Tetrahedron: *Asymmetry* 22 (2011) 1225–1230

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Asymmetric addition of diethylzinc to aldehydes catalyzed by new zinc-amides prepared by a rhodium-catalyzed asymmetric addition

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ARTICLE INFO

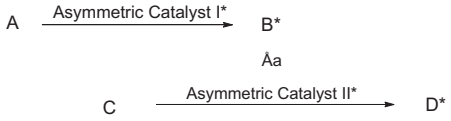
Article history:
Received 3 June 2011
Accepted 30 June 2011
Available online 6 August 2011

ABSTRACT

A new chiral zinc-amide **2s**′ was found to be an effective catalyst for the asymmetric addition of diethylzinc to aldehydes **3** through a screening method for asymmetric catalysts, in which two catalytic asymmetric reactions are connected. The chiral zinc catalyst can be readily prepared catalytically from achiral imine **1** by the chiral rhodium–diene complex mediated asymmetric addition of dimethylzinc.

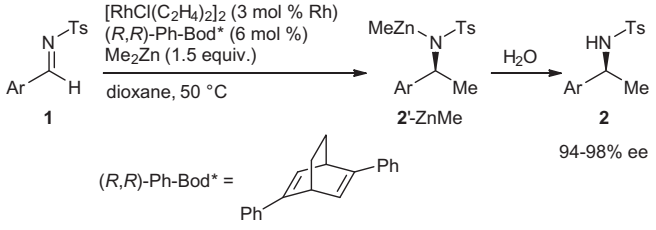
1. Introduction

Catalytic asymmetric synthesis has attracted a great deal of attention because small amounts of chiral catalysts can induce the formation of large amounts of optically active compounds in this system.[1] If the chiral catalysts are prepared catalytically, an enhanced amplification of the chirality can be expected due to the multiplication of two catalytic asymmetric reactions.[2] Herein we report a new type of chiral zinc catalyst for the asymmetric addition of diethylzinc to aldehydes, which was found by our recent catalyst screening method,[3] which connects two different catalytic asymmetric reactions (Scheme 1).



Scheme 1. Connection of two catalytic asymmetric reactions for catalyst screening.

The asymmetric addition[4] of dimethylzinc to *N*-tosylarylimines **1** catalyzed by the Rh/(*R*,*R*)-Ph-bod* complex,[5] which was reported by Hayashi et al. in 2006, was our choice of reaction for the preparation and screening for new chiral zinc catalysts (Scheme 2). This highly reliable reaction produces various 1-arylethylamines **2** with high enantioselectivities; chiral zinc-amide intermediates **2**′-ZnMe were assumed to be formed prior to work-up with H_2O. Herein, we attempted to use chiral zinc-amide **2**′ as a catalyst for the asymmetric addition[6,7] of diethylzinc to aldehydes **3**.



Scheme 2. Asymmetric addition of dimethylzinc to *N*-tosylarylimines **1** catalyzed by an Rh/(*R*,*R*)-Ph-bod* complex.

2. Results and discussion

The catalyst screening[8,9] was performed with the following one-pot procedure. First, *N*-tosylarylimine **1** was reacted with dimethylzinc in the presence of Rh/(*R*,*R*)-Ph-bod* catalyst at 50 °C for 3 h to give chiral zinc-amide **2**′-ZnMe. Next, all of the volatile materials were removed under reduced pressure from the reaction flask. Benzaldehyde, diethylzinc, and hexane were then introduced into the same flask and the mixture was stirred at 30 °C for 24 h. Finally, the mixture was quenched by adding 1 M HCl aq and purified by silica gel chromatography after extraction.

