34. *Researches in the Menthone Series. Part XVII.** *Configurations of Menthols and Menthylamines.*

By NEAL L. MCNIVEN and JOHN READ.

Each of the four stereoisomeric menthyltrimethylammonium hydroxides on thermal decomposition affords one of three *p*-menthenes. Menthyl- and *iso*menthyltrimethylammonium hydroxides give isomeric *p*-menth-2-enes which on hydrogenation yield isomeric *p*-menthanes. Application of von Auwers's rule to the physical properties of these *p*-menthanes indicates that menthone and its derivatives have the *trans*-configuration on carbon atoms 1 and 4 while *iso*menthone and its derivatives have the *cis*-configuration. Since quaternary ammonium hydroxides have been shown to decompose by a bimolecular mechanism dependent wholly on *trans*-elimination, additional evidence for the accepted configurations on carbon atoms 3 and 4 of the four menthylamines, and hence also of the four menthols, is now presented (cf. Read and Grubb, *J.*, 1934, 1779). *neoiso*Menthylamine has been prepared by a new method. New optical constants have been calculated for (+)-*trans*- and (+)-*cis*-*p*-menth-2-ene.

THE methyl and *iso*propyl groups on carbon atoms 1 and 4 respectively of menthone and *iso*menthone have been assigned the *trans*- and the *cis*-configuration respectively by applying the rule of von Auwers (*Annalen*, 1920, **420**, 92) to their physical properties and to those of their derivatives. Zeitschel and Schmidt (*Ber.*, 1926, **59**, 2298), using optically pure materials, found that (+)-*iso*menthone had a higher density and refractive index than (—)-menthone. This was confirmed by Hiraidzumi (Chikashige Anniv. Vol. Kyoto, 1930, 87). If von Auwers's rule is assumed to hold for cyclic compounds, *iso*menthone should be assigned the *cis*- and menthone the *trans*-configuration. Additional evidence for these configurations was presented by Keats (*J.*, 1937, 2003) who converted (—)-menthone and (±)-*iso*menthone into the corresponding menthanes by electrolytic reduction using Scholl and Kirst's procedure (*Z. Electrochem.*, 1923, **29**, 537). (±)-*iso*Menthone gave the menthane having the higher density and refractive index : as before, this indicates a

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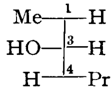
* Part XVI, *J.*, 1939, 1306.

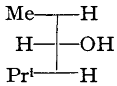
cis-configuration. Hückel and his co-workers (*Annalen*, 1939, **537**, 126; *Ber.*, 1941, **74**, 657) prepared *p*-menth-2-enes by treating (—)-menthyl and (+)-*iso*menthyl toluene-*p*-sulphonate with alcoholic sodium ethoxide. In this case also the menthene derived from the *iso*menthyl compound had the higher density and refractive index, indicating that it and the related *iso*menthone should be assigned the *cis*-configuration.

Read and Grubb (*loc. cit.*) used the comparative rates of esterification of the menthols with *p*-nitrobenzoyl chloride to determine the configurations of the groups on carbon atom 3. They found that the two *neo*menthols esterified much more slowly than either menthol or *iso*menthol. On the assumption that steric hindrance by the *iso*propyl group is the main factor adverse to esterification, the hydroxyl group on carbon atom 3 is assigned the *cis*-position relative to the *iso*propyl group in the two *neo*menthols, and the *trans*-position in menthol and *iso*menthol.

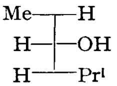
Since (—)-menthol and (+)-*neo*menthol have been related configurationally to (—)-menthone (Zeitschel and Schmidt, *Ber.*, 1926, **59**, 2303), and since (+)-*iso*menthol and (+)-*neoiso*menthol have been related to (+)-*iso*menthone (Read, Robertson and Cook, *J.*, 1927, 1276; Read and Grubb, *J.*, 1934, 313), the relative configurations of the menthols can be written as shown :



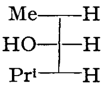
(—)-Menthol



(+)-*iso*-



(+)-*neo*-



(+)-*neoiso*-

The four menthylamines have been assigned corresponding configurations partly on the basis of similarities of values for optical rotation between the menthylamine and the menthols (Read and Grubb, *J.*, 1934, 314). Attempts to use the rate of formation of acyl derivatives of the amines as a criterion for the relative configurations on carbon atoms 3 and 4 led to anomalous results (Read and Grubb, *J.*, 1934, 1779).

