MASS SPECTRAL FRAGMENTATION OF SOME INDOLE DERIVATIVES

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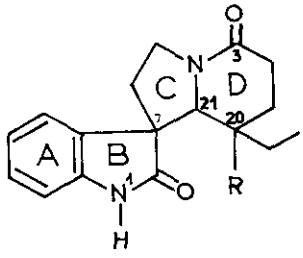
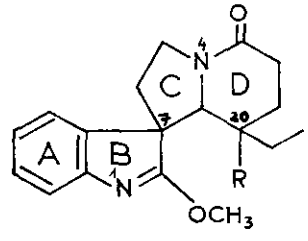
Abstract - EI mass spectra of oxindoles C, iminoethers D, and dihydro β-carbolines E, arising from chloroindolenines B are analysed.

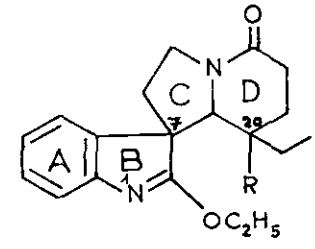
Chloroindolenines B, obtained from 4-oxo indolo (2,3-a) quinolizidines A, rearrange to oxindoles C, iminoethers D, and dihydro β-carbolines E[2] (TABLE 1), in which R=H, C_2H_5 or $CH_2CH_2CO_2R'$. Some oxindoles C may also be prepared after HARLEY MASON[3], through condensation of 2-hydroxy tryptamine with the suitable aldehydo-ester. Iminoethers D (R'=CH_3 or C_2H_5) are available from C, using the appropriate MEERWEIN'S reagent. All these coupounds exhibit very simple EI spectrum upon a 70 eV energy electron beam[4].

Then,it became obvious to compare the behaviour of each class, in order to deduce the fragmentation pattern and mechanism. Only one natural base, i.e. the alkaloid vincatine, is know to possess the same skeleton as ester 1c. Its mass spectrum has already been published[5]. However, oxindoles 1,a,b,c, which bear a supplementary lactame carbonyl groupe at C(3), follow a fragmentation mode drastically differing from that of vincatine.

