842. *Stereochemistry of* cyclo*Hexane Derivatives. Part IV.* Some Secondary Tertiary* 1 : 2-*Diols.*

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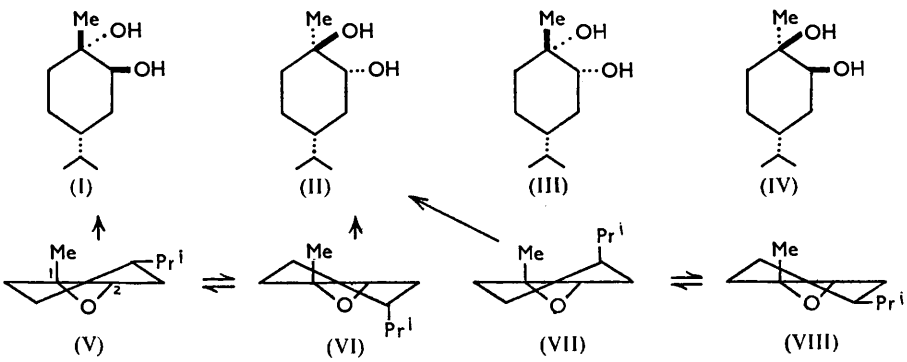
The hydroxylation of (±)-*p*-menth-1-ene is described and some evidence for the structures of the *trans*-diols is presented. Equilibration of a series of glycols with sodium in decalin is described and an explanation of some apparent anomalies is suggested. The rates of oxidation of the diols by periodate have been measured.

To provide a series of closely related secondary tertiary 1 : 2-diols we have examined the hydroxylation of (±)-*p*-menth-1-ene. Some details about the active diols are available,[1] but the racemic forms have not been described. Although the stereochemistry of the carvomenthols has not been completely clarified[2] we have adopted Bose's nomenclature,[3] and on this basis the menthols and carvomenthols are conformationally analogous. The *p*-menthane-1 : 2-diols are referred to as 1-hydroxycarvomenthols (I—IV). Hydroxylation of *p*-menth-1-ene by way of the epoxide or directly with peracetic acid gave mainly 1-hydroxy*neo*carvomenthol (I) and some 1-hydroxy*iso*carvomenthol (II). The production of a mixture of diols is expected on the basis of application[4] of the Fürst–Plattner[5] principle to rupture of the oxide mixture. The half-chair conformations (V, VI) of one oxide would undergo attack at positions 2 and 1, respectively. The conformation (V) will exist in larger proportion and will be attacked more readily than (VI) where attack at $C_{(1)}$ is hindered by both steric and inductive effects of the methyl group. This oxide should yield almost entirely 1-hydroxy*neo*carvomenthol (I), corresponding to rupture of form (V).



The oxide (VII, VIII) will be more stable in the form (VIII), but the rates of rupture could be similar since attack of epoxide (VIII) at $C_{(1)}$ is hindered by the methyl group and in form (VII) the approach to $C_{(2)}$ is hindered by the axial *iso*propyl group and a mixture of the diols (I) and (II) by rupture of conformations (VII) and (VIII), respectively, is expected.

Structures cannot be established by relation to (±)-carvomenthols or *p*-menthan-1-ols at present as no reliable information about these isomers exists. Hydroxylation of *p*-menth-1-ene with osmium tetroxide and esterification gave 1-hydroxy*neoiso*carvomenthol (IV) as the di-*p*-nitrobenzoate. Both *cis*-diols (III and IV) were obtained by hydroxylation

* Part III, *J.*, 1956, 2363.

[1] Schmidt, *Chem. Ber.*, 1949, **82**, 11; Meerwein, Ogait, Prang, and Serini, *J. prakt. Chem.*, 1926, **113**, 9.

[2] Orloff, *Chem. Rev.*, 1954, **54**, 375.

[3] Bose, *Experientia*, 1952, 8, 458.

[4] Bose, Chaudhuri, and Bhattacharyya, *Chem. and Ind.*, 1953, 869; Newth, *ibid.*, p. 1257; Cookson, *ibid.*, 1954, 223, 1512; Angyal, *ibid.*, p. 1230; Stevens and Dykstra, *J. Amer. Chem. Soc.*, 1953, **75**, 5975.

[5] Fürst and Scotoni, *Helv. Chim. Acta*, 1953, **36**, 1332, 1410.

by iodine–silver acetate–water,[6] or, less well, by *tert.*-butyl hydroperoxide [7] or by inversion of the bromohydrins derived from the epoxide mixture.[8] Much evidence for the configurations of the *cis*-diols is described in the following paper. The formation of the diol (IV) from osmium tetroxide follows attack *trans* to the *iso*propyl group although the product is less stable conformationally than the isomer (III).

