

The acylketene  $t\text{-BuC}(\text{CO}_2\text{Et})=\text{C}=\text{O}$  is also persistent<sup>26a</sup> and is found to be considerably more reactive than **3** in hydration, but less reactive than  $n\text{-BuCH}=\text{C}=\text{O}$  (Table I).<sup>17c</sup> Other studies of acylketenes have recently appeared.<sup>26b,c</sup>

The second golden age of ketene chemistry is just beginning. New syntheses of ketenes are being developed,<sup>27</sup> new classes and reactions of ketenes are being

(26) (a) Newman, M. S.; Zuech, E. A. *J. Org. Chem.* **1962**, *27*, 1436-1438. (b) Clemens, R. J.; Witzeman, J. S. *J. Am. Chem. Soc.* **1989**, *111*, 2186-2193. (c) Meier, H.; Wengenroth, H.; Laurer, W.; Krause, V. *Tetrahedron Lett.* **1989**, *30*, 5253-5256.

(27) Masters, A. P.; Sorensen, T. S. *Tetrahedron Lett.* **1989**, *30*, 5869-5872.

found, and there is a better understanding of ketene structure and reactivity. But many potentially useful ketenes have not yet been made, and many attractive reactions have not been explored, so the thrill of discovery still awaits the investigator of these fascinating compounds.

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## Gas-Phase Ion/Molecule Reactions as Studied by Fourier Transform Ion Cyclotron Resonance

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### Introduction

Studies of reactions between ions and molecules in the gas phase have received considerable interest over many years. This derives mainly from the fact that such studies in principle can provide a detailed and often quantitative insight into the intrinsic reactivity and properties of the ions and molecules involved based upon their interactions in the absence of solvent molecules or counterions. This insight in turn may lead to a better understanding of the role of solvent molecules or counterions in reactions that take place in the condensed phase and is very relevant to theoretical considerations and calculations.

Equally important to note is that the research interest in gas-phase ion/molecule reactions has grown because of the development of instrumental methods such as chemical-ionization mass spectrometry,<sup>1</sup> flowing afterglow,<sup>2</sup> and Fourier transform ion cyclotron resonance (FT-ICR).<sup>3</sup> The last method, first introduced by Comisarow and Marshall in 1974,<sup>4</sup> has blossomed since 1980.

This paper will give an account of a variety of results of research carried out in my group<sup>5</sup> concerning gas-phase organic ion/molecule reactions as studied by the FT-ICR method. The principles of this method have been described in other recent reviews.<sup>3,6-8</sup>

Nico M. M. Nibbering was born in Zaandam, The Netherlands, in 1938. He studied physical organic chemistry at the University of Amsterdam, where he received his Ph.D. degree in 1968 under the direction of Thymen J. de Boer. Since 1966 he has been a faculty member in the Department of Chemistry at the University of Amsterdam, where he became associate professor in 1975 and full professor of organic mass spectrometry in 1980. He is director of the Institute of Mass Spectrometry, founded in 1988 by the Department of Chemistry at the University of Amsterdam. In 1989 he became a member of the Royal Netherlands Academy of Arts and Sciences. His current research interests include unimolecular gas-phase ion chemistry as studied by time-resolved mass spectrometry via the method of field-ionization kinetics and bimolecular gas-phase ion chemistry as studied by chemical-ionization and Fourier transform ion cyclotron resonance mass spectrometry.

### Experimental Method

The heart of an FT-ICR spectrometer is the so-called trapped-ion cell, which may have different geometries, one of them being cubic (usually 2.54 cm long) (Figure 1). Ions in this cell, which is located in a high-vacuum chamber ( $\leq 10^{-5}$  Pa) between the poles of an electromagnet or a superconducting magnet, are generated from gas-phase sample molecules by an electron beam pulse or from solid samples by, for example, a laser pulse. The ions move in circular orbits perpendicular to the direction of the magnetic field,  $B$ , and are trapped in the cell by a potential of about  $-1$  V, in the case of anions, on the trapping plates. The angular or cyclotron frequency  $\omega_c$  of the ions, which have nearly thermal translational energies and random phases in their cyclotron motion, is given to a first approximation by eq 1, where  $q$  is the charge,  $v$  the velocity,  $m$  the mass of the ion, and  $r$  the radius of its circular orbit.

$$\omega_c = v/r = qB/m \quad (1)$$

One of the methods used to detect the ions after a certain trapping time (1-100 ms), i.e., the time between ion formation and ion detection (Figure 2), is to apply a fast-swept radio-frequency field of 1-2 MHz/ms to one of the pair of plates of the cell parallel to the magnetic field lines (transmitter plates). This excites the ions translationally and brings them into a large

(1) Harrison, A. G. *Chemical Ionization Mass Spectrometry*; CRC Press: Boca Raton, FL, 1983.

(2) DePuy, C. H.; Grabowski, J. J.; Bierbaum, V. M. *Science* **1982**, *218*, 955.

(3) Wilkins, C. L.; Chowdhury, A. K.; Nuwaysir, L. M.; Coates, M. L. *Mass Spectrom. Rev.* **1989**, *8*, 67.

(4) Comisarow, M. B.; Marshall, A. G. *Chem. Phys. Lett.* **1974**, *25*, 282; *Can. J. Chem.* **1974**, *52*, 1997.

(5) Nibbering, N. M. M. *Adv. Phys. Org. Chem.* **1988**, *24*, 1.

(6) Wanczek, K.-P. *Int. J. Mass Spectrom. Ion Processes* **1989**, *95*, 1.

(7) Marshall, A. G. *Acc. Chem. Res.* **1985**, *18*, 316.

(8) Gross, M. L.; Rempel, D. L. *Science* **1984**, *226*, 261.

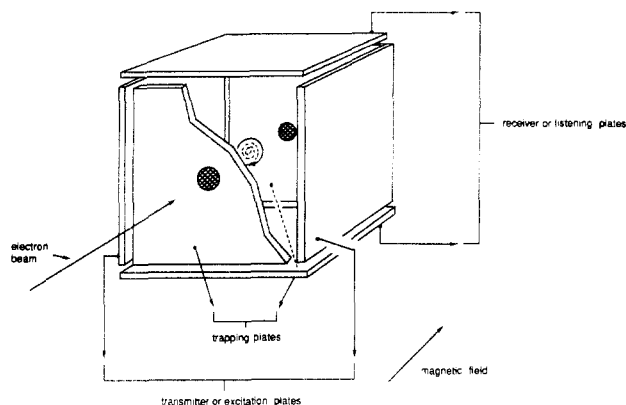


Figure 1. Schematic drawing of a cubic FT-ICR trapped-ion cell.

