

## Comparison of Halide Receptors Based on H, Halogen, Chalcogen, Pnicogen, and Tetrel Bonds

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### ABSTRACT

A series of halide receptors are constructed and the geometries and energetics of their binding to  $F^-$ ,  $Cl^-$ , and  $Br^-$  assessed by quantum calculations. The dicationic receptors are based on a pair of imidazolium units, connected via a benzene spacer. The imidazoliums each donate a proton to a halide in a pair of H-bonds. Replacement of the two bonding protons by Br leads to binding via a pair of halogen bonds. Likewise, chalcogen, pnicogen, and tetrel bonds occur when the protons are replaced, respectively, by Se, As, and Ge. Regardless of the binding group considered,  $F^-$  is bound much more strongly than are  $Cl^-$  and  $Br^-$ . With respect to the latter two halides, the binding energy is not very sensitive to the nature of the binding atom, whether H or some other atom. But there is a great deal of differentiation with respect to  $F^-$ , where the order varies as tetrel > H ~ pnicogen > halogen > chalcogen. The replacement of the various binding atoms by their analogues in the next row of the periodic table enhances the fluoride binding energy by 22-56%. The strongest fluoride binding agents utilize the tetrel bonds of the Sn atom, whereas it is I-halogen bonds that are preferred for  $Cl^-$  and  $Br^-$ . After incorporation of thermal and entropic effects, the halogen, chalcogen, and pnicogen bonding receptors do not represent much of an improvement over H-bonds with regard to this selectivity for  $F^-$ , even I which binds quite strongly. In stark contrast, the tetrel-bonding derivatives, both Ge and Sn, show by far the greatest selectivity for  $F^-$  over the other halides, as much as  $10^{13}$ , an enhancement of six orders of magnitude when compared to the H-bonding receptor.

## INTRODUCTION

The detection, extraction, and transport of anions is of paramount importance in a wide diversity of applications, whether biological or chemical, medical or environmental <sup>1</sup>. But it is one thing to detect the presence of a generic anion, and quite another to do this in a highly selective fashion. For example, it may be necessary to bind, transport, or extract a Cl<sup>-</sup> anion in a given process, over and above another halide, or simply to measure its concentration without regard to that of other anions. Another process may hinge upon a HCO<sub>3</sub><sup>-</sup> anion, which must be selectively chosen out of a sea of other anions. It is for this reason that biological evolution has developed a panoply of anion binding proteins. The sulphate-binding protein of *Salmonella typhimurium* <sup>2</sup> is an example of one which binds this anion via a number of H-bonds. Another protein is responsible for the binding and transport of phosphate <sup>3</sup> with very high specificity. Still another protein, present in blue-green algae, is highly specific for the nitrate anion <sup>4</sup>, and another binds specifically to bicarbonate <sup>5</sup>.

Whereas the evolutionary process has developed some very specific and selective anion binding agents, modern technology lags behind. Many receptors make use of general electrostatic interactions, and sometimes of H-bonds <sup>6-11</sup>. The thiourea molecule, for example, is a widely used <sup>12-16</sup> anion binder, taking advantage of its H-bonding capability. The guanidinium cation and its derivatives <sup>17, 18</sup> have also found use in this regard.

However, the anion receptors that have been developed to date still suffer from certain disadvantages. Their selectivity is not optimal, or they are unable to detect the presence of a particular anion below a given concentration threshold. In fact, at this point in time, the biggest need is the development of highly selective receptors that can function in an aqueous, rather than organic or biological environment. As mentioned in a recent review <sup>1</sup>, “examples of receptors that are neutral or of low charge and operate in organic–aqueous mixtures are uncommon, and those that function in 100% water are rarer still”.

One major, and fairly recent, advance in this field has arisen with the growing recognition of the phenomenon of halogen bonds <sup>19-30</sup>, wherein an attractive force occurs between a halogen atom and an electron donor, such as the lone pair of an amine. These halogen bonds (XBs) have been thoroughly dissected by experiment and theoretical calculations over the past years, and are now rather well understood.

