

STUDIES IN MASS SPECTROMETRY¹

STEREOCHEMISTRY AND ELIMINATION REACTIONS OF HYDROXY AND ACETOXY COMPOUNDS

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The relative rates of loss of water or acetic acid from different ions in the mass spectrometer vary through a wide range. For example, in the mass spectra of aliphatic straight-chain² and non-fused six-membered ring alcohols³ and their corresponding acetates³ the parent peaks due to molecular ions are generally very weak, especially compared with the M-18 or M-60 peaks due to loss of water or acetic acid. However, with ions of fused cyclic alcohols and acetates elimination is often, but not always, less facile. It has been observed⁴ that with some compounds in this latter class mass spectra indicate more ready elimination when axial and not equatorial hydroxyl or acetoxy groups are present. We now report results which indicate that these phenomena are associated with the occurrence of 1,4- or 1,3-elimination processes in the molecular ions.

Hydroxy Compounds

It had already been shown^{5,6} from a study of the mass spectra of

¹Part VI. For Part V, see J.S. Shannon, Tetrahedron Letters 801 (1963).

²R.A. Friedel, J.L. Shultz, and A.G. Sharkey Jr., Anal. Chem. **28**, 926 (1956).

³For example, alkyl-substituted cyclohexanols, menthols, etc., and corresponding acetates (J.S. Shannon, unpublished data).

⁴K. Biemann and J. Seibl, J. Amer. Chem. Soc. **81**, 3149 (1959).

⁵W.H. McFadden, M. Lounsbury, and A.L. Wahrhaftig, Canad. J. Chem. **36**, 990 (1958).

⁶E.L. Eliel and T.J. Prosser, J. Amer. Chem. Soc. **78**, 4045 (1956).

butan-1,1-d₂-1-ol and butan-2-d-1-ol, that neither hydrogen attached to C-1 nor hydrogen attached to C-2 was involved in the elimination of water from the molecular ion of butan-1-ol (I), and a mechanism involving 1,4-elimination was proposed⁵. In order to distinguish between 1,4- and 1,3-elimination we synthesized butan-4,4,4-d₃-1-ol, which mass spectral analysis showed to contain 21% d₀, 5% -4-d₁, 17% -4,4-d₂ and 56% -4,4,4-d₃. Using the relative heights of mass peaks⁷ due to loss of H₂O or HOD from the molecular ions and neglecting secondary isotope effects it was calculated that loss of water was due to approximately 80% 1,4- and 20% 1,3-elimination processes.

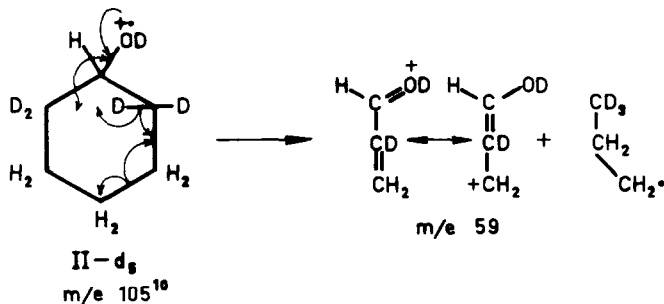
We have now studied the mass spectra of some cyclic alcohols - for example, cyclohexanol (II), which, like the aliphatic straight-chain compounds, gave a very weak molecular but strong M-18 peak. M-18 but not M-19 peaks were found in the spectra of II-1-d and II-2,2,6,6-d₄ but both M-18 and M-19 peaks of relative intensities 1.4 to 1 were found in the spectrum of II-1,4,4-d₃, indicating the simultaneous operation of 1,3- and 1,4-elimination processes. With II-1,4,4-d₃, since the two pairs of hydrogen atoms attached to C-3 and C-5 are equivalent, the ratio of the rate of abstraction of a C-3 hydrogen to that of a C-4 hydrogen is 0.7. Further, since with II-d₀ there is no primary isotope effect favouring 1,3-elimination as there is with II-1,4,4-d₃, the ratio of the rate of 1,3- to that of 1,4-elimination in the ion of II-d₀ should be appreciably lower than 0.7 to 1⁸.

In view of the prevalence of random hydrogen migration in some

⁷From spectra, obtained using low-energy electrons, in which peaks due to M-H₂O ions were eliminated.

⁸For discussion of order of magnitude of isotope effects in ion reactions see F.H. Field and J.C. Franklin, "Electron Impact Phenomena and the Properties of Gaseous Ions", p.210. Academic Press Inc., New York (1957).

aliphatic ions⁹ the following evidence was obtained which, it is suggested, shows that the above results were not due to the occurrence of such migration before or during the elimination of water. The strongest peak in the spectrum of II, which is at m/e 57, is shifted to m/e 58 in the spectra of II-0-d, II-1-d, II-1,4,4-d₂, and II-2,2,6,6-d₄, and to m/e 59 in the spectra of the O-deuterated derivatives of these latter three compounds. These data indicated that the molecular ion of II was cleaved as follows to form a stabilized allylic ion - for example, with II-0,2,2,6,6-d₅ (O = oxygen).

