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New Chemistry News

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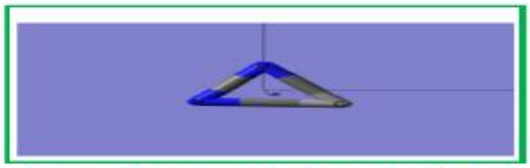
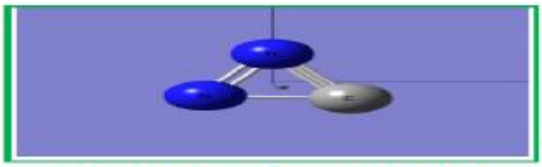


New News of Chem (NNC)



ChemNewsNew (CNN)

CNN –40: *Halogen bond- Weak or strong?*

Information Source	ACS.org ; sciencedirect.com
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KLab

rsr.chem1979

I. Select Research Titles (2000 to 2021) in X-bonds

		halogen bonding
Interactions	**If**	Binary Solvent system: acetic acid + water

		Then	ATMBA forms a strong halogen bond with acetate ion
			ATMBA : alpha-(Trichloromethyl) benzyl acetate
Methods	Radial distribution function (RDF); MD evidence for a halogen bond between the solute and acetate ion		
KeyLrn_Bits	, σ-profile analysis	molecular dynamic simulation	

Deep analysis of the solubility behaviour mechanism of alpha-(trichloromethyl) benzyl acetate in three binary aqueous solvents	The Journal of Chemical Thermodynamics, 151(2020)106246 doi.org/10.1016/j.jct.2020.106246
Ning Wei and Zeren Shang and Nuoyang Zhang and Jingkang Wang and Songgu Wu	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding
Synth	4-bromobenzaldehyde arylhydrazones + CCl4 +Cu catalyst → 1-Aryl-3-(4-bromophenyl)-4,4-dichloro-1,2-diazabuta-1,3- dienes
Interactions	Non-covalent Cl···Br interactions in the crystalline state → formation of 3D supramolecular framework
Dichlorodiazadiene	Strong halogen bond donor
Methods	DFT ; Bader's theory (QTAIM method) X-ray diffraction
KeyLrn_Bits	Non-covalent interactions, crystal engineering

Supramolecular organic frameworks derived from bromoaryl-substituted dichlorodiazabutadienes via Cl···Br halogen bonding	Mendeleev Communications, 31(2021)191-193 doi.org/10.1016/j.mencom.2021.03.015
Namiq G. Shikhaliyev and Abel M. Maharramov and Khanim N. Bagirova and Gulnar T. Suleymanova and Biligma D. Tsyrenova and Valentine G. Nenajdenko and Alexander S. Novikov and Victor N. Khrustalev and Alexander G. Tskhovrebov	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding
	Halophilic reaction
Substrates	CBr4, Cl3CCN, Cl3CCOCl, CCl4, Cl3CF
Nucleophile	Cl−
For halophilic reactionto occur	strong halogen bond is a necessary but not sufficient condition

On the role of halogen bond in the halophilic reaction: A theoretical study	Journal of Molecular Structure: Theochem, 961,(2010)6-8 doi.org/10.1016/j.theochem.2010.08.039
Yu Zhang	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding
Synth	➔ Dichloroacetylated prodrugs ➔ Control compounds
Interactions	🕮 Weak halogen bond formation between

	➔ 17-O-dichloroacetylated 2-methoxyestradiol with GTP in the a-tubulin subunit
Methods	▶ MD
KeyLrn_Bits	Anticancer agent : 2-methoxyestradiol

Synthesis and biotesting of new carrier prodrugs of 2-methoxyestradiol	Mendeleev Communications, 30(2020)7-9 doi.org/10.1016/j.mencom.2020.01.002
Natalia A. Lozinskaya and Natalia A. Maximova and Daniil R. Bazanov and Sergey E. Sosonyuk and Birgit Wobith and Nikolay A. Zefirov and Elena V. Kharitonashvili and Olga N. Zefirova and Sergey A. Kuznetsov and Marina V. Proskurnina	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding
Neutral heteroleptic cluster	Mo3(μ3-S)(μ-S2)3Br4(bpy)
Interactions	By Unsymmetrical substitution of the bromide ligands in [Et4N]2[Mo3(μ3-S)(μ-S2)3Br6] by the 2,2′-bipyridine(bpy) is responsible

Heteroleptic bipyridine complex: Synthesis, spectral and structural analyses, and interconversion of its {Mo3S7} core to {Mo3S4} core	Journal of Molecular Structure, 1234(2021)130138 doi.org/10.1016/j.molstruc.2021.130138
Goutam Nandi and Sabyasachi Sarkar and Bezawada Sridhar Reddy and TaeYoung Kim and Kumud Malika Tripathi	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding
Copper-based antitumor drug	3-formylchromone pharmacophore Substituted with X ((F−, Br−)
Structure detn	Spectroscopy; single X-ray crystallography
Interactions	Strong halogen bonding
Stability of X bond	Rationalized by sigma hole region of positive electrostatic potential on surface of C-X covalent bond
Methods	DFT (B3LYP) gas phase computations

Copper (II)-based halogen-substituted chromone antitumor drug entities: Studying biomolecular interactions with ct-DNA mediated by sigma hole formation and cytotoxicity activity	Bioorganic Chemistry, 104(2020)104327 doi.org/10.1016/j.bioorg.2020.104327
FarukhArjmand and Salman khursheed and Thierry Roisnel and Hifzur R. Siddique	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding	
Interactions	CI···Cl− halogen-bonding interactions	
KeyLrn_Bits	✓ Halogen bonding ✓ Solid phase extraction	✓ Strong anion exchange sorbent Perfluorinated iodine alkanes

Halogen bonding: A new retention mechanism for the solid phase extraction of perfluorinatediodoalkanes	Analytica Chimica Acta, 753(2012)48-56 doi.org/10.1016/j.aca.2012.09.024

Xiao Qing Yan and Qian Jin Shen and Xiao Ran Zhao and Hai Yue Gao and Xue Pang and Wei Jun Jin

Halogen bond-strong weak-- Halogen bond-strong weak--

	halogen bonding
Interactions	Strong halogen bonding between Iodine atoms of TIP and iodide anions XB energies are up to 4.3 kcal/mol.
Methods	DFT
KeyLrn_Bits	Non-covalent interactions, Supramolecular chemistry

Synthesis		
▪ tri(n-propyl)ammonium (1) or ▪ 1,3,5-trimethylpyridinium (2) iodides	2,3,4,5-tetraiodopyrrole (TIP)	hybrids CatI•TIP•xEtOH (X = 0.5 (1) and 0.33 (2)

2,3,4,5-Tetraiodopyrrole as a building block for halogen bonding: Formation of supramolecular hybrids with organic iodide salts in solid state	Journal of Molecular Structure, 1230(2021)129931 doi.org/10.1016/j.molstruc.2021.129931
Mikhail A. Bondarenko and Alexander S. Novikov and Pavel A. Abramov and Ilyas F. Sakhapov and Maxim N. Sokolov and Sergey A. Adonin	

Halogen bond-strong weak-- Halogen bond-strong weak–

		halogen bonding
Interactions	➔ Br atom in Li3Br is a stronger halogen acceptor than Cl atom in Li3Cl when it interacts with dihalogen molecules ➔ Li3I is the strongest Lewis base	
Li3M–XY	▪ M=Cl, Br, I; ▪ XY=ClCl, BrBr, ClF, BrCl, BrF	
Methods	▪ MP2/aug-cc-pVTZ level	
	▪ Natural bond orbital (NBO) ▪ Atoms in molecules (AIM) ▪ Energy decomposition	▪ Formation of halogen bonding
KeyLrn_Bits	▪ Superatom ▪ Orbital interaction,	▪ LiCl, LiBr

Superalkali Li3M (M=Cl, Br, I) as a Lewis base in halogen bonding: A heavier halogen is a stronger Lewis base than a lighter halogen	Computational and Theoretical Chemistry, 1012(2013)41-46 doi.org/10.1016/j.comptc.2013.03.002
WenKai Tian and Qin Miao and QingZhong Li and WenZuo Li and JianBo Cheng	

Halogen bond-strong weak-- Halogen bond-strong weak–

	halogen bonding
System	1,8-naphthyridine + diiodine
Non-Cov bonds	➔ Hydrogen bond ➔ Tetrel bond ➔ Stacking interaction

	➔ Cooperativity and anticooperativity between strong halogen bond and other noncovalent interactions
Interactions	➔ Strong halogen bond
	N···I halogen bond interaction energy : −21.41 kcal/mol
KeyLrn_Bits	Organic semiconductor,
Appl	☞ Strong halogen bond is useful to design organic semiconductor materials

Theoretical rationale for the role of the strong halogen bond in the design and synthesis of organic semiconductor materials	Computational and Theoretical Chemistry, 1194(2021)113074 doi.org/10.1016/j.comptc.2020.113074
Yu Zhang and Weizhou Wang	

Halogen bond-strong weak-- Halogen bond-strong weak—

		halogen bonding
System	N-bromosuccinimide + electron-donating groups	
Non-Cov bonds		
Interactions	➔ N—Br in H2N—Br…NH3 form a much stronger halogen-bonding than C—Br.	
Methods	AIM	MP2/Lanl2DZ*
KeyLrn_Bits	Interaction energy	

Ab Initio Calculations on Halogen Bond Between N—Br and Electron-donating Groups	Chemical Research in Chinese Universities, 23(2007)355-359 doi.org/10.1016/S1005-9040(07)60075-0
Yan-hua WANG and Xue-song CHEN and Jian-wei ZOU and Qing-sen YU	

Halogen bond-strong weak-- Halogen bond-strong weak--

		halogen bonding
System	Formamidine + XY	X=Cl, Br, I; Y=F, CCH, CF3, CN, NC
Complexes	FA-(Z) through a halogen bond,	FA-(E) complex stabilized by both a halogen bond and X···H interaction.
Non-Cov bonds	FA-(E) more stable than FA-(Z) counterpart with interaction energy of −3.4 to −23.4kcal/mol	
Expl	Stability of stronger halogen bonding is due to electrostatic and polarization energies	

Prediction and characterization of halogen bonds involving formamidine and its derivatives	Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy, 138(2015)195-202 doi.org/10.1016/j.saa.2014.11.064
Xiulin An and Lixia Jiang and Qingzhong Li and Wenzuo Li and Jianbo Cheng	

Halogen bond-strong weak-- Halogen bond-strong weak—

		halogen bonding
KeyLrn_Bits	Human fertilization Calmodulin-dependent protein kinase	Molecular design
Appl		

Design and verification of halogen-bonding system at the complex interface of human fertilization-related MUP PDZ5 domain with CAMK's C-terminal peptide	Computational Biology and Chemistry, 72(2018)164-169 doi.org/10.1016/j.compbiolchem.2017.11.007
Juan Wang and Yunjie Guo and Xue Zhang	

Halogen bond-strong weak-- Halogen bond-strong weak—

		halogen bonding
System	14N2···ICF3 15N2···ICF3	Symmetric-top complexes
Interactions	Weak halogen bond	
since	🕮 Distance rN···I=3.443(1)Å slightly < sum of the N and I van der Waals radii 🕮 Intermolecular stretching force constant kσ=2.94Nm−1 is small 🕮 Negligible charge redistribution on complex formation	
Methods	Rotational spectroscopy	

Characterisation of the weak halogen bond in N2···ICF3 by pure rotational spectroscopy	Chemical Physics Letters, 625(2015)179-185 doi.org/10.1016/j.cplett.2015.02.023
Jonathan P. Anable and David E. Hird and Susanna L. Stephens and Daniel P. Zaleski and Nicholas R. Walker and Anthony C. Legon	

Halogen bond-strong weak-- Halogen bond-strong weak—

			halogen bonding
System	Azaaromatic chloride crystals		
Synth	✓ bis-2,4-[(2-formoyl)phenoxyl]-6-chloro-[1,3,5]triazine (1) ✓ bis-2,4-(4-carbomethoxyphenoxyl)-6-chloro-[1,3,5]triazine (2)		
Non-Cov bonds	➔ N···Cl halogen bonding ➔ lone pair···π interaction ➔ π–π stack ➔ C–H···O hydrogen bonding in the directionality of supramolecular self-assembly		
Interactions	Strong halogen bonding		
since	🕮 unusually short intermolecular N···Cl distance of 3.095(2) and 3.088(3)Å		
Methods	Theoretical calculations		
KeyLrn_Bits	☞ Directionality ☞ Site selectivity	☞ DFT calculations ☞ Molecular electrostatic potential	

Directionality and site selectivity of N···Cl halogen bonding in two azaaromatic chloride crystals	Journal of Molecular Structure, 975(2010)274-279 doi.org/10.1016/j.molstruc.2010.04.035
Yi-Min Zhu and Ti-Fang Miao and Yang-Yi Yang and Dong-Yue Zhuang and Kang-Cheng Zheng and Wing-Tak Wong	

Halogen bond-strong weak-- Halogen bond-strong weak—

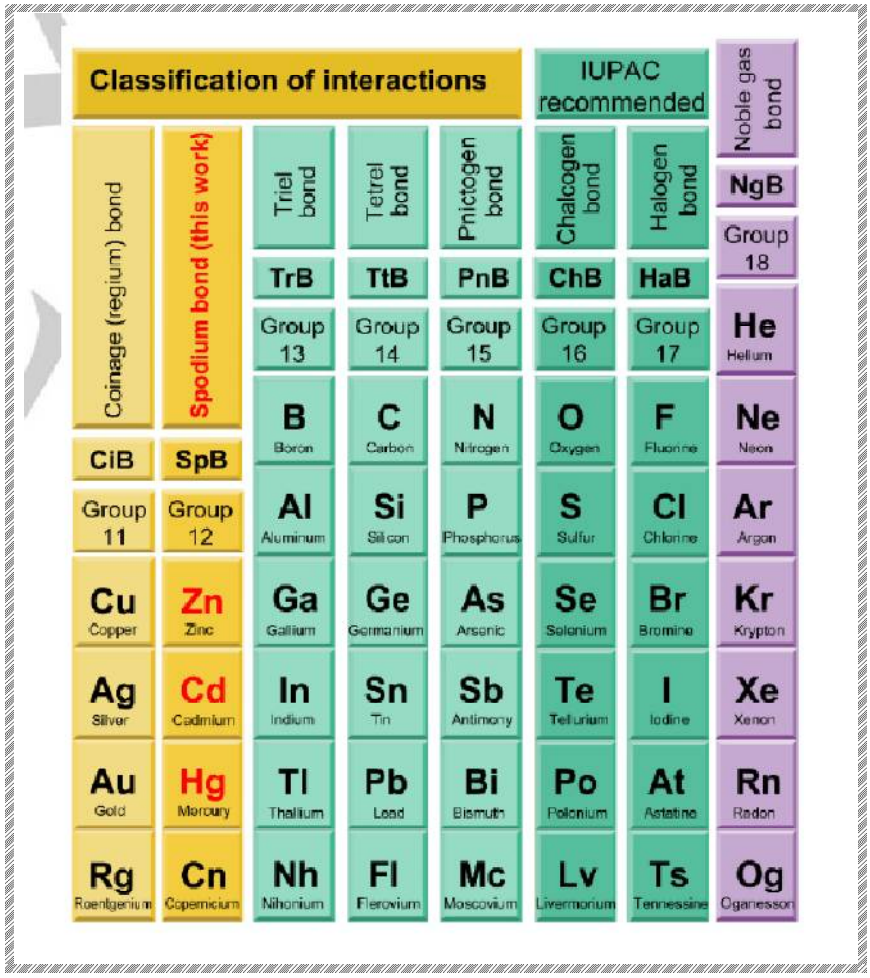
II. Object oriented terminology (OOT) for X-bonds

Interactions within in and between chemical moieties	
!	|chemical biological|
!	|Vander_wall dispersion stacking hydrophobic|
!	|quantum ||relativistic|| nano || gravity||

Interactions	Energy (kcal/mol) in biomolecules
Van der Waals contact	<1
Hydrophobic force	1.5–2
Salt-bridge	0.5–5
Stacking	5–7
H-bonding	0.25–40
Xbonding	1–40
Covalent bond	>80
Electrovalent	>700

Classification of

non-covalent interactions

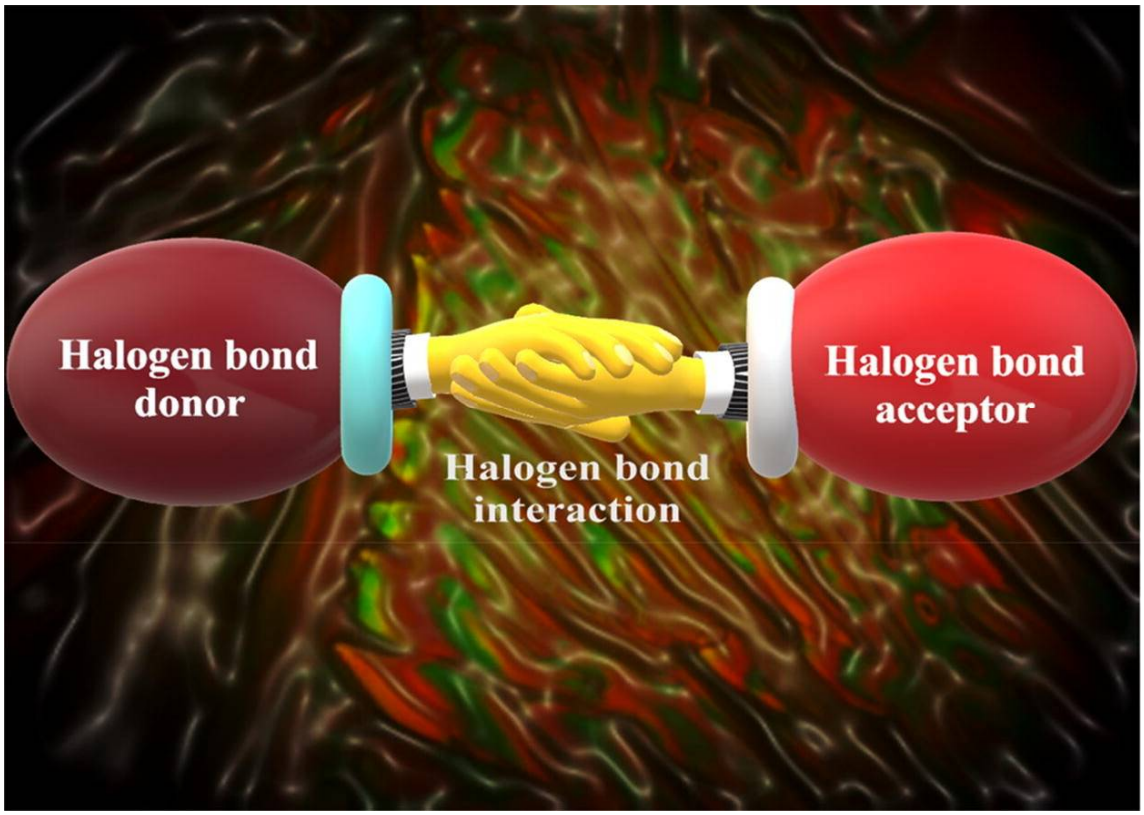


LA | Interaction | LB		
|Interaction |	| Bond No_Bond|	
	|Bond|	|CovBNonCovBElectroStatic|
	|Electrostatic|	|ion-ion, ion-Multi_poleMultipole_multipole| Multipole : |dipole ……hexadecapole|
LA | NCB| LB		NCB : Non-covalent bond
| NCB|	| HB XB [G11-G18] B|	
| HB|	| HB invHB|	
XB	| F Cl Br I At|	

Interactions	
Lewis acid (LA)	**Lewis base (LB)**
Hard acid (HA)	Hard base (HB)
Electrophile	Nucleophile
Cation	Anion
σ-hole	Base
Acid	σ-hole
σ-hole positive	σ-hole negative
Electron density acceptor	Electron density donor

# column of Chem elements in periodic table	Abbrev	$$ Bonds

18G	NgB	Nobel gas
17G @	HaB	Halogen
16G @	ChB	Chalcogen
15G	PnB	Pnicogen or Pnictogen
14G	TTb	Tetrel
13G	TrB	Triel
12G	SPb	Spodium
11G	CiB or Rg	Regium or Coinage
1G	HB	Hydrogen
		@ IUPAC recommened



	halogen bond		
Synonyms	Halogen bond Halogen molecule bridges		
Abbreviation	HaB	IUPAC approved	Group 17 in 18Column-Periodic table
	XB	popular	

Chem Elements in Halogen (X) group	[F, Cl, Br, I] [At] [Ts]

Halogen atom	☞ Plays the role of electron acceptor to electron donor atoms in a molecule (NH3) ✓ Ex: nitrogen, oxygen, even anions such as halides
	☞ Plays the role of electron density donor to electron acceptor atoms in a molecule
Halogen bonding	☞ A specific subset of inter- and intramolecular interactions ☞ Attractive interaction ☞ Non-covalent interactions ☞ A subset of σ-hole interactions
	☞ Halogen bonds are a highly directional class of bonds ! **Reason:** X- bonds formed in line with the halogen's molecular bond (R-X) ☞ Hydrogen bonds on the other hand, are non-directional
Halogen bond	A halogen bonded molecular system consists one of halogen atoms and has a σ-hole in one moiety and a base in other species in inter-molecular interaction associated with energy transactions.
	A halogen atom (Hal) in one molecule and an atom or a group of atoms with rich electron density (Y) in another molecule

X-atom	Behaves as	Complex
Electrophile	When there is positive ESP region (σ-hole)	Halogen bond X…Y
Nucleophile	When there is negative ESP region	Halogen atoms have high electronegativity. Thus, they behave as electron rich (nucleophilic) sites Ex: A halogen atom functions as hydrogen bond acceptor
Both electrophile and nucleophile	When there is negative ESP region and also positive ESP region (σ-hole) on the same halogen atom	One halogen bond and another halogen…nucleophile complex

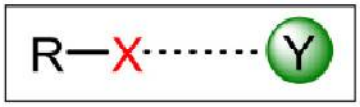
Halogen bond	Type I	✓ Net attractive interaction between ! An electrophilic region associated with a halogen and ! Electrophile region of another molecule
	Type II	✓ Net attractive interaction between ? A nucleophilic region associated with a halogen atom (σ-hole) in a molecular entity/fragment and ? A nucleophilic region of another molecule (Lewis base) or the same, molecular entity

Origin of electrophilic region on halogen	**when** a halogen atom makes a covalent bond in a molecule **Then** electron distribution density around the atom shifts a bit toward the bond **Consequence**: This leaves an area (opposite the bond)—of diminished of electron density, which is christened as the σ-hole.

