Tetrahedron Letters No. 4, pp. 173-179, 1963. Pergamon Press Ltd.
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STUDIES IN MASS SPECTROMETRY[1]

TRITERPENOIDS : STRUCTURE ASSIGNMENT TO FRIEDELAN-Y-ONE (Y-AL) AND DERIVATIVES

J.S. Shannon and C.G. Macdonald, Division of Coal Research,
C.S.I.R.O., Chatswood, New South Wales
and J.L. Courtney, University of New South Wales, Sydney

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IN 1956 there were isolated from the bark of Siphonodon australe Benth some derivatives of the pentacyclic triterpene friedelane (I). These were divided into two groups - friedelan-x-one and friedelan-y-one derivatives[2,3]. Owing to the uncertain conformation of rings D and E optical rotatory dispersion measurements did not provide definite information on the positions of C-x and C-y in the friedelane skeleton[4]. However, a recent communication[5] has described the assignment of position 21 or 22, with preference for the latter, to the x-substituents by mass-spectrometric methods. Mass spectra obtained by the method described in that communication are now reported for friedelan-y-one[6] and derivatives. These spectra have been interpreted to show that the carbonyl group

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[1] Part IV. For Part III see ref. 5.

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

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

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

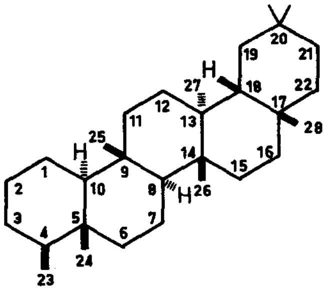
[5] J.L. Courtney and J.S. Shannon, Tetrahedron Letters No.1, 13 (1963).

[6] Henceforth termed "friedelan-y-al".

at C-y is not in fact a keto group, as previously assumed[2,3,4], but is an angular aldehyde group replacing in friedelane (I) the axial methyl group attached at either C-5 or, preferably, C-9 (see below).

Table and Figure 1 illustrate the friedelane derivatives referred to in the text.

Table and Figure 1



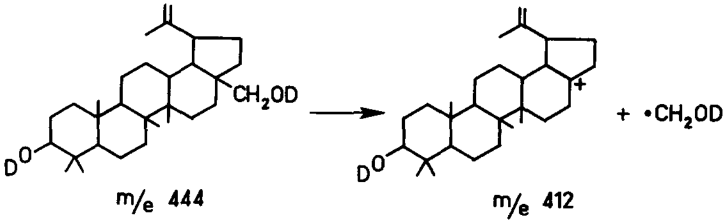
R1 is at C-3

R2 is at C-y where y = 24 or 25

R3 is at C-x where x = 21 or 22

	I	II	III	IV	V	VI	VII	VIII	IX	X	XI	XII	XIII	XIV
R1	H_2	H_2	O	H_2	O	O	H_2	O	O	O	H_2	O	O	O
R2	H_2	O	O	O	O	O	OH	OH	OH	H_2	H_2	H_2	O	O
R3	H_2	H_2	H_2	OH	OH	OAc	H_2	H_2	O	H_2	OH	OH	H_2	O

The mass-spectrometric evidence for the presence of the aldehyde group was the appearance of strong M-29 peaks in the spectra of friedelan-y-al (II) and friedelan-y:al:3-one (III) due to the elimination of a CHO radical from the molecular ions. With the x-hydroxy- or x-acetoxy friedelan-y-al derivatives there was, first, loss of H_2O from compounds IV and V, and, secondly, of CH_3CO_2H from compound VI before the main elimination of the CHO radicals; the sequence of these reactions was confirmed by the presence of corresponding meta-stable peaks in the spectra. In those compounds where the C-y carbonyl had been reduced to a hydroxyl group, as in compounds VII, VIII and IX, the M-29 were replaced by M-31 peaks, which became M-32 when the y-hydroxyl group was O-deuterated, this sequence being entirely consistent with the elimination from the molecular ions of a CH_2OH or a CH_2OD radical. Independent evidence that angular hydroxymethylene groups are readily eliminated from ions of triterpenes was provided by study of the mass spectrum of betulin. This had an intense M-31 peak, which was changed to M-32 in the spectrum of the $O,O'-d_2$ derivative. For example,



A meta-stable peak at m/e 382.2 in the spectrum of betulin and at m/e 382.3 in the spectrum of betulin-O-d_2 confirmed the single-step nature of the reaction.

