VIP Reactivity of Dications

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Fast and Efficient Fluorination of Small Molecules by SF_4^{2+}**

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As a result of fluorine's high electronegativity, fluorination can have a dramatic effect on molecular properties. Nowhere is this perturbation more important than for organic compounds, where fluorination can impart substantial metabolic stability to prospective pharmaceutically active species.[1] However, because of their stability and inertness,[1c,2] facile synthesis of C–F bonds still provides a considerable challenge for chemists.[1a,3]

Gas-phase reactions monitored in a mass spectrometer provide a unique environment to study chemical reactivity free from the effects of solvents or counterions.[4] Gozzo et al. have shown that gas-phase SF_3^+ ions donate F^+ to heteroaromatic compounds,[5] and F_2^+ has been observed to fluorinate some molecules.[6] In contrast, fluorination by gaseous molecular dications has never been specifically investigated, despite the current interest in the bond-forming reactivity of these species;[7] for example, collisions of $C_2H_2^{2+}$ with Ar form ArC_2H^{2+},[8] $C_2O_3^{2+}$ is observed from CO_2^{2+} and CO_2,[9] and NH^+ is formed upon collisions of N_2^{2+} with H_2.[10] However, the rates of these bond-forming reactions are usually much lower than those for single-electron transfer between the dication and the neutral [Eq. (1)]. In contrast to this weak dicationic bond-forming reactivity, herein we report a series of very efficient reactions involving the fluorination of a variety of neutral species upon collisions with SF_4^{2+}.

The electron transfer [Eq. (1)] and bond-forming reactions [Eq. (2)] displayed by dicationic systems commonly generate pairs of monocations as reaction products:[7,11]

$$SF_4^{2+} + CH_4 \rightarrow SF_4^+ + CH_4^+ \text{ then } SF_4^+ \rightarrow SF_3^+ + F \qquad (1)$$

$$SF_4^{2+} + H_2 \rightarrow SF_3^+ + H_2F^+ \qquad (2)$$

We have used a time-of-flight mass spectrometer (TOFMS) to detect these pairs of product monocations formed upon collisions of SF_4^{2+} with Ar, H_2, D_2, CO, N_2, H_2O, CH_4, C_2H_4, and C_2H_6.[7a,12] For each collision system, this experimental method measures the masses and the initial velocities of each pair of product monocations formed upon a dication–neutral collision. Thus, our raw data for each collision system is a two-dimensional mass spectrum (examples shown in Figure 1), a histogram of the number of ion-pair counts against the masses of the two ions that form each pair. The signals in such spectra clearly characterize the reactions of SF_4^{2+} that result in pairs of product ions.

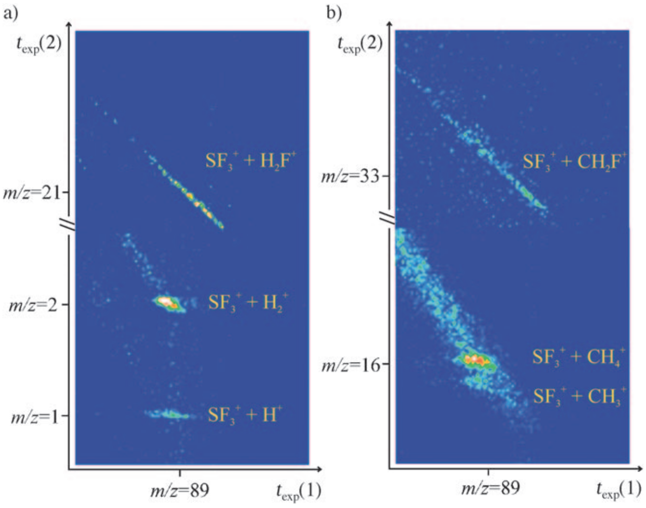

Figure 1. Two-dimensional mass spectra showing the ion pairs formed upon collisions of SF_4^{2+} with a) H_2 and b) CH_4.[17]

In all the collision systems investigated we observe intense fluorination channels (Table 1), which compete effectively with single-electron transfer.[13] Of special note are those reactions of SF_4^{2+} with hydrocarbons that exhibit the facile formation of C–F bonds (Table 1, entries 4, 7–9). The efficiency of electron transfer following collisions of SF_4^{2+} with neutral species has been observed before,[14] and SF_4^{2+} has also been shown to be reactive at surfaces.[15] Indeed, when thermodynamically accessible, single-electron transfer between dications and neutral species usually proceeds very rapidly and efficiently.[11,16] Our experimental method does not allow direct measurement of rate constants.[10] However, from the comparable branching ratios measured (Table 1) for electron transfer and fluorination, it is clear that the

Table 1: Fluorination reactions observed following reactions of SF_4^{2+} at collision energies E_{CM}.

