

Supramolecular Control of Photochemical Enantiomeric Induction and Radical Pair Recombination in Zeolites

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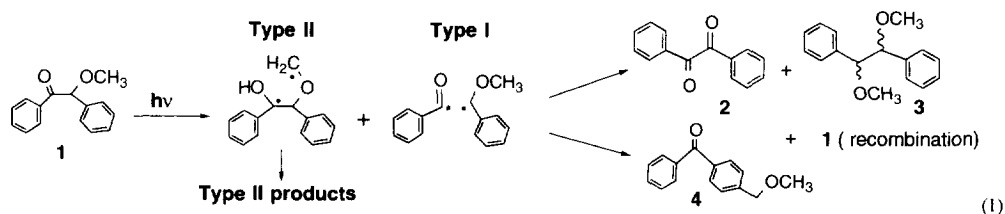
Abstract: Geminate radical pairs are formed from the α -photocleavage of aryl ketones within the supercage of zeolites which has been modified with chiral guest molecules. Herein, we report the supramolecular structure and dynamic control of both the enantiomeric selectivity and probability of the recombination of the radical pairs. © 1997 Elsevier Science Ltd.

Introduction.

Photochemical enantiomerically selective reactions have been attempted utilizing circularly polarized light, chiral photosensitizers, chiral solvents and chiral auxiliaries.¹ Among these, the most enantioselective reactions were achieved in the crystalline state and with solid host-guest assemblies.² Ramamurthy and Scheffer have demonstrated that Norrish-Type II photoreactions, when conducted in zeolites modified with chiral guest molecules, can yield cyclobutanols with low to moderate enantiomeric excess.³ Stereospecificity in photochemical reactions involving *geminate radical pairs*, although attractive as a synthetic strategy in principle, is very rare in practice. The free radicals produced by geminate pair separation are incapable of retaining configuration at the carbon radical center during the time scale of diffusional excursions between the creation of the pair and the combination reactions of free radicals. Thus, in order to develop general synthetic approaches for efficient enantioselective reactions involving geminate radical pairs, at least two features of the supramolecular structure dynamics of the pair must be controlled: (a) the separation of the geminate pair must be restrained so that geminate recombination has a high probability of occurrence and (b) the geminate recombination must be made enantiomerically selective. In this report, we present the results of the supramolecular control of both enantiomeric selectivity and the probability of recombination of geminate radical pairs produced by the α -photocleavage of aryl ketones included in zeolites.

Results and Discussion

I. Enantiomeric Induction in the Photolysis of (\pm) Benzoin Methyl Ether (1). The mechanism of photolysis of aryl ketones in zeolites appears to follow the same paradigm for primary photochemical processes which are observed in solution. The differences in products observed in solution *vs* zeolites are explained in terms of conformational influences of the supramolecular structure of the zeolite/ketone complex. For example, **1** (eq. 1) produces geminate radical pairs via Type I cleavage and biradicals via Type II hydrogen abstraction in both homogeneous solution and zeolites. In homogeneous solutions, the geminate radical pairs separate to create free radicals which after subsequent combination form products **2** (23%) and **3** (70 %) and, presumably, some **1**.⁴ In zeolites, the free radical, combination products are strongly suppressed and the geminate rearrangement product **4** (eq. 1) is formed in yields of up to 70%.⁵ The reported results are "silent" on the extent of geminate radical recombination to regenerate **1**. In the absence of any chiral influences, there is no stereoselectivity expected for regeneration of **1** by geminate radical pair recombination. Therefore, the observation of enantiomeric excess in **1** when photolyzed in zeolites in the presence of chiral molecules would be a demonstration of both recombination of geminate radical pairs and the ability of a chiral supramolecular structure to induce enantiomeric selectivity during the geminate recombination process.



