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# Recyclable fluorous chiral ligands and catalysts: asymmetric addition of diethylzinc to aromatic aldehydes catalyzed by fluorous BINOL–Ti complexes

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**Abstract**—Fluorous chiral BINOLs were prepared and used as the ligands for the titanium catalyzed asymmetric addition of  $\text{Et}_2\text{Zn}$  to aromatic aldehydes. Consecutive reactions were examined by utilizing fluorous–organic biphasic and fluorous solid phase extraction techniques. Enantioselectivities were similar in consecutive reactions and were close to that attained in the non-fluorous system. The solid phase extraction method also enabled us to perform a simultaneous screening procedure. © 2002 Elsevier Science Ltd. All rights reserved.

The fluorous–organic biphasic system and the solid phase extraction with fluorous reverse phase silica gel were originated by Horváth and Curran, respectively. These are very attractive techniques<sup>1</sup> for researchers who are seeking practical and environmentally friendly catalytic systems of asymmetric reactions.<sup>2</sup> Chiral ligands for metal catalysts are usually laborious to prepare and expensive. Therefore, fluorous chiral ligands that are reusable have a potential to afford catalytic systems that fit the needs of the researchers.

We have focused our attention on preparation of effective and recyclable fluorous chiral ligands and their application to catalytic asymmetric reactions. We have prepared a fluorous chiral BINOL (FBINOL) and obtained interesting results by using it for the ligand of Ti-complex which catalyzed an asymmetric addition of diethylzinc to aromatic aldehydes in an organic and FC-72 ( $\text{CF}_3(\text{CF}_2)_4\text{CF}_3$ ) biphasic system.<sup>2h</sup> Although the chemical yields and the enantioselectivities in consecutive reactions paralleled the original non-fluorous reaction, a certain amount of FBINOL leached to the organic phase from the fluorous phase in every run. The measurement of partition coefficient suggested that the leaching was caused by insufficient fluorous content of the chiral ligand. Therefore, we have tried to prepare another fluorous chiral BINOL that has higher fluorine content in order to improve the immobilizability of the ligand and catalyst in the fluorous phase.

Fluorous solid phase extraction is a very useful method to

separate organic products from a fluorous catalyst or ligand, especially in cases where the fluorine content is not high enough to carry out the catalytic reaction in fluorous–organic biphasic system successfully. Thus, we also employed the fluorous solid phase extraction method in order to reuse the fluorous chiral BINOLs more effectively. The simple and clear-cut separation of the organic products and the fluorous BINOL with the fluorous reverse phase silica gel prompted us to perform a high throughput analysis of the products which contained the corresponding enantiomeric pairs derived from a mixture of different aromatic aldehydes. GC analysis with chiral capillary column enabled us to determine the enantiomeric excesses of each product simultaneously.

We report here the usefulness of these techniques for creating practical and environmentally benign catalytic asymmetric reaction systems.

## 1. Results and discussion

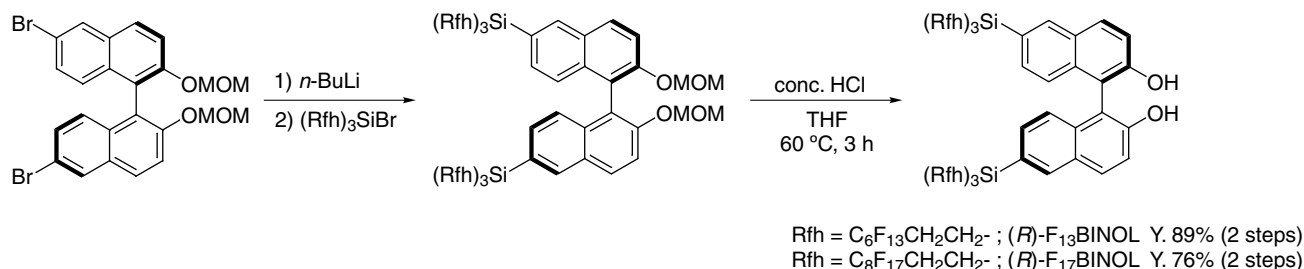
Fluorous chiral BINOLs, (*R*)- $\text{F}_{13}\text{BINOL}$  and (*R*)- $\text{F}_{17}\text{BINOL}$ , were prepared by the following route shown in Scheme 1.

(*R*)- $\text{F}_{17}\text{BINOL}$  was obtained in 76% overall yield by the same procedures reported in the previous paper for (*R*)- $\text{F}_{13}\text{BINOL}$ .<sup>2g</sup> The approximate partition coefficients of FBINOLs were determined by the simple method described in the footnote of Table 1, and the results are summarized in Table 1.

