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Lithium Binaphtholate-Catalyzed Asymmetric Addition of Lithium Acetylides to Carbonyl Compounds

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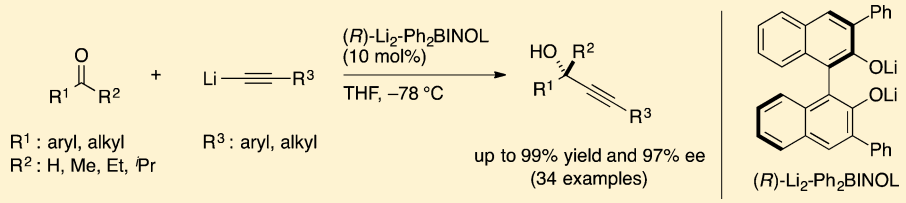
Supporting Information

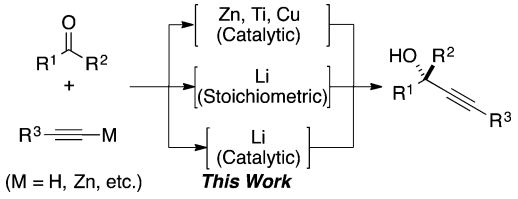


ABSTRACT: The asymmetric addition of lithium acetylides to carbonyl compounds in the presence of a chiral lithium binaphtholate catalyst was developed. A procedure involving the slow addition of carbonyl compounds to lithium acetylides improved the enantioselectivity. This reaction afforded diverse chiral secondary and tertiary propargylic alcohols in high yields and with good to high enantioselectivities.

INTRODUCTION

Organolithiums are versatile reagents and commonly used as nucleophiles or bases in organic synthesis.[1] The cationic property of lithium leads to higher reactivity than Grignard or organozinc reagents; however, this property is simultaneously disadvantageous for achieving high stereoselectivity. Lithium acetylide, an organolithium reagent, is used in alkynylations of carbonyl compounds to afford the corresponding propargylic alcohols that are useful building blocks in the synthesis of pharmaceuticals, agrochemicals, and natural products.[1] Therefore, asymmetric alkynylations have been developed.[2,3] Because of recent significant progress in asymmetric catalysis, highly stereoselective alkynylations of terminal alkynes have been achieved using other metal cocatalysts such as Zn,[4,5] Ti,[6] Cu,[7] and several other metals.[8] However, the asymmetric alkynylation using lithium acetylides without other metals has been rarely examined despite the high reactivity of alkynyllithiums (Scheme 1). In 1979, Mukaiyama and coworkers developed the first enantioselective alkynylation with lithium acetylide in the absence of other metals.[9] They used lithium acetylides and chiral ligands, affording propargylic alcohols with high enantioselectivity. In 1995, the enantioselective alkynylation of ketones was applied to synthesize efavirenz, an HIV-1 reverse transcriptase inhibitor.[10,11] In both cases, more than stoichiometric amounts of acetylide and ligand were required to achieve high enantioselectivity. Recently, we reported that a catalytic amount of chiral lithium binaphtholate complex efficiently catalyzed the asymmetric alkynylation of ketones with lithium acetylides, affording the corresponding tertiary propargylic alcohols with high enantioselectivity.[12] In this paper, we report the details of lithium binaphtholate-catalyzed enantioselective alkynylation of carbonyl compounds using a slow addition procedure, thus dramatically increasing the enantioselectivity.

Scheme 1. Methods for Asymmetric Alkynylation of Carbonyl Compounds



RESULTS AND DISCUSSION

Survey of Substrates and Catalysts for Enantioselective Alkynylations. First, we investigated the addition of lithium phenylacetylide (**4u**) to benzaldehyde (**2a**) or acetophenone (**3a**) in the presence of 10 mol % of lithium binaphtholate (**1b**) (Table 1). Both the lithium reagents **1b** and **4u** were prepared in situ by adding *n*-butyllithium to a solution of (*R*)-3,3′-diphenyl-2,2′-binaphthol (**1b′**) and phenylacetylene (**4u′**) (Scheme 2). To the resulting solution was added a solution of carbonyl compound **2a** or **3a**, affording the corresponding propargylic alcohols **5au** or **6au**, respectively. In the toluene solution, no selectivity was observed in the alkynylation of **2a** and **3a** (Table 1, entries 1 and 3). In contrast, the reaction in THF afforded **5au** with moderate enantioselectivity (32% ee, Table 1, entry 2). Furthermore, the alkynylation of ketone **3a** afforded the corresponding tertiary

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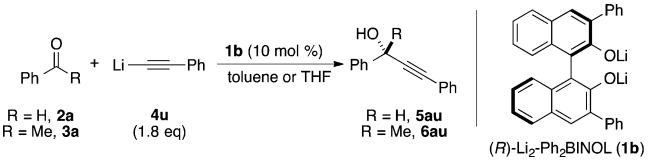
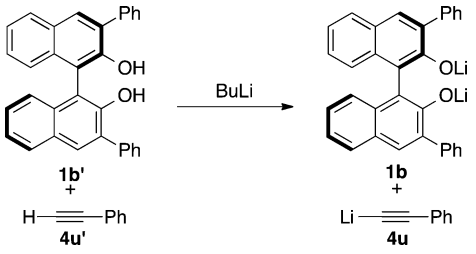
Table 1. Asymmetric Alkynylation of Carbonyl Compounds with Lithium Binaphtholate 1b[a]



entry	carbonyl compd	solvent	yield (%)	ee[b] (%)
1	PhCHO (**2a**)	toluene	89	1
2		THF	95	32
3	$PhCOCH_3$ (**3a**)	toluene	72	3
4		THF	87	67

[a]The reaction was conducted by adding a solution of carbonyl compound **2a** or **3a** over 1 min to a solution of acetylene **4u′** (2.0 equiv), (*R*)-Ph_2-BINOL **1b′** (10 mol%), and *n*-BuLi (2.0 equiv) in the above-mentioned solvent at 0 °C (entries 1 and 2) or at 23 °C (entries 3 and 4). [b]Determined by chiral HPLC.

Scheme 2. In Situ Generation of Lithium Binaphtholate and Lithium Acetylide

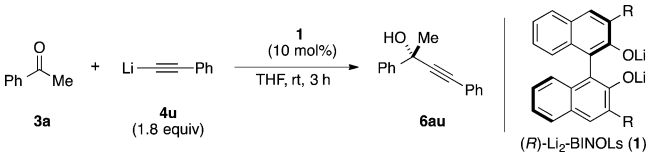


alcohol **6au** with good enantioselectivity (67% ee, Table 1, entry 4).

