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PAPER

Dinuclear zinc complex catalyzed asymmetric methylation and alkynylation of aromatic aldehydes

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A general AzePhenol dinuclear zinc catalytic system has been successfully developed and introduced into the asymmetric addition of dimethylzinc and alkynylzinc to aromatic aldehydes. In this system, an azetidine derived chiral ligand has proven to be effective enantioselective promoter. Under the optimal reaction conditions, a series of chiral 1-hydroxyethyl (up to 99% *ee*) and secondary propargylic alcohols (up to 96% *ee*) were generated with good yields and enantioselectivities. Additionally, this novel catalytic system showed good functional group compatibility. Remarkably, the substituent's electronic nature alone is not sufficient to allow for exclusive enantioselectivity, an additional substituent's location also had an effect. We proposed that the formation of a stable and structural rigid transition state by the chelation of *ortho* substitued benzaldehydes to the zinc atom was responsible for the observed higher enantioselectivity. The possible catalytic cycles of both transformations accounted for the stereoselectivity was described accordingly.

Introduction

Asymmetric addition of organometallic reagents to prochiral carbonyl compounds has emerged as one of the most effective transformations to construct new C–C bond with a stereogenic center in one step.[1] Organozinc reagents such as alkylzinc and alkynylzinc serve as attractive alternatives to the corresponding lithium and magnesium counterparts because of their easily accessible and well functional group tolerance.[2] Dimethylzinc and diethylzinc compounds are commercially available. The alkynylzinc reagents can be prepared in situ through the reaction of acidic terminal alkynes and a zinc reagent.[3]

Catalytic asymmetric methylation of aldehydes with dimethylzinc reagents generates a tremendous amount of interest,[4] since it allows chemists to synthesis of chiral 1-hydroxyethyl moiety which is important sub-structure in many natural products and drug precursors.[5] In addition, the corresponding adducts are also useful intermediates for further preparation of chiral ligands.[6] The relative lower reactive dimethylzinc compared to the ethyl alternative and the sensitivity of the reaction to the ligand motivated chemists to examine the catalytic efficiency of the chiral ligand in the asymmetric addition of aldehydes. A variety of ligands[4], such as amino alcohols,[4a] diamines,[4b] diols,[4c] and phosphine catalysts[4d] were prepared to induce this asymmtric synthesis. Among them, the β-amino alcohols generally showed better performance with excellent level of reactivity and enantioselectivity.

Chiral secondary propargylic alcohols are important precursors of a range of natural products and pharmaceutical compounds.[7] Methods of allowing access to this target molecular are usually based on 1) alkynylation *via* the lithiated alkynes and subsequent kinetic resolution; 2) [2,3]- σ - rearrangement; 3) asymmetric reduction; 4) the catalytic asymmetric alkyne additions to carbonyl compounds in the presence of titanium reagents.[8] However, the use of lithiated alkynes always suffers from substrate compatibility. The limitation of the asymmetric reduction is the unstability of the ethynyl – ketone intermediate, which is prone to undergo decomposition to form diene ketone. The disadvantage of the rearrangement is the requirement of chiral substrates synthesis *via* kinetic resolution. Alternatively, direct catalytic asymmetric alkynylation of aldehydes has proven as the most straightforward approach to access desired alcohols.[1b]

Based on the known methods, the asymmetric catalysis crucially depends on the discovery of remarkable chiral ligands.[1b–1f,9] Since Corey and Cimprich reported the first enantioselective addition of alkynylzinc reagents to aldehydes using chiral oxazaborolidines,[10] the development of efficient catalysts for alkynylation of aldehydes attracted much attention. Carreira and co-workers disclosed an addition of acetylide to aliphatic aldehydes with stoichiometric (+)-*N*-methylephedrine, $Zn(OTf)_2$, and triethylamine.[11] Furthermore, 1,1'-bi-2-

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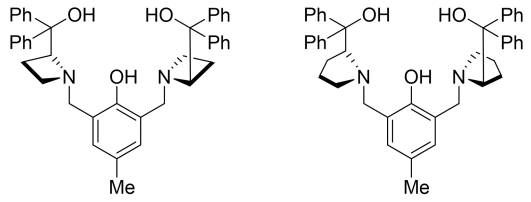
Electronic Supplementary Information (ESI) available: All chiral HPLC chromatograms data and spectra for methylation products and alkynylation products. See DOI: 10.1039/x0xx00000x



Scheme 1 Proline (right) and azetidines-derived (left) dinuclear chiral ligands by Trost and our group respectively.

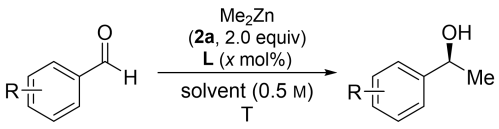
naphthol (BINOL) in conjunction with Ti(O-*i*-Pr)$_4$[12a–c] and (*S*)-BINOL in combination with indium[12d] were found to be excellent in the alkynylation of aromatic aldehydes. The Wang group described that sulfoamido alcohols could efficiently catalyze the asymmetric addition of phenyl acetylene to aldehydes. Other ligands have been employed in the asymmetric alkynylzinc additions to aldehydes, including amino alcohols, hydroxy carboxamides, bifunctional salen catalysts, phosphine catalyst, as well as nitrogen heterocycles.[13] A few years ago, Trost and co-workers reported a general alkynylation of aldehydes by using proline-derived dinuclear zinc catalyst system (Scheme 1, Zn_2Me**L2**) as an effective promoter in the absence of an additive,[14] a variety of aldehydes and alkynes were employed to give propargylic alcohols in good yield and enantioselectivity.[15]

In the last decade, our group have successfully developed a series of chiral azaheterocycle-based ligands for catalytic asymmetric synthesis use.[16–21] As expected, a highly enantioselective methylation, ethylation and arylation of aldehydes were achieved in the presence of catalytic amounts of azetidino alcohols bearing ferrocenyl or phenyl group on the nitrogen atom of the heterocycle skeleton[16,17]. We recently developed an interesting azetidines-derived dinuclear zinc catalyst system (Scheme 1,Zn_2Me**L1**). This promising catalytic combination has led to several efficient enantioselective transformations, including asymmetric domino Michael/ Hemiketalization reaction,[18] Friedel–Crafts alkylation,[19] enantioselective co-polymerization.[20] It was noteworthy that much higher enantioselectivity was achieved by using our novel chiral auxiliaries than that of Trost's dinuclear zinc-ProPhenol catalyst in the asymmetric co-polymerization of cyclohexene oxide with carbon dioxide,[21] which might attribute to the lower flexibility azetidine ring skeleton and appropriate sterically hindered microenvironment compared with that of pyrrolidine. This more rigid ligand has shown to be superior for this type of chemistry. Considering further demonstrating the value of our AzePhenol dinuclear zinc catalyst system, our studies on the asymmetric addition of alkynylzinc and dimethylzinc to various aromatic aldehydes were described herein.

Results and discussion

Asymmetric addition of dimethylzinc to aromatic aldehydes

Table 1 Identification of the catalyst system and substrate scope for the catalytic asymmetric addition of dimethylzinc to various aromatic aldehydes.[a]



Entry	R	*x*	Solvent	T (°C)	Yield (%)[b]	*ee* (%)[c]
1	H (**1a**)	5	toluene	0	trace (**3aa**)	–
2	H (**1a**)	5	toluene	30	81 (**3aa**)	43
3[d]	H (**1a**)	5	toluene	30	34 (**3aa**)	31
4	H (**1a**)	10	toluene	30	77 (**3aa**)	42
5	H (**1a**)	5	DCM	30	trace (**3aa**)	–
6	H (**1a**)	5	THF	30	18 (**3aa**)	30
7	2-Cl (**1b**)	5	toluene	30	48 (**3ba**)	14
8	2-Me (**1c**)	5	toluene	30	92 (**3ca**)	27
9	2-OMe (**1d**)	5	toluene	30	99 (**3da**)	73
10	3-OMe (**1e**)	5	toluene	30	68 (**3ea**)	56
11	4-OMe (**1f**)	5	toluene	30	67 (**3fa**)	60
12	4-NMe_2 (**1g**)	5	toluene	30	78 (**3ga**)	79

[a] Unless otherwise noted, all reactions were processed using **L1** as chiral ligand under argon in corresponding solvent at 30 °C for 48–72 h. [b] Isolated yield reported. [c] The *ee* values were determined by HPLC analysis (refer to the experimental part for detail). The absolute configuration of **3aa** was assigned by comparison of optical rotation and chiral HPLC traces with the literature,[16, 22] while the absolute configurations of products **3ba**–**3ga** were assigned by analogy to **3aa**. [d] Trost's dinuclear zinc-ProPhenol catalyst system (Zn_2Me**L2**) was introduced instead for comparison.

