PCCP

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/pccp

The properties of Substituted 3D-Aromatic Neutral Carboranes: The Potential for σ-Hole Bonding

Rabindranath Lo,[†] Jindřich Fanfrlík,[†] Martin Lepšík,[†] Pavel Hobza[†,‡*]

[†]Institute of Organic Chemistry and Biochemistry (IOCB) and Gilead Sciences and IOCB Research Center, Academy of Sciences of the Czech Republic, v.v.i., Flemingovo nám. 2, 16610 Prague 6, Czech Republic
‡Regional Center of Advanced Technologies and Materials, Department of Physical Chemistry, Palacký University, 77146 Olomouc, Czech Republic

*Corresponding Author: hobza@uochb.cas.cz

Abstract

The calculated properties of substituted carboranes such as dipole moment, polarisability, the magnitude of the σ-hole and the desolvation free energy are compared with these properties in comparable aromatic and cyclic aliphatic organic compounds. Dispersion and charge transfer energies are similar. However, the predicted strength of the halogen bonds with the same electron donor (based on the magnitude of the σ-hole) is larger for neutral C-vertex halogen-substituted carboranes than for their organic counterparts. Furthermore, the desolvation penalties of substituted carboranes are smaller than those of the corresponding organic compounds, which should further strengthen the halogen bonds of the former in the solvent. It is predicted that substituted carboranes have the potential to form stronger halogen bonds than comparable aromatic hydrocarbons, which will be even more pronounced in the medium. This theoretical study thus lays ground for the rational engineering of halogen bonding in inorganic crystals as well as in biomolecular complexes.

Introduction

Polyhedral boron clusters (boron hydrides, boranes) and their derivatives (heteroboranes) are a large class of inorganic compounds with unique properties, which are distinct from carbon-based compounds. These include especially their hydrophobicity,[1] low nucleophilicity,[2] Lewis acidity, high symmetry and spherical shape, 3D aromaticity[3] and the ability to form special types of noncovalent interactions, such as dihydrogen[4,5] and σ-hole bonding.[6,7] For this reason, they have found many applications, e.g. in radioactive waste extraction,[8] nanotechnology and medicinal chemistry.[9-10]

An important class of parental borane clusters comprises dianionic *closo*-$B_nH_n^{2-}$ compounds, known for n=5-12.[11] Neutral *closo*-carboranes can be obtained by replacing two formally neutral BH vertices with heteroatom vertices, such as isolobal CH^+.[12] The partial charges on B-bound H atoms are slightly negative because of the electropositive character of B, whereas those on the C-bound H atoms are slightly positive.[4] Exoskeletal H atoms, bound both to B and C, can be substituted by various organic moieties, such as halogens or a hydroxyl.[12-15]

Substituted carboranes are promising new structures for use not only in crystal engineering but also in medicinal chemistry.[13,16] The reasons are their low toxicity, metabolic stability and their ability to participate in various unique noncovalent interactions.[4,7] Indeed, substituted carboranes have been found to bind to proteins, where they serve as 'hydrophobic pharmacophores'.[16-17] Structural details about their binding are only known for a few proteins – HIV-1 protease,[18] dihydrofolate reductase[19] (DHFR), carbonic anhydrase[20-21] and vitamin D receptor.[22] The types of noncovalent interactions that they form range from standard electrostatic B-H…Na^+ and dispersion interactions to still unusual dihydrogen bonding.[5,23] The interaction repertoire of heteroboranes has, however, been recently expanded by unconventional σ-hole bonding, specifically halogen, chalcogen[7] and pnictogen bonding.[6]

Halogen bonds (X-bonds), the best known among various σ-hole bonding types, are an interesting type of noncovalent interaction that has received a lot of attention in crystal engineering.[24-25] Such noncovalent interactions were found first with amine complexes of dihalides in the 19th century,[26-27] however, the term 'X-bond' was used after the work of Dumas *et al.*[28-29] and the nature of the X-bond was explained via the σ-hole in 2007.[30-31] In 2004, they were also discovered in protein–ligand complexes.[32] Since then, the number of applications in biomolecular systems has been growing.[33-38] The X-bond occurs between a halogen atom (X) covalently bonded to an electronegative element, mostly carbon, and an electron donor (O, N, S, etc.). The X-bond might thus seem counterintuitive, because both the X atom and the electron donor are electronegative elements with a negative partial charge. Electron distribution in X atoms covalently bound to an electronegative atom (Y) is anisotropic, which gives rise to a region of positive electrostatic potential (ESP), located on the axis of the X-Y covalent bond and distal from atom Y. The positively charged region is called the σ-hole[30-31] and is characterised by its magnitude and size.[39] The strength of the X-bond increases with the σ-hole magnitude, whereas the directionality of the bond decreases when the σ-hole size increases. Passing from Cl to I, the magnitude (and also size) of the σ-hole increases; Br and especially I thus form the strongest X-bonds. The tunability of X-bonds has already been demonstrated in small molecular complexes[39-41] as well as in complex biomolecular systems.[36,38] The IUPAC definition[42] of X-bond emphasises the dominant role of the electrostatic interaction between the positively charged σ-hole and the negatively charged electron donor. Nevertheless, we have shown that characteristic features of the X-bond result from a concerted action of electrostatic, polarization, dispersion and exchange-repulsion energy terms.[43] Dispersion energy is mostly dominant, which is caused by the fact that two heavy atoms with large polarisabilities (X and the electron donor) are close together; their distance is shorter than the sum of their van der Waals radii.

So far, we have discussed the ability of boranes and carboranes to bind a partner via electrostatic and dispersion-energy terms. Besides these energy terms, boranes and carboranes can interact via charge-transfer interaction since both are good electron acceptors.

The efficiency of boranes and carboranes to bind a partner molecule noncovalently is, however, affected not only by their properties but also by their solvation/desolvation energies. If the system is strongly polar or even charged, the solvation/desolvation energies in water medium are much higher than those of less polar or nonpolar systems. Specifically for H-bonded complexes, the dehydration penalty weakens the interaction substantially. In contrast, X-bonds are less prone to be dampened[44] due to their lower polarity and also the larger role of dispersion,[41,45-46] which is not as much affected by the solvent.

The aim of the present paper is to predict computationally the ability of substituted carboranes to be efficient binders in noncovalent complexes, specifically in X-bonded, dispersion-bound or charge-transfer-dominated complexes. We will compare the studied carborane molecules with similar (with respect to the charge and the number of heavy atoms) carbon-based aromatic and cyclic aliphatic organic compounds (Fig. 1). For this comparison, we will use various one-electron properties: the dipole moment (μ), the most positive value of the electrostatic potential $V_{s,max}$ on the X atom as well as on the H atom of the hydroxyl group, polarisability and the energy of the LUMO. μ determines the strength of the electrostatic interactions, $V_{s,max}$ implies the strength of the X-bonding, polarisability provides information on the strength of the dispersion energy and the LUMO energy determines the charge-acceptor behaviour. Finally, we will calculate the solvation/desolvation free energy and thus estimate the effects of the water environment on the formation of noncovalent interactions.

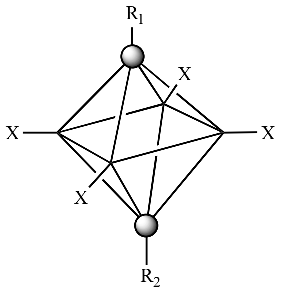
Materials and Methods

The systems investigated

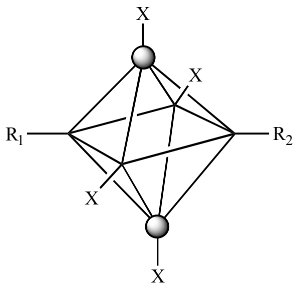
Two halogen atoms (X = Br, I) and a hydroxyl were chosen as representative moieties that would form halogen and hydrogen bonds, respectively. In the series of neutral *closo*-dicarbaboranes, $C_2B_{n-2}H_n$, six- and twelve-vertex species (i.e. n= 6, 12), were considered as they are the most stable of the cluster sizes.[47] The *exo*-substituents were added (as mono- and di- species) on either boron or carbon atoms, thus comprising both existing[12] and theoretical compounds. Their schematic structures are shown in Fig. 1.

