

Cite this: *CrystEngComm*, 2011, **13**, 3682

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Tetrabenzylcyclen as a receptor for fluoride†

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Received 3rd March 2011, Accepted 11th April 2011

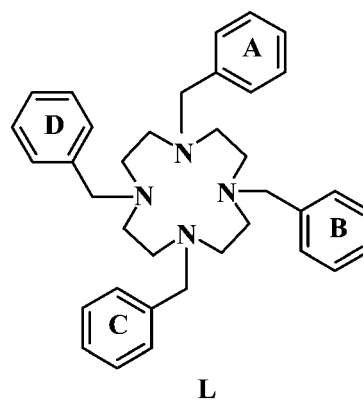
DOI: 10.1039/c1ce05279a

A tetraazacyclic ligand, tetrabenzylcyclen (L), was synthesized using an improved method with a higher yield by treatment of cyclen with benzylchloride in the presence of potassium carbonate. The reaction of L with an aqueous solution of fluorosilicic acid yielded a mixed-anionic salt with the composition $[\text{H}_3\text{L}][\text{F}][\text{SiF}_6] \cdot 4\text{H}_2\text{O}$ (1). The single crystal X-ray study revealed that the macrocyclic trication essentially changes the conformation compared to the free ligand in order to tightly accommodate the fluoride inside and to keep the hexafluorosilicate anions and water molecules outside in the solid state complex.

Recent years demonstrate the steady interest in the various aspects of supramolecular chemistry of anions, and, in particular, in halide anions due to their important role in chemical engineering and biological processes.^{1–3} Among the halide anions the smallest in size, fluoride, occupies a special place due to its specific properties: in aprotic media it acts as a very strong Lewis base and a nucleophile, and it has a strong acceptor ability in the formation of hydrogen bonds. Intensive studies of the complexation of the fluoride ion with various organic receptors were stimulated by the participation of fluoride in the processes of biological catalysis^{4,5} and organic synthesis,^{6–9} and also due to search for new selective and sensitive sensors for analytical monitoring of fluoride in the environment, as well as in biological and chemical processes.^{10–12} The aza-cycles, azacryptands and relative molecules, easily protonated in the acidic medium, proved themselves as effective receptors for fluoride.^{13–15} For years we have been involved in the physicochemical studies of fluorides and fluoro-containing complexes of the 3A, 4A and 5A group elements with an emphasis on the stabilizing function of spacious macrocyclic cations in the retention of hydrolytically unstable and even unique fluoro-containing anions. The aqueous solutions of

fluorosilicic acid, H_2SiF_6 , represent important products of fluoride technology being used as reagents for the fluorination of potable water¹⁶ as well as industrial fluorinating agents. Solutions of fluorosilicic acid represent an equilibrium mixture of the fluoride anions and fluoro-complexes with the general formula $[\text{SiF}_{6-n}(\text{H}_2\text{O})_n]^{2-}$ ($n = 0–2$). The interaction of this system with a macrocyclic receptor is possible, resulting in the competitive coordination of fluoro-containing anionic complexes with the macrocycle. However, our previous investigations demonstrated the exclusive formation of azonia hexafluorosilicates in the case of ‘all-N-containing’ cycles such as cyclen, 3,6,9-triaza-1(2,6)-pyridinacyclododecaphane and tet b (*meso*-5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane),¹⁷ while the extraction of the hydrolytically unstable anionic $[\text{SiF}_3]^-$, $[\text{SiF}_5 \cdot \text{H}_2\text{O}]^-$ and neutral $[\text{SiF}_4 \cdot 2\text{H}_2\text{O}]$ species was registered when aza-crown ethers or ‘all-O’ crown ethers were used.¹⁸

