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Asymmetrically Modified Zeolite As a Medium For Enantioselective Photoreactions: Reactions From Spin Forbidden Excited States

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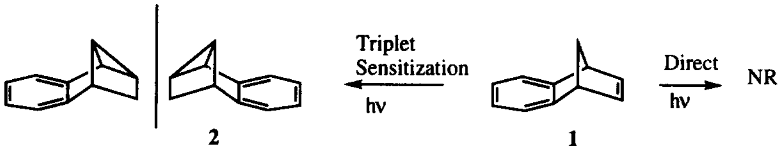
Moderate enantioslectivity has been achieved on two photochemical reactions that involve molecules reacting from spin forbidden excited states. Zeolite is found to be a unique medium in this context. © 1997 Elsevier Science Ltd.

A multitude of elegant and extremely efficient chiral induction strategies have been designed for numerous thermal reactions during the last decade.[1] There are considerably less number of examples of photochemical asymmetric inductions.[2] A recent successful approach in this context has been to make use of a confined medium such as inclusion complexes and crystals. Two approaches have been used to achieve chiral induction in the crystalline state. In one, from the Weizmann Institute Group, the achiral reactant is crystallized into a chiral space group.[3] The chances of this happening are limited and therefore this approach is less general. In the second approach, due to Scheffer, an ionic chiral auxiliary is used to create an asymmetric environment.[4] This limits the approach to those acidic molecules that form crystallizable salts with chiral amines or *vice versa*. Zeolites, when functionalized with chiral inductors, can be more general with respect to the types of molecules that can be made to undergo enantioselective photoreactions. Another moderately successful approach has been to make use of organic hosts that contain chiral centers (deoxycholic acid, cyclodextrin, 1,6-bis(o-chlorophenyl)-1,6-diphenyl-2,4-diyne-1,6-diol) or crystallize in a chiral space group (urea).[5] The success of this approach is limited to guests that can form solid solutions with the host without disturbing the host's macro-structure. Zeolites, on the other hand, 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. Thus while crystalline and host–guest assemblies have been useful to conduct enantioselective photoreactions, their general applicability has been limited. We believe that zeolites offer a solution to this limitation.[6]

The lack of availability of chiral zeolites has led us to explore the utility of chiral inductors included in zeolites to effect enantioselectivity.[7] Thus far no strategy has been reported for achieving enantioselectivity during photoreactions that involves a reactive excited state that can not be reached by direct light excitation. We report below two strategies towards this end. The first strategy utilizes a heavy cation to induce transition from an excited singlet to the reactive triplet state.[8] In the second approach the classic sensitization technique is used.[9]

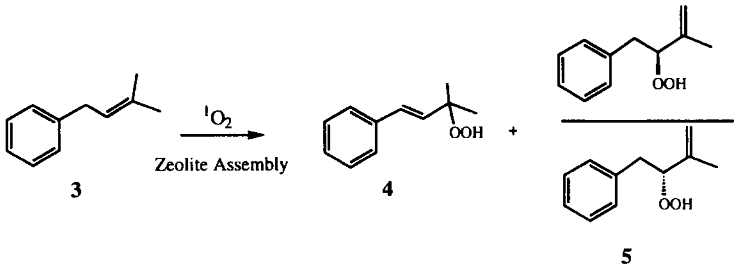
The first example, involves the well known rearrangement of benzonorbornadiene (**1**) to benzonorbonene (**2**).[10] This system was chosen because not only does this rearrangement occur only via the triplet excited state (direct irradiation does not give any products), but additionally it produces a chiral photoproduct (Scheme 1). In order to examine the feasibility of inducing enantioselectivity during the rearrangement of **1** to **2** it was necessary to generate the triplet state of **1**. As anticipated, irradiation (48 hours, 450W medium pressure mercury lamp, Pyrex tube) of **1** included in NaY did not yield any products. Previous experiments have shown that the production of triplet state is triggered within zeolites exchanged with heavy cations.[8] Indeed, photolysis of **1** within TlY provided **2**. The reaction was clean and efficient; 40% conversion was achieved within 30 minutes of irradiation.



Scheme 1

The asymmetric induction of the product benzonorbornene was attempted with (+) ephedrine as the chiral inductor. The experiment consisted of irradiating a hexane (5 mL) slurry of TlY (300 mg) included with benzonorbornadiene and (+) ephedrine in 1:5 ratio.[11] The irradiation resulted in a complex mixture of products. Although no detailed investigation was carried out to probe the reasons for such a complex product mixture, quenching of the excited state of benzonorbornadiene by the amine, ephedrine, seemed like an obvious possibility. To alleviate this complication, ephedrine hydrochloride was used as the chiral inductor. Indeed, a remarkable result was obtained when ephedrine hydrochloride was used instead of free amine ephedrine as the chiral agent. (+) Ephedrine hydrochloride was introduced into TlY by an exchange process.[12] The exchange level was maintained such that every supercage on an average contained one molecule of ephedrine hydrochloride. Irradiation of benzonorbornadiene included into the ephedrine hydrochloride exchanged TlY gave benzonorbornene as the single product. HPLC analysis showed that the product obtained was enriched in one of the optical isomers (e.e. ~14%). This is the first example in which two strategies (heavy cation effect and chiral induction) have been coupled to obtain a modest enantioselectivity on a photoreaction that originates from a state that can not be reached by direct light excitation. This, when viewed in the context of our failure to achieve enantioselectivity during solution irradiation is important.

