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# Halogen Bonding between Anions and Iodoperfluoroorganics: Solution-Phase Thermodynamics and Multidentate-Receptor Design

Mohammed G. Sarwar, Bojan Dragisić, Elena Dimitrijević, and Mark S. Taylor\*<sup>[a]</sup>

**Abstract:** The interactions of iodoperfluoroarenes and -alkanes with anions in organic solvent were studied. The data indicates that favorable halogen-bonding interactions exist between halide anions and the monodentate model compounds C<sub>6</sub>F<sub>5</sub>I and C<sub>8</sub>F<sub>17</sub>I. These data served as a basis for the development of preorganized multidentate receptors capable of high-affinity

anion recognition. Several new receptor architectures were prepared, and the multidentate-iodoperfluorobenzoate-ester design, as described in a preliminary communication, was evalu-

**Keywords:** anions • molecular recognition • noncovalent interactions • perfluoroarenes • thermodynamics

ated in more detail. Computation was employed to better interpret the structure–activity relationships arising from these studies. Investigations of the thermodynamics of anion binding (by van't Hoff analysis) and solvent effects reveal details of these halogen bonding interactions.

## Introduction

Halogen bonding (XB) occurs “when there is evidence of a net attractive interaction between an electrophilic region on a halogen atom X belonging to a molecule or molecular fragment R–X and a nucleophilic region of a molecule, or molecular fragment, Y–Z.”<sup>[1]</sup> R–X...Y–Z interactions are most thermodynamically favorable when X is a heavy halogen atom (I > Br > Cl > F) and R is either an electronegative or polarizable substituent, and display a pronounced preference for 180° noncovalent R–X–Y angles.<sup>[2]</sup> Both charge-transfer<sup>[3]</sup> (donation of electron density to low-lying σ\*<sub>R–X</sub> orbitals) and electrostatic models<sup>[4]</sup> (interaction with the ‘σ-hole’ region of electron deficiency centered on X) have been advanced to account for these interactions. The utility of XB for directing self-assembly in condensed phases is established,<sup>[5]</sup> and includes applications in crystal engineering,<sup>[6]</sup> liquid crystals,<sup>[7]</sup> chiral discrimination,<sup>[8]</sup> topochemical polymerization,<sup>[9]</sup> and organic materials design.<sup>[10]</sup> Applications of XB in solution have been developed more slowly; the scarcity of thermodynamic data for interactions of organic donors (as opposed to inorganic donors RX, where R is also a halogen atom<sup>[11]</sup>) has likely been a contributing factor. In recent years, the body of data of this type for interactions of haloalkynes,<sup>[12]</sup> haloarenes,<sup>[13]</sup> and haloalkanes<sup>[13b,14]</sup> has grown, and demonstrations of the utility of

XB in medicinal chemistry,<sup>[15]</sup> self-assembly,<sup>[16]</sup> and catalysis<sup>[17]</sup> are emerging rapidly.<sup>[18]</sup>

Our research group has explored anion recognition using multidentate XB donors. The crystallographic literature indicates that halogen bonds to anionic acceptors are highly directional and that a single anion may accept multiple halogen bonds in the solid state.<sup>[19]</sup> Evidence that XB interactions of anions are thermodynamically favorable in solution includes the formation of trihalide anions, for example, the interaction of I<sub>2</sub> with KI to form KI<sub>3</sub>, an interaction that is exothermic by 4 kcal mol<sup>−1</sup> in water,<sup>[20]</sup> and the handful of reported association constant (K<sub>a</sub>) values for interactions of anions with organic XB donors.<sup>[21]</sup> Iodoperfluoroarene-functionalized podand **1a** stands as a pioneering example of the incorporation of XB donor groups into molecular receptors; C—I...I<sup>−</sup> halogen bonding was estimated to contribute roughly 1.8 kcal mol<sup>−1</sup> to the free energy of interaction with NaI in CDCl<sub>3</sub>, as judged by K<sub>a</sub> values determined for **1a** and control receptor **1b** (Figure 1).<sup>[22]</sup> The geometry of this receptor precludes bi- or tridentate halogen bonding with anions, a conclusion supported by X-ray crystallography of the **1a**–NaI complex and by the modest estimated contribution of XB to the thermodynamics of binding. In compari-

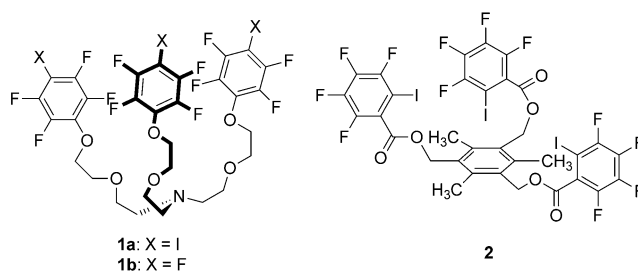


Figure 1. Structures of iodoperfluoroarene-based halogen-bonding receptors for NaI (**1a**, Ref. [22]) and Bu<sub>4</sub>NCl (**2**, Ref. [26]).

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son to hydrogen bonding,<sup>[23]</sup> Lewis acid–Lewis base<sup>[24]</sup> and anion–arene<sup>[25]</sup> interactions, XB interactions have arguably been underexploited in the design of synthetic anion receptors.

We thus set out to design hosts bearing XB donor groups oriented appropriately for multidentate anion recognition, and in 2010 reported that tris(iodoperfluorobenzoate) ester **2** acts as a tridentate anion receptor, with  $K_a$  value of  $1.9 \times 10^4 \text{ M}^{-1}$  for  $n\text{Bu}_4\text{N}^+\text{Cl}^-$  in acetone solvent at 295 K.<sup>[26]</sup> Values of  $K_a$  for interactions of **2** with tetra-*n*-butylammonium halide salts,  $n\text{Bu}_4\text{N}^+\text{X}^-$ , decreased in the order  $\text{Cl}^- > \text{Br}^- > \text{I}^-$ , and oxoanions ( $\text{HSO}_4^-$ ,  $\text{TsO}^-$ ,  $\text{NO}_3^-$ ) did not interact with **2** to a measurable extent under these conditions. We have since employed partially fluorinated variants of **2** to obtain quantitative data for XB interactions of weak donors<sup>[27]</sup> and have prepared urea-based iodoperfluorobenzoate receptors that interact with anions through combinations of halogen bonding and hydrogen bonding.<sup>[28]</sup> Studies of haloimidazolium- and halotriazolium-based receptors have demonstrated that XB may be employed for anion recognition in either polar or protic solvents.<sup>[29,30,31]</sup> The interactions have been employed to template the assembly of catenanes and rotaxanes,<sup>[16]</sup> to mediate anion transport across lipid bilayers,<sup>[32]</sup> and to accelerate Ritter-type reactions of benzylic halides.<sup>[33]</sup>

Here, we present a full account of our studies of the influence of iodoperfluoroorganic halogen-bond-donor structure on solution-phase association constants with anionic acceptors. Association constants of simple monodentate donors, iodoperfluorobenzene ( $\text{C}_6\text{F}_5\text{I}$ ) and 1-iodoperfluorooctane ( $\text{C}_8\text{F}_{17}\text{I}$ ), with salts,  $\text{Bu}_4\text{N}^+\text{X}^-$ , in a range of solvents are reported, along with thermodynamic data obtained by van't Hoff analysis. Computational modeling of such interactions in the gas phase is also presented. The evaluation of various multidentate anion-receptor architectures is described, and implications of these results for the design of selective and high-affinity receptors are discussed.

