

The Hydrogen Bridge

Interactions without borders

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Hydrogen bond, $X-H\dots A$

Pauling definition (1939)

Under certain conditions an atom of hydrogen is attracted by rather strong forces to two atoms instead of only one, so that it may be considered to be acting as a bond between them.

Hydrogen bond, $X-H\dots A$

Pimentel–McClellan definition (1960)

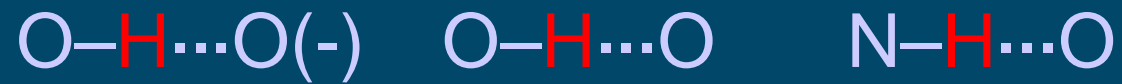
A hydrogen bond is said to exist when (1) there is evidence of a bond, and (2) there is evidence that this bond sterically involves a hydrogen atom already bonded to another atom

Hydrogen bond, X–H...A

Steiner–Saenger definition (1993)

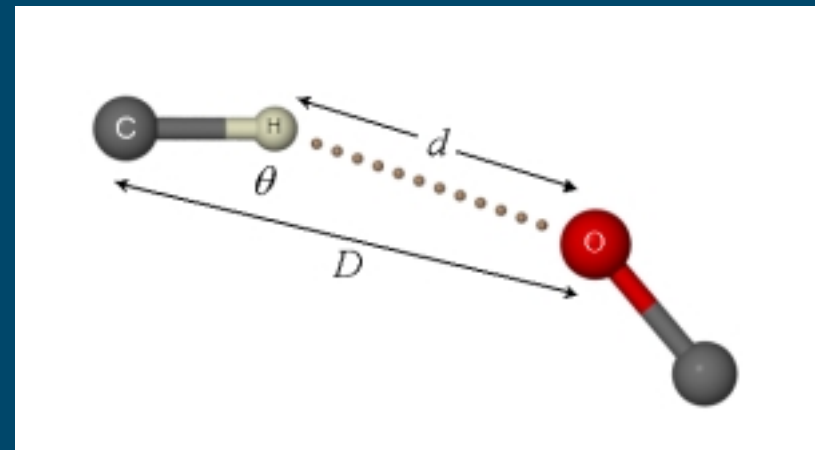
Any cohesive interaction where H carries a positive charge and A a negative charge (partial or full) and the charge on H is more positive than on X

Hydrogen bond



How to assess hydrogen bonds?

- Energy
- Spectroscopy
- Geometry
- Structure
- Function



A **complex** interaction

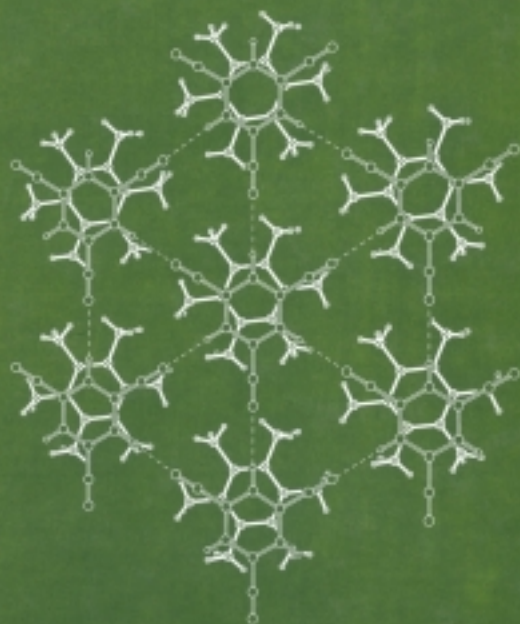
	Very strong	Strong	Weak
	$[F-H...F]^-$	$N-H...O=C$	$C-H...O$
Energy (kcal/mol)	-15 to -40	- 4 to - 15	< - 4
IR, ν_s	>25%	5-25%	<5%
$\Delta(X-H)$, Å	0.05 to 0.2	0.01 to 0.05	< 0.01
$H...A$, Å	1.2 to 1.5	1.5 to 2.2	2.0 to 3.0
Shorter than van der Waals	100%	~100%	30-80%
Effect on crystal packing	Pronounced	Distinctive	Variable

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The Weak Hydrogen Bond

In Structural Chemistry and Biology

Gautam R. Desiraju
and Thomas Steiner



INTERNATIONAL UNION OF CRYSTALLOGRAPHY
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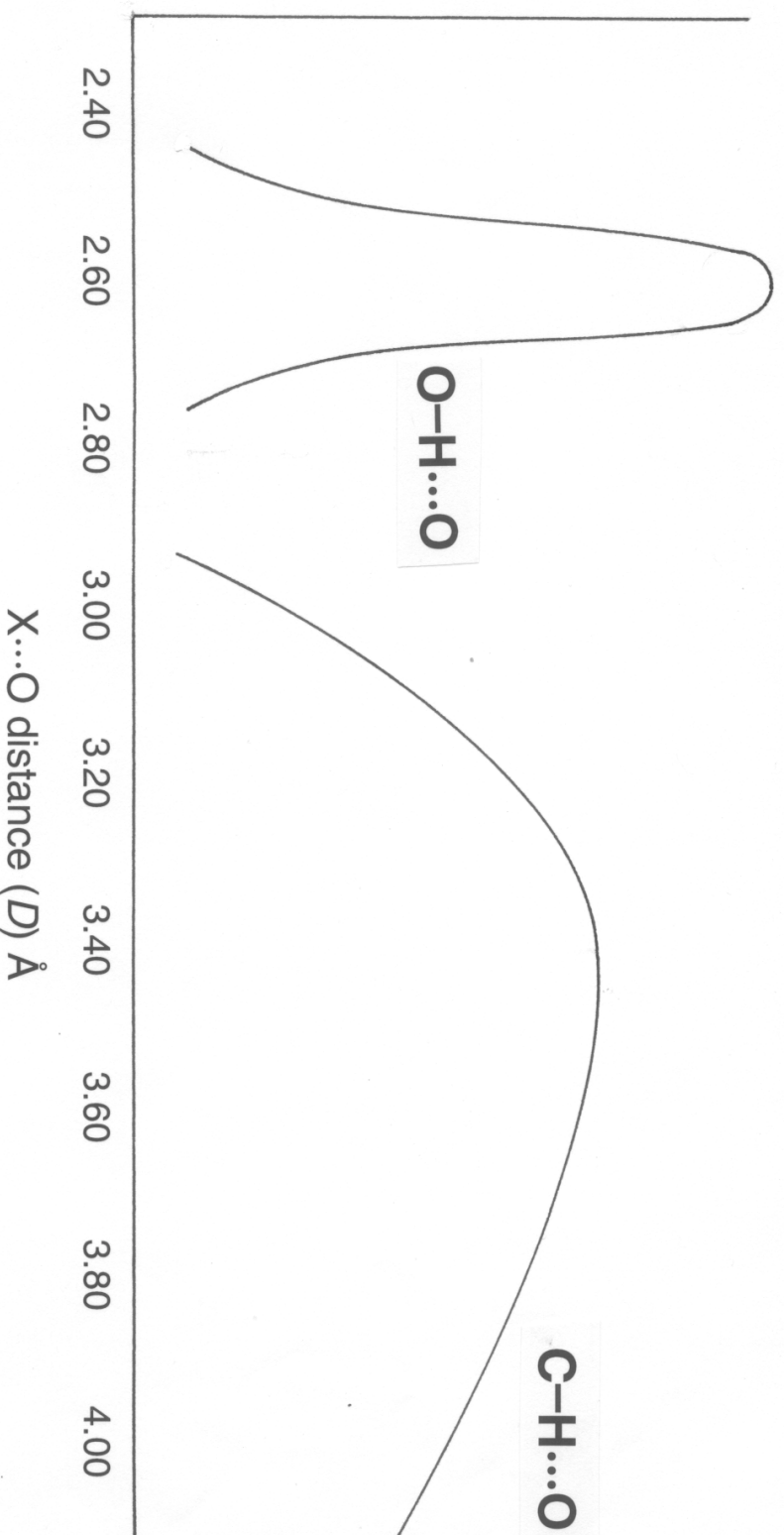


