ALKALOIDS OF *VOACANGA SCHWEINFURTHII* STAPF

PART I. VOACAMINE AND VOBTUSINE

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Two alkaloids, voacamine and vobtusine, have been isolated from the stem bark of *Voacanga schweinfurthii* Stapf (Apocynaceae).

THE presence of alkaloid in plants of the genus *Voacanga* was noted by Greshoff[1] in 1890, but detailed investigations have only recently been made on several species, especially *V. africana* Stapf from which ten alkaloids have been isolated[2]. Vobtusine and voacamine were isolated from *V. africana* and *V. thouarsii* Roem and Schult (var. *obtusa* K. Schum) by Janot and Goutarel[3]. Vobtusine and voacangine were reported in *V. dregei* E. Mey by Schuler and others[4], but these alkaloids were not found by Neuss and Cone[5] who isolated a new base, dregamine. Vobtusine has also been reported[6] in the Apocynaceous plant *Callichilia subsessilis* Stapf.

Stem bark of *Voacanga schweinfurthii* was kindly supplied by Dr. D. B. Fanshawe, Division of Forest Ecology, Forest Department, Kitwe, N. Rhodesia through Mr. J. J. Lewis, of the University of Glasgow. Isolation of voacamine and vobtusine from this material was by the method of Percheron[7]. Two strongly basic fractions were chromatographed on alumina to give voacamine and vobtusine, each verified by melting point, rotation, ultra-violet and infra-red spectra, and micro-analysis.

EXPERIMENTAL

The bark (2·4 kg.), in No. 60 powder, was percolated to exhaustion (negative Meyer's Reagent) with ethanol (70 per cent, 45 l.). The first 15 l. of percolate was reduced to about 1 l. by distillation under reduced pressure at a temperature below 50°. The remaining thick dark brown, aqueous suspension was shaken with ethyl acetate (1·25 l.) in which most of the solid matter dissolved. The aqueous fraction was separated and shaken with further quantities of ethyl acetate (2 × 500 ml., 1 × 200 ml.). The bulked ethyl acetate solutions, after washing with distilled water (400 ml.), constituted Solution I.

To the partially extracted aqueous fraction above was added ethyl acetate (1 l.) and sufficient sodium carbonate to adjust to pH 9. After shaking and separating, the aqueous fraction was extracted with further quantities of ethyl acetate (1 l., 800 ml., 400 ml., and 5 × 200 ml.). The bulked ethyl acetate solution was divided, to facilitate handling, and each half washed with distilled water (400 ml.). The two ethyl acetate solutions constituted Solution II.

Solution I was extracted with acetic acid (5 per cent, 4 × 500 ml., 1 × 200 ml.) each extract being washed with the same ethyl acetate

(500 ml.). The combined acid fractions were basified with solution of ammonia (20 per cent) in the presence of ethyl acetate (1 l.). After shaking, the aqueous portion was separated and further extracted with ethyl acetate (2 × 500 ml., 1 × 200 ml.), the combined extracts being washed with distilled water (400 ml.). The ethyl acetate solution was dried (Na_2SO_4) and filtered, and the solvent removed under reduced pressure, to leave a residue of crude strong base (Residue IA, 3·66 g.).

Solution I, after acetic acid extraction, was extracted with hydrochloric acid (5 per cent, 2 × 500 ml., 6 × 200 ml.), the acid fractions washed with ethyl acetate (500 ml.), bulked, basified with solution of ammonia (20 per cent) and extracted with ethyl acetate (1 l., 2 × 500 ml., 1 × 200 ml.). The combined extract, after washing with distilled water (400 ml.), was dried (Na_2SO_4), filtered, and evaporated to dryness under reduced pressure to leave a residue of crude weak base (Residue IB, 0·73 g.).

Each half of Solution II was subjected to the extraction procedure described for Solution I, using different volumes of solvent. Acetic acid (5 per cent, 500 ml., 7 × 200 ml.) followed, after basifying, by ethyl acetate (500 ml., 3 × 250 ml.) gave a residue of crude strong base (Total Residue IIA, 12·22 g.). Hydrochloric acid (5 per cent, 500 ml., 8 × 250 ml.) followed, after basifying, by ethyl acetate (500 ml., 250 ml.) gave a small residue of crude weak base (Total Residue IIB, 1·51 g.).