One of the more intriguing and potentially useful applications of XBs is associated with the development of receptors that are highly selective for one anion over another <sup>31-41</sup>. In an early effort in this direction, the Beer group <sup>42</sup> found that substitution of H by Br enabled the consequent halogen bond to more effectively bind chloride. They later showed <sup>43</sup> receptors of this type could recognize both chloride

and bromide ions, purely by virtue of XBs, and an increased affinity over H-bonding analogues in a picket-fence scaffold<sup>44</sup> or rotaxane motif<sup>45</sup>. Chudzinski et al<sup>46</sup> obtained quantitative estimates of the contribution of halogen bonding to the binding of anions to bipodal receptors, along with noting a preference for halides over oxoanions. This group later<sup>47</sup> applied I halogen bonds to develop preorganized multidentate receptors capable of high-affinity anion recognition. Huber's group compared<sup>48</sup> entropic with enthalpic contributions to such binding. Halogen bonding exerts selectivity for bromide over chloride, or other anions in a set of tripodal receptors<sup>49</sup>. Our own group<sup>50-52</sup> has applied quantum chemical calculations to this issue, showing that the replacement of H in a series of H-bonding bidentate receptors by halogen atoms can indeed influence their binding to halides. The work detailed a remarkable enhancement of both binding and selectivity, most particularly when the H atom is replaced by I.

It seems clear, then, that halogen bonding has enormous potential to enhance the ability of receptors to bind anions, a facility which begs to be exploited. But just as the switchover from H to halogen bonding introduced a new dimension to the field, extending this same philosophy to another sort of bonding may offer even more important added benefits. More specifically, just as the elements of the halogen family (Cl, Br, I, etc) can replace H as a bridging atom in strongly bound complexes, the same is equally true for other families in the periodic table. There is rapidly growing evidence that chalcogen atoms such as S and Se engage in bonding of a parallel sort<sup>53-64</sup>. The pnicogens (P, As, etc) can function in a similar manner<sup>65-73</sup>, and there is a growing avalanche of data that demonstrate the same is true of tetrrels (Si, Ge, etc)<sup>74-82</sup>. These findings should not be entirely surprising, as all of these atoms, like halogens, display highly asymmetric charge distributions when bound to another atom, and are even less electronegative than the halogens, so have a better native ability to generate a positive electrostatic potential region directed toward an approaching nucleophile. And indeed their propensity to engage in such noncovalent bonding can occur in the context of anion receptors, as shown by the very recent publication of a work<sup>83</sup> wherein it is a set of chalcogen bonds (to S in this case) that enable a newly synthesized set of molecules to bind to and transport anions.

It was just this idea that motivated our group to very recently perform a set of calculations to examine how the latter sorts of bonds might compare with chalcogens in this context. The transition from chalcogen to pnicogen to tetrel yielded<sup>84</sup> not only progressively stronger binding to anions, but also greater selectivity. In a quantitative sense, the binding energy of halides to a Ge-bonding bidentate receptor was as high as 63 kcal/mol, and preferentially bound F<sup>-</sup> over other halides with a selectivity of 27 orders of magnitude. These quantities are especially impressive, given the fact that the receptor was electrically neutral, forgoing the positive charge on many other such candidates.

At this point then, there is every reason to believe that the recent opening of the field of anion receptors to halogen bonding represents only the tip of the proverbial iceberg. It seems opportune to expand the anion receptor horizon not only to halogen atoms, but also to their chalcogen, pnictogen, and tetrel cousins, which appear to offer perhaps even greater opportunities. In brief then, this work employs the power of high-level quantum calculations to explore the capabilities of all of these bonding types for the design of new anion binding agents.

## SYSTEMS AND METHODS

As a prototype system, we consider the bipodal receptors wherein a pair of imidazolium groups engage in HBs with an incoming anion. The two imidazoliums are connected via a benzene spacer group, as illustrated at the top of Fig 1, for which the sample anion is a chloride. The imidazoliums and benzene groups were chosen first because of their resemblance to receptors studied earlier<sup>1, 11, 33, 48, 49, 85-87</sup>, and also because prior calculations<sup>52</sup> had indicated they represent an optimal choice for this purpose. The influence upon anion binding of different sorts of noncovalent bonds was examined first by replacing the H atoms involved in H-bonding by third-row atoms Ge, As, Se, and Br as representative of tetrel, pnictogen, chalcogen, and halogen bonds respectively. The effect of moving down one row of the periodic table was facilitated by replacing Ge and Br by their fourth-row analogues Sn and I. All receptors carried a formal charge of +2, again consistent with prior experimental and computational studies of these systems. The three halides F<sup>-</sup>, Cl<sup>-</sup>, and Br<sup>-</sup>, were each allowed to interact with these various dicationic receptors, leading to a total of 21 different receptor/halide combinations.

