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An asymmetric catalytic carbon–carbon bond formation in a fluorous biphasic system based on perfluoroalkyl-BINOL

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Abstract

Asymmetric diethylzinc addition to arylaldehydes in a fluorous biphasic system catalyzed by perfluoroalkyl-BINOL has been accomplished. © 2000 Elsevier Science Ltd. All rights reserved.

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 prepare, 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.[3]

In our previous work, we had synthesized perfluoroalkyl-BINOLs and examined the catalytic reactivities of BINOL-metal complexes.[4] Herein, we report the asymmetric carbon–carbon bond formation in a fluorous biphasic system catalyzed by a titianium perfluoroalkyl-BINOL complex.

A highly perfluorinated BINOL derivative, 4,4′,6,6′-tetraperfluorooctyl-BINOL **3** which contains 32 perfluorocarbons was designed for asymmetric FBC. Bromination of 4,4′-dibromo-BINOL **1**[5] at −78°C[6] gave tetrabromide **2** in good yield, which underwent a copper-mediated cross-coupling reaction with perfluorooctyl iodide[7] at high temperature to yield compound **3**. The resolution of *rac*-**3**[8] was accomplished by column chromatography of the corresponding diastereomeric bis-(*S*)-10-camphorsulfonates **4a** and **4b**,[9] followed by alkaline hydrolysis to yield the optically pure (*S*)-**3** and (*R*)-**3** (Scheme 1).[10]

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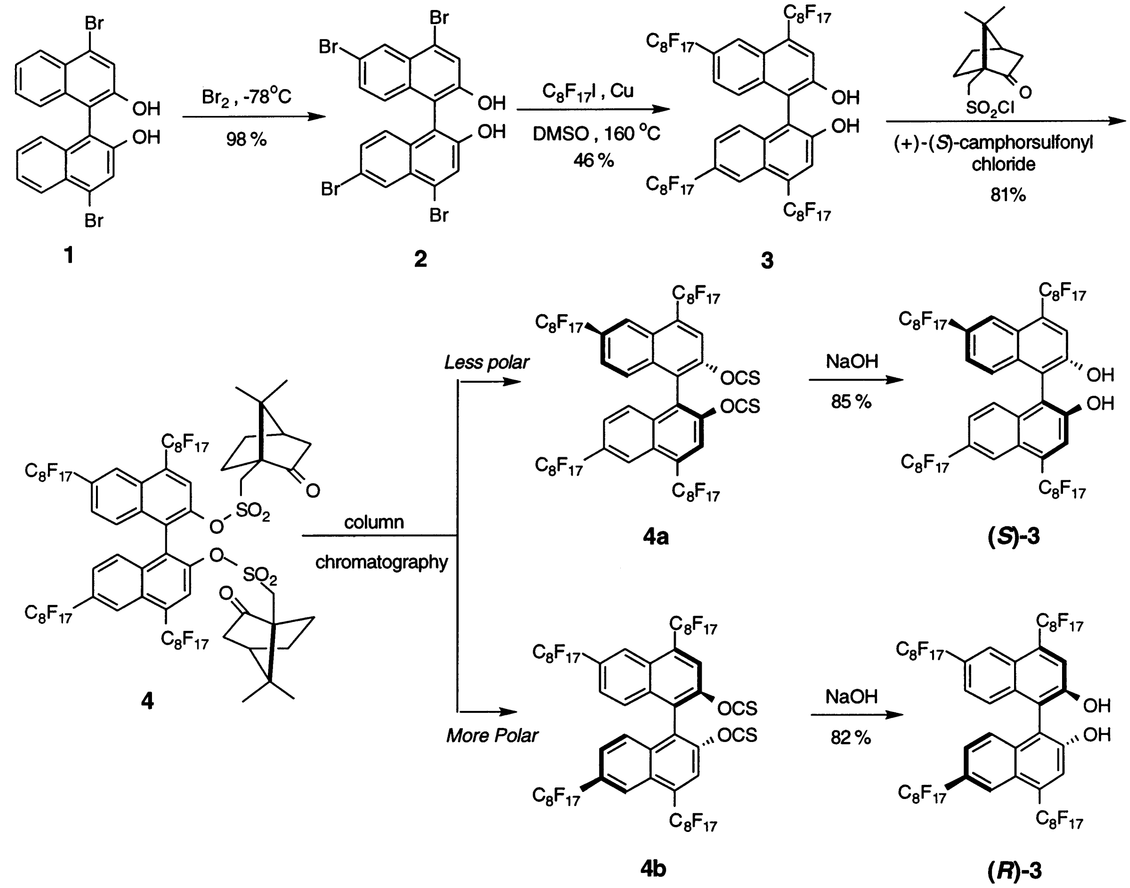
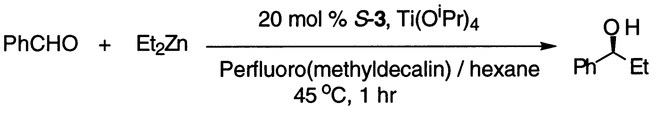


Scheme 1.

