OPENING THE DOOR ON MOLECULAR HINGES

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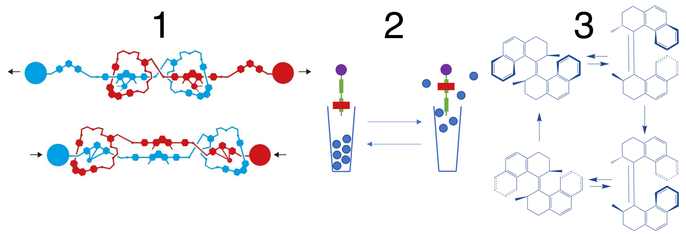
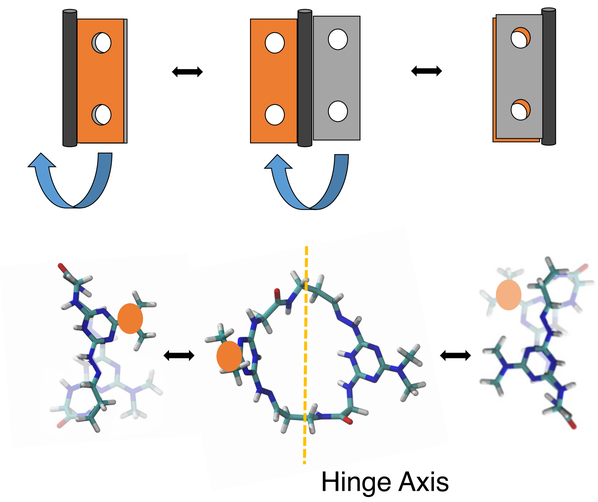
MOLECULAR MACHINES NOBEL LAUREATES

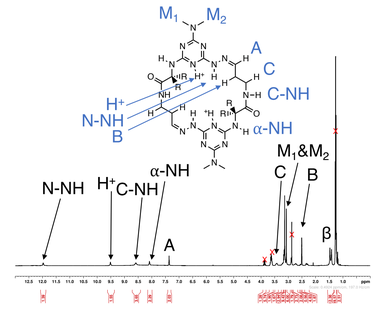


Number	Explanation
1	• **Chemist**: Jean-Pierre Sauvage (Univ. of Strasborg) • **Name of Structure**: Molecular Muscle • **Description of Activity**: Capable of expanding and contracting depending on the type of ion chelated to the molecule.
2	• **Chemist**: Sir J. Frasier Stoddart (Northwestern Univ.) • **Name of Structure**: Nanovalve • **Description of Activity**: Capable of opening or closing depending on the pH of the environment - allowing for precise control of pharmaceutical delivery.
3	• **Chemist**: Bernard Feringa (Univ. of Gronigen) • **Name of Structure**: Molecular Motor • **Description of Activity**: Capable of cycling through different conformations using light and heat.

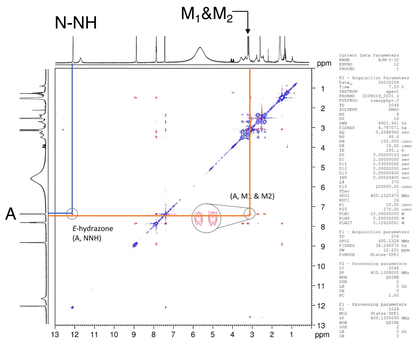
HINGING MOTION

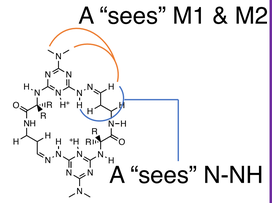


MOLECULE IMAGING



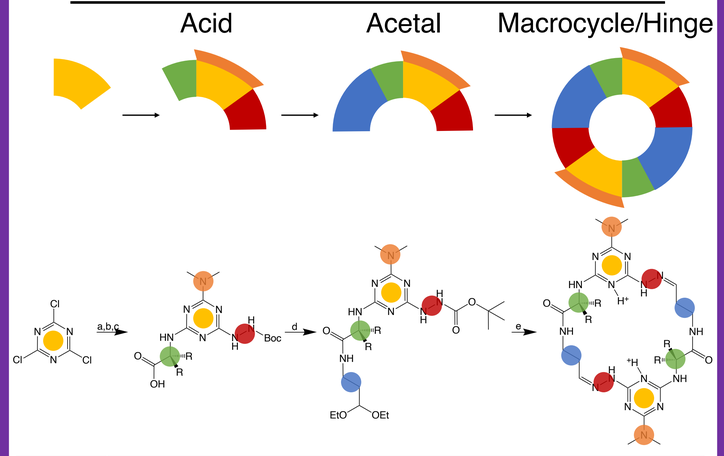
The ^{1}H NMR spectrum of the **AIB-AIB** macrocycle in DMSO-d_6. Position of proton A at 7.3 ppm indicates formation of hydrazone, and loss of protecting group indicates complete cyclization.





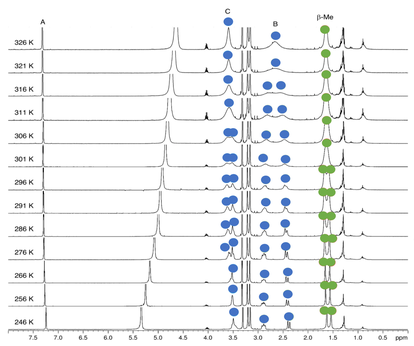
ROESY spectrum indicates that macrocycle adopts folded conformation in solution, which is consistent with hinging.

SYNTHETIC APPROACH



Letter	Reagents
a	Tert-butyl carbamate (Boc) added over 4.5 hours at -10˚C
b	2-aminoisobutyric acid added over 2 hours at 25˚C
c	Dimethylamine added over 5 minutes at 25˚C
d	HOBT, HBTU, DIPEA added and stirred for 1 hour, then 3,3-diethoxypropylamine added
e	1:1 solution of dichloromethane and trifluoroacetic acid added

HINGING RATE CALCULATIONS



Variable Temperature NMR in CD_3OD shows coalescence of the C (blue), B (blue), and β-Me (green) protons.

$$k_{exch} = \frac{\pi \Delta v}{\sqrt{2}}$$

Equation 1

$$\Delta G^{\ddagger} = -ln\frac{hk_{exch}}{k_B T_c} * RT_c$$

Equation 2

The rate at which the protons exchange is calculated using **Equation 1**, then the energy required for the hinging motion to occur can be calculated using **Equation 2** (Eyring's equation).

k_{exch} for β-Me: 106 sec^{-1}
$\Delta G^{\ddagger}$ for **AIB-AIB**: 15.3 kcal/mol

CONCLUSION & FUTURE WORK

1) Three step process used to successfully and efficiently synthesize **AIB-AIB** macrocycle.
2) Characterization of hinging motion possible using various techniques.
3) Steric congestion and solvent effects allows for control of hinging motion.
4) Measurement of logP and other biological properties will help determine hinging motion's impact on bonding to important intracellular factors.
5) Information on bonding and interactions with intracellular elements could inform future therapeutic uses.

ACKNOWLEDGMENT

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