Pergamon

Tetrahedron 55 (1999) 12657–12698

TETRAHEDRON

Tetrahedron report number 508

Organic Transformations using Zeolites and Zeotype Materials

Stephanie E. Sen,* Sarah M. Smith, and Katherine A. Sullivan

Department of Chemistry, Indiana University – Purdue University at Indianapolis (IUPUI)
402 North Blackford Street, Indianapolis, IN 46202, USA

Received 10 June 1999

Contents

Email:sen@chem.iupui.edu

PII: S0040-4020(99)00747-4

1. Introduction

Although zeolites have been known for their adsorption properties for over a century, it was not until 1952, when the first synthetic zeolite was prepared, that their utility in chemical transformations was explored. Since that time, zeolites have been used for a multitude of purposes, and to this day they are essential catalysts in the petroleum industry, converting large and small hydrocarbons into high-octane compounds. As an outgrowth of this work, zeolites have found utility in industrial fine chemical synthesis for the construction of aromatics, heterocycles, aliphatic amines, and ethers.

This paper will not provide a comprehensive summary of past applications of zeolites to industrial chemistry, as many excellent reviews are already available.[1] Instead, it will summarize contemporary applications of zeolites and related materials to organic synthesis, with particular emphasis on work appearing in synthetic journals since 1996. Although many related materials have been prepared and studied, only commercially available zeolites, MCM-type materials, and titanium-containing zeotypes will be discussed.

2. Zeolite Types

Many naturally occurring zeolites are known and a vast array of synthetic zeolites have been prepared.[2] All share a characteristic aluminosilicate framework, composed of $[SiO_4]^{-4}$ and $[AlO_4]^{-5}$ tetrahedra that are linked together through oxygen bridges. Depending on the preparative method used, several predictable 3-dimensional structures are obtained. Zeolites that are commonly used for synthetic transformations include zeolites X/Y, beta, mordenite, and ZSM-5. Zeolite A, whose pore dimensions preclude absorption of larger molecules, is typically used only as a water scavenger.

Zeolites A and X/Y have as their basic structure the sodalite cage, a truncated octahedron that has 8 hexagonal and 6 square faces. Zeolite A is formed when the cages are connected through each of the 6 square faces, while X/Y zeolites are formed when half of the octahedral faces are joined together to form hexagonal prisms. For zeolites X and Y (also known as synthetic faujasites), the spherical internal cavity generated when 8 sodalite cages are joined is called the α-cage (or supercage) and is about 13Å in diameter. Entry into the spherical α-cage can occur through 4 identical openings that are 7-8Å wide. In contrast to zeolite A, the dimensions of X/Y zeolites allow reasonably large molecules to penetrate the internal pores, since compounds may extend through a prism into 2 connecting α-cages.

Zeolites ZSM-5 and mordenite are pentasil zeolites, consisting of units composed of 5 membered T-rings or O-linked tetrahedra. ZSM-5 has two types of interconnecting channels, a smaller one that is elliptical and linear, and a larger one that is close to circular, but zigzags through the aluminosilicate framework. Mordenite also has two interconnecting channels, although one is too small to accommodate organic molecules.

Although zeolites have high surface areas (500-700 m^2g^{-1}), most of this area is internal (Figure 1). This is an unusual property for solid materials and, fortunately, it allows the chemist to perform selective chemistry *within* a zeolite cavity, often resulting in differences in reaction selectivity. The pore and/or cavity dimensions of several zeolites, derived from crystallographic data,[3] are provided in Table 1, and have been correlated with examples of included organic molecules. Although these numbers provide a rough understanding of how zeolites selectively include (or exclude) compounds based on size, they are somewhat misleading. This is due to the fact that the zeolite pores are flexible (as a result of Si-O-Si bending) and because the type of cation present effects both the pore and cavity dimensions. In many cases, molecules seemingly too large may enter zeolite cavities, particularly at higher temperatures. A more appropriate measure of zeolite dimensions is the "effective" pore size, which may be estimated as 110% of the zeolite's crystallographic dimensions.

Zeolite	Pore type	Dimensions	Commercial products	Si/Al ratio, cation present	Molecules absorbed
Zeolite A (LTA)	Interconnected spheres	4.1Å diameter pore 11.4Å diameter cavity	Linde Type 4A, 3A, 5A molecular sieves	1, Na^+ Na^+/K^+, Na^+/Ca^+	water, methanol
Zeolite X/Y (Faujasite, FAU)	Interconnected spheres	7.4Å diameter pore 11.8Å diameter cavity	13X, CBV-100, HSZ-320NAA CBV-400 HSZ-390HUA	5, Na^+ 5, H^+ 200, H^+	naphthalene various steroids
ZSM-5 (MFI)	Interconnected channels	5.3 x 5.6Å channel 5.1 x 5.5Å channel	CBV-3020 CBV-30014	30, H^+ or NH_4^+ 300, H^+ or NH_4^+	cyclohexane biphenyl
Mordenite (MOR)	Interconnected channels	6.5 x 7Å channel 2.6 x 5.7Å channel	HSZ-620HOA CBV-10A HSZ-690HOA	15, H^+ 13, Na^+ 200, H^+	neopentane
Zeolite beta (BEA)	Interconnected channels	7.6 x 6.4Å channel 5.5 x 5.5Å channel	CP-811BL-25	25, H^+	*cis*-4-*tert*-butyl cyclohexanol

Table 1. General Characteristics of Several Zeolite Types

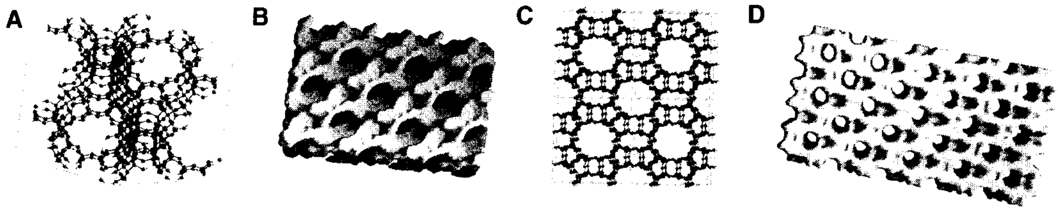


Figure 1. Zeolite Structures. A: Faujasite, Unit Cell; B: Faujasite, 4:2:3 Surface View; C: Mordenite 2:2:3 Structure; D: Mordenite 4:4:3 Surface View

By strict definition, only those materials that are porous aluminosilicates are defined as zeolites. Materials that are structurally similar to zeolites, but do not have an aluminosilicate composition, are called *zeotypes*. A large number of zeotypes have been prepared, including materials where Ga, B, Ti, Cr, V, and P have been substituted into the aluminosilicate framework. In many cases, these materials are derivatives of well-established zeolite structures. In contrast, other zeotypes have no structural analogs, such as the siliceous MCM-41.[4] This material is defined as mesoporous and its structure consists of hexagonal, elliptical, or spherical, parallel channels that vary from 15-110Å in diameter, depending on the templating method chosen for the crystallization process. Titanium-substituted and MCM-derived zeotypes have some distinct advantages over traditional zeolites and selected applications of these materials to organic synthesis have been provided in this review.

3. General Properties of Zeolites: Acidity, Basicity, and Hydrophobicity

Substitution of Al for Si in any silicalite structure creates an anionic site within the inorganic framework. Charge neutralization may occur by either protonation or by interaction with a metal cation or a hydronium ion. Thus, both Brönsted and Lewis acidity may be present within the zeolite framework. Brönsted acidity is typically viewed as resulting from protonation of the Al-O-Si oxygen center or by reaction of water with a proton or metal center to generate a hydronium ion, which interacts with the anionic framework aluminum center. Lewis acidity is typically conferred by the metal ions that compensate for the anionic aluminum centers. For zeolites A, X, and Y, these cations are localized at several distinct positions within the zeolite cages. Much stronger Lewis acid sites are created when defects in the aluminosilicate framework are present, causing the generation of unsaturated trigonal aluminum centers.

Zeolite acidity (both the number of sites and their strength) can be quantified by spectroscopic (NMR, IR, UV-vis) and calorimetric methods.[5] H-Form zeolites, prepared by ion exchange with NH_4Cl, followed by thermal decomposition of the ammonium ions at ≥400 °C, are highly acidic species and were once considered to be the solid equivalents of superacids. However, results from recent studies would indicate that the Brönsted acidity of H-form zeolites is much lower, being in the range of 70% sulfuric acid.[6] A convenient procedure has recently been developed for determining the number of acidic sites in zeolites, by titrating zeolite with base (e.g. pyridine or diethylamine) using retinol as indicator.[7] With this method, it was determined that anhydrous NaY retains residual Brönsted acidity, in the order of about 1 Brönsted site per 2 supercages.

Acidity can be modulated in several ways: i) by cation exchange, ii) by exchange of framework aluminum for other metals (e.g., Ga, Fe, B, P), iii) by the presence of water, and iv) by changing the Si/Al ratio.[8] Cation exchange using alkali metals (i.e., Li, K, Rb, Cs), transition metals, and rare earth metals (e.g., La, Ce, Y, Nb, Yb) is a convenient method for modulating zeolite acidity. The zeolite is first soaked in an aqueous salt solution for several hours (sometimes at higher temperatures), then filtered, washed, and dried. Thorough drying is extremely important when preparing metal-exchanged zeolites, as the presence of trace amounts of water can result in the generation of active (and usually unwanted) Brönsted sites. Although a comprehensive acidity scale is not available, the order of increasing acidity for alkali metal-exchanged zeolites is $Cs^+<Rb^+<K^+<Na^+<Li^+$.

Changes in the Si/Al ratio within the zeolite framework also cause subtle changes in acidity. As one might expect, the more aluminum is present, the greater the number of acidic sites are present within the zeolite. However, higher aluminum content also *decreases* the strength of the acidic centers present, since positive charge is more effectively dispersed by the higher number of adjacent anionic centers. Changes in Si/Al content are simply performed by modifying the amount of silica and alumina present during the zeolite synthesis. Alternatively, higher Si/Al ratio zeolites may be obtained by dealumination of pre-existing materials; however, this often results in the enlargement of micropores and the formation of mesopores and satellite aluminum centers.[9]

Although zeolites are usually considered acid catalysts, cation substitution with Rb and Cs, as well as metal-doping, creates a basic zeolite.[10] The presence of heavy metal cations is believed to increase the negative charge on the aluminum center, which is transferred to the adjacent oxygen atom, creating a basic site. The structure and location of the basic sites for metal-doped zeolites is not well understood; however, they are believed to be surface-bound metal oxides. Basic zeolites catalyze deprotonation chemistry, and studies indicate that their basicity is between pyridine (pK_b 8.8) and piperidine (pK_b 11.12).[11] The basicity of zeolites was determined by examining the Knoevenagel condensation of benzaldehyde with several dicarbonyl compounds, including ethyl acetoacetate, ethyl malonate, and ethyl cyanoacetate.

Whether zeolites are hydrophilic or hydrophobic can have a profound influence on their chemical reactivity. Organic molecules rely on H-bonding, electrostatics, and π-cation interactions for effective zeolite absorption and these interactions will clearly be influenced by the number of acidic sites present. As expected, the more Si is present, the more hydrophobic the zeolite and therefore the greater the ability these materials have to interact with hydrophobic organic molecules or to exclude hydrophilic molecules, such as water. Zeolite A and zeolites X/Y have a Si/Al content at or close to 1 (Table 1) and are highly hydrophilic absorbants. Pentasil zeolite ZSM-5, which can have very high Si content, has significant hydrophobic character and has poor affinity for water. Mesoporous materials, such as MCM-41, are unusual in that they possess terminal silanols *within* their cavities. Although one might expect these materials to be highly hydrophilic (i.e., behaving like hydroxylated silica), MCM-41 has only moderate affinity for highly polar compounds.[4c]

4. Why use Zeolites?

There are several reasons for using zeolites over other possible reagents/catalysts. From an industrial standpoint, zeolites offer the advantages of having (i) high thermal stability, ii) being insoluble versions of noxious Brönsted and Lewis acids, and iii) providing shape selectivity by possessing identical, well-defined reaction cavities. These features are of utility to the synthetic organic chemist, who is continuously dealing with issues of reagent compatibility and reaction selectivity. However, the less obvious benefit to using zeolites involves their (controlled) variability. Through the processes of cation exchange, metal framework substitution, covalent modification, and organic templating, the chemist can fine-tune zeolite dimensions, acidity, and electrostatics. The latter is particularly important for electron and energy transfer processes, or for stabilizing reactive cationic intermediates.

The shape selectivity observed for zeolite catalysis has been categorized into 3 different types:[12]

2. *Reactant selectivity.* From a mixture of reactants, only those of the appropriate dimensions will enter the zeolite cavity and undergo chemical transformation. A classic example is the selective cracking and absorption of *n*-alkanes from paraffin mixtures.
3. *Product selectivity or molecular trafficking.*[13] From a mixture of products formed during the zeolite-catalyzed reaction, only those of appropriate dimension may diffuse out of the pores. An important application of this process is seen in zeolite-mediated electrophilic aromatic substitutions, exemplified by the *para*-selective Friedel-Crafts monoalkylation of toluene using zeolite ZSM-5.
4. *Transition state shape selectivity.* This last type of selectivity, also termed *restricted transition state selectivity*, requires the reaction to occur either at[14] or within the zeolite pore. Similar to enzyme catalysis, the zeolite will stabilize one transition state over another, either by size or shape effects.

Thus, by one or more of the above methods, zeolites can control the selectivity of chemical transformations, by changing either the products formed or the ratio of the product(s) formed. The extent of reactant and transition state shape selectivity has been quantified by examining the zeolite-mediated dehydration of 1- *versus* 2-butanol. Using this as a benchmark, it would appear that zeolites can discriminate between differences in structure of less than 1Å.[15]

5. Mechanistic Pathways of Zeolite-Catalyzed Transformations

5.1. Carbonium and carbenium ions

Zeolites often confer reactivity by generating carbonium, carbenium, and radical cation intermediates. This ability to stabilize electron deficient species is due to both the zeolite (anionic) framework and the fact that zeolite cavities are highly polar and possess strong electric fields.[16]

Zeolite-mediated carbonium ion formation was first discovered in petroleum cracking processes.[17] The mechanism of aliphatic hydrocarbon fragmentation is analogous to superacid-promoted decomposition of hydrocarbons, involving protonation of a saturated carbon center to generate a transient carbonium ion intermediate, which decomposes to yield hydrocarbon and carbenium ion.[18] An application of this chemistry to fine chemical synthesis is the isomerization of tricyclo[5.2.1.$0^{2,6}$]decane (**1**) to adamantane with rare-earth (RE) exchanged zeolite Y, under a reducing atmosphere (H_2/HCl) and at elevated (250 °C) temperature (Figure 2).[19] Deuterium labeling experiments support a mechanism involving the intermediacy of pentacoordinate carbonium ions, which subsequently dehydrogenate and undergo a series of 1,2 shifts to generate adamantane.[20]

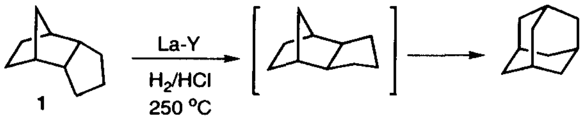


Figure 2. Skeletal Isomerization of Tricyclo[5.2.1.$0^{2,6}$]decane (1) to Adamantane with RE-Y

Carbenium ion stabilization within the zeolite cavity is pronounced and in certain cases, the generation of persistent carbenium ions can occur, which can be monitored spectroscopically and even by X-ray diffraction.[21] For example, indene (**2**), 1,1-diphenylethylene (**3**), and 4-vinylanisole (**4**) all react with CaY to generate highly colored materials that result from initial protonation and condensation (through electrophilic aromatic substitution) to generate persistent cations (lasting for weeks to several months, Figure 3).[22]

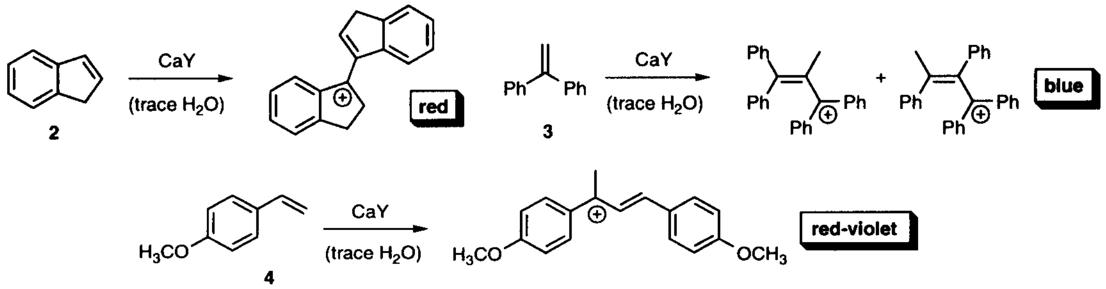


Figure 3. Examples of Persistent Carbenium Ions

Olefin reduction, isomerization, and addition (e.g., hydration) reactions occur under acid-catalyzed conditions, using a variety of zeolites, including Li- and CaY.[23] In these cases, Brönsted sites have been cited as the source of zeolite reactivity, where the presence of trace amounts of water creates a hydrated metal cation (Figure 4). Olefin reduction occurs by protonation followed by solvent-mediated quenching of the resulting cation.

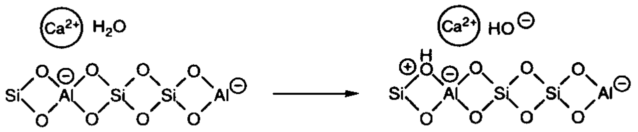


Figure 4. Formation of Brönsted Sites in Hydrated Zeolites

5.2. *Radical Cations*

Zeolites have the capacity to accept electrons (*via* their metal ion centers) and, in the presence of a suitable donor, can generate radical cations. Like persistent carbenium ions, certain species are stable within the zeolite cavity for up to several months and can be monitored spectroscopically.[24] For example, electron transfer occurs with conjugated aromatic systems, using NH_4Y, HY, and Na-ZSM-5 as acceptors.[25] Although electron transfer does not spontaneously occur with NaY or NaX, Ca-, Mg-, and Sr-exchanged faujasites are susceptible to electron transfer chemistry. Because the supercages of zeolites X/Y are relatively large, the radical cations can subsequently react to generate either addition or dimeric products. Thus, reaction of benzonorbornadiene (**5**) with CaY yielded a mixture of structurally diverse compounds, the amount of which depended on the reaction conditions employed (Figure 5).[26] Using 450 °C activated zeolites in dry hexane, two products resulting from olefin reduction were obtained (**7** and **8**), while under wet or methanolic conditions, reduction to the corresponding alcohol or ether (**9**) occurred. As expected, increased loading of the faujasite with benzonorbornadiene resulted in a linear increase in the [2+2] cycloaddition product.

