

of a variety of vinyl methyl groups. Treatment of the oil with *n*-hexane-ether and storage at  $-23^{\circ}$  for 2 days gave 27 mg. of crude crystalline material which, after recrystallization from *n*-hexane-ether, gave 13.5 mg. of dihydrocostunolide (**1**), m.p.  $76.0-78.0^{\circ}$ . Chromatography ( $-23^{\circ}$ ) of the mother liquors on 2.3 g. of silicic acid gave an additional 6 mg. of **1**, m.p.  $74.5-78^{\circ}$ ; total yield, 19.5 mg. (10%) based on amount of diene **10** actually transformed on photolysis.

Recrystallization afforded pure synthetic dihydrocostunolide (**1**), m.p.  $76.5-78.0^{\circ}$ ,  $[\alpha]^{26D} +110.8^{\circ}$  (*c* 0.8) (lit.<sup>3</sup> m.p.  $77-78^{\circ}$ ,  $[\alpha]_D +113.6^{\circ}$  (*c* 3.0,  $\text{CHCl}_3$ )); the n.m.r. spectrum of **1** exhibited peaks at 1.19 (3 H, doublet,  $J = 6.5$  c.p.s.), 1.40 (3 H, doublet,  $J \approx$

1.5 c.p.s.), 1.67 (3 H, doublet,  $J \approx 1.0$  c.p.s.), 4.39 and 4.52 (2 H, multiplet), and 4.75 (1 H, multiplet) p.p.m. The synthetic material showed no depression in its melting point when admixed with an authentic specimen prepared from costunolide (**2**)<sup>3</sup>; it was identical in all respects with this specimen in its infrared and ultraviolet ( $\epsilon$  10,300 at 207  $m\mu$ ) spectra.

In another experiment 56 mg. of dihydrocostunolide (**1**), m.p.  $74.5-76.0^{\circ}$ , was obtained in the same manner as described above from the photolysis of 1.20 g. of the diene **10**.

*Acknowledgment.* This work was supported by the National Institutes of Health and the National Science Foundation.

## Studies in Mass Spectroscopy. III.<sup>1</sup> Mass Spectra of $\beta$ -Keto Esters

J. H. Bowie, S.-O. Lawesson, G. Schroll, and D. H. Williams

Contribution from the University Chemical Laboratory,  
Cambridge, England, and the Department of Organic Chemistry,  
Aarhus University, Aarhus C, Denmark. Received August 9, 1965

The spectra of 16  $\beta$ -keto esters are reported and discussed. Ethyl acetoacetate and its derivatives, in which one of the active methylene hydrogens has been replaced by a substituent, break down in a well-defined manner upon electron impact. The spectra of some substituted ethyl benzoylacetates are noteworthy for the probable occurrence of an intramolecular acylation of the aromatic ring which takes place in an acylium ion fragment.

In view of the importance of  $\beta$ -keto esters and their derivatives as synthetic intermediates, it was thought desirable that the mass spectra of representative members of this class should be determined and interpreted. Prior to the present study, the only mass spectrum of a member of this series which has been discussed appears to be that of methyl 3-oxooctadecanoate.<sup>2</sup>

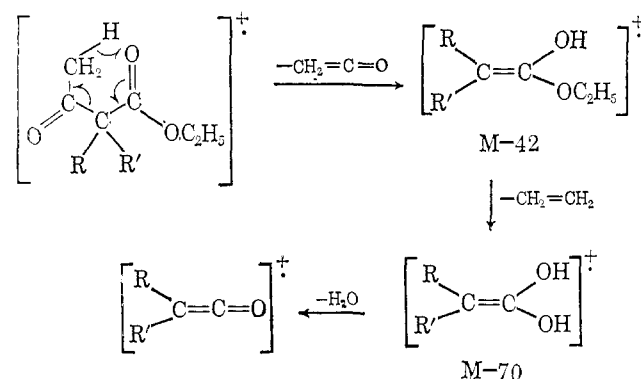
The mass spectra of ethyl acetoacetate (**I**) and seven derivatives (**II-VIII**) are recorded in Table I and Figures 1 and 2. The parent compound **I** and all the derivatives **II-VI** break down to a large extent by the general sequence which is outlined in Scheme I. The formation of enolic fragment ions (see  $M - 42$ ), from processes involving hydrogen rearrangement in the mass spectrometer, has previously been demonstrated.<sup>3a</sup> Moreover, the elimination of ethylene from the  $M - 42$  ion closely parallels the loss of an olefin from vinyl ethers<sup>3a</sup> and acetals.<sup>3b</sup>

(1) Part II: R. Grigg, M. V. Sargent, J. Knight, and D. H. Williams, *Tetrahedron*, in press.

(2) R. Ryhage and E. Stenhagen, *Arkiv Kemi*, **15**, 545 (1960).

