

# Asymmetric Photoreactions within Zeolites: Role of Confinement and Alkali Metal Ions<sup>†</sup>

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Received November 21, 2002

## ABSTRACT

In this Account strategies using zeolites as media to achieve chiral induction are presented. Diastereomeric excesses as high as 90% and enantiomeric excesses up to 78% have been obtained with selected systems within zeolites. The same systems show no asymmetric induction in solution. Chiral induction is dependent on the alkali ions present in the zeolites. Alkali ions control not only the extent of asymmetric induction but often the isomer being enhanced. Results of ab initio computations have allowed us to gain an insight into the observed selectivity within zeolites.

## Introduction

Following the communication by Hammond and Cole in 1965 on the use of optically active sensitizers in the photosensitized isomerization of *cis*-diphenylcyclopropane,<sup>1</sup> several groups have performed enantio- and diastereoselective phototransformations, both in solution and the solid state.<sup>2</sup> Despite considerable efforts, the enantiomeric excesses (ee's) obtained under ambient conditions in solution continue to be less than 50%. The best results in solution have been obtained via the chiral auxiliary methodology, yielding in select examples diastereomeric excesses (de's) close to 100%.<sup>3</sup> Asymmetric photochemistry in the crystalline state is based on the "chance" crystallization of achiral molecules in chiral space groups.<sup>4</sup> Because of the limited probability of this

happening, there are relatively few examples of asymmetric induction during photolysis of achiral molecules in the crystalline state.<sup>5</sup> A more general methodology known as the "ionic chiral auxiliary approach" introduced by Scheffer facilitates the crystallization of achiral molecules in chiral space groups.<sup>6</sup> On the basis of this strategy, Scheffer and co-workers have provided a number of examples that yield photoproducts in very high ee (or de) in the crystalline state.

Recognizing the problem of crystallizing achiral molecules in chiral space groups, several researchers have explored chiral hosts as the reaction medium. The earliest such report is that of Natta on the photopolymerization of 1,3-dienes included in the channels of optically active perhydrotriphenylene,<sup>7</sup> and the most successful ones are those of Toda using chiral diol hosts.<sup>8</sup> While crystalline and host-guest assemblies have been extremely useful to conducting enantioselective photoreactions, their general applicability has been limited. Not all molecules crystallize either alone or in the presence of organic host systems. The reactivity of molecules in the crystalline state and in solid host-guest assemblies is controlled by the details of molecular packing. Currently, molecular packing, and consequently the chemical reactivity in the crystalline state, cannot be reliably predicted. Therefore, even after successfully crystallizing a molecule in a chiral space group or complexing a molecule with a chiral host or a chiral auxiliary, there is no guarantee that the guest will react in the crystalline state.

Our approach has been to employ readily available and inexpensive zeolites as media to bring about asymmetric induction in photochemical reactions. The internal structure of the faujasite class of zeolites is characterized by a three-dimensional network of supercages (ca. 13 Å in diameter) interconnected by tetrahedrally disposed windows (ca. 8 Å diameter, Figure 1).<sup>9</sup> Due to the difference in charge between the [SiO<sub>4</sub>]<sup>4-</sup> and [AlO<sub>4</sub>]<sup>5-</sup> tetrahedra which form the framework of the zeolite, the net charge of an aluminum containing zeolite is negative and hence must be balanced by a cation. Charge compensating cations are located at three different sites within the zeolite framework, of which only two (types II and III) are expected to be readily accessible to the adsorbed organic molecule. The Y zeolite used in this study has only type I and II sites occupied. The results of our studies within zeolites in the context of asymmetric photochemistry are highlighted in this Account.<sup>10</sup>

## The Chiral Inductor Method

To provide the asymmetric environment lacking in zeolites during the reaction, a chiral source must be introduced. For this purpose, in the approach we refer to as the chiral inductor method (CIM), the nonchiral interior surface of the zeolite is rendered "locally chiral" by adsorption of a

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<sup>†</sup> Dedicated to Professor N. J. Turro on the occasion of his 65th birthday.

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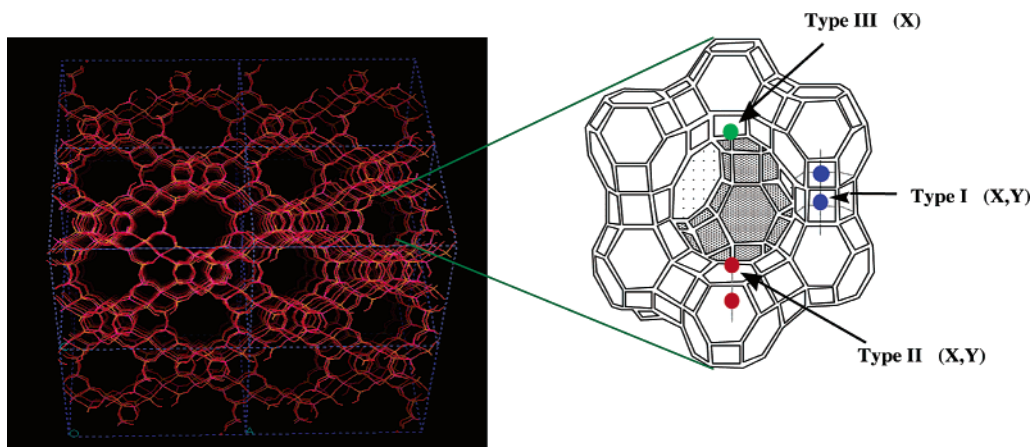


FIGURE 1. Structure of the faujasite zeolite (left) and the zeolite supercage (right). Positions of cations are identified as types I, II, and III.

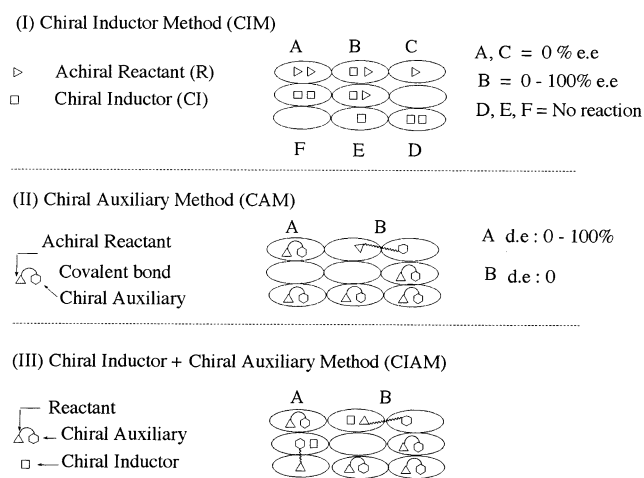


FIGURE 2. Probable occupancy of reactant and chiral inducers within zeolites. The three models represent the three approaches used in this study.

chiral inductor such as ephedrine.<sup>11,12</sup> This simple method affords easy isolation of the product, as the chiral inductor and the reactant are not connected through either a covalent or an ionic bond. The chiral inductor that is used to modify the zeolite interior will determine the magnitude of the enantioselectivity of the photoproduct.

