747. *The Preparation of Novel Decalin Derivatives from* 10β-(1,2-*Dihydroxyethyl*)-trans-1β-*decalol.*

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The above named triol, as its isopropylidene derivative, was oxidised to the *trans*-1-decalone from which 9-(1,2-dihydroxyethyl)-*cis*-decalin was obtained by Wolff–Kishner reduction and subsequent acid hydrolysis. This change of configuration was observed again when the *trans*-1-decalone (VI) was condensed with ethane-1,2-dithiol. Other derivatives of *cis*- and *trans*-decalin are described (see V and IX ⟶ XII).

Previous work [1] on the products of oxidation of 10β-vinyl-*trans*-decalin 1β,1′-oxide, the primary product of the interaction of decalin and a Friedel–Crafts acetylating agent, included the isolation of 10β-(1,2-dihydroxyethyl)-*trans*-1β-decalol (I) and its isopropylidene derivative (II). Our previous communications have been concerned only with those derivatives of *trans*-decalin which were involved in the determination of the structure of the oxide; we now report the preparation of other novel derivatives of both *cis*- and *trans*-decalin from the isopropylidene derivative (II).

Compound (II), a *trans*-1β-decalol, with chromium trioxide in pyridine gave, almost quantitatively, the corresponding *trans*-decalone (III) from which the isopropylidene derivative (IV) of 9-(1,2-dihydroxyethyl)-*cis*-decalin was obtained by the Huang-Minlon modification of the Wolff–Kishner reduction. The structure of the decalone (III) was established by showing that with lithium aluminium hydride it regenerated the *trans*-decalol (II), while that of the product (IV) was determined as follows: acid hydrolysis gave a glycol, which with periodic acid gave formaldehyde and an aldehyde, $C_{11}H_{18}O$, from which *cis*-decalin-9-carboxylic acid [2] was obtained by oxidation with permanganate.

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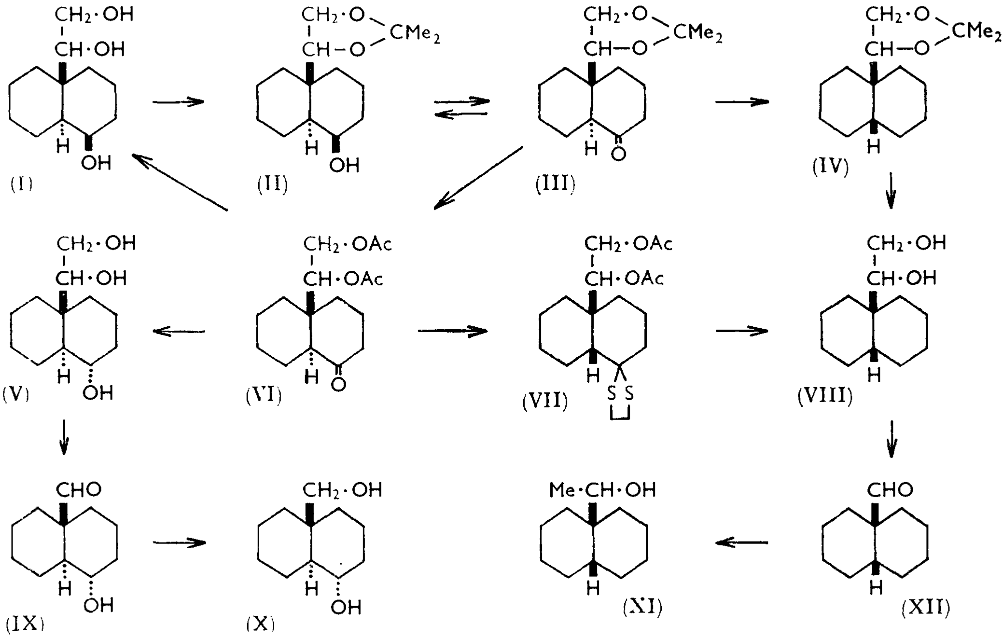
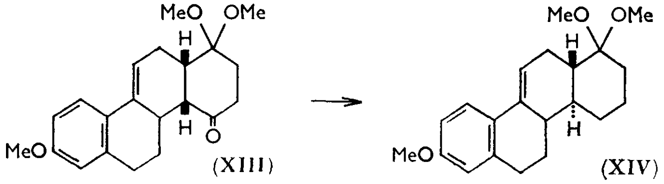
[1] Baddeley, Heaton, and Rasburn, *J.*, 1960, 4713.

