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SHORT COMMUNICATION

ALKALOIDS AND TERPENOIDS OF *BLEEKERIA VITIENSIS**

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Abstract—The alkaloidal components of the Ochrosiinae subtribe of the Rauvolfieae are reviewed and the phytochemical investigation of *Bleekeria vitiensis* has yielded ellipticine, 9-methoxyellipticine, isoreserpiline isoreserpiline-ψ-indoxyl and ursolic acid

THE TAXONOMY of the thirty-six or so small trees of the Ochrosiinae (tribe Rauvolfieae, subfamily Plumerioideae of the Apocynaceae) is complex.[1] Individual species are often referred to the genera *Ochrosia*, *Excavatia*, *Bleekeria* or *Bleekaria* but there is a good deal of synonymy involved.

Table 1 lists the members of the Ochrosiinae which have been subjected to chemical scrutiny and shows the part of the plant examined, the alkaloids which have been characterized and the amount (where known) expressed as a percentage of the dry plant material. Unfortunately, only rarely have different parts of the same plant been studied and, in most cases, quantitative results have not been quoted. Nevertheless, all species contain indole alkaloids of which ellipticine, 9-methoxyellipticine, reserpine and isoreserpiline are the most important Isoreserpiline occurs in eight of the ten species examined so far, 9-methoxyellipticine in six, ellipticine in five and reserpine in three.

Interest in the Ochrosiinae has been stimulated by the fact that ellipticine and 9-methoxyellipticine have wide spectrum antitumour activity, and it is the intention of the present study to evaluate the Ochrosiinae as a commercial source of these alkaloids. In this, the first of a series of papers, we report upon the extractives of *Bleekeria vitiensis* a small tree indigenous to the island of Fiji. In three separate experiments, the leaves and leaf stems, the bark and trunk wood and the roots and root bark have been studied, the results are included in Table 1.

Ellipticine is not present in the leafy material but occurs in the other organs of the plant whereas isoreserpiline is richest in the leaves but only present in trace amounts in the trunk and roots 9-Methoxyellipticine is the major alkaloidal component and occurs in all parts of the plant examined Moreover, the bark and wood of *Bleekeria vitiensis* would appear to represent the best natural source of this alkaloid yet discovered.

The only other alkaloid isolated from this plant is isoreserpiline-ψ-indoxyl, but whether this compound is a true natural product or merely an artefact of isoreserpiline is a matter

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* Part I in a projected series "Extractives of the Ochrosiinae"

[1] G H SVOBODA, G A POORE and M L MONTFORT, *J Pharm Sci* 1720 (1963)

Table 1

Plant and source	Part of plant	Ellipticine	9-Methoxy-ellipticine	Isoreserpiline	Other alkaloids	Ref
Ochrosia elliptica Labill Florida, U S A	Leaves and leaf stems	√(0 004%)	√(0 007%)	√(0 28%)	Elliptinine ($C_{20}H_{24}O_2N_2$)	4, 5
Ochrosia moorei F Muel Australia (These are specimens of *O elliptica* transplanted originally from Trinidad)		—	—	√	Elliptamine ($C_{24}H_{30}O_5N_2$)	6
Ochrosia coccinea (Tejsmann & Binnendijk) Kiq (syn *Excavatia coccinea* (Tejsmann & Binnendijk) Mgf New Guinea	Bark and leaves	—	√	—		5
		—	—	—	Reserpine	8
		—	—	√	Elliptamine	6
Ochrosia sandwicensis (ADC A Gray (syn *Bleekaria calocarpa*) Hawaii	Leaves	√	√	—		4
	Trunk and root bark	√(0 04%)	√	—	10-Hunterburnine-α-methochloride (0 007%), 10-Hydroxydihydrocorynantheol methochloride	9
	Bark	—	—	—	N-(b)-Methylisoreserpilinium chloride	10
Ochrosia malculata Jacq (syn *Ochrosia borbonica* Gmel or *Cerbera undulata* Reunion Island	Bark	—	√(0 015%)	—	Reserpine	1, 2, 3
Ochrosia poweri Bailey Queensland, Australia	Leaves and twigs	—	—	√	Reserpine, powerine ($C_{21}H_{26}O_4N_2$), poweridine ($C_{24}H_{30}O_5N_2$), poweramine ($C_{23}H_{30}O_4N_2$), elliptamine	6
	Stem	—	—	√(0 3%)	Elliptamine, ochropamine ($C_{22}H_{26}O_3N_2$), ochropine ($C_{23}H_{25}O_4N_2$), powerchrine ($C_{22}H_{26}O_3N_2$)	12
Ochrosia oppositifolia (Lamk) K Schum Mascarene and Seychelle Islands	Bark	—	√	—		7
Ochrosia Vieillardii Guil New Caledonia	Leaves	√(0 0079%)	—	√(0 085%)	10-Methoxydihydrocorynantheol	11
Ochrosia glomerate Valeton New Guinea	—	—	—	√	Elliptamine	6
Ochrosia silvation Dan New Caledonia	Trunk bark	√(0 13%)	—	√(0 58%)	Apparicine (0 012%)	13
Bleekeria vitiensis (Markgraf) A C Smith syn *Ochrosia vitiensis* or *Excavatia vitiensis* Fiji	Leaves and leaf stems	—	√(0 003%)	√(0 05%)	Isoreserpiline-ψ-indoxyl (0 001%)	
	Bark and wood	√(0 001%)	√(0 083%)	√(0 002%)	Isoreserpiline-ψ-indoxyl (trace)	
	Roots and root bark	√(0 005%)	√(0 024%)	√(trace)	Isoreserpiline-ψ-indoxyl (trace)	

