

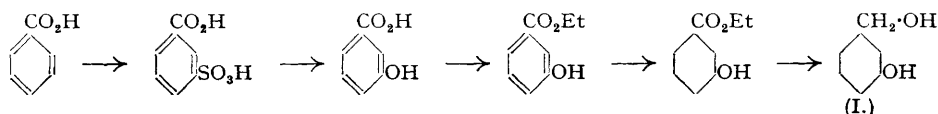
**434. Alicyclic Glycols. Part V. 3-Hydroxymethylcyclohexanol.**

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The synthesis of 3-hydroxymethylcyclohexanol (I) from *m*-hydroxybenzoic acid is described. Several derivatives of the *cis*- and the *trans*-form have been obtained and their reactions studied. Toluene-*p*-sulphonyl and methanesulphonyl substituted into the primary hydroxyl group undergo normal replacement by alkoxy-, acetoxy-, chloro-, and iodo-groups; sulphonate esters of the secondary group more readily undergo the elimination reaction, but substitution, when it occurs, is accompanied by inversion of configuration. The cyclic ether, 1 : 3-*endo*-methyleneoxy-cyclohexane (XII) has been obtained by the action of alkali on the primary monotoluene-*p*-sulphonate and on the primary monochloride (3-chloromethylcyclohexanol).

THE synthesis and properties of 4-hydroxymethylcyclohexanol were recorded in Part III (Owen and Robins, *J.*, 1949, 326). The synthesis of 3-hydroxymethylcyclohexanol (I) has now been accomplished by a similar series of reactions. Benzoic acid was converted in 90% yield

into *m*-hydroxybenzoic acid by sulphonation, and fusion of the sodium benzene-*m*-sulphonate with potassium hydroxide, the use of sodium hydroxide for the fusion having given unsatis-



factory results (cf. Offermann, *Annalen*, 1894, **280**, 5). An alternative route to the *m*-hydroxyacid, involving diazotisation of *m*-aminobenzoic acid, was also investigated, but the overall yield was small. Esterification, followed by hydrogenation over Raney nickel, gave ethyl 3-hydroxycyclohexanecarboxylate in good yield; this compound had previously been obtained, in very poor yield, from 3-aminocyclohexanecarboxylic acid by Bauer and Einhorn (*ibid.*, 1901, **319**, 324). Bouveault-Blanc reduction then gave the diol (I) as a viscous liquid from which, unlike the 4-hydroxymethyl isomer, no solid form could be separated. The overall yield of diol, from benzoic acid, was nearly 50%.

As a by-product from the Bouveault-Blanc reduction, a small amount of 3-hydroxycyclohexanecarboxylic acid was recovered, which after purification was the *cis*-form, m. p. 132° (cf. Einhorn and Coblitz, *ibid.*, 1896, **291**, 297; Perkin and Tattersall, *J.*, 1907, **91**, 480). This was esterified, and then reduced by the Bouveault-Blanc method, but again, as shown by the preparation of derivatives (see below), the resulting diol was a mixture of stereoisomers; not unexpectedly, therefore, some isomerisation had occurred during the reduction. The mixed diol was also prepared by reduction of the hexahydro-ester with lithium aluminium hydride (cf. Nystrom and Brown, *J. Amer. Chem. Soc.*, 1947, **69**, 1197, 2548).

Since the diol itself could not be obtained directly in any one pure stereochemical form, attention was directed towards the preparation of suitable derivatives. In this way it was eventually possible to achieve the desired separation, and also, on the basis of certain reactions, to allocate the appropriate stereochemical structures to the derivatives.

The diacetate and dibenzoate were liquids, but the di-*p*-nitrobenzoate, dimethanesulphonate and bisphenylurethane were solids, each of which by fractional crystallisation was separated into two forms, m. p.s 141° and 162°; 103·5° and 103°; 162° and 122°, respectively. The bis-3 : 5-dinitrobenzoate, m. p. 181°, and ditoluene-*p*-sulphonate, m. p. 95°, were also solids, but only the one form of each could be crystallised. By distillation of one of the bisphenylurethanes (m. p. 162°) with sodium hydroxide, the corresponding form of the diol was obtained as a liquid; from this, a bis-3 : 5-dinitrobenzoate, m. p. 181°, a dimethanesulphonate, m. p. 103·5°, and a ditoluene-*p*-sulphonate, m. p. 95°, were prepared, each of which was identical with the derivative of similar melting point obtained from the mixed diol. Furthermore, hydrolysis of the di-*p*-nitrobenzoate, m. p. 141°, also gave the same stereoisomer of the diol, as shown by formation of the dimethanesulphonate, m. p. 103·5°. (The similar melting points of the two stereoisomeric dimethanesulphonates did not introduce any uncertainty, since a mixture of the two had m. p. ca. 86°; either form could therefore be readily recognised.) This diol also gave a bis- $\alpha$ -naphthylurethane, m. p. 166·5°. Hydrolysis of the di-*p*-nitrobenzoate, m. p. 162°, gave the other form of the diol, from which the different dimethanesulphonate, m. p. 103°, was obtained, thus providing additional confirmation of the inter-relationships.

Six derivatives were therefore known of one form, and three of the other form, of the diol; these are summarised in the Table, the stereochemical structures recorded being those assigned later.