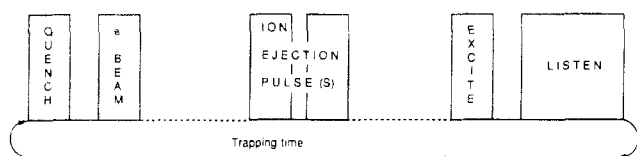


Figure 2.

circular orbit where they move coherently in phase. This motion induces so-called image currents in the other pair of plates (receiver plates) that are also parallel to the magnetic field lines. These image currents will decrease with time because of collisions of the ions with neutral molecules which destroy the coherent ion motion. A transient signal is obtained which is amplified, digitized, and stored. The ions are then removed from the cell with a quench pulse by inverting the polarity of the potential applied to one of the trapping plates. The pulse sequence, schematically shown in Figure 2, is then repeated to improve the signal-to-noise ratio. Fourier transformation of the summed transient will give the excited ion cyclotron frequencies  $\omega_c$  and therefore via eq 1 the masses of the ions.

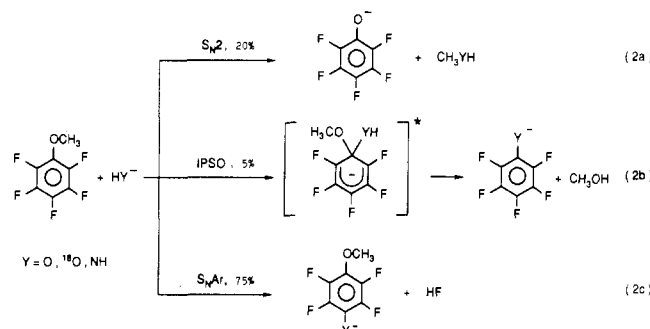
During the trapping time, ion/molecule reactions can take place. Unwanted ions can be removed from the cell during this time by application of a series of ion ejection pulses<sup>9</sup> (see Figure 2) to the transmitter plates of the cell, which increase the radii of the orbits so much that the ions strike the cell walls and are lost. Other methods to remove unwanted ions from the cell are notch ejection<sup>10,11</sup> and tailored window excitation.<sup>12</sup> FT-ICR permits study of ion/molecule reactions as a function of trapping time, i.e., evolution of the chemistry. As the concentration of ions is  $10^4$  that of the molecules, pseudo-first-order kinetics is observed for the ion/molecule reactions. These reactions proceed much faster in the gas phase than in solution:<sup>13</sup> at low pressures the ion/dipole and ion/induced dipole energy gained as the ion and molecule approach is not carried off by third-body collisions. With this energy the initial ion/molecule complex can overcome barriers in the potential-energy surface, which should not be higher

- (9) de Koning, L. J.; Fokkens, R. H.; Pinkse, F. A.; Nibbering, N. M. *Int. J. Mass Spectrom. Ion Processes* **1987**, *77*, 95.  
 (10) Noest, A. J.; Kort, C. W. F. *Comput. Chem.* **1983**, *7*, 8.  
 (11) Marshall, A. G.; Lin Wang, T. C.; Lebatuan Ricca, T. *Chem. Phys. Lett.* **1984**, *105*, 233.  
 (12) Marshall, A. G.; Wang, T.-C. L.; Ricca, T. L. *J. Am. Chem. Soc.* **1985**, *107*, 7893.  
 (13) Bohme, D. K.; Mackay, G. I. *J. Am. Chem. Soc.* **1981**, *103*, 978.

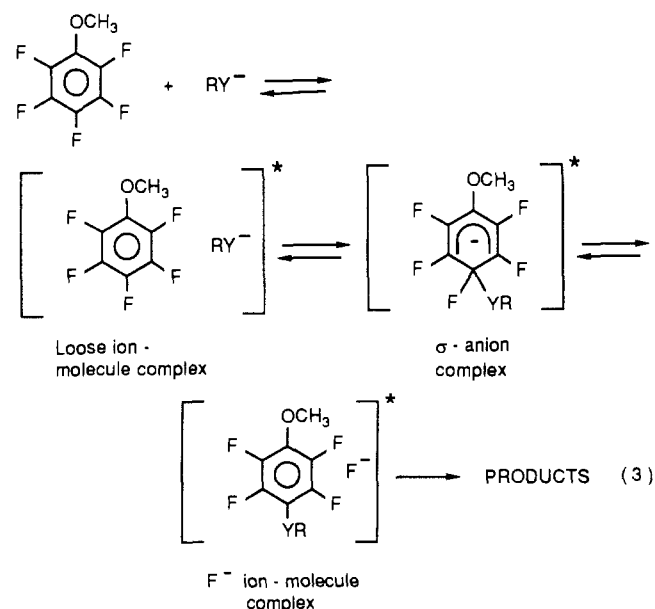
than the potential energies of the separated reactants, to yield products. The ion/molecule reactions should be overall either thermoneutral or exothermic in order to occur. However, it is the combination of the ion/(induced) dipole energy and local energy barriers in the potential-energy surface lower than the energies of the separated reactants that makes the ion/molecule reactions in the gas phase much faster, even proceeding by reaction channels unexpected by analogous reactions in the condensed phase.

Other methods<sup>1,2</sup> have been applied extensively to study the kinetics, mechanisms, and thermodynamics of gas-phase ion/molecule reactions. Together with FT-ICR, they have contributed to today's profound understanding of gas-phase ion chemistry.

**Nucleophilic Aromatic Substitution.** One of our first studies with the University of Amsterdam FT-ICR instrument<sup>14</sup> which came into operation in mid 1980 concerned the reactions of nucleophiles with methyl pentafluorophenyl ether.<sup>15</sup> Most nucleophiles ( $\text{OH}^-$ , alkoxide, thiolate, enolate, and (un)substituted allyl anions) attacked the fluorine-substituted carbon atoms. Hydroxide reacts as summarized in eq 2.