The data in Table 1 show that (*R*)- $\text{F}_{13}\text{BINOL}$  and

**Keywords:** addition reactions; asymmetric reactions; fluorine and compounds; perfluoroalkyl compounds.

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Scheme 1.

**Table 1.** Partition coefficients of (*R*)-FBINOLs in organic solvent and FC-72

FBINOL	Rfh	F (%)	Organic solvent	Organic solvent/FC-72
( <i>R</i> )-F <sub>13</sub> BINOL	C <sub>6</sub> F <sub>13</sub> CH <sub>2</sub> CH <sub>2</sub> -	61.16	CHCl <sub>3</sub> Toluene	5/95 2/98
( <i>R</i> )-F <sub>17</sub> BINOL	C <sub>8</sub> F <sub>17</sub> CH <sub>2</sub> CH <sub>2</sub> -	64.10	CH <sub>2</sub> Cl <sub>2</sub> Toluene	1/99 1/99

A mixture of 100 mg of (*R*)-FBINOLs in FC-72 (2 mL) and organic solvent (2 mL) was stirred at room temperature for 10 min. Then the two phases were separated and the solvents were evaporated in vacuo. The contents of the fluororous compound in each phase were determined by weighing the residue.

(*R*)-F<sub>17</sub>BINOL are highly fluororous. Therefore, the amount of catalysts and/or the ligands which leak to the organic phase should be small in the organic and fluororous biphasic systems.

We chose the asymmetric addition of diethylzinc to aromatic aldehydes catalyzed by a BINOL–Ti complex to examine usefulness of the FBINOLs. The reaction has been reported by Nakai and Chan independently.<sup>3</sup> It was selected for testing the FBINOLs by utilizing the fluororous–organic biphasic and solid phase extraction techniques because the reaction occurs in high enantiomeric excess and yield by a simple procedure and with the use of commercially available reagents.

At the outset, a standard reaction was carried out under the same reaction conditions as those reported except that the FBINOLs and benzotrifluoride (BTF) were used as the

chiral ligand and the solvent. The products and FBINOLs were simply and cleanly separated with 1*H*,1*H*,2*H*,2*H*-perfluoro-octyldimethylsilyl bonded silica gel (fluororous reverse phase silica gel; FRP silica gel) by washing successively with acetonitrile and FC-72 and the results for several aromatic aldehydes are summarized in Table 2.

The chemical yields and the enantioselectivities are similar to those reported by Nakai (97 and 85% ee for benzaldehyde, respectively)<sup>3a</sup> and the recoveries of the FBINOLs were quantitative. 1-Naphthylaldehyde afforded higher enantioselectivity (91% ee) than that of 2-naphthylaldehyde (78% ee), which may be caused by the difference in steric hindrance around their aldehyde carbon atoms.

The successful results in the uniphase reaction encouraged us to examine a toluene and FC-72 biphasic system. Thus,

**Table 2.** Catalytic asymmetric addition of diethylzinc (1 M in hexane) to several aromatic aldehydes using FBINOL–Ti complexes

Entry	Solvent	FBINOL	Ar	Yield (%) <sup>a</sup>	% ee <sup>b</sup>	Recovered FBINOL (%) <sup>c</sup>
1	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	Ph	92	84	99
2	BTF/hexane (1:1 v/v)	F <sub>17</sub> BINOL	Ph	86	83	100
3	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	2-MeO-C <sub>6</sub> H <sub>4</sub> -	93	78	98
4	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	3-MeO-C <sub>6</sub> H <sub>4</sub> -	95	85	100
5	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	4-MeO-C <sub>6</sub> H <sub>4</sub> -	97	80	96
6	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	4-Me-C <sub>6</sub> H <sub>4</sub> -	91	81 <sup>d</sup>	100
7	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	1-Naphthyl	98	91	98
8	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	2-Naphthyl	93	78	98
9	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	4-Cl-C <sub>6</sub> H <sub>4</sub> -	93	82 <sup>d</sup>	100
10	BTF/hexane (1:1 v/v)	F <sub>13</sub> BINOL	4-Br-C <sub>6</sub> H <sub>4</sub> -	93	86 <sup>d</sup>	100

Substrate/FBINOL/Ti(O-*i*Pr)<sub>4</sub>/Et<sub>2</sub>Zn = 1:0.2:1.2:3 (molar ratio).

<sup>a</sup> Isolated yield.

