

434. Alicyclic Glycols. Part XVI.* Decalin 2 : 3-Ketols.

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A new route to each stereoisomer of *cyclohexane-1 : 2*-diacetic acid is described. Acyloin cyclisation of the *cis*- and the *trans*-dimethyl ester leads to 2 : 3-ketols in the *cis*- and the *trans*-decalin series. Elimination of the keto-group furnishes the corresponding decalol and enables an assignment of configuration to be made to the hydroxyl group in each ketol; the results are in accordance with conformational requirements.

IN connection with studies on the decalin-2 : 3-diols, reported in the following paper, convenient sources of the 3-oxodecalin-2-ols were required. By hydrolysis of 2-chloro-3-oxo-*trans*-decalin Lehmann and Krätschell¹ obtained two ketols, m. p.s 84° and 134°, and by a similar method in the *cis*-series Cook and Lawrence² prepared one, m. p. 88—90°, of the two possible *cis*-fused isomers; the higher-melting ketol in the *trans*-series was also obtained³ by reduction of *trans*-decalin-2 : 3-dione, but no configuration was allocated to the hydroxyl group in any of these compounds. In our hands, Lehmann and Krätschell's procedure gave only one product, m. p. 82°. The overall yields from the decalones are very poor, and an alternative approach was therefore desirable.

An obvious synthetic route is the acyloin cyclisation of an ester of *cyclohexane-1 : 2*-diacetic acid, but when the present investigation was begun neither the *cis*- nor the *trans*-acid was readily obtainable in quantity, both having been prepared hitherto by oxidation of Δ^2 -octalin or of suitable oxygenated decalin derivatives; very recently Stork and Hill⁴ have reported an improved method for the *cis*-acid which involves the ozonolysis of an oxalyl derivative of *cis*-decalin-2-one. Attempts to apply the Arndt-Eistert method to *cyclohexane-cis-1 : 2*-dicarboxyl chloride were unpromising, but the availability of the two stereoisomers of 1 : 2-bishydroxymethylcyclohexane⁵ opened a new and convenient route. By reaction of the *trans*-ditoluene-*p*-sulphonate (I) with potassium cyanide in ethanol the dinitrile (II) and a small amount of the ethoxy-nitrile (III) were obtained; hydrolysis of the former gave *cyclohexane-trans-1 : 2*-diacetic acid in good yield. The *cis*-ditoluene-*p*-sulphonate was similarly converted into the *cis*-acid, the *cis*-ethoxy-nitrile (V) being obtained as a by-product at the intermediate stage. Hydrolysis of each ethoxy-nitrile (III) and (V) with boiling 50% sulphuric acid gave the same lactonic product, as shown by the formation of identical *S*-benzylisothiuronium salts of the corresponding hydroxy-acid. The most likely explanation of the change in configuration which must have occurred with one isomer is that under the vigorous conditions elimination occurs to give the unsaturated acid (IV), which could then give either a γ - or a δ -lactone. The infrared spectrum showed a peak at 1735 cm.⁻¹ characteristic of a δ -lactone, and the product is therefore formulated as the lactone (VI) of (*cis* or *trans*)-2-hydroxymethylcyclohexylacetic acid. In acyclic γ -unsaturated acids with a terminal double bond lactonisation occurs preferentially at the γ - rather than the δ -position,⁶ but in the present instance the production of a bicyclic system evidently favours the formation of a second six-membered ring.

By the use of Sheehan's⁷ convenient modification of the acyloin cyclisation, dimethyl *cyclohexane-trans-1 : 2*-diacetate was converted in 70% yield into a ketol, m. p. 82—83°, identical with that obtained from 3-chloro-*trans*-decalin-2-one. The presence of a

* Part XV, Ali and Owen, *J.*, 1958, 1074.

¹ Lehmann and Krätschell, *Ber.*, 1934, **67**, 1857.

² Cook and Lawrence, *J.*, 1937, 817.

³ Ganapathi, *J. Indian Chem. Soc.*, 1938, **15**, 407.

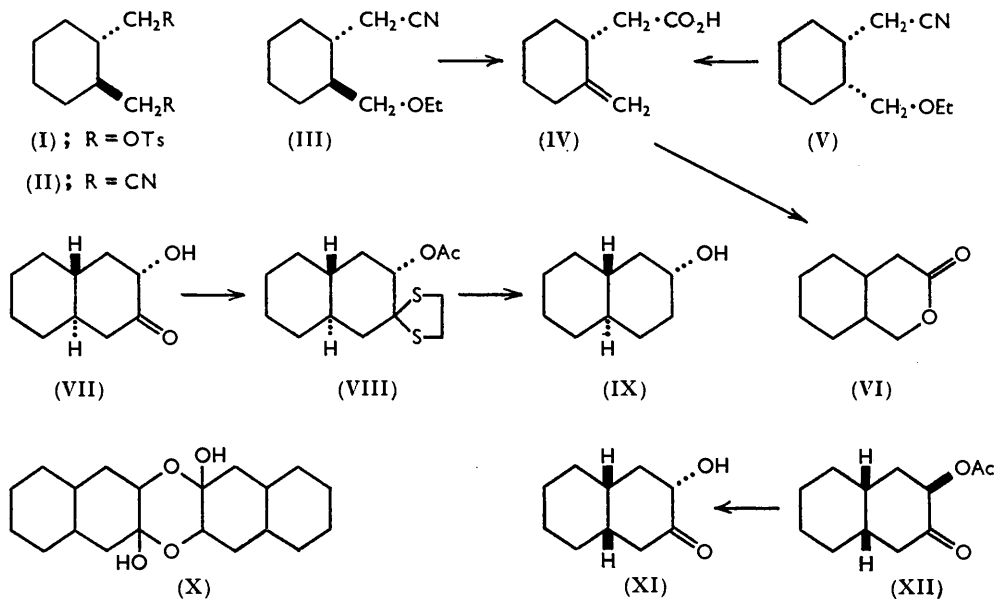
⁴ Stork and Hill, *J. Amer. Chem. Soc.*, 1957, **79**, 495.