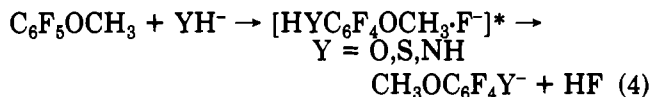
In attack upon the fluorine-substituted carbon atoms, a  $\text{F}^-$  ion is displaced via a  $\sigma$ -anion complex to form a  $\text{F}^-$  ion/molecule complex, but that does not dissociate into  $\text{F}^-$  as ionic product. Instead, the displaced  $\text{F}^-$  ion reattacks the newly formed molecule, leading eventually to the products visualized in eq 3. Thus the poten-



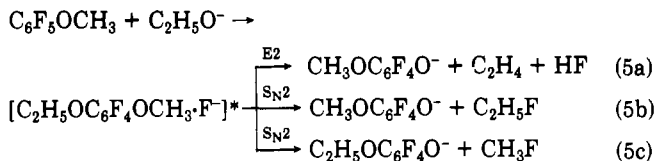
- (14) Dawson, J. H. *J. Lect. Notes Chem.* **1982**, *31*, 331.  
 (15) Ingemann, S.; Nibbering, N. M. M.; Sullivan, S. A.; DePuy, C. H. *J. Am. Chem. Soc.* **1982**, *104*, 6520.

tial-energy surface for reaction can contain a series of minima. The lifetime of the  $F^-$  ion/molecule complexes must be sufficiently long to allow secondary reactions to occur. Depending upon the nature of the original nucleophile, the reattack by the displaced  $F^-$  ion can involve proton transfer,  $S_N2$  substitution, and E2 elimination.

Proton transfer to the displaced  $F^-$  ions is the dominant reaction if the neutral species in the complex is more acidic than HF, as is the case when the primary reactant ions are  $NH_2^-$ ,  $OH^-$ , and  $SH^-$ :

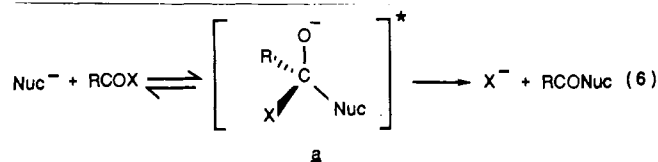


The formation of relatively long-lived  $F^-$  ion/molecule complexes is demonstrated by the reaction of  $CD_3O^-$  with  $C_6F_5OCH_3$ . This reaction yields  $CH_3OC_6F_4O^-$  and  $CD_3OC_6F_4O^-$  in a 1:1 ratio. There is therefore sufficient time for the displaced  $F^-$  ions to attack via  $S_N2$  both the  $CH_3O$  group and the  $CD_3O$  group of the newly formed  $CH_3OC_6F_4OCD_3$  molecule with equal probability. The decisive role of the  $F^-$  ion/molecule complexes is further corroborated by the observation that the same  $[CH_3OC_6F_4O^-]/[CH_3CH_2OC_6F_4O^-]$  (9:1) ratio is obtained when  $CH_3CH_2O^-$  reacts with  $C_6F_5OCH_3$  and when  $CH_3O^-$  reacts with  $C_6F_5OCH_2CH_3$ .<sup>16</sup> This observed ratio also indicates that the  $CH_3OC_6F_4O^-$  ions are formed predominantly, if not exclusively, by an E2 elimination:



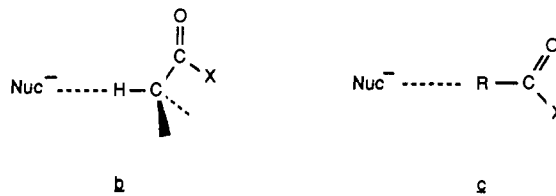
Valuable insight into competing intramolecular reactions can be obtained in this fashion. For example, neopentoxide ions  $(CH_3)_3CCH_2O^-$  react with  $C_6F_5OCH_3$  to give, via the  $F^-$  ion/molecule complex, the ions  $(CH_3)_3CCH_2OC_6F_4O^-$  and  $CH_3OC_6F_4O^-$  in a ratio of 96:4, which clearly reflects the steric effect of the neopentyl group in the  $S_N2$  reactions required to form the ions.<sup>15</sup> Similarly, a striking selectivity in the reattack by  $F^-$  is found in the reaction of  $CH_3S^-$  with  $C_6F_5OCD_3$ , where the observed product ions  $CH_3SC_6F_4O^-$  and  $CD_3OC_6F_4O^-$  are formed in a ratio of more than 99:1.<sup>15</sup>

**Addition-Elimination to Carbonyl Centers.** The addition-elimination of nucleophiles to carbonyl centers is important for the interconversion of carbonyl compounds.<sup>17</sup> Such a reaction is thought to proceed through tetrahedral species a (eq 6). Gas-phase

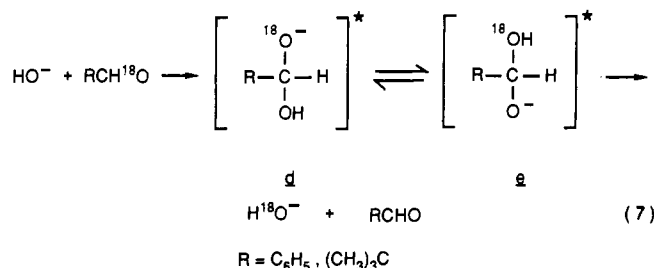


$CH_3COCl_2^-$  ions, generated by  $Cl^-$  transfer from  $Cl_2^-$  or  $COCl^-$  to acetyl chloride, must have had a tetrahedral structure, as they transfer either chlorine with equal probability as  $Cl^-$  to  $CF_3COCl$ .<sup>18</sup> Does the tetrahedral

structure correspond to a minimum or maximum of some barrier in the potential-energy surface? Loosely associated proton-bound structures or ion-dipole complexes, such as structures b and c, could also well be long-lived stable structures.<sup>19</sup> Support for this view is



provided by the observation that the chlorines in the adducts between  $Cl^-$  and  $CF_3COCl$  or  $CH_3OCOCl$  are nonequivalent.<sup>20</sup> Theoretical studies<sup>21,22</sup> indicate that the stability of a tetrahedral species depends on two key factors, (i) the energy difference between the  $\pi_{C=O}^*$  molecular orbital (MO) of the carbonyl group and the  $\sigma_{CX}^*$  MO of the bond between the carbonyl carbon atom and the leaving group X and (ii) the difference in gas-phase basicities between the attacking nucleophile and the tetrahedral anion. Thus tetrahedral intermediates are expected in reactions of strong nucleophiles, such as amide, hydroxide, or alkoxide, with carbonyl compounds having large energy differences between the  $\pi_{C=O}^*$  and  $\sigma_{CX}^*$  MOs, such as amides and esters. In reactions, however, of weak nucleophiles, such as thiolate, chloride, bromide, or iodide ions, with carbonyl compounds having small energy differences between the  $\pi_{C=O}^*$  and  $\sigma_{CX}^*$  MOs, such as acyl halides and thioesters, tetrahedral transition states will occur. These predictions are supported by the following experimental observations. If unlabeled hydroxide ions react with either benzaldehyde or pivaldehyde labeled with  $^{18}O$ , then not only does simple proton abstraction take place, but also unlabeled deprotonated benzaldehyde or pivaldehyde species and  $^{18}O$ -labeled hydroxide ions are generated.<sup>23</sup> The last observation is rationalized in eq 7, where the proton transfer required to interconvert the tetrahedral structures d and e can take place only if these structures are sufficiently long-lived, i.e., if they correspond to a potential-energy minimum.



