Janus Face Aspect of All-cis 1,2,3,4,5,6-Hexafluorocyclohexane Dictates Remarkable Anion and Cation Interactions In the Gas Phase

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Ⓢ *Supporting Information*

ABSTRACT: Experiments have been carried out in which electrospray ionization has been used to generate ionic complexes of all-cis 1,2,3,4,5,6 hexafluorocyclohexane. These complexes were subsequently mass isolated in a quadrupole ion trap mass spectrometer and then irradiated by the tunable infrared output of a free electron laser in the 800−1600 cm^{-1} range. From the frequency dependence of the fragmentation of the complexes, vibrational signatures of the complexes were obtained. Computational work carried out in parallel reveals that the complexes formed are very strongly bound and are among the most strongly bound complexes of Na$^+$ and Cl$^-$ ever observed with molecular species. The dipole moment calculated for the heaxafluorocyclohexane is very large (∼7 D), and it appears that the bonding in each of the complexes has a significant electrostatic contribution.

A detailed knowledge of the nature of the interaction of ions with molecules in the gas phase is especially useful to understand the forces which drive molecular structure and energetics in ionic complexes. Previous contributions from this and other laboratories have provided considerable data on the energetics of interaction between ions and neutral molecules.[1] From these data, an understanding has emerged of the importance of gas-phase acidity and basicity of the relevant binding sites leading to covalent binding as well the role of polarizability and dipole and quadrupole moments for electrostatic binding. For example, an examination of Na$^+$ binding energetics to a series of molecules with a range of functionality and heteroatoms reveals a better correlation with dipole moment than with gas-phase proton basicity, thus demonstrating the importance of the electrostatic interactions in such complexes.[2] Similarly, an examination of the binding energetics of chloride ion to a series of *n*- and cycloalkanes has shown a very good correlation with the polarizability of the alkane with the exception that the cycloalkanes exhibit a slightly higher binding enthalpy to chloride than the corresponding *n*-alkane, despite the fact that they have a slightly lower polarizabilty. This can be seen to be due to the somewhat closer approach possible for the total of the individual C−H···Cl$^-$ interactions in the cycloalkanes.[3] In the study of chloride ions bound to alkanes, experimental and computational energetics were in excellent agreement. Lisy et al. have also carried out studies of Li$^+$, Na$^+$, and K$^+$ bound to cyclohexane in which vibrational spectra were obtained in the C−H stretching region, and these were compared to computed spectra.[4] Somewhat surprisingly, the computational work supports assignment of the structures as involving two axial and one equatorial hydrogen rather than three axial hydrogens. Interestingly, the computed binding energy for Na$^+$ with cyclohexane is essentially identical to that computed for Cl$^-$, which is very well reproduced by an ion-induced dipole potential.

Prior studies of halide ions binding to a variety of molecules had also shown, not surprisingly, that substitution of hydrogen by an electronegative substituent gave rise to a significant increase in the binding enthalpy. For example, the binding enthalpy of Cl$^-$ to acetone has been determined as ∼58 kJmol^{-1}.[5] Substitution of fluorine for hydrogen, for example, in 1,1,3,3 tetrafluoroacetone, results in an increase of roughly 30 kJ mol^{-1} in binding enthalpy.[6,7] Moreover, in the fluorinated acetone case, bidentate binding occurs. With this consideration in hand, when the studies of Cl$^-$ binding to cyclohexane had been carried out, it had been deemed to be of interest to carry out an experiment in which hydrogen was symmetrically substituted by fluorine in order to appreciably enhance the binding energy. Unfortunately, at that time, such compounds were not readily available. Most recently, however, O'Hagan et al. demonstrated the synthesis of all-cis 1,2,3,4,5,6 hexafluorocyclohexane, **1**, which can be considered to be the epitome of the type of compound sought in order to enhance halide ion binding in cyclohexanes.[8] The orientation of the fluorine atoms in **1** entails a 1,3,5 triaxial orientation and a 2,4,6 triequatorial orientation such that the molecule can be considered to have a fluorine face as well as a hydrogen face (Figure 1). Accompanying computational work[8] yielded a dipole moment of ∼6.2 D for **1**, leading to the expectation that the binding of anions should be substantially enhanced at the hydrogen face of the molecule. Moreover, it was deemed likely that the binding of cations to the fluorine face of the molecule would be realized.