1 . Mass spectral fragmentation of oxindoles C and iminoethers D







1a R = H — 3a

1b R = C_2H_5 — 2c — 3b

1c R = $(CH_2)_2COOCH_3$ — 3c

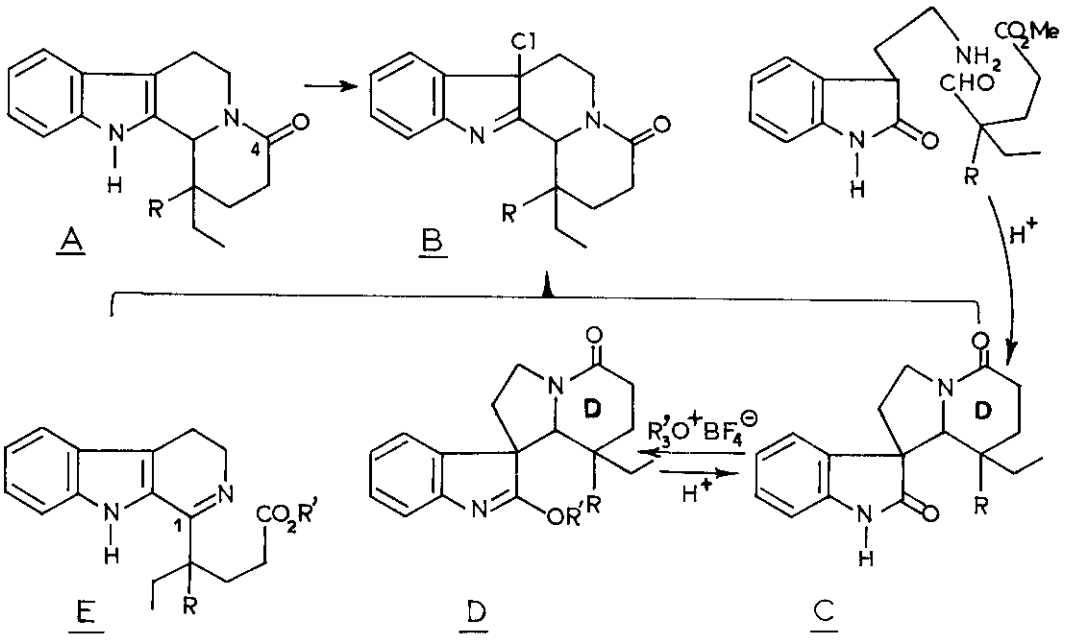
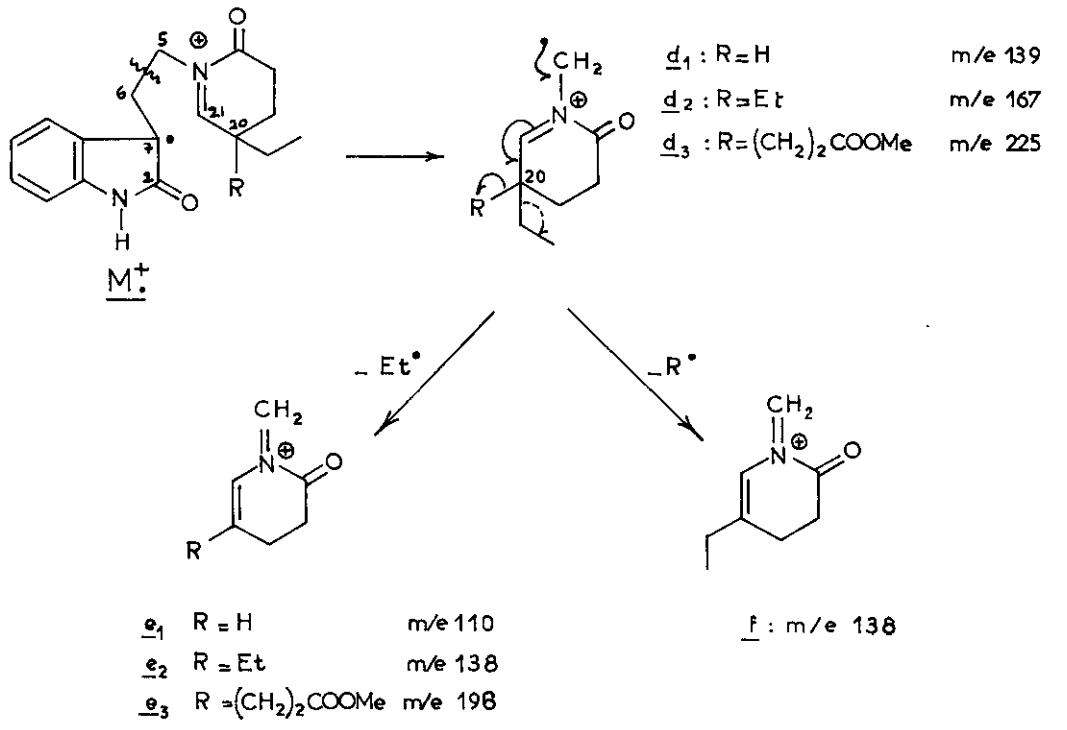


Table **1**



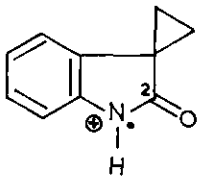
e1	R = H	m/e 110
e2	R = Et	m/e 138
e3	R = $(CH_2)_2COOMe$	m/e 198

f : m/e 138

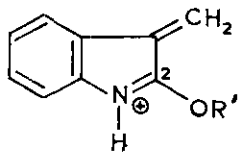
Table 2

Oxindoles 1a,b,c and iminoethers 2c and 3a,b,c are concerned in this study. They differ only by the nature of R on C(20)[2,6]. In each case, many stereoisomers exist, due to the chiral carbons 7,20 and 21. Yet, the mass spectra of the stereoisomers are quite similar, and throughout this paper, the relative configuration of the discussed molecules will not be further taken in account. Some fragments vary with R, some other do not.