This systematic study was started with mono-halogenated carboranes. In analogy to the organic systems studied previously,[41] the σ-hole tuning was examined by fluorination (as *exo*-substituents) of the other vertices. For hydroxyl systems, we took mono-hydroxyl systems and their corresponding fluorinated counterparts. We considered 1,2-*cis* and 1,6-*trans* isomers of the 6-vertex carborane cages[14] and 1,2-*ortho*, 1,7-*meta* and 1,12-*para* carboranes for 12-vertex carborane.[12] The calculated properties of the carboranes were compared with those of substituted aromatic and cyclic aliphatic hydrocarbons having the same charge (neutral) and number of heavy atoms (6 or 12) (Fig. 1).

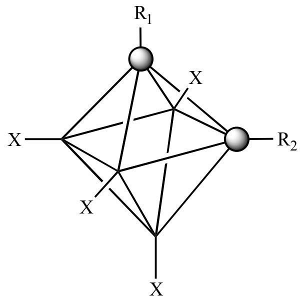
For a better orientation of the reader, the studied systems are systematically referred to with descriptive abbreviations. For example in 6_T-Br^CH, 6 stands for the number of heavy atoms (for 12-vertex carboranes and acenapthyl systems, it becomes 12) and the subscript 'T' denotes *trans*-isomer carborane (similarly 'C', 'O', 'M' and 'P' stand for *cis*-, *ortho*-, *meta*- and *para*- isomer carboranes, respectively). The saturated hydrocarbons are designated with an 'S' superscript. The systems may be *exo*-substituted by Br, I or OH and the number of substituent groups is also part of the abbreviation. The superscript 'C' (or B) denotes the skeletal atom to which the substituent (Br/I/OH) is bonded. The last position of the abbreviation is taken by either ‘H’ or ‘F’, indicating the parent or per-fluorinated system, respectively.



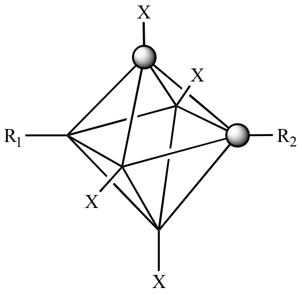
6_T-Br^{C}H: R$_1$= Br, R$_2$= X= H
6_T-Br^{C}F: R$_1$= Br, R$_2$= X= F
6_T-2Br^{C}H: R$_1$= R$_2$= Br, X= H
6_T-2Br^{C}F: R$_1$= R$_2$= Br, X= F
6_T-I^{C}H: R$_1$= I, R$_2$= X= H
6_T-I^{C}F: R$_1$= I, R$_2$= X= F
6_T-2I^{C}H: R$_1$= R$_2$= I, X= H
6_T-2I^{C}F: R$_1$= R$_2$= I, X= F
6_T-OH^{C}H: R$_1$= OH, R$_2$= X= H
6_T-OH^{C}F: R$_1$= OH, R$_2$= X= F



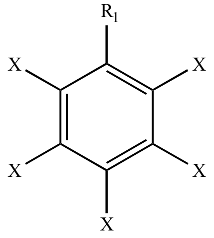
6_T-Br^{B}H: R$_1$= Br, R$_2$= X= H
6_T-Br^{B}F: R$_1$= Br, R$_2$= X= F
6_T-2Br^{B}H: R$_1$= R$_2$= Br, X= H
6_T-2Br^{B}F: R$_1$= R$_2$= Br, X= F
6_T-I^{B}H: R$_1$= I, R$_2$= X= H
6_T-I^{B}F: R$_1$= I, R$_2$= X= F
6_T-2I^{B}H: R$_1$= R$_2$= I, X= H
6_T-2I^{B}F: R$_1$= R$_2$= I, X= F
6_T-OH^{B}H: R$_1$= OH, R$_2$= X= H
6_T-OH^{B}F: R$_1$= OH, R$_2$= X= F



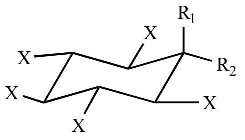
6_C-Br^{C}H: R$_1$= Br, R$_2$= X= H
6_C-Br^{C}F: R$_1$= Br, R$_2$= X= F
6_C-OH^{C}H: R$_1$= OH, R$_2$= X= H
6_C-OH^{C}F: R$_1$= OH, R$_2$= X= F



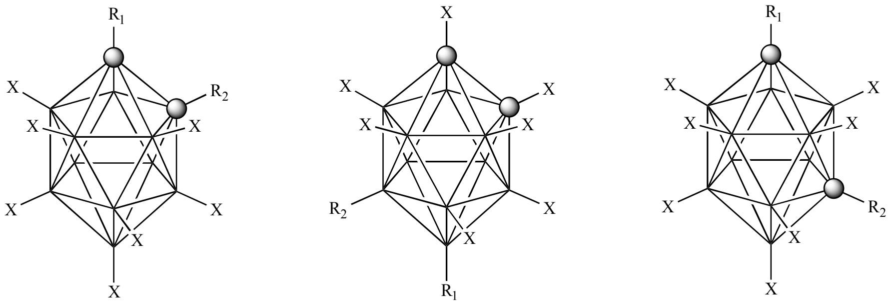
6_C-Br^{B}H: R$_1$= Br, R$_2$= X= H
6_C-Br^{B}F: R$_1$= Br, R$_2$= X= F
6_C-OH^{B}H: R$_1$= OH, R$_2$= X= H
6_C-OH^{B}F: R$_1$= OH, R$_2$= X= F



6-Br^{C}H: R$_1$= Br, X= H
6-Br^{C}F: R$_1$= Br, X= F
6-I^{C}H: R$_1$= I, X= H
6-I^{C}F: R$_1$= I, X= F
6-OH^{C}H: R$_1$= OH, X= H
6-OH^{C}H: R$_1$= OH, X= F



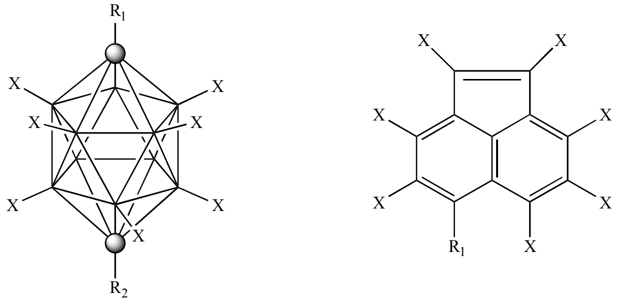
6^s-Br^{C}H: R$_1$= Br, R$_2$= X= H
6^s-Br^{C}F: R$_1$= Br, R$_2$= H, X= F
6^s-I^{C}H: R$_1$= I, R$_2$= X= H
6^s-I^{C}F: R$_1$= I, R$_2$= H, X= F
6^s-OH^{C}H: R$_1$= OH, R$_2$= X= H
6^s-OH^{C}F: R$_1$= OH, R$_2$= H, X= F



12_{O}-Br^{C}H: R_1= Br, R_2= X= H
12_{O}-Br^{C}F: R_1= Br, R_2= X= F
12_{O}-I^{C}H: R_1= I, R_2= X= H
12_{O}-I^{C}F: R_1= I, R_2= X= F
12_{O}-2I^{C}H: R_1= R_2= I, X= H
12_{O}-2I^{C}F: R_1= R_2= I, X= F
12_{O}-OH^{C}H: R_1= OH, R_2= X= H
12_{O}-OH^{C}F: R_1= OH, R_2= X= F