In order to examine these possibilities, a combined experimental and computational approach was undertaken in which the energetics of binding of both sodium and chloride ions to **1** was determined. This also gave detailed information
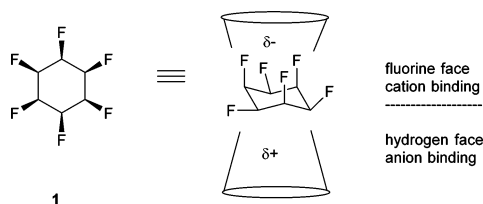
Figure 1. Structures and two faced Janus polarity of **1**.

for the structures and vibrational spectra of the ion-neutral molecule adducts which, in the latter case, could be compared to infrared multiple photon dissociation (IRMPD) spectra obtained for these adducts at the CLIO free electron facility in Orsay, France.[9] Briefly, ions of interest were generated by electrospray ionization and subsequently trapped in a Bruker Esquire ion trap mass spectrometer where they were irradiated by the output of the free electron laser (typically for 150 ms), which was scanned from 800 to 1800 cm^{-1}. In each of the Na$^+$ and Cl$^-$ cases, it was possible to generate both the mono- and di-coordinated adducts with **1**. The photoproducts resulting from the IRMPD process involved loss of either one or two molecules of **1** to generate either the bare ion or the ion coordinated to **1**.

To gain an understanding of the strength of binding in these adducts, the thermochemistry of reactions 1−4 was calculated using the Gaussian 09 program package[10] in which geometry optimizations were carried out at the B3LYP level of theory with a 6-311+G(d,p) basis set followed by single point calculations of energies at the MP2(full)/6-311+G(2d,2p) level of theory. In the case of sodium cation and adducts containing sodium cation, the single point energy calculations employed the MP2(full)/aug-cc-pCVTZ on sodium.[2c] The results for energetics of interaction from the computational analysis are given in Table 1. In the cases of both positive ion and negative ion complexes, the addition of the second molecule of **1** is less favorable than the first, as expected is such systems.[11]

Table 1. Energetics of Association Reactions

Na$^+$ + C$_6$H$_6$F$_6$ → [C$_6$H$_6$F$_6$]Na$^+$ (1)

[C$_6$H$_6$F$_6$]Na$^+$ + C$_6$H$_6$F$_6$ → [C$_6$H$_6$F$_6$]$_2$Na$^+$ (2)

Cl$^-$ + C$_6$H$_6$F$_6$ → [C$_6$H$_6$F$_6$]Cl$^-$ (3)

[C$_6$H$_6$F$_6$]Cl$^-$ + C$_6$H$_6$F$_6$ → [C$_6$H$_6$F$_6$]$_2$Cl$^-$ (4)

eq	ΔH^o_{298} kJ mol^{-1}	ΔS^o_{298} J mol^{-1} K^{-1}	ΔG^o_{298} kJ mol^{-1}
1	−175.9	−116.3	−141.3
2	−145.4	−132.9	−105.8
3	−156.5	−97.2	−127.5
4	−114.5	−112.5	−81.0

The magnitudes of the binding enthalpies in each case are impressively large. Some of the strongest molecular binding to Na$^+$ is that found for amino acids, and the data for the complexes investigated here have binding enthalpies comparable to those of the smaller aliphatic amino acids. The only compounds found to exceed significantly the magnitude observed for Na$^+$ binding to **1** are polyethers such as diglyme, 12-crown-4, 12-crown-5, and 18-crown-6.[11,12]

