358. *Proton Magnetic Resonance Spectral Studies of Some Amaryllidaceae Alkaloids of the* 5,10b-*Ethanophenanthridine Series and of Criwelline and Tazettine*

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A comparison of the proton magnetic resonance spectra of a number of alkaloids and their derivatives based on the 5,10b-ethanophenanthridine skeleton and of criwelline (VIIIa) and tazettine (IX) has given useful information which supports gross structural and stereochemical assignments for these compounds. The correlations, used in conjunction with double-resonance experiments, have allowed the assignment of the structure and stereochemistry of 6-hydroxycrinamine (IId) in an unequivocal manner.

Amaryllidaceae alkaloids based on the 5,10b-ethanophenanthridine ring system [1] constitute a large class of structurally and stereochemically inter-related compounds. The stereochemistry of these alkaloids has been established as shown [cf. structure (Ia)]. The rigid nature of rings A, B, and D in this structure make the alkaloids of this series well suited to a study of their proton magnetic resonance (p.m.r.) spectra. The alkaloids in general contain both unsaturation and an oxygen function in ring C. A series of wide occurrence possessing a 1,2-double bond and a C_3-oxygen function was chosen for our initial study.

Experimental.—All spectra were obtained with a Varian DP 60 or A 60 spectrometer at 60 Mc./sec. for approximately 10% (w/v) solutions in deuteriochloroform with tetramethylsilane as an internal standard. Double-resonance studies were performed as described by Johnson [2] using the DP 60 spectrometer. All compounds used had physical constants in agreement with those reported.

Discussion

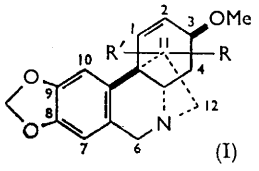
The relevant features in the p.m.r. spectra of the alkaloids hæmanthamine (Ia),[1] crinamine (IIa),[1] buphanadrine (III),[1] and their derivatives whose structures have been firmly established, will be discussed first.

The Hæmanthamine and Crinamine Series, and Buphanidrine.—The series of derivatives (Ib—Ie) and (IIb—IIc) obtained from hæmanthamine and crinamine differ only at position 11, and thus provided useful probes for investigating various aspects of the stereochemistry of both series.

[1] For a review of these alkaloids, see Wildman, "The Alkaloids," ed. Manske, Academic Press, New York, 1960, Vol. VI.

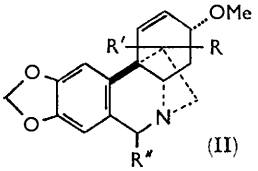
[2] Johnson, *Varian Technical Bulletin*, 1962, Vol. 3, No. 3, p. 5.

Aromatic hydrogens. The chemical shifts of the signals of the aromatic hydrogens at C-7 and C-10 are typical of signals of aryl hydrogens adjacent to oxygen functions.[3] The 10-proton signal occurred as a sharp singlet and was located at consistently lower field than the 7-proton signal. Furthermore, the latter was slightly shorter and broader than



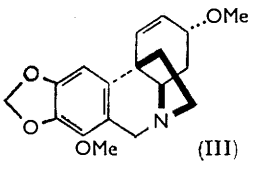
(I)

a: R = OH, R′ = H
b: R = OAc, R′ = H
c: R = R′ = O
d: R = H, R′ = OH
e: R = H, R′ = OAc



(II)

a: R = OH, R′ = R″ = H
b: R = OAc, R′ = R″ = H
c: R = R′ = O, R″ = H
d: R = R″ = OH, R′ = H
e: R = R″ = OAc, R′ = H



(III)

the former, indicative of weak splitting, presumably from coupling with one or both of the benzylic hydrogens.[4] The assignment of the lower-field signal to the 10-hydrogen was made on the basis of the effect on its chemical shift associated with hydrogenation of the 1,2-double bond. The p.m.r. spectra of the dihydro-products revealed a diamagnetic shift of the low-field aryl hydrogen signal. Since the 1,2-double bond would be expected to have a greater effect on the more proximate 10- than on the 7-proton, the downfield singlet was assigned to the former.

