60. *Researches in the Carvone Series. Part I. Some Ketones and Amines.*

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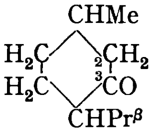
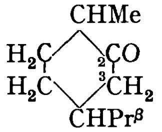
A GOOD deal of new light has recently been thrown upon the chemistry and stereochemistry of the menthones, menthols, and menthylamines (J., 1925, **127**, 2782; 1933, 170). Of almost equal interest in the terpene chemistry are the similar substances derived theoretically by interchanging the groups 2 and 3 of the menthones and their derivatives :


Menthones.


Carvomenthones.

A cursory knowledge is all that can be claimed at present for the resulting carvomenthones and their congeners. It is now hoped to extend the knowledge of this group by the application of methods which have been elaborated in studying the menthone chemistry, and possibly in other ways. The acquisition of a detailed stereochemical knowledge of two groups of substances related so closely as these is a matter of general interest in stereochemistry and of special interest in the chemistry of terpenes. Since members of both groups occur as natural products, the subject has also a biochemical aspect.

Of the two readily accessible natural substances which have been used as points of departure in the menthone chemistry, *l*-menthol affords entry to the menthone series and *l*-piperitone to the *iso*menthone series; piperitone, moreover, has the great advantage of being available in *l*-, *d*-, and *dl*-forms. In the carvone chemistry, the conditions are less favourable, the two most useful natural substances being *d*- and *l*-carvone, obtained from oil of caraway and oil of spearmint, respectively: effective entry to the *iso*-series thus presents difficulty in this group, although it may ultimately be attained by hydrogenating suitable unsaturated substances.

d-Carvone is readily hydrogenated, yielding *l*-rotatory carvomenthone with $[\alpha]_D$ about − 25°. The rotatory power varies over a small range, according to the conditions; and the experiments outlined below indicate that specimens of carvomenthone prepared in this way consist of equilibrium mixtures of two stereoisomeric carvomenthones. The variations observed in these experiments were much smaller than those recorded for menthone (J., 1926, 2214), and there was no inversion in the sense of the optical rotation, all the equilibrated specimens being *l*-rotatory. The purest specimens of *l*-menthone and its dynamic stereoisomeride, *d*-*iso*menthone, are made by oxidising *l*-menthol and *d*-*iso*menthol, respectively, with Beckmann's reagent. Similarly, *l*-carvomenthone, with $[\alpha]_D^{17^\circ}$ − 6·0°, has now been made by oxidising *d*-carvomenthol, a stereochemically homogeneous substance prepared from the equilibrium mixture of *l*-rotatory carvomenthones *via* *l*-carvomenthone oxime (m. p. 99—100°) and its main product of reduction, *d*-carvomenthylamine. This is the lowest numerical value of $[\alpha]_D$ yet recorded for a carvomenthone, and it is noteworthy that the Indian herb, *Blumea Malcomii*, yielded *l*-carvomenthone having $[\alpha]_D^{30^\circ}$ − 9·33° (Simonsen and Rau, J., 1921, **119**, 876). *l*-Carvomenthone oxime has m. p. 99—100°, $[\alpha]_D^{16^\circ}$ − 38·7° (alcohol). We assign this oxime to *l*-carvomenthone because the ketones of low numerical rotatory power give the highest yields. From a study of these yields, and using the value $[\alpha]_D$ −6° for the first isomeride, the value of $[\alpha]_D$ for the second isomeride has been estimated approximately at − 90°; a direct and more satisfying determination must be deferred until an appropriate carvomenthol becomes available for oxidation. It is shown below that *d*-carvone was most readily hydrogenated in presence of a palladium hydroxide–calcium carbonate catalyst; the product had $[\alpha]_D$ −30·6°, which is the highest numerical value yet recorded for a specimen of carvomenthone. The dynamic isomerism of the menthones and carvomenthones may be summarised in a preliminary form as follows:

d-menthone $\rightleftarrows$ *l*-*iso*menthone ($[\alpha]_D$ + 30°) (− 92°)

l-carvomenthone $\rightleftarrows$ *l*-*iso*carvomenthone (− 6°) (? − 90°)

In the carvomenthone series the equilibrium appears to lie further to the left and to be attained more rapidly than in the menthone series.

The precise knowledge of carvomenthylamines is very limited. Wallach (*Annalen*, 1893, **277**, 138) and also Brunel (*Compt. rend.*, 1907, **145**, 1437) prepared optically inactive carvomenthylamine by reducing *dl*-carvomenthone oxime (m. p. 105°) with sodium and alcohol; Wallach (*Annalen*, 1900, **313**, 361) obtained a similar material by reducing terpinene nitrosite; moreover, he found that optically active carvomenthylamine was formed in the reduction of optically active α-phellandrene nitrosite or nitro-α-phellandrene (*Annalen*, 1895, **287**, 377; 1904, **336**, 32). We have now obtained stereochemically pure specimens of the last base, for which we propose the name *d*-carvomenthylamine, by reducing *l*-carvomenthone oxime with sodium and alcohol.

