The C–F···Cation Interaction: An Ammonium Complex of a Hexafluoro Macrocyclic Cage Compound

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Abstract: An ammonium complex of the hexafluoro cage compound **1** was isolated and its structure was elucidated by X-ray crystallographic analysis. The C–F bonds are elongated by the complexation, which is clear evidence of C–F···cation interaction. The driving force of NH_4^+ inclusion is the C–F···cation interaction, but the C–F···HN^+ hydrogen bond does not contribute to this complexation. The crystal structure of the $NH_4^+ \subset$ **1** shows short C–F···HN^+ contacts (2.286–2.662 Å). Furthermore, it shows that closer F···H^+(–N) distances give a larger F···H^+–N angle. Although such structural features seem to indicate the existence of C–F···HN^+ hydrogen bonds, the spectral data (^{1}H NMR, ^{19}F VT-NMR, and IR spectroscopy) did not support the existence of hydrogen bonds. Thermodynamic parameters, log K_s (4.6 ± 0.1, 298 K), ΔH (-5.3 ± 0.1 kcal mol^{-1}), and ΔS (3.2 ± 0.3 cal mol^{-1} K^{-1}), of the complexation were obtained in $CDCl_3/CD_3CN$ mixture.

Keywords: cryptands · cyclophanes · fluorine · host–guest chemistry · macrocyclic ligands

Introduction

The C–F···H–N^+ hydrogen bond has become of interest in recent years in bio-organic chemistry with respect to the base-pairing interactions in DNA replication. The discussion on whether there are hydrogen bonds between adenine and a thymine isostere are currently in progress.[1] However, several research results suggest the weak C–F···H–N^+ hydrogen bond. Shimoni et al. performed a search of the crystal structure database and showed that the hydrogen bonds between C–F and H–X (X = C, N, O) are weak but cannot be ignored in the prediction of the molecular packing mode in crystals.[2] They also predicted the $CH_mF_n \cdots NH_4^+$ interaction by ab initio MO calculations and concluded that the "near-linear interactions C–F···H^+–N are sufficiently strong to play a role in the alignment of molecules in crystals and complexes". They estimated the dissociation energy ΔH_{298} of $CH_mF_n \cdots NH_4^+$ to be 8.1–13.5 kcal mol^{-1}.[3] On the other hand, Dunitz and Taylor carried out a search of the crystal structure database and concluded "organic fluorine hardly ever accepts hydrogen bonds".[4] Howard et al. also carried out the search of CSDS (Cambridge Structural Database System) and ab initio calculations, and they found very rare case of C–F···HX (X = O, N) hydrogen bonds.[5] Plenio et al. observed short C–F···H–N^+ contacts in their protonated cryptands, but they could not obtain unambiguous spectral evidence of the hydrogen bond.[6]

On the other hand, in a previous report, we clarified C–F··· cation (alkali metal ions, NH_4^+, and Ag^+) interactions through the use of hexafluoro macrocyclic compound **1** (Figure 1).[7] The specific spectral features (^{1}H, ^{13}C and ^{19}F NMR spectroscopy) of the cation complexes reflected clear evidence of a C–F···M^+ interaction. Comparison of the structures between cation-free **1** and its potassium complex, $K^+ \subset$ **1**, showed precise structural differences on complexation.[8] These are summarized as follows:

1) Short C–F···K^+ distances were observed.
2) The shorter C–F···K^+ distance tends to make the bond angle C–F···K^+ closer to linear.
3) Coordination of six fluorine atoms to the K^+ ion resulted in the change of ligand structure so as to accommodate the coordination sphere of K^+.
4) The average C–F bond length (1.377 Å) of $K^+ \subset$ **1** is slightly longer than that found in metal-free **1** (1.348 Å).

