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6,6′-Bisperfluoroalkylated BINOLs promoted asymmetric allylation of aldehydes

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Abstract

6,6′-Bis(1*H*, 1*H*, 2*H*, 2*H*-perfluorooctyl)-1, 1′-bi-2-naphthol (Rf_6-BINOL) and 6,6′-bis(1*H*, 1*H*, 2*H*, 2*H*-perfluorodecyl)-1,1′-bi-2-naphthol (Rf_8-BINOL) were used in allylation of aldehydes in fluorous biphase system. Good enantioselectivity was obtained and the ligands could be recovered by continuos liquid–liquid extraction.

Keywords: Rf-BINOL; Fluorous biphase; Asymmetric allylation

1. Introduction

Homogeneous asymmetric catalysis is a powerful tool for enantioselective transformations. Although a variety of homogeneous chiral catalysts have been developed for enantioselective reactions, recovery and purification of these catalysts are always problematic. In the last few years, fluorous chiral catalysts were discovered and applied in fluorous biphase system to solve this problem. Several fluorous catalysts were used for asymmetric carbon–carbon bond formation [1–5], protonation [6], epoxidation [7] and hydrogenation reaction [8]. Herein, we wish to report the 6,6′-bisperfluoroalkylated BINOLs promoted asymmetric allylation of aldehydes in fluorous biphase systems. Good enantioselectivity was obtained and the ligands could be recovered by liquid–liquid extraction. The recovered ligands were reused without loss of activity.

2. Results and discussion

2.1. Asymmetric allylation of aldehydes catalyzed by Rf-BINOL/Ti(IV) in fluorous biphase system

In continuation of our efforts in Rf-BINOL catalyzed asymmetric reactions [9], we conducted the asymmetric allylation reaction of aldehydes in fluorous biphase systems (FBS) according to Keck's procedure [10a–d]. But the BINOL–Ti(IV) complex (either 2:1 or 1:1) showed inferior yields and enantioselectivities to those of Keck's, irrespective to the presence of molecular sieve, at 0 or −20 °C. The best result obtained in our hands was 67% yield and 89% e.e. with 10% Ti complex (BINOL/Ti(IV) = 2 : 1). Inferior yield and e.e. were also reported by other groups [11,12a–d] (BINOL-derivative/Ti(IV) complex). The Rf-BINOL/Ti(IV) catalyzed allylation of benzaldehy (as indicated in Table 1) in dichloromathane (entry 3, Table 1) delivered even worse result. One reason might be that this BINOL–Ti(IV) system is too much sensitive to air and moisture, the other might be that the solubility of the Rf-BINOL/Ti(IV) complex in dichloromathane is not good. Although the Rf-BINOLs could be totally dissolved in CH_2Cl_2, either BINOL or Rf-BINOL could not be dissolved completely in hexane, not to mention their Ti complexes (entries 1 and 2). The Rf-BINOLs and their Ti(IV) complexes could be dissolved in toluene, but the reaction was very sluggish (entry 4). Reaction in benzotrifluoride as homogenous system delivered good yield but no better enantiomeric selectivity (entry 5). We found that the Rf-BINOL/Ti(IV) complex showed good solubility in the fluorous biphase systems. With hexane, dichloromethane and toluene as the organic phase and, FC-72 (perfluorohexane, $CF_3(CF_2)_4CF_3$), perfluoromethylcyclohexane and perfluorodecalin as the fluorous phase respectively, the hexane-FC-72 solvent system was found to be the best choice (entries 6–12) Scheme 1.

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Table 1
Asymmetric allylation of benzaldehyde catalyzed by Rf-BINOL/Ti(IV) in homogenous and fluorous biphase system

Entry	Ligand (20 mol%)	Solvents (ml)	Time (h)	Yield (%)	e.e.% (R)[a]
Homogenous					
1	BINOL	Hexane	24	74	77.9
2	**1**	Hexane	24	75	82.6
3	**1**	CH_2Cl_2	24	40	76.6
4	**1**	Toluene	24	26	70.6
5	**1**	$C_6H_5CF_3$	24	81	72.6
Biphase					
6	**1**	CH_2Cl_2:$C_{10}F_{18}$	24	27	75.6
7	**2**	CH_2Cl_2:$C_{10}F_{18}$	24	20	74.9
8	**1**	Hexane:$C_{10}F_{18}$	12	76	83.2
9	**1**	Hexane:$C_6F_{11}CF_3$	10	78	87.7
10	**1**	Hexane:FC-72	10	85	90.1
11	**2**	Hexane:FC-72	5	83	89.8
12	**1**	Toluene:FC-72	12	52	48.2
13	**1** (10 mol% 1:1)[b]	Hexane:FC-72	24	81	81.3
14	**1** (5 mol% 2:1)	Hexane:FC-72	24	26	49.1

[a] The absolute configuration was determined by comparison with reported specific rotation [10a]. The enaotioselectivities were determined by chiral HPLC.
[b] The ratio referred to that of Ti to benzaldehyde.