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[2] C C J Culvenor and J W Loder, *Abstracts 152nd Meeting of Amer Chem Soc* p 29 Med Chem Sect , New York (1966)

[3] J Poisson and C Miet, *Ann Pharm Franc* **25,** 523 (1967)

[4] S Goodwin, A F Smith and E C Horning, *J Am Chem Soc* **81,** 1903 (1959)

[5] J W Loder, *Austral J Chem* **19,** 1947 (1966)

[6] F A Doy and B P Moore, *Austral J Chem* **15,** 548 (1962)

[7] A Buzas, M Osowiecki and O Schindler, *Compt Rend* **247,** 1390 (1958)

[8] E Macko and R F Raffauf, *J Med Pharm Chem* **2,** 585 (1960)

[9] W Jordan and P J Scheuer, *Tetrahedron* **21,** 3731 (1965)

[10] P J Scheuer and J T H Metzger, *J Org Chem* **26,** 3069 (1961)

[11] C Kan Fan, B C Das, P Potier and M Schmid, *Phytochem* **9,** 1351 (1970)

[12] B Douglas, J L Kirkpatrick, B P Moore and J A Weisbach, *Austral J Chem* **17,** 248 (1964)

[13] J. P Cosson and M Schmid, *Phytochem* **6,** 1353 (1970)

for conjecture Isoreserpiline-ψ-indoxyl has been reported to co-occur with isoreserpiline in *Aspidosperma discolor*[14] but the compound has not been isolated before from members of the Ochrosiinae

Bleekeria vitiensis has also been examined for non-alkaloidal compounds, the leaves contain a large amount of waxes which form a complex mixture GLC analysis shows at least twelve components. The bark and root bark also contain waxy materials although in much smaller quantities than the leaves Phenolic derivatives were not found in amounts sufficient for characterization but the triterpenoid ursolic acid was isolated from the leaves in 0·34% yield

EXPERIMENTAL

All m ps are uncorrected SiO_2 refers to MN silica gel and Al_2O_3 to Merck basic alumina grade 1

Leaves and leaf stems 3 kg extracted exhaustively first with petrol (60–80°) (A), then EtOAc (B) and finally with MeOH (C)

Extract A Removal of the solvent gave dark green gum which was chromatographed on SiO_2 and eluted with petrol (60–80°) (1), 15% $CHCl_3$/petrol (2) and 20% $CHCl_3$/petrol (3).

(1) This afforded a gummy residue, GLC analysis of which showed at least 12 components High vac distillation afforded several fractions, one of which crystallized to give colourless solid, m p 53° Precision mass measurement of this material indicated the molecular formula $C_{31}H_{64}$ Other fractions could not be purified but mass and IR spectroscopy showed the presence of hydrocarbon derivatives of high molecular weight (2) Evaporation yielded a waxy solid which recrystallized from acetone as colourless prisms, m p 76°. (3) From this fraction a similar compound m p 70° (acetone) was obtained Spectral analysis shows that both of these compounds are saturated aliphatic esters with molecular weights above 800