This reduction yields about 92·5% of *d*-carvomenthylamine and 7·5% of a second base, which, as shown below, may be conveniently called *l*-*neo*carvomenthylamine. The best source of the latter base is the mixture of stereoisomeric formylcarvomenthylamines which is formed when *l*-rotatory carvomenthone is heated with ammonium formate; the new base was isolated by fractionally crystallising the derived mixture of hydrogen *d*-tartrates. The relationships existing between *d*- and *l*-*neo*carvomenthylamine are strikingly similar to those shown by *l*- and *d*-*neo*menthylamine (J., 1930, 2764):

	$d_{4^\circ}^{25^\circ}$.	$n_D^{25^\circ}$.	$[\alpha]_D^{25^\circ}$.
d-Carvomenthylamine	0·8505	1·4578	+12·47°
l-*neo*Carvomenthylamine	0·8558	1·4596	−26·55
l-Menthylamine	0·8525	1·4600	−44·53
d-*neo*Menthylamine	0·8551	1·4614	+15·12

When treated with nitrous acid, *d*-carvomenthylamine gives *d*-carvomenthol * as the main product, together with small amounts of *l*-*neo*carvomenthol * and *l*-Δ^1-menthene. The same three substances are given by *l*-*neo*carvomenthylamine : here, however, the terpene is the main product. Thus, in the deamination process, *d*-carvomenthylamine resembles the menthylamines and *l*-*neo*carvomenthylamine resembles the *neo*menthylamines. The capacity for crystallisation which distinguishes *neo*menthylamine derivatives (J., 1926, 2224) reappears in the derivatives of *l*-*neo*carvomenthylamine. Salicylidene-*d*-carvomenthylamine, like salicylidene-*d*-menthylamine, is strongly phototropic; the corresponding derivatives of *l*-*neo*carvomenthylamine and *d*-*neo*menthylamine are not phototropic. The evidence which has been summarised enables the appended parallel arrangement to be advanced for characteristic members of the two series of substances :

Values of $[\alpha]_D$ (homogeneous substances).

d-Menthol *	+50°	*d*-Carvomenthol	+28°
d-Menthylamine	+45	*d*-Carvomenthylamine	+12
d-Menthone	+30	*l*-Carvomenthone	− 6
l-*neo*Menthylamine	−15	*l*-*neo*Carvomenthylamine	−27
l-*neo*Menthol	−20	*l*-*neo*Carvomenthol	−42

* In alcohol (J., 1933, 193).

It is noteworthy that a transition from the menthone to the carvomenthone series throughout the above table is accompanied by a fairly regular shift in the value of $[\alpha]_D$, varying from 12 to 36 units in the *l*-rotatory sense.

All the available evidence points to the stereochemical analogy of these five pairs of substances. Consideration of their molecular configuration may be conveniently deferred until more experimental evidence, bearing upon the Auwers–Skita rule and other points (cf. J., 1927, 1278), has been collected; if, however, the prefix *iso*- is allocated, as in the menthone series, to the saturated ketone having the higher numerical rotatory power, the nomenclature adopted above falls naturally to the two carvomenthylamines now described. As shown below, it is possible that a third carvomenthylamine has also been isolated, in the form of a benzoyl derivative with m. p. 151—152° and $[\alpha]_D$ − 38·8° (chloroform).

The above classification suggests a correspondence in molecular configuration between *l*-carvomenthone and *d*-menthone, and therefore between *d*-carvomenthone and *l*-menthone : now while *l*-menthone occurs in peppermint oil, *d*-carvomenthone is obtained by hydrogenating *l*-carvone, which occurs in oil of spearmint. These relationships point to the possible existence of an interesting biochemical correspondence (cf. *Chemical Reviews*, 1930, **7**, 42).

A secondary base, ***dicarvomenthylamine***, $(C_{10}H_{19})_2NH$, is also produced when *l*-carvomenthone is heated with ammonium formate; this does not readily yield characteristic derivatives, possibly because it may consist of a mixture of ten stereoisomeric substances.

Wallach (*Annalen*, 1893, **275**, 121) obtained specimens of dihydrocarvylamine, which must necessarily have been mixtures of four stereoisomerides, by reducing *d*-carvoxime with sodium, and also by heating *d*-carvone with ammonium formate under pressure. From the product of the former reaction a stereochemically homogeneous *d*-dihydrocarvylamine (*d*-$\Delta^{8(9)}$-*p*-menthenyl-2-amine) has now been isolated; the configurational correspondence of this base with *d*-carvomenthylamine is shown by the exclusive hydrogenation of its benzoyl derivative to benzoyl-*d*-carvomenthylamine. The melting points and rotatory powers of corresponding derivatives of these two bases are very similar, and in each case the salicylidene derivative shows marked anomalous rotatory dispersion. Thus, the double bond in the *iso*propylidene side-chain appears to exert little influence upon certain of the physical properties of the unsaturated base and its derivatives.

