than 30°. During the addition of the aldehyde, the solution turned deep lemon yellow. After the addition was complete, the solution was stirred at room temperature for 20 min after which 100 ml of water was added. The resultant mixture was extracted with ether, the ether solution was dried, and the solvent was evaporated. The crude esters were distilled to yield 6.84 g (67%) of material [bp 88–92° (0.55 mm)] which was mainly a 1:1 mixture of the two title compounds.

The isomers were separated by gas–liquid partition chromatography (glpc) using an Autoprep A-700 chromatograph equipped with a 20 ft × $^3/_8$ in. aluminum column charged with 30% SE-30-coated firebrick. The temperature of separation was 175° at *ca.* 200-cc/min helium flow rate. The nmr spectrum of the Δ^2 ester shows a singlet at δ 7.13 (aromatics), a complex multiplet at δ 6.91 (vinyl proton), a quartet at δ 4.08 ($\mathrm{O}\mathit{CH}_2\mathrm{CH}_3$), a multiplet at δ 3.38 ($\mathrm{Ar}\mathit{CH}_2\mathrm{CH}{=}$), a multiplet at δ 1.88 ($-\mathrm{HC}{=}\mathrm{C}(\mathit{CH}_3)\mathrm{CO_2Et}$), and a triplet at δ 1.12 ($\mathrm{OCH_2}\mathit{CH}_3$). The coupling constant between the vinyl hydrogen and the allylic methyl was 1.4 cps. The coupling constant between the benzylic methylene and the allylic methyl was 1.6 cps. These data, along with the value of the coupling constant between the benzylic methylene and vinyl proton (7.8 cps), indicate that the double bond is *trans* with relation to the vinyl hydrogen and allylic methyl.[25]

Anal. Calcd for $C_{13}H_{16}O_2$; C, 76.44; H, 7.90. Found: C, 76.17; H, 8.02.

The nmr spectrum of the Δ^3 ester had a multiplet at δ 7.25 (aromatics), a multiplet at δ 6.30 (vinyl proton), a multiplet centered at δ 3.31 (methine proton), and a doublet at δ 1.31 [$\mathrm{CH}{-}\mathit{CH}_3)\mathrm{CO_2Et}$]. The ester ethyl group gave normal patterns. The infrared spectrum showed a medium absorption at 965 cm^{-1} (*trans* $-\mathrm{HC}{=}\mathrm{CH}-$) and the ultraviolet spectrum shows $\lambda_{\max}$ 246 mμ (ϵ 11,460).

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.17; H, 8.02.

Ethyl 4-(*p*-Alkylphenyl)-2-methyl-2- and -3-butenoates.—The title compounds were prepared in the same manner as described for ethyl 4-phenyl-2-methyl-2- and -3-butenoates. The mixture of *p*-alkylphenylacetaldehyde and *p*-alkylbenzaldehyde were added to equimolar amounts of the anion generated from sodium hydride and ethyl α-diethylphosphonopropionate in glyme. After working-up in the normal manner, mixtures of the title compounds and ethyl *p*-alkyl-2-methylcinnamates were isolated. These were separated *via* glpc. The ethyl 4-(*p*-alkylphenyl)-2-methyl-2-butenoates were then treated with sodium ethoxide in ethanol and the products were again separated by glpc to give finally pure ethyl 4-(*p*-alkylphenyl)-2-methyl-2-butenoates and ethyl 4-(*p*-alkylphenyl)-2-methyl-3-butenoates.

Analyses and major nmr absorptions for the compounds are listed in Table V.

Equilibrations of Unsaturated Esters (Table VI).—Sodium (sufficient to make a 3 *M* sodium ethoxide) was added to dried ethanol in a 10-ml flask which was protected from carbon dioxide and moisture with a Drierite–Ascarite drying tube. After the sodium had disappeared, the unsaturated ester was added (~20 mg for each 5 ml of 3 *M* sodium ethoxide). The equilibration mixture was then placed in a constant temperature bath (77.3 ± 0.5) for 12 hr. After that time, the mixture was treated with 10% solution of sodium carbonate solution and finally with water. The ether layer was dried and the solvent was removed. The residual ester mixture was then weighed and analyzed using a Wilkins Autoprep A-700 gas chromatograph fitted with a 20 ft × $^3/_8$ in. aluminum column filled with 30% SE-30 on firebrick. The yields were determined by comparing the ester peaks to an internal standard. The glpc traces corresponding to the esters were then cut-out and weighed. The ratio of the weights of α–β to β–γ isomers was taken as the K_{obsd} which are tabulated herein. The relative thermal conductivity response was found to be 1.01 ± 0.01 for known mixtures of the isomeric *p*-hydrogen, *p*-methyl, and *p*-*t*-butyl compounds. The yield of isomeric esters for all tabulated runs was >85%. Each run was chromatographed twice and equilibrium constants were calculated for each glpc trace.