Entry	Reactant	Products	E_{CM} [eV]	B [%][a]
1	Ar	$SF_3^+ + ArF^+$	3.0	13
2	H_2	$SF_3^+ + H_2F^+$	0.2	24
3	D_2	$SF_3^+ + D_2F^+$	0.4	29
4	CO	$SF_3^+ + FCO^+$	2.5	8
5	N_2	$SF_3^+ + N_2F^+$	2.5	13
6	H_2O	$SF_3^+ + H_2OF^+$	1.7	3
7	CH_4	$SF_3^+ + CH_2F^+ + 2H$	1.0	19
8	C_2H_4	$SF_3^+ + C_2H_2F^+ + 2H$	2.5	4
		$SF_3^+ + C_2H_3F^+ + H$	2.5	1
9	C_2H_6	$SF_3^+ + C_2H_3F^+ + 3H$	2.6	2

[a] The branching ratio B is the percentage of the ion pairs in the fluorination channel with respect to the total number of pairs that are detected after bimolecular reactive events.

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fluorination reactions of SF_4^{2+} are very fast and efficient. Indeed, the calibrated and normalized rate[10] of formation of product-ion pairs indicates that SF_4^{2+} reacts upon nearly every collision with the target molecule.

Our experimental technique allows us to probe the mechanisms of the fluorination reactions by revealing correlations between the velocity vectors of the reactant and the product ions.[12] We show these correlations using scattering diagrams in the center-of-mass (CM) frame. These scattering diagrams (Figure 2) are radial histograms that plot the magnitude of the product-ion velocity and the angle θ ($0 < \theta < 180°$) between that velocity and the velocity vector of the reactant dication.[7a] These scattering diagrams (e.g. Figure 2) for all the fluorination reactions (Table 1) clearly show that there is no correlation between the product velocities and the original velocity of the reactant SF_4^{2+} ion. This scattering shows that all the fluorination reactions involve the initial formation of a complex between the reactants; this complex lives for at least a few rotational periods before decaying to the observed products.

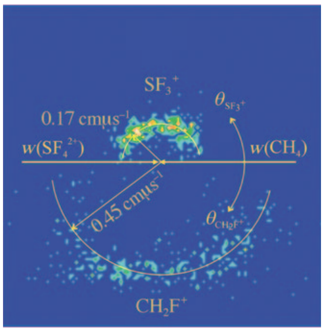

Figure 2. CM scattering diagram for the formation of CH_2F^+ and SF_3^+ following the interaction of SF_4^{2+} with CH_4. The diagram is a radial histogram showing the orientation of the velocities of SF_3^+ and CH_2F^+ with respect to the direction of the reactant velocities $w(SF_4^{2+})$ and $w(CH_4)$ (see text for details).

Examination of the correlations between the velocities of the products[7a] shows that fluorination arises through the fragmentation of the collision complex $[SF_4{-}X]^{2+}$ into $SF_3^+ + FX^+$, followed by subsequent decay of the FX^+ ion [Eq. (3) and (4)].

$$SF_4^{2+} + CH_4 \rightarrow [SF_4\text{-}CH_4]^{2+} \rightarrow SF_3^+ + CH_4F^+ \tag{3}$$