Desiraju–Steiner definition

The weak hydrogen bond is an interaction $X-H\cdots A$ wherein a hydrogen atom forms a bond between two structural moieties X and A , of which one or even both are of moderate to low electronegativity (1999)

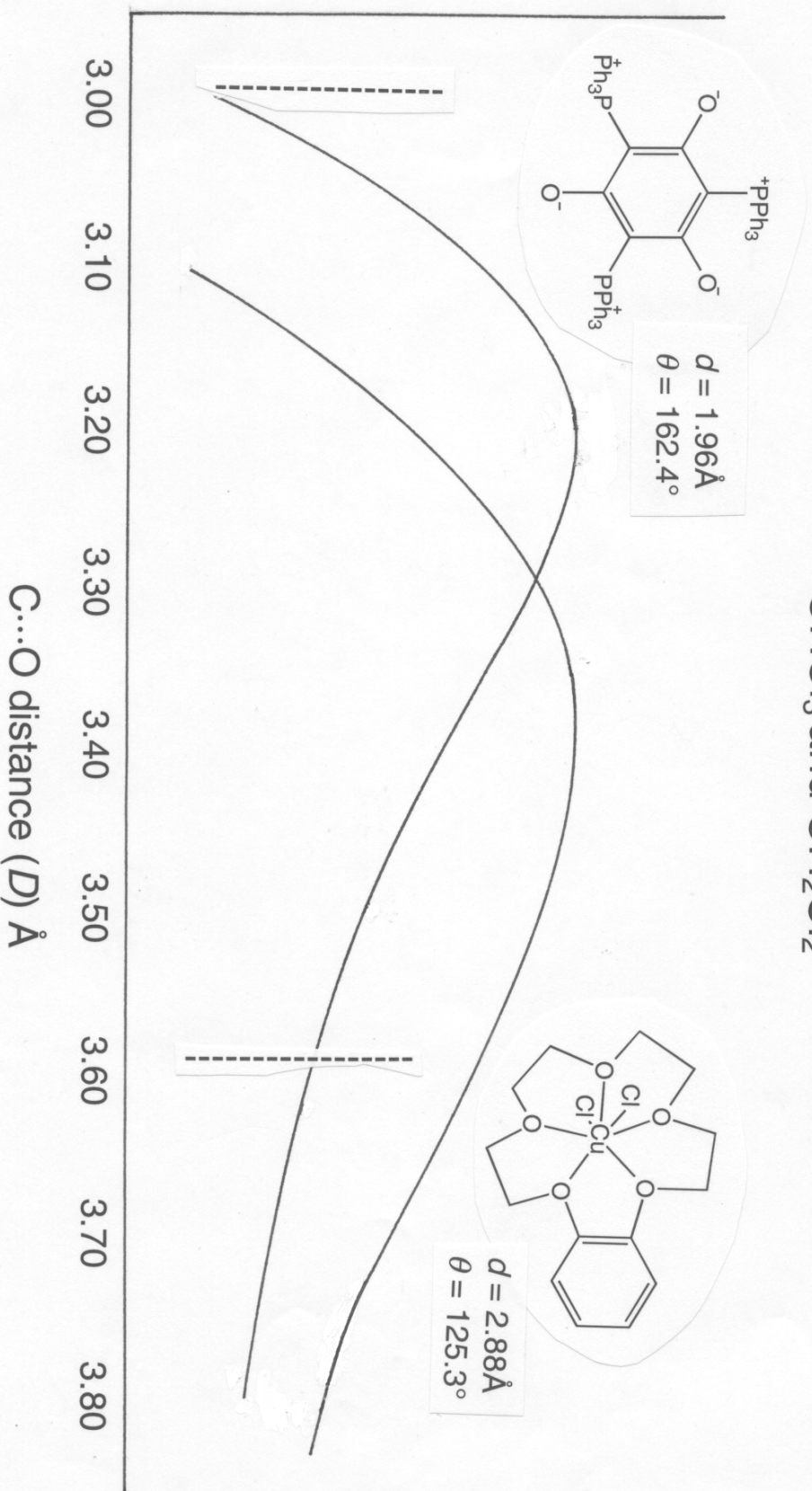