The runs in *t*-butyl alcohol were treated in the same way but the recoveries of esters were somewhat lower (70–75%).

Registry No.—Ethyl 2-methyl-4-phenyl-2-buteneoate, 14182-67-3; ethyl 2-methyl-4-phenyl-3-buteneoate, 14182-68-4; ethyl α-diethylphosphonopropionate, 3699-66-9.

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[25] M. S. Newman, G. Fraenkel, and W. N. Kirn, *J. Org. Chem.*, **28**, 1851 (1963).

Mass Spectrometry in Structural and Stereochemical Problems. CXL.[1] Competitive McLafferty Rearrangements in Bifunctional Compounds[2]

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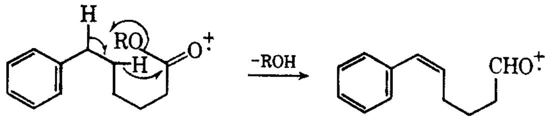
Received May 18, 1967

An investigation of the competition between different functional groups in the same molecule for electron impact induced γ-hydrogen transfer indicates that rearrangement takes place preferentially to the carbonyl moiety in both the phenylalkyl methyl ketones and the keto esters studied. However, the dominant fragmentation process in some of these compounds is a 1:6 elimination analogous to that observed in an earlier publication[4] with 6-phenylhexanoic acid.

Although a considerable amount of recent work in organic mass spectrometry has been devoted to the study of the site-specific hydrogen-transfer process known as the McLafferty rearrangement,[3] scant attention has been paid to the competitive aspect of this electron impact induced fragmentation. The analysis by Meyerson and Leitch[4] of the competition for the common γ-hydrogens between the carboxyl group and the aromatic nucleus in the mass spectra of 6-phenylhexanoic acid (I) and its methyl ester (II) was hindered by the presence of a dominant alternative fragmentation which involved initial expulsion of the elements of water (from I) or methanol (from II) *via* a 1:4, 1:5, or preferentially a 1:6 elimination (I or II → a).



I, R = H
II, R = CH_3

a

By replacing the carboxylate function by a methyl ketone group as in 7-phenyl-2-heptanone (III) it was thought that the interference of such elimination

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[1] For paper CXXXIX, see G. Schroll, S.-O. Lawesson, A. M. Duffield, and C. Djerassi, *Arkiv Kemi*, in press.

[2] We are grateful to the National Institutes of Health for financial assistance (grants No. AM-04257 and CA-07195). The purchase of the Atlas CH-4 mass spectrometer was made possible by NASA grant NsG 81-60.

[3] For a recent review and leading references see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1967, section 3-7.

[4] S. Meyerson and L. C. Leitch, *J. Am. Chem. Soc.*, **88**, 56 (1966).

