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# Stereoselective Photochemical Reaction of Cyclohexyl Phenyl Ketone within Lytropic Liquid Crystals Formed by Chiral Ionic Liquids

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Irradiation of cyclohexyl phenyl ketone (**1**) results in either intra- or intermolecular hydrogen abstraction to afford compounds 1-phenylhept-6-en-1-one (**2**) and $\alpha$-cyclohexyl benzyl alcohol (**3**) as photoproducts, in which **3** has a pair of enantiomers. Herein, two types of chiral hexagonal liquid crystals were prepared to direct the enantioselective photochemical reaction of **1**. One of the hexagonal liquid crystals is composed of 1-tetradecyl-3-methylimidazolium bromide/*p*-xylene/$H_2O$ with the modification by a chiral inductor. The other one is formed by chiral (*S*)-3-hexadecyl-1-(1-hydroxy-propan-2-yl)-imidazolium bromide/*p*-xylene/$H_2O$. The product analysis shows that the latter one can be used as a microreactor to achieve stereoselective photochemical reaction, while the former one produced compound **3** with no enantioselectivity at all.

**Keywords** enantioselectivity, chiral ionic liquid, liquid crystal, microreactor

## Introduction

Enantioselectivity in ground-state reactions is commonly achieved by developing appropriate catalytic systems, and great success has been made in the past decades.[1,2] However, there are fewer examples of asymmetric photochemical transformations.[3,4] In an effort to achieve stereoselective photochemistry, scientists have made use of inherently chiral hosts,[5-7] or chiral-modified media[8-12] as microreactors. It has been established that chiral cavities and/or surfaces are able to bias the course of photochemical reactions, and thus leading to stereoselective chemical transformation. Cyclodextrins,[5-7] chirally modified zeolites[8] and chiral lactams[10-12] are the most successful chiral microreactors.

Ionic liquids (ILs) represent an important class of molecular assemblies that have been widely used as environmentally benign solvents for organic chemical and enzymatic reactions,[13-16] and as media in extraction process.[17-19] It has been known that ILs enable surfactants self-assembly to form lyotropic liquid crystals either in water or in oil solutions. For example, 1-tetradecyl-3-methylimidazolium bromide ($[C_{14}mim]Br$) can form anisotropic lamellar liquid crystals (LLCs) and hexagonal liquid crystals (HLCs) with *p*-xylene and water (Figure 1).[20] The assemblies are optically transparent amenable to photochemical study. Owing to the large interfaces and various microdomains with different polarities presented in liquid crystals (LCs), these ordered aggregates could incorporate various kinds of substrates in high concentration. Furthermore, LCs have

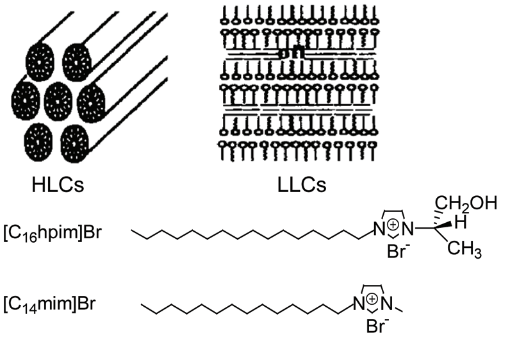

**Figure 1** Schematic representation of the structure of HLC and LLC. The structures of $[C_{16}hpim]Br$ and $[C_{14}mim]Br$ are also shown in the figure.

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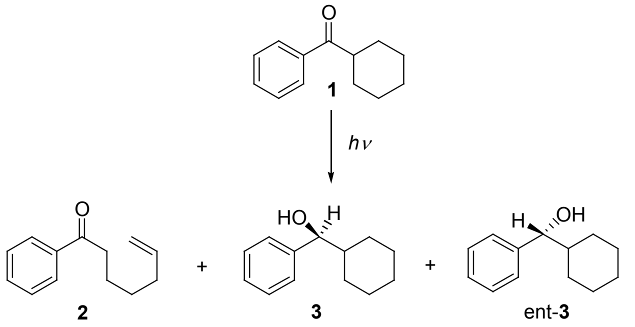
very high viscosity, and the "stiff" structure would influence the arrangement and orientation of substrates.[20-22] In particular, one may synthesize chiral ILs to prepare LCs, or incorporate a chiral inductor into the LCs formed by achiral ILs. The prepared LCs might serve as chiral microreactors to conduct stereoselective photochemical reactions.[21] However, the use of lyotropic liquid crystals (LCs) as chiral-confined media is rarely reported.[23-25]

