# ALKALOIDS OF *RAUWOLFIA VERTICILLATA* (LOUR.) BAIL. OF HONG KONG.

## IDENTIFICATION OF VELLOSIMINE AND PERAKSINE, AND DEMONSTRATION FROM N.M.R. DATA THAT PERAKSINE IS A MIXTURE OF TWO EPIMERS*

By H. R. ARTHUR,† S. R. JOHNS,‡ J. A. LAMBERTON,‡ and (in part) S. N. Loo†

The known alkaloids yohimbine, δ-yohimbine, reserpine, serpentine, and ajmaline were previously isolated from *Rauwolfia verticillata* (Lour.) Bail. of Hong Kong, as well as three alkaloids of unknown constitution.[1] One of the latter alkaloids (RW47) has been shown to be a monoterpenoid alkaloid of the actinidine group,[2] but the alkaloids initially designated RB19 and RB20 remained for more detailed investigation.

Alkaloid RB19 was originally considered[1] to have the molecular formula $C_{26}H_{29}N_3O$, but the presence of a strong molecular ion peak at *m/e* 292 in the mass spectrum requires this formula to be revised to $C_{19}H_{20}N_2O$, and the physical constants re-determined on the purified alkaloid indicate that RB19 is identical with vellosimine[3] (I). The identification of RB19 as vellosimine has been confirmed by comparison with authentic vellosimine supplied by Professor H. Rapoport. Vellosimine was originally isolated from *Geissospermum vellosii*, and it was also obtained as an hydrolysis product from the alkaloid geissolosimine.[3]

The mass spectrum of alkaloid RB20 shows a molecular ion peak at *m/e* 310, indicating that it has the molecular formula $C_{19}H_{22}N_2O_2$, and not the previously assigned $C_{21}H_{28}N_2O_5$. The analytical results previously reported for this alkaloid[1] are misleading as they were determined on a sample of the chloroform adduct that is obtained when RB20 crystallizes from chloroform solution. Consideration of the spectroscopic evidence now available indicates that RB20 is identical with peraksine, an alkaloid isolated from *Rauwolfia perakensis* King & Gamble,[4] and purified RB20 was found to have the same melting point as that reported for peraksine. Comparison of RB20 with authentic peraksine has confirmed the identity of the two alkaloids.

* Manuscript received January 8, 1968.

† Chemistry Department, University of Hong Kong, Hong Kong.

‡ Division of Applied Chemistry, CSIRO Chemical Research Laboratories, P.O. Box 4331, Melbourne, Vic. 3001.

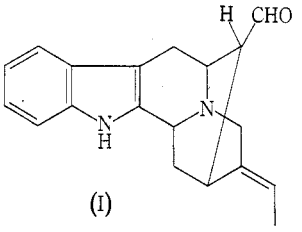
[1] Arthur, H. R., and Loo, S. N., *Phytochemistry*, 1966, **5**, 977.

[2] Arthur, H. R., Johns, S. R., Lamberton, J. A., and Loo, S. N., *Aust. J. Chem.*, 1967, **20**, 2505.

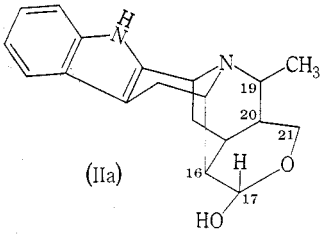
[3] Rapoport, H., and Moore, R. E., *J. org. Chem.*, 1962, **27**, 2981.

[4] Kiang, A. K., Loh, S. K., Demanczyk, M., Gemenden, C. W., Papariello, G. J., and Taylor, W. I., *Tetrahedron*, 1966, **22**, 3293.

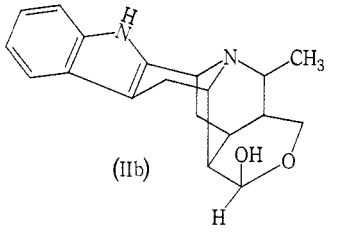
The structure (IIa) assigned to peraksine[4] was based on an X-ray crystallographic study of peraksine methiodide, but an interesting point has emerged from a study of the 100-Mc/s spectra of peraksine and *O*-acetylperaksine. In $CDCl_3$–$CD_3OD$ solution the C 17 proton of the cyclic hemiacetal system of peraksine gives rise to two




(I)




(IIa)




(IIb)

distinct signals at δ 4·58 and δ 4·98, and this observation is considered to depend upon the presence of an equilibrium mixture of the epimeric forms (IIa) and (IIb). The signal at δ 4·58 is a sharp singlet showing minimal coupling to the adjacent C 16 proton, while that at δ 4·98 is a doublet showing a small coupling of approximately 2 c/s. The assignment of both these signals to the C 17 proton is confirmed by the n.m.r. spectrum of *O*-acetylperaksine in $CDCl_3$ solution, as both signals show the expected downfield "acylation shift" to δ 5·53 and δ 5·92 respectively. Assignment of the individual signals from the C 17 proton to the epimers (IIa) and (IIb) cannot be made with any certainty, but the relative intensities of the two signals indicate that (IIa) and (IIb) are present in approximately 1 : 1 ratio. In the n.m.r. spectrum of *O*-acetylperaksine two distinct signals are observed from *O*-acetyl groups.