The second example is the well know 'ene' reaction. A supramolecular structure of an olefin, a thiazine dye (thionin) and oxygen was assembled within the zeolite framework. Excitation of the dye (450 W mercury lamp with filter to cut off the light below 500 nm), followed by energy transfer to ground state oxygen, results in the spin forbidden species, singlet oxygen. In this assembly, singlet oxygen has been shown to undergo a highly regioselective hydroperoxidation reaction (Scheme 2).[13] For example, oxidation of olefin **3** while in solution gives two hydroperoxides **4** and **5** in a 1:1 ratio, within NaY a single hydroperoxide **5** was obtained. Having achieved regioslective oxidation of the olefin **3**, our interest turned to the possibility of generating predominantly one enantiomer of **5**. The olefin **3** was placed in a slurry of hexane and dry dye-exchanged zeolite (NaY/thionin). (+)-ψ-Ephedrine hydrochloride was added to the hexane slurry and irradiation took place while stirring and bubbling with oxygen.[14] A modest enantioselectivity (~15% e.e) was observed in the presence of (+)-ψ-ephedrine hydrochloride. As in the previous example, the free amine of ephedrine not only failed to bring about enantioselectivity but also quenched the oxidation reaction.



Scheme 2

Approaches to achieving enantioslectivity during photoreactions that involve spin forbidden states are provided in this report. Although the enantioselectively realized in the two systems examined is at best modest, it is encouraging that it is not zero. In spite of low enantioselectivity, these experiments serve as a basis for further exploration to establish ground rules for achieving enantioselectivity during phototransformations within zeolites. We believe that further experiments are necessary in order to uncover the underlying principles of chiral induction within the modified zeolite matrix. These principles will help in developing a model which in turn will help design, enhance predictions of the outcome of future enantioselective photochemical reactions.

Acknowledgment

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11. Ephedrine (25mg, 0.15M) was loaded into TlY (300mg) from CH_2Cl_2 : hexane (1:4). This complex was filtered and vac. dried ($<10^{-3}$ Torr). Benzonorbornadiene (5mg, 0.04mM) was introduced into this complex by stirring in hexane. The resulting complex was filtered, washed with hexane and irradiated (after degassing) as a slurry in hexane (4mL) for 2-3h (conversion ~ 80%). The hexane portion was removed and the product was extracted with diethyl ether (15mL) and analyzed by HPLC (Column: Chiralcel OJ; Eluent: hexane; Analysis wavelength: 270 nm).
12. Ephedrine hydrochloride (160mg, 0.79 M) and the zeolite (2.4 g) were stirred in water (120 mL) for 18h at 65° C. After filtering, this complex was stirred again with ephedrine hydrochloride (160mg, 0.79 M) in water (120 mL) for 18h at 65° C. The chiral auxillary/zeolite complex (300 mg) was dried under vacuum (<3 mTorr) for 12h. The substrate benzonorbornadiene (5mg, 0.04M) was stirred with the dried chiral auxillary/zeolite complex in hexane (5mL) for 12h. The resulting complex was filtered and washed with minimum amount of hexane (~2mL) and irradiated (after degassing) as a slurry in hexane (4mL) for 2-3h . The hexane portion was removed and the product was extracted with diethyl ether (15mL) and analyzed by HPLC .
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14. Dry NaY/thionin (308 mg) was suspended in 9 mL of hexane. Chiral inductor (+)-ψ-ephedrine hydrochloride (~9 mg) was added and slurry was stirred at room temperature for one hour. 1-Methyl-4-phenyl-2-butene (0.1 mL) was added to stirring slurry. After an additional hour of stirring reaction mixture was placed in irradiation chamber, oxygen gas was bubbled through as irradiation took place. After four hours, the irradiation was stopped. Triphenylphospine was added with diethyl ether. The reaction mixture was allowed to stir for 1 hour to reduce and extract the oxidation products. Analysis was done by GC with a β-Dex chirasil column. The optimum separation condition was found to be an isotherm at 100° C. Assignments were made based on the behavior of the authentic alcohol. The retention times for the chiral 2° alcohols were 11.30 and 11.75 minutes.

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