All the calculations were carried out with the M06-2X DFT functional<sup>88</sup> in conjunction with the aug-cc-pVDZ basis set, within the framework of the Gaussian-09<sup>89</sup> program. For the heavy atoms I and Sn, the aug-cc-pVDZ-PP pseudopotential was taken directly from the EMSL library<sup>90, 91</sup> so as to incorporate relativistic effects. This level of theory is appropriate for this task, as evident by previous work by others<sup>92-101</sup> and very recently by ourselves in dealing with very similar sorts of systems<sup>50-52</sup>. The geometries of the receptors and complexes were fully optimized without any restriction, taking into account only true minima with all positive vibrational frequencies. The binding energy,  $E_b$ , of each halide with its receptor was calculated as the difference between the energy of the complex and the sum of the energies of separately optimized monomers. Each binding energy was corrected for basis set superposition error using the counterpoise<sup>102</sup> procedure. To account for solvent effects, the polarizable conductor calculation model (CPCM) was applied<sup>103</sup>, with water as the solvent. Molecular electrostatic potential maps were visualized and quantified with the Chemcraft and WFA-SAS programs<sup>104, 105</sup> and charge transfer assessed via the Natural Bond Orbital (NBO) technique<sup>106</sup>.

## RESULTS

Geometry optimizations led to structures like those samples illustrated in Fig 1 for the  $\text{Cl}^-$  halide, wherein the halide engages in noncovalent bonds with the pair of Z atoms on the receptor. In most cases, the halide was symmetrically disposed as in Fig 1, but there were a number of cases where the halide was closer to one Z atom than the other. The  $R(\text{Z}\cdots\text{X})$  distances are displayed in Table 1 where asymmetrical structures are indicated by a pair of distances. The highest degree of asymmetry was associated with the fluoride anion where the two  $R(\text{Z}\cdots\text{F})$  distances can differ by 1 Å or more, but this asymmetry only occurs with certain Z atoms. With respect to the three different halides, the distances involving the fluoride are the shortest by a good deal; distances to the bromide are longer than those to chloride, but only by a small amount. The H-bonding distances in the first row of Table 1 are quite a bit shorter than the other noncovalent bonds. Within the group of third-row Z atoms, one sees a tendency for gradual shortening:  $\text{Ge} > \text{As} > \text{Se} > \text{Br}$ , but the increments from one to the next are rather small. Jumping down to the next row in the periodic table is associated with a small noncovalent bond contraction, despite the larger size of I and Sn, relative to their third-row congeners Br and Ge. It may finally be noted that the tetrel atoms Ge and Sn are particularly disposed toward asymmetric complexes, occurring in five of the six cases.

The binding energies reported in Table 2 obey a number of systematic trends. In the first place, these complexes are strongest for  $\text{F}^-$  and weakest for  $\text{Br}^-$ , with the largest gap occurring between  $\text{F}^-$  and  $\text{Cl}^-$ . This pattern mirrors the noncovalent bond lengths in Table 1. With regard to the nature of the Z atom, the trends are more subtle. Within the subset of  $\text{Cl}^-$  and  $\text{Br}^-$ , there is not much sensitivity to Z, although the Br halogen bonds are the strongest, and As pnictogen bonds the weakest. The pattern is quite different for the fluoride anion, where there are substantial differences from one bond to the next. The Ge tetrel bond is clearly the strongest, followed by pnictogen, halogen, and lastly chalcogen. Moving down to the next row of the periodic table strengthens all bonds, but retains the patterns of the third row. Specifically, the halogen bonds are stronger for  $\text{Cl}^-$  and  $\text{Br}^-$  but the reverse is true for fluoride. Indeed, the strongest binding of all, amounting to 30 kcal/mol, occurs for the  $\text{Sn}\cdots\text{F}$  tetrel bonds.

### Analysis of Contributing Factors

Given the charged nature of the halides and receptor, one would anticipate the binding to involve a great deal of Coulombic attraction. One measure of this quantity arises from analysis of the molecular electrostatic potential (MEP) of the receptor in the region where the halide is attracted. The MEP of each of the various receptors is illustrated in Fig 2 on a surface that corresponds to 1.5 times the van der Waals radius of each atom, which makes visible the point where the halide will ultimately reside between the pair of Z atoms. As the receptor contains a total charge of +2, the potential is quite positive; the blue regions in

Fig 2 refer to a potential of +0.25 au, and red to +0.20. Focusing on this particular location, the potential is clearly the bluest, i.e. most positive, for Z=H. Within the context of the third-row atoms, it would appear this region becomes somewhat more positive in the order Ge < As < Se < Br. There is little change evident in moving down to the next period, Sn and I. These patterns are partially consistent with the binding energies in Table 2 for Cl<sup>-</sup> and Br<sup>-</sup> where halogen bonds tend to be stronger. But the MEPs do not comport with the much stronger binding of the fourth-row Z atoms Sn and I, nor are they consistent with the binding of fluoride.

