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MASS SPECTRA OF AMARYLLIDACEAE ALKALOIDS. THE STRUCTURE OF NARCISSIDINE.

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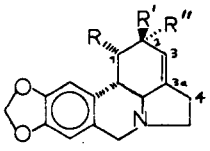
Although mass spectrometry has been used extensively for alkaloid structure determination (1), application of the technique to the Amaryllidaceae (2) has been limited to alkaloids derived from the crinine-, montanine- and tazettine-type nuclei (3). The mass spectra of these alkaloids were found to be very dependent on small structural or stereochemical changes, which often necessitated isotope labeling studies before structural conclusions could be formulated. We wish to report a mass spectral study of the most common of the eight different ring systems which have been encountered in the Amaryllis, namely the pyrrolo[de]-phenanthridine nucleus which is present in the lycorine-type alkaloids. These spectra are not greatly effected by small structural changes and application to structure determination is exceptionally straightforward.

The mass spectrum of lycorine (Ia) is shown in Figure 1. The parent ion appears as an intense peak at m/e 287.



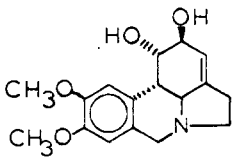
Ia, R=R'=OH; R"=H

Ib, R=OH; R'=R"=H

Ic, R=OAc; R'=OH; R"=H

Id, R=OAc; R'=R"=H

Ie, R=R"=OH ; R'=H



II

Essentially twin base peaks occur at m/e 227 (M-60) and m/e 226 (M-61). The only other fragment ion of reasonable intensity is m/e 268 (M-19). The spectrum of caranine (Ib), shown in Figure 2, exhibits a very similar pattern of fragments in the high mass region with essentially no fragments below m/e 220.

Substituent labeling proved to be very useful in understanding the fragmentation. Methylpseudolycorine (II), whose spectrum is shown in Figure 3, also suffers the loss of 19, 60 and 61 mass units which shows that ring A is not suffering fragmentation. 1-Acetyllycorine (Ic), acetylcaranine (Id) and 1-acetyl-2-^{2}H-lycorine all gave very intense ions at m/e 226 and 227. The only different major fragment ions which appeared in the spectra of these acetylated derivatives were due to the loss of acetic acid.

FIG. 1

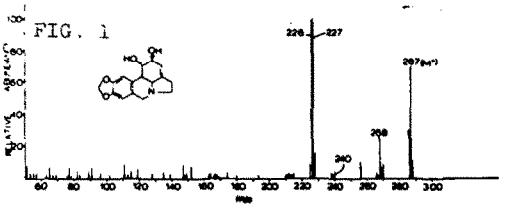


FIG. 2

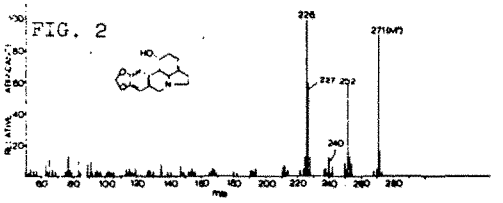


FIG. 3

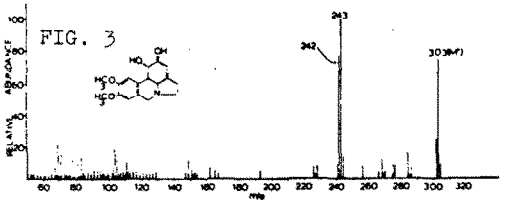
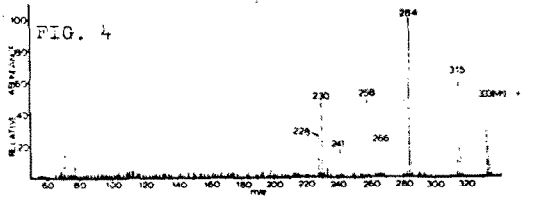
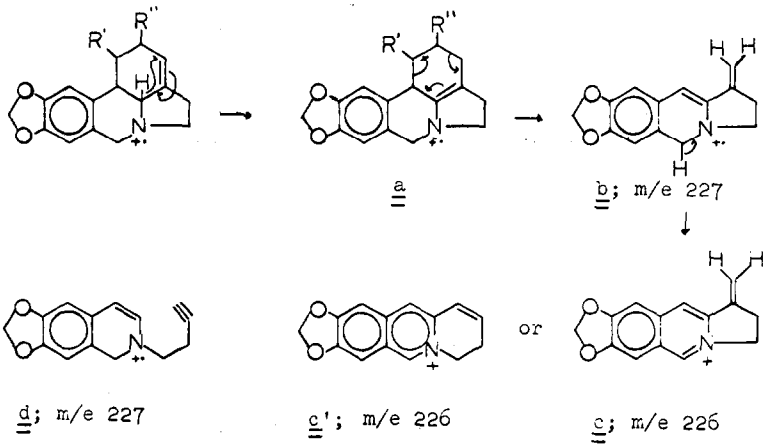


FIG. 4

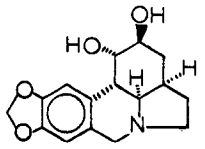


The formation of these intense fragment ions can be shown to result from the loss of carbon atoms C_1 and C_2 and their substituents. The presence of a strong metastable ion at m/e 179.8 (m^*_c = 179.6 for 287 → 227) in the spectrum of lycorine supports this postulate. Corresponding metastable ions have been detected in the spectra of all lycorine-type alkaloids containing 3,3a-unsaturation. Another metastable at m/e 225.0 in the spectra of these compounds relates the m/e 227 ion to the m/e 226 ion. Spectra measured at lowered electron energies exhibit a much decreased 226/227 intensity ratio. The loss of the C_1-C_2 bridge is the lowest energy fragmentation. A reasonable mechanism for this loss and possible structures for the resulting ions are shown in Scheme I.