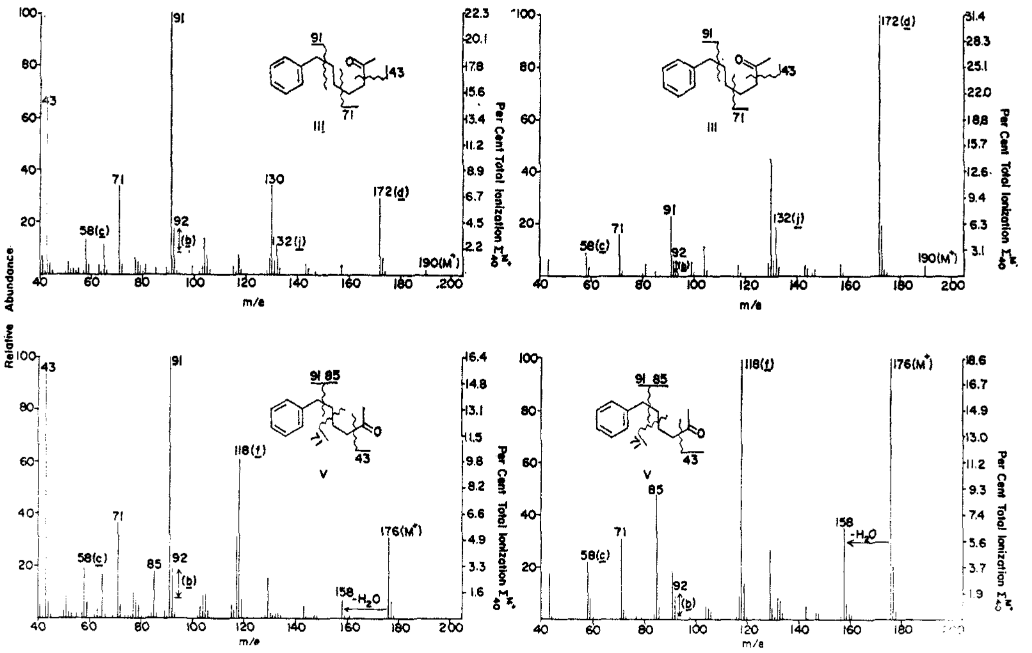
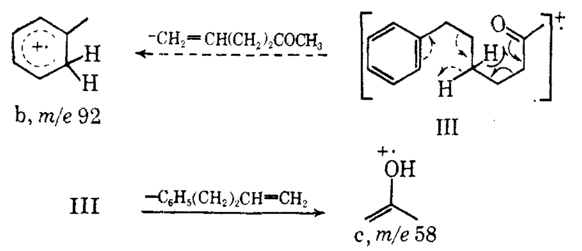


Figure 1.—Mass spectrum of 7-phenyl-2-heptanone (III) at 70 ev (upper left quadrant), at 12 ev (upper right quadrant); mass spectrum of 6-phenyl-2-hexanone (v) at 70 ev (lower left quadrant), at 12 ev (lower right quadrant).

pathways as I → a, would be minimized and thus allow a better comparison of the two competing McLafferty rearrangements (III → b and III → c) in the mass spectrum of this compound.



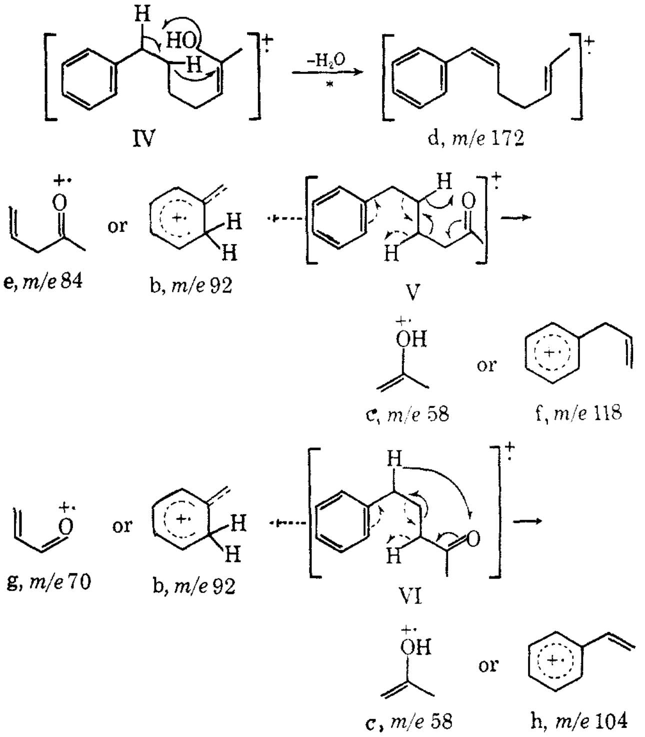
However, Figure 1 (upper quadrants) shows that the loss of water (*m/e* 172) from III (presumably through the enol form (IV) for which one may write a mechanism (IV → d) similar to that proposed[4] for the elimination of water from the acid (I), is moderately intense at 70 ev (Figure 1 (upper left)) and becomes the base peak in the spectrum (Figure 1 (upper right)) at 12 ev, while both McLafferty processes to furnish ions b (*m/e* 92) and c (*m/e* 58) are of relatively small abundance at 70 ev and lower ionizing voltages (Table I).

TABLE I
COMPETITIVE MCLAFFERTY REARRANGEMENT IONS IN THE MASS SPECTRA OF THE PHENYLALKYL METHYL KETONES III, V, AND VI

Ion	m/e	70 ev[a]	12 ev [a,b]
IIIc	58	2.9	2.8
IIIb	92	2.0	1.3
Vc	58	3.3	4.1
Vb	92	1.8	1.5
VIc	58	2.3	1.4
VIb	92	0.5	0.4

[a] Percent total ionization ($\Sigma_{40}^{M^+}$) corrected for natural ^{13}C isotope abundance. Measured on an A.E.I. MS-9 mass spectrometer. [b] Nominal electron voltage values.

