Highly enantioselective alkynylation of aldehydes catalyzed by a new oxazolidine–titanium complex†

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The readily available and inexpensive new chiral oxazolidine **2a** in combination with Ti(O^{i}Pr)$_4$ was found to catalyze the reaction of an alkynylzinc reagent with various types of aldehydes to generate chiral propargylic alcohols with high enantioselectivities (up to 95%) and excellent yields (up to 98%).

Introduction

The asymmetric alkynylzinc addition to aldehydes can simultaneously form a new C–C bond and a stereogenic centre in one step, which has become the preferred way of synthesizing useful chiral propargylic alcohols.[1] In recent years, the catalytic enantioselective addition of terminal alkynes to aldehydes has generated great amount of interest, and some impressive results have been obtained since the leading example reported by Corey.[2]

Among the catalysts developed, those based on ephedrine or 1,1′-bi-2-naphthol are the outstanding representatives.[3] Since axially chiral symmetric ligands have proved to be exceptionally versatile and effective in many asymmetrically catalytic processes,[4] development of such catalysts for asymmetric alkynylation additions is meaningful.

Recently, Du has developed the complex of a C_3-symmetric tris(β-hydroxyamide) ligand (**A**, Fig. 1) and Ti(O^{i}Pr)$_4$ for asymmetric alkynylation, and moderate to excellent enantioselectivities (up to 92% ee) have been obtained.[5] Under the same conditions, the ligand **A** afforded higher chemical selectivity and enantioselectivity than the corresponding C_2- or C_1-symmetric ligands. Wang and co-workers also reported that the C_2-symmetric bissulfonamide ligand **B** catalyzed the asymmetric alkynylation of aldehydes and ketones to give chiral products with high ee values.[6] In addition, C_2-symmetric bisoxazolidine ligand **C** has been used for highly enantioselective addition of alkynes to aldehydes, while oxazolidine ligand **D** afforded the corresponding product with only 17% ee.[7]

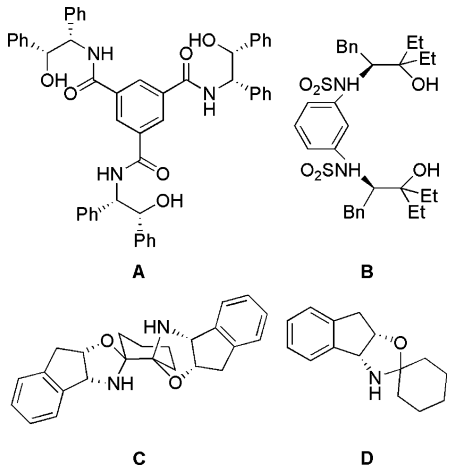

Fig. 1 Previously reported chiral axial symmetric ligands.[5–7]

However, it is a dilemma that C_2 or C_3-symmetric ligands definitely have higher synthetic cost and are more difficult to synthesize than C_1-symmetric ligands. Therefore, the development of easily accessible and operationally simple ligands is still a challenge. In the long run, we are interested in ligands which are easily prepared by a short pathway from readily available starting materials, and their applications in asymmetric transition processes.[8]

With the current interest in oxazolidine catalysts, we have designed and synthesized chiral ligands derived from (1*R*,2*S*)-*cis*-1-amino-2-indanol (**1**).[9] However, poor results were obtained during their application to asymmetric alkynylzinc additions to benzaldehyde.

In contrast to the traditional oxazolidine or bisoxazolidine catalysts, which did not require Ti(O^{i}Pr)$_4$, addition of Ti(O^{i}Pr)$_4$ to the reaction unexpectedly provided a highly effective catalytic system. In this paper, we report an example of highly enantioselective addition of terminal alkynes to aldehydes using a very simple oxazolidine–titanium complex catalyst with high yields and excellent enantioselectivities.