Our initial attempts began with the examination of temperature on the asymmetric addition of dimethylzinc to benzaldehyde (**1a**) in the presence of **L1** as potential chiral ligand. As illustrated, however, only trace amounts of methylated product was obtained at 0 °C (Table 1, entry 1). We found that elevated temperature could greatly promote desired product formation, affording 1-phenylethan-1-ol (**3aa**) in higher yield and enantioselectivity through the activation of organozinc reagent (**2a**, Table 1, entry 2). The catalytic activities of azetidine ligand **L1** and pyrrolindine ligand **L2** were also compared under the identical conditions. As showed in Table 1, behaving as an effective promoter, azetidine ligand **L1** performed more effective than Trost's pyrrolindine ligand **L2** (entries 2 *vs* 3). Intriguingly, doubling chiral ligand loading did not yield more product with roughly the same enantioselectivity (Table 1, entry 4). Solvent screening revealed that toluene was the choice of reaction medium to promote transformation in modest enantioselectivity, whereas, neither DCM nor THF gave acceptable results (Table 1, entries 5 and 6). Notably, the relative reactive carbonyl group was untouched in DCM medium (Table 1, entry 5). After extensive reaction optimization, the reaction of benzaldehyde (**1a**) and dimethylzinc (**2a**) was achieved with modest enantioselectivity

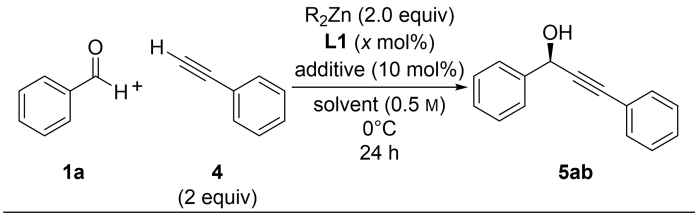
by using a combination of 2.0 equivelants of Me_2Zn and 5 mol% of **L1** dissolved in toluene at 30 °C.

The range of arylaldehyde starting materials **1b**–**1g** was further extended under the optimized reaction conditions as outlined in the lower part of Table 1. Both electron rich and electron poor arylaldehydes were carefully investigated with good yields and modest to good enantioselectivities. These results revealed a correlation between the catalytic efficiency and the electronic nature of aromatic substituents. Electron-donating substituents (**1c** → **3ca**) generally provided better results than electron-withdrawing ones (**1b** → **3ba**). For instance, 2-chloro substituted benzaldehyde (**1b**) generated product **3ba** with only 14% enantiomeric excess (*ee*), while a higher *ee* was achieved when a more electron donating substituent was employed instead (Table 1, entries 7 *vs* 8). To our delight, a methoxy substituent in the *ortho* position of aldehyde **1d** substrate was found to be beneficial in both yield and enantioselectivity (Table 1, entry 9). Importantly, this *ortho*-methoxy substituted benzaldehyde (**1d**) afforded slightly better enantioselectivities than *meta*- (**1e**) and *para*- (**1f**) positions, probably due to the formation of a stable and structural rigid transition state by the chelation of *ortho* methoxyl benzaldehyde to the zinc atom. (Table 1, entries 9 *vs* 10 and 11). In addition, as expected, an electron rich NMe_2 group was found to be more reactive even located far away from the carbonyl group (**1g** → **3ga**, Table 1, entry 12). The electron donating substituents led to higher enantioselectivity because the increasing electron density might enhance the affinity of aldehyde to the zinc atom, which would activate the carbonyl group and stablize the transition state in the asymmetric induction.

Asymmetric addition of alkynylzinc to aromatic aldehydes

The above achievements promoted us to address other transformations. Our further studies turned into the application of this azetidines-derived dinuclear zinc catalyst system in the asymmetric addition of alkynylzinc to arylaldehydes (**1a** → **5ab**). Extensive screening was carried out to find suitable reaction conditions. Based on our current knowledge, the eventually reactive alkynylzinc species was generated prior to use in situ through the reaction between dialkylzinc reagent and terminal alkyne. Accordingly, we examined different dialkylzinc reagents. Compared with aforementioned methylation, the alkynylation can be performed under even milder conditions. Comparable enantioselectivity was observed when dimethylzinc (**2a**) or diethylzinc (**2b**) was employed (Table 2, entries 1 and 2). Although It has been reported that the titanium complex can be used to catalyze the alkyne addition to aldehydes with high enantioselectivity. However, in our case, the product was obtained in only 8% *ee* when $Ti(OiPr)_4$ was added.(Table 2, entry 3). To our delight, the reaction proceeded efficiently with slightly higher enantiomeric excess when DiMPEG was used as a Lewis basic additive to facilitate the formation of the alkynylzinc (Table 2, entry 4). No significant influence of temperature on the reaction enantioselectivity was observed. Unfortunately, decreasing the reaction temperature did not improve any enantioselectivity, whereas yielded less product

Table 2 Identification of the catalyst system for the asymmetric addition of alkynylzinc to benzaldehyde.[a]



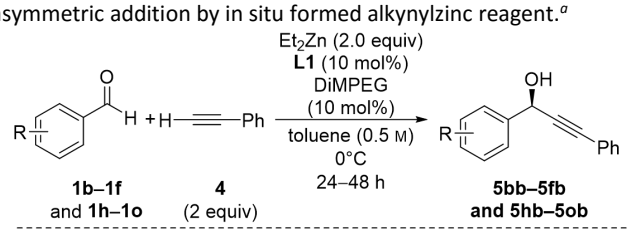
Entry	*x*	R_2Zn	Additive	Solvent	T (°C)	Yield (%)[b]	*ee* (%)[c]
1	10	Et_2Zn	–	toluene	0	90	67
2	10	Me_2Zn	–	toluene	0	99	70
3	10	Et_2Zn	$Ti(OiPr)_4$	toluene	0	84	8
4	10	Et_2Zn	DiMPEG	toluene	0	92	73
5	10	Et_2Zn	DiMPEG	toluene	-10	85	70
6	10	Et_2Zn	DiMPEG	toluene	-40	43	68
7	10	Et_2Zn	DiMPEG	DCM	0	92	37
8	10	Et_2Zn	DiMPEG	THF	0	58	26
9	10	Et_2Zn	DiMPEG	MeCN	0	64	16
10	20	Et_2Zn	DiMPEG	toluene	0	96	76

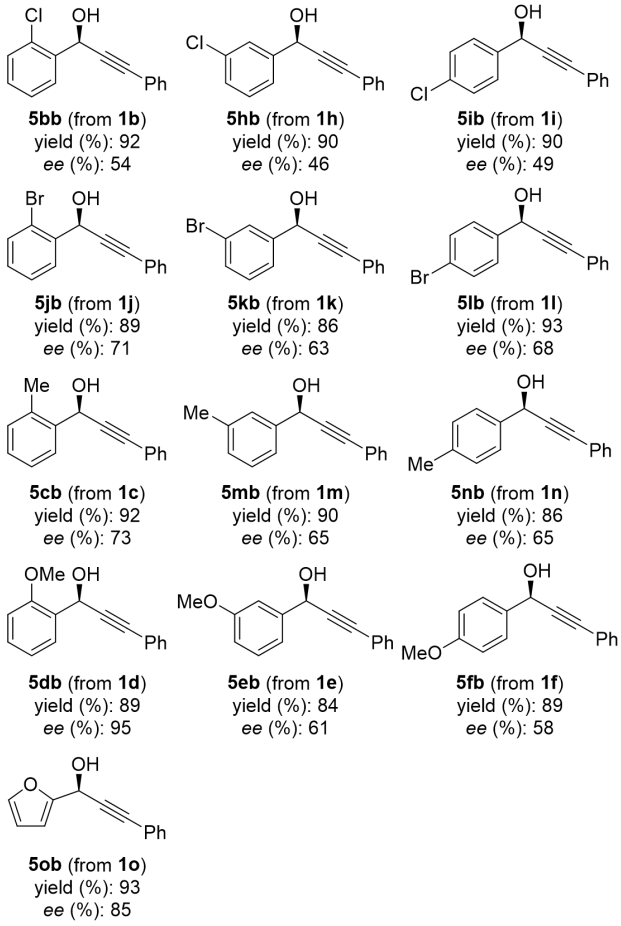
[a] Unless otherwise noted, all reactions were processed under argon in corresponding solvent at 0 °C for 24 h. [b] Isolated yield reported. [c] The *ee* values were determined by HPLC analysis (seeing the experimental part for detail). Absolute configuration was assigned by comparison of optical rotation and chiral HPLC traces with the literature.[14a] DiMPEG = polyethyleneglycol dimethyl ether.

