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STUDIES IN MASS SPECTROMETRY[1]

TRITERPENOIDS : STRUCTURE ASSIGNMENT TO SOME FRIEDELANE DERIVATIVES

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RECENT publications have demonstrated the power of mass spectrometry as a research tool for elucidating the structure of steroids,[2] alkaloids,[3,4] and some unsaturated triterpenes,[5] using a technique in which these compounds were introduced into the ion source via some type of heated-inlet system. For recording the mass spectra reported in this communication a different technique was adopted, in which the sample in its solid state was introduced directly into the ion source and then vaporized by heating it close to the fringe of the ionizing electron beam. By means of a vacuum lock the samples could be introduced into and withdrawn from the ion source without breaking the vacuum of the analyser tube.

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[1] Part III. For Part II see C.G. Macdonald and J.S. Shannon, Aust.J.Chem. **15**, No.4 (1962).

[2] H. Budzikiewicz and C. Djerassi, J.Amer.Chem.Soc. **84**, 1430 (1962); R. Ryhage and E. Stenhagen, J.Lipid Res. **1**, 361 (1960).

[3] K. Biemann, Angew. Chem. **74**, 102 (1962).

[4] B. Gilbert, J.M. Ferreira, R.J. Owellen, C.E. Swanholm, H. Budzikiewicz, L.J. Durham and C. Djerassi, Tetrahedron Letters No.2, 59, (1962).

[5] C. Djerassi, H. Budzikiewicz and J.M. Wilson, Tetrahedron Letters No.7, 263 (1962) and references therein.

The present note deals with the mass spectroscopy of some triterpenes of the friedelane series - in particular, friedelane-x-one derivatives[6,7,8] - and is probably the first communication to be published on mass spectra of saturated triterpene derivatives (however, see ref.[5]). Although the relationship of friedelane-x-one (II) to friedelane (I) was established[6,7] in 1956 the exact position of the keto group has remained in doubt. Owing to the existence of a D/E "cis" juncture in friedelane[7] and its derivatives the large steric interference between 13-α and 20-α methyl groups precludes a chair form of ring E and also leaves the conformation of ring D in doubt. Consequently consideration of substituents in ring E from optical rotatory dispersion measurements was not possible,[8] and thus it could only be concluded that chemical and optical rotatory dispersion results were compatible with a keto group in position 6 or position 16[8]. Mass-spectral studies reported herein have now disclosed that the keto group is in fact in ring E and is at either position 21 or position 22, with preference for the latter.

Table 1 presents the friedelane derivatives referred to in the text. The positions of cleavage of the ions of these, the elucidation of which led

TABLE 1

	I	II	III	IV	V	VI	VII	VIII
R_1	H_2	H_2	O	O	O	H_2	H_2	O
R_2	H_2	O	H_2	O	OH	OH	OAc	OAc

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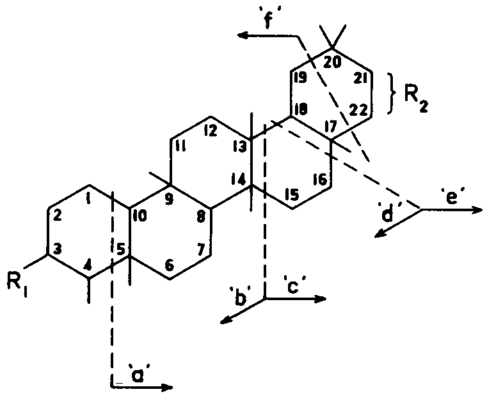
[6] J.L. Courtney and R.M. Gascoigne, J.Chem.Soc. 1956, 2115.

[7] J.L. Courtney, R.M. Gascoigne and A.Z. Szumer, J.Chem.Soc. 1956, 2119.

[8] C. Djerassi, Jeanne Osiecki and W. Closson, J.Amer.Chem.Soc. 81, 4594 (1959).

to the assignment of position "x", are shown below. The masses of the



resultant fragment ions are given in Table 2.