⁵ Haggis and Owen, *J.*, 1953, 389.

⁶ Linstead and Rydon, *J.*, 1933, 580.

⁷ Sheehan and Coderre, *J. Amer. Chem. Soc.*, 1953, **75**, 3997.

carbonyl and a hydroxyl group was shown by the infrared spectrum and confirmed by the preparation of a semicarbazone, a 2:4-dinitrophenylosazone, a toluene-*p*-sulphonate, a 3:5-dinitrobenzoate, an acetate (from which the same ketol was regenerated on deacetylation), and an acetate 2:4-dinitrophenylhydrazone; oxidation with bismuth trioxide⁸ gave *trans*-decalin-2:3-dione. Lehmann and Krätschell¹ reported failure to acetylate their ketols, and claimed to have obtained the lower-melting ketol from the isomer by treatment with toluene-*p*-sulphonyl chloride in pyridine; it is difficult to understand why they did not obtain the toluene-*p*-sulphonate under these conditions. The ketol showed no tendency to enolise, since it gave no colour with ferric chloride, and its infrared spectrum was devoid of absorption attributable to an ethylenic linkage.



In the double-chair form of the *trans*-decalin system each hydrogen atom or substituent has one definite conformation, axial or equatorial, which is determined by its configuration, and the isolation of only one of the two possible ketols suggested that this was the 2 α -compound (VII),* in which the hydroxyl group is in the more stable equatorial position; † the configurational stability of the ketol was confirmed by its resistance towards epimerisation by sodium ethoxide. The position of the C-O stretching band in the infrared spectrum of sterols has been shown to depend upon the conformation of the hydroxyl group, an equatorial and an axial disposition giving rise to absorption at *ca.* 1040 and *ca.* 1000 cm.⁻¹, respectively.^{9,10} The absorption of the acetates is also characteristic, those with an equatorial group giving a single band in the 1200—1250 cm.⁻¹ region,

* In this and the following paper the designations α and β are used to indicate configurations in the same sense as in the steroid field, the decalin skeleton being always represented with a β -orientated hydrogen atom at C₍₉₎.

† It seems unlikely that dipole interaction between the equatorial hydroxyl and the carbonyl group, which it almost eclipses, would be sufficiently strong to favour the axial conformation, as occurs with certain bromo-ketones (cf. ref. 15); the equatorial conformation would also permit stabilisation by hydrogen bonding.

⁸ Rigby, *J.*, 1951, 793.

⁹ Cole, Jones, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 5571; Rosenkrantz, Milhorat, and Farber, *J. Biol. Chem.*, 1952, **195**, 509.

¹⁰ Fürst, Kuhn, Scotoni, and Gunthard, *Helv. Chim. Acta*, 1952, **35**, 951; Braude and Waight in "Progress in Stereochemistry", ed. Klyne, Butterworths, 1954, Vol. I, p. 126.

whilst for an axial conformation the band is complex.^{10,11} For the decalols the distinction is not so clearly defined, though their acetates conform to the above generalisation.¹² The infrared spectrum of the ketol (VII) showed no band near 1000 cm^{-1} , but several between 1025 and 1087 cm^{-1} ; the acetate showed a strong single maximum at 1233 cm^{-1} . These results therefore supported the α -configuration, and confirmatory chemical evidence was provided by reaction of the ketol acetate with ethane-1 : 2-dithiol, and desulphurisation of the product (VIII) to give, after deacetylation, *trans*-decalin-2 α -ol (IX), the configuration of which rests on a sound basis.¹²

When the product from the acyloin reaction was worked up under acidic conditions a very sparingly soluble compound was obtained instead of the ketol; it was also slowly formed when the pure ketol was stored, and more rapidly from the crude ketol. It showed no carbonyl band in the infrared spectrum and gave no immediate reaction with 2 : 4-dinitrophenylhydrazine, but when heated with this reagent it gave the 2 : 4-dinitrophenylosazone of *trans*-decalin-2 : 3-dione and was readily converted into the dione by oxidation with bismuth trioxide. With pyridine-acetic anhydride at 100° it gave the monomeric ketol acetate identical with that described above. Although the apparent molecular weight (Rast method) was approximately that of the monomeric ketol this is no doubt due to dissociation by heat, and the compound is evidently the dimer (X) analogous to that formed¹³ from 2-hydroxycyclohexanone.