Screening of BINOLs for the Asymmetric Alkynylation of Ketones. We investigated the alkynylation of ketone **3a** with lithium acetylide **4u** using diverse BINOLs **1** because the alkynylations of ketones have not been well established compared to those of aldehydes (Table 2). The parent BINOL (R = H, **1a**) was ineffective (Table 2, entry 1). Introduction of bromo, methyl, or different substituents on the phenyl group did not improve the enantioselectivity. The best result was obtained with **1b** (R = Ph). Since no enantioselectivity was achieved by using O-methylated BINOL derivatives **7** and **8** (structures shown below Table 2), a bisphenol motif is absolutely essential for the asymmetric alkynylation (Table 2, entries 9 and 10). When the reaction was performed at −78 °C, both the product yield and enantioselectivity dramatically increased (Table 2, entry 11). We reported these reaction conditions (standard conditions: catalyst, **1b**; solvent, THF; reaction temperature, −78 °C) in our previous communication.[12] After further detailed investigation, we discovered that a slow addition of a solution of ketone **3a** over 1 h (slow addition procedure) improved the enantioselectivity to 96% ee (Table 2, entry 12). A further increase in the addition time did not improve the enantioselectivity (Table 2, entry 13). Even when the catalyst loading was reduced to 2 mol %, the product was obtained without loss of both yield and enantioselectivity (Table 2, entry 14).

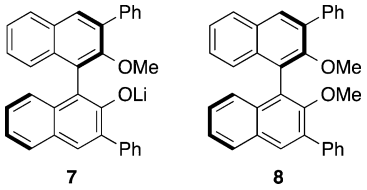
Asymmetric Alkynylation of Ketones with Alkynes. With the optimized reaction conditions and catalyst **1b**, we performed the asymmetric alkynylation of various ketones **3** (Table 3). The results obtained by using standard conditiosn[12]

Table 2. Screening of Catalysts[a]



	(*R*)-Li_2-BINOLs			
entry	**1**	R	yield (%)	ee[b] (%)
1	**1a**	H	90	2
2	**1b**	Ph	87	67
3	**1c**	Br	78	17
4	**1d**	Me	94	15
5	**1e**	4-tolyl	90	60
6	**1f**	3,5-xylyl	77	28
7	**1g**	4-FC_6H_4	81	63
8	**1h**	4-$MeOC_6H_4$	80	57
9	**7**	Ph	95	0
10	**8**	Ph	96	0
11[c]	**1b**	Ph	96	92
12[c,d]	**1b**	Ph	95	96
13[c,e]	**1b**	Ph	91	96
14[c,d,f]	**1b**	Ph	96	96

[a]The reaction was conducted by adding a THF solution of ketone **3a** over 1 min to a THF solution of **4u′** (2.0 equiv), (*R*)-BINOL **1′** (10 mol%), and *n*-BuLi (2.0 equiv) at rt. [b]Determined by chiral HPLC. [c]At −78 °C for 2 h. [d]A THF solution of ketone **3a** was added over 1 h. [e]A THF solution of ketone **3a** was added over 3 h. [f]2 mol % of **1b** was used.



(addition over 1 min) are also listed in Table 3 for comparison with those of the slow addition procedure (addition over 1 h). Ethyl ketone **3b** still afforded good enantioselectivity (Table 3, entry 2), whereas isopropyl ketone **3c** decreased the selectivity because of less enantiodifferentiation by ketone **3c** (Table 3, entry 3). Although *ortho*-substituted ketone **3d** slightly decreased the yield, high enantioselectivity was achieved in the reaction of tolylaldehydes **3d−f** irrespective of the substituent position (Table 3, entries 4−6). Aryl methyl ketones **3g−m** also afforded the corresponding tertiary propargylic alcohols in both high chemical and optical yields (Table 3, entries 7−13). In the reactions of ketones **3l** and **3m**, the slow addition procedure decreased the product yields (Table 3, entries 12 and 13). When the reactions were quenched with deuterium oxide, deuterated ketones **3l-dα** and **3m-dα** could be obtained. The observation indicated that the enolization of ketones was preferred over alkynylation because of low electrophilicity of the carbonyl groups (Figure 1).[13] Even the alkynylation of ketone **3n**, with a small steric difference between the carbonyl substituents, afforded good enantioselectivity (Table 3, entry 14). The alkynylation of aliphatic ketone **3o** was successful, affording good enantioselectivity (Table 3, entry 15). Notably, ketones bearing heteroaromatic rings afforded high yields and enantioselectivity because other metal catalysts were less selective (Table 3, entries 16−18). Propargylic alcohol **6qu**, which exhibits antifungal activity,

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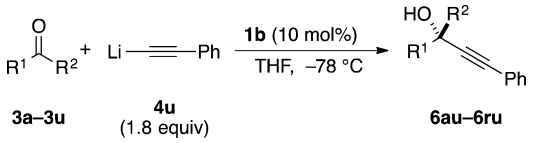
Table 3. Asymmetric Alkynylation of Ketones[a]



	ketone			standard conditions			slow addition procedure[b]	
entry	3	R^1	R^2	6	yield (%)	ee[c] (%)	yield (%)	ee[c] (%)
1	**3a**	Ph	Me	**6au**	96	93	95	96
2	**3b**	Ph	Et	**6bu**	93	73	95	89
3[d]	**3c**	Ph	^{i}Pr	**6cu**	99	7	95	8
4	**3d**	2-MeC_6H_4	Me	**6du**	53	87	66	91
5	**3e**	3-MeC_6H_4	Me	**6eu**	97	94	90	96
6	**3f**	4-MeC_6H_4	Me	**6fu**	93	88	94	96
7	**3g**	4-$MeOC_6H_4$	Me	**6gu**	95	92	92	95
8	**3h**	4-$CF_3C_6H_4$	Me	**6hu**	95	76	92	95
9	**3i**	4-FC_6H_4	Me	**6iu**	89	91	93	95
10	**3j**	4-BrC_6H_4	Me	**6ju**			94	94
11	**3k**	2-naphthyl	Me	**6ku**	94	85	93	93
12[d]	**3l**	1-naphthyl	Me	**6lu**	76	70	21	78
13[d]	**3m**	3,4,5-$(MeO)_3C_6H_2$	Me	**6mu**	90	97	21	98
14	**3n**	$PhCH_2CH_2$	Me	**6nu**	99	39	96	55
15	**3o**	^{i}Pr	Me	**6ou**	95	33	89	81
16	**3p**	2-thienyl	Me	**6pu**			92	95
17	**3q**	3-pyridyl	Me	**6qu**	96	87	96	94
18	**3r**	4-pyridyl	Me	**6ru**	90	71	90	92

[a]The reaction was conducted by adding a THF solution of ketone **3** to a THF solution of alkyne **4u′** (2.0 equiv), (*R*)-**1b′** (10 mol%), and *n*-BuLi (2.0 equiv) at −78 °C. [b]A THF solution of ketone **3** was added over 1 h. [c]Determined by chiral HPLC. [d]For 6 h.