1.1 Fragments non varying with R : ions a,b,b',c,c'

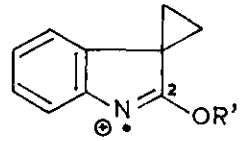


a : m/e 159



b R' = CH_3 : m/e 160

b' R' = C_2H_5 : m/e 174



c R' = CH_3 : m/e 173

c' R' = C_2H_5 : m/e 187

When bearing only one nitrogen (N(1)), they retain carbons from cycles A,B or C.

The abundant ions are :

from oxindoles 1a-c : ion a, m/e 159

from iminoether 2c : ions b, m/e 160 and c m/e 173 (base peak)

from iminoether 3a-c : ions b', m/e 174 and c'm/e 187 (base peak).

Ion a is commonly encountered in oxindole alkaloids[7]. The nature of b,b' and c,c' is deduced from the gain of 14 m.u. from the methyl iminoether 2 to the ethyl derivate 3.

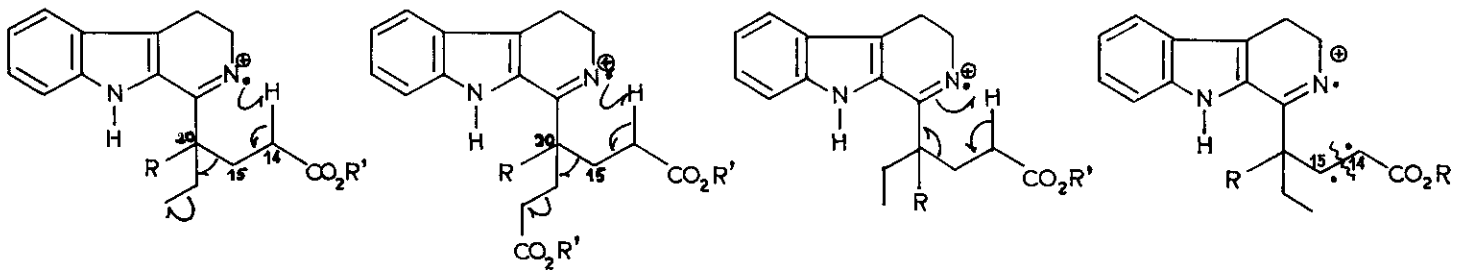
1.2 Fragments varying with R : ions d,e,f

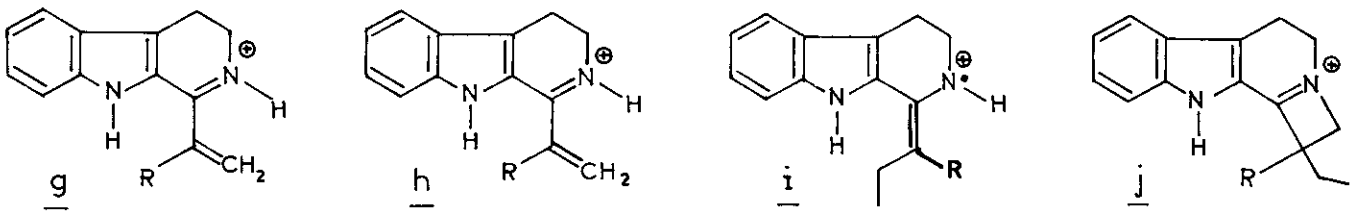
When bearing only are nitrogen (N(4)), they involve carbons of cycle D. They arise from oxindole 1 and its iminoethers 2 and 3. Their alleged genesis and structures are shown on TABLE 2. Radical cations d result from the homolytic cleavage of bonds 6-5 and 7-21 in the molecular ion. These unstable species rearrange to the more stable ions e and f through the loss of one of the two radicals attached to C(20).

These assumptions are deduced from the correlative variations of d and R : d_1 (m/e 139) d_2 (m/e 167) d_3 (m/e 225).

Then d_{1-3} lead to the corresponding ions e through loss of 29 m.u. : e_1 (m/e 110) ; e_2 (m/e 138) ; e_3 (m/e 196).

