Mass Spectrometry in Structural and Stereochemical Problems. CCVIII.[1] The Effect of Double Bonds upon the McLafferty Rearrangement of Carbonyl Compounds[2]

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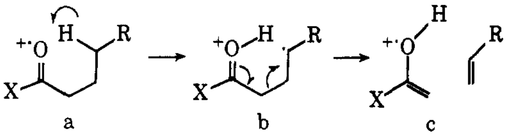
Abstract: The present study is concerned with an evaluation of the effect that a nonconjugated double bond can exert on the well-known fragmentation behavior of carbonyl compounds. Through examination of suitable model compounds and labeled analogs it was demonstrated that double bond migration to the δ,ϵ position (with respect to the carbonyl groups) is favored and leads to a McLafferty rearrangement with charge retention by the hydrocarbon rather than the carbonyl-containing fragment Since this "complementary" McLafferty rearrangement requires prior double bond movement, this process is enhanced at lower ionizing voltages. Loss of water, which is absent in the saturated aliphatic ketones, is also favored by double bond movement to the δ,ϵ position and lower ionizing voltages. An example of a facile proton exchange between the activated positions of 8-nonen-2-one is presented. All three processes illustrate the profound effect that an isolated double bond can cause in aliphatic carbonyl compounds.

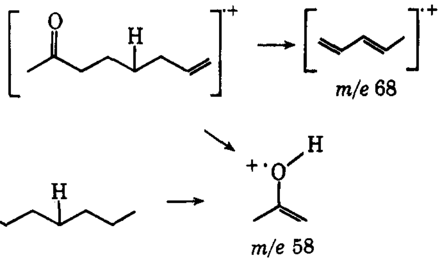
The mass spectra of aliphatic ketones possessing a γ-hydrogen exhibit an important peak resulting from a McLafferty rearrangement (a → c).[4] Increasing the positive ionic charge on the carbonyl group with electron-withdrawing substituents on X[5] or stabilizing the γ-radical site of the intermediate b with electron-releasing substituents at R[6] results in an enhancement of this process. Systematic study of bifunctional carbonyl compounds is necessary to specifically determine: (1) the effect of the presence of other groups on the McLafferty process and (2) the formation of fragments not common to either functional group but resulting from some cooperative interplay.[7] Knowledge of these factors will increase the scope of manual and computerized interpretation of mass spectra,[8] the latter being one of the primary goals of this work.



Since the McLafferty rearrangement is directed by the charge localized on the carbonyl group, the presence of another functional group in the molecule can give rise to three situations: the second functional group can have (1) a higher, (2) approximately the same, or (3) a lower ionization potential (IP) than the carbonyl group. The first case is primarily uneventful, the second case is the subject of this work, and the third alternative causes suppression of the McLafferty rearrangement by localizing the ionic charge far from the carbonyl function.[9]

Results

In the normal McLafferty rearrangement of ketones, esters, and acids, the charge is retained by the carbonyl-containing fragment.[4] In this study of carbonyl compounds containing an isolated double bond (Table I), it was revealed that a substantial amount of charge is retained by the severed hydrocarbon portion. Compare the mass spectra of 2-octanone and 7-octen-2-one (IIIa), first at high and then at low ionizing voltage (Figures 1 and 2). At 70 eV the *m/e* 41, 43, and 71 peaks are essentially comparable for both compounds. The most obvious difference in these spectra is that the base peak resulting from the McLafferty rearrangement (*m/e* 58) in 2-octanone (Figure 1) becomes approximately equally divided in 7-octen-2-one (Figure 2) into *m/e* 58 and *m/e* 68 (M − 58), the latter peak corresponding to a McLafferty rearrangement with charge retention on the hydrocarbon moiety.



The *m/e* 83 and 111 peaks in 7-octen-2-one (IIIa) correspond to the *m/e* 85 and 113 peaks in 2-octanone

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[1] For preceding paper, see J. P. Morizur and C. Djerassi, *Org. Mass. Spectrom.*, **5**, 895 (1971).

[2] Financial assistance by the National Institutes of Health (Grants No. GM-06840 and AM-04257) is gratefully acknowledged.

[3] (a) Postdoctoral Fellow, 1970–1971; (b) Postdoctoral Fellow, 1969–1971

[4] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 3.

[5] F. W. McLafferty and T. Wachs, *J. Amer. Chem. Soc.*, **89**, 5043 (1967).

[6] A. Budzikiewicz, C. Fenselau, and C. Djerassi, *Tetrahedron*, **22**, 1391 (1966); H. Fritz, H. Budzikiewicz, and C. Djerassi, *Chem. Ber.*, **99**, 35 (1966).

[7] For work with related motives see: (a) S. Meyerson and J. McCollum, "Advances in Analytical Chemistry & Instrumentation," C. Reilley, Ed., Interscience, New York, N. Y., 1963, Chapter 4; (b) G. Remberg and G. Spiteller, *Chem. Ber.*, **103**, 3640 (1970); (c) U. Bhalerao and H. Rapoport, *J. Amer. Chem. Soc.*, **93**, 105 (1971).

[8] A. M. Duffield, A. V. Robertson, C. Djerassi, B. G. Buchanan, G. L. Sutherland, E. A. Feigenbaum, and J. Lederberg, *ibid.*, **91**, 2977 (1969); R. Venkataraghavan, F. W. McLafferty, and G. E. Van Lear, *Org. Mass Spectrom.*, **2**, 1 (1969); A. Buchs, A. B. Delfino, A. M. Duffield, C. Djerassi, B. G. Buchanan, E. A. Feigenbaum, and J. Lederberg, *Helv. Chim. Acta*, **53**, 1394 (1970).

[9] T. Wachs and F. W. McLafferty, *J. Amer. Chem. Soc.*, **89**, 5044 (1967); R. J. Highet and P. F. Highet, *Tetrahedron Lett.*, 1803 (1970).

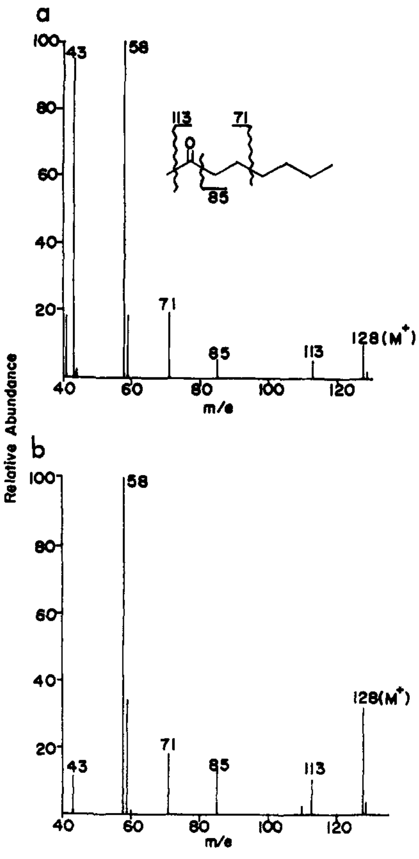


Figure 1. Mass spectrum of 2-octanone: (a) 70 eV; (b) 12 eV.

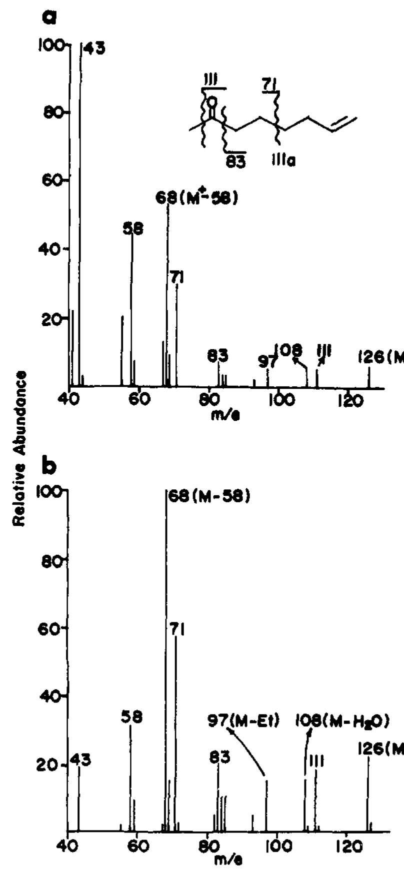


Figure 2. Mass spectrum of 7-octen-2-one: (a) 70 eV; (b) 12 eV.