12_{O}-Br^{B}H: R_1= Br, R_2= X= H
12_{O}-Br^{B}F: R_1= Br, R_2= X= F
12_{O}-I^{B}H: R_1= I, R_2= X= H
12_{O}-I^{B}F: R_1= I, R_2= X= F
12_{O}-2I^{B}H: R_1= R_2= I, X= H
12_{O}-2I^{B}F: R_1= R_2= I, X= F
12_{O}-OH^{B}H: R_1= OH, R_2= X= H
12_{O}-OH^{B}F: R_1= OH, R_2= X= F

12_{M}-Br^{C}H: R_1= Br, R_2= X= H
12_{M}-Br^{C}F: R_1= Br, R_2= X= F
12_{M}-OH^{C}H: R_1= OH, R_2= X= H
12_{M}-OH^{C}F: R_1= OH, R_2= X= F



12_{P}-Br^{C}H: R_1= Br, R_2= X= H
12_{P}-Br^{C}F: R_1= Br, R_2= X= F
12_{P}-OH^{C}H: R_1= OH, R_2= X= H
12_{P}-OH^{C}F: R_1= OH, R_2= X= F

12-Br^{C}H: R_1= Br, X= H
12-Br^{C}F: R_1= Br, X= F
12-I^{C}H: R_1= I, X= H
12-I^{C}F: R_1= I, X= F
12-OH^{C}H: R_1= OH, X= H
12-OH^{C}F: R_1= OH, X= F

Fig. 1. Schematic structures of the systems studied. The circles shown in carborane systems denote carbon atoms.

Calculations

All the structures considered in this study, i.e. carboranes and the aromatic and cyclic aliphatic hydrocarbon systems (Fig. 1), were optimised at the B3LYP/def2-TZVPP level of theory in Gaussian 09.[48] The def2-TZVPP basis set was chosen, as it efficiently considers the effective-core potentials for X atoms.[49] Frequency calculations were performed for all the geometries to characterise them as minima with no imaginary frequency. The dipole moment (μ), the linear polarisability (α) and LUMO energies were obtained at the same level of theory. Furthermore, Grimme's advanced dispersion-corrected approach[50] (DFT-D3) with a basis set (def2-TZVPP) was taken for the optimization of some systems to determine the effect of dispersion energy in these isolated systems. The electrostatic potentials were generated on the molecular surfaces defined by Bader et al.,[51] as the 0.001 a.u. (electrons/bohr^3) contour of the electron density. The most positive value of the potentials (the local maximum) can be characterised as well as quantified on the molecular surfaces and is designated as $V_{s,max}$. In this study, the electrostatic potentials were calculated at the HF/cc-pVDZ level of theory and the HF/cc-pVDZ-PP basis set was employed for Br and I atoms to account for the relativistic effects in this study. The HF functional was utilised to generate the electrostatic potentials so as to keep the consistency with earlier study.[6] The solvent effects were taken into account in these calculations by using the SMD continuum model with the HF/6-31G* level of theory.[52] The SMD solvent model was chosen as one of the most accurate implicit solvent methods[53] with relatively low error bars for charged as well as neutral molecules.[52] LANL2DZ basis set was used for iodine atom in these solvent calculations. However, the SMD solvent model was not parameterised on iodine compounds.[54] So, special care should be taken when using such iodinated systems, as we aimed at a comparable level of accuracy.

Results and Discussion

The molecular properties (μ, $V_{s,max}$, polarisability, LUMO energy and solvation free energy) of the *exo*-substituted carboranes are compared with those of the corresponding aromatic and cyclic aliphatic organic compounds.

Electrostatic properties

Dipole moment (μ). The vector μ describes the charge distribution in a molecule, gives clues about its potential electrostatic interactions and also partially influences the solvation free energy. For the 6-vertex carborane cages (Table 1A), the 1,6-C_2B_4 molecules have obviously lower μ than the 1,2-isomers (6_T- vs. 6_C-, respectively). In the former group, the mono-hydroxyl penta-fluoro compounds, 6_T-OH^{C}F and 6_T-OH^{B}F, have the highest μ of nearly 2.0 D. The latter class attains the μ of ca 2.4 D for 6_C-OH^{C}H, 6_C-OH^{C}F and 6_C-Br^{B}H for two hydroxylated and one brominated compound. The μ for hydrocarbons is similar, for the aromatic ones it ranges from 0.5 to 2.0 D and for the cyclic aliphatic (6^S-compounds) it is 1.4–2.9 D. The μ of the 12-vertex cages is larger, up to 6.0 D (Table 1B), increasing from the *para*- via *meta*- to the *ortho*-carboranes. The largest values are obtained for iodinated compounds, especially for the iodo compound 12_O-I^{B}H (6.0 D, Fig. 2B). The increase in the polarity of 12-vertex carborane cages (not only in comparison with the 6-vertex cages but also in the absolute values) is dramatic and gives evidence about the significant electrostatic (and thus total stabilisation) energy of the complexes formed between these carboranes and polar systems.

Electrostatic potential. A useful way of describing the electrostatic properties of a molecule is to use its electrostatic potential (ESP). It can show either a uniform electron distribution, e.g. the skeletal part of bromo-cyclohexane (Fig. 2A), or various anisotropies. The global anisotropy can be evaluated and visualised as the dipole moment (μ), as exemplified here for 12_O-I^BH (the blue arrow in Fig. 2B). A local anisotropy can take the form of e.g. a σ-hole as in 12_O-I^CF (Fig. 2C).

