

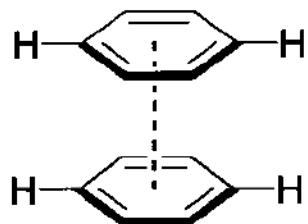
Molekuly jsou „předpogramované cihly“, které jsou schopny se samy, prostřednictvím mezimolekulární interakcí, spojovat ve vyšší celky

## **SUPRAMOLEKULY**

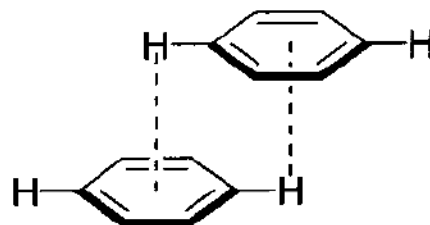
Supramolekulární chemie je multidisciplinární obor, který se snaží odhalit tajemství přírody, která jsou s tímto spojená, a využít je ve svůj prospěch.



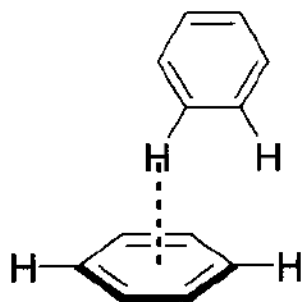
# Types of arene interactions - benzene dimers



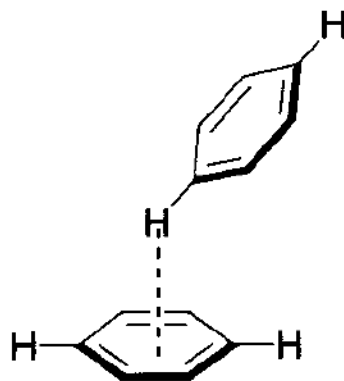
parallel stacking  
face-to-face  
planar sandwich  
face-to-face/center-to-center



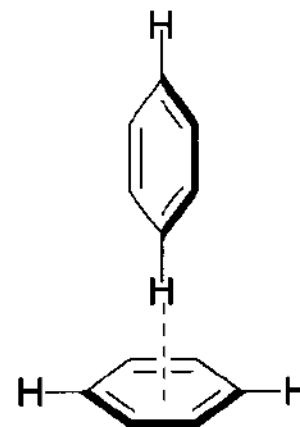
offset parallel stacking  
parallel-displaced  
face-to-face/center-to-edge



edge-titled-T

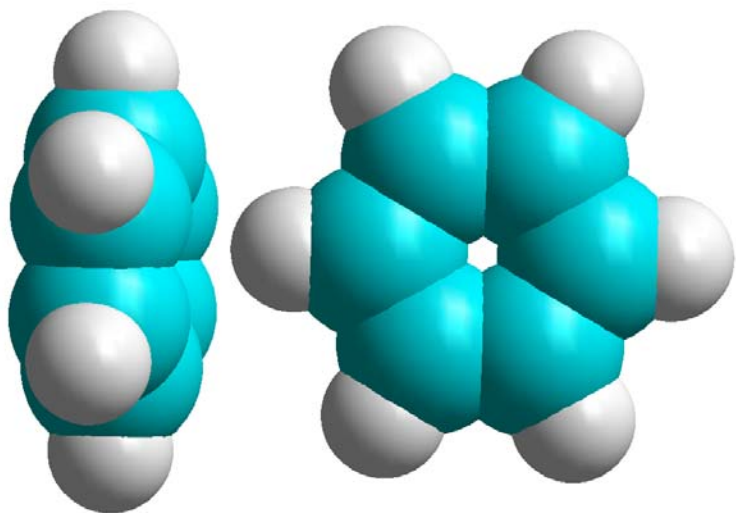


face-titled-T



T-shaped  
edge-to-face  
point-to-face

# Types of Arene interactions



face-to-edge

T-stacking

perpendicular aromatic interactions

phenyl interactions (in biology)

harringbone (crystal engineering)

hybrid interactions (crystal engineering)

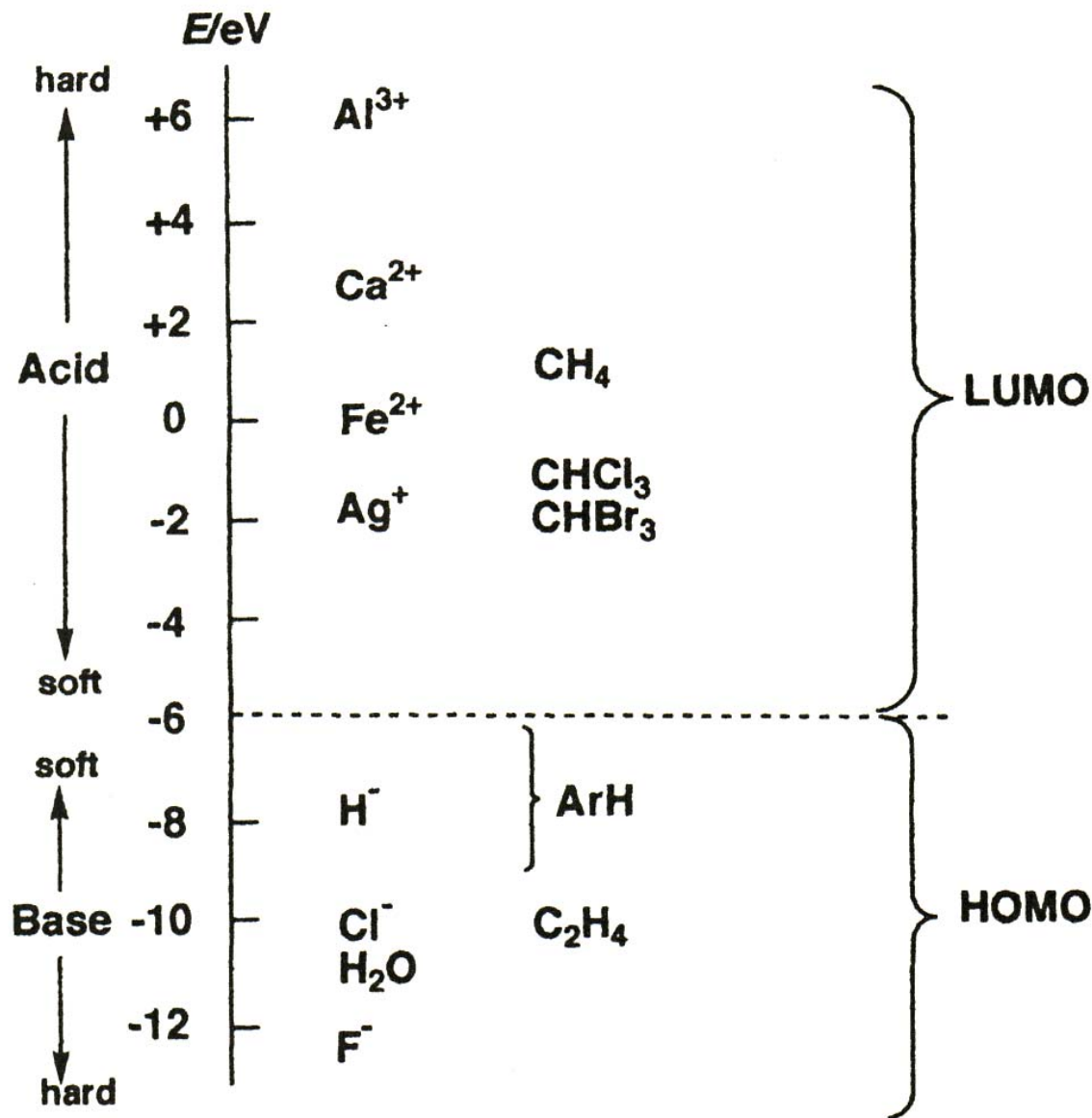
„CH- $\pi$  interaction (CH/ $\pi$ )“ ☹️

„CH- $\pi$  hydrogen bond“ 😊

„hydrophobic interaction“ ☹️

1. „Hydrogen bridges in crystal engineering: interactions without borders“  
Acc. Chem. Res. **2002**, 35, 565-573.
2. „The CH/ $\pi$  interaction: evidence, nature and consequences“  
Wiley-VCH, Inc., **1998**, ISBN 0-471-25290-5.
3. „The weak hydrogen bond in structural chemistry and biology“  
Oxford University Press Inc., **1999**, ISBN 0-19-850970-7.
4. „The CH-Pi interaction: Significance in Molecular Recognition“  
Tetrahedron **1995**, 51 (32), 8665-8701.

# Face-to-edge ... .. Hard-Soft-Acid-Base (HSAB) Concept



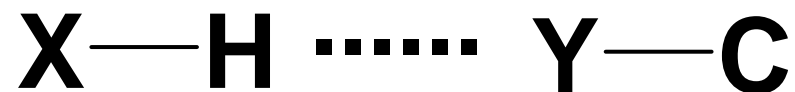
1. „Chemical Hardness: Applications from Molecules to Solids“ R. G. Pearson, Wiley-VCH, **1997**
2. „Hard and Soft Acids and Bases“ R.G. Pearson: *J. Am. Chem. Soc.* **1963**, 85(22), 3533-3539.
3. „Hard and soft acids and bases, HSAB“ R.G. Pearson: *J. Chem. Educ.* **1968**, 45, 581-587.

# Face-to-edge ... Hydrogen bond

	<b>O-H...O</b> hard acid ... hard base	<b>C-H...O</b> soft acid ... hard base	<b>O-H...<math>\pi</math></b> hard acid ... soft base	<b>C-H...<math>\pi</math></b> soft acid ... soft base
<b>Interaction energy</b> [ kcal.mol <sup>-1</sup> ]	<b>10 - 3</b>	<b>&lt; 3</b>	<b>~ 2</b>	<b>&lt; 2.5</b>
<b>Delocalization</b> (charge-transfer)	<b>variable</b>	<b>unimportant</b>	<b>important</b>	<b>important</b>
<b>Electrostatic</b> (Coulombic)	<b>strong</b>	<b>important</b>	<b>weak</b>	<b>unimportant</b>
<b>Dispersion</b> (London)	<b>unimportant</b>	<b>unimportant</b>	<b>important</b>	<b>important</b>
<b>Repulsive</b> <b>van der Waals</b>	<b>similar</b>			

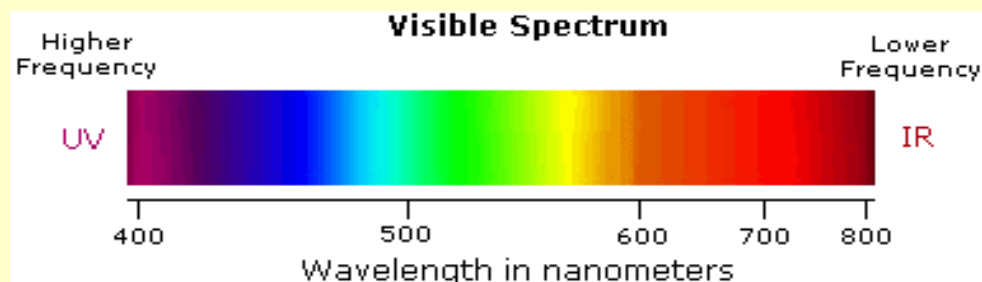
1. „Hydrogen bridges in crystal engineering: interactions without borders“  
Acc. Chem. Res. **2002**, 35, 565-573.
2. „The CH/ $\pi$  interaction: evidence, nature and consequences“  
Wiley-VCH, Inc., **1998**, ISBN 0-471-25290-5.
3. „The weak hydrogen bond in structural chemistry and biology“  
Oxford University Press Inc., **1999**, ISBN 0-19-850970-7.

# Blue-shift *versus* Red-shift Hydrogen Bond



## Klasická vodíková vazba (standard hydrogen bond)

Red shift (batochromní), delší vazebná délka, zvýšení intenzity  
EDT z  $\pi$  nebo  $n$  do  $\sigma^*$  vazby X-H  $\rightarrow$  přímé oslabení vazby X-H



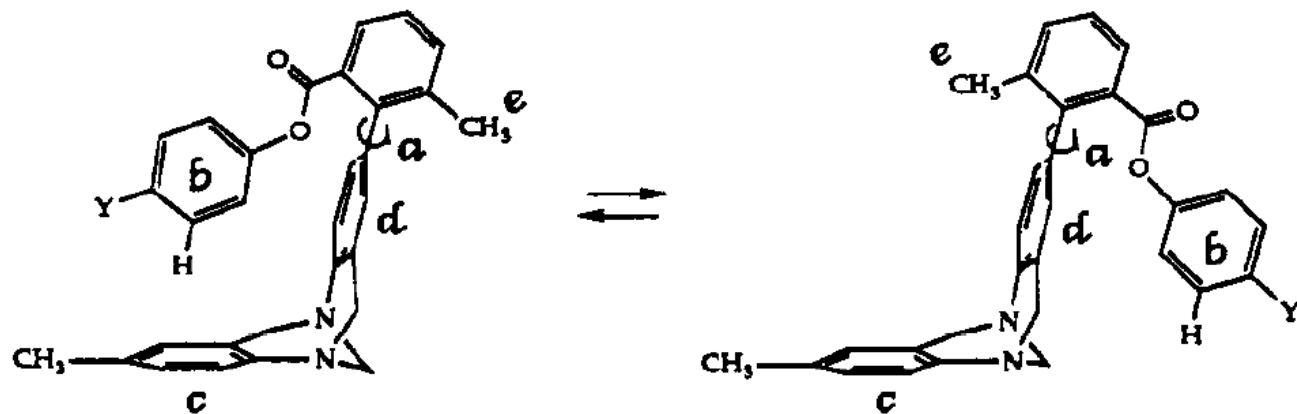
## Neklasická vodíková vazba (improper hydrogen bond)

Blue shift (hypsochromní), kratší vazebná délka, snížení intenzity  
Nedochází k EDT do  $\sigma^*$  vazby X-H, ale ...