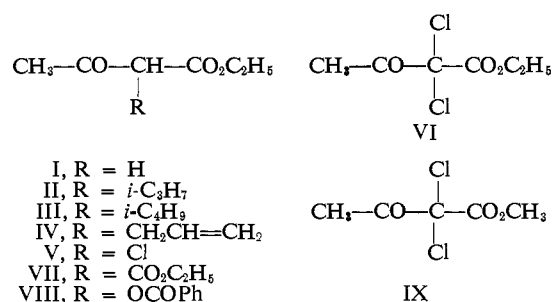
(3) (a) S. Meyerson and J. D. McCollum, *Advan. Anal. Chem. Instr.*, **2**, 179 (1963); (b) R. A. Friedel and A. G. Sharkey, *Anal. Chem.*, **28**, 940 (1956).

Scheme I<sup>a</sup>



<sup>a</sup> Throughout this paper, specific structures have been drawn for fragment ions primarily to give a self-consistent rationale for the interpretation of the spectra. Although exact mass measurements confirm the composition of the fragment ions in many instances, some structures are nominal only.

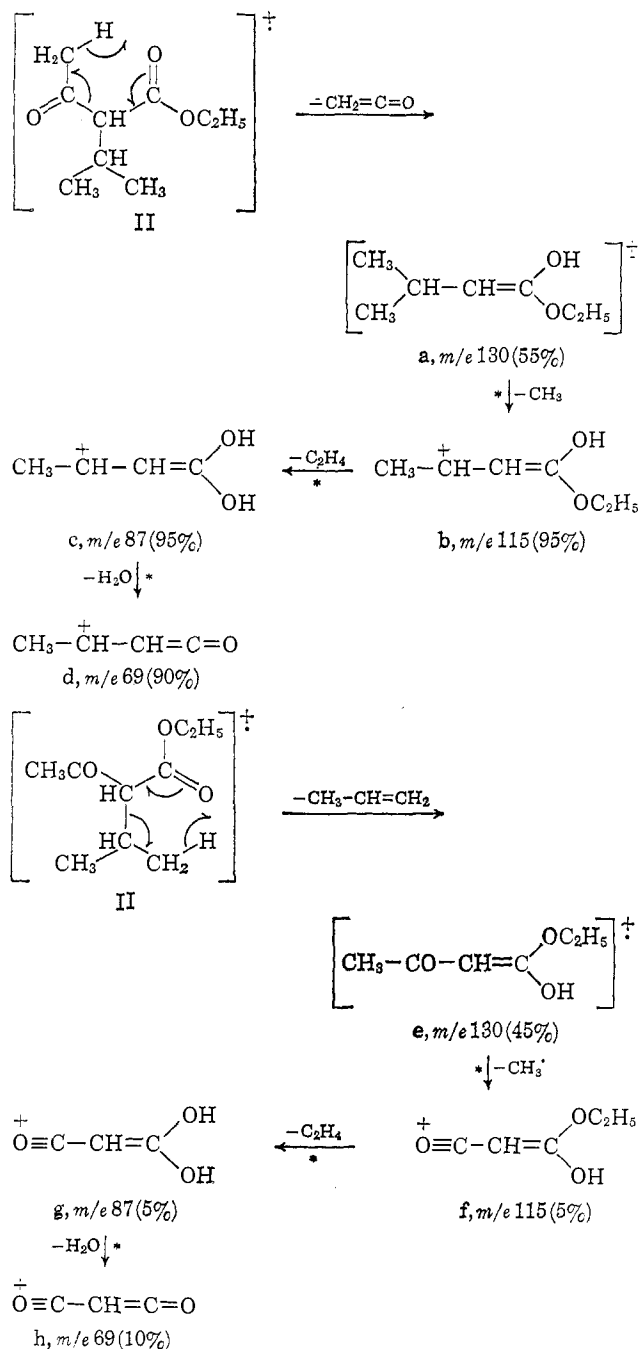
The sequence indicated in Scheme I is supported by a number of appropriate metastable peaks in many of the



spectra. It is noteworthy that the  $M - 42$ ,  $M - 70$ , and  $M - 88$  ions are all odd electron fragments and therefore, depending on the nature of R and R', a

radical may be expelled from one of these substituents at some stage in the sequence. This behavior may be illustrated by reference to the spectrum (Figure 1) of ethyl 2-isopropyl-3-oxobutyrates (II). The abundant  $m/e$  130 ion is associated in part (55%, as established by high-resolution measurements) with the loss of ketene to afford a (Scheme II). This ion then decom-

**Scheme II\***



\* Transitions supported by an appropriate metastable peak are indicated with an asterisk (\*).

poses by loss of a methyl radical from the isopropyl substituent to give **b** ( $m/e$  115), which undergoes the previously described losses of ethylene and then water to yield  $m/e$  87 (**c**) and  $m/e$  69 (**d**). High-resolution measurements on  $m/e$  130, 115, 87, and 69 establish that all these peaks are doublets whose compositions are indicated in Scheme II. The alternative decomposition path  $\text{e} \rightarrow \text{f} \rightarrow \text{g} \rightarrow \text{h}$  accounts for the lower mass