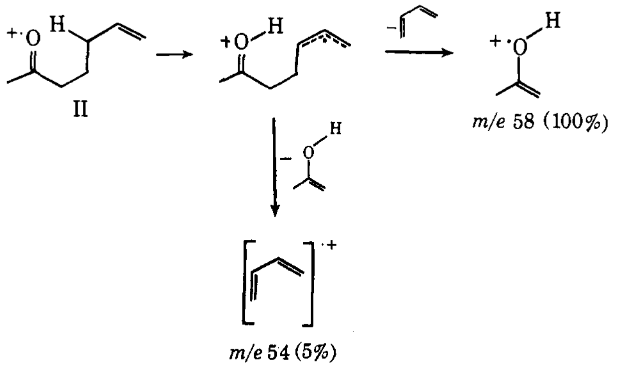
and result from simple cleavage around the carbonyl group. Analogs of the *m/e* 97 and 108 peaks in 7-octen-2-one (IIIa) do not exist in the spectrum (Figure 1) of 2-octanone and formally correspond to the loss of ethyl and water, respectively. In going from 70 (Figure 1a) to 12 eV (Figure 1b), 2-octanone shows little change other than appreciable reduction of the high-energy cleavage fragments of mass 41 and 43; but in 7-octen-2-one (IIIa) the *m/e* 68 and 71 peaks approximately double in intensity and the high-energy peak corresponding to the cyclopropylcarbinyl cation (*m/e* 55) vanishes.

Consider the homologous series of olefinic ketones Ia–VI (Table I). When a critical separation (four carbon atoms)[10] between the double bond and the carbonyl group is obtained as in IIIa, the M − 58 (C_5H_8) peak becomes more dominant than its *m/e* 58 (C_3H_6O) counterpart. Furthermore, in the low-voltage spectra of IIIa (Figure 2b) and its higher homologs (IV–VI), the M − 58 peak becomes the most intense one and the ratio of M − 58 to *m/e* 58 decreases from a value of 3.5 in IIIa to a value of 1.1 in VI; this decline is somewhat more dramatic in the 70-eV spectra where this ratio is 1.0 in IIIa and 0.1 in VI. Thus, charge retention among the two products of the McLafferty rearrangement is a function of the distance separating the double bond and the carbonyl group.

Discussion

A Fragmentation Process Complementary to the McLafferty Rearrangement. The mass spectrum of I does not contain the M − 58 (*m/e* 40) or *m/e* 58 peaks because cleavage of the vinylic γ proton is not a favorable process.[11] Since a McLafferty rearrangement shows a preference for abstraction of a tertiary proton over a secondary proton which in turn is preferred over a primary one,[6] it might be speculated that the low-voltage spectrum of II (Table I) fails to exhibit an appreciable M − 58 (*m/e* 54) peak because the allylic γ-proton results (see Scheme I) in an enhanced McLafferty rearrangement (II → *m/e* 58). However, examination of the high- and low-voltage spectra (Table I) of 6-octen-2-one (IX), which also possesses a γ proton, unequivocally excludes this possibility by displaying its base peak at *m/e* 68 (M − 58). The weak M − 58 (*m/e* 54) peak in the spectrum of II would seem to imply that product stability control was not an impor-

Scheme I



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(10) For a further example of a minimum chain length requirement in styryl ketones see: C. Fenselau, A. Baum, and D. Cowans, *Org. Mass Spectrom.*, 4, 229 (1970).

(11) Reference 4, p 10.

Table I. Partial Spectra of Nonconjugated Olefinic Carbonyl Compounds

	M⁺		M − 58		m/e 58		M − 18		M − 19	m/e 71	
Olefinic ketone	70 eV	12 eV	70 eV	12 eV	70 eV	12 eV	70 eV	12 eV	12 eV	70 eV	12 eV
Ia, $CH_2{=}CH(CH_2)_2COCH_3$	98 (4)	(12)	40 (0)	(0)	(0)	(0)	(0)	(0)		(0)	(0)
b, $CH_2{=}CHCH_2CD_2COCD_3$ (86% d_5)	103 (2)	(21)	40 (0)	(0)	63 (0)	(0)	(0)	(0)		(0)	
II, $CH_2{=}CH(CH_2)_3COCH_3$	112 (5)	(43)	54 (8)	(5)	(49)	(100)	(3)	(29)		(4)	(11)
IIIa, $CH_2{=}CH(CH_2)_4COCH_3$	126 (5)	(20)	68 (42)	(100)	(42)	(29)	(4)	(16)		(30)	(57)
b, $CH_2{=}CH(CH_2)_3CD_2COCD_3$ (90% d_5)	131 (2)	(21)	68 (44)	(100)	63 (34)	(18)	(3)	(25)	(4)^{b}	75 (12)	(29)
c, $CH_2{=}CHCD_2(CH_2)COCH_3$ (97% d_2)	128 (2)	(17)	70 (23)	(100)	(40)	(42)	(2)	(13)	(5)	75 (21)	(76)
d, $CD_2{=}CH(CH_2)_4COCH_3$ (95% d_2)	128 (1)	(10)	70 (30)	(100)	(37)	(32)	(2)	(11)	(0)	(21)	(52)
IVa, $CH_2{=}CH(CH_2)_5COCH_3$	140 (2)	(8)	82 (29)	(100)	(60)	(57)	(2)	(12)		(34)	(73)
b,^{a} $CH_2{=}CH(CH_2)_4CD_2COCD_3$ (91% d_5)	145 (2)	(20)	82 (14), 83 (11)	(81), (69)	63 (50)	(50)	(3)	(12)	(2)^{b}	75 (21)	(100)
c, $CH_2{=}CHCD_2(CH_2)_4COCH_3$ (90% d_2)	142 (1)	(19)	83 (9), 84 (15)	(70), (100)	(57)	(50)	(1)	(21)	(9)	(14)	(93)
d, $CH_2{=}CHCD_2(CH_2)_3CD_2COCD_3$ (80% d_7)	147 (1)	(14)	84 (11)	(100)	63 (53)	(63)	(1)	(23)	(9)^{b}	75 (14)	(66)
V, $CH_2{=}CH(CH_2)_6COCH_3$	154 (2)	(10)	96 (14)	(100)	(72)	(43)	(1)	(15)		(29)	(47)
VI, $CH_2{=}CH(CH_2)_8COCH_3$	182 (2)	(22)	124 (9)	(100)	(90)	(90)	(1)	(24)		(37)	(70)
VII,^{a} $CH_2{=}CH(CH_2)_3C(CH_3)_2(CH_2)_4COCH_3$	210 (<1)	(1)	152 (2)	(11)	(34)	(27)	(0)	(0)		(42)	(22)
VIII, $CH_3CH{=}CH(CH_2)_2COCH_3$	112 (15)	(100)	54 (2)	(0)	(11)	(14)	(7)	(43)		(2)	(1)
IX, $CH_3CH{=}CH(CH_2)_3COCH_3$	126 (7)	(30)	68 (100)	(100)	(30)	(10)	(8)	(23)		(10)	(13)
Xa, $CH_3(CH_2)_2CH{=}CH(CH_2)_2COCH_3$	140 (6)	(31)	82 (32)	(100)	(5)	(4)	(1)	(6)		(10)	(22)
b, $CH_3CH_2CD_2CH{=}CH(CH_2)_2COCH_3$ (98% d_2)	142 (5)	(88)	83 (17), 84 (10)	(100), (96)	(4)	(8)	(1)	(16)		(5)	(50)
XI, $CH_3CH_2CH{=}CH(CH_2)_4COCH_3$	154 (4)	(23)	96 (24)	(100)	(22)	(15)	(3)	(24)		(59)	(89)
XII, $CH_2{=}CHCH_2CH(CH_3)CH_2COCH_3$	126 (2)	(13)	68 (39)	(100)	(12)	(8)	(3)	(25)		85 (2)	(5)
XIII, $CH_2{=}CHCH(CH_3)(CH_2)_3COCH_3$	140 (2)	(6)	82 (54)	(100)	(31)	(6)	(6)	(21)		(19)	(17)
XIV, $(CH_3)_2C{=}CH(CH_2)_2CH(CH_3)CH_2COCH_3$	168 (7)	(29)	110 (42)	(100)	(10)	(1)	(3)	(12)		85 (35)	85 (23)