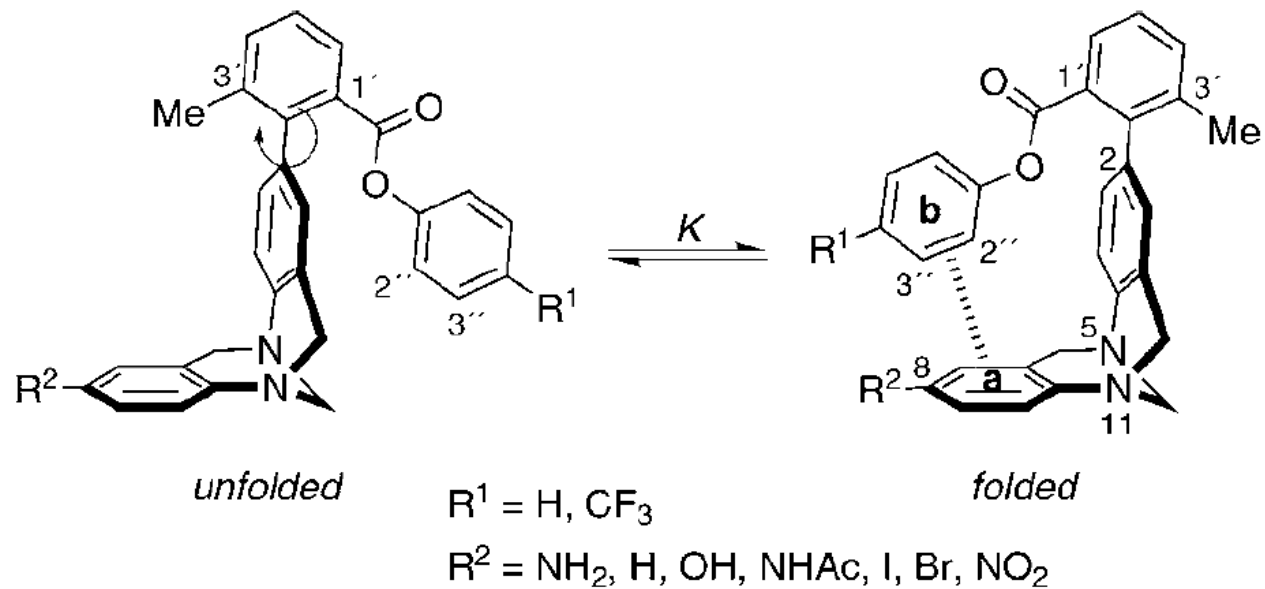
P. Hobza, *Chem. Rev.* **2000**, *100*, 4253-4264

E.D. Jammis, *J. Am. Chem. Soc.* **2007**, *129*, 4620-4632

# Face-to-edge ... Molecular torsion balances



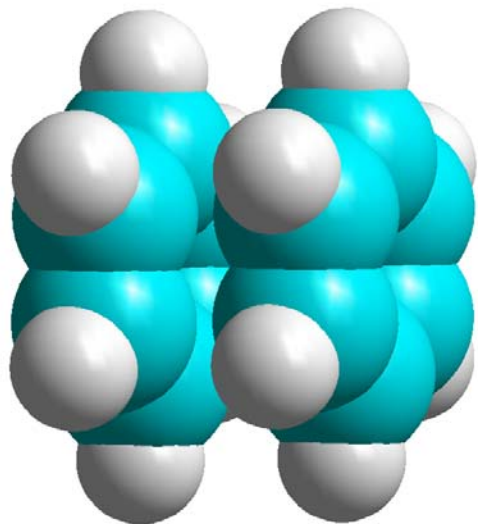
C. S. Wilcox, *J. Am. Chem. Soc.* **1994**, *116*, 4497-4498



F. Diederich, *Chem. Commun.* **2008**, 4031-4033



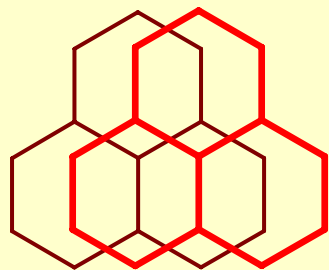
# Types of Arene interactions



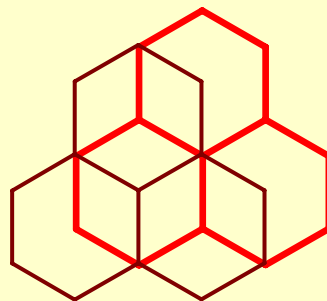
face-to-face  
 $\pi$ - $\pi$  interaction  
parallel aromatic interactions  
 $\pi$ -acid/ $\pi$ -base  
molecular complex  
charge-transfer complex (CT)  
electron donor acceptor (EDA) interactions  
“hydrophobic interaction” 😞

$\pi$ -stacking  
 $\pi$ -sandwich  
stacking interaction  
phenyl-stacking

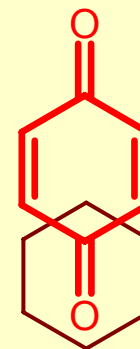
$\pi$ - $\pi$  Interactions in Self-Assembly, *J. Phys. Org. Chem.* **1997**, 10, 254-272



Pyrene, coronene

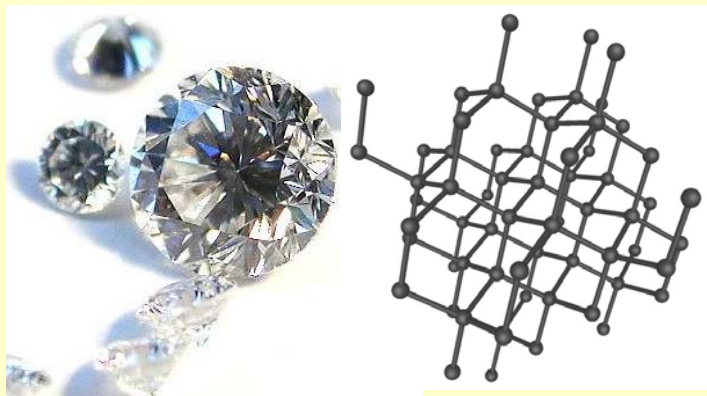


Graphite

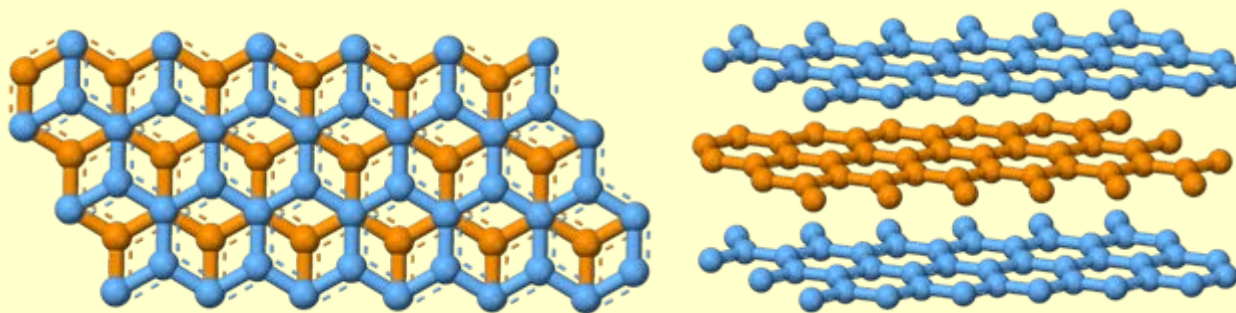


*p*-benzoquinone

# $\pi$ - $\pi$ ... Graphite versus diamond



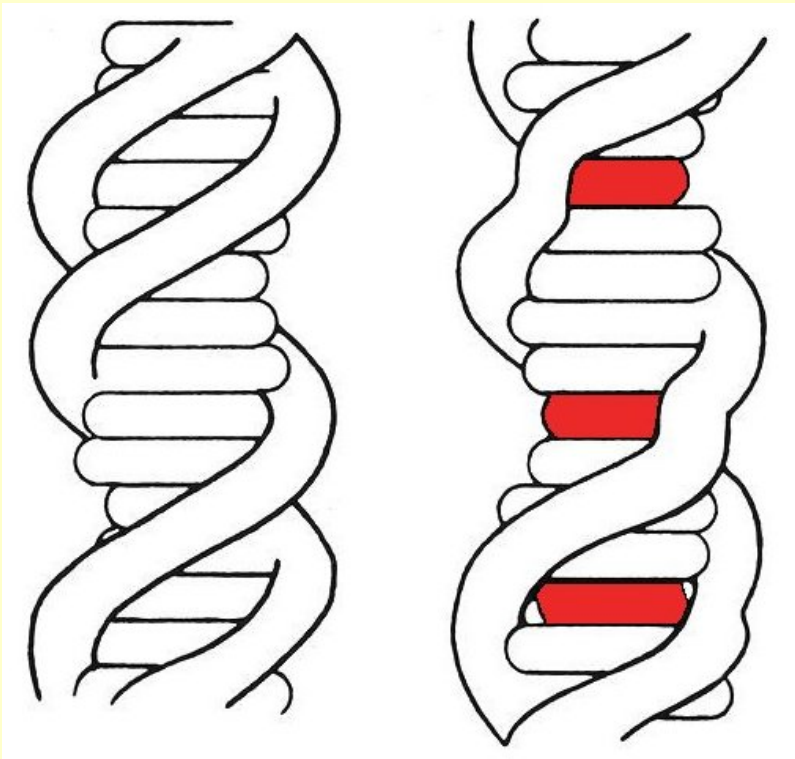
Délka vazby 0,154 nm, vzdálenost rovin < 0,154 nm,  
kovalentní vazba, hybridizace uhlíku  $sp^3$   
Tvrđost 10, bezbarvý  
Měrný elektrický odpor  $2,7 \times 10^9$   
X-ray hustota  $3,52 \text{ g.cm}^{-3}$   
Teplota tání  $3550 \text{ }^\circ\text{C}$ , teplota varu  $4827 \text{ }^\circ\text{C}$



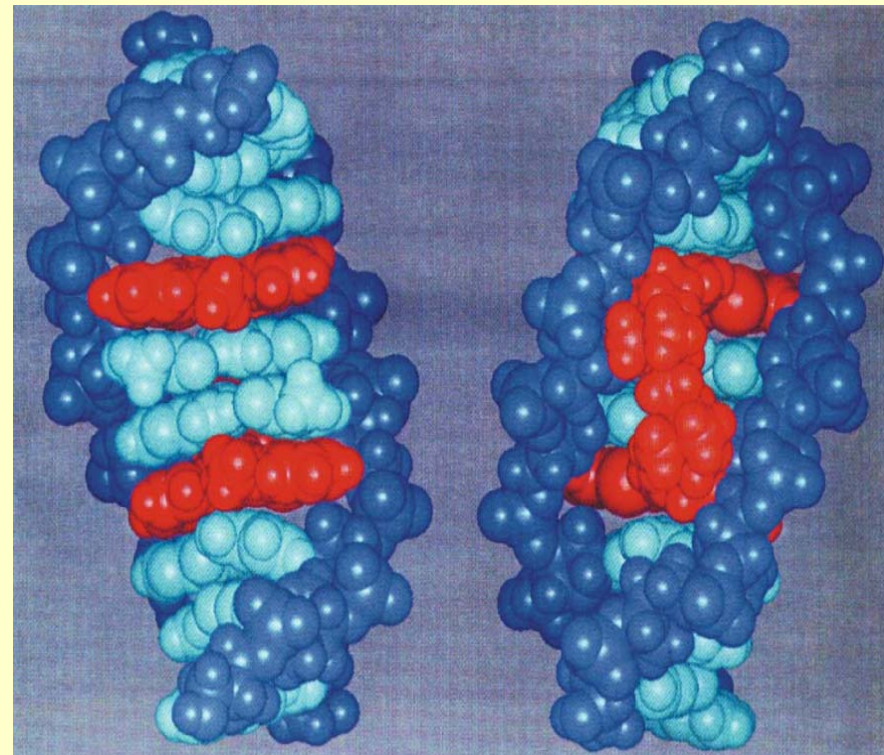
Délka vazby 0,142 nm, vzdálenost rovin 0,335 nm,  
van der Waals síly,  $\pi$ - $\pi$  stacking (?), hybridizace  $sp^2$   
Tvrđost 1-2, superlubrikant, černý  
Měrný elektrický odpor  $1,4 \times 10^3$   
X-ray hustota  $2,27 \text{ g.cm}^{-3}$   
Teplota tání  $3652 - 3697 \text{ }^\circ\text{C}$ , teplota varu  $4200 \text{ }^\circ\text{C}$

# DNA intercalation

Intercalation induces structural distortion



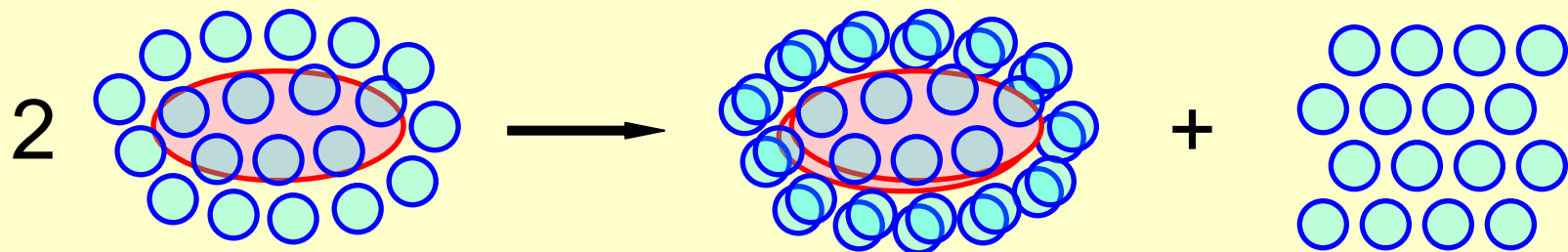
Double intercalation into DNA



*Top. Curr. Chem.* **2005**, 258, 161-204

*Nucleic Acids Research* **2005**, 33 (6), 1779–1789

# Nature of $\pi$ - $\pi$ ... Solvophobic Effect



$$\Delta G = \Delta H - T \cdot \Delta S$$

Je významný ve vodném prostředí (hydrofobní efekt) – významný entropický člen.

*Angew. Chem. Int. Ed.* **1984**, 23, 908-910

*J. Chem. Soc., Chem. Commun.* **1987**, 219-221

*J. Am. Chem. Soc.* **1990**, 112, 339-343

V organickém prostředí není solvofobní efekt významný – přesto dochází k vazbě.

*J. Am. Chem. Soc.* **1989**, 111, 1082-1090

Efekt minimalizuje povrch – přesto je obvykle pozorován offset stacking.

*J. Am. Chem. Soc.* **1989**, 112, 5525-5534

Arene-arene interakce spojené s DNA jsou řízeny převážně entalpicky.

Classical versus Nonclassical hydrophobic effect

*Angew. Chem. Int. Ed.* **2003**, 42 (11), 1210-1250

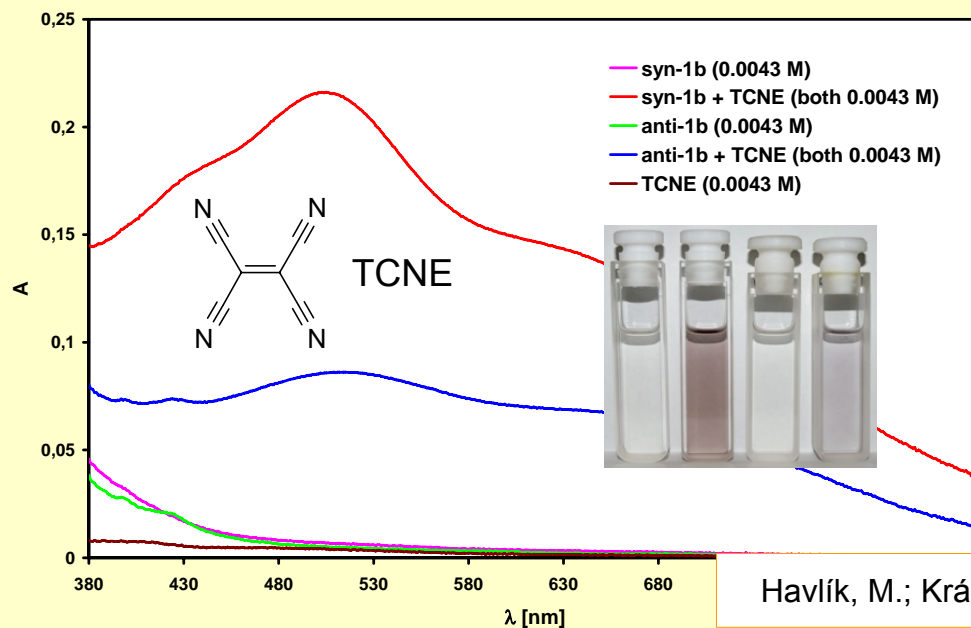
# Nature of $\pi$ - $\pi$ ... Charge-Transfer Complex

Charge transfer complex (CT komplex) je definován jako komplex elektron-donoru s elektron-akceptorem, který je charakterizován elektronovým přechodem do excitovaného stavu. V excitovaném stavu dochází k parciálnímu přenosu náboje z donoru na akceptor. Toto je provázeno vnikem nového pásu (CT pásu) v UV-Vis spektru nebo alespoň rozšířením stávajících.