EXPERIMENTAL.

Ketones.

l-*Rotatory Carvomenthone.*—*d*-Carvone of $[\alpha]_D$ *ca.* + 62°, from caraway oil, was hydrogenated (40 lb./sq. in.) in the presence of a palladium catalyst in three different ways (Hughesdon, Smith, and Read, J., 1923, **123**, 2916; Wallach, *Annalen*, 1911, **381**, 64; Hartung, *J. Amer. Chem. Soc.*,

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* The nomenclature and characteristics of these new alcohols will be discussed in a later paper.

1928, **50**, 3370; Ott and Schröter, *Ber.*, 1929, **60**, 633). In each instance about 60% of the calculated volume of hydrogen was absorbed, and a second treatment with fresh catalyst raised the quantity only to about 70%. It was unprofitable to isolate carvomenthone from the product. The incomplete hydrogenation seems to be due largely to the isomerisation of carvone to carvacrol during the process.

A successful result was achieved with a palladium hydroxide–calcium carbonate catalyst (Busch, *Ber.*, 1916, **49**, 1063; 1929, **62**, 1458), using 40 g. of *d*-carvone, 200 c.c. of methyl alcohol, and 8 g. of catalyst (equivalent to 0·16 g. $PdCl_2$), followed by an additional 4 g. of catalyst after an hour's shaking. In 2 hours a 96% absorption of hydrogen had occurred. The distilled product had b. p. 98—99°/16 mm., $n_{D}^{20^\circ}$ 1·4552, $\alpha_{D}^{20^\circ}$ – 27·66°, $[\alpha]_{D}^{20^\circ}$ – 30·62°.* It is advisable to remove any carvacrol by extraction with aqueous alkali.

Much of the *l*-rotatory carvomenthone used in this work was made by hydrogenating *d*-carvone with the aid of a nickel catalyst supported on powdered porous pot, according to the effective method of Rupe (*Helv. Chim. Acta*, 1918, **1**, 452; *Annalen*, 1927, **459**, 210; H. Rupe, "Anleitung zum Experimentieren," Braunschweig, 1930, p. 168). The purified ketone made in this way gave values of $[\alpha]_{D}^{20^\circ}$ falling between – 24·9° and – 25·1°; since $d_{4^\circ}^{20^\circ}$ = 0·9033, the values of $\alpha_{D}^{20^\circ}$ fall between – 22·5° and – 22·7°.

l-*Carvomenthone*.—*d*-Carvomenthol (10 g., $\alpha_{D}^{13^\circ}$ + 25·08), obtained by treating *d*-carvomenthylamine with nitrous acid and purifying the product through the **3** : 5-dinitrobenzoate, was shaken with chromic acid mixture (70 c.c.) in the way used by Beckmann for oxidising *l*-menthol (*Annalen*, 1889, **250**, 335). The mixture was warmed, with continual shaking, to 61°; the black addition compound then liquefied. The product was cooled rapidly, and an ethereal extract of the resulting ketone was washed with water and dilute sodium carbonate solution, and dried with sodium sulphate. The ketone (9·0 g.) distilled almost completely at 97—97·5°/17 mm., and had $n_{D}^{17^\circ}$ 1·4545, $\alpha_{D}^{17^\circ}$ – 9·71°; in absolute alcohol (*c* 8·0), the value of $[\alpha]_{D}^{18^\circ}$ was – 11·9°. In a second experiment the ketone had b. p. 96—96·5°/16 mm., $n_{D}^{17^\circ}$ 1·4548, $\alpha_{D}^{17^\circ}$ – 5·46, $[\alpha]_{D}^{17^\circ}$ – 6·0°; this was the purest specimen of *l*-carvomenthone prepared. The oxime obtained from it in 85% yield by treatment for several days with hydroxylamine acetate in aqueous alcohol at room temperature appeared to be homogeneous: m. p. 99—100°, $[\alpha]_{D}^{16^\circ}$ – 38·7° (absolute alcohol).

Dynamic Equilibrium between l- *and* l-iso*Carvomenthone*.—The carvomenthone used in experiments 1 to 5 below was prepared from *d*-carvone by Rupe's method, and had b. p. 91·5—92·0°/10 mm., $n_{D}^{13^\circ}$ 1·4570, $n_{D}^{20^\circ}$ 1·4554, $d_{4^\circ}^{20^\circ}$ 0·9033, $\alpha_{D}^{20^\circ}$ – 22·54°, $[\alpha]_{D}^{20^\circ}$ – 24·85°. In absolute alcohol (*c* 7·9), the value of $[\alpha]_{D}^{14^\circ}$ was – 26·6°, and the rotatory powers recorded below were determined under these conditions.

