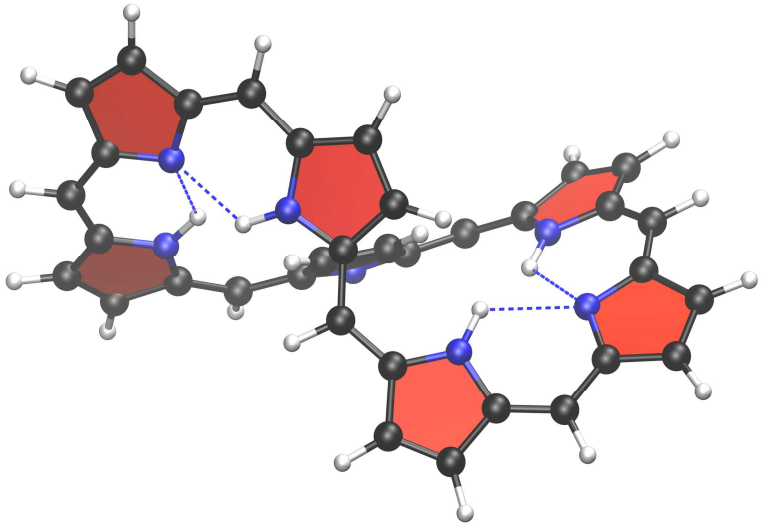
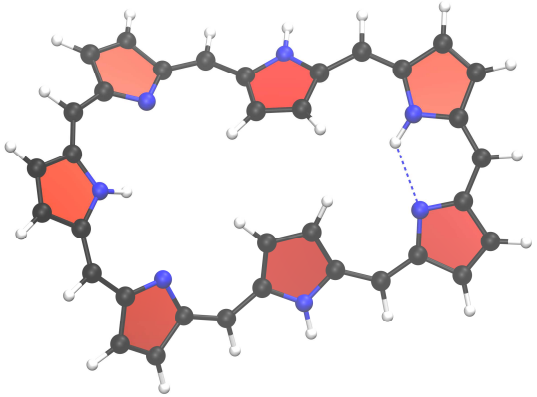
Fine-tuning of the conformation of expanded porphyrins using conceptual DFT descriptors and non-covalent index

Mercedes Alonso, Frank De Proft and Paul Geerlings





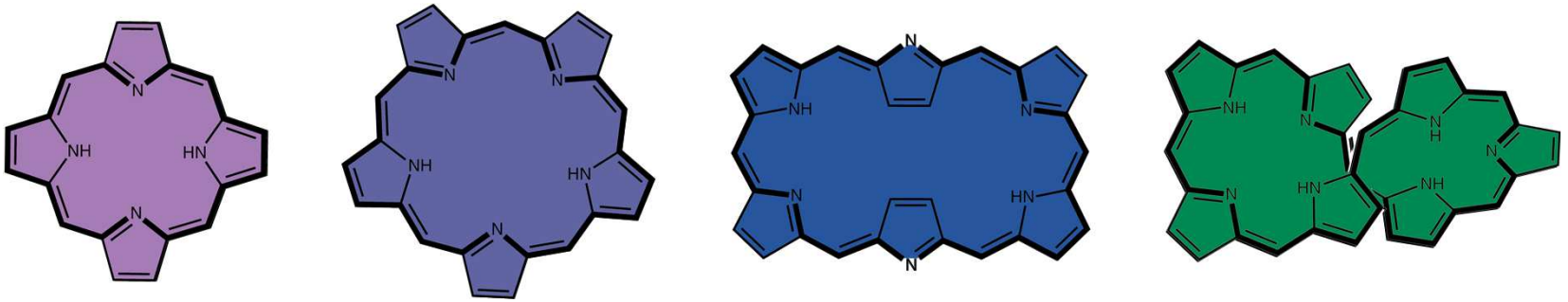
Topological Approaches to Intermolecular Interactions, Paris 2013

Overview

- Introduction
- Computational approach
- Results and discussion
- Conclusions

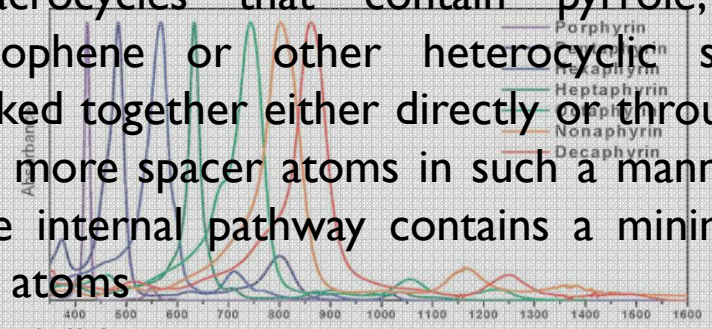
Expanded Porphyrins

porphyrin (*N* = 4) **pentaphyrins** (*N* = 5) **hexaphyrins** (*N* = 6) **heptaphyrins** (*N* = 7)



expansion

Macrocycles that contain pyrrole, furan, thiophene or other heterocyclic subunits linked together either directly or through one or more spacer atoms in such a manner that the internal pathway contains a minimum of 17 atoms



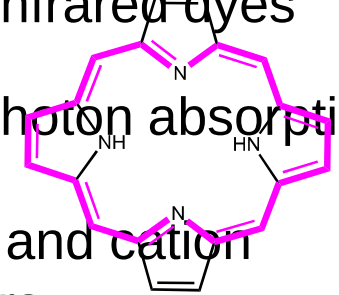
Visible NIR

J. L. Sessler, D. Seidel, *Angew. Chem. Int. Ed.* 2003, *42*, 5134

Near-infrared dyes

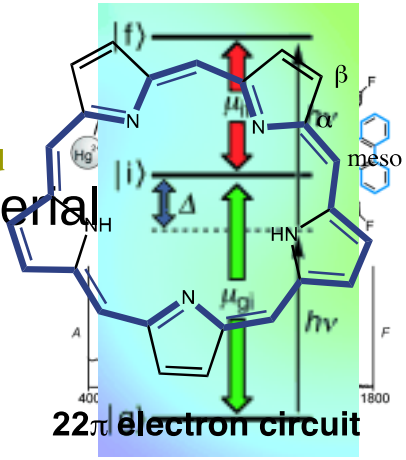
Two-photon absorption material

Anion and cation sensors



18π electron circuit

Expanded

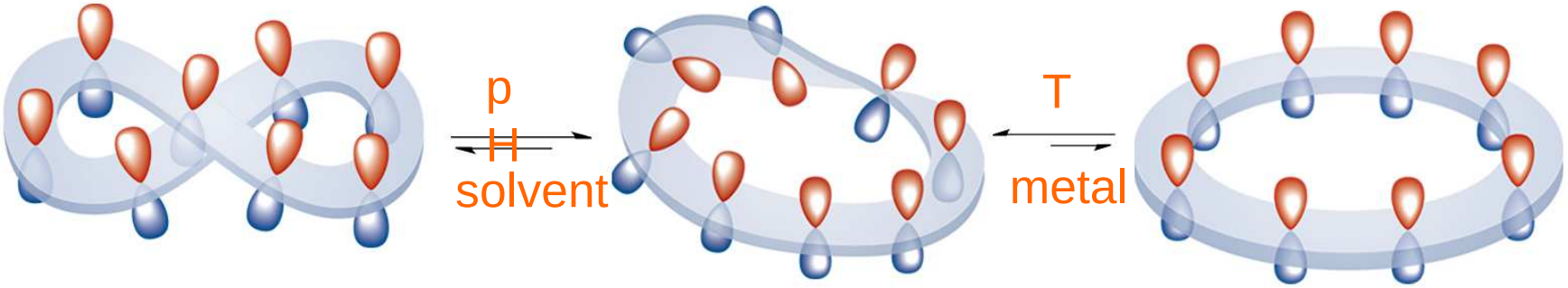


22π electron circuit

Large σ_{TPA}

A. Osuka et al. *Angew. Chem. Int. Ed.* 2011, 50, 4342
K. Rurack *Angew. Chem. Int. Ed.* 2008, 47, 193
L. Latos-Grazynski *et al. Angew. Chem. Int. Ed.* 2011, 50, 4288