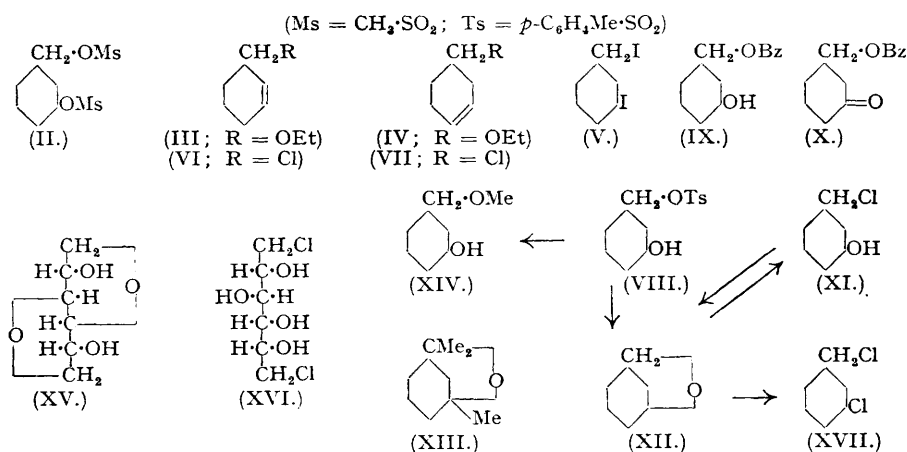
*Derivatives of 3-hydroxymethylcyclohexanol.*

	M. p.			M. p.	
	<i>cis.</i>	<i>trans.</i>		<i>cis.</i>	<i>trans.</i>
Di- <i>p</i> -nitrobenzoate .....	141°	162°	Ditoluene- <i>p</i> -sulphonate .....	95°	—
Bis-3 : 5-dinitrobenzoate .....	181	—	Bisphenylurethane .....	162	122°
Dimethanesulphonate .....	103·5	103	Bis- $\alpha$ -naphthylurethane .....	166·5	—

The reactivities of the sulphonyloxy-groups in the methanesulphonyl and toluene-*p*-sulphonyl derivatives were then examined. The *cis*-dimethanesulphonate (II) reacted rapidly and completely when heated with ethanolic potassium hydroxide, and gave an ethoxymethylcyclohexene (III) or (IV) as the main product; the primary group thus underwent solvolysis, whilst the secondary group was lost by elimination. With aqueous alkali, however, although some hydroxymethylcyclohexene was probably formed, a small amount of the free *trans*-diol was obtained, identified as the di-*p*-nitrobenzoate; under these conditions, therefore, the

secondary group to some extent undergoes replacement with inversion. Somewhat similar results were obtained by treatment with aqueous alkali of the (*cis* + *trans*)-ditoluene-*p*-sulphonate, when, in addition to unsaturated material, some free diol was formed which was shown to consist mainly of the *trans*-form by conversion into the di-*p*-nitrobenzoate, m. p. 161°. Since the original mixed diol, and hence the mixed ditoluene-*p*-sulphonate, appears to contain predominantly the *cis*-isomer (as judged from the proportions of *cis*-derivatives formed from it), inversion has occurred in the hydrolysis.

When the *cis*-dimethanesulphonate was treated with potassium acetate in boiling ethanol, the solution became acid to an extent corresponding to the formation of 0.9 mole of methanesulphonic acid. The main product isolated was ethoxymethylcyclohexene (III) or (IV), but some *trans*-diacetate was also formed, characterised by hydrolysis to *trans*-diol and formation of the di-*p*-nitrobenzoate. The *trans*-dimethanesulphonate, on similar treatment, gave ethoxymethylcyclohexene and the *cis*-diacetate. Thus, although the possible products were not all isolated and may not all have been formed, it is clear that the primary sulphonyloxy-group undergoes replacement both by the acetoxy- and by the ethoxy-group, whilst the secondary sulphonyloxy-residue undergoes both elimination and replacement (the latter with inversion).



The *cis*-dimethanesulphonate reacted readily with sodium iodide in acetone to give 3-iodomethylcyclohexyl iodide (V), but with lithium chloride in ethanol a high yield of the elimination product, chloromethylcyclohexene (VI) or (VII), was obtained. The behaviour of the secondary group towards these two reagents is similar to that observed with methanesulphonates of cyclohexane-1 : 3-diol (Part IV, preceding paper).

Mono-esters of 3-hydroxymethylcyclohexanol were prepared by methods similar to those used for the 4-hydroxymethyl isomer (Owen and Robins, *loc. cit.*). The  $\omega$ -toluene-*p*-sulphonate (VIII) and the  $\omega$ -benzoate (IX) were liquids; the latter derivative on oxidation with chromic acid gave 3-benzoyloxymethylcyclohexanone (X). The  $\omega$ -methanesulphonate was a water-soluble oil which could not be satisfactorily purified. When the *cis*-diol was heated with fuming hydrochloric acid, *cis*-3-chloromethylcyclohexanol (XI) was formed, which gave an  $\alpha$ -naphthylurethane, m. p. 142°; the reaction was slower than had been observed in the preparation of 4-chloromethylcyclohexanol. The chloride was also prepared, as a *cis-trans*-mixture, from the mixed diol; only the *cis*- $\alpha$ -naphthylurethane, m. p. 142°, could be isolated in a pure state from this chloride, although indications of another solid isomer were observed. It was also possible to obtain the chloride by reaction of the  $\omega$ -toluene-*p*-sulphonate (VIII) with lithium chloride.

