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Commercially available neat organozincs as highly reactive reagents for catalytic enantioselective addition to ketones and aldehydes under solvent free conditions

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ABSTRACT

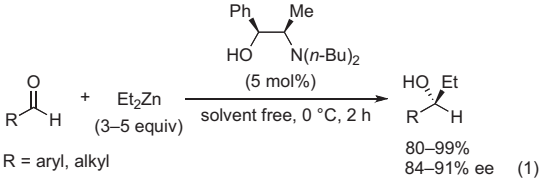
Neat Et_2Zn, Ph_2Zn, and highly concentrated Me_2Zn are highly reactive organozinc reagents, which are commercially available in bulk quantities. We here report a catalytic enantioselective Et_2Zn, Ph_2Zn, and Me_2Zn addition to ketones and aldehydes under solvent free or highly concentrated conditions without Ti(O*i*-Pr)$_4$ as a conventional activator of organozinc reagents. The desired optically active tertiary and secondary alcohols were obtained in good yield with high enantioselectivity when compared to the conventional solvent-use conditions. From the viewpoint of ecological and environmental reasons in green chemistry, this catalysis would be practical for not only academic but also industrial use.

1. Introduction

A catalytic enantioselective organozinc addition to carbon electrophiles is an important reaction in asymmetric catalysis.[1] It has been extensively documented since the discovery of the reaction by Oguni and Noyori 25 years ago.[2] To date, a variety of highly effective chiral ligands have been developed for the enantioselective organozinc addition to aldehydes to provide optically active secondary alcohols under the mild reaction conditions.[3] However, organozinc addition to much less reactive ketones to provide optically active tertiary alcohols, in place of more reactive aldehydes, is still challenging. This difficulty is caused by both steric and electronic factors between ketones and organozinc reagents, and low reactivity and/or low enantioselectivity are sometimes observed.[4,5] Most chiral ligands, which are effective for the addition to aldehydes, often cannot be used for ketones due to a formation of reduction byproducts (i.e., secondary alcohols). Moreover, Zn(II)-enolates are often generated from ketones via α-deprotonation, and the corresponding self-aldol compounds or recovery of starting ketones after acidic workup procedure is observed.

To improve the reactivity of substrates and reagents, solvent free organic synthesis has generally received much attention.[6] Since solvents in organic synthesis often might be wastes, solvent free conditions are favorable from the viewpoint of ecological and environmental reasons in green chemistry. Although catalytic enantioselective reactions using organometallic reagents under solvent free conditions have not yet been common,[6c] a few pioneering examples in catalytic enantioselective organozinc addition to aldehydes and ketones have been reported by Soai[7] and Walsh.[8]

Soai and co-workers reported, for the first time, the enantioselective addition of Et_2Zn to aldehydes using chiral β-amino alcohols as chiral ligands under solvent free conditions without Ti(O*i*-Pr)$_4$ (Eq. 1).[7] They used neat Et_2Zn (3–5 equiv) at 0 °C under homogeneous reaction conditions, and the desired secondary alcohols were obtained from both aromatic and aliphatic aldehydes in high yields with high enantioselectivities.



Later, Walsh and co-workers reported the first enantioselective addition of organozinc reagents to ketones using a chiral bis(hydroxyalkanesulfonamide) as a chiral ligand under solvent free conditions (Eq. 2).[8] They used a variety of neat organozinc reagents (3–5 equiv), although co-presence of liquid Ti(O*i*-Pr)$_4$ (1.2 equiv) was necessary. Significant benefits in catalytic activity (0.25–1 mol

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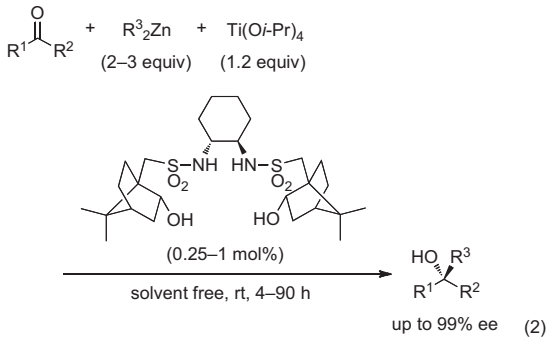
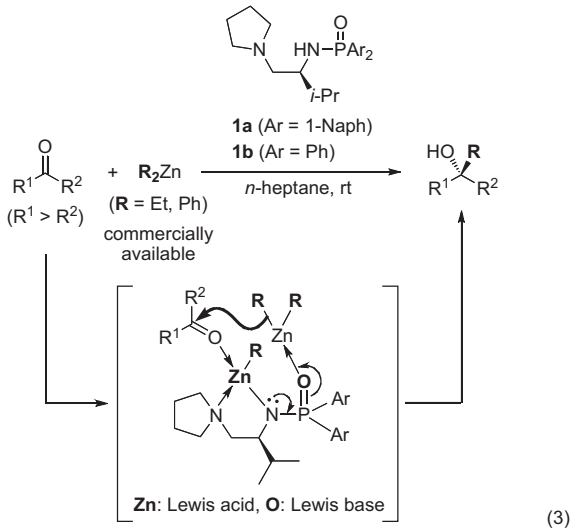
%) were observed under solvent free conditions with Ti(O*i*-Pr)$_4$, and the corresponding tertiary alcohols were obtained with high enantioselectivities (up to 99% ee).



(2)

Meanwhile, we recently developed L-valine-derived chiral phosphoramide ligands **1**, which gave chiral conjugate Lewis acid–Lewis base catalysts[9] in situ, for commercially available Et_2Zn and Ph_2Zn addition to ketones as well as aldehydes under *n*-heptane solvent conditions (Eq. 3).[10a,b] As an advantageous point in our catalysis with **1**, the addition of Ti(O*i*-Pr)$_4$ was not required as an activator of organozinc reagents even for less reactive ketones. Later, we reported a catalytic enantioselective alkyl addition to aldehydes and ketones with commercially unavailable neat di(1°-alkyl)zinc and di(2°-alkyl) zinc reagents that were prepared from Grignard reagents by using a refined Charette's method (Eq. 4).[10c,d,11] Although this method is highly attractive on a small scale in laboratory, the centrifugation of the prepared suspension including organozinc reagents and inorganic salts might be unlikely on a larger scale, particularly in industry. In sharp contrast, more useful and popular Et_2Zn, Ph_2Zn, and Me_2Zn are commercially available even in bulk quantities in neat (or highly concentrated) and solid states from many suppliers. In particular, in the reaction of less reactive ketones unlike more reactive aldehydes, reactivity of organozinc reagents is critical. In this context, with the use of commercially available neat or highly concentrated Et_2Zn, Ph_2Zn, and Me_2Zn, we here report the catalytic enantioselective organozinc addition to ketones and aldehydes under solvent free or highly concentrated conditions by simple procedure without Ti(O*i*-Pr)$_4$ (Eq. 5). Although the use of pyrophoric organozinc reagents without solvent is somewhat hazardous, these reactive neat organozinc reagents are significantly attractive for not only academic but also industrial use since they are practically provided in bulk quantities without serious problems in industry.