We next examined this system for allylation of other aldehydes. Disappointedly, only substrates with strong electron withdrawing groups showed good yields and enantioselectivities (entries 1–3, Table 2). The conversions of *p*-chloro, *p*-bromo and 2,4-dicloro-benzaldehydes were rather poor (entries 4, 5 and 7) and most of the substrates were recovered. Aldehydes with electron donating groups showed no better results as could be predicted (entries 8–10).

The mechanism of this reaction is still controversial. Thus, the reasons for the unsatisfactory results are ambiguous. The BINOL/Ti(IV) complex is also believed to be easily decomposed [11]. Bidentate complex and BINOL-derivative/Ti(IV) complex showed better results [12c, e]. Optimization of this system is undergoing in our group Scheme 2.

3. Experimental

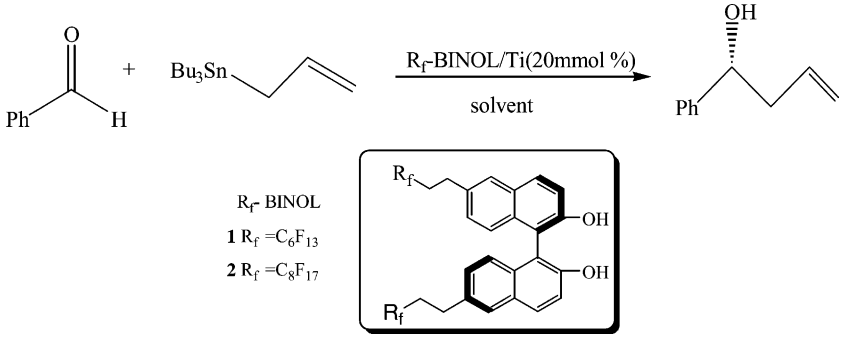
3.1. General

All experiments were carried out under argon atmosphere using Schlenk techniques. Commercial reagents were used as received without further purification. Aldehydes were distilled or recrystallized before use. Solvents were freshly distilled by standard method. The ^{1}H-NMR spectra were obtained on a Bruker, AMX-300 spectrometer (TMS as ^{1}H internal reference). IR spectra were recorded with a Bio-Rad FTS-185 spectrometer by films or KBr discs.

3.2. Typical procedure for asymmetric allylation of aldehydes

Rf-BINOL **1** (196 mg, 0.2 mmol) was added into FC-72 (2 ml), which could not be totally dissolved, followed by Ti(OPr-i)$_4$ (30 μl, 0.1 mmol) in freshly distilled hexane (2 ml) (entry 10 in Table 1 as an example). The mixture (dark brown biphase system) was stirred at room temperature for 1 h then cooled to 0 °C and benzaldehyde (102 μl, 1 mmol) was added and stirred for 10 min. Then allytributyltin (0.34 ml, 1.1 mmol) was added and the reaction mixture was kept at 0 °C until TLC inferred the disappearance of benzaldehyde. The organic layer was moved out by syringe and quenched by saturated $NaHCO_3$ solution (1.5 ml). After filtration, methanol (4 ml) and FC-72 (3 ml) were added for three-phase extraction. Another two portions of FC-72 (3 ml) were added for a second and a third extraction. The separated organic layer was washed with saturated $NaHCO_3$ and brine and dried over anhydrous Na_2SO_4. After evaporation, the residue was purified by flash chromatography. Optical rotation of the product was $[\alpha]_D^{20}$ + 64.9 (c 3.3, $CHCl_3$). Ligand **1** recovered from the organic phase was 24% (47 mg). The combined fluorous solvent was distilled with little solvent left. Ethyl acetate and saturated $NaHCO_3$ were added. After extraction, evaporation and column purification, 49% (96 mg) of **1** was recovered.

(*R*)-1-Phenyl-3-buten-1-ol $[\alpha]_D^{20}$ + 64.8 (c, 3.3, $CHCl_3$); IR (film, cm^{-1}) 3388, 3076, 2925, 2854, 1641, 1492, 1453, 1260, 1196, 1049, 914, 872; ^{1}H NMR ($CDCl_3$) δ 7.25–7.38



Scheme 1. Asymmetric allylation of benzaldehyde promoted by Rf-BINOL/Ti(IV).