The results of the screening are shown in Table 1. When *N*-tosyl-1-phenylimine **1a** was employed as the substrate for the first step of the reaction, the desired 1-phenyl-1-propanol **4a** was obtained in 79% yield as the final product (entry 1). In this case, the enantiomeric excess (ee) of **4a** was found to be 20%. The screening for **1** with a substituent at the 4-position of the aromatic ring also gave **4a** in good yields, but unsatisfactory results were obtained in terms of enantioselectivity (entries 2–12). On the other hand, whereas similar results were observed in most of the screening for **1** with a substituent at the 2-position (entries 13–16), remarkable enantioselectivity (73% ee) was observed with **1q**,

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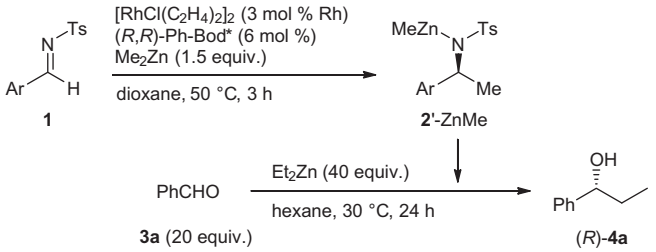
doi:10.1016/j.tetasy.2011.06.031

Table 1
Screening for asymmetric catalysts **2′**-ZnMe by connecting two reactions[a]



Entry	Ar	**2′**-ZnMe	Yield[b] of **4a** (%)	ee[c,d] of **4a** (%)
1	Ph **1a**	**2a′**	79	20
2	4-MeC_6H_4 **1b**	**2b′**	76	8
3	4-EtC_6H_4 **1c**	**2c′**	61	16
4	4-*i*-PrC_6H_4 **1d**	**2d′**	92	9
5	4-PhC_6H_4 **1e**	**2e′**	73	19
6	4-$CF_3C_6H_4$ **1f**	**2f′**	67	5
7	4-FC_6H_4 **1g**	**2g′**	76	6
8	4-ClC_6H_4 **1h**	**2h′**	85	7
9	4-$MeOC_6H_4$ **1i**	**2i′**	78	5
10	4-$EtOC_6H_4$ **1j**	**2j′**	78	16
11	4-$BuOC_6H_4$ **1k**	**2k′**	70	22
12	4-$BnOC_6H_4$ **1l**	**2l′**	57	10
13	2-MeC_6H_4 **1m**	**2m′**	83	19
14	2-EtC_6H_4 **1n**	**2n′**	79	10
15	2-ClC_6H_4 **1o**	**2o′**	80	30
16	2-BrC_6H_4 **1p**	**2p′**	82	3
17	2-$MeOC_6H_4$ **1q**	**2q′**	79	73
18	2-$EtOC_6H_4$ **1r**	**2r′**	83	53
19	2,3-$(MeO)_2C_6H_3$ **1s**	**2s′**	82	86
20	2,4-$(MeO)_2C_6H_3$ **1t**	**2t′**	80	78
21	2,6-$(MeO)_2C_6H_3$ **1u**	**2u′**	76	13
22	2,6-$Me_2C_6H_3$ **1v**	**2v′**	85	12
23	1-Naphthyl **1w**	**2w′**	77	10
24	2-Naphthyl **1x**	**2x′**	88	19

[a] Catalyst **2′**-ZnMe was prepared by the asymmetric addition of Me_2Zn (1.5 equiv) to **1** in the presence of $[RhCl(C_2H_4)_2]_2$ (3 mol % Rh) and (*R*,*R*)-Ph-bod* (6 mol %) in dioxane at 50 °C for 3 h. After concentration of the mixture of **2′**-ZnMe, hexane, Et_2Zn (40 equiv), and benzaldehyde **3a** (20 equiv) were added to the residue. The resulting mixture was stirred at 30 °C for 24 h.
[b] Isolated yield.
[c] Chiral HPLC analysis.
[d] Absolute configuration was determined by comparison of the sign of the specific rotation and the chiral HPLC retention time with data in the literature.

