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MAJVININE: A NEW INDOLE ALKALOID OF *VINCA MAJOR*

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Key Word Index—*Vinca major*; Apocynaceae; periwinkle; indole alkaloids; majvinine.

Abstract—A new alkaloid, majvinine, was isolated from the aerial parts of *Vinca major*. Its structure was determined by chemical and spectroscopic investigations.

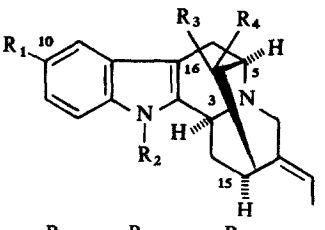
INTRODUCTION

Our previous work on the alkaloidal principles of *Vinca major*. L. var. *major* [1] led to the isolation of a number of indole alkaloids [2] and the monoterpenoid alkaloid venoterpine (RW-47) [3]. In the present paper we report the isolation and structure elucidation of another new indole alkaloid from the same source.

RESULTS

The new alkaloid, majvinine, was isolated in 0.0002% yield from the petrol-soluble fraction of the methanolic extract of the aerial parts of *Vinca major* L. var. *major*. Majvinine, $C_{21}H_{24}N_2O_2$, gave the colour reactions (Fröhde: deep green, Hopkins–Cole: deep blue) characteristic of 2,3-disubstituted indole derivatives. The alkaloid showed the typical UV spectrum of a 10-methoxytetrahydro-β-carboline derivative (λ_{max}^{EtOH} 225, 283 nm; log ε 4.42, 3.99; $\lambda_{max}^{1\%HClO_4/EtOH}$ 221, 277 nm; log ε 4.52, 3.99).

The presence of an aldehyde group attached to a —CH— group in majvinine was indicated by its IR (ν_{max}^{Nujol} 2700, 1718 cm^{-1}) and 60 MHz NMR spectra (δ 9.73, 1H, *d*, *J* 1.5 Hz). Borohydride reduction of majvinine afforded a dihydro derivative, $C_{21}H_{26}N_2O_2$ (M^+ 338.1980, calc. for $C_{21}H_{26}N_2O_2$: 338.1994), which lacked the carbonyl absorption in its IR spectrum, and showed a M—CH_2OH peak (*m/e* 307) in its mass spectrum.



	R_1	R_2	R_3	R_4
(1)	MeO	H	H	CHO
(2)	MeO	H	H	CH_2OH
(3)	MeO	H	CH_2OH	H
(4)	MeO	Me	H	CHO
(5)	H	H	H	CHO
(6)	MeO	Me	H	CH_2OH

The 60 MHz NMR spectrum ($CDCl_3$) of the new alkaloid was very similar to that of 10-methoxyvellosimine (1) [2, 4], previously isolated from this plant source [2]. The only difference was the absence of the indole —NH— signal in majvinine, and the appearance instead of a three-proton singlet at δ 3.60 due to the $N_{(a)}$-methyl grouping. The absence of the indole —NH— was also indicated by its IR spectrum. The mass spectral fragmentation of majvinine and dihydromajvinine were very similar to those observed for 10-methoxyvellosimine (1) [2, 4], and lochnerine (2) [2] and lochvinerine (3) [2] respectively. However, the fragments containing the indole moiety in the former series were displaced to higher mass regions by 14 units compared to the latter, an observation in agreement with the presence of a $N_{(a)}$-methyl group in majvinine. The structure and stereochemistry of the new base could thus be settled as $N_{(v)}$-methyl-10-methoxyvellosimine (4) from the spectral data discussed above and from the following considerations. The absolute stereochemistry at C-15 is suggested from biogenetic theory [5, 6]. The configuration at this centre also determines those at C_3 and C_5, as depicted in (4), as otherwise the formation of the rigid pentacyclic ring system would not be possible. The appearance of the formyl proton signal at the normal value of δ 9.73 resembling the chemical shift (δ 9.58 in liq. SO_2) of the aldehyde proton in vellosimine (5) [7] demonstrated that the formyl group at C-16 in (4) must be situated away from the aromatic nucleus. Had the formyl group been towards the indole nucleus the shielding effect from the π-electrons of the aromatic system would have caused the signal to shift upfield by about 1 ppm.

EXPERIMENTAL

Plant material. The plant *Vinca major* L. var. *major* was collected from the Long Islands in the Andamans situated in the Indian Ocean. The plant was identified by Dr. P. C. Dutta, Botany Department, Calcutta University. A voucher specimen, No. VM, has been preserved in our laboratory.