For comparison, the two lower homologs 6-phenyl-2-hexanone (V) and 5-phenyl-2-pentanone (VI) were prepared and examined mass spectrometrically. The per cent contribution to the total ionization ($\Sigma_{40}^{M^+}$) of the McLafferty species b and c in the spectra of these compounds (Figure 1 (lower quadrants) and Figure 2 (upper quadrants)) is shown in Table 1. In the absence of deuterium labeling it must be assumed that all of the ions of composition C_3H_6O (*e.g.*, c) and C_7H_8 (*e.g.*, b) arise *via* the two illustrated McLafferty rearrangement routes (III, V, and VI → b or c) although it is possible that part of the *m/e* 58 and 92 peaks could be formed through secondary fragmentation. If so, the low electron voltage studies should provide a better comparison of the two competing primary rearrangements.



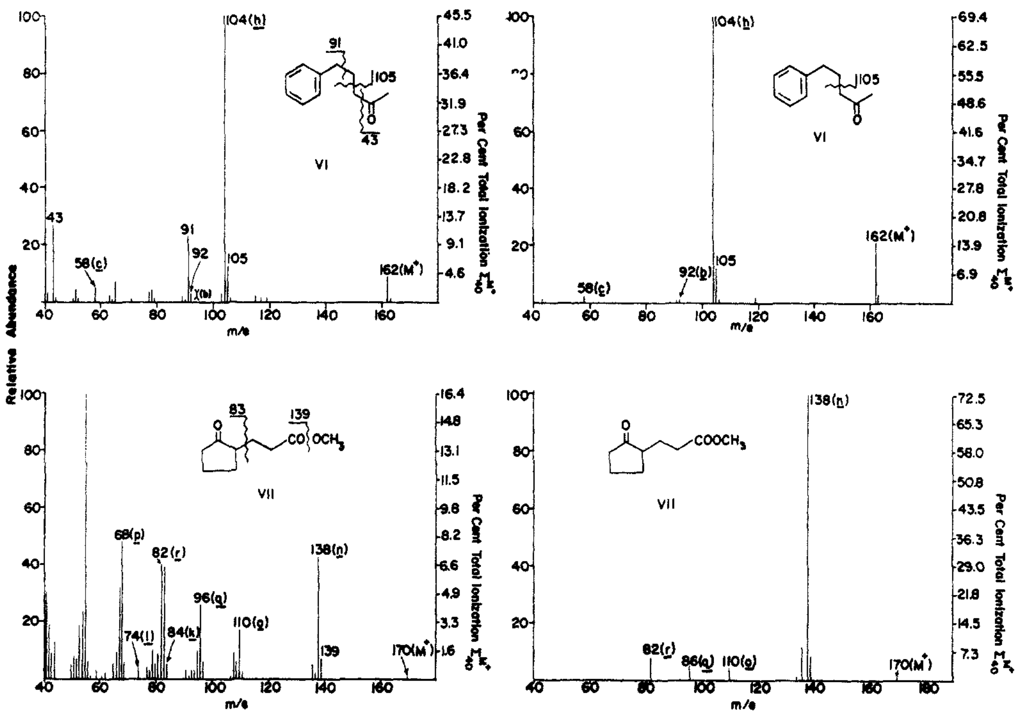
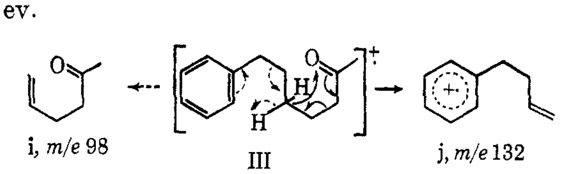


Figure 2.—Mass spectrum of 5-phenyl-2-pentanone (VI) at 70 ev (upper left quadrant), at 12 ev (upper right quadrant); mass spectrum of 3-(2-oxocyclopentyl)propionate (VII) at 70 ev (lower left quadrant), at 12 ev (lower right quadrant).

