"Naked" Fluoride

B-Octamethyl-[12]Mercuracarborand-4 as Host for "Naked" Fluoride Ions[**]

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Despite the fact that naked fluoride ions cannot exist either in solution or in the solid state, terms such as "naked fluoride ions" or "noncoordinating ion" are frequently used to describe fluoride-ion sources.[1–4] The first reliable source for "naked" fluoride ions, reported by Christe et al., describes a procedure for the preparation of anhydrous Me_4NF.[2] Since then, several other fluoride-ion sources have been prepared which show a higher reactivity of their component fluoride ions than that of Me_4NF.[3,5] The increased reactivity was explained by the "cesium effect"[4] in which the reactivity of

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the fluoride ion increases with the increasing size of the counterion, thereby providing more-exposed fluoride ions and resulting as well in their increased solubility in aprotic organic solvents. More recently, an in situ method for the preparation of anhydrous fluoride-ion solutions,[6] the solvent dependency of the ^{19}F NMR chemical shifts of the fluoride ion,[7] and a quantitative measure for the donor abilities, or “nakedness”, of fluoride ion donors[8] have been reported.

Mercuracarborands,[9] cyclic multidentate Lewis acids composed of alternating units of carborane cages and mercury atoms (Figure 1), readily form complexes with electron-donor species such as tetrahydrofuran,[10] acetonitrile,[11] nitrate ion,[12] halide ions (Cl^-, Br^-, I^-),[13] and the polyhedral *closo*-$[B_{10}H_{10}]^{2-}$ ion, among others.[14]

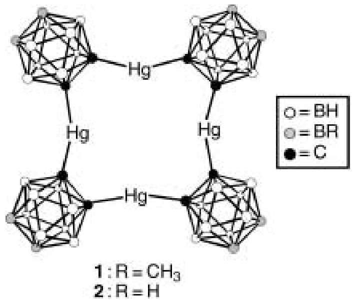

Figure 1. Representation of mercuracarborands, **1** and **2**.

Furthermore, mercuracarborands have been demonstrated to form self-assembled microporous channels,[15] and a hydrogen-bonded π-sandwich complex,[16] and to complex and activate an uncharged nucleophilic species for catalysis.[17]

Herein we report the structural characterization of the tetramethylammonium salt of the fluoride ion-complexed tetrameric B-octamethyl-[12]mercuracarborand-4 **1** (Figure 1), in which the mercuracarborand is η^4-coordinated by a weakly bonded fluoride ion and thus serves as the host for a “naked” fluoride ion.

In contrast to the method outlined in earlier publications[13d,14a] the decomplexation of **1**-I_2Li_2[13d] was accomplished using silver tetrafluoroborate in acetone rather than silver acetate, thereby providing pure **1** in quantitative yield. Treatment of **1** in dichloromethane with an aqueous solution of tetramethylammonium fluoride led to the quantitative formation of [**1**-F][Me_4N] as an air- and moisture stable solid (Scheme 1).

$$\mathbf{1}\text{–}I_2Li_2 \xrightarrow{AgBF_4} \mathbf{1} \xrightarrow{Me_4NF} [\mathbf{1}\text{–}F][Me_4N]$$

Scheme 1. Synthesis of **1**-F(Me_4N).

The most informative data concerning anion binding by mercuracarborand hosts has been obtained from ^{199}Hg and ^{19}F NMR spectroscopy studies. Other NMR spectroscopic methods, using ^{1}H, ^{13}C, or ^{11}B nuclei, are not sensitive to the guest's presence, but ^{199}Hg NMR is highly sensitive to small changes in the electronic environment surrounding the mercury centers.[18] The ^{199}Hg NMR spectrum of **1** exhibits a highfield signal at $\delta = -1280$ ppm (in [D$_6$]acetone) and -1213 ppm (in CH_2Cl_2), respectively, compared to **1**-I_2Li_2 ($\delta = -667$ ppm[13d] in [D$_6$]acetone). However the observed resonance is not in agreement with that earlier reported for **1** ($\delta = -1145$ ppm, in [D$_6$]acetone).[13d] This disparity in chemical shifts is now explained by the fact that the decomplexation of **1**-I_2Li_2 with silver acetate, as previously reported, does not afford guest-free **1**, but forms [**1**-CH_3COO]$^-$, in which the acetate ion is weakly coordinated to the Hg centers. This result and an X-ray diffraction study of [**1**-CH_3COO]$^-$ will be published elsewhere.