The diethylzinc addition to benzaldehyde catalyzed by perfluoroalkyl-BINOL/$Ti(O^iPr)_4$[11] was demonstrated in a fluorous biphasic system (Eq. (1)). To 20 mol% of (*S*)-perfluoroalkyl-BINOL **3** dissolved in perfluoro(methyldecalin), 1.4 equiv. of $Ti(O^iPr)_4$ in hexane solution was added to give a two-layer system. After heating to 45°C, a homogenous reaction system was obtained. Then 3 equiv. of Et_2Zn in a hexane solution and PhCHO were added sequentially. After stirring for 1 hour at 45°C, the reaction was cooled to 0°C and two layers were obtained. The upper organic layer was withdrawn for analysis. Repeated addition of $Ti(O^iPr)_4$ and reactants completed another reaction cycle. Nine cycles of the reaction were performed and no significant decrease in the chemical yield or the enantiomeric excess of the product was observed (Table 1). Poor results were obtained when $Ti(O^iPr)_4$ was absent in the tenth cycle. This observation is consistent with previously reported work and it is suggested that this is due to the requirement for free $Ti(O^iPr)_4$ as a co-catalyst in the reaction.[12]



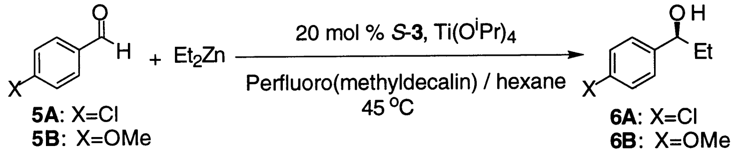
(1)

Table 1
FBC result of Et_2Zn addition to benzaldehyde catalyzed by *S*-**3**

Reaction cycle	Yield (%)[a]	e.e.[b]
1	69	54
2	80	57
3	79	58
4	79	58
5	80	55
6	79	58
7	80	57
8	79	56
9	79	55
10[c]	51	5

[a] Determined by HPLC integration against 4-methoxyphenethyl alcohol as the internal standard.
[b] Determined by HPLC using Daicel Chiralcel OD-H column, the major isomer had the (*S*) configuration.
[c] $Ti(O^iPr)_4$ was absent.

Other aryl aldehydes also underwent Et_2Zn addition in this fluorous biphasic system catalyzed by (*S*)-perfluorooctyl-BINOL **3** (Eq. (2)). For the more electron deficient 4-chlorobenzaldehyde, the reaction was a little faster than that with benzaldehyde and was completed in 45 minutes according to TLC analysis with a quantitative yield of **6A** being obtained. On the contrary, the reaction of the more electron rich 4-methoxybenzaldehyde was slower. The yield of **6B** was around 90% after 2 hours. The FBC phenomena 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 2).



(2)

Table 2
FBC of Et_2Zn addition to arylaldehydes catalyzed by *S*-**3**

Reaction cycles	**6A**[a]		**6B**[d]	
	Yield (%)[b]	e.e.[c]	Yield (%)[e]	e.e.[c]
1	99	54	91	37
2	98	51	92	41
3	99	51	91	40

[a] Reaction time was 45 minutes.
[b] Determined by HPLC integration against 4-methoxyphenethyl alcohol as the internal standard.
[c] Determined by HPLC using Daicel Chiralcel OD-H column, the major isomer had the (*S*) configuration.
[d] Reaction time was 2 hours.
[e] Determined by HPLC integration against 3-nitrobenzyl alcohol as the internal standard.

In summary, we have synthesized a new type of tetraperfluorooctyl-BINOL and demonstrated asymmetric catalytic carbon–carbon bond formation in a fluorous biphasic system. Further studies are being carried out.

Acknowledgements

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8. For *rac*-**3**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (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); ESIMS: m/z 1959 (M+1).
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10. For (*S*)-**3**: $[\alpha]_D^{20}=-15.7$ ($c=0.15$, ethyl acetate); for (*R*)-**3**: $[\alpha]_D^{20}=+15.6$ ($c=0.96$, ethyl acetate). The optical purity of compounds (*S*)-**3** and (*R*)-**3** was determined from the ^{1}H NMR of the corresponding camphorsulfonates. The absolute configuration of compound **3** was assigned based on the comparison of the R_f values of the camphorsulfonates,[9] the Cotton effect and the sign of optical rotation of BINOLs.[5]
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