Pergamon

Tetrahedron 58 (2002) 3951–3961

TETRAHEDRON

Asymmetric catalytic carbon–carbon bond formations in a fluorous biphasic system based on perfluoroalkyl-BINOLs

Yuan Tian, Qing Chuan Yang, Thomas C. W. Mak and Kin Shing Chan*

Department of Chemistry, Open Laboratory of Chirotechnology of the Institute of Molecular Technology for Drug Discovery and Synthesis (University Grants Committee Area of Excellence Scheme, Hong Kong), The Chinese University of Hong Kong, Shatin New Territories, Hong Kong, People's Republic of China

Received 20 November 2001; revised 23 January 2002; accepted 30 January 2002

Abstract—Optically active 1,1′-binaphthols (BINOLS) substituted at the 4,4′; 6,6′ and 4,4′,6,6′ positions with perfluoroalkyl groups have been synthesized. Asymmetric diethylzinc and triethyl aluminum addition to aryl aldehydes in a fluorous biphasic system catalyzed by these perfluoroalkyl-BINOL–titanium complexes have been accomplished with good enantiomeric excess obtained.

1. Introduction

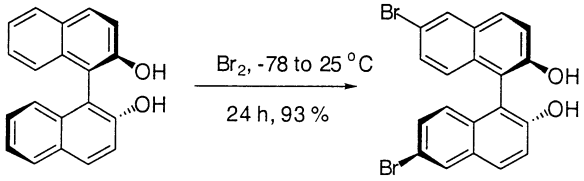
Homogeneous asymmetric catalysis has been applied in countless bench-scale and commodity chemical transformations. However, for chiral catalysts, which are often expensive and not easy to be prepared, there remains a need for improving their recovery methodologies. In 1994, a new type of two-phase catalytic system–fluorous biphasic catalysis (FBC) was developed,[1] based on the temperature-dependent phase separation of common organic and perfluorous solvents. A prerequisite is the use of a perfluorinated catalyst that shows preferential solubility in the perfluorous phase. Nowadays, an increasing number of academic and industrial groups are working on the design and application of perfluorinated catalysts.[2] To our knowledge, however, only a few papers have been reported describing asymmetric fluorous biphasic catalysis which include carbon–carbon bond forming reaction,[3] protonation[4] and epoxidation.[5]

We have reported the asymmetric carbon–carbon bond formation in a fluorous biphasic system (AFBC) catalyzed by a titanium perfluoroalkyl-BINOL complex[6] and now disclose the full details of our investigation.

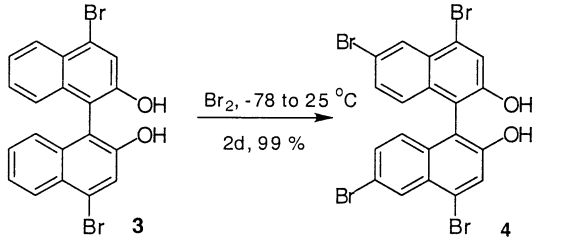
2. Results and discussion

2.1. Synthesis of ligands

Perfluorobutyl and perfluorooctyl BINOL derivatives substituted at the 4,4′; 6,6′ and 4,4′,6,6′ positions were prepared by perfluoroalkylation of the corresponding bromo-BINOL with Cu/R_fI in DMSO at elevated temperature of 90 to 160°C.[7] The bromo-BINOLs were prepared according to literature methods. Bromination of BINOL **1** and 4,4′-dibromo-BINOL **3** at −78°C[8] gave 6,6′-dibromo-BINOL **2** and 4,4′, 6, 6′-tetrabromo-BINOL **4**[9] in excellent yields (Eqs. (1) and (2)). The bromination of optically active (*R*)- and (*S*)-**1** gave (*R*)- and (*S*)-**2** with excellent optical purity of over 99% ee.



(*R*)-1 (*R*)-2 (1)



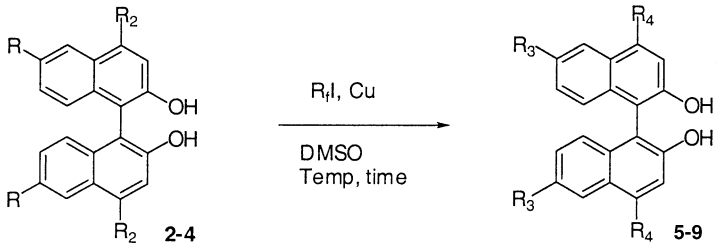
3 4 (2)

Copper-mediated cross-coupling reactions of (*R*)- and (*S*)-**2**

Keywords: asymmetric fluorous biphasic catalysis; perfluoroalkyl-binaphthols.

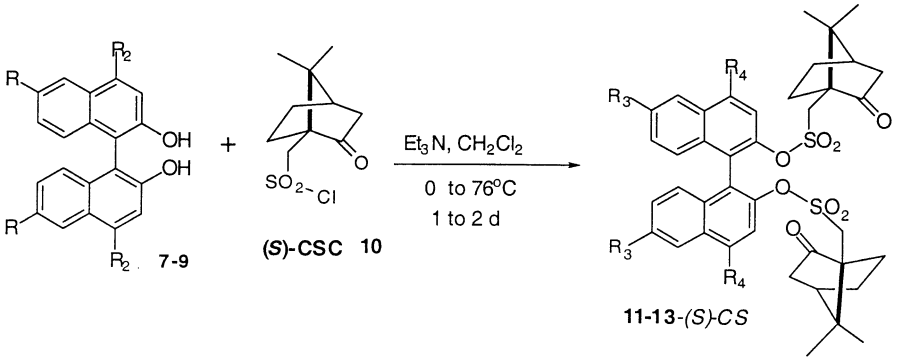
* Corresponding author. Tel.: +852-2609-6376; fax: +852-2603-5057; e-mail: ksc@cuhk.edu.hk

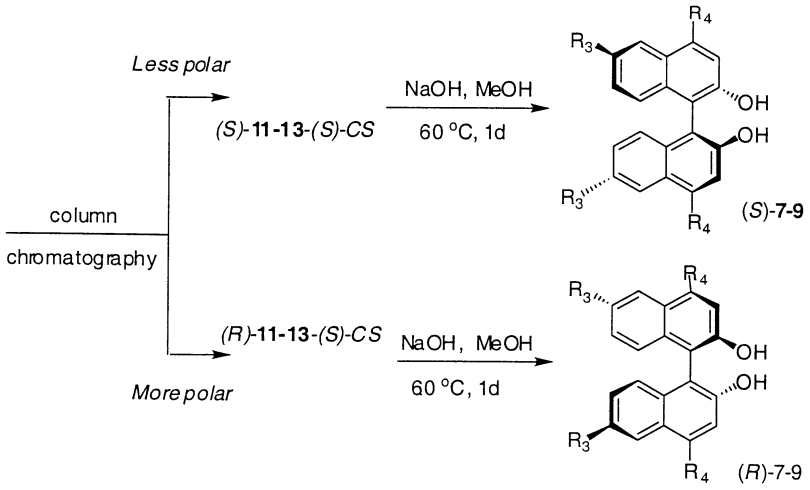
0040–4020/02/$ - see front matter
PII: S0040-4020(02)00218-1



R		R_2	Temp	time/d		R_3	R_4	%yield	% ee
(*S*)-**2**	Br	H	90 °C	5	(*S*)-**5**	C_4F_9	H	54	> 99
(*R*)-**2**	Br	H	90 °C	5	(*R*)-**5**	C_4F_9	H	52	> 99
(*S*)-**2**	Br	H	90 °C	8	(*S*)-**6**	C_8F_{17}	H	21	
3	H	Br	120 °C	4	**7**	H	C_4F_9	50	
4	Br	Br	120 °C	5	**8**	C_4F_9	C_4F_9	36	
4	Br	Br	160 °C	3	**9**	C_8F_{17}	C_8F_{17}	46	

Scheme 1.





R_3	R_4		Sulphonation %yield		Saponification %yield (% e.e.)		
H	C_4F_9	**11**	85	(*S*)-**7**	82	(*R*)-**7**	83
C_4F_9	C_4F_9	**12**	83	(*S*)-**8**	75	(*R*)-**8**	71
C_8F_{17}	C_8F_{17}	**13**	76	(*S*)-**9**	85	(*R*)-**9**	77

Scheme 2.