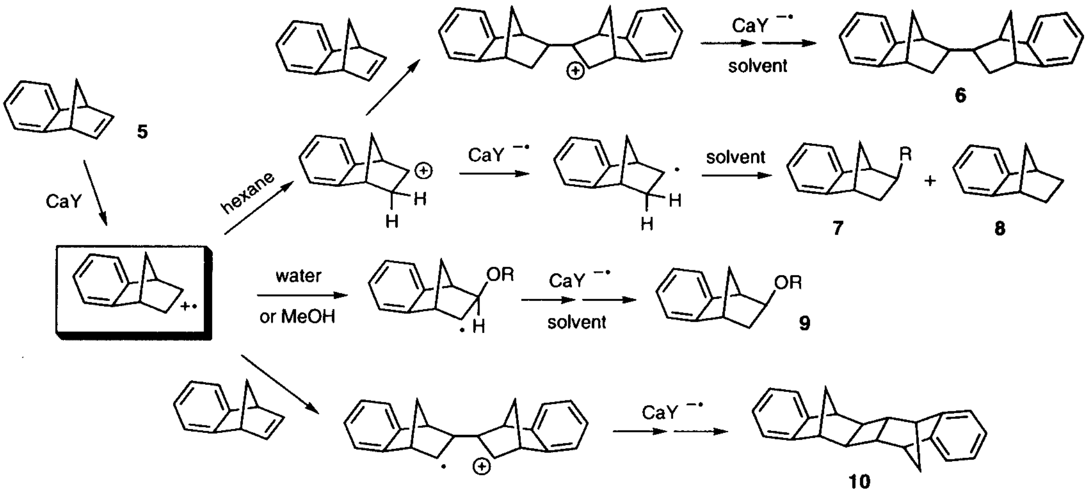


Figure 5. Intermediacy of Radical Cations in Reduction, Addition, and Dimerization Chemistry with Zeolites

6. Zeolites in Organic Synthesis

6.1. Zeolites as small molecule absorbents and as acid catalysts

Zeolites have been used for the selective absorption of small molecules, particularly polar compounds and olefinic compounds that have high binding affinity for zeolite cavities. Although initially conceived for the selective absorption of small, linear hydrocarbons, zeolite A is widely used as a water and acid (HCl, HBr) scavenger. The ability of zeolite A to shift equilibria, as exemplified by its use in imine, acetal, ester, and enamine formation, and for transacetalization and transesterification reactions, is well known. 4Å Molecular sieves are added to metal-mediated organic transformations, such as the Sharpless-Katsuki asymmetric epoxidation,[27] to minimize inhibition and/or decomposition of the organometallic catalyst.[28]

Recent uses of zeolites as small molecule scavengers utilize their acidic properties as well. Zeolites have been shown to be effective catalysts for the preparation of acetates,[29] dioxolanes,[30] dimethylacetals,[31] and for ketal, hydrazone,[32] and benzyl ether[33] deprotections. Zeolites that contain trace amounts of water (and presumably have enhanced Brönsted acidity) have been used for the preparation of the chiral Lewis acid, BINOL-Ti, and to increase diastereoselectivity in the Pd(II)-catalyzed coupling of 1,2-divinylcyclohexane with various chiral acids.[34] In each case the zeolite appears to function as a replacement for conventional Brönsted and Lewis acids, resulting in milder reaction conditions and better reaction selectivity.

The zeolite-promoted hydrolysis of several acetals was studied to determine whether there were any mechanistic differences between the heterogeneous and corresponding homogeneous (e.g., aqueous HCl) reactions.[35] A comparison of the rates of hydrolysis showed little dependence on acetal structure for the zeolite-promoted reaction (Figure 6). This surprising result suggests that the heterogeneous deprotection is under stereoelectronic control, where specific acetal-zeolite interactions result in loss of conformational freedom, favoring conformers having an anti-periplanar arrangement of the oxygen electron lone pairs.[34]

acetal	relative rate	
	homogenous conditions	heterogenous conditions
2-phenyl-1,3-dioxolane	1	1
benzaldehyde diethyl acetal	39	5

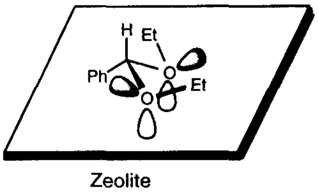


Figure 6. Conformational Control in the Zeolite-Mediated Deprotection of Acetals

An unusual acid-catalyzed spiroketalization was recently reported using acidic pentasil zeolite.[36] Tricarbonyl dihydropyran derivative **11** was reacted with H-ZSM-5 (40 wt%) in refluxing benzene for 36 h, yielding novel tricylic spiroketal **12** (Figure 7). Proof of structure was obtained by X-ray crystallography. This reaction is apparently the result of shape selectivity, since reaction of **11** with *p*-TsOH in refluxing benzene did not yield **12**, but rather a mixture of phenolic or cyclohexenone-containing materials. Although the spiroketal is too large to form within the pores of ZSM-5, surface adsorption appears to play an important role in reactivity. The authors speculate that formation of **12** is due, in large part, to stabilization of intermediate **13**.

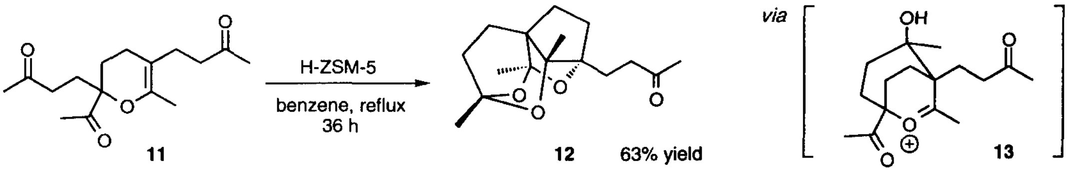


Figure 7. Zeolite-Mediated Spiroketalization

The stereoselective dehydration of aliphatic, aromatic, and heteroaromatic 2-hydroxy-nitroalcohols (e.g., **14**) was recently demonstrated using zeolites Y, ZSM-5, beta, and mordenite (Figure 8).[37] The reaction is performed by refluxing nitroalcohol and zeolite (10 wt%) in toluene, with azeotropic removal of water. No side products were formed and the reaction was stereoselective, providing only (*E*)-nitroolefin. H-Form zeolites were found to the best catalysts, followed by rare-earth exchanged Y and small pore H-ZSM-5. The zeolites could be reused several times, after reactivation at 400 °C, without any discernable loss in activity.

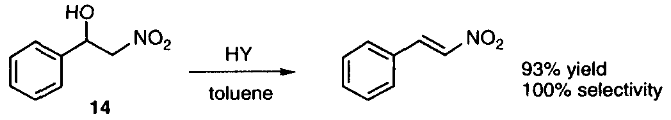
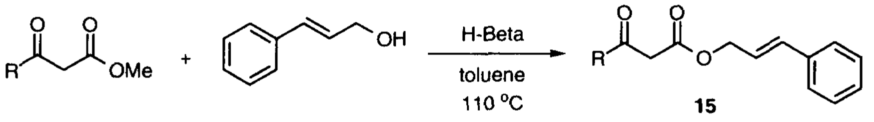


Figure 8. Nitroolefin Formation *via* Zeolite-Promoted Dehydration of Nitroalcohols

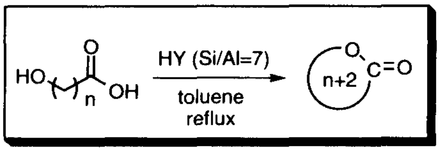
The transesterification of several β–keto esters, using a variety of alcohols, is effectively catalyzed by acidic zeolites.[38] The reaction is most amenable to sterically unencumbered esters, and is mild enough to be used for the formation of labile allylic β-ketoesters (**15**, Figure 9). Transesterification is performed by reacting ester and alcohol with 10 mol% zeolite in refluxing toluene, with azeotropic removal of alcohol. Zeolite H-beta was a better catalyst than either H-ZSM-5 or HY, providing 95% yield in the reaction of methyl acetoacetate with cinnamyl alcohol. The use of larger reactants resulted in a steady decline in reactivity, possibly due to the lower diffusability of these compounds within the zeolite cavities. This reaction appears to be limited to β-keto esters, as α–keto, α-bromo, and γ-keto esters did not undergo transesterification.



R = CH_3, 95% yield
R = Ph, 66% yield

Figure 9. β-Keto Allylic Esters by Zeolite-Promoted Transesterification

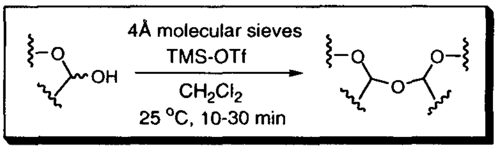
Zeolite-catalyzed esterification was recently extended to the macrolactonization of long chain (C_{12}-C_{19}) hydroxyalkanoic acids.[39] Using dealuminated zeolite Y, HSZ-360HUA (Si/Al=7), macrolactonization occurred in generally high yield (Figure 10), and unlike typical homogeneous reaction conditions, could be performed at relatively high concentrations. The reaction is mediated on the surface of the zeolite (probably at surface mesopores), as seen by the inhibition in lactone formation upon addition of 4,7-diphenyl-1,10-phenanthroline, which can deactivate surface acid sites but is too large to penetrate the supercages of zeolite Y.



n	yield (%)
11	10
14	50
15	55
18	45

Figure 10. Macrolactonization of Hydroxyacids using Dealuminated Zeolite HY

High stereoselection is achieved in the TMS-OTf promoted dimerization of pyranose and furanose sugars to yield α,α-disaccharides when molecular sieves are added (Figure 11).[40] Posner and Bull examined various 4Å molecular sieves and found that Davison SP 7-8461 zeolites were superior to those obtained from Aldrich, Janssen, and Lancaster. The reason for the observed difference in reactivity is unclear, although a study of the effects of intrinsic water content indicates that this is not a factor. The chemical composition of each of the zeolites was determined and variability in the amount of trace metals present, such as Fe_2O_3, was found.



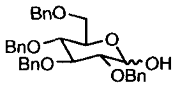
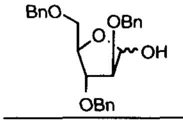
		1,1'-disaccharide ratio		
sugar	yield (%)	α,α	α,β	β,β
	76	2.8	1.0	0.1
	62	only	---	---

Figure 11. TSM-OTf Promoted α,α-Disaccharide Formation, Using Zeolite A as Additive

6.2. *Electrophilic aromatic substitution*

A variety of industrially-useful synthetic transformations, which rely on both the acidic and shape selective properties of zeolites, were developed as an outgrowth of petroleum cracking. In particular, zeolites have been used as Lewis acid substitutes for electrophilic aromatic substitutions of benzene, substituted benzenes, aromatic heterocycles, and naphthalenes. The greatest advantage to using zeolites is environmental, where highly noxious acids are replaced by recyclable solid catalysts. Another advantage, which is of particular importance in the preparation of disubstituted arenes, is that *para*-selectivity is typically observed.[41]

The Mobil-Badger process, which forms ethylbenzene from benzene and ethylene, is a classic example of a zeolite-catalyzed Friedel-Crafts alkylation.[42] Although polyalkylations occur, these materials are typically trapped within the zeolite (often clogging the pores and creating polymeric materials known as coke) or undergo acid-catalyzed isomerization/fragmentation to yield the desired product. Other zeolite-catalyzed electrophilic aromatic substitutions include acylation (using acids and anhydrides as acylating agents), nitration (using NO_2), and halogenation (using Cl_2 or Br_2).[43]

The zeolite-mediated Friedel-Crafts acylation and alkylation of naphthalene has received considerable attention, because many products of these reactions are used as starting materials for synthesis of polymers and pharmaceuticals. Although further study of these reactions is required, differences in reactivity, which can be directly attributed to shape selectivity, have been noted. For example, in the formation of diisopropylnaphthalenes from naphthalene and isopropanol, ZSM-5 was not reactive, zeolite Y and mordenite provided varying mixtures 1,3-, 2,6- and 2,7-diisopropylnaphthalenes, and zeolite beta yielded several polycycles resulting from acid-catalyzed skeletal rearrangements.[44]

Zeolites are useful catalysts for the preparation of chromans and 2*H*-1-benzopyrans.[45] Thus, a series of aryl α-alkynols and substituted phenol and naphthol derivatives condense to form 2*H*-1-benzopyrans (**16**) when refluxed at 130 °C in chlorobenzene, in the presence of H-form faujasites (Figure 12). The reaction, which is *ortho* selective, involves three sequential steps: i) enyne formation (by acid-catalyzed dehydration), ii) electrophilic aromatic substitution between phenol and alkyne, and iii) *O*-alkylation. Although a number of alternative methods are known for the synthesis of these bicyclic ring systems, the zeolite reactions typically result in higher reaction yields and selectivity.

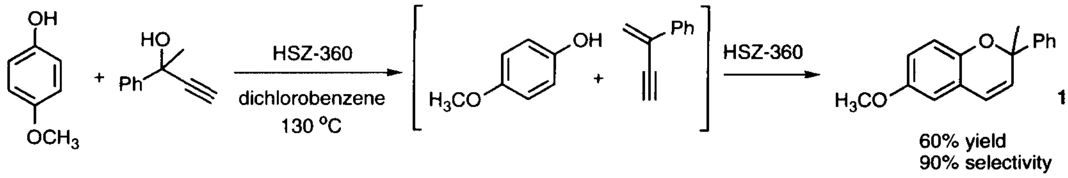
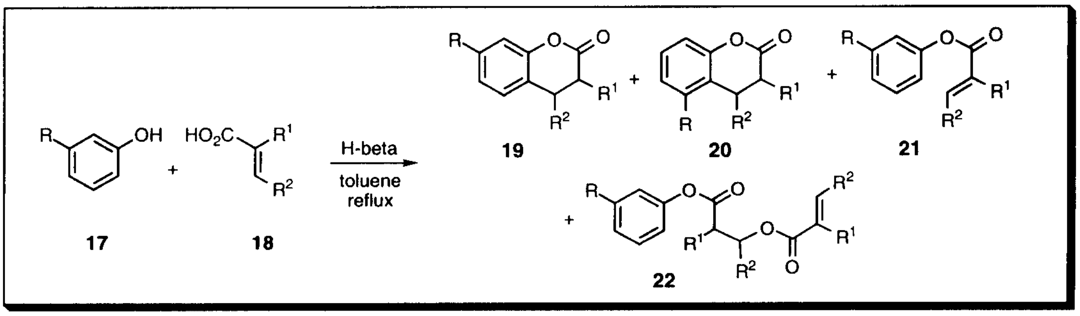


Figure 12. Zeolite-Promoted Cyclizations for the Preparation of 2*H*-1-Benzopyrans

Tandem esterification and electrophilic aromatic substitution of phenols with α,β-unsaturated carboxylic acids is effectively performed with a variety of solid acid catalysts. van Bekkum and co-workers have recently examined the preparation of several coumarin derivatives (e.g., **19** and **20**) by this method, using zeolite H-beta as acid catalyst (Figure 13).[46] The reaction works best with highly activated phenols, such as 3-methoxyphenol, and with sterically uncongested acids. Because water is generated as a by-product in the esterification step, azeotropic distillation is required to limit deactivation of the catalyst. Despite these precautions, the reaction reaches maximal conversion within 80 minutes, in part because of product inclusion within the zeolite cavities.



R	R^1	R^2	% Conversion			
			19	20	21	22
OH	H	H	73	-	-	-
OCH_3	H	H	64	14	-	-
H	H	H	2	-	10	4
OH	H	CH_3	-	-	10	-

Figure 13. Zeolite-Catalyzed Coumarin Formation

6.3. *Zeolite-Catalyzed Rearrangements*

As previously mentioned, zeolites catalyze a number of skeletal rearrangements, resulting from the formation of transient carbenium and/or carbonium ion intermediates. The *para*-selective isomerization of xylenes, anilines, and chlorobenzenes,[47] and the Beckman rearrangement of cyclohexanone oxime to ε-caprolactam[48] are two industrially-significant rearrangements that are effectively catalyzed by zeolites. The mechanism of arene isomerization involves initial arene protonation, followed by 1,2-alkyl migration of the resulting benzenium ion.[49]

The acid-catalyzed rearrangement of epoxides to either aldehydes or ketones may be performed by zeolites, which are excellent alternatives to conventional protic and Lewis acids. For example, α-pinene oxide (**23**) is efficiently converted to campholenic aldehyde using a variety of zeolitic materials (Figure 14).[50]

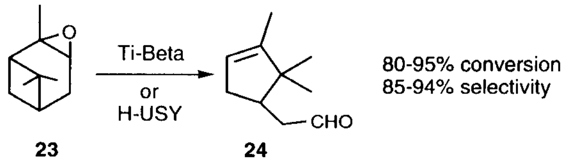


Figure 14. An Example of Zeolite-Catalyzed Epoxide Rearrangements

Zeolites can be used to promote sequential acid catalyzed reactions. As an example, spirolactone **25** is converted in 90% isolated yield to tricylic enone **26** upon treatment with zeolite HY at 300-400 °C in hexane (the reaction was performed in a Teflon-lined autoclave, Figure 15).[51] This multi-step transformation, which involves the intermediacy of an acylium ion, occurs within the supercages, as seen by both loss of starting material from solution and by the inability of small pore zeolite H-ZSM-5 to catalyze the reaction. Because the product does not readily diffuse through the pore openings and requires extraction with methanol for recovery, the reaction must be performed with excess zeolite (10X w/w). Although excess acid catalyst is required, the zeolite may be reused upon reactivation.

