848. *Carveol and Related Substances.*

By A. Blumann and W. R. Wood.

Optically active *cis*- and *trans*-carveol are readily racemised by acid. The carveol from autoxidised (+)-limonene is mainly the (±)-*trans*-epimer. It is also formed by thermal decomposition of *trans*-sobreryl acetate, and on hydration it forms (±)-*trans*-sobrerol.

Thermal decomposition of the acetate of *cis*-*p*-menth-8-ene-1 : 2-diol gives (±)-*trans*-carveol accompanied by an isomer which is probably *p*-mentha-1(7) : 8-dien-2-ol.

(±)-*cis*-Carveol is formed by thermal decomposition of the acetate of (±)-*p*-menthane-1 : 2 : 8-triol and on hydration it forms *cis*-sobrerol, which, however, changes slowly into the *trans*-form.

Carveol, first isolated from the products of autoxidation of (+)-limonene in a racemic form (Blumann and Zeitschel, *Ber.*, 1914, **47**, 2624) and later prepared by Ponndorf (*Z. angew. Chem.*, 1926, **39**, 138) by reduction of (+)-carvone with aluminium *iso*propoxide, was considered uniform till Johnston and Read (*J.*, 1934, 233) proved that Ponndorf's product was a mixture of (+)-*cis*- and (+)-*trans*-carveol. It has now been shown that this mixture is readily racemised by cold sulphuric acid in ether and that, with phthalic anhydride, it forms mainly (±)-*trans*-carveyl hydrogen phthalate.

The identity of the carveol from autoxidised limonene with (±)-*trans*-carveol has also been proved by preparation of its 3 : 5-dinitrobenzoate. It is remarkable that the bulk of this carveol is no longer optically active, and Wallach (*Annalen*, 1891, **281**, 132) was puzzled by the fact that he obtained (±)-carvone by oxidation of the active carveyl methyl ether which he prepared from (+)-1 : 2 : 8-tribromo-*p*-menthane. Our experiments indicate that it is not the carvone which is racemised by acid, but the carveol, *cis* as well as *trans*, since acetic and phthalic anhydrides at elevated temperatures and sulphuric acid in ether at low temperatures, and even the mild acids produced during autoxidation, readily induce racemisation.

It was found by Blumann and Zeitschel (*loc. cit.*) that carveol, when hydrated with dilute sulphuric acid, yielded a diol, the constitution of which was not then determined. It was suggested (Beilstein, 4th edn., 1st Suppl., **6**, 377) that this diol is identical with (±)-sobrerol, and this has now been demonstrated by mixed m. p. with an authentic sample. We consider it to be the *trans*-form, although Wagner (*Ber.*, 1899, **32**, 2088) claimed that it was the *cis*-. We have also prepared it from the mixture of (—)-carveols prepared by Ponndorf reduction, but we could not isolate the corresponding *cis*-sobrerol in this case as it appears to form pinol with greater ease than the *trans*-epimer. (±)-*cis*-Sobrerol was later prepared from (±)-*cis*-carveol.

Dehydration of *trans*-sobrerol, first observed by Sobrero (*Compt. rend.*, 1851, **33**, 67) and later studied by Armstrong and Pope (*J.*, 1891, **59**, 315) and by Wallach (*Annalen*, 1893, **277**, 133), has been found to give pinol. We have found, however, that when the diol was acetylated and distilled at atmospheric pressure, acetic acid was split off and (±)-*trans*-carveol was obtained, the hydration being simply reversed.

Another autoxidation product of limonene, (+)-*cis*-*p*-menth-8-ene-1 : 2-diol, recently described in detail by Schmidt (*Chem. Ber.*, 1949, **82**, 11), when acetylated and subjected to thermal decomposition yields a mixture of carveols, amongst which (±)-*trans*-carveol has been identified (phenylurethane and hydrogen phthalate) in a preparation with a low positive rotation. This confirms Simonsen and Owen's suggestion ("The Terpenes," 2nd edn., 1947, Vol. 1, p. 154) that *cis*-*p*-menth-8-ene-1 : 2-diol is the primary oxidation product of limonene in moist air.

In this preparation (±)-*trans*-carveol is accompanied by a product which seems to be a hitherto unknown carveol in which a $CH_2\colon$ group is attached to $C_{(1)}$ and is isomerised by acid to the Δ^1-compound. This is indicated by the difference in odour from *trans*-carveol, the odour of which is somewhat similar to that of crude naphthalene, and by the fact that it is not racemised so readily with cold acid. Furthermore, it did not give a crystalline phenylurethane and on oxidation afforded, in poor yield, an optically active ketone, which gave a semicarbazone with a very wide melting range. Hydrolysis of the semicarbazone gave an odour reminiscent of cuminaldehyde and quite different from that of carvone.

Considerable dehydration of this new carveol took place during the thermal decomposition, and the optically active hydrocarbon formed is probably another terpene of formula $C_{10}H_{14}$ (cf. Wallach's hydrocarbon, *Annalen*, 1891, **264**, 27; verbenene, *Ber.*, 1921, **54**, 887; and camphenene, *Ber.*, 1928, **61**, 1491).