Similarly, the binding enthalpy for the second molecule of **1** is among the largest ever reported for binding of two molecules to sodium.[11,13] The binding of chloride ion to **1** is also found to

be very strong. The binding enthalpy of 156.5 kJ mol^{-1} is comparable to that found for very strong gas-phase Brønsted and Lewis acid species. For example, the largest molecular binding enthalpy to Cl$^-$ found in the NIST database is that for *p*-cyanophenol[11,14] at 148 kJ mol^{-1}. Similarly, the binding enthalpies of chloride ion to Lewis acids such as BF$_3$ (109 kJ mol^{-1}), AsF$_3$ (108 kJ mol^{-1}), and SiCl$_4$ (101 kJ mol^{-1}) are all substantially weaker than that of **1**.[11,15] Thus, **1** is a contender for the molecule with the strongest molecular binding to Cl$^-$. Once again very few, if any, second molecule binding enthalpies are stronger than that of **1**. For example, the binding of a second molecule of HCN to the Cl$^-$(HCN) complex[16] is found to be 75 kJ mol^{-1}, considerably less than that found here for a second molecule of **1** of 114.5 kJ mol^{-1}.

It is also of considerable interest to examine the details of the structures of the complexes formed between Na$^+$ and Cl$^-$ with **1**. Consistent with the decrease in binding enthalpy for the second addition of **1** relative to the first addition to Na$^+$, it can be seen (Table 2, Figure 2) that the contact distance between

Table 2. Calculated Covalent Bond Distances (Å)

	1	MNa$^+$	M$_2$Na$^+$	MCl$^-$	M$_2$Cl$^-$
C−C	1.532	1.530	1.530	1.526	1.527
C−H$_{ax}$	1.098	1.097	1.097	1.099	1.097
C−H$_{eq}$	1.094	1.090	1.091	1.093	1.093
C−F$_{ax}$	1.380	1.418	1.409	1.396	1.392
C−F$_{eq}$	1.384	1.377	1.378	1.400	1.397
X−H/F		2.282	2.341	2.532	2.604

Na$^+$ and each of the axial fluorines increases from 2.28 Å in the monomer to 2.34 Å in the dimer. Similarly, the second addition
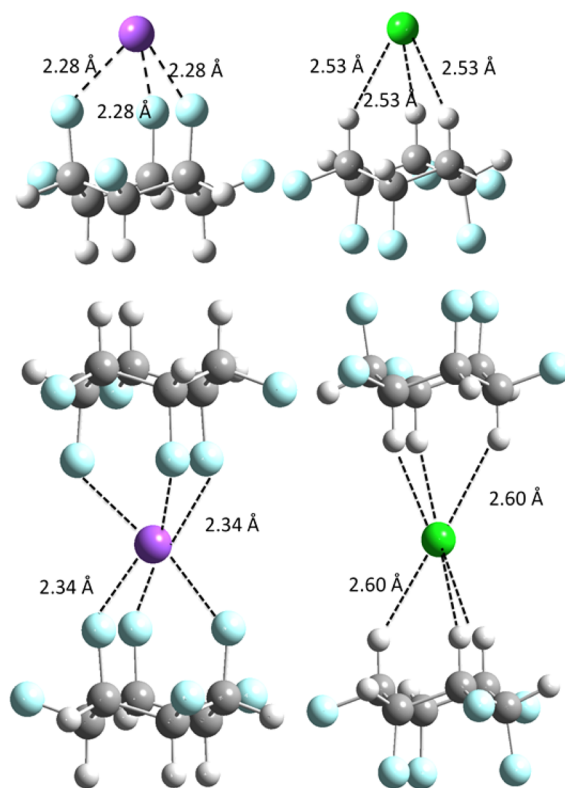

Figure 2. Structures of the Na$^+$ and Cl$^-$ ions coordinated to one and two molecules of **1**.

of **1** to its monomeric complex with Cl$^-$ increases the contact distance between Cl$^-$ and the axial hydrogens in the dimer complex from 2.53 to 2.60 Å. Interestingly, the magnitude of the contact distance changes in the Na$^+$ and Cl$^-$ complexes is relatively similar (0.06 Å for Na$^+$ and 0.07 Å for Cl$^-$), while the changes in binding enthalpies are somewhat larger for Cl$^-$ (42 kJ mol^{-1}) than for Na$^+$ (30 kJ mol^{-1}).

