iodide-2-d_1 prepared by iodination of the labeled alcohol[27] with constant boiling hydriodic acid.

Methyl Valerate-γ-d_1 (XVII). The Grignard reagent prepared from n-butyl bromide-3-d_1 (0.7 ml) and magnesium (150 mg) in ether was carbonated by pouring onto Dry Ice and the reaction mixture worked up in the usual way for acidic products. After methylation with diazomethane, the deuterated methyl ester of valeric acid was purified by vpc.

Labeled benzyl alkyl ethers (XXV to XXIX) were synthesized by the reaction of benzyl chloride, sodium hydroxide, and the appropriately labeled alcohol,[28] i.e., for XXV, ethanol-1-d_1; for XXVI, propyl alcohol-1-d_1 (from NaBD$_4$ reduction of propionaldehyde); for XXVII, propyl alcohol-1-d_2 (from LAD reduction of propionic acid); for XXVIII, methanol-d_1 (prepared from NaBD$_4$ reduction of paraformaldehyde); and for XXIX, methanol-d_2 (prepared by cautious reduction of formic acid with LAD). The unlabeled ethers were prepared by the same method using unlabeled methanol, ethanol, and 1-propanol.

n-Methylbenzylamine-3'-d_2 (XXXI). n-Formylbenzylamine was synthesized by the method of Blicke and Lu[29] and converted to the required N-methylbenzylamine-3'-d_2 by reduction with LAD in the usual way.

1-n-Butyl-3'-d_1-isoquinoline (XXXII). The method described by Sample, et al.,[21] employing alkylation of lithium-metalated 1-

methylisoquinoline, was used to prepare this compound from n-propyl bromide-2-d_1. The corresponding dideuterated derivative was made available by Dr. S. Sample.[21]

Methyl Thionvalerate-γ-d_1 (XXXIV). Methyl chlorothioformate[30] (0.3 ml) in ether solution was added slowly to a cooled (0°) ethereal solution of the Grignard reagent composed of n-butyl bromide-3-d_1 (0.5 ml) and magnesium (100 mg). The reaction mixture was allowed to warm up to room temperature, left stirring for a further 2 hr, then decomposed by dropwise addition of saturated sodium sulfate solution. After filtration and removal of the solvent in vacuo, the product was purified by preparative vpc on a silicon rubber column at 80° (retention time, 5.5 min). The unlabeled thion ester XXXIII was obtained in the same manner.

Anal. Calcd for C$_6$H$_{12}$OS: C, 54.5; H, 9.1; S, 24.2. Found: C, 54.66; H, 8.91; S, 24.31.

The γ-d_2 derivative XXXV was synthesized by the same route from methyl thiochloroformate and n-butyl bromide-γ-d_2.[31]

(27) A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., London, 1956, p 285.

(28) W. T. Olson, H. F. Hipster, C. M. Buess, I. A. Goodman, I. Hart, J. H. Lamneck, and L. C. Gibbons, *J. Am. Chem. Soc.*, **69**, 2541 (1947).

(29) I. F. Blicke and C. J. Lu, *ibid.*, **74**, 3933 (1952).

(30) M. Delépine, *Bull. Soc. Chim. France*, 904 (1911), and preceding papers.

(31) 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. CXXXVII.[1] Examples of Interaction of Remote Functional Groups after Electron Impact[2]

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Abstract: Oxygen rearrangement on electron impact has been found to be an important fragmentation pathway in various (I–VII) cyclic ketones containing methoxyl and hydroxyl groups. This oxygen migration, which produces, for example, the m/e 60 ion (C$_2$H$_4$O$_2$) from the molecular ion of 4-hydroxycyclohexanone (II), occurs in six- and seven-membered rings, with the two functional groups in both a 1,3 and 1,4 relationship. Heavy substitution around the ketone group appears to enhance the rearrangement while substitution adjacent to the hydroxyl or methoxyl group acts as a depressant. Deuterium labeling of 4-methoxy- and 4-hydroxycyclohexanone (I and II) suggested the intermediacy of the molecular ion of methyl Δ^5-hexenoate (XIII) in the case of 4-methoxycyclohexanone (I) and support for this proposal was provided by the synthesis of XIII. The rearrangement has been found to be unimportant in acyclic ketones containing primary methyl ether groups.

The attraction of organic chemists to rearrangement reactions is in no small way related to the important driving forces revealed by way of these processes.[4] Even if this were not the case, one is frequently stimulated to study these reactions for the intellectual challenge they provide.[5]

These reasons are no less binding in the study of electron impact produced ion reactions. Indeed, the developing use of mass spectrometery for structure determination adds further to the need for understanding these processes.[6]
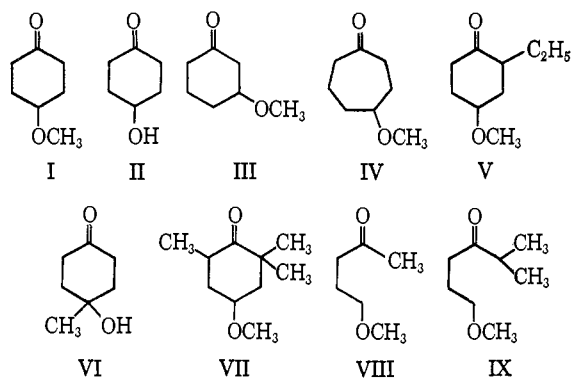
There has been no scarcity of rearrangements in mass spectrometry, but most of these have involved hydrogen migration. Although recent work has uncovered rearrangements of larger groups,[7] these are far

(1) For paper CXXXVI see J. K. MacLeod and C. Djerassi, *J. Am. Chem. Soc.*, **89**, 5182 (1967).

(2) Financial support from the National Institutes of Health (Grant No. AM-04257) is gratefully acknowledged. The purchase of the Atlas CH-4 mass spectrometer was made possible through NASA Grant No. NsG 81-60.

(3) National Institutes of Health Postdoctoral Fellow, 1966–1967.

(4) Ample examples are found in "Molecular Rearrangements," P. deMayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963.

(5) See, for example, a recent popular book providing this stimulation:

S. Ranganathan, "Fascinating Problems in Organic Reaction Mechanisms," Holden-Day, Inc., San Francisco, Calif., 1967.

(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967.

less prevalent. It is therefore of great interest that the base (largest) peak in the mass spectrum of 4-methoxy-cyclohexanone (I) occurs at m/e 74 and has the elemental composition $C_3H_6O_2$.[8] Since a rearrangement must occur to bring the two oxygen functions in closer proximity than they were in I, it was of obvious interest to study in detail the mechanism of this rearrangement and also to determine its applicability to other compounds.[9] As will be shown in the sequel, this was done by examining the mass spectra (Figures 1–9) of I and the related compounds II–IX. The latter part of this paper reports the efforts we have made to determine the detailed mechanism of the rearrangement in I and 4-hydroxycyclohexanone (II) (Scheme I).

Scheme I

I OCH₃; II OH; III OCH₃; IV OCH₃; V C₂H₅ OCH₃;
VI CH₃ OH; VII CH₃ CH₃ OCH₃; VIII CH₃ OCH₃; IX CH₃ CH₃ OCH₃

The energetically navigable nature of the path involved in the interaction of the two remote oxygen groups in the molecular ion of 4-methoxycyclohexanone (I) is amply demonstrated by the fact that the ion of mass 74 carries 10% of the total ionizing current (Σ_{40}).[10] Since the composition of this ion is $C_3H_6O_2$ and since the two oxygen atoms are connected by four carbon atoms in the starting material, a rearrangement must have occurred. This becomes even clearer in the mass spectrum (Figure 2) of 4-hydroxycyclohexanone (II). In this case, a peak appears at m/e 60 (Σ_{40} 7.8%) which is due exclusively to the ion $C_2H_4O_2$.[8] Thus, in the absence of the methyl group it is seen that the two oxygen atoms must at least reside on adjacent carbons in the product.[11] Furthermore, this remote group interaction manifests itself by the presence of at least one other rearrangement ion at m/e 73 (Σ_{40} 2.8%, $C_3H_5O_2$) in the spectrum (Figure 2) of II. Analogously, an ion of mass m/e 87 in I (Figure 1) carries 1.5% of the total ionization.[12] These processes are represented in Scheme II.

