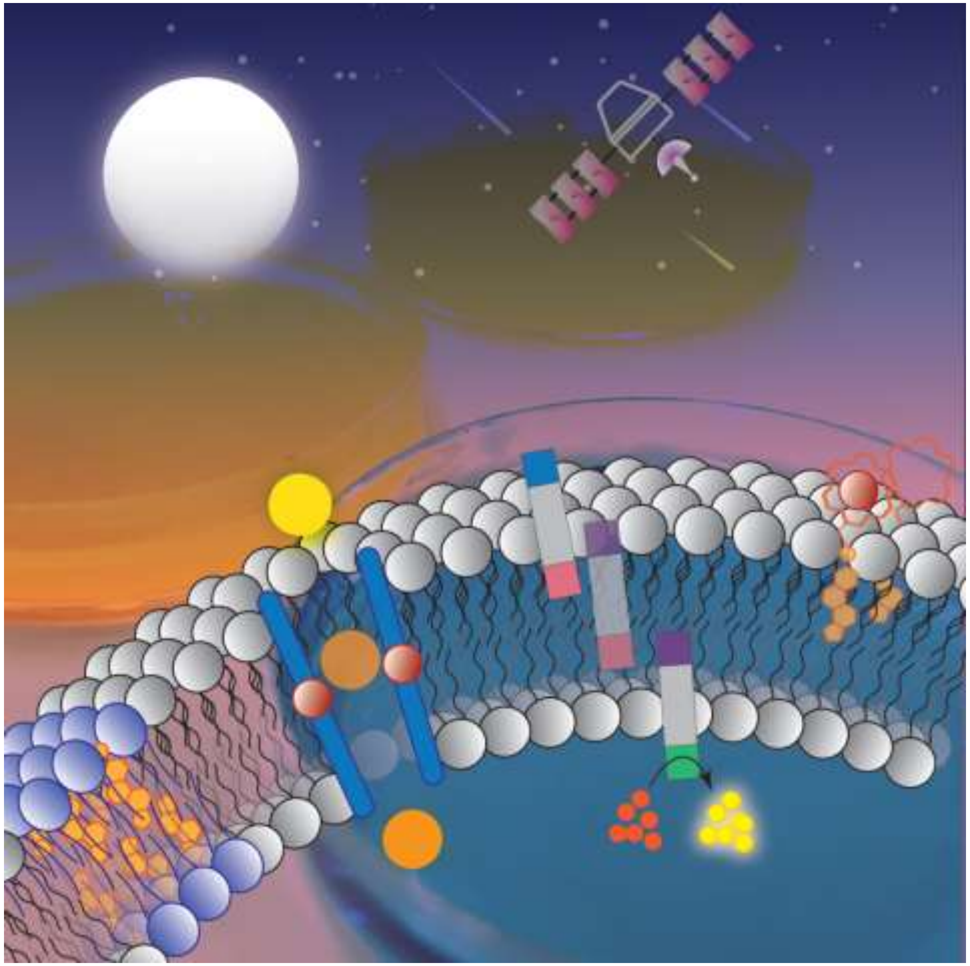
Biosupramolekulska hemija

BioS



Biosupramolekulska hemia

Dr Veselin Maslak, vanredni profesor

Cilj ovog predmeta je da se studenti upoznaju sa interakcijama između molekula u supermolekulima koje su zastupljene u biološkim sistemima. Zatim, proučavanje molekulskog prepoznavanja koje predstavlja osnovu domaćin gost hemije. U okviru ovog kursa izučavaće se enkapsulacija kao motiv u procesima supramolekulske katalize i biokatalize, kao i molekulsko samouređivanje različitih biomolekula (agregacija).

Fond časova: tri časa predavanja (3+0+0)

predavanja 10; seminarski rad 20; usmeni ispit 70;

ESPB: 5

Биосупрамолекулска хемија (242В2)
школска 2020/21. година

Презиме и име	Индекс	Предиспитне обавезе				Полагање испита	Кон. оцена
		П (10)	С (20)	Ост.	Збир		
ОАС: Биохемија (2014)							
1. Банђур (Ненад) Дуња	БХ11/2016	0	0		0		
ОАС: Биохемија (2020)							
2. Алексић (Сретен) Љубодраг	БХ26/2018	0	0		0		
3. Бићанин (Срећко) Маша	БХ04/2018	0	0		0		
4. Врачар (Предраг) Алекса	БХ39/2018	0	0		0		
5. Друловић (Миланко) Ненад	БХ29/2018	0	0		0		
6. Костић (Бранка) Анђела	БХ30/2018	0	0		0		
7. Пановић (Милојко) Лазар	БХ10/2016	0	0		0		
8. Петронијевић (Саша) Наталија	БХ06/2018	0	0		0		
9. Хаџи-Ристић (Никола) Тања	БХ09/2018	0	0		0		
10. Чолаковић (Владан) Маша	БХ01/2018	0	0		0		
11. Џалета (Марко) Александар	БХ48/2018	0	0		0		

Укупан број студената: **11**, положило: **0**, пролазност: **0.00 %**

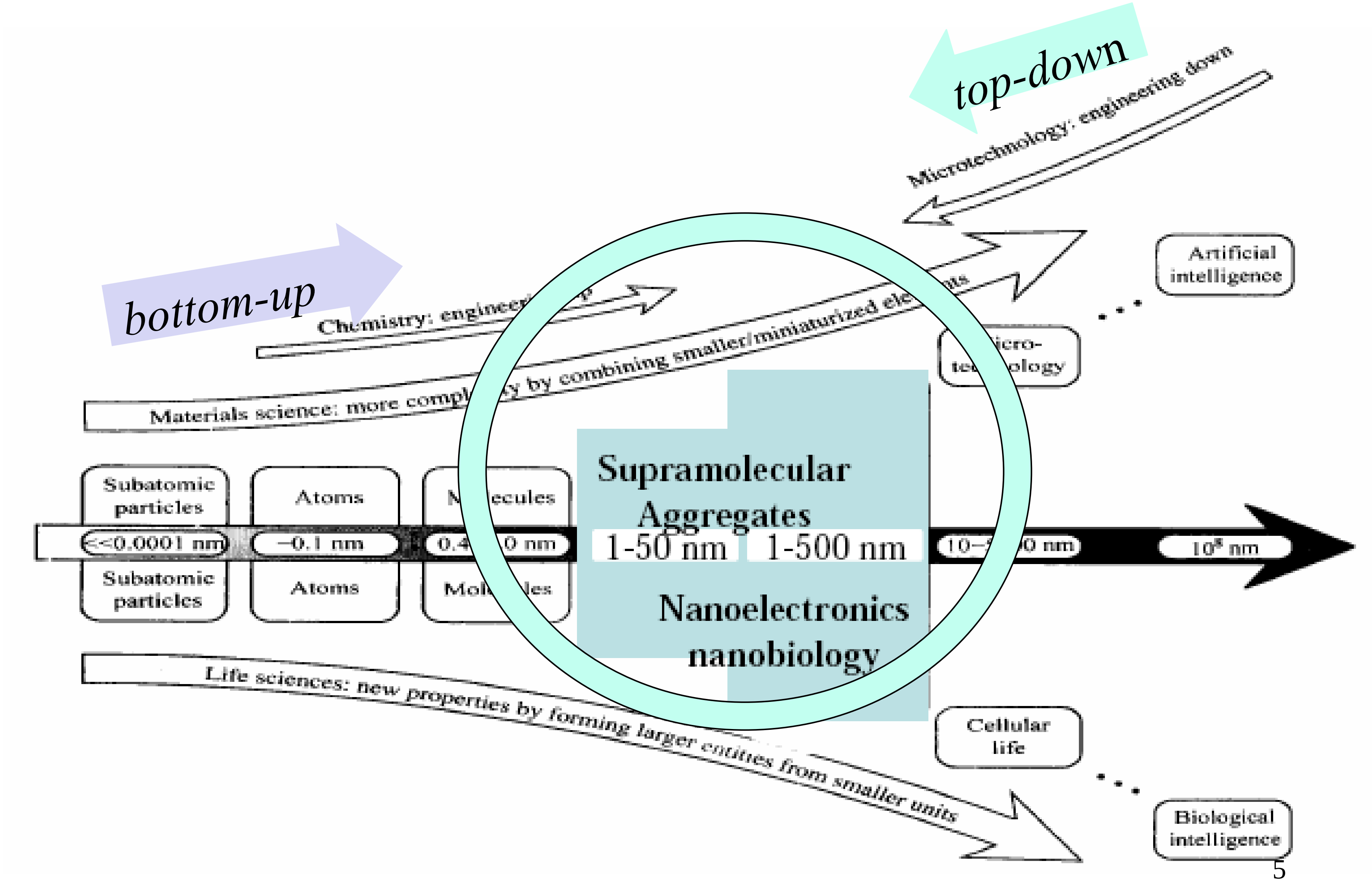
PLAN I PROGRAM

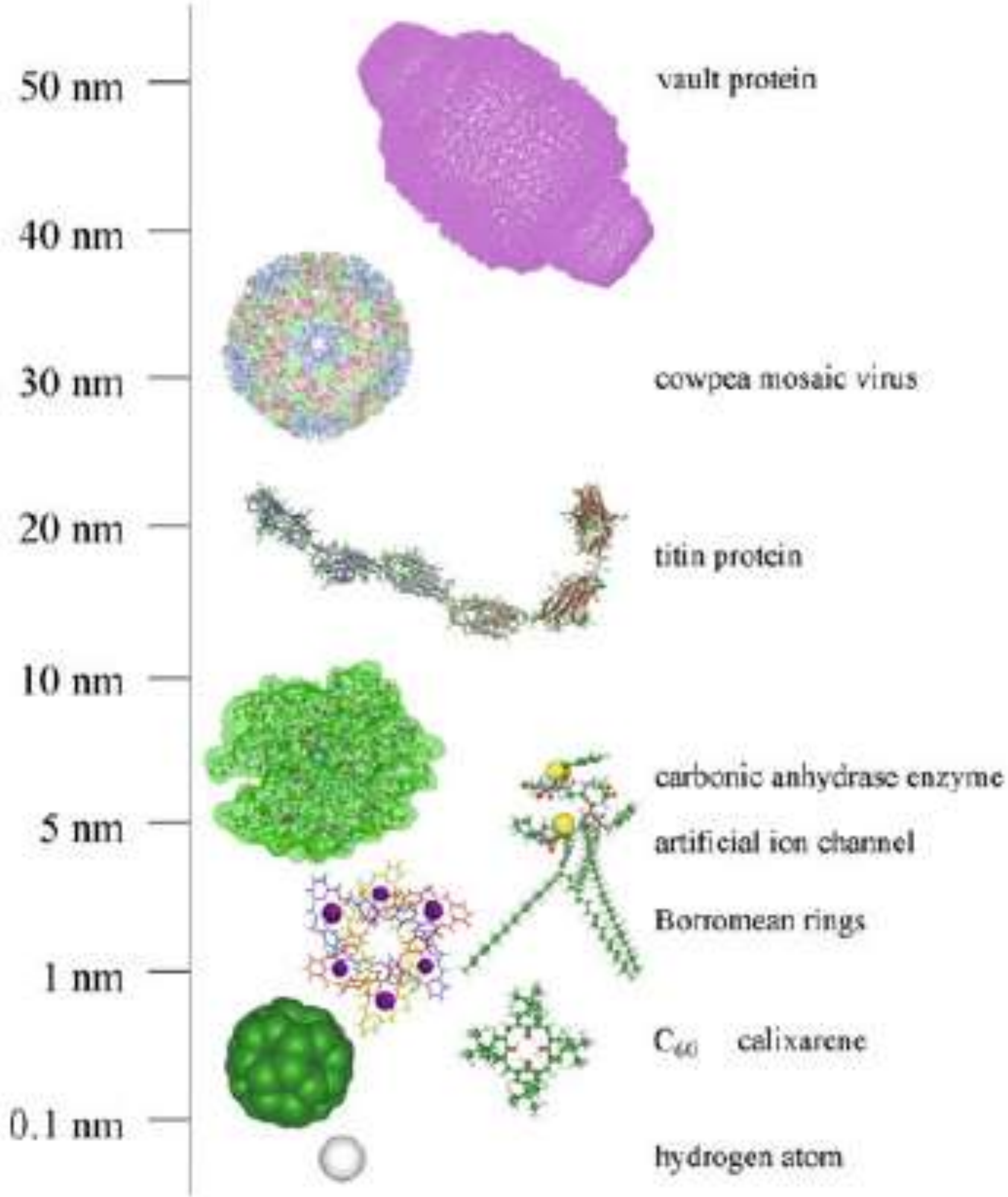
- Osnovne supramolekulske interakcije u biološkim sistemima.
- Biološki sistemi kao inspiracija u supramolekulskoj hemiji.
- Transport katjona, anjona i neutralnih molekula u biološkim sistemima.
- Supramolekulska kataliza.
- Ciklodekstrini kao modeli za delovanje enzima.
- Samouređivanje u biološkim sistemima (membrane i vezikule).Uvod u supramolekulsku hemiju-osnovni pojmovi

Literatura:

1. J. W. Steed, D. R. Turner, K. J. Wallace, Core concepts in supramolecular chemistry and nanochemistry
2. Peter J. Cragg: Supramolecular chemistry. From biological inspiration to biomedical applications. Springer 2010,

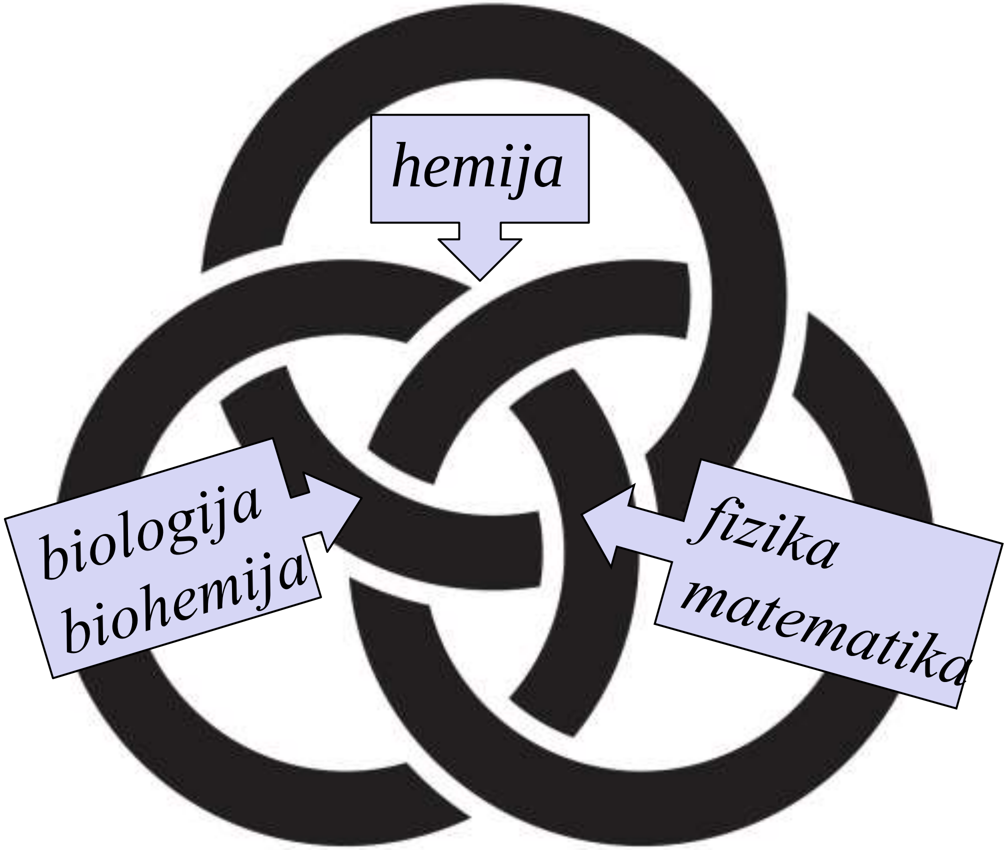
Supramolekuli su vrste nanometarskih dimenzija




50 nm
40 nm
30 nm
20 nm
10 nm
5 nm
1 nm
0.1 nm
vault protein
cowpea mosaic virus
titin protein
carbonic anhydrase enzyme
artificial ion channel
Borromean rings
C60 calixarene
hydrogen atom