Halogen bond 'donor'	Halogen bearing molecule
Halogen bond 'acceptor'	Nucleophilic molecule

Applications of X-bonded systems

Crystal engineering	🕮 Designed Mechanical properties
	🕮 Co-crystals with specific desired features of structure and composition → ☞ Non-linear optical activity ☞ Enhanced conducting properties
Liquid crystals	🕮 Dimeric 🕮 Trimeric
Materials	🕮 Soft, Smart ☞ Magnetic ☞ Conducting ☞ Supramolecular polymers
Electronics	🕮 Magnetic and conducting materials 🕮 Liquid-crystal displays 🕮 Organic semiconductors
Biomedicine	🕮 Biological Systems 🕮 Functional systems 🕮 Rational drug design 🕮 Anion binding
Recognition	🕮 Molecular 🕮 Anion
Chemistry	🕮 Macromolecular chemistry ☞ Supramolecular chemistry ☞ Supramolecular host-guest complexes ☞ Interlocked XB host molecules 🕮 Biochemistry 🕮 Solid state chemistry 🕮 Organic synthesis, catalysis 🕮 Separation science

Halogen(Ha) bond Representation		X or Ha: ☞ Halogen atom ✓ Cl, Br, I, At ✓ F; ☞ Lewis acid
	OR **R—Ha···Y**	R: Electron withdrawing group

		R-X	R is covalently bonded to X
		Y	✓ Lewis base ✓ Halogen bond acceptor possessing at least one nucleophilic (electron rich) region.

Chemical species with X-bond	🕮 Molecular entity or any constitutionally or isotopically distinct atom, molecule, ion, ion pair, radical, radical ion, complex, conformer etc., which is detectable and can be quantified as a distinct entity
Evidence for X-bond	• Experimental • CQC (Computational quantum chemistry) • Combination of both
	! Greater the number of features satisfied ✓ More reliable is characterization of interaction as a halogen bond

Features	**R-X + Y → R-X…Y**
	Geometric characteristics
Interatomic distance between X…Y	→ Greater than covalent bond distance → Less than sum of van der Waals radii
Angle R–X…Y	→ Nearer to 180° i.e., the halogen bond acceptor Y → Approaches X along the extension of R–X bond
Length of the R–X covalent bond in R–X…Y	→ More than bond distance in simple R–X

Spectral response		
Infrared Raman scattering	Absorption	Formation of the X…Y bond results in new vibrational modes
UV–vis	Absorption bands	Of halogen bond donor shifts to shorter wavelengths
X-ray photoelectron spectrum	Binding energies of peaks	Complex shift to lower energies relative to unbonded X
NMR(@)	Chemical shift values	Of nuclei in both R–X and Y, in solution as well as in solid state change
(@) NMR spectroscopy requires high concentrations (up to ~1 M) of solute for signal measurement + It had advantage that weaker interactions also can be detected at higher concentrations.		

Ha-Bond strength	Bond strength **of X…Y in R-X…Y-Z**
Forces in Ha-Bond	→ Electrostatic → Polarization → Charge transfer → Dispersion
Correlated	Function of (magnitudes of the positive and negative electrostatic potentials of σ-hole and the negative site)

Variation	Highly variable over a wide range of energies
Decreases as	☞ Electronegativity of X increases ☞ Electron withdrawing ability of R decreases

Strength of XB	Changes with
Increases	✓ Size and polarizability of atoms (Cl < Br < I < At) ✓ Size of σ-hole
Increases	Increasing the electron withdrawing ability of covalently bonded R group Ex: C(sp)-X > C(sp2)-X > C (sp3)-X).
Depends on nature of halogen atom	Greater in order of F < Cl < Br < I < At
Depends on nature of Lewis bases	✓ Conventional electron donors such as oxygen-And nitrogen-containing molecules ✓ Aromatic compounds, metal hydrides, radicals ✓ Carbenes

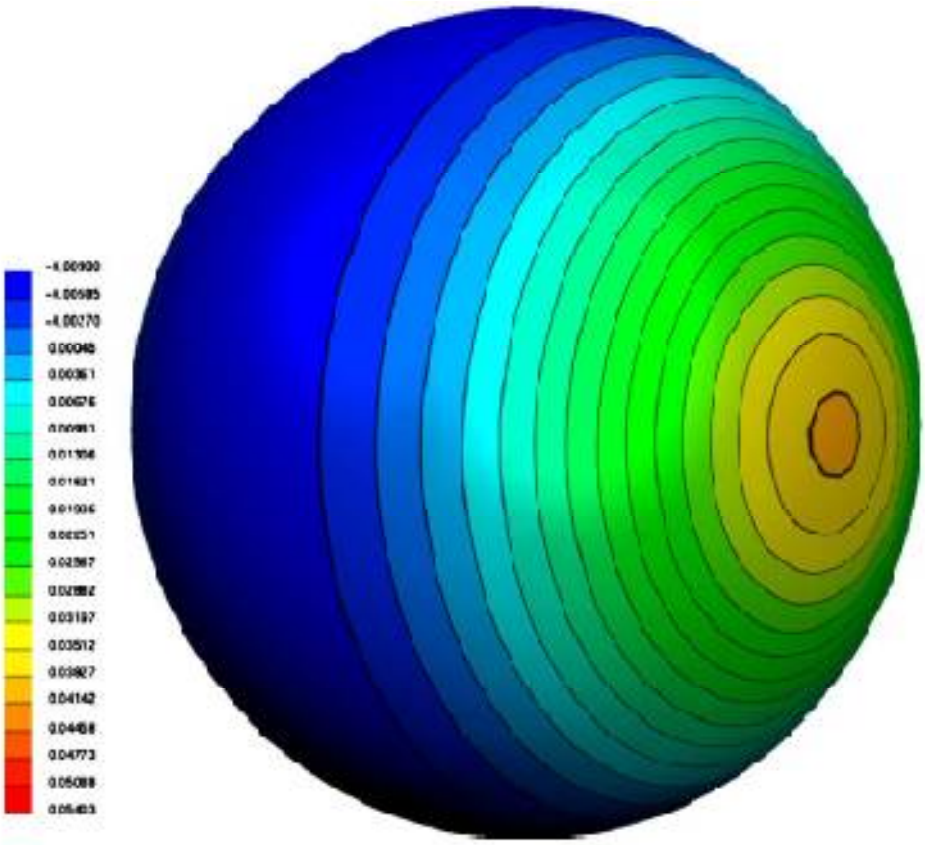
R–X	CBr4, CHI3, CnF2n+1I	Haloalkane
	Iodobenzene, halopyridinium And haloimidazolium cations	Haloarene or haloheteroarene
	Diiodoacetylene	1-haloalkyne
	Diphenyliodonium or bromonium derivatives	Halonium ion
	N-bromo- or N-iodosuccinimide	Haloimide
	I2, Br2, ICl, ClF	Dihalogen molecule
	CBr4, CHI3, CnF2n+1I	Haloalkane
Y	lone pair	Possessing atom N atom of a pyridine or an amine
	O atom of a	Carbonyl group
	Pi system	Double or triple bonds, arene moiety
	anion	S

III. Supplementary Information
X-bonded chemical species

Sup Inf 1: σ-hole in Single atom

MEP (Hartrees)	isodensity surface (0.001 electrons $Bohr^{-3}$)		XB-02

Cl atom



Electronic configuration	s2 p2x p2y p1z
σ-hole	Formed in z-direction
σ-hole is clearly visible, surrounded by a belt of negative potential	

σ-hole in X atoms of molecules—Positive ESP region

- ➔ σ-hole is due to the anisotropy of the atom's charge distribution
- ➔ The three pairs of unshared electrons on the halogen atom X form a belt of negative electrostatic potential around its central region.
- ➔ It leaves a positive "σ-hole" on the outermost portion of its surface centered around the R–X axis.

- o This region of lower electron density is known as the σ-hole.
- o Its position accounts for the highly directional interaction with the XB acceptor, and the stricter

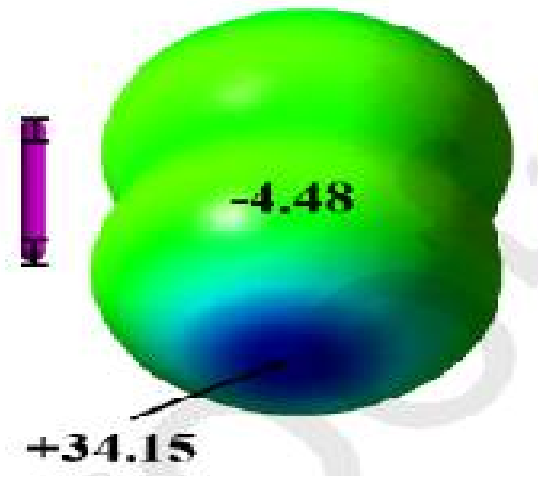
preference for linear interactions of XB in comparison to HB

Calculated molecular electrostatic potential surfaces of these R—X bonds show a clear anisotropic distribution of electrons, with a highly localised region of positive electrostatic potential positioned on the halogen atom at the head/terminal end of the R—X bond

Diatomic halogen molecule

ESP of single molecules	I2			XB-10

Most positive ESP (34.15) of I_2 is located on one Iodine atom of molecule



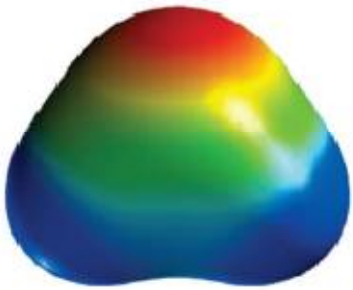
Number σ-holes in atom	o Elements in groups 16, 15, and 14 of the periodic table have ✓ two, three, and four σ-holes o if hypervalent, even more σ-holes

ESP of single molecules	ClF			XB-121

SP of single molecules	NH3			XB-121

Negative values shown in red	positive values in blue
ESP	MP2/augcc-pVDZ

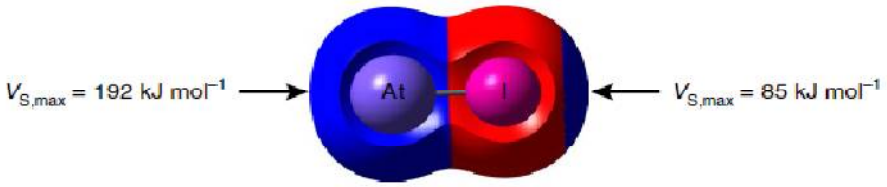
Isodensity surfaces (0.02 a.u.)



Negative values shown in red	positive values in blue
ESP	MP2/augcc-pVDZ

Isodensity surfaces (0.02 a.u.)

Molecule	AtI			XB-16

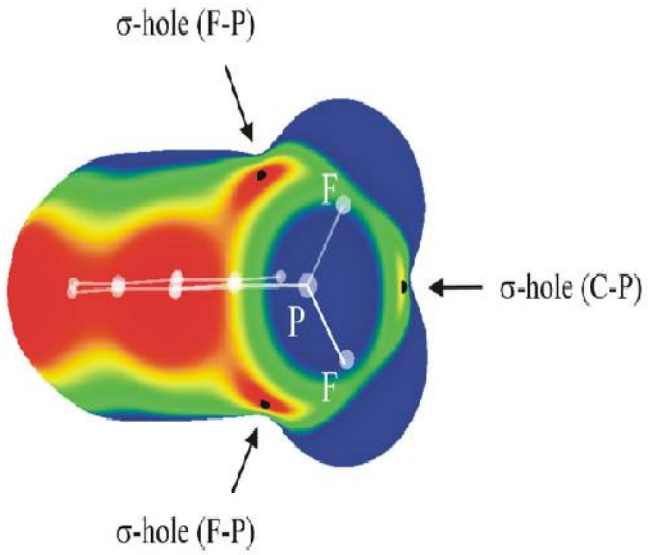


Astatine iodide

Side view of the	
DFT	B3LYP/AVDZ
.Molecular electrostatic potential	Isovalue of the electron density (0.001 e bohr-3)
Negative values shown in red	positive values in blue

Theory	Spin–orbit DFT (SODFT)	Relying on relativistic pseudo-potentials
Functional	B3LYP55 PW6B9556	For Astatine
Basis set	polarized double zeta basis sets, referred as AVDZ	Explicitly treated electrons were described
	AVDZ, augmented with Diffuse functions	For non-hydrogen atoms
	AVDZ, supplemented with two-component extensions	For astatine, iodine
Software		

MEP	PF2C6H5		X-Bonding



Molecule	PF2C6H5	
	Theory	Post-HF
MEP	Level	MP2
	BS	aug-ccpVTZ
red	>15	
yellow	Between 8 and 15	
green	0 and 8	
blue	below 0 kcal/mol	

σ-hole limitations	However, the σ-hole model does not show the complete picture of the halogen bond, Future and the exact nature of the bonding interaction has yet to be confirmed

If	electron-attracting power of X is greater than that of the remainder of its molecule (R)
Then	halogen atom may gain enough electronic charge to neutralize the σ-hole
Why	Fluorine does not participate in halogen bonding
Because	sp-hybridization of the unshared s-valence electrons of F neutralization of the σ-hole
Why	σ-hole is observed for the Cl in CF3Cl σ-hole is not observed for the Cl in CH3Cl
Because	➔ Cl, Br and I atoms in these molecules closely approximate the s2p2x p2y p1z configuration, where the z-axis is along the R–X bond. ➔ The three unshared pairs of electrons produce a belt of negative electrostatic potential around the central part of X, leaving the outermost region positive, the σ-hole.
	This is not found in the case of fluorine, for which the combination of its high electronegativity plus significant sp-hybridization → causes an influx of electronic charge that neutralizes the σ-hole
Trend	These factors become progressively less important in proceeding to Cl, Br and I,

Why	σ-hole not found CF4
Because	higher electronegativity of fluorine gives it a disproportionately large share of the σCX bonding electrons

	→ leads to neutralize the σ-hole →does not form halogen bond
Why	CH3Cl does not form halogen bond
Because	CH3Cl does not have a σ-hole
Why	CF3Cl form X-bond
Because	Electronattracting power of the chlorine is overwhelmed by that of the three fluorines.

Why	it's much more difficult in the protein to establish a strong halogen bond than a strong hydrogen bond
Because	halogen bonds have a strong geometric requirement

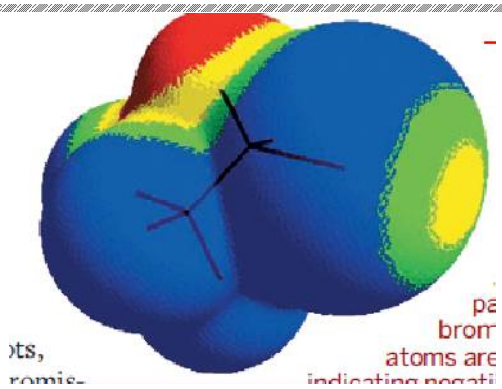
Tuning of σ-hole	This r-hole can be tuned through substitution of atoms or chemical groups in the vicinity of a halogen Ex: bromine in 5-bromo-4,6-dicyano pyrimidine shows a more positive σ-hole than the corresponding one in 5-bromopyrimidine

σ-hole bond XB-24	A σ-hole bond is a noncovalent interaction between a covalently-bonded atom of Groups IV–VII and a negative site e.g. of negative site: a lone pair of a Lewis base or an anion.
	It involves a region of positive electrostatic potential, labeled a σ-hole, on the extension of one of the covalent bonds to the atom.

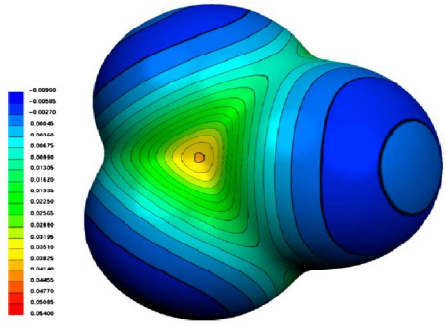
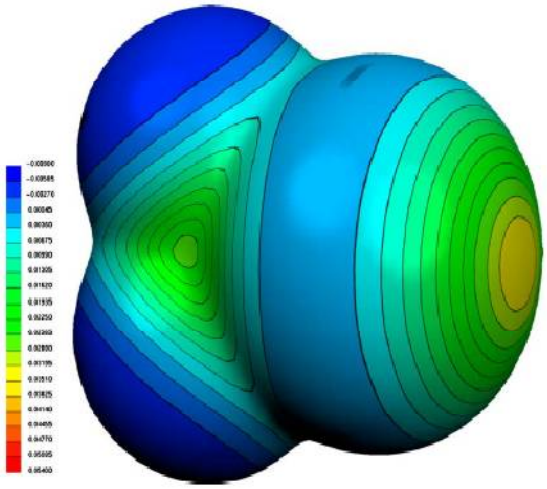
Number of X-bonds	= < number of σ-holes in X atom of Lewis acid (LA)

Single molecules containing halogen atoms

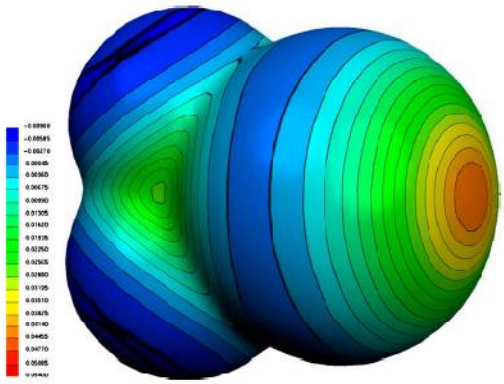
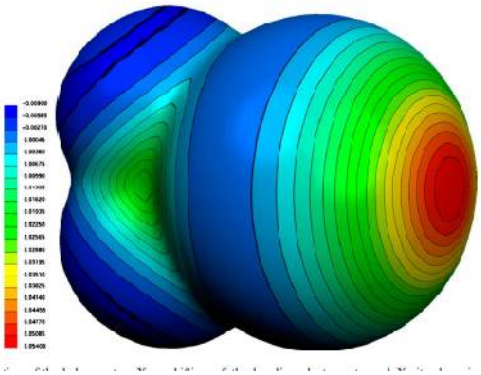
Molecule	CF3CH2Br			XB



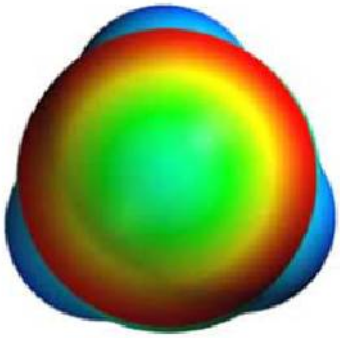
Bromine	electropositive yellow tip (right)	amenable to form X bond with Lbase
Sides of bromine	Full negative charge (indicated in blue)	No halogen bond
Fluorine atoms		
Hydrogen atom	most positive region of molecule (indicated in red)	Capable of forming hydrogen bond

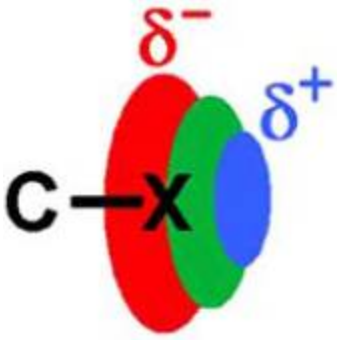
MEP (Hartrees)	isodensity surface (0.001 electrons $Bohr^{-3}$)		XBS-02
CF_4		CF_3Cl	
			

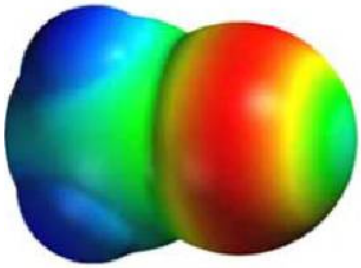
MEP (Hartrees)	Isodensity surface (0.001 electrons Bohr^{-3})		XBS-02

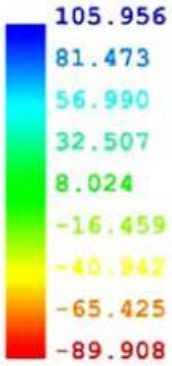
CF_3Br	CF_3I
	

XB feasibility	Methyl bromide		XB



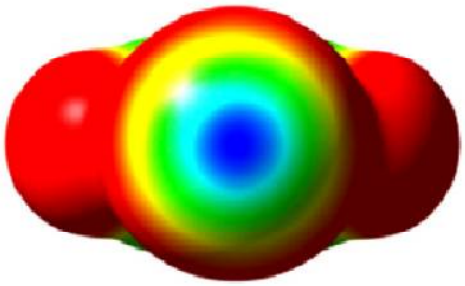


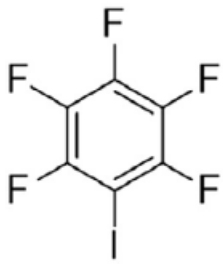




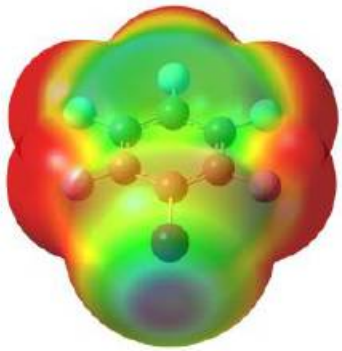
Geo opt	Basis set	HF/6-31G(d)
ESP surface		Spartan'08 v1.0.0

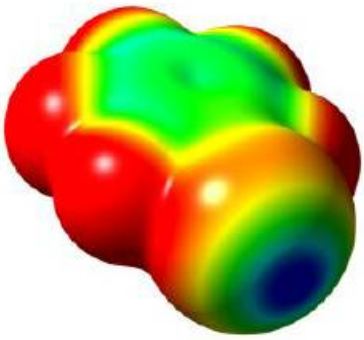
ESP map	Blue:positive Red: negative		Iodo-pentafluoro-benzene	B97D3/Def2-TZVP	XB





ESP map	CQC, Raman ; NMR		Iodo-pentafluorobenzene		XBS-15





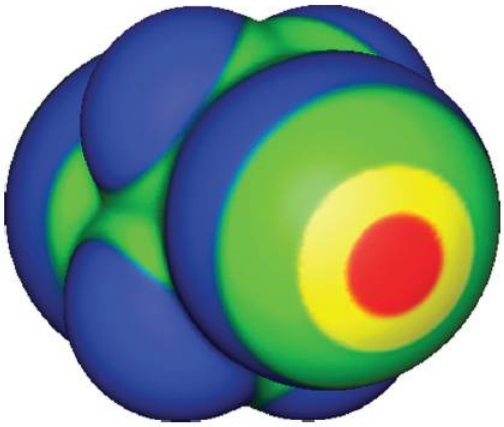
solid surface included to clearly show both positive
and negative ESP regions.

