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THE NMR SPECTRA OF TAXININE AND ITS DERIVATIVES

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Abstract—The 60 and 100 Mc NMR spectra of taxinine and several of its more important derivatives are assigned and discussed.

IN SEVERAL recent communications, evidence for the proposed structure[1,2,3,4] and stereochemistry[5] of taxinine (I) has been briefly reported. Much of our earlier evidence[1,5] was obtained from the NMR spectra[2] of taxinine and its derivatives, and in this paper we discuss in more detail the assignment of these spectra and some of the conclusions that may be drawn from them.

EXPERIMENTAL

Preparation of new compounds discussed in this paper will be described elsewhere. The spectra[6] were measured at 60 Mc and 100 Mc, using $CDCl_3$ solutions with tetramethylsilane (TMS) as internal standard. In each case, only a first-order analysis of spin–spin multiplets was made, in some cases with the aid of spin–spin decoupling techniques (nuclear magnetic double resonance or NMDR).

Assignment of the methyl signals

The 12-Me signal is easily distinguished since in the case of taxinine (I)* and those of its derivatives which contain the ring A C=C—C=O grouping, it is the methyl signal which appears at lowest field (2·05–2·43 ppm). When the 11,12-double bond has been reduced, as in taxinol tetraacetate (V) and oxonortaxinol tetraacetate (VI), this methyl signal shifts to higher field (near 1·4 ppm) and appears as a doublet ($J = 7$ c/s). The signals due to the *gem*-methyls at $C_{(15)}$ are readily identified since they are appreciably coupled to each other. Irradiation of the methyl signal at 1·50 ppm, in the spectrum of oxonortaxinol tetraacetate (Fig. 6), causes the 0·97 ppm

* The numbering system used throughout this paper is the one agreed on previously.[7]

[1] M. Kurono, Y. Nakadaira. S. Onuma, K. Sasaki and K. Nakanishi, *Tetrahedron Letters* 2153 (1963).
[2] K. Nakanishi, M. Kurono and N. S. Bhacca, *Tetrahedron Letters* 2161 (1963).
[3] K. Ueda, S. Uyeo, Y. Yamamoto and Y. Maki, *Tetrahedron Letters* 2167 (1963).
[4] D. H. Eyre, J. W. Harrison, R. M. Scrowston and B. Lythgoe, *Proc. Chem. Soc.* 271 (1963).
[5] M. Kurono, Y. Maki, K. Nakanishi, Mo. Ohashi, K. Ueda, S. Uyeo, M. C. Woods and Y. Yamamoto, *Tetrahedron Letters* 1917 (1965).
[6] Some of the spectra have already been discussed: S. Uyeo, K. Ueda, Y. Yamamoto and Y. Maki, *Yakugaku Zasshi* **84**, 762 (1964); **85**, 404 (1965).
[7] B. Lythgoe, K. Nakanishi and S. Uyeo, *Proc. Chem. Soc.* 301 (1964).

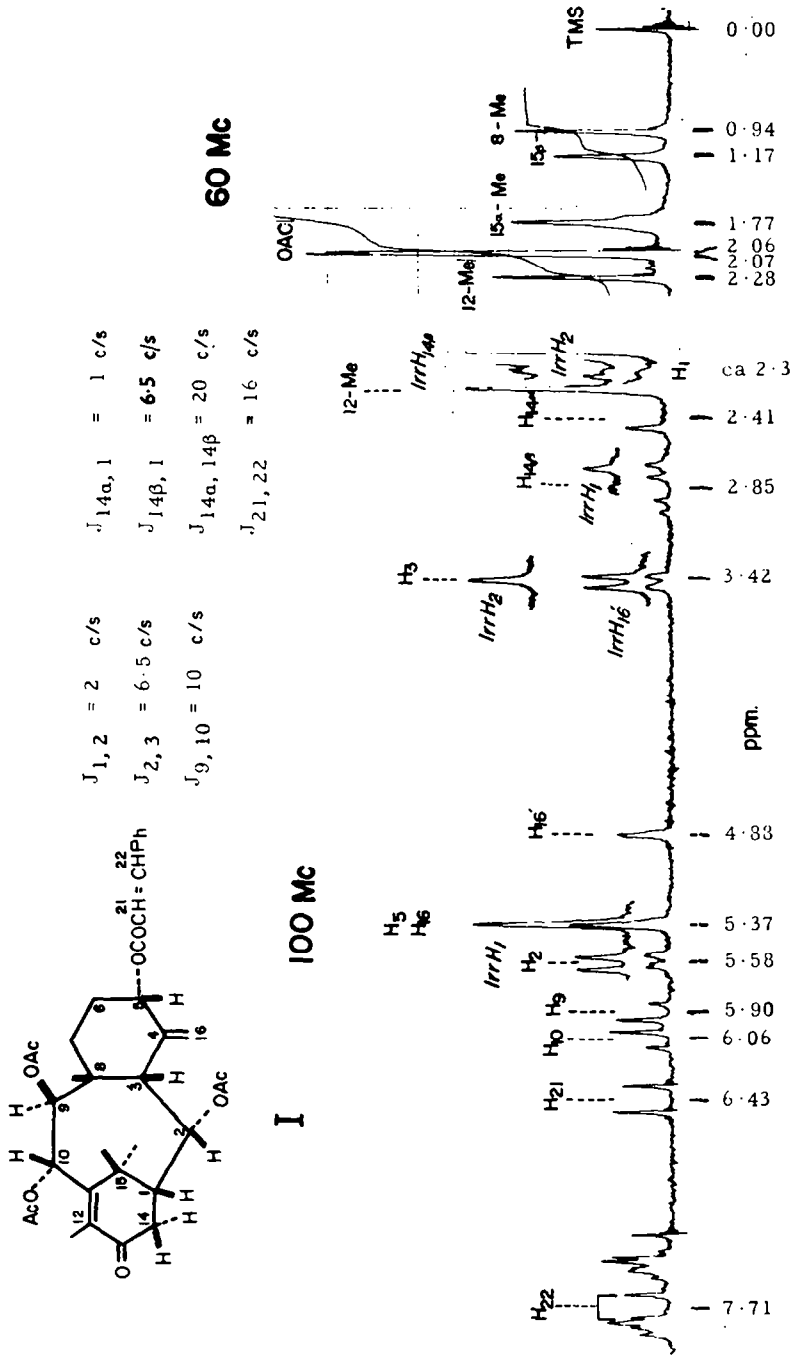


FIG. 1. NMR spectrum of taxinine (I).

