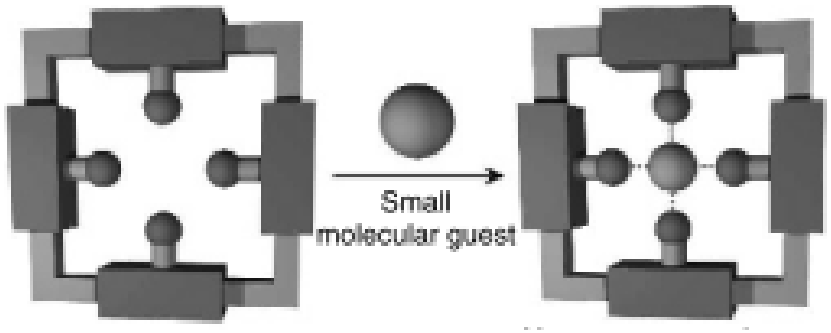
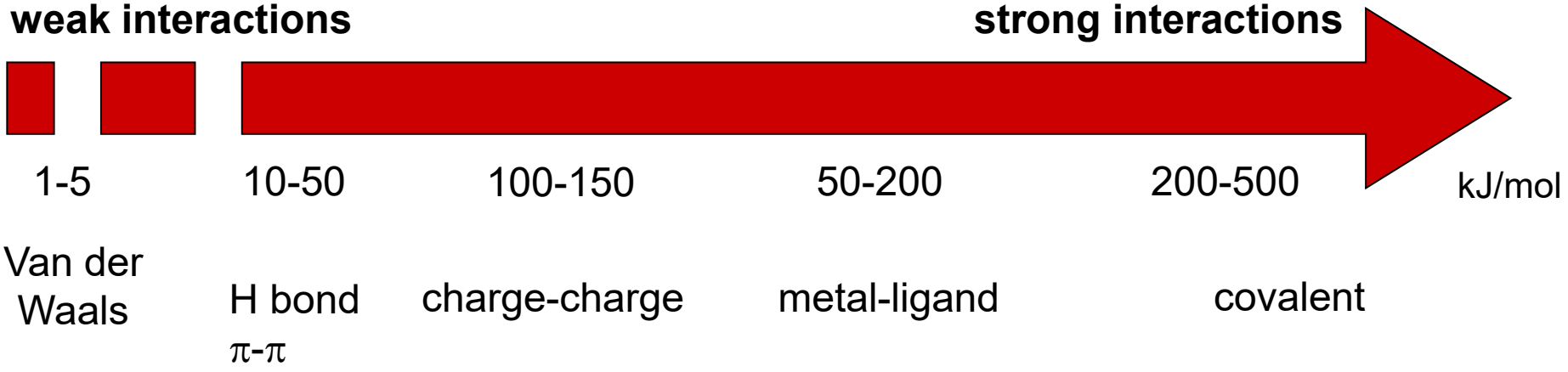

Small
molecular guest

Weak (Reversible) Intermolecular Interactions

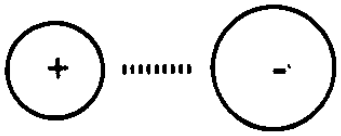
- Electrostatic
- π-π
- Cation-π/ Anion-π/CH-π
- H Bonding
- Halogen Bonding
- Metal-Ligand Coordination
- Reversible Covalent Bonding
- Chelate Effect
- Macrocyclic Effect
- Hydrophobic Effect

Weak (Reversible) Intermolecular Interactions

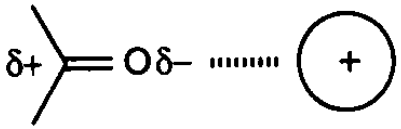


Reminder: to convert kJ in kcal, divide by 4.18

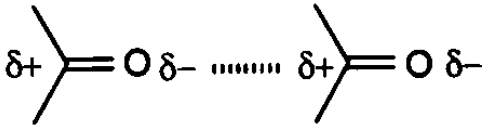
Electrostatic Interactions



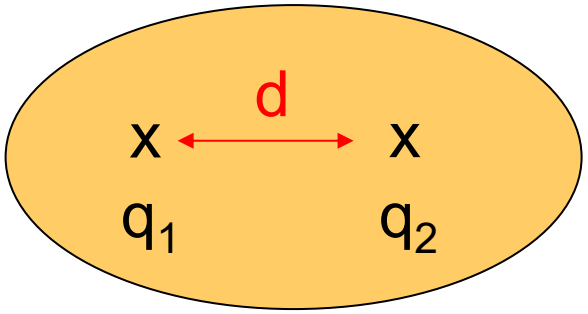
Charge-Charge Interactions 100-350 kJ/mol



Dipole-Charge Interactions 50-200 kJ/mol



Dipole-Dipole Interactions 5-50 kJ/mol



$$W = \frac{1}{4\pi\varepsilon_0}\frac{q_1 q_2}{\varepsilon d} \text{ (J)}$$

vacuum permittivity

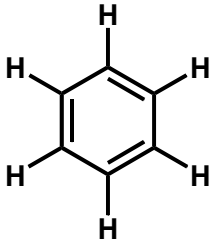
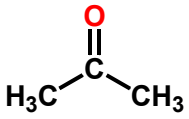
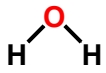
dielectric constant (nature of solvant)

ε(vacuum) = 1

apolar medium ⇔ ε small (~ 2)

polar medium ⇔ ε big (H_2O ~ 80)

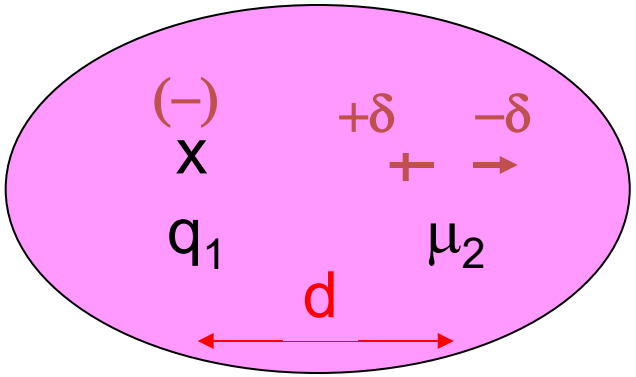
dielectric constant of the solvant

		ε
Benzene		2,3
Acetone		20,7
Ethanol	CH_3CH_2OH	24,3
water		78,5

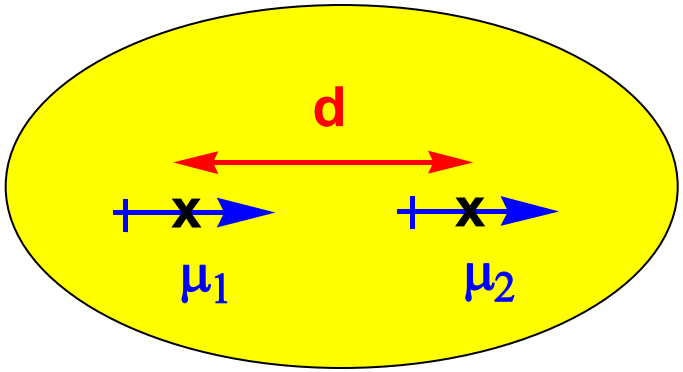
apolar ↓ polar

ε = 78.5 d = 0.5 nm => W = 3.75 kJ.mol^{-1}

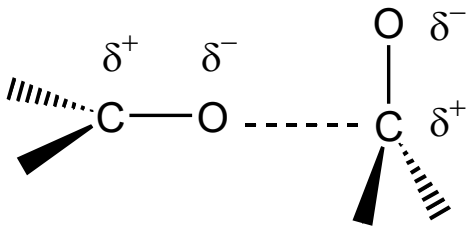
ε = 2 d = 0.5 nm => W = 140 kJ.mol^{-1}

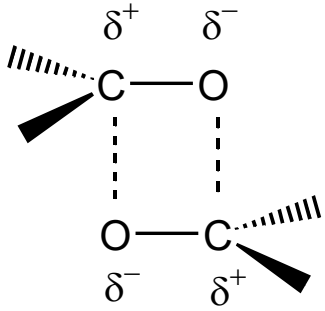


$$W = - C^{te} \times \frac{|q|\mu_2}{\varepsilon d^2}$$

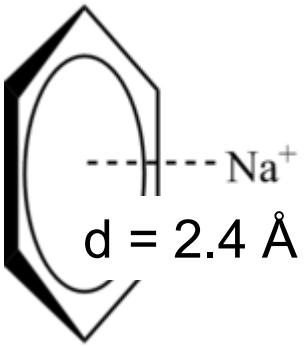


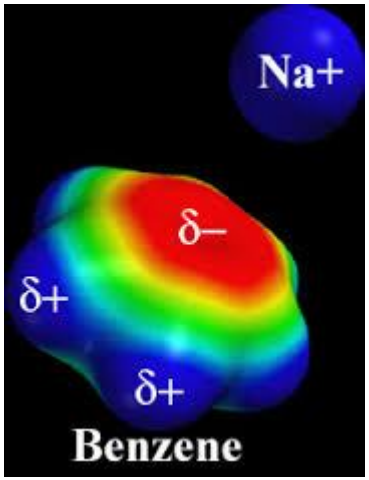
$$W = - C^{te} \frac{\mu_1 \mu_2}{\varepsilon d^3}$$