Table 1. Chemical shifts of the diastereomers (*S*)- and (*R*)-**11**–**13**-(*S*)-CS (ppm)

Compound	Methylene-H		$\Delta\delta$	$\delta_S-\delta_R$	Methyl-H		$\Delta\delta$	$\delta_S-\delta_R$
(*S*)-**11**-(*S*)-CS	3.00	2.58	0.42	−0.39	0.79	0.55	0.24	0.14
(*R*)-**11**-(*S*)-CS	3.39	2.51	0.88	0.07	0.65	0.54	0.11	0.01
(*S*)-**12**-(*S*)-CS	3.16	2.76	0.40	−0.33	0.82	0.61	0.21	0.13
(*R*)-**12**-(*S*)-CS	3.49	2.63	0.86	0.13	0.69	0.58	0.11	0.03
(*S*)-**13**-(*S*)-CS	3.17	2.77	0.40	−0.32	0.81	0.60	0.21	0.13
(*R*)-**13**-(*S*)-CS	3.49	2.64	0.85	0.13	0.68	0.58	0.10	0.02

with perfluorobutyl iodide[7] in DMSO at 90°C for 5 days yielded (*R*)- and (*S*)-**5** in about 50% yield with excellent optical purity as determined by chiral HPLC on a Diacel OD-H column (Scheme 1). The perflurooctylation of (*S*)-**2** required a longer time of 8 days at 90°C to give (*S*)-**6** with a poorer yield of 21%. The optical purity (*S*)-**6** was not determined as racemic forms of **6** were not resolvable by chiral HPLC (Diacel OD and AD columns) and (*S*)-**6** was assumed to be optically pure.

Since the copper-mediated cross-coupling reactions required elevated temperature which would ruin the optical purity of the starting bromo-BINOLs, the perfluoroalkylations of **3** and **4** were carried out using racemic mixtures. Furthermore, the optical resolution of **3** and **4** were not very practical due to their poor solubility in organic solvents[9] and our unsuccessful diastereomeric resolution by fractional recrystallization with *N*-benzylcinchonidium chloride,[10] $H_3B{\cdot}SMe_2$-quinine,[11] and H_3BO_3-proline.[12] The perfluorobutylation and perfluorooctylation of **3** and **4** required a higher temperature of 120°C to give satisfactory yields of **7**–**9**.

2.2. Optical resolution and determination of absolute configuration of ligands

The resolution of optically active ligands of **7**–**9** were achieved by sulphonation of racemic **7**–**9** with (*S*)-camphorsulphonyl chloride[13] to yield **11**–**13**. Careful chromatographic separation of **11**–**13** yielded the diastereomerically pure compounds which were further converted to the optically pure **7**–**9** by saponification (Scheme 2). Since chiral HPLC using Diacel OD or AD columns was not able to resolve the racemates **7**–**9**, the optical purities were determined by ^{1}H NMR spectroscopy on the re-formed camphorsulphonates.

The absolute configuration of **7**–**9** were determined based on four kinds of physical evidence: relative chromatographic mobility, proton chemical shift correlation, X-ray diffraction studies of BINOL camphor sulphonate (*S*)-**12**-(*S*)-CS and circular dichorism (CD) of BINOLs.

The proton NMR spectra of the diastereomeric mixtures of **11**–**13**-(*S*)-CS exhibited two AX systems arising from the diastereotopic methylene groups adjacent to the sulfonyl moiety and two pairs of singlet peaks contributing to the diastereotopic methyl groups of camphor with their relative integrations in the ration of 1:1, indicating the relative percentage of the two diastereomers. Chow, in the study of the absolute configuration of BINOLs, has concluded that 'The axis of all of the faster running isomers (less polar diastereomers) BINOLs had an (*S*)-configuration while those of the slower running isomers (more polar diastereomers) BINOLs had an (*R*)-configuration'.[14] For the less polar diastereomer (*S*)-**11**-(*S*)-CS, the methylene group adjacent to the sulfonyl moiety appeared as an AX system (J=14.8 Hz) at 3.00 and 2.58 ppm and the two methyl groups appeared at 0.55 and 0.79 ppm as a pair of singlet peaks. The chemical shift difference between these AX system peaks was 0.42 ppm. On the contrary, for the more polar (*R*)-**11**-(*S*)-CS, the chemical shifts of methylene group were 3.39 and 2.51 ppm, and those of two methyl groups were 0.54 and 0.65 ppm. The chemical shift difference between these AX system peaks was 0.88 ppm. In addition, comparing with the two spectra of (*S*)-**11**-(*S*)-CS and (*R*)-**11**-(*S*)-CS, most of the chemical shifts of aromatic protons of (*S*)-**11**-(*S*)-CS were further down field than those of (*R*)-**11**-(*S*)-CS, the differences range from 0.004 to 0.058 ppm (Table 1). Similar chromatographic and spectral characteristics were also observed in NMR spectra of **12**- and **13**-(*S*)-CS.

The structure of the less polar 4,4′,6,6′-tetraperfluorobutyl-BINOL camphorsulfonate (*S*)-**12**-(*S*)-CS was characterized by single crystal X-ray diffraction analysis. In this molecule, the absolute configuration of camphor was confirmed to be *S*, due to the configuration of (*S*)-(+)-camphorsulfonyl chloride used. Based on the IUPAC tentative rule for the nomenclature of organic chemistry,[15] the absolute configuration of the chiral axis in compound (*S*)-**12**-(*S*)-CS was confirmed to be *S*. The torsion angle of C1–C8–C18–C11 was found to be 97.6°. The crystal structure of (*S*)-**12**-(*S*)-CS is highly disordered due to the four perfluorobutyl chains.

CD spectra of optically active 4,4′-diperfluoroalkyl- and 4,4′,6,6′-tetraperfluoroalkyl-BINOLs revealed that all of the less polar diastereomeric camphorsulfonates related perfluoroalkyl-BINOLs of (*S*)-**7**–**9** exhibited negative Cotton effects at λ=208–225 nm and positive Cotton effects at λ=238–246 nm. On the contrary, more polar diastereomeric camphorsulfonates related perfluoroalkyl-BINOLs (*R*)-**7**–**9** had corresponding mirror-image CD spectra with positive Cotton effects at λ=208–225 nm and negative Cotton effects at λ=238–246 nm. The absolute configurations of (*S*)-**7**–**9** were further confirmed to be *S* by their CD spectra based on the comparison with the spectra of other optically active BINOL derivatives.[14]

2.3. Asymmetric fluorous biphasic catalytic diethylzinc addition

The diethylzinc addition of aldehydes is classical in asymmetric catalysis and serves as the testing ground for the efficiency of a newly developed catalytic system.

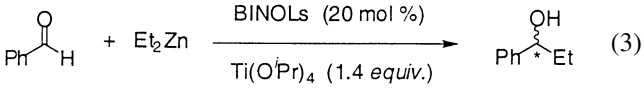
Table 2. The result of asymmetric diethylzinc addition to benzaldehyde catalyzed by BINOL derivatives in dichloromethane

Entry	Ligand	Conversion[a]	ee (%)	Conf.[b]
1	(*R*)-**1**	99[a]	88[b]	*R*
2[c]	(*R*)-**1**	100[c,d]	92[c,d]	*R*
3	(*R*)-**5**	97[a]	77[b]	*R*
4	(*S*)-**7**	99[a]	79[b]	*S*
5	(*S*)-**8**	97[a]	70[b]	*S*

[a] Determined by proton NMR.
[b] Determined by HPLC on a Chiracel OD-H column.
[c] Data were from Ref. 17.
[d] Determined by GLC.

Ti–BINOL complex has been used in this catalysis to give good to excellent yields and good enantioselectivities.[16,17] The application of the newly synthesized optically pure perfluoroalkyl-BINOLs as chiral ligands system has been studied in Ti–BINOL catalyzed reaction in fluorous biphasic version.