In order to examine whether liquid crystal chiral microreactor could be used as a confined medium for enantioselective photochemical reactions, we synthesized (*S*)-3-hexadecyl-1-(1-hydroxy-propan-2-yl)imidazolium bromide ([C$_{16}$hpim]Br),[26] a chiral IL, and made use of the surfactant to prepare LCs with *p*-xylene and $H_2O$ (chiral microreactor mode 1). At the same time, we also prepared LCs by [C$_{14}$mim]Br, which was modified by a chiral inductor (chiral microreactor mode 2). The photoreaction of cyclohexyl phenyl ketone (**1**, Scheme 1) was studied, which undergoes intramolecular and intermolecular hydrogen abstraction to yield product 1-phenylhept-6-en-1-one (**2**) and *α*-cyclohexyl benzyl alcohol (**3**), respectively. The ratio of **2**/**3** mainly depends on whether a hydrogen donor is presented in the reaction. Irradiation of **1** gives **2** exclusively in the absence of hydrogen donor. However, in the presence of a large amount of hydrogen donors, **3** is yielded as the only product. Prolonged irradiation leads to secondary reactions of **2**. In our experiments, we focused on the enantioselectivity of product **3**, and the conversion of the reaction was kept in the range of 20%—30%.

**Scheme 1** Photochemical reaction of cyclohexyl phenyl ketone



## Experimental

### Materials

The amphiphilic ionic liquids, [C$_{14}$mim]Br and [C$_{16}$hpim]Br were synthesized according to the procedure reported in the previous work.[26] Cyclohexyl phenyl ketone, triethylamine, (−)-*N*-methylephedrine, (−)-norephedrine, (−)-prolinol and (−)-menthol were purchased from Acros and were used without further purification. *p*-Xylene was provided by Beijing Chemical Reagent Company. Double-distilled water was used throughout the experiment.

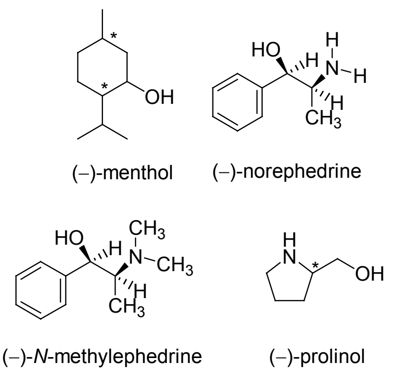
### Apparatus and procedures

To investigate the microemulsion regions, a phase diagram was constructed by the titration of a series of [C$_{16}$hpim]Br/*p*-xylene mixtures with water at room temperature. Appropriate amounts of [C$_{16}$hpim]Br and *p*-xylene were weighed into bottles. Samples were shaken for sufficient time to attain equilibrium and then progressively enriched with water (added drop by drop). The amount of added water at which transition occurred was derived from weight measurements. By repeating this experimental procedure for other combinations of [C$_{16}$hpim]Br to *p*-xylene weight ratio, the phase boundaries were determined. The presence of liquid crystalline mesophase structures was determined by using cross polarizers. Temperature was thermostatted at (25±0.1) ℃. The textures of samples were obtained by polarized optical microscopy (POM, Olympus BX51p) with a cooled CCD (Evolution MP5.1RTV, Q-imaging, Canada) for image capture, and temperature was controlled at 25 ℃ with a Linkam THSME600 liquid crystal freezing and heating stage system with a TP94 temperature controller (Linkam Scientific Instrument Ltd., UK). Small-angle X-ray scattering (SAXS) measurements were performed using a Kratky Compact Camera (HMBG, Austria) with Ni and W filtered Cu Kα radiation (wavelength $\lambda = 0.15418$ nm) generated by a PW3830 X-ray generator (5 kV×40 mA). Scattering intensities were plotted versus reciprocal spacing ($q = 4\pi \cdot \sin \theta/\lambda$), where $\theta$ was the scattering angle. The exposure time was 600 s for all samples. $^1$H NMR measurements were carried out with a Brucker 400 NMR spectrometer at 298 K.

### Photoirradiation of cyclohexyl phenyl ketone

Irradiation of cyclohexyl phenyl ketone (**1**) in the hexagonal liquid crystals was carried out in Pyrex reactors. The samples used for the photochemical reaction of **1** were simply prepared by sonicating the mixture of *p*-xylene, the IL ([C$_{14}$mim]Br or [C$_{16}$hpim]Br), water, chiral inductor (if necessary), cyclohexyl phenyl ketone (**1**) and hydrogen donor (Scheme 2) at room temperature over 24 h till the mixture became uniformly transparent. The concentration of the ketone (**1**) was 2 mg/g of LC sample. Prior to irradiation, the samples were degassed by freeze-thaw cycles. A 500 W high-pressure mercury lamp was used as the light source. After the conversion reached *ca*. 30%, the products were obtained by extrac-

**Scheme 2** Chemical structures of chiral inductors



tion with ether for gas chromatograph (GC) detection using a chiral column Supelco $\beta$-dex 325. The structure of products was identified mainly by GC-MS and $^1H$ NMR spectra.