	M⁺		M − 60		m/e 60		m/e 73	
Olefinic carboxylic acid	70 eV	12 eV	70 eV	12 eV	70 eV	12 eV	70 eV	12 eV
XV, $CH_2{=}CH(CH_2)_5CO_2H$	142 (1)	(5)	82 (69)	(100)	(48)	(17)	(22)	(16)
XVI, $CH_2{=}CH(CH_2)_6CO_2H$	156 (1)	(6)	96 (35)	(100)	(42)	(40)	(29)	(50)
XVII, $CH_2{=}CH(CH_2)_8CO_2H$	184 (1)	(5)	124 (14)	(82)	(28)	(18)	(25)	(32)
XVIII, $CH_3CH{=}CH(CH_2)_2CO_2H$	114 (63)	(100)	54 (11)	(0)	(57)	(5)	(18)	(7)
XIX, $CH_3CH{=}CH(CH_2)_3CO_2H$	128 (10)	(38)	68 (100)	(48)	(33)	(4)	(8)	(4)
XX, $CH_3CH_2CH{=}CH(CH_2)_2CO_2H$	128 (9)	(25)	68 (100)	(28)	(29)	(1)	(6)	(2)

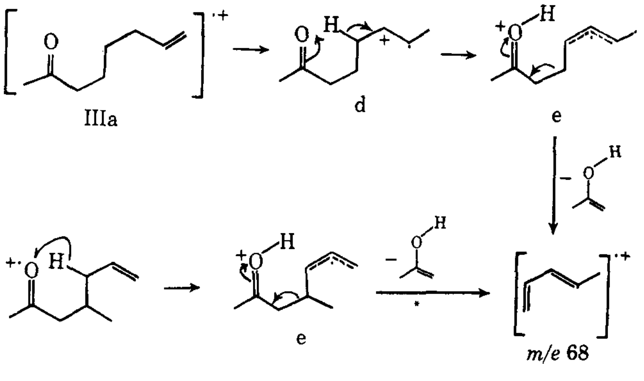
	M⁺		M − 88		m/e 88		m/e 101	
Olefinic Ester	70 eV	12 eV	70 eV	12 eV	70 eV	12 eV	70 eV	12 eV
XXI, $CH_2{=}CH(CH_2)_4CO_2Et$	156 (6)	(15)	68 (80)	(24)	(100)	(62)	(16)	(12)
XXII, $CH_2{=}CH(CH_2)_5CO_2Et$	170 (2)	(4)	82 (55)	(50)	(93)	(85)	(31)	(30)
XXIII, $CH_2{=}CH(CH_2)_6CO_2Et$	184 (2)	(7)	96 (48)	(49)	(100)	(42)	(39)	(25)
XXIV, $CH_2{=}CH(CH_2)_8CO_2Et$	212 (1)	(3)	124 (28)	(59)	(100)	(100)	(44)	(45)
XXV, $CH_2{=}CH(CH_2)_3C(CH_3)_2CH_2CO_2Et$	198 (1)	(1)	110 (66)	(100)	(73)	(56)	129 (22)	(19)
XXVI, $(CH_3)_2C{=}CH(CH_2)CH(CH_3)CH_2CO_2Et$	198 (6)	(13)	110 (45)	(28)	(25)	(6)	115 (9)	(1)

[a] Base peak at 12 eV is at mass 123. [b] Approximately 50% M − H_2O and 50% M − CD_3.

tant factor since this ion would be the only diene of this series with assured conjugation (Scheme I). However this interpretation is negated by the spectrum (Table I) of its branched analog XII which gives (Scheme II) a base peak at *m/e* 68 (M − 58). Apparently, II does not exhibit a significant M − 58 peak because the appearance potential of the unsubstituted butadiene (*m/e* 54) in Scheme I is sufficiently higher than that of the substituted diene corresponding to *m/e* 68 in Scheme II.[12] Thus, the governing factor for this inverse charge retention is product stability[13] with the minimum chain length requirement being determined by IP of the dissociated products rather than the ability of one functional group to coil back on the other as observed in other systems.[10]

A mechanism for this complementary McLafferty rearrangement, which is in accord with the data obtained, is illustrated with IIIa (Figure 2) in Scheme II. Isomerization of the double bond after ionization

Scheme II



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(12) This conclusion follows from a comparison of the ionization potentials of the compounds shown below ("Ionization Potentials, Appearance Potentials, Heats of Formation of Gaseous Positive Ions," NSRDS-NBS 26, U. S. Government Printing Office, Washington, D. C., 1969): $CH_2{=}CHCH_3$, 9.8 eV; $PrCOCH_3$, 9.4 eV; $CH_3CH{=}CHCH_3$, 9.2 eV; $CH_2{=}CHCH{=}CH_2$, 9.1 eV; $CH_2{=}C(CH_3)CH{=}CH_2$, 8.9 eV.

(13) This identical rationale was proposed in ref 7a, pp 187, 189, and 198 for the M − 74 peak observed in a limited number of nonconjugated methyl olefinic esters.

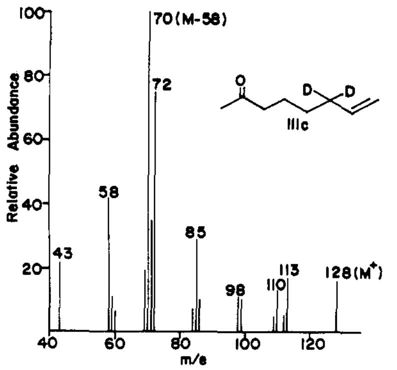

Figure 3. Mass spectrum of 7-octen-2-one-*6,6-d_2* (12 eV).

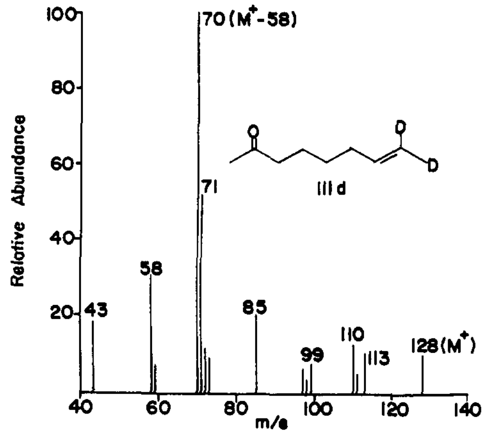

Figure 4. Mass spectrum of 7-octen-2-one-*8,8-d_2* (12 eV).