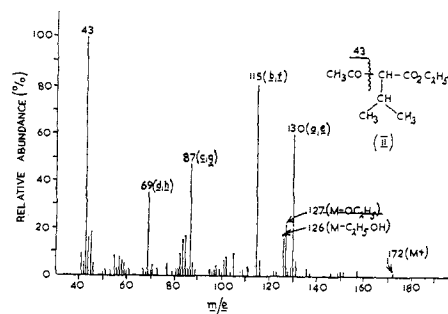


Figure 1. Mass spectrum of ethyl 2-isopropyl-3-oxobutyrates (II).

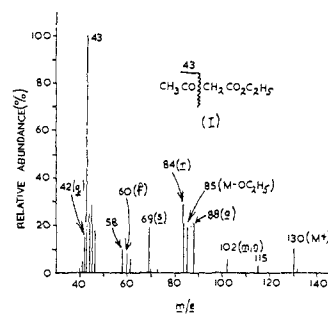


Figure 2. Mass spectrum of ethyl acetoacetate (I).

portions of all these doublets, and indeed is identical in form with the first sequence with the exception that the first step involves elimination of propylene instead of the isobaric ketene fragment. Evidence for the participation of ester-enols in these fragmentation sequences is available in the decomposition of  $m/e$  87 (**c** or **g**) to  $m/e$  69 (**d** or **h**) by loss of water; if the  $m/e$  87 species were simply the  $\text{CH}_2\text{COOC}_2\text{H}_5$  ion, formed by elimination of the isopropyl and acetyl groups from the molecular ion with a hydrogen rearrangement to carbon, then this certainly would not fragment specifically by loss of water. Moreover, the very pronounced loss of a methyl group from  $\text{C}_7\text{H}_{14}\text{O}_2^+$  (**a**,  $m/e$  130) to afford **b** ( $m/e$  115) is consistent with the presence of two allylic methyl groups in the enol **a**.

The self-consistent behavior of these compounds is illustrated by the spectrum (Table I) of the isobutyl derivative III. The  $\text{M} - \text{CH}_2=\text{C}=\text{O}$  ion (**i**,  $m/e$  144) should now eliminate an isopropyl radical to give **j** ( $m/e$  101) which is anticipated to decompose by successive losses of ethylene (to **k**,  $m/e$  73) and water (to **l**,

