sults also reflect the relative thermodynamic affinities (*i.e.*, β subunits prefer carbon monoxide to oxygen as ligands by a larger margin than do α subunits), we should expect carbon monoxide to be replaced by oxygen more readily from α than from β subunits. Accordingly, if Gibson's kinetic results do reflect the differential thermodynamic affinities for oxygen *vs.* carbon monoxide of α and β subunits, we tentatively conclude that the resonance at lower field (which is the one more readily removed by oxygen) represents ^{13}CO bound to α subunits of rabbit hemoglobin.

In summary, this work indicates that significant differences exist in the nature of the environment experienced by carbon monoxide when bound to α or β subunits of a variety of hemoglobins. These differences do not appear to be significantly affected over the range pH 6.5–7.5 and, at least in the case of rabbit HbCO, are not affected by 2,3-diphosphoglycerate. Moreover, the ease of displacement of CO by O_2 differs markedly for CO bound to the α or β subunits of rabbit hemoglobin.

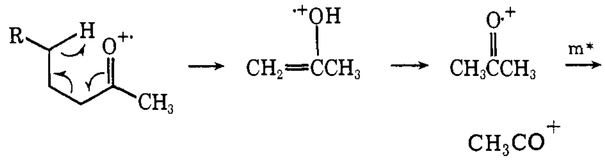
Acknowledgment. We wish to thank K. Dill for providing myoglobin samples and Dr. D. Powars of the Los Angeles County-USC Medical Center for providing samples of fetal blood.

Richard B. Moon, John H. Richards*
Contribution No. 4449
Gates and Crellin Laboratories of Chemistry
California Institute of Technology
Pasadena, California 91109
Received April 21, 1972

Reketonization of a McLafferty Product Ion Studied by Ion–Molecule Reactivity

Sir:

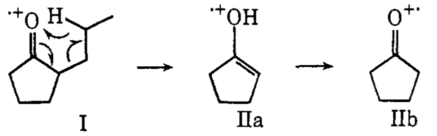
The nature of the McLafferty product of a ketone molecular ion has been inferred to be of enolic structure at its time of formation.[1] Recently it has been determined that for at least some aliphatic ketones the metastable McLafferty product decomposing by loss of methyl scrambles in such a way as to suggest reketonization of the enolic form (eq 1).[2] In the case of an aryl alkyl ketone, the ion kinetic energy spectrum indicates that the metastable McLafferty product which loses methyl is not reketonized.[3] A distinction may therefore be made between the behavior of purely aliphatic ketones and that of aryl alkyl ketones during loss of methyl from the metastable McLafferty product.[2c]



(1)

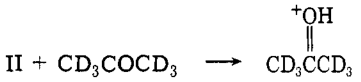
Previous studies of aliphatic ketones by ion cyclotron resonance (icr), however, have not led to observation of reketonization of a large fraction of the McLafferty product ions, for the keto and enol forms remain distinguishable by their ion-molecule chemistry.[4] We now report on a McLafferty rearrangement whose product, monitored by its ion-molecule reactivity, is found to change structure as the time scale of the icr experiment is increased. Standard[4] reactions for distinguishing keto and enol structures of ions were used to follow this transformation. It is, to our knowledge, *the first reported example of structural change followed by ion-molecule reactions.*

The mass and icr spectra of 2-propylcyclopentanone (I) contain an ion of *m/e* 84 (II) resulting from the loss of propylene in a McLafferty rearrangement (eq 2).

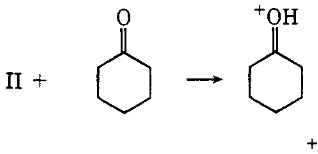


I IIa IIb (2)

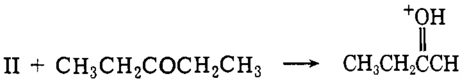
Under conventional conditions for operation (5 × 10^{-6} Torr for I, 5 × 10^{-6} Torr for the other ketone, total calculated transit time[5] (τ_T) *ca.* 4 × 10^{-4} sec to *ca.* 1 × 10^{-3} sec, ionizing voltage 12–30 V) the product behaves like the expected enol, as the following observed reactions typical of enolic structure[4] suggest (eq 3–5). Double resonance experiments confirm these assignments.



$$\text{II} + CD_3COCD_3 \longrightarrow CD_3\overset{\overset{+}{O}H}{\overset{\|}{C}}CD_3 \qquad (3)$$

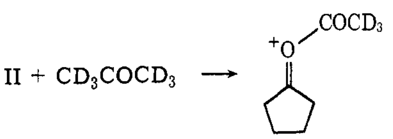


(4)

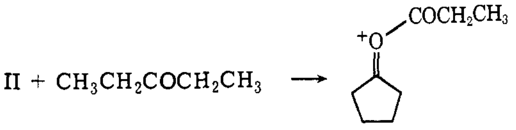


$$\text{II} + CH_3CH_2COCH_2CH_3 \longrightarrow CH_3CH_2\overset{\overset{+}{O}H}{\overset{\|}{C}}CH_2CH_3 \qquad (5)$$

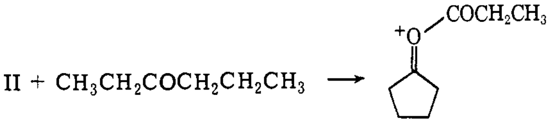
When the residence time of the ions is increased by adjustment[5] of the drift voltages (τ_T *ca.* 5 × 10^{-3} sec to *ca.* 1.6 × 10^{-1} sec) and all other conditions are maintained the same, eq 3–5 can no longer be detected in the analyzer. In their place, new reactions appear.