(Table 2, entries 5 and 6). The use of DCM or THF as solvent resulted in a notable decrease both in reactivity and enantioselectivity, whereas in CH_3CN the optical purity of the adduct was only 16% (Table 2, entries 7–9). Catalytic alkynylation of benzaldehyde (**1a**) proceeded with 96% yield and 75% *ee* by the introduction of a combination of DiMPEG/Et_2Zn in toluene at 0 °C (Table 2, entry 10). The results were comparable with the same transformation in Trost's report with the aid of pyrroline-derived dinuclear zinc catalyst.[14]

We then extensively examined aldehyde coupling partners for this transformation. Adopting the conditions of table 2, entry 4 as optimal one, the results of alkynylation of a series of aromatic aldehydes with phenyl acetylene (**4**) were documented in Scheme 2. According to these results, we observed that the enantioselectivity exhibited a strong dependence of the substrates' electronic properties. Starting materials with electron-donating substituents generated products with better enantioselectivities. Additionally, the enantioselectivities improved along with the raising of electron-donating abilities (OMe > Me > Br > Cl), thus the desired chiral alcohol has been synthesized in enantiopure form from common precursor. The alkynylation of methoxy substituents **1d**–**1f** with phenyl acetylene (**4**) displayed high enantioselectivity, while the same ring with a chloro group **1b**, **1h** and **1i** was alkynylated with poor enantioinduction due to its electron-deficient effect. What's more, the location of substituents had a significant influence on the enantioselectivity. *Ortho* substituted arylaldehydes (**1b**-**1d** and **1j**)

Scheme 2 Variation of the aromatic aldehydes and alkynes for the asymmetric addition by in situ formed alkynylzinc reagent.[a]

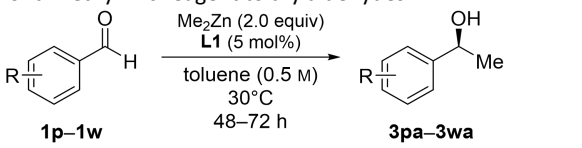


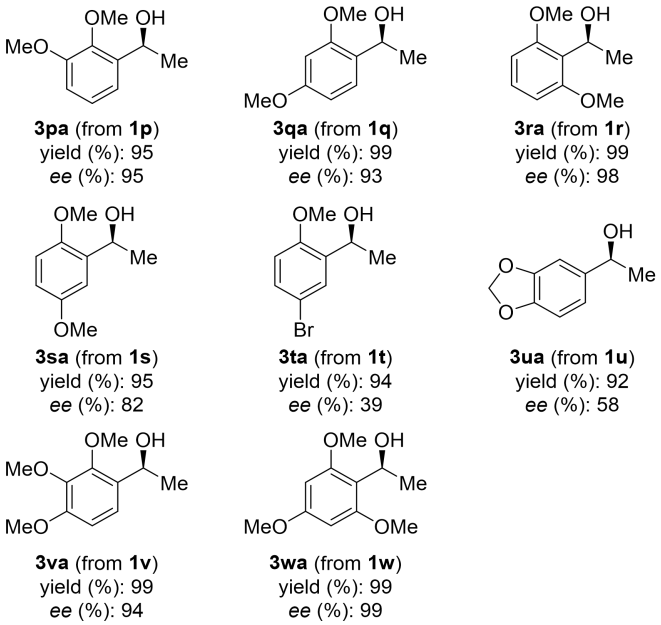


[a] Reaction conditions: **1a** (0.5 mmol), **4** (2.0 equiv), **2b** (2.0 equiv), **L1** (10 mol%), DiMPEG (10 mol%) in toluene. Unless otherwise noted, all reactions were processed under argon for indicated reaction time. Isolated yield reported. The *ee* values were determined by HPLC analysis (refer to the experimental part for detail). The absolute configurations of products were assigned by analogy to product in Table 2.

with appropriate steric bulk provided products with higher enantioselectivity than *meta*- (**1e**, **1h**, **1k** and **1m**) and *para*- (**1f**, **1i**, **1l** and **1n**) substitutions that resulted in comparable enantioselectivities. To our delight, alkynylation of the *ortho*-methoxy substituent gave a very promising enantioselectivity (**1d** → **5db**, 95% *ee*) largely owing to both the electronic effect and the chelate effect. Interestingly, a similar effect was observed for the aforementioned asymmetric methylation of aromatic aldehydes (Table 1, entry 9).

Scheme 3 *Ortho* substituted effect studies for the asymmetric addition of dimethylzinc reagent to arylaldehydes.





[a] Reaction conditions: **1p**–**1w** (0.5 mmol), **2a** (2.0 equiv), **L1** (5.0 mol%) in toluene. Unless otherwise noted, all reactions were processed under argon in toluene at 30 °C for 48–72 h. Isolated yield reported. The *ee* values were determined by HPLC analysis (refer to the experimental part for detail). The absolute configurations of products were assigned by analogy to product in Table 1.

The *ortho* substituted effect on enantioselectivity

Generally in our study, arylaldehydes with *ortho* methoxyl substituents generated desired methylation and alkynylation products in higher enantioselectivity. Encouraged by these results, we expanded the substrate scope by using a number of methoxy substituted arylaldehydes for both methylation and alkynylation (Scheme 3 and 4). Methylation of 5-Br-2-OMe benzaldehyde (**1t**) showed poor enantioselectivity, while 2,5-dimethoxy substituted starting material **1s** restored high enantioinduction due to its electron density increasing. 3,4-Dialkyl sunstituted benzaldehyde **1u** was methylated with only 58% *ee*, however, 2,3-dimethoxy **1p**, 2,4-dimethoxy **1q**, 2,5-dimethoxy **1r** and 2,6-dimethoxy **1s** substituents generated desired methylated products (**3pa**–**3sa**) in impressive enantioselectivity. In a word, very promising *ee* values were obtained for the *ortho* substituted benzaldehyde irrespective of di- or tri- methoxy substituents (Scheme 3, **1p**–**1s** and **1v**–**1w**). Similarly, multiple methoxy substituted benzaldehyde bearing an *ortho* substitution led to alkynylated products (**1p**–**1s** → **5pb**–**5sb** and **1v**–**1x** → **5vb**–**5xb**) in satisfied enantioselectivity which attribute to both the strong electron donating effect and the chelate effect (Scheme 4). It is

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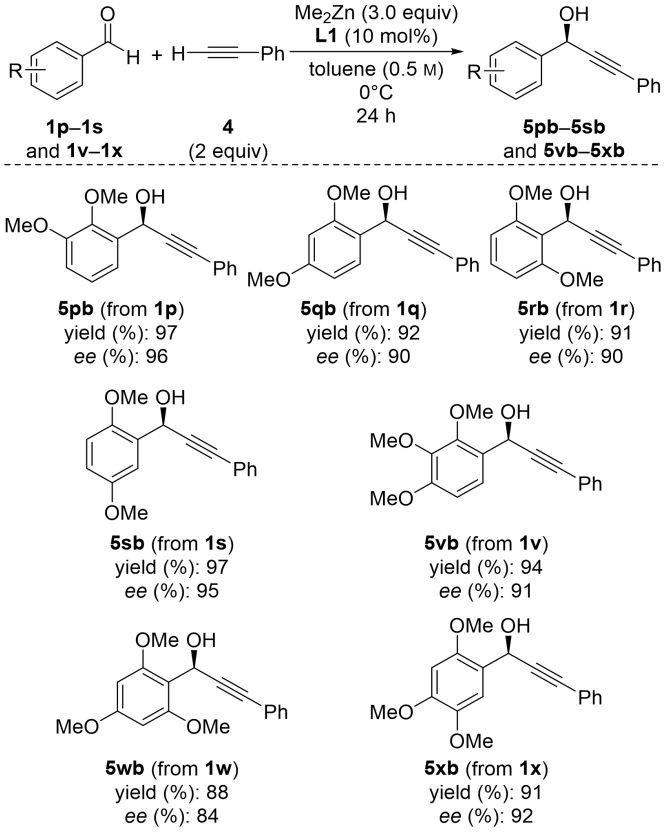
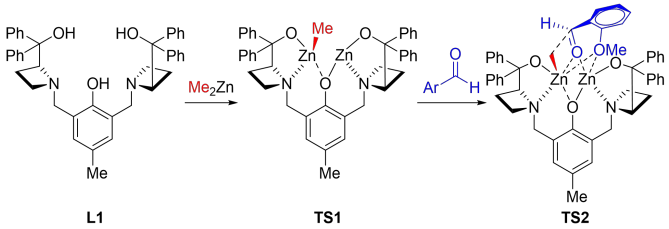
Scheme 4 *Ortho* substitution effect studies for the asymmetric addition of alkynylzinc reagent to arylaldehydes.[a]



[a] Reaction conditions: **1p**–**1s** or **1v**–**1x** (0.5 mmol), **4** (2.0 equiv), **2a** (3.0 equiv), **L1** (10 mol%) in toluene. Unless otherwise noted, all reactions were processed under argon in toluene at 0 °C for 24 h. Isolated yield reported. The *ee* values were determined by HPLC analysis (refer to the experimental part for detail). The absolute configurations of products were assigned by analogy to product in Table 2.

