A statistical analysis of halide $\cdots$ H–A (A = OR, NR_2, N^+R_3) hydrogen bonding interactions in the solid state

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The interaction between F^-, Cl^-, Br^- and I^- and organic H-bond donors OH, NH and N^+H are examined in detail using the Cambridge Structural Database. The ammonium group is shown to be the most effective H-bond donor to the halides, followed by the hydroxy group and neutral NH. Comparison of the H-bonding requirements of the anions in each case shows trends in $X^- \cdots HA$ distances (*r*), with the Δr interval between F^- and Cl^- being the greatest, and that between Cl^- and Br^- the least. Mean H-bonding angles $\angle AHX^-$ are *ca.* 160 ° and tend towards greater linearity with increasing quality of the hydrogen bond. Interactions of halide ions with macrocyclic H-bonding receptors and the potential for host selectivity are discussed.

Introduction

Among the many disciplines which make up modern supramolecular chemistry, the classic example of the self assembling system, *i.e.* the macrocyclic host–guest complex, remains a focal point of attention. Although the original Peterson–Lehn–Cram work dealt with metal ion inclusion, a subsequent awareness that analogous anion complexation might be effected has prompted the synthesis of a number of ingenious receptors incorporating ion-pairing, H-bonding and/or Lewis acidic binding sites.[1] The key role of anion transport in biological systems, for example in the cystic fibrosis transmembrane conductance regulator protein, also fuels interest in the possibility of synthetic anion channel design.[2]

The most obvious targets for anion inclusion studies would be the halide anions, and a systematic study of their H-bonding properties would aid in the design of selective receptors based on this most well defined of the supramolecular design principles.[3] Recent work has shed light on the weak interactions between covalently bound halogens and nitrogen or oxygen,[4] as well as the relationship of H_2O bridged halide ions to each other,[5] but no comparative account of the H-bonding properties of the halide anion series has apparently been undertaken. We thus now report a statistical analysis of the solid state interactions of fluoride, chloride, bromide and iodide anion with the common H-bond donors O–H, N–H and N^+–H derived from the Cambridge Structural Database,[6] thereby evaluating the prospects of halide discrimination by H-bonding receptors.

Method

Structures were retrieved from the Cambridge Structural Database, using the query dialogue within QUEST3D[5] represented in Fig. 1. In the first instance, in order to obtain statistically meaningful distributions for the individual $H \cdots X^-$ distances (*r*), no limiting value of *r* was defined and a dataset of all structures containing X^- and HA was analysed with the sole condition that the $X \cdots HA$ angle (α) be greater than 90 °. Prominent maxima were observed in all cases near the expected H-bonding distances, and these values were noted. An arbitrary range of 1.00 Å beyond the observed maximum was then set for each anion, representing the distance beyond which would not constitute a significant interaction. The lower limit for $H \cdots X^-$ contact was simply set to 0 Å. In order to avoid hits involving halide polyanions, the number of connections to X^- had to be specified as 'exact'. Organic-only structures with coordinate sets and *R* values < 0.10 were then analysed using the VISTA[5] program, the results of which are summarised in Table 1.

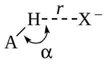

Fig. 1

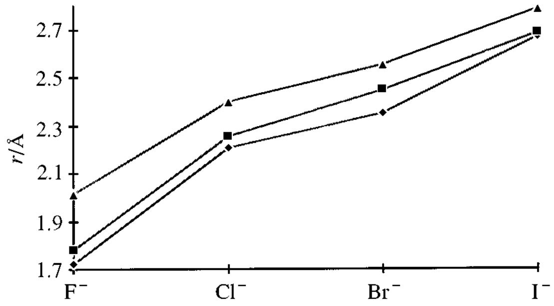

Fig. 2 $H \cdots X^-$ distance (*r*) *vs.* X^-, (–◆–) $N^+H \cdots X^-$, (–■–) $OH \cdots X^-$, (–▲–) $NH \cdots X^-$

