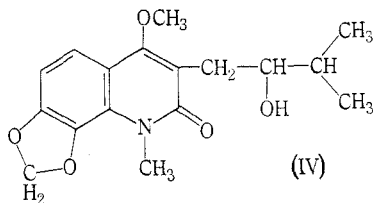
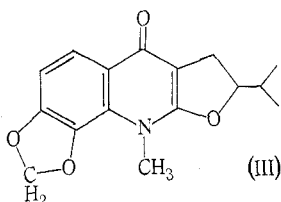
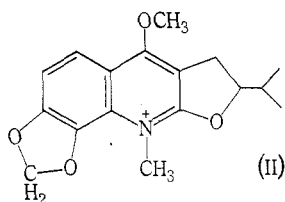
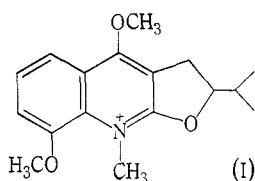


ALKALOIDS OF THE AUSTRALIAN RUTACEAE: *LUNASIA QUERCIFOLIA**

III.† ISOLATION OF (–)-O-METHYLLUNINIUM SALTS

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Extraction of the bark of *Lunasia quercifolia* (Warb.) Lauterb. & K. Schum., a species closely allied to *Lunasia amara*, affords water-soluble bases (3–3.5%) which were shown¹ to contain (–)-lunasine (I) as a major component. It has now been found that leaves of *L. quercifolia* contain about 1% quaternary bases composed partly of (–)-lunasine (I) but mainly of the (–)-O-methyluninium base (II), which may be



regarded as derived from the known alkaloid (–)-lunine (III). Although (–)-O-methyluninium salts have not been isolated previously, Rüeegger and Stauffacher² obtained (+)-O-methyluninium perchlorate as reaction product from the alkaloid (+)-lunidine (IV) isolated from a New Guinea species identified as *Lunasia amara* Blanco var. *repanda* (Lauterb. & K. Schum) Lauterb.

The structure of the (–)-O-methyluninium ion is readily deduced from comparison of its n.m.r. spectrum with that of lunasine and with the published spectra³ of lunine and lunacrine. Conversion of the iodide into the known tertiary

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¹ Price, J. R., *Aust. J. Chem.*, 1959, **12**, 458.

² Rüeegger, A., and Stauffacher, D., *Helv. chim. Acta*, 1963, **46**, 2329.

³ Goodwin, S., Shoolery, J. N., and Johnson, L. F., *J. Am. chem. Soc.*, 1959, **81**, 3065.

base, (–)-lunine (III), confirmed the structural assignment based on spectroscopic data. The picrate and other (–)-*O*-methyluninium salts are converted in alkaline solution into a dextrorotatory, weakly basic substance, $C_{17}H_{21}NO_5$, the properties of which are in close agreement with those reported² for (+)-lunidine (IV). Because of the ease with which this conversion takes place, the possibility remains that the alkaloid (+)-lunidine isolated by Rügger and Stauffacher may be an artefact. This suggestion is in accordance with the positive rotation reported² for lunidine and the *O*-methyluninium salt derived from it.

Experimental

Microanalyses were carried out by the Australian Microanalytical Service, Melbourne. N.m.r. spectra were measured in deuterochloroform solution on a Varian A60 spectrometer, and chemical shifts are relative to tetramethylsilane (δ 0.00).

(a) Isolation of (–)-*O*-Methyluninium Salts

Dried leaves of *L. quercifolia* (40 lb) were extracted by continuous percolation with methanol, and the extracts concentrated under reduced pressure to 6 l. The concentrated methanolic extract (300 ml) was diluted with 1% aqueous hydrochloric acid (400 ml), and filtered. The aqueous acid solutions were basified with sodium bicarbonate to pH < 9, extracted rapidly with chloroform (4 × 400 ml), and immediately reacidified to prevent decomposition of the water-soluble bases. A saturated solution of picric acid was added to the acidic solution until there was no further separation of picrate. Fractional crystallization of the mixed picrates from methanol and methyl acetate gave (–)-lumasine picrate (16 g), yellow needles, m.p. and mixed m.p. with an authentic specimen 143–144°, (–)-*O*-methyluninium picrate (24 g), yellow needles which melted at 159–161°, resolidified in crystalline form and then melted at 170–172°, and 21 g of a mixture of picrates (Found for (–)-*O*-methyluninium picrate: C, 52.1; H, 4.2; N, 10.4; O, 33.0; CH_3O , 5.7; $CH_3(N)$, 2.8; $[\alpha]_D^{24} - 18.5^\circ$ (c, 0.56 in methanol). Calc. for $C_{17}H_{20}O_4N^+C_6H_3O_7N_3^-$: C, 52.1; H, 4.2; N, 10.6; O, 33.2; CH_3O , 5.9; $CH_3(N)$, 2.8%).

(–)-*O*-Methyluninium picrate (1 g) was dissolved in methanol (40 ml) and passed through an ion exchange column (Permutit Deacidite FF, iodide form). Evaporation of the methanolic eluate yielded (–)-*O*-methyluninium iodide (0.77 g), which after recrystallization from ethanol melted at 176–179° (dec.), resolidified, and melted at 216–220°; $[\alpha]_D^{24} - 27.4^\circ$ (c, 1.0 in ethanol) (Found: C, 47.6; H, 4.9; I, 29.3; N, 3.2; O, 14.9; CH_3O , 7.5; $CH_3(N)$, 4.3. Calc. for $C_{17}H_{20}INO_4$: C, 47.6; H, 4.7; I, 29.4; N, 3.4; O, 14.9; CH_3O , 7.2; $CH_3(N)$, 3.5%). Ultra-violet absorption in ethanol: λ_{max} 218, 260, and 336 m μ ($\log \epsilon$ 4.65, 4.67, and 3.80 respectively), λ_{min} 237 and 279 m μ ($\log \epsilon$ 4.05 and 3.40 respectively). Infrared spectrum in chloroform: 6.08s, 6.22m, 6.44vs, 6.65s, 6.72s, 6.86m, 7.32s, 7.75s, 9.35m, 9.51m, and 9.97w μ .