The known examples of mixed-anionic fluoride-containing complexes are scarce and refer mainly to the complexes of 18-membered azacryptands containing aromatic fragments^{13,14,19} and oxa,azacryptands.²⁰ We previously reported the mixed-anionic salt $[\text{H}_6[18]\text{aneN}_4][\text{F}][\text{BF}_4] \cdot 3.5\text{H}_2\text{O}$,²¹ which represents an interesting example of fluoride ion encapsulation by the hexaazonia macrocycle, $[\text{H}_6[18]\text{aneN}_4]^{6+}$. The fluoride perfectly centres the macrocyclic cavity while the tetrafluoroborate anions form the second coordination sphere of the $\{[\text{H}_6[18]\text{aneN}_4][\text{F}]\}^{5+}$ complex cation. In continuation of this research, we describe herein the improved synthetic procedure and crystal structure of the tetraazacycle 1,4,7,10-tetrabenzyl-1,4,7,10-tetraazacyclododecane (L), as well as the crystal structure of its mixed-anionic salt with the composition $[\text{H}_3\text{L}][\text{F}][\text{SiF}_6] \cdot 4\text{H}_2\text{O}$ (1), where the ligand in the form of trication encapsulates the fluoride, thus



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† CCDC reference numbers 815104–815105. For crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ce05279a

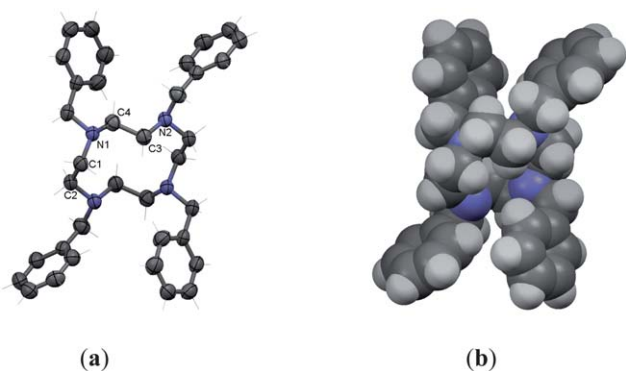


Fig. 1 ORTEP plot (with ellipsoids at 50%) (a), and space-filling presentation (b) for L with partial numbering scheme. Selected torsion angles: C(4)–N(1)–C(1)–C(2) $-157.0(1)$, N(1)–C(1)–C(2)–N(2)' $91.0(2)$, C(1)–C(2)–N(2)'–C(3)' $-77.4(2)$, C(2)'–N(2)–C(3)–C(4) $154.0(1)^\circ$. Symmetry transformation: $i - x, -y, -z$.

demonstrating a crucial change of its conformation in comparison with the free molecule. Compound **1** represents the unprecedented metal-free complex where the tetrabenzylcyclen manifests its facilities as a promising anionic and in particular fluoride receptor.

To obtain 1,4,7,10-tetrabenzyl-1,4,7,10-tetraazacyclododecane (L); to the boiling mixture of cyclen (2.6 g, 0.015 mol)^{22,23} and potassium carbonate (9.95 g, 0.072 mol) in anhydrous acetonitrile (100 mL), the solution of benzylchloride (7.6 mL, 0.066 mol) in acetonitrile (30 mL) was added dropwise over half an hour, and then the reaction mixture was boiled for 10 h. The reaction mixture was left overnight. The precipitate was filtered off, chloroform (200 mL) was added, the mixture was boiled and after cooling the inorganic salts were filtered off. The chloroform was evaporated to dryness. The product was extracted with boiling heptane (2×150 mL), and after distillation of the heptane it was recrystallized from acetonitrile. Yield 6 g (75%). M. p. 145–147 °C. FAB mass MH^+ 533. 1H NMR ($CDCl_3$, ppm) δ 2.69 (16 H, br s, CH_2N), 3.53 (8H, br s, $CH_2-C_6H_5$), 7.19–7.29 (20H, m, C_6H_5). Monocrystals of L were obtained by recrystallization from methanol/ethylacetate (50 mL : 20 mL), m.p. 136–138 °C. The given improved method results in a higher yield compared with the previously reported synthesis (yield 54%), which was completed in the

medium of methylene chloride using NaOH as a main reagent.²⁴ Complex **1**, with the composition $[LH_3][F][SiF_6] \cdot 4H_2O$ (**1**), was obtained by mixing a boiling methanol solution (75 mL) of 1,4,7,10-tetrabenzyl-1,4,7,10-tetraazacyclododecane (L, 53 mg, 0.1 mmol) and 5 mL of a 45% solution of fluorosilicic acid. The spontaneous evaporation of the reaction mixture at room temperature led to single crystals of the complex with the yield being close to quantitative and m.p. 212–215 °C (with decomposition). Anal. found, %: Si 3.71, N 7.15, F 17.86. Calc. for **1**, %: Si 3.65, N 7.29, F 17.30.