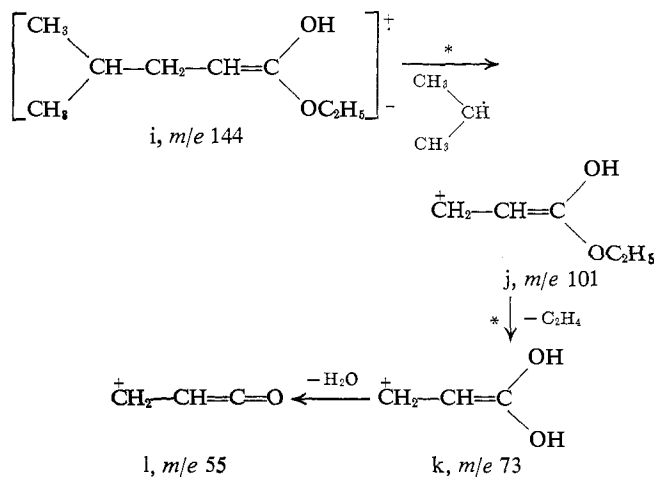


Table I<sup>a</sup>

III	<i>m/e</i>	41	42	43	44	45	46	55	56	57	58	69
	<i>I (%)</i>	15	6	87	15	13	7	32	4	10	11	9
		70	71	73	83	84	85	87	97	98	99	101
		10	7	40	5	10	10	5	22	6	8	100
		102	115	125	130	131	140	141	143	144	157	171
	9	9	9	35	4	8	11	17	31	9	4	
	186(M)											
	3											
IV	<i>m/e</i>	39	41	43	45	53	54	55	56	58	69	81
	<i>I (%)</i>	9	11	100	10	11	11	22	6	4	3	22
		82	83	95	96	97	99	100	101	106	109	124
		14	16	4	7	14	20	21	5	4	6	6
		125	127	128	152	155	170(M)					
	5	51	29	2	2							
V	<i>m/e</i>	42	43	44	45	69	76	78	92	94	96	118
	<i>I (%)</i>	4	100	11	12	3	7	3	20	6	6	6
		119	120	122	124	136	138	164(M)	166(M)			
	4	3	23	8	3	1	3		1			
VI	<i>m/e</i>	42	43	44	45	62	73	76	94	110	112	114
	<i>I (%)</i>	4	100	7	4	2	2	3	3	5	3	1
		122	124	126	128	130	132	155	156	158	160	
	4	2	4	21	14	2	2	18	10	2		
VII	<i>m/e</i>	41	42	43	44	46	55	56	58	69	84	85
	<i>I (%)</i>	9	5	39	15	19	5	3	10	34	58	100
		86	87	88	102	103	113	115	130	143	157	
	11	35	8	34	3	16	25	34	7	18		
VIII	<i>m/e</i>	43	51	77	105	106	122	205	208	209	250(M)	
	<i>I (%)</i>	10	4	16	100	9	2	3	21	3	3	
IX	<i>m/e</i>	42	43	44	45	47	49	59	61	63	76	
	<i>I (%)</i>	4	100	8	3	3	4	7	4	4	3	
		77	79	83	85	110	112	114	127	129	131	141
		7	3	5	3	5	3	1	5	2	1	3
		142	144	146								
	10	6	2									
X	<i>m/e</i>	43	44	45	46	50	51	77	78	105	106	120
	<i>I (%)</i>	6	9	9	5	3	9	26	3	100	8	7
		146	147	192(M)	193							
	12	5	9		2							
XI	<i>m/e</i>	41	44	45	51	77	78	105	106	120	145	146
	<i>I (%)</i>	3	3	4	6	24	3	100	9	7	3	6
		192	193	201	202	248(M)						
	17	3	3	7	1							
XII	<i>m/e</i>	42	51	69	77	105	106	120	145	146	192	193
	<i>I (%)</i>	7	6	3	25	100	9	5	3	4	14	3
XIV	<i>m/e</i>	42	51	57	77	78	105	106	117	218	368(M)	
	<i>I (%)</i>	2	4	2	25	2	100	9	2	4	4	
XV	<i>m/e</i>	39	40	41	42	43	44	45	46	50	51	52
	<i>I (%)</i>	24	14	43	27	32	100	88	43	5	9	5
		53	54	55	56	57	58	67	68	69	70	71
		10	10	93	39	24	5	16	16	22	24	6
		77	79	81	82	83	84	85	94	95	96	97
		5	5	9	10	33	25	5	10	13	9	12
	<i>m/e</i>	98	101	105	109	110	111	112	113	125	127	128
	<i>I (%)</i>	5	6	4	7	12	6	44	7	9	3	4
		129	134	138	139	142	156	184(M)	185			
		5	6	47	24	4	8	10	3			

<sup>a</sup> All ions having an abundance greater than 2% of the base peak are recorded; molecular ions (and fragment ions of diagnostic value) of lesser abundance are included in the table.

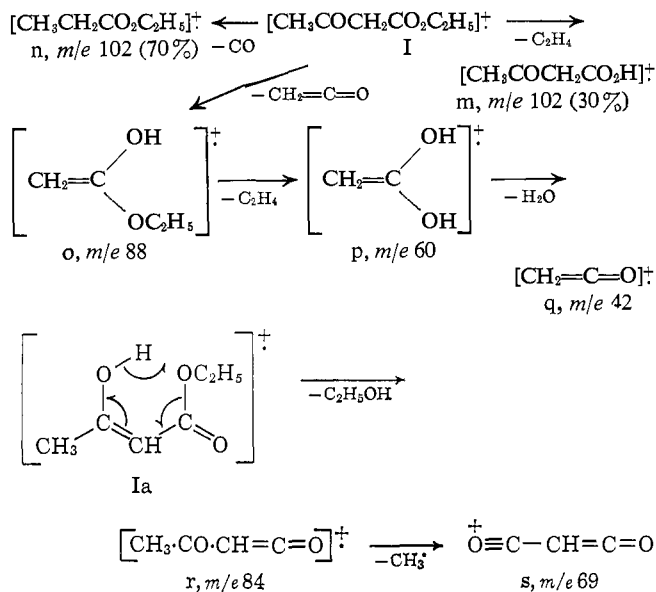
*m/e* 55). In fact this sequence describes the main breakdown path of III (*m/e* 101 is the base peak). It can be seen that the difference of 14 mass units between the ions b, c, d, and j, k, l reflects the  $\alpha$ -branching (methyl group) of the C-alkyl chain in II.

Additional evidence that the  $C_6H_{10}O_3$  ion should be formulated as e rather than as the ethyl acetoacetate molecular ion is provided by the mass spectrum (Figure 2) of ethyl acetoacetate (I) itself, which indicates that the molecular ion of I fragments to a prominent *m/e* 88 ion, almost absent in the spectrum (Figure 1) of the isopropyl derivative II. The formation of most of the fragment ions in the ethyl acetoacetate spectrum is summarized in Scheme III. Particularly important are the  $M - C_2H_5O$  (*m/e* 85) and  $M - C_2H_5OH$