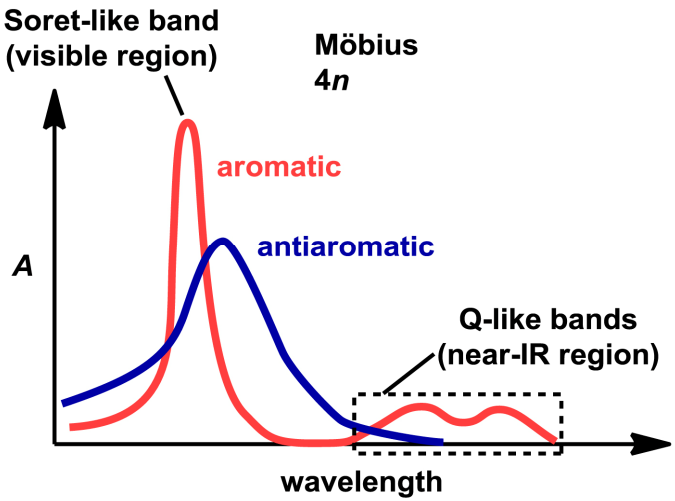
Molecular switches

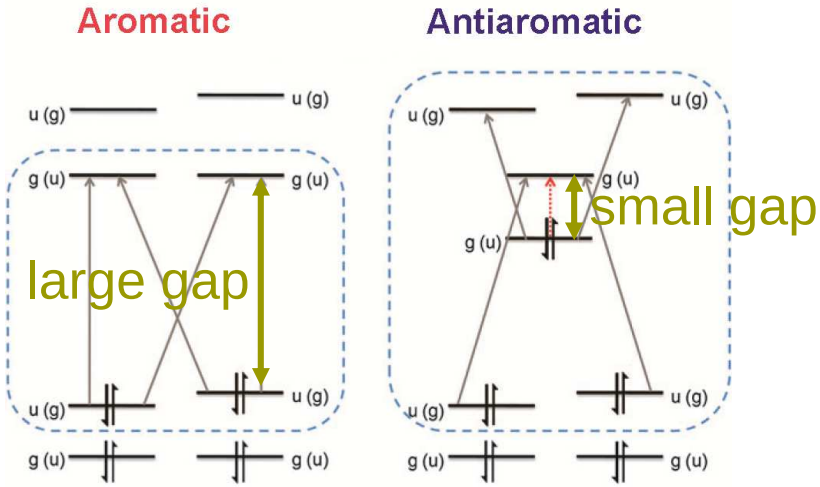


twisted Hückel
$L_k = 2$

Möbius
$L_k = 1$

Hückel
$L_k = 0$



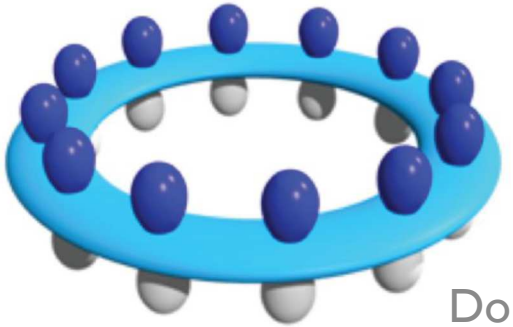


S. Saito, A. Osuka *Angew. Chem. Int. Ed.* **2011**, *50*, 4342

H. S. Rzepa *et al. J. Am. Chem. Soc.* 2008, 130, 7613

Hückel and Möbius aromaticity

Hückel



Doubled-sided

[4*n* + 2] π : **aromatic**

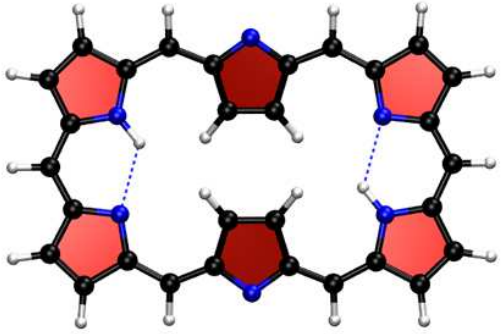
[4*n*] π : **antiaromatic**

Möbius

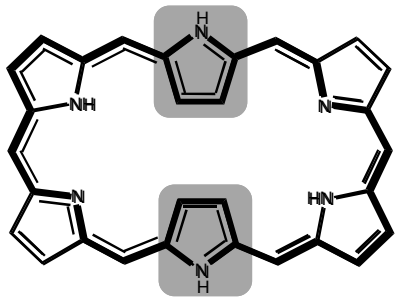
Single-sided

[4*n*] π : **aromatic**

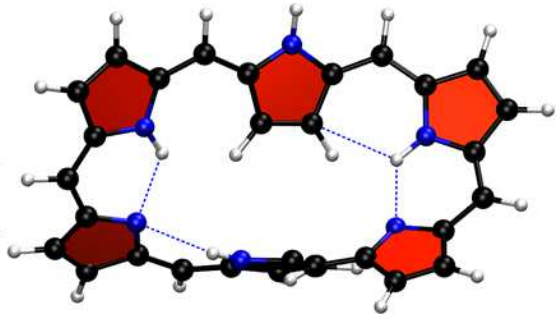
[4*n* + 2] π : **antiaromatic**



antiaromatic



26π



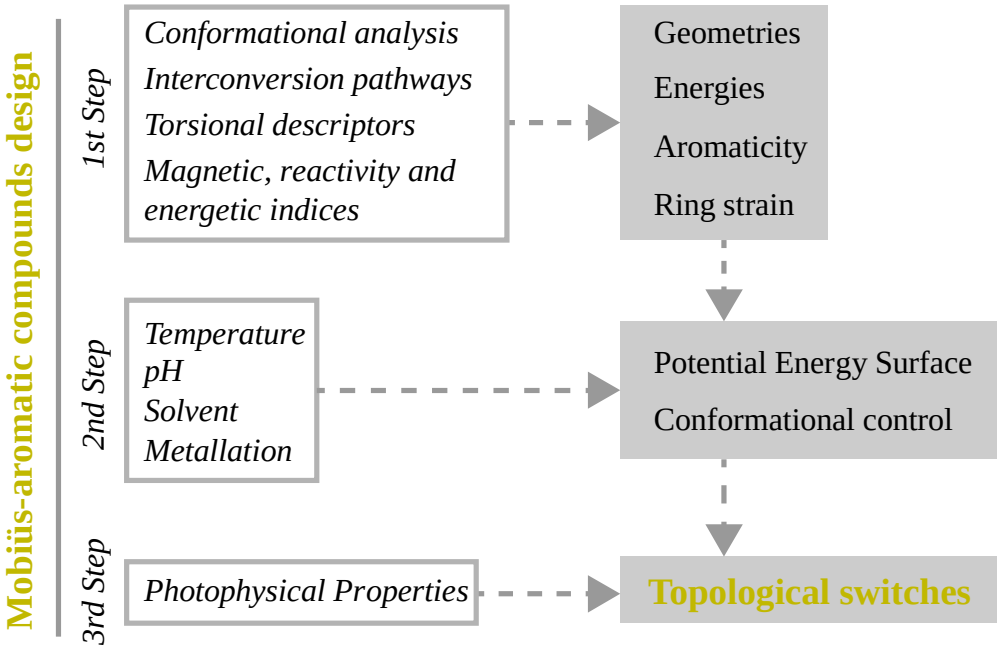
aromatic

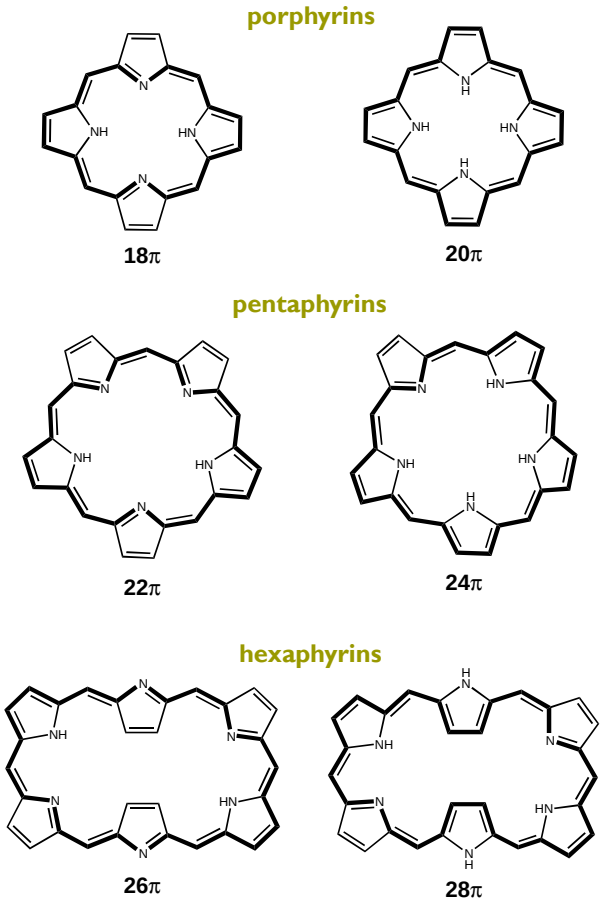
E. Heilbroner, *Tetrahedron Lett.* **1964,** *29*, 1923

M. Alonso, P. Geerlings, F. De Proft, *Chem. Eur. J.* **2012,** *18*, 10916

APPROACH

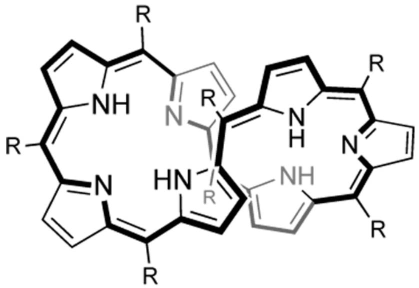
Optimum conditions for **Möbius aromatic compounds** and **topological switches** with unique magnetic properties using DFT



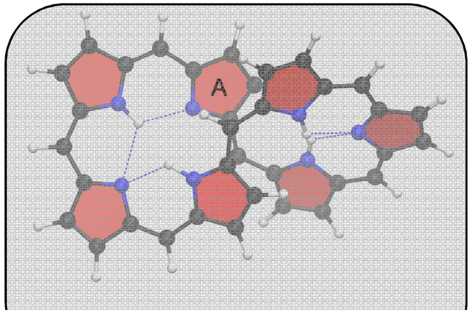
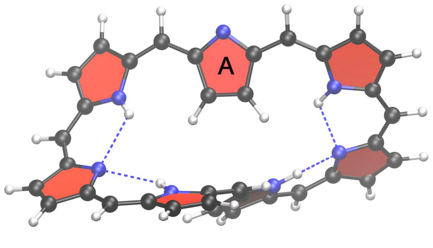
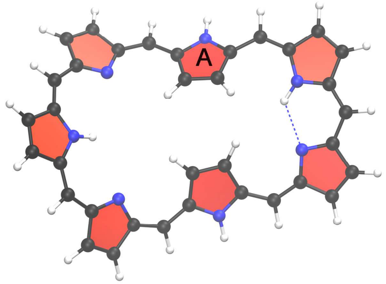


Conformational stability

B3LYP/6-31++G**



R = CF_3, CH_3, H, Phe, C_6F_5

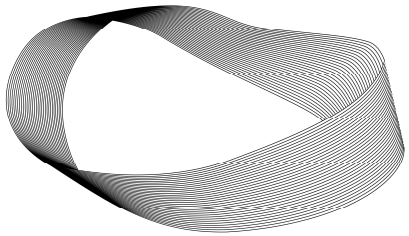
	two half-twists 0.0	one half-twist 5.2	no twist 25.7
			
	Figure-eight	**Möbius**	**Hückel**
Ring strain ➔ Φ_P	**19.0**	28.0	24.3
Hydrogen bonding ➔ N_H	**3.5**	3.0	1.0
Effective p overlap ➔ Π	**0.72**	-0.57	0.59

