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Intramolecular Fluorine Migration via Four-Member Cyclic Transition States

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Gaseous CF_3^+ interchanges F^+ for O with simple carbonyl compounds. CF_3^+ reacts with propionaldehyde in the gas phase to produce $(CH_3)_2CF^+$ via two competing pathways. Starting with 1-^{13}C-propionaldehyde, the major pathway (80%) produces $(CH_3)_2CF^+$ with the carbon label in one of the methyl groups. The minor pathway (20%) produces $(CH_3)_2CF^+$ with the carbon label in the central position. The relative proportions of these two pathways are measured by ^{19}F NMR analysis of the neutral $CH_3CF{=}CH_2$ produced by deprotonation of $(CH_3)_2CF^+$ at $<10^{-3}$ Torr in an electron bombardment flow (EBFlow) reactor. Formation of alkene in which carbon is directly bonded to fluorine means that (in the minor product, at least) an F^+ for O transposition occurs via adduct formation followed by 1,3-atom transfer and then isomerization of $CH_3CH_2CHF^+$ to the more stable $(CH_3)_2CF^+$. Use of CF_4 as a chemical ionization (CI) reagent gas leads to CF_3^+ adduct ions for a variety of ketones, in addition to isoelectronic transposition of F^+ for O. Metastable ion decompositions of the adduct ions yield the metathesis products. Decompositions of fluorocycloalkyl cations formed in this manner give evidence for the same kinds of rearrangements as take place in $CH_3CH_2CHF^+$. Density functional calculations confirm that F^+ for O metathesis takes place via addition of CF_3^+ to the carbonyl oxygen followed by transposition via a four-member cyclic transition state. A computational survey of the effects of different substituents in a series of aldehydes and acyclic ketones reveals no systematic variation of the energy of the transition state as a function of thermochemistry, but the Hammond postulate does appear to be obeyed in terms of progress along the reaction coordinate. Bond lengths corresponding to the central barrier correlate with overall thermochemistry of the F^+ for O interchange, but in a sense opposite to what might have been expected: the transition state becomes more product-like as the metathesis becomes increasingly exothermic. This reversal of the naive interpretation of the Hammond postulate is accounted for by the relative positions of the potential energy wells that precede and follow the central barrier.

Methods for incorporation of fluorine into an organic molecule are of widespread interest and utility. Potential applications of site-specifically fluorinated compounds include high-resolution ^{19}F NMR imaging and positron emission tomography (PET scanning) using the short-lived isotope ^{18}F. Development of new synthetic approaches depends on more detailed understanding of the mechanisms by which fluorine can be introduced.

Some of the most useful reactions transpose fluorine for oxygen. In solution, a variety of Lewis acidic reagents of the general form XF_{n+1} accomplish this with carbonyl compounds as starting materials.[1,2] Equation 1 portrays two intermediates in a general scheme. The Lewis acid forms an adduct (**A**) with the carbonyl oxygen. In subsequent steps fluorine shifts onto the carbonyl carbon, and the carbon−oxygen bond heterolyzes to form an intermediate α-fluorinated cation (**B**, which may be contained within an ion pair). The final product forms either via nucleophilic attack on **B** or by deprotonation.

If there is a single rate-determining step in this reaction, it is likely to occur somewhere in the conversion of **A** to **B**, corresponding to the transposition of fluorine from center X to carbon. One of the best known reagents, sulfur tetrafluoride ($SF_4 = XF_{n+1}$), is believed to require a bimolecular reaction to move fluorine from sulfur onto carbon,[3] which should render the overall reaction second-order in fluorine-containing reagent (even though stoichiometrically the reaction is first-order in SF_4). A reaction whose kinetic order is greater than its stoichiometric order would be a poor choice for incorporation of a rare isotope, where the limiting reagent is typically used in high dilution.

$$R_2C{=}O + XF_{n+1} \xrightarrow{-F^-} \underset{\mathbf{A}}{R_2C{=}OXF_n^+} \longrightarrow \underset{\mathbf{B}}{R_2CF^+} \qquad (1)$$

A gas-phase analogue of eq 1 exhibits an intramolecular transposition of fluorine onto the carbonyl cation in the course of an ion−molecule reaction. Some years ago, Eyler, Ausloos, and Lias reported the metathesis of F^+ for oxygen (which are isoelectronic substituents) in the reaction of a perfluorinated cation (such as CF_3^+ or $C_2F_5^+$) with a variety of aldehydes and ketones in the gas phase.[4] As eq 2 depicts, the Eyler−Ausloos−Lias reaction demonstrates that fluorine appears to be capable of undergoing a unimolecular 1,3-transfer to a sufficiently electrophilic carbon. In a subsequent ion−molecule reaction, the

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[1] Hasek, W. R.; Smith, W. C.; Engelhardt, V. A. *J. Am. Chem. Soc.* **1960**, *82*, 543−555.

[2] Rozen, S.; Mishani, E.; Bar-Haim, A. *J. Org. Chem.* **1994**, *59*, 2918.

[3] (a) Martin, D. G.; Kagan, F. *J. Org. Chem.* **1962**, *27*, 3164−3168. (b) Boswell, G. A., Jr.; Ripka, W. C.; Scribner, R. M.; Tullock, C. W. *Org. React.* **1974**, *21*, 1−124.

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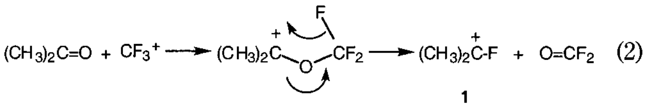
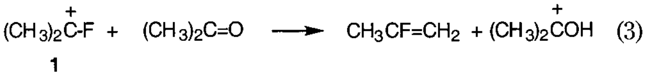
fluorinated ion **1** transfers a proton to another molecule of acetone, as portrayed by eq 3.[5]



$$(CH_3)_2C{=}O + CF_3^+ \longrightarrow (CH_3)_2\overset{+}{C}\overset{F}{\underset{O}{\frown}}CF_2 \longrightarrow \underset{\mathbf{1}}{(CH_3)_2\overset{+}{C}\text{-}F} + O{=}CF_2 \quad (2)$$



$$\underset{\mathbf{1}}{(CH_3)_2\overset{+}{C}\text{-}F} + (CH_3)_2C{=}O \longrightarrow CH_3CF{=}CH_2 + (CH_3)_2\overset{+}{C}OH \quad (3)$$

Intramolecular 1,3-halogen transpositions are comparatively unusual.[6] The fluorine shift in eq 2 has to take place via a four-member cyclic transition state, for which there are not many precedents. Only recently has a four-member cyclic bromonium ion been exhibited in the gas phase,[7] even though halonium ions of both smaller and larger ring sizes have been well characterized for many years.[8,9] The question arises whether unimolecular 1,3-shift can compete effectively with other rearrangement pathways. We present evidence that 1,3-fluorine transfer operates in the reaction of CF_3^+ with propionaldehyde, even though competing, lower energy pathways are accessible.

We have previously reported the detection of $CH_3CF{=}CH_2$ as a neutral product from the reaction of CF_3^+ with acetone in the gas phase.[5] Surprisingly, we observed that the reaction of CF_3^+ with propionaldehyde also yields the same neutral product in addition to a lower yield of $CH_3CH{=}CHF$. This result is analogous to rearrangements reported in the course of reactions of some aldehydes (such as chloral) with SF_4 in solution,[10] and it could be explained in two ways. Either the $CH_3CH_2CHF^+$ ion, **4**, is generated (analogous to eq 2) and subsequently undergoes rearrangement, or else a rearrangement takes place in the intermediate stages of the metathesis (as eq 4 represents). For instance, adduct **2** might isomerize to intermediate **3** via a hydrogen shift, which would then permit fluorine transfer to take place via a five-member cyclic transition state, as drawn.