With respect to other geometric parameters within these complexes, it is of interest to note the relative lack of changes in covalent bond distances within the **1** moieties which accompany the complexation with these ions, despite the very strong energies of binding. As can be seen from Table 2, there is no change in bond distance >0.04 Å. The largest changes occur in the axial C−F bond distances with a lengthening of 0.04 and 0.03 Å in the Na$^+$ complexes and 0.01 to 0.02 Å in the Cl$^-$ complexes. Relative to isolated **1**, a very small contraction occurs in the equatorial C−F bonds in the Na$^+$ complexes of ~0.007 Å and a minor lengthening in the Cl$^-$ complexes of 0.016 and 0.013 Å. The fact that the covalent bond system of **1** remains essentially unchanged in the complexation process supports the conclusion that the interaction of the ions with the molecule via the axial fluorine or hydrogen atoms is largely electrostatic in origin, involving ion−dipole and ion-induced−dipole potentials. A calculation of the ion-induced−dipole interaction between Cl$^-$ and cyclohexane gives, within experimental error, the experimentally determined value of 40 kJ mol^{-1}. Given the very large dipole moment of **1** and the distances of approach of these monatomic ions to the molecule, it is likely that the charge−dipole and charge-induced−dipole interactions contribute substantially to the overall energetics of interaction.

Vibrational frequencies for the ion−molecule adducts obtained from the IRMPD experiments have been compared to computed spectra for the same adducts as well as to the computed spectrum of **1** itself. One such spectrum, for the $[C_6H_6F_6]_2Cl^-$ species, is shown in Figure 3, where the red lines represent the computed frequencies (with a scaling factor of 0.986) and relative intensities.
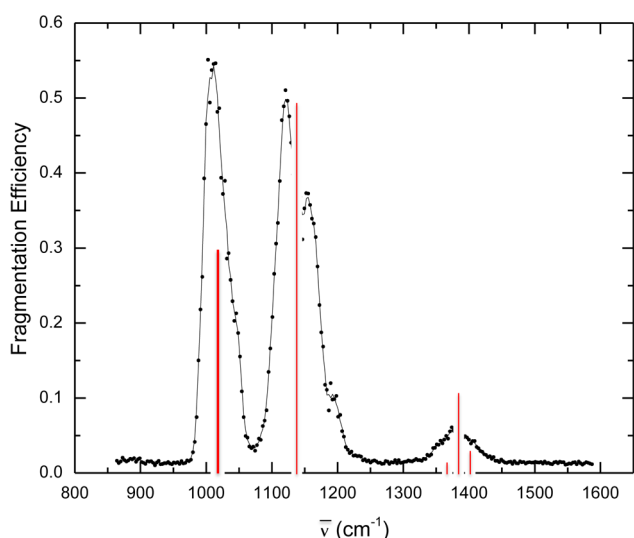

Figure 3. IRMPD spectrum of the complex of Cl$^-$ bound to two molecules of **1**. The black points represent the actual experimental data points and the red lines the computed vibrational frequencies (scaled by 0.986).

