SECTION C

Organic Chemistry

The Chemistry of *Ottonia vahlii,* Kth. Part I. The Volatile Constituent [1]

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The shrub *Ottonia vahlii,* Kth. contains a volatile oil, proved by structural study and synthesis to be 1-butyl-3,4-methylenedioxybenzene.

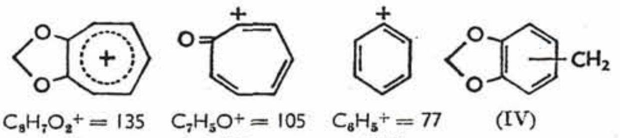
VIA VAHLII, Kth. [syn. *Piper ovatum* (Vahl)] is a which is native to the West Indies, Trinidad in cular.[2] The sole report concerning its chemical tuents is that of Dunstan and Garnett.[3] The possessed an aromatic taste, and on steam distill- yielded an oil with an aromatic odour. It was ted, on very slender evidence, that the oil was terpenoid in nature. From the leaves was ex- d an alkaloid, piperovatine, apparently responsible e physiological properties of the plant. We are vestigating the chemical constituents of this plant, escribe here the elucidation of the structure of the e constituent.

e combined leaves, stems, and roots on steam distill- afforded an oil with a pleasant odour reminiscent frole, which distilled sharply and virtually com- y at 119°/14 mm. (lit.,[3] b. p. 245° at atmospheric e); gas chromatography revealed it to be a geneous product. The molecular weight (mass ometry) was 178, and this, and elemental analysis, rted a molecular formula $C_{11}H_{14}O_2$. The neutral cter of the compound, its failure to form derivatives cteristic of an aldehyde or ketone, and its stability t aqueous alkali, suggested the oxygen atoms were al; this was confirmed by the infrared spectrum, showed neither hydroxy nor carbonyl bands, but ng ether band at 1250 cm.$^{-1}$. In agreement with an and Garnett [3] we found the compound gave an e crimson colour with concentrated sulphuric acid; ethylenedioxybenzene, safrole, and dihydrosafrole ve similarly. These observations suggest the pres- of a 1,2-methylenedioxybenzene group in the struc- Since the compound was saturated, it seemed y that it was an alkyl-1,2-methylenedioxybenzene. e ultraviolet absorption spectrum of the compound ethanol) showed maxima at 205·5, 233, and mμ (ε 17,800, 4900, and 4100), the general shape of curve agreeing well with that expected for a 1,2-methylenedioxybenzene substituted in the aromatic ring.[4]

The infrared spectrum showed bands at 813, 1042, 1100, 1190, and 1616 cm.$^{-1}$, all characteristic of a 1,2,4-substituted benzene ring.[5] Cyclic ether bands were present at 935, 1250, and 2778 cm.$^{-1}$.[6]

The n.m.r. spectrum in deuteriochloroform at 60 Mc./sec. (tetramethylsilane = 0) showed a multiplet (3H) centred at δ 6·55, almost identical in position, appearance, and intensity with the aromatic proton pattern of safrole [7] and isosafrole.[8] A characteristic methylenedioxy-proton singlet (2H) occurred at 5·7 p.p.m.; in 1,2-methylenedioxybenzene this signal appears in the same position. A benzylic proton signal (2H) appeared as a triplet (J = 6·5 c/sec.) centred at 2·42 p.p.m., and a high-field triplet signal (3H) centred at 0·83 p.p.m. (J = 6·5 c./sec.), is ascribed to the terminal methyl group in a side chain. Finally, a broad multiplet (4H) ranging from 1·0 to 1·6 p.p.m. is assigned to two chain-methylene groups.

The evidence so far accumulated points to the structure 1-butyl-3,4-methylenedioxybenzene for the natural product. Confirmation of the 1,2,4-orientation of the benzene ring was obtained by permanganate oxidation of the compound, which led to piperonylic acid (3,4-methylenedioxybenzoic acid), identical with an authentic sample.