Discussion

Twelve searches were performed using the query defined in Fig. 1 inputting OH, N–H, and N^+–H as the hydrogen bond donors and for each case F^-, Cl^-, Br^- and I^- as the acceptors. Table 1 shows that the $H \cdots X^-$ distance increases as expected going down the periodic table. A median value is also given in each case, since the mean is influenced by contributions from longer range interactions which were included in the overall analysis. A comparison of the median *r* values for each halide acceptor is presented in Fig. 2. Here it is conspicuous that the most effective H-donor is the ammonium cation, whose hydrogen bond is reinforced by an ion-pairing interaction, followed by the O–H and finally the neutral N–H function, which is entirely consistent with the status of these species with respect to non-ionic Brønsted acceptors. The angle of the H-bonding axes show no significant trends, although those for $NH \cdots X^-$ contact are generally the most acute. Minimum values of *r* and the accompanying angle are quoted to give an indication of the lower limit on these interactions. It is worth noting that although the average hydrogen bond lengths are shortest for the N^+H donor group, all four minimum values for $OH \cdots X^-$ distances are shorter than those for N^+H. Histograms and scatterplots of H-bonding angle *vs.* bond distance are given for comparison of all three cases involving the chloride ion (Fig. 3).

Table 1 Hydrogen bond lengths and angles with sample standard deviations for all combinations of $X^- \cdots HA$

$O–H \cdots X^-$				
X^-	Observations	r/Å mean (median) ± s	$\angle OHX^-$/° mean (median) ± s	r/Å min., $\angle$/°
F^-	7	1.757 (1.779) ± 0.223	162.4 (162.5) ± 8.2	1.346, 167.0[a]
Cl^-	325	2.271 (2.257) ± 0.244	161.8 (165.3) ± 16.2	1.594, 169.7[b]
Br^-	85	2.482 (2.448) ± 0.255	156.9 (163.0) ± 17.7	1.909, 170.6[c]
I^-	24	2.723 (2.689) ± 0.305	153.7 (160.5) ± 20.7	2.233, 164.3[d]

$N^+–H \cdots X^-$				
X^-	Observations	r/Å mean (median) ± s	$\angle N^+HX^-$/° mean (median) ± s	r/Å min., $\angle$/°
F^-	6	1.763 (1.720) ± 0.151	171.2 (172.4) ± 5.0	1.577, 173.1[e]
Cl^-	636	2.257 (2.210) ± 0.241	159.1 (163.0) ± 17.0	1.797, 176.2[f]
Br^-	141	2.384 (2.350) ± 0.161	159.9 (162.4) ± 13.0	2.049, 168.8[g]
I^-	16	2.672 (2.674) ± 0.122	160.8 (161.3) ± 14.8	2.477, 179.4[h]

$N–H \cdots X^-$				
X^-	Observations	r/Å mean (median) ± s	$\angle NHX^-$/° mean (median) ± s	r/Å min., $\angle$/°
F^-	7	1.964 (2.017) ± 0.115	156.8 (148.5) ± 12.0	1.786, 169.6[i]
Cl^-	230	2.472 (2.403) ± 0.298	154.0 (157.5) ± 17.7	1.927, 153.9[j]
Br^-	52	2.616 (2.555) ± 0.250	154.0 (157.0) ± 18.3	2.285, 164.8[k]
I^-	15	2.805 (2.792) ± 0.125	155.4 (153.0) ± 11.2	2.653, 158.5[l]

The CDS reference codes for the minima are: [a] BULGEU. [b] PASHOC01. [c] GARVOK. [d] LUPMIA10. [e] DEHSOY10. [f] VEFXIN01. [g] DHMBHC10. [h] MPTHNA. [i] JEFWAS. [j] FUMGOJ. [k] ADENIC. [l] VEPVIV.