<sup>b</sup> Determined by HPLC analysis using DAICEL CHIRALCEL OD or OD-H. (*R*)-configuration of the product in each case.

<sup>c</sup> Separated from the organic compounds by solid phase extraction with FRP silica gel.

<sup>d</sup> Determined by capillary GC analysis using SUPELCO β-DEX 120.

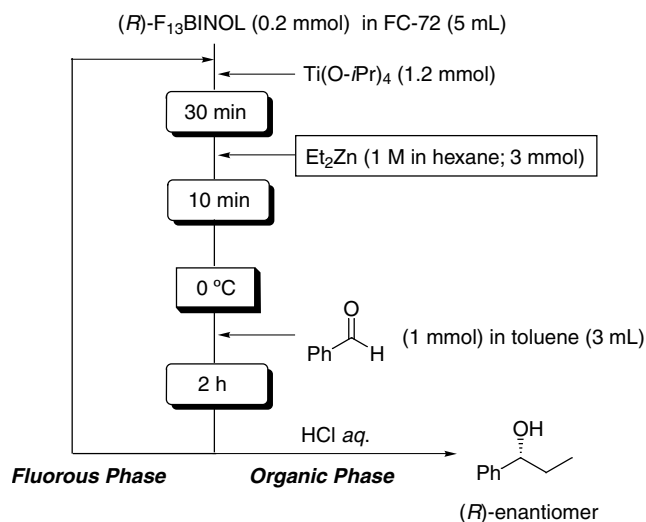


Figure 1.

the reaction was carried out repeatedly by using benzaldehyde and (*R*)-F<sub>13</sub>BINOL as shown in Fig. 1.

When Ti(O-*i*Pr)<sub>4</sub> was added to the solution of (*R*)-F<sub>13</sub>BINOL in FC-72, the reaction mixture first became a light red and homogeneous and then a colorless oily material separated out on the surface of the FC-72 solution. A 1 M solution of Et<sub>2</sub>Zn in hexane was then added. After cooling to 0 °C, a benzaldehyde solution in toluene was added. The organic phase (toluene and hexane) became pale yellow-brown and the FC-72 phase remained light red. The reaction mixture was stirred vigorously at 0 °C for 2 h, and then the organic phase was withdrawn with syringe and was quenched with 1N hydrochloric acid to ensure

removal of any residual (*R*)-F<sub>13</sub>BINOL and to liberate the product alcohol from the Ti complex. The products and residual (*R*)-F<sub>13</sub>BINOL were separated with FRP silica gel by washing successively with acetonitrile and FC-72. The product alcohol was obtained from the acetonitrile eluate. Fresh Ti(O-*i*Pr)<sub>4</sub>, the Et<sub>2</sub>Zn and benzaldehyde solution were added to the fluorous phase, and the reaction was carried out in the same way. The reaction was repeated five times and the results are summarized in Table 3.

As seen in Table 3, the enantioselectivity remained at 80% or above through run 5. However, about 10% of (*R*)-F<sub>13</sub>BINOL was recovered from the organic phase in every experiment. Therefore, it seems likely that a significant amount of the chiral catalyst was in the organic phase and the asymmetric reaction took place only in that phase. That the organic phase had a pale brown color also supports this conclusion. To test this postulate, we carried out the reaction separately in the organic phase and in a toluene–FC-72 biphasic system. The procedure was the same until the reaction mixture was cooled at 0 °C after the addition of Et<sub>2</sub>Zn solution. Toluene was added to the reaction mixture and the two phases were separated. The benzaldehyde solution was added to the organic phase and the reaction was carried out as described above. The Et<sub>2</sub>Zn solution and the benzaldehyde solution were added to the FC-72 phase and the reaction was carried out in the same way. From the organic phase the product was obtained in 73% ee (88% yield) and 10% of (*R*)-F<sub>13</sub>BINOL was recovered. From the toluene–FC-72 biphasic system the product was obtained in 77% ee (81% yield) and 88% of (*R*)-F<sub>13</sub>BINOL was recovered. Therefore, it is clear that some of the chiral complex was actually in the organic phase but that the amount of the complex was too little to give the expected 83% ee. On the other hand, the enantioselectivity in the toluene–FC-72 biphasic system was somewhat higher in

**Table 3.** Catalytic asymmetric addition of diethylzinc (1 M in hexane) to benzaldehyde using a (*R*)-F<sub>13</sub>BINOL–Ti complex in FC-72/organic solvent biphasic system