Tetrabenzylcyclen, L,²⁵ crystallizes in the monoclinic space group $P2_1/n$. The molecule resides on an inversion centre and adopts 1,2-alternate conformation with all N-atoms being displayed in the same plane. The two neighbouring benzyl groups attached to N(1) and N(2) and their symmetry-related counter-parts are situated on opposite sides of this plane (Fig. 1). The T-shape mutual arrangement of the one-side oriented phenyl rings is described by the Ar(A)/Ar(B) dihedral angle of $89.22(7)^\circ$ and Cg(A)···H–Ar(B) distance of 3.84 Å. The conformation of the heterocycle and the arrangement of the aromatic substituents in L are very similar to those found in 1,4,7,10-tetrakis(4-nitrobenzyl)-1,4,7,10-tetraazacyclododecane²⁶ and 1,4,7,10-tetrakis(4-vinylbenzyl)-1,4,7,10-tetraazacyclododecane.²⁷

The interaction of L with an aqueous solution of fluorosilicic acid resulted in the mixed-anionic salt with the composition $[H_3L][F][SiF_6] \cdot 4H_2O$ (**1**), whose crystal structure was determined by single crystal X-ray diffraction. The compound **1** crystallizes in the monoclinic $C2/c$ space group with one formula unit in the asymmetric unit. The structure is built of the globular cation $[(H_3L)(F)]^{2+}$ keeping the fluoride deeply encapsulated into the tricationic azacycle, the outer-sphere hexafluorosilicate anion, and four water molecules, two of which, O(3w) and O(4w), are subject to crystal disorder. The most interesting feature of this structure is the trapping of the fluoride by the tetraazacycle accompanied by the crucial changing of the ligand conformation in comparison with its free state as well as with the known metal-containing complexes.^{24,28} The ligand adopts an asymmetric shape with three of four nitrogen atoms being protonated (as follows from the objective location of three H-atoms in close proximity to the N-atoms) and a cone conformation of the phenyl substituents, all being situated on one side of the cyclic cavity. The conformation of the 12-membered framework refers to the four-angular type,²⁹ which is characterised by the four *gauche,gauche*-