- Positive ESP indicated by blue at the terminus of the moleculule
- Nucleophilic region of negative ESP perpendicular to the R-X covalent bond

Theory	DFT	
Functional	M06-2X	
Basis set	Augmented with diffuse functions (aug-cc-pVTZ)	
	small-core energy-consistent relativistic pseudo-potential (aug-cc-pVTZ-PP).	bromine[42] and iodine
Software	Gaussian09	

		σ-hole		
MEP (Hartrees)	Isodensity surface (0.001 electrons $Bohr^{-3}$)	Red > 25; yellow 15 to 25;	green 0 to 15; blue < 0 (negative).	XB

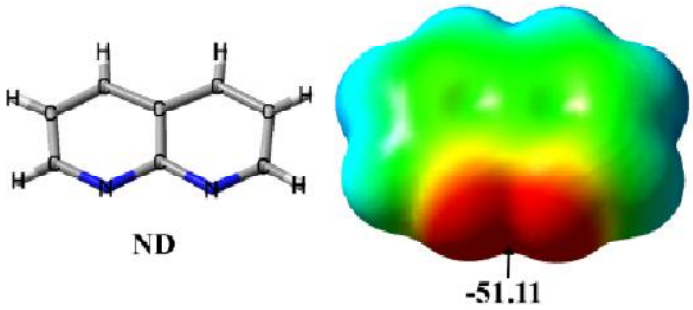
1,2-diiodoperfluoroethane



		Theory	DFT
VS,max	31 kcal mol	Functional	M06-
Fluorines	Entirely negative	Basis set	2X/6-311G(d)
		Software	Gaussian09
σ-hole	Iodine is along extension of a C–I Shown in red		

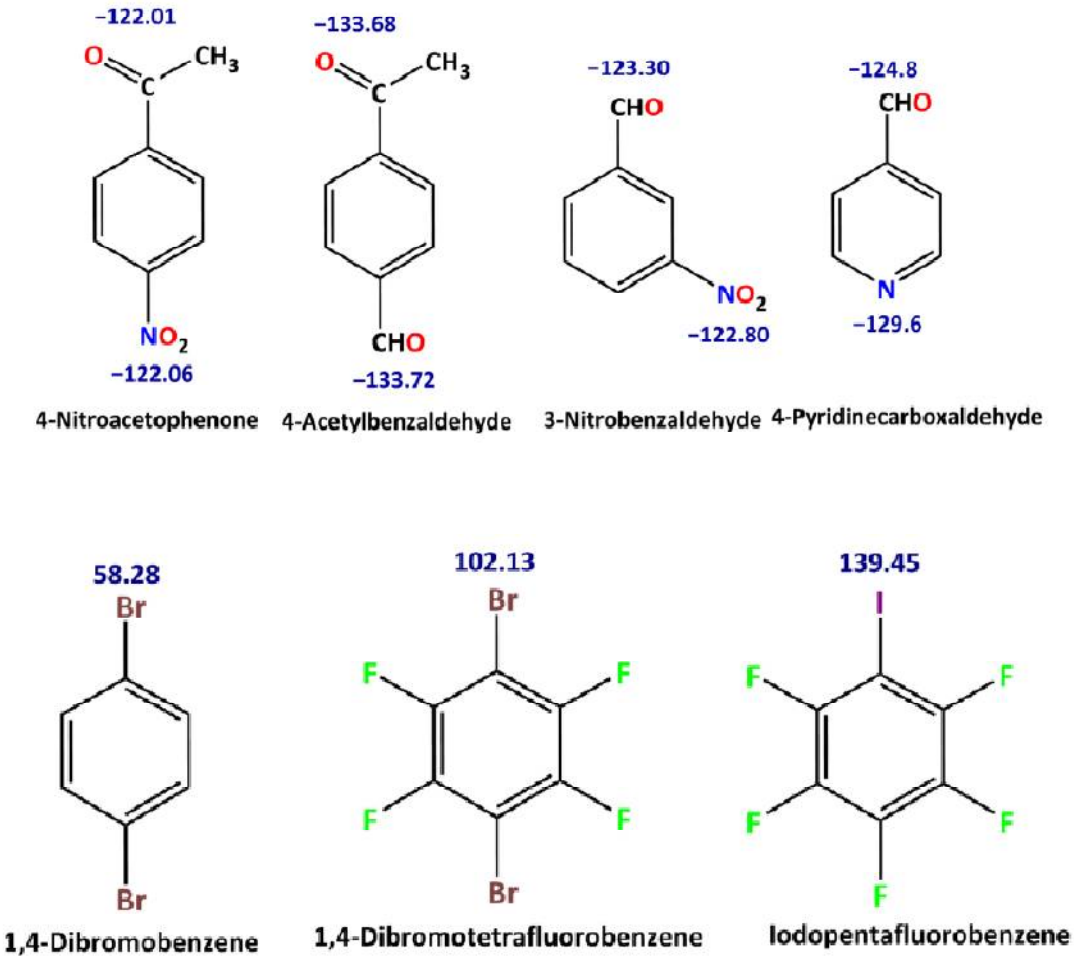
ESP of Single Molecules
LA and LB →RX…YZ

ESP of single molecules	ND			XB

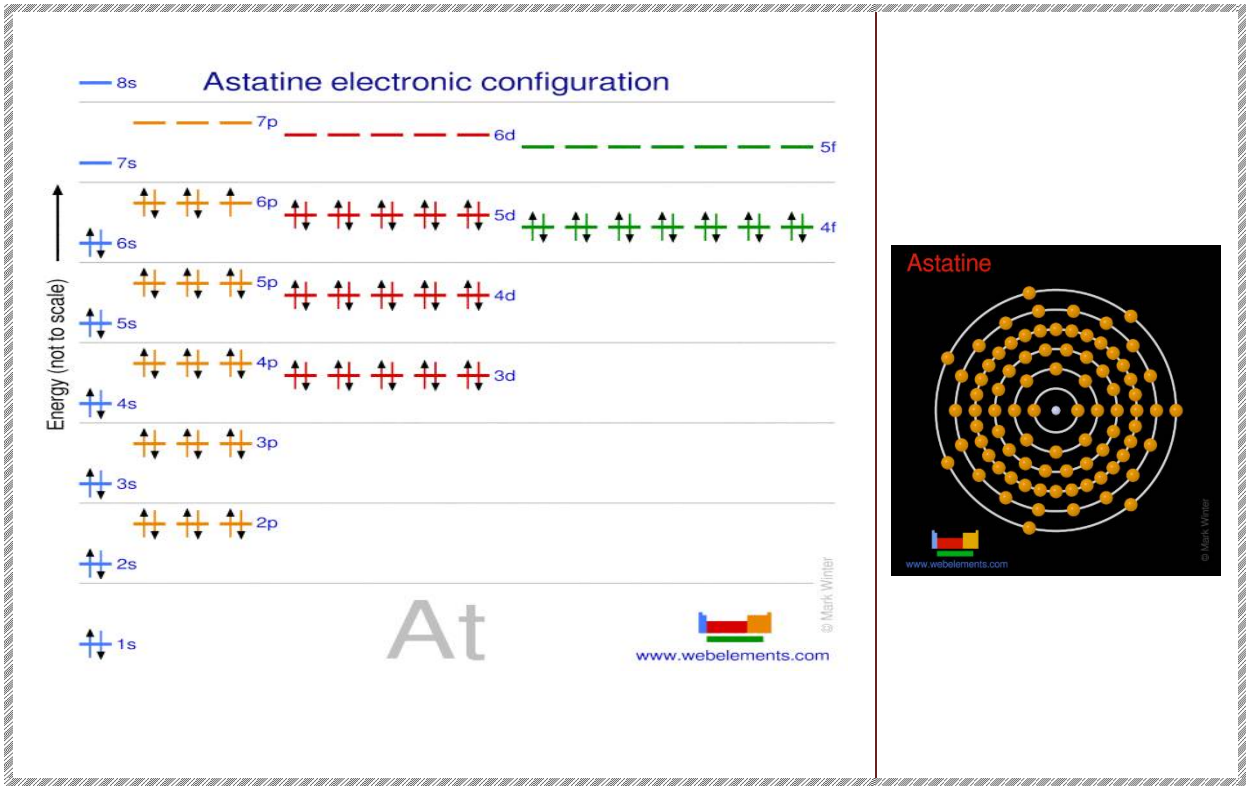


Most negative ESP (-51.11) of ND is located at the middle point between two N atoms

XB-42



Electronic configuration of Halogen atoms


Astatine electronic configuration
8s
7p
6d
5f
7s
6p
5d
4f
6s
5p
4d
5s
4p
3d
4s
3p
3s
2p
2s
1s
Energy (not to scale)
At
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Astatine
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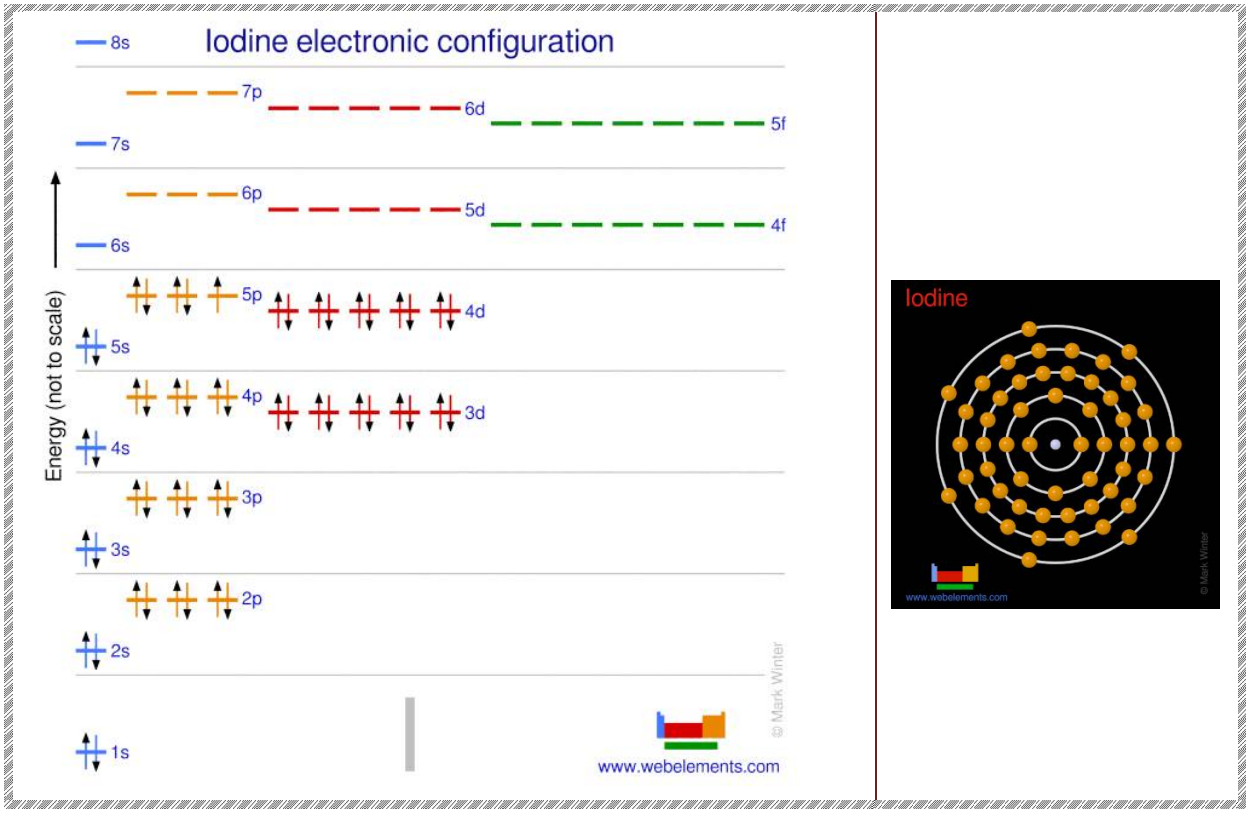
Iodine electronic configuration
8s
7p
6d
5f
7s
6p
5d
4f
6s
5p
4d
5s
4p
3d
4s
3p
3s
2p
2s
1s
Energy (not to scale)
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Iodine
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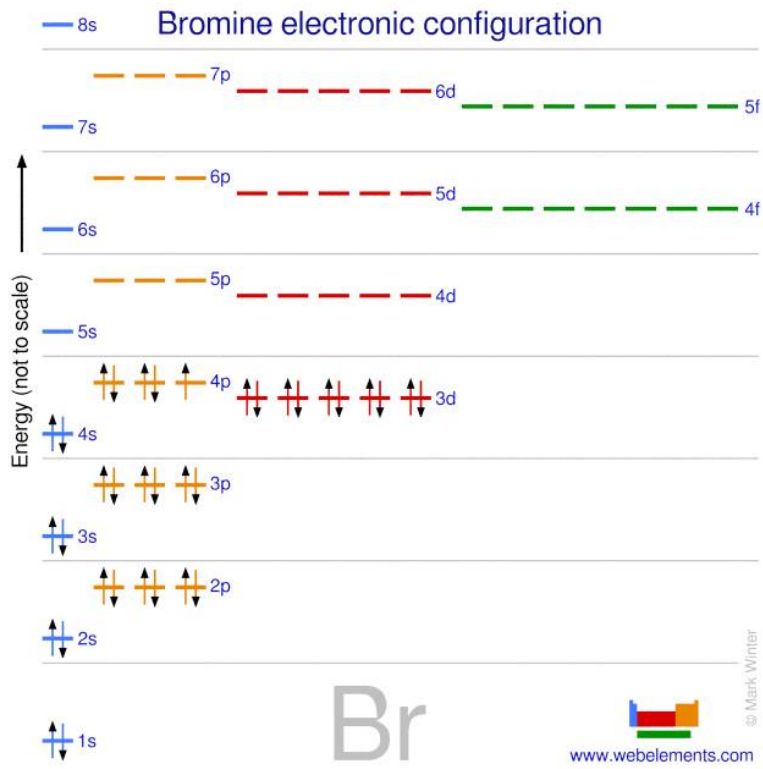
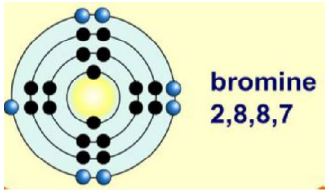
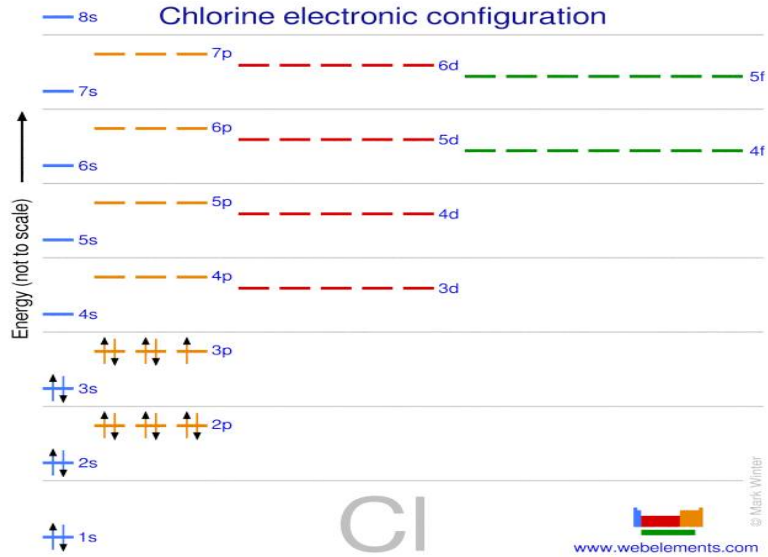
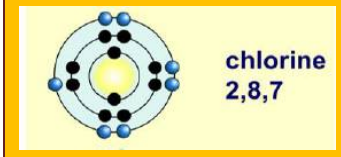
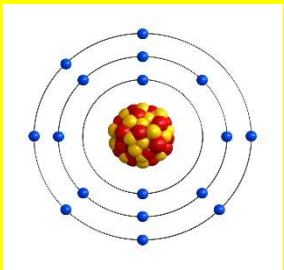


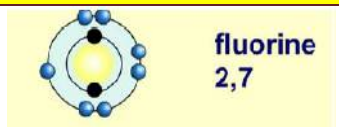








Chlorine -Bhor model



Sup Inf 2: Molecular structures of X-bonded chemical species

Layout	
X-bond formation necessary conditions	✓ Topology
	✓ Orbital character
	sup inf.1 ✓ Molecular Electro-static potential ✓ Electron density
	✓ Hundred years time line of Hydrogen-, Halogen-, no-bonding Interactions

Chemical Systems with X-bonding	
Intra-molecular X-bond	
Homo-dimer molecules	
Single crystal	
Co-crystals	Binary
	Ternary
Liquid-crystals	
Super-atoms/molecules	
Linear chains	
Molecular tapes	

Adducts (complexes)	Binary	
	Ternary	
Halogen (F, Cl, Br, I, At)-bonding	Fluorine	F
	Chlorine	Cl
	Bromine	Br
	Iodine	I
	Astatine	At
Rotaxane X-complexes		

Bio-Molecules
Bio-systems

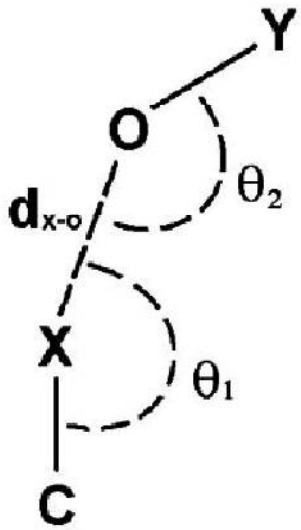
X-bonding + Another non-covalent bonding

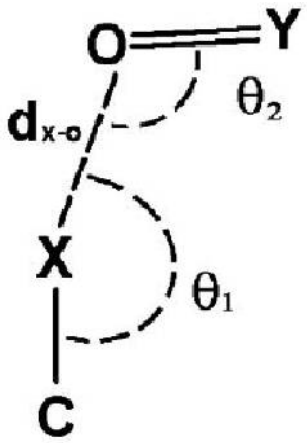
sup inf.3
H…bonds
Weak… … …Interactions

X...bonds topology

X-bond	Topology		XBS-01

Function(.)	
Geometrical aspects of interaction	☞ Distance of C-X bond ☞ Angle (oxygen relative to the C-X bond) ☞ Angle (halogen relative to the O-Y bond)