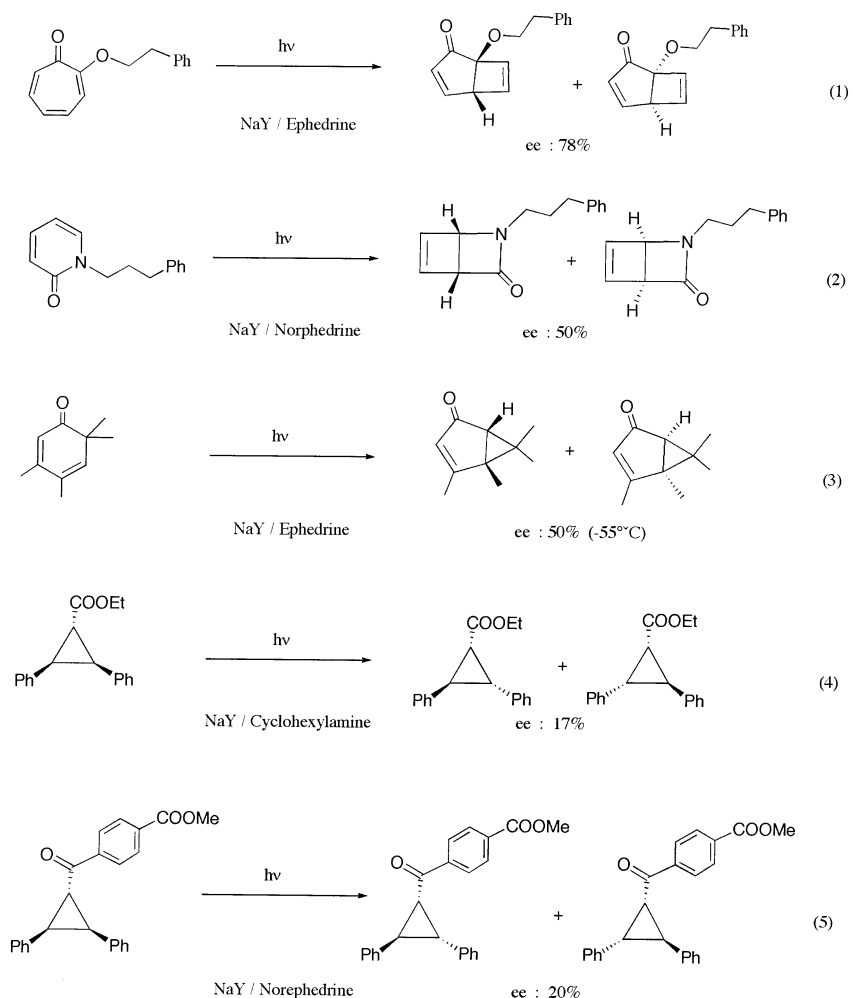
The strategy of employing chirally modified zeolites as reaction media requires the inclusion of two different molecules, a chiral inductor (CI) and a reactant (R), within the interior space of an achiral zeolite and by its very nature does not allow quantitative asymmetric induction. The six possible occupancies of two different molecules CI and R included within a given zeolite are shown in Figure 2I: cages containing two R molecules (type A), one R and one CI (type B), single R (type C), two CI (type D), a single CI (type E), and no CI or R molecules (type F). The products obtained from the photoreaction of R represent the sum of reactions that occur in cages of type A, B, and C, of which B alone leads to asymmetric induction. Obtaining high asymmetric induction therefore requires the placement of each reactant molecule next to a chiral inductor (type B situation), i.e., enhancement of the ratio of type B cages to the sum of types A and C.

To examine the viability of CIM, we have explored a number of photoreactions (electrocyclic reactions,<sup>13,14</sup> the Zimmerman (di- $\pi$ -methane) reaction,<sup>15</sup> the oxa-di- $\pi$ -methane rearrangement,<sup>16</sup> Yang cyclization,<sup>17,18</sup> geometric isomerization of 1,2-diphenylcyclopropane derivatives,<sup>19</sup> and the Schenk reaction<sup>15</sup>) which yield racemic products even in the presence of chiral inducers in solution (see Schemes 1 and 2 for selected examples). Although most systems gave moderate enantiomeric excesses (15–50%), two reactions gave respectable ee's within NaY, namely, the photocyclization of tropolone ethyl phenyl ether (78%, eq 1, Scheme 1)<sup>14</sup> and photocyclization of 1-(3-phenyl propyl)-2-pyridone (50%, eq 2, Scheme 1).<sup>20</sup> Considering that in solution all systems gave racemic products even in the presence of a chiral inductor, the CIM results within zeolites are both significant and mechanistically interesting. In general best results were obtained with ephedrine, norephedrine or pseudoephedrine as the chiral inductor (for structures of chiral inducers and chiral auxiliaries, see Scheme 3).

## The Chiral Auxiliary Method

We reasoned that unless a strategy which places each reactant molecule next to a chiral inductor within a zeolite is developed, high stereoselectivity is unlikely by CIM. This led us to explore the chiral auxiliary method (CAM) in which the chiral perturber is connected to the reactant via a covalent bond.<sup>21</sup> In this approach, most cages are expected to contain both the reactant as well as the chiral inductor components within the same cage (Figure 2II). We have tested CAM with several systems (for selected examples see Scheme 4; for the sake of variety, we have provided examples with different chiral auxiliaries) and have found that the diastereomeric excesses obtained within zeolites are far superior to those in solution. de's of >75% have routinely been obtained within MY zeolites for systems that yield photoproducts in 1:1 diastereomeric ratio in solution.

Scheme 1



## A Combination of Chiral Auxiliary and Chiral Inductor Methods

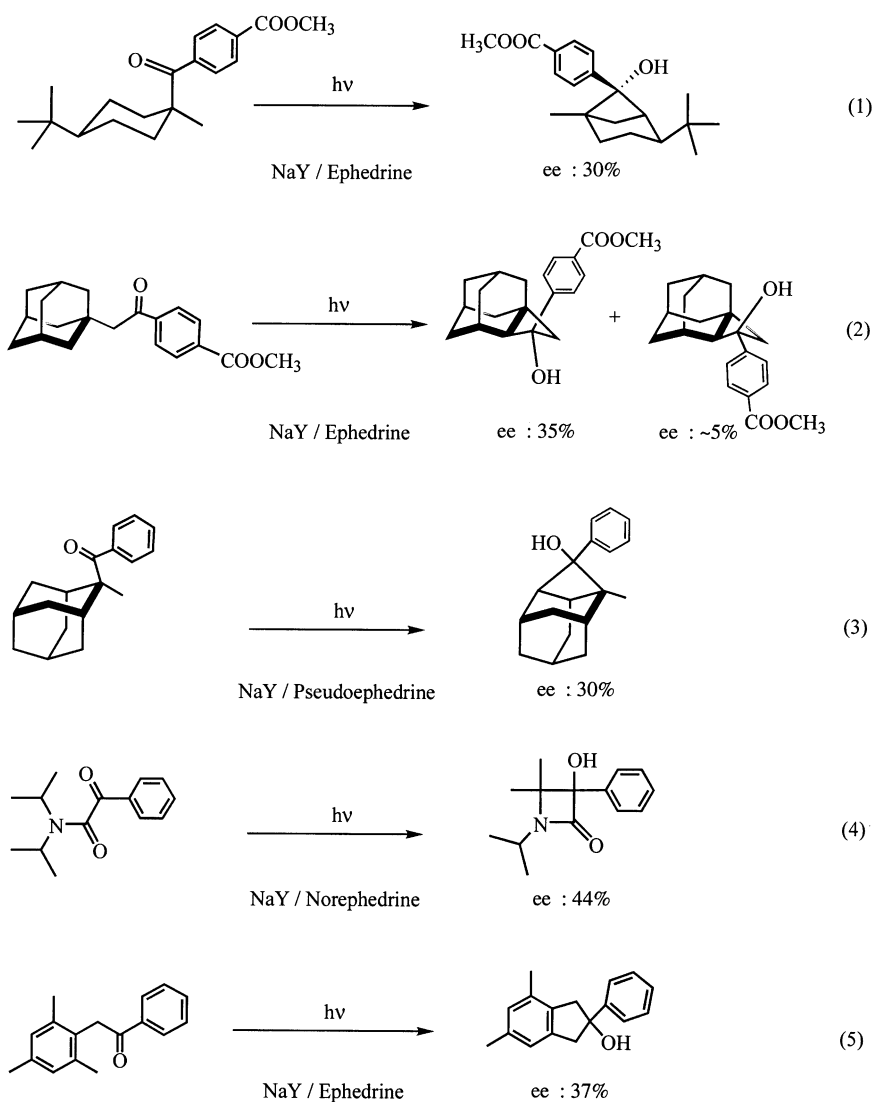
By adopting an extended conformation, it is possible that the reactant and its covalently linked chiral inductor may reside in different cages that could result in <100% de (type B in Figure 2II). We have attempted to provide an asymmetric environment to such molecules by using chirally modified Y zeolites as the reaction media (Figure 2III). Within (–)-ephedrine modified NaY, the de in the photoproduct from tropolone-2-methylbutyl ether increased from 53% to 90% (Figure 3),<sup>21a</sup> while it decreased from 59% to 3% in the case of the 1-phenylethylamide of 2,6,6-trimethylcyclohexa-2,4-diene-1-one-4-carboxylic acid (eq 1 Scheme 4 where the chiral auxiliary is 1-phenylethylamide).<sup>16</sup> Several tropolone derivatives which gave >80% de in NaY (e.g., eq 3 in Scheme 4) did not give higher de's when irradiated within chirally modified Y zeolites. Thus, the combination of the chiral inductor and the chiral auxiliary approach had led to a limited success, and it is still somewhat unpredictable (see Scheme 4 for selected examples). As shown in Figure 3, the 20% decrease in the maximum de obtained with (+) ephedrine from that with its antipode (90% in (–)-ephedrine and 70% in (+)-ephedrine) suggests that the reactions occur in two types of cages, one that contains the reactant alone and

