Ethyl ε-ferrocenylcaproate was prepared from 300 mg (1.0 mmole) of ε-ferrocenylcaproic acid, yielding 285 mg (88%), and was recrystallized from hexane: mp 27.5–29°; ν^{KBr} 3085, 1735, 1110, and 1008 cm^{-1}; nmr, τ 8.77 (t, CH_3), 8.54 (m, $CH_2CH_2CH_2$), 7.72 (m, CH_2, CH_2), 5.98 (broad s, C_5H_4), 5.93 (s, C_5H_5), and 5.89 (q, CH_2).

Anal. Calcd for $C_{18}H_{24}O_2Fe$: C, 65.86; H, 7.37. Found: C, 66.35; H, 7.43.

Methyl β-ferrocenoylpropionate was prepared from 286 mg (1.0 mmole) of β-ferrocenoylpropionic acid, mp 166–169° (lit.[18] mp 166.5–167.5°), yielding 224 mg (75%) upon recrystallization from hexane, mp 60–61° (lit.[23] mp 60°).

Acknowledgments. We thank Messrs. Laurence R. Dusold and Thomas A. Elwood for recording many of the spectra. D. T. R. thanks E. I. du Pont de Nemours and Co., Inc., for a Du Pont Teaching Fellowship and the American Enka Corp. for an Enka Summer Fellowship.

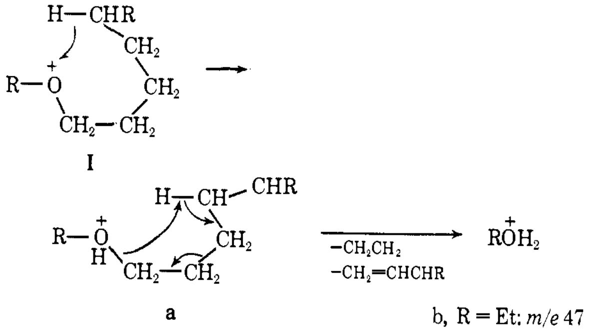
Mass Spectrometry in Structural and Stereochemical Problems. CXLIII.[1] Unusual Fragmentations in the Mass Spectra of Some Aliphatic Ethers[2]

Wayne Carpenter,[3] A. M. Duffield, and Carl Djerassi

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received June 26, 1967*

Abstract: The mass spectra of a series of aliphatic ethers ROR′ (R′ $\geqslant$ n-C_5) contain a peak involving transfer of two hydrogen atoms from R′ such that the charged species formally corresponds to ROH_2. In ethyl n-hexyl ether deuterium labeling demonstrated that the major amounts of both transferred hydrogen atoms arise from C-5 of the hexyl chain and that a seven-membered intermediate is preferred over all other ring sizes. A mechanistic rationalization is presented for this fragmentation and for the loss of ethanol from ethyl n-hexyl ether which proceeds preferentially through five- and six-membered intermediates.

The first detailed study of the electron impact promoted decomposition of aliphatic ethers is due to McLafferty.[4] Further work,[5] utilizing deuterium labeling, delineated some of the hydrogen rearrangement processes occurring during the mass spectrometric fragmentation of aliphatic ethers. During this study,[5,6] an interesting peak in the mass spectrum of ethyl n-hexyl ether was observed at m/e 47 which formally corresponds[6] to protonated ethyl alcohol and must involve a double hydrogen migration from the hexyl chain. At the time of our previous publication,[5] the origin of this peak was not commented upon since the requisite deuterium labeling of the hexyl chain remained to be completed. We have now determined that this apparently bizarre rearrangement is in fact of general occurrence in aliphatic ethers provided one alkyl chain possesses at least five carbon atoms and, furthermore, that this rearrangement is enhanced at low ionizing voltages. Spiteller-Friedmann and Spiteller[7] observed the same phenomena in symmetrical dialkyl ethers and suggested the mechanism given in (1) without the benefits of deuterium labeling.



(1)

The present study utilizing deuterium labeling of all positions of the hexyl chain of ethyl n-hexyl ether (IV) invalidates the above proposal for all but a minor portion (17%, see Table I) of the ion yield at m/e 47.

The mass spectra of seven aliphatic ethers with at least one n-alkyl chain of five carbon atoms or longer have been measured and all display evidence of a peak corresponding to $(ROH_2)^+$ (Table II). At low electron energy these peaks all increase in ion yield relative to the values obtained with 70-ev electrons.