We now present additional evidence in favour of the above configurations for the menthols and the menthylamines. Optically active menthenes were prepared from each of the four menthylamines by way of the quaternary ammonium hydroxides, Read and Hendry's method (*Ber.*, 1938, **71**, 2544) being used with some modifications. The menth-2-ene derived in this way from (+)-*iso*menthylamine had a higher density and a higher refractive index than that derived from (—)-menthylamine. By von Auwers's rule, the *cis*-configuration of carbon atoms 1 and 4 is accordingly assigned to (+)-*iso*menthylamine, as also to the related (+)-*iso*menthone, and the *trans*-configuration to (—)-menthylamine and (—)-menthone. This result confirms the conclusion drawn from the work of Hückel and his co-workers (*loc. cit.*), who prepared the isomeric menth-2-ene by a different method.

Since von Auwers's rule is applied with greater certainty when the disubstituted ring is saturated, the menth-2-enes prepared as above were hydrogenated to the corresponding *p*-menthanes. Again, the menthane derived from (+)-*iso*menthone had a higher density and a higher refractive index than that from (—)-menthone. This work, in which optically pure starting materials and purely chemical reactions were used throughout, confirms the results of Keats (*loc. cit.*), who used electrolytic reduction.

Recently it has been shown by Rossini and Pitzer (*Science*, 1947, 647) that the general application of von Auwers's rule to cyclic compounds is susceptible to error. In a study of the thermodynamic properties of isomeric 1 : 3-dimethyl*cyclo*hexanes they found that the *cis*-configuration is less strained and has a lower energy content than the *trans*-configuration. Accordingly they assigned the *cis*-configuration to the lower-boiling isomer, which also had the lower density and refractive index. This is contrary to von Auwers's rule. Mousseron and Granger (*Bull. Soc. chim.*, 1938, **5**, 1618) arrived at the same conclusion from a study of the optically active forms of 1 : 3-dimethyl*cyclo*hexane.

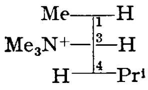
However, Rossini and Pitzer concluded that the *trans*-1 : 2- and *trans*-1 : 4-dimethyl-*cyclo*hexanes should have the lower energy content and hence should follow von Auwers's rule. Since the menthanes are 1 : 4-disubstituted *cyclo*hexanes it is very probable that they also follow von Auwers's rule and that the configurations on carbon atoms 1 and 4 deduced for the menthones, menthylamines, and menthols are correct.

The identification of the menthenes prepared by pyrolysis of the four optically active quaternary ammonium hydroxides of the menthylamines gives additional evidence for the configuration of the groups on carbon atom 3. It has been established that quaternary ammonium hydroxides on thermal decomposition form olefins by a bimolecular ionic mechanism associated with *trans*-elimination (Dhar, Hughes, Ingold, Mandour, Maw, and Woolf, *J.*, 1948, 2117).

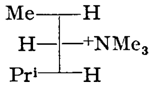
The appended table shows the composition, determined by Hückel's method (*Annalen*, 1940, **543**, 191), of the olefins formed by pyrolysis of each of the four quaternary ammonium hydroxides from the menthylamines :

Quaternary ammonium compound	(+)-*trans-p*-Menth-2-ene	(+)-*cis-p*-Menth-2-ene	(+)-*p*-Menth-3-ene
Menthyl	96	—	4
*iso*Menthyl	—	99	1
*neo*Menthyl	10·5	—	89·5
*neoiso*Menthyl	—	present	mainly

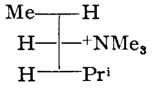
The accepted relative configurations for the four quaternary ammonium ions are :



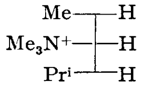
(−)-Menthyl-



(+)-*iso*-



(+)-*neo*-



(+)-*neoiso*-

Examination of these formulæ shows that with the menthyl and *iso*menthyl compounds *trans*-elimination can occur only between carbon atoms 2 and 3. This has been found to be substantially the case, since very little *p*-menth-3-ene is formed. With the *neo*menthyl and the *neoiso*menthyl compounds *trans*-elimination can occur either between carbon atoms 3 and 4 or between atoms 2 and 3. Elimination occurs by both routes, but in each case elimination predominates between carbon atoms 3 and 4, towards the tertiary carbon.

Since these results fit in well with the accepted configuration for carbon atom 3 it can be concluded that these configurations of the quaternary ammonium compounds, the menthylamines, and the menthols are probably correct.

EXPERIMENTAL

(M. p.s are uncorrected. Analyses are by Drs. Weiler and Strauss, Oxford.)

Menthyltrimethylammonium Hydroxide.—(−)-Menthol (45 g.), $[\alpha]_D^{16}$ −48·9° (*c*, 3·83 in ethanol), was converted by Beckmann's method (*Annalen*, 1889, **250**, 325) into (−)-menthone (42 g., 95%), α_D^{15} −25·62° (*l* = 1 dm.; homogeneous). (−)-Menthone (332 g.), α_D^{16} −23·9° (*l* = 1 dm.; homogeneous), from several similar preparations, with hydroxylamine acetate in ethyl alcohol at room temperature gave a crystalline oxime (267 g., 73%), m. p. 49—50°, $[\alpha]_D^{15}$ −42·0° (*c*, 2·47 in ethanol), and an oily oxime (79 g., 22%), $[\alpha]_D^{18}$ −36·6° (*c*, 2·48 in ethanol). The crystalline oxime (112 g.) was reduced by sodium and ethanol (Wallach, *Annalen*, 1893, **276**, 301) to (−)-menthylamine (58 g., 57%), α_D^{17} −31·51° (*l* = 1 dm.; homogeneous). The hydrochloride, after recrystallising once from water, had $[\alpha]_D^{11}$ −32·4° (*c*, 1·88 in water), and (−)-*menthylamine hydrobromide* had $[\alpha]_D^{11}$ −26·9° (*c*, 2·74 in water) (Found: Br, 33·8. $C_{10}H_{22}NBr$ requires Br, 33·9%). The salicylidene derivative was phototropic and had m. p. 57—58°, $[\alpha]_D^{13}$ −118·2° (*c*, 2·17 in chloroform).

The oily oxime (79 g.) was reduced by the same procedure to (−)-menthylamine (48 g., 66%), α_D^{17} −29·67° (*l* = 1 dm.; homogeneous). Its salicylidene derivative was phototropic and had m. p. 56—57°, $[\alpha]_D^{16}$ −119·9° (*c*, 1·99 in chloroform). No depression in m. p. was obtained when this derivative was mixed with the salicylidene derivative of authentic (−)-menthylamine.

Since both oximes give (−)-menthylamine on reduction they are probably *syn*- and *anti*-isomers. This type of isomerism has already been reported by Hückel and Doll (*Annalen*, 1936, **526**, 103) who isolated *syn*- and *anti*-forms of carvomenthone oxime and *iso*carvomenthone oxime.

(−)-Menthylamine (67 g.) was converted into (−)-menthyltrimethylammonium iodide (129 g., 93%) by the method of Read and Hendry (*Ber.*, 1938, **71**, 2544) except that a 50%

excess of methyl iodide was used to ensure higher yields. After recrystallising from acetone the methiodide had m. p. 193—194°, $[\alpha]_D^{17}$ −37·6° (*c*, 2·59 in water). Read and Hendry (*loc. cit.*) give m. p. 190° (decomp.), $[\alpha]_D^{17}$ −39·3° (*c*, 2 in water).

The methiodide (56 g.) in aqueous solution was converted into the quaternary ammonium hydroxide by treating it with excess of freshly prepared moist silver oxide. The precipitated silver iodide and excess of silver oxide were filtered off, leaving the menthyltrimethylammonium hydroxide in solution.

Pyrolysis of Menthyltrimethylammonium Hydroxide.—The above menthyltrimethylammonium hydroxide solution was concentrated on a steam-bath and then distilled under atmospheric pressure at a bath-temperature of 130—140°. Two fractions were recovered which on being washed with dilute hydrochloric acid, aqueous sodium carbonate, and water and dried (Na_2SO_4) gave colourless liquids: 2·3 g., α_D^{14} +107·87° (*l* = 1 dm.; homogeneous); and 1·8 g., α_D^{17} +99·34° (*l* = 1 dm.; homogeneous). A third fraction (3·0 g.), α_D^{17} +104·30° (*l* = 1 dm.; homogeneous), was obtained on continuing the distillation at 200° (bath-temp.)/20 mm. The overall yield of menthene was 7·1 g. (30%). After distillation of the combined fractions three times from sodium under a vacuum, (+)-*trans*-*p*-menth-2-ene having the following properties was obtained: α_D^{16} +107·18° (*l* = 1 dm.; homogeneous), $[\alpha]_D^{16}$ +132·5° (homogeneous), d_4^{20} 0·8096, n_D^{20} 1·4492, $[R_L]_D$ 45·78 (Calc., 45·71). As found by Read and Hendry (*loc. cit.*), the distillate also contained (−)-menthyldimethylamine which was removed in the acid wash.

Racemisation of (+)-trans-p-*Menth-2-ene.*—Hückel (*Annalen*, 1940, **543**, 191) has shown that on being refluxed with alcoholic toluene-*p*-sulphonic acid (+)-*p*-menth-3-ene and (+)-*p*-menth-1-ene are completely racemised, whereas (+)-*trans*- and (+)-*cis*-*p*-menth-2-ene are not affected. The above (+)-*trans*-*p*-menth-2-ene (0·6 ml.) was refluxed with toluene-*p*-sulphonic acid solution (0·8 ml.) (29·4 g. of p-$C_6H_4Me{\cdot}SO_3H,4H_2O$ in 100 ml. of ethanol solution) for 4·5 hours. After recovery by addition of water, washing with aqueous sodium carbonate, and drying (Na_2SO_4), the menthene had α_D^{18} +103·6° (*l* = 1 dm.; homogeneous). A series of racemisation tests on another sample of (+)-*trans*-*p*-menth-2-ene showed that little further drop in rotation occurred after 4 hours' refluxing. If the value α_D +88·0° is assumed for optically pure (+)-*p*-menth-3-ene, as calculated by Hückel (*loc. cit.*), the composition of the *p*-menthene having α_D^{16} +107·18° (*l* = 1 dm.; homogeneous) can be estimated by using the relation given by Landolt ("Optical Rotation of Organic Substances," 2nd. edn., 1902, p. 240). This was found to be (+)-*trans*-*p*-menth-2-ene 95·9 and (+)-*p*-menthene-3-ene 4·1%. By the same relation it can be estimated that optically pure (+)-*trans*-*p*-menth-2-ene should have α_D +108·0° (*l* = 1 dm.; homogeneous).

trans-p-*Menthane.*—(+)-*trans*-*p*-Menth-2-ene (2·7 g.), α_D^{18} +107·18° (*l* = 1 dm.; homogeneous), in glacial acetic acid (10 ml.), was hydrogenated at 4 atm. at room temperature over Adams's platinum oxide (16 mg.). The absorption stopped when one molecular equivalent of hydrogen had been taken up in 12 minutes. After the catalyst had been removed by filtration the *trans*-*p*-menthane was recovered by adding water, washing with aqueous sodium carbonate and with aqueous potassium permanganate, and drying (Na_2SO_4). It had α_D^{15} −0·38° (*l* = 1 dm.; homogeneous), d_4^{20} 0·7936, n_D^{20} 1·4366, $[R_L]_D$ 46·24 (calc., 46·18).

Dibromide of (+)-trans-p-*Menth-2-ene.*—(+)-*trans*-*p*-Menth-2-ene (1·57 g.), α_D^{18} +104·10° (*l* = 1 dm.; homogeneous), in glacial acetic acid (5 ml.), was titrated at room temperature with bromine in glacial acetic acid (3·27 g.-atoms per l.); 2·00 atomic equivalents of bromine were absorbed with liberation of heat. The dibromide was recovered by addition of water, washing with aqueous sodium carbonate, and drying (Na_2SO_4), to give (+)-2 : 3-dibromo-*trans*-*p*-menthene (2·74 g., 81%), α_D^{17} +60·70° (*l* = 1 dm.; homogeneous), $[\alpha]_D^{17}$ +41·4° (homogeneous), d_4^{20} 1·4686, n_D^{20} 1·5239, $[R_L]_D$ 62·07 (calc., 61·71). This dibromide was probably a mixture of stereoisomers.

Debromination of (+)-2 : 3-*Dibromo*-trans-p-*menthene.*—Debromination was carried out by Linnemann's procedure (*Ber.*, 1877, **10**, 1113). (+)-2 : 3-Dibromo-*trans*-*p*-menthane (2·74 g.), α_D^{17} +60·70° (*l* = 1 dm.; homogeneous), was refluxed with water (1 ml.), ethanol (7 ml.), and zinc dust (1·0 g.) for 3 hours. After filtration, washing with water, and drying (Na_2SO_4), the resulting (+)-*trans*-*p*-menth-2-ene had α_D^{18} +102·20° (*l* = 1 dm.; homogeneous).

neo*Menthyltrimethylammonium Hydroxide.*—(+)-Formyl*neo*menthylamine (180 g.), m. p. 116—118°, was converted by the method of Read and Robertson (*J.*, 1926, 2217) into *neo*menthylamine (158 g., 100%). The hydrochloride, recrystallised twice from water, had $[\alpha]_D^{15}$ +18·9° (*c*, 1·78 in water). The free base, α_D^{15} +11·38° (l = 1 dm.; homogeneous), from this salt (100 g.) was converted into (−)-*neo*menthyltrimethylammonium iodide (160 g., 76%)

by the method used for (−)-menthylamine. After recrystallising from acetone it had m. p. 161—162°, $[\alpha]_D^{18}$ −20·6° (*c*, 3·35 in water). Read and Hendry (*loc. cit.*) reported m. p. 160·5° (decomp.), $[\alpha]_D^{17}$ −19·5° (*c*, 2 in water). The quaternary ammonium hydroxide was prepared by the method used for the menthyl compound.

Pyrolysis of neo*Menthyltrimethylammonium Hydroxide.*—The quaternary ammonium hydroxide from 40 g. of the above iodide was distilled initially at atmospheric pressure and 120° (bath-temp.) and finally at 180°/20 mm. The greater part of the colourless oily distillate came over at the lower temperature. On working up of the distillate and distillation from sodium, (+)-*p*-menth-3-ene (86%) was obtained having α_D^{16} +90·09° (l = 1 dm.; homogeneous), $[\alpha]_D^{16}$ +110·8° (homogeneous), d_4^{20} 0·8138, n_D^{20} 1·4519, $[R_L]_D$ 45·79 (calc., 45·71). No tertiary amine was found in the distillate from this pyrolysis. The nitrosochloride, prepared by the method of Richtman and Kremers (*Amer. Chem. J.*, 1896, **18**, 762), was obtained in 41% yield as a colourless crystalline solid. After three recrystallisations from ethanol–chloroform it had m. p. 124—126°, $[\alpha]_D^{19}$ +226° (*c*, 1·8 in benzene) [Found : *M* (cryoscopic in benzene), 415. Calc. for $(C_{10}H_{18}ONCl)_2$: *M*, 407].

Racemisation of (+)-p-*Menth*-3-*ene.*—The above (+)-*p*-menth-3-ene was subjected to a series of racemisation tests with alcoholic toluene-*p*-sulphonic acid by Hückel's method (*loc. cit.*). The rotation dropped in 5·75 hours to a constant value of α_D^{17} +11·26° (l = 1 dm.; homogeneous). The composition of this menthene is estimated by the previously described method to be (+)-*p*-menth-3-ene 89·5 and (+)-*trans*-*p*-menth-2-ene 10·5%.

Hydrogenation of (+)-p-*Menth*-3-*ene.*—(+)-*p*-Menth-3-ene (4·33 g.), α_D^{16} +90·08° (l = 1 dm.; homogeneous), was hydrogenated by the method used for (+)-*trans*-*p*-menth-2-ene. Absorption of hydrogen stopped after one molecular equivalent had been added. The resulting *p*-menthane (4·3 g., 99%), after distillation over sodium at 15 mm., had α_D^{17} −0·06° (l = 1 dm.; homogeneous), d_4^{20} 0·7996, n_D^{20} 1·4407, $[R_L]_D$ 46·26 (calc., 46·18). This *p*-menthane is estimated to contain *cis*-*p*-menthane 55 and *trans*-*p*-menthane 45%, on the assumption of a linear variation of density and refractive index with concentration.

Dibromide of (+)-p-*Menth*-3-*ene.*—(+)-*p*-Menth-3-ene (1·0 g.), α_D^{16} +90·08° (l = 1 dm.; homogeneous), was brominated by the procedure used for (+)-*trans*-*p*-menth-2-ene: 1·94 atomic equivalents were absorbed with evolution of heat. The dibromide (1·95 g., 90%) had α_D^{18} +35·87° (l = 1 dm.; homogeneous), $[\alpha]_D^{18}$ +24·8° (homogeneous), d_4^{20} 1·4443, n_D^{20} 1·5260, $[R_L]_D$ 63·32 (calc., 61·71). This dibromide was probably a mixture of stereoisomers.

Debromination of (+)-p-*Menth*-3-*ene Dibromide.*—The above dibromide was debrominated by Linnemann's method (*loc. cit.*). The resulting *p*-menth-3-ene had $[\alpha]_D^{18}$ +28·1° (*c*, 2·99 in ethanol).

iso*Menthyltrimethylammonium Hydroxide.*—(−)-Piperitone (500 ml.), α_D^{16} −41·22° (l = 1 dm.; homogeneous), was hydrogenated by the method of Hughesdon, Smith, and Read (*J.*, 1923, **123**, 2921), using colloidal palladium as catalyst. Absorption was complete after 18 hours when one molecular equivalent of hydrogen had been added. After steam-distillation and drying (Na_2SO_4), (+)-*iso*menthone (467 g., 99%), α_D^{17} +49·0° (l = 1 dm.; homogeneous) was recovered. This was converted into the oxime by the method used for (−)-menthone. (+)-*iso*Menthone oxime (525 g., 100%), $[\alpha]_D^{18}$ +25·0° (*c*, 5·76 in ethanol), was obtained as an oil. The oxime (121 g.) was reduced with sodium and ethyl alcohol, by the method used for (−)-menthone oxime, to (+)-*iso*menthylamine (89 g., 80%), α_D^{15} +12·10° (l = 1 dm.; homogeneous). This was converted into the salicylidene derivative (Read and Robertson, *J.*, 1926, 2221), which after recrystallising three times from ethyl alcohol attained the constant rotation $[\alpha]_D^{15}$ +78·6° (*c*, 2·16 in chloroform). Hydrolysis of this derivative (118 g.) by refluxing it with aqueous sulphuric acid using the procedure of Read and Robertson (*J.*, 1927, 2171) afforded (+)-*iso*menthylamine (64 g., 100%). This was converted by the method used for (−)-menthylamine into (+)-*iso*menthyltrimethylammonium iodide (139 g., 100%). After two recrystallisations from acetone it formed long needles with the constant properties : m. p. 185°, $[\alpha]_D^{16}$ +0·6° (*c*, 3·46 in water). Read and Cuthbertson (*Rec. Trav. chim.*, 1950, **69**, 539) reported m. p. 184°, $[\alpha]_D^{18}$ +2·0° (*c*, 1·5 in water). The methiodide was converted into *iso*menthyltrimethylammonium hydroxide by moist silver oxide as described previously.

Pyrolysis of iso*Menthyltrimethylammonium Hydroxide.*—The quaternary ammonium hydroxide prepared from the iodide (40 g.) was distilled at 20 mm. and a maximum bath-temperature of 200°. An oil started to distil at a bath-temperature of 145°. After being washed with dilute hydrochloric acid and then aqueous sodium carbonate and dried (Na_2SO_4), (+)-*cis*-*p*-menth-2-ene (9·9 g., 58%) was obtained. After distilling from sodium at 15 mm. it had α_D^{16} +37·98° (l = 1 dm.; homogeneous), $[\alpha]_D^{16}$ +46·5° (homogeneous), d_4^{20} 0·8187, n_D^{20} 1·4530,

$[R_L]_D$ 45·61 (calc., 45·71). Besides the menthene there was obtained an oily base (4·6 g., 20%), α_D^{18} +38·64° (l = 1 dm.; homogeneous), probably *iso*menthyldimethylamine.

Racemisation of (+)-cis-p-*Menth*-2-ene.—A series of racemisation tests on the above menthene using Hückel's method (*loc. cit.*) showed that a constant value of α_D^{17} +37·20° (l = 1 dm.; homogeneous) was reached in 4 hours. This indicates that the menthene contains (+)-*cis*-*p*-menth-2-ene 99 and (+)-*p*-menth-3-ene 1%, and that optically pure (+)-*cis*-*p*-menth-2-ene has α_D^{17} +37·5° (l = 1 dm.; homogeneous).

Hydrogenation of (+)-cis-p-*Menth-2-ene.*—(+)-*cis*-*p*-Menth-2-ene (2·91 g.), α_D^{16} +37·98° (l = 1 dm.; homogeneous), was hydrogenated by the method used for (+)-*trans*-*p*-menth-2-ene. Absorption of hydrogen stopped after one molecular equivalent had been taken up. *cis*-*p*-Menthane (2·6 g., 88%) was obtained, which on distillation over sodium had α_D^{18} ±0·00° (l = 1 dm.; homogeneous), d_4^{20} 0·8047, n_D^{20} 1·4421, $[R_L]_D$ 46·10 (calc. 46·18).

Dibromide of (+)-cis-p-*Menth-2-ene.*—(+)-*cis*-*p*-Menth-2-ene (1·9 g.), α_D^{16} +37·98° (l = 1 dm.; homogeneous), was brominated by the procedure used for (+)-*trans*-*p*-menth-2-ene: 2·20 atomic equivalents of bromine were taken up with liberation of heat. The dibromide (4·08 g., 99%) had α_D^{18} −53·99° (l = 1 dm.; homogeneous), $[\alpha]_D^{18}$ −36·1° (homogeneous), d_4^{20} 1·4948, n_D^{20} 1·5299, $[R_L]_D$ 61·56 (calc., 61·71), b. p. 194°(decomp.)/760 mm. On debromination by the method used for (+)-2 : 3-dibromo-*trans*-*p*-menthane the resulting (+)-*cis*-*p*-menth-2-ene had α_D^{18} +31·85° (l = 1 dm.; homogeneous).

neoiso*Menthyltrimethylammonium Hydroxide.*—(+)-*iso*Menthone oxime (239 g.), α_D^{18} +25·7° (c, 5·47 in ethanol), in methyl alcohol (500 ml.) was hydrogenated at 106°/100 atm., 2 teaspoonsfuls of Raney nickel catalyst being used. The absorption of hydrogen stopped after 15 hours, when two molecular equivalents had been taken up. After steam-distillation an oily amine (58 g., 26%), α_D^{20} +2·01° (l = 1 dm.; homogeneous), was recovered from the distillate. An acid-insoluble oily ketone, α_D^{18} +3·82° (l = 1 dm.; homogeneous), made up the remainder of the distillate. The amine was converted into the salicylidene derivative, which after recrystallising seven times from light petroleum (b. p. 40—60°) to constant m. p. and rotation had m. p. 98—99°, $[\alpha]_D^{19}$ −19·5° (c, 2·43 in chloroform). No depression in m. p. was obtained when this derivative was mixed with authentic salicylidene*neoiso*menthylamine, prepared by the original method of Read and Robertson (*J.*, 1927, 2168). The salicylidene derivative (5·2 g.) was hydrolysed, giving *neoiso*menthylamine (2·3 g., 74%). This was converted by the method used for (−)-menthylamine into the methiodide, which after recrystallising once from acetone gave (+)-*neoiso*menthyltrimethylammonium iodide (2·9 g., 60%) having the constant properties: m. p. 195° (decomp.), $[\alpha]_D^{18}$ +16·5° (c, 1·88 in water) (Found: I, 39·4. Calc. for $C_{13}H_{28}NI$: I, 39·1%). Read and Cuthbertson (*loc. cit.*) reported m. p. 195°, $[\alpha]_D^{25}$ +16·8° (c, 1·5 in water). The quaternary ammonium hydroxide was prepared by the method used for the (−)-menthyl compound.

Pyrolysis of neoiso*Menthyltrimethylammonium Hydroxide.*—The quaternary ammonium hydroxide from 2·9 g. of iodide was distilled at 20 mm. and 195° (maximum bath-temp.). (+)-*p*-Menth-3-ene (0·16 g., 30%), $[\alpha]_D^{16}$ +94·1° (c, 1·39 in ethanol), was obtained along with an oily amine (0·30 g., 42%), α_D^{17} −13·34° (l = 1 dm.; homogeneous), probably *neoiso*menthyldimethylamine.

Racemisation of (+)-p-*Menth*-3-*ene.*—When the above menthene was refluxed for 4 hours with alcoholic toluene-*p*-sulphonic acid according to Hückel's procedure (*loc. cit.*), the rotation dropped to $[\alpha]_D^{16}$ +9·6° (c, 1·14 in ethanol). This low rotation, especially in view of the enhanced rotatory powers of such menthenes in ethanol (cf. Read and Robertson, *J.*, 1926, 2217), indicates that the menthene consisted essentially of (+)-*cis*-*p*-menth-2-ene with a little (+)-*cis*-*p*-menth-2-ene.

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