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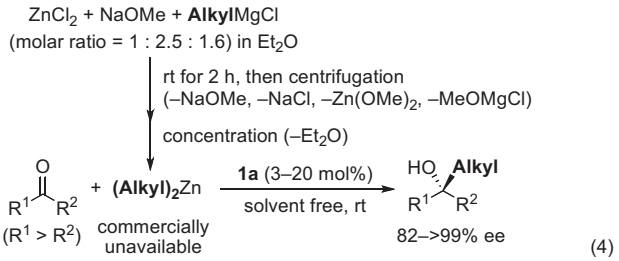

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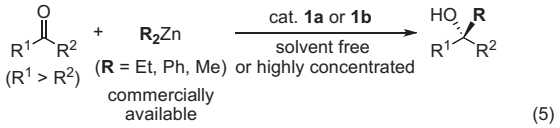
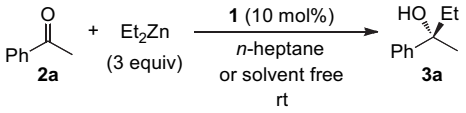


(5)

2. Results and discussion

As an initial stage of the study, we examined a prove reaction between acetophenone **2a** and Et_2Zn under conventional *n*-heptane conditions or solvent free conditions (Table 1). Since neat Et_2Zn is commercially available, relatively less reactive and less pyrophoric than other organometallic reagents like EtLi, EtMgX, Et_3Al, etc., and non-viscous liquid at room temperature, the handling of it under the inert gas atmosphere is not technically difficult even in laboratory. As expected, homogeneous solvent free conditions with neat Et_2Zn were found to be effective to increase the catalytic activity when **1a** was used (entries 1 and 2). The reaction proceeded within 8 h under solvent free conditions and the corresponding product **3a** was obtained in 89% yield with 94% ee, while **3a** was obtained in 80% yield with 93% ee within 24 h under conventional *n*-heptane conditions. In sharp contrast, less bulky ligand **1b** in place of more bulky **1a** showed lower reactivity and enantioselectivity even if the reaction was conducted under solvent free conditions, since **1b**-catalysis gave undesired self-aldol product and recovered **2a** (entries 3 and 4). Therefore, the bulkiness of ligand **1a** might be critical for the selective organozinc addition to ketones.

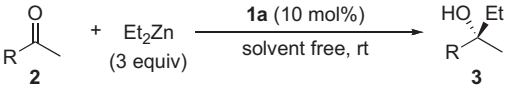
Table 1
Et_2Zn addition to acetophenone **2a**



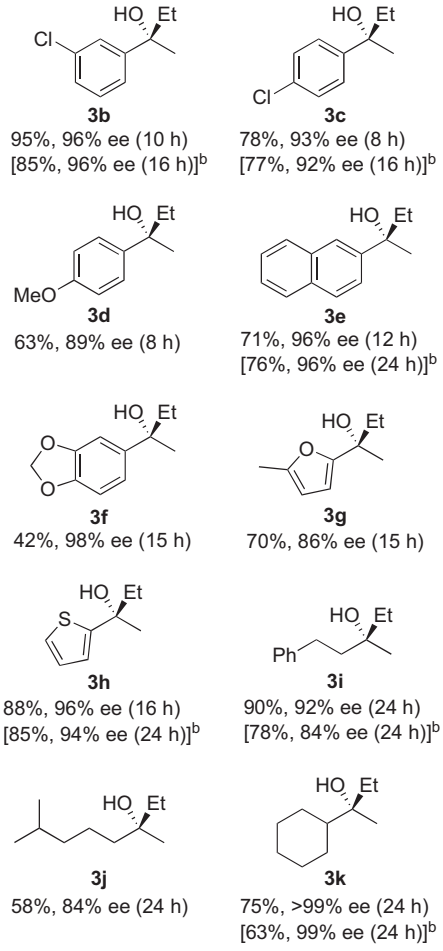
Entry	Ligand	Et_2Zn	Time (h)	Yield (%)	ee (%)
1[a]	**1a**	1 M in *n*-heptane	24	80	93
2[b]	**1a**	Solvent free	8	89	94
3[a]	**1b**	1 M in *n*-heptane	24	21	87
4[b]	**1b**	Solvent free	24	19	73

[a] Reaction was conducted in 1 M Et_2Zn solution in *n*-heptane without additional solvent.
[b] Neat Et_2Zn was used under solvent free conditions.

By using **1a**, not only aromatic ketones (see **3b**–**f**) but also heteroaromatic ketones (see **3g** and **3h**) were used under the solvent free conditions, and the desired tertiary alcohols were obtained in high yields with high enantioselectivities (Scheme 1). To clearly compare the results to those in our conventional catalysis,[10a] results under the *n*-heptane solution conditions are shown in brackets. In particular, ketones with an electron-donative group,



Product, yield, enantioselectivity, and reaction time[a]



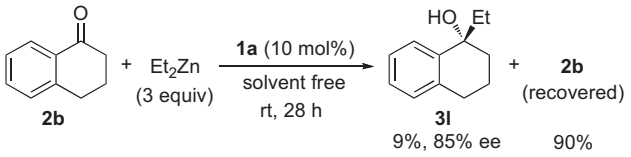
Scheme 1. Enantioselective Et_2Zn addition to methylketones **2** under solvent free conditions. Conditions: (a) unless otherwise noted **2** (1 mmol) and neat Et_2Zn (0.31 mL, 3 mmol) were used in the presence of **1a** (10 mol %). (b) Data in the brackets are the results when 1 M Et_2Zn in *n*-heptane (3 mL, 3 mmol) was used in place of neat Et_2Zn. See Ref. 10a for **3c**, **3e**, and **3h**.

which were generally unsuitable under less reactive solvent conditions, could be applied under solvent free conditions although the yields were still moderate (see **3d**, **3f**, and **3g**). Moreover, aliphatic ketones, which we have not used so far, could be used, and improvements on yield and/or enantioselectivity were observed (see **3i**–**k**). Reduction to secondary alcohols, as a possible serious problem, was scarcely observed in those reactions with the use of **1a**, although the starting ketones were often recovered (see **3b**–**k**).

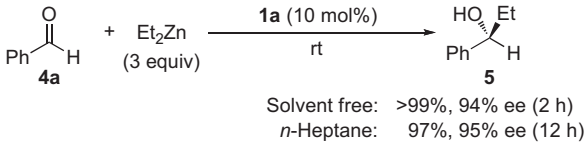
In place of acetylarenes and 2-alkanones in Scheme 1, α-tetralone **2b** was examined (Scheme 2). Unfortunately, however, the desired product **3l** was obtained in only 9% yield although its enantioselectivity was high (85% ee). In this case, **2b** was fully recovered after acidic workup procedure, and thus it would be α-deprotonated in situ.