When the variable radical R is lost from d, ion f arises. Actually, f (m/e 138) is present on the spectrum of any compound C and D. Moreover, the ubiquitous ion m/e 138 is notably more abundant on the spectra of compounds 1b and 3b. In these compounds, the two substituents attached to C(20)





g h i j

	R	m/e	Intensity	R	m/e	Intensity
4a,b	H	197	100			
5a,b	Et	225	100			
6a	$(CH_2)_2CO_2Me$	283	40	Et	225	100
7a,b	$(CH_2)_2CO_2Et$	297	15	Et	225	100

	R	m/e	Intensity a	Intensity b
4a,b	H	212	35	35
5a,b	Et	240	35	35
6a	$(CH_2)_2CO_2Me$	298	30	
7a,b	$(CH_2)_2CO_2Et$	312	30	

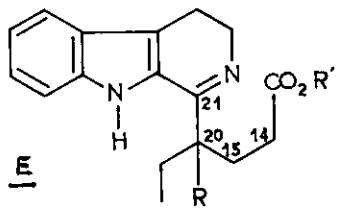
	R	m/e	Intensity a	Intensity b
4a,b	H	225	20	20
5a,b	Et	253	80	85
6a	$(CH_2)_2CO_2Me$	311	30	
7a,b	$(CH_2)_2CO_2Me$	325	30	

a : $R' = CH_3$
b : $R' = C_2H_5$

Table 3

are identical ; then $\underline{d}_2$ leads to identical ions $\underline{e}_2$ and $\underline{f}$.

2 . Mass spectral fragmentation of dihydro-β-carbolines E



E

4 : R = H

5 : R = C_2H_5 a : R' = CH_3

6 : R = $(CH_2)_2CO_2CH_3$ b : R' = C_2H_5

7 : R = $(CH_2)_2CO_2C_2H_5$

Series a consist of *methyl* esters, series b of *ethyl* esters.

Compounds 7a and 7b could not be separated : then the spectrum of the mixture was measured.

The fragmentation of coumpounds E appears to proceed through three competive mechanisms (TABLE 3):

2.1 Loss of an acrylic ester plus homolytic cleavage : ions g et h

Peaks M -101, i.e. M -(86 + 15) are to be seen on the spectra of 4a,5a,6a,7a, whereas peaks M -115, i.e. M -(100 + 15) are to be seen on the spectra of 4b,5b, and 7b. These ions may result from the simultaneous loss of methyl (a series) *vs* ethyl (b series) acrylate and a methyl radical. Ions g give rise to the base-peak in the spectra of 4a,b and 5a,b. Their genesis may result from the cleavage of the 15,20- bond with hydrogen radical transfer on N(4) (loss of an acrylic ester), followed with the loss of a methyl radical from the ethyl chain at C(20), thus leading to the very stable species g.

In the case of diesters 6a and 7a,b, the same process (i.e. loss of an acrylic ester and a methyl radical) can occur : ions g m/e 283 *vs* 297, but the main process is the loss of an acrylic ester and an acetate ester radical : h m/e 225 (base-peak). The latter process requires less activation energy.

2.2 Loss of an acrylic ester through a MAC LAFFERTY's rearrangement : ions i

The ions i appear at m/e M-86 (4a,5a,6a and 7a) or M-100 (4b,5b,7b), in every case with the same relative intensity (about 30 % of the base peak). These relatively abundant radical cations are suggested to be generated through an electrocyclic process such as path 2 outlined on TABLE 3.

2.3 Homolytic cleavage of the 14-15 bond

The classical scission β to a carbonyl group accounts for the loss of a methyl acetate radical (a series) or an ethyl acetate radical (b series) from the molecular ion and gives rise to ions j. The strikingly high abundance of j from 5a (80 %) and 5b (85 %) could not be interpreted.

The above results are of interest for the structure elucidation and recognition of the intermediates C,D,E in the total synthesis of indole alkaloid performed in this[8-9] and other[10] laboratories.

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