1. The ketone was kept in contact with concentrated hydrochloric acid at room temperature for 6 hours, with occasional shaking; it was recovered by extraction with ether, and dried over sodium sulphate. The value of $[\alpha]_{D}^{14^\circ}$ had changed from – 26·6° to – 16·6°.

2. The ketone was dissolved in 90% sulphuric acid at – 9°, and the pale yellow solution was gradually warmed to 30° and then poured on ice; the recovered substance, after steam distillation, had $[\alpha]_D$ – 16·8°.

3. The ketone (3 c.c.) was added to a cold solution of sodium (0·5 g.) in absolute alcohol (12 c.c.); when recovered after 20 hours, it had $[\alpha]_D$ – 14·9°. A similar treatment of a fresh sample gave $[\alpha]_D$ – 15·8°.

4. After being shaken for 2 hours with an excess of 40% aqueous sodium hydroxide, the recovered and distilled ketone had $[\alpha]_D$ – 23·3°.

5. When heated in a silica test-tube at 200° for 3, 5, and 12 hours, the ketone had $[\alpha]_D$ – 23·8°, – 23·4°, and – 23·0°, respectively.

6. A specimen of *l*-carvomenthone made by oxidising *d*-carvomenthol had $[\alpha]_{D}^{18^\circ}$ – 11·9° in absolute alcohol (*c* 8·0); when this was treated with alcoholic sodium ethoxide as in (3) above, the value altered to – 17·8°.

7. Carvomenthone having $\alpha_{D}^{17^\circ}$ – 21·2° reacted rapidly with semicarbazide acetate in aqueous solution at room temperature, and after 24 hours 12 g. of ketone had deposited 17·2 g. of crystalline semicarbazone having $[\alpha]_{D}^{16}$ – 30·4° (chloroform), m. p. 170—176°. After five successive recrystallisations from hot ethyl alcohol, the constant values m. p. 192°, $[\alpha]_{D}^{16}$ – 13·25° (chloroform) were attained. The purified semicarbazone (6·3 g.) when steam distilled with 20%

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* Unless otherwise stated, values of α quoted in these researches refer to a 1-dcm. tube, and values of $[\alpha]$ to solutions having $c = 2·0$, approximately; when a value for α is mentioned, the homogeneous liquid substance was used.

aqueous oxalic acid (1·1 mols.) underwent rapid hydrolysis and yielded carvomenthone having $\alpha_D^{16^\circ}$ − 14·46°.

Amines.

d-*Carvomenthylamine.*—A specimen of chemically pure carvomenthone prepared by Rupe's method had $[\alpha]_D$ − 24·85° and gave a 72% yield of solid oxime when left with hydroxylamine acetate in cold aqueous solution for 2 days; recrystallisation from light petroleum furnished large transparent rhombohedra of *l*-carvomenthone oxime, m. p. 99—100°, $[\alpha]_D$ − 37·0° (absolute alcohol). A syrupy product, apparently an oxime, was also formed in this reaction. The yield of solid oxime was found to increase with decreasing optical rotation of the carvomenthone; it is therefore advisable, if this oxime is required, to treat the hydrogenated carvone with alcoholic sodium ethoxide before converting it into oxime.

When reduced with sodium in boiling absolute alcohol, which had been dried over quicklime, 80 g. of the above recrystallised oxime yielded 72 g. of crude carvomenthylamine hydrochloride; by using dried alcohol which had also been heated under reflux for 4 hours with calcium shavings (1 g. to 200 c.c.), the yield of hydrochloride was increased almost to the theoretical quantity. The values of $[\alpha]_D$ (water) for such preparations ranged from + 8·7° to + 9·2°. The product was very soluble in water, alcohol, or chloroform; readily soluble in benzene; and progressively less soluble in ethyl acetate, acetone, light petroleum, and ether. This approximate order of solubilities holds for all the amine hydrochlorides described in this paper. Recrystallisation from hot ethyl acetate containing a little alcohol readily yielded long glistening needles of *d*-carvomenthylamine hydrochloride, m. p. above 250°, $[\alpha]_D^{16^\circ}$ + 12·2°, $[M]_D^{16^\circ}$ + 24·4°; these constant values were reached after two recrystallisations. *d*-Carvomenthylamine was liberated from hydrochloride having $[\alpha]_D^{16^\circ}$ + 12·2°, which had been recrystallised six times; the base has to be handled carefully owing to the ease with which it absorbs carbon dioxide, forming a crystalline deposit. It is a colourless, limpid liquid, with an odour closely resembling that of the menthylamines, and it is only very slightly soluble in water: b. p. 89·8—90·0°/16·5 mm., $d_{4^\circ}^{25^\circ}$ 0·8505, $n_D^{25^\circ}$ 1·4578, $[R_L]_D$ 49·70 (calc. for $C_{10}H_{21}N$, 49·53), $\alpha_D^{25^\circ}$ + 10·61°, $[\alpha]_D^{25^\circ}$ + 12·47°, $\alpha_{5461}^{25^\circ}$ + 12·40°, $[\alpha]_{5461}^{25^\circ}$ + 14·58; in chloroform solution (*c* 3·8), $[\alpha]_D^{25^\circ}$ + 13·09°, $[\alpha]_{5461}^{25^\circ}$ + 15·29°.

