76. *Alicyclic Glycols. Part III.* 4-*Hydroxymethyl*cyclo*hexanol.*

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The synthesis of 4-*hydroxymethyl*cyclo*hexanol* (I) from *p*-hydroxybenzoic acid is described. From the *cis*- and *trans*-forms, several mono- and di-substituted derivatives have been obtained, and, by making use of the greater reactivity of the primary hydroxyl group, structurally isomeric compounds such as the 1-*benzoate*-ω-*toluene*-p-*sulphonate* and ω-*benzoate*-1-*toluene*-p-*sulphonate* have been prepared, their structures proved, and their properties studied. The difference in behaviour between primary and secondary toluene-*p*-sulphonyl groups has been demonstrated in several reactions. On treatment with methanolic alkali, a tosyloxy-group in the primary position is replaced, to give the methyl ether, whilst one in the secondary position is eliminated, with formation of an ethylenic linkage (cf. Parts I and II). Smooth replacement of the primary tosyloxy-group by acetoxy-, chlorine, and iodine has also been observed, in contrast to the results obtained with secondary toluene-*p*-sulphonyl compounds. The configuration of the *trans*-form of the glycol (I) has been proved by relating it to the *trans*-forms of 4-hydroxy*cyclo*hexanecarboxylic acid and 4-hydroxy*cyclo*hexanol.

*cyclo*Hexane-1 : 4-diol, the simplest analogue of 1 : 4-terpin, has been discussed in Part II (preceding paper). The present account is concerned with the homologue, 4-*hydroxymethyl*-cyclo*hexanol* (I), a compound which is similarly related to 1 : 8-terpin (II), and also of interest because it contains both a primary and a secondary hydroxyl group.

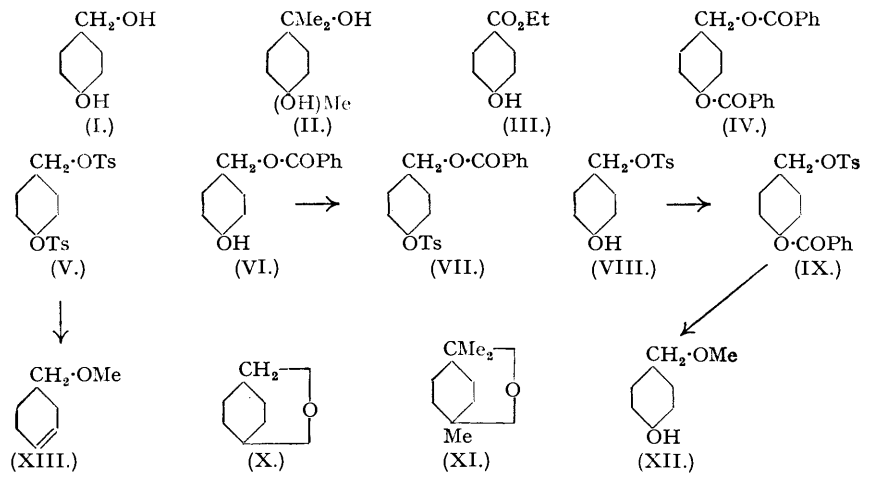
The glycol was synthesised from *p*-hydroxybenzoic acid, and it was necessary to make a preliminary study of the hydrogenation of this acid and of its ethyl ester under various conditions. Balas and Srôl (*Coll. Czech. Chem. Comm.*, 1929, **1**, 658) and Edson (*J. Soc. Chem. Ind.*, 1934, **53**, 138T) reported that reduction of the acid proceeded slowly in aqueous or ethanolic solution over a platinum catalyst at ordinary pressure to give poor yields of 4-hydroxy*cyclo*hexane-carboxylic acid, simultaneous hydrogenolysis leading to the formation of *cyclo*hexanecarboxylic acid. We have confirmed these observations, and have failed to effect any marked improvement by increasing the pressure to 100 atm. Attempted reduction of an alcoholic solution of the potassium salt of the hydroxy-acid at 150° and 125 atm., over Raney nickel, resulted only in the formation of phenol; this decarboxylation was found to occur merely on heating the alcoholic solution of the salt to 150°, and it is evidently related to the production of *cyclo*hexanol in attempted reduction of the acid, under somewhat similar conditions, by Ipatieff and Razuvaieff (*Ber.*, 1926, **59**, 306) and Levin and Pendergrass (*J. Amer. Chem. Soc.*, 1947, **69**, 2436). Mitsui

(*Mem. Coll. Sci. Kyoto Imp. Univ.*, 1935, *A*, **18**, 329) claimed good results for the hydrogenation of ethyl *p*-hydroxybenzoate over a supported nickel catalyst, though Martin and Robinson (*J.*, 1943, 491) found Raney nickel unsuitable, and recommended palladium on strontium carbonate (cf. Hardegger, Heuser, and Blank, *Helv. Chim. Acta*, 1946, **29**, 477). In our hands, however, Raney nickel has been quite satisfactory, and has given ethyl 4-hydroxy*cyclo*hexanecarboxylate (III) in consistently good yield.

The carbethoxy-group in (III) was reduced both by the Bouveault–Blanc method (yield 60%, with sodium and ethanol) and by hydrogenation in alcoholic solution over copper chromite at 250° and 200 atm. With the latter method, however, it was impossible to obtain consistent results; of seven experiments, all carried out under apparently identical conditions, one gave a yield of 61%, and two of about 5%, whilst the remainder gave practically none of the desired material, but mainly 4-methyl*cyclo*hexanol. This hydrogenolysis is similar to the observation by Adkins (*J. Amer. Chem. Soc.*, 1932, **54**, 4678) that hydrogenation of ethyl 2-hydroxy*cyclo*hexanecarboxylate over copper chromite gave a 92% yield of 2-methyl*cyclo*hexanol, but the latter result is not unexpected, since the primary reduction product is 2-hydroxy*cyclo*hexylcarbinol and it is known that 1 : 2- and 1 : 3- glycols readily undergo hydrogenolysis under these conditions. Similar behaviour by a 1 : 5-glycol, however, is surprising.

