Molecular Lamps and Molecular Golf Balls

ULRICH LÜNING⋆, MARTIN HAGEN, FRANK LÖFFLER, TORSTEN
MARQUARDT and BERND MEYNHARDT
Institut für Organische Chemie, Olshausenstr. 40, D-24098 Kiel, Germany

Abstract. The concave shielding of the active site of enzymes has been transferred to standard reagents of organic chemistry and concave reagents have been synthesized which possess a lamp-like geometry (concave 1,10-phenanthrolines **1**–**2**, concave pyridines **3**). The special concave geometry of these reagents is responsible for their selectivity in metal ion catalyzed (Pd-catalyzed allylations, Cu(I)-catalyzed cyclopropanations) and base catalyzed (acylation of alcohols by ketenes) reactions. For an easier recovery, these reagents have been attached to Merrifield polymers and to dendrimers. Higher generations of dendrimers loaded with concave reagents will possess a golf ball geometry.

Key words: allylation, calixarenes, concave reagents, cyclopropanation, dendrimers, metal ion catalysis.

1. Introduction

The high selectivities of enzymatic reactions are largely caused by the concave environment of the active site. The feature of concave shielding has been exploited in concave reagents [1] which combine standard reagents of organic chemistry with a concave geometry around the functional group. The overall geometry of such concave reagents resembles that of a lamp, with the light bulb as the functional group, the active site, and the lampshade as the shielding.

The minimum structural requirement for a concave reagent is the construction of a bimacrocycle. One macrocycle forms the rim of the lamp shade which is then spanned by a bridge carrying the functional group. As functional groups acids, bases and transition metal binding sites have been incorporated, some examples are shown in Figure 1. These concave reagents have then been used as catalysts in model reactions.

2. Transition Metal Ion Catalysis

A vast number of reactions can be catalyzed by transition metals. Therefore the complex formation between concave 1,10-phenanthrolines **1** and transition metal ions has been studied [2] and the resulting complexes have been used in model

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Figure 1. 2,9-Diaryl substituted concave 1,10-phenanthrolines **1**, 1,10-phenanthroline bridged calix[6]arenes **2** and concave pyridines **3** as examples of concave reagents with a lamp geometry.

L	unlike-5a : like-5a R = Me	unlike-5b : like-5b R = Et
L¹	75 : 25	54 : 46
L²	81 : 19	69 : 31
L³	92 : 8	-
L⁴	94 : 6	91 : 9
L⁵	93 : 7	91 : 9
PPh₃	81 : 19	70 : 30
-	84 : 16	71 : 29

Chart 1.

reactions. Cobalt and nickel complexes are effective Lewis acids to catalyze Diels-Alder reactions between cyclopentadienes and pyrazole acrylates. The concave 1,10-phenanthroline ligand shifts the *exo/endo*-selectivity towards *exo* [3].

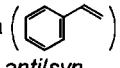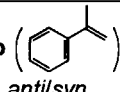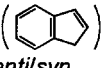A second model reaction exploits the ability of palladium to catalyze the allylation of nucleophiles with allyl acetate. As nucleophile a substituted deprotonated cyano acetate **4** was chosen which contains a chiral center. In the course of the allylation a new chiral quarternary center is formed. The product is a mixture of *like-* and *unlike*-diastereomers **5**.

4   **a**: R = Me
        b: R = Et

unlike/like -**5**

Using allyl compounds with better leaving groups (e.g. bromide) this allylation can also be carried out without palladium. As Chart 1 shows the 1,2-asymmetric induction then leads to *unlike/like*-ratios of 71 : 29 and 84 : 16 for the ethyl and methyl compounds **5b** and **5a** respectively. Changing the reaction conditions using palladium catalysis does not change the *unlike/like*-ratios very much, when triphenylphosphines are the additional ligands at the palladium. But when these ligands are exchanged by concave 1,10-phenanthrolines the ligands L³–L⁵ can enhance the fraction of the *unlike*-isomer up to 94%.

The third transition metal ion catalysis whose selectivity can be governed by concave 1,10-phenanthrolines **1** or **2** is the copper(I)-catalyzed cyclopropanation of alkenes **6** [4].

