# **221.** *Leptospermone. Part I.*

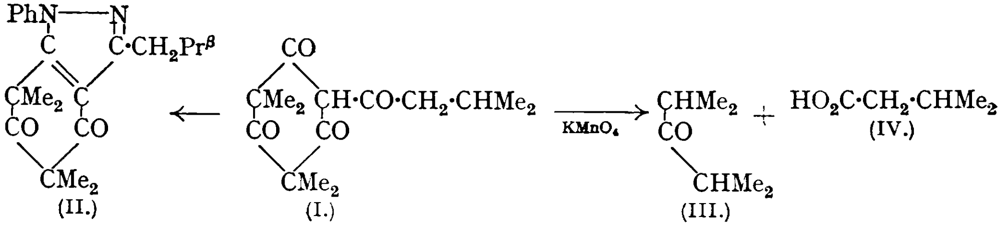
By L. H. Briggs, A. R. Penfold, and W. F. Short.

Various oils of the genus *Leptospermum* contain *leptospermone*, $C_{15}H_{22}O_4$, which is shown to be a β-diketone. A provisional formula for this compound is suggested.

During an investigation of the oil of *Leptospermum flavescens*, which grows in New South Wales, Penfold (*J. Proc. Roy. Soc. New South Wales*, 1921, **45**, 51) isolated an acidic compound, $C_{14}H_{20}O_4$, which was considered to be a phenol and was therefore termed leptospermol. The leptospermol content of different samples of the oil showed somewhat large variations (0·2—14%), but there are insufficient data to show whether this variation is seasonal. Leptospermol was subsequently isolated from two members of the genus *Leptospermum* growing in New Zealand, *viz.*, *Leptospermum ericoides* (" manuka-rauriki "), which contains 0·9—2·5% (Johnson and Short, *Rep. Austr. Assoc. Sci.*, 1923, **16**, 223; Short, *J. Soc. Chem. Ind.*, 1926, **45**, 96T), and *Leptospermum scoparium* (" manuka "; " tea-tree "), different samples of which contained 7·2—11% of leptospermol (R. H. Inder, Thesis, University of New Zealand, 1923; Short, *loc. cit.*; Gardner, *J. Soc. Chem. Ind.*, 1924, **43**, 34T; 1925, **44**, 828T). Gardner (*loc. cit.*), who also advocated the formula $C_{14}H_{20}O_4$, concluded that leptospermol is a monobasic acid, since it could be titrated with alkali and afforded a stable barium salt.

The essential oil of *L. scoparium* contains *iso*valeric, cinnamic, and acetic acids (4%) and the crude leptospermol was freed from these impurities by washing with saturated aqueous sodium bicarbonate, so that it cannot be an acid. The crystalline copper salt was soluble in chloroform and the *anhydro-phenylhydrazone*, m. p. 118°, contained a pyrazole ring, since on reduction it afforded a compound which gave the well-known Knorr pyrazoline reaction (*Ber.*, 1893, **26**, 100). It was clear that the compound was a β-diketone (Briggs, Thesis, University of New Zealand, 1928) and therefore belongs to the same group as the two ketones, angustione and dehydroangustione, isolated by Penfold (*J. Proc. Roy. Soc. New South Wales*, 1924, **57**, 300) from the oil of *Backhousia angustifolia* and subsequently investigated by Cahn, Gibson, Penfold and Simonsen (J., 1930, 1184; 1931, 286). We therefore propose to change the name of this compound to *leptospermone*.

Leptospermone has now been found to have the composition $C_{15}H_{22}O_4$ and not $C_{14}H_{20}O_4$ and this has been substantiated by the preparation and analysis of a number of solid derivatives. Like angustione and dehydroangustione, leptospermone shows a large exaltation in its molecular refraction. With boiling aniline in presence of zinc chloride it afforded *anilinoleptospermone*, $C_{21}H_{27}O_3N$, m. p. 91°, which was insoluble in alkali and gave no coloration with ferric chloride. The ketone underwent extensive degradation when oxidised with nitric acid and only dimethylmalonic acid was isolated from the product. Oxidation with potassium permanganate produced di*iso*propyl ketone (III) and *iso*valeric acid (IV), which were identified by direct comparison of solid derivatives with synthetic specimens. Twelve of the fifteen carbon atoms of leptospermone are present in these oxidation products and we suggest that the ketone may be represented by (I) and the anhydro-phenylhydrazone by (II).



Evidence for the presence of the six-membered ring and the remaining carbonyl groups will be submitted in a subsequent communication. On the basis of this formulation leptospermone is related both to angustione and to the phloroglucinol derivatives of the Filix group (Boehm, *Annalen*, 1898, **302**, 171; 1899, **307**, 250; 1901, **318**, 230).

## EXPERIMENTAL.

*Leptospermone*, separated from the oils by extraction with 4% aqueous sodium hydroxide and purified by washing with saturated aqueous sodium bicarbonate and fractional distillation, had b. p. 146°/10 mm., $d_{4°}^{19·5°}$ 1·0688, $n_D^{19·5°}$ 1·5000, $\alpha_D$ 0°, $[R_L]_D$ 73·27 (Found: C, 67·7, 67·6; H, 8·3, 8·4; *M*, cryoscopic in benzene, 246. $C_{15}H_{22}O_4$ requires C, 67·7; H, 8·3%; *M*, 266). The ketone is a faintly yellow, viscous liquid with a weak, somewhat unpleasant smell. Its alcoholic solution gave an intense orange-red coloration with ferric chloride. Determinations of active hydrogen (Zerewitinoff method) afforded the following results: 0·2037 and 0·1473 g. of leptospermone evolved 39·75 and 28·8 c.c. of methane at 12°/758 mm., corresponding to 2·0 and 2·0 atoms of active hydrogen per mole respectively.