(*m/e* 84) ions; the former is present in the spectra of all the ethyl acetoacetate derivatives examined, whereas the formation of the latter is dependent on the presence of an active methylene hydrogen, *i.e.*, no  $M - C_2H_5OH$  ion occurs in the spectrum of the dichloro derivative VI. These observations are consistent with the formation of *m/e* 84 via a six-membered transition state involving the enol form Ia. The spectrum (Figure 2) is remarkable for the appearance of an  $M - 28$  ion (*m/e* 102) which corresponds to only a small extent (*ca.* 30%) to loss of ethylene ( $I \rightarrow m$ ), and mainly (*ca.* 70%) to the elision of carbon monoxide from the keto group as established by  $^{18}O$  labeling<sup>4</sup> and high-

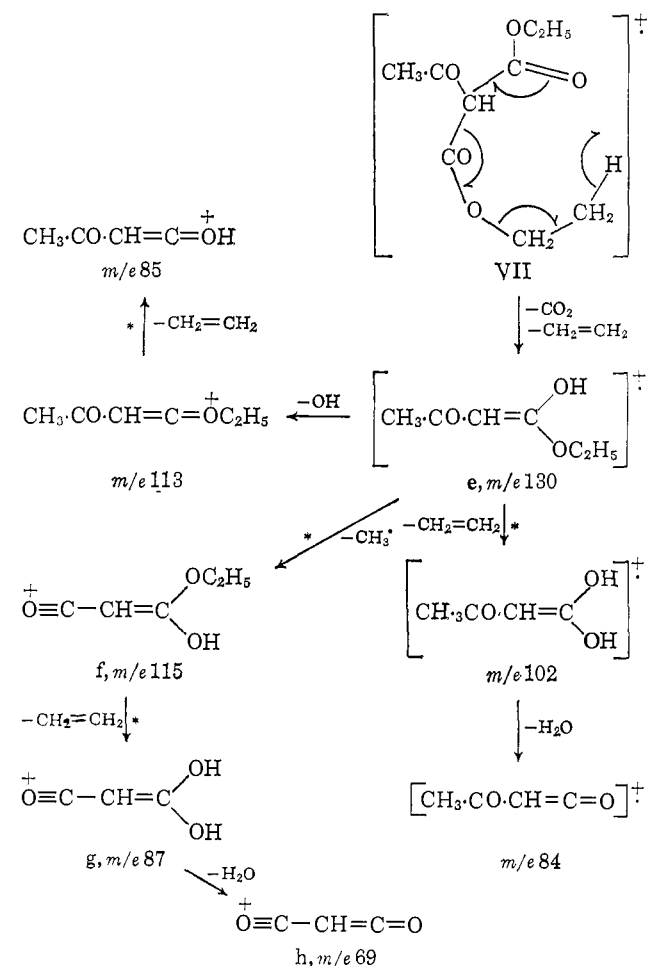
(4) W. J. Richter, M. Senn, and A. L. Burlingame, *Tetrahedron Letters*, 1235 (1965).

**Scheme III**



resolution measurements. This latter process (perhaps I → n) requires an alkyl migration, examples of which are relatively few in mass spectroscopy.<sup>5</sup>

**Scheme IV**

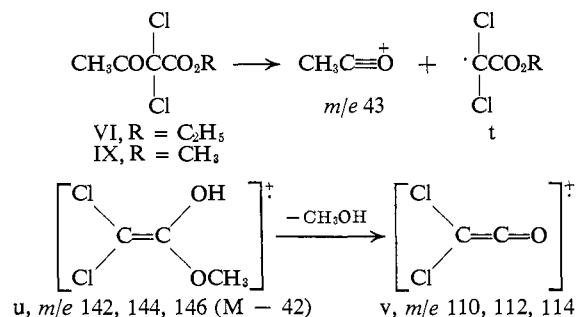


M - 72 ions, corresponding to the elimination of CO<sub>2</sub>C<sub>2</sub>H<sub>4</sub> fragments, occur in the spectra of ethyl

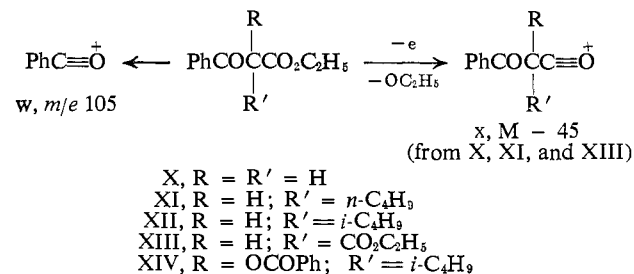
(5) (a) A. S. Newton and P. O. Strom, *J. Phys. Chem.*, **62**, 24 (1958); (b) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1399 (1965); (c) P. Brown, C. Djerassi, G. Schroll, H. J. Jakobsen, and S.-O. Lawesson, *ibid.*, **87**, 4559 (1965).

acetoacetate (I), the chloro analogs V and VI, and diethyl acetylmalonate (VII), but are absent in the spectra of the alkyl derivatives (II, III, IV) and the benzoyloxy compound VIII. The absence of any M - CO<sub>2</sub>C<sub>2</sub>H<sub>4</sub> ion in the spectrum of the one methyl ester examined (IX) points to the participation of the β-hydrogen of the ethyl group in this rearrangement. In the instance of diethyl acetylmalonate (VII), there is evidence which indicates that the rearrangement takes place to oxygen with formation of the ester-enol e (m/e 130). Thus, m/e 130 decomposes as outlined previously in Scheme II to m/e 115 (f), m/e 87 (g), and m/e 69 (h) and additionally as indicated in Scheme IV. The compositions of all pertinent ions have been checked by high-resolution measurements and the majority of transitions indicated are supported by appropriate metastable peaks.