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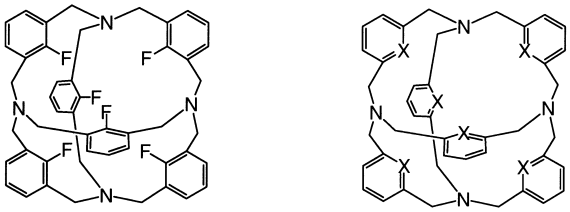

1 **2a** X = CH **2b** X = N

Figure 1. Structures of compounds **1** and **2**.

The pioneering work on macrocyclic systems that contain fluorine as a donor was performed by Plenio et al.[9] They clarified the C–F···cation interaction by means of ^{19}F NMR spectra, crystallographic analyses, and complexation studies. Although several metal-cation complexes (alkali, alkaline earth, or silver cations) were discussed in detail, the ammonium complex has not yet appeared. In the studies of C–F···M^+ interactions, the ammonium ion provides additional interest with the C–F···HN^+ hydrogen bond.

Our work revealed that **1** strongly binds an NH_4^+ ion ($\log K_s = 4.37$ in $CHCl_3$), and spectroscopic features on complexation indicate the C–F···cation interaction. However, information about the hydrogen bond between C–F and the ammonium proton was not obtained from these data. In order to ensure the contribution of the C–F···H–N^+ hydrogen bond to the inclusion of the NH_4^+ ion, we carried out X-ray crystallographic analysis of $NH_4^+ \subset$ **1** and spectroscopic evaluation. In this report, we describe the comparison of the structures among $NH_4^+ \subset$ **1**, $K^+ \subset$ **1**, and cation-free **1** and discuss the possibility of the C–F···NH_4^+ hydrogen bond.

Results and Discussion

The crystal structure of $NH_4^+ \subset$ **1** is depicted in Figure 2. Selected bond lengths, bond angles, and interatomic distances are shown in Table 1. As in $K^+ \subset$ **1**, the lone pairs of four nitrogen atoms are directed inward (one of four nitrogen atoms is directed outward in metal-free **1** in order to reduce F···F repulsion).[8] Also in the case of $NH_4^+ \subset$ **1**, reorganization of the ligand structure occurs, and F···F repulsion is reduced by the cation complexation. The four bridgehead nitrogen atoms are arranged in a tetrahedral fashion, and the ammonium ion is placed at the center of the cavity. The six fluorine atoms are coordinated to NH_4^+ in distorted octahedral manner similar to that found in $K^+ \subset$ **1**. The average C–F bond length (1.373 Å) is comparable with that in $K^+ \subset$ **1**

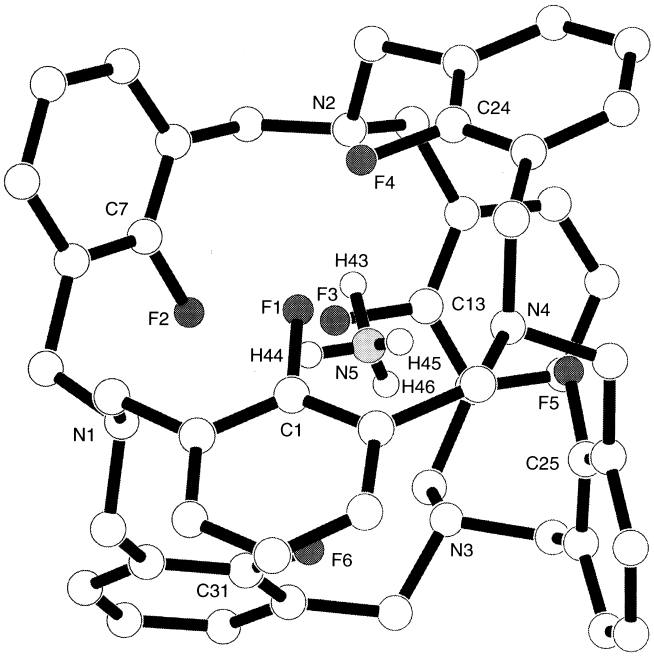

Figure 2. Crystal structure of $NH_4^+ \subset \mathbf{1} \cdot BF_4^-$ (H atoms are omitted for clarity).