the second that contains the reactant and a chiral inductor (Figure 3 bottom). Had all the photoreactions occurred in a single type of cage, complete switch would be expected with the antipode. This implies that we have not yet reached a condition in which every reactant site is adjacent to a chiral center.

## Localizing Photoreactions to Specific Cages

One of the drawbacks of the use of zeolites as reaction media is the difficulty in controlling the distribution of reactants and chiral inductors (Figure 2I). In principle, this problem can be overcome by localizing the photoreaction to those cages in which the reactant is next to a chiral inductor (type B in Figure 2I). We have explored this concept with the photoreduction of ketones by amines as a probe reaction.<sup>22</sup> The ketone we have examined is phenyl cyclohexyl ketone (Scheme 5). Upon excitation in solution, this ketone gives Norrish type II products. However, when included within a chirally modified zeolite (ephedrine, pseudoephedrine or norephedrine as chiral inductors), it gave the intermolecular reduction product,  $\alpha$ -cyclohexyl benzyl alcohol. The ratio of photoreduction to Norrish type II product was dependent on the nature (primary, secondary, or tertiary) and amount of the chiral

Scheme 2



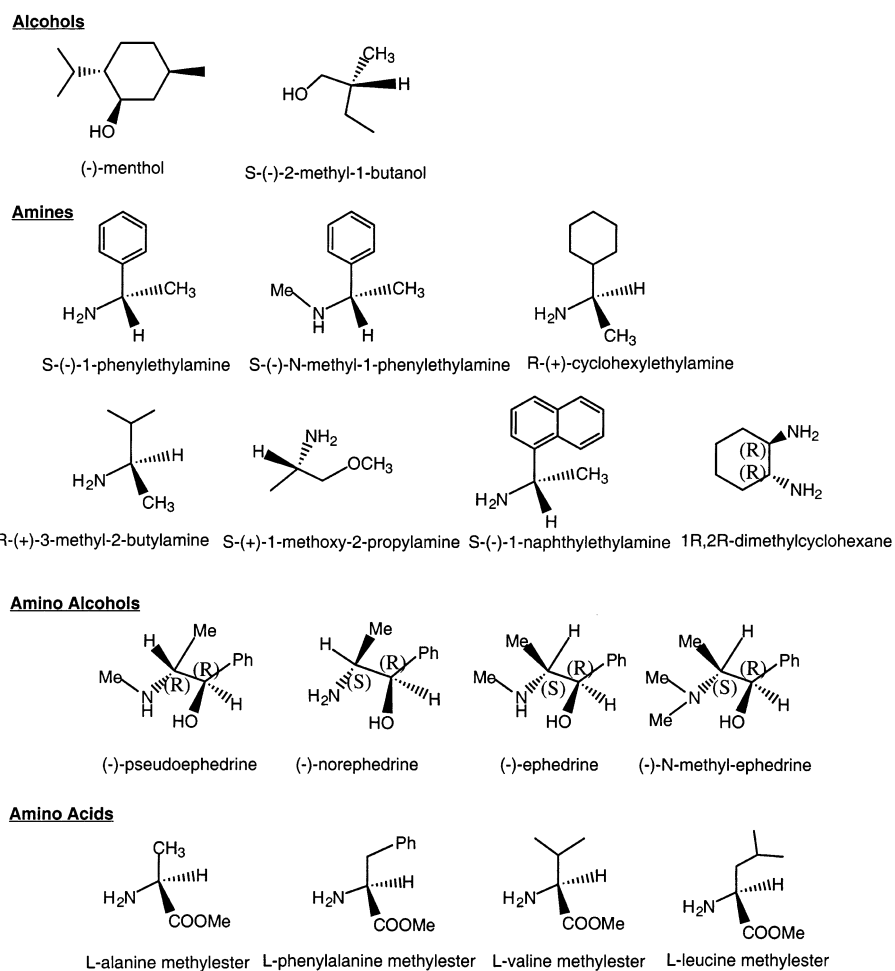
amine that acts as an electron donor. These observations indicate that photoreduction occurs only in cages that contain a chiral inductor. Using norephedrine as the chiral inductor, the ee obtained for the reduction product was 68%. As expected, the configuration of the photoproduct was reversed by using the antipode of the chiral inductor. It is important to note that under similar conditions in solution no ee was obtained in the reduction product which is formed in minor amounts. We have shown that the strategy presented above with phenyl cyclohexyl ketone is general by investigating a number of aryl alkyl and diaryl ketones (for selected examples, see Scheme 6). Despite the fact that the entire reaction occurs within chirally modified cages, the ee is still not quantitative, suggesting that there are yet unknown factors that need to be optimized.

## Role of Metal Ions

Having established the superiority of zeolites over solution media for asymmetric induction during photoreactions,

we need to gain an insight into how zeolites enhance the power of chiral inductors and chiral auxiliaries. Of the four methods discussed above, the chiral auxiliary method is more general, normally gives high de ( $>70\%$ ), and is more amenable to mechanistic understanding. In this context, we have carried out detailed investigations of seven independent systems within alkali ion exchanged Y zeolites (photocyclization of tropolone alkyl ethers,  $\gamma$ -hydrogen abstraction reaction of 2-benzoyladamantane-2-carboxylic acid derivatives and *N,N*-bis(1-methylethyl)- $\alpha$ -oxo-benzeneacetamide-4-carboxylic acid derivatives, oxa-di- $\pi$ -methane rearrangements of 2,2-dimethyl-1-(2H)-naphthalenone derivatives and 2,6,6-trimethylcyclohexa-2,4-diene-1-one-4-carboxylic acid derivatives, and photoisomerization of 2 $\beta$ ,3 $\beta$ -diphenylcyclopropane-1 $\alpha$ -carboxylic acid derivatives and 2 $\beta$ ,3 $\beta$ -diphenyl-1 $\alpha$ -benzoylcyclopropane derivatives; Scheme 4) with a variety of appended chiral auxiliaries. Studies with these systems have allowed us to reach a few generalizations which are presented below. However, we are still far from developing a model with predictive powers.

