ALKALOIDS OF THE AUSTRALIAN LEGUMINOSAE*

III. THE OCCURRENCE OF PHENYLETHYLAMINE DERIVATIVES IN ACACIA SPECIES

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Many species of *Acacia* have been tested by Mr. E. P. White for the presence of alkaloids in plants grown in New Zealand. He identified tryptamine, phenylethylamine, and *N*-methylphenylethylamine.

Acacia kettlewelliae Maiden was found by White[1] to contain about 1·5% base in its leaves and stems, 92% of which was 2-phenylethylamine. A sample of leaves collected at Creswick, Victoria, gave 0·9% base which was identified as *N*-methyl-2-phenylethylamine from consideration of its nuclear magnetic resonance spectrum and the properties of its picrate and oxalate. It is relevant that White[2] found that the proportions of these two bases varied between plants of the species *A. prominens*, and in the one plant at different times of the year.

Acacia adunca A. Cunn. ex G. Don is a valid species though there has been botanical confusion with other species. No record of its alkaloid content has been found. Leaves obtained from Stanthorpe in south-eastern Queensland yielded 2·4% of a base which proved to be *N*-methyl-2-phenylethylamine.

Acacia harpophylla F. Muell. (brigalow) predominates in parts of Queensland to such an extent that these areas have become known as the Brigalow country. Although the tree has been studied by those seeking methods of control, its constituent bases have not previously been examined. It has now been shown that the leaves contain 2-phenylethylamine and [2-(*p*-hydroxyphenyl)ethyl]dimethylamine (hordenine) in the proportions of 2 : 3, the crude base amounting to 0·6% of the dry weight of leaf.

Poor recoveries resulted when the milled plant was extracted with methanol, but much higher yields of base were obtained by extraction with ammoniacal chloroform. From some experiments a small amount of crystals separated while the chloroform solution of the crude base was being concentrated. These proved to be the chloromethyl bromide of hordenine, presumably formed by reaction of the base with chlorobromomethane present in the chloroform as an impurity. This would support the suggestion of Williams[3] that the supposed interaction of chloroform and tertiary bases is due to this impurity.

Previously hordenine has been reported only from the families Cactaceae and Gramineae, although its methyl ether was recently found by Badger, Christie, and Rodda[4] in a member of the Rutaceae (*Teclea simplicifolia*).

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[1] White, E. P., *N.Z. J. Sci. Tech.* B, 1957, **38**, 719.

[2] White, E. P., *N.Z. J. Sci. Tech.* B, 1954, **35**, 451.

[3] Williams, H., *Chem. & Ind.*, 1960, 900.

[4] Badger, G. M., Christie, B. J., and Rodda, H. J., *Aust. J. Chem.*, 1963, **16**, 734.

Acacia holoserica A. Cunn. yielded 1·2% of base from a sample of bark collected near Mackay in Queensland. It was found to consist of one component which proved to be hordenine.

Experimental

Microanalyses were made by the CSIRO and University of Melbourne Microanalytical Laboratory.

(*a*) *Acacia kettlewelliae.*—Methanol extraction of leaves of this species, worked up to the crude base by the usual extraction process, gave 0·9% of a pungent-smelling liquid. Gas chromatography over a Silicone E–301 column showed one peak, slightly later than that for 2-phenylethylamine; a mixture with the latter base gave two peaks.

Nuclear magnetic resonance spectra for the two bases measured at 60 Mc/s in carbon tetrachloride solution with tetramethylsilane as internal reference, are consistent with the base of *A. kettlewelliae* being *N*-methyl-2-phenylethylamine. Peaks and assignments are as follows:

Phenylethylamine			*A. kettlewelliae* Base		
δ (p.p.m.)	Integration step	Assignment	δ (p.p.m.)	Integration step	Assignment
1·65	2	$-NH_2$	1·05*	1·2	>NH
			2·3	2·3	$>N-CH_3$
2·55–3·05 (septet)	4	$-CH_2-CH_2-$	2·7	4	$-CH_2-CH_2-$
7·22	5	Ph–	7·15	5	Ph–

A picrate was formed from the *A. kettlewelliae* base, m.p. 144·5–145·5° (from water) (Found: C, 49·8; H, 4·7; N, 15·0%. Calc. for $C_9H_{13}N.C_6H_3N_3O_7$: C, 49·5; H, 4·4; N, 15·4%) (*N*-methyl-2-phenylethylamine picrate, m.p. 140–141° lit.).