This paper presents data that show there are at least two pathways leading to **1** from propionaldehyde plus CF_3^+. Isotopic labeling demonstrates that one pathway consists of isomerization of initially formed **4** via methyl shift, as eq 5 portrays. Alternatively, **4** might isomerize via fluoride shift in competition with methyl shift (as we have observed in other monofluorinated propyl cations[5]). The fluoride shift product is indistinguishable from that of eq 4.

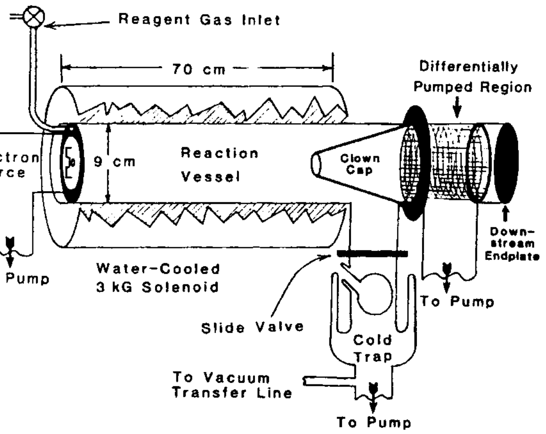
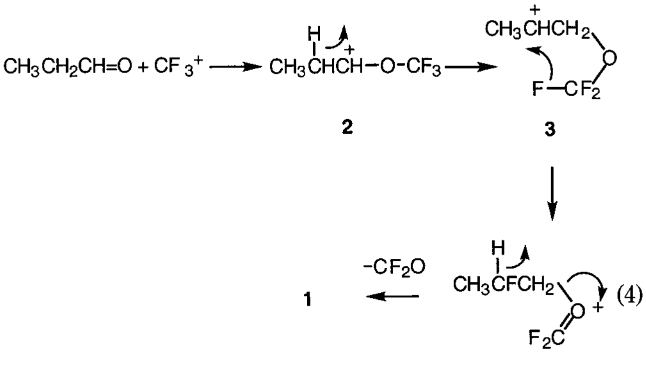


Figure 1. Schematic diagram of an electron bombardment flow (EBFlow) reactor. An external solenoid electromagnet keeps the electrons on the axis of the cylindrical reaction vessel, and the electrical charge of the beam (along with the magnetic field) prevents collisions from driving ions to the walls. At the far end of the vessel electrons and ions exit to a differentially pumped chamber via a conical Faraday plate ("clown cap"), while neutrals find their way into a liquid nitrogen cooled trap, where they are collected. Efficiency of neutral product collection has been estimated to be on the order of 85%.[11]



Experimental Section

Electron bombardment flow (EBFlow) experiments were performed as previously described.[5,11] The cylindrical EBFlow reaction vessel is modeled on a conventional electron ionization (EI) source, but with the path of electron beam enlarged by a factor of 1000. A simplified schematic of the apparatus is diagrammed in Figure 1. Briefly, a flowing mixture of acetone or propionaldehyde (2×10^{-4} Torr) was bombarded continuously with 10−100 μA of 70 eV electrons and condensed into a liquid nitrogen-cooled trap. The recovered sample was vacuum transferred to a 5 mm Pyrex NMR tube containing acetone-d_6, which was sealed and examined by ^{19}F NMR.

For mass spectrometric experiments, MIKE spectra were taken on a VG ZAB 2F reverse Nier-Johnson double-focusing instrument. Where appropriate, exact masses were measured for ions in the CI source. For instance, *m/z* 43 and 93 from CF_4 CI of 1,1,1-trifluoroacetone show those ions to be acetyl cation (calcd for $C_2H_3O^+$ 43.0184; found 43.0177) and $C_3H_3F_2O^+$ (calcd 93.0152; found 93.0155). Collisionally activated decomposition (CAD) fragmentation patterns were examined by colliding an 8 kV mass-selected ion beam from the CI source with helium gas in the second field-free region. Relative intensities of overlapping peaks were determined by fitting as a set of equally spaced Gaussians using the Multi-peak fit function of the IGOR Pro 3.03 software.

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(4) (a) Eyler, J. R.; Ausloos, P.; Lias, S. G. *J. Am. Chem. Soc.* **1974**, *96*, 3673−3675. (b) Ausloos, P.; Lias, S. G.; Eyler, J. R. *Int. J. Mass Spectrom. Ion Proc.* **1975**, *18*, 261−271.

(5) Shaler, T. A.; Morton, T. H. *J. Am. Chem. Soc.* **1991**, *113*, 6771−6779.

(6) Reinecke, C. E.; McCarthy, J. R., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 6376−6378.

(7) Heck, A. J. R.; Nibbering, N. M. M. *J. Am. Soc. Mass Spectrom.* **1995**, *6*, 11−18.

(8) (a) Prakash, G. K. S.; Aniszfeld, R.; Hashimoto, T.; Bausch, J. W.; Olah, G. A. *J. Am. Chem. Soc.* **1989**, *111*, 8726−8727. (b) Angelini, G.; Lilla, G.; Speranza, M. *J. Am. Chem. Soc.* **1989**, *111*, 7393−7399. (c) Nguyen, V.; Cheng, X.; Morton, T. H. *J. Am. Chem. Soc.* **1992**, *114*, 7127−7132.

(9) (a) Olah, G. A. Halonium Ions; Wiley-Interscience: New York, 1975. (b) Staley, R. H.; Wieting, R. D.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1977**, *99*, 5964−5972.

(10) (a) Sargeant, P. B. *J. Org. Chem.* **1970**, *35*, 678−682. (b) Guenter, S. *Liebigs Ann. Chem.* **1979**, 1280−1290.

(11) Morton, T. H. In *Techniques for the Study of Ion−Molecule Reactions*; Farrar, J. M., Saunders, W. H., Jr., Eds.; Techniques of Chemistry XX; Wiley-Interscience: New York, 1988; pp 119−164.

Unless otherwise specified, all reagents and isotopically labeled compounds were purchased from Aldrich Chemical Co. CF_4 gas (Semiconductor Grade, >99%) was obtained from Air Products & Chemical Inc. Propionaldehyde-1-^{13}C was prepared from propionic-1-^{13}C acid (Cambridge Isotope Laboratory) by reduction with lithium aluminum hydride in diethylene glycol diethyl ether, followed by workup, filtration, and oxidation in the same solvent using solid $K_2Cr_2O_7{\cdot}2H_2O$ with dropwise addition of 10% H_2SO_4. Product was distilled from the reaction mixture: ^1H NMR (300 MHz, $CDCl_3$) δ 1.2 (dt, $J_{CH} = 2$ Hz, 3*H*), 2.4 (dq, $J_{CH} = 8$ Hz, 2*H*), 9.7 (d, $J_{CH} = 171$ Hz, 1*H*). Propionaldehyde-*1-d*$_1$ was prepared in similar fashion starting with $LiAlD_4$ reduction of propionic acid.