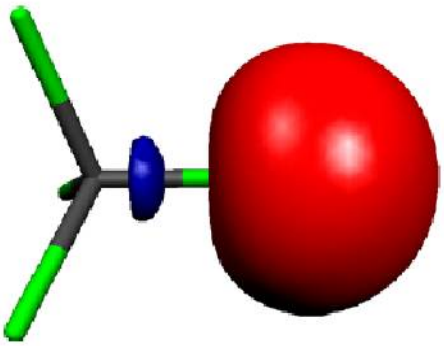


Interaction	lone pair of the oxygen atom with … halogen

Interaction	Pi system of the double bond between O … Y

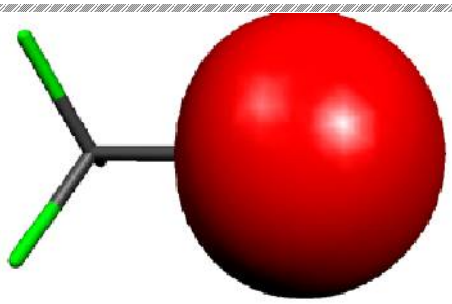
Orbital character

	CF3X		XBS-02
CF_4		CF_3Br	



unshared s-electron pair(75.12%) in CF_4

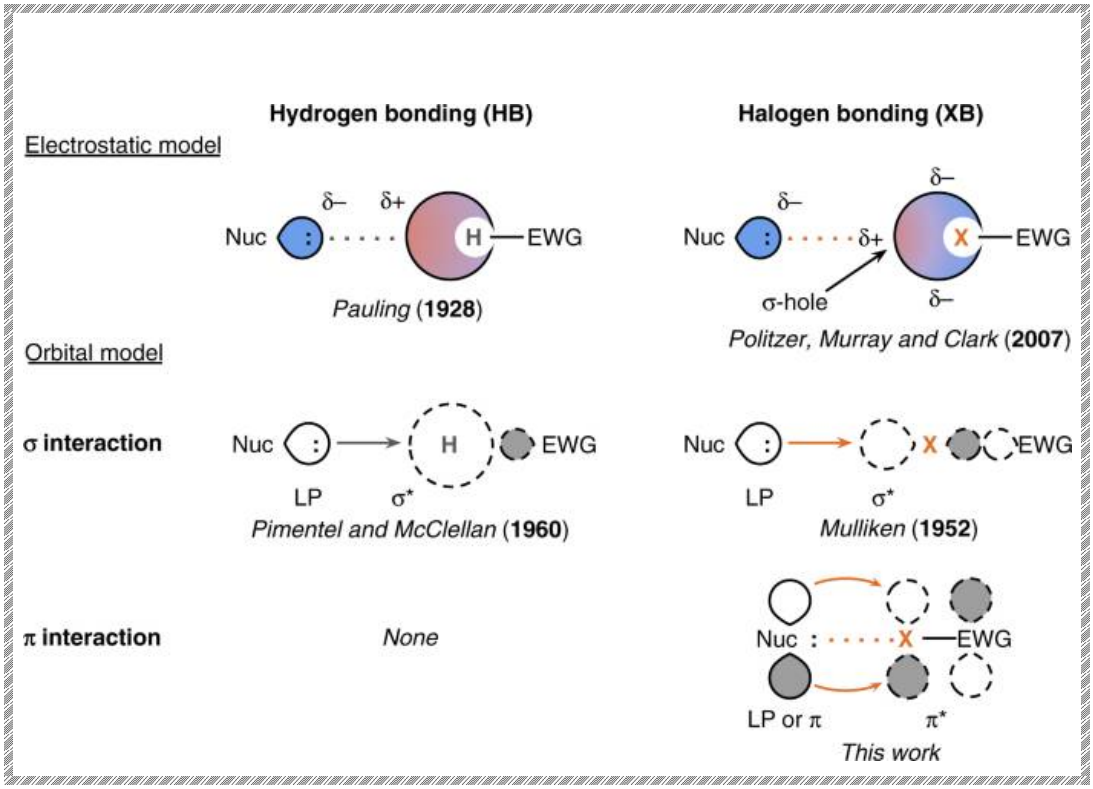
p-character (25%) more than that in CF_3Br (8%)



unshared s-electron pair in CF_3Br

p-character less than that in CF_4

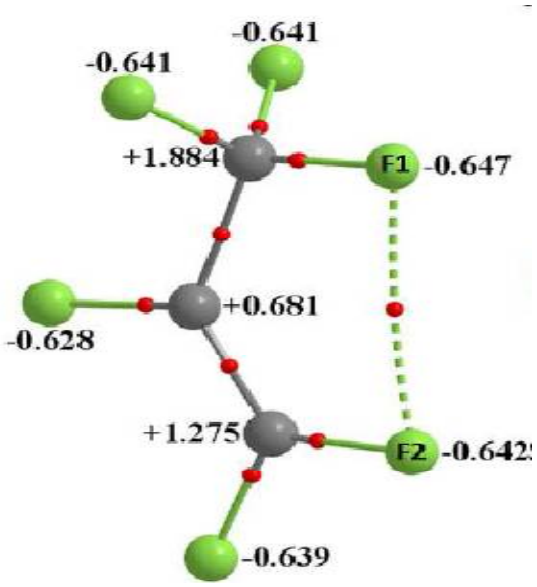
Hundred years Time line of H-, Ha-, no-bonding Interactions



Chemical Systems with X-bonding

Intra-molecular X-bond (Flourine)

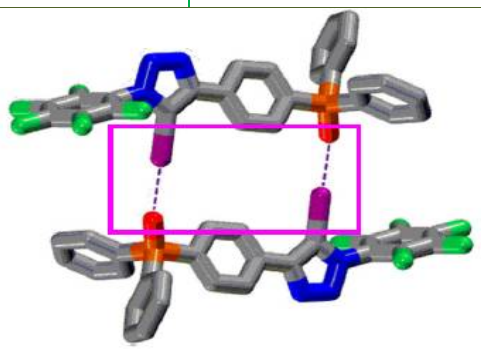
Monomer	C3F6	F3C-CF=CF2	XBS-03



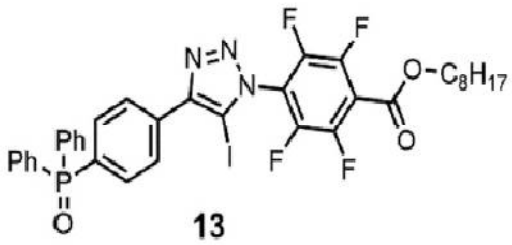
halogen bond	F1…. F2 bond
Method. CQC	QTAIM
Probe: BCP bond path between two covalently bound fluorine atoms	Confirmed ✓ intramolecular interaction of two negatively charged F-atoms
Dist F1…F2:2.624 Å, rb = 0.0137 a.u. Ñ2rb = 0.0629 a.u.	Inference : closed-shell bonding interaction since positive value of Ñ2rb & small value of rb

Homo-dimer molecules

Homodimer	CQC calculated structure	Phosphine oxide receptor 13		XBS-04



Theory	DFT
Hybrid functional	TPSSh
Basis set	def2TZVP

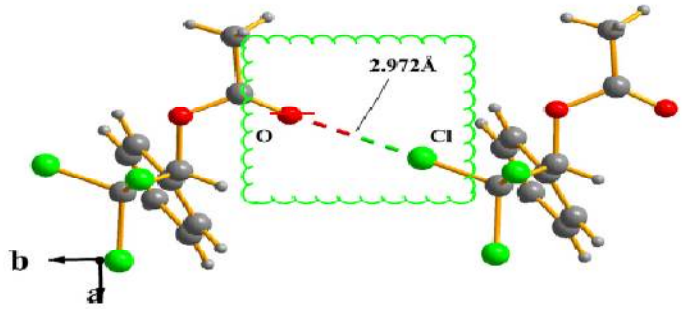


13

Crystal	Chemical species	
✓ Single crystal	Monomer	
✓ Cocrystal	➔ Adduct	➔ Binary
		➔ Ternary

Single crystal

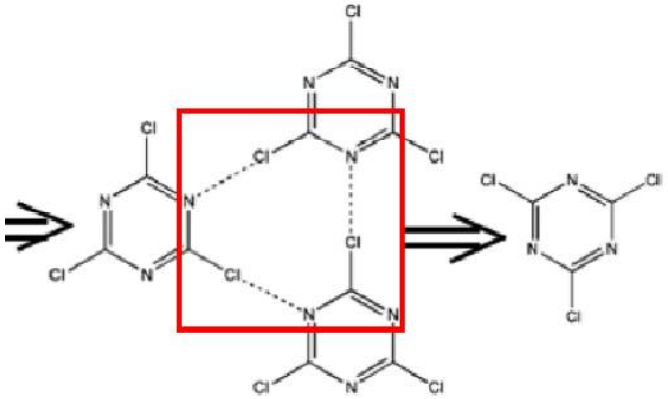
single crystal	ATMBA	Cl…O		XBS-05



alpha-(Trichloromethyl) benzyl acetate (ATMBA)

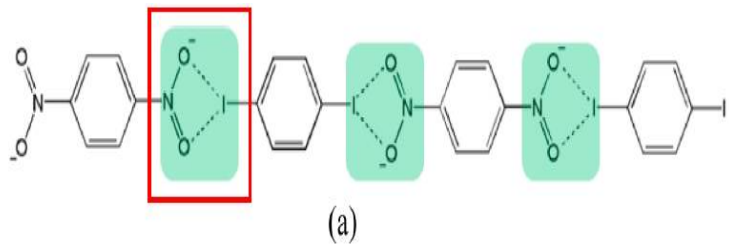
Co-crystals binary

1:1 cocrystal	1,3,5-tricyanobenzene	hexamethylbenzene	XBS-06



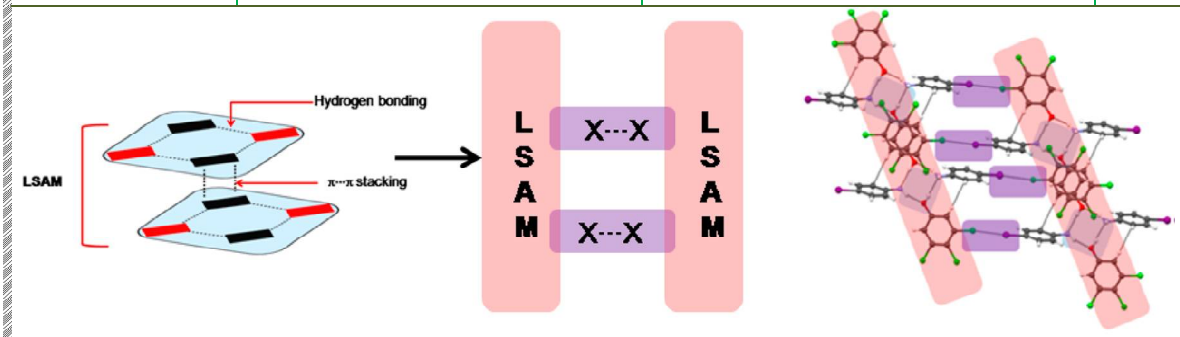
halogen bond	C-Cl…NY

Cocrystal of 1:1 (a)	1,4-dinitrobenzene	1,4-diiodobenzene	XBS-06



halogen bond	I···O1 of NO2 I···O2 of NO2

1:1 cocrystal	3,4,5-trichlorophenol	4-iodoaniline	XBS-06



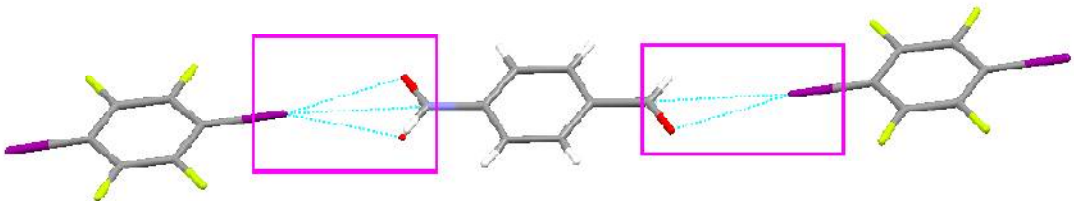
halogen bond	I···O
LSAMs :long range synthon aufbau module	

Binary cocrystal	4-ANLD	DITFB	XBS-07

halogen bond	C=O···I
H-Bond	C−H···O
	Methoxy group of 4-ANLD
Chain type structure	

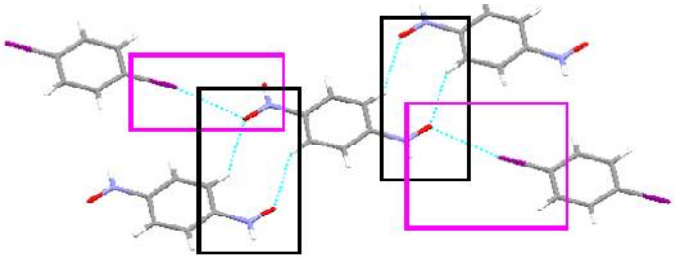
Binary cocrystal	4-NBD	DITFB	XBS-07

halogen bond	C=O···I



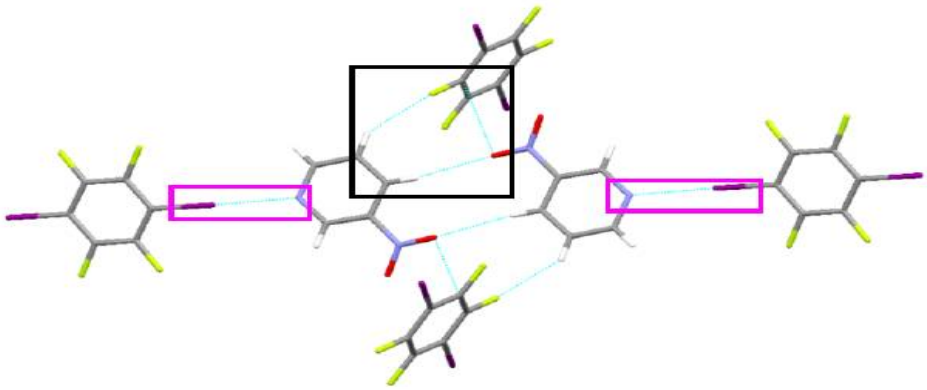
Binary cocrystal	4-NBD	DIB	XBS-07

halogen bond (pink)	C=O···I I of DIB molecule O of CHO-Ph
H-bond weak (black)	C−H···O oxygen atom of (CHO/NO2)



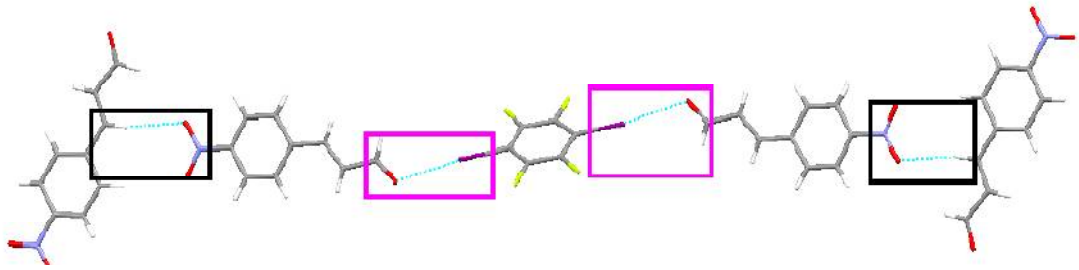
Binary cocrystal [AB3]	DITFB	3-NPY	XBS-07

halogen bond (pink)	N…I	pyridine N …. I of
H-bond weak (black)	C-H…O	3-NPY moiety … NO2 group
	RH…F	C-H of 3-NPY … F of DITFB



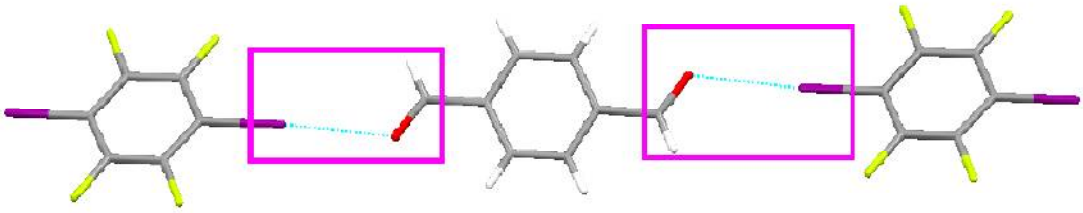
Binary cocrystal (AB4)	DITFB	NCAD	XBS-07

halogen bond (pink)	C=O···I	aldehyde O…
H-bond weak (black)	C–H···O	NO2 group



Binary cocrystal (AB)	DITFB	TA	XBS-07

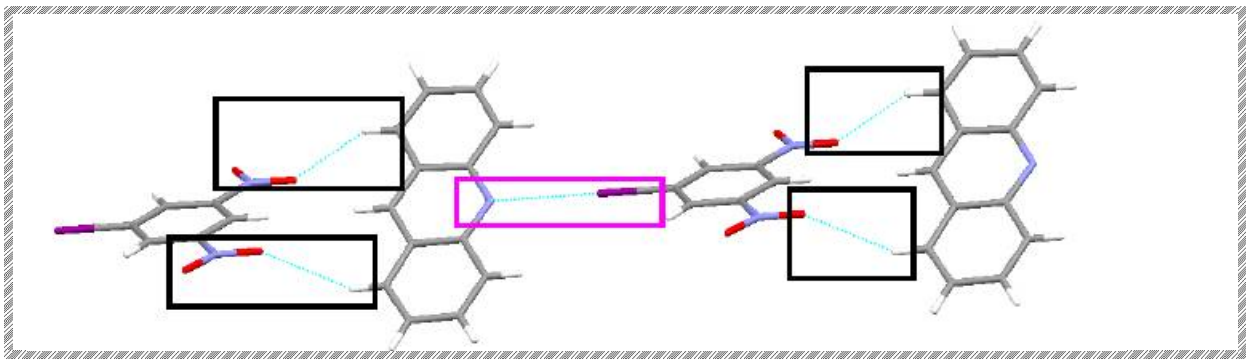
halogen bond (pink)	C=O···I	Both aldehyde groups



Exptal failure	**Failed to get any crystal**from the TA+DIB mixture
Reason	✓ strong-strong and weak-weak interactions are favoured ➔ compared with strong-weak ones in binary cocrystals

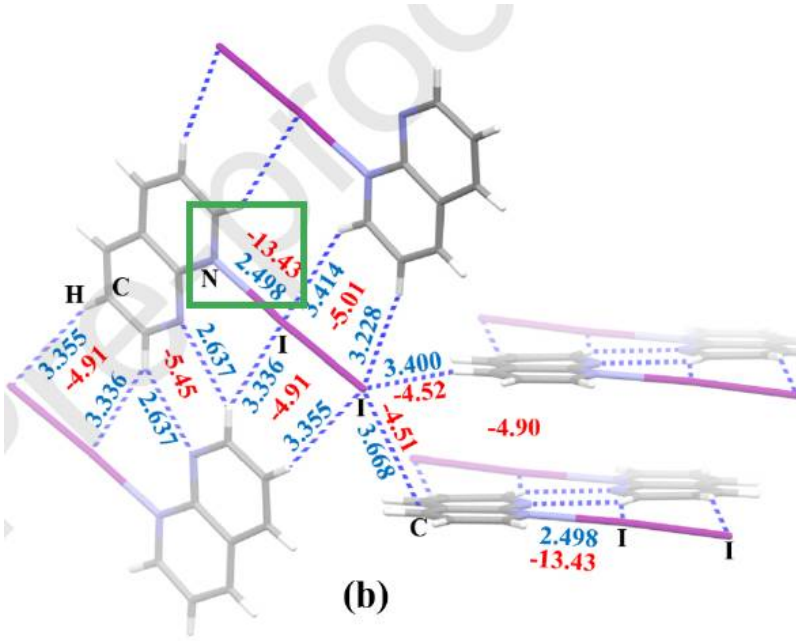
Binary cocrystal (AB)	IDNB:	ACR	XBS-07

halogen bond (pink)	C=N···I	N atom of ACR … I-atom of IDNB
H-bond weak (black)	C–H···O	phenyl H-atom… O of NO2 group
! two molecules are not planar ! bisect each other at an angle of 35.38°		



Probe: CQC	XBS-07
➔ Geo.optimization ➔ Electronic energy	Theory: DFT Functional: wB97XD Basis set: def2-TZVP Software: Gaussian09
➔ Proton affinity (PA)	Same level as opt
➔ ESP	Geometry opt: wB97XD Software: WFA-SAS software
➔ Charges on individual atoms	Natural Bond Orbital (NBO) analysis
➔ Interaction energy of ternaries (only involving halogen bonds)	Optimized geometries

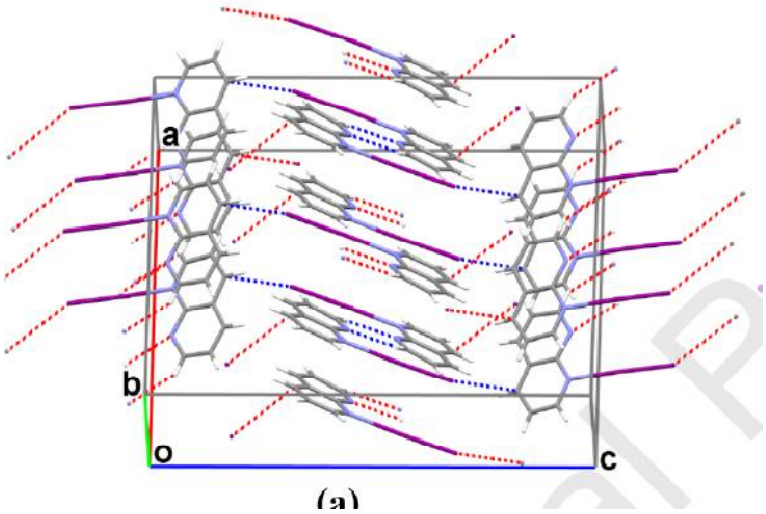
cocrystal	ND	I2	X-bond	XBS-10



halogen bond strong	N···I
H-bond	C–H···N C–H···I

one-dimensional (1D) sheet structure

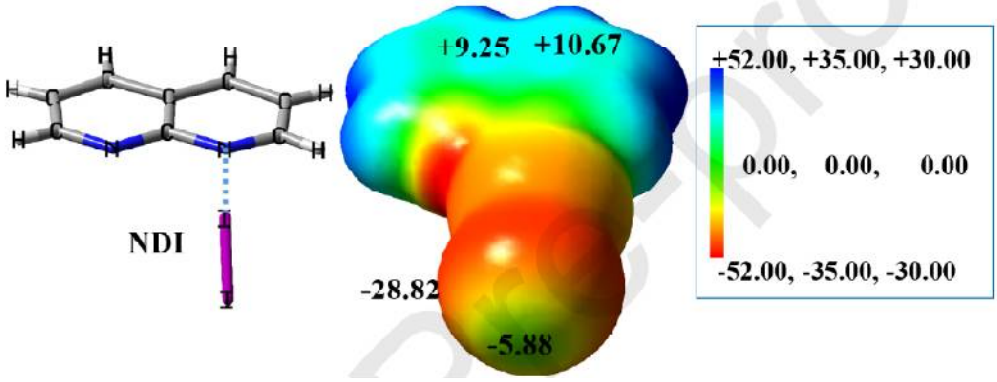
cocrystal	ND	I2	**X-bond**	XBS-10



(a)

Tetrel bonds	C···I
H-bond	C–H···I
2D layer structures → 3D supramolecular architecture	

Co crystal (AB)	ND	I2	**X-bond**	XBS-10



X-Bond	N…I
H-bond	C–H···I
Tetrel bonds	C···I
stacking interaction	

- → Monocoordinate N···I halogen bond not the symmetrical bifurcated halogen bond
- → N···I halogen bond is not an electrostatically dominated noncovalent interaction

N···I halogen bond

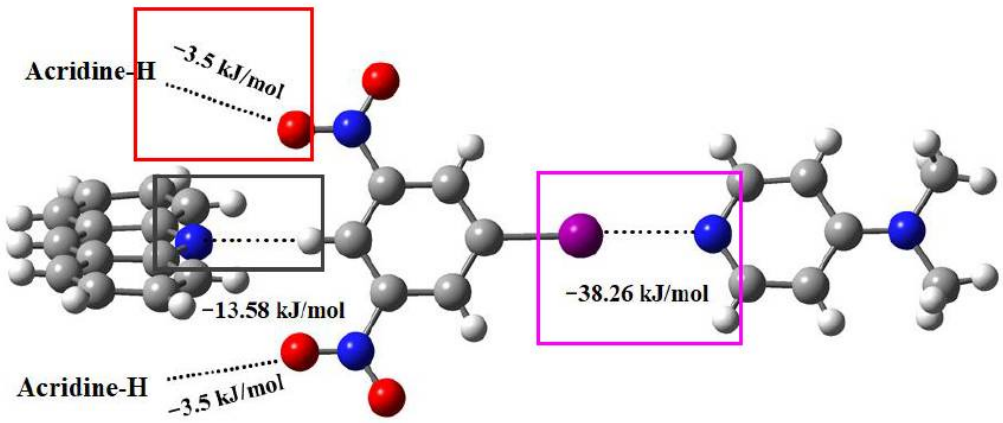
- 🕮 Upon the formation of the halogen-bonded complex NDI
  - ✓ σ hole of the other I atom of I2 is changed from positive to negative
  - ✓ same time the electrostatic potentials on the C atoms of the aromatic ring become more positive
    - ➔ This explains the formation of C···I tetrel bond in crystal structure

- 🕮 The electrostatic potentials around the two I atoms of NDI are much negative
  - ➔ supports formation of the C–H···I hydrogen bonds in the crystal structure.

