AN ANALYSIS OF TWEEZER MOLECULES ARE PROJECTED TO PROVIDE SENSORS WITH A FLEXIBLE STERIC PROPERTY SUITABLE TO ENTRAP GUESTS WITH EFFICIENCY

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Abstract

Supramolecular interaction in chemistry is described as "chemistry beyond the molecule1 which involve non-covalent association between different molecules2 probably the most famous and comprehensive definition of supramolecular chemistry was given in 1985 by JeanMarie Lehn, Nobel prize winner in 1987, together with Cram and Pedersen. This branch of chemistry investigates systems based predominantly on weak and reversible interactions between molecules: i.e. electrostatic interaction, Hydrogen bonding, coordination bonds, Van der Waals interactions, π-π interactions, ion-dipole interactions, etc. Naturally occurring macromolecules like enzymes and membrane receptors have been a great source of inspiration in the design of supramolecular systems. The terms receptor and substrate, borrowed from natural systems are still commonly used to indicate two different molecular units interacting by means of non-covalent interactions. The receptor is usually the bigger molecular unit whereas the substrate is the smaller one.

Paper Identification

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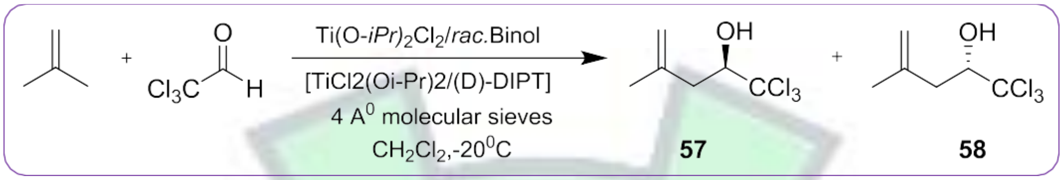
Introduction

The asymmetric activation of catalysts can occur according to several different strategies: (a) starting from a racemic catalyst, it is possible to introduce a chiral de-activating catalyst or (b) a chiral activating ligand, or (c) starting from a chiral catalyst, it is possible to add a racemic orchiral activating ligand.

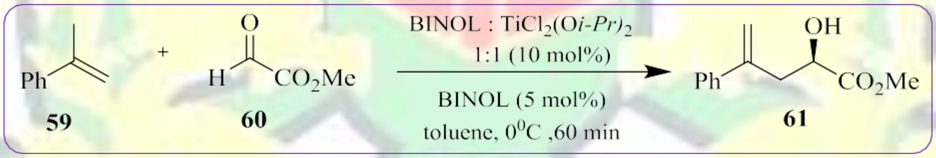


Scheme 1.13: poisoning of catalysts by adding Ti(O-i-Pr)2C12 / diisopropyl-D- tartrate

The first approach, known as the chiral poisoning strategy, was used successfully by Faller.

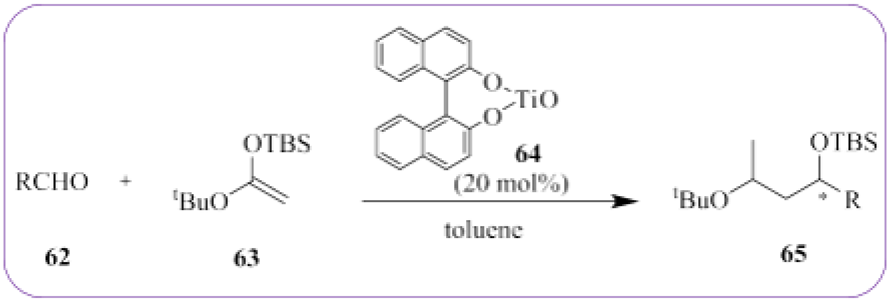
Starting from chloral, he established that a *rac*-BINOL/TiCl2- (O*i*-Pr)2 catalyst can be poisoned by an inactive enantiopure catalyst [TiCl2(O*i*-Pr)2/(D)-DIPT] to yield a catalyst capable of a better asymmetric induction than the one obtained from catalysts directly prepared from enantiopure BINOL.[35-36]

Mikami and group applied second and third strategy to study kinetic of reaction that the catalyst prepared from (*R*)-BINOL and TiCl2-O*i*-Pr)2 could be activated by adding (*R*)-BINOL, *rac*- BINOL, or other chiral diols [37-38]