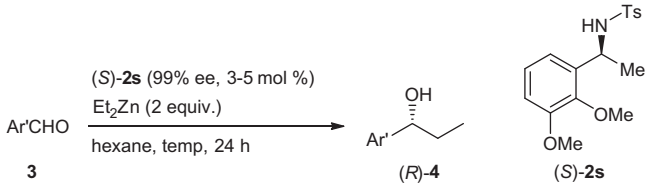
which has a methoxy group at the 2-position (entry 17). The screening result for **1r** with an ethoxy group was likewise notable, but the selectivity was lower than that of **1q** (entry 18). These results indicate that the coordination ability of the alkoxy group to the zinc metal center is likely to be important for high enantioselectivity. Moreover, the introduction of an additional methoxy group at the 3- or 4-position of **1q** was found to further improve the enantioselectivity (entries 19 and 20). In particular, the highest enantioselectivity (86% ee) was observed when *N*-tosyl-2,3-dimethoxyphenylimine **1s** was employed as the substrate for the first step of the reaction (entry 19). Other substrates with substituents at the 2,6-positions or a naphthyl moiety gave poor enantioselectivity (entries 21–24).

The generality of the ethylation of aldehydes **3** using organozinc **2s′**, which was found to be the best catalyst in the screening in Table 1, was examined (Table 2). First, we prepared 99% ee of **2s** by recrystallization of the enantiomerically enriched (95% ee) **2s** obtained by the Rh-catalyzed asymmetric addition with H_2O quenching. Next, organozinc catalyst **2s′**-ZnMe was prepared by mixing 99% ee of **2s** with dimethylzinc. When we applied this catalyst (5 mol %) to the ethylation of benzaldehyde (**3a**) at 30 °C, **4a** was produced with 83% ee (entry 1). A similar result was obtained with the **2s′**-ZnEt catalyst, which was prepared from 99% ee of **2s** and diethylzinc (entry 2). Lowering the temperature when using **2s′**-ZnEt catalyst generally improved the enantioselectivity (entries 3–5). At the end of the optimization, it was found that 95% ee of **4a** could be obtained by performing the reaction at 0 °C in the presence of 3 mol % of **2s′**-ZnEt catalyst (entry 6).[10] Under these conditions, the reaction of various aldehydes **3** gave corresponding alcohols with high enantioselectivities (entries 7–14). In particular, the ethylation of 2-naphthaldehyde **3i** gave **4i** with the highest enantioselectivity (96% ee) (entry 14).

3. Conclusion

We have found a new chiral zinc catalyst for the asymmetric addition of diethylzinc to aldehydes through a screening method in which two catalytic asymmetric reactions were connected. Performance of multiple asymmetric reactions consecutively is an effective approach to amplify the asymmetric source. The fact that chiral zinc catalyst **2s′** can be prepared from inexpensive reagents by a Rh-catalyzed asymmetric addition underscores the advantage of this catalyst over other catalysts.

Table 2
Asymmetric addition of diethylzinc to aldehydes **3** catalyzed by (*S*)-**2s**'[a]



Entry	**3**	(*S*)-**2s** (mol %)	Temp (°C)	Yield[b] of **4** (%)	ee[c,d] of **4** (%)
1[e]	Benzaldehyde **3a**	5	30	73	83
2		5	30	73	85
3		5	20	84	88
4		5	0	77	94
5		5	−20	48	95
6		3	0	74	95
7	4-Methylbenzaldehyde **3b**	3	0	68	94
8	4-Chlorobenzaldehyde **3c**	3	0	60	90
9	4-Methoxybenzaldehyde **3d**	3	0	70	91
10	2-Methylbenzaldehyde **3e**	3	0	72	91
11	2-Chlorobenzaldehyde **3f**	3	0	77	75
12	2-Methoxybenzaldehyde **3g**	3	0	69	80
13	1-Naphthaldehyde **3h**	3	0	79	89
14	2-Naphthaldehyde **3i**	3	0	90	96

[a] A mixture of (*S*)-**2s** (3–5 mol %) and diethylzinc (2 equiv) in hexane was stirred at room temperature for 1 h. Then, aldehyde **3** was added and the resulting mixture was stirred for 24 h at the reaction temperature.
[b] Isolated yield.
[c] Chiral HPLC analysis.
[d] Absolute configuration was determined by the comparison of the sign of the specific rotation and the chiral HPLC retention time with the data in the literature.
[e] The catalyst was prepared from (*S*)-**2s** and dimethylzinc.