Mass Spectra of Deuterated Analogs of Ethyl n-Hexyl Ether. The mass spectra of ethyl n-hexyl ether taken at 70 and 12 ev using a heated inlet system (ion source temperature 200°) are reproduced in Figures 1 and 2. It will be observed that at high electron voltage (Figure 1) the molecular ion peak (m/e 130) is of low abundance and that a substantial M − 1 fragment is obtained. If, however, the spectrum (Figure 3) is repeated using direct sample insertion into a relatively cold (70°) ion source, a much more pronounced molecular ion is obtained and virtually no M − 1 fragment is visible. The Spitellers have already commented in

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[1] Part CXLII: W. S. Briggs and C. Djerassi, *J. Org. Chem.*, in press.

[2] Financial assistance (Grant No. AM-04257) from the National Institutes of Health of the U. S. Public Health Service is gratefully acknowledged. The purchase of the Atlas CH-4 mass spectrometer was made possible by National Aeronautics and Space Administration Grant NsG 81-60.

[3] Recipient of a Senior Postdoctoral Fellowship while on leave from the U. S. Naval Ordnance Test Station, China Lake, Calif.

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

[5] C. Djerassi and C. Fenselau, *J. Am. Chem. Soc.*, 87, 5747 (1965).

[6] C. Fenselau, Ph.D. Thesis, Stanford University, 1965, pp 37, 46, 47, and 61.

[7] M. Spiteller-Friedmann and G. Spiteller, *Chem. Ber.*, 100, 79 (1967).

Table I. Mass Distribution of Ion b in Deuterated Analogs of Ethyl *n*-Hexyl Ether

	Isotopic purity[a]	—Transfer of the peak at *m/e* 47,[b] %— 70 ev	15 ev	12 ev
1,1-d_2	98% d_2	47 (88%)	47 (88%)	47 (88%)
	2% d_1	48 (12%)	48 (12%)	48 (12%)
2,2-d_2	95% d_2	47 (95%)	47 (95%)	47 (95%)
	5% d_1	48 (5%)	48 (5%)	48 (5%)
3,3-d_2	98% d_2	47 (96%)	47 (96%)	47 (96%)
	2% d_1	48 (4%)	48 (4%)	48 (4%)
4,4-d_2	90% d_2	47 (93%)	47 (83%)	47 (83%)
	10% d_1	48 (17%)	48 (17%)	48 (17%)
5,5-d_2	96% d_2	47 (10%)	47 (12%)	47 (9%)
	2% d_1	48 (45%)	48 (41%)	48 (40%)
	2% d_0	49 (45%)	49 (47%)	49 (51%)
6,6,6-d_3	97% d_3	47 (100%)	47 (100%)	47 (100%)
	3% d_0			

[a] Isotopic purities were calculated from the spectra determined using direct sample introduction into a cool (70°) ion source. The labeled hexyl bromides used in the syntheses of these ethers were converted to the corresponding methyl ketones (W. Carpenter, A. M. Duffield, and C. Djerassi, *J. Am. Chem. Soc.*, in press) and the latter compounds afforded an independent check of the isotopic purity of the labeled alkyl bromides and hence of the labeled ethers. [b] Calculated from spectra measured with the ion source temperature at 200°. There were no significant changes in the retention of deuterium when a cool (70°) ion source was utilized.

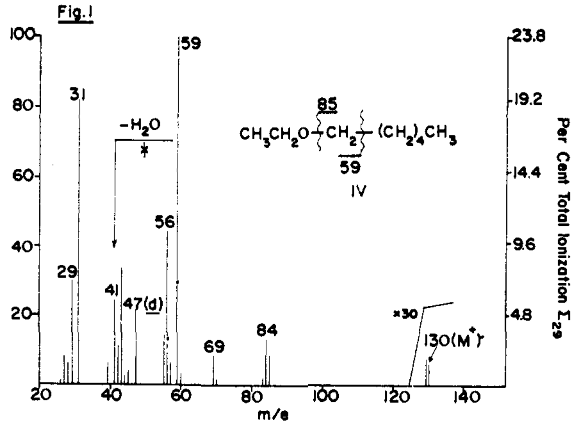
Table II. Effect on the Rearrangement Peak (b) of Changing the Electron Energy in a Series of Aliphatic Ethers