Initially, monophasic experiments were carried out in dichloromethane to test the effectiveness of chiral induction. Optically pure perfluoroalkyl-BINOLs (20 mol%) was treated with 1.4 mol equiv. of titanium tetraisopropoxide at room temperature for 30 min in dichloromethane to form the co-catalyst, which promoted the addition of diethylzinc (3.0 mol equiv.) to benzaldehyde at 0°C for 5 h to afford 1-phenyl-propanol (Eq. (3), Table 2). Optically pure (*R*)-BINOL (*R*)-**1**, (*R*)-6,6′-diperfluorobutyl-BINOL (*R*)-**5**, (*S*)-4,4′-diperfluorobutyl-BINOL (*S*)-**7** and (*S*)-4,4′,6,6′-tetraperfluorobutyl-BINOL (*S*)-**8** have been employed as the chiral ligands. The results showed that all perfluoroalkyl-BINOLs were active in the catalytic diethylzinc addition of benzaldehyde. The enantioselectivities of the reactions catalyzed by (*R*)-**5** and (*S*)-**7** were similar (entries 3 and 4) and a little higher than that by 4,4′,6,6′-tetraperfluorobutyl-BINOL **8** (entry 5). All perfluoroalkyl-BINOLs exhibited a slightly poorer enantioselectivities than the parent BINOL **1**.



(3)

When (*R*)-BINOL derivatives were used as the ligands, the absolute configurations of obtained products were *R*, while (*S*)-BINOL derivatives gave (*S*)-products. Among BINOL analogs, the substituents at 4 or 6 positions should not affect the absolute configuration of product during the same reaction system. Therefore, the absolute configurations of **5**–**8** were further confirmed.

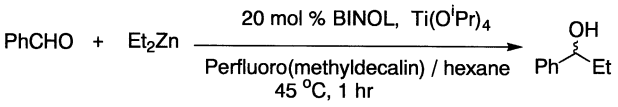
Table 3. Partition coefficients of perfluoroalkyl-BINOLs in organic and fluorous solvent

BINOL	Hexane/ perfluoro-(methyldecalin)[a]
6,6′-Diperfluorobutyl-BINOL **5**	1:2
4,4′,6,6′-Tetraperfluorobutyl-BINOL **8**	1:15
6,6′-Diperfluorooctyl-BINOL **6**	1:23
4,4′,6,6′-Tetraperfluorooctyl-BINOL **9**	1:53

[a] A mixture of 50 mg perfluoroalkyl-BINOL in perfluoro(methyldecalin) (1 mL) and hexane (1 mL) was heated to 45°C to give a clear solution. Then the solution was cooled down to 0°C to obtain a biphasic mixture. The two phases were separated and the solvents were evaporated in vacuo. The contents of the BINOLs in each phase were determined by weighing the residue.

With the optically active perfluoroalkyl-BINOLs in hand, the fluorous biphasic catalysis was attempted. Perfluoro-(methyldecalin) and hexane were used as the fluorous and organic solvent, respectively. The approximate partition coefficients of perfluoroalkyl-BINOLs which contain the different number of fluorocarbons were determined[18] and the results are shown in Table 3. The compounds which contained more perfluorocarbons, are more soluble in fluorous solvent but less soluble in hexane.

The asymmetric catalytic diethylzinc additions to benzaldehyde in fluorous biphasic system using perfluoroalkyl-BINOLs as chiral ligands were carried out in a mixture of perfluoro(methyldecalin) and hexane (Eq. (4), Table 6). Optically pure perfluoroalkyl-BINOL (20 mol%) was dissolved in the fluorous solvent, $Ti(O^iPr)_4$ (0.5 M solution in hexane, 1.4 equiv.) was then added to form a two-layer system at room temperature. Heating the mixture to 45°C gave a deep red or orange one-layer solution. Then, Et_2Zn (1.0 M solution in hexane, 3.0 equiv.) was added and the reaction mixture was stirred at 45°C for 15 min. The color of the reaction mixture changed into dark gray. After freshly distilled benzaldehyde (1.0 equiv.) was added, the mixture changed yellow in color immediately. The reaction mixture was stirred at 45°C as a homogeneous phase for another 30 min. After the reaction mixture was cooled down to 0°C, a two-layer mixture formed. The light color upper layer was withdrawn with a syringe and added into 10% HCl solution. 1-Phenylpropanol was obtained by usual work up. To the deep color bottom layer, a new batch of $Ti(O^iPr)_4$ (0.5 M solution in hexane, 1.4 equiv.) was added. The second and subsequent reaction cycle was then carried out similarly (Table 4).



(4)

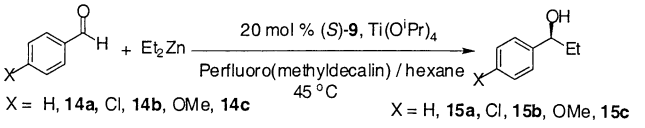
For the parent BINOL **1**, which has no fluorocarbon, after the first reaction run, BINOL was removed from the reaction system since BINOL prefers to dissolve in hexane rather than fluorous solvent. Therefore, the enantioselectivity of the second run was almost lost. When the ligand was changed to 6,6′-diperfluorobutyl-BINOL (*R*)-**5**, which contained eight fluorocarbons and whose partition coefficient in hexane/perfluoro(methyldecalin) is only 1:2, the enantiomeric excess of product decreased from 70% in the first run to 28% in the second run and then to 5% in the third run. When 6,6′-diperfluorooctyl-BINOL (*S*)-**6** was used, which contains 16 fluorocarbons and whose partition coefficient in hexane/perfluoro(methyldecalin) is 1:23, the decrease of % ee of product along with the reaction runs was a little slower than that of **1** and **5**. After six runs, the enantioselectivity was lost. 4,4′,6,6′-Tetraperfluorobutyl-BINOL (*S*)-**8**, which has 16 fluorocarbons, behaved

Table 4. AFBC of diethylzinc addition to benzaldehyde catalyzed by optically pure perfluoroalkyl-BINOL–titanium complexes

Cpd	(*R*)-**1**		(*R*)-**5**		(*S*)-**6**		(*S*)-**8**		(*S*)-**9**	
Run	Con.[a]	ee (%)[b]	Con.[a]	ee (%)[b]	Con.[a]	ee (%)[c]	Con.[a]	ee (%)[c]	Con.[a]	ee (%)[c]
1	98	68	99	70	99	64	98	41	69[d]	54
2	71	5	98	28	99	58	99	53	80	57
3	–	–	57	5	99	41	99	31	79	58
4	–	–	–	–	83	15	95	15	76	55
5	–	–	–	–	51	4	76	7	80	60
6	–	–	–	–	–	–	63	3	79	58
7	–	–	–	–	–	–	61	3	80	57
8									79	56
9									79	55
10									73[e]	25
11									51[e,f]	5

[a] Conversion determined by HPLC on a Chiracel OD–H column using *para*-methoxy-phenethyl alcohol as the internal standard.
[b] The product was in (*R*)-configuration.
[c] The product was in (*S*)-configuration.
[d] The reaction temperature was 40°C, the reaction was not homogeneous.
[e] Fresh $Ti(O^iPr)_4$ was not added.
[f] The reaction was carried out at 45°C for 14 h.

similarly. When 4,4′,6,6′-Tetraperfluorooctyl-BINOL (*S*)-**9**, which contains 32 fluorocarbons and whose partition coefficient [hexane/perfluoro(methyldecalin)] is more than 1:50, was tested in AFBC, to our delight, the enantiomeric excess of product as well as the chemical yields were maintained after nine reaction runs, no significant decrease along with the reaction run was observed (Table 4). The critical temperature for this biphasic system was 45°C, lower chemical yield and enantioselectivity were obtained when the reaction temperature was lower than 45°C as the reaction proceeded heterogeneously (Run 1). The addition of fresh titanium complex in each run was necessary to maintain the reactivity and selectivity of the catalysis.[17] When the fresh titanium complex was not added, the reaction rate was slower, and the % ee of product decreased dramatically (runs 10 and 11).



(5)

Other aryl aldehydes also underwent Et_2Zn addition in this fluorous biphasic system catalyzed by (*S*)-**9** (Table 5, Eq. (5)). For the more electron-deficient 4-chlorobenzaldehyde, the reaction was a little faster than that with benzaldehyde and was completed in 45 min according to TLC analysis with a quantitative yield of **15b** being obtained. On the contrary, the reaction of the more electron-rich 4-methoxybenzaldehyde was slower. The yield of **15c** was around 90% after 2 h. The FBC phenomenon has been observed in both cases. There were no significant changes in the chemical yield as well as in the enantioselectivities of products after three reaction cycles.