## Results and Discussion

**Thermodynamics of halogen-bonding interactions of anions with iodoperfluorobenzene and iodoperfluorooctane:** As preliminary steps towards developing multidentate receptors, we undertook computational modeling and experimental determinations of binding constants for interactions of commercially available perfluoroiodooctane and perfluoroiodobenzene with halide anions. Gas-phase energies of interaction were calculated at the DFT/B3LYP and MP2 levels of theory, using the 6-31+G(d,p) basis set for all atoms except iodine, for which the LANL2DZdp effective core potential was employed. The basis set superposition error (BSSE) was estimated by the counterpoise method.<sup>[34]</sup> To simplify the calculations, complexes of iodoperfluorobutane  $\text{C}_4\text{F}_9\text{I}$  rather than  $\text{C}_8\text{F}_{17}\text{I}$  were modeled. We have found that gas-phase calculations of this type provide useful levels of correlation with experimental free energies of halogen

bonding for uncharged donor/acceptor pairs in alkane solvent.<sup>[35]</sup>

Noncovalent bond distances and angles were calculated at the B3LYP and MP2 levels of theory for each of the complexes studied (Table 1). In all cases, the calculated  $\text{I}\cdots\text{X}^-$  distances are significantly shorter than the sums of van der Waals radii ( $\Sigma_{\text{vdw}} = 3.73 \text{ \AA}$  for  $\text{I}/\text{Cl}$ ,  $3.83 \text{ \AA}$  for  $\text{I}/\text{Br}$ , and  $3.96 \text{ \AA}$  for  $\text{I}/\text{I}$ ). The calculated  $\text{C-I-X}^-$  angles are close to

Table 1. Calculated, gas-phase halogen bond lengths ( $\text{I}\cdots\text{X}^-$ ) and angles ( $\text{C-I-X}^-$ ) for complexes of  $\text{C}_6\text{F}_5\text{I}$  and  $\text{C}_4\text{F}_9\text{I}$  with halides.

Complex	B3LYP <sup>[a]</sup>		MP2 <sup>[a]</sup>	
	XB distance [Å]	XB angle [°]	XB distance [Å]	XB angle [°]
$\text{C}_4\text{F}_9\text{I}\cdots\text{Cl}^-$	2.82	177.2	2.85	177.7
$\text{C}_4\text{F}_9\text{I}\cdots\text{Br}^-$	3.02	177.0	3.04	177.6
$\text{C}_4\text{F}_9\text{I}\cdots\text{I}^-$	3.24	177.0	3.28	177.6
$\text{C}_6\text{F}_5\text{I}\cdots\text{Cl}^-$	2.83	180.0	2.84	180.0
$\text{C}_6\text{F}_5\text{I}\cdots\text{Br}^-$	3.02	180.0	3.02	180.0
$\text{C}_6\text{F}_5\text{I}\cdots\text{I}^-$	3.25	180.0	3.26	180.0

[a] Calculations carried out using the 6-31+G(d,p)-LANL2DZdp basis set (see text).

$180^\circ$ , in accordance with previous experimental and computational results. This preference appears to be slightly stronger for halide complexes of  $\text{C}_6\text{F}_5\text{I}$  relative to those of  $\text{C}_4\text{F}_9\text{I}$ . The B3LYP and MP2 levels of theory resulted in similar optimum geometries, although the noncovalent bond lengths that were calculated using the former were shorter. The counterpoise-corrected energies of interaction ( $\Delta E$ , along with the BSSE values) for each complex were calculated at the two levels of theory employed (Table 2). Among the trends evident from these data is the greater calculated hal-

Table 2. Calculated gas-phase energies of interaction ( $\Delta E$ ,  $\text{kcal mol}^{-1}$ ) and basis set superposition errors (BSSE,  $\text{kcal mol}^{-1}$ ) for complexes at the B3LYP and MP2 levels of theory.

Complex	B3LYP <sup>[a]</sup>		MP2 <sup>[a]</sup>	
	$\Delta E$	BSSE	$\Delta E$	BSSE
$\text{C}_4\text{F}_9\text{I}\cdots\text{Cl}^-$	−24.4	0.27	−19.2	2.76
$\text{C}_4\text{F}_9\text{I}\cdots\text{Br}^-$	−23.3	0.88	−18.6	6.18
$\text{C}_4\text{F}_9\text{I}\cdots\text{I}^-$	−20.3	0.27	−16.0	4.49
$\text{C}_6\text{F}_5\text{I}\cdots\text{Cl}^-$	−22.6	0.30	−18.1	2.89
$\text{C}_6\text{F}_5\text{I}\cdots\text{Br}^-$	−21.6	0.89	−17.6	6.26
$\text{C}_6\text{F}_5\text{I}\cdots\text{I}^-$	−18.6	0.28	−15.0	4.55

[a] Calculations carried out using the 6-31+G(d,p)-LANL2DZdp basis set; basis set superposition errors estimated by the counterpoise method (see text).

ogen-bond donor ability of  $\text{C}_4\text{F}_9\text{I}$  relative to  $\text{C}_6\text{F}_5\text{I}$  towards the halide anions and the higher acceptor ability of the lighter more charge-dense halides ( $\text{I}^- < \text{Br}^- < \text{Cl}^-$ ). Whereas similar trends hold for the B3LYP and MP2 methods, the latter level of theory generally results in lower interaction energies and higher basis-set superposition errors.

$K_a$  values of  $\text{C}_6\text{F}_5\text{I}$  and  $\text{C}_8\text{F}_{17}\text{I}$  with  $\text{Bu}_4\text{N}^+$  salts of various anions were determined by  $^{19}\text{F}$  NMR titrations in acetone solvent at 295 K (Table 3). Upon addition of halogen-accept-

Table 3. Association constants ( $K_a$ ) for interactions of  $C_6F_5I$  and  $C_8F_{17}I$  with  $Bu_4N^+X^-$  in acetone at 295 K.

$C_6F_5I$ donor		$C_8F_{17}I$ donor	
$X^-$	$K_a [M^{-1}]^{[a,b]}$	$X^-$	$K_a [M^{-1}]^{[a]}$
$Cl^-$	$1.5 \times 10^2$	$Cl^-$	$2.2 \times 10^3$
$Br^-$	$1.0 \times 10^2$	$Br^-$	$1.0 \times 10^3$
$I^-$	$4.4 \times 10^1$	$I^-$	$3.3 \times 10^2$
$TsO^-$	$< 0.5 \times 10^1$	$TsO^-$	—
$NO_3^-$	$< 0.5 \times 10^1$	$NO_3^-$	—
$HSO_4^-$	$< 0.5 \times 10^1$	$HSO_4^-$	—
$AcO^-$	— <sup>[c]</sup>	$AcO^-$	—
$H_2PO_4^-$	— <sup>[c]</sup>	$H_2PO_4^-$	—

[a]  $K_a$  values were determined by fitting changes in  $^{19}F$  NMR chemical shift to a 1:1 binding isotherm. Experiments were carried out in duplicate; uncertainties in  $K_a$  values estimated to be  $\pm 10\%$ . [b]  $K_a$  values for interactions of  $C_6F_5I$  with  $Bu_4N^+X^-$  were previously reported in the Supporting Information of Ref. [26]. [c] The halogen-bond donor decomposed upon addition of  $Bu_4N^+X^-$ .

