlated with those of the hexahydro-acids. The diol has also been obtained, again as a mixture of stereoisomers, by high-temperature hydrogenation of the hexahydro-ester over a chromite catalyst (U.S.P. 2,105,664).

In the present work the diols were prepared by the method of Malachowski *et al.*, except that they were regenerated from the dibenzoates more conveniently, and in almost quantitative yield, by catalytic solvolysis with methanolic sodium methoxide, rather than by alkaline hydrolysis. The *cis*-isomer was also obtained by reduction of dimethyl *cis*-hexahydroterephthalate with lithium aluminium hydride. Since this method of reduction is known to occur with complete retention of configuration (see Parts VIII and IX, *J.*, 1953, 389, and *loc. cit.*), this provides independent proof of the configurations of the diols, because those of the hexahydroterephthalic acids are known with certainty (Mills and Keats, *J.*, 1935, 1373).

The diols were characterised by four derivatives from each, the melting points of the *trans*-compounds all being higher than those of their *cis*-isomers. The *trans*-diol also gave a solid diacetate. The dimethanesulphonates (II) reacted smoothly with sodium iodide in boiling acetone to give the corresponding *cis*- or *trans*-di-iodide (III), the latter being solid. The *trans*-ditoluene-*p*-sulphonate with lithium bromide in ethanol gave the *trans*-dibromide, m. p. 55°, previously prepared by Malachowski *et al.* from the diol and hydrobromic acid.

In Parts VIII and IX (*locc. cit.*) it was shown that intramolecular ethers are formed from both the *cis*- and the *trans*-1 : 2-bishydroxymethyl*cyclo*hexane, but only from the *cis*-1 : 3-isomer. Steric considerations make it clear that with the 1 : 4-compounds a cyclic oxide (IV) could only be derived from the *cis*-form, and it would necessarily be of the boat conformation (a similar structure must apply to the anhydride of *cis*-hexahydroterephthalic acid). Compounds containing seven-membered oxide rings are uncommon, and attempts to prepare them sometimes result in the formation of isomers containing smaller rings. Thus Franke and Kroupa (*Monatsh.*, 1936, **69**, 167) found that dehydration of hexane-1 : 6-diol with 50% sulphuric acid gave a mixture of 2-ethyltetrahydrofuran, 2-methyltetrahydropyran, and hexamethylene oxide, in which the first two predominated; pure hexamethylene oxide was later obtained as a by-product of the action of hydrobromic acid on hexane-1 : 6-diol (Müller and Vanc, *Ber.*, 1944, **77**, 669). Wittig and Pook (*Ber.*, 1937, **70**, 2485) found that dehydration of the *cis*- and the *trans*-tetraphenyl-substituted diol (V) with sulphuric acid in acetic acid gave the unsaturated hydrocarbon (VI), though in this case the tertiary nature of both hydroxyl groups probably favours the elimination. On the other hand, diols of the type (VII; R = H, Me, or Ph), in which olefin-formation is

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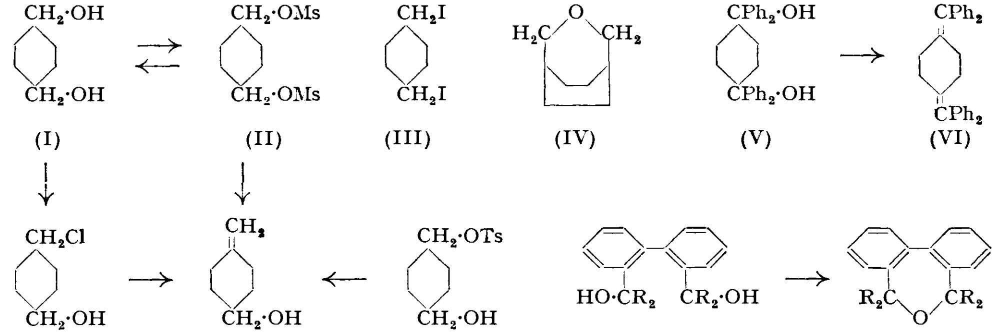
* Part IX, preceding paper.

impossible, are readily dehydrated to the corresponding oxides (VIII) (Wittig and Petri, *Annalen,* 1933, **505**, 17; Bennett and Wain, *J.*, 1936, 1114; Hall and Turner, *J.*, 1951, 3072).