Run	Solvent	FBINOL	Yield (%) <sup>a</sup>	% ee <sup>b</sup>	Recovered ( <i>R</i> )-F <sub>13</sub> BINOL (%) <sup>c</sup>
1	Toluene/hexane/FC-72 (3:3:5 v/v)	F <sub>13</sub> BINOL	81	83	10
2	Toluene/hexane/FC-72 (3:3:5 v/v)	F <sub>13</sub> BINOL	89	82	12
3	Toluene/hexane/FC-72 (3:3:5 v/v)	F <sub>13</sub> BINOL	87	82	12
4	Toluene/hexane/FC-72 (3:3:5 v/v)	F <sub>13</sub> BINOL	87	81	11
5	Toluene/hexane/FC-72 (3:3:5 v/v)	F <sub>13</sub> BINOL	87	80	10

<sup>a</sup> Isolated yield.

<sup>b</sup> Determined by HPLC analysis using DAICEL CHIRALCEL OD. (*R*)-configuration of the product in each case.

<sup>c</sup> Separated from the organic compounds by solid phase extraction with FRP silica gel.

**Table 4.** Catalytic asymmetric addition of diethylzinc (1.1 M in toluene) to benzaldehyde using a (*R*)-F<sub>13</sub>BINOL–Ti complex in FC-72/organic solvent biphasic system

Run	Solvent	FBINOL	Yield (%) <sup>a</sup>	% ee <sup>b</sup>	Recovered ( <i>R</i> )-F <sub>13</sub> BINOL (%) <sup>c</sup>
1	Toluene/FC-72 (3:5 v/v)	F <sub>13</sub> BINOL	85	78	<1
2	Toluene/FC-72 (3:5 v/v)	F <sub>13</sub> BINOL	85	78	<1
3	Toluene/FC-72 (3:5 v/v)	F <sub>13</sub> BINOL	80	77	<1

Substrate/F<sub>13</sub>BINOL/Ti(O-*i*Pr)<sub>4</sub>/Et<sub>2</sub>Zn=1:0.2:1.2:3 (molar ratio).

<sup>a</sup> Isolated yield.

<sup>b</sup> Determined by HPLC analysis using DAICEL CHIRALCEL OD. (*R*)-configuration of the product in each case.

<sup>c</sup> Separated from the organic compounds by solid phase extraction with FRP silica gel.

spite of the lack of excess amount of  $\text{Ti}(\text{O}-i\text{Pr})_4$ . The presence of excess amount of  $\text{Ti}(\text{O}-i\text{Pr})_4$  was reported to be indispensable for the reaction to result in high enantioselectivity and yield.<sup>3b</sup>

When a consecutive reaction was carried out by using  $\text{Et}_2\text{Zn}$  solution in toluene (1.1 M) instead of hexane solution in order to clarify a role of hexane in the biphasic system, the enantioselectivities were lowered to 77–78% ee, but the amount of (*R*)- $\text{F}_{13}\text{BINOL}$  that leached into the toluene phase decreased to less than 1%, as shown in Table 4.

This reaction was also carried out in the toluene phase and in the toluene–FC-72 biphasic system separately in the same way as described above. The enantioselectivity in the biphasic system, 78% ee (85% yield), was similar to the values in Table 4. However, the enantioselectivity in the separated toluene phase was dramatically reduced to 30% ee (49% yield) and the recovery of (*R*)- $\text{F}_{13}\text{BINOL}$  from the phase was negligible. Results (ee, recovery of (*R*)- $\text{F}_{13}\text{BINOL}$  from organic phase) seem to suggest that hexane dissolves the catalyst much better than toluene. Therefore, it is deduced that both phases are necessary to get the enantioselectivity higher than 83% ee in the biphasic system and that hexane plays an important role to bring about the high enantiomeric excess.

When the reaction was carried out consecutively by using (*R*)- $\text{F}_{17}\text{BINOL}$  and  $\text{Et}_2\text{Zn}$  solution in hexane as in Table 3, leaching of (*R*)- $\text{F}_{17}\text{BINOL}$  into the organic phase was only

about 1% in each experiment, while the enantioselectivities were consistently 78–79% ee as shown in Table 5.

Judging from all these results, it is concluded that a certain amount of FBINOLs are necessary to exist in the organic phase for getting enantioselectivity as high as 83% ee in the organic and FC-72 biphasic system. However, it is also clear that the enantioselectivity was slightly improved and the immobilization of the  $\text{F}_{17}\text{BINOL}$  in FC-72 phase was much improved compared to the results of  $\text{F}_{13}\text{BINOL}$  in toluene–FC-72 and in organic (toluene and hexane)–FC-72 biphasic systems, respectively, as a result of the increased fluorine content of the ligand.