Derivatives of d-*Carvomenthylamine.*—Unless otherwise indicated, all the rotatory powers given for these derivatives were determined at 25°: for salts, the solvent was water (*c* 2·0); for other derivatives, chloroform (*c* 1·0). When two rotatory powers are recorded, the first is $[\alpha]_D^{25^\circ}$ and the second is $[\alpha]_{5461}^{25^\circ}$; when one only is given, it is $[\alpha]_D^{25^\circ}$. All derivatives made from the hydrochloride having $[\alpha]_D^{16^\circ}$ + 12·2° behaved as homogeneous substances when fractionally crystallised; most of them formed small, colourless needles from aqueous acetone or aqueous alcohol. The *formyl* derivative distilled at 160—170°/12—17 mm. when the dry formate was heated under diminished pressure to about 300°; it crystallised from aqueous acetone in fine needles, m. p. 95°, $[\alpha]_D^{25^\circ}$ + 62·1°, $[\alpha]_{5461}^{25^\circ}$ + 72·8° (Found: C, 71·8; H, 11·2. $C_{11}H_{21}ON$ requires C, 72·0; H, 11·6%). *Acetyl* derivative, m. p. 160—161°, + 67·8°, + 79·6° (Found: C, 72·9; H, 11·4. $C_{12}H_{23}ON$ requires C, 73·0; H, 11·7%). Propionyl derivative, m. p. 128—129°; + 65·7°, + 77·0°. *n*-Butyryl derivative, m. p. 123—124°; + 59·4°, + 71·2°. *n*-Hexoyl derivative, m. p. 104°; + 55·5°, + 63·8°. *n*-Octoyl derivative, m. p. 97—98°; + 50·0°, + 56·6°. Phenylacetyl derivative, m. p. 177°; + 41·7°, + 47·7°. *Benzoyl* derivative, m. p. 161°; + 45·1°, + 52·6° (Found: C, 78·3; H, 9·7. $C_{17}H_{25}ON$ requires C, 78·7; H, 9·7%). *d*-Camphor-10-sulphonyl derivative, m. p. 95°; + 61·2°. Carbimide, m. p. 206—207°. The salicylidene derivative separated from rectified spirit in short prisms. The substance is phototropic, behaving similarly to salicylidene-*d*-dihydrocarvylamine. The optical rotatory dispersion is anomalous: $[\alpha]_C^{16^\circ}$ + 18·0°, $[\alpha]_C^{25^\circ}$ + 14·8°; $[\alpha]_D^{16^\circ}$ + 18·6°, $[\alpha]_D^{25^\circ}$ + 15·0°; $[\alpha]_{5461}^{16^\circ}$ + 19·0°, $[\alpha]_{5461}^{25^\circ}$ + 15·1°; $[\alpha]_F^{16^\circ}$ + 12·1°, $[\alpha]_F^{25^\circ}$ + 8·8°. The salicylidene derivatives of *l*-, *d*-*neo*-, and *d*-*iso*-menthylamine were examined also, but their rotatory dispersions were normal.

The formate separated in fine leaflets when the acid and the base were mixed in ether; m. p. 152°, $[\alpha]_D^{16^\circ}$ + 12·1°, $[M]_D^{16^\circ}$ + 24·3°. The *hydrogen* d-*tartrate* was deposited as a thick syrup when its alcoholic solution was evaporated; it separated slowly from an aqueous solution at room temperature in large, transparent, monoclinic prisms, m. p. 143—144°, $[\alpha]_D^{16^\circ}$ + 20·1°, $[M]_D^{16^\circ}$ + 64·9° (Found: C, 52·0; H, 9·1. $C_{14}H_{27}O_6N,H_2O$ requires C, 52·0; H, 9·0%). The *d*-camphor-10-sulphonate, m. p. 138—140°, $[\alpha]_D^{16^\circ}$ + 19·5°, $[M]_D^{16^\circ}$ + 75·5°, formed a thick syrup which set to a hard crystalline mass; this was too soluble to be fractionally crystallised. The *l*-camphor-10-sulphonate, m. p. 144—145°, $[\alpha]_D^{16^\circ}$ − 8·4°, $[M]_D^{16^\circ}$ − 32·5°, was less soluble, and could be crystallised from a little light petroleum.

l-neo*Carvomenthylamine.*—Separate quantities of 30 g. of *l*-rotatory carvomenthone, made by