$C_8H_7O_2^+ = 135$ (I) $C_7H_5O^+ = 105$ (II) $C_6H_5^+ = 77$ (III) (IV)

Support for the presence of a methylenedioxybenzyl group was found in the mass spectrum. In addition to the parent ion peak at m/e 178 there were peaks at m/e 135, 105, and 77. They correspond satisfactorily to the ions (I), (II), and (III); of these the first two can be

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A. H. R. Grisebach, 'Flora of the British West Indian ds,' Lovell, Reeve and Co., London, 1864, reprinted 1963, er Publishing Co., New York, p. 172.

W. R. Dunstan and H. Garnett, *J. Chem. Soc.*, 1895, **67**, see also W. R. Dunstan and F. H. Carr, *Proc. Chem. Soc.*, 177.

[4] A. I. Scott, 'Ultraviolet Spectra of Natural Products,' Pergamon Press, New York, 1964, p. 322.

[5] L. J. Bellamy, 'Infra-red Spectra of Complex Molecules,' Methuen, London, 1958, ch. 5.

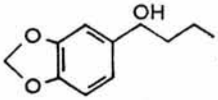
[6] Ref. 5, ch. 7, and K. Nakanishi, 'Infrared Absorption Spectroscopy,' Holden-Day, San Francisco, 1962, pp. 36 and 169.

[7] Varian Associates, N.M.R. Spectral Catalogue, 1962, vol. I, Spectrum No. 253.

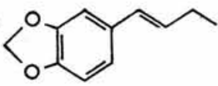
[8] Ref. 7, Spectrum No. 252.

found only if the original compound contains a methylenedioxybenzyl moiety (IV), according to a detailed study of the mass spectra of a series of 3,4-methylenedioxyphenyl compounds carried out by Willhalm *et. al.*[9]

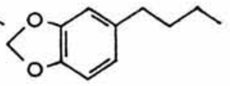
The proposed structure was confirmed by synthesis. Piperonal was condensed with propylmagnesium bromide to give the alcohol (V) mixed with its dehydration product (VI). On heating the mixture in dimethyl sulphoxide[10] the dehydration to (VI) was completed; on infrared evidence this compound was shown to be the *trans*-isomer, which was smoothly reduced catalytically to (VII), identical in all respects (i.r., n.m.r., mass spectral, and g.l.c. comparison) with the natural material. Attempts to make a crystalline derivative of both natural and synthetic products for mixed m. p. comparison were unsuccessful, though the compound clearly formed bromo- and nitro-derivatives, a picrate, and a picrolonate, as evidence by colour changes.



(V)



(VI)



(VII)

By analogy with the physiological properties of similarly constituted compounds,[11] it was to be expected that the natural product would have insecticidal synergist properties. An evaluation kindly carried out by Dr. L. Priester (Department of Entomology, Clemson University) revealed pyrethrum synergist activity of moderate order; the knock-down power of a 0·017% solution of pyrethrum in acetone towards five-day old *Musca domestica* was increased fourfold by the presence of 0·1% 1-buty-3,4-methylenedioxybenzene.

EXPERIMENTAL

Melting points are uncorrected. Ultraviolet spectra relate to solutions in 95% ethanol, and were measured on a Perkin-Elmer 202 instrument. Infrared spectra were measured as liquid films on a Perkin-Elmer 137 instrument. Gas–liquid chromatographic analysis was carried out on a Perkin-Elmer Vapor Fractometer, model 154, using an Apiezon 'L' column and helium as carrier gas. Nuclear magnetic resonance spectra were measured in deuteriochloroform solution, using tetramethylsilane as internal standard ($\delta = 0$), on a Varian A-60 instrument.

Isolation of the Essential Oil.—Air-dried leaves, stems, and roots (50 g.) of *Ottonia Vahlii*, Kth., were pulverised and steam distilled until a clear, homogeneous distillate resulted (about 1 hr.). The steam distillate was extracted thrice with ether, the combined extracts were dried, and the solvent evaporated through a 12 in. Vigreux column, leaving the oil (0·3 g.), which distilled entirely at 119°/14 mm.; g.l.c. at 198° showed a single peak (Found: C, 74·0; H, 7·9. Calc. for $C_{11}H_{14}O_2$: C, 74·1; H, 7·9%). The spectral properties of the compound are referred to in the Discussion.