The 10-proton signal in 11-epihæmanthamine acetate was located at slightly higher field (τ 3·33) than the corresponding signal in other compounds of the hæmanthamine and crinamine series (τ 3·15—3·25). This result is most readily explicable in terms of long-range shielding by the carbonyl of the acetoxyl group. Molecular models reveal that the acetate of an 11-hydroxy-group directed toward the aromatic ring, as portrayed in structure (Ie), places the carbonyl of the acetate in close proximity to the 10-hydrogen. Thus, this result provides corroboration of the previously assigned[5] orientation of the 11-hydroxyl function in the " normal " and epi-series.

The lone aromatic hydrogen at C-10 in buphanidrine appears as a singlet whose chemical shift is at higher field than that of the 10-proton in the hæmanthamine and crinamine series. This diamagnetic shift is in accord with the presence of an additional oxygen function on the aromatic ring.[6a]

Methylenedioxy- and benzylic-hydrogens. The methylenedioxy-group was characterised in each compound by a sharp two-proton signal in the range τ 4·10—4·18. An exception to this was once again 11-epihæmanthamine acetate whose spectrum showed the signal as a pair of doublets with only a small difference in their chemical shift. The magnetic non-equivalence of the two hydrogens in this compound may be attributed to the perturbation of the α-oriented hydrogen of this group by the acetate carbonyl.

The non-equivalence of the benzylic hydrogens was apparent in the spectra of compounds of both series (I) and (II) from a pair of doublets showing large geminal coupling, of distinctly different chemical shift.

As expected from 3-oxo- and 7-oxo-10-methyl steroid and diterpene models[7] the presence of an 11-oxo-function [cf. (Ic) and (IIc)] produces a paramagnetic shift of the two 6-proton signals. Whilst the positions of the benzylic hydrogen signals are only mildly affected by the stereochemistry of 11-hydroxy-functions, a somewhat greater

[3] Bredenberg and Shoolery, *Tetrahedron Letters*, 1961, 285.
[4] Rottendorf and Sternhell, *Tetrahedron Letters*, 1963, 1289.
[5] Fales and Wildman, *J. Amer. Chem. Soc.*, 1960, **82**, 197.
[6] Jackman, " Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, New York, 1959, (*a*) p. 63; (*b*) p. 89.
[7] Shoolery and Rogers, *J. Amer. Chem. Soc.*, 1958, **80**, 5121; Bhacca, Wolf, and Kwok, *ibid.*, 1962, **84**, 4976; Brieskorn, Fuchs, McChesney, and Wenkert, *J. Org. Chem.*, 1964, **29**, 2293.

change could be observed in a pair of 11-epimeric acetates. The spectrum of 11-epi-hæmanthamine acetate revealed a paramagnetic shift of one of the 6-proton doublets. Presumably the acetoxyl carbonyl group is responsible for the deshielding of the 6α-hydrogen.

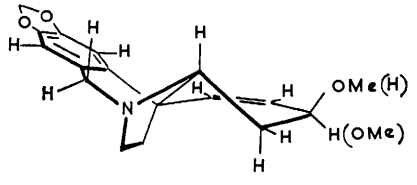
Olefinic hydrogens. The major differences revealed in the p.m.r. spectra of the hæmanthamine and crinamine series are associated with the signals resulting from the 1- and 2-protons.

The 1-, 2-, and 3-hydrogens of the hæmanthamine series, with one exception (Ic), gave rise to an ABX pattern which is amenable to a simple analysis since not only are the chemical shifts well separated but $J_{AX'} = 0$. Thus, chemical shifts and coupling constants are determinable by direct measurement and first-order considerations.