Scheme 3

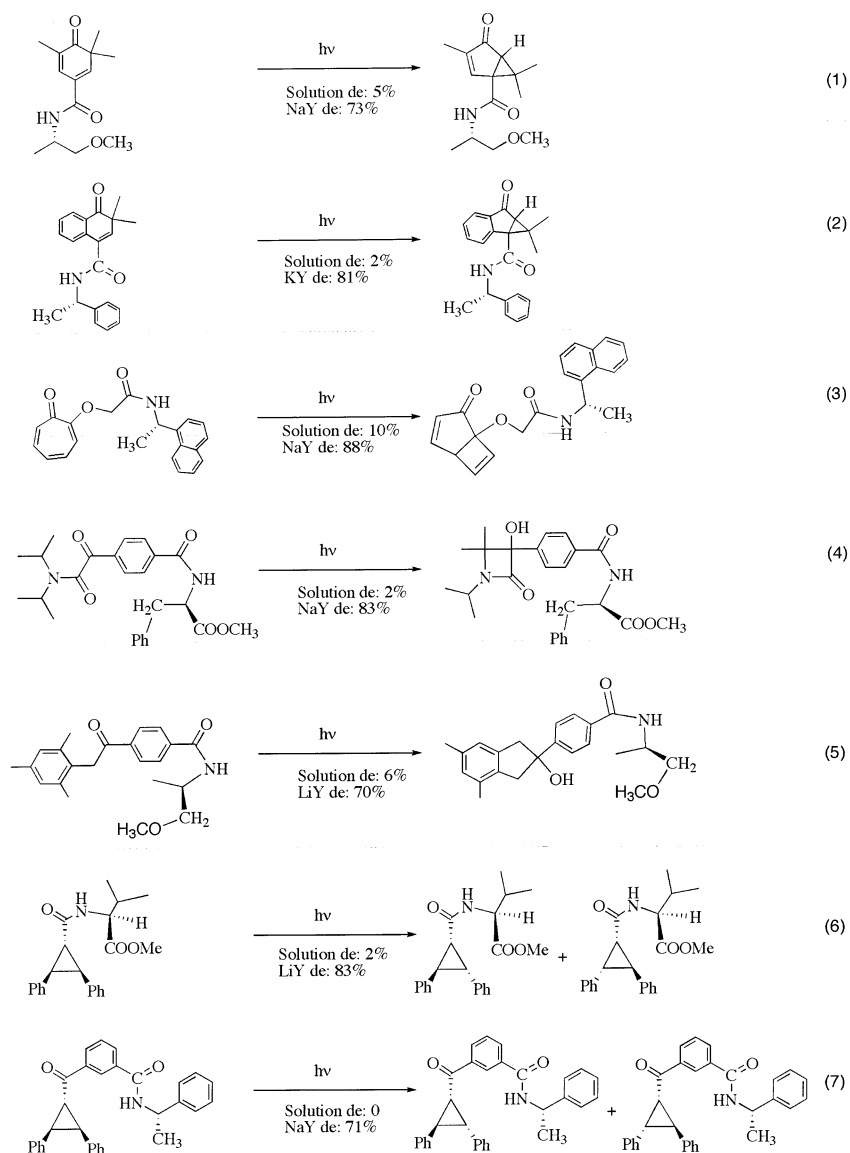


For all the systems investigated, the effectiveness of a chiral auxiliary is enhanced within a zeolite compared to that in solution. As representative of the behavior of all the molecules investigated, results from one system (photocyclization of the amide derived from tropolone acetic acid and 1-phenylethylamine; Scheme 7) are highlighted below:<sup>23</sup> (a) The de was dependent on the nature of the alkali metal ion. (b) The de varied with the water content of the NaY used. (c) The de was dependent on the number of alkali ions present within a zeolite. (d) The de upon irradiation of the tropolone derivative adsorbed on silica gel, a surface that does not contain alkali metal cations, was negligible (<5%). These observations lead us to conclude that alkali ions present in zeolites play an important role in the asymmetric induction process. Water molecules that hydrate the alkali ions probably disrupt the close interaction between the alkali ion and the reactant molecule and thus decrease the observed de.

Our inference that alkali ions present in zeolites interact with the guest reactant molecules has precedent. A variety of techniques has demonstrated that the alkali ion–guest interaction plays an important role during the adsorption of organic molecules within MY zeolites. Cation– $\pi$  interactions<sup>24</sup> have been recognized as the main force of binding between aromatic guest molecules (e.g., benzene, pyridine, etc.) and the zeolite supercage.<sup>25</sup> However, when

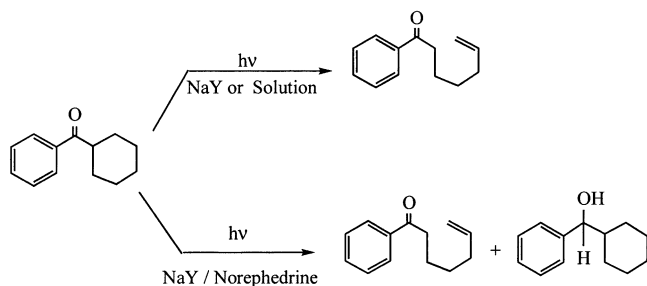
a benzene ring is substituted with a polar group such as nitro or carbonyl (dinitrobenzene, acetophenone), the primary interaction is between the alkali ions and the oxygen atoms of the nitro or carbonyl groups (due to cation–dipolar interaction).<sup>26</sup> How does the alkali ion–reactant interaction influence the power of a chiral auxiliary? A recent report based on computational studies indicates that the conformations of free and Na<sup>+</sup> bound phenylalanine are different.<sup>27</sup> Further, in this case, alkali ion $\cdots\pi$ , alkali ion $\cdots$ O=C dipolar, and alkali ion $\cdots$ nitrogen lone pair interactions restrict the conformational mobility of Na<sup>+</sup> bound phenylalanine. We believe that the enhanced asymmetric induction within a zeolite (with respect to that in solution) can be understood on a similar basis. Two examples discussed below provide a glimpse of how an alkali ion might influence asymmetric induction within a zeolite.

The enhanced de in the products derived via  $\gamma$ -hydrogen abstraction from several chiral esters of 2-benzoyladamantane-2-carboxylic acid within a zeolite compared to that in solution (Scheme 8) may be understood on the basis of conformational restriction brought forth by the alkali ion–reactant interaction.<sup>18</sup> For example, density functional calculations (B3LYP/6-31G\*) suggest that the menthyl ester of 2-benzoyladamantane-2-carboxylic acid has two conformations, differing by 2.3 kcal/mol, in which

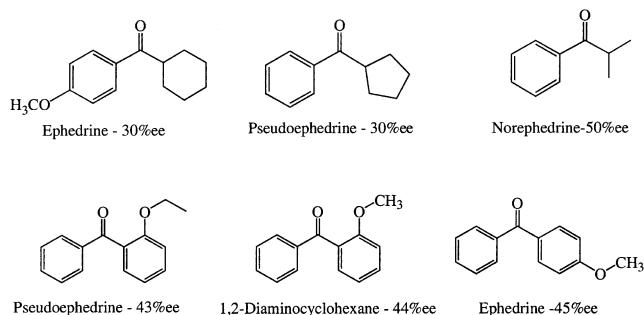
Scheme 4. Selected Examples of Chiral Inductors and Chiral Auxiliaries Used in this Study<sup>a</sup>

<sup>a</sup> Alcohols were connected to the reactants as esters and the rest as amides.

