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INDOLE ALKALOIDS XII : THE TEMPERATURE DEPENDENCE OF 2-ACYLINDOLE ALKALOIDS NMR SPECTRA.

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Certain unexpected features have been reported in the litterature for room-temperature NMR spectra of some 2-acylindole alkaloids (1,2,3,4).

2-Acylindole alkaloids and their derivatives in table I can be grouped in three classes according to the spectral characteristics of their methyl signals.

Class A[x] : compounds whose NMR spectra can be interpreted straightforwardly on the basis of their accepted structures.

Class B[x] : compounds whose NMR spectra are remarkable by the absence of one or more singlet signals expected for $COOCH_3$, $N_\beta COCH_3$, $N_\beta CH_3$ and/or $N_\beta CHO$ groups.

Class C[x] : compounds in the NMR spectra of which one or more of the above groups give rise to two distinct signals.

It is to be noted that in the three categories integration fits the required number of protons.

The suggested classification is somewhat arbitrary as one single compound may be included either in class B or in class C depending on the proton group under consideration. For instance, the spectrum of O,N-diacetylvoacarpine (VIII) recorded for a deuteriochloroform solution at room temperature shows a 3H singlet (acetate), 3 protons distributed between two singlets (acetamide) and no "visible" signal for the methoxycarbonyl group (see figure 1).

One can assume that the unexpected spectral behaviour of compounds in classes B and C is due to the occurence of interconverting conformers.

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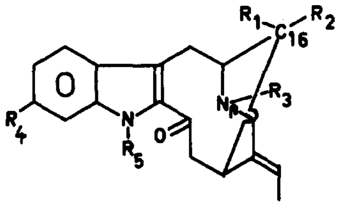
[x] see table I.

TABLE I.

2-ACYLINDOLE ALKALOIDS AND DERIVATIVES.



CLASS	COMPOUND	R_1	R_2	R_3	R_4	R_5	REFERENCES
A	I	COOCH$_3$	CH$_2$OH	H	H	H	(1,2)
	II	COOCH$_3$	H	CH$_3$	H	H	(7)
	III	COOCH$_3$	H	CH$_3$	OCH$_3$	CH$_3$	(8)
	IV	COOCH$_3$	H	CH$_3$	H	CH$_3$	(8)
	V	H	COOCH$_3$	H	H	H	(3)
B	VI	COOCH$_3$	CH$_2$OH	CH$_3$	H	H	(2,5,6)
	VII	COOCH$_3$	CH$_2$OCOCH$_3$	CH$_3$	H	H	(2,5,6)
	VIII	COOCH$_3$	CH$_2$OCOCH$_3$	COCH$_3$	H	H	(1,2)
	IX	COOCH$_3$	CH$_2$OCOCD$_3$	COCD$_3$	H	H	(1,2)
	X	COOCH$_3$	CH$_2$OTs	Ts	H	H	(1)
	XI	COOCH$_3$	H	H	H	H	(3)
C	XII	COOCH$_3$	H	COCH$_3$	H	H	(3,4)
	XIII	COOCH$_3$	H	CHO	H	H	(4)

In this case, the pattern of the observed signals is known to be dependent on the interconversion rate and on the $\Delta\nu$ of the signals corresponding to the same proton group in the different conformers (9).

NMR spectra of all compounds, except compounds III, IV and XIII, have been measured at several increasing temperatures in nitrobenzene or tetrachloroethylene. At 120° all the compounds of classes B and C give spectra that can be immediately interpreted and contain singlets of relative area 3H for the COOCH$_3$, OCOCH$_3$, N$_\beta$COCH$_3$ and/or N$_\beta$CH$_3$ groups present in these molecules.

The pattern of the observed signals varies with increasing temperatures according to the scheme: two signals → coalescence → one signal (see table II). On the other hand, the spectrum of vobasine (II)(class A) scanned at -40° becomes similar to that of the compounds of classes B recorded at room temperature (important broadening of the $COOCH_3$ and $N_\beta CH_3$ signals).

