IUPAC *Workshop*

Hydrogen Bonding and Other Molecular Interactions

San Giuliano Terme, Pisa, Italy
5-9 September 2005

Lecture

Leitmotifs in Strong Hydrogen Bonding

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HB BASIC NOMENCLATURE

(a1) X—H----X

homonuclear

(a1') R_1—X—H----X—R_1

homonuclear
homomolecular

(a1") R_1—X—H----X—R_2

homonuclear
heteromolecular

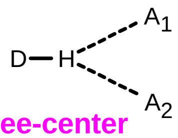
(a2) X—H----Y

heteronuclear

(b1) D—H-------A

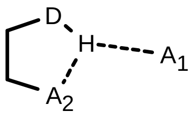
two-center
(monodentate)

(b2)



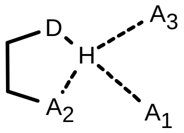
three-center
(bifurcated, bidentate)

(b2')



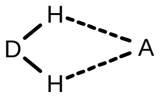
three-center
(bifurcated, bidentate)

(b3)



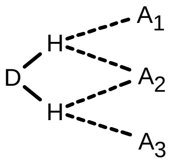
four-center
(tridentate)

(c1)



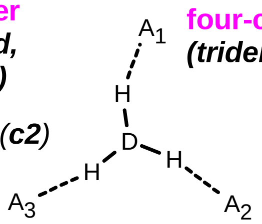
double (*chelated*)

(c1')



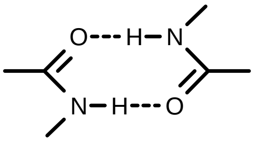
double and three-center

(c2)



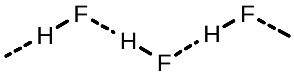
triple

(d1)



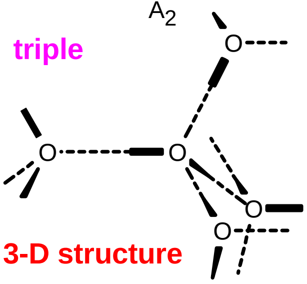
0-D dimer

(d2)



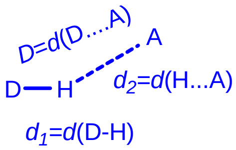
1-D chain

(d3)

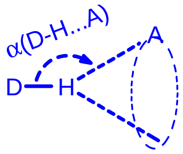


3-D structure

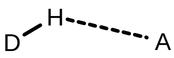
(e1)



(e2)



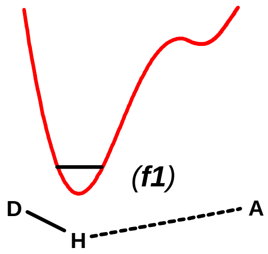
(e3)



dissymmetric
and bent

(e4) D---H---A

symmetric
and linear

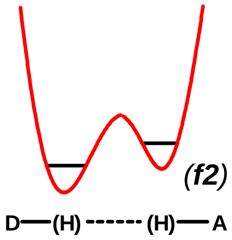


aSW-HB

Asymmetric Single-Well
High-Barrier H-Bond

Properties:

Weak, long and
strongly dissymmetric.
Ordered both in solution
and in crystals.
Essentially elecrostatic.

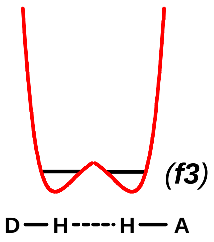


aDW-MB

Asymmetric Double-Well
Mid-Barrier H-Bond

Properties:

Moderate strength.
Tautomeric exchange
in solution and static
disorder in crystals.
Partially covalent.

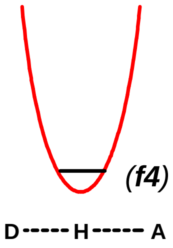


sDW-LB

Symmetric Double-Well
Low-Barrier H-Bond

Properties:

Strong and short.
Tautomeric exchange
in solution and dynamic
disorder in crystals.
Partially covalent.



sSW-NB

Symmetric Single-Well
No-Barrier H-Bond

Properties:

Very strong and short.
Symmetric and linear.
Ordered crystals.
Essentially Covalent.

A CHEMICO-TOPOLOGICAL CLASSIFICATION OF THE HYDROGEN BOND

TAXONOMY OF SHARED-PROTON INTERACTIONS

1st Category. 3-Centre-4-electon bonds

$$X\bullet - \bullet H \cdots :Y \longleftrightarrow {}^{-}X: \cdots H\bullet - \bullet Y^{+}$$

