Mass Spectrometry in Structural and Stereochemical Problems. Part CLXXV.[1] Evidence against Electron Impact-induced Alkyl Shifts in the Mass Spectra of α-Hydroxy-ketones

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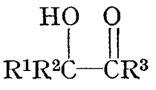
Recently the mass spectra of simple α-hydroxy-ketones were reported to contain peaks arising from isomeric ketols attributed to electron impact-induced 1,2-alkyl migrations. These peaks have now been shown to be an artifact of thermal rearrangements in the inlet systems. The mass spectra of simple tertiary ketols from A.E.I. model MS-9 and Finnigan model 1015 mass spectrometers are compared and contrasted.

THE electron impact-induced fragmentations in mass spectrometry have been determined for most simple functional groups.[2] However, one of the current limitations upon the application of this wealth of information to structure elucidation is the influence which one functional group may exert upon the 'normal' fragmentation of another. The mass spectra of α-hydroxy-ketones provide an excellent example: the standard McLafferty [3] rearrangement is absent in these substrates.[4]

The most abundant ions in the fragmentation of α-hydroxy-ketones arise from α-cleavage with charge retention on the carbinol moiety, and fragments thereof.[4,5] During a study on the effect of structure upon the electron impact-induced fragmentations of dialkylacetyl carbinols (I), ions corresponding to α-cleavage of isomeric ketols were observed, [see Table 1: *m/e* 59 in (Ib) and (Ic), *m/e* 73 in (Id)]. Similar results have been



$R^1R^2C(OH)-C(=O)R^3$

(I)

a; $R^1 = R^2 = R^3 = Me$

b; $R^1 = R^3 = Me, R^2 = Et$

c; $R^1 = R^3 = Me, R^2 = Pr$

d; $R^1 = R^2 = Et, R^3 = Me$

reported by Frearson and Brown,[5] with the same type of spectrometer (A.E.I. model MS-9); in fact the spectra from this study are in good agreement with those published in ref. 5 (see Table 1). However, our respective conclusions differ considerably.

Frearson and Brown [5] concluded that these rearrangements are electron impact-induced as shown in the Scheme, since thermal rearrangements were apparently precluded by (i) lack of change in spectra with increased resonance time in the inlet system, (ii) failure of the material to rearrange (n.m.r. analysis) during g.l.c. or when heated with glass beads in a sealed tube, and (iii) observation of rearrangement peaks in (I; $R^1 = R^3 = Ph$, $R^2 = Me$) even with direct-insertion techniques at temperatures below 110°. Here we present our own conclusions, which demonstrate the difficulty of differentiating between electron impact-induced and other (catalytic or thermal) processes.

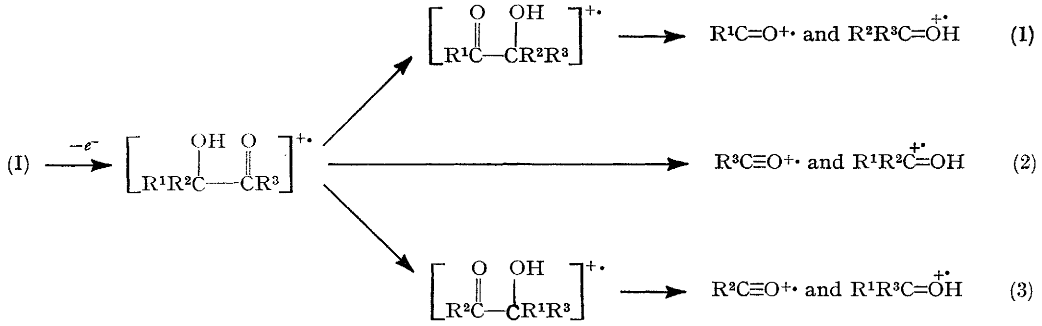
TABLE 1

Salient fragment ions from α-hydroxy-ketones (MS-9)[a] at 70 ev

m/e		41	43	45	55	57	59	69	71	73	83	87	101	102	116	130
(Ia)	*	18	36	2		2	100	2				4		0·7		
	†	18	39	3			100	4				4		0·8		
(Ib)	*	17	81	15	82		70	6		100	2	11			0·6	
	†	17	72	18	62		80	7		100		10			0·6	
(Ic)	*	30	55	97	3	4	100	4	4			49				0·5
	†	Not available														
Id)	*	15	60	52	56	19		12		100	6	31	8			0·1
	†	12	36	40	47			9		100	3	26	7			0·2

* This study. † From ref. 5.