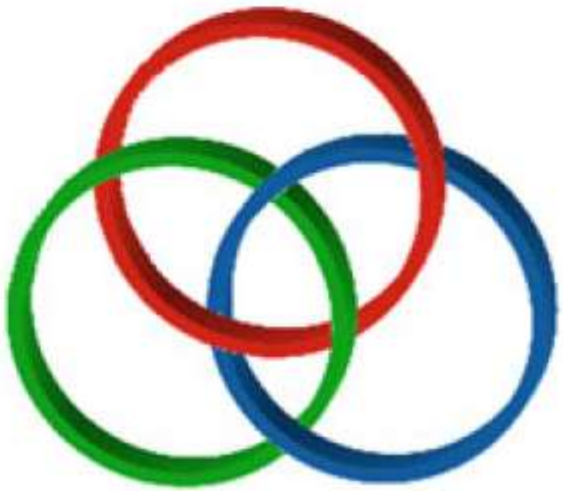
Supramolekulska hemija-hemija više od molekula

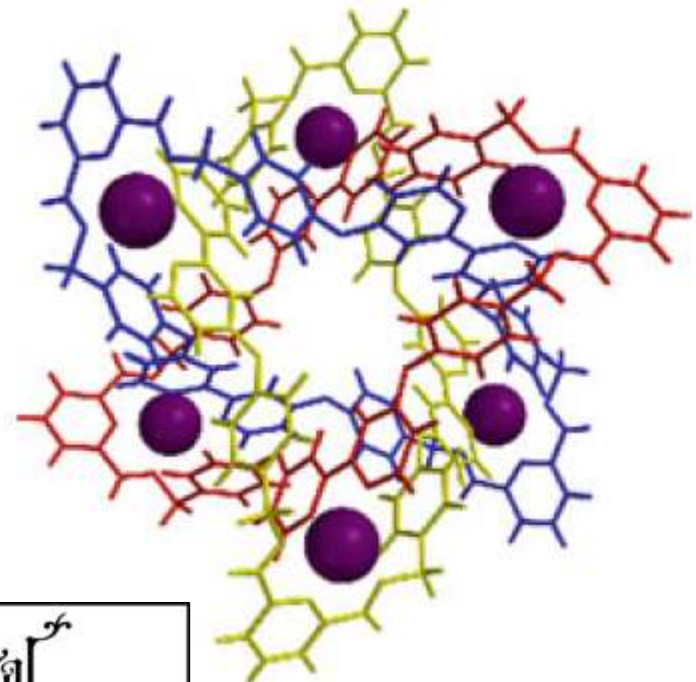
Interdisciplinarna naučna disciplina



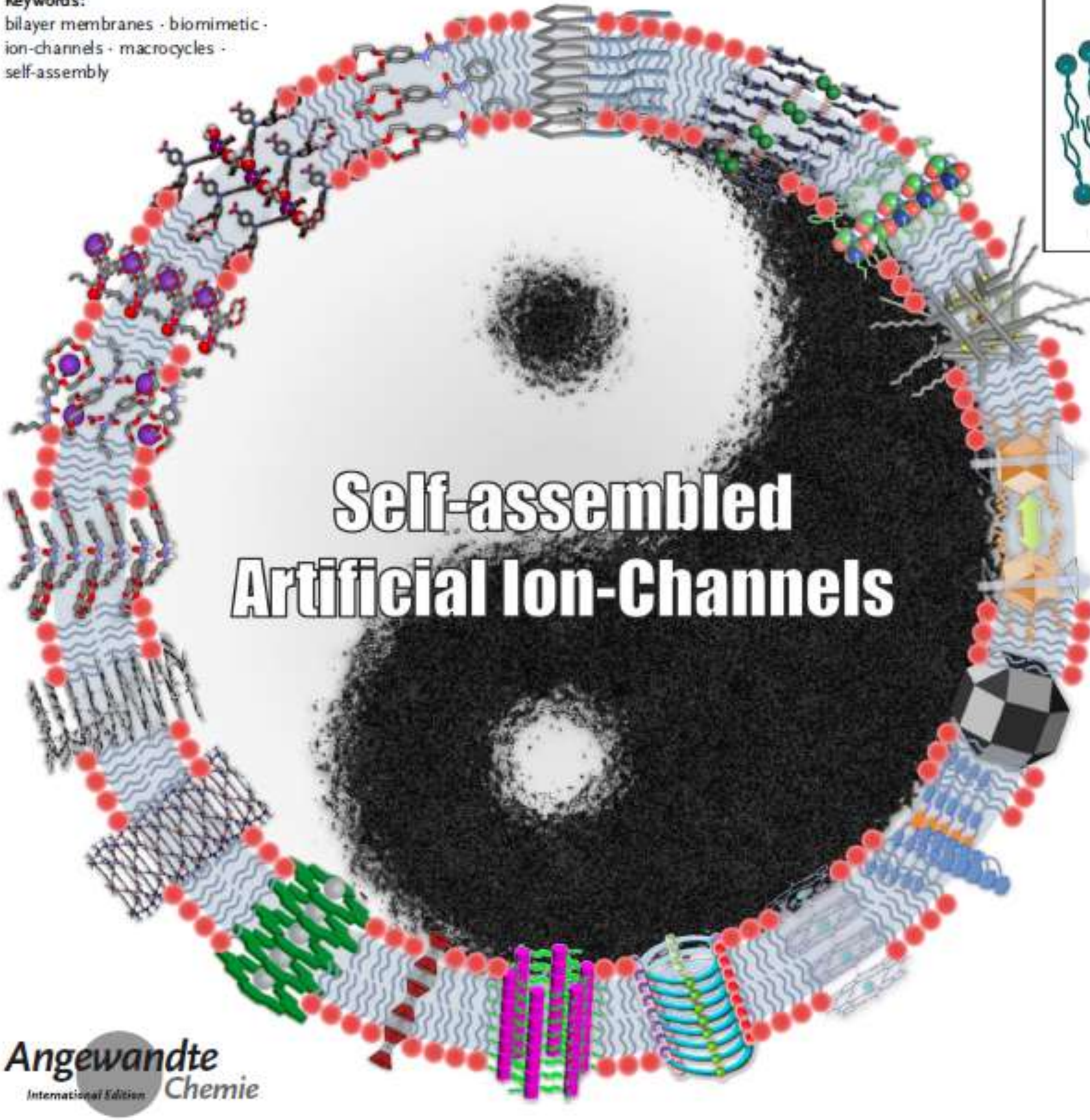
20-30% radova u vodećim časopisima kao *J. Am. Chem. Soc., Angew. Chem., Chem. Commun., Chem. Eur. J.*

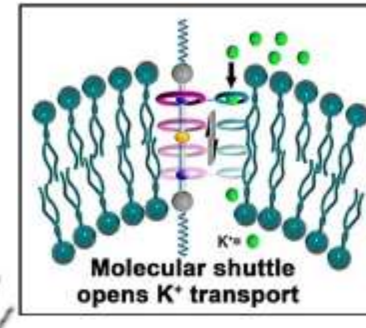
Boromejski prstenovi





Keywords:
bilayer membranes · biomimetic · ion-channels · macrocycles · self-assembly



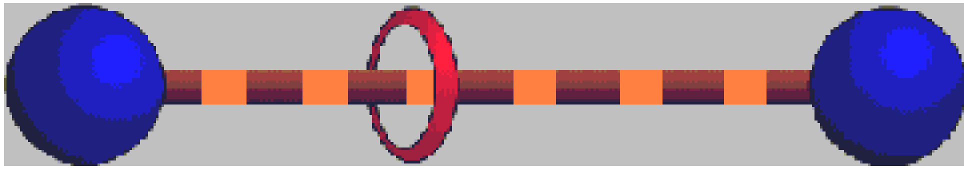


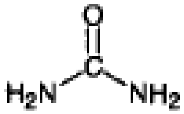
Angewandte
International Edition Chemie

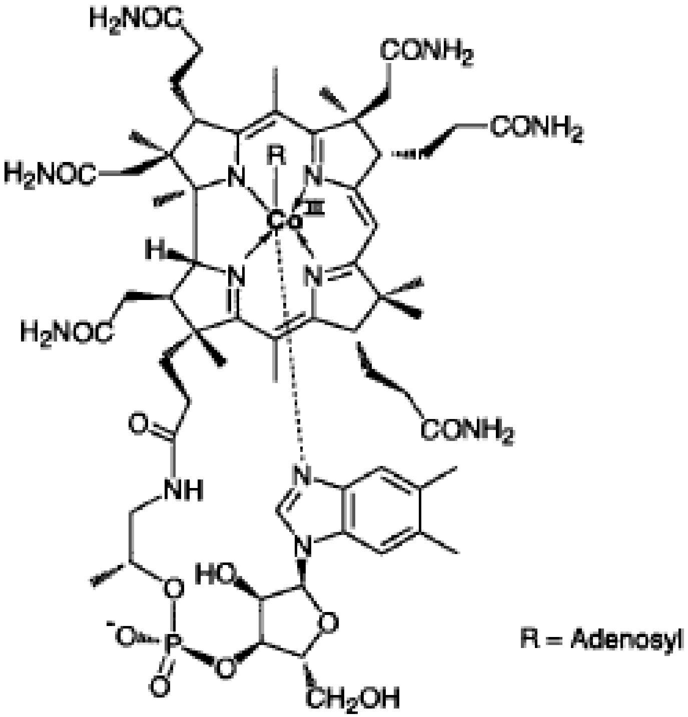
❖1829. Wohler sinteza uree

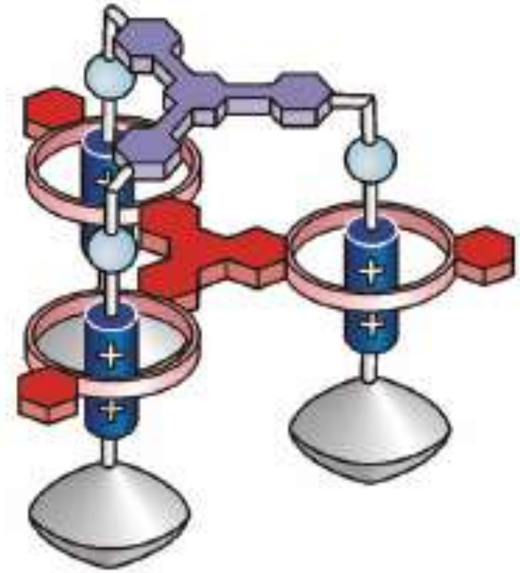
❖Sredinom prošlog veka sinteze kompleksnih molekula na kojima je radio veliki broj istraživača- primer je Woodward i Eschenmoserova sinteza vitamina B12 (1972)

❖Supramolekulska hemija!------(1967)





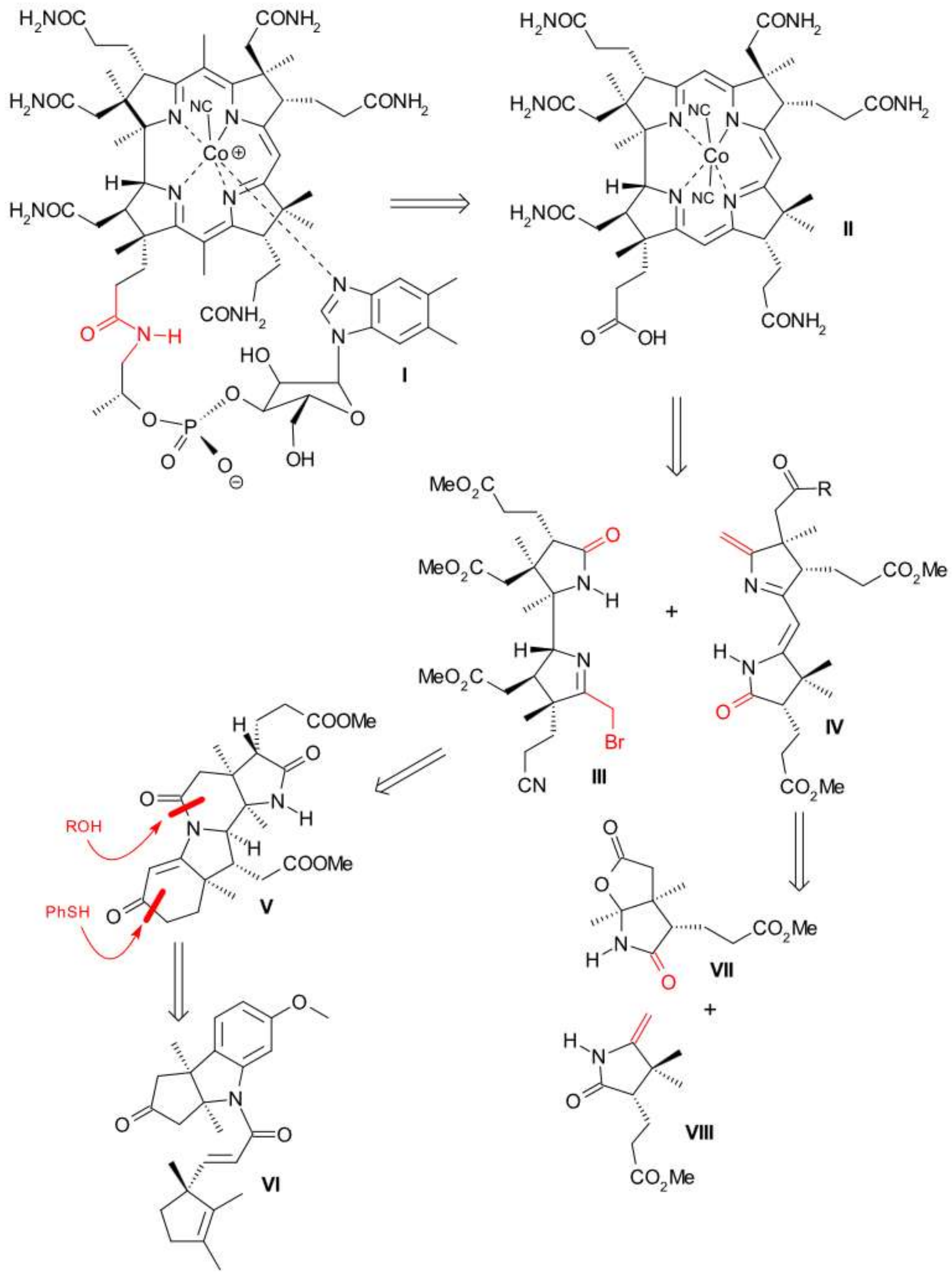




Totalnu sintezu vitamina B12 su izveli Woodward i Eschenmoser uz pomoć 91 postdoktoranada

12 doktoranada

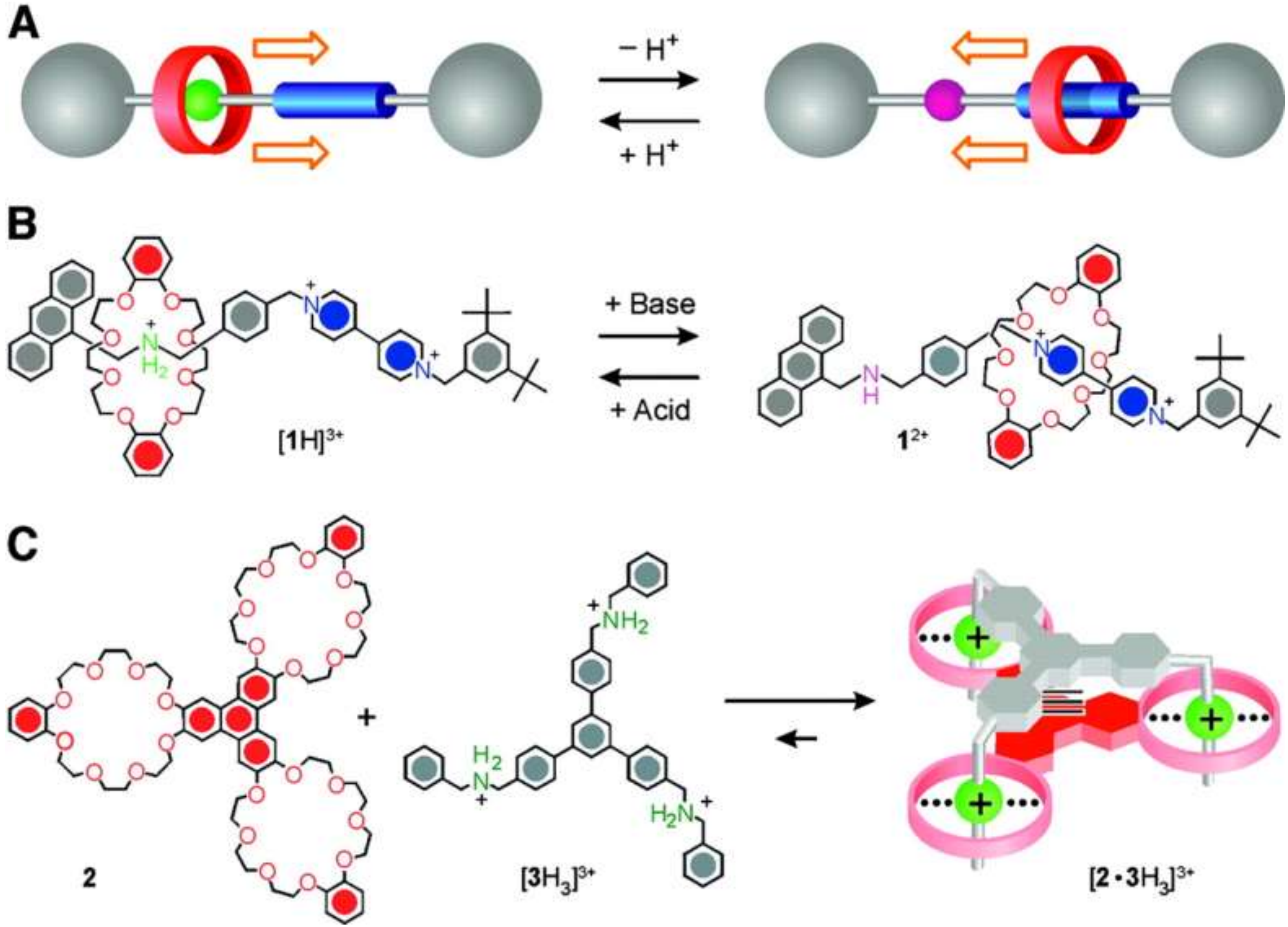
Sintezu počeli 1960. a završili je 1972. godine