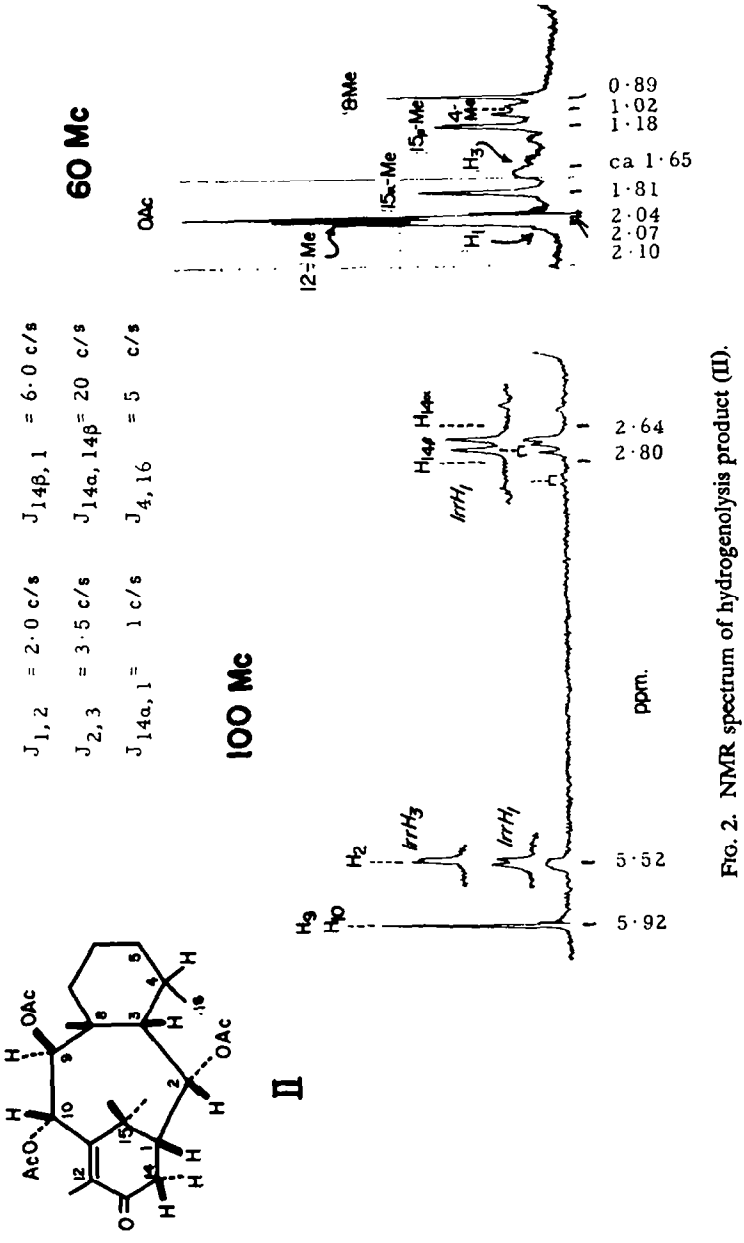


FIG. 2. NMR spectrum of hydrogenolysis product (II).

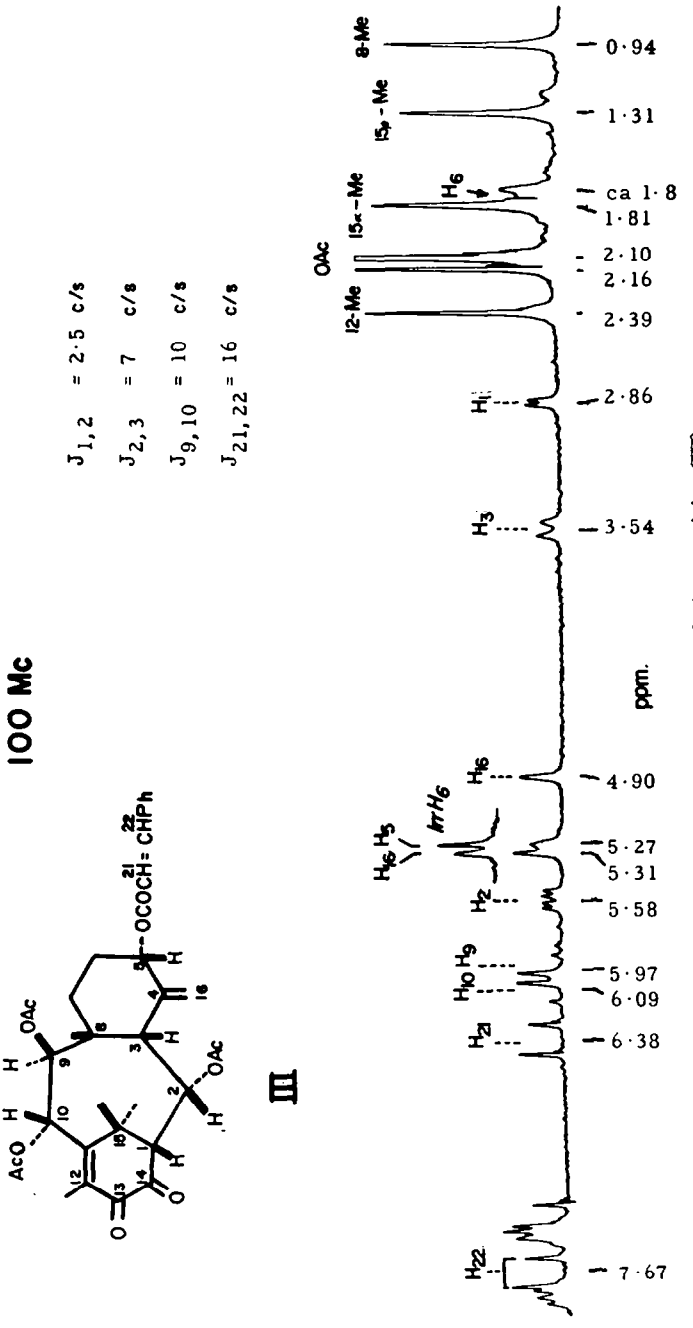


FIG. 3. NMR spectrum of 14-oxotaxinine (III).

