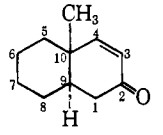
Mass Spectrometry in Structural and Stereochemical Problems. CXXXII.[1] Electron Impact Induced Alkyl and Aryl Rearrangements in α,β-Unsaturated Cyclic Ketones[2]

R. L. N. Harris,[3a] F. Komitsky, Jr.,[3b] and Carl Djerassi

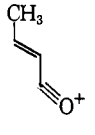
Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received February 13, 1967*

Abstract: The mass spectra of a number of alkyl- and aryl-substituted Δ^2-cyclohexenones and related bicyclic ketones, together with deuterium-labeled analogs, have been measured and the course and scope of an electron impact induced 1,2-alkyl (aryl) rearrangement occurring in these compounds discussed. Ketene elimination and other fragmentation processes in the mass spectra of these compounds are also described.

Electron impact induced alkyl and aryl rearrangements have received wide attention,[4] principally because of their mechanistic interest, but also because of the possible limitations which they may impose on the element map technique for the presentation of mass spectral data. Most of the examples so far documented involve expulsion of a neutral species (*e.g.*, CO, CO_2, SO_2, etc.) from the molecular ion accompanied by a rearrangement of the remainder to give a charged fragment having a different arrangement of carbon atoms from that existing in the original molecule. Authentic 1,2 rearrangements that take place within the molecule without concomitant loss of a neutral fragment are much less commonly observed. One of the first examples of such a rearrangement was observed in the mass spectra of Δ^3-2-octalones bearing a 10-methyl substituent. Thus, a prominent peak (Σ_{40} = 11%) in the mass spectrum of I occurs at *m/e* 69 and has been shown by high resolution and deuterium labeling[5] to correspond to the ion a, which arises by a 1,2 shift of the angular methyl group from C-10 to C-4 prior to fragmentation. Several plausible rationaliza-



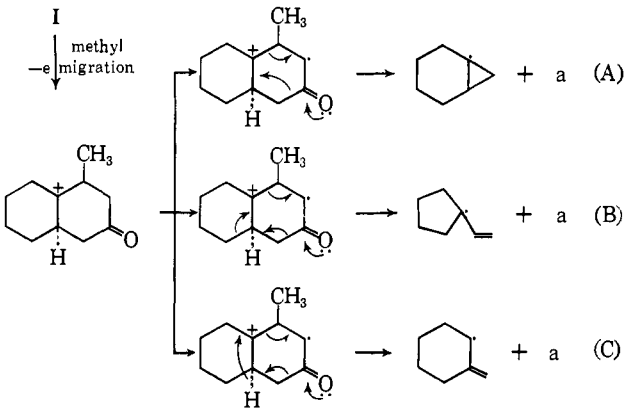
I



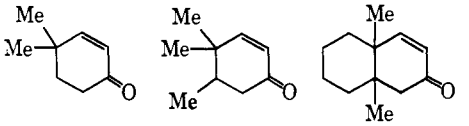
a

tions have been proposed to account for the formation of the *m/e* 69 peak (see Scheme I). The principal difference between them is the nature of the neutral (undetectable) fragment produced. However, a distinction can be drawn by considering the structural requirements necessary for the rearrangement to take place. For example, if process A[5] operates, the ketone II should also undergo such a rearrangement. If the concerted 1,2 shifts implicit in process B[6] are involved,

Scheme I



then the ketone III should show the rearrangement even if II did not. If process C[6] were the correct one, then the ketone IV might not be expected to exhibit an *m/e* 69 peak (a). Accordingly, the appropriate ketones and some deuterated analogs were synthesized and their



II III IV

mass spectra measured. The present paper discusses the mechanistic implications of these results; in addition, the scope of the rearrangement has been further delineated by a consideration of the mass spectra of many related α,β-unsaturated cyclic ketones, in which the migrating group is methyl, ethyl, or aryl (see Table I).

Synthesis of the Ketones

Δ^3-Octalones and Related Compounds. Most of these substances have been reported previously (see footnotes to Table I). *trans*-10-d_3-Methyl-2-octalone (Ib) was prepared by the following sequence. The magnesium salt of cyclohexanone cyclohexylimine was alkylated[7] with d_3-methyl iodide to give 2-d_3-methylcyclohexanone. This was condensed[8] with methyl vinyl ketone; the intermediate ketol was dehydrated[8] and the product re-

(1) For paper CXXXI see J. O. Madsen, S.-O. Lawesson, A. M. Duffield, and C. Djerassi, *J. Org. Chem.*, **32**, 2054 (1967).

(2) Financial assistance by the National Institutes of Health (Grants No. AM-04257 and GM-06840) is gratefully acknowledged. The purchase of the Atlas mass spectrometer was made possible through NASA Grant NsG 81-60.

(3) Postdoctoral Research Fellow: (a) 1965–1966; (b) 1964–1965.

(4) For a recent review, see P. Brown and C. Djerassi, *Angew. Chem.*, in press.

(5) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1398 (1965).

(6) First proposed by Dr. W. J. Richter (Hoffmann-La Roche, Basel) in a private discussion with one of the authors.

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

(8) J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964).

Table I. Per Cent Total Ionization (Σ_{40}) and Relative Abundance (*RA*) of Alkyl and Aryl Rearrangement Ions in the Mass Spectra of Δ^3-Cyclohexenones and Related Ketones

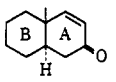
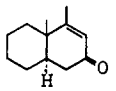
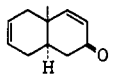
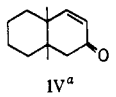
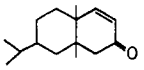
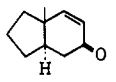
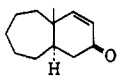
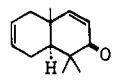
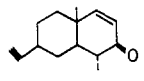
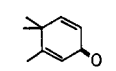
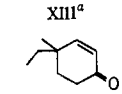
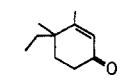
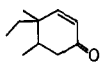
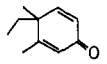
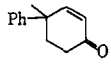
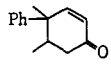
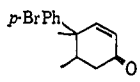
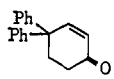
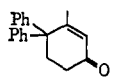
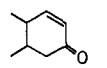
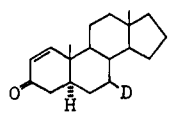
Compound	—M+, 70 ev— % Σ_{40}	% RA	—M+, 12 ev— % Σ_{40}	% RA	—Rearr ion, 70 ev— *m/e*	% Σ_{40}	% RA	Rearr ion, 12 ev % Σ_{40}	% RA	Deuterated analogs	Ref
 I[a]	2.6	24	19.2	45	69	11.0	100	6.8	16	1,1,3-d_3 (Ia) *m/e* 69 → *m/e* 70 10-d_3-Me (Ib) *m/e* 69 → *m/e* 72	*b*
 V[a]	3.14	35			83	9.0	100			1,1,3-d_3 (Va) *m/e* 83 → *m/e* 84 4-d_3-Me (Vb) *m/e* 83 → *m/e* 87	*c*
 VI[a]	4.2	60			69	5.8	84			4-d_1 (VIa) *m/e* 69 → *m/e* 70	*b*
 IV[a]	3.3	47	36	100	69	6.4	92	1.1	3	9-d_3-Me (IVa) *m/e* 69 unchanged	*d*
 VII[a]	1.6	21	19.8	100	69	7.8	100	2.0	10		*d*
 VIII[a]	2.6	23	18.3	38	69	5.74	51	4.34	9		
 IX[a]	1.5	19	13.4	33	69	7.6	96	4.5	11		*e*
 X[a]	1.4	18			69	1.3	17				*b*
 XI[f]	4.1	76			69	3.8	70				*g*
 II[a]	10.9	51	67.6	100	69	1.1	5				
 XII[a]	6.3	42	34.9	68	83	0.5	3				
 III[a]	5.4	22	34.5	91	69	9.3	38	2.7	7	2,6,6-d_3 (IIIa) *m/e* 69 → *m/e* 70 4,4-Di-d_3-Me (IIIb) *m/e* 69 → *m/e* 72	
 XIII[a]	12.1	84	43.2	100	83						
 XIV[a]	3.2	23			69 83	0.6 0.3	4 2				
 XV[a]	3.5	19			83 97	0.2	1				

Table I (*Continued*)

