

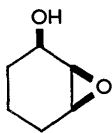
672. Aspects of Stereochemistry. Part X.* The Preparation and Hydration of a Ditertiary Vicinal Epoxide of the Decalin Series.

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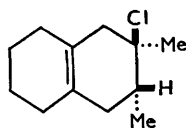
Acid-catalysed hydration of the bicyclic ditertiary epoxide (V) gave a mixture of the *trans*-diaxial diol (71%) and the *trans*-diequatorial diol (23%), the *cis*-diol (prepared separately) not being detected.

Nomenclature.—As a result of consultation with the Editors, whose assistance is gratefully acknowledged, the following proposals for the consistent naming of variously substituted *racemic* alicyclic compounds are made and used in this and later papers:

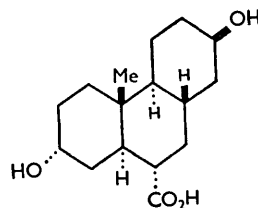
1. Racemic composition to be designated by the prefix (\pm).
2. General numbering to follow established rules (cf. Editorial Nomenclature Reports).
3. Relative configurations to be expressed as α or β (or ξ if unknown) for all groups, the reference position (arbitrarily designated as β) being chosen in the following descending order of preference: (a) a single group or atom other than hydrogen at the lowest-numbered position, (b) of two dissimilar groups at the lowest-numbered position that one which is named as a suffix, (c) of two dissimilar groups at the lowest-numbered position both named as prefixes, that which is named first in alphabetical order, and (d) if identical groups are present at the lowest-numbered position, apply (a)—(c) to the next higher-numbered positions until a decision can be reached. Three examples are as shown.



(\pm)-2 β :3 β -Epoxy-
cyclohexan-1 β -ol
(reference group:
1 β -OH).



(\pm)-2 β -Chloro-
2 α :3 α -dimethyl- Δ^9 -octalinal
(reference group:
2 β -Cl).



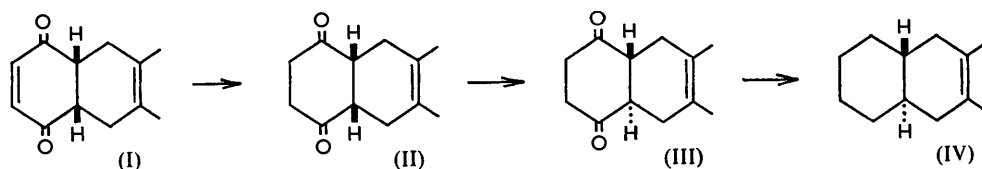
(\pm)-11 β :12 α :14 α -Tetradecahydro-
2 β :7 α -dihydroxy-13 β -methylphen-
anthrene-9 α -carboxylic acid (reference
group:
2 β).

As illustrated by these examples, in the representation of racemic compounds by formulæ, the enantiomer can be chosen which conforms to its racemic name when heavy lines indicate " β " and dotted lines " α "-substituents. However, in a series of reactions rigid application of this could sometimes lead (in the formulæ) to the inversion of the other

* Part IX, *J.*, 1957, 4765.

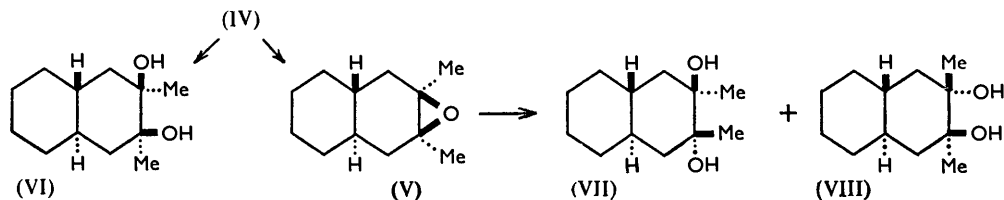
centres of asymmetry not involved in particular reactions: in such cases it may be more convenient to keep to one enantiomeric series of formulæ throughout. Thus the diol (VIII; below) is written as shown in order to show its relation with the epoxide (V) from which it is prepared, although for nomenclatural purposes the positions 2 and 3 are reversed in the two racemic compounds. Previous uses of $\alpha\beta$ -nomenclature in cyclic systems may be noted.¹⁻⁴

THE purpose of the present investigation was to prepare a group of three isomeric cyclic ditertiary diols of defined conformation (*i.e.*, VI, VII, and VIII) with a view to under-



standing better the stereochemical requirements of the glycol fission reaction. *En route* to these diols the stereochemical course of the hydration of the simple bicyclic ditertiary epoxide (V) could be examined.

