

1003. Alkaloids of the Leguminosae. Part XXVIII.¹ Virgiline and O-(2-Pyrrolylcarbonyl)virgiline in *Virgilia oroboides*.

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Virgiline is corrected to $C_{15}H_{24}N_2O_2$ and further derivatives are made. O-(2-Pyrrolylcarbonyl)virgiline is identified in *Virgilia oroboides* branchlets.

VIRGILINE² was assigned the formula $C_{16}H_{26}N_2O_2$. Gerrans and Harley-Mason³ isolated this base from seeds of *Virgilia oroboides* (Berg.) Salter (*V. capensis* Lam.) and showed it to be 13-hydroxyaphylline (OH axial), $C_{15}H_{24}N_2O_2$. They also obtained "orobidine," the pyrrole-2-carboxylic ester of 13-hydroxylupanine from the seeds, and Goosen⁴ reported a base of this structure as "calpurnine" from the allied *Calpurnia subdecandra*. Independent studies of the alkaloids of *V. oroboides* branchlets supported the formula $C_{15}H_{24}N_2O_2$ for virgiline and led to preparation of further derivatives which might be reducible to known quinolizidine bases. A second crystalline ester base, usually the dominant "acetone-insoluble" base was identified as O-(2-pyrrolylcarbonyl)virgiline. The proportions of virgiline and ester varied greatly in the several plant samples examined.

EXPERIMENTAL

Infrared measurements were made on a Perkin-Elmer Infracord 137 spectrophotometer. R_F values are for the butan-1-ol-36% hydrochloric acid-water (50 : 7.5 : 17) system on Whatman No. 1 discs.⁵ Identities were established by infrared spectroscopy and mixed m. p. determinations.

Isolation of Bases.—Flowering branchlets (3.49 kg.) were extracted continuously with 70% ethanol and the extract concentrated to 4 l. Acetic acid (30 ml.) was added and the precipitate filtered off. The solution was made alkaline (NaOH), extracted with chloroform, and the bases extracted into dilute hydrochloric acid. Basification and chloroform extraction gave the alkaloids (37.7 g., R_F 0.58, 0.71, 0.81, and 0.90). A further 0.7 g. of alkaloid was extracted from the first aqueous phase after reduction with zinc and hydrochloric acid. Treatment of the total alkaloid with acetone left a crystalline fraction (9.0 g., R_F 0.58, 0.90). This was put on an alumina column (Grade IV; 26 × 4.5 cm.) in chloroform, and eluted with this solvent. Recrystallizations, and further chromatography of mixed fractions, gave, from the first-eluted fractions, the ester base (4.75 g.), m. p. 271°, R_F 0.90, and, from later fractions, virgiline (1.9 g.), m. p. 248°, R_F 0.58. Separation of bases was also achieved on large Whatman No. 3 discs with butan-1-ol-acetic acid-water (50 : 5 : 15); virgiline, R_F 0.35; ester base, R_F 0.73.

Virgiline.—Recrystallized from methanol-acetone, this had m. p. 248—249°, $[\alpha]_D^{25} -39^\circ$ (c 0.9 in EtOH) [Found: C, 66.4, 67.1; H, 9.0, 9.3; N, 10.7%; equiv. (titration with HCl) 277. Calc. for $C_{15}H_{24}N_2O_2$: C, 67.1; H, 9.1; N, 10.6%; equiv. 264], ultraviolet end-absorption from 240 m μ (log ϵ at 210 m μ , ca. 4), ν_{max} . (Nujol) 3400 (OH), 1615 cm.⁻¹ (lactam C:O), faint "trans-bands" ⁶ in the 2700—2800 cm.⁻¹ region. The hydrochloride, prepared by titration of the base with dilute hydrochloric acid and recrystallized from acetone, had m. p. 268—272° [Found: (dried at 80°/20 mm.) C, 59.8; H, 8.1; N, 8.6. Calc. for $C_{15}H_{25}ClN_2O_2$: C, 59.9; H, 8.3; N, 9.3%, ν_{max} . (Nujol) 3430; (OH), 3210s, 2750w, 2190w, 1680m, 1600 cm.⁻¹ (lactam C:O). The methiodide² had m. p. 172—176° (decomp.) (from methanol-acetone) [Found: C, 44.9; H, 6.8; N, 6.7. Calc. for $C_{16}H_{27}IN_2O_2 \cdot H_2O$: C, 45.3; H, 6.8; N, 6.6%].