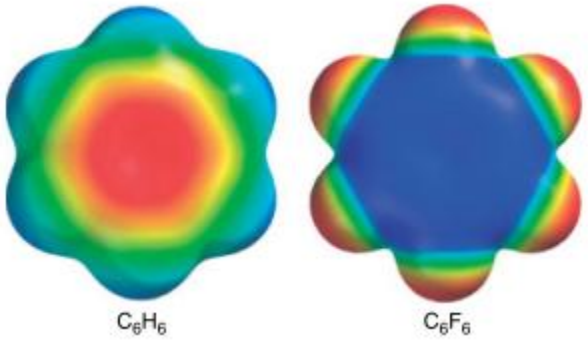




Cation-π Interactions







CHEMICAL REVIEWS

Review

pubs.acs.org/CR

dx.doi.org/10.1021/cr300222d | *Chem. Rev.* 2013, 113, 2100–2138

Cation–π Interaction: Its Role and Relevance in Chemistry, Biology, and Material Science

A. Subha Mahadevi and G. Narahari Sastry*

ACCOUNTS of chemical research

Vol. 46, No. 4 ■ 2013 ■ 885–893 ■ ACCOUNTS OF CHEMICAL RESEARCH

The Cation–π Interaction

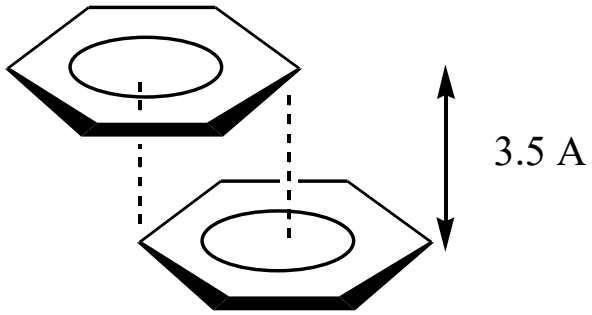
DENNIS A. DOUGHERTY

Chem. Rev. **1997,** *97,* 1303–1324

The Cation–π Interaction

Jennifer C. Ma and Dennis A. Dougherty*

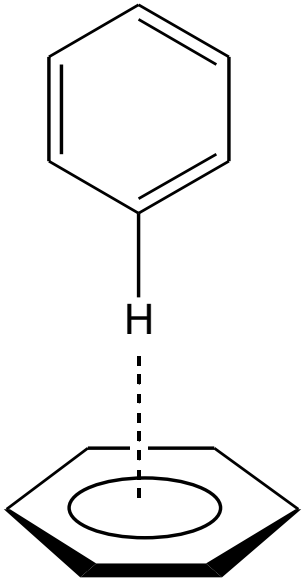
π-π Interactions up to 50 kJ/mol

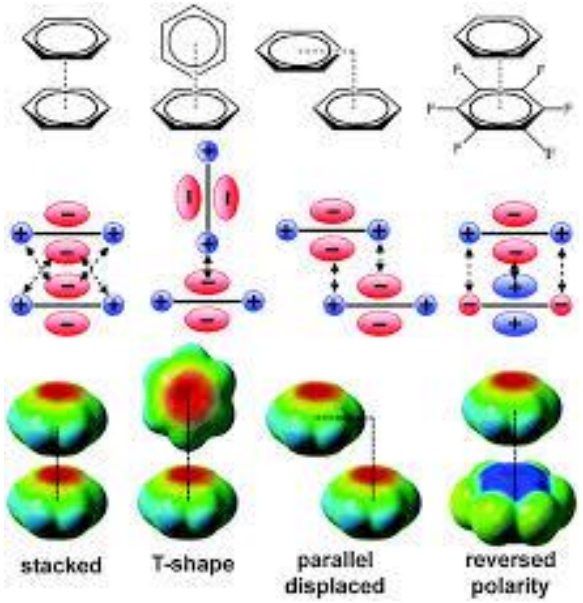


face to face

3.5 A

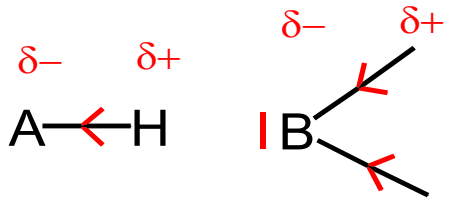
edge to face



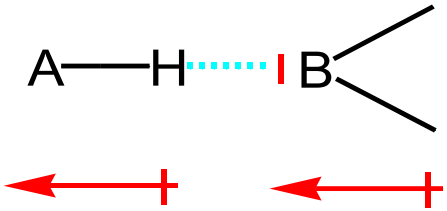


- C.A. Hunter and J.K.M. Sanders, ***The Nature of π - π interactions***, *J. Am. Chem. Soc.,* **1990**, *112*, 5525;
- E.-I. Kim, S. Paliwal and C.S. Wilcox, ***Measurements of molecular electrostatic field effects in edge-to-face aromatic interactions and CH- π interactions with implications for protein folding and molecular recognition***, *J. Am. Chem. Soc.*, **1998**, *120*, 11192.

