Alkylation of Enolate Ions

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Abstract: We describe a procedure for studying gas-phase ion-molecule chemistry in which the neutral reaction products are collected and identified. Our experiment uses a flowing afterglow device configured with a cryogenic trapping column; material collected on this column is separated by capillary chromatography and the individual components are identified by their retention time and their electron impact mass spectrum. We have used this device to study the reaction of the cyclohexanone enolate ion with CH₃Br. We find that reaction of this enolate proceeds with a rate constant of 3.9×10^{-10} cm³ molecule⁻¹



 s^{-1} to produce only the product resulting from O-alkylation, 1-methoxycyclohexene; there is no evidence for the product resulting from C-alkylation.

I. Introduction

The study of ion-molecule reactions in the gas phase is a broad enterprise¹ and involves a variety of experimental techniques such as ion cyclotron resonance (ICR), high-pressure mass spectrometry, and the flowing afterglow. All of these methods permit reactions to be investigated without being obscured by the effects of solvents or counterions. Consequently, the intrinsic reactivities of ions can be directly studied. These techniques are also useful in that they provide a direct test for the modeling of chemical reactions; calculations typically correspond to isolated molecules in the gas phase and should be directly comparable to experimental results obtained from gas-phase ion-molecule studies.

As powerful as the various techniques are for studying ionmolecule reactions, all have individual disadvantages. When taken together they form a complementary set which greatly reduces the limitations imposed by the separate methods. However, since all of these devices monitor the ion reactions solely by the detection of charged particles, none can identify the neutral reaction products. Thus one directly observes only "half" of the final ion-molecule products in all cases. As a result the reaction channels and products of a large number of ion-molecule reactions are not rigorously known and a great deal of information is lost.

Several research groups have devised means of identifying neutral products resulting from ion reactions. In the pioneering work,^{2,3} the neutrals resulting from negative ion reactions in an ICR were identified by electron impact (EI) ionization of the background gas. The neutral reaction products were identified on the basis of their distinctive positive ions. Experiments were done to verify that nucleophilic displacement reactions of the form $X^- + RY \rightarrow RX + Y^-$ generated RX as the neutral products. The reaction of Cl⁻ with both *cis*- and *trans*-4-bromocyclohexanol was reported to proceed with predominate inversion of configuration. Morton's laboratory⁴⁻⁶ has developed an electron bombardment

(6) T. H. Morton, J. Am. Chem. Soc., 102, 1596 (1980)

Scheme I

0

$$N_2 O + e^- \longrightarrow O^- + N_2$$
 (1)

$$0^{-} + CH_4 \longrightarrow CH_3 + OH^{-}$$
(2)

$$H^{-} + \bigcup^{0} \longrightarrow \bigcup^{0^{-}} + H_{2}0 \qquad (3)$$

$$\begin{array}{c} 0 \\ + \ CH_3Br \longrightarrow \end{array} \begin{array}{c} CCH_3 \\ + \ Br^- \ (a) \end{array}$$



flow reactor to study the neutrals generated by positive ion chemistry. He has recently reviewed⁷ gas-phase analogues of solvolysis reactions. The products of gas-phase positive-ionmolecule reactions have also been detected by radioactive labeling techniques.⁸⁻¹¹ Infrared chemiluminescence and laser-excited fluorescence from vibrationally excited reaction products have been studied as well.¹² In reactions of the type $X^- + HY \rightarrow XH +$ Y^- , the neutral reaction products XH can be characterized in a small number of cases. Reaction products that have been optically detected are HF, HCl, HBr, HO, HCN, and CNH.

We have developed a technique¹³ for neutral collection and detection based on a flowing afterglow device configured with a cryogenic trapping column (Figure 1) and a gas chromatograph/mass spectrometer (GC/MS) for product separation and

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⁽¹³⁾ M. A. Smith, R. M. Barkley, and G. B. Ellison, J. Am. Chem. Soc., 102, 6851 (1980).



Figure 1. Schematic diagram of the flowing afterglow device configured with a trapping column.



Figure 2. A sketch of the gas chromatograph/mass spectrometer used to separate and identify the reaction products.

identification (Figure 2). Ion-molecule reactions are carried out in the afterglow, and a small fraction of the neutrals present in the flow tube are collected on the trapping column (Figure 1). Collected material is thermally desorbed from the trapping column onto a chromatographic column (Figure 2). Separation of this mixture of neutrals then takes place, and the resulting individual components are identified by their retention times and by their EI mass spectra. The flowing afterglow¹⁴⁻¹⁶ is especially well suited for neutrals collection since a relatively large number of ions and consequently neutral products can be produced. Under the typical operating conditions employed in a flowing afterglow, a large flow of helium buffer gas ($\simeq 200 \text{ STP cm}^3 \text{ s}^{-1}$) is continuously pumped through the flow tube along with lesser amounts of the neutral reagents. The partial pressure of helium is roughly 0.4 torr while all other neutrals are maintained at pressures of about 1 mtorr or less. When operated in this manner the afterglow produces about 10⁹ ions cm⁻³ at the electron gun; this density falls to approximately 107 ions cm⁻³ near the reaction zone 45 cm downstream from the ion source. Consequently ion densities of 10⁷ ions cm⁻³ can be produced and undergo reaction to afford an equal number of neutral products.