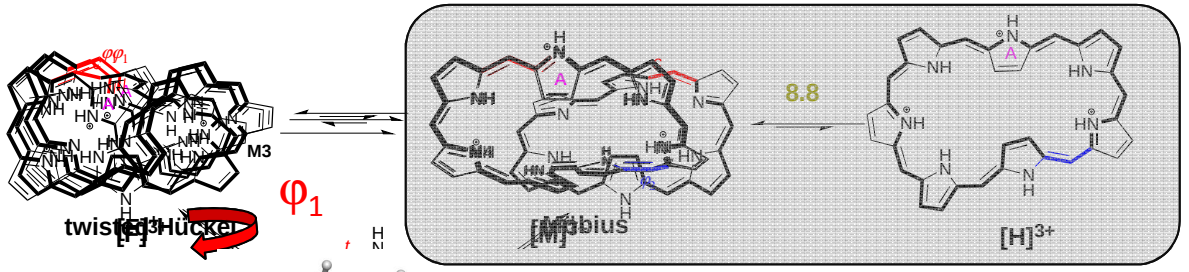
Aromaticity ➔ ASE, Λ, NICS, HOMA, $\Delta\eta$

$$\Pi = \prod_i \cos\varphi_i$$

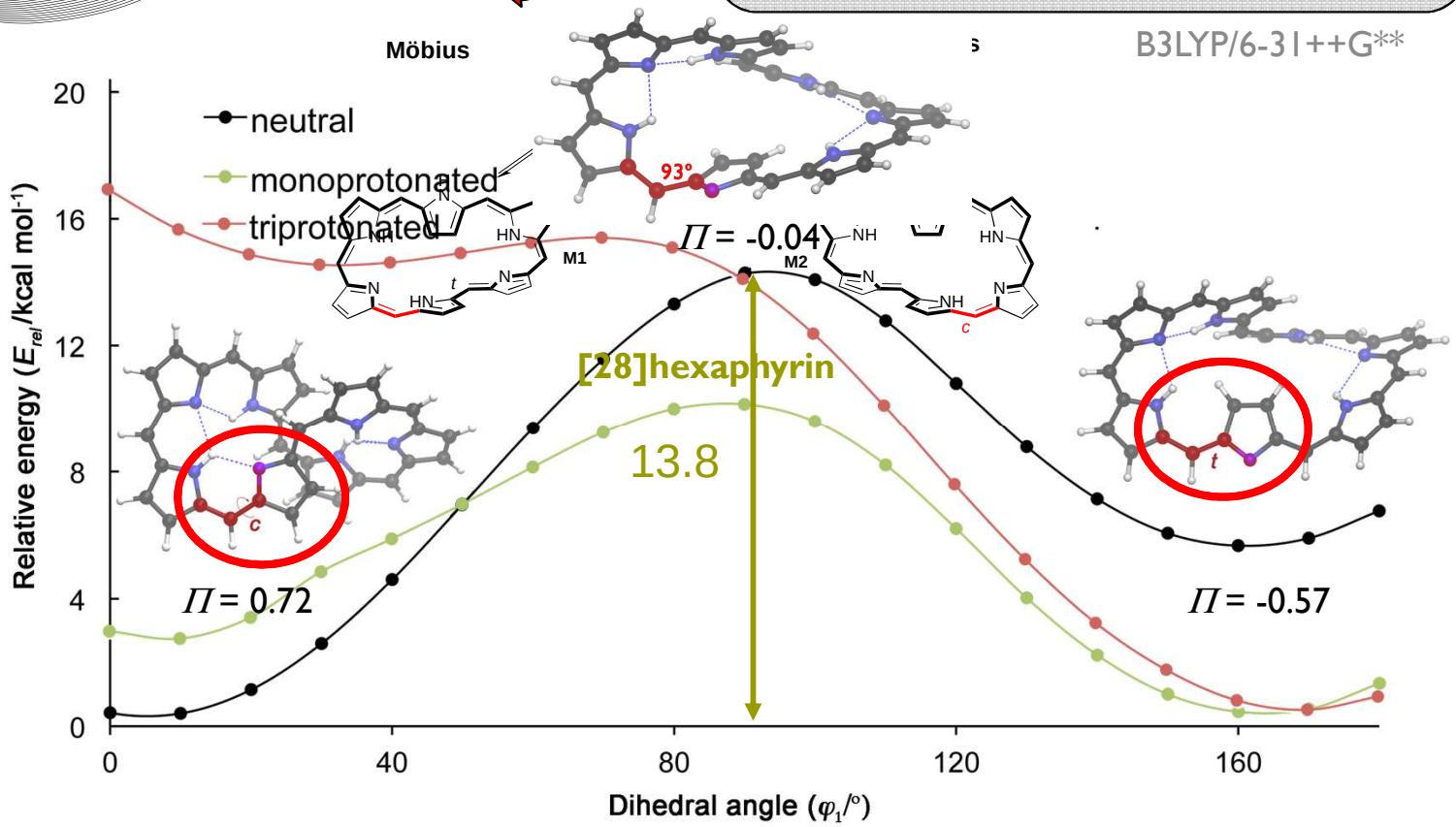
Steric effects of *meso*-substituents ➔ NCI index

Hückel-Möbius topology switch





B3LYP/6-31++G**

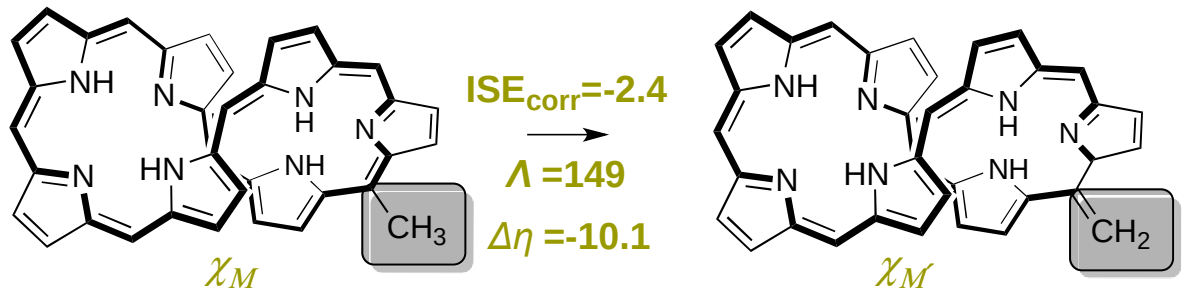


Protonation is an effective way for controlling the conformation!

Aromaticity descriptors

Aromaticity is a **multidimensional** property cannot be quantified with a single-index

ENERGETIC



ISE > 0 : **aromatic**
ISE < 0 : **antiaromatic**

syn/anti corrections

P. v. R. Schleyer *et al. Org. Lett.* 2002, *4*, 2873

MAGNETIC

Λ : Diamagnetic Susceptibility Exaltation $\Lambda = \chi_M - \chi_{M'}$

Λ < 0 : **aromatic**
Λ > 0 : **antiaromatic**

H. J. Dauben *et al. J. Am. Chem. Soc.* 1968, *90*, 811

REACTIVITY

$\Delta\eta$: Relative hardness $\eta = I - A \approx \varepsilon_{LUMO} - \varepsilon_{HOMO}$

$\Delta\eta$ > 0 : **aromatic**
$\Delta\eta$ < 0 : **antiaromatic**

F. De Proft, P. Geerlings, *Phys. Chem. Chem. Phys.* 2004, *6*, 242.

X. Alonso *et al Phys. Chem. Chem. Phys.* **2010**, *12*, 1305; *J. Comput. Chem.* 2010, 31, 917.
P. v. R. Schleyer *et al J. Am. Chem. Soc.* **2013**, *135*, 315

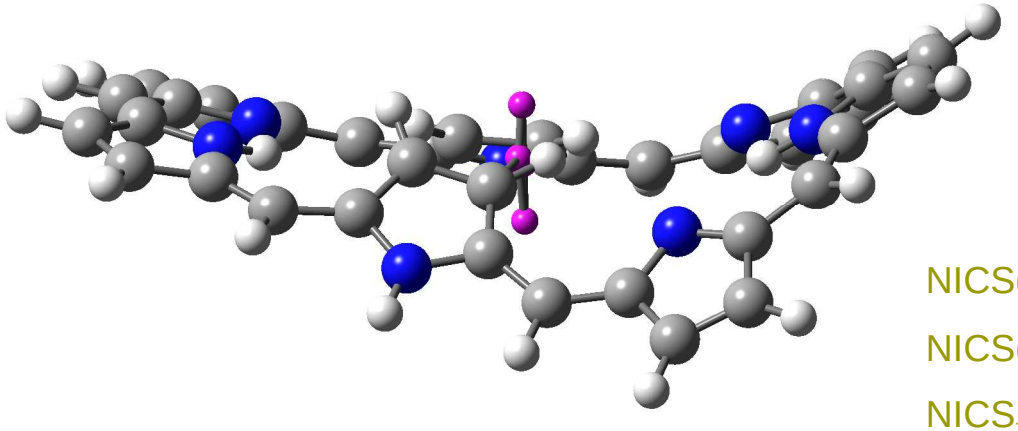
First time that these descriptors are computed for expanded porphyrins !

Aromaticity descriptors

MAGNETIC

NICS: Nucleus-independent chemical shift

GIAO/B3LYP/6-311+G**



NICS < 0 : **aromatic**
NICS > 0 : **antiaromatic**

NICS(0) = 19.1

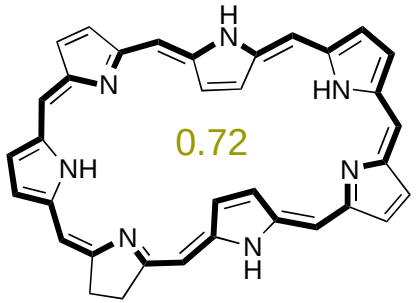
NICS(±1) = 17.3

$NICS_{zz}(\pm 1)$ = 57.3

P. v. R. Schleyer *et al.* *J. Am. Chem. Soc.* 1996, *118*, 6317

ESTRUCTURAL

HOMA



$$HOMA = 1 - \frac{\alpha}{n}\sum_{i=1}^{n}(R_{opt} - R_i)^2$$

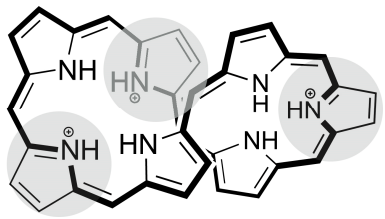
HOMA = 1 : **fully aromatic**
HOMA = 0 : **nonaromatic**

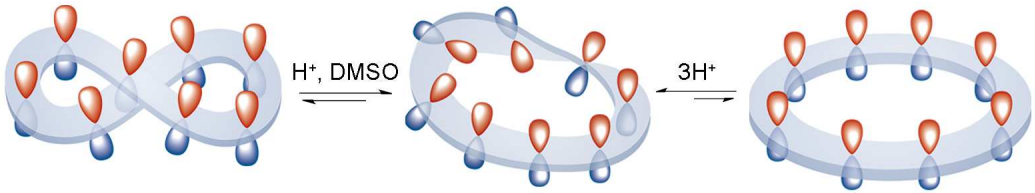
T. M. Krygowski *et al.*, *Tetrahedron Lett.* 1972, *13*, 3

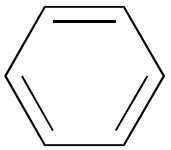
Performance of these indices to describe Möbius aromaticity??