noteworthy that in this asymmetric alkynylation system, no additive was needed when the dimethlyzinc (**2a**) was introduced instead as an activator. Better enantioselectivity of the *ortho* substitution was observed not only in the substrates bearing electron donating groups but also electron-withdrawing groups. The possible reasons were outlined as follows: (i) The *ortho* bromo substituent was more hindered than other positions to enhance the enantioselectivity, while the steric effect was not obvious in case of *ortho* methoxyl, methyl, or chloro substituents. (ii) An *ortho* substitution such as a methoxy or halogen group would coordinate to the metal center to decrease the structural flexibility of the transition state in the asymmetric induction, which facilitated the attack from the more desirable face. (iii) The *ortho* substituents had more electronic donating effect than *meta* and *para* substitutions in case of methoxy group, while there should be more electron withdrawing effect on the *ortho* position than that of *other* positions in terms of a halogen. However, better results of *ortho* substitution in both cases indicated that the electronic factor was not dominant. Therefore in case of

Scheme 5 Possible transition state in the asymmetric methylation with the aid of **L1**.



methoxy and halogen substitution, we believe the chelate effect play as the main reason for the observed better enantioselectivity. In terms of methyl group, there have been no chelate effect, so no dramatically improved enantioselectivity was observed on *ortho* position than that on other positions. The catalytic transition state of asymmetric methylation of arylaldehydes would involve the formation of a dinuclear zinc-AzePhenol complex Zn_2Me**L** (**TS1**), followed by the coordination of aromatic aldehyde to the other zinc atom to generate the intermediate **TS2** (Scheme 5). In this case, the *ortho* substitution such as methoxy and halogen group would coordinate to the same zinc atom to form a stable six-membered ring. The transition state would be more stable.and structural rigid, which is responsible for the largely enhancement of enantioselectivity. Subsequently, the methyl group attacked the more sterically accessible face of aldehyde. Finally, the desired product was released by another dimethylzinc transfer (not shown).

Based on Trost's report,[14a] the asymmetric alkynylation of aromatic aldehyde should undergo the generation of a dinuclear zinc-AzePhenol complex Zn_2Et**L1** by treatment of the chiral ligand **L1** with 2 equivalents of diethylzinc (**2b**) wherein a dynamic equilibrium between the $(Zn_2EtL1)_n$ and Zn_2Et**L1** existed by our previous studies.[19] Subsequently, coordination of 2 equivalents of zinc alkynylide formed a complex and followed by the coordination of aldehyde to the zinc atom from the more sterically accessible site. Finally, alkyne attacks the aldehyde and followed by the transfer of another zinc alkynylide to release an alkoxide of the product and restarts the cycle.

Conclusions

In conclusion, we reported herein an application of dinuclear zinc-AzePhenol catalyst into the asymmetric addition of organozinc to aromatic aldehydes. Results showed that an azetidine derived chiral ligand was quite efficient for the asymmetric addition of both dimethylzinc and alkynylzinc to prochiral aromatic aldehydes with good yields and enantioselectivities. The protocol provided an effective and straightforward access to the chiral 1-hydroxyethyl and secondary propargylic alcohols. Various arylaldehydes were tolerated under standard catalytic conditions. We observed that the enantioselectivity was influenced not only by the electronic nature, but also by the position of substituents. It was worth noting that the *ortho* substituted arylaldehydes generated both methylated and alkynylated products in promising enantioselectivity. An interesting effect of *ortho* substituents on the enatioselectivity was

investigated and a possible transition state was proposed accordingly.

Experimental

General remarks

All reactions were performed in flame-dried glassware using conventional Schlenk techniques under a static pressure of argon. All starting materials, ligands, and racemic products were prepared according to known procedures. Liquids and solutions were transferred with (micro)syringes. Solvents were purified and dried following standard procedures. All aldehydes and alkynes were purchased from *Acros* or *Fluka*. Diethylzinc was prepared from EtI with Zn and then diluted with toluene to 1.0 mol/L. Technical grade solvents for extraction and chromatography were distilled prior to use. Analytical thin-layer chromatography (TLC) and Flash column chromatography were performed on silica gel using the indicated solvents. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on *Bruker DPX 400*/*300*. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and are referenced to the residual solvent resonance as the internal standard (δ = 7.26 ppm for ^{1}H and δ = 77.16 ppm for ^{13}C). Data are reported as follows: chemical shift, multiplicity (br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. Optical rotations were recorded on a *Perkin-Elmer 341* polarimeter. Mass spectra were recorded on *VG-FAB* mass spectrometer. The *ee* value determination was carried out using chiral HPLC on a *Chiralcel OB*, *OD, or OD-H Column* (for all the columns: 4.6mmϕ × 250 mm, Daicel Chemical Ind., LTD, Japan) combined with a *JASCO model PU-1580 intelligent HPLC pump* and a *JASCO model UV-1575 intelligent UV-vis detector* (216nm).

General Procedure for the Catalytic Asymmetric Addition of Dimethylzinc to Aromatic Aldehydes. In a flame-dried Schlenk tube equipped with a magnetic stir bar, a solution of dimethylzinc (**2a**, 0.83 mL, 1.2 mol/L in hexane, 1.0 mmol, 2.0 equiv) is added to a solution of the chiral ligand **L1** (15.3 mg, 0.025 mmol, 5.0 mol%) in dry toluene (1.0 mL, 0.5 M) under nitrogen at 0 °C. The mixture is stirred at 40 °C for 30 min. Then a newly distilled aromatic aldehyde (**1a**–**1f or 1p**–**1w**, 0.5 mmol, 1.0 equiv) is added by a micro syringe to the mixture at 0 °C. The solution is stirred at 30 °C for 48–72 h. After complete consumption of the aldehyde starting material, as monitored by TLC analysis, the reaction mixture is allowed to cool to room temperature, quenched with aqueous NH_4Cl (5.0 mL), and extracted with diethyl ether (3 × 10 mL). The combined organic phases are washed with brine (5.0 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, purification of the residue by column chromatography on silica gel using mixtures of petroleum ether and ethyl acetate as eluents affords the analytically pure title compounds. All these products are known compounds.

(*S*)-1-Phenylethan-1-ol (**3aa**): A pale yellow oil, 49.5 mg, 81% yield, 43% *ee*; $[\alpha]_D^{20}$ = -10.3 (C = 0.5, CH_2Cl_2); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 95/5, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 10.70 min, t_R(*R*) = 8.64 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.48 (d, *J* = 6.6 Hz, 3H), 1.82 (d, *J* = 3.3 Hz, 1H), 4.88 (dq, *J* = 3.3 Hz, *J* = 6.6 Hz, 1H), 7.24–7.28 (m, 1H), 7.31–7.41 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* = (major + minor) 22.2, 69.0, 125.2, 126.8, 128.0, 143.6 ppm.

(*S*)-1-(2-Chlorophenyl)ethan-1-ol (**3ba**): A pale yellow oil, 37,6 mg, 48% yield, 14% *ee*; HPLC (Chiralcel OB column, hexane/*i*-PrOH = 15/1, flow rate: 0.5 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 13.71 min, t_R(*R*) = 10.38 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.39 (d, *J* = 6.4 Hz, 3H), 2.55 (br s, 1H), 5.11 (q, *J* = 6.4 Hz, 1H), 7.08 (td, *J* = 1.9 Hz, *J* = 7.8 Hz, 1H), 7.15–7.18 (m, 2H), 7.44 (dd, *J* = 1.9 Hz, *J* = 8.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* (major + minor) = 23.2, 67.0, 126.2, 126.9, 128.3, 128.9, 131.0, 143.0 ppm.

(*S*)-1-(*o*-Tolyl)ethan-1-ol (**3ca**): A pale yellow oil, 62.6 mg, 92% yield, 27% *ee*; HPLC (Chiralcel OB column, hexane/*i*-PrOH = 15/1, flow rate: 0.5 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 11.73 min, t_R(*R*) = 16.75 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.46 (d, *J* = 6.5 Hz, 3H), 1.84 (br s, 1H), 2.34 (s, 3H), 4.80–4.89 (m, 1H), 7.03–7.10 (m, 1H), 7.12–7.17 (m, 2H), 7.20–7.28 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* (major + minor) = 18.9, 23.5, 66.1, 124.8, 125.8, 126.5, 130.9, 134.6, 144.2 ppm.

(*S*)-1-(2-Methoxyphenyl)ethan-1-ol (**3da**): A pale yellow oil, 75.3 mg, 99% yield, 73% *ee*; HPLC (Chiralcel OB column, hexane/*i*-PrOH = 15/1, flow rate: 0.5 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 8.38 min, t_R(*R*) = 14.09 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.50 (d, *J* = 6.4 Hz, 3H), 2.68 (br s, 1H), 3.89 (s, 3H), 5.03–5.12 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.91–6.98 (m, 1H), 7.18–7.25 (m, 1H), 7.28–7.34 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* (major + minor) = 21.8, 56.0, 66.3, 109.8, 120.1, 125.2, 127.5, 132.8, 155.9 ppm.