The product was a viscous liquid which partly crystallised. The solid portion, amounting to *ca.* 30%, was subsequently proved, as described later, to be trans-4-*hydroxymethyl*cyclo*hexanol*; the residual liquid, purified by distillation, contained the cis-*form*, and was characterised as the *bisphenylurethane*.

The *trans*-glycol gave a *dibenzoate* (IV) and a *bistoluene*-p-*sulphonate* (V); with one mol. of benzoyl chloride it gave the ω-*monobenzoate* (VI) as a liquid, which reacted with toluene-*p*-sulphonyl chloride to give the crystalline ω-*benzoate*-1-*toluene*-p-*sulphonate* (VII); similarly, one mol. of toluene-*p*-sulphonyl chloride yielded a crude ω-monotoluene-*p*-sulphonate (VIII) which could not be purified, but on benzoylation gave the 1-*benzoate*-ω-*toluene*-p-*sulphonate* (IX). The *cis*-glycol, probably not stereochemically pure, was also converted into the corresponding derivatives, but only the *bistoluene*-p-*sulphonate* was obtained in crystalline form. The structures assigned to the mixed derivatives (VII) and (IX), based on the expected preferential reactivity of the primary hydroxyl group, were confirmed by evidence which is considered at the end of this paper.



(Ts = *p*-$CH_3 \cdot C_6H_4 \cdot SO_2$.)

1 : 4-*endo*Oxymethylene*cyclo*hexane (X), which is not described in the literature, may be considered to be the simple analogue of 1 : 8-cineole (XI) in the same way as 1 : 4-epoxy*cyclo*hexane is related to 1 : 4-cineole (see Part II). Since it appeared from the experiments described in Part II that a toluene-*p*-sulphonyl group in a secondary position, on treatment with alkali, gave an unsaturated product rather than an ether or anhydro-compound, it was clear that the behaviour of the primary toluene-*p*-sulphonyl derivative (IX) would be of more interest than that of the structural isomer (VII), which would probably give only 4-hydroxymethyl*cyclo*hexene. Whereas, however, the formation of the 1 : 4-epoxide, had it occurred, would

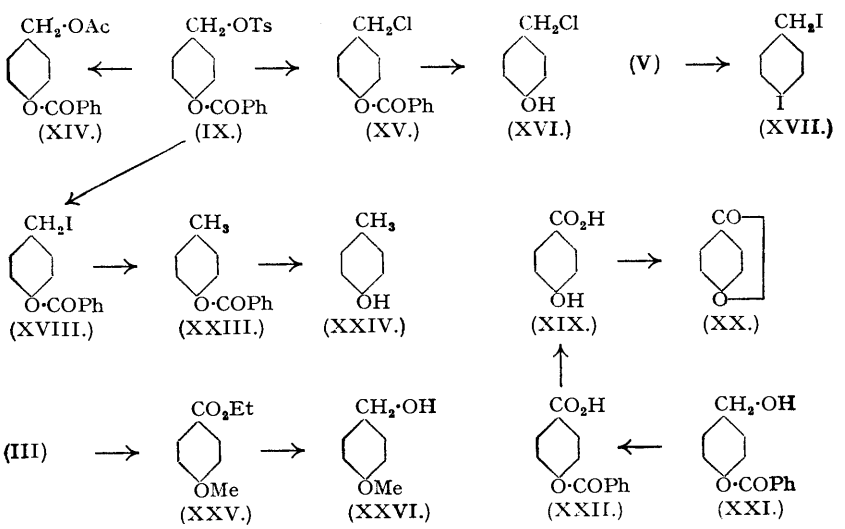
presumably have been easier from the *trans*-monotoluene-*p*-sulphonyl derivative of *cyclo*hexane-1 : 4-diol, in the present case it would be expected that ring formation would occur most readily from the *cis*-primary monotoluene-*p*-sulphonate, since the inversion accompanying removal of the toluene-*p*-sulphonyl group would not reverse the configuration at C_4. Both the *cis*- and *trans*-forms of (IX), however, reacted with methanolic potassium hydroxide to give 4-*methoxymethyl*cyclo*hexanol* (XII), indicating that ether formation had occurred intermolecularly with the solvent, rather than intramolecularly with the hydroxyl group at C_1.

The difference in reactivity between the primary and secondary toluene-*p*-sulphonyl groups was well demonstrated by reaction of the bistoluene-*p*-sulphonate (V) with methanolic potassium hydroxide, whereby the primary group was replaced to form an ether, whilst the secondary was eliminated with the introduction of a double bond, the product being 4-*methoxymethyl*cyclo*hexene* (XIII).

The *trans*-1-benzoate-ω-toluene-*p*-sulphonate (IX) reacted with methanolic potassium acetate to yield the 1-*benzoate*-ω-*acetate* (XIV), only a trace of acid being liberated. The replacement thus proceeds normally, in striking contrast to the behaviour of a secondary toluene-*p*-sulphonyl group under such conditions (cf. Part II).

Two experiments were carried out on the reaction of the toluene-*p*-sulphonyl-groups with lithium chloride. The *cis*-isomer of (IX) gave the *benzoate* (XV) of *cis*-4-chloromethyl*cyclo*hexanol (XVI) as an oil, which after removal of the benzoyl group by cautious saponification was characterised as the α-*naphthylurethane*. Similarly, the *trans*-ω-monotoluene-*p*-sulphonate (VIII) gave trans-4-*chloromethyl*cyclo*hexanol* (XVI), characterised as the *phenylurethane*, and the α-*naphthylurethane*. The *cis*- and *trans*-forms of the chloride (XVI) were also obtained from the corresponding forms of the glycol (I) by reaction with fuming hydrochloric acid, the urethanes being respectively identical with those described above.