Aromaticity of [32]heptaphyrin

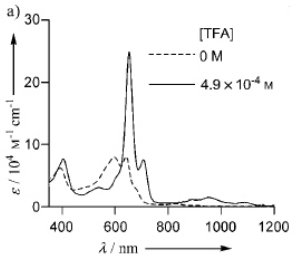
triprotonated







benzene



UV/VIS spectra upon TFA addition

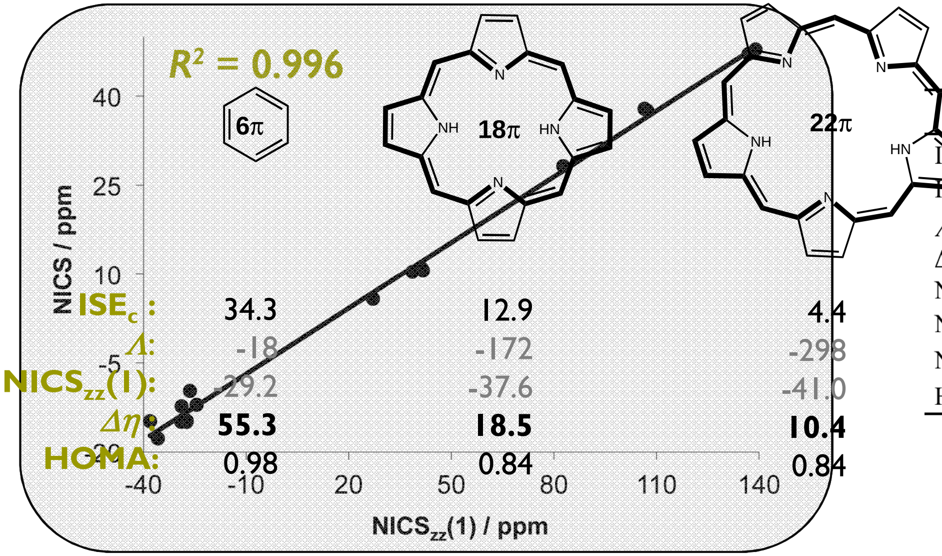
	twisted Hückel		Möbius		Hückel		benzene
ISE_{corr}	-2.4	-11.0	5.8	3.1	-3.4	-4.4	34.3
Λ	149	408	-219	-315	584	1176	-17.8
NICS(0)	9.8	16.1	-11.0	-12.7	19.1	28.2	-8.0
$NICS_{zz}(1)$	23.8	57.9	-24.1	-30.2	57.3	93.9	-29.2
HOMA	0.71	0.74	0.84	0.81	0.72	0.74	0.98
$\Delta\eta$	-10.1	-9.7	4.9	4.1	-5.9	-9.2	55.3
	weakly antiaromatic		**aromatic**		**antiaromatic**		**aromatic**
	σ_{TPA} = 1800 GM		σ_{TPA} = 5100 GM				

ISE_{corr} and Δ are given in kcal mol^{-1}, α in ppm cgs and NICS indices in ppm

Close relationship between the topology and aromaticity

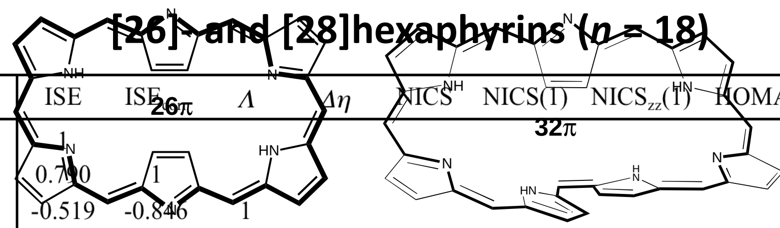
A. Osuka, *Angew. Chem. Int. Ed.* **2008**, *47*, 9681

Correlation between aromaticity indices



	6π	18π	22π	26π	32π
ISE_c:	34.3	12.9	4.4	7.4	5.8
Λ:	-18	-172	-298	-400	-219
$NICS_{zz}(1)$:	-29.2	-37.6	-41.0	-35.8	-24.1
$\Delta\eta$:	55.3	18.5	10.4	7.1	4.9
HOMA:	0.98	0.84	0.84	0.88	0.84

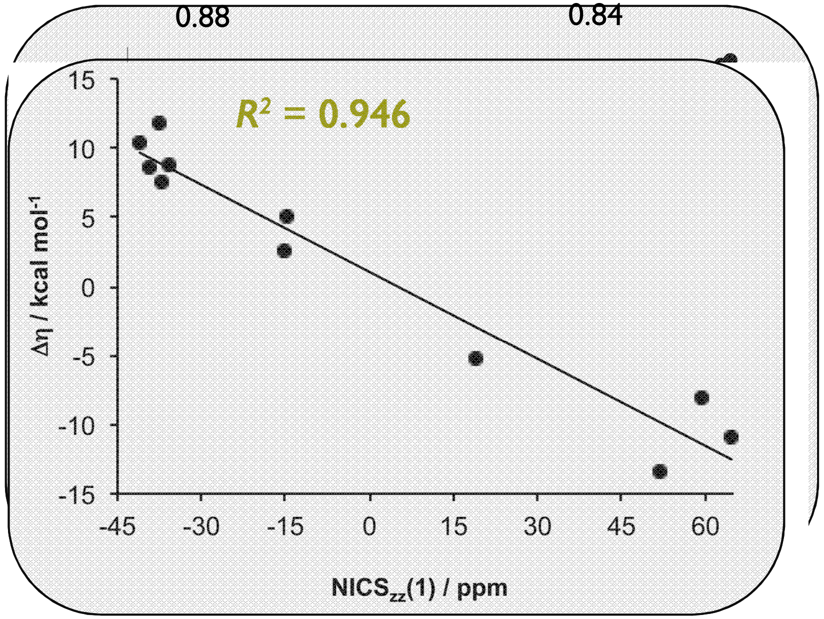
[26]- and [28]hexaphyrins (n = 18)



	ISE	ISE_{corr}	Λ	$\Delta\eta$	NICS	NICS(1)	$NICS_{zz}(1)$	HOMA
ISE	1							
ISE_{corr}	0.790	1						
Λ	-0.519	-0.846	1					
$\Delta\eta$	0.676	0.967	-0.879	1				
NICS(0)	-0.509	-0.870	**0.993**	**-0.909**	1			
NICS(1)	-0.497	-0.868	**0.991**	**-0.905**	**0.999**	1		
$NICS_{zz}(1)$	-0.530	-0.878	**0.992**	**-0.910**	**0.998**	**0.999**	1	
HOMA	0.855	0.926	-0.728	**0.898**	-0.753	-0.753	-0.772	1

[22]- and [24]pentaphyrins (n = 11)

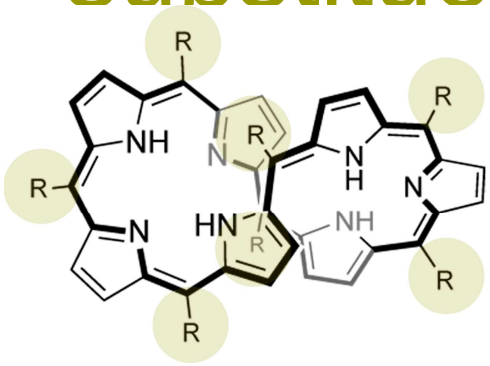
	ISE	ISE_{corr}	Λ	$\Delta\eta$	NICS	NICS(1)	$NICS_{zz}(1)$	HOMA
ISE	1							
ISE_{corr}	**0.919**	1						
Λ	-0.743	-0.885	1					
$\Delta\eta$	0.746	0.884	**-0.992**	1				
NICS(0)	-0.733	-0.883	**0.985**	**-0.973**	1			
NICS(1)	-0.734	-0.885	**0.986**	**-0.973**	**1.000**	1		
$NICS_{zz}(1)$	-0.719	-0.875	**0.989**	**-0.973**	**0.998**	**0.998**	1	
HOMA	0.772	0.834	**-0.948**	**0.931**	**-0.908**	**-0.910**	**-0.913**	1



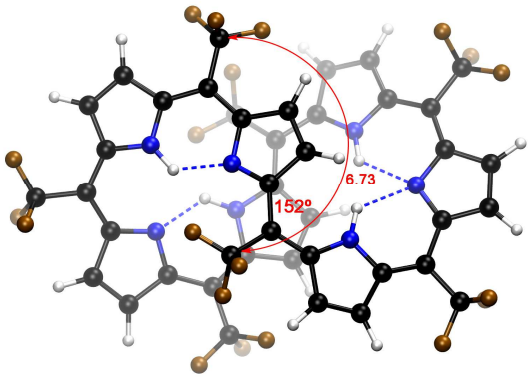
Good correlation between aromaticity indices!

$\Delta\eta$ is not size-dependent and easy to compute!