The reduction of ketones with sodium and alcohol leads to the same mixture of alcohols as is obtained by direct equilibration with sodium,[9] the distribution of the isomers corresponding to their relative stability. We have been unable to obtain sufficient of the diol (III) to equilibrate it with sodium but the isomers (I), (II), and (IV) all yield the same product, 1-hydroxy*iso*carvomenthol (II), when treated in this way. Examination of the infrared spectrum of the equilibration product failed to indicate the presence of any other *p*-menthane-1 : 2-diol. As a model, the reaction was applied to the isomeric 1-methyl*cyclo*hexane-1 : 2-diols. The product was the *trans*-diol and no evidence for the presence of the *cis*-isomer could be obtained, indicating a close relation between the most stable conformations of 1-hydroxy*iso*carvomenthol and 1-methyl*cyclo*hexane-*trans*-1 : 2-diol. The inversion of configuration at $C_{(1)}$ in equilibration of (I) however is unexpected since tertiary alcohols are normally unaffected by the reaction,[10] which for secondary alcohols proceeds through ketonic intermediates. Without further experimental results it seems profitless to attempt to distinguish between possible mechanisms for this inversion at $C_{(1)}$. Although the equilibration product is 1-methyl*cyclo*hexane-*trans*-1 : 2-diol (IX; R = Me), yet if the size of the substituent is increased a stage will be reached where equilibration will yield the *cis*-diol (XI) as indicated for the 1-phenyl*cyclo*hexane-1 : 2-diols.[11] We accordingly extended the study to 1-ethyl- and 1-*iso*propyl-*cyclo*hexane-1 : 2-diols. The isomeric ethyldiols were prepared by standard methods. 2-Ethyl-2-hydroxy*cyclo*hexanone was obtained from a Grignard reaction with *cyclo*hexane-1 : 2-dione and was reduced with sodium and alcohol. The *trans*-isomer was isolated from this equilibrating reduction. Infrared analysis of the products from the sodium–decalin equilibration indicated at least 70% of *trans*-isomer. The 1-*iso*propyl*cyclo*hexane-1 : 2-diols were prepared in the usual manner and on equilibration afforded mainly the *cis*-diol. An attempt to gain a closer insight into these results was made by summing the energy differences between the *trans*-conformations (IX) and (X) and the *cis*-conformation (XI) by using the free-energy differences for groups in axial and equatorial positions at 39° recently given by Winstein and Holness,[12] allowing the approximate value 0·4 kcal./mole for the skew interaction between two hydroxyl groups and neglecting solvent effects. In the tabulated results no allowance is made for

Free energy differences (kcal./mole).

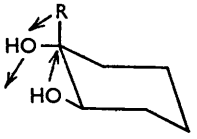
R	Me	Et	Pr^i
E_{IX-X}	0·6	0·9	>2·1
E_{IX-XI}	1·0	1·3	>2·5
E_{X-XI}	0·4	0·4	0·4

hydrogen bonding since this effect will not be present during equilibration. They show a stability order (XI) > (X) > (IX), regardless of the alkyl group. Although the nature of this equilibration is not fully understood it seems probable that the product will be the most stable disodium salt and not necessarily the most stable diol. Values of the free-energy difference between ONa in an axial and an equatorial position are unknown, but may be assumed to be rather larger than the value [12] (0·8 kcal./mole) for the hydroxyl group. As a result, conformation (IX) could be stabilised with respect to (X) and (XI) for the sodium salts derived from the *p*-menthane-, ethyl*cyclo*hexane-, and methyl*cyclo*hexane-1 : 2-diol. An electrostatic effect resulting in repulsion of the oxygen substituents would favour conformation (IX) over (XI) since the resultant deformation, indicated by arrows, would

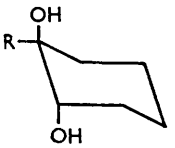
[6] Ginsburg, *J. Amer. Chem. Soc.*, 1953, **75**, 5746.
[7] Milas and Sussman, *ibid.*, 1936, **58**, 1302; 1937, **59**, 2345.
[8] Winstein and Buckles, *ibid.*, 1942, **64**, 2787.
[9] Vavon, *Bull. Soc. chim. France*, 1931, **49**, 937; Hückel, *Annalen*, 1937, **533**, 1.
[10] Stevens, *J. Amer. Chem. Soc.*, 1932, **54**, 3733; Doering, Cortes, and Knox, *ibid.*, 1947, **69**, 1700.
[11] Verkade, *Annalen*, 1928, **467**, 217.
[12] Winstein and Holness, *J. Amer. Chem. Soc.*, 1955, **77**, 5562.

increase axial group interactions in the latter but decrease them in the former, corresponding to the reverse of the situation described by Angyal and Macdonald [13] for formation of cyclic complexes from *cis*- but not *trans*-1 : 2-diols.

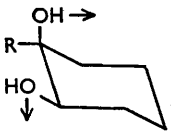
Dehydration of the four *p*-menthane-1 : 2-diols with dilute sulphuric acid gave a (±)-carvomenthone as the only identifiable product.