(Ms = $CH_3·SO_2$; Ts = *p*-$C_6H_4Me·SO_2$·.)

In view of these facts, and of the results obtained with the 1 : 3-isomers (Part IX, *loc. cit.*), attention was concentrated on the hydrolysis of the mono- and di-esters of the diol, rather than on methods involving direct dehydration, and although cyclisation was likely to occur only in the *cis*-series, the *trans*-compounds were also studied for comparative purposes. Hydrolysis of the *cis*- or the *trans*-dimethanesulphonate (II) with aqueous potassium hydroxide gave the corresponding diol as the major product, but a small amount of a lower-boiling liquid was also formed. The latter, although having the correct composition for the expected cyclic oxide (IV), $C_8H_{14}O$, contained one double bond (quantitative hydrogenation), a hydroxyl group (3 : 5-dinitrobenzoate) and an exocyclic methylene group (evolution of formaldehyde on ozonolysis), and was therefore 4-methylene*cyclo*hexylmethanol (IX). Its formation is of interest because it arises from the unusual process of elimination from a primary methanesulphonate.

Monoesterification of the *cis*- and the *trans*-diol was carried out under mild conditions by slow addition of 1 mol. of toluene-*p*-sulphonyl chloride to the diol in chloroform–pyridine at 0°. The resulting liquid monotoluene-*p*-sulphonates were characterised as the solid *cis*-*p*-nitrobenzoate–toluene-*p*-sulphonate and *trans*-methanesulphonate–toluene-*p*-sulphonate. Treatment of the *cis*-monotoluene-*p*-sulphonate (X) with boiling 2 : 6-lutidine, according to the method used by Reynolds and Kenyon (*J. Amer. Chem. Soc.*, 1950, **72**, 1593; U.S.P. 2,544,899) for the formation of tetrahydro-furan and -pyran rings, gave only the unsaturated alcohol (IX), identified as the 3 : 5-dinitrobenzoate. Hydrolysis of the *trans*-monotoluene-*p*-sulphonate with aqueous sodium hydroxide gave the *trans*-diol and a small amount of unsaturated material.

When heated with a limited amount of fuming hydrochloric acid, the *trans*-diol gave 4-chloromethyl*cyclo*hexylmethanol (XI), characterised as the crystalline *p*-nitrobenzoate; treatment of this monochloride with aqueous sodium hydroxide gave the *trans*-diol and unsaturated material, probably mainly (IX).

The formation of (IX) in our attempts to form a cyclic oxide is of interest in view of the results of Malachowski *et al.* (*loc. cit.*) : in the hope of obtaining a cyclic imine analogous to (IV) they heated the hydrochloride of the diamine corresponding to *cis*-(I), but obtained only 4-methylene*cyclo*hexylmethylamine, the amino-analogue of (IX).

EXPERIMENTAL

Diethyl Hexahydroterephthalate.—Diethyl terephthalate (49 g.) in ethanol (400 c.c.) was hydrogenated over Raney nickel (5 g.) at 200°/100 atm. Distillation gave the crude hexahydro-ester (47 g.), b. p. 75—115° (mainly 105—115°)/0·4 mm., n_D^{18} 1·4615.

Dimethyl cis-*Hexahydroterephthalate.*—The crude hexahydro-ester was hydrolysed by boiling aqueous-alcoholic sodium hydroxide, and the solution was acidified and steam-distilled to remove hydrogenolysis products; the hexahydro-acid was then isolated from the aqueous solution by continuous ether-extraction. The *cis*-acid, m. p. 160—161° (recorded m. p.s vary from 161—162° to 170—171°), was separated from a small quantity of *trans*-acid by crystallisation from chloroform (in which the latter is insoluble) and converted into the dimethyl ester, b. p. 110°/1 mm., n_D^{16} 1·4595, by methanol and sulphuric acid (cf. Baeyer, *Annalen*, 1888, **245**, 174).

1 : 4-*Bishydroxymethyl*cyclo*hexane*.—(i) Crude diethyl hexahydroterephthalate was reduced with sodium in alcohol according to Malachowski *et al.* (*loc. cit.*). The crude diol was benzoylated in pyridine, and the dibenzoates separated by fractional crystallisation from methanol and acetone into the *trans*-, m. p. 125°, and the *cis*-isomer, m. p. 84°.