An application of the above device to the study of the reaction of F^- with neopentyl chloride found the nucleophilic product, neopentyl fluoride, to be the lone reaction product.¹³ Since this preliminary report the technology of our experiment has evolved. In this paper we wish to fully describe the flowing afterglow together with the cryogenic collection columns and GC/MS. Using this device, we have completed a study of the reaction of cyclohexanone enolate anion with methyl bromide. The reaction we have studied is shown in Scheme I. By a series of steps (eq 1–3), we have generated the enolate anion of cyclohexanone. Our goal was to deduce whether the enolate ion reacted via O-al-



Figure 3. The low-resolution spectrum of positive ions observed by the flowing afterglow quadrupole mass spectrometer in Figure 1.



Figure 4. The low-resolution spectrum of negative ions observed by the flowing afterglow quadrupole mass spectrometer in Figure 1.

kylation, C-alkylation (eq 4a or 4b), or a combination of the two. Both of these reactions are quite exothermic (see Appendix): $\Delta H^{\circ}_{298}(4a) = -26.9$ kcal mol⁻¹ and $\Delta H^{\circ}_{298}(4b) = -43.8$ kcal mol⁻¹. From an analysis of the neutral reaction products, we conclude that O-alkylation is the exclusive reaction pathway (eq 4a); of the two plausible channels (eq 4) 1-methoxycyclohexene is the only product that was detected. This product was unambiguously identified by the sample's proper retention time on a fused silica capillary column and a corresponding EI mass spectrum.

II. Experimental Section

A. Flow Reactor. These experiments were performed on a flowing afterglow system¹⁴⁻¹⁶ which has been previously described. The reaction vessel is a 100×7.6 cm i.d. stainless steel cylinder (see Figure 1) through which purified helium was passed. A helium flow of 200 STP cm³ s was used at a pressure of 0.4 torr and with a linear velocity ($\langle v_{\rm He} \rangle$) of around 8400 cm s⁻¹. Hydroxide ion $(m/z \ 17)$ was produced and maximized (\approx 15 pA) by adding 1 mtorr of N₂O and 2 mtorr of CH₄ past the electron gun (Figure 1) while operating the quadrupole mass filter at relatively low resolution. The positive ions detected by the afterglow quadrupole mass spectrometer are shown in Figure 3. Positive ions resulting from admitting N₂O and CH₄ past the electron gun are shown in trace A, trace B shows the positive ions when cyclohexanone was added downstream, and trace C depicts the resultant positive ions when CH₃Br was finally added to the flow tube. Traces B and C of Figure 3 demonstrate that the positive ions were invariant to methyl bromide addition. Figure 4 shows the variation of the negative ions in the flow tube; HOwas the only ion produced when N_2O and CH_4 were added to the ion source (trace A). Cyclohexanone was added 10 cm downstream in sufficient quantity (<0.1 mtorr) to quench all of the hydroxide ion signal (trace B, Figure 4), producing roughly 15 pA of the enolate ion (m/z 97)and only a few pA of the enolate-cyclohexanone cluster $(m/z \ 195)$. Methyl bromide was then added 35 cm downstream (<0.1 mtorr) to quench all of the enolate ion signal at m/z 97 and generate roughly 8 pA of the bromide ion at m/z 79 (trace C, Figure 4). Figures 3 and 4 suggest that the only important ion reaction when CH₃Br is added to the flow tube is one that destroys cyclohexanone enolate (m/z 97) and generates Br⁻ (m/z 79, 81).

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B. Collection Technology. The neutrals were collected on glass columns (14 \times 0.4 cm i.d.) which were attached to the flow tube via a high-conductance valve¹⁷ on one end and a liquid N_2 -trapped 1397 Welch mechanical pump at the other. The tubes were loosely filled with glass wool which had been treated with a saturated methylene chloride solution of Tenax-GC^{18,19} (Applied Science Labs., Deerfield, IL) and then baked out at 190 °C under vacuum. Used in this way Tenax-GC is not employed as a porous polymer, but it is an inert coating on the glass wool. The glass wool proved to be too reactive in our control experiments to be used uncoated. Several chromatographic stationary phases were tested as coatings for the glass wool, but Tenax-GC proved to be the best. These tubes had a conductance of roughly 8×10^{-2} STP cm³ s⁻¹. Three tubes were collected simultaneously by attachment to a small manifold. During the collection each column was individually cooled by liquid N₂ in a styrofoam cup.