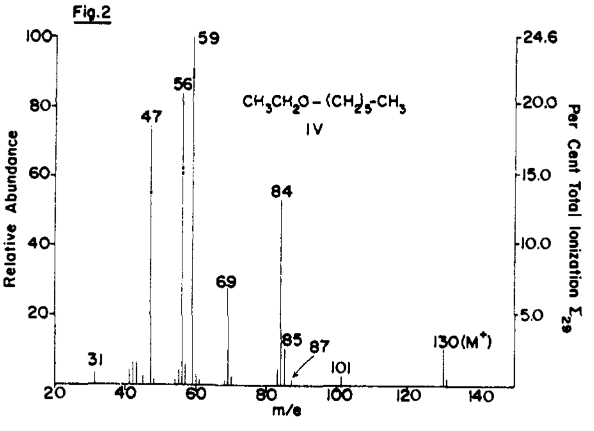
R′-O-R	Ion b, *m/e*	Relative abundance of $(ROH_2)^+$, %[a] 70 ev	15 ev	12 ev
R′ = *n*-C_6H_{13}; R = CH_3 (II)	33	4	7	15
R′ = *n*-C_5H_{11}; R = C_2H_5 (III)	47	12	15	18
R′ = *n*-C_6H_{13}; R = C_2H_5 (IV)	47	21	35	74
R′ = *n*-C_7H_{15}; R = C_2H_5 (V)	47	24	42	95
R′ = *n*-C_6H_{13}; R = *i*-C_3H_7 (VI)	61	5	41	79
R′ = *n*-C_5H_{11}; R = *n*-C_3H_7 (VII)	61	2	7	13
R′ = *n*-C_5H_{11}; R = *n*-C_4H_9 (VIII)	75	2	4	7

[a] Determined using the heated inlet system (ion source temperature 200°).

detail upon such temperature effects in ethers[7] and other compounds.[8] The other principal difference between the spectra is that the per cent total ionization of the *m/e* 47 peak is enhanced (Figure 3) when a cool ion source is used. It is also noteworthy that at low ionizing energy the peak at *m/e* 47 increases progressively in intensity and becomes the most abundant one at 10 ev.

The effects on the *m/e* 47 peak (b = protonated ethanol) of specifically labeling the hexyl chain with deuterium in ethyl *n*-hexyl ether (Figure 1) are collected in Table I. It will be observed that some transfer of the label occurs in the 1,1-, 2,2-, 3,3-, 4,4-, and 5,5-d_2 analogs with the major site of transfer being C-5. Interestingly, a substantial amount (45%) of the peak at *m/e* 47 is located at *m/e* 49 in the 5,5-d_2 compound and hence the virtually unprecedented transfer of both hydrogen atoms from one methylene group must occur in this double hydrogen rearrangement process. A mechanistic rationalization to satisfy this requirement is depicted by IV → c → d, in which transfer to oxygen is twice accomplished using a seven-membered intermediate.





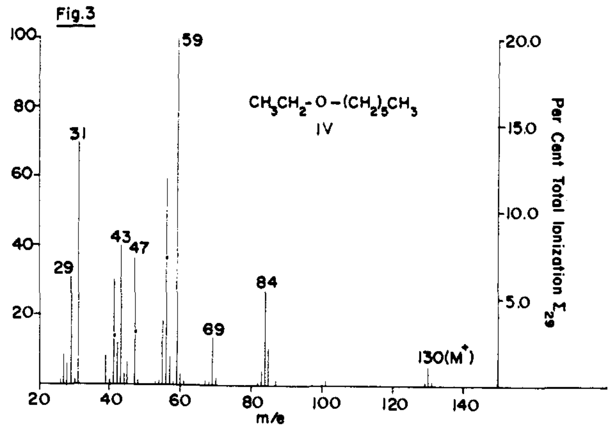
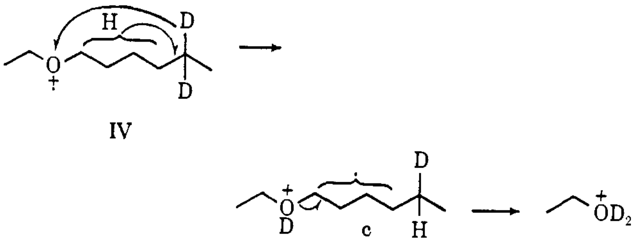


Figure 1. Mass spectrum of ethyl *n*-hexyl ether, ion source 200°, 70 ev.

Figure 2. Mass spectrum of ethyl *n*-hexyl ether, ion source 200°, 12 ev.

Figure 3. Mass spectrum of ethyl *n*-hexyl ether, ion source 70°, 70 ev.