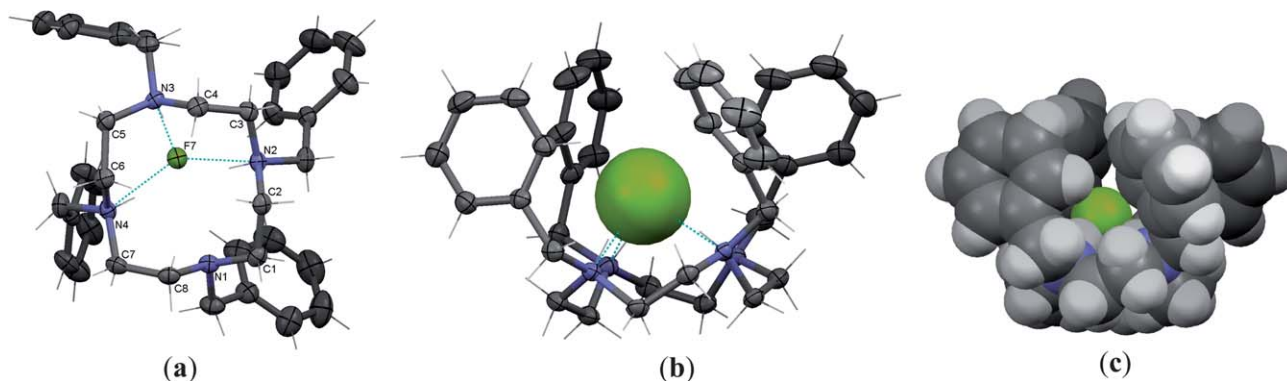


Fig. 2 ORTEP plot (with ellipsoids at 30%), bottom (a) and side (b) views, and space-filling presentation (c) for $[(H_3L)(F)]^{2+}$ complex cation with partial numbering scheme. Torsion angles along the 12-membered framework: C(1)–C(2)–N(2)–C(3) $164.4(2)$, C(2)–N(2)–C(3)–C(4) $-67.1(2)$, N(2)–C(3)–C(4)–N(3) $-74.5(2)$, C(3)–C(4)–N(3)–C(5) $150.5(2)$, C(4)–N(3)–C(5)–C(6) $-65.9(2)$, N(3)–C(5)–C(6)–N(4) $-66.0(3)$, C(5)–C(6)–N(4)–C(7) $167.9(2)$, C(6)–N(4)–C(7)–C(8) $-71.7(2)$, N(4)–C(7)–C(8)–N(1) $-61.3(2)$, C(7)–C(8)–N(1)–C(1) $158.9(2)$, C(8)–N(1)–C(1)–C(2) $-79.3(2)$, N(1)–C(1)–C(2)–N(2) $-60.6(2)^\circ$.

Table 1 Hydrogen bonds for **1** (Å and °)

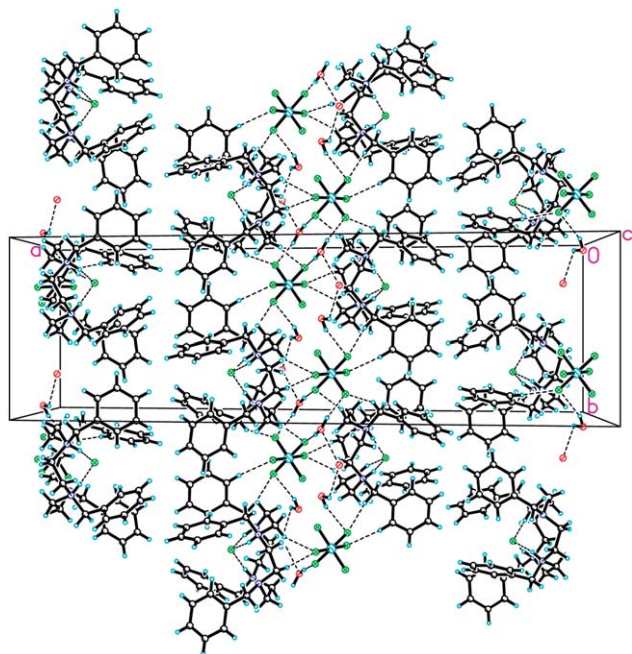
| D–H...A | d(D–H) | d(H...A) | d(D...A) | ∠(DHA) |
|-----------------------------------|---------|----------|----------|--------|
| N(2)–H(2N)...F(7) | 0.98(2) | 1.68(2) | 2.630(2) | 161(2) |
| N(3)–H(3N)...F(7) | 0.97(2) | 1.55(2) | 2.507(2) | 167(2) |
| N(4)–H(1N)...F(7) | 0.92(2) | 1.75(2) | 2.647(2) | 164(2) |
| O(1W)–H(1W1)...F(5) | 0.89(2) | 1.87(2) | 2.753(2) | 174(2) |
| O(1W)–H(2W1)...F(2) ^b | 0.85(2) | 2.02(2) | 2.856(2) | 169(3) |
| O(2W)–H(1W2)...F(6) ^c | 0.87(2) | 2.17(3) | 2.945(3) | 148(3) |
| O(2W)–H(1W2)...F(1) ^c | 0.87(2) | 2.22(2) | 2.982(3) | 146(3) |
| O(2W)–H(2W2)...O(3W) | 0.92(2) | 2.28(4) | 2.753(4) | 111(3) |
| O(4W)–H(1W4)...F(3) | 0.90(2) | 1.98(4) | 2.777(5) | 147(6) |
| O(4W)–H(2W4)...O(3W) ^a | 0.90(2) | 2.00(3) | 2.814(6) | 151(6) |

Symmetry transformations used to generate equivalent atoms:

^a 1–x, y, 1/2–z; ^b 1–x, 2–y, 1–z; ^c 1–x, 1–y, 1–z.