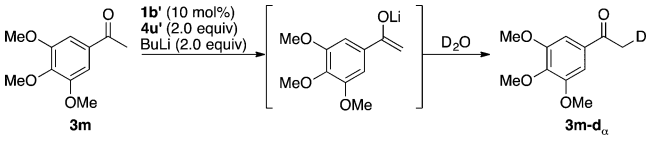


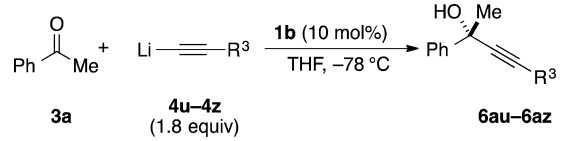
Figure 1. Enolization of **3m** with lithium acetylide.

could be readily synthesized.[14] The slow addition procedure was quite efficient for diverse substrates, affording the corresponding products with improved enantioselectivity.

The alkynylations of diverse alkynes with acetophenone (**3a**) are summarized in Table 4. *n*-Alkynes such as 1-hexyne (**4v**) and 1-decyne (**4w**) afforded the corresponding tertiary propargylic alcohols in high yields and with good enantioselectivities (Table 4, entries 2 and 3). In the reaction of cyclohexenylacetylene (**4x**), excellent selectivity was obtained (Table 4, entry 4). Alkynes containing an oxygen or a silicon atom also afforded the corresponding products with high enantioselectivity (Table 4, entries 5 and 6). In the reaction with alkyne **4z**, the slow addition procedure dramatically improved the enantioselectivity from 44% to 91% ee. This alkynylation method of ketones has a broad substrate scope in terms of both ketones and alkynes.

Determination of the Absolute Configuration of Chiral Tertiary Propargylic Alcohols. Several asymmetric alkynylations of ketones have been reported; however, the determination of the absolute configurations of tertiary propargylic alcohols has not been well established. This is because the volume of the optical rotation data of this series of compounds is small. To determine the absolute configurations, the derivatives of product **6** were prepared by following the procedure as shown in Scheme 3.[15] Propargylic alcohol **6bu** was reduced with Red-Al to afford the corresponding allylic alcohol, followed by the ozonolysis and oxidation to afford the corresponding ester **7b**. The optical rotation of **7b** was compared with the reported value in the literature,[16] and the absolute configuration of **4bu** was determined to be *S*. Following the same procedure, the absolute configurations of several products were determined, resulting in the *S* configuration in all the cases.[17]

Table 4. Asymmetric Alkynylation of Acetophenone with Alkynes[a]



	lithium acetylide			standard conditions		slow addition procedure[b]	
entry	4	R^3	6	yield (%)	ee[c] (%)	yield (%)	ee[c] (%)
1	**4u**	Ph	**6au**	96	93	95	96
2	**4v**	^{n}Bu	**6av**	89	87	95	90
3	**4w**	^{n}octyl	**6aw**	92	86	99	92
4	**4x**	cyclohexenyl	**6ax**	80	84	99	95
5	**4y**	$BnOCH_2$	**6ay**	97	86	99	87
6	**4z**	TMS	**6az**	88	44	93	91

[a]The reaction was conducted by adding a THF solution of ketone **3a** to a THF solution of alkyne **4′** (2.0 equiv), (*R*)-**1b′** (10 mol%), and *n*-BuLi (2.0 equiv) at −78 °C. [b]A THF solution of ketone **3** was added over 1 h. [c]Determined by chiral HPLC.

Asymmetric Alkynylation of Aldehydes with Alkynes. Because the slow addition procedure was quite efficient for the

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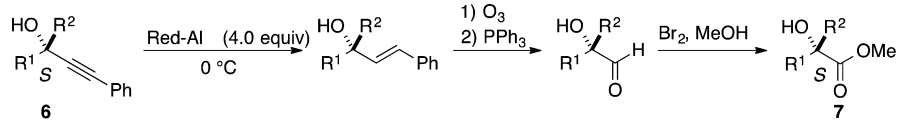
Scheme 3. Derivatization of 6

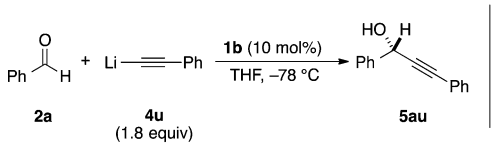


R^1 = Ph, R^2 = Et: **6bu**
R^1 = 4-$CH_3C_6H_4$, R^2 = Me: **6fu**
R^1 =4-$CF_3C_6H_4$, R^2 = Me: **6hu**
R^1 = 2-naphthyl, R^2 = Me: **6ku**
R^1 = $PhCH_2CH_2$, R^2 = Me: **6nu**

R^1 = Ph, R^2 = Et: (*S*)-**7b**
R^1 = 4-$CH_3C_6H_4$, R^2 = Me: (*S*)-**7f**
R^1 =4-CF_3-C_6H_4, R^2 = Me: (*S*)-**7h**
R^1 = 2-naphthyl, R^2 = Me: (*S*)-**7k**
R^1 = $PhCH_2CH_2$, R^2 = Me: (*S*)-**7n**

alkynylation of ketones, we applied this procedure to the asymmetric alkynylation of aldehydes (Table 5). When the

Table 5. Effect of Slow Addition Procedure for the Alkynylation of Benzaldehyde 2a[a]



entry	addition time	yield (%)	ee[b] (%)
1	1 min	96	49
2	10 min	97	75
3	1 h	91	74

[a]The reaction was conducted by adding a THF solution of aldehyde **2a** over the above-mentioned addition time to a THF solution of alkyne **4u**′ (2.0 equiv), (*R*)- **1b**′ (10 mol %), and *n*-BuLi (2.0 equiv) at −78 °C. [b]Determined by chiral HPLC.

