

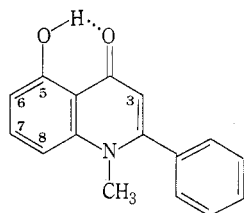
ALKALOIDS OF THE AUSTRALIAN RUTACEAE:

LUNASIA QUERCIFOLIA*

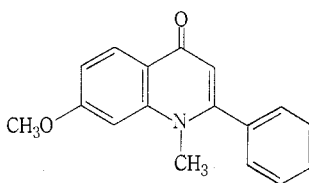
IV.† IDENTIFICATION OF A MINOR CONSTITUENT AS 5-HYDROXY-1-METHYL-2-PHENYL-4-QUINOLONE AND THE PREPARATION OF AN ANGULAR ISOMER OF (-)-LUNINE

By N. K. HART,‡ S. R. JOHNS,‡ J. A. LAMBERTON,‡ and J. R. PRICE‡§

A very weakly basic minor constituent, $C_{16}H_{13}NO_2$, isolated from the alkaloidal fraction from leaves of *Lunasia quercifolia* (Warb.) Lauterb. & K. Schum., has been identified by spectroscopic examination as 5-hydroxy-1-methyl-2-phenyl-4-quinolone (I). The structure of (I) follows from the close resemblance between its spectroscopic properties and those of the alkaloid eduleine (II), previously isolated from *L. quercifolia*.^{1,2} Evidence for placing the hydroxyl group at C5 where it is strongly hydrogen-bonded to the quinolone oxygen atom comes from the n.m.r. spectrum of (I). The



(I)



(II)

60-Mc/s spectrum ($CDCl_3$ solution) shows a sharp one-proton singlet at very low field (δ 14.0), and this signal could be assigned to the hydroxyl proton as this proton was shown to be exchangeable with deuterium oxide. This conclusion was supported by the dark colour, similar to that seen with 5-hydroxyflavones, which developed on adding ferric chloride to an ethanolic solution of (I). In accord with the hydrogen-bonded structure assigned, (I) has only slight solubility in aqueous acid, resembling in this respect the 1-hydroxy-10-methylacridones which are much more weakly basic than the corresponding 1-methoxy compounds.³ A three-proton singlet at δ 3.56 in the n.m.r. spectrum of (I) was assigned to the *N*-methyl group, and a one-proton singlet at δ 6.17 to the C3 proton.

* Manuscript received January 8, 1968.

† Part III, *Aust. J. Chem.*, 1966, **19**, 2185.

‡ Division of Applied Chemistry, CSIRO Chemical Research Laboratories, P.O. Box 4331, Melbourne, Vic. 3001.

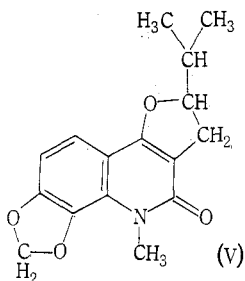
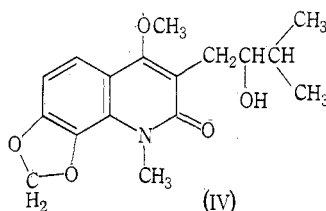
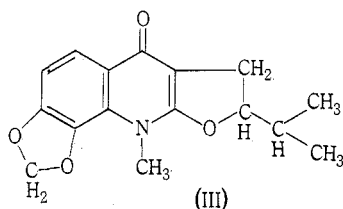
§ Present address: CSIRO, 314 Albert Street, East Melbourne, Vic. 3002.

¹ Johnstone, R., Price, J. R., and Todd, A. R., *Aust. J. Chem.*, 1958, **11**, 562.

² Goodwin, S., Smith, A. F., Velasquez, A. A., and Horning, E. C., *J. Am. chem. Soc.*, 1959, **81**, 6209.

³ Crow, W. D., and Price, J. R., *Aust. J. scient. Res. A*, 1949, **2**, 255.

Although the *O*-methyl ether of (I) has not been isolated the possibility remains that (I) may be an artefact, as it is known that similarly situated methoxyl groups in 10-methylacridones and *N*-methylfuro-4-quinolones are easily demethylated.^{3,4} The yield of (I) was low but because of its low basicity the normal method of work-up for alkaloids may not be suitable for its isolation. Despite these uncertainties, the isolation of (I) is of interest, as the oxygen substitution pattern found in (I) differs from that of other *Lunasia* alkaloids.