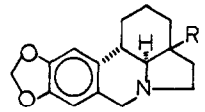
Scheme I



In agreement with this scheme, dihydrolycorine (III), as well as other derivatives lacking the 3,3a-unsaturation, do not lose the C_1-C_2 bridge. The base peak in the spectrum of III



III



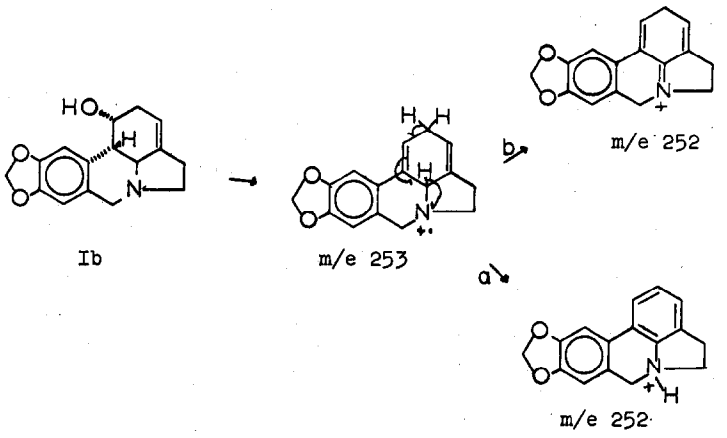
IV V

R= ···· H R= ◄ H

is 288 (M-1). No other fragment greater than 8% of this intensity was observed. Alternative formulations for the fragment ions (such as d in place of b) will be tested by isotope labeling studies currently underway.

The M-19 ion, which is the second largest fragment in the spectra of Ia, Ib, and II, is not present in the spectra of Ic or Id or the diacetyl derivatives of I or II. It can be attributed to the loss of water followed by the loss of an additional proton as shown by the presence of the appropriate metastable transitions in all cases. Although substantiation by isotope labeling is not yet complete, possible mechanisms for this fragmentation are shown in Scheme II using caranine as a model.

Scheme II

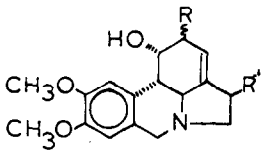


The ease of water loss from the molecule ion was found to be greatly dependent on the stereochemistry of the C_2 hydroxyl group. In the mass spectrum of lycorine the relative intensity of m/e 269 (M-18) is less than 10%, while in 2-epilycorine (Ie), it is the base peak. This difference is even more pronounced at low electron energies. Using 15ev electrons the M-18 ion from lycorine (Ia) or methylpseudolycorine (II) is negligibly small, while in 2-epilycorine (Ie), it remains the base peak and five times as intense as the molecule ion. Studies now in progress suggest that this technique will be useful in assigning the stereochemistry of a C_2 hydroxyl group. The stereochemical differences present

in α- and β-lycorane (IV and V, respectively) do not result in significant differences in their mass spectra.

These findings insure that in the future mass spectrometry will provide a rapid and convenient determination of the substituent composition (but not position) at C_1 and C_2. Of paramount importance is the ease with which the presence or absence of the lycorine-type ring system can be detected in an Amaryllidaceae alkaloid of unknown structure, since other types fragment quite differently. Further confirmation of the presence of this ring system is available from the absence of the diagnostic fragment ions in the spectra of the 3,3a-dihydro derivatives. The diagnostic value of this technique is considerable since available chemical methods are extremely costly in both time and material (2).

Structure of Narcissidine. On the basis of extensive chemical interrelations structure VI was assigned to narcissidine (4). The mass spectrum of narcissidine (Figure 4) confirmed the



VI, R=OH; R'=OCH_3

VII, R=OCH_3; R'=OH

VIII, R=R'=H

molecular weight, but seemed anomalous since there were no peaks at m/e 272 or 273 due to loss of the C_1, C_2 bridge. However intense ions in the m/e 257-259 region combined with metastable peaks at m/e 200.9 and 257.0, which interrelate $333 \rightarrow 259$ ($m^*_c = 201.0$) and $259 \rightarrow 258$ ($m^*_c = 257.0$), requires the loss of $C_3H_6O_2$ and requires that C_1 and C_2 bear hydroxyl and methoxyl substituents. A hydroxyl group must be located at C_1 since narcissidine has been converted to pluviine (VIII) by sodium and amyl alcohol. The remaining hydroxyl group is placed at C_4 from arguments cited in our earlier paper (4) and narcissidine is best represented by the revised structure VII.

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