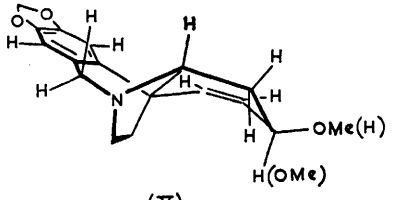
The olefinic spectral region showed six peaks, albeit one or more peaks were obscured in some spectra, usually by overlapping with other signals. The pair of resonance lines located at the low-field end of the olefinic hydrogen multiplet is a one-proton doublet ($J_{1,2} = 10{\cdot}0$ c./sec.) associated with the 1-hydrogen. The remaining four lines are a doublet of doublets resulting from H-2 coupling with H-1 ($J_{1,2} = 10{\cdot}0$ c./sec.) and with H-3 ($J_{2,3} = 4{\cdot}5$—$5{\cdot}0$ c./sec.).

The one exception, the spectrum of oxohæmanthamine (Ic), showed a 1-proton doublet but an eight-line 2-proton signal. The magnitude of the additional coupling in the latter signal is very small ($J = 0{\cdot}8$ c./sec.) and was shown by a double-resonance experiment to result from long-range coupling to one of the 4-hydrogens. This is an unusual case of coupling through four σ-bonds for which a specific stereochemical requirement of the coupled hydrogens has recently been demonstrated,[8] and indicates it is probably the 4α-hydrogen that is involved.

At this stage it is pertinent to discuss the possible conformations of ring c in the 5,10b-ethanophenanthridine ring systems. In the presence of a 1,2-double bond two conformations, (IV) and (V), are possible.[9] The half-chair form (IV) is expected to be the more



(IV)



(V)

stable, and considerations of the magnitude of the coupling between the 2- and 3-hydrogens support this contention. With ring c in the half-chair conformation the 2- and 3-hydrogens subtend an angle of *ca.* 45° for which $J_{2,3}$ is calculated [10] to be *ca.* 4·5 c./sec. This value is in good agreement with the observed range (4·0—5·0 c./sec.) for the compounds (Ia)—(Ic).

The olefinic hydrogen pattern in the crinamine series showed marked differences from their hæmanthamine analogues. In the p.m.r. spectrum of crinamine itself the observed signal for both hydrogens was a broadened singlet (half-height band-width 1·0 c./sec.). If $J_{1,2}$ (10·0 c./sec.) is considered an invariant value,[11] the unusual appearance of a singlet can be interpreted as a consequence of the near coincidence of the inner two lines of the pair of doublets in an AB system and the virtual disappearance of the outer two lines.[6b] The greater non-equivalence of the olefinic hydrogens of the acetate (IIb) and oxocrinamine (IIc) leads to six-line multiplets in their p.m.r. spectra whose appearances, however, differ from those of the corresponding hæmanthamine analogues. If the relative chemical shifts of the olefinic hydrogens in the two series are unchanged, analysis of the multiplet

[8] Phiney and Sternhell, *Tetrahedron Letters*, 1963, 275.
[9] Fales and Wildman, *J. Amer. Chem. Soc.*, 1963, **85**, 784.
[10] Williamson and Johnson, *J. Amer. Chem. Soc.*, 1961, **85**, 784.
[11] O. L. Chapman, *J. Amer. Chem. Soc.*, 1963, **85**, 2014.