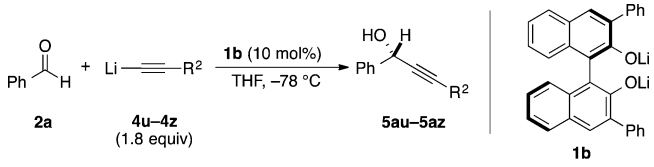
asymmetric alkynylation of aldehyde **2a** was performed with lithium acetylide **4u** at −78 °C, the standard conditions afforded the corresponding product with only 49% ee (Table 5, entry 1). The slow addition procedure dramatically improved the enantioselectivity (Table 5, entries 2 and 3), and the best result was obtained by the addition over 10 min (Table 5, entry 2).

The reactions of diverse alkynes **4** with benzaldehyde (**2a**) were conducted (Table 6). The reactions of 1-hexyne (**4v**) and 1-decyne (**4w**) afforded almost racemic products (Table 6, entries 2 and 3). Moderate enantioselectivity was observed in the reaction with 1-cyclohexenylacetylene (**4x**) (Table 6, entry 4). The enantioselectivities of 3-(benzyloxy)prop-1-yne (**4y**) and (trimethylsilyl)acetylene (**4z**) were moderate (Table 6, entries 5 and 6).

Next, we investigated the alkynylation of diverse aldehydes **2** (Table 7). The nucleophilicity of lithium acetylide severely affected the product selectivity. The enantioselectivity of aromatic aldehydes depends on the steric and electronic effects of the substituents on the phenyl groups (Table 7, entries 2−5). Although the aldehydes with electron-withdrawing groups decreased the enantioselectivity, the aldehydes with electron-donating groups afforded good to high enantioselectivity. The best enantioselectivity was achieved in the reaction with 3,4,5-trimethoxybenzaldehyde (Table 7, entry 5). Aliphatic aldehyde **2f** was less selective, affording moderate enantioselectivity (Table 7, entry 6).

Conclusion. The chiral lithium binaphtholate-catalyzed enantioselective alkynylation of ketones and aldehydes with lithium acetylides afforded the corresponding optically active tertiary propargylic alcohols with high enantioselectivity. In addition, we showed that the slow addition procedure efficiently improved the enantioselectivity. This procedure was useful for the alkynylation of carbonyl compounds with lithium acetylide without using other metals. The study paved the path to develop enantioselective reactions of organolithium reagents.

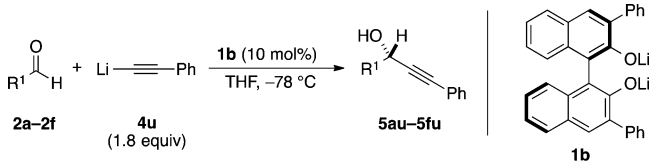
Table 6. Asymmetric Alkynylation of Aldehydes with Alkynes[a]



	lithium acetylide		secondary propargylic alcohol		
entry	4	R^2	5	yield (%)	ee[b] (%)
1	**4u**	Ph	**5au**	97	75
2	**4v**	^{n}Bu	**5av**	99	15
3	**4w**	^{n}octyl	**5aw**	94	21
4	**4x**	1-cyclohexenyl	**5ax**	92	61
5	**4y**	$BnOCH_2$	**5ay**	98	42
6	**4z**	TMS	**5az**	91	44

[a]The reaction was conducted by adding a THF solution of aldehyde **2a** over 10 min to a THF solution of an acetylene **4**′ (2.0 equiv), (*R*)-**1b**′ (10 mol%), and *n*-BuLi (2.0 equiv) at −78 °C. [b]Determined by chiral HPLC.

Table 7. Asymmetric Alkynylation of Aldehydes with Alkynes[a]



	aldehyde		secondary propargylic alcohol		
entry	2	R^1	5	yield (%)	ee[b] (%)
1	**2a**	Ph	**5au**	97	75
2	**2b**	4-$MeOC_6H_4$	**5bu**	99	75
3	**2c**	4-ClC_6H_4	**5cu**	98	71
4	**2d**	2-naphthyl	**5du**	96	65
5	**2e**	3,4,5-$(MeO)_3C_6H_2$	**5eu**	95	82
6	**2f**	^{c}hex	**5fu**	90	58

[a]The reaction was conducted by adding a THF solution of aldehyde **2a** over 10 min to a THF solution of an acetylene **4u**′ (2.0 equiv), (*R*)-**1b**′ (10 mol%), and *n*-BuLi (2.0 equiv) at −78 °C. [b]Determined by chiral HPLC.

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EXPERIMENTAL SECTION

Representative Procedure for Asymmetric Alkynylations of Ketones. Lithium acetylide **4u** and lithium binaphtholate **1b** were prepared by the addition of *n*-BuLi (1.65 M in hexane, 0.52 mL, 0.86 mmol) to the solution of (*R*)-3,3′-diphenyl-1,1′-binaphthalene-2,2′-diol (19 mg, 0.043 mmol) and phenylacetylene (0.10 mL, 0.86 mmol) in THF (1.0 mL) at −78 °C. To the resulting solution was added acetophenone (**3a**) (0.05 mL, 0.43 mmol) in THF (1.0 mL) over 1 h at the same temperature, and the resulting solution was stirred for an additional 3 h. After being quenched with saturated aq NH_4Cl, the reaction mixture was extracted with EtOAc. The organic layer was washed with saturated aq $NaHCO_3$ and saturated aq NaCl. After drying over Na_2SO_4, the solvent was removed under vacuum, and the residue was purified by silica gel column chromatography (hexane/CH_2Cl_2 = 1/1) to afford **6au** (90.2 mg, 95% yield) as an oil. The enantiomeric excess (ee) was determined to be 96% by chiral HPLC with Daicel Chiralcel OD-H column.

*(S)-(−)-2,4-Diphenylbut-3-yn-2-ol (**6au**).* The experimental data are in accordance with those reported in the previous literature.[15] 90.2 mg (95% yield). $[\alpha]^{30}_D$ −7.4 (*c* 1.3, $CHCl_3$) for 96% ee [lit. $[\alpha]^{22}_D$ −6.6 (*c* 1.0, $CHCl_3$) for 82% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.87 (s, 3H), 2.46 (s, 1H), 7.30−7.50 (m, 8H), 7.73−7.75 (d, 2H, *J* = 7.3 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.3, 70.4, 84.9, 92.4, 122.5, 125.0, 127.7, 128.29, 128.34, 128.5, 131.7, 145,6. HPLC: Daicel Chiralcel OD-H, hexane/isopropyl alcohol (IPA) = 19:1, 1.0 mL/min, 254 nm, t_R = 8.8 min (*R*), t_R = 10.9 min (*S*).