Other experimental support for the existence of stable tetrahedral intermediates is provided by the reactivity of the long-lived methoxide adduct ions of formaldehyde, pivaldehyde, and benzaldehyde toward tri-deuteriomethyl pentafluorophenyl ether.<sup>23</sup> These adduct ions were generated by reaction with meth-

(18) Asubiojo, O. I.; Blair, L. K.; Brauman, J. I. *J. Am. Chem. Soc.* **1975**, *97*, 6685.

(19) Bowie, J. H. *Mass Spectrom. Rev.* **1984**, *3*, 1.

(20) Han, C. C.; Brauman, J. I. *J. Am. Chem. Soc.* **1987**, *109*, 589.

(21) Yamabe, S.; Minato, T.; Kawabata, Y. *Can. J. Chem.* **1984**, *62*, 235.

(22) Blake, J. F.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1987**, *109*, 3856.

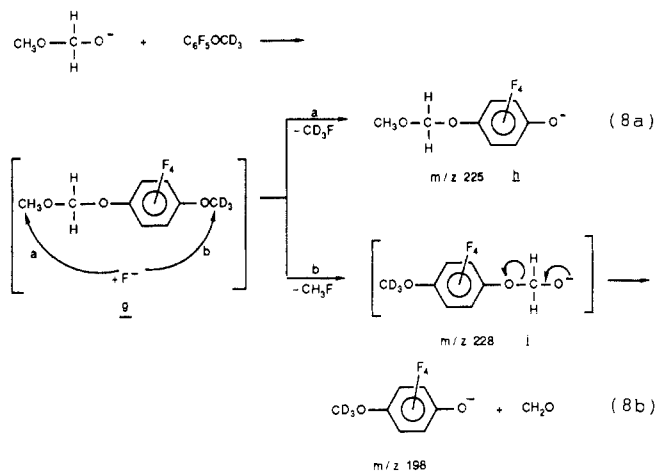
(23) van der Wel, H.; Nibbering, N. M. M. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 491.

(16) Ingemann, S.; Nibbering, N. M. M. *Nouv. J. Chim.* **1984**, *8*, 299.

(17) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, 1981; Chapter 8.

oxide/methanol cluster ions, which in turn were prepared by reaction of methoxide with methyl formate via the Riveros reaction.<sup>24</sup> The methoxide/methanol cluster ions themselves react with  $C_6F_5OCD_3$ <sup>23</sup> to produce via nucleophilic aromatic substitution (*vide supra*) the ions  $m/z$  195 ( $CH_3OC_6F_4O^-$ ) and  $m/z$  198 ( $CD_3OC_6F_4O^-$ ) in a 1:1 ratio.

The adduct ions between methoxide and the various aldehydes, however, react quite differently with  $C_6F_5OCD_3$ <sup>23</sup> in the sense that the  $m/z$  195 and 198 ions are not produced any more in a 1:1 ratio. For example, the methoxide adduct ions of formaldehyde react with  $C_6F_5OCD_3$  to give the ions  $m/z$  195 and 198 in a 1:12 ratio. The latter observation points to an intermediate in which the methoxy and trideuteriomethoxy groups are not chemically equivalent any more rather than to an isotope effect: the adduct ions between tri-deuteriomethoxide and formaldehyde react similarly with unlabeled  $C_6F_5OCH_3$  to produce the ions  $m/z$  195 and  $m/z$  198 in a 10:1 ratio. These facts together with the observation of  $m/z$  225 ions **h** in the  $[CH_3O^- + CH_2O]/C_6F_5OCD_3$  reaction system (see eq 8a) and  $m/z$  228 ions in the  $[CD_3O^- + CH_2O]/C_6F_5OCH_3$  reaction system support the presence of a stable tetrahedral structure for at least part of the generated methoxide-aldehyde adduct ions. A mechanism for the reaction



between the tetrahedral  $[CH_3O^- + CH_2O]$  adduct ions and  $C_6F_5OCD_3$  is presented in eq 8. The  $m/z$  228 ions with the proposed tetrahedral structure **i** in eq 8b were not detected, probably because of their fast decomposition to  $m/z$  198 ions.

The  $m/z$  195 ions, however, are probably not generated via the  $m/z$  225 ions, intermediate structure **h**, because no fragmentation of the latter ions could be achieved by collision-induced dissociation. The  $m/z$  195 ions, therefore, are assumed to be generated exclusively via the cluster structure  $[CH_3O^- \cdots RCHO]$  of the adduct ion. With this assumption and the assumption that the adduct ions with the cluster structure will generate the  $m/z$  195 and 198 ions in a 1:1 ratio, it is possible to estimate the relative amounts of ions having the cluster and tetrahedral structures from the relative abundances of the  $m/z$  195 and 198 ions. In this way it has been calculated that at least ~90% of the methoxide ions of formaldehyde, ~35% of those of pivaldehyde, and ~20% of these of benzaldehyde have the tetrahedral

structure. These data suggest the following stability order for the tetrahedral versus cluster adduct ions:  $[CH_3O^- + CH_2O] > [CH_3O^- + (CH_3)_3CCHO] > [CH_3O^- + C_6H_5CHO]$ . This order reflects the calculated bond strength order for the cluster structures as being 105, 188, and 218 kJ/mol,<sup>23</sup> the structures should become more stable as the acidity difference between methanol and the aldehyde decreases.<sup>25</sup>