Ethylation of benzaldehyde **4a** was also examined (Scheme 3). Under solvent free conditions, the corresponding product **5** was obtained in quantitative yield within 2 h, while **5** was obtained in 97% yield for 12 h under *n*-heptane conditions.

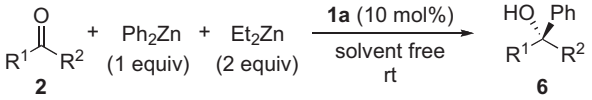
Next, phenylation of ketones was examined under solvent free conditions (Scheme 4). Although Ph_2Zn (1 equiv) is solid at room



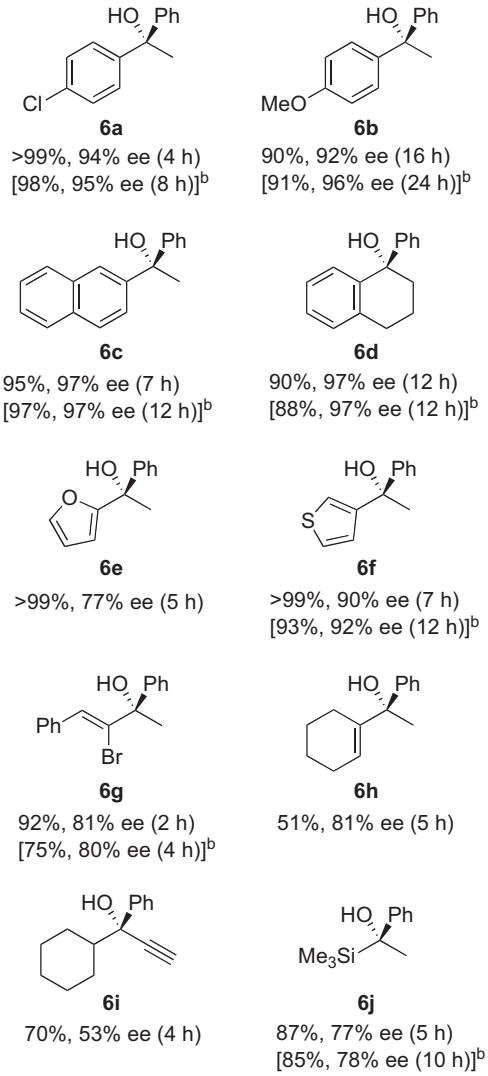
Scheme 2. Et_2Zn addition to α-tetralone **2b**.



Scheme 3. Et_2Zn addition to benzaldehyde **4a**.



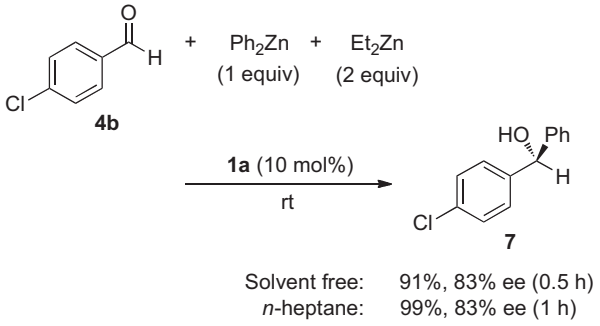
Product, yield, enantioselectivity, and reaction time[a]



Scheme 4. Enantioselective Ph_2Zn addition to ketones **2** under solvent free conditions. Conditions: (a) unless otherwise noted **2** (1 mmol), neat Et_2Zn (0.21 mL, 2 mmol), and Ph_2Zn (1 mmol) were used in the presence of **1a** (10 mol %). (b) Data in the brackets are the results when 1 M Et_2Zn in *n*-heptane (2 mL, 2 mmol) was used in place of neat Et_2Zn. See Ref. 10a for **6a**–**d** and **6f**.

temperature, the solvent free conditions could be realized since liquid Et_2Zn (2 equiv) would serve as a solvent as well as a co-reagent for Ph_2Zn.[12,3c] Similar to the **1a**-catalyzed ethylation under solvent free conditions, the phenylation proceeded smoothly under the homogeneous solvent free conditions, and the catalytic activity was increased expectedly when compared from the *n*-heptane solution conditions as shown in the brackets in Scheme 4. In almost all the cases that were examined, reactions were further promoted under solvent free conditions rather than conventional *n*-heptane conditions[10a] (see the results in brackets). Acetylarenes (see **6a**–**c**), α-tetralone (see **6d**), and acetylheteroarenes (see **6e** and **6f**) gave the corresponding tertiary alcohols in high yields with high enantioselectivities without side products. α,β-Unsaturated enones (see **6g** and **6h**), which we have not examined so far, were also used, although complicated mixtures including a 1,4-addition compound were accompanied in the case of **6h** even under solvent free conditions. For other substrates that we have not examined, 1-cyclohexylprop-2-yn-1-one as an α,β-unsaturated ynone substrate was also used and **6i** was obtained with moderate enantioselectivity (53% ee). Moreover, as a heteroaliphatic ketone, acetyltrimethylsilane could be used in this catalysis, and the corresponding Ph-adduct **6j** was obtained with good enantioselectivity (77% ee) within 5 h under solvent free conditions.

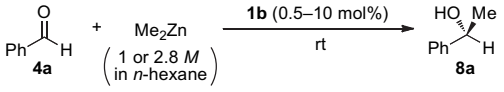
For phenylation of an aldehyde in place of a ketone, *p*-chlorobenzaldehyde **4b** reacted more rapidly under the solvent free conditions (within 30 min) than under the *n*-heptane solution conditions (within 1 h) (Scheme 5).



Scheme 5. Ph_2Zn addition to *p*-chlorobenzaldehyde **4b**.

In the preliminary investigation, Me_2Zn addition to simple unactivated ketones, such as propiophenone, α-tetralone, etc. was significantly sluggish, and the starting ketones were fully recovered.[13] Unfortunately, even when commercially available highly concentrated (2.8 M) Me_2Zn (bp 44–46 °C) solution in *n*-hexane was used, the reaction to ketones did not proceed. This is strongly owing to the low reactivity of Me_2Zn unlike other dialkylzinc(II) reagents, such as Et_2Zn.[14] Actually, there are a few excellent examples of catalytic enantioselective Me_2Zn addition to aldehydes.[15] Therefore, we next used aldehydes in place of ketones in catalytic enantioselective Me_2Zn addition. In sharp contrast to ketones, methylation of benzaldehyde **4a** could proceed quite smoothly in the presence of more accessible chiral ligand **1b** (10 mol %) in place of **1a** and 2.8 M Me_2Zn in *n*-hexane (3 equiv) without any side reactions (Table 2, entry 2). As expected, 2.8 M Me_2Zn in *n*-hexane was apparently more effective than 1 M Me_2Zn in *n*-hexane (entry 1). The amount of Me_2Zn and **1b** could be reduced, 2–1.5 equiv of Me_2Zn and 2–1 mol % of **1b** were still effective (entries 3 and 4), although 2 equiv of Me_2Zn and 0.5 mol % of **1b** showed low reactivity (entry 5).