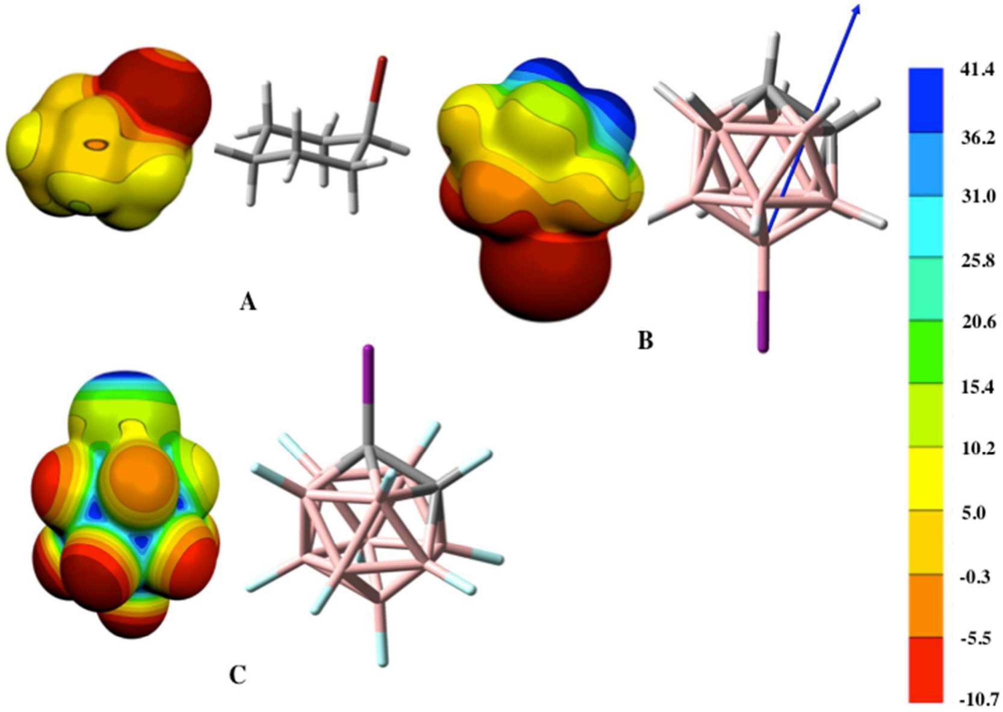


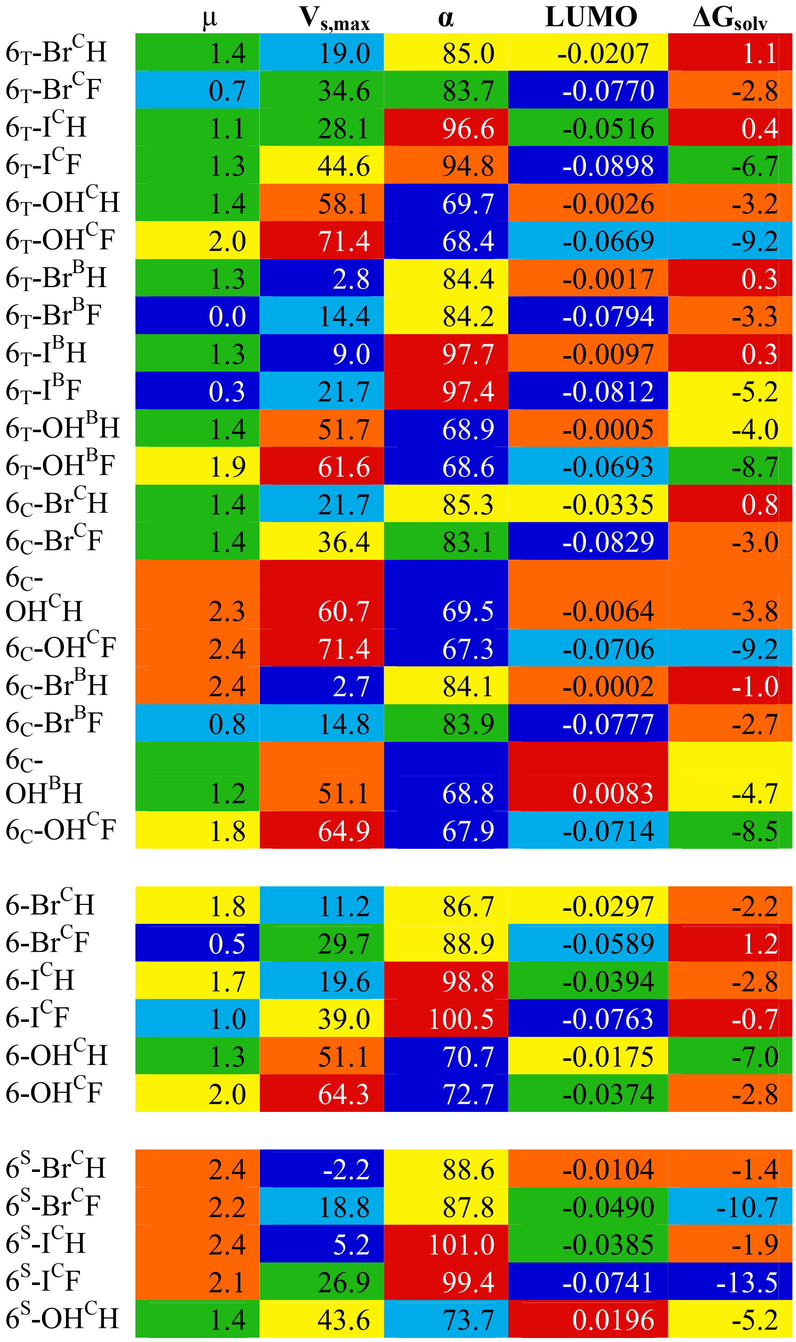
Fig. 2. Computed electrostatic potentials on 0.001a.u. molecular surfaces of selected systems. A) Bromo-cyclohexane; B) Iodo-o-carborane 12_O-I^BH with a high μ of 6.0 D, which is represented by the arrow; C) 12_O-I^CF. The colour of the ESP ranges in kcal/mol. Atom colour coding: [C: grey; H: white; B: light pink; Br: dark-red; I: magenta; F: cyan]. Fig. prepared with GaussView and MOLEKEL.[55]

It is known that the strength of X-bonds increases with the increasing magnitude (the most positive value of ESP on the X atom, $V_{s,max}$).[39] This finding makes it possible to predict the capabilities of the studied molecules to form X-bonds by calculating this one-electron property.

The results are summarised in Table 1. They show that the point of attachment of the X atom to the carborane cage has a crucial role. The B-bound Br atoms have consistently smaller $V_{s,max}$ as compared to C-bound Br atoms, in line with our previous finding[6] (Table 1). The B-bound X atoms have only slightly positive or even negative $V_{s,max}$ values, which are however less negative in the belt around the X atom (cf. Fig. 2). Additionally, the properties of the σ-holes significantly differ between the *cis* and *trans* isomers in the 6-vertex cages and the *ortho*, *meta* and *para* isomers in the 12-vertex cages. The $V_{s,max}$ is systematically larger for the C-bound X atoms of *cis* and *ortho* carborane compounds. For example, the $V_{s,max}$ of 6_T-Br^CH and 6_C-Br^CH is 19.0 and 21.7 kcal/mol, respectively. The $V_{s,max}$ of C-bound X atoms of *cis* and *ortho* carboranes is also found to be systematically more positive than that of comparable organic compounds, e.g. the $V_{s,max}$ of bromo-benzene (6-Br^CH) of 11.2 kcal/mol.[41] It is even more pronounced in the case of bigger molecules. $V_{s,max}$ of 12-Br^CH is 12.4 kcal/mol while that of 12_O-Br^CH is 31.6 kcal/mol.

Table 1: Various physical–chemical properties (dipole moment, μ in D; $V_{s,max}$ in kcal/mol; polarisability α in a.u.; LUMO energy in a.u.; solvation free energy, ΔG_{solv} in kcal/mol) are given as ranges. A – systems with six heavy atoms, B – systems with twelve heavy atoms. Colour coding: The ranges of values for all molecular characteristics in A and B were separated into 6 bins of equal size. In the order of descending values, the corresponding colours are: red, orange, yellow, green, cyan and blue.

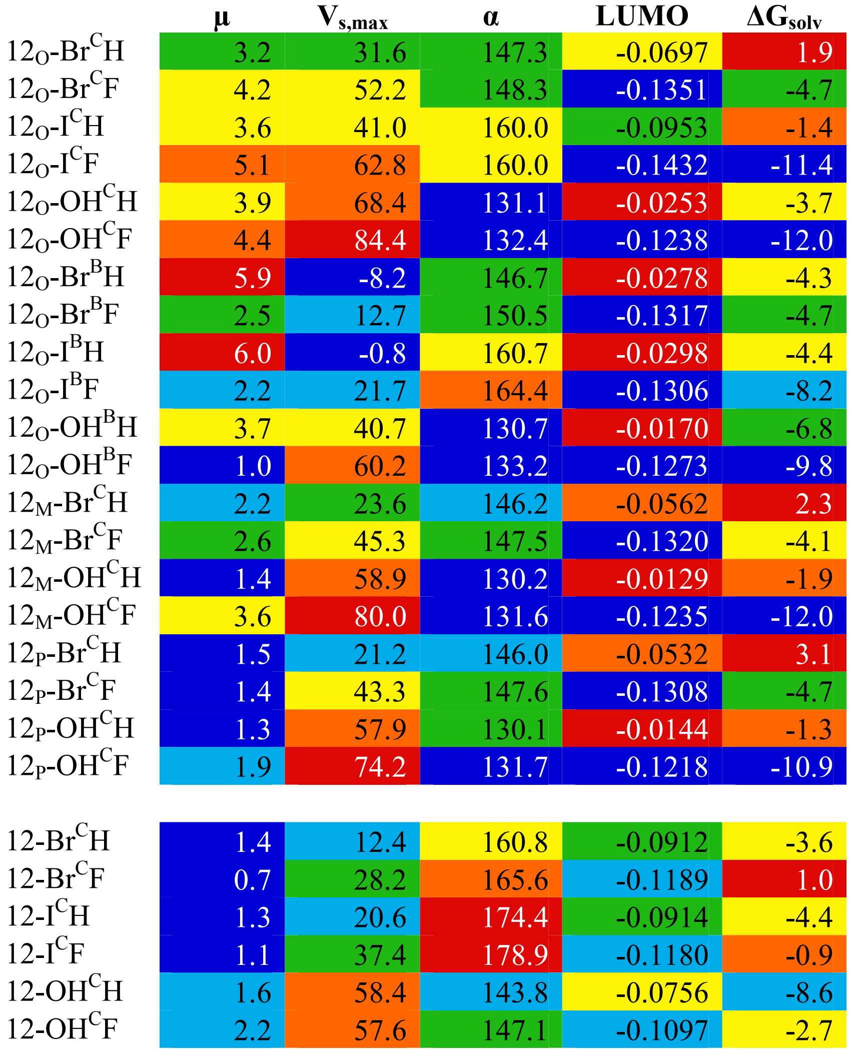
A, Six-vertex carboranes and small organic systems