Strong and Weak Hydrogen Bonds, X-H...O

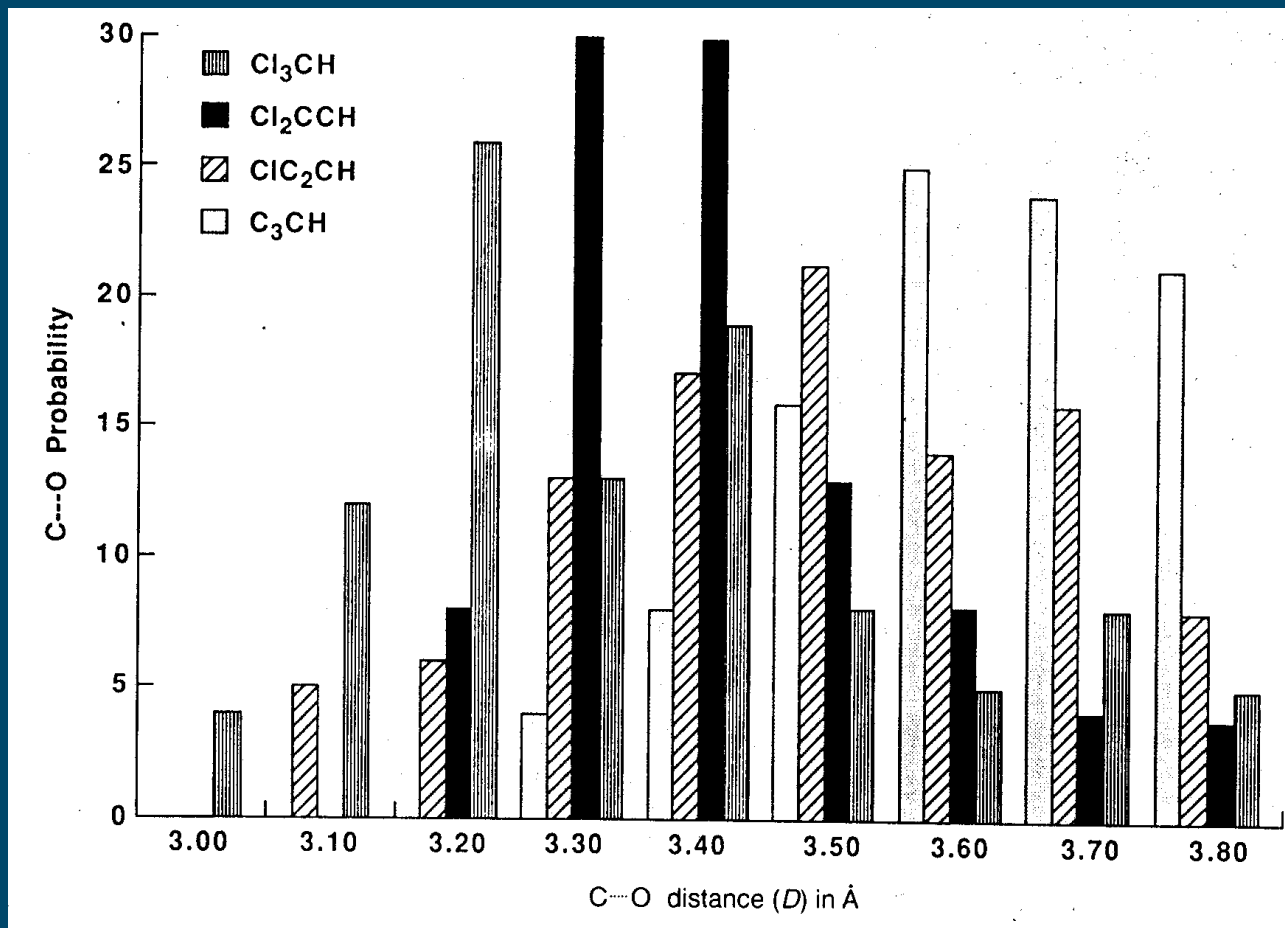
An important difference



C-H...O Hydrogen Bonds

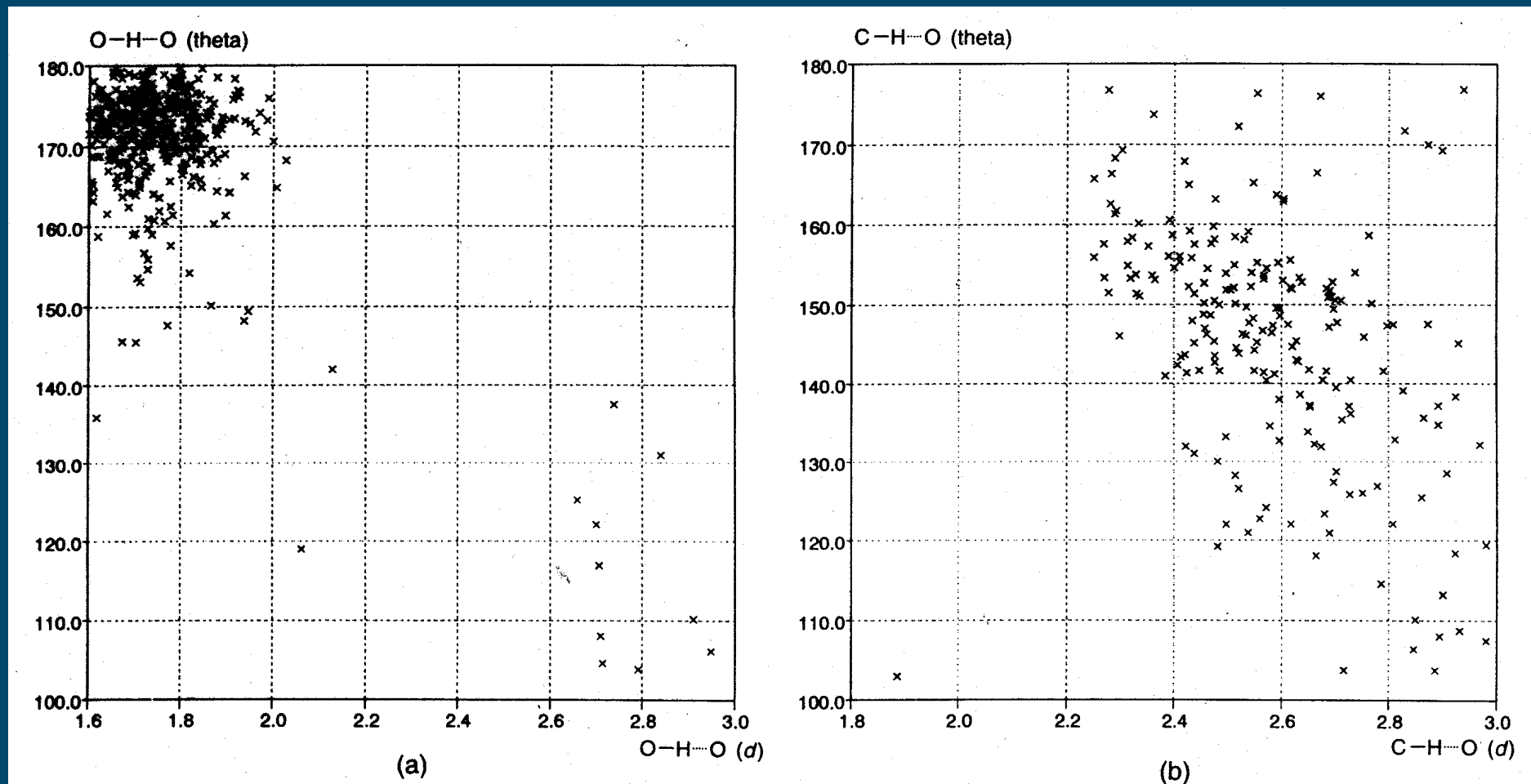
CHCl₃ and CH₂Cl₂



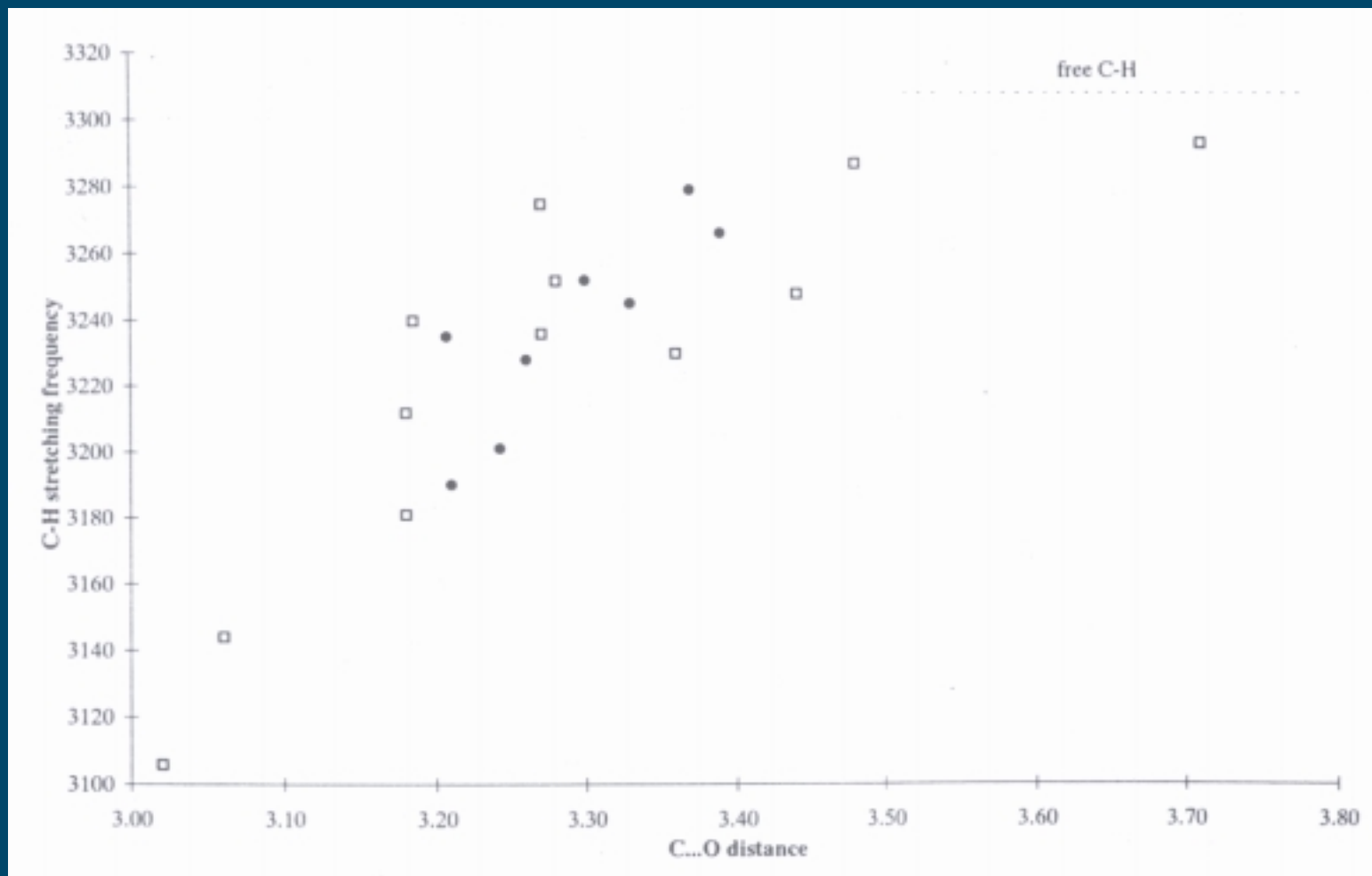


G. R. Desiraju, J. Chem. Soc., Chem. Comm., 179, 1989

Angles, X-H...O