Scheme 5

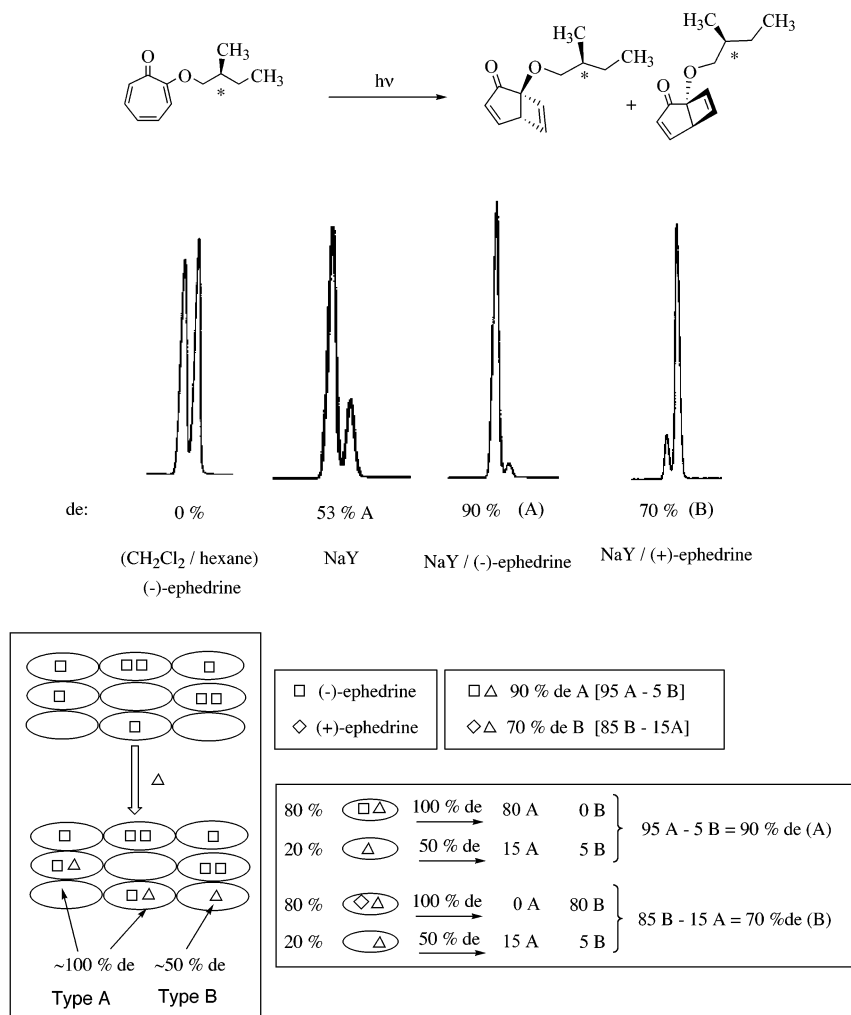


Scheme 6



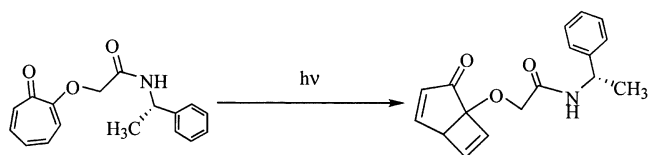
the carbonyl chromophore is tilted toward one or the other diastereotopic hydrogen at C4 and C6 (Figure 4). This would allow equilibrium between the two conformers leading to negligible de in solution. On the other hand, in the presence of  $\text{Li}^+$  there is a larger difference in energy between the two conformers (Figure 5; 10.4 kcal/mol). Closer examination of the two structures indicates that the nature of the interaction between  $\text{Li}^+$  and the menthyl

ester of 2-benzoyladamantane-2-carboxylic acid is different in the two conformers. In structure "a" the interaction is between  $\text{Li}^+$  and the oxygen atoms of the ketone and the ether oxygens of the ester group ( $\text{CO}-\text{O}-\text{C}$ ), and in structure "b" the interaction is between  $\text{Li}^+$  and the carbonyl oxygens of the keto and the ester ( $\text{CO}-\text{O}-\text{C}$ ) groups. In these structures the cation acts as "glue" to



**FIGURE 3.** Results on the photocyclization of (*S*)-tropolone 2-methylbutyl ether within chirally modified Na Y zeolite. The % de (diastereomeric excess) and the isomer enhanced are shown on the GC traces. Note that the extent of chiral induction brought forth by the antipodes are not the same with achiral and chiral tropolone ether. The lower de obtained with (+)-ephedrine could be understood on the basis of the model presented in the bottom part of the figure.

**Scheme 7**

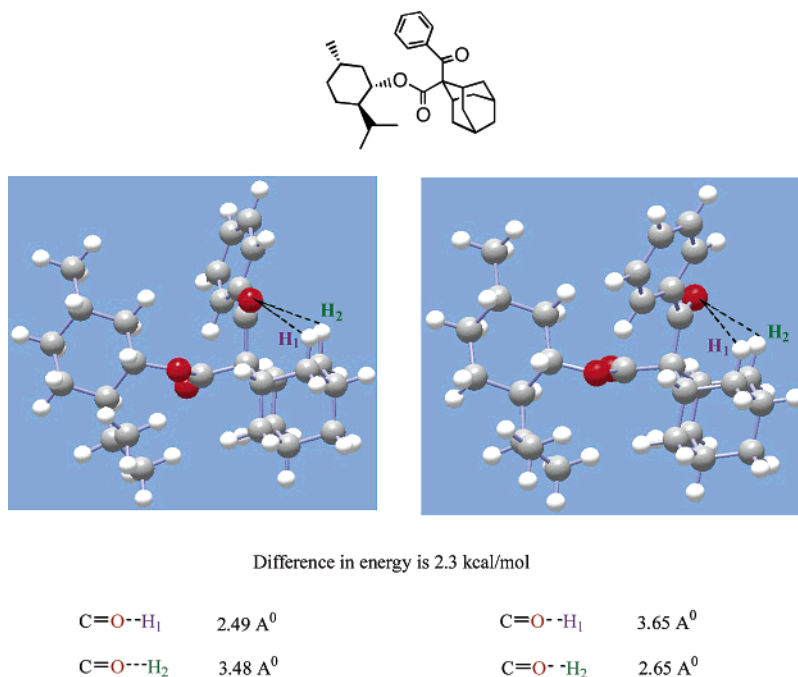


Medium	% de	NaY (Si/Al ratio)	%de
Solution	2	2.4	85
LiY	64	6	22
NaY	85	15	16
KY	26	40	4
RbY	5	NaY, 2.4, hydrated	3
CsY	5		

restrict the relative motions of the reactive and chiral auxiliary portions of the molecule (Figure 5). By this process the chiral auxiliary is able to exert a strong influence on the  $\gamma$ -hydrogen abstraction reaction. Once interconversion between the conformers is restricted, the reaction will take place from the more stable of the two conformers. Thus, while the chiral auxiliary is essential

to differentiate the two diastereotopic hydrogens, the cation is important to restrict bond rotations and freeze the molecule in a conformation that leads primarily to a single cyclobutanol diastereomer.

