Last Name	
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Legi-No.	
Program of Study	

Written Exam
Supramolecular Chemistry
Summer 2016

F. Diederich, Y. Yamakoshi

Please check:
This exam paper includes 4 printed pages (4 questions) in addition to the cover.

Please note:
- All problems have to be solved.
- Unreadable texts or drawings will not yield any points.
- If you use additional sheets, make sure to mark them with your name and to attach them to this paper.

Points

Problem 1	
Problem 2	
Problem 3	
Problem 4	
Total	

Grades

Written	
Oral	
Final	

Problem 1 (20 points).

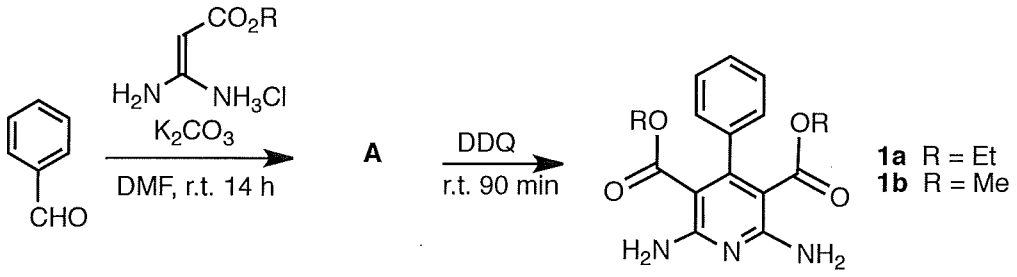
(1) Propose a structure of the intermediate **A** formed in the shown reaction of benzaldehyde to give **1a** and **1b**. Propose a mechanism for the first step. (5 pts)

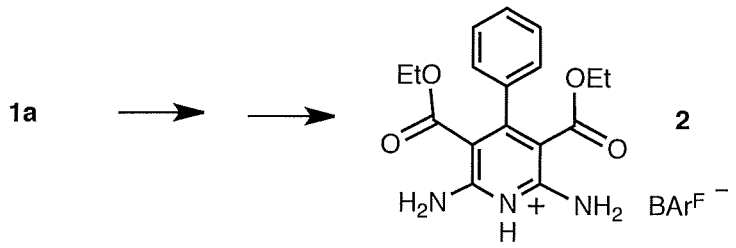
(2) Propose the (simple) two-step synthesis of **2** starting from **1a.**
In **2**, the counteranion BAr^F is tetrakis[3,5-bis(trifluoromethyl)phenyl]borate. (3 pts)

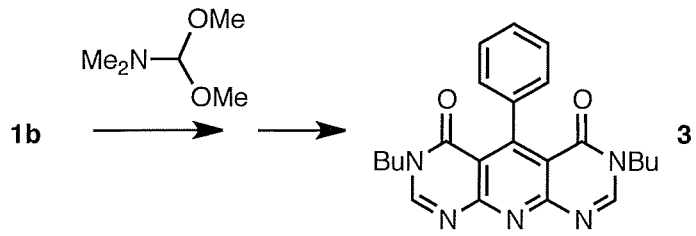
(3) Propose the two-step synthesis of **3** starting from **1b**.
In the synthesis of **3** from **1b**, please use as reagent $Me_2N–CH(OMe)_2$ in the first step. Suggest a mechanism for the two steps. (5 pts)

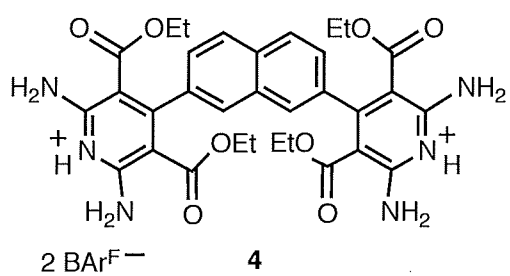
(4) Compounds **2** and **3** form a 1:1 complex with $K_a = 10^7\ M^{-1}$ in CD_2Cl_2 at 288 K. Suggest its structure and indicate the intra- and intermolecular bonding interactions in the complex. Comment on the strength of the intermolecular interactions. (4 pts)