It was shown in Parts I and II that a secondary toluene-*p*-sulphonyloxy-group can be replaced by iodine, though in rather poor yield, and the effect of sodium iodide in acetone solution on both *cis*- and *trans*-bistoluene-*p*-sulphonates (V) was therefore investigated. In each case an almost theoretical amount of sodium toluene-*p*-sulphonate was precipitated, with formation of the rather unstable 4-*iodomethyl*cyclo*hexyl iodide* (XVII). The product was a liquid, the physical properties of which were almost identical in the two preparations, so it was not possible to determine to what extent inversion had occurred at C_1 during the reaction. The *trans*-1-benzoate-ω-toluene-*p*-sulphonate (IX) reacted with sodium iodide in acetone to give a good yield of trans-4-*iodomethyl*cyclo*hexyl benzoate* (XVIII). Difference in reactivity between a primary and a secondary toluene-*p*-sulphonyl group was again evident in these reactions, and from the accumulated evidence it is now clear that at the temperature of boiling acetone the



precipitation of sodium toluene-*p*-sulphonate from a primary group is complete after 2—3 hours, whilst for a secondary group 12 hours or longer are necessary. In the latter case, decomposition

of the product invariably occurs, and better results with a secondary toluene-*p*-sulphonyl group are usually obtained by carrying out the reaction in a sealed tube at 100° for 2—3 hours.

The allocation of a *trans*-configuration to the solid form of the glycol (I) was subsequently confirmed by relating the compound to particular stereoisomers both of 4-hydroxy*cyclo*hexanecarboxylic acid and of 4-methyl*cyclo*hexanol. This hydroxy-acid (XIX) is known in two forms, m. p.s 120° and 152°, and the latter, despite its higher m. p. and lower solubility, was assigned the *cis*-configuration by Balas and Srôl (*loc. cit.*) on the grounds of the formation from it of a lactone (XX), m. p. 109—110°. Perkin (*J.*, 1904, **85**, 430) had earlier observed that dry distillation of the lower-melting form gave a solid product (m. p. not stated) which was said not to be a lactone; he had therefore assumed this acid, m. p. 120°, to be the *trans*-form. It has now been found, however, that this solid product described by Perkin is identical with the lactone described by Balas and Srôl. The previous evidence of configuration, which would in any event appear to have been rather dubious in view of the very vigorous conditions of lactonisation, is therefore nullified, but we have also observed that solution of the lactone in cold aqueous alkali, followed by acidification and extraction with ether, yields the acid, m. p. 152°. Since the opening of a lactone ring under mild conditions, considered as a simple saponification of a carboxylic ester, must occur without inversion, it follows that the acid, m. p. 152°, has the *cis*-configuration.

The pure *trans*-acid was converted into its ethyl ester and reduced by the Bouveault–Blanc method, but the glycol obtained was a mixture of stereoisomers, partial inversion having occurred, not unexpectedly, during the process. Attempts to oxidise the solid glycol preferentially at the primary hydroxyl group, in an endeavour to obtain one of the stereoisomeric hydroxy-acids, were not successful, but by cautious saponification of the *trans*-dibenzoate (IV) with one mol. of sodium hydroxide in aqueous acetone, the secondary *monobenzoate* (XXI) was obtained in good yield and identified by conversion of a sample into the ω-benzoate-1-toluene-*p*-sulphonate already described. Oxidation of (XXI) with chromic acid gave the *benzoate* (XXII) of 4-hydroxy*cyclo*hexanecarboxylic acid. Attempts to prepare this benzoate from either of the hydroxy-acids were unsuccessful, owing to their resistance to benzoylation; furthermore, the derivative itself was very resistant to saponification, but on refluxing for 24 hours with 20% methanolic potassium hydroxide it gave the *trans*-acid (XIX), m. p. 120°. A control experiment showed that the *cis*-acid, m. p. 152°, was not converted into the *trans*- under the vigorous treatment with alkali; isolation of the *trans*-acid therefore proves conclusively the *trans*-configuration of the original solid glycol.

Correlation between the glycol and the stereoisomeric forms of 4-methyl*cyclo*hexanol was readily achieved by hydrogenation of the *trans*-4-iodomethyl*cyclo*hexyl benzoate (XVIII) in methanol, with a platinum catalyst, to the trans-*benzoate* (XXIII) of 4-methyl*cyclo*hexanol, m. p. 34—35°. [The liquid benzoate of 4-methyl*cyclo*hexanol described by Zaki (*J.*, 1932, 1184) was probably a mixture of stereoisomers.] This compound, in contrast to the benzoate (XXII), readily underwent alcoholysis by the Zemplén method, and the resulting 4-methyl*cyclo*hexanol (XXIV) was identified as the *trans*-form by conversion into the phenylurethane and the α-naphthylurethane,. The allocation of the *cis*- and *trans*-configurations to the 4-methyl*cyclo*hexanols was previously based on physical properties (Skita and Faust, *Ber.*, 1931, **64**, 2878), but the present work has confirmed these earlier conclusions by relating the *trans*-alcohol, through the *trans*-glycol (I), to the *trans*-hydroxy-acid (XIX).

Confirmation of the structures assigned to the structurally isomeric benzoyl-toluene-*p*-sulphonyl derivatives (VII) and (IX) is afforded by the following observations. Methylation with methyl iodide and silver oxide of ethyl (*cis* + *trans*)-4-hydroxy*cyclo*hexanecarboxylate (III) afforded the *methyl ether* (XXV), which on reduction by the Bouveault–Blanc method gave (cis + trans)-4-*hydroxymethyl*cyclo*hexyl methyl ether* (XXVI) as a liquid, the α-naphthylurethane of which was separated by fractional crystallisation into two *stereoisomers*, cis(?)-, m. p. 95—96°; and *trans*(?) m. p. 113—114°. Neither of these derivatives was identical with the *α-naphthylurethane* obtained from the methyl ether (XII), which therefore must be structurally different, and consequently has the formula assigned to it; it follows that the toluene-*p*-sulphonyl derivative (IX) is correctly formulated. Independent evidence is also afforded by the fact that the monobenzoate (XXI), which on toluene-*p*-sulphonation gives (IX), must have a free primary hydroxyl group, since it is oxidised to the benzoyloxy-acid (XXII).