A comparison of the effectiveness of aryl and alkyl amides as chiral auxiliaries further reveals the importance of alkali ion–chiral auxiliary interaction within zeolites. Results on three systems are highlighted in Scheme 9.<sup>23</sup> Generally higher de is obtained with aryl amides than with alkyl amides as chiral auxiliaries. The important question concerning the reason for the differential behavior of the aryl and the alkyl chiral auxiliaries was answered with the help of *ab initio* computations at the Hartree–Fock level (HF/3-21G). Results on one system discussed below illustrate the point. Computations carried out with 2 $\beta$ ,3 $\beta$ -diphenylcyclopropane-1 $\alpha$ -carboxamides of 1-phenylethylamine and 1-cyclohexylethylamine revealed that Li<sup>+</sup> binds to the substrate in several different geometries, and of these the one shown in Figure 6 is the most stable. In the structure shown for the 1-phenylethylamide, Li<sup>+</sup> interacts simultaneously with both the phenyl group and the amide carbonyl oxygen. Such an interaction is expected to reduce



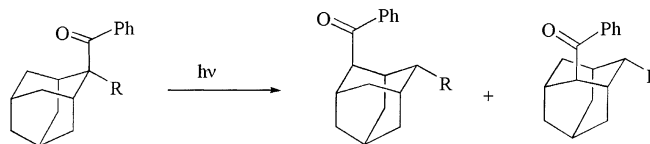
**FIGURE 4.** Two conformations of the menthyl ester of 2-benzoyladamantane-2-carboxylic acid as computed at the RB3LYP/6-31G(d) level. Note that the two conformations in which the carbonyl group is tilted toward the two prochiral hydrogens have different energies. The distances between the carbonyl oxygen and the prochiral hydrogens are included.

the rotational freedom of the chiral auxiliary and thus make it “rigid”. On the other hand, in the case of the 1-cyclohexylethylamide, the cation interacts primarily with the amide carbonyl oxygen via a dipolar type interaction and does not interact with the chiral auxiliary part (cyclohexyl group). Such a type of interaction would have no effect on the rotational mobility of the chiral auxiliary. Thus, a model based on the difference in flexibility of the chiral auxiliary due to differences in cation binding between aryl and alkyl chiral auxiliaries accounts for the

observed variation in *de* between the two classes of chiral auxiliary (Scheme 9). The prominent interaction between the alkali metal ion and the aryl group can be characterized as a cation- $\pi$  interaction.<sup>24</sup>

While one might question the relevancy of the computed “free-space” cation-organic structures to those within a “confined space”, the fact that the photochemical behavior of a large number of molecules can be understood on the basis of a model developed with computed structures suggests that simple *ab initio* computations are

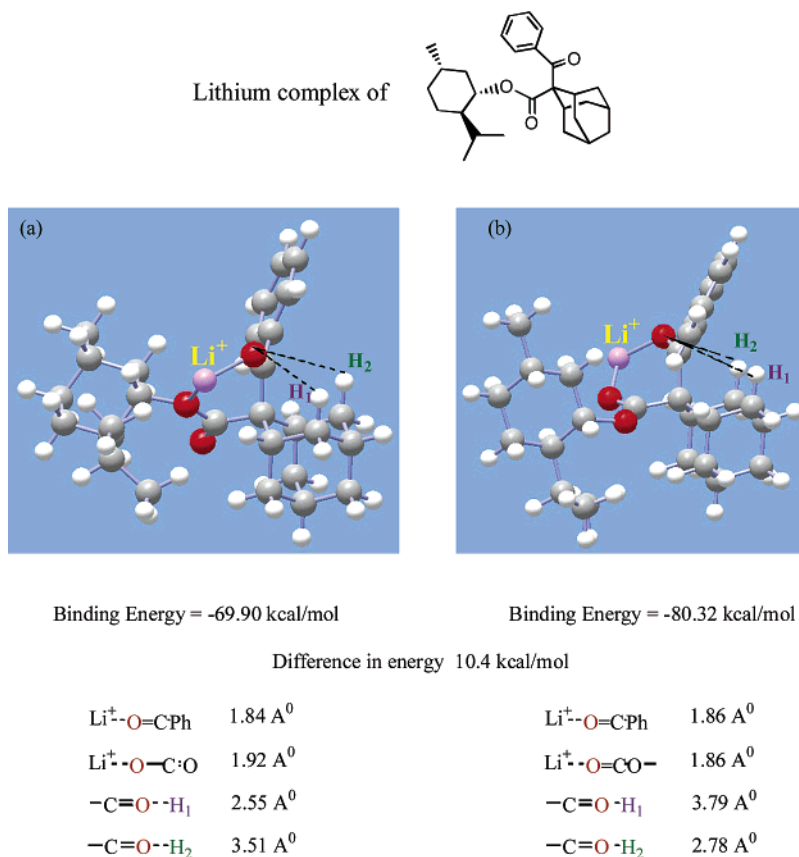
**Scheme 8**



Diastereomeric excess on the product  $\delta$ -ketoesters upon irradiation of the chiral esters of 2-benzoyladamantane-2-carboxylic acids

Medium	(-)-menthyl ester	(+)-isomenthyl ester	S(-)-2-methylbutylester	(+)-isopinocampheol ester
CH <sub>3</sub> CN	22(A)	14(B)	5(A)	5(B)
LiY	79(B)	65(A)	26(B)	52(B)
NaY	60(B)	79(A)	54(B)	62(B)
KY	31(B)	3(A)	30(B)	4(A)





**FIGURE 5.** The most stable structure computed (RB3LYP/6-31G\*) for the  $\text{Li}^+$  complex of the menthyl ester of 2-benzoyladamantane-2-carboxylic acid. In the two structures the sites of interaction of  $\text{Li}^+$  are different. The carbonyl group is tilted toward different prochiral hydrogens in the two structures. Note that the binding energies are considerably different for the two structures.

useful in understanding reactions within zeolites. We are currently limited by computational power to perform ab initio level calculations that include the zeolite framework. We are in the process of obtaining experimental support for the above proposed model based on cation-organic interactions. The proposed model is based on the concept that alkali ion-reactant interactions are (at least partially) responsible for the asymmetric induction within zeolites. The alkali ion enhances the power of a chiral auxiliary by restricting the conformational flexibility of the chiral auxiliary and/or the reacting parts of the molecule.

### An Alkali Ion and Reactive State-Dependent Diastereomer Switch

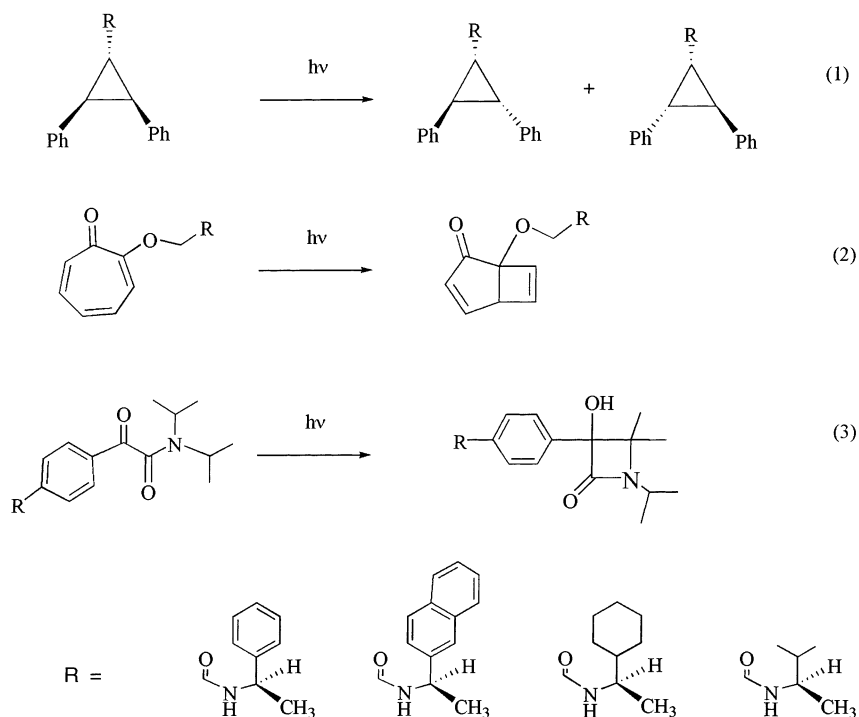
The alkali ions control not only the extent of de but also the diastereomer that is enhanced. Eight of the 11 amides of 2 $\beta$ ,3 $\beta$ -diphenylcyclopropane-1 $\alpha$ -carboxylic acid examined displayed alkali ion dependent diastereomer switch (for selected examples, see Scheme 10).<sup>21d</sup> The most remarkable example is provided by the amide derived from L-valine methyl ester (Figure 7). In this case the de in LiY is 83% favoring the B isomer, whereas in KY it is 80% in favor of the A isomer (A and B refer to the first and the second diastereomer peaks in the GC trace). A similar alkali ion-dependent diastereomer switch was observed in the case of the amides derived from N, N-bis(1-methylethyl)- $\alpha$ -oxo-benzeneacetamide-4-carboxylic acid

(eq 4, Scheme 4).<sup>28</sup> We believe that the diastereomer switch reflects a difference in site to which the two alkali ions bind.