The dichloro compounds VI and IX do not exhibit molecular ions in their spectra, presumably because of the extremely facile cleavage which affords the acetyl ion (m/e 43, base peak) and the tertiary radical t. The M - 42 ion (u) formed from methyl 2,2-dichloro-3-oxobutyrates (IX), unable to eliminate ethylene like its ethyl analog (see Scheme I), decomposes directly to v (m/e 110, 112, 114) by loss of methanol.



The base peak in the spectra of ethyl benzoylacetate (X) and its derivatives (XI-XIV) is due to the benzoyl ion w (m/e 105), which decomposes in the established manner<sup>6</sup> to the phenyl cation (m/e 77) and C<sub>4</sub>H<sub>3</sub><sup>+</sup> (m/e 51). M - 45 ions (x), arising from the loss of an ethoxyl radical, are present in the spectra of X, XI, and XIII.



M - C<sub>2</sub>H<sub>5</sub>OH (M - 46) peaks are evident in the spectra of X, XI, and XIII. In the cases of XI and XIII, appropriate metastable ions indicate that the M - 46 ion is formed, at least in part, by the loss of a hydrogen radical from the M - OC<sub>2</sub>H<sub>5</sub> species. Moreover, in the spectrum (Figure 3) of XIII, the M - C<sub>2</sub>H<sub>5</sub>OH ion decomposes by the loss of a second molecule of ethanol to m/e 172, as indicated by an appropriate metastable ion. This latter observation de-

(6) See, for example: (a) T. Aczel and H. E. Lumpkin, *Anal. Chem.*, **33**, 386 (1961); (b) S. Meyerson and P. Rylander, *J. Am. Chem. Soc.*, **79**, 1058 (1957).

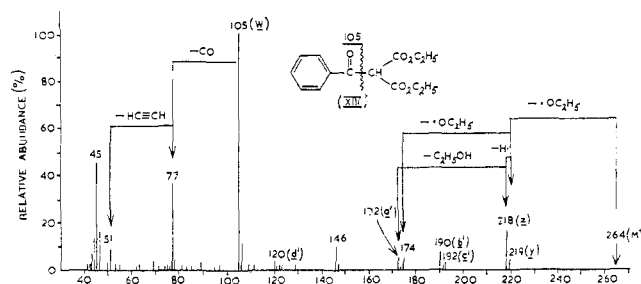
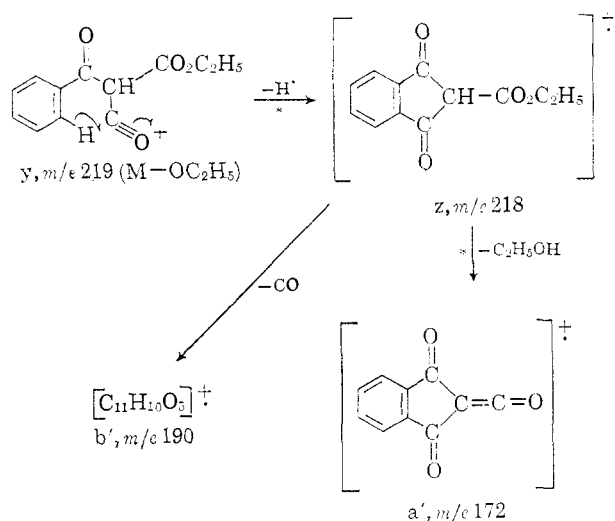


Figure 3. Mass spectrum of diethyl benzoylmalonate (XIII).

mands that the  $m/e$  172 ion has lost a hydrogen from the phenyl ring, as confirmed by high-resolution measurements. Thus, it appears that in the spectra of XI and XIII, the  $M - OC_2H_5$  acylium ion (e.g., y) is eliminating a hydrogen radical from the aromatic ring to give what is probably a bicyclic ion-radical (e.g., z). This process obviously bears some analogy to a Friedel-Crafts acylation, except that a hydrogen radical is lost instead of a proton.