Schmidt (*loc. cit.*) also describes (+)-*trans-p*-menth-8-ene-1 : 2-diol, first prepared by Ginzberg from (+)-*p*-menthane-1 : 2 : 8-triol, an oxidation product of (+)-α-terpineol (*Ber.*, 1896, **29**, 1198). Acetylation of this triol, without isolation of the diol, has now been found to yield (±)-*cis*-carveol by thermal decomposition.

On hydration, (±)-*cis*-carveol yielded a sobrerol; as the m. p. 107—108° was much lower than that of (±)-*trans*-sobrerol, we consider it to be the *cis-form*. When heated with dilute sulphuric acid it formed pinol. After (±)-*cis*-sobrerol had been kept for 2 years its melting point had changed into that of the *trans-form*.

EXPERIMENTAL

Light petroleum refers to the fraction of b. p. 40—60°. All optical rotations are measured in 1-dm. tubes.

(−)-Carvone [isolated from oil of spearmint; α_D^{20} −57·8° (homogeneous)] was reduced by Ponndorf's method as described by Macbeth and Mills (*J.*, 1949, 2646). The mixture of *cis*- and *trans*-carveol obtained had α_D^{20} −122·1° (homogeneous).

Racemisation.—A solution of sulphuric acid (1 g.) in dry ether (9 g.) was cooled to 2° and slowly added to the above carveol mixture (2 g.) in dry ether (8 g.), also at 2°, and the whole kept at 6°; the optical rotation was −4·9° after 2½ hours and only −0·8° after 24 hours. A corresponding 10% solution in dry ether had α_D −7·3° initially and this was unchanged after 24 hours.

(±)-trans-*Carveol.*—(*a*) The carveol mixture (α_D −122·1°; 55 g.) was heated with phthalic anhydride (50 g.) and pyridine (2·5 g.) for 6 hours at 120°. The only crystalline product obtained was a hydrogen phthalate, m. p. 136—137° (9·5 g.), which on hydrolysis gave (±)-*trans*-carveol, b. p. 95—100°/5 mm., d_4^{18} 0·950, n_D^{20} 1·4956, α_D ±0°. This formed a phenylurethane, m. p. 94—95°, identical (m. p. and mixed m. p.) with that of carveol from autoxidised limonene. This was identified by its 3 : 5-dinitrobenzoate, m. p. 119° (Johnston and Read, *loc. cit.*).

(*b*) (±)-*trans*-Sobrerol (2·5 g.) and acetic anhydride (5 g.) were refluxed for 5 hours and slowly distilled at 80 mm. pressure. Two fractions were obtained : (i) b. p. 71°, (ii) b. p. up to 178°. The latter was distilled at atmospheric pressure, and the distillate washed till neutral and hydrolysed with excess of alcoholic sodium hydroxide. After steam-distillation, extraction with light petroleum, and drying at 100°/80 mm., it had d_4^{23} 0·950, n_D^{20} 1·4949, α_D ±0°, and had the typical unpleasant odour of *trans*-carveol. It formed a phenylurethane, m. p. 94—95°, undepressed by authentic (±)-*trans*-carveol phenylurethane.

(±)-trans-*Sobrerol.*—Carveol mixture (α_D −122·1°; 12 g.) was shaken with a solution of benzenesulphonic acid (30 g.) in 5% sulphuric acid (1200 c.c.) at room temperature for 24 hours. The solution was extracted with light petroleum (50 c.c.), the solvent removed *in vacuo*, and the residue distilled, forming fractions : (i) b. p. <73°/100 mm. (2 g.), and (ii) b. p. 80—135°/100 mm., α_D −14·1° (homogeneous), mostly carveol but containing 10·1% of ketones estimated as carvone (3 g.), and a residue (0·5 g.). The last crystallised on cooling and formed shiny scales, m. p. 119—121°, from light petroleum. It is insoluble in water.

Fraction (i) contained pinol, which formed the dibromide, m. p. 94—95°, on treatment with bromine in carbon tetrachloride, evaporation *in vacuo*, and crystallisation from light petroleum.

The acid aqueous solution was made alkaline with sodium carbonate and twice extracted with ethyl acetate. On evaporation, the extracts left a waxy residue of (±)-*trans*-sobrerol which, crystallised from ethyl acetate, had m. p. 131—131·5°, α_D±0°. This was identical (m. p. and mixed m. p.)with an authentic sample from Americal oil of turpentine.

