ORGANIC
LETTERS

2007
Vol. 9, No. 21
4219−4222

Oxa-Bicyclocalixarenes: A New Cage for Anions via C–H···Anion Hydrogen Bonds and Anion···π Interactions

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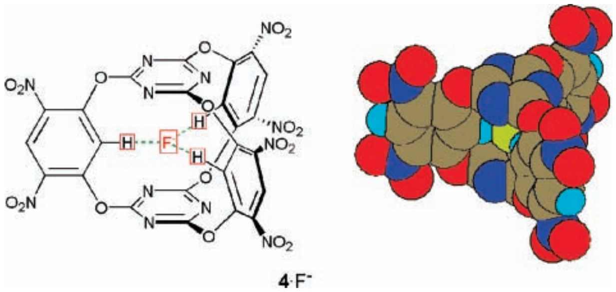
Received July 26, 2007

ABSTRACT



4·F⁻

Density functional theory calculations indicate that the cage molecule 4 can trap F⁻ in the gas phase (–80.5 kcal/mol) as well as in CH_2Cl_2 (–14.7 kcal/mol) via strong C–H···F⁻ hydrogen bonds and π···F⁻ interaction.

Anion binding processes are important in anion recognition, electrochemical or optical sensing, synthetic templates, anion-directed assembly, and catalysis.[1] In the past decade, there was a boom in the design and synthesis of receptors for specific anions.[1a−e,h,i,o] Many moieties, such as Lewis acid metal ions,[1a,1c,1d,1j] π-acidic aromatic rings,[2] positively charged groups,[3] and hydrogen bonds, especially N−H and O−H proton donors,[1d−e,g,h,m,n,p,4] are introduced into the design of anion receptors. Although there are some reports on the studies of C−H···anion hydrogen bonds by theoretical and experimental methods in the gas phase,[5] recent experimental studies of C−H···anion binding in the condensed phase usually utilize imidazolium cations, where cation−anion interactions potentially play important roles.[1p,6] It is, therefore, still challenging and conceptually novel to use neutral C−H···anion interactions in the design of anion receptors.

Inspired by the development of oxa-bridged calixarenes,[7] a recent report by Katz et al.[8] on the easy synthesis of oxa-bicyclocalixarenes, and a proposal by Mascal on potential anion binding with positively charged cyclophane-like

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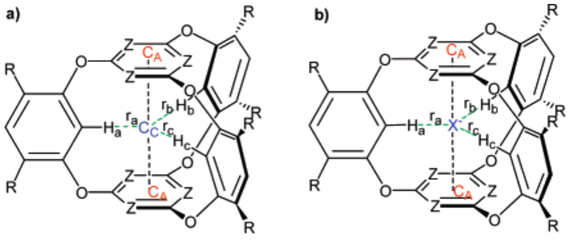
10.1021/ol701740p CCC: $37.00

molecules,[9] we have carried out a computational study on oxa-bicyclocalixarenes, **1**−**4** (Scheme 1), to address their halide binding potential and selectivity.

Scheme 1[a]



1 Z = CH, R = H **3** Z = CH, R = NO_2
2 Z = N, R = H **4** Z =N, R = NO_2

X = F, Cl Z = CH,N R = H, NO_2

[a] C_C is the center of the cavity, and C_A is the center of the parallel aromatic ring.

All calculations were performed with the Gaussian03[10] program. The density functional theory (DFT)[11] method of B3LYP/6-31G*[12] was employed to perform full geometrical optimizations unless specified otherwise. All structures (see the Supporting Information) were confirmed to be minima in the gas phase with vibrational analyses. Energies were further evaluated with the B3LYP/6-311++g** method including Boy's[13] counterpoise (CP) correction for basis set superposition errors (BSSE) of interaction energies. The solvent effect of CH_2Cl_2 (dielectric constant $\epsilon = 8.93$) on energies was estimated by the integral equation formalism polarizable continuum model (IEFPCM)[14,15] (with UAHF[16] molecular cavity atomic radii) at the latter level.