IR bathochromic shifts, C–H...O



G. R. Desiraju and B. N. Murty, Chem. Phys. Lett., 139, 360, 1987

Thermal parameters

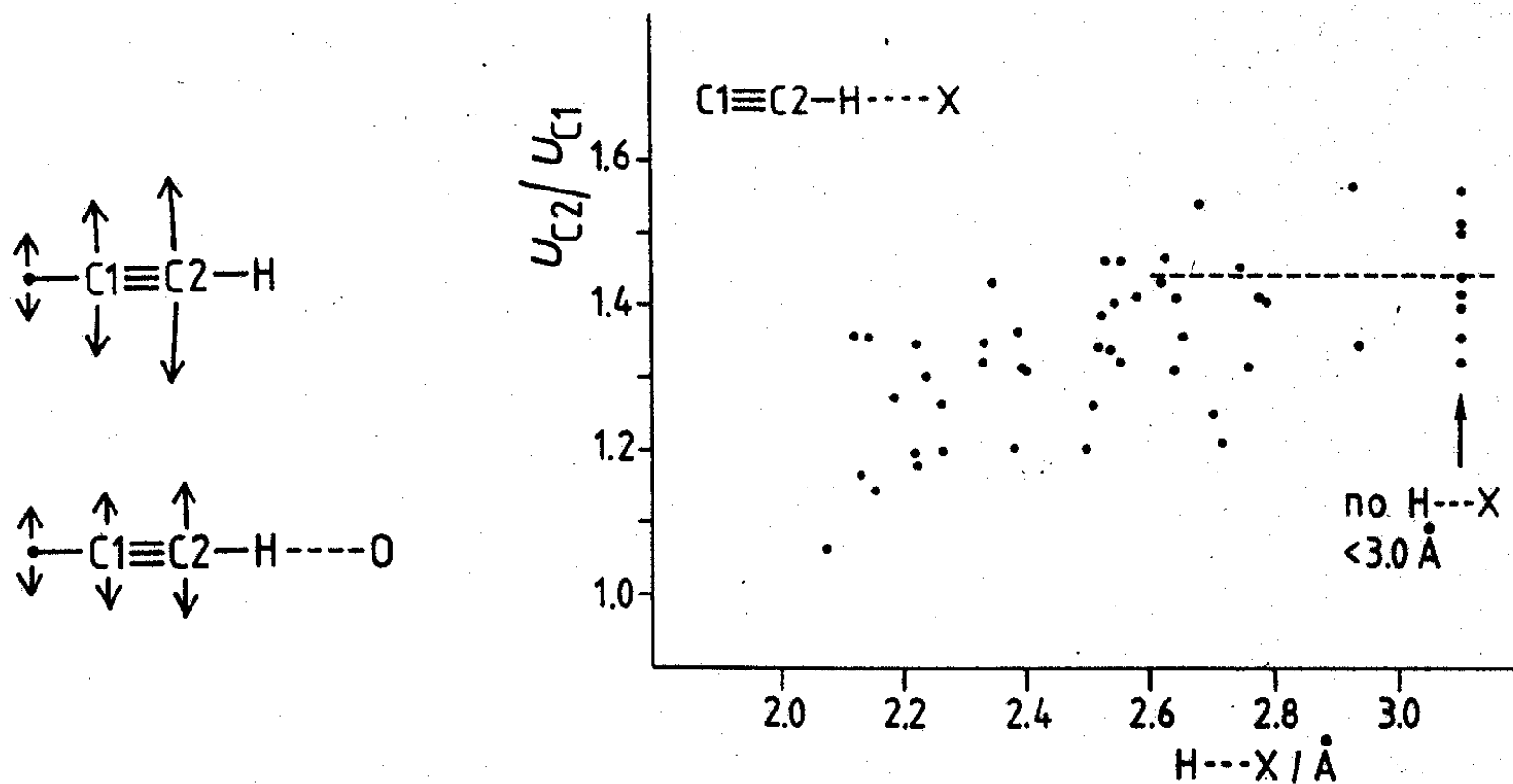
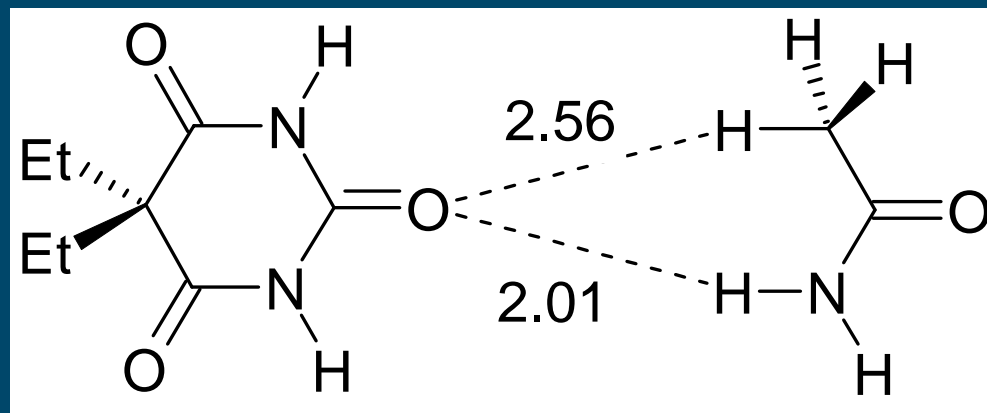
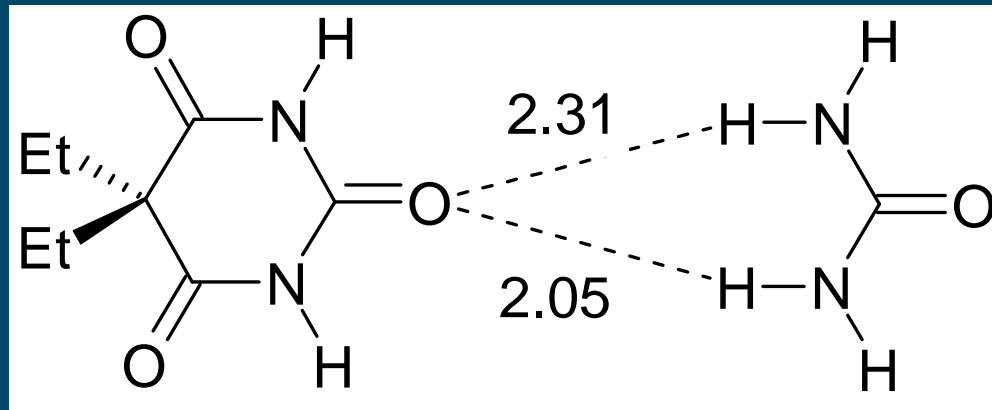
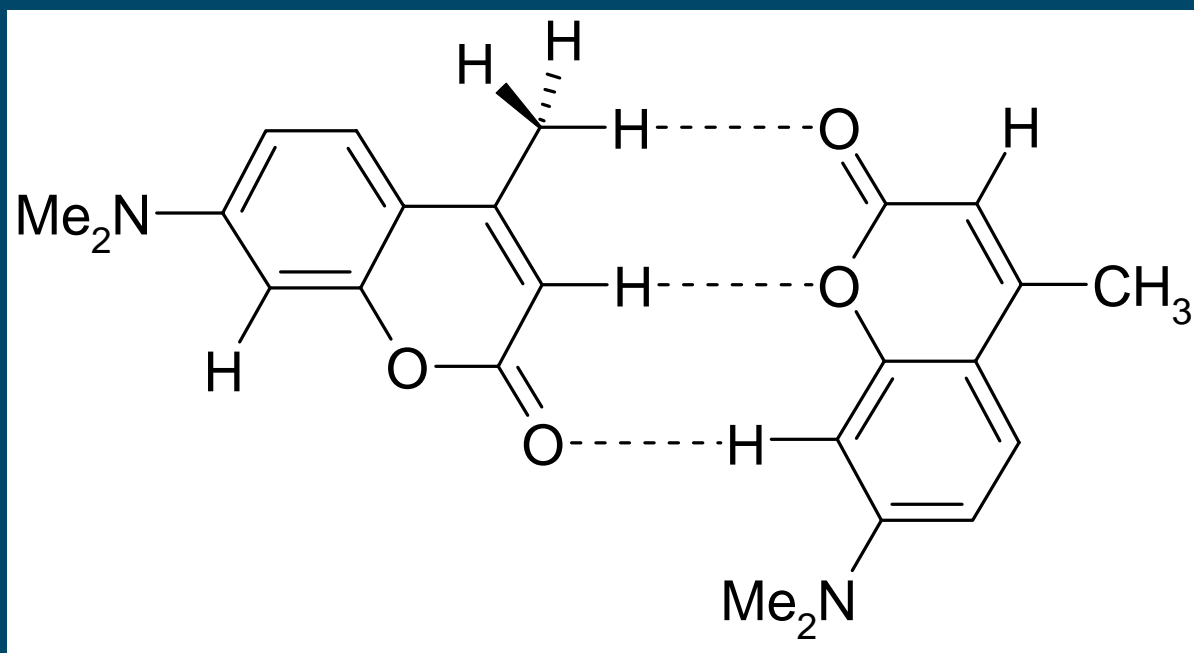