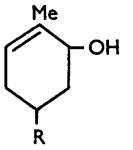
(IX)



(X)



(XI)



(XII)

The preparation of a (±)-carvotanacetol (XII; R = Pr^i) has been described previously.[14] Further examination of the products has provided the epimeric carvotanacetols, characterised by oxidation to carvotanacetone. The structure of the *trans*-isomer is indicated by its hydrogenation to a carvomenthol isolated by Johnston and Read [15] by similar treatment of (±)-*trans*-carveol (XII; R = $CMe{:}CH_2$). The assignment of the *trans*-configuration to the latter, originally based on the Auwers–Skita rule, is substantiated by its reactions.[2] Reaction of the mono-*p*-nitrobenzoates of both the diols (I) and (IV) with phosphorus oxychloride in pyridine gave the corresponding derivative of *trans*-carvotanacetol, providing evidence for the configurations of these two diols.

The rates of oxidation of some of the diols with periodate have been determined (see Table). The *cis*-diols are all oxidised faster than their *trans*-isomers and the very slow rate for 1-hydroxy*neo*carvomenthol is in agreement with a stable diaxial conformation.[16] The observed rate would correspond to presence of about 3% of the diequatorial conformation oxidising at the same rate as 1-hydroxy*iso*carvomenthol. The rates for two *p*-menthane-3 : 4-diols prepared by standard methods are included for comparison.

Rates of oxidation of diols with periodate at 25° (k_2 in $mole^{-1}$ l. min.).

Diol	pH 10·5	pH 2	Diol	pH 10·5	pH 2
1-Hydroxy*neo*carvomenthol	~0·25	2·5	1-Methyl*cyclo*hexane-*trans*-1 : 2-diol	~2·0	60
1-Hydroxy*iso*carvomenthol	2·5	70	1-*iso*Propyl*cyclo*hexane-*cis*-1 : 2-diol	—	53
1-Hydroxycarvomenthol	6·5	—	,, ,, -*trans*- ,,	—	1·0
1-Hydroxy*neoiso*carvomenthol ...	8·8	—	*cis*-*p*-Menthane-3 : 4-diol	—	5·0
1-Methyl*cyclo*hexane-*cis*-1 : 2-diol	26	—	*trans*-*p*- ,, ,, ...	—	0·055

As a possible route to *p*-menthane-3 : 4-diols we have examined reduction of the 4-hydroxymenthone, prepared by Kötz and Steinhorst [17] by hydrolysis of 4-bromomenthone. *trans*-2-Hydroxymenthol was obtained by using sodium and alcohol. Rearrangement during hydrolysis of the bromide with production of 2-hydroxymenthone probably occurred.

Experimental

Unless otherwise stated alumina, type H from Messrs. P. Spence, was used for chromatography, and light petroleum had b. p. 60—70°. Microanalyses were by C.S.I.R.O. Microanalytical Laboratory, Melbourne.

trans-*Hydroxylation of* (±)-p-*Menth*-1-*ene*.—(±)-*p*-Menth-1-ene was prepared from dihydrocryptone.[14] (*a*) The hydrocarbon (23 g.) was treated with peracetic acid by the usual method, and the resulting monoacetates (16·5 g.) were hydrolysed with alkali. The crude diol gave fractions: (i) b. p. 98—128°/6·0 mm. (1·0 g.) and (ii) b. p. 128—132°/6·0 mm. (10·3 g.). Fraction (ii) yielded a partly crystalline *p*-nitrobenzoate. After being washed with light petroleum,

[13] Angyal and Macdonald, *J.*, 1952, 686.
[14] Macbeth, Milligan, and Shannon, *J.*, 1953, 2574.
[15] Read and Johnston, *J.*, 1935, 1138.
[16] Jefferies and Milligan, *J.*, 1956, 2363.
[17] Kötz and Steinhorst, *Annalen*, 1911, **379**, 13.

the crystalline ester (7·5 g.) was chromatographed in light petroleum–benzene (4 : 1; 150 c.c.) on alumina (150 g.). Elution with these solvents gave the *di*-p-*nitrobenzoate* of 1-hydroxy*iso*carvomenthol (1·20 g.) as pale yellow needles, m. p. 164°, after two crystallisations from methanol–chloroform (Found : C, 61·5; H, 5·4; N, 6·0. $C_{24}H_{26}O_8N_2$ requires C, 61·3; H, 5·5; N, 6·0%). Benzene eluted the *di*-p-*nitrobenzoate* of 1-hydroxy*neo*carvomenthol (0·50 g.), needles (from methanol–chloroform), m. p. 185° (Found : C, 61·6; H, 5·6; N, 5·9%). The *mono*-p-*nitrobenzoate* of 1-hydroxy*neo*carvomenthol (2·00 g.) was eluted with ether–benzene (1 : 4). It crystallised as needles, m. p. 107°, from light petroleum (b. p. 40—60°) (Found : C, 63·9; H, 7·2; N, 4·5. $C_{17}H_{23}O_5N$ requires C, 63·6; H, 7·1; N, 4·4%).