DFT, G3, and Hartree–Fock based calculations were performed using the GAUSSIAN98 code, and DFT zero point energies were used without scaling. Unless otherwise specified, all computed enthalpy changes were computed using DFT (B3LYP/6-31G**)[12] and correspond to 0 K values of ΔH. Basis set superposition errors (BSSE) were estimated using counterpoise and found to be in the range 4–7 kcal/mol. Bond critical points were found using DFT wave functions by means of the AIMPAC program package, kindly provided by J. Cheeseman and R. F. W. Bader.

Results

EBFlow Experiments. The gas-phase reaction between CF_3^+ and propionaldehyde yields neutral products, which demonstrate that simple fluorine–oxygen metathesis occurs, followed by isomerization to structure **1**. First, we establish the stability of ion **1** by examining the neutral product formed by 70 eV electron impact on a mixture of 2-^{13}C-acetone and CF_4 at pressure of 10^{-3} Torr in our specially constructed Electron Bombardment Flow (EBFlow) reactor.[11] Under these conditions, CF_3^+ is the principal ion produced initially,[13] and the reactions depicted in eqs 2 and 3 take place. The recovered neutral C_3H_5F has ^{13}C-label exclusively in position 2, consistent with our previous observation that ion **1** does not transpose hydrogen between its methyl groups.[14]

The first labeling experiment on propionaldehyde was designed to test whether the recovered 2-fluoropropene comes from **1**. The symmetry of **1** dictates that a deuterium label should be randomly distributed in the recovered neutral product. EBFlow radiolysis of a mixture of CF_4 and CH_3CH_2CDO gave a mixture of $CH_2{=}CFCH_2D$:$CHD{=}CFCH_3$:$CH_2{=}CFCH_3$ of 2.7:2:1, consistent with the intermediacy of **1**.

A ^{13}C-labeling experiment on propionaldehyde can thus be expected to yield meaningful results. If the carbonyl is specifically tagged, eq 4 predicts that the ^{13}C should end up in one of the methyl groups of **1** and, hence, in either the CH_3 or the CH_2 of the recovered $CH_3CF{=}CH_2$. By contrast, if rearrangement takes place within a free $C_3H_6F^+$ ion via eq 5 (in which a corner-protonated cyclopropane is hypothesized as an intervening structure), then the ^{13}C will remain connected to fluorine.

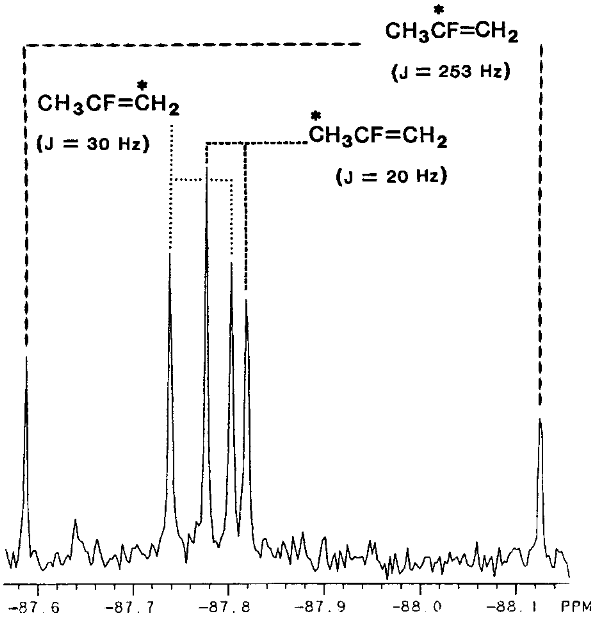
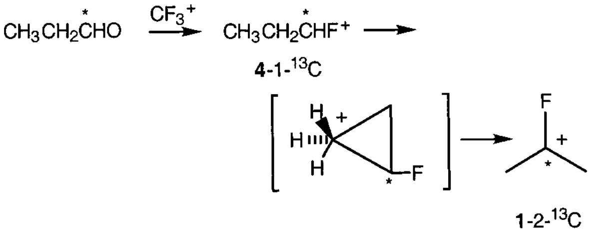


Figure 2. 470 MHz proton-decoupled ^{19}F NMR spectrum of 2-fluoropropene (in acetone-d$_6$) recovered from 70 eV EBFlow radiolysis of 1-^{13}C-propionaldehyde with CF_4. Identifications are based upon chemical shifts (relative to $CFCl_3$) and the observed carbon–fluorine spin–spin splittings.



(5)

The distribution of ^{13}C-label was assessed by examining the ^{19}F NMR of the recovered product.[5,15,16] The outcome is shown in Figure 2, which reproduces the proton-decoupled ^{19}F NMR spectrum. Three doublets can be discerned, corresponding to $CH_3CF{=}CH_2$ with ^{13}C in positions 1, 2, and 3. Assignments were made on the basis of ^{13}C-^{19}F spin–spin coupling constants.

The peak areas are in the ratio 1.2 ± 0.1:0.65 ± 0.05: 1.4 ± 0.1, respectively. Within experimental uncertainty, the proportion with labeled carbon in position 1 is equal to that with label in position 3; together these constitute 80% of the recovered C_3H_5F. The other 20% has ^{13}C in position 2, which, we infer, comes from skeletal rearrangement of $C_3H_6F^+$ after loss of CF_2O. While it is conceivable that all of the product may result from isomerization of free $CH_3CH_2CHF^+$ via competing pathways (without any involvement of eq 4), it is clear that the distribution of label does not reflect complete carbon randomization.

Mass Spectrometric Experiments. Chemical ionization (CI) with CF_4 reagent gas was studied for a half-dozen carbonyl compounds: acetone, propionaldehyde, cyclopentanone (both *d*$_0$ and *d*$_4$), cyclohexanone, and 1,1,1-trifluoroacetone. In every case at least two ions were observed in the CI source resulting from ion–molecule reactions: CF_3^+ adduct ions (*m/z* 127 from C_3H_6O; *m/z* 153 from C_5H_8O; *m/z* 167 from $C_6H_{10}O$; *m/z* 181 from $C_3H_3F_3O$) and the product of F^+ for O metathesis (*m/z* 61 from C_3H_6O; *m/z* 87 from C_5H_8O; *m/z* 101 from $C_6H_{10}O$; *m/z* 115 from $C_3H_3F_3O$). We presume that the adduct ion from propionaldehyde has structure **2** and that the adducts of the other carbonyl compounds have analogous structures.

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(12) Kohn, W.; Becke, A. D.; Parr, R. G. *J. Phys. Chem.* **1996**, *100*, 12974–12980.

(13) Bruce, M. R.; Bonham, R. A. *Int. J. Mass Spectrom. Ion Proc.* **1993**, *123*, 97–100.

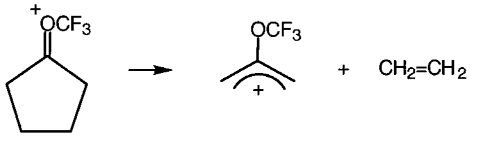
(14) (a) Redman, E. W.; Johri, K. K.; Morton, T. H. *J. Am. Chem. Soc.* **1985**, *107*, 780–784. (b) Stams, D. A.; Johri, K. K.; Morton, T. H. *J. Am. Chem. Soc.* **1988**, *110*, 699–706.

(15) Shaler, T. A.; Morton, T. H. *J. Am. Chem. Soc.* **1994**, *116*, 9222–9226.

(16) Shaler, T. A.; Borchardt, D.; Morton, T. H. *J. Am. Chem. Soc.* **1999**, *121*, 7907–7913.