The precursor of the diols was the bicyclic olefin (IV) which was synthesised in the following way. Reduction of the Diels-Alder adduct (I) with zinc in aqueous acetic acid yielded the *cis*-ring diketone (II). This, on suitable treatment with alkali, was converted into its higher-melting *trans*-isomer (III). Wolff-Kishner reduction then gave the desired olefin (IV), from which the epoxide (V) and the *cis*-diol (VI) were readily obtained.



Hydration of the epoxide (V) in aqueous acetone solution with sulphuric acid as catalyst and chromatography of the products gave two crystalline diols which, being different from the *cis*-diol (VI), could be assigned *trans*-configurations. The higher-melting isomer of the pair has been assigned the diaxial diol structure (VII) as (*a*) it is formed in larger amount (71% as opposed to 23% of the diequatorial diol, VIII), (*b*) it is more easily eluted from an alumina chromatogram, and (*c*) it is the most resistant of the three isomers to pinacolic dehydration.

Owing to the possibility of ring inversion there are in the monocyclic series only two isomers related to the diols (VI—VIII). Both of these give 1-acetyl-1-methylcyclopentane (IX; monocyclic) on treatment with acid, but significantly the *trans*-diol, where both hydroxyl groups can be equatorial, reacts the more rapidly.^{5, 6} Clearly, these pinacolic reactions leading to ring contraction depend on the migration of an annular C-C bond which is parallel to the equatorial C-OH bond undergoing acid-induced ionisation. Observations with the bicyclic diols have amplified these previous findings. The diaxial diol was largely unchanged under conditions which caused almost sole production of a ketone

¹ Fieser, *J. Amer. Chem. Soc.*, 1950, **72**, 623.

² Fodor and Nádor, *J.*, 1953, 721.

³ Cookson, *J.*, 1954, 282.

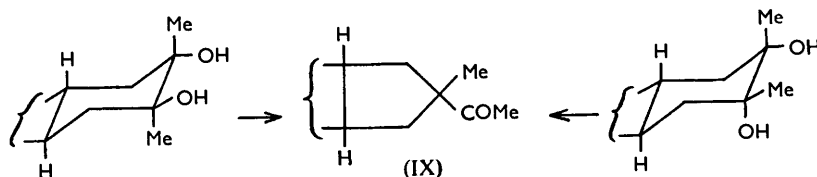
⁴ Lemieux, Kullnig, and Moir, *J. Amer. Chem. Soc.*, 1958, **80**, 2237.

⁵ Bartlett, quoted by Klyne in "Progress in Stereochemistry," Butterworths Scientific Publ., London, 1954, p. 73.

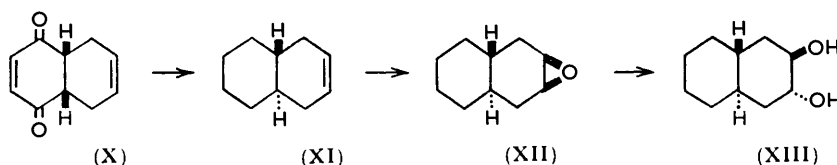
⁶ Meerwein, *Annalen*, 1939, **542**, 123.

from the other two isomers containing one or two equatorial hydroxyl groups. This ketone (formulated as IX; bicyclic) was characterised as its 2 : 4-dinitrophenylhydrazone, the overall yield of derivative being higher from the diequatorial than from the mono-equatorial diol.