Experimental support for tetrahedral transition states in the reactions between weak nucleophiles and pivaloyl chloride and *S*-methyl thiopivalate for which the energy difference between the  $\pi_{C=O}^*$  and  $\sigma_{CX}^*$  MOs is small, e.g., ~0.4 V, was obtained from rate measurements.<sup>26</sup> The efficiency of  $Cl^-$  and  $CH_3S^-$  production, respectively, varied with the basicity of the nucleophiles; the more basic ones react more rapidly. Thus, the reaction rate for the generation of  $Cl^-$  and  $CH_3S^-$  via nucleophilic addition-elimination to the carbonyl center appears to depend on the basicity of the nucleophile and consequently on the reaction enthalpy. This dependence points to the presence of one or more significant intrinsic barriers in the potential-energy surface. The double-well potential model in which the tetrahedral structure is situated at the top of the central energy barrier<sup>27</sup> is the simplest model to account for the results. The more exothermic the reaction becomes, the larger the reaction rate will be as the central energy barrier will be less significant as shown for the reaction between  $F^-$  and acetyl chloride on the basis of *ab initio* calculations. Confidence in this interpretation is also provided by the observation that reactions of nucleophiles with 1-pivaloyl-1,2,4-triazole (for which the energy difference between  $\pi_{C=O}^*$  and  $\sigma_{CX}^*$  is 1.3 eV<sup>21</sup>) either occur at every collision for exothermic reactions or do not occur at all for endothermic reactions. This potential-energy surface must have no barriers or very small barriers to the formation of the tetrahedral intermediate. Similar observations from rate data have been made for reactions of various nucleophiles with methyl iodide and trimethylchlorosilane.<sup>28</sup> For the former substrate the  $S_N2$  reactivity of the various nucleophiles varies with their basicity, the more basic ones reacting most rapidly. This order is consistent with a concerted nucleophilic substitution reaction and with the double-well potential model for the  $S_N2$  reaction<sup>29</sup> having the pentacoordinate transition state as the central energy barrier. For the latter substrate, however, the nucleophiles appear to react either at the collision rate for exothermic reactions or not at all for endothermic reactions, which points to a potential-energy surface having no barriers or very small barriers to the formation of the pentacoordinate silicon intermediate.<sup>30</sup>

**Elimination Reactions.** Gas-phase elimination reactions studied so far are facile processes. It is often difficult to distinguish them from  $S_N2$  substitution reactions: both reactions lead to the same product ions. They do not lead to the same neutral products, but in

(25) Caldwell, G.; Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 4660.

(26) van der Wel, H.; Bruin, G. J. M.; van der Linde, S. J. J.; Nibbering, N. M. M.; Engberts, J. B. F. N. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 370.

(27) Asubiojo, O. I.; Brauman, J. I. *J. Am. Chem. Soc.* **1979**, *101*, 3715.

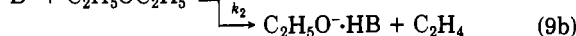
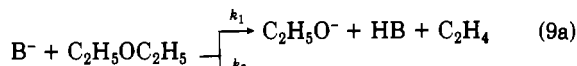
(28) Damrauer, R.; DePuy, C. H.; Bierbaum, V. M. *Organometallics* **1982**, *1*, 1553.

(29) Olmstead, W. N.; Brauman, J. I. *J. Am. Chem. Soc.* **1977**, *99*, 4219.

(30) Sheldon, J. C.; Hayes, R. N.; Bowie, J. H. *J. Am. Chem. Soc.* **1984**, *106*, 7711.

(24) Faigle, J. F. G.; Isolani, P. C.; Riveros, J. M. *J. Am. Chem. Soc.* **1976**, *98*, 2049.

most experiments these are not known.<sup>31</sup> In that respect the reactions of cyclic compounds, such as cyclic ethers, are good probes to study elimination reactions because the "leaving group" remains in the anion.<sup>32</sup> Dialkyl ethers containing  $\beta$ -hydrogens react rapidly with bases, such as amide and hydroxide ions, to form alkoxide ions, whereas ethers lacking  $\beta$ -hydrogens are comparatively unreactive. This observation demonstrates that these are elimination reactions, not substitution. In the case of diethyl ether, abundant water-solvated ethoxide ions and free ethoxide ions are generated in the reaction with  $\text{OH}^-$ .<sup>33,34</sup> These channels, eqs 9a and 9b, have been studied recently by FT-ICR,<sup>35</sup> to understand the formation of water-solvated ethoxide ions in the absence of third-body collisions.



The overall kinetic isotope effects associated with reactions 9a and 9b between  $\text{OH}^-$  and  $\text{RNH}^-$  ( $\text{R} = \text{H}, \text{CH}_3, \text{C}_2\text{H}_5$ ) and diethyl ether agree very well<sup>35</sup> with those measured for the  $\text{NH}_2^-$  and  $\text{OH}^-$ /diethyl ether systems by flowing afterglow<sup>36</sup> and permit calculation of the overall  $k_{\text{H}}/k_{\text{D}}$  ( $\text{H}_\beta$ ), the  $k_{\text{H}}/k_{\text{D}}$  (secondary  $\text{H}_\alpha$ ), and  $k(\text{OCH}_2\text{CH}_3)/k(\text{OCD}_2\text{CD}_3)$  values for the reactions listed in Table I. The overall  $k_{\text{H}}/k_{\text{D}}$  ( $\text{H}_\beta$ ) value corresponds to the product of  $[k_{\text{H}}/k_{\text{D}} (\text{primary } \text{H}_\beta)] \times [k_{\text{H}}/k_{\text{D}} (\text{secondary } \text{H}_\beta)]$ , where  $k_{\text{H}}/k_{\text{D}}$  (primary  $\text{H}_\beta$ ) refers to the rates of  $\text{H}_\beta$  versus  $\text{D}_\beta$  abstraction and  $k_{\text{H}}/k_{\text{D}}$  (secondary  $\text{H}_\beta$ ) is the ratio of reaction rates upon substitution of the two remaining  $\text{H}_\beta$ 's by D. Similarly,  $k_{\text{H}}/k_{\text{D}}$  (secondary  $\text{H}_\alpha$ ) corresponds to the ratio of reaction rates if both  $\text{H}_\alpha$ 's are substituted by D, while  $k(\text{OCH}_2\text{CH}_3)/k(\text{OCD}_2\text{CD}_3)$  reflects the kinetic effect which arises from replacing H's by D's in the leaving group.

The results show that  $k_{\text{H}}/k_{\text{D}}$  ( $\text{H}_\beta$ ) is a smooth function of the base strength and spans a scale from 2.2 for  $\text{OH}^-$  to 5.6 for  $\text{NH}_2^-$  in the generation of ethoxide. For both bases,  $k_{\text{H}}/k_{\text{D}}$  (secondary  $\text{H}_\alpha$ ) is found to be unity. The same is true for  $k(\text{OCH}_2\text{CH}_3)/k(\text{OCD}_2\text{CD}_3)$  if  $\text{NH}_2^-$  is the base, but the value found for  $\text{OH}^-$  points at a leaving-group effect. These observations indicate a shift from an  $\text{E1cB}$  type mechanism toward a more central  $\text{E2}$  mechanism when going from the strong base  $\text{NH}_2^-$  to the weaker base  $\text{OH}^-$ , as illustrated by transition-states i and k.