A perhaps more quantitative measure of the MEP can be derived by evaluating the maximum of the potential on a surface of constant electron density. These maxima are contained in the last column of Table 2 for each of the receptors, on the surface corresponding to  $\rho=0.001$  au. Like the diagrams in Fig 2, the potential is most positive for Z=H. They do not, however, indicate much of a difference as one moves along the third row atoms with Ge, As, Se, and Br all within 3% of one another. There is a small increment for moving down to the fourth period, particularly for Sn for which  $V_{s,max}$  is some 11% higher than for Ge. On the other hand, there is nothing in the MEPs which would predict that the Sn tetrel atoms bind the halides more strongly than do the H-bonds. One might conclude that the MEPs offer only a partial and incomplete explanation of the comparative binding strengths. This finding is not entirely surprising as the charged nature of the anions and receptors will strongly polarize one another, perturbing each other's charge distributions upon interaction.

Concerning the perturbations of the monomer electron distributions, the NBO formalism offers a means of quantifying this phenomenon. In particular, H-bonds and their analogues typically involve a good deal of charge transfer from the lone pairs of the electron donor to the  $\sigma^*(Z-C)$  antibonding orbital, and this transfer often tracks well with the strength of the noncovalent bond. The energetic measures of this charge transfer,  $E(2)$ , is displayed in the first three columns of Table 3. Before considering this data, it must be pointed out that the quantities must be viewed in the context of whether the complex is symmetric or asymmetric. In the former case,  $E(2)$  is the same for both of the  $X \rightarrow Z$  transfers, i.e. both  $Z_1$  and  $Z_2$ . On the other hand, this term is quite large when the halide closely approaches one of the two Z atoms, at the expense of the other; the larger of these two quantities is reported in Table 3. Indeed, if the halide approaches the Z atom more closely, the NBO formalism views their interaction as a covalent bond, and no  $X_{lp} \rightarrow \sigma^*(Z-C)$  term can be evaluated.

With the forgoing as a backdrop, one can consider how the charge transfers may influence the binding energies. Both  $E_b$  and  $E(2)$  diminish with the size of the halide:  $F^- > Cl^- > Br^-$ . Considering only symmetric systems, there is a steady reduction of  $E(2)$  from tetrel to halide: Ge > As > Se > Br, whereas the

binding energy pattern is less systematic. Like the interaction energies, moving down from the third to the fourth period raises  $E(2)$ .

Although perhaps not of predictive value, the strengths of noncovalent bonds are typically strongly correlated with the electron density at the AIM bond critical point connecting the two atoms of interest. Certain such correlations are observed in the halide receptor complexes here as well, with the same caveat that it is only the stronger of the two bonds that is reported for the asymmetric systems in Table 3. As may be observed in the last three columns of Table 3, these densities diminish as  $F^- > Cl^- > Br^-$ , similar to binding energy. But the binding energy patterns observed for different Z atoms are not well matched by  $\rho_{BCP}$ . For example, Br forms the strongest bonds with Cl, whereas  $\rho_{BCP}$  is largest for Ge. With respect to  $Br^-$ ,  $\rho_{BCP}$  is smallest for Ge whereas the same is not true for  $E_b$ . Nor is the stronger binding of both of these anions with I vs Sn adequately reflected in  $\rho_{BCP}$ .

#### Free Energy Comparisons and Selectivity

By including entropic and thermal effects, it is possible to extract the free energies of binding of the various halides to the receptors. These quantities are reported in Table 4 at 25 C and may be seen to be negative (with only one minor exception), suggesting the binding ought to be a spontaneous process in water. The inclusion of entropy tends to raise  $\Delta G$  relative to  $\Delta E$ , with the former less negative than the latter by roughly 10 kcal/mol. Importantly, the patterns of the free energies in Table 4 closely mimic those of  $\Delta E$ . For example, the binding of  $F^-$  is much stronger than that of  $Cl^-$  or  $Br^-$ . The former anion is also bound much more strongly by the Ge and Sn tetrel bonds than by the corresponding halogen, chalcogen, or pnictogen bonds, while the same is not true of  $Cl^-$  and  $Br^-$ , for which halogen bonding has a slight edge.

