Enantioselective Photopinacolization of Benzophenone and Benzhydrol Intercalated in Mg–Al LDH Interlayers

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A novel enantioselective photochemical pinacolization utilizing the interlayer spaces of layered double hydroxide (LDH) was investigated. UV irradiation of (+)-4-(α-hydroxy-α-phenyl)-methylbenzoate [benzhydrol-4-carboxylate] ions (*d*-**BHA**) with 4-benzoylbenzoate ions (**BBA**) gave rise to the formation of (−)-1,2-bis(4-carboxyphenyl)-1,2-bisphenyl-1,2-ethanediol (*l*-benzopinacol) in the LDH interlayers. Similarly, *l*-**BHA** reacts with **BBA** to give *d*-benzopinacol in the LDH. A maximum optical yield of over 60%ee was observed at the initial reaction stage.

Photopinacolization is one of the most classical reactions known since the 18th century.[1] Many studies have been reported since then and the reaction mechanism has been well established.[2,3] However, enantioselective photopinacolization is not commonly observed, though some aromatic ketones undergo diastereoselective photopinacolizations.[4,5] This is due to the fact that the ketyl radical intermediates are sufficiently persistent and stable that they can move freely in solution. However, in confined reaction fields such as solid or viscous matrices which suppress the molecular movement, the stereochemistry can be anticipated by controlling the molecular arrangements in the reaction system.

In the present study, the photochemical reduction of 4-benzoylbenzoate (**BBA**) by chiral benzhydrol-4-carboxylate (*d*- or *l*-**BHA**),[6] which yields *dl*- and/or *meso*-pinacols, was examined in the confined spaces of Mg–Al layered double hydroxide (Mg–Al LDH), and the enantioselectivity is discussed in terms of the molecular arrangement of the cavities.
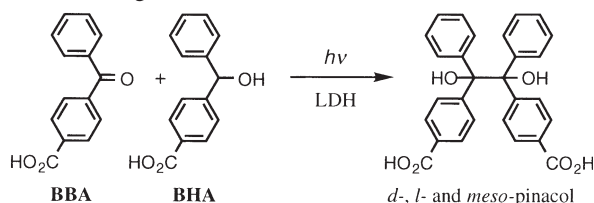
Mg–Al LDH, $[Al_{1/3}Mg_{2/3}(OH)_2]Cl_{1/3}$, is an anion-exchangeable layered compound.[7] The laminating structure consists of $Mg(OH)_2$ octahedral sheets, a part of which is replaced by $Al(OH)_2^+$ with exchangeable interlayer anions (Figure 1). Organic anions such as carboxylates can be adsorbed into the LDH interlayers by ion exchange of the interlayer anions and assembled as molecular aggregates, thus enabling stereoselective chemical reactions.[8–10]

0.05 mmol of both **BHA** and **BBA** was dissolved in 10 mL of a NaOH aqueous solution (10 mM) followed by the addition of equivalent amounts of LDH powder with an anion exchange capacity (AEC) of 3.50 mmol/g. The aqueous suspension was then
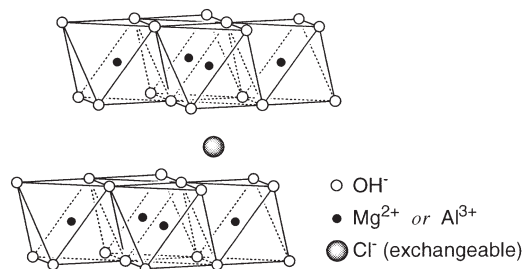

Figure 1. Structure of Mg–Al layered double hydroxide (LDH).