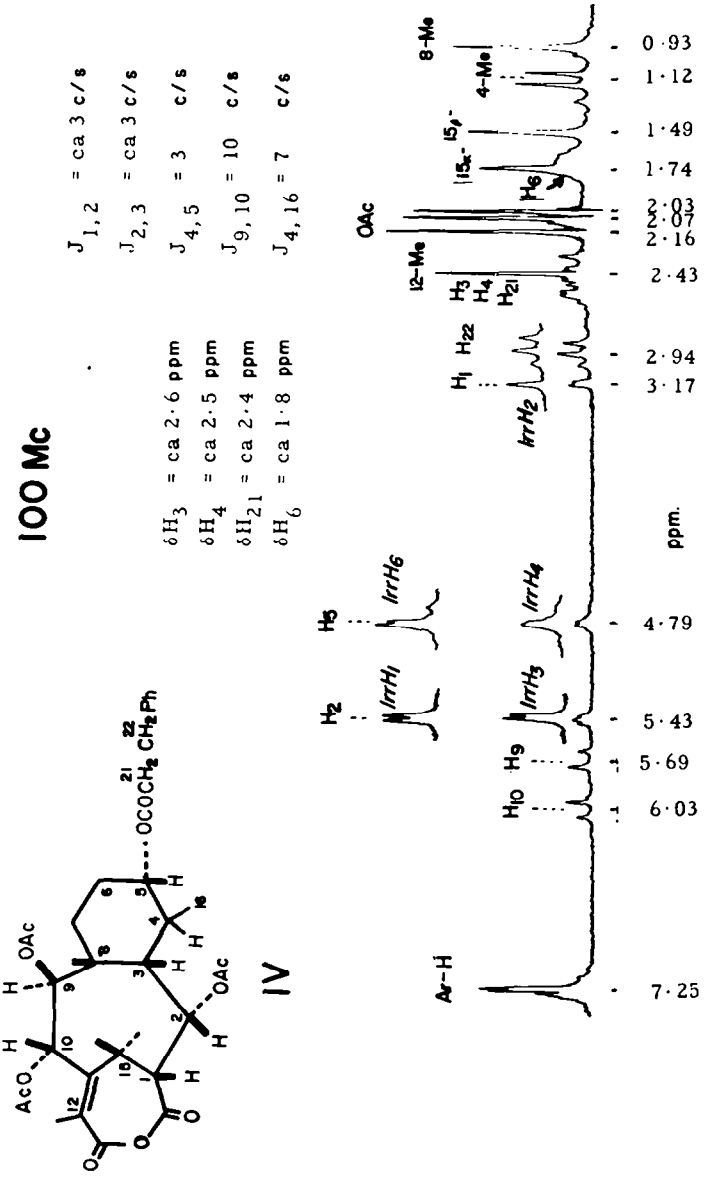


FIG. 4. NMR spectrum of the acid anhydride (IV).

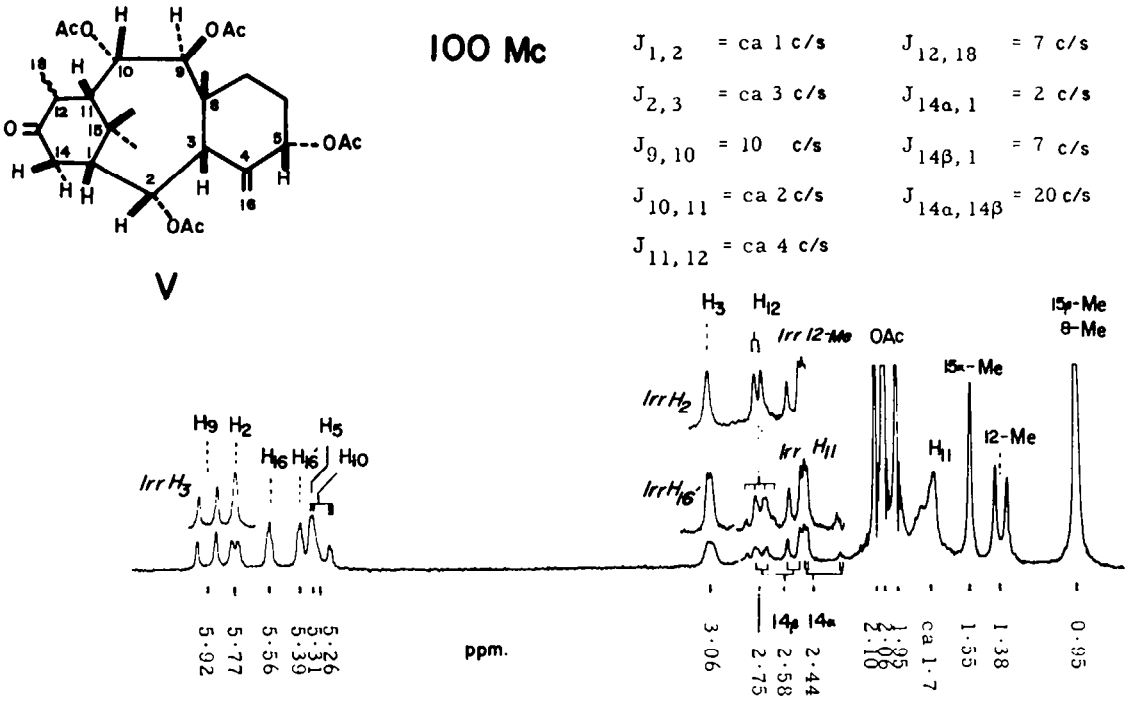


FIG. 5. NMR spectrum of taxinol tetraacetate (V).

methyl signal to increase in height; conversely, irradiation of the latter signal increases the height of the 1·50 ppm signal. This weak coupling is also apparent from an examination of the half-band widths of the methyl signals in the spectra of taxinine and its derivatives; in each case the 15α- and 15β-methyl signals are shorter and broader than the other unsplit methyl signals. Moreover, one of the signals arising from the *gem*-methyls is invariably displaced to much lower field (1·50–1·81 ppm)