*(S)-(−)-1,3-Diphenylpent-1-yn-3-ol (**6bu**).* The experimental data are in accordance with those reported in the previous literature:[7c] 84.4 mg (95% yield). $[\alpha]^{30}_D$ −10.9 (*c* 3.3, $CHCl_3$) for 89% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.03 (t, 3H, *J* = 7.3 Hz), 1.95−2.13 (m, 2H), 2.45 (s, 1H), 7.30−7.40 (m, 6H), 7.48−7.51 (m, 2H), 7.68−7.77 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 9.2, 38.4, 74.3, 86.1, 91.3, 122.6, 125.6, 127.7, 128.2, 128.3, 128.5, 131.7, 144.5. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 49:1, 1.0 mL/min, 254 nm, t_R = 13.5 min (*R*), t_R = 17.0 min (*S*).

*(−)-4-Methyl-1,3-diphenylpent-1-yn-3-ol (**6cu**).* The experimental data are in accordance with those reported in the previous literature.[15] 79.0 mg (95% yield). $[\alpha]^{30}_D$ −1.8 (*c* 0.90, $CHCl_3$) for 8% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.89 (d, 3H, *J* = 7.2 Hz), 1.14 (d, 3H, *J* = 6.7 Hz), 2.14−2.23 (qq, 1H, *J* = 6.7, 7.2 Hz), 2.41 (s, 1H), 7.28−7.39 (m, 6H), 7.47−7.53 (m, 2H), 7.66−7.71 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 17.5, 18.1, 40.5, 77.5, 86.9, 90.3, 122.7, 126.2, 127.6, 127.9, 128.3, 128.4, 131.7, 143.9. HPLC: Daicel Chiralpak AD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 9.9 min (minor), t_R = 14.6 min (major).

*(−)-2-(2-Methylphenyl)-4-phenylbut-3-yn-2-ol (**6du**).* The experimental data are in accordance with those reported in the previous literature.[7c] 59.6 mg (66% yield). $[\alpha]^{30}_D$ −9.4 (*c* 1.4, $CHCl_3$) for 91% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.94 (s, 3H), 2.40 (s, 1H), 2.69 (s, 3H), 7.19−7.33 (m, 6H), 7.41−7.46 (m, 2H), 7.74−7.77 (m, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 21.3, 31.0, 70.0, 84.6, 92.8, 122.7, 125.0, 125.8, 127.7, 128.3, 128.4, 131.6, 132.3, 135.7, 142.3. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 9.6 min (minor), t_R = 10.7 min (major).

*(−)-2-(3-Methylphenyl)-4-phenylbut-3-yn-2-ol (**6eu**).* The experimental data are in accordance with those reported in the previous literature.[7c] 78.2 mg, (90% yield). $[\alpha]^{30}_D$ −5.6 (*c* 0.86, $CHCl_3$) for 96% ee. [lit. $[\alpha]^{20}_D$ +5.8 (*c* 1.21, $CHCl_3$) for 86% ee]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.86 (s, 3H), 2.39 (s, 3H), 2.45 (s, 1H), 7.12 (d, 1H, *J* = 7.3 Hz), 7.25−7.35 (m, 4H), 7.47−7.54 (m, 4H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 21.6, 33.3, 70.3, 84.8, 92.6, 122.1, 122.6, 125.6, 128.2, 128.3, 128.4, 128.5, 131.7, 138.0, 145.6. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 8.2 min (minor), t_R = 9.9 min (major).

*(S)-(−)-2-(4-Methylphenyl)-4-phenylbut-3-yn-2-ol (**6fu**).* The experimental data are in accordance with those reported in the previous literature.[7c] 83.4 mg (94% yield). $[\alpha]^{28}_D$ −5.8 (*c* 0.65, $CHCl_3$) for 96% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.86 (s, 3H), 2.36 (s, 3H), 2.41 (s, 1H), 7.19 (d, 2H, *J* = 8.2 Hz), 7.28−7.33 (m, 3H), 7.47−7.49 (m, 2H), 7.62 (d, 2H, *J* = 8.2 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 21.0, 33.2, 70.2, 84.8, 92.6, 122.6, 124.9, 128.3, 128.4, 129.0, 131.7, 137.5, 142.8. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 8.1 min (*R*), t_R = 10.9 min (*S*).

*(−)-2-(4-Methoxyphenyl)-4-phenylbut-3-yn-2-ol (**6gu**).* The experimental data are in accordance with those reported in the previous literature.[4h] 104.5 mg (92% yield). $[\alpha]^{30}_D$ −6.9 (*c* 1.3, $CHCl_3$) for 95% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.86 (s, 3H), 2.39 (s, 1H), 3.82 (s, 3H), 6.91 (m, 2H, *J* = 9.2 Hz), 7.32−7.35 (m, 3H), 7.47−7.49 (m, 2H), 7.64−7.67 (d, 2H, *J* = 9.2 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.2, 55.3, 70.1, 84.8, 92.6, 113.6, 122.6, 126.3, 128.3, 128.5, 131.7, 137.9, 159.2. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 12.4 min (minor), t_R = 19.8 min (major).

*(S)-(−)-2-[(4-Trifluoromethyl)phenyl]-4-phenylbut-3-yn-2-ol (**6hu**).* The experimental data are in accordance with those reported in the previous literature.[7c] 114.2 mg (92% yield). $[\alpha]^{16}_D$ −12.1 (*c* 0.65, $CHCl_3$) for 95% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.87 (s, 3H), 2.57 (s, 1H), 7.31−7.36 (m, 3H), 7.47−7.49 (m, 2H), 7.65 (d, 2H, *J* = 8.3 Hz), 7.85 (d, 2H, *J* = 8.3 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.5, 70.1, 85.5, 91.6, 122.1, 124.1 (q, *J* = 269 Hz), 125.3 (q, *J* = 39 Hz), 128.3, 128.8, 130.4 (q, *J* = 3 Hz), 131.7, 149.5. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm), t_R = 7.6 min (*R*), t_R = 9.0 min (*S*).