Compound	—M+, 70 ev— % Σ_{40}	% RA	—M+, 12 ev— % Σ_{40}	% RA	—Rearr ion, 70 ev— *m/e*	% Σ_{40}	% RA	Rearr ion, 12 ev % Σ_{40}	% RA	Deuterated analogs	Ref
 XVI[a]	2.2	11			69 83	3.4 4.0	17 20			2,6,6-d_3 (XVI) *m/e* 69 → *m/e*[f] 70 *m/e* 83 → *m/e* 84	
 XVII[a]	6.7	33			69 83 97						
 XVIII[f]	11.2	82	25.9	76	69 131	0.1 0.4	1 3	0.3	0.5		
 XIX[a]	6.2	32	35.8	100	69 131	0.8 8.0	4 41	14.7	41	2,6,6-d_3 (XIXa) *m/e* 69 → *m/e* 70 *m/e* 131 → *m/e* 132	
 XX[f]	6.7	31	25.7	100	69 209 211	0.6 7.7	3 36	0.3 17	1 66		
 XXI[f]	2.0	16	8.1	16	131	0.3	2				*h*
 XXII[f]	10.4	100			145	0.1	1				
 XXIII[f]	7.5	36	20	100	69	2.7	13	1.6	8	2,4,6,6-d_4 (XXIIIa) *m/e* 69 → *m/e* 70	
 XXIV[f]	1.5	28			69	1.2	23				*i*

[a] Mass spectrum measured on Atlas CH-4 spectrometer. [b] C. Djerassi and D. Marshall, *J. Am. Chem. Soc.*, **80**, 3986 (1958). [c] L. H. Zalkow, F. X. Markley, and C. Djerassi, *ibid.*, **82**, 6354 (1960). [d] The authors wish to thank Professor J. A. Marshall for a generous gift of this compound; see J. A. Marshall, W. I. Fanta, and H. Roebke, *J. Org. Chem.*, **31**, 1016 (1966). [e] C. Djerassi and J. E. Gurst, *J. Am. Chem. Soc.*, **86**, 1755 (1964). [f] Mass spectrum measured on AEI MS-9 mass spectrometer using direct inlet method. [g] The authors wish to thank Professor T. Nozoe for a generous gift of this compound; see T. Nozoe, Y. S. Cheng, and T. Toda, *Tetrahedron Letters*, 3663 (1966). [h] H. E. Zimmerman and D. I. Schuster, *J. Am. Chem. Soc.*, **84**, 4527 (1962). [i] R. H. Shapiro and C. Djerassi, *ibid.*, **86**, 2865 (1964).

duced with lithium in liquid ammonia.[9] Oxidation[10] of the resulting saturated alcohol gave the corresponding decalone which was brominated (pyridinium perbromide in acetic acid) and dehydrobrominated (calcium carbonate in N,N-dimethylacetamide[11]) to give the required Δ^3-10-d_3-methyloctalone. *cis*-9-d_3-Methyl-10-methyl-Δ^3-2-octalone (IVa) was prepared in a manner analogous to that used for the 1-methyl compound.[9] The deuterated ketones Ia and Va were obtained by refluxing the appropriate ketone with sodium in methanol-d_1 and heavy water.[12]

4,4-Disubstituted Cyclohexenones. Two general methods of synthesis were employed. The first involved base-catalyzed condensation of methyl vinyl ketone with the appropriately substituted aldehyde and is satisfactory only when either or both C-4 substituents are aryl (XVIII–XXII). 4,4-Dialkylcyclohexenones (II and XIV) were synthesized by alkylation–cyclization of the appropriate aldehyde enamine with methyl vinyl ketone.[13]

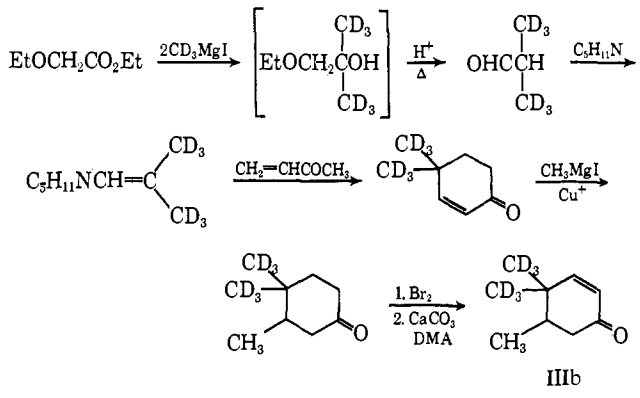
4,4,5-Trisubstituted Cyclohexenones. 4,5-Dimethyl-4-aryl-Δ^2-cyclohexenones (XIX and XX) were prepared by condensing the appropriate aldehyde with pent-2-en-3-one. The trialkylcyclohexenones (III and XVI) were obtained by 1,3 addition of methylmagnesium iodide to the corresponding 4,4-dialkylcyclohexenone, fol-

(9) See G. Stork and S. D. Darling, *J. Am. Chem. Soc.*, **86**, 1761 (1964).
(10) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(11) G. F. H. Green and A. G. Long, *ibid.*, 2532 (1961).
(12) R. H. Shapiro, J. M. Wilson, and C. Djerassi, *Steroids*, 1, 1 (1963).
(13) G. Stork, A. Brizzolara, H. Landesman, J. Smuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, **85**, 207 (1963).

lowed by bromination and dehydrobromination. This second route was complicated by the formation of the 1,2-addition product in the first step and of both isomeric α,β-unsaturated ketones (*e.g.*, III and XII) and the corresponding dienone (*e.g.*, XIII) in the second step. In most instances, however, separation of these compounds was accomplished readily by gas–liquid partition chromatography.

Deuterated Cyclohexenones. The hydrogen atoms α to the carbonyl group were exchanged with deuterium by refluxing a solution of the ketone in methanol-d_1 and heavy water containing a trace of potassium carbonate. The synthesis of 4,4-di-(d_3-methyl)-5-methyl-Δ^2-cyclohexenone (IIIb) was achieved as follows (Scheme II).

Scheme II



Ethyl ethoxyacetate was treated with 2 equiv of d_3-methylmagnesium iodide and the resulting propanediol monoethyl ether heated with aqueous sulfuric acid. Steam distillation gave the labeled aldehyde which was immediately condensed with piperidine in ether in the presence of anhydrous potassium carbonate[14] to afford the enamine in which there was no scrambling of the deuterium as shown by nmr and mass spectrometry. The desired ketone IIIb was prepared from this enamine by the procedure used for the undeuterated analog.

Discussion of the Mass Spectra

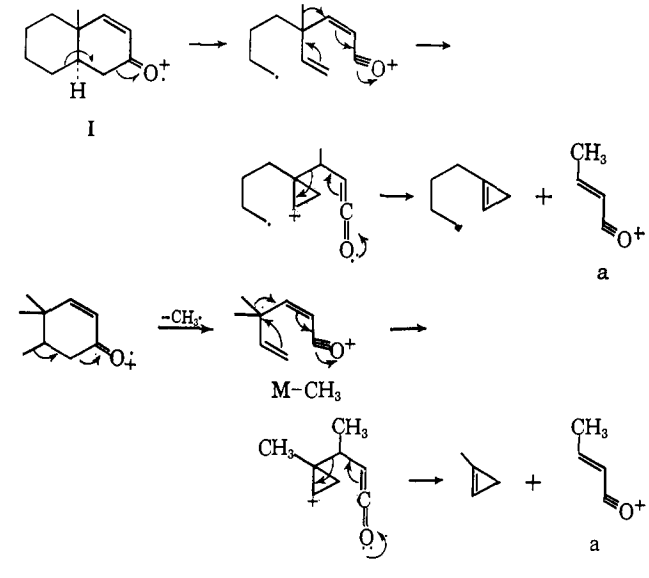
The Rearrangement Ion a. The main feature of interest in the mass spectra of the α,β-unsaturated cyclic ketones is the occurrence of the rearrangement ion a, and the discussion will first be concerned with it. The intensity of fragment a in the mass spectra of the ketones studied is recorded in Table I both as per cent total ionization (% $\Sigma_{40}{}^{M^+}$) and per cent abundance relative to the most intense peak (% RA). The intensity of the molecular ion is included for comparison. In many cases the spectra were measured at low voltage (12 ev) as well as at the customary 70 ev.

High-resolution mass spectral measurements confirmed the elemental composition of the rearrangement ion in all relevant examples. Furthermore, the inclusion of the implicated carbon atoms in the rearrangement ion a was substantiated in most cases by deuterium labeling, as shown in Table I. The migration of the phenyl group in XIX was confirmed by labeling this group with a *p*-bromine atom (see XX). The aryl rearrangement ion shifted from *m/e* 131 to *m/e* 209–211 as would be expected. All the bicyclic ketones show the rearrangement ion in their mass spectra; in fact, the ion is in most cases of greater than 90% relative abundance.