Conformational control by substituents



R = CF_3



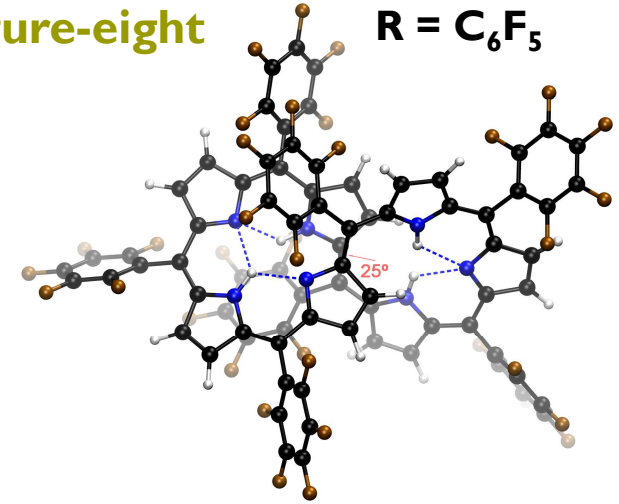
ΔE_{M-F} = 6.8

TFA

$\Delta E_{(M-F)^+}$ = 0.9

figure-eight

R = C_6F_5



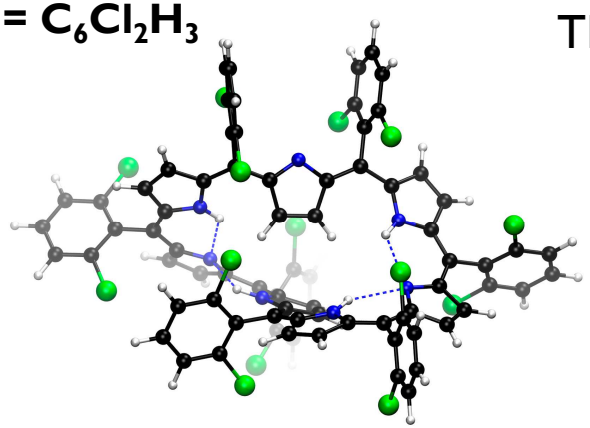
ΔE_{M-F} = 2.8

TFA

$\Delta E_{(M-F)^+}$ = -2.8

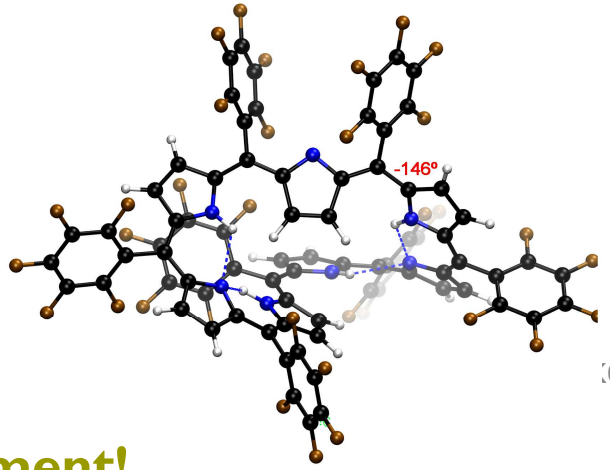
Möbius

R = $C_6Cl_2H_3$



ΔE_{M-F} = -10.0 ⇒ $\Delta E_{(M-F)^+}$ = -16.7

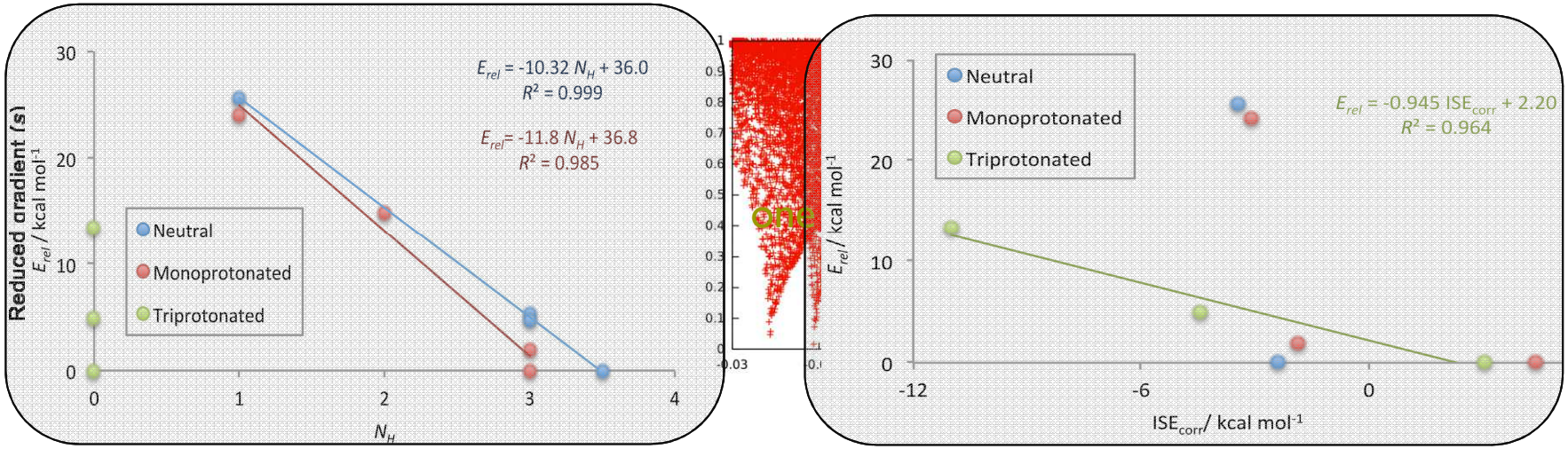
A. Osuka, *Angew. Chem. Int. E*
2006, 12, 9095

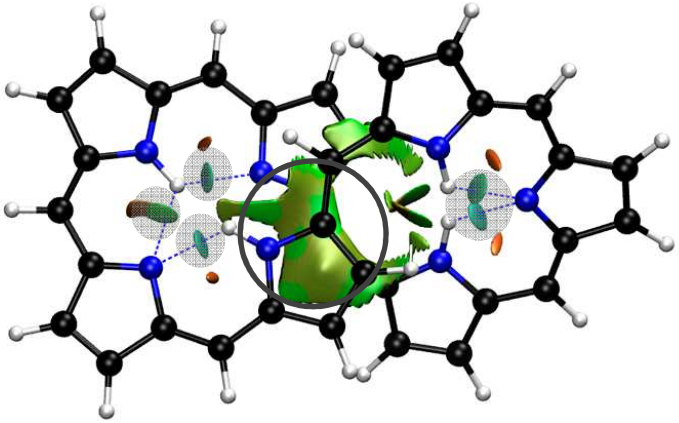


ΔE_{M-F} is the energy difference between the Möb

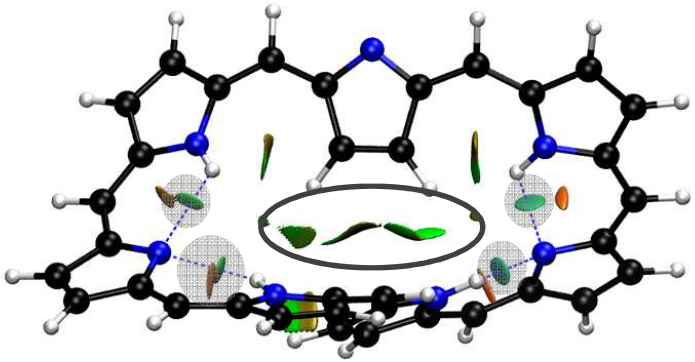
Excelent agreement with the experiment!

NCI index in heptaphyrins





N_H = 3.5 ISE$_c$ = -2.4



N_H = 3.0 ISE$_{corr}$ = 5.8

Aromaticity controls the E_{rel} of [32]heptaphyrin!

W. Yang *et al. J. Am. Chem. Soc.* 2010, *132*, 6498
J. Contreras-García *et al. Chem. Theory Comput.* 2011, *7*, 625

NCI of meso-substituted heptaphyrins

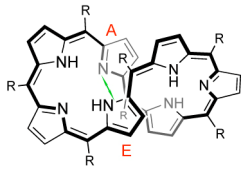
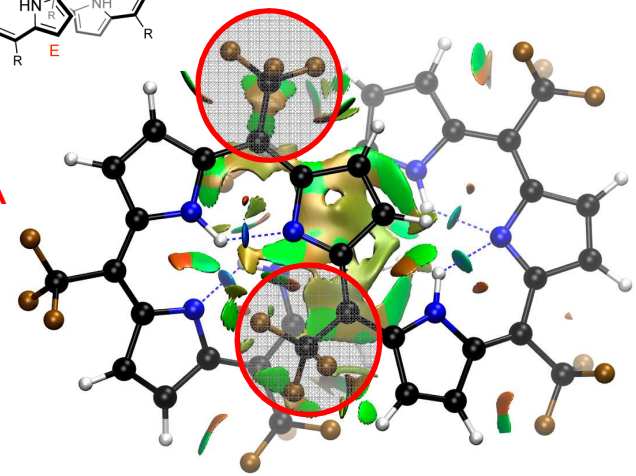


figure-eight



6.7 Å

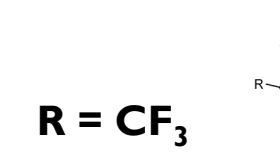
$R = CF_3$

hydrogen bonds

π–π interactions

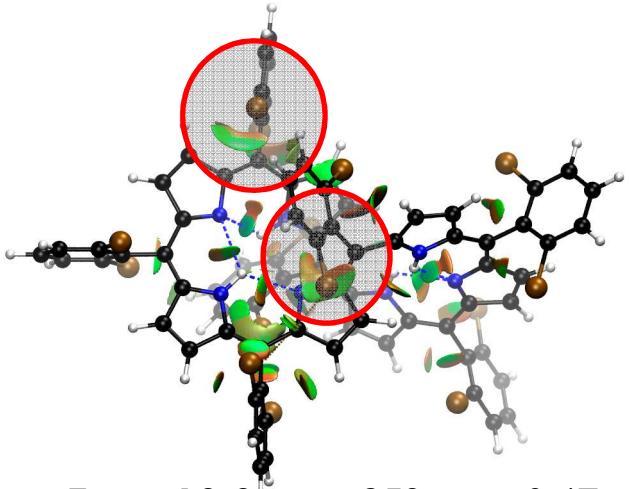
CF···X (X=N, H)