$M - 72$  ions ( $M - CO_2CH_2CH_2$ ), corresponding to loss of the ethyl ester substituent with hydrogen rearrangement, are also present in the spectra of X, XI, and XIII. In these cases the hydrogen rearrangement may well be taking place to carbon, since the  $M - 72$  ion ( $m/e$  192) in the spectrum (Figure 3) of XIII decomposes in the same manner as the ethyl benzoylacetate molecular ion; these and other fragmentation modes of XIII are summarized in Scheme V and Figure 3. The alkyl derivatives XI and XII also of course yield  $m/e$  192 ions from elimination of the alkyl group with hydrogen rearrangement.

Scheme V

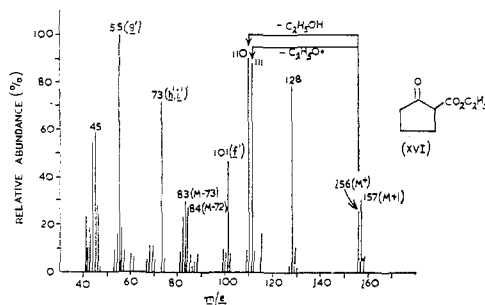
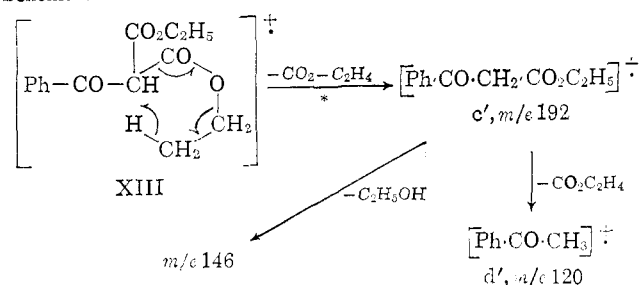
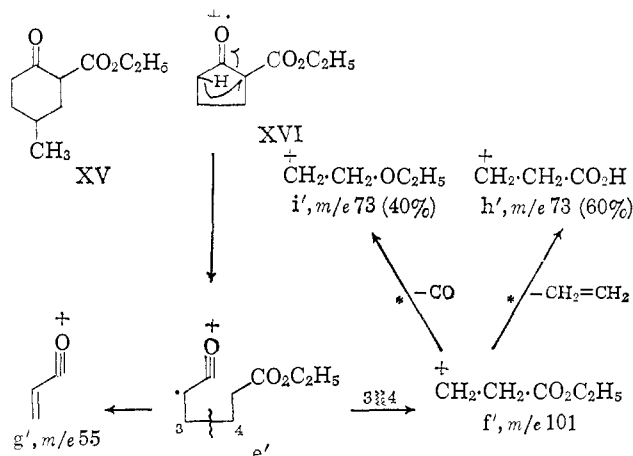


Figure 4. Mass spectrum of ethyl cyclopentanone-2-carboxylate (XVI).

In the spectra of the cyclic  $\beta$ -keto esters XV and XVI, peaks due to the loss of an ethoxyl radical ( $M - 45$ ) and ethanol ( $M - 46$ ) are important features of the high mass regions. Ethyl cyclopentanone-2-carboxylate (XVI, see Figure 4) affords an  $M - 28$  ion which is associated with elimination of carbon monoxide (80%) and ethylene (20%). In analogy to the behavior of cyclopentanone itself,<sup>7</sup> the  $m/e$  101 ion ( $C_5H_9O_2^+$ ) can be formed by the process of  $\alpha$ -cleavage and hydrogen transfer (XVI  $\rightarrow$  e'), followed by heterolysis of the 3-4 bond to give f'; homolysis of the same linkage affords g' ( $m/e$  55, base peak). The  $m/e$  73 peak is a doublet ( $C_3H_3O_2^+$ , 60%;  $C_4H_9O^+$ , 40%); the latter fragment can only reasonably be formed by an ethoxyl migration, and, since a metastable ion indicates the transition  $m/e$  101  $\rightarrow$   $m/e$  73, it appears that f' decomposes by loss of both ethylene and carbon monoxide to give h' and i', respectively.



## Experimental Section

All spectra were determined using an A.E.I. MS 9 mass spectrometer operating at 70 e.v. and with the heated inlet system and source at a temperature of approximately 150°.

*Ethyl 3,3-d<sub>2</sub>-2-<sup>18</sup>O-Oxobutyrate (Ib).* Ethyl acetate (100 mg.) and D<sub>2</sub><sup>18</sup>O (400 mg., 82% <sup>18</sup>O) were applied<sup>4</sup> to a tandem g.l.p.c. column (two-coiled stainless steel 0.25 in.  $\times$  5 ft. columns packed with (a) Celite (60-80) coated with 5% phosphoric acid and (b) Apiezon L on Celite (60-80) (1:4), contained in an Autoprep Model A700 (Wilkins Instruments, Walnut Creek, Calif.). The column temperature was 60°, and

(7) P. Natalis, *Bull. soc. chim. Belges.*, **67**, 599 (1958).

the hydrogen flow rate was 50 cc./min. The labeled ester Ib was collected from the column after 16 min. This method gave 66% incorporation of  $^{18}\text{O}$ .<sup>4</sup>

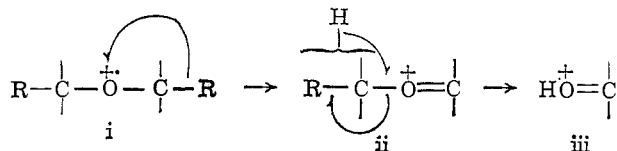
*Acknowledgment.* We wish to thank Professor D. Samuel of the Weizmann Institute for a generous gift of  $\text{D}_2^{18}\text{O}$ .