Scheme II[13]

R = H, CH₃, m/e 114, 128 → a (R = H, CH₃, m/e 60, 74) and b (R = H, CH₃, m/e 73, 87)

Within a few electron volts of the ionization potential, the rearrangement ions of I are still responsible for 8 and 4% of the total ionization. At this impact energy the molecular ion contributes 40% to the total ionization. One cannot say which of the other major ions owe their strength to the remote group interaction which gives rise to m/e 74, since at this point we can only detect these phenomena when they result in rearrangement products.[17]

That the two oxygen functions need not be related 1,4 in a six-membered ring can be seen from the spectrum (Figure 3) of 3-methoxycyclohexanone (III). In this case, the ion of mass 74 (a) carries 4.5% of the total ionization while the mass 87 ion (b) is of negligible abundance. It is apparent from the spectrum (Figure 3) of III that the fragmentation modes are similar to those available to I, but in this case the distribution is

Scheme III

III (OCH₃) → c (O⁺, O–CH₃) —C₂H₄, –CH₂CO→ d, m/e 58 (=O⁺ CH₃)
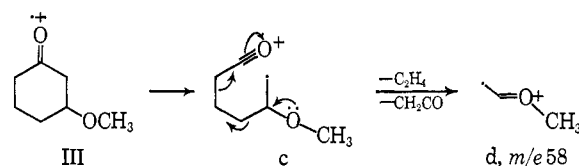
different.[18] This can be understood to a limited extent for the production (see Scheme III) of ion d (m/e 58, Σ_{40} 12%, C_3H_6O). Let us suppose that α cleavage is important as a first step in the rearrangement process. The resulting ion c may be captured in a likely process (Scheme III) which defeats the production of m/e 74. Indeed, if α cleavage is important with participation of the methoxyl oxygen following, the difference in rearrangement for I and III could in part represent the propensity for five- over six-membered ring closure (Scheme IV).

The still wider applicability of this rearrangement is demonstrated by its occurrence in the fragmentation of the molecular ion of 4-methoxycycloheptanone (IV).

(7) See P. Brown and C. Djerassi, *Angew. Chem.*, **79**, 481 (1967); *Angew. Chem. Intern. Ed. Engl.*, **6**, 477 1967.
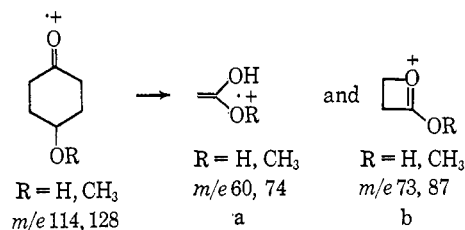
(8) The composition of all relevant peaks was determined by high-resolution measurements.

(9) A preliminary account of a portion of this work has appeared: M. M. Green, D. S. Weinberg, and C. Djerassi, *J. Am. Chem. Soc.*, **88**, 3883 (1966).

(10) In this paper, per cent of total ionization refers to that region of the spectrum above m/e 40 (Σ_{40}).

(11) It is assumed in this work that the rearrangement ions of I and II are homologous in every sense (*i.e.*, structure and mechanism of formation).

(12) A few other such ions ($C_2H_3O_2$ and $C_4H_5O_2$) appear which are of lower intensity. These were noted in an element map of I for which we are indebted to Professor K. Biemann of Massachusetts Institute of Technology.

(13) (a) Although there exist at least two choices for localizing the charge, the resonance hybrid shown is favored since the ionization potentials of ketones are usually lower than those of alcohols and ethers.[14,15] A forceful case for the use of the localized charge concept[6] has recently been published.[16] (b) The ions are assigned structures for reasons given later in the paper.

(14) F. H. Field and J. L. Franklin, "Electron Impact Phenomena," Academic Press Inc., New York, N. Y., 1957, pp 110, 111.

(15) R. W. Kiser, "Introduction to Mass Spectrometry and Its Applications," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 308 ff.

(16) H. J. Svec and G. A. Junk, *J. Am. Chem. Soc.*, **89**, 790 (1967).

(17) Specifically, a process of this sort can only be detected if it culminates in an ion in which the heteroatoms are connected by fewer carbons than in the starting material. This state of affairs would be analogous to the unavailability of all kinetic methods to detect, for example, anchimeric assistance in ground-state solvolysis.

(18) 3-Methoxycyclohexanone (III) suffers from thermal decomposition in the heated inlet system since the M − CH₃OH peak is nearly twice as intense as the one in the spectrum obtained by inserting the sample directly into the ion source. A recently described molecular beam inlet system may result in even greater elimination of the M − CH₃OH peak. See C. Brunee, Abstracts, ASTM Committee E-14, 14th Annual Conference on Mass Spectrometry, Dallas, Texas, 1966, p 410.

Fig.1

100 41 74 128(M⁺) 10
80 58 8
60 43 68 6
40 99 4
20 59 87 113(M-15) 2
40 60 80 100 120 140
m/e

Per Cent Total Ionization Σ₄₀

(structure I: 4-methoxycyclohexanone, O with OCH₃)

Fig.2

100 57 10
80 60 9
60 43 114(M⁺) 8
7
6
5
40 4
20 73 3
96 99(M-15) 2
1
40 60 80 100 120
m/e

Per Cent Total Ionization Σ₄₀

(structure II: 4-hydroxycyclohexanone, O with OH)

Fig.3

100 58 12
71
80 68 9
60
40 74 96(M-CH₃OH) 6
20 85 128(M⁺) 3
40 60 80 100 120 140
m/e

Relative Abundance

Per Cent Total Ionization Σ₄₀

(structure III: 4-methoxycyclohexanone with OCH₃)

Fig.4

100 71 10
55
80 41 58 8
60 6
40 74 110 114 4
87
20 142(M⁺) 2
40 60 80 100 120 140 160
m/e

Per Cent Total Ionization Σ₄₀

(structure IV: 4-methoxycycloheptanone with OCH₃)

Fig.5

100 74 9
80 8
41 7
60 55 6
67 87 5
40 156(M⁺) 4
45 3
20 102 128 2
1
40 60 80 100 120 140 160
m/e

Per Cent Total Ionization Σ₄₀

(structure V: CH₃, CH₂, OCH₃ substituents)

Fig.6

100 71 12
80 43 10
60 55 85 8
73 128(M⁺) 6
30 60 110 4
2
40 60 80 100 120 140
m/e

Per Cent Total Ionization Σ₄₀

(structure VI: CH₃ and OH)

Fig.7

100 88 16
80 14
12
60 CH₃ CH₃ 10
CH₃ 8
40 55 69 83 102 OCH₃ 6
VII 4
20 115 138(M-32) 170(M⁺) 2
40 60 80 100 120 140 160 180
m/e