Results and discussion

Initially, ligand **2a** was synthesized from **1**, a readily available chiral source (see the Experimental section). When **2a** was used as the ligand to catalyze the asymmetric addition of phenylacetylene to benzaldehyde, only (*S*)-product with 21% ee was obtained.[10] To our surprise, the addition of an equivalent of Ti(O^{i}Pr)$_4$ not only resulted in reversal of the configuration of the product, but also enhanced ee values greatly. Thus this ligand, traditionally believed to be rather poor, became an excellent catalyst (Fig. 2). The reaction used THF as the solvent, with a reagent ratio of phenylacetylene–Et$_2$Zn–benzaldehyde–ligand–Ti(O^{i}Pr)$_4$ = 1 : 1 : 0.5 : 0.1 : 0.2, and was conducted under argon at room temperature. We also synthesized three similar ligands (**2b–2d**), all of which

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† Electronic supplementary information (ESI) available: ^{1}H NMR, ^{13}C NMR and IR spectra of ligands and products; HPLC data; expanded version of Table 1; crystal structure data in CIF format (CCDC reference number 667689. See DOI: 10.1039/b719624e

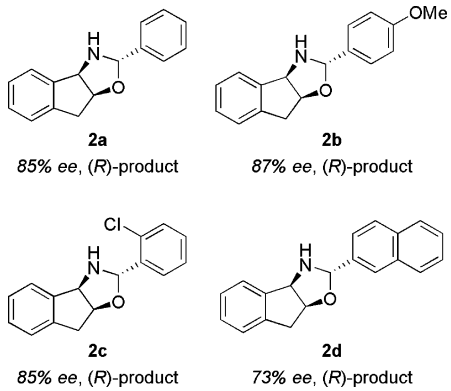


Fig. 2 The chiral ligands evaluated in this paper, and the results of using them in the asymmetric addition of phenylacetylene to benzaldehyde.

afforded good enantioselectivities in the presence of $Ti(O^iPr)_4$, as can be seen from Fig. 3.

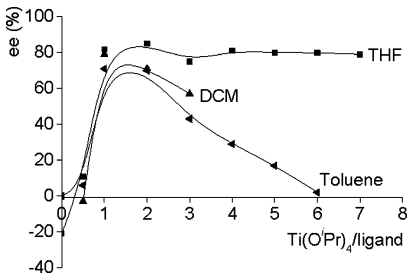


Fig. 3 The relationship between ee values and the $Ti(O^iPr)_4$–ligand ratio when different solvents were used in the asymmetric addition of phenylacetylene to benzaldehyde.

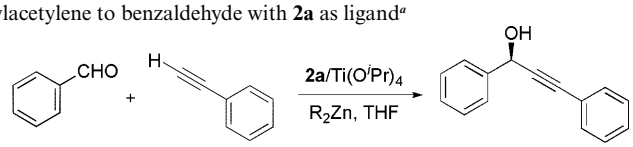
Since similar results were obtained for all ligands (**2a–2d**), ligand **2a** was chosen as the model ligand for further investigations due to its inexpensiveness. The effects of the reaction conditions such as the choice of solvent and the $Ti(O^iPr)_4$–**2a** ratio were also investigated. As can be seen from Fig. 3, the $Ti(O^iPr)_4$–**2a** ratio was important in determining the enantioselectivities of the products; in addition, the optimal $Ti(O^iPr)_4$–ligand ratios varied between solvents. The best result (85% ee) was obtained when the $Ti(O^iPr)_4$–ligand ratio was 2 : 1 with THF as solvent.

Other reaction conditions employing ligand **2a** were then explored, and are summarized in Table 1. Enhancement of the amounts of Et_2Zn and phenylacetylene had no effect on the enantioselectivity (entries 1–4). Increasing the amount of **2a** gave enhanced ee (entries 5–9), but further increasing the ligand amount from 20 to 30 mol% did not lead to a dramatic increase in ee. Thus, 20 mol% was chosen as the optimal loading of ligand. Reducing the reaction temperature gave enhanced enantioselectivity (entries 10 and 11). Replacement of Et_2Zn with Me_2Zn at room temperature boosted the enantioselectivity to 90% ee (entries 12 and 13). At this time, reducing the reaction temperature from room temperature to 0 °C gave the best enantioselectivity (at the expense of chemical yield) of the product (entry 14).