Table 1. Selected bond lengths, bond angles, and interatomic distances.

Bond lengths [Å]	Bond angles [°]	Interatomic distances [Å]
C1–F1 1.367(5)	N5–H43···N2 168.7(8)	N1···N5 3.727(7)
C7–F2 1.362(6)	N5–H44···N1 165.9(5)	N2···N5 3.421(7)
C13–F3 1.370(6)	N5–H45···N4 176.0(1)	N3···N5 3.375(7)
C24–F4 1.370(5)	N5–H46···N3 173.2(9)	N4···N5 3.357(8)
C25–F5 1.384(5)		
C31–F6 1.385(5)	N5–H45···F1 109.8(5)	F1···N5 2.856(8)
H43–N5 0.987(5)	N5–H44···F2 121.6(2)	F2···N5 2.824(7)
H44–N5 0.847(6)	N5–H43···F3 110.3(5)	F3···N5 2.895(7)
H45–N5 0.705(6)	N5–H45···F5 105.3(7)	F4···N5 2.891(6)
H46–N5 0.804(6)		F5···N5 2.783(7)
	N5···F1–C1 113.5(3)	F6···N5 2.928(6)
	N5···F2–C7 107.0(3)	
	N5···F3–C13 102.7(3)	N1···H44 2.900(4)
	N5···F4–C24 99.9(3)	N2···H43 2.448(4)
	N5···F5–C25 102.4(3)	N3···H46 2.575(4)
	N5···F6–C31 104.5(3)	N4···H45 2.653(5)
		F1···H45 2.539(4)
		F2···H44 2.286(3)
		F3···H43 2.401(4)
		F4···H43 2.561(3)
		F5···H45 2.513(3)
		F6···H44 2.662(3)

Abstract in Japanese:

フッ素 6 つを含むかご型化合物 **1** のアンモニウム錯体を単離し，その構造を X 線結晶構造解析により明らかにした。アンモニウムイオンと錯形成することにより C-F 結合が伸長し，これは C-F ··· カチオン相互作用の明らかな証拠となる。アンモニウムイオン包接の Driving Force は C-F ··· カチオン相互作用によるものであるが，C-F ··· HN^+水素結合はこの包接に寄与していない。結晶構造から短い C-F ··· HN^+ 距離 (2.286 ～ 2.662 Å)が認められ，さらに，F ··· H^+(-N) 距離が短いほど F ··· H^+-N 角は大きくなる傾向が見られた。これらの事実からは C-F ··· HN^+水素結合の存在が認められるように思われる。しかしながら，スペクトルデータ(^1H, ^{19}F VT-NMR, IR)からはこの水素結合を支持する結果は得られなかった。併せてアンモニウム錯形成反応の熱力学的パラメーター，log K_S, ΔH, ΔS を $CDCl_3$–CD_3CN 中で測定した。

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(1.377 Å), which is longer than that of **1** (1.348 Å). Also here, the C–F···cation interaction elongates the C–F bond. The F···H$^+$(–N) distance is shorter (2.286 – 2.662 Å) than the sum of van der Waals radii (2.67 Å).[10] In constrast to K$^+$⊂**1**, the relationship between the C–F bond lengths and the angles C–F···N$^+$ or C–F···H$^+$(–N) was not observed. However, the shorter F···H$^+$(–N) distances give larger F···H$^+$–N angles (Shimoni et al. reported the nearly linear relationship between F···H$^+$ distances and F···H$^+$–N angles in CH_mF_n···NH_4^+ complexes[3]). If one considers only these structural features, the C–F···H–N$^+$ hydrogen bond is possible in this complex, although the F···H$^+$–N angles (105.3 – 121.6°) are far from linear.