	μ	$V_{s,max}$	α	LUMO	ΔG_{solv}
6_T-Br^{C}H	1.4	19.0	85.0	-0.0207	1.1
6_T-Br^{C}F	0.7	34.6	83.7	-0.0770	-2.8
6_T-I^{C}H	1.1	28.1	96.6	-0.0516	0.4
6_T-I^{C}F	1.3	44.6	94.8	-0.0898	-6.7
6_T-OH^{C}H	1.4	58.1	69.7	-0.0026	-3.2
6_T-OH^{C}F	2.0	71.4	68.4	-0.0669	-9.2
6_T-Br^{B}H	1.3	2.8	84.4	-0.0017	0.3
6_T-Br^{B}F	0.0	14.4	84.2	-0.0794	-3.3
6_T-I^{B}H	1.3	9.0	97.7	-0.0097	0.3
6_T-I^{B}F	0.3	21.7	97.4	-0.0812	-5.2
6_T-OH^{B}H	1.4	51.7	68.9	-0.0005	-4.0
6_T-OH^{B}F	1.9	61.6	68.6	-0.0693	-8.7
6_C-Br^{C}H	1.4	21.7	85.3	-0.0335	0.8
6_C-Br^{C}F	1.4	36.4	83.1	-0.0829	-3.0
6_C-OH^{C}H	2.3	60.7	69.5	-0.0064	-3.8
6_C-OH^{C}F	2.4	71.4	67.3	-0.0706	-9.2
6_C-Br^{B}H	2.4	2.7	84.1	-0.0002	-1.0
6_C-Br^{B}F	0.8	14.8	83.9	-0.0777	-2.7
6_C-OH^{B}H	1.2	51.1	68.8	0.0083	-4.7
6_C-OH^{C}F	1.8	64.9	67.9	-0.0714	-8.5
6-Br^{C}H	1.8	11.2	86.7	-0.0297	-2.2
6-Br^{C}F	0.5	29.7	88.9	-0.0589	1.2
6-I^{C}H	1.7	19.6	98.8	-0.0394	-2.8
6-I^{C}F	1.0	39.0	100.5	-0.0763	-0.7
6-OH^{C}H	1.3	51.1	70.7	-0.0175	-7.0
6-OH^{C}F	2.0	64.3	72.7	-0.0374	-2.8
6^S-Br^{C}H	2.4	-2.2	88.6	-0.0104	-1.4
6^S-Br^{C}F	2.2	18.8	87.8	-0.0490	-10.7
6^S-I^{C}H	2.4	5.2	101.0	-0.0385	-1.9
6^S-I^{C}F	2.1	26.9	99.4	-0.0741	-13.5
6^S-OH^{C}H	1.4	43.6	73.7	0.0196	-5.2

6^S-OH^CF	2.9	57.0	73.2	-0.0003	-14.1

B. 12-vertex carboranes and big organic systems.



	μ	$V_{s,max}$	α	LUMO	ΔG_{solv}
12_{O}-Br$^{\mathrm{C}}$H	3.2	31.6	147.3	-0.0697	1.9
12_{O}-Br$^{\mathrm{C}}$F	4.2	52.2	148.3	-0.1351	-4.7
12_{O}-I$^{\mathrm{C}}$H	3.6	41.0	160.0	-0.0953	-1.4
12_{O}-I$^{\mathrm{C}}$F	5.1	62.8	160.0	-0.1432	-11.4
12_{O}-OH$^{\mathrm{C}}$H	3.9	68.4	131.1	-0.0253	-3.7
12_{O}-OH$^{\mathrm{C}}$F	4.4	84.4	132.4	-0.1238	-12.0
12_{O}-Br$^{\mathrm{B}}$H	5.9	-8.2	146.7	-0.0278	-4.3
12_{O}-Br$^{\mathrm{B}}$F	2.5	12.7	150.5	-0.1317	-4.7
12_{O}-I$^{\mathrm{B}}$H	6.0	-0.8	160.7	-0.0298	-4.4
12_{O}-I$^{\mathrm{B}}$F	2.2	21.7	164.4	-0.1306	-8.2
12_{O}-OH$^{\mathrm{B}}$H	3.7	40.7	130.7	-0.0170	-6.8
12_{O}-OH$^{\mathrm{B}}$F	1.0	60.2	133.2	-0.1273	-9.8
12_{M}-Br$^{\mathrm{C}}$H	2.2	23.6	146.2	-0.0562	2.3
12_{M}-Br$^{\mathrm{C}}$F	2.6	45.3	147.5	-0.1320	-4.1
12_{M}-OH$^{\mathrm{C}}$H	1.4	58.9	130.2	-0.0129	-1.9
12_{M}-OH$^{\mathrm{C}}$F	3.6	80.0	131.6	-0.1235	-12.0
12_{P}-Br$^{\mathrm{C}}$H	1.5	21.2	146.0	-0.0532	3.1
12_{P}-Br$^{\mathrm{C}}$F	1.4	43.3	147.6	-0.1308	-4.7
12_{P}-OH$^{\mathrm{C}}$H	1.3	57.9	130.1	-0.0144	-1.3
12_{P}-OH$^{\mathrm{C}}$F	1.9	74.2	131.7	-0.1218	-10.9
12-Br$^{\mathrm{C}}$H	1.4	12.4	160.8	-0.0912	-3.6
12-Br$^{\mathrm{C}}$F	0.7	28.2	165.6	-0.1189	1.0
12-I$^{\mathrm{C}}$H	1.3	20.6	174.4	-0.0914	-4.4
12-I$^{\mathrm{C}}$F	1.1	37.4	178.9	-0.1180	-0.9
12-OH$^{\mathrm{C}}$H	1.6	58.4	143.8	-0.0756	-8.6
12-OH$^{\mathrm{C}}$F	2.2	57.6	147.1	-0.1097	-2.7

In the case of halogenated hydrocarbons, it has been shown that the properties of the σ-holes can be modulated by increasing the atomic number of the X atom and by introducing electron-withdrawing F atoms on the ring with the X atom.[40] When comparing the $V_{s,max}$ in Br- and I-substituted compounds, the latter is consistently larger by 6.7 to 10.6 kcal/mol (Table 1). It is worth mentioning here that it is possible to compare Br and I in this study only due to the use of a basis set including effective core potentials. The ability to tune the X-bond by Br-to-I substitution in boron clusters is thus similar to the situation known from hydrocarbons. It has already been used to increase the inhibition activity of halogenated organic inhibitors.[33,34,36,38] Similarly, the presence of the electron-withdrawing groups has comparable effects in the carboranes and the hydrocarbons. Upon the perfluorination of both the boron clusters and hydrocarbons, the $V_{s,max}$ consistently increases by 9–23 kcal/mol (Table 1). The combination of both effects, Br-to-I substitution and the addition of the electron-withdrawing F atoms, leads to the remarkable $V_{s,max}$ value of 62.8 kcal/mol for 12_O-I^CF (Table 1B).