(*b*) (±)-*p*-Menth-1-ene (18 g.) was added to ethereal monoperphthalic acid (1·1 mol.) and after 20 hr. the epoxide was isolated in the usual way and heated with water (60 ml.) at 120° during 3 hr. Isolation with ether and distillation gave a fraction (10 g.), b. p. 102—108°/0·4 mm. Crystallisation from hexane gave needles (6·7 g.) of 1-*hydroxy*neo*carvomenthol*, m. p. 77° (Found : C, 69·9; H, 11·7. $C_{10}H_{20}O_2$ requires C, 69·8; H, 11·6%). The *mono*-3 : 5-*dinitrobenzoate* crystallised from aqueous methanol as pale yellow plates, m. p. 51° (Found : C, 56·0; H, 6·0; N, 7·8. $C_{17}H_{22}O_7N_2$ requires C, 55·7; H, 6·0; N, 7·7%). The *acetate* of the *p*-nitrobenzoate, prepared by use of boiling acetic anhydride, crystallised from aqueous methanol as plates, m. p. 107° (Found : C, 63·3; H, 6·9; N, 4·2. $C_{19}H_{25}O_6N$ requires C, 62·8; H, 6·9; N, 3·9%). The glycol isolated from the mother-liquors was esterified and the *p*-nitrobenzoates were separated as above into the di-*p*-nitrobenzoates of 1-hydroxy*neo*carvomenthol (0·2 g.) and of 1-hydroxy-*iso*carvomenthol (0·7 g.). Hydrolysis of the latter ester with methanolic potassium hydroxide gave 1-*hydroxy*iso*carvomenthol*, b. p. 118°/5 mm., m. p. 53° (Found : C, 70·3; H, 11·7%).

(*c*) A similar result was obtained when the epoxide mixture was shaken for 10 hr. with 5% aqueous perchloric acid.

cis-*Hydroxylation of* (±)-p-*Menth*-1-*ene*.—(*a*) The hydrocarbon (1·0 g.) was treated with osmium tetroxide in the usual way. The product (0·68 g.) in light petroleum (40 ml.) was adsorbed on acid-washed alumina and elution with light petroleum–benzene (4 : 1) afforded the diol which was characterised as the *di*-p-*nitrobenzoate* of 1-hydroxy*neoiso*carvomenthol which separated from methanol as cream-coloured needles, m. p. 186° (Found : C, 61·2; H, 5·5; N, 6·3%).

(*b*) *p*-Menth-1-ene (20 g.) was added to a solution of *tert.*-butyl hydroperoxide (1·1 mol.) in *tert.*-butanol (200 ml.) and a 1% solution of osmium tetroxide in *tert.*-butanol (0·5 ml.). After 4 weeks water was added and the butanol removed by distillation. The aqueous residue was extracted continuously with ether, the dried extract evaporated, and the residue distilled. The following fractions were collected : (i) b. p. 96—113°/2·5 mm. (4·6 g.), (ii) b. p. 113—123°/2·5 mm. (4·7 g.), (iii) b. p. 123—143°/2·5 mm. (3·8 g.), (iv) b. p. 143—160°/2·5 mm. (1·0 g.), (v) residue (3·5 g.). Fractions (ii) and (iii) were esterified with *p*-nitrobenzoyl chloride in pyridine, and the crude ester chromatographed in light petroleum–benzene (10 : 1; 200 c.c.) and on alumina (200 g.). This solvent eluted the *di*-p-*nitrobenzoate* of 1-hydroxycarvomenthol (880 mg.) as pale yellow prisms, m. p. 126° (after repeated fractionation from ethanol) (Found : C, 61·3; H, 5·5; N, 6·1%). Elution with light petroleum–benzene (4 : 1) yielded the di-*p*-nitrobenzoate of 1-hydroxy*neoiso*carvomenthol (1·12 g.; m. p. 186° after repeated crystallisation). Fractions (i), (iv), and (v) gave no crystalline ester. Distillation of the product from another oxidation on the same scale gave a main fraction, b. p. 102—152°/30 mm. (8·2 g.). The crude *p*-nitrobenzoates derived from this fraction were chromatographed as before. Elution with light petroleum–benzene (4 : 1) gave a mixture (1·8 g.) as needles, m. p. 165—167°, from methanol–chloroform. Ether–benzene (1 : 4) afforded the *mono*-p-*nitrobenzoate* of 1-hydroxycarvomenthol (0·5 g.) which crystallised either as pale yellow plates or clusters of needles m. p. 83°, from light petroleum (Found : C, 63·7; H, 7·1; N, 4·5%).