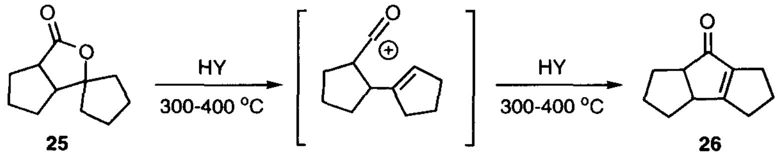
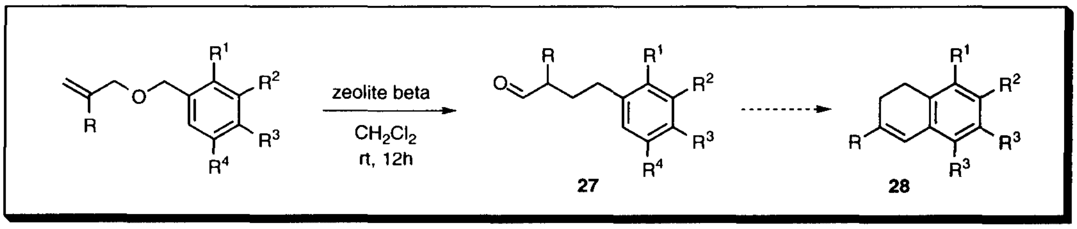


Figure 15. Zeolite Catalyzed Rearrangement of Spirolactone 25

Activated zeolite beta has been found to be an excellent substitute for Lewis acids (e.g., $BF_3 \cdot Et_2O$, $SnCl_4$) in the rearrangement of benzyl allyl ethers to 4-arylbutanals (**27**, Figure 16).[52] Mechanistically, the reaction proceeds by initial 1,4-migration of the allyl moiety to the benzylic position, followed by a 1,2-hydride shift. A number of substitution patterns are tolerated on the aromatic ring and when highly activated rings are present, further cyclization (by acid-catalyzed electrophilic aromatic substitution) may occur to yield dihydronaphthalene derivatives (e.g., **28**). Interestingly, only certain compounds undergo this secondary reaction. In these cases, differences in reactivity have been attributed to transition state shape selectivity, where it is proposed that only dihydronaphthalenes with widths <7.4Å are accommodated within the zeolite cavity.

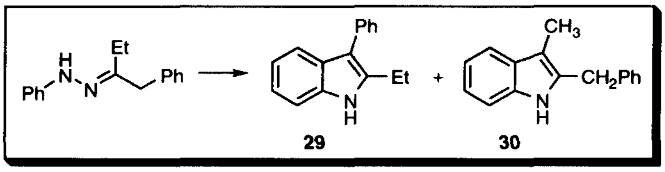


benzyl ether	yield (%)	
	27	28
R=CH_3, R^1=OMe, R^2-R^4=H	83	-
R=CH_3, R^2,R^3=OMe, R^1,R^4=H	-	63

Figure 16. Zeolite-Promoted "BenzAll" Rearrangement of Allyl Methoxybenzyl Ethers

6.4. *Cyclodehydrations*

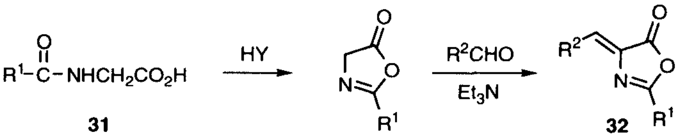
Because of their dual properties, namely acidity and porosity, zeolites have found utility as cyclization catalysts. An example of this reactivity is seen in the Fischer indole synthesis, an industrially important method for preparing substituted heterocycles.[53] The reaction involves a series of steps: i) condensation of phenylhydrazine with ketone or aldehyde, ii) acid-catalyzed tautomerization and cyclization of the resulting hydrazone, and iii) loss of ammonia to generate indole. As one would predict based on shape selectivity arguments, substituted indoles are formed with varying isomeric selectivity, depending on zeolite type used (Figure 17).[54]



conditions	29:30
CH_3CO_2H	76:24
HY	62:38
H-beta	31:69

Figure 17. Zeolite-Catalyzed Fischer Indole Synthesis

Zeolite HY has been used for the two-step synthesis of 2-oxazolin-5-ones (Figure 18).[55] The reaction is performed by impregnating zeolite with melted *N*-acylamino acid **31**, then microwaving the mixture for several minutes. The resulting lactone is extracted from the zeolite with benzene and condensed with various benzaldehyde derivatives in the presence of triethylamine. Unlike conventional cyclodehydration methods, which require the use of acids and often produce a number of by-products, the zeolite-catalyzed reaction affords 4-arylidene-2-oxazolin-5-ones in 70-85% isolated yield. The use of microwave irradiation to accelerate this reaction may be of applicability to other zeolite-mediated processes.



R^1 = Ph, Me, CH=CHPh
R^2 = Ph, 4-NMe_2Ph, 2-furyl, 3,4-$(OMe)_2$Ph
70-85% yield

Figure 18. HY-Promoted Cyclodehydration of *N*-Acylamino acids

Considerable efforts have been made to develop methodology related to zeolite-catalyzed ether formation, since ethers, such as methyl *tert*-butyl ether (MTBE), are manufactured as high octane additives for gasoline. This known chemistry can be applied to the synthesis of cyclic ethers, where the formation of either 5- or 6-membered ring systems may occur. For example, diethylene glycol and several of its derivatives are cyclodehydrated using zeolites.[56] The reaction appears to proceed in two steps, first by covalent attachment to the zeolite surface, followed by acid-catalyzed etherification (Figure 19).

catalyst	diethylene glycol conversion (%)	1,4-dioxane formed (%)
HY	16.3	13
Cu-NaY	8.1	27
K10 clay	46.5	38.6
H-ZSM-5	100	73

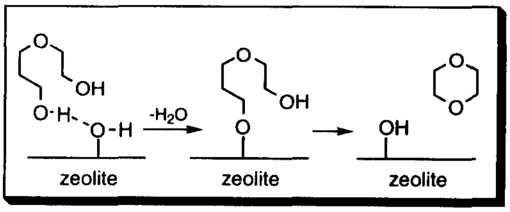


Figure 19. Cyclodehydration of Diethylene Glycol with Various Zeolites

6.5. *N*- and *S*-Alkylation Chemistry

Nitrogen and sulfur substitutions are effectively promoted by zeolites. The former is performed with acidic zeolites, often using ammonia as an external nitrogen source, while the latter is typically performed under basic conditions. Although zeolites have been studied as hydrosulfuration catalysts, their intrinsic acidity often results in competing side reactions, such as dehydration and sulfide formation.[57]

Zeolite-catalyzed *O*-to-*N* and *N*-to-*S* conversions are rather facile, and several industrially-relevant examples include tetrahydrothiophene from THF, 2-pyrrolidinone from γ-butyrolactone, aniline from phenol, and either pyrrole or thiophene from furan.[1a,g] Unsymmetrical organic sulfides are efficiently synthesized from thiols and either alkyl or aryl halides, using Ce-exchanged NaY (CeNa-Y, 72% Ce, Figure 20).[58] Na-exchanged zeolite X catalyzes the regioselective ring opening of several substituted thiiranes (e.g., **33**) by thiols.[59] Both of these reactions occur by S_N2 displacement, with the latter involving the formation of an ion pair intermediate. Compared to other methods, the zeolite-catalyzed reactions provide generally higher yields and are often less prone to by-product formation, which results from additional alkylation chemistry.

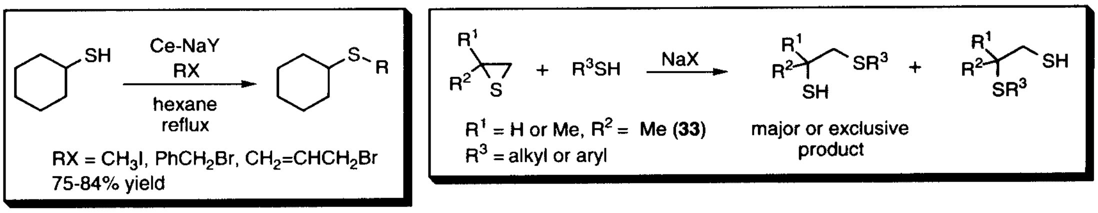


Figure 20. Thiol Alkylations Catalyzed by Basic Zeolites

Zeolite-catalyzed *N*-alkylations are particularly useful for the preparation of 1° and 2° amines since trialkylation typically does not proceed, due to size constraints within the zeolite cavity. As a recent example, the monomethylation of substituted anilines with excess dimethyl carbonate was studied using zeolite X and Y as catalysts (Figure 21).[60] The reaction is highly selective compared to the corresponding base-catalyzed reaction, which is not only slower, but provides a significant amount of *N*-methyl carbamate product. The observed differences in selectivity between zeolite and typical preparation methods are apparently due to restricted product diffusion. While *N*-methyl aniline can freely exit the zeolite supercages, the carbamate that also forms does not. Instead, it undergoes both *N*-methylation and demethoxycarbonylation to generate the desired monomethylated aniline derivative.

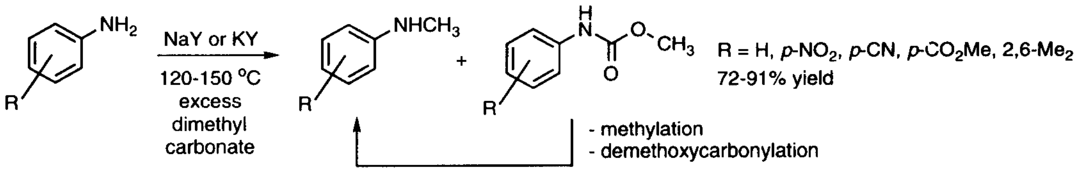


Figure 21. Zeolite Promoted *N*-Methylation of Anilines with Dimethyl Carbonate

Acidic zeolites are effective catalysts of amidation reactions and have found applicability in the preparation of organic nitriles under high temperature (300-400 °C) conditions.[61] Recently, this methodology has been extended to the preparation of substituted ureas.[62] For example, diphenylurea is obtained by heating ethyl acetoacetate with aniline in the presence of HY, followed by MeOH/water extraction. A time course of this reaction supports a two-step mechanism, where formation of an intermediate acetoacetanilide occurs, which subsequently reacts with additional aryl amine to produce urea and acetone. Although benzyl and alkylamines do not amidate β-ketoesters (instead, condensation of benzylamine with ethyl acetoacetate yielded exclusively ethyl β-benzylaminocrotonate), a broad range of 1° amines will react with acetoacetamide **35** to provide symmetrical *N,N'*-dialkylureas (Figure 22). Compared to analogous protic and Lewis acid promoted condensations, the zeolite reaction provides higher yields and much higher selectivity towards urea formation.

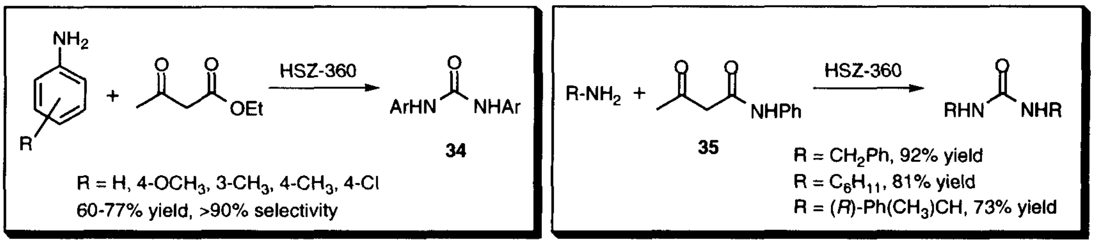


Figure 22. Symmetrical Urea Formation Using Zeolites

6.6. *Base-Catalyzed reactions*

A variety of condensation reactions may be performed with zeolites of appropriate basicity.[10] These reactions proceed by either base catalysis, or by dual involvement of acidic and basic sites that are present in the zeolite structure. Aldol condensation, such as the condensation of acetone to give mesityl oxide, using zeolites X and Y, can been effected under high temperature conditions.[63] The product ratios are modulated by Si/Al ratio and zeolite size, with greater amounts of isophorone being formed when larger pore zeolites are used. Knoevenagel condensations and Michael additions are also catalyzed by basic zeolites.[64]

A great disadvantage to using zeolites as base catalysts is that they are inherently acidic materials. As a result, they can be converted into only *weakly* basic materials by exchange with heavier metals cations, such as cesium. While basic zeolites can be used to deprotonate activated carbon centers, they have low reactivity in the condensation of non-activated materials. This is exemplified in the Claisen-Schmidt condensation of 2-hydroxyacetophenone with benzaldehyde to yield 2'-hydroxychalcone, where a comparison of Cs-NaX with hydrotalcites of varying Mg/Al ratios indicated that clays were superior as basic heterogeneous catalysts.[65] While highly basic zeolites can be prepared by metal doping,[66] the resulting materials are usually air and moisture sensitive and of limited synthetic applicability.

Recently, Jacobs, *et al.* have developed a strongly basic (pK_a~25) heterogeneous catalyst by covalently attaching the guanidine base, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD, **36**) to the free hydroxyls of MCM-41.[67] This material effectively catalyzes several condensation reactions, including Michael addition, Robinson annulation, and Knoevenagel condensations, as well as the base-catalyzed epoxidation of enals with H_2O_2 (Figure 23). High selectivity towards 1,4-addition was seen in the Michael addition of ethyl cyanoacetate and diethyl malonate with various enones in the presence of modified MCM-41, in CH_3CN at room temperature. Aldol condensations could also be catalyzed by this catalyst, as demonstrated by the Robinson annulation of 1,3-cyclohexanedione with methyl vinyl ketone. A comparison of the reactivity of the TBD-modified MCM-41 with TBD-modified amorphous silica indicates that this reaction occurs within the mesopores and that transition state shape selectivity is operational.

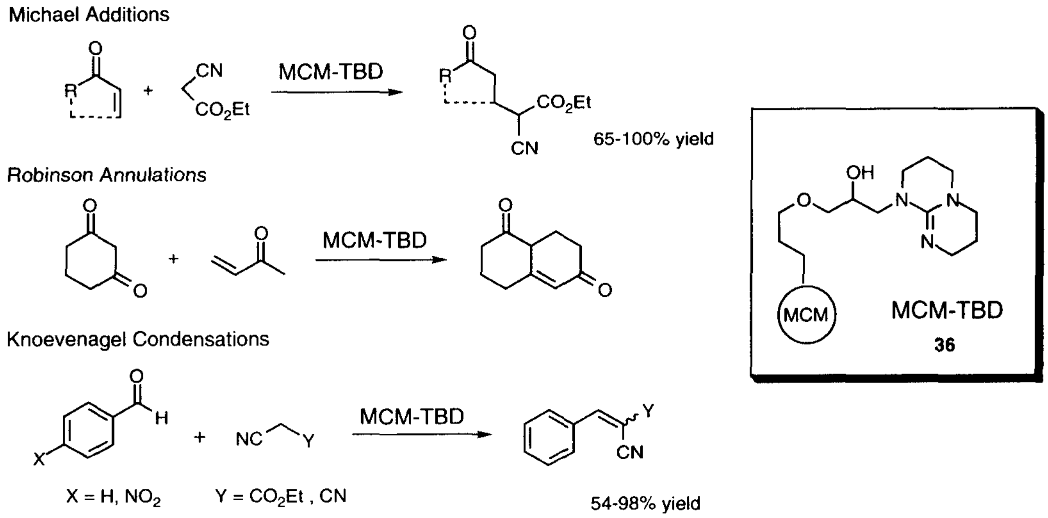
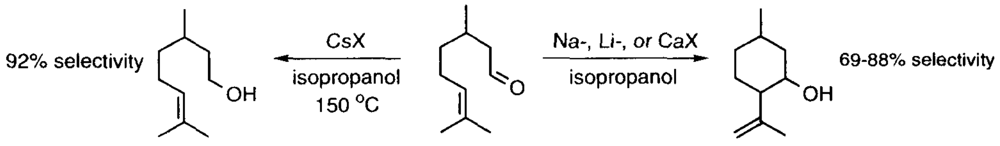


Figure 23. Scope of Condensation Reactions Catalyzed by Guanidine-Modified MCM-41

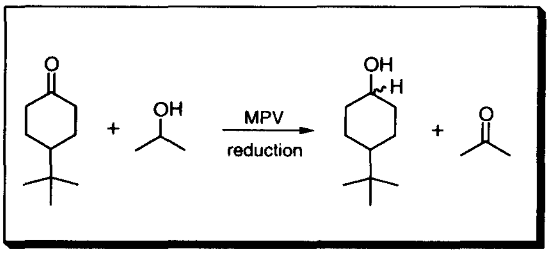
The Meerwein-Ponndorf-Verley (MPV) reduction converts aldehydes or ketones to alcohols, using an aluminum alkoxide as hydride donor. The reaction can be performed with zeolite catalysts, but requires the proper balance of basicity and Lewis acidity. In the reduction of citronellal (**37**) with isopropanol, the use of the basic zeolite, CsX, results in selective reduction (Figure 24).[68] In contrast, reaction of citronellal and isopropanol with Li-, Ca, or Na-exchanged X results in acid-catalyzed cyclization to isopulegol (**38**).