Addition of the percentage transfer of hydrogen obtained with 70-ev electrons (Table I) accounts for only 1.73 of the two transferred hydrogen atoms and the discrepancy is probably attributable to an isotope



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(8) M. Spiteller-Friedmann, S. Eggers, and G. Spiteller, *Monatsh.*, 95, 1740 (1964); G. Spiteller and M. Spiteller-Friedmann, *Ann.*, 690, 1 (1966).

effect.[9] It should also be noted that at low ionizing energies (Table I) the results of deuterium transfer from ethyl *n*-hexyl-5,5-d_2 ether in the formation of the peak at *m/e* 47 vary from the figures obtained with 70-ev electrons. This parallels previous findings of different specificities of hydrogen transfer with low electron energies in the elimination of hydrogen sulfide from aliphatic thiols[10] and in the decomposition of nitroarenes.[11] Evidently differing isotope effects operate at low voltage.

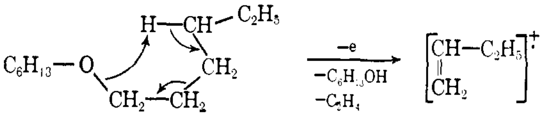
In view of the significant transfer of deuterium from C-5 (Table I) of the hexyl chain in the formation of the peak at *m/e* 47 in the spectrum of ethyl *n*-hexyl ether (IV), it was of interest, because of the known preference in mass spectrometry for transfer of a secondary (methylene) rather than primary (methyl) hydrogen atom,[5] to investigate the mass spectrum of the 5,5-d_2 labeled analog of ethyl *n*-heptyl ether (V). In this instance the peak at *m/e* 47 was dispersed between *m/e* 47 (24%), 48 (57%), and 49 (19%). This result strongly suggests that the transfer of deuterium depicted in IV → c and again in c → d (*m/e* 49) will proceed by larger ring intermediates when the option of transferring a secondary (methylene, V) rather than a primary (methyl, IV) hydrogen atom exists.

An important fragmentation at low electron voltage (12 ev) in the mass spectrum (Figure 2) of ethyl *n*-hexyl ether (IV) involves the loss of ethanol from the molecular ion generating a peak at *m/e* 84. This loss of the elements of alcohol from aliphatic ethers is quite an important process at low voltage (12 ev) and a further discussion of this process will appear in a subsequent publication.[12]

At this stage, it is only necessary to point out that the availability of deuterated analogs of ethyl *n*-hexyl ether labeled in all positions of the hexyl chain made it possible to examine the specificity of hydrogen abstraction in the electron impact controlled alcohol elimination of these compounds. Loss of butanol from di-*n*-butyl ether or of hexanol from di-*n*-hexyl ether has been envisaged[7] as occurring either through a four- or five-membered intermediate, but deuterated analogs were not available to confirm this postulate. We find that hydrogen abstraction in the elimination of ethanol from the molecular ion of ethyl *n*-hexyl ether (IV) occurs from C_3 (41%), C_4 (35%), and C_5 (18%) with no detectable loss from other positions of the hexyl chain.[3] This shows that five- and six-membered transition states are almost equally favored, but that a seven-membered ring is also feasible. The postulated[7] four-membered intermediate is thus excluded.

In the case of ethyl *n*-heptyl ether (V) the loss of ethanol occurs by abstraction of a C-5 hydrogen to the extent of 28%[13] as was calculated from the appropriately labeled compound. Thus, the elimination of ethanol from ethyl *n*-hexyl and *n*-heptyl ethers is mechanistically dissimilar to the loss of water from aliphatic alcohols[14,15] which is known to occur in over 90% yield through a six-membered intermediate.

The peak at *m/e* 56 in the 12-ev mass spectrum (Figure 2) of ethyl *n*-hexyl ether (IV) is of considerable abundance. While a portion of this ion at 70 ev is produced by decomposition of a precursor of mass 84 (as shown by the appropriate metastable ion[5]), the Spitellers[7] have pointed out that at low electron voltages such secondary fragmentation would be repressed or entirely eliminated. In the case of di-*n*-hexyl ether they postulated the rearrangement (IX → e) for the origin of the ion of mass 56.