Significantly, substitution of the C-9 hydrogen atom by a methyl group in the Δ^3-2-octalones (IV and VII) does not restrict the migration of the C-10 methyl substituent. In view of this observation, process C in Scheme I, which requires the migration of a secondary hydrogen atom from C-9, is either not operative or at least cannot be the only process by which such methyl rearrangements take place. The deuterated analog IVa still shows the rearrangement ion at *m/e* 69, indicating that the d_3-methyl group at C-9 is not part of this charged species. As reported previously,[5] the presence of a double bond (*cf.* VI) in ring B of the bicyclic ketones has no effect on the rearrangement process. Furthermore, a consideration of the mass spectra of ketones I, VIII, and IX reveals that the size of ring B also has very little effect on the abundance of the rearrangement ion. All the observations discussed so far can be accommodated by either process A or B in Scheme I.

However, only one of these reaction sequences offers a rationale for the mass spectra of the monocyclic ketones and their deuterated derivatives listed in Table I. Thus, ions due to the rearrangement of methyl, ethyl, or phenyl substituents (*m/e* 69, 83, and 131, respectively) are almost absent in the mass spectra of ketones II, XIV, and XVIII, whereas in the C-5-methyl homologs III, XVI, and XIX, these rearrangement ions now account for Σ_{40} = 7.3–9.3% and thus are of the same order of abundance as that observed for rearrangement ions in the octalone series. Therefore alkyl substitution at C-5 in the cyclohexenones appears to be necessary for the rearrangement ion a to be produced. This corresponds to one of the sites of attachment of ring B in the octalone series. Clearly, the results implicate the C-5 substituent in the rearrangement process, and of the three reaction paths proposed so far, only the second (B in Scheme I) remains valid. A more recent variant[15] of B for the course of the rearrangement process is shown in Scheme III. In this sequence the

Scheme III



(14) C. Mannich and H. Davidsen, *Ber.*, **69**, 2106 (1936).

(15) Suggested by Drs. P. Brown and M. M. Green in our laboratory.

molecular ion is depicted with charge localization on oxygen rather than the carbon–carbon double bond. Again, the C-5 substituent is involved, and in the octalone series there is no way in which this proposal can be distinguished from that embodied in B of Scheme I.

In the cyclohexenones, however, preliminary cleavage as depicted in Scheme III will result in the generation of an intermediate M − CH_3 fragment, and the rearrangement ion would be formally derived from this species in a secondary process. A careful investigation of the relevant spectra reveals no metastable ions to support this hypothesis, whereas the concerted nature of the rearrangement process from molecular ion to phenyl rearrangement ion (*m/e* 131) in the mass spectrum of XIX is substantiated by a prominent metastable peak at *m/e* 85.8. It should be noted, however, that in the d_6-labeled ketone IIIb ejection of the C-5 methyl group occurs to a greater extent than loss of one of the allylically activated d_3-methyl substituents, and so fragmentation, as depicted in the first step of Scheme III, is not an unreasonable process.

It has been established that a C-5 substituent is necessary for the rearrangement ion to be produced. Variation of substituents at C-4 has shown that both alkyl and aryl groups are able to migrate. To further define the scope of the rearrangement the mass spectra of the ketone XXIII and its deuterated d_4-analog XXIIIa were measured, and the results (Table I) show that both the C-4 hydrogen atom and the C-4 methyl group undergo migration giving rearrangement ions at *m/e* 55 (*m/e* 57 in XXIIIa) and *m/e* 69 (*m/e* 70 in XXIIIa), respectively. Migration of a hydrogen atom (Σ_{40} = 8.7%) is preferred over that of the methyl group (Σ_{40} = 2.7%).

The mass spectra of many of the ketones were also run at low voltages so that favored, primary fragmentations could be distinguished from subsequent or higher energy processes. The results (Table I) do not permit any generalization, but the large increase in the per cent total ionization of the phenyl rearrangement ion (*m/e* 131) in the 12-ev mass spectrum of XIX is worthy of note. This result suggests that the aryl rearrangement is an energetically favorable primary fragmentation process and corroborates the evidence from the metastable peak described above. In conclusion, therefore, it may be stated that the 1,2 rearrangement ion in the mass spectra of 4,5-disubstituted and 4,4,5-trisubstituted Δ^2-cyclohexenones and related bicyclic ketones is generated in a process involving participation of the C-5 alkyl substituent, and that it is most probably of a concerted nature from the molecular ion to the rearrangement ion.

The mass spectra of a number of other alkyl- and aryl-substituted cyclohexenones were measured (see Table I), and it was found that the rearrangement ion occurred to a significant extent only when the basic 4,5-disubstitution pattern was present in the molecule. For example, XII, although isomeric with III, exhibits only a minor peak at *m/e* 69. The mass spectra of two cyclohexadienones (XIII and XVII), obtained as side products in our synthetic work, were also measured and no rearrangement ion was observed.

Of considerable interest is the question of relative migratory aptitudes in electron impact promoted alkyl and aryl migrations. It is not surprising that in the

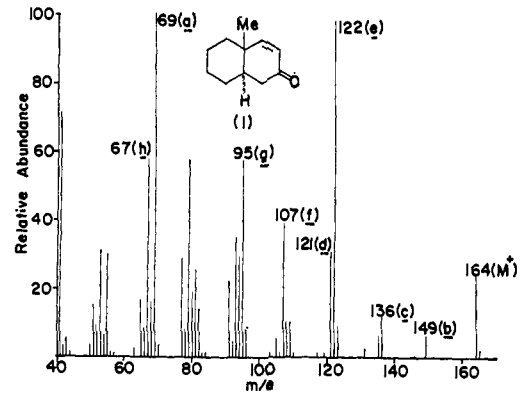


Figure 1. Mass spectrum of *trans*-10-methyl-Δ^3-2-octalone (I); see Scheme IV.

mass spectrum of XIX, the phenyl rearrangement ion (*m/e* 131) is much more intense than the methyl rearrangement ion (*m/e* 69), whereas in the spectrum of XVI, both methyl and ethyl migrations occur to a similar extent. However, a quantitative comparison of migratory aptitudes cannot be inferred from a comparison of rearrangement ion intensities in this class of compounds because of the possible influence of stereochemical factors on the rearrangement process and the different subsequent fragmentations of the respective rearrangement ions.

Other Principal Fragmentation Processes

The mass spectra of several of the ketones will be considered in detail to define the nature of other important fragmentation processes in cyclic α,β-unsaturated ketones.

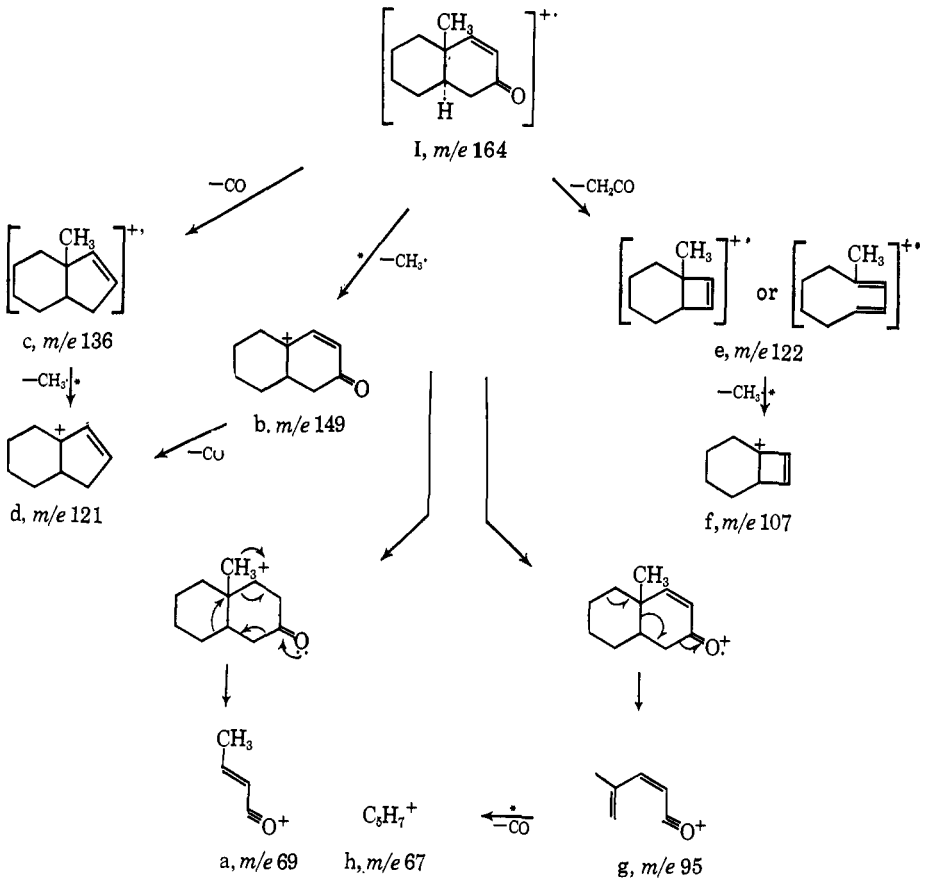
trans-**10-Methyl-Δ^3-2-octalone (I).** Some aspects of the mass spectrum (Figure 1) of this compound have been discussed previously.[16] However, further information is now available and a more complete evaluation of its spectrum is possible. The principal fragmentation processes are outlined in Scheme IV. The composition of the ions shown was established by high-resolution mass measurements and in some instances metastable ions (shown by asterisks) support the postulated fragmentation pathways. Further evidence for these processes has been obtained from consideration of the mass spectra of the two deuterated derivatives Ia and Ib (see Table II).