ing anions, the resonances corresponding to the 2-fluoro groups of  $C_6F_5I$  and the  $CF_2I$  group in iodoperfluorooctane underwent significant upfield shifts; the maximum values of the complexation-induced changes in chemical shift,  $\Delta\delta$ , as determined by nonlinear curve fitting to a 1:1 binding isotherm, were roughly 1.2 ppm for the  $C_6F_5I \cdots Cl^-$  interaction and 12 ppm for that of  $C_8F_{17}I \cdots Cl^-$ . The halogen-bond donors decomposed in the presence of basic anions such as fluoride and dihydrogenphosphate under the conditions of the NMR titrations. The  $K_a$  values for interactions of  $C_8F_{17}I$  with halides are roughly consistent with those determined recently for 1,6-diiodoperfluorohexane,  $I(CF_2)_6I$  in acetonitrile solvent, the latter values being determined using UV/Vis absorbance spectroscopy ( $K_a = 250, 150$ , and  $80 M^{-1}$  for  $Cl^-$ ,  $Br^-$  and  $I^-$ , respectively, as their  $Bu_4N^+$  salts).<sup>[36]</sup> In our hands, addition of  $Bu_4N^+$  halides to  $C_8F_{17}I$  in acetone did not lead to UV/Vis spectral changes that would be suitable for determining  $K_a$  values.

In agreement with the gas-phase calculated results, the experimental solution-phase data show that  $C_8F_{17}I$  interacts more favorably with halides relative to  $C_6F_5I$ . Similarly, the relative affinities for the halides,  $Cl^- > Br^- > I^-$ , are in line with the computationally predicted trend. However, the oxoanions for which binding constants could be determined showed only weak interactions with  $C_6F_5I$ , despite that such species are often good hydrogen-bond acceptors (for example, the enthalpy of transfer of  $NO_3^-$  from water to acetonitrile is higher than that of  $I^-$ ).<sup>[37]</sup> It has also been noted that a bromimidazolium-based receptor displays high levels of discrimination for halides over oxoanions in aqueous methanol.<sup>[29b]</sup> In another study, a monodentate iodoimidazolium compound was found to bind more tightly to dihydrogenphosphate and acetate than to halides in  $[D_6]DMSO$ , thus indicating that XB of oxoanions is favorable in certain instances.<sup>[30]</sup> In any case, we speculate that the high affinities of the perfluorinated donors towards halide anions, as evident herein, reflect either significant charge-transfer contributions, dispersion contributions, or both, to their interactions. Such proposals have been advanced to rationalize other trends in XB thermodynamics that do not follow pre-

dictions of electrostatic models,<sup>[11,13b,35]</sup> and are supported by computational studies.<sup>[38]</sup>

We studied the temperature dependence of the  $K_a$  values of  $C_6F_5I$  and  $C_8F_{17}I$  with  $Bu_4N^+Cl^-$  in acetone to obtain enthalpies and entropies of interaction using van't Hoff plots. To obtain accurate thermodynamic parameters, we investigated as wide a temperature range as was experimentally accessible (238–308 K, Figure 2). Several features of the data

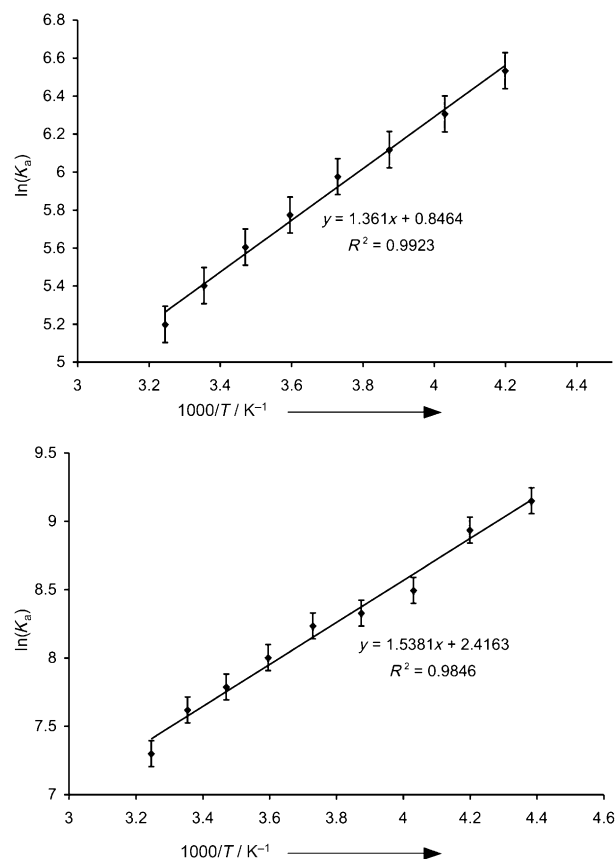


Figure 2. van't Hoff plots ( $\ln(K_a)$  versus  $1000/T$ ) for interactions of  $C_6F_5I$  (top) and  $C_8F_{17}I$  (bottom) with  $Bu_4N^+Cl^-$  in acetone. Values of  $K_a$  were determined by  $^{19}F$  NMR titrations at temperatures ranging from 238 to 308 K.

are noteworthy (Table 4). The interactions are entropically favorable (that is,  $\Delta S > 0$ ), a result that is in contrast to the complexation of group 10 fluorides by  $C_6F_5I$  in toluene, as studied by Perutz, Brammer, and co-workers and for which  $\Delta S$  values ranged from  $-10$  to  $-17 \text{ cal mol}^{-1} \text{ K}^{-1}$ .<sup>[13c]</sup> Several examples of positive entropies of interaction for anion binding by neutral receptors have been reported; receptor desol-

Table 4. Enthalpies ( $\Delta H$ ) and entropies ( $\Delta S$ ) of interaction between  $Bu_4N^+Cl^-$  and  $C_6F_5I$  or  $C_8F_{17}I$  in acetone, as determined by van't Hoff plot analysis. Values of  $K_a$  were determined by  $^{19}F$  NMR titrations at temperatures ranging from 238 to 308 K.

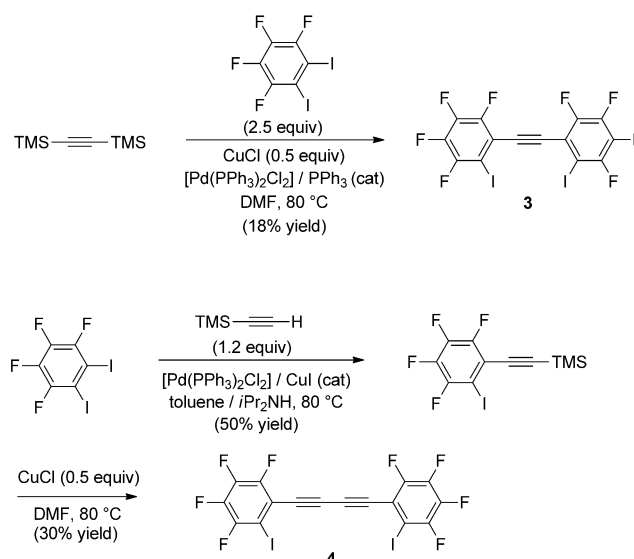
XB donor	$\Delta H [\text{kcal mol}^{-1}]$	$\Delta S [\text{cal mol}^{-1} \text{ K}^{-1}]$
$C_6F_5I$	-2.7	1.7
$C_8F_{17}I$	-3.0	4.8

