

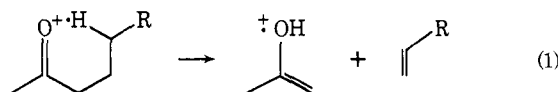
Mass Spectrometry of Organic Compounds. IX.^{1a} McLafferty Rearrangements in Some Bicyclic Ketones

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Abstract: An examination of the mass spectra of isotopically labeled bicyclo[4.2.1]nonan-9-one (1), bicyclo[5.2.1]decan-10-one (2), bicyclo[4.3.1]decan-10-one (3), and bicyclo[5.3.1]undecan-11-one (4) has shown that the ions of *m/e* 84 and 98 in the spectra of 2 and 4 most probably arise by McLafferty rearrangement. This conclusion is noteworthy in view of the large angle that the γ hydrogens must make with the plane of the carbonyl group in these compounds.

Among the many and varied itinerations undergone by hydrogen atoms on electron impact of organic molecules,² none has received as much attention as the rearrangement that has become known as the McLafferty rearrangement (eq 1). A recent review³ lists



over 250 references dealing with the mechanistic aspects of this and related rearrangements, and the rearrangement has been used times without number for purposes of structural elucidation. It has become important for diagnostic purposes precisely because it is so well documented and well understood. Thus, it is known³ that rearrangement involves the specific migration of a γ -hydrogen atom to the carbonyl oxygen atom, followed by cleavage of the bond between the carbon atoms α and β to the carbonyl group, to yield (usually) an ionized enol fragment and an olefin. Structural effects on the rearrangement are well documented; formation of stable product ions provides a substantial driving force for the reaction, while the greater tendency for secondary hydrogens to migrate compared with primary hydrogens, or hydrogen atoms compared with deuterium atoms, is well known. Steric effects on the rearrangement are less well understood, however, and the study of one aspect of these effects forms the subject of this paper.

Previous studies of the effect of the stereochemistry of the substrate on the McLafferty rearrangement have been limited almost exclusively to an investigation of the maximum value possible for the H_γ -O interatomic distance. In a definitive series of papers⁴ Djerassi and his coworkers showed from their investigation of the rearrangement of various steroids that rearrangement

did not occur if the interatomic distance between the γ hydrogen and the receptor oxygen was greater than 1.8 Å. Similar conclusions were drawn from a study of the rearrangement of the exo and endo isomers of 2-acetylnorbornane.⁵

The other major steric factor which might influence the rearrangement is the angle τ between the itinerant hydrogen atom and the plane of the carbonyl group (Figure 1). In normal acyclic aldehydes and ketones this angle can approach 0°, and it has been stated⁶ that "the observed specificity for rearrangement of the γ hydrogen is in accord with steric requirements for overlap of the highly directional orbital of the unpaired electron on oxygen." The point of interest in the current work concerns the effect of increasing the angle τ from 0° to its maximum value of 90°. Will McLafferty rearrangement still occur or will it become inoperative at some value of τ between 0 and 90°? If the latter statement is correct, at what angle does the rearrangement become essentially inoperative?

The only work that bears directly on this question is the theoretical study of the McLafferty rearrangement by Boer, Shannon, and McLafferty.⁷ These investigators used nonempirical molecular orbital calculations to estimate the energy of the transition state for hydrogen transfer and showed that transition states in which τ is appreciably greater than 0° have significantly higher energies than those in which τ is close to 0°. They concluded that the planar transition state is the favored one. While this conclusion is undoubtedly valid for the simple system for which the calculations were made, it does not solve the problem of what happens when a molecule is constrained to approach rearrangement through a nonplanar transition state. Some insight into this question may be obtained from studies on various monocyclic ketones.⁸ In these studies it has been shown that McLafferty rearrangement can take place, albeit with reduced ion abundance, in ketones as small as cyclononane. A study of a

(1) (a) Part VIII: D. G. I. Kingston, H. P. Tannenbaum, and H. G. Kuivila, *Org. Mass Spectrom.*, **9**, 31 (1974); (b) abstracted from the Ph.D. Thesis of J. D. Henion, State University of New York at Albany; (c) Virginia Polytechnic Institute and State University.

(2) J. T. Bursey, M. M. Bursey, and D. G. I. Kingston, *Chem. Rev.*, **73**, 191 (1973).