Relative Abundance

Per Cent Total Ionization Σ₄₀

Fig.8

100 43 20
80 45 59 CH₃
OCH₃ 15
60 58 VIII 10
40
20 69 85 101(M-15) 116(M⁺) 5
40 60 80 100 120
m/e

Per Cent Total Ionization Σ₄₀

Fig.9

100 69 16
80 101 CH₃ 14
CH₃ 12
60 43 59 10
71 OCH₃ 8
40 IX 6
86 4
20 112(M-32) 144(M⁺) 2
40 60 80 100 120 140
m/e

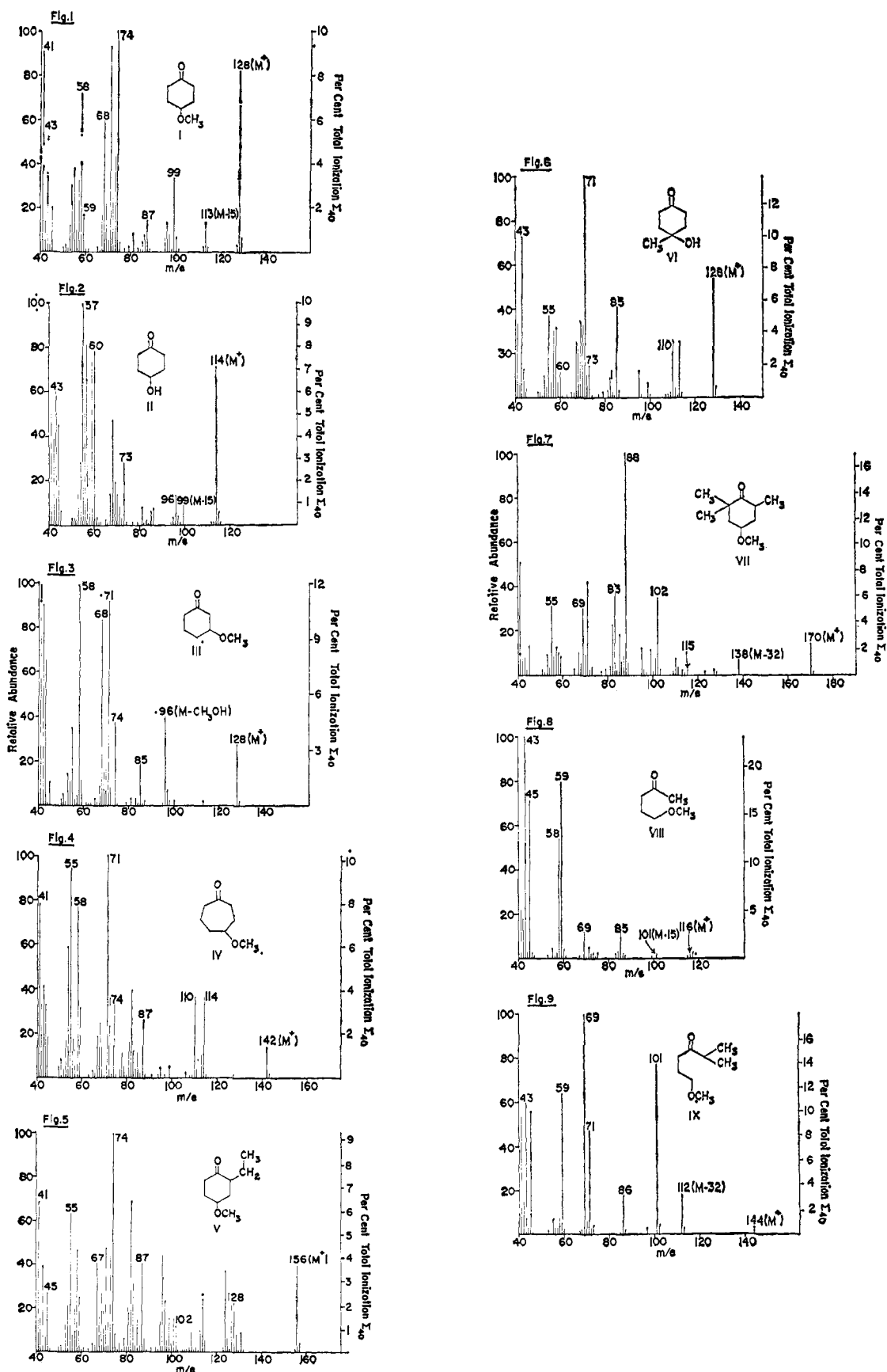Per Cent Total Ionization Σ₄₀

Figure 1. 4-Methoxycyclohexanone (I) (A.E.I., MS-9).
Figure 2. 4-Hydroxycyclohexanone (II) (C.E.C., 21-103C).
Figure 3. 4-Methoxycyclohexanone (III) (Atlas CH-4, direct inlet).
Figure 4. 4-Methoxycycloheptanone (IV) (Atlas CH-4).
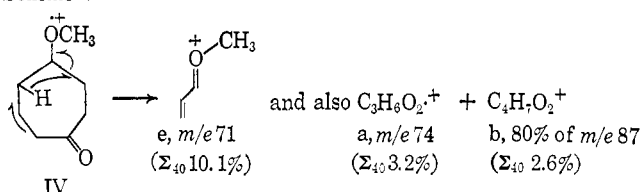Figure 5. 2-Ethyl-4-methoxycyclohexanone (V) (A.E.I., MS-9).

Figure 6. 4-Methyl-4-hydroxycyclohexanone (VI) (A.E.I., MS-9).
Figure 7. 2,2,6-Trimethyl-4-methoxycyclohexanone (VII) (A.E.I., MS-9).
Figure 8. 5-Methoxy-2-pentanone (VIII) (C.E.C., 21-103C).
Figure 9. 6-Methoxy-2-methyl-3-hexanone (IX) (C.E.C., 21-103C).

Scheme IV

$$\text{I} \longrightarrow \longrightarrow \quad \text{rearrangement process}$$

$$\text{III} \longrightarrow \longrightarrow$$
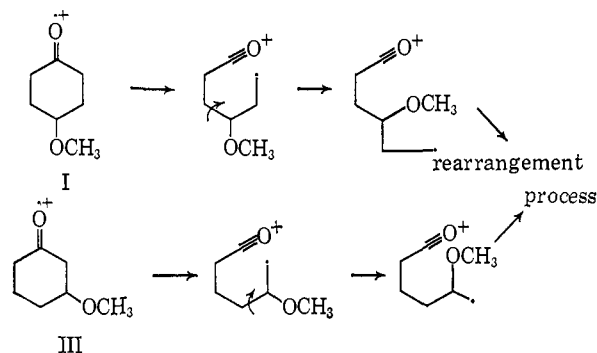
Although the base peak (Σ_{40} 10.1%) in its spectrum (Figure 4) corresponds to the expected[19] m/e 71 (e in Scheme V) the two rearrangement ions a and b of mass m/e 74 and 87 still carry 3.2 and 2.6% of the total ionization, respectively.

Scheme V

$$\text{IV} \longrightarrow$$

e, $m/e\,71$	and also $C_3H_6O_2\cdot^+$	$+$ $C_4H_7O_2^+$
(Σ_{40}10.1%)	a, $m/e\,74$	b, 80% of m/e 87
	(Σ_{40}3.2%)	(Σ_{40} 2.6%)

To further test the prevalence of this oxygen rearrangement, we have examined the mass spectra of three substituted cyclohexanones: 2-ethyl-4-methoxycyclohexanone (V), 4-methyl-4-hydroxycyclohexanone (VI), and 2,2,6-trimethyl-4-methoxycyclohexanone (VII). The ethyl homolog V is especially interesting for at least two reasons. First, 2-ethylcyclohexanone, the analog of V devoid of the 4-methoxy substituent, undergoes a facile McLafferty rearrangement[20] and it would be instructive to determine how this rearrangement competes with the oxygen transfer in the presence of the methoxyl group. Second, because of its unsymmetrical nature, V could give rise to the ethyl homologs of the rearrangement ions in addition to or instead of the mass 74 and 87 ions.

