A New pH-Switchable Dimannosyl[c2]Daisy Chain Molecular Machine

Introduction of Rotaxane

- concept
- synthesis
- potential applications
- research groups

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- concept
- synthesis of precursor 4
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Introduction of Rotaxane
1. Concept

• A rotaxane is a mechanically-interlocked molecular architecture.

• The two components of a rotaxane are kinetically trapped.
2. Synthesis

- Preorganized the components utilizing supramolecular interaction forces.

- The three most common strategies to synthesize rotaxane are "capping", "clipping", and "slipping".
Synthesis via the capping method relies strongly upon a thermodynamically driven template effect; that is the "thread" is held within the "macrocycle" by non-covalent interactions. This dynamic complex or pseudorotaxane is then converted to the rotaxane by reacting the ends of the threaded guest with large groups preventing disassociation.

The clipping method is similar to the capping reaction except that in this case the dumbbell-shaped molecule is complete and is bound to a partial macrocycle. The partial macrocycle then undergoes a ring-closing reaction around the dumbbell shaped molecule forming the rotaxane.
3. Potential applications

• Molecular machines (molecular electronics, muscles)

• Ultrastable dyes (long lasting dyes)

4. Research groups

- Bradley Smith Research Group.
  Developing Rotaxanes as a means to image cancer cells using dyes normally unstable to aqueous environments.

- Stoddart Research Group.
  Active in the development and application of unusual molecular topologies. Particularly towards the development of molecular machines.

- Leigh Research Group.
  Amide based rotaxanes and catenanes, peptide rotaxanes, transition-metal-based mechanically-interlocked architectures, "active metal template" rotaxane formation. Molecular machines: unidirectional molecular motors, molecular information ratchets.

- Anderson Research Group.
  Developing rotaxanes with enhanced stabilities and luminescence efficiency.

- Vögtle Research Group.
  Researching the construction of amide based rotaxanes and investigated their reactivity.

- Beer Research Group.
  Anion-templated rotaxane and catenane formation.

- Sauvage Research Group.
  Transition-metal-based rotaxanes and catenanes.

- Dawson Research Group.
  Protein rotaxanes and catenanes.

- Coutrot Research Group.
  Synthesis and Structure-Activity relationship of glycorotaxane molecular machines for their lectin receptors.
pH-Switchable Dimannosyl[c2]Daisy Chain Molecular Machine
1. Concept

The term ‘daisy chain’ has been introduced into the chemical literature to describe compounds such as those illustrated below.

The prefix ‘[c2]’ denotes cyclic dimers, be they supramolecular or molecular.
2. Synthesis of [c2]Daisy Chain Precursor 4

1) NH₂, toluene
2) NaBH₄, MeOH

3: X = NH, 76%
4: X = NH₂⁺ PF₆⁻, quantitative
Crown ether 1

Amine linker 2

The three possible [c2]daisy chain stereoisomers 4a-c.
4b Diastereoisomers

4a Enantiomers

4c Diastereoisomers
a: b: c 86 : 7 : 7

a) DMSO-d6

b) CDCl3

18 isomers b, c

δ/ppm

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
3. Synthesis of Mannosyl[c2]Daisy Chains 8a and 9a

Cu(CH3CN)4PF6
2,6-Lutidine
CH2Cl2

6a: \( X = \text{NH}_2 \cdot \text{PF}_6, 92\% \)
1. HCl, Et₂O
2. NH₄PF₆, H₂O / CH₂Cl₂

NaOH, H₂O / CH₂Cl₂

7a: Y = I, quantitative
8a: Y = PF₆, 86%

9a: quantitative
4. pH-Switchable Molecular Machine

a). 8u

b). 8a

c). 9a

d). 9u

DB24C8

ammonium station

triazolium station

amine moiety

mannosyl moiety
5. Conclusion

a). A very efficient access to glyco[c2]daisy chains using the end-capping method via click chemistry.

b). Depending of the pH, the different affinities of the macrocycle for the two molecular stations allowed the contracted and the stretched co-conformations of the molecule.

c). The affinity of the macrocycle is much better for the ammonium template than for the triazolium one by hydrogen bonding.
Thank you