(3) D. G. I. Kingston, M. M. Bursey, and J. T. Bursey, *Chem. Rev.*, **74**, 215 (1974).

(4) D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Amer. Chem. Soc.*, **85**, 2091 (1963); D. H. Williams and C. Djerassi, *Steroids*, **3**, 259 (1964); C. Djerassi, G. von Mutzenbecher, J. Fajkos, D. H. Williams, and H. Budzikiewicz, *J. Amer. Chem. Soc.*, **87**, 817 (1965); C. Djerassi and L. Tökés, *ibid.*, **88**, 536 (1966); L. Tökés, R. T. LaLonde, and C. Djerassi, *J. Org. Chem.*, **32**, 1020 (1967).

(5) A. F. Thomas and B. Willhalm, *Helv. Chim. Acta*, **50**, 826 (1967).

(6) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, p 155.

(7) F. P. Boer, T. W. Shannon, and F. W. McLafferty, *J. Amer. Chem. Soc.*, **90**, 7239 (1968).

(8) (a) D. H. Williams, H. Budzikiewicz, Z. Pelah, and C. Djerassi, *Monatsh. Chem.*, **95**, 166 (1964); (b) K. H. Schulte-Elte, B. Willhalm, A. F. Thomas, M. Stoll, and G. Ohloff, *Helv. Chim. Acta*, **54**, 1759 (1971).

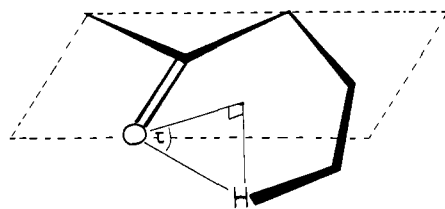
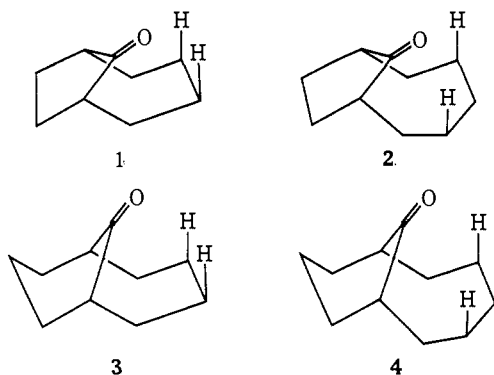


Figure 1. Approach of a γ hydrogen at an angle τ to the plane of the carbonyl group.

Dreiding model of cyclononane shows that the γ hydrogen cannot approach the carbonyl oxygen in the plane of the carbonyl group but must instead approach it at a significant angle. However, these compounds are not entirely suitable for a detailed study of steric effects on the rearrangement. This is so because the many conformations available to such flexible molecules together with the large amounts of energy associated with an ionized molecule preclude an accurate evaluation of τ values in reacting ions. We therefore turned our attention to the more rigid bicyclic systems described below.

Results and Discussion

Any model system for the study of steric effects on the McLafferty rearrangement must meet a number of criteria. In the first place, it should be a system which would undergo rearrangement in an unambiguous manner, if it rearranges at all. Secondly, it should be reasonably rigid, so that conformational effects are reduced to a minimum. Thirdly, it should be possible to prepare a series of compounds of related structure, differing significantly only in the angle of interest τ . Fourthly, all members of the series should have γ -hydrogen to oxygen internuclear distances of 1.8 Å or less. Finally, it should be possible to prepare specifically deuterated molecules to test the specificity of the rearrangement. The compounds which most nearly meet these requirements are the bicycloalkanes 1-4.⁹⁻¹¹ The salient features of the geometry of these



molecules (as measured from Dreiding models) are summarized in Table I. It should be noted that the actual geometries obtainable in an excited ion will vary to some extent from those given in the table, but the values given should be fairly close to the mean values of the parameters in the excited ion.

(9) C. D. Gutsche and T. D. Smith, *J. Amer. Chem. Soc.*, **82**, 4067 (1960).

(10) R. D. Sands, *J. Org. Chem.*, **34**, 2794 (1969).

(11) E. W. Warnhoff, C. M. Wong, and W. T. Tai, *J. Org. Chem.*, **32**, 2664 (1967).