C. Neutrals Separation and Identification. Once a collection was completed, the three collection tubes were removed from the flow tube and sealed with Swagelok fittings. The tubes remained in the liquid \mathbf{N}_2 filled styrofoam cups prior to thermal desorption onto the chromatographic column to avoid loss of collected material. Connections which enabled introduction of a sample into the injection port of the GC/MSwere made with a cup full of liquid N_2 still in place. Once connected to the injection port the cup was cut away and a heater installed to desorb trapped material from the column (see Figure 2).

A Hewlett-Packard 5993B (Hewlett-Packard, Palo Alto, CA)²⁰ combined gas chromatograph/mass spectrometer/data system was used for the separation and analysis of the collected neutrals (Figure 2). Data were accumulated and handled with use of standard Hewlett-Packard 5993B, Revision F software. This software package allows chromatograms to be obtained in either full scanning or selected ion modes. In a full scanning mode, the operator sets the mass range and scan speed to allow collection of complete EI mass spectra for the eluting chromatographic peaks. In selected ion monitoring (SIM) runs only a particular ion or group of ions is monitored. Several computer routines are available for the dynamic reduction of acquired data. These include background subtraction, selected ion display, and similar routines. These are particularly useful either when background counts are high or when close to the detection limit of the instrument. An automatic mass spectrometer calibration/tuning routine and associated hardware are included as well.

Several modifications to the mass spectrometer have been made so that the chromatographic column is directly coupled into the mass spectrometer; this capillary column/MS interface is shown in Figure 5. The Model 5993B was originally designed for use with packed chromatographic columns, and as such it has a pneumatically controlled, bellows seal isolation valve between the end of the column and the ion source. This valve is normally under computer control, but due to the time required for pressure equalization when the valve is first opened, we have bypassed the control such that the valve normally remains open between runs. We have added another pneumatically controlled bellows seal valve which is interlocked with the isolation valve. Labelled "VENT VALVE" in Figure 5, it allows column effluent to be vented when we do not want it in the high-vacuum region. The chromatographic column ends approximately 1 cm below the isolation valve. The distance from the end of the column to the ion source has been lengthened over the standard configuration by 5 cm. The total distance in our instrument is roughly 13 cm. This change was effected by lengthening the high-vacuum region and the entrance tube to accommodate an ionization gauge in the mass spectrometer. In this directly coupled configuration, all material placed on the column enters the mass spectrometer ion source; no carrier gas separator is used. Automatic tuning of the MS is done by admitting perfluorotributylamine (PFTBA) into the high-vacuum region with the isolation valve closed. PFTBA [N(CF2CF2CF2CF3)] is commonly used for tuning mass spectrometers because it has a simple EI fragmentation pattern which covers a wide molecular weight range. The direct coupling of the column to the MS and the unavoidable flow of helium into the ion source cause autotuning to give poor mass spectra. Thus, the modifications to the mass spectrometer require that it be tuned manually with use of PFTBA while carrier gas is flowing into the ion source. Ionization is accomplished with a 220 μ A emission current of 70 eV electrons from a rhenium filament. The mass spectrometer consists of a quadrupole mass filter with 20.3-cm hyperbolic rods and a continuous dynode electron multiplier. For full scanning runs, the mass spectrometer was



Figure 5. The interface used for direct coupling of the WCOT column to the mass spectrometer. The construction material is either 304 or 316 stainless steel; all joints are silver brazed.

scanned at 120.8 amu s⁻¹ over the range of 33-150 amu.

Helium carrier gas (UHP Grade, Matheson, East Rutherford, NJ) with a linear flow velocity of 34 cm s⁻¹ was used in the GC/MS. The column used for the analysis consisted of a 1 m precolumn of 0.25 mm i.d., 1.0 μ m film thickness, DB-5²¹ fused silica wall-coated open tubular (WCOT) column (J and W Scientific, Rancho Cordova, CA) connected to a 30 m, 0.32 mm i.d., 0.25 μ m film thickness DB-1701²² fused silica WCOT (J and W Scientific, Rancho Cordova, CA) column. This connection was made by using a single ferrule capillary column butt connector (Supelco, Bellefonte, PA). The precolumn was required to effect cold trapping of the compounds of interest because the more polar DB-1701 does not do so efficiently. Trapping was done on the nonpolar DB-5 phase by cooling the entire column to -30 °C with use of a subambient cooling attachment to the GC with subsequent temperature programmed separation on the DB-1701 analytical column.

Chromatographic retention times and mass spectra of authentic samples of 1-methoxycyclohexene²³ and 2-methylcyclohexanone (Columbia Organic Chemicals, Columbia, SC) were obtained with the following temperature program: cold trap at -30 °C (20 min), ramp at 20 °C min⁻¹ to 60 °C, and hold for 16 min. Under these conditions, 1-methoxycyclohexene elutes at 29.4 min and 2-methylcyclohexanone elutes at 34.3 min. A chromatogram of an authentic mixture of 1-methoxycyclohexene (a), cyclohexanone (b), and 2-methylcyclohexanone (c) is displayed in Figure 6. The associated full scanning mass spectrum of features a and c are shown in Figures 7 and 8. Notice that several distinctive mass peaks characterize each of these substances; 1-methoxycyclohexene (Figure 7) has intense peaks at 112 (M), 111 (M - 1), 97 (M - 15), and 84 (M - 28) while 2-methylcyclohexanone (Figure 8) shows features at 112 (M), 97 (M - 15), 84 (M - 28), and 68 (M - 44). A long separation between b and c was required since large amounts of

⁽¹⁷⁾ Whitey stainless steel 45F8 ball valve with 10.3 mm diameter orifice (Whitey Co., Highland Heights, OH).