vation is among the phenomena that have been invoked to rationalize such behavior.<sup>[39]</sup> In particular, Huber and co-workers have used isothermal titration calorimetry to obtain thermodynamic data for charge-assisted XB interactions of bis(imidazolium) receptors with halides in a variety of organic solvents, and have found favorable (in certain cases, dominant) entropic contributions to the thermodynamics of binding.<sup>[31]</sup> Interestingly, the data herein shows that the different halogen bond donor ability of C<sub>8</sub>F<sub>17</sub>I and C<sub>6</sub>F<sub>5</sub>I towards Bu<sub>4</sub>N<sup>+</sup>Cl<sup>−</sup> in acetonitrile appears to arise from both modest enthalpic ( $\Delta\Delta H = -0.3$  kcal mol<sup>−1</sup>) and entropic ( $T\Delta\Delta S = 0.9$  kcal mol<sup>−1</sup> at 298 K) contributions, with the magnitude of the latter being perhaps slightly greater. Whereas the more favorable enthalpy of interaction for the iodoperfluoroalkane–chloride complex is consistent with the computational data discussed above, the difference in entropic contributions is somewhat surprising and highlights the dangers of neglecting entropy when interpreting structure-activity relationships for noncovalent interactions.

**Multidentate halogen-bond donors as anion receptors:** Despite the lower halide affinity of C<sub>6</sub>F<sub>5</sub>I relative to C<sub>8</sub>F<sub>17</sub>I, we felt that the former could be chemically modified more readily for the purpose of preorganized receptor design. While S<sub>N</sub>Ar reactions of C<sub>6</sub>F<sub>5</sub>I provide ready access to *para*-substituted C<sub>6</sub>F<sub>4</sub>I donor groups,<sup>[40]</sup> this substitution pattern may not be ideal for orienting donors to bind to an anion in a convergent fashion: for example, receptor **1a** described above does not act as a multidentate halogen bond donor. We instead elected to pursue *ortho*-substituted iodoperfluoroarenes.

**Ethynylene and diynylene-linked iodoperfluoroarenes as bidentate halogen-bond donors:** Drawing on the structures of hydrogen-bonding dimerization motifs developed by Ducharme and Wuest,<sup>[41]</sup> we investigated ethynylene and butadiynylene groups as linkers for 2-iodoperfluoroarene halogen-bond donors. Among the attractive features of these linker groups are their low steric demand, electron-withdrawing ability, which is beneficial for halogen bond donation, and their conformational rigidity. The syntheses of receptors **3** and **4** from 1,2-diiodotetrafluorobenzene are depicted in Scheme 1. A modified Sonogashira coupling using copper(I) chloride in DMF to promote alkynylsilane activation<sup>[42]</sup> enabled the synthesis of **3** in a single step from C<sub>6</sub>F<sub>4</sub>I<sub>2</sub> and bis(trimethylsilyl)acetylene. Receptor **4** was prepared by conventional Sonogashira coupling of C<sub>6</sub>F<sub>4</sub>I<sub>2</sub> with trimethylsilylacetylene,<sup>[43]</sup> followed by oxidative alkynylsilane dimerization. Both syntheses led to low yields owing to diethynylation of C<sub>6</sub>F<sub>4</sub>I<sub>2</sub> in the presence of the Pd catalyst, and the resulting challenging purification of the products. However, the synthetic route shown in Scheme 1 enabled relatively rapid access to sufficient quantities of material for anion-binding studies.

K<sub>a</sub> values of **3** and **4** with anions were determined by <sup>19</sup>F NMR titrations with Bu<sub>4</sub>N<sup>+</sup> salts as described above (Table 5). Comparing this data with that for interactions of



Scheme 1. Synthesis of bidentate halogen-bond donors **3** and **4**.

C<sub>6</sub>F<sub>5</sub>I (Table 2) shows that both **3** and **4** act as bidentate anion receptors: for a given anion, the K<sub>a</sub> values for interactions of the diiodo compounds are roughly an order of magnitude higher than those of C<sub>6</sub>F<sub>5</sub>I. Geometry optimizations of **3**⋯Cl<sup>−</sup> and **4**⋯Cl<sup>−</sup> complexes in the gas phase (B3LYP/6-

Table 5. Association constants (K<sub>a</sub>) for interactions of receptors **3** and **4** with Bu<sub>4</sub>N<sup>+</sup>X<sup>−</sup> in acetone at 295 K.

Receptor <b>3</b>		Receptor <b>4</b>	
X <sup>−</sup>	K <sub>a</sub> [M <sup>−1</sup> ] <sup>[a]</sup>	X <sup>−</sup>	K <sub>a</sub> [M <sup>−1</sup> ] <sup>[a]</sup>
Cl <sup>−</sup>	1.7 × 10 <sup>3</sup>	Cl <sup>−</sup>	1.2 × 10 <sup>3</sup>
Br <sup>−</sup>	1.0 × 10 <sup>3</sup>	Br <sup>−</sup>	8.5 × 10 <sup>2</sup>
I <sup>−</sup>	–	I <sup>−</sup>	3.5 × 10 <sup>2</sup>
NO <sub>3</sub> <sup>−</sup>	–	NO <sub>3</sub> <sup>−</sup>	< 0.5 × 10 <sup>1</sup>
HSO <sub>4</sub> <sup>−</sup>	–	HSO <sub>4</sub> <sup>−</sup>	< 0.5 × 10 <sup>1</sup>

[a] K<sub>a</sub> values were determined by fitting changes in <sup>19</sup>F NMR chemical shift to a 1:1 binding isotherm. Experiments were carried out in duplicate; uncertainties in K<sub>a</sub> values estimated to be ± 20%.

31+G(d,p)-LANL2DZdp) revealed the expected bidentate coordination (Figure 3). The calculated geometry of the **3**⋯Cl<sup>−</sup> complex was characterized by an average I⋯Cl<sup>−</sup> distances of 3.18 Å, C-I-Cl<sup>−</sup> angles of 166°, and a I-Cl<sup>−</sup>-I angle of 76°. For **4**⋯Cl<sup>−</sup>, the calculations revealed halogen bonds that were shorter (*d*<sub>I⋯Cl</sub> = 3.14 Å) and more linear (*θ*<sub>C-I-Cl</sub> = 174°), with a less acute I-Cl<sup>−</sup>-I angle of 94°. Similar trends were observed for geometry optimizations of the **3**⋯Br<sup>−</sup> and **4**⋯Br<sup>−</sup> complexes in the gas phase: the bromide complex of **4** was calculated to possess shorter I⋯Br distances (3.25 versus 3.29 Å), more linear C-I-Br<sup>−</sup> angles (174° versus 167°) and a less acute I-Br<sup>−</sup>-I angle (92° versus 74°). The calculated geometries also indicate that bidentate coordination of Cl<sup>−</sup> by **4** is accompanied by bending of the butadiynylene group (average C≡C–C bond angles of 174°).