TABLE 1. ASSIGNMENT OF PROTON SIGNALS IN THE 60 Mc SPECTRA OF DERIVATIVES IX—XIV

Derivative	IX	X	XI	XII	XIII	XIV
δH_2	5·55 (q)	5·59 (q)	4·20 (q)		5·57 (q)	5·43 (q)
δH_3	3·37 (d)	3·21 (d)	3·23 (d)	4·22 (s)	2·82 (d)	3·12 (d)
δH_5[a]	5·34	5·35	4·20	4·22	5·2 or 5·1	5·75
δH_9	4·20 (d)	4·33 (d)	4·19 (d)	3·98 (d)	4·18 (d)	9·42 (s)[b]
δH_{10}	4·90 (d)	4·91 (d)	4·90 (d)	4·96 (d)	3·75 (q)[c]	10·30 (s)[d]
δH_{16}, $\delta H_{16'}$[e]	5·34	5·35	5·22	5·02	5·2	5·25
	4·86	4·82	5·22	4·77	5·1 or 5·2	5·15
δH_{21}	6·47 (d)	6·41 (d)	—	—	—	6·53 (d)
δH_{22}	7·67 (d)	7·65 (d)	—	—	—	7·77 (d)
δ8-Me	1·10 (s)	1·05 (s)	1·02 (s)	1·13 (s)	1·02 (s)	[f]
δ12-Me	2·12 (s)	2·15 (s)	2·05 (s)	2·12 (s)	1·22 (d)	2·15 (s)
δ15α-Me	1·71 (s)	1·75 (s)	1·65 (s)	1·52 (s)	1·27 or 1·34 or 1·39 (s)	[f]
δ15β-Me	1·23 (s)	1·23 (s)	1·22 (s)	1·26 (s)	0·92 (s)	[f]
Acetates	2·05 (s)	2·04 (s)	—	—	1·80 (s) 1·97 (s)	1·96 (s)
$J_{9,10}$	9	9·5	9·5	9	9	—
$J_{1,2}$	1·5	2	2	—	1–2	2 or 6·5
$J_{2,3}$	6	6	6	—	4	6·5 or 2
$J_{21,22}$	16	16	—	—	—	16

[a] In IX–XIII, the H_5 signal is a multiplet with half-band width 3–4 c/s; in XIV, the half-band width is ca 16 c/s.
[b] $C_{(8)}$–CHO signal.
[c] H_{10} is weakly coupled (J = ca 1 c/s) to H_{11}.
[d] $C_{(11)}$–CHO signal.
[e] In each case, the $C_{(16)}$-protons appear as a pair of unresolved multiplets (half-band width 2–4 c/s).
[f] Unassigned methyl signals at 1·43, 1·38 and 1·08 ppm.

than the other (0·95–1·49 ppm); the lower field signal can be assigned to the 15α-Me which is almost in the plane of the $C_{(13)}$ C=O grouping, and hence subject to strong deshielding, whereas the 15β-Me is more out of plane and is probably shielded to some extent (cf. structure XV).

The 8-Me is responsible for the absorption of 0·89–0·95 ppm in compounds I–VI, and as can be seen from Figs 1, 3, 4 and 5, its signal is unaffected by changes in ring A. Removal of the $C_{(5)}$-oxygen function causes a small up field shift of 0·05 ppm (Figs 1 and 2), and in dideacetyl taxinine (IX) the 8-Me has suffered an 0·16 ppm downfield shift (cf. Fig. 1 and Table 1).

Acetate groupings, when present, gave rise to signals in the range 1·95–2·16 ppm but have not been assigned to individual groupings.

Cinnamate grouping

In the spectra of taxinine and those derivatives still containing a cinnamate grouping, the aromatic protons appear as a broad multiplet at 7·2–7·9 ppm. The 21- and 22-protons on the double bond, however, show as an AB-quartet, typically at 6·38–6·53 ppm (H_{21}) and 7·65–7·77 ppm (H_{22}), with J = 16 c/s (*trans* olefinic protons); the signal at lowest field is assigned to the proton (H_{22}) nearest the benzene ring. These ethylenic absorptions are not present in this region when the double bond has been reduced, as in IV, but instead appear as an A_2X_2 pattern between 2·0 and 3·0 ppm. Moreover, the aromatic protons now give rise to a group of closely packed signals centered near 7·2–7·3 ppm.

The 9- and 10-proton signals

In taxinine and derivatives I–IV, the 9- and 10-protons absorb at 5·69–5·97 and 5·92–6·09 ppm, respectively, whereas in the 9,10-diol (IX), these protons absorb at 4·20 and 4·90 ppm, the large upfield shift being due to hydrolysis of the acetate groupings. In each case, the allylic proton, H_{10}, absorbs at lower field than H_9, and the signals appear as a characteristic AB quartet (see Figs 1–4).* As can be seen from these spectra, the higher field doublet is invariably shorter and broader than the lower field doublet, suggesting that H_9 is weakly coupled to an additional proton or protons. The only protons likely to be involved in such long-range coupling are the 8-Me protons and these will be coupled only when H_9 and the 8-Me are in *anti-trans* relationship[8–10] (cf. structure XV).

In the case of taxinol tetraacetate (V) and oxonortaxinol tetraacetate (VI), the H_{10} proton signal is subject to an additional small splitting (1–2 c/s) due to the newly introduced 11-proton, and has suffered an upfield shift of about 0·8 ppm resulting from removal of the 11,12-double bond; the 9-proton, on the other hand, still absorbs at about the same postion (5·82, 5·92 ppm) as taxinine. Irradiation of H_{11} in oxonortaxinol tetraacetate (see Fig. 6) converts the H_{10} signal to a doublet.

Periodate cleavage of the 9,10-diol in IX produces a dialdehyde (XIV) which exhibits sharp singlets at 10·30 and 9·42 ppm, the former being due to the C_{11}-aldehyde (H_{10}) and the latter to the C_8-aldehyde (H_9). The sharpness of these signals indicates that both aldehyde groupings are attached to carbons bearing no hydrogens; however the H_9 signal is somewhat shorter and broader than the H_{10} signal suggesting that the former proton is subject to a weak long range coupling. Splittings of up to 1·5 c/s have been observed in certain cases[8,11] where tertiary aldehydes are involved in long range couplings.

Assignment of other protons

(i) *Taxinine.* The lowfield signals (2 to 6 ppm) have been unequivocally assigned with the aid of NMDR as follows.

* The hydrogenolysis product (II) is an exception since H_9 and H_{10} absorb at the same position.

[8] S. Sternhell, *Rev. Pure and Appl. Chem.* **14**, 15 (1964).

[9] N. S. Bhacca and D. H. Williams, *Application of NMR Spectroscopy in Organic Chemistry* p. 108. Holden-Day, San Francisco (1964).

[10] C. W. Shoppee, F. P. Johnson, R. Lack and S. Sternhell, *Tetrahedron Letters* 2319 (1964).

[11] W. T. de Kock, P. R. Enslin, K. B. Norton, D. H. R. Batron, B. Sklarz and A. A. Bothner-By, *J. Chem. Soc.* 3828 (1963); C. A. Henrick and P. R. Jefferies, *Austr. J. Chem.* 915, **17** (1964).