[2] Dauben and Rogan, *J. Amer. Chem. Soc.*, 1957, **79**, 5002; Haworth and Turner, *J.*, 1958, 1240.

These transformations, therefore, had provided the novel compounds, 9-(1,2-dihydroxyethyl)-*cis*-decalin (VIII) and 9-formyl-*cis*-decalin (XII). The change of configuration of the decalin moiety in the Wolff–Kishner reduction (III ⟶ IV) is not unexpected. A recently reported example of a similar change (see XIII ⟶ XIV) occurred in the stereoselective total synthesis [3] of œstrone.





Having previously prepared 9-1′-hydroxyethyl-*trans*-decalin,[4] we have now, for comparison, prepared the *cis*-isomer (XI) by treating the aldehyde (XII) with methylmagnesium iodide.

Acid hydrolysis of the isopropylidene derivative (III) and acetylation of the product gave a compound, $C_{16}H_{24}O_5$, which is 10-(1,2-diacetoxyethyl)-*trans*-1-decalone (VI) since alkaline hydrolysis of the product of its reaction with potassium borohydride gave the *trans*-decalol (I). Interaction of the decalone (VI) and ethane-1,2-dithiol in glacial acetic acid containing zinc chloride involved a configurational change since the resulting crystalline thioketal (see VII) gave the *cis*-decalin derivative (VIII) when desulphurised with Raney nickel. Comparable configurational changes in thioketal formation are well known, *e.g.*, 5β- and 5α-cholestan-4-one give the same thioketal from which 5α-cholestane is obtained by desulphurisation. Applying views previously expressed by Djerassi and Gorman [5] we suggest that the condensation is suitably represented by the annexed scheme.

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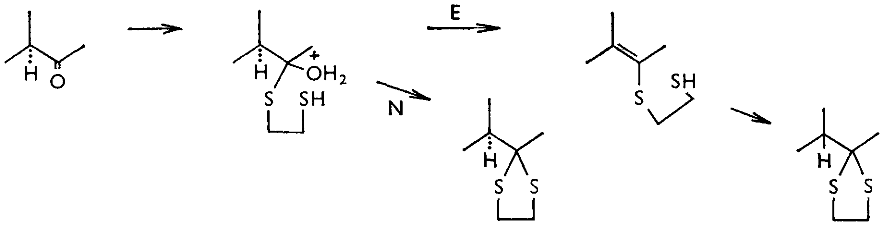
[3] Cole, Johnson, Robins, and Walker, *Proc. Chem. Soc.*, 1958, 114.

[4] Baddeley and Wrench, *J.*, 1959, 1324.

[5] Djerassi and Gorman, *J. Amer. Chem. Soc.*, 1953, **75**, 3704.



If the nucleophilic displacement (N) is hindered, elimination (E) may intervene and result in thioketal formation with change of configuration. The condensation of the decalone (III) with ethane-1,2-dithiol by means of the boron trifluoride–ether complex as catalyst did not give a solid product; the reaction was not studied further.

Reduction of the diacetate (VI) with lithium aluminium hydride afforded the triol (V) which is stereoisomeric with (I). It is noteworthy that the transfer of hydride ion from lithium aluminium hydride to $C_{(1)}$ occurred at the α-position for the isopropylidene derivative (III) and at the β-position for the diacetate (VI). Since it occurred at the α-position for the ketone (VI) when potassium borohydride was used, we suggest that lithium aluminium hydride attacked first the ester groups of (VI) and thereafter reduced the carbonyl group at $C_{(1)}$ intramolecularly. The *trans*-1α-decalol (V) thus obtained gave 10β-formyl- (IX) and 10β-hydroxymethyl-*trans*-1α-decalol (X) by reaction with periodic acid and lithium aluminium hydride successively.