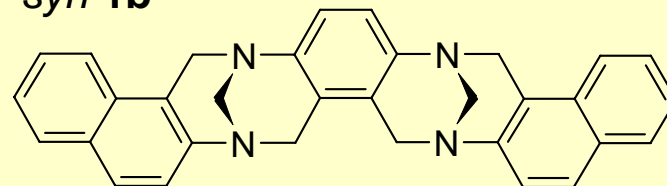
R. S. Mulliken, *J. Am. Chem. Soc.* **1952**, 74, 811-824.

R. S. Mulliken, W. B. Person, *Molecular Complexes*, Wiley, New York, **1969**

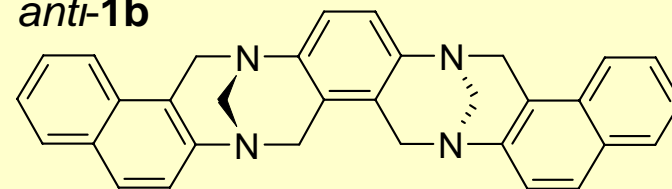
M. D. Newton, *Electron Transfer in Chemistry*, vol. 1, Wiley-VCH, New York, **2001**



*syn-1b*



*anti-1b*



Havlík, M.; Král, V.; Kaplánek, R.; Dolenský, B. *Org. Lett.* **2008**, in press

## Nature of $\pi$ - $\pi$ ... Charge Transfer Complex

<b>DONOR</b>	$\lambda_{CT}$ [nm]	$\epsilon_{CT}$ [L.mol <sup>-1</sup> cm <sup>-1</sup> ]	$K_{ass}$
Benzen	340	9180	0.30
Toluen	365	1920	0.50
<i>p</i> -Xylen	410	1960	0.89
Mesitylen	410	2250	1.17
Hexamethylbenzen	505	2880	9.08

1. Čím intenzivnější CT pás tím méně stabilnější komplex
2. Mnohé stabilní komplexy nevykazují žádné CT pásy

## $\pi$ - $\pi$ ... Atomic Charge Model

Hypotéza je založena na nestejně distribuci náboje v  $\pi$ -systému. Orientací kladných (záporných) parciálních nábojů jedné molekuly k záporným (kladným) parciálním nábojům druhé molekuly dochází k elektrostatické interakci.

*J. Am. Chem. Soc.* **1988**, 110, 6561-6562

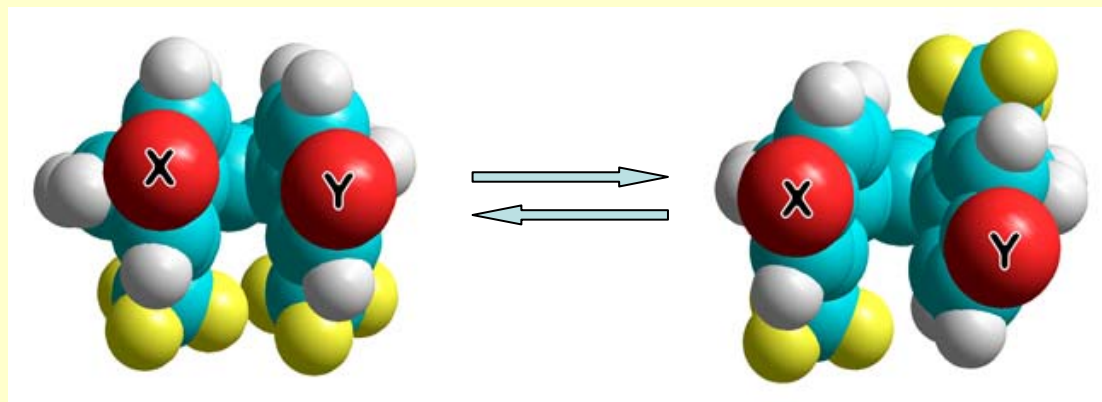
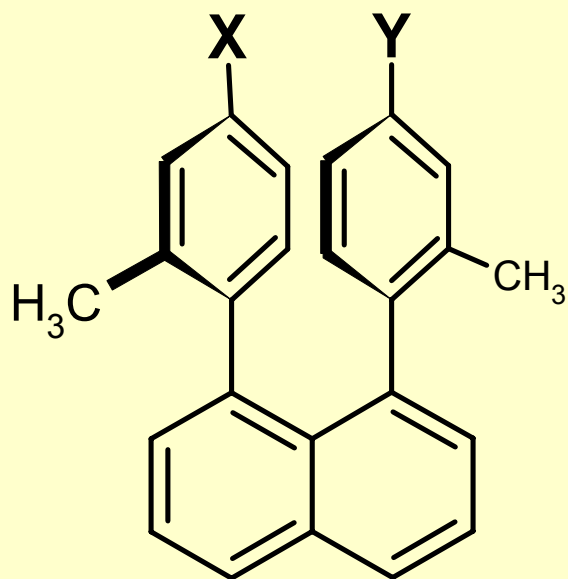
Energetické bariéry mezi jednotlivými isomery jsou však oproti experimentálně nalezeným hodnotám nezanedbatelně menší

ca. **1**  $\ll$  **50** kJ.mol<sup>-1</sup>

*J. Am. Chem. Soc.* **1990**, 112, 5525-5534

# $\pi$ - $\pi$ ... Electrostatic or Charge Transfer?

( polar/ $\pi$  versus  $\pi$ - $\pi$  )



X	Y	stability
Acceptor	Acceptor	
Acceptor	Donor	
Donor	Donor	

*J. Am. Chem. Soc.*  
**1992**, 114, 5729-5733

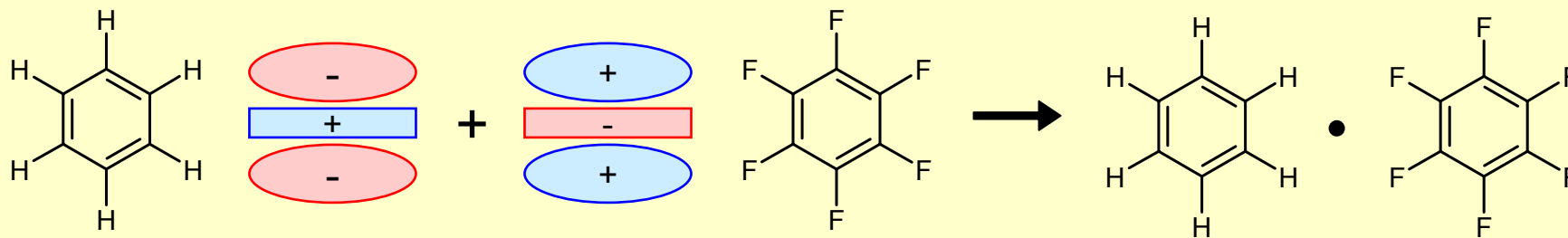
*J. Am. Chem. Soc.*  
**1993**, 115, 5330-5331

*Pure Appl. Chem.*  
**1995**, 67 (5), 683-689

**!!! ELECTROSTATIC !!!**



Patrick, C.R.; Prosser, G. S. *Nature*, **1960**, 187, 1021



Bod tání  
**5,5 °C**

Bod tání  
**4,1 °C**

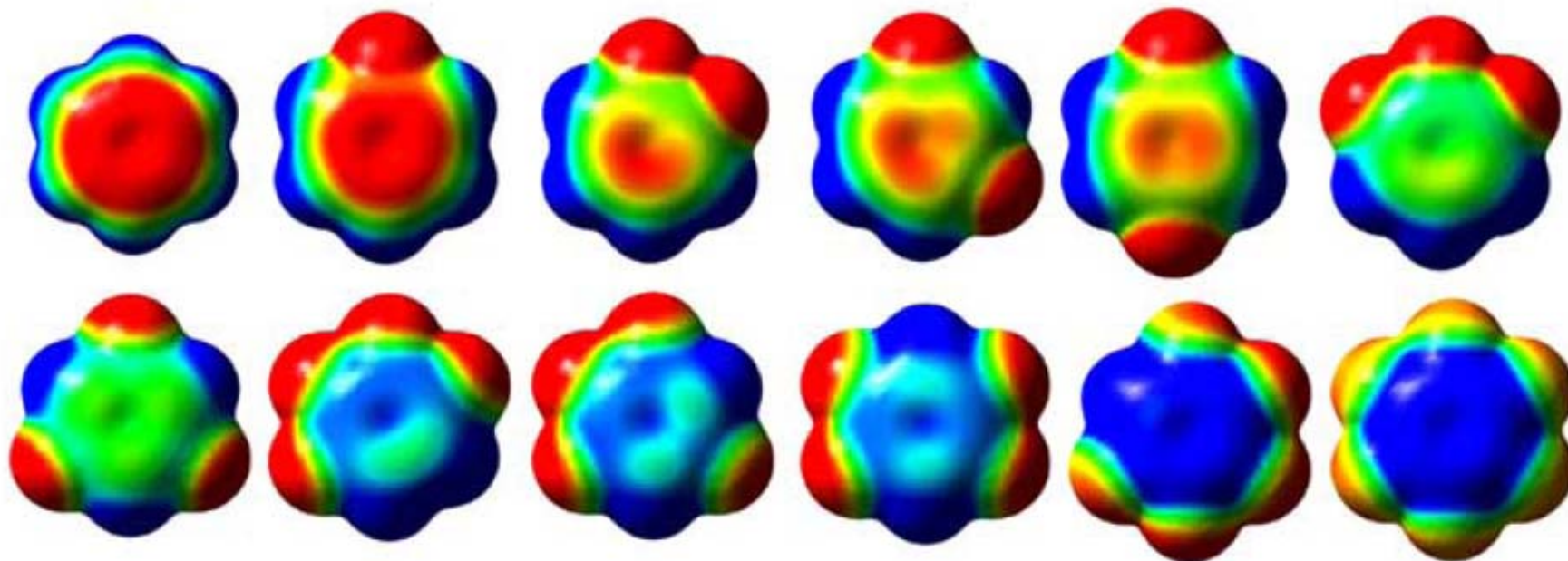
Bod tání  
**23,7 °C**

## UV-Vis spektra

→ Žádné rozšíření ani nový pás = nejsou to charge transfer komplexy

*J. Phys. Chem. A* **2006**, 110, 2027-2033 → **ELEKTROSTATICKÁ INTERAKCE**

## Electrostatic Potential Energy Surfaces (PES) of Benzene and Fluorobenzenes

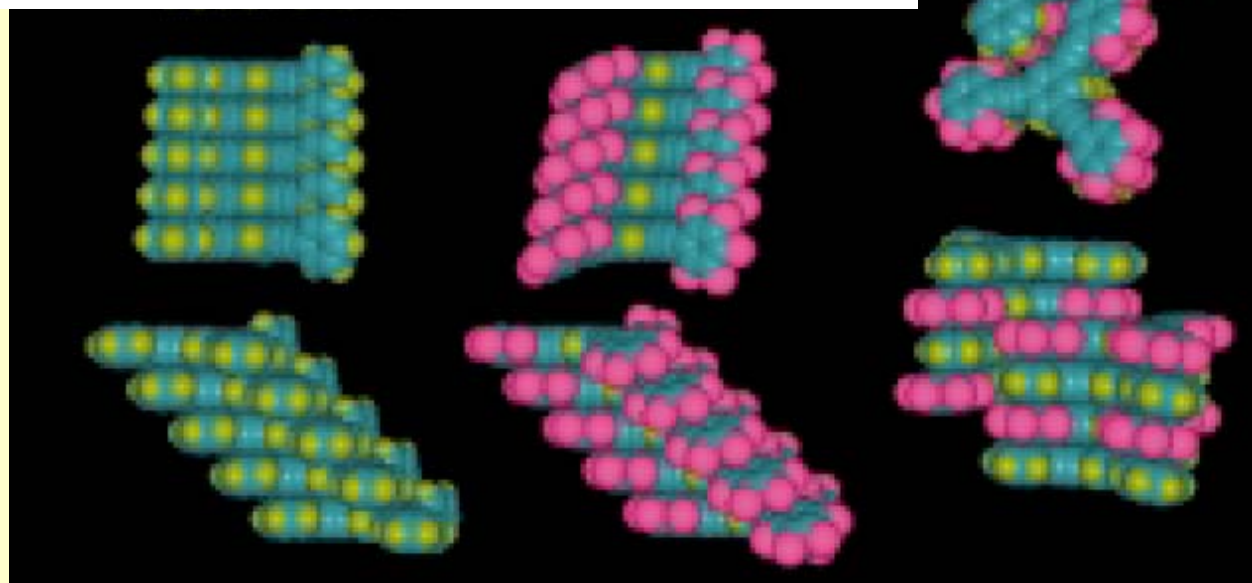
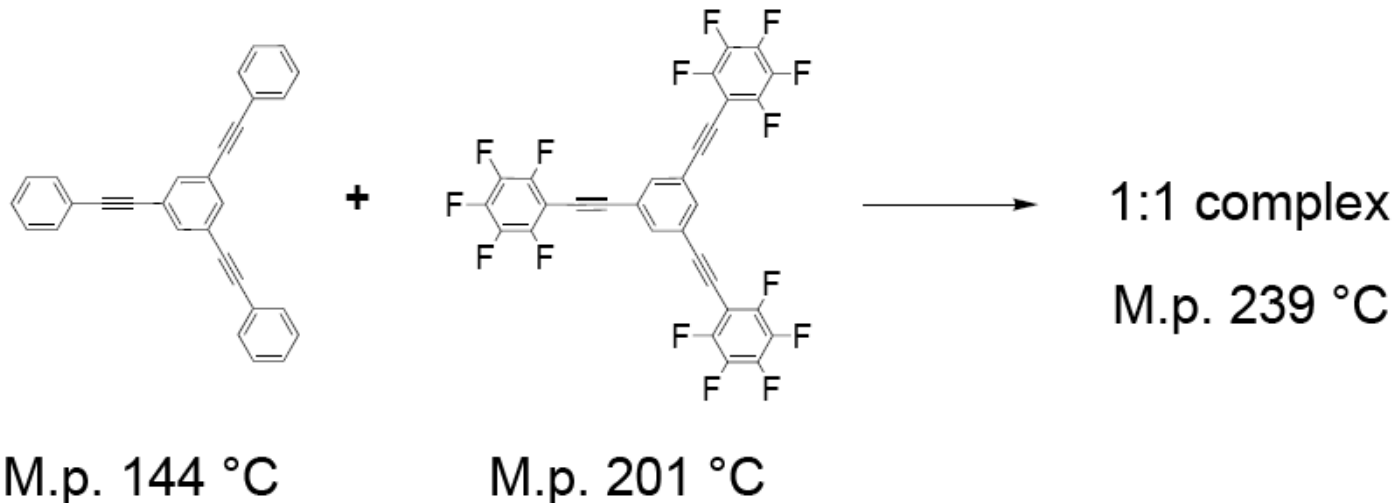