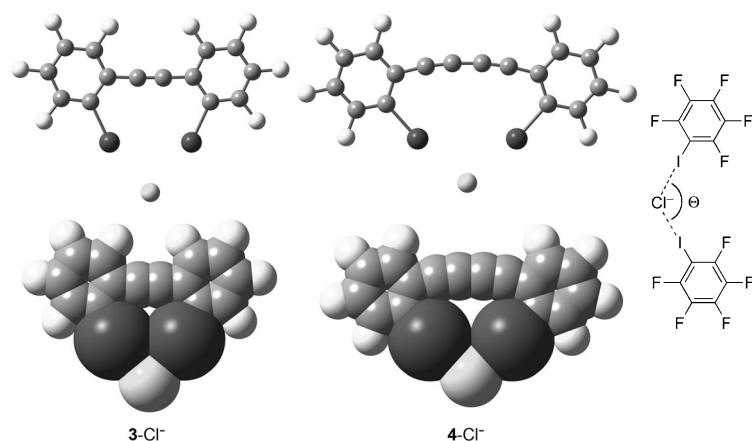


Figure 3. Calculated gas-phase geometries of the **3**·Cl<sup>−</sup> and **4**·Cl<sup>−</sup> complexes, as depicted by ball-and-stick (top) and space-filling models (bottom). Calculations were carried out with the B3LYP functional using the 6-31+G(d,p)-LANL2DZdp split basis set.

The ability of alkyne and diyne groups to undergo distortions of this type is established.<sup>[44]</sup>

Although the preference for halogen-bonding systems to adopt noncovalent bond angles of 180° is known to be stringent, the question of the preferred I-X-I angle was less clear. An analysis of the Cambridge Crystallographic Date Centre Structural Database (CSD) by Beer and co-workers suggested that bifurcated halogen bonds of chloride and bromide tend to adopt I-X-I angles of 180°, whereas those of iodide tends to show a larger range (70–180°).<sup>[45]</sup> As the I-X-X angle becomes smaller, it appears that steric interactions between iodine atoms destabilize the bifurcated system, an effect that is more pronounced for smaller halides X<sup>−</sup>. Examination of space-filling models of the calculated **3**·Cl<sup>−</sup> and **4**·Cl<sup>−</sup> complexes supports this idea, with the iodo groups incurring a significantly closer approach in **3**·Cl<sup>−</sup>. To further probe this issue, we have carried out gas-phase computational modeling of the bifurcated halogen bond C<sub>6</sub>F<sub>5</sub>I...Cl<sup>−</sup>...IC<sub>6</sub>F<sub>5</sub> while constraining the I-Cl-I angle to values from 70° to 170° in ten-degree increments (Figure 4).<sup>[46]</sup> The calculations suggest that bifurcated complexes having angles less than 80 degrees are significantly destabilized.

Computational modeling thus appears to indicate that butadiynylene-linked receptor **4** is better suited than **3** to accommodate the distance and angle preferences of bifurcated halogen bonds involving Cl<sup>−</sup> and Br<sup>−</sup>. However, this trend was not borne out in the experimental binding data in acetone: the *K<sub>a</sub>* values of **3** and **4** for a given anion were found to differ by less than a factor of two, with **3** interacting more tightly with both Cl<sup>−</sup> and Br<sup>−</sup> under the conditions of the <sup>19</sup>F NMR titration.

**Multidentate halogen-bond donors based on 2-iodoperfluorobenzaldehyde and 2-iodoperfluorobenzoic acid:** In search of donor groups that could lend themselves to rapid evaluation of multidentate XB receptor architectures, we turned to perfluorinated derivatives of 2-iodoperfluorobenzoic acid (**5**)

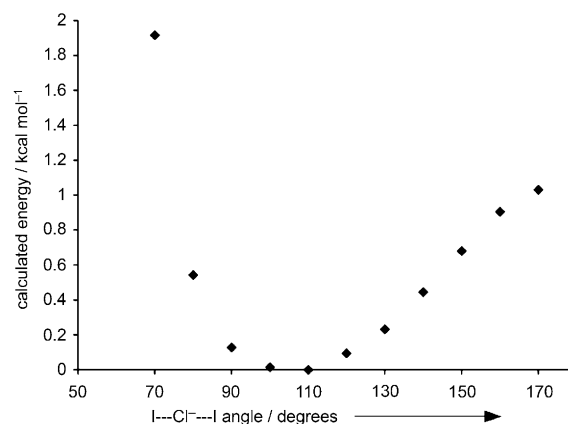
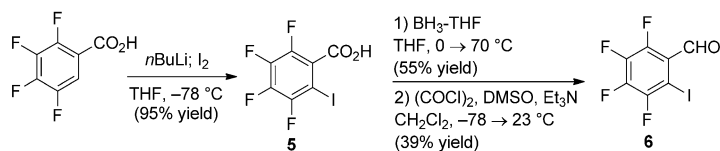


Figure 4. Plot of calculated energy versus I...Cl<sup>−</sup>...I angle for the bifurcated halogen bond shown. Calculations were carried out at the B3LYP/6-31+G(d,p)-LANL2DZdp level of theory.

and 2-iodobenzaldehyde (**6**). The synthesis of **5** was accomplished using a reported protocol;<sup>[47]</sup> reduction of **5** with borane followed by Swern oxidation yielded the volatile aldehyde **6** (Scheme 2). Receptors **7–11** and **13** were synthe-



Scheme 2. Synthesis of iodoperfluoroarenes **5** and **6**. DMF = *N,N*-dimethylformamide, TMS = trimethylsilyl.

sized from **5**, by condensations mediated by diisopropylcarbodiimide and catalytic 4-(dimethylamino)pyridine (Figure 5). Condensation of **6** with *trans*-1,2-diaminocyclohexane (toluene, 105 °C) generated bis(imine) **12** in 67% yield. Triesters **14** and **15** were prepared by alkylation of **5** with the corresponding tris(bromomethyl)arene.

The anion-recognition properties of receptors **7–14** (assessed by *K<sub>a</sub>* values determined in acetone solvent as described above) are summarized in Table 6. Benzyl ester **7** displayed chloride affinity that was marginally higher than that of amide **8**. Ester-based receptors capable of acting as bidentate halogen-bond donors (**9–11**) had *K<sub>a</sub>* values with Bu<sub>4</sub>N<sup>+</sup>Cl<sup>−</sup> ranging from 1.1–1.8 × 10<sup>3</sup> M<sup>−1</sup>, affinities similar to those of the ethynylene- and butadiynylene-based bidentate receptors **3** and **4** discussed in the previous section. Dramatic effects of the linker length and flexibility on *K<sub>a</sub>* were not evident in this series of compounds. On the other hand, bis(imine) **12** displayed a relatively low *K<sub>a</sub>* value with chloride. DFT modeling of the **12**·Cl<sup>−</sup> complex in the gas phase revealed a bifurcated halogen bond having a I-Cl-I angle of 83°; we speculate that the suboptimal angle combined with the flexibility of **12** (in comparison to **3**) may be contributing factors.

Esters **13–14** and **2**, which are capable of donating three halogen bonds, displayed *K<sub>a</sub>* values for chloride that were

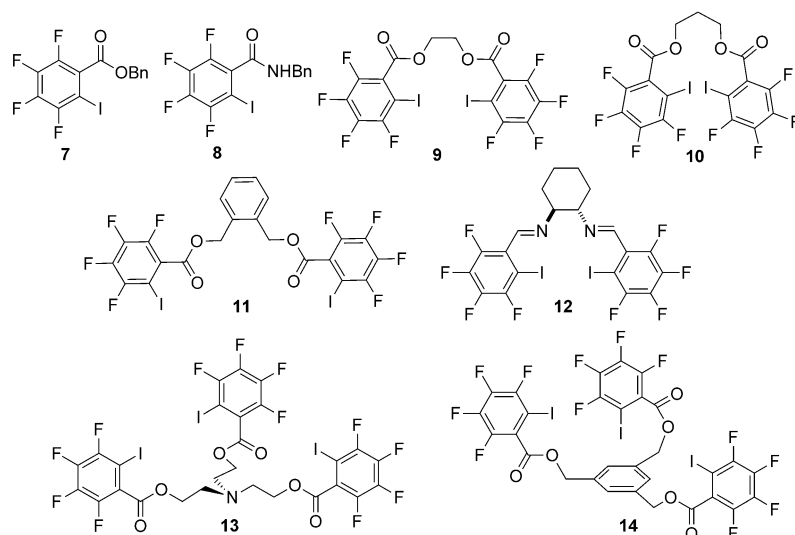


Figure 5. Structures of anion receptors **7–14**.

