Note

Enantioselectivity of Photochemical Reactions within Polymer Microcapsules

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Polymer microcapsule was employed as a reaction medium to achieve enantioselectivity in photochemical reduction of phenyl cyclohexyl ketone and photoelectrocyclization of tropolone methyl ether under the influence of various chiral inductors. In all cases, low but evident enantioselectivity was observed. The poor enantioselectivity is probably due to the facts that not all the capsules include simultaneously both the chiral inductor and the reactant molecules, and the wall of the microcapsule is not rigid enough to hold the reactant and the chiral inductor molecules in close contact.

Keywords microcapsule, enantioselectivity, photochemical reduction, photoelectrocyclization, phenyl cyclohexyl ketone, tropolone methyl ether

Enantioselectivity of chemical reactions continues to be one of the main concerns of chemists. While many elegant and efficient chiral induction strategies have been developed for a variety of thermal reactions, there are, however, considerably fewer examples of asymmetric induction in photochemical transformations.[1] Short excited state lifetime and low activation energy for reactions in the exited states leave very little room for manipulating the diastereomeric transition states when the photochemical reaction is carried out in solution. On the other hand, impressive chiral induction of photochemical reactions in confined media such as inclusion complexes and crystals has been achieved.[2] In several examples, the enantioselectivity of the photochemical reactions in such media can be as high as 100% enantiomeric excess (*ee*). However, these approaches are less general due to the fact that not all the molecules can form crystallizable salts or host-guest complexes. Recently Ramamurthy and co-workers used the supercages of zeolites as microreactors to enhance the influence of chiral inductor on the photochemical reaction course of several substrates, and moderate to high asymmetric induction has been obtained.[3] However zeolites can only include molecules whose sizes are smaller than the dimension of the zeolite pores. This to a great extent limits the applications of this approach.

Here, we report the possibility of employing polymer microcapsule as a medium for achieving enantioselectivity in photochemical reactions. This attempt was motivated by the facts that microcapsule can be readily prepared at ambient conditions, and it can envelop almost any kind of guest molecules, regardless of their shapes and sizes. We expect that in the confined space offered by the microcapsules, the reactant and the chiral inductor molecules could interact intimately so as to yield enantiomerically enriched products.

The reactions we chose to study are the photochemical reduction of phenyl cyclohexyl ketone (**1**) and the photoelectrocyclization of tropolone methyl ether (**2**). It has been well established that in the presence of a hydrogen donor, irradiation of **1** gives intermolecular hydrogen abstraction product **3** in addition to the intramolecular hydrogen abstraction product **4** (Scheme 1).[4] Product **3** exists in two enantiomers. In this study *L*-(−)-α-methylbenzylamine, *D*-(−)-α-methylbenzylamine, *L*-(−)-proline, *D*-prolinol, *L*-menthol or *L*-(−)-ephedrine was used as the chiral inductor. These chiral inductors contain either an amino or a hydroxy group and may serve as a hydrogen donor. On the other hand, upon exposure to UV light, **2** undergoes 4π-electron electrocyclic ring closure[5] to yield the bicyclic photoisomers **5** and **6** (Scheme 1), and **5** exists in two enantiomers. The photochemistry of **2** in the presence of the chiral inductor *L*-(−)-α-methylbenzylamine or *D*-(−)-α-methylbenzylamine was investigated.

The microcapsules were prepared as follows:[6] polystyrene (1 g) (Aldrich, molecular weight, *ca.* 280000) was dissolved in cyclohexane (20 mL) at 40 ℃, and to this solution was added the weighed reactant (*ca.* 1 mmol) and the chiral inductor (*ca.* 10 mmol). The mixture was stirred for 1 h at this temperature and then was slowly cooled to 0 ℃. Phase separation was observed. The polystyrene capsules enveloping the reactant and the inductor were dispersed in cyclohexane. To the dispersion solution 100 mL of methanol was added to harden the capsule walls. The mixture was stirred at room temperature for 1 h, and the capsules were then washed with methanol several times and dried under reduced pressure. The amounts of the uptake of the reactant and the inductor were determined by the difference between the initially added weights and those left in the solution.