A Molecular Elevator

Jovica D. Badjić, Vincenzo Balzani, Alberto Credi, Serena Silvi, J. Fraser Stoddart

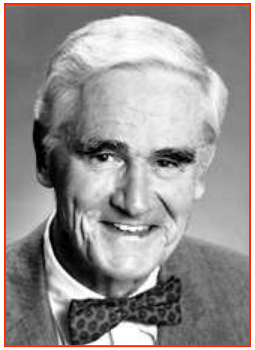
Science 19 Mar 2004: Vol. 303, Issue 5665, pp. 1845-1849



Istorijat supramolekulske hemije

1967- Charles Pedersen:
otkriće krunskih etara
1968- Park i Simmonds:
katapinandi: domaćin molekuli za anjone
1969- Jean-Marie Lehn:
sinteza prvog kriptanda
1969- Donald Cram:
sinteza sferanda
1978- Jean-Marie Lehn:
uveo pojam supramolekulska hemija
1979- Gokel i Okahara:
sinteza lariatnih etara
1981- Vogtle i Weber:
podandi kao domaćini; nomenklatura
1987-Nobelova nagrada
Cram-Lehn-Pedersen
1996-Comprehensive Supramolecular chemistry
1996-Nobelova nagrada
Kroto, Smalley i Curl hemija fulerena
2003-Nobelova nagrada
Agre, MacKinnon kanali ćelijskih membrana
2016-Nobelova nagrada
Stoddart, Feringa, Sauvage

Charles Pedersen



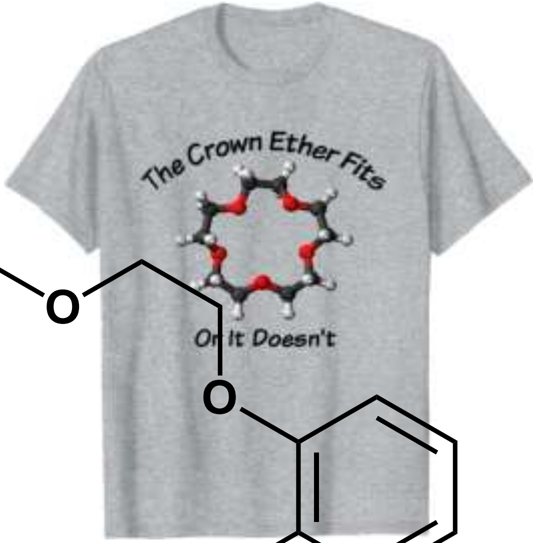
Donald Cram

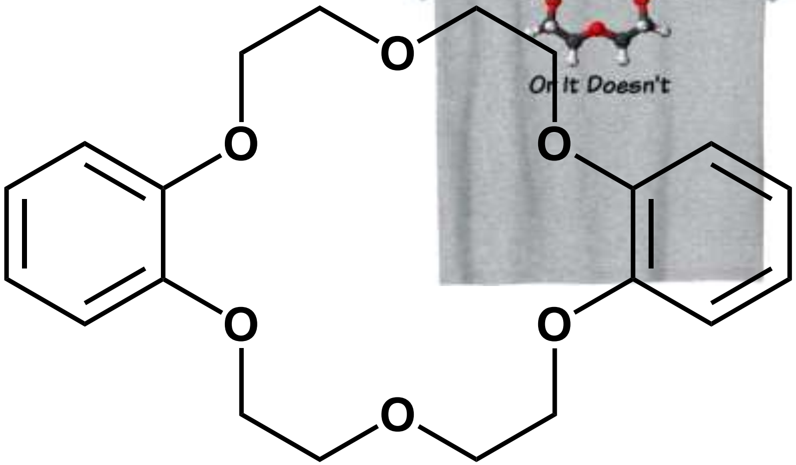
Jean-Marie Lehn

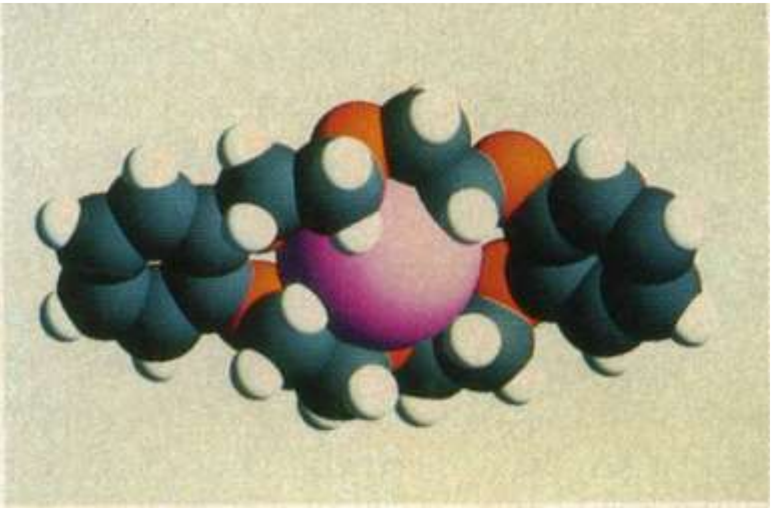
Supramolekulski sistemi pre 1960-ih

- 1810. Sir Humphrey Davy: inkluzija molekula hlora u ledu
- 1893 Alfred Werner Koordinaciona hemija
- 1894 Emil Fischer koncept ključ-brava
- 1891 Villiers & Hebd ciklodekstrini
- 1906 Paul Ehrlich koncept receptora
- 1937 Wolf supermolekul (übermolekül)

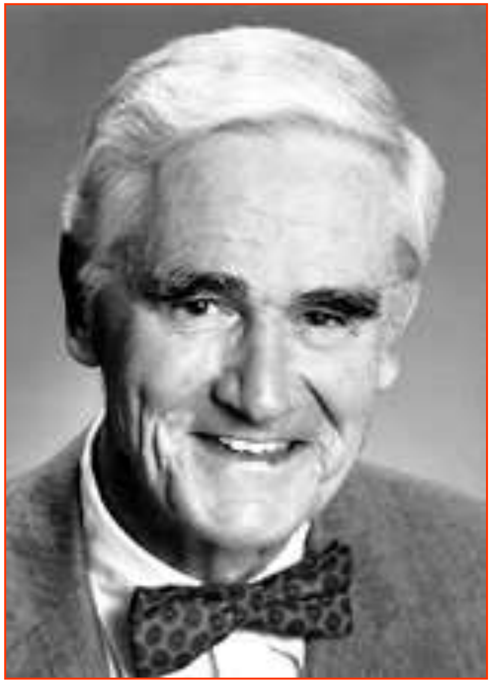
1967- Charles Pedersen
otkriće krunskih etara





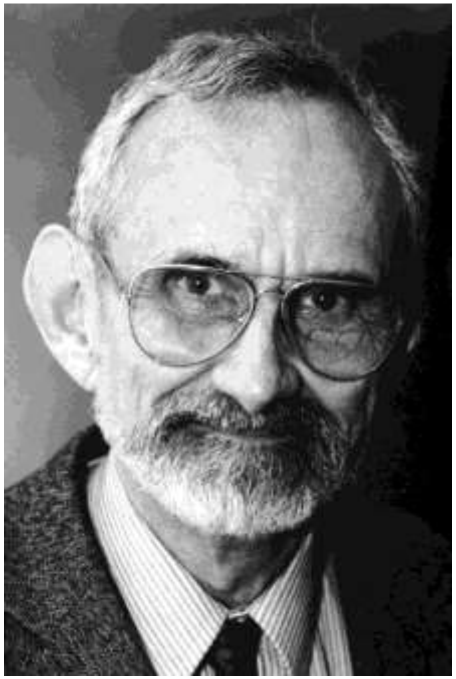


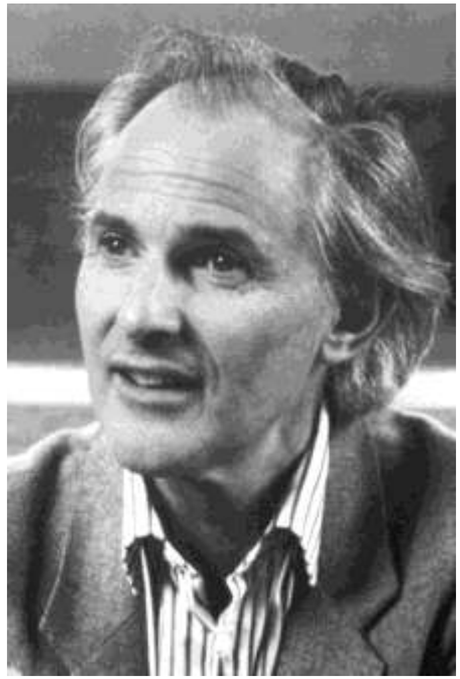
The Nobel Prize in Chemistry 1987

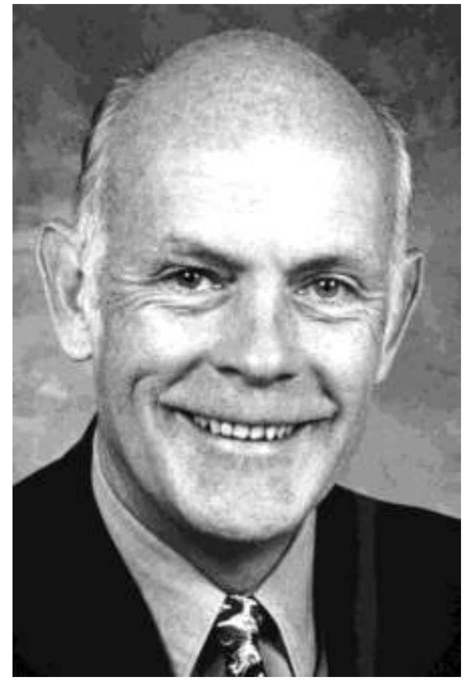


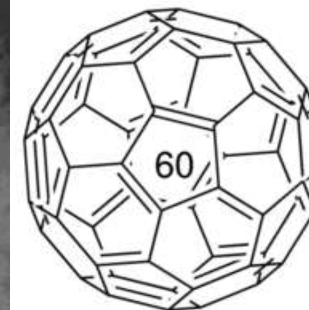
The Nobel Prize in Chemistry 1987 was awarded jointly to Donald J. Cram, Jean-Marie Lehn and Charles J. Pedersen
"for their development and use of molecules with structure-specific interactions of high selectivity."

The Nobel Prize in Chemistry 1996



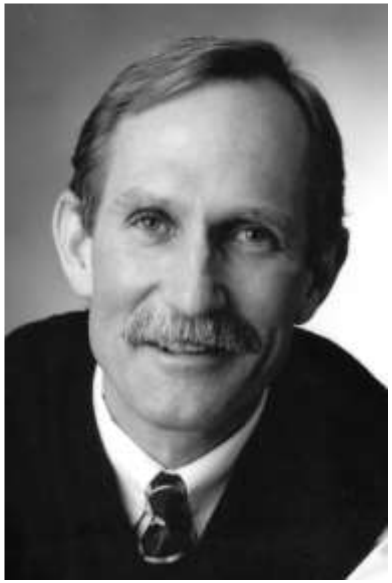






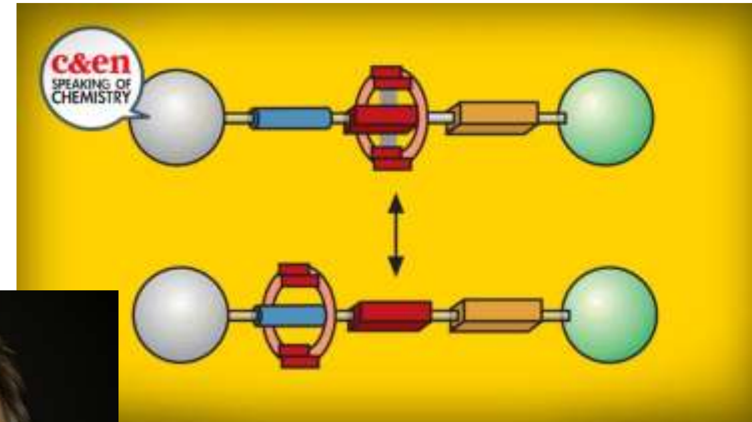
The Nobel Prize in Chemistry 1996 was awarded jointly to Robert F. Curl Jr., Sir Harold W. Kroto and Richard E. Smalley **"for their discovery of fullerenes."**

The Nobel Prize in Chemistry 2003

The Nobel Prize in Chemistry 2003 was awarded
"for discoveries concerning channels in cell membranes"
Peter Agre:
"for the discovery of water channels"
Roderick MacKinnon:
"for structural and mechanistic studies of ion channels."

The Nobel Prize in Chemistry 2016



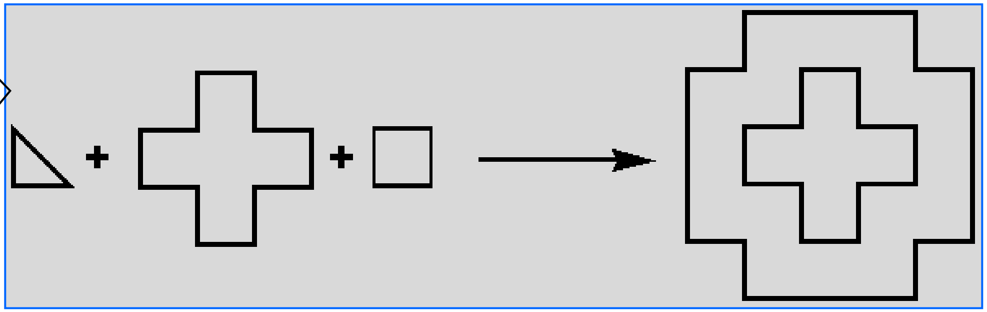
The Nobel Prize in Chemistry 2016 was awarded jointly to Jean-Pierre Sauvage, Sir J. Fraser Stoddart and Bernard L. Feringa

"for the design and synthesis of molecular machines".

Molekulska hemija : Supramolekulska hemija

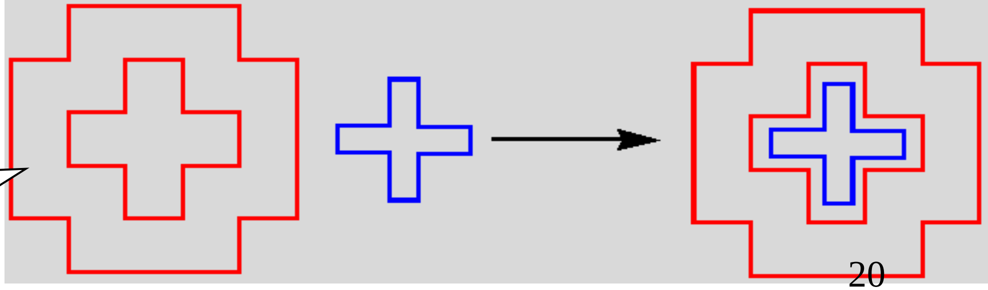
Molekulska hemija, hemija kovalentnih veza, proučava strukturu, osobine I transformacije molekulskih vrsta.

Kovalentni molekuli: **hemijske osobine, priroda, oblik, redoks potencijal, polarnost, vibracije i rotacije, magnetizam, hiralnost**



Supramolekulska hemija se može definisati kao hemija više od molekula (chemistry beyond the molecule) dve ili više molekulskih vrsta drže se zajedno intermolekulskim silama.