(*c*) *p*-Menth-1-ene (5 g.) was hydroxylated by the iodine–silver acetate method as described in Part III. The crude diol (4·5 g.), b. p. 140—154°/24 mm., was esterified with *p*-nitrobenzoyl chloride, and the ester chromatographed in light petroleum–benzene (4 : 1; 150 c.c.) on alumina (150 g.). Elution with this solvent gave the di-*p*-nitrobenzoate of 1-hydroxycarvomenthol (0·2 g.), m. p. 126° after three crystallisations from ethanol. Light petroleum–benzene (1 : 1) eluted crystals, m. p. 165—167° (1·0 g.). The mono-*p*-nitrobenzoate of 1-hydroxy*neoiso*carvomenthol (0·8 g.) was eluted with ether–benzene (1 : 4).

(*d*) 1 : 2-Epoxy-*p*-menthane mixture (12 g.) in ether (100 ml.) at 0° was saturated with hydrogen bromide and ice added. The ether extract was washed with sodium hydrogen carbonate. Distillation gave the bromohydrin mixture (14·0 g.), b. p. 78—83°/0·3 mm. Acetylation of the bromohydrin (10 g.) and treatment with silver acetate in moist acetic acid was carried out as

described for 2 : 3-epoxy-*p*-menthane.[16] The mixture of diols (4·1 g.) was separated by fractionation of the derived *p*-nitrobenzoates from alcohol, yielding the diester of 1-hydroxy*neoiso*carvomenthol (1·4 g.) and the monoester of 1-hydroxycarvomenthol (1·9 g.).

1-*Hydroxycarvomenthol.*—Hydrolysis of either the above di-*p*-nitrobenzoate, m. p. 126°, or the mono-*p*-nitrobenzoate, m. p. 83°, yielded 1-*hydroxycarvomenthol*, b. p. 88—90°/1·0 mm., needles, m. p. 49°, which could not be recrystallised (Found: C, 69·8; H, 11·6%). The *mono*-3 : 5-*dinitrobenzoate* crystallised as fine white needles, m. p. 117° from hexane (Found: C, 56·1; H, 6·1; N, 7·9%). The *monotoluene*-p-*sulphonate* crystallised as needles, m. p. 56°, from hexane (Found: C, 62·9; H, 8·3; S, 9·7. $C_{17}H_{26}O_4S$ requires C, 62·6; H, 8·0; S, 9·8%).

1-*Hydroxy*neoiso*carvomenthol.*—Hydrolysis of the di-*p*-nitrobenzoate, m. p. 186°, gave 1-*hydroxy*neoiso*carvomenthol* as needles, m. p. 72·5° after crystallisation from light petroleum (b. p. 40°) (Found: C, 69·5; H, 11·8%). Hydrolysis of the mixture, m. p. 165—167°, from methods (*b*) and (*c*) of *cis*-hydroxylation yielded needles, m. p. 70° after two crystallisations from light petroleum (b. p. 40°). The m. p. was undepressed on admixture with a sample of 1-hydroxy*neoiso*carvomenthol, m. p. 72—75°. The *mono*-p-*nitrobenzoate*, obtained from equimolar portions of the glycol and acid chloride crystallised from light petroleum as needles, m. p. 107° (Found: C, 63·4; H, 7·0; N, 4·3%).

Equilibration of p-*Menthane*-1 : 2-*diols.*—Sodium (1 g.) was added to a solution of 1-hydroxy-*neo*carvomenthol (2·0 g.) in decalin (10 ml.) and the mixture boiled in oxygen-free nitrogen for 10 hr. Alcohol was added and the mixture evaporated to dryness *in vacuo* at 100°. The diol was separated by addition of water, isolation with ether, and distillation. The infrared absorption spectrum of the product in carbon disulphide was measured in the region 8—12 μ. 1-Hydroxy*iso*carvomenthol was the only diol which could be identified although about 10% of an unidentified component was present. Esterification of the glycol afforded the di-*p*-nitrobenzoate of this diol. The reaction was repeated but for periods of 16 and 24 hr., with the same result. The absorption spectra of the different samples were identical. The same result was obtained when 1-hydroxy*iso*- and 1-hydroxy*neoiso*-carvomenthol were treated similarly.

Dehydration of p-*Menthane*-1 : 2-*diols.*—The diols (0·1 g.) were heated individually with 10% sulphuric acid (1 ml.) at 100° for 2 hr. Treatment of the products with 2 : 4-dinitrophenylhydrazine sulphate solution and crystallisation of the product from methanol gave orange plates, m. p. 157°, alone or mixed with a sample of a *carvomenthone* 2 : 4-*dinitrophenylhydrazone* prepared from carvacrol by hydrogenation with W-7 Raney nickel at 100°/1000 lb. per sq. in. for 3 hr. After separation from hydrocarbon the carvomenthol mixture was oxidised with sodium dichromate–sulphuric acid, and the ketone isolated with ether. The 2 : 4-dinitrophenylhydrazone had m. p. 157° (Found: N, 16·6. $C_{16}H_{22}O_4N_4$ requires N, 16·8%).