Table 5. AFBC of Et_2Zn addition to aryl aldehydes catalyzed by (*S*)-**9**

Run	**15b**[a]		**15c**[b]	
	% Yield[c]	ee (%)[d]	% Yield[e]	ee (%)[d]
1	99	54	91	37
2	98	51	92	41
3	99	51	91	40

[a] Reaction time was 45 min.
[b] Reaction time was 2 h.
[c] Determined by chiral HPLC using 4-methoxyphenethyl alcohol as the internal standard.
[d] The major isomer had the (*S*) configuration.
[e] Determined by chiral HPLC using 3-nitrobenzyl alcohol as the internal standard.

From the above results, the number of fluorocarbon is important to ensure the reusability of the ligands in FBC. Optically pure 4,4′,6,6′-tetraperfluorooctyl-BINOL **9**, which contains 32 fluorocarbons, has been found a good ligand in titanium catalyzed asymmetric diethylzinc addition to aromatic aldehydes in fluorous biphasic system.

2.4. Asymmetric fluorous biphasic catalytic triethylaluminum addition

In 1997, the first example of an asymmetric catalytic ethylation of aldehydes with triethylaluminum in the presence of a chiral titanium alkoxide catalyst prepared from $Ti(O^iPr)_4$ and optically pure BINOL was reported by Chan.[17a] In comparison with asymmetric catalytic diethylzinc addition, the reaction conditions were quite similar and the enantioselectivities were a little lower. Therefore, studies extended to the fluorous biphasic system were carried out.

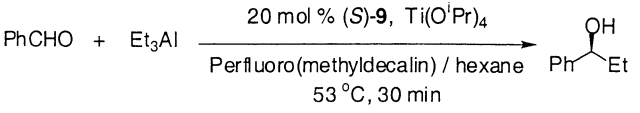
Optically pure (*S*)-4,4′,6,6′-tetraperfluorooctyl-BINOL (*S*)-**9** was used as the chiral ligands in perfluoro(methyldecalin)/hexane biphasic system (Eq. (6), Table 6). Although the mixture of (*S*)-**9** (20 mol%) in fluorous solvent and $Ti(O^iPr)_4$ (0.5 M solution in hexane) was heated to 45°C to become homogeneous deep orange solution, when Et_3Al (1.0 M solution in hexane, 3.0 equiv.) was added, the mixture could not remain as one-layer solution at 45°C any more. After the addition of benzaldehyde, the reaction proceeded heterogeneously at 45°C for 30 min and gave 59% yield and 63% ee (Run 1). When the temperature was increased to 53°C, the reaction system became homogeneous and the yields and ees of product were improved to

Table 6. AFBC of Et_3Al addition to benzaldehyde catalyzed by (*S*)-**9**-titanium complex

Run	Yield (%)[a]	ee (%)[b]
1[c]	59	63
2	76	77
3	88	79
4	82	77
5	79	82
6	82	80
7[d]	47	58
8[e]	65	10
9[e]	78	0

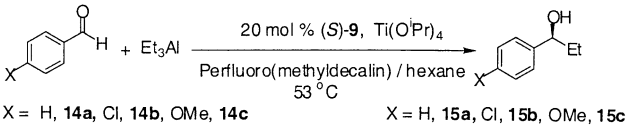
[a] Determined by chiral HPLC using *para*-methoxy-phenethyl alcohol as the internal standard.
[b] The product was in (*S*)-configuration.
[c] The reaction temperature was 45°C, the reaction was not homogeneous.
[d] The reaction was carried out at 25°C for 20 h.
[e] Fresh $Ti(O^iPr)_4$ was not added.

76 and 77%, respectively (Run 2). The following reaction runs were therefore carried out at 53°C and gave the similar results. No significant difference along with the reaction run was observed during six runs. Therefore, chiral ligand (*S*)-**9** was demonstrated to be a good ligand for AFBC triethylaluminum addition of benzaldehyde. Moreover, the ees of product were a little higher than that in the AFBC diethylzinc addition using the same ligand. When the temperature was decreased to room temperature (25°C), the reaction was completed after 20 h, low yield and ee were obtained (Run 7). If the fresh titanium complex was not added, the enantioselectivities of the reaction was lost (runs 8 and 9) (Table 6).



(6)

Similarly, other aromatic aldehydes were also used as the substrates in AFBC triethylaluminum addition and the results are shown in Table 7. The procedure was the same as the reaction of benzaldehyde. For the electron-deficient 4-chlorobenzaldehyde, the yield was similar and the enantioselectivity was lower than that of benzaldehyde. However, for the electron-rich 4-methoxy-BINOL, after 2 h reaction at 53°C, only 10% product was obtained. The ee of product was around 38%. Comparing with AFBC diethylzinc addition, for the chloro- or methoxy-benzaldehydes, the enantioselectivities were similar or slightly lower than that of benzaldehyde.



(7)

3. Conclusion

The asymmetric catalytic carbon–carbon bond formation in fluorous biphasic system based on BINOL chemistry has been developed. A series of perfluoroalkyl-BINOLs has been investigated in AFBC diethylzinc and triethylaluminum addition to aromatic aldehydes. The number of fluorocarbons in the ligand molecules has been found to be very important to ensure the reusability of the ligands in FBC. Optically pure 4,4′,6,6′-tetraperfluorooctyl-BINOL **9**, which contains 32 fluorocarbons and whose partition coefficient in hexane/perfluoro(methyldecalin) is 1:53, has been found to be an effective ligand in asymmetric diethylzinc and triethylaluminum additions to aromatic aldehydes in fluorous biphasic system.

4. Experimental

4.1. General

Melting points were measured on an Electrothermal melting apparatus and were uncorrected. ^1H NMR spectra were recorded on a Bruker DPX 300 (300 MHz) spectrometer. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm), or with tetramethylsilane (TMS, δ 0.00 ppm) as internal standard. Coupling constants (J) were reported in Hertz (Hz). ^{13}C NMR spectra were obtained on a Bruker DPX 300 (75 MHz) spectrometer and were referenced to $CDCl_3$ (δ 77.00 ppm). Mass spectra (EIMS and FABMS) were recorded on a HP 5989B Mass Spectrometer. High-resolution mass spectra (HRMS) were recorded on a Bruker APEX 47e FT-ICR Mass Spectrometer (ESI-MS). Specific rotation were measured on a Perkin–Elmer 341 polarimeter. The HPLC analyses were conducted on a Waters 486 system using a Daicel chiral column. CD spectra were recorded on a JASCO J-20C spectropolarimeter. Elemental Analysis was performed by the Medac Ltd., Department of Chemistry, Brunel University, United Kingdom.

Table 7. AFBC of Et_3Al addition to aryl aldehydes using (*S*)-**9**-titanium complex

Reaction	Benzaldehyde[a]		4-Cl-Benzaldehyde[a]		4-MeO-benzaldehyde[b]	
Run	Yield (%)[c]	ee (%)[d]	Yield (%)[c]	ee (%)[d]	Yield (%)[e]	ee (%)[d]
1	59	63	66	48	10	38
2	76	77	67	52	13	37
3	88	79	–	–	–	–

[a] The reaction was carried out at 53°C for 30 min.
[b] The reaction was carried out at 53°C for 2 h.
[c] Determined by chiral HPLC using *para*-methoxy-phenethyl alcohol as the internal standard.
[d] The product was in (*S*)-configuration.
[e] Determined by chiral HPLC using 3-nitrobenzyl alcohol as internal standard.

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl immediately prior to use. Hexane was distilled over calcium chloride. Toluene was distilled from sodium and dichloromethane was distilled over calcium hydride. Thin layer chromatography was performed on Merck precoated silica gel 60 F_{254} plates. Silica gel (70–230 and 230–400 mesh) was used for column chromatography.

