

SUBSTITUTED BENZOPHENONES FROM *LEPTOSPERMUM*  
*LUEHMANNII* (F. M. BAILEY)\*

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Jones and White<sup>1</sup> in 1931 noted a small quantity of yellow crystalline solid in the pot residue from a distillation of the essential oil of *Agonis luehmannii* (now *L. luehmannii*), a shrub or small tree of the Myrtaceae family which grows on one only of the Glasshouse Mountains, SE. Queensland. Re-isolation of this material in much higher yield from a garden specimen of *L. luehmannii* has now permitted its structure to be determined as 6-hydroxy-2,4-dimethoxy-3-methylbenzophenone. The 2-hydroxy-4,6-dimethoxy isomer is also present in much smaller quantity.

The principal alkali-soluble phenol (greenish black ferric reaction) formed pale yellow plates, m.p. 110°C, analysing for  $C_{14}H_{10}O_2(OCH_3)_2$ . The *C*-methyl estimation yielded 1.7 moles of volatile acids, shown by gas chromatography of the butyl esters, to be a mixture of acetic and benzoic acids only. Although the infrared spectrum of the phenol showed no carbonyl absorption, an appropriate band ( $1661\text{ cm}^{-1}$ ) appeared after conversion to the colourless acetate (m.p. 96°C,  $C_{18}H_{18}O_5$ ) revealing the phenol as an *o*-hydroxy aromatic ketone. On the basis of Birch's acetate rule, feasible alternative structures are 6-hydroxy-2,4-dimethoxy-3-methylbenzophenone and 2-hydroxy-4,6-dimethoxy-3-methylbenzophenone, the n.m.r. spectrum being consistent with either in showing two methoxyls ( $6.12$  and  $6.83\tau$ ), an aromatic-bound methyl ( $8.02\tau$ ), six aromatic protons and a hydrogen-bonded phenolic proton ( $-1.61\tau$ ). The latter alternative is however a known and distinct substance (m.p. 137°C) having been prepared by Ciamician and Silber<sup>2</sup> and by McGookin, Robertson, and Simpson.<sup>3</sup> The *Leptospermum* phenol, m.p. 110°C, is therefore formulated as 6-hydroxy-2,4-dimethoxy-3-methylbenzophenone, a conclusion consistent with the negative Gibbs' test.

Confirmation of the proposed structure follows from its methylation with diazomethane to 2,4,6-trimethoxy-3-methylbenzophenone (m.p. 96–97°C) identical with a synthetic specimen prepared from 2,4,6-trihydroxy-3-methylbenzophenone (m.p. 146–147°C, McGookin *et al.*<sup>3</sup> reported m.p. 139–140°C) by prolonged treatment with potassium carbonate and dimethyl sulphate. On the other hand, diazomethane treatment of the trihydric phenol yields the Gibbs-positive isomer (m.p. 137°C)<sup>2-4</sup> thereby confirming its 2-hydroxy-4,6-dimethoxy-3-methyl arrangement. It follows that the easily methylated *Leptospermum* phenol has the arrangement in which the phenolic hydroxyl is not that sheltered between the *C*-methyl and the carbonyl.

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<sup>1</sup> Jones, T. G. H., and White, M. (1931).—*J. Proc. Roy. Soc. Qd.* **43**: 24.

<sup>2</sup> Ciamician, G., and Silber, P. (1894).—*Ber. dtsh. chem. Ges.* **27**: 417.

<sup>3</sup> McGookin, A., Robertson, A., and Simpson, T. H. (1951).—*J. Chem. Soc.* **1951**: 2021.

<sup>4</sup> Pollak, J. (1901).—*Mh. Chem.* **22**: 998.

The isomeric phenol, m.p. 137°C, is also a constituent of *L. luehmannii* being isolable in small yield from the mother liquors of the more abundant phenol. The ratio of isomers in the essential oil was shown by gas chromatography (QF1 at 200°C) to be 13 : 1. The ultraviolet spectra could not be directly compared with the literature data for related hydroxybenzophenones reviewed by van Allen and Tinker<sup>5</sup> presumably because of lack of coplanarity due to the crowding of the adjacent substituents.<sup>6</sup>

Karrer<sup>7</sup> lists other substituted benzophenones, e.g. cotoin from coto bark and paracotoin from paracoto bark, which differ from the *Leptospermum* phenols in their *O*-methylation and/or *C*-methylation patterns.

### Experimental

*Extraction of the 6-Hydroxy-2,4-dimethoxy-3-methylbenzophenone.*—Leaves (34 lb) were steam distilled with cohobation for 52 hr yielding 59 ml of essential oil which on standing at 10°C deposited yellow crystals. The oil was extracted several times with 10% NaOH soln. to yield 8.3 g of oil which deposited 2.6 g of yellow crystals. Recrystallization from ethanol and ethyl acetate yielded 0.61 g of pale yellow plates or prisms (Found: C, 70.5; H, 6.0; OCH<sub>3</sub>, 21.2%. Calc. for C<sub>14</sub>H<sub>10</sub>O<sub>2</sub>(OCH<sub>3</sub>)<sub>2</sub>: C, 70.6; H, 5.9; OCH<sub>3</sub>, 22.7%). The ultraviolet absorption spectrum measured in ethanol showed  $\lambda_{\max}$  340, 291, and 256 m $\mu$  ( $\epsilon$  9890; 10,930, and 7920). The Gibbs' test in borate buffer was negative.