1-*Methyl*cyclo*hexane*-cis- *and* -trans-1 : 2-*diol.*—The *trans*-diol[11] was prepared with peracetic acid as described for *p*-menth-1-ene. Esterification with *p*-nitrobenzoyl chloride and chromatography afforded the *monoester*, needles (from aqueous methanol), m. p. 103° (Found: C, 60·6; H, 6·0; N, 5·1. $C_{14}H_{17}O_5N$ requires C, 60·2; H, 6·1; N, 5·0%), and the *diester*, prisms (from methanol), m. p. 194° (Found: C, 59·4; H, 4·9; N, 6·4. $C_{21}H_{20}O_8N_2$ requires C, 58·9; H, 4·7; N, 6·5%). The *cis*-diol[18] was obtained in 50% yield by the iodine–silver acetate–water method. The crude diol (2·5 g.) obtained by sodium–alcohol reduction of 2-hydroxy-2-methyl*cyclo*hexanone[19] gave the *trans*-diol (1·1 g.), m. p. and mixed m. p. 84°, on crystallisation from light petroleum. Esterification of the mother-liquors gave only the di-*p*-nitrobenzoate (0·5 g.) of this diol. Samples of the *cis*- and the *trans*-diol (2·0 g.) were heated with sodium (0·8 g.) in decalin (15 ml.) for 8 and 16 hr. Alcohol was added, the mixtures were evaporated and decomposed with water, and the products were isolated with ether. The distilled products all had identical absorptions in the 8—12 μ region, corresponding to the *trans*-diol. No bands of the *cis*-isomer could be detected. Chemical separation of the products gave the *trans*-diol and its esters in all cases.

1-*Ethyl*cyclo*hexane*-cis- *and* -trans-1 : 2-*diol.*—The *trans*-diol was prepared by hydration of the epoxide with water at 110° during 5 hr. It crystallised on refrigeration for some days and formed prisms, m. p. 47°, from hexane (Found: C, 66·4; H, 11·0. $C_8H_{16}O_2$ requires C, 66·7; H, 11·1%). Esterification in pyridine at 100° during 3 hr. gave the *di*-p-*nitrobenzoate*, prisms, m. p. 222° (from benzene–light petroleum) (Found: C, 59·7; H, 4·9; N, 6·6. $C_{22}H_{22}O_8N_2$ requires C, 59·7; H, 5·0; N, 6·3%), and the *mono*-p-*nitrobenzoate*, prisms (from light petroleum) m. p. 101° (Found: C, 61·4; H, 6·3; N, 4·9. $C_{15}H_{19}O_5N$ requires C, 61·4; H, 6·3; N, 4·8%).

[18] Boeseken and Mann, *Ber.*, 1923, **56**, 2409.
[19] Wilson and Read, *J.*, 1935, 1269.

The *cis*-diol was prepared in 40% yield from 1-ethyl*cyclo*hexene by the iodine–silver acetate–water method. It crystallised from light petroleum as prisms, m. p. 81° (Found: C, 67·0; H, 11·1. $C_8H_{16}O_2$ requires C, 66·7; H, 11·1%). The *di*-p-*nitrobenzoate* separated from light petroleum–chloroform as needles, m. p. 142° (Found: C, 59·9; H, 5·1; N, 6·6%). *cyclo*Hexane-1 : 2-dione (35 g.) in ether (200 ml.) was added to ethylmagnesium iodide (from 105 g. of ethyl iodide) during 2 hr. After 15 hr. at the b. p. the mixture was worked up in the usual way. *2-Ethyl-2-hydroxy*cyclo*hexanone* (17·2 g.) had b. p. 104—105°/25 mm., n_D^{25} 1·4728, d_4^{25} 1·0334 (Found: C, 68·1; H, 10·1. $C_8H_{14}O_2$ requires C, 67·6; H, 9·9%). This ketol (7·5 g.) in absolute alcohol (200 ml.) was reduced with sodium (20 g.). Water was added, the alcohol distilled off, and the residue extracted with ether. Distillation gave the diol (3·5 g.) which was esterified with *p*-nitrobenzoyl chloride. Chromatography on alumina and elution with benzene gave the diester (3·0 g.), m. p. and mixed m. p. 222°, of the *trans*-glycol. Ether–benzene (1 : 10) yielded the monoester (0·7 g.), m. p. and mixed m. p. 101°. Other fractions failed to crystallise. The *cis*- and *trans*-diols, heated with sodium in decalin for 16 hr., afforded some *trans*- and some *cis*-diol: the infrared absorption spectra of both samples indicated approximately 70% of *trans*- and 30% of *cis*-diol.