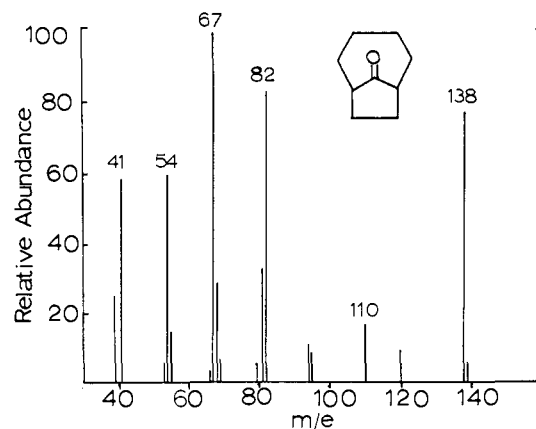


Figure 2. Mass spectrum of bicyclo[4.2.1]nonan-9-one (1) at 70 eV.

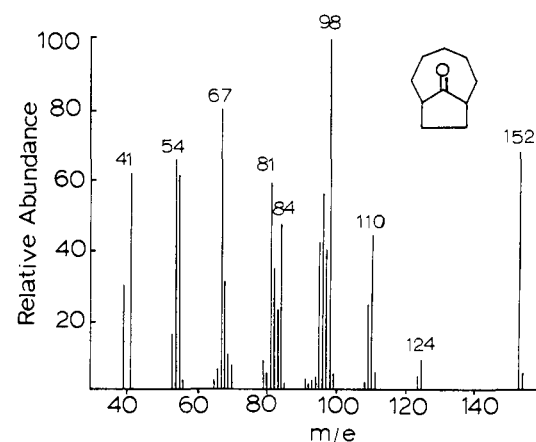


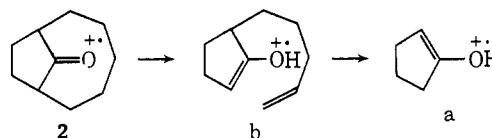
Figure 3. Mass spectrum of bicyclo[5.2.1]decan-10-one (2) at 70 eV.

Table I. Molecular Parameters of the Ketones 1-4

Ketone	$H_\gamma-O$, Å ^a	τ° ^a
Bicyclo[4.2.1]nonan-9-one (1)	1.6	80
Bicyclo[5.2.1]decan-10-one (2)	1.6	50
Bicyclo[4.3.1]decan-10-one (3)	2.0	80
Bicyclo[5.3.1]undecan-1-one (4)	1.5	50

^a Distance and angle measured at the position of closest approach of H_γ to O.

A study of Table I indicates that a comparison of the behavior on electron impact of ketones 1 and 2 should be especially rewarding since both of them meet the requirement that the γ -hydrogen to oxygen distance should be less than 1.8 Å, while they differ substantially in their interatomic angle τ . Any rearrangement undergone, for example, by ketone 2 would be manifested by further rearrangement of the initial rearranged ion to give an ion of m/e 84 ($2 \rightarrow a \rightarrow b$).^{3,12}

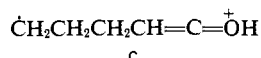


An examination of the mass spectra of ketones 1 and 2 (Figures 2 and 3) provided striking evidence for the importance of the interatomic angle τ on the McLafferty rearrangement. Compound 1 shows no ion at

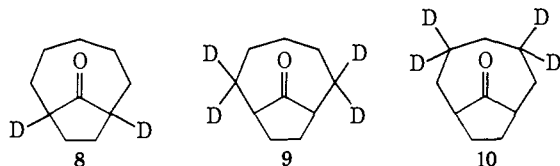
(12) Reference 6, p 160.

m/e 84, while in compound **2** the ion at m/e 84 is relatively very intense, amounting to about 50% of the intensity of the base peak at m/e 98. The absence of an ion at m/e 84 in the spectrum of ketone **1** may be taken as conclusive proof that McLafferty rearrangement is not occurring in this compound. In addition, it also proves that alternate pathways to m/e 84 (involving, for example, prior cleavage of one of the rings followed by appropriate hydrogen rearrangements) do not occur in this molecular ion. Since fragmentations involving prior ring cleavage would presumably be less likely to occur in the less strained ketone **2**, it may be inferred that formation of m/e 84 by pathways other than the McLafferty rearrangement will not occur in this molecular ion either. The observation of a significant peak of m/e 84 in the mass spectrum of compound **2** is thus strong evidence that the McLafferty rearrangement ($2 \rightarrow a \rightarrow b$) is taking place in its molecular ion.¹³