The ^{199}Hg-signal of [**1**-F][Me_4N] in CH_2Cl_2 is shifted downfield relative to **1** and appears as a doublet (Hg–F coupling) at $\delta = -1181.72$ with a coupling constant of $^1J = 698$ Hz. The ^{19}F NMR spectrum of [**1**-F][Me_4N] is, in principle, coupled to ^{199}Hg (16.8 % natural abundance, $S = 1/2$) and ^{201}Hg (13.2 % natural abundance, $S = 3/2$). Experimentally, a singlet (an apparent quintet) at $\delta = -102.27$ ppm is observed arising from Hg_4, $S = 0$ isotopic arrays superimposed upon a doublet and a triplet arising from $^{199}HgHg_3$ and $^{199}Hg_2Hg_2$ structures, respectively, with $^1J = 698$ Hz. Coupling with ^{19}F to $^{199}Hg_3Hg$ and $^{199}Hg_4$ structures is not observable nor is coupling of any sort with ^{201}Hg species under the conditions employed. This experimental demonstration of ^{19}F-^{199}Hg coupling involves species containing more ^{199}Hg centers per ^{19}F nucleus than any other structures previously examined. The ^{1}H, ^{13}C, and ^{11}B NMR spectra of [**1**-F][Me_4N] revealed a highly symmetrical structure in solution. The negative-ion fast atom bombardment mass spectrum exhibits a base peak centered at $m/z = 1502$, with the isotopic pattern expected for [**1**-F]$^-$.

Compound [**1**-F][Me_4N] crystallized from a CH_2Cl_2 solution in the orthorhombic space group *Ibam*. The atoms of the tetramethylammonium cation are severely disordered.[19]. The structure of the ion [**1**-F]$^-$ is presented in Figure 2.

The anion consists of four bivalent *closo*-[9,12-$(CH_3)_2$-1,2-$C_2B_{10}H_8$] cages linked by four Hg atoms in a cyclic tetramer

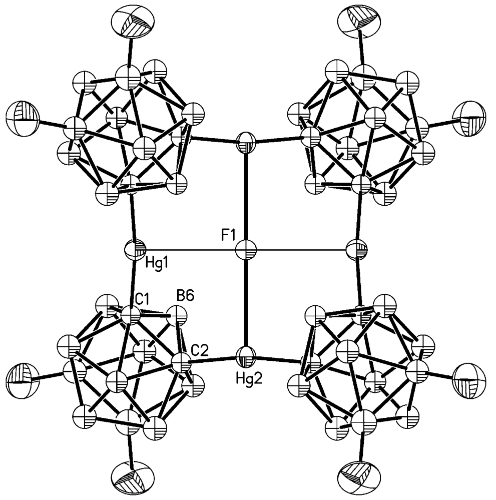

Figure 2. Structure of [**1**-F]$^-$ (ORTEP plot; hydrogen atoms omitted for clarity thermal ellipsoids set at 30 % probability). Selected interatomic distances [Å]: Hg1-F1 2.6544(6), Hg2-F1 2.5567(5), Hg1-C1 2.057(8), Hg2-C2 2.059(9), Hg1⋯Hg2 3.6855(6), Hg1⋯Hg1* 5.3088(11), Hg2⋯Hg2* 5.1135.