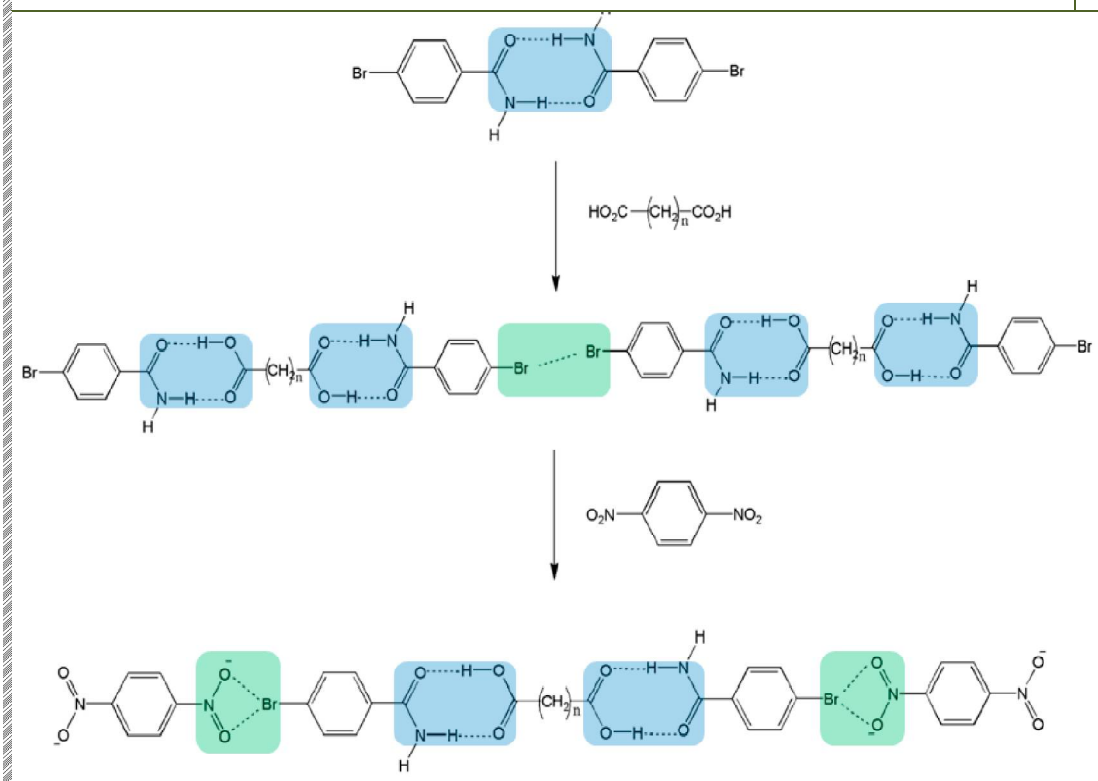
Co-crystals ternary

cocrystal (ABC) ternary	A	B	C	XBS-07

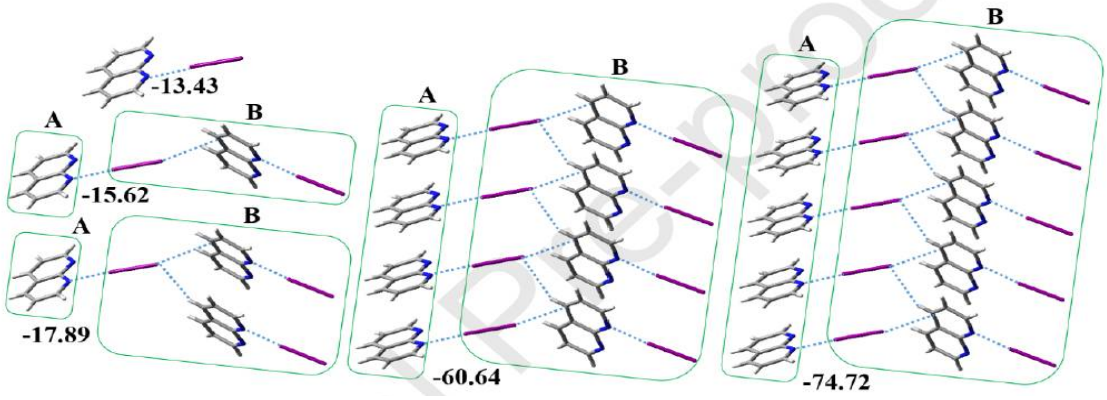
halogen bond (pink)		
H-bond weak (black)	Acridine	



Graded halogen and hydrogen bonds in the ternary cocrystal	XBS-06



Cocrystal (AB)n n=1 to 10	ND	I2	X-bond	XBS-10



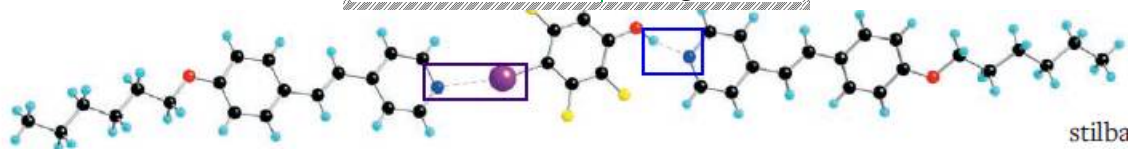
Interaction energies (kcal/mol)

$(AB)_m$	#X-bonds
NDI,	1
(NDI)2,	1
(NDI)3,	1
(NDI)8	4
(NDI)10	5

Liquid-crystals

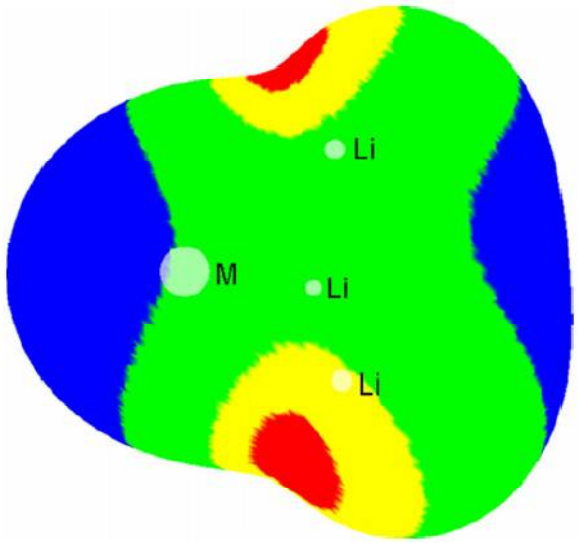
Liquid crystal	4-iodotetrafluorophenol	alkoxystilbazole		XBS-08

halogen bond (pink)	N···I
H-bond weak (black)	N···H
I = purple F = yellow C = black	O = red N = blue H = light blue



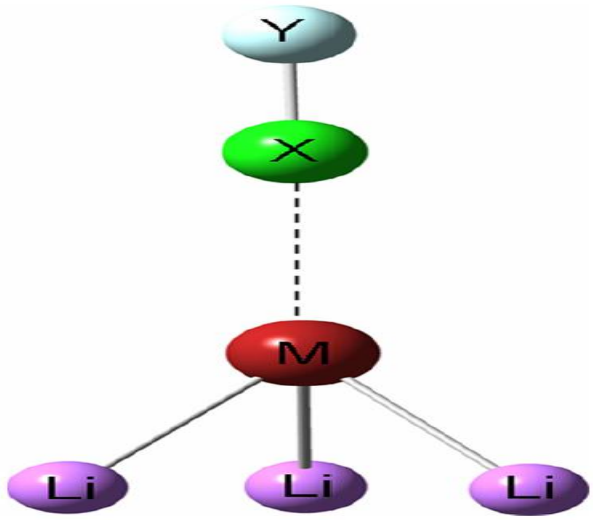
Super-atoms/molecules

Molecule	ESP	Li3M	XBS

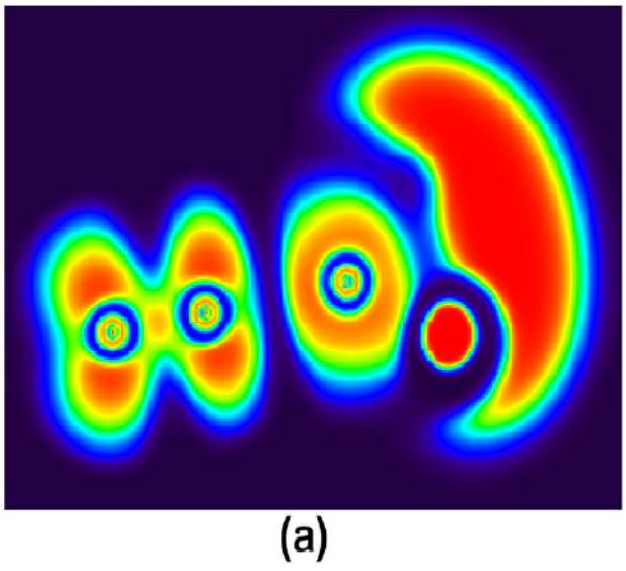


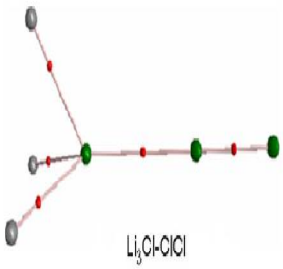
Molecule	Li3M	
	Theory	HF
ESP	Level	MP2
Blue	<0	
Red	>0.12	
Yellow	0.12	0.06
Green	0.06	0

	Li3M–XY		X-bond	XBS-10



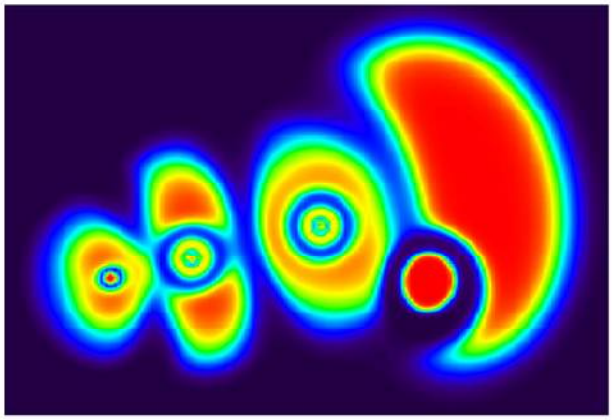
	Li3Cl–ClCl	electron localization functions	XBS



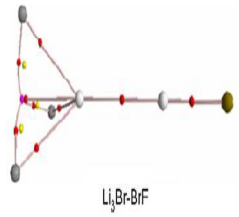


Molecule	Li3Cl–ClCl	
	Theory	HF
ESP	Level	MP2
	BS	aug-ccpVTZ
Bond critical points		Red dots
ring critical points		yellow dots

	Li3Br–BrF	electron localization functions	XBS



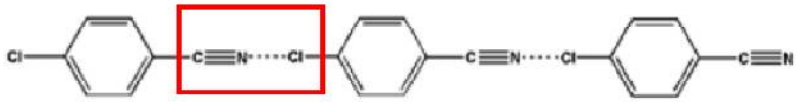
(b)



Molecule	Li3Br–BrF	
	Theory	HF
ESP	Level	MP2
	BS	aug-ccpVTZ
Bond critical points		Red dots
ring critical points		yellow dots

Linear chains

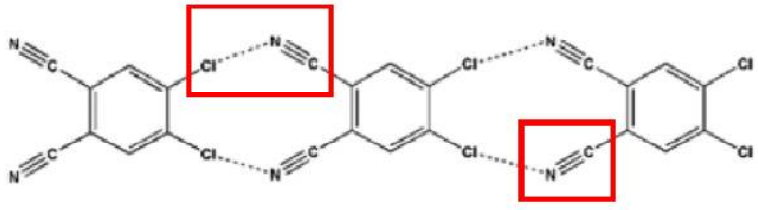
Linear chain	p-cyano-chlorobenzene			XBS-06



halogen bond	Cl…N
	R-Cl…NY

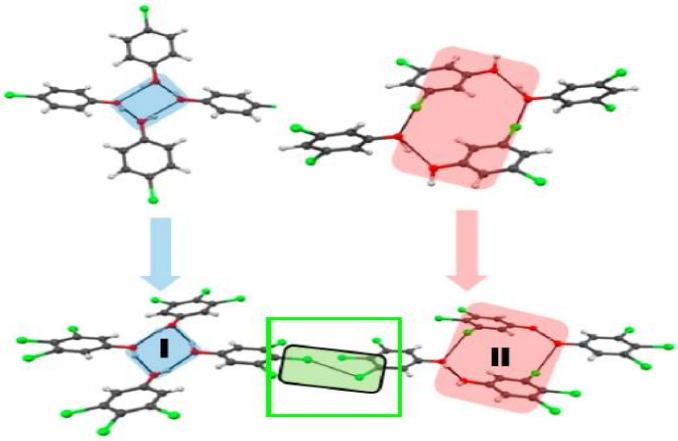
Molecular tapes

Molecular tape	1,2 dichloro, 4,5 dicyano-benzene			XBS-06



halogen bond	Cl…N
	R-Cl…NY
Cyclic X-bonded structure	

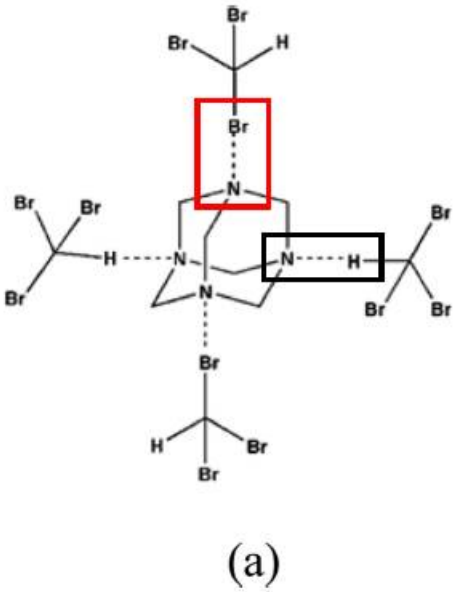
3,4,5-trichlorophenol	4-chlorophenol	3,5- dichlorophenol	XBS-06



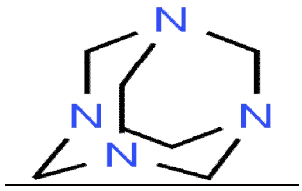
halogen bond	I … II

Binary adducts (complexes)

4:1 adduct	bromoform an	urotropin		XBS-06



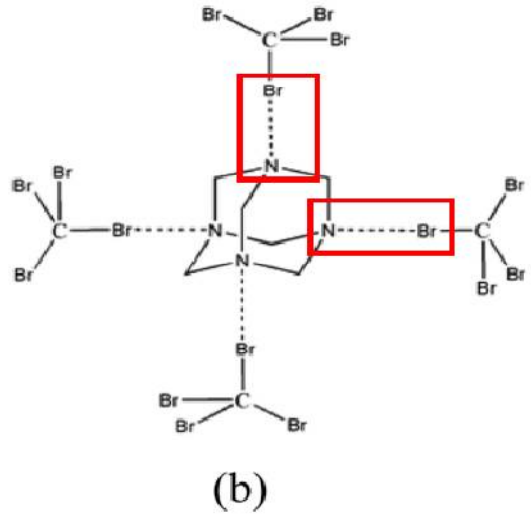
halogen bond	Br…N
	Br_2HC-Br…N of Ur
H-bond	Br_3C–H···N of Uro



urotropin

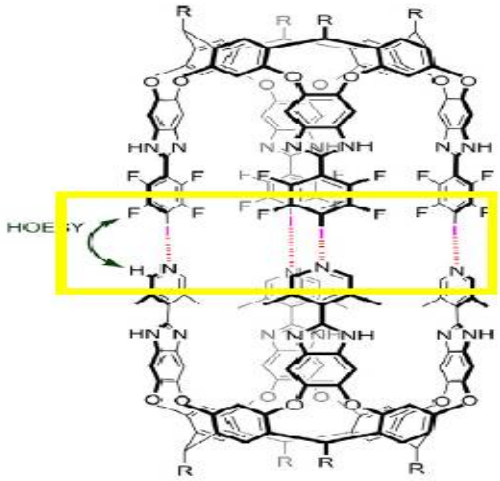
4:1 adduct	carbon tetrabromide	urotropin		XBS-06

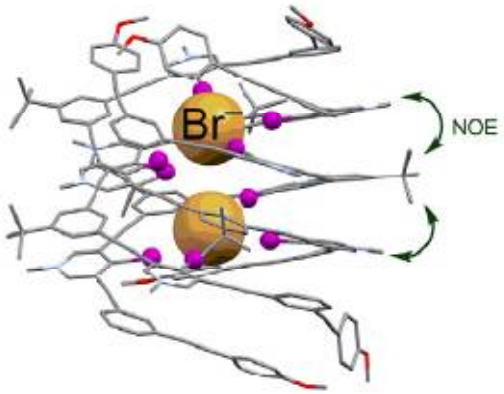
halogen	Br…N



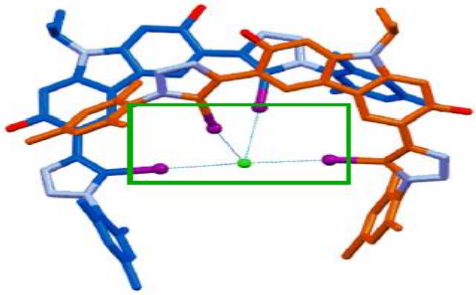
bond	Br3C-Br…N-Y

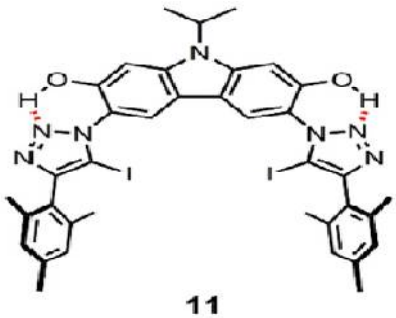
Dimeric capsule halogen bonding	Triple helix halogen bonding	XBS-09





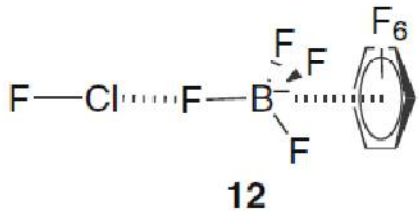
dimer–Cl^- complex	solid state structure	carbazole receptor 11		XBS





Ternary molecular adducts (complexes)

1:1:1 complex	Hexafluorobenzene	BF_4^- anion	ClF	XBS-41



12

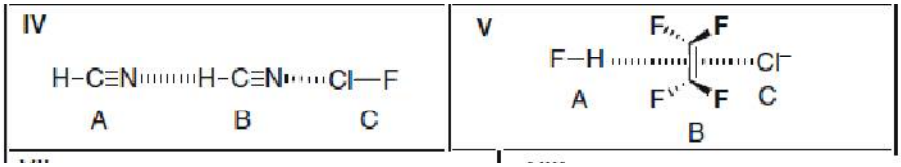
- leads to unfavorable cooperativity energy

halogen bond	Cl…F	Cl of F-Cl F of F-B
anion–p interaction		

111

1:1:1 complex	H-CN	Cl-F		XBS-41

111



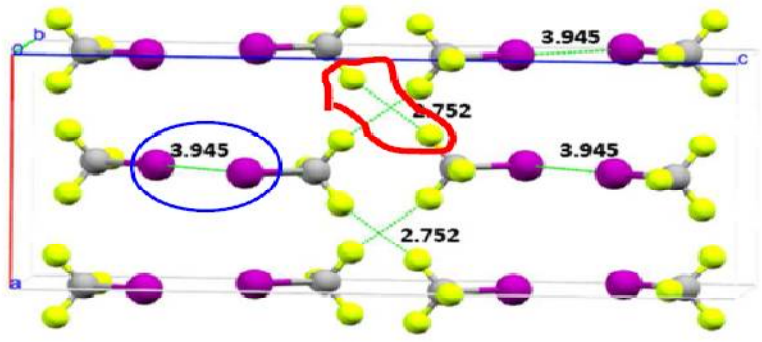
Cl…F Halogen bond	Pi…Cl⁻ Halogen bond
N…H H-bond	H…Pi H-bond

Omom

Flourine | Halogen (X)