4. Experimental

4.1. General

All anaerobic and moisture-sensitive manipulations were carried out using standard Schlenk techniques or glove box techniques under argon. NMR spectra were recorded on a JEOL JNM ECA-500 spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C) and ECS-400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) at Chemical Analysis Center, Chiba University. Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$ standard for ^{1}H NMR and chloroform-*d* (δ 77.0) for ^{13}C NMR. High-resolution mass spectra were recorded on Thermo Fisher Scientific Exactive Orbitrap mass spectrometers at Chemical Analysis Center, Chiba University. Optical rotations were measured with a JASCO P-1020 polarimeter.

4.2. Materials

Toluene and 1,4-dioxane were distilled from sodium benzophenone-ketyl under argon and stored in a glass flask with a Teflon stopcock. $[RhCl(C_2H_4)_2]_2$ was prepared according to the reported procedures.[11] Hexane, *p*-toluenesulfonamide, boron trifluoride diethyl ether complex, dimethylzinc (1 M solution in hexane), diethylzinc (1 M solution in hexane), and (1*R*,4*R*)-2,5-dibenzylbicyclo[2.2.2]octa-2,5-diene [(*R*,*R*)-Ph-bod*] were used as received.

4.3. Procedures for the preparation of *N*-tosylarylimines 1[12]

4.3.1. General procedure A

To a mixture of *p*-toluenesulfonamide (10.0 mmol) and aldehyde (10.0 mmol) in toluene (20 mL) was slowly added boron trifluoride diethyl ether complex (0.80 mmol, 0.098 mL) at reflux under argon and the mixture was stirred for 12 h. After cooling to room temperature, the mixture was quenched with 1 N NaOH aq and extracted with EtOAc three times. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was then recrystallized (EtOAc/hexane) to give *N*-tosylarylimines **1**.

4.3.2. *N*-Phenylmethylidene-4-methylbenzenesulfonamide 1a

Yield, 95%. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.35 (d, *J* = 7.9 Hz, 2H), 7.46–7.52 (m, 2H), 7.59–7.64 (m, 1H), 7.87–7.95 (m, 4H), 9.03 (s, 1H).

4.3.3. *N*-(4-Methylphenyl)methylidene-4-methylbenzenesulfonamide 1b

Yield, 77%. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 2.44 (s, 3H), 7.26–7.29 (m, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 2H), 7.87–7.90 (m, 2H), 8.99 (s, 1H).

4.3.4. *N*-(4-Ethylphenyl)methylidene-4-methylbenzenesulfonamide 1c

Yield, 63%. ^{1}H NMR ($CDCl_3$) δ 1.25 (t, *J* = 7.6 Hz, 3H), 2.43 (s, 3H), 2.71 (q, *J* = 7.6 Hz, 2H), 7.30–7.34 (m, 4H), 7.80–7.89 (m, 4H), 8.99 (s, 1H).

4.3.5. *N*-(4-Isopropylphenyl)methylidene-4-methylbenzenesulfonamide 1d

Yield, 56%. ^{1}H NMR ($CDCl_3$) δ 1.26 (d, *J* = 7.1 Hz, 6H), 2.44 (s, 3H), 2.93–3.01 (m, 1H), 7.31–7.35 (m, 4H), 7.81–7.88 (m, 4H), 8.99 (s, 1H).

4.3.6. *N*-(4-Phenylphenyl)methylidene-4-methylbenzenesulfonamide 1e

Yield, 44%. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 7.35 (d, *J* = 8.2 Hz, 2H), 7.40–7.49 (m, 3H), 7.62 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.7 Hz, 2H), 9.00 (s, 1H).