A fraction of the metathesis products lose HF in the CI source, as has previously been reported in ion cyclotron resonance (ICR) experiments,[4] to yield $C_3H_5^+$ (m/z 41) from C_3H_6O, $C_5H_7^+$ (m/z 67) from C_5H_8O, $C_6H_9^+$ (m/z 81) from $C_6H_{10}O$, and $C_3H_2F_3^+$ (m/z 95) from $C_3H_3F_3O$. Also, depending on the partial pressure of the carbonyl compound, the protonated parent ions $C_3H_7O^+$ (m/z 59), $C_5H_9O^+$ (m/z 85), $C_6H_{11}O^+$ (m/z 99), and $C_3H_4F_3O^+$ (m/z 113), respectively, are observed. Those ions arise via the exothermic proton-transfer exemplified by eq 3.[4] The metastable HF-elimination decompositions from acyclic ions exhibit flat-topped peaks, indicative of translational kinetic energy releases $T_{0.5} \geq 0.8$ eV, which suggest that the energy barriers to those dissociations are much higher than the thermodynamic thresholds. By contrast, the metastable ion decompositions from cyclic precursors display much narrower, Gaussian peaks characteristic of much smaller translational kinetic energy releases (e.g., $T_{0.5} = 0.03$ and 0.08 eV for ethylene and HF-elimination, respectively, from the metastable $C_6H_{10}F^+$ ions produced by metathesis on cyclohexanone). Those peak shapes imply that rearrangement opens up pathways whose kinetic barriers are not much greater than the thermodynamic threshold.

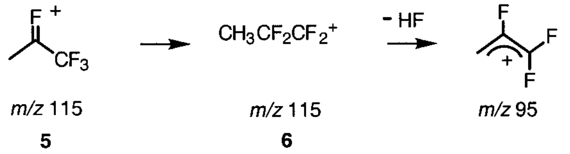
The CF_3^+ adducts have not been reported in the published ICR experiments[4] (probably because the pressure was too low for them to experience collisional stabilization prior to expulsion of CF_2O), but adduct ions have been reported in ion-beam studies of CF_3^+ with benzaldehyde, acetophenone, and methyl benzoate (though not with propiophenone or ethyl benzoate under the same conditions).[17] In the present study, metastable decompositions of these adduct ions were examined by mass-analyzed ion kinetic energy (MIKE) spectroscopy, in which an ion of given mass is separated and the fragments of its subsequent decompositions are mass analyzed. All exhibited CF_2O loss, but only the cycloalkanone adducts displayed metastable loss of the elements of CF_2O and HF together. The adduct from cyclopentanone also loses ethylene, and the cycloreversion drawn in eq 6 presents a tempting hypothesis. However, we find that the CF_3^+ adduct of cyclopentanone-2,2,5,5-d_4 (m/z 157) loses C_2D_3H, $C_2D_2H_2$, and C_2DH_3 as well as C_2H_4, in an approximate ratio of 3:5:4:3. Hence, eq 6 does not represent a major decomposition pathway, and we surmise that a more complicated rearrangement is taking place. Moreover, loss of HF and CF_2O accompanies loss of DF and CF_2O, and we conclude that those two neutrals are not expelled simultaneously. The adduct from cyclohexanone exhibits propylene loss in competition with ethylene loss. Once again, this implicates a skeletal rearrangement.



(6)

The CF_3^+ adduct of acetone shows CF_3^+ ion in its MIKE spectrum, with an intensity much weaker than that of metastable CF_2O loss. In turn, the intensity of $C_3H_5^+$ is <0.05 as intense as CF_3^+, even though the MIKE spectrum of $C_3H_6F^+$ does display $C_3H_5^+$ (which, based on our previously published EBFlow experiments, has the 2-propenyl cation structure[13]).

The analogous elimination from 1,1,1-trifluoroacetone plus CF_3^+, however, would be endothermic.[18] Although the MIKE spectrum of the adduct ion of 1,1,1-trifluoroacetone (m/z 181) does not show appreciable $C_3F_3H_2^+$, this ion is observed in the ion source, and we speculate that it may arise via the rearrangement represented in eq 7.



(7)

The MIKE spectrum of m/z 181 does display metastable loss of CF_2O to give what we believe to be ion **5**, and we also observe the production of $C_3H_3F_2O^+$ (m/z 93) from metastable expulsion of CF_4. Collisionally activated decomposition on m/z 93 from the CI source yields an intense m/z 43 peak (which we believe to be acetyl cation rather than C_2F^+, based on an exact mass measurement on m/z 43 from the ion source); the sequence m/z 181 → m/z 93 → m/z 43 corresponds to the overall reaction of CF_3^+ with 1,1,1-trifluoroacetone to yield m/z 43, which has been reported in ICR experiments.[19]

The fluorocycloalkyl ions produced by F^+ for O metathesis on cyclic ketones (m/z 101 from cyclohexanone; m/z 87 from cyclopentanone) undergo two competing metastable decompositions in comparable proportions: ethylene loss and HF loss. The m/z 101 from cyclohexanone exhibits ethylene loss versus HF loss in proportions of 0.5:1. The m/z 87 from cyclopentanone displays these losses in proportions of 0.8:1, as well as a much less intense peak (m/z 41) from expulsion of vinyl fluoride. A pathway for ethylene loss analogous to eq 6 is again tempting, but the ion from cyclopentanone-d_4 (m/z 91) shows loss of a mixture of ethylene isotopomers: m/z 59: m/z 60: m/z 61: m/z 62: m/z 63 in a ratio of approximately 1: 10: 20: 9: 3.5. The m/z 91 ion also loses HF in preference to DF, in proportions of 5:1.

Finally, we have examined the $C_3H_5^+$ ions (m/z 41) in the source from CF_4 CI of propionaldehyde and acetone by means of collisionally activated decomposition. The collisional fragmentation patterns of allyl cation and the isomeric 2-propenyl cations can be distinguished on the basis of the m/z 26: m/z 27 intensity ratio, 1.3 for the allyl cation and 2.3 for 2-propenyl,[20] ratios that we reproduce in our apparatus for the ions from allyl bromide and 2-bromopropene, respectively. Our published neutral product studies confirm that the electron ionization of the latter bromide yields 2-propenyl cation exclusively, as does the unimolecular elimination of HF from ion **1**.[14] We find that m/z 41 from propionaldehyde and CF_4 in the CI source gives an m/z 26: m/z 27 intensity ratio close to that allyl bromide, while m/z 41 from acetone and CF_4 gives a ratio of 1.5:1, demonstrating that it is a mixture of allyl and 2-propenyl cations. Since **1** does not produce allyl cation, we infer that a

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[17] Tsuji, M.; Aizawa, M.; Nishimura, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1055−1063.

[18] (a) McAllister, M.; Tidwell, T. T.; Peterson, M. R.; Czizmadia, I. G. *J. Org. Chem.* **1991**, *56*, 575−580. (b) Apeloig, Y.; Biton, R.; Zuilhof, H.; Lodder, G. *Tetrahedron Lett.* **1994**, *35*, 265−268.

[19] Drummond, D. F.; McMahon, T. B. *Int. J. Mass Spectrom. Ion Proc.* **1982**, *42*, 265−284.

[20] Bowers, M. T.; Shuying, L.; Kemper, P.; Stradling, R.; Webb, H.; Aue, D. H.; Gilbert, J. R.; Jennings, K. R. *J. Am. Chem. Soc.* **1980**, *102*, 4830−4832.

