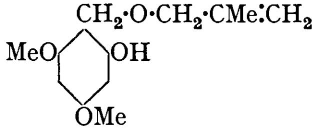
91. *The Structure and Synthesis of Bæckeol.*

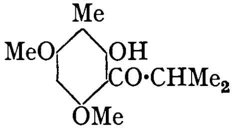
By G. R. Ramage and W. J. I. Stowe.

Bæckeol has been synthesised and shown to have structure (II). It is closely related to aspidinol and other synthetic substances known to possess anthelmintic properties.

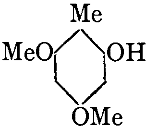
The essential oils from various species of *Myrtaceæ*, more especially *Bæckea crenulata* and *Darwinia grandiflora*, contain a phenol, bæckeol, $C_{13}H_{18}O_4$ (Penfold and Morrison, *J. Proc. Roy. Soc., New South Wales*, 1922, **56**, 87), which was examined by Penfold and Simonsen (*ibid.*, 1938, **71**, 291) and considered to be (I). An attempt to synthesise it failed owing to difficulty in the preparation of 2 : 4 : 6-trimethoxybenzyl alcohol (Ramage, Simonsen, and Stowe, J., 1939, 89). It was suggested by Professor Simonsen that the phenol was possibly represented by (II) and the synthesis of this substance has shown this to be correct.



(I.)



(II.)

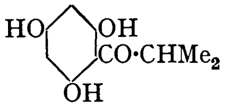


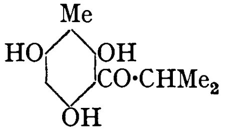
(III.)

The new formulation satisfies the degradation of bæckeol on fusion with sodium ethoxide to methylphloroglucinol dimethyl ether (III) and on oxidation with hydrogen peroxide in alkaline solution to *iso*butyric acid. It has not been possible to prove the presence of a carbonyl group, since the phenol was recovered unchanged after treatment with hydroxylamine, semicarbazide or 2 : 4-dinitrophenylhydrazine. Baum (*Ber.*, 1895, **28**, 3207), Meyer (*ibid.*, 1896, **29**, 830) and others have shown that ketones substituted in the two ortho-positions frequently do not yield oximes or hydrazones.

Karrer (*Helv. Chim. Acta*, 1919, **2**, 466) has prepared many compounds closely related to (II), *e.g.*, phloro*iso*butyrophenone (IV) from phloroglucinol and *iso*butyronitrile, but no ketonic derivatives are recorded. By substituting methylphloroglucinol it has been possible to isolate *methylphloro*iso*butyrophenone* (V), m. p. 160—161°. Since bæckeol itself is not affected by an ethereal solution of diazomethane, (V) has been similarly treated; the resulting dimethyl ether crystallised in pale yellow needles, m. p. 102—103°, and gave an acetyl derivative, m. p. 73°, identical respectively with bæckeol and its acetyl derivative. Methylation of only two of the hydroxyl groups in (V) occurs, but it is almost certain that (II) would result.

(IV.)





(V.)

EXPERIMENTAL.

*Methylphloro*iso*butyrophenone.*—Dry hydrogen chloride was passed for 12 hours into a well-stirred ice-cold mixture of methylphloroglucinol (5 g., dried at 100° for 1 hour), *iso*butyronitrile (5 g.), and finely powdered anhydrous zinc chloride (3 g.) in dry ether (100 c.c.). After standing for 48 hours at room temperature, the ether was decanted, and the dark red viscous oil washed twice with dry ether before being decomposed by warming with water (300 c.c.). The solution was neutralised with aqueous ammonia, heated on the sand-bath for 30 minutes, treated with charcoal, and filtered. On cooling, *methylphloro*iso*butyrophenone* crystallised, and a further quantity was obtained by extracting the mother-liquor with ether, dissolving the red oil, remaining after removal of the solvent, in hot water (20 c.c.), and allowing the solution to cool. The total product (2·6 g.), recrystallised from water, formed light brown needles, m. p. 160—161° (Found : C, 57·8; H, 6·9; H_2O, 8·0. $C_{11}H_{14}O_4,H_2O$ requires C, 57·9; H, 7·0; H_2O, 7·9%). After drying in a vacuum at 100°, the anhydrous substance had m. p. 161—162° (Found : C, 62·7; H, 6·6. $C_{11}H_{14}O_4$ requires C, 62·8; H, 6·7%).

*Methylphloro*iso*butyrophenone Dimethyl Ether* (II).—The above anhydrous phenol (2·2 g.) was treated in ether with an ice-cold ethereal solution of diazomethane. Nitrogen was rapidy evolved and after 1 hour the ether and the excess of diazomethane were distilled. The residual dark red oil was stirred with cold dilute aqueous sodium hydroxide (bæckeol is very sparingly soluble in cold alkali), and the resulting solid (0·5 g.) filtered off, sublimed under reduced pressure, and crystallised from methyl alcohol; it formed faintly yellow, long needles, m. p. 102—103°, both alone and in admixture with natural bæckeol (Found : C, 65·2; H, 7·7. Calc. for $C_{13}H_{18}O_4$: C, 65·5; H, 7·5%). The acetate, prepared by digesting the phenol with acetic anhydride and a drop of pyridine, crystallised from aqueous methyl alcohol in prisms, m. p. 73°, not depressed by the acetate of bæckeol (Found : C, 64·0; H, 7·3. Calc. for $C_{15}H_{20}O_5$: C, 64·3; H,7·1%).

The authors thank Prof. J. L. Simonsen, F.R.S., for his interest and Imperial Chemical Industries Ltd. for a grant.

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[*Received, January 9th,* 1940.]