4.3.7. *N*-(4-Trifluoromethylphenyl)methylidene-4-methylbenzenesulfonamide 1f

Yield, 81%. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 7.37 (d, J = 7.9 Hz, 2H), 7.75 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 8.05 (d, J = 8.2 Hz, 2H), 9.08 (s, 1H).

4.3.8. *N*-(4-Fluorophenyl)methylidene-4-methylbenzenesulfonamide 1g

Yield, 70%. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.15–7.19 (m, 2H), 7.35 (d, J = 7.9 Hz, 2H), 7.87–7.89 (m, 2H), 7.93–7.97 (m, 2H), 9.00 (s, 1H).

4.3.9. *N*-(4-Chlorophenyl)methylidene-4-methylbenzenesulfonamide (1h)

Yield, 91%. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.35 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 8.6 Hz, 2H), 7.86 (d, J = 8.6 Hz, 2H), 7.88 (d, J = 8.3 Hz, 2H), 8.99 (s, 1H).

4.3.10. *N*-(4-Methoxyphenyl)methylidene-4-methylbenzenesulfonamide 1i

70% yield. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.88 (s, 3H), 6.95–6.99 (m, 2H), 7.33 (d, J = 8.2 Hz, 2H), 7.86–7.90 (m, 4H), 8.94 (s, 1H).

4.3.11. *N*-(4-Ethoxyphenyl)methylidene-4-methylbenzenesulfonamide 1j

Yield, 38%. ^{1}H NMR ($CDCl_3$) δ 1.44 (t, J = 6.9 Hz, 3H), 2.43 (s, 3H), 4.11 (q, J = 7.3 Hz, 2H), 6.93 (d, J = 4.6 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 7.87 (d, J = 7.8 Hz, 4H), 8.93 (s, 1H).

4.3.12. *N*-(4-Butoxyphenyl)methylidene-4-methylbenzenesulfonamide 1k

Yield, 38%. ^{1}H NMR ($CDCl_3$) δ 0.97 (t, J = 7.3 Hz, 3H),1.44–1.54 (m, 2H), 1.75–1.82 (m, 2H), 2.43 (s, 3H), 4.03 (t, J = 6.4 Hz, 2H), 6.95 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.85–7.88 (m, 4H), 8.93 (s, 1H).

4.3.13. *N*-(4-Benzyloxyphenyl)methylidene-4-methylbenzenesulfonamide 1l

Yield, 42%. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 5.14 (s, 2H), 7.04 (d, J = 5.0 Hz, 2H), 7.22–7.42 (m, 7H), 7.86–7.90 (m, 4H), 8.94 (s, 1H).

4.3.14. *N*-(2-Methylphenyl)methylidene-4-methylbenzenesulfonamide 1m

Yield, 55%. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 2.60 (s, 3H), 7.25–7.31 (m, 2H), 7.33–7.36 (m, 2H), 7.45–7.49 (m, 2H), 8.00 (d, J = 7.8 Hz, 2H), 9.34 (s, 1H).

4.3.15. *N*-(2-Ethylphenyl)methylidene-4-methylbenzenesulfonamide 1n

Yield, 77%. ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 7.6 Hz, 3H), 2.44 (s, 3H), 2.97 (q, J = 7.7 Hz, 2H), 7.29 (d, J = 7.6 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 7.49–7.53 (m, 1H), 7.89 (d, J = 8.4 Hz, 2H), 8.04–8.06 (m, 1H), 9.35 (s, 1H).

4.3.16. *N*-(2-Chlorophenyl)methylidene-4-methylbenzenesulfonamide 1o

Yield, 75%. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 7.34–7.37 (m, 3H), 7.46–7.52 (m, 2H), 7.90 (d, J = 8.5 Hz, 2H), 8.14–8.17 (m, 1H), 9.50 (s, 1H).