cis-**9,10-Dimethyl-Δ^3-2-octalone (IV).** The mass spectrum (Figure 2) is similar to that of the octalone I; again ejection of carbon monoxide, a methyl radical, and ketene are important although the base peak is now at *m/e* 95 (g). At 12 ev the only significant fragmentation is loss of ketene.

4,4,5-Trimethyl-Δ^2-cyclohexenone (III). The mass spectrum (Figure 3) shows clearly that again the same principal fragmentation pathways operate. Ions resulting from elimination of carbon monoxide, methyl radical, and ketene are evident, and the ion e produced by expulsion of propene contributes substantially (Scheme V) to the base peak (*m/e* 96). This cleavage is analogous to that leading to the peak at *m/e* 95 in the octalone series. The most significant fragmentation

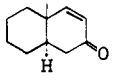
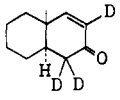
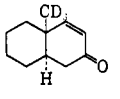
(16) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, p 157.

Scheme IV.[a] Major Fragmentation Pathways of *trans*-10-Methyl-Δ^{8}-2-octalone (I)



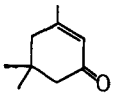
[a] Many of the cyclic structures in this (*e.g.*, ions c, e, and f) and subsequent schemes can also be written in an open form [see B. J. Millard and D. F. Shaw, *J. Chem. Soc., Sect. B.*, 664 (1966)]. The cyclic structures are used here solely for the sake of convenience.

Table II. *m/e* Values for Various Fragment Ions of *trans*-10-Methyl-Δ^{8}-2-octalone (I) and Deuterated Derivatives

Compound	*m/e* values of fragment ions[a]						
	b	c	e	d	g	a	h
 I	149	136	122	121	95	69	67
 Ia	152	139	123	124	96	70	68
 Ib	149	139	125	121	98	72	70

[a] See Scheme IV.

processes are shown in Scheme IV and supporting evidence from deuteration studies is listed in Table III. These studies show that loss of a methyl radical occurs both from C-4 (b) and C-5 (b′) and both resulting ions subsequently expel carbon monoxide to give an ion (d) of mass 95. The mass spectrum of isophorone (XXV) has recently been published[17] and differs significantly from that of its isomer III. Although ions resulting from loss of carbon monoxide, methyl radical, and isobutene (*cf.* propene in III) are abundant, loss of ketene is a very minor process (*vide infra*).



XXV

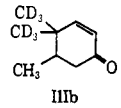
4,4-Dimethyl-Δ^{2}-cyclohexenone (II). The mass spectrum (Figure 4) resembles that of the trimethyl homolog III. All principal peaks are derived by loss of ethylene, ketene, or carbon monoxide and/or a methyl radical. The rearrangement ion (*m/e* 69) is now insignificant. The mass spectrum of II differs in one important respect from that published for Δ^{2}-cyclohexenone;[17] namely, in the former loss of ketene furnishes the base peak, whereas in the latter the M − 42 ion is only of 3% relative abundance.

4,5-Dimethyl-4-phenyl-Δ^{2}-cyclohexenone (XIX). The mass spectrum (Figure 5) resembles that of the ketone III; loss of ketene, propene, and carbon monoxide followed by loss of a methyl radical are important processes. Migration of the C-4 methyl group (giving the rearrangement ion a, *m/e* 69) is now overshadowed by rearrangement of the C-4 phenyl substituent, leading to an analogous ion of mass 131.

Loss of Ketene. One of the more prominent modes of fragmentation of many of the Δ^{2}-cyclohexenones studied is the elimination of ketene. This process has been observed already in steroidal α,β-unsaturated

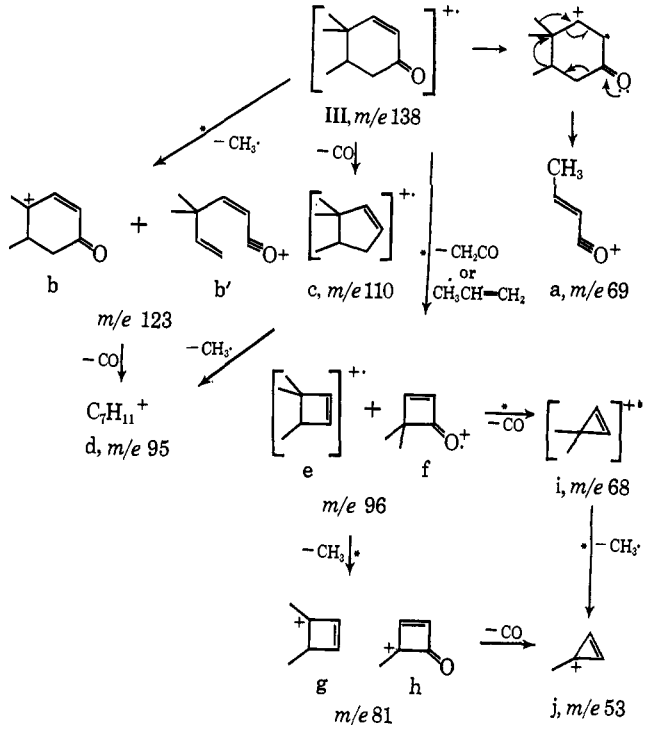
(17) J. H. Bowie, *Australian J. Chem.*, **19**, 1619 (1966).

Table III. *m/e* Values for Various Fragment Ions of 4,4,5-Trimethyl-Δ^2-cyclohexenone (III) and Deuterated Derivatives

Compound	*m/e* values of fragment ions[a]							
	b, b′	c	e, f	d	g, h	a	i	j
 III	123	110	96	95	81	69	68	53
 IIIa	126	113	97	98	82	70	69	54
 IIIb	126, 129	116	102	98, 101	84	72	74	56

[a] See Scheme V.

Scheme V. Major Fragmentation Pathways of 4,4,5-Trimethyl-Δ^2-cyclohexenone (III)

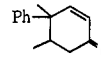
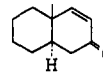
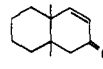


ketones (*e.g.*, XXVII)[18] and occurs in the mass spectra of all the ketones in the present study. It was surprising, therefore, to find that elimination of ketene from Δ^2-cyclohexenone itself proceeds only to a negligible extent, an observation first reported by Bowie[17] and confirmed in our own laboratories. Table IV lists the per cent total ionization of the species produced by ketene elimination (*i.e.*, the M − 42 ion) from several Δ^2-cyclohexenones. It should be noted that 5-methyl-substituted Δ^2-cyclohexenones also eliminate propene, giving rise to an oxygen-containing M − 42 species and high-resolution mass measurements were necessary, therefore, to distinguish this process from ketene elimination (see Table IV).

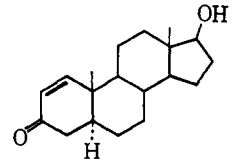
From the table it is clear that alkyl or aryl substitution at C-4 is necessary for ketene elimination to occur. Recently Egger has shown[19] that ketene elimination

(18) See footnote *i*, Table I.
(19) H. Egger, *Monatsh.*, **97**, 1201 (1966).