Rupe's method and purified from carvomenthols by treatment with Beckmann's chromic acid mixture (*Annalen*, 1927, **459**, 210), were each heated with 36 g. of ammonium formate at 130° for 48 hours in a flask provided with an air-condenser. When cold, the contents of six flasks were mixed, and the brown syrup forming the upper layer was extracted with ether, dried, and fractionally distilled under diminished pressure. The fraction distilling up to 160°/10 mm. consisted mainly of unchanged carvomenthone, and it was treated again with ammonium formate. The second fraction (90—120 g.), b. p. 163—185°/11 mm., was hydrolysed by boiling it under reflux for 12 hours with 5—6 equivs. of 10% alcoholic hydrogen chloride. The alcohol was then distilled, and the residue basified with sodium hydroxide and steam-distilled; the neutral solution obtained by adding hydrochloric acid to the volatile base was evaporated to dryness on the water-bath. The non-volatile base consisted of dicarvomenthylamine. The crude hydrochloride had $[\alpha]_D$ −12° to − 16° (water), m. p. *ca.* 180—190°; 180 g. of fresh carvomenthone furnished 36—46 g. In a fractional hydrolysis, the first fraction of crude hydrochloride (13 g.) had $[\alpha]_D$ −16·1°, and the second fraction (10 g.) had $[\alpha]_D$ − 12·1°.

Unsuccessful attempts were made to separate the constituents of this product by fractionally distilling the free bases and by fractionally crystallising and fractionally extracting the hydrochloride. Successive fractional distillation and crystallisation of the formyl derivative (26 g.) led to the separation of a small amount (0·7 g.) of formyl-*d*-carvomenthylamine, m. p. 94—95°, $[\alpha]_D$ + 61·5° (chloroform). The crude benzoyl derivative had m. p. 93—96·5°, $[\alpha]_D$ − 6·6° (absolute alcohol, *c* 2·0); after six fractional crystallisations these values had changed to m. p. 102—103°, $[\alpha]_D$ + 45·7°. The Schiff's bases obtained by condensing the crude base with salicylaldehyde, vanillin, and *p*-dimethylaminobenzaldehyde did not crystallise. Certain aldehydes of higher molecular weight (see below) were therefore prepared and condensed with the crude base. β-Naphthalenesulphonylsalicylaldehyde yielded a derivative which crystallised with difficulty; the other complex aldehydes described below gave syrupy products with the crude mixture of carvomenthylamines.

The perchlorate, benzoate, and hydrogen oxalate of the crude base gave no definite separation, and the *l*-menthoxyacetate appeared to undergo dehydration on the water-bath, yielding the *l*-menthoxyacetyl derivative. The crude formate (118 g.), m. p. 75—87°, $[\alpha]_D$ − 14·0° (water), when fractionally crystallised from acetone, first showed a fall in the numerical value of $[\alpha]_D$, but eventually it gave a small yield (5·6 g.) of pure *l-neo*carvomenthylamine formate, m. p. 131·5—132°, $[\alpha]_D$ − 31·5°, $[M]_D$ − 63° (water). The hydrogen *d*-tartrate (380 g.) of the mixed bases had $[\alpha]_D$ + 8·2° (water); when it was recrystallised once from hot 50% aqueous alcohol and three times from hot water, with systematic inoculation, it yielded l-neo*carvomenthylamine hydrogen* d-*tartrate* (102 g.), having m. p. 162°, $[\alpha]_D$ − 5·7°, $[M]_D$ − 18° (water) (Found: C, 52·3; H, 9·1. $C_{14}H_{27}O_6,H_2O$ requires C, 52·0; H, 9·0%).

*l-neo*Carvomenthylamine closely resembles *d*-carvomenthylamine in its general properties. The following physical constants were determined: b. p. 87·8—88·0°/16 mm., $d_{4°}^{25°}$ 0·8558, $n_D^{25°}$ 1·4596, $[R_L]_D$ 49·58 (calc. for $C_{10}H_{21}N$, 49·53), $\alpha_D^{25°}$ − 22·72°, $[\alpha]_D^{25°}$ − 26·55°, $\alpha_{5461}^{25°}$ − 26·53°, $[\alpha]_{5461}^{25°}$ − 31·00°; in chloroform solution (*c* 4·0), $[\alpha]_D^{25°}$ − 20·13°, $[\alpha]_{5461}^{25°}$ −23·94°. The hydrochloride had $[\alpha]_D^{16°}$ − 31·9°, $[M]_D^{16°}$ − 61·1° (water, *c* 2·0).