In the reaction with  $\text{NH}_2^-$ , the  $\beta$ -hydrogen is situated more or less symmetrically between the  $\beta$ -carbon and  $\text{NH}_2^-$  and the  $\text{C}_\alpha\text{-O}$  bond is only minimally stretched in the (reactant-like) transition state. In the reaction with  $\text{OH}^-$ , however, the  $\beta$ -proton is more than half transferred and the  $\text{C}_\alpha\text{-O}$  bond breaking is substantial in the (product-like) transition state. The results in Table I also show a significant difference in  $k_{\text{H}}/k_{\text{D}}$  ( $\text{H}_\beta$ ) for the production of free and solvated ethoxide ions

(31) Jones, M. E.; Kass, S. R.; Filley, J.; Barkley, R. M.; Ellison, G. B. *J. Am. Chem. Soc.* 1985, 107, 109.

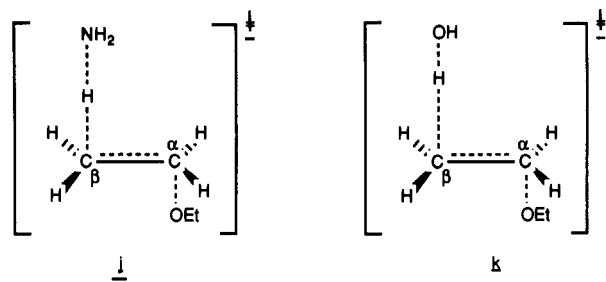
(32) DePuy, C. H.; Beedle, E. C.; Bierbaum, V. M. *J. Am. Chem. Soc.* 1982, 104, 6483.

(33) van Doorn, R.; Jennings, K. R. *Org. Mass Spectrom.* 1981, 16, 397.

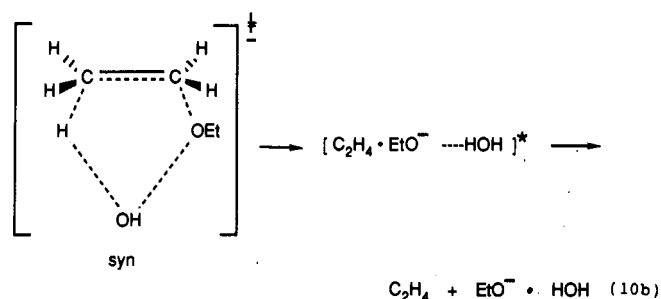
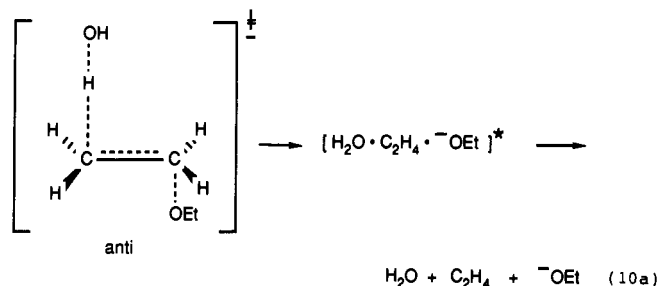
(34) DePuy, C. H.; Bierbaum, V. M. *J. Am. Chem. Soc.* 1981, 103, 5034.

(35) de Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* 1987, 109, 1715.

(36) Bierbaum, V. M.; Filley, J.; DePuy, C. H.; Jarrold, M. F.; Bowers, M. T. *J. Am. Chem. Soc.* 1985, 107, 2818.



in the reactions with  $\text{OH}^-$ . These ions then are formed by different elimination mechanisms. An anti elimination has been proposed for the free ethoxide formation and a syn elimination for the water-solvated ethoxide ion formation (eqs 10a and 10b). In the syn



elimination no complicated reorganization of the reaction complex is required to arrive at the water-solvated ethoxide ion, and the assignment also agrees with isotope effect model calculations for anti and syn eliminations.<sup>37</sup> The importance of base/leaving group association in the transition state for syn elimination (eq 10b) is further corroborated by the observation that diethyl ether and dimethylamine-solvated hydroxide ions  $\text{OH}^- \cdot \text{HN}(\text{CH}_3)_2$  yield mostly the free ethoxide, rather than solvated ethoxide.<sup>35</sup>

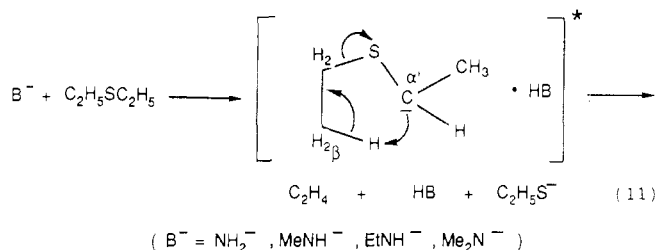
These elimination reactions of diethyl ether are suggested to proceed by a periplanar transition state. This hypothesis has been tested by studying stereoelectronic control in the base-induced elimination reactions of *cis*- and *trans*-1,4-*tert*-butylmethoxycyclohexane.<sup>35</sup> Both compounds give free and water-solvated methoxide by reaction with  $\text{OH}^-$ .

If the bulky *tert*-butyl group fixes the methoxy group spatially, a perfect antiperiplanar relationship exists between the methoxy group and the  $\beta$ -hydrogens in the *cis* compound, but not in the *trans*. The formation of free methoxide from the *cis* compound will then be preferred over formation from the *trans* compound. Indeed, the ratio is 2.6 in favor of the *cis* compound. The formation of water-solvated methoxide from the *cis* compound also has been found to be more favored, by a factor of 4.2, over formation from the *trans* com-

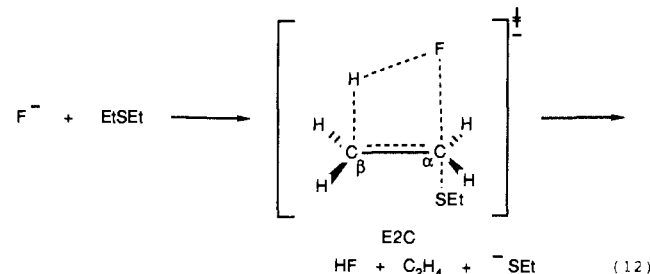
(37) Melander, L.; Saunders, W. H., Jr. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980.

ound. Then in the syn elimination the methoxy group leaves preferentially from an axial position as well. A significant leaving-group effect has been observed in the formation of both free and water-solvated methoxide from the trans compound, where the periplanarity required for elimination cannot be readily achieved. This indicates a drastic shift of the transition state toward the carbenium ion or E1 region of the E2 spectrum. For further details the reader is referred to the original publication.<sup>35</sup>