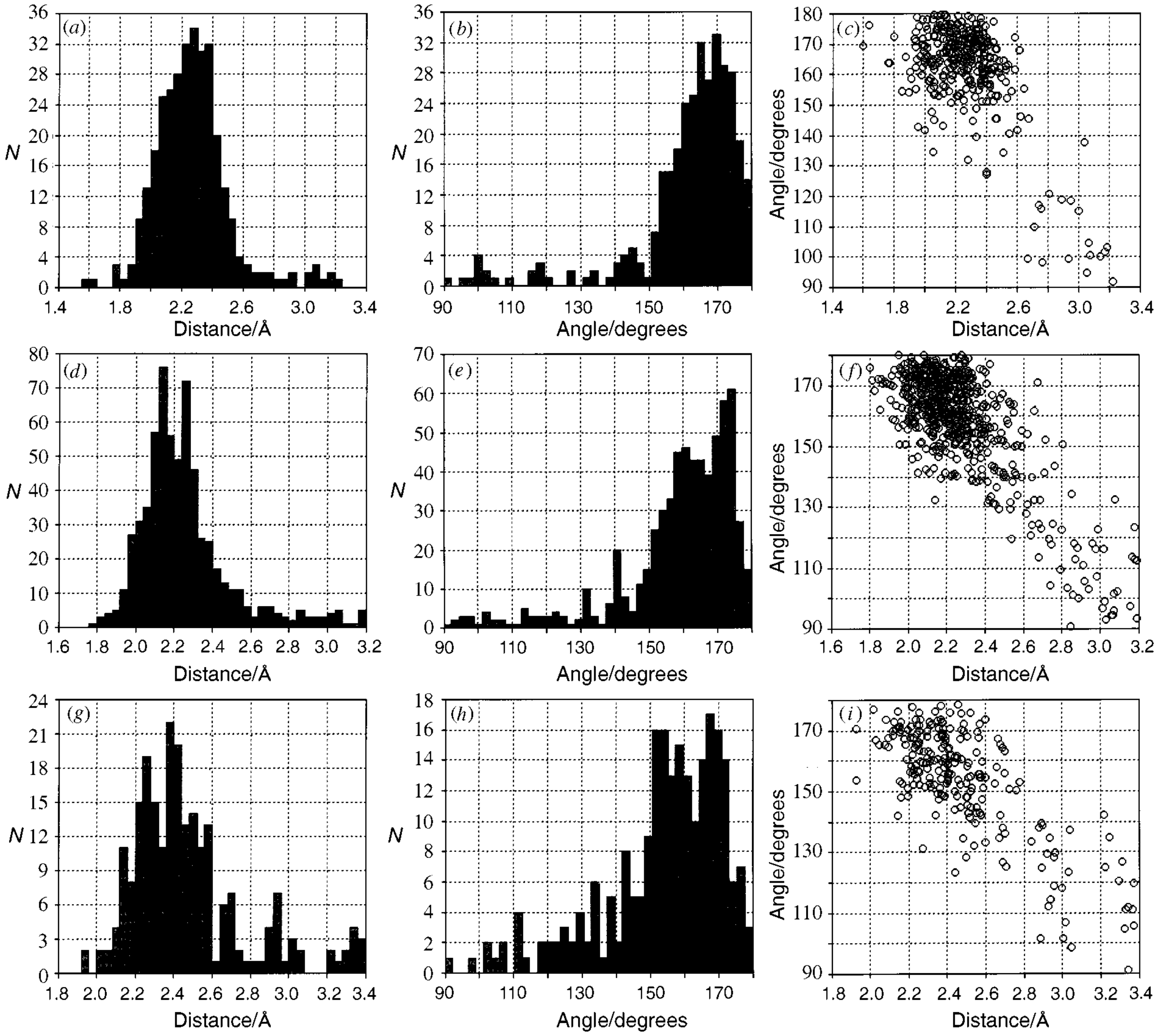

Fig. 3 (*a*) Histogram for the $Cl^- \cdots HO$ distance; (*b*) histogram for $\angle OHCl^-$; (*c*) scatterplot $\angle OHCl^-$ *vs.* $Cl^- \cdots HO$ distance; (*d*) histogram for the $Cl^- \cdots HN^+$ distance; (*e*) histogram for $\angle N^+HCl^-$; (*f*) scatterplot $\angle N^+HCl^-$ *vs.* $Cl^- \cdots HN^+$ distance; (*g*) histogram for the $Cl^- \cdots HN$ distance; (*h*) histogram for $\angle NHCl^-$; (*i*) scatterplot $\angle NHCl^-$ *vs.* $Cl^- \cdots HN$ distance

Table 2 Stepped differences in the median values (Δr/Å) of the $X^- \cdots HA$ distances. Single steps are emboldened