It is well-known that anion selectivity of macrocyclic compounds is highly dependent on the size of the cavity.[1d,i] In the present case, the size of the cage is described by two parameters: one is the distance between the parallel aromatic rings (C_A−C_A, Scheme 1), defined as r_1, and another is the distance between the center of the cage (C_C) and the inward hydrogens (H_a, H_b, and H_c in Scheme 1), designated as r_a, r_b, and r_c. Table 1 shows the structural features for the empty oxa-bicyclocalixarenes and anion-bound complexes. The optimized structure of **3** agrees well with the reported crystal structure (Figure 1).[8] The calculated r_1 and r_{a-c} are 4.807 and 1.694 Å, respectively. The corresponding values are 4.827 and 1.740 Å, respectively, in the crystal structure. Both **1** and **3** adopt pseudo-D_{3h} symmetry. All three hydrogens H_{a-c} point toward C_C, whereas the structures **2** and **4** are distorted. The hydrogens H_{a-c} deviate significantly from the central direction, pointing along the edge of the triazine (TZ) ring, as indicated by the large deviation of the angles A_1, A_2, and A_3(C−H···C_C or C−H···X angles) from linearity (Table 1).

These results indicate that the electronic character of the aromatic rings exerts a large influence on the geometries of the molecules. Benzene is π-electron rich, and triazine is π-electron deficient.[2a−e,9] The acidic hydrogens H_{a-c} point toward the electron-rich center in **1** and **3**, gaining attractive electrostatic interactions, whereas the acidic hydrogens H_{a-c} avoid the electron-poor center in **2** and **4**. They prefer to point along the edge of the triazine ring to gain attractive

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Table 1. Structural Features at the B3LYP/6-31g* Level[a]

structure	r_1	r_a	r_b	r_c	A_1	A_2	A_3
1	4.928	1.617	1.617	1.617	176.2	176.2	176.2
2	4.953	1.863	1.874	1.855	129.9	122.0	123.5
3	4.807	1.681	1.681	1.694	178.4	178.4	180.0
4	4.841	1.805	1.688	1.885	131.5	142.4	125.5
1·F$^-$	5.022	1.582	1.579	1.579	180.0	178.9	178.4
1·Cl$^-$	5.324	2.149	2.555	2.433	178.2	87.7	91.6
2·F$^-$	4.913	1.557	1.559	1.559	167.3	166.3	166.9
2·Cl$^-$	5.201	2.133	2.496	2.668	174.0	87.2	80.9
3·F$^-$	4.955	1.614	1.610	1.605	178.6	179.5	179.2
3·Cl$^-$	5.224	1.968	2.004	2.465	169.1	172.3	81.0
4·F$^-$	4.810	1.572	1.574	1.572	178.9	179.7	178.3
4·Cl$^-$	5.177	2.157	2.522	2.704	177.3	87.3	79.1
3·F$^{-(\mathrm{TS})}$	4.909	2.801	1.524	1.525	180.0	150.5	150.4
4·F$^{-(\mathrm{TS})}$	4.802	3.543	1.467	1.874	164.6	174.7	110.8

[a] Distances in Å, angles in °. Fluorine in **3**·F$^{-(\mathrm{TS})}$ and **4**·F$^{-(\mathrm{TS})}$ using 6-31+g* basis sets during geometry optimization.

interactions with the nitrogen atoms. The average H···N distance in **2** is about 2.75 Å and about 2.60 Å in **4**.

Upon F$^-$ binding, the centers of **2** and **4** become electron rich. Therefore, the acidic hydrogens H$_{a-c}$ are more favorable to point toward the center just like the situations in **1** and **3**. The cages of **2** and **4** are slightly contracted because of the attraction between F$^-$ and the electron-deficient triazine rings, which are reflected by the smaller r_1 value (Table 1). As expected, the geometries of F$^-$-bound **1**·F$^-$ and **3**·F$^-$ do not change obviously with respect to the empty **1** and **3**. The orientation of the hydrogens H$_{a-c}$ does not change in **1** and **3**, but the cages are slightly swelled due to the repulsion between the negatively charged F$^-$ and the electron-rich benzene ring. The influence of the electronic character of the aromatic rings on the binding of F$^-$ can also be shown by the interaction energies between F$^-$ and these compounds (Table 2). The triazine-containing compounds **2** and **4** have about 15.0 kcal/mol stronger binding affinities with F$^-$ than the corresponding benzene analogues. In all cases, **4**·F$^-$ is the most stable, and it is predicted to have about −15.0 kcal/mol of interaction energy even in CH$_2$Cl$_2$.[17]