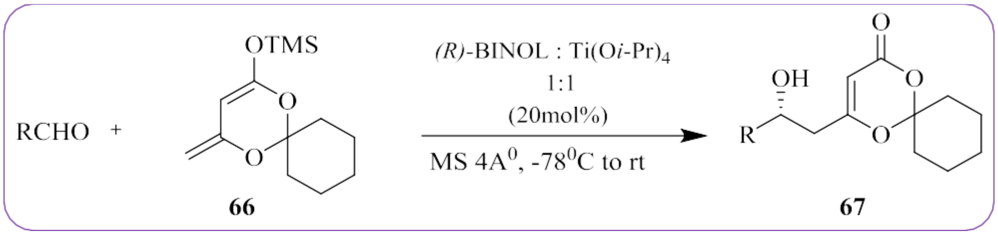
Scheme 1.14: Asymmetric Activation of Catalysts in the organic Reaction

The Lewis acid-promoted aldol-type reaction of nucleophilic alkenes with carbonyl compounds has been known since the late 1930s, the introduction of silyloxyalkenes by Mukaiyama in 1973 marked a major breakthrough. Mukaiyama reported enantioselective reaction with encouraging results using Binol-Ti complex[39] Up to 85% ee's were reported with a complex formed from (*R*)-BINOL and (*i*-PrO)2- Ti(O) and for which structure **64** was proposed



Scheme 1.15: Enantioselective Mukaiyama Reaction

BINOL complexes have also been used in various vinylogous aldol reactions involving acyclicor cyclicenol ethers. Thus, in the presence of BINOL-Ti catalyst, silyoxydioxine **66** and benzaldehyde led to the corresponding alcohol **67** with very good yield and enantiomeric excess.



UV-Vis spectroscopy

UV-vis spectroscopy is one of the widely used methods for ion / molecular recognition as it provides high sensitivity and simplicity to the host-guest binding study. In this case the host molecule should contain a chromophoric group with the absorption band(s) in the UV-Vis range, while the host-guest complex generally has the absorption band at different wavelength. This deviation is generally used for determination of the extent and strength of binding in a quantitative manner.

The association constants related to the binding process of each enantiomeric guest with the chiral host can be calculated by using the modified Benesie–Hildebrand equation[4] as follows.

(I0/I- I0) = (b/a-b)[1/K[G]+1]

Where: **I0** is the initial emission intensity of host (without any presence of guest) **I** is the emission of host of host on treating with guest [G] concentration. **K** is the association constant for system.

The value of **(b/a-b)** is a constant term and can be found out by plotting **(I0/I- I0)** versus inverse of guest concentration term, where intercept gives the constant term. The graph is equated with that for the straight line equation **y= mx + C;** the slope of the graph obtained indicates the overall 'association constant' **K** for the system. I0 and I are the emission intensities observed experimentally, whereas the changing guest concentration is known. Similar treatment can beapplied for fluorescence spectroscopy.

Fluorescence

Fluorescence spectroscopy received considerable attention so far because it is able to provide special advantages which include simplicity, low cost, high sensitivity, adaptation to automation and real-time analysis, diverse signal output modes and small quantities of host and guest. This technique allows multiple detection modes such as emission, excitation and lifetime measurements.

For ion sensing analysis/recognition, the appropriate fluorophores (fluorescent chromophoric systems) should be either intrinsically chiral or chirally modified by attaching an enantiopure moiety, if chiral species is being studies; for studies of non-chiral species the host molecule need not be chiral. The corresponding non-bonded interactions with the concerned analyte give different fluorescence responses; *i.e.* the recognition. Such sensors generally respond via the fluorescence enhancement or quenching. The fluorescence quenching is observed due to loss of the energy of the excited state by a non-radiative decay. Such systems are commonly analyzed by the Stern-Volmer equation (see below).

I0/I = 1+K[G]

I0 = Initial emission intensity of the host

I = Intensity of the host after addition of analyte (Guest)

K= Stern-Volmer constant / Stability constant for the complex

[G] = Concentration of the analyte (Guest)

The Stern-Volmer plot of fluorescence intensity ratio, **I0/I** Vs concentration of guest enantiomers, **[G]** exhibits linear relationship, from which the Stern-Volmer constant is obtained experimentally, and hence **K** can then be easily calculated.

In general, BINOL and Benzimidazole based chromophoric systems are chiral fluorophores widely used in chiral recognition via fluorescence. Karnik[5] *et al.* reported the furo-fused BINOL based crown ethers for enantioselcetive fluorescence recognition of Phenyl ethyl amine and Ethyl ester of valine in their protonated ammonium salt form with enhancement inemission intensity.