From Table I, it appears that there is a definite preference for migration of hydrogen to the carbonyl group rather than to the aromatic nucleus when the charge radical is retained on the hydrogen receptor group (c > b). This preference is even more striking when a comparison is made of the alternative pairs of ions, e *vs.* f, or g *vs.* h which can result from this rearrangement when charge localization remains on the hydrogen donor portion of the molecular ions V and VI.[5] Whereas species e (*m/e* 84) and g (*m/e* 70) from V and VI, respectively, make negligible contributions to the spectra at high or low voltage (Figure 1 (lower quadrants) and Figure 2 (upper quadrants)), both ions f (*m/e* 118) and h (*m/e* 104) are the base peaks in the 12-ev spectra of V and VI. The corresponding ions i and j from fragmentation of III (Figure 1 (upper quadrants)) show relative abundances of 0% and 11%, respectively, at 70 ev, the latter increasing to 19% at 12 ev.

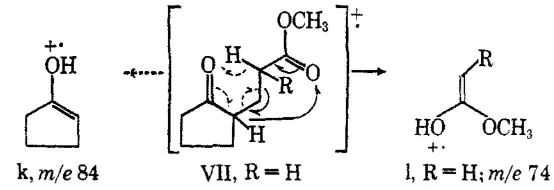


i, *m/e* 98 III j, *m/e* 132

Loss of water in V (*m/e* 158 in Figure 1 (lower quadrants)), indicating a 1:5 elimination, was considerably lessened compared with the higher homolog III (7% *vs.* 30% at 70 ev, 35% *vs.* 100% at 12 ev) and was entirely suppressed in VI. These findings are in reasonable accord with the labeling results of Meyerson[4] who found that initial loss of water from I took place *via* 1:6 (64%), 1:5 (21%) and 1:4 (10%) elimination as calculated from the spectra of the 6-d_1, 5-d_2 and 4-d_1 derivatives.

As a further extension of this study, we chose to look at the competition for γ-hydrogen rearrangement between the carbonyl and the methoxycarbonyl groups in the mass spectra (Figure 2 (lower quadrants) and Figure 3 (upper quadrants)) of 3-(2-oxocyclopentyl)-propionate (VII) and its 2-methyl derivative VIII. The contributions of the rearrangement ions k and l from VII and k and m from VIII at differing electron energies are compared in Table II, p 3488.

The most obvious aspect of these results is the large difference in the extent of the rearrangements in the two compounds VII and VIII for what is only a minor structural change. In VII, where competition exists between secondary hydrogen transfer to the carbonyl group (VII → k) and tertiary hydrogen transfer to the methoxycarbonyl moiety (VII → l), the per cent total ionization of the two ions k and l together amounts to less than 2% $\Sigma_{40}{}^{M^+}$, with some predominance of the former ion k at 15 ev (statistically 0.8 *vs.* 0.3), whereas ions k and m from VIII together contribute over 10% $\Sigma_{40}{}^{M^+}$, being of equal intensity at 70 ev, but again rearrangement to the carbonyl group predominates over transfer to methoxycarbonyl at lower ionizing voltages. Overall it may be concluded that the McLafferty rearrangement to the cyclic ketone shows a significant enhancement over the alternative transfer process to the ester at low electron energies, even where the competition involves an energetically less favorable transfer of a



k, *m/e* 84 VII, R = H VIII, R = CH_3 l, R = H; *m/e* 74 m, R = CH_3; *m/e* 88

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[5] See R. D. Grigsby, M. C. Hamming, E. J. Eisenbraun, D. V. Hertzler, and N. Bradley, 14th Annual Meeting of the American Society for the Testing of Materials Committee E-14 on Mass Spectrometry, Dallas, Texas, May 1966, and G. Spiteller and M. Spiteller-Friedman, *Monatsh.*, **95**, 257 (1964), for data on the same phenomenon of retention of charge on the aromatic moiety as a result of an external hydrogen rearrangement to another possible charge-localizing group observed in the mass spectra of methylxylylbutyric acids.