Red is negative, green is neutral, blue is positive charged surfaces

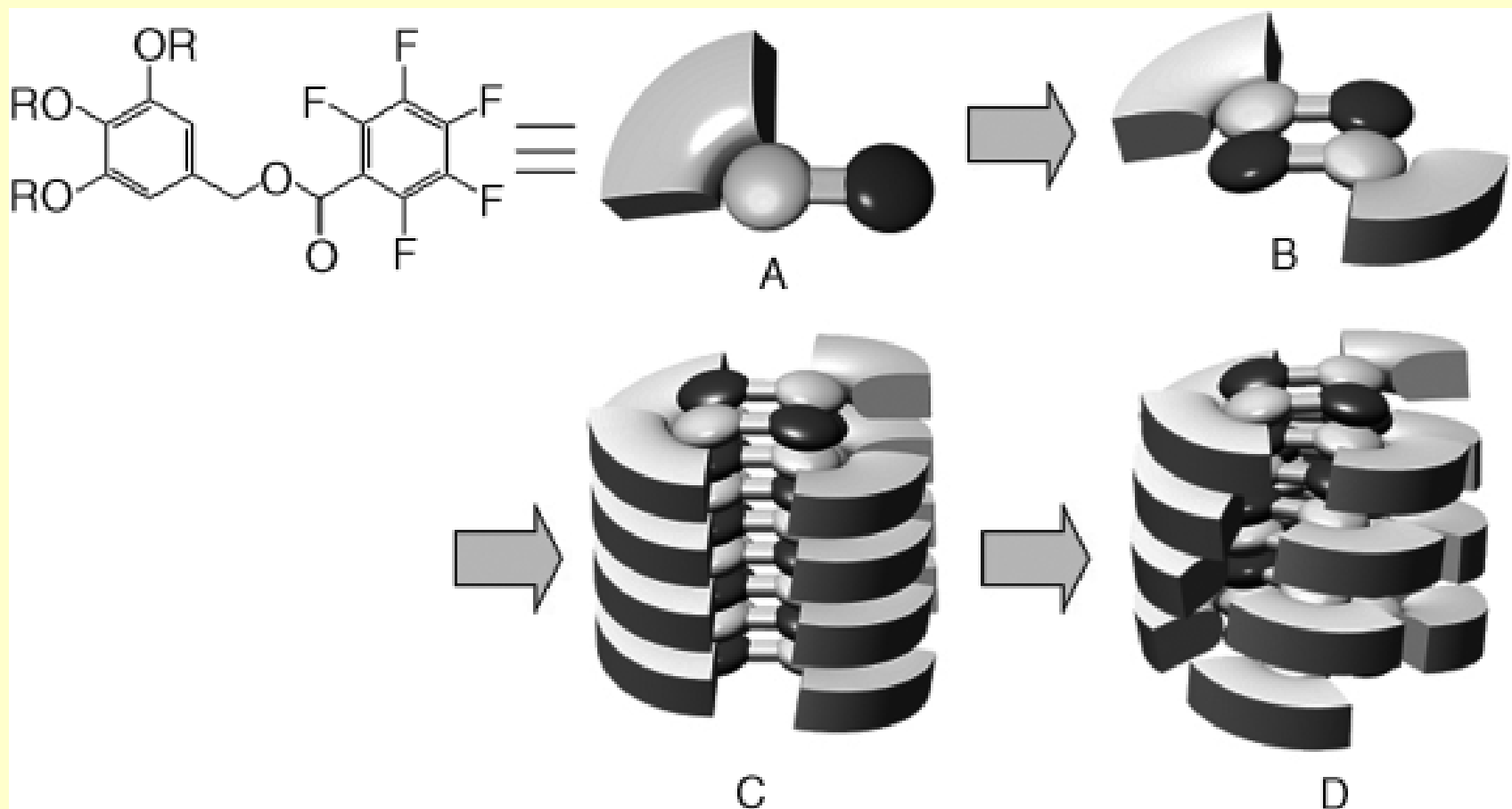
**The Strength of Weak Interactions: Aromatic Fluorine in Drug Design**

*Current Topics in Medicinal Chemistry*, 2006, 6, 1473-1482

# Arene-Perfluoroarene Interactions



# Arene-perfluorarene interactions



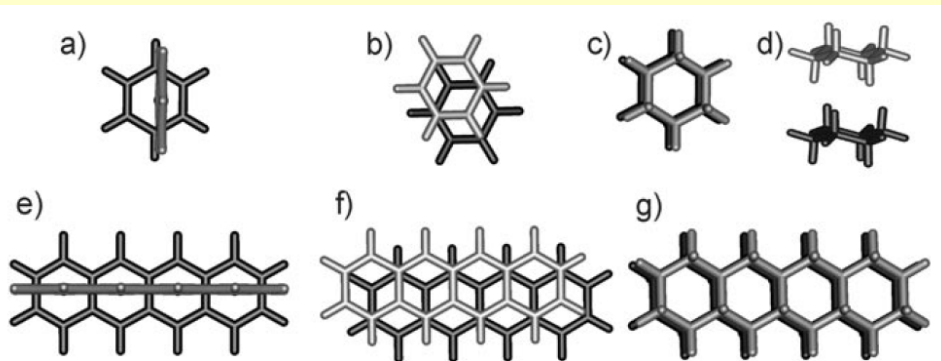
*Angew. Chem. Int. Ed.* **2007**, 46 (5), 764-768

# $\pi$ - $\pi$ ... Does it really exist?

Stefan Grimme:

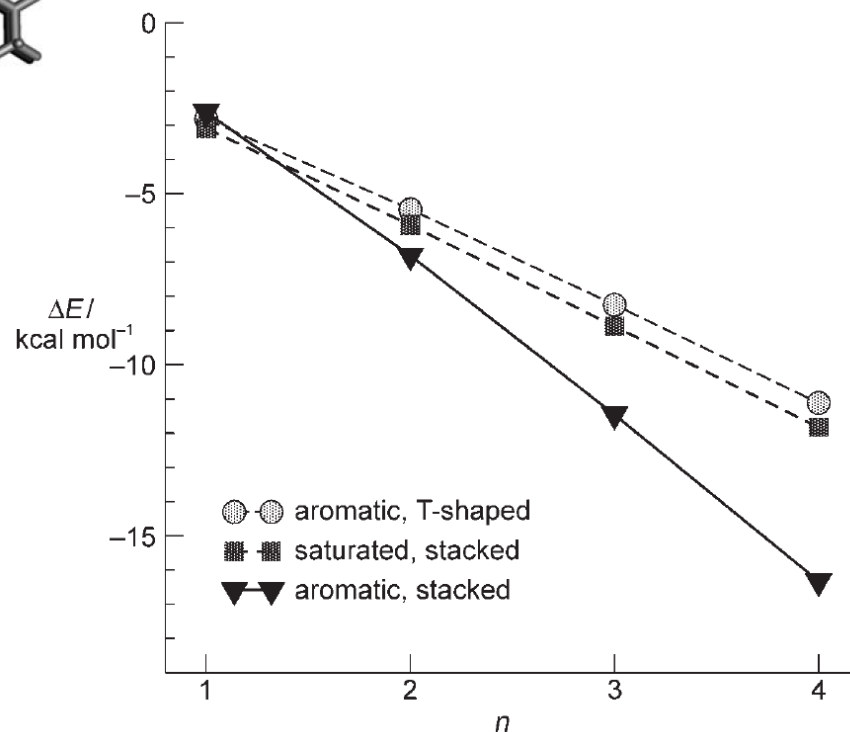
Do Special Noncovalent  $\pi$ - $\pi$  Stacking Interactions Really Exist?

**Yes!**



**Figure 1.** Energy-minimized structures of the benzene dimer: a) T-shaped and b)  $\pi$ - $\pi$  stacked. c), d) The cyclohexane dimer in two projections. The tetracene dimer: e) T-shaped and f)  $\pi$ - $\pi$  stacked. g) The octadecahydrotetracene dimer.

*Angew. Chem. Int. Ed.*  
**2008**, 47, 3430-3434



## $\pi$ - $\pi$ Interaction

 **!!! TOTO NENÍ PRAVDA !!!** 

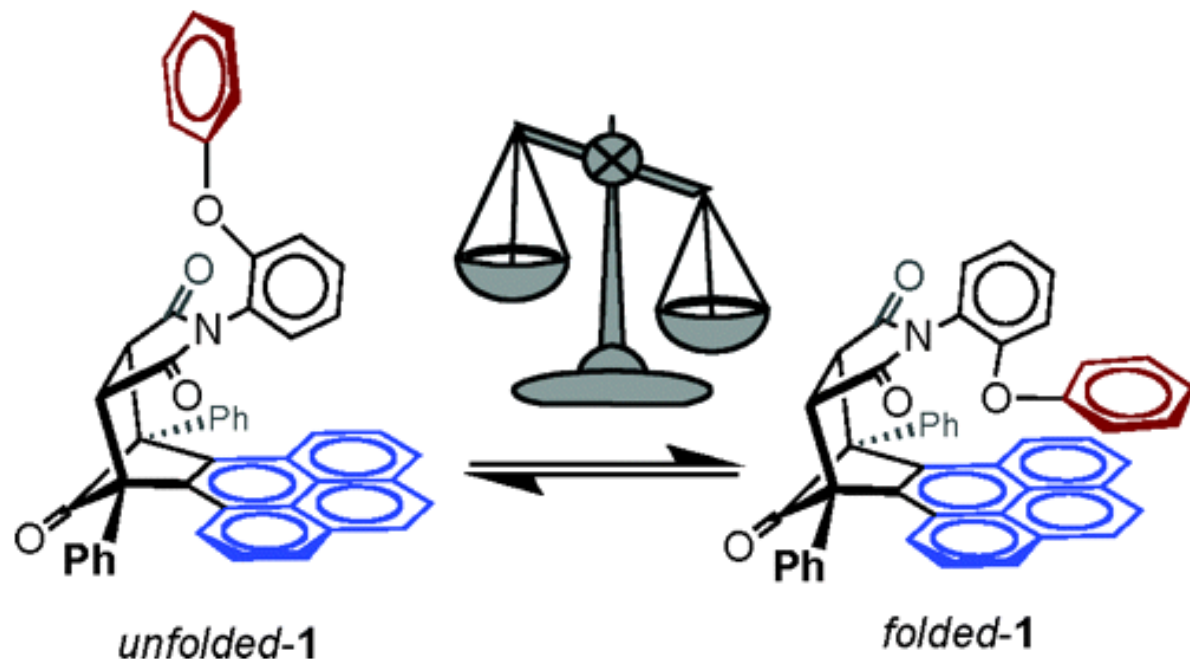
The  $\pi$ - $\pi$  interactions are caused by intermolecular overlapping of p-orbitals in  $\pi$  conjugated systems, so they become stronger as the number of  $\pi$  electron increases.

 **!!! TOTO JE PRAVDA !!!** 

The prototypical benzene dimer is nowadays considered a typical van der Waals complex in which the long-range dispersion interactions play the major role.

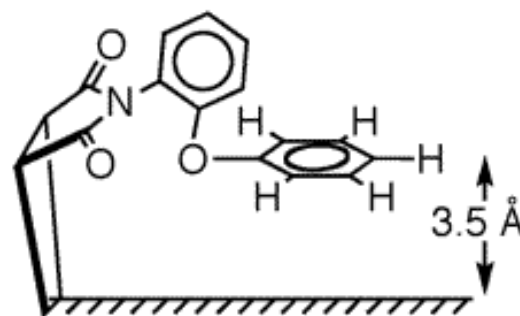
*Angew. Chem. Int. Ed.* **2008**, 47, 3430-3434

# Molecular balances of $\pi$ - $\pi$ interactions

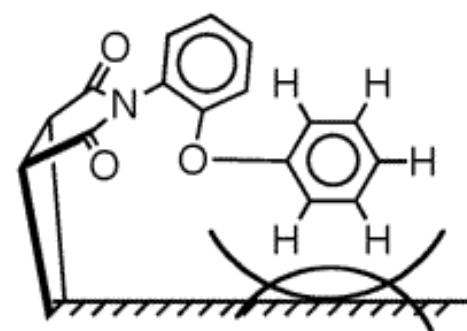


Face to Face

Edge to Face



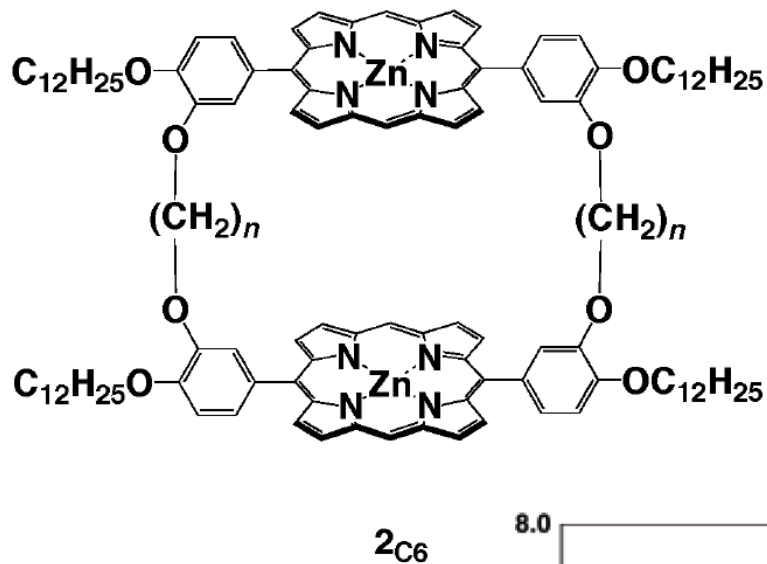
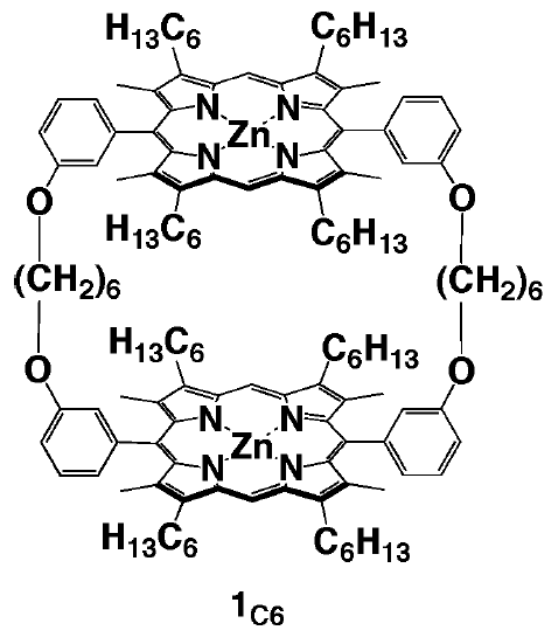
Arene Shelf