The remaining 30 l. of initial percolate, extracted as above, gave the following yields of crude base: IA, 1·46 g.; IB, 0·72 g.; IIA, 0·70 g.; IIB, 0·02 g.

Purification of Strong Bases

The dried crude strong bases from the first 15 l. of percolate were shaken with warm benzene (Residue IA, 25 ml.; Residue IIA, 75 ml.) and after cooling the small amount of insoluble material was filtered off and the filtrates evaporated to dryness under reduced pressure. The residues were redissolved in benzene (IA, 15 ml., IIA, 50 ml.) and the solutions chromatographed on alumina (Merck) using 100 g. and 360 g. of adsorbent for residues IA and IIA respectively.

Development and elution of each chromatogram began with benzene, followed by ether, ether: methanol, and methanol. The various fractions of eluant were evaporated to dryness, the residues weighed (Table I) and attempts made to crystallise each from dry methanol.

The residues from the second fraction from each column gave, after several re-crystallisations from methanol and drying *in vacuo* over phosphorus pentoxide, white acicular crystals of voacamine (from IA, 0·06 g.; from IIA, 0·91 g.).

The residues from the third fraction from each column were shaken with methanol, the insoluble material filtered off and dissolved in methylene chloride. On addition of methanol to this solution and warming, white crystals of vobtusine were obtained and these were purified by repeating the above process. (Yield from IA, 0·10 g.; from IIA, 1·25 g.)

Voacamine. Recrystallised from methanol, corrected m.p. 223° (decomp.) readily soluble in chloroform, sparingly soluble in methanol. $[\alpha]_D^{20} = -50°$ (c = 1 in chloroform) ultra-violet spectrum (absolute ethanol) with absorption peaks at 225 mμ (log ε = 4·72) and 295 mμ (log ε = 4·28) and infra-red spectrum with absorption bands at 3,380, 2,900, 1,725, 1,710, 1,460, 1,370, and 736 cm.$^{-1}$, agreed with published[7] results. (Found: C, 71·00; H, 7·5; N, 7·8, $C_{45}H_{56}O_6N_4$ requires C, 72·3; H, 7·6; N, 7·8 per cent.)

Vobtusine. Precipitated from methylene chloride, uncorrected m.p. 305° (decomp.), readily soluble in chloroform, insoluble in methanol, deep blue colour with concentrated nitric acid. $[\alpha]_D^{20} = -295°$ (c = 1 in chloroform). Ultra-violet spectrum (absolute ethanol) with absorption peaks at 220, 265, 300, and 325 mμ agreed with results of Janot and Goutarel[3] and infra-red spectrum with absorption bands at 3,340, 1,680, 1,610, 772, 746, 732, corresponded to published[4,6] spectra. (Found: C, 70·3; H, 7·1; N, 7·65. $C_{42}H_{48}O_6N_4$ requires C, 71·6; H, 6·9; N, 7·95 per cent.) The $[\alpha]_D^{20}$ value, although lower than the published[3] figure (− 321°), was the same as that obtained by us on a genuine sample of vobtusine. The slightly low analysis is accounted for by the method of drying which has an effect on the results[6]. Our sample was dried (P_2O_5) *in vacuo* at 55° for 4 hours and at 20° for 24 hours.

TABLE I

WEIGHT OF ALKALOID REMOVED FROM CHROMATOGRAMS OF CRUDE BASE BY VARIOUS SOLVENTS

Material	Fraction	Eluant	Volume (ml.)	wt. (g.)
Residue IA	1	benzene	600	0·314
	2	ether	800	0·736
	3	ether/methanol (1 per cent)	800	1·014
	4	ether/methanol (2 per cent)	400	0·230
	5	ether/methanol (5 per cent)	400	0·166
	6	ether/methanol (10 per cent)	300	0·123
	7	methanol	100	0·167
Residue IIA	1	benzene	900	0·045
	2	ether	3,000	2·192
	3	ether/methanol (1 per cent)	3,000	2·701
	4	ether/methanol (5 per cent)	1,200	1·241
	5	methanol	300	1·121

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After Mr. Newcombe presented the paper there was a DISCUSSION. The following points were made.

Voacamine and vobtusine were the main alkaloids of *V. schweinfurthii* Stapf. Vocamine was known to have a 3-methoxy di- indole structure, and vobtusine was also a double indole structure with methoxy groups. Neither had been tested pharmacologically and the claimed cardiotonic activity of the alkaloids of *V. africana* had not been confirmed by others.