Support for the formulation of the ion at m/e 84 in the mass spectrum of compound **2** as the enolic product ion of a McLafferty rearrangement came from a study of the decomposition of this and related ions in the first field-free region of a double focusing mass spectrometer. A study of the fragmentations of the m/e 84 ions generated from cyclopentanone (**5**), 2-*n*-propylcyclopentanone (**6**), and 2-ethyl-5-*n*-propylcyclopentanone (**7**) showed that the fragmentation m/e 84 \rightarrow m/e 69 occurs from the presumably enolic ions of the latter two compounds, but *no* such fragmentation could be detected for the keto ion generated from cyclopentanone. The m/e 84 ion formed from **2**, however, did give a strong metastable peak for the m/e 84 \rightarrow m/e 69 transition, supporting its formulation as an enolic ion. It should be noted, however, that other structures such as the open-chain isomer **c** are not excluded by this evidence.



Although the evidence outlined above provides strong support for the formulation of the m/e 84 ion as the product of a McLafferty rearrangement, it was judged desirable to study the fragmentation of some deuterated analogs of **2**. To this end **8-10** were pre-



pared and their mass spectra obtained. Since there is significant interference in the region m/e 81-83 from hydrocarbon ions, the relative abundances of the oxygen-containing ions in the region m/e 81-87 were obtained for each of the compounds **2** and **8-10** at a resolution of 2000. The results of this study are given in Table II. Inspection of the data of Table II indicates that formation of the ion **b** is occurring largely, but not completely, with the specificity associated with the McLafferty rearrangement. Thus, essentially both the deuterium atoms of **8** are retained in the ion **b** (shift to m/e 86) while almost none of the deuterium atoms of **9**

(13) A metastable peak was observed for this transition and all other transitions discussed in this paper.

Table II. Oxygen-Containing Ions from the Ketones **2** and **8-10**

m/e	Relative intensity of selected ions ^a							
	2		8^b		9^c		10^d	
	70 eV	14 eV	70 eV	14 eV	70 eV	14 eV	70 eV	14 eV
82	0.148		0.025		0.080		0.038	
83	0.306	0.220	0.104		0.146	0.045	0.124	
84	0.576	0.780	0.047	0.058	0.462	0.893	0.245	0.208
85			0.314	0.210	0.312	0.062	0.400	0.510
86			0.510	0.732			0.192	0.282

^a Corrected for natural abundance ¹³C and normalized in the region of interest. ^b 96% d_2 , and 4% d_1 . ^c 94.4% d_4 , 1.9% d_3 , 0.7% d_2 , and 2.9% d_0 . ^d 50.2% d_4 , 29% d_3 , 12.7% d_2 , 1.5% d_1 , and 5.5% d_0 .

are retained (at 14 eV the major peak remains at m/e 84). The case of compound **10** is more difficult to interpret because of the low deuterium incorporation that was obtained by the synthetic method used. A statistical analysis of the data indicates that approximately 45% of the ions at m/e 84 in the unlabeled compound must be formed by pathways involving the transfer of *two* hydrogens from the γ position; the remaining $\text{C}_6(\text{H},\text{D})_6\text{O}$ ions are formed by processes involving transfer of one or none of the γ hydrogens to this ion.¹⁴ It thus appears that rearrangement of **2** to the m/e 84 ion occurs with the specificity associated with the McLafferty rearrangement at least to the extent of 45%. It is not possible on the present evidence to determine whether the remaining nonspecific rearrangement is due to hydrogen scrambling prior to specific rearrangement or to the occurrence of various nonspecific rearrangement pathways. If the former explanation is the case, then hydrogen scrambling must not involve the hydrogens α and β to the carbonyl group to any significant extent, since these hydrogens were specifically retained or lost in the m/e 84 ion. A further objection to the hydrogen scrambling rationalization is that scrambling in aliphatic ketones has been shown to become more extensive as the ionizing voltage is lowered.¹⁵ In the case of ketone **2**, however, the specificity of the rearrangement to give m/e 84 increases slightly as the ionizing voltage is lowered; at a nominal 14 eV the rearrangement proceeds with approximately 50% specificity for the transfer of two γ -hydrogen atoms. This suggests that competing higher energy fragmentation pathways become less important at lower energies of the ionizing voltage. This effect must be more than enough to counterbalance any increase in hydrogen scrambling that takes place.