Unlike the reaction in the *trans*-series, the acyloin cyclisation of dimethyl cyclohexane-*cis*-1 : 2-diacetate gave a mixture. One product, m. p. 89—90°, isolated in 27% yield, was a monomeric ketol which gave derivatives of the keto- and the hydroxy-function, but the infrared spectrum, which included a group of bands with frequencies ranging from 1010 to 1087 cm^{-1} , was not configurationally decisive. The acetate, m. p. 74—75°, however, showed a strong *single* peak at 1227 cm^{-1} , indicating¹² the α -configuration, and this was confirmed by reaction with ethane-1 : 2-dithiol, followed by desulphurisation and deacetylation to give *cis*-decalin-2 α -ol. The ketol is therefore 3-oxo-*cis*-decalin-2 α -ol (XI), and is probably identical with that described by Cook *et al.*² The second product isolated was a dimer, which showed no carbonyl absorption in the infrared region, but this compound was not derived from the ketol (XI) since on vigorous acetylation it gave an isomeric ketol acetate, m. p. 98—99°, whose infrared spectrum differed significantly from that of the lower-melting isomer in that the acetate band showed *twin* peaks at 1231 and 1223 cm^{-1} , consistent¹² with a β -configuration (XII). Each acetate gave an individual 2 : 4-dinitrophenylhydrazone, and, with an excess of the reagent, the same 2 : 4-dinitrophenylosazone of *cis*-decalin-2 : 3-dione. An interesting observation was that the 2 α - and the 2 β -acetate by solvolysis in the presence of sodium ethoxide gave the same 3-oxo-*cis*-decalin-2 α -ol (XI). In the flexible *cis*-decalin system there are two interconvertible double-chair forms, and in passing from one to the other an axially disposed group becomes equatorial and *vice versa*. Consequently a hydroxyl group in either the 2 α - or the 2 β -configuration can take up the stable equatorial position, and at first sight the exclusive formation of the one isomer (XI) from both acetates under epimerisation conditions seems unexpected. It is necessary, however, to take account of the important non-bonded interactions which occur between certain axially disposed groups attached to different rings.¹⁴ In conformation (XIII) of the 2 α -ketol ($\alpha = \text{OH}$; $\beta = \text{H}$) there are three such interactions, *viz.*, $\text{O}_{(2)}\text{-H}_{(6)}$, $\text{H}_{(6)}\text{-H}_{(4)}$, and $\text{H}_{(4)}\text{-H}_{(6)}$, and in the first of these the oxygen-hydrogen distance (centre to centre) is only 1.7 Å, a situation which must result in

¹¹ Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1951, **73**, 3215; Jones and Herling, *ibid.*, 1956, **78**, 1152.

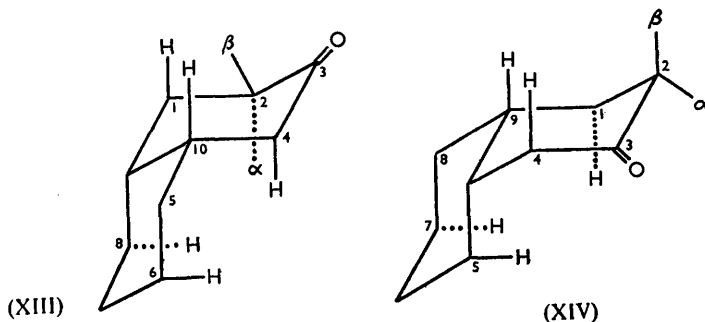
¹² Dauben, Hoerger, and Freeman, *J. Amer. Chem. Soc.*, 1952, **74**, 5206.

¹³ Sheehan, O'Neill, and White, *ibid.*, 1950, **70**, 3376.

¹⁴ Mills, *J.*, 1953, 260; Dauben, Tweit, and Mannerskantz, *J. Amer. Chem. Soc.*, 1954, **76**, 4420; Dauben and Pitzer, Ch. 1 of "Steric Effects in Organic Chemistry," ed M. S. Newman, Chapman and Hall Ltd., 1956.

considerable steric repulsion; the distance between the hydrogen atoms involved in the other two is 1.85 Å, which would result in smaller but still significant repulsions each equivalent to a skew-butane interaction. The alternative conformation (XIV) exhibits only the two interactions $H_{(5)}-H_{(1)}$ and $H_{(1)}-H_{(7)}$ (there being no inter-ring effect involving the carbonyl group¹⁵), and furthermore lacks the ordinary 1:3-diaxial repulsion $O_{(2)}-H_{(4)}$ present in (XIII). With the 2 β -ketol ($\alpha = H$; $\beta = OH$), conformation (XIII) has three inter-ring repulsions, $H_{(2)}-H_{(8)}$, $H_{(8)}-H_{(4)}$, and $H_{(4)}-H_{(6)}$, whilst (XIV) has $H_{(5)}-H_{(1)}$ and $H_{(1)}-H_{(7)}$ plus the two ordinary diaxial interactions $O_{(2)}-H_{(4)}$ and $O_{(2)}-H_{(9)}$. Although some interaction may occur between the carbonyl group and an equatorial hydroxyl at $C_{(2)}$ (as mentioned above in connection with the *trans*-decalin isomer), this would be the same for both the 2 α -ketol in conformation (XIV) and the 2 β -ketol in conformation (XIII). Thus, of the four possibilities, the 2 α -ketol in conformation (XIV) would be expected to be the most stable, having one fewer skew-butane interaction than the 2 β -ketol in conformation (XIII).

Some further points arising from the spectroscopic results are of interest. In agreement with the conclusions, by Dickson and Page,¹⁶ that a vicinal acetoxy-group, whether axial or equatorial, raises the C=O stretching frequency, the three ketol acetates all showed a carbonyl absorption maximum at 1733 cm^{-1} , compared with *ca.* 1720 cm^{-1} for *cis*- and *trans*-decalin-2-one.¹⁷ The C=O and C-O stretching frequencies in the acetate group, which in the three compounds were at *ca.* 1750 and 1230 cm^{-1} respectively, also showed the expected¹⁶ displacement from the normal values (*ca.* 1730 and 1240 cm^{-1}).



In the ultraviolet region, the weak carbonyl band in a simple steroid ketone at *ca.* 280 $\text{m}\mu$ is displaced to a lower wavelength by a vicinal equatorial hydroxyl or acetoxy-group, to the extent of *ca.* 12 $\text{m}\mu$ and 5 $\text{m}\mu$ respectively.¹⁸ Both *cis*- and *trans*-decalin-2-one show this band at 283 $\text{m}\mu$; ^{19,20} the maxima for the *cis*- and the *trans*-decalin ketol were at 273 and 275 $\text{m}\mu$, respectively, in good agreement with prediction, but the two stereoisomeric *cis*-decalin ketol acetates both showed a maximum at 282 $\text{m}\mu$ and the *trans*-decalin ketol acetate one at 287 $\text{m}\mu$. Since, from the arguments advanced above, the vicinal group in all these compounds is in the equatorial position, the generalisation evidently cannot be safely applied to acetates, though it is still true that acetylation of the equatorial hydroxyl group in the ketols results in a marked shift of the carbonyl band to a longer wavelength.