37 **38**

Figure 24. Reduction *versus* Cyclization of Citronellal, as a Function of Zeolite Type

Recently, the zeolite-promoted MPV reduction of substituted cyclohexanones by isopropanol was studied to better understand the nature of the aluminum centers involved in this chemistry.[69] Compared to other aluminosilicates tested, zeolite beta was highly active, and for the reduction of 4-*tert*-butylcyclohexanone, generated the less stable *cis*-cyclohexanol with high selectivity (Figure 25). NMR and IR measurements indicate that the reaction is not catalyzed by extra-matrix, octahedral aluminum centers. While a variety of 4-substituted cyclohexanones were reduced by zeolite H-beta to the corresponding *cis*-cyclohexanols, 3-methylcyclohexanone was reduced with only 68% selectivity and 2-*tert*-butylcyclohexanone was unreactive. For the reduction of 4-*tert*-butylcyclohexanone, the regioselectivity was influenced by the cation present, with heavy atom substitution producing almost complete selectivity towards the *cis* isomer. These results, in conjunction with amine deactivation studies, indicate that the reaction occurs within the zeolite cavity and that zeolites can catalyze disfavored reactions based on transition state shape selectivity. The reaction is believed to proceed though a *cis* restricted six-membered transition state (Figure 26) and requires the intermediacy of transient trivalent aluminum centers that function as the active Lewis acid catalysts.



heterogeneous catalysts	conversion (%)	*cis*:*trans*
Na-beta	32	96:4
NH_4-beta	30	95:5
USY	24	9:91
H-Al-MCM-41	10	10:90
Na-Al-MCM-41	10	10:90
Al_2O_3	45	9:91

Figure 25. Zeolite-Promoted Meerwein-Ponndorf-Verley Reduction of Substituted Cyclohexanones

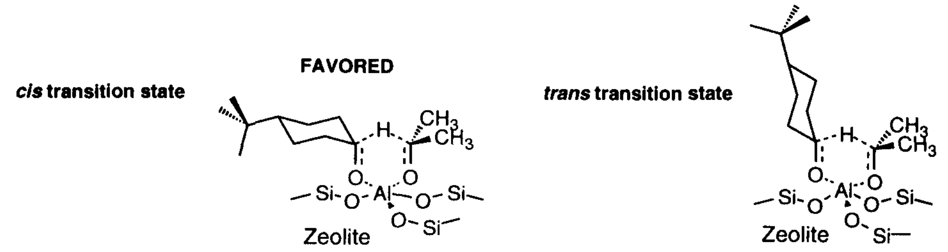
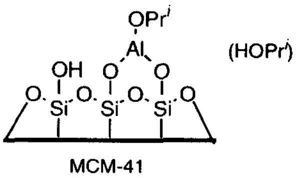


Figure 26. Proposed Transition State Selectivity in Zeolite Beta Mediated Reduction of 4-*tert*-Butylcyclohexanone

Although the H- and Na-forms of Al-MCM-41 are poor catalysts for MPV reductions, reaction of siliceous MCM-41 with $Al(OPr^i)_3$ produces a material that effectively reduces 4-*tert*-butylcyclohexanone to the corresponding alcohol within 5 hours at room temperature, in 86% yield (Figure 27).[70]



39

catalyst	time, temp	conversion (%)
$Al(OPr^i)_3$	24h, rt	59
MCM-41	24h, rt	<1
39	5h, rt	86 (>99)*

* reaction performed at 80 °C

Figure 27. $Al(OPr^i)_3$ Modified MCM-41 for MPV Reductions

As an extension of zeolite-mediated MPV chemistry, the biporous mesoporous zeolite, H-MCM-22, was found to be a bifunctional catalyst for the reductive etherification of ketones.[71] The reaction proceeds in two steps, by acid-catalyzed (hemi)acetal formation, followed by MPV reduction (Figure 28). This novel reaction appears to be unique to MCM-22 and is believed to be the result of the zeolite's high acidity. Typical reaction conditions involve refluxing ketone and catalyst with a secondary alcohol. Both *i*-PrOH and *sec*-BuOH were effective reducing agents, and increased selectivity for ether formation was obtained when the water by-product was removed by NaA absorption. Interestingly, the reaction was found to be sensitive to ketone structure, with only 4-*tert*-butyl- and the sterically similar 4-trimethylsilylcyclohexanones providing ether **41** in high yield and selectivity. The reaction is believed to occur within the zeolite mesopores, where specific orientation of aluminum and carbonyl centers is required for the reaction to proceed.

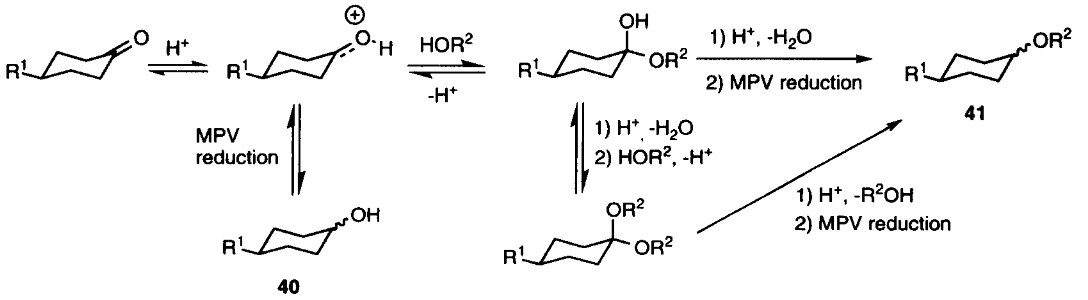
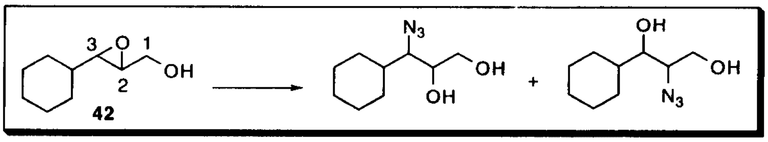


Figure 28. Reductive Etherification of Cyclohexanones

6.7. *Supported reagents*

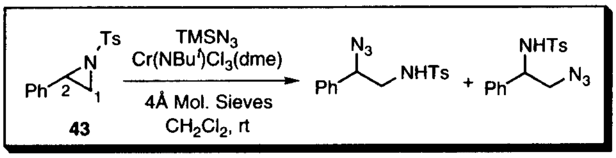
Epoxides are useful intermediates in organic synthesis, being commonly transformed to other materials by either acid-catalyzed rearrangement or by regioselective addition of nucleophiles. Inorganic solids, such as alumina, silica, and zeolites that are "doped" with reactive compounds are often selective reagents. As an example, the reaction of 3-cyclohexyl-1,2-epoxypropan-1-ol (**42**) with NaN_3-doped zeolites was studied (Figure 29).[72] Compared to other reagents, NaN_3-doped CaY was the most effective, with nucleophilic attack occurring preferentially at the more substituted carbon center. This high selectivity is believed to be due to both carbocation stabilization and bidentate Ca^{2+} coordination to the oxygen centers.



reagent	yield (%)	C3/C2 addition
NaN_3 doped CaY	85	94/6
NaN_3 doped alumina	65	66/34
NaN_3–NH_4Cl	88	76/24
Me_3SiN_3-$Ti(OPr^i)_4$	91	89/11

Figure 29. Azide Addition to Epoxides

Other azide-addition reactions are enhanced by the use of zeolites. Sodium azide-doped zeolite HY, H-beta, and H-ZSM-5 are all effective catalysts for the preparation of alkyl and aryl azides from alkenes or alcohols.[73] The reaction is regiospecific, with azide addition occurring at the more substituted carbon center. In the conversion of styrene to 1-azido-1-phenylethane, higher reactivity was seen for catalysts having lower azide loading (<10 wt%) and residual water present. Interestingly, no reaction occurred when unsupported zeolite was added to a solution of styrene and sodium azide. 4Å Molecular sieves were shown to increase both the yield and regioselectivity of the $\mathrm{Cr(NBu^t)Cl_3(dme)}$ catalyzed addition of azide to substituted *N*-tosylaziridines (Figure 30).[74] While there is no selectivity in the absence of zeolite, the addition of 2 equivalents by weight of NaA to the Cr-catalyzed reaction of $\mathrm{TMSN_3}$ with styrene *N*-tosylaziridine (**43**) resulted in almost exclusive formation of the 2-azido product.



reaction conditions	yield (%)	C2/C1 addition
without zeolite	40	1/1
2 equiv (w/w) NaA	86	40/1
NaA only	0	--

Figure 30. Zeolite-Mediated Ring Opening of Aziridines

The reactivity and selectivity of hydride reagents can also be modulated with zeolites. For example, when H-ZSM-5 is added to a mixture of $\mathrm{NaCNBH_3}$ and nitroalkene, all side products resulting from the Michael addition of reduced nitronate intermediate to starting material are eliminated.[75] Despite the inherent acidity of ZSM-5, the reaction is compatible with nitroalkene acetal **44** (Figure 31). Recently, zeolite Y and zeolite beta were treated with zinc borohydride to generate novel supported reagents, which reduce both epoxides and enones with high selectivity.[76] As expected from other zeolite-mediated epoxide ring opening reactions, hydride addition to unsymmetrical epoxides occurred preferentially at the less hindered carbon position. Whereas the reduction of enones (e.g., **45**) with zinc borohydride yields only 1,4-addition product, the zeolite-supported hydride reduces the enone carbonyl to yield allylic alcohol.

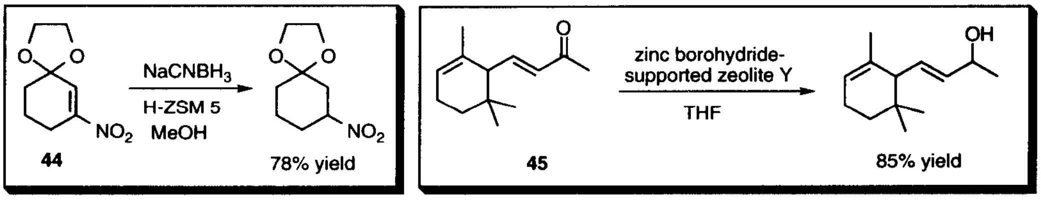


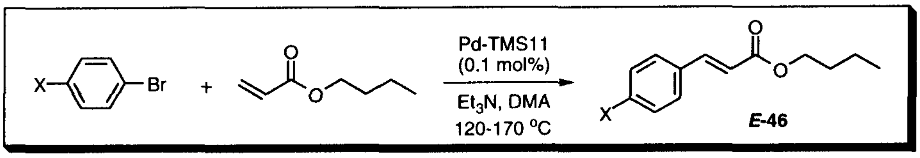
Figure 31. Examples of Zeolite-Mediated Hydride Reductions

6.8. *Zeolite-supported metal catalysts*

The incorporation of metallic catalysts (as opposed to metal-cation exchange or metal-framework replacement) provides bifunctional materials that can be used for (de)hydrogenation, oxidation, isomerization, and hydroformylation. These materials are typically formed by ion exchange with an appropriate metal salt (e.g., metal carbonyls, metal allyl complexes, and metal acetates), followed by thermal decomposition to yield the deposited metal.[77] Chemical vapor deposition is also a useful method for placing catalytic metal centers onto zeolites.

The reduction of cinnamaldehyde with Rh- and Pt-doped zeolite NaY has been studied.[78] Compared to Rh or Pt on carbon, which preferentially reduces the carbon-carbon double bond, Pt-impregnated zeolite Y reduces the carbonyl moiety of cinnamaldehyde, providing 96% selectivity at 75% conversion. Because the metal particles are within the zeolite supercage, the reduction is believed to proceed through an "end-on" absorption of the carbonyl, through the zeolite pore.

A novel heterogeneous Heck catalyst has recently been prepared using siliceous MCM-41.[79] Pd was deposited onto the mesoporous material by chemical deposition of $[Pd(\eta\text{-}C_5H_5)(\eta^3\text{-}C_3H_5)]$, followed by reduction with H_2. This, as well as the surface silanized material (Pd-TMS), was tested for its ability to couple aryl halides with either styrene or *n*-butyl acrylate. Compared to commercially available catalysts (Pd on silica, alumina, or carbon), Pd-TMS was superior, providing higher catalytic turnover, yield, and stability (Figure 32).



X	yield (%)	*E*/*Z*	turnover number
H	62	99/1	624
NO_2	99	99/1	1000
$C(O)CH_3$	99	99/1	1000

Figure 32. MCM-41 Supported Pd as Heck Coupling Catalyst

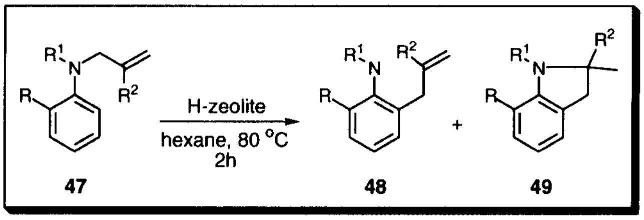
6.9. *Cycloaddition Reactions*

Despite the potential of zeolites as shape selective reagents, there are few examples of zeolite-promoted cycloadditions, such as the Diels-Alder reaction. This is due, in part, to the intrinsic acidity of the zeolite lattice, which causes olefin polymerization to occur in preference to cycloaddition. Cu(I)-Exchanged and non-acidic zeolites have been studied as heterogeneous catalysts for the cyclocondensation of 1,3-butadiene to yield 4-vinylcyclohexene.[80] Zeolites have also been used in Diels-Alder reactions of isoprene,[81] and for the cyclocondensation of (-)-menthyl acrylate with cyclopentadiene.[82] *Endo* selectivity is typically observed, as seen in the reaction of cyclopentadiene with methyl acrylate, using $ZnBr_2$ doped zeolite Ce-Y.[83]

Early attempts to utilize Cu-exchanged zeolites X/Y for the cyclopropanation of olefins using ethyl diazoacetate met with limited success. Results indicated that shape selectivity was outweighed by zeolite acidity, which caused polymerization rather than regioselective cyclopropanation.[84] Recent attempts to prepare heterogeneous Cu(II) catalysts suggest that clays are better solids for cyclopropanation chemistry than zeolites.[85]

6.10. *Sigmatropic Rearrangements*

As with cycloaddition reactions, there are limited examples of zeolite-promoted sigmatropic rearrangements. An early example of how zeolites can promote sigmatropic rearrangements is the Fries rearrangement of phenyl esters to yield *o*- and *p*-acylphenols, using H-form zeolites.[86] As an extension of this chemistry, the aza-Cope rearrangement of allyl-aniline derivative **47** has been studied, using several H-form zeolites as both reaction hosts and acidic promoters.[87] Because the starting material and products are strongly included within the zeolite cavities, excess promoter is required. Reaction of **47** with H-form zeolites in anhydrous hexane at 80 °C (using a Teflon-lined autoclave) yielded two products – the Cope rearrangement product (**48**) along with bicycle **49**, which is formed by subsequent acid-catalyzed cyclization of **48** (Figure 33). Zeolite Y provided consistently better selectivity than the corresponding beta structure, although the reason for this selectivity is unclear (i.e., whether due to differences in zeolite shape selectivity or acidity).



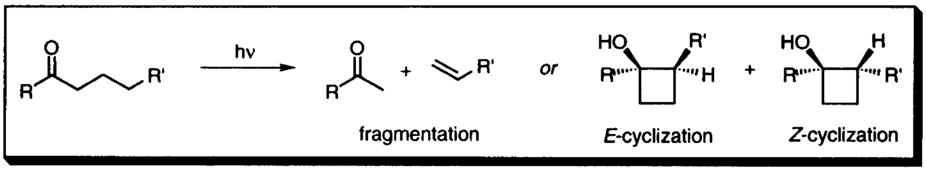
R	R^1	R^2	zeolite	% conversion 48	% conversion 49
CH_3	H	H	H-Y	11	78
CH_3	H	H	H-beta	18	58
H	CH_3	H	H-Y	6	80
H	CH_3	H	H-beta	23	52
H	CH_3	CH_3	H-Y	17	64
H	CH_3	CH_3	H-beta	31	48

Figure 33. Zeolite Mediated Aza-Cope Rearrangement

6.11. Photochemical Transformations

Numerous examples of zeolite-mediated photochemical transformations have appeared in the literature over the past several years. While zeolites impose shape selectivity for many of these reactions, they can also change the electronic properties of reactant molecules, which can itself lead to differences in the products formed and the stereoselectivity of the chemical transformation. Photochemical reactions typically require a change in the excited electronic state – this is done by either electron or energy transfer. The former involves the movement of electrons from one molecule to another to generate radical cation and anion intermediates. In energy transfer, energy transfer between two molecules allows movement of electrons from singlet to triplet (or *vice verse*) states. In solution, photochemical processes often lead to mixtures of products due to the presence of both transfer mechanisms.

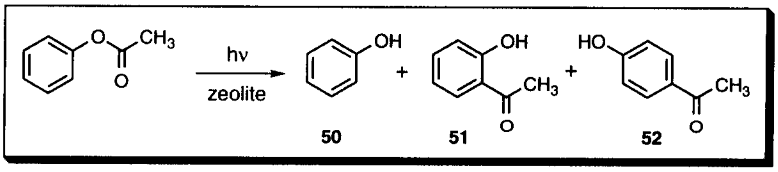
Photochemical transformations, such as the Norrish type II reaction, have been examined by Ramamurthy and co-workers, utilizing zeolites as shape-selective hosts.[88] Normally, excited ketones that possess a γ-hydrogen will undergo competitive fragmentation or cyclization reactions, the amount of each depending on both electronic and steric properties of the ketone. This product ratio is altered when the reaction is performed within a zeolite cavity – for example, aromatic ketones (e.g., valerophenone, R=Ph R'=Me, Figure 34) only undergo fragmentation when reacted in the presence of pentasil zeolites. Alkyl-substituted ketones that are included in either ZSM-5 or zeolites X/Y were found to undergo both fragmentation and cyclization, with cyclization occurring more readily in the presence of faujasites. Interestingly, for sterically congested ketones, inclusion within ZSM-5 resulted in very high selectivity for the *E*-cyclobutanol. These differences in reactivity are attributed to the zeolite structure, where aromatic and alkyl-substituted ketones must adopt a transoid or *cis*-cisoid conformation, respectively, within the pentasil pores.



			product ratios	
R	**R'**	**zeolite**	**fragmentation/ cyclization**	***E/Z* cyclobutanol**
Ph	Me	none	2.8/1	not determined
		NaX	1.2/1	not determined
		ZSM-5	only fragmentation	-
nonyl	Pr	none	1.9/1	1.7/1
		NaX	0.3/1	0.7/1
		ZSM-5	4/1	70/1

Figure 34. Stereoselectivity in Norrish Type II Reactions Using Zeolites as Shape-Selective Hosts

Sigmatropic rearrangements are common synthetic methods employed in compound construction. Recently, the photo-Fries and photo-Claisen reactions were studied, using zeolites as shape selective hosts.[89] Substrates were first included within zeolite X/Y or pentasils ZSM-5 or ZSM-11, then irradiated using a 450-W mercury lamp. Compared to the corresponding non-included reactions, remarkable regioselectivity for the *ortho* isomer was observed, as exemplified in the zeolite KY-mediated photo-Fries rearrangement of phenyl benzoate and phenyl acetate (Figure 35).[88b] The observed selectivity is attributed to restricted mobility of the radical pairs, which form upon photolysis within the zeolite cavities.