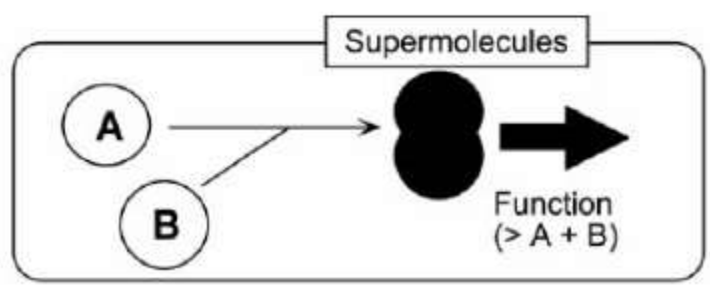
Supramolekuli: **specifične funkcije kao prepoznavanje, kataliza, transport (hemija lego kockica)**



TIM BOLJI OD IGRAČA

Tim čije su performanse bolje od prostog zbira osobina članova tima

Ovaj koncept “good team being greater than the sum of its parts” može se primeniti i na supermolekule

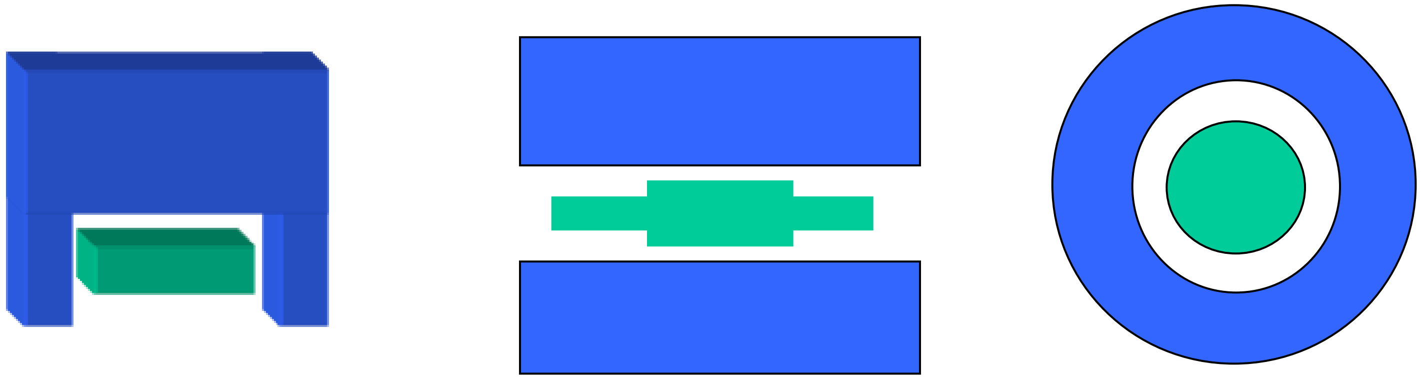


Supramolekulska hemija se može podeliti na dve velike oblasti

- *Domaćin-gost hemija*
- *Hemija molekulskog uredjivanja*

Domaćin-gost:

ukoliko je jedan od molekula znatno veći od drugog

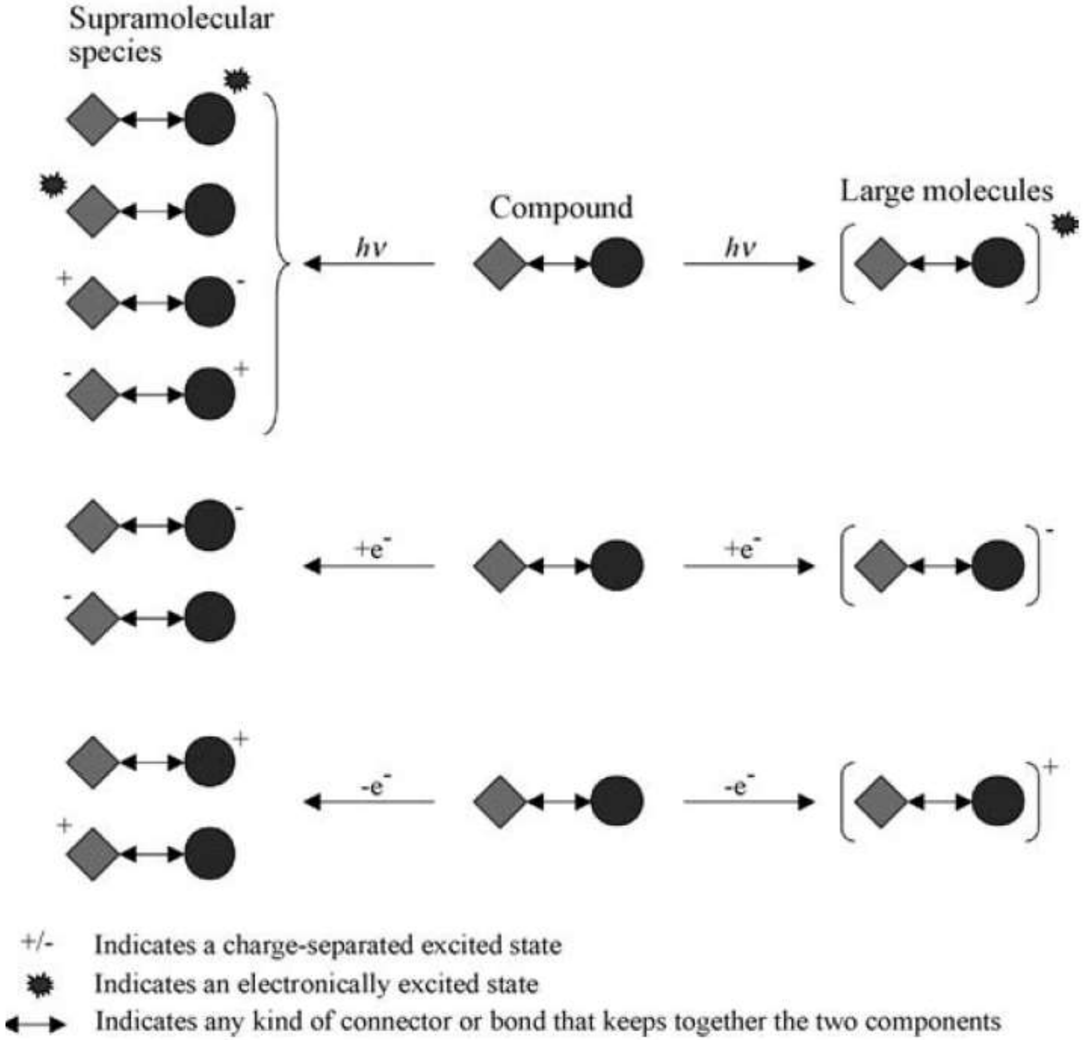


Molekulsko uređivanje:

Nema bitne razlike u veličini molekula koji su povezani nekovalentnim vezama

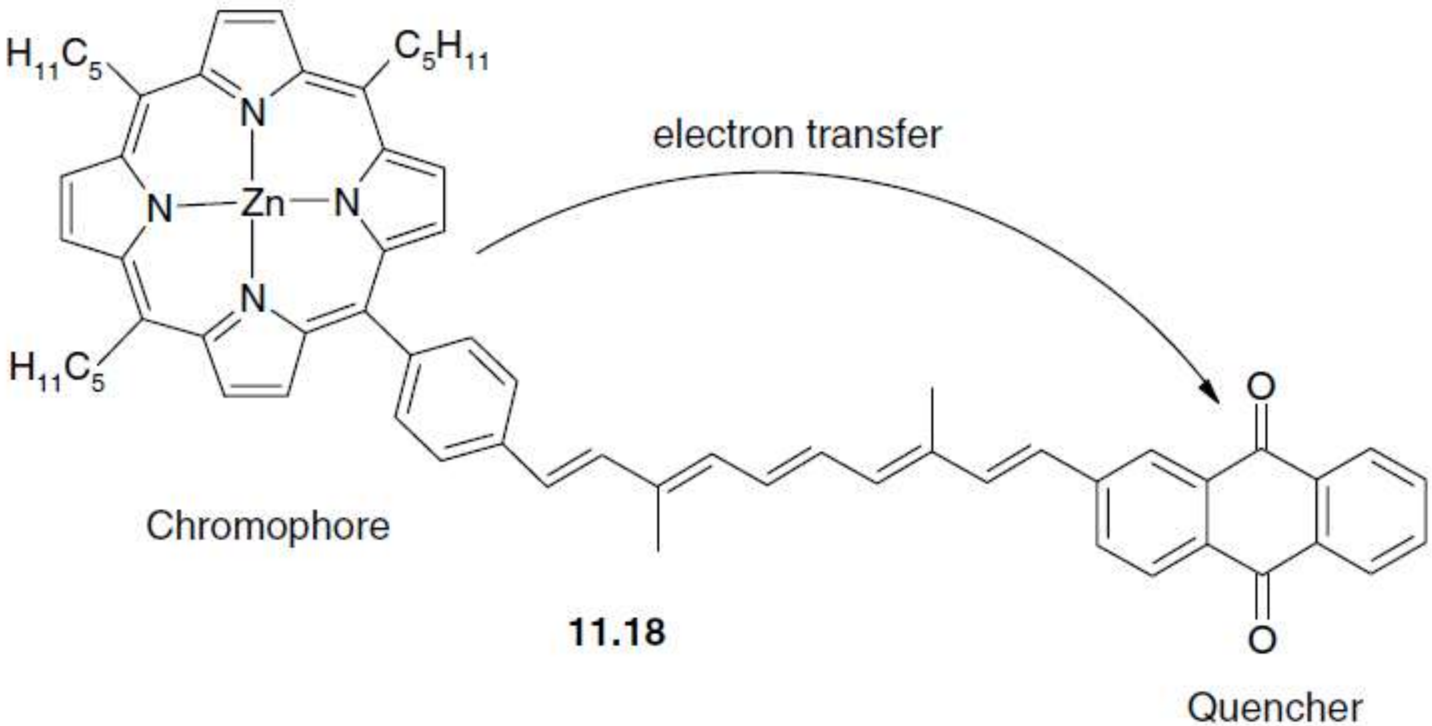
Kovalentni molekul kao super molekul

složeni sistemi koji se sastoje od određenih komponenti sa karakterističnim osobinama

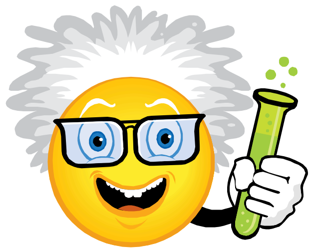


Povezana dva ključna elementa značajna za fotosintezu:

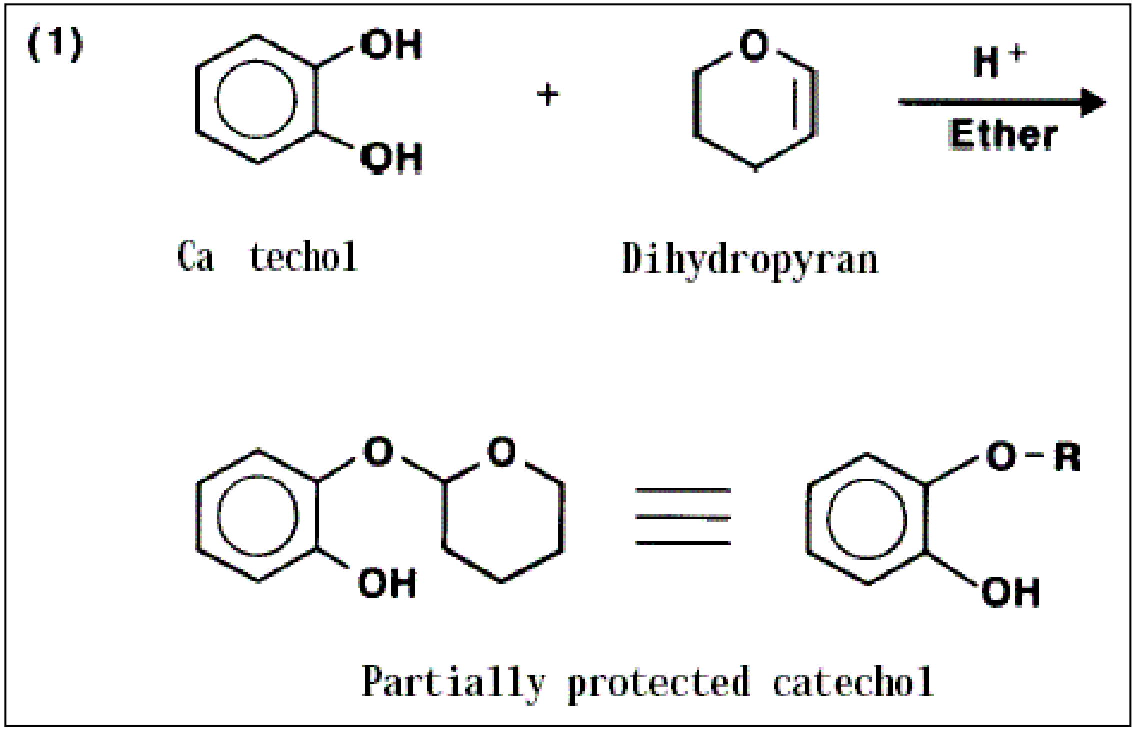
porfirinska hromofora i hinonski elektron-akceptor

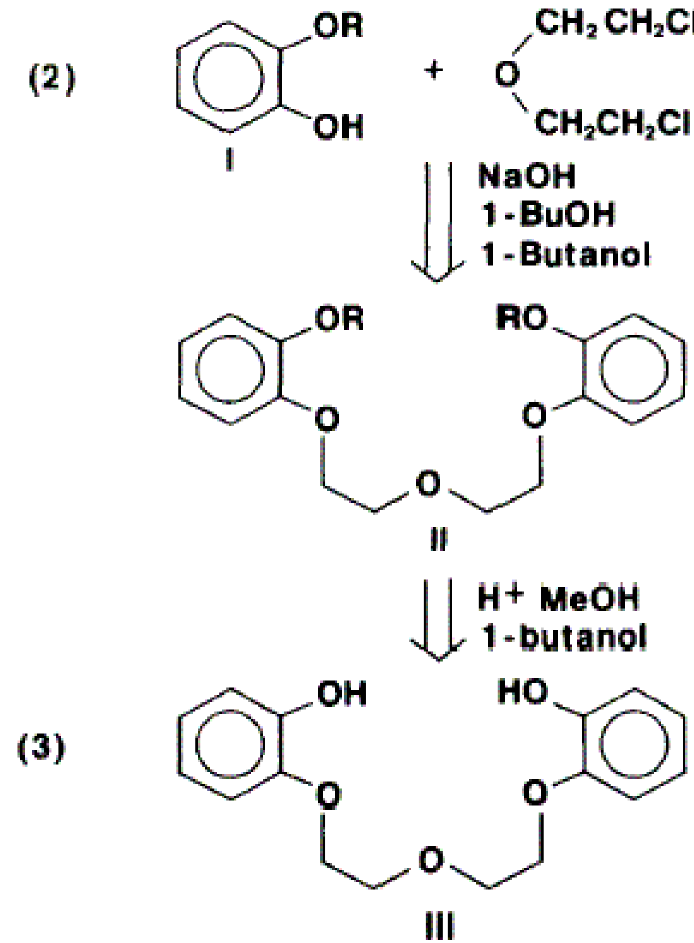


11.18



Neočekivana sinteza krunskih etara

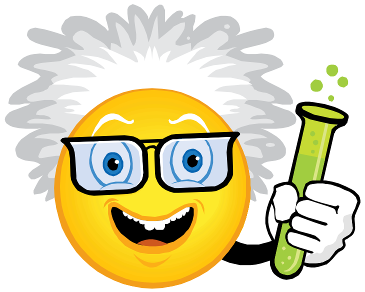




10% unreacted catechol

"But I decided to use this mixture for the second step anyway since purification would be required at the end."