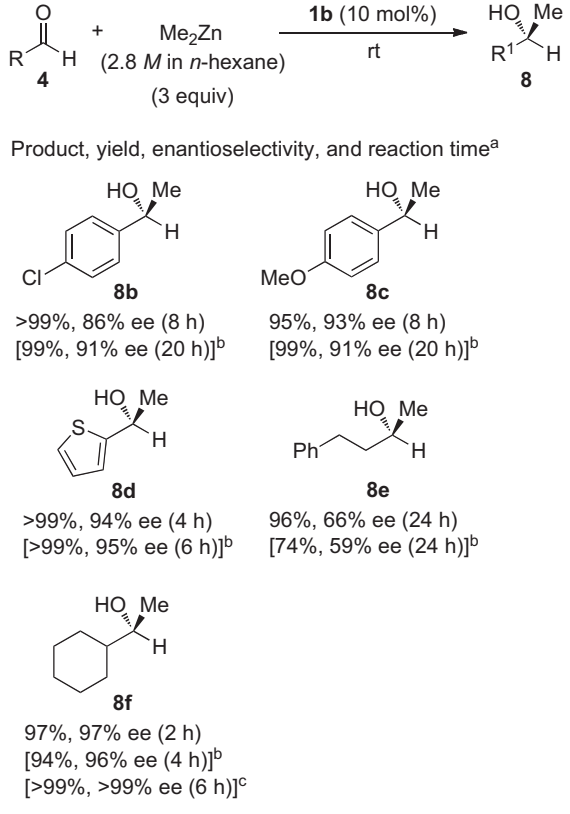
Table 2
Me_2Zn addition to benzaldehyde **4a**



Entry	Me_2Zn [equiv][a]	**1b** (mol %)	Time (h)	Yield (%)	ee (%)
1	1 M in *n*-hexane [3]	10	4	>99	90
2	2.8 M in *n*-hexane [3]	10	2	>99	92
3	2.8 M in *n*-hexane [2]	2	4	98	90
4	2.8 M in *n*-hexane [1.5]	1	5	84	89
5	2.8 M in *n*-hexane [2]	0.5	8	29	83

[a] Reaction was conducted in 1 or 2.8 M Me_2Zn solution in *n*-hexane without additional solvent.

For other aromatic, heteroaromatic, and aliphatic aldehydes, Me_2Zn addition smoothly proceeded under highly concentrated reaction conditions, and the corresponding secondary alcohols were obtained in high yields with high enantioselectivities by using **1b** (Scheme 6). Since we have not examined Me_2Zn addition to aldehyde under solvent conditions with **1b**, results under the *n*-heptane solution conditions are shown in brackets. Ligand **1a** was also effective, and **8f** was obtained in quantitative yield with >99% ee when 2 mol % of **1a** was used at 0 °C for 6 h, while the reaction was completed within 2 h with the use of 10 mol % of **1b** under *n*-hexane solvent conditions.



Scheme 6. Enantioselective Me_2Zn addition to aldehydes **4** under highly concentrated conditions. Conditions: (a) Unless otherwise noted **4** (1 mmol) and 2.8 M Me_2Zn in *n*-hexane (1.07 mL, 3 mmol) were used in the presence of **1b** (10 mol %). (b) Data in the brackets are the results when 1 M Me_2Zn in *n*-hexane (3 mL, 3 mmol) was used. (c) Data in the bracket is the result when the reaction was conducted with 2 mol % of **1a** in place of **1b** at 0 °C.

Finally, possible transition states are shown in Fig. 1. In particular, *si*-face attack via TS-**9** should be favored exclusively without terrible steric repulsion between the *i*-Pr moiety of **1a** and a substrate [$R^1(=O)R^2$, $R^1>R^2$].

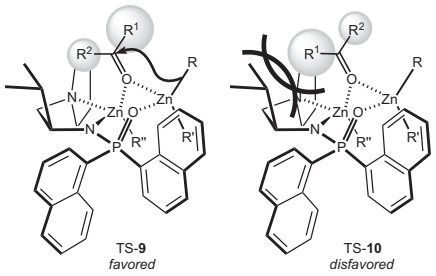


Fig. 1. Possible transition states ($R^1>R^2$).

3. Conclusion

In summary, we have developed the catalytic enantioselective addition of commercially available neat organozinc reagents (Et_2Zn, Ph_2Zn, and Me_2Zn) to ketones and aldehydes under solvent free or highly concentrated conditions without $Ti(O\textit{i}\text{-}Pr)_4$ as a conventional activator of organozinc reagents. The desired optically active tertiary and secondary alcohols were smoothly obtained with high enantioselectivity when compared to the conventional solvent-use conditions. From the viewpoint of ecological and environmental reasons in green chemistry, this catalysis would be practical for not only academic but also industrial use.

4. Experimental section

4.1. General

^{1}H NMR spectra were measured on a JEOL ECS-400 (400 MHz) spectrometer at ambient temperature. Data were recorded as follows: chemical shift in parts per million from internal tetramethylsilane on the δ scale, multiplicity (s=singlet; d=doublet; t=triplet; q=quartet; m=multiplet; br=broad), coupling constant (Hz), integration, and assignment. ^{13}C NMR spectra were measured on JEOL ECS-400 (100 MHz) spectrometer. Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (deuterochloroform at 77.10 ppm). High resolution mass spectral analyses (HRMS, FAB, and EI) were performed at Chemical Instrument Center, Nagoya University (JEOL JMS-700). IR spectra were determined by a FT-IR spectrometer. High performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-MA-10A-VP and chiral column of Daicel CHIRALCEL, CHIRALPAK; AD-H, OD-H, OJ-H. GC analysis was performed with Shimadzu 17A instruments using CP-Cyclodextrin-β-2,3,6-M-19 (i.d. 0.25 mm×25 m; CHROMPACK; GL Science Inc.) or CHIRALDEX B-DM, B-TA (i.d. 0.25 mm×20 m; Tokyo Kasei Kogyo Co., Ltd). All experiments were carried out under an atmosphere of dry nitrogen. For thin-layer chromatography (TLC) analysis throughout this work, Merck TLC plates (silica gel 60G F_{254} 0.25 mm) were used. The products were purified by neutral column chromatography on silica gel (Kanto Chemical Co., Inc. 37560). Visualization was accomplished by UV light (254 nm), anisaldehyde, $KMnO_4$, and phosphomolybdic acid. All dry solvents were obtained from commercial source and were distilled before use.