steric clashes

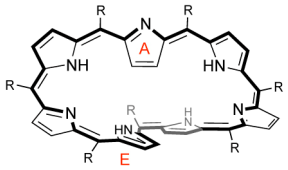


-0.04 sign(λ_2)ρ / a.u. 0.02

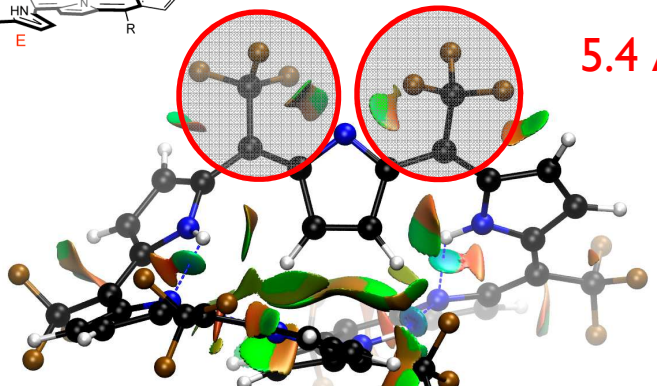
$R = C_6Cl_2H_3$



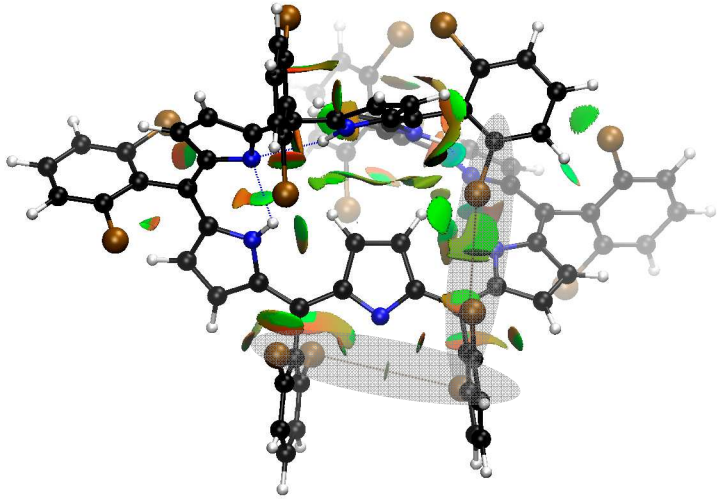
E_{rel} = **-10.0** Φ_P = 25° Π = 0.47



Möbius



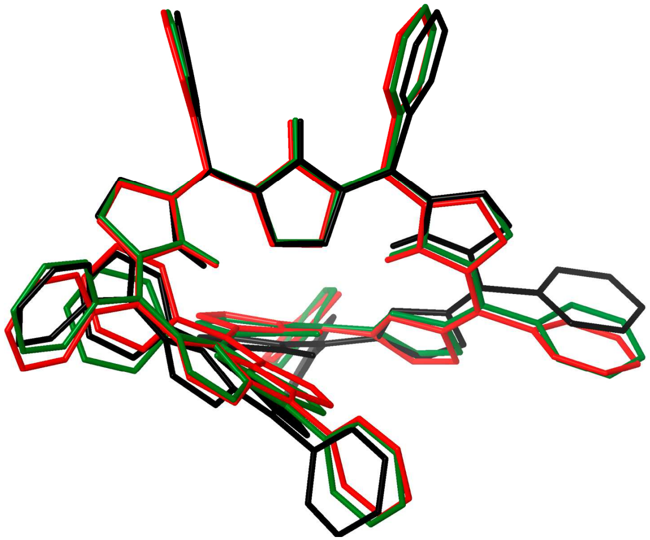
5.4 Å



E_{rel} = **0.0** Φ_P = 30° Π = -0.50

Performance of density functionals

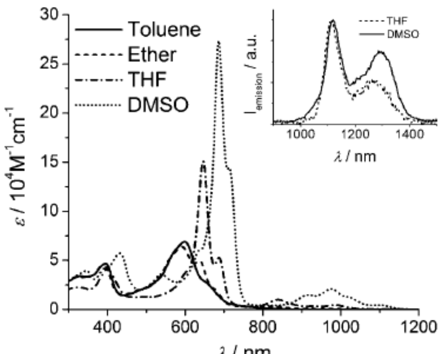
B3LYP ➔lack of medium and long-range dispersion➔M06-2X and DFT-D



	RMSDs	HOMA	R_{A-E}	R_{G-Ar}
RX		0.83	4.65	3.82
B3LYP	0.69	0.78	4.65	4.15
M06-2X	0.89	0.74	3.88	3.52
B3LYP-D	0.77	0.80	3.91	3.50

Overestimate π-π stacking interactions!

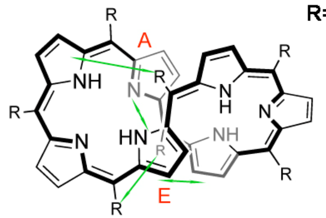
n

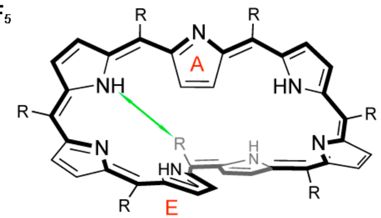


Absorption spectra in various solvents

[32]heptaphyrins

R=C_6F_5





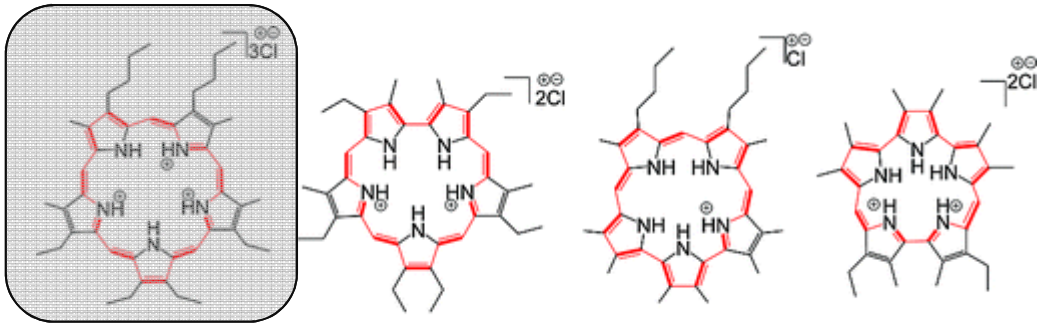
neutral	B3LYP	0.0	(2.8)	2.8	(0.0)
(monoprotonated)	M06-2X	0.0	(0.0)	16.2	(6.0)
	B3LYP-D	0.0	(0.0)	13.5	(6.0)

Relative energies in kcal mol⁻¹

B3LYP shows the best overall performance

A. Osuka et al. *Chem. Eur. J.* 2011, 17, 6707

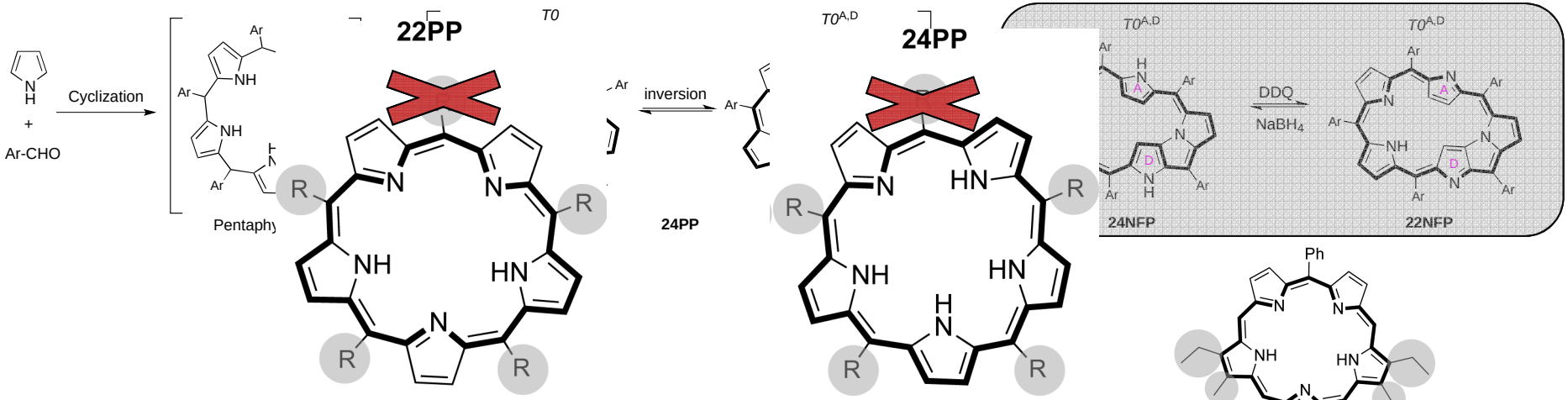
[22]- and [24]pentaphyrins



1 Pentaphyrin **2** Sapphyrin **3** Isosmaragdyrin **4** Orangarin

σ_{TPA} (GM) : 3300 2900 2700 1200

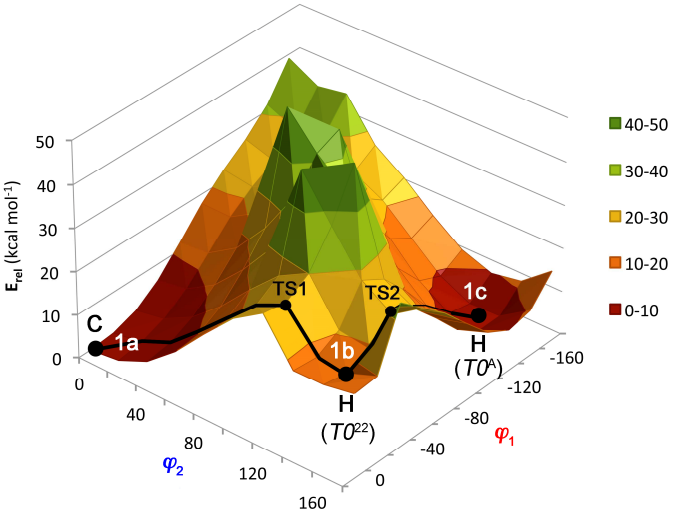
→ Photodynamic therapy



Removing one meso-substituent provides non-fused pentaphyrins

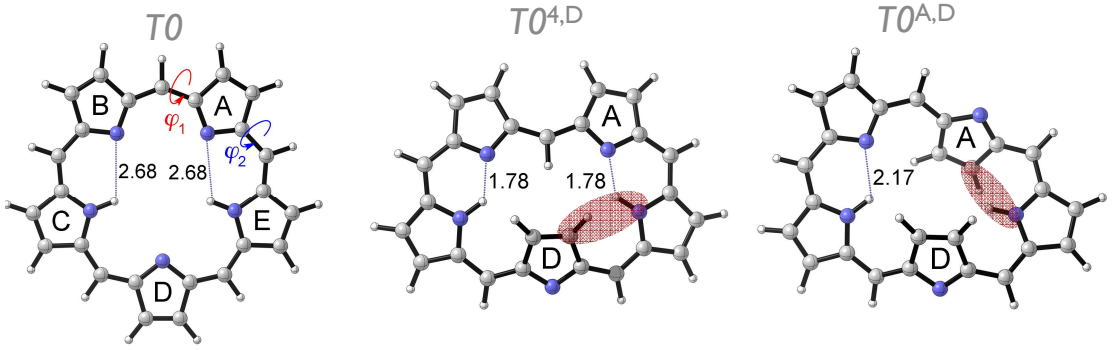
M. Stępień et al. Angew. Chem. Int. Ed. 2006, 45, 1091; M. Stępień et al. Chem. Eur. J. 2007, 13, 1596; M. Stępień et al. Tetrahedron 2006, 62, 8147; M. Stępień et al. J. Org. Chem. 2005, 70, 1214; M. Stępień et al. J. Am. Chem. Soc. 2008, 130, 6930