The above, admittedly speculative, model has some support. On the basis of computational and experimental results, a difference in binding pattern between  $\text{Li}^+$  and  $\text{K}^+$  ions with glycine, valine, and arginine has been proposed.<sup>29</sup> For example,  $\text{Li}^+$  binds to these molecules through CO and  $\text{NH}_2$  (N, O coordination), whereas  $\text{K}^+$  binds to the oxygens of the COOH group (O, O coordination). A similar switch in the binding site is found between  $\text{Li}^+$  and  $\text{Cs}^+$  in the case of arginine.<sup>29b</sup> Such a phenomenon may be involved within zeolites and could be the cause of the observed cation-controlled diastereomer switch. Before leaving this section, we wish to point out that the alkali ion-dependent diastereomer switch can be turned off by methylating the amide nitrogen. For example while the 2 $\beta$ ,3 $\beta$ -diphenylcyclopropane-1- $\alpha$ -carboxamide derived from S(-)-1-phenylethylamine (**1a**) and (-)-norephedrine (**1c**) showed an alkali ion-dependent diastereomer switch, the amides derived from S(-)-N-methyl-1-phenylethylamine (**1d**) and (-)-pseudoephedrine (**1e**) did not (Scheme 10). We do not yet understand the role of N-CH<sub>3</sub> in this process. To our knowledge no alkali ion-dependent diastereomer switch has been reported previously, and it is clear that this unusual phenomenon needs further study.

The geometric isomerization of the amides of 2 $\beta$ ,3 $\beta$ -diphenylcyclopropane-1 $\alpha$ -carboxylic acid within zeolites

Scheme 9



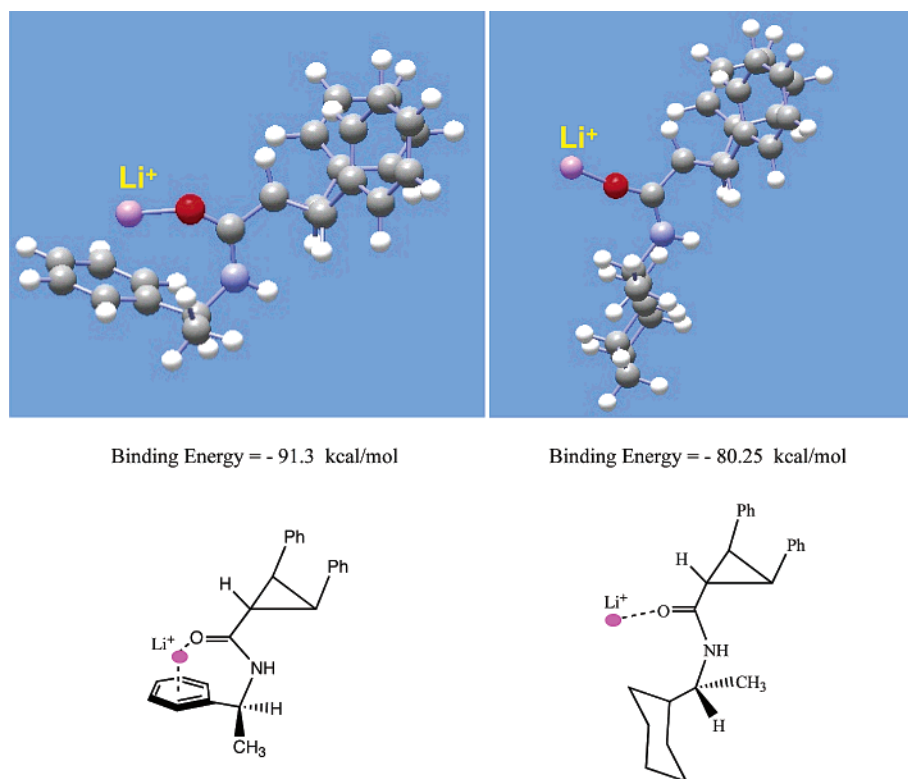
Reaction 1	de in LiY	85%	70%	29%	7%
Reaction 2	de in NaY	85%	88%	45%	45%
Reaction 3	de in NaY	62%	54%	22%	30%

could also be brought about by triplet sensitization with *para*-methoxyacetophenone as the triplet sensitizer. Three examples (**1a–c**) were investigated in this context.<sup>30</sup> As seen in Scheme 10, the de obtained under direct excitation and *para*-methoxyacetophenone sensitization were different; however, between the three examples no clear pattern emerges. Remarkably, within NaY, direct excitation of **1c** resulted in a 60% excess of diastereomer A, whereas upon triplet sensitization diastereomer B was favored in 59% excess. Since the mechanism of isomerization need not be the same from S<sub>1</sub> and T<sub>1</sub> states, the reactive state-dependent diastereomer switch is not totally unexpected. By investigating the time dependent photochemistry of the pure diastereomers of 2 $\alpha$ ,3 $\beta$ -diphenylcyclopropane-1 $\alpha$ -carboxamide of 1-phenyl ethylamine within zeolites, we have been able to establish that the isomerization from the S<sub>1</sub> state proceeds through a zwitterionic intermediate while that from the T<sub>1</sub> state proceeds via a triplet diradical (Scheme 11). The observed switch in the favored diastereomer in the case of **1c** (Scheme 10) under the two conditions is most likely the result of variations in the ability of the chiral auxiliary to stabilize the intermediates with different characters, i.e., diradical and zwitterionic. It is important to note that the alkali ion and reactive state-dependent diastereomer switch is not universal; only a few systems we investigated showed this phenomenon.

## A Few Experimental Tips

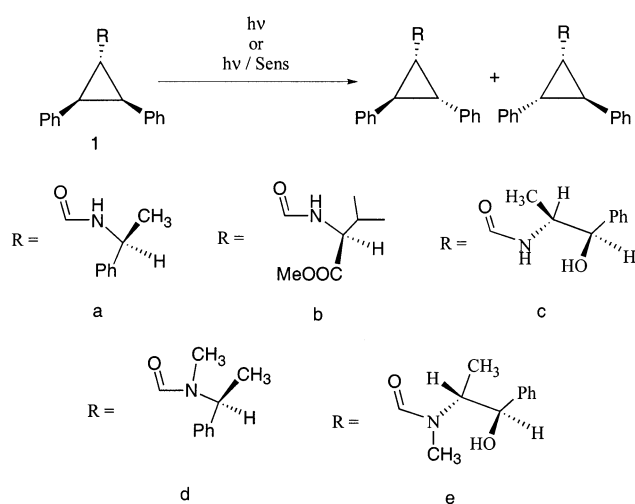
It would not be surprising if one had the feeling at this stage that asymmetric photochemistry within zeolites lacks predictability. While this may be true, we believe that there is enough information available for this strategy to be used generally. While quantitative ee's or de's are unlikely, modest enantio- and diastereoselectivities are a distinct possibility. For best results one should use "dry" conditions. That is, zeolites must be activated at ~500 °C prior to use, sample loading, and washing should be carried out with dry hexane and the reactant loaded zeolite should be dried using a vacuum line (>10<sup>-3</sup> Torr) prior to irradiation. During the chiral inductor strategy, one should try to achieve a loading level of one chiral inductor molecule per supercage. Chiral inducers that have worked well for us are ephedrine, pseudoephedrine, and norephedrine (Scheme 3).

