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## Studies on Orchidaceae Alkaloids

### XIV.\* A Phthalide Alkaloid from *Dendrobium pierardii* Roxb.

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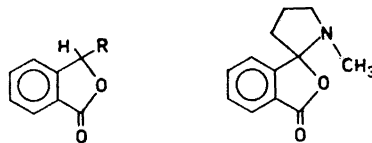
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An optically active alkaloid, pierardine, a 3-(3-dimethylaminopropyl)phthalide, has been isolated from *Dendrobium pierardii* Roxb. Its structure (I) resembles that of shihunine (II),<sup>2-4</sup> isolated from *Dendrobium lohohense* Tang et Wang.

The free base I was obtained as a viscous oil by purification through its hydrochloride. The molecular formula, C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub>, was established by high resolution mass spectrometry of the base and elemental analysis of its hydrochloride and its methiodide.

The presence of a phthalide group in I was indicated by its UV spectrum, which is almost superimposable on that of phthalide,<sup>5</sup> and supported by its IR spectrum showing a strong carbonyl band at

\* No. XIII of this series, see Ref. 1.



I R = -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>

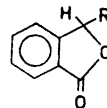
II

III R = -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N<sup>⊕</sup>(CH<sub>3</sub>)<sub>2</sub>  
O<sup>⊖</sup>

IV R = -CH<sub>2</sub>CH=CH<sub>2</sub>

V R = -CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>

1777 cm<sup>-1</sup> in carbon tetrachloride, shifted to 1767 cm<sup>-1</sup> in acetonitrile. The NMR spectrum shows four aromatic protons (τ 2.0–2.7, multiplet) and a one proton signal at τ 4.46 (multiplet) due to the benzylic hydrogen in the phthalide group. On basis of the above evidence, the following partial structure of I was indicated:



A 6 H singlet (τ 7.81) in the NMR spectrum and the base peak *m/e* 58 in the mass spectrum strongly suggest the presence of the -CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub> grouping in I. Oxidation of I with hydrogen peroxide afforded an oily *N*-oxide, which gave an NMR spectrum in which the 6 H singlet was shifted to τ 6.77. Without further purification the *N*-oxide was pyrolyzed giving the nitrogen free compound IV. The NMR spectrum of IV shows four aromatic protons, four protons in the region τ 3.9–5.1 and two allylic protons centered at τ 7.35. Catalytic hydrogenation of IV afforded V, which was indistinguishable from 3-propylphthalide (IR, NMR and MS) obtained by catalytic hydrogenation of propylidenephthalide, and hence pierardine has structure I. Attempts to elucidate the absolute configuration of pierardine are in progress.

*Experimental.* All melting points are corrected. Mass spectra were measured on an LKB 9000 spectrometer (ionization energy 70 eV), and with a double focussing Atlas SM 1 mass spectrograph. IR spectra were recorded

on a Perkin Elmer 257 instrument, the UV spectra on a Beckman DK2 instrument, and the NMR spectra on a Varian A60-A spectrometer.

**Isolation of pierardine (I).** Fresh plants of *Dendrobium pierardii* Roxb. (6 kg) were extracted with methanol (12 l). The extract was concentrated to 0.3 l, acidified and washed with carbon tetrachloride ( $4 \times 0.2$  l). The aqueous solution was made alkaline (pH 10) with sodium hydroxide and extracted with ether ( $5 \times 0.2$  l). The combined ether solutions were dried ( $\text{Na}_2\text{SO}_4$ ), concentrated and filtered through neutral alumina ( $3 \times 15$  cm) using chloroform as eluent. Concentration of the eluate gave the crude alkaloid, which was dissolved in ether and treated with hydrogen chloride in ether. The precipitate (1.1 g) was washed with ether and recrystallized twice from ethanol giving pierardine hydrochloride (0.8 g), from which the free base was obtained as a colourless viscous oil.

**Characterization of I.** Viscous oil,  $[\alpha]_{\text{D}}^{25} - 69^\circ$  (c 1.2, chloroform). (Found: 219.1264. Calc. for  $\text{C}_{13}\text{H}_{17}\text{NO}_2$ : 219.1259.  $^{12}\text{C} = 12.00000$ ). UV spectrum:  $\lambda_{\text{max}}$  (ethanol) 280.5 nm (log  $\epsilon$  3.29), 273 nm (log  $\epsilon$  3.29), 227 nm (log  $\epsilon$  4.09). IR spectrum:  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 1777(s)  $\text{cm}^{-1}$ ;  $\nu_{\text{max}}$  ( $\text{CH}_3\text{CN}$ ) 1767(s)  $\text{cm}^{-1}$ . NMR spectrum ( $\text{CDCl}_3$ ):  $\tau$  2.0–2.7 (m, 4 H),  $\tau$  4.46 (m, 1 H), 7.81 (s, 6 H),  $\tau$  7.5–9.0 (m, 6 H). Pertinent mass spectral peaks  $m/e$  (rel. intensity): 219 (5), 169 (3), 133 (3), 105 (2), 77 (4), 71 (2), 58 (100).