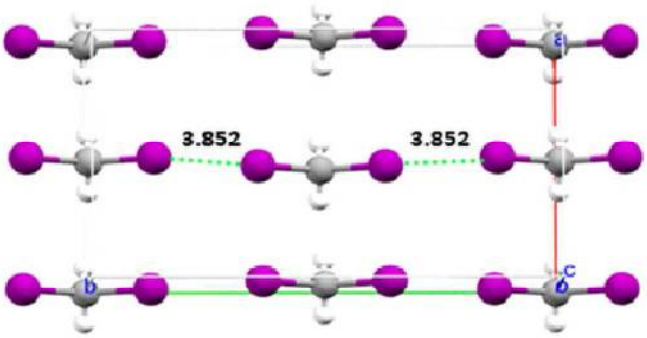
Non-covalent Bond

	CF3I	CSDsearch	XBS-03



halogen bond	F…F

	CH2I2	CSDsearch	XBS-03

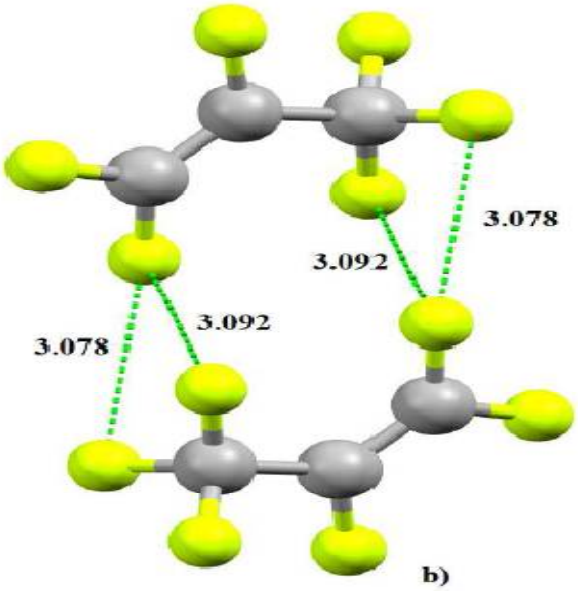


CH2I2

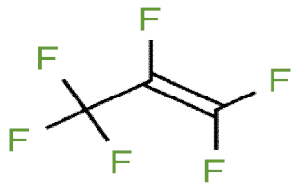
I….I Bond

halogen bond	I…I

Binary cluster	C3F6	F3C-CF=CF2	XBS-03

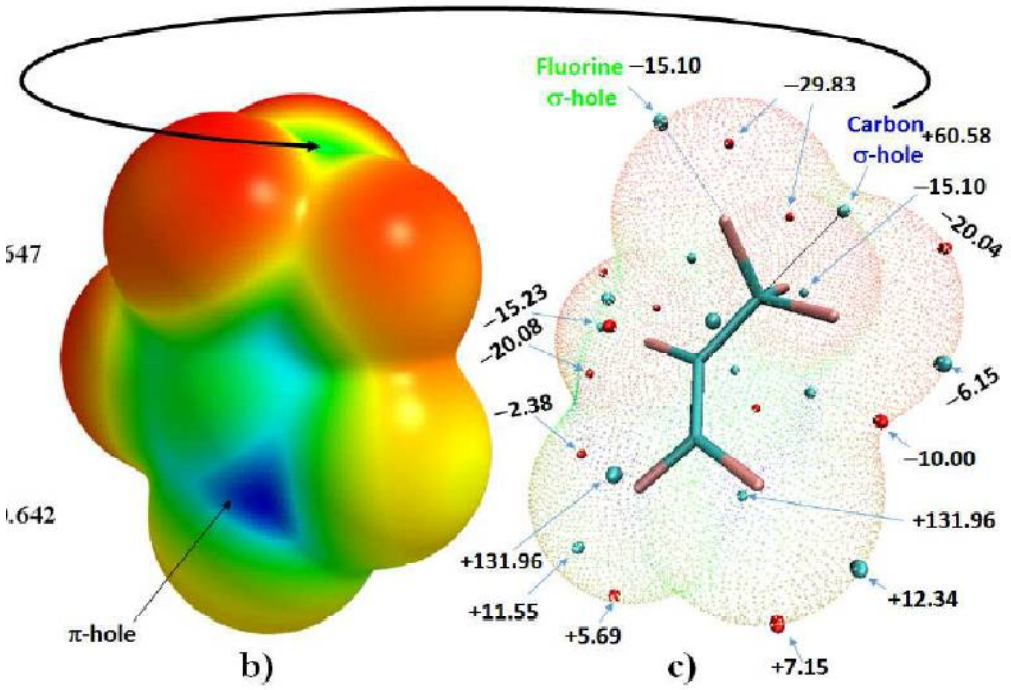


Halogen bond	F …. F bond (3.08)
Expt	XRD At Temp: 95 K
F atom	! 1 covBond with C ! 2 XBs with two F atoms



Hexafluoropropylene

MESP	C3F6 monomer		XBS

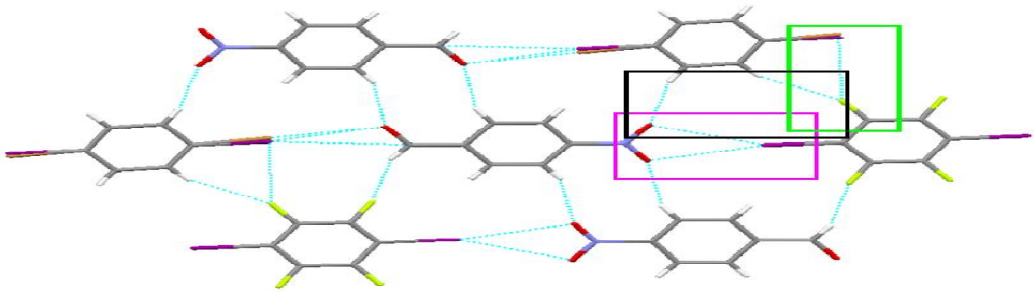


QTAIM based

M06-2X/6-311++G(2d,2p) molecular graph for the C3F6 monomer, showing the

- Bond critical points as tiny spheres in red
- Bond paths (solid and dotted lines in atom color; fluorine: green; carbon: dark-gray).
- Atomic charges are given in e.
- b) and c: solid and dotted versions of the 0.001 a.u. (electrons bohr–3) isodensity map of the molecular electrostatic surface potential of C3F6

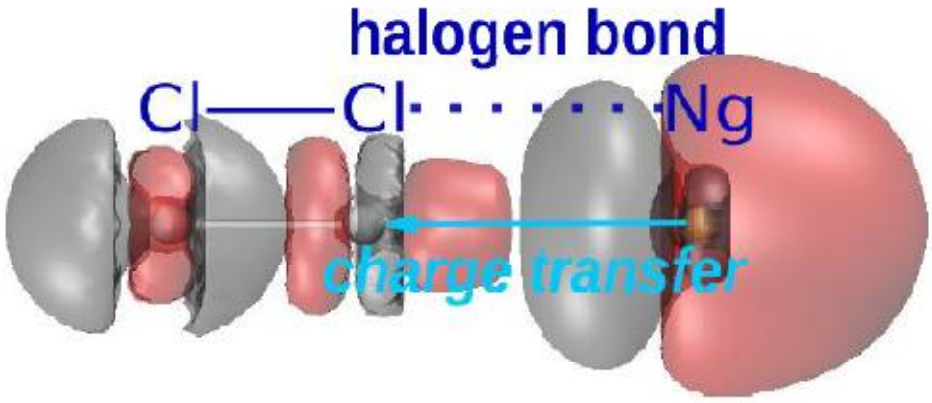
X-bond	1,4-diiodotetrafluorobenzene	1-iodo-3,5-dinitrobenzene ???	XBS



Chlorine | | Halogen (X)

Non-covalent Bond

Cl-Cl…Ng	Noble gas (Ng)		XBS-12



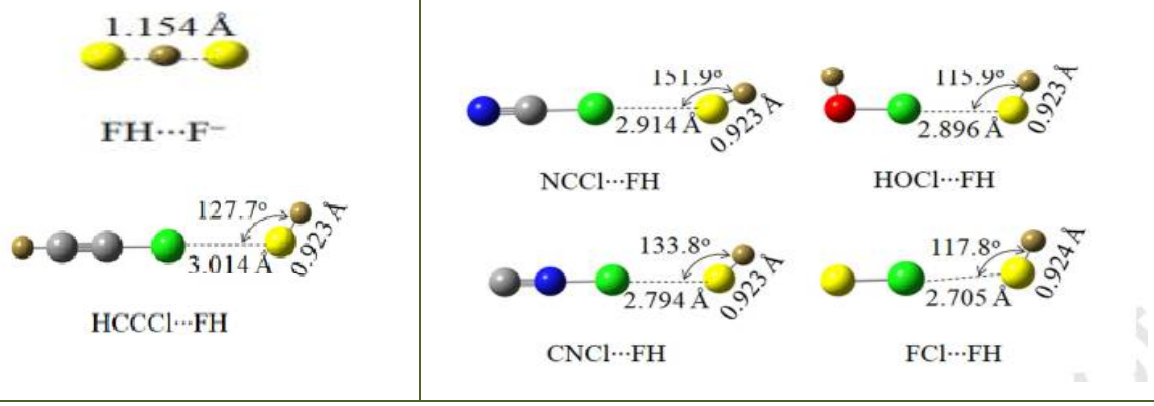
Experiments	Molecular Beam Scattering
Computational	CQC
Theory	DFT ab initio

convergent XB donors	chloride complex		XB

Theory	DFT

dyads AB				XB-13

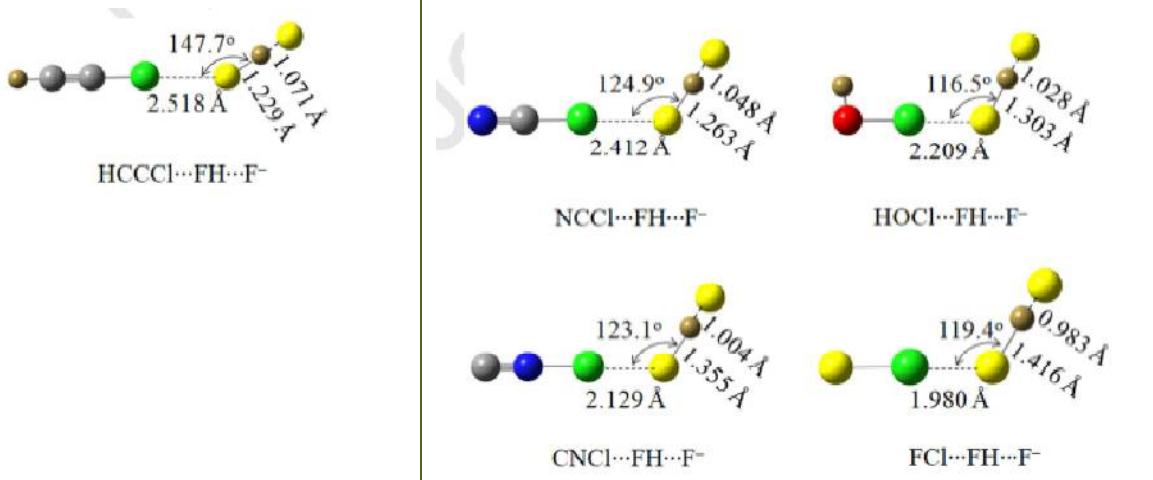
halogen bond	Cl…F	Cl of RCl…F of FH
R in RCl	F, CN, NC, OH, CCH	

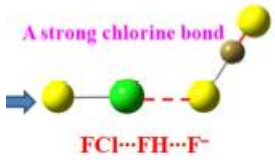


Data	The Cl···F distance is from 2.705 Å in FCl···FH to 3.014 Å in HCCCl···FH
Information	These Cl···F distances are shorter than the sum of the van der Waals Radii of both atoms (~3.15 Å).
Inference	Halogen bond is present between both molecules

Triads ABC	RCl	FH	F^-	XBS-13

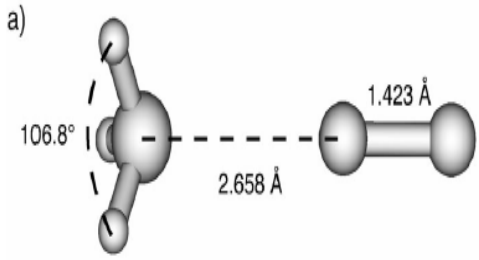
halogen bond (pink)	RCl…F…F	Cl of RCl…F of FH…F of fluoride anion
R in RCl	F, CN, NC, OH, CCH	



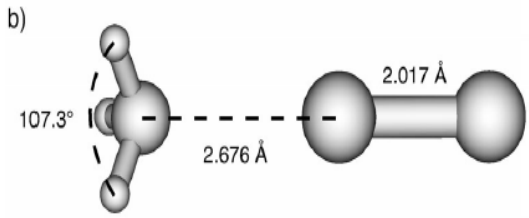
RCl···FH	R-Cl	F-H	FH···F–	F-Cl	F-H…F$^-$	XBS-13
						
[R = F, CCH, CN, OH, NC]			very strong hydrogen bond in FH···F–.			

Theory	DFT	XBS-25
Functional	B3LYP	
Basis set	6–311+G(d)	CF4 CF3Cl CF3Br
	DGDZVP	CF3I
Software		

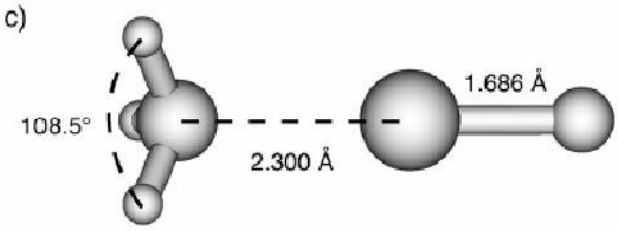
X…NH3	Cl2, Br2,ClF			XBS-14
	Feo opt	CP-CCSD(T)-F12b/VTZ-F12b		



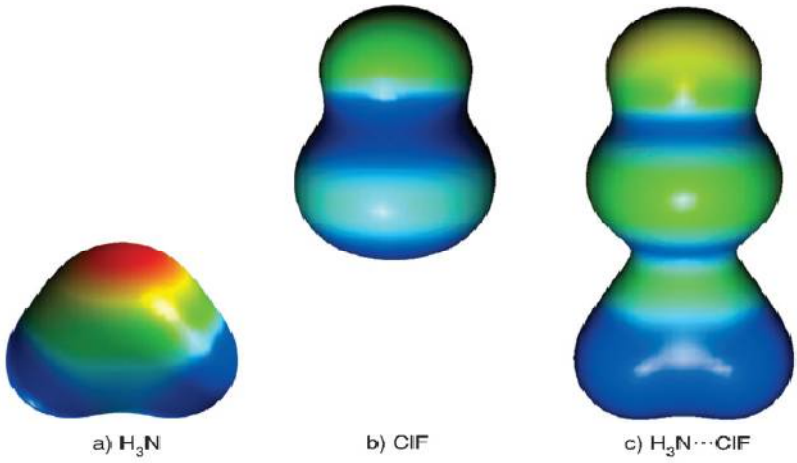
a) H3N···F2



b) H3N···Cl2



c)H3N···ClF

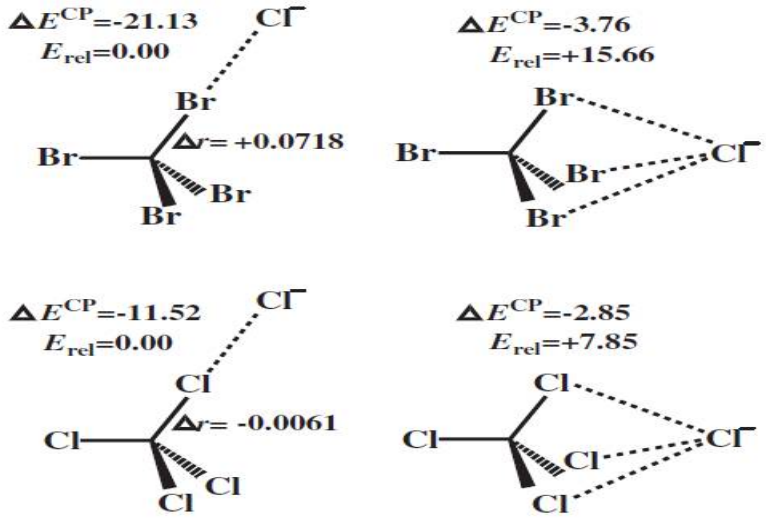


ESP	MP2/augcc-pVDZ
Red	<-0.01 au
Blue	>0.01 au
Isodensity surfaces (0.02 a.u.)	

Bromine | Halogen (X)

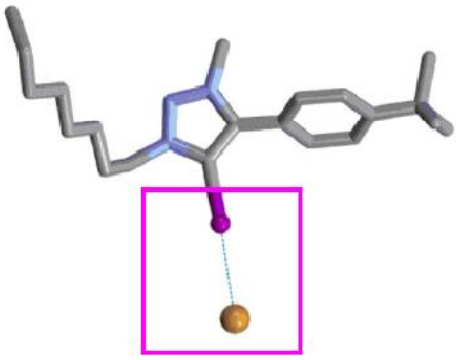
Non-covalent Bond

X…Cl	CBr4 or CCl4	Cl^-	X-bond	XB

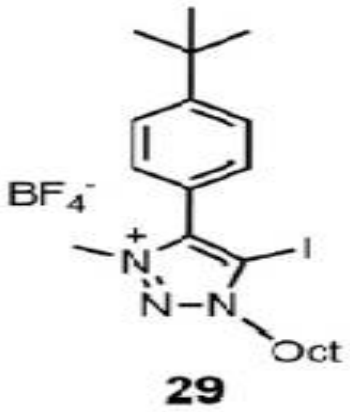


(r, Å)	Means
Positive value	Elongation
Negative value	Contraction

Bromide complex	Solid-state structure	iodotriazolium unit 29	XB

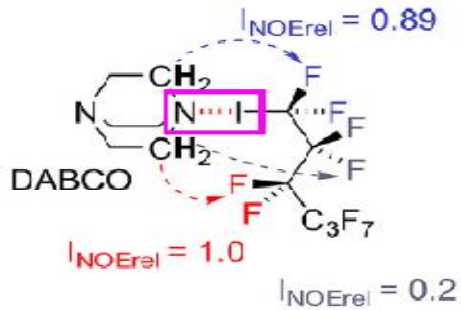


Hydrogen atoms and counterion omitted for clarity

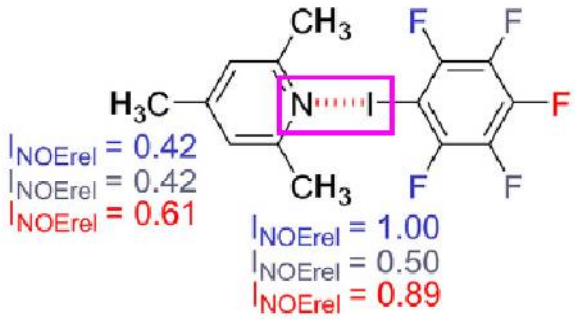


AB	DABCO	1-iodoperfluorohexane	AB	2,4,6-trimethylpyridine	iodoperfluorobenzene	XB

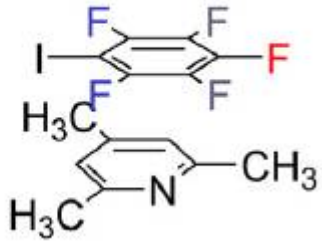
XB and HB



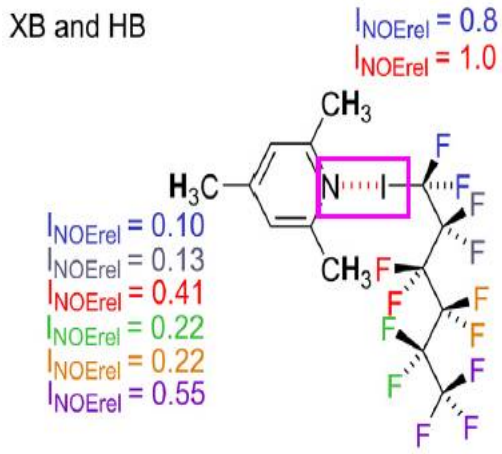
XB and HB

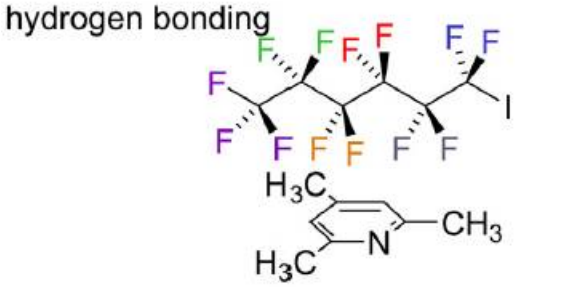


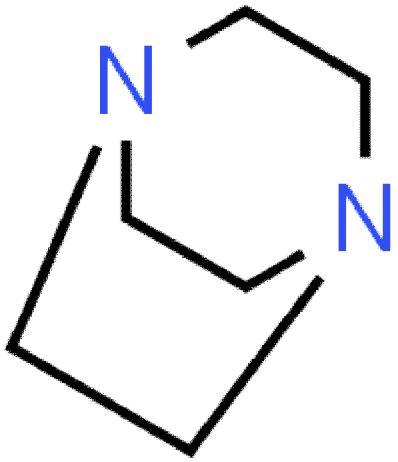
π-stacking and HB



AB	2,4,6-trimethylpyridine XBS-22	1-iodo perfluorohexane		AB	DABCO	

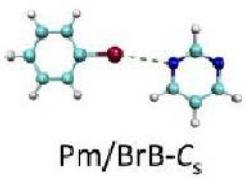


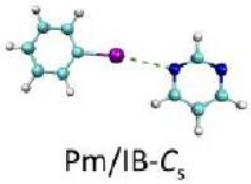


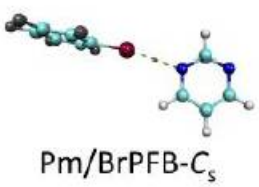


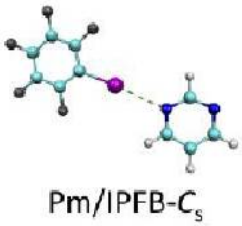
1,4-Diazabicyclo[2.2.2]octane (DABCO)