The stronger binding of fluoride has important implications for the selectivity of these receptors. The selectivity for  $F^-$  over another anion  $X^-$  can be evaluated by the equilibrium constant  $K = \exp\{\{\Delta G(X^-) - \Delta G(F^-)\}/RT\}$ , and the resulting quantities are reported in the two last columns of Table 4. This selectivity is rather large, ranging from a minimum of 200 all the way up to  $2 \times 10^{13}$ . The largest selectivities are exhibited by the tetrel-bonding receptors  $Z=Ge$  and especially Sn. Note also that like the binding energies, the selectivities for fluoride are also enhanced on going from third to fourth-row Z atoms. In comparison to the H-bonding receptors in the first row of Table 4, it may be noted that only the tetrel bonding receptors provide an enhanced selectivity, but this increase is quite large, 4 orders of magnitude for Ge and 6 orders of magnitude for Sn.

As one final issue, inspection of Fig 2 suggests that the region lying in between the two Z atoms does not necessarily carry the most positive MEP. One might wonder then whether this location is indeed the preferred binding site for an incoming halide. Pilot calculations examined this question for the sample

system where a  $\text{Cl}^-$  is combined with the  $\text{Z}=\text{Br}$  receptor. Despite several bluer regions in Fig 2 for  $\text{Z}=\text{Br}$ , the site lying between the two Br atoms is indeed the most stable. Optimization of the geometry in which the  $\text{Cl}^-$  is placed on the exterior of the receptor, in the plane of one of the Im rings, leads to a structure with a pair of  $\text{CH}\cdots\text{Cl}$  HBs, 5.4 kcal/mol higher in energy than the favored site. A position where a  $\text{CH}\cdots\text{Cl}$  HB is formed with the CH of the central phenyl ring, meta to both C-N bonds, is disfavored by 7.8 kcal/mol. An alternate position, wherein a  $\text{CH}\cdots\text{Cl}$  bond with the CH of the phenyl ring lying between the two C-N bonds, is combined with an attractive interaction wherein this chloride lies above the plane of one Im ring, is a bit more stable, but still higher in energy than the globally favored site by 1.9 kcal/mol.

### Other Systems and Environments

As mentioned above, the data presented above pertains to aqueous systems, where each receptor/halide is immersed in a dielectric continuum designed to model water with  $\epsilon=78$ . One might wonder about the intrinsic binding properties without the influence of a surrounding solvent. A comparison of Figs 3a and 3b provide the necessary information, wherein Fig 3a illustrates the binding energies in solution, from data in Table 2, and the same quantities were calculated *in vacuo* in Fig 3b. Without the solvent to help stabilize the isolated charged entities, the halide and the dicationic receptor, the binding energies are greatly enlarged rising to as much as 200 kcal/mol. But what is of greater interest is the comparison of the patterns in the aqueous and vacuum environments.

In either case, the fluoride binding is much stronger than that of the other two halides, which are similar to one another. Also in either environment, there is little to differentiate the tetrel, pnictogen, chalcogen or halogen bonding of  $\text{Cl}^-$  and  $\text{Br}^-$ , but one sees a substantial degradation in this sequence for  $\text{F}^-$ . Both environments show enhanced binding of fourth over third-row Z atoms. There are differences as well. In solution, the H-bonded systems are bound about as tightly as the other Z atoms, but the former are considerably stronger than the latter in the gas phase. Whereas Sn makes for stronger complexes than I in the gas phase, the opposite is true for both  $\text{Cl}^-$  and  $\text{Br}^-$  in solution.

Instead of displacing the dicationic receptors from water to vacuum, one can also remove the +2 charge from the receptor. This was done by removing the two methyl groups on the N atom of each imidazole. The binding energies were again computed in aqueous solution, and these values are contained in Table 5. Graphic display of these quantities in Fig 3c facilitates comparison with the corresponding dicationic binding in Fig 3a. Very similar patterns are immediately obvious, although of course the neutral receptor engages in uniformly weaker binding without the benefit of a strong Coulombic attraction. The stronger binding of the 4<sup>th</sup> row atoms is clear in either case, as is the similarity of H-bonding with any of the 3<sup>rd</sup> row atoms for all but  $\text{F}^-$ . Importantly, the strong preference of  $\text{F}^-$  for  $\text{Z}=\text{Sn}$  is preserved even without the +2

charge on the receptor. The  $V_{s,max}$  quantities in the last column of Table 5 are of course markedly smaller than those for the dicationic receptors in Table 2, but nonetheless exhibit similar trends. In either case, the potentials for the Z=H receptors are disproportionately large, compared to the binding energy. Also, the potentials are larger for 4<sup>th</sup> row than for 3<sup>rd</sup> row binding atoms, largest of all for the tetrels.