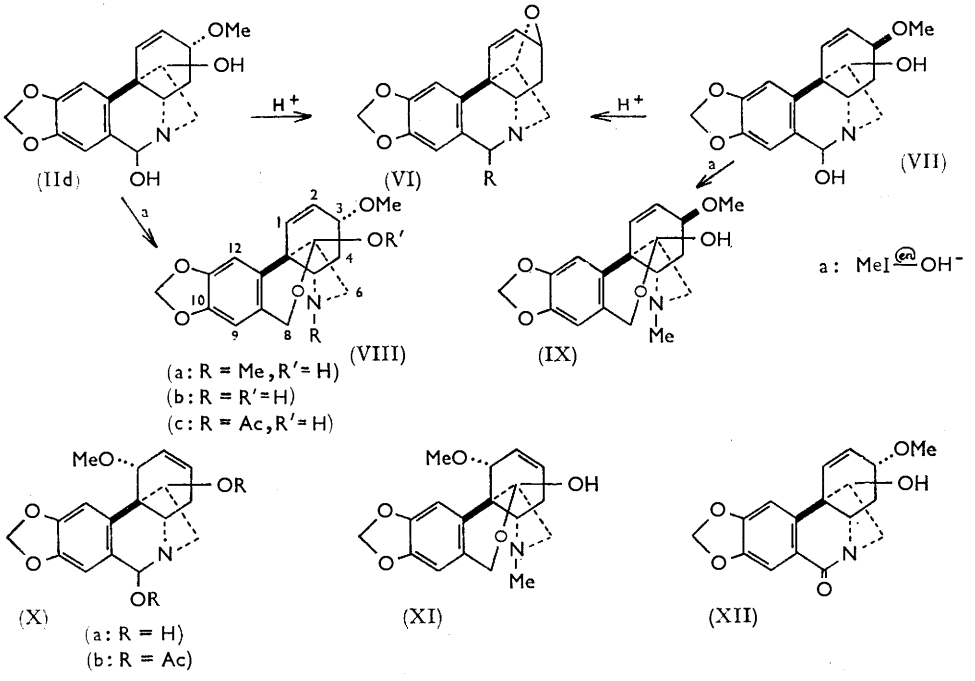
of (IIb) and (IIc) yields $J_{1,2} = 10{\cdot}0$ c./sec., $J_{1,3} = 2{\cdot}0$ c./sec. and $J_{2,3} = 0$ c./sec. Thus, these are unusual examples of allylic coupling being greater than vicinal coupling; a fact fully consistent with a half-chair form of ring C, a β-orientation of the 3-hydrogen, and a dihedral angle subtended by the 1-, 2-, and 3-hydrogens of *ca.* 80°.[12]

The six-line multiplet of the olefinic hydrogens in the acetate (IIb) could be made to collapse to a symmetrical AB quartet by saturation at the 3-proton resonant frequency and served to determine the precise location of the latter signal at τ 5·92. Similarly, decoupling of the 1-proton with a large side-band component effected the collapse of the diffuse doublet of the 3-proton resonance to a singlet.

The six-line multiplet of the olefinic hydrogens in the p.m.r. spectrum of buphanidrine showed a doublet ($J_{1,2} = 10{\cdot}0$ c./sec.) for the 1-proton signal and a pair of doublets ($J_{1,2} = 10{\cdot}0$, $J_{2,3} = 5{\cdot}0$ c./sec.) for the 2-proton resonance. These data are fully consistent with a quasi-axial 3-methoxyl group, as expected for structure (III) in which ring C is in the half-chair form.

4-*Protons.* The signals of the 4-protons were located at higher magnetic field than those of other hydrogen signals and were well resolved in most cases, but have not been analysed.

6-*Hydroxycrinamine.*—Independent studies by two groups [13,14] led to the proposal of structure (IId) for 6-hydroxycrinamine, which occurs in *Hæmanthus natalensis* B and certain *crinum* species. One of the key reactions in the elucidation of its structure was its conversion by acid treatment into the known compound anhydrodemethylhæmanthidine



(VI; R = OH), which was also obtained by a similar acid-catalysed reaction from hæmanthidine (VII).[15] Further support for the structural relation of alkaloid (IId) with hæmanthidine came from the ready base-catalysed rearrangement of its methiodide to the

[12] Collins, Hobbs, and Sternhell, *Tetrahedron Letters*, 1963, 197.
[13] Fales, Horn, and Wildman, *Chem. and Ind.*, 1959, 1415.
[14] Jeffs, Warren, and Wright, *J.*, 1960, 1090.
[15] Uyeo, Fales, Highet, and Wildman, *J. Amer. Chem. Soc.*, 1958, **80**, 2591.

alkaloid criwelline. The latter was formulated as (VIIIa) on the basis of an analogous conversion of hæmanthidine methiodide into tazettine (IX) [15] (see Scheme).