Isolation and properties of majvinine. The procedure for the isolation of the alkaloids has been described previously [2]. The basic material obtained from the petrol-soluble fraction of the methanolic extract was chromatographed over Brockmann Al_2O_3. The characterisation of reserpinine obtained in the

petrol–C_6H_6 (1:3) eluates, and 10-methoxyvellosimine (1) occurring in the C_6H_6–$CHCl_3$ (1:1) eluates have been reported earlier [2]. The C_6H_6 eluate from the same column contained a mixture of bases, which on careful rechromatography over Al_2O_3 furnished majvinine (yield: 15 mg; 0.0002%). Majvinine (4) crystallised as needles, mp 195–97° (dec) from C_6H_6. MS: M^+ 336.1818 (70%) ($C_{21}H_{24}N_2O_2$; calc. 336.1836), *m/e* 335.1765 (39%) ($C_{21}H_{23}N_2O_2$, calc. 335.1761), 321.1621 (8%) ($C_{20}H_{21}N_2O_2$, calc. 321.1605), 307.1831 (100%) ($C_{20}H_{23}N_2O$, calc. 307.1811), 293.1618 (17%) ($C_{19}H_{21}N_2O$, calc. 293.1654), 226.1118 (10%) ($C_{14}H_{14}N_2O$, calc. 226.1108), 198.0805 (12%) ($C_{12}H_{10}N_2O$, calc. 198.0795). IR (Nujol, cm^{-1}): 2700, 1718 (—CHO); 1620, 1585, 853, 837, 800 (1,2,4-tri-substituted C_6H_6). NMR (60 MHz, $CDCl_3$) (δ): 9.73 (1H, *d*, *J* 1.5 Hz, CHO), 7.17 (1H, *d*, J_o 8 Hz, C-12-H), 6.93 (1H, *d*, J_m 2.5 Hz, C-9-H), 6.80 (1H, *dd*, J_o 8 Hz, J_m 2.5 Hz, C-11-H), 5.36 (1H, *q* with further fine splitting, *J* 7 Hz, =CH—Me), 3.84 (3H, *s*, Ar—OCH_3), 3.60 (3H, *s*, $N_{(a)}$—CH_3), 1.61 (3H, double triplet, J_1 7 Hz, J_2 2 Hz, =CH—CH_3). The dihydroderivative 6, obtained by $NaBH_4$ reduction of 4, was obtained as an amorphous powder. MS: M^+ 338.1980 (calc. for $C_{21}H_{26}N_2O_2$, 338.1994) (72%), 337 (M—H) (70%), 323 (M—Me) (7%), 307 (M—CH_2OH) (36%), 293 (12%), 226 (11%), 213 (100%), 212 (85%), 198 (12%), 197 (16%).

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FUROQUINOLINE ALKALOIDS FROM *TYLOPHORA ASTHMATICA*

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Key Word Index—*Tylophora asthmatica*; Asclepiadaceae; furoquinoline alkaloids; γ-fagarine and skimmianine.

Furoquinoline alkaloids, *e.g.* γ-fagarine and skimmianine, have so far been found only in plants of the Rutaceae, [1] with one exception: skimmianine has been found as a minor alkaloid of *Vinca herbaceae* (Apocynaceae) [2] It is thus of some interest that we now report the isolation of two such alkaloids from *Tylophora asthmatica* of the Asclepiadaceae. We separately isolated basic material from the roots and aerial parts of the plant. The major alkaloids were the phenanthroindolizidine alkaloids reported previously [3, 4] One of the minor alkaloids of the roots, however, proved to be γ-fagarine and a minor base of the aerial parts was shown to be skimmianine.

This is a surprising observation since the Rutaceae and Asclepiadaceae are taxonomically unrelated (although the latter family is closely allied to the Apocynaceae). [5] Moreover, the biosynthesis of furoquinoline [6] and phenanthroindolizidine [7] alkaloids is quite different. The validity of our results is strengthened by the isolation of different furoquinoline bases from roots and aerial parts.

EXPERIMENTAL

Plant Source. Tylophora asthmatica, Wight et Arn, obtained originally through Dr. T. R. Govindachari, Ciba Research Centre, Bombay, India; greenhouse grown in Leeds.

Alkaloids were isolated as reported previously [3] except that initial fractionation by column chromatography was carried out on Kieselgel G nach Stahl [8] using MeOH in $CHCl_3$. The furoquinoline alkaloids appeared in front of tylophorine. Skimmianine was purified on Woelm Al_2O_3 (neutral; grade 1; benzene–chloroform) (yield: 9×10^{-4}% of dried plant material) and γ-fagarine by preparative TLC (Kieselgel G, 5% MeOH in $CHCl_3$) (yield: 8×10^{-4}%). The NMR and MS (including accurate mass determination on the molecular ions) corresponded to the authentic alkaloids [9]. In addition, direct comparison established identity on TLC (3 solvent systems) and HPLC; in the case of γ-fagarine further proof of identity was obtained by mp mmp and IR spectra.

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