Under the optimized conditions of entry 12 in Table 1, the reactions of phenylacetylene with a variety of aldehydes catalyzed by **2a**–$Ti(O^iPr)_4$ were investigated. As shown by the results summarized in Table 2, high enantioselectivities (ranging from 90–95% ee) were achieved for the addition of phenylacetylene to aromatic aldehydes. Substituents of aromatic aldehydes containing electron-donating or electron-withdrawing groups at the *ortho*, *meta*, or *para* positions have little effect on the enantioselectivity. Good enantioselectivity (77%) was also obtained with an aliphatic aldehyde (entry 11).

Good results can also be obtained for this asymmetric addition reaction with other acetylenes. For example, 83% ee was obtained for the addition of 4-phenyl-1-butyne to 2-naphthaldehyde, while 88% ee was obtained when trimethylsilylacetylene was used as the substrate (Fig. 4).

Table 1 Asymmetric addition of phenylacetylene to benzaldehyde with **2a** as ligand[a]



Entry	Cat. (%)	T/°C	PhC≡CH (equiv.)	R_2Zn (equiv.)	ee (%)[b]
1	20	rt	1.4	Et_2Zn (1.4)	85
2	20	rt	2.0	Et_2Zn (2.0)	86
3	20	rt	3.0	Et_2Zn (3.0)	86
4	20	rt	4.0	Et_2Zn (4.0)	87
5	5	rt	2.0	Et_2Zn (2.0)	66
6	10	rt	2.0	Et_2Zn (2.0)	81
7	15	rt	2.0	Et_2Zn (2.0)	83
8	25	rt	2.0	Et_2Zn (2.0)	85
9	30	rt	2.0	Et_2Zn (2.0)	87
10	20	0	2.0	Et_2Zn (2.0)	89
11	20	−25	2.0	Et_2Zn (2.0)	90
12	20	rt	2.0	Me_2Zn (2.0)	90
13	30	rt	2.0	Me_2Zn (2.0)	90
14[c]	20	0	2.0	Me_2Zn (2.0)	93

[a] All the reactions were processed in THF under argon at room temperature. $Ti(O^iPr)_4$ was freshly distilled. Ligand **2a**–$Ti(O^iPr)_4$–benzaldehyde = 1 : 2 : 5. GC indicated the complete conversion of benzaldehyde after the reaction time of 20 h. [b] The enantiomeric excess was determined by chiral HPLC analysis of the corresponding products on a Chiralcel OD-H column. [c] The yield of the product was 46%.

Table 2 Enantioselective alkynylation of various aldehydes with phenylacetylene using ligand **2a**[a]

Entry	Aldehyde	Yield (%)[b]	ee (%)[c]
1	Benzaldehyde	98	90
2	2-Anisaldehyde	91	92
3	4-Anisaldehyde	91	95
4	4-Tolualdehyde	87	90
5	2-Chloroaldehyde	96	93
6	3-Chloroaldehyde	97	91
7	α-Naphthaldehyde	96	90
8	β-Naphthaldehyde	97	93
9	2,3-Dimethoxybenzaldehyde	91	90
10	2-Furaldehyde	91	90
11	Hydrocinnamaldehyde	81	77

[a] All the reactions were carried out under argon at room temperature for 20 h. Phenylacetylene–Et_2Zn–aldehyde–**2a**–$Ti(O^iPr)_4$ = 2 : 2 : 0.5 : 0.1 : 0.2. [b] Isolated yield. [c] The enantiomeric excess was determined by chiral HPLC analysis of the corresponding products on a Chiralcel OD-H column.

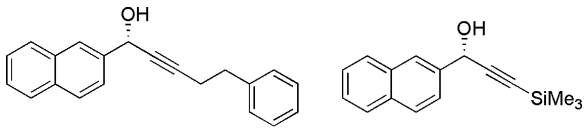


Fig. 4 Products of the reactions of 4-phenyl-1-butyne and trimethylsilylacetylene with 2-naphthaldehyde.