4.2. General procedure for the catalytic enantioselective addition of Et_2Zn to ketones

A well-dried Pyrex Schlenk tube was charged with **1a** (45.6 mg, 0.10 mmol) under nitrogen atmosphere. Then, Et_2Zn (0.31 mL, 3.0 mmol) was added at room temperature. This solution was stirred for 30 min, and ketone (**2**) (1.0 mmol) was added. The mixture was stirred for 8–24 h. Ether (or *n*-hexane, toluene, EtOAc, etc.) (10 mL) and satd NH_4Cl aqueous solution (10 mL) were poured into the mixture at 0 °C. The product was extracted with ether or EtOAc (10 mL×3) and washed by brine (10 mL). The combined extracts were dried over $MgSO_4$. The organic phase was concentrated under reduced pressure and the crude product was purified by neutral silica gel column chromatography (eluent: *n*-hexane/EtOAc), to give the desired products (**3**). The enantiomeric purity was determined by GC or HPLC on chiral column.

4.3. Analytical data for the Et-adducts

*4.3.1. (S)-2-Phenyl-2-butanol (**3a**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.75 (t, *J*=7.5 Hz, 3H), 1.48 (s, 3H), 1.73–1.81 (m, 2H), 2.16 (br, 1H), 7.25–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.3, 29.7, 36.7, 74.9, 124.9, 126.5, 128.1, 147.8. IR (neat) 3407, 2970, 1446, 1374, 1029 cm^{-1}. HRMS (FAB^+) calcd for $C_{10}H_{13}$ $[M-OH]^+$ 133.1017, found 133.1020. Chiral GC CHIRALDEX B-DM, 100 °C, t_R=9.1 min (major, *S*), 9.7 min (minor, *R*).

*4.3.2. (S)-2-(3-Chlorophenyl)butan-2-ol (**3b**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.78 (t, *J*=7.5 Hz, 3H), 1.51 (s, 3H), 1.79 (q, *J*=7.5 Hz, 1H), 1.80 (q, *J*=7.5 Hz, 1H), 1.95 (br, 1H), 7.16–7.31 (m, 3H), 7.43 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.2, 29.6, 36.6, 74.7, 123.2, 125.4, 126.6, 129.4, 134.1, 149.9. IR (neat) 3408, 2972, 2935, 1683, 1473, 1419 cm^{-1}. HRMS (FAB^+) calcd for $C_{10}H_{12}Cl$ $[M-OH]^+$ 167.0628, found 167.0626. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=99/1, 0.3 mL/min, t_R=48.9 min (major, *S*), 58.1 min (minor, *R*).

*4.3.3. (S)-2-(4-Chlorophenyl)butan-2-ol (**3c**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.77 (t, *J*=7.5 Hz, 3H), 1.53 (s, 3H), 1.77–1.83 (m, 2H), 1.82 (br, 1H), 7.28 (d, *J*=8.7 Hz, 2H), 7.35 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.3, 29.6, 36.7, 74.7, 126.6, 128.2, 132.3, 146.4. IR (neat) 3419, 2971, 2934, 1489, 1094 cm^{-1}. HRMS (FAB^+) calcd for $C_{10}H_{12}Cl$ $[M-OH]^+$ 167.0628, found 167.0630. Chiral GC CHIRALDEX B-TA, 90 °C, t_R=47.4 min (minor, *R*), 60.6 min (major, *S*).

*4.3.4. (S)-2-(4-Methoxyphenyl)butan-2-ol (**3d**)*[16]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (t, *J*=7.8 Hz, 3H), 1.52 (s, 3H), 1.70 (br, 1H), 1.75–1.90 (m, 2H), 3.80 (s, 3H), 6.87 (d, *J*=9.0 Hz, 2H), 7.35 (d, *J*=9.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.4, 29.6, 36.7, 55.3, 74.7, 113.4, 126.1, 139.9, 158.2. IR (neat) 2968, 2934, 1610, 1508, 1456, 1248, 1179, 1034 cm^{-1}. HRMS (FAB^+) calcd for $C_{11}H_{15}O$ $[M-OH]^+$ 163.1123, found 163.1124. Chiral GC CHIRALDEX G-TA, 110 °C, t_R=16.3 min (minor, *R*), 17.7 min (major, *S*).

*4.3.5. (S)-2-(Naphthalen-2-yl)butan-2-ol (**3e**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (t, *J*=7.5 Hz, 3H), 1.61 (s, 3H), 1.80–2.05 (m, 2H), 1.92 (br, 1H), 7.38–7.55 (m, 3H), 7.76–7.86 (m, 3H), 7.89 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.3, 29.7, 36.4, 75.1, 123.2, 123.8, 125.6, 126.0, 127.5, 127.8, 128.1, 132.2, 133.2, 145.1. IR (neat) 3420, 2970, 2932, 1457, 1375, 1130 cm^{-1}. HRMS (FAB^+) calcd for $C_{14}H_{15}$ $[M-OH]^+$ 183.1174, found 183.1173. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=9/1, 1.0 mL/min, t_R=14.4 min (major, *S*), 15.6 min (minor, *R*).

*4.3.6. (S)-2-(Benzo[d][1,3]dioxol-5-yl)butan-2-ol (**3f**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.79 (t, *J*=7.2 Hz, 3H), 1.50 (s, 3H), 1.74–1.84 (m, 3H), 5.93 (s, 2H), 6.76 (d, *J*=8.1 Hz, 1H), 6.88 (d, *J*=8.1 Hz, 1H), 6.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.4, 29.8, 36.8, 74.9, 101.0, 106.1, 107.7, 118.0, 142.0, 146.0, 147.6. IR (neat) 3435, 2972, 2881, 1610, 1432, 1239, 1107, 1039 cm^{-1}. HRMS (EI^+) calcd for $C_{11}H_{14}O_3$ $[M]^+$ 194.0943, found 194.0948. Chiral GC CHIRALDEX B-DM, 130 °C, t_R=42.9 min (major, *S*), 43.8 min (minor, *R*).

*4.3.7. (S)-2-(5-Methylfuran-2-yl)butan-2-ol (**3g**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J*=7.5 Hz, 3H), 1.50 (s, 3H), 1.78–1.93 (m, 2H), 1.95 (br, 1H), 2.27 (s, 3H), 5.87 (m, 1H), 6.05 (d, *J*=2.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.7, 13.6, 25.7, 34.3, 71.8, 105.4, 105.9, 151.2, 157.6. IR (neat) 3390, 2973, 2936, 2880, 1561, 1455, 1220, 1021 cm^{-1}. HRMS

(EI$^+$) calcd for $C_9H_{14}O_2$ [M]$^+$ 154.0994, found 154.0995. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 95 °C, t_R=11.6 min (major, *S*), 12.1 min (minor, *R*).