Since allylic rearrangement cannot be excluded in the conversion of the alkaloid (IId) into the ether (VI; R = OH), the allyl isomer (Xa) must still be considered as a possible structure for 6-hydroxycrinamine * and (XI) as an alternative structure for criwelline.

A priori the p.m.r. spectrum of a compound of structure (IId) would be expected to show strong similarities, particularly in the aromatic and olefinic regions, with that of crinamine (IIa). This in fact proved to be the case, not only for the alkaloids but also their acetates (IIb) and (IIe).

The p.m.r. spectrum of 6-hydroxycrinamine di-*O*-acetate (IIe) had an olefinic hydrogen region of a simplicity quite incompatible with that expected for a compound of structure (Xb). It consisted of a pair of doublets whose two low-field lines were broad, indicative of further small coupling. A double-resonance experiment involving saturation of the signal of the allylic hydrogen on the methoxy-substituted carbon [H-3 in (IIe) or H-1 in (Xb)], fortunately well separated from other signals in this spectrum, resulted in an alteration of the olefinic hydrogen multiplet to a symmetrical AB quartet. Irradiation of the C-4 two-proton multiplet by a large side-band component left the olefinic hydrogen region unchanged but reduced the four-line signal of the allylic hydrogen on the methoxy-bearing carbon to a broad singlet. These results establish unequivocally (IIe) as the structure of the 6-hydroxycrinamine derivative and confirm previous structural and stereochemical proposals for the alkaloid.[13,17]

The decrease of $J_{1,3}$ (<0·5 c./sec.) in the spectra of the 6-hydroxycrinamine derivatives, as compared to that of the crinamine series ($J_{1,3}$ = 2·0 c./sec.) probably indicates a slight deformation of the half-chair conformation of ring C from the direction of a dihedral angle of the 2- and 3-hydrogens of 90°.

Since the base-catalysed rearrangement of 6-hydroxycrinamine methiodide to criwelline is unlikely to involve rearrangement of the allyl ether system, the above double-resonance experiments constitute, also, good evidence for retaining the original structure proposal of (VIIIa) for criwelline.[14,17]

The spectrum of 6-oxocrinamine (XII) showed the expected paramagnetic shift (τ 0·82) of the 7-proton signal due to the peri-carbonyl group [18] and a similar, although smaller shift (τ 0·12) of the methylenedioxy-group hydrogens.

Anhydrodemethylhæmanthamine (VI; R = H) is a completely rigid system in which ring C is locked in the boat form by the 3,11-ether bridge. Such a conformational change in ring C is reflected in several ways in the p.m.r. spectrum of this compound. The characteristic appearance of the pattern of the olefinic hydrogens in the hæmanthamine series was somewhat modified in the ether (VI; R = H). Whilst the same six-line multiplet appeared, increases in coupling constants resulted in a change in the relative line positions and led to an overlap of signals. The increase in $J_{1,2}$ (12·6 c./sec.) is of interest since the coupling constants of the olefinic hydrogens in cyclohexene systems [11] fall in the range 9·9—10·5 c./sec. Thus, the increase in coupling in this compound is possibly a reflection of the torsional strain of the 1,2-double bond imposed by the ether bridge between rings C and D.

The second factor responsible for the different appearance of this multiplet is the increase in the coupling constant of the 2- and 3-protons to 6·5 c./sec. The magnitude of this coupling suggests a dihedral angle for these hydrogens of *ca.* 30°, which is not in very good agreement with that (5°) revealed by a model. This deviation may be a

* Consideration of this structure is particularly important since buphanamine is known [16] to have a 1-oxygen function and 2,3-double bond.

[16] Fales and Wildman, *J. Org. Chem.*, 1961, **26**, 881.
[17] Goosen, Graham, Jeffs, Warren, and Wright, *J.*, 1960, 1090.
[18] Jeffs and Hawksworth, *Tetrahedron Letters*, 1963, 217; Hawksworth, Jeffs, Tidd, and Toube, preceding Paper.