It may thus reasonably be concluded that the available evidence points strongly to the formation of the ion at m/e 84 from **2** by a McLafferty rearrangement. In view of the later discussion of the mass spectrum of the isomeric compound bicyclo[4.3.1]decan-10-one, we wish specifically to point out that the ring-opening pathway below ($2 \rightarrow d \rightarrow b$) does *not* give the m/e 84 ion with the labeling patterns observed.¹⁶

(14) Full details of this calculation are given in the Ph.D. thesis of J. D. Henion, State University of New York at Albany, 1972. Ignoring isotope effects, transfer of deuterium atoms from the γ position would be in the ratio $d_2:d_1:d_0 = 0.74:0.22:0.04$ for completely specific rearrangement.

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

(16) The failure of compound **1** to yield an ion at m/e 84 may be due to the fact that the increased ring strain in this compound makes other fragmentation processes more favorable than the McLafferty rearrangement. A study of the spectra of compounds **1** and **2** at low-ionizing

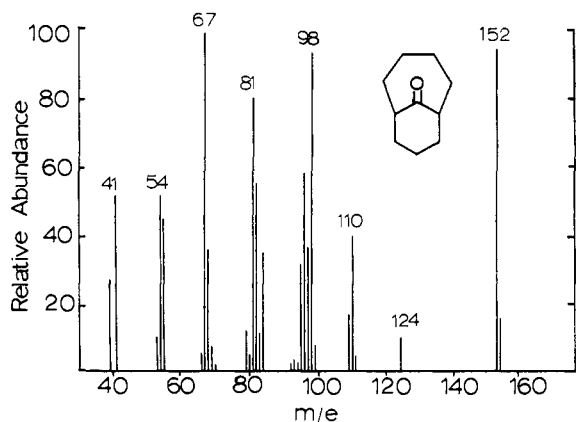
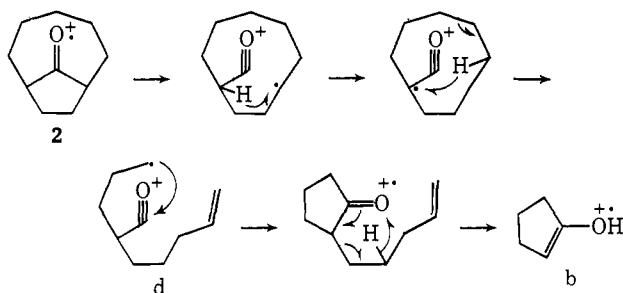
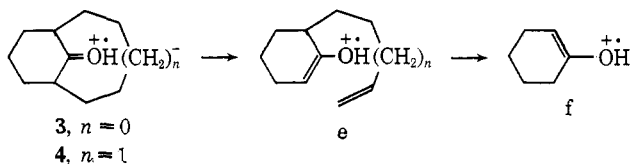


Figure 4. Mass spectrum of bicyclo[4.3.1]decan-10-one (**3**) at 70 eV.

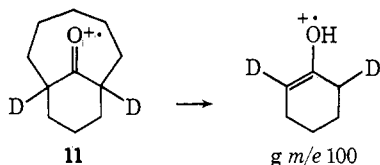


As a further test of the effect of the interatomic angle τ on the McLafferty rearrangement, the mass spectra of the ketones **3** and **4** were obtained. In these cases rearrangement would be expected to give an ion **f** at m/e 98 (**3**, **4** \rightarrow e \rightarrow f). According to the data of Table



I, however, McLafferty rearrangement of **3** should be precluded by the $H_{\gamma}-O$ distance of 2.0 Å, while **4** would be expected to undergo rearrangement in a comparable manner to **2**. We were thus surprised to observe that *both* **3** and **4** showed significant ions at m/e 98; in compound **4** this ion represented the base peak of the spectrum (Figures 4 and 5).