## Results and Discussion

The ternary phase diagram of [$C_{16}$hpim]Br, *p*-xylene and water system is constructed and presented in Figure 2a. There is a region of liquid crystalline phase in the phase diagram. Figure S1 shows the POM picture of sample (the ratio of *p*-xylene/[$C_{16}$hpim]Br/water is 0.25 : 0.50 : 0.25), indicating the formation of a hexagonal liquid crystalline phase. SAXS experiment was also carried out to understand the internal structure of the liquid crystalline phases. From the scattering spectra in Figure S2, the values of the scattering vector $q$ corresponding to the scattering peaks of the sample (the ratio of *p*-xylene/[$C_{16}$hpim]Br/water is 0.25 : 0.50 : 0.25) appear in the ratio $q_1 : q_2 : q_3 = 1 : \sqrt{3} : 2$, a characteristic of hexagonal periodicity, indicating that the sample is hexagonal liquid crystalline (HLCs). For comparison, the ternary phase diagram of [$C_{14}$mim]Br, *p*-xylene and water was also examined (Figure 2b),[20] where LLCs and HLCs are clearly shown. Herein, we use HLCs as microreactors to carry out photochemical reaction of cyclohexyl phenyl ketone (**1**, Scheme 1). As mentioned above, the chiral microreactors of liquid crystals (LCs) were constructed by two modes: 1) HLCs microreactors were prepared by chiral ionic liquids (ILs), [$C_{16}$hpim]Br (mode 1 microreactor); 2) HLCs microreactors were prepared by achiral ionic liquids (ILs), [$C_{14}$mim]Br with a chiral inductor (mode 2 microreactor). The samples for the photochemical reaction of cyclohexyl phenyl ketone (**1**) were simply prepared by sonicating the mixture of *p*-xylene, ILs ([$C_{14}$mim]Br or [$C_{16}$hpim]Br), water, chiral inductor (if necessary), cyclohexyl phenyl ketone (**1**) and hydrogen donor (Scheme 2) at room temperature over 24 h till the mixtures became uniformly transparent. Generally, the weight ratio of *p*-xylene : ILs : water was 20 : 40 : 40 or 25 : 50 : 25. In mode 1 microreactor, the mole ratio of hydrogen donor to substrate was fixed at 7 : 1, while in mode 2 microreactor, the concentration of the chiral inductor was 7 times that of the ketone (**1**).

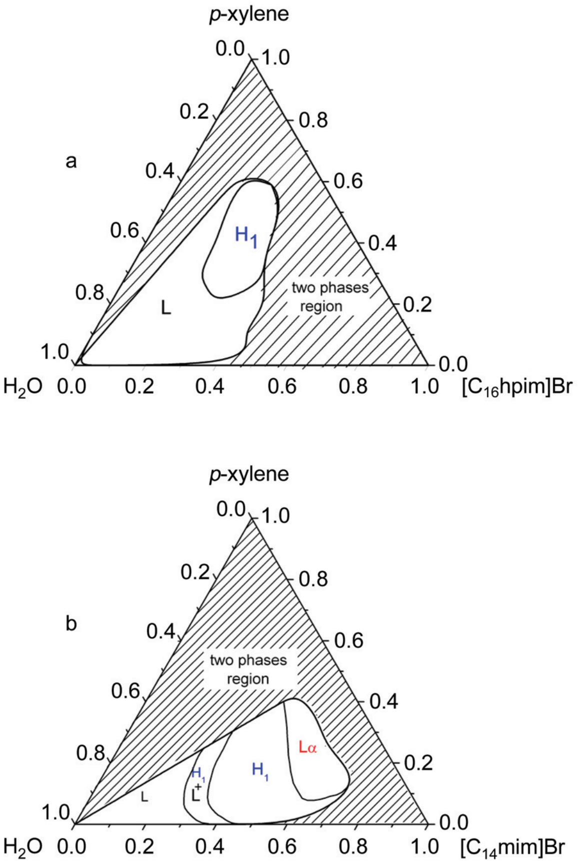


**Figure 2** Ternary phase diagram of [$C_{16}$hpim]Br/*p*-xylene/$H_2O$ (a) and [$C_{14}$mim]Br/*p*-xylene/$H_2O$ (b) at room temperature.