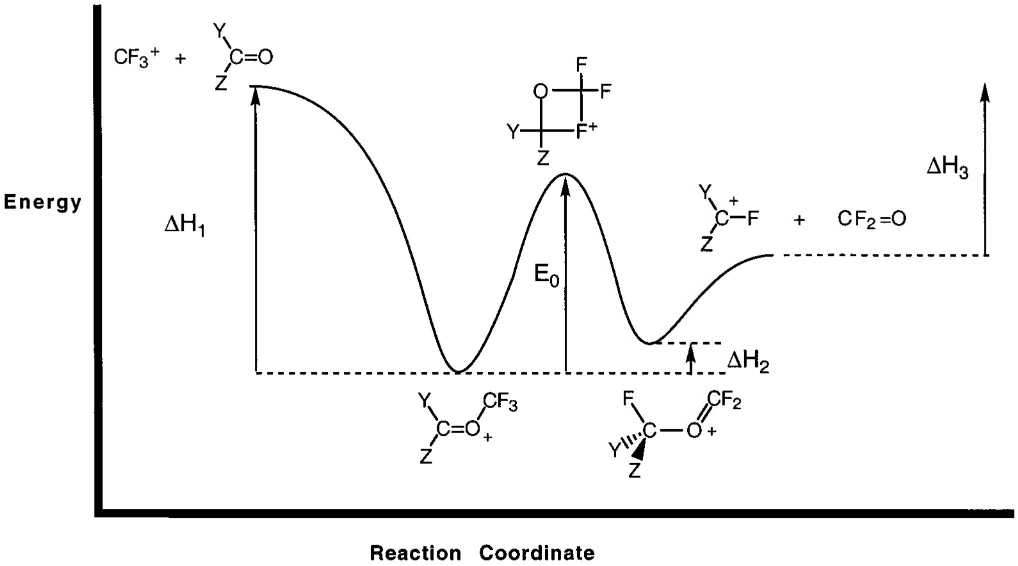
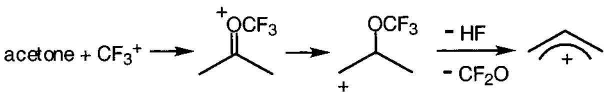


Figure 3. Reaction coordinate diagram for interchange of F^+ with O in the gas-phase ion−molecule reaction of a simple carbonyl compound (YZC═O) with CF_3^+, showing the enthalpy of association of the reactants ΔH_1, the height of the central barrier E_0, the enthalpy of unimolecular isomerization of the adduct ion ΔH_2, and the overall enthalpy of the metathesis ΔH_3.

substantial fraction of m/z 41 in the ion source forms directly from the CF_3^+-adduct ion as allyl cation, perhaps by the pathway drawn in eq 8. We fit the m/z 24:25:26:27 relative peak intensities to those of known mixtures of allyl bromide and 2-bromopropene and conclude that CF_4 CI of propionaldehyde yields 2-propenyl and allyl cations in a 8:92 ratio, while acetone yields the isomeric ions in a 42:58 ratio.



(8)

Theoretical Calculations. The transition states for fluorine transfer have been probed computationally. Figure 3 summarizes the contour of the potential energy surface along the reaction coordinate for the metathesis reaction. CF_3^+ is an extremely strong Lewis acid, and it can attach to a carbonyl oxygen as eq 2 depicts. The subsequent elimination of CF_2O proceeds with the four-member cyclic transition state representing the principal barrier. The top of this barrier lies well below the energy of the separated reactants, so the net ion−molecule metathesis reaction should operate with nearly unit efficiency. In other words, the exothermicity of adding gaseous CF_3^+ to a carbonyl oxygen, ΔH_1, is greater in magnitude than the activation barrier E_0.

The unimolecular transfer of fluorine from the CF_3 to the carbonyl carbon (concomitant with shift of the carbonyl oxygen in the opposite direction) is endothermic. This transposition moves the charge from a carbon on one side of the oxygen to the carbon on the other side. Since that isomerization puts positive charge onto a CF_2 group, it is not surprising that the enthalpy change, ΔH_2, is positive. Cleavage of this isomerized ion to the final products, is also endothermic, as are virtually all dissociations of singly charged positive ions in the gas phase. The net exothermicity of the metathesis of F^+ for O, ΔH_3, is sufficiently great that a fraction of the product ions have enough internal energy to expel HF.[4,14] From thermochemical values ΔH_3 for acetone is −50 kcal/mol (based on ΔH_f values for CF_3^+ of 95 kcal mol^{-1}; acetone −52 kcal mol^{-1}; CF_2O −145 kcal mol^{-1}; and Me_2CF^+ 138 kcal mol^{-1}).[4] Some controversy remains concerning the heat of formation of gaseous CF_2O,[21] however, and the measured ΔH_f values for the pertinent ions are subject to uncertainties of ±2 kcal/mol. Thus, the DFT and G3 values for ΔH_3 in Table 1 must be considered as being within the error limits of the experimental value.

Table 1. DFT-Calculated Zero Kelvin Enthalpy Differences (B3LYP/6-31G//B3LYP/6-31G** Electron Energies plus Unscaled Zero-Point Energy Differences) (kcal mol^{-1})**

	ΔH_1[a]	ΔH_2	E_0	ΔH_3[b]
Y = Z = F	−21.08	0	30.27	0 (0)
Y = Z = $(CH_2)_5$	−72.29	5.42	35.53	−64.35
Y = Z = $(CH_2)_4$	−73.00	7.05	39.81	−59.56
Y = Z = CH_3	−65.80	5.54	35.29	−56.32 (−54.38)
Y = C_2H_5, Z = H	−61.19	9.90	36.19	−43.62 (−42.26)
Y = CF_3, Z = CH_3	−45.27	2.76	29.79	−28.20
Y = CF_3CH_2, Z = H	−49.60	4.38	35.73	−27.72
Y = Z = CF_3	−24.26	−5.20	29.65	1.10

[a] Includes counterpoise correction for basis set superposition error. [b] Numbers in parentheses represent G3-calculated values of ΔH_3.

Fluorocycloalkyl cations undergo rearrangements in the course of metastable ion decompositions, as attested by the extensive isotopic scrambling seen in the dissociations of the m/z 91 produced by CF_4 CI of cyclopentanone-2,2,5,5-d_4. In the CF_4 CI of cyclohexanone we speculate that ethylene loss from 1-fluorocyclohexyl cation, **7**, involves hydride shift to structure **8**. Ion **8** could expel C_2H_4 to give the fluorinated homoallylic ion **10** (which computation shows to possess a cyclopropyl fluorocarbinyl structure having a plane of symmetry). Alternatively **8** might undergo ring contraction to 2-fluoro-1-methylcyclopentyl cation, **9**, as drawn in Scheme 1, which could expel ethylene to yield the fluoromethallyl cation **11** (*E* or *Z*). Such a ring contraction is a well-known, low-barrier rearrangement of cyclohexyl cation itself,[22,23] which takes

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[21] Schneider, W. F.; Wallington, T. J. *J. Phys. Chem.* **1994**, *98*, 7448−7451.

[22] Saunders, M.; Rosenfeld, J. *J. Am. Chem. Soc.* **1969**, *91*, 7756−7758.

