Photochemistry of a Tropolone Ether and 2,2-Dimethyl-1-(2*H*)-naphthalenones within a Zeolite: Enhanced Diastereoselectivity via Confinement

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In the past, chiral solvents, chiral auxiliaries, circularly polarized light, and chiral sensitizers have been utilized to conduct asymmetric photoreactions.[1] Of the many organized media, the most encouraging results have been provided by the crystalline state and solid host−guest assemblies.[2] In the context of asymmetric induction, zeolites offer advantages over other organized assemblies.[3,4] Zeolites can include a large number of different types of molecules, with the only limitation being that the dimensions of the guest must be less than the pore dimensions of the zeolite. In this communication, employing photorearrangements of the optically pure tropolone ether **1**[5] and 2,2-dimethyl-1-(2*H*)-naphthalenone derivatives **4**[6] as probe reactions, we illustrate the uniqueness of the confined space within a zeolite in effecting asymmetric induction during photochemical reactions. More importantly, the amplification of the effect of a chiral auxiliary by the zeolite medium suggests that the confinement strategy is effective even when the chiral auxiliary fails to act in isotropic solution medium.

Scheme 1

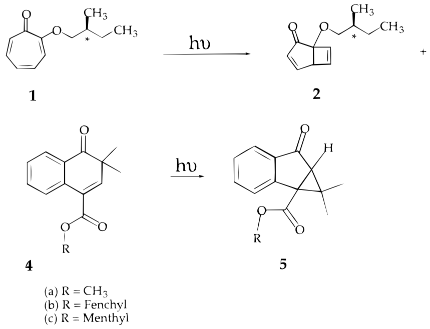

Table 1. Diastereoselectivity during the Irradiation of (*S*)-Tropolone-2-methylbutyl Ether

s. no.	medium[a]	chiral inductor[b]	loading level of tropolone ether	diastereom. excess[c,d]
1	NaY		0.28	51 (A)
2	NaY		0.56	41 (A)
3	NaY (22 °C)		0.83	28 (A)
4	NaY (0 °C)		0.28	59 (A)
5	NaY (−20 °C)		0.28	68 (A)
6	KY		0.28	21 (A)
7	RbY		0.28	12 (A)
8	CsY		0.28	17 (B)
9	NaY	(−)-ephedrine (1)	0.28	90 (A)
10	NaY	(+)-ephedrine (1)	0.28	70 (B)
11	NaY	(−)-norephedrine (1)	0.28	92 (A)
12	NaY	(+)-norephedrine (1)	0.28	70 (B)
13	silica gel	(−)-ephedrine		0
14	hexane	(−)-ephedrine		0

[a] All irradiations unless indicated otherwise were conducted at 22 °C. Note rows 4 and 5. [b] Loading level of the chiral inductor (average number of chiral inductor per supercage) indicated in the bracket, note rows 9 to 12. [c] The first of the two diastereomeric peaks on the HPLC was assigned to be the A isomer. [d] Conversion was estimated by GC using dodecane as the calibrant, ∼30%.

Irradiation of a hexane solution of (*S*)-tropolone-2-methylbutyl ether **1** results in a electrocyclization to yield the bicyclo[3.2.0] product, **2** (Scheme 1). Prolonged irradiation leads to **3** via a secondary rearrangement process.[5a] The ratio of **2:3** varied with the duration of irradiation. For example, the ratio was ∼24:1 at 10 min and 7:1 at 45 min of irradiation. Most samples were irradiated for ∼20 min and studies focused on the diastereoselectivity in **2**. Irradiation in solution yields a 1:1 diastereomeric mixture of **2**. Clearly, in solution, the presence of the chiral auxiliary (note the alkyl chain in **1**) has no influence on the product stereochemistry. On the other hand, the same molecule included within “dry” NaY zeolite and irradiated as a hexane slurry gave **2** in ∼51% diastereomeric excess (d.e.) at room temperature (Table 1), which increased to ∼68% at −20 °C.[8] As shown in the table, the cation plays a very important role; the extent of diastereoselectivity is inversely dependent on the size of the cation. This is the first clear indication of the cation controlling both the extent and the direction (A or B) of diastereoselectivity (note that in CsY the isomer that is enhanced has switched from A to B). The importance of the zeolite cation is also evident when one recognizes that the d.e. obtained on silica gel surface is zero (Table 1). The ability to improve the diastereoselectivity from zero in solution to 68% (at −20 °C) using an *achiral* zeolite as a reaction medium is remarkable. We propose that it is the small “active reaction cavity studded with cations” that controls the behavior of the reacting molecule.

In zeolite chemistry, one suffers from a lack of knowledge concerning the distribution of guests within the zeolite. The

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[8] The detailed experimental procedure is provided as part of the Supporting Information.