As can be seen from an inspection of Figure 5, only a small peak appears at m/e 102 (Σ_{40} ca. 1%), the position of the ethyl homolog of the rearrangement ion. On the other hand, m/e 74 is the base peak (Σ_{40} 9.3%) while m/e 87 corresponds to 3.8% of the total ionization. Further the ion (m/e 128) derived from the McLafferty rearrangement is considerably diminished, now carrying only 2% of the total ionization.[21]

(19) Unsubstituted cyclic alcohols yield on mass spectral fragmentation the lower homolog of e (m/e 71), namely m/e 57 as the base peak (see section 2-2A in ref 6).
(20) J. K. MacLeod, J. B. Thomson, and C. Djerassi, *Tetrahedron*, 23, 2095 (1967).
(21) It is conceivable that the McLafferty rearrangement peak is depressed due to its subsequent decomposition to m/e 74. Formally the m/e 128 ion corresponds to the enol of 4-methoxycyclohexanone. The question of enol–keto interconversion in mass spectral processes has been treated in ref 20 and in section 3-7 of ref 6.

$$\text{V} \longrightarrow \text{m/e 128} \xrightarrow{?} \text{I} \longrightarrow \text{a, m/e 74}$$
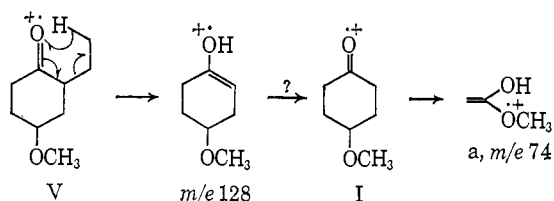
Substitution of another sort as in 4-methyl-4-hydroxycyclohexanone (VI) appears more damaging to the rearrangement pathway. The depression of the m/e 60 ion a (Σ_{40} 1.5%) and the virtual absence (see Figure 6) of b, $C_3H_5O_2^+$ (m/e 73 is 90% C_4H_9O), is surprising since one possible mechanism for the rearrangement might seem the migration of the hydroxyl group to C-1. If this were the case one might hypothesize that the C-4 methyl function would exert a stabilizing influence. On the contrary, the inhabitants of C-4 reside together throughout the fragmentation process giving rise to the base peak (Σ_{40} 13.8%) at m/e 71 (f). This pathway, again homologous to the decomposition of cyclohexanol on electron bombardment,[19] is depicted in Scheme VI.

Scheme VI

$$\longrightarrow \longrightarrow \quad f, m/e\,71$$
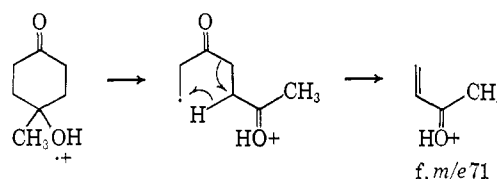
Since the ionization potentials of alcohols decrease with substitution[14] (*e.g.*, ionizing potential of n butyl alcohol is 10.3 ev while that of t-butyl alcohol is 9.9 ev) one could argue that while in 4-hydroxycyclohexanone (II) the major resonance hybrid has charge localized on the ketonic oxygen, this is not the case in the molecular ion of VI. Thus, the lowered ionization potential of the tertiary hydroxyl could act to produce more fragmentation associated with that site in the molecule (*i.e.*, f = m/e 71) at the expense of fragmentation directed by charge localization at the ketone function (*i.e.*, a = m/e 60).

In the highly substituted 2,2,6-trimethyl-4-methoxycyclohexanone (VII, Figure 7), the rearrangement may manifest itself in two possible ways according to the incorporation of the methyl groups on C-2 or C-6 (assuming of course that these carbons are involved). Indeed, the decomposition pattern is dominated by radical ions of mass 88 (Σ_{40} 17% $C_4H_8O_2$) and 102 (Σ_{40} 5.8% $C_5H_{10}O_2$). These two homologs of m/e 74 (a in Scheme II) are in the ratio of about 3:1. Their presence strongly suggests incorporation of one of the α carbons in the rearrangement.

Inspection of the mass spectrum (Figure 7) of VII demonstrates that while the homologs (m/e 88 and 102) of a (m/e 74) carry together almost 23% of the total ionization, the homologs (m/e 101 and 115) of b (m/e 87) are very small. One may conclude only tentatively that this side road of rearrangement is less favorable in VII relative to I, since in this case (VII) the remaining hydrocarbon ions may carry relatively more charge.[22] In fact, m/e 69 (90% of which is C_5H_9) and m/e 55 (90% of this peak is C_4H_7) carry portions of the total ionization of about 5% each. It is interesting though that whereas in I ion b (m/e 87) persists (see Table I) at low voltages, in the case of VII the hydrocarbon peaks at m/e 69 and 55 virtually disappear.

(22) Stevenson's rule[23] predicts that in a mass spectral fragmentation reaction the radical of lowest ionization potential will carry a disproportionate amount of the charge. The hydrocarbon fragments in the case of VII are more highly substituted than those in I (*i.e.*, they will have lower ionization potentials in the case of VII).
(23) D. P. Stevenson, *Discussions Faraday Soc.*, 10, 35 (1951).

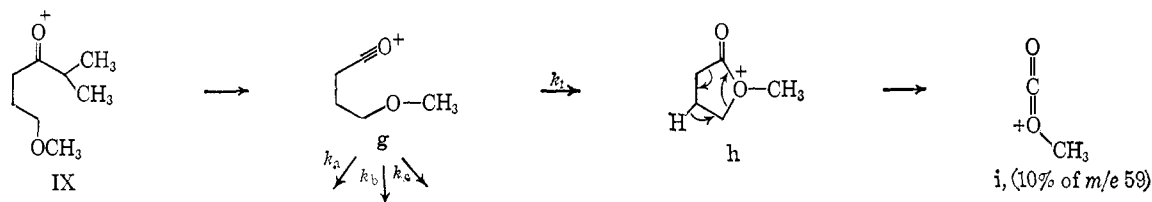**Table I.** Compilation of Intensities of Rearrangement Ions

| | Rearrangement ion[a] | | | |
| | a (Scheme II) | | b (Scheme II) | |
Compd	m/e	$\% \Sigma_{40}$	m/e	$\% \Sigma_{40}$
I	74	10.0 (at 10 ev, 8.0)	87	1.5 (at 10 ev, 4.0)
II	60	7.8	73	2.8
III	74	4.5 (at 12 ev, 6.0)	87	<0.3 (at 12 ev, <0.5)
IV	74	3.2	87	2.6
V	74	9.3	87	3.8
VI	60	1.5	73	<0.2 (10% of m/e 73)
VII	88 + 102	22.8 (at 12 ev, 32.0)	101 + 115	1.2 (at 12 ev, 3.5)
VIII	No rearrangement apparent			
IX	m/e 59, Σ_{40} ~1.1% (10% of peak at m/e 59)			

[a] Data at 70 ev unless otherwise indicated.

Their oxygen counterparts at m/e 101 and 115 remain unperturbed at 12 ev.[24]

While the rearrangement first described in I makes at least a reasonable contribution to the total fragmentation in the alicyclic systems studied so far, it is absent in the two acyclic methoxy ketones VIII and IX. In the case of 5-methoxy-2-pentanone (VIII) the spectrum (Figure 8) is unexceptionable. The acylium ion (m/e 43) and the McLafferty rearrangement product (m/e 58) are among the largest peaks. In addition, α cleavage to the methyl ether gives the standard m/e 45 (C_2H_5O) species.[25] The even-electron ion of mass 59 amounts formally to loss of a $CH_3COCH_2\cdot$ radical.