⁽¹⁸⁾ Tenax-GC is a polymer of 2,6-diphenyl-p-phenylene oxide.
(19) E. D. Pellizzari, J. E. Bunch, B. H. Carpenter, and E. Sawicki, Environ. Sci. Technol., 9, 552 (1975).

⁽²⁰⁾ D. L. Forest, Environmental Protection Agency Report No. EPA-600/4-81-04, 1981.

⁽²¹⁾ DB-5 is a cross-linked 1% vinyl, 5% phenyl, methyl polysiloxane; a nonpolar stationary phase.

⁽²²⁾ DB-1701 is a cross-linked 86% dimethyl, 14% cyanopropylphenyl polysiloxane; an intermediate polarity phase.

⁽²³⁾ Our sample of 1-methoxycyclohexene was synthesized and graciously donated by Allison M. Fisher. The synthetic method of R. A. Wohl [Syn-thesis, 1, 38 (1978)] was followed. The compound was identified by its 90-MHz NMR spectrum.



Figure 6. The chromatogram resulting from injection of an authentic mixture of 1-methoxycyclohexene (a), cyclohexanone (b), and 2-methylcyclohexanone (c) onto a fused silica column (described in the text). Each component is characterized by a retention time and a complete EI mass spectrum.



Figure 7. The EI mass spectrum of peak a in Figure 6 which elutes at 29.4 min; the mass range was scanned from 10 to 150 amu. This peak is identified as 1-methoxycyclohexene.

reactant cyclohexanone elute at 31.2 min; this often caused automatic shutdown of the mass spectrometer. The separation attained with this temperature program allowed the MS to be restarted without loss of significant data. At 60 °C, the 2-methylcyclohexanone was adequately resolved from the cyclohexanone tail to allow accurate identification.

The samples from the afterglow tubes were desorbed by using a thermostated heater held at 200 °C (Omega Engineering type 6100 controller, Stamford, CT). The desorbed material was placed on the column by diverting the normal flow of helium carrier gas through the collection tube which was fitted with a stainless steel needle for insertion into the injection port. When authentic samples of 1-methoxycyclohexene and 2-methylcyclohexanone were desorbed from Tenax at 200 °C, we found no evidence that these compounds were isomerized or degraded. Connections were made by using Swagelok tube fittings with Teflon ferrules. The standard Hewlett-Packard 18740B injection port was used in splitless mode with a straight, unpacked glass liner. The collection tube was flushed for 20 min, during which time the column was at -30 °C. Experiments indicate that the collection column is efficiently flushed within 15 min, but the additional time allows for elution (from the chromatographic column) of the lower boiling components in the reagent gases, as well as CO₂, substantially improving the base line. After 20 min the port was flushed, the normal flow configuration was resumed, and the collection column was removed. The rapid temperature ramp, 20 °C min⁻¹, to 60 °C was begun. This temperature program was used throughout the scanning and SIM runs. At the end of each run, the



Figure 8. The EI mass spectrum of peak c in Figure 6 which elutes at 34.3 min; the mass range was scanned from 10 to 150 amu. This peak is identified as 2-methylcyclohexanone.

column temperature was raised and held at 100 $^{\circ}$ C for 3 min to allow all material remaining on the column to elute.

D. Signal Estimate. It is instructive to estimate the number of neutral molecules that are the products of ion-molecule reactions. In the flowing afterglow there are approximately 10^7 ions cm⁻³ in the reaction zone; these will be converted into neutral products by chemical reaction. Since $\langle v_{\rm He} \rangle \simeq 8400$ cm s⁻¹ and the area of the flow tube is 45.4 cm², the flux of ions down the flow reaction is about 3.8×10^{12} ions s⁻¹; following chemical reaction this is the flux of neutral reaction products (23 nmol h⁻¹). The flow through each collection column was roughly 8×10^{-2} STP cm³ s⁻¹ which is much smaller than the 200 STP cm³ s⁻¹ that passes through the afterglow. Consequently, we expect that our cooled collection columns will trap no more than 1.5×10^9 product molecules s⁻¹ or 10 pmol h⁻¹. This conjecture assumes that the Tenax-GC columns trap 100% of the reaction products.