Finally, we examined a consecutive reaction by using the (*R*)- $\text{F}_{13}\text{BINOL}$  recovered from the fluorine silica gel separation. The reaction was carried out in BTF at 0°C for 1 h and the (*R*)- $\text{F}_{13}\text{BINOL}$  was separated from the product with FRP silica gel. The recovered (*R*)- $\text{F}_{13}\text{BINOL}$  was reused for the next reaction without further purification. The results of four consecutive reactions are summarized in Table 6.

As seen in Table 6, the enantioselectivities were the same as those reported by Nakai<sup>3a</sup> and the recoveries of (*R*)- $\text{F}_{13}\text{BINOL}$  were quantitative.

Liscamp and co-workers have reported a simultaneous substrate screening procedure for the ability to enantioselectively catalyze the  $\text{Ti}(\text{O}-i\text{Pr})_4$ -mediated addition of

**Table 5.** Catalytic asymmetric addition of diethylzinc (1 M in hexane) to benzaldehyde using a (*R*)- $\text{F}_{17}\text{BINOL}$ –Ti complex in FC-72/organic solvent biphasic system

Run	Solvent	FBINOL	Yield (%) <sup>a</sup>	% ee <sup>b</sup>	Recovered ( <i>R</i> )- $\text{F}_{17}\text{BINOL}$ (%) <sup>c</sup>
1	Toluene/hexane/FC-72 (1:1:2 v/v)	$\text{F}_{17}\text{BINOL}$	82	79	1
2	Toluene/hexane/FC-72 (1:1:2 v/v)	$\text{F}_{17}\text{BINOL}$	82	78	1
3	Toluene/hexane/FC-72 (1:1:2 v/v)	$\text{F}_{17}\text{BINOL}$	77	78	1

Substrate/ $\text{F}_{17}\text{BINOL}$ / $\text{Ti}(\text{O}-i\text{Pr})_4$ / $\text{Et}_2\text{Zn}$ =1:0.2:1.2:3 (molar ratio).

<sup>a</sup> Isolated yield.

<sup>b</sup> Determined by GC analysis using SIPELCO  $\beta$ -DEX 120. (*R*)-configuration of the product in each case.

<sup>c</sup> Separated from the organic compounds by solid phase extraction with FRP silica gel.

**Table 6.** Catalytic asymmetric addition of diethylzinc (1 M in hexane) to benzaldehyde reusing the same (*R*)- $\text{F}_{13}\text{BINOL}$

Run	Solvent	FBINOL	Yield (%) <sup>a</sup>	% ee <sup>b</sup>	Recovered ( <i>R</i> )- $\text{F}_{13}\text{BINOL}$ (%)
1	BTF/hexane (1:1 v/v)	$\text{F}_{13}\text{BINOL}$	92	84	99
2	BTF/hexane (1:1 v/v)	$\text{F}_{13}\text{BINOL}$	93	85	97
3	BTF/hexane (1:1 v/v)	$\text{F}_{13}\text{BINOL}$	96	84	99
4	BTF/hexane (1:1 v/v)	$\text{F}_{13}\text{BINOL}$	89	83	99

Substrate/ $\text{F}_{13}\text{BINOL}$ / $\text{Ti}(\text{O}-i\text{Pr})_4$ / $\text{Et}_2\text{Zn}$ =1:0.2:1.2:3 (molar ratio).

<sup>a</sup> Isolated yield.

**Table 7.** Simultaneous catalytic asymmetric addition of diethylzinc (1 M in hexane) to various aromatic aldehydes

Entry	Ar	(R)-F <sub>13</sub> BINOL		(R)-F <sub>17</sub> BINOL	
		Yield (%) <sup>a</sup>	% ee <sup>a</sup>	Yield (%) <sup>a</sup>	% ee <sup>a</sup>
1	Ph	97 (92)	82 (84) <sup>b</sup>	91 (86)	83 (83)
2	4-Me-C <sub>6</sub> H <sub>4</sub> -	85 (93)	83 (81)	81	83
3	2-MeO-C <sub>6</sub> H <sub>4</sub> -	94 (91)	76 (78) <sup>b</sup>	73	79
4	4-Cl-C <sub>6</sub> H <sub>4</sub> -	94 (93)	83 (82)	87	84
5	4-Br-C <sub>6</sub> H <sub>4</sub> -	96 (93)	84 (86)	83	85

Substrate/FBINOL/Ti(O-*i*Pr)<sub>4</sub>/Et<sub>2</sub>Zn=1:0.2:1.2:3 (molar ratio).