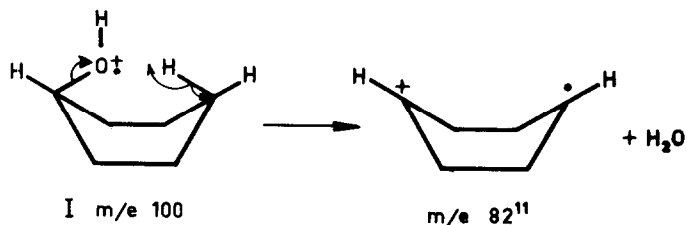


Since the ion m/e 59 was formed without the accompaniment of an ion m/e 58 it followed that there was no significant amount of random hydrogen rearrangement prior to or during this reaction. Further, since by measurement it was determined that the appearance potential of the peak at m/e 57 in the spectrum of II was significantly higher (by approximately 0.5 eV) than that of the peak at m/e 58 it followed that the molecular ion of II had to be slightly more activated to produce the allylic than the $M-H_2O$ ion. Thus, since excess energy did not cause random hydrogen rearrangement in the former ion, it seemed highly improbable that it would produce it in the latter.

⁹For an excellent review of random hydrogen migration in aliphatic ions see F.W. McLafferty, "Determination of Organic Structures by Physical Methods", vol. 2, chap.2. Academic Press Inc., New York (1962).

¹⁰The arrow ↘ represents the shift of one electron and the arrow ↙ the shift of two.

For 1,4- or 1,3-elimination to occur without initial ring opening it was apparent that the molecular ion of II had to assume a boat form; for example, the process could be visualized thus:



If the elimination from the ions of 4- substituted cyclohexanols was also 1,4- in type, the above mechanism would require that the trans- should eliminate more readily than the cis-isomer. This hypothesis was confirmed with cyclohexane-1,4-diol (III)-1,4-d₂, where the loss of HOD from the molecular ion was clearly due to 1,4-elimination, the proportion of ion yield associated with the M-HOD peak in the spectrum of trans- III-1,4-d₂ being eight times (7.3/0.9, see Table 1) greater than the corresponding proportion from the

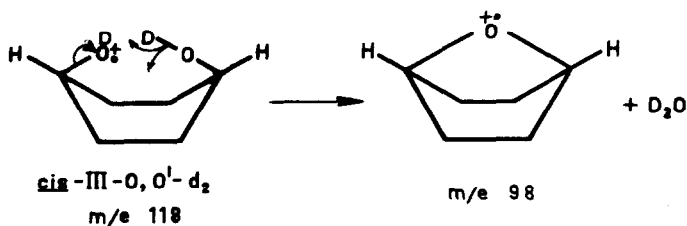
Table 1. Proportion (%) of Ion Yield due to M-HOD and M-H₂O peaks

Compound	M-HOD	M-H ₂ O
<u>cis</u> -III-1,4-d ₂	0.9	0.9
<u>trans</u> -III-1,4-d ₂	7.3	0.8

spectrum of cis-III-1,4-d₂. Further, comparison of the spectrum of cis-III with that of cis-III-0,0¹-d₂ showed that the proportion (0.9%) of ion yield due to loss of H₂O from the molecular ion of cis-III-1,4-d₂ was mainly due to interaction of the two hydroxyl groups, which may occur as follows or by an

¹¹The possibility of bond formation between C-1 and C-4 to yield a more stable bicyclic (2.2.0) hexane ion is not excluded.

equivalent mechanism:



Further, the spectrum of trans-III-O, O¹-d₂ showed no M-D₂O peak; thus the ionization (0.8%, Table 1) was probably mainly associated with 1,3-elimination.

The mass spectra of dl-menth-2,2,3-d₃-ol¹², and of the fused-ring compounds friedelan-2,2,4-d₃-3-ol¹², friedelan-d₃-x-ol^{12,13}, all showed that H₂O and not HOD was mainly lost from the respective molecular ions due to elimination processes which were not 1,2- in type. Thus, since in fused-ring compounds models show that axial would be more favourably situated than equatorial hydroxyl groups for participation in 1,4- or 1,3-processes, it followed that the former should be preferentially eliminated, as has already been noted from certain mass spectra⁴.