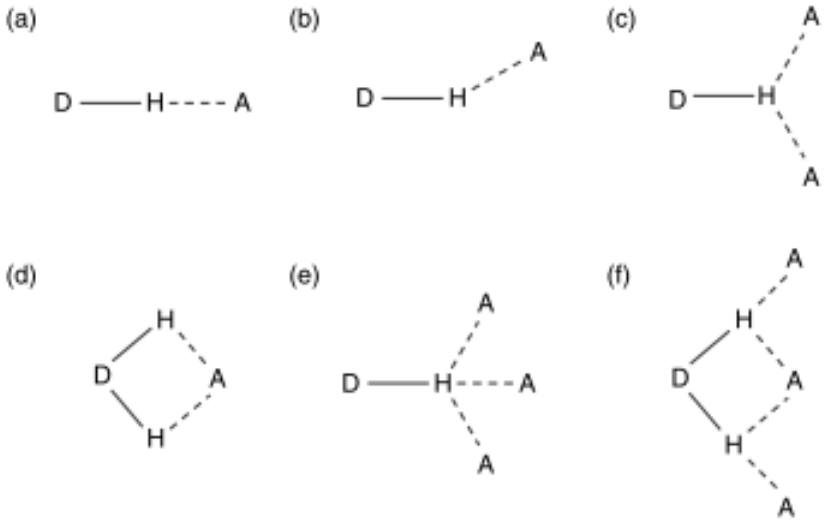
H Bond 4-120 kJ/mol

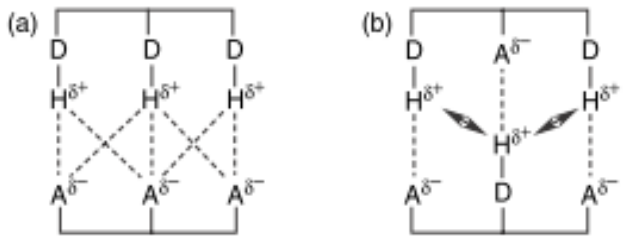


A, B electronegative or electrondeficient atoms



permanent dipoles



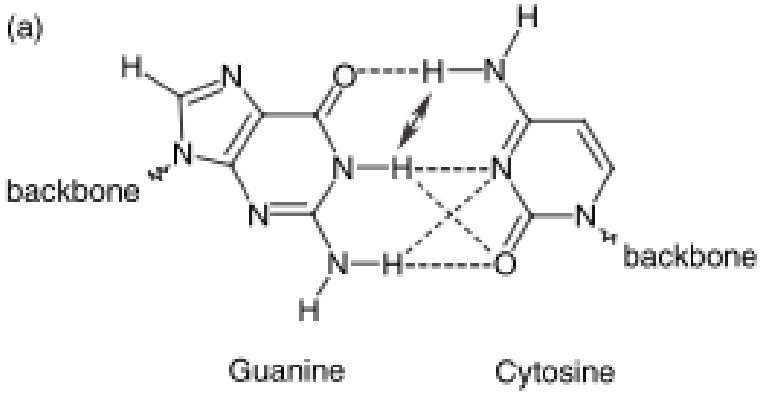


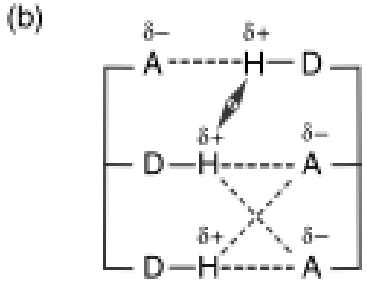
D Donor

A Acceptor

Attractive interaction

Repulsive interaction





	Strong	Moderate	Weak
interaction type	strongly covalent	mostly electrostatic	electrostat./ dispers.
bond lengths [Å]			
H ··· A	1.2 – 1.5	1.5 – 2.2	> 2.2
lengthening of X–H [Å]	0.08 – 0.25	0.02 – 0.08	< 0.02
X–H versus H ··· A	X–H ≈ H ··· A	X–H < H ··· A	X–H ≪ H ··· A
X ··· A [Å]	2.2 – 2.5	2.5 – 3.2	> 3.2
directionality	strong	moderate	weak
bond angles [°]	170 – 180	> 130	> 90
bond energy [kcal mol^{-1}]	15 – 40	4 – 15	< 4
relat. IR shift $\Delta\tilde{\nu}_{XH}$ [cm^{-1}]	25 %	10 – 25 %	< 10 %
^{1}H downfield shift	14 – 22	< 14	

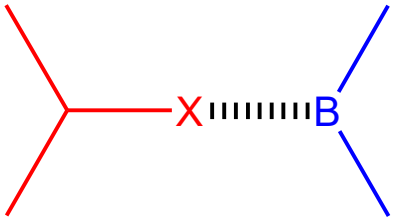
Halogen Bond

In 2009 the International Union of Pure and Applied Chemistry (IUPAC) started a project (project no. 2009-032-1-100) having the aim “ to take a comprehensive look at intermolecular interactions involving halogens as electrophilic species and classify them”
http://www.halogenbonding.eu/
http://www.iupac.org/web/ins/2009-032-1-100

An IUPAC recommendation defining these interactions as halogen bonds was issued in 2013 when the project was concluded: This definition states that

“ A halogen bond occurs when there is evidence of a net attractive interaction between an electrophilic region associated with a halogen atom in a molecular entity and a nucleophilic region in another, or the same, molecular entity. ”

Halogen Bond



B : Lewis base (neutral or anionic)

X : electron-poor halogen atom

- Very directional (180°, but also other geometries)
- As strong as H-bond
- Often encountered in solid state, more rarely in solution

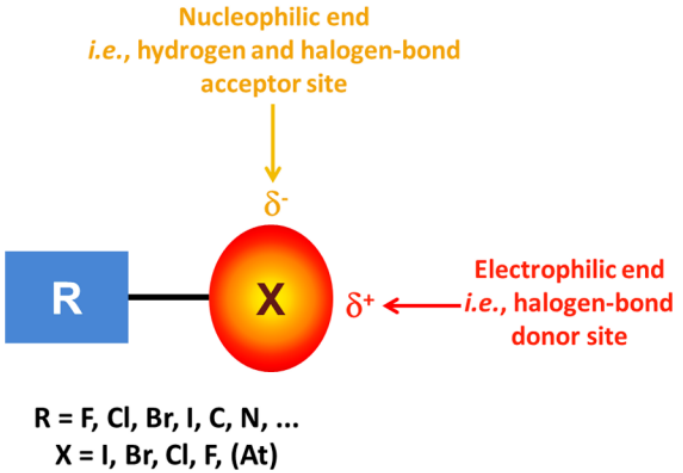
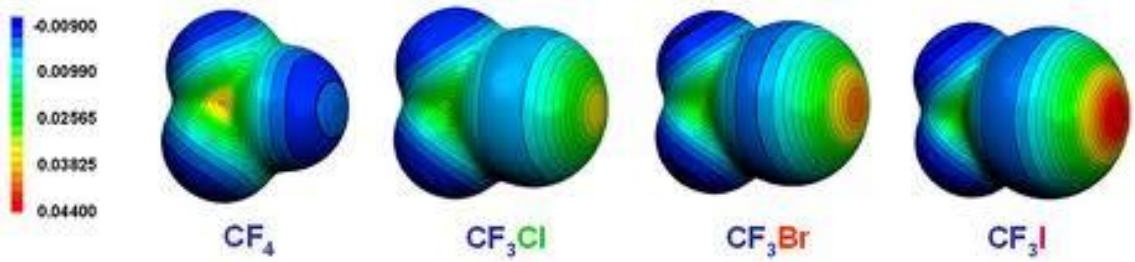


Figure 21. Schematic representation of the anisotropic distribution of the electron density around covalently bound halogen atoms and the pattern of the resulting interactions.



molecule	atom	bond producing a σ-hole
H_3C-F	F	C−F
H_3C-Cl	Cl	C−Cl
H_3C-Br	Br	C−Br
H_3C-I	I	C−I
F_3C-F	F	C−F
F_3C-Cl	Cl	C−Cl
F_3C-Br	Br	C−Br
F_3C-I	I	C−I
NC−F	F	C−F
NC−Cl	Cl	C−Cl
NC−Br	Br	C−Br
NC−I	I	C−I
		Dihalogens
F−F	F	F−F
Cl−Cl	Cl	Cl−Cl
Br−Br	Br	Br−Br
		Focus on Bromine
Br—C≡C—Br	Br	C−Br
H_3Si-Br	Br	C−Br
F_3Si-Br	Br	Si−Br
H_3Ge-Br	Br	Ge−Br
H_2N-Br	Br	N−Br
F_2N-Br	Br	N−Br
H_2P-Br	Br	P−Br
F_2P-Br	Br	P−Br
HO−Br	Br	O−Br
FO−Br	Br	O−Br
HS−Br	Br	S−Br
FS−Br	Br	S−Br
F−Br	Br	F−Br
Cl−Br	Br	Cl−Br