$$CH_4F^+ \rightarrow CH_2F^+ + 2\,H \text{ or } H_2 \tag{4}$$

To rationalize these facile fluorination reactions we have probed the structure of SF_4^{2+} computationally.[18] These calculations (Figure 3) show that the lowest lying triplet state of SF_4^{2+} has C_s symmetry with one highly extended, and presumably weak, S–F bond. We could also locate (Figure 3) a higher lying C_{2v} triplet state and a lower-lying T_d singlet state.[19] The fact the SF_4^{2+} ions in our beam readily donate F^+ ions strongly hints that the ^3C_s structure is responsible for fluorination. Indeed, the calculations show that the distinct F atom in the ^3C_s structure bears a considerably higher ($+0.37e$) charge than the other fluorine atoms ($+0.05e$). Similar structural arguments have been used to explain the propensity of CF_3^{2+} to lose a neutral F atom in collisions.[20] Further to these qualitative arguments, as explained below, the energetics revealed by our coincidence experiments strongly point to the ^3C_s state of SF_4^{2+} being the fluorinating agent and a major species in our dication beam.

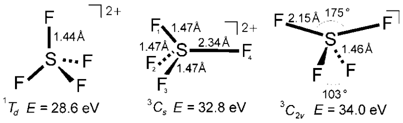

Figure 3. Calculated geometries of SF_4^{2+}. The point group of each structure, and their energy relative to the ground state of SF_4, are shown. For the ^3C_s state, the bond angles are: $\measuredangle F_1F_2 = \measuredangle F_1F_3 = \measuredangle F_2F_3 = 108°$, $\measuredangle F_2F_4 = \measuredangle F_3F_4 = 109°$, and $\measuredangle F_1F_4 = 112°$.

From the velocities of the product ions we can derive the translational-energy release of a given reactive process.[7a] Translational-energy release is readily related to the reaction exothermicity, given the known velocity of the SF_4^{2+} ion, if the internal excitation of the reactants and products is negligible. The reaction of SF_4^{2+} with Ar to form $SF_3^+ + F + Ar^+$ should involve minimal vibrational excitation of the products, as two of the products are atoms. Since the energies of the other products and the reactants are known, the translational-energy release that we measure for this reaction yields a double ionization energy for SF_4 of 32.8 eV, in excellent agreement with the calculated energy of the ^3C_s minimum (Figure 3), thus supporting the conclusion that the lowest triplet (^3C_s) electronic state of the dication is responsible for the fluorination reactions. The large count rates of product-ion pairs that we measure, given the ion-beam current and the neutral-gas density,[10] strongly hint that the state of SF_4^{2+} responsible for the fluorination, the ^3C_s state, is the dominant configuration of this reagent in our dication beam. This observation therefore suggests that the population of the ground ^1T_d state of SF_4^{2+} from SF_6 is significantly disfavored, possibly on Franck–Condon grounds.

Our results show that gas-phase SF_4^{2+} ions are very efficient fluorinating agents for a wide variety of molecules. The next challenge is to transfer this reactivity into solution. Methods to achieve this could involve the selective in situ photoionization of SF_4 or SF_6 or the generation of zwitterions of the form $R^{2-}{-}SF_4^{2+}$. Certainly our observation of the efficient fluorination of neutral molecules by SF_4^{2+} prompts further investigation of the chemistry of this unusual class of ions.

Experimental Section

We generated the SF_4^{2+} ions by 150 eV electron ionization of SF_6. These ions were energy selected, mass selected, and pulsed before interacting with the neutral target gas in the source region of a TOFMS. Typical transit times for SF_4^{2+} ions from the ion source to collision with the neutral species are 0.1 to 0.2 ms. After a dication pulse has interacted with the neutral gas we used the TOFMS, which was equipped with a position-sensitive detector, to identify the pairs of product ions formed. The detector gives the time and position of each ion's arrival, thus allowing the determination of the masses and velocities of the product ions.[7a,12]