(*S*)-1-(3-Methoxyphenyl)ethan-1-ol (**3ea**): A pale yellow oil, 51.8 mg, 68% yield, 56% *ee*; HPLC (Chiralcel OB column, hexane/*i*-PrOH = 15/1, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 15.36 min, t_R(*R*) = 20.74 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.46 (d, *J* = 6.4 Hz; 3H), 1.71 (br s, 1H), 3.78 (s, 3H), 4.80–4.88 (m, 1H), 6.86 (d, *J* = 7.6 Hz, 2H), 7.28 (d, *J*=7.6 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* (major + minor) = 25.5, 55.2, 68.9, 111.0, 113.3, 117.6, 131.1, 148.0, 159.8 ppm.

(*S*)-1-(4-Methoxyphenyl)ethan-1-ol (**3fa**): A pale yellow oil, 51.0 mg, 67% yield, 60% *ee*; HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 50/1, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 31.60 min, t_R(*R*) = 26.53 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.49 (d, *J* = 6.4 Hz, 3H), 1.72 (br s, 1H), 3.78 (s, 3H), 4.80–4.88 (m, 1H), 6.85 (d, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 7.6 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* (major + minor) = 24.0, 55.3, 69.7, 113.4, 126.2, 137.9, 159.1 ppm.

(*S*)-1-(4-(Dimethylamino)phenyl)ethan-1-ol (**3ga**): A pink solid, 64.4 mg, 78% yield, 79% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 98/2, flow rate: 0.7 mL/min, UV detection at 216 nm); Retention time: t_R(S) = 45.55 min, t_R(*R*) = 41.70 min; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* (major + minor) = 1.47 (d, *J* = 6.3 Hz, 3H), 1.59 (br s, 1H), 2.98 (s , 6H), 4.78 (q, *J* = 6.3 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) *δ* (major + minor) = 23.5, 39.4, 69.6, 112.0, 125.4, 135.9, 151.8 ppm.

(*S*)-1-(2,3-Dimethoxyphenyl)ethan-1-ol (**3pa**): A pale yellow oil, 86.6 mg, 95% yield, 95% *ee*; $[\alpha]_D^{20}$ = -16.9 (C = 2.0, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 15/1, flow rate: 1.0 mL/min,

UV detection at 216 nm); Retention time: t_R(*S*) = 10.75 min, t_R(*R*) = 12.08 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 1.49 (d, *J* = 6.2 Hz, 3H), 2.77 (br s, 1H), 3.90 (s, 3H), 3.93 (s, 3H), 5.15 (q, *J* = 6.2 Hz, 1H), 6.81 (dd, *J* = 2.1 Hz, *J* = 7.4 Hz, 1H), 7.01 (dd, *J* = 2.1 Hz, *J* = 7.4 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H) ppm.

(*S*)-1-(2,4-Dimethoxyphenyl)ethan-1-ol (**3qa**): A white solide, 90.0 mg, 99% yield, 93% *ee*; $[\alpha]_D^{20}$ = -36.9 (C = 1.9, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 15/1, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 11.88 min, t_R(*R*) = 17.89 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 1.49 (d, 3H), 2.61 (s, 1H), 3.80 (s, 3H), 3.85 (s, 3H), 5.09 (q, *J* = 6.2 Hz, 1H), 6.41–6.45 (m, 2H), 7.18–7.22 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 22.2, 54.9, 64.4, 66.8, 97.1, 103.5, 118.8, 131.9, 158.4, 160.1 ppm.

(*S*)-1-(2,6-Dimethoxyphenyl)ethan-1-ol (**3ra**): A white solide, 90.1 mg, 99% yield, 98% *ee*; m.p. = 95–96 °C; $[\alpha]_D^{20}$ = -15.2 (C = 0.7, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 9/1, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 23.38 min, t_R(*R*) = 11.00 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 1.49 (d, *J* = 6.2 Hz, 3H), 1.52 (br s, 1H), 3.78 (s, 6H), 5.28 (q, *J* = 6.2 Hz, 1H), 6.51 (d, *J* = 8.3 Hz, 2H), 7.19 (t, J = 8.3 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 22.5, 54.2, 62.8, 102.8, 122.7, 126.6, 158.7 ppm.

(*S*)-1-(2,5-Dimethoxyphenyl)ethan-1-ol (**3sa**): A pale yellow oil, 86.6 mg, 95% yield, 82% *ee*; $[\alpha]_D^{20}$ = -12 (C = 1.2, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 15/1, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 15.71 min, t_R(*R*) = 28.19 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 1.49 (d, *J* = 6.4 Hz, 3H), 2.58 (d, *J* = 5.5 Hz, 1H), 3.70 (s, 3H), 3.81 (s, 3H), 5.00 (q, *J* = 6.4 Hz, 1H), 6.58 (dd, *J* = 2.6 Hz, *J* = 8.6 Hz, 1H), 6.64 (d, *J* = 8.6 Hz, 1H), 6.99 (d, *J* = 2.6 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 22.3, 54.5, 55.1, 64.6, 111.9, 112.2, 112.9, 133.3, 149.7, 154.6 ppm.

(*S*)-1-(5-Bromo-2-methoxyphenyl)ethan-1-ol (**3ta**): A pale yellow oil, 108.5 mg, 94% yield, 39% *ee*; HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 95/5, flow rate: 0.8 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 20.50 min, t_R(*R*) = 18.56 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 1.51 (d, *J* = 6.4 Hz, 3H), 2.58 (br s, 1H), 3.79 (s, 3H), 5.09 (q, *J* = 6.2 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 1H), 7.34 (dd, *J* = 2.5 Hz, *J* = 8.7, 1H), 7.44 (d, *J* = 2.5 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ (major + minor) = 21.9, 55.9, 66.4, 113.0, 113.6, 129.0, 130.7, 138.1, 156.0 ppm.

(*S*)-1-(Benzo[*d*][1,3]dioxol-5-yl)ethan-1-ol (**3ua**): A pale yellow oil, 76.4 mg, 92% yield, 58% *ee*; HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 50/1, flow rate: 0.5 mL/min, UV detection at 216 nm); Retention time: t_R(S) = 73.89 min, t_R(*R*) = 66.14 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 1.47 (d, *J* = 6.4 Hz, 3H), 2.35 (br s, 1H), 4.95 (q, *J* = 6.4 Hz, 1H), 5.85 (s, 2H), 6.77–6.82 (m, 2H), 6.94 (d, *J* = 2.1 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 25.9, 69.1, 101.6, 108.2, 108.8, 119.6, 141.2, 148.4, 149.1 ppm.

(*S*)-1-(2,3,4-Trimethoxyphenyl)ethan-1-ol (**3va**): A pale yellow oil, 104.9 mg, 99% yield, 94% *ee*; $[\alpha]_D^{20}$ = -20.6 (C = 2.1, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 9/1, flow rate: 0.2 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 36.80 min, t_R(*R*) = 40.26 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 1.47 (d, *J* = 6.7 Hz, 3H), 2.37 (br s, 1H), 3.82 (s, 3H), 3.84 (s, 3H), 3.91 (s, 3H), 5.01–5.04 (m, 1H), 6.64 (d, *J* = 8.7 Hz, 1H), 7.00 (d, *J* = 8.7 Hz, 1H) ppm.

(*S*)-1-(2,4,6-Trimethoxyphenyl)ethan-1-ol (**3wa**): A white solid, 104.8 mg, 99% yield, 99% *ee*; $[\alpha]_D^{20}$ = -27 (C = 0.95, $CHCl_3$); HPLC (Chiralcel OD-H column, hexane/*i*-PrOH = 25/1, flow rate: 1.0 mL/min, UV detection at 216 nm); Retention time: t_R(*S*) = 21.13 min, t_R(*R*) = 22.58 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 1.41 (d, *J* = 6.4 Hz, 3H), 2.50 (br s, 1H), 3.77 (s, 6H), 3.81 (s, 3H), 4.90–4.97 (m, 1H), 6.12 (s, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ (major + minor) = 24.8, 55.3, 55.7, 69.2, 91.0, 112.7, 158.5, 160.1 ppm.

General Procedure for the Catalytic Asymmetric Addition of Alkynylzinc to Aromatic Aldehydes. A flame-dried Schlenk tube equipped with a magnetic stir bar is successively charged with the chiral ligand **L1** (30.5 mg, 0.05 mmol, 10.0 mol%), DiMPEG (100 mg, 0.10 mmol, 10 mol%), dimethylzinc (**2a**, 0.83 mL, 1.2 mol/L in hexane, 1.0 mmol, 2.0 equiv) or diethylzinc (**2b**, 1.0 mL, 1.0 mol/L in hexane, 1.0 mmol, 2.0 equiv), alkyne (**4**, 1.0 mmol, 2.0 equiv), and dry toluene (1.0 mL, 0.5 M) under nitrogen at 0 °C. The mixture is stirred at 25 °C for 2 h. Then a newly distilled aromatic aldehyde (**1a**–**1f** or **1h**–**1s** or **1v**–**1x**, 0.5 mmol, 1.0 equiv) is added by a micro syringe to the mixture at 0 °C. The solution is stirred at 0 °C for 20 or 24 h. After complete consumption of the aldehyde starting material, as monitored by TLC analysis, the reaction mixture is allowed to cool to room temperature, quenched with aqueous NH_4Cl (5.0 mL), and extracted with diethyl ether (3 × 10 mL). The combined organic phases are washed with brine (5.0 mL) and dried over anhydrous Na_2SO_4. After evaporation of the solvent under reduced pressure, purification of the residue by column chromatography on silica gel using mixtures of petroleum ether and ethyl acetate as eluents affords the analytically pure title compounds. All these products are known compounds.