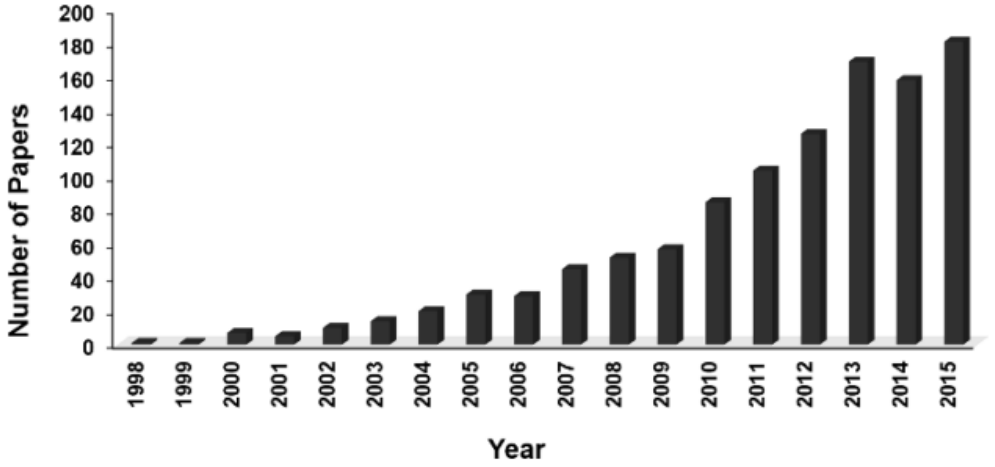
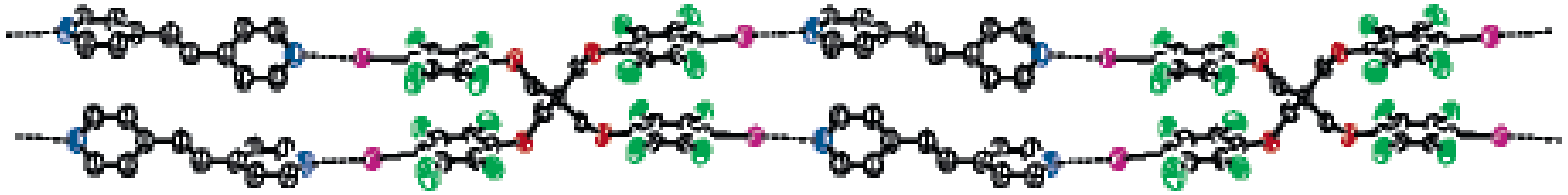
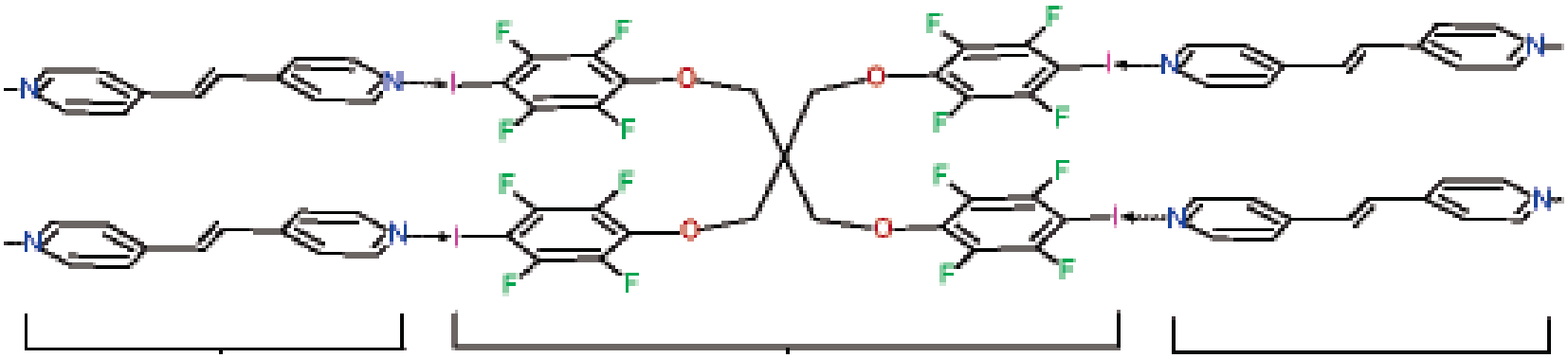
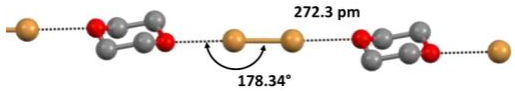


Figure 5. Number of papers per year having "halogen bonding" in the title and/or abstract (source SciFinder, search performed in November 2015).



14





Anion-π Interactions

Proposed by three research groups of theoreticians independently in 2002 based on their theoretical calculations, anion −π interactions are defined as attractive interactions between negatively charged species and electron-deficient aromatic rings.

Typical anion−π interaction indicates the attraction of an anion species to the centroid of an aromatic ring.

In comparison to a plethora of theoretical calculations of anion−π interactions, experimental studies on these intriguing noncovalent bond interactions are limited.

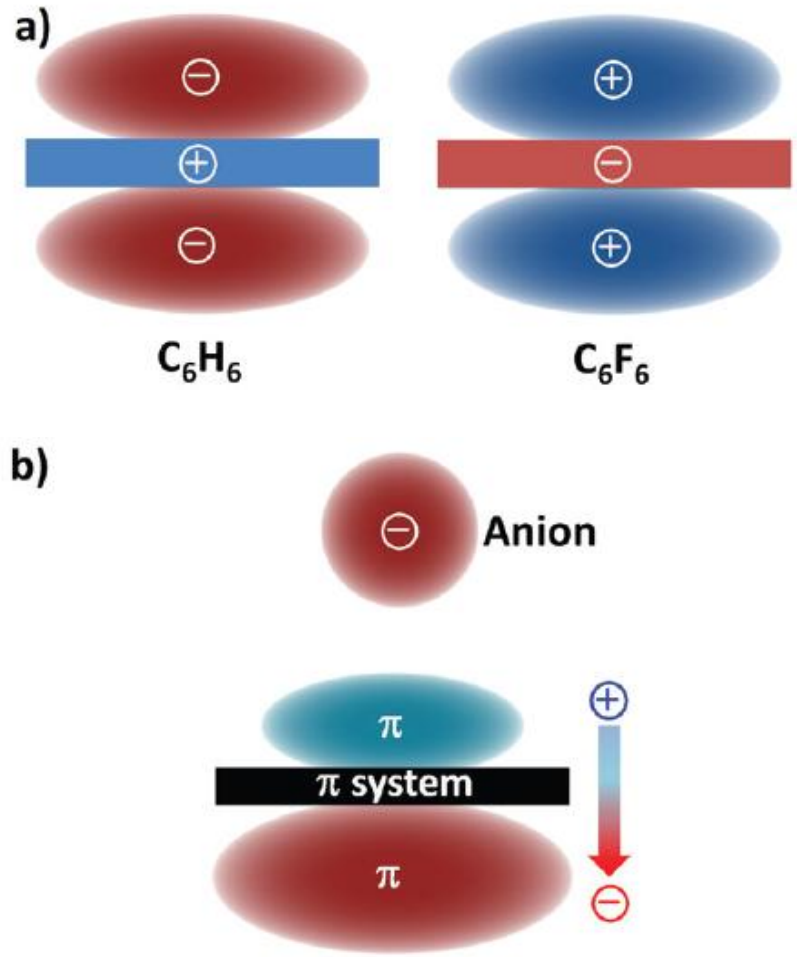


Fig. 1 (a) Schematic representation of the quadrupole moments of benzene (C_6H_6; Q_{zz} = −8.45 B) and hexafluorobenzene (C_6F_6; Q_{zz} = +9.50 B)[21] and (b) the ion-induced dipole[22] (the molecular polarizabilities parallel to the main symmetry axis are $\alpha_{\|}$ = 41.5 and 37.7 a.u (a.u. stands for atomic units), for benzene and hexafluorobenzene respectively).

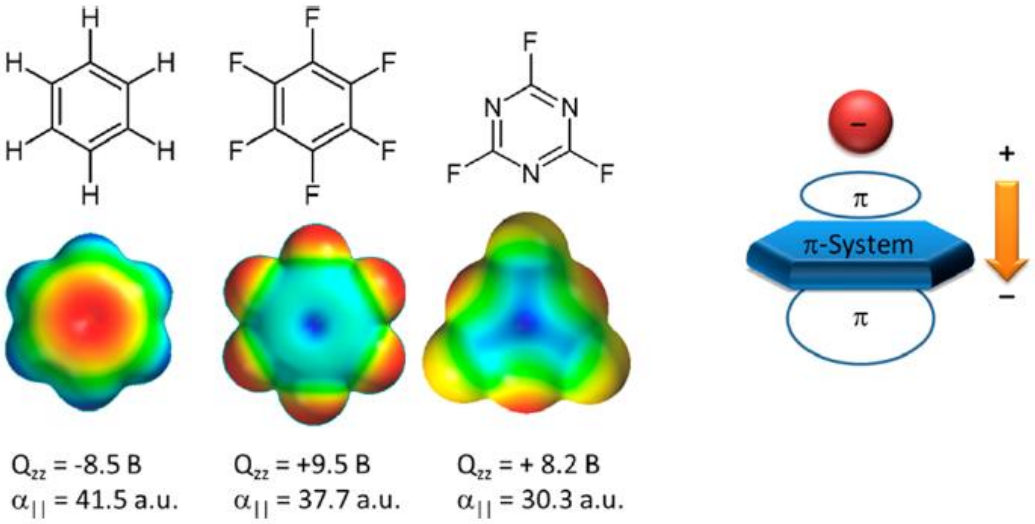


Figure 5. Structures and electron-density surfaces of selected arenes showing low electron density (blue region) in the aromatic core of C_6F_6 and $C_3N_3F_3$ (left). In addition the concept of "anion-induced dipole moment" is illustrated (right).[88]