The ammonium protons are directed toward the bridgehead nitrogen, and the N–H$^+$···N angles (165.9 – 176.0°) are almost linear. Judging from the atomic distances N···H$^+$(–N) (2.448 – 2.900 Å) and the sum of van der Waals radii (2.75 Å), hydrogen bonds between N–H$^+$···N are possible. However, it is not the main factor in the binding of ammonium ion. This is clearly recognized from the fact that fluorine-free compound **2a**[11] (Figure 1) does not bind the NH_4^+ ion. The complex formation between compound **2a** and the NH_4^+ ion was attempted by the reaction of **2a** with ammonium picrate in $CDCl_3/CD_3CN$, but evidence of the interaction was not observed. Nevertheless, the direction of the ammonium protons of NH_4^+⊂**1** seems to be determined by the weak N–H$^+$···N hydrogen bonds.

In order to obtain the experimental value of the C–F··· cation interaction, the stability constant K_s of NH_4^+⊂**1** and its thermodynamic parameters, ΔH^o and ΔS^o, were determined by ^{1}H NMR spectroscopy. The reaction between **1** and ammonium picrate in $CDCl_3/CD_3CN$ resulted in new peaks that correspond to the those of newly formed complex. Thus the association constant K_s could be easily determined. The complexation reaction proceeded very slowly in [D$_6$]DMSO; therefore, the mixed solvent was employed. Despite this, the reaction occurs slowly, and the reaction required three days at 60 °C and seven days at 30 °C until it had equilibrated. The thermodynamic measurements were performed at every 10 °C over the range of 30 – 60 ± 0.1 °C. The van't Hoff's plots of each $\ln K_s$ verus $1/T$ afforded a linear relationship that gave the parameters $\log K_s$ (298 K) = 4.6 ± 0.1, $\Delta H^o = -5.3 \pm 0.1$ kcal mol^{-1}, and $\Delta S^o = 3.2 \pm 0.3$ cal mol^{-1} K^{-1}. The positive ΔS^o shows that desolvation of the cation is one of the dominant factors for the complexation. This is recognized by the fact that the complexation rate strongly depends on the solvent. From this experiment, the actual value of the C–F··· cation (NH_4^+) interaction ($\Delta H^o = 0.88$ kcal mol^{-1} for each F atom) has been evaluated for the first time.[12] Undoubtedly, it is not a pure value of the C–F···NH_4^+ interaction because the ΔG of this reaction contains free-energy terms of the reorganization of the ligand structure.

In the $CD_3CN/CDCl_3$ mixture (1:1, v/v), the NH_4^+ proton signal appeared at $\delta = 6.38$ as a broad singlet in the absence of **1**, while the signal of NH_4^+⊂**1** appears at $\delta = 5.28$ as a triplet ($J = 53.5$ Hz). Intermolecular proton exchange of NH_4^+ is sufficiently suppressed by the inclusion. On the other hand, in the case of pyridine cage **2b**,[11] (Figure 1) the NH_4^+ signal of NH_4^+⊂**2b** appears at $\delta = 8.34$ (t, $J = 52.7$ Hz, $CD_3CN/CDCl_3$ 1:1, v/v). The low-field shift of the ammonium proton is easily understood by considering the hydrogen bond between ammonium protons and the nitrogen atoms of **2b**. However, in the case of NH_4^+⊂**1**, the NH$^+$···N or NH$^+$···F hydrogen bonds are very weak, since the NH_4^+ proton signal is shifted to higher field through the complexation. The-high field shift of the signal suggests that hydrogen bonds between the solvents and the NH_4^+ ion are broken by the inclusion. The ^{1}H NMR spectrum of NH_4^+⊂**1** at low temperatures showed only slight broadening and very small shift (≈0.1 ppm) of the NH_4^+ signal. The ^{19}F-^{1}H coupling that would imply the formation of a C–F···HN$^+$ hydrogen bond was not observed. The ^{19}F NMR spectrum of NH_4^+⊂**1** showed a sharp singlet at 25 °C which splits into a doublet and a triplet (intensity = 2 : 1, J = 50 Hz) at −90 °C. This is consistent with the ^{1}H NMR spectrum at −90 °C, in which the methylene signal appears as two sets of broad, overlapped doublets (intensity = 2:1). Therefore, the splitting of the ^{1}H and ^{19}F signals at low temperatures results from freezing of the molecular movement of the ligand **1**, but not from ^{19}F-^{1}H (ammonium proton) coupling. Furthermore, the IR spectrum also shows the weak hydrogen-bonded nature of NH_4^+⊂**1** ($\nu_{NH} = 3293$ cm^{-1}) as compared with NH_4^+⊂**2b** ($\nu_{NH} = 3160$ cm^{-1}).