4.3.17. *N*-(2-Bromophenyl)methylidene-4-methylbenzenesulfonamide 1p

Yield, 23%. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H), 7.36–7.46 (m, 4H), 7.66 (d, J = 6.4 Hz, 1H), 7.91 (d, J = 6.4 Hz, 2H), 8.15 (d, J = 6.4 Hz, 1H), 9.43 (s, 1H).

4.3.18. *N*-(2-Methoxyphenyl)methylidene-4-methylbenzenesulfonamide 1q

Yield, 73%. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.93 (s, 3H), 6.94–7.00 (m, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.52–7.59 (m, 1H), 7.89 (d, J = 8.4 Hz, 2H), 8.06–8.07 (m, 1H), 9.54 (s, 1H).

4.3.19. *N*-(2-Ethoxyphenyl)methylidene-4-methylbenzenesulfonamide 1r

Yield, 60%. ^{1}H NMR ($CDCl_3$) δ 1.47 (t, J = 7.3 Hz, 3H), 2.43 (s, 3H), 4.14 (q, J = 7.3 Hz, 2H), 6.92–7.01 (m, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.50–7.55 (m, 1H), 7.89 (d, J = 7.8 Hz, 2H), 8.04–8.07 (m, 1H), 9.53 (s, 1H).

4.3.20. *N*-(2,3-Dimethoxyphenyl)methylidene-4-methylbenzenesulfonamide 1s

Yield, 60%. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.89 (s, 3H), 3.96 (s, 3H), 7.06–7.16 (m, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.61–7.64 (m, 1H), 7.89 (d, J = 8.0 Hz, 2H), 9.44 (s, 1H).

4.3.21. *N*-(2,4-Dimethoxyphenyl)methylidene-4-methylbenzenesulfonamide 1t

Yield, 68%. ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3H), 3.87 (s, 3H), 3.89 (s, 3H), 6.40 (s, 1H), 6.51 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 2H), 7.87 (d, J = 8.0 Hz, 2H), 8.03 (d, J = 8.0 Hz, 1H), 9.41 (s, 1H).

4.3.22. *N*-(2,6-Dimethoxyphenyl)methylidene-4-methylbenzenesulfonamide 1u

Yield, 75%. ^{1}H NMR ($CDCl_3$) δ 2.42 (s, 3H), 3.88 (s, 6H), 6.54 (d, J = 8.7 Hz, 2H), 7.31 (d, J = 8.2 Hz, 2H), 7.46 (t, J = 8.2 Hz, 1H), 7.89 (d, J = 8.0 Hz, 2H), 9.55 (s, 1H).

4.3.23. *N*-(2,6-Dimethylphenyl)methylidene-4-methylbenzenesulfonamide 1v

Yield, 68%. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 2.56 (s, 6H), 7.10 (d, J = 7.8 Hz, 2H), 7.27–7.35 (m, 3H), 7.89 (d, J = 7.8 Hz, 2H), 9.50 (s, 1H).

4.3.24. *N*-(1-Naphthyl)methylidene-4-methylbenzenesulfonamide 1w

Yield, 90%. ^{1}H NMR ($CDCl_3$) δ 2.43 (s, 3H), 7.35 (d, J = 8.4 Hz, 2H), 7.57 (t, J = 7.8 Hz, 1H), 7.58 (t, J = 7.8 Hz, 1H), 7.67 (t, J = 8.1 Hz, 1H), 7.91 (d, J = 7.7 Hz, 1H), 7.95 (d, J = 8.4 Hz, 2H), 8.09 (d, J = 8.2 Hz, 1H), 8.15 (d, J = 7.2 Hz, 1H), 8.98 (d, J = 8.2 Hz, 1H), 9.61 (s, 1H).