4.1.1. Preparation of (*R*)-6,6′-diperfluorobutyl-1,1′-binaphthyl-2,2′-diol (*R*)-5. A mixture of optically pure (*R*)-6,6′-dibromo-BINOL (**2**)[20] (2.22 g, 5.0 mmol), copper bronze (3.2 g, 50 mmol) and perfluorobutyl iodide (6.92 g, 3.44 mL, 20 mmol) in anhydrous DMSO (50 mL) was degassed three times, and then heated to 90°C for 5 days. After cooling down, ethyl acetate (150 mL) was added and the mixture was filtered through Celite, the filtrate was washed with 10% HCl, water, brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane=1:6) to give (*R*)-**5** (1.25 g, 52%) as a white solid. Mp 65–66°C; R_f=0.28 (ethyl acetate/hexane/dichloromethane=1:3:0.2); $[\alpha]_D^{20}=-25.7°$ (*c* 1.0, $CHCl_3$); optical purity >99% ee {chiral Daicel OD-H column (0.46×15 cm), hexane/2-propanol=9:1, flow rate: 1.0 mL/min, T_R=5.51 min}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.30 (brs, 2H), 7.22 (d, 2H, *J*=8.9 Hz), 7.45 (d, 2H, *J*=8.8 Hz), 7.51 (d, 2H, *J*=9.0 Hz), 8.11 (d, 2H, *J*=9.0 Hz), 8.18 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 110.62, 115.80 (q, *J*=31.7 Hz), 119.29, 124.53, 124.61, 124.77, 128.33, 132.69, 135.05, 154.73; EIMS: *m/z* (relative intensity) 723 ($[M+H]^+$, 82), 704 (7), 553 (100), 525 (7), 485 (5), 333 (12); FABMS: *m/z* (relative intensity) 722 (M^+, 100), 704 (8), 694 (2), 584 (2), 569 (2), 553 (59); HRMS (M^+) Calcd for $C_{28}H_{12}O_2F_{18}$ 722.0544. Found 722.0513.

4.1.2. Preparation of (*S*)-6,6′-diperfluorobutyl-1,1′-binaphthyl-2,2′-diol (*S*)-5. The procedure was the same as that for the preparation of (*R*)-isomer. Mp 60–63°C; $[\alpha]_D^{20}=+26.1°$ (*c* 0.5, $CHCl_3$); optical purity >99% ee (HPLC: Daicel OD-H column (0.46×15 cm), hexane/2-propanol=9:1, flow rate: 1.0 mL/min, T_R=3.61 min).

4.1.3. Preparation of (*S*)-6,6′-diperfluorooctyl-1,1′-binaphthyl-2,2′-diol (*S*)-6. A mixture of optically pure (*S*)-6,6′-dibromo-BINOL **2**[20] (2.22 g, 5.0 mmol), copper bronze (3.2 g, 50 mmol) and perfluorobutyl iodide (10.9 g, 5.3 mL, 20 mmol) in anhydrous DMSO (50 mL) was degassed three times, and then heated to 90°C for 8 days. After the reaction mixture was cooled down to room temperature, ethyl acetate (200 mL) was added and the mixture was filtered through Celite. The filtrate was washed with 10% HCl, water, brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane/dichloromethane=1:8:1) to give (*S*)-**6** (1.2 mg, 21%) as a yellow solid. Mp 137–139°C; R_f=0.36 (ethyl acetate/hexane/dichloromethane=1:3:0.2); $[\alpha]_D^{20}=+24.4°$ (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 5.26 (br, 2H), 7.23 (t, 2H, *J*=8.8 Hz), 7.45 (d, 2H, *J*=9.2 Hz), 7.48 (d, 2H, *J*=9.2 Hz), 8.10 (d, 2H, *J*=9.0 Hz), 8.18 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 110.46, 110.92, 111.38, 116.09, 119.04, 119.29, 124.55, 124.74, 125.01, 125.65, 127.23, 128.33, 130.89, 132.56, 132.75, 134.98, 154.73; SIMS: 1122 (M^+); Anal. Calcd for $C_{36}H_{12}F_{34}O_2$: C, 38.52; H, 1.08. Found: C, 38.78; H, 1.33.

4.1.4. Preparation of racemic 4,4′-diperfluorobutyl-1,1′-binaphthyl-2,2′-diol (7). A mixture of 4,4′-dibromo-BINOL **3**[21] (111 mg, 0.25 mmol), copper bronze (160 mg, 2.5 mmol) and perfluorobutyl iodide (346 mg, 0.18 mL, 1.0 mmol) in anhydrous DMSO (3 mL) was degassed three times, and then heated to 120°C for 4 days in a Telfon stopper flask. After cooling down, ethyl acetate (10 mL) was added and the mixture was filtered through Celite. The filtrate was washed with 10% HCl, water, brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane/dichloromethane=1:10:0.2) to give **7** (90 mg, 50%) as a yellow oil. R_f=0.59 (ethyl acetate/hexane/dichloromethane=1:4:0.2); ^1H NMR (300 MHz, $CDCl_3$) δ 5.43 (brs, 2H), 7.20 (d, 2H, *J*=8.3 Hz), 7.41 (dt, 2H, *J*=0.7, 7.1 Hz), 7.52 (td, 2H, *J*=1.3, 7.2 Hz), 7.77 (s, 2H), 8.29 (d, 2H, *J*=8.5 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 115.63, 115.76, 117.26, 119.45, 120.34 (t, *J*=10.3 Hz), 124.86, 125.43, 125.47, 125.51, 125.56, 125.60, 125.64, 125.88, 126.13, 128.30, 128.33, 133.93, 151.02; FABMS: *m/z* (relative intensity) 723 ($[M+H]^+$, 100), 704 (3), 553 (30); HRMS (M^+) Calcd for $C_{28}H_{12}O_2F_{18}$ 722.0544. Found 722.0503.

4.1.5. Preparation of diastereomeric 2,2′-di-[(1*S*)-camphor-10-sulfonyl]-4,4′-diperfluorobutyl-1,1′-binaphthyl (*S*)-11-(*S*)-CS and (*S*)-11-(*S*)-CS.[14b] To a solution of 4,4′-diperfluorobutyl-BINOL **7** (680 mg, 0.94 mmol) and (1*S*)-camphor-**10**-sulfonyl chloride **10** (948 mg, 3.8 mmol) in dry CCl_4 (15 mL) at 0°C, triethylamine (476 mg, 0.66 mL, 4.7 mmol) was added. The yellow solution was stirred overnight. Water (15 mL) was added and the reaction mixture was extracted with CCl_4. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane=1:8) to give a mixture of diastereomers **11**-(*S*)-CS (922 mg, 85%) as a white solid. SIMS: *m/z* 1151 ($[M+H]^+$).

Careful column chromatography (hexane/dichloromethane=3:5) gave less polar diastereomer (*S*)-**11**-(*S*)-CS. Mp 78–80°C; R_f=0.33 (hexane/dichloromethane=3:5); ^1H NMR (300 MHz, $CDCl_3$) δ 0.55 (s, 6H), 0.79 (s, 6H), 1.25–1.41 (m, 4H), 1.81 (d, 2H, *J*=18.5 Hz), 1.81–1.90 (m, 2H), 1.96–2.04 (m, 4H), 2.23 (dt, 2H, *J*=18.6, 3.6 Hz), 2.58 (d, 2H, *J*=14.8 Hz), 3.00 (d, 2H, *J*=14.8 Hz), 7.34 (d, 2H, *J*=8.5 Hz), 7.49 (t, 2H, *J*=8.3 Hz), 7.66 (t, 2H, *J*=8.1 Hz), 8.14 (s, 2H), 8.35 (d, 2H, *J*=8.6 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.06, 19.17, 24.71, 26.64, 42.13, 42.54, 47.67, 49.27, 57.58, 123.47 (t, *J*=10.3 Hz), 125.21, 127.24, 127.78, 128.27, 128.40, 133.76, 143.98, 212.79.

More polar diastereomer (*R*)-**11**-(*S*)-CS. Mp 80–82°C; R_f=0.27 (hexane/dichloromethane=3:5); ^1H NMR (300 MHz, $CDCl_3$) δ 0.54 (s, 6H), 0.65 (s, 6H), 1.20–1.31 (m, 4H), 1.77 (d, 2H, *J*=18.4 Hz), 1.75–1.77 (m, 4H),

1.94–1.96 (m, 2H), 2.22 (dt, 2H, J=3.1, 18.6 Hz), 2.51 (d, 2H, J=14.9 Hz), 3.39 (d, 2H, J=14.9 Hz), 7.28 (d, 2H, J=8.3 Hz), 7.45 (t, 2H, J=8.1 Hz), 7.64 (td, 2H, J=8.5, 1.1 Hz), 8.17 (s, 2H), 8.35 (d, 2H, J=8.6 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.91, 24.42, 26.51, 42.03, 42.42, 47.55, 49.41, 57.49, 123.28 (t, J=9.8 Hz), 125.12, 127.18, 127.78, 128.15, 128.40, 133.82, 143.80, 212.74.