Table 6. Association constants ( $K_a$ ) for interactions of receptors **7–14** and **2** with  $\text{Bu}_4\text{N}^+\text{X}^-$  in acetone at 295 K.

XB donor	$\text{X}^-$	$K_a [\text{M}^{-1}]^{[a,b]}$
<b>7</b>	$\text{Cl}^-$	$7.0 \times 10^1$
<b>8</b>	$\text{Cl}^-$	$4.0 \times 10^1$
<b>9</b>	$\text{Cl}^-$	$1.2 \times 10^3$
<b>10</b>	$\text{Cl}^-$	$1.1 \times 10^3$
<b>11</b>	$\text{Cl}^-$	$1.8 \times 10^3$
<b>12</b>	$\text{Cl}^-$	$2.0 \times 10^2$
<b>13</b>	$\text{Cl}^-$	$8.0 \times 10^3$
<b>14</b>	$\text{Cl}^-$	$3.0 \times 10^3$
<b>2</b>	$\text{Cl}^-$	$1.9 \times 10^4$
<b>2</b>	$\text{Br}^-$	$3.8 \times 10^3$
<b>2</b>	$\text{I}^-$	$7.6 \times 10^2$
<b>2</b>	$\text{TsO}^-$	$1.0 \times 10^1$
<b>2</b>	$\text{NO}_3^-$	$< 1.0 \times 10^1$
<b>2</b>	$\text{HSO}_4^-$	$< 1.0 \times 10^1$

[a]  $K_a$  values were determined by fitting changes in  $^{19}\text{F}$  NMR chemical shift to a 1:1 binding isotherm. Experiments were carried out in duplicate; uncertainties in  $K_a$  values estimated to be  $\pm 20\%$ . [b]  $K_a$  values for interactions of **7**, **10**, **11** and **2** were previously reported in Ref. [26].

higher than those of the bidentate receptors. The chloride affinity of triethanolamine triester **13** was intermediate between those of the tris(hydroxymethyl)arene derivatives, **14** and **2**. The  $K_a$  value of hexasubstituted benzene derivative **2** with chloride was six times higher than that of its trisubstituted congener **14**, thus suggesting that the methyl substituents provide a degree of preorganization consistent with previous studies of related hexasubstituted benzene-based receptors.<sup>[48]</sup> As discussed in our preliminary report,<sup>[26]</sup> computational modeling of the  $\mathbf{2} \cdots \text{Cl}^-$  adduct in the gas phase revealed a binding mode in which the anion accepts a halogen bond from each of the three iodoperfluorobenzoate groups.  $K_a$  values of **2** with various  $\text{Bu}_4\text{N}^+\text{X}^-$  salts indicated the same trends that were observed for the simple monodentate donors,  $\text{C}_6\text{F}_5\text{I}$  and  $\text{C}_8\text{F}_{17}\text{I}$ , that is, halide affinities de-

creased down the group ( $\text{Cl}^- > \text{Br}^- > \text{I}^-$ ) and the oxoanion affinities were low. Because the  $K_a$  values of **2** with halides are significantly higher than those of  $\text{C}_6\text{F}_5\text{I}$  and  $\text{C}_8\text{F}_{17}\text{I}$ , the tridentate donor provides a better indication of the magnitude of this effect. The observation of similar trends for the mono- and tridentate donors suggests that the geometry of triester **2** does not play a major role in influencing its selectivity as an anion receptor.

The thermodynamics of the  $\mathbf{2} \cdots \text{Cl}^-$  interaction were further probed using a van't Hoff plot, from which a  $\Delta H_{\text{binding}}$  of  $-3.9 \text{ kcal mol}^{-1}$  and  $\Delta S_{\text{binding}}$  of  $+6.1 \text{ cal mol}^{-1} \text{ K}^{-1}$  were inferred

(Figure 6). The positive  $\Delta S_{\text{binding}}$  is consistent with the data described above for the  $\text{C}_6\text{F}_5\text{I} \cdots \text{Cl}^-$  interaction, and its magnitude is roughly three times that of the latter. We note that this quantitative comparison is an approximation, given that  $\text{C}_6\text{F}_5\text{I}$  is not an ideal substitute for the iodoperfluorobenzoate groups of **2**. Subject to a similar qualification, comparison of  $\Delta H_{\text{binding}}$  for  $\mathbf{2} \cdots \text{Cl}^-$  and  $\text{C}_6\text{F}_5\text{I} \cdots \text{Cl}^-$  suggests that the enthalpy contributions of each successive halogen bond are not additive.

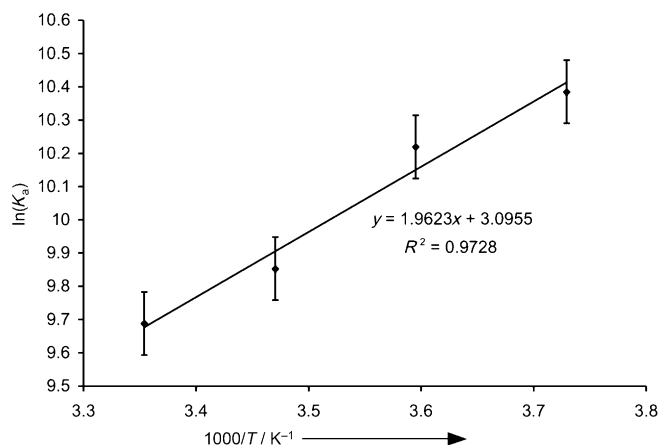


Figure 6. van't Hoff plot ( $\ln(K_a)$  versus  $1000/T$ ) for the interaction of tridentate receptor **2** with  $n\text{Bu}_4\text{N}^+\text{Cl}^-$  in acetone. Values of  $K_a$  were determined by  $^{19}\text{F}$  NMR titrations at temperatures ranging from 268 to 298 K.

**Solvent effects on halogen bonding of iodoperfluoroorganics with anions:** The  $K_a$  value of **2** with  $\text{Bu}_4\text{N}^+\text{Cl}^-$  showed considerable variation as a function of solvent identity (Table 7). Whereas the  $K_a$  value for chloride binding in acetonitrile was within a factor of five of that for acetone, those for chlorinated solvents ( $\text{CH}_2\text{Cl}_2$  and  $\text{CHCl}_3$ ) and for di-

Table 7. Association constants ( $K_a$ ) for interactions of receptor **2** and  $C_8F_{17}I$  with  $Bu_4N^+Cl^-$  in various solvents at 295 K.