Experimental.

(Light petroleum, unless otherwise stated, refers to the fraction, b. p. 40—60°.)

Attempted Hydrogenation of Potassium p-*Hydroxybenzoate.*—*p*-Hydroxybenzoic acid (50 g.) and potassium hydroxide (24·5 g.) were dissolved in ethanol (300 c.c.) and stirred with hydrogen in the

presence of Raney nickel (10 g.) at 150°/150 atm. for 24 hours. After removal of solvent from the filtered solution, the residue was acidified with sulphuric acid and extracted with ether. Distillation of the product gave phenol (31·3 g.), m. p. 40°.

Decarboxylation of p-*Hydroxybenzoic Acid.*—The acid (5 g.), potassium hydroxide (2·5 g.), and ethanol (30 c.c.), heated for 24 hours at 150° and worked up as above, gave phenol (3 g.), m. p. 41°.

Ethyl 4-*Hydroxy*cyclo*hexanecarboxylate.*—Ethyl *p*-hydroxybenzoate (70 g., m. p. 112—114°) in ethanol (200 c.c.) was hydrogenated at 150°/85 atm. (initial pressure at room temperature) for 20 hours over Raney nickel (5 g.). The hydrogenated ester (55 g.) obtained by distillation of the product had b. p. 142—145°/15 mm., $n_D^{18°}$ 1·4673, and was mainly the *trans*-form, since on saponification with boiling 10% aqueous potassium hydroxide it gave a crude solid acid, m. p. 110—112°, raised on recrystallisation from ethyl acetate to 119·5° (*trans*-4-hydroxy*cyclo*hexanecarboxylic acid has m. p. 120°).

4-*Hydroxymethyl*cyclo*hexanol* (I).—(*a*) To a solution of ethyl 4-hydroxy*cyclo*hexanecarboxylate (172 g.) in anhydrous ethanol (1500 c.c.), contained in a 3 l. flask fitted with a large reflux condenser, was added sodium (138 g.). The reaction was allowed to proceed as vigorously as possible without mechanical loss, some cooling being necessary in the early stages. Finally, the mixture was heated on the steam-bath until all the sodium had dissolved (*ca.* 3 hours). After addition of water (200 c.c.), most of the alcohol was removed under reduced pressure. The residue, diluted with more water (400 c.c.), was continuously extracted with ether for 40 hours. Evaporation of the dried extracts gave an oil (106 g.) which partly solidified on treatment with acetone (50 c.c.) and ether (150 c.c.). The solid material was triturated with more acetone (50 c.c.), washed with a little ether, and recrystallised from ethyl acetate to give trans-4-*hydroxymethyl*cyclo*hexanol* in prisms, m. p. 103° (Found: C, 64·5; H, 10·6. $C_7H_{14}O_2$ requires C, 64·6; H, 10·8%). The combined mother liquors were diluted with ether until cloudy; the small quantity of precipitated solid was removed, and the filtrate evaporated to an oil (70 g.), which on distillation gave 56 g., b. p. 135—147°/3 mm., $n_D^{14°}$ 1·4910, of (mainly) *cis*-4-hydroxymethyl*cyclo*hexanol (Found: C, 65·1; H, 10·5). With excess of phenyl *iso*cyanate for 24 hours, it gave a *bisphenylurethane*, crystallising from benzene, m. p. 179—181° (Found: C, 68·2; H, 6·7. $C_{21}H_{24}O_4N_2$ requires C, 68·4; H, 6·6%). 4-Hydroxy*cyclo*hexanecarboxylic acid (18·9 g.) was recovered after acidification of the original aqueous residues.

(*b*) Ethyl 4-hydroxy*cyclo*hexanecarboxylate (50 g.) in ethanol (100 c.c.), with copper chromite catalyst (10 g., containing barium, prepared according to *Org. Synth.*, Coll. Vol. II, p. 142), was sealed in an autoclave under hydrogen at 125 atm. The autoclave was heated as rapidly as possible to 250°, the pressure then being 210 atm., whereupon stirring was begun. Pressure rose rapidly to 280 atm., and then fell slowly during 2 hours to 186 atm. Stirring and heating were then discontinued. Removal of solvent from the cooled and filtered mixture gave 23 g. of the glycol, b. p. 156—165°/15 mm., which was separated as above into the solid (7 g.) and liquid (14 g.) forms. Repetition of this hydrogenation failed to give comparable results, the products obtained containing much *p*-cresol and 4-methyl*cyclo*hexanol.

Derivatives of the trans-*Glycol.*—(*a*) With excess of benzoyl chloride in pyridine it gave the trans-*dibenzoate*, plates from aqueous methanol, m. p. 80—81° (Found: C, 74·5; H, 6·5. $C_{21}H_{22}O_4$ requires C, 74·5; H, 6·55%), and with excess of toluene-*p*-sulphonyl chloride in pyridine, the trans-*bistoluene*-p-*sulphonate* was obtained, crystallising from methanol in needles, m. p. 94° (Found: C, 57·4; H, 5·9. $C_{21}H_{26}O_6S_2$ requires C, 57·5; H, 6·0%).