The *cis*-dibenzoate (15·5 g.) was boiled under reflux for 4 hours in dry methanol (250 c.c.) containing sodium (0·2 g.). The solution was then steam-distilled, and the diol was isolated by continuous extraction of the residual aqueous solution with ether. Evaporation of the dried (Na_2SO_4) extract gave the *cis*-diol (6 g., 96%) as a non-crystallisable oil. Malachowski *et al.* (*loc. cit.*) reported m. p. 43°. The *trans*-dibenzoate (69 g.) in dry methanol (600 c.c.) containing sodium (0·2 g.) similarly gave the *trans*-diol (28 g., 99%), m. p. 62—64°, raised to 66° by crystallization from anhydrous ether. Malachowski *et al.* (*loc. cit.*) gave m. p. 67°.

(ii) Dimethyl *cis*-hexahydroterephthalate (4·1 g.) in dry ether (30 c.c.) was added slowly, with stirring, to a cooled solution of lithium aluminium hydride (1 g.) in dry ether (50 c.c.). After an hour, dilute sulphuric acid was added until, after shaking, no solid remained, and the ethereal layer was separated. The aqueous layer was continuously extracted with ether overnight, and the combined ethereal solutions were dried (K_2CO_3) and evaporated to give the *cis*-diol (2·7 g., 91%) as an oil; benzoylation of a portion gave the dibenzoate, m. p. and mixed m. p. 84°.

Derivatives of cis-1 : 4-*Bishydroxymethyl*cyclo*hexane*.—The *cis*-diol (0·5 g.), treated with toluene-*p*-sulphonyl chloride (1·45 g.) in pyridine (5 c.c.) for 20 hours at 0°, followed by precipitation with ice, gave the *ditoluene*-p-*sulphonate* (0·62 g., 40%), which crystallised from methanol in needles, m. p. 95° (Found : C, 58·3; H, 6·3; S, 13·9. $C_{22}H_{28}O_6S_2$ requires C, 58·4; H, 6·2; S, 14·2%). Similarly prepared, the *dimethanesulphonate* (74%) formed needles, m. p. 69°, from methanol (Found : C, 40·2; H, 6·75; S, 21·2. $C_{10}H_{20}O_6S_2$ requires C, 40·0; H, 6·7; S, 21·35%). The *cis*-diol (0·5 g.) and phenyl *iso*cyanate (1 g.), heated for 1 hour at 100°, gave the *bisphenylurethane* (0·95 g., 72%), which crystallised from benzene-light petroleum (b. p. 60—80°) in needles, m. p. 147—148° (Found : C, 69·2; H, 7·1; N, 7·3. $C_{22}H_{26}O_4N_2$ requires C, 69·1; H, 6·85; N, 7·3%).

Derivatives of trans-1 : 4-*Bishydroxymethyl*cyclo*hexane*.—Under conditions described for the *cis*-isomer, there were obtained the *ditoluene*-p-*sulphonate* (77%), needles, m. p. 162—163° (Found : C, 58·7; H; 6·4, S, 13·5%), the *dimethanesulphonate* (71%), needles, m. p. 158° (Found : C, 40·2; H, 6·9; S, 21·05%), and the *bisphenylurethane* (70%), plates, m. p. 197° (Found : C, 69·0; H, 6·5; N, 7·6%), all from acetone.

The *trans*-diol (pyridine–acetic anhydride) gave the *diacetate* (55%), needles, m. p. 70°, from aqueous methanol (Found : C, 63·2; H, 8·8. $C_{12}H_{20}O_4$ requires C, 63·2; H, 8·8%).

1 : 4-*Bisiodomethyl*cyclo*hexanes*.—(i) The *cis*-dimethanesulphonate (1 g.) was refluxed for 16 hours in acetone (25 c.c.), containing sodium iodide (2·5 g.). The precipitated sodium methanesulphonate (0·9 g.) was removed, and the filtrate evaporated. Water was added to the residue, and the iodide extracted into chloroform and dried (Na_2SO_4). Removal of solvent followed by distillation of the residual oil gave the cis-*di-iodide* (0·5 g., 41%) as a yellow liquid, b. p. 103—105°/10^{-4} mm., n_D^{29} 1·6082 (Found : C, 27·1; H, 4·1; I, 69·3. $C_8H_{14}I_2$ requires C, 26·4; H, 3·9; I, 69·7%).