Virgiline (93 mg.), acetic anhydride (0.2 ml.), and pyridine (0.1 ml.) were shaken for 4 days at 25° until virgiline had dissolved. The residue after evaporation was dissolved in very dilute sodium hydroxide and the basic fraction extracted with chloroform. Recrystallization from acetone-water gave waxy plates of O-acetylvirgiline, m. p. 181° [Found: C, 66.4; H, 8.55; N, 9.3. Calc. for $C_{17}H_{26}N_2O_3$: C, 66.6; H, 8.5; N, 9.1%], ν_{max} . (Nujol) 1635 (lactam C:O), 1725 (acetate), 1245 cm.⁻¹ (acetate), no O-H stretching bands.

¹ Part XXVII, *J.*, 1964, 4613.

² White, *New Zealand J. Sci. Technol.*, 1946, **27**, B, 478.

³ Gerrans and Harley-Mason, *Chem. and Ind.*, 1963, 1546.

⁴ Goosen, *J.*, 1963, 3067.

⁵ White, *New Zealand J. Sci. Technol.*, 1957, **38**, B, 707.

⁶ Wicwiorowski and Skolik, *Bull. Acad. polon. Sci., Ser. Sci. chim.*, 1962, **10**, 1.

5244 *White: Alkaloids of the Leguminosae. Part XXVIII.*

Virgiline (174 mg.), methanesulphonyl chloride (0.2 ml.), and pyridine (1 ml.) were kept at 0° for 2 days. The residue after evaporation was dissolved in aqueous sodium carbonate and chloroform, and the chloroform layer was shaken with dilute hydrochloric acid. Addition of sodium hydroxide to the acid layer and extraction with chloroform gave a basic fraction (179 mg.). This was put on an alumina column (Grade IV; 12 × 1.1 cm.) in benzene. Elution with benzene gave two dark zones separated by a colourless middle band which was collected, giving crystals (133 mg.). Recrystallization from benzene gave plates of *O-methanesulphonyl-virgiline*, m. p. 149° (Found: C, 56.2; H, 8.2; N, 8.0. $C_{16}H_{26}N_2O_4S$ requires C, 56.1; H, 7.9; N, 8.2), ν_{max} (Nujol) 1630 (lactam C=O), 1330, 1170 cm^{-1} (sulphonate), no O-H stretching bands. A toluene-*p*-sulphonyl derivative was not obtained by several procedures.

Virgiline (100 mg.) was heated at 60° for 1 hr. with thionyl chloride (0.3 ml.). The residue after evaporation was dissolved in ice-cold dilute hydrochloric acid and chloroform. Chloroform extraction removed a coloured impurity. The aqueous layer was made alkaline and extracted with chloroform to give a crystalline residue (95 mg.), which recrystallized from acetone as colourless plates (30 mg.) of 13-chloroaphylline, m. p. 180° (Found: C, 63.7; H, 8.2; Cl, 13.1; N, 9.35. $C_{15}H_{23}ClN_2O$ requires C, 63.7; H, 8.2; Cl, 12.6; N, 9.9%), ν_{max} (Nujol) 1635 (lactam C=O), faint "trans-bands" in the 2700–2800 cm^{-1} region, no O-H stretching bands. 13-Chloroaphylline was unaltered after refluxing with alcoholic potassium hydroxide and after catalytic hydrogenation (PtO₂) in methanol or dilute hydrochloric acid.