Group 1.1 a
Conventional HBs

$D{-}H\cdots A$

D, A = N, O, F, Cl, Br

$F{-}H\cdots F$

$O{-}H\cdots O$

$O{-}H\cdots N$

$N{-}H\cdots O$

$N{-}H\cdots N$

Group 1.1 b
Weak HB-Donors

$WD{-}H\cdots A$

W D = C, S, P, Se, Si

$C{-}H\cdots O$

$C{-}H\cdots N$

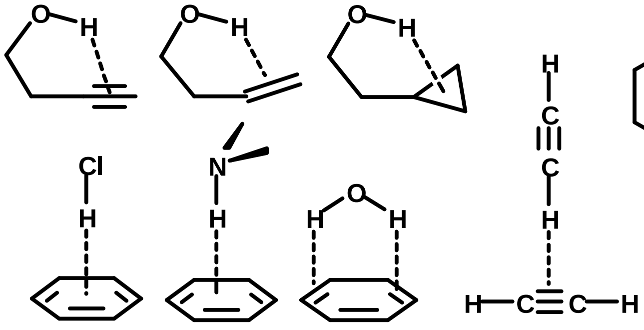
Group 1.1 c
Weak HB-Acceptors

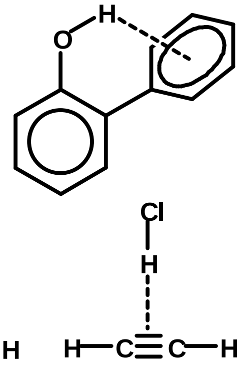
$D{-}H\cdots WA$

W A = organic F, Cl and Br,
S, Se, Te,
P, As, Sb,
isonitriles, carbenes

Group 1.1 d
Weak HBs with π- HB-Acceptors

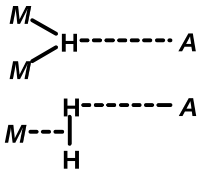
$D{-}H\cdots\pi$- *Bond*





Group 1.2 a
Metals as HB-Donors

$\overset{\delta-}{M}{-}\overset{\delta+}{H}\cdots A$



M = Transition Metal

Group 1.2 b
Metals as HB-Acceptors

$D{-}H\cdots\overset{\delta-}{M}$

M = Fe, Co, Ir, Pd, Pt
in low oxidation states

Group 1.3
Dihydrogen Bonds

$D{-}H\cdots\overset{\delta-}{H}{-}\overset{\delta+}{M}$

M = B, Ga, Al,
Trasition Metal

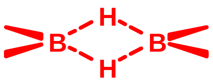
2nd Category. 3-Centre-2-electon bonds

$$X\bullet - \bullet H \cdots Y \longleftrightarrow {}^{-}X \cdots H\bullet - \bullet Y^{+}$$

Group 2.1
Agostic Interactions

M = Transition Metal

Group 2.2
Boranes



Group 2.3
Inverse H-Bond

$Li{-}\overset{\delta-}{H}\cdots\overset{\delta+}{Li}{-}H$

$Li{-}\overset{\delta-}{H}\cdots Na^{+}$

The Hydrogen Bond (HB)

Definitions

The HB is a

Three-Center-Four-Electron
Proton-Shared Interaction

having the general form

$$\mathbf{R_1{-}D{-}H \cdot \cdot \cdot \cdot \cdot :A{-}R_2}$$

where

D is the **HB Donor**

{ An **electronegative atom** such as
F, O, N, C, S, Cl, Br and I }

and

:A the HB Acceptor or **Lone Pair Carrier**

{ A second **electronegative atom**
or
a **multiple bond**, that is π**-bond**) }

The HB can also be seen as

a single proton sharing
two lone electron pairs
from two adjacent
electronegative atoms or groups

$$\mathbf{R_1{-}D^{-}: \cdot \cdot \cdot H^{+} \cdot \cdot \cdot :A{-}R_2}$$

The Most Striking HB Property: Its Modulability

☛ Chemical bonds have **nearly invariant lengths and energies**, in the sense that they are weakly affected by **chemical substitution** or **chemical environment.**

☛ HBs have completely different properties.

First Example

R_1–O–H · · · · · :O–R_2 bond

<u>in the gas phase</u> and <u>in molecular crystals</u>

1a. Changes of the Substituents R_1 and R_2 can modify

☛ the **HB Energy (E_{HB})** from **1 to some 30 kcal/mol**,

and the **O...O Contact Distance** from **3.10 to 2.38 Å**.

1b. Changes of Acid-Base Properties of the Environment

can cause even more astonishing effects:

☛ Neutral Environment (Simple Dimer):

HO–H...OH_2 **E_{HB}≈ 5** kcal/mol, **d(O...O)≈ 2.75** Å

☛ Acid Environment (Protonated Dimer):

$[H_2O...H...OH_2]^+$, **E_{HB}≈ 31** kcal/mol, **d(O...O)≈ 2.38** Å

☛ Basic Environment (Deprotonated Dimer):

$[HO...H...OH]^-$, **E_{HB}≈ 30** kcal/mol, **d(O...O)≈ 2.40** Å

Second Example

F–H · · · · · :F–H bond

in the gas phase and in molecular crystals

☛ Neutral Environment (Simple Dimer):

F–H...FH **E_{HB}≈ 5** kcal/mol, **d(F...F)≈ 2.49** Å

☛ Basic Environment (Deprotonated Dimer):