(*b*) Treatment of the *trans*-glycol (5 g.) in pyridine (40 c.c.) and pure chloroform (25 c.c.) with a solution of benzoyl chloride (5 g.) in chloroform (40 c.c.), added with stirring at 0° during 1 hour, followed by standing overnight at room temperature, gave a liquid product which on fractional distillation gave the trans-*ω-monobenzoate* (6·2 g.) as a viscous oil, b. p. 95° (bath temp.)/10^{-5} mm., $n_D^{18°}$ 1·5346 (Found: C, 71·45; H, 8·0. $C_{14}H_{18}O_3$ requires C, 71·35; H, 7·75%). The higher-boiling material (1·2 g.), b. p. 120—125° (bath temp)/10^{-5} mm., solidified, and was the dibenzoate, m. p. 80—81°, identical with that described above. Treatment of the monobenzoate with toluene-*p*-sulphonyl chloride in pyridine gave the trans-*ω-benzoate*-1-*toluene*-p-*sulphonate*, which crystallised from benzene–light petroleum (b. p. 60—80°) in stout needles, m. p. 82—83° (Found: C, 64·9; H, 6·1. $C_{21}H_{24}O_5S$ requires C, 64·9; H, 6·2%).

(*c*) The *trans*-glycol (5 g.) in pyridine (40 c.c.) was treated at 0° with toluene-*p*-sulphonyl chloride (8·8 g.) added in small portions during 1 hour. After standing at room temperature overnight, the product was isolated as an oil, which on solution in methanol and cooling to 0° deposited a small quantity of the *trans*-bistoluene-*p*-sulphonate. Evaporation of the methanol then left a crude *ω*-monotoluene-*p*-sulphonate, which failed to crystallise and could not be distilled without decomposition; it was therefore dissolved in pyridine and treated with excess of benzoyl chloride, and gave the trans-1-*benzoate*-*ω*-*toluene*-p-*sulphonate* (11·1 g.) as long prisms from ethanol, m. p. 110—111° (Found: C, 65·1; H, 6·3. $C_{21}H_{24}O_5S$ requires C, 64·9; H, 6·2%).

Derivatives of the cis-*Glycol.*—(*a*) Treatment of the glycol (5 g.) dissolved in pyridine (50 c.c.) with excess of benzoyl chloride (15 g.) during 1·5 hours at 0° gave a deep purple mixture which was left at room temperature for 40 hours and then worked up to give an oil (18·1 g.). Distillation gave a lower fraction (5·3 g.) of a brown viscous nitrogenous oil, b. p. 85° (bath temp.)/5×10^{-6} mm., and a second fraction (9·1 g.) of a yellow nitrogen-free oil, b. p. 140—160° (bath temp.)/5×10^{-6} mm., which on redistillation gave the cis-*dibenzoate*, 7·5 g., b. p. 140—150° (bath temp.)/5×10^{-6} mm., $n_D^{15°}$ 1·5562, as an almost colourless viscous oil (Found: C, 74·95; H, 6·5. $C_{21}H_{22}O_4$ requires C, 74·5; H, 6·55%).

(*b*) The cis-*bistoluene*-p-*sulphonate*, prepared by reaction with excess of toluene-*p*-sulphonyl chloride in pyridine, crystallised from methanol in needles, m. p. 98·5°, depressed to 84° on admixture with the *trans*-isomer (Found: C, 57·6; H, 5·9. $C_{21}H_{26}O_6S_2$ requires C, 57·5; H, 6·0%).

(*c*) Treatment of the *cis*-glycol with 1 mol. of benzoyl chloride under the same conditions as those used for the preparation of the *trans*-monobenzoate gave the cis-*ω-monobenzoate* as a colourless viscous oil, b. p. 105° (bath temp.)/5×10^{-5} mm., $n_D^{20°}$ 1·5332 (Found: C, 71·2; H, 7·85. $C_{14}H_{18}O_3$ requires C, 71·75; H, 7·75%).

(*d*) The *cis*-glycol (10 g.) was treated in pyridine–chloroform solution with toluene-*p*-sulphonyl chloride (14·6 g.) under the usual conditions for the preparation of the mono-derivative. After being

left at room temperature for 24 hours the mixture was again cooled to 0°, and treated with benzoyl chloride (13·5 g.) in chloroform (50 c.c.). The product was isolated as a dark red oil (30 g.) which failed to solidify. It was decolourised by filtration of a solution in benzene–light petroleum through a column of activated alumina, but the *cis*-1-benzoate-ω-toluene-*p*-sulphonate failed to crystallise and could not be purified by distillation (Found: C, 68·0; H, 7·1. Calc. for $C_{21}H_{24}O_5S$: C, 64·9; H, 6·2%).

Action of Alkali on (IX).—(*a*) The *trans*-1-benzoate-ω-toluene-*p*-sulphonate (11 g.) was heated under reflux for 3 hours with 5% methanolic potassium hydroxide (100 c.c.). On cooling, and addition of ether, a crystalline mass of potassium toluene-*p*-sulphonate separated and was removed. The filtrate was neutralised with carbon dioxide, again filtered, concentrated to small bulk, and diluted with water. Extraction with ether gave trans-4-*methoxymethyl*cyclo*hexanol* (1·5 g.), b. p. 114—116°/18 mm., $n_D^{18°}$ 1·4652 (Found: C, 66·5; H, 11·3. $C_8H_{16}O_2$ requires C, 66·65; H, 11·2%). The *α-naphthylurethane* crystallised from light petroleum (b. p. 60—80°) in fine needles, m. p. 117—118° (Found: C, 72·95; H, 7·3. $C_{19}H_{23}O_3N$ requires C, 72·8; H, 7·4%).

(*b*) The crude *cis*-1-benzoate-ω-toluene-*p*-sulphonate (25 g.) was heated under reflux for 6 hours with 5% methanolic potassium hydroxide (200 c.c.). Working up as before gave a liquid product (7 g.), b. p. 124—128°/18 mm, $n_D^{19°}$ 1·4673, which was presumably mainly *cis*-4-methoxymethyl*cyclo*hexanol, although good analytical figures could not be obtained (Found: C, 67·3, 67·6; H, 11·2, 11·1. Calc. for $C_8H_{16}O_2$: C, 66·65; H, 11·2%). The product reacted readily with α-naphthyl *iso*cyanate, but a solid urethane could not be obtained.