Table 2. Single-Point Interaction Energies without (ΔE) and with BSSE Correction (ΔE^{cp}), Gibbs Free Energy Correction ($\Delta\Delta G^{\mathrm{gas}}$) in the Gas Phase, Solvation Free Energy Contribution ($\Delta\Delta G^{\mathrm{sol}}$) in CH$_2Cl_2$, and Total Interaction Energy ($\Delta_r G^{\mathrm{sol}}$) in CH$_2Cl_2$[a]

structure	ΔE^{b}	$\Delta E^{\mathrm{cp},b}$	$\Delta\Delta G^{\mathrm{gas},c}$	$\Delta\Delta G^{\mathrm{sol},b}$	$\Delta_r G^{\mathrm{sol},d}$
1·F$^-$	−32.10	−28.55	7.66	55.64	34.75
1·Cl$^-$	44.64	47.02	7.69	33.48	88.19
2·F$^-$	−45.52	−41.41	7.49	52.12	18.20
2·Cl$^-$	21.74	24.11	8.83	31.54	64.48
3·F$^-$	−73.67	−70.13	9.12	71.15	10.14
3·Cl$^-$	11.57	13.86	9.00	49.60	72.45
4·F$^-$	−90.85	−86.66	6.15	65.84	−14.68
4·Cl$^-$	−18.32	−15.87	11.20	46.37	41.70
3·F$^{-(\mathrm{TS})e}$	−60.61	−56.98	8.90	70.87	22.80
4·F$^{-(\mathrm{TS})e}$	−71.11	−67.61	9.84	63.96	6.19

[a] Energies in kcal/mol. [b] At the B3LYP/6-311++g** level. [c] At the B3LYP/6-31 g* level. [d] $\Delta_r G^{\mathrm{sol}} = \Delta E^{\mathrm{cp}} + \Delta\Delta G^{\mathrm{gas}} + \Delta\Delta G^{\mathrm{sol}}$. [e] $\Delta\Delta G^{\mathrm{gas}}$ for fluorine using the 6-31+g* basis set here.

Obviously, the cages of **1**−**4** are too small to accommodate the chloride anion. Though the minimum can be located for all **1**·Cl$^-$, **2**·Cl$^-$, **3**·Cl$^-$, and **4**·Cl$^-$, the structures of these complexes deform significantly compared to the empty cages (Figure 1). The interaction energies are positive even in the gas phase, except for **4·Cl**$^-$. These complexes are about 70.0 and 50.0 kcal/mol less stable than the fluoride complexes in the gas phase and in CH$_2$Cl$_2$, respectively, implying that these cages have a very high selectivity for fluoride over chloride. These results can be understood by the simple model studies in the gas phase, in which the r_1 is about 6.98 Å for the TZ···Cl$^-$···TZ sandwich complexes,[9] which is much larger than the average r_1 value of about 4.88 Å in cages **1**−**4**, whereas the r_1 is about 5.40 Å for the TZ···F$^-$···TZ sandwich complexes, close to that in cages **1**−**4**. Therefore, these cages are nearly ideal for the binding of F$^-$. However, the inclusion of Cl$^-$ causes large deformations to the cages, and such deformation disrupts the normal C−H···Cl$^-$ bond, which in turn decreases the binding affinity of Cl$^-$ with the cages. In addition, the intrinsic electronic characters of halide ions also