fragments separated by C–N bonds in *anti*-conformations, which maximises the distances between the charged NH⁺-sites (Fig. 2). The phenyl substituents are arranged in a T-shape mode again with the dihedral angles between the phenyl rings equal to 68.6(1), 59.2(1), 89.6(1), and 57.1(1)° for the A/B/C/D/A sequence. The fluoride sits 1.583(1) Å from the N₄-mean plane (the r.m.s. deviation of the fitted atoms of 0.059 Å). The three NH-binding sites are involved in similar strength NH...F hydrogen bonds, with N...F separations ranging within 2.507(2)–2.647(2) Å (Table 1). The N(1)...F(7) separation, to the non-protonated nitrogen atom, is equal to 3.148(2) Å. The degree of protonation, as well as the conformation of the macrocyclic cation, is quite similar to the 1,4,7,10-tetraallyl-10-aza-1,4,7-triazoniacyclododecane in its trichloride complex.³⁰

The solid state structure of **1** demonstrates the pronounced demarcation of hydrophilic and hydrophobic regions. The hydrophilic regions represent the negatively charged inorganic sheets expanded parallel to the *bc* plane and built of the hydrogen-bonded hexafluorosilicate anions and water molecules (Table 1), the hydrophobic regions represent the cyclic azonia-cations centred by fluoride

**Fig. 3** Fragment of crystal packing for **1**.

(Fig. 3). Between the regions the strongest interactions are the numerous CH...F interactions.

In summary, the tetrabenzylcyclen has manifested itself as a promising fluoride receptor, as it demonstrates the deep accumulation of the anion inside the nest-shaped cyclic trication due to the cumulative effect of three NH⁺...F⁻ hydrogen bonds and the shielding effect of four pendant benzyl arms. Compound [H₃L][F][SiF₆]-4H₂O represents the first metal-free complex of this ligand selected in the crystal state.

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- Crystal data for **L**: C₃₆H₄₄N₄, M_r = 532.75, monoclinic, P2₁/n, λ = 0.71073 Å, a = 15.285(3), b = 6.467(1), c = 16.654(2) Å, V = 1540.6(4) Å³, Z = 2, D_c = 1.148 g cm⁻³, μ = 0.067 mm⁻¹, θ range 1.56–25.07°, GOF = 1.025, R₁ = 0.0488, wR₂ = 0.1210 for 1962 reflections with I > 2σ(I), R₁ = 0.0726, wR₂ = 0.1363 for all 2719 unique reflections. Crystal data for **1**: C₃₆H₅₅F₇N₄O₄Si, M_r = 768.93, monoclinic, C2/c, λ = 0.71073 Å, a = 37.0414(14), b = 11.1521(4), c = 19.2636(7) Å, V = 7835.6 (5) Å³, Z = 8, D_c = 1.304 g cm⁻³, μ = 0.136 mm⁻¹, θ range 2.95–25.50°, GOF = 0.841, R₁ = 0.0399, wR₂ = 0.0809 for 3577

reflections with $I > 2\sigma(I)$, $R_1 = 0.0950$, $wR_2 = 0.0896$ for all 7297 unique reflections. The single crystal X-ray data for **L** and **1** were collected at room temperature on Bruker SMART-APEX and Xcalibur Oxford Diffraction diffractometers, both equipped with a CCD area detector and a graphite monochromator utilizing Mo-K α radiation. Final unit cell dimensions were obtained and refined on an entire data set. All calculations to solve the structures and to refine the model proposed were carried out with the programs SHELXS97 and SHELXL97. Empirical absorption correction was applied. In **1**, two water molecules are disordered over two orientations with the partial occupancies of 0.918(5) and 0.082(5) for O(3w) and 0.638(17) and 0.362(17) for O(4w), respectively. For O(3w) the hydrogen atoms were not localised. The C-bound H atoms were placed in calculated positions and were treated using a riding model approximation with $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{C})$, while the O- and N-bound H-atoms of the water molecules and amino groups were found from

differential Fourier maps and were refined with isotropic displacement parameters $U_{\text{iso}}(\text{H}) = 1.5 U_{\text{eq}}(\text{O})$, $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{N})$ and DFIX restraints for O–H distances ($d(\text{O}–\text{H}) = 0.86$, $d(\text{H}\cdots\text{H}) = 1.46 \text{ \AA}$). CCDC 815104 and 815105 contain the crystallographic data for **L** and **1**.

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