$C_2H_3O_2$ (Σ_{40} ca. 1.1%). This ion may be formulated as i as shown in Scheme VII. Although its intensity does not indicate a strong remote group interaction, the abundance of i could be limited by a small k_2 and a reversible k_1. In that case other decomposition modes (k_a, k_b, k_c, etc.) may predominate. Certainly the intermediacy of h (Scheme VII) is at least as interesting as the telltale fragment ion (i, $C_2H_3O_2$) it produces. Indeed in all cases studied there may be an abundance of precursor ions of this type. One way to detect them might be to accurately measure the appearance potentials of standard cleavages such as the loss of methyl from VIII as a function of the distance of a remote group.[27]

Scheme VII

The lack of any evidence for interaction between these remote functions in VIII may be due to several causes. Among the most obvious ones are: (i) the methoxyl group is primary in VIII vs. secondary in I and therefore less prone to migrate in VIII, and (ii) the facile α cleavage of the ketone with loss of CH_3CO^+ precludes interaction. We have not investigated any secondary acyclic ethers, but since a more highly substituted group adjacent to the ketone will favor α cleavage giving the dioxygenated ion (M − 43 in Scheme VII), we chose to prepare the isopropyl ketone IX. Again we find (Figure 9) that all the major peaks except for m/e 101 (g) contain one oxygen and therefore lend no support to any remote group interaction.[26] The isopropyl group though effects some change since about 10% of the peak at m/e 59 has the composition

A summary of the extent of rearrangement encountered in compounds I–IX is found in Table I.

We are now left with the question of the mechanism of the rearrangement in I and II. Some understanding of the details of this process may shed more light on the results in Table I.

One can propose numerous rationalizations to account for the production of a (m/e 60, $C_2H_4O_2$) from 4-hydroxycyclohexanone (II). One of the more plausible possibilities is shown below (Scheme VIII). α Cleavage at the ketone would lead to considerable electron deficiency at C-1. This situation could be relieved by participation of the electron-rich hydroxyl oxygen in a manner similar to that encountered in ground-state solvolysis of disubstituted cyclohexanes.[28] Homolytic cleavage with formation of the cyclopropyl ring (j) followed by McLafferty rearrangement would lead to the abundant mass 60 ion (a).

To test if this process is indeed responsible for the rearrangement we have specifically deuterated[29] the

(24) It should be pointed out that in every case the rearrangement pathway may be more heavily trodden than is apparent from the strengths of the obvious heteroatomic products.[17] Any hydrocarbon ion may be seen to be a rearrangement product if it holds so many carbon atoms as to require the removal of a heteroatom from one position to another in the starting material. In this case though a metastable ion would be required to show that it is not just the result of a stripping process.

(25) For a recent publication discussing the formation and possible structure of C_2H_5O ions, see T. W. Shannon and F. W. McLafferty, J. Am. Chem. Soc., 88, 5021 (1966).

(26) Migrations of methoxyl groups to other functionalized sites have been recently uncovered in some acyclic molecules. See R. G. Cooks and D. H. Williams, Chem. Commun., 51 (1967), and M. Vandewalle, N. Schamp, and M. Francque, Bull. Soc. Chim. Belges, 75, 848 (1966).

(27) For a very accurate determination of appearance potentials for α cleavages of simple ketones using photoionization, see E. Murad and M. G. Inghram, J. Chem. Phys., 41, 404 (1964). High accuracy would probably be necessary to detect what are likely to be small energy changes associated with these interactions.

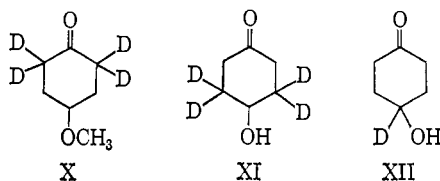(28) D. S. Noyce and B. N. Bastian, J. Am. Chem. Soc., 82, 1246 (1960).

(29) The details of the deuteration are discussed in the Experimental Section. In all cases, high-resolution measurements were used to elucidate the composition of overlapping peaks.

Scheme VIII
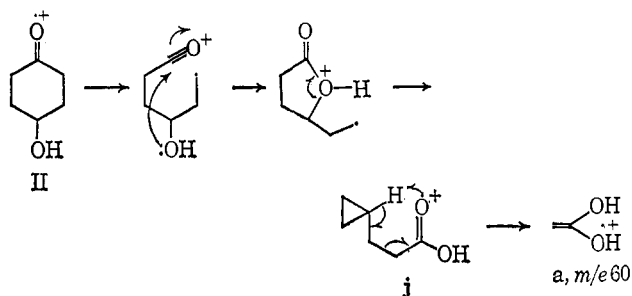
various ring positions in I and II[11] as depicted in Scheme IX.

Scheme IX

The mass spectrum (Figure 7) of VII suggested that one of the α-cleavage carbons (C-2 or C-6) is present in the rearrangement ion. This hypothesis is borne out by the mass spectral shifts (see Table II) observed on deuteration of C-2 and C-6 in I. In this case (X), most of

Table II. Deuterium Labeling Data for Compounds X–XII

Compd	Deuterium content	Rearrangement ions	
		a (%)	b (%)
X	>95% d_4	74 → 77 (22)	87 → 89 (35)
		74 → 76 (72)	87 → 87 (42)
XI	>98% d_4	60 → 60 (47)	73 → 75 (94)
		60 → 61 (53)	73 → 73 (<5)
XII	>99% d_1	60 → 60 (58)	73 → 73 (80)
		60 → 61 (42)	73 → 74 (20)

m/e 74 undergoes a two mass unit shift to m/e 76. However, 22% of m/e 74 is shifted to m/e 77. One possible explanation for this fact is deuterium scrambling in the molecular ion analogous to that observed in 3,3,5,5-d_4-cyclohexanol.[30] This compound loses some D_2O on electron impact and therefore undergoes exchange between the hydroxyl and ring hydrogens. Scheme X outlines how a similar process could give rise to m/e 77 from X.
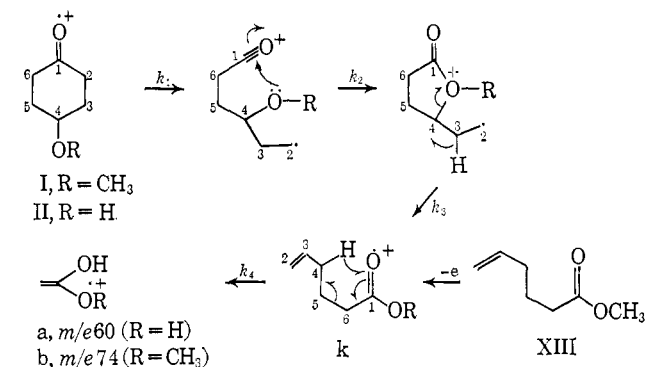
Scheme X
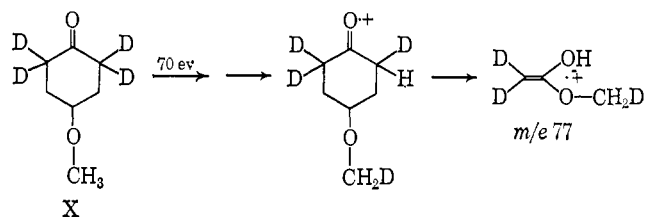
Of crucial importance to the mechanism proposed in Scheme VIII is the observation that deuteration α to the hydroxyl group (XI) leads to splitting (see Table II) of the rearrangement ion between m/e 60 and m/e 61. The latter result requires either the operation of two

(30) H. Budzikiewicz, Z. Pelah, and C. Djerassi, *Monatsh.*, **95**, 158 (1964).

mechanisms (*i.e.*, one incorporating one of the C-3(5) hydrogens and the other not) or if only one reaction path operates, the data exclude the one outlined in Scheme VIII. The deuterium shift encountered in XI is reinforced by the behavior of XII on electron impact. Here again the rearrangement ion is split between m/e 60 and 61. Table II summarizes the precise labeling results in compounds X–XII.[31]

It is clear that if a single mechanism is to account for the major rearrangement ion, it must incorporate as its essential feature the approximate equivalence of one of the C-3(5) hydrogens with the lone hydrogen atom on C-4. In addition, in the case of II the only carbons involved are C-1 and C-2. One process which satisfies these criteria is shown in Scheme XI.