Conformations of [22]pentaphyrins



B3LYP/6-31++G(d,p) potential energy surface

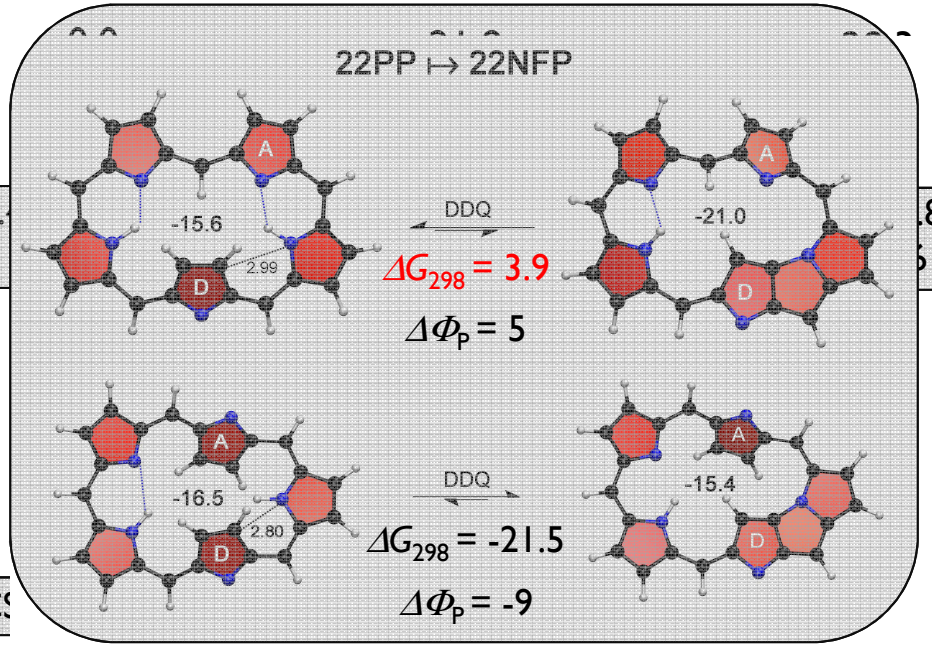
Hückel



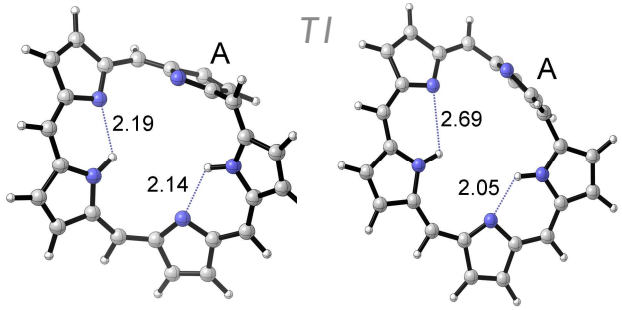
E_{rel}	0.0	0.1	15.2
Φ_P			
Π			

ISE$_c$=4.
Δη

.82



Möbius

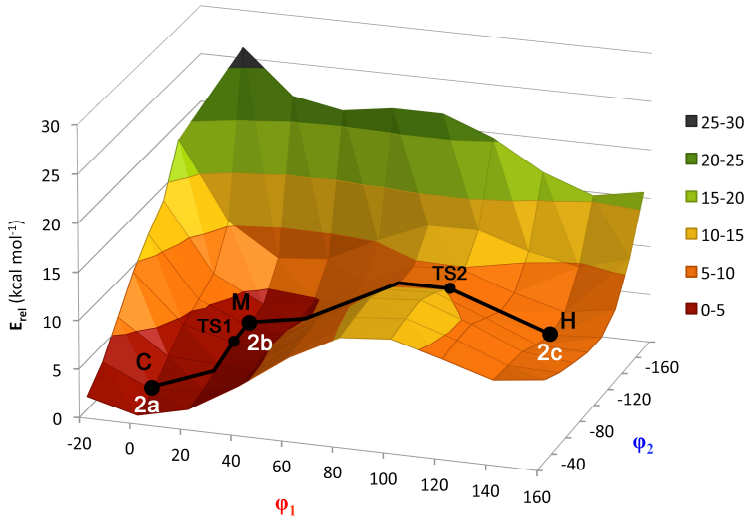


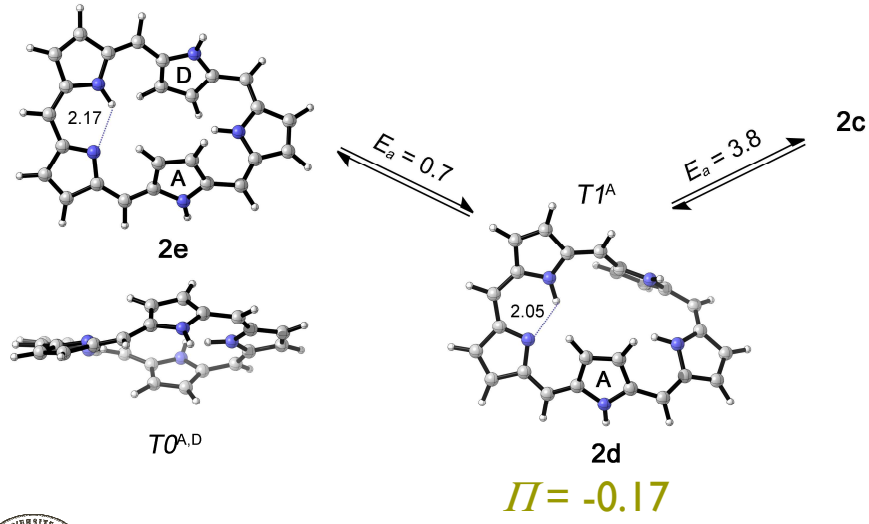
	TS1	TS2
ΔG	26.6	25.8

HOMA= 0.56 NICS

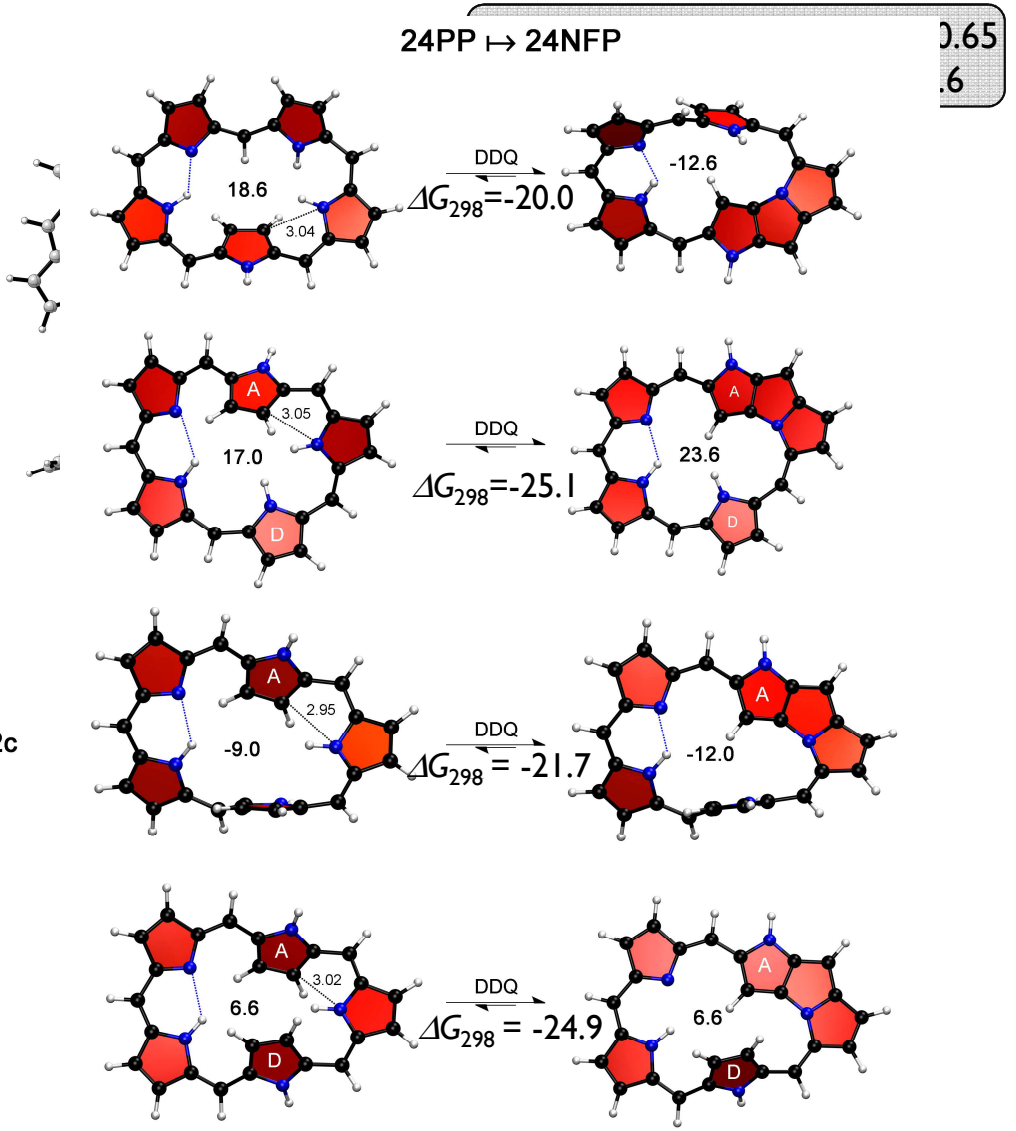
$T0^{4,D}$ conformer does not undergo the N-fusion reaction