IX

e, *m/e* 56

Our results (Table III) obtained from the 12-ev spectra of the deuterated analogs of ethyl *n*-hexyl ether (IV) show that only approximately 40–50% of the ion yield at *m/e* 56 is associated with such a process. The distribution of the peaks in the range *m/e* 56–59 in these deuterated compounds may be due to either of two factors. First, the hydrogen-transfer process may well occur from various positions of the hexyl chain other than C-4 (see IX → e) as was found for the origin of ion b and in the loss of ethanol from the molecular ion of ethyl *n*-hexyl ether (IV). Second, at 12 ev (Figure 2), there still exists the possibility that a part of the ion yield at mass 56 arises from a decomposition of the fragment of mass 84.[5]

Table III. Mass Distribution at 12 ev of the *m/e* 56 Peak in Deuterated Analogs of Ethyl *n*-Hexyl Ether[a]

	Isotopic purity	Transfer of peak at *m/e* 56, %, 12 ev
1,1-d_2	98% d_2 2% d_1	56 (40%) 57 (27%) 58 (33%)
2,2-d_2	95% d_2 5% d_1	56 (50%) 57 (27%) 58 (23%)
3,3-d_2	98% d_2 2% d_1	56 (20%) 57 (33%) 58 (47%)
4,4-d_2	90% d_2 10% d_1	56 (25%) 57 (52%) 58 (23%)
5,5-d_2	96% d_2 2% d_1 2% d_0	56 (11%) 57 (40%) 58 (49%)
6,6,6-d_3	97% d_3 3% d_0	57 (12%) 58 (24%) 59 (64%)

[a] Owing to the presence of a small peak at *m/e* 55 (Figure 2) whose location in the deuterated analogs is unknown, the values at *m/e* 55 and 56 in the dideuterated compounds are reliable to ±4%. A similar uncertainty exists in the figures quoted for the 6,6,6-d_3 analog.

A fragmentation common to most of the ethers investigated is the loss of water from the initially formed α-cleavage product (*e.g.*, *m/e* 59 → *m/e* 41 in Figure 1) as indicated by the appropriate metastable ion. This sequence of events can be depicted by eq 2.

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[9] J. K. McLeod and C. Djerassi, *J. Am. Chem. Soc.*, **89**, 5182 (1967).

[10] A. M. Duffield, W. Carpenter, and C. Djerassi, *Chem. Commun.*, 109 (1967).

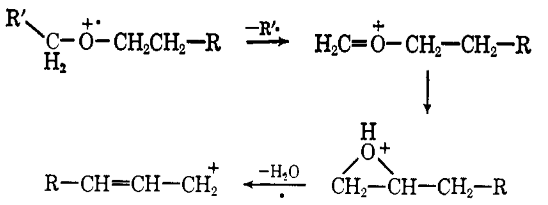
[11] S. Meyerson, I. Puskas, and E. K. Fields, *J. Am. Chem. Soc.*, **88**, 4974 (1966).

[12] W. Carpenter, A. M. Duffield, and C. Djerassi, *ibid.*, in press.

[13] Calculated from the 12-ev spectra of the deuterated analogs determined with an ion source temperature of 200°.

[14] W. Benz and K. Biemann, *J. Am. Chem. Soc.*, **86**, 2375 (1964).

[15] S. Meyerson and L. C. Leitch, *ibid.*, **86**, 2555 (1964).



(2)

It is not intended to imply by this hypothetical rationalization that loss of water in the final step would be site specific. Indeed our results with the rearrangement ion b, the elimination of ethanol, and the formation of the ion of mass 56 from ethyl *n*-hexyl ether suggest that hydrogen abstraction would occur from various positions of the alkyl chain and that the contributions from any one position would in all probability depend upon the alkyl chain length.

Experimental Section[16,17]

Alkyl Ethers. All the ethers were made by the Williamson synthesis with the larger alkyl group present as the bromide and the smaller group as the alkoxide. The alkoxides of methanol and ethanol were generated with sodium metal in an excess of the alcohol; those of isopropyl alcohol, propanol, and butanol were generated with sodium hydride in excess alcohol. The following procedure is typical.

Ethyl *n*-Hexyl Ether. Sodium (0.1 g, 4.3 g-atoms) was dissolved in 5 ml of absolute ethanol in a 15-ml test tube and *n*-hexyl bromide (65 mg, 3.9 mmoles) was added. The tube was sealed and heated in a steam bath for 2 hr. The reaction mixture was diluted with 25 ml of water and extracted twice with ether. The ether extracts were washed with water, dried over anhydrous magnesium sulfate, and evaporated to an oil. Purification for mass spectrometry was performed by gas chromatography using a 10 ft × 0.25 in. column packed with 20% silicone gum SE-52 on DMCS-Chromsorb W at a temperature of 130°.