TABLE 2

Compounds	Masses of Ion Fragments from Reactions					
	'a'	'b'	'c'	'd'	'e'	'f'
III	341	273	-	302	-	-[9]
III-2,2′,4-d_3	341	276	-	305	-	-
IV	355	273	-	-	-	355
IV-2,2′,4,21,21′-d_5[10]	357	276	-	-	-	358
V	-	273	-	-	139	-
VI	-	259	149	-	139	-
VI-O-d	-	259	149	-	140	-
VII	-	259	149	-	-	-
VIII	-	273	-	-	-	-

To indicate how the break-down pattern shown on the previous page was established it may be mentioned that with friedelane-3-one(III),

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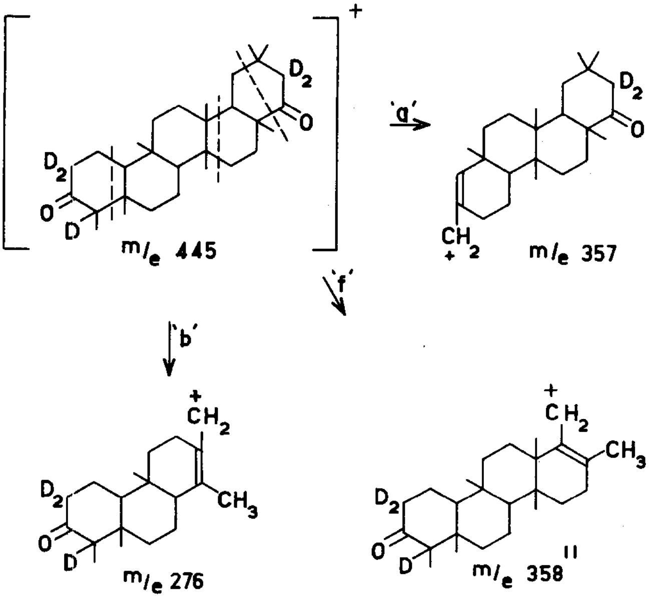
[9] Where a dash is shown there may be small peaks present but there is no evidence to relate these to reactions 'a' to 'f'.

[10] Alternatively, -2,2′,4,22,22′-d_5 (see discussion).

evidence that the ion of mass 341 originated by the loss of ring A (reaction 'a'), the ion of mass 302 by the loss of ring E (reaction 'd') and the ion of mass 273 by the loss of rings D and E (reaction 'b') was provided by the fact that in the spectrum of friedelane-3-one-2,2',4-d_3 the ion of mass 341 showed no change whereas the ion of mass 302 was increased to 305 and the ion of mass 273 to 276.

In the spectrum of friedelane-3:x-dione(IV) there is a peak at mass 355 corresponding to the loss of C_5H_9O (reaction 'a') and a peak at mass 273 (reaction 'b') but no peak at mass 302 (reaction 'd'). When the dione IV was reacted with NaOD,D_2O in dioxane solution, five hydrogen atoms were exchanged with deuterium. The presence of the 3-keto group accounts for



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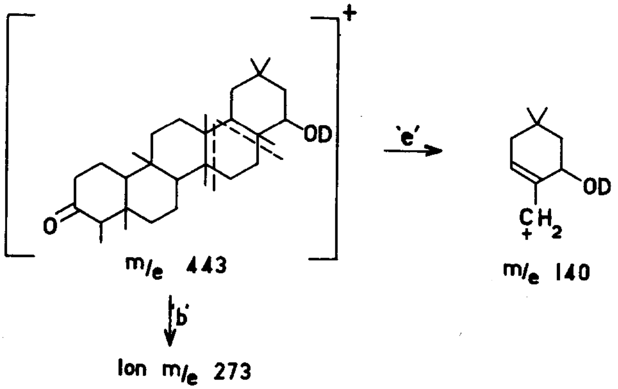
[11] No distinction is made between this and the alternative structure where the positions of the $-CH_3$ and $-\overset{+}{C}H_2$ groups are interchanged.

three of these exchangeable hydrogens, and hence the x-keto group was in a position where there are only two adjacent exchangeable hydrogens. Further, study of the mass spectrum of IV-d_5 showed that the peak corresponding to the peak at mass 355 in the spectrum of the undeuterated compound had been not only shifted but resolved into two peaks - one at mass 357 and the other at mass 358. The peak at mass 273 was shifted to mass 276. These results may be explained if the x-keto group is at either position 21 or position 22.

Further evidence that position "x" is in ring E was provided by study of the mass spectra of compounds V, VI, VII and VIII. In the spectrum of x-hydroxyfriedelane-3-one(V) the peak at mass 273 (reaction 'b') is retained but there is also a strong peak at mass 139 (reaction 'e') which is shifted to mass 140 in the O-deuterated compound[12].