Scheme XI

This mechanism embodies the same driving forces described in the first proposed rationalization (Scheme VIII). In this case though, instead of forming a cyclopropane ring on homolytic cleavage of the carbon–oxygen bond, a hydrogen atom is shifted instead from C-3(5) thus producing an intact double bond (k). The McLafferty process (k → a) now involves an activated allylic hydrogen instead of the cyclopropyl hydrogen (see j). However it is apparent from the data in Table II that k_3 (Scheme XI) or its equivalent must be slowly reversible since XI and XII show excess transfer of deuterium and protium, respectively.[32]

The reaction sequence outlined in Scheme XI proposes in essence that in the case of the 4-methoxy analog I, the six-membered ring opens to form the molecular ion k of methyl Δ^5-hexenoate (XIII). The question immediately arises whether one can produce ion k directly by electron bombardment of XIII and we have, therefore, prepared XIII in order to examine its mass spectrum (Figure 10).

At the most cursory level of comparison of the mass spectra (Figures 1 and 10) of I and XIII one notes that the base peak in both is at m/e 74. This ion (a) is the expected McLafferty rearrangement product of XIII. Furthermore, there are no peaks present in the spectrum (Figure 10) of XIII, which are not also discernible in that (Figure 1) of I and the relative intensities of many ions present in XIII are similar to those of the same ions found in the mass spectrum of I.

In addition to the major rearrangement ion of I (*i.e.*, a = m/e 74), mention has been made in this paper

(31) The shifts shown have been adjusted to 100% deuterium incorporation in the case of X.

(32) It is less plausible that the transferred hydrogen from C-3 forms a vibrationally excited bond to C-4 and therefore is more easily transmitted in the subsequent McLafferty step (k_4, Scheme XI).

Table III. Metastable Ion Data for Methyl Δ^5-Hexenoate (XIII) and 4-Methoxycyclohexanone (I)

Obsd		Calcd for process shown	Parent$^+$ $\rightarrow$ daughter$^+$ + neutral[a]			Rel inten[b]	
XIII	I		Parent$^+$ $\rightarrow$	daughter$^+$ +	neutral[a]	XIII	I
24.5	24.5	24.36	C_5H_9 $\rightarrow$	C_3H_5 +	C_2H_4	26	26
25.0	25.1	24.99	$C_3H_6O_2$ $\rightarrow$	C_2H_3O +	CH_3O	50	50
34.7	34.8	34.77	$C_4H_7O_2$ $\rightarrow$	C_3H_3O +	CH_3OH	10	10
36.2	36.2	36.13	$C_7H_{12}O_2$ $\rightarrow$	C_5H_8 +	$C_2H_4O_2$	12	80
37.1	37.1	37.10	C_3H_5 $\rightarrow$	C_3H_3 +	H_2	27	32
48.2	48.2	48.17	C_6H_8O $\rightarrow$	C_5H_8 +	CO	4	10
49.1	49.1	49.08	C_6H_9O $\rightarrow$	C_5H_9 +	CO	39	20
66.1	66.2	66.01	C_5H_8 $\rightarrow$	C_5H_7 +	H	20	40
72.0	72.0	72.00	$C_7H_{12}O_2$ $\rightarrow$	C_6H_8O +	CH_3OH	20	>70
99.8	99.9	99.76	$C_7H_{12}O_2$ $\rightarrow$	$C_6H_9O_2$ +	CH_3	6	35

[a] The transitions were matched to the metastable ion positions using a computer program written in this laboratory by Mr. S. H. Brown. Copies of this program are available on request. [b] m/e 25 in both I and XIII is arbitrarily made equal to 50.

(see Table I) of a second less prominent ion (b) at m/e 87 (m/e 73 in II). At this point it is appropriate to direct our attention to its genesis. Since XIII also gives rise to b (m/e 87) by allylic cleavage (see Scheme XII), one may be tempted to assign its formation in I
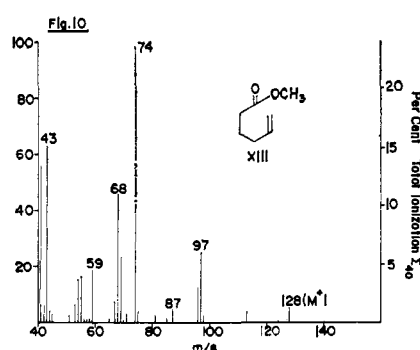

Figure 10. Mass spectrum of methyl Δ^5-hexenoate (XIII) (A.E.I., MS-9).

to the intermediacy of the molecular ion (k) of XIII. Certain data dampen this hypothesis. The ratio of m/e 74:87 in XIII (Figure 10) is 24:1 while in the mass spectrum (Figure 1) of I this ratio is 6.6:1. The deuterium labeling results in Table II on the other hand suggest that C-1, C-6, and C-5 are involved as would be required by the intermediacy of the molecular ion k of XIII (Scheme XII).[33] Whether these results indicate the presence of alternative routes to m/e 87 in I or whether the species represented by k is formed in different energy and/or geometric states on ionization of XIII and rearrangement of ionized I cannot be said.

Scheme XII
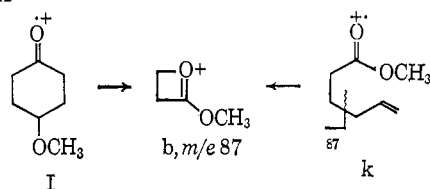
In regard to these conjectures, a second level of comparison between the mass spectral behavior of I and

(33) We find here that the deuterium shifts are not clean. In the case of XII about 20% of m/e 73 shifts to 74, while in X 42% of m/e 87 does not shift at all. In XII this could be caused by the effective reversal (Scheme XI) of k_3 which would place at least one deuterium atom on C-5.

XIII is of interest. *Every* metastable ion found in the mass spectrum of XIII is also detected in that of I and the shapes of the various metastable peaks are similar in the two spectra.[34] Table III is a compilation of all the prominent[35] metastable ions in XIII and the matching metastable ions in I.

The last two columns of Table III are a comparison of the relative intensity of the various metastables encountered *within each series*. In each case the metastable ion at m/e 25.0 was set to an intensity of 50 units.[36]

It is interesting to note that the three worst fits (*i.e*, 36.2, 72.0, and 99.8) all involve the molecular ion and in each case the metastable ion from I is too intense. In the latter two the m/e 128 ion can lose methyl or methanol before or after rearrangement. In that manner two routes are opened to m/e 72.0 and 99.8 in the case of I but only one route in the case of XIII.

The data suggest that there exist common ions in the fragmentation of I and XIII. It is not however borne out that all of I$\cdot^+$ rearranges to a species *identical* with that formed from XIII on ionization. The differences between rearranged I$\cdot^+$ and XIII$\cdot^+$ may be conveniently used to justify the ratio differences of m/e 74:87 encountered in the electron impact induced fragmentation of I and XIII.[37] It is also of interest to compare the ratio of m/e 60:73 in 4-hydroxycyclohexanone (II) and Δ^5-hexenoic acid (free acid corresponding to XIII). In II, m/e 60:73 is about 3:1 while in the free acid it is about 5.4:1. Thus, while the proposed rearrangement product (Δ^5-hexenoic acid in the case of II) is again less efficient in producing the second rearrangement ion (b in Scheme

(34) No major flat-topped peaks were encountered and we therefore could not carry out a comparison such as has been accomplished recently. See ref 25 as well as J. H. Beynon, R. A. Saunders, and A. E. Williams, Z. *Naturforsch.*, **20a**, 180 (1965).