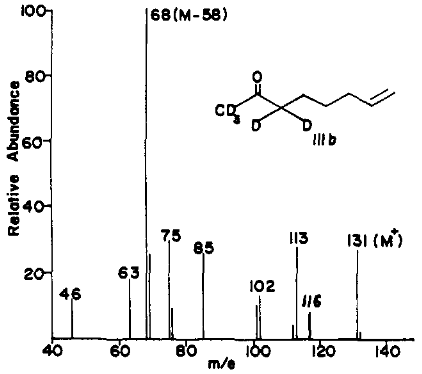

Figure 5. Mass spectrum of 7-octen-2-one-*1,1,1,3,3-d_5* (12 eV).

by 1,3-hydrogen shift in IIIa can lead to the more stable disubstituted olefin ion d. Though the charge may be localized initially on the oxygen of the molecular ion IIIa, 1,3-hydrogen shift is probably a process of low-charge density requirement.[14] Subsequent to isomerization, proton abstraction from the activated "acidic" position in ion d *via* the favorable six-membered transition state gives the allylic radical ion e, acquiring additional stabilization.[15] Expulsion of the neutral enol of acetone then affords the ionized diene of mass 68. Deuterium labeling in the allyl (IIIc, Figure 3) and terminal vinyl (IIId, Figure 4) positions of IIIa results in the expected shift from *m/e* 68 to 70,

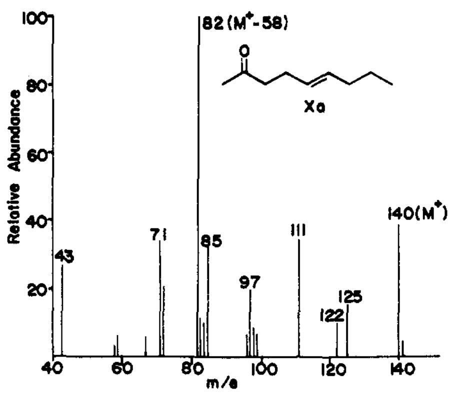

Figure 6. Mass spectrum of 5-nonen-2-one (12 eV).

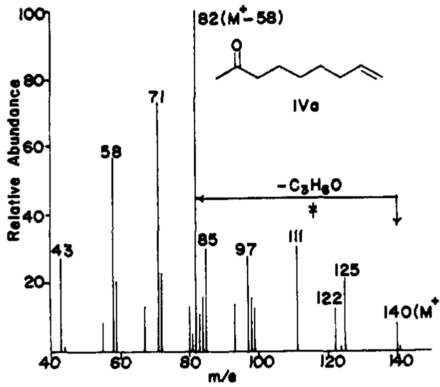

Figure 7. Mass spectrum of 8-nonen-2-one (12 eV).

whereas the *m/e* 68 peak remained unchanged when all the hydrogens α to the carbonyl were exchanged by deuterium (IIIb, Figure 5). These results establish that only a β or γ hydrogen is incorporated in the departing acetone molecule. Support that the *m/e* 68 (M − 58) peak is derived from the molecular ion (*m/e* 126) was provided by the metastable defocusing technique.[16]

Since the *m/e* 58 and M − 58 ions both emanate directly from the molecular ion, the ratio of the intensities of the M − 58 to *m/e* 58 peaks should be approximately comparable among related olefinic ketones run under similar conditions, especially in spectra obtained at low ionizing voltages where the high-energy processes are suppressed. In this regard, it is worthwhile to consider the differences reflected in the ratio of the M − 58 to *m/e* 58 peaks observed for the analogs in Table I.

The mechanism of Scheme II is further substantiated by the electron impact promoted fragmentation of the isomeric ketones Xa and IVa (Figures 6 and 7). The ratio of *m/e* 82 (M − 58) to *m/e* 58 in IVa and Xa at 12 eV is 1.7 and 25, respectively, and indicates that most of the normal McLafferty rearrangement product (IVa → *m/e* 58 in Scheme III) is produced before the double bond migrates from the terminal position in IVa. Once it has migrated to a more highly substituted position (g, f) the charge is mainly localized on the substituted double bond of lower IP (*e.g.*, g and f). The intermediacy of ion f in the production of the ionized diene fragment of mass 82 is supported by the

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(14) W. Vetter, W. Meister, and W. J. Richter, *Org. Mass Spectrom.*, 3, 777 (1970).

(15) Other mechanistic interpretations are possible, but we find this one most convenient.

(16) M. Barber and R. Elliot, 12th Annual Conference on Mass Spectrometry, Montreal, Canada, ASTM-E-14, 1964; K. R. Jennings, *J. Chem. Phys.*, 43, 4176 (1965).

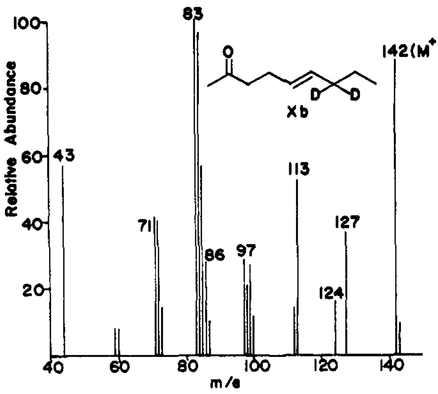


Figure 8. Mass spectrum of 5-nonen-2-one-*7,7*-d_2 (12 eV).

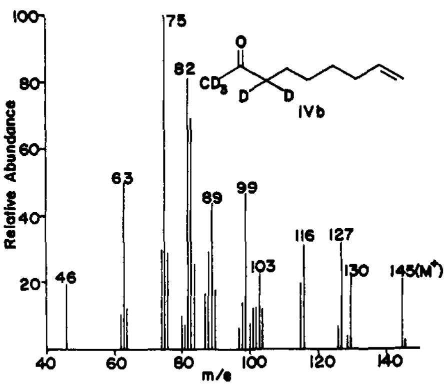


Figure 9. Mass spectrum of 8-nonen-2-one-*1,1,1,3,3*-d_5 (12 eV).

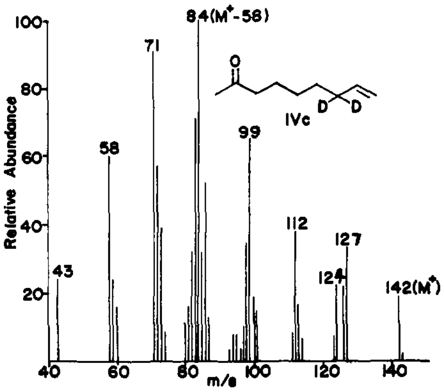
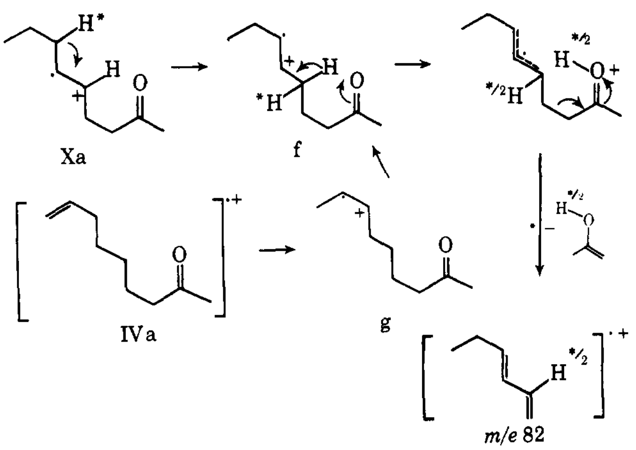


Figure 10. Mass spectrum of 8-nonen-2-one-7,7-d_2 (12 eV).

mass spectrum (Figure 8) of the labeled ketone Xb in which the *m/e* 82 peak was replaced by a 1:1 ratio of *m/e* 83 and 84 peaks.

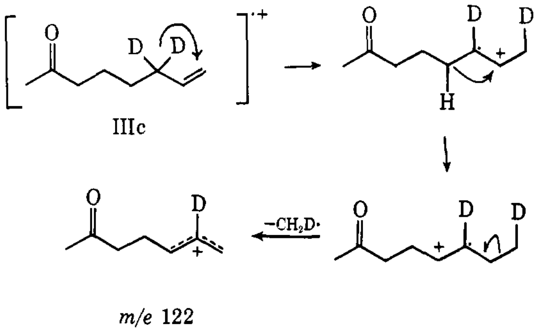
Scheme III



That double bond migration (intermediates d and f in Schemes II and III) to the δ,ε position is a necessary requirement for manifestation of the loss of the elements of acetone with charge retention on the diene moiety was corroborated further by the reduction of this process (see Table I) in the ketone VII in which the two geminal methyl substituents on position 7 retarded (*cf.* VI which lacks such a quaternary block) movement of the double bond beyond this point on the hydrocarbon chain.