In order to discuss the hydration of the tetrasubstituted epoxide (V) it was desirable to determine the yield of diaxial diol to be expected as the main product from hydration



of the related disubstituted epoxide (XII). This epoxide was prepared from the octalin (XI), obtained in turn from the Diels-Alder adduct (X) by a route analogous to that used for the tetrasubstituted olefin (IV); however, the yields in the *cis* \rightarrow *trans* isomerisation and the Wolff-Kishner reduction steps were lower. Acid-catalysed hydration of



disubstituted epoxide (XII) gave a diol (90%) to which the diaxial structure (XIII) may be assigned by analogy with similar reactions in the steroid series. The *cis*- and the *trans*-diequatorial isomers of (XIII) were not detected on alumina chromatography of the total hydration product. [A product, clearly the diaxial diol (XIII), has been obtained ⁷ by hydroxylation of the olefin (XI) prepared by a different route starting from β -decalol. Ali and Owen ⁸ have recently prepared the olefin by this route and have fully characterised the three possible racemic diols derivable by direct or indirect hydroxylation. Melting-point comparisons confirmed that the *cis*- and the *trans*-diaxial diols prepared from our olefin and from Ali and Owen's olefin were identical.]

Electronic and steric effects influence the direction of opening of unsymmetrically substituted epoxides.⁹ The general trends are that strongly nucleophilic reagents tend to attack the less substituted carbon atom whereas electrophilic agents promote Markownikow ring opening, an anion becoming linked to the more alkylated carbon atom. The latter type of reaction receives a simple explanation in terms of carbonium-ion intermediates, and support comes from recent studies on the kinetics of the acid-catalysed hydration of epoxides where it was concluded that, as the reaction velocity could be related to Hammett's acidity function H_0 , carbonium-ion formation from the epoxide conjugate acid represents the rate-determining step.¹⁰

When, however, the stereochemistry of epoxide ring opening under acidic conditions is considered it seems unlikely that "carbonium-ion formation" is the whole story. Thus disubstituted epoxycycloalkanes yield *trans*-products with little or none of the *cis*-products that could equally well be formed *via* simple carbonium ions. Moreover disubstituted epoxycyclohexanes, *e.g.*, (XII), yield *trans*-diaxial compounds, the specificity suggesting that the solvent, as a nucleophile, is intimately concerned in the reactions, which may be

⁷ Hückel and Naab, *Annalen*, 1933, **502**, 151.

⁸ Ali and Owen, *J.*, 1958, 2119.

⁹ For a recent discussion see Eliel in "Steric Effects in Organic Chemistry," Wiley & Sons, New York, 1956.

¹⁰ Pritchard and Long, *J. Amer. Chem. Soc.*, 1956, **78**, 2663, 2667, 6008.

regarded as displacement processes where the reacting groups take up a linear arrangement most readily when a diaxial compound is being formed. Further evidence indicating that nucleophilic solvent participation is not excluded by dependence of rate on H_0 comes from studies on the acid-catalysed racemisation of active butan-2-ol in $H_2^{18}O$ where although $\log k$ and H_0 are related linearly, every hydroxyl exchange is accompanied by inversion.¹¹

Even in the tetrasubstituted epoxide (V) where the presence of tertiary carbon atoms could more easily give rise to open carbonium ions, specific *trans*-opening of the ring still takes place.* However, compared with the disubstituted compound (XII), the extra methyl groups in (V) cause the formation of an appreciable amount of the diequatorial diol although the diaxial compound is still the major product. Displacement reactions are still involved and the formation of some diequatorial product appears due to the methyl groups' somewhat inhibiting solvent approach and favouring larger fractional positive charges on either carbon in the transition states for reaction; more random ring opening therefore occurs. It is hoped that further work will help to clarify the situation.

In discussing the formation of diequatorial products in six-membered ring systems it may be noted that small amounts of these isomers frequently accompany diaxial products in reactions of ammonia with some benzyldienehexoses;¹⁴ *cis*-products have again not been detected. The most extreme example of equatorial ring opening appears to be the reduction of $5\beta : 6\beta$ -epoxycoprostan-5 β -ol with lithium aluminium hydride in 60% yield;¹⁵ special steric factors are thought to cause this result.

EXPERIMENTAL

M. p.s were determined on a Kofler hot stage. Alumina (P. Spence, Grade H) was deactivated with dilute acetic acid.¹⁶ Light petroleum refers to the fraction, b. p. 60—80°.