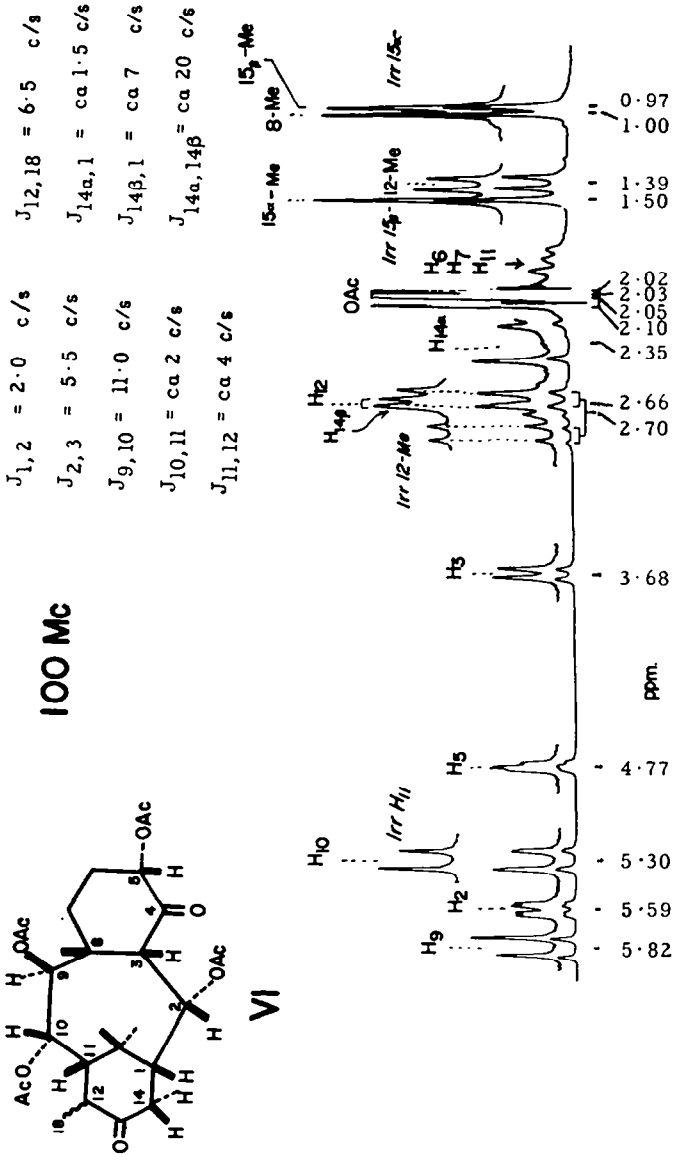


FIG. 6. NMR spectrum of 4-oxonortaxinol tetraacetate (VI).

As can be seen from Fig. 1, irradiation of the quartet (J = 2; 6·5 c/s) at 5·58 ppm (H_2) causes the doublet (J = 6·5) at 3·42 ppm (H_3) to collapse to a singlet when $\Delta\omega$ = 210 c/s, and with $\Delta\omega$ = 332 c/s results in marked change in signal shape near 2·3 ppm (H_1), thus locating the protons H_1, H_2 and H_3. Conversely, irradiation of the H_1 signal near 2·3 ppm ($\Delta\omega$ = 332) converts the 5·58 ppm quartet to a doublet (J = 6·5). The H_3 signal at 3·42 ppm is a rather diffuse doublet which is considerably sharpened by irradiation of the rather broad one-proton peak (H_{16}) at 4·88 ppm ($\Delta\omega$ = 145 c/s), indicating the existence of weak allylic coupling between these two protons. The two proton peak at 5·37 ppm can be then safely assigned to the other H_{16} proton and the H_5 proton. The quartet (J = 6·5, 20) at 2·85 ppm is assigned to the 14β-proton since irradiation of H_1 near 2·3 ppm ($\Delta\omega$ = 54 c/s) reduces the quartet to a doublet (J = 20) which is observed to be the lowfield half of an AB quartet; the high-field half of which is partly obscured by the 12-Me signal and is located at 2·41 ppm ($H_{14\alpha}$). Inspection of Dreiding models of taxinine suggests that the 14β-proton would be almost in the plane of the $C_{(13)}$ carbonyl group and have a dihedral angle (ϕ) of about 35° with respect to the 1β-proton. This would account for the rather large J value (6·5 c/s) and for the fact that it absorbs at lower field than the 14α-proton which is more out of the plane of the carbonyl. Moreover, $\phi_{14\alpha,1}$ appears to be near 80° (cf. XV) which would explain the small $J_{14\alpha,1}$ observed (< 1 c/s). The large value (20 c/s) found for the $H_{14\alpha}$, $H_{14\beta}$ geminal coupling constant appears to be a normal one for methylene groups adjacent to a carbonyl function.[12]

(ii) *The hydrogenolysis product* II. The unresolved multiplet at 5·52 ppm (H_2) becomes a doublet (J = 2·0) on irradiating near 1·65 ppm (assigned to H_3). Irradiation near 2·1 ppm (H_1) converts the 5·52 ppm multiplet to a doublet (J = 3·5 c/s) when $\Delta\omega$ = 386, whereas irradiation at 2·1 ppm (H_1) with $\Delta\omega$ = 60 c/s converts the quartet (J = 6·0; 20) at 2·80 ppm to a doublet (J = 20) which is the lower field half of an AB quartet having its higher field pair at 2·64 ppm. The protons H_1, H_2, H_3, $H_{14\alpha}$ and $H_{14\beta}$ can accordingly be assigned as indicated in Fig. 2.

(iii) 14-*Oxotaxinine* (III). Assignment of the H_1, H_2, H_3, H_5 and H_{16} proton signals in the spectrum of III can be made with confidence by comparison with the spectrum of taxinine. Introduction of the carbonyl at $C_{(14)}$ has removed the signals due to the 14-protons and has caused a large down-field shift (ca. 0·7 ppm) of the H_1 signal which now appears as a doublet (J = 2·5) at 2·86 ppm.

(iv) *The anhydride* (IV). Assignment of H_2 to the triplet (ca. 3 c/s splittings) at 5·43 ppm in the spectrum of IV is straightforward (see Fig. 4). Decoupling experiments show that H_1 and H_3 must be at 3·17 ppm (doublet; J = ca. 3 c/s) and ca. 2·6 ppm (obscured) but do not establish which is which. However, it seems more reasonable to assign H_1 to the doublet at 3·17 ppm (a 0·3 ppm down-field shift from its position in the case of III) than to the signal at ca. 2·6 ppm (which would mean it had undergone a 0·3 ppm *up-field* shift). This means that H_3 is responsible for the signal near 2·6 ppm and has suffered an up-field shift of ca. 1·0 ppm due to removal of the $C_{(4)}$ double bond (cf. spectrum of III).

