Abstract

This study draws attention to supramolecular catalysts. Cram, Lehn, and Pedersen's pioneering works evolved around the use of supramolecules for molecular recognition and catalysis. Supramolecules offer defined binding pockets and noncovalent interactions such as hydrogen bonding, van der Waals forces, and π-π interactions, thus generating a reaction microenvironment for catalysis. Moreover, macrocycles can provide a preorganized arrangement of functional groups, such as binding sites or catalytically active groups, thus enabling a defined and possibly multivalent binding and activation of substrates. Various supramolecules such as calixarene, cryptands, cucurbiturils, and COFs, have been studied for a variety of applications for environmental and catalytic applications.

Among various supramolecules, calixarene is the most important molecule for constructing conformationally rigid supramolecular catalysts. The unique properties of calix[4]arene lead to a rational design of homogeneous catalysts and due to the absence of metals, these methods are attractive for the preparation of pharmaceutical compounds, and chemical reactions that are of high value in the biological, and chemical industries. With the increasing demand for chiral products, many efficient catalysts have been developed for a wide range of organic transformations. The major part of asymmetric catalysis is homogeneous catalysts as they facilitate molecular reactions in an efficient manner with high chirality transfer. Calix[4]arene appended catalysts are easily recoverable, separable, and can be purified as well and these catalysts could be recycled with a good number of recyclable cycles.

Out of various studies on asymmetric homogeneous organocatalyzed reactions, asymmetric Michael addition of acetylacetone to β-nitrostyrene is one of the key reactions with wide applications in pharmaceutical industries. Mono and dicationic *Cinchona* alkaloid-anchored calix[4]arenes as organocatalysts were effective and gave high enantiomeric induction (~99% yield and >99% ee). Phase Transfer catalysts (PTC) based on calixarene supramolecules offer special advantages due to their unique properties with a rigid and stable aromatic cavity. Additionally, four phenolic hydroxyl groups of calix [4] arene provide synthetic adaptability and noncovalent interactions and a new catalyst designed utilizing quaternary ammonium Cinchona-functionalized crown ether-strapped calix[4]arenes as PTCs for asymmetric α-alkylation of glycine imines to α-alkylated glycinates with remarkable selectivity under ambient conditions (~98% yield and >99% ee). Another PTC designed a highly selective α-methylbenzylamine functionalized crown-ether-appended calix [4]arene is harnessed for asymmetric nitroaldol reaction to provide nitroaldol adducts in high yields (up to 99 % yield) with good to excellent enantioselectivities (up to 99.8 % ee). Organocatalysis has gained noteworthy attention due to its efficiency, selectivity, and gratifying results at sub-stoichiometric amounts of the chiral catalyst and calixarene-derived enantioselective organocatalytic one-pot Strecker reaction catalyzed by camphor sulfonyl functionalized crown-ether-tethered calix [4] arene and provide the desired cyano adducts in high yields up to 99.9% yield and 99.2% ee. The synthetic utility of the Strecker reaction was used in the synthesis of Clopidogrel.