Conclusions

In conclusion, we have developed a very simple catalyst system for the highly enantioselective synthesis of propargylic alcohols by alkynylzinc addition to various aldehydes. The study has shown that a combination of **2a** with $Ti(O^iPr)_4$ generated a highly enantioselective and chemically active catalyst that could afford products with up to 95% ee and 98% yield. The application of this catalyst system to other asymmetric catalytic reactions is in progress.

Experimental

General methods

All manipulations were carried out under an argon atmosphere in dried and degassed solvents. All solvents were dried and degassed by the standard methods; all aldehydes, as well as dimethylzinc and diethylzinc, were commercially available. Melting points were determined using a standard melting point apparatus and are uncorrected. The reactions were monitored by thin layer chromatography (TLC). NMR spectra were measured in $CDCl_3$ on a Varian-Inova-400 NMR spectrometer (400 MHz) with TMS as an internal reference. Optical rotations were measured with a HORIBA SEPA-200 high sensitivity polarimeter. Enantiomeric excess (ee) determination was carried out using a chiral OD-H column: solvent, hexane–isopropanol; flow rate, 1 cm^3 min^{-1}; UV detection, 254 nm. High resolution mass spectra (HRMS) were performed using EI.

General procedure for the synthesis of chiral ligands 2a–2d (Fig. 5)

A solution of (1*R*,2*S*)-*cis*-1-amino-2-indanol (**1**) (10 mmol) and the corresponding aldehyde (10 mmol) in DCM (20 mL) was stirred at room temperature for 24 h. After evaporation of the solvent, the residue was purified by recrystallization from isopropanol–petroleum ether (1 : 6).

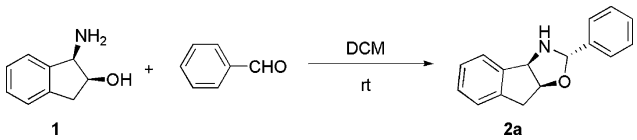


Fig. 5 Synthesis of chiral ligand **2a**.

Ligand 2a. Mp 69–70 °C; $[a]_D^{25}$ = +82.8 (*c* 1.02, abs. EtOH); dr = 1 : 5 (determined by ^1H NMR); ^1H NMR (400 MHz, $CDCl_3$) δ 8.58–7.07 (m, 9H), 5.12–5.07 (m, 2H), 4.81 (d, J = 4.4 Hz, 1H), 3.24–3.17 (m, 2H), 2.53 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.8, 141.3, 136.6, 133.7, 130.3, 130.0, 129.2, 129.0, 128.0, 127.8, 127.6, 127.4, 126.3, 126.1, 125.9, 125.3, 90.7, 89.8, 81.2, 80.6, 69.5, 39.8, 38.7; IR (cm^{-1}): 3280, 1026, 895, 756; HRMS (EI$^+$) calc. for $[C_{16}H_{15}NO]^+$ requires *m*/*z* 237.1154, found 237.1165.

Single-crystal X-ray structure (Fig. 6). Careful evaporation of a solution of **2a** in isopropanol–petroleum ether (1 : 6) gave a single crystal of **2a** suitable for crystallographic analysis.† Selected crystal structure data: $C_{16}H_{15}NO$, monoclinic, space group C_2, a = 19.246(6) Å, b = 5.8447(16) Å, c = 14.509(5) Å, α = 90.00°, β = 129.844(4)°, γ = 90.00°, V = 1253.1(7) $Å^3$, Z = 4, ρ_{calcd} = 1.258 g cm^{-3}, T = 223(2) K.