## Mass Spectrometry in Structural and Stereochemical Problems. LXXXIV.<sup>1</sup> The Nature of the Cyclic Transition State in Hydrogen Rearrangements of Aliphatic Ethers<sup>2,3</sup>

Carl Djerassi and Catherine Fenselau

Contribution from the Department of Chemistry, Stanford University, Stanford, California. Received July 6, 1965

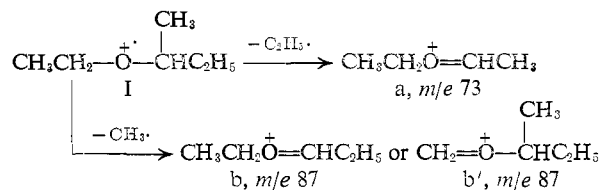
As recognized first by McLafferty,<sup>4</sup> the two most characteristic fragmentation processes of aliphatic ethers (i) upon electron impact are  $\alpha$ -fission to an oxonium ion (ii) and subsequent hydrogen rearrangement to a second oxonium ion (iii) with expulsion of an olefin fragment.



The second step (ii  $\rightarrow$  iii), also noted in amines and thioethers, has generally been accepted as the prototype of a four-membered cyclic transition state in mass spectrometric rearrangement processes. By means of deuterium labeling in suitable ethers with sufficiently long side chains, it has now been demonstrated that three-, four-, five-, and six-membered cyclic transition states are feasible, with the latter three occurring to approximately the same extent. When a choice between abstraction of primary (methyl) or secondary (methylene) hydrogen is available, the latter is favored. Other features of the mass spectrometric fragmentation of aliphatic ethers are also discussed in the light of the spectra of their deuterated analogs.

The behavior of aliphatic ethers upon electron bombardment in the mass spectrometer has been studied in detail by McLafferty,<sup>4</sup> who was the first to call attention to the two most diagnostic processes, namely  $\alpha$ -fission next to the oxygen atom and subsequent hydrogen transfer with ejection of an olefin molecule. The  $\alpha$ -fission process can be illustrated conveniently in the mass spectrum (Figure 1) of an unsymmetrical ether such as ethyl *sec*-butyl ether (I),<sup>4</sup> and it will be noted that following the usual generalization in mass spectrometry,<sup>4,5</sup> the more highly substituted radical (in

this instance, ethyl) is lost preferentially to give the second most intense ion (a,  $m/e$  73) in the spectrum (Figure 1). Alternate  $\alpha$ -cleavage with expulsion of a methyl radical ( $m/e$  87 in Figure 1) occurs to a much smaller extent. By labeling individually the two carbon atoms in the ethyl chain, it has now been possible to answer unambiguously the remaining question<sup>5</sup> concerning this  $\alpha$ -fission, namely whether the methyl group is lost from the *sec*-butyl (b) or ethyl (b') chain or from both sites. The present results (Table I) demonstrate the exclusive origin from the more highly substituted locus (see b).



Theoretically, the  $m/e$  73 peak could also arise by O-C cleavage with loss of the ethyl chain, but such a process would lead to an unfavored species where the heteroatom possesses only an electron sextet and the labeling results (Table I) confirm the absence of such a decomposition path. In fact when O-C fission does occur, as is particularly noted<sup>4</sup> in higher alkyl ethers (see also Figure 4), the charge remains predominantly with the alkyl portion (see  $m/e$  29 and 57 in Figure 1) and an alkoxy radical is lost.

Mechanistically, by far the most intriguing reaction of ethers in the mass spectrometer is the subsequent decomposition of the  $\alpha$ -fission products by hydrogen transfer to oxygen and olefin expulsion. McLafferty<sup>4</sup> noted that such a process did not occur with methyl ethers and thus required at least a  $\beta$ -hydrogen. Using the  $\alpha$ -cleavage product a as progenitor, the reaction was visualized as a  $\rightarrow$  c and apparently has been accepted in the literature<sup>6-8</sup> as the prototype of a four-membered cyclic transition state even in those com-

(1) Paper LXXXIII: J. Poisson, M. Plat, H. Budzikiewicz, L. J. Durham, and C. Djerassi, in press.

(2) Taken in part from the Ph.D. Thesis of C. F., Stanford University, 1965.

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(4) F. W. McLafferty, *Anal. Chem.*, **29**, 1782 (1957).

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, pp. 50-52.

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(7) F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959).

(8) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 116.