Recently the base-induced gas-phase elimination reactions of diethyl sulfide have been studied.<sup>38</sup> Reaction with the nitrogen bases  $\text{NH}_2^-$ ,  $\text{CH}_3\text{NH}^-$ ,  $\text{C}_2\text{H}_5\text{NH}^-$ , and  $(\text{CH}_3)_2\text{N}^-$  preferentially proceeds via an  $\alpha',\beta$ -elimination mechanism. Abstraction of the relatively acidic  $\alpha'$  proton of the sulfide results in the formation of an  $\alpha$ -thio carbanion, which subsequently undergoes an intramolecular syn elimination to generate the ethanethiolate anion (eq 11). Reaction with  $\text{OH}^-$ ,  $\text{MeO}^-$ ,



and  $\text{F}^-$ , however, exclusively proceeds via an E2 mechanism with a variable E2 transition state. In the case of  $\text{OH}^-$ , the transition state is preceded by a rapid exchange between the  $\alpha$ -hydrogens of the sulfide and the hydroxide hydrogen. With  $\text{F}^-$ , both free and HF-solvated ethanethiolate anions are generated. The latter ions are formed via a syn elimination involving a two-side attack of  $\text{F}^-$  on the  $\beta$ -hydrogen and the leaving group. This picture is consistent with the isotope and leaving-group effects and is similar to the mechanism for the formation of water-solvated ethoxide ions (eq 10b). With  $\text{F}^-$  as base, however, an extremely large secondary  $\alpha$ -deuterium isotope effect  $k_{\text{H}}/k_{\text{D}}$  (secondary  $\text{H}_\alpha$ ) of 1.30 for  $\text{C}_2\text{H}_5\text{S}^-$  formation was found; this is incompatible with an E2H mechanism, where  $\text{F}^-$  would interact only with a  $\beta$ -hydrogen. Instead, the large secondary  $\text{H}_\alpha$  isotope effect points to an interaction of  $\text{F}^-$  with the  $\alpha$ -carbon in the transition state. This isotope effect and the relatively small  $\beta$ -deuterium isotope effect  $k_{\text{H}}/k_{\text{D}}$  ( $\text{H}_\beta$ ) of 1.68 are best explained by an E2C-like mechanism involving a bent proton transfer and covalent interaction of  $\text{F}^-$  with the  $\alpha$ -carbon (eq 12).



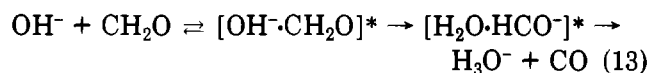
Finally, by studying cyclic thioethers from hexamethylene to dimethylene sulfide,<sup>39</sup> the E2 elimination

(38) van Berkel, W. W.; de Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1987**, *109*, 7602.

and  $\alpha',\beta$ -elimination have been found to occur under stereoelectronic control favoring a transition state in which the  $\text{C}_\beta\text{-H}$  and  $\text{C}_\alpha\text{-(leaving group)}$  bonds are periplanar. The small strained trimethylene and dimethylene sulfides show such a low E2 reactivity that  $\text{S}_\text{N}2$  substitution, not observed in the reactions of the unstrained cyclic and diethyl sulfide, competes effectively with the E2 elimination in them.<sup>39</sup>

**Hydride-Transfer Reactions.** Hydride transfer from  $\text{HCO}^-$  to formaldehyde,<sup>40</sup> from  $\text{DNO}^-$  as deuteride to  $(\text{CH}_3)_3\text{B}$ ,<sup>41</sup> from the conjugate base of 1,4-cyclohexadiene to benzaldehyde,<sup>42</sup> from alkoxide ions to singlet oxygen,<sup>43</sup> and from the 1-phenylethyl, formate, and isobutyronitrile anions to iron pentacarbonyl<sup>44</sup> has been observed. Similarly, it has been found possible to transfer a hydride from methoxide ions to formaldehyde, benzaldehyde, 2,2-dimethylpropanal, and 1-adamantylcarboxaldehyde.<sup>45</sup> The reaction trajectory of the hydride transfer from methoxide ion to formaldehyde has also been studied by ab initio calculations.<sup>46</sup>

An interesting hydride-transfer step has been observed in the reaction of hydroxide ion with formaldehyde.<sup>47</sup> Once the corresponding collision complex is formed, the solvation energy allows a proton transfer from the formaldehyde molecule to  $\text{OH}^-$ . The water-solvated formyl anion so generated cannot separate since water is more acidic than formaldehyde. Instead, hydride transfer from the formyl anion to the water molecule in the complex occurs, leading to  $\text{H}_3\text{O}^-$  and carbon monoxide (eq 13). The  $\text{H}_3\text{O}^-$  ion, which has also



been prepared independently in an ion-beam experiment,<sup>48</sup> contains exclusively the oxygen atom of the hydroxide while the hydrogen atoms are not equivalent. For example, the  $\text{H}_2\text{DO}^-$  ion generated by reaction of  $\text{OD}^-$  with  $\text{CH}_2\text{O}$  transfers a hydride, but not a deuteride, to formaldehyde. These observations and those for the  $\text{OH}^-/\text{CD}_2\text{O}$  system are consistent with the picture of the  $\text{H}_3\text{O}^-$  ion as a hydride ion solvated by water. Both photoelectron spectroscopy<sup>49</sup> and theoretical calculations<sup>50-52</sup> confirm this. According to the latter, the

(39) de Koning, L. J.; Nibbering, N. M. M. *J. Am. Chem. Soc.* **1988**, *110*, 2066.

(40) Karpas, Z.; Klein, F. S. *Int. J. Mass Spectrom. Ion Phys.* **1975**, *18*, 65.

(41) Murphy, M. K.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 1433.

(42) DePuy, C. H.; Bierbaum, V. M.; Schmitt, R. J.; Shapiro, R. H. *J. Am. Chem. Soc.* **1978**, *100*, 2920.

(43) Schmitt, R. J.; Bierbaum, V. M.; DePuy, C. H. *J. Am. Chem. Soc.* **1979**, *101*, 6443.

(44) Lane, K. R.; Sallans, L.; Squires, R. R. *Organometallics* **1985**, *4*, 408.

(45) Ingemann, S.; Kleingeld, J. C.; Nibbering, N. M. M. *J. Chem. Soc., Chem. Commun.* **1982**, 1009.

(46) Sheldon, J. C.; Bowie, J. H.; Hayes, R. N. *Nouv. J. Chim.* **1984**, *8*, 79.

(47) Kleingeld, J. C.; Nibbering, N. M. M. *Int. J. Mass Spectrom. Ion Phys.* **1983**, *49*, 311.

(48) Paulson, J. F.; Henchman, M. J. *Bull. Am. Phys. Soc.* **1982**, *27*, 108.