## *Experimental*

### *Vellosimine*

Alkaloid RB19 crystallized from methanol as faintly yellow prisms, m.p. 303–305°, $[\alpha]_D$ +49° (*c*, 0·39 in methanol) (Found: C, 77·9; H, 7·3; N, 10·1. Calc. for $C_{19}H_{22}N_2O$: C, 78·1; H, 6·9; N, 9·6%). For vellosimine, m.p. 305–306° and $[\alpha]_D$ +48° in methanol were reported.[3] No melting point depression was observed on a mixture of RB19 with authentic vellosimine and the i.r. spectra of the two samples were identical. The n.m.r. spectrum of RB19 measured in $CDCl_3$–$CD_3OD$ solution was fully consistent with data reported from the spectrum of vellosimine in liquid sulphur dioxide,[3] and the aldehydic proton signal appeared as a sharp singlet at δ 9·62. The mass spectrum of vellosimine showed peaks at *m/e* 292 ($M^+$, 85% of base peak), 291 (46%), 263 (base peak, 100%), 249 (13), 169 (60), 168 (40), and 149 (17).

### *Peraksine*

Alkaloid RB20 crystallized from chloroform containing a trace of methanol as glistening colourless prisms, m.p. 196–197°, $[\alpha]_D$ +19°, uncorrected for chloroform of crystallization (*c*, 0·48

in methanol). As previously reported for peraksine,[4] RB20 crystallized as a chloroform adduct which strongly retained chloroform on drying (Found: C, 64·5; H, 6·8; N, 8·0%). The analytical results are close to the mean values reported for the chloroform adduct of peraksine:[4] C, 64·0, 64·9; H, 6·4, 6·5; N, 7·9, 7·9%. The mass spectrum of RB20 shows a molecular ion peak at *m/e* 310, with a very strong $(M-1)^+$ peak at *m/e* 309 as previously reported for peraksine.[4] The crystalline nitrate of alkaloid RB20 was found to be identical with a specimen of peraksine nitrate supplied by Professor A. K. Kiang, and alkaloid RB20 and peraksine prepared from authentic peraksine nitrate had identical i.r. and n.m.r. spectra, and there was no depression of m.p. on mixing samples of the crystalline chloroform adduct.

The 100-Mc/s n.m.r. spectrum of peraksine (both RB20 and that prepared from Professor Kiang's peraksine nitrate) in $CDCl_3$–$CD_3OD$ (1 : 1) showed a four-proton multiplet between 696–750 c/s (four aromatic protons), a doublet (*J* 6·7 c/s) at δ 1·40 ($CH_3CHN$), and separate signals at δ 4·58 and δ 4·98 (C 17–H). Double irradiation at δ 3·22 caused the *C*-methyl doublet at δ 1·40 to collapse to a singlet, while irradiation near the frequency of the C 16 proton at approximately δ 1·50 reduced the signal at δ 4·98 to a sharp singlet.

O-*Acetylperaksine* was obtained as a colourless gum by acetylation of peraksine at room temperature with acetic anhydride–pyridine. It was characterized by its i.r. spectrum which showed ν ($CHCl_3$) 1735 $cm^{-1}$ (ester carbonyl) and 3500 $cm^{-1}$ (indole NH). The 100-Mc/s n.m.r. spectrum ($CDCl_3$ solution) showed a four-proton multiplet at 700–750 c/s (four aromatic protons), a broad one-proton signal at δ 7·93 (indole NH, exchangeable with $D_2O$), a doublet (*J* 2 c/s) at δ 5·92 and a singlet at δ 5·53 (both assigned to C 17–H), two sharp singlets at δ 2·14 and δ 2·02 (both assigned to $OCOCH_3$), and a doublet (*J* 6·7 c/s) at δ 1·41 ($CH_3CHNH$). Double irradiation at δ 3·13 reduced the *C*-methyl doublet at δ 1·41 to a singlet.

Peraksine methiodide crystallized from methanol in colourless prisms, m.p. 310°, and not m.p. 210° as reported in the literature,[4] but Professor A. K. Kiang has confirmed (personal communication) that peraksine methiodide in fact has m.p. 310°.

*Acknowledgments*

The authors are indebted to Professor H. Rapoport for the gift of a sample of vellosimine, and to Professor A. K. Kiang for a sample of peraksine nitrate.