<sup>a</sup> Numbers in parentheses are the data obtained by the separately performed experiments for each substrate. Determined by capillary GC analysis using SUPELCO β-DEX 120.

<sup>b</sup> Determined by HPLC analysis using DAICEL CHIRALCEL OD-H.

Et<sub>2</sub>Zn to aldehydes.<sup>4a</sup> They used polymer-bound chiral ligand for the catalyst and gas chromatography with a chiral column for the analysis. The report and the successful results of consecutive reaction shown in Table 6 prompted us to apply Liscamp's methodology to our reaction system of fluorous solid extraction method. Thus we carried out the reaction by using five different aldehydes as substrates. The product mixture was first separated on FRP silica gel, and then analyzed by gas chromatography with a chiral column. The enantiomer pairs of the corresponding products were well separated under the GC conditions described in Section 3 and the results are summarized in Table 7 together with the data obtained by the separately performed experiments for each substrate.

As seen in Table 7, the chemical yields and the enantioselectivities were very similar to those obtained by the reaction of each substrate.

## 2. Conclusions

We have prepared fluorous chiral BINOLs, (R)-F<sub>13</sub>BINOL and (R)-F<sub>17</sub>BINOL, and examined the consecutive reactions by using fluorous–organic biphasic and fluorous solid phase extraction techniques. In the biphasic system, we obtained an enantioselectivity near maximum value that was attained in non-fluorous uniphase system and a good immobilization of the catalyst in the fluorous phase by tuning the fluorine atom content of the ligands. The FBINOLs were easily recovered by the solid phase extraction with FRP silica gel and

reusable without further purification to give almost the same chemical yield and enantioselectivity as the first use. The solid phase extraction technique was applied successfully to a simultaneous screening procedure.

## 3. Experimental

### 3.1. General

The melting point was determined by Yanagimoto micro-melting point apparatus and was uncorrected. The IR spectra were recorded on a Perkin–Elmer 1720-X FT-IR spectrometer. The <sup>1</sup>H NMR spectra were obtained on a JEOL JNM-A400 spectrometer in CDCl<sub>3</sub> with tetramethylsilane as an internal standard. The optical rotations were measured with a Perkin–Elmer 241 polarimeter. HPLC analysis was performed with Hitachi L-7100 flow system and L-7400 UV detector or JASCO CD-1595 CD detector using DAICEL CHIRALCEL OD or OD-H column. GC analysis was carried out on a Shimadzu GC-18APFsc gas chromatograph with SUPELCO β-DEX capillary column. Preparative TLC was run on a Wakogel B-5F and column chromatography was performed using a Wakogel C-300. Tetrahydrofuran (THF) was distilled prior to use from sodium benzophenone ketyl under argon. Hexane and toluene were distilled from sodium. FC-72 and benzotrifluoride were distilled from phosphorous pentoxide under argon. The fluorous reverse phase silica gel was prepared by Curran's method.<sup>5</sup>

### 3.1.1. (*R*)-6,6'-Bis[tris(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl)silyl]-2,2'-dihydroxy-1,1'-binaphthyl ((*R*)-F<sub>17</sub>BINOL).

