Enantioselective photoelectrocyclization within zeolites: tropolone methyl ether in chirally modified NaY

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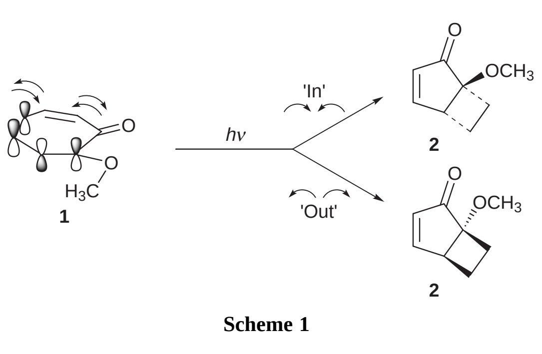
Tropolone methyl ether, included within chirally modified Y zeolite, upon irradiation yields a product of 4e electrocyclization in *ca.* 40% ee.

During the past decade, many elegant and efficient chiral induction strategies have been developed for a variety of thermal reactions.[1] There are, however, considerably fewer examples of asymmetric induction in photochemical transformations.[2] A recent successful approach in this latter context has been to make use of confined media such as inclusion complexes and crystals.[3–5] Zeolites offer advantages over other confined media in that they can be used for catalysis,[6] and our long range objective is to prepare reusable zeolite-based materials for asymmetric catalysis of photochemical processes. First, however, we must establish the feasibility of employing zeolite matrices for non-catalytic asymmetric induction, and here we illustrate our strategy with the well known photocyclization of α-tropolone methyl ether **1** as an example.[7,8]

Upon exposure to UV light, α-tropolone methyl ether undergoes 4π-electron disrotatory electrocyclic ring closure to yield the bicyclic photoisomer **2** (Scheme 1).[7] Irradiation in solution results in a racemic mixture as the result of an equal probability of ‘in’ and ‘out’ rotation as illustrated in Scheme 1. An obvious approach to control the mode of cyclization is to adsorb compound **1** on a surface, since under these conditions, it is possible that the surface could interfere with one of the two modes of disrotation. Even then racemic products would be expected because compound **1** should not show any preference for adsorption from either enantiotopic face. On the other hand, when the surface is chiral, preferential adsorption from one of the two enantiotopic faces is likely, and under such conditions, one might anticipate enantioselectivity in the formation of photoproduct **2**. This is illustrated in Fig. 1. Enantioselectivity has indeed been achieved in this system by this strategy and the results are presented below. The medium we have used to achieve the desired goal is a zeolite. In the absence of readily available chiral zeolites, we have created an asymmetric environment within a zeolite by the adsorption of chiral organic molecules.[9]

A typical experimental procedure consisted of stirring tropolone methyl ether (0.01 M) and a chiral inductor (0.1 M) with activated NaY (300 mg) in dichloromethane–hexane (1 : 4) for 12 h at room temperature. The zeolite containing both the reactant and a chiral inductor was collected by filtration, washed with an excess of hexane and irradiated (450 W medium pressure mercury lamp, Pyrex filter) as a hexane slurry for 2 h. Sample handling was carried out under laboratory conditions (temperature = 20 °C, humidity 55%). The product was extracted with dichloromethane and analyzed by chiral GC (Supelco β-DEX column). The results are presented in Table 1.



Scheme 1

Independent control experiments established that the numbers reported here are not skewed due to preferential adsorption of one enantiomer of the product within the chirally modified zeolite. The system is well behaved in the sense that, as expected, the optical antipode of the chiral inductor always gave the opposite enantiomer of the product (compare entries 2 and 7; 8 and 9; and 10 and 11 in Table 1). The need for a chiral inductor was clear, since irradiation of compound **1** in unmodified NaY gave racemic **2**. The zeolite is also essential as shown by the fact that none of the chiral inductors listed in Table 1 led to any enantioselectivity when photolyzed with compound **1** in solution (dichloromethane–hexane).

Examination of Table 1 reveals that not all chiral inductors are equally effective. Those that contain only one functional group (entries 15–18, Table 1) gave low or negligible chiral induction; more effective were those that contain both an amine and an alcohol functionality, and of these, norephedrine consistently gave good results. As a result, several additional experiments were carried out with norephedrine as the chiral inductor. In one set of experiments (entries 1, 2, 5–7, Table 1), the effect of changing the nature the alkali metal cation present within the zeolite was explored. While no clear trend was evident, this did indicate that NaY and RbY give the best results. In a second set of experiments (entries 2–4), the effect of temperature was briefly examined, which showed that −20 °C is optimum; above room temperature the enantiomeric excess (ee) also decreases and becomes zero at 60 °C.

At low conversions (< 10%, NaY, room temp.), the ee was relatively low (*ca.* 20%), which may be the result of reaction occurring faster at unencumbered sites with no chiral inductor

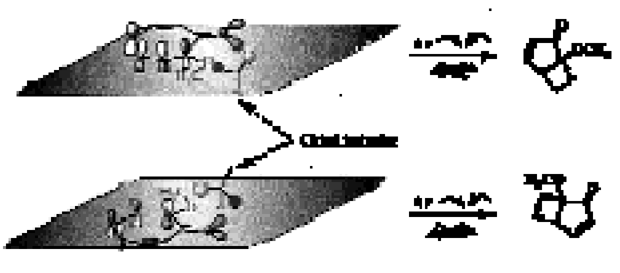


Fig. 1 Influence of a chiral agent on the mode of adsorption of tropolone methyl ether on a surface. On the top surface interactions are between methoxy and dark grey substituent, and carbonyl and light grey substituent. On the bottom surface they are reversed. Assuming one pair of interactions is preferred over the other, tropolone methyl ether will prefer to adsorb in this mode over the other.