*4.3.8. (S)-2-(Thiophen-2-yl)butan-2-ol (**3h**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J*=7.5 Hz, 3H), 1.60 (s, 3H), 1.88 (q, *J*=7.5 Hz, 2H), 2.18 (br, 1H), 6.89 (dd, *J*=3.6, 1.5 Hz, 1H), 6.93 (dd, *J*=4.8, 3.6 Hz, 1H), 7.17 (dd, *J*=4.8, 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.5, 29.6, 37.4, 74.0, 122.3, 123.6, 126.5, 153.2. IR (neat) 3408, 2971, 2932, 1457, 1375, 1235, 1125 cm^{-1}. HRMS (FAB$^+$) calcd for $C_8H_{11}S$ [M−OH]$^+$ 139.0581, found 139.0580. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=98/2, 0.4 mL/min, t_R=26.6 min (minor, *R*), 29.4 min (major, *S*).

*4.3.9. (S)-3-Methyl-1-phenylpentan-3-ol (**3i**)*[17]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J*=7.5 Hz, 3H), 1.21 (s, 3H), 1.39 (br, 1H), 1.55 (q, *J*=7.5 Hz, 2H), 1.75 (m, 2H), 2.67 (m, 2H), 7.12–7.32 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.3, 26.3, 30.3, 34.4, 43.2, 72.8, 125.7, 128.3, 128.4, 142.6. IR (neat) 3389, 2966, 2936, 1455, 1375, 1147 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{12}H_{17}$ [M−OH]$^+$ 161.1330, found 161.1334. Chiral GC CHIRALDEX B-DM, 100 °C, t_R=36.1 min (major, *S*), 38.2 min (minor, *R*).

*4.3.10. (S)-3,7-Dimethyloctan-3-ol (**3j**)*[18]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (d, *J*=6.9 Hz, 6H), 0.89 (t, *J*=7.2 Hz, 3H), 1.15 (s, 3H), 1.15–1.70 (m, 8H), 1.49 (q, *J*=7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.3, 21.7, 22.7, 26.5, 28.0, 34.3, 39.6, 41.6, 73.1. IR (neat) 3387, 2956, 1464, 1367, 1154 cm^{-1}. HRMS (EI$^+$) calcd for $C_{10}H_{20}$ [M−H_2O]$^+$ 140.1565, found 140.1564. Chiral GC CHIRALDEX B-DM, 75 °C, t_R=12.2 min (major, *S*), 13.1 min (minor, *R*).

*4.3.11. (S)-2-Cyclohexylbutan-2-ol (**3k**)*[19]. ^{1}H NMR (400 MHz, CDCl_3) δ 0.89 (t, *J*=7.2 Hz, 3H), 0.90–1.38 (m, 7H), 1.07 (s, 3H), 1.49 (t, *J*=7.2 Hz, 2H), 1.62–1.86 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.6, 23.4, 26.6, 26.8, 26.9, 27.5, 32.1, 46.7, 74.5. IR (neat) 3420, 2965, 2926, 2853, 1450, 1375, 1142 cm^{-1}. HRMS (EI$^+$) calcd for $C_{10}H_{18}$ [M−H_2O]$^+$ 138.1409, found 138.1411. Chiral GC CHIRALDEX B-DM, 80 °C, t_R=26.9 min (major, *S*), 28.5 min (minor, *R*).

*4.3.12. (R)-1-Ethyl-1,2,3,4-tetrahydronaphthalen-1-ol (**3l**)*[20]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J*=7.2 Hz, 3H), 1.75–2.15 (m, 4H), 1.71 (s, 1H), 1.87 (q, *J*=7.2 Hz, 2H), 2.60–2.90 (m, 2H), 7.07 (m, 1H), 7.16 (td, *J*=7.2, 1.8 Hz, 1H), 7.19 (td, *J*=7.2, 1.8 Hz, 1H), 7.52 (dd, *J*=7.2, 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.6, 19.8, 30.0, 34.9, 35.4, 72.7, 126.3, 127.0, 128.9, 136.9, 142.3. IR (neat) 3445, 2935, 1677, 1455, 1287, 1161 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{12}H_{15}$ [M−OH]$^+$ 159.1174, found 159.1174. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 140 °C, t_R=18.0 min (minor, *S*), 18.8 min (major, *R*).

*4.3.13. (S)-1-Phenylpropan-1-ol (**5**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J*=7.5 Hz, 3H), 1.69–1.77 (m, 2H), 2.24 (br, 1H), 4.56 (t, *J*=6.9 Hz, 1H), 7.25–7.38 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.2, 31.9, 75.9, 126.0, 127.5, 128.4, 144.7. IR (neat) 3360, 2963, 1492, 1454, 1377, 1200, 1097, 1013 cm^{-1}. HRMS (FAB$^+$) calcd for $C_9H_{13}O$ [M+H]$^+$ 137.0966, found 137.0964. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 115 °C, t_R=13.3 min (minor, *R*), 13.7 min (major, *S*).

4.4. General procedure for the catalytic enantioselective addition of Ph_2Zn to ketones

A well-dried Pyrex Schlenk tube was charged with diphenylzinc (220 mg, 1.0 mmol) and neat Et_2Zn (0.20 mL, 2.0 mmol) at the room temperature under nitrogen atmosphere. The mixture was stirred for 30 min, and then **1a** (45.6 mg, 0.10 mmol) was added to the mixture. This solution was stirred for another 30 min, and then ketone (**2**) (1.0 mmol) was added. The resulting heterogeneous solution was stirred at room temperature for 2–16 h. Ether (or *n*-hexane, toluene, EtOAc, etc.) (10 mL) and satd NH_4Cl aqueous solution (10 mL) were poured into the mixture at 0 °C. The product was extracted with ether or EtOAc (10 mL×3) and washed by brine (10 mL). The combined extracts were dried over $MgSO_4$. The organic phase was concentrated under reduced pressure and the crude product was purified by neutral silica gel column chromatography (eluent: hexane/EtOAc=20/1 to 1/2), to give the desired products (**6**). The enantiomeric purity was determined by GC or HPLC on chiral column.

4.5. Analytical data for the Ph-adducts

*4.5.1. (S)-1-(4-Chlorophenyl)-1-phenylethanol (**6a**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (s, 3H), 2.38 (br, 1H), 7.18–7.40 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 75.8, 125.8, 127.2, 127.3, 128.2, 128.3, 132.7, 146.6, 147.5. IR (neat) 3419, 2979, 1489, 1446, 1093, 1013 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{14}H_{12}Cl$ [M−OH]$^+$ 215.0628, found 215.0626. Chiral GC CHIRALDEX B-DM, 150 °C, t_R=30.6 min (major, *S*), 31.9 min (minor, *R*).