(*R*)-6,6'-Dibromo-2,2'-dimethoxy-methoxy-1,1'-binaphthyl (640 mg, 1.20 mmol) was dissolved in THF (6 mL) and cooled to  $-78^{\circ}\text{C}$  under argon. *n*-Butyl lithium (1.59 mol dm<sup>-3</sup>, 1.7 mL, 2.7 mmol) was added dropwise, and the resulting yellow solution was stirred at that temperature for 50 min. A mixture of bromo tris(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptafluorodecyl)silane<sup>6</sup> (4.18 g, 2.88 mmol) in Et<sub>2</sub>O (50 mL) was added to the reaction mixture. After stirring at room temperature for 1.5 h, the reaction mixture was quenched with a saturated aqueous NH<sub>4</sub>Cl solution (30 mL). The volatiles were removed in vacuo and CHCl<sub>3</sub> (30 mL) was added. The mixture was washed with FC-72 (20 mL×5), the combined FC-72 layer was concentrated in vacuo to give a syrup. A mixture of the syrup, conc. HCl (10 mL) and THF (30 mL) was stirred vigorously at  $60^{\circ}\text{C}$  for 5 h. After addition of CH<sub>2</sub>Cl<sub>2</sub> (50 mL), the cloudy biphasic mixture was washed with FC-72 (20 mL×5). The combined FC-72 layer was concentrated in vacuo to give a syrup, which was purified on a silica gel column (hexane/Et<sub>2</sub>O=10:1 then 4:1) to afford (*R*)-F<sub>17</sub>BINOL as a colorless waxy solid (2.75 g, 76% overall yield): mp  $85-88^{\circ}\text{C}$ ;  $[\alpha]_{\text{D}}^{19} = -21.4^{\circ}$  (c 1.0, BTF); IR (KBr) 3501, 2974, 2947, 2912, 1615, 1470, 1242, 1205, 1147, 1072, 901, 705, 657 cm<sup>-1</sup>; <sup>1</sup>H NMR  $\delta$  1.15–1.30 (m, 6H,  $-\text{CH}_2\text{C}-$ ), 2.00–2.20 (m, 6H,  $-\text{CF}_2\text{CH}_2-$ ), 5.19 (s, 2H,  $-\text{OH}$ ), 7.22 (d, 2H, Ar-*H*, *J*=8.6 Hz), 7.33 (d, 2H, Ar-*H*, *J*=8.6 Hz), 7.47 (d, 2H, Ar-*H*, *J*=9.0 Hz), 8.00 (s, 2H, Ar-*H*), 8.05 (d, 2H, Ar-*H*, *J*=9.0 Hz); Anal. calcd for C<sub>80</sub>H<sub>36</sub>F<sub>102</sub>O<sub>2</sub>Si<sub>2</sub>: C, 31.78; H, 1.20; F, 64.10. Found: C, 31.81; H, 1.12; F, 64.00.

### 3.2. General procedure for the enantioselective addition of diethylzinc to aromatic aldehydes catalyzed by FBINOL in BTF

Ti(O-*i*Pr)<sub>4</sub> (341 mg, 1.20 mmol) was added to a solution of (*R*)-F<sub>13</sub>BINOL (485 mg, 0.200 mmol) in BTF (3 mL) under argon at room temperature. After stirring for 30 min, 1 M Et<sub>2</sub>Zn hexane solution (3.0 mL, 3.0 mmol) was added to the reaction mixture and the mixture was stirred for another 10 min. The reaction mixture was cooled to  $0^{\circ}\text{C}$  and the aldehyde (1.0 mmol) was added to the mixture. After stirring for 1 h at that temperature, the reaction mixture was quenched with 1N hydrochloric acid (6 mL) and extracted with Et<sub>2</sub>O (15 mL×4). The combined organic layer was washed with brine (10 mL×3), dried over anhydrous MgSO<sub>4</sub> and concentrated in vacuo. The residue was dissolved in Et<sub>2</sub>O (2 mL). ((1*H*,1*H*,2*H*,2*H*)-perfluorooctyl)-dimethylsilyl bound silica gel (1 g) was added to the solution, then the solvent was evaporated to dryness. The powder obtained was loaded on a column of ((1*H*,1*H*,2*H*,2*H*)-perfluorooctyl)dimethylsilyl bound silica gel (5 g) and then eluted successively with acetonitrile (30 mL) and FC-72 (40 mL). The acetonitrile fraction was evaporated in vacuo, and purified by preparative TLC (hexane/EtOAc=4:1) to give the corresponding alcohol. The enantiomeric excess of the product was determined by HPLC analysis using DAICEL CHIRALCEL OD or OD-H column or by GC analysis using SUPELCO  $\beta$ -DEX capillary column.<sup>2d,7</sup> (*R*)-F<sub>13</sub>BINOL was recovered almost

quantitatively from FC-72 fraction without a loss of optical purity.

### 3.3. Typical procedure for the enantioselective addition of diethylzinc to benzaldehyde catalyzed by FBINOL in FC-72/organic solvent biphasic system