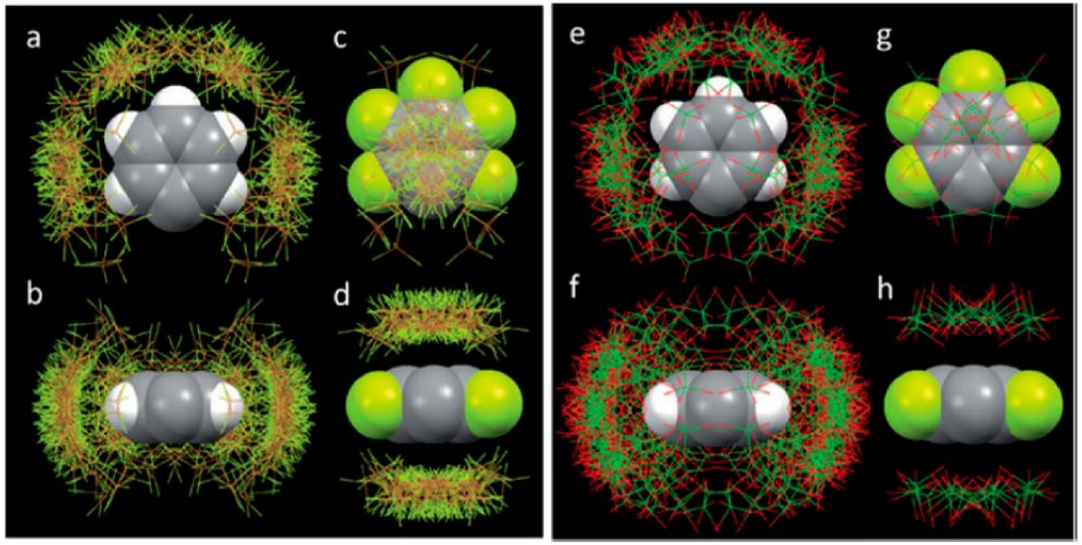


Figure 20. IsoStar plots showing anion contacts between C_6H_5 and BF_4^- (a and b) and ClO_4^- (e and f) as well as anion−π interactions between C_6F_5 and BF_4^- (c and d) and ClO_4^- (g and h). Reproduced and adapted with permission from ref 22. Copyright 2011 John Wiley and Sons.

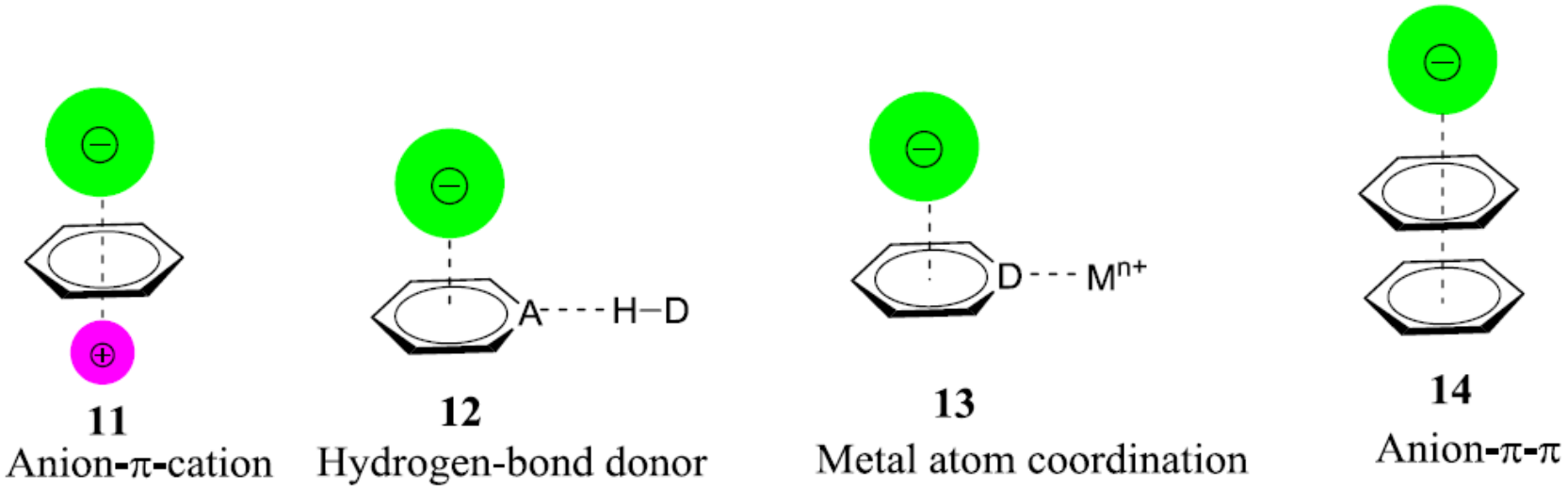


Fig. 4. Illustration of diverse factors affecting the strength of anion-π interactions.

Review Coordination Chemistry Reviews 415 (2020) 213327

Emergence of anion-π interactions: The land of opportunity in supramolecular chemistry and beyond

Ishfaq Ahmad Rather, Shafieq Ahmad Wagay, Rashid Ali *

Anion–π Interactions with Fluoroarenes

Michael Giese,*,† Markus Albrecht,*,‡ and Kari Rissanen*,§

DOI: 10.1021/acs.chemrev.5b00156
Chem. Rev. 2015, 115, 8867–8895

The anion–π interaction: naissance and establishment of a peculiar supramolecular bond

Patrick Gamez[a,b]

Cite this: *Inorg. Chem. Front.*, 2014, **1**, 35

Supramolecular Chemistry

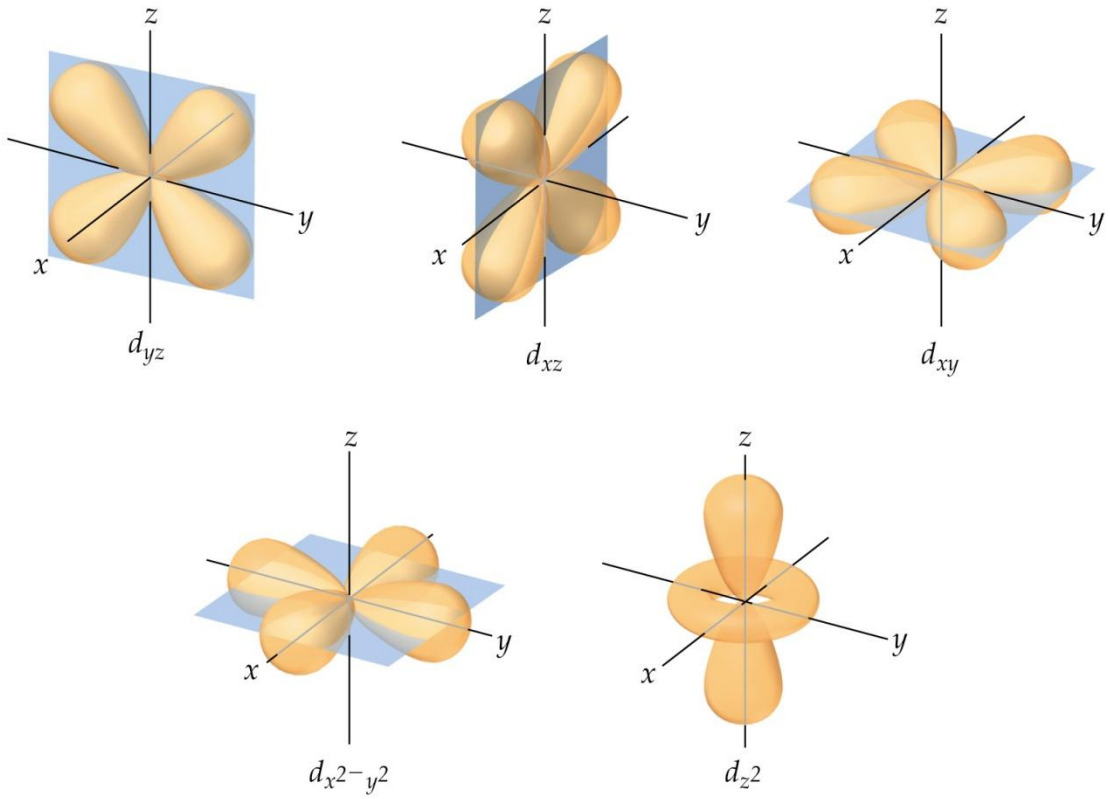
DOI: 10.1002/anie.201100208

Putting Anion–π Interactions Into Perspective

Antonio Frontera, Patrick Gamez,* Mark Mascal,* Tiddo J. Mooibroek,* and Jan Reedijk**

