

# Zeolite as a host for chiral induction

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**By employing a strategy that involves the use of chirally modified zeolite as the reaction medium, modest enantioselectivity is achieved during photolysis of two ketones capable of undergoing the Norrish–Yang reaction.**

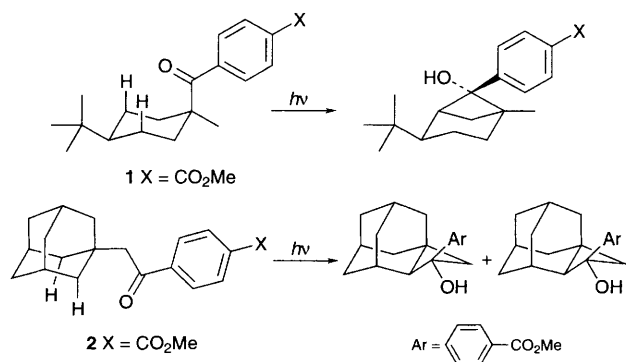
In the past, chiral solvents, chiral auxiliaries, circularly polarized light and chiral sensitizers have been utilized to conduct enantioselective photoreactions.<sup>1</sup> Organized media have also been used for such purposes, and of these, the crystalline state and solid host–guest assemblies have provided the most encouraging results.<sup>2</sup> We have established recently that zeolites, when modified with chiral inductors such as ephedrine, yield photoproducts with low to moderate enantiomeric excess.<sup>3</sup> The results presented here indicate that the free volume of the cavity in which the reaction occurs and the relative sizes and shapes of the products are important parameters that determine enantioselectivity during photoproduct formation within zeolites.

Two ketones **1** and **2**, capable of undergoing the Norrish–Yang reaction upon direct excitation, have been chosen as probes (Scheme 1).<sup>4,5</sup> Both ketones yield only cyclobutanols as the type II product. Since it was clear from our previous studies that ephedrine is by far the best chiral inductor and that it is most effective when the occupancy number is one, the present investigation utilized ephedrine as the co-guest at a loading level of one molecule per supercage.<sup>3</sup> Photoreactions were investigated within the supercages of faujasites, which are large enough to accommodate simultaneously both ephedrine and either one of the ketones **1** and **2** (Fig. 1). Of the two ketones chosen for investigation, **1** gives only one cyclobutanol diastereomer, both in solution and within zeolites. Since this photoreaction is devoid of any complication, we have used this ketone to probe the effect of the supercage free volume on enantioselectivity. Ketone **2** gives both cyclobutanol diastereomers, and since these two isomers have different molecular size and shape, we have used this ketone to establish the effect of the product molecular volume on the enantioselectivity and diastereoselectivity.

The experimental procedure consisted of stirring known amounts of ephedrine and the activated (*ca.* 470 °C) zeolite (X or Y) in hexane, followed by washing with excess hexane and

drying under reduced pressure ( $10^{-4}$  Torr). A known amount of the ketone (**1** or **2**) was included into these functionalized zeolites by stirring them together in hexane. Filtration and thorough washing with hexane gave zeolites loaded with ephedrine and the ketone. These were irradiated (*ca.* 15 min) in hexane as a slurry. The absence of ephedrine or ketone in the hexane washings was established by GC and by recording UV absorption spectra. Following irradiation, the products were extracted with ether and analysed on HPLC columns (Chiralcel OD or OJ). Enantioselectivity was calculated on the basis of analyses of the sample on both columns. Mass balances were excellent (>90%). Spectral data for the product cyclobutanols agreed well with the reported data.<sup>4,5</sup>

Results obtained with ketone **1** are presented in Scheme 2. The most important observations relates to the nature of the enantiomer that is enhanced in the two zeolites Na X and Na Y. While in Na Y, (–)-ephedrine showed enantioselectivity in favour of the (+) isomer, the same chiral inductor favoured, although to a much lesser extent, the (–)-isomer in Na X.† A similar reversal is also seen when (+)-ephedrine is used as the chiral inductor. We attribute this remarkable effect to the differences in supercage free volume between Na X and Na Y and to the number of type III cations. We speculate that the larger dimension of the supercages in Na X (852 Å<sup>3</sup>) compared to that in Na Y (827 Å<sup>3</sup>) favours an orientation between the reactant and the chiral inductor which is different from that in Na Y. Supporting this interpretation are the results obtained with K X (800 Å<sup>3</sup>), Rb X (770 Å<sup>3</sup>) and Cs X (732 Å<sup>3</sup>).<sup>6</sup> When the supercage free volume was reduced until it was the same as or smaller than that of Na Y by exchanging Na X with different

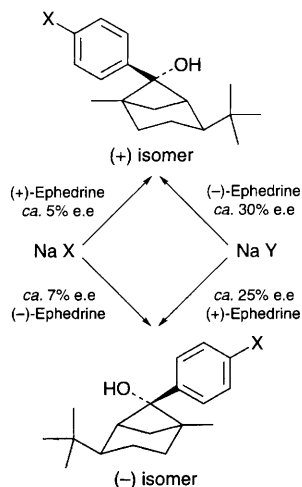


**Fig. 1** Molecular model diagram of ephedrine and ketone **1** within the supercage of X or Y zeolite. Guest structures have been minimized but the guest–host assembly has not. The figure shows that both the ephedrine and ketone can fit within zeolite cages.