**Table 1** Product distributions of **1** in hexagonal liquid crystals

| Entry | Hydrogen donor | Reaction media | Molar ratio of **2** : **3** | *ee* in **3** |
|---|---|---|---|---|
| 1 | No | HLC-1[a] | 95 : 5 | — |
| 2 | triethylamine | HLC-1[a] | 0 : 100 | 13% A |
| 3 | No | HLC-2[b] | 100 : 0 | — |
| 4 | triethylamine | HLC-2[b] | 3 : 97 | 0% |
| 5 | (−)-*N*-methylephedrine | HLC-2[b] | 40 : 60 | 1% B |
| 6 | (−)-prolinol | HLC-2[b] | 42 : 58 | 1% B |
| 7 | (−)-norephedrine | HLC-2[b] | 100 : 0 | — |
| 8 | (−)-menthol | HLC-2[b] | 100 : 0 | — |

[a] The ratio of *p*-xylene : [$C_{16}$hpim]Br : $H_2O$ is 0.25 : 0.50 : 0.25.
[b] The ratio of *p*-xylene : [$C_{14}$mim]Br : $H_2O$ is 0.20 : 0.40 : 0.40, the molar ratio of chiral inductor to substrate is fixed at 7 : 1.

The product distributions both in mode 1 and mode 2 microreactors are given in Table 1. Evidently, in the absence of a hydrogen donor, irradiation of **1** in HLCs prepared by [$C_{14}$mim]Br led to intramolecular hydrogen abstraction to produce compound **2** (Table 1, entry 3, Figure S3), while in HLCs formed by [$C_{16}$hpim]Br, small amount of **3** (5%, Table 1, entry 1) is also detected. In the later case, **3** is probably produced by hydrogen abstraction from the hydrocarbon chain of the IL and/or the methyl group of *p*-xylene. In the presence of a hydrogen donor, the intermolecular hydrogen abstraction product becomes dominant. Irradiation of **1** in mode 1 microreactor exclusively gave **3** in the presence of triethylamine (Table 1, entry 2). On the other hand, the photochemical reaction of **1** in HLCs made of [$C_{14}$mim]Br in the presence of triethylamine only yielded trace of **2** (3%) (Table 1, entry 4, Figure S4). The chiral inductor, (−)-prolinol, (−)-*N*-methylephedrine, (−)-norephedrine and (−)-menthol (Scheme 2) can also act as hydrogen donor. However, in the model 2 microreactors shown in Table 1 (entries 5—8), compound **3** was detected as a part of products or even absent. This observation suggests that ketone **1** and the hydrogen

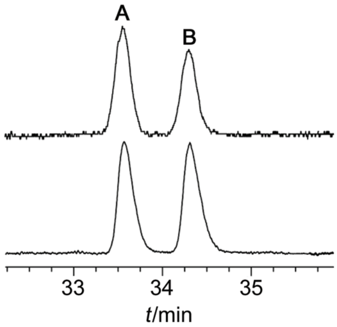


**Figure 3** GC trace of product **3** obtained in HLC-1 (up) and HLC-2 (down) microreactors in the presence of triethylamine.

donor are located in different domains of the HLCs.

Of particular interests is the enantioselective photochemical reaction of **1** was examined using mode 1 and mode 2 microreactors. Figure 3 shows the GC trace of product **3** upon irradiation of **1** in mode 1 microreactor. The first of the two enantiomeric peaks on GC trace is arbitrarily assigned to be isomer **A**, and the second peak is isomer **B**. **A** was enriched to the extent of *ca*. 13% *ee*. The *ee* value is small but evident, considering the difficulty to achieve asymmetric induction in photochemical transformations. In contrast, the photochemical reaction of **1** in mode 2 microreactors shows negligible enantioselectivity (Table 1, entries 5 and 6). This might arise from the fact that ketone **1** and the molecules of chiral inductor are located in different domains of the model 2 microreactors. The separation of the chiral inductor and ketone would not prefer to direct the reaction toward one of the enantiomers.

## Conclusions

In summary, HLCs constructed by long chain ILs can be used as microreactors to incorporate cyclohexyl phenyl ketone **1**. Irradiation of the samples without hydrogen donor resulted in intramolecular hydrogen abstraction product exclusively. In the presence of hydrogen donor (such as triethylamine), however, the main product is switched to intermolecular hydrogen abstraction one(s). The chiral model 1 microreactor made of inherently chiral ILs induced enantioselectivity of the intermolecular hydrogen abstraction product **3**. On the other hand, the photochemical reaction of ketone **1** in the chiral model 2 microreactor shows no chiral induction, possibly due to the fact that the substrate and chiral inductor molecules are located in different domains of the HLCs. These results remind us that it is possible to achieve enantioselectivity of photochemical reactions using chiral ILs to form LC systems. The closer contact between substrates and chiral inductors is, the higher stereoselectivity will be. It is anticipated this research line would realize asymmetric photochemical transformation, which is undergoing in our laboratory.

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