(6)



(7)



(8)

These are analogous to the reactions shown to be indicative of the keto form,[4] and in fact are also observed

---

[1] (a) J. A. Gilpin and F. W. McLafferty, *Anal. Chem.*, **29**, 990 (1957); (b) P. P. Manning, *J. Amer. Chem. Soc.*, **79**, 5151 (1957); (c) S. Meyerson and J. D. McCollum, *Advan. Anal. Chem. Instrum.*, **2**, 179 (1963).

[2] (a) D. J. McAdoo, F. W. McLafferty, and J. S. Smith, *J. Amer. Chem. Soc.*, **92**, 6343 (1970); (b) F. W. McLafferty, D. J. McAdoo, J. S. Smith, and R. Kornfeld, *ibid.*, **93**, 3720 (1971); (c) see, however, S. Meyerson and E. K. Fields, *Org. Mass Spectrom.*, **2**, 1309 (1969).

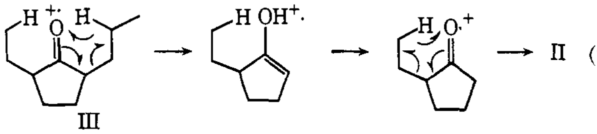
[3] J. H. Beynon, R. M. Caprioli, and T. W. Shannon, *ibid.*, **5**, 967 (1971).

[4] (a) J. Diekman, J. K. MacLeod, C. Djerassi, and J. D. Baldeschwieler, *J. Amer. Chem. Soc.*, **91**, 2069 (1969); (b) G. Eadon, J. Diekman, and C. Djerassi, *ibid.*, **91**, 3986 (1969); (c) G. Eadon, J. Diekman, and C. Djerassi, *ibid.*, **92**, 6205 (1970).

[5] T. B. McMahon and J. L. Beauchamp, *Rev. Sci. Instrum.*, **42**, 1362 (1971).

with the molecular ion of cyclopentanone, while eq 3–5 are not. We conclude that the average lifetime of the enolic product ion IIa is on the order of 1-5 × 10^{-3} sec, and that it rearranges to a form characterized by the same chemistry as the molecular ion of cyclopentanone, *i.e.*, reketonizes.

The *m/e* 84 ion in the spectrum of 2-ethyl-5-propylcyclopentanone (III), which arises from two consecutive McLafferty rearrangements (eq 9), behaves like an enol



III

(9)

at short lifetimes as expected from earlier studies of consecutive rearrangements,[4] but at τ_T *ca.* 10^{-1} sec, this ion also behaves like a keto form, undergoing, for example, eq 7.

Straight-chain aliphatic ketones produce McLafferty products which do not reketonize on such a scale that they can be detected by icr. For example, the acetone enol ion formed from 2-hexanone still undergoes reactions typical of the enolic form, *e.g.*, protonation of acetone-d_6, even for τ_T on the order of 10^{-1} sec with ionizing voltages in the range of 13 and 20 V. The lifetime of the acetone enol ion is thus in excess of 10^{-1} sec when the total population of McLafferty products is considered, even though it may be[2] on the order of 10^{-5}–10^{-6} sec for the metastable fraction losing methyl.

In the presence of a collision gas (air) at 10^{-5} Torr, the reaction product of I retains its enolic structure even at residence times on the order of 10^{-2}–10^{-1} sec. The presence of the collision gas may alter the residence time of the ion, and we are conducting experiments to distinguish between this and chemically more interesting explanations relating to collisional stabilization of the enol form.

The difference in reactivity between I and 2-hexanone suggests that the reketonization process is a function of ion structure even within nonaromatic ketones. We are beginning to examine other systems in order to determine whether information about the preferred geometry of the activated complex for reketonization may be gathered in this way.

Acknowledgment. The ion cyclotron resonance spectrometer was purchased through the generosity of Hercules, Inc., the Shell Companies Foundation, the National Science Foundation (GU 2059), and the North Carolina Board of Science and Technology (159). Partial support of this study by the National Science Foundation (GP 28570) and the Alfred P. Sloan Foundation is gratefully acknowledged.

(6) Research Fellow of the Alfred P. Sloan Foundation.