The diffuse doublet at 4·79 ppm, which can only be assigned to H_5, becomes a diffuse singlet when the signal near 2·5 ppm (H_4) is irradiated ($\Delta\omega$ = 230 c/s). Alternatively, if the signal near 1·8 ppm (H_6) is irradiated ($\Delta\omega$ = 300 c/s) the doublet at 4·79 ppm becomes much sharper (J = 3 c/s).

[12] T. Takahashi, *Tetrahedron Letters* 565 (1964).

(v) *The taxinol derivatives* (V) *and* (VI). With some assistance from double resonance experiments, the assignment of the high-field signals in the spectrum of V (Fig. 5) is straightforward. Once again, NMDR showed H_3 to be weakly coupled to one of the H_{16} protons (at 5·39 ppm). Irradiation of the 12-Me (doublet at 1·38 ppm) converted the multiplet at 2·75 ppm to a doublet (J = 4), whereas irradiation near 1·7 ppm (H_{11}) caused the 2·75 ppm multiplet to become a quartet (partly obscured by overlap of the $H_{14\beta}$ signal).

In compound VI (see Fig. 6), H_2 gives rise to a quartet (J = 2·0, 5·5) at 5·59 ppm, and H_3 now appears as a sharp doublet (J = 5·5) which has shifted down-field due to the adjacent ketone. The H_5-proton appears as an unresolved "triplet" at 4·77 ppm. As in the previous compound (V), signals due to H_{12} and H_{14} overlap. However, irradiation of the 12-Me locates the 12-proton signal which now appears as a doublet (J = 6·5) at 2·66 ppm; the quartet due to $H_{14\beta}$ (at 2·70 ppm) and the doublet from $H_{14\alpha}$ (at 2·35 ppm) are now discernable.

(vi) *Secotaxinol diacetate* (VII). The assignment indicated in Fig. 7 for secotaxinol diacetate is straightforward. The most important feature to be noticed is the appearance of the H_5 proton signal as a broad multiplet, indicating that the 5-hydrogen is axial in this compound and strongly coupled to the adjacent methylene protons at $C_{(6)}$. Small long-range couplings between H_5 and the protons at $C_{(16)}$ and $C_{(3)}$, as well as the fact that H_5 forms part of an AA'BB'X (protons at $C_{(7)}$, $C_{(6)}$ and $C_{(5)}$) type system, account for the complex nature of the H_5 signal.

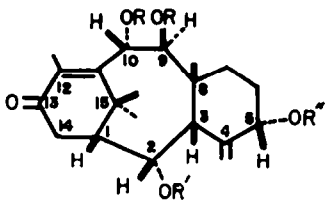
(vii) *Anhydrotaxininol* (VIII). The doublets at 6·05 ppm (J = 9) and 3·55 ppm (J = 9) in the spectrum of anhydrotaxininol (VIII) are easily assigned, since addition of D_2O caused the former (due to 9-OH) to disappear and the latter to become a singlet (9-H); the peak near 2·1 ppm, due to the 5-OH, also vanished after D_2O treatment (see Fig. 8). The low-field position of the 9-OH signal and the fact that it appears as a doublet whereas the 5-OH signal is a singlet (i.e. proton exchange is inhibited with the former but not with the latter) constitute good evidence that the 9-OH is involved in strong intramolecular hydrogen-bonding with the carbonyl at $C_{(13)}$. The broad singlet at 4·33 ppm obviously belongs to H_5, since irradiation near 1·88 ppm (H_6) with $\Delta\omega$ = 245 c/s causes marked sharpening of the 4·33 ppm signal; the two signals at 5·12 and 4·85 ppm can therefore be assigned to the $C_{(16)}$-protons. Irradiation ($\Delta\omega$ = 760 c/s) of the doublet (J = 3) at 9·73 ppm (aldehyde proton) reduces the quartet (J = 2·5 and 12 c/s) at 2·13 ppm to a doublet (12 c/s spacing), and irradiation of the 12-Me doublet at 1·10 ppm with $\Delta\omega$ = 146 ppm similarly reduces the multiplet (doublet of quartets) at 2·62 ppm to a doublet (12 c/s spacing). These two doublets constitute an AB quartet and are due to H_{11} and H_{12}, respectively.

(viii) *Compounds* IX–XIV. The NMR spectra of compounds IX–XIV have been assigned by analogy with the compounds described above; the relevant data are given in Table 1.

Comments of the above spectra

The chemical degradations and other evidence discussed in the previous paper[1] did not lead conclusively to the structure of ring C in taxinine, apart from showing that the exocyclic methylene group and cinnamate group are on adjacent carbons. However, NMR evidence[2] does provide convincing proof for the ring C structure shown in structure I (see Fig. 1). As indicated in Fig. 1 (see earlier discussion),

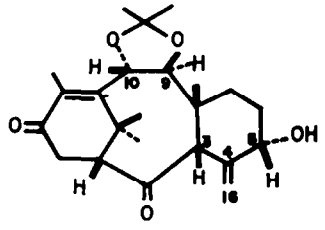
NMDR experiments on taxinine demonstrate that the C_3-proton (at 3·42 ppm) is coupled weakly to a proton absorbing at 4·88 ppm. From its down-field position, this proton must be one of the protons attached to the exocyclic methylene or to the carbon bearing the cinnamate grouping. A similar conclusion can be drawn from the



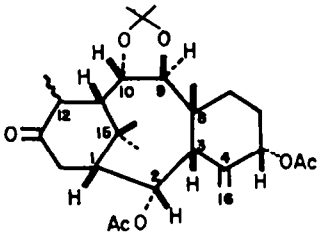
IX R=H, R'=Ac, R''= -COCH=CHPh

X R, R= >CMe$_2$, R'=Ac, R''= -COCH=CHPh

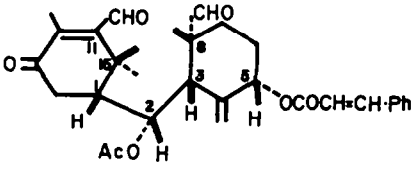
XI R, R= >CMe$_2$, R'=R''=H



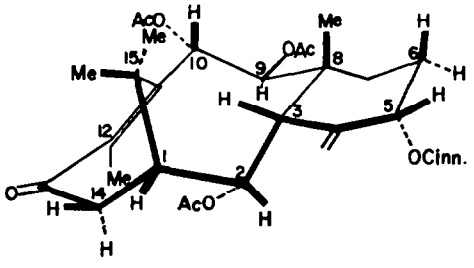
XII



XIII



XIV



XV

results of decoupling experiments carried out on taxinol tetraacetate (see Fig. 5). Accordingly, in taxinine (and in taxinol tetraacetate) there must be either an exocyclic methylene group or an oxygen function attached to $C_{(4)}$, and of these two possibilities only the former can adequately explain the low-field absorption of H_3 (at 3·42 ppm in taxinine and at 3·06 ppm in taxinol tetraacetate); hence taxinine has the ring C structure shown in I. This conclusion is supported by the fact that in the 14-keto