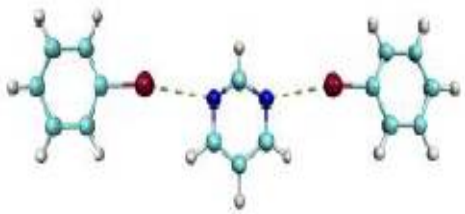
XB	CQC, Raman ; NMR		Iodo-pentafluorobenzene	pyrimidine	XBS-15



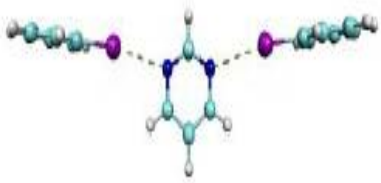




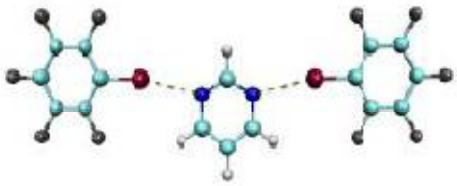




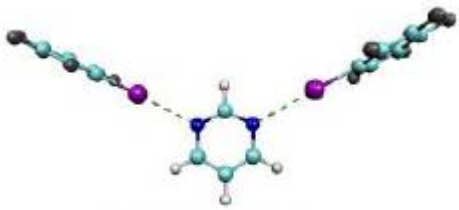
Pm/(BrB)$_2$-C_2-B



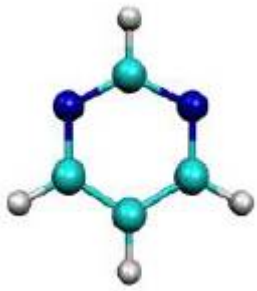
Pm/(IB)$_2$-C_s



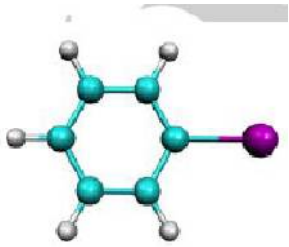
Pm/(BrPFB)$_2$-C_{2v}



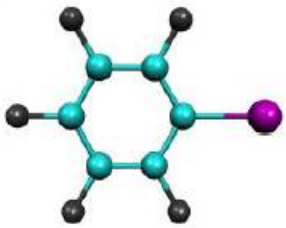
Pm/(IPFB)$_2$-C_2



pyrimidine (Pm)

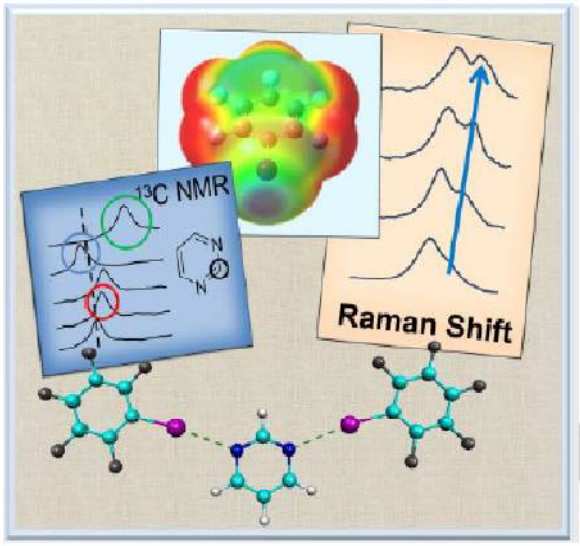


bromobenzene (BrB) or iodobenzene (IB)



bromo- (BrPFB) or iodopentafluorobenzene (IPFB)

Theory	DFT	
Functional	M06-2X aVTZ	
Basis set	Augmented with diffuse functions (aug-cc-pVTZ)	
	small-core energy-consistent relativistic pseudo-potential (aug-cc-pVTZ-PP).	bromine[42] and iodine
Software	Gaussian09	

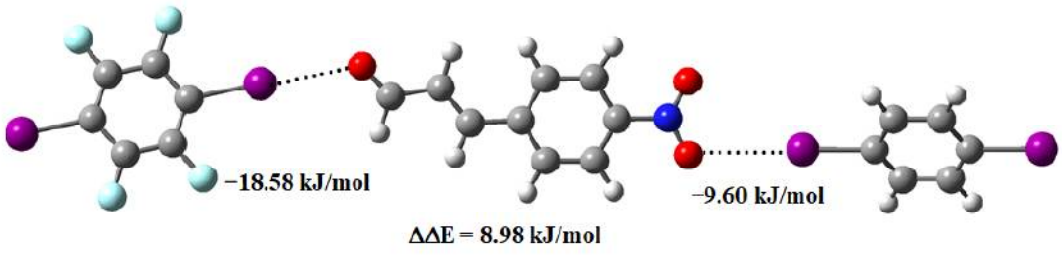


Iodine | Halogen (X)

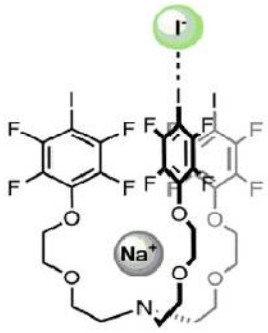
Non-covalent Bond

ABC	DITFB	4-NCAD	DIB	XBS-07

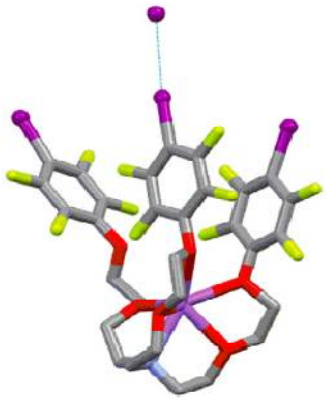
CQC-	Inference: failure of formation of ABC	
	Reason	➔ DDE (8.98 kJ/mol) is positive ➔ DDE: Difference between DEs of binaries



AB	Perfluoroaryl receptor 2	NaI		XBS-10



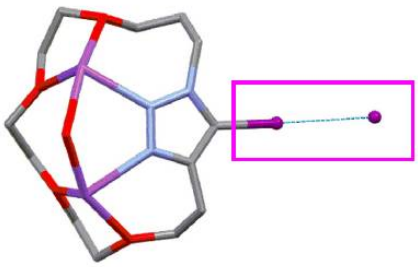
2a.NaI

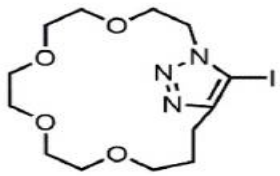


halogen bond strong	I…. I bond
Na+ cation coordination	

Appl	anion recognition in solution	halogen bonding as a specific interaction

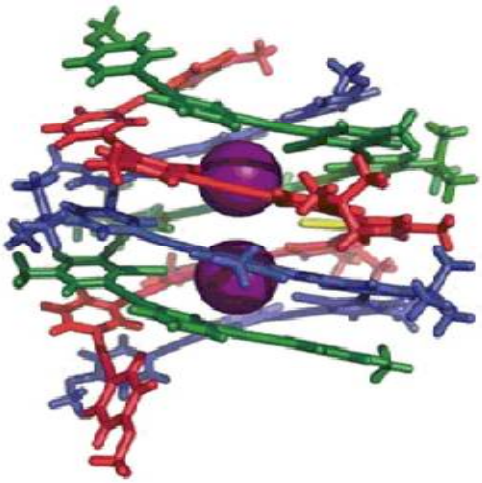
12.2 (NaI) complex	Solid state structure	Iodotriazole crown ether macrocycle 12		XBS-10

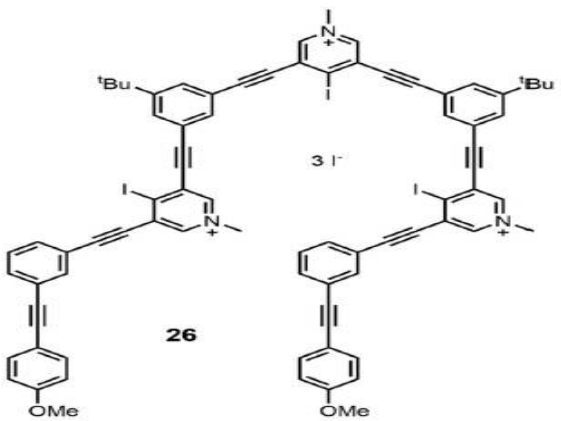




12

Triple helicate binding two intrachannel iodides	Solid-state structure	Berryman's iodopyridinium receptor 26	XBS-10



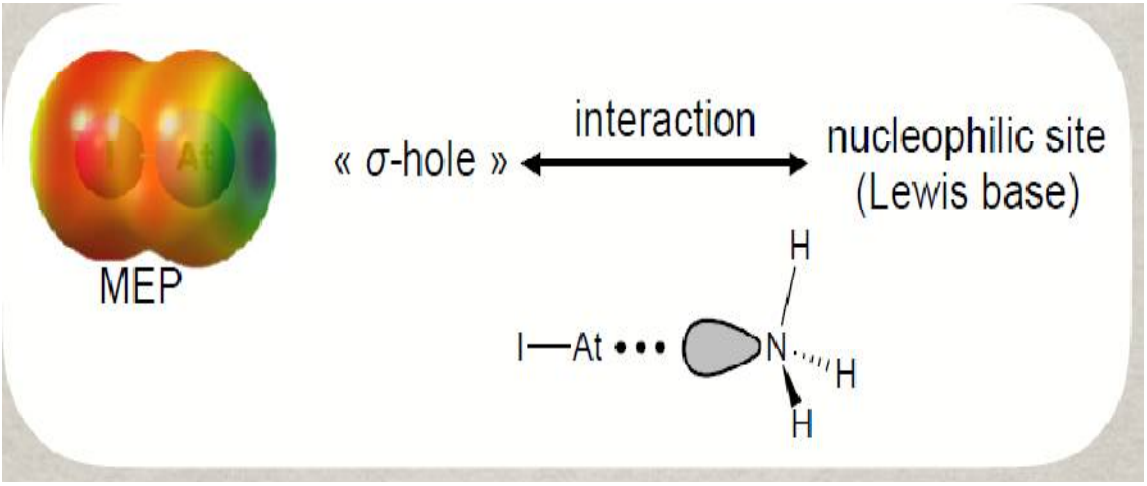


26

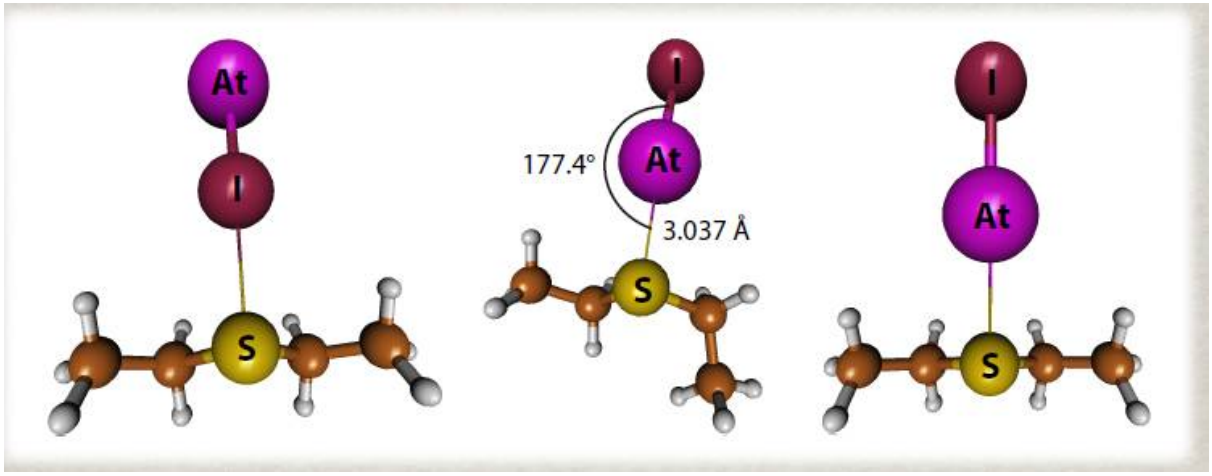
	Fact base. σ-bond
CF_4	fluorine hemispheres are negative
CF_3Cl	➔ positive potential develops on the outermost portion of its surface, around its intersection with the C–Cl axis. ➔ This positive region, which is centered on the C–X axis, as the "σ-hole" in the belt of negative potential that encompasses the chlorine
CF_3Br CF_3I	➔ σ-holes on the bromine and the iodine are progressively larger and more positive
Consequence ➔	these positive regions that are responsible for the halogen-bonding capabilities of CF3Cl, CF3Br and CF3I, as well as other halogen-bearing molecules
	halogen bonding by CF3Cl, CF3Br and CF3I is greatly enhanced by the three electron withdrawing fluorines
CH_3Cl	CH3Cl does not even have a σ-hole [13, 15–17],
CH_3Br CH_3I	σ-hole on the bromine and iodine & σ-hole in CH3Br and CH3I are much weaker
CH_4	

Astatine Halogen (X)

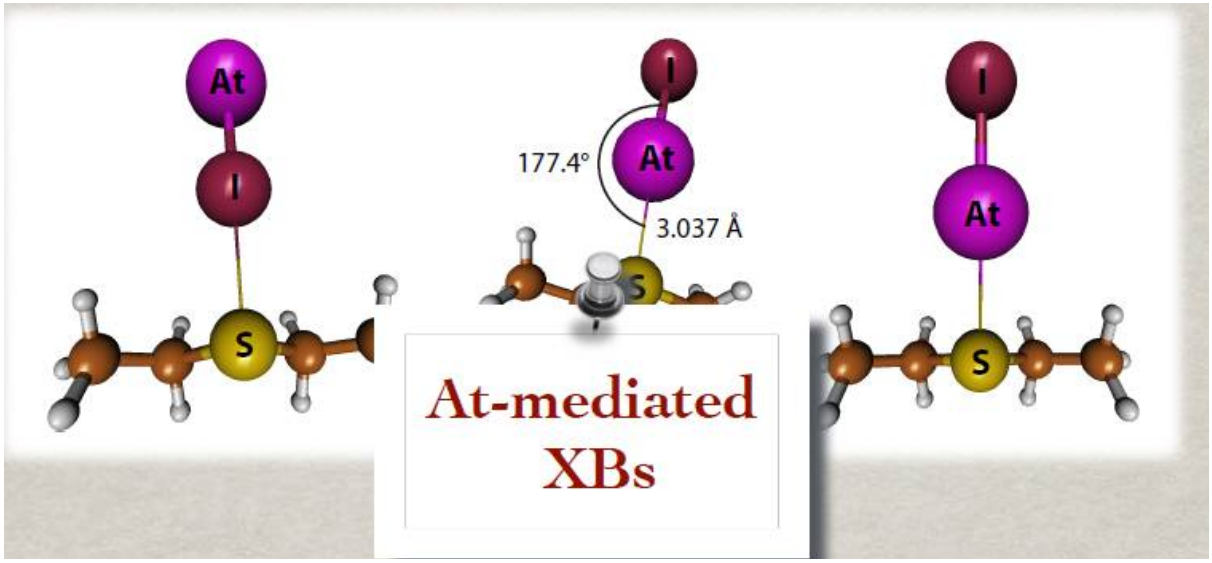
		XBS-16



				XBS-



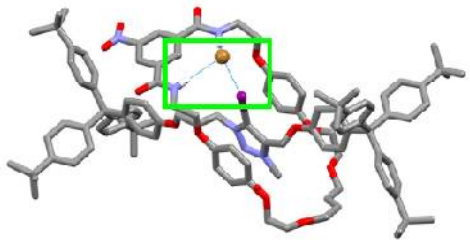
				XBS-



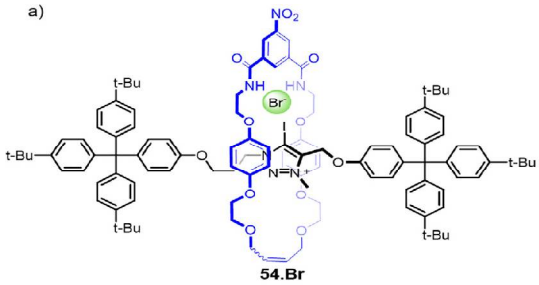
- ! Astatine is potentially the strongest XB donor
- ! Extend the range of the XB basicity scale
- ! Influence of relativistic effects on At-mediated XBs
- ! At-mediated XBs relevant to targeted alpha immunotherapy

Rotaxane X-complexes

XB	rotaxane	Solid-state structure	XBS-10



First example of an XB in rotaxane 54



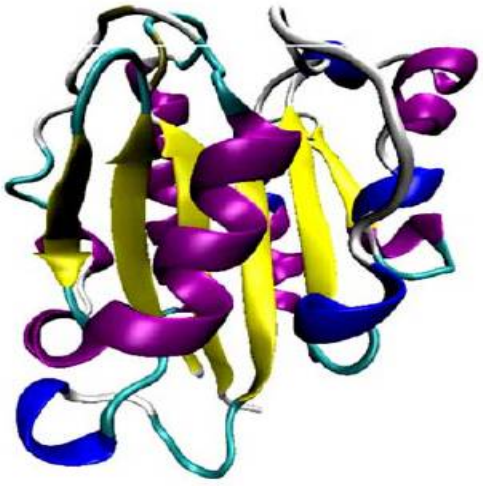
Disorder and non-polar hydrogen atoms omitted for clarity

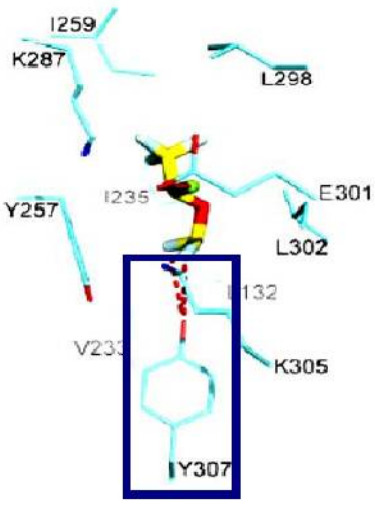
Bio-systems
Bio-Molecules

XB		Crystal structure of the LFA-1 bound to the Sstereoisomer isoflurane	XBS-01

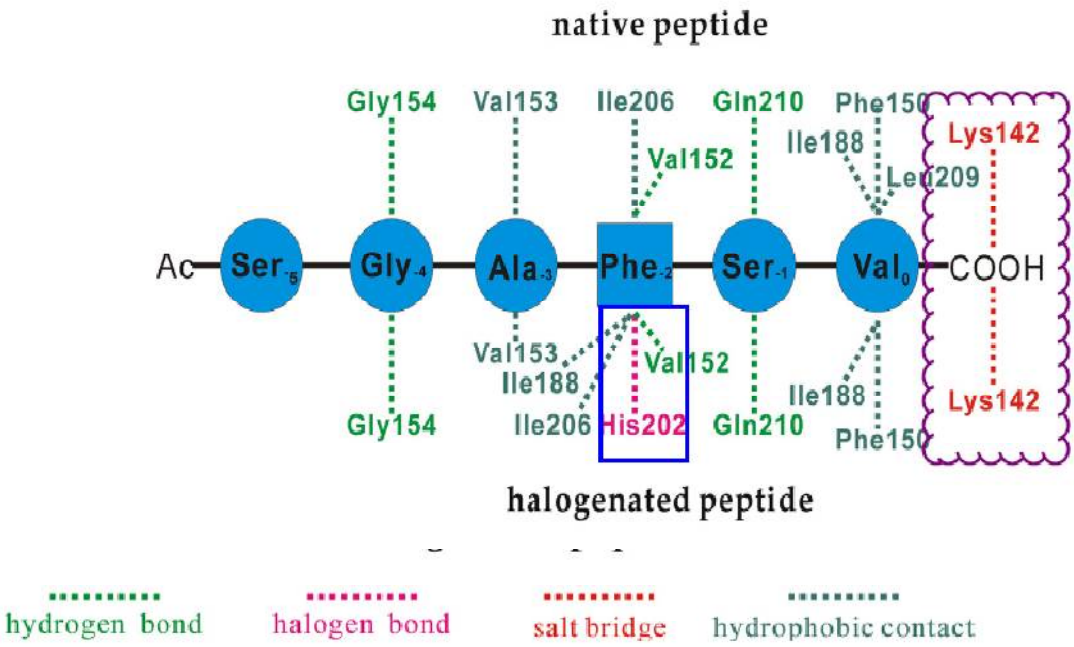
Integrin lymphocyte function- associated antigen-1 (LFA-1)

Ribbon representation

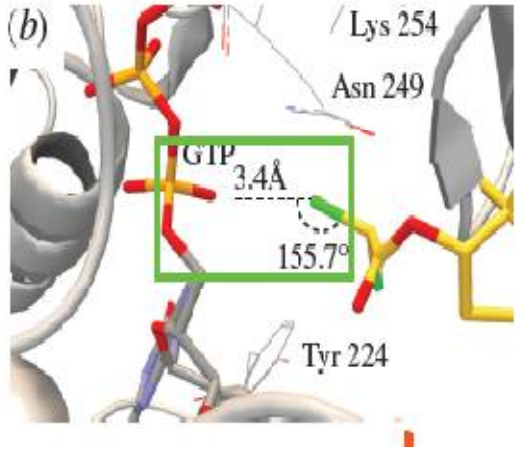




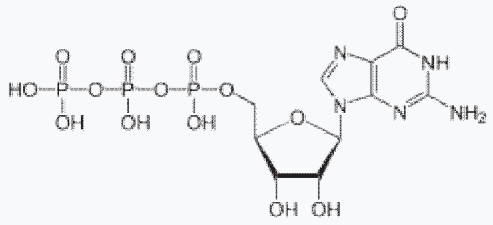
X-bond	Native sga (P-2F) peptide	Intermolecular noncovalent interactions	XB



Guanosine triphosphate (GTP)	X…Cl	X-bond Putative	XBS-04



Guanosine triphosphate (GDP)