The n.m.r. spectrum showed doublet signals at δ 1.11 and δ 1.13 (each J 6.5 c/s) for the two *C*-methyl groups, a one-proton multiplet at 120–158 c/s (Me_2CH-), a two-proton multiplet at 201–230 c/s ($-CH_2CH-$ of the dihydrofurano ring), two three-proton singlets at δ 4.18 and δ 4.51 (the *N*-methyl- and methoxyl-groups), a one-proton multiplet at 309–333 c/s ($-CH_2CH-$ of the dihydrofurano ring), a two-proton singlet at δ 6.30 (methylenedioxy group), and a pair of doublets at δ 7.12 and δ 7.80 (J 9 c/s) (aromatic protons H 5 and H 6).

(–)-*O*-Methyluninium perchlorate was prepared by dissolving the picrate in boiling methanol, adding a small excess of perchloric acid, and diluting with ether. Repeated crystallization from methanol/ether gave colourless microcrystals, m.p. 208–209°, $[\alpha]_D^{24} - 23.8^\circ$ (c, 1.2 in methanol) (Found: C, 50.9; H, 5.2; Cl, 8.5; N, 3.1; O, 31.6. Calc. for $C_{17}H_{20}O_4N^+ClO_4^-$: C, 50.8; H, 5.1; Cl, 8.8; N, 3.5; O, 31.7%).

(b) (–)-Lunine from (–)-*O*-Methyluninium Salts

(–)-*O*-Methyluninium iodide (0.2 g) in anhydrous pyridine (4 ml) was maintained at 80° for 16 hr and then evaporated to dryness in a vacuum. The residue was partitioned between

chloroform (10 ml) and water (4 ml), and the aqueous phase extracted again with chloroform (2×10 ml). The combined chloroform extracts were dried and evaporated, the residue dissolved in ethanol/chloroform (1:2), and the solution filtered through a small column of alumina. Evaporation of the filtrate yielded crude lunine (III) (0.13 g), which crystallized from ethyl acetate in prisms, m.p. and mixed m.p. with authentic lunine 223–224°; $[\alpha]_D^{24} - 39^\circ$ (c, 1.5 in chloroform) (Found: C, 67.0; H, 6.1; N, 4.6; O, 21.8. Calc. for $C_{16}H_{17}NO_4$: C, 66.9; H, 6.0; N, 4.9; O, 22.3%). Ultraviolet absorption in ethanol: $\lambda_{\max}$ 222, 247, 267sh, 313, and 323 m μ ($\log \epsilon$ 4.35, 4.60, 4.06, 4.08, and 4.07 respectively), $\lambda_{\min}$ 211, 228, 280, and 318 m μ ($\log \epsilon$ 4.24, 4.32, 3.69, and 4.06 respectively).

(c) (+)-Lunidine from (–)-O-Methyluninium Salts

(–)-O-Methyluninium picrate (1 g) was dissolved in warm methanol (25 ml), aqueous sodium hydroxide (10 ml; 5% solution) added, and the methanol removed under reduced pressure. The mixture was diluted with water, extracted with chloroform, and the chloroform evaporated. Crystallization of the residue (0.6 g) from light petroleum (boiling range 60–80°) gave (+)-lunidine as colourless crystals, m.p. 64–66°; $[\alpha]_D^{24} + 28.6^\circ$ (c, 1.3 in ethanol) (Found: C, 64.0; H, 6.7; N, 4.7; O, 24.8. Calc. for $C_{17}H_{21}NO_5$: C, 63.9; H, 6.6; N, 4.4; O, 25.1%). Ultraviolet absorption in ethanol: $\lambda_{\max}$ 216sh, 228, 237sh, 258, 266sh, 317, and 331 m μ ($\log \epsilon$ 4.31, 4.41, 4.34, 4.30, 4.33, 3.82, and 3.78 respectively), $\lambda_{\min}$ 248 and 279 m μ ($\log \epsilon$ 4.12 and 3.57 respectively). The n.m.r. spectrum was identical with that published by Rütgger and Stauffacher.²

(d) Preparation of (–)-O-Methyluninium Iodide from Lunine

Lunine (200 mg) was refluxed with methyl iodide (10 ml) and ethanol (10 ml) for 8 hr, and then allowed to stand for 16 hr in a refrigerator. (–)-O-Methyluninium iodide (294 mg) crystallized and after recrystallization from ethanol had m.p. 175–180° (dec.) and 217–220°; the mixed m.p. with (–)-O-methyluninium iodide was not depressed. $[\alpha]_D^{24} - 28^\circ$ (c, 1.3 in ethanol) (Found: C, 47.8; H, 4.9; N, 3.5; CH_3O , 7.3. Calc. for $C_{17}H_{20}INO_4$: C, 47.6; H, 4.8; N, 3.4; CH_3O , 7.2%). The infrared and ultraviolet spectra were identical with those for (–)-O-methyluninium iodide.