(35) Easily detectable above the noise on an AEI MS-9 mass spectrometer.

(36) After dividing these numbers by the % Σ_{40} of their respective parent ions, no improvement in fit was found. In fact for any one parent peak in the case of I one may have at least two ion structures (of the same composition) of unknown proportion. Ideally one should divide the relative intensities of the metastables by the entire parent peak in the case of XIII and by some fraction of the parent peak in the case of I. This does not work here since to match the two columns requires in a few cases higher values of % Σ_{40} than those observed in I.

(37) A third level of comparison between I and XIII is also available. One could determine the enthalpy change for the rearrangement step (the heat of formation of neutral I and XIII could be calculated with sufficient accuracy) by accurately measuring the difference between the ionization potentials of I and XIII and the appearance potentials of m/e 74 in I and in XIII. It would be interesting to compare that value with one obtained by using the difference between the appearance potentials of the m/e 87 ions in I and in XIII.

II), it is better in the free acid than in the ester XIII. This parallels the behavior of the 4-hydroxy- vs. the 4-methoxycyclohexanone. That at least part of m/e 87 is produced in one step in I and XIII is demonstrated by a low-intensity metastable ion at m/e 59.1 (calcd 59.13).

It seems probable that the mechanism outlined in Scheme XI is a close approximation of the actual state of events. Since the hydrogen transfer (k_3) is central to this process we decided to test its mettle for production of m/e 60 by forcing the molecule to transfer a methyl group instead. We therefore prepared 3,3,5,5-tetramethyl-4-hydroxycyclohexanone (XIV). It suffices to say with regard to the present work that the ion at m/e 60 is not present. Indeed a mixture of the compounds containing one and two methyl groups less than XIV also shows no m/e 60 ion. Other workers though have observed oxygen rearrangements in various cyclic molecules.[38] A likely explanation for the lack of rearrangement is that in XIV, just as in VI, charge localization (i.e., the preferred resonance hybrid) is favored at other sites (e.g., tertiary carbonium ion) than the carbonyl oxygen. As indicated in Scheme XI, charge localization on the carbonyl oxygen with concomitant α fission appears to be a likely prerequisite for the occurrence of the oxygen rearrangement.

XIV   a, m/e 60
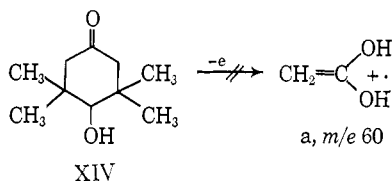
Experimental Section

Low-resolution mass spectra were obtained by Drs. Alan M. Duffield and John K. MacLeod, using an Atlas CH-4 spectrometer; by Mr. R. G. Ross, using an A.E.I. MS-9 double-focussing spectrometer; and by Mr. N. S. Garcia, using a C.E.C. Model 21-103C mass spectrometer. High-resolution measurements with the A.E.I. MS-9 instrument were secured by Mr. R. G. Ross. The inlet system in the Atlas and MS-9 instruments were heated to ca. 150°, and the all-glass inlet of the C.E.C. spectrometer was held at 200°. Source temperatures varied from below 200° in the Atlas and MS-9 to ca. 250° in the C.E.C. spectrometer. Unless noted otherwise an ionizing energy of 70 ev was employed.

Proton resonance spectra were recorded using a Varian A-60 nmr spectrometer with TMS as internal standard. Carbon tetrachloride was used for VIII and IX while all other spectra were taken in deuteriochloroform. Infrared spectral data were recorded with a Perkin-Elmer Infracord. All compounds for mass spectra analyses were purified and checked for purity by vpc.

The preparation of 4-hydroxycyclohexanone (II) and its ketal followed that of the literature,[39] while the oxidation of the ketal was performed according to Prins.[40]

Δ^5-Hexenoic acid[41] was synthesized by carbonation of the Grignard reagent prepared from 1-chloro-4-pentene. Diazomethane converted the acid to the methyl ester XIII. Infrared, nmr, and mass spectral data agreed with the structures.

4-Methoxycyclohexanone (I). To 3.3 g of the ethylene ketal of II was added slowly, in benzene, with stirring 2.6 g of 50% sodium hydride dispersion in mineral oil. The resulting suspension was heated under reflux overnight and then heated again overnight

with 7.6 g of methyl iodide. This reaction was worked up in a standard manner and the resulting colorless oil (3 g) was deketalized with p-toluenesulfonic acid in acetone–water at room temperature overnight. The resulting ketone was purified by distillation and vpc on a 6-ft polybutylene glycol column at 130°; n^{24}D 1.4550 (lit.[42] n^{20}D 1.4560).

3-Methoxycyclohexanone (III). To 5 g of cyclohexane-1,3-diol (K & K Chemical Company) in benzene was added 1 g of 50% sodium hydride dispersion. The resulting suspension was heated under reflux and then treated with excess methyl iodide. After reaction for 3 days and work-up, a light yellow oil was obtained which was purified by vpc to yield ca. 3 g of a colorless hydroxy ether (characterized by its infrared spectrum (λ_{max} 3.0 and 9.1 μ)). A portion of this material was oxidized with Jones regent[43] at 0° to yield a colorless oil which was purified by vpc on a "DC-200" column (10 ft) at 135° ($\sim$60 cc/min, retention time 9 min). This ketone (λ_{max} 5.85 μ) gave a nmr spectrum (in δ values) which showed a singlet at 3.35 (3 H), a multiplet between 1.7 and 2.7 (8 H), and a broad multiplet near 3.7 (1 H). There was no evidence for olefinic hydrogens. The molecular weight by mass spectroscopy was 128.

4-Methoxycycloheptanone (IV). To 200 mg of I in ca. 100 ml of ether was added ca. 5 ml of diazomethane in ether (ca. 0.0003 mole/cc). About 10 cc of anhydrous methanol was added and the solution allowed to stand 1 week. Evaporation of the solvent yielded a yellow oil which was fractionated by vpc on SE-30 (5-ft column, retention time 6 min) at 130°. The product was shown by mass spectrometry to have a molecular weight of 142, and infrared verified the presence of a ketone (λ_{max} 5.85 μ) and an ether group (λ_{max} 9.1 μ).

2-Ethyl-4-methoxycyclohexanone (V). The following procedure is modeled after related alkylations in the literature.[44,45] Cyclohexylamine (640 mg) and 720 mg of I were used to form the imine. Ethylmagnesium bromide was prepared from 80 mg of magnesium and a slight excess of ethyl bromide. To the organometallic intermediate in ether was added 400 mg of the above prepared crude imine, causing a yellow-red precipitate to form. After stirring for 2 hr, 300 mg of ethyl iodide was added and the resulting suspension heated for 20 hr. After adding 20% hydrochloric acid two layers formed which were stirred for 1 hr. The system was neutralized with sodium carbonate and extracted with ether. There was thus obtained 260 mg of a brown oil which was distilled in a short-path apparatus at ca. 100° and fractionated by vpc on a PDEAS column at 150°. The peak of second longest retention time was cleanly separated from starting material and shown to have molecular weight of 156 by mass spectroscopy and contain both ketone (λ_{max} 5.85 μ) and ether groups (λ_{max} 9.15 μ) by infrared. Equilibration with basic D_2O only incorporated up to three deuterium atoms.