### CONCLUSIONS

In summary, bipodal dicationic receptors based upon the motif of a pair of imidazoliums connected via a benzene spacer can bind halide anions both strongly and effectively. The replacement of the H-bonds of the two imidazoliums with tetrel, pnictogen, chalcogen, and halogen atoms can enhance certain features of the halide binding. For all receptors, F<sup>-</sup> is bound much more strongly than are Cl<sup>-</sup> and Br<sup>-</sup>. While the binding of the latter two halides is not very sensitive to the nature of the binding atom, there is a great deal of differentiation with respect to F<sup>-</sup>, where the order varies as tetrel > H ~ pnictogen > halogen > chalcogen. Transitioning the binding atom from third to fourth row of the periodic table (Ge→Sn and Br→I) further enhances the fluoride binding energy. Overall, the strongest fluoride binding is associated with the tetrel bonds of Sn, in contrast to Cl<sup>-</sup> and Br<sup>-</sup> which show a preference for halogen bonds with I. The tetrel-bonding derivatives, both Ge and Sn, show the greatest selectivity for F<sup>-</sup> over the other halides, as much as 10<sup>13</sup>, an enhancement of six orders of magnitude when compared to the H-bonding receptor.

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Table 1. Interatomic distances (Å) between indicated Z atom of receptor and halide

Z	F <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>
H	1.770	2.360	2.534
Ge	1.924/3.165	3.179/3.194	3.399
As	2.022/3.165	3.187	3.361
Se	2.432/2.616	3.164	3.313/3.317
Br	2.523	3.120	3.290
Sn	2.105/3.155	2.988/3.036	3.229/3.255
I	2.509	3.103	3.260

Table 2. Binding energies between dicationic receptors using indicated Z atom to interact with the halide, and maximum in MEP of isolated receptor (all in kcal/mol)

Z	F <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>	V <sub>s,max</sub>
H	-18.85	-10.36	-9.15	290
Ge	-24.73	-9.32	-8.55	251
As	-17.19	-8.87	-8.44	248
Se	-13.94	-9.36	-8.95	243
Br	-15.73	-10.07	-9.54	245
Sn	-30.11	-13.79	-11.87	275
I	-24.47	-15.75	-14.84	256

Table 3. NBO values of E(2) for X<sub>lp</sub>→σ\*(Z-C) and AIM density at bond critical point

Z	E(2), kcal/mol			ρ <sub>BCP</sub> , 10 <sup>-3</sup> au		
	F <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>	F <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>
H	24.21	15.52	14.12	35.4	18.3	15.9
Ge	a	11.91	10.06	84.7	23.0	11.0
As	91.14	10.75	9.84	77.1	14.7	13.2
Se	24.41	9.30	9.01	37.1	15.7	14.5
Br	12.68	7.39	6.74	30.4	16.3	14.4
As	91.14	10.75	9.84	77.1	14.7	13.2
Sn	a	a	19.30	71.8	21.9	17.3
I	21.41	14.20	13.42	37.3	20.5	18.7

<sup>a</sup>NBO formulation does not consider halide as fully separate from receptor

Table 4. Free energy of binding between dicationic receptors and halide, and equilibrium constant favoring the binding of F<sup>-</sup> over indicated halide

Z	$\Delta G(298\text{ K}), \text{ kcal/mol}$			$K(\text{F}^-/\text{X}^-)$	
	F <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>
H	-10.89	-1.74	-1.19	5.5E+06	1.4E+07
Ge	-14.84	-0.80	+0.28	2.2E+10	1.3E+11
As	-9.01	-1.09	-1.30	6.7E+05	4.7E+05
Se	-5.40	-1.68	-2.26	5.5E+02	2.1E+02
Br	-6.72	-2.64	-2.39	1.0E+03	1.5E+03
Sn	-20.55	-4.01	-2.41	1.5E+12	2.3E+13
I	-16.61	-8.42	-8.49	1.1E+06	9.5E+05

Table 5. Binding energies of neutral receptors using indicated Z atom to interact with the halide, and maximum in MEP of isolated receptor (all in kcal/mol)

Z	F <sup>-</sup>	Cl <sup>-</sup>	Br <sup>-</sup>	$V_{s,\text{max}}$
H	-8.79	-3.99	-3.46	30.3
Ge	-10.08	-3.47	-3.46	21.7
As	-4.94	-3.82	-4.09	18.1
Se	-4.89	-4.18	-4.40	18.6
Br	-6.07	-4.40	-4.30	14.9
Sn	-17.80	-4.74	-4.40	30.0
I	-11.80	-7.67	-7.46	24.2