Jones and White<sup>1</sup> reported yellow prisms from ethanol, m.p. 104°C (C, 70.5; H, 6.5; OCH<sub>3</sub>, 22.8%).

*6-Acetyl-2,4-dimethoxy-3-methylbenzophenone.*—The *Leptospermum* phenol, m.p. 110°C (100 mg), was refluxed in acetic anhydride with dry sodium acetate for 10 min. Working up in the usual way yielded colourless plates, m.p. 96°C, from ethanol (Found: C, 68.7; H, 5.8%. Calc. for C<sub>15</sub>H<sub>12</sub>O<sub>5</sub>: C, 68.8; H, 5.8%).

*Alkali Fusion.*—The *Leptospermum* phenol, m.p. 110°C (94 mg), was fused in NaOH under nitrogen at 300°C for 2 hr. The melt was cooled, dissolved in water, acidified, and extracted with ether to give a residue from which 23 mg of benzoic acid (m.p. and mixed m.p. 122°C) was readily sublimed. Phloroglucinol derivatives could not be isolated.

*2,4,6-Trimethoxy-3-methylbenzophenone.*—(i) The *Leptospermum* phenol, m.p. 110°C (50 mg), was treated with an excess of diazomethane in ether at room temperature for 1 hr. Working up yielded 47 mg of alkali-insoluble material, crystallizing as long colourless needles, m.p. 96–97°C, from light petroleum (Found: C, 70.9; H, 6.4; OCH<sub>3</sub>, 32.6%. Calc. for C<sub>14</sub>H<sub>9</sub>O<sub>2</sub>(OCH<sub>3</sub>)<sub>3</sub>: C, 71.3; H, 6.3; OCH<sub>3</sub>, 31.8%). There was no depression of the melting point with the trimethyl ether, m.p. 98°C, obtained from 2,4,6-trihydroxy-3-methylbenzophenone as described below.

(ii) 2,4,6-Trihydroxy-3-methylbenzophenone, yellow crystals, m.p. 146–147°C (Found: C, 68.7; H, 5.0%. Calc. for C<sub>14</sub>H<sub>12</sub>O<sub>4</sub>: C, 68.8; H, 4.9%) after vacuum sublimation, was prepared as described by McGookin *et al.*<sup>3</sup> Of this, 261 mg was treated with dimethyl sulphate in refluxing acetone in the presence of K<sub>2</sub>CO<sub>3</sub> for 42 hr. Isolation of the alkali-insoluble material (254 mg) yielded colourless needles, m.p. 98°C (Found: C, 71.2; H, 6.4; OCH<sub>3</sub>, 31.5%. Calc. for C<sub>14</sub>H<sub>9</sub>O<sub>2</sub>(OCH<sub>3</sub>)<sub>3</sub>: C, 71.3; H, 6.3; OCH<sub>3</sub>, 32.6%).

*2-Hydroxy-4,6-dimethoxy-3-methylbenzophenone.*—(i) The alkali-soluble products (32 mg) from the previous experiment crystallized from aqueous ethanol as pale yellow needles, m.p. 136–137°C (Found: C, 70.5; H, 5.9; OCH<sub>3</sub>, 22.2%. Calc. for C<sub>14</sub>H<sub>10</sub>O<sub>2</sub>(OCH<sub>3</sub>)<sub>2</sub>: C, 70.6; H, 5.9; OCH<sub>3</sub>, 22.7%) giving a positive Gibbs' test and greenish black ferric test.

<sup>5</sup> van Allen, J., and Tinker, J. F. (1954).—*J. Org. Chem.* **19**: 1243.

<sup>6</sup> O'Shaughnessy, M. T., and Rodebush, W. H. (1940).—*J. Amer. Chem. Soc.* **62**: 2906.

<sup>7</sup> Karrer, W. (1958).—"Konstitution und Vorkommen der Organischen Pflanzenstoffe." p. 187. (Birkhäuser A. G.: Basel.)

(ii) 2,4,6-Trihydroxy-3-methylbenzophenone (293 mg) was treated with ethereal diazomethane as above to yield 281 mg of alkali-soluble residue which crystallized from aqueous ethanol as pale yellow needles, m.p. 136–137°C, showing no depression of the melting point with product under (i).

The brown alkali-insoluble material (23 mg) obtained from the reaction was not further examined.

(iii) The mother liquors from the isolation of the *Leptospermum* phenol, m.p. 110°C, yielded on standing, a small amount of yellow needles, m.p. 137°C, from ethanol, showing no depression of the melting point with product under (ii) (Found: C, 70.7; H, 6.0; OCH<sub>3</sub>, 22.4%. Calc. for C<sub>14</sub>H<sub>10</sub>O<sub>2</sub>(OCH<sub>3</sub>)<sub>2</sub>: C, 70.6; H, 5.9; OCH<sub>3</sub>, 22.7%).