Double bond migration was also made evident by the presence of M − 29 (ethyl loss) peaks in the low voltage spectra of II (8%), IIIa (15%), IVa (30%, as compared with 34% for X), V (25%), VI (3%), and IX (16%), and the presence of M − 16 (CH_2D loss) and M − 17 (CD_2H loss) peaks in the spectra IIIc or IVc and IIId, respectively, due to allylic cleavage. As expected the spectrum of I had no M − 29 peak.

The presence of M − 30 (loss of C_2H_4D) peaks in the spectra (Figures 5, 9, 8) of IIIb, IVb, Xb, and M − 29 as well as M − 30 or M − 31 peaks in the spectra (Figures 3, 10, 4) of IIIc, IVc, or IIId, respectively, shows that there is another concomitant process involving skeletal rearrangement by which ethyl loss was occurring. The decline in the ratio of M − 58 to *m/e* 58 observed in going from IIIa to VI (Table I) is due to the greater distance the terminal double bond must move before the favorable δ,ε position with respect to the carbonyl group is reached. Greater relative intensification of the M − 58 (ionized diene) peak at lower ionizing voltage is the result of more extensive hydrogen migration[17] leading to more facile



double bond movement. The M − 58 peak in the spectrum of IX was the most intense one at 70 as well as at 12 eV because no prior double bond movement was necessary before cleavage (compare with IIIa); *i.e.*, the double bond in IX already occupies the requisite δ,ε position. Since methyl substitution of the diene (see XII in Scheme II) should lower the IP of the diene fragment, one would expect that alkyl substituents on the β, γ, δ, or ε positions between the double bond and the carbonyl group would enhance the ratio of M − 58 to *m/e* 58.[7a] This is supported by the observed (Table I) ratios of 12 and 16 for XII and XIII, respectively, compared to 3.5 for IIIa.

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(17) A. Yeo, *Chem. Commun.*, 987 (1970), and leading references therein.

Table II. Composition of Principal (>80%) Ions Determined by Precise Mass Measurements

Ion	IIIa	IVa	XIII	Ion	XV	Ion	XXII
M^+	$C_8H_{14}O$	$C_9H_{16}O$	$C_9H_{16}O$	M^+	$C_8H_{14}O_2$	M^+	$C_{10}H_{18}O_2$
M − 15	$C_7H_{11}O$	$C_8H_{13}O$	$C_8H_{13}O$	M − H_2O	$C_8H_{12}O$	M − EtOH	$C_8H_{12}O$
M − 18	C_8H_{12}	C_9H_{14}	C_9H_{14}	M − C_3H_6	$C_5H_8O_2$	101	$C_6H_9O_2$
M − 29	$C_6H_9O_1$	$C_7H_{11}O$	$C_7H_{11}O$	96	C_6H_8O	96	C_6H_8O
M − 41	C_5H_9O	$C_6H_{11}O$	None	83	C_6H_{11}	88	$C_4H_8O_2$
M − 42	C_5H_8O	$C_6H_{10}O$	None	82	C_6H_{10}	82	C_6H_{10}
M − 43	C_6H_{11}	C_7H_{13}	C_7H_{13}	73	$C_3H_5O_2$	60	$C_2H_4O_2$
M − 44	C_6H_{10}	C_7H_{12}	None	67	C_5H_7	55	C_4H_7
M − 55	C_4H_7O	C_5H_9O	C_5H_9O	60	$C_2H_4O_2$		
M − 57	C_5H_9	C_6H_{11}	C_6H_{11}	55	C_4H_7		
M − 58	C_5H_8	C_6H_{10}	C_6H_{10}				
72	None	C_4H_8O	None				
71	C_4H_7O	C_4H_7O	C_4H_7O				
67	C_5H_7	C_5H_7	C_5H_7				
59	C_3H_7O	C_3H_7O	C_3H_7O				
58	C_3H_6O	C_3H_6O	C_3H_6O				
Misc		84, C_5H_8O 55, C_4H_7	70, C_5H_{10}				

Nonconjugated carboxylic acids and ethyl esters[18] (Table I) exhibit prominent peaks located at M − 60 (loss of $C_2H_4O_2$) (Figure 11 and Table II) and M − 88 ($C_4H_8O_2$ loss) (Figure 12 and Table II) respectively, which again correspond to the ionized diene portions of the McLafferty rearrangement. The M − 88 ions of the olefinic ethyl esters, though abundant, were weaker than the analogous diene ions of the olefinic acids and ketones. However, β-methyl substitution in XXV did enhance this cleavage as compared to its unsubstituted analog XII because of the lower ionization potential of the corresponding diene product. 4-Hexenoic acid (XVIII) gave no appreciable M − 60 peak, since the critical hydrocarbon length was only reached in 5-heptenoic acid (XIX). It is pertinent to note that whereas the 70-eV spectra of the isomeric heptenoic acid XIX and XX were identical, the 12-eV spectrum of XIX displayed an *m/e* 68 peak with approximately twice the relative abundance as that of XX because the former requires no double bond migration prior to cleavage.

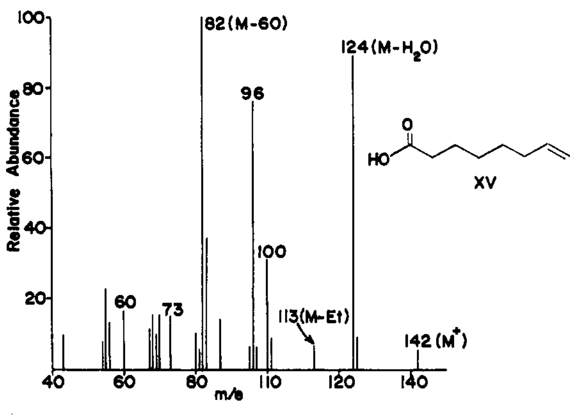

Figure 11. Mass spectrum of 7-octenoic acid (12 eV).

Loss of Water from the Molecular Ion. Inspection of Table I reveals that loss of water in ketones increases greatly at lower ionizing voltages. Furthermore, no water loss is noticeable in the saturated ketone 2-octanone (Figure 1) or in 5-hexen-2-one (I), but extension of the hydrocarbon chain by one carbon atom as in 6-hepten-2-one (II) results in a substantial elimination of water. These results demonstrate that the presence of a mobile (nonvinylic) γ-hydrogen atom is critical before a progression of hydrogen movements can be initiated leading to the eventual placement of two hydrogens on the carbonyl oxygen for final expulsion of water.

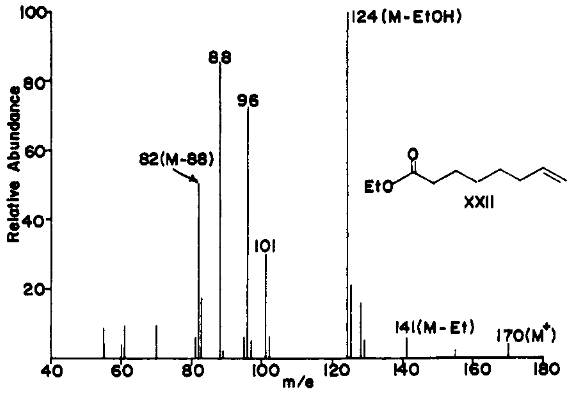

Figure 12. Mass spectrum of ethyl 7-octenoate (12 eV).

More information about this process was garnered from the mass spectra of the labeled ketones IIIb, IIIc, IIId, IVb, IVc, and IVd. Only water was expelled from the terminally deuterated IIId, and approximately 40% of the total water lost from IIIb, IIIc, and IVb, IVc, IVd was monodeuterated (M − 19). Thus, the main hydrogen donors in this process are β and γ positions. A possible mechanism consistent with these data is illustrated with 7-octen-2-one (IIIa) in Scheme IV and is based on the production of an ionized conjugated triene (*e.g.*, *m/e* 108 in Scheme IV). Generation of such a triene is impossible in saturated ketones as well as in the geminally substituted unsaturated ketone VII, which prevents double bond migration required for a conjugated system. These are precisely the ketones which show no water loss from M^+ even at low voltage.