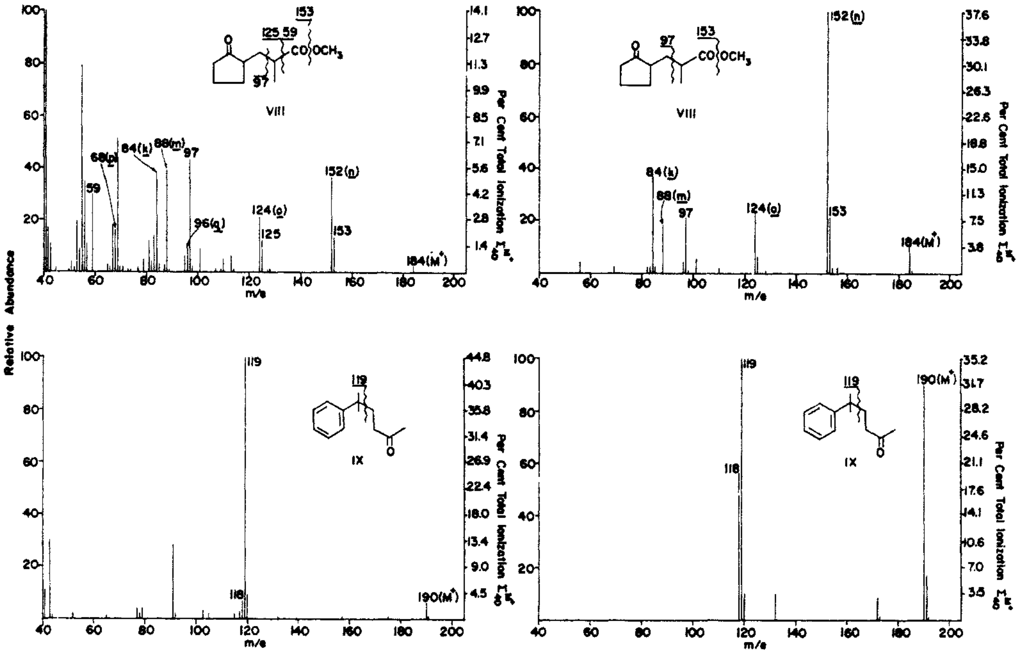
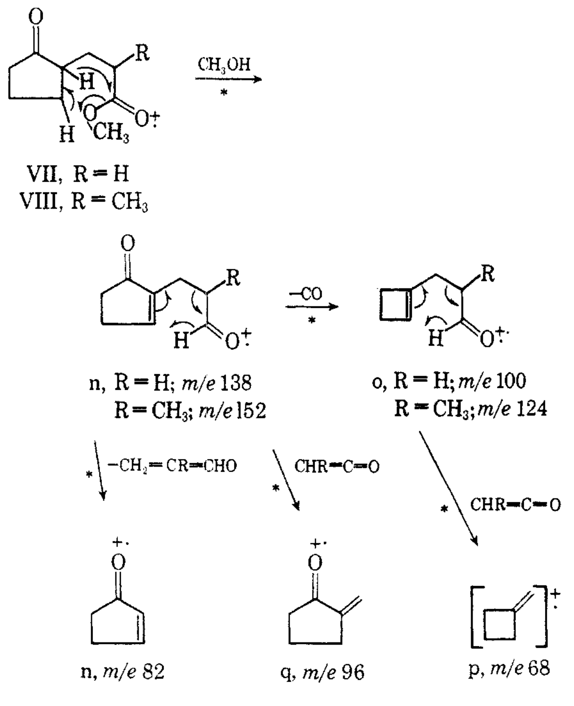


Figure 3.—Mass spectrum of 2-methyl-3-(2-oxocyclopentyl)propionate (VIII) at 70 ev (upper left quadrant), at 12 ev (upper right quadrant); mass spectrum of 5-phenyl-5-methyl-2-hexanone (IX) at 70 ev (lower left quadrant), at 12 ev (lower right quadrant).

secondary hydrogen to the carbonyl group (VII → k). The results at 70 ev may be somewhat distorted by the possible formation of part of the species k, l, and m by secondary fragmentation processes and this could well account for the decrease in the per cent of the total ionization of ions l and m compared with the increase of k as the electron energy is lowered (Table II).

However it is apparent from Figures 2 (lower quadrants) and Figure 3 (upper quadrants) that the preferred fragmentation in the mass spectra of VII and VIII is the loss of methanol (VII, VIII → n) which may be visualized as being analogous to the process proposed by Meyerson for the expulsion of methanol from methyphenyl hexanoate (II → a). The primary fragmentaltion ion n appears to be responsible for directing much of the subsequent cleavage of compounds VII and VIII, especially at low electron voltage as outlined above.



