ORGANIC LETTERS

2000
Vol. 2, No. 2
119−121

# Chirally Modified Zeolites as Reaction Media: Photochemistry of an Achiral Tropolone Ether

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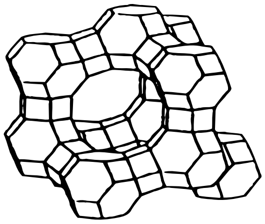
**Received October 26, 1999**

## ABSTRACT



**Zeolites modified with chiral inductors serve as media for performing chiral induction during photochemical reactions of organic molecules. The photochemical behavior of achiral tropolone ethyl phenyl ether illustrates this unique feature of a zeolite.**

During the past decade numerous elegant and extremely efficient chiral induction strategies have been designed for ground-state reactions. Asymmetric photochemical reactions have not, however, enjoyed the same level of attention or success.[1] In the past, chiral solvents, circularly polarized light, and chiral sensitizers have been utilized to conduct enantioselective photoreactions in solution. The highest chiral induction achieved by any of these approaches (excluding the approach in which a chiral auxiliary is covalently linked to the reactant)[2] at ambient temperature and pressure has been ∼50% (2−10% enantiomeric excesses being more common in photochemical reactions under the above conditions).[1,3] A recent successful approach in this context has been to make use of confined media such as inclusion complexes and crystals.[4] Although crystalline solids and host−guest assemblies have been useful in conducting enantioselective photoreactions, their general applicability is limited. We believe zeolites offer a remedy to this limitation. 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.[5] To establish the utility of zeolites as media for asymmetric induction in photochemistry, we have investigated the photoelectrocyclization of tropolone ethyl phenyl ether **1** (Scheme 1).[6] We have obtained enantiomeric excesses (ee) of up to 78% of the primary photoproduct **2** at room

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(3) Most successful chiral induction strategies have made use of chiral auxiliaries (see ref 2). Photosensitization of (*Z*)-cyclooctene with chiral aromatic sensitizers has been shown to afford its *E*-isomer in 50% ee: Inoue, Y., Yamasaki, N., Yokayama, T., Tai, A. *J. Org. Chem.* **1993**, *58*, 1011.

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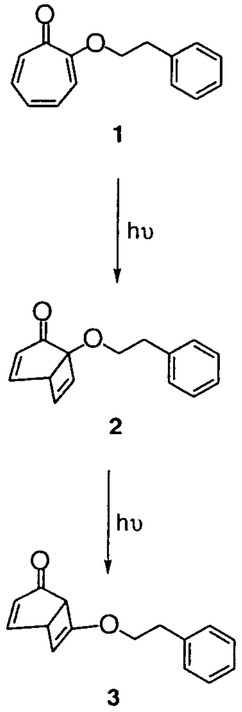
10.1021/ol9903335 CCC: $19.00

**Scheme 1**



temperature in NaY (as medium) and with optically pure ephedrine as the coadsorbent. The ee achieved in this study is the highest thus far reported for a photoproduct from an achiral reactant in a noncrystalline medium.[1,3]

Upon excitation, the achiral tropolone ethyl phenyl ether **1** undergoes a four $\pi$-electron disrotatory ring closure to yield the chiral bicyclo[3.2.0] product **2**. Prolonged irradiation leads to **3** via a secondary rearrangement process (Scheme 1).[6] In our experiments with short irradiation times (10 min), the ratio of **2**:**3** was 25 and all our studies focused on the enantioselectivity of the formation of **2**. Irradiation of a hexane−methylene chloride solution of **1** yields racemic **2**. Remarkably, however, irradiation (450 W medium-pressure mercury lamp, Pyrex filter, 10 min) of a hexane slurry of compound **1** adsorbed on “dry” NaY along with the chiral inductor (−)-ephedrine gave product **2** (conversion ∼50% based on GC calibration) enantiomerically enriched to the extent of 78%.[7] The extent of ee was dependent on the duration of irradiation. For example, the ee decreased from 78% to 68% when the irradiation time was increased to 45 min (ratio of **2**:**3** = 10).[8] The use of (+)-ephedrine afforded the optical antipode of photoproduct **2**, indicating that the system is well behaved (Figure 1). The possibility that the observed enantioselectivity may be due to an experimental artifact was eliminated by including a racemic mixture of **2** within ephedrine containing NaY and showing that the extracted **2** is still racemic. A comparison of the results observed in isotropic solution (hexane−methylene chloride), on the surface of silica gel, and in the zeolite clearly brings out the importance of the zeolite to the process of chiral induction (Figure 1). In both former cases, ephedrine did not bring about any enantioselectivity. The unique aspect of the current study is the ability of an achiral medium (NaY) to bring about enantioselectivity in the reaction of an *achiral* compound. The chiral inductor that induces enantioselectivity is only loosely held by the zeolite and is not linked to the reactant through covalent or ionic bonds.