TABLE 1

Proton magnetic resonances (τ values) and coupling constants (c./sec.) of hæmanthamine and related alkaloids

Compound	H-1	H-2	H-3	4-Protons	6-Protons	H-7	H-10	H-11	$-O\cdot CH_2\cdot O-$	OMe
(Ia)	3·60d $J_{1,2} = 10{\cdot}0$,	3·77d.d $J_{2,3} = 5{\cdot}0$	*ca.* 6·20m	7·83—8·07m	(α) 6·35d (β) 5·65d $J = 16{\cdot}0$	3·60s	3·25s	6·05d.t	4·18s	6·68s
(Ib)	3·47d $J_{1,2} = 10{\cdot}0$,	3·91d.d $J_{2,3} = 5{\cdot}0$	6·21m	7·87—8·16m	(α) 6·35d (β) 5·65d $J = 17{\cdot}0$	3·58s	3·17s	5·16d.t	4·17s	6·64s
(Ic)	3·47d $J_{1,2} = 9{\cdot}8$, $J_{2,3} = 4{\cdot}5$, $J_{2,4} = 0{\cdot}8$	3·82q.d	6·18m	7·75b.d	(α) 6·22d (β) 5·42d $J = 17{\cdot}0$	3·52s	3·20s	—	4·15s	6·65s
(Id)	3·41d $J_{1,2} = 10{\cdot}0$,	3·89d.d $J_{2,3} = 5{\cdot}0$	6·23o	7·98—8·17m	(α) 6·24d (β) 5·58d $J = 17{\cdot}0$	3·50s	(3·18s)	5·620	4·10s	6·68s
(Ie)	3·53d $J_{1,2} = 10{\cdot}0$,	4·05d.d $J_{2,3} = 4{\cdot}5$	6·20m	7·88—8·30m	(α) 6·18d (β) 5·58d $J = 17{\cdot}0$	3·60s	3·33s	4·82—5·11 *	4·17d 4·21d $J = 1{\cdot}2$	6·70s
Dihydro-(Ia)			*ca.* 6·30o		(α) 6·36d (β) 5·70d $J = 17{\cdot}0$	3·62s	3·32s	*ca.* 5·800	4·14s	6·72s
(IIa)	3·78 (calc.) assumed $J_{1,2} = 10{\cdot}0$, obs. 3·81s	3·84 (calc.)	*ca.* 6·08m	7·78—8·12m	(α) 6·35d (β) 5·76d $J = 17{\cdot}0$	3·59s	3·25s	*ca.* 6·00m	4·15s	6·64s
(IIb)	3·82d.d $J_{1,2} = 9{\cdot}8$,	4·05d $J_{2,3} = 2{\cdot}0$	5·92b.d	7·85—8·08m	(α) 6·30d (β) 5·69d $J = 17{\cdot}0$	3·57s	3·15s	5·05d.t	4·13s	6·60s
(IIc)	3·66d.d $J_{1,2} = 10{\cdot}0$,	3·94d $J_{2,3} = 2{\cdot}0$	6·17o.m	7·75m	(α) 6·20d (β) 5·45d $J = 17{\cdot}0$	3·50s	3·22s	6·08o	4·11s	6·65s
Dihydro-(IIa)			6·03o.m		(α) 6·34d (β) 5·78d $J = 17{\cdot}0$	3·59s	3·30s	5·78o.m	4·13s	6·64s
(IId)	3·78 (calc.) assumed $J_{1,2} = 10{\cdot}0$, obs. 3·80s	3·84 (calc.)	*ca.* 6·15o	7·70—8·05m	5·00s	3·29s	3·21s	5·98o.m	4·09s	6·63s

TABLE 1 (*Continued*)