The possibility of preparing cyclic oxides by intramolecular elimination of a sulphonylic acid between a sulphonyloxy-group and a suitably disposed hydroxyl group has been discussed in earlier papers in this series, but only in the case of 1 : 2-epoxycyclohexane has the method been successful. During the present work, in one preparation of the monotoluene-*p*-sulphonate (VIII) an odour suggestive of a cyclic oxide was observed, and it was found that when (VIII) was heated with solid or aqueous sodium hydroxide a small yield of a volatile crystalline compound, C<sub>7</sub>H<sub>12</sub>O, m. p. 96—97°, was obtained. This material, which has a pronounced camphor-

aceous odour, is the hitherto unknown 1 : 3-*endomethyleneoxycyclohexane* (XII), the simplest analogue of *m*-cineole (XIII). In this reaction, which was carried out on the mixed stereoisomers of (VIII), unsaturated by-products were formed, but a proportion of the monotoluene-*p*-sulphonate was recovered from the reaction mixture; the recovered ester was largely unaffected by further treatment with alkali and was possibly the *trans*-form, since only the *cis*-compound would be expected to give the oxide (inversion accompanying removal of the primary sulphonyloxy-group does not affect the stereochemistry of the ring system). The oxide was also formed when (VIII) was treated with methanolic sodium hydroxide, but the main product then was 3-methoxymethylcyclohexanol (XIV), intermolecular reaction with the solvent evidently occurring more readily than intramolecular reaction with the secondary hydroxyl group. The possibility that (XIV) was formed *via* the oxide is very unlikely in view of the stability of the latter (see below).

A more convenient method of preparing the oxide was to treat the chloride (XI) with solid sodium hydroxide, and, since the oxide could be obtained in this way from the chloride derived, as mentioned above, from one stereoisomer of the diol, it follows that this stereoisomer is probably the *cis*-form, since the dehydrochlorination would not be expected to cause any inversion on the carbon atom carrying the hydroxyl group. It is on this evidence, supported by a further observation considered below, that the configurations, already assumed, have been based.

The oxide ring in (XII) is of the type encountered in tetrahydrofuran and in the 3 : 6-anhydro-sugars, and in common with such compounds it shows considerable stability. The oxide was unaffected by water at 100°, even in the presence of perchloric acid, or by methanesulphonic or toluene-*p*-sulphonic acid in ether or boiling benzene. Montgomery and Wiggins (*J.*, 1946, 392) found that, when 1 : 4-3 : 6-dianhydrosorbitol (XV), which possesses two such ring systems and is also very stable, is heated with fuming hydrochloric acid, it undergoes ring fission in a direction such that the 1 : 6-dichloro-compound (XVI) is obtained. When the oxide (XII) was similarly treated it gave, according to the amount of hydrochloric acid used, either 3-chloromethylcyclohexanol (XI) or 3-chloromethylcyclohexyl chloride (XVII). The ring-opening to give the former compound would not be expected to lead to inversion, and consequently the monochloride formed in this reaction is probably the *cis*-form; it gave an  $\alpha$ -naphthylurethane, m. p. 142°, identical with that described above, which, on evidence of oxide-formation, had already been allotted a *cis*-configuration.

#### EXPERIMENTAL.

*m*-Hydroxybenzoic Acid.—Sodium hydrogen *m*-sulphobenzoate (239 g.), prepared by the method of Offermann (*loc. cit.*), was mixed to a paste with 45% aqueous sodium hydroxide (95 c.c.) contained in a basin heated on the steam-bath, and powdered sodium hydroxide (48 g.) was then stirred into the mixture, which solidified when allowed to cool. The product was broken into small pieces and added during  $\frac{1}{2}$  hour to fused potassium hydroxide (335 g.) contained in an iron vessel, the internal temperature being maintained at 210–220° during the addition and for a further 2½ hours. The cooled mass was then dissolved in water (1 l.), and the solution filtered and acidified with hydrochloric acid. *m*-Hydroxybenzoic acid (133 g., 91%), m. p. 198–200°, was precipitated. It was collected and washed with a little cold water. The use of sodium hydroxide for the fusion gave only a 17% yield.

Ethyl *m*-Hydroxybenzoate.—Esterification of the acid (126 g.) with ethanol (150 c.c.) and sulphuric acid (24 c.c.) under reflux for 6 hours, followed by dilution with water, gave the ester as a solid (118 g., 89%). After recrystallisation from light petroleum (b. p. 80–100°) it had m. p. 72°.

Ethyl 3-Hydroxycyclohexanecarboxylate.—A solution of ethyl *m*-hydroxybenzoate (145 g.) in ethanol (400 c.c.) was stirred in the presence of Raney nickel (*ca.* 15 g.) with hydrogen at 140°/130 atm. Absorption ceased after 30 hours, and the filtered solution was concentrated and fractionally distilled. Ethyl hexahydrobenzoate (18.5 g.) was collected at 84–90°/16 mm.,  $n_D^{20}$  1.4500, followed by ethyl 3-hydroxycyclohexanecarboxylate (105 g., 70%), b. p. 117–122°/1 mm.,  $n_D^{20}$  1.4651. There was a small residue (17.5 g.) of ethyl *m*-hydroxybenzoate.