We conclude this section by stating that C-bound X atoms as the *exo*-substituents of the neutral carboranes possess σ-holes with larger magnitudes than the corresponding hydrocarbons. This unambiguously means that these substituted carboranes should form, as compared to organic compounds, stronger X-bonds with the same electron donors (D). The tuning of the magnitude of the σ-hole by e.g. fluorination is comparably efficient in the substituted carboranes and in hydrocarbons. This means that the strength of the X-bonds formed can be efficiently and largely modulated. The significantly larger σ-hole at the C-bound X atoms on carboranes indicates the existence of strong C-X…D halogen bonds, which could be the structure-making motif. This will not be the case for the B-X…D motif.

Dispersion Energy

Dispersion energy between two systems is proportional to their polarisability. For the 6-vertex cages, the calculated molecular polarisabilities of carboranes are comparable with those of small aromatic and cyclic aliphatic organic systems (e.g. the α of 6_T-Br^CH, 6-Br^CH and 6_S-Br^CH equals 85.0, 86.7 and 88.6 a.u., respectively, Table 1A). In the case of larger organic aromatic molecules, the polarisabilities are about 10 % smaller (e.g. the α of 12_O-Br^CH and 12-Br^CH equals 147.3 and 160.8 a.u., respectively, Table 1B). This indicates that the complexes of substituted carboranes should be stabilised by dispersion energy comparable to or only slightly smaller than the corresponding complexes of similarly large organic molecules with the same charge. This is a surprising finding, because it is known that the dispersion energy of 2D aromatic organic compounds is large and forms a dominant part of the substantial stabilisation of the respective complexes. Evidently, a similar phenomenon will also appear for 3D aromatic carboranes.

An easy alternative to generate molecular polarisabilities of extended systems is to use the known additivity of molecular polarisability.[56-57] The calculated molecular polarisabilities of organic compounds using the average atomic polarisability[56] are found in agreement with the calculated values obtained from the DFT methods. For example, compare the values for 6-Br^CH (89.1 a.u.), 6-Br^CF (90.8 a.u.), 6-OH^CH (71.9 a.u.), and 6-OH^CF (73.6 a.u.) with those in Table 1. Similarly, the average BH-group polarisability of carborane systems can also be determined with the help of the calculated polarisability of small organic molecules. For example, the average BH-group polarisability of brominated carboranes can be calculated by using the polarisability of monobromoacetylene (C_2HBr: 39.5 a.u.). The average BH-group polarisability of 6_T-Br^CH is 11.4 a.u., whereas for 12_O-Br^CH, the value is 10.8 a.u.

Charge transfer

Charge transfer is a mathematical formulation of polarization, which help predict the polarization and strength in noncovalently bound complexes. The charge-transfer energy, which is part of polarization occurs between an electron donor and an electron acceptor and is proportional to the ionisation potential of the former and the electron affinity of the latter. In the first approximation, the electron affinity of a system is proportional to the energy of the lowest unoccupied molecular orbital (LUMO) – the lower the energy of the LUMO, the higher the charge-transfer energy is expected.

The LUMO energies of the parental 6-vertex cages are found to be comparable with those of the corresponding organic compounds in the cases where the Br atom is bound to the C vertex (e.g. the LUMO of 6_T-Br^CH, 6_C-Br^CH, 6-Br^CH and 6^S-Br^CH is -0.0207, -0.0335, -0.0297 and -0.0104 a.u., respectively, Table 1A). The compounds with Br bound to the B vertex have the LUMO energy significantly less negative (i.e. these systems are worse electron acceptors). The introduction of the electron-withdrawing F atoms to the boron cage has made the LUMO-energy levels systematically more negative (i.e. better electron acceptors). Significantly lower LUMO energy levels have been found for the 12-vertex carboranes than for the 6-vertex cages. However, the LUMO-energy levels were less negative than those of large organic compounds (for example, the LUMO of 12_O-Br^CH and 12-Br^CH was -0.0697 and -0.0912 a.u., respectively; see Table 1B).

It may be concluded that the carboranes *exo*-substituted on the C vertex are comparable or slightly worse electron acceptors than the organic compounds studied. Consequently, the charge-transfer binding energy of these carboranes is predicted to be similar to or slightly smaller than that of comparable organic compounds.

Solvation

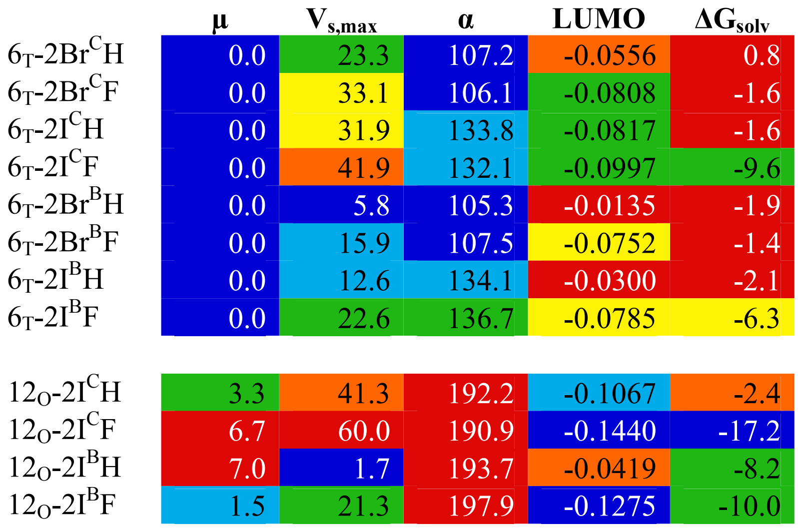
High polarity or even the presence of charge on one of the subsystems indicates a higher gas-phase interaction energy. In the presence of a solvent, the respective electrostatic interaction is damped and this damping can be dramatic (for example, in protein–ligand interactions; see Reference 38). It has also been shown that the hydrogen bonds formed between organic ligands and the protein may be stronger in the gas-phase than halogen bonds but the desolvation penalty renders them weaker.[44] It is thus important to study the solvation in conjunction with the gas-phase characteristics.

The calculated solvation free energy ΔG_{solv} shows that carboranes are solvated worse than hydrocarbons. Moreover, halogenated systems are solvated worse than hydroxylated compounds (the ΔG_{solv} is less negative or even positive; see Table 1). These compounds will thus have a smaller desolvation penalty when forming a complex in water environment. Consequently, the final binding free energy of carboranes is expected to be larger (more favourable) than that of hydrocarbons. An inspection into the studied trends within the brominated carboranes reveals that they are solvated better when the Br atom is bound to the B vertex (the ΔG_{solv} of 12_O-Br^CH and 12_O-Br^BH is 1.9 and -4.3 kcal/mol, respectively; see Table 1B), which correlates with the μ of these molecules. Similarly, the *cis*-carboranes are solvated better than the *trans* isomers and the *ortho*-carboranes are solvated better than the *meta* and *para* isomers. Additionally, the results show that fluorination can make ΔG_{solv} more negative (with the ΔG_{solv} of 12_O-Br^CH and 12_O-Br^CF being 1.9 and -4.7 kcal/mol, respectively). This finding should be considered when the fluorination is used to tune the X-bond strength, because it might simultaneously increase the desolvation penalty.