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[1] a) P. M. Pihko, *Angew. Chem.* **2006**, *118*, 558; *Angew. Chem. Int. Ed.* **2006**, *45*, 544; b) K. Müller, C. Faeh, F. Diederich, *Science* **2007**, *317*, 1881; c) B. K. Park, N. R. Kitteringham, P. M. O'Neill, *Annu. Rev. Pharmacol. Toxicol.* **2001**, *41*, 443.
[2] P. Jeschke, *ChemBioChem* **2004**, *5*, 570.
[3] a) V. A. Brunet, D. O'Hagan, *Angew. Chem.* **2008**, *120*, 1198; *Angew. Chem. Int. Ed.* **2008**, *47*, 1179; b) H. Sun, S. G. DiMagno, *Angew. Chem.* **2006**, *118*, 2786; *Angew. Chem. Int. Ed.* **2006**, *45*, 2720; c) D. D. Steiner, N. Mase, C. F. Barbas, *Angew. Chem.* **2005**, *117*, 3772; *Angew. Chem. Int. Ed.* **2005**, *44*, 3706; d) M. Shimizu, T. Hiyama, *Angew. Chem.* **2005**, *117*, 218; *Angew. Chem. Int. Ed.* **2005**, *44*, 214; e) S. Rozen, *Acc. Chem. Res.* **1996**, *29*, 243.
[4] a) N. Dietl, M. Engeser, H. Schwarz, *Angew. Chem.* **2009**, *121*, 4955; *Angew. Chem. Int. Ed.* **2009**, *48*, 4861; b) J. Roithová, D. Schröder, *Angew. Chem.* **2009**, *121*, 8946; *Angew. Chem. Int. Ed.* **2009**, *48*, 8788.
[5] F. C. Gozzo, D. R. Ifa, M. N. Eberlin, *J. Org. Chem.* **2000**, *65*, 3920.
[6] R. Cipollini, M. E. Crestoni, S. Fornarini, *J. Am. Chem. Soc.* **1997**, *119*, 9499.
[7] a) S. D. Price, *Int. J. Mass Spectrom.* **2007**, *260*, 1; b) D. Schröder, H. Schwarz, *J. Phys. Chem. A* **1999**, *103*, 7385.
[8] J. F. Lockyear, K. Douglas, S. D. Price, M. Karwowska, K. J. Fijalkowski, W. Grochala, M. Remes, J. Roithová, D. Schröder, *J. Phys. Chem. Lett.* **2010**, *1*, 358.
[9] J. Roithová, C. L. Ricketts, D. Schröder, S. D. Price, *Angew. Chem.* **2007**, *119*, 9476; *Angew. Chem. Int. Ed.* **2007**, *46*, 9316.
[10] J. Lockyear, C. Ricketts, M. Parkes, S. D. Price, *Chem. Sci.* **2010**, DOI: 10.1039/c0sc00344a.
[11] Z. Herman, *Int. Rev. Phys. Chem.* **1996**, *15*, 299.
[12] W. P. Hu, S. M. Harper, S. D. Price, *Meas. Sci. Technol.* **2002**, *13*, 1512.
[13] We also observe the formation of $F^+ + SF_3^+$ ion pairs. Reactions without collision gas indicate that there is a large contribution to these ion signals from the unimolecular dissociation of SF_4^{2+} but also a component resulting from collision-induced dissociation processes.
[14] R. Sparrapan, M. A. Mendes, I. P. P. Ferreira, M. N. Eberlin, C. Santos, J. C. Nogueira, *J. Phys. Chem. A* **1998**, *102*, 5189.
[15] L. Feketeová, V. Grill, F. Zappa, N. Endstrasser, B. Rasul, Z. Herman, P. Scheier, T. D. Märk, *Int. J. Mass Spectrom.* **2008**, *276*, 37.
[16] S. D. Price, *Phys. Chem. Chem. Phys.* **2003**, *5*, 1717.
[17] The tails from some of the signals result from reactions of SF_4^{2+} at higher collision energies, which are reached after the dications have been accelerated in the mass spectrometer.
[18] Optimizations used the CCSD/cc-VTZ method [Gaussian09 (Gaussian Inc., Pittsburgh, USA, **2009**)]. Stationary points were characterized by frequency analysis. Energies at 0 K were then determined at the CCSD(T)/VTZ level, thus including corrections for zero-point energy. To test this theoretical approach for SF_4, the first ionization energy of SF_4 was computed $IE(SF_4) = 11.6$ eV and found to be in good agreement with the experimental value $IE(SF_4) = 11.7$ eV.
[19] B. Bapat, V. Sharma, S. V. K. Kumar, *Phys. Rev. A* **2008**, *78*, 042503.
[20] a) N. Kaltsoyannis, S. D. Price, *Chem. Phys. Lett.* **1999**, *313*, 679; b) S. D. Price, M. Manning, S. R. Leone, *Chem. Phys. Lett.* **1993**, *214*, 553.