Table IV. Per Cent Total Ionization of Ions Produced by Ketene and Propene Elimination from Δ^2-Cyclohexenones

Compound	Loss of ketene (% Σ_{40})	Loss of propene (% Σ_{40})
	0.27	1.53
 XXIII	4.2	16.7
 II	20.1	...
 III	6.8	12.7
 XIX	9.7	14.7
 I	10.3	~1
 IV	6.2	~1

from steroidal α,β-unsaturated ketones may depend on the stereochemistry of the A/B ring junction. For example, in the spectrum of Δ^1-5α-androsten-17β-ol-3-one (XXVII) the M − 42 peak is of 56% relative



XXVII

abundance (the molecular ion being responsible for the base peak), whereas in the 5β isomer loss of ketene is negligible. Similarly, in the corresponding 17-keto

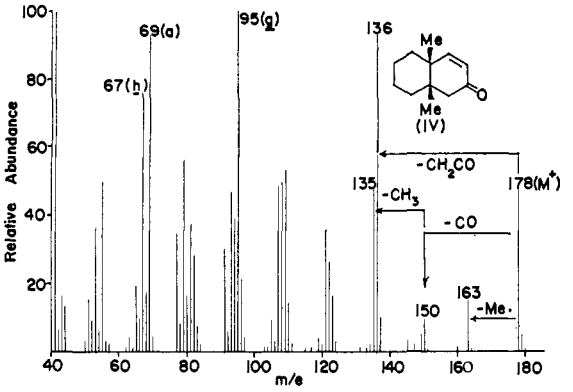


Figure 2. Mass spectrum of *cis*-9,10-dimethyl-Δ^3-2-octalone (IV). The ions of mass 163, 150, 136, and 135 are analogs of ions b, c, e, and d in Scheme IV. Ions a, h, and g are identical with those depicted in Scheme IV

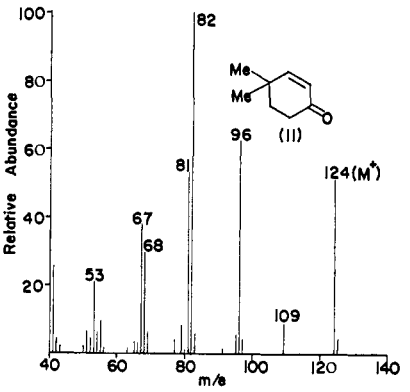


Figure 4. Mass spectrum of 4,4-dimethyl-Δ^2-cyclohexenone (II). The ions of mass *m/e* 109, 96, 82, 81, and 67 are analogs of ions b, c, e, d, and g in Scheme V. Ions of mass 96, 81, 68, and 53 correspond to ions f, g, i, and j of Scheme V.

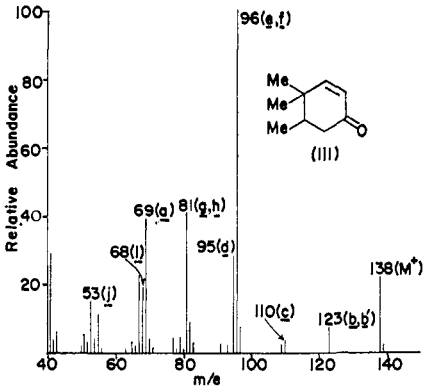


Figure 3. Mass spectrum of 4,4,5-trimethyl-Δ^2-cyclohexenone (III); see Scheme V.

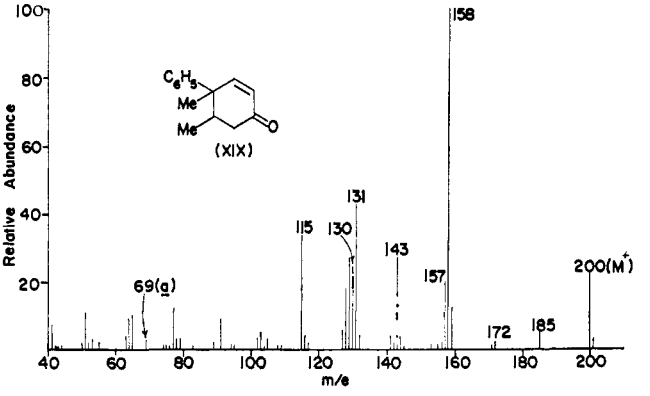
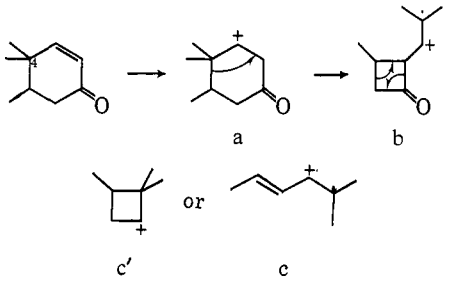


Figure 5. Mass spectrum of 4,5-dimethyl-4-phenyl-Δ^2-cyclohexenone (XIX). Ions of mass 185, 172, 158, 157, 143, 130, and 115 are analogs of ions b, c, e–f, d, g–h, i, and j in Scheme V. Ions of mass 69 and 131 are the methyl rearrangement ion a and the corresponding phenyl rearrangement product, respectively.

steroids the 5α isomer has a prominent M − 42 peak (84% relative abundance), whereas the 5β isomer exhibits a very weak M − 42 peak (4% relative abundance). A possible rationale for these observations is outlined in Scheme VI. Direct fission of the bond connecting the vinylic carbon to the carbonyl group is an unlikely process and almost certainly implies that a prior rearrangement of the molecular ion a occurs. Thus, rearrangement of a to b, with its highly substituted ionized double bond, provides a cyclobutanone species from which ketene elimination would be a most favorable process (b → c). The resulting M − 42 ion c is a resonance-stabilized ionized butadiene and may also be visualized as the ionized cyclobutene form c′. Such a concerted sequence will probably only operate when there is a suitable driving force for rearrangement of the molecular ion a to species b, such as alkyl or aryl substitution at C-4. This would explain the failure of Δ^2-cyclohexenone itself to eliminate ketene on electron impact.[20] The failure of the 5β- (but not 5α-) Δ^1-3-keto steroids[19] to undergo ketene elimination may be associated with the "frozen" conformation of *cis*-octalones in steroidal systems. By comparison, the flexible *cis*-octalone (IV) shows an intense peak in its mass spectrum (see Table IV) corresponding to the loss of ketene, possibly because it may assume the proper conformation required for the initial rearrangement (a → b).

Scheme VI



Experimental Section[21]

trans-**10-d_3-Methyl-Δ^3-2-octalone (Ib).** A solution of 0.7 *M* methylmagnesium iodide in tetrahydrofuran (138 ml) was stirred

(20) After completion of our manuscript, Professor A. L. Burlingame (University of California) sent us a copy of a paper by A. L. Burlingame, C. Fenselau, W. J. Richter, W. G. Dauben, G. W. Shaffer, and N. D. Vietmeyer [*J. Am. Chem. Soc.*, **89**, 3346 (1967)] in which the same results with a different interpretation are recorded.

(21) Melting points (uncorrected) were determined on the Kofler block. Ultraviolet absorption spectra were determined with a Bausch and Lomb Spectronic 505 spectrophotometer, and the infrared absorption spectra were measured with a Perkin-Elmer Model 137 Infracord spectrophotometer. Mass spectra measured with an Atlas CH-4 spectrometer were run by Dr. J. K. MacLeod and Dr. A. M. Duffield, using a TO-4 ion source equipped with a gas cartridge. The ion source was maintained at 200°. Spectra measured on the AEI MS-9 instrument were run by Dr. J. K. MacLeod and Mr. R. G. Ross. The samples were inserted through the heated inlet system unless otherwise stated. Gas–liquid partition chromatography (glpc) was carried out on a Varian Aerograph 202 machine using helium as carrier gas at a flow rate of 150 cc/min. The nmr spectra were measured by Mr. J. H. Freed using a Varian A-60 nmr spectrometer. Microanalyses were performed by Messrs. E. Meier and J. Consul.

under nitrogen and a solution of cyclohexanone cyclohexylimine (16.94 g) in tetrahydrofuran (50 ml) was added slowly during 20 min while the solution was brought to reflux. The mixture was heated under reflux for 2 hr and cooled to 0° and a solution of 89% isotopically pure d_3-methyl iodide (13.4 g) in ether (30 ml) added dropwise with stirring over a period of 20 min. The mixture was heated for 9 hr, cooled, and treated with water (10 ml) followed by 5% hydrochloric acid (30 ml). After stirring for 30 min, 10% hydrochloric acid (25 ml) was added and the mixture stirred a further 20 min, then poured into a saturated solution of sodium chloride (75 ml). The product was extracted into ether (four 50-ml portions); the combined ether extracts were washed with saturated aqueous sodium bicarbonate solution and dried over anhydrous magnesium sulfate. The ether was removed and the residue distilled through a short Vigreux column. The fraction bp 160–164° (8.87 g, 82%) was collected and shown by infrared and mass spectra and glpc (10-ft free fatty acid phase column, 150°) to be pure 2-d_3-methylcyclohexanone.