Scheme 1

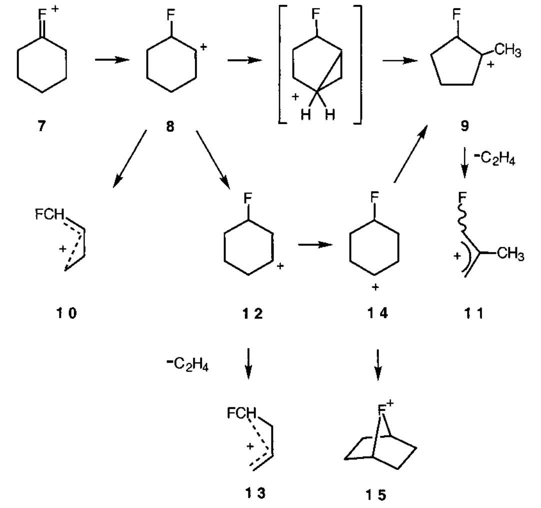


Table 2. Relative DFT 0 K Heats of Formation of $C_6H_{10}F^+$ Species (B3LYP/6-31G)**

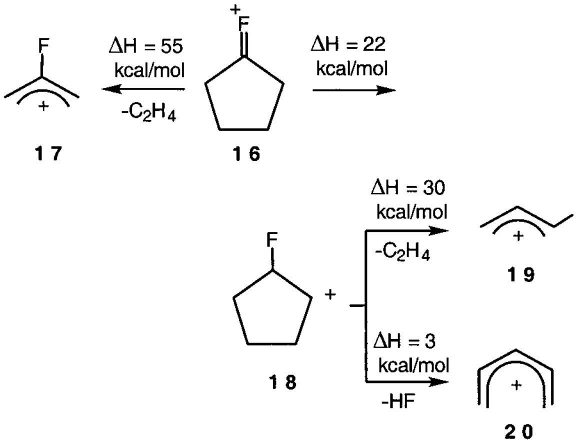
7	0	(*Z*)-**11** + C_2H_4	40.12
8 (axial F)	17.87	(*E*)-**11** + C_2H_4	42.19
9	6.20	**13** + C_2H_4	52.38
12 (axial F)	13.51	(*Z*)-$CH_2{=}CFCHCH_3^+$ + C_2H_4	40.47
14 (equatorial F)	14.12	(*E*)-$CH_2{=}CFCHCH_3^+$ + C_2H_4	44.41
15	12.00	(*E*,*E*)-$FCH{=}CHCHCH_3^+$ + C_2H_4	30.96
(*Z*)-**10** + C_2H_4	45.28	(*Z*)-$CH_2{=}CHCFCH_3^+$ + C_2H_4	28.55
(*E*)-**10** + C_2H_4	45.97	(*E*)-$CH_2{=}CHCFCH_3^+$ + C_2H_4	29.82

place via a corner-protonated cyclopropane. Further hydride shift would form **12**, which could eject ethylene to form the fluorinated homoallylic cation **13** (which adopts a fluorocyclopropylcarbinyl structure; the cis and trans isomers have the same heats of formation within 0.1 kcal mol^{-1}). Ion **12** could also undergo hydride shift to give **14**, which might also rearrange to **9** via a corner-protonated cyclopropane.

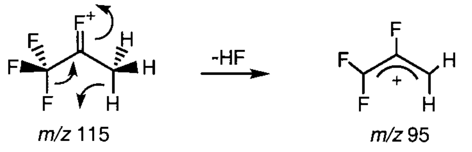
Calculated energies of a large number of fluorocyclohexyl cation geometries have been reported at the MP2/6-31G* level.[24] The DFT results in Table 2 agree with the published energetic ordering, in which **7** is the most stable structure, and the symmetrically bridged ion **15** is the next most stable. We find that **9** (which was not included in the previously published survey) has a stability intermediate between **7** and **15**. The 5-center elimination of ethylene from **9** is analogous to eq 6. We have not calculated activation energies for these cycloreversions but note that the exothermicity of forming **9** from CF_3^+ plus cyclohexanone, $\Delta H = -58$ kcal mol^{-1}, provides enough energy to surmount most barriers.

It is worth remarking that ring contraction of ion **12** would form 3-fluoro-1-methylcyclopentyl cation (whose calculated $\Delta H^\circ_{f_{0K}}$ is 3 kcal mol^{-1} lower than that of **9**), which cannot expel ethylene without further rearrangement. Although allylic fluorobutenyl ions have heats of formation lower than **10**, **11**, or **13** (as Table 2 summarizes) it is hard to see how a conjugated fluorobutenyl structure could arise via direct elimination of ethylene from either a tertiary cation or from any of the fluorocyclohexyl cations. In any event, the exothermicity of F^+ for O interchange is great enough that all of the C_2H_4 elimination products listed in Table 2 are thermodynamically accessible.

We have probed the thermochemistry of other 5-center eliminations. Simple cleavage of the 1-fluorocyclopentyl cation, **16**, could give 2-fluoroallyl cation **17**. This dissociation is endothermic by 55 kcal mol^{-1}, as eq 9 summarizes. Isomerization to the 2-fluorocyclopentyl cation, **18**, is 22 kcal mol^{-1} endothermic, but it can cleave to yield the more stable 1-fluoroallyl cation, **19**, with an overall endothermicity of $\Delta H_{0K} = 52$ kcal mol^{-1}. Alternatively **18** could undergo a vicinal or a 1,3-syn elimination of hydrogen fluoride with ring opening to afford the pentadienyl cation, **20**. Despite the fact that ethylene loss is at least 25 kcal mol^{-1} more endothermic than HF loss, those two dissociations are observed to compete to nearly equal extents in the metastable dissociation of fluorocyclopentyl cation, signaling that formation of **20** must have a substantial activation barrier. We calculate a DFT energy barrier for 1,3-elimination of HF of 33.2 kcal/mol for the acyclic ion shown in eq 10, 5.0 kcal greater than the corresponding magnitude of ΔH_1. Nevertheless that elimination is observed in the MIKE spectrum of **5**. By contrast, we calculate that the isomerized adduct **6** has a heat of formation 8 kcal/mol higher than **5** and surmise that HF elimination from **5** takes place via isomerization to **6** followed by vicinal elimination, as eq 7 depicts. In other words, there is no basis at the present time for supposing that 1,3-eliminations have lower barriers than do vicinal eliminations.



(9)



(10)

Discussion

The CF_3^+ ion acts as an "ionic Lewis superacid" in the gas phase.[25] Chemical ionization of simple carbonyl compounds with CF_4 reagent gas yields a variety of ions whose structures have been determined by experiment or predicted by theory. The present results demonstrate

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(23) (a) Marinelli, W. J.; Morton, T. H. *J. Am. Chem. Soc.* **1978**, *100*, 3536–3539; **1979**, *101*, 1908. (b) Attiná, M.; Cacace, F.; Giacomello, P. *J. Am. Chem. Soc.* **1981**, *103*, 4711–4714.

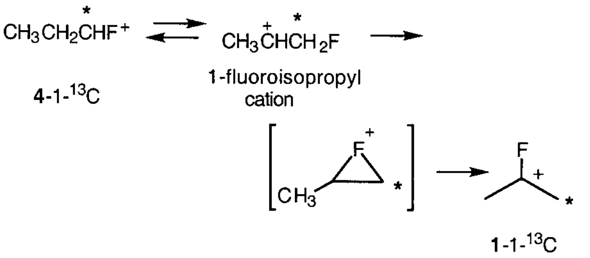
(24) Damrauer, R.; Leavell, M. D.; Hadad, C. M. *J. Org. Chem.* **1998**, *63*, 9476–9488.