4.3.25. *N*-(2-Naphthyl)methylidene-4-methylbenzenesulfonamide 1x

Yield, 34%. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 7.33–7.39 (m, 2H), 7.55–7.60 (m, 1H), 7.60–7.66 (m, 1H), 7.85–7.90 (m, 2H), 7.90–7.98 (m, 3H), 8.00–8.06 (m, 1H), 8.33 (s, 1H), 9.07 (s, 1H).

4.4. Procedure for the screening for the asymmetric catalysts 2′ by connecting two reactions

4.4.1. General procedure B

A mixture of $[RhCl(C_2H_4)_2]_2$ (0.400 mg, 0.00100 mmol, 3 mol % Rh) and (*R*,*R*)-Ph-bod* (1.00 mg, 0.00400 mmol, 2 equiv to Rh) in 1,4-dioxane (0.30 mL) was placed in a 20 mL Schlenk tube and stirred for 5 min at room temperature. To this solution were added *N*-tosylarylimine **1** (0.0660 mmol), additional 1,4-dioxane (0.40 mL), and Me_2Zn (0.10 mL, 0.10 mmol; 1.02 M solution in hexane). The mixture was stirred for 3 h at 50 °C. After cooling to room temperature, the mixture was thoroughly concentrated under reduced pressure. To the mixture were added hexane (2.0 mL), diethylzinc (2.70 mL 2.70 mmol; 1.05 M solution in hexane), and benzaldehyde **3a** (0.134 mL, 1.32 mmol). After stirring for 24 h at 30 °C,

the mixture was quenched by 1 M HCl aq and extracted with EtOAc three times. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude product was purified by PTLC on silica gel (EtOAc/hexane = 1:4) to give **4a**.

4.5. Procedure for the asymmetric addition of dimethylzinc to *N*-tosylarylimines 1 catalyzed by a rhodium–diene complex[4]

4.5.1. General procedure C

A mixture of $[RhCl(C_2H_4)_2]_2$ (1.20 mg 0.00300 mmol, 3 mol % Rh) and (*R*,*R*)-Ph-bod* (3.10 mg, 0.0120 mmol, 2 equiv to Rh) in 1,4-dioxane (0.30 ml) was placed in a 20 mL Schlenk tube and stirred for 5 min at room temperature. To this solution were added successively *N*-tosylarylimine **1** (0.200 mmol), additional 1,4-dioxane (0.40 mL), and Me_2Zn (0.30 mL, 0.30 mmol; 1.02 M solution in hexane). After stirring for 3 h at 50 °C, the resulting mixture was quenched with 7% NH_3 aq and extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The residue was purified by PTLC (EtOAc/hexane = 1:2) to give **2**.

4.5.2. *N*-[(1*S*)-1-(2,3-Dimethoxyphenyl)ethyl]-4-methylbenzenesulfonamide (*S*)-2s

Yield, 41%, 95% ee. The ee was determined by HPLC analysis with a stationary phase column Chiralcel OD-H column (hexane/2-propanol = 4:1, flow = 0.3 mL/min, wavelength = 254 nm, retention times = 25.0 min [(*R*)-enantiomer], 28.9 min [(*S*)-enantiomer]). ^{1}H NMR ($CDCl_3$) δ 1.43 (d, J = 7.1 Hz, 3H), 2.33 (s, 3H), 3.79 (s, 3H), 3.80 (s, 3H), 4.55–4.62 (m, 1H), 5.34 (d, J = 8.7 Hz, 1H), 6.56–6.58 (m, 1H), 6.70–6.73 (m, 1H), 6.82–6.86 (m, 1H), 7.10 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 21.5, 23.8, 51.2, 55.8, 60.8, 111.7, 119.6, 124.0, 127.0, 129.2, 135.5, 137.6, 142.8, 146.0, 152.5; HRMS (ESI) calcd for $C_{17}H_{21}O_4NNaS$ ([M+Na]$^+$) 358.1084, found 358.1078. Crystallization in EtOAc/hexane (1:2) increased the ee to >99% ee; $[\alpha]_D^{20} = -20.8$ (c 0.300, $CHCl_3$); mp 131–136 °C.