III. Results

Before considering the results of our neutral collection let us examine the kinetics of the reaction of cyclohexanone enolate with CH_3Br (eq 4). The rate coefficient for the reaction of the enolate (m/z 97) with methyl bromide was measured by monitoring the ion signal at m/z 97 as a function of time.¹⁴ Plots of the logarithm of the ion intensity vs. the reaction distance afforded straight lines for four different flows of the neutral reagent. The results were averaged to afford $k_4 = (3.9 \pm 0.3) \times 10^{-10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$ which corresponds to a reaction efficiency $(k_{obsd}/k_{ADO})^{24,25}$ of 31%. This rate constant is entirely consistant with the known chemistry of other enolate ions. The reaction of acetone enolate with CH₃Br has been studied in an ICR spectrometer,²⁶ and the rate constant was reported to be 1.8×10^{-10} cm³ molecule⁻¹ s⁻¹; this reaction has also been scrutinized in a flowing afterglow device²⁷ wherein the displacement rate constant was found to be 1.6×10^{-10} cm³ molecule⁻¹ s⁻¹.

All afterglow samples consisted of three tubes collected simultaneously. Comparisons of impurity peaks present in three such commonly collected tubes gives an indication of how consistent the collection process is. Unfortunately, small differences in the collection tubes manifest themselves as seemingly large deviations in the amount of material detected by the GC/MS. Our experience shows that deviations in chromatographic peak area of a factor of 4 are not uncommon. Care must therefore be taken to compare blanks and samples which show similar amounts of the background impurities to ensure comparison of similar runs. Blanks were completed (a) with all reagents (N_2O , CH₄, CH₃Br, cyclohexanone) added to the flow tube and with the ion source off, (b) the ion source on with CH₃Br off, and (c) the ion source

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⁽²⁵⁾ k_{ADO} was calculated as 1.26×10^{-9} cm³ molecule⁻¹ s⁻¹; we used μ_D = 1.81 D and α = 5.53 Å³. C. G. Le Févre, R. J. W. Le Févre, and A. J. Williams, J. Chem. Soc., 4188 (1965).

⁽²⁶⁾ M. J. Pellerite and J. I. Brauman, J. Am. Chem. Soc., 105, 2672 (1983).



Figure 9. The chromatogram resulting from analysis of a sample collected over 1 h from the flowing afterglow. The reaction sequence of Scheme I is used to prepare cyclohexanone enolate which is then quenched with CH_3Br . The peak labeled a is identified as 1-methoxycyclohexene by its retention time and by its EI mass spectrum (Figure 10).



Figure 10. The EI mass spectrum of the peak labeled a in Figure 9 which elutes at 29.4 min; the mass range was scanned from 33 to 150 amu. This species is identified as 1-methoxycyclohexene (see Figure 7).

on with both cyclohexanone and CH_3Br off. Collection times were 1 h for all blanks and either 1 or 2 h for the samples.

Full scanning sample and blank runs were completed and analvzed. One such run is shown in Figure 9. Positive identification is claimed only when the retention time and the mass spectrum match those of the authentic standard. Care must be taken to ensure correct identification of the small quantities of material present; ions of low relative abundance frequently will not be detected in full scanning mode. Thus, comparison of mass spectra taken at low abundance will differ from those taken when larger amounts of material are present. In the case presented here, a reasonably strong parent ion $(m/z \ 112)$ is a great aid in making positive identification. Leaks and breakdown products from vacuum fluids give a background which can also serve to confuse mass spectral identification at low levels. Working close to the detection limit in a system which contains impurities can cause some problems. Most notable of these is the large number of chromatographic peaks observed. The origin of all peaks present can be assigned. Impurities in the reagents, background levels in the flow tube, and residual solvents in the collection tubes are responsible for most of the peaks seen in Figure 9. The mass spectrum of the peak labeled a in Figure 9 is shown in Figure 10. This peak is assigned as 1-methoxycyclohexene. The correct retention time and the close spectral match (see Figure 7) allow this assignment; the presence of 1-methoxycyclohexene was not detected in any of the blanks. In fact, m/z 112 was not detected in any of the full scanning blanks. The full scanning runs made it apparent that 1-methoxycyclohexene was present and was the



Figure 11. A SIM chromatogram. A sample collected from the afterglow is analyzed with the GC/MS programmed to monitor four selected ions which are diagnostic (see Figure 7) for 1-methoxycyclohexene: m/z= 84, 97, 111, and 112. All features are normalized to the m/z 84 peak which has a peak height of 35 counts.

product of a chemical reaction. A match of both mass spectrum and retention time did not occur for the 2-methylcyclohexanone which means it is below our detection limit. The detection limit for both compounds is approximately 5 pmol in the full scanning mode.