	$NH^+ \cdots Cl^-$	$NH^+ \cdots Br^-$	$NH^+ \cdots I^-$		$OH \cdots Cl^-$	$OH \cdots Br^-$	$OH \cdots I^-$		$NH \cdots Cl^-$	$NH \cdots Br^-$	$NH \cdots I^-$
$NH^+ \cdots F^-$	**0.490**	0.630	0.954	$OH \cdots F^-$	**0.478**	0.669	0.910	$NH \cdots F^-$	**0.386**	0.538	0.775
$NH^+ \cdots Cl^-$	—	**0.140**	0.464	$OH \cdots Cl^-$	—	**0.191**	0.432	$NH \cdots Cl^-$	—	**0.152**	0.389
$NH^+ \cdots Br^-$	—	—	**0.324**	$OH \cdots Br^-$	—	—	**0.241**	$NH \cdots Br^-$	—	—	**0.237**

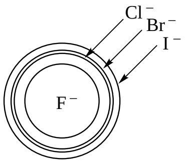

Fig. 4 A graphical representation of the data in Table 2 for the $X^- \cdots HN^+$ system, where the diameter of the innermost ring represents the H-bonding distance to F^-, the next Cl^-, followed by Br^- and finally I^-

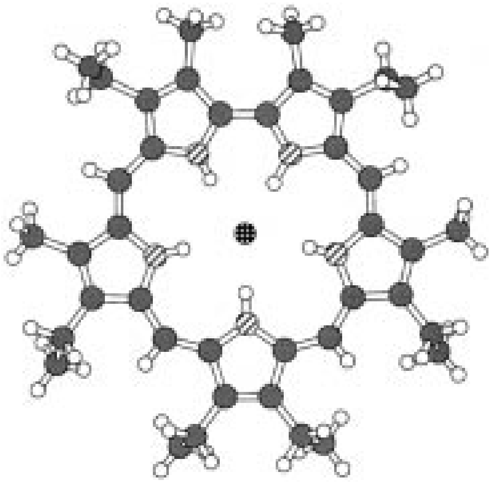

Fig. 5 Dihydrosapphyrinium fluoride

The latter make clear the preference of the hydrogen bond for approximate linearity, in that the cases where the bonding distance indicates a more subtle interaction are exclusively associated with the more acute angles.

The question of potential selectivity in the recognition of these spherical anions is addressed by the data in Table 2, which shows the steps in the median H-bonding distance from one ion to the next for all three types of donor hydrogen. The Δr interval between fluoride and chloride is large; nearly 0.5 Å in the case of the better donors, which is numerically comparable to that of the two steps between chloride and iodide. However, the difference between the preferred hydrogen bonding distances of chloride and bromide, as little as 0.14 Å for the NH^+ group, makes the prospect of distinguishing these anions based solely on H-bonding properties difficult. A somewhat larger gap is observed finally between bromide and iodide in all three cases. The separations are compared graphically in Fig. 4.

A number of synthetic receptors capable of recognising anions have been described,[7] based mainly on protonated azamacrocycles and expanded porphyrins, and X-ray structures of complexes have in some cases demonstrated multiple, good quality hydrogen bonds to NH and N^+H. Although selectivity between chloride and fluoride has been noted,[7g,h] no study has yet compared chloride with bromide. No macrocyclic host possessing OH donors has yet been applied to anion recognition, although two clefts with convergent OH functions have been observed to bind chloride.[7d,f] Perhaps the most impressive example of the H-bonding approach to anion recognition is found in the complex dihydrosapphyrinium fluoride (Fig. 5),[7k] which possesses a nearly planar, pentagonal array of $N-H \cdots F^-$ bonds whose mean $H \cdots F$ distance of 1.89 Å is nearly ideal for this interaction (*cf.* Table 1).

Conclusions

A survey of the Cambridge Structural Database gives over 1500 observations of close contacts between halide anions and OH, NH and N^+H functions consistent with hydrogen bonding. Analysis shows consistent trends in all three cases, with greatest difference in H-bonding distance being between fluoride and chloride, and the least between chloride from bromide. These data should be of assistance in the future design of selective anion receptors.

Acknowledgements

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