(ii) The *trans*-dimethanesulphonate (0·35 g.) similarly gave the trans-*di-iodide* (0·4 g., 94%), which, however, solidified on the addition of water; it crystallised from methanol as fine needles, m. p. 77—78° (Found : C, 26·5; H, 4·0; I, 69·9%).

trans-1 : 4-*Bisbromomethyl*cyclo*hexane*.—The *trans*-ditoluene-*p*-sulphonate (0·25 g.) was refluxed for 16 hours in ethanol (10 c.c.) containing lithium bromide (0·2 g.). Ethanol was distilled off, and water added to precipitate a solid, which on crystallisation from aqueous methanol gave the *trans*-dibromide (0·1 g.), m. p. 55°. Malachowski *et al.* (*loc. cit.*) give m. p. 55°.

Hydrolysis of the trans-*Dimethanesulphonate*.—The dimethanesulphonate (11·5 g.) was boiled under reflux for 5 hours with 16% aqueous potassium hydroxide (50 c.c.), and the solution was then steam-distilled. The distillate was extracted with ether, dried (Na_2SO_4), and evaporated to give 4-*methylene*cyclo*hexylmethanol* (0·4 g.), b. p. 128—130°/57 mm., n_D^{19} 1·4825 (Found : C, 76·3; H, 11·1%; ╒0·95 by catalytic hydrogenation. $C_8H_{14}O$ requires C, 76·1; H, 11·2%; ╒1·0). The 3 : 5-*dinitrobenzoate* crystallised from methanol in needles, m. p. 97—98° (Found : C, 55·9; H, 5·0; N, 8·6. $C_{15}H_{16}O_6N_2$ requires C, 56·2; H, 5·0; N, 8·75%). The residue from the steam-distillation was continuously extracted with ether to give the *trans*-diol (4 g., 73%), identified as ditoluene-*p*-sulphonate, m. p. and mixed m. p. 163°.

Hydrolysis of the cis-*Dimethanesulphonate.*—The dimethanesulphonate (1·1 g.), similarly hydrolysed, gave 4-methylene*cyclo*hexylmethanol (20 mg.) (3 : 5-dinitrobenzoate, m. p. and mixed m. p. 97—98°), and *cis*-diol (0·3 g.).

Ozonolysis of 4-*Methylene*cyclo*hexylmethanol.*—The alcohol (0·25 g.) in acetic acid (10 c.c.) was treated with ozonised oxygen for 15 minutes; absorption had then ceased. Zinc dust (2 g.) was added, and the mixture steam-distilled into aqueous 2 : 4-dinitrophenylhydrazine sulphate. The yellow precipitate was collected and chromatographed on alumina from benzene, to give impure formaldehyde 2 : 4-dinitrophenylhydrazone (70 mg.), m. p. 155°. The m. p. could not be raised by further treatment, but it was not depressed on admixture with an authentic sample, m. p. 165° (Found : C, 40·7; H, 3·2; N, 25·4. Calc. for $C_7H_6O_4N_4$: C, 40·0; H, 2·9; N, 26·7%). Light absorption : max. 3440 Å, ε 18,900 (in $CHCl_3$).

Monotoluene-p-*sulphonates of* 1 : 4-*Bishydroxymethyl*cyclo*hexane.*—(i) The *cis*-diol (3 g.), in chloroform–pyridine (1 : 1; 50 c.c.), was cooled to 0° and treated with toluene-*p*-sulphonyl chloride (4 g.) in the same solvent (50 c.c.), dropwise, with stirring, during 4 hours. Chloroform and pyridine were then removed under reduced pressure below 35° and the residue was dissolved in chloroform and washed with dilute sulphuric acid, aqueous hydrogen sodium carbonate, and water. After being dried (Na_2SO_4), the chloroform was removed, and the residue dissolved in a small volume of methanol and cooled to 0°. After filtration from a small quantity of ditoluene-*p*-sulphonate, removal of methanol gave the crude cis-*monotoluene*-p-*sulphonate* (3·1 g.) as a viscous yellow oil (Found : S, 9·05. $C_{15}H_{22}O_4S$ requires S, 10·7%). Reaction of a portion with *p*-nitrobenzoyl chloride in pyridine gave the cis-p-*nitrobenzoate–toluene*-p-*sulphonate*, needles (from methanol), m. p. 81° (Found : C, 59·6; H, 6·1; N, 3·2. $C_{22}H_{25}O_7NS$ requires C, 59·0; H, 5·6; N, 3·1%).