XB donor	Solvent	$K_a [M^{-1}]^{[a]}$
<b>2</b>	acetone	$1.9 \times 10^4$
<b>2</b>	acetonitrile	$5.0 \times 10^3$
<b>2</b>	dichloromethane	$3.1 \times 10^1$
<b>2</b>	dimethylsulfoxide	$1.3 \times 10^1$
<b>2</b>	chloroform	$0.6 \times 10^1$
$C_8F_{17}I$	acetone	$2.2 \times 10^3$
$C_8F_{17}I$	acetonitrile	$1.3 \times 10^2$
$C_8F_{17}I$	dimethylsulfoxide	$3.2 \times 10^1$
$C_8F_{17}I$	dichloromethane	$3.1 \times 10^1$

[a]  $K_a$  values were determined by fitting changes in  $^{19}F$  NMR chemical shift to a 1:1 binding isotherm. Experiments were carried out in duplicate; uncertainties in  $K_a$  values estimated to be  $\pm 10$ –20%.

methyl sulfoxide were suggestive of significant deleterious effects on binding.<sup>[49]</sup> Similar effects were observed for the monodentate iodoperfluoroalkane donor  $C_8F_{17}I$ .

The data for chlorinated solvent are particularly striking because most scales of solvent polarity and polarizability, including Kosower's  $Z$  scale,  $E_T(30)$ , and  $\pi^*$ , place both dichloromethane and chloroform lower than acetone and acetonitrile.<sup>[50]</sup> Competition with hydrogen-bond donation by the chlorinated solvents is possible, although values of  $\alpha$ , a measure of solvent hydrogen-bond donor ability, are not entirely consistent with this proposition; for example, acetonitrile possesses a value of  $\alpha$  that is higher than that of dichloromethane. Halogenated solvents, particularly  $CHCl_3$ , are also known to act as halogen-bond donors.<sup>[51]</sup> Given the complexity of receptor–anion interactions in solution (desolvation, ion pairing, etc.), the significant entropic contributions to the interactions in acetonitrile, as revealed by van't Hoff plot analysis, and the relatively small number of solvents examined in the present study, our ability to interpret these data is somewhat limited. Interesting solvent effects were also evident in studies of halogen bonding between iodoperfluorocarbons and the neutral acceptor, triethylamine,<sup>[13b]</sup> and between anions and bis(haloimidazolium) receptors.<sup>[31]</sup>

## Conclusion

Halogen-bonding interactions between halide anions and iodoperfluoroalkanes and iodoperfluoroarenes are of appreciable strength in moderately polar organic solvents such as acetone and acetonitrile, and they may be employed as the basis for the development of multidentate anion receptors. The monodentate donors,  $C_8F_{17}I$  and  $C_6F_5I$ , display  $K_a$  values for anions in acetone solvent ranging from 40–2200  $M^{-1}$ ; trends include the interactions of the iodoperfluoroalkane with a given anion being characterized by higher  $K_a$  values than those of the corresponding arenes, a preference for binding to the lighter halides ( $Cl^- > Br^- > I^-$ ), and relatively weak binding of oxoanions. Analysis of the temperature dependence of the  $C_8F_{17}I \cdots Cl^-$  and  $C_6F_5I \cdots Cl^-$   $K_a$  values reveals several noteworthy features: anion binding is entropi-

cally favorable; both entropic and enthalpic factors appear to contribute to the differences in behavior observed in the two classes of iodoperfluoroorganic donors.

Several multidentate receptor architectures based on *ortho*-substituted iodoperfluoroarene donors have been evaluated. Solution-phase binding data indicate that ethynylene, butadiynylene, imine, and ester linking groups are useful for the construction of iodoperfluoroarene-derived bidentate anion receptors. Tridentate receptors show still higher  $K_a$  values with halides: structure-activity relationships suggest that the preorganized nature of the hexasubstituted benzene-based triester **2** contributes to its high chloride affinity in organic solvent. Studies of both tridentate **2** and  $C_8F_{17}I$  reveal significant solvent effects on halogen bonding interactions with anions, including a surprising deleterious effect of chlorinated solvents such as dichloromethane and chloroform.

The bi- and tridentate receptors described in this study display the same trends in anion affinity as were observed for the simple monodentate model compounds; it is likely that more rigid iodoperfluoroarene-based architectures would be needed to overcome the intrinsic preferences of the donor groups that underlie this behavior. Beer and co-workers' observations that the levels of anion selectivity of conformationally restricted haloimidazoliophanes and catenanes are influenced by receptor geometry indicate that this goal is achievable. Computational studies suggest that several features of the halogen-bonding interaction should be taken into account when considering the design of multidentate receptors: in addition to the generally recognized preference for linear  $C-I \cdots X^-$  noncovalent bonds, the  $I-X-I$  angle is likely to contribute meaningfully to the strength of bifurcated interactions with anions. The predicted destabilization of complexes having small  $I-X-I$  angles (apparently a result of steric interactions between iodo groups) is consistent with previous crystallographic studies, and may be a productive line of investigation in terms of developing selective anion receptors. Identifying new halogen bond donor groups either that give rise to strong interactions with anions (especially in competitive solvents), that are readily incorporated into modular architectures, or both, and applying halogen bonding of anions in functional contexts (e.g. in the development of synthetic ion transporters and catalysts) represent interesting directions for future study.

## Experimental Section

**General considerations:** Reactions were carried out in oven-dried glassware fitted with rubber septa under an atmosphere of dry argon, unless otherwise indicated. Toluene (HPLC grade) and tetrahydrofuran were purchased from Caledon Laboratories and purified by passing through two columns of activated alumina under argon (Innovative Technology, Inc.). Stainless steel syringes were used to transfer air- and moisture-sensitive liquids.

$^1H$  and  $^{19}F$  NMR spectra were obtained using either a Varian Mercury 400 MHz or Agilent 500 DD2MHz spectrometer, with an HX 5 mm OneNMR probe.  $^1H$  NMR spectra are reported in parts per million



(ppm) relative to tetramethylsilane and referenced to residual protium in the solvent. Chemical shifts for fluorine were recorded in parts per million (ppm) relative to CFC<sub>3</sub> using trifluorotoluene ( $\delta$  63.72 ppm) as an internal standard. High-resolution mass spectra (HRMS) were obtained on a VS 70–250S (double focusing) mass spectrometer at 70 eV. Infrared (IR) spectra were obtained on a PerkinElmer Spectrum 100 instrument equipped with a single-reflection diamond/ZnSe ATR accessory, either in the solid state or as neat liquids, as indicated.

**Synthesis:** 2-Iodoperfluorobenzoic acid **5**<sup>[47]</sup> and receptors **2**, **7**, **10**, and **11**<sup>[26]</sup> were prepared as previously reported. Receptors **8–9** and **13–14** were prepared in analogy to the procedures for **10–11** and **2**, respectively, and their characterization data are provided in the Supporting Information.

**1,2-Bis(2,3,4,5-tetrafluoro-6-iodophenyl)ethyne (3):** To an oven-dried Schlenk tube equipped with a stir bar and cooled under an atmosphere of argon were added 1,2-bis(trimethylsilyl)ethyne (1 equiv, 0.9 mmol, 205  $\mu$ L), [Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>] (5 mol %, 0.045 mmol, 32 mg), PPh<sub>3</sub> (10 mol %, 0.09 mmol, 24 mg), 1,2-diiodo-3,4,5,6-tetrafluorobenzene (2.5 equiv, 2.25 mmol, 905 mg), and CuCl (0.5 equiv, 0.45 mmol, 45 mg) in dry DMF (0.5 mL). After stirring for 6 h at 80 °C, the solvent was evaporated and the residue was subjected to flash column chromatography (silica gel, pentane), affording a white solid. (92 mg, 0.16 mmol, 18 % yield). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = –113.4 (m, 2F), –128.8 (m, 2F), –149.2 (m, 2F), –153.6 ppm (m, 2F); IR (powder):  $\tilde{\nu}$  = 1620 (s), 1498 (s), 1473 (s), 1412 (s), 1376 (s), 1082 (s), 986 (s), 799 (s), 608 cm<sup>–1</sup> (m); HRMS (EI):  $m/z$  calcd for C<sub>14</sub>F<sub>8</sub>I<sub>2</sub>: 573.7962; found: 573.7952.