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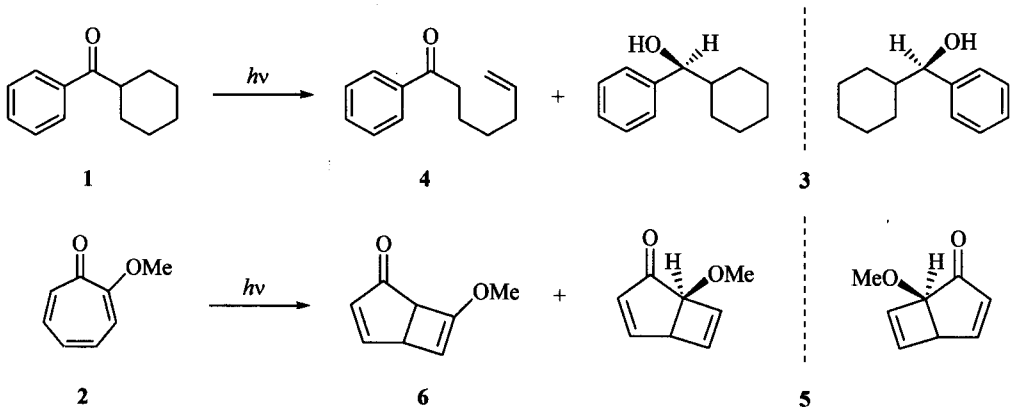
Scheme 1



The prepared microcapsules were added to acetonitrile (20 mL) in a quartz reactor. The mixture was allowed to stir under nitrogen for 1 h, and then irradiated with a 500-W high-pressure mercury lamp for 3 h to 6 h. The capsules were filtered, and extracted with cyclohexane for several times at 40 ℃. The extracted solution was concentrated and analyzed by GC on a Schimadzu GC-14B equipped with a Sepelco β-dex 325 or a Chiraldex-B-PH GC-columns.

The photochemical reaction of **1** in the microcapsule medium mainly gave **4** as the product, and **3** was produced in less than 10% yield. The *ee* values of **3** are listed in Table 1 for all the chiral inductors studied. On the other hand, in the photochemical reaction of **2**, the yield of **5**was determined to be *ca*. 50%. The *ee* values of **5** are also given in Table 1. In all cases, the chiral induction is low, but evident. One reason for the poor enantioselectivity is probably due to the fact that not all the capsules include simultaneously both the chiral inductor and the reactant molecules. Another possible reason may be attributed to the microcapsule, the wall of which is not rigid enough to hold the reactant and the chiral inductor molecules in close contact.

Table 1 Enantiomeric excess (*ee*, %) obtained with various chiral inductors within microcapsules

Chiral inductor	Product **3** (%)[a]	Product **5** (%)[a]
L-(−)-α-methylbenzylamine	5 (A)	1 (B)
D-(−)-α-methylbenzylamine	2 (B)	1 (A)
L-(−)-proline	1 (B)	
D-prolinol	2 (A)	
L-menthol	1 (B)	
L-(+)-ephedrine	2 (B)	

[a] Peak with shorter retention time is arbitrarily assigned to be isomer A, and A or B in the parentheses represents the main isomer.

To summarize, an enantiomeric excess was obtained during the photochemical reactions of phenyl cyclohexyl ketone and tropolone methyl ether within polymer microcapsules, although the enantioselectivity is low. Now we are actively trying to improve the capsule materials and reaction conditions to enhance the enantioselectivity of photochemical reactions.

References

1 (a) Inoue, Y. *Chem. Rev.* **1992**, *92*, 741.
(b) Rau, H. *Chem. Rev.* **1983**, *83*, 535.
2 (a) Leibovith, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *Pure Appl. Chem.* **1997**, *69*, 815.
(b) Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480.
3 Abraham, J.; Ramamurthy, V. *Chem. Eur. J.* **2000**, *6*, 1287.
4 (a) Lewis, F. D.; Johnson, R. W.; Johnson, D. E. *J. Am. Chem. Soc.* **1974**, *96*, 6090.
(b) Stocker, J. H. *J. Chem. Soc., Chem. Commun.* **1969**, 204.
5 Dauben, W. G.; Koch, K.; Smith, S. L.; Chapman, O. L. *J. Am. Chem. Soc.* **1963**, *85*, 2616.
6 (a) Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.* **1999**, *121*, 1129.
(b) Donbrow, M. *Microcapsules and Nanoparticles in Medicine and Pharmacy*, CRC press, Boca Raton, Florida, **1992**.

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