EXPERIMENTAL

Microanalyses in this and the following paper were by Miss J. Cuckney and staff, and absorption spectra by Mr. R. L. Erskine, B.Sc., A.R.C.S., and Mrs. A. I. Boston.

¹⁵ Klyne, *Experientia*, 1956, **12**, 119.

¹⁶ Dickson and Page, *J.*, 1955, 447.

¹⁷ Lecomte, *J. Phys. Radium*, 1945, **6**, 257.

¹⁸ Cookson and Dandegaonker, *J.*, 1955, 352; Baumgartner and Tamm, *Helv. Chim. Acta*, 1955, **38**, 441.

¹⁹ Biquard, *Bull. Soc. chim. France*, 1941, **8**, 725.

²⁰ Tsatsas, *Ann. Chim.*, 1944, **19**, 247.

trans-Decalin-2 : 3-dione 2 : 4-Dinitrophenylosazone.—The diketone, prepared by Ganapathi's³ method, had m. p. 99—100° (lit.,³ m. p. 99—100°); λ_{max} in ethanol 269 m μ (ϵ 7500); disemicarbazone, m. p. 264° (lit.,³ m. p. 264—265°). Reaction with 2 : 4-dinitrophenylhydrazine (2 mol.) in methanolic sulphuric acid for a few minutes under reflux gave red needles (from chloroform-methanol) of the 2 : 4-dinitrophenylosazone, m. p. 218—219° (decomp.) (Found: C, 50.4; H, 4.45; N, 21.5. $\text{C}_{22}\text{H}_{22}\text{O}_8\text{N}_8$ requires C, 50.2; H, 4.2; N, 21.3%); λ_{max} in chloroform 243, 260, 353, 400 m μ (ϵ 21,000, 21,500, 34,000, 24,000, respectively).

Reaction of 2-Chloro-3-oxo-trans-decalin with Aqueous Sodium Hydroxide.—The chloro-ketone²⁰ (3.4 g.) was boiled under reflux for 1 hr. with a deficiency (70 c.c.) of 1% aqueous sodium hydroxide, according to the conditions described by Lehmann and Krättschell.¹ The mixture, which had become neutral, was cooled, and the solid (2.6 g.), m. p. 63—69°, was collected; it contained halogen. Fractional crystallisation from methanol and from aqueous methanol gave only 3-oxo-*trans*-decalin-2 α -ol (1.2 g.), m. p. and mixed m. p. 82°, and a trace of the dimer, m. p. 122° (see below). Evaporation of the mother liquors, and recrystallisation of the residue from light petroleum (b. p. 60—80°), gave more ketol (0.2 g.), m. p. 82°. The halogen-containing residue obtained by evaporation of the petroleum mother liquors was re-treated with boiling alkali as before, and gave a further quantity (0.3 g.) of ketol, m. p. 80—82°. No higher-melting epimer was encountered.

Ditoluene-p-sulphonates of 1 : 2-Bishydroxymethylcyclohexane.—Improved yields were obtained by a modification of the original⁵ method. The *trans*-diol (71.5 g.) in dry pyridine (260 c.c.) was added drop by drop to a vigorously stirred solution of toluene-*p*-sulphonyl chloride (215 g.) in dry pyridine (450 c.c.) at 0° during 4 hr. The stirring was continued for 2 hr. at room temperature, and the mixture was then poured into ice-water. The precipitate was washed with water and recrystallised from methanol to give the *trans*-ditoluene-*p*-sulphonate (200 g., 89%), m. p. 108° (lit.,⁵ m. p. 108°).

The *cis*-ditoluene-*p*-sulphonate, m. p. 83—84° (lit.,⁵ m. p. 84—85°), was similarly prepared (yield, 68%) from *cis*-1 : 2-bishydroxymethylcyclohexane.

trans-1 : 2-Biscyanomethylcyclohexane.—The *trans*-ditoluene-*p*-sulphonate (200 g.), potassium cyanide (83.5 g.), ethanol (1200 c.c.), and water (120 c.c.) were boiled under reflux for 60 hr. The alcohol was then removed under reduced pressure and the residue was diluted with water and extracted with ether. Removal of solvent from the dried (Na_2SO_4) extract, followed by careful distillation of the residue through a short Vigreux column, gave (i) 3.7 g., b. p. 90—108°/0.4 mm., and (ii) *trans-1 : 2-biscyanomethylcyclohexane* (49.5 g., 69%), b. p. 143—144°/0.4 mm., n_{D}^{20} 1.4829 (Found: C, 73.6; H, 8.8; N, 17.1. $\text{C}_{10}\text{H}_{14}\text{N}_2$ requires C, 74.0; H, 8.7; N, 17.3%). Redistillation of (i) gave *trans-2-ethoxymethylcyclohexylmethyl cyanide*, b. p. 76°/0.2 mm., n_{D}^{20} 1.4600 (Found: C, 72.8; H, 10.4; N, 7.85. $\text{C}_{11}\text{H}_{19}\text{ON}$ requires C, 72.9; H, 10.6; N, 7.7%).

cycloHexane-trans-1 : 2-diacetic Acid.—A mixture of *trans-1 : 2-biscyanomethylcyclohexane* (49.5 g.) and 50% sulphuric acid (1200 c.c.) was boiled under reflux for 8 hr. The mixture was cooled and the solid, m. p. 166—167°, was collected and recrystallised from aqueous methanol to give *cyclohexane-trans-1 : 2-diacetic acid* (50 g., 82%), m. p. 167° (lit.,²¹ m. p. 167°).