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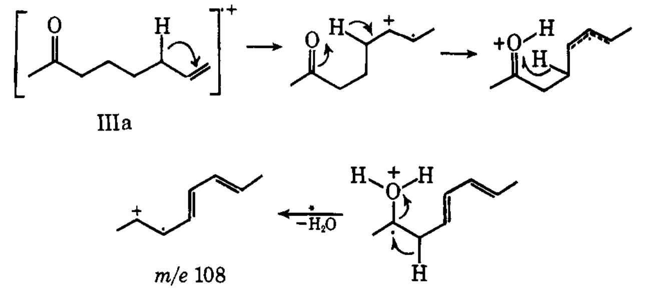
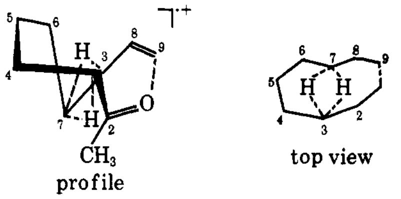
[18] For related work and pertinent spectra of unsaturated carboxylic esters see: W. Rohwedder, A. Mabouk, and E. Selke, *J. Phys. Chem.*, **69**, 1711 (1965); M. Hamming, *Arch. Mass Spectrom.*, **1**, 166 (1970); E. Von Sydow, K. Anjou,and G. Karlsson, *ibid.*, **2**, 63 (1971).

Scheme IV



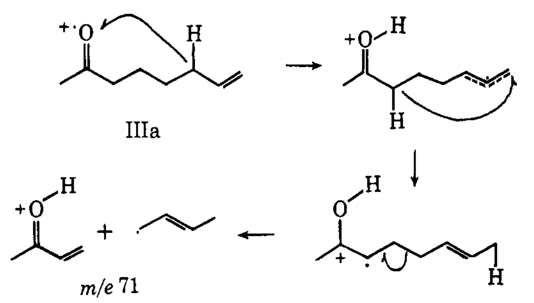
Facile Proton Exchange between Activated Positions. Deuterated analogs (IVb and IVc) of 8-nonen-2-one (IVa) gave complex spectra (Figures 9 and 10), particularly in the M − 58 region due to a facile proton exchange at the activated positions *via* a possible tricyclo[3.2.1.1] intermediate in which the π clouds may be held together as a charge-transfer complex.[19] Some involvement of protons at positions 4, 5, and 6 in this proton exchange must be inferred by the presence



of the moderately intense *m/e* 85 peak in the spectrum (Figure 13) of IVd.

***m/e* 71 Peak.** Comparison of the 12-eV spectra of 2-octanone and IIIa (Figures 1 and 2) shows that the *m/e* 71 peak is approximately two times as intense in the latter (Σ_{40} is 8 and 14%, respectively). That this ion of mass 71 (C_4H_7O) in IIIa and IVa originated by a reciprocal hydrogen transfer (Scheme V) similar to that observed in saturated ketones[20] was substantiated by deuterium labeling (*m/e* 71 → *m/e* 75 in IIIb, IVb, and IVf; *m/e* 71 → *m/e* 72 in IIIc).[10] It follows that an α hydrogen was lost and a δ hydrogen gained. The presence of a substantial *m/e* 72 peak (Figure 10) in IVc shows that some ϵ-allylic hydrogens are also capable of migration. Ketones II, VIII, and XII exhibit (Table I) hardly any *m/e* 71 peaks because of the unavailability of δ hydrogens which are not also vinylic. The weak peaks that are present emanate by direct cleavage.

Scheme V



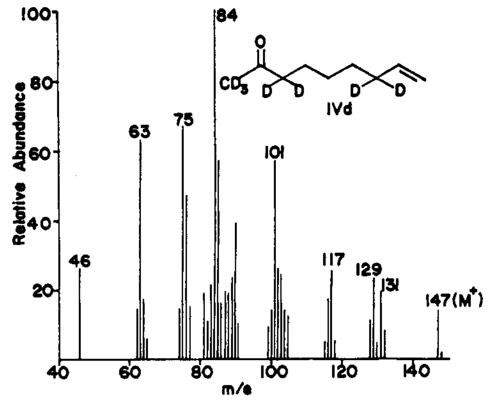
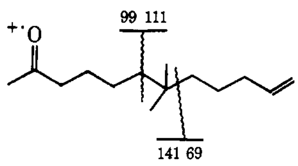


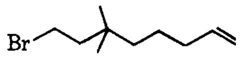
Figure 13. Mass spectrum of 8-nonen-2-one-*1,1,1,3,3,7,7-d*$_7$ (12 eV).

This counter hydrogen transfer is also operating in the olefinic esters (*m/e* 101, $C_5H_9O_2$) and acids (*m/e* 73, $C_3H_5O_2$) of Table I. As observed with the olefinic ketones, the *m/e* 73 peaks in acids XV–XVII are significantly larger than in XVIII–XX because in this group the δ hydrogens are vinylic.

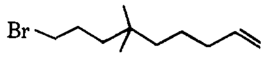
Cleavages Products Associated with Branching in VII. Branching in VII generates ions which have no counterparts in the spectrum of its analog VI. Prominent peaks associated with simple cleavage around the quaternary center were observed at *m/e* 69 (C_5H_9), 99 ($C_6H_{11}O$), 111 (C_8H_{15}), and 141 ($C_9H_{17}O$), and peaks for rearrangement ions were observed at *m/e* 83 (C_6H_{11}) and 123 (C_9H_{15}). Whereas the *m/e* 69 and 111 peaks were also prominent in the mass spectra of 3,3-dimethyl-1-bromo-7-octene (XXVII) and 4,4-dimethyl-1-bromo-8-nonene (XXVIII), only the latter possessed an *m/e* 83 peak of significant intensity. This observation and the existence of a metastable peak at *m/e* 48.8 (*m/e* 141 → *m/e* 83) suggest that Scheme VI may constitute a possible rationale for its genesis. The metastable peak observed at *m/e* 107.2 confirms the operation of the *m/e* 141 → *m/e* 123 sequence.[21]



IIIa



XXVIII



XXVII

***m/e* 70 Ion of XII.** The *m/e* 70 peak (C_5H_{10}) in XII has no counterpart in the spectra (Figures 2b and 7) of III or IV and is postulated to derive from a McLafferty rearrangement involving the double bond[22] after its initial migration to an adjacent, internal position, impetus for migration being provided by

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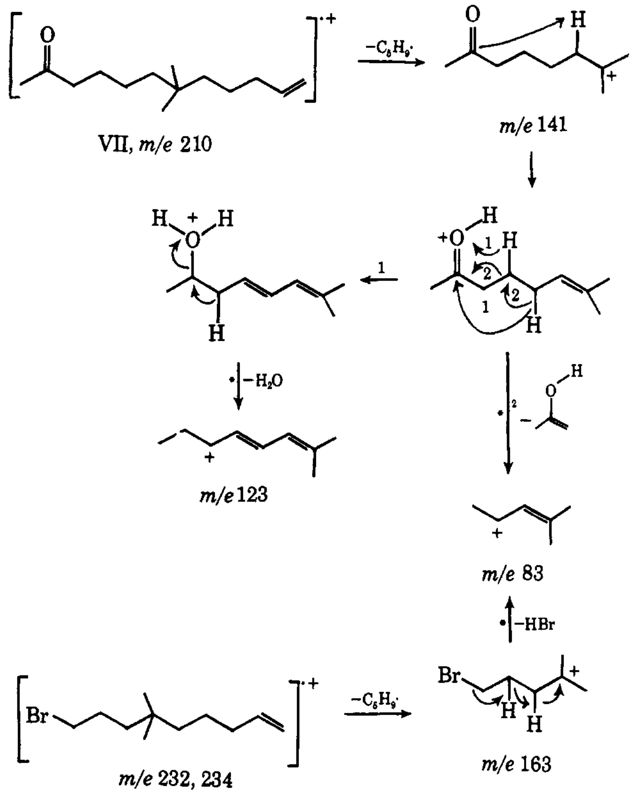
[19] For a similar exchange in *N-n*-(butyl-*3,3-d*$_2$)-pyrrole see A. M. Duffield, R. Beugelmans, H. Budzikiewicz, D. A. Lightner, D. H. Williams, and C. Djerassi, *J. Amer. Chem. Soc.*, **87**, 805 (1965); A. Yeo, *Chem. Commun.*, 1154 (1970).