VII, R = H
VIII, R = CH_3

n, R = H; m/e 138
R = CH_3; m/e 152

o, R = H; m/e 100
R = CH_3; m/e 124

n, m/e 82

q, m/e 96

p, m/e 68

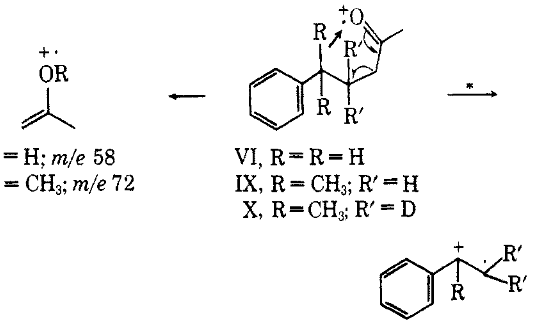
Table II

Competitive McLafferty-Rearrangement Ions in the Mass Spectra of 3-(2-Oxocyclopentyl)propionate (VII) and its 2-Methyl Homolog (VIII)

Ion	m/e	70 ev[a]	15 ev[a,b]	12 ev[a,b]
VIIk	84	0.5	1.6	
VIIl	74	0.7	0.3	
VIIIk	84	5.4	13.6	13.9
VIIIm	88	5.5	9.4	6.8

[a] Percent total ionization ($\Sigma_{40}{}^{M^+}$) corrected for natural ^{13}C abundance. Measured on an Atlas CH-4 mass spectrometer. [b] Nominal electron voltage values.

As a consequence of the foregoing study we became interested in the nature of the rearrangement VI → h in which hydrogen transfer to the carbonyl oxygen atom results in a large proportion of the charge being transferred to the aromatic nucleus and very little being retained on the ketone moiety to give species c.[6]



c, R = H; m/e 58
u, R = CH_3; m/e 72

VI, R = R = H
IX, R = CH_3; R′ = H
X, R = CH_3; R′ = D

h, R = R = H; m/e 104
s, R = CH_3; R′ = H; m/e 118
t, R = CH_3; R′ = D; m/e 120

The above representation of this rearrangement as a hydride ion transfer to a positively charged center is

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[6] The reason for postulating initial charge localization on the carbonyl oxygen atom is discussed in detail in pp 12–21 in ref 3.

similar to the type of situation[7] in which alkyl rearrangement has been shown to occur. With this in mind we prepared the dimethyl derivative IX and examined its mass spectrum. The base peak in this spectrum (Figure 3 (lower quadrants)) is due to benzylic cleavage to give the dimethyltropylium ion of mass 119, while the relative abundance of the anticipated alkyl rearrangement ion s of mass 118 is small at 70 ev but increases at low electron energies (Figure 3 (lower left)). However the mass spectrum of 5-phenyl-5-methyl-2-hexanone-4,4-d_2 (X) showed no shift of the m/e 118 peak to m/e 120 as would be expected if the alkyl rearrangement X → t were operative. It seems, therefore, that alkyl and other groups suffer migration to carbonium ion centers,[8] but not to radical ion sites.[9]

Experimental Section[10]

7-Phenyl-2-heptanone (III).—The Grignard reagent from 5-phenylpentyl bromide (2.3 g; prepared by ethylene oxide chain extension[11] of hydrocinnamyl bromide followed by bromination with 48% HBr–concentrated H_2SO_4) and magnesium (0.23 g) in ether was treated with acetaldehyde (0.6 ml) in ether and worked up in the usual way. Oxidation of the resulting alcohol with Jones reagent[12] gave 7-phenyl-2-heptanone which was purified by vpc on Apiezon L at 190° (retention time of 10 min).

6-Phenyl-2-hexanone (V).—Following the above procedure, using the Grignard derivative of 4-phenylbutyl bromide (from LAH reduction of 4-phenylbutyric acid followed by bromination in the usual manner) gave 6-phenyl-2-hexanone (V), purified by vpc on Apiezon L at 185° (retention time 14 min).

5-Phenyl-2-pentanone (VI).—This compound was prepared by the same procedure outlined for III, using hydrocinnamyl bromide as a starting material. Purification of the product was carried out by vpc on an Apiezon L column at 175° (retention time of 11 min).

3-(2-Oxocyclopentyl)propionate (VII) and 2-methyl-3-(2-oxocyclopentyl)propionate (VIII).—Both compounds were prepared by the Stork enamine procedure[13] employing alkylation of cyclopentanone pyrrolidine enamine with methyl acrylate and methyl methacrylate, respectively. The compounds were purified by vpc on Apiezon L at 180° (retention times of 5 and 5.5 min).

5-Phenyl-5-methyl-2-hexanone (IX).—β-Phenylisovaleric acid, prepared by the method of Dippy and Young,[14] was reduced with LAH to the alcohol and brominated using 48% HBr–concentrated H_2SO_4 (4:1). Treatment of the Grignard reagent of this bromide with acetaldehyde and subsequent oxidation (as for III, V, and VI) gave the required ketone IX, which was purified by vpc on a 20% polybutylene glycol column at 170° (retention time 12.5 min). The structure of the compound was verified by nmr and mass spectrometry.