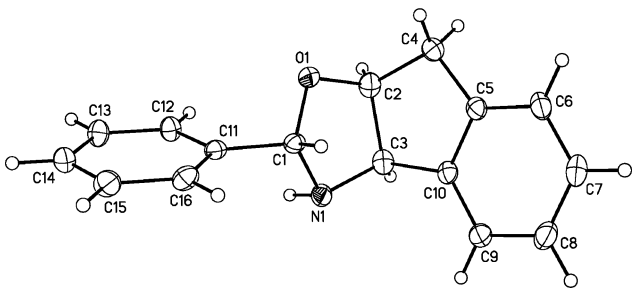


Fig. 6 X-Ray crystal structure of ligand **2a**.†

Ligand 2b. Mp 87–88 °C; $[a]_D^{25}$ = +52.0 (*c* 1.00, abs. EtOH); dr = 1 : 3 (determined by ^1H NMR); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78–7.06 (m, 8H), 5.10–5.06 (m, 2H), 4.94 (m, 1H), 3.86–3.77 (m, 3H), 3.31–3.16 (m, 2H), 2.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.3, 159.9, 142.6, 141.5, 141.5, 141.2, 130.8, 128.8, 128.7, 128.5, 128.2, 127.7, 127.5, 127.5, 127.4, 127.3, 126.7, 126.0, 125.7, 125.7, 125.3, 124.9, 124.5, 114.2, 113.8, 93.4, 91.5, 80.8, 79.9, 75.6, 74.6, 68.9, 55.4, 40.0, 39.5, 38.5; IR (cm^{-1}): 3272, 2917, 1613, 1513, 1428, 1243, 1034, 756; HRMS (EI$^+$) calc. for $[C_{17}H_{17}NO_2]^+$ requires *m*/*z* 267.1259, found 267.1248.

Ligand 2c. Mp 91–92 °C; $[a]_D^{25}$ = +70.0 (*c* 1.00, abs. EtOH); dr = 1 : 5 (determined by ^1H NMR); ^1H NMR (400 MHz, $CDCl_3$) δ 7.63–7.09 (m, 8H), 5.45 (s, 1H), 5.38–5.12 (m, 1H), 4.95–4.94

(m, 1H), 3.53–3.19 (m, 2H), 2.66 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.7, 141.7, 141.3, 136.5, 133.6, 130.2, 129.9, 129.2, 128.9, 128.0, 127.8, 127.6, 127.4, 126.2, 126.0, 125.8, 125.3, 90.7, 89.8, 81.2, 80.6, 69.5, 39.8, 38.7; IR (cm^{-1}): 3319, 2948, 1436, 1027, 749; HRMS (EI^+) calc. for $[C_{16}H_{14}NOCl]^+$ requires m/z 267.1259, found 267.1248.

Ligand 2d. Mp 129–130°C; $[a]_D^{25} = +46.7$ (c 0.42, abs. EtOH); dr = 1 : 4 (determined by ^{1}H NMR); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74–7.10 (m, 11H), 5.29 (s, 1H), 5.13 (d, J = 5.2 Hz, 1H), 4.98 (s, 1H), 3.37–3.20 (m, 2H), 2.70 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.6, 141.2, 136.2, 133.5, 133.2, 131.1, 129.0, 128.9, 128.9, 128.8, 128.8, 128.7, 128.6, 128.4, 128.3, 128.3, 128.1, 127.8, 127.7, 127.4, 126.8, 126.4, 126.3, 126.1, 125.8, 125.5, 125.0, 124.5, 123.8, 93.7, 91.9, 81.6, 80.2, 74.8, 69.0, 39.6, 38.6; IR (cm^{-1}): 3442, 1651, 1250, 1189, 756; HRMS (EI^+) calc. for $[C_{20}H_{17}NO]^+$ requires m/z 287.1310, found 287.1304.

General procedure for the addition of phenylacetylene to aldehydes

All manipulations were carried out under an argon atmosphere using dried and degassed solvent. The ligand **2a** (23.8 mg, 0.1 mmol) and $Ti(O^iPr)_4$ (60 µl, 0.2 mmol) were mixed in dry THF (2.0 ml) at room temperature. Then, a solution of Me_2Zn (1.2 M in toluene, 0.84 ml) was added. After the mixture was stirred at room temperature for 1.5 h, phenylacetylene (109 µl, 1.0 mmol) was added and the stirring continued for another 1.5 h. The yellow solution was cooled to 0 °C and treated with benzaldehyde (50 µl, 0.5 mmol), and then the resultant mixture was allowed to warm up to room temperature naturally and stirred for 20 h. After the reaction was complete, it was cooled to 0 °C again and quenched by 5% aqueous HCl (2 ml). The mixture was extracted with ethyl acetate (2 × 10 ml). The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, EtOAc–petroleum ether = 1 : 6) to give the pure product.