*Action of Alkali on the Bistoluene-*p*-sulphonate* (V).—The *trans*-bistoluene-*p*-sulphonate (15 g.) and 5% methanolic potassium hydroxide (150 c.c.) were heated under reflux for 2 hours. After cooling, and removal of precipitated potassium toluene-*p*-sulphonate, the solution was concentrated to 20 c.c., diluted with ether, washed twice with water, dried, and evaporated to an oil, which on distillation gave 4-*methoxymethyl*cyclo*hexene*, 1·5 g., b. p. 86—88°/100 mm., $n_D^{23°}$ 1·4519 (Found: C, 76·6; H, 11·5. $C_8H_{14}O$ requires C, 76·15; H, 11·2%). The methanolic distillate contained unsaturated material, and a further small quantity of the methyl ether was recovered from it by dilution with water and extraction with ether; its evident volatility probably accounts for the poor yield.

Reaction of (IX) *with Potassium Acetate.*—The *trans*-1-benzoate-ω-toluene-*p*-sulphonate (3 g.) and potassium acetate (3 g.) in ethanol (30 c.c.) were refluxed for 3 hours. Water and chloroform were then added, and the lower layer separated. The aqueous layer contained only a trace of acid, requiring only 0·5 c.c. of N-sodium hydroxide for neutralisation to phenolphthalein. The chloroform layer was dried and evaporated to a solid residue (2·33 g.) of the trans-1-*benzoate-ω-acetate* (XIV) which crystallised from aqueous methanol in prisms, m. p. 78—79° (Found: C, 69·45; H, 7·3. $C_{16}H_{20}O_4$ requires C, 69·55; H, 7·3%).

Reaction of (IX) *with Lithium Chloride.*—The crude *cis*-1-benzoate-ω-toluene-*p*-sulphonate (6·4 g.) in ethanol (30 c.c.) was refluxed with lithium chloride (3 g.) for 5·5 hours. After concentration and dilution with water, ether extraction gave an oil (3·8 g.), which on distillation yielded the *benzoate* of *cis*-4-chloromethyl*cyclo*hexanol as a colourless oil, 2·9 g., b. p. 127—130°/0·3 mm., $n_D^{21°}$ 1·5288 (Found: C, 66·1; H, 6·9. $C_{14}H_{17}O_2Cl$ requires C, 66·5; H, 6·8%). Saponification of this compound (1 g.) by refluxing for 0·5 hour with 5% methanolic potassium hydroxide (20 c.c.) gave *cis*-4-chloromethyl*cyclo*hexanol as an oil (0·58 g.) which was characterised as the *α-naphthylurethane*, needles from light petroleum (b. p. 100—120°), m. p. 123° (Found: C, 68·05; H, 6·2. $C_{18}H_{20}O_2NCl$ requires C, 68·0; H, 6·3%).

Reaction of (VIII) *with Lithium Chloride.*—Crude *trans*-ω-monotoluene-*p*-sulphonate (14 g., prepared by toluene-*p*-sulphonation of the *trans*-glycol) was refluxed in ethanol (50 c.c.) for 7·5 hours with lithium chloride (9 g.). The product was a yellow oil (11·7 g.) which on distillation furnished trans-4-*chloromethyl*cyclo*hexanol* as a colourless oil, b. p. 98—99/4 mm., $n_D^{16°}$ 1·4931 (Found: C, 55·9; H, 9·0. $C_7H_{13}OCl$ requires C, 56·6; H, 8·8%). The *phenylurethane* separated from light petroleum (b. p. 60—80°) in needles, m. p. 129—130° (Found: C, 62·9; H, 6·6. $C_{14}H_{18}O_2NCl$ requires C, 62·8; H, 6·8%). The *α-naphthylurethane* crystallised from light petroleum (b. p. 100—120°) in leaflets, m. p. 183—184° (Found: N, 4·5. $C_{18}H_{20}O_2NCl$ requires N, 4·4%).

4-*Chloromethyl*cyclo*hexanol from the Glycol.*—(*a*) The *trans*-glycol (10 g.) dissolved in fuming hydrochloric acid (20 c.c., *d* 1·19) was heated in a sealed tube at 80—90° for 6 hours, during which time two layers were formed. The upper layer was diluted with ether, washed with sodium hydrogen carbonate, dried, evaporated, and distilled to give *trans*-4-chloromethyl*cyclo*hexanol, 8·9 g., b. p. 98—100°/3 mm., $n_D^{23°}$ 1·4910, $n_D^{33°}$ 1·4884, characterised as the phenylurethane, m. p. 129—130°, identical with that described above.

(*b*) The *cis*-glycol (15 g.), similarly treated, gave cis-4-*chloromethyl*cyclo*hexanol*, 11·5 g., b. p. 106—112°/12 mm., $n_D^{14°}$ 1·4940 (Found: C, 56·8; H, 8·6. $C_7H_{13}OCl$ requires C, 56·55; H, 8·8%), which gave an α-naphthylurethane, m. p. 122°, identical with that obtained by the other route.

*Action of Sodium Iodide on the Bistoluene-*p*-sulphonate* (V).—(*a*) The *cis*-bistoluene-*p*-sulphonate (3 g.) and sodium iodide (4 g.) in dry acetone (20 c.c.) were heated in a sealed tube at 100° for 1·5 hours. The product, isolated in the usual way, on distillation gave 4-*iodomethyl*cyclo*hexyl iodide* (1·3 g.) as a deep yellow liquid, b. p. 40—50° (bath temp.)/10^{-4} mm., $n_D^{22°}$ 1·6209 (Found: I, 72·6. $C_7H_{12}I_2$ requires I, 72·5%).