3-Hydroxymethylcyclohexanol.—(i) Ethyl 3-hydroxycyclohexanecarboxylate (105 g.) was dissolved in dry ethanol (800 c.c.) contained in a 3-l. flask fitted with a large and efficient reflux condenser. Sodium (85 g.) was added in one portion and the reduction was allowed to proceed as vigorously as possible, the flask being heated on the steam-bath when the initial violence had subsided. When all the sodium had disappeared (6 hours), water (150 c.c.) was added and the alcohol was removed by distillation under reduced pressure. The semi-solid residue was dissolved in a further portion of water (250 c.c.) and continuously extracted with ether for 48 hours. Removal of solvent from the dried (Na<sub>2</sub>SO<sub>4</sub>) extract gave an oil, which on distillation gave a main fraction (67.0 g., 84%) of 3-hydroxymethylcyclohexanol, b. p. 117–122°/0.5 mm., 165–166°/27 mm.,  $n_D^{20}$  1.4900 (Found: C, 64.3; H, 10.7. C<sub>7</sub>H<sub>14</sub>O<sub>2</sub> requires C, 64.6; H, 10.85%). Acidification of the remaining alkaline solution, and extraction with ether, gave a solid acid, m. p. 125°. Repeated recrystallisation from ethyl acetate gave *cis*-3-hydroxycyclohexanecarboxylic acid (7.5 g.), m. p. 131–132°.

(ii) The recovered *cis*-acid was converted into the ethyl ester, which was then reduced under the conditions described above. The glycol so obtained, b. p. 115–119°/0.5 mm., was shown to be a mixture of stereoisomers by formation of the two *di-p*-nitrobenzoates (see below).

(iii) To a solution of lithium aluminium hydride (0.2 g.) in dry ether (10 c.c.), ethyl 3-hydroxycyclohexanecarboxylate (2.0 g.) in dry ether (2 c.c.) was added, and the mixture was stirred for 40 minutes. Water (10 c.c.) was then added, followed by 10% sulphuric acid (12 c.c.), and the aqueous layer was removed, washed once with ether to remove unchanged ester, and then continuously extracted with ether. The latter extracts gave the glycol (0.78 g., 52%), b. p. 120–122°/0.5 mm., which was characterised by formation of the two dimethanesulphonyl derivatives (see below).

**Diacetate.** Acetyl chloride (0.75 g.) was added to a solution of 3-hydroxymethylcyclohexanol (0.5 g.) in pyridine (5 c.c.), and the mixture was set aside for a few hours. Chloroform was then added, and the solution was washed with dilute hydrochloric acid and with water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated. Distillation of the residual oil gave the *diacetate* as a mobile liquid (0.7 g.), b. p. 60–70°/0.005 mm.,  $n_D^{20}$  1.4511 (Found: C, 62.1; H, 8.7.  $\text{C}_{11}\text{H}_{18}\text{O}_4$  requires C, 61.7; H, 8.5%).

**Dibenzoate.** Prepared in a similar way, this was an oil, which decomposed on attempted distillation.

**Di-*p*-nitrobenzoate.** The diol (6.0 g.) in pyridine (150 c.c.) was treated with *p*-nitrobenzoyl chloride (16.5 g.) at 60° for 8 hours, followed by 4 days at room temperature. It was then worked up, as previously described for the diacetate, in chloroform (200 c.c.), and gave an oil (16.5 g.) which solidified when triturated with methanol. Recrystallisation from dioxan (30 c.c.) gave two crops of crystals (9.1 g.), m. p. 137–140°, which when recrystallised from methanol gave the *cis-di-p-nitrobenzoate* as needles, m. p. 141° (Found: N, 6.2.  $\text{C}_{21}\text{H}_{20}\text{O}_8\text{N}_2$  requires N, 6.5%). Progressive dilution of the dioxan mother-liquors with methanol gave first a small crop of the same material, followed by a new compound, m. p. 155–156°; recrystallisation of the latter from ethanol gave the *trans-di-p-nitrobenzoate* as prisms, m. p. 162° (Found: N, 6.2%). A mixture of the two forms had m. p. 128°.

**Bis-3:5-dinitrobenzoate.** The diol (0.4 g.) in pyridine (10 c.c.) was treated with 3:5-dinitrobenzoyl chloride (1.4 g.) under the same conditions as for the *p*-nitrobenzoate. The product (1.3 g., 83%) was crystallised from dioxan to give the *cis-bis-3:5-dinitrobenzoate*, which after recrystallisation from ethanol formed needles (0.6 g.), m. p. 181° (Found: C, 48.25; H, 3.4.  $\text{C}_{21}\text{H}_{18}\text{O}_{12}\text{N}_4$  requires C, 48.65; H, 3.5%). The only other crystalline product obtained on dilution of the dioxan mother-liquor with methanol was the *ω*-3:5-dinitrobenzoate, which crystallised from ethanol in needles, m. p. 100° (Found: N, 8.6.  $\text{C}_{14}\text{H}_{16}\text{O}_7\text{N}_2$  requires N, 8.6%).

**Dicinnamate.** Treatment of the diol with cinnamoyl chloride in pyridine gave a solid product from which only one stereoisomer of the *dicinnamate* could be isolated; it formed rosettes of needles, m. p. 106°, from ethanol (Found: C, 76.5; H, 6.7.  $\text{C}_{28}\text{H}_{28}\text{O}_4$  requires C, 76.8; H, 6.7%).