*(−)-2-(4-Fluorophenyl)-4-phenylbut-3-yn-2-ol (**6iu**).* The experimental data are in accordance with those reported in the previous literature.[4m] 93.4 mg (93% yield). $[\alpha]^{30}_D$ −8.3 (*c* 1.6, $CHCl_3$) for 95% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.85 (s, 3H), 2.48 (s, 1H), 7.04−7.08 (m, 2H), 7.31−7.35 (m, 3H), 7.47−7.49 (m, 2H), 7.68−7.71 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.5, 70.0, 85.1, 92.1, 115.1 (d, *J* = 21 Hz), 122.4, 126.8 (d, *J* = 7 Hz), 128.4, 128.6, 131.7, 141.5 (d, *J* = 4 Hz), 162.2 (d, *J* = 244 Hz). HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 8.3 min (minor), t_R = 10.4 min (major).

*(−)-2-(4-Bromophenyl)-4-phenyl-but-3-yn-2-ol (**6ju**).* The experimental data are in accordance with those reported in the previous literature.[18] 128.5 mg (94% yield). $[\alpha]^{29}_D$ −5.9 (*c* 0.88, $CHCl_3$) for 94% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.84 (s, 3H), 2.42 (s, 1H), 7.30−7.35 (m, 3H), 7.45−7.52 (m, 4H), 7.58−7.61 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.5, 70.0, 85.2, 91.8, 121.7, 122.2, 126.9, 128.3, 128.7, 131.4, 131.7, 144.8. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 9.3 min (minor), t_R = 11.4 min (major).

*(S)-(−)-2-(2-Naphthyl)-4-phenylbut-3-yn-2-ol (**6ku**).* The experimental data are in accordance with those reported in the previous literature.[4m] 109.1 mg (93% yield). $[\alpha]^{29}_D$ −16.5 (*c* 1.4, $CHCl_3$) for 93% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.95 (s, 3H), 2.58 (s, 1H), 7.31−7.35 (m, 3H), 7.46−7.52 (m, 4H), 7.78−7.88 (m, 4H), 8.18 (s, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.2, 70.5, 85.1, 92.4, 122.5, 123.4, 123.5, 126.1, 126.2, 127.6, 128.2, 128.3, 128.5, 131.8, 132.9, 133.0, 142.9. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 8.6 min (*R*), t_R = 11.1 min (*S*).

*(+)-2-(1-Naphthyl)-4-phenylbut-3-yn-2-ol (**6lu**).* The experimental data are in accordance with those reported in the previous literature.[4m] 27.0 mg (21% yield). $[\alpha]^{29}_D$ +17.8 (*c* 0.73, $CHCl_3$) for 78% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.15 (s, 3H), 2.67 (s, 1H), 7.24−7.29 (m, 3H), 7.42−7.55 (m, 5H), 7.83 (d, 1H, *J* = 8.2 Hz), 7.89 (d, 1H, *J* = 8.0 Hz), 7.98 (dd, 1H, *J* = 1.2, 7.3 Hz), 8.86 (d, 1H, *J* = 8.9 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 31.8, 70.4, 85.5, 93.2, 122.6, 122.9, 124.9, 125.4, 125.5, 126.3, 128.3, 128.4, 129.0, 129.2, 130.1, 131.6, 134.7, 140.0. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 12.5 min (minor), t_R = 15.8 min (major).

*(+)-4-Phenyl-2-(3,4,5-trimethoxyphenyl)but-3-yn-2-ol (**6mu**).* 37.0 mg (26% yield). $[\alpha]^{30}_D$ +7.0 (*c* 1.2, $CHCl_3$) for 98% ee. IR (neat): ν (cm^{-1}) 3431, 2935, 2835, 1593. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.87 (s, 3H), 2.50 (s, 1H), 3.86 (s, 3H), 3.90 (s, 6H), 6.98 (s, 2H), 7.31−7.35 (m, 3H), 7.46−7.48 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.3, 56.1, 60.8, 70.5, 84.9, 92.3, 102.3, 122.4, 128.4, 128.6, 131.6, 137.4, 141.4, 153.0. LRMS (FAB): *m*/*z* 335 $(M + Na)^+$, 312, 129, 77. HRMS: calcd for $C_{19}H_{20}O_4Na$ 335.1259, found

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335.1269. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 10.6 min (minor), t_R = 14.1 min (major).

*(S)-(+)-3-Methyl-1,5-diphenylpent-1-yn-3-ol (**6nu**).* The experimental data are in accordance with those reported in the previous literature.[4e] 80.3 mg (96% yield). $[\alpha]^{28}_D$ +7.4 (*c* 1.9, $CHCl_3$) for 55% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.63 (s, 3H), 2.01−2.10 (m, 3H), 2.91−2.95 (m, 2H), 7,18−7.32 (m, 8H), 7.43−7.46 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 30.1, 31.3, 45.4, 68.5, 83.9, 92.4, 122.6, 125.9, 128.27, 128.33, 128.4, 131.7, 141.9. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 11.5 min (*R*), t_R = 15.6 min (*S*).

*(+)-3,4-Dimethyl-1-phenylpent-1-yn-3-ol (**6ou**).* The experimental data are in accordance with those reported in the previous literature.[4e] 78.6 mg (81% yield). $[\alpha]^{30}_D$ +5.9 (*c* 0.98, $CHCl_3$) for 81% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.07 (d, 3H, *J* = 6.7 Hz), 1.11 (d, 3H, *J* = 6.7 Hz), 1.54 (s, 3H), 1.90 (qq, 1H, *J* = 6.7, 6.7 Hz), 2.02 (s, 1H), 7.28−7.31 (m, 3H), 7.40−7.44 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 17.5, 18.0, 27.2, 39.1, 72.1, 84.0, 92.0, 122.9, 128.17, 128.21, 131.6. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 6.0 min (minor), t_R = 8.2 min (major).

*(−)-2-(2-Thienyl)-3-phenylbut-3-yn-2-ol (**6pu**).* The experimental data are in accordance with those reported in the previous literature.[19] 98.3 mg (92% yield). $[\alpha]^{22}_D$ −7.7 (*c* 0.65, $CHCl_3$) for 95% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.99 (s, 3H), 2.66 (s, 1H), 6.96−6.98 (m, 1H), 7.25−7.35 (m, 5H), 7.47−7.50 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.1, 67.7, 84.3, 91.7, 122.3, 124.0, 125.1, 126.7, 128.3, 128.7, 131.8, 150.6. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 10.6 min (minor), t_R = 13.4 min (major).