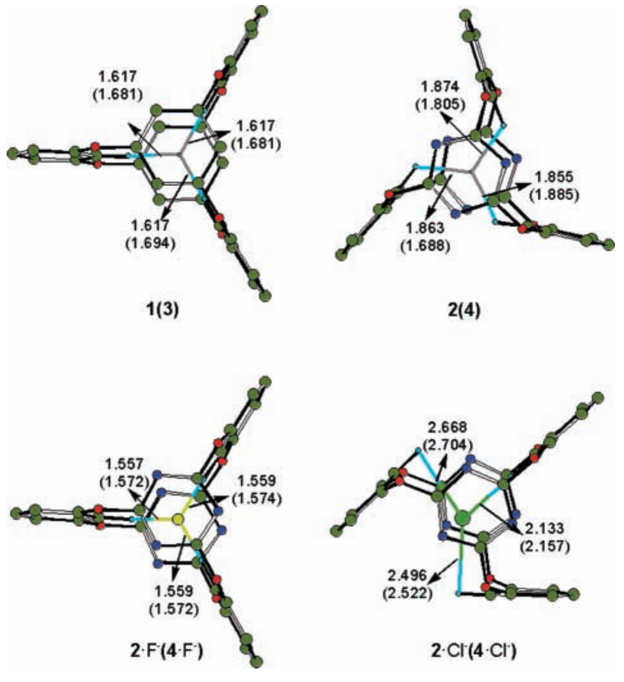

Figure 1. Selected calculated structures of **1**−**4** and anion binding species (nitro groups and some hydrogen atoms omitted for clarity; the values in parentheses are for nitro-substituted bicyclocalixarenes).

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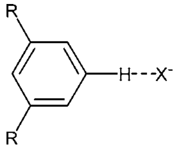
(17) We have also optimized structures **4** and **4**·F$^-$ with the MP2 method using the 6-31+G* basis set for F and the 6-31G* basis set for other atoms. The calculated geometrical parameters are very close to those shown in Table 1. The calculated electronic interaction energy between **4** and F$^-$ is about −85.3 kcal/mol (see Supporting Information for details).

influence their binding properties. For example, the interaction energy of TZ···Cl$^-$···TZ is about 8.9 kcal/mol less than that of TZ···F$^-$···TZ,[9] and the C−H···Cl$^-$ bond is about 7.6−13.0 kcal/mol less stable than C−H···F$^-$(Figure 2).



	R(X$^-$-H)	ΔE_{bind}
X = F, R = H	1.673 (1.693)	-15.4 (-13.7)
X = F, R = NO$_2$	1.469 (1.484)	-34.9 (-32.9)
X = Cl, R = H	2.491 (2.497)	-6.5 (-6.1)
X = Cl, R = NO$_2$	2.236 (2.242)	-20.3 (-19.9)

Figure 2. Calculated H···X distances (Å) and binding energies (kcal/mol) obtained at the B3LYP/6-311++g** level without and with BSSE correction (in parentheses) for benzene and 1,3-dinitrobenzene (DNB) with F$^-$ and Cl$^-$.

As shown in Table 2, the interaction energy difference between **2**·F$^-$ and **1**·F$^-$ is −12.9 kcal/mol, whereas that between **4**·F$^-$ and **3**·F$^-$ is −16.5 kcal/mol. These are close to the interaction energy of about −16.5 kcal/mol in the TZ···F$^-$···TZ model.[9] Considering the possible Ph···F$^-$···Ph repulsion, the real TZ···F$^-$···TZ stabilization in this system should be somewhat less than the above estimated value. This result indicates that the contribution of C−H···F$^-$ bonds to the total interaction energy is dominant (−10.0 to −25.0 kcal/mol per bond) in complexes **1**·F$^-$, **2**·F$^-$, **3**·F$^-$, and **4**·F$^-$. Figure 2 shows the calculated strength of the C−H···F$^-$ and C−H···Cl$^-$ bonds in the model systems of benzene and 1,3-dinitrobenzene in the gas phase. The values are −13.7 and −32.9 kcal/mol (Figure 2) for F$^-$ with benzene and 1,3-dinitrobenzene, respectively. These interaction energies calculated by the B3LYP/6-311++G** method are similar to those calculated by the MP2 method by Hay et al.,[5j,k] and the former is consistent with the experimental value of −15.3 kcal/mol.[5b] The calculated anion binding energies in **1**·F$^-$ to **4**·F$^-$ are somewhat less than the corresponding optimal C−H···F$^-$ bonds. We can also analyze the influence of the nitro groups on the C−H···F$^-$ bond through the comparison of **3**·F$^-$ and **1**·F$^-$, or **4**·F$^-$ and **2**·F$^-$, which brings about 14.0−15.0 kcal/mol stabilization, indicating that the electron-withdrawing groups on the aromatic rings significantly contribute to the binding of F$^-$ to the cages. Again these energies are somewhat smaller than those calculated based on benzene and 1,3-dinitrobenzene.