Initial attempts at purification gave a small quantity (about 0.4 percent yield) of white crystals, silky, fibrous structure

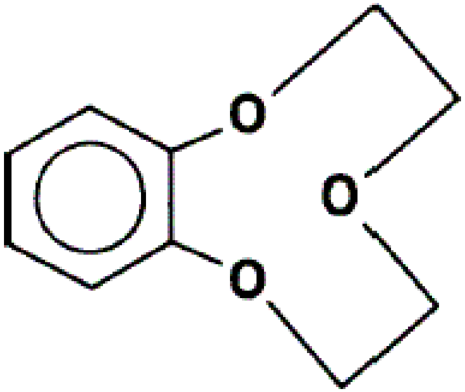


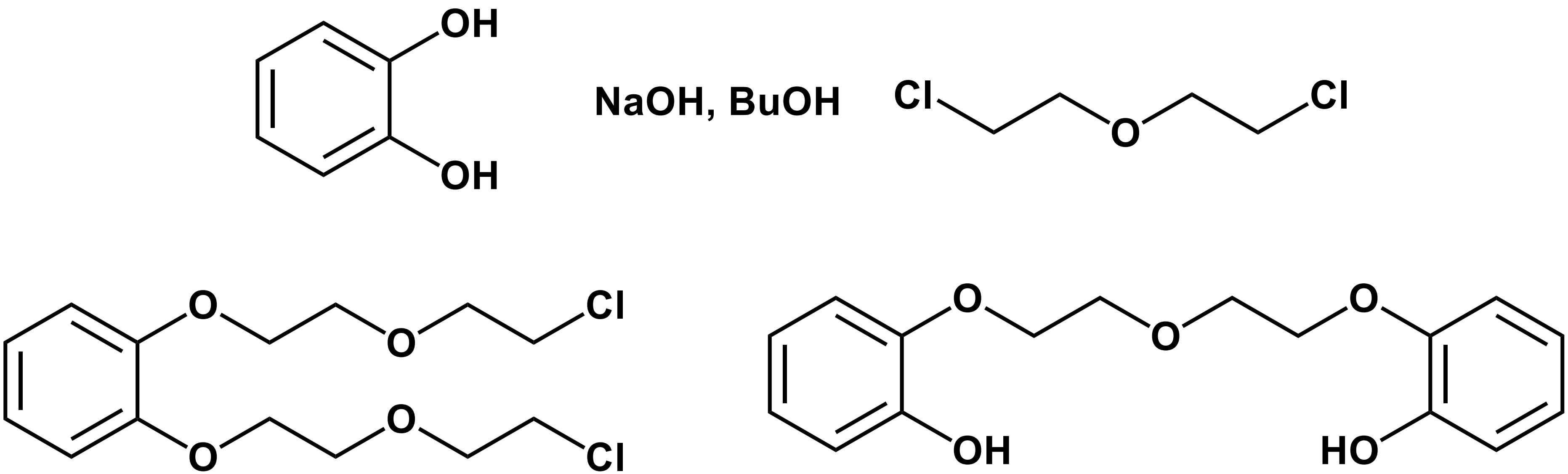
"It probably was not the target compound because thatwould be obtained in a higher yield. Because of my natural curiosity, I began study of the unknown."

Nepoznato jedinjenje ????????????????

- **Osobine nepoznatog jedinjenja:**

- Nepoznato jedinjenje veoma slabo rastvorno u metanolu
- Dobro se rastvara u metanolu u prisustvu natrijum-hidroksida
- Ne sadrži slobodne OH grupe (IR i NMR spektri).
- Rastvorno u metanolu koji sadrži bilo koju rastvornu natrijumovu so.
- Elementalna analiza, $C_{10}H_{12}O_3$




OH
OH
NaOH, BuOH
Cl
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Cl
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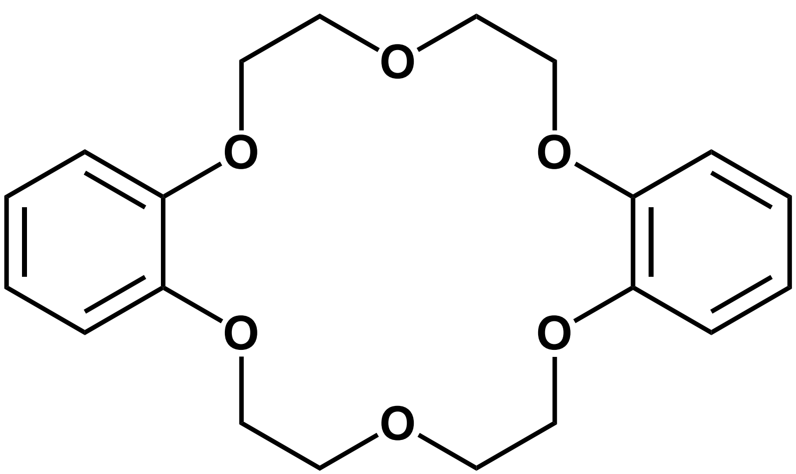
O
OH
HO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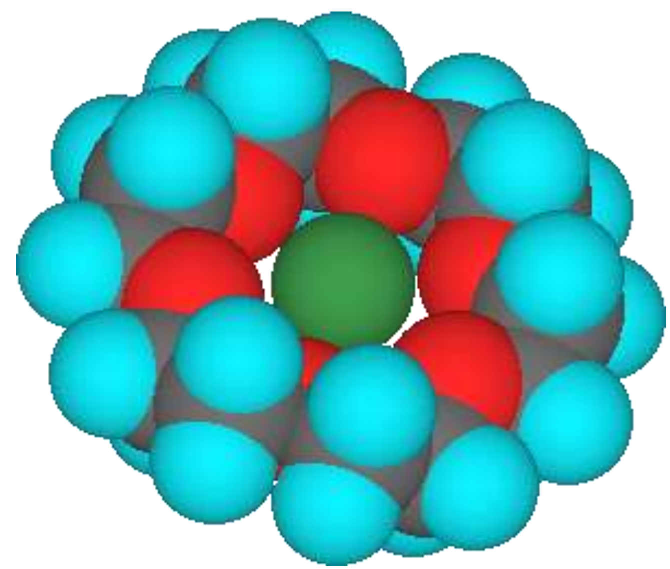
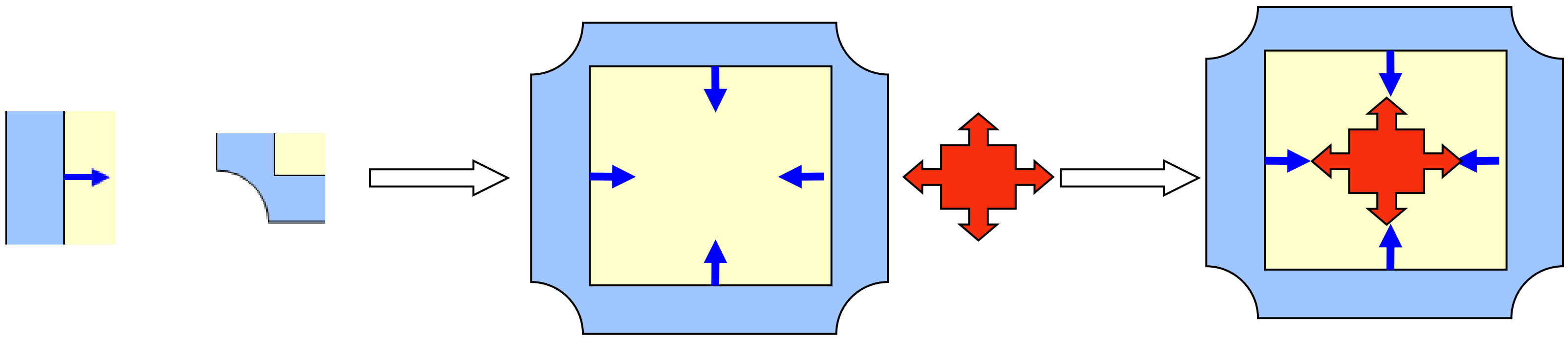
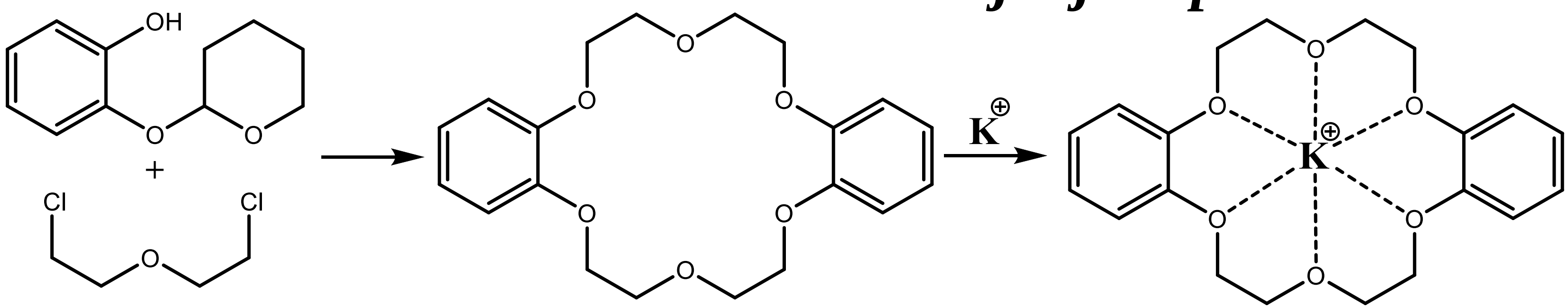


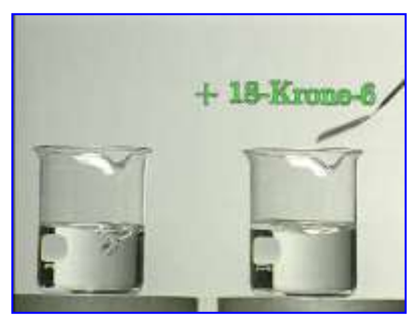
Kovalentni molekuli : Supermolekuli



Kovalentna sinteza *Nastajanje supermolekula*



Ljubičasti benzen



Supramolekulska hemija?!

Jean-Marie Lehn (Nobel Prize 1987):

"Chemistry of Molecular Assemblies and of the Intermolecular Bond."

- **Supramolekulske interakcije**

Pregled supramolekulskih interakcija

Interaction	Strength (kJ mol^{-1})	Example
Ion–ion	200–300	Tetrabutylammonium chloride
Ion–dipole	50–200	Sodium [15]crown-5
Dipole–dipole	5–50	Acetone
Hydrogen bonding	4–120	(See Table 1.2)
Cation–π	5–80	K^+ in benzene
π–π	0–50	Benzene and graphite
van der Waals	< 5 kJ mol^{-1} but variable depending on surface area	Argon; packing in molecular crystals
Hydrophobic	Related to solvent–solvent interaction energy	Cyclodextrin inclusion compounds

Nekovalentne interakcije su slabe!

Agnew. Chem. Int. Ed. 2001, *40*, 2382-2426
Leonard J. Prins, David N. Reinhoudt, Peter Timmerman

Jon–Jon interakcije (100-350 kJ/mol)

- Veoma jake veze, mogu biti i jače od kovalentnih veza.
- Mogu biti privlačne i odbojne.
- Nisu usmerene
- Deluju na relativno velikom rastojanju (1/r)
- Veoma zavise od dielektrične konstante sredine

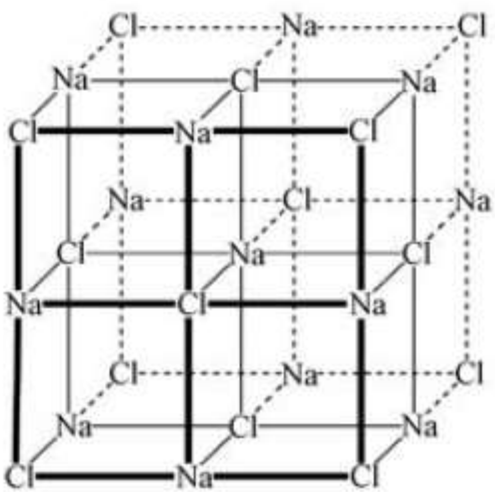
$$\text{Energija} = (k \cdot z_1 \cdot z_2 \cdot e^2) / (\varepsilon \cdot r_{12})$$

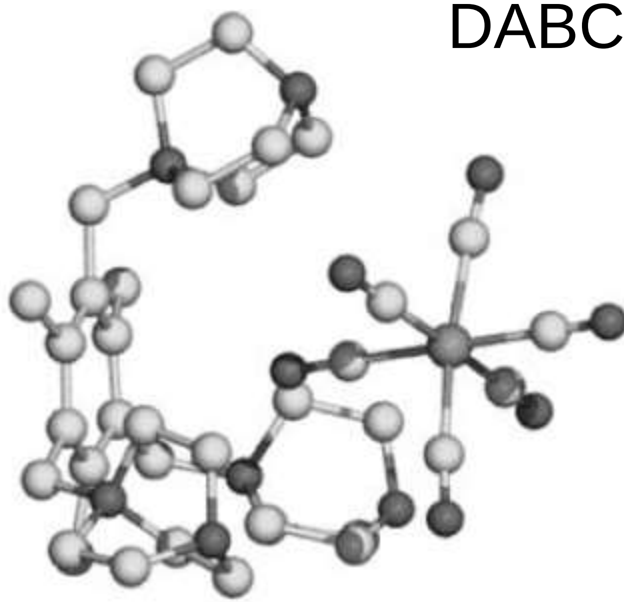
$k = 1 / 4\pi\varepsilon_o$ = Coulomb-ova constanta = $9 \cdot 10^9$ $N \cdot m^2/C^2$

e = elementarno naelektrisanje = $1.6 \cdot 10^{-19}$C

ε = dielektrična konstanta

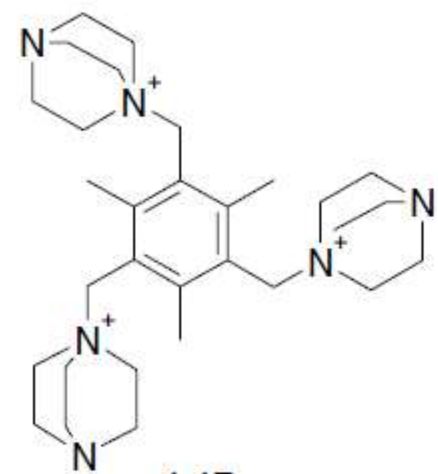
r_{12} = rastojanje između naelektrisanja





(b)

DABCO - $[Fe(CN)_6]^{3-}$



1.17

Jon–Jon interakcije u rastvaračima različite polarnosti

1 nm u vodi?

Energija = $(k \cdot z_1 \cdot z_2 \cdot e^2) / (\varepsilon \cdot r_{12})$

$= 9 \cdot 10^9 \cdot 1 \cdot (-1) \cdot (1.6 \cdot 10^{-19})^2 / \mathbf{78.5} \cdot 1 \cdot 10^{-9}$

$= -2.3 \cdot 10^{-28} / 0.8 \cdot 10^{-7}$

$= -29.4 \cdot 10^{-22}$ J

-1.74 kJ/mol = -0.42 kcal/mol

1 nm u hloroformu?

$= 9 \cdot 10^9 \cdot 1 \cdot (-1) \cdot (1.6 \cdot 10^{-19})^2 / \mathbf{4.8} \cdot 1 \cdot 10^{-9}$

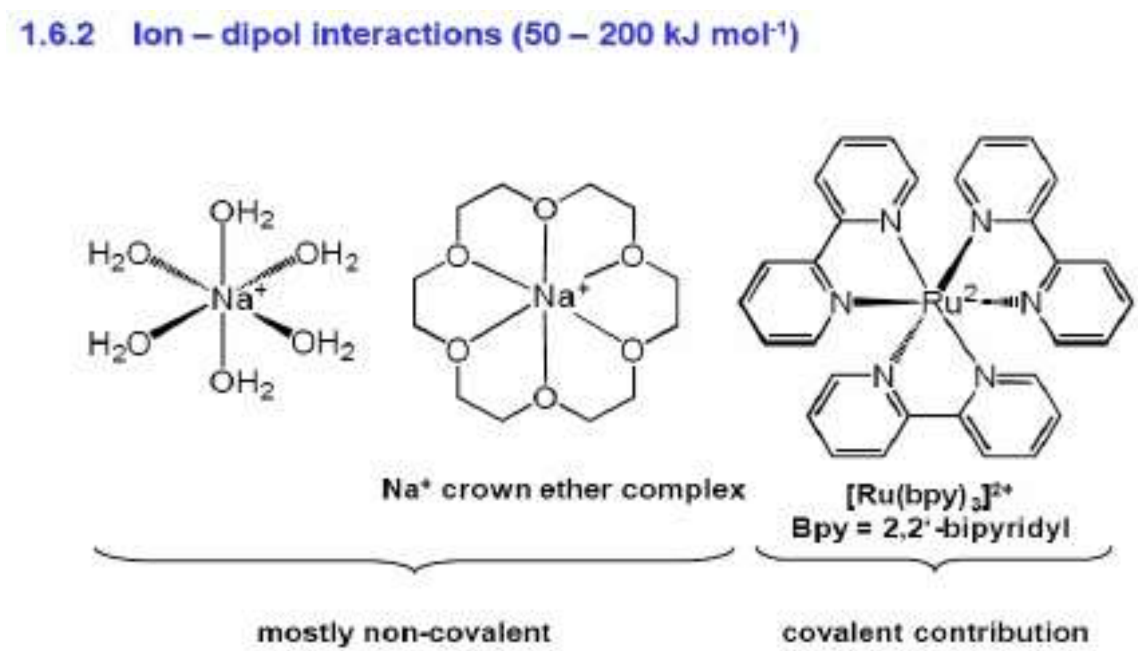
$= -2.3 \cdot 10^{-28} / 4.8 \cdot 10^{-9}$