Ti(O-*i*Pr)<sub>4</sub> (341 mg, 1.20 mmol) was added to a solution of (*R*)-F<sub>13</sub>BINOL (485 mg, 0.200 mmol) in FC-72 (5 mL) under argon at room temperature. After stirring for 30 min, 1 M Et<sub>2</sub>Zn hexane solution (3.0 mL, 3.0 mmol) was added to the reaction mixture and the mixture was stirred for another 10 min. The reaction mixture was cooled to  $0^{\circ}\text{C}$  and solution of benzaldehyde (110 mg, 1.03 mmol) in toluene (3 mL) was added to the mixture. After vigorously stirring for 2 h at that temperature, the organic phase was separated with a cannula and was quenched with 1N hydrochloric acid (6 mL). The mixture was extracted with Et<sub>2</sub>O (15 mL×4). The combined organic layer was washed with brine (10 mL×3), dried over anhydrous MgSO<sub>4</sub> and concentrated in vacuo. The residue was dissolved in Et<sub>2</sub>O (2 mL). ((1*H*,1*H*,2*H*,2*H*)-perfluorooctyl)-dimethylsilyl bound silica gel (1 g) was added to the solution, then the solvent was evaporated to dryness. The powder obtained was loaded on a column of ((1*H*,1*H*,2*H*,2*H*)-perfluorooctyl)dimethylsilyl bound silica gel (5 g) and then eluted successively with acetonitrile (30 mL) and FC-72 (40 mL). The acetonitrile fraction was evaporated in vacuo, and purified by preparative TLC (hexane/EtOAc=4:1) to give 1-phenyl-1-propanol (116 mg, 83% yield) in 82% ee as colorless oil. (*R*)-F<sub>13</sub>BINOL (50 mg 10%) was recovered from FC-72 fraction. To the fluorous phase Ti(O-*i*Pr)<sub>4</sub>, the Et<sub>2</sub>Zn solution and benzaldehyde solution were added, and the reaction was carried out in the same way.

### 3.4. Multisubstrate screening in catalytic asymmetric addition of diethylzinc to various aromatic aldehydes

Ti(O-*i*Pr)<sub>4</sub> (243 mg, 0.591 mmol) was added to a solution of (*R*)-F<sub>13</sub>BINOL (243 mg, 0.100 mmol) in BTF (1.5 mL) under argon at room temperature. After stirring for 30 min, 1 M Et<sub>2</sub>Zn hexane solution (1.5 mL, 1.5 mmol) was added to the reaction mixture and the mixture was stirred for another 10 min. The reaction mixture was cooled to  $0^{\circ}\text{C}$  and a mixture of benzaldehyde, 4-tolylaldehyde, 2-methoxybenzaldehyde, 4-chlorobenzaldehyde, and 4-bromobenzaldehyde in BTF (0.5 mL, each 0.2 mol L<sup>-1</sup>, total 0.50 mmol) was added to the reaction mixture. After stirring for 2 h at that temperature, the reaction mixture was quenched with 1N hydrochloric acid (6 mL) and extracted with Et<sub>2</sub>O (15 mL×4). The combined organic layer was washed with brine (10 mL×3), dried over anhydrous MgSO<sub>4</sub> and concentrated in vacuo. The residue was dissolved in Et<sub>2</sub>O (2 mL). ((1*H*,1*H*,2*H*,2*H*)-perfluorooctyl)-dimethylsilyl bound silica gel (1 g) was added to the solution, then the solvent was evaporated to dryness. The powder obtained was loaded on a column of ((1*H*,1*H*,2*H*,2*H*)-perfluorooctyl)dimethylsilyl bound silica gel (5 g) and then eluted successively with acetonitrile (30 mL) and FC-72 (40 mL). The acetonitrile fraction was evaporated in vacuo, and the residue was dissolved with CH<sub>2</sub>Cl<sub>2</sub>. *n*-Dodecane (17.0 mg, 0.100 mmol) was added to

the solution as an internal standard and the solution was used for GC analysis (SUPELCO  $\beta$ -DEX 120, He=1.0 mL min<sup>-1</sup>, DET=250°C, INJ=240°C, OVEN=110°C (1 min) to 170°C, 2°C min<sup>-1</sup>, Split=100:1):  $t_R$ =19.1 min for (*R*)-1-phenyl-1-propanol,  $t_R$ =19.4 min for (*S*)-1-phenyl-1-propanol,  $t_R$ =22.6 min for (*R*)-1-(4-methylphenyl)-1-propanol,  $t_R$ =23.2 min for (*S*)-1-(4-methylphenyl)-1-propanol,  $t_R$ =28.9 min for (*S*)-1-(2-methoxyphenyl)-1-propanol,  $t_R$ =29.8 min for (*R*)-1-(2-methoxyphenyl)-1-propanol,  $t_R$ =30.9 min for (*R*)-1-(4-chlorophenyl)-1-propanol,  $t_R$ =31.5 min for (*S*)-1-(4-chlorophenyl)-1-propanol,  $t_R$ =37.8 min for (*R*)-1-(4-bromophenyl)-1-propanol, and  $t_R$ =38.6 min for (*S*)-1-(4-bromophenyl)-1-propanol.

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