The supramolecular zeolite/ketone structure consists of the host zeolite (framework, supercage and exchangeable cations), guest substrate (**1**) and invited guests (chiral molecules such as diethyl tartrate or ephedrine). The amount of chiral guest was selected to achieve an occupancy number of *ca.* 1 ($\langle S \rangle \sim 1$).⁶ Samples were prepared by stirring ephedrine (25 mg) or diethyl tartrate (21 μ L) in hexane (10 mL) with zeolite NaY (200 mg, activated at 500 °C) for 3 hours. The samples were dried with a stream of nitrogen, and then washed with excess hexane. Next, a known amount of **1** (5 mg, hexane solution, 10 mL) was loaded into the chirally modified zeolite by stirring overnight. Drying and washing were repeated as previously described. The zeolites loaded with both inductor and ketone were irradiated for 20 minutes in a hexane slurry (10 mL).⁷ The absence of the chiral guest molecule or **1** in the hexane washings was established by either GC or UV. Following irradiation, hexane was evaporated by using a stream of nitrogen, and the products were extracted with ether (20 mL) after dissolving the zeolite framework in aqueous HCl solution (0.8N, 10 mL). At this point, conversion based on the disappearance of **1** was measured ($\sim 50\%$) by GC using an internal standard. Compound **1** was isolated from the reaction mixture with preparatory TLC (hexane:ether, 7:3) and analyzed for enantiomeric excess with HPLC (Chiracel OD-H column, hexane:isopropanol 9:1) and GC (Chiracel-Dex CB column, isothermal at 125 °C). Control experiments demonstrated that acid does not induce any racemization of optically active **1**. The results are summarized in Table 1.

Table 1. Enantiomeric Excesses (ee%) obtained from Photolysis of **1** in Zeolite NaY with Chiral Guest Molecules.

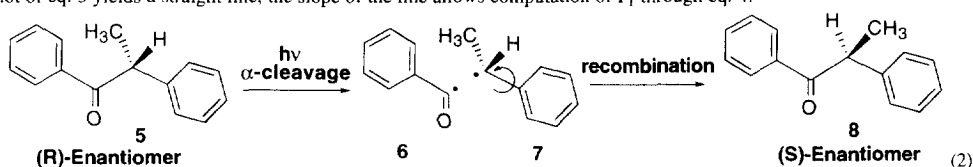
| Zeolite | Chiral Guest | ee% ^a |
|---------|----------------------|------------------|
| NaY | (-) Ephedrine | 3.3 (1, S) |
| | (+) Ephedrine | 4.9 (1, R) |
| | (D)-Diethyl-Tartrate | 9.2 (1, S) |
| | (L)-Diethyl-Tartrate | 8.4 (1, R) |

^a The assignment of stereochemistry was confirmed by comparison with authentic enantiomers. Enantiomeric excess was measured and confirmed independently with both HPLC and GC at least twice from separate samples. Experimental error is $\sim 10\%$. In each case 5 mg of **1** was complexed with 200 mg of NaY. As it would be expected, the excess optical antipode is switched when the chiral molecule is changed from (-) to (+) or (D) to (L). In the case of (+) Ephedrine, the hemihydrate salt was used.

From the various combinations of zeolites and conditions explored, definitive examples of enantiomeric excess is only found in NaY. For example, within the experimental error, there is no measurable enantiomeric selectivity when **1** is photolyzed in LiY or KY containing ephedrine or diethyl tartrate under conditions identical to those reported in Table 1. Although the percent enantiomeric excesses are low at this juncture, the results demonstrate that photochemical enantiomeric selectivity through geminate radical pair recombination in zeolites is possible. This is an important result since a wide range of features of the zeolite/ketone supramolecular structure may be varied systematically in order to optimize the efficiency of enantiomeric control. Indeed, the sensitivity of enantioselection to the exchangeable cation is an indication of the sensitivity of the system to subtle features of the supramolecular structure. For example, Ramamurthy and Scheffer have shown in a recent study that a tight fit between the reactant and chiral inductor could be a prerequisite to achieve significant enantioselectivity.⁸