$= -4.79 \cdot 10^{-20}$ J

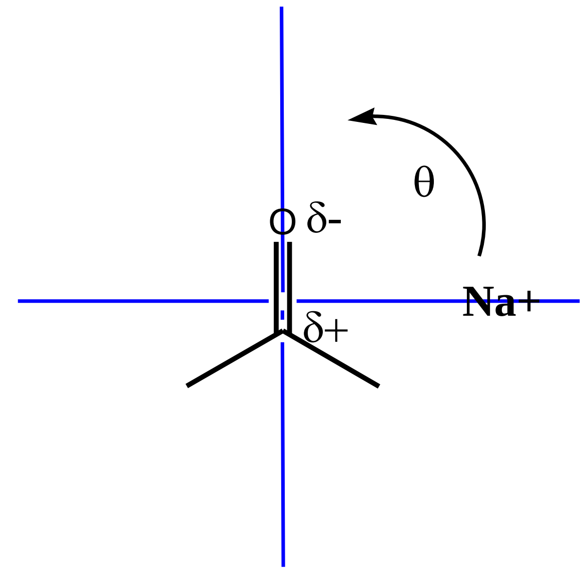
-28.94 kJ/mol = -6.89 kcal/mol ≅ *8 % od energije C-C veze*

Jon-Dipol Interakcije (50-200 kJ/mol)

- Slabo usmerene
- Mogu biti odbojne i privlačne
- Deluju na manjem rastojanju od jon-jon interakcija($1/r^2$)
- Znatno su slabije od jon-jon interakcija



Energija = $-(k \cdot Q \cdot u \cdot \cos\theta / \varepsilon \cdot r^2)$



Maksimum za $\theta = 0$ ili 180 stepeni
nula za $\theta = 90$ stepeni

$u = q \cdot \ell$
u = dipolni moment
ℓ = dužina dipola
q = parcijalno naelektrisanje dipola
r = rastojanje od centra naelektrisanja do centra dipola
Q = naelektrisanje jona

Primer: Delovanje između acetona i Na^+ jona (θ = nula) na rastojanju od 1 nm (u hloroformu)

Energija = $-(k \cdot Q \cdot u \cdot \cos\theta / \varepsilon \cdot r^2)$
Ako je θ = nula
-1.76 kJ/mol= = -0.42 kcal/mol

Dipol-Dipol interakcije (5-50 kJ/mol)

Usmerene interakcije

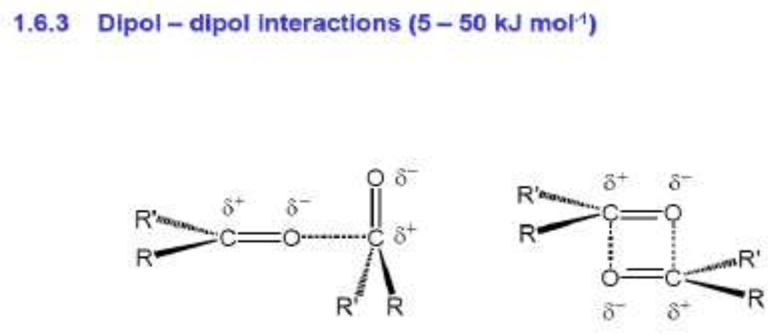
Mogu biti privlačne i odbojne

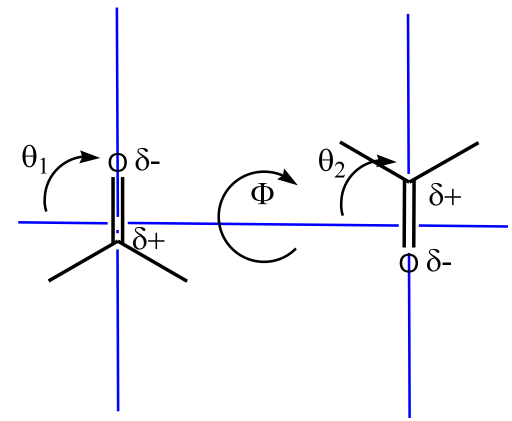
Deluju na malom rastojanju ($1/r^3$)

Značajno slabije od jon-dipol interakcija

Javljaju se između molekula koji imaju permanentni dipol (polarni molekuli)

Na primer, dipol-dipol interakcije se javljaju između SCl_2, PCl_3, $(CH_3)_2CO$



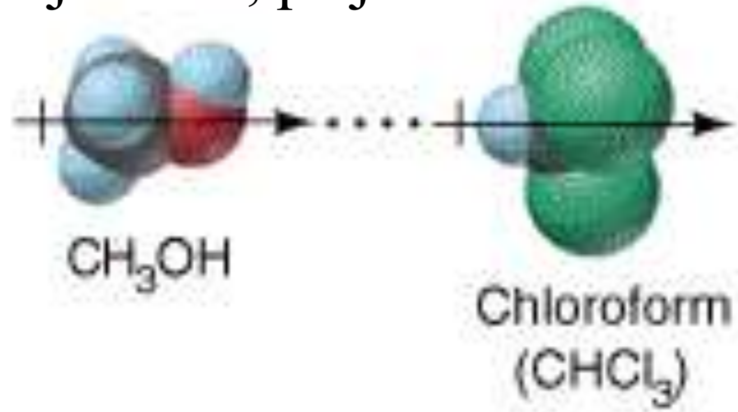


$$\text{Energija} = -\left(k \cdot u_1 \cdot u_2 / \varepsilon \cdot r^3\right) \cdot \left(\left(2\cos\theta_1\cos\theta_2 - \sin\theta_1\sin\theta_2\right) \cdot \cos\phi\right)$$

$$\text{Energija} = -(k \cdot u_1 \cdot u_2 / \varepsilon \cdot r^3) \cdot ((2\cos\theta_1\cos\theta_2 - \sin\theta_1\sin\theta_2) \cdot \cos\phi)$$

Maksimum za dipole “u liniji” gde je $\theta = 0$, pa je izraz za energiju

$$= -2k \cdot u_1 \cdot u_2 / (\varepsilon \cdot r^3)$$



Primer:

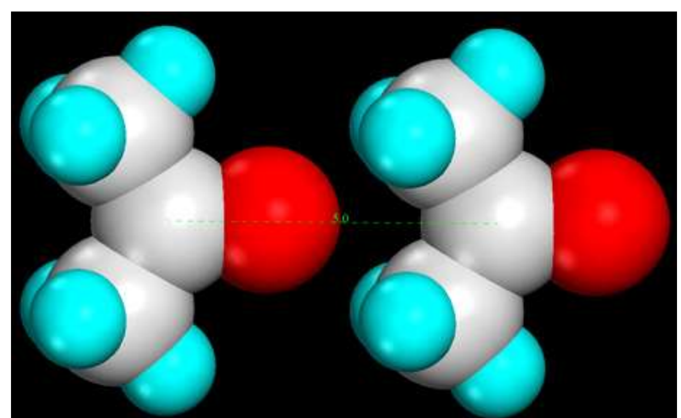
dva molekula acetona u $CHCl_3$ na rastojanju od 0.5 nm:

$= \text{Energija} = -2k \cdot u_1 \cdot u_2 / (\varepsilon \cdot r^3)$

$= -2 \cdot 9 \cdot 10^9 \cdot (2.88 \cdot 3.34 \cdot 10^{-30})^2 / (4.8 \cdot (0.5 \cdot 10^{-9})^3)$

$= -28.08 \cdot 10^{-22}$ J

-1.68 kJ/mol= -0.4 kcal/mol

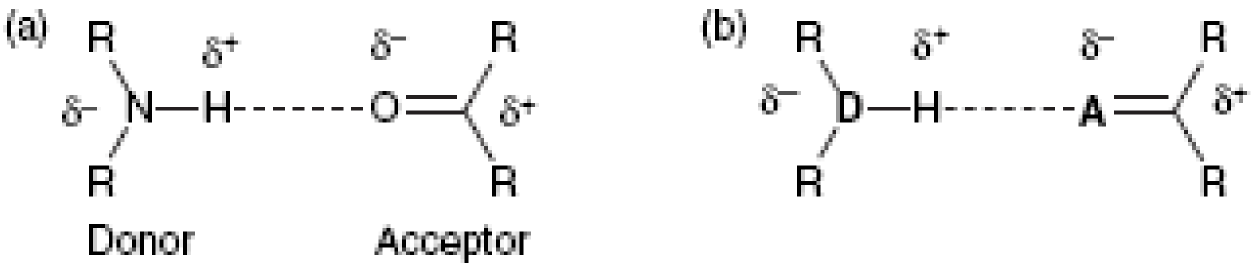


Vodonične veze (4-120 kJ/mol)

Vodonične veze su najznačajnije nekovalentne interakcije u supramolekulskim sistemima
Donori za vodonične veze su grupe u kojima je vodonikov atom vezan za elektronegativniji atom (azot ili kiseonik).

Akceptori za vodonične veze su grupe koje sadrže elektron privlačne atome koji interaguju sa pozitivno naelektrisanim atomom vodonika.

prirodni „blokova za izgradnju“ supramolekulskih sistema (amino-kiseline, ugljeni hidrati, nukleotidi...).

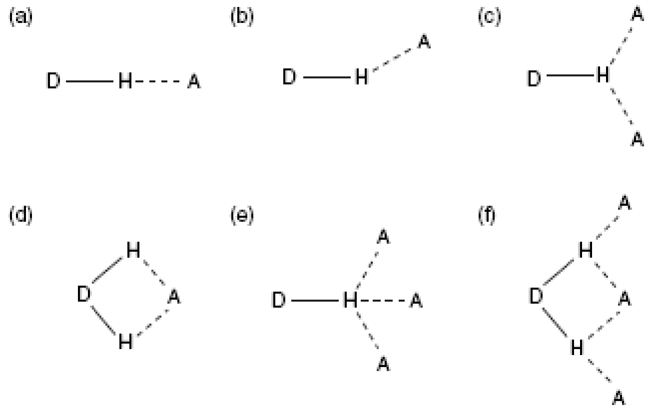


The International Union of Pure and Applied Chemistry (IUPAC) has recently established the hydrogen bond as

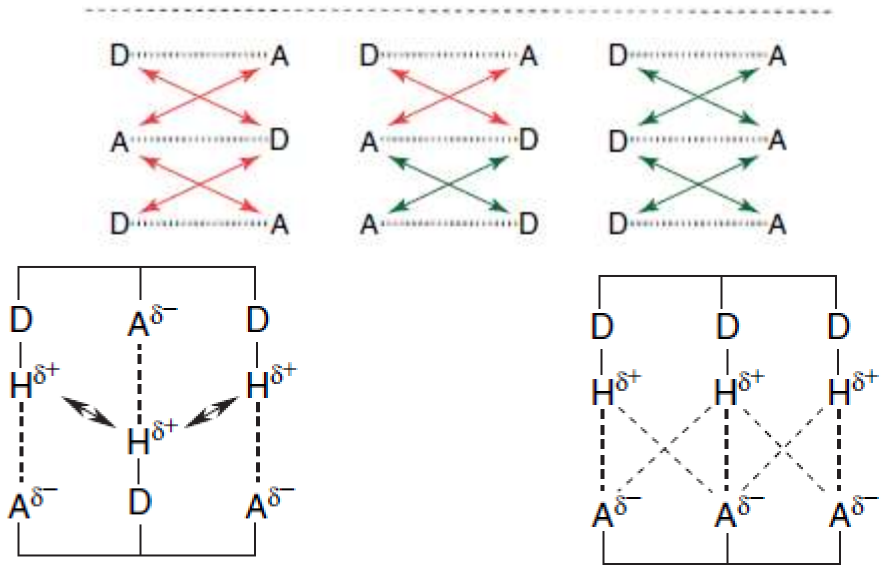
“an attractive interaction between a hydrogen atom from a molecule or a molecular fragment X–H in which X is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.”

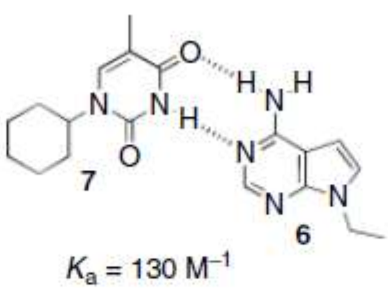
Angew. Chem. Int. Ed. **2011,** *50*, 52

Primarne vodonične veze



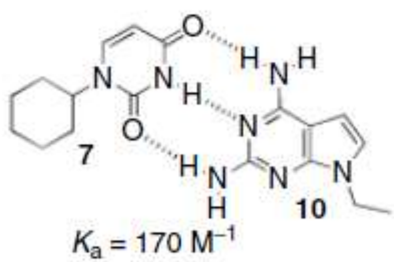
Sekundarne vodonične veze



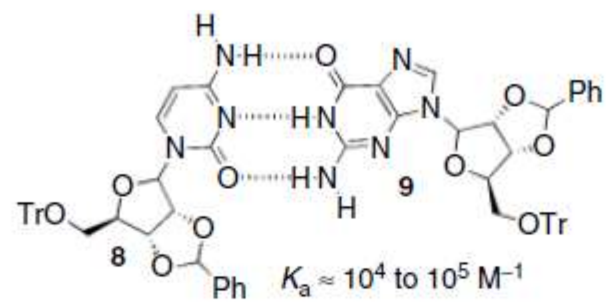


DA : AD

adenin-timin



DAD : ADA



DAA : AAD

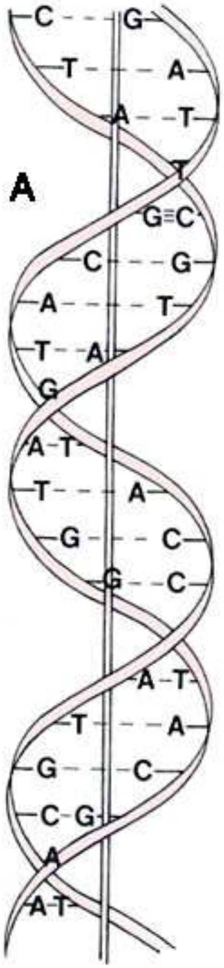
citozin-guanin

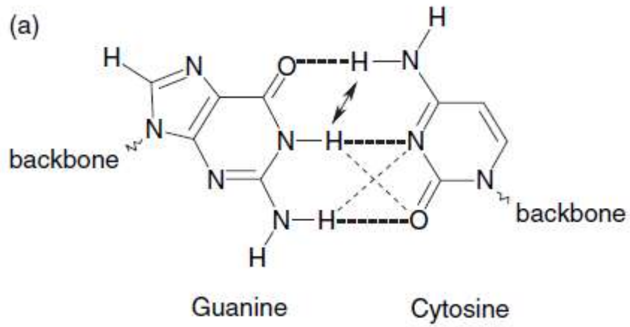
Osobine vodoničnih veza: jačina i geometrija

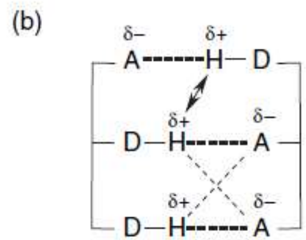
	Strong	Moderate	Weak
A—H···B interaction	Mainly covalent	Mainly electrostatic	Electrostatic
Bond energy (kJ mol^{-1})	60–120	16–60	<12
Bond lengths (Å)			
H···B	1.2–1.5	1.5–2.2	2.2–3.2
A···B	2.2–2.5	2.5–3.2	3.2–4.0
Bond angles (°)	175–180	130–180	90–150
Relative IR vibration shift (stretching symmetrical mode, cm^{-1})	25%	10–25%	<10%
^{1}H NMR chemical shift downfield (ppm)	14–22	<14	?
Examples	Gas phase dimers with strong acids/bases	Acids	Minor components of bifurcated bonds
	Proton sponge	Alcohols	C—H hydrogen bonds
	HF complexes	Biological molecules	O—H···π hydrogen bonds