Two classes of concave 1,10-phenanthrolines have been applied leading select-ively to *both* isomers of **8**. 2,9-Diaryl substituted 1,10-phenanthrolines **1** [2] prefer the formation of the *anti*-cyclopropanes **8** with selectivities up to 99 : 1, while 1,10-phenanthroline bridged calix[6]arenes **2** [5] preferentially form the *syn*-isomers **8**. The difference between these two classes of ligands is the flexibility of the bridge. In contrast to the stiff diarylphenanthrolines **1**, the bridge across the calixarene in **2** can bend and thus allows another orientation of the carbene moiety in the reactive copper-carbene intermediate. With the first ligands **1**, the ester function and the attacking alkene **6** can avoid each other explaining (i) the *anti*-selectivity and (ii) the fact that better results are obtained with large esters. In contrast with the latter ligands **2**, the alkene **6** attacks from the side of the ester groups (i) leading preferentially to *syn*-**8** and (ii) explaining why the best selectivities are found with the smallest ester, the methyl ester **7a**. See Table I.

3. Base Catalyzed Addition of Alcohols to Ketenes

The selectivitiy enhancing effect of concave reagents has also been demonstrated in a base catalyzed reaction. When alcohols are reacted with bases like pyridines, hydrogen bonded complexes are formed which possess an increased reactivity towards ketenes.

Table I. anti/syn Diastereoselective cyclopropanation of alkenes **6** by diazoacetates **7** catalyzed by copper(I) complexes of concave 1,10-phenanthrolines **1** and **2**.

Catalysis by	with	6a ( ) anti/syn	6b ( ) anti/syn	6c ( ) anti/syn
	7a	57:43	-	66:34
Cu⊕	**7b**	57:43	51:49	70:30
	7c	61:39	72:28	75:25
	7a	-	-	-
Cu⊕ · **1**	**7b**	83:17	-	97:3
	7c	87:13	68:32	>99:1
	7a	28:74	-	14:86
Cu⊕ · **2**	**7b**	33:67	35:65	24:76
	7c	46:34	-	31:69

In numerous investigations [6] the bimacrocyclic pyridine catalysts and the ketene were optimized for inter- and intramolecular selective acylations. With the concave pyridine **3** the partially protected glucose derivative **9a** can be acylated in 2-position exclusively to form **9b** [6c].

9a R^2 = H, R^3 = H
9b R^2 = CO—CHPh$_2$, R^3 = H
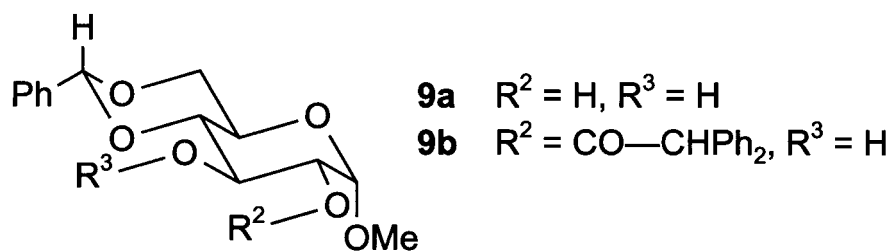
For an economical application of these concave catalysts, the synthetic effort of their synthesis must be minimized. The logical development is therefore the fixation of the concave pyridines to polymers [7] which has been realized for soluble or insoluble polymers. Which polymer will be the best choice? Insoluble

polymers of the Merrifield type [7] are inhomogeneous which may lower the selectivity due to reagents depletion. These problems can be overcome with soluble polymers but here the separation of products and catalysts is more difficult. Nanofiltration should be able to solve the separation problem for soluble polymers but here threading of a linear soluble polymer through the membrane, reptation, may occur. Such a leakage of catalyst will be prevented when the polymer is branched. Therefore concave pyridines have been attached to Fréchet type dendrimers [8]. A first generation dendrimer containing six concave pyridines on its surface could already be restrained by a nanofiltration membrane with up to 90% effectivity [9]. A second generation dendrimer **10** covered with twelve concave pyridines has now been synthesized. Analogously also other sterically shielded pyridines like 2,6-di-*tert*-butylpyridines have been attached to the dendrimer framework.