The 4-d_2 derivative (X) was prepared by NaOD–MeOD exchange of the methyl ester of β-phenylisovaleric acid (esterification being carried out with diazomethane) followed by $LiAlH_4$ reduction, bromination, and Grignard reaction as outlined above for the nondeuterated compound.

Registry No.—III, 14171-88-1; V, 14171-89-2; VI, 2235-83-8; VII, 10407-36-0; VIII, 14128-60-0; IX, 14128-61-1.

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[7] C. Djerassi, A. M. Duffield, F. Komitsky, and L. Tökes, *J. Am. Chem. Soc.*, **88**, 860 (1966). For a general review of alkyl rearrangements see P. Brown and C. Djerassi, *Angew. Chem.*, **79**, 481 (1967).

[8] R. G. Cooks and D. H. Williams, *Chem. Commun.*, 51 (1967) have established a generalized pattern for the migration of hydroxyl and alkoxyl groups to carbonium ion centers.

[9] R. R. Arndt and C. Djerassi, *ibid.*, 578 (1965).

[10] Conditions for operation of the Atlas CH-4 mass spectrometer were: inlet line temperature, 150°; reservoir temperature, 90°; ion source temperature, 200° (except compounds IX and X which were run at 175°); ionizing current, 10 μA; electron voltage as specified. For the A.E.I. MS-9: inlet line and ion source temperature, *ca.* 200°; ionizing current, 100 μA; electron voltage as specified. Processes for which metastable ions were observed are marked with an asterisk (*) in the text. High resolution measurements were carried out where necessary to determine the composition and homogeneity of relevant peaks.

[11] A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co. Ltd., London, 1956, p 253.

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

[13] G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrel, *J. Am. Chem. Soc.*, **85**, 207 (1963).

[14] J. F. J. Dippy and J. T. Young, *J. Chem. Soc.*, 3919 (1955).

Benzylic Chlorides in the Darzens Reaction

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Received March 28, 1967

The alkoxide-promoted reactions between four *para*-substituted benzyl chlorides and five carbonyl compounds have been studied. p-Nitrobenzyl chloride and benzaldehyde was the only combination of reactants that yielded an epoxide; all other pairs gave ethers or stilbenes. The factors influencing the course of these reactions are discussed.

The Darzens reaction, as usually applied, involves the base-promoted condensation of an aldehyde or ketone with an α-halo ester to produce an α,β-epoxy ester. The general scope mechanism of this reaction have been reviewed up to 1954.[2,3] The reaction has also been extended to benzylic halides in a few cases. Kleucker[4] obtained two isomeric epoxides and a small amount of 4,4′-dinitrostilbene when p-nitrobenzyl chloride was condensed with cinnamaldehyde or furfural in methanol using potassium carbonate as the base. Bergmann and Hervey[5] made a more extensive study of this reaction; however, in most cases yields of epoxides were not reported. Benzyl chloride with p-nitrobenzaldehyde and methanolic potassium hydroxide gave predominantly p-nitrobenzyl methyl ether. Hanna and co-workers[6] obtained nearly quantitative yields of 4,4′-dinitrostilbene when p-nitrobenzyl chloride was treated with alkali in aqueous acetone. Feldstein and Vander Werf[7] treated benzyl chloride with p-chlorobenzaldehyde in attempts to prepare p-chlorostilbene oxide; however in ethereal sodium methoxide a chlorohydrin was obtained while with sodium ethoxide in butyl ether the product was p-chlorobenzoic acid in 67% yield. When benzaldehyde was condensed with p-chlorobenzyl chloride in the

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[1] To whom inquiries should be addressed.

[2] M. S. Newman and B. J. Magerlein, *Org. Reactions*, **5**, 413 (1949).

[3] M. Ballester, *Chem. Rev.*, **55**, 283 (1955).

[4] E. Kleucker, *Chem. Ber.*, **55**, 1634 (1922).

[5] E. Bergmann and J. Hervey, *ibid.*, **62**, 893 (1929).

[6] S. B. Hanna, Y. Iskander, and Y. Riad, *J. Chem. Soc.*, 217 (1961).

[7] A. Feldstein and C. A. Vander Werf, *J. Am. Chem. Soc.*, **76**, 1626 (1954).