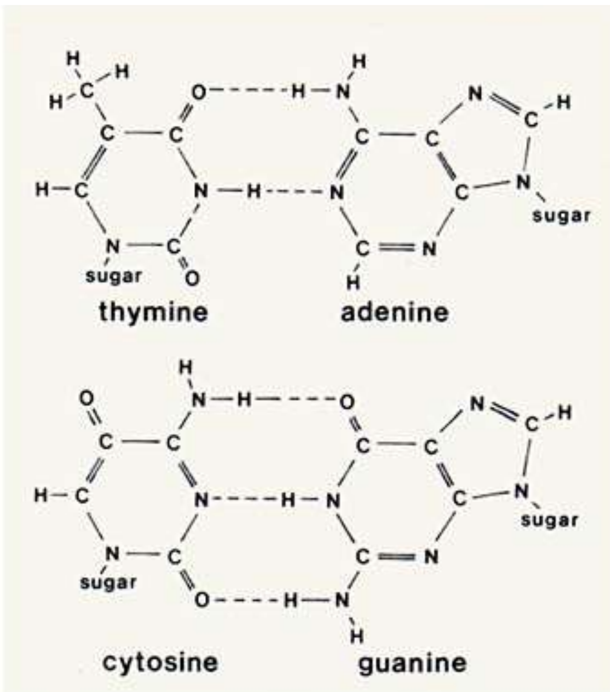
HF_2^- 170 kJ/mol

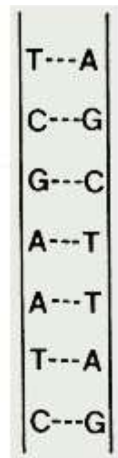
DNA

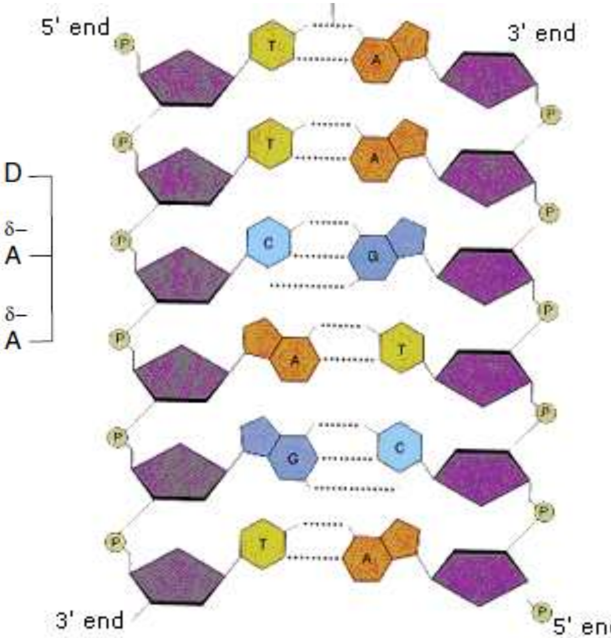

A

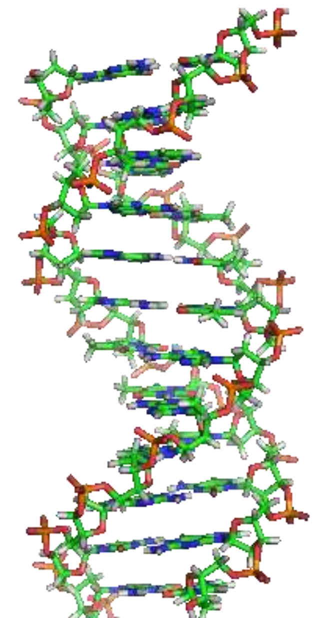

(a)
backbone
backbone
Guanine
Cytosine


(b)


sugar
sugar
thymine
adenine
sugar
sugar
cytosine
guanine


T---A
C---G
G---C
A---T
A---T
T---A
C---G


5' end
3' end
3' end
5' end



Primeri veoma stabilnih supramolekulskih sistema

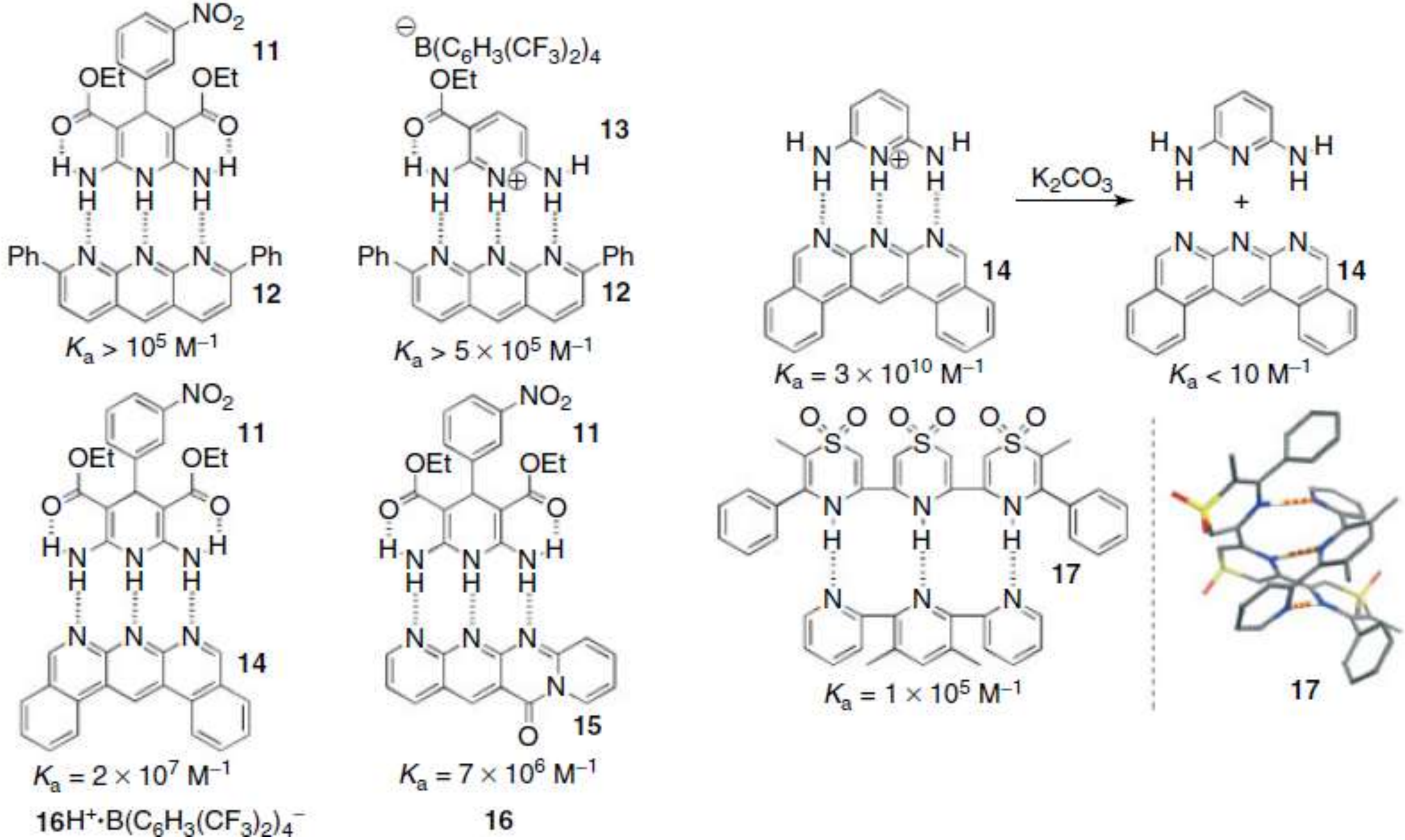
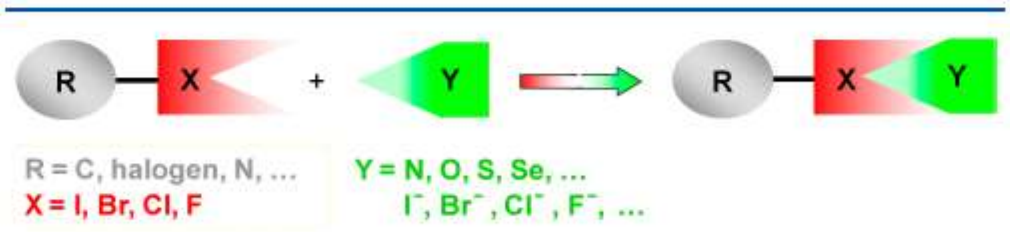


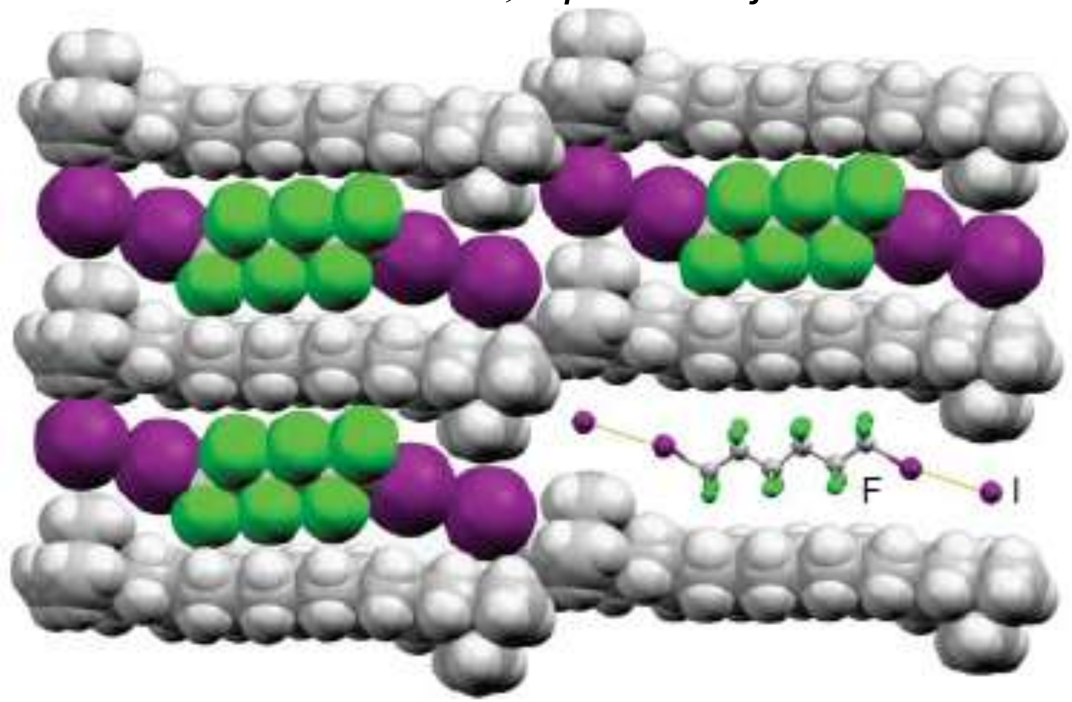
Figure 4 Chemical structures of DDD–AAA triply H-bonded pairs **11.12**, **12.13**, **11.14**, **11.15**, **14.16**H$^+$, and **17** studied by the Zimmerman, Anslyn, Leigh, and Wisner groups.

Halogenidne veze (Resnati, Metrangolo)

- Privlačne interakcije između elektron-deficitarnih halogena (donora) i elektron-bogatih atoma (akceptora)
- Jačina 10-200 kJ/mol u gasnoj fazi i 10-50 kJ/mol u čvrstom stanju
- Linearna geometrija



Kristalna struktura α,ω-perfluorojodalakana



Chem. Rev. **2015**, *115*, 7118

Review

pubs.acs.org/CR

Halogen Bonding in Supramolecular Chemistry

Lydia C. Gilday, Sean W. Robinson, Timothy A. Barendt, Matthew J. Langton, Benjamin R. Mullaney, and Paul D. Beer*

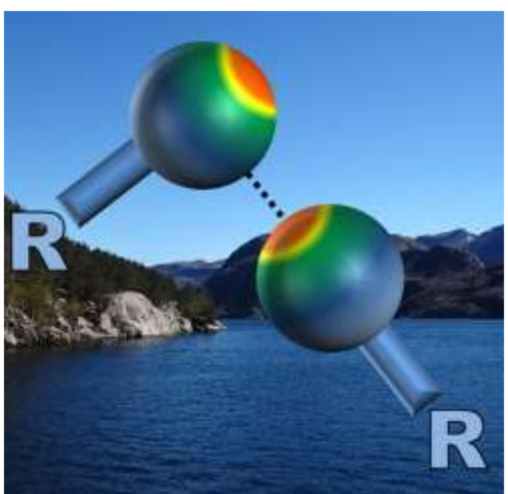
Chem. Rev. **2016**, *116*, 2478

Review

pubs.acs.org/CR

The Halogen Bond

Gabriella Cavallo,[†] Pierangelo Metrangolo,*[,†,‡] Roberto Milani,[‡] Tullio Pilati,[†] Arri Priimagi,[§] Giuseppe Resnati,*[,†] and Giancarlo Terraneo[†]



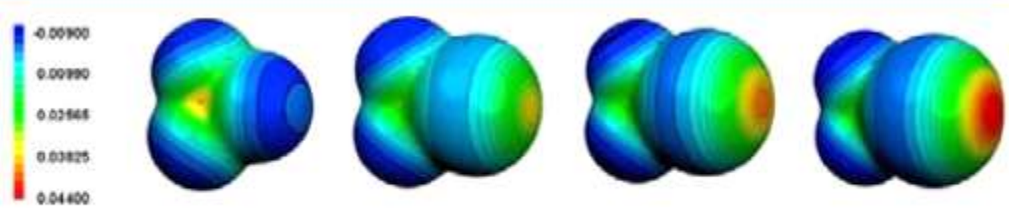


Figure 1. Molecular electrostatic potential, in hartrees, at the 0.001 e/bohr^3 isodensity surface of CF_3X (from left to right, X = F, Cl, Br, I). Reprinted with permission from ref 43b. Copyright 2007 Springer.

„σ-hole“ koncept
Deformacija elektronske gustine na donorskom atomu halogena

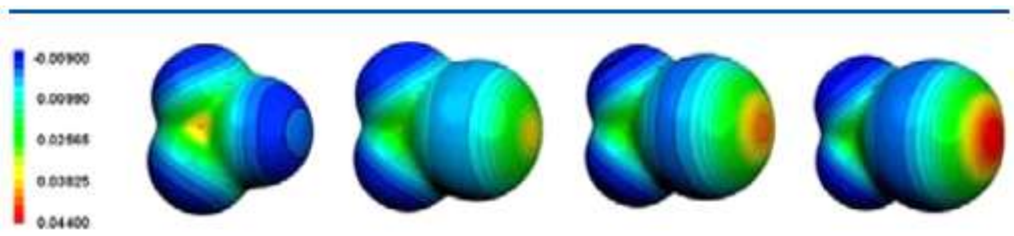
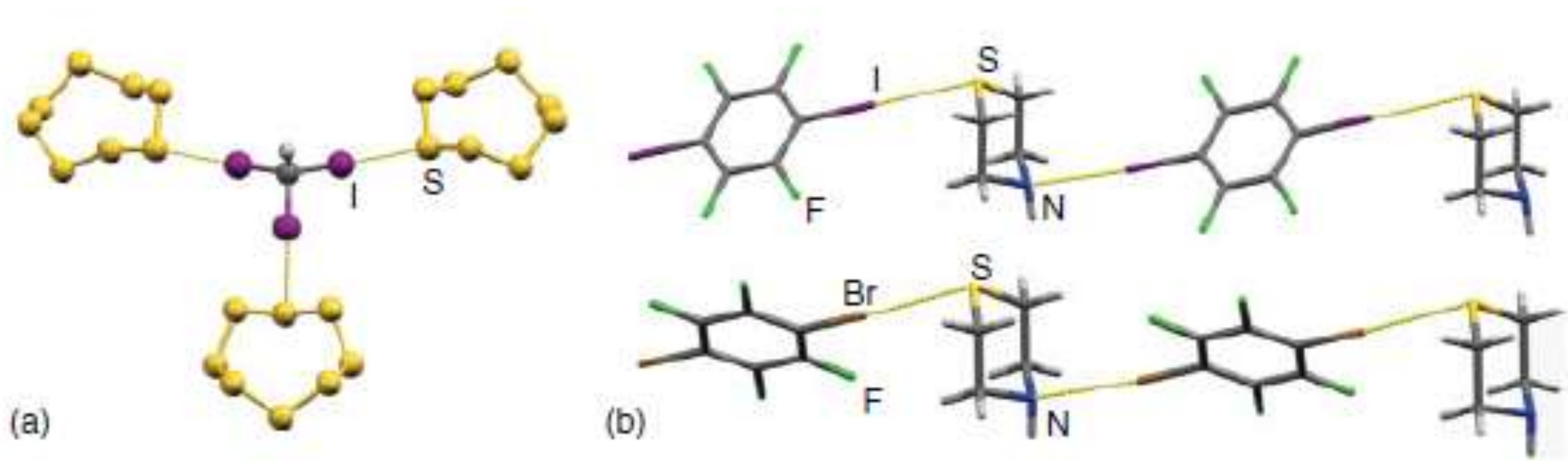


Figure 1. Molecular electrostatic potential, in hartrees, at the 0.001 e/bohr^3 isodensity surface of CF_3X (from left to right, X = F, Cl, Br, I). Reprinted with permission from ref 43b. Copyright 2007 Springer.