The hydrogen tartrate with $[\alpha]_D$ − 5·7° readily yielded other homogeneous derivatives of the base, including the formate, already described. The formyl derivative distilled at 298—299°/775 mm. when the formate was heated; it is very soluble, and was deposited from a little light petroleum as a white crystalline powder, m. p. 50°, $[\alpha]_D^{25°}$ − 61·2°, $[\alpha]_{5461}^{25°}$ − 74·2° (chloroform, *c* 2·0). In general, the derivatives of this base crystallised better than those of *d*-carvomenthylamine, being deposited in long transparent needles from alcohol or acetone containing a little water. In the following list of constants, the rotatory powers are given as for the formyl derivative above. *Acetyl* derivative, m. p. 114°; − 61·9°, − 75·4° (Found: C, 73·0; H, 11·8. $C_{12}H_{23}ON$ requires C, 73·0; H, 11·8%). Propionyl derivative, m. p. 101°; − 60·1°, − 72·4°. *n*-Butyryl derivative, m. p. 98°; − 57·6°, − 69·0°. *Benzoyl* derivative, m. p. 126°; − 33·0°, − 38·3° (Found: C, 78·5; H, 9·7. $C_{17}H_{25}ON$ requires C, 78·7; H, 9·7%). Phenylacetyl derivative, m. p. 81°; − 40·6°, − 48·0°. The *salicylidene* derivative formed stout yellow prisms, m. p. 36—37°, which were not phototropic, thus agreeing with salicylidene-*d-neo-* and salicylidene-*d-neoiso*-menthylamine (J., 1927, 2174). Like salicylidene-*d*-carvomenthylamine, it exhibited anomalous rotatory dispersion: $[\alpha]_C^{25°}$ − 6·00°, $[\alpha]_D^{25°}$ − 5·85°, $[\alpha]_{5461}^{25°}$ − 5·40°; $[\alpha]_F^{25°}$ could not be determined, owing to the marked absorption in this region of the spectrum (Found: C, 78·6; H, 9·5. $C_{17}H_{25}ON$ requires C, 78·7; H, 9·7%).

Attempts to isolate Other Carvomenthylamines.—1. The mixed carvomenthylamine hydrochlorides recovered from the mother-liquors of the above hydrogen tartrates had $[\alpha]_D$ − 8·3°

(water). No effective separation attended a prolonged extraction of this material with boiling light petroleum, although from the less soluble portion some pure acetyl-*d*-carvomenthylamine was prepared. The hydrogen *l*-malate did not crystallise satisfactorily. By fractionally crystallising the hydrogen *l*-tartrate from water, about 22% of the material was isolated as *d*-carvomenthylamine hydrogen *l*-tartrate, m. p. 176°, $[\alpha]_D$ − 7·0° (water).

2. The syrupy product formed in the oximation of carvomenthone having $[\alpha]_D$ − 24·85° (see above) was dried and distilled in a vacuum; the main product passed over at 135—140°/17 mm. and had $[\alpha]_D$ − 43·5° (absolute alcohol, *c* 2·0), and when kept for some days it deposited a small amount of the oxime of m. p. 99—100°. When dissolved in dry ethyl alcohol, reduced with sodium, and worked up in the usual way, it gave in good yield a crystalline hydrochloride with $[\alpha]_D$ − 6·8° (water). The corresponding hydrogen *d*-tartrate (90 g.) had $[\alpha]_D$ + 8·2°; after two recrystallisations from 50% aqueous methyl alcohol this gave a fraction (16·5 g.) with m. p. 166°, $[\alpha]_D$ + 5·4°. The derived hydrochloride had $[\alpha]_D$ − 11·8° (water), and the benzoyl derivative had $[\alpha]_D$ − 33·7° (chloroform); when recrystallised, the latter had m. p. 151—152°, $[\alpha]_D$ − 38·8°. This result, taken in conjunction with the properties of the tartrate, suggests that a new base had been obtained, and this conclusion was supported by a study of the deamination of this base, which will be described in a later paper.

Dicarvomenthylamine.—*l*-*neo*Carvomenthylamine and its stereoisomerides, formed by heating *l*-carvomenthone with ammonium formate, are accompanied by a basic oil which is not volatile in steam (see above). This material distilled almost completely at 178—179°/11 mm., 185—186°/14 mm., or 187—188°/16 mm., and had the following physical constants after distillation: $d_{4°}^{18°}$ 0·8956, $n_D^{18°}$ 1·4787, $[R_L]_D$ 92·71, $\alpha_D^{18°}$ − 3·15°, $[\alpha]_D^{18°}$ − 3·5°. It appeared to consist of a mixture of stereoisomeric *dicarvomenthylamines*, $(C_{10}H_{19})_2NH$ (Found: C, 81·8; H, 13·3; N, 4·9. $C_{20}H_{39}N$ requires C, 81·9; H, 13·3; N, 4·8%). The material is a fairly limpid, colourless liquid, which darkens slightly when exposed to light, and possesses a feeble but characteristic odour. Its basic properties are much less pronounced than those of the carvomenthylamines; it does not absorb carbon dioxide from the air, but in aqueous-alcoholic solution it turns red litmus blue. When shaken with mineral acids, the small globules which form become coated with a thin layer of the insoluble salt. The hydrochloride, prepared by passing hydrogen chloride into an ethereal solution of the base, was a glass. The salts with inorganic acids are very soluble in organic solvents; no crystalline salts with formic, acetic, or picric acid were obtained, and syrupy products were formed also by the action of acetyl or benzoyl chloride. In chloroform solution the base reacts rapidly with half a molecular proportion of bromine, apparently giving rise to the *N*-bromo-derivative and the hydrobromide; the hydrochloride of the base does not react with bromine.