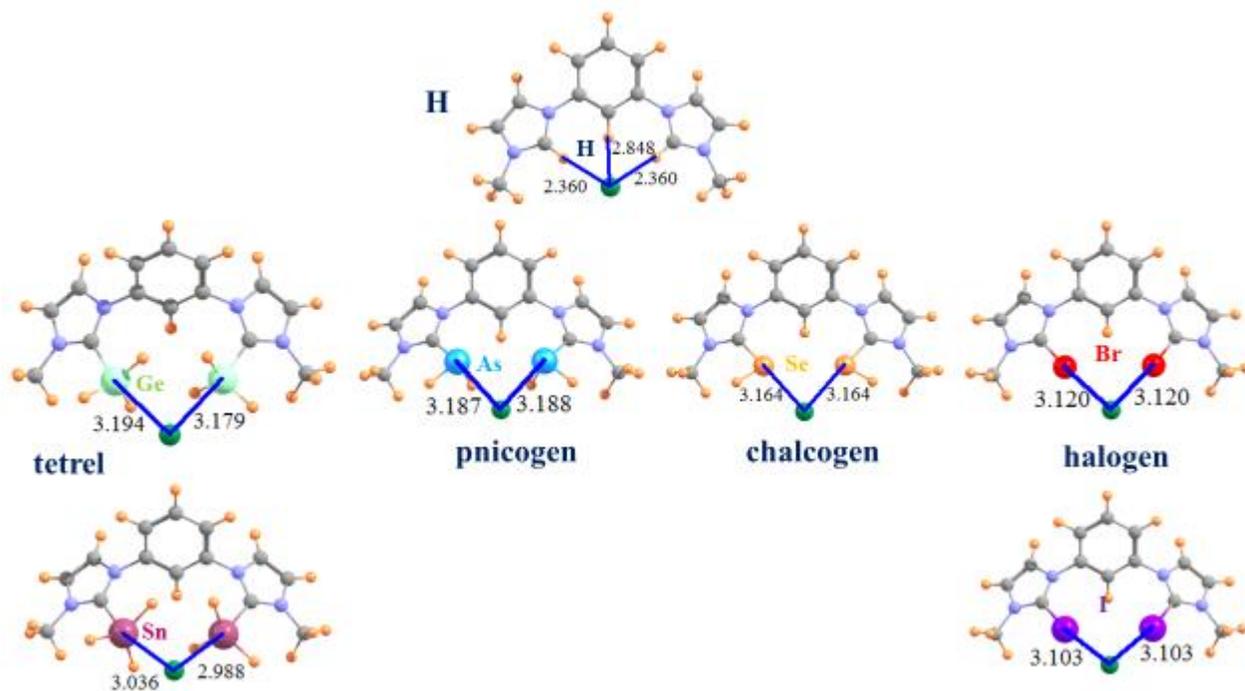


Fig 1. Optimized geometries of  $\text{Cl}^-$  anion with receptors. Distances in Å.