Table 2
Asymmetric allylation of aldehydes catalyzed by Rf-BINOL/Ti(IV) in fluorous biphase system

Entry	Substrate	Time (h)	Yield %	e.e.%[a]	$[\alpha]_D^{20}$ $CHCl_3$
1	4-Fluorobenzaldehyde	3	91	80.9	54.0
2	3-Fluorobenzaldehyde	3	86	87.6	47.0
3	3-Fluoro-5-trifluoromethyl-benzaldehyde	3	81	n.d.[b]	31.4
4	4-Chlorobenzaldehyde	10	51	82.6	33.9
5	4-Bromobenzaldehyde	12	12	58.6	24.0
6	2-Chlorobenzaldehyde	12	83	n.d.	53.8
7	2,4-Dichlorobenzaldehyde	12	16	n.d.	43.9
8	4-Methoxybenzaldehyde	12	47	54.6	32.1
9	4-Ethylbenzaldehyde	24	25	51.0	33.9
10	4-Ethoxybenzaldehyde	24	21	62.7	24.5
11	Octanalaldehyde	24	Trace	n.d.	−11.6[c]
12	3-Bromobenzaldehyde	12	31	76.0	38.7

The catalysts can be recovered by continuous extraction. Recovered ligands were used without obvious loss of activity.

[a] The absolute configurations were determined by comparison with reported specific rotation [10a]. The enantioselectivities were determined by chiral HPLC.

[b] Not determined.

[c] In benzene.

(m, 5H, ArH), 6.73–6.89 (m, 1H, CH=CH_2), 5.20–5.32 (m, 2H, CH=CH_2), 4.70–4.78 (m, 1H, CHOH), 2.48–2.57 (m, 2H, CH_2), 2.12 (s, 1H, OH).

(*R*)-1-(4-Fluorophenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 54.0 (c, 1.1, $CHCl_3$); IR (film, cm^{-1}) 3385, 2927, 1641, 1605, 1510, 1431, 1224, 1157, 1051, 836; ^1H NMR ($CDCl_3$) δ 7.28–7.36 (m, 2H, ArH), 6.97–7.08 (m, 2H, ArH), 5.71–5.86 (m, 1H, CH=CH_2), 5.12–5.20 (m, 2H, CH=CH_2), 4.72 (t, $J = 6.6$ Hz, 1H, CHOH), 2.40–2.56 (m, 2H, CH_2), 2.09 (s, 1H, OH).

(*R*)-1-(3-Fluorophenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 47.0 (c, 2.3, $CHCl_3$); IR (film, cm^{-1}) 3380, 3078, 2980, 2929, 1642, 1615, 1591, 1488, 1248, 1139, 1052, 992, 920, 873; ^1H NMR ($CDCl_3$) δ 7.25–7.34 (m, 1H, ArH), 7.05–7.13 (m, 2H, ArH), 6.91–6.99 (m, 1H, ArH), 5.70–5.85 (m, 1H, CH=CH_2), 5.12–5.20 (m, 2H, CH=CH_2), 4.70 (t, $J = 6.3$ Hz, 1H, CHOH), 2.38–2.57 (m, 2H, CH_2), 2.25 (s, 1H, OH).

(*R*)-1-(3-Fluoro-5-trifluoromethylphenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 31.4 (c, 1.6, $CHCl_3$); IR (film, cm^{-1}) 3392, 3084, 2983, 2916, 1643, 1607, 1455, 1344, 1229, 1172, 1092, 1055, 924, 877; ^1H NMR ($CDCl_3$) δ 7.25–7.53 (M, 3H, ArH), 5.72–5.86 (m, 1H, CH=CH_2), 5.15–5.24 (m, 2H, CH=CH_2), 4.80 (t, $J = 6.3$ Hz), 2.38–2.51 (m, 2H, CH_2), 2.20 (s, 1H, OH).

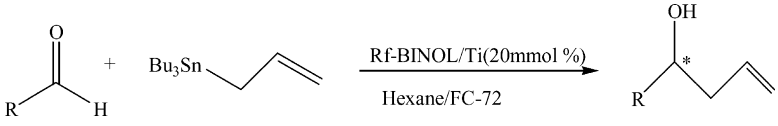
(*R*)-1-(4-Chlorophenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 33.9 (c, 1.1, $CHCl_3$); IR (film, cm^{-1}) 3377, 3078, 2979, 2928, 1641, 1596, 1492, 1411, 1091, 1050, 919, 870, 829; ^1H NMR ($CDCl_3$) δ 7.25–7.34 (m, 4H, ArH), 5.70–5.84 (m, 1H, CH=CH_2), 5.11–5.19 (m, 2H, CH=CH_2), 4.70 (t, $J = 6.6$ Hz, 1H, CHOH), 2.38–2.55 (m, 2H, CH_2), 2.20 (s, 1H, OH).