(*b*) The *trans*-bistoluene-*p*-sulphonate (3 g.) on reaction with sodium iodide (4 g.) as for the *cis*-compound, also gave 4-iodomethyl*cyclo*hexyl iodide (2·5 g.), $n_D^{22°}$ 1·6180, identical in properties with that obtained from the *cis*-bis-*p*-toluenesulphonate.

*Action of Sodium Iodide on the Benzoate-toluene-*p*-sulphonate* (IX).—The *trans*-1-benzoate-ω-toluene-*p*-sulphonate (5 g.) and sodium iodide (3·3 g.) in acetone (50 c.c.) were heated under reflux for 5 hours. After addition of ether, the filtered solution was washed with aqueous sodium thiosulphate, dried, and evaporated to a solid residue (3 g.) of trans-4-*iodomethyl*cyclo*hexyl benzoate*, m. p. 49—53°, raised to 56—57° by sublimation at 70°/10^{-4} mm., or by recrystallisation from aqueous methanol (Found: C, 48·9; H, 4·85. $C_{14}H_{17}O_2I$ requires C, 48·85; H, 5·0%).

4-*Hydroxy*cyclo*hexanecarboxylic Acid.*—(*a*) *p*-Hydroxybenzoic acid (5 g.) in ethanol (30 c.c.) was shaken with hydrogen in the presence of Adams's platinum catalyst for a total of 28 hours, by which time

the theoretical volume of gas (2·6 l.) had been absorbed, the catalyst being renewed at intervals when the rate of absorption became slow. Crystallisation of the product from acetone gave *cis*-4-hydroxy-*cyclo*hexanecarboxylic acid (2·7 g.), m. p. 152° From the mother liquors a small quantity of the *trans*-isomer, m. p. 120°, was obtained.

(*b*) Ethyl 4-hydroxy*cyclo*hexanecarboxylate (65 g.) was saponified by refluxing with 20% aqueous potassium hydroxide (400 c.c.) for 3 hours. After removal of unchanged ester by extraction with ether, the aqueous solution was acidified and constantly extracted with ether for several hours, to yield a solid acid (51 g.). This on crystallisation from acetone gave mainly the *trans*-acid, m. p. 120°.

Lactone of 4-*Hydroxy*cyclo*hexanecarboxylic Acid* (XX).—The *trans*-acid, m. p. 120° (4 g.), was distilled at atmospheric pressure over a free flame. The distillate, b. p. 250—270°, largely solidified, and unlike the acid was readily soluble in a small amount of boiling ether, from which it separated in leaflets, m. p. 108—112°, unchanged on recrystallisation (Balas and Srôl, *loc. cit.*, give m. p. 109—110° for the lactone prepared from the *cis*-acid). This lactone dissolved slowly in cold 10% aqueous potassium hydroxide solution, and acidification of the solution, followed by saturation with salt and continuous extraction with ether, gave an extract which on cooling deposited prisms of the *cis*-acid, m. p. 152—153°. Concentration of the extract to small bulk gave a further quantity, m. p. 147—149°, raised to 152° by recrystallisation from ethyl acetate. Evaporation of the mother liquors to dryness gave no indication of the lower melting (*trans*) form.

Reduction of Ethyl trans-4-*Hydroxy*cyclo*hexanecarboxylate*.—The ester (21 g.), b. p. 143—144°/12 mm., $n_D^{14°}$ 1·4678, prepared by esterification of the pure *trans*-acid with ethanol and sulphuric acid, was reduced with sodium and alcohol as previously described to give a semi-solid product (13 g.) which on crystallisation from acetone gave the *trans*-glycol (I) (4·5 g.), m. p. 102°. The remaining material, recovered from the mother liquors, failed to crystallise and, in the light of the earlier experiments, evidently consisted largely of the *cis*-glycol.

Partial Saponification of the Dibenzoate (IV).—To a solution of the *trans*-dibenzoate (8·16 g.) in acetone (80 c.c.), N-aqueous sodium hydroxide (25 c.c.) was added. After being shaken at room temperature for 48 hours, the solution was no longer alkaline to phenolphthalein and it was diluted with water and extracted with chloroform. Removal of solvent from the dried extracts, and distillation of the resulting oil, gave the slightly impure trans-1-*monobenzoate* (XXI), 3·5 g., b. p. 120—130° (bath temp.)/10^{-5} mm., $n_D^{18°}$ 1·4351 (Found: C, 72·5; H, 7·75. $C_{14}H_{18}O_3$ requires C, 71·75; H, 7·75%). The residue in the distillation flask (0·7 g.) crystallised, and was identified as unchanged *trans*-dibenzoate, m. p. 80° after crystallisation from methanol. The monobenzoate, treated with toluene-*p*-sulphonyl chloride in pyridine, gave the *trans*-1-benzoate-*ω*-toluene-*p*-sulphonate (IX), m. p. 110—111°, identical with that previously obtained.

Benzoate of trans-4-*Hydroxy*cyclo*hexanecarboxylic Acid*.—The 1-monobenzoate (2·3 g.) was heated at 100° for 1 hour with a solution of chromium trioxide (1·5 g.) in acetone (25 c.c.). After addition of a few drops of methanol to destroy excess of oxidising agent, the mixture was poured into water and extracted twice with ether. The extracts, after being washed with water, were extracted with saturated sodium hydrogen carbonate solution, and the latter then acidified and extracted twice with ether. These extracts were dried and evaporated to a solid residue (1·4 g.) which on recrystallisation from ethyl acetate gave the *benzoate* of *trans*-4-hydroxy*cyclo*hexanecarboxylic acid as long laths, m. p. 145—146° (Found: C, 67·7; H, 6·5. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·45%). This compound (2·9 g.) was saponified by being heated under reflux with 20% methanolic potassium hydroxide (10 c.c.) for 24 hours. Most of the solvent was removed, and 10% sulphuric acid was added in slight excess (Congo-red). After cooling, benzoic acid (1·32 g.), m. p. and mixed m. p. 122°, was removed, and the filtrate was evaporated to dryness. The residue, extracted continuously with ether for 6 hours, gave a solid (0·72 g.) which was dissolved in the minimum amount of boiling ethyl acetate On cooling, a small quantity (0·1 g.) of unchanged benzoate separated in prisms, m. p. 142—144°. The ethyl acetate solution was then evaporated to dryness and the residue crystallised from ether to yield *trans*-4-hydroxy*cyclo*hexanecarboxylic acid, m. p. and mixed m. p. 119—120°.