The decalol (II) and thionyl chloride (1 mol.) in benzene and pyridine at 0° afforded only the sulphite ester of the decalol. Attempts to prepare the toluene-*p*-sulphonate by reaction with toluene-*p*-sulphonyl chloride in pyridine at room temperature during several days and for 2 hours at 100° gave only unchanged decalol.

EXPERIMENTAL

10β-(1,2-*Isopropylidenedioxyethyl*)-trans-1-*decalone* (III).—The isopropylidene derivative (II) [1] (3·3 g.) of 10β-(1,2-dihydroxyethyl)-*trans*-1β-decalol, in pyridine (15 ml.), was added dropwise to a stirred mixture of chromium trioxide (4·0 g.) and pyridine (50 ml.). After a week at room temperature, the mixture was added to ice (200 g.), and the excess of oxidant was destroyed with sulphur dioxide. The *isopropylidene derivative* (III) separated and crystallised from light petroleum (b. p. 60—80°) in plates (2·9 g.), m. p. 107° (Found: C, 71·3; H, 9·6. $C_{15}H_{24}O_3$ requires C, 71·4; H, 9·5%), $\nu_{max.}$ at 1714 (cyclohexanone), 1368, 1242, 1215, 1065, and 1046 cm.$^{-1}$. Apart from the first, all these bands are given also by compound (II). The product (III) (34 mg.) was refluxed with lithium aluminium hydride (250 mg.) in ether (50 ml.) for 1·5 hr. The excess of hydride was destroyed with ethyl acetate and the mixture was added to N-sodium hydroxide (50 ml.). The organic layer was separated, dried (K_2CO_3), and evaporated. The light petroleum extract of the residue gave compound (II) (15 mg.), m. p. and mixed m. p. 120—121°.

9-(1,2-*Dihydroxyethyl*)-cis-*decalin* (VIII).—The isopropylidene derivative (III) (0·60 g.), 100% hydrazine hydrate (1·5 ml.), potassium hydroxide (1·5 g.), and diethylene glycol (15 ml.) were heated under a short air-condenser. In 9 hr. the temperature rose from 150° to 190°, and the mixture was heated for a further 9 hr. at 190—195°, then allowed to cool. After addition of water (50 ml.) and 2N-sulphuric acid (50 ml.) the mixture was immediately extracted with ether, the extract was dried (K_2CO_3), and the solvent was removed. The residual pale yellow oil was heated with water (1 ml.), dilute sulphuric acid (0·5 ml.), and ethanol (15 ml.) on the steam-bath for 2 hr. and the ethanol was removed under reduced pressure. The residue gave the *diol* (VIII) (0·45 g.) which crystallised from light petroleum in needles (0·35 g.), m. p. 101—102° (Found: C, 72·8; H, 11·2. $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·1%), $\nu_{max.}$ 3360 (hydrogen-bonded OH), and 1450 and 1467 (*cis*-decalin) [6] cm.$^{-1}$. The same compound was obtained in similar yield when the potassium hydroxide was added only after the other components had been heated together for 3 hr. at 140—150°.

[6] Baker, Minckler, and Hussey, *J. Amer. Chem. Soc.*, 1959, **81**, 2379.

9-*Formyl*-cis-*decalin* (XII).—A mixture of the above diol (49 mg.) and 0·206M-periodic acid (1·5 ml.) in ethanol (2·5 ml.) was kept at room temperature for 3 days. Water (20 ml.) and excess of sodium hydrogen carbonate solution (5%) were added and the mixture was extracted with ether. The extract was dried ($MgSO_4$) and gave formaldehyde and the required compound as an oil of camphor-like odour. The 2,4-*dinitrophenylhydrazone* separated from methanol–ethyl acetate (1 : 1) in orange-yellow needles, m. p. 163—164° (Found: C, 58·9; H, 6·8; N, 16·3. $C_{17}H_{22}N_4O_4$ requires C, 59·0; H, 6·4; N, 16·2%). In a further experiment, the crude 9-formyl-*cis*-decalin from the diol (0·60 g.) was heated with water (30 ml.) and 40% sodium hydroxide solution (0·5 ml.) on the steam-bath and vigorously stirred while potassium permanganate (1·2 g.) in hot water (35 ml.) was added until the permanganate colour persisted for several minutes. The manganese dioxide was separated and the filtrate was decolorised with a trace of sodium hydrogen sulphite and acidified with 2N-sulphuric acid. The ice-cold mixture gave *cis*-decalin-9-carboxylic acid [2] which separated from aqueous ethanol in needles (0·32 g.), m. p. 120—121° (Found: C, 72·5; H, 9·8%; equiv., 182. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%; equiv., 182) Admixture with *trans*-decalin-9-carboxylic acid,[4] m. p. 132—134°, gave m. p. 85—105°. The methyl ester, obtained by means of diazomethane, was an oil of ginger-like odour which did not afford the amide when heated with concentrated ammonia solution (*d* 0·880).