d-*Dihydrocarvylamine.*—*d*-Carvoxime (30 g.) was reduced with sodium (38 g.) and absolute alcohol (Wallach, *Annalen*, 1893, **275**, 121). The product (25·5 g.) had $n_D^{16°}$ 1·4827, $\alpha_D^{16°}$ + 24·20°. Most of it (21 g.) distilled at 86—92·5°/12 mm.; a little unchanged oxime was present. The customary evaporation of aqueous solutions of the hydrochloride was avoided, owing to the accompanying hydration of the double bond (Willstätter, *Annalen*, 1903, **326**, 6). The crude acetyl derivative had m. p. 90—95°, $[\alpha]_D$ + 58·4°; after 5 recrystallisations from petroleum (b. p. 60—80°), this material gave 15% of its weight of pure acetyl-*d*-dihydrocarvylamine, m. p. 131—132°, $[\alpha]_D$ + 91·8° (chloroform) (cf. Wallach, *loc. cit.*).

Neither the hydrogen *d*-tartrate nor the hydrogen oxalate of the crude base responded to fractional crystallisation. The formate (68 g.), made by mixing the base and anhydrous formic acid in ether, gave, after four recrystallisations from ethyl acetate–alcohol, d-*dihydrocarvylamine formate* (15·3 g.), having m. p. 145°, $[\alpha]_D$ + 21·2° (water) (Found: C, 66·1; H, 10·8. $C_{11}H_{21}O_2N$ requires C, 66·3; H, 10·6%). This readily yielded the pure acetyl derivative noted above.

Benzoyl-d-*dihydrocarvylamine* crystallised from alcohol in long, transparent needles, m. p. 182°, $[\alpha]_D$ + 48·3° (chloroform) (Found: C, 79·1; H, 9·1. $C_{17}H_{23}ON$ requires C, 79·3; H, 9·0%). Salicylidene-*d*-dihydrocarvylamine, m. p. 58°, forms lemon-yellow needles from alcohol; these become orange in sunlight, and revert to the original colour in diffused light. The substance displays anomalous rotatory dispersion, as illustrated by the following values, determined in chloroform solution at 17°: $[\alpha]_C$ + 8·6°, $[\alpha]_D$ + 6·0°, $[\alpha]_{5461}$ + 1·7°, $[\alpha]_F$ − 17·1°. *d*-Dihydrocarvylamine, liberated from the formate having $[\alpha]_D$ + 21·2° (water), is a colourless liquid with a strong smell, which, however, is less unpleasant than that of *d*-carvomenthylamine; it absorbs carbon dioxide readily from the air. Constants: b. p. 111°/35 mm., $n_D^{17°}$ 1·4781, $d_{4°}^{17°}$ 0·8775, $[R_L]_D$ 49·21 (calc. for $C_{10}H_{19}N$, 49·13), $\alpha_D^{17°}$ + 14·4°, $[\alpha]_D^{17°}$ + 16·4° (*c* 5·8, chloroform).

When hydrogenated in methyl alcohol with a palladium hydroxide–calcium carbonate catalyst under a pressure of 4 atmospheres, benzoyl-*d*-dihydrocarvylamine gave an almost quantitative yield of benzoyl-*d*-carvomenthylamine, m. p. 160—161°; this product suffered no depression of melting point when mixed with an authentic specimen of benzoyl-*d*-carvomenthylamine.

Aldehydes of High Molecular Weight.—These substituted aldehydes were made by mixing a simple hydroxy-aldehyde with an appropriate acid chloride in dry pyridine. After 24 hours the mixture was treated with dilute hydrochloric acid and extracted with chloroform; the extract was washed successively with dilute hydrochloric acid, water, sodium hydroxide solution, and water, and then dried. *d*-Camphor-10-sulphonylsalicylaldehyde (J., 1909, 337) was obtained in 88% yield; when crystallised from rectified spirit it had m. p. 125°, $[\alpha]_D^{12°}$ + 43·1° (chloroform). d-*Camphor*-10-*sulphonyl*-m-*hydroxybenzaldehyde* had m. p. 67° (Found: C, 60·4; H, 6·0. $C_{17}H_{20}O_5S$ requires C, 60·7; H, 6·0%). d-*Camphor*-10-*sulphonylvanillin* had m. p. 128°, $[\alpha]_D^{14°}$ + 35·8° (Found: C, 59·0; H, 6·1. $C_{18}H_{22}O_6S$ requires C, 59·0; H, 6·0%). β-Naphthalenesulphonylsalicylaldehyde, m. p. 74—75°, and β-naphthalenesulphonylvanillin, m. p. 98°, were also prepared. β-Naphthalenesulphonylsalicylidene-*d*-carvomenthylamine, when crystallised from acetone, had m. p. 104°, $[\alpha]_D^{18°}$ + 44·5° (chloroform).

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