[20] W. Carpenter, A. M. Duffield, and C. Djerassi, *J. Amer. Chem. Soc.*, **90**, 160 (1968).

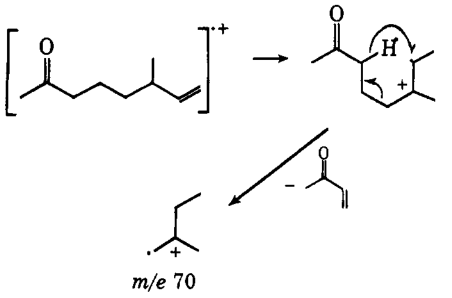
[21] For a discussion concerning the intense loss of water subsequent to α cleavage from ketones branched beyond the γ position, see: G. Eadon and C. Djerassi, *ibid.*, **92**, 3084 (1970).

[22] F. W. McLafferty, *Anal. Chem.*, **31**, 2072 (1959).

Scheme VI



increased stability of the more highly substituted double bond.



Conclusion

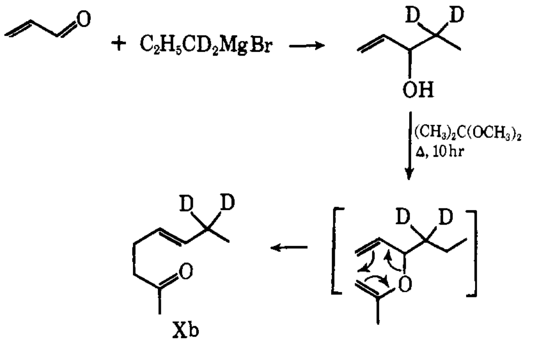
In general, α cleavage (m/e 43 and M − 15) of the methyl ketones was little affected by the presence of the double bond. The base peak in the 70-eV spectra of the olefinic ketones in Table I was located at m/e 43 (C_2H_3O), corresponding to severance of the larger alkyl branch; its greater reduction at lower ionizing voltage relative to the M − CH_3 peak proceeded in accord with earlier observations[23] among saturated ketones. The presence of a mobile double bond in the aliphatic ketones resulted in a McLafferty rearrangement with inverse charge retention which prevailed over the ordinary McLafferty rearrangement until the distance (number of intervening methylenes) between these functional groups became sufficiently great so as to preclude the double bond from reaching the δ,ϵ position within a reasonable time period.

It has been observed[17] that hydrogen migration occurs more extensively at lower ionizing voltages than at higher ones. These results suggest with other factors being equal that processes which require double bond migrations or hydrogen transfers should become relatively more important in going from high- to low-voltage spectra than similar processes that do not. The enhancement of the M − 58 and M − 18 ions with decreasing ionizing voltage observed in our study is in agreement with this generalization.

Synthesis of Labeled Ketones

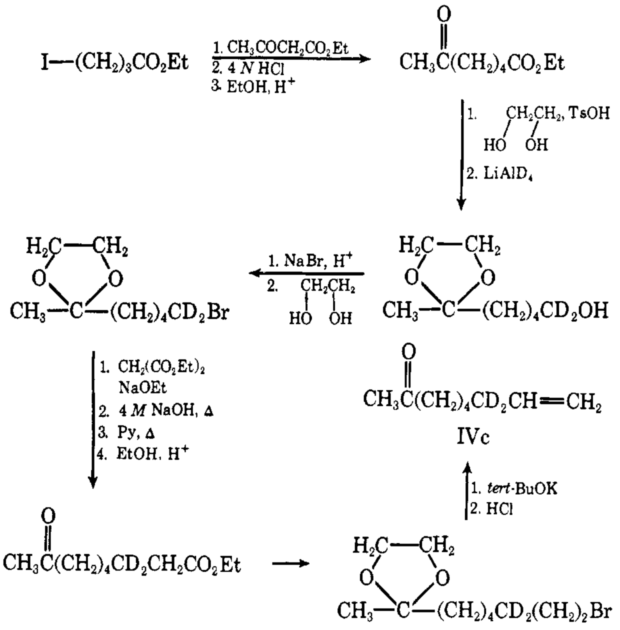
Synthetic Schemes VII and VIII typify the syntheses employed in this work.

Scheme VII



Xb

Scheme VIII



Experimental Section

The mass spectra were obtained by Mr. R. G. Ross using an AEI MS-9 double focusing mass spectrometer (heated inlet 150°, ion source temperature 180°). Metastable transitions in the first field free region were observed with the aid of the metastable defocusing technique.[16] All spectral measurements were performed on substances which were purified by vpc (5 ft × $^1/_4$ in. SE-30, on Chromosorb G; 5 ft × $^1/_4$ in. Carbowax 20M, 15% on Chromosorb P).

Infrared spectral data were recorded with a Perkin-Elmer Model 700 spectrophotometer, and nmr spectra were obtained with a Varian Model T-60 spectrometer (60 MHz). All infrared spectra were made neat or in $CHCl_3$ solution with matched cells, and nmr measurements were made neat or in $CDCl_3$ solutions using 1% TMS as an internal standard. Infrared absorptions are given in Kaysers (K = cm^{-1}), and chemical shifts are reported in δ (parts per million).

All d_5 compounds were prepared by equilibration (24-hr reflux followed by vigorous room temperature stirring for 3 days) of approximately 0.4 g of parent ketone with 15 ml of heavy water and 5 ml of dry tetrahydrofuran to which 0.2 g of anhydrous sodium carbonate was added. The product was recovered by extraction

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[23] W. Carpenter, A. M. Duffield, and C. Djerassi, *J. Amer. Chem. Soc.*, **89**, 6167 (1967).

with ether, and the concentrated oil was purified by vapor phase chromatography through a column preequilibrated with heavy water. The characteristic nmr triplet at δ 2.2 (t, α protons) and singlet at 2.1 (acetyl methyl) were absent. The ketones not available commercially were made by the acetoacetic ester synthesis from the appropriate bromide followed by saponification and decarboxylation by vigorously stirring with 3 equiv of 1.4 *M* sodium hydroxide solution at room temperature for 10–15 hr and steam distillation. The appropriate bromides were either obtained from commercial sources or made from available olefinic alcohols with pyridine and phosphorous tribromide.[24] The vinyl olefins exhibited the spectral features expected: λ_{max} 1640, 990, and 905 K; nmr 5.7 (m, 1p), 5.0 (d, 1p, J = 17 Hz), and 4.9 (d, 1p, J = 10 Hz). All internal double bonds were trans: λ_{max} 970 K; nmr 5.4 (peak, 2p).

7-Octen-2-one-*6,6*-d_2 (IIIc). The alkylation product of ethyl acetoacetate and ethyl 3-bromopropanoate was heated under reflux with 3 equiv of 4 *N* hydrochloric acid for 5 hr. The isolated crude acid was esterified by heating for 2 hr with absolute ethanol containing sulfuric acid as a catalyst. Distillation of the isolated crude ester gave a 65% yield of ethyl 5-oxohexanoate: bp 123–127° (35 Torr); λ_{max} 1730 (broad); nmr 4.1 (q, 2p), 2.2 (m, 4p), 2.1 (s, 3p), 1.5 (m, 2p), and 1.3 (t, 3p); mass spectrum *m/e* 158 (5%, M$^+$ = $C_8H_{14}O_3$), 112 (100%, M = EtOH).