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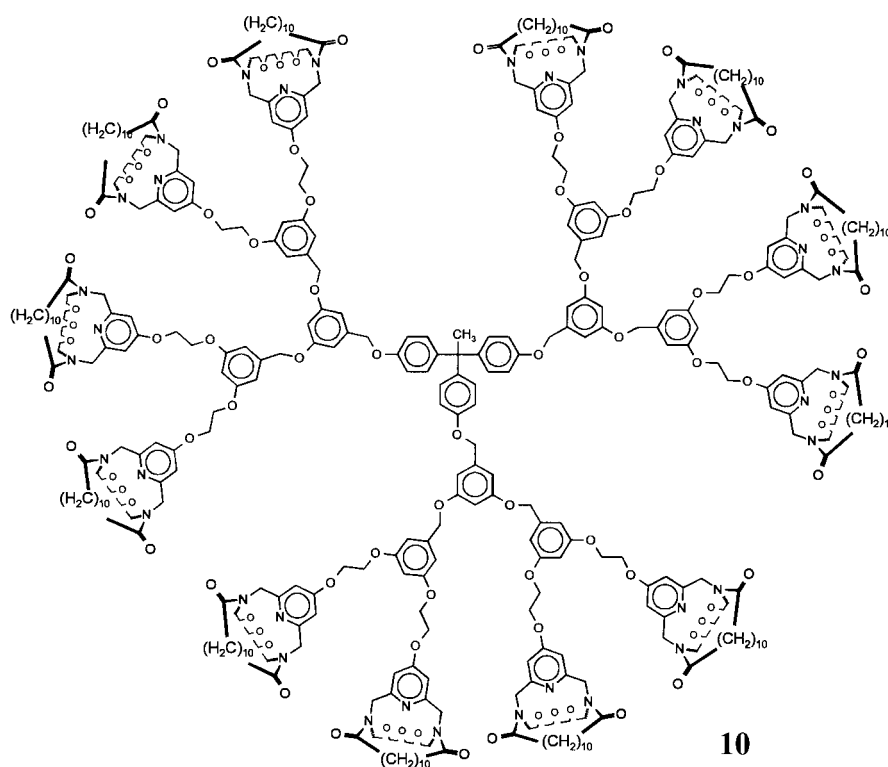
In future work the construction of dendrimers with concave reagents will be extended to other catalysts, e.g. for metal ion catalyzed reactions. In higher generations all these dendrimer catalysts will possess the geometry of a golf ball [9] with each deepening being a concave reagent.

Acknowledgement

References

1. (a) U. Lüning: *Liebigs Ann. Chem.* 949 (1987). (b) U. Lüning: *Top. Curr. Chem.* **175**, 57 (1995). (c) U. Lüning: *J. Mater. Chem.* **7**, 175 (1997).
2. U. Lüning, M. Müller, M. Gelbert, K. Peters, H. G. von Schnering, and M. Keller: *Chem. Ber.* **127**, 2297 (1994).
3. M. Gelbert and U. Lüning: *Supramol. Chem.*, in press.
4. M. Hagen and U. Lüning: *Chem. Ber./Recueil* **130**, 231 (1997).
5. H. Ross and U. Lüning: *Tetrahedron Lett.* **38**, 4539 (1997).
6. (a) U. Lüning, R. Baumstark, and W. Schyja: *Liebigs Ann. Chem.* 999 (1991). (b) W. Schyja, S. Petersen, and U. Lüning: *Liebigs Ann.* 2099 (1996). (c) U. Lüning, S. Petersen, W. Schyja, W. Hacker, T. Marquardt, K. Wagner, and M. Bolte: *Eur. J. Org. Chem.* 1077 (1998).
7. U. Lüning and M. Gerst: *J. Prakt. Chem./Chem.-Ztg.* **334**, 656 (1992).
8. J. M. J. Fréchet and C. Hawker: *J. Am. Chem. Soc.* **112**, 7638 (1990).
9. (a) T. Marquardt and U. Lüning: *J. Chem. Soc. Chem. Commun.* 1681 (1997). (b) U. Lüning and T. Marquardt: *J. Prakt. Chem.* **341**, 222 (1999).