Compound	H-1	H-2	H-3	4-Protons	6-Protons	H-7	H-10	H-11	$-O\cdot CH_2\cdot O-$	OMe
(IIe)	3·86b.d	4·07d	6·02d.q	7·80—8·10m	3·92o	3·40s	3·18s	5·15d.t	4·08s	6·65s
	$J_{1,2} = 9{\cdot}8$, $J_{1,3} < 0{\cdot}5$									
(XII)	3·75o.d.d	3·83d	*ca.* 5·90o	7·82—8·18m	—	2·58s	3·16s	*ca.* 6·05o	3·97s	6·66(C-3)
	$J_{1,2} = 9{\cdot}8$, $J_{1,3} = 1{\cdot}2$									
(III)	3·41d	4·02d.d			(α) 6·25d	—	3·43s	—	4·16s	6·64(C-3)
	$J_{1,2} = 10{\cdot}0$, $J_{2,3} = 5{\cdot}0$				(β) 5·71d					
					$J = 17{\cdot}5$					6·03(C-7)
Dihydro-(Id)			*ca.* 6·75o.m		5·04s	3·38s	3·27s	6·04m	4·13s	6·65s
(V; R = H)	3·27d	3·40d.d	5·60m	8·08—8·22m	(α) 6·28d	3·55s	3·18s	6·30m	4·10s	—
	$J_{1,2} = 12{\cdot}5$, $J_{2,3} = 6{\cdot}5$				(β) 5·72d					
					$J = 17{\cdot}0$					
Dihydro-(V; R = H)			6·10m	8·01—8·38m	(α) 6·28d	3·58s	3·20s	5·91m	4·12s	—
					(β) 5·75d					
					$J = 17{\cdot}0$					

* 4-line signal.

s, singlet; d, doublet; d.d, doublet of doublets; m, multiplet; d.t, diffuse triplet; b.d, broad doublet, d.q, diffuse quartet; o, obscured signal (*e.g.* o.m, obscured multiplet); q.d, quartet of doublets.

TABLE 2

Proton magnetic resonances (τ values) and coupling constants (c./sec.) of tazettine and related alkaloids

Compound	H-1	H-2	H-3	H-4	6-Protons	8-Protons	H-9	H-12	$-O\cdot CH_2\cdot O-$	OMe	*N*-Me
(IX)	4·41b.d	3·90b.d	5·74—6·13m		6·71d	5·06d	3·56s	3·19s	4·16s	6·59s	7·63s
	$J_{1,2} = 10{\cdot}5$				7·32d	5·38d					
					$J = 10{\cdot}5$	$J = 15{\cdot}0$					
(VIIIa)	4·40b.d	3·81d.d	6·04—6·29m	8·00m	6·72d	5·11d	3·51s	3·46s	4·11s	6·59s	7·65s
	$J_{1,2} = 10{\cdot}0$, $J_{2,3} = 3{\cdot}5$				7·29d	5·38d					
					$J = 10{\cdot}5$	$J = 15{\cdot}0$					
(VIIIb)	4·08b.d	3·76d.d	6·12—6·25m	8·00m		5·02d	3·57s	3·53s	4·17s	6·62s	—
	$J_{1,2} = 10{\cdot}0$, $J_{2,3} = 4{\cdot}0$					5·44d					
						$J = 15{\cdot}0$					
(VIIIc)	*ca.* 4·12o	3·72d.d	6·14m	8·00m	6·31d	5·05d	3·57s	3·47s	4·08s	6·67s	—
	$J_{1,2} = 10{\cdot}0$, $J_{2,3} = 4{\cdot}0$				6·50d	5·42d					
					$J = 10{\cdot}5$	$J = 15{\cdot}0$					

Abbreviations as in Table 1.

consequence of the strain in this system since similar deviations are found in the spectra of other strained oxide ring systems.[19]

The 3-proton signal was located with certainty at τ 5·60 by appropriate double-resonance studies in which the multiplicity of this signal could be reduced by decoupling the signal from the 2- and 4-hydrogens. Similar decoupling of the 5-line multiplet at τ 6·30 by irradiation of the signal at τ 6·75—6·90 reduced the multiplet to a broad singlet. This showed it to be the signal of the 11-hydrogen which is considered to be the X part of an ABX system in which the 12-hydrogens at higher field form the AB part.