$[F...H...F]^-$, **E_{HB}≈ 40-45** kcal/mol, **d(F...F)≈ 2.26-2.28** Å

A New Classification of the HB:
By HB Strength

	Strong	*Moderate*	*Weak*
H-bond nature	*mostly covalent*	*mostly electrostatic*	*electrostatic*
Bond lengths	$D-H \approx H\cdots A$	$D-H < H\cdots A$	$D-H << H\cdots A$
$H\cdots A$ (Å)	1.2-1.5	1.5-2.2	2.2-3.2
$D\cdots A$ (Å)	2.2-2.5	2.5-3.2	3.2-4.0
$D-H-A$ *angle* (°)	165-180	130-180	90-150
Energy (kcal mol^{-1})	15-45	4-15	< 4
Relative decrease of the IR $\nu(D-H)$ *frequency*	> 25%	10-25%	< 10%
NMR $\delta(DH)$ *chemical shift (ppm)*	14-22	< 14	-
Typical donors	$[=O-H]^+$, $[\equiv N-H]^+$	$-O-H$, $=N-H$, $P-O-H$	$C-H$, $Si-H$
Typical acceptors	$[F]^-$, $[-O]^-$, $[P-O]^-$	$=O$, $\equiv N$, $P=O$	$C\equiv C$, *phenyl*
Typical H-bonds	*Charge-assisted:* $[H_2O\cdot\cdot H\cdot\cdot OH_2]^+$; *proton sponges* $[\equiv N\cdot\cdot H\cdot\cdot N\equiv]^+$; $[R-COO\cdot\cdot H\cdot\cdot OOC-R]^-$; $[O_3SO\cdot\cdot H\cdot\cdot OSO_3]^-$; $R_3N^+-H\cdots{}^-OOCR$; *Resonance-assisted:* $\cdots O=C-C=C-OH\cdots$ $\cdots O=C-C=C-NRH\cdots$	$-O-H\cdots O=$; $-O-H\cdots N\equiv$; $-N-H\cdots O=$; $-N-H\cdots N\equiv$; *σ-cooperative or polarization-assisted:* \ \ $\cdots O-H\cdots O-H\cdots$	$C-H\cdots O$; $C-H\cdots N$; $O/N-H\cdots\pi$ *bonds*

The Five HB Chemical Leitmotifs (CLs)

☛ ***The most interesting aspect of a HB classification based on HB strength*** is that we discover that strong HBs belong only to a small number of chemical scheme that we have called **Chemical Leitmotifs**.

The Alchemic Piper plays the Five Magic Tunes that make any Hydrogen Bond stronger:

The Chemical Leitmotifs

☛ ☛ Results are published in

JACS 1989, 1991, 1994, 2000, 2002, and 2004
ActaCrystB 1993, 1995, 1998, 1999, and 1999
JCSPerkinT 1993, 1997
JMolStruct 2000
Chemistry 1996
NJC 1994, 1999

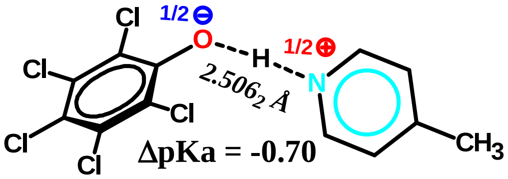
☛ The interested reader can retrieve them from the **ISI Web of Science** by looking for the names of the main contributors, that is

☛ ☛ **P. GILLI, V. BERTOLASI, V. FERRETTI, and G. GILLI**

The Five HB Chemical Leitmotifs (CLs)

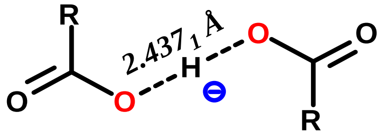
Charge - Assisted HBs

CL # 1: (+/−)CAHB ☛ SHB, VSHB
Positive/Negative Charge-Assisted HBs
Short and Very Short HBs



ΔpKa = -0.70

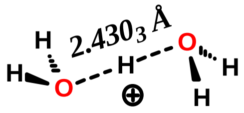
PENTACHLOROPHENOL -
p-TOLUIDINE



CARBOXYLIC ACID -
CARBOXYLATE

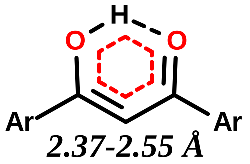
CL # 2: (−)CAHB ☛ SHB, VSHB
Negative Charge -Assisted HBs
Short and Very Short HBs

CL # 3: (+)CAHB ☛ SHB, VSHB
Positive Charge -Assisted HB
Short and Very Short HBs



WATER -
HYDRONIUM

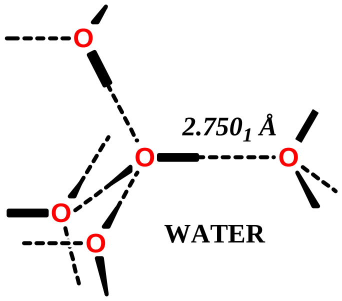
Π/Σ-Bond Polarization - Assisted HBs



DIBENZOYLMETHANE
ENOLS

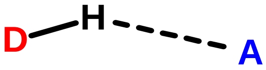
CL # 4: RAHB ☛ SHB, VSHB
Resonance - Assisted HBs
Short and Very Short HBs

CL # 5: PAHB ☛ MSHB
Polarization - Assisted HB
Mid - Short HBs



WATER

Neither Charged- Nor Π/Σ-Bond-Polarization-Assisted HBs



CL # 6: OHB or IHB ☛ WHB
Ordinary or Isolated HBs

THE WONDERFUL WORLD OF CHEMICAL LEITMOTIFS

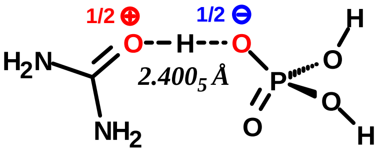
Chemical Leitmotif # 1:

(+/-)CAHB

Positive/Negative Charge-Assisted HB

$R\text{-}^{1/2-}D....H^{+}....A^{1/2-}\text{-}R$

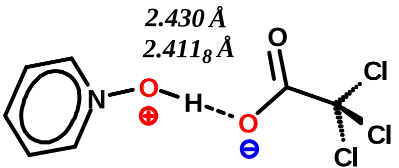
HOMONUCLEAR O-H...O



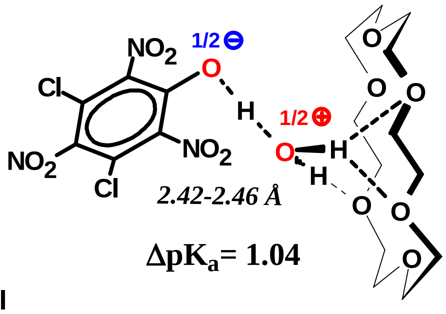
ΔpK$_a$= 2.1

UREA - PHOSPHORIC ACID

PYRIDINE-*N*-OXIDE - TRICHLOROACETIC ACID



ΔpK$_a$= -0.1

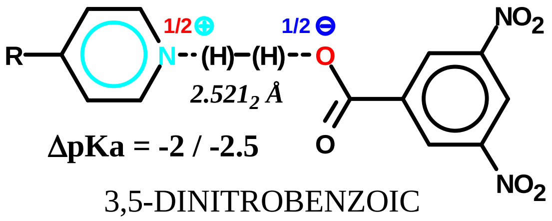


ΔpK$_a$= 1.04

3,5-DICHLOROPICRIC ACID - WATER(CROWN)

HETERONUCLEAR N-H...O/O-H...N

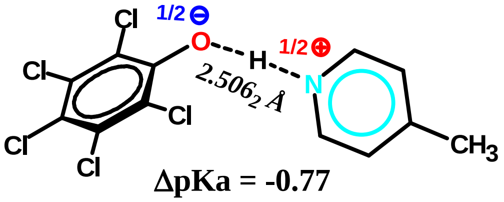
(+/–)CAHB



ΔpKa = -2 / -2.5

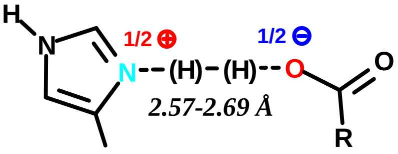
3,5-DINITROBENZOIC ACID - 4-ALKYLPYRIDINES

Aminoacids and Peptides



ΔpKa = -0.77

PENTACHLOROPHENOL - *p*-TOLUIDINE



ΔpKa = -1.7 / -2.1

ASPARTIC ACID - HISTIDINE

CLASS 6: OHB/IHB. Ordinary or Isolated HB

OHB/IHB

Bond	O-H...O	N-H...N	N-H...O	S-H...S
Intermolecular	2.70-2.84	2.85-3.10	2.87-3.30	
Intramolecular	2.55-2.90	2.80-3.00	2.71-2.85	

THE WONDERFUL WORLD OF CHEMICAL LEITMOTIFS

Chemical Leitmotif # 2:
(-)CAHB
Negative Charge-Assisted HB

$[R\text{-}D....H....A\text{-}R]^-$

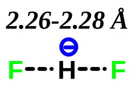
Chemical Leitmotif # 3:
(+)CAHB
Positive Charge-Assisted HB

$[R\text{-}D....H....A\text{-}R]^+$

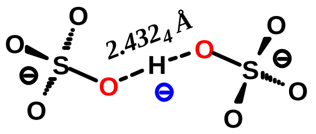
CLASS 2: (-)CAHB. Negative charge-assisted HB

(–)CAHB

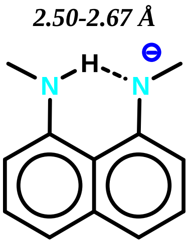
HOMONUCLEAR X-H...X (X= F, O, N, S)



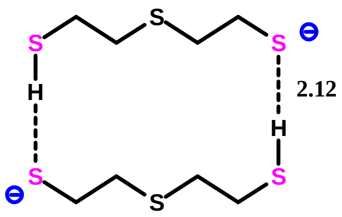
HYDROGEN
FLUORIDE

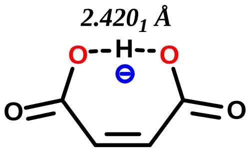


HYDROGEN SULPHATE

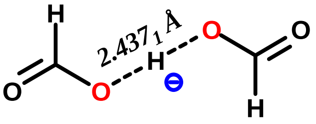


1,8-NAPHTYL-
DIAMINES





HYDROGEN
MALEATE

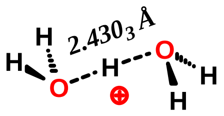


CARBOXYLIC ACID -
CARBOXYLATE

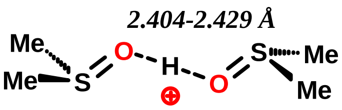
CLASS 3: (+)CAHB. Positive charge-assisted H-bond

(+)CAHB

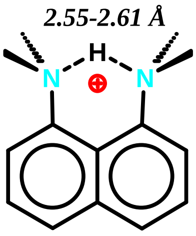
HOMONUCLEAR X-H...X (X= O, N)

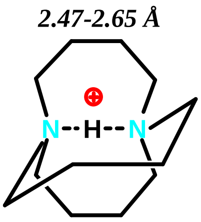


WATER -
HYDRONIUM

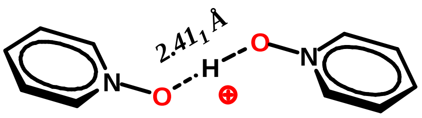


H^+- BIS(DIMETHYL-
SULPHOXIDE)

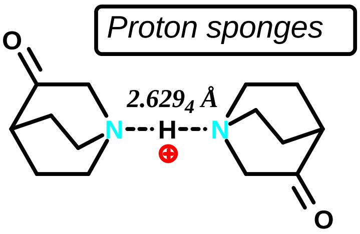




Proton sponges



H^+- BIS(PYRIDINE-N-OXIDE)