6 : 7-Dimethyl- Δ^6 -*cis*-octalin-1 : 4-dione (II).—Finely powdered 6 : 7-dimethyl- $\Delta^2 : 6$ -*cis*-hexalin-1 : 4-dione (I) (50 g.) was dissolved in acetic acid at 50°, and immediately poured into a vigorously stirred suspension of zinc dust (50 g.) in water (200 c.c.) also at 50°. Stirring was continued for 2 min., during which the yellow colour disappeared and the temperature rose to 75°. The hot mixture was filtered, and water (1 l.) was added to the filtrate, which was cooled to 0°. The product (44.5 g., 88%), m. p. 120°, crystallised as needles. An analytical sample of the *cis*-diketone had m. p. 119—120° (from light petroleum) (Found: C, 74.95; H, 8.3. $C_{12}H_{16}O_2$ requires C, 75.0; H, 8.4%).

(\pm)-6 : 7-Dimethyl- Δ^6 -9 β : 10 α -octalin-1 : 4-dione (III).—N-Sodium hydroxide (280 c.c.) was added during 10 min. to a vigorously stirred solution of the *cis*-diketone (50 g.) in dioxan (250 c.c.) at 80° under nitrogen. The mixture was neutralised with hydrochloric acid, diluted with water (1 l.), and cooled to 0°. The product (45.5 g., 91%) had m. p. 168—169°. The pure *trans*-diketone had m. p. 169° (change of form at 120°) (from light petroleum) (Found: C, 75.2; H, 8.45%).

(\pm)-2 : 3-Dimethyl- Δ^2 -9 β : 10 α -octalin (IV).—A solution of the *trans*-diketone (129 g.) and 90% hydrazine hydrate (130 c.c.) in diethylene glycol (1250 c.c.) was heated under reflux for 1 hr. Potassium hydroxide (130 g.) was added in portions during 20 min., and then the mixture was distilled until the vapour temperature reached 180°. The mixture was heated under reflux for 5 hr. (two layers formed). Water and pentane were added to the cooled mixture. Distillation of the product from the pentane extract yielded the *olefin* (78 g., 70%), b. p. 61°/0.3 mm., n_D^{21} 1.4926 (Found: C, 87.85; H, 12.25. $C_{12}H_{20}$ requires C, 87.8; H, 12.2%).

* As far as the possible formation of *cis*-diol is concerned, hydration of the monocyclic 1 : 2-epoxy-1 : 2-dimethylcyclohexane could equally well be studied. This reaction has been reported to give the *trans*-diol (80%).¹² The formation of cholestane-3 α : 5 α -diol from the acid-catalysed hydration of 3 α : 5 α -epoxycholestane shows that a *cis*-diol can be produced from 1 : 3-epoxide probably *via* an "open carbonium ion."¹³

¹¹ Bunton, Konasiewicz, and Llewellyn, *J.*, 1955, 604.

¹² Nametkin and Delektorsky, *Ber.*, 1924, 57, 583.

¹³ Clayton, Henbest, and Smith, *J.*, 1957, 1982.

¹⁴ For references see Overend and Vaughan, *Chem. and Ind.*, 1955, 995.

¹⁵ Hallsworth and Henbest, *J.*, 1957, 4604.

¹⁶ Farrar, Hamlet, Henbest, and Jones, *J.*, 1952, 2657.

(\pm)-2 α : 3 α -Dimethyl-9 β : 10 α -decalin-2 β : 3 β -diol (VI).—A solution of the olefin (0.63 g.) and osmium tetroxide (1 g.) in ether (50 c.c.) was kept at 20° for 48 hr. The ether was evaporated, and the residue was dissolved in tetrahydrofuran (50 c.c.) and shaken with a solution of mannitol (10 g.) and potassium hydroxide (10 g.) in water (50 c.c.) for 8 hr. The product (isolated with ether) was dissolved in light petroleum and adsorbed on deactivated alumina (10 g.). Elution with light petroleum gave some oil. Elution with ether–light petroleum (1 : 1) gave the *cis*-diol (0.4 g.), m. p. 83–89° (from pentane) (Found: C, 72.55; H, 10.85. C₁₂H₂₂O₂ requires C, 72.7; H, 11.2%).