9-1′-*Hydroxyethyl*-cis-*decalin* (XI).—9-Formyl-*cis*-decalin from the diol (VIII) (0·31 g.) was added, in ether (20 ml.), to the Grignard reagent prepared from magnesium (0·3 g.), methyl iodide (1 ml.), and ether (40 ml.). The mixture was refluxed for 2 hr., cooled, and decomposed with saturated ammonium chloride solution (15 ml.). The organic layer was dried (K_2CO_3) and gave the required compound as an oil of camphor-like odour; it gave the α-*naphthylurethane* (0·33 g.), m. p. 154·5—155·5° (Found: C, 78·6; H, 8·4; N, 4·3. $C_{23}H_{29}NO_2$ requires C, 78·6; H, 8·3; N, 4·0%). A mixture of this derivative and the α-naphthylurethane, m. p. 161—162°, of 9-1′-hydroxyethyl-*trans*-decalin [4] melted at 133—142°.

10β-(1,2-*Diacetoxyethyl*)-trans-1-*decalone* (VI).—The isopropylidene derivative (III) (1·37 g.), ethanol (15 ml.), water (9·5 ml.), and 2N-sulphuric acid (0·5 ml.) were heated on the steam-bath for 1·5 hr. Most of the ethanol was evaporated under reduced pressure and a gum, which was moderately soluble in water and insoluble in light petroleum, was isolated. It was kept in acetic anhydride (5 ml.) in pyridine (10 ml.) and at room temperature for 2 days and then heated at 100° for 1 hr. Addition of 2N-sulphuric acid (150 ml.) to the cooled mixture gave the required *diacetate*, needles (0·75 g.) (from aqueous ethanol), m. p. 136·5—137·5° (Found: C, 64·9; H, 8·2. $C_{16}H_{24}O_5$ requires C, 64·9; H, 8·1%), $\nu_{max.}$ (in Nujol) 1730 (OAc), 1703 (CO of cyclohexanone), and 1238 cm.$^{-1}$. In another experiment, compound (III) (2·0 g.) was heated in glacial acetic acid (10 ml.) containing 2N-hydrochloric acid (0·4 ml.) at 100° for 1 hr. and then under reduced pressure until the volume was halved. Acetic anhydride (5 ml.) was added and the mixture was heated at 100° for 3·5 hr. The product obtained by addition of water (50 ml.) was washed with water and crystallised from aqueous alcohol in needles (1·75 g.), m. p. and mixed m. p. 136—137°.

Interaction of the Diacetate (VI) *and Potassium Borohydride*.—A solution of the borohydride (0·1 g.) and 2N-sodium hydroxide solution (0·1 ml.) in water (2 ml.) was gradually added to the diacetate (VI) (0·10 g.) in methanol (5 ml.). After 2 hr. at room temperature, the mixture was warmed for 5 min. to complete the reduction. Alkaline hydrolysis of the product gave a gum from which 10β-(1,2-dihydroxyethyl)-*trans*-1β-decalol [1] (I) (2 mg.), m. p. and mixed m. p. 155—156°, was obtained. The low yield of product (I) was caused by incomplete hydrolysis and a better yield was obtained by further hydrolysis of the recovered material.

10β-(1,2-*Dihydroxyethyl*)-trans-1α-*decalol* (V).—This *compound* was obtained as needles (0·75 g.), m. p. 180—181°, from ethyl acetate (Found: C, 67·4; H, 10·4. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·4%), by reduction of the diacetate (VI) (1·5 g.) in tetrahydrofuran (50 ml.) with lithium aluminium hydride (1·6 g.) in ether (90 ml.). Unlike the stereoisomeric triol (I), it does not readily form an isopropylidene derivative.