4.1.6. Preparation of (*S*)-4,4′-diperfluorobutyl-1,1′-binaphthyl-2,2′-diol (*S*)-7.[14b] To a suspension of (*S*)-**11**-(*S*)-CS (413 mg, 0.36 mmol) in methanol (20 mL), NaOH (1 M, 5 mL) was added. The resulting yellow solution was refluxed for 24 h. After cooling down, 10% HCl was added to neutralize the solution to pH 7. Methanol was removed in vacuo and the residue was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the product was purified by column chromatography (ethyl acetate/hexane=1:10) to give (*S*)-**7** (213 mg, 82%) as a pale yellow solid. Mp 78–80°C; $[\alpha]_D^{20}=-10.7°$ (c 1.0, $CHCl_3$); ^{1}H NMR spectrum was identical with the spectrum of racemic **7**.

4.1.7. Preparation of (*R*)-4,4′-diperfluorobutyl-1,1′-binaphthyl-2,2′-diol (*R*)-7. To a suspension of (*R*)-**11**-(*S*)-CS (407 mg, 0.35 mmol) in methanol (15 mL), NaOH (1 M, 5 mL) was added. The resulting yellow solution was refluxed for 24 h. After cooling down, 10% HCl was added to neutralize the solution to pH 7. Methanol was removed in vacuo and the residue was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the product was purified by column chromatography (ethyl acetate/hexane=1:10) to give (*R*)-**7** (211 mg, 83%) as a pale yellow solid. Mp 78–80°C; $[\alpha]_D^{20}=+10.6°$ (c 1.1, $CHCl_3$); ^{1}H NMR spectrum was the same as the spectrum of racemic **7**.

4.1.8. Preparation of 4,4′,6,6′-tetrabromo-1,1′-binaphthyl-2,2′-diol (4).[21] To a solution of 4,4′-dibromo-BINOL **3**[21] (2.22 g, 5 mmol) in dichloromethane (50 mL) at −78°C, bromine (2.40 g, 0.78 mL, 15 mmol) in dichloromethane (5 mL) was added dropwise. The resulting brown solution was stirred and warmed up to room temperature for 2 days. Saturated sodium thiosulfate solution (10 mL) was added and the solution was stirred for 30 min. The organic layer was separated and aqueous layer was extracted with ethyl acetate (2×20 mL), the combined organic layer was washed with water, brine and dried over $MgSO_4$. After removal of solvent, the crude product was purified by column chromatography (ethyl acetate/hexane=1:8) to give **4** (2.98 g, 99%) as a pale brown solid. Mp 129–133°C (decomp.); R_f=0.31 (hexane/ethyl acetate=3:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.56 (brs, 2H), 6.96 (d, 2H, J=8.9 Hz), 7.41 (dd, 2H, J=8.9, 2.0 Hz), 7.73 (s, 2H), 8.45 (d, 2H, J=1.9 Hz); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 110.6, 119.8, 123.0, 124.7, 126.2, 129.3, 130.0, 131.8, 132.4, 152.5; FABMS: m/z (relative intensity) 603 (2), 601 (M^+, 5), 414 (18), 391 (100), 307 (24), 289 (29), 279 (31), 261 (15); HRMS (M^+) Calcd for $C_{20}H_{10}O_2Br_4$ 597.7414. Found 597.7361.

4.1.9. Preparation of 4,4′,6,6′-tetraperfluorobutyl-1,1′-binaphthyl-2,2′-diol (8). A mixture of 4,4′,6,6′-tetrabromo-BINOL **4** (4.6 g, 7.6 mmol), copper bronze (7.3 g, 114.6 mmol) and perfluorobutyl iodide (15.9 g, 7.9 mL, 45.8 mmol) in anhydrous DMSO (40 mL) was degassed three times, and then heated to 120°C for 5 days. After cooling down, ethyl acetate (100 mL) was added and the mixture was filtered through Celite, the filtrate was washed with 10% HCl, water, brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane=1:10) to give **8** (3.16 g, 36%) as a yellow oil. R_f=0.32 (ethyl acetate/hexane=1:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93 (brs, 2H), 7.28 (d, 2H, J=8.9 Hz), 7.55 (d, 2H, J=9.0 Hz), 7.88 (s, 2H), 8.55 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 112.17, 115.55, 115.78, 115.99, 116.88, 119.36, 121.83 (t, J=9.7 Hz), 124.93, 125.21, 125.57, 125.91, 126.23, 126.55, 129.21, 129.50, 129.81, 135.68, 153.05; FABMS: m/z (relative intensity) 1159 ($[M+H]^+$, 85), 1141 (17), 990 (100), 853 (3), 820 (19), 772 (18); SIMS: m/z 1158 (M^+); Anal. Calcd for $C_{36}H_{10}F_{36}O_2$: C, 37.33; H, 0.87. Found: C, 37.27; H, 0.92.

4.1.10. Preparation of diastereomeric 2,2′-di-[(1*S*)-camphor-10-sulfonyl]-4,4′,6,6′-tetraperfluorobutyl-1,1′-binaphthyl (*S*)-12-(*S*)-CS and (*R*)-12-(*S*)-CS. To a solution of 4,4′,6,6′-tetraperfluorobutyl-BINOL **8** (702 mg, 0.61 mmol) and (1*S*)-camphor-**10**-sulfonyl chloride (609 mg, 2.4 mmol) in dry CCl_4 (15 mL) at 0°C, triethylamine (306 mg, 0.57 mL, 3.0 mmol) was added. The yellow solution was stirred at room temperature for 10 h and then refluxed overnight. Water (15 mL) was added and the reaction mixture was extracted with CCl_4. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane=1:8) to give a mixture of diastereomers **12**-(*S*)-CS (800 mg, 83%) as a white solid. SIMS: m/z 1625 ($[M+K]^+$), 1609 ($[M+Na]^+$); APCIMS: m/z 1609 ($[M+Na]^+$), 1587 ($[M+H]^+$), 1586 (M^+).

Careful column chromatography (hexane/dichloromethane=3:5) gave less polar diastereomer (*S*)-**12**-(*S*)-CS. Mp 134–135°C; R_f=0.19 (hexane/dichloromethane=3:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.61 (s, 6H), 0.82 (s, 6H), 1.21–1.30 (m, 4H), 1.81 (d, 2H, J=18.5 Hz), 1.86–2.03 (m, 6H), 2.23 (dt, 2H, J=18.5, 2.7 Hz), 2.76 (d, 2H, J=14.9 Hz), 3.16 (d, 2H, J=14.9 Hz), 7.43 (d, 2H, J=9.0 Hz), 7.65 (t, 2H, J=8.9 Hz), 8.27 (s, 2H), 8.63 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.09, 19.19, 24.67, 26.58, 42.06, 42.57, 47.72, 49.71, 57.63, 115.90, 119.28, 124.82 (t, J=10.3 Hz), 125.36, 127.34, 127.44, 127.90, 128.40, 128.72, 128.83, 129.12, 129.43, 130.91, 135.15, 145.80, 212.59; Anal. Calcd for $C_{56}H_{38}F_{36}S_2O_8$: C, 42.38; H, 2.41. Found: C, 42.15; H, 2.39. A single crystal was obtained from hexane/dichloromethane solution. X-Ray crystallographic data is shown in the supporting information and has been deposited in Cambridge Crystallographic Data Centre.

More polar diastereomer (*R*)-**12**-(*S*)-CS. Mp 102–103°C; R_f=0.08 (hexane/dichloromethane=3:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.58 (s, 6H), 0.69 (s, 6H), 1.11–1.34 (m, 4H), 1.80 (d, 2H, J=18.5 Hz), 1.79–1.81 (m, 4H), 1.99–2.00 (m, 2H), 2.26 (dt, 2H, J=2.7, 18.6 Hz), 2.63 (d, 2H,

J=14.9 Hz), 3.49 (d, 2H, J=14.9 Hz), 7.40 (d, 2H, J=8.9 Hz), 7.63 (t, 2H, J=9.0 Hz), 8.30 (s, 2H), 8.63 (s, 2H); Anal. Calcd for $C_{56}H_{38}F_{36}S_2O_8$: C, 42.38; H, 2.41. Found: C, 42.56; H, 2.54.