(\pm)-2 β : 3 β -Epoxy-2 α : 3 α -dimethyl-9 β : 10 α -decalin (V).—The olefin (25 g.) was added dropwise to a stirred 2N-etheral solution of monoperphthalic acid (170 c.c.) maintained below 10°. The mixture was then kept at 20° for 1 hr., whereafter the phthalic acid was removed by filtration. The filtrate was washed with dilute alkali and dried. Distillation afforded the *epoxide* (24.2 g., 88%), b. p. 60.5°/0.2 mm., n_D^{19} 1.4776 (Found: C, 79.5; H, 11.1. C₁₂H₂₀O requires C, 79.9; H, 11.2%).

Hydration of the *Epoxide* (V).—The *epoxide* (2.81 g.), acetone (5 c.c.), water (5 c.c.) and concentrated sulphuric acid (66 mg.) were shaken together at 20° for 1 hr. to give a homogeneous solution. This was kept at 20° for 23 hr., then the products were isolated with ether and chromatographed on deactivated alumina (250 g.). Elution with benzene–light petroleum gave unchanged *epoxide* (45 mg., 1.5%) (infrared evidence). Elution with benzene (1.6 l.) gave (\pm)-2 α : 3 α -dimethyl-9 β : 10 α -decalin-2 β : 3 α -diol (VII) (2.199 g., 71%), m. p. 119–121° (from light petroleum) (Found: C, 72.8; H, 10.9. Further elution with benzene (1.1 l.) and with ether (400 c.c.) afforded (\pm)-2 α : 3 β -dimethyl-9 α : 10 β -decalin-2 β : 3 α -diol (VIII) (0.701 g., 23%), m. p. 81–85° (from pentane) (Found: C, 72.5; H, 11.05%). Separate careful chromatography of an artificial mixture of the three diols gave a good separation, the *cis*-diol being eluted after the diaxial diol. The benzene eluate from chromatography of the product from the hydration experiment was collected in fractions, but a plot of fraction weight against number gave no evidence for the presence of the *cis*-diol. [A strong depression of m. p. (to 50–60°) was recorded on admixture of the *cis*- and the *trans*-diequatorial diol.] The infrared absorption of the total reaction product exhibited the bands of the two *trans*-diols; no extra bands due to an *isopropylidene* compound were present. The *cis*-diol was recovered unchanged (96%) on treatment with the acetone–sulphuric acid mixture used in the hydration experiment (therefore no *isopropylidene* derivative was formed).

Pinacolic Dehydration of the Diols.—Each diol (50 mg.) in water (12.5 c.c.), dioxan (5 c.c.), and concentrated sulphuric acid (0.25 c.c.) was heated under reflux for 15 hr. The products were isolated with ether and examined by infrared spectroscopy. The diaxial diol was about 80% unchanged, as there was only a small carbonyl band near 1700 cm.⁻¹. The products from the other two diols showed no hydroxyl bands but each had a strong carbonyl band at 1700 cm.⁻¹ and another medium band at 1355 cm.⁻¹ (*C*-acetyl groups, *e.g.*, 21-methyl-20-oxo-steroids, give a band at 1357 cm.⁻¹). The products from the *cis*-diol and from the diequatorial diol both gave the same 2 : 4-dinitrophenylhydrazone (70 and 88% yields respectively), m. p. 128–129°, of the ketone (IX) (Found: C, 59.65; H, 6.8; N, 15.2. C₁₈H₂₄O₄N₄ requires C, 60.0; H, 6.7; N, 15.55%).

Δ^2 :⁶-*cis*-Hexalin-1 : 4-dione (X).—*p*-Benzoquinone (100 g.) and butadiene (100 g.) in benzene (1 l.) were kept at 20° for 2 weeks. The solution was filtered, the solvent removed, and the residue recrystallised from light petroleum–benzene to give the diketone (141 g., 94%), m. p. 57° (lit., m. p. 58°).

Δ^6 :*cis*-Octalin-1 : 4-dione.—Finely powdered Δ^2 :⁶-*cis*-hexalin-1 : 4-dione (100 g.) was dissolved in acetic acid (200 c.c.) at 50° and poured into a vigorously stirred suspension of zinc (125 g.) in water (250 c.c.) at 50°. Stirring was continued for 2 min., during which the yellow colour disappeared and the temperature rose to *ca.* 75°. The hot mixture was filtered, and water (1.5 l.) was added to the filtrate, which was kept at 0° overnight. The product (70 g., 70%), m. p. 90–108°, was dried and recrystallised from light petroleum to give the diketone, m. p. 105–108° (lit., m. p. 108°).