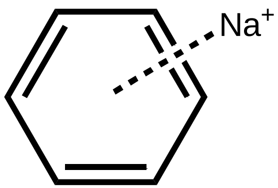


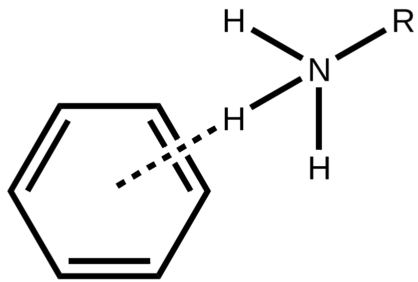
Sumpor + jodoform

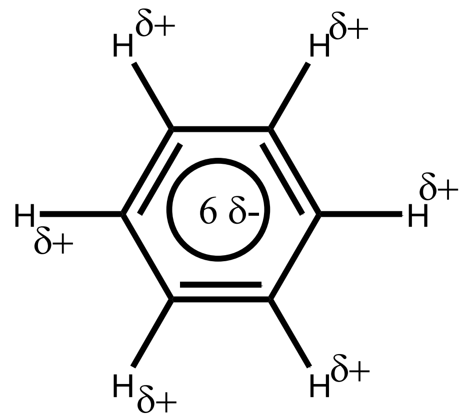
π interakcije

katjon π interakcije, π– π interakcije, anjon- π interakcije

katjon π interakcije

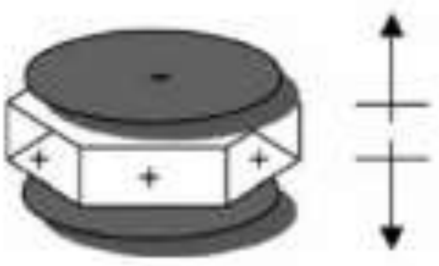


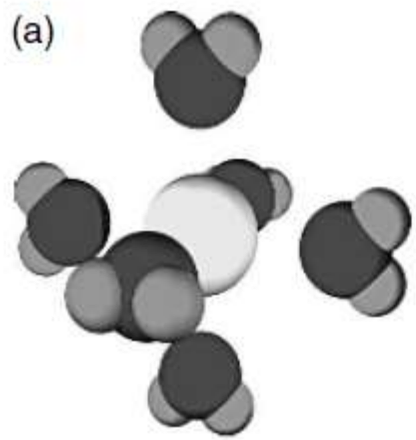


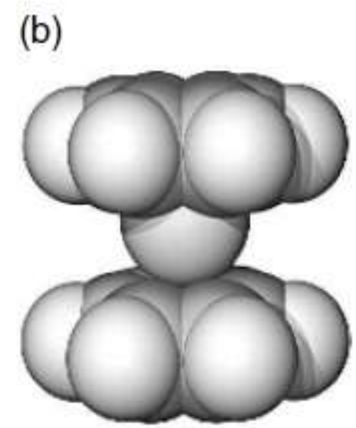


U gasnoj fazi!!!

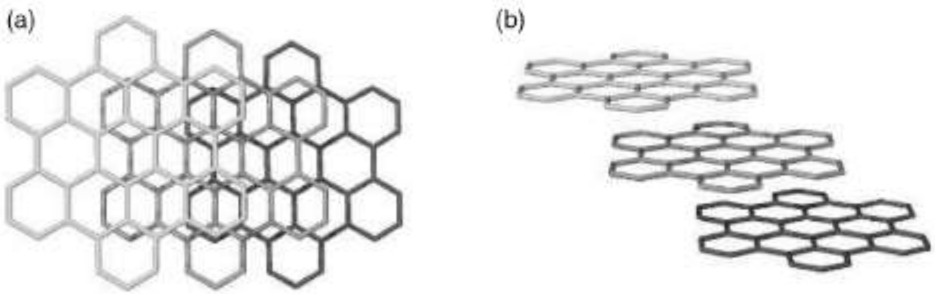
K^+----benzen	80 KJ/mol
K^+----voda	75 KJ/mol

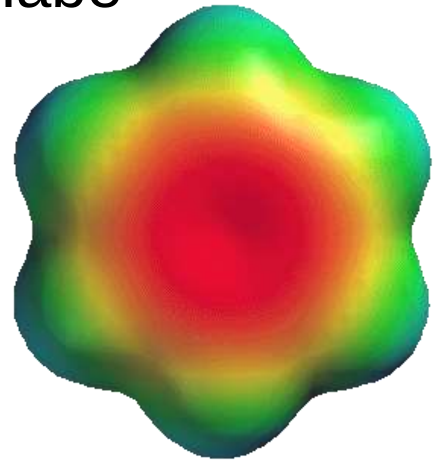




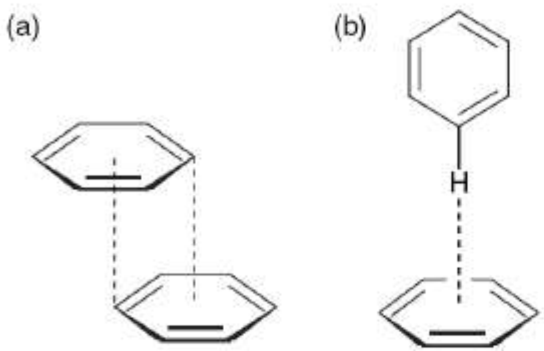


π–π interakcije (0-10 kcal/mol), slabe elektrostaičke interakcije

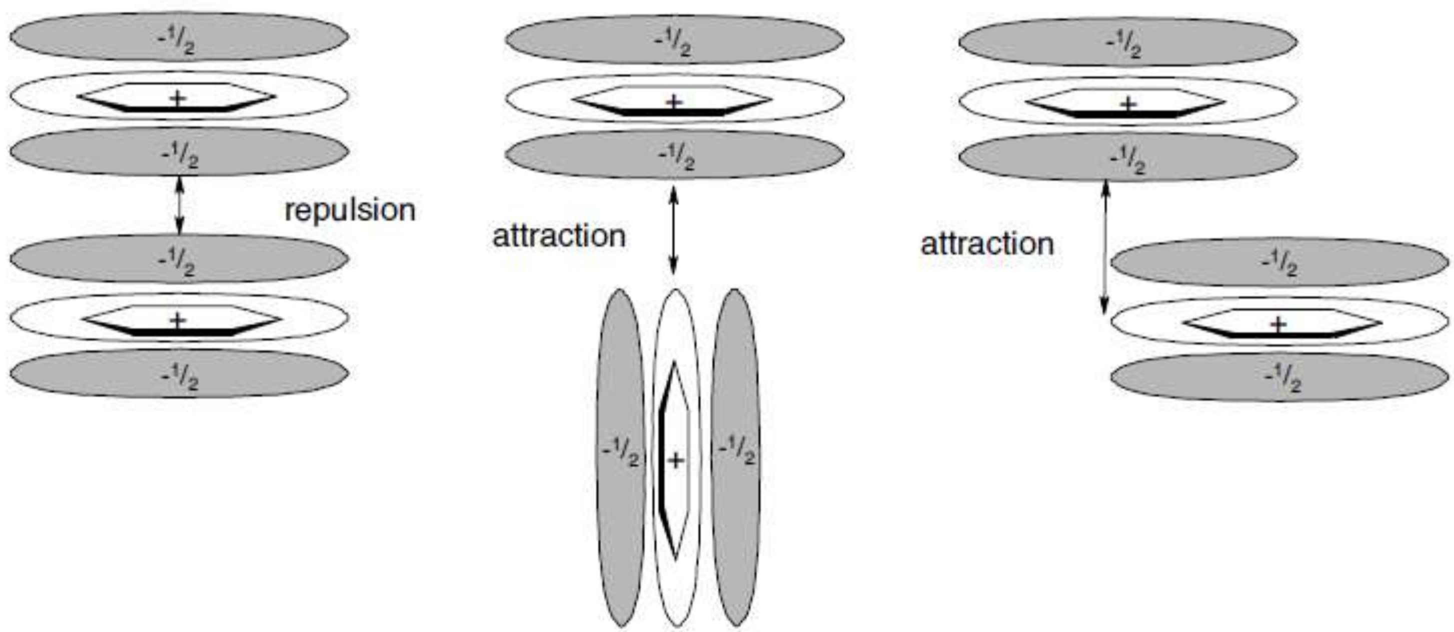




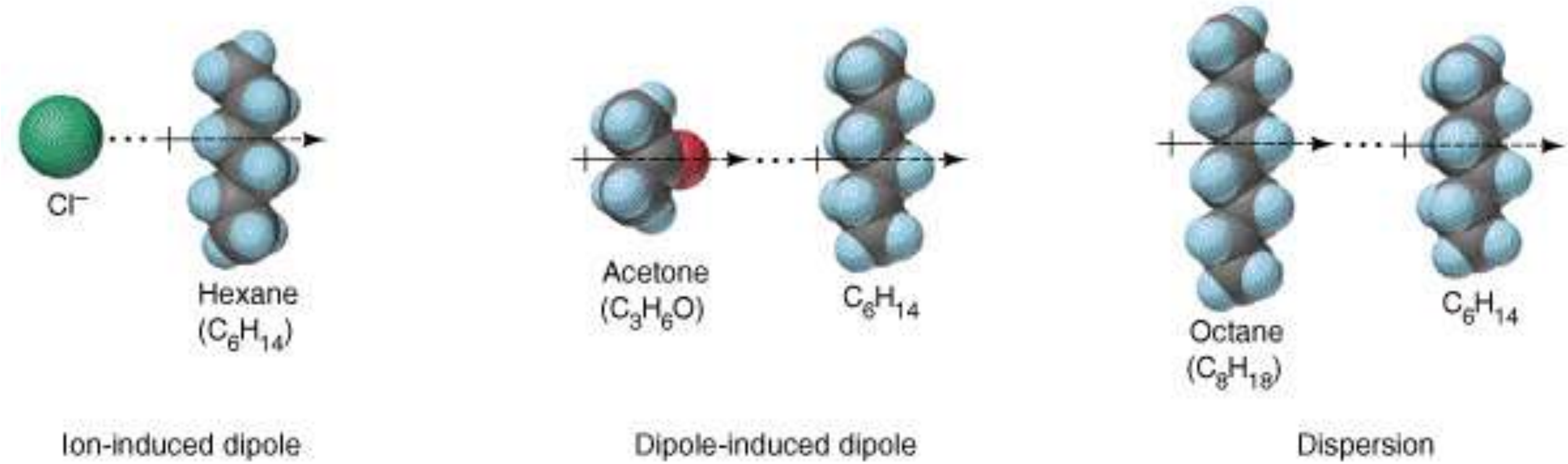
Gustina elektrona u benzenu

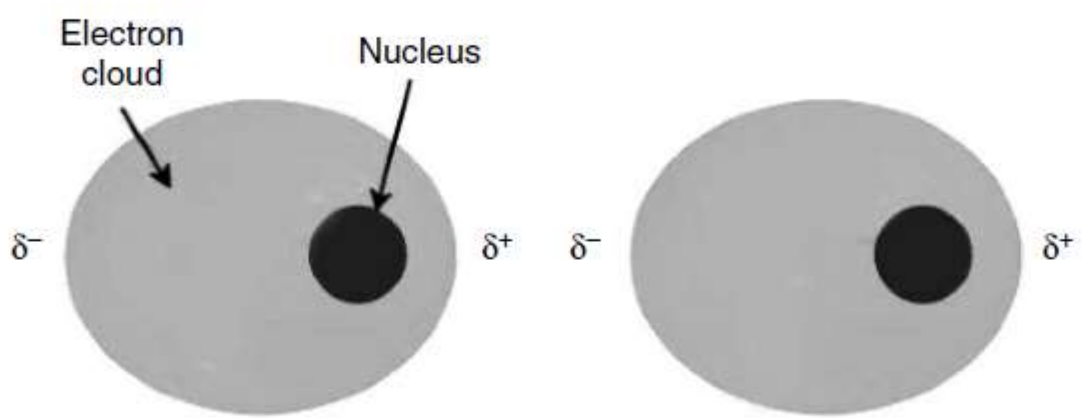


Pakovanje antracena (riblja kost)


-1/2
+
-1/2
repulsion
-1/2
+
-1/2
-1/2
+
-1/2
attraction
-1/2
+
-1/2
-1/2
+
-1/2
attraction
-1/2
+
-1/2

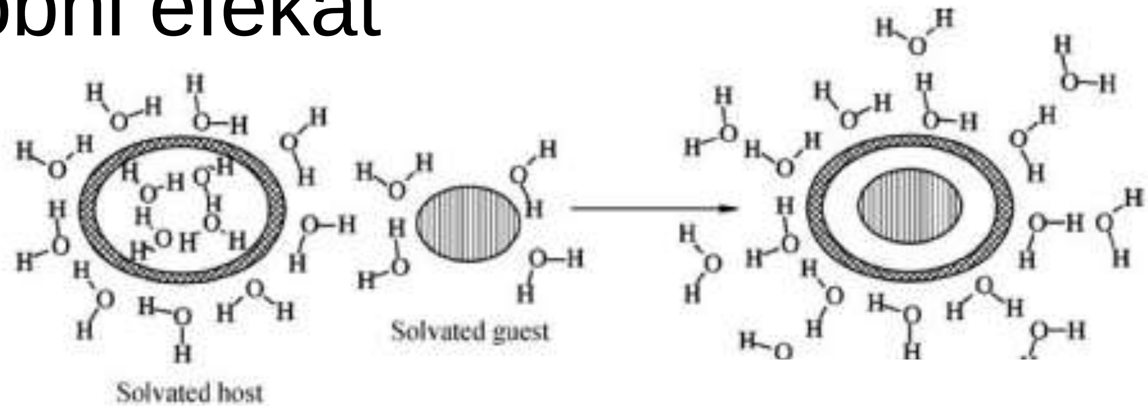
van der Waals-ove (disperzione) sile

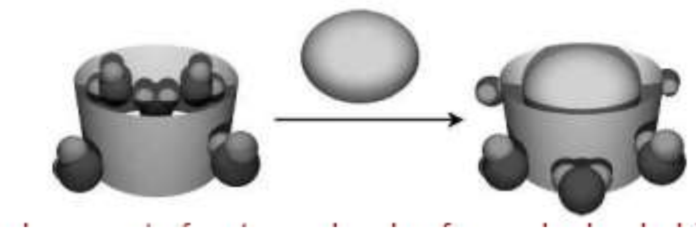


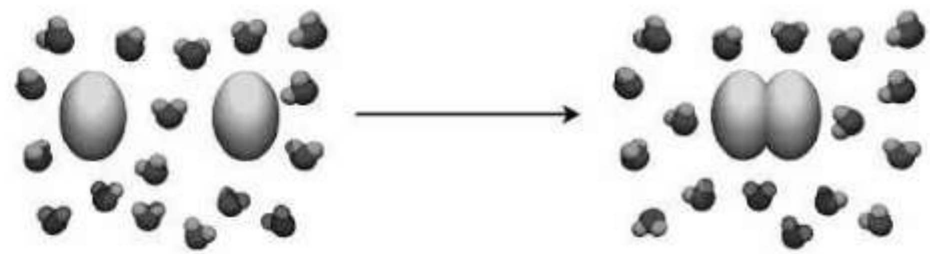


London-ove interakcije između dva atoma argona

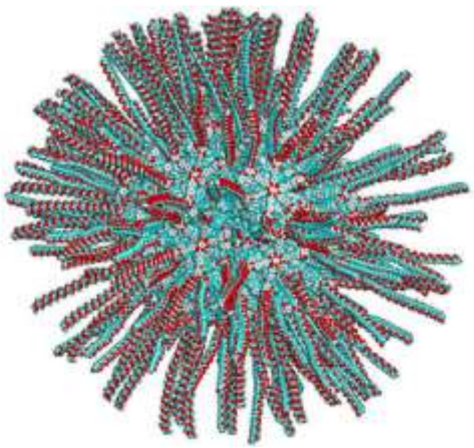
Hidrofobni efekat





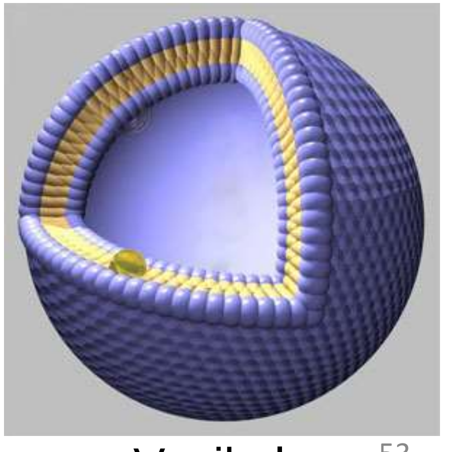


Hidrofobni efekat se može iskoristiti za dobijanje veoma dobro definisanih supramolekulskih struktura



Sverna micela

Cilindrična micela



Vezikula