with a fluoride ion located in the center of the array. The shortest Hg–F separation is 2.5567(5) Å. The four Hg atoms and F are coplanar and the four cages lie alternately up-down-up-down with respect to this plane. The fluorine atom lies on the intersection of three mutually perpendicular twofold axes. Two of these intersecting axes pass through the Hg-F-Hg vectors. The four Hg atoms form an approximate square. In contrast to the fluoride-ion mercuracarborand complex,[9,13c,g,14b] the chloride and mono-bromide[14a] mercuracarborand complexes have the halide ion displaced above the plane containing the four Hg atoms, while the di-iodide[9,13c,e,g,14b] complex has halide ions both above and below the plane containing the four Hg atoms. Each Hg in [**1**-F][Me$_4$N] links carbon atoms of two carborane icosahedra with Hg–C separations of 2.057(8) Å (Hg1-C1) and 2.059(9) Å (Hg2-C2). The Hg-C-C angles are 118.8(5)° and 120.1(6)° while the C-Hg-C angles are 173.9(4)° and 172.4(4)°, respectively. In comparison, the parent B-unsubstituted [12]mercuracarborand-4 hosting a chloride ion, [**2**-Cl]$^-$, possesses an average C–Hg separation of 2.09 Å, a C-Hg-C angle of 162.0°, and a Hg-C-C angle of 125.7°.[13g,14a] The distance between adjacent mercury atoms is 3.6855(6) Å, which is longer than the van der Waals distance (3.46 Å) and significantly shorter than in [**2**-Cl]$^-$ (4.129(1) Å).[14a] The diagonal Hg···Hg distances are 5.3088(11) and 5.1135(11) Å, respectively. The torsion angle involving Hg-C-C-Hg is 1.5(9)° which is comparable with those found in [**2**-Cl]$^-$ (0.0°)[13g,14a] The shortest distance between the nitrogen atom of the cation and the fluoride atom of the anion is 6.92 Å, ruling out the possibility that the fluoride is complexed as its tetramethylammonium salt.

Preliminary evaluation of the fluorination potential of **1**-F(Me$_4$N) using NMR spectroscopy analyses showed that treatment of this complex with two equivalents of tetra-*n*-butyl ammonium iodide in dry deuterated acetonitrile (to produce [**1**-I$_2$]$^{2-}$) in the presence of a tosylated sugar (1,2,3,4-tetra-*O*-acetyl-6-*p*-tolylsulfonoxy-β-D-glucopyranose) led to a partial displacement (up to 49.4 %) of the tosylate group of the sugar derivative.[20] The ^{19}F NMR spectrum of the product has a signal at $\delta = -234$ ppm which is in agreement with that reported[21] for the 6-fluoro derivative. Separate experiments showed that the sugar tosylate group does not react with [**1**-F][Me$_4$N] in dry CD$_3$CN alone. In addition, treatment of the sugar tosylate with tetra-*n*-butyl ammonium iodide gave less than 2 % displacement of the tosylate.[20] These results show that the tetra-*n*-butyl ammonium iodide serves to activate the complexed fluoride ion by releasing "naked fluoride".

An optimized fluorination procedure using [**1**-F][Me$_4$N] as a source for "naked fluoride" is currently under investigation in our laboratories and will be reported elsewhere.

The simplicity of the synthesis of [**1**-F][Me$_4$N] using aqueous conditions provides a complexed fluoride ion with outstanding properties, such as air- and moisture-stability, solubility in common organic solvents, and utility as a source for "naked fluoride" under controlled circumstances by the addition of two equivalents of tetra-*n*-butyl ammonium iodide. It may be possible that these properties of [**1**-F][Me$_4$N] can be utilized for the synthesis of ^{18}F-labeled carbohydrates and other species required for positron-emission-tomography (PET)[22] allowing the investigation of metabolic processes in vivo as a routine diagnostic tool or in the study of physiological processes.

Experimental Section

1: The complex **1**-I$_2$Li$_2$ (3.00 g, 1.713 mmol) in dry acetone (100 mL) was treated with AgBF$_4$ (0.70 g, 3.596 mmol) and stirred at room temperature for 12 h. The yellow precipitate (AgI) was removed by filtration, washed with several portions of acetone, and the solvent was removed under vacuum. Recrystallization from acetone afforded **1** as a white solid in quantitative yield. ^{1}H NMR (400 MHz, [D$_6$]acetone, 25 °C): $\delta = 0.03$ (s, BCH$_3$), 2.5–3.0 ppm (br, BH); ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]acetone, 25 °C): $\delta = 0.8$ (br, BCH$_3$), 86.3 ppm (HgC); ^{11}B{^{1}H} NMR (160 MHz, acetone, 25 °C, BF$_3$·Et$_2$O): $\delta = -13.5$ (2 B), −10.4 (4 B), −5.5 (2 B), 8.8 ppm (2 B); ^{199}Hg{^{1}H} NMR (89.6 MHz, 25 °C, external 0.5 M PhHgCl in [D$_6$]DMSO: chemical shift $\delta = -1187$[18] upfield from neat Me$_2$Hg): $\delta = -1280$ in [D$_6$]acetone and −1213 in CH$_2$Cl$_2$.