Fig. 2.24. Correlation of the U -ratio defined as $U_{eq}(C2)/U_{eq}(C1)$ with the distance d in 51 $C\equiv C-H\cdots X$ hydrogen bonds ($X = O, N, \pi$). The horizontal line shows the mean value for $C\equiv C-H$ groups that donate no hydrogen bond with $d < 2.8 \text{\AA}$ (adapted from Steiner 1994b).

Isostructurality



Two molecules in the asymmetric unit ($Z'=2$)



Electronegativity and Hardness

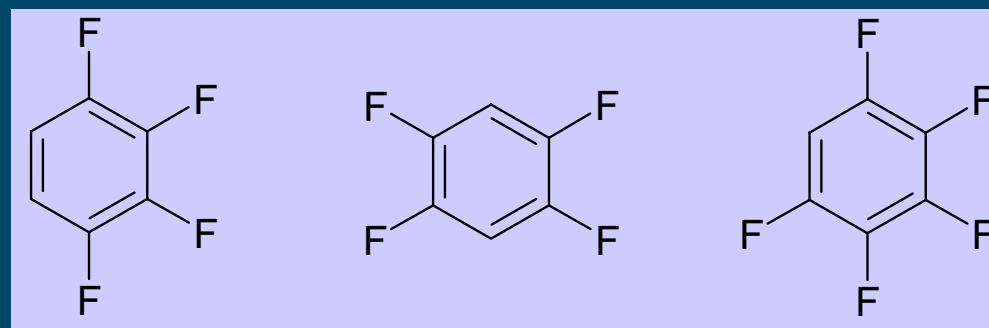
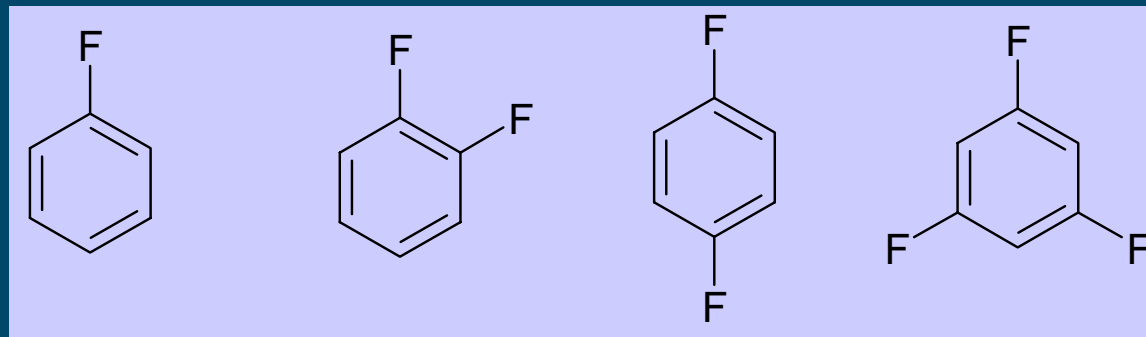
Fluorine