4.1.11. Preparation of (*S*)-4,4′,6,6′-tetraperfluorobutyl-1,1′-binaphthyl-2,2′-diol (*S*)-8. To a suspension of (*S*)-**12**-(*S*)-CS (1.22 g, 0.77 mmol) in methanol (40 mL), NaOH (1 M, 10 mL) was added. The resulting yellow solution was refluxed for 24 h. After cooling down, 10% HCl was added to neutralize the solution to pH 7. Methanol was removed in vacuo and the residue was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the product was purified by column chromatography (ethyl acetate/hexane=1:10) to give (*S*)-**8** (0.67 g, 75%) as a pale yellow semi-solid. $[\alpha]_D^{20}=-2.3°$ (*c* 0.7, $CHCl_3$); ^1H NMR spectrum is the same as the spectrum of racemic **8**.

4.1.12. Preparation of (*R*)-4,4′,6,6′-tetraperfluorobutyl-1,1′-binaphthyl-2,2′-diol (*R*)-8. To a suspension of (*R*)-**12**-(*S*)-CS (392 mg, 0.25 mmol) in methanol (15 mL), NaOH (1 M, 5 mL) was added. The resulting yellow solution was refluxed for 24 h. After cooling down, 10% HCl was added to neutralize the solution to pH 7. Methanol was removed in vacuo and the residue was extracted with ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the product was purified by column chromatography (ethyl acetate/hexane=1:10) to give (*R*)-**8** (204 mg, 71%) as a pale yellow semi-solid. $[\alpha]_D^{20}=+2.1°$ (*c* 1.0, $CHCl_3$); ^1H NMR spectrum is the same as the spectrum of racemic **8**.

4.1.13. Preparation of racemic 4,4′,6,6′-tetraperfluorooctyl-1,1′-binaphthyl-2,2′-diol (9). A mixture of 4,4′,6,6′-tetrabromo-BINOL **4** (1.0 g, 1.66 mmol), copper bronze (1.6 g, 25 mmol) and perfluorobutyl iodide (5.46 g, 2.6 mL, 10 mmol) in anhydrous DMSO (15 mL) was degassed three times, and then heated to 160°C for 3 days. After cooling down, ethyl acetate (50 mL) was added and the mixture was filtered through Celite, the filtrate was washed with 10% HCl, water, brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane=1:10) to give **9** (1.48 g, 46%) as a yellow oil. R_f=0.17 (ethyl acetate/hexane=1:10); ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (brs, 2H), 7.27 (d, 2H, J=7.6 Hz), 7.56 (d, 2H, J=8.9 Hz), 7.87 (s, 2H), 8.55 (s, 2H); FABMS: *m/z* (relative intensity) 1159 ($[M+H]^+$, 85), 1141 (17), 990 (100), 853 (3), 820 (19), 772 (18); SIMS: *m/z* 1959 ($[M+H]^+$); Anal. Calcd for $C_{52}H_{10}F_{68}O_2$: C, 31.89; H, 0.89. Found: C, 32.02; H, 0.73.

4.1.14. Preparation of diastereomeric 2,2′-di-[(1*S*)-camphor-10-sulfonyl]-4,4′,6,6′-tetraperfluorooctyl-1,1′-binaphthyl (*S*)-13-(*S*)-CS and (*R*)-13-(*S*)-CS. At 0°C, to a solution of 4,4′,6,6′-tetraperfluorooctyl-BINOL **9** (1.18 g, 0.60 mmol) and (1*S*)-camphor-**10**-sulfonyl chloride (605 mg, 2.4 mmol) in dry CCl_4 (20 mL), triethylamine (304 mg, 0.57 mL, 3.0 mmol) was added. The yellow solution was refluxed for 2 days. After cooling down, water (15 mL) was added and the reaction mixture was extracted with CCl_4. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography (ethyl acetate/hexane=1:6) to give a mixture of diastereomers **13**-(*S*)-CS (1.1 g, 76%) as a white solid.

Careful column chromatography (hexane/dichloromethane=10:7) gave less polar diastereomer (*S*)-**13**-(*S*)-CS. Mp 127–128°C; R_f=0.25 (hexane/dichloromethane=10:7); ^1H NMR (300 MHz, $CDCl_3$) δ 0.60 (s, 6H), 0.81 (s, 6H), 1.27–1.30 (m, 4H), 1.80 (d, 2H, J=18.6 Hz), 1.85–2.02 (m, 6H), 2.22 (dd, 2H, J=18.6, 2.9 Hz), 2.77 (d, 2H, J=14.9 Hz), 3.17 (d, 2H, J=14.9 Hz), 7.43 (d, 2H, J=8.9 Hz), 7.65 (t, 2H, J=9.1 Hz), 8.29 (s, 2H), 8.64 (s, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 19.11, 19.18, 24.72, 26.58, 42.06, 42.63, 47.71, 49.77, 57.65, 107.76, 110.94, 114.87, 124.89, 125.34, 127.50, 127.94, 128.85, 129.23, 135.18, 145.86, 212.57; Anal. Calcd for $C_{72}H_{38}F_{68}S_2O_8$: C, 36.23; H, 1.60. Found: C, 36.12; H, 1.86.

More polar diastereomer (*R*)-**13**-(*S*)-CS. Mp 109–110°C; R_f=0.19 (hexane/dichloromethane=3:5); ^1H NMR (300 MHz, $CDCl_3$) δ 0.58 (s, 6H), 0.68 (s, 6H), 1.23–1.34 (m, 4H), 1.80 (d, 2H, J=18.6 Hz), 1.78–1.81 (m, 4H), 1.98–1.99 (m, 2H), 2.25 (dt, 2H, J=18.6, 2.6 Hz), 2.64 (d, 2H, J=14.9 Hz), 3.49 (d, 2H, J=15.0 Hz), 7.40 (d, 2H, J=8.9 Hz), 7.63 (t, 2H, J=9.1 Hz), 8.30 (s, 2H), 8.64 (s, 2H); Anal. Calcd for $C_{72}H_{38}F_{68}S_2O_8$: C, 36.23; H, 1.60. Found: C, 36.11; H, 1.52.

4.1.15. Preparation of (*S*)-4,4′,6,6′-tetraperfluorooctyl-1,1′-binaphthyl-2,2′-diol (*S*)-9. To a suspension of (*S*)-**13**-(*S*)-CS (239 mg, 0.10 mmol) in methanol (10 mL) and CCl_4 (10 mL), NaOH (1 M, 5 mL) was added. The resulting yellow solution was stirred at 60°C for 24 h. After cooling down, 10% HCl was added to neutralize the solution to pH 7. Methanol was removed in vacuo and the residue was extracted with CCl_4 and ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the product was purified by column chromatography (ethyl acetate/hexane=1:10) to give (*S*)-**9** (167 mg, 85%) as a yellow oil. $[\alpha]_D^{20}=-15.7°$ (*c* 0.15, ethyl acetate); ^1H NMR spectrum is the same as the spectrum of racemic **9**.

4.1.16. Preparation of (*R*)-4,4′,6,6′-tetraperfluorooctyl-1,1′-binaphthyl-2,2′-diol (*R*)-9. To a suspension of (*S*)-**13**-(*S*)-CS (184 mg, 0.08 mmol) in methanol (5 mL) and CCl_4 (5 mL), NaOH (1 M, 2 mL) was added. The resulting yellow solution was refluxed for 24 h. After cooling down, 10% HCl was added to neutralize the solution to pH 7. Methanol was removed in vacuo and the residue was extracted with CCl_4 and ethyl acetate. The combined organic layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the product was purified by column chromatography (ethyl acetate/hexane=1:10) to give (*R*)-**9** (122 mg, 79%) as a yellow oil. Mp $[\alpha]_D^{20}=+15.6°$ (*c* 0.96, ethyl acetate); ^1H NMR spectrum is the same as the spectrum of racemic **9**.