(25) (a) Grandinetti, F.; Occhiucci, G.; Crestoni, M. E.; Fornarini, S.; Speranza, M. *Int. J. Mass Spectrom. Ion Processes* **1993**, *127*, 123–136. (b) Grandinetti, F.; Occhiucci, G.; Crestoni, M. E.; Fornarini, S.; Speranza, M. *Int. J. Mass Spectrom. Ion Processes* **1993**, *127*, 137–145. (c) Grandinetti, F.; Crestoni, M. E.; Fornarini, S.; Speranza, M. *Int. J. Mass Spectrom. Ion Processes* **1993**, *130*, 207–222.

that, as a free ion, **4** isomerizes to **1** in the gas phase when it has sufficient internal energy. In our previous work,[5,15,16] we used this as a basis for characterizing the EBFlow products of ion–neutral complexes containing **4** (in which this rearrangement does not take place). The experiments reported here confirm what we have heretofore supposed: at least 20% of the **1** formed from propionaldehyde plus CF_3^+ must come from isomerization of **4**. Otherwise, it is hard to imagine how labeled **1** might be formed from propionaldehyde-1-^{13}C with the labeled carbon bonded directly to fluorine. Therefore, four-member cyclic transition states for fluoride transfer are accessible, even when alternative pathways can operate.

We note the parallelism between the isomerization of **4** to **1** in eq 5 and the ring contraction of **8** to **9** in Scheme 1. Skeletal rearrangements that proceed via protonated cyclopropanes have long been attested in simple carbocations.[22,26] The present work confirms their occurrence in monofluorinated carbocations, as well.

The fact that the majority of ^{13}C-label ends up in the methyl groups of **1** cannot be taken as proof that eq 4 occurs. The isomerization of **4** to 1-fluoroisopropyl cation, drawn in eq 11, is nearly thermoneutral and occurs rapidly (and reversibly) within ion–neutral complexes.[5,16] Bridging by fluorine has ample precedent,[8c,15] and subsequent 1,2-hydride shift could form **1**.

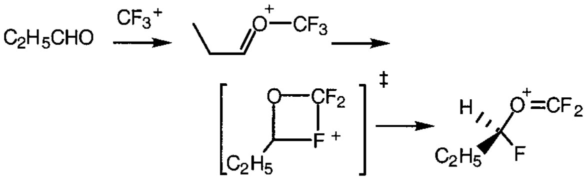


(11)

Equation 12 generalizes the mechanism drawn in eq 2. Computation of the energetics for eq 12 using density functional theory (DFT), summarized in Table 1, shows a substantial activation energy E_0 (electronic energy difference plus zero point energy difference) for 1,3-fluorine transfer (step ***ii***). In the thermoneutral transposition of F^+ and O between CF_3^+ and CF_2O ($Y = Z = F$) the symmetrical transition state presents a DFT-calculated barrier of $E_0 = 30.3$ kcal mol^{-1} with respect to the simple adduct $CF_3OCF_2^+$. This transition state is 5.5 kcal mol^{-1} greater than the calculated exothermicity ΔH_1 of the addition reaction (step ***i***). Hence we should not expect that the degenerate exchange of F^+ and oxygen between CF_3^+ and CF_2O can occur under ordinary conditions. Equation 13 portrays the four-member cyclic transition state for the case of propionaldehyde (Y = ethyl, Z = H). Here the DFT-calculated activation energy is 36.0 kcal mol^{-1}, but it presents a barrier 29.5 kcal mol^{-1} lower than the exothermicity of step ***i***.

$$\mathrm{YZC{=}O + CF_3^+ \overset{i}{\rightleftarrows} YZ\overset{+}{C}\text{-}O\text{-}CF_3 \overset{ii}{\rightleftarrows} YZCF\text{-}O\text{-}\overset{+}{C}F_2 \xrightarrow{iii} YZCF^+ + O{=}CF_2} \qquad (12)$$

Bimolecular metathesis of F^+ for O in the gas phase takes place via eq 12 through a four-member cyclic transition state as drawn in eq 13.



(13)

Our calculations suggest that in order for the overall reaction to be exothermic, the unimolecular isomerization represented by step ***ii*** of eq 12 should be endothermic, as Figure 3 depicts schematically. This stands to reason, since the heterolysis represented by step ***iii*** transfers positive charge from a CF_2 group to a CYZ group. If the overall conversion of CF_3^+ to $YZCF^+$ is energetically favorable (i.e., $\Delta H_3 < 0$), then the approximate reverse of that reaction, step ***ii***, ought to be unfavorable (i.e., $\Delta H_2 > 0$). This qualitative picture is confirmed by thermochemical calculations for the case where $Y = Z = CF_3$. Here, step ***ii*** is exothermic, while the overall metathesis is about 1 kcal mol^{-1} endothermic. The calculated barrier height E_0 is higher than the exothermicity of association ΔH_1, so (as in the case of degenerate exchange between CF_3^+ and CF_2O) it seems unlikely that this reaction will operate under ordinary conditions.

We have performed calculations for substitutents Y and Z, including examples for which the metathesis has yet to be studied experimentally. The outcomes of Hartree–Fock based computations are much the same as for DFT, and we report only the latter. Ring strain plays a significant role, and the four-member transition state for interchange between CF_3^+ and cyclopentanone has the highest value of E_0 in the series on which we have performed calculations. Among the remaining examples listed in Table 1 eq 13 has the highest E_0. Nevertheless, our experimental results demonstrate that eq 13 indeed takes place. Even if we confine our attention to metatheses of aldehydes and acyclic ketones the activation energies display no obvious trend as a function of substitution or thermochemistry, although the degree of progress along the reaction coordinate does do so.

The Hammond postulate addresses the question of how small changes in overall thermochemistry affect the position of a barrier along the reaction coordinate.[27] In its simplest form, the postulate states that the top of the barrier moves toward the product as ΔH increases and toward the reactant as ΔH decreases, but it does not posit a correlation of barrier height with ΔH. A prima facie expectation based on the Hammond postulate would suggest that as net F^+ for O metathesis becomes more exothermic (ΔH_3 becomes more negative), the cyclic transition state should more closely resemble the reactant. This naive interpretation is exactly the reverse of what Figure 3 implies. Step ***ii*** represents the unimolecular isomerization of a cation, and the position of the barrier top reflects the stabilization of the charge in $-OCF_2^+$ relative to $-OCYZ^+$. Since ΔH_2 becomes positive as ΔH_3 becomes negative, the transition state ought to resemble the product more closely as the overall reaction becomes more exothermic.

To test this hypothesis we need to measure how much the reaction has progressed when it reaches the transi-

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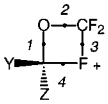
[26] Baird, R. L.; Aboderin, A. A. *J. Am. Chem. Soc.* **1964**, *86*, 252–255.

[27] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper & Row: New York, 1987; pp 211–229.