Weak donor

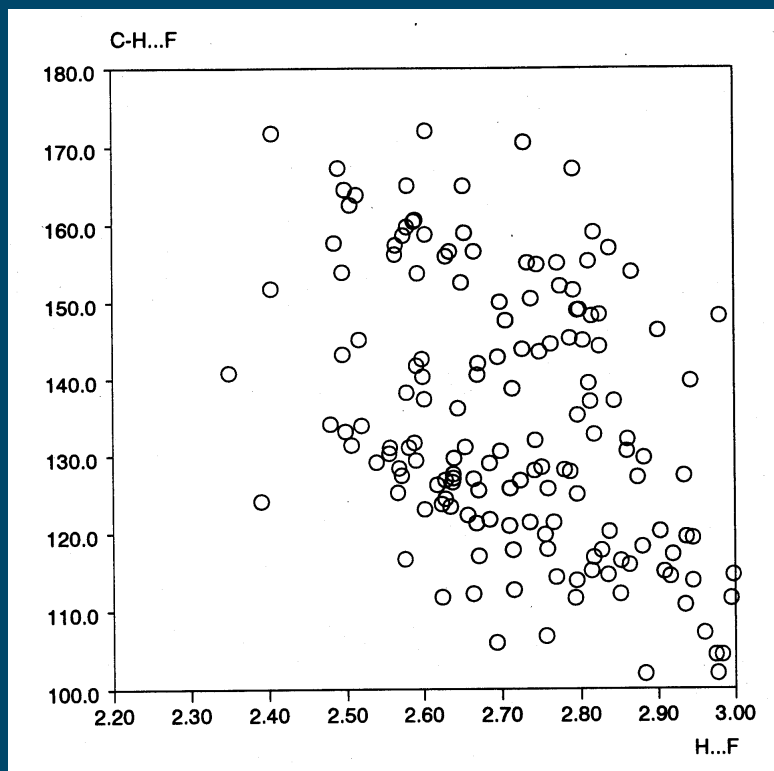
Very weak acceptor

C–H...F–C Interactions in Fluorobenzenes

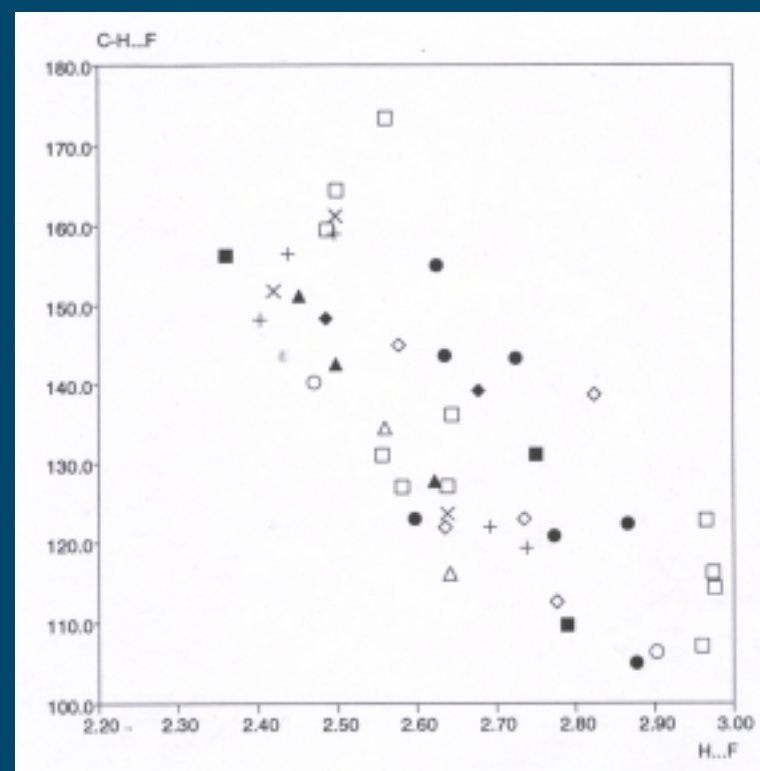


Thalladi, Weiß et al, JACS, 120, 8702, 1998

C-H...F-C Hydrogen Bonds

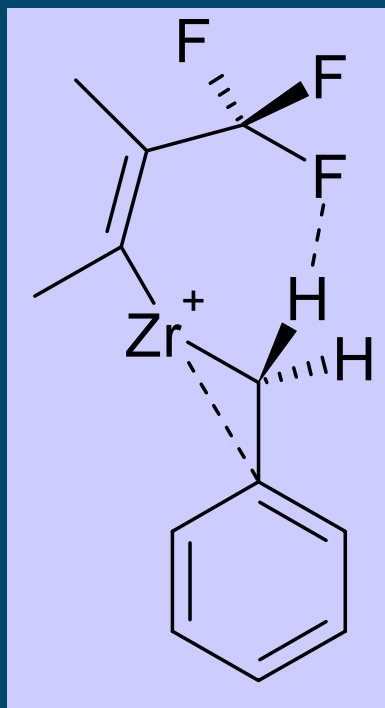


All C, H, F compounds

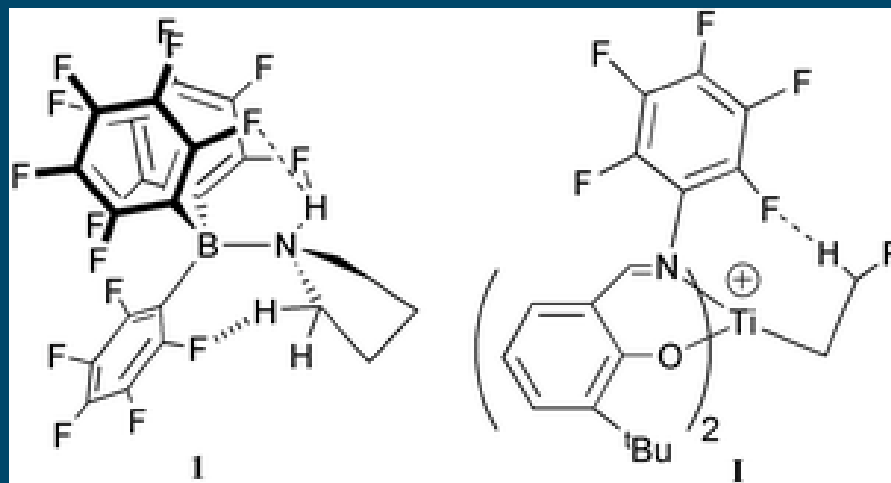


Fluorobenzenes

Weak and reversible C–H...F–C Hydrogen Bridge Applications. Polymerization catalyst.