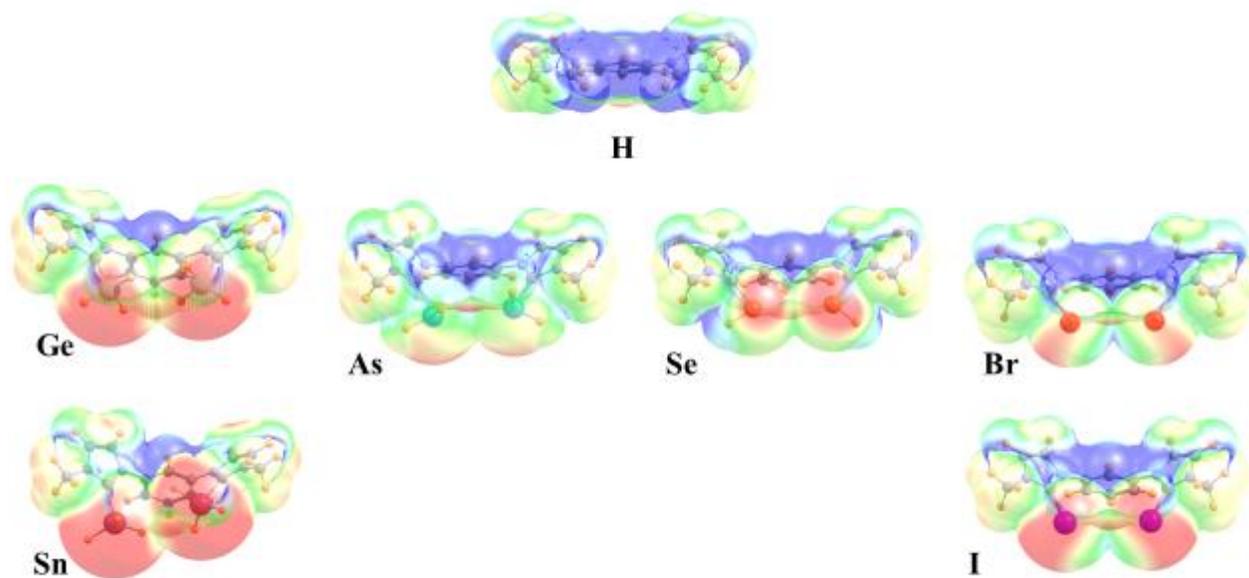


Fig 2. Molecular electrostatic potentials (MEPs) of receptors on surface corresponding to  $1.5 \times \text{vdW}$  radius. Blue and red regions correspond respectively to  $+0.25$  and  $+0.20$  au, respectively.

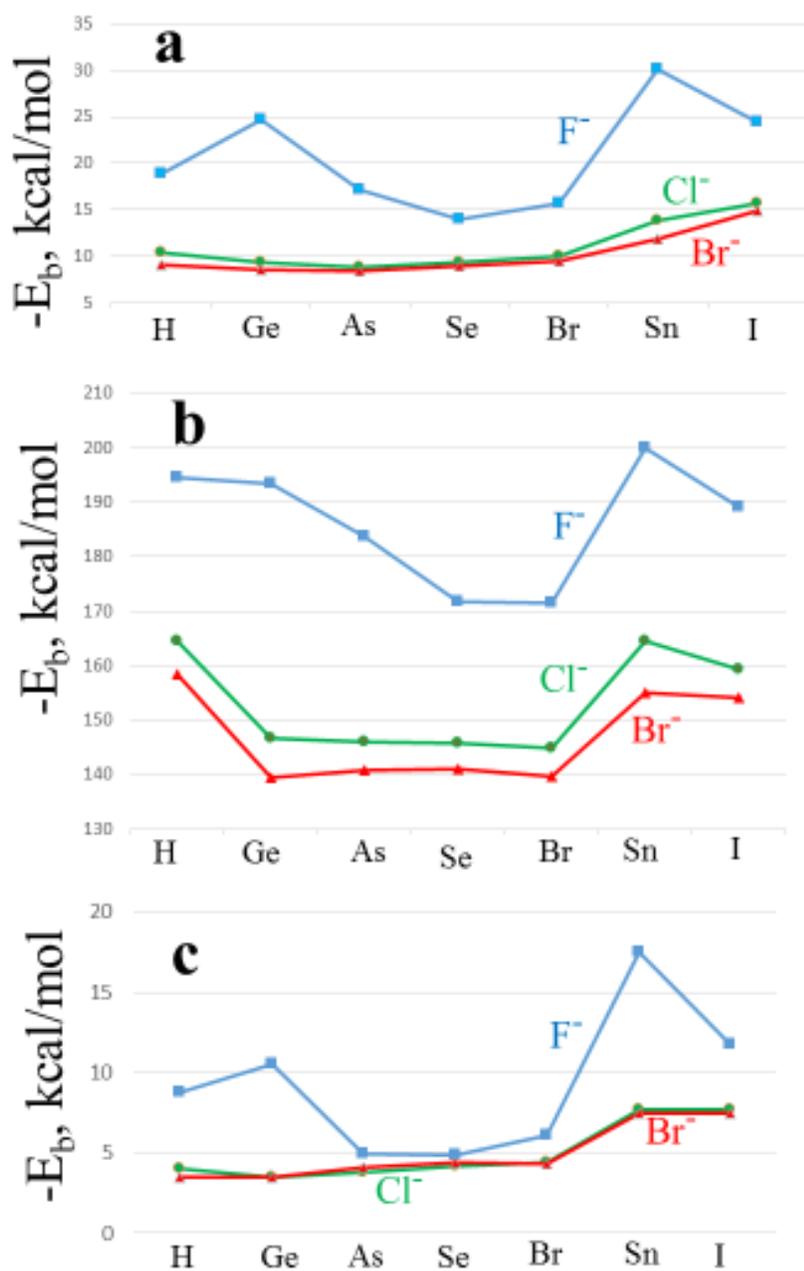


Fig 3. Binding energies of halides with receptors utilizing indicated atoms for binding to halide. Data for dicationic receptors are displayed in aqueous solution and *in vacuo* in a and b, respectively. Neutral receptors in water are shown in c.