Di-brominated and di-iodinated carboranes

So far, we have only studied the properties of mono-halogenated compounds in order to be able to compare them with the more-studied and better-known organic compounds. However, it is often more difficult to synthesise mono-halogenated carboranes than di-halogenated species. In the case of the 6-vertex cages, 2-X-1,6-$C_2B_4H_5$ and 2,4-X-1,6-$C_2B_4H_4$ have been synthesised.[58] In the case of 12-vertex cages, 1-X-1,2-$C_2B_{10}H_{11}$ and 9,10-X_2-1,2-$C_2B_{10}H_{10}$ have been synthetised.[12] Therefore, we extend our study by selected di-brominated and di-iodinated carboranes. The properties of these compounds are summarised in Table 2. Obviously, they are similar to the properties of mono-brominated and mono-ionidated carboranes with the exception of polarisability. As could be expected, α is considerably larger in di-halogenated compounds. Consequently, the dispersion energy of complexes formed by di-halogenated systems will be considerably larger than that of the complexes of monohalogenated systems. Furthermore, we have calculated quadrupole moments for the dihalogenated systems, where the overall dipole moment becomes zero due to symmetry (Table S1, ESI). The results show that in-plane components Q_{xx} and Q_{yy}, become strong when X-atoms bound to C atoms. The B-bound X atoms have positive out-of-plane component Q_{zz}.

Table 2: Various physico-chemical properties (dipole moment, μ in D; $V_{s,max}$ in kcal/mol; polarisability α in a.u.; LUMO energy in a.u.; solvation free energy, ΔG_{solv} in kcal/mol) are given for dibrominated and diiodinated carboranes.



	μ	$V_{s,max}$	α	LUMO	ΔG_{solv}
6_T-2Br^{C}H	0.0	23.3	107.2	-0.0556	0.8
6_T-2Br^{C}F	0.0	33.1	106.1	-0.0808	-1.6
6_T-2I^{C}H	0.0	31.9	133.8	-0.0817	-1.6
6_T-2I^{C}F	0.0	41.9	132.1	-0.0997	-9.6
6_T-2Br^{B}H	0.0	5.8	105.3	-0.0135	-1.9
6_T-2Br^{B}F	0.0	15.9	107.5	-0.0752	-1.4
6_T-2I^{B}H	0.0	12.6	134.1	-0.0300	-2.1
6_T-2I^{B}F	0.0	22.6	136.7	-0.0785	-6.3
12_O-2I^{C}H	3.3	41.3	192.2	-0.1067	-2.4
12_O-2I^{C}F	6.7	60.0	190.9	-0.1440	-17.2
12_O-2I^{B}H	7.0	1.7	193.7	-0.0419	-8.2
12_O-2I^{B}F	1.5	21.3	197.9	-0.1275	-10.0

Moreover, we have optimized the geometries of some selected systems at DFT-D3/B3LYP/def2-TZVPP level of theory and compared with the geometries obtained at B3LYP/def2-TZVPP level of theory. We only optimized isolated molecules in this study. Consequently, the consideration of the empirical dispersion had negligible effect on the optimized geometries. The calculated root-mean-square deviation (RMSD) is in the order of 10^{-3} -10^{-4} Å (Table S2, ESI). The largest deviations occur in 6^S-Br^{C}H and 6^S-I^{C}H of rmsd values 0.012 and 0.011 Å, respectively. Even in these molecules, the molecular properties (μ, $V_{s,max}$, α, LUMO energy and ΔG_{solv}) remain unchanged in optimized geometries (Table 1 and Table S3, ESI).

Conclusions

We have shown that carbon-bound halogen (X) atoms as *exo*-substituents of neutral *ortho*- 1,2-$C_2B_{10}H_{12}$ and *cis*- 1,2-$C_2B_4H_6$ carboranes possess σ-holes with a considerably larger magnitude than X atoms in the corresponding hydrocarbons. This means that X-substituted carboranes are predicted to form stronger X-bonds with the same electron donor than organic compounds. Moreover, the tuning of the $V_{s,max}$ of the σ-hole by e.g. fluorination is similarly efficient for substituted carboranes and for hydrocarbons. This means that the strength of the X-bonds formed can be efficiently and largely modulated. Furthermore, the desolvation penalties of substituted carboranes are smaller than those of the corresponding organic compounds while dispersion and charge-transfer energies are predicted to be comparable or slightly smaller. Putting everything together, it may thus be predicted that substituted carboranes have a potential to form stronger X-bonds than the comparable hydrocarbons, which will be even more pronounced in the medium. This study lays ground for the predictions of the noncovalent binding potential of substituted carboranes based on quantum chemical calculations. Such an approach can find its use in the engineering of novel materials or the design of new biomolecular ligands.

Electronic supplementary information (ESI) available: B3LYP/def2-TZVPP optimized Cartesian coordinates of isolated systems, including electronic energies and ESP surfaces.

Acknowledgements

This work was supported by the research project RVO 61388963, awarded by the Academy of Sciences of the Czech Republic. We acknowledge the financial support of the Czech Science Foundation (grant number P208/12/G016). We also thank the Gilead Sciences and IOCB Research Center for financial support. This work was also supported by the Operational Program Research and Development for Innovations—European Science Fund (grant number CZ.1.05/2.1.00/03.0058).

References

1 K. Karki, D. Gabel and D. Roccatano, *Inorg. Chem*. 2012, **51**, 4894−4896.
2 C. A. Reed, *Acc. Chem. Res.*, 1998, **31**, 325−332.
3 Z. Chen and R. B. King, *Chem. Rev*. 2005, **105**, 3613−3642.
4 J. Fanfrlík, M. Lepšík, D. Horinek, Z. Havlas and P. Hobza, *ChemPhysChem*, 2006, **7**, 1100−1105.
5 A. Pecina, M. Lepšík, J. Řezáč, J. Brynda, P. Mader, P. Řezáčová, P. Hobza and J. Fanfrlík, *J. Phys. Chem. B*, 2013, **117**, 16096−16104.
6 A. Pecina, M. Lepšík, D. Hnyk, P. Hobza and J. Fanfrlík, *J. Phys. Chem. A*, 2015, **119**, 1388−1395.

7 J. Fanfrlík, A. Přada, Z. Padělková, A. Pecina, J. Macháček, M. Lepšík, J. Holub, A. Růžička, D. Hnyk and P. Hobza, *Angew. Chem. Int. Ed.* 2014, **53**, 10139–10142.

8 B. Grüner, J. Rais, P. Selucký and M. Lučaníková, in Boron Science: New Technologies and Applications, ed. N. S. Hosmane, CRC Press, Boca Raton, New York, 2011, pp. 463–490.

9 P. Řezáčová, P. Cígler, P. Matějíček, M. Lepšík, J. Pokorná, B. Grüner and J. Konvalinka, in Boron Science: New Technologies and Applications, ed. N. S. Hosmane, CRC Press, New York, 2011, pp. 41–70.

10 J. Plešek, *Chem. Rev*. 1992, **92**, 269–278.

11 W. N. Lipscomb, in Boron Hydrides: The Physical Inorganic Chemistry Series. W. A. Benjamin, Inc.: New York. 1963.

12 R. N. Grimes, in *Carboranes*, (2nd Ed.), Academic Press Publications (Elsevier, Inc.), London-Amsterdam- Burlington- San Diego-Oxford. 2011.

13 M. Scholz and E. Hey-Hawkins, *Chem. Rev*. 2011, **111**, 7035–7062.

14 W. Preetz and G. Peters, *Eur. J. Inorg. Chem.* 1999, 1831–1846.

15 V. I. Bregadze, *Chem. Rev*. 1992, **92**, 209–223.

16 F. Issa, M. Kassiou and L. M. Rendina, *Chem. Rev*. 2011, **111**, 5701–5722.

17 Z. J. Lesnikowski, *Collect. Czech. Chem. Commun.* 2007, **72**, 1646–1658.

18 P. Cígler, M. Kožíšek, P. Řezáčová, J. Brynda, Z. Otwinowski, J. Pokorná, J. Plešek, B. Grüner, L. Dolečková-Marešová, M. Máša, J. Sedláček, J. Bodem, H.-G. Kräusslich, V. Král and J. Konvalinka, *Proc. Natl. Acad. Sci. U.S.A*. 2005, **102**, 15394–15399.