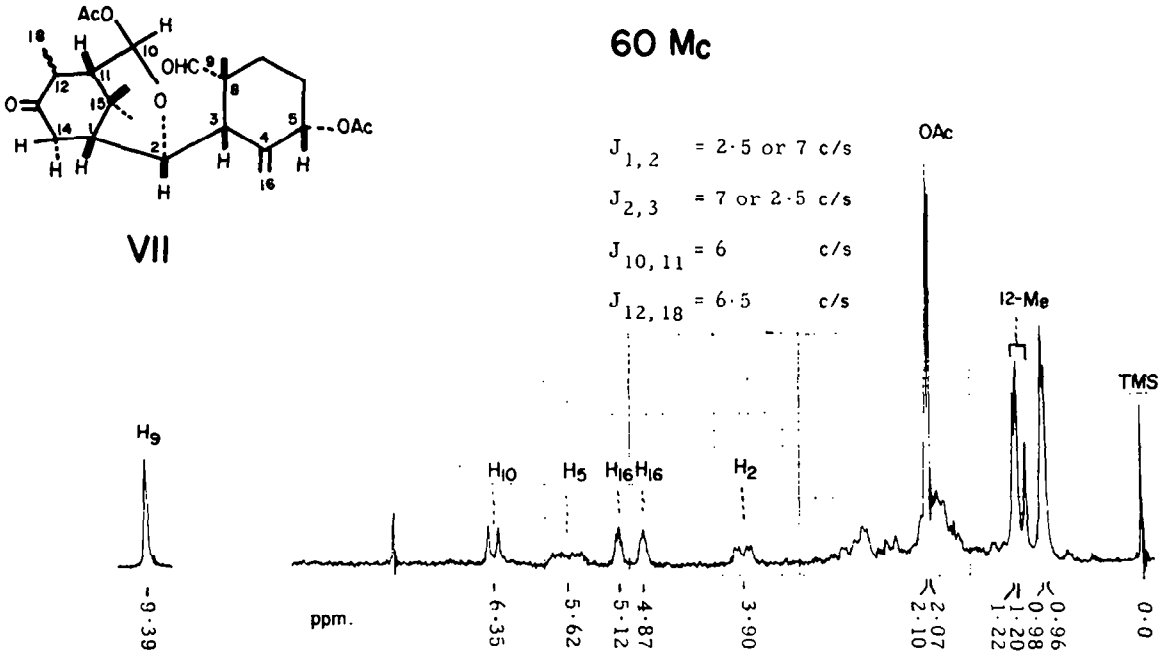


FIG. 7. NMR spectrum of secotaxinol diacetate (VII).

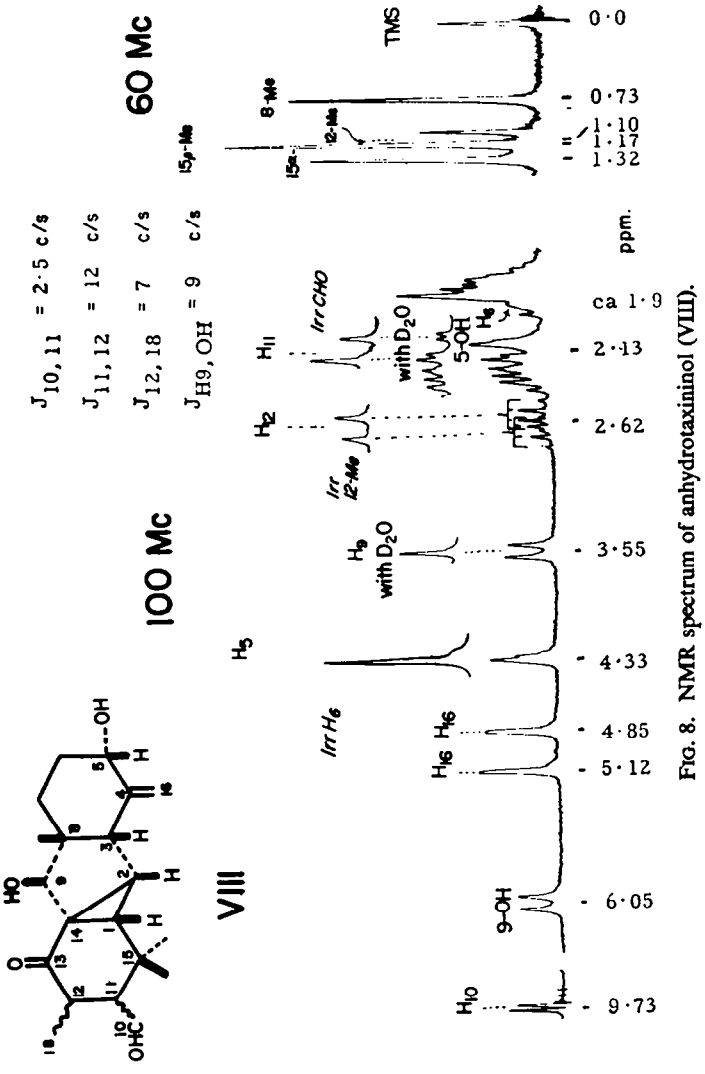


FIG. 8. NMR spectrum of anhydrotaxininol (VIII).

derivative (III), which still retains exocyclic methylene, H_8 appears at 3·54 ppm, and in the 4-keto derivative (VI) H_3 absorbs at 3·68 ppm, but in compounds II and IV which have a methyl group at $C_{(4)}$ the 3-proton signal is shifted to a much higher field position at 1·65 and 2·6 ppm, respectively. Moreover, the marked sharpening of the broad peak at 5·27 ppm, on irradiating near 1·8 ppm in the spectrum of 14-oxotaxinine (see Fig. 3), is in accord with the presence of an oxygen function at $C_{(5)}$ but not at $C_{(4)}$, since an allylic or ethylenic proton is unlikely to absorb at a field as high as 1·8 ppm whereas a CH_2, such as that at $C_{(6)}$ in structure III (Fig. 3), may do so. Decoupling of H_5 from the adjacent methylene protons at $C_{(6)}$ has also been carried out with anhydrotaxininol (Fig. 8) and the anhydride IV (Fig. 4).