*(−)-4-Phenyl-2-(3-pyridinyl)but-3-yn-2-ol (**6qu**).* The experimental data are in accordance with those reported in the previous literature.[20] 97.9 mg (96% yield). $[\alpha]^{33}_D$ −2.5 (*c* 0.89, $CHCl_3$) for 94% ee [lit. $[\alpha]^{24}_D$ −0.9 (*c* 1.0, $CHCl_3$) for 75% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.88 (s, 3H), 3.51 (s, 1H), 7.27−7.35 (m, 4H), 7.46−7.51 (m, 2H), 8.01−8.03 (m, 1H), 8.54−8.56 (m, 1H), 8.97 (m, 1H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.4, 68.7, 85.6, 91.4, 122.1, 123.1, 128.4, 128.7, 131.7, 132.9, 141.3, 147.0, 148.8. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 9.9 min (minor), t_R = 12.3 min (major).

*(−)-4-Phenyl-2-(4-pyridinyl)but-3-yn-2-ol (**6ru**).* The experimental data are in accordance with those reported in the previous literature.[21] 85.7 mg (90% yield). $[\alpha]^{30}_D$ −4.3 (*c* 0.52, $CHCl_3$) for 92% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.82 (s, 3H), 4.01−6.21 (brs, 1H), 7.27−7.35 (m, 3H), 7.41−7.44 (m, 2H), 7.62 (d, 2H, *J* = 6.1 Hz), 8.59 (d, 2H, *J* = 6.1 Hz). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.1, 68.9, 85.0, 91.6, 120.2, 122.1, 128.3, 128.6, 131.6, 149.2, 155.6. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 4:1, 1.0 mL/min, 254 nm, t_R = 7.2 min (minor), t_R = 11.0 min (major).

*2-Phenyloct-3-yn-2-ol (**6av**).* The experimental data are in accordance with those reported in the previous literature.[22] 82.3 mg (95% yield). $[\alpha]^{30}_D$ −0.3 (*c* 1.2, $CHCl_3$) for 90% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.93 (t, 3H, *J* = 7.3 Hz), 1.39−1.58 (m, 4H), 1.74 (s, 3H), 2.25−2.34 (m, 3H), 7.26−7.37 (m, 3H), 7.65−7.67 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 13.6, 18.4, 22.0, 30.7, 33.6, 70.1, 83.7, 85.7, 125.0, 127.5, 128.2, 146.2. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 200:1, 1.0 mL/min, 254 nm: t_R = 20.7 min (minor), t_R = 22.5 min (major).

*(−)-2-Phenyldodec-3-yn-2-ol (**6aw**).* The experimental data are in accordance with those reported in the previous literature.[23] 110.1 mg (99% yield). $[\alpha]^{32}_D$ −2.3 (*c* 0.95, $CHCl_3$) for 92% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, 3H, *J* = 6.7 Hz), 1.28−1.42 (m, 10H), 1.51−1.58 (m, 2H), 1.74 (s, 3H), 2.25−2.29 (m, 3H), 7.25−7.39 (m, 3H), 7.64−7.67 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 14.1, 18.7, 22.7, 28.6, 28.9, 29.1, 29.2, 31.8, 33.5, 70.1, 83.7, 85.8, 125.0, 127.5, 128.2, 146.2. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 99:1, 1.0 mL/min, 254 nm, t_R = 12.3 min (minor), t_R = 13.3 min (major).

*(−)-4-(1-Cyclohexenyl)-2-phenylbut-3-yn-2-ol (**6ax**).* The experimental data are in accordance with those reported in the previous literature.[19] 101.2 mg (99% yield). $[\alpha]^{25}_D$ −2.0 (*c* 1.3, $CHCl_3$) for 95% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.56−1.68 (m, 4H), 1.77 (s, 3H), 2.07−2.17 (m, 4H), 2.34 (s, 1H), 6.16 (t, 1H, *J* = 1.9 Hz), 7.25−7.39 (m, 3H), 7.65−7.67 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 21.4, 22.2, 25.6, 29.2, 33.4, 70.3, 86.7, 89.8, 120.1, 125.0, 127.5, 128.2, 135.4, 146.0. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 99:1, 1.0 mL/min, 254 nm, t_R = 16.1 min (minor), t_R = 17.5 min (major).

*(−)-1-(Benzyloxy)-4-phenylpent-2-yn-4-ol (**6ay**).* The experimental data are in accordance with those reported in the previous literature.[24] 115.0 mg (99% yield). $[\alpha]^{31}_D$ −4.5 (*c* 2.0, $CHCl_3$) for 87% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.76 (s, 3H), 2.51 (s, 1H), 4.23 (s, 2H), 4.61 (s, 2H), 7.24−7.36 (m, 8H), 7.63−7.65 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ 33.1, 57.4, 69.9, 71.7, 80.8, 90.0, 124.8, 127.7, 127.9, 128.1, 128.3, 128.4, 137.3, 145.3. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 14.2 min (minor), t_R = 16.0 min (major).

*(+)-2-Phenyl-4-(trimethylsilyl)but-3-yn-2-ol (**6az**).* The experimental data are in accordance with those reported in the previous literature.[25] 88.7 mg (91% yield). $[\alpha]^{28}_D$ +6.1 (*c* 1.5, $CHCl_3$) for 91% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.21 (s, 9H), 1.76 (s, 3H), 2.33 (s, 1H), 7.27−7.31 (m, 1H), 7.34−7.38 (m, 2H), 7.64−7.66 (m, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125 MHz): δ −0.1, 33.3, 70.2, 89.3, 108.7, 124.9, 127.7, 128.3, 145.4. HPLC: Daicel Chiralpak AS-H, hexane/IPA = 99:1, 0.5 mL/min, 254 nm, t_R = 24.0 min (minor), t_R = 26.2 min (major).

Representative Procedure for Preparation of Esters 7a. Reduction of alkynes to alkenes: A solution of Red-Al in toluene (65%, 4.0 equiv) was added to a solution of propargyl alcohol **6bu** in anhydrous Et_2O at 0 °C via a syringe. The reaction mixture was allowed to warm slowly to room temperature and stirred for 4 h. Then, the mixture was cooled to 0 °C and quenched by dropwise addition of MeOH. The resulting solution was allowed to warm to rt and diluted with EtOAc. The solution was washed with saturated aq Rochelle's salt (sodium potassium tartrate), and the organic layer was dried over $MgSO_4$. After filtration and concentration, the resulting yellowish oil was purified by column chromatography (eluent: hexane/EtOAc = 8:1) to afford the corresponding alkene.