The labeled cyclohexanone (8.71 g) and 3 *N* ethanolic sodium ethoxide solution (0.47 ml) was stirred under nitrogen and cooled to −10°. Freshly distilled methyl vinyl ketone (5.55 g) was added during 6 hr at this temperature and the thick mixture kept at −10° a further 6 hr. Ether was added; the mixture was washed with brine and the organic layer dried over anhydrous magnesium sulfate. The ether was slowly evaporated on a steam bath, the level being maintained by the addition of hexane. A small amount of polymeric material precipitated and was removed by filtration. On cooling the filtrate 9-hydroxy-10-d_3-methyl-2-decalone crystallized as colorless needles, mp 120–121°. The identity of the ketol was confirmed by comparison of its mass spectrum with that of the authentic unlabeled analog.[8] The crude ketol was heated under reflux with a solution of potassium hydroxide (10.3 g) in water (100 ml) and the mixture steam distilled until the distillate was clear. The distillate (1 l.) was saturated with sodium chloride and extracted with ether (four 250-ml portions) and the ether extract washed with brine and dried over anhydrous magnesium sulfate. The residue on removal of the ether was purified by chromatography on silica gel (100 g/g of product), eluting with successive 100-ml portions of 1:1 hexane–benzene, benzene, 5% ether in benzene, 10% ether in benzene, and finally 300 ml of 10% ether in benzene. The latter solvent eluted the required octalone which was used directly in the next step.

The octalone (1.88 g) in ether (50 ml) was added dropwise during 20 min to a solution of lithium (1 g) in liquid ammonia (100 ml) cooled in Dry Ice. After the addition was complete, the cooling bath was removed; the solution was stirred for 80 min as the ammonia evaporated, and methanol (15 ml) in ether (75 ml) was then added, followed by water (75 ml). The mixture was stirred until clear and extracted with ether (three 100-ml portions). The ether extracts were combined, dried over anhydrous magnesium sulfate, and evaporated. The residue was dissolved in acetone (60 ml), treated with a slight excess of Jones reagent,[10] and poured into saturated aqueous bicarbonate solution and the product extracted into ether. The ether extract was dried and evaporated and the residue bulb-distilled to give ***trans*-10-d_3-methyl-2-decalone** (1.1 g).

A solution of the decalone (1.1 g) in acetic acid (20 ml) was stirred at room temperature, and pyridinium hydrobromide perbromide (2.12 g) was added in portions during 20 min. The solution was stirred a further 30 min, then poured into water and the precipitated bromo ketone collected and recrystallized from acetone–water as colorless needles, mp 135–137° (1.14 g). The recrystallized bromo ketone was dissolved in N,N-dimethylacetamide (5 ml) and added to a suspension of calcium carbonate (1.75 g) in N,N-dimethylacetamide (15 ml). The mixture was heated under reflux for 15 min, then poured into water (70 ml) containing hydrochloric acid (10%; 30 ml). The mixture was extracted with ether (three 25-ml portions); the ether extract was washed successively with 10% hydrochloric acid, saturated aqueous sodium bicarbonate solution, and brine and dried over anhydrous magnesium carbonate and the ether removed. The residual oil was purified by glpc (10-ft 5% diethylene glycol succinate on 60–80 Chromosorb W, 140°) to give a small amount of recovered decalone and the required *trans*-10-d_3-methyl-Δ^3-2-octalone as shown by mass (Figure 1) and ultraviolet (λ_{max} 227 mμ) spectra.

***trans*-8-Methyl-Δ^6-hydrinden-5-one (VIII).** A solution of *trans*-8-methylhydrindan-5-one[22] (0.1 g) in glacial acetic acid (3.5 ml) was stirred at room temperature and a solution of bromine in acetic acid (10% v/v; 0.36 ml, 1 mole equiv) was added during 5 min. The mixture was stirred a further 5 min and poured into water, and the bromo ketone extracted into ether (two 10-ml portions). The ethereal extract was washed with water (10 ml) and saturated aqueous sodium bicarbonate solution (10 ml) and dried over anhydrous magnesium sulfate. The ether was removed and the crude product heated under reflux for 30 min with N,N-dimethylacetamide (5 ml) containing a suspension of powdered calcium carbonate (0.1 g). After filtration, the mixture was poured into water and the product extracted with ether (two 10-ml portions). The ethereal extracts were combined, washed with water (two 15-ml portions), and dried. Removal of the ether gave the hydrindenone as an oil which was purified by glpc (5-ft 10% SE 30 on 60–80 Chromosorb W; 200°). The nmr spectrum ($CDCl_3$ solution) showed a quadruplet centered at δ 6.5 (J = 9 cps) due to the two vinylic protons at C-6 and C-7. *Anal.* Calcd for $C_{10}H_{14}O$: C, 79.95; H, 9.39; mol wt, 150. Found: C, 80.29; H, 9.19; mol wt (mass spectroscopy), 150.

***cis*-10-Methyl-9-d_3-methyl-Δ^3-2-octalone (IVa).** This ketone was prepared by 1,4 addition of d_3-methylmagnesium iodide to 10-methyl-$\Delta^{1(9)}$-2-octalone,[23] followed by bromination and dehydrobromination of the resulting decalone by the procedure used for the unlabeled analog.[23]

4,4-Dimethyl-Δ^2-cyclohexenone (II). The enamine from isobutyraldehyde and piperidine was prepared by the general method of Mannich and Davidsen[14] and was obtained as colorless oil, bp 77–78° (28 mm). This enamine (11 g) was stirred under nitrogen at 0° and redistilled methyl vinyl ketone (6.1 g) added dropwise during 5 min. The mixture was stirred 4 days at room temperature under nitrogen, dissolved in 15% aqueous hydrochloric acid (85 ml), left at room temperature for 24 hr, and finally heated on a steam bath for 1 hr. The cooled mixture was extracted with ether (two 50-ml portions), and the extracts were combined, washed with water (two 25-ml portions), and dried over anhydrous magnesium sulfate. After removal of the ether the residual oil was distilled under reduced pressure to give 4,4-dimethyl-Δ^2-cyclohexenone (II) as a colorless oil (6.8 g, 69%), bp 81–83° (26 mm) [lit.[24] 72.5–73.5° (20 mm)]. *Anal.* Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74; mol wt, 124. Found: C, 77.51; H, 9.76; mol wt (mass spectroscopy), 124.

4,4,5-Trimethyl-Δ^2-cyclohexenone (III). 4,4-Dimethyl-Δ^2-cyclohexenone (0.7 g) and copper acetate monohydrate (0.214 g) were dissolved in anhydrous tetrahydrofuran (20 ml) and stirred under nitrogen in a Dry Ice–acetone bath while (15 min) the Grignard reagent from methyl iodide (1.0 ml) and magnesium (0.4 g) in ether (20 ml) was added dropwise. The mixture was allowed to warm to room temperature, left for 1 hr, heated under reflux for 30 min, and finally decomposed by the addition of excess saturated aqueous ammonium chloride solution. The product was taken into ether (two 15-ml portions), and the combined ether layers were washed with water (two 15-ml portions) and dried (anhydrous magnesium sulfate). The infrared spectrum of the crude product showed that both 1,2- and 1,4-addition products (*i.e.*, allylic alcohol and saturated ketone) were present These were separated by preparative glpc (10-ft 20% Carbowax 20M on 60–80 Chromosorb W, 150°). The first fraction (15%) was shown to be the allylic alcohol (infrared spectrum) and was not characterized further. The second fraction (85%) was shown to be 4,4,5-trimethylcyclohexanone (γ_{max}^{film} 5.80 μ). *Anal.* Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50; mol wt, 140. Found: C, 76.83; H, 11.44; mol wt (mass spectroscopy), 140.

The above saturated ketone (0.5 g) was dissolved in glacial acetic acid (10 ml), protected from moisture, and stirred during the dropwise addition of a solution of bromine in acetic acid (10% w/v, 5.8 ml). The mixture was stirred a further 10 min and poured into water and the bromo ketone taken into ether (two 50-ml portions). The ethereal extracts were combined, washed with water (50 ml) and saturated aqueous sodium bicarbonate solution (50 ml), and dried (anhydrous magnesium sulfate), and the ether was removed. The crude bromo ketone mixture was dissolved in N,N-dimethylacetamide (20 ml); calcium carbonate (0.5 g) was added, and the mixture heated under reflux for 30 min. After filtration the mixture was poured into water and the product taken into ether (two 50-ml portions); the combined ether extracts were washed with water (three 50-ml portions) and dried. The ether was removed, and the mixture of unsaturated ketones thus obtained was separated by

(22) C. Djerassi, D. Marshall, and T. Nakano, *J. Am. Chem. Soc.*, 80, 4853 (1958).