To evaluate the barrier for F$^-$ to enter cages **3** and **4** in solution, the transition states **3**·F$^{-(TS)}$ and **4**·F$^{-(TS)}$ were located (Figure 3). F$^-$ lies between the edges of the two parallel benzene rings in **3**·F$^{-(TS)}$. It forms two strong C−H···F$^-$ hydrogen bonds. However, F$^-$ locates outside the two parallel triazine rings in **4**·F$^{-(TS)}$. It forms a linear C−H···F$^-$ hydrogen bond with the top benzene ring and a nonlinear hydrogen bond with the bottom benzene ring. Overall, **4**·F$^{-(TS)}$ can be considered as an earlier transition state than **3**·F$^{-(TS)}$. The calculated barriers for F$^-$ entering cages **3** and **4** are about 22.8 and 6.4 kcal/mol, respectively, in solution. These calculated low barriers for F$^-$ inclusion into **3** and **4** are remarkable considering that they have to overcome large desolvation energies (70.9 and 64.0 kcal/mol, respectively). Thus, the two C−H···F$^-$ hydrogen bonds in the transition structures **3**·F$^{-(TS)}$ and **4**·F$^{-(TS)}$ are indeed very strong.

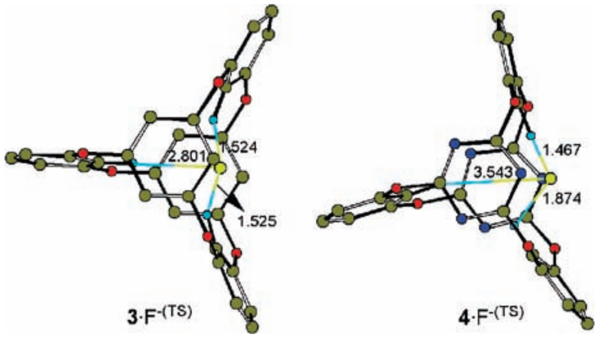


Figure 3. Transition state structures for F$^-$ entering the cages **3** and **4** at the B3LYP/6-31+G*(for F)/6-31G*(for others) level.

Thus, we propose that oxa-bicyclocalixarenes can selectively bind with the fluoride ion in the gas phase and in the condensed phase. The C−H···F$^-$ hydrogen bonds contribute to the primary stabilization for the anion binding. In addition, the π acidity of the triazine ring also improves greatly the encapsulation of F$^-$. The cavity of **4** is nearly ideal for the encapsulation of F$^-$ in terms of both C−H···F$^-$ and π···F$^-$ interactions. Thus, it is remarkable that despite a calculated desolvation destabilization of about 65.8 kcal/mol for the **4**·F$^-$ formation (Table 2, $\Delta\Delta G^{sol}$) a sizable stabilization energy of −14.7 kcal/mol is predicted in CH$_2$Cl$_2$ solution. This invites experimental tests to see whether **4** can be the first neutral cage with only C−H···F$^-$ and π···F$^-$ interactions to trap the fluoride anion in solution.

Acknowledgment. This research was supported by the National Science Foundation of China (20225312). We thank Prof. M. X. Wang of CASIC for helpful discussions.

Supporting Information Available: Detailed geometries and energetics of the structures. This material is available free of charge via the Internet at http://pubs.acs.org.

OL701740P