**Bisphenylurethane.** The diol (1.2 g.) was heated at 80° for 2 hours with phenyl isocyanate (2.9 g.) in a sealed tube. The resulting white solid was crystallised from *ca.* 150 c.c. of 1:1 benzene–light petroleum (b. p. 60–80°) and gave 1.95 g. (58%) of the *cis-bisphenylurethane* as needles, m. p. 162° (Found: C, 68.6; H, 6.3.  $\text{C}_{21}\text{H}_{24}\text{O}_4\text{N}_2$  requires C, 68.5; H, 6.6%). Removal of solvent from the mother-liquors gave a sticky solid, which after several recrystallisations from benzene–light petroleum gave the *trans-bisphenylurethane*, m. p. 122° (Found: N, 7.65.  $\text{C}_{21}\text{H}_{24}\text{O}_4\text{N}_2$  requires N, 7.6%). A mixture of the two forms had m. p. 120–122°.

**Dimethanesulphonate.** A solution of methanesulphonyl chloride (22 g.) and the diol (12 g.) in pyridine (80 c.c.) was left at 0° overnight and then worked up in the usual way with chloroform (150 c.c.). The product (26 g.) solidified and was crystallised from ethyl acetate. Two more recrystallisations from this solvent, followed by several from ethanol, gave the *cis-dimethanesulphonate* (16.1 g., 61%) as rosettes of needles (from ethyl acetate), m. p. 103.5° (Found: C, 38.0; H, 6.2.  $\text{C}_9\text{H}_{18}\text{O}_6\text{S}_2$  requires C, 37.8; H, 6.3%). Concentration of the original ethyl acetate mother-liquor gave a crop of crystals, m. p. *ca.* 90°, which after several recrystallisations from methanol gave the *trans-dimethanesulphonate* (3.8 g., 14.5%), m. p. 103° (Found: C, 38.1; H, 6.5%). A mixture of the two forms had m. p. 86–87°.

**Ditoluene-*p*-sulphonate.** The diol (3.8 g.) and toluene-*p*-sulphonyl chloride (11.2 g.) in pyridine, under the conditions described for the methanesulphonate, gave a viscous oil which was taken up in a small quantity of methanol. Crystals slowly separated out, and recrystallisation from methanol gave the *cis-ditoluene-*p*-sulphonate* as needles, m. p. 95° (Found: C, 57.4; H, 6.1.  $\text{C}_{21}\text{H}_{26}\text{O}_6\text{S}_2$  requires C, 57.5; H, 6.0%). No other crystalline material could be isolated.

**ω-Benzate.** Benzoyl chloride (2.2 g.) in pure chloroform (70 c.c.) was slowly added with good stirring to the diol (2.0 g.) in pyridine (15 c.c.) at –10°. The solution was set aside at room temperature for 2 days and then heated on the steam-bath for 1 hour. The product, isolated as above, was an oil, distillation of which gave the *ω-benzoate* as a viscous liquid (2.3 g.), b. p. 100° (bath)/0.0006 mm.,  $n_D^{20}$  1.5287 (Found: C, 71.7; H, 7.9.  $\text{C}_{14}\text{H}_{18}\text{O}_3$  requires C, 71.8; H, 7.8%), which failed to give a crystalline methanesulphonate.

**ω-Toluene-*p*-sulphonate.** Toluene-*p*-sulphonyl chloride (14.3 g.) in pyridine (20 c.c.) was added during 20 minutes to a stirred solution of the diol (9.8 g.) in pyridine (90 c.c.) at 0°. After a further 40 minutes at 0° the solution was poured into 5*N*-sulphuric acid (300 c.c.) containing some crushed ice. The precipitated oil was taken up in chloroform and washed with water, and the extract was then dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated under reduced pressure to constant weight (14.1 g., 66%). The *ω-toluene-*p*-sulphonate* was an almost colourless viscous oil (Found: S, 10.8.  $\text{C}_{14}\text{H}_{20}\text{O}_6\text{S}$  requires S, 11.3%). A yield of only 43% was obtained when the reaction was carried out at room temperature.

The derivative was also prepared by the gradual addition of powdered potassium hydroxide (3.7 g.) to a stirred solution of the diol (2.95 g.) and toluene-*p*-sulphonyl chloride (4.3 g.) in pure chloroform



(30 c.c.) at 0°. After 24 hours, the chloroform solution was decanted, washed with ice-water, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated. The  $\omega$ -toluene-*p*-sulphonate (4.0 g., 62%) contained an odoriferous by-product, later recognised to be an oxide.

**$\omega$ -Methanesulphonate.** Methanesulphonyl chloride (1.77 g.) in carbon tetrachloride (100 c.c.) was slowly added to a stirred solution of the diol (2.0 g.) in pyridine (20 c.c.) at 0°. The solution was set aside at 0° overnight, filtered from pyridine hydrochloride, and evaporated under reduced pressure to remove pyridine and carbon tetrachloride. Chloroform (60 c.c.) was then added, and the solution was stirred with solid sodium hydrogen carbonate and a few drops of water to decompose a little residual pyridine hydrochloride. The solution was filtered and evaporated, to give a pyridine-free oil (1.45 g.). Some dimethanesulphonate (0.38 g.) was removed by crystallisation from methanol; evaporation of the solution then gave a water-soluble oil which, although containing combined sulphur, was contaminated with some unchanged diol, since it gave a small yield of the *cis*-di-*p*-nitrobenzoate, m. p. 140°, on treatment with *p*-nitrobenzoyl chloride in pyridine.