[a] Heated (150°) inlet system with ion-source temperature of 200°.



$$[R^1R^2C(OH)-C(=O)R^3]^{+\cdot} \rightarrow [R^1C(=O)-C(OH)R^2R^3]^{+\cdot} \longrightarrow R^1C{=}O^{+\cdot} \text{ and } R^2R^3C{=}\overset{+\cdot}{O}H \quad (1)$$

$$(I) \xrightarrow{-e^-} [R^1R^2C(OH)-C(=O)R^3]^{+\cdot} \longrightarrow R^3C{\equiv}O^{+\cdot} \text{ and } R^1R^2\overset{+\cdot}{C}{=}OH \quad (2)$$

$$[R^1R^2C(OH)-C(=O)R^3]^{+\cdot} \rightarrow [R^2C(=O)-C(OH)R^1R^3]^{+\cdot} \longrightarrow R^2C{\equiv}O^{+\cdot} \text{ and } R^1R^3C{=}\overset{+\cdot}{O}H \quad (3)$$

SCHEME

From the stability of the mass spectrum with time we infer that complete equilibration of the isomeric ketols has occurred prior to fragmentation. In fact, ^{2}H- and

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[1] Paper CLXXIV, *Org. Mass Spectrometry*, in the press.

[2] H. Budzikiewicz, C. Djerassi, and D. H. Williams, 'Mass Spectrometry of Organic Compounds,' Holden-Day, San Francisco, 1967.

[3] Ref. 2, p. 155.

[4] C. A. Brown, unpublished observations.

[5] M. J. Frearson and D. M. Brown, *J. Chem. Soc.* (*C*), 1968, 2909.

^{18}O-labelled substrates were found [5] to have the label distributed in a nearly statistical manner; however, this does not distinguish between rearrangement prior or subsequent to ionization. The absence of isomerization when the ketols are heated with glass beads suggests that the reaction is not thermal; however, the MS-9 spectrometer has metal in the inlet system, and hot metal or metal oxide could easily catalyse the rearrangement (see below). The failure to detect rearrangement in the g.l.c. (presumably with metal contact involved) by n.m.r. spectroscopy does not preclude metal catalysis; a few percent rearrangement—undetected by n.m.r. spectroscopy—in g.l.c. purification corresponds in quantity to the conversion of many times the *amount* of material passing through the mass spectrometer. The presence of a small amount (5% reported) of rearranged product in PhCO·C(OH)MePh introduced by the direct probe if anything tends to support the possibility of rearrangements being thermal and metal catalysed rather than electron impact-induced. If the latter were operative, there is no reason why direct insertion should produce only 5% of rearranged fragments while vapour introduction produces 16%. However, the opportunity for contact with hot metal is reduced with direct insertion (although not eliminated in the MS-9 spectrometer).

In fact, we have obtained two strong pieces of evidence in support of the occurrence of metal-catalysed thermal rearrangement.

First, the mass spectra of α-ketols (I) obtained on a Finnigan 1015 quadrupole mass spectrometer with a cool (75°) *all-glass* inlet system show only low-intensity peaks for fragments from isomeric ketols (Table 2). The most striking difference is noted with 3-ethyl-3-hydroxypentan-2-one (Id), for which the ratio of protonated butan-2-one (from rearranged ketol) to protonated pentan-3-one (from unrearranged ketol) is 3 (or 4) : 1 in the MS-9 instrument but only 0·07 : 1 in the Finnigan 1015 spectrometer. This difference cannot be attributed simply to a much longer ion-residence time in the source of the MS-9 spectrometer. Beynon *el al.*[6] have estimated MS-9 source residence-time to be *ca.* 0·7—2·1 μsec. under the operating conditions employed. The corresponding value for the Finnigan source is 0·6—1·2 μsec.[7]

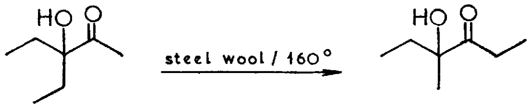
TABLE 2

Salient fragment ions from α-hydroxy-ketones (Finnigan 1015)* at 70 ev

m/e	41	43	45	55	57	59	69	71	73	83	87	101	102	116	130
(Ia)	11	20	2		5	100	2				5		1		
(Ib)	3	41	15	70	4	6	2	2	100		12			1	
(Ic)	15	36	97	3	5	7	25	3			100				<0·5
(Id)	16	43	73	7	20	3	40		7		100				<0·5

* All-glass vapour inlet system (75°) with ion-source temperature of 150°.

Secondly, we have found that the rearrangement of 3-ethyl-3-hydroxypentan-2-one (Id) to 4-hydroxy-4-methylhexan-3-one (II) occurs thermally in the presence of finely divided steel wool at 160° but not over glass wool.