Dimethyl cycloHexane-trans-1 : 2-diacetate.—The acid (30 g.), dry methanol (19 g.), dry benzene (56 c.c.), and concentrated sulphuric acid (9 g.) were boiled under reflux overnight. Water was then added and the benzene layer was washed with aqueous sodium hydrogen carbonate, and water, and dried (Na_2SO_4). Removal of the solvent and distillation of the residue gave the *trans-dimethyl ester* (30.8 g., 90%), b. p. 115°/0.7 mm., n_{D}^{19} 1.4625 (Found: C, 62.95; H, 8.9. $\text{C}_{12}\text{H}_{20}\text{O}_4$ requires C, 63.1; H, 8.8%).

cis-1 : 2-Biscyanomethylcyclohexane.—A mixture of *cis-1 : 2-bishydroxymethylcyclohexane* ditoluene-*p*-sulphonate (163.5 g.), potassium cyanide (70 g.), ethanol (900 c.c.), and water (90 c.c.) was boiled under reflux for 24 hr. The product was isolated as described for the corresponding *trans*-compound, and was distilled through a short Vigreux column to give (i) 7.5 g., b. p. 50—130°/0.2 mm., and (ii) the *cis-dinitrile* (23.1 g., 39.4%), b. p. 130°/0.2 mm., n_{D}^{20} 1.4865 (Found: C, 74.1; H, 8.9; N, 17.6. $\text{C}_{10}\text{H}_{14}\text{N}_2$ requires C, 74.0; H, 8.7; N, 17.3%). The lower-boiling fraction on redistillation gave *cis-2-ethoxymethylcyclohexylmethyl cyanide* (2 g.), b. p. 70°/0.2 mm., n_{D}^{21} 1.4624 (Found: C, 72.6; H, 10.4; N, 7.8. $\text{C}_{11}\text{H}_{19}\text{ON}$ requires C, 72.9; H, 10.6; N, 7.7%).

cycloHexane-cis-1 : 2-diacetic Acid.—A mixture of *cis-1 : 2-biscyanomethylcyclohexane*

²¹ Hüchel, *Annalen*, 1925, **444**, 1.

(23 g.) and 50% sulphuric acid (552 g.) was boiled under reflux for 3 hr., and then cooled. The precipitated solid on recrystallisation from aqueous methanol gave the *cis*-diacetic acid (26 g., 91.5%), m. p. 159—161° (lit.,⁴ m. p. 160—161°).

Dimethyl cycloHexane-cis-1 : 2-diacetate.—Esterification of the above acid (26 g.), as described for the corresponding *trans*-compound, gave the *cis*-dimethyl ester (26.4 g., 90%), b. p. 91°/0.1 mm., n_D^{20} 1.4645 (Found: C, 62.7; H, 8.9. $C_{12}H_{20}O_4$ requires C, 63.1; H, 8.8%).

Hydrolysis of a sample of this ester regenerated *cyclohexane-cis-1 : 2-diacetic acid* (80%), m. p. 160—161°.

2-Hydroxymethylcyclohexylacetic Acid Lactone.—(i) A mixture of *cis*-2-ethoxymethylcyclohexylmethyl cyanide (0.7 g.) and 50% sulphuric acid (10 g.) was boiled under reflux for 8 hr., then cooled, diluted with water, and extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate and with water, and evaporated. The residue was dissolved in 10% aqueous sodium hydroxide (10 c.c.), with shaking, and the solution was washed once with ether, then acidified with sulphuric acid and extracted with ether to give an oil, which on distillation furnished 3-oxo-4-oxabicyclo[4 : 4 : 0]decane (0.25 g.), b. p. 122°/4 mm., n_D^{19} 1.4915 (Found: C, 70.15; H, 9.1. Calc. for $C_9H_{14}O_2$: C, 70.1; H, 9.15%); ν_{max} . (liquid film) 1735 cm^{-1} (δ -lactone). For the *cis*-lactone, Stork and Hill⁴ give b. p. 115—120°/4 mm., ν_{max} . 1727 cm^{-1} .

A solution of the lactone (0.1053 g.) in ethanol (10 c.c.) was treated with 0.0900N-aqueous potassium hydroxide, added 2 c.c. at a time, phenolphthalein being used as indicator. The colour disappeared slowly after each addition and became permanent after 8 c.c. had been added. The solution was then heated (steam-bath) for a few minutes and the excess of alkali was back-titrated with 0.1095N-hydrochloric acid (0.42 c.c.) (Found: equiv., 152. Calc.: equiv., 154). The titrated solution was concentrated and mixed with a solution of *S*-benzylisothiuronium chloride (0.15 g.) in water (1 c.c.). The precipitate was recrystallised from aqueous methanol to give the *S*-benzylisothiuronium salt, m. p. 140°, of 2-hydroxymethylcyclohexylacetic acid (Found: C, 60.6; H, 7.7; N, 8.3. $C_{17}H_{26}O_3N_2S$ requires C, 60.3; H, 7.7; N, 8.3%).

(ii) *trans*-2-Ethoxymethylcyclohexylmethyl cyanide (0.8 g.), on similar hydrolysis, gave a slightly impure lactone (0.35 g.), b. p. 112—116°/3 mm., n_D^{20} 1.4849 (Found: C, 69.4; H, 9.6%; equiv., determined as described above, 147), which furnished the same *S*-benzylisothiuronium salt, m. p. and mixed m. p. 139°.