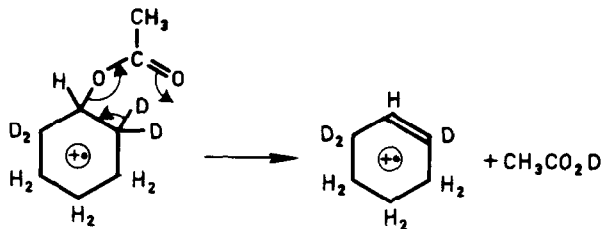
Acetoxy Compounds

The mass spectra of n-butyl acetate (IV) and cyclohexyl acetate (V) have weak parent but strong M-60 peaks, the latter due to loss of acetic acid from the molecular ions. The spectrum of n-butyl-4,4,4-d₃ acetate also has an M-60 peak, whereas in that of cyclohexyl-2,2,4,4-d₄ acetate the corresponding peak was shifted to M-61 owing to loss of CH₃CO₂D by a reaction probably

¹² These are epimeric mixtures, which contain compounds with both equatorial and axial hydroxyl (or acetoxy) groups.

¹³ x = 21 or 22 and the deuterium is substituted on the two neighbouring carbon atoms (see J.L. Courtney and J.S. Shannon, Tetrahedron Letters, **1**, 13 (1963)).

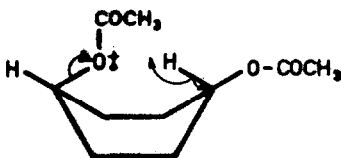
involving a six-membered ring transition state, which we suggest must be planar¹⁴.



The spectra of cis- and trans-cyclohexane-1,4-diol (III) diacetate, unlike the spectra of the corresponding diols, had no marked distinguishing features. They both had strong $M-120$ peaks due to double elimination and very weak $M-60$ peaks due to single elimination of acetic acid. From the spectra of cis- and trans-III-1,4- d_2 diacetate it was seen that the single elimination occurred by a 1,4-process, but this was not true of the more favoured double elimination, which was therefore probably 1,2- in type, like the elimination from the ion of cyclohexyl acetate (V). Models showed that cis- and trans-diacetates could both assume boat conformations in which C-1 and C-4 oxygen atoms were eclipsed by C-2 and C-5 hydrogen atoms, so that bi-six-membered ring transition states in which both six-membered rings were planar could be formed in each case. The 1,4-elimination, which accounted for only 0.2% of the ion yield in the spectrum of cis-III-1,4- d_2 diacetate, and 0.5% in the spectrum of the corresponding trans- compound, may proceed by a mechanism analogous to that

¹⁴An analogous transition state is well known in the unimolecular pyrolysis of esters; see P. de Mayo, in "The Chemistry of Natural Products", vol.2, p.78 (K.W. Bentley ed.). Interscience Publishers, New York (1959). For discussion of similar transition states in ions formed in the mass spectrometer see F.W. McLafferty⁹.

suggested above for 1,4-elimination of water, for example



Further evidence that the 1,2-elimination proceeded via a planar cyclic transition state was obtained by comparing the proportion of ionization due to 1,2- with that due to 1,4- (and/or 1,3-) elimination from ions derived from compounds of different structural rigidity. For example, with cyclohexyl acetate ions only 1,2-elimination occurred whereas with 3-hydroxyfriedelan-2,2,4-d₃ acetate¹² and x-hydroxyfriedelan-d₃ acetate^{12,13} there was no 1,2-elimination. With an ion derived from a compound of intermediate rigidity, namely dl-menthyl-2,2,4-d₃ acetate¹², both 1,2- and 1,4- (and/or 1,3-) processes occurred in the ratio of 4 to 1 respectively. Since with the above ions of rigid non-planar structure there was no 1,2-elimination¹⁵, the preferential reaction of axial acetate groups in x-hydroxyfriedelan acetate and other fused-ring ions⁴ may be due to the greater ease demonstrated by models with which these groups participate in 1,4- (and/or 1,3-) elimination.

Butan-4-d₃-1-ol was obtained by malonic ester synthesis from CD₃CH₂I followed by reduction with lithium aluminium hydride. Cyclohexane-1,4,4-d₃-ol was synthesized from cyclohexane-1,4-dione by lithium aluminium¹⁵. The recent proposal¹⁵ that the greater ease of elimination from the ion of the equatorial compared with the axial epimer of x-hydroxyfriedelan-3-one acetate was due to the operation of a mechanism involving 1,2-elimination, must now be considered invalid. Further, the ion of the axial epimer of the closely related x-hydroxyfriedelan acetate eliminates acetic acid 2.4 faster than that of the equatorial epimer.

deuteride reduction, partial esterification with tosyl chloride, and reaction with Na I followed by reduction with zinc and acetic acid-d. All hydroxy or acetoxy compounds which were deuterated in the α -positions were obtained by treatment of the corresponding keto-derivatives with NaOD, D₂O (and dioxan if necessary) followed by reduction with lithium aluminium hydride. The O-deuterated derivatives were made by exchange with D₂O within the ion source of the mass spectrometer.

Acknowledgments - Grateful thanks are due to Mr. H.R. Brown, Chief, Division of Coal Research, C.S.I.R.O., for support and encouragement, to Mr. J. Wilmshurst for preparative V.P.C. experiments, and to Dr. W.D. Crow for the gift of cyclohexane-1,4-dione.