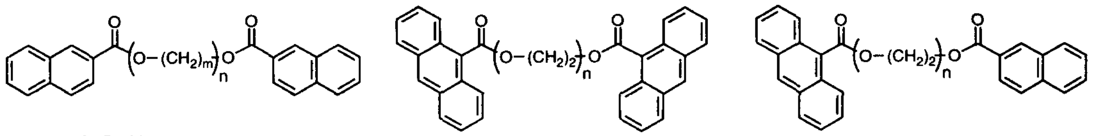


	product distribution*		
	50	**51**	**52**
Hexanes	20	53	27
LiY - Hexanes	7	87	6
NaY-Hexanes	5	91	4

* at 30% conversion

Figure 35. Zeolite-Mediated Photo-Fries Rearrangement

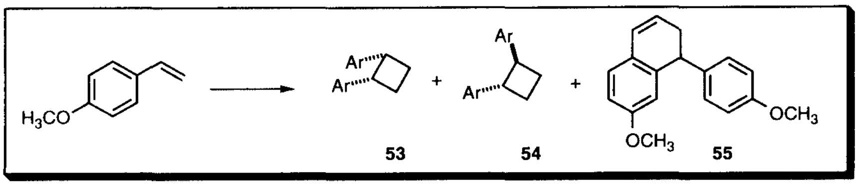
The preparation of large-ring compounds by intramolecular photocycloaddition is difficult due to competing intermolecular processes. To determine the utility of zeolites in suppressing the intermolecular photocycloaddition pathway, Tung and co-workers examined the photocyclization of several flexible diaryl (naphthalene and/or anthracene) compounds, having polyethylene- or polymethylene glycol tethers of varying chain lengths (Figure 36).[90] The diaryl compounds were included within the supercages of zeolite NaY at a loading level of 1 molecule per 10 cages. Subsequent irradiation at >280 nm induced macrocyclization; however, the products formed were too large to diffuse from the zeolite cavity and required isolation by sequential acid-treatment (to destroy the zeolite framework), followed by extraction. Despite these technical difficulties, product recovery was excellent and unlike analogous solution reactions, only macrocycles resulting from intramolecular [4+4] cycloaddition were obtained.



N-P$_n$-N m=2, n=4,5,10,12
N-M$_n$-N m=1, n=3,5,8,10
A-M$_n$-A n=6,10
A-P$_n$-N n=3,4,5

Figure 36. Flexible Diaryls Examined for Zeolite-Mediated Intramolecular Photochemical Macrocyclizations

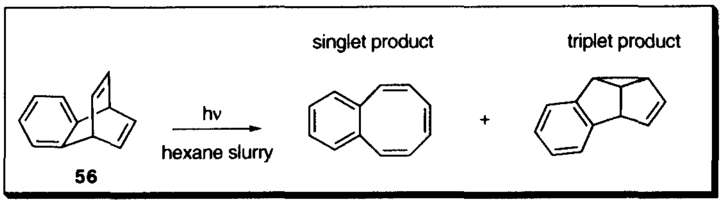
The zeolite-mediated [2+2] cycloaddition of several styrene derivatives has recently been studied.[91] By inclusion of both olefin substrate and the sensitizer, 9-cyanoanthracene, within zeolite NaX, a significant difference was seen for the zeolite-mediated photocyclization compared to the solution reaction, where for the zeolite-mediated reaction, the *cis*-cyclobutane was the major product (Figure 37). This difference in stereoselectivity is directly attributed to size restrictions within the zeolite cavity.



reaction conditions	product ratio 53/54/55
Acetonitrile/PET sensitized	4/90/6
NaX/9-cyanoanthracene	66/26/7

Figure 37. [2+2] Cycloadditions with Zeolites as Hosts

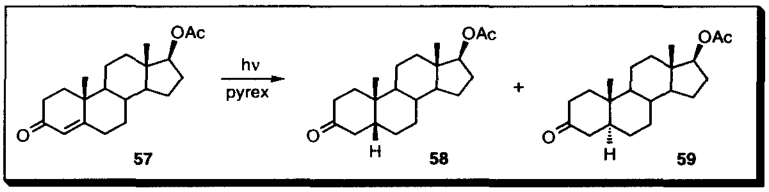
Heavy atom-substitution has proven effective for several photochemically-induced rearrangements, where the efficiency of intersystem crossing determines the types of products formed.[92] For example, benzobarrelene (**56**) is converted to two different compounds, depending on whether the olefin is in the singlet or triplet excited state (Figure 38).[93] Using LiX or NaX, a mixture of products forms; however, when a heavy atom-exchanged zeolite is used, the triplet-derived product is formed predominantly. The photochemical oxa-di-π-methane rearrangement of bicyclic enones has also been examined using heavy atom-exchanged zeolites.[94] In this case, heavy-atom substitution increased the amount of triplet-derived product, although the zeolite-mediated reaction was not as efficient as the corresponding homogeneous photo-rearrangement.



conditions	conversion (%)	singlet-derived product	triplet-derived product
Hexane	-	96	4
Acetophenone	-	0	100
NaX	77	95	5
TlX	90	8	92

Figure 38. Heavy Atom Effect in Zeolites – Singlet *versus* Triplet Photochemistry

Specific binding interactions between substrate and zeolite may be utilized to induce selective chemical transformations, as seen in the photoreduction of testosterone acetate (**57**, Figure 39), cholestenone, and androstenedione.[95] The steroids were first included within faujasite-type zeolites or mesoporous MCM-41, then irradiated as a hexane slurry. Interestingly, it was found that the zeolite-mediated reaction was selective and that reduction had occurred from the more hindered face of the steroid. Differences in the regioselectivity of olefin reduction were also seen, where irradiation of zeolite-included androstenedione resulted in exclusive A ring photoreduction. This unusual result is believed to be due to strong π-cation interaction between olefin and zeolite, which lowers the π-π* electronic transition and exposes the more hindered side for photoreduction.



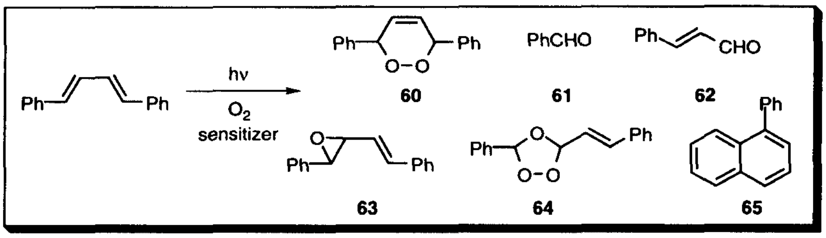
reaction conditions	product distribution* 58	59
2-Propanol	27	73
MCM-41	0	0
NaY/Hexanes (Si/Al=2.5)	85	15

* at 15% conversion

Figure 39. Stereoselective Photoreduction of Steroids

The photooxidation of alkenes has been investigated using either doubly-loaded (i.e., alkene and sensitizer) or singly-loaded (i.e., alkene) zeolites, and recently, the mechanism of photooxidation of 1-alkenes, using BaY and H-ZSM-5 has been described.[96] An example of a doubly-loaded photooxidation is the reaction of stilbene and stilbene derivatives with O_2, using zeolites X/Y and thionin as sensitizer.[97] After sequentially loading sensitizer and alkene, the zeolite was irradiated as a hexane slurry under an O_2 atmosphere. Compared to the homogeneous reaction, the zeolite-mediated photooxidation was more efficient, yielding the corresponding benzaldehyde in near quantitative yield. The reaction was found to be sensitive to several variables – the presence of heavier cations (e.g., Cs$^+$ *versus* Na$^+$), water, and the use of higher loading levels all inhibited the photooxidation process. These results are consistent with an electron transfer mechanism (i.e., $O_2^{\bullet-}$ formation), where proper orientation of sensitizer and alkene within the zeolite supercage is also important for reactivity.

Alkene photooxidation using ZSM-5 and 9,10-dicyanoanthracene has also been studied.[98] In this case, the zeolite is too small to allow entry of the sensitizer and therefore oxidation *via* an energy transfer pathway is expected. Inclusion of *trans*-1,4-diphenyl-1,3-butadiene, followed by irradiation using oxygenated pentaerythritol trimethyl ether ($(CH_3OCH_2)_3CCH_2OH$, a bulky solvent) yielded endoperoxide **60** as the sole product (Figure 40). This remarkable selectivity is contrasted to the homogenous reaction, where a mixture of products, derived from electron transfer is obtained.



zeolite	yield (%) 60	61 / 62	63	64	65
none	3	73	16	4	4
ZSM-5	100	0	0	0	0

Figure 40. Photooxidation Under Sensitizer-*Excluded* Conditions

Alkene oxidation, by singlet-oxygen mediated hydrogen abstraction, has also been investigated using zeolite Y.[99] Both sensitizer and alkene were included within the zeolite supercage, then irradiated in the presence of O_2. The hydroperoxide products thus generated were extracted and reduced to the corresponding alcohols with PPh_3. Compared to the homogeneous reaction, the zeolite reaction displayed remarkable selectivity, with H-abstraction occurring selectively from the less sterically congested allylic carbon position. The zeolite-mediated oxidation of limonene exemplifies the utility of this methodology. Reaction of limonene with O_2, using Rose Bengal as sensitizer, produces a complex mixture of products that result from all possible ene reactions to the trisubstituted double bond. However, using zeolite NaY (in the presence of a small amount of pyridine, which neutralizes all residual Brönsted sites), the photochemical oxidation of limonene (**66**) is regioselective, yielding only the *cis* and *trans* products that result from hydrogen abstraction from the least hindered allylic carbon center (Figure 41).[90] Two possible mechanistic rationales have been put forward to explain the selectivity of this oxidation process. One is a conformational argument, where interaction between olefin and zeolite cation creates steric repulsion between the larger sidechain and the zeolite surface, restricting H-abstraction to the less hindered positions. The second explanation for the observed selectivity relates to the relative stability of intermediate perepoxides **A** and **B** and the ability of the perepoxide functionality to polarize the allylic hydrogens of more substituted carbon centers (making them more reactive towards abstraction).[100]

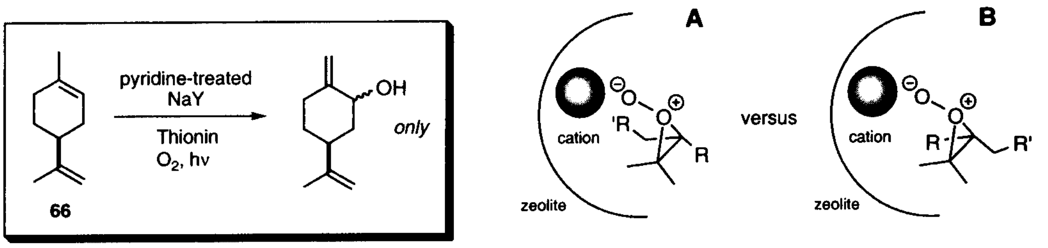


Figure 41. Allylic Oxidations with Zeolites

6.12. Chemistry Involving Titanium-Substituted Zeotypes

The incorporation of a redox active transition metal within the zeolite (or zeotype) framework provides novel bifunctional materials that can be used as shape selective oxidation catalysts.[101] A number of metals have been examined, including early (Ti, Zr, Mo, W) and late (Cr, Mn, Fe) transition metals. Of these, the most well studied and characterized are the titanium-substituted zeolites, including TS-1 and Ti-beta, and Ti-MCM-41. Although these materials are not yet commercially available, they can be prepared by chemical modification or by direct hydrothermal synthesis. For the former, framework titanium is incorporated into a pre-existing zeolite structure by chemical modification with $TiCl_4$ or $Ti(OPr^i)_4$ under gas or liquid phase conditions. A novel approach to generating a mesoporous epoxidation catalyst, which involves grafting titanium within the pores by decomposition of included titanocene dichloride, has been described.[102]

TS-1, the titanium analog of ZSM-5, is used extensively for a variety of chemical oxidations.[98a,103] As with all Ti-mediated oxidations, these reactions require a stoichiometric amount of oxidant, and for TS-1 oxidations, H_2O_2, urea hydrogen peroxide (UHP), or *tert*-butyl hydrogen peroxide (TBHP) are used. Because of TS-1's low hydrophilicity (due to its high silica content), higher concentrations of aqueous H_2O_2 solutions are preferred.

The two major disadvantages to using TS-1 as an oxidation catalyst are its acidity, which often causes rearrangement chemistry, and its small pore dimensions, which restrict its use to small organic reactants. To circumvent these problems, Ti-beta and Ti-MCM-41 have been developed.[104] Ti-beta is a titanium-containing aluminosilicate having a beta type structure. Its pore size is larger than TS-1 and therefore this material can tolerate larger reactant molecules. Ti-MCM-41, which does not possess aluminum within its framework, is not only less acidic, but also more hydrophobic. This feature, in addition to its mesoporous structure, should provide a broader range of synthetic applications. Oxidation reactions using titanium-containing zeolites include epoxidation, arene hydroxylation, nitrogen and sulfur oxidation, allylic and benzylic oxidation, alcohol oxidation, and alkane oxidation.[4c,98a,100]

The mechanism of TS-1 catalyzed epoxidation has recently been studied using chiral allylic alcohols as probes.[105] The diastereoselectivity of the reaction (quantified by determining the *threo*:*erythro* ratio of the products formed) was compared to other reagents, including $VO(acac)_2$/TBHP, $Ti(OPr^i)_4$/TBHP, *m*-CPBA, and dimethyldioxirane. The results of these studies support a mechanism that is similar to peracid epoxidation, where 1,3-allylic strain plays a central role in diastereoselection (Figure 42).

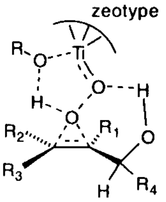
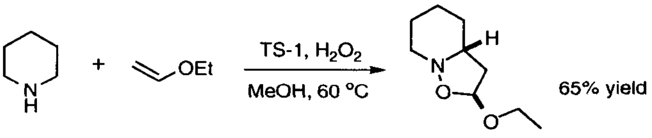


Figure 42. Proposed Transition State for Ti-beta Mediated Epoxidation with H_2O_2

The epoxidation of unsaturated fatty acids has been studied using Ti-beta and Ti-MCM-41, to determine what factors contribute to optimal selectivity.[106] An examination of several different samples of Ti-beta, having varying Si/Al ratios, using methyl oleate as reactant, demonstrated that increased aluminum content results in both decreased epoxide selectivity and increased H_2O_2 decomposition. Solvent was also found to play a role in the reaction outcome. Compared to acetonitrile, methanol inhibited the epoxidation process and facilitated product decomposition. Materials containing no aluminum, such as Ti-MCM-41, were typically more selective when H_2O_2 was replaced by the more hydrophobic oxidant, TBHP. These results are consistent with the notion that epoxide degradation is enhanced by more hydrophilic zeotypes and by protic solvents.

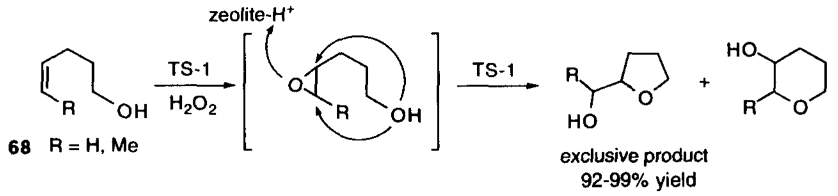
Although the intrinsic acidity of Ti-containing zeolites is usually an undesirable property, in some cases it is a benefit that may facilitate tandem chemical transformations. An example of this is seen in the oxidation of secondary amines to nitrones using TS-1/H_2O_2.[107] In addition to mediating both the *N*-oxidation and dehydration that are required for this conversion, the reagent may be used for tandem nitrone formation and 1,3-dipolar cycloaddition chemistry. For example, TS-1/H_2O_2 mediates the condensation of piperidine and ethyl vinyl ether to yield isoxazolidine **67** in 65% yield (Figure 43).



67

Figure 43. Isoxazolidine Formation using TS-1

Although the epoxidation of alkenes by TS-1 and related materials often leads to by-product formation (e.g., diol and/or carbonyl compound), due to zeolite acidity and the presence of water in the reaction medium, tandem epoxidation/cyclization chemistry utilizing titanium zeolites can provide an efficient route to cyclic ethers. The conversion of several unsaturated alcohols (e.g., **68**) to tetrahydrofuranols and tetrahydropyranols has recently been demonstrated with TS-1 and H_2O_2 as oxidant (Figure 44).[108] The product distribution of these reactions parallels that obtained using protic and Lewis acids[109] and is therefore not the result of zeolite-imposed shape selectivity.

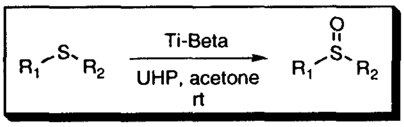


68 R = H, Me

Figure 44. Tetrahydrofuran Formation from 68, Using TS-1/H_2O_2

The development of new reagents for the selective oxidation of silanes to silanols is of interest to synthetic chemists since it is known that product dimerization readily occurs under acidic or basic conditions. Ti-beta has been shown to be a highly effective oxidation catalyst for the conversion to silanes to silanols, with negligible amount of disiloxane being produced.[110] The reaction is performed using aqueous H_2O_2 and appears to be a pore selective process, as seen by the inability of Ti-beta to oxidize (+)-Me(α-Np)PhSiH.

The oxidation of sulfides to sulfoxides has also been examined using Ti-containing zeotypes. TS-1, Ti-beta, and Ti-MCM-41 have been studied for their ability to selectivity catalyze this transformation, as well as the molybdenum ZSM-5 analog, MoS-1.[111] Excellent yield and selectivity were obtained for sulfide oxidation using Ti-beta/urea hydrogen peroxide (Ti-beta/UHP, Figure 45).[112] The reaction is performed by stirring sulfide with 10 wt% Ti-beta, 1.2 equiv. UHP, in acetone at room temperature. This reaction is applicable to a broad range of sulfides and unlike other methods, produces negligible amounts of sulfone by-product.



	yield (%)
R_1, R_2 = Pr^i	89
R_1, R_2 = Bu^n	94
R_1 = Me, R_2 = cyclohexyl	85
R_1 = Ph, R_2 = benzyl	95

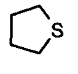
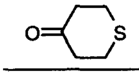
	yield (%)
	95
	82

Figure 45. Ti-Beta Mediated Sulfide Oxidation

6.13. Asymmetric Synthesis Using Zeolites

Because zeolites are both heterogeneous and shape selective catalysts, these materials have been studied for their utility in asymmetric transformations. Although zeolites are not chiral, they can serve as a stabilizing host for chiral molecules and for homogeneous asymmetric catalysts, thus making the *zeolite complex* a potential chiral catalyst. A number of strategies to prepare chiral zeolite catalysts have been examined, and many have provided promising results. Unfortunately, the ee's of these transformations are usually lower than already established methods; therefore, more work is needed before these materials are useful to synthetic chemists.