THE WONDERFUL WORLD OF CHEMICAL LEITMOTIFS

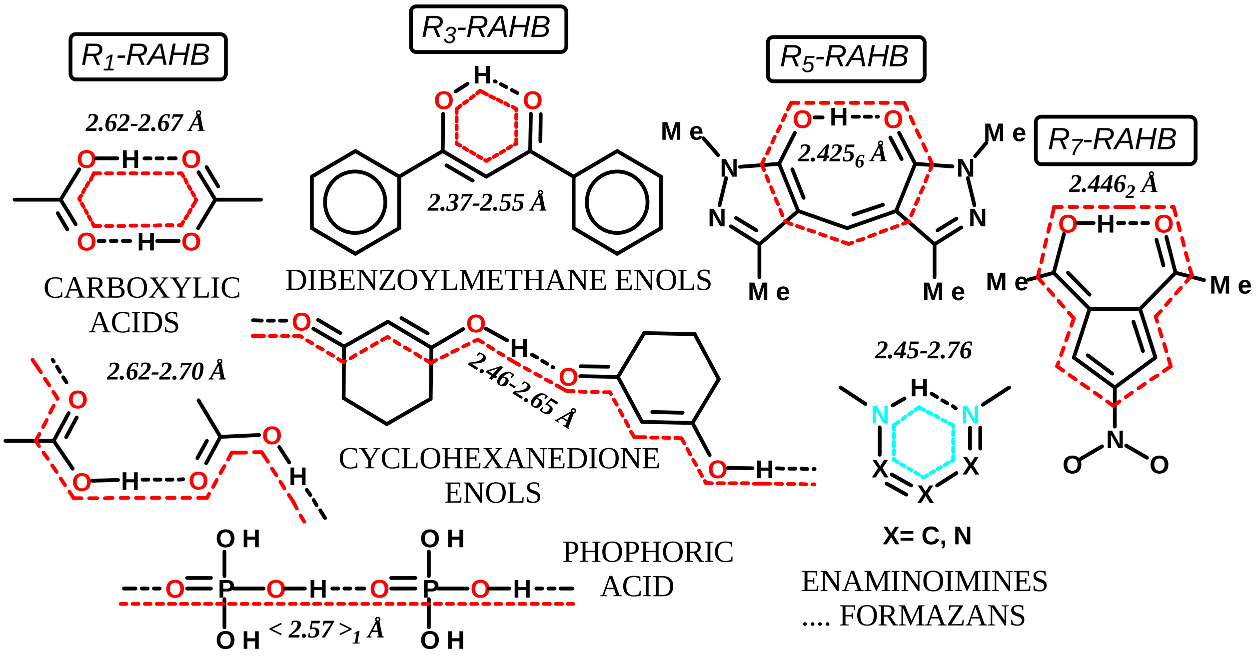
Chemical Leitmotif # 4:

RAHB

Resonance-Assisted or π-Bond Cooperative HB

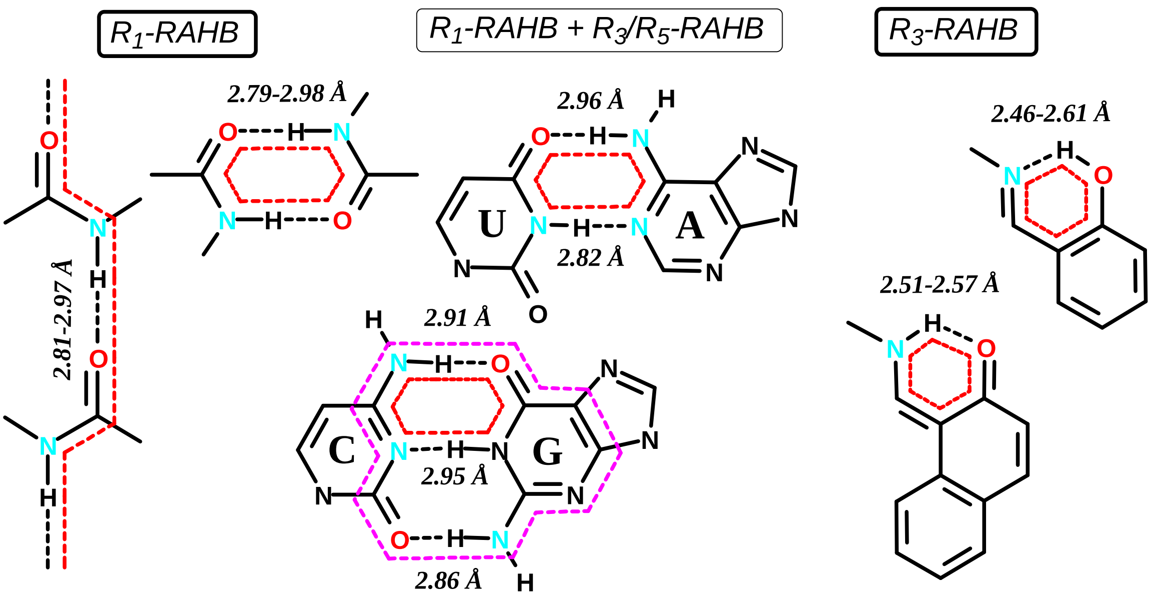
R-D-H...A=R ⇔ R=D...H-A-R

HOMONUCLEAR X-H...X (X= O, N)



HETERONUCLEAR X-H...Y (X, Y= O, N)