Thermal Decomposition of Acetylated (+)-cis-p-*Menth*-8-*ene*-1 : 2-*diol.* This diol (m. p. 72·5—73·5°; prepared from orange-oil terpenes; 67 g.) and acetic anhydride (70 g.) were refluxed for 8 hours, and the mixture then distilled very slowly at atmospheric pressure, yielding fractions b. p. <133° (mainly acetic acid), b. p. 133—150° (α_D +37·9°), and b. p. 150—210°. The last two fractions were washed till neutral, and the oil (35 g.) refluxed with excess of sodium hydroxide in alcohol for 2 hours. After distillation in steam and separation, there were obtained two fractions: (i) α_D +37·7°, (ii) α_D +40·2°. Fraction (i) was fractionated *in vacuo*, giving fractions (*a*) b. p. 46—56°/3 mm., 172—174° 766 mm., d_4^{20} 0·8802, n_D^{20} 1·4982, α_D +41·9° (6 g.), and (*b*) b. p. 56—83°/3 mm., α_D +32·3° (3·5 g.); (*a*) is obviously a hydrocarbon but no crystalline bromide or nitrosite could be prepared from it. After about 3 months it had polymerised to an amorphous, brittle substance melting indefinitely about 68—70°.

Redistillation of the higher-boiling fractions (ii) and (i) (*b*) gave a rather viscous end-fraction, b. p. 93°/3 mm., α_D +52·2°, d_4^{20} 0·956, n_D^{20} 1·4967. It did not form a crystalline phenylurethane, but considerable diphenylurea was formed; a 3 : 5-dinitrobenzoate, however, m. p. 80—80·5°, was obtained. The optical rotation of this carveol was unaffected by sulphuric acid in ether at 6° but fell from 52·2° to 51·1° when the product itself was kept for 3 months in a closed vessel.

In a second experiment, the carveol fraction had α_D +14° and yielded (±)-*trans*-carveol phenylurethane, m. p. 94—95°, and (±)-*trans*-carveyl hydrogen phthalate, m. p. 136—137°, although only in small quantities. The hydrocarbon fraction, purified by fractionation and by repeated washing with 70% alcohol, had α_D +47·6°, d_4^{17} 0·878, n_D^{17} 1·4956.

In a third experiment the carveol fraction had α_D +35·4°. When it (9·5 g.) was oxidised in 50% acetic acid solution (10 g.) with chromium trioxide (9 g.) in 75% acetic acid at 0°, the ketone obtained on steam-distillation (1·75 g.) had α_D +37·4°. The m. p. of its semicarbazone (softening at 155°, m. p. 175—180°) indicated that it was not uniform and heating with aqueous phthalic acid produced an odour resembling that of cuminaldehyde, quite different from that of carvone.

(±)-cis-*Carveol*.—(±)-*p*-Menthane-1 : 2 : 8-triol [86 g.; m. p. 122—124°, prepared by oxidation of (±)-α-terpineol] and acetic anhydride (150 g.) were refluxed for 8 hours. After slow distillation at atmospheric pressure and washing with brine, an oil (79 g.) was obtained; this was hydrolysed with excess of sodium hydroxide in alcohol, and steam-distillation then removed a volatile oil, leaving a substantial residue of diol and triol. The volatile oil on distillation gave: (i) b. p. <84°/3 mm., $n_D^{23 \cdot 5}$ 1·5004 (3 g.); (ii) b. p. 84—87°/3 mm., $d_4^{23 \cdot 5}$ 0·9497, $n_D^{23 \cdot 5}$ 1·4978, (9 g.); (iii) b. p. 90—92°/3 mm., $n_D^{23 \cdot 5}$ 1·4988 (2·5 g.); (iv) b. p. mainly 103—108°/3 mm., $n_D^{23 \cdot 5}$ 1·4939 (5 g.).

Fraction (i) with phthalic anhydride (2 g.) gave (±)-*cis*-carveyl hydrogen phthalate, which formed needles, m. p. 114—116°, from light petroleum. The corresponding *trans*-ester is hardly soluble in this solvent. On refractionation of (ii), the main product had b. p. 92—94°/3 mm., d_4^{25} 0·954, n_D^{25} 1·4970, and when oxidised with chromium trioxide as described above yielded a steam-volatile ketone, which formed a semicarbazone, m. p. 154—156°, after recrystallisation. This was identical (m. p. and mixed m. p.) with an authentic specimen of (±)-carvone semicarbazone.

(±)-*cis*-Carveol does not form a crystalline phenylurethane.

(±)-cis-*Sobrerol*.—(±)-*cis*-Carveol (4 g.) was shaken with dilute sulphuric acid (5%, 400 g.) for 24 hours at room temperature. Unchanged oil (2 g.) was separated and re-treated, and the solutions were combined, washed twice with light petroleum, made alkaline with sodium carbonate, and concentrated *in vacuo*. By exhaustive extraction with ethyl acetate (±)-cis-*sobrerol* was obtained as a viscous oil, which crystallised in the presence of a drop of water. It formed short, sparkling prisms, m. p. 107—108°, from water (Found: C, 70·8; H, 10·6. $C_{10}H_{18}O_2$ requires C, 70·5; H, 10·7%). Mixed with (±)-*trans*-sobrerol, it melted from 92° to 110°. A pure sample after 2 years had m. p. 131—131·5°, undepressed by authentic (±)-*trans*-sobrerol.

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