1-iso*Propyl*cyclo*hexane*-cis- *and* -trans-1 : 2-*diol*.—The *cis*-isomer, obtained in 50% yield from 1-*iso*propyl*cyclo*hexene by the iodine–silver acetate–water method, separated from light petroleum as prisms, m. p. 106° (Found: C, 68·8; H, 11·6. $C_9H_{18}O_2$ requires C, 68·4; H, 11·4%). The *trans*-diol was prepared from the hydrocarbon by reaction with monoperphthalic acid and hydration of the epoxide with water at 120° during 4 hr. Crystallisation from light petroleum gave prisms, m. p. 98° (Found: C, 68·7; H, 11·8%). The *di*-p-*nitrobenzoate* had m. p. 181° (Found: C, 60·7; H, 5·2; N, 6·3. $C_{23}H_{24}O_8N_2$ requires C, 60·5; H, 5·3; N, 6·1%).

The *trans*-diol was heated with sodium and decalin as above for 8 and 16 hr. The crystalline product separated from light petroleum as prisms, m. p. 106° alone or mixed with a sample of the *cis*-diol. Similar treatment of 1-*iso*propyl*cyclo*hexane-*cis*-1 : 2-diol resulted in recovery of the starting material.

(±)cis- *and* (±)trans-*Carvotanacetol*.—The mixed 3 : 5-dinitrobenzoates derived from mercuric acetate oxidation of (±)-*p*-menth-1-ene [20] were crystallised from methanol, affording the *trans*-isomer, m. p. 94°, which was hydrolysed with potassium hydroxide in boiling ether–methanol to (±)-*trans*-carvotanacetol, b. p. 106°/17 mm., d_4^{20} 0·9290, n_D^{20} 1·4786 (Found: C, 78·2; H, 11·9. $C_{10}H_{18}O$ requires C, 77·8; H, 11·8%). A sample (0·5 g.) was hydrogenated in ethanol with W.4. Raney nickel at 100°/500 lb. per sq. in. After dilution with water the alcohol was removed and the product isolated with ether. The "*iso*carvomenthyl" 3 : 5-dinitrobenzoate [15] had m. p. 93° (Found: C, 58·8; H, 6·4. Calc. for $C_{17}H_{22}O_6N_2$: C, 58·3; H, 6·3%). The *p*-nitrobenzoate had m. p. 85° (lit.,[15] 85°).

The mother-liquors from the separation of the *trans*-ester afforded the *cis*-isomer as plates, m. p. 75° after four crystallisations from aqueous methanol (Found: C, 59·0; H, 5·7%). The ester was hydrolysed as for the *trans*-isomer and the product (0·35 g.) shaken with manganese dioxide (7 g.) in hexane (70 ml.) for 10 hr. The hexane residue afforded (±)-carvotanacetone semicarbazone, m. p. and mixed m. p. 174°. Oxidation of (±)-*trans*-carvotanacetol in the same way gave the identical result.

Dehydrations by Phosphorus Oxychloride.—1-Hydroxy*neo*carvomenthyl mono-3 : 5-dinitrobenzoate (0·04 g.) in pyridine (1·5 ml.) was treated with phosphorus oxychloride (0·15 ml.) during 24 hr. Isolation in the usual way and crystallisation from methanol gave (±)-*trans*-carvotanacetyl 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 94°. Similar treatment of the mono-*p*-nitrobenzoate afforded the (±)-*trans*-carvotanacetol derivative, as plates (from hexane), m. p. 100° (Found: C, 67·2; H, 6·8; N, 4·6. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 6·9; N, 4·6%). The mono-*p*-nitrobenzoate of 1-hydroxy*neoiso*carvomenthol (0·04 g.) was treated as above. Crystallisation from hexane gave the *p*-nitrobenzoate of (±)-*trans*-carvotanacetol m. p. and mixed m. p. 100°. Under the same conditions the mono-3 : 5-dinitrobenzoate of 1-hydroxy-carvomenthol was recovered unchanged.

cis- *and* trans-p-*Menthane*-3 : 4-*diol*.—(±)-*p*-Menth-3-ene was prepared from 4-methyl*cyclo*hexanone by Grignard reaction with *iso*propylmagnesium bromide followed by dehydration with aqueous oxalic acid as described for (±)-*p*-menth-1-ene.[14] A cis-*diol* was obtained in 40% yield by the iodine–silver acetate–water method, described above. Esterification of the product with *p*-nitrobenzoyl chloride in the usual way, absorption on alumina, and elution with benzene gave the *mono*-p-*nitrobenzoate* which crystallised from light petroleum as prisms, m. p.

[20] Treibs and Bast, *Annalen*, 1948, **561**, 165.