4-Methyl-4-hydroxycyclohexanone (VI). This material was prepared from the monoethylene ketal of cyclohexane-1,4-dione[40] by reaction with excess methylmagnesium iodide and subsequent removal of the ketal group by heating (steam bath) the product of the Grignard reaction (100 mg) with 40 ml of 90% acetic acid for 1 hr. Infrared analyses showed the presence of both hydroxyl and ketone functions. The molecular weight (mass spectroscopy) was 128.

2,2,6-Trimethyl-4-methoxycyclohexanone (VII). To 2.4 g of 50% sodium hydride dispersion in toluene was added slowly 800 mg of II. Excess methyl iodide was added and the suspension heated under reflux for 4 days. After work-up the resulting yellow oil (1.5 g) was subjected to fractionation by vpc on "Dowfax" at 170° (10-ft column). The highest boiling component was cleanly separated and shown by mass spectroscopy to have a molecular weight of 170 and to contain ketone (λ_{max} 5.89 μ) and ether (λ_{max} 9.15 μ) functions by infrared. In addition the nmr spectrum showed three lines in the methyl region at 72, 65, and 59 cps. Their relative intensities may be explained by the superposition of a doublet ($J = 7$ cps) centered at 72 cps on two singlets at 72 and 65 cps. The methyl region comprises 9 H. Further a singlet appears at δ 3.4 (3 H) and multiplets near δ 2 (ca. 4 H) and near δ 3.7 (1 H). This spectrum supports[46] the structure of VII.

5-Methoxy-2-pentanone (VIII). The ketal of methyl levulinate was prepared from 7 g of the ester and 5 g of ethylene glycol with a

(38) See K. Heyns and D. Müller, *Tetrahedron*, **21**, 55 (1965); *Tetrahedron Letters*, 449 (1966); 6061 (1966); N. K. Kochetkov and O. S. Chizhov, *Tetrahedron*, **21**, 2029 (1965); H. F. Grützmacher, J. Winkler, and K. Heyns, *Tetrahedron Letters*, 6051 (1966).

(39) (a) L. N. Owen and P. A. Robins, *J. Chem. Soc.*, 320 (1949); (b) E. R. H. Jones and F. Sondheimer, *ibid.*, 615 (1949); (c) H. Plieninger and H. J. Grasshoff, *Ber.*, **90**, 1973 (1957).

(40) D. A. Prins, *Helv. Chim. Acta*, **40**, 1621 (1957).

(41) F. B. LaForge, N. Green, and W. A. Gersdorff, *J. Am. Chem. Soc.*, **70**, 3707 (1948).

(42) C. S. Marvel and W. L. Walton, *J. Org. Chem.*, **7**, 88 (1942).

(43) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(44) G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963).

(45) H. Fritz, H. Budzikiewicz, and C. Djerassi, *Chem. Ber.*, **99**, 35 (1966).

(46) M. Fétizon, J. Goré, P. Laszlo, and B. Waegell, *J. Org. Chem.*, **31**, 4047 (1966).

trace of *p*-toluenesulfonic acid in boiling benzene. This material was reduced with lithium aluminum hydride in the conventional manner (work-up with saturated sodium sulfate). The resulting alcohol (2 g) was methylated with the use of 3 g of 50% sodium hydride dispersion and 7 g of methyl iodide under reflux in benzene. The ketal group was removed with *p*-toluenesulfonic acid in acetone–water at 250° and the product purified by vpc on a "Carbowax column" (10 ft) at 120° (retention time 9 min). Infrared analyses showed the presence of ketone and ether function and mass spectroscopy gave the correct molecular weight (116). The nmr spectrum showed a singlet at δ 2.1 ($CH_3C=O$) and a singlet superimposed on a multiplet at *ca.* δ 3.25 (OCH_3). In addition multiplets appeared centered at *ca.* δ 2.45 and 1.75.

6-Methoxy-2-methyl-3-hexanone (IX). 4-Methoxy-1-butanol, prepared by reaction of 1,4-butanediol with 1 equiv of sodium hydride dispersion in benzene under reflux overnight followed by 24-hr heating with excess methyl iodide, was oxidized with Jones reagent[48] to the acid. This acid (500 mg) was treated with 1 equiv of isopropyllithium[47] (from isopropyl chloride and lithium metal dispersion in ether) in ether at 0°. The mixture was stirred for 1 hr and worked up with aqueous ammonium chloride. The product was purified by vpc on a 10-ft Apiezon L column (helium flow rate 100 cc/min) at 150° (retention time 12 min). The presence of ketone (λ_{max} 5.9 μ) and ether (λ_{max} 9.0 μ) functions was verified by infrared. Mass spectrometry gave the correct molecular weight (144). The nmr spectrum (in δ values) showed a prominent doublet ($J = 7$ cps) at 1.05 (6 H) and a singlet superimposed on a multiplet at *ca.* 3.25 (5 H). In addition multiplets appeared at about δ 2.5 and 1.7 (total 5 H).

3,3,5,5-Tetramethyl-4-hydroxycyclohexanone (XIV). To 500 mg of the monoethylene ketal of cyclohexane-1,4-dione[40] in toluene was added 700 mg of dry sodium hydride and excess (20-fold) methyl iodide. This suspension was heated under reflux for 4 days. After work-up there was obtained about 700 mg of a colorless oil. This oil was reduced with excess lithium aluminum hydride in

ether. The partially crystalline product was deketalized with 50 ml of 90% acetic acid (steam bath for 1 hr). There was thus obtained 300 mg of a colorless oil after distillation in a short path apparatus. This material was fractionated on a 10-ft "DC-200" vpc column at 190° and ∼60 cc/min. The highest boiling component crystallized in the collection tube. Mass spectral analysis showed it to have a molecular weight of 170 (contaminated with less than 20% of the trimethyl analog as judged by the peak at *m/e* 156). Infrared analyses showed the presence of a hydroxyl group and two bands in the carbonyl region (λ_{max} 5.8 and 5.9 μ). The nmr spectrum confirmed the structure. Two lines appeared at δ 0.95 and 1.15 of equal intensity (12 H together). In addition a singlet occurs at δ 2.3 (4 H) and broad peaks at δ 3.55 (1 H) and 1.9 (1 H).

2,2,6,6-Tetradeuterio-4-methoxycyclohexanone (X).[48] Compound I was subjected to exchange in basic (sodium carbonate) deuterium oxide at 25°.[49] After two exchange procedures, for a total of 50 hr, the isotopic composition as measured by mass spectroscopy was >95% d_4. Attempts to incorporate deuterium by vpc with an acid column[50] failed as the material (I) would not elute; cyclohexanone performed satisfactorily under these conditions.

3,3,5,5-Tetradeuterio-4-hydroxycyclohexanone (XI).[48] The monoethylene ketal of cyclohexane-1,4-dione[40] was subjected to two exchanges in basic (sodium carbonate) deuterium oxide at 25°. The resulting crystalline solid was reduced with lithium aluminum hydride in ether. The ketal group was removed with *p*-toluenesulfonic acid in acetone–water at 25° overnight. Mass spectral analysis showed >98% d_4.

4-Deuterio-4-hydroxycyclohexanone (XII).[48] The monoethylene ketal of cyclohexane-1,4-dione was reduced with lithium aluminum deuteride (Metal Hydrides, Inc.) in ether. The resulting alcohol was deketalized as in the preparation of XI. The product had >99% d_1 by mass spectroscopic analysis.

(47) For a general discussion of organolithium compounds, including references to isopropyllithium, see E. A. Braude, *Progr. Org. Chem.*, **3**, 172 (1955), and references included therein.

(48) In all cases the deuterated compounds were identical with the protium compounds by vpc criteria.

(49) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. 1, Holden-Day, Inc., San Francisco, Calif., 1964, p 19.

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