A laevorotatory isomer of (–)-lunine (III) has been prepared by converting (–)-lunine methiodide into (+)-lunidine (IV) in alkaline solution,⁵ and then heating (+)-lunidine in aqueous hydrochloric acid solution. The product of this reaction sequence was characterized as (V), the angular isomer of (–)-lunine, and its formation parallels the conversion of (–)-lunacrine methiodide into (+)-lunacridine and thence by heating with acid into a mixture of (+)-lunacrine and a laevorotatory angular isomer of lunacrine.⁶ The angular isomer (V) predominates, however, in the reaction products from (+)-lunidine, and its structure can be deduced by comparison of its n.m.r. spectrum with that of (–)-lunine.

Experimental

(i) In the course of processing residues remaining from the isolation of alkaloids of *L. quercifolia* leaves,¹ the crude material was partitioned between organic solvents (chloroform, benzene) and aqueous acid. The relatively non-basic fractions deposited small amounts of a faintly yellow crystalline substance and crystallization from methanol afforded 5-hydroxy-1-methyl-2-phenyl-4-quinolone as pale yellow needles, m.p. 174–176° (Found: C, 76.2; H, 5.3; N, 5.4. Calc. for C₁₅H₁₃NO₂: C, 76.5; H, 5.2; N, 5.6%).

⁴ Lahey, F. N., Lamberton, J. A., and Price, J. R., *Aust. J. scient. Res. A*, 1950, **3**, 155.

⁵ Hart, N. K., and Price, J. R., *Aust. J. Chem.*, 1966, **19**, 2185.

⁶ Price, J. R., *Aust. J. Chem.*, 1959, **12**, 458.

The molecular weight was confirmed by the mass spectrum which showed a very strong molecular ion peak at m/e 251 and fragmentation peaks at m/e 250, 223, 208, 194, 180, 165, 152, and 111.5. For comparison, eduleine (II) showed a strong M^+ peak at m/e 265 with fragmentation peaks at m/e 237, 222, 194, 165, 152, and 118.5. The n.m.r. spectrum of (I) showed a three-proton singlet at δ 3.56 ($N-CH_3$), a one-proton singlet at δ 6.17 (C 3-H), a complex multiplet at 395–462 c/s (eight aromatic protons), and a one-proton singlet at δ 14.00 (OH). For comparison, eduleine showed three-proton singlets at δ 3.55 ($N-CH_3$) and δ 3.95 (OCH_3) and a one-proton singlet at δ 6.22 (C 3-H).

(ii) A solution of (+)-lunidine⁵ (110 mg) in hydrochloric acid (5N; 8 ml) was refluxed for 6 hr, then diluted with water, basified (NH_3), and extracted with chloroform. The residue remaining on evaporation of the chloroform was dissolved in a small volume of methanol, the solution poured into dilute hydrochloric acid solution (2N), and the methanol removed under reduced pressure. The material insoluble in hydrochloric acid was crystalline, and it was recovered by filtration, dried, dissolved in benzene, and the benzene solution passed through a short column of neutral alumina. The benzene-eluted fractions (91 mg) on crystallization from diethyl ether gave (V) as colourless needles, m.p. 123.5–125.5°; $[\alpha]_D$ 47.3° (c, 0.56 in methanol); λ_{max} 232 m μ ($\log \epsilon$ 4.50), 253 (4.41), 262sh (3.89), 267sh (4.13), 295sh (5.87), and 312 (3.94) (Found: C, 66.8; H, 6.1; N, 4.7. Calc. for $C_{18}H_{17}NO_4$: C, 66.9; H, 6.0; N, 4.9%). The n.m.r. spectrum of (V) shows a three-proton singlet at δ 3.85 ($N-CH_3$), a two-proton singlet at δ 6.02 (methylenedioxy group), a pair of AB doublets (J 8.3 c/s) at δ 6.78 and δ 7.31 (H 6, H 5), two three-proton doublets (each J 6.5 c/s) at δ 1.05 and δ 1.00 (non-equivalent *C*-methyl groups), a one-proton multiplet at δ 2.05 (methine proton of isopropyl group), a two-proton multiplet at 160–200 c/s (CH_2 group), and a one-proton multiplet at 270–300 c/s ($-CH-O$). The n.m.r. spectrum of (V) closely resembles that of (–)-lunine, except that in the spectrum of (–)-lunine there is a relative downfield displacement of the doublet signal for C 5-H to δ 7.98 due to the deshielding influence of the quinolone carbonyl group.