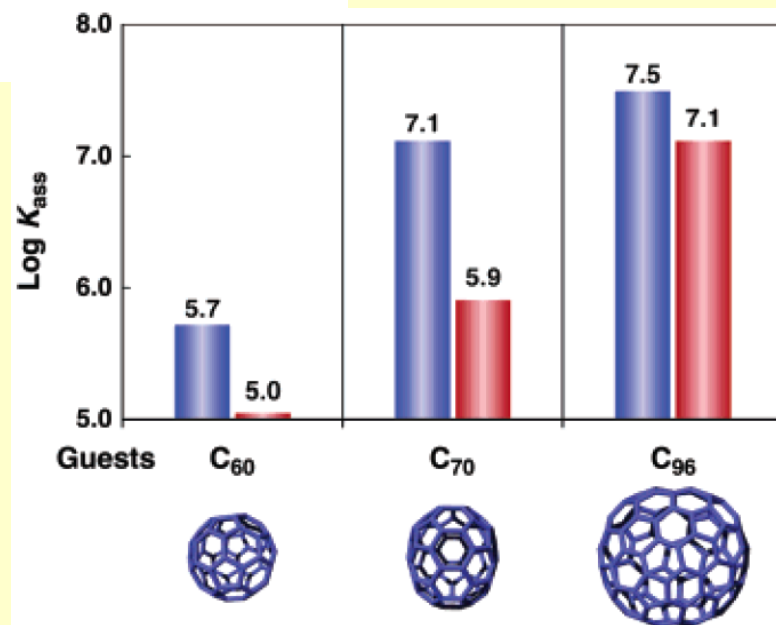
Arene Shelf

*Org. Lett.* **2008**  
10 (16), 3547–3550

# Arene interactions – Fullerene separation



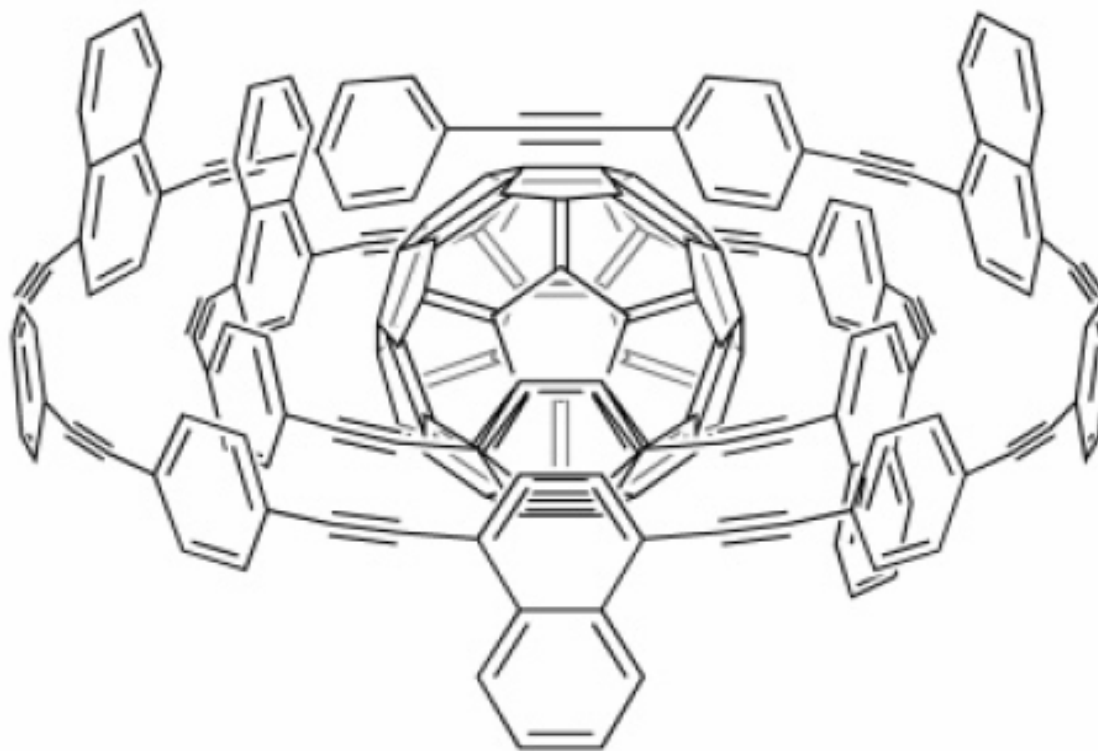
*J. Am. Chem. Soc.* **2004**  
126 (21), 6570–6571





# Arene interactions – Fullerene complexation

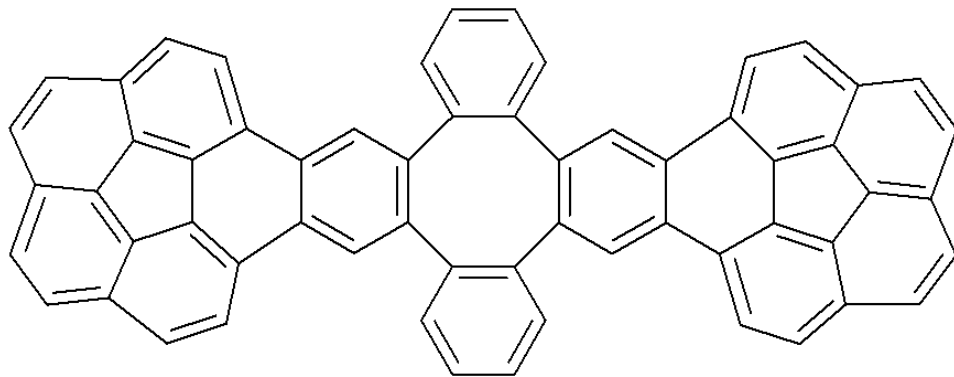
Ball-, Bowl-, and Belt-Shaped Conjugated Systems and Their Complexing Abilities: Exploration of the Concave-Convex  $\pi$ - $\pi$  Interaction



Onion-type complex

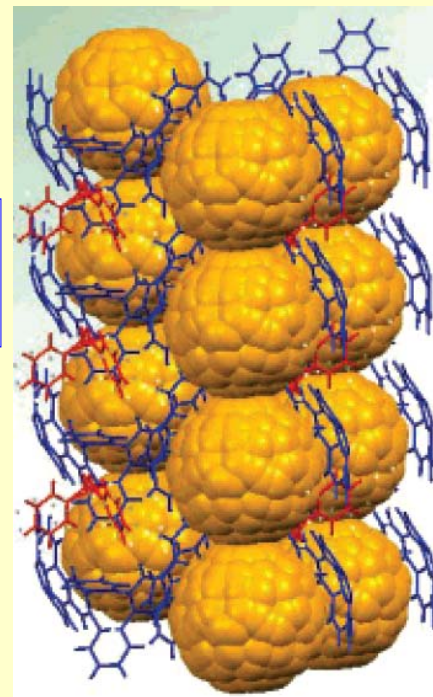
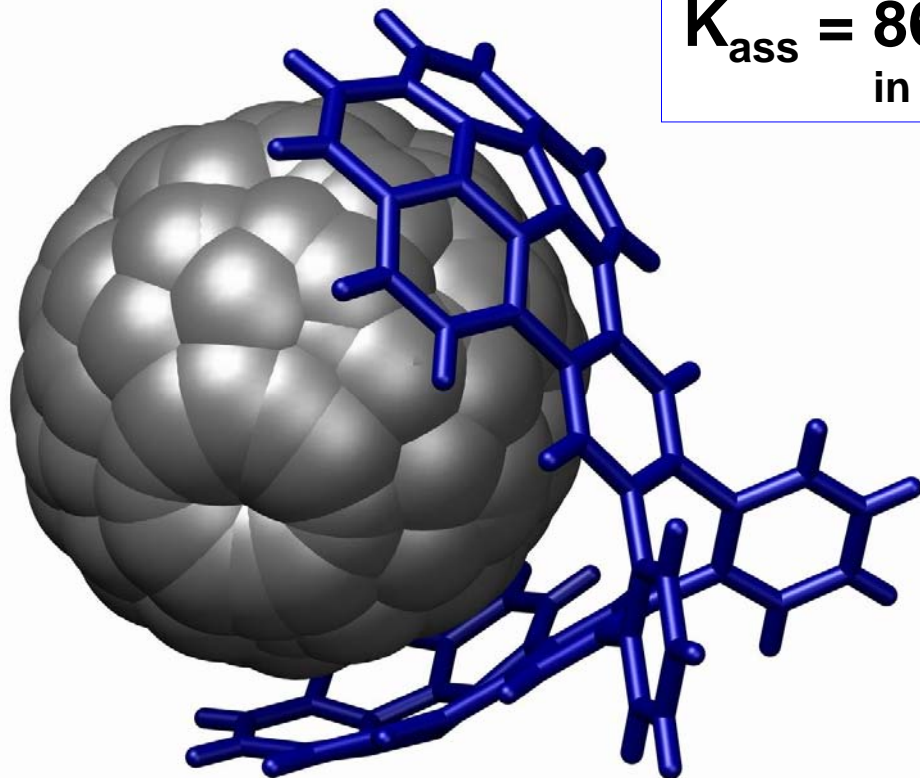
Chem. Rev. **2006**, *106*, 5250-5273

# Arene interactions – Fullerene C<sub>60</sub>



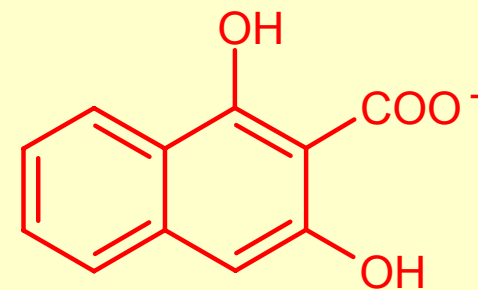
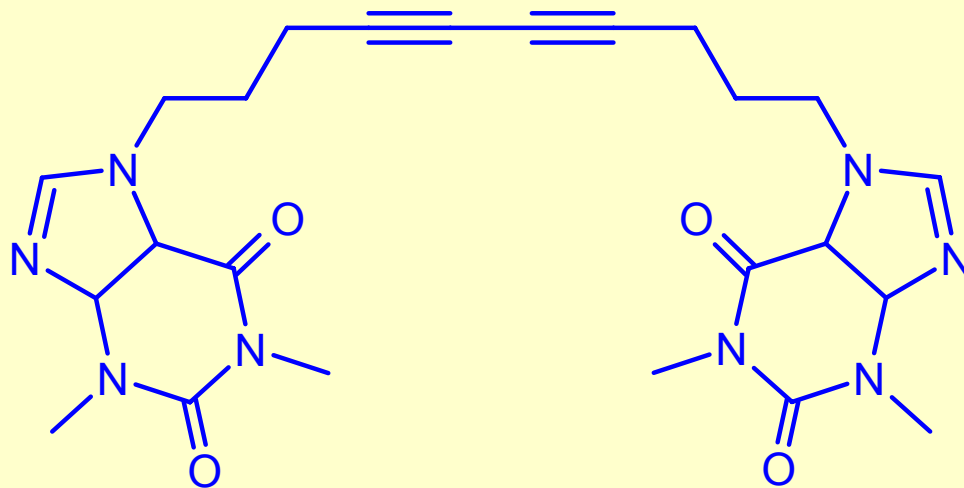
$$K_{\text{ass}} = 8600 \text{ M}^{-1}$$

in toluene



*J. Am. Chem. Soc.* **2007**  
129 (13), 3842–3843.

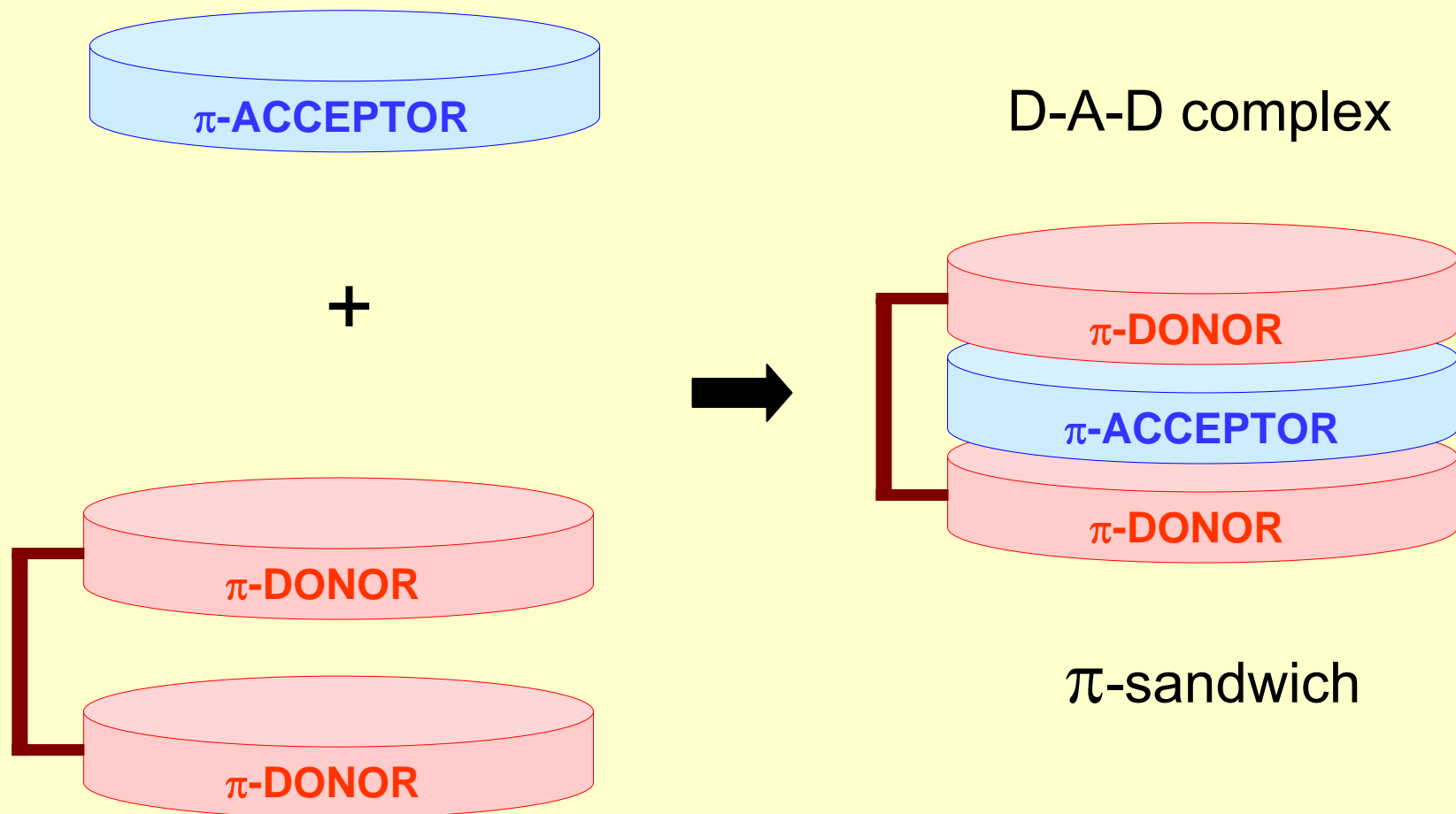
# Molecular Tweezers – The Original Idea