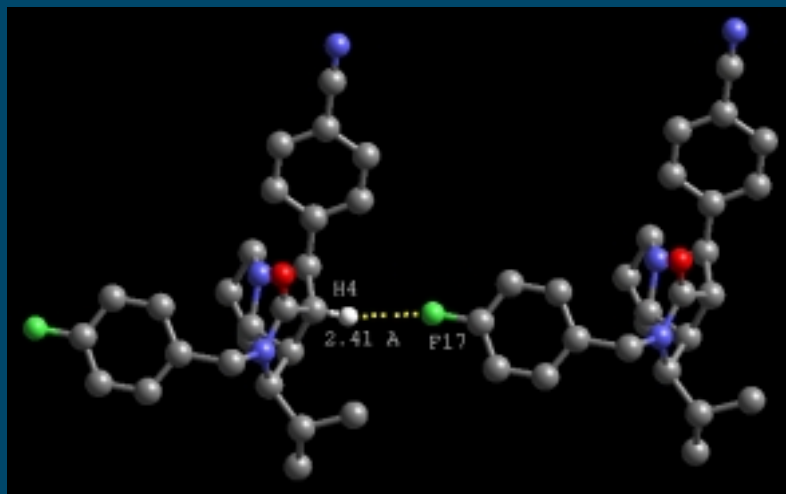
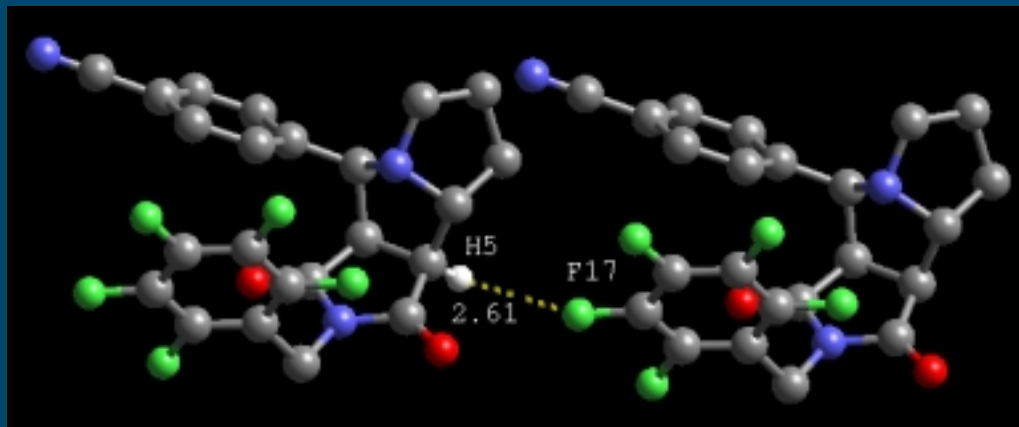
Stereoselective polymerisation
Chan et al,
Angew. Chem. Int. Ed.,
42, 1628, **2003**



Boron adducts
Lancaster et al, Chem. Comm.,
2148, **2003**

Decrease of β -H transfer
T. Fujita et al,
JACS, 124, 3327, **2002**
JACS, 125, 4293, **2003**

Weak and reversible C–H...F–C Hydrogen Bridge Applications. Molecular recognition.



Binding in thrombin
Diederich et al,
Angew. Chem. Int. Ed.,
42, 2507, 2003

Hydrogen bridge (*Wasserstoffbrücke*)

Electrostatics

Charge transfer
(covalency)

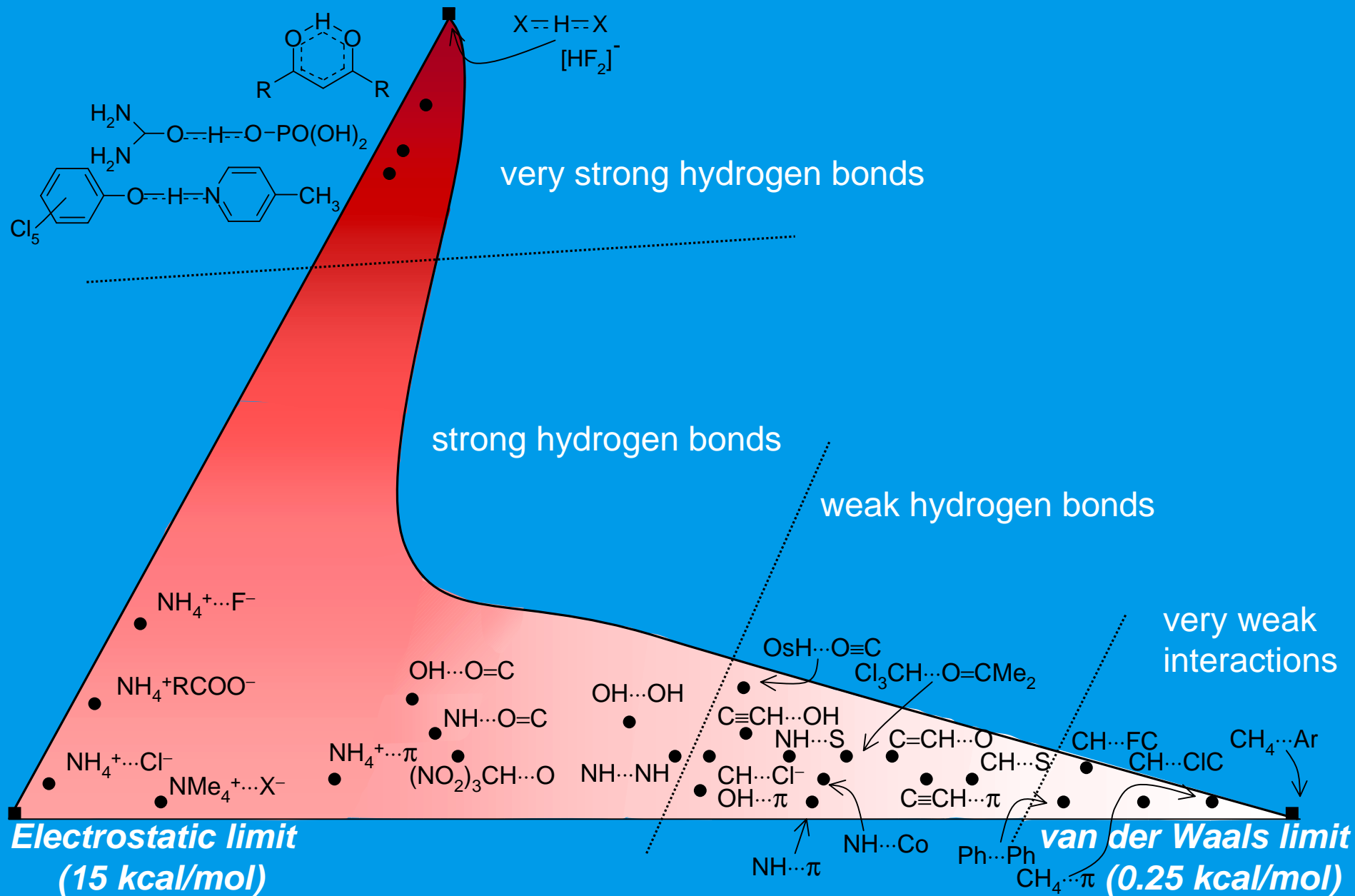
Dispersion/repulsion
(van der Waals)

Polarisation



A **composite** interaction

Covalent limit (40 kcal/mol)



Hydrogen bond (bridge)



A complex interaction that involves several atoms

A composite interaction that spans wide ranges of geometry and energy

Great chemical variations among the donor **D—H** and acceptor **A** groups

However, all hydrogen bonds (bridges) have several features in common; notably, their effect on crystal structure and packing

The above discussion shows that hydrogen bonds of differing strengths have broadly similar if graded effects in the building up of crystals from molecules. Indeed it is at the functional level rather than at a geometrical, energetic or spectroscopic level that all hydrogen bonds are similar, and it is little surprise that it is in the fields of crystal engineering and supramolecular chemistry that the hydrogen bond is most clearly identified as an interaction type without internal borders.

Hydrogen bridge

The master-key of molecular recognition

Strength

Directionality

Weakness

Flexibility

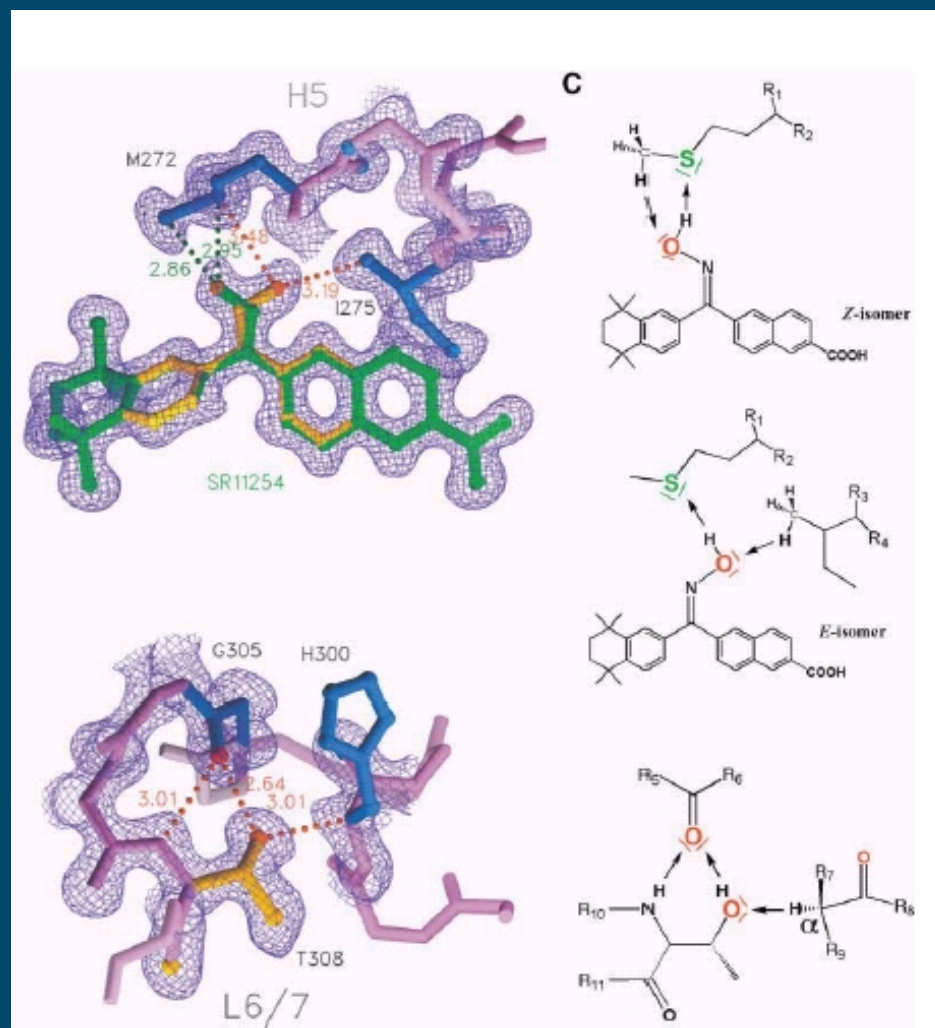
C–H...O Hydrogen Bonds in the Nuclear Receptor RAR γ

Specificity

Reversibility

Affinity

Hydrophobicity



Klaholz and Moras, Structure, 10, 1197-1204, 2002

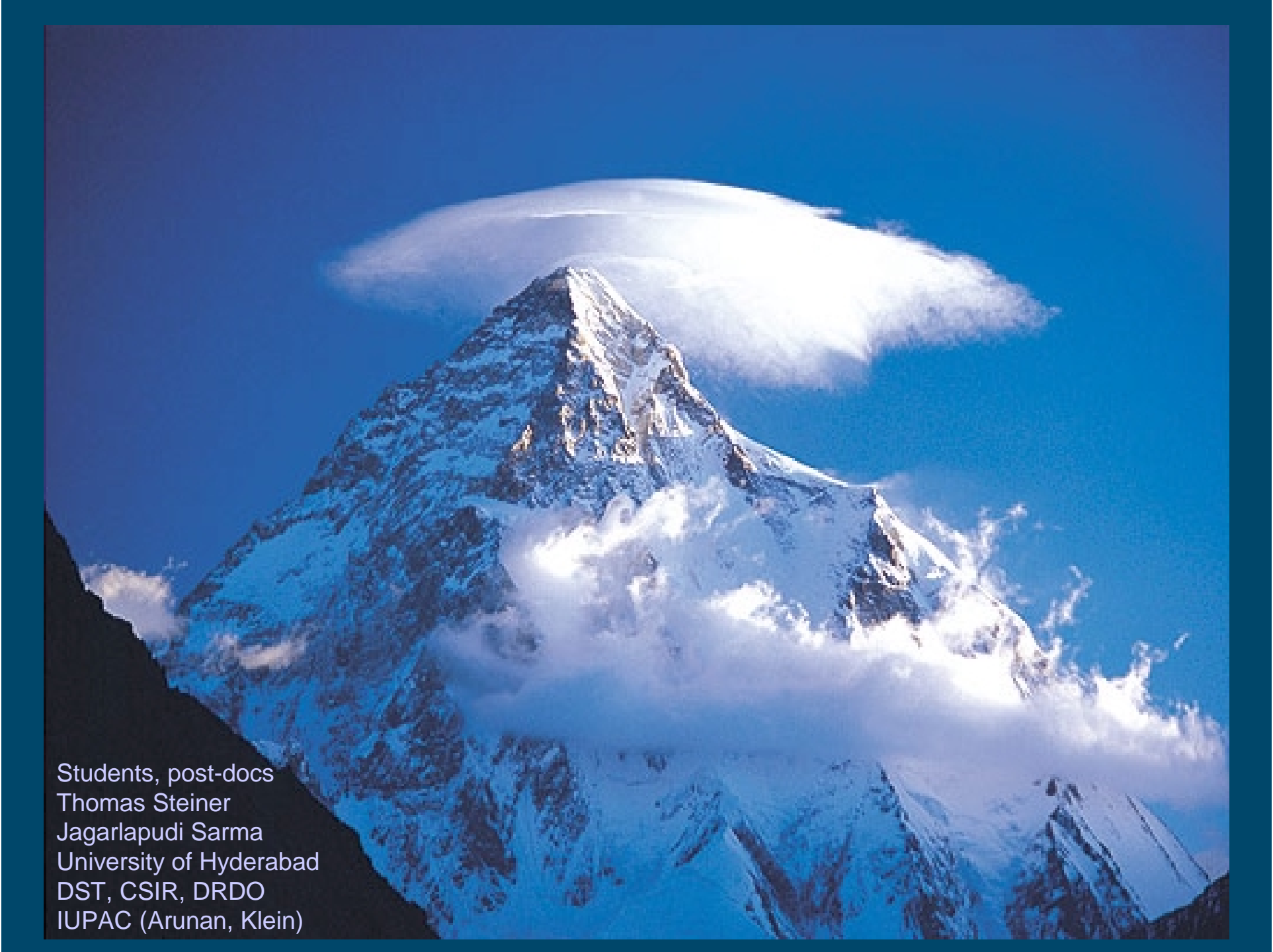
Bonds and bridges

Pauling's definition

Under certain conditions an atom of hydrogen is attracted **by rather strong forces** to two atoms instead of only one, so that it may be considered to be acting as a **bond** between them.

Modern definition

Under certain conditions an atom of hydrogen is attracted to two atoms instead of only one, so that it may be considered to be acting as a bridge between them.



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IUPAC (Arunan, Klein)