The oxalate separated from ethanolic solution as plates, m.p. 185–186° (depressed 20° on admixture with phenylethylamine oxalate) (Found: C, 58·6; H, 6·8%. Calc. for $C_9H_{13}N.C_2H_2O_4$: C, 58·7; H, 6·7%) (*N*-methylphenylethylamine oxalate, m.p. 183–184° lit.).

(*b*) *Acacia adunca.*—The base was obtained in 2·4% yield from the dried, milled leaves either by extraction with warm methanol, or by direct extraction with chloroform after moistening the plant with ammonium hydroxide. The bulk of the crude base was obtained as a clear liquid by distilling over solid sodium hydroxide at 120° and 100 mm Hg in a sublimation apparatus.

The nuclear magnetic resonance spectrum in carbon tetrachloride was essentially identical with that of the base from *A. kettlewelliae.*

The picrate, m.p. 141–143°, and the oxalate, m.p. 188–189°, did not depress the melting point of the corresponding salts of the *A. kettlewelliae* base (Found: for the picrate, C, 49·6; H, 4·5; N, 15·3%. Calc. for $C_9H_{13}N.C_6H_3N_3O_7$: C, 49·5; H, 4·4; N, 15·4%. Found, for the oxalate; C, 59·1; H, 6·8; N, 6·1%. Calc. for $C_9H_{13}N.C_2H_2O_4$: C, 58·7; H, 6·7; N, 6·2%).

(*c*) *Acacia harpophylla.*—Leaves and twigs collected at Meandarra in Queensland yielded 0·6% of crude base when extracted with chloroform after moistening the milled plant with aqueous ammonia. The bases were extracted from the chloroform with dilute sulphuric acid and taken back into chloroform after basifying with ammonia. In some instances the crude base was semicrystalline, and crystals could be separated by washing with cold benzene. A more complete separation was brought about by extraction of the chloroform solution with sodium hydroxide solution; recovery from the latter phase gave the crystalline base while the chloroform retained a liquid base.

* Not present after solution shaken with D_2O.

Recrystallization of the solid from water gave [2-(*p*-hydroxyphenyl)ethyl]dimethylamine (hordenine) as needles, m.p. 119–120°, undepressed on admixture with pure hordenine (Found: C, 72·7; H, 9·2; N, 8·3; (*N*)-Me; 14·8%. Calc. for $C_{10}H_{15}NO$: C, 72·7; H, 9·2; N, 8·5; (*N*)-Me, 18·2%). No explanation can be offered for the very low *N*-methyl result, which was obtained on a second sample and also from authentic hordenine. The following derivatives were formed: hydrochloride, plates from acetone containing 5% ethanol, m.p. 180–181° (lit. m.p. 177°) (Found: C, 59·2; H, 7·7; N, 6·9%. Calc. for $C_{10}H_{15}NO.HCl$: C, 59·6; H, 8·0; N, 7·0%); methiodide, from acetone with 20% methanol, m.p. 228–229° (lit. m.p. 230–231°) (Found: C, 42·7; H, 5·8; N, 4·7%). Calc. for $C_{10}H_{15}NO.CH_3I$: C, 43·0; H, 5·9; N, 4·6%); picrate, lemon yellow needles from water, m.p. 140° (lit. m.p. 139–140°) (Found: C, 48·9; H, 4·7; N, 14·2%. Calc. for $C_{10}H_{15}NO.C_6H_3N_3O_7$: C, 48·7; H, 4·6; N, 14·2%); picrolonate, m.p. 221–224° from ethanol (lit. m.p. 220°) (Found: C, 56·1; H, 5·3; N, 16·4%. Calc. for $C_{10}H_{15}NO.C_{10}H_8N_4O_5$: C, 55·9; H, 5·4; N, 16·3%). The nuclear magnetic resonance spectrum, measured at 60 Mc/s in carbon tetrachloride with tetramethylsilane as internal reference, showed peaks at δ 2·4 (6 protons; NMe_2), δ 2·6 (4 protons; CH_2–CH_2), δ 6·75 (4 proton quadruplet; *p*-substituted aromatic), and δ 8·0 (1 proton, not shown in the presence of D_2O; hydroxyl). The infrared spectrum of hordenine and of the crystalline base, measured in chloroform solution, were identical.