**Regeneration of 3-Hydroxymethylcyclohexanol from its Derivatives.**—(i) The bisphenylurethane of m. p. 162° (1.7 g.) was mixed with powdered sodium hydroxide (0.52 g.) in a 25-c.c. distilling flask and heated at ordinary pressure to a bath-temperature of 200°, water and aniline being collected; a further quantity of the latter was removed at 100°/30 mm. The *cis*-diol (0.37 g., 62%) was then collected at 200° (bath)/0.3 mm. Small portions were converted into the bis-3:5-dinitrobenzoate, m. p. 181°, dimethanesulphonate, m. p. 103.5°, and ditoluene-*p*-sulphonate, m. p. 95°, all of which were identical with the *cis*-forms previously described.

(ii) The di-*p*-nitrobenzoate of m. p. 141° (5.8 g.) was heated under reflux with 0.5*N*-methanolic potassium hydroxide (100 c.c.) for 4 hours. Water (10 c.c.) was added, and the solution was neutralised with hydrochloric acid and evaporated under reduced pressure. Extraction with chloroform then gave 1.77 g. of *cis*-diol, b. p. 115–117°/0.2 mm.,  $n_D^{25}$  1.4902. A small portion was converted into the dimethanesulphonate, m. p. 103.5°, identical with the *cis*-derivative already described. Another portion gave the *cis*-bis- $\alpha$ -naphthylurethane, which crystallised from benzene-light petroleum (b. p. 60–80°) in needles, m. p. 166.5° (Found: C, 74.3; H, 6.3.  $\text{C}_{29}\text{H}_{28}\text{O}_4\text{N}_2$  requires C, 74.3; H, 6.0%).

(iii) The di-*p*-nitrobenzoate of m. p. 161–162° (1.6 g.) was hydrolysed in the same way and gave the *trans*-diol (0.46 g.) as a viscous oil. With methanesulphonyl chloride in pyridine, a portion gave the *trans*-dimethanesulphonate, m. p. 103°, identical with the *trans*-derivative previously described.

**3-Benzoyloxymethylcyclohexanone.**—A solution of chromic anhydride (0.45 g.) in acetic acid (30 c.c.), containing a few drops of water, was slowly added to a stirred solution of the  $\omega$ -benzoate (1.35 g.) in acetic acid (20 c.c.), and the whole set aside overnight. Ether (300 c.c.) was then added, and the acid was washed out with water and finally with aqueous sodium hydrogen carbonate. The ethereal solution was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to give 3-benzoyloxymethylcyclohexanone (1.3 g., 97%), b. p. 95° (bath)/0.0001 mm.,  $n_D^{20}$  1.5287 (Found: C, 72.3; H, 7.3.  $\text{C}_{14}\text{H}_{16}\text{O}_3$  requires C, 72.4; H, 6.9%). The semicarbazone formed needles, m. p. 145°, from aqueous methanol (Found: C, 61.7; H, 6.5.  $\text{C}_{15}\text{H}_{18}\text{O}_3\text{N}_2$  requires C, 62.3; H, 6.6%). The 2:4-dinitrophenylhydrazones crystallised from ethyl acetate in yellow needles, m. p. 201° (Found: C, 58.2; H, 4.8.  $\text{C}_{20}\text{H}_{20}\text{O}_6\text{N}_4$  requires C, 58.3; H, 4.9%).

**Reaction of the Dimethanesulphonate with Alkali.**—(i) The *cis*-dimethanesulphonate (10 g.) was heated under reflux with 4% ethanolic potassium hydroxide (200 c.c.) for 2 hours. The precipitated potassium methanesulphonate was removed, and the ethanol was distilled off through a Vigreux column (the distillate was unsaturated). The semi-solid residue was extracted with ether, to give ethoxymethylcyclohexene (2.6 g., 51%), b. p. 103°/102 mm.,  $n_D^{24}$  1.4500 (Found: C, 76.5; H, 11.6.  $\text{C}_9\text{H}_{16}\text{O}$  requires C, 77.1; H, 11.5%).

(ii) The *cis*-dimethanesulphonate (3.8 g.) was stirred for 2½ hours at 90° with 5% aqueous sodium hydroxide (42 c.c.). The resulting clear solution was extracted once with ether, this extract being rejected, and then continuously extracted with ether for 18 hours. Evaporation of the ethereal extract gave an oil (0.43 g.), which on treatment with *p*-nitrobenzoyl chloride in pyridine furnished the di-*p*-nitrobenzoate, m. p. and mixed m. p. 161°, of the *trans*-diol.

**Reaction of the Ditoluene-*p*-sulphonate with Alkali.**—The (*cis* + *trans*)-ditoluene-*p*-sulphonate (11.6 g.) was stirred for 6 hours at 90° with 5% aqueous potassium hydroxide (120 c.c.). From the resulting emulsion, unchanged starting material (6.85 g.) was recovered; this was boiled under reflux for 16 hours with 10% aqueous potassium hydroxide (70 c.c.). Continuous ether-extraction of the combined alkaline solutions then gave 3-hydroxymethylcyclohexanol (0.75 g.), b. p. 114–117°/1 mm., and an undistillable residue (2 g.) of unattacked ditoluene-*p*-sulphonate. The glycol was characterised as the di-*p*-nitrobenzoate, m. p. 161°, identical with the *trans*-derivative previously described.