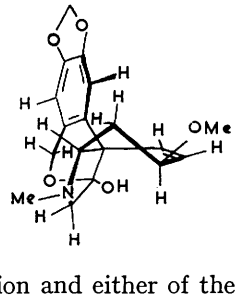
All foregoing p.m.r. data are summarised in Table 1.

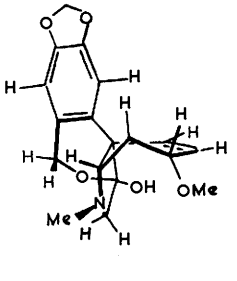
Tazettine and Criwelline.—These alkaloids are thus far the only known representatives of the [2]benzopyrano[3,4-*c*]indole ring system. Their relationship with the 5,10b-ethanophenanthridine alkaloids hæmanthidine (VI) and 6-hydroxycinamine (IId), respectively, made inspection of their p.m.r. spectra of interest.

The p.m.r. spectrum of tazettine is fully consistent with the proposed[20] structure (IX). The aromatic 9- and 12-hydrogens give rise to singlets at τ 3·56 and 3·19, respectively. These assignments can be made on the assumption of the broader of the two singlets being ascribable to the 9-hydrogen on the basis of its weak coupling with the benzylic hydrogens.[4] The signals of the olefinic 1- and 2-hydrogens appeared as an AB quartet in which small coupling with the 3-hydrogen results in considerable peak broadening of this multiplet.* The 3-proton signal is a very broad, diffuse quartet at τ 5·73—6·13 in which the half-band width of *ca.* 11·0 c./sec. suggests its axial conformation. Inspection of a Drieding model of tazettine indicates that an axial 3-hydrogen is allowed only in the half-boat ring C conformation [cf. (XIII)]. This relationship appears to be independent of the two possible ring B conformations of the alkaloid. The half-boat ring C conformation relieves an otherwise energetically unfavourable, non-bonded interaction of the 3β-methoxyl group and the 12-hydrogen. Furthermore, this conformation is in agreement with the weak coupling between the 2- and 3-hydrogens whose dihedral angle is *ca.* 108°.

The p.m.r. spectrum of criwelline (VIIIa) and its derivatives reveal $J_{2,3} = 3{\cdot}5$—4·0 c./sec., characteristic of a 2,3-dihedral angle of *ca.* 50 or 118°, and a half-band width of less than 5 c./sec. of the 3-proton signal, indicative of an other than axial 3-hydrogen conformation. These facts limit criwelline's structure to one possessing a half-chair

(XIII)





(XIV)

ring C conformation and either of the two possible ring B conformations. However, the fact that the 12-proton signal in the p.m.r. spectra of criwelline and its derivates are *ca.* 0·33 p.p.m. upfield of the corresponding signal of tazettine, indicating that the 12-hydrogen in criwelline is located close to and above the plane of the ring C double bond,

* Since only small quantities of this alkaloid were available, the spectra were not of good quality. The *J* value of the small coupling in the olefinic hydrogen and 3-hydrogen multiplets conceivably could be determined under more optimum operating conditions. This also applies to the spectra of criwelline and its derivatives.

[19] Reilly and Swalen, *J. Chem. Phys.*, 1961, **35**, 1522; Tori, Komeno, and Nakagawa, *J. Org. Chem.*, 1964, **29**, 1136.

[20] Ikeda, Taylor, Tsuda, Uyeo, and Yujima, *J.*, 1956, 4749; Tsuda and Uyeo, *J.*, 1961, 2485.

restricts the structure of the alkaloid to one (XIV) whose ring B conformation places the $C_{(8)}$–O bond below the plane of the benzene ring. Inspection of Dreiding models of criwelline and its derivatives and consideration of the many possible, unfavourable, non-bonded interactions in the various conformations also show the stereostructure (XIV) deduced by p.m.r. arguments to be the most stable.

Further assignments of hydrogen resonances are listed in Table 2.

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