R_n-RAHB



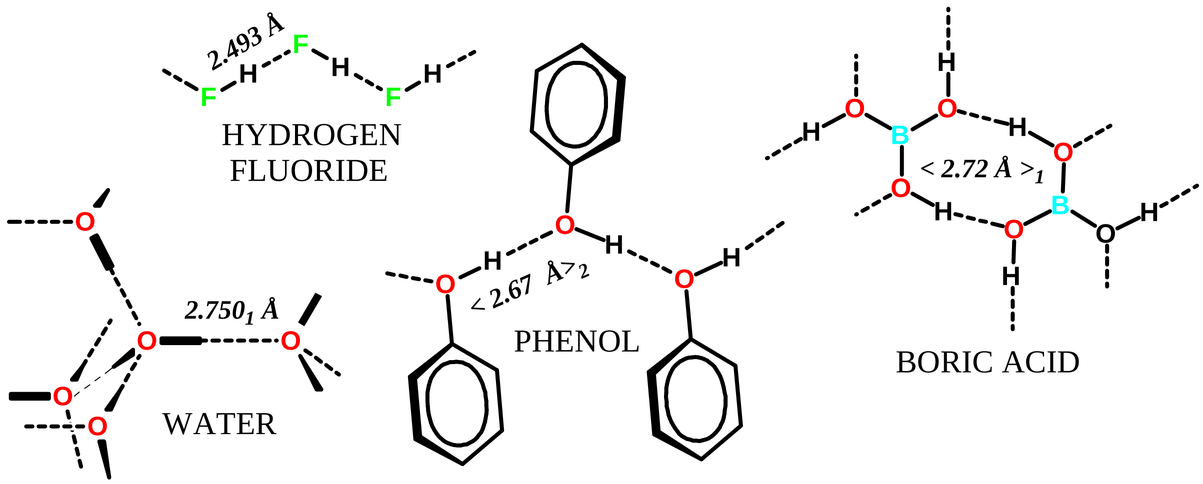
THE WONDERFUL WORLD OF CHEMICAL LEITMOTIFS

Chemical Leitmotif # 5:

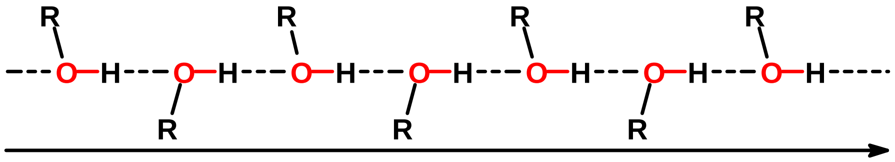
PAHB

Polarization-Assisted or σ-Bond Cooperative HB

...X-H...X-H...X-H...



The most known HB of this type is the ***σ-Bond-Cooperative** Chain* ***of H-bonded ...O(R)H.. groups*** (Jeffrey and Saenger, 1991)



(R= alkyl, aryl or H in, respectively, alcohols, phenols or water).

Because of the ***rather low polarizability of the σ bond***, this Leitmotif can provide a ***only a small enhancement of the HB energy*** of some 20-40% with a moderate O...O shortening from 2.75 to 2.62 Å.

THE INTERPRETATION OF CHEMICAL LEITMOTIFS:
THE PA/pKa EQUALIZATION PRINCIPLE

Chemical Leitmotif # 1:
(+/-)CAHB
Positive/Negative Charge-Assisted HB
Direct Acid-Base PA/pK_a Matching
$R\text{-}^{1/2-}D....H^{+}....A^{1/2-}\text{-}R$

The basis for the interpretation of the mechanism of action of chemical leitmotifs
is given by the **(+/-)CAHB chemical leitmotif.**
Acid-base pairs having a **pK_a matching within 0-2 units**
are all known to give very strong HBs.

But what about the other leitmotifs?

Why the weak water-water HB (of some 5 kcal/mol)
can be transformed,
by both acquiring and loosing a proton,
into HBs with energies as large as 30-31 kcal/mol?

And why the weak R-O-H...O=CR_2 alcohol-ketone HB
may undergo a fourfold increase of its energy
when the donor and acceptors atoms
are connected through an ...O=C-C=C-OH...
π-conjugated group?

The reason is always PA/pK_a matching,
all ***chemical leitmotifs*** being ***simple artifices***
that molecules can use to obliterate the normally
very large ΔpK_a between HB donor and acceptor atoms.

THE INTERPRETATION OF CHEMICAL LEITMOTIFS: THE PA/pKa EQUALIZATION PRINCIPLE

Chemical Leitmotif # 2:

(-)CAHB

Negative Charge-Assisted HB

Acid-Base PA/pK_a Matching by Proton Loss

$[R\text{-}D....H....A\text{-}R]^-$

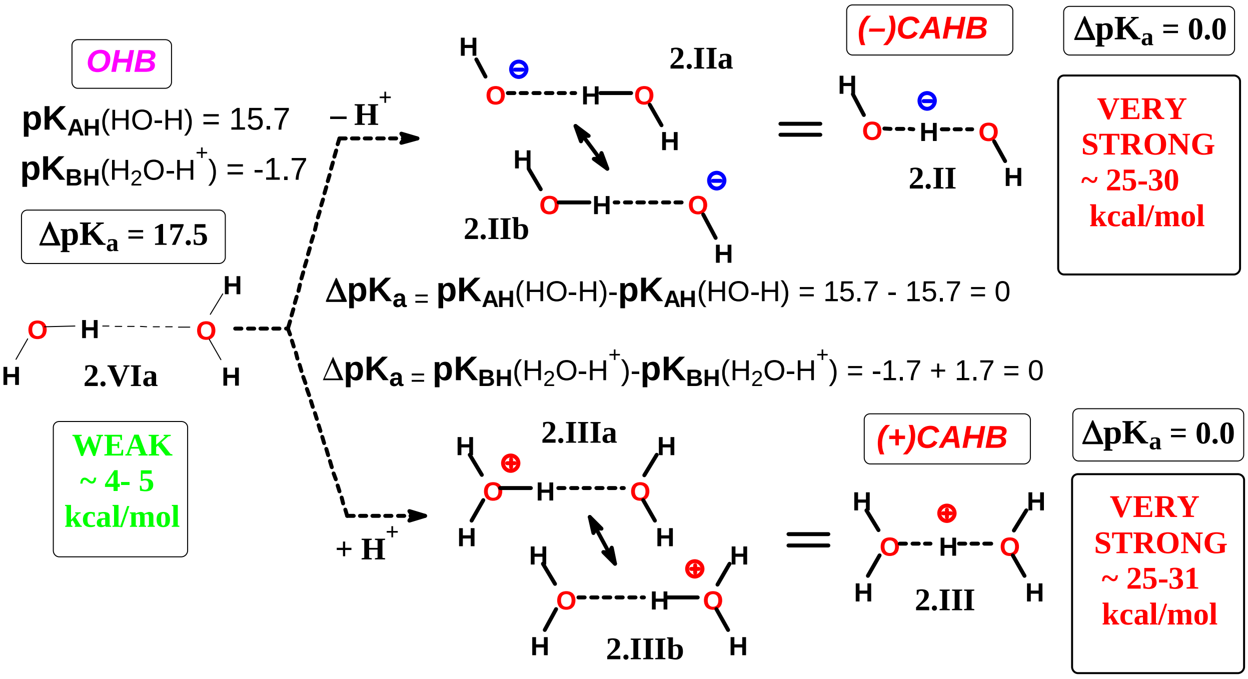
Chemical Leitmotif # 3:

(+)CAHB

Positive Charge-Assisted HB

Acid-Base PA/pK_a Matching by Proton Gain

$[R\text{-}D....H....A\text{-}R]^+$



$pK_{AH}(HO\text{-}H) = 15.7$

$pK_{BH}(H_2O\text{-}H^+) = -1.7$

$\Delta pK_a = 17.5$

$\Delta pK_a = 0.0$

$\Delta pK_a = pK_{AH}(HO\text{-}H)\text{-}pK_{AH}(HO\text{-}H) = 15.7 - 15.7 = 0$

$\Delta pK_a = pK_{BH}(H_2O\text{-}H^+)\text{-}pK_{BH}(H_2O\text{-}H^+) = -1.7 + 1.7 = 0$

$\Delta pK_a = 0.0$

THE INTERPRETATION OF CHEMICAL LEITMOTIFS: THE PA/pKa EQUALIZATION PRINCIPLE

Chemical Leitmotif # 4:

RAHB

Resonance-Assisted or π-Bond Cooperative HB

PA/pK_a Matching by π-Conjugated-Bond Polarization

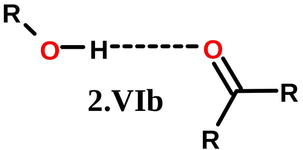
R-D-H...A=R ⇔ R=D...H-A-R

OHB

pK_{AH}(RO-H) = 15/18

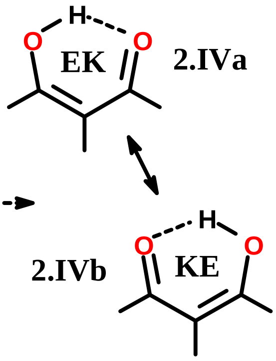
pK_{BH}(R_2C=O-H^+) = -(6/7)

ΔpK_a = ~ **21-25**



2.VIb

WEAK
~ 4- 5
kcal/mol

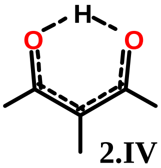


2.IVa

2.IVb

R_n-RAHB

ΔpK_a = 0.0



2.IV

STRONG
~ 15-22
kcal/mol

ASSESSING A COMPREHENSIVE HB MODEL 1

EXPERIMENTAL FACTS ON THE HB STRENGTH

It is of fundamental importance to realize that
there are not strong or weak HB in themselves.
Rather, ***any given D-H...A system***
may form HBs having a
wide range of strengths, lengths, symmetries **and** ***proton locations***,
the two extremes of this range being
represented by
1. the weak, long, dissymmetric and proton-outcentered HB
of electrostatic nature
and the
2. the very strong, very short, symmetric and proton-centered HB
classifiable as a true 3-center-4-electron covalent bond.

THE INDEPENDENT VARIABLE DRIVING THE HB STRENGTH

We now know that ***the driving variable*** which transforms
very strong into weak HBs is
dimensionally a free enthalpy
and is represented by the
difference between the Proton Affinities (ΔPA)
or related
Acid-Base Dissociation Constants (ΔpK_a)
of the Donor and Acceptor moieties.

LOGICAL CONSEQUENCE

The strongest HB formed by any given D-H...A system occurs only when
ΔPA (or ΔpK_a) approaches zero.
This limit corresponds to the condition by which
the proton is equally shared by the two groups
so that the HB is transformed from a weak electrostatic interaction into a
strong proton-centred 3-centre-4-electron $R\text{-}D^{1/2-}\text{---}H\text{---}{}^{1/2+}A\text{-}R$ covalent bond.

ASSESSING A COMPREHENSIVE HB MODEL 2

THE
“PROTON-AFFINITY EQUALIZATION”
PRINCIPLE

Let’s consider a generic HB of the form

$$R_1\text{--D--H.....:A--}R_2$$

where **D** and **:A** are the ***HB Donor*** and ***Acceptor Atoms***
and $\mathbf{R_1}$ and $\mathbf{R_2}$ any, however complex, molecular fragment.