*4.5.2. (S)-1-(4-Methoxyphenyl)-1-phenylethanol (**6b**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 3H), 2.21 (br, 1H), 3.77 (s, 3H), 6.78–6.87 (m, 2H), 7.18–7.44 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.0, 55.2, 75.9, 113.4, 125.8, 126.8, 127.2, 128.1, 140.3, 148.3, 158.5. IR (neat) 3464, 2974, 1610, 1509, 1446, 1250, 1178, 1029 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{15}H_{15}O$ [M−OH]$^+$ 211.1123, found 211.1128. Chiral HPLC OJ-H, *n*-hexane/*i*-PrOH=9/1, 1.0 mL/min, t_R=39.8 min (minor, *R*), 51.2 min (major, *S*).

*4.5.3. (S)-1-(2-Naphthalenyl)-1-phenylethanol (**6c**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.42 (br, 1H), 7.15–7.48 (m, 8H), 7.66–7.84 (m, 3H), 7.93 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.7, 76.3, 123.7, 125.0, 125.9, 126.0, 126.1, 127.0, 127.5, 127.9, 128.2, 128.3, 132.3, 133.0, 145.3, 147.7. IR (neat) 3433, 3056, 1493, 1446, 1373, 1126, 1065 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{18}H_{15}$ [M−OH]$^+$ 231.1174, found 231.1174. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=20/1, 0.5 mL/min, t_R=34.2 min (major, *S*), 39.8 min (minor, *R*).

*4.5.4. (S)-1-Phenyl-1,2,3,4-tetrahydronaphthalen-1-ol (**6d**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.78 (m, 1H), 1.90–2.20 (m, 3H), 2.16 (s, 1H), 2.80–2.96 (m, 2H), 7.00–7.40 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 29.9, 41.5, 75.4, 126.4, 126.5, 126.6, 127.5, 127.8, 128.9, 129.0, 137.7, 142.1, 149.0. IR (neat) 3444, 2936, 1488, 1445, 1324, 1068 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{16}H_{15}$ [M−OH]$^+$ 207.1174, found 207.1171. Chiral GC CHIRALDEX B-DM, 160 °C, t_R=18.1 min (minor, *R*), 19.4 min (major, *S*).

*4.5.5. (S)-1-(Furan-2-yl)-1-phenylethanol (**6e**)*[21]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.87 (s, 3H), 2.59 (br, 1H), 6.25 (d, *J*=3.3 Hz, 1H), 6.33 (m, 1H), 7.19–7.40 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.3, 73.1, 106.4, 110.1, 125.3, 127.4, 128.3, 142.2, 145.8, 158.9. IR (neat) 3388, 1665, 1594, 1500, 1470, 1447, 1368, 1224, 1155, 1069, 1010 cm^{-1}. HRMS (EI$^+$) calcd for $C_{12}H_{12}O_2$ [M]$^+$ 188.0837, found 188.0829. Chiral GC CHIRALDEX B-DM, 120 °C, t_R=14.5 min (minor, *R*), 15.6 min (major, *S*).

*4.5.6. (S)-1-Phenyl-1-(3-thiophenyl)ethanol (**6f**)*[10a]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.92 (s, 3H), 2.28 (br, 1H), 6.97 (dd, *J*=5.1, 1.5 Hz, 1H), 7.17 (dd, *J*=3.0, 1.5 Hz, 1H), 7.20–7.36 (m, 4H), 7.38–7.46 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.1, 74.6, 120.8, 125.4, 126.0, 126.7, 127.0, 128.2, 147.4, 149.7. IR (neat) 3418, 2978, 1492, 1446, 1370, 1231, 1069 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{12}H_{11}S$ [M−OH]$^+$ 187.0581, found 187.0584. Chiral GC CHIRALDEX B-DM, 140 °C, t_R=18.3 min (minor, *R*), 19.1 min (major, *S*).

*4.5.7. (S)-3-Bromo-2,4-diphenylbut-3-en-2-ol (**6g**)*[22]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.91 (s, 3H), 2.76 (br, 1H), 7.29–7.34 (m, 3H), 7.38

(t, J=8.1 Hz, 4H), 7.52 (d, J=7.8 Hz, 2H), 7.59 (d, J=7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.0, 78.8, 125.5, 127.7, 127.9, 128.2, 128.3, 128.5, 129.2, 134.6, 135.6, 145.1. IR (neat) 3446, 2925, 1716, 1493, 1446, 1323, 1100, 1072 cm^{-1}. HRMS (EI$^+$) calcd for $C_{16}H_{15}BrO$ [M]$^+$ 302.0306, found 302.0307. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=19/1, 1.0 mL/min, t_R=13.3 min (major, *S*), 16.4 min (minor, *R*).

*4.5.8. (R)-1-(Cyclohex-1-en-1-yl)-1-phenylethanol (**6h**)*[21]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52–1.59 (m, 4H), 1.64 (s, 3H), 1.69–1.95 (m, 3H), 2.09–2.15 (m, 2H), 5.90 (m, 1H), 7.22 (t, J=7.8 Hz, 1H), 7.31 (t, J=7.8 Hz, 2H), 7.41 (d, J=7.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.3, 22.9, 24.6, 25.3, 28.8, 77.3, 121.8, 125.4, 126.7, 128.1, 142.2, 146.8. IR (neat) 3481, 2930, 1447, 1384, 1351, 1272, 1244 cm^{-1}. HRMS (EI$^+$) calcd for $C_{14}H_{18}O$ [M]$^+$ 202.1358, found 202.1363. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=19/1, 0.5 mL/min, t_R=13.6 min (minor, *S*), 14.3 min (major, *R*).

*4.5.9. (S)-1-Cyclohexyl-1-phenylprop-2-yn-1-ol (**6i**)*[23]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01–1.30 (m, 5H), 1.48 (m, 1H), 1.59–1.81 (m, 4H), 1.97 (m, 1H), 2.34 (s, 1H), 2.69 (s, 1H), 7.30 (t, J=7.2 Hz, 1H), 7.36 (t, J=7.2 Hz, 2H), 7.60 (d, J=7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.2, 26.3, 27.3, 27.8, 49.8, 74.9, 76.6, 85.5, 126.2, 127.8, 128.0, 143.4. IR (neat) 3440, 3304, 2929, 2853, 1448, 1317, 1015 cm^{-1}. HRMS (EI$^+$) calcd for $C_{15}H_{18}O$ [M]$^+$ 214.1358, found 214.1360. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=19/1, 0.5 mL/min, t_R=10.5 min (major, *S*), 15.3 min (minor, *R*).