This spectrum and, in fact, all of the IRMPD spectra obtained for the extensive series of ionic adducts examined exhibit a very strong resemblance to the computed spectrum of isolated monomeric **1** with some minor shifts depending upon the ion involved. The broadening of the peaks in the 1000−1100 and 1100−1200 cm^{-1} ranges, as well as the shoulder on the latter feature, suggests that there may in fact be two species present with this composition. Additional computational work has revealed a structure in which a neutral dimer of **1** is bound to the chloride ion which lies 15 kJ mol^{-1} higher in energy that the species described above. This structure is shown in the Supporting Information (SI). Given the more favorable energetics of the structure shown in Figure 2, it is likely that this species dominates in the spectrum. The computed vibrational spectrum of **1** as well as those of the two possible $[C_6H_6F_6]_2Cl^-$ species described above are also provided in the SI.

In the cases of the four ionic species discussed above, the most intense modes involve vibrations which are substantially C−F stretch in character, and, significantly, the primarily axial and equatorial C−F stretches occur at different frequencies. In Table 3, the computed values for the modes of highest intensity

Table 3. Computed Vibrational Frequencies[a]

species	C−F$_{eq}$	C−F$_{ax}$	C−H$_{wag}$
all-*cis*-$C_6H_6F_6$	1039	790, 1150	1363, 1355
$[cis\text{-}C_6H_6F_6]Na^+$	1050	767, 1055	1362
$[cis\text{-}C_6H_6F_6]_2Na^+$	1048	1065	1363
$[cis\text{-}C_6H_6F_6]Cl^-$	999	774, 1107	1347, 1369
$[cis\text{-}C_6H_6F_6]_2Cl^-$	1027	779, 1137[17]	1352, 1367

[a]Scaled by 0.986 (cm^{-1}).

are summarized for the isolated molecule and each of the adducts of **1**. Consistent with the slight shortening of the C−F$_{eq}$ bonds in the two sodium cation complexes, the frequency of the C−F$_{eq}$ stretch vibration increases slightly. Similarly, those same bonds for the chloride complexes are lengthened somewhat, and the corresponding frequencies are lower relative to the isolated molecule.

In analogous fashion, the axial C−F mode frequencies follow the slight shifts in equilibrium bond distances among the set of complexes described here, where the bond distances in the ionic complexes are each somewhat longer and the corresponding frequencies are somewhat lower.

The analogous changes for axial and equatorial C−H stretching frequencies could not be probed experimentally due to the limited frequency range accessible with the FEL. However, computationally, the expected result is seen with variations <20 cm^{-1} relative to **1**, consistent with the minimal changes observed in C−H bond distances.

Analogous IRMPD experiments were carried out for each of the atomic alkali cations, and halide anions with both one and two molecules of **1** with, for the most part, similar vibrational spectra observed. Computational work is currently underway to explore further the structures and energetics of these complexes. The one notable exception to this commonality for atomic anion complexes is that for the fluoride ion, where considerably more structure is observed in the 900−1200 cm^{-1} region of the IRMPD spectrum. It seems clear that, even though the masses of the adducts observed are consistent with formation of the analogous anionic association adducts, either chemical reaction or alternative binding modes are being

observed here. Gas-phase ion—molecule reactions of fluoride ions with fluoroalkanes are known to be rich, involving proton abstraction and FHF^- formation accompanied by hydrogen-bond formation to C—H bonds.[18] Potential complexes resulting from addition of F^- to **1** are also the subject of ongoing experimental and computational investigation. As well, a number of complexes involving polyatomic anions have also been the subject of the IRMPD studies, including BF_4^-, HCO_2^-, and $B_{12}F_{12}^{2-}$.

In summary, all-cis hexafluorocyclohexane displays an extraordinary propensity to bind both cations and anions. This is a consequence of its differentially polarized faces which suggests that **1**, or analogous derivatives, has potential to act as a complexation motif to associate with or deliver cations and anions in both polar and nonpolar media and in supramolecular chemistry.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b02856.

Experimental data (PDF)

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Notes

The authors declare no competing financial interest.

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(17) The shoulder on this peak in Figure 3 is likely due to a small amount of binding of Cl^- to a neutral dimer of **1** (see SI).

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