Sulphuric acid was added to dissolve virgiline (0.59 g.) in water (30 ml.), and solid potassium permanganate added at 50° until a pink colour persisted for a few minutes. The precipitate was dissolved with sulphur dioxide and the solution was extracted with chloroform. The glass from evaporation of this solvent was repeatedly recrystallized from benzene giving radiating blades of a neutral hydroxy-dilactam, probably 17-oxovirgiline, m. p. 206° [Found: (for compound dried at 80°/20 mm.) C, 64.6, 64.7; H, 7.9, 7.8; N, 9.9, 9.4. $C_{18}H_{22}N_2O_3$ requires C, 64.7; H, 7.85; N, 9.9%], ν_{max} (Nujol) 3500 (OH), 1620s cm^{-1} (lactam C=O), no bands characteristic of an organic- or amino-acid.

(-)-*O*-(2-Pyrrolylcarbonyl)virgiline.—The fraction, R_F 0.90, of the plant extract, recrystallized from ethanol, formed plates of the (-)-*ester*, m. p. 271°, $[\alpha]_D^{20} -23^\circ$ (c 0.7 in EtOH) (Found: C, 67.5; H, 8.1; N, 11.6. $C_{20}H_{27}N_3O_3$ requires C, 67.2; H, 7.55; N, 11.8%), λ_{max} (MeOH) 267 $m\mu$ ($\log \epsilon$ 4.23) and end-absorption to 210 $m\mu$, ν_{max} (Nujol) 3230 (NH), 1695 (ester C=O), 1620 (lactam C=O), 1550 cm^{-1} (pyrrole nucleus). The base, treated with an excess of dilute hydrochloric acid and recrystallized from ethanol-acetone, formed needles of the *hydrochloride*, m. p. 293° (decomp.) (Found: C, 60.9; H, 7.3; N, 10.1. $C_{20}H_{28}ClN_3O_3$ requires C, 61.0; H, 7.15; N, 10.7%), ν_{max} (Nujol) 3130 (NH), 2470w, 2510w, 1695 (ester C=O), 1640 cm^{-1} (lactam C=O). Usual procedures failed to give an acetyl derivative or methiodide.

The ester (126 mg.), ethanol (10 ml.), and aqueous sodium hydroxide (8*N*; 2 ml) were refluxed for 2 hr., water was added, and the base extracted with chloroform giving virgiline (83 mg.). The aqueous phase, on acidification and extraction with ether, gave an acid (35 mg.) which recrystallized from ether as colourless plates, m. p. 206° (subliming and decomp. to oily droplets), λ_{max} (EtOH) 263 $m\mu$ ($\log \epsilon$ 4.1), λ_{max} (water and NaOH) 257 $m\mu$, ν_{max} (Nujol) 3400 (NH), 2750–2550 (acid), 1660br (acid C=O), 1550 cm^{-1} (pyrrole nucleus); these properties are close to reported values^{4,7,8} for pyrrole-2-carboxylic acid, and identity was established by comparison with a synthetic specimen.⁹

Virgiline (13.7 mg.), pyrrole-2-carboxylic acid (8 mg.), and dicyclohexylcarbodi-imide (18 mg.) in dichloromethane (1 ml.) were kept at 20° for 4 days. The urea was filtered off, the solution evaporated, and the part soluble in dilute hydrochloric acid washed with ether. The basic fraction (11 mg.), extracted by chloroform, was put on an alumina column (Grade IV). Elution with chloroform gave first the ester (3.2 mg.), later fractions gave virgiline (4.6 mg.).

[*Note added in proof*: Gerrans and Harley-Mason (*J.*, 1964, 2202) accept the name calpurnine for the base, and establish the structure of virgiline.]

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⁷ Scrocco and Nicolaus, *Atti. Acad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1956, 20, 795.

⁸ Hodge and Rickards, *J.*, 1963, 2543.

⁹ McCay and Schmidt, *J. Amer. Chem. Soc.*, 1926, 48, 1935.