(49) Miller, T. M.; Leopold, D. G.; Murray, K. K.; Lineberger, W. C. *Bull. Am. Phys. Soc.* **1985**, *30*, 880.

(50) Squires, R. R. In *Ionic Processes in the Gas Phase*; Almoester Ferreira, M. A., Ed.; Reidel: Dordrecht, 1984; p 337.

(51) Cremer, D.; Kraka, E. *J. Phys. Chem.* **1986**, *90*, 33.

(52) Chalasiński, G.; Kendall, R. A.; Simons, J. *J. Chem. Phys.* **1987**, *97*, 2965.

Table I  
Kinetic Isotope and Leaving-Group Effects Associated with the Reaction between B<sup>-</sup> and Diethyl Ether

B <sup>-</sup>	$k_{1H}/k_{1D}$ (H <sub>β</sub> )	$k_{2H}/k_{2D}$ (H <sub>β</sub> )	$k_{1H}/k_{1D}$ (H <sub>α</sub> )	$k_{2H}/k_{2D}$ (H <sub>α</sub> )	$k_1(\text{OC}_2\text{H}_5)/k_1(\text{OC}_2\text{D}_5)$	$k_2(\text{OC}_2\text{H}_5)/k_2(\text{OC}_2\text{D}_5)$
NH <sub>2</sub> <sup>-</sup>	5.60 ± 0.03		1.01 ± 0.01		1.00 ± 0.01	
OH <sup>-</sup>	2.20 ± 0.03	1.55 ± 0.03	1.00 ± 0.02	1.00 ± 0.02	1.05 ± 0.02	1.10 ± 0.03

hydride ion is bonded to one of the hydrogen atoms of the water molecule in the most stable form of H<sub>3</sub>O<sup>-</sup>.

Similarly, reaction of NH<sub>2</sub><sup>-</sup> with formaldehyde generates the NH<sub>4</sub><sup>-</sup> ion.<sup>53</sup> Here, however, the proton abstraction from formaldehyde by NH<sub>2</sub><sup>-</sup>, now exothermic, forms HCO<sup>-</sup>. This ion then transfers a hydride to ammonia to give NH<sub>4</sub><sup>-</sup> and carbon monoxide (eqs 14a and 14b). The hydride ion transferred to ammonia retains



its identity; the NH<sub>4</sub><sup>-</sup> ion, like the H<sub>3</sub>O<sup>-</sup> ion is best described as a hydride ion solvated by an ammonia molecule. This description is confirmed by photoelectron spectroscopy<sup>54</sup> and by theoretical calculations.<sup>50,51,55,56</sup>

Recently the SiH<sub>5</sub><sup>-</sup> ion has been prepared in a flowing afterglow instrument.<sup>57</sup> Hydride ions were added to alkylsilanes, such as *n*-C<sub>5</sub>H<sub>11</sub>SiH<sub>3</sub> and (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>SiH, and the products collisionally stabilized by He buffer. The resulting *n*-C<sub>5</sub>H<sub>11</sub>SiH<sub>4</sub><sup>-</sup> and (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>SiH<sub>2</sub><sup>-</sup> ions could transfer a hydride to SiH<sub>4</sub> to generate SiH<sub>5</sub><sup>-</sup> in addition to SiH<sub>3</sub><sup>-</sup>. The hydrogen atoms bonded to silicon in the (C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>SiH<sub>2</sub><sup>-</sup> and *n*-C<sub>5</sub>H<sub>11</sub>SiH<sub>4</sub><sup>-</sup> ions are chemically equivalent.

Finally, reduction of carbonyls by hydride transfer from BH<sub>4</sub><sup>-</sup> has been studied recently. BH<sub>4</sub><sup>-</sup> cannot reduce formaldehyde<sup>58</sup> or other simple aliphatic carbonyls<sup>59</sup> in the gas phase. However, difluoroformaldehyde, hexafluoroacetone, and methylmaleic anhydride can be reduced by BH<sub>4</sub><sup>-</sup>.<sup>60</sup> The carbonyl group

neighboring the methyl substituent in methylmaleic anhydride is reduced preferentially, as its higher LUMO coefficient suggests.

### Concluding Remarks

Among the many experiments possible with FT-ICR mass spectrometry are those used to study evolution of ion/molecule chemistry as a function of reaction time. Often a close correspondence is found with reactions in solution, but there are also examples where unexpected and unprecedented chemistry happens. The ion-(induced) dipole energy gained upon approach of the ion and neutral molecule serves as the fuel for the ion/molecule complex to surmount not only traditional reaction barriers but also reaction barriers which are otherwise difficult (or impossible) to overcome. The interest in studying organic (and also organometallic) ion/molecule reactions will therefore continue as such studies may aid in understanding chemical reactivity. Moreover, FT-ICR is quite compatible with the use of lasers as others have shown, so that experiments of this type are expected to become increasingly important in studies of organic and organometallic ion/molecule reactions in the near future. Together with the recent rapid development of FT-ICR as an analytical method, this branch of mass spectrometry is blossoming as before, and new, very exciting technical and chemical progress will be made.

*It is a great pleasure for me to thank all my previous and present co-workers whose contributions far exceeded the merely experimental and without whom the work carried out at the University of Amsterdam could not have been completed. Many of their names are listed in the references. I am also indebted to my many colleagues in the field for their cooperation in various projects over many years. Last, but certainly not least, I thank the Netherlands Organization for Pure Research (SON/NWO) for continuous financial and personal support over many years to perform the research described in this Account.*

(60) van der Wel, H.; Nibbering, N. M. M.; Kayser, M. M. *Can. J. Chem.* 1988, 66, 2587.

(53) Kleingeld, J. C.; Ingemann, S.; Jalonen, J. E.; Nibbering, N. M. *J. Am. Chem. Soc.* 1983, 105, 2474.

(54) Coe, J. V.; Snodgrass, J. T.; Freidhoff, C. B.; McHugh, K. M.; Bowen, K. H. *J. Chem. Phys.* 1985, 83, 3169.

(55) Kalcher, J.; Rosmus, P.; Quack, M. *Can. J. Phys.* 1984, 62, 1323.

(56) Cardy, H.; Larrien, C.; Dargeloo, A. *Chem. Phys. Lett.* 1986, 131, 507.

(57) Hajdasz, D. J.; Squires, R. R. *J. Am. Chem. Soc.* 1986, 108, 3139.

(58) Kayser, M. M.; McMahan, T. B. *Tetrahedron Lett.* 1984, 25, 3379.

(59) Workman, D. B.; Squires, R. R. *Inorg. Chem.* 1988, 27, 1846.