19 R. C. Reynolds, S. R. Campbell, R. G. Fairchild, R. L. Kisliuk, P. L. Micca, S. F. Queener, J. M. Riordan, W. D. Sedwick, W. R. Waud, A. K. W. Leung, R. W. Dixon, W. J. Suling and D. W. Borhani, *J. Med. Chem*. 2007, **50**, 3283–3289.

20 P. Mader, A. Pecina, P. Cígler, M. Lepšík, V. Šícha, P. Hobza, B. Grüner, J. Fanfrlík, J. Brynda and P. Řezáčová, *Biomed. Res. Int.* 2014, 389869.

21 J. Brynda, P. Mader, V. Šícha, M. Fábry, K. Poncová, M. Bakardiev, B. Grüner, P. Cígler and P. Řezáčová, *Angew. Chem. Int. Ed.* 2013, **52**, 13760–13763.

22 S. Fujii, H. Masuno, Y. Taoda, A. Kano, A. Wongmayura, M. Nakabayashi, N. Ito, M. Shimizu, E. Kawachi, T. Hirano, Y. Endo, A. Tanatani and H. Kagechika, *J. Am. Chem. Soc*. 2011, **133**, 20933–20941.

23 J. Fanfrlík, J. Brynda, J. Řezáč, P. Hobza and M. Lepšík, *J. Phys. Chem. B* **2008**, *112*, 15094–15102.

24 P. Metrangolo, G. Resnati, *Chem.-Eur. J.* 2001, **7**, 2511−2519.

25 L. H. Nguyen, P. N. Horton, M. B. Hursthouse, A. C. Legon, D. W. Bruce, *J. Am. Chem. Soc*. 2004, **126**, 16−17.

26 F. Guthrie, *J. Chem. Soc*., 1863, **16**, 239–244.

27 I. Remsen and J. F. Norris, *Am. Chem. J*., 1896, **18**, 90–96.

28 J.-M. Dumas, M. Kern and J. L. Janier-Dubry, *Bull. Soc. Chim. Fr*., 1976, 1785–1787.

29 J.-M. Dumas, H. Peurichard and M. J. Gomel, *Chem. Res. (S)*, 1978, 54–57.

30 P. Politzer, P. Lane, M. C. Concha, Y. Ma, J. S. Murray, *J Mol Model* 2007, **13**, 305–311.

31 T. Clark, M. Hennemann, J. S. Murray, P. Politzer, *J Mol Model* 2007, **13**, 291–296.

32 P. Auffinger, F. A. Hays, E. Westhof and P. S. Ho, *Proc. Natl. Acad. Sci. U.S.A*. 2004, **101**, 16789–16794.

33 R. Wilcken, M. O. Zimmermann, A. Lange, A. C. Joerger and F. M. Boeckler, *J. Med. Chem*. 2013, **56**, 1363−1388.

34 R. Wilcken, X. Liu, M. O. Zimmermann, T. J. Rutherford, A. R. Fersht, A. C. Joerger and F. M. Boeckler, *J. Am. Chem. Soc.* 2012, **134**, 6810−6818.

35 L. A. Hardegger, B. Kuhn, B. Spinnler, L. Anselm, R. Ecabert, M. Stihle, B. Gsell, R. Thoma, J. Diez, J. Benz, J.-M. Plancher, G. Hartmann, D. W. Banner, W. Haap and F. Diederich, *Angew. Chem. Int. Ed.* 2011, **50**, 314–318.

36 L. A. Hardegger, B. Kuhn, B. Spinnler, L. Anselm, R. Ecabert, M. Stihle, B. Gsell, R. Thoma, J. Diez, J. Benz, J.-M. Plancher, G. Hartmann, Y. Isshiki, K. Morikami, N. Shimma, W. Haap, D. W. Banner and F. Diederich, *ChemMedChem* 2011, **6**, 2048–2054.

37 P. Dobeš, J. Řezáč, J. Fanfrlík, M. Otyepka and P. Hobza, *J. Phys. Chem. B* 2011, **115**, 8581–8589.

38 J. Fanfrlík, M. Kolář, M. Kamlar, D. Hurný, F. X. Ruiz, A. Cousido-Siah, A. Mitschler, J. Řezáč, E. Munusamy, M. Lepšík, P. Matějíček, J. Veselý, A. Podjarny and P. Hobza, *ACS Chem. Biol.* 2013, **8**, 2484−2492.

39 M. Kolář, J. Hostaš and P. Hobza, *Phys. Chem. Chem. Phys.*, 2014, **16**, 9987–9996.

40 K. E. Riley, J. S. Murray, J. Fanfrlík, J. Řezáč, R. J. Solá, M. C. Concha, F. M. Ramos and P. Politzer, *J. Mol. Model.*, 2011, **17**, 3309–3318.

41 K. E. Riley, J. S. Murray, J. Fanfrlík, J. Řezáč, R. J. Solá, M. C. Concha, F. M. Ramos and P. Politzer, *J. Mol. Model.*, 2013, **19**, 4651–4659.

42 G. R. Desiraju, P. S. Ho, L. Kloo, A. C. Legon, R. Marquardt, P. Metrangolo, P. Politzer, G. Resnati and K. Rissanen, *Pure Appl. Chem.*, 2013, **85**, 1711–1713.

43 M. H. Kolář, P. Deepa, H. Ajani, A. Pecina, P. Hobza, *Top. Curr. Chem.*, 2015, **359**, 1–26.

44 J. Fanfrlík, F. X. Ruiz, A. Kadlčíková, J. Řezáč, A. Cousido-Siah, A. Mitschler, S. Haldar, M. Lepšík, M. H. Kolář, P. Majer, A. D. Podjarny and P. Hobza, *ACS Chem. Biol.* 2015, (DOI: 10.1021/acschembio.5b00151).

45 K. E. Riley, J. Řezáč and P. Hobza, *J. Mol. Model.* 2013, **19**, 2879–2883.

46 P. Deepa, B. V. Pandiyan, P. Kolandaivel and P. Hobza, *Phys. Chem. Chem. Phys.*, 2014, **16**, 2038–2047.

47 P. v. R. Schleyer and K. Najafian, *Inorg. Chem.* 1998, **37**, 3454–3470.

48 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, OÅN. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Gaussian 09, Revision D.01, Gaussian, Inc., Wallingford, CT, 2009.

49 F. Weigend and R. Ahlrichs, *Phys. Chem. Chem. Phys.* 2005, **7**, 3297–3305.

50 S. Grimme, J. Antony, S. Ehrlich, H. Krieg, *J. Chem. Phys.*, 2010, **132**, 154104.

51 R. F. W. Bader, M. Carroll, J. R. Cheeseman and C. Chang, *J. Am. Chem. Soc.*, 1987, **109**, 7968–7979.

52 A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys Chem. B.*, 2009, **113**, 6378–6396.

53 M. Kolář, J. Fanfrlík, M. Lepšík, F. Forti, F. J. Luque and P. Hobza, *J. Phys. Chem. B* 2013, **117**, 5950−5962.

54 R. F. Ribeiro, A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Comput. Aided. Mol. Des.* 2010, **24**, 317–333.

55 MOLEKEL, 4.3; Swiss Center for Scientific Computing: Manno, Switzerland, 2000.

56 R. Bosque and J. Sales, *J. Chem. Inf. Comput. Sci.* 2002, **42**, 1154–1163.

57 J. Wang, X.-Q. Xie, T. Hou and X. Xu, *J. Phys. Chem. A* 2007, **111**, 4443–4448.

58 G. A. Beltram and T. P. Fehlner, *J. Am. Chem. Soc.*, 1979, **101**, 6237–6244.