J. Ronald Hass, Maurice M. Bursey[*6]
Venable and Kenan Chemical Laboratories
University of North Carolina
Chapel Hill, North Carolina 27514

David G. I. Kingston
Department of Chemistry, Virginia Polytechnic Institute
Blacksburg, Virginia 24061

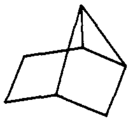
Harvey P. Tannenbaum
Department of Chemistry, State University of New York at Albany
Albany, New York 12203

Received February 28, 1972

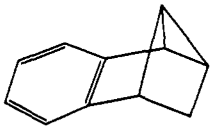
Silver(I)-Assisted Methoxyl Group Ionization. Some Mechanistic and Synthetic Considerations Derived from the Behavior of *endo*-2-Methoxytricyclo[4.1.0.0^{3,7}]heptanes[1]

Sir:

Although Ag$^+$ is now recognized to be capable of catalyzing spectacular bond rearrangements of bicyclo[1.1.0]butane derivatives under exceedingly mild conditions,[2] bicyclo[2.1.0]pentane is characterized by inertness toward this noble metal ion.[3,4] Consistent with this reactivity order are our more recent findings that **1**[5a,b] and **2**[5c] are likewise unreactive toward catalytic amounts of silver perchlorate in benzene.[6]



1



2

As regards ether **5a**, however, quantitative rapid isomerization exclusively to *anti*-7-methoxynorbornene (**6a**) occurs under these conditions. We have now devised a general synthesis of *endo*-2-methoxytricyclo-[4.1.0.0^{3,7}]heptanes (**5**) which permits: (a) conclusive demonstration of the fact that this rearrangement and the general **5** → **6** isomerization proceed by initial ionization of the methoxyl substituent and not by any Ag$^+$-strained bond interaction; and (b) realization of facile synthetic entry to a variety of formerly elusive anti-7-substituted norbornenes.

The brief synthetic scheme is founded upon stereoselective dibromocarbene addition[7] to readily available 3-methoxycyclohexenes (**3**) and subsequent stereoselective carbene–hydrogen insertion (**4** → **5**).[8–10] The very characteristic nmr features of **5a**, particularly the low-field quartet ($J_{1,2}$ = 3.5 and $J_{2,3}$ = 7.0 Hz),[11] are also readily apparent in the spectra of **5c** and **5d**. Independent confirmation of structure **5c** was derived from catalytic hydrogenation (Pd/C, ethanol, 1 atm) to *endo*-1-methyl-3-methoxynorbornane (100%). As a result of their inherent structural features, this low-field

---

(1) Silver(I) Ion Catalyzed Rearrangements of Strained σ Bonds· XI. For the previous paper, see L. A. Paquette, R. E. Wingard, Jr., and R. K. Russell, *J. Amer. Chem. Soc.*, **94**, 4739 (1972).

(2) (a) L. A. Paquette and S. E. Wilson, *ibid.*, **93**, 5934 (1971), and earlier work; (b) M. Sakai, H. H. Westberg, H. Yamaguchi, and S. Masamune, *ibid.*, **93**, 4611 (1971), and preceding papers.

(3) L. A. Paqeutte, *Accounts Chem. Res.*, **4**, 280 (1971).

(4) Appropriate substitution with labilizing substituents does result, however, in skeletal rearrangement: L. A. Paquette and L. M. Leichter, *J. Amer. Chem. Soc.*, **94**, 3653 (1972).

(5) (a) H. C. Brown and H. M. Bell, *ibid.*, **85**, 2324 (1963); (b) S. Winstein, A. H. Lewin, and K. C. Pande, *ibid.*, **85**, 2324 (1963); (c) R. Edman, *ibid.*, **91**, 7103 (1969).

(6) G. Zon, unpublished observations.

(7) D. Seyferth and V. A. Mai, *J. Amer. Chem. Soc.*, **92**, 7412 (1970).

(8) W. R. Moore and B. J. King, *J. Org. Chem.*, **36**, 1877, 1882 (1971); W. R. Moore, H. R. Ward, and R. F. Merritt, *J. Amer. Chem. Soc.*, **83**, 2019 (1961).

(9) Not unexpectedly, methoxyl-substituted tricyclo[4.1.0.0^{2,7}]heptanes are also produced in this step. The relative yields of such products vary with substitution. Complete details will be elaborated upon in a future full paper.

(10) Satisfactory combustion analyses have been obtained for all new compounds described herein except for the deuterium-labeled substrates for which accurate mass spectral determinations were secured.

(11) (a) H. Tanida, T. Tsuji, and T. Irie, *J. Amer. Chem. Soc.*, **88**, 864 (1966); (b) M. Brookhart, A. Diaz, and S. Winstein, *ibid.*, **88**, 3135 (1966). We thank Dr. Tanida for a copy of the nmr spectrum of **5a**. High resolution nmr spectra reveal that each component of this doublet of doublets is further split ($J \cong 0.5$ Hz) by long-range coupling.