The inclusion or support of a homogeneous asymmetric catalyst within zeolite cavities has been the most common strategy employed to develop chiral zeolite catalysts. Corma and co-workers have prepared a series of heterogeneous catalysts utilizing zeolite-supported proline derivatives as chiral ligands. For example, reaction of siloxane-modified proline derivative **69** with $[RhCl(cod)]_2$, then ultra-stable zeolite Y (USY), yielded a covalently-modified zeolite (**70**, Figure 46) that catalyzed the hydrogenation of several α-acylaminocinnamate derivatives.[113] Compared to the homogeneous reaction or the use of a silica-modified catalyst, both the yield and enantioselection for the zeolite catalyst were higher, suggesting that catalyst inclusion within the 12-30Å supermicropores of the highly dealuminated zeolite had occurred. This methodology has been extended to the chiral conjugate addition to enones and to asymmetric allylic epoxidation.[114]

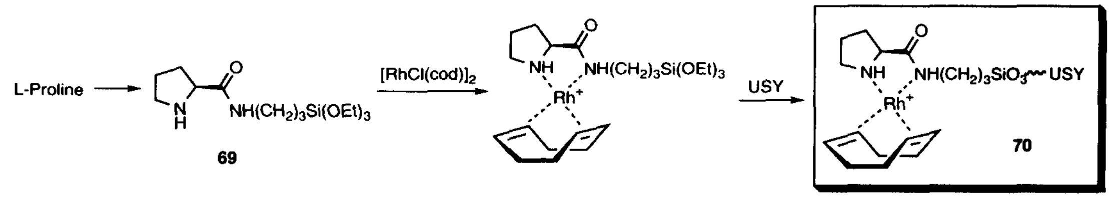


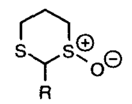
Figure 46. Preparation of a Zeolite-Supported Asymmetric Hydrogenation Catalyst

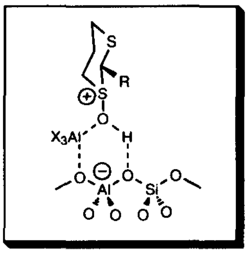
Another strategy for preparing chiral zeolite catalysts is to include previously developed organometallic catalysts within zeolites. Due to the size limitations of most zeolites, this process is usually performed in sequential steps, known as "ship-in-a-bottle" synthesis. As described by Bedioui, there are three methods used for ship-in-a-bottle synthesis: (i) flexible ligand method, (ii) template method, and (iii) zeolite synthesis method.[115] In the flexible ligand method, the zeolite is subjected to ion exchange with the desired metal, followed by diffusion of the ligand into the zeolite cavity to generate the active metal complex. The template method is similar to the flexible ligand method, except in this case the macrocyclic ligand is prepared by *in situ* condensation of the monomeric subunits within the zeolite cavity. The zeolite synthesis method requires the presence of metal complex or ligand during the zeolite crystallization process. In this case, the ligand is believed to function as a templating agent. Ligands utilized in ship-in-a-bottle synthesis of zeolite catalysts include Schiff bases, amino acids, bipyridyls, phthalocyanines, and porphyrins.

An important application of the ship-in-a-bottle methodology in zeolite-mediated asymmetric transformations is the preparation of heterogeneous manganese catalysts.[116] Chiral Mn(III)salen complexes are synthetically useful catalysts for the enantioselective epoxidation of aromatic alkenes.[117] The encapsulation of these compounds within zeolite Y and the related zeolite, EMT, by *in situ* condensation of (*R*,*R*)- or (*S*,*S*)-1,2-*trans*-diaminocyclohexane with the appropriate salicylaldehyde derivative, has provided several shape-selective chiral epoxidation catalysts.[118] This method has recently been extended to the preparation of a Mn(III)salen-included Al-MCM-41 (prepared by reaction of Mn-exchanged zeolite with chiral salen ligand).[119] Unfortunately, none of these catalysts are as good as the homogenous ones, although the EMT-included material appears to provide comparable enantioselectivity in the epoxidation of styrene and its derivatives.

Cu-Mediated processes, such as the cyclopropanation and aziridination of olefins have also been investigated using zeolite-included chiral ligands. For example, using 2,2-bis[2-[(4*R*)-1-phenyl-1,3-oxazolinyl]]propane as ligand and [*N*-(*p*-tolylsulfonyl)imino)]phenyliodinane (PhI=NTs) as nitrogen source, the aziridination of *trans*-methyl cinnamate occurred in 61% ee.[120] Recently, a chiral Pd(II) complex was prepared by surface modification of MCM-41 with the chiral ligand, 1,1'-bis(diphenylphosphino)ferrocene, which was shown to be an efficient catalyst of allylic amination.[121]

As an extension of zeolite-catalyzed dehydration reactions, Hutchings and co-workers have recently studied the ability of modified zeolites to perform kinetic resolution of racemic alcohols by an enantioselective dehydration.[122] The inclusion of 1,3-dithiane-1-oxides within zeolite HY (loaded at 1 molecule per supercage) results in the formation of highly reactive catalysts that were found to dehydrate (*R*)- and (*S*)-2-butanol at different rates (Figure 47). From spectroscopic and computational studies, a model has been proposed to explain catalyst activity, where interaction of both Lewis and Brönsted acid sites within the zeolite cavity with the 1,3-dithiane-1-oxide moiety appears to generate the actual acid dehydration catalyst.

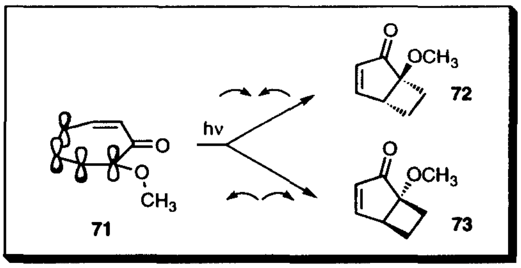
modifier		reaction temp (˚C)	relative dehydration rate (*R*)- / (*S*)-2-butanol
	(*R*)-R=H 83% ee	110	1 / 17.5
		150	1 / 39.3
	(*S*)-R=Ph 99% ee	110	18.4 / 1



Proposed catalyst structure

Figure 47. Enantioselective Dehydration of 2-Butanol with Chirally-Modified Zeolites

The development of methodology related to asymmetrical photochemical transformations has seen promising results with the use of confined (or solid state) media. This work has recently been extended to the use of chirally-modified zeolites for two distinct photochemical reactions, the Norrish/Yang type II cyclization of *cis*-4-*tert*-butylcyclohexyl ketones to cyclobutanols, and the photocyclization of α-tropolone methyl ether.[123] The strategy employed for both of these reactions was to sequentially include a chiral modifier and reactant within the zeolite cavity (loading at about 1 chiral inducer per supercage) prior to photolysis, such that a ternary complex between zeolite, chiral inducer, and reactant would form, leading to facial selectivity in the photochemical process. Of a number of chiral inducers tested, ephedrine and norepehdrine produced the best results (Figure 48). Both reactions show modest enantioselectivity (20-50%), and the reaction was found to be sensitive to the size of the zeolite cavity, where steric compression typically led to higher selectivity.



71 72 73

chiral inducer/zeolite/temp	ee (%)	favored enantiomer*
(-)-norephedrine/NaY/-20°C	50	72
(-)-norephedrine/RbY/22°C	40	72
(+)-norephedrine/NaY/22°C	34	73

*Arbitrarily assigned configuration based on GC retention times

Figure 48. Asymmetric Photochemical Transformations with Zeolites

6.14. *Biomimetic Chemistry*

The fact that zeolites possess well-defined cavities, in which shape-selective reactions may occur, suggests that these materials could function as enzyme mimics. The development of *zeozymes*, in particular compounds that mimic redox enzymes, has been an important area of zeolite research. The outcome of these studies has been the preparation of several transition metal-containing zeolites that catalyze alkene epoxidation and/or and arene and alkane oxidations.[112]

To mimic cytochrome P-450 enzymes, metalloporphyrin-zeolites have been prepared by inclusion of the redox active center into zeolites X/Y or mesoporous MCM-41. The reactivity of these materials is often superior to the corresponding homogeneous system, presumably because the metal complexes are highly dispersed and are sequestered within the zeolite cavities, making them less susceptible to decomposition (e.g., formation of oxo-bridged dimers). Because metalloporphyrins are large, standard ship-in-a-bottle synthetic methodology usually leads to low incorporation within the zeolite cavities. Recently, a new method to overcome these difficulties was developed, whereby tetrakis(*N*,*N*,*N*-trimethylanilinium)porphyrin was added as an organic template during the synthesis of zeolite Y.[124]

Mesoporous metalloporphyrin complexes are excellent catalysts and, like their microporous counterparts, appear to confer shape selectivity. As an example, MCM-41-immobilized ruthenium tetrakis(2,6-dichlorophenyl)porphyrin (Ru/M-41(m)) was found to epoxidize a variety of alkene substrates, using 2,6-dichloropyridine *N*-oxide as oxidant.[125] The reaction is stereospecific and is selective for sterically unencumbered, terminal olefins (Figure 49), features which are characteristic of many epoxidases. The Ru/M-41(m) catalyzed epoxidation of (+)-limonene provided the 8,9-epoxide as the major product, in sharp contrast to both the homogenous metalloporphyrin reaction and to the *m*-CPBA epoxidation of limonene.

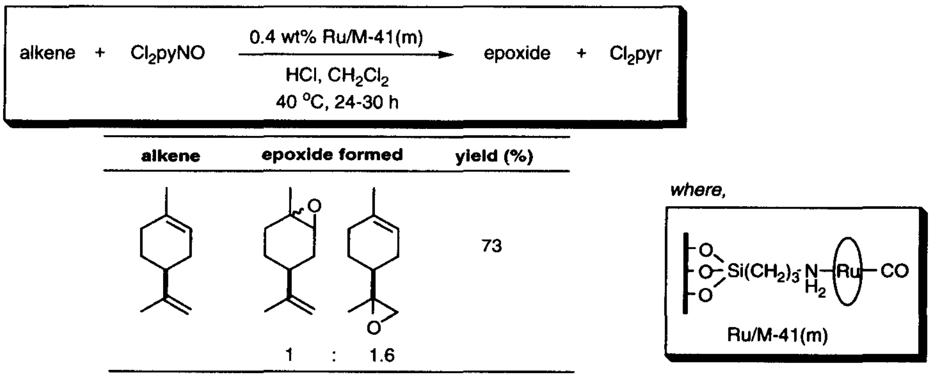


Figure 49. MCM-41 Immobilized Ru-Porphyrin Complex– an Epoxidase Mimic

Other biomimetic redox active materials include Cu-Y and Fe-ZSM-5.[126] The former, which contains dimeric copper centers, catalyzes O_2-dependent arene oxidations with selectivity that parallels naturally-occurring tyrosinases. The latter, which possesses an iron environment that is similar to methane monooxygenases, catalyzes the N_2O-dependent hydroxylation of benzene and methane.

Epoxide cyclizations are important enzymatic transformations that are catalyzed by a family of related cyclases. Zeolites have been shown to mimic several naturally occurring cyclases, including the steroid forming enzyme, oxidosqualene cyclase. Corma and co-workers have utilized Ti-beta and Ti-MCM-41 to effect the tandem epoxidation/cyclization of linalool, to generate a mixture of furanols and pyranols (**74** and **75**, respectively, Figure 50).[127] While typical chemical cyclization routes using protic acids, such as TFA, provide ratios of **74**/**75** of up to 9, the zeolite-mediate process generates the cyclic ethers in almost equal quantities. In the case of Ti-MCM-41/TBHP, the reaction yields more pyranol, as observed for the cyclization of 6,7-epoxylinalool in plants.

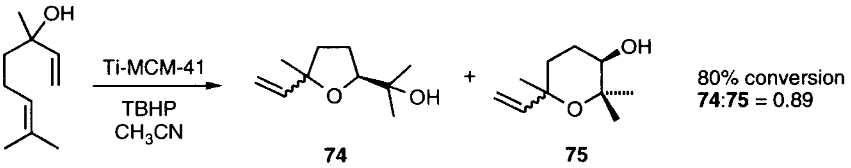


Figure 50. Tandem Epoxidation/Cyclization of Linalool with Ti-Containing Zeolites

Zeolites can be used for the construction of fused ring systems and in these cases, not only do the zeolites effectively replace traditional protic and Lewis acid promoters, but they can also provide shape selectivity in the cyclization process. In this sense, zeolites are true replacements of naturally occurring cyclases, since these enzymes usually confer high stereoselectivity in the cyclization process. The cyclization of epoxypolyenes **76** and **77** have been studied (Figure 51), using several different zeolites.[128] In both cases, the product yields are excellent and, for the cyclization of **77**, very high stereoselectivity for the all *trans* isomer (**78a**) is observed. Based on pyridine treatment studies, it appears that the tricyclization of **77** is initiated at the zeolitic pores, with concurrent interaction of the polyene tail with the exterior surface of the zeolite.

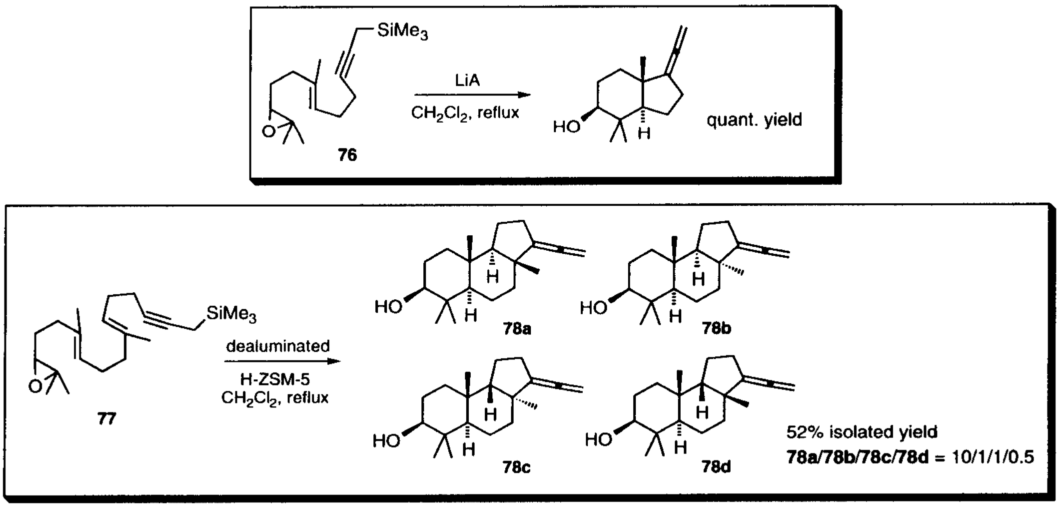


Figure 51. Zeolite as Cyclase Mimics for Epoxypolyene Cyclizations

6.15. Covalently-Modified Zeolites as Synthetic Catalysts

Although zeolites can be used for a number of synthetic transformations, they do not always provide the proper balance of porosity, hydrophobicity, and acidity. Reactions often occur on the zeolite surface, and both the hydrophilicity and high acidity of these materials can cause leaching and unwanted chemistry to occur. Each of these factors will result in lower yield and selectivity, and therefore significant efforts have been made to modify zeolite structure to modulate their intrinsic properties. A common method for increasing pore dimensions of microporous materials, to facilitate entry of larger molecules into the zeolite, is to create larger micropores or mesopores by dealumination. This process may be performed on commercial zeolite by steam treatment, acid treatment, or treatment with metal chelators, such as EDTA.[8] In all cases, Si-O-Al bond cleavage occurs, creating defects or "holes" in the zeolite structure of ill-defined structure. For example, dealumination of X/Y by steam treatment creates mesopores of 15-20 nm in dimension.[129] To eliminate surface chemistry, zeolites can be treated with bulky siliconizing agents, which will react with surface silanols, but are too large to enter and react within the zeolite cavity. Mesoporous materials, such as Ti-MCM-41, also benefit from surface modification. For example, silylation of the internal cavity by treatment with hexamethyldisilazane increases the material's hydrophocity, resulting in a dramatic increase in product yield for the epoxidation of cyclohexene with TBHP, concurrent with a decrease in product decomposition (*via* epoxide hydrolysis).[130] A similar procedure was also shown to greatly reduce leaching of the homogeneous epoxidation catalyst, titanium(IV) silsesquioxane, which was heterogenized by inclusion within MCM-41.[131]

The preparation of "organic-functionalized" molecular sieves represents a novel approach to modifying zeolite structure. In this case, covalently modified silicalites are prepared by the incorporation of organosiloxanes into the hydrothermal synthesis (Figure 52).[132] This procedure, which was initially utilized to prepare derivatives of MCM-41, can be extended to microporous materials as well. Si-Methylated Ti-MCM-41, prepared by co-condensation of $MeSi(OEt)_3$ with $Si(OMe)_4$ and $Ti(OEt)_4$ in the presence of base and surfactant, produces the most active and selective mesoporous epoxidation catalyst known to date.[133]

$$\mathrm{RSi(OEt)_3 + Si(OEt)_4 + surfactant + NaOH} \longrightarrow \boxed{\text{organo-functionalized MCM-41}}$$

R = Me, Et, *n*-octyl, phenyl,
CH_2CH_2Ph, $(CH_2)_3SH$, $(CH_2)_3NH_2$

Figure 52. Preparation of Organic-Functionalized MCM-41

Novel zeolite catalysts have recently been prepared that utilize covalently-linked appendages as their reactive centers. For example, a piperidine-MCM-41 adduct has been been prepared as a heterogeneous catalyst for monoglyceride synthesis.[134] The material was synthesized in several steps by: i) functionalizing the silanols with (3-chloropropyl)triethyoxysilane, ii) *N*-alkylating with piperidine, and iii) capping the remaining silanols with hexamethyldisilazane (Figure 53). The resulting material catalyzed the esterification of lauric acid with glycidol in 90% yield.

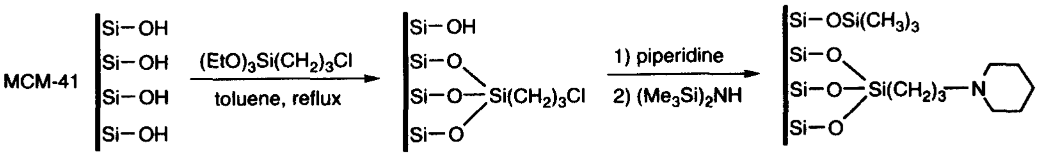


Figure 53. Preparation of Piperidine-Modified MCM-41

Covalent attachment of the trimeric cobalt complex $[Co_3(\mu_3\text{-}O)(OAc)_5(\mu_2\text{-}OH)(pyr)_3]PF_6$ to MCM-41 was performed by treatment of surface silanols with (3-bromopropyl)trichlorosilane, then glycine.[135] The resulting carboxylate tethers served as ligands, displacing the bridging OH group to generate a heterogeneous oxidation catalyst. Turnover number and selectivity for the oxidation of cyclohexane to cyclohexanone with TBHP was high and minimal catalyst leaching was observed.