In the case of compound **4**, there is reason to believe that the ion at m/e 98 is indeed formed by the McLafferty rearrangement (**4** \rightarrow e). Thus, in the spectrum of the α - d_2 -[5.3.1] ketone (**11**) the rearrangement ion



g appeared at m/e 100; such an ion would appear at m/e 99 if rearrangement occurred by a ring-opening pathway such as **11** \rightarrow h. The m/e 98 ion most probably

voltage suggests that the formation of the m/e 110 ion from **1** has a lower appearance potential than the formation of the m/e 84 ion from **2**. However, in view of the complete absence of the m/e 84 ion from the spectrum of **1**, we believe that the tendency for the McLafferty rearrangement has indeed been reduced in this compound. We thank a referee for bringing this point to our attention.

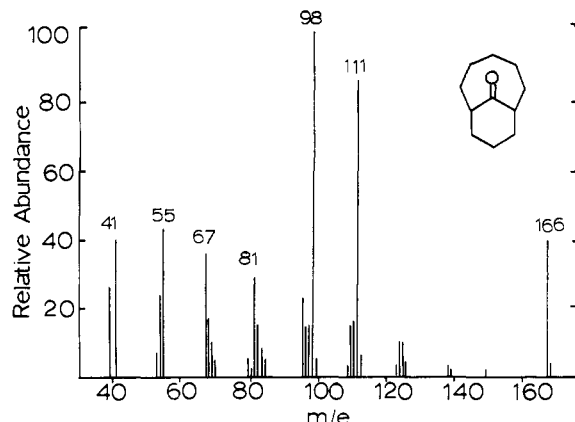
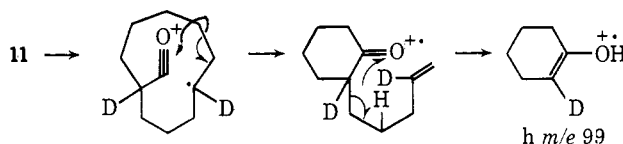
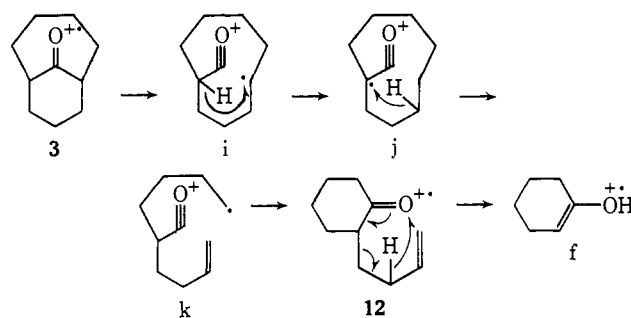


Figure 5. Mass spectrum of bicyclo[5.3.1]undecan-11-one (**4**) at 70 eV.



has an enolic structure, since a metastable peak was observed for its conversion to the ion at m/e 70 by the retro-Diels-Alder reaction, while *no* metastable peak was observed for its conversion to m/e 97, even when metastable peaks formed in the first field-free region were examined. Since the transition m/e 98 \rightarrow m/e 97 is not observed for the enol ion,^{8b} while the transition m/e 98 \rightarrow m/e 70 is typical of the enol ion,¹⁷ this evidence suggests an enolic structure for the m/e 98 ion. An analogous conclusion is drawn for the case of the m/e 98 ion derived from bicyclo[9.3.1]pentadecan-15-one by double McLafferty rearrangement.^{8b}

Since the observation of an intense ion at m/e 98 in the mass spectrum of ketone **3** cannot be explained by the McLafferty rearrangement, the best rationalization involves ring opening followed by hydrogen rearrangements as indicated below (**3** \rightarrow i \rightarrow j \rightarrow k \rightarrow 12 \rightarrow f). Unfortunately, deuterium labeled compounds



were not available to test this pathway, but exact mass measurement established the composition of the ion as $C_6H_{10}O$. A process similar to the conversion of **3** to **12** has previously been proposed to account for the formation of the ion $C_4H_5O^+$ in the mass spectrum of cyclohexanone.¹⁸ Certainly if the ketone **12** were formed, its rearrangement to the ion **f** would be expected to be very facile. This indeed proved to be the

(17) H. Budzikiewicz, J. I. Brauman, and C. Djerassi, *Tetrahedron*, **21**, 1855 (1965).

(18) J. Seibl and T. Gaumann, *Z. Anal. Chem.*, **197**, 33 (1963); *Helv. Chim. Acta*, **46**, 2857 (1963).

case; on electron impact an independently synthesized sample of **12**¹⁹ gave an ion at *m/e* 98 as its base peak.