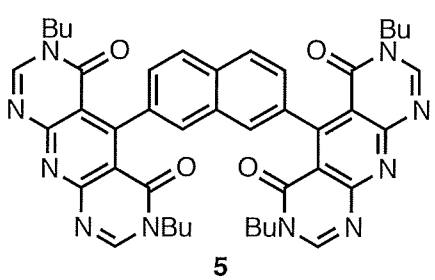
(5) Starting from 2,7-naphthalenedicarbaldehyde (not shown), the same synthetic procedures afford compounds **4** and **5**. In CD_2Cl_2, **4** and **5** undergo supramolecular assembly to give a four-component [2+2] macrocyclic structure of high stability. Suggest a schematic structure of the asssembly, showing the intermolecular interactions. (3 pts)
(Angew. Chem. Int. Ed. **2016**, *55*, 1685-1689)



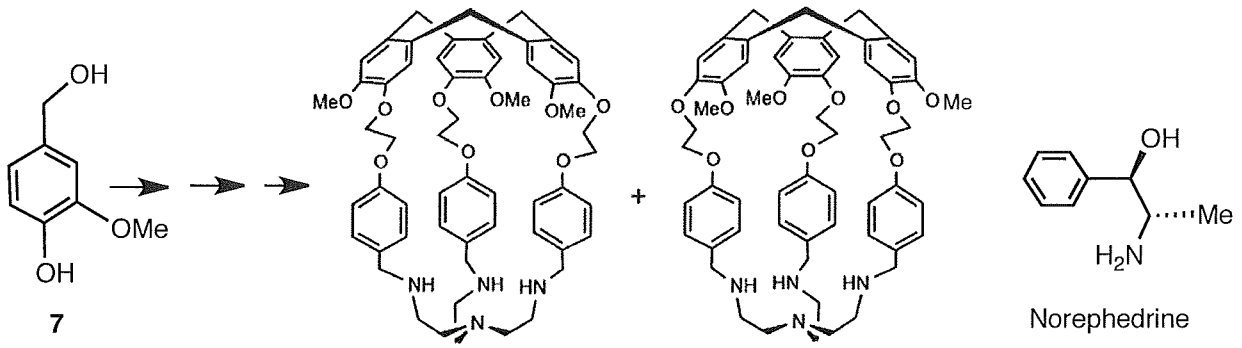








Problem 2 (20 points). The neurotransmitter norephedrine is complexed with high enantioselectivity by the cryptophane derivatives (*M*)-**6** and (*P*)-**6**.



(1) Suggest a synthesis of the two receptor enantiomers (*M*)-**6** and (*P*)-**6** starting from benzene derivative **7** including detailed reagents, solvent, and reaction conditions. Propose at which step of the synthesis you would separate the initially racemic material into the enantiomers. (15 pts)

(2) What is the point group of the receptors? (1 pt)

(3) Titration curves in $CDCl_3$/MeOD 95:5 at 298 K, with the receptors added to norephedrine held at constant concentration (0.5 mM) give $K_a = 4.9 \times 10^7$ M^{-1} for the complex of (*M*)-**6** and $K_a = 5.1 \times 10^6$ M^{-1} for the complex of (*P*)-**6**, resulting in an enantioselectivity of 91:9. Larger upfield shifts in the titration at fast exchange were recorded for the protons shown in bold in the aliphatic side chain of norephedrine, C**H**(OH)C**HMe**NH_2. Suggest, how norephedrine could bind and what unit in the receptor is primarily responsible for chiral recognition. (4 pts).