Molecular Tweezers: A Simple Model of Bifunctional Intercalation

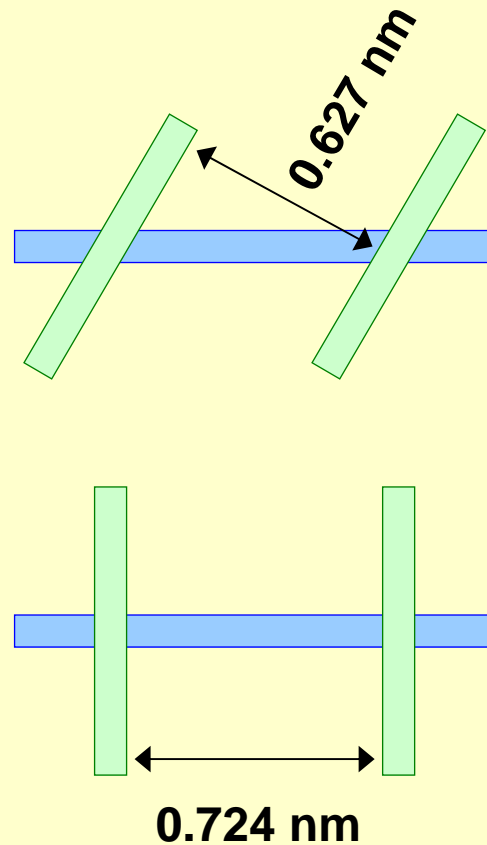
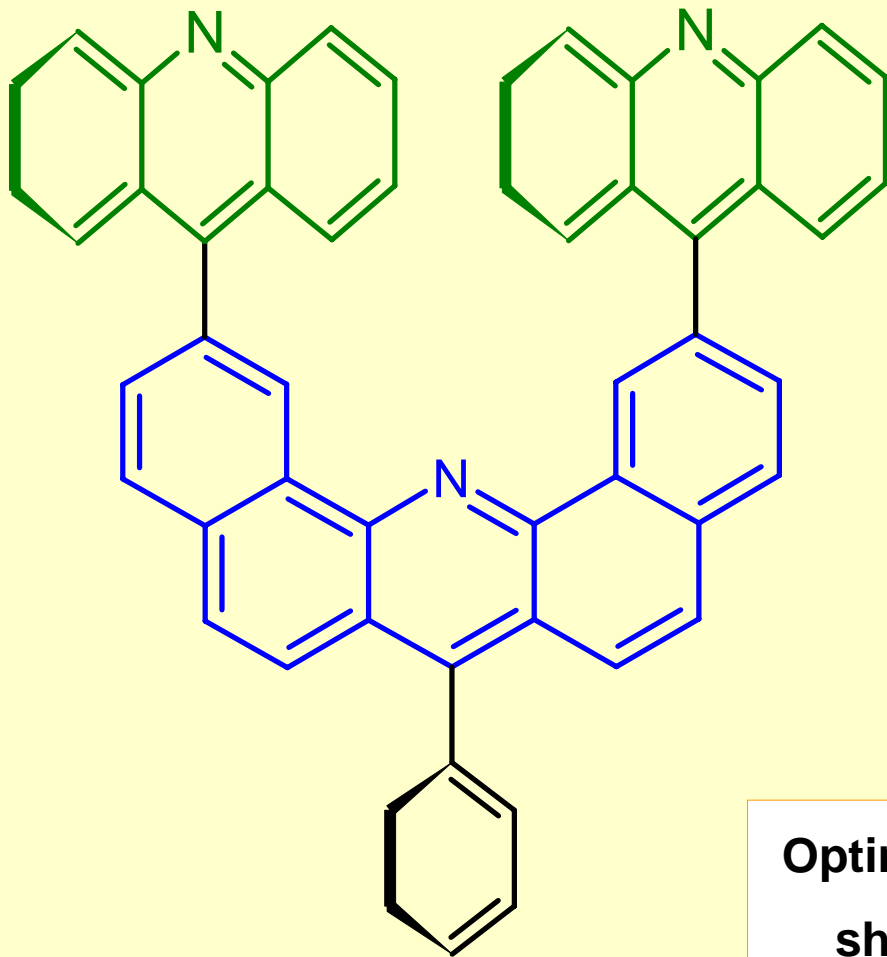
C.-W. Chen, H. W. Whitlock, *J. Am. Chem. Soc.* **1978**, *100*, 4921-4922

# Idea of Rigid Molecular Tweezers



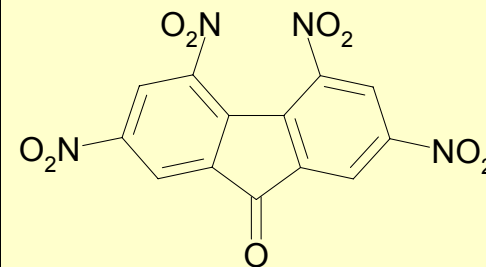
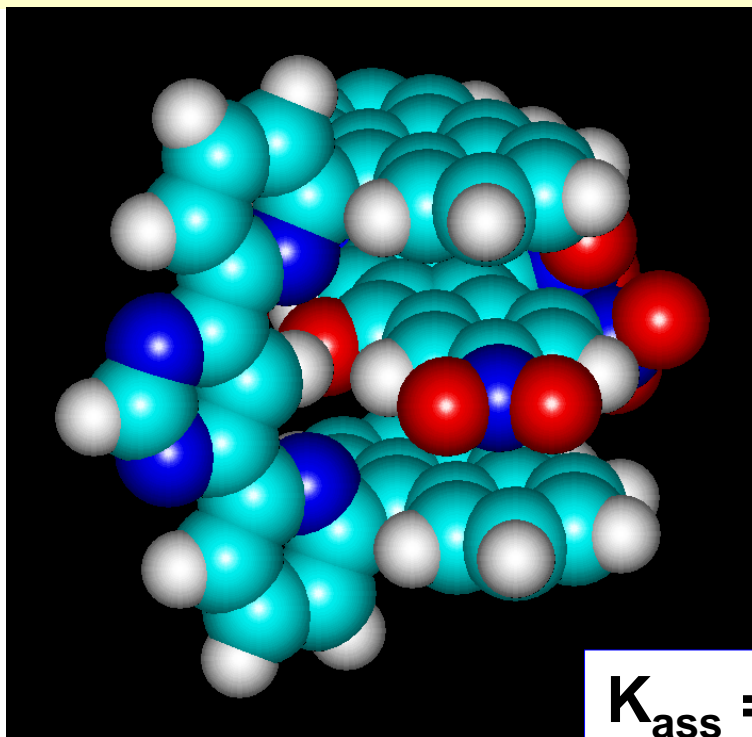
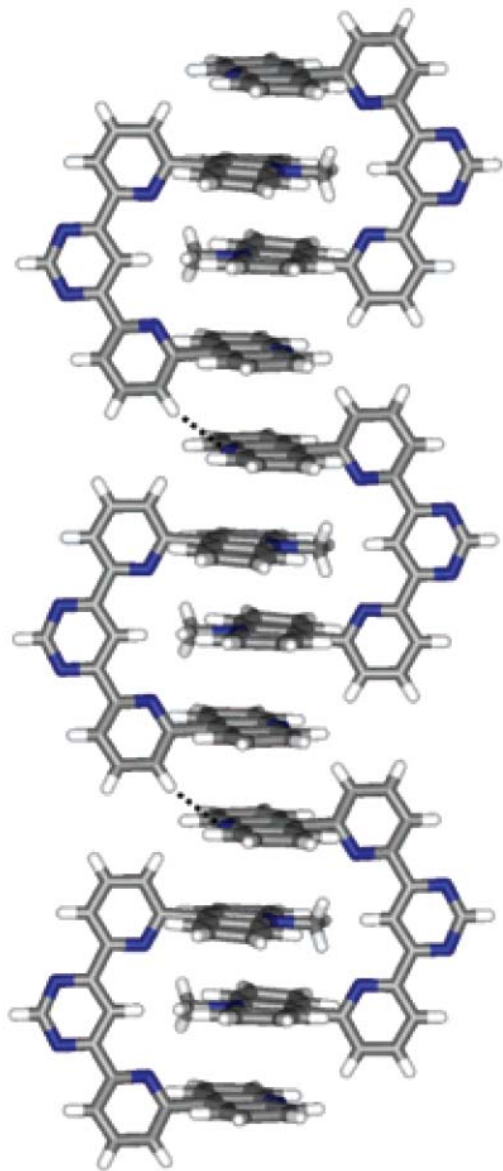
# Rigid Molecular Tweezers

S. C. Zimmerman, *Bioorg. Chem. Front.* **1991**, 2, 33-71  
S. C. Zimmerman, *Top. Curr. Chem.* **1993**, 165, 71-102



Optimum distance in „ideal“ tweezers  
should be from 0.64 to 0.70 nm

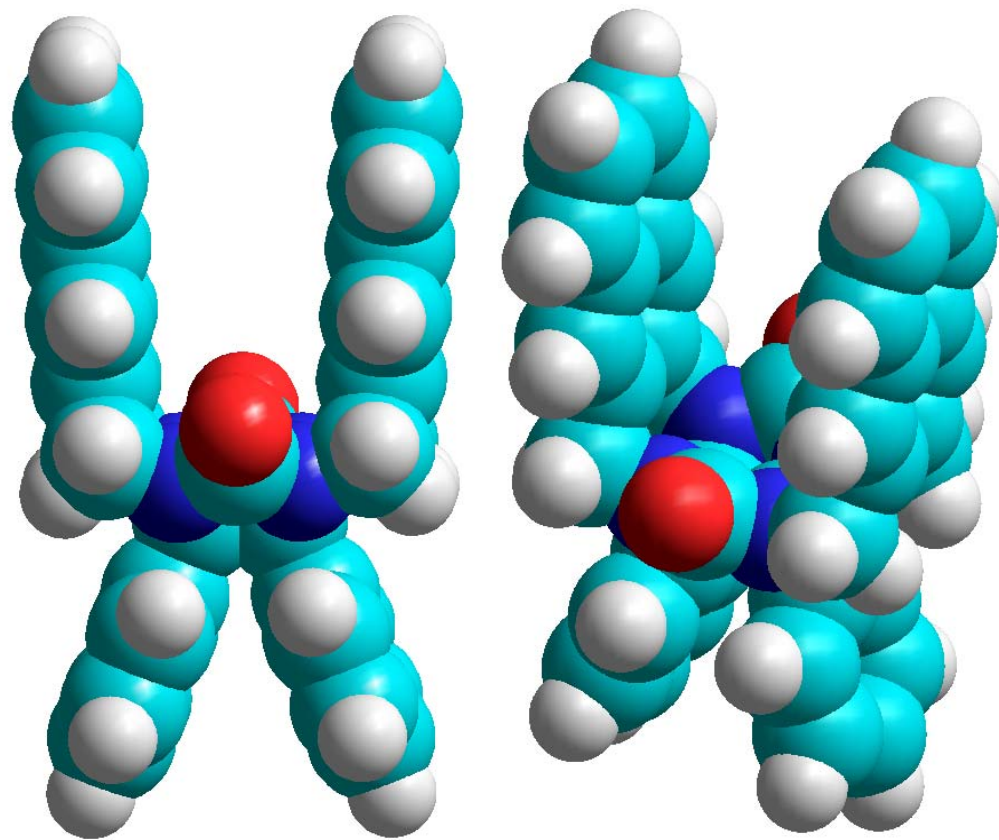
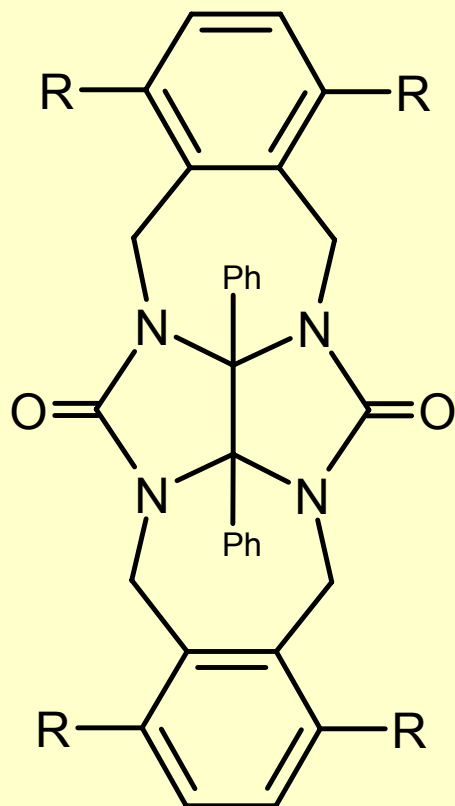
# Arene interactions – Tweezers



$K_{\text{ass}} = 2500 \text{ M}^{-1}$   
in chloroform

*J. Am. Chem. Soc.* **2004**, 126 (21), 6637–6647

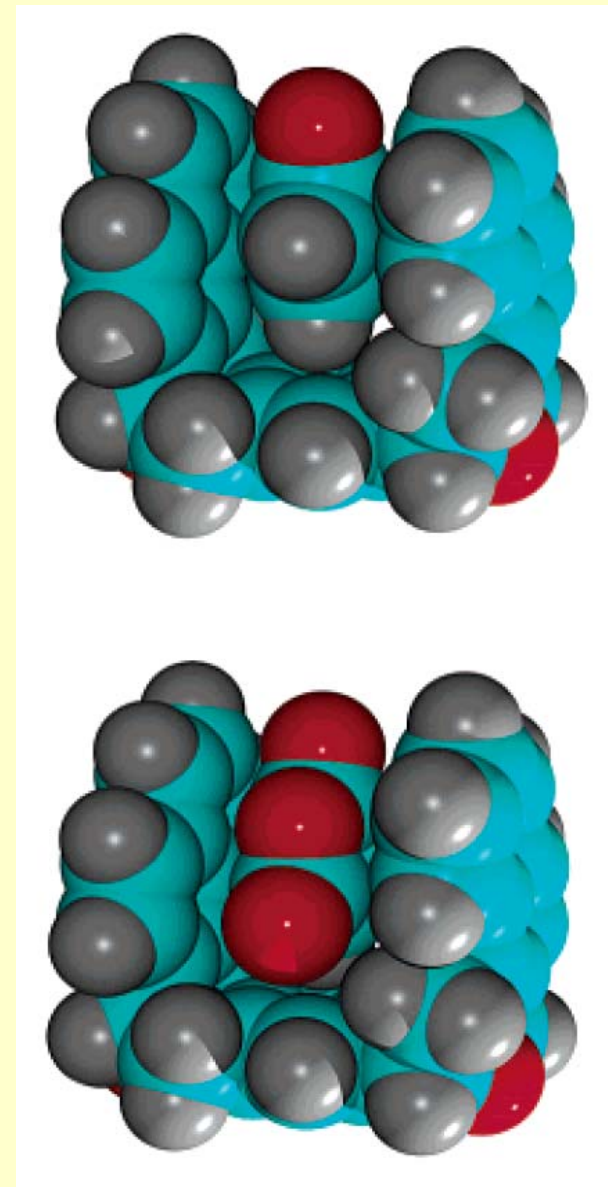
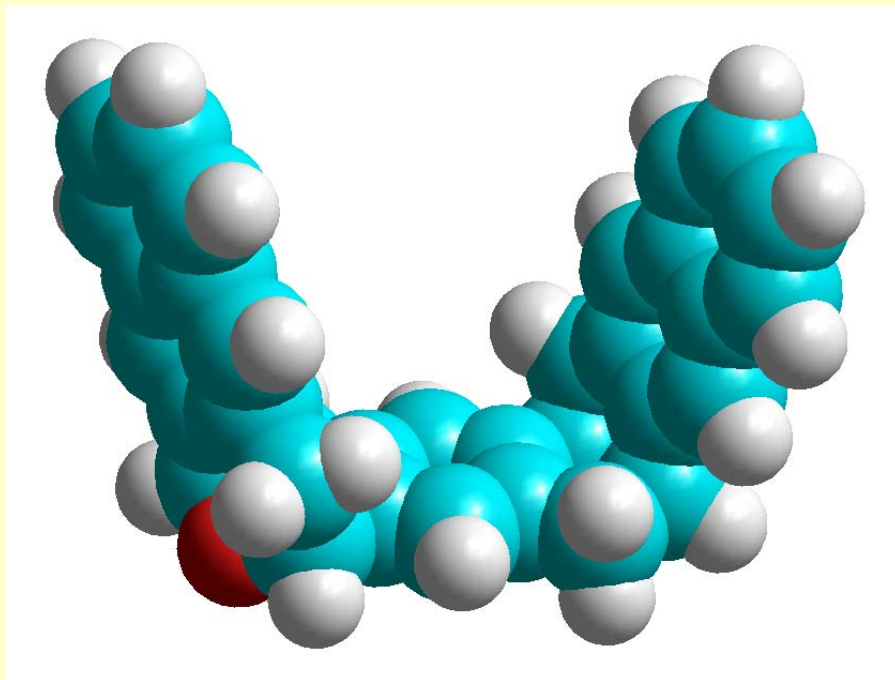
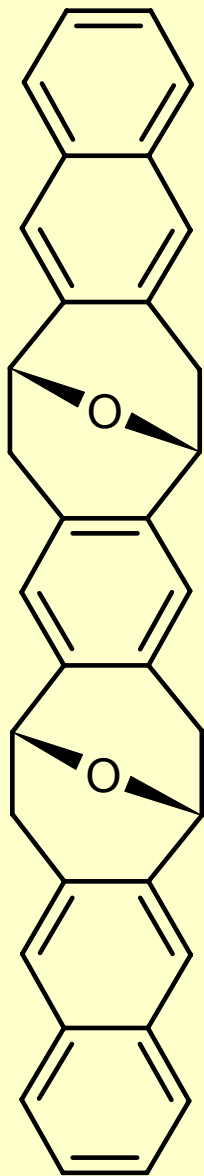
# Rigid Molecular Tweezers – Glycoluril



Smeets, J. W. H.; Sijbesma, R. P.; Niele, F. G. M.; Spek, A. L.; Smeets, W. J. J.; Nolte, R. J. M., *J. Am. Chem. Soc.* **1987**, *109*, 928-929

Rowan, A. E.; Elemans, J. A. A. W.; Nolte, R. J. M.  
*Acc. Chem. Res.* **1999**, *32*, 995-1006.