stirred at 70 °C overnight. The adsorption degree of the carboxylate was estimated at 85% (1.49 mmol/g-LDH) for **BBA** and 45% (0.788 mmol/g-LDH) for **BHA** from the UV-vis spectral intensities of the filtrate. Powder XRD analysis of the intercalated composite showed a weak (001) diffraction peak in the smaller diffraction angle region (Figure 2). The basal spacing of the LDH intercalated composites of **BBA** and *dl*-**BHA** was estimated to be 21 Å which is comparable to the cases of *l*- or *d*-**BHA**. Since LDH originally has a basal spacing of 8 Å, the interlayer was opened by 13 Å, which is somewhat larger than the molecular lengths of **BBA** (10.4 Å) and **BHA** (9.7 Å), implying that the carboxylates may be loosely packed as bilayers.
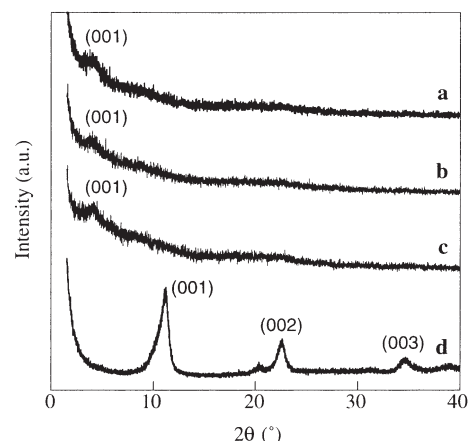

Figure 2. Powder XRD patterns of (a) *l*-**BHA/BBA/**LDH, (b) *d*-**BHA/BBA/**LDH, (c) *dl*-**BHA/BBA/**LDH and (d) LDH before intercalation.
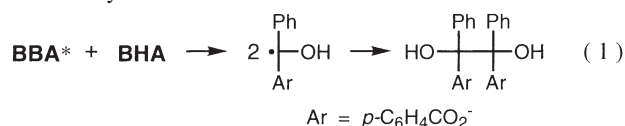
The resulting **BBA** and **BHA** containing composite was suspended in water and irradiated by a 300 W medium pressure mercury lamp through a Pyrex filter (>300 nm) under Ar atmosphere. After UV irradiation for 2 h, the reaction mixture was added into 1 mol dm^{-3} HCl to decompose the LDH layers, then extracted with Et_2O–CH_2Cl_2 (3 × 50 mL), and analyzed by HPLC equipped

**Table 1.** Photoreaction of **BBA** with chiral **BHA** intercalated on LDH interlayers[a]

BHA	Medium	Conv. of **BHA** /%[b]	Selectivity/%[b]			ee/%[c]
			meso-	*d-*	*l-*	
d-BHA	LDH	66	68	12	20	−25
	H_2O	78	64	19	17	6
l-BHA	LDH	74	68	20	12	25
	H_2O	76	66	15	18	−8
dl-BHA	LDH	83	68	15	17	−6

a Irradiation: 300 W medium pressure Hg lamp/Pyrex, 2 h, Ar atm.
b Conversions and selectivities were calculated from HPLC analysis.
c Enantiomeric excesses are based on *d*-pinacol: ee $= (d − l)/(d + l)$.

with an optical resolution column (Daicel, CHIRALCEL OD). The stereochemical distributions of the photoproducts are summarized in Table 1. Under the present conditions, *dl*- and *meso*-pinacols were formed as a 1:2 diastereomeric mixture. In contrast, the enantioselectivity was strongly affected by the reaction environment. In the case of chiral **BHA** in LDH, significant enantioselectivities of 25%ee, could be observed in the formation of *d*- or *l*-pinacol, which shows a great contrast to the case in aqueous solution without LDH. Stereochemical control of the photopinacolization can reasonably be explained by the confinement effect of the LDH host interlayers.

$$\mathbf{BBA^*} + \mathbf{BHA} \longrightarrow 2\ \overset{\mathrm{Ph}}{\underset{\mathrm{Ar}}{\cdot\!\!-\!\!\mathrm{OH}}} \longrightarrow \mathrm{HO}\!\!-\!\!\overset{\mathrm{Ph}}{\underset{\mathrm{Ar}}{}}\!\!-\!\!\overset{\mathrm{Ph}}{\underset{\mathrm{Ar}}{}}\!\!-\!\!\mathrm{OH} \quad (1)$$