The chiral auxiliary strategy generally works better than the chiral inductor approach. With some manipulation, de's in the range 70–90% could be achieved for most systems. The best chiral auxiliaries are derived from alcohols such as menthol, amines such as 1-phenylethylamine, amino alcohols such as ephedrine, pseudoephedrine, norephedrine, and amino acid derivatives such as valine methyl ester, alanine methyl ester, phenylalanine



**FIGURE 6.** RHF/3-21G optimized structures of  $\text{Li}^+$  bound  $2\beta,3\beta$ -diphenylcyclopropane-1 $\alpha$ -carboxamides of 1-phenylethylamine (a) and 1-cyclohexylethylamine (b). Binding affinities are included at the bottom of each structure.

### Scheme 10



compound	mode	LiY	NaY	KY
1a	Direct	80-B	28-A	14-A
1a	Sens	33-B	40-A	61-A
1b	Direct	83-B	21-A	80-A
1b	Sens	52-B	18-A	81-A
1c	Direct	25-B	60-A	13-A
1c	Sens	23-B	59-B	43-B
1d	Direct	17-A	30-A	20-A
1e	Direct	58-A	89-A	15-A

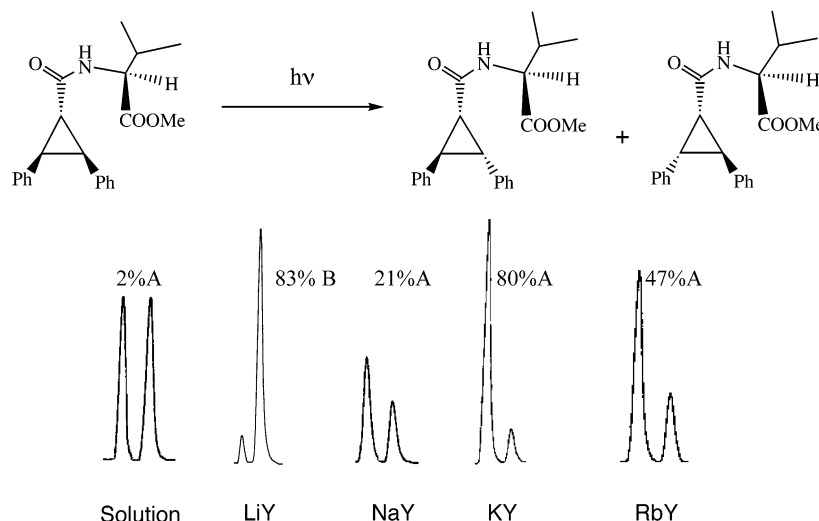
Sens. = *para*-methoxyacetophenone

methyl ester, and leucine methyl ester (Scheme 3). The suitability of a chiral inductor or chiral auxiliary for a particular study depends on its inertness under the given

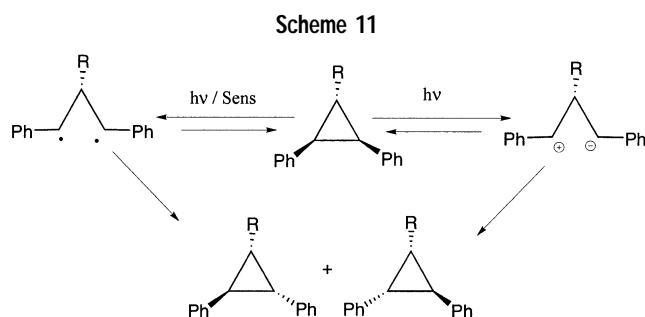
photochemical condition, its shape and size (in relation to that of the reactant molecule and the free volume of the zeolite cavity), and the nature of the interaction(s) that will develop between the chiral agent and the reactant molecule/transition state/reactive intermediate. One should recognize that no single chiral agent will be ideal for two different reactions or for structurally differing substrates undergoing the same reaction. These are inherent problems of chiral chemistry. Use of LiY, NaY, and KY is recommended over RbY and CsY. Best results are obtained with commercial Y zeolite (Si/Al: 2.4) and zeolites with higher or lower Si/Al ratio have yielded significantly lower ee's or de's in our hands. Irradiations should be conducted as a zeolite-hexane slurry, and products can be extracted with polar solvents such as acetonitrile, tetrahydrofuran, and diethyl ether.

## Summary

We have explored four strategies for asymmetric induction in organic photochemistry that derive their success from the use of a confined reaction cavity. In the first, more general approach, the achiral supercages of the zeolite are loaded with an optically active, photoinactive chiral inductor molecule, so that a reactant residing in the same cage senses the asymmetry created and reacts enantioselectively. This approach can in principle accommodate a wide variety of chiral inductors, reactants and zeolites of different internal shapes and sizes. In the second approach, the chirally modified reactant is included within an achiral zeolite. The cation and confined space coerce



**FIGURE 7.** GC traces of the trans diastereomers of the amide derived from L-valine methyl ester and 2,3,3-diphenylcyclopropane-1 $\alpha$ -carboxylic acid formed by irradiation of the corresponding cis isomer. Note the difference in the peaks being enhanced within LiY and KY.



Sens = *para*-methoxyacetophenone

the molecule to adopt a geometry in which there is an enhanced interaction between the chiral center and the site of reaction. This approach yields best results but requires the extra synthetic steps of linking and delinking the chiral auxiliary to the reactant molecule. In the third approach, a chirally modified reactant is included within a chirally modified zeolite. The generality of this approach is yet to be established. The fourth and potentially most promising approach limits the photoreaction to those cages that contain the achiral reactant and a chiral inductor. The methods described here complement the elegant work of Scheffer on the ionic chiral auxiliary approach in the crystalline state,<sup>6</sup> Toda and others<sup>8</sup> on the use of optically active host compounds as well as the work of the Weizmann Institute group and others on absolute asymmetric photoreactions in pure molecular crystals.<sup>4</sup>

Examination of the zeolite interior, in which the reactant molecule is held, suggests that the most likely factor responsible for the change in de or ee between solution and zeolite is the difference in conformational preference for the reactant molecules (and chiral inductors) in the two media. Changes in conformation are brought about by alkali ion–reactant interactions. In solution the influence of the alkali ions is wiped out by coordination of the cations to the solvent molecules. Cations present in zeolites, being only partially coordinated to the surface oxygens, are free to interact with

included guest molecules. X and Y zeolites contain high concentrations ( $\sim 5$  M) of exchangeable cations, making them resemble open structures of alkali salts with the zeolite framework as the anion. We believe that alkali ions present in zeolites can be cleverly exploited to control the photochemical behavior of organic molecules. The cost and environmentally benign nature of the medium and the “greenness” of the reagent (light) used to register the chirality of the product justify further exploration of zeolite-mediated asymmetric induction processes.

*We thank G. Sundarababu, R. J. Robbins, K. Ponchot, S. Karthik, T. Shichi, and Y. Yoshimi for their intellectual and experimental contributions. It is a pleasure to acknowledge the long-standing and valuable collaboration with J. R. Scheffer and his research group. Discussions with J. R. Scheffer have helped us shape the project at various stages of its development and his studies in the crystalline state have been a motivating force for ours in zeolites. The authors thank the National Science Foundation (CHE-9904187 and CHE-0212042) and the Petroleum Research Foundation for support of the research summarized here. V.R. thanks the Department of Organic Chemistry, Indian Institute of Science, Bangalore, for providing an ICOS Visiting professorship (October–November, 2002) during which time the manuscript was completed.*

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AR020269I