In an attempt to increase the sensitivity of the GC/MS, the quadrupole mass spectrometer was programmed to monitor only selected ions (SIM) rather than scan over the entire mass range. An order of magnitude increase in signal intensity, as measured by the m/z 112 area, is observed in SIM runs over full scanning runs with identically dilute samples. Prior to running the SIM experiments, full scanning runs of authentic samples were completed to enable correct choice of the ions to be monitored to within 0.1 amu. This is necessary to correct for any irregularities in the mass axis calibration of the mass spectrometer. For 1-methoxycyclohexene, the following ions (see Figure 7) were chosen: 84.1, 97.1, 111.1, and 112.1 amu. For 2-methylcyclohexanone, 68.2, 84.1, and 112.1 amu were selected (see Figure 8). The groups were scanned only over that period of time when the compounds of interest would elute: 28.5 to 30.5 min for 1methoxycyclohexene and 33 to 36 min for 2-methylcyclohexanone. The four ions chosen for 1-methoxycyclohexene were each monitored for 100 ms, giving a total scan time of 400 ms. In order to have identical scan times, 68.2 amu was monitored for 100 ms, while 84.1 and 112.1 amu were monitored for 150 ms in the 2-methylcyclohexanone group. In the SIM mode, the detection limit for both compounds is roughly 0.5 pmol. Blank SIM runs were always completed prior to a sample collection. Typical results are shown in Figure 11; this clearly shows the presence of 1methoxycyclohexene.

The ratio of the areas of the monitored ions peaks is an important tool for making positive identifications of compounds in SIM work. The ratio observed in the sample runs (Figure 11) match those observed by using dilute solutions of authentic 1methoxycyclohexene to within statistical error. These ratios also nicely correspond to the area ratios observed for the selected ions in the full scanning runs for the feature identified as 1-methoxycyclohexene (a in Figure 9). The SIM runs suggest that the amount of material collected in a 2-h sample is between 4 and 10 pmol. The other possible product, 2-methylcyclohexanone, was again undetected in both the SIM samples and blanks.

There is no doubt that a chemical reaction is producing 1methoxycyclohexene in the afterglow. Can we be sure that ionmolecule reactions are the source of this product? Radical chemistry may perhaps be responsible. One might conjecture that hydroxyl radicals (which are surely present in the flow tube) will generate cyclohexanone enol radical by α -hydrogen abstraction. This enol might react with CH₃Br to produce 1-methoxycyclohexene and bromine atoms. Radical reactions such as this are quite implausible; we feel that there is no chance that radical chemistry is the source of our 1-methoxycyclohexene. Combining



known $\Delta H_{f^{\circ}298}$ values for CH₃Br, Br, and the cyclohexanone enol radical together with an estimated heat of formation for 1methoxycyclohexene, we compute $\Delta H^{\circ}_{298}(5) \simeq +15 \text{ kcal mol}^{-1}$ (see Appendix).

The reactions of OH with several ketones have been studied.²⁸ The rate constants are smaller than those for ions and are usually in the range of 10^{-11} to 10^{-13} cm³ molecule⁻¹ s⁻¹. The reaction of OH with CH₃COCH₃ has been examined,²⁹ and a rate constant of 6.6 (± 0.9) \times 10⁻¹³ cm³ molecule⁻¹ s⁻¹ reported. If OH were to react with cyclohexanone, we conjecture that the rate constant for α -hydrogen abstraction would be about this magnitude. While OH will certainly be a background radical in our flow tube, it is not likely to be in high concentrations. The OH number density has been directly measured³⁰ by laser-excited fluorescence spectroscopy in a flowing afterglow. The concentration of background OH radicals was estimated to be 2×10^6 cm⁻³. Taken together, all of these observations suggest that background OH radicals are present in low concentrations, react slowly with cyclohexanone, and do not produce the observed 1-methoxycyclohexene.

Our initial experiments suggest that the O-alkylation product (eq 4a) is 100% of the reaction. How precise can we be about the branching ratio of products between eq 4a and 4b? From calibrated standards we know that our detector is slightly more sensitive for 2-methylcyclohexanone than for 1-methoxycyclohexene. As mentioned earlier, our detection limit for both of these substances is roughly 5 pmol in full scanning mode and at least 0.5 pmol in the SIM option. Our SIM runs show between 4 and 10 pmol of the product 1-methoxycyclohexene; this indicates that if C-alkylation (eq 4b) occurs, it can represent no more than 13% of the total products formed in (4). Consequently in reaction 4, 1-methoxycyclohexene is 100% of the observed product.

IV. Discussion

The competition between C- and O-alkylation in the reactions of enolate anions in solution has been extensively investigated.^{31,32} This is a very important problem to understand because the alkylation of enolates is one of the most common ways to form carbon-carbon bonds (C-alkylation) and also finds use in the protection of ketones via their vinyl ethers (O-alkylation). Therefore, it is important to examine the conditions that can be contrived to favor one or the other of the two pathways. It has been found that polar aprotic solvents tend to favor the alkylation of the more electronegative O atom since they can complex the positive counterion and leave the oxygen relatively unhindered. On the other hand, protic solvents have been found to lead to the thermodynamically more favored C-alkylation products.