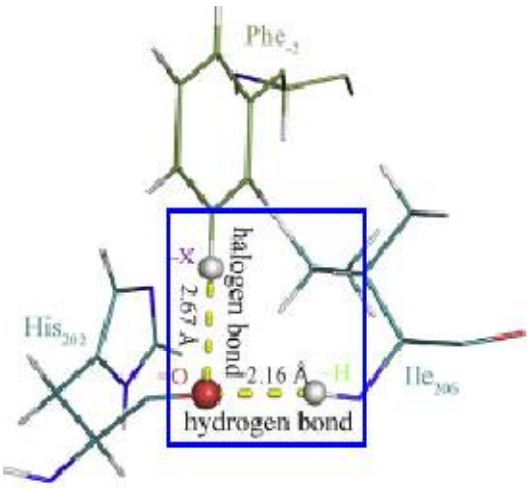


IUPAC name

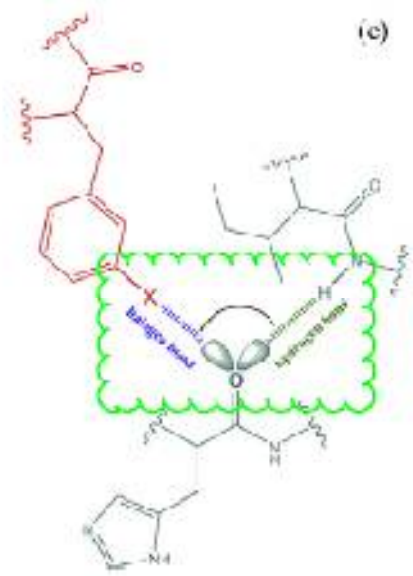
O[1]-{[(2*R*,3*S*,4*R*,5*R*)-5-(2-Amino-6-oxo-1,6-dihydro-9*H*-purin-9-yl)-3,4-dihydroxy oxolan-2-yl]methyl} tetrahydrogen triphosphate

Halogen bond	**Cl…O**	**R-Cl…O of GTP**	

human fertilization			XB



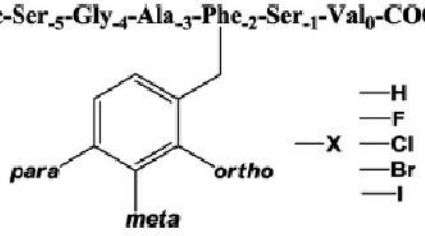
	Residues	
Halogen bond	domain His202	peptide Phe-2
H-bond	domain His202	Ile206



X- bond/H-bond system at complex interface

Weak Interactions →	**H-bond**	**π-π**	XB

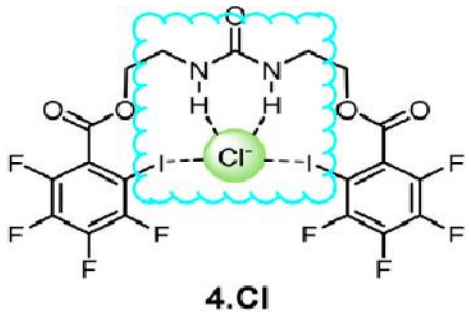
Ac-Ser$_{-5}$-Gly$_{-4}$-Ala$_{-3}$-Phe$_{-2}$-Ser$_{-1}$-Val$_{0}$-COOH



Peptide		
ortho	*meta*	*para*
H	H	H
F	H	H
Cl	H	H
Br	H	H
I	H	H
H	F	H
H	Cl	H
H	Br	H
H	I	H
H	H	F
H	H	Cl
H	H	Br
H	H	I

X-bonding + Another non-covalent bonding

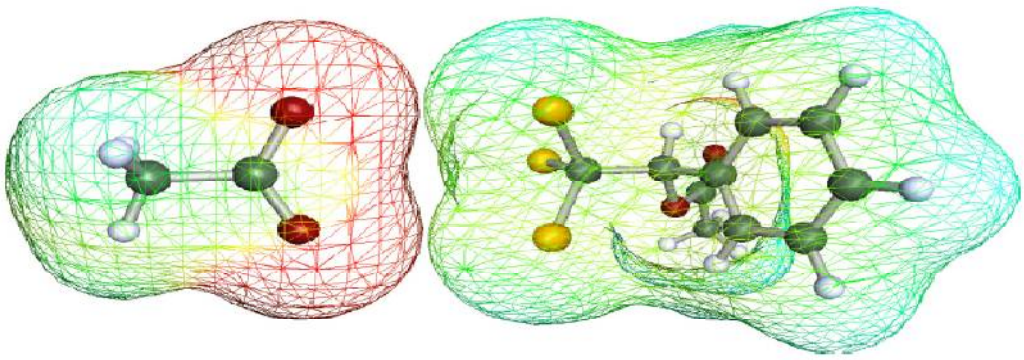
Taylor's mixed HB-XB acyclic 4 host bound to Cl		XBS-10



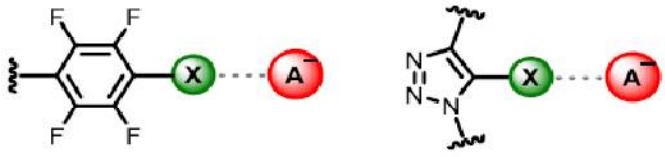
4.Cl

	acetate ion	ATMBA		XB

halogen bond	Cl…O (around 3 Ã)	O on acetate ion …Cl on ATMBA
	strong interaction	kinetically feasible



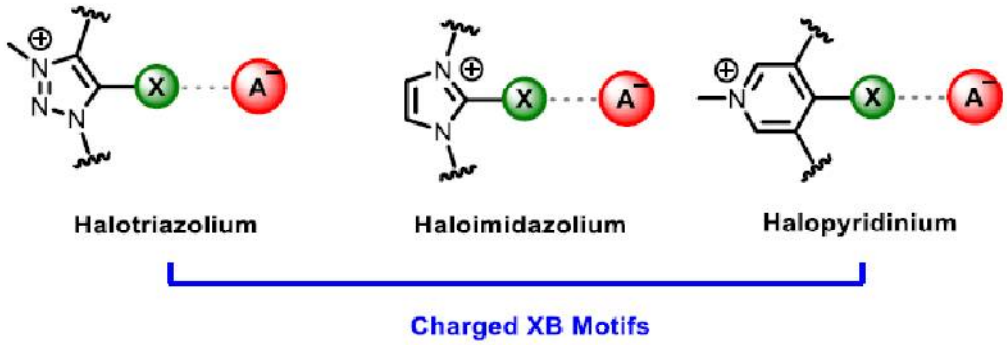
X-bond	Neutral XB			XBS-10



Haloperfluoroarene Halotriazole

Neutral XB Motifs

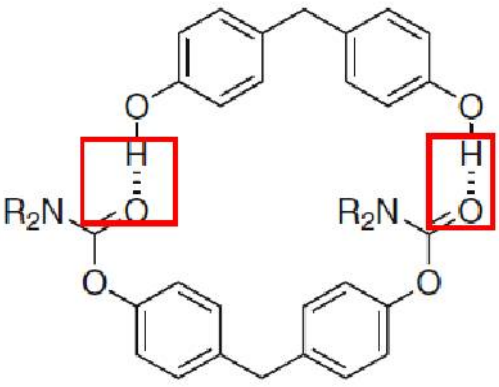
X-bond	charged XB			XBS-10

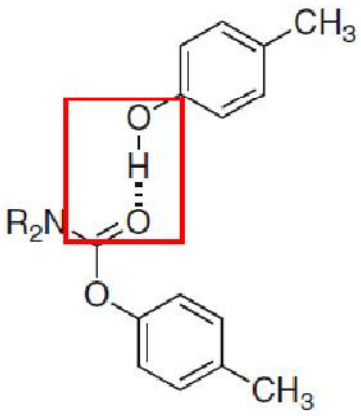


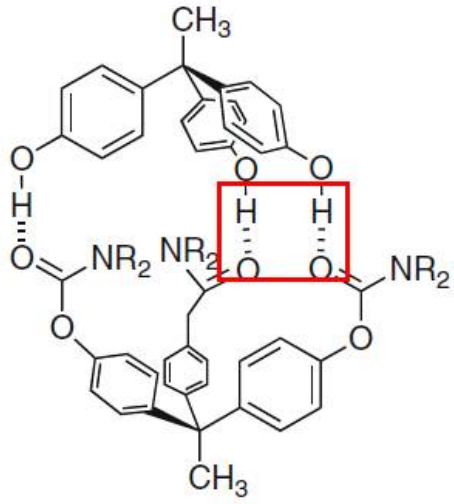
Sup Inf 3:
H…bonds&Weak… … … Interactions

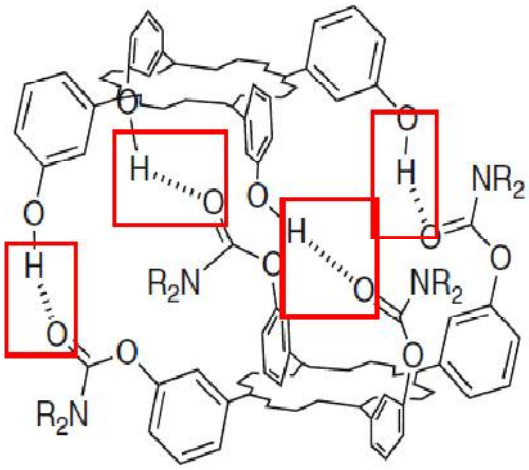
H...bonds
Co-operative
Weak
Strong
Convergent

H-Bonds	cooperativity		XB

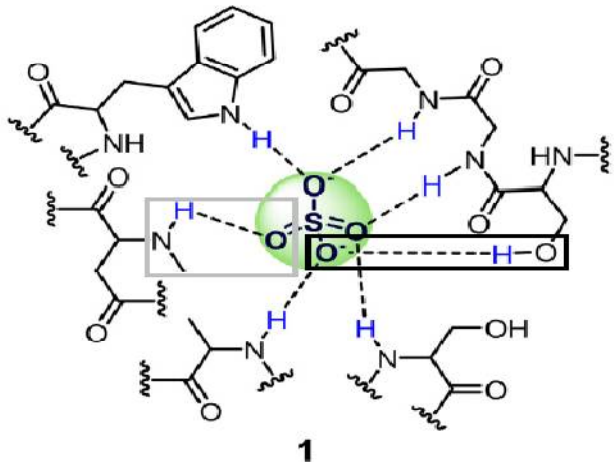








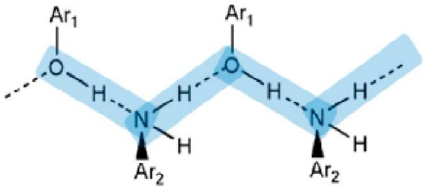
H-Bond Convergent	sulfate binding protein (SBP) of Salmonella typhimurium	XBS-04

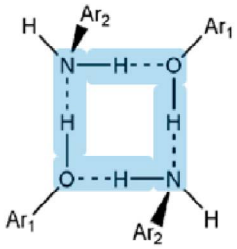


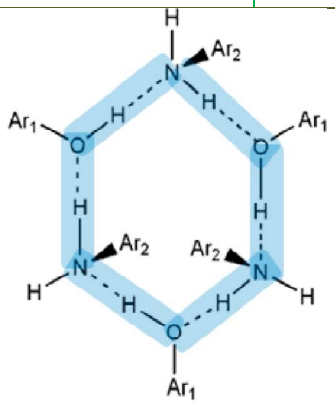
1

Cooperative hydrogen bonds

amine	phenol		XB-06

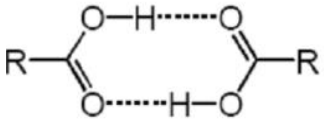


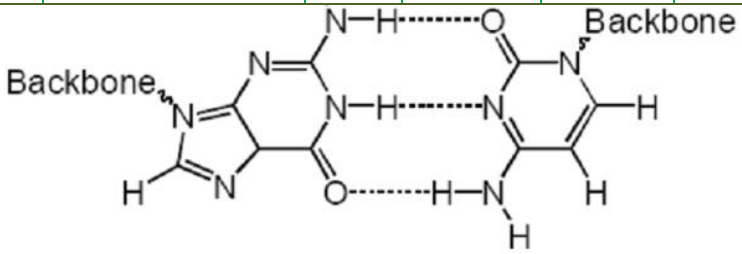




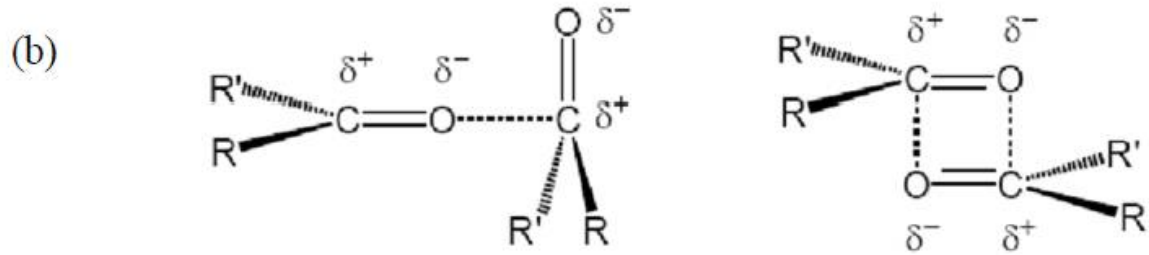
Hydrogen bond	PhN-H…O-Ph

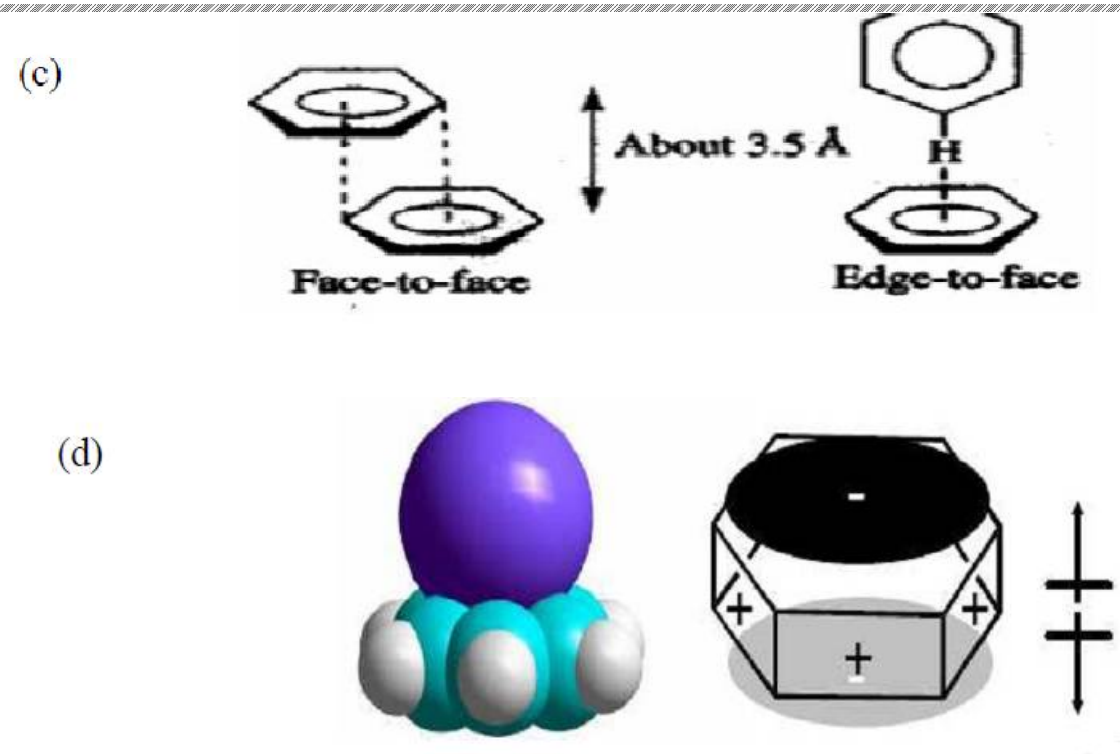
Interactions →	**H-bond**	**Electrostic**	**π -**		XB-16
		Dipole-dipole	π-π	C-H---π	C^+- π





Guanine **Cytosine**

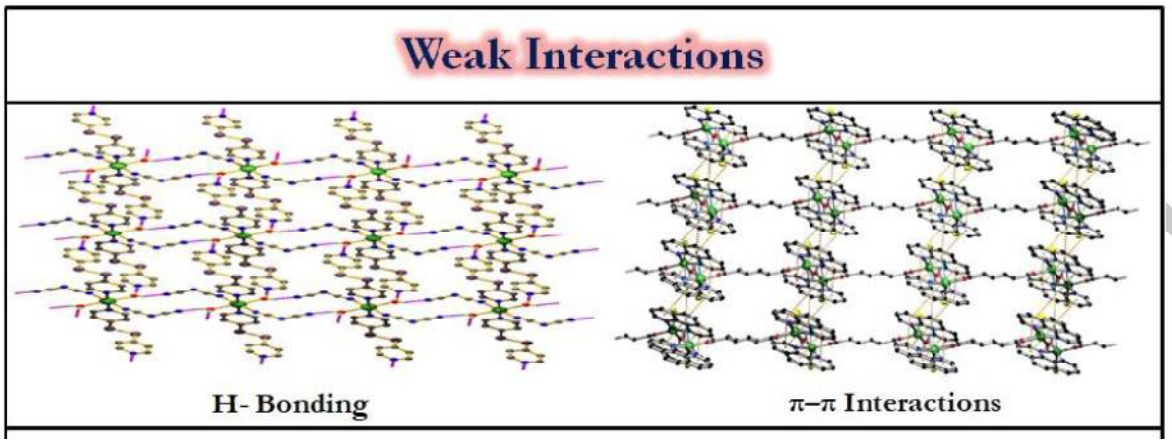




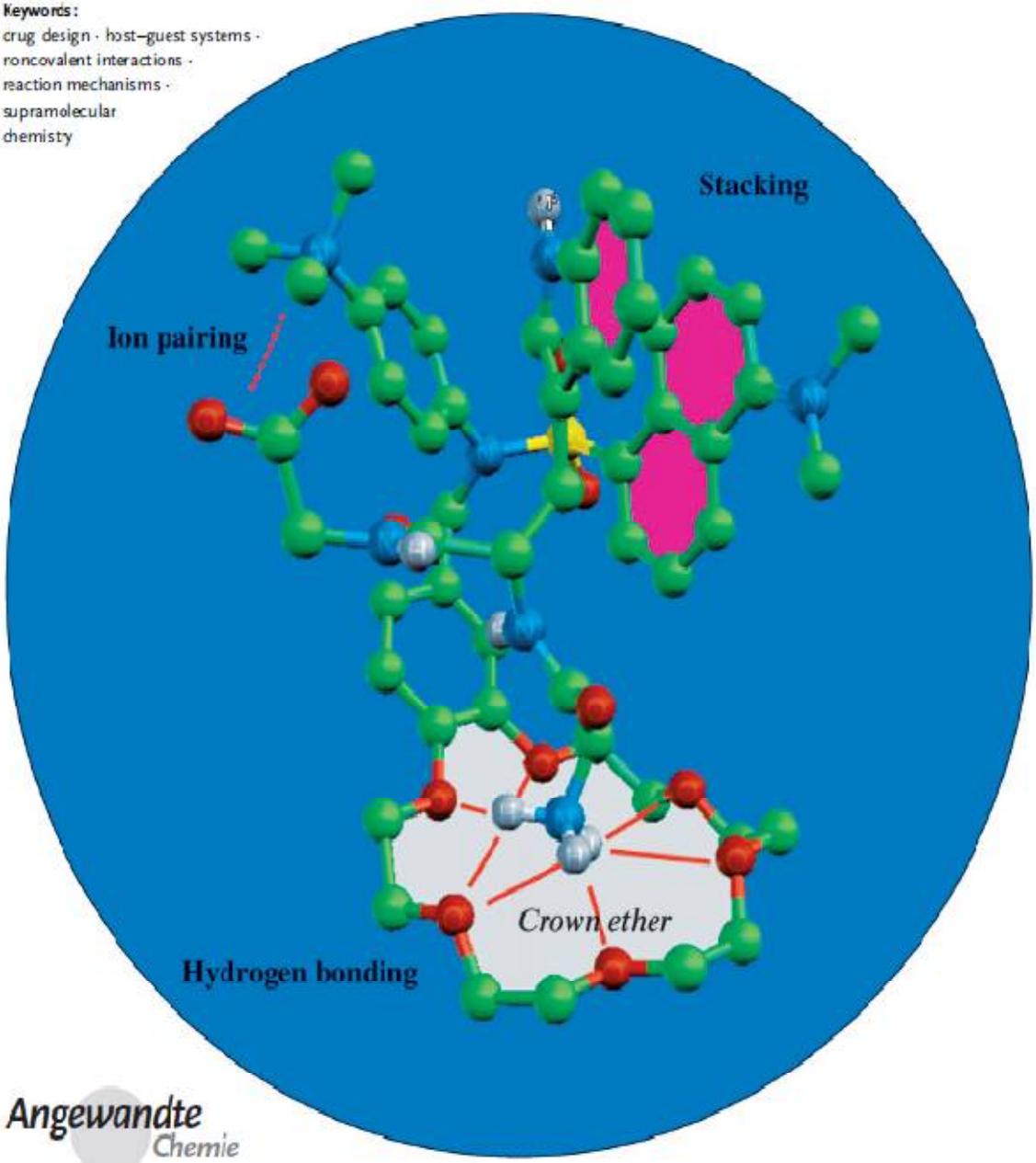
(a) Hydrogen bonding, (b) Dipole-Dipole electrostatic interaction,
(c) π-π and C-H---π stacking, (d) Cation- π interaction

Weak... ... ...Interactions

Weak Interactions →	H-bond	π-π	XB



Keywords:
drug design · host–guest systems · noncovalent interactions · reaction mechanisms · supramolecular chemistry



Sup Inf 4:
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