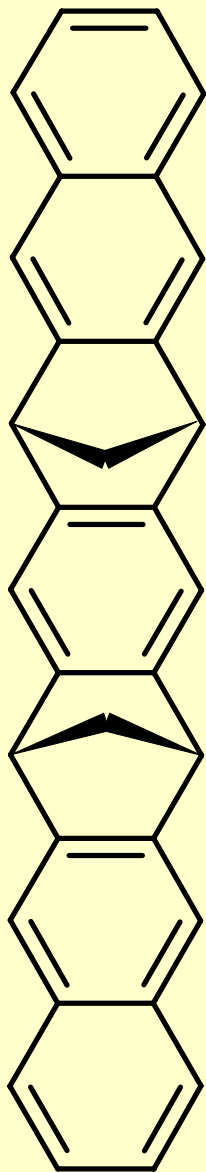
# Rigid Molecular Tweezers – Kagan's ether



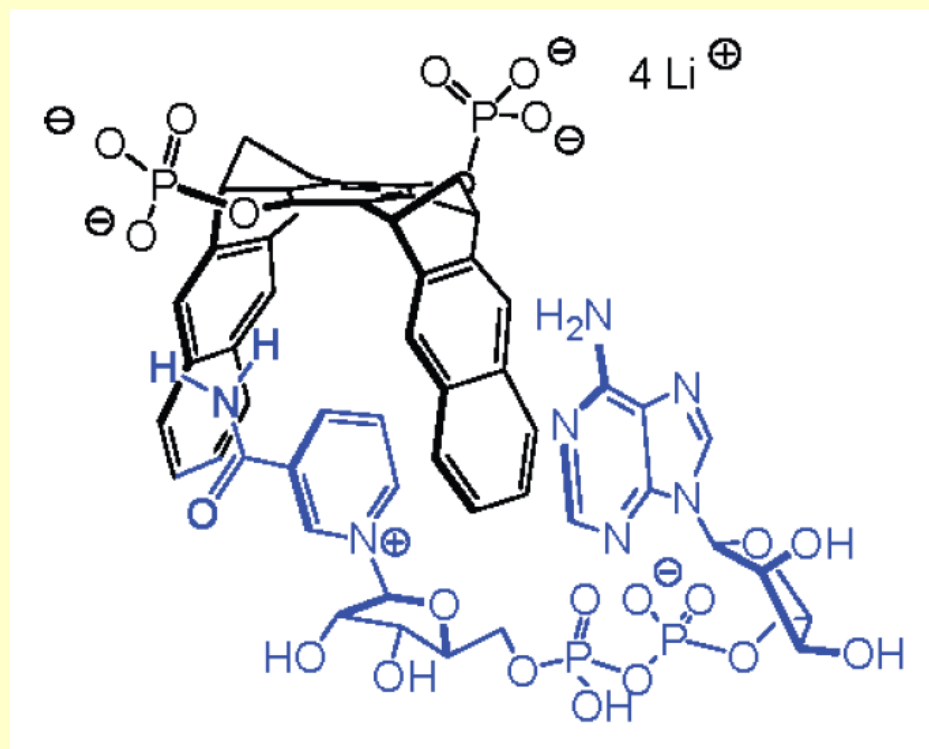
*Acc. Chem. Res.*  
**2004**, 37, 862-873



# Rigid Molecular Tweezers – methanoanthracenes

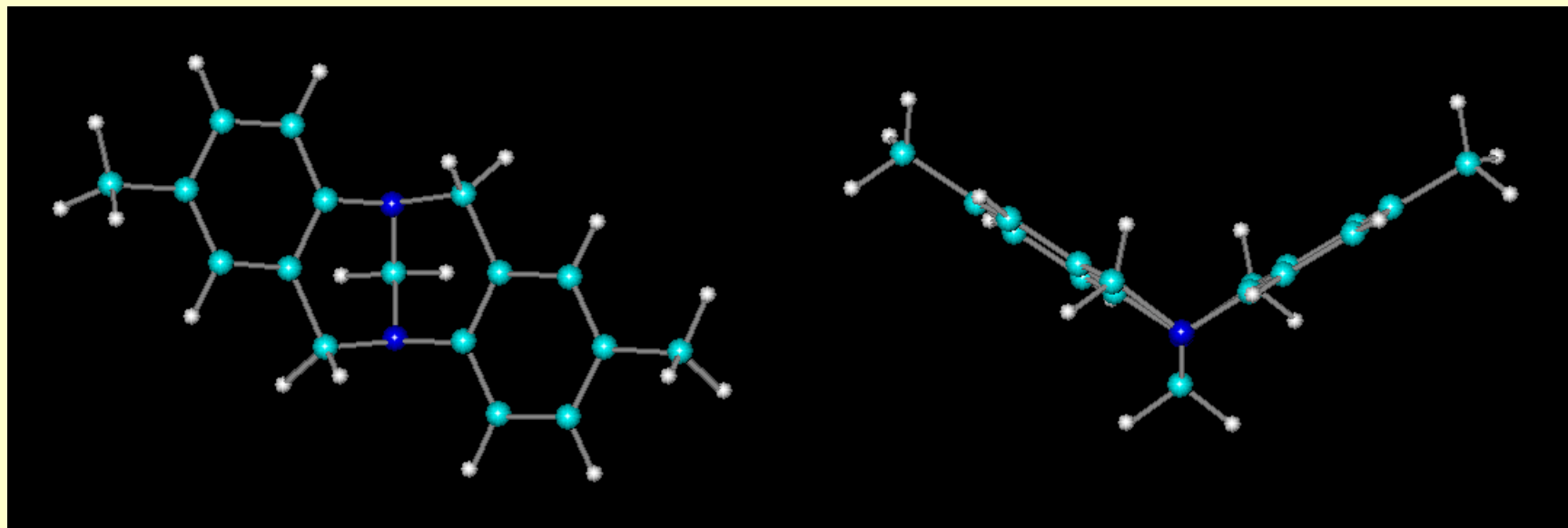


## Molecular Clips and Tweezers Introduce New Mechanisms of Enzyme Inhibition



*Acc. Chem. Res.* **2003**, 36, 919-932  
*J. Am. Chem. Soc.* **2006**, 128, 4831-4841  
*J. Am. Chem. Soc.* **2008**, 130, 9824-9828

# Rigid Molecular Tweezers – Tröger's base derivatives

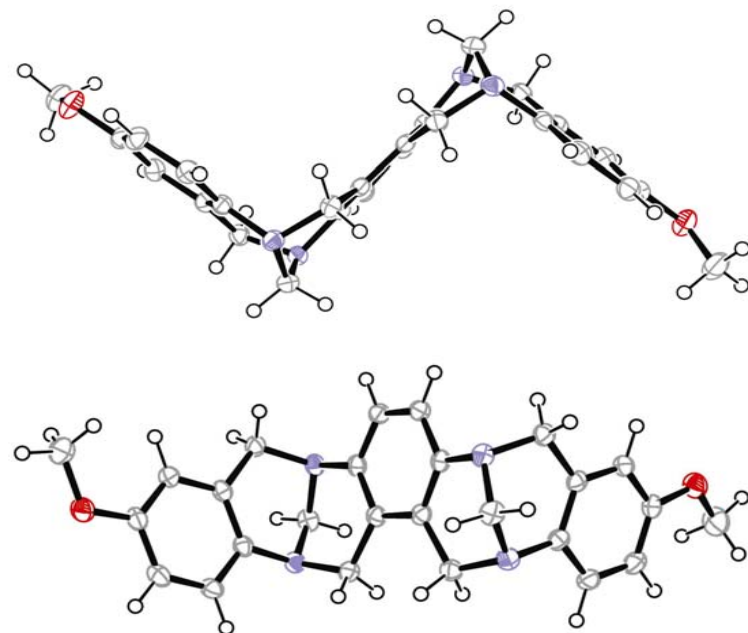
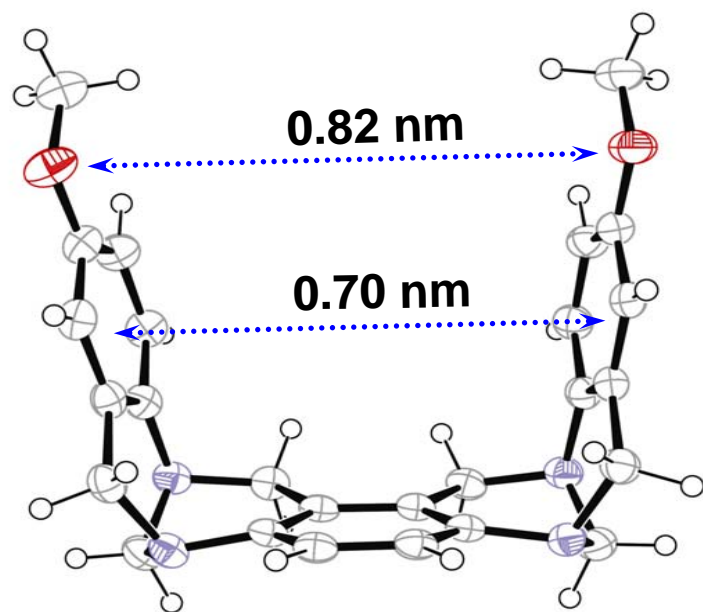
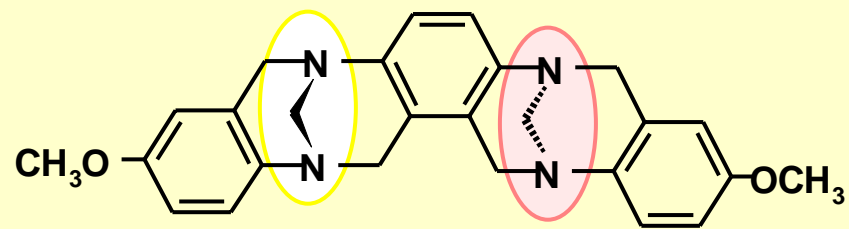
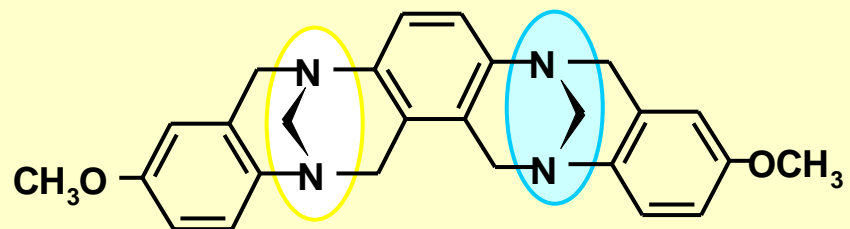


## Current Tröger's Base Chemistry

Dolenský, B.; Elguero, J.; Král, V.; Pardo, C.; Valík, M.

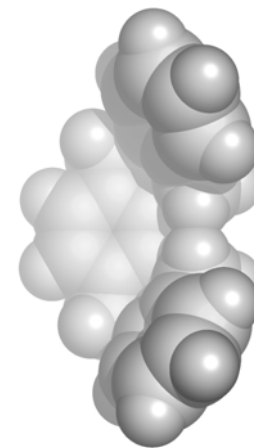
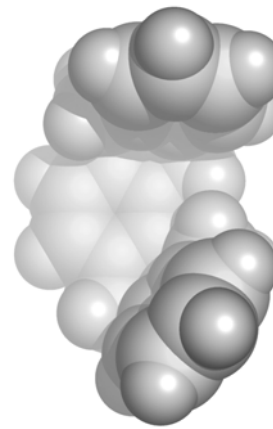
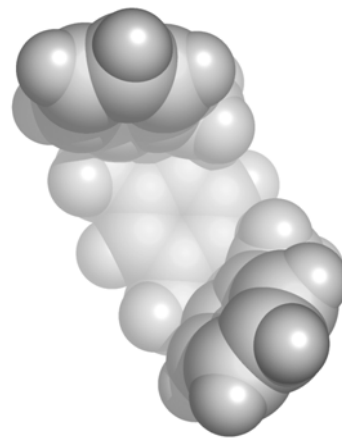
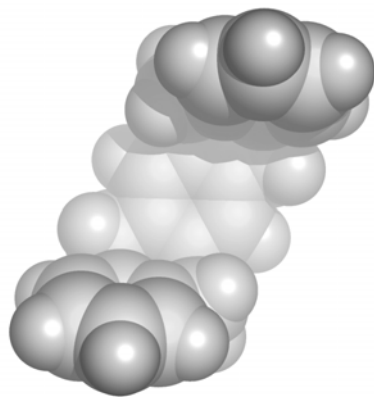
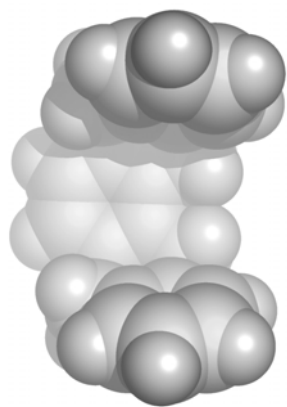
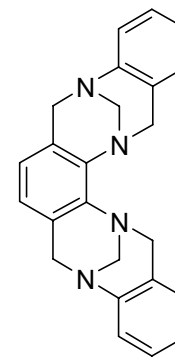
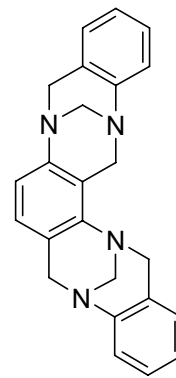
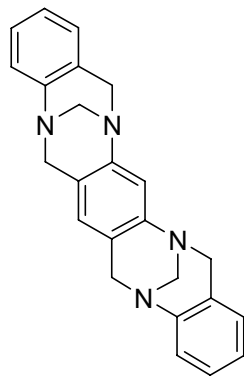
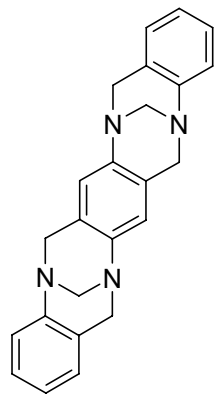
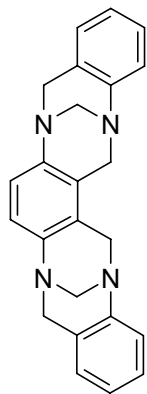
*Advances in Heterocyclic Chemistry* **2007**, 93, 1-56