(*R*)-1,3-Diphenylprop-2-yn-1-ol (**5ab**): A white solid, 95.7 mg, 92% yield, 73% *ee*; $[\alpha]_D^{20}$ = +4.0 (C = 1.0, CH_2Cl_2); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*R*) = 11.34 min, t_R(*S*) = 21.20 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.91 (br s, 1H), 5.59 (s, 1H), 7.29–7.41 (m, 6H), 7.43–7.46 (m, 2H), 7.55–7.57 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 63.4, 86.5, 88.2, 123.1, 126.8, 128.2, 128.5, 128.7, 128.9, 131.1, 140.8 ppm.

(*S*)-1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-ol (**5bb**): A white solid, 111.6 mg, 92% yield, 54% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 0.5 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 10.46 min, t_R(*R*) = 11.56 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.55 (d, *J* = 5.0 Hz, 1H), 6.00 (d, *J* = 5.0 Hz, 1H), 7.30–7.33 (m, 5H), 7.38 (dd, *J* = 1.8 Hz, *J* = 7.4 Hz, 1H), 7.48–7.51 (m, 2H), 7.85 (dd, *J* = 2.0 Hz, *J* = 7.4 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 61.5. 86.0, 87.9, 121.5, 126.4, 128.0, 128.3, 128.4, 129.7, 129.8, 131.1, 132.2, 137.5 ppm.

(*S*)-3-Phenyl-1-(*o*-tolyl)prop-2-yn-1-ol (**5cb**): A white solid, 102.1 mg, 92% yield, 73% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 10.02 min, t_R(*R*) = 23.36 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 2.29 (d, *J* = 5.0 Hz, 1H), 2.51 (s, 3H), 5.88 (d, *J* =

4.8 Hz, 1H), 7.16–7.28 (m, 6H), 7.40–7.43 (m, 2H), 7.66–7.70 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ (major + minor) = 19.4, 62.5, 85.6, 88.1, 122.0, 126.0, 126.1, 127.8, 128.0, 128.4, 130.1, 131.2, 135.5, 138.2 ppm.

(*S*)-1-(2-Methoxyphenyl)-3-phenylprop-2-yn-1-ol (**5db**): A pale yellow oil, 105.9 mg, 89% yield, 94% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 13.91 min, t_R(*R*) = 17.02 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 3.01 (d, *J* = 6.1 Hz, 1H), 3.88 (s, 3H), 5.89 (d, *J* = 6.0 Hz, 1H), 6.99–7.04 (m, 2H), 7.21–7.28 (m, 4H), 7.41–7.46 (m, 2H), 7.59–7.62 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 55.2, 61.0, 86.7, 88.0, 110.1, 121.1, 122.2, 128.1, 128.2, 128.5, 128.6, 128.9, 129.2, 157.1 ppm.

(*S*)-1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-ol (**5eb**): A white solid, 100.0 mg, 84% yield, 61% *ee*; (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 16.49 min, t_R(*R*) = 25.91 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.99 (d, *J* = 4.7 Hz, 1H), 3.70 (s, 3H), 5.59 (d, *J* = 4.7 Hz, 1H), 6.78–6.82 (m, 1H), 7.11–7.15 (m, 2H), 7.18–7.23 (m, 4H), 7.35–7.40 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 54.9, 65.1, 86.5, 88.6, 112.2, 114.0, 119.2, 122.5, 128.0, 128.5, 129.6, 131.4, 142.5, 160.6. ppm.

(*S*)-1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-ol (**5fb**): A white solid, 106.0 mg, 89% yield, 58% *ee*; (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 14.42 min, t_R(*R*) = 31.71 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 2.77 (s, 1H), 3.81 (s, 3H), 5.61(s, 1H), 6.85–6.88 (m, 2H), 7.22–7.24 (m, 2H), 7.42–7.48 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ (major + minor) = 55.1, 64.9, 86.8, 89.2, 113.2, 122.0, 128.1, 128.3, 128.4, 131.4, 132.5, 159.9 ppm.

(*R*)-1-(3-Chlorophenyl)-3-phenylprop-2-yn-1-ol (**5hb**): A white solid, 109.1 mg, 90% yield, 46% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*R*) = 9.84 min, t_R(*S*) = 38.07 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 2.49 (d, *J* = 5.4 Hz, 1H), 5.60 (d, *J* = 5.0 Hz, 1H), 7.28–7.36 (m, 5H), 7.47–7.52 (m, 3H), 7.61 (s, 1H) ppm.

(*R*)-1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-ol (**5ib**): A white solid, 109.2 mg, 90% yield, 49% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*R*) = 9.07 min, t_R(*S*) = 30.03 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 3.00 (br s, 1H), 5.58 (s, 1H), 7.21–7.27 (m, 5H), 7.35–7.40 (m, 2H), 7.42–7.47 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 65.5, 89.2, 89.9, 122.0, 128.1, 128.3, 128.6, 129.0, 131.7, 134.2, 139.9 ppm.

(*S*)-1-(2-Bromophenyl)-3-phenylprop-2-yn-1-ol (**5jb**): A white solid, 127.7 mg, 89% yield, 71% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 0.5 mL/min, UV detection at 254 nm); Retention time: t_R(S) = 17.73 min, t_R(*R*) = 20.10 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.49 (d, *J* = 5.9 Hz, 1H), 5.98 (d, *J* = 5.8 Hz, 1H), 7.18–7.26 (m, 2H), 7.36–7.47 (m, 5H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 63.8, 86.1, 87.1, 122.5, 122.8, 127.1, 127.6, 128.2, 128.4, 129.6, 131.7, 132.9, 139.6 ppm.

(*R*)-1-(3-Bromophenyl)-3-phenylprop-2-yn-1-ol (**5kb**): A white solid, 123.4 mg, 86% yield, 63% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*R*) = 8.96 min, t_R(*S*) = 25.92 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.31 (d, *J* = 6.0 Hz, 1H), 5.60 (d, *J* = 6.0 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.23–7.28 (m, 2H), 7.41–7.48 (m, 4H), 7.59 (d, *J* = 7.4 Hz, 1H), 7.83 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 62.8, 86.3, 87.3, 121.6, 122.6, 124.4, 128.3, 128.6, 129.0, 129.8, 131.5, 131.8, 142.9 ppm.

(*R*)-1-(4-Bromophenyl)-3-phenylprop-2-yn-1-ol (**5lb**): A white solid, 133.5 mg, 93% yield, 68% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*R*) = 9.07 min, t_R(*S*) = 25.05 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.29 (d, *J* = 6.1 Hz, 1H), 5.66 (d, *J* = 6.2 Hz, 1H), 7.28–7.34 (m, 3H), 7.45–7.51 (m, 2H), 7.52–7.58 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 62.8, 86.1, 88.5, 121.3, 122.5, 128.2, 128.3, 128.5, 131.8, 131.2, 139.8 ppm.

(*S*)-3-Phenyl-1-(*m*-tolyl)prop-2-yn-1-ol (**5mb**): A white solid, 99.9 mg, 90% yield, 65% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 9.72 min, t_R(*R*) = 19.41 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.41 (s, 3H), 2.82 (s, 1H), 5.68 (s, 1H), 7.08–7.11 (m, 1H), 7.26–7.29 (m, 4H), 7.38–7.40 (m, 2H), 7.45–7.47 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 20.8, 64.2, 86.8, 88.5, 121.6, 123.0, 127.9, 128.1, 128.3, 129.6, 131.5, 138.9, 141.2 ppm.

(*S*)-3-Phenyl-1-(*p*-tolyl)prop-2-yn-1-ol (**5nb**): A white solid, 95.5 mg, 86% yield, 65% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 8.85 min, t_R(*R*) = 15.79 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.42 (s, 3H), 2.45 (d, *J* = 4.4 Hz, 1H), 5.60 (d, *J* = 2.8 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.33–7.37 (m, 3H), 7.46–7.48 (m, 2H), 7.52 (d, *J* = 8.0 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 19.9, 64.2, 86.5, 88.2, 122.0, 126.1, 128.5, 128.9, 129.2, 131.5, 137.8, 139.0 ppm.