Molecular Tweezers

Whitlock is the person who coined the term molecular tweezer. Molecular tweezers are synthetic molecular receptors with an open cavity defined by two interactions for substrate binding bridged by a spacer.

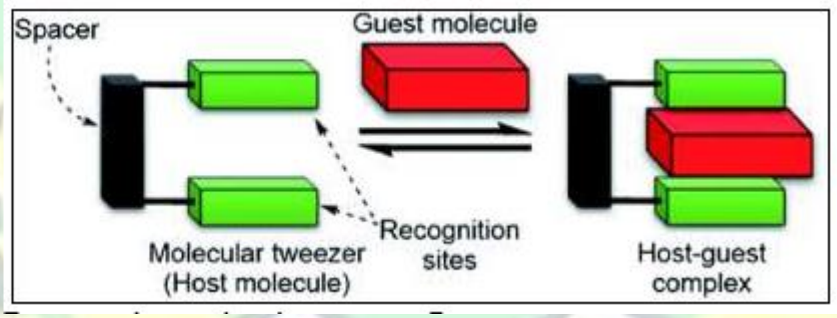


Figure 1.1: Representing molecular tweezers

Molecular tweezers must possess the three general factors for the enhancement of the bindingof an aromatic guest molecules, i) the presence of spacer that prevent self-association. ii) a spacer that establish a distance between the pincer of the tweezers of about 7A^{o} (plane to plane or centroid to centroid) ideal for the inclusion of a single aromatic guest. iii) Spacer thatholds the pincer rigidly in a syn-conformation. Tweezers have open cavities that are capable ofbinding guest molecules via non-covalent bonding interaction which includes hydrogen bonding, metal coordination, hydrophobic forces, Van der waals forces, π-π interaction or electrostatic effect. Particularly in case of π-π interaction tweezers must possess an inner voidof ca. 7A^{o} in order to facilitate the complexation of aromatic substrate via π-stackingintersection as aromatic group stack at an average inter-planar distance 3.5A^{o} . Depending on the type of their terminal unit and on the number and form of functional group constituting thespacer, a broad range of tweezers are now known.

So far the synthetic chiral molecular tweezers are rare. Maitra[8] and coworkers have reported the synthesis of such tweezers using a bile acid as a scaffold. These tweezers bind electron deficient aromatic species with reasonable affinity. Another chiral molecular tweezers was developed by Pardo[8] and coworkers using Tröger's base as a scaffold around with the tweezerswas built. The crystal structure shows that two molecules interact with each other in the solid state**.**

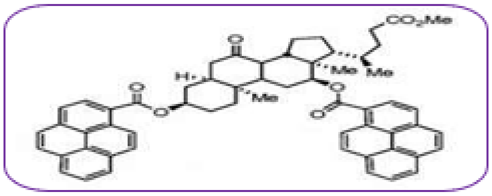


Figure 1.2: Chiral molecular Tweezer by Maitra and coworkers

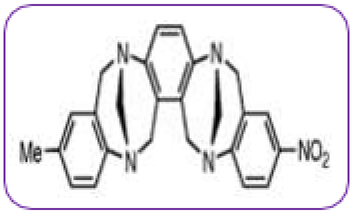
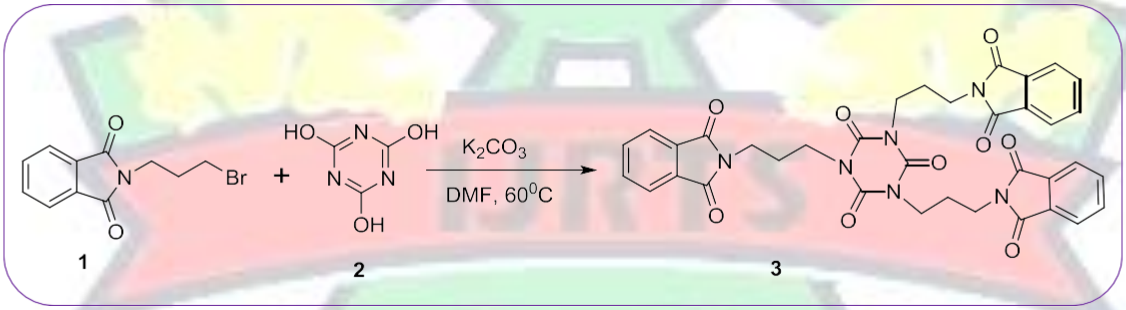


Figure 1.3: Chiral molecular Tweezer by Pardo and coworkers.