**1,4-Bis(2,3,4,5-tetrafluoro-6-iodophenyl)buta-1,3-diyne (4):** To an oven-dried Schlenk tube equipped with a stir bar and cooled under an atmosphere of argon were added 1-iodo-2-[(trimethylsilyl)ethynyl]-3,4,5,6-tetrafluorobenzene<sup>[43]</sup> (1 equiv, 0.48 mmol, 177 mg) and CuCl (0.48 equiv, 1.25 mmol, 190  $\mu$ L) in 0.5 mL DMF. After stirring for 6 h at 80 °C, the solvent was evaporated and the residue was subjected to flash column chromatography (silica gel, pentane), affording a white solid. (48 mg, 0.19 mmol, 30 % yield). <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = –113.5 (m, 2F), –129.0 (m, 2F), –148.6 (m, 2F), –153.4 ppm (m, 2F); IR (powder):  $\tilde{\nu}$  = 1618 (s), 1491 (s), 1460 (s), 11363 (s), 948 (s), 797 cm<sup>–1</sup> (s); HRMS (EI):  $m/z$  calcd for C<sub>16</sub>F<sub>8</sub>I<sub>2</sub>: 697.79616; found: 697.79686.

**2,3,4,5-Tetrafluoro-6-iodobenzaldehyde (6):** To a solution of 2,3,4,5-tetrafluoro-6-iodobenzoic acid (1 equiv, 1.58 mmol, 500 mg) in THF (2 mL) was added BH<sub>3</sub>·THF (1.4 equiv, 2.2 mmol, 2.2 mL) at 0 °C. The solution temperature was raised to 70 °C and heated with stirring for 7 h. Excess hydride was destroyed by the addition of THF/H<sub>2</sub>O (4 mL). The combined organic solution was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated in vacuo. The crude mixture was purified by flash column chromatography, using pentane/diethyl ether (9:1) as the eluent affording tetrafluoro-6-iodophenyl-methanol as a white solid (276 mg, 0.87 mmol, 55 %). To a stirred solution of oxalyl chloride (30  $\mu$ L, 0.34 mmol, 1.2 equiv) in dichloromethane (1.5 mL) cooled to –78 °C was added a solution of dimethyl sulfoxide (2.4 equiv, 0.68 mmol, 49  $\mu$ L). The mixture was stirred for 10 min, and (2,3,4,5-tetrafluoro-6-iodophenyl)methanol (1 equiv, 0.28 mmol, 87 mg; see above) in dichloromethane (0.5 mL) was added dropwise. The solution was stirred 1.5 h at –78 °C after which triethylamine (4.8 equiv, 1.3 mmol, 188  $\mu$ L) was added over 5 min. The resulting mixture was allowed to warm to room temperature for 1.5 h after which water (2 mL) was added. The phases were separated, and the organic layer was successively washed with water (2 mL), a saturated aqueous sodium bisulfate solution (2  $\times$  5 mL), and brine and dried with anhydrous sodium sulfate. The solvents were removed in vacuo and the crude residue purified by flash column chromatography, eluting with pentane (34 mg, 0.11 mmol, 39 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 10.05 ppm (s, 1H); [<sup>19</sup>F]<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 187.9 (d,  $J$ (C,H) = 140 Hz), 149.1, 147.8, 142.8, 140.7, 119.7, 78.3 ppm; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = –115.5 (m, 1F), –145.1 (m, 1F), –146.0 (m, 1F), –154.6 ppm (m, 1F); IR (powder):  $\tilde{\nu}$  = 1742 (m), 1706 (s), 1614 (m), 1499 (s), 1457 (s), 1338 (s), 1137 (m), 1074 (m), 1051 (m), 939 (m), 814 (m), 780 (m) 760 cm<sup>–1</sup> (m).

**N<sup>1</sup>,N<sup>2</sup>-bis(2,3,4,5-tetrafluoro-6-iodobenzylidene)-cyclohexane-1,2-diamine (12):** To an oven-dried reaction tube equipped with a stir bar and cooled under an atmosphere of argon were added trans-(1*R*,2*R*)-diaminocyclo-

hexane (0.084 mmol, 10  $\mu$ L), 2,3,4,5-tetrafluoro-6-iodobenzaldehyde (2 equiv, 0.17 mmol, 51 mg) and dry toluene (1 mL). The tube was sealed and the solution heated to 105 °C for 20 h. Solvent was removed in vacuo and the resulting crude product crystallized from cyclohexane affording the title compound (39 mg, 67 %). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.13 (s, 2H), 3.56 (m, 2H), 1.89 (m, 6H), 1.52 ppm (m, 2H); [<sup>1</sup>H]<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 157.0, 74.9, 32.7, 24.3 ppm; [<sup>19</sup>F]<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 157.0, 147.2, 147.1, 145.9, 140.9, 139.9 ppm; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>):  $\delta$  = –114.6 (m, 2F), –139.0 (m, 2F), –151.0 (m, 2F), –153.3 ppm (m, 2F); IR (powder):  $\tilde{\nu}$  = 2931 (m), 2963 (m) 1639 (m), 1618 (m), 1494 (s), 1469 (s), 1358 (m), 1149 (m), 1129 (m), 1071 (s), 958 (m) 802 cm<sup>–1</sup> (m); HRMS (ESI):  $m/z$  calcd for C<sub>20</sub>H<sub>13</sub>F<sub>8</sub>I<sub>2</sub>N<sub>2</sub>: 686.90403; found: 686.90135.

**Anion-binding titrations:** <sup>19</sup>F NMR titrations were carried out as described previously.<sup>[28]</sup> Representative plots of <sup>19</sup>F NMR chemical shift versus concentration of *n*Bu<sub>4</sub>N<sup>+</sup>X<sup>–</sup> are provided in the Supporting Information.

**Computational details:** Calculations were carried out with the Gaussian '09 software package,<sup>[52]</sup> on a Linux workstation equipped with two quad-core AMD Shanghai processors. Cartesian coordinates of all calculated structures are provided in the Supporting Information.

## Acknowledgements

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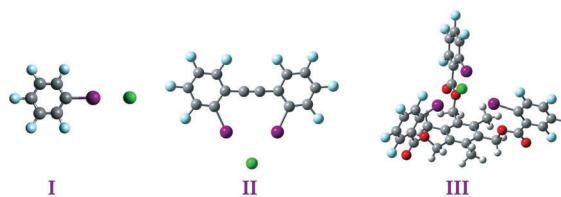
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## Halogen Bonding

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### Halogen Bonding between Anions and Iodoperfluoroorganics: Solution-Phase Thermodynamics and Multidentate-Receptor Design

**Halogen-bonding interactions** between halide anions and iodoperfluoroalkanes and iodoperfluoroarenes in moderately polar organic solvents, such as acetone and acetonitrile, are of appreciable strength (see figure). Sev-

eral multidentate-receptor architectures were also evaluated. Structure-activity relationships, computational studies, thermodynamics from van't Hoff plot analysis, and solvent effects are presented.