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LETTERS

The influence of chiral auxiliaries is enhanced within zeolites

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Abstract

Zeolites significantly enhance the influence of chiral auxiliaries during photochemical reactions. The generality of this phenomenon has been tested with three independent examples. Chiral auxiliaries that lead to 1:1 mixtures of diastereomers in solution give products in up to 80% diastereomeric excess in the presence of faujasite type zeolites. © 2000 Elsevier Science Ltd. All rights reserved.

Asymmetric induction continues to be one of the main concerns of organic chemists. While the basic rules of asymmetric induction have been reasonably well established for ground state reactions, the same is not true of photochemical processes.[1] Short excited state lifetimes and low activation energies for reactions in the excited state make manipulation of the diastereomeric transition states difficult. Nevertheless impressive asymmetric induction has been achieved with photochemical reactions in the solid state.[2] In contrast, asymmetric induction of photochemical reactions in solution continues to be inefficient under ambient conditions. Among the various approaches employed to achieve asymmetric induction in solution phase photoreactions, the ‘chiral auxiliary’ strategy (wherein the chiral auxiliary is covalently linked to the reactant molecule) has been most promising.[1,3] By this method, diastereomeric excesses (des) above 90% have been achieved during addition of olefins to excited enones and other carbonyl and thiocarbonyl compounds in solution.[1,3] We recently showed that moderate levels of asymmetric induction can be obtained by using zeolites as the reaction medium through the ‘chiral inductor’ approach as well. In this method the chiral inductor is not linked to the reactant molecule.[4] For example, photocyclization of tropolone-2-phenylethyl ether within ephedrine-modified NaY gave the bicyclo[3.2.0] product in 69% enantiomeric excess (ee), while in hexane/methylene chloride solution in the presence of ephedrine, a racemic mixture was obtained. This observation

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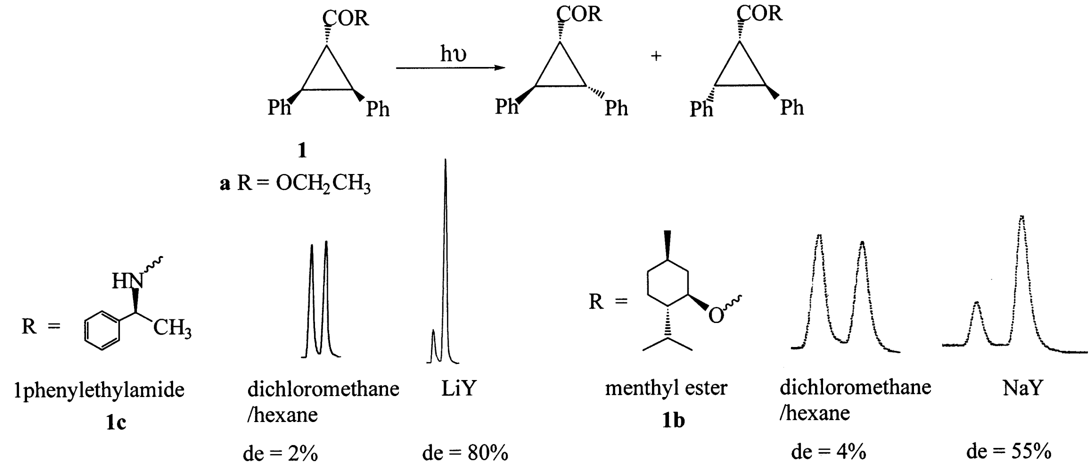
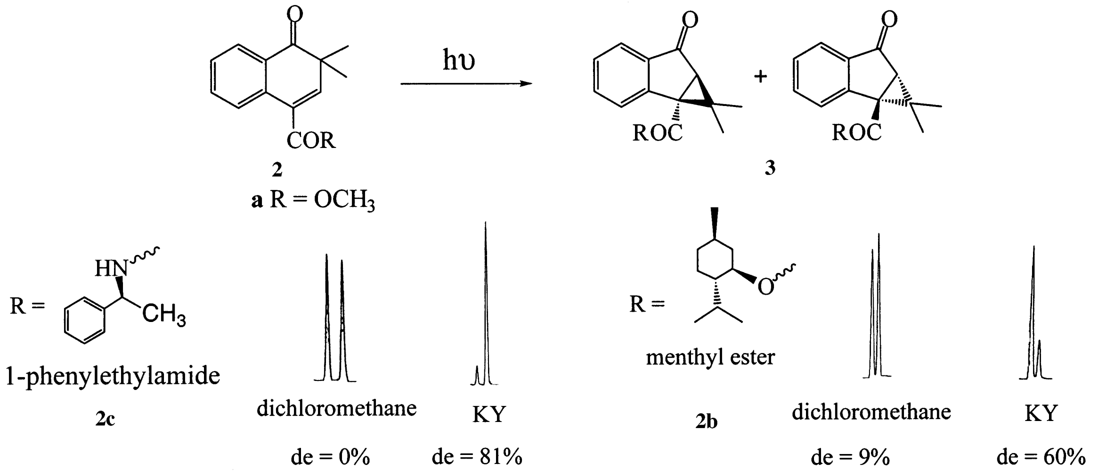
suggested to us that zeolites could also be used to enhance the influence of covalent chiral auxiliaries during photochemical reactions. We have tested this possibility with three independent photochemical reactions and confirmed that, compared to isotropic solution, zeolites significantly enhance the influence of a covalent chiral auxiliary. The results of this study are presented in this letter.