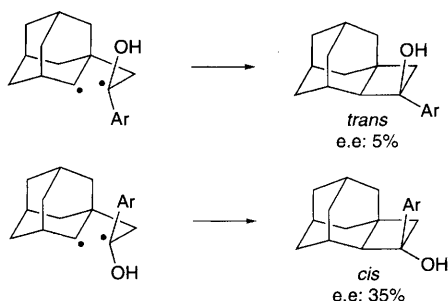
cations such as K<sup>+</sup>, Rb<sup>+</sup> and Cs<sup>+</sup>, the enantioselectivity was found to be the same as that obtained in Na Y.

Unlike **1**, ketone **2** gives both cyclobutanol diastereomers upon irradiation. The ratio of the two isomers depends greatly on the medium in which the irradiation is conducted. For example, in hexane solution the ratio of *trans*- to *cis*-cyclobutanol is 2.8, whereas within Na Y zeolite the ratio is 1. Such a dependence is not unprecedented.<sup>7</sup> For example, we have observed earlier with a number of aralkyl ketones that the relative yield of *cis*-cyclobutanol increases within Na X and Na Y zeolites with respect to isotropic solvents (e.g. *trans*- to *cis*-cyclobutanol ratio for octanophenone: hexane, 3.1; methanol, 2.5; Na X, 1.0 and Na Y, 1.0; dodecanophenone: hexane, 2.8; methanol, 1.7; Na X, 0.6 and Na Y, 0.7).<sup>8</sup> Such variations have been attributed to the differences in size and shape of the two isomers and the influence of the supercage free volume on the partitioning of the 1,4-diradical intermediates resulting from  $\gamma$ -hydrogen abstraction. *cis*-Cyclobutanol, with the aryl and adamantyl groups on the same side, is expected to be spherical in shape whereas the *trans* isomer is expected to be elliptical. The 1,4-diradical precursors of the two isomers will also have closely similar shapes and sizes. We propose, therefore, that the elliptically shaped *trans*-cyclobutanol and its precursor diradical require two cages, whereas the *cis*-cyclobutanol and its precursor diradical can fit within a single cage. On the basis of such reasoning, one would expect a difference in enantioselectivity between the two diastereomeric cyclobutanols within chiral modified zeolites. *cis*-Cyclobutanol and its precursor, which fit well within a single cage, should be subjected to a greater influence by the chiral inductor ephedrine than *trans*-cyclobutanol and its precursor, which are accommodated within two cages.

The above prediction is borne out experimentally. Photolysis of 1-adamantyl-*p*-carbomethoxyacetophenone within Na Y containing one (–)-ephedrine molecule per supercage gave the *trans*- and *cis*-cyclobutanols in the ratio 1.4. A slight increase in



Scheme 2 Results of photolysis of ketone **1** in Na Y and Na X



Scheme 3 Photolysis of ketone **2** within Na Y–ephedrine

the *trans* isomer is once again consistent with the decrease in free volume of the cage due to the presence of ephedrine.<sup>‡</sup> Most interestingly, the optical induction properties of the two cyclobutanols are not the same. While *cis*-cyclobutanol is formed in moderate enantioselectivity, the *trans* isomer is formed with very low enantioselectivity. The results are summarized in Scheme 3. As would be expected, with the change in ephedrine from the (–) to the (+) isomer, the opposite enantiomer is enhanced. Neither of the optical isomers of the two cyclobutanols were selectively included/retained within zeolites. This was checked by including and re-extracting racemic-cyclobutanols from Na Y.

In summary we have shown with two examples that the extent and sense of enantioselectivity in the Norrish–Yang reaction within zeolites depend on how well the reactant, the type II diradicals and the products fit within a supercage. A tight fit between the reactant and the chiral inductor may be a prerequisite to achieve significant enantioselectivity. At the moment, the enantioselectivity achieved by the strategy of utilizing chirally modified zeolites as the supramolecular assembly is low. However, information gained from studies such as the one presented here is expected to help refine the system to achieve higher enantioselectivity.

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## Footnotes

† The first enantiomeric peak on the HPLC trace (Chiralcel OJ or OD) is laevorotatory and the second peak is dextrorotatory. Peaks were identified by measuring the optical rotation of the pure enantiomers, obtained by photolysis in the crystalline state (ref. 3). However, the absolute configurations of the isomers are unknown at this time.

‡ An increase in *trans*- to *cis*-cyclobutanol ratio has been observed when the supercage free volume is decreased by exchanging Na<sup>+</sup> by Cs<sup>+</sup> (see ref. 8).

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