(23) See footnote *d*, Table I.

(24) E. D. Bergmann and R. Corrett, *J. Org. Chem.*, 23, 1507 (1958).

glpc (10-ft 20% Carbowax 20M on 60–80 Chromosorb W, 150°). The products isolated in their order of elution were: (a) **4,4,5-trimethyl-Δ²-cyclohexenone**, 62%, λ_{max}^{film} 5.95 μ [*Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21; mol wt, 138. Found: C, 7790; H, 9.93; mol wt (mass spectroscopy), 138. The nmr spectrum ($CDCl_3$ solution) showed a quadruplet centered at δ 6.25 (J = 10 cps) due to the two vinylic protons at C-2 and C-3]; (b) **3,4,4-trimethyl-Δ²-cyclohexenone (XII)**, 16.5%, λ_{max}^{film} 5.95 μ [*Anal.* Calcd for $C_9H_{14}O$: mol wt, 138. Found: mol wt (mass spectroscopy), 138; $n^{24}D$ 1.4839 (lit.[25] 1.4840)]; (c) **4,4,5-trimethyl-2,5-cyclohexadienone (XIII)**, 19.5%, λ_{max}^{film} 6.02 μ [*Anal.* Calcd for $C_9H_{12}O$: mol wt, 136. Found: mol wt (mass spectroscopy), 136].

In an analogous sequence the enamine from 2-methylpropanal and piperidine was condensed with methyl vinyl ketone to give **4-methyl-4-ethyl-Δ²-cyclohexenone (XIV)**, 61%, a colorless oil, bp 106–109° (31 mm). *Anal.* Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21; mol wt, 138. Found: C, 77.94; H, 10.27; mol wt (mass spectroscopy), 138. 1,4 Addition of methylmagnesium iodide to this cyclohexenone afforded **3,4-dimethyl-4-ethylcyclohexanone**, 73%, as a colorless oil, λ_{max}^{film} 5.78 μ. *Anal.* Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.71; H, 11.82. The 1,2-addition product was also obtained in this reaction, but was not characterized further. The above saturated ketone was brominated and dehydrobrominated as described above and the resulting mixture of unsaturated ketones separated by glpc (10-ft 20% Carbowax 20M on 60–80 Chromosorb W, 150°). Again three products were isolated: (a) **4,5-dimethyl-4-ethyl-Δ²-cyclohexenone (XVI)**, 66%, λ_{max} 228 mμ [*Anal.* Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59; mol wt, 152. Found: C, 78.97; H, 10.54; mol wt (mass spectroscopy), 152]; (b) **3,4-dimethyl-4-ethyl-Δ²-cyclohexenone (XV)**, 21%, λ_{max}^{film} 5.95 μ, λ_{max} 238 mμ [*Anal.* Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59; mol wt, 152. Found: C, 78.60; H, 10.36; mol wt (mass spectroscopy), 152]; (c) **4,5-dimethyl-4-ethyl-Δ²,⁵-cyclohexadienone (XVII)**, 13%, λ_{max}^{film} 6.05 μ, λ_{max} 238 mμ [*Anal.* Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39; mol wt, 150. Found: C, 79.60; H, 9.3; mol wt (mass spectroscopy), 150].

4,4-Di-(d_3-methyl)-5-methyl-Δ²-cyclohexenone (IIIb) (See Scheme II). The Grignard reagent from d_3-methyl iodide (3.1 ml) and magnesium (1.2 g) in ether (40 ml) was stirred under nitrogen and a solution of ethyl ethoxyacetate (3.3 g) in ether (20 ml) was added during 30 min. The reaction mixture was heated under reflux for 30 min, then left overnight at room temperature. A saturated aqueous solution of ammonium chloride was added and the ethereal layer separated. The aqueous layer was extracted with ether; the combined ether layers were dried over anhydrous magnesium sulfate, and the ether was removed. The residual oil was suspended in 15% sulfuric acid (25 ml) and stirred under nitrogen, and the mixture slowly distilled until the temperature of the distillate reached 100°. The distillate was taken up in ether (25 ml), dried over anhydrous potassium carbonate, and filtered. A further quantity of anhydrous potassium carbonate (5 g) was added, the mixture was cooled in ice, and piperidine (5 ml) added with swirling. The mixture was kept at 0° overnight, filtered, and distilled under reduced pressure. The fraction bp 97–99° (90 mm) was collected and shown by mass spectrum and glpc (5-ft 15% Apiezon on 60–80 Chromosorb W, 100°) to be 95% 1,1-di-(d_3-methyl)-2-piperidinoethene (0.76 g, 22%). The foregoing enamine (0.76 g) was cooled and stirred under nitrogen and redistilled methyl vinyl ketone (0.4 g) added. The mixture was stirred at room temperature under nitrogen for 90 hr, then 15% hydrochloric acid (6 ml) added. The mixture was left a further 24 hr, heated on a steam bath for 1 hr, diluted to 75 ml with water, and thoroughly extracted with ether. The ether extracts were washed with water and dried over anhydrous magnesium sulfate; the ether was removed and the residual oil bulb distilled under reduced pressure. **4,4-Di-(d_3-methyl)-Δ²-cyclohexenone** was obtained as a colorless oil (0.42 g, 62%), bp 120–140° (bath) (28 mm), λ_{max}^{film} 5.95 μ. The nmr and mass spectra indicated deuterium incorporation of 98% with no rearrangement of deuterium from the two 4-d_3-methyl substituents. **4,4-Di-(d_3-methyl)-5-methyl-Δ²-cyclohexenone (IIIb)** was prepared from the preceding ketone by the procedure used for the synthesis of the unlabeled analog III described earlier. The nmr spectrum showed a quadruplet at δ 6.25 (J = 10 cps) (two vinylic protons) and a doublet at δ 0.95 (J = 6 cps) (three methyl protons). The nmr and mass spectra indicated that deuterium incorporation was 98% with no rearrangement of deuterium from the two 4-d_3-methyl substituents.

(25) E. R. Buchman and H. Sargent, *J. Org. Chem.*, 7, 140 (1942).

4-Methyl-4-phenyl-Δ²-cyclohexenone (XVIII). A solution of α-phenylpropionaldehyde (25.0 g) and redistilled methyl vinyl ketone (15.0 g) in *t*-butyl alcohol (125 ml) was stirred under nitrogen and cooled in ice during the dropwise addition of 30% aqueous Triton B hydroxide (31 ml). The addition required 15 min and the mixture was stirred at 0° a further 2 hr. The reaction mixture was poured into water and extracted thoroughly with ether. The ether extract was washed with water and dried over anhydrous magnesium sulfate and the ether removed. The crude residue was distilled at reduced pressure to give **4-methyl-4-phenyl-Δ²-cyclohexenone** as a colorless oil which crystallized on scratching, bp 110–120° (0.5 mm). On recrystallization from ether at low temperature the ketone afforded colorless needles, mp 40°. *Anal.* Calcd for $C_{13}H_{14}O$: mol wt, 186. Found: mol wt (mass spectroscopy), 186.

4,5-Dimethyl-4-phenyl-Δ²-cyclohexenone (XIX). A stirred solution of α-phenylpropionaldehyde (1.34 g) and pent-2-en-3-one[26] (0.84 g) in *t*-butyl alcohol (5 ml) was cooled to 5° in ice and 30% aqueous Triton B hydroxide (1.5 ml) was added during 30 min. The mixture was stirred at 5–10° a further 2 hr and poured into water, and the product was extracted into ether. The ether extract was washed with water and dried and the ether removed. The residue was bulb distilled at bath temperature, 145–150° (0.5 mm), to give **4,5-dimethyl-4-phenyl-Δ²-cyclohexenone** as a pale yellow viscous oil which did not crystallize at room temperature. A portion was purified by glpc (5-ft 20% silicone rubber on 60–80 Chromosorb W, 175°). *Anal.* Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05; mol wt, 200. Found: C, 83.75; H, 8.01; mol wt (mass spectroscopy), 200.