4.2. The typical procedure of the asymmetric catalytic addition of diethylzinc to aryl aldehyde in fluorous biphasic system

To a solution of optically pure BINOL derivative (0.025 mmol) in dry perfluoro(methyldecalin) (1 mL), titanium tetraisopropoxide (350 μL, 0.5 M in hexane, 0.175 mmol) was added and the resulting solution was heated to 45°C to form a one-layer solution. Diethylzinc in hexane (1 M, 375 μL, 0.375 mmol) was added and the mixture was stirred at 45°C for 15 min. An aryl aldehyde (0.125 mmol) was added and the reaction mixture was stirred at 45°C homogeneously and checked by TLC until aldehyde was completely consumed. After the reaction was cooled down to 0°C, a two-layer mixture was obtained. To the lower layer, a new batch of titanium tetraisopropoxide (350 μL, 0.5 M in hexane, 0.175 mmol) was added and the second reaction cycle was then carried out similarly. The upper layer was withdrawn with a syringe and added into HCl (1 M, 1 mL). The resulted reaction mixture was extracted with diethyl ether (3 mL×3). The combined organic layer was washed with water, brine and dried over $MgSO_4$. After removal of solvent, the residue was mixed with the internal standard solution (50 μL, 50 mg/mL), and the mixture was determined by HPLC on a Chiracel OD-H column.

4.3. The typical procedure of the asymmetric catalytic addition of triethylaluminum to aryl aldehyde in fluorous biphasic system[19]

To a solution of optically pure 4,4′,6,6′-tetraperfluorooctyl-BINOL (*S*)-**9** (49 mg, 0.025 mmol) in dry perfluoro(methyldecalin) (1 mL), titanium tetraisopropoxide (350 μL, 0.5 M in hexane, 0.175 mmol) was added and the resulting solution was heated to 45°C to form a one-layer solution. Triethylaluminum in hexane (1 M, 375 μL, 0.375 mmol) was added and the mixture was stirred at 53°C for 15 min. An aryl aldehyde (0.125 mmol) was added and the reaction mixture was stirred at 53°C homogeneously and checked by TLC until aldehyde was completely consumed. After the reaction was cooled down to 0°C, a two-layer mixture was obtained. To the lower layer, a new batch of titanium tetraisopropoxide (350 μL, 0.5 M in hexane, 0.175 mmol) was added and the second reaction cycle was then carried out similarly. The upper layer was withdrawn with a syringe and added into HCl (1 M, 1 mL). The resulted reaction mixture was extracted with diethyl ether (3 mL×3). The combined organic layer was washed with water, brine and dried over $MgSO_4$. After removal of solvent, the residue was mixed with the internal standard solution (50 μL, 50 mg/mL), and the mixture was determined by HPLC on a Chiracel OD-H column as the same as above.

5. Supplementary materials

Supporting information available: X-ray collection parameters for compound (*S*)-**12**-(*S*)-CS and ORTEP diagram. The CIF has been deposited at Cambridge Crystallographic Data Centre. CD spectra for compounds (*R*)- and (*S*)- for **5**, **7**, **8** and **9** and (*S*)-**6** (4 pages).

Acknowledgements

We thank Hong Kong Research Grants Council of Hong Kong for financial support (CUHK4023/98P).

References

1. Horvath, I. T.; Rabai, J. *Science* **1994**, *266*, 72.
2. For recent review and leading references, see: (a) Wolf, E. D.; Koten, G. V.; Deelman, B. *J. Chem. Soc. Rev.* **1999**, *28*, 37. (b) Fish, R. H. *Chem. Eur. J.* **1999**, *5*, 1677. (c) Crich, D.; Neelanmkavil, S. *J. Am. Chem. Soc.* **2001**, *123*, 7449. (d) Haddleton, D. M.; Jackson, S. G.; Bon, S. F. A. *J. Am. Chem. Soc.* **2000**, *122*, 1542. (e) Betzeimer, B.; Cavazzini, M.; Quici, S.; Knochel, P. *Tetrahedron Lett.* **2000**, *41*, 4343. (f) Wende, M.; Meier, R.; Gladysz, J. A. *J. Am. Chem. Soc.* **2001**, *123*, 11490.
3. For asymmetric carbon–carbon bond formation: (a) Klejin, H.; Rijinberg, E.; Jastrzebski, J. T. B. H.; Koten, G. V. *Org. Lett.* **1999**, *1*, 853. (b) Nakamura, Y.; Takeuchi, S.; Ohgo, Y.; Curran, D. P. *Tetrahedron Lett.* **2000**, *41*, 57.
4. For asymmetric protonation: (a) Takeuchi, S.; Nakamura, Y.; Ohgo, Y.; Curran, D. P. *Tetrahedron Lett.* **1998**, *39*, 8691. (b) Nakamura, Y.; Takeuchi, S.; Ohgo, Y.; Curran, D. P. *Tetrahedron* **2000**, *56*, 351.
5. For asymmetric epoxidation: (a) Pozzi, G.; Cinato, F.; Montanari, F.; Quici, S. *Chem. Commun.* **1998**, 877. (b) Pozzi, G.; Cavazzini, M.; Cinato, F.; Montanari, F.; Quici, S. *Eur. J. Org. Chem.* **1999**, 1947. (c) Cavazzini, M.; Manfre, A.; Montanari, F.; Quici, S.; Pozzi, G. *Chem. Commun.* **2000**, 2171.
6. Tian, Y.; Chan, K. S. *Tetrahedron Lett.* **2000**, *41*, 8813.
7. (a) Mathivet, T.; Monflier, E.; Castanet, Y.; Mortreux, A.; Couturier, J. L. *Tetrahedron Lett.* **1999**, *40*, 3885. (b) Mathivet, T.; Monflier, E.; Castanet, Y.; Mortreux, A.; Couturier, J. L. *Tetrahedron Lett.* **1998**, *39*, 9411.
8. Chow, H. F.; Ng, M. K. *Tetrahedron: Asymmetry* **1996**, *7*, 2251.
9. Cuntze, J.; Owens, L.; Alcazar, V.; Seiler, P.; Diederich, F. *Helv. Chim. Acta* **1995**, *78*, 367.
10. (a) Cai, D.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. *Tetrahedron Lett.* **1995**, *36*, 7991. (b) Cai, D.; Hughes, D. L.; Verhoeven, T. R.; Reider, P. *Org. Synth.* **1998**, *76*, 1.
11. Shan, Z.; Wang, G.; Duan, B.; Zhao, D. *Tetrahedron: Asymmetry* **1996**, *7*, 2847.
12. Shan, Z.; Xiong, Y.; Li, W.; Zhao, D. *Tetrahedron: Asymmetry* **1998**, *9*, 3985.
13. Commercially available (1*S*)-(+)-**10**-camphorsulfonyl chloride (Aldrich 21,957-6) is 97% pure, which is not pure enough for resolution. The transformation of camphorsulfonic acid to camphorsulfonyl chloride, see: Bartlett, P. D.; Knox, L. H. *Organic Syntheses*, Collect. Vol. 5; Wiley: New York, 1973 p 196.
14. (a) Ng, M. K.; Chow, H. F.; Chan, T. L.; Mak, T. C. W. *Tetrahedron Lett.* **1996**, *37*, 2979. (b) Chow, H. F.; Wan, C. W.; Ng, M. K. *J. Org. Chem.* **1996**, *61*, 8712. (c) Chow, H. F.; Ng, M. K. *Tetrahedron: Asymmetry* **1996**, *7*, 2251.
15. IUPAC Tentative Rule for the Nomenclature of Organic Chemistry. *J. Org. Chem.* **1970**, *35*, 2849.
16. For reviews, see: (a) Noyori, R.; Kitamura, M. *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49–69. (b) Soai, K.; Niwa, S. *Chem. Rev.* **1992**, *92*, 833–856. (c) Noyori, R. *Asymmetric Catalysis*

in Organic Synthesis; Wiley: New York, 1994. (d) Soai, K.; Shibata, T. *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999; Vol. 2, pp. 911–922. (e) Mori, M.; Nakai, T. *Teterahedron Lett.* **1997**, *38*, 6233–6236.

17. (a) Chan, A. S. C.; Zhang, F. Y.; Yip, C. W. *J. Am. Chem. Soc.* **1997**, *119*, 4080. (b) Zhang, F. Y.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1998**, *9*, 1179. (c) Zhang, F.; Yip, C.; Cao, R.; Chan, A. S. C. *Tetrahedron: Asymmetry* **1997**, *8*, 585.
18. Nakamura, Y.; Takeuchi, S.; Ohgo, Y.; Curran, D. P. *Tetrahedron Lett.* **2000**, *41*, 57.
19. Seeback, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, 2171.
20. Cuntze, J.; Owens, L.; Alcazar, V.; Seiler, P.; Diederich, F. *Helv. Chim. Acta* **1995**, *78*, 367.
21. Noji, M.; Nakajima, M.; Koga, K. *Tetrahedron Lett.* **1994**, *35*, 7983.