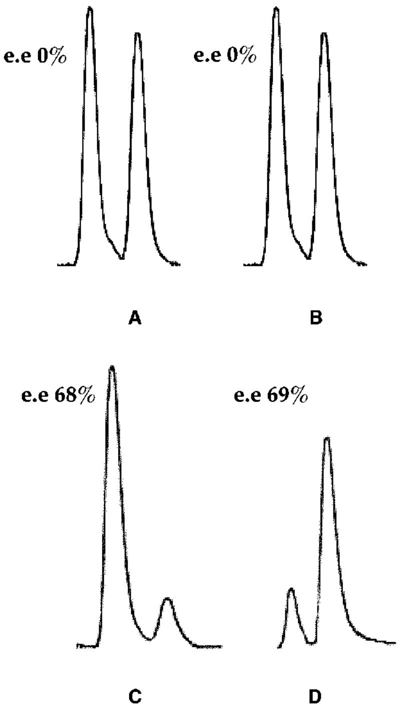


**Figure 1.** HPLC traces (the region corresponding to the product **2**) of the irradiated samples of tropolone ethyl phenyl ether and ephedrine in various media: A, hexane−methylene chloride and (−)-ephedrine; B, silica gel and (−)-ephedrine; C, NaY and (−)-ephedrine; and D, NaY and (+)-ephedrine. The % ee is shown on each trace.

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[7] The chiral inductor (30 mg, 182 mM) was dissolved in a mixture of methylene chloride and hexane (1:4). NaY (300 mg) dried at 500 °C was added to the above. The slurry was stirred for 8 h, filtered, and washed. The zeolite modified with the chiral inductor was dried under vacuum and added to **1** (4 mg, 20 mM) dissolved in methylene chloride−hexane (1:4). The slurry was stirred for 12 h, filtered, and washed. After the chiral inductor and the tropolone ether were loaded, the zeolite sample was dried under vacuum at 60 °C. The resulting zeolite sample complexed with the chiral inductor and the tropolone ether was irradiated in hexane for 10 min. The products were extracted from the zeolite with diethyl ether. The chiral auxiliary was removed from the product mixture before evaluating the enantiomeric excess. In a typical run, the loading levels (number of molecules per supercage) of ephedrine and **1** within NaY were 1 and 0.1, respectively. Efforts to increase the loading level of ephedrine higher than this level resulted in exclusion of **1** from the zeolite. In all runs prior to and following irradiation, the hexane layer was checked for the absence of **1** by GC. This ensured that the photoreaction occurs on the surface of the zeolite.

[8] The variation in ee with respect to the length of irradiation could be due to several factors. For example, the reaction could occur from different sites with different efficiencies. The contribution of these sites to the total ee may vary with time. As indicated in Scheme 1, as a result of seconadry photoreaction product **3** is formed from **2**. As expected, longer irradiation times result in higher amounts of **3**. Conversion of **2** to **3** could occur enantioselectively, resulting in a time dependence of the ee of isolated **2**. Presently we have not identified the origin of the variation in ee with the length of irradiation.

The model we have adopted to understand the role of the zeolite in the enantioselective process is shown in Figure 2.