The n.m.r. spectrum of friedelan-y-al (II) and of friedelan-y:al:x-ol (IV) showed bands at τ-0.12 and τ-0.19 respectively which were not affected by exchange with deuterium oxide[7]. These results were consistent with the presence of aldehydic protons[8,9].

<u>Position of -CHO or -CH_2OH Substituent</u>

One of the prominent ion reactions of friedelane derivatives in the mass

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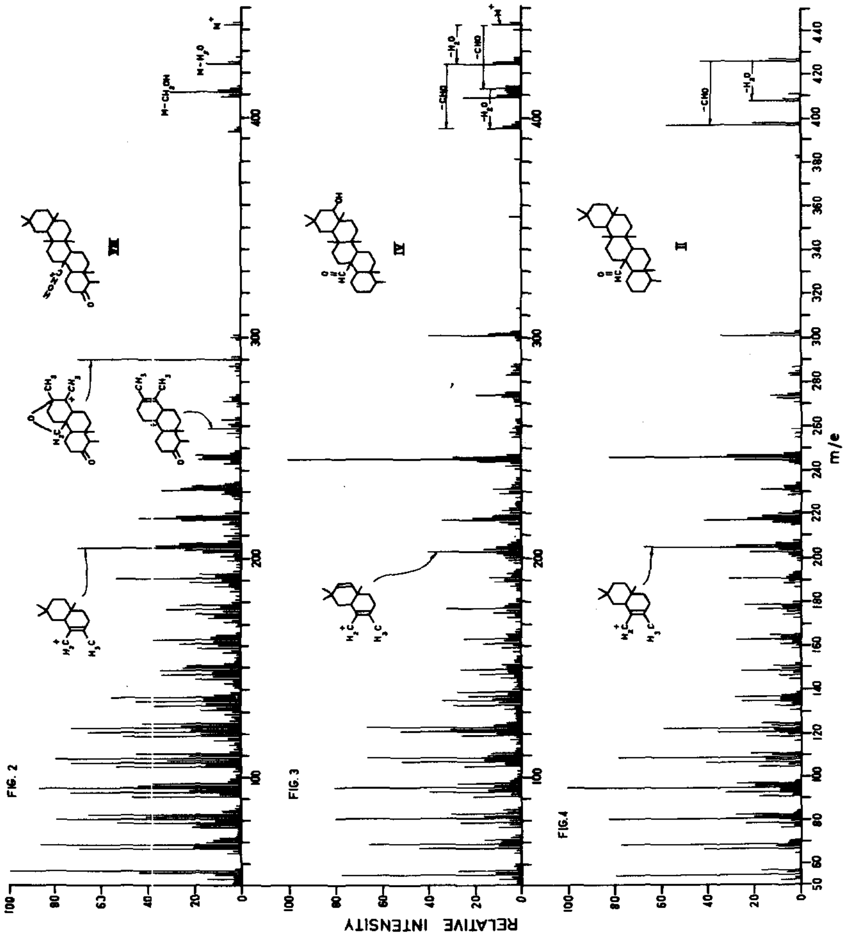
[7] H.M. Fales and A.V. Robertson, Tetrahedron Letters No. 3, 111, (1962).

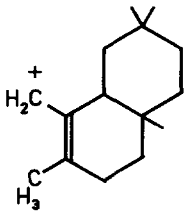
[8] L.M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", p.71 (Pergamon Press, New York, 1959).

[9] Nuclear-magnetic-resonance information kindly supplied by Dr. S. Sternhell.

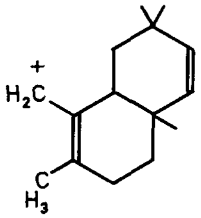
STUDIES IN MASS SPECTROMETRY
FRIEDELANE DERIVATIVES



spectrometer produces fragment ions of m/e 203 and m/e 205. For example, in the spectra of compound X and its 2,2,4-d_3 derivative there are peaks at m/e 205 while in the spectra of compounds XI and XII which contain hydroxyl groups in ring E at C-x there are peaks at m/e 203. Thus occurrence of cleavage across ring C is indicated, with the production of ions which may be formulated thus:

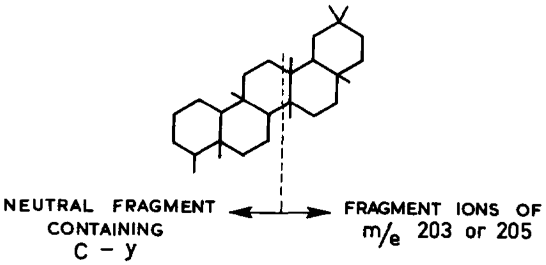


m/e 205[10]



m/e 203[10]