TABLE II.

NUMBER OF SINGLET SIGNALS FOR EACH CH_3 IN THE SPECTRA RECORDED AT DIFFERENT TEMPERATURES.

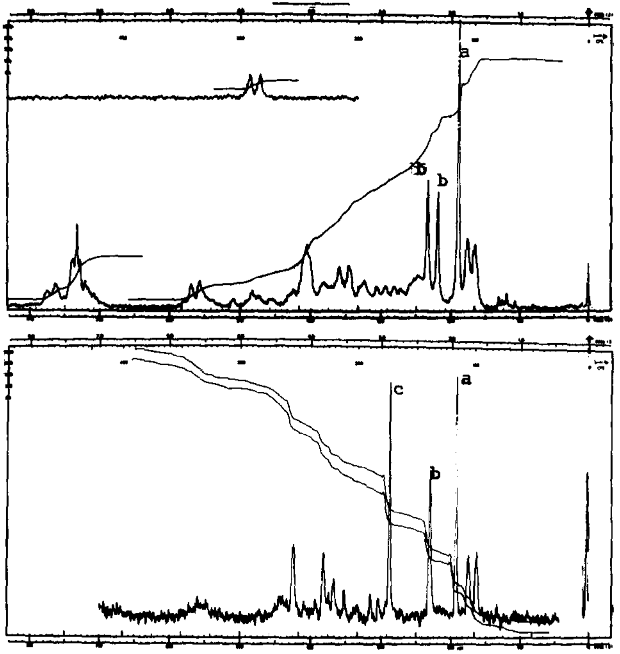
ALKALOID	GROUPS	NUMBER OF SINGLET SIGNALS		
		-40°	+35°	+120°
II	$COOCH_3$	broadening	1	
	$N_\beta CH_3$	broadening	1	
VI	$COOCH_3$		0	1
	$N_\beta CH_3$		1	1
VII	$COOCH_3$		0	1
	$OCOCH_3$		1	1
	$N_\beta CH_3$		1	1
VIII	$COOCH_3$	2	0	1
	$OCOCH_3$	1	1	1
	$N_\beta COCH_3$	2	2	1
IX	$COOCH_3$	2	0	1
X	$COOCH_3$		0	1
XI	$COOCH_3$		0	1
XII	$COOCH_3$	2	2	1
	$N_\beta COCH_3$	2	2	1

The observed phenomenon seems therefore to be general for 2-acylindole alkaloids and is indeed to be attributed to the occurence of several conformers. Three types of conformational equilibria may be involved: the inversion of the alicyclic part of the molecule (9) (in this particular case the azabicyclo [5,3,1] undecane system), the inversion of the N_β nitrogen atom (10) and/or the hindered rotation about the N_β-C=O, C_{16}-C=O bounds (11). A choice between these possibilities is hardly possible at the present time, and a full investigation is now in hand.

The situation can be even more intricate when a carbinolamine $\rightleftharpoons$ ketoamine equilibrium is possible. However, when the carbinolamine structure is higly favored at room temperature the NMR spectrum is immediatly interpretable, the rigid alicyclic system no longer allowing conformational changes (eg. voacarpine (I) and 16-epiperivine (V)). On the other hand, perivine (XI) which has essentially the keto-amine structure, belongs to class B.

The occurence of compounds of classes B and C shows that the greatest care is needed when interpreting the NMR spectra of 2-acylindole alkaloids.

FIG.1



VARIAN A60 NMR spectrum of O,N-diacetylvoacarpine (VIII) in $CDCl_3$ solution at +35° (upper curve) and in nitrobenzene solution at +120° (lower curve). Peak (a) : $OCOCH_3$ group. Peak(s) (b) : $N_\beta COCH_3$ group. Peak (c) : $COOCH_3$ group.

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