Conclusion

The arguments presented above lead to the conclusion that at least part of the mass 84 ions from compound **2** arise through a double McLafferty rearrangement. The evidence from deuterium labeling supports a mechanism for the formation of these ions which has the specificity associated with the McLafferty rearrangement and excludes any simple mechanism involving prior ring opening of the bicyclic system. The structure of the mass 84 ion has not been established unambiguously, but it clearly is not a keto structure and may most probably be assigned as an enol. We thus find that the rearrangement process to form the mass 84 ion from compound **2** meets all the tests for the McLafferty rearrangement, and it seems safe to conclude that it is in fact a McLafferty rearrangement.

In the case of compound **4** the evidence for the formation of the mass 98 ion by a double McLafferty rearrangement is less clear-cut. However, the limited deuterium labeling evidence available does exclude the most obvious ring-opening pathway to this ion, and the evidence from metastable peaks is consistent with an enolic structure for it. We thus conclude that the evidence for compound **4** is consistent with (but does not demand) formation of the mass 84 ion by a double McLafferty rearrangement.

The observation that McLafferty rearrangement can and does occur in at least one compound where the

(19) J. M. Conia and F. Leyendecker, *Bull. Soc. Chim. Fr.*, 830 (1967).

angle τ between the plane of the carbonyl group and the γ -hydrogen atom is as high as 50° indicates that this particular steric effect is of less importance than had previously been calculated⁷ in determining occurrence of rearrangement. Clearly further theoretical investigations are needed before we can be said fully to understand this remarkable reaction.

Experimental Section

All mass spectra were recorded with an AEI-MS-902 double focusing mass spectrometer (heated inlet 225°, ion source temperature 50°). Metastable transitions in the first field-free region were observed with the aid of the metastable defocusing technique.²⁰ All spectral measurements were performed on substances which were purified by vapor phase chromatography (vpc) (8 ft \times 0.25 in. SE-30, 20% on 60–80 mesh Chromosorb P or 8 ft \times 0.25 in. Apiezon L, 10% on 5% H₃PO₄ washed 60–80 mesh Chromosorb W).

Deuterated Compounds. Deuterated compounds were prepared by suitable modifications of published procedures.^{9–11} The α -deuterated compounds **8** and **11** were prepared by deuterium exchange of the parent compound. The β -deuterated compound **9** was prepared by diazo insertion⁹ into cyclohexanone-2,2,6,6-*d*₄, and the γ -deuterated compound **10** was similarly prepared by diazo insertion into cyclohexanone-3,3,5,5-*d*₄.^{8a}

Acknowledgment. We thank Dr. R. D. Sands for a gift of 1-carboxybicyclo[4.3.1]nonan-9-one, Dr. E. Warnhoff for a gift of bicyclo[5.3.1]undecan-11-one, and Dr. A. W. Herriott for assistance with a deuterium exchange experiment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

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Molecular Design by Cycloaddition Reactions. IV.¹ Cycloaddition Reactions of Cycloheptatriene with 2-Pyrene Derivatives

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Abstract: Cycloaddition reactions of cycloheptatriene with coumalic acid and its ester afforded two bridged tetracycoundecadiene derivatives **3** and **4** together with [6 + 4] cycloadduct **5**, respectively. Similar reactions with 4,6-dimethylcoumalic acid and its ethyl ester gave only compounds **11**, and **12**, respectively. The structures of these cage adducts were deduced from spectral evidence.

Among Diels–Alder reactions of 2-pyrene derivatives with a variety of dienophiles, those with acetylenic compounds have been reported to give benzene derivatives by loss of carbon dioxide from the intermediate adducts.² In the case of alkyl coumalate, the reactions of electron-rich dienophiles (*i.e.*, dieno-

philes with inverse electron demand) give readily cycloadducts as suggested by extended Hückel MO calculation of the net charge distribution on methyl coumalate.³ Recently, double Diels–Alder reactions of coumalic acid with 1,3-dienes have been documented.⁴ However, similar reactions with conjugated trienes

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(3) J. A. Reed, C. L. Schilling, Jr., R. F. Tarcin, T. A. Rettig, and J. K. Stille, *J. Org. Chem.*, 34, 2188 (1969).

(4) (a) T. Imagawa, M. Kawanishi, and K. Sisido, *Chem. Commun.*, 1292 (1971); (b) *ibid.*, 288 (1972).