1,2-Diphenylcyclopropane has played an important role in the development of methods of asymmetric induction in photochemical reactions.[5] The highest ee thus far reported during the photoconversion of the optically inactive *cis*-1,2-diphenylcyclopropane to the chiral *trans*-isomer has been ~10%. *cis*-1,2-Diphenylcyclopropane was not suitable for the present study since it is not appreciably converted to the *trans*-isomer upon irradiation in MY zeolites.[6] Therefore we selected 2β,3β-diphenylcyclopropane-1α-carboxylic acid derivatives as the model (Scheme 1). Both esters and amides were used. When ethyl ester **1a** included in zeolite NaY was irradiated (450W medium pressure mercury lamp, quartz test tube), the corresponding *trans*-isomer was formed within 90 minutes (conversion: 5–20%) as a racemic mixture.[7] Of the various chiral auxiliaries investigated, the results obtained with the menthyl ester **1b** and 1-phenylethyl amide **1c** are described in detail. Irradiation of **1b** and **1c** in dichloromethane/hexane solution gave the corresponding *trans*-isomers in 4 and 2% de, respectively. In startling contrast, when ester **1b** and amide **1c** were included in zeolites and irradiated as solids or hexane slurries, the corresponding *trans*-isomers were formed in much higher des. The maximum de for the menthyl ester **1b** was obtained in NaY (LiY: 50; NaY: 55; KY: 30 and RbY: 22%) and for 1-phenylethylamide **1c** in LiY (LiY: 80; NaY: 28; KY: 14 and RbY: 5%). The GC traces of the solution and zeolite irradiations of menthyl ester **1b** and 1-phenylethylamide **1c** reproduced in Scheme 1 illustrate the remarkable control zeolites exert on the chiral induction process.



Scheme 1. The GC traces for the solution and zeolite irradiations are shown (since the chart speed was faster, the GC traces for **1b** appear broader). For conditions of analysis see reference 7. The first peak from the left is identified as A

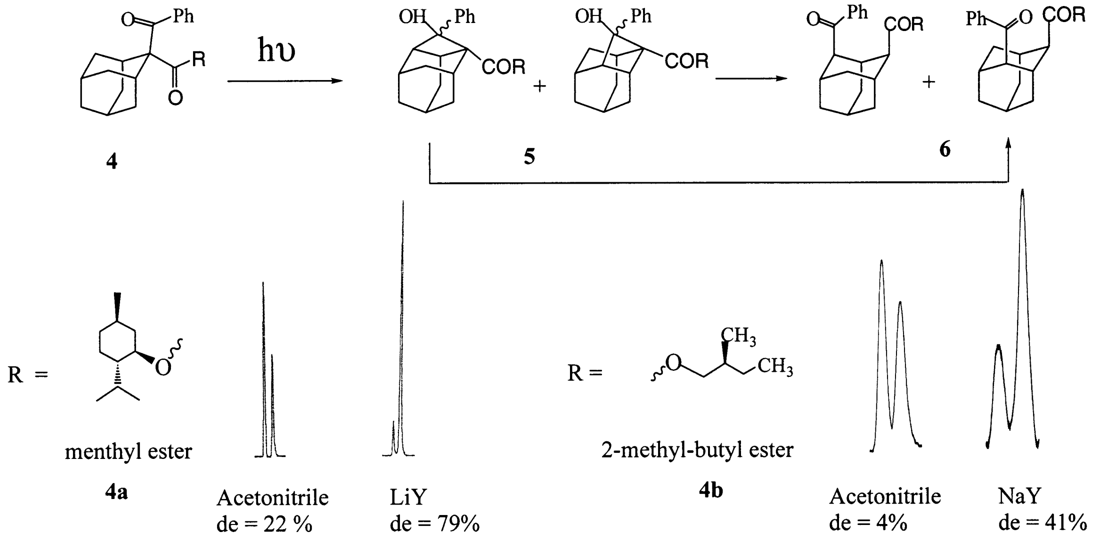
The second photoreaction we have examined is the rearrangement of the achiral 1,2-dihydro-2,2′-dimethylnaphthalenone derivative **2** to the chiral benzobicyclo[3.1.0]hexenone derivative **3** (Scheme 2).[8] As in the case of ester **1a**, the chiral inductors menthol and 1-phenylethylamine failed to give significant ee in product **3a** on irradiation of the methyl ester **2a** in their presence



Scheme 2. The GC traces for the solution and zeolite irradiations are shown. For conditions of analysis see reference 7

in dichloromethane solution (<5%) or within NaY. However, when these inductors were covalently linked to compound **2** as menthyl ester **2b** and 1-phenylethylamide **2c**, a dramatic influence on the photorearrangement process within zeolites was observed (450W medium pressure mercury lamp, uranyl filter; 5 minutes; 30% conversion). Within zeolite KY the des were 60 and 81%, and once again the extent of de depended on the cation (**2b**: LiY: 12; NaY: 46; KY: 60; and RbY: 48%; **2c**: LiY: 49; NaY: 59; KY: 81; and RbY: 57%).