A number of conclusions regarding the stereochemistry of ring C in taxinine and its derivatives can be drawn from the spectra discussed above. In the spectra of those derivatives of taxinine which have an uncleaved B-ring and an oxygen function at $C_{(5)}$ but no proton at $C_{(4)}$ (see Figs. 1, 3, 5, 6 and 8), the H_5 signal appears as an ill-defined triplet with a half-band width of about 4 c/s. Compounds XIV, X, XI, XII, and XIII also give rise to a similar type of H_5 signal. On the other hand, in the spectra of *seco*-taxinol diacetate (Fig. 7) and *seco*-dideacetyl taxinine (XIV; spectrum not shown) the H_5 signal is a broad multiplet with half-band width 16–22 c/s. A 5-hydrogen whose bond bisects the angle between the adjacent methylene hydrogens would explain the narrow band width of the H_5 signal,* but in the case of the two *seco*-derivatives (VII and XIV) the 5-hydrogen is obviously axial since it is strongly coupled to the adjacent methylene hydrogens. From the substitution pattern of ring C in VII and XIV, it can be assumed that ring C will adopt the stable chair form with the bulky $C_{(3)}$-substituent in an equatorial conformation. This means that the 3- and 5-hydrogens are both axial and therefore in a *cis* relationship. In taxinine and taxinol derivatives the same relative stereochemical relationship will hold for the substituents at $C_{(3)}$ and $C_{(5)}$, but exactly which conformation will be the most stable one for ring C can not be predicted with any certainty. An examination of Dreiding models of taxinine, based on the stereochemistry depicted in I, indicates that interactions between the 8- and 15α-methyls would prevent ring C from adopting the chair form having axial hydrogens at $C_{(3)}$ and $C_{(5)}$. In the alternative chair conformation, a large 1,3-diaxial interaction between the 5-acyl group and the $C_{(2)}$-hydrogen, in addition to the close proximity of the hydrogen at $C_{(3)}$ and the methyl at $C_{(8)}$, would be expected to destabilize this conformation. It is therefore suggested that ring C exists in a deformed chair or twist-boat conformation in which the 5-hydrogen bisects the $C_{(6)}$ methylene hydrogens (projection along $C_{(5)}$–$C_{(6)}$ bond) and the $C_{(2)}$–$C_{(3)}$ bond and the 5-acyl group are pseudo equatorial (see for example the stereo drawing XV).

The narrow band-width (6 c/s) of the H_5 signal in the spectrum of anhydrotaxininol provides evidence for a *cis*-B/C ring junction in this compound, since an examination of Dreiding models of anhydrotaxininol with *cis* 3,5-hydrogens indicates that only in those models having a *cis*-B/C ring junction is it possible for ring C to exist in a stable conformation with the 5-hydrogen in a bisectional relationship to the methylene hydrogens at $C_{(6)}$. In models having a *trans*-B/C ring junction, the most stable

* In this connection, it is interesting to note that $J_{e,e}$ and $J_{e,a}$ for a equatorial proton attached to a carbon bearing an axial acyl group have been observed to be quite small (ca 2·5 c/s) in the steriod series.[18]

[18] D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.* **86**, 2742 (1964).

conformation is with ring C in the chair form and the 5-hydrogen axial; a severe 1,4-interaction between the 8-Me and 5-hydroxyl would prevent ring-C from assuming any of the available boat or twist-boat conformations. A study of Dreiding models of anhydrotaxininol, with the stereochemistry depicted in structure VIII, suggests that ring C would probably be stable in a conformation similar to that in taxinine (cf. structure XV).

From the appearance of the H_{16} signals in the spectra of taxinine (Fig. 1), 14-oxotaxinine (Fig. 3), taxinol tetraacetate (Fig. 5) and anhydrotaxininol (Fig. 8) it is apparent that the exocyclic methylene protons are involved in a small but significant (ca. 1 c/s) amount of allylic coupling to one or both of the protons at $C_{(3)}$ and $C_{(5)}$. If there were no allylic couplings the H_{16} signals should appear as sharp singlets or doublets, depending on the extent of geminal coupling, and not as poorly resolved triplets which appears to be the case. The fact that the H_3 signal appears as a broad doublet (in those cases where it is visible), which becomes much sharper on irradiating one of the H_{16} signals, clearly indicates that the 3-proton is coupled to one or both of the 16-protons. Unfortunately, the H_5 signal is overlapped by other absorption in the spectra of taxinine and taxinol tetraacetate, but in the spectra of 14-oxotaxinine (Fig. 3) and anhydrotaxininol (Fig. 8), both with the H_5 signal clearly visible, the sharpness of the H_5 signal after decoupling from the protons at $C_{(6)}$ seems to indicate that there is little or no allylic coupling between H_5 and H_{16}. This apparent lack of significant coupling between H_5 and H_{16} could be attributed to the 5-hydrogen not having the same orientation as the 3-hydrogen with respect to the exocyclic double bond or possibly to the presence of an oxygen function at $C_{(5)}$. The steric requirements for allylic coupling have been reviewed recently.[8]

The large vicinal coupling constant (9–10 c/s) found for H_9 and H_{10} in taxinine (Fig. 1), the diol IX, and the acetonides X and XI (see Table 2) requires the dihedral angle between these two protons to be near 180°, i.e. the 9,10 hydrogens are *anti-trans*. A cis arrangement of these hydrogens is unlikely since the eight-membered B-ring in taxinine and taxinol tetraacetate is not sufficiently rigid to force these protons into the eclipsed conformation required to produce a large $J_{9,10}$. As mentioned earlier in this paper, the 8-Me and H_9 are thought to be in an *anti-trans* relationship since they appear to be weakly coupled. However, attempts to confirm the presence of this weak coupling by NMDR has so far only led to inconclusive results; the problem is still being investigated.

In those derivatives of taxinine still having the 11,12-double bond, there exists a possibility of homoallylic coupling between the 12-Me and H_{10}. Although Dreiding models of 14-oxotaxinine (III) and the anhydride (IV) indicate that the 10-hydrogen is coplanar with the 11,12-double bond (i.e. homoallylic coupling is minimal),[8] inspection of the spectra of these compounds (see Figs. 3 and 4) shows that the 12-Me signal is appreciably shorter than the nearby acetate signals and hence must be subject to a small coupling. Decoupling experiments to determine the nature of this coupling have not so far been carried out.

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