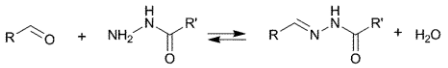
Angew. Chem. Int. Ed. **2011**, 50, 9564 – 9583

Metal-Ligand Interaction

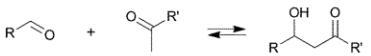


Covalent Reversible reactions

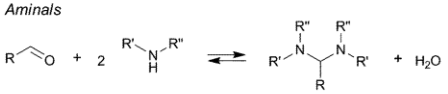
Acylhydrazones



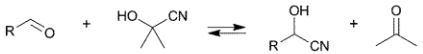
Aldols



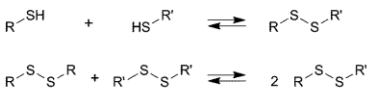
Aminals



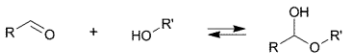
Cyanohydrins



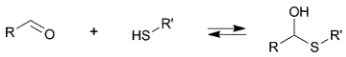
Disulfides



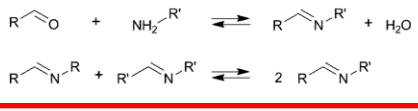
Hemiacetals



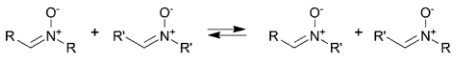
Hemithioacetals



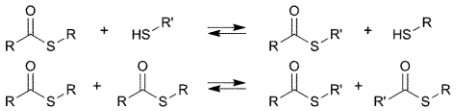
Imines (Schiff bases)



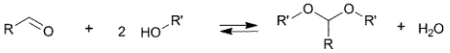
Nitrones



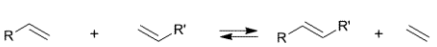
Thioesters



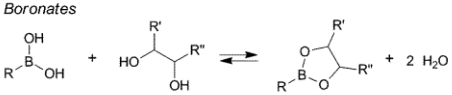
Acetals



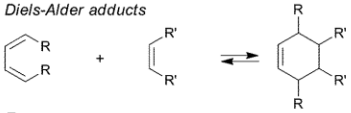
Alkenes



Boronates



Diels-Alder adducts



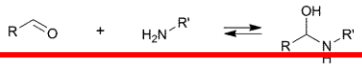
Esters



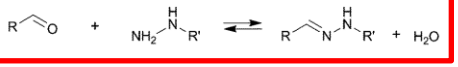
Formamidines:



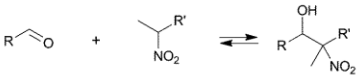
Hemiaminals



Hydrazones



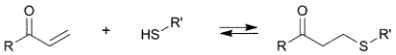
Nitroaldols



Oximes



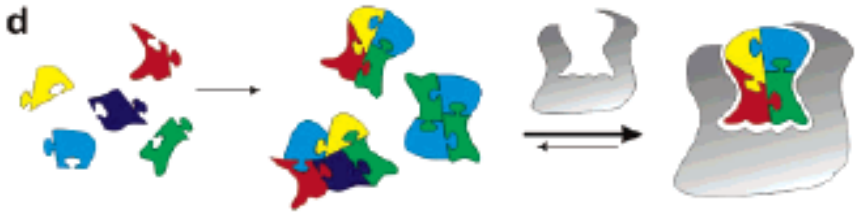
Thioethers



To facilitate the analysis of a library, and in particular to avoid shifting of its composition, DCLs can be "frozen" after having reached equilibrium in the presence of the target substrate. This can be achieved by changing the conditions of the reversible reactions, *e.g.* by further irreversible functionalisation of the labile reaction products, such as by reducing reversibly formed imines to their corresponding amines (reductive amination),[97,102,103] or by derivatising them in an Ugo reaction.[104] Other reversible systems have been slowed down by pH changes, *e.g.* by decreasing the pH of a mixture of disulfides, which easily interchange under neutral or slightly alkaline conditions but are stable at low pH,[98,105,106] or by increasing the pH of a mixture of acetals,[107] hydrazones[89,108–111] and others,[111,112] which readily hydrolyse under acidic conditions and which are stable at neutral pH. In catalysed reversible reactions, the removal or inactivation of the catalyst will transform the DCL into a static library, which can then be screened and analysed.[85,113]

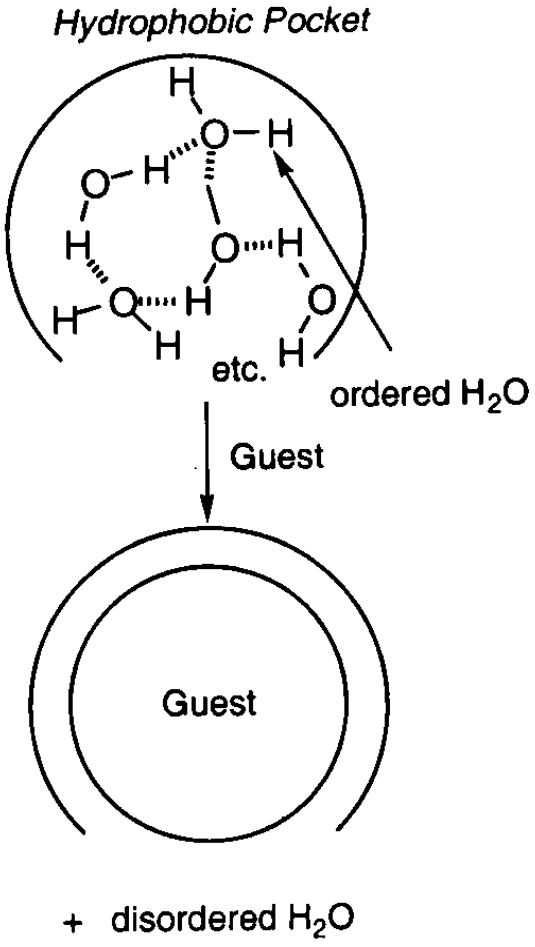
Selection of a host by a separately introduced guest