Now the spectra of friedelane derivatives substituted at C-y are also characterized by peaks at m/e 203 and m/e 205. Two examples may be cited: (i) at m/e 203, with compound IV and its O-d derivative and with compound V and its 2,2,4-d_3 and O-d derivative; and (ii) at m/e 205, in the spectra of compounds II, VII, and XIII and the latter's 2,2,4-d_3 derivative. Thus C-y is in that part of the friedelane skeleton which is eliminated as a neutral fragment in the cleavage reaction across ring C:



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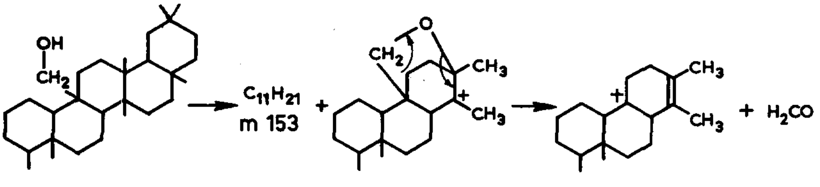
[10] No distinction is made between this and the alternative structure where the positions of the $-CH_3$ and $-\overset{+}{C}H_2$ groups are interchanged.

Since friedelane-3:x dione-y-al (XIV) may be reduced to friedelan-3-one (X)[2] it follows that the aldehyde group in the former replaces a methyl group which may be attached at C-4, C-5 or C-9. When friedelan-y-al (II) was reacted with NaOD,D_2O in dioxane solution no hydrogen atoms were exchanged, which indicated that the aldehyde group was attached to C-5 or C-9, especially since no difficulty was experienced in exchanging the hydrogen atom at C-4 in friedelan-3-one (X).[5] Of these two possible positions it is suggested that C-9 is the correct one, for the following reasons: One of the most intense peaks in the spectrum of y-hydroxy friedelane (VII) is at m/e 275, which is shifted to m/e 289 in the spectrum of y-hydroxy friedelan-3-one (VIII) and to m/e 292 in the spectrum of VIII-2,2,4-d_3. Further, there is no increase of one mass number of the corresponding peaks in the spectra of IV-O-d and VIII-O-d but there is in the spectrum of VII-d, where the deuterium atom is located on the hydroxymethylene carbon atom[11]. Thus the ions of m/e 275 and m/e 289 contained ring A and the methylene of the hydroxymethlene group but not the O-hydrogen atom of this latter group. Since the ions of m/e 275 and 289 were formed in single-step reactions from the molecule ion of VII and VIII respectively (meta-stable peaks at m/e 176.7 and m/e 189.0 in the spectra of VII and VIII respectively) the O-hydrogen atoms were probably transferred to the neutral fragments of mass 153 which were concurrently formed during the reactions involving cleavage across ring D. For example,



VII m/e 428 m/e 275 m/e 245

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[11] Synthesis by reduction of friedelane-y-al (II) with lithium aluminium deuteride.

Models suggest that the distance through which the O-hydrogen would have had to migrate if the hydroxymethylene group had been at C-5 would have been prohibitive. Models further showed that the proposed bridged ions of m/e 275 and m/e 289 have relatively strain-free structures. In the spectra of compounds VII and VII-d there were prominent peaks at m/e 245 and in the spectra of compounds VIII and VIII-2,2,4-d_3 corresponding peaks appeared at m/e 259 and m/e 262 respectively. These peaks could be due to loss of CH_2O from the bridged ions illustrated by the arrows in the above formulae.

The positioning of the aldehyde group at C-25, where it would be subject to 1:3 interaction by the two axial methyl groups attached at C-5 and C-14, may account for the large amount of steric hindrance which was encountered in the study of the chemistry of these friedelane derivatives. For example, while it proved possible to reduce y-al derivatives to y-ol derivatives and to isolate some friedelan-3-one (X) from the Wolff-Kishner reduction of the 3-ketal of friedelane-3:x-dione-y-al (XIV)[2,3], all other attempts so far to prepare chemical derivatives of the aldehyde group or to oxidize it to a carboxyl group have failed[12].

Full details of the mass spectral investigations reported in Parts III and IV of this series, including further ion structure proposals, will be published elsewhere.

Acknowledgements - The authors are grateful to Mr. H.R. Brown, Chief, Division of Coal Research, C.S.I.R.O. for support and encouragement, and to Dr. S. Sternhell for stimulating discussions.

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[12] J.L. Courtney, C.G. Macdonald and J.S. Shannon - unpublished work.