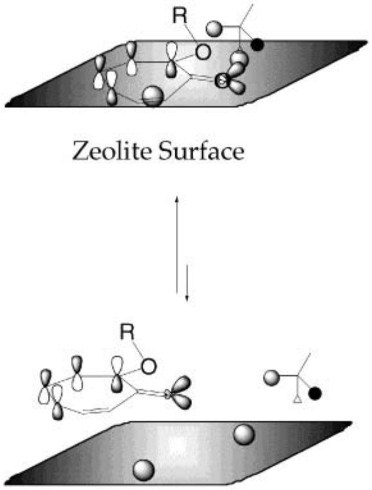

**Figure 2.** Model for chiral induction by a chiral inductor adsorbed on a zeolite surface. Adsorption of reactant tropolone alkyl ether and a chiral inductor on a zeolite surface is shown. Spheres on the surface represent cations present in zeolites, and the chiral inductor is shown in the form of a carbon with four different substituents (dark sphere, shaded sphere, a triangle, and a stick). Figure on the top represents the state in which the reactant and the chiral inductor are adsorbed and on the bottom the desorbed state.

The basic premise is the need for a "three-point interaction" between the prochiral reactant and the chiral inductor.[9] Two of the three interactions that we visualize in the case of ephedrine and **1** are the hydrogen bonding between the carbonyl and ether oxygens of **1** and the hydroxyl and amino hydrogens of ephedrine. The third interaction, we believe, occurs through the surface. Both **1** and ephedrine are most likely held on the zeolite surface via cation$-\pi$ interactions.[10] Consistent with this model, chiral inductors with a single functional group such as borneol, menthol, bornylamine, and methylbenzylamine gave no chiral induction. On the other hand, chiral inductors with three functionalities such as ephedrine, norephedrine, pseudoephedrine, and diethyl tartrate gave ee values above 30%.

The hydrogen-bonding interactions between tropolone ether **1** and the chiral inductor alone are insufficient to bring about enantioselectivity. Despite the fact that such interactions very likely persist even on a silica surface, no ee was obtained in this medium (Figure 1). We conclude that the surface of silica is unable to prevent the dissociation of the ephedrine−**1** complex (Figure 2). A feature that distinguishes the zeolite surface from that of silica is the presence of cations. Our postulate that the cations present on the surface of a zeolite play a crucial role in inducing chirality is supported by the following important observation: for the same chiral inductor (ephedrine) the extent of ee obtained in **2** decreased with the decrease in charge density of the cation: NaY, 68%; KY, 11%; and RbY, 2%. This behavior can be rationalized on the basis of the reported relationship between the binding energy of cations with aromatics and alkenes and the size of the cations; smaller cations bind more strongly.[11] If the cation$-\pi$ interaction is indeed important, one would expect a decrease in ee when such an interaction is turned off. This can be done by introducing water into the zeolite. The ee did in fact decrease from 68 to 17% when a "wet" sample of NaY−**1**−(−)ephedrine was irradiated.[12] Under "wet" conditions, in addition to the decreased ee, the enantiomer present in excess shifted from A to B. The origin of this effect is presently not understood. The remarkable effect of water observed in this study highlights the importance of using "dry" conditions to obtain the maximum influence of a zeolite.[13]

In summary, we have documented a strategy for asymmetric induction in organic photochemistry that derives its success from the use of a confined active reaction cavity.[14] In the absence of readily available chiral zeolites, our approach has made use of a chirally modified zeolite. The achiral supercages of the zeolite are loaded with an optically active and non-light-absorbing guest molecule, so that a reactant residing in the cage senses the asymmetric field created within the zeolite and reacts enantioselectively. This approach can, in principle, accommodate a wide variety of chiral inductors, reactants, and zeolites. The technique reported here complements the crystalline ionic chiral auxiliary approach being developed in the laboratory of one of the authors.[15]

**Acknowledgment.** V.R. thanks the National Science Foundation (CHE-9904187) and the Petroleum Research Foundation for financial support. J.R.S. thanks the Natural Sciences and Engineering Research Council of Canada for support of the program.

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[12] The sample prepared as described in ref 7 was exposed to laboratory humidity by placing it on the pan of a Mettler balance. The weight increase indicated the adsorption of water. The water-included sample did not displace the chiral inductor and **1** to the external surface. This was evident from the analysis of the hexane wash. For routine "wet" experiments, samples were prepared as in ref 7 but were not dried under vacuum, and all operations were performed on a laboratory benchtop instead of a drybox.

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