Based on the work that has been done in solution, one might expect that O-alkylation would predominate in the gas phase since the negative charge resides primarily on the more electronegative oxygen³³ atom and it is unhindered by solvent or counterion. On the other hand, the formation of 2-methylcyclohexanone as shown in eq 4b is exothermic by 43.8 kcal mol⁻¹ while the formation of 1-methoxycyclohexene is less energetic ($\Delta H_{4a} = -26.9 \text{ kcal mol}^{-1}$) (see Appendix). Therefore, the C-alkylated product would be expected to be favored on the basis of thermodynamics.

Other investigators have considered the possibility of gas-phase O-alkylation of enolate ions.^{27,34} As part of an extended study of $S_N 2$ displacements, the reactions of a set of naked (and clustered) negative ions with CH₃Br or CH₃Cl were examined.²⁷ The reactivities of most of the nucleophiles were found to be correlated³⁵ with their methyl cation affinities; the sole exception in the correlation was CH₃COCH₂⁻. It was conjectured that acetone enolate might instead undergo O-alkylation. Our direct measurement of the alkylation of cyclohexanone enolate suggests that Bohme and Raskit's postulate is correct. We have calculated the methyl cation affinity of acetone enolate and find it to be 248 kcal mol^{-1} (see Appendix); this is precisely in the predicted range.

Recently the addition of carbanions to carbonyl-containing compounds was studied in an ICR spectrometer.³⁴ It was found that the enolate of acetone reacted with trifluoroethylacetate via a transesterification reaction (O-alkylation; $\Delta H^{\circ} = -12$ kcal mol⁻¹) or a Claisen condensation (C-alkylation; $\Delta H^{\circ} = -29 \text{ kcal mol}^{-1}$). Using acetone- d_5 enolate the authors were able to demonstrate that only the Claisen product $(m/z \ 103, eq \ 6a)$ was formed and that none of the ester arising from transesterification $(m/z \ 104,$ eq 6b) was produced. These results are in contrast with our

$$CD_3 - COCD_2^- + CH_3 - CO - OCH_2CF_3$$

$$\longrightarrow [CD_3CO - CD - COCH_3]^- + CF_3CH_2OD \qquad (6a)$$

$$m/z \ 103$$

$$\longrightarrow [CD_2^- = C(CH_3) - O - COCH_2]^- + CF_3CH_2OH \qquad (6b)$$

$$m/z \ 104$$

finding of the O-alkylation of cyclohexanone enolate by CH₃Br. Perhaps the Claisen condensation involves the reversible formation of a covalently bound intermediate (most likely a tetrahedral intermediate³⁶); under these conditions it is likely that the thermodynamically more favored C-alkylation product would be produced. Our reaction (eq 4) is probably mechanistically distinct; it proceeds to product by "direct" displacement.

Our results along with data in the literature seem to suggest that the alkylation of enolates proceeds via kinetic control in nonreversible systems and by thermodynamic control in equilibrating ones. This is similar to the behavior found in solution and provides a striking parallel. It is apparent that the study of differences in reactivity between gas phase and solution chemistry is enhanced by examining the neutral products of ion-molecule reactions.

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Appendix

This appendix collects our thermochemical calculations. We must calculate the heats of reaction for the channels in eq 4a and 4b. Standard heats of formation are available^{37,38} as $\Delta H_{\rm f}^{\circ}_{298}(\rm Br^{-})$ = -50.8 kcal mol⁻¹ and $\Delta H_{f^{\circ}298}(CH_{3}Br)$ = -8.4 kcal mol⁻¹. One can employ the gas-phase acidity of cyclohexanone to find the heat of formation of cyclohexanone enolate. Acetone enolate will slowly abstract a proton from cyclohexanone; this suggests that $\Delta H^{\circ}_{acid}(cyclohexanone) = 366 \pm 3 \text{ kcal mol}^{-1}$. Use³⁷ of

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 $\Delta H_f^{\circ}_{298}(\mathrm{H}^+) = 367.2 \text{ kcal mol}^{-1} \text{ together with}^{39} \Delta H_f^{\circ}_{298}(\text{cyclo-}$ hexanone) = -54.04 kcal mol⁻¹ leads to $\Delta H_{f^{\circ}298}$ (cyclohexanone enolate anion) = $-55.2 \pm 3 \text{ kcal mol}^{-1}$. We have not been able to find experimental heats of formation for 1-methoxycyclohexene and 2-methylcyclohexanone. However, they can be estimated by applying Benson's method of group equivalents:⁴⁰ $\Delta H_{f^{\circ}_{298}}^{\circ}(1$ methoxycyclohexene) = -39.7 kcal mol⁻¹ and $\Delta H_{f_{298}}^{\circ}(2$ methylcyclohexanone) = -56.6 kcal mol⁻¹. These are likely to be reasonable estimates. The liquid phase heat of formation for 2-methylcyclohexanone is reported³⁹ to be -68.8 kcal mol⁻¹. If one assumes that the heat of vaporization³⁹ will be nearly the same as that for the isomeric cycloheptanone ($\Delta H^{\circ}_{vap} = 12.4 \text{ kcal mol}^{-1}$), the estimated $\Delta H_{f}^{\circ}_{298}(2\text{-methylcyclohexanone})$ is -56.4 kcal mol}{-1}. This is quite close to Benson's estimate. Use of these heats of formation directly leads to $\Delta H^{\circ}_{298}(4a) = -26.9 \pm 3 \text{ kcal mol}^{-1}$ and $\Delta H^{\circ}_{298}(4b) = -43.8 \pm 3 \text{ kcal mol}^{-1}$.