Conclusively, the inclusion of NH_4^+ occurs by C–F··· cation interaction, but not by the C–F···HN$^+$ or N···HN$^+$ hydrogen bonds. Furthermore, the reduction of F···F repulsion by cation complexation contributes to the inclusion of the NH_4^+ ion. The formation of the C–F···HN$^+$ hydrogen bond could be expected from the crystal structure, but its presence was not observed from NMR (^{1}H, ^{19}F) and IR spectra.

Experimental Section

The ^{1}H and ^{19}F NMR spectra were recorded at 400.1 MHz and 376.5 MHz with TMS and $CFCl_3$ as internal references, respectively. The IR spectra were measured as KBr pellets. The thermodynamic measurements were performed in a temperature-controlled water bath every 10 °C over the range of 30 – 60 ± 0.1 °C. The initial concentrations of **1** and ammonium picrate were 9.51×10^{-3} and 7.55×10^{-3} mol dm^{-3}, respectively ($CDCl_3$/CD_3CN 1:1, v/v). The NMR spectra were recorded at the over the time range of three (60 °C) to seven days (30 °C) until the reaction equilibrated.

NH_4^+⊂1·BF_4^-·CH_3CN: A mixture of **1** (50.2 mg, 6.4×10^{-2} mmol) and an excess of NH_4BF_4 in MeOH was heated under reflux for 24 h. After removal of the solvent, the residue was washed with water and recrystallized from CH_2Cl_2/CH_3CN (colorless prisms, 47.5 mg, 79.4 %). A single crystal suitable for X-ray crystallographic analysis was obtained by slow evaporation of the CH_3CN solution of the complex.

Crystal data for NH_4^+⊂1·BF_4^-·CH_3CN: $C_{50}H_{49}F_{10}N_6B$, $T = 23 \pm 1$°, $Mo_{K\alpha}$ (Rigaku RAXIS-IV diffractometer, $\lambda = 0.71070$ Å), crystal dimensions $0.60 \times 0.40 \times 0.40$ mm^3 (colorless prism), $a = 14.36(1)$, $b = 20.540(6)$, $c = 16.10(1)$ Å, $\beta = 106.62(6)$°, $V = 4551.5(1)$ Å^3, $Z = 4$, monoclinic, space group $P2_1/c$ (No. 14), $\mu_{Mo} = 1.09$ cm^{-1}, $M_w = 934.78$ g mo1^{-1}, $\rho_{calcd} = 1.364$ g cm^{-3}, $2\theta_{max} = 55.0$°, $F(000) = 1944.00$. Number of reflections measured, 7707; number of reflections observed, 5846 [$I > 3.00\sigma(I)$]; number of parameters 653. The structure was solved by direct methods and refined on Sir92. Data were corrected for Lorentz polarizations. The data/parameter ratio was 8.95. $R = 0.077$, $wR = 0.077$, GOF = 2.53, max/min residual electron density, +0.89/−0.42 e Å^{-3}. All calculations were performed by using the TEXSAN crystallographic software package of the Molecular Structure Corporation. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-119349. Copies of the data can be obtained free of charge on

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application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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