Table 3. Bond Critical Point Electron Densities (ρ in Atomic Units) and Bond Lengths (r, in Å) for Aldehyde and Acyclic Ketone Reactants Calculated Using Density Functional Theory (DFT) at B3LYP/6-31G//B3LYP/6-31G****



	ρ_1	$\boldsymbol{r}_1$	ρ_2	$\boldsymbol{r}_2$	ρ_3	$\boldsymbol{r}_3$	ρ_4	$\boldsymbol{r}_4$
Y = Z = F	0.318	1.368	0.318	1.368	0.146	1.628	0.146	1.628
Y = Z = CH_3	0.242	1.455	0.354	1.319	0.120	1.704	0.148	1.591
Y = H, Z = C_2H_5	0.268	1.415	0.338	1.341	0.148	1.622	0.131	1.637
Y = CH_3, Z = CF_3	0.285	1.394	0.323	1.360	0.167	1.572	0.115	1.695
Y = H, Z = CF_3CH_2	0.290	1.386	0.322	1.361	0.171	1.563	0.110	1.710
Y = Z = CF_3	0.326	1.335	0.280	1.410	0.216	1.470	0.077	1.865

tion state. One option might be to examine changes of hybridization along the reaction coordinate,[28] as measured (for instance) by the F−C−F bond angle of the CF_2 group at the top of the central barrier. This angle changes from 120° in the reactant (CF_3^+) to 112°−113° in the adduct ion (step ***i***), then to 113°−114° in the isomerized adduct (step ***ii***) and finally to 108° in the product (step ***iii***). The F−C−F bond angle in the transition state opens up relative to the intermediates that precede and follow it. Nevertheless, for acyclic reactants its value, 114.5°, remains constant within ±0.1° as Y and Z are varied. Hence the hybridization criterion does provide a useful test of how to apply the Hammond postulate here.

Bond lengths offer a more conventional measure of progress along the reaction coordinate, which Table 3 summarizes for the transition states. At the barrier top the carbonyl C═O bond length of the reactant lengthens ($\boldsymbol{r}_1$) as the oxygen approaches the carbon of the CF_3^+ (distance $\boldsymbol{r}_2$). Likewise, the CF_2−F bond length ($\boldsymbol{r}_3$) lengthens as the itinerant fluorine approaches the carbonyl carbon (distance $\boldsymbol{r}_4$). Our calculations predict that $\boldsymbol{r}_1$ and $\boldsymbol{r}_3$ get shorter as the reaction becomes less exothermic (i.e., as ΔH_3 becomes less negative), while $\boldsymbol{r}_2$ and $\boldsymbol{r}_4$ get longer. As noted above, this stands in contrast to what the Hammond postulate might at first be thought to predict. The bond lengths for the symmetrical transition state for degenerate exchange (Y = Z = F), however, do not fall within this trend. Therefore, we consider the degenerate exchange as a case separate from the aldehydes and ketones.

The theory of atoms in molecules[29] offers another probe of the properties of the computed transition states, which confirms the trend manifested by bond lengths. Between each pair of bonded atoms lies an extremum of the electron density (called a bond critical point), which is a minimum in the path between the two atoms and a maximum in the directions orthogonal to that path. In the present case the electron densities at those extrema (ρ) can be compared in order to examine relative progress along the coordinate that transfers F in one direction and O in the other. As overall metathesis becomes less exothermic (reading from the second line of Table 3 to the bottom) ρ for the CYZ-O bond gets larger (ρ_1) and ρ for the CF_2−O bond gets smaller (ρ_2). At the same time, ρ for the C−F bond to CF_2 gets larger (ρ_3) and ρ for the bond to CYZ gets smaller (ρ_4). The calculated bond lengths ($\boldsymbol{r}$) for the aldehyde and acyclic ketone transition states vary linearly with ρ (correlation coefficients ranging from $\boldsymbol{r}^2 = 0.999$ for $\boldsymbol{r}_1$ versus ρ_1 to 0.984 for $\boldsymbol{r}_4$ versus ρ_4). The corresponding ρ values, in turn, vary linearly with ΔH_3 ($\boldsymbol{r}^2$ ranging from 0.988 for ρ_2 to 0.996 for ρ_4).

The correlation of ρ values with ΔH_3 implies that the structure of the transition state responds systematically to the charge-stabilizing properties of substituents Y and Z. It turns out that transition state properties correlate poorly with the thermochemistries of addition (step ***i***) or isomerization (step ***ii***), probably because structural features of the intermediates at the bottoms of the potential wells undergo substantial structural alterations in response to substituent variations. For instance, the calculated CFYZ−OCF_2 bond length in the isomerized adduct jumps from 1.75 Å in the case of propionaldehyde (eq 12, Y = H, Z = ethyl) to 2.53 Å in the case of acetone (X = Y = CH_3). The latter ion looks like a loosely held aggregate of **1** with CF_2O. Owing to the stability of **1**, step ***ii*** is not as endothermic starting with acetone as it is with propionaldehyde. This large geometric alteration does not begin to manifest itself at the top of the barrier, however. Hence, it turns out that progress along the reaction coordinate correlates very well with ΔH_3.

Transposition of F^+ for O is calculated to be slightly endothermic in the reaction of CF_3^+ with hexafluoroacetone, and the barrier height E_0 is about 5 kcal mol^{-1} greater than the magnitude of ΔH_1. With a central barrier higher than the energy of the reactants, interchange should not take place. The reported failure of this ion−molecule reaction to be observed in competition with fluoride abstraction[19] confirms that prediction. Computation appears to provide a useful model for intramolecular fluorine migration via four-member cyclic transition states.

Conclusions

Isoelectronic metathesis of F^+ for O takes place between gaseous CF_3^+ and a variety of ketones. The same transposition between propionaldehyde and CF_3^+ also occurs, but yields ion **1** as well as ion **4**. Isotopic labeling demonstrates that at least one-fifth of **1** comes from rearrangement of **4** following interchange. Evidence for analogous rearrangements in fluorocycloalkyl cations is provided by those ions' subsequent decompositions.

Other reactions besides transposition take place in the course of CF_4 CI of ketones, e.g., formation of allyl cation from acetone and CF_4 loss from the adduct of CF_3^+ with 1,1,1-trifluoroacetone. The ions formed by metathesis can also undergo further dissociation, because the interchange of F^+ for O is so highly exothermic. Loss of HF is ubiquitous. Expulsion of HF from **1** corresponds to vicinal elimination, but deuterium labeling shows that HF loss from fluorocycloalkyl cations follows a more complicated

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[28] Haddon, R. C.; Chow, S.-Y. *J. Am. Chem. Soc.* **1998**, *120*, 10494−10496.

[29] Bader, R. F. W. *Atoms in Molecules − a Quantum Theory*; Oxford University Press: New York, 1990.

sequence of steps. Fluorine-containing ions derived from cycloalkanones also lose ethylene.

A survey of computed potential energy surfaces shows that interchange of F^+ for O obeys the Hammond postulate. Owing to thermochemical features within the potential energy well a later transition state correlates with a more exothermic overall reaction. This ostensible anomaly is, in fact, consistent with expectation, since endothermic unimolecular isomerization of the CF_3^+ adduct of a carbonyl corresponds to a net exothermic metathesis. Viewed from this perspective, the Hammond postulate applies as well to gas-phase ion−molecule reactions as it does to other realms of chemistry.

Acknowledgment. This work was supported by NSF Grant CHE 9983610.

Supporting Information Available: Mass-analyzed ion kinetic energy (MIKE) spectra showing unimolecular metastable ion decompositions of F^+-for-O metathesis ions; collisionally activated decomposition (CAD) spectra of *m*/*z* 41 ions produced by HF-elimination from the metathesis ions of acetone and propionaldehyde compared with those from authentic samples and mixtures of bromopropenes. This material is available free of charge via the Internet at http://pubs.acs.org.

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