(*R*)-1-(4-Bromophenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 24.0 (c, 3.5, $CHCl_3$); IR (film, cm^{-1}) 3384, 3077, 2978, 2929, 1641, 1592, 1488, 1404, 1296, 1070, 1010, 918, 825; ^1H NMR ($CDCl_3$) δ 7.46 (dd, $J_1 = 8.4$ Hz, $J_2 = 2.0$ Hz, 2H, ArH), 7.22 (dd, $J_1 = 8.7$ Hz, $J_2 = 2.1$ Hz, 2H, ArH), 5.70–5.85 (m, 1H, CH=CH_2), 5.12–5.20 (m, 2H, CH=CH_2), 4.68 (t, $J = 6.5$ Hz), 2.38–2.52 (m, 2H, CH_2), 2.22 (s, 1H, OH).

(*R*)-1-(2-Chlorophenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 53.8 (c, 1.1, $CHCl_3$); IR (film, cm^{-1}) 3396, 3074, 2979, 2923, 1641, 1574, 1473, 1438, 1196, 1131, 1048, 987, 917, 872; ^1H NMR ($CDCl_3$) δ 7.56 (dd, $J_1 = 7.5$ Hz, $J_2 = 1.5$ Hz, 1H, ArH), 7.17–7.35 (m, 3H, ArH), 5.80–5.97 (m, 1H, CH=CH_2), 5.15–5.26 (m, 3H,), 2.58–2.69 (m, 1H), 2.32–2.42 (m, 1H), 2.21 (s, 1H, OH).

(*R*)-1-(2, 4-Dichlorophenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 43.9 (c, 3.2, $CHCl_3$); IR (KBr, cm^{-1}) 3382, 2999, 2939, 1639, 1590, 1470, 1220, 1070, 927, 823; ^1H NMR ($CDCl_3$) δ 7.25–7.53 (m, 3H, ArH), 5.75–5.92 (m, 1H, CH=CH_2), 5.07–5.22 (m, 3H,), 2.56–2.67 (m, 1H), 2.27–2.39 (m, 1H), 2.21 (s, 1H, OH).

(*R*)-1-(4-Methyloxyphenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 32.1 (c, 2.5, $CHCl_3$); IR (film, cm^{-1}) 3398, 2931, 2836, 1639, 1612, 1513, 1302, 1175, 1036, 916, 832; ^1H NMR ($CDCl_3$) δ 7.24 (dd, $J_1 = 8.7$ Hz, $J_2 = 2.0$ Hz,.2H, ArH), 6.89 (dt, $J_1 = 8.4$ Hz, $J_2 = 2.4$ Hz,.2H, ArH), 5.71–5.86 (m, 1H, CH=CH_2), 5.07–5.18 (m, 2H, CH=CH_2), 4.68 (t, $J =$



Scheme 2. Asymmetric allylation of aldehyde promoted by Rf-BINOLs in FBS.

6.6 Hz, 1H, CHOH), 3.80 (s, 3H, OCH_3), 2.48 (t, J = 7.1 Hz, 2H, CH_2), 2.12 (s, 1H, OH).

(*R*)-1-(4-Ethylphenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 33.9 (c, 1.1, $CHCl_3$); IR (film, cm^{-1}) 3385, 3076, 3011, 2965, 2931, 1641, 1514, 1456, 1418, 1206, 1042, 1000, 914, 871; 832; ^1H NMR ($CDCl_3$) δ 7.21 (dd, J_1 = 8.1 Hz, 4H, ArH), 5.74–5.89 (m, 1H, $CH{=}CH_2$), 5.10–5.20 (m, 2H, $CH{=}CH_2$), 4.70 (t, J = 7.5 Hz), 2.64 (q, J = 7.7 Hz, 2H, CH_2CH_3), 2.46–2.54 (m, 2H, $CH_2CH{=}CH_2$), 2.04 (s, 1H, OH), 1.42 (t, J = 7.5 Hz, 3H, CH_3).

(*R*)-1-(4-Ethyloxyphenyl)-3-buten-1-ol $[\alpha]_D^{20}$ + 24.5 (c, 3.1, $CHCl_3$); IR (film, cm^{-1}) 3418, 2980, 2929, 1641, 1612, 1512, 1393, 1244, 1174, 1116, 1048, 920, 834; ^1H NMR ($CDCl_3$) δ 7.25 (dt, J_1 = 8.7 Hz, J_2 = 2.1 Hz, 2H, ArH), 6.89 (dt, J_1 = 8.7 Hz, J_2 = 2.7 Hz, 2H, ArH), 5.85–5.94 (m, 1H, $CH{=}CH_2$), 5.09–5.18 (m, 2H, $CH{=}CH_2$), 4.66 (t, J = 6.7 Hz, 1H, CHOH), 4.00 (q, J = 6.9 Hz, 2H, OCH_2), 2.44 (t, J = 6.6 Hz, 2H, CH_2), 2.12 (s, 1H, OH), 1.40 (t, J = 7.1 Hz, 3H, CH_3).

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