Conformations of [24]pentaphyrins





$\Pi = -0.17$



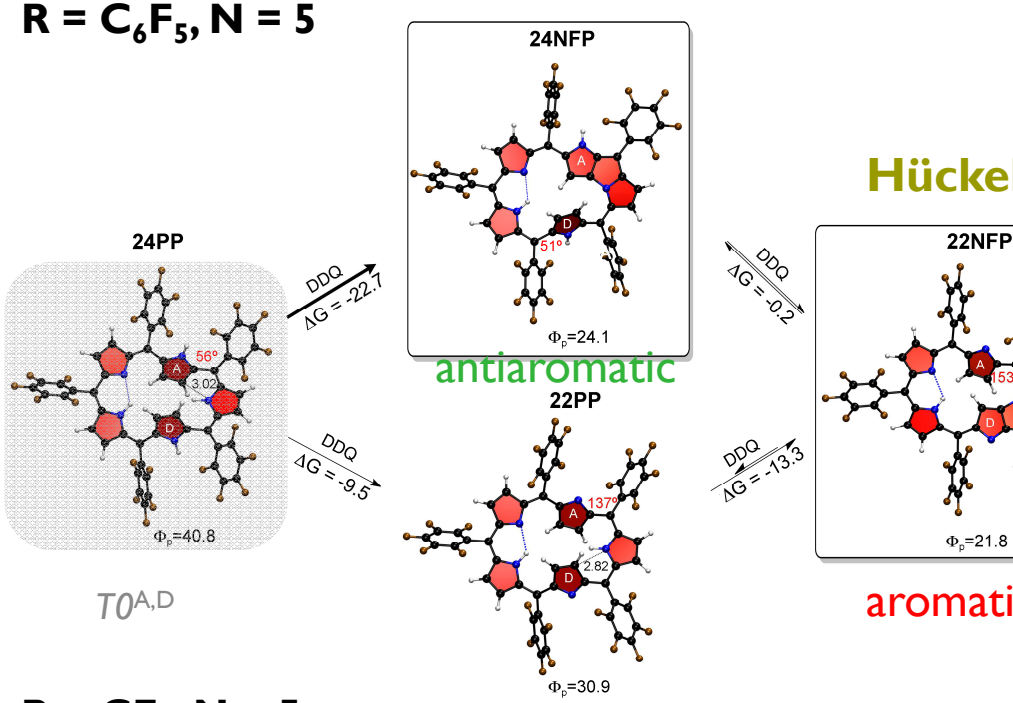
Möbius conformers undergo N-fusion reaction

[24]Pentaphyrin with enhanced aromaticity

Conformation controlled by substituents

R = C_6F_5, N = 5

Hückel



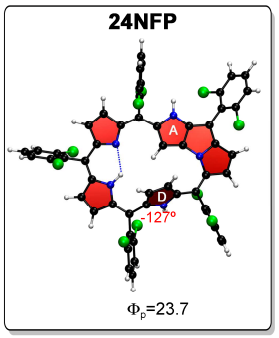
antiaromatic

aromatic

$T0^{A,D}$

R = $C_6H_3Cl_2$, N = 5

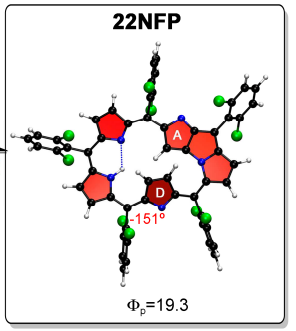
Hückel



antiaromatic

DDQ
ΔG = -5.2

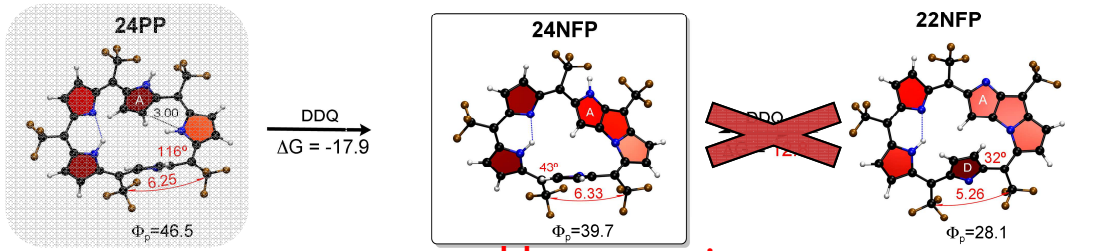
Hückel



aromatic

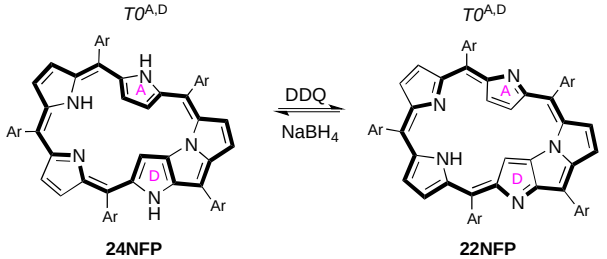
R = CF_3, N = 5

Möbius



weakly aromatic

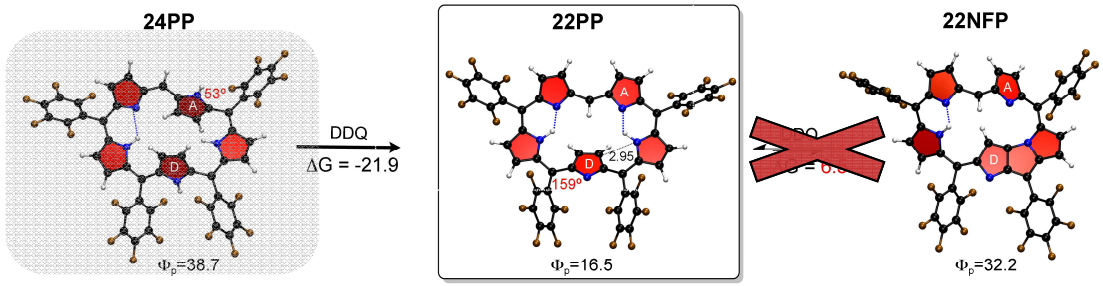
$T1^{A}$



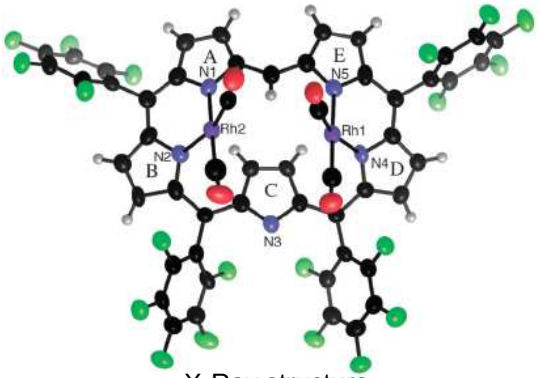
Five substituents → N-fused pentaphyrins

Conformation controlled by substituents

R = C_6F_5, N = 4



T0^{A,D}

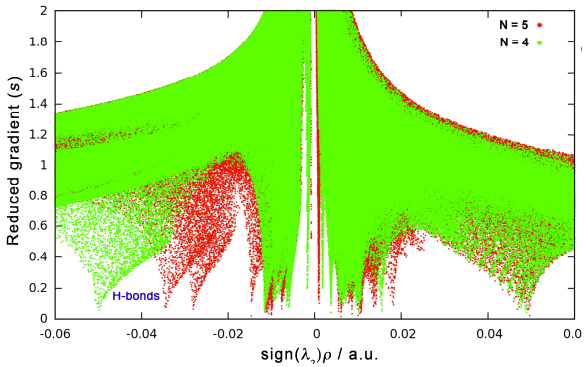


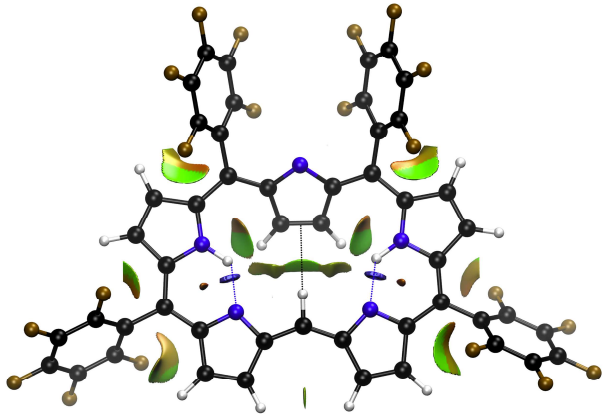
X-Ray structure

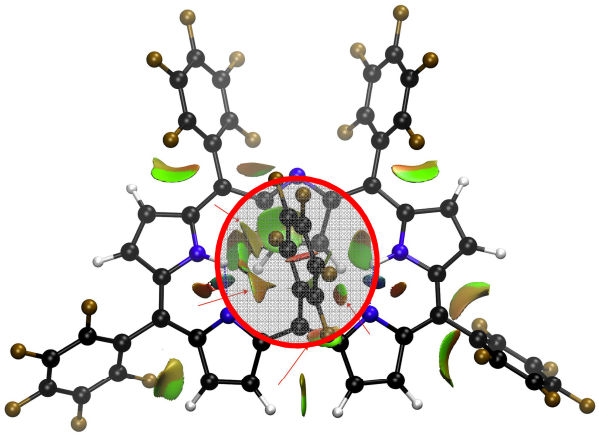
(A. Osuka *et al. Chem. Commun*. 2012, 48, 6785)

N = 4

N = 5







Φ_P = 16.5

Φ_P = 34.1

Four aryl groups ➔ Non-fused [22]pentaphyrins

Conclusions

Conformation strongly depends on the oxidation state and *meso*-substituents

[32]heptaphyrin is a promising molecular switch, that can be induced by protonation

A close relationship exist between molecular topology and aromaticity

Magnetic descriptors and $\Delta\eta$ are the best indices to quantify Möbius and Hückel aromaticity

B3LYP shows the best overall performance for geometries and thermochemistry of expanded porphyrins

NCI is a powerful tool to analyze the steric effects

Aromatic Möbius structures are easily achievable by [32]heptaphyrin and [28]hexaphyrin

M. Alonso, P. Geerlings, F. De Proft *Chem. Eur. J.* **2012,** *18*, 10916-10928.
M. Alonso, P. Geerlings, F. De Proft *Chem. Eur. J.* **2013,** *19*, 1617-1628.
M. Alonso, P. Geerlings, F. De Proft. *J. Org. Chem.* **2013**, 78, 4419-443.

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Prof. Frank De Proft

Dr. Julia Contreras-García

MARIE CURIE ACTIONS

FP7-PEOPLE-2010-IEF-273527

FWO VLAANDEREN

Fonds Wetenschappelijk Onderzoek
Research Foundation – Flanders

Thank you very much for your attention!