(*S*)-1-(Furan-2-yl)-3-phenylprop-2-yn-1-ol (**5ob**): A pale brown oil, 92.1 mg, 93% yield, 85% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 9.73 min, t_R(*R*) = 18.20 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 3.00 (br s, 1H), 5.59 (s, 1H), 6.53–6.56 (m, 1H), 7.21–7.26 (m, 3H), 7.46 (dd, *J* = 2.0 Hz, *J* = 2.3 Hz, 1H), 7.47–7.51 (m, 2H), 7.59–7.62 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 57.5, 85.0, 88.1, 109.2, 122.6, 126.6, 128.3, 128.8, 132.6, 141.2, 144.9 ppm.

(*S*)-1-(2,3-Dimethoxyphenyl)-3-phenylprop-2-yn-1-ol (**5pb**): A pale yellow oil, 130.0 mg, 97% yield, 96% *ee*; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 85/15, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 9.93 min, t_R(*R*) = 12.51 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 3.14 (s, 1H), 3.92 (s, 3H), 3.98 (s, 3H), 5.80 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 7.05 (t, *J* = 7.8 Hz, 1H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.31–7.34 (m, 3H), 7.49–7.52 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 55.8, 61.5, 62.1, 85.6, 89.2, 113.1, 119.5, 123.4, 124.5, 128.5, 128.7, 132.6, 135.7, 147.6, 154.5 ppm.

(*S*)-1-(2,4-Dimethoxyphenyl)-3-phenylprop-2-yn-1-ol (**5qb**): A pale yellow oil, 123.3 mg, 92% yield, 90% *ee*; $[\alpha]_D^{20}$ = +1.6 (C = 0.35, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(S) = 14.88 min, t_R(*R*) = 36.23 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 2.90 (br s, 1H), 3.81 (s, 6H), 5.59 (d, *J* = 5.6 Hz, 1H), 6.52 (d,

J = 9.9 Hz, 2H), 7.25–7.58 (m, 6H) ppm; MS m/z (ESI): 290.6 (M + Na)$^+$, 306.5 (M + K)$^+$, 558.1 (2M + Na)$^+$.

(*S*)-1-(2,6-Dimethoxyphenyl)-3-phenylprop-2-yn-1-ol (5rb): A white solid, 121.9 mg, 91% yield, 90% *ee*; m.p. = 98–100 °C; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 24.90 min, t_R(*R*) = 18.69 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 2.11 (br s, 1H), 3.90 (s, 6H), 4.04 (d, *J* = 9.6 Hz, 1H), 6.19 (d, *J* = 9.6 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 2H), 7.24–7.34 (m, 3H), 7.38–7.42 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 55.5, 57.2, 82.3, 90.6, 104.1, 117.4, 123.8, 128.1, 128.3, 129.0, 131.2, 157.9 ppm.

(*S*)-1-(2,5-Dimethoxyphenyl)-3-phenylprop-2-yn-1-ol (**5sb**): A white solid, 129.9 mg, 97% yield, 95% *ee*; m.p. = 85–87 °C; HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 13.39 min, t_R(*R*) = 18.43 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (major + minor) = 3.19 (d, *J* = 6.0 Hz,1H), 3.88 (s, 3H), 3.93 (s, 3H), 5.79 (d, *J* = 5.8 Hz, 1H), 6.85–6.88 (m, 2H), 7.23–7.28 (m, 3H), 7.49–7.52 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ (major + minor) = 55.3, 56.1, 62.6, 86.1, 88.4, 112.9, 114.2, 114.3, 122.2, 128.3, 128.5, 130.6, 132.7, 151.7, 154.6 ppm.

(*S*)-3-Phenyl-1-(2,3,4-trimethoxyphenyl)prop-2-yn-1-ol (**5vb**): A pale yellow oil, 140.1 mg, 94% yield, 91% *ee*; $[\alpha]_D^{20}$ = +5.0 (C = 0.26, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 13.28 min, t_R(*R*) = 20.11 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 3.07 (br s, 1H), 3.87 (s, 9H), 5.74 (d, *J* = 5.5 Hz, 1H), 6.69 (d, *J* = 8.6 Hz, 1H), 7.24–7.46 (m, 6H) ppm; MS m/z (ESI): 320.7 (M + Na)$^+$, 336.6 (M + K)$^+$, 618.9 (2M + Na)$^+$.

(*S*)-3-Phenyl-1-(2,4,6-trimethoxyphenyl)prop-2-yn-1-ol (**5wb**): A white solid, 131.1 mg, 88% yield, 84% *ee*; m.p. = 96-97 °C; $[\alpha]_D^{20}$ = -15.0 (C = 0.24, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 14.51 min, t_R(*R*) = 20.02 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 1.56 (br s, 1H), 3.83 (s, 9H), 5.74 (d, *J* = 5.5 Hz, 1H), 6.11 (d, *J* = 11.2 Hz, 2H), 7.24–7.41 (m, 5H) ppm; MS m/z (ESI): 320.7 (M + Na)$^+$, 336.6 (M + K)$^+$, 618.9 (2M + Na)$^+$.

(*S*)-3-Phenyl-1-(2,4,5-trimethoxyphenyl)prop-2-yn-1-ol (**5xb**): A white solid, 135.6 mg, 91% yield, 92% *ee*; $[\alpha]_D^{20}$ = +22.0 (C = 0.15, $CHCl_3$); HPLC (Chiralcel OD column, hexane/*i*-PrOH = 90/10, flow rate: 1.0 mL/min, UV detection at 254 nm); Retention time: t_R(*S*) = 24.48 min, t_R(*R*) = 31.50 min; ^{1}H NMR (400 MHz, $CDCl_3$) δ (major + minor) = 2.87 (br s, 1H), 3.88 (s, 9H), 5.92 (d, *J* = 5.4 Hz, 1H), 6.56 (s, 1H), 7.23–7.48 (m, 6H) ppm; MS m/z (ESI): 320.7 (M + Na)$^+$, 336.6 (M + K)$^+$, 618.1 (2M + Na)$^+$.

Conflicts of interest

There are no conflicts of interest to declare.

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Notes and references

View Article Online DOI: 10.1039/C7OB01717K

1 (*a*) J.-C. Kizirian, *Chem. Rev*., 2008, **108**, 140−205; (*b*) E. Tyrrell, *Curr. Org. Chem*., 2009, **13**, 1540−1552; (*c*) B. M. Trost, A. H. Weiss, *Adv. Synth. Catal*., 2009, **351**, 963−983; (*d*) L. Pu, *Acc. Chem. Res*., 2014, **47**, 1523−1535; (*e*) T. Bauer, *Coord. Chem. Rev*., 2015, **299**, 83−150; (*f*) V. Bisai, V. K. Singh, *Tetrahedron Lett*., 2016, **57**, 4771−4784.

2 X.-F. Wu, H. Neumann, *Adv. Synth. Catal.*, 2012, **354**, 3141−3160.

3 M. Turlington, L. Pu, *Synlett*, 2012, **23**, 649−684.

4 For enantioselective addition of Me_2Zn to aldehydes, see: (*a*) G. Blay, I. Fernández, V. Hernández-Olmos, A. Marco-Aleixandre, J. R. Pedro, *Tetrahedron: Asymmetry*, 2005, **16**, 1953−1958; (*b*) P. G. Cozzi, P. Kotrusz, *J. Am. Chem. Soc*., 2006, **128**, 4940−4941; (*c*) N. Garćia-Delgado, M. Fontes, M. A. Pericàs, A. Riera, X. Verdaguer, *Tetrahedron: Asymmetry*, 2004, **15**, 2085−2090; (*d*) C. M. Sprout, M. L. Richmond, C. T. Seto, *J. Org. Chem*., 2004, **69**, 6666−6673; (*e*) G. Blay, I. Fernández, V. Herández-Olmos, A. Marco-Aleixandre, J. R. Pedro, *J. Mol. Catal. A-Chem.*, 2007, 276. 235–243; for an unique example for Me_2Zn addition to ketones, see: (*f*) C. Garcia, L. K. LaRochelle, P. J. Walsh, *J. Am. Chem. Soc*., 2002, **124**, 10970−10971; for addition of Me_2Zn to ketoesters, see: (*g*) L. C. Wieland, H. Deng, M. L. Snapper, A. H. Hoveyda, *J. Am. Chem. Soc*., 2005, **127**, 15453−15456; (*h*) G. Blay, I. Fernández, A. Marco-Aleixandre, J. R. Pedro, *Org. Lett*., 2006, **8**, 1287–1290; (*i)* Y. S. Sokeirik, H. Mori, M. Omote, K. Sato, A. Tarui, I. Kumadaki, A. Ando, *Org. Lett*., 2007, **9**, 1927−1929; (*j*) M. Hatano, T. Miyamoto, K. Ishihara, *Synlett*., 2006, 1762−1764.

5 Examples of the total synthesis of natural products having a chiral methylcarbonyl moiety, see: (*a*) M. S. Scott, C. A. Luckhurst, D. J. Dixon, *Org. Lett*., 2005, **7**, 5813−5816; (*b*) F. Cohen, L. E. Overman, *J. Am. Chem. Soc*., 2006, **128**, 2604−2608.