1,3-Diphenylprop-2-yn-1-ol. 98% yield. 90% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 7.63, t_{minor} = 11.69. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, J = 7.2 Hz, 2H), 7.48–7.25 (m, 8H), 5.69 (s, 1H), 2.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.1, 132.2, 129.2, 129.1, 128.9, 128.8, 127.2, 122.9, 89.1, 87.2, 65.6.

1-(2-Methoxyphenyl)-3-phenylprop-2-yn-1-ol. 91% yield. 92% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 8.05, t_{minor} = 9.11. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 7.2 Hz, 2H), 7.36–7.28 (m, 4H), 6.98 (t, J = 7.6 Hz, 1H), 6.88 (d, J = 8.4 Hz, 1H), 5.93 (s, 1H), 3.85 (s, 3H), 3.27 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 132.1, 130.0, 129.1, 128.7, 128.6, 128.3, 123.1, 121.2, 111.3, 88.8, 86.3, 61.8, 55.9.

1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-ol. 91% yield. 95% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 7.20, t_{minor} = 11.83. ^{1}H NMR (400 MHz, $CDCl_3$) (δ, ppm): 7.55 (d, J = 8.4 Hz, 2H), 7.49–7.48 (m, 2H), 7.33–7.27 (m, 3H), 6.93 (d, J = 8.4 Hz, 2H), 5.65 (d, J = 6.0 Hz, 1H), 3.83 (s, 3H), 2.24 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 133.4, 132.2, 129.0, 128.7, 128.6, 122.9, 114.4, 89.4, 86.8, 65.1, 55.7.

1-(4-Methylphenyl)-3-phenylprop-2-yn-1-ol. 87% yield. 90% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 10 : 90). Retention time: t_{major} = 8.38, t_{minor} = 16.31. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 8.0 Hz, 2H), 7.47 (t, J = 7.2 Hz, 2H), 7.32–7.21 (m, 5H), 5.65 (d, J = 6.4 Hz, 1H), 2.37 (s, 3H), 2.24 (d, J = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.2, 132.2, 130.0, 129.0, 128.7, 127.2, 122.9, 89.4, 86.9, 65.4.

1-(2-Chlorophenyl)-3-phenylprop-2-yn-1-ol. 96% yield. 93% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 10 : 90). Retention time: t_{major} = 8.25, t_{minor} = 9.51. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 7.42–7.28 (m, 6H), 6.05 (d, J = 4.8 Hz, 1H), 2.36 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 133.3, 132.2, 130.2, 129.1, 128.9, 128.8, 127.7, 122.7, 88.1, 87.1, 62.8.

1-(3-Chlorophenyl)-3-phenylprop-2-yn-1-ol. 97% yield. 91% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 15 : 85). Retention time: t_{major} = 6.61, t_{minor} = 16.90. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.48 (t, J = 7.6 Hz, 3H), 7.34–7.27 (m, 5H), 5.67 (d, J = 5.6 Hz, 1H), 2.36 (d, J = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 135.0, 132.3, 130.4, 129.3, 129.0, 128.8, 127.4, 125.3, 122.5, 88.5, 87.5, 64.9.

1-(2-Naphthyl)-3-phenylprop-2-yn-1-ol. 97% yield. 93% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 7.72, t_{minor} = 18.35. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.91–7.85 (m, 3H), 7.73 (d, J = 8.4 Hz, 1H), 7.51–7.33 (m, 7H), 5.87 (d, J = 6.0 Hz, 1H), 2.40 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4, 133.7, 132.3, 129.1, 128.8, 128.7, 128.2, 126.8, 126.0, 125.1, 122.8, 89.2, 87.4, 65.7.