The methyl cation affinity (MCA) was calculated by using the following relation: MCA(cyclohexanone enolate) = $\Delta H_{f_{298}}^{\circ}$ -(cyclohexanone enolate anion) + $\Delta H_{f}^{\circ}_{298}(CH_{3}^{+}) - \Delta H_{f}^{\circ}_{298}(1-$ methoxycyclohexene). Adoption³⁸ of $\Delta H_{f}^{\circ}_{298}(CH_{3}^{+}) = 264$ kcal mol^{-1} leads to MCA(cyclohexanone enolate) = 248 kcal mol^{-1} .

The thermochemistry of reaction 5 is calculated by using the heats of formation of the cyclohexanone enol radical, CH₃Br, 1-methoxycyclohexene, and bromine atom. We use³⁸ $\Delta H_{f^{\circ}298}^{\circ}(Br)$ = 26.74 kcal mol⁻¹; the heat of formation of cyclohexanone enol radical can be extracted from the EA. Zimmerman et al.³⁴ find EA(cyclohexanone enol radical) = 35.8 ± 1.2 kcal mol⁻¹; use of $\Delta H_{\rm f}^{\circ}_{298}$ (cyclohexanone enolate anion) yields $\Delta H_{\rm f}^{\circ}_{298}$ (cyclohexanone enol radical) = -19.4 ± 3.2 kcal mol⁻¹. The heat of reaction 5 can then be calculated as $+14.8 \pm 3.2$ kcal mol⁻¹.

Registry No. CH₃Br, 74-83-9; cyclohexanone enolate, 55886-84-5; hydroxide ion, 14280-30-9; cyclohexanone, 108-94-1.

Correlation of Acyl Ion Intensities with Product Enthalpies from Collisionally Activated Decomposition of Molecular Ions of Small Aliphatic Ketones

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Abstract: Previously observed correlations of collisionally activated decomposition (CAD) fragment ion intensities of proton-bound pairs of bases with product enthalpies are extended to competitive cleavages of aliphatic ketones to acyl ions. The ratio of intensities of the acyl ions formed by CAD of the molecular ions of acetone, 2-butanone, 3-methyl-2-butanone, and 2methyl-3-pentanone has an excellent correlation (r = 0.997) with the difference between the heats of formation of the sets of products.

Enthalpy differences can be predicted from fragment ion intensities when an accelerated gaseous ion decomposes after activation by collision with a thermal noble gas atom. For eq 1, the ratio of intensities of B_1H^+ and B_2H^+ in both the unimolecular mass-analyzed ion kinetic energy (MIKE) spectrum and in the collisionally activated decomposition (CAD) MIKE spectrum of $B_1HB_2^+$ formed in a chemical ionization (CI) source correlates with the difference between the proton affinities of B_1 and B_2 .

$$\mathbf{B}_{1}\mathbf{H}^{+} + \mathbf{B}_{2} \leftarrow \mathbf{B}_{1}\mathbf{H}\mathbf{B}_{2}^{+} \rightarrow \mathbf{B}_{1} + \mathbf{B}_{2}\mathbf{H}^{+}$$
(1)

Unknown proton affinities of other bases, B_x , can, therefore, be determined from the MIKE spectrum of the proton-bound base pair $B_1HB_x^+$ when the proton affinity of B_1 is known.¹⁻³

The slope of this kind of correlation of ion intensities has been extended to reactions in which stronger, covalent bonds are broken and to reactions in which the colliding ion has been formed by electron ionization (EI).⁴ That extension required a reformulation of the supporting theory, which previously had used the concept of equivalent temperature. Although for CI ions this concept is certainly tenable,^{5,6} for EI ions it has much less physical meaning. The correlation, which was observed for substituted ions related to eq 2, was not nearly as satisfactory (r = 0.82) as those observed in CI studies nor was the correlation of intensities of the same ions produced by unimolecular decomposition.⁷ One kind of

$$C_4(C_6H_5)_4^+ \rightarrow C_6H_5C \equiv CC_6H_5^+ \rightarrow C_6H_5C \equiv CC_6H_5$$
(2)

qualitative correlation of EI ions might have been expected, for CAD spectra often resemble EI spectra, and correlations of EI fragment ion intensities from substituted aromatic compounds with, for example, Hammett σ constants have long been known.^{8,9}

On the other hand, little has been done to correlate the intensities of aliphatic fragment ions produced in an EI source.¹⁰ Further, the proposed requirement⁴ that k(E) functions for competitive decompositions be sufficiently parallel that the ratio of rates does not vary significantly over the energy range of colli-

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