A different approach to generating pore-selective acid catalysts, also involving chemical modification, was recently developed by Davis and co-workers.[136] To eliminate surface acidity, aluminum-free zeolite beta, which was organically functionalized by adding phenethyltrimethoxysilane during the liquid crystal template synthesis, was prepared. Prior to template removal, the zeolite was treated with base to remove the *surface* organic functionality, and after removal of the template, the internal aromatics were sulfonated. The resulting zeotype was found to be a shape selective acid catalyst, which acetalated cyclohexanone, but not 1-pyrenecarboxaldehyde.

7. Conclusions

Although the application of zeolites to synthetic organic chemistry is still at its infancy, it is clear that these materials are more than water scavengers and may be used to catalyze a wide variety of difficult chemical transformations. The advantages to using zeolitic materials include their ease of handling, their ability to replace acids (in the case of redox zeotypes, replacing homogeneous redox catalysts), their ability to modulate electronics, and their shape selectivity. The fact that zeolites can be modified by metal substitution, organic functionalization, or catalyst immobilization expands their utility to enantioselective and tandem chemical transformations. In many cases, zeolitic materials catalyze reactions better than other known methods, with turnover numbers and selectivity paralleling that of naturally-occurring enzymes.

As an outgrowth of zeolite-catalyzed transformations, clays,[137] organic zeolites,[138] and sol-gels,[139] have also been investigated for their ability to mediate organic transformations. Future work in the area of zeolite catalysts will undoubtedly focus on the preparation of "tailor-made" zeozymes, immobilized zeolites (e.g., zeolite membranes),[140] and chiral zeolites (where chirality is imparted directly within the framework structure). Although chiral zeolites do not occur naturally, zeolite beta possesses a helical polymorph that, if made homogenous, would produce a chiral material.[1f] The preparation of chiral zeotypes, such as cobalt aluminophosphates phosphate, are also currently under investigation.[141]

References

1. a) Feast, S.; Lercher, J.A. *Stud. Surf. Sci. Catal.* **1996**, *102*, 363-412; b) Prins, R. *Chimia* **1996**, *50*, 79-85; c) Vaughan, D.E.W., in *Comprehensive Supramolecular Chemistry*, Pergamon: NewYork, 1996, Chapt. 13, pp. 379-388; d) Sheldon, R.A. *J. Mol. Catal. A: Chem.* **1996**, *107*, 75-83; e) Martin-Luengo, M.A.; Yates, M. *J. Mat. Sci.* **1995**, *30*, 4483-4491; f) Dartt, C.B.; Davis, M.E. *Catal. Today* **1994**, *19*, 151-186; g) Hölderich, W.F.; van Bekkum, H. *Stud. Surf. Sci. Catal.* **1991**, *58*, 631-726.
2. a) Dyer, A. *An Introduction to Zeolites Molecular Sieves*, John Wiley: Chichester, 1988; b) Breck, D.W. *J. Chem Educ.* **1964**, *41*, 678-689.
3. Meier, W.M.; Olson, D.H. *Atlas of Zeolite Structure Types*, Butterworth-Heinemann: London, 1992.
4. a) Kresge, C.T.; Leonowicz, M.E.; Roth, W.J.; Vartuli, J.C.; Beck, J.S. *Nature* **1992**, *359*, 710-712; b) Beck, J.S.; Vatuli, J.C.; Roth, W.J.; Leonowicz, M.E.; Kresge, C.T.; Schmitt, K.D.; Chu, C.T.-W.; Olson, D.H.; Sheppard, E.W.; McCullen, S.B.; Higgins, J.B.; Schlenker, J.L. *J. Am. Chem. Soc.* **1992**, *114*, 10834-10843; c) Corma, A. *Chem. Rev.* **1997**, *97*, 2373-2419; d) Sayari, A; Yang, Y; Kruk, M.; Jaroniec, M. *J. Phys. Chem. B* **1999**, *103*, 3651-3658.
5. a) Li, P; Xiang, Y.; Grassian, V.H.; Larsen, S.C. *J. Phys. Chem. B* **1999**, *103*, 5058-5062; b) Drago, R.S.; Dias, S.C.; Torrealba, M.; de Lima L. *J. Am. Chem. Soc.* **1997**, *119*, 4444-4452; c) Savitz, S.; Myers, A.L.; Gorte, R.J. *J. Phys. Chem. B* **1999**, *103*, 3687-3690; d) Savitz, S.; Myers, A.L.; Gorte, R.J.; White, D. *J. Am. Chem. Soc.* **1998**, *120*, 5701-5703; e) Lee, C.; Parrillo, D.J.; Gorte, R.J.; Farneth, W.E. *J. Am. Chem. Soc.* **1996**, *118*, 3262-3268; f) Parrillo, D.J.; Gorte, R.J.; Farneth, W.E. *J. Am. Chem. Soc.* **1993**, *115*, 12441-12445; g) Xu, T.; Munson, E.J.; Haw, J.F. *J. Am. Chem. Soc.* **1994**, *116*, 1962-1972.
6. Corma, A.; García H. *Catal. Today* **1997**, *38*, 257-308.
7. Thomas, K.J.; Ramamurthy, V. *Langmuir* **1998**, *14*, 6687-6692.
8. Ribeiro, F.R.; Alvarez, F.; Henriques, C.; Lemos, F.; Lopes, J.M.; Ribeiro, M.F. *J. Mol. Catal. A: Chem.* **1995**, *96*, 245-270.
9. a) Zukal, A.; Patzelová, V.; Lohse, U. *Zeolites* **1986**, *6*, 133-136; b) Wouters, B.H.; Chen, T.-H.; Grobet, P.J. *J. Am. Chem. Soc.* **1998**, *120*, 11419-11425.
10. Ono, Y.; Baba, T. *Catal. Today* **1997**, *38*, 321-337.
11. Corma, A.; Fornés, V.; Martín-Aranda, R.M.; García, H.; Primo, J. *Appl. Catal.* **1990**, *59*, 237-248.
12. a) Csicsery, S.M. *Zeolites* **1984**, *4*, 202-213; b) Csicsery, S.M. *Pure Appl. Chem.* **1986**, *58*, 841-856.
13. Derouane, E.G.; Gabelica, Z. *J. Catal.* **1980**, *65*, 486-489.
14. Martens, J.A.; Souverijns, W.; Verrelst, W.; Parton, R.; Froment, G.F.; Jacobs, P.A. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2528-2530.
15. Davis, M.E. *Acc. Chem. Res.* **1993**, *26*, 111-115.
16. a) Ortiz, W.; Cozens, F.L.; Schepp, N.P. *Org. Lett.* **1999**, *1*, 531-534; b) Barrachin, B.; Cohen de Lara, E. *J. Chem. Soc. Faraday Trans. 2* **1986**, *82*, 1953-1966; c) Ramamuthy, V.; Sanderson, D.R.; Eaton, D.F. *Photochem. Photobiol.* **1992**, *56*, 297-303.
17. a) Biswas, J.; Maxwell, I.E. *Appl. Catal.* **1990**, *63*, 197-258.
18. a) Kiricsi, I.; Förster, H.; Tasi, G.; Nagy, J.B. *Chem. Rev.* **1999**, *ASAP article*; b) Hogeveen, H.; Gaasbeek, C.J.; Bickel, A.F. *Rec. Trav. Chim. Pays-Bas* **1969**, *88*, 703-718; c) Chen, C.S.H.; Bridger, R.F. *J. Catal.* **1996**, *161*, 687-693.
19. Honna, K.; Sugimoto, M.; Shimizu, N.; Kurisaki, K. *Chem. Lett.* **1986**, 315-318.
20. Lau, G.C.; Maier, W.F. *Langmuir* **1987**, *3*, 164-173.
21. a) Cano, M.L.; Corma, A.; Fornés, V; García, H.; Miranda, M.A.; Baerlocher, C.; Lengauer, C. *J. Am. Chem. Soc.* **1996**, *118*, 11006-11013; b) Cano, M.L.; Cozens, F.L.; Esteves, M.A.; Márquez, F.; García, H. *J. Org. Chem* **1997**, *62*, 7121-7127.
22. a) Pitchumani, K.; Ramamurthy, V. *Chem. Commun.* **1996**, 2763-2764; b) Rao, V.J.; Prevost, N.; Ramamurthy, V.; Kojima, M.; Johnston, L.J. *Chem. Commun.* **1997**, 2209-2210.; c) Lakshminarasimhan, P.; Thomas, K.J.; Brancaleon, L.; Wood, P.D.; Johnston, L.J.; Ramamurthy, V. *J. Phys. Chem. B* **1999**, *ASAP article*.
23. a) Pitchumani, K.; Joy, A.; Prevost, N.; Ramamurthy, V. *Chem. Commun.* **1997**, 127-128; b) Pitchumani, K.; Ramamurthy, V. *Tetrahedron Lett.* **1996**, *37*, 5297-5300.
24. a) Stamires, D.N.; Turkevich, J. *J. Am. Chem. Soc.* **1964**, *86*, 749-757; b) Roth, H.D.; Shen, K.; Lakkarruju, P.S.; Fernández, L. *Chem. Commun.* **1998**, 2447-2448; c) Martí, V.; Fernández, L.; Fornés, V.; García, H.; Roth, H.D. *J. Chem. Soc., Perkin Trans. 2* **1999**, 145-152; d) Gener, I.; Buntinx, G.; Brémard, C. *Angew. Chem. Int. Ed.* **1999**, *38*, 1819-1821.
25. Ramamurthy, V.; Caspar, J.V.; Corbin, D.R. *J. Am. Chem. Soc.* **1991**, *113*, 594-600.

26. Pitchumani, K.; Corbin, D.R.; Ramamurthy, V. *J. Am. Chem. Soc.* **1996**, *118*, 8152-8153.
27. Katsuki, T.; Sharpless, K.B. *J. Am. Chem. Soc.* **1980**, *102*, 5974-5976.
28. Hanson, R.M.; Sharpless, K.B. *J. Org. Chem.* **1986**, *51*, 1922-1925.
29. a) Ballini, R.; Bosica, G.; Carloni, S.; Ciaralli, L.; Maggi, R.; Sartori, G. *Tetrahedron Lett.* **1998**, *39*, 6049-6052; b) Ballini, R.; Bordoni, M.; Bosica, G.; Maggi, R.; Sartori, G. *Tetrahedron Lett.* **1998**, *39*, 7587-7590; c) Kumar, P.; Hegde, V.R.; Kumar, T.P. *Tetrahedron Lett.* **1995**, *36*, 601-602.
30. Ballini, R.; Bosica, G.; Frullanti, B.; Maggi, R.; Sartori, G.; Schroer, F. *Tetrahedron Lett.* **1998**, *39*, 1615-1618.
31. Tanaka, Y.; Sawamura, N.; Iwamoto, M. *Tetrahedron Lett.* **1998**, *39*, 9457-9460.
32. Farzaneh, F.; Soleimannejad, J.; Ghandi, M. *J. Mol. Catal. A: Chem.* **1997**, *118*, 223-227.
33. Itoh, A.; Kodama, T.; Maeda, S.; Masaki, Y. *Tetrahedron Lett.* **1998**, *39*, 9461-9464.
34. a) Posner, G.H.; Dai, H.; Bull, D.S.; Lee, J.-K.; Eydoux, F.; Ishihara, Y.; Welsh, W.; Pryor, N.; Petr, Jr, S. *J. Org. Chem.* **1996**, *61*, 671-676; b) Terada, M.; Matsumoto, Y.; Nakamura, Y.; Mikami, K. *Chem. Commun.* **1997**, 281-282; c) Tottie, L.; Baeckström, P.; Moberg, C.; Tegenfeldt, J.; Heumann, A. *J. Org. Chem.* **1992**, *57*, 6579-6587.
35. Moreau, C.; Lecomte, J.; Mseddi, S.; Zmimita, N. *J. Mol. Catal. A: Chem.* **1997**, *125*, 143-149.
36. Reddy, P.V.; Manisekaran, T.; Bhat, S.V. *Tetrahedron Lett.* **1998**, *39*, 1629-1632.
37. Anbazhagan, M.; Kumaran, G.; Sasidharan, M. *J. Chem. Res. (S)* **1997**, 336-337.
38. Balaji, B.S.; Sasidharan, M.; Kumar, R.; Chanda, B. *Chem Commun.* **1996**, 707-708.
39. Ookoshi, T.; Onaka, M. *Tetrahedron Lett.* **1998**, *39*, 293-296.
40. Posner, G.H.; Bull, D.S. *Tetrahedron. Lett.* **1996**, *37*, 6279-6282.
41. Sugi, Y.; Toba, M. *Catal. Today* **1994**, *19*, 187-212.
42. Dwyer, F.G. *Chem. Ind.* **1981**, *5*, 39-50.
43. a) Chiche, B.; Finiels, A.; Gauthier, C.; Geneste, P. *J. Org. Chem.* **1986**, *51*, 2128-2130; b) Bertea, L.; Kouwenhoven, H.W.; Prins, R. *Appl. Catal.* **1995**, *129*, 229-250; c) Smith, K.; He, P.; Taylor, A. *Green Chem.* **1999**, 35-38; d) Smith, K.; Bahzad, D. *Chem Commun.* **1996**, 467-477; e) Singh, A.P.; Sharma, A.; Kale, S.M. *J. Mol Catal. A: Chem.* **1997**, *127*, 101-111.
44. a) Katayama, A.; Toba, M.; Takeuchi, G.; Mizukami, F.; Niwa, S.-i.; Mitamura, S. *J. Chem. Soc., Chem. Commun.* **1991**, 39-40; b) Gunnewegh, E.A.; Gopie, S.S.; van Bekkum, H. *J. Mol. Catal. A: Chem.* **1996**, *106*, 151-158; c) He, C.; Liu, Z.; Fajula, F.; Moreau, P. *Chem. Commun.* **1998**, 1999-2000.
45. a) Bigi, F.; Carloni, S.; Maggi, R.; Muchetti, C.; Rastelli, M.; Sartori. G. *Synthesis* **1998**, 301-304; b) Bigi, F.; Carloni, S.; Maggi, R.; Muchetti, C.; Sartori, G. *J. Org. Chem.* **1997**, *62*, 7024-7027.
46. Gunnewegh, E.A.; Hoefnagel, A.J.; van Bekkum, H. *J. Mol. Catal. A: Chem.* **1995**, *100*, 87-92.
47. a) Weigert, F.J. *J. Org. Chem.* **1986**, 51, 2653-2655; b) Weigert, F.J. *J. Org. Chem.* **1987**, 52, 3296-3298; c) Pardillos, J.; Brunel, D.; Coq, B.; Massiani, P.; de Ménorval, L.C.; Figueras, F. *J. Am. Chem. Soc.* **1990**, *112*, 1313-1318.
48. a) Aucejo, A.; Burguet, M.C.; Corma, A.; Fornes, V. *Appl. Catal.* **1986**, *22*, 187-200; b) Thangaraj, A.; Sivasanker, S.; Ratnasamy, P. *J. Catal.* **1992**, *137*, 252-256; c) Dai, L.-X.; Hayasaka, R.; Iwaki, Y.; Koyano, K.A.; Tatsumi, T. *Chem. Commun.* **1996**, 1071-1072.
49. a) Xu, T.; Barich, D.H.; Goguen, P.W.; Song, W.; Wang, Z.; Nicholas, J.B.; Haw, J.F. *J. Am. Chem. Soc.* **1998**, *120*, 4025-4026; b) Nicholas, J.B.; Haw, J.F. *J. Am. Chem. Soc.* **1998**, *120*, 11804-11805; c) Goguen, P.W.; Xu, T.; Barich, D.H.; Skloss, T.W.; Song, W.; Wang, Z.; Nicholas, J.B.; Haw, J.F. *J. Am. Chem. Soc.* **1998**, *120*, 2650-2651.
50. a) Liebens, A.T.; Mahaim, C.; Hölderich, W.F. *Stud. Surf. Sci. Catal.* **1997**, *108*, 587-594; b) Kunkeler, P.J.; van Der Waal, J.C.; Bremmer, J.; Zuurdeeg, B.J.; Downing, R.S.; van Bekkum, H. *Catal. Lett.* **1998**, *53*, 135-138.
51. Sreekumar, R.; Narayana Murthy, Y.V.S; Narayana Pillai, C. *J. Chem. Soc., Chem. Commun.* **1992**, 1624-1625.
52. a) Wennerberg, J.; Ek, F.; Hansson, A.; Frejd, T. *J. Org. Chem.* **1999**, *64*, 54-59; b) Wennerberg, J.; Eklund, L.; Polla, M.; Frejd, T. *Chem. Commun.* **1997**, 445; c) Wennerberg, J.; Olofsson, C.; Frejd, T. *J. Org. Chem.* **1998**, *63*, 3595-3598.
53. a) Kunkeler, P.J.; Rigutto, M.S.; Downing, R.S.; de Vries, H.J.A.; van Bekkum, H. *Stud. Surf. Sci. Catal.* **1997**, *105*, 1269-1275; b) Prochazka, M.P.; Eklund, L.; Carlson, R. *Acta Chem. Scand.* **1990**, *44*, 610-613.
54. Rigutto, M.S.; de Vries, H.J.A.; Magill, S.R.; Hoefnagel, A.J.; can Bekkum, H. *Stud. Surf. Sci. Catal.*, **1993**, *78*, 661-668.
55. Boruah A.; Baruah, P.P.; Sandhu, J.S. *J. Chem. Research (S)* **1998**, 614-615.
56. Wali, A.; Pillai, S.M.; Unnikrishnan, S.; Satish, S. *J. Mol. Cat. A: Chem.* **1996**, *109*, 149-155.
57. Ziolek, M.; Nowak, I.; Decyk, P.; Kujawa, J. *Stud. Surf. Sci. Catal.* **1998**, *117*, 509-516.
58. Reddy, T.I.; Varma, R.S. *Chem. Commun.* **1997**, 621-622.