(Chem. Eur. J. **2016**, *22*, 2068-2074)

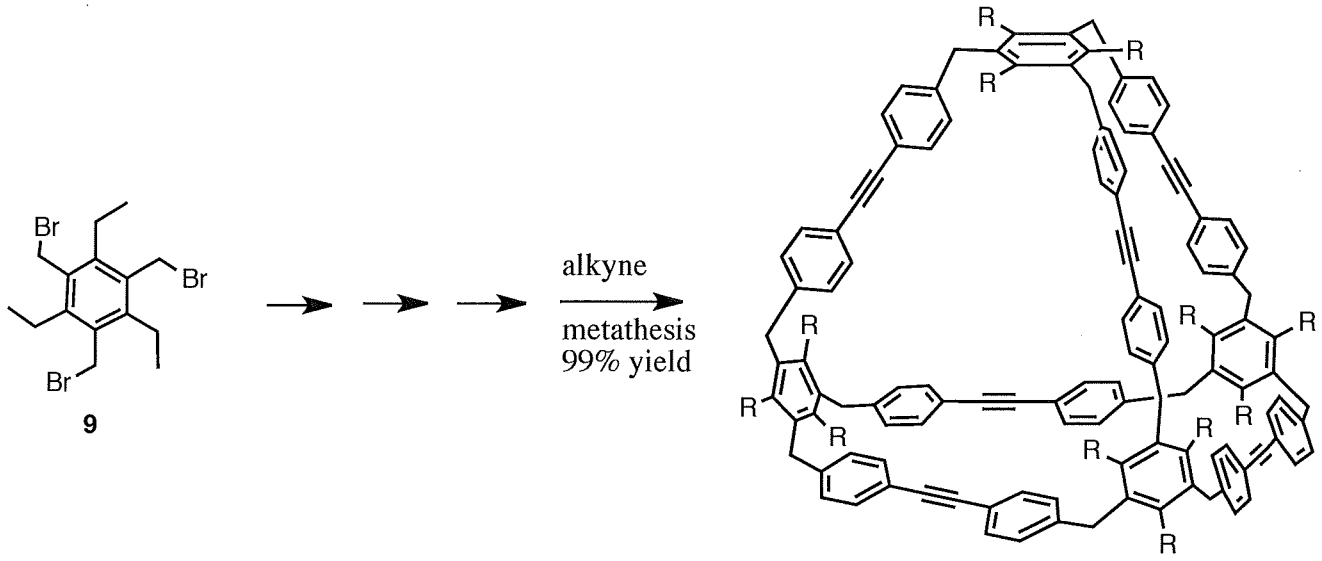
Problem 3 (10 points). We have seen in class that alkyne metathesis using aromatic building blocks with bis-propyne side chains under [Mo] catalysis (Mo = molybdenum) is a versatile dynamic covalent synthesis method to produce macrocycles that are thermodynamic sinks. The inventor of this method, Prof. Jeffrey S. Moore has now applied it to a short synthesis of the remarkable tetrahedral cage **8**.

(1) Starting from hexasubstituted benzene **9**, he was able to construct **8** in 4 high-yielding steps. Suggest the 4-step synthesis of **8** starting from hexasubstituted benzene **9** and introducing at some stage propynyl residues (–CC–Me) to a key building block derived from **9**, giving reagents and conditions. The conditions for the alkyne metathesis step are: [Mo] catalyst (5 mol-%), Ph_3SiOH, 1,2,4-trichlorobenzene as solvent, and molecular sieves 5 Å to capture the 2-butyne byproducts and shift the equilibrium. (8 pts)

(2) What is the distinct conformational property of **9** which enables this synthesis? (2 pts)

If you do not remember alkyne metathesis, try to work towards a more classical synthesis for partial credit.

(*J. Am. Chem. Soc.* **2016**, *138*, 2182-2185)



9

8 R = Et

Problem 4 (10 pts)

Prof. J. Fraser Stoddart prepared new box-type cationic receptors for guest inclusion.

(1) Suggest the synthesis of **10** starting from bis(pyridinyl)acetylene **11**. Give reagents, solvent, and conditions. (8 pts)

(2) In the final step, either starting material is obtained or the bis-adamantyl functionalized receptor. No mono-adamantyl derivative could ever be detected. Suggest why. (2 pts)

(*J. Am. Chem. Soc.* **2016**, *138*, 3667-3670)