Extract B The solvent volume was reduced from 10 l to approx 2 l and this was then re-extracted with 2 N HCl Basification of the aqueous phase yielded 6 g of crude alkaloids The residual EtOAc extract was evaporated almost to dryness and allowed to cool, whereupon a solid (11 3 g) separated This was collected and purified by chromatography (SiO_2) and repeated recrystallization from EtOH affording, eventually, colourless needles of ursolic acid, m p 276–278° Further purification by sublimation gave material m p 280–282° (lit,[15] 280°) (Yield 10 g, 0 34%) R_f 0 4 SiO_2, 5% MeOH/$CHCl_3$ (red colour when developed with 50% H_2SO_4/EtOH followed by heating at 100°) (Found C, 78 9, H, 10 4 Calc for $C_{30}H_{48}O_3$ C,78 95, H, 10 5%)

The crude alkaloids were purified by chromatography on Al_2O_3 and individual compounds were characterized as follows

Isoreserpiline (eluting solvent 50% $CHCl_3$/petrol) 1 5 g (0 05%) colourless needles from ether m p 210° (lit,[11] 213°) R_f 0 85 Al_2O_3 (red fluorescence in UV) (Found C,66 75, H, 6 95, N, 6 8 Calc for $C_{23}H_{28}N_2O_5$ C, 67 0, H, 6 8, N, 6 8%)

Isoreserpiline-ψ-indoxyl (60% $CHCl_3$/petrol) 30 mg (0 001%), pale yellow needles from ether, m p 243–247°, sublimation raised m p 250–252° dec (lit,[14] 250–253°) R_f 0 83 Al_2O_3, $CHCl_3$ (bright green fluorescence in UV) (Found G, 64 8, H, 6 5, N, 6 6 Calc for $C_{23}H_{28}N_2O_6$ C, 64 5, H, 6 6, N, 6 5%) This material was identical (mixed m p, IR, NMR, TLC) with an authentic specimen

9-Methoxyellipticine (4 8% MeOH/$CHCl_3$) 30 mg yellow prisms from EtOAc, m p 273–276°, further purified by sublimation, m p 283–285° (lit,[4] 280–285°) R_f 0 7 Al_2O_3, 6% MeOH/$CHCl_3$ (red fluorescence in UV, maroon colour in I_2 vap) (Found C, 78 1, H, 5 8, N, 10 4 Calc for $C_{18}H_{16}N_2O$ C, 78 2, H, 5 8, N, 10 1%) This material was identical (mixed m p, IR, NMR, TLC) with natural 9-methoxyellipticine

Extract C The combined extracts were evaporated and the residue dissolved in $CHCl_3$ and re-extracted with 2 N HCl Basification of the aqueous extracts followed by chromatographic purification yielded a further 60 mg of 9-methoxyellipticine (total 90 mg, 0 003%) Trace amounts of isoreserpiline and isoreserpiline-ψ-indoxyl were also detected The base free extract was evaporated to give a small quantity of ursolic acid (10 mg) Further evaporation afforded intractible tars

Bark and wood 8 kg extracted first with petrol to remove waxes and then with MeOH The work-up procedure of the methanol extract parallels that of *C* above and yielded isoreserpiline (160 mg, 0 002%) and a mixture of ellipticine and 9-methoxyellipticine together with trace amounts of isoreserpiline-ψ-indoxyl The mixture of ellipticine and 9-methoxyellipticine was separated by chromatography on Al_2O_3 eluting with $CHCl_3$ First fractions contained ellipticine (80 mg, 0 001%), pale yellow prisms from benzene m p 310–312° (lit,[4] 311–315°) R_f 0 6, Al_2O_3, $CHCl_3$ (blue–green fluorescence under UV) (Found C, 82 5, H, 5 9, N, 11 3

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[14] N Dastoor and H Schmid, *Experientia* **19**, 297 (1963)

[15] R E Corbett, H Young and R. S Wilson, *Austral J Chem* **17**, 712 (1964)

calc. for $C_{17}H_{14}N_2$ C, 82.9, H, 5.7, N, 11.4%.) From the remaining fractions 9-methoxyellipticine (6.65 g, 0.083%) was isolated.

Roots and root bark. 2 kg. This material was treated in the same manner as the bark and wood. In this way ellipticine (100 mg, 0.005%) and 9-methoxyellipticine (480 mg, 0.024%) were isolated. Additionally trace amounts of isoreserpiline and isoreserpiline-ψ-indoxyl were detected.

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Key Word Index—*Bleekeria vitiensis*, Apocynaceae, ellipticine, isoreserpiline, indole alkaloids.