Acyloin Cyclisation of Dimethyl cycloHexane-trans-1 : 2-diacetate.—Sodium (10.5 g.) was added in small portions with stirring during 15 min. to dry ether (1000 c.c.) and liquid ammonia (1400 c.c.), and after a further 15 min. the stirring was stopped and all air was displaced by a rapid stream of oxygen-free dry nitrogen. The nitrogen flow was then reduced, and maintained until after the final acidification stage. The *trans*-dimethyl ester (15 g.) in dry ether (1000 c.c.) was added dropwise during 8 hr. with vigorous stirring. The ammonia was allowed to evaporate at room temperature (ca. 24 hr.) and the flask was then warmed at 45—50° to remove the remaining ether. When the contents of the flask became dry, more dry ether (100 c.c.) was added and subsequently removed in a similar way. This process of addition and removal of ether was repeated 3 or 4 times until all the ammonia was removed. Finally, dry ether (300 c.c.) was added, followed by the gradual addition, during 20 min., of acetic acid (32 g.) in dry ether (200 c.c.). The precipitated sodium acetate was filtered off and washed with ether. The combined filtrate and washings were washed with aqueous sodium hydrogen carbonate, then with water, and were dried (Na_2SO_4) and evaporated under reduced pressure to give 3-oxo-*trans*-decalin-2 α -ol (8 g., 72%), which after recrystallisation from ether-light petroleum (b. p. 40—60°) had m. p. 82—83° (Found: C, 71.9; H, 9.9. Calc. for $C_{10}H_{16}O_2$: C, 71.4; H, 9.6%); λ_{max} . in ethanol 275 μ (ϵ 28); ν_{max} . in paraffin mull 3385 (O—H stretching), 1708 (C=O stretching), 1087, 1080, 1064, 1047, 1025 cm^{-1} . It readily reduced Fehling's solution, and bismuth oxide in boiling acetic acid. With aqueous 2 : 4-dinitrophenylhydrazine sulphate it immediately gave a yellow precipitate which, when heated with excess of the reagent on the steam-bath for a few minutes, gave the 2 : 4-dinitrophenylosazone of *trans*-decalin-2 : 3-dione, m. p. and mixed m. p. 219° (decomp.).

After storage for 2 months a sample of the originally pure ketol had m. p. 78—80°; it was extracted with boiling ether, and filtered from a small amount of insoluble residue. The filtrate, on concentration and dilution with light petroleum (b. p. 40—60°) gave the original ketol, m. p. 82°. The ether-insoluble material was washed several times with boiling methanol to give the dimer, *trans*-A/B : *trans*-D/E-5a : 12a-dihydroxy-6 : 13-dioxaperhydropentacene, a white powder,

m. p. 122—123° (Found: C, 71.1; H, 9.7%; *M* in camphor, 178. $C_{20}H_{32}O_4$ requires C, 71.4; H, 9.6%; *M*, 336); dissociation to the monomer is evidently almost complete in molten camphor. Infrared absorption (in paraffin mull): ν_{\max} . 3413 cm^{-1} (O—H stretching) (no carbonyl band). It slowly reduced boiling Fehling's solution and bismuth oxide in boiling acetic acid. It gave no precipitate with alcoholic 2 : 4-dinitrophenylhydrazine sulphate (in which the compound was insoluble) in the cold, but on continued boiling with excess of the reagent the 2 : 4-dinitrophenylosazone of *trans*-decalin-2 : 3-dione, m. p. and mixed m. p. 219°, was formed.

A sample of crude ketol, stored for about a month, gave a much greater proportion of insoluble material, which was washed with ether to give the same dimer, m. p. and mixed m. p. 122—123°.

On one occasion, the product of the acyloin condensation, in the ethereal solution, was not washed with sodium hydrogen carbonate to free it from excess of acetic acid and the acidic ethereal solution was as such evaporated at 50° under reduced pressure; only the dimer, m. p. and mixed m. p. 122—123° (after being washed with ether) was obtained.

Derivatives of 3-Oxo-trans-decalin-2 α -ol.—The *semicarbazone* formed prisms (from methanol), m. p. 177° (Found: C, 58.9; H, 8.15; N, 19.0. $C_{11}H_{19}O_2N_3$ requires C, 58.65; H, 8.5; N, 18.7%).

The *toluene-p-sulphonate*, prepared from the ketol (0.2 g.) and toluene-*p*-sulphonyl chloride (0.27 g.) in pyridine (0.6 c.c.) (12 hr. at room temperature) and isolated by precipitation with ice (yield 0.3 g.), formed needles (from methanol), m. p. 101° (Found: C, 63.5; H, 7.1; S, 9.9. $C_{17}H_{22}O_4S$ requires C, 63.3; H, 6.9; S, 9.9%).

The 3 : 5-*dinitrobenzoate*, similarly prepared (yield, 72%), formed prisms (from acetone-ethanol), m. p. 147° (Found: C, 56.5; H, 5.2; N, 7.75. $C_{17}H_{18}O_7N_2$ requires C, 56.35; H, 5.0; N, 7.7%).

Reaction of the ketol (4 g.) in pyridine (13 c.c.) with acetic anhydride (5 g.) for 10 min. on the steam-bath, followed by storage at room temperature overnight, and dilution with crushed ice, gave the *acetate* (3.9 g., 77%), needles (from aqueous methanol), m. p. 64—65° (Found: C, 68.6; H, 8.7. $C_{12}H_{18}O_3$ requires C, 68.5; H, 8.6%); λ_{\max} . in ethanol 287 $m\mu$ (ϵ 33); ν_{\max} . in carbon tetrachloride 1749 and 1733 ($C=O$ stretching in ester and in ketone), 1233 ($C-O$ stretching in acetate) cm^{-1} .

Similar treatment of the dimeric ketol (0.22 g.) with acetic anhydride (1 g.) and pyridine (1.6 c.c.) gave the same acetate (0.21 g., 76%), m. p. and mixed m. p. 64—65°.

Reaction of the ketol acetate (0.044 g.) in methanol (1 c.c.) with 2 : 4-dinitrophenylhydrazine sulphate (0.040 g. of 2 : 4-dinitrophenylhydrazine in 0.3 c.c. of concentrated sulphuric acid and 3 c.c. of methanol) gave a precipitate which on recrystallisation from dioxan gave the *acetate* 2 : 4-*dinitrophenylhydrazone* (0.065 g., 79%) as yellow needles, m. p. 202° (Found: C, 55.1; H, 5.7; N, 13.9. $C_{18}H_{22}O_6N_4$ requires C, 55.4; H, 5.7; N, 14.35%).