*Anilinoleptospermone.*—A mixture of the ketone (5 c.c.), aniline (5·5 c.c.), and zinc chloride (0·5 g.) was boiled for 5 minutes, and the product cooled, shaken with dilute hydrochloric acid, and dissolved in ether. The ethereal solution was washed with dilute acid, alkali, and water, dried, and evaporated. The crystalline residue separated from light petroleum (b. p. 40—60°) in clusters of long rods, m. p. 91° (Found: C, 73·85, 74·0; H, 8·0, 8·2; N, 4·2, 4·2; *M*, cryoscopic in benzene, 329. $C_{21}H_{27}O_3N$ requires C, 73·9; H, 7·9; N, 4·1%; *M*, 341).

*Anhydroleptospermonephenylhydrazone.*—Addition of phenylhydrazine (1·5 mols.) to leptospermone caused a rise in temperature and separation of water. After heating on the water-bath for ½ hour, the mixture was extracted with ether, washed with dilute acid and alkali, and dried, and the solvent evaporated. Recrystallisation from light petroleum (b. p. 60—80°) gave clusters of long rods, m. p. 118° (Found: C, 74·6; H, 7·7; N, 8·4, 8·5. $C_{21}H_{26}O_2N_2$ requires C, 74·6; H, 7·7; N, 8·3%).

*Oxidation of Leptospermone.*—(1) *With nitric acid.* Concentrated nitric acid (11 c.c.) was slowly added to a solution of the ketone (5 g.) in concentrated sulphuric acid (25 c.c.) at 50° and the resulting solution was poured into water (200 c.c.). The solution was extracted once with ether and then concentrated to a small volume in a current of air. The crystalline residue melted at 189° (decomp.) after recrystallisation from acetone–benzene; it was readily soluble in water, acid in reaction, and afforded an insoluble silver salt (Found: *M*, by titration, 132. Calc. for $C_5H_8O_4$: *M*, 132). The m. p. agreed with that (190°) of dimethylmalonic acid (Perkin, J., 1903, **83**, 1237) and the identity of the product with this acid was confirmed by the preparation of dimethylmalonamide, m. p. 263° (Fischer and Dilthey, *Ber.*, 1902, **35**, 854).

(2) *With potassium permanganate.* 5% Aqueous potassium permanganate (equiv. to 4·2 atoms of oxygen) was added to a mechanically stirred solution of the ketone (25·2 g.) in sodium hydroxide solution (10N; 50 c.c.) so that the temperature remained below 45°. The manganese dioxide sludge was extracted with hot water (200 c.c.), and the aqueous layer exhaustively extracted with ether. Most of the neutral extract distilled at 124—124·5°/762 mm. and had a pleasant camphor-like odour. It afforded a semicarbazone, which separated from 50% aqueous alcohol in white plates, m. p. 156—156·5° (Found: N, 24·6. Calc. for $C_8H_{17}ON_3$: N, 24·6%). The properties of this compound indicated that it was either di*iso*propyl ketone or ethyl *tert.*-butyl ketone and, owing to the discordant and overlapping values recorded in the literature for the m. p.'s of the semicarbazones of these compounds, each ketone was synthesised so that a direct comparison could be instituted. Di*iso*propyl ketone, b. p. 123—124°/760 mm., was

prepared from *iso*butyric acid (Senderens, *Compt. rend.*, 1909, **148**, 929) and afforded a semicarbazone, m. p. 156·5—157°. Ethyl *tert.*-butyl ketone was prepared from pinacol (Holleman, *Rec. Trav. chim.*, 1906, **25**, 206; Hill, Spear, and Lachowicz, *J. Amer. Chem. Soc.*, 1923, **45**, 1559), which was successively converted into pinacolin and methylated as described by Haller (*Compt. rend.*, 1901, **150**, 582). The semicarbazone of this ketone melted at 144° (Found : C, 56·2; H, 10·0. Calc. for $C_8H_{17}ON_3$ : C, 56·1; H, 9·9%). Admixture of the semicarbazone of the ketone from leptospermone with that of di*iso*propyl ketone caused no depression in m. p., but the m. p. of the semicarbazone of ethyl *tert.*-butyl ketone was depressed to 114—130°.

The aqueous alkaline layer from the oxidation was concentrated and acidified, and the acids collected in ether. Distillation of the extract afforded a main fraction (1), b. p. 172—173°/762 mm., and a small fraction (2), b. p. 95—105°/10 mm. A portion (1 g.) of fraction (1) was boiled for 1 hour with thionyl chloride (1·3 g.), and the product cooled, mixed with aniline (0·9 g.), and heated at 150—160° for ½ hour. The anilide, isolated in the usual way and recrystallised from ligroin, had m. p. 110·5—111° (Found : C, 74·5; H, 8·7. Calc. for $C_{11}H_{15}ON$ : C, 74·6; H, 8·5%). Similar m. p.'s are recorded in the literature for *iso*valeranilide and α-methylbutyranilide, and the two acids were therefore synthesised. *iso*Valeric acid was prepared from *iso*propylmalonic ester (Fischer and Dilthey, *Annalen*, 1904, **335**, 337) and α-methylbutyric acid from methylethylmalonic ester. The corrresponding anilides melted at 112·5° and 105—106·5° respectively and the first of these did not depress the m. p. of the anilide from leptospermone, whereas the second caused a depression of 14°.

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THE TECHNOLOGICAL MUSEUM, SYDNEY, N.S.W.
AUCKLAND UNIVERSITY COLLEGE, NEW ZEALAND.
THE COLLEGE OF TECHNOLOGY, MANCHESTER.

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