(ii) Interaction of the *trans*-diol (5 g.) with toluene-*p*-sulphonyl chloride (6·6 g.) under similar conditions gave the trans-*monotoluene*-p-*sulphonate* (2·9 g.) as a yellow oil (Found: S, 10·1%). Methanesulphonyl chloride in pyridine then gave the trans-*methanesulphonate–toluene*-p-*sulphonate*, needles (from methanol), m. p. 105° (Found : C, 51·1; H, 6·2; S, 17·0. $C_{16}H_{24}O_6S_2$ requires C, 51·0; H, 6·4; S, 17·0%).

Reaction of the cis-*Monotoluene*-p-*sulphonate with* 2 : 6-*Lutidine.*—The monotoluene-*p*-sulphonate (2·5 g.) and 2 : 6-lutidine (7 c.c.) were boiled under reflux for 2 hours, the initially homogeneous solution then having separated into two layers. Excess of concentrated hydrochloric acid was added, with cooling, and the solution extracted with ether. Evaporation of the dried (Na_2SO_4) extracts followed by distillation gave a strongly unsaturated product (0·3 g.), b. p. 120—130°/25 mm., n_D^{20} 1·4802, which was shown to be mainly 4-methylene*cyclo*hexylmethanol by preparation of the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 97—98°.

Hydrolysis of the trans-*Monotoluene*-p-*sulphonate.*—The monotoluene-*p*-sulphonate (2 g.) was boiled under reflux for 16 hours with 10% aqueous potassium hydroxide (10 c.c.); steam-distillation then removed unsaturated material but in quantity insufficient for identification. Continuous extraction of the alkaline solution with ether gave the *trans*-diol (0·7 g., 73%), identified as dimethanesulphonate, m. p. 158°.

trans-4-*Chloromethyl*cyclo*hexylmethanol.*—The *trans*-diol (10 g.) and fuming hydrochloric acid (13 c.c.; *d* 1·19) were heated at 100° for 20 hours (sealed tube). The product was extracted with chloroform, and the dried (Na_2SO_4) solution evaporated and distilled to give the trans-*monochloride* (7·2 g.), b. p. 75—90°/0·04 mm., n_D^{23} 1·4858—1·4908. A fraction, b. p. 78—82°/0·04 mm., n_D^{23} 1·4897, was analysed (Found: C, 59·2; H, 9·18; Cl, 21·4. $C_8H_{15}OCl$ requires C, 59·1; H, 9·30; Cl, 21·8%). It gave a p-*nitrobenzoate*, needles, m. p. 64—65°, from ethanol (Found : C, 58·2; H, 6·05; N, 4·4. $C_{15}H_{18}O_4NCl$ requires C, 57·8; H, 5·8; N, 4·5%).

Hydrolysis of trans-4-*Chloromethyl*cyclo*hexylmethanol.*—The monochloride (7·1 g.) was boiled under reflux for 30 hours with 10% aqueous potassium hydroxide (50 c.c.); the resulting suspension was steam-distilled and the distillate extracted with ether. Distillation of the dried (Na_2SO_4) extract gave a liquid (2·2 g.), b. p. 100—138°/20 mm., n_D^{18} 1·4801—1·4861, which was unsaturated and contained chlorine. Ozonolysis in acetic acid at room temperature, followed by steam-distillation with zinc, gave formaldehyde (dimedone derivative, m. p. and mixed m. p. 189—190°; 2 : 4-dinitrophenylhydrazone, m. p. 155°). The residual alkaline solution from the hydrolysis was continuously extracted with ether to give the *trans*-diol (2·7 g.), identified as the dimethanesulphonate, m. p. and mixed m. p. 158°.

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