Ozonolysis of alkenes to aldehydes: Ozone was bubbled into a solution of the alkene in CH_2Cl_2 at −78 °C until a blue color persisted. Oxygen was then passed through the solution to remove the ozone, and then triphenylphosphine (1 equiv) was added at −78 °C. The resulting mixture was stirred for 1 h at rt. The mixture was concentrated under reduced pressure to afford an oil, which was purified by column chromatography (eluent: hexane/EtOAc = 6:1) to afford the corresponding aldehyde as an oil.

Oxidation of aldehyde to ester: $NaHCO_3$ (33 equiv) was added to a solution of the aldehyde in MeOH/water (9:1 v/v), followed by the addition of bromine (7.5 equiv) over 30 min under vigorous stirring at rt. After the solution was stirred for 2 h, the excess bromine was decomposed with $Na_2S_2O_3$. The resulting solution was filtered, and the filtrate was extracted with EtOAc. The organic layer was washed with brine and dried over Na_2SO_4. After concentration in vacuo, the crude product obtained was purified by column chromatography (eluent: hexane/CH_2Cl_2 = 3:2 to 1:3) to afford **7b** (38 yield from **6bu**) as a colorless oil.

*(S)-(+)-Methyl 2-hydroxy-2-phenylbutanoate (**7b**).* The experimental data are in accordance with those reported in the previous literature.[16] 38% yield from **6bu**. $[\alpha]^{24}_D$ +21.5 (*c* 0.50, $CHCl_3$) for 71% ee [lit. $[\alpha]_D^{25}$ +34.1 (*c* 0.49, $CHCl_3$) for 83% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.92 (t, 3H, *J* = 7.2 Hz), 1.99−2.12 (m, 1H), 2.19−2.28 (m, 2H), 3.72 (s, 1H), 3.78 (s, 3H), 7.26−7.37 (m, 3H), 7.59 (d, 2H, *J* = 8.2 Hz). HPLC: Daicel Chiralpak AD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm: t_R = 7.8 min (*S*), t_R = 8.5 min (*R*).

*(S)-(+)-Methyl 2-hydroxy-2-(4-methylphenyl)propanoate. (**7f**).* The experimental data are in accordance with those reported in the previous literature.[17] 11% yield from **6fu**. $[\alpha]^{24}_D$ +25.3 (*c* 0.16, $CHCl_3$) for 81% ee [lit. $[\alpha]^{25}_D$ +54 (*c* 1.6, $CHCl_3$) for 85% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.77 (s, 3H), 2.34 (s, 3H) 3.68 (s, 1H), 3.77 (s, 3H), 7.16 (d, 2H, *J* = 8.2 Hz), 7.42 (d, 2H, *J* = 8.2 Hz). HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 0.5 mL/min, 254 nm, t_R = 15.0 min (*S*), t_R = 18.3 min (*R*).

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*(S)-(+)-Methyl 2-Hydroxy-2-[4-(trifluoromethyl)phenyl]-propanoate (**7h**).* The experimental data are in accordance with those reported in the previous literature.[17] 21% yield from **6hu**. $[\alpha]^{24}_{D}$ +28.9 (*c* 0.36, $CHCl_3$) for 71% ee [lit. $[\alpha]^{24}_{D}$ +6.1 (*c* 1.8, $CHCl_3$) for 16% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.80 (s, 3H), 3.80 (s, 3H), 3.82 (s, 1H), 7.60−7.62 (m, 2H), 7.69−7.71 (m, 2H). HPLC: Daicel Chiralcel OD-H, hexane/IPA = 49:1, 0.5 mL/min, 254 nm, t_R = 16.5 min (*R*), t_R = 17.8 min (*S*).

*(S)-(+)-Methyl 2-Hydroxy-2-(2-naphthyl)propanoate. (**7k**).* The experimental data are in accordance with those reported in the previous literature.[17] 31% yield from **6ku**. $[\alpha]^{18}_{D}$ +43.4 (*c* 0.90, $CHCl_3$) for 88% ee [lit. $[\alpha]^{26}_{D}$ +45 (*c* 1.7, $CHCl_3$) for 82% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.89 (s, 3H), 3.79 (s, 3H), 3.86 (s, 1H), 7.46−7.51 (m, 2H), 7.64 (dd, 1H, *J* = 1.8, 8.7 Hz), 7.81−7.87 (m, 3H), 8.01−8.07 (m, 1H). HPLC: Daicel Chiralcel OJ-H, hexane/IPA = 9:1, 0.5 mL/min, 254 nm, t_R = 52.2 min (*S*), t_R = 67.3 min (*R*).

*(S)-(+)-Methyl 2-Hydroxy-2-methyl-4-phenylbutanoate. (**7n**).* The experimental data are in accordance with those reported in the previous literature.[17] 59% yield from **6nu**. $[\alpha]^{25}_{D}$ +17.7 (*c* 1.5, $CHCl_3$) for 39% ee [lit. $[\alpha]^{25}_{D}$ +7.2 (*c* 1.5, $CHCl_3$) for 19% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.45 (s, 3H), 1.94−2.10 (m, 2H), 2.42−2.50 (m, 1H), 2.75−2.83 (m, 1H), 3.25 (s, 1H), 3.73 (s, 3H), 7.15−7.19 (m, 3H), 7.25−7.30 (m, 2H). HPLC: Daicel Chiralcel OJ-H, hexane/IPA = 49:1, 0.5 mL/min, 254 nm, t_R = 25.8 min (*R*), t_R = 27.1 min (*S*).

Representative Procedure for Asymmetric Alkynylations of Aldehydes. Lithium acetylide **4u** and lithium binaphtholate **1b** were prepared by the addition of *n*-BuLi (1.65 M in hexane, 0.59 mL, 0.98 mmol) to the solution of (*R*)-3,3′-diphenyl-1,1′-binaphthalene-2,2′-diol (22 mg, 0.049 mmol) and phenylacetylene (0.11 mL, 0.98 mmol) in THF (1.0 mL) at −78 °C. A solution of benzaldehyde **2a** (0.050 mL, 0.49 mmol) in THF (1.0 mL) was added to the reaction mixture over 10 min at the same temperature and stirred for an additional 1 h. After quenching with saturated aq NH_4Cl, the resulting solution was extracted with EtOAc. The organic layer was washed with saturated aq $NaHCO_3$ and brine. After drying over Na_2SO_4, the solvent was removed under vacuum, and the residue was purified by silica gel column chromatography (hexane/CH_2Cl_2 = 1:1 v/v), affording **5au** (99.2 mg, 97%) as an oil. The ee was determined to be 75% by chiