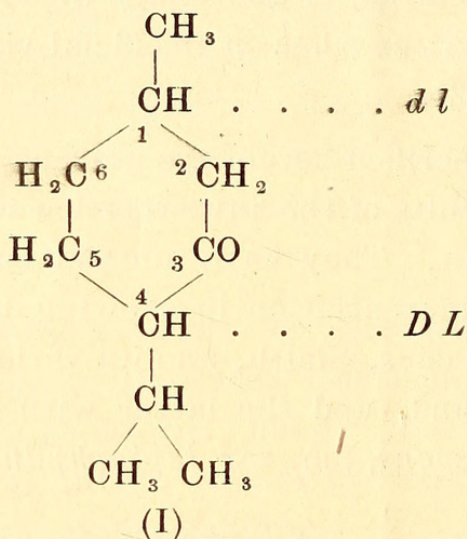


THE STEREOISOMERIC FORMS OF MENTHONE.  
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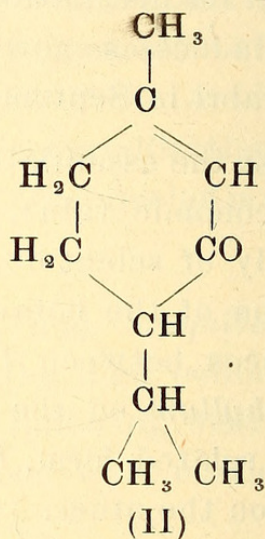
[Read before the Royal Society of N. S. Wales, November 1, 1922.]

FROM a stereochemical point of view the molecular constitution of menthone (*p*-menthan-3-one) is of particular interest, since it presents one of the best known examples of a cyclic structure containing two dissimilar asymmetric carbon atoms (Nos. 1 and 4, Formula I):



Menthone.

(*p*-menthan-3-one)



Piperitone.

( $\Delta^1$ -*p*-menthen-3-one)

The presence in the molecule of two such atoms should permit of the existence of four optically active forms of menthone. The two enantiomorphous spacial environments, and the corresponding right- and left-handed optical effects of carbon atom No. 1 may conveniently be indicated by the symbols *d* and *l*, respectively, whilst the symbols *D* and *L* may be used similarly for carbon atom No. 4. The four

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optically active menthones are then represented by the symbols *Dd*, *Ll*; *Ld*, and *Dl*. The first two of these optical isomers are wholly uncompensated substances, possessing the maximum rotatory power for the structure concerned, whilst the last two may be regarded as partially internally compensated compounds of lower rotatory power. Furthermore, these four optically active forms may combine in pairs to give rise to two fully racemic menthones, represented by the symbols *Dd,Ll* and *Ld,Dl*.

Menthone occurs in essential oils in dextro- and lævo- gyrate forms which are generally supposed to correspond with each other and with the *l*-menthone obtained from natural *l*-menthol by oxidation with chromic acid (Beckmann, *Annalen*, 1889, 250, 325). Since, however, the menthones do not combine with sodium bisulphite, and since, further, they are liable to undergo "inversion" when regenerated from derivatives, such as the oximes and semi-carbazones, the stereochemical characterisation of natural or synthetic forms of this ketone is a problem of considerable difficulty.

*l*-Menthone obtained by the oxidation of natural *l*-menthol has a maximum optical rotatory power of  $[\alpha]_D -28.46^\circ$ , and by treatment with cold 90 per cent. sulphuric acid a maximum inversion value of  $[\alpha]_D +28.14^\circ$  is exhibited (Beckmann, *loc. cit.*, 335; Ber., 1909, 42, 846). The inversion, which is conditioned by alkali as well as by acid, has been attributed to enolisation and consequent loss of asymmetry of carbon atom No. 4: it appears, therefore, that *l*-menthone should be assigned the configuration *Ld* (compare Barrow-cliff, *Trans. Chem. Soc.*, 1907, 91, 875; also Gardner, Perkin and Watson, *Trans. Chem. Soc.*, 1910, 97, 1756). *d*-Menthone would thus be *Dl*, and the configurations *Dd* and *Ll* would correspond, respectively, with the dextro- and lævo-rotatory forms of *isomenthone*, that is, with *d*- and *l*-*isomenthone*.



From the inversion results, if the above explanation is correct, it follows that the optical rotatory effect of carbon atom No. 1 is less than that of No. 4, and hence the sense of the optical rotation is determined by the spacial distribution of the groups about No. 4. In other words, the optical effects of the two asymmetric carbon atoms are opposed in the active menthones and conjoined in the active isomenthones.

Inverted *l*-menthone appears to consist of a mixture of *l*-menthone and *d*-isomenthone. By oxidising *l*-isomenthol Beckmann (J. pr. Chem., 1897, 55, 18) obtained isomenthones having values of  $[\alpha]_D$  from  $+30^\circ$  to  $+35^\circ$ , whilst a preparation made by an indirect method from *l*-menthone oxime had the remarkably high value,  $[\alpha]_D +93.2^\circ$  (Ber., 1909, 42, 846). Furthermore, Barrowcliff (*loc. cit.*), by means of the reaction with semicarbazide, isolated an isomenthone having  $[\alpha]_D +47.1^\circ$  from the essential oil of American pennyroyal (*Hedeoma pulegioides*), and estimated the value for the optically pure ketone at about  $[\alpha]_D +97^\circ$ .

It has already been shown (Smith and Penfold, this Journal, 1920, 54, 40) that the eucalyptus ketone, piperitone, can be hydrogenated in the presence of finely divided nickel at  $175-180^\circ$ , without the keto-group undergoing alteration. In the course of a recent series of investigations, as yet unpublished, in which by the application of a method independent of oxidative breakdown we have been able to confirm the structural identity of *dl*-piperitone with  $\Delta^1$ -*p*-menthen-3-one (Formula II), it became necessary to prepare comparatively large quantities of menthone from *dl*-piperitone. Among the successful methods employed was that of direct hydrogenation by the catalytic method of Paal, in the presence of colloidal palladium. The menthone obtained in this way was optically inactive and consisted mainly, or perhaps wholly, of isomenthone. It



yielded a sparingly soluble semicarbazone melting, after careful purification, at  $219 - 220^{\circ}$ , and was apparently identical with the inactive menthone obtained by Wallach (a) from  $\triangle^1$ -*p*-menthen-3-one, synthesised in turn from 1,3,4-trioxyterpane, and (b) from 1,4-methylhexanone (Annalen, 1908, 362, 272). The semicarbazone described by Wallach melted in each instance at  $210 - 212^{\circ}$ , but the lower value is readily accounted for by the presence of a more fusible isomeric semicarbazone (compare Wallach, "Terpene und Campher," 1914, 377), which we have now isolated in a state of purity. The same optically inactive isomenthone was evidently also obtained by Pickard and Littlebury (Trans. Chem. Soc., 1912, 101, 109), by the catalytic hydrogenation of thymol, the melting point of the semicarbazone in this instance being  $217^{\circ}$ .

Hitherto, no definite correlation appears to have been established between inactive isomenthone and the various preparations of *d*-isomenthone which have been described from time to time. It was therefore of considerable interest to find that lævo-rotatory piperitone, extracted from the essential oil of *Eucalyptus dives*, yielded a highly dextro-rotatory isomenthone when hydrogenated in the presence of colloidal palladium. As an example, a specimen of *l*-piperitone having  $\alpha_D^{20} - 48.05^{\circ}$  yielded a menthone which after purification had  $\alpha_D^{20} + 58.33^{\circ}$ . This result indicates that optically active piperitone, when hydrogenated under appropriate conditions, yields an optically active isomenthone having a reversed and enhanced rotatory power. Through the courtesy of Dr. Simonsen, of the Forest Research Institute, Dehra Dun, India, we were able to submit a specimen of *d*-piperitone, obtained from the essential oil of the Himalayan grass, *Andropogon Jwar-*



*ancusa*, to similar treatment (compare Trans. Chem. Soc., 1921, 119, 1644; 1922, 121, 582). A specimen of the dextro-*gyrate* piperitone, having  $\alpha_D^{17} + 47.46^\circ$ , was thereby converted into a *lævo-gyrate isomenthone*, having  $\alpha_D^{19} - 57.40^\circ$ , thus confirming the previous result.

The work of Pope and Read (Trans. Chem. Soc., 1913, 103, 1515) on partially racemic compounds of the non-electrolytic type suggested the possibility of the optically active *isomenthones* now described belonging to this type. In such an event these isomers would be represented by the symbols *Dd, Dl* and *Ld, Ll* respectively, and the catalytic hydrogenation of the optically active forms of piperitone would not be an asymmetric synthesis. Correspondingly, a second pair of partially racemic *menthones* can be imagined, in which carbon atom No. 4 fails to exert its potential activity; these would be represented by the symbols *Dd, Ld* and *Dl, Ll* respectively. All such isomers might perhaps be classified most simply as partially racemic *isomenthones*: 1-racemic in the first instance, and 4-racemic in the second.

On the whole it appears unlikely that the catalytic hydrogenation of the optically active forms of piperitone should occur otherwise than as an asymmetric, or, at least, a partially asymmetric synthesis. Further investigations, including inversion experiments, are being undertaken in order to test this point and other closely associated ideas. In addition, attention is being devoted to the characteristics of the optically active and inactive *menthols* which it has been found possible to derive in various ways from piperitone. It may be stated that preliminary work has resulted in the isolation of an inactive *menthol*, which in view of its melting point ( $39 - 41^\circ$ ) is probably to be classified as an *isomenthol*, derived from *isomenthone* (compare Pickard and Littlebury, *loc. cit.*).



In concluding this preliminary paper it is convenient to summarise the various stereoisomeric forms of menthone which appear on theoretical grounds to be capable of existing:—

- |                   |   |   |
|-------------------|---|---|
| 1. <i>Dd</i>      | } | Wholly uncompensated compounds: <i>d</i> - and <i>l</i> -iso-menthones, respectively.         |
| 2. <i>Ll</i>      |   |   |
| 3. <i>Dl</i>      | } | Partially internally compensated compounds: <i>d</i> - and <i>l</i> -menthones, respectively. |
| 4. <i>Ld</i>      |   |   |
| 5. <i>Dd, Dl</i>  | } | Partially racemic compounds: 1-racemic iso-menthones.   |
| 6. <i>Ld, Ll</i>  |   |   |
| 7. <i>Dd, Ld</i>  | } | Partially racemic compounds: 4-racemic iso-menthones.   |
| 8. <i>Dl, Ll</i>  |   |   |
| 9. <i>Dd, Ll</i>  | } | Wholly racemic compounds: <i>i</i> -isomenthone and <i>i</i> -menthone, respectively.         |
| 10. <i>Ld, Dl</i> |   |   |

We are continuing the detailed investigation of the whole field of work indicated in this paper.

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Smith, Henry George, Hughesdon, Reginald Slater, and Read, John. 1922. "The stereoisomeric forms of menthone." *Journal and proceedings of the Royal Society of New South Wales* 56, 170–175. <https://doi.org/10.5962/p.359819>.

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