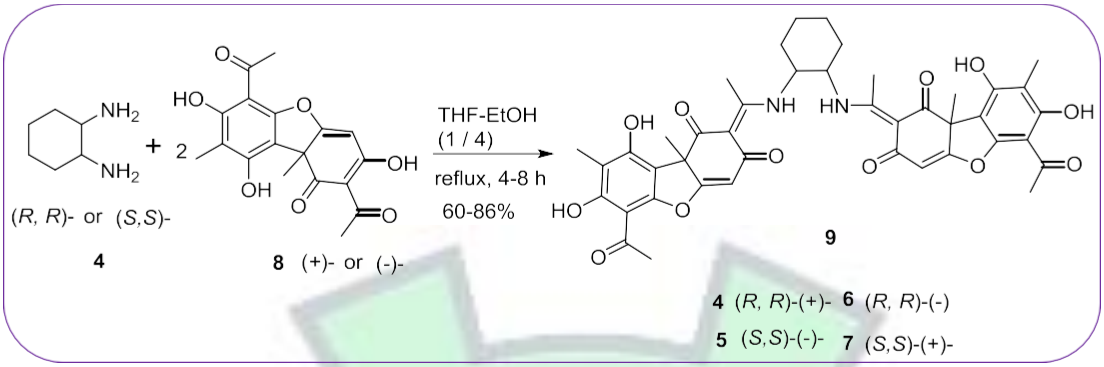
From the last three decades molecular tweezers have received immense attention due to the applications in asymmetric synthesis, recognition of neutral organic molecules, chiral molecules and metal ion sensing. Different spacers have different types of flexibility due to this different recognition properties can be achieved[9].

A. Gaurav[9] and co-workers developed tripodal tweezer **3** prepared from cyanuric acid **2** and propylene as a linker and pthalimide hetrocycle **1** as terminal for conformational applications.



Scheme 1.1: Synthesis of flexible tripodal tweezer

B. Legouin[10] et al have successfully prepared four stereoisomers of potential chiral molecular tweezers from trans-1, 2-diaminocy-clohexane as a spacer and two molecules of usnic acid as a pincer. Only the combinations (R, R)-(+) **4** and (S, S)-(-) **7** lead to the formation of molecular tweezers. The ability of this molecular tweezer to bind various electron-poor aromatic compounds such as 2, 4, 7-trinitrofluorenone (TNF) has been studied. The behavior of **4** as a chiral complexing agent was evaluated with chiral esters. This molecular tweezer **9** and its host–guest chiral complex were fully characterized and both substrates afforded crystals suitable for X-ray diffraction analysis**.**



Scheme 1.2: Synthesis of flexible tripodal tweezer

Cyclophanes

Cyclophanes[13, 14] are strained organic compounds with aromatic rings and aliphatic units. The structure of these molecules is made rigid by the aromatic rings, while the overall structure is made flexible by the aliphatic units that act as bridges between the aromatic rings.

It was seen that structure of cyclophane has aromatic ring in the cyclophane system which canbe either carbocyclic or heterocyclic in nature. If there is a heteroatom present in the aromatic ring system then the system is called heterophane **9** whereas if hetero atom is present in the alkyl chain of the bridge, then it is called heterophane **10**. If heteroatom is present in both the aromatic ring and alkyl chain, it is called a hetero-heterophane **11**. Number of cyclophanes derivatives have been employed as hosts, and their guest binding properties have been widely investigated.[15] The characteristic feature of cyclophane include symmetry, unusual structural features, synthetic challenge, through space interaction between aromatic system, conformational behavior, the physical and chemical consequence of strain and inherent planer chirality. Such robust chiral scaffold has been used as building blocks for construction of chiral architecture, functional material, chiral sensors and asymmetric catalyst.[16] Cyclophanes plays an important role in host guest chemistry and supramolecular assembly. “Phane”- containing molecules show interactions with π system, and they can also bind to large no cations, anions,and neutral molecules.

Conclusion

The work presented in the thesis pertains to development of tweezers and cyclophanes and their applications as ion sensors. BINOL, 1,2,3-triazoles and some other heterocycles have been incorporated in the synthetic host molecules. A brief idea about origin of supramolecular interactions and methods of qualitative and quantitative evaluation of sensing using UV and fluorescence techniques has been provided in the chapter on Introduction. The selection of BINOL and 1,2,3-triazoles as a part of host molecules is based on certain properties of these molecules. A brief idea about their synthetic routes and applications has been provided in this chapter. Tweezer molecules are projected to provide sensors with a flexible steric property suitable to entrap guests with efficiency; carefully designed tweezers provide more sensitive readouts.

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