59. Takeuchi, H.; Nakajima, Y. *J. Chem. Soc. Perkin Trans. 2* **1998**, 2441-2446.
60. Selva, M.; Bomben, A.; Tundo, P. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1041-1045.
61. Nagaiah, K.; Kulkarni, S.J.; Subrahmanyam, M.; Rama Rao, A.V. *Ind. J. Chem. Tech.* **1996**, *3*, 128-130.
62. a) Bigi, F.; Maggi, R.; Sartori, G.; Zambonin, E. *Chem. Commun.* **1998**, 513-514; b) Bigi, F.; Frullanti, B.; Maggi, R.; Sartori, G.; Zambonin, E. *J. Org. Chem.* **1999**, *64*, 1004-1006.
63. Veloso, C.O.; Monteiro, J.L.F.; Sousa-Aguiar, E.F. *Stud. Surf. Sci. Catal.* **1994**, *84*, 1913-1920.
64. a) Posner, L.S.; Augustine, R.L. *Chem. Ind.* **1995**, *62*, 531-534; b) Sreekumar, R.; Rugmini, P.; Padmakumar, R. *Tetrahedron Lett.* **1997**, *38*, 6557-6560; c) Wang, Q.L.; Ma, Y.; Zuo, B. *Synth. Commun.* **1997**, *27*, 4107-4110; d) Reddy, T.I.; Varma, R.S. *Tetrahedron Lett.* **1997**, *38*, 1721-1724.
65. Climent, M.J.; Corma, A.; Iborra, S.; Primo, J. *J. Cat.* **1995**, *151*, 60-66.
66. Martens, L.R.M.; Vermeiren, W.J.M.; Grobet, P.J.; Jacobs, P.A. *Stud. Surf. Sci. Catal.* **1987**, *31*, 531-542.
67. Rao, Y.V.S.; De Vos, D. E.; Jacobs, P.A. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2661-2663.
68. Shabtai, J.; Lazar, R.; Biron, E. *J. Mol. Catal.* **1984**, *27*, 35-43.
69. Creyghton, E.J.; Ganeshie, S.D.; Downing, R.S.; van Bekkum, H. *J. Mol. Catal. A: Chem.* **1997**, *115*, 457-472.
70. Anwander, R.; Palm, C.; Gerstberger, G.; Groeger, O.; Engelhardt, G. *Chem. Comm.* **1998**, 1811-1812.
71. Verhoef, M.J.; Creyghton, E.J. Peters, J.A.; van Bekkum, H. *Chem. Comm.* **1997**, 1989-1990.
72. Onaka, M.; Sugita, K.; Izumi, Y. *J. Org. Chem.* **1989**, *54*, 1116-1123.
73. Sreekumar, R.; Padmakumar, R.; Rugmini, P. *Chem. Commun.* **1997**, 1133-1134.
74. Leung, W.-H.; Yu, M.-T.; Wu, M.-C.; Yeung, L.-L. *Tetrahedron Lett.* **1996**, *37*, 891-892.
75. Gupta, A.; Haque, A,; Vankar, Y.D. *Chem. Commun.* **1996**, 1653-1654.
76. Sreekumar, R.; Padmakumar, R.; Rugmini, P. *Tetrahedron Lett.* **1998**, *39*, 5151-5154.
77. Psaro, R.; Recchia, S. *Catal. Today* **1998**, *41*, 139-147.
78. Gallezot, P.; Giroir-Fendler, A.; Richard, D. *Catal Lett.* **1990**, *5*, 169-174.
79. Mehnert, C.P.; Weaver, D.W.; Ying, J.Y. *J. Am. Chem. Soc.* **1998**, 120, 12289-12296.
80. Dessau, R.M. *J. Chem. Soc., Chem. Commun.* **1986**, 1167-1168.
81. a) Eklund, L.; Axelsson, A.-K.; Nordahl, Å.; Carlson, R. *Acta Chem. Scand.* **1993**, *47*, 581-591; b) Genske, D.; Bornholdt, K.; Lechert, H. *Stud. Surf. Sci. Catal.* **1998**, *117*, 421-428.
82. a) Figueras, F.; Cativiela, C.; Fraile, J.M.; Garcia, J.I; Mayoral, J.A.; de Ménorval, L.C.; Pires, E. *Stud. Surf. Sci. Catal.* **1994**, *83*, 391-398; b) Cativiela, C.; Figueras, F.; Fraile, J.M.; Garcia, J.I; Mayoral, J.A.; de Ménorval, L.C.; Pires, E. *Appl. Catal., A* **1993**, *101*, 253-267.
83. Narayana Murthy, Y.V.S.; Pillai, C.N. *Synth. Commun.* **1991**, *21*, 783-791.
84. Oudejans, J.C.; Kaminska, J.; Kock-van Dalen, A.C.; van Bekkum, H. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 421-427.
85. Fraile, J.M.; García, J.I.; Mayoral, J.A. *Chem. Commun.* **1996**, 1319-1320.
86. Vogt, A.; Kouwenhoven, H.W.; Prins, R. *Appl. Catal. A* **1995**, *123*, 37-49.
87. Sreekumar, R.; Padmakumar, R. *Tetrahedron Lett.* **1996**, *30*, 5281-5282.
88. Ramamurthy, V.; Sanderson, D.R. *Tetrahedron Lett.* **1992**, *33*, 2757-2760.
89. a) Tung, C.-H.; Ying, Y.-M. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1319-1322; b) Pitchumani, K.; Warrier, M.; Ramamurthy, V. *J. Am. Chem. Soc.* **1996**, 118, 9428-9429; c) Pitchumani, K.; Warrier, M.; Cui, C.; Weiss, R.G.; Ramamurthy, V. *Tetrahedron Lett.* **1996**, 37, 6251-6254.
90. Tung, C-H.; Wu, L-Z.; Yuan, Z-Y.; Su, N. *J. Am. Chem. Soc* **1998**, 120, 11594-11602.
91. Ramamurthy, V.; Lakshminarasimhan, P.; Grey, C.P.; Johnston, L.J. *Chem. Commun.* **1998**, 2411-2424.
92. Anderson, M.A.; Grissom, C.B. *J. Am. Chem. Soc.* **1996**, *118*, 9552-9556.
93. Pitchumani, K.; Warrier, M.; Scheffer, J.R.; Ramamurthy, V. *Chem. Commun.* **1998**, 1197-1198.
94. Sadeghpoor, R.; Ghandi, M.; Mahmoudi Najafi, H.; Farzaneh, F. *Chem. Commun.* **1998**, 329-330.
95. Rao, V.J.; Uppili, S.R.; Corbin, D.R.; Schwarz, S.; Lustig, S.R.; Ramamurthy, V. *J. Am. Chem. Soc.* **1998**, *120*, 2480-2481.
96. a) Xiang, Y.; Larsen, S.C.; Grassian, V.H. *J. Am. Chem. Soc.* **1999**, *121*, 5063-5072; b) Steilemann, M.; Armor, J.N.; Hölderich, W.F. *Chem. Commun.* **1999**, 697-698.
97. Li, X.; Ramamurthy, V. *Tetrahedron Lett.* **1996**, *37*, 5235-5238.
98. Tung, C.-H.; Wang, H.; Ying, Y.-M. *J. Am. Chem. Soc.* **1998**, *120*, 5179-5186.
99. a) Robbins, R.J.; Ramamurthy, V. *Chem. Commun.* **1997**, 1071-1072; b) Li, X.; Ramamurthy, V. *J. Am. Chem. Soc.* **1996**, *118*, 10666-10667.
100. Clennan, E.L.; Sram, J.P. *Tetrahedron Lett.* **1999**, *40*, 5275-5278.

101 a) Arends, I.W.C.E.; Sheldon, R.A.; Wallau, M.; Schuchardt, U. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1144-1163; b) Murugavel, R.; Roesky, H.W. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 477-479.

102. a) Maschmeyer, T.; Rey, F.; Sankar, G.; Meurig Thomas, J. *Nature* **1995**, *378*, 159-162; b) Corma, A.; Díaz, U.; Fornés, V.; Jordá, J.L.; Domine, M.; Rey, F. *Chem. Commun.* **1999**, 779-780.

103. Kumar, P.; Kumar, R.; Pandey, B. *Synlett.* **1995**, 289-98.

104. a) Camblor, M.A.; Corma, A.; Martínez, A.; Pérez-Pariente, J. *J. Chem. Soc., Chem. Commun.* **1992**, 589-590; b) Camblor, M.A.; Costantini, M.; Corma, A.; Gilbert, L.; Esteve, P.; Martínez, A.; Valencia, S. *Chem. Commun.* **1996**, 1339-1340; c) Zhang, W.; Fröba, M.; Wang, J.; Tanev, P.T.; Wong, J.; Pinnavaia, J. *J. Am. Chem. Soc* **1996**, *118*, 9164-9171.

105. a) Adam, W.; Kumar, R.; Reddy, T.I.; Renz, M. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 880-882; b) Adam, W.; Corma, A.; Reddy, T.I.; Renz, M. *J. Org. Chem.* **1997**, *62*, 3631-3637.

106. Camblor, M.A.; Corma, A.; Esteve, P.; Martínez, A.; Valencia, S. *Chem. Commun.* **1997**, 795-796.

107. Joseph, R.; Sudalai, A.; Ravindranathan, T. *Synlett* **1995**, 1177-1178.

108. Bhaumik, A.; Tatsumi, T. *Chem. Commun.* **1998**, 463-464.

109. Coxon, J.M.; Hartshorn, M.P.; Swallow, W.H. *Aust. J. Chem.* **1973**, *26*, 2521-2526.

110. Adam, W.; Garcia, H.; Mitchell, C.M.; Saha-Möller, C.R.; Weichold, O. *Chem. Commun.* **1998**, 2609-2610.

111. a) Reddy, R.S.; Reddy, J.S.; Kumar, R.; Kumar, P. *J. Chem. Soc. Chem. Commun.* **1992**, 84-85; b) Corma, A.; Iglesias, M.; Sánchez, F. *Catal. Lett.* **1996**, *39*, 153-156; c) Raghavan, P.S.; Ramaswamy, V.; Upadhya, T.T.; Sudalai, A.; Ramaswamy, A.V.; Sivasanker, S. *J. Mol. Catal. A: Chem.* **1997**, *122*, 75-80.

112. Reddy, T.I.; Varma, R.S. *Chem. Commun.* **1997**, 471-472.

113. Corma, A.; Iglesias, M.; del Pino, C.; Sánchez, F. *J. Chem. Soc., Chem. Commun.* **1991**, 1253-1255.

114. a) Corma, A.; Iglesias, M.; Martín, M.V.; Rubio, J.; Sánchez, F. *Tetrahedron: Asym.* **1992**, *3*, 845-848; b) Corma, A.; Fuerte, A.; Iglesias, M.; Sánchez, F. *J. Mol. Catal. A: Chem.* **1996**, *107*, 225-234.

115. Bedioui, F. *Coord. Chem. Rev.* **1995**, *144*, 39-68.

116. Knops-Gerrits, P.-P.; De Vos, D.E.; Jacobs, P.A. *J. Mol. Catal. A: Chem.* **1997**, *117*, 57-70.

117. a) Zhang, W.; Loebach, J.L.; Wilson, S.R.; Jacobsen, E.N. *J. Am. Chem. Soc.* **1990**, *112*, 2801-2803; b) Zhang, W.; Jacobsen, E.N. *J. Org. Chem.* **1991**, *56*, 2296-2298; c) Canali, L.; Sherrington, D.C. *Chem. Soc. Rev.* **1999**, *28*, 85-93.

118. a) Sabater, M.J.; Corma, A.; Domenech, A.; Fornés, V.; García, H. *Chem. Commun.* **1997**, 1285-1286; b) Ogunwumi, S.B.; Bein, T. *Chem. Commun.* **1997**, 901-902.

119. Piaggio, P.; McMorn, P.; Langham, C.; Betell, D.; Bulman-Page, P.C.; Hancock, F.E.; Hutchings, G.J. *New J. Chem.* **1998**, 1167-1169.

120. a) Langham, C.; Taylor, S.; Bethell, D.; McMorn, P.; Bulman Page, P.C.; Willock, D.J.; Sly, C.; Hancock, F.E.; King, F.; Hutchings, G.J. *J. Chem. Soc., Perkin Trans 2* **1999**, 1043-1049; b) Langham, C.; Piaggio, P.; Bethell, D.; Lee, D.F.; McMorn, P.; Bulman-Page, P.C.; Willock, D.J.; Sly, C.; Hancock, F.E.; King, F.; Hutchings, G.J. *Chem. Commun.* **1998**, 1601-1602.

121. Johnson, B.F.G.; Raynor, S.A.; Shephard, D.S.; Mashmeyer, T.; Meurig Thomas, J.; Sankar, G.; Bromley, S.; Oldroyd, R.; Gladden, L.; Mantle, M.D. *Chem. Commun.* **1999**, 1167-1168.

122. a) Feast, S.; Bethell, D.; Bulman Page, P.C.; King, F.; Rochester, C.H.; Siddiqui, M.R.H.; Willock, D.J.; Hutchings, G.J. *J. Chem. Soc., Chem. Commun.* **1995**, 2409-2411; b) Hutchings, G.J. *Chem. Commun.* **1999**, 301-306; c) Feast, S.; Bethell, D.; Bulman Page, P.C.; King, F.; Rochester, C.H.; Siddiqui, M.R.H.; Willock, D.J.; Hutchings, G.J. *J. Mol. Catal. A: Chem.* **1996**, *107*, 291-295.

123. a) Sundarababu, G.; Leibovitch, M.; Corbin, D.R.; Scheffer, J.R.; Ramamurthy, V. *Chem. Commun.* **1996**, 2159-2160; b) Leibovitch, M.; Olovsson, G.; Sundarababu, G.; Ramamurthy, V.; Scheffer, J.R.; Trotter, J. *J. Am. Chem. Soc.* **1996**, *118*, 1219-1220; c) Joy, A.; Scheffer, J.R.; Corbin, D.R.; Ramamurthy, V. *Chem. Commun.*, **1998**, 1379-1380.

124. Zhan, B.-Z.; Li, X.-Y. *Chem. Commun.* **1998**, 349-350.

125. Lin, C.-J.; Yu, W.-Y.; Li, S.-G.; Che, C.-M. *J. Org. Chem.* **1998**, *63*, 7364-7369.

126. a) Robert, R.; Ratnasamy, P. *J. Mol. Catal. A: Chem.* **1995**, *100*, 93-102; b) Panov, G.I.; Sobolev, V.I.; Dukkov, K.A.; Kharitonov, A.S. *Stud. Surf. Sci. Catal.* **1996**, *101*, 493-502.

127. Corma, A.; Iglesias, M.; Sánchez, F. *J. Chem. Soc., Chem. Commun.* **1995**, 1635-1636.

128. a) Sen, S.E.; Zhang, Y.z.; Roach, S.L. *J. Org. Chem.* **1996**, *61*, 9534-9537; b) Sen, S.E.; Zhang, Y.-z.; Smith, S.M.; Huffman, J.C. *J. Org. Chem.*, **1998**, *63*, 4459-4465.

129. Sasaki, Y.; Suzuki, T.; Takamura, Y.; Saji, A.; Saka, H. *J. Catal.* **1998**, 178, 94-100.

130. Corma, A.; Domine, M.; Gaona, J.A.; Jordá, J.L.; Navarro, M.T.; Rey, F.; Pérez-Pariente, J.; Tsuji, J.; McCulloch, B; Nemeth, L.T. *Chem. Commun.* **1998**, 2211-2212.
131. Krijnen, S.; Abbenhuis, H.C.L.; Hanssen, R.W.J.M.; van Hooff, J.H.C.; van Santen, R.A. *Angew. Chem. Int. Ed.* **1998**, *37*, 356-358.
132. a) Burkett, S.L.; Sims, S.D.; Mann, S. *Chem. Commun.* **1996**, 1367-1368; b) Fowler, C.F.; Burkett, S.L.; Mann, S. *Chem. Commun.* **1997**, 1769-1770; c) Hall, S.R.; Fowler, C.E.; Lebeau, B.; Mann, S. *Chem. Commun.* **1999**, 201-202.
133. Corma, A.; Jordá, J.L.; Navarro, N.T.; Rey, F. *Chem. Commun.* **1998**, 1899-1900.
134. Cauvel, A.; Renard, G.; Brunel, D. *J. Org. Chem.* **1997**, *62*, 749-751.
135. Maschmeyer, T.; Oldroyd, R.D.; Sankar, G.; Thomas, J.M.; Shannon, I.J.; Klepetko, J.A.; Masters, A.F.; Beattie, J.K.; Catlow, C.R.A. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1639-1642.
136. Jones, C.W.; Tsuji, K.; Davis, M.E. *Nature* **1998**, *393*, 52-54.
137. Laszlo, P. *Science* **1987**, *235*, 1473-1477.
138. a) Janiak, C. *Angew. Chem. Int. Ed. Engl* **1997**, *36*, 1431-1434; b) Lee, S.; Venkataraman, D. *Stud. Surf. Sci. Catal.* **1996**, *102*, 75-95.
139. Corriu, R.J.P.; Leclercq, D. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1420-1436.
140. a) Clet, G.; Jansen, J.C.; van Bekkum, H. *Chem. Mater.* **1999**, *11*, 1696-1702; b) Muñoz, Jr, T.; Balkus, Jr, K. J. *J. Am. Chem. Soc.* **1999**, *121*, 139-146.
141. Feng, P.; Bu, X.; Tolbert, S.H.; Stucky, G.D. *J. Am. Chem. Soc.* **1997**, *119*, 2497-2504.

Biographical sketch

Stephanie Sen was born in 1962 in New York City, New York. She received her BA degree in chemistry at Bryn Mawr College and her Ph.D. in organic chemistry from the State University of New York at Stony Brook. After working as a postdoctoral researcher at both the Scripps Research Institute and Stanford University, she joined the faculty at Indiana University-Purdue University at Indianapolis in 1992, where she is now an associate professor of chemistry. Her research interests are in bioorganic chemistry, with current projects related to biomimetic polyene cyclizations and insect juvenile hormone biochemistry.

Sarah M. Smith was born in 1970 in Chicago, Illinois. She received her BS degree in chemistry at St. Joseph's College in 1992 and after working as an analytical chemist for 3 years, decided to obtain her graduate degree in chemistry. She is currently pursuing her Ph.D. degree in the area of zeolite-mediated polyene cyclizations.

Katherine A. Sullivan was born in 1978 in Muncie, Indiana. She is currently an undergraduate majoring in chemistry at Indiana Univerity-Purdue University at Indianapolis and is a research assistant under the direction of Dr. S. Sen. She plans to continue her studies and obtain a graduate degree in chemistry.