6 E. J. Corey, C. J. Helal, *Angew. Chem., Int. Ed. Engl*., 1998, **37**, 1986−2012.

7 (*a*) B. M. Trost, M. J. Krische, *J. Am. Chem. Soc*., 1999, **121**, 6131−6141; (*b*) P. J. Stang, F. Diederich, *Modern Acetylene Chemistry*, VCH: Weinheim, Germany, 1995; (*c*) G. Lu, Y.-M. Li, X.-S. Li, A. S. C. Chan, *Coord. Chem. Rev*., 2005, **249**, 1736−1744.

8 For selected examples, see: (*a*) K. Matsumura, S. Hashguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc*., 1997, **119**, 8738−8739; (*b*) S. Hu, L. P. Hager, *J. Am. Chem. Soc*., 1999, **121**, 872−873; (*c*) A. Ford, S. Woodward, *Angew. Chem., Int. Ed*., 1999, **38**, 335−336; (*d*) C. F. Thompson, T. F. Jamison, E. N. Jacobsen, *J. Am. Chem. Soc*., 2001, **123**, 9974−9983; (*e*) V. B. Birman, L. Guo, *Org. Lett*., 2006, **8**, 4859−4861; (*f*) R. S. Coleman, X. Lu, I. Modolo, *J. Am. Chem. Soc*., 2007, **129**, 3826−3827; (*g*) Y. Xing, G. A. Doherty, *Org. Lett*., 2009, **11**, 1107−1110; for a related review, see: (*h*) T. Nakai, K. Mikami, *Chem. Rev*., 1986, **86**, 885−902; (*i*) P. G. Cozzi, S, Alesi, *Chem. Commun.*, 2004, 2448−2449.

9 For selected reviews, see: (*a*) J.-C. Kizirian, *Chem. Rev.*, 2008, **108**, 140−205; (*b*) C. M. Binder, B. Singaram, *Org. Prep. Proced. Int*., 2011, **43**, 139–208; (*c*) T. Ohshima, *To Catalytic Asymmetric 1,2-Alkynylation* in *Comprehensive Chirality*, E. M. Carreira and H. Yamamoto eds, Elsevier, Amsterdam, Nederland, 2012, vol. 4, pp. 355–377; (*d*) A. Lumbroso, M. L. Cooke, B. Breit, *Angew. Chem., Int. Ed.*, 2013, **52**, 1890–1932; (*e*) T. Hirose, K. Kodama, *Recent advances in organozinc reagents* in *Comprehensive Organic Synthesis (2nd Edition)*, P. Knochel and G. Molander eds. Elsevier, Amsterdam, Nederland, 2014, vol. 1, pp. 204−266; (*f*) D. Łowicki, S. Baś, J. Mlynarski, *Tetrahedron*, 2015, **71**, 1339−1394; (*g*) L. Hong, W. Sun, D. Yang, G. Li, R. Wang, *Chem. Rev.*, 2016, **116**, 4006−4123.

10 E. J. Corey, K. A. Cimprich, *J. Am. Chem. Soc*., 1994, **116**, 3151−3152.

11 (*a*) D. E. Frantz, R. Fässler, E. M. Carreira, *J. Am. Chem. Soc*., 2000, **122**, 1806−1807; (*b*) D. E. Frantz, R. F ssler, C. S. Tomooka, E. M. Carreira, *Acc. Chem. Res*., 2000, **33**, 373−381; (*c*) N. K.

View Article Online
DOI: 10.1039/C7OB01717K

Anand, E. M. Carreira, *J. Am. Chem. Soc*., 2001, **123**, 9687−9688; (*d*) D. Boyall, D. E. Frantz, E. M. Carreira, *Org. Lett*., 2002, **4**, 2605−2606; (*e*) R. Fässler, C. S. Tomooka, D. E. Frantz, E. M. Carreira, *Proc. Natl. Acad. Sci. USA*, 2004, **101**, 5843−5845.

12 (*a*) X. Li, G. Lu, W. H. Kwok, A. S. C. Chan, *J. Am. Chem. Soc*., 2002, **124**, 12636−12637; (*b*) M. Turlington, Y. Du, S. G. Ostrum, V. Santosh, K. Wren, T. Lin, M. Sabat, L. Pu, *J. Am. Chem. Soc*., 2011, **133**, 11780−11794; (*c*) W.-C. Huang, W. Liu, X.-D. Wu, J. Ying, L. Pu, *J. Org. Chem*., 2015, **80**, 11480−11484; (*d*) R. Takita, K. Yakura, T. Ohshima, M. Shibasaki, *J. Am. Chem. Soc*., 2005, **127**, 13760–13761.

13 For selected examples, see: (*a*) Z. Xu, R. Wang, J. Xu, C.-S. Da, W.-J. Yan, C. Chen, *Angew. Chem., Int. Ed.*, 2003, **42**, 5747–5749; (*b*) C. Chen, L. Hong, Z.-Q. Xu, R. Wang, *Org. Lett*., 2006, **8**, 2277–2280; (*c*) C. Wolf, S. Liu, *J. Am. Chem. Soc*., 2006, **128**, 10996–10997; (*d*) D. L. Usanov, H. Yamamoto, *J. Am. Chem. Soc*., 2011, **133**, 1286–1289; (*e*) B. Zheng, S.-N. Li, J.-Y. Mao, B. Wang, Q.-H. Bian, S.-Z. Liu, J.-C. Zhong, H.-C. Guo, M. Wang, *Chem. Eur. J*., 2012, **18**, 9208–9211; (*f*) J. Yuan, J. Wang, G. Zhang, C. Liu, X. Qi, Y. Lan, J. T. Miller, A. J. Kropf, E. E. Bunelb, A. Lei, *Chem. Commun*., 2015, **51**, 576–579; (*g*) N. Xu, D.-W. Gu, J. Zi, X.-Y. Wu, X.-X. Guo, *Org. Lett*., 2016, **18**, 2439−2442; (*h*) A. M. Cook, C. Wolf, *Angew. Chem., Int. Ed.*, 2016, **55**, 2929−2933.

14 (*a*) B. M. Trost, A. H. Weiss, A. J. von Wangelin, *J. Am. Chem. Soc*., 2006, **128**, 8−9; for a review, see: (*b*) B. M. Trost, M. J. Bartlett, *Acc. Chem. Res*., 2015, **48**, 688−701.

15 (*a*) B. M. Trost, A. H. Weiss, *Org. Lett.,* 2006, **8**, 4461−4464; (*b*) B. M. Trost, V. S. Chan, D. Yamamoto, *J. Am. Chem. Soc*., 2010, **132**, 5186−5192; (*c*) B. M. Trost, A. Quintard, *Angew. Chem., Int. Ed*., 2012, **51**, 6704–6708; (*d*) B. M. Trost, M. J. Bartlett, A. H. Weiss, A. J. von Wangelin, V. S. Chan, *Chem. Eur. J*., 2012, **18**, 16498–16509; (*e*) J. Liu, H. Li, C. Zheng, S. Lu, X. Guo, X. Yin, R. Na, B. Yu, M. Wang, *Molecules*, 2017, **22**, 364–379.

16 M.-C. Wang, Q.-J. Zhang, W.-X. Zhao, X.-D. Wang, X. Ding, T.-T. Jing, M.-P. Song, *J. Org. Chem*., 2008, **73**, 168−176.

17 J.-L. Niu, M.-C. Wang, L.-J. Lu, G.-L. Ding, H.-J. Lu, Q.-T. Chen, M.-P. Song, *Tetrahedron: Asymmetry*, 2009, **20**, 2616–2621.

18 Y.-Z. Hua, M.-M. Liu, P.-J. Huang, X. Song, M.-C. Wang, J.-B. Chang, *Chem. Eur. J*., 2015, **21**, 11994–11998.

19 Y.-Z. Hua, X.-W. Han, X.-C. Yang, X. Song, M.-C. Wang, J.-B. Chang, *J. Org. Chem*., 2014, **79**, 11690–11699.

20 (*a*) Y.-Z. Hua, L.-J. Lu, P.-J. Huang, D.-H. Wei, M.-S. Tang, M.-C. Wang, J.-B. Chang, *Chem. Eur. J.,* 2014, **20**, 12394–12398; (*b*) Y.-Z. Hua, X.-C. Yang, M.-M. Liu, X. Song, M.-C. Wang, J.-B. Chang, *Macromolecules*, 2015, **48**, 1651–1657.

21 (*a*) Y. Xiao, Z. Wang, K. Ding, *Chem. Eur. J*., 2005, **11**, 3668–3678; (*b*) Y. Xiao, Z. Wang, K. Ding, *Macromolecules* 2006, **39**, 128–136.

22 M. J. Palmer, J. A. Kenny, T. Walsgrove, A. M. Kawamoto, M. Wills, *J. Chem. Soc., Perkin Trans. 1,* 2002, 416–427.