Having fixed the atomic nature of D and A, and making allowance
for specific effects of **steric** stretching or compression,

HB STRENGTH (HB dissociation energy),
GEOMETRY (D...A, D-H, H...A distances and D-H-A angle)
and ***SYMMETRY*** (linear or bent, proton-centered or less)

ARE COMPLETELY DETERMINED

by the DIFFERENCE OF TWO FREE ENTHALPIES which
may be equally related to Proton Affinities (PA)

$$\Delta PA = PA\ (R_1\text{-}D^-) - PA\ (R_2\text{-}A)$$

or Acid-Base Dissociation Constants (pK$_a$)

$$\Delta pK_a = pK_{AH}\ (R_1\text{-}D\text{-}H) - pK_{BH}\ (R_2\text{-}A\text{-}H^+).$$

The strongest possible HB (the intrinsic HB)
which may be formed in any given H-bonded system
is always associated with the condition

$$\Delta PA \text{ or } \Delta pK_a = 0$$

FINAL CONSIDERATIONS - CRITERIA FOR A CLASSIFICATION OF THE CHEMICAL LEITMOTIFS

There are three different ways for subdividing chemical leitmotifs:

1. BY THE STRENGTH OF THE HB FORMED

   a) ***Strong and very strong HBs***
      i) **CL # 1: (+/-)CAHB, Positive/Negative Charge-Assisted HB**
      j) **CL # 2: (-)CAHB, Negative Charge-Assisted HB**
      k) **CL # 3: (+)CAHB, Positive Charge-Assisted HB**
      l) **CL # 4: RAHB, Resonance-Assisted or π-Bond Cooperative HB**
   b) ***Mid-strong HB***
      i) **CL # 5: PAHB, Polarization-Assisted or σ-Bond Cooperative HB**
   c) ***Weak HB***
      i) **CL # 6: OHB or IHB, Ordinary or Isolated HB**

2. BY THEIR MECHANISM OF HB STRENGTHENING

   a) ***Charge-Assisted HBs***
      i) **CL # 1: (+/-)CAHB, Direct Acid-Base PA/pK_a Matching**
      j) **CL # 2: (-)CAHB, Acid-Base PA/pK_a Matching by Proton Loss**
      k) **CL # 3: (+)CAHB, Acid-Base PA/pK_a Matching by Proton Gain**
   b) ***Π/Σ-Bond Polarization-Assisted HBs***
      i) **CL # 4: RAHB, PA/pK_a Matching by π-Conjugated-Bond Polarization**
      j) **CL # 5: PAHB, PA/pK_a Matching by σ-Conjugated-Bond Polarization**
   c) ***Neither Charged- nor Π/Σ-Bond Polarization-Assisted HB***
      i) **CL # 6: OHB or IHB, No PA/pK_a Matching**

FINAL CONSIDERATIONS - CRITERIA FOR A CLASSIFICATION OF THE CHEMICAL LEITMOTIFS

3) BY THEIR RELATIONSHIPS WITH THE $\Delta PA/\Delta pK_a$ EQUALIZATION PRINCIPLE

a) Proton-Transfer HBs (Class PT)

- i) **CL # 1: (+/-)CAHB, Positive/Negative Charge-Assisted HB (Reaction A)**
- j) **CL # 6: OHB or IHB, Ordinary or Isolated HB (Reaction A)**

b) Proton-Shared HBs (Class PS)

- i) **CL # 2: (-)CAHB, Negative Charge-Assisted HB (Reaction B1)**
- j) **CL # 3: (+)CAHB, Positive Charge-Assisted HB (Reaction B2)**
- k) **CL # 4: RAHB, Resonance-Assisted or π-Bond Cooperative HB (Reaction B3)**
- l) **CL # 5: PAHB, Polarization-Assisted or σ-Bond Cooperative HB (Reaction B4)**

Class PT. Proton Transfer Reaction

$$R_1\text{-}D\text{-}H....:A\text{-}R_2 \leftrightarrows R_1\text{-}{}^{1/2-}D...H^{+}...A^{1/2-}\text{-}R_2 \leftrightarrows R_1\text{-}{}^{-}D:....H\text{-}A^{+}\text{-}R_2 \qquad \text{(PT)}$$

Class PS. Proton Sharing Reactions

$$R_1\text{-}D\text{-}H....:D^{-}\text{-}R_2 \leftrightarrows [R_1\text{-}D...H...D\text{-}R_2]^{-} \leftrightarrows R_1\text{-}{}^{-}D:....H\text{-}D\text{-}R_2 \qquad \text{(PS1)}$$

$$R_1\text{-}{}^{+}A\text{-}H....:A\text{-}R_2 \leftrightarrows [R_1\text{-}A...H...A\text{-}R_2]^{+} \leftrightarrows R_1\text{-}A:....H\text{-}A^{+}\text{-}R_2 \qquad \text{(PS2)}$$

$$..:A{=}R_n\text{-}D\text{-}H... \leftrightarrows ...H...A:::R_n:::D...H... \leftrightarrows ....H\text{-}A\text{-}R_n{=}D:... \qquad \text{(PS3)}$$

$$..:X(R)\text{-}H\ldots:X(R)\text{-}H.. \leftrightarrows ..X(R)\ldots H\ldots X(R)\ldots H.. \leftrightarrows ..H\text{-}(R)X:\ldots H\text{-}(R)X:.. \qquad \text{(PS4)}$$