**Reaction of the Dimethanesulphonates with Potassium Acetate.**—(i) The *cis*-derivative (2.5 g.) was heated under reflux with anhydrous potassium acetate (4.3 g.) in ethanol (80 c.c.) for 24 hours. Water (30 c.c.) was then added to dissolve the precipitated sodium methanesulphonate, and the solution was neutralised to phenolphthalein by titration with 0.216*N*-sodium hydroxide (35.7 c.c.; corresponding to 0.87 mole of acetic acid). It was then distilled to remove ethanol, the residual aqueous solution (A) being reserved. The distillate, which was unsaturated and had the characteristic odour of ethoxymethylcyclohexene, was diluted with water and continuously extracted with ether for several hours. Solvent was removed from the extract through a Vigreux column, and the residue on distillation gave ethoxymethylcyclohexene (0.62 g., 51%), b. p. 105–110°/105 mm.,  $n_D^{22}$  1.4515. Extraction of the aqueous solution (A) with ether gave mainly the diacetate of 3-hydroxymethylcyclohexanol (0.46 g., 25%), b. p. 136–138°/28 mm.,  $n_D^{20}$  1.4538, which contained traces of an unsaturated impurity. Hydrolysis by heating with 10% aqueous potassium hydroxide, followed by continuous ether-extraction, gave the diol, characterised as the *trans*-di-*p*-nitrobenzoate, m. p. and mixed m. p. 160°.

(ii) The *trans*-dimethanesulphonate (2.5 g.) on similar treatment gave 0.3 g. of ethoxymethylcyclohexene, b. p. 120° (bath)/80 mm., and 0.7 g. of diacetate, b. p. 136–139°/30 mm.,  $n_D^{25}$  1.4522. The latter was hydrolysed and characterised as the *cis*-di-*p*-nitrobenzoate, m. p. and mixed m. p. 139–140°.

**Reaction of the Dimethanesulphonate with Sodium Iodide.**—The *cis*-derivative (0.75 g.), sodium iodide (2 g.), and acetone (15 c.c.) were heated in a sealed tube at 100° for 2 hours. The precipitated sodium methanesulphonate was removed and washed with acetone. Evaporation of the filtrate and washings gave a semi-solid residue which was diluted with water and extracted with ether. The extract was washed with aqueous sodium thiosulphate to remove free iodine, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated to an oil, which on distillation furnished 3-iodomethylcyclohexyl iodide (0.5 g.) as an almost colourless liquid, b. p. 65–70° (bath)/0.0006 mm.,  $n_D^{17}$  1.6233 (Found: I, 71.6.  $\text{C}_7\text{H}_{12}\text{I}_2$  requires I, 72.5%). It gradually decomposed on storage.

**Reaction of the Dimethanesulphonate with Lithium Chloride.**—The *cis*-derivative (1.0 g.), lithium chloride (0.75 g.), and ethanol (35 c.c.) were boiled under reflux for 40 hours. The alcohol was then distilled off (the distillate was unsaturated), and the residue was diluted with water and extracted with ether. Removal of solvent from the dried ( $\text{Na}_2\text{SO}_4$ ) extract gave chloromethylcyclohexene (0.37 g., 81%), b. p. 215–220°,  $n_D^{25}$  1.4840 (Found: Cl, 28.9.  $\text{C}_7\text{H}_{11}\text{Cl}$  requires Cl, 27.2%).

**3-Chloromethylcyclohexanol.**—(i) 3-Hydroxymethylcyclohexanol (14.5 g.; mixture of stereoisomers) was heated with fuming hydrochloric acid (30 c.c.;  $d$  1.19) at 110° for 14 hours in a sealed tube. The oil was separated from the aqueous portion, and the latter was extracted with chloroform, which was then added to the oil and washed with sodium hydrogen carbonate solution, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated to a liquid, distillation of which gave 3-chloromethylcyclohexanol (13.8 g., 83%), b. p. 73°/0.5 mm., 127–130°/36 mm.,  $n_D^{24}$  1.4910 (Found: C, 56.3; H, 8.9; Cl, 24.0.  $\text{C}_7\text{H}_{13}\text{OCl}$  requires C, 56.6; H, 8.8; Cl, 23.9%); a higher-boiling residue (1.9 g.) consisted of unchanged diol. Treatment of a portion of the chloride with  $\alpha$ -naphthyl isocyanate gave a solid product which on fractional crystallisation from light petroleum (b. p. 80–100°) gave the  $\alpha$ -naphthylurethane, m. p. 142°, as rosettes of fine needles (Found: N, 4.5.  $\text{C}_{18}\text{H}_{20}\text{O}_2\text{NCl}$  requires N, 4.4%). From the mother-liquors there was obtained some material, m. p. ca. 127–128° (Found: N, 4.6%), which probably contained the other stereoisomer, but the quantity was insufficient for further purification.

(ii) Similar treatment of the *cis*-diol (1.3 g.) gave *cis*-chloromethylcyclohexanol (0.7 g.), b. p. 119–123°/30 mm.,  $n_D^{30}$  1.4858. It gave an  $\alpha$ -naphthylurethane, m. p. 142°, identical with that described above.

(iii) The  $\omega$ -toluene-*p*-sulphonate (3.0 g.; mixture of stereoisomers) and lithium chloride (1.35 g.) in ethanol (20 c.c.) were boiled under reflux for 6 hours. The solvent was then distilled off through a Vigreux column, the residue was treated with water and chloroform, and the chloroform extract was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The chloromethylcyclohexanol (1.4 g., 90%) had b. p. 76–80°/0.5 mm.,  $n_D^{21}$  1.4913, and gave an  $\alpha$ -naphthylurethane which was mainly the *cis*-form, m. p. 142°.