[**1**-F][Me$_4$N]: Me$_4$NF·4 H$_2$O (1 mL of a 0.035 mM solution in H$_2$O) was added to a solution of **1** (51.6 mg, 0.035 mmol) in CH$_2$Cl$_2$ (1 mL) and the mixture was stirred for 5 min. The aqueous layer was extracted with CH$_2$Cl$_2$ (2 × 2 mL) and the combined organic phase was evaporated to dryness under vacuum. Traces of water were removed azeotropically by adding CH$_2$Cl$_2$ (3 × 2 mL) and removing the solvent to give [**1**-F][Me$_4$N] in quantitative yield as a white solid. ^{1}H NMR (400 MHz, [D$_6$]acetone, 25 °C): $\delta = 0.03$ (s, BCH$_3$), 2.5–3.0 ppm (br, BH); ^{13}C{^{1}H} NMR (100 MHz, [D$_6$]acetone, 25 °C): $\delta = 0.8$ (br, BCH$_3$), 86.3 ppm (HgC); ^{11}B{^{1}H} NMR (160 MHz, acetone, 25 °C, BF$_3$·Et$_2$O): $\delta = -13.5$ (2 B), −10.4 (4 B), −5.5 (2 B), 8.8 ppm (2 B); ^{19}F{^{1}H} NMR (376.50 MHz, CH$_2$Cl$_2$, 25 °C, CFCl$_3$): $\delta = -102.27$ ppm (apparent quintet, see discussion, ^1J with ^{199}Hg = 698 Hz); ^{199}Hg{^{1}H} NMR (89.6 MHz, CH$_2$Cl$_2$, 25 °C, external 0.5 M PhHgCl in [D$_6$]DMSO: chemical shift $\delta = -1187$[18] upfield from neat Me$_2$Hg): $\delta = -1181.72$ in [D$_6$]acetone (d, ^1J(Hg,F) = −698 Hz); MS (negative ion FAB) $m/z = 1501.8$ [**1**-F]$^-$.

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[19] Crystallographic data collection for **1**-F(Me_4N): $C_{20}H_{56}B_{40}FHg_4N$, $M_r = 1564.42$, crystal dimensions: $0.10 \times 0.30 \times 0.35\ mm^3$, orthorhombic, space group *Ibam*, $a = 10.5888(7)$, $b = 21.8950(15)$, $c = 26.2498(18)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 6085.8(7)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.707\ mg\,cm^{-3}$, $T = 298(2)$ K, absorption coefficient $\mu = 10.083\ mm^{-1}$. Data were collected on a Bruker SMART 1000 ccd diffractometer using $Mo_{K\alpha}$ radiation. to a maximum $2\theta = 56.66°$, giving 3762 unique reflections. A total of 3762 unique reflections were measured, of which 1968 reflections were considered observed with $I > 2\sigma(I)$. All reflections were used in the subsequent structure analysis. Data were corrected for Lorentz and polarization effects and for secondary extinction and absorption. Atoms were located by use of direct methods. Hg, F, and the 2 methyl C atoms of the anion were refined anisotropically. The tetramethylammonium cation is disordered and methyl H atoms were not located. All other H atoms were placed in calculated positions. H atoms were assigned isotropic displacement values based approximately on the value for the attached atom. Scattering factors for H atoms were obtained from Stewart et al.[23] and for other atoms were taken from The International Tables for X-ray Crystallography.[24] The final discrepancy index was $R = 0.045$, $R_w = 0.1772$ ($w = 1/\sigma^2|F_o|$) for 1968 independent reflections with $I > 2\sigma(I)$. The largest peak maximum and minimum on a final difference electron density map were 2.39 and -1.34 e Å^{-3}, both near Hg. Programs used in this work include SMART, SAINT, and SHELXTL, all supplied by Bruker for the SMART system. CCDC-219630 ([**1**-F][Me_4N]) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

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