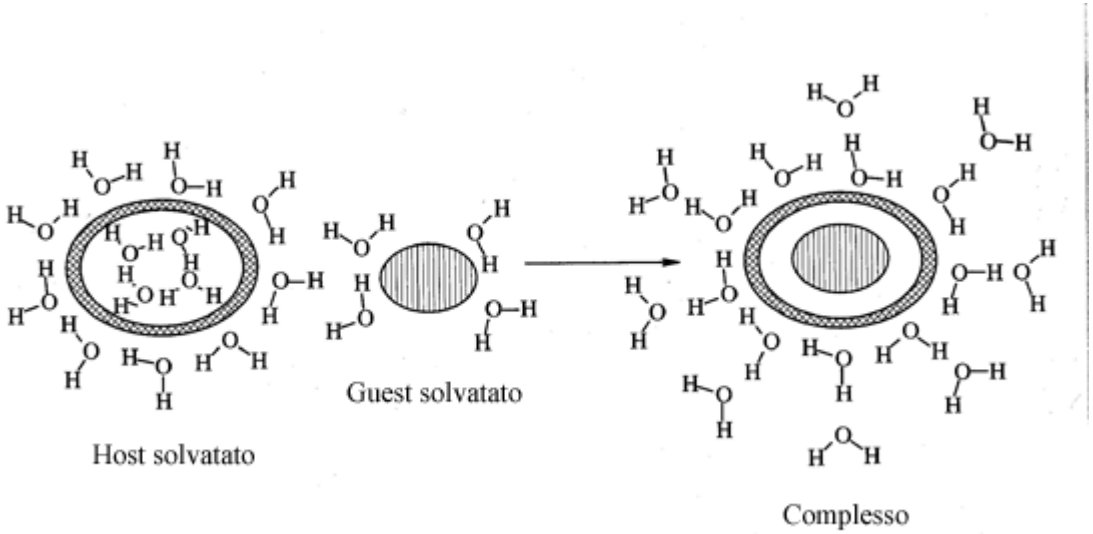




Selection of a guest by a separately introduced host

Hydrophobic Effect





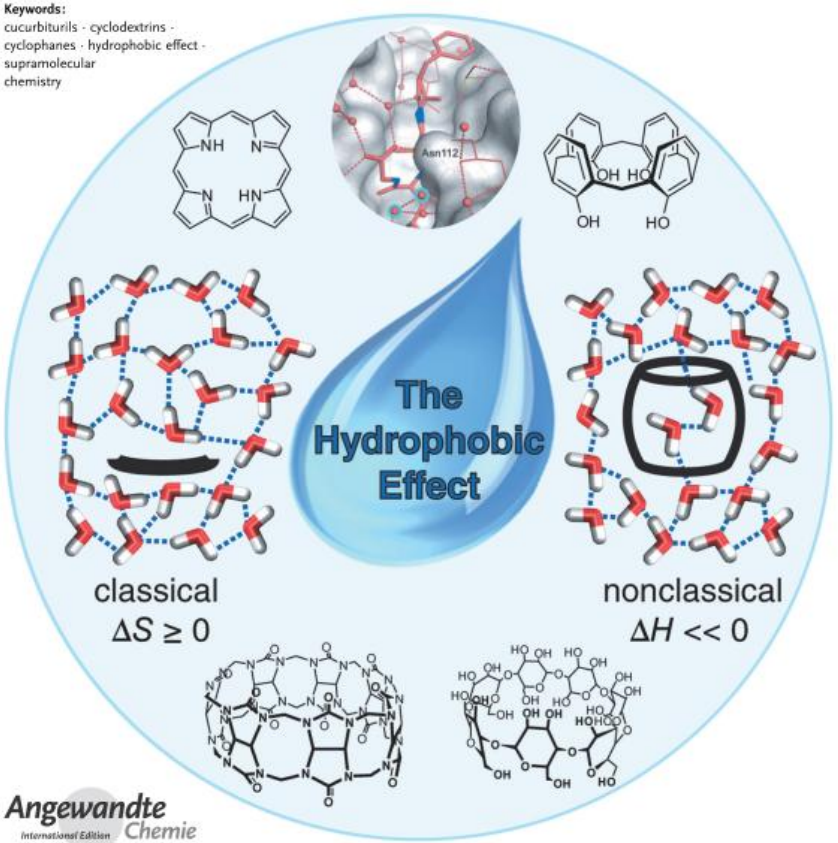
Hydrophobic Effect

DOI: 10.1002/anie.201310958

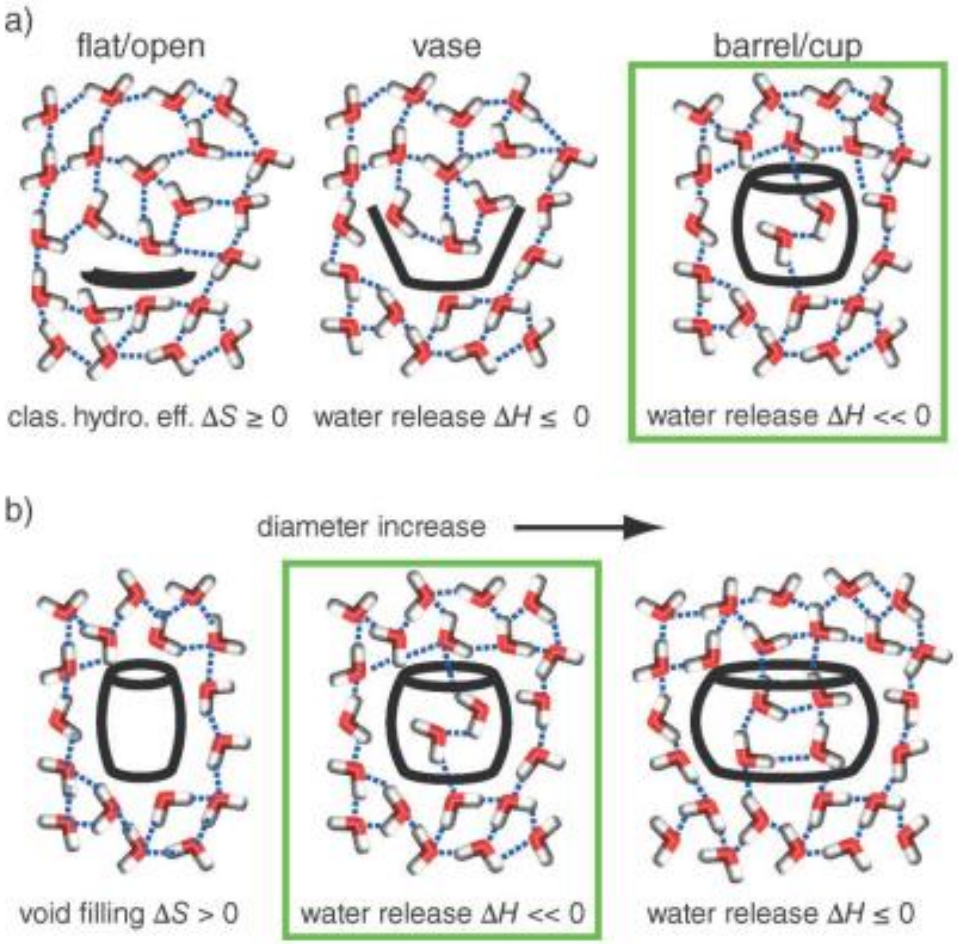
The Hydrophobic Effect Revisited—Studies with Supramolecular Complexes Imply High-Energy Water as a Noncovalent Driving Force

Frank Biedermann, Werner M. Nau,* and Hans-Jörg Schneider**

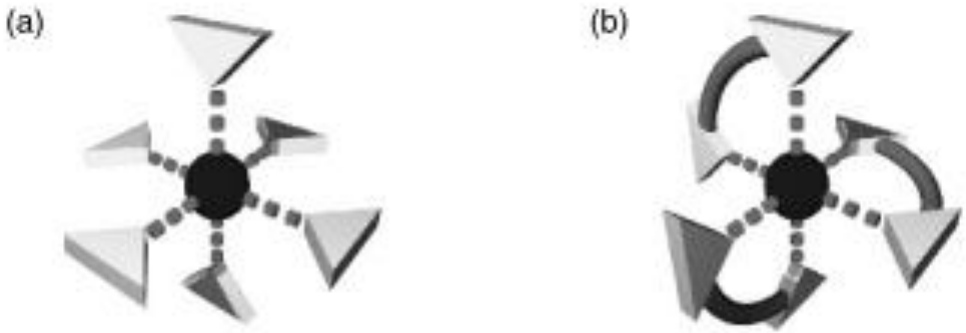
Keywords:
cucurbiturils · cyclodextrins · cyclophanes · hydrophobic effect · supramolecular chemistry



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a)
flat/open
vase
barrel/cup
clas. hydro. eff. ΔS ≥ 0
water release ΔH ≤ 0
water release ΔH << 0
b)
diameter increase
void filling ΔS > 0
water release ΔH << 0
water release ΔH ≤ 0