II. Enhancement of Geminate Pair Recombination Probability in Zeolites. There are two possible reasons for the low enantiomeric selectivity achieved in the photolysis of **1** in a chiral zeolite host: (a) the geminate radical pair may be

a zeolite cage occupied by a chiral guest, but its ability to induce enantiomeric selection is low. The first possibility requires the generation of the geminate radical pair in the same supercage with a guest chiral molecule. This issue will be the subject of future investigations. The second possibility is related to the probability of recombination (P_r) of the geminate radical pair. It has been demonstrated that the value of P_r may be determined experimentally by measuring the extent of racemization of an optically active ketone as a function of conversion of the ketone.⁹ Here the idea is that efficient enantiomeric induction by a chiral molecule may be achieved best in systems for which there is a high probability of geminate radical pair return. Thus, in exploring systems for optimization, knowledge of P_r is valuable. Because of its previous use to measure P_r in micellar systems,¹⁰ the optically active ketone **5** (eq. 2) was selected to determine P_r in the parent zeolite systems.¹¹ Photolysis of **5** leads to the formation of a geminate radical pair (**6** and **7**, eq. 2), which can either recombine to form the original enantiomer or undergo inversion and recombine to form the opposite enantiomer **8**. From this model, the value of P_r is simply obtained by measuring the extent of racemization (A/A_0) as a function of conversion of the ketone (f).¹² The enantiomeric excess (A/A_0) and conversion of ketone **5** were measured by chiral GC. If a plot of eq. 3 yields a straight line, the slope of the line allows computation of P_r through eq. 4.



$$\log (A/A_0) = S [\log (1-f)] \quad (3)$$

$$S = P_r / (1 - P_r) \quad (4)$$

Figure 1(a) shows that $\log(A/A_0)$ varies linearly with $\log(1-f)$. Figure 1(b) shows the influence of occupancy number on the value of P_r for the photolysis of **5** in NaY. There are two salient results: (a) the value of P_r in zeolite is much higher than the value for solution and (b) the value of P_r increases monotonically with increasing occupancy number. These results are straightforward to interpret. First, the zeolite cage serves as a constrained space which discourages diffusional separation of geminate radical pairs and encourages geminate recombination; second, when the loading is increased the internal surface is occupied with ketone and solvent molecules which reduce the available free volume for diffusional separation and thus, probability of recombination is increased. Figure 1(c) shows the influence of exchangeable cation on the value of P_r . The value of P_r is highest for NaY. This result may be related to the observations of Table 1, where measurable enantiomeric selectivity was found for NaY, but not for LiY or KY.

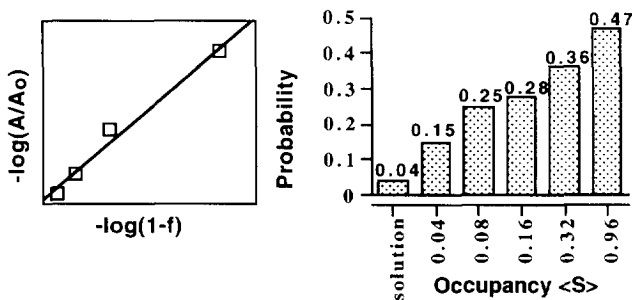


Figure 1(a). Representative plot of racemization of **5** as a function of conversion in NaY at $\langle S \rangle \geq 0.08$.

Figure 1(b). Probability of recombination of **5** in NaY at various loadings and solution. Experimental error is ~10%.

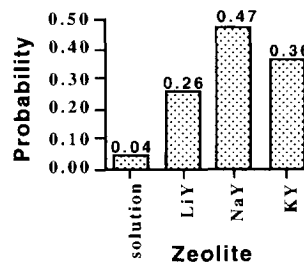


Figure 1(c). Probability of recombination of **5** at $\langle S \rangle = 0.96$ in various zeolites and solution. Experimental error is ~10%.

Conclusion

Enantiomeric selectivity can be achieved when guest radical pairs recombine within chirally modified supercages of zeolites. The results speak (a) to the sensitivity of recombination and enantiomeric selectivity to subtle features of the supramolecular structure and dynamics and (b) to our limited knowledge of the details of "supramolecular structure-reactivity" relationships for molecule/zeolite complexes.

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References and Notes

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6. The occupancy number, which is presented as $\langle S \rangle$, is defined as the average number of guests molecules per supercage.
7. The output of a 450-W Hanovia medium pressure mercury lamp and pyrex filter were used for the irradiation of samples. The samples were stirred during photolysis.
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