Deuterated *n*-Hexyl and *n*-Heptyl Bromides. *n*-Hexyl bromide-1,1-d_2 was prepared by lithium aluminum deuteride reduction of *n*-hexanoic acid followed by treatment of the alcohol with a 4:1 (v/v) mixture of 48% hydrobromic acid–98% sulfuric acid at 100° for 4 hr. *n*-Hexyl bromide-2,2-d_2 was prepared by first making *n*-pentyl bromide-1,1-d_2 from *n*-pentanoic acid as described above. The *n*-pentyl bromide was converted to the Grignard reagent and carbonated to give *n*-hexanoic acid-2,2-d_2 which was reduced to the hexanol with lithium aluminum hydride and then converted to the bromide as described above. *n*-Hexyl-3,3-d_2, *n*-hexyl-4,4-d_2, *n*-hexyl-5,5-d_2, and *n*-hexyl-6,6,6-d_3 bromide were prepared from the labeled 1-bromobutanes[18] by the following general sequence. The formation of the butylmalonic ester was followed by hydrolysis, decarboxylation, reduction with lithium aluminum hydride, and formation of the bromide as described above. Ethyl *n*-hexyl-4,4-d_2 ether has previously been synthesized by a slightly different proprocedure.[5] *n*-Heptyl bromide-5,5-d_2 was prepared by carbonation of the Grignard reagent of *n*-hexyl-4,4-d_2 bromide, followed by reduction to the alcohol and conversion to the bromide.

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(16) Mass spectra were determined with an Atlas CH-4 mass spectrometer using either the heated inlet system (TO-4 ion source at 200° with a gas cartridge) or the direct inlet system (TO-4 ion source with sample absorption on activated charcoal, ion source temperature approximately 70°). Metastable peaks were observed with the aid of a logarithmic transfer recorder.[17] All low-voltage spectra correspond to nominal electron volt values and were recorded with zero potential on the drawout plates of the gas cartridge.

(17) R. T. Aplin, H. Budzikiewicz, H. S. Horn, and J. Lederberg, *Anal. Chem.*, 37, 776 (1965).

(18) A. M. Duffield, R. Beugelmans, H. Budzikiewicz, D. A. Lightner, D. H. Williams, and C. Djerassi, *J. Am. Chem. Soc.*, 87, 805 (1965).

Mass Spectrometry in Structural and Stereochemical Problems. CXLV.[1] Factors Governing the Preferential Loss of Small *vs.* Large Radicals in Ketones, Schiff Bases, and Ethers[2]

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Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received July 31, 1967*

Abstract: Study of the low-voltage (10 ev) spectra of a series of aliphatic ketones with regard to the α-cleavage process (I → a + b) reveals that the smallest alkyl radical is preferentially eliminated, contrary to the situation existing at 70 ev. A series of aliphatic Schiff bases at low voltage behave in a similar fashion. Aliphatic ethers lose an alkyl radical by α-cleavage (II → c) in preference to a methyl radical but when a choice between two alkyl radicals (ethyl or larger) exists, it is the smallest group which is preferentially eliminated at 9–12 ev. In all the classes of compounds examined loss of an alkyl group from the most highly substituted carbon atom has precedence over the loss of larger alkyl groups both at 70 and 10 ev. Possible rationalizations are presented for these observations.

The mass spectra of ketones have been extensively investigated using both deuterium labeling and high-resolution measurements.[4] One of the earliest recognized fragmentation modes of aliphatic ketones is α cleavage of the molecular ion (I → a + b)[5] and it has always been accepted (based on experience with 70-ev electron-impact spectra)[4] that the larger alkyl group is preferentially lost as a radical provided the same degree

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(1) Part CXLIV: W. Carpenter, A. M. Duffield, and C. Djerassi, *J. Am. Chem. Soc.*, in press.

(2) Financial assistance (Grant No. AM-04257) from the National Institutes of Health of the U. S. Public Health Service is gratefully acknowledged. The purchase of the Atlas CH-4 mass spectrometer was made possible by the National Aeronautics and Space Administration, Grant NsG 81-60.

(3) Recipient of a Senior Postdoctoral Fellowship while on leave from the U. S. Naval Ordnance Test Station, China Lake, Calif.

(4) For a review of the mass spectra of ketones see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day Inc., San Francisco, Calif., 1967, Chapter 3.

(5) R_s represents the smaller and R_L the larger alkyl group throughout this paper and both, unless indicated otherwise, have the same degree of substitution at the α-carbon atom.