Oxidation of the Natural Product.—The distilled oil (1·0 g.), water (30 c.c.), potassium permanganate (10·0 g.), and anhydrous sodium carbonate (5·0 g.) were heated gently under reflux for 2 hr. The cooled mixture was treated with sufficient conc. hydrochloric acid to render it distinctly acid, followed by sufficient powdered sodium sulphite to destroy the excess of permanganate and to dissolve the precipitated manganese dioxide. The fine, white precipitate which remained was collected, washed with water, and crystallised from a little hot water, from which it separated as long needles, m. p. 229—230° (decomp.), alone or mixed with an authentic sample of piperonylic acid, obtained by oxidation of piperonal.[12]

1-[3,4-*Methylenedioxyphenyl*]*butanol* (V) *and* 1-(3,4-*Methylenedioxyphenyl*)*but*-1-*ene* (VI).—A Grignard reagent was prepared from magnesium (4·3 g.) in ether (30 c.c.) and n-propyl bromide (18·5 g.) in ether (50 c.c.). To the stirred reagent, with ice-cooling, was added piperonal (22·5 g.) in ether (200 c.c.) during 45 min. After stirring for a further hour the mixture was decomposed with 10% aqueous hydrochloric acid, and the ether layer was separated, washed with water, dried, and evaporated. The alcohol (V) suffered partial dehydration when distilled under reduced pressure (b. p. 84—85°/0·15 mm.), as evidenced by the n.m.r. spectrum, which showed both vinyl and hydroxy-proton signals. The once-distilled product (2·38 g.) and dimethyl sulphoxide (15 c.c.) were heated at 155—165° (bath) for 16 hr. under reflux.[10] The cooled solution was diluted with water (250 c.c.) and the product was isolated by several extractions with light petroleum (b. p. 30—60°). Removal of the solvent yielded the *olefin* (VI), b. p. 130—131°/14 mm. (1·42 g.) (Found: C, 75·4; H, 7·15. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9), $\lambda_{max.}$(EtOH) 210, 260, and 302 mμ (ε 22,500, 11,800, and 5900), $\nu_{max.}$ 960 (*trans* CH=CH), 925, 1245, and 2710 cm.$^{-1}$ (cyclic ether). The n.m.r. spectrum (in deuteriochloroform, $\delta_{TMS} = 0$) showed signals at δ 6·6—6·8 (multiplet, 3H, aromatic protons), 5·9—6·2 (multiplet, 2H, olefinic protons), 5·7 (singlet, 2H, OCH_2O), 1·8—2·3 (multiplet, 2H, allylic CH_2), and 1·0 p.p.m. (triplet, $J = 7·5$ c./sec., 3H, terminal CH_3).

1-*Butyl*-3,4-*methylenedioxybenzene* (VII).—The above olefin (1·0 g.) in 95% ethanol (10 c.c.) was shaken with Adams catalyst at s.t.p. in hydrogen until absorption ceased (3 hr.; uptake 1 mol.). Filtration, dilution with water, and ether extraction afforded, after evaporation of the ether *via* a column, 1-butyl-3,4-methylenedioxybenzene (0·9 g.), b. p. 119°/14 mm. (Found: C, 74·0; H, 7·9%), identical with the natural product (i.r., n.m.r., mass spectral, and g.l.c. comparison).

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[9] B. Wilhalm, A. F. Thomas, and F. Gautschi, *Tetrahedron*, 1964, **20**, 1185.

[10] V. J. Traynelis, W. L. Hergenrother, J. R. Livingston, and J. A. Valicenti, *J. Org. Chem.*, 1962, **27**, 2377.

[11] B. P. Moore and P. S. Hewlett, *J. Sci. Food Agric.*, 1958, **9**, 666; M. Beroza and W. F. Barthel, *J. Agric. Food Chem.*, 1957, **5**, 855; L. O. Hopkins and D. R. Maciver, *Pyrethrum Post*, 1966, **8** (4), 10.

[12] *Org. Synth.*, Coll. Vol. II, p. 538.