Table 1 Dependence of enantiomeric excess on chiral inductor, zeolite and temperature[a–c]

Entry	Chiral auxiliary/zeolite/temp.[d]	ee (%)	Favored isomer[e]
1	(−)-Norephedrine/LiY	15	A
2	(−)-Norephedrine/NaY	35	A
3	(−)-Norephedrine/NaY/−20 °C	50	A
4	(−)-Norephedrine/NaY/−40 °C	31	A
5	(−)-Norephedrine/KY	31	A
6	(−)-Norephedrine/RbY	40	A
7	(−)-Norephedrine/CsY	20	A
8	(+)-Norephedrine/NaY	34	B
9	(−)-Ephedrine (anhydrous)/NaY	7	B
10	(+)-Ephedrine (hemihydrate)/NaY	5	A
11	(−)-Ephedrine hydrochloride/NaY	5	B
12	(+)-Ephedrine hydrochloride/NaY	5	A
13	(+)-Prolinol/NaY	6	B
14	L-Proline *tert*-butyl ester/NaY	7	B
15	(+)-Bornylamine/NaY	2	B
16	(−)-Camphorquinone-3-oxime/NaY	2	B
17	(−)-Menthol/NaY	< 1	—
18	(−)-Borneol/NaY	< 1	—

[a] All irradiations were done on samples that contained 1 mg of tropolone methyl ether and 25 mg of the chiral inductor in 200 mg of dry NaY. [b] Samples were irradiated for 2 h and conversions were within 50%. [c] Tropolone methyl ether and the chiral inductor were co-induced within NaY by three methods. In the first tropolone methyl ether and the chiral inductor were added simultaneously to a suspension of NaY and stirred, in the second the tropolone methyl ether was included into NaY and to the dried sample of tropolone methyl ether-NaY, the chiral inductor was added and stirred. In the third method the sequence in the second approach was reversed. [d] Unless indicated otherwise, the temperature of the reaction was 22 °C. [e] The peak with shorter retention time is arbitrarily assigned to be isomer A.

nearby. Beyond this point, the ee increased and reached a plateau of *ca.* 35% ee at 30% conversion; conversions beyond 50% were not attempted owing to secondary photoreactions of product **2**.[7] Values reported in Table 1 correspond to conversions in the range 35–50%.

From the results presented in Table 1, we tentatively conclude that a three point interaction between the reactant molecule, the chiral inductor and the zeolite interior is necessary to induce preferential adsorption of **1** from a single prochiral face. The fact that monofunctional chiral inductors fail to yield significant enantioselectivity supports this idea. The recognition points in the case of norephedrine are most likely the hydroxyl, amino and aryl groups of the inductor, the cations of the zeolite and the carbonyl and methoxy groups of tropolone methyl ether. The cations present in the zeolite help to anchor the chiral inductor to the interior surface. The overall arrangement as we visualize it is illustrated in Fig. 2,[10] which shows the hydrogen bonding between norephedrine and tropolone methyl ether as well as the electrostatic interaction between the cation on the zeolite and the phenyl group of norephedrine. This view reveals that one of the faces of tropolone methyl ether is fairly open while the other is encumbered by the zeolite surface. Such an arrangement is expected to favor one of the two modes of disrotatory cyclization. The fact that 100% enantioselectivity is not observed suggests that not all molecules are present in this idealized arrangement.

The results presented here provide encouragement for further exploration of chiral induction within modified zeolites.[11] For the first time, the phenomenon of asymmetric induction within a zeolite appears to be amenable to a simple model, a model that can be used to plan future experiments exploring the utility of zeolites as media for enantioselective photoreactions. Such research is under way in our laboratories.

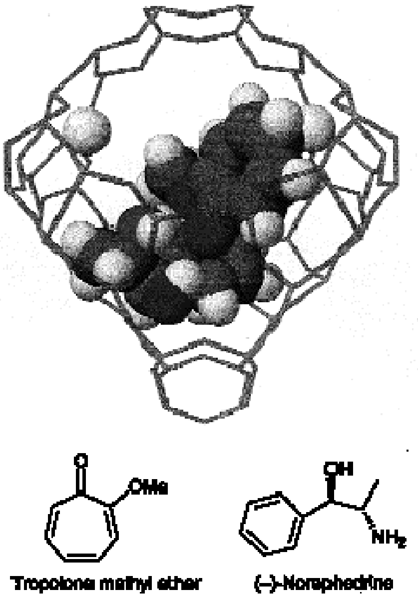


Fig. 2 Tropolone methyl ether and norephedrine included within a supercage of a NaY zeolite. The model shows hydrogen bonding interactions between the reactant and the chiral inductor and electrostatic interaction between the zeolitic cation and the chiral inductor. The cations help to anchor the chiral inductor and the chiral inductor helps to adsorb tropolone methyl ether preferentially from one enantiotopic face.

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10 Calculations were performed on a CAChe STEREO Worksystem using the standard software programs, including molecular mechanics employing MM2 parameters.

11 Very recently we found that ee could be improved to 65% when the samples are very dry. Experiments are underway to examine the effect of water on the extent of ee.

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