The keto ester was heated under reflux with an equivalent amount of ethylene glycol in benzene containing a catalytic quantity of *p*-toluenesulfonic acid using a Dean–Stark water separator. The ketal ester was added to lithium aluminum deuteride in ether and stirred overnight at room temperature before decomposing with a minimum amount of ice water; the ether phase was separated from the white paste which was subsequently washed well with more ether and the combined ether phases were concentrated. The residue of hydroxy ketal was combined with sodium bromide (4 equiv) and 40% sulfuric acid and heated under reflux for 4 hr before steam distilling out the product of 6-bromo-2-hexanone-*6,6*-d_2 in 85% yield (based on keto ester): λ_{max} 1705 and 2150 (wk); nmr 2.4 (t, 2p), 2.1 (s, 3p), 1.8 (m, 2p), and 1.4 (m, 2p); mass spectrum *m/e* 101 (22%, M$^+$ − Br), 58 (1%), 43 (100%).

The bromo ketone was converted to the ketal and allowed to react with the sodium salt of diethylmalonate which was saponified by refluxing with 4 *M* sodium hydroxide solution for 6 hr. The isolated diacid was decarboxylated by heating in pyridine for 1 hr, and the monoacid was esterified with ethanol to finally give a 42% yield of ethyl 7-oxooctanoate-*3,3*-d_2: bp 136–138° (20 Torr); λ_{max} 2200 (wk) and 1730. Octanone-*6,6*-d_2 was made from this keto ester by repetition of previous steps: bp 124–126° (25 Torr); λ_{max} 2200 (wk doublet) and 1710; nmr 3.2 (t, 2p), 2.2 (t, 2p), 2.1 (s, 3p), 1.8 (m, 2p), and 1.4 (m, 4p); mass spectrum *m/e* 129 (15%, M − Br), 58 (100%), 43 (77%).

The corresponding ketal was dehydrobrominated with freshly prepared potassium *tert*-butoxide in refluxing toluene for 45 hr; removal of the excess toluene by fractional distillation and acidifying the residue with diluted sulfuric acid followed by steam distillation gave a 70% yield of IIIc.

7-Octen-2-one-*8,8*-d_2 (IIId). This ketone was synthesized as described for IIIc but the order of reduction of the keto ester intermediates with $LiAlD_4$ and $LiAlH_4$ was reversed.

8-Nonen-2-one-*7,7*-d_2 (IVc). Ethyl 4-iodobutanoate was transformed into IVc exactly as was described for the conversion of ethyl 3-bromopropanoate into IIIc: ethyl 6-oxoheptanoate, bp 92–93° (15 Torr); λ_{max} 1730 (broad); mass spectrum *m/e* 172 (5%, M$^+$ = $C_9H_{16}O_3$), 115 (32%, M − 57), 43 (100%); 7-bromo-2-heptanone-*7,7*-d_2, bp 140–143° (50 Torr); λ_{max} 2200 (wk) and 1710; nmr 4.1 (q, 2p), 2.4 (m, 4p), 2.1 (s, 3p), 1.8 (m, 2p), and 1.2 (t, 3p); mass spectrum *m/e* 115 (16%, M$^+$ − Br), 58 (98%), 43 (100%); ethyl 8-oxononanoate-*3,3*-d_2, bp 165–168° (45 Torr); λ_{max} 2200 (wk doublet) and 1730 (broad); nmr 4.1 (q, 2p), 2.4 (t, 2p), 2.3 (s, 2p), 2.1 (s, 3p), 1.3 (m, 6p), and 1.2 (t, 3p); mass spectrum *m/e* 202 (1%, M$^+$ = $C_{11}H_{18}O_3D_2$), 145 (67%, M − 57), 43 (100%); 9-bromo-2-nonanone-*7,7*-d_2, bp 166–168° (45 Torr); λ_{max} 2200 (wk doublet) and 1710; mass spectrum *m/e* 143 (1.0%, M − Br), 58 (100%), 43 (66%).

11-Dodecen-2-one (VI). Dimethylcadmium was treated with the acid chloride of 10-undecenoic acid to give VI.

7,7-Dimethyl-11-dodecen-2-one (VII). 2-(2-Methyl-6-heptenyl)-malonic acid was prepared from 1-bromo-4-pentene and diethyl isopropylidenemalonate[25] and decarboxylated in refluxing pyridine to give a 70% yield of 3,3-dimethyl-7-octenoic acid which was converted to the ethyl ester with triethyl orthoformate: bp 121–123° (35 Torr); λ_{max} 1725, 1640, 995, and 915; nmr δ 5.7 (m, 1p), 5.0 (d, J = 18 Hz, 1p), 4.9 (d, J = 11 Hz, 1p), 4.1 (q, 2p), 2.1 (s, 2p), 1.9 (m, 2p), 1.3 (m, 4p), 1.1 (t, 3p), and 1.0 (s, 6p); mass spectrum 198 (1%, M$^+$ = $C_{12}H_{22}O_2$), 183 (5%, M − CH_3), 153 (16%, M − OEt), 110 (66%), 88 (73%), 69 (100%). Reduction with lithium aluminum hydride and treatment of the alcohol with phosphorus tribromide in pyridine yielded 3,3-dimethyl-1-bromo-7-octene (XXVII): bp 66–69° (20 Torr); λ_{max} 1640, 995, and 915; mass spectrum *m/e* 111 (18%, M − C_2H_4Br), 69 (100%). Carbonation of the Grignard reagent generated from this halide yielded 4,4-dimethyl-8-nonenoic acid (λ_{max} 3200 (broad), 1705, 1640, 1000, and 915; mass spectrum *m/e* 184 (1%, M$^+$ = $C_{11}H_{20}O_2$), 115 (50%), 97 (52%), 69 (100%)) which was reduced with $LiAlH_4$, the resulting alcohol transformed into 4,4-dimethyl-1-bromo-8-nonene (XXVIII) (λ_{max} 1640, 1000, and 915; mass spectrum *m/e* 111 (43%, M$^+$ − C_3H_6Br), 83 (65%), 69 (100%)) and then converted with ethyl acetoacetate and base treatment into 7,7-dimethyl-11-dodecen-2-one (VII): λ_{max} 1710, 1640, 1000, and 915; nmr 5.7 (m, 1p), 5.0 (d, J = 18 Hz, 1p), 4.9 (d, J = 11 Hz, 1p), 2.4 (t, 2p), 2.1 (s, 3p), 1.9 (m, 2p), 1.2 (m, 10p), and 0.9 (s, 6p); mass spectrum *m/e* 210 (1%, M$^+$ = $C_{14}H_{26}O$), 141 (10%), 123 (55%), 111 (17%), 83 (55%), 71 (40%), 69 (100%), 59 (43%), 58 (33%), 55 (68%), 43 (98%).

Anal. Calcd for $C_{14}H_{26}O$: C, 79.93; H, 12.46; O, 7.61. Found: C, 80.21; H, 12.26; O, 7.53.

5-Nonen-2-one-*7,7*-d_2 (Xb). The Grignard reagent of 1-bromopropane-*1,1*-d_2[26] was treated with acrolein in ether to give a 82% yield of 1-hexen-3-ol-*4,4*-d_2. This alcohol was combined with 10 equiv of acetone dimethyl acetal and 1 equiv of 2,4-dinitrophenol and diluted with twice its volume of toluene. After heating this mixture under mild reflux for 8–12 hr the reaction mixture was cooled, diluted with ether, extracted with 2 *M* sodium hydroxide solution, dried, and concentrated to yield 60% 5-nonen-2-one-*7,7*-d_2 (Xb): λ_{max} 220 (wk), 1710, and 970; mass spectrum *m/e* 142 (5%, M$^+$ = $C_9H_{14}OD_2$), 43 (100%).

4,9-Dimethyl-7-nonen-2-one (XIV). Citronelloic acid was converted into its acid chloride with thionyl chloride followed by reaction with dimethylcadmium to yield XIV: bp 120–124° (30 Torr); λ_{max} 1710; nmr 5.1 (crude t, 1p), 2.3 (m), 2.1 (s, 3p), 1.9 (m), 1.7 (s, 3p), 1.6 (s, 3p), 1.3 (m), and 0.9 (d, 3p); mass spectrum *m/e* 168 (7%, M$^+$), 43 (100%).

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