**Hydrochloride of I.** Needles from ethanol, m.p. 185–186°. (Found: C 61.0; H 7.18; Cl 13.8; N 5.61; O 12.5. Calc. for  $\text{C}_{13}\text{H}_{18}\text{ClNO}_2$ : C 61.1; H 7.09; Cl 13.9; N 5.48; O 12.5). IR spectrum:  $\nu_{\text{max}}$  (KBr) 1756(s)  $\text{cm}^{-1}$ .

**Methiodide of I.** M.p. 199–200°;  $[\alpha]_{\text{D}}^{25} - 64^\circ$  (c 0.22, methanol). (Found: C 46.8; H 5.40; I 35.5; N 3.73; O 9.04. Calc. for  $\text{C}_{14}\text{H}_{20}\text{INO}_2$ : C 46.6; H 5.58; I 35.1; N 3.88; O 8.86).

**Oxidation of I.** Hydrogen peroxide (30 %, 0.6 ml) was added to a solution of I (383 mg) in methanol (0.3 ml) and the solution kept overnight at room temperature. The excess of hydrogen peroxide was destroyed by the addition of platinum black. The solution was filtered and evaporated leaving the crude *N*-oxide (III). IR spectrum:  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 1765(s)  $\text{cm}^{-1}$ . NMR spectrum ( $\text{CDCl}_3$ ):  $\tau$  6.77 (s, 6 H).

**Pyrolysis of III.** Without further purification the *N*-oxide (obtained from 383 mg I) was pyrolyzed (160°, 0.4 mm Hg). The distillate was purified by preparative GLC (column: 20 % SE-52 on Chromosorb AW DMCS, 60–80 mesh; 4 mm  $\times$  2.0 m; retention time 7.5 min at 207°; gas flow rate 40 ml/min) and IV

(100 mg) was collected as an oil,  $[\alpha]_{\text{D}}^{25} - 65^\circ$  (c 1.2, chloroform). IR spectrum:  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 1781(s), 1645(w), 997(m) and 922(m)  $\text{cm}^{-1}$ . NMR spectrum ( $\text{CCl}_4$ ):  $\tau$  2.1–2.8 (m, 4 H),  $\tau$  3.8–5.1 (m, 4 H),  $\tau$  7.1–7.5 (m, 2 H). Pertinent mass spectral peaks  $m/e$  (rel. intensity): 174 (0.4), 133 (100), 105 (14), 77 (15), 76 (4), 51 (9).

**Hydrogenation of IV.** A solution of IV (87 mg) in methanol (10 ml) was hydrogenated over palladium (50 mg, 5 % Pd/ $\text{BaSO}_4$ ) at room temperature and atmospheric pressure. After 20 min 1 molar equivalent of hydrogen had been consumed. The catalyst was filtered off and the solvent evaporated leaving V, which was purified by preparative GLC using the same conditions as above (retention time 8 min) and collected as an oil,  $[\alpha]_{\text{D}}^{25} - 55^\circ$  (c 1.0, chloroform). IR spectrum:  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 1778(s)  $\text{cm}^{-1}$ . NMR spectrum ( $\text{CCl}_4$ ):  $\tau$  2.0–2.7 (m, 4 H),  $\tau$  4.4–4.7 (m, 1 H),  $\tau$  7.7–8.9 (m, 4 H),  $\tau$  9.05 (deformed triplet, 3 H,  $J = 6$  cps). Pertinent mass spectral peaks  $m/e$  (rel. intensity): 176 (4), 133 (100), 105 (36), 77 (16), 76 (5), 51 (9).

**Synthesis of 3-propylphthalide.** Propylidene-phthalide<sup>6</sup> was hydrogenated under the same conditions as IV, giving 3-propylphthalide, previously prepared by Gucci<sup>7</sup> and Tasman.<sup>8</sup> Its spectral properties (NMR, IR, MS) were identical with those of IV.

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