On some occasions a small amount of crystals separated from the chloroform solution of the crude alkaloid. Without further purification they had m.p. 173·5–175° (Found: C, 45·3; H, 5·9; N, 4·6; O, 6·8; Cl, 10 (approx.); Br, 28 (approx.)%. Calc. for $C_{11}H_{17}NOClBr$: C, 44·8; H, 5·8; N, 4·8; O, 5·4; Cl, 12·0; Br, 27·2%). *[2-(p-hydroxyphenyl)ethyl]dimethylamine chloromethyl bromide*, m.p. 175–175·5°, was prepared by refluxing hordenine in acetone or chloroform solution with chlorobromomethane for about 1 hr. It gave no depression of melting point when mixed with the artefact from the natural base solution. No satisfactory solvent was found for recrystallizing the chloromethyl bromide, but pure crystals were obtained from the acetone solution of reactants decanted after a portion of the quaternary salt had formed. (Found: C, 45·0; H, 6·0; N, 4·3%).

The liquid base, distilled over solid sodium hydroxide in a sublimation apparatus at 120° and 100 mm Hg, gave 2-phenylethylamine, the infrared spectrum being identical with that of authentic material. The melting points of the following derivatives were not depressed on admixture with authentic samples: picrate, m.p. 167–170°, yellow plates from water (lit. m.p. 169–171°) (Found: C, 48·3; H, 4·1; N, 16·0%. Calc. for $C_8H_{11}N.C_6H_3N_3O_7$: C, 48·0; H, 4·0; N, 16·0%); oxalate m.p. 218–222°, platelets from boiling ethanol (lit. m.p. 218°, normal salt is formed in boiling ethanol) (Found: C, 64·9; H, 7·3%. Calc. for $(C_8H_{11}N)_2.C_2H_2O_4$: C, 65·0; H, 7·3%); picrolonate, m.p. 220–224°, golden yellow prisms from 30% ethanol (Found: C, 56·4; H, 5·0; N, 17·4%. Calc. for $C_8H_{11}N.C_{10}H_8N_4O_5$: C, 56·1; H, 5·0; N, 18·2%). *2-Phenylethylamine picrolonate* was prepared similarly, m.p. 223–225° (Found: C, 56·3; H, 5·1; N, 18·0%).

(*d*) *Acacia holoserica*.—Dried, milled bark was moistened with 5% aqueous ammonia and extracted by percolation with chloroform. The base was extracted from the solution by dilute sulphuric acid, and after this had been basified with ammonia it was extracted with chloroform. The base remaining after removal of the chloroform was solid and could be partially purified by solution in dilute aqueous sodium hydroxide, filtration to remove a small amount of tarry matter, and re-precipitation by the addition of ammonium chloride. Further purification was effected by sublimation or by crystallization from water, which gave prisms, m.p. 119°, not depressed on admixture with hordenine (Found: C, 72·7; H, 9·2; N, 8·4%. Calc. for $C_{10}H_{15}NO$: C, 72·7; H, 9·2; N, 8·5%).

Confirmation was found in the identity of the infrared spectra of the base and authentic hordenine, run as dispersions in KCl disks.

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