# BisTB ... Diastereoisomers



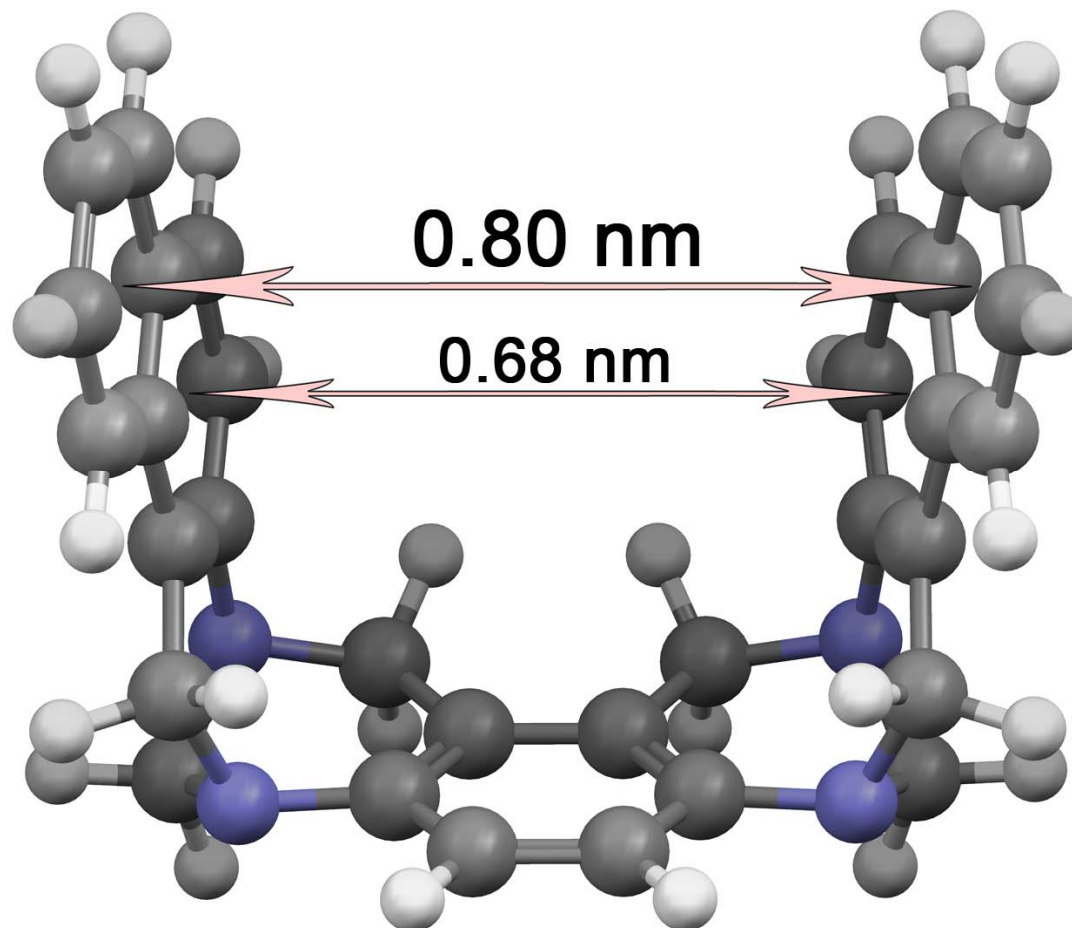
Dolenský, B.; Valík, M.; Matějka, P.; Herdtweck, E.; Král, V.  
*Coll. Czech Chem. Comm.* **2006**, *71*, 1278-1302

# BisTB ... Regioisomers



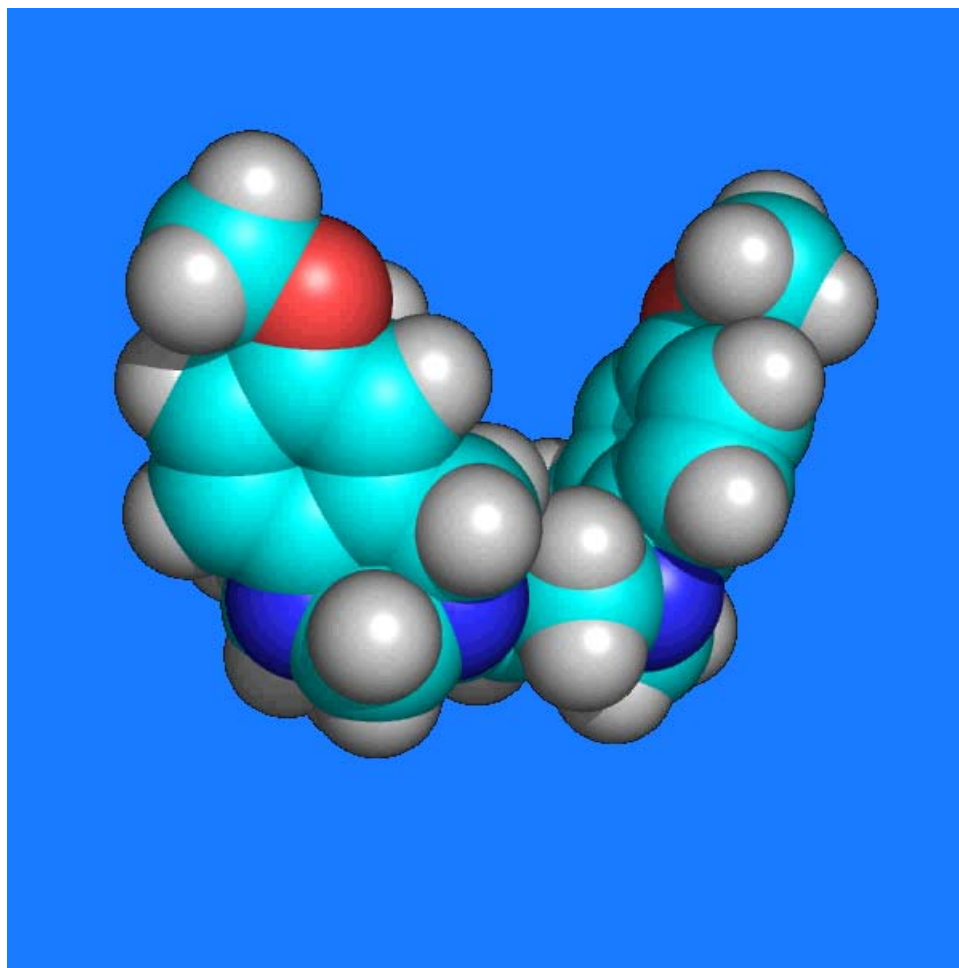
Havlík, M.; Král, V.; Dolenský, B. *Org. Lett.* **2006**, 8 (21), 4867-4870

# BisTB ... Molecular tweezers



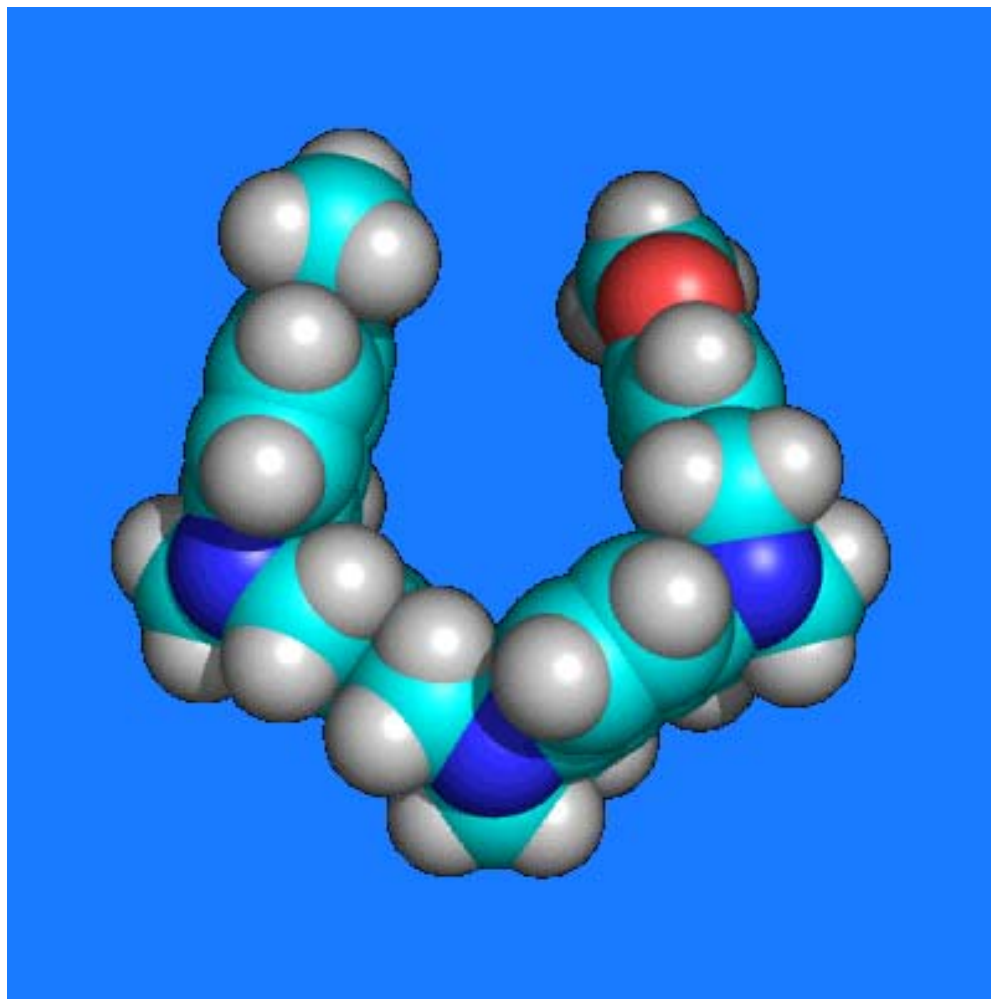
Havlík, M.; Král, V.; Kaplánek, R.; Dolenský, B. *Org. Lett.* **2008**, in press

# TrisTB ... Molecular cavitands



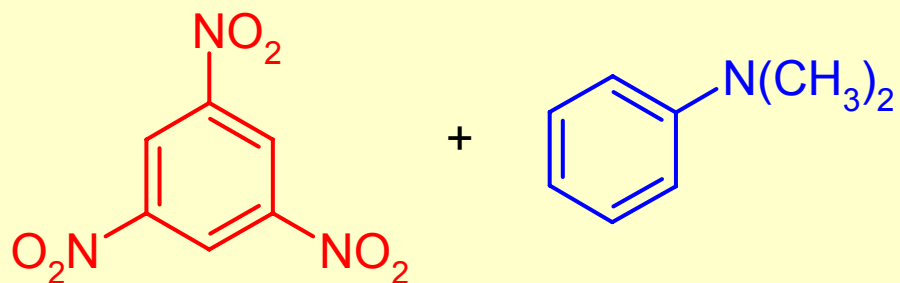
Valík, M.; Čejka, J.; Havlík, M.; Král, V.; Dolenský, B.  
*Chemical Communications* **2007**, 37, 3835-3837

## TrisTB ... Molecular clips



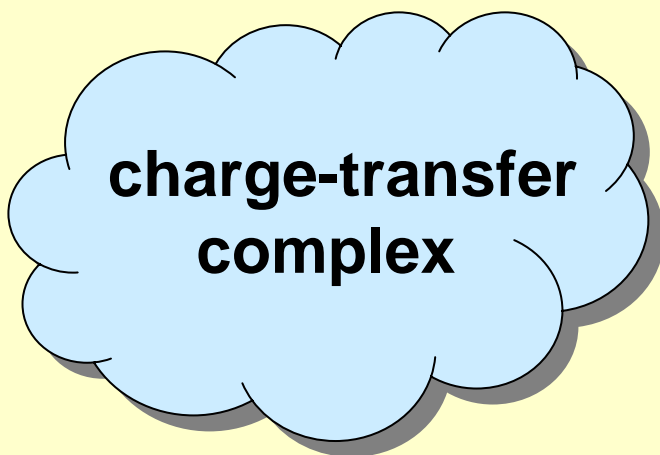
Dolenský, B.; Valík, M.; Sýkora, D.; Král, V. *Organic Letters* **2005**, 7(1), 67-70

# $\pi$ - $\pi$ ... CT ... Solvent influence



$\pi$ -acceptor  
 $\pi$ -acid

$\pi$ -donor  
 $\pi$ -base



$$K_{\text{ass}} = 9,6 \text{ M}^{-1}$$

v cyklohexanu

$$K_{\text{ass}} = 8,2 \text{ M}^{-1}$$

v hexanu

$$K_{\text{ass}} = 7,2 \text{ M}^{-1}$$

v dekalinu

$$K_{\text{ass}} = 3,4 \text{ M}^{-1}$$

v  $\text{CCl}_4$

$$K_{\text{ass}} = 1,3 \text{ M}^{-1}$$

v  $\text{CHCl}_3$

$$K_{\text{ass}} = 0,2 \text{ M}^{-1}$$

v  $\text{CHCl}_2\text{CHCl}_2$

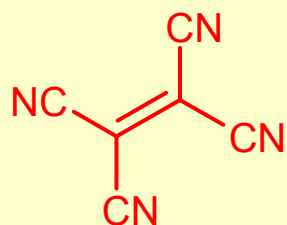
$$K_{\text{ass}} = 0,15 \text{ M}^{-1}$$

v dioxanu

Volné electronové páry jsou konkurenční donor nebo-li  $\pi$ -báze

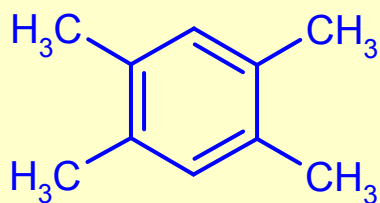


# $\pi$ - $\pi$ ... CT ... Solvent influence

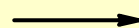


$\pi$ -acceptor  
 $\pi$ -acid

+



$\pi$ -donor  
 $\pi$ -base



**charge-transfer  
complex**

$$K_{\text{aas}} \text{ (v plynné fázi)} = 11800 \pm 5900$$
$$K_{\text{ass}} \text{ (v CH}_2\text{Cl}_2) = 54,2$$

$K_{\text{ass}} = 8600 \text{ M}^{-1}$   
in toluene

$K_{\text{ass}} = 8600 \text{ M}^{-1}$   
in toluene

*J. Am. Chem. Soc.* **1968**, 90 (5), 1097-1105

*J. Am. Chem. Soc.* **1958**, 80 (11), 2778-2782

# Arene interactions – Fullerene separation

Separace C60 – C70

*Chem. Lett.* **1994**, 699-702  
*Nature* **1994**, 368, 229-231