Deacetylation of 3-Oxo-trans-decalin-2 α -yl Acetate.—Treatment of the ketol acetate (0.1 g.) with methanolic sodium methoxide (*ca.* 0.01 g. of sodium in 10 c.c. of methanol) at room temperature overnight, followed by neutralisation with carbon dioxide, evaporation to dryness under reduced pressure at room temperature, and extraction of the residue with ether, regenerated the *trans*-ketol (0.055 g., 68%), which after one recrystallisation from light petroleum (b. p. 60—80°) had m. p. and mixed m. p. 82°.

Dimethylene Thioketal of 3-Oxo-trans-decalin-2 α -yl Acetate.—A mixture of the ketol acetate (0.30 g.), ethane-1 : 2-dithiol (0.13 g.), acetic acid (3 c.c.), a small drop of sulphuric acid, and a little anhydrous sodium sulphate was kept for 24 hr. at room temperature, then diluted with ether, washed with water, then with aqueous sodium hydrogen carbonate, and again with water, and dried (Na_2SO_4). Removal of the ether afforded an oil (0.33 g., 64%) which solidified, and on recrystallisation from pentane gave the *dimethylene thioketal*, plates, m. p. 96° (Found: C, 58.7; H, 7.9; S, 22.0. $C_{14}H_{22}O_2S_2$ requires C, 58.7; H, 7.7; S, 22.4%).

Desulphurisation. A solution of the thioketal (0.25 g.) in dry ethanol (100 c.c.) was boiled under reflux with Raney nickel catalyst (10 g.) for 24 hr. The mixture was filtered and the catalyst was thoroughly washed with ethanol. The filtrate and washings were combined and evaporated to an oil (which had a strong characteristic odour of a decalinyll acetate); this was deacetylated by treatment with a catalytic amount of sodium methoxide in dry methanol (5 c.c.) under reflux for 30 min. to give a solid (0.085 g., 63%), m. p. 71—73°. One recrystallisation from light petroleum (b. p. 60—80°) gave *trans*-decalin-2 α -ol, m. p. and mixed m. p. 74—75°.

Attempted Epimerisation of 3-Oxo-trans-decalin-2 α -ol.—(i) A solution of the ketol (0.15 g.) in 1.5N-ethanolic sodium ethoxide (10 c.c.) was boiled under reflux for 10 min. Neutralisation of the cooled mixture with carbon dioxide, followed by evaporation to dryness under reduced pressure, extraction with ether, and evaporation of the dried extract, gave a residue which crystallised from light petroleum (b. p. 60–80°) to give the starting material (0.07 g.), m. p. and mixed m. p. 82–83°.

(ii) A mixture of the ketol (0.30 g.), 10% aqueous sodium hydroxide (7 c.c.), and dioxan (3 c.c.) was heated on the steam-bath for 30 min. The dioxan was removed under reduced pressure and the aqueous solution was acidified with dilute sulphuric acid. Extraction with ether again gave the starting material (0.2 g.), m. p. and mixed m. p. 82°.

Oxidation of 3-Oxo-trans-decalin-2 α -ol with Bismuth Oxide.—The ketol (0.10 g.), bismuth trioxide (0.17 g.), and acetic acid (1.5 c.c.) were boiled under reflux for 10 min., then cooled and filtered. The filtrate was diluted with 2N-sulphuric acid and extracted with ether to give a semisolid, which when sublimed at 140°/0.3 mm. gave *trans*-decalin-2 : 3-dione (0.045 g., 46%), m. p. and mixed m. p. 98–100°; 2 : 4-dinitrophenylosazone, m. p. and mixed m. p. 219°.

Similar oxidation of the dimeric form of the above ketol (0.5 g.) with bismuth trioxide (0.7 g.) in acetic acid (5 c.c.) gave the same diketone, m. p. and mixed m. p. 99–100°.

Acyloin Cyclisation of Dimethyl cycloHexane-cis-1 : 2-diacetate.—The method was the same as for the corresponding *trans*-compound. The *cis*-ester (4 g.) gave on evaporation of the washed ethereal solution a paste which was dissolved in hot light petroleum (b. p. 60–80°) and cooled; the solid which crystallised out was collected, and the mother-liquor was preserved. Recrystallisation of the solid from ether–light petroleum (b. p. 40–60°) gave 3-oxo-*cis*-decalin-2 α -ol (0.8 g., 27%), m. p. 89–90° (Found: C, 71.0; H, 9.6. Calc. for C₁₀H₁₆O₂: C, 71.4; H, 9.6%); a mixed m. p. with the *trans*-isomer, m. p. 82°, was 59° (reported² m. p. for one of the two possible ketols: 88–90°); λ_{\max} . in ethanol 273 m μ (ϵ 23); ν_{\max} . in paraffin mull, 3425 (O–H stretching), 1709 (C=O stretching), 1089, 1080, 1047, 1040, 1010 cm.⁻¹. It readily reduced Fehling's solution, and with excess of aqueous 2 : 4-dinitrophenylhydrazine sulphate it gave the 2 : 4-dinitrophenylosazone of *cis*-decalin-2 : 3-dione, red needles (from chloroform–methanol), m. p. 226–227° (Found: C, 50.2; H, 4.3; N, 20.8. C₂₂H₂₂O₆N₈ requires C, 50.2; H, 4.2; N, 21.3%).

Unlike the *trans*-analogue, 3-oxo-*cis*-decalin-2 α -ol was unchanged after storage for several months.