10β-*Formyl*-trans-1α-*decalol* (IX).—This compound was obtained as an oil when the triol (V) was oxidised with periodic acid. The 2,4-*dinitrophenylhydrazone* was obtained as orange plates, m. p. 156—157°, from aqueous ethanol (Found: C, 56·2; H, 6·3. $C_{17}H_{22}N_4O_5$ requires C, 56·35; H, 6·1%).

10β-*Hydroxymethyl*-trans-1α-*decalol* (X).—This *diol* was prepared by the reduction with lithium aluminium hydride of compound (IX) obtained by the oxidation of the triol (V) (0·20 g.)

with periodic acid. It separated from ethyl acetate–light petroleum in needles (0·10 g.), m. p. 107—107·5° (Found: C, 71·9; H, 10·9. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·9%). A mixture with the isomeric diol 10β-hydroxymethyl-*trans*-1β-decalol,[1] m. p. 110°, melted at 80—82°. The infrared analysis of compound (X) showed intramolecular hydrogen bonding to be absent.

The Ethylene Thioketal (VII) *of the Keto-diacetate* (VI).—A mixture of the keto-diacetate (1·60 g.), ethane-1,2-dithiol (1·3 g.), anhydrous zinc chloride (2·0 g.), anhydrous sodium sulphate (4 g.), and glacial acetic acid (8 ml.) was kept at room temperature for 14 days, then shaken with ether (100 ml.) and an excess of 2N-sodium hydroxide. The ether extract was dried (K_2CO_3) and gave the required *thioketal* which separated from light petroleum in prisms (1·70 g.), m. p. 120·5—121° (Found: C, 58·3; H, 7·7. $C_{18}H_{28}O_4S_2$ requires C, 58·1; H, 7·5%). In a further experiment this compound was obtained as prisms, m. p. 93—94°, which did not depress the m. p. of the previous sample and gave this higher-melting form when melted and cooled. Both experiments gave also a *substance* (*ca.* 1%), m. p. 117—118° (Found: C, 57·4; H, 7·2. $C_{18}H_{28}O_4S_2$ requires C, 58·1; H, 7·5%), which was almost insoluble in ether and ethanol and was only slightly soluble in dimethylformamide.

Desulphurisation of the Thioketal (VII).—This compound (0·50 g.), m. p. 120—121°, with Raney nickel (*ca.* 10 g.) and ethanol (100 ml.) was vigorously stirred and refluxed for 9 hr. The liquid phase was separated and reduced to a small volume (15 ml.) by evaporation. 40% Sodium hydroxide solution (3 ml.) was added, the mixture was heated on the steam-bath for 2 hr., and most of the alcohol was removed under reduced pressure. Water (30 ml.) was added and the mixture was extracted with ether. The extract was dried (K_2CO_3) and gave 10-(1,2-dihydroxyethyl)-*cis*-decalin (VIII) (0·25 g.) as needles, m. p. and mixed m. p. 101—102°, from light petroleum.

Interaction of the Isopropylidene Derivative (II) *and Thionyl Chloride.*—Redistilled thionyl chloride (0·55 g.) was slowly added during 20 min. to a cold (0°) solution of compound (II) (1·0 g.) in pyridine (5 ml.) and benzene (10 ml.). The mixture was decomposed with ice and water, and the product was extracted with ether. The extract was washed successively with dilute acetic acid, water, sodium hydrogen carbonate solution, and water, and the solvent was removed at room temperature under reduced pressure. The product crystallised from light petroleum as prisms (0·3 g.), m. p. 154·5—155° (Found: C, 64·9; H, 8·7. $C_{30}H_{50}O_7S$ requires C, 65·0; H, 9·0%). It was shown, by a mixed m. p., not to be the triol (I), m. p. 155—156°; it does not contain halogen and is established as the *sulphite* of compound (II) since it gave the triol (I) as plates, m. p. and mixed m. p. 155—156°, on hydrolysis with dilute acid and then with alkali. The infrared spectrum (in CS_2) has a strong absorption band at 1210 cm.$^{-1}$ (S=O).[7]

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[7] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1954.