The surprisingly high stability of the ion of mass 139, despite the well-known tendency of hydroxylated ions to eliminate a molecule of water, may point to the hydroxyl group being at position 22 where it could rearrange to produce a resonance-stabilized structure, for example:

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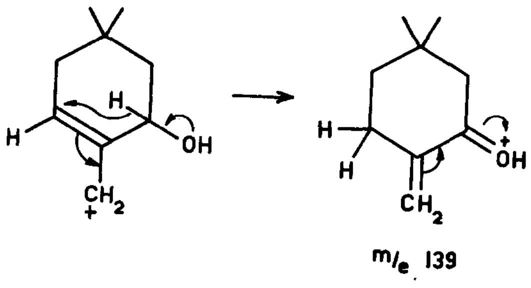
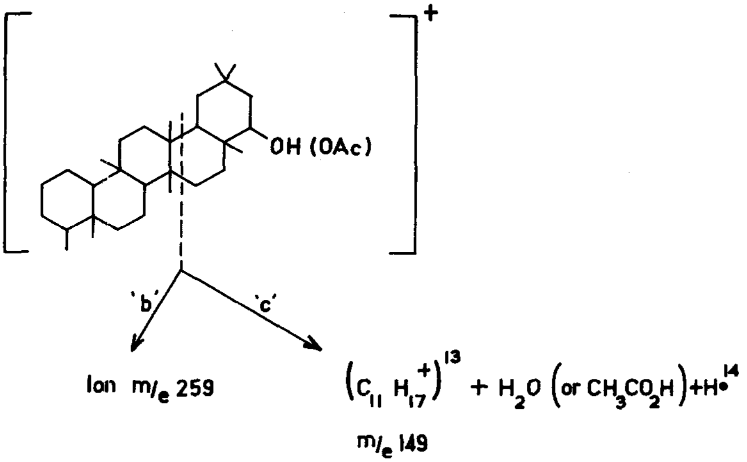
[12] Prepared by passing D_2O through the gas inlet system of the mass spectrometer into the ion source where the sample was being evaporated.



With the keto-acetate (VIII) there is no peak at mass 139. However, with the acetate (VII) there is a large peak at mass 149 and also at 259, as there also is in the spectra of the corresponding alcohol.



The corresponding 3-one derivative (VIII) formed an ion of mass 273 corresponding to the ion of mass 259 (reaction 'b'), but no ion of mass 149.

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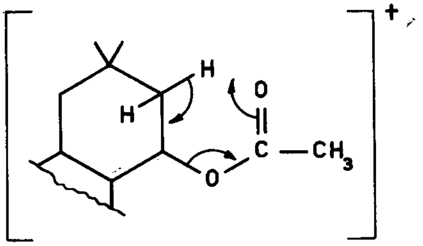
[13] No attempt has been made to formulate a structure for this ion.

[14] The formation of each fragment ion in reactions 'a', 'b', 'c', 'e' and 'f' is accompanied by the loss of a hydrogen atom.

Presumably the keto group reduces the ionization potential of the fragment of mass 273 below that of the fragment of mass 259 and causes reaction 'b' to take precedence over reaction 'c'.

Stereochemical Considerations

With compounds VI, VII and VIII epimeric pairs, i.e. modifications containing both equatorial and axial x-substituents, were studied. A marked difference was observed between the mass spectra of the equatorial and axial compounds. Although these spectra were the same as far as position of peaks was concerned (except M-15 peaks) there were significant differences in relative intensities between corresponding peaks at equal mass positions. For example, the equatorial form of the keto-acetate (VIII) has no M-15 peak but a strong M-60 peak, whereas the spectrum of VIII (ax) has an M-15 peak but a relatively weaker M-60 peak. Although the greater ease of elimination of acetic acid from an equatorial compared with an axial acetate is contrary to previous findings, with other compounds[15], the present results are explicable in the light of the more ready formation of a cyclic transition state in the ion from the equatorial acetate compared with the ion from the axial acetate.



With the epimeric pairs VI(ax) and VI(eq) elimination of the ion of mass 139 (reaction 'd') is strongly favoured with the axial compound, as is the ion of mass 149 (reaction 'c') with VII(ax) and VII(eq). Further, with all three

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[15] K. Biemann and J. Seibl, J. Amer.Chem.Soc. 81, 3149 (1959).

pairs studied reaction 'b' produced ions of greater relative abundance from the axial derivatives. It follows that these ring cleavage reactions are facilitated by ring strain, which is greater in the axial than in the equatorial compounds.

Further mass-spectral studies are in progress with friedelane-y-one derivatives and results will be published shortly.

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