4,5-Dimethyl-4-(*p*-bromophenyl)-Δ²-cyclohexenone (XX). A mixture of *p*-bromoacetophenone (10 g), ethyl chloroacetate (6.75 g), and *t*-butyl alcohol (50 ml) was stirred under nitrogen and cooled to 15°. A solution of potassium *t*-butoxide (6.15 g) in *t*-butyl alcohol (50 ml) was added during 1.5 hr. A gelatinous precipitate formed and made stirring difficult. The mixture was left at 21° for 2 days, poured into water (200 ml), and extracted with ether (two 100-ml portions). The ether extract was washed with water and dried over anhydrous magnesium sulfate and the ether removed. The residue was distilled (3 mm) and the fraction bp 140–155° collected and redistilled (1 mm). The glycidic ester (5.6 g) was obtained as an oil, bp 125–140°, and was used directly in the next step. The crude ester (5.3 g) was dissolved in dry ethanol (10 ml) and sodium methoxide (1 g) was added. Upon addition of water (0.34 ml), the sodium salt of the glycidic acid began to precipitate, and was collected after 24 hr, washed with ether, and air dried. The salt was suspended in ether (50 ml), and dry hydrogen chloride was bubbled through the mixture for 30 min. Heat was evolved; the salt dissolved, and finely divided sodium chloride separated. The mixture was filtered on Kieselguhr; the residue was washed with ether and the combined ethereal solutions were evaporated, leaving a yellow gum which crystallized on trituration with pentane. A solution of sodium bicarbonate (4 g) in water (20 ml) was added and the mixture allowed to stand for 2 hr, then heated on a steam bath for 15 min. The cooled mixture was extracted with ether, and the ether extract washed with water, dried over anhydrous magnesium sulfate, and evaporated. The residual oil was distilled under reduced pressure to give α-(*p*-bromophenyl)propionaldehyde as a pale yellow oil (1.72 g), bp 158–163° (36 mm). *Anal.* Calcd for C_9H_9BrO: C, 50.73; H, 4.26. Found: C, 50.54; H, 4.01. **4,5-Dimethyl-4-(*p*-bromophenyl)-Δ²-cyclohexenone** was prepared from aldehyde (1 g) and pent-2-en-3-one (0.4 g) in a manner analogous to that described above for the preparation of 4,5-dimethyl-4-phenyl-Δ²-cyclohexenone. It was obtained as colorless needles, mp 118°. *Anal.* Calcd for $C_{14}H_{15}BrO$: C, 60.23; H, 5.42. Found: C, 60.36; H, 5.73.

3-Methyl-4,4-diphenyl-Δ²-cyclohexenone (XXII). This ketone was prepared from 4,4-diphenyl-Δ²-cyclohexenone[27] by 1,4 addition of methylmagnesium iodide, followed by bromination and dehydrobromination of the resulting saturated ketone using procedures already described in the synthesis of 4,4,5-trimethyl-Δ²-cyclohexenone (III). The 1,4-addition product in the first step was separated from some 1,2-addition product (allylic alcohol) by fractional crystallization from methanol. Separation of the mixture of unsaturated ketones obtained in the final step was achieved by repeated thin layer chromatography on silica gel GF_{254} (Stahl)

(26) S.-O. Lawesson, E. H. Larsen, G. Sundstrom, and H. J. Jakobsen, *Acta Chem. Scand.*, 17, 2216 (1963).

(27) See footnote *h*, Table I.

containing 5% silver nitrate, using 20% ether in benzene as eluent. Bands were detected by ultraviolet light, separated, and extracted with ether. Only two products were isolated, and both were shown by infrared spectroscopy to be unsaturated ketones. The more easily eluted product was not obtained free from saturated ketone even on repeated chromatography. The less mobile product crystallized from methanol–water as colorless prismatic needles, mp 106°. The nmr spectrum showed a singlet at δ 6.2 integrating for one proton (vinylic) and a doublet at δ 1.61 (J = 1 cps) integrating for three protons (methyl group attached to double bond), indicating that the compound was **3-methyl-4,4-diphenyl-Δ^2-cyclohexenone (XXII)**. *Anal.* Calcd for $C_{19}H_{18}O$: C, 86.99; H, 6.92; mol wt, 262. Found: C, 86.57; H, 6.86; mol wt (mass spectroscopy), 262.

4,5-Dimethyl-Δ^2-cyclohexenone (XXIII). 3,4-Dimethylcyclohexanol was oxidized by Jones' reagent[10] to 3,4-dimethylcyclohexanone. Bromination and dehydrobromination as already described gave a mixture of unsaturated ketones, which was separated by glpc (10-ft 20% IGEPAL on 60–80 Chromosorb W, 150°). The most abundant product was shown by infrared (λ_{max}^{film} 5.95 μ) and ultraviolet (λ_{max} 228 mμ) spectra to be 4,5-dimethyl-Δ^2-cyclohexenone. *Anal.* Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74; mol wt, 124. Found: C, 77.24; H, 9.57; mol wt (mass spectroscopy), 124. The other isomer was not characterized further.

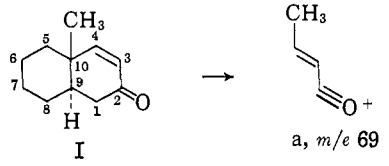
Mass Spectrometry in Structural and Stereochemical Problems. CXXXIV.[1] Electron Impact Induced Alkyl and Aryl Rearrangements in α-Arylidene Cyclic Ketones[2]

R. L. N. Harris,[3a] F. Komitsky, Jr.,[3b] and Carl Djerassi

Contribution from the Department of Chemistry, Stanford University, Stanford, California 94305. *Received April 4, 1967*

Abstract: The mass spectra of a number of alkyl- and aryl-substituted α-arylidene cyclic ketones have been measured and the mechanism and scope of an electron impact induced alkyl (aryl) rearrangement occurring in these compounds is examined. Other fragmentation processes occurring in this class of compounds are also discussed.

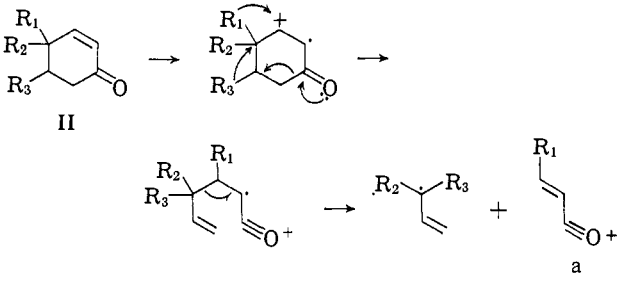
Ketones of type I display a prominent peak in their mass spectra at m/e 69 which has been shown[4] to be due to the formation of the ion a, arising from a 1,2 rearrangement of the angular methyl group from C-10 to C-4 prior to fragmentation. In an earlier paper[5] the mechanism and scope of this rearrangement was discussed and it was found to occur in ketones of general formula II where R_1 = H, Me, Et, and Ph, and R_2 and R_3 are either methyl groups or part of a second alicyclic ring (five, six, or seven membered) Of particular interest was the fact that certain closely related ketones (II, R_3 = H) did not display any significant



I a, m/e 69

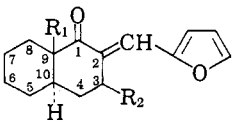
rearrangement ions in their mass spectra. From this and other evidence it was concluded that the C-5 alkyl substituent was implicated in the rearrangement process; of the various plausible mechanistic rationalizations outlined earlier[5] only that summarized in Scheme I is compatible with all of the experimental results.

Scheme I

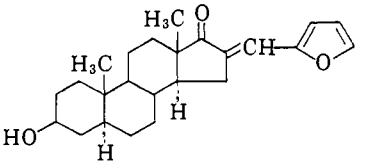


II a

An earlier communication[6] has drawn attention to the occurrence of a related rearrangement in the mass spectra of 2-arylidene-1-decalones. Thus, the base peak in the mass spectrum of *trans*-2-furfurylidene-9-methyl-1-decalone (III) and the analogous steroidal D-homo ketone IV occurs at m/e 121 and was shown by exact mass measurements to correspond to C_8H_9O. This peak was shifted to m/e 124 in the spectrum of the 9-d_3-methylated analog IIIa and to m/e 122 in that of the 3-d_1 analog IIIb, whereas in the spectrum of the compound lacking the angular methyl group (V) the base



III, R_1 = Me, R_2 = H
IIIa, R_1 = CD_3, R_2 = H
IIIb, R_1 = Me, P_2 = D
V, R_1 = H, R_2 H



IV

(1) For paper CXXXIII see P. Brown and C. Djerassi, *Angew. Chem.*, in press.

(2) Financial assistance by the National Institutes of Health (Grants No. AM-04257 and CA-07195) is gratefully acknowledged. The purchase of the Atlas mass spectrometer was made possible through NASA Grant NsG 81-60.

(3) Postdoctoral Research Fellow: (a) 1965–1966; (b) 1964–1965.

(4) F. Komitsky, Jr., J. E. Gurst, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 1398 (1965).

(5) R. L. N. Harris, F. Komitsky, Jr. and C. Djerassi, *ibid.*, **89**, 4765 (1967).

(6) C. Djerassi, A. M. Duffield, F. Komitsky, Jr., and L. Tökes, *ibid.*, **88**, 860 (1966).