**1:3-endoMethyleneoxycyclohexane.**—3-Chloromethylcyclohexanol (6.7 g.; mixture of stereoisomers) was mixed to a paste with finely powdered sodium hydroxide (11 g.) and heated at 60–70°/35 mm. in a sublimation apparatus, the condensing surface being cooled with water at 0°. After 45 minutes, the hard transparent solid sublimate was collected, and on resublimation gave 1:3-endoMethyleneoxycyclohexane (2.2 g., 44%), m. p. 96–97° (Found: C, 74.7; H, 10.9.  $\text{C}_7\text{H}_{12}\text{O}$  requires C, 74.9; H, 10.8%). Further sublimation from the original reaction mixture gave an additional small quantity of the oxide, but prolonged heating merely resulted in contamination of the product with water. The alkaline residue, which had a very strong odour of the oxide, was dissolved in water, neutralised with hydrochloric acid, and extracted with ether. Removal of ether from the dried extracts gave an oil (2.1 g.), which was unsaturated and contained chlorine; it was not possible to obtain any pure oxide from this.

Similar treatment of the 3-chloromethylcyclohexanol (0.58 g.), from the *cis*-diol, with powdered sodium hydroxide, gave 0.21 g. of oxide.

1:3-endoMethyleneoxycyclohexane was very readily soluble in all common solvents, including cold water and cold light petroleum, and could only be satisfactorily purified by sublimation. It had a strong camphoraceous odour and was quite volatile even at ordinary temperatures, small quantities soon disappearing when exposed to the air. It was unaffected by treatment for 8 hours with methanesulphonic acid or toluene-*p*-sulphonic acid, in ether at 20° or in boiling benzene. It did not react with water in the presence of catalytic amounts of perchloric acid at 20° or 100°, but when heated with water in a sealed tube at 195° for 16 hours it gave an unsaturated oil which decomposed on attempted distillation at 100°/0.0002 mm.

**Reactions of 1:3-endoMethyleneoxycyclohexane with Hydrochloric Acid.**—(i) The oxide (1.05 g.) and fuming hydrochloric acid (6.8 c.c.;  $d$  1.19) were heated in a sealed tube at 115° for 21 hours. The oil was separated from the aqueous portion by extraction with chloroform ( $3 \times 7$  c.c.), and the extracts were washed with sodium hydrogen carbonate solution, dried ( $\text{Na}_2\text{SO}_4$ ), and evaporated. Distillation of the residue then gave 3-chloromethylcyclohexyl chloride (1.5 g., 96%), b. p. 102–104°/23 mm.,  $n_D^{20}$  1.4940 (Found: C, 50.8; H, 7.1; Cl, 42.3.  $\text{C}_7\text{H}_{12}\text{Cl}_2$  requires C, 50.3; H, 7.2; Cl, 42.4%).

(ii) The oxide (1.0 g.) was heated with fuming hydrochloric acid (2.3 c.c.) in a sealed tube for 14 hours at 112° and then worked up as in the previous experiment, to yield 3-chloromethylcyclohexanol (1.1 g., 83%), b. p. 120°/23 mm.,  $n_D^{23}$  1.4910. It gave the  $\alpha$ -naphthylurethane, m. p. 142°, identical with that previously described.

**Reactions of the  $\omega$ -Toluene-*p*-sulphonate with Alkali.**—(i) The monotoylene-*p*-sulphonate (0.64 g.) was mixed with powdered sodium hydroxide (0.6 g.) and heated at 60°/32 mm. in the sublimation apparatus used for the preparation of 1:3-endoMethyleneoxycyclohexane from the chloride (see above). The yield of oxide was 0.06 g. (24%); a further amount present in the residue could not be isolated.

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(ii) The monotoluene-*p*-sulphonate (7.4 g.) was stirred at 70° for 2 hours with 30% aqueous sodium hydroxide (14 c.c.). The resulting emulsion was extracted with ether, and the extract was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to an oil, from which a small amount of oxide (0.15 g.) was obtained by sublimation; the ether distillates had a strong odour of oxide, and much of the latter had probably been lost owing to its high volatility. The non-volatile residue (2.3 g.) appeared to consist of unchanged toluene-*p*-sulphonate and was recovered almost quantitatively after further treatment for 4 hours at 70° with 30% aqueous sodium hydroxide; it reacted with benzoyl chloride in pyridine, but no solid derivative could be obtained.

(iii) The monotoluene-*p*-sulphonate (5.9 g.) was heated with 0.5N-methanolic sodium methoxide (72 c.c.) at 60° for 8 hours; much sodium toluene-*p*-sulphonate was precipitated. Water (0.5 c.c.) was added, and the solution was neutralised with carbon dioxide and filtered. Methanol was removed by distillation through a Vigreux column (the distillate had a strong odour of the oxide), and the residue was taken up in ether, which was then dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated to an oil. On distillation there was obtained 3-methoxymethylcyclohexanol (2.04 g., 67%), b. p. 78—79°/0.1 mm.,  $n_D^{21}$  1.4700 (Found: C, 66.6; H, 11.2.  $\text{C}_8\text{H}_{16}\text{O}_2$  requires C, 66.6; H, 11.2%). There was an undistilled residue of unchanged monotoluene-*p*-sulphonate (0.6 g.), and some 1 : 3-*endomethyleneoxycyclohexane* (0.1 g.) was recovered from the liquid-air trap in the vacuum system.

Acknowledgment is made to the Department of Scientific and Industrial Research for the award of a maintenance grant (to M. F. C.).

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[Received, May 10th, 1950.]