$$\mathrm{Ar} = p\text{-}\mathrm{C_6H_4CO_2^-}$$

Excited triplet benzophenone is well known to be able to abstract the α-hydrogen of benzhydrol to yield two ketyl radicals which recombine into pinacol (Eq 1). In solution, these two ketyl radicals can move freely in the solvent cage and sometimes escape out of the cage,[3] resulting in the loss of enantioselectivity. However, when the pinacolization of **BBA** and **BHA** is carried out in the confined LDH interlayers, since they are well-concentrated and assembled, an excited **BBA** may abstract the hydrogen of **BHA** more preferably from one side of the molecular plane, as depicted in Scheme 1. The preferable formation of *d*- or *l*-pinacol suggests that rotation and diffusion of the resulting ketyl radicals are suppressed by the upper and lower layers of the LDH.
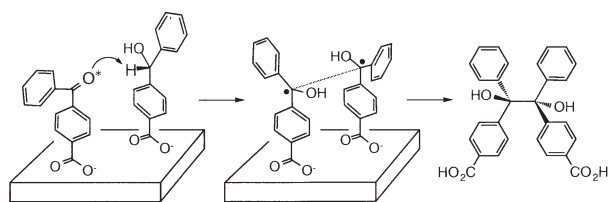
Scheme 1.

The enantioselectivity of the pinacolization depends considerably on the irradiation time (Figure 3). The dependence of the percentages of the enantiomeric excess of the *dl*-pinacol on the irradiation times under various reaction conditions are shown in Figure 3A. At the initial reaction stage, the optical yield reached 40%ee The irradiation time dependency of the ee values can be considerable because of the collapse of the regular alignment in the organized **BBA** and **BHA** molecular assembly during the pinacolization. Furthermore, there is a possibility of photopinacolization outside the interlayers, since **BHA** (45% adsorption degree) in the
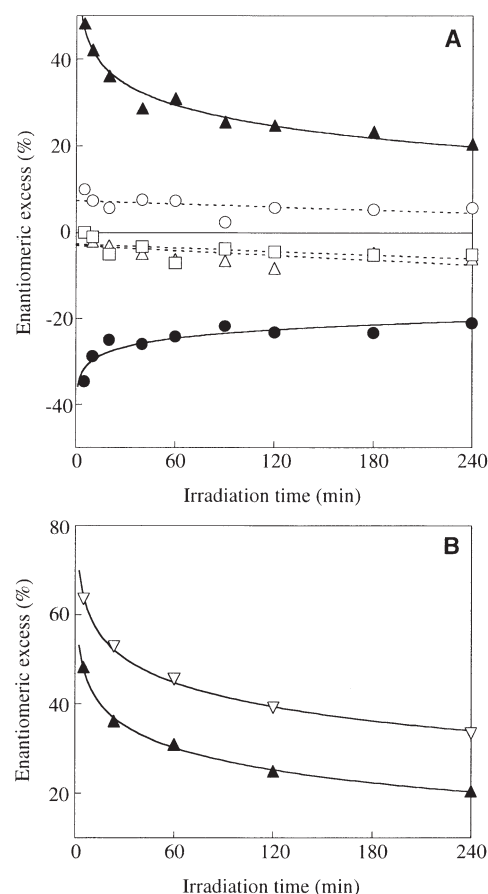
Figure 3. (A) Time dipendence of enantioselectivities of the photoreactions of **BBA** with *l*-**BHA**/LDH (▲), *l*-**BHA**/H_2O (△), *d*-**BHA**/LDH (●), *d*-**BHA**/H_2O (○) and *dl*-**BHA**/LDH (□). (B) Enanitoselectivities of filtrated (▽) and not filtrated (▲) samples of **BBA**/*l*-**BHA**/LDH.

bulk leads to racemic pinacol which may lower the optical purity of the interlayer pinacolization. In order to observe the net enantiomeric excess of the pinacol within the LDH interlayers, the **BBA** and **BHA** not intercalated in the LDH were filtered off before UV irradiation. The obtained dispersion in water improved the optical yield considerably, i.e., 63%ee could be observed, which is much higher than the original yield of 47%ee.

In conclusion, 4-benzoylbenzoate (**BBA**) and benzhydrol-4-carboxylate (**BHA**) ions could be intercalated in the Mg–Al LDH interlayers, and irradiation of the intercalated mixture gave rise to a corresponding pinacol. By employing chiral **BHA**, the chirality could induce the formation of chiral pinacol by the confinement of the **BBA** and **BHA** molecules in the LDH interlayers.

References and Notes
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