Stability of cis-4-*Hydroxy*cyclo*hexanecarboxylic Acid to Alkali*.—The *cis*-acid (0·5 g.) was refluxed with 20% methanolic potassium hydroxide (5 c.c.) for 24 hours. The solution was then concentrated, acidified with a slight excess of 2N-sulphuric acid (Congo-red), and evaporated to dryness under reduced pressure. The solid residue, extracted continuously with ether for 6 hours, furnished stout needles of the unchanged acid (0·43 g.), m. p. and mixed m. p. 152°.

Hydrogenation of trans-4-*Iodomethyl*cyclo*hexyl Benzoate*.—The compound (2·5 g.) and potassium acetate (1·1 g.) in methanol (40 c.c.) were shaken with hydrogen in the presence of Adams's platinum catalyst (0·1 g.) for 3 hours, by which time 1·01 mols. had been absorbed. The filtered solution was concentrated, diluted with water, and extracted with ether. The dried extracts on evaporation yielded a yellow oil (1·4 g.) which solidified on standing at 0°. The solid was very soluble in organic solvents but sublimed at 30—40°/10^{-4} mm. to give the *benzoate* (XXIII) of *trans*-4-methyl*cyclo*hexanol as a white powder, m. p. 34—35° (Found: C, 77·0; H, 8·4. $C_{16}H_{18}O_2$ requires C, 77·0; H, 8·3%).

trans-4-*Methyl*cyclo*hexanol* (XXIV).—The above benzoate (0·5 g.) was dissolved in dry methanol (5 c.c.) and treated with a trace of sodium methoxide (0·1 c.c. of a 20% solution in methanol). After 40 hours at room temperature, the solvent was evaporated, and the residual *trans*-4-methyl*cyclo*hexanol was identified as the phenylurethane, m. p. 123—124°, and the α-naphthylurethane, m. p. 158° (Found: C, 76·0; H, 7·5. Calc. for $C_{18}H_{21}O_2N$: C, 76·3; H, 7·5%). Skita and Faust (*loc. cit.*) give m. p. 124—125° for the *trans*-phenylurethane, and m. p. 116—117° for the *cis*; Ungnade and McLaren (*J. Amer. Chem. Soc.*, 1944, **66**, 118) give m. p. 124—124·5° for the *trans*-phenylurethane, and m. p. 156·5—157·5° for the *trans*-α-naphthylurethane.

Ethyl 4-*Methoxy*cyclo*hexanecarboxylate* (XXV).—Ethyl 4-hydroxy*cyclo*hexanecarboxylate (20 g., *cis* and *trans*) was dissolved in methyl iodide (50 g.) and refluxed during the addition, in small quantities, of silver oxide (41 g.). Dry ether (50 c.c.) was added after the addition of half the silver oxide. Finally, the mixture was refluxed for 2·5 hours. Silver compounds were then removed by filtration and thoroughly extracted with ether. Evaporation of the filtrate and washings and fractionation of the residue gave

ethyl 4-*methoxy*cyclo*hexanecarboxylate* (10·3 g.), b. p. 118—122°/16 mm., $n_D^{15°}$ 1·4541 (Found: C, 64·6; H, 9·45. $C_{10}H_{18}O_3$ requires C, 64·5; H, 9·75%). A higher-boiling fraction (6·5 g.), b. p. 140—146°/16 mm., consisted of unchanged hydroxy-ester.

4-*Hydroxymethyl*cyclo*hexyl Methyl Ether* (XXVI).—The above methoxy-ester (10 g.) dissolved in ethanol (96 c.c.) was reduced by the addition of sodium (7·5 g.), the mixture being warmed on the steam-bath. When all the sodium had reacted, water (30 c.c.) was added, and most of the alcohol distilled off. The residual solution was saturated with salt and extracted with ether to give 4-*hydroxymethyl*cyclo*hexyl methyl ether* as a colourless oil (5·1 g.), b. p. 116—118°/13 mm., $n_D^{15°}$ 1·4699 (Found: C, 66·8; H, 11·4. $C_8H_{16}O_2$ requires C, 66·65; H, 11·2%). This product, a mixture of *cis*-and *trans*-forms, gave a solid α-naphthylurethane which was successively extracted with (i) cold light petroleum, (ii) boiling light petroleum (b. p. 60—80°), (iii) boiling light petroleum (b. p. 80—100°), (iv) boiling light petroleum (b. p. 100—120°). On concentration, (i) yielded fine needles, (ii) deposited a mixture of needles and dense concretions, (iii) gave a mass of dense concretions, and (iv) gave no solid. The two forms in (ii) were readily separated by flotation. Recrystallisation of the needles from light petroleum gave stellate clusters of the (cis?)-*α-naphthylurethane*, m. p. 95—96° (Found: C, 72·7; H, 7·4. $C_{19}H_{23}O_3N$ requires C, 72·8; H, 7·4%). The concretions, recrystallised from light petroleum (b. p. 60—80°), gave long prisms of the (trans?)-*α-naphthylurethane*, m. p. 113—114° (Found: C, 72·7; H, 7·4%). The m. p. of the latter compound was depressed to *ca.* 100° on admixture with the α-naphthylurethane, m. p. 117—118°, of the structurally isomeric methyl ether (XII).

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