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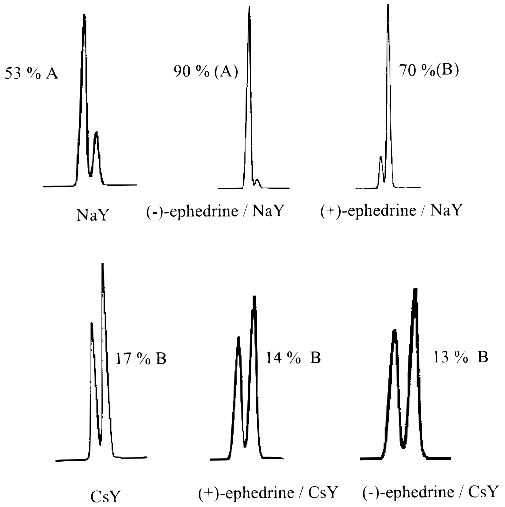

Figure 1. GC traces (Supelco β-Dex 325 column) of the product **2** upon irradiation of **1** in chirally modified NaY and CsY zeolites. The first peak on the trace is termed A. The percentage disteromeric excess and the isomer that is enhanced are marked on each trace.

distribution of guest molecules included within NaY supercages is varied. Singly and doubly occupied supercages as well as cages with no guest molecules may be encountered within the same zeolite. Because the extent of diastereoselectivity in the first two types of cages may not be the same, and because the distribution of the above three types of cages varies with the loading level of the guest, one predicts that the measured d.e. may depend on the loading level (the average number of molecules per cage). Consistent with this expectation, the d.e. decreases with increasing loading level (Table 1), suggesting that the cages containing two molecules give rise to lower diastereoselectivity.

The most exciting result was obtained when tropolone ether **1** was irradiated within a chirally modified NaY zeolite. The zeolite was modified by adsorbing chiral inductors such as optically pure ephedrine on its interior surfaces. When a chirally modifed NaY zeolite (coadsorbed with (−) ephedrine or (−) norephedrine) was used as the medium for irradiation of **1**, the photoproduct diastereomer A was obtained in ~90% d.e (Figure 1).[8] The significance of this result is apparent when one recognizes that irradiation of **1** in solution or on a silica surface in the presence of optically pure ephedrine or norephedrine gave a 1:1 diastereomeric mixture. To our knowledge, the diastereomeric excesses obtained in this study are the highest thus far reported for any photochemical reaction that shows zero d.e. in solution, in a noncrystalline medium.

A comparison of the behavior of **1** within chirally modified NaY and CsY zeolites (coadsorbed with the optical antipodes of ephedrine and norephedrine) suggests that to achieve asymmetric induction, the chiral inductor and **1** must be adjacent. While in NaY the isomer that is enhanced is reversed upon replacing the chiral inductor with its enantiomer, within CsY the d.e. as well as the isomer that is enhanced remain the same independent of the absolute configuration of the chiral inductor (Figure 1). The lack of influence by chiral inductors within CsY, we believe, is due to space limitations within the supercage for occupation by both **1** and the chiral inductor.[9]

An insight into the process of asymmetric induction within chirally modified NaY zeolite is obtained by comparing the d.e. in the presence of the antipodes of ephedrine and norephedrine. As shown in Table 1 the maximum d.e. obtained with the (+) isomer is ~70%, a 20% decrease from the corresponding (−) isomer (90%). We believe that the reactions occurring in singly and doubly (reactant and chiral inductor) occupied cages contribute to significant differences in d.e. When **1** is alone in a cage it cyclizes to give the A isomer in 53% d.e. The A isomer is also favored by the (−) isomers of ephedrine and norephedrine resulting in enhanced d.e. Thus the 90% d.e. is a sum of cyclization in cages where the reactant **1** is alone and with (−) ephedrine as well. On the other hand, when **1** is placed next to (+) ephedrine within a supercage it yields the B isomer preferentially. The 20% difference in d.e. observed between the optical antipodes of the chiral inductors most likely is the result of reactions from cages in which **1** is present alone.[10]

The generality of the "diastereoselectivity via confinement" strategy is illustrated with the photochemical behavior of 2,2-dimethyl-1-(2*H*)-naphthalenone-3-carboxylic acid esters (**4**, Scheme 1). The molecule is made asymmetric by introducing chiral auxiliaries (fenchyl and menthyl groups) as the ester functionality. Irradiation of the (1*R*)-endo-(+) fenchyl ester **4b** in hexane and on silica gel gave the product **5b** in <5% d.e. Similar irradiation of the (−) menthyl ester **4c** in hexane, on silica gel, highly silaceous Y zeolite, and MCM-41 gave the product **5c** in d.e. of <5%. Remarkably, photolysis of hexane slurries of **4b** and **4c** included in achiral NaY (dry) gave **5b** and **5c** in 57% and 47% d.e. (B isomer favored), respectively. As in the case of tropolone ether **1**, the extent of d.e. depends on the cation. Since **5b** and **5c** were too large to fit into a zeolite cage with chiral inductors, further improvements on the d.e. could not be made by using chirally modified zeolites.

The confined space offered by the zeolite supercage forces a reactant and the chiral inductor to interact intimately to yield diastereomerically enriched products. Owing to the transitory nature of the reaction cavity in solution, such close interactions are less likely in isotropic solvent media. The power of the chiral auxiliary strategy can be tremendously enhanced within the confined spaces of a zeolite.

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Supporting Information Available: Experimental details, comparative HPLC traces (figure) of the photoproducts upon irradiation of **1** in cation exchanged (Li^+, Na^+, K^+, Rb^+ and Cs^+) Y zeolites and a tabulation of results of irradiation of 2,2-dimethyl-1-(2*H*)-naphthalenone-3-carboxylic acid esters in zeolites (PDF). These materiala are available free of charge via the Internet at "http://pubs.acs.org."

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(10) A referee has suggested that the difference in d.e. between the (+) and (−) chiral inductors might arise due to differences in chiral recognition of the chiral reactant by the two chiral inductors. Such a difference could alter the distribution pattern of singly and doubly (reactant and chiral inductor) occupied cages and thereby the observed d.e. At this stage we have no way of eliminating this possibility.