The third reaction we have explored is the Norrish–Yang reaction of 2-benzoyladamantane-2-carboxylic acid derivative **4** (Scheme 3).[9] The chiral auxiliaries were introduced as ester functionalities. Irradiation of the menthyl ester **4a** and 2-methylbutyl ester **4b** in acetonitrile gave **6** as the final product. Phenyl ketone **6** is formed via cyclobutanol **5**, a product of a



Scheme 3. The GC and HPLC traces for the solution and zeolite irradiations are shown. For conditions of analysis see reference 7

Norrish–Yang reaction. Owing to the photolabile nature of product **6**, conversions beyond 15% resulted in secondary products. Therefore all irradiations were limited to ~10% conversion. Irradiation of **4a** in acetonitrile resulted in **6a** with 22% de. When the same molecule was included in LiY and irradiated (450W medium pressure mercury lamp, Pyrex filter; 5 minutes; 10% conversion), product **6a** was formed in 79% de. It is important to note that the isomers enhanced in LiY and in acetonitrile differ (Scheme 3). The extent of de varied with the cation: NaY:62%; and KY:17%. The ester of *S*-(−)-2-methylbutan-1-ol **4b** behaved similarly, resulting in product **6b** whose de was significantly improved compared to that observed in acetonitrile solution (LiY:37; NaY:41 KY:29; RbY:28%).

The three examples provided here, along with our recent report on tropolone-2-methylbutyl ether (de in solution 0% and in NaY 51%)[10] convincingly demonstrate that the influence of a chiral center present as a chiral auxiliary can be significantly enhanced when the photoreaction is carried out within a zeolite. We have shown examples in which the chiral auxiliary, with little or no influence in solution, enhances product formation to ~80% de in zeolites. The observed generality suggests that the phenomenon responsible for the enhanced chiral induction within zeolites must be independent of the reaction and the chiral auxiliary. Examination of the zeolite interior (Fig. 1), in which the reactant molecule is expected to be present, suggests that the most likely factor responsible for the change in de between solution and zeolite is a difference in conformational preference for the reactant molecule in these two media. Properties such as intermolecular interactions and the nature and structure of the reaction cavity, which contribute to the immediate surroundings of a reactant molecule, differ between solution and zeolites. In solution the intermolecular interactions (with the solvent molecules) are expected to be weak and transient, whereas they are likely to be strong and more permanent within zeolites.[11] Furthermore, while the 'reaction cavity' in solution is soft and time-dependent, that in zeolites is hard and relatively time independent. We are currently examining the conformational differences of the reactants described here by semi-empirical theoretical calculations and solid state NMR.

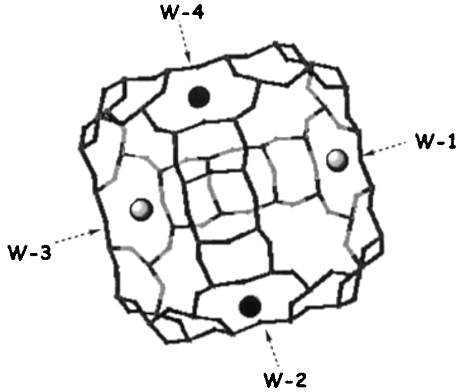


Figure 1. The internal structure of a zeolite supercage. The four windows that connect adjacent supercages are marked. The dark circles represent the Type II cations. Darker lines represents the front atoms and the lighter lines represents the ones at the back

Acknowledgements

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7. Known amounts of the compound (**1b**, **1c**, **2b**, **2c**, **4a**, or **4b**) were dissolved in 0.5 ml of dichloromethane and 12 ml of hexane was added followed by the addition of 300 mg of MY zeolite activated at 500°C with stirring. The slurry was stirred for 8 h, filtered and washed thoroughly with fresh hexane (supernatant was analyzed for the presence of starting material). The zeolite was dried in high vacuum (2×10^{-3} torr) at 65°C for 8–12 h. The sample was transferred to a test-tube (quartz test-tube-**1a**, **1b**, **1c**) inside a dry box, fresh dry-hexane added, and the test-tube stoppered. The slurry was then irradiated (450W medium pressure mercury lamp), filtered and washed again with fresh hexane (supernatant was again analyzed using GC for the presence of products/reactants). Then the zeolite was stirred with acetonitrile or ether for 6–8 h to extract the products. The extract was concentrated and analyzed.
   GC/HPLC condition: **1b**-SPB-5/HP-5890-Series II; **1c**-SE-30/Shimadzu-GC-17A; **2b**-SE-30/Shimadzu-GC-17A; **2b**-SE-30/Shimadzu-GC-17A; **4a**-SPB-5/HP-5940-Series-II; **4b**-ChiralPak OJ/Rainin HPLC/Hexane: 2-propanol = 98:02.
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