(Id) (II)

Thus, when samples of (Id) were heated in sealed tubes over washed glass wool at 160° (under 0·5 atmos. of argon) for 48 hr., the recovered ketol had an n.m.r. spectrum identical to that of pure (Id). Over steel wool on the other hand, the product showed new signals at δ 1·28 (sharp s), 1·07 (t, J_{obs} 7 Hz), and 2·55 p.p.m.) J_{obs} 7 Hz). These new signals are consistent with a tertiary carbinol methyl group and an ethyl ketone, as in (II). The ratio of (Id) to (II) in this product was 1 : 2·2 from the heights of the tertiary methyl signals. G.l.c. showed two components in the ratio 1 : 2·1. The minor peak had a retention time identical to (Id) (separate or co-injection). The major peak was collected and examined by mass spectrometry.* Its spectrum resembled that of (Id) run on the MS-9 instrument, possessing strong peaks (70 ev) at *m/e* 73 (protonated butan-2-one) and 57 (propionyl ion) consistent with structure (II).

It is possible that the small amounts of isomeric ketol fragments produced even with the Finnigan instrument are the result of an electron impact-induced rearrangement; they may also be due to metal-catalysed isomerizations of molecules striking the hot walls of the ionizer before entering the electron beam. However, our data strongly suggest that the rearrangement observed by Frearson and Brown was thermal and that electron impact-induced alkyl migrations are a very minor, or non-existent, reaction of α-ketols in the mass spectrometer.†

EXPERIMENTAL

^1H.n.m.r. spectra were recorded on a 60 MHz instrument.

The ketols were prepared by hydration of the corresponding dialkyl carbinols with mercury(II) methanesulphonate–methanesulphonic acid in aqueous isopropyl alcohol.[8] The following procedure is typical.

3-Methylpent-1-yn-3-ol ‡ (4·9 g., 5·6 ml., 55 mmoles) was added during 10 min. to a stirred mixture of mercury(II) oxide (0·38 g., 2·0 mmoles), isopropyl alcohol (8·5 ml.), water (1·5 ml.), and methanesulphonic acid (0·52 ml., 8·0 mmoles) at 45°. The mixture was stirred and heated for 30 min. after which it was cooled to room temperature and treated with anhydrous sodium carbonate (1·5 g.); it was then stirred for a further 30 min. and finally filtered. The

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* Spectra determined on an Atlas CH-4 instrument with a cold (50°) direct-insertion probe. This system gives slightly more isomeric ketol fragments than the Finnigan machine.

† One of us (C. A. B.) is currently studying the effects of different metals upon the thermal rearrangement.

‡ Air-Reduction Co.

[6] J. H. Beynon, J. A. Hopkinson, and G. R. Lester, *J. Mass Spectrometry and Ion Physics*, 1968, **1**, 393.

[7] Personal communication from M. Story, Finnegan Instruments Corporation.

[8] C. A. Brown, unpublished observations; adapted from G. F. Hennion and E. J. Watson, *J. Org. Chem.*, 1958, **23**, 656.

resulting solution contained 3-hydroxy-3-methylpentan-2-one in 90% yield (v.p.c., external standard) with no significant impurities; $\nu_{max.}$ (liq.) 3450br, s (OH) and 1685s (CO); δ (CCl_4; D_2O exchange) 0·80 (t, *J* 7 Hz, CH_2CH_3), 1·27 (s, carbinol CH_3), 1·69 (q, *J* 7 Hz, CH_2CH_3), and 2·17 p.p.m. (s, $COCH_3$), intensity ratio 2·1 : 3·0 : 2·0 : 3·0. There appeared no evidence for the isomeric ketol 2-hydroxy-2-methylpentan-3-one. The other ketols possess appropriately similar spectra.

Thermal rearrangement studies were carried out by heating (Id) (0·25 g.) in sealed tubes with washed and dried glass and steel wool (0·25 and 0·5 g., respectively) under 0·5 atmos. of argon at 160° for 48 hr. After being cooled, the packed end of the tubes were warmed while the other end was cooled in ice–salt in order to collect the product for g.l.c., n.m.r., and m.s. examination.

G.l.c. (Carbowax on Chromosorb W) of the steel wool rearrangement product showed two nearly resolved materials in the ratio 1 : 2·1. The smaller peak had the same retention time as (Id). Enough of the larger peak could be collected by analytical g.l.c. for mass spectrometry. At 70 ev it showed peaks at *m/e* 73 (protonated butanone), 57 (propionyl ion), and 55 (protonated butanone minus water), confirming the structure 4-hydroxy-4-methylhexan-3-one produced from (Id) by ethyl and hydrogen migration.

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