Chelate Effect



$$[Ni(H_2O)_6]^{2+} + 6NH_3 = [Ni(NH_3)_6]^{2+} + 6H_2O$$

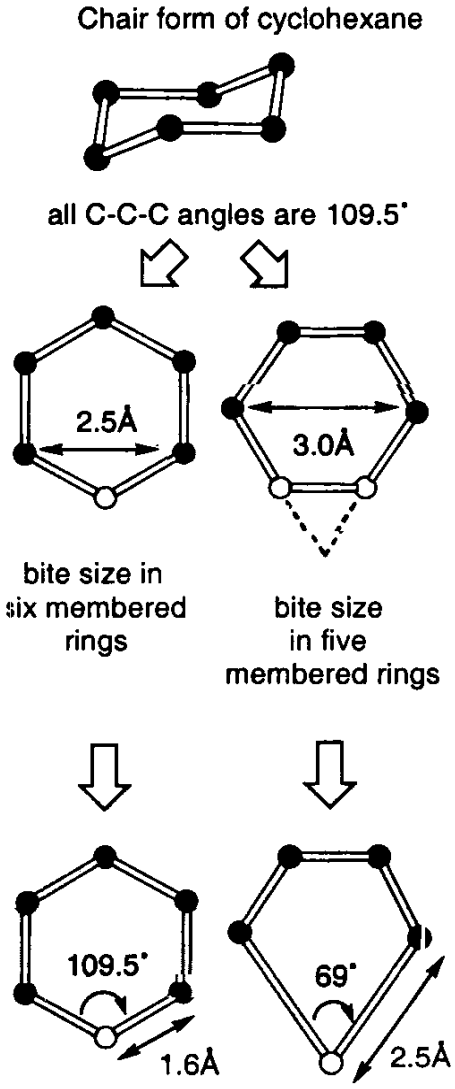
$$\beta \sim 10^9,\ \Delta G = -51.8\ \text{kJ mol}^{-1},$$

$$\Delta H = -100\ \text{kJ mol}^{-1},\ \Delta S = -163\ \text{J mol}^{-1}\text{K}^{-1}$$

$$[Ni(H_2O)_6]^{2+} + 3en = [Ni(en)_3]^{2+} + 6H_2O$$

$$\beta \sim 10^{18},\ \Delta G = -101.8\ \text{kJ mol}^{-1},$$

$$\Delta H = -117\ \text{kJ mol}^{-1},\ \Delta S = -42\ \text{J mol}^{-1}\text{K}^{-1}$$



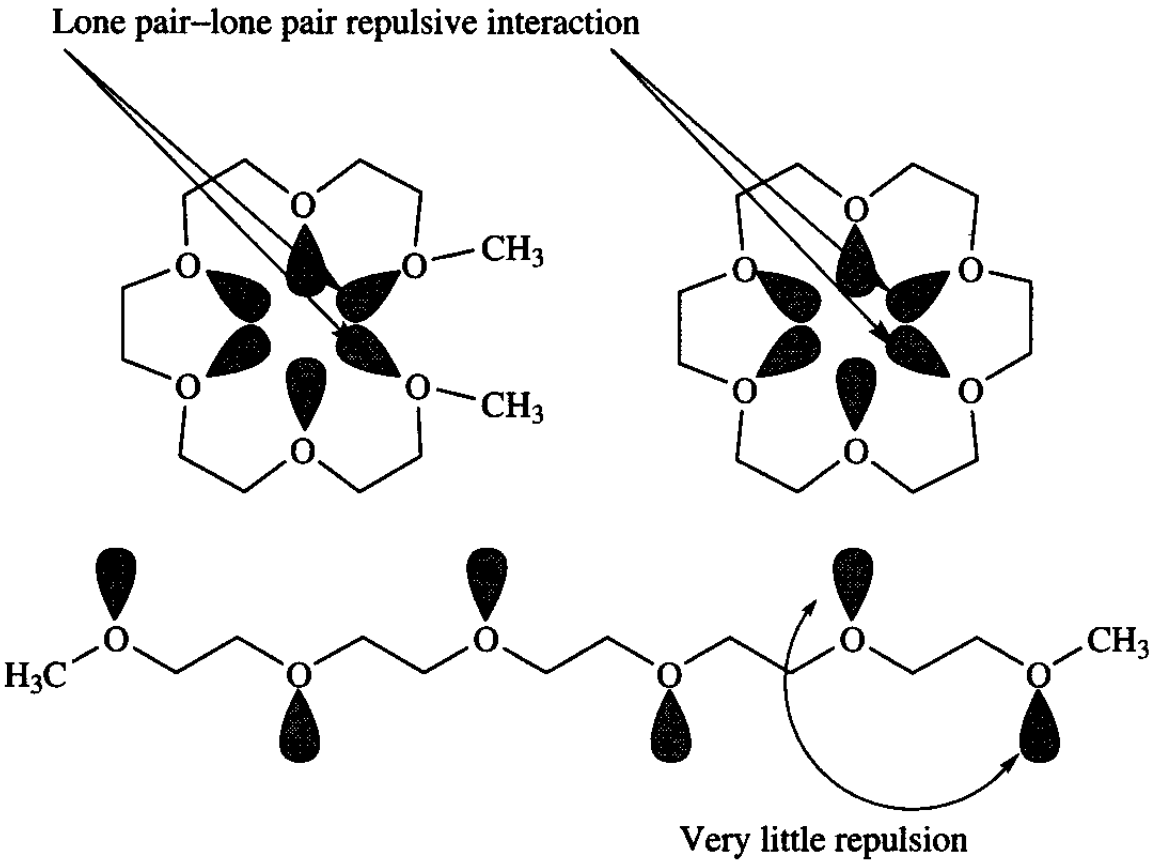
The general rule is that five-membered rings are more stable, the optimal ring size for maximum stability and chelate effect is influenced by the specific metal ion's size and coordination preferences, as well as the ligand's electronic and steric properties.

The bond angles in a (flexible) five-membered ring are closer to the ideal tetrahedral geometry, resulting in minimal strain compared to smaller or larger rings; the space offered is compatible with wider range of cations.

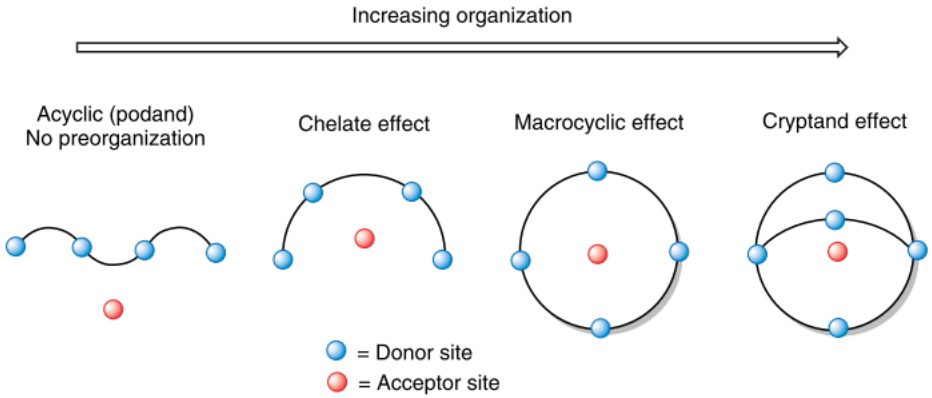
$$[Ni(H_2O)_6]^{2+} + 3en \rightleftharpoons [Ni(en)_3]^{2+} + 6H_2O(l) \qquad K_f = 6.76 \times 10^{17}$$
$$[Ni(H_2O)_6]^{2+} + 3tn \rightleftharpoons [Ni(tn)_3]^{2+} + 6H_2O(l) \qquad K_f = 1.86 \times 10^{12}$$

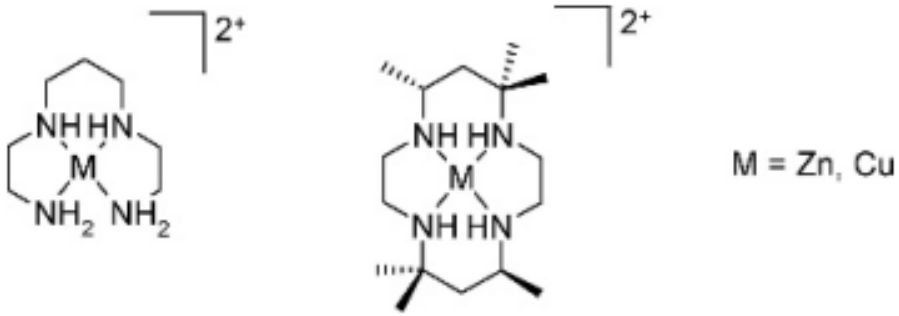
tn = $NH_2CH_2CH_2CH_2NH_2$
en = $NH_2CH_2CH_2NH_2$

Macrocyclic Effect



Macrocyclic Effect





Stability: Cyclic System 10^4 higher than the Acyclic one

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Assessing cooperativity in supramolecular systems†

Larissa K. S. von Krbek,‡[a] Christoph A. Schalley *[a] and Pall Thordarson *[b]

In general, positive allosteric cooperativity can be achieved either by making the first binding event less favorable or by making subsequent binding events more favorable (e.g. conformational changes, electronic polarization of the receptor, or long-range electrostatic interactions between the ligands.)

Chelate cooperativity in the assembly of a supramolecular system is driven by the difference in strength between the intermolecular and intramolecular interactions