4.6. Procedures for the asymmetric addition of diethylzinc to aldehydes 3 catalyzed by 2s′

4.6.1. General procedure D

A mixture of **2s** (0.0060 mmol) and diethylzinc (0.40 mL, 0.40 mmol; 1.05 M solution in hexane) in hexane (1.00 mL) was stirred at room temperature for 1 h. Then the mixture was cooled to appropriate temperature, added aldehyde **3** (0.200 mmol), and stirred for 24 h. The mixture was then quenched by NH_4Cl aq and extracted with EtOAc three times. The combined organic layers were washed with brine and dried over Na_2SO_4. The crude product was purified by PTLC on silica gel (EtOAc/hexane = 1:4) to give **4**.

4.6.2. (*R*)-1-Phenylpropanol 4a

This product was characterized by the comparison of the spectroscopic data with those reported previously[13]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OD-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 26.0 min [(*R*)-enantiomer]], 30.8 min [(*S*)-enantiomer].[14]

4.6.3. (*R*)-1-(4-Methylphenyl)-1-propanol 4b

This product was characterized by the comparison of the spectroscopic data with those reported previously[13]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OB-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 21.8 min [(*S*)-enantiomer], 26.5 min [(*R*)-enantiomer].[15]

4.6.4. (*R*)-1-(4-Chlorophenyl)-1-propanol 4c

This product was characterized by the comparison of the spectroscopic data with those reported previously[13]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OB-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 22.0 min [(*S*)-enantiomer], 24.4 min [(*R*)-enantiomer] or Daicel Chiralcel OD-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 8.9 min [(*S*)-enantiomer], 10.5 min [(*R*)-enantiomer].[16]

4.6.5. (*R*)-1-(4-Methoxyphenyl)-1-propanol 4d

This product was characterized by the comparison of the spectroscopic data with those reported previously[13]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OD-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 36.0 min [(*R*)-enantiomer], 41.7 min [(*S*)-enantiomer].[16]

4.6.6. (*R*)-1-(2-Methylphenyl)-1-propanol 4e

This product was characterized by the comparison of the spectroscopic data with those reported previously[17]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OB-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 15.9 min [(*S*)-enantiomer], 21.9 min [(*R*)-enantiomer].[18]

4.6.7. (*R*)-1-(2-Chlorophenyl)-1-propanol 4f

This product was characterized by the comparison of the spectroscopic data with those reported previously[16]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OB-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 14.0 min [(*S*)-enantiomer], 17.6 min [(*R*)-enantiomer].[14]

4.6.8. (*R*)-1-(2-Methoxyphenyl)-1-propanol 4g

This product was characterized by the comparison of the spectroscopic data with those reported previously[13]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OD-H, hexane/2-propanol = 500:1, flow = 0.5 mL/min, retention times = 122.5 min [(*R*)-enantiomer], 152.8 min [(*S*)-enantiomer].[17]

4.6.9. (*R*)-1-(1-Naphthyl)-1-propanol 4h

This product was characterized by the comparison of the spectroscopic data with those reported previously[16]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OD-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 38.8 min [(*S*)-enantiomer], 54.9 min [(*R*)-enantiomer].[16]

4.6.10. (*R*)-1-(2-Naphthyl)-1-propanol 4i

This product was characterized by the comparison of the spectroscopic data with those reported previously[19]; the ee value was determined by HPLC analysis with a stationary phase column Daicel Chiralcel OD-H, hexane/2-propanol = 98:2, flow = 0.5 mL/min, retention times = 55.8 min [(*S*)-enantiomer], 64.5 min [(*R*)-enantiomer].[14]

Acknowledgments

We thank Dr. Takeharu Toyoshima for some initial experiments. We appreciate the financial support from JGC-S Scholarship Foundation (No. 2208) to K.Y.

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