*4.5.10. (R)-1-Phenyl-1-(trimethylsilyl)ethanol (**6j**)*[24]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.00 (s, 9H), 1.41 (br, 1H), 1.62 (s, 3H), 7.14–7.40 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ −4.2, 25.9, 69.8, 124.5, 125.3, 127.9, 148.1. IR (neat) 3444, 2956, 1491, 1444, 1247, 1040 cm^{-1}. HRMS (EI) calcd for $C_{11}H_{18}OSi$ [M]$^+$ 194.1127, found 194.1124. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 120 °C, t_R=12.9 min (minor, *S*), 13.7 min (major, *R*).

*4.5.11. (S)-(4-Chlorophenyl)(phenyl)methanol (**7**)*[25]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.69 (br, 1H), 5.78 (s, 1H), 7.18–7.40 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.6, 125.4, 126.6, 127.9, 128.6, 128.7, 133.3, 142.3, 143.5. IR (KBr) 3358, 3026, 1485, 1453, 1402, 1346, 1189, 1082, 1071 cm^{-1}. HRMS (FAB$^+$) calcd for $C_{13}H_{12}ClO$ [M+H]$^+$ 219.0577, found 219.0579. Chiral HPLC OB-H, *n*-hexane/*i*-PrOH=9/1, 0.5 mL/min, t_R=31.5 min (minor, *R*), 49.5 min (major, *S*).

4.6. General procedure for the catalytic enantioselective addition of Me_2Zn to aldehydes

A well-dried Pyrex Schlenk tube was charged with **1b** (35.6 mg, 0.10 mmol) under nitrogen atmosphere. Then, 2.8 M Me_2Zn in *n*-hexane (1.07 mL, 3.0 mmol) was added at room temperature. This solution was stirred for 30 min, and aldehyde (**4**) (1.0 mmol) was added. The mixture was stirred at room temperature for 2–24 h. Ether (or *n*-hexane, toluene, EtOAc, etc.) (10 mL) and satd NH_4Cl aqueous solution (10 mL) were poured into the mixture at 0 °C. The product was extracted with ether or EtOAc (10 mL×3) and washed by brine (10 mL). The combined extracts were dried over $MgSO_4$. The organic phase was concentrated under reduced pressure and the crude product was purified by neutral silica gel column chromatography (eluent: *n*-hexane/EtOAc), to give the desired products (**8**). The enantiomeric purity was determined by GC on chiral column.

4.7. Analytical data for the Me-adducts

*4.7.1. (S)-1-Phenylethanol (**8a**)*[25]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (d, J=6.6 Hz, 3H), 2.03 (br, 1H), 4.86 (q, J=6.6 Hz, 1H), 7.22–7.36 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3, 70.6, 125.4, 127.5, 128.5, 145.9. IR (neat) 3358, 2973, 1698, 1558, 1507, 1451, 1369, 1283, 1203, 1077, 1011, 899 cm^{-1}. HRMS (FAB$^+$) calcd for $C_8H_{11}O$ [M+H]$^+$ 123.0810, found 123.0809. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 110 °C, t_R=10.0 min (minor, *R*), 10.6 min (major, *S*).

*4.7.2. (S)-1-(4-Chlorophenyl)ethanol (**8b**)*[25]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (d, J=6.3 Hz, 3H), 2.00 (br, 1H), 4.86 (q, J=6.3 Hz, 1H), 7.23–7.33 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.3, 69.8, 126.9, 128.7, 133.1, 144.3. IR (neat) 3356, 2973, 1652, 1492, 1455, 1406, 1371, 1294, 1201, 1088, 1013, 904 cm^{-1}. HRMS (FAB$^+$) calcd for $C_8H_{10}ClO$ [M+H]$^+$ 157.0420, found 157.0421. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 130 °C, t_R=14.5 min (minor, *R*), 15.5 min (major, *S*).

*4.7.3. (S)-1-(4-Methoxyphenyl)ethanol (**8c**)*[15c]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.49 (d, J=6.3 Hz, 3H), 2.13 (br, 1H), 3.78 (s, 3H), 4.82 (q, J=6.3 Hz, 1H), 6.86 (d, J=8.7 Hz, 2H), 7.27 (dd, J=8.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 55.2, 69.9, 113.8, 126.6, 138.0, 158.9. IR (neat) 3389, 2969, 1612, 1512, 1245, 1176, 1034 cm^{-1}. HRMS (EI) calcd for $C_9H_{12}O_2$ [M]$^+$ 152.0837, found 152.0833. Chiral GC CHIRALDEX B-DM, 100 °C, t_R=28.6 min (minor, *R*), 30.9 min (major, *S*).

*4.7.4. (S)-1-(Thiophen-2-yl)ethanol (**8d**)*[26]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (d, J=6.3 Hz, 3H), 2.3 (br, 1H), 1.88 (q, J=6.3 Hz, 1H), 6.90–7.01 (m, 2H), 7.22 (dd, J=4.5, 1.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.2, 66.2, 123.2, 124.4, 126.6, 149.9. IR (neat) 3358, 2973, 1435, 1371, 1311, 1233, 1069 cm^{-1}. HRMS (EI) calcd for C_6H_8OS [M]$^+$ 128.0296, found 128.0300. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 110 °C, t_R=10.6 min (minor, *R*), 11.1 min (major, *S*).

*4.7.5. (S)-4-Phenylbutan-2-ol (**8e**)*[27]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (d, J=6.0 Hz, 3H), 1.40 (br, 1H), 1.70–1.83 (m, 2H), 2.60–2.82 (m, 2H), 3.82 (sextet, J=6.0 Hz, 1H), 7.15–7.33 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 32.2, 40.9, 67.5, 125.8, 128.4, 142.1. IR (neat) 3365, 2926, 1716, 1495, 1455, 1128, 1053 cm^{-1}. HRMS (EI) calcd for $C_{10}H_{14}O$ [M]$^+$ 150.1045, found 150.1038. Chiral HPLC OD-H, *n*-hexane/*i*-PrOH=9/1, 0.5 mL/min, t_R=15.0 min (minor, *R*), 20.5 min (major, *S*).

*4.7.6. (S)-1-Cyclohexylethanol (**8f**)*[15c]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90–1.33 (m, 6H), 1.15 (d, J=6.3 Hz, 3H), 1.52 (br, 1H), 1.62–1.90 (m, 5H), 3.54 (quintet, J=6.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.4, 26.1, 26.2, 26.5, 28.4, 28.7, 45.1, 72.2. IR (neat) 3363, 2924, 2852 cm^{-1}. HRMS (EI) calcd for C_8H_{14} [M−OH_2]$^+$ 110.1096, found 110.1091. Chiral GC CP-Cyclodextrin-β-2,3,6-M-19, 90 °C, t_R=17.5 min (minor, *R*), 17.8 min (major, *S*).

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.02.042.

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