138° (Found: C, 63·6; H, 7·3; N, 4·8. $C_{17}H_{23}O_3N$ requires C, 63·6; H, 7·1; N, 4·4%). Hydrolysis with methanolic potassium hydroxide, isolation with ether, and crystallisation from light petroleum gave prisms of the *diol*, m. p. 78·5° (Found: C, 70·1; H, 11·7. $C_{10}H_{20}O_2$ requires C, 69·8; H, 11·6%). The *mono*-3 : 5-*dinitrobenzoate* separated from light petroleum as needles, m. p. 98° (Found: C, 56·2; H, 6·2; N, 7·9. $C_{17}H_{22}O_7N_2$ requires C, 55·7; H, 6·0; N, 7·65%). *trans*-Hydroxylation was carried out as described by Ogata [21] except that the epoxide (13·0 g.) was hydrated with water at 120° during 18 hr. The diol mixture (7·0 g.) was taken up in light petroleum (b. p. < 40°) and on refrigeration a *trans-p*-menthane-3 : 4-diol separated as prisms, m. p. 74° (73·5—76° [21]) (Found: C, 70·0; H, 11·6. Calc. for $C_{10}H_{20}O_2$: C, 69·8; H, 11·6%). The *mono*-3 : 5-*dinitrobenzoate* separated from light petroleum as needles, m. p. 156° (Found: C, 56·1; H, 5·9; N, 7·7%). The mother-liquors from the original diol crystallisation were esterified with *p*-nitrobenzoyl chloride, and the ester was washed with methanol; the precipitate (0·8 g.) when crystallised from ethanol–ethyl acetate gave a *diester* as prisms, m. p. 188° (Found: C, 61·4; H, 5·6; N, 6·0. $C_{24}H_{26}O_8N_2$ requires C, 61·3; H, 5·5; N, 6·0%). A further quantity (0·2 g.) was obtained from the mother-liquors after removal of the methanol, dissolution in light petroleum–benzene (1 : 5), and elution with this solvent. Elution with ether–benzene (1 : 5) afforded the *mono*-p-*nitrobenzoate*, m. p. 117° (Found: C, 63·9; H, 7·1; N, 4·8%), of the diol, m. p. 74°. Hydrolysis of the diester, m. p. 188°, afforded a further *diol* which separated from light petroleum as heavy prisms, m. p. 82° (Found: C, 70·0; H, 11·8%), unaffected by periodic acid at pH. 2. The infrared absorption spectrum showed the absence of a carbonyl group.

4-Bromomenthone was prepared from (±)-menthone by the method described for bromination of formyl*cyclo*hexane.[22] The hydroxy-ketone (A) was prepared by hydrolysis with aqueous potassium hydroxide.[23] Treatment with 2 : 4-dinitrophenylhydrazine sulphate gave the derivative of (±)-*p*-menth-3-en-5-one, crystallising from alcohol as red needles, m. p. 144° (Found: C, 58·0; H, 6·3. $C_{16}H_{22}O_4N_4$ requires C, 57·8; H, 6·0%) alone or mixed with a sample obtained from ketone prepared by dehydrobromination of 4-bromomenthone.[17] The same derivative was obtained when 2-hydroxymenthone [24] was converted into the 2 : 4-dinitrophenylhydrazone. The hydroxy-ketone (A) (12·0 g.) was reduced with sodium (25 g.) and alcohol (200 ml.). The bulk of the alcohol was removed, water added, and the product isolated with ether. Distillation gave a diol fraction (4·0 g.), b. p. 104—114°/2·5 mm. Esterification with *p*-nitrobenzoyl chloride, chromatography, and fractional crystallisation gave (±)-*trans*-2-hydroxymenthyl di-*p*-nitrobenzoate (2·0 g.), m. p. and mixed m. p. 117—118°, and (±)-*trans*-2-hydroxy*iso*menthyl di-*p*-nitrobenzoate [25] (0·4 g.), m. p. and mixed m. p. 164°, together with the ester of (±)-menthol (0·3 g.).

Periodate Titrations.—Rate constants at pH 10·5 were obtained as described previously.[16] Measurements in buffer pH 2 [obtained by dilution of potassium chloride (3·725 g.) in 0·100N-hydrochloric acid (106 ml.) to 1 l.] were made in the same way except that samples were quenched in a solution of potassium iodide (0·1—0·2 g.) in 0·1N-hydrochloric acid (20 ml.) and the iodine titrated with 0·01N-sodium thiosulphate.

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[21] Ogata, *J. Chem. Soc. Japan*, 1942, **45**, 428.
[22] Heilbron, Jones, Richardson, and Sondheimer, *J.*, 1954, 705.
[23] Wallach, *Annalen*, 1918, **414**, 354.
[24] Jefferies, Macbeth, and Milligan, *J.*, 1954, 705.
[25] Macbeth and Robertson, *J.*, 1953, 895; 3512; 1954, 701.