1-(1-Naphthyl)-3-phenylprop-2-yn-1-ol. 96% yield. 91% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 15 : 85). Retention time: t_{major} = 9.87, t_{minor} = 17.45. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, J = 8.4 Hz, 1H), 7.94–7.86 (m, 3H), 7.61–7.48 (m, 5H), 7.47–7.32 (m, 3H), 6.36 (d, J = 4.4 Hz, 1H), 2.43 (d, J = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.1, 134.5, 132.3, 131.1, 129.9, 129.2, 129.1, 128.8, 127.0, 126.4, 125.7, 125.2, 124.4, 122.9, 89.0, 87.8, 63.9.

1-(2,3-Dimethoxyphenyl)-3-phenylprop-2-yn-1-ol. 91% yield. 90% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 8.30, t_{minor} = 9.92. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46–7.44 (m, 2H), 7.31–7.29 (m, 3H), 7.17 (d, J = 8.0 Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 5.80 (s, 1H), 3.91 (s, 3H), 3.89 (s, 3H), 3.26 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 147.1, 135.2, 132.1, 128.9, 128.7, 124.8, 123.1, 120.1, 113.3, 89.8, 86.2, 62.5, 61.6, 56.3.

1-(Furan-2-yl)-3-phenylprop-2-yn-1-ol. 91% yield. 90% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 5.85, t_{minor} = 8.55. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.45 (m, 3H), 7.34–7.33 (m, 3H), 6.53 (d, J = 2.8 Hz, 1H), 6.39 (s, 1H), 5.69 (d, J = 6.8 Hz, 1H), 2.44 (d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 153.3, 143.5, 132.2, 129.2, 128.7, 122.5, 110.9, 108.3, 86.6, 86.1, 59.0.

1,5-Diphenylpent-1-yn-3-ol. 81% yield. 77% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 6.34, t_{minor} = 9.40. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, J = 7.2 Hz, 2H), 7.33–7.19 (m, 8H), 4.60 (q, J = 5.6 Hz, 1H), 2.87 (t, J = 8.0 Hz, 2H), 2.15 (q, J = 3.6 Hz, 2H), 1.95 (d, J = 5.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.7, 132.1, 128.9, 128.8, 128.7, 126.4, 123.0, 90.3, 85.7, 62.6, 39.7, 31.9.

1-(Naphthalen-6-yl)-5-phenylpent-2-yn-1-ol. 67% yield. 83% ee determined by HPLC analysis (Chiralcel OD-H column, isopropanol–hexane = 20 : 80). Retention time: t_{major} = 9.67, t_{minor} = 17.74. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.79 (d, J = 6.4 Hz, 3H), 7.55 (d, J = 8.4 Hz, 1H), 7.47–7.45 (m, 2H), 7.25–7.18 (m, 5H), 5.54 (s, 1H), 2.84 (t, J = 7.2 Hz, 2H), 2.56 (t, J = 7.2 Hz, 2H), 2.46 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.9, 138.7, 133.5, 133.4, 129.1, 129.0, 128.9, 128.8, 128.6, 128.1, 126.8, 126.6, 125.7, 125.1, 87.4, 81.1, 65.2, 35.2, 21.4.

3-(Trimethylsilyl)-1-(naphthalen-6-yl)prop-2-yn-1-ol. 53% yield. 88% ee determined by HPLC analysis (Chiralcel AD-H column, isopropanol–hexane = 15 : 85). Rentention time: t_{minor} = 4.65, t_{major} = 5.91. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.88–7.84 (m, 3H), 7.54 (d, J = 8.4 Hz, 1H), 7.50 (dd, J = 6.4 Hz, J = 3.2 Hz, 2H), 5.62 (d, J = 5.2 Hz, 1H), 2.46 (d, J = 5.2 Hz, 1H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.0, 138.6, 133.5, 129.0, 128.7, 128.1, 126.8, 126.7, 126.0, 125.1, 105.3, 92.3, 65.6, 0.31.

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