The light petroleum mother-liquors spontaneously evaporated to dryness in 14 days, and the residue was boiled with ether to give an ether-insoluble solid (soluble in hot methanol) which was a *cis*-dimer, *cis*-A/B : *cis*-D/E-5a : 12a-dihydroxy-6 : 13-dioxaperhydropentacene (0.32 g.), m. p. 110–112° (Found: C, 71.1; H, 9.7. C₂₀H₃₂O₄ requires C, 71.4; H, 9.6%); ν_{\max} . in paraffin mull 3552 and 3437 (O–H stretching) cm.⁻¹.

Concentration of the ethereal solution and crystallisation of the residue from ether gave *cis*-decalin-2 α : 3 β -diol (0.06 g.), m. p. and mixed m. p. 125° (Found: C, 70.3; H, 10.7. Calc. for C₁₀H₁₈O₂: C, 70.5; H, 10.65%) (for proof of configuration see following paper).

Derivatives of 3-Oxo-cis-decalin-2 α -ol.—The *semicarbazone*, needles (from methanol), m. p. 195–196° (Found: C, 58.5; H, 8.55; N, 18.3%), the *toluene-p-sulphonate*, needles (from methanol), m. p. 109° (Found: C, 63.2; H, 7.2; S, 9.8%), the *acetate*, needles (from aqueous methanol), m. p. 74–75° (Found: C, 68.6; H, 8.8%), and the *acetate 2 : 4-dinitrophenylhydrazone*, yellow needles (from ethyl acetate–methanol), m. p. 203–204° (Found: C, 55.3; H, 5.8; N, 14.3%), were all prepared as described for the corresponding *trans*-derivatives. Light absorption of the acetate: λ_{\max} . in ethanol 282 m μ (ϵ 25); ν_{\max} . in carbon tetrachloride 1752 and 1732 (C=O stretching in ester and in ketone), 1227 (C–O stretching in acetate) cm.⁻¹.

Dimethylene Thioketal of 3-Oxo-cis-decalin-2 α -yl Acetate.—Prepared from the acetate (0.66 g.) by the same procedure as for the *trans*-decalin analogue, the *dimethylene thioketal* crystallised from pentane in prisms (0.70 g., 77%), m. p. 84–85° (Found: C, 58.9; H, 7.9; S, 22.6. C₁₄H₂₂O₂S₂ requires C, 58.7; H, 7.7; S, 22.4%).

Desulphurisation. The thioketal (0.64 g.), Raney nickel catalyst (W6) (10 g.), and dry ethanol (100 c.c.) were boiled under reflux for 24 hr. The product was isolated and deacetylated as described for the *trans*-isomer to give *cis*-decalin-2 α -ol, m. p. 100–102°; the m. p. of a mixture with an authentic sample (m. p. 104°) was 100–102°.

3-Oxo-cis-decalin-2 β -yl Acetate.—A mixture of the dimeric *cis*-ketol (m. p. 110–112°; 0.47 g.), acetic anhydride (2.5 c.c.), and pyridine (3.6 c.c.) was heated on the steam-bath for

10 min. The mixture was kept for 18 hr. at room temperature and was then diluted with ice-water. The solid was recrystallised from aqueous methanol to give 3-oxo-cis-decalin-2 β -yl acetate (0.46 g., 79%), needles, m. p. 98—99° (Found: C, 68.5; H, 8.8. C₁₂H₁₈O₃ requires C, 68.5; H, 8.6%); λ_{max} in ethanol 282 m μ (ϵ 27); ν_{max} in carbon tetrachloride 1750 and 1733 (C=O stretching in ester and ketone), 1231 and 1223 (C—O stretching in acetate) cm.⁻¹.

This ketol acetate (0.028 g.) with 2:4-dinitrophenylhydrazine sulphate in methanolic sulphuric acid gave a solid which on recrystallisation from dioxan-methanol (1:2) gave the 2:4-dinitrophenylhydrazone of 3-oxo-cis-decalin-2 β -yl acetate (0.036 g., 69%), yellow needles, m. p. 217—218° (Found: C, 55.4; H, 5.7; N, 14.3. C₁₈H₂₂O₆N₄ requires C, 55.4; H, 5.7; N, 14.35%). The m. p. of a mixture with the 2:4-dinitrophenylhydrazone of 3-oxo-cis-decalin-2 α -yl acetate was 195°.

Deacetylation of the Acetates of 3-Oxo-cis-decalin-2 α - and -2 β -ol.—(i) The 2 α -acetate (0.062 g.) was treated with methanolic sodium methoxide (ca. 0.003 g. in 10 c.c. of methanol) for 18 hr. at room temperature. The solution was then neutralised with carbon dioxide and evaporated to dryness under reduced pressure. The residue was stirred with a little water and extracted with ether. Removal of the solvent from the dried extract and crystallisation of the residue from light petroleum (b. p. 60—80°) gave 3-oxo-cis-decalin-2 α -ol, m. p. and mixed m. p. 88—89°.

(ii) Exactly similar treatment of the 2 β -acetate (0.060 g.) also gave 3-oxo-cis-decalin-2 α -ol, m. p. and mixed m. p. 89—90°.

Formation of cis-Decalin-2:3-dione 2:4-Dinitrophenylosazone from the Acetates of 3-Oxo-cis-decalin-2 α - and -2 β -ol.—(i) The 2 α -acetate (0.02 g.) in methanol (1 c.c.) was treated with ca. 5 mol. of methanolic 2:4-dinitrophenylhydrazine sulphate. The mixture was heated on the steam-bath whereupon the yellow precipitate quickly turned orange-red. The heating was continued for 1 hr. and then the precipitate was collected, washed with methanol, and crystallised from chloroform-methanol, to give cis-decalin-2:3-dione 2:4-dinitrophenylosazone (0.04 g.), m. p. and mixed m. p. 226—227°.

(ii) Similar treatment of the 2 β -acetate (0.02 g.) gave the same 2:4-dinitrophenylosazone (0.04 g.), m. p. and mixed m. p. 226—227°.

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