(\pm) Δ^6 -9 β : 10 α -Octalin-1 : 4-dione.— Δ^6 :*cis*-Octalin-1 : 4-dione (100 g.) was dissolved in dioxan (400 c.c.) at 80° and *N*-sodium hydroxide solution (648 c.c.) was added to the vigorously stirred solution under nitrogen during 10 min. Some *trans*-compound (2 g.; obtained in smaller-scale experiments) and water (300 c.c.) were added, and the solution was neutralised with 1.3N-hydrochloric acid. More water (1 l.) was added and the solution kept at 0° overnight to

give a product (20 g., 20%), m. p. 150—160°. The pure *trans-diketone* had m. p. 157—160° (from light petroleum) (Found: C, 73.05; H, 7.0. $C_{10}H_{12}O_2$ requires C, 73.15; H, 7.35%).

(\pm) Δ^2 -9 β : 10 α -*Octalin* (XI).—The *trans*-diketone (16 g.) and hydrazine hydrate (21 c.c., 85%) in diethylene glycol (160 c.c.) were refluxed for 1 hr. The excess of hydrazine hydrate and water was distilled off, the vapour temperature reaching 180°. Potassium hydroxide (19.5 g.) was added in portions during 5 min., and the mixture was refluxed for 5 hr. The cold mixture was diluted with water and extracted with light petroleum (1 l.), and the extract percolated through alumina (70 g.). Removal of the solvent at atmospheric pressure left a product which on distillation at a bath-temperature of 110°/15 mm. gave the olefin (5.06 g., 38%), n_D^{20} 1.4865 (Found: C, 88.30; H, 11.6. Calc. for $C_{10}H_{16}$: C, 88.15; H, 11.85%).

(\pm)9 β : 10 α -*Decalin-2 β* : 3 β -*diol*.—The olefin (0.52 g.) and osmium tetroxide (1 g.) in ether (50 c.c.) were kept at room temperature for 48 hr. The ether was evaporated, and the residue dissolved in dioxan (50 c.c.) and shaken with a solution of mannitol (10 g.) and potassium hydroxide (10 g.) in water (50 c.c.) for 8 hr. The solid product (isolated with ether) was dissolved in benzene and adsorbed on deactivated alumina (20 g.). Elution with benzene gave a trace of oil. Elution with ether (300 c.c.) gave the *cis*-diol (0.37 g., 57%), m. p. 140—141° (from benzene-light petroleum) (lit.,¹⁷ m. p. 141°).

(\pm)2: 3-*Epoxy-9 β* : 10 α -*decalin* (XII).—The olefin (1.5 g.) in ether (5 c.c.) was added to a stirred solution of monoperphthalic acid (0.356M; 42 c.c.) at 0°. The mixture was kept at 20° for 1.5 hr., washed with dilute alkali, then water, and dried ($MgSO_4$). Distillation afforded the *epoxide* (1.17 g., 70%), b. p. 95°/12 mm., n_D^{24} 1.4872 (Found: C, 78.65; H, 10.7. $C_{10}H_{16}O$ requires C, 78.9; H, 10.6%).

Hydration of the Epoxide.—The epoxide (0.628 g.), dioxan (6 c.c.), water (4 c.c.), and concentrated sulphuric acid (57 mg.) were shaken at room temperature for 24 hr. The solid product (isolated with ether) was chromatographed on deactivated alumina (65 g.). Elution with benzene-light petroleum gave unchanged epoxide (16 mg., 2%) (identified by formation of further diol, m. p. 161—163°, on acid hydrolysis). Elution with benzene-ether (1:1) (680 c.c.) gave (\pm)9 β : 10 α -*decalin-2 β* : 3 α -*diol* (XIII) (0.63 g., 90%), m. p. 163—164° (from benzene-light petroleum) (lit.,⁷ m. p. 163°). The m. p.s of this diol and of the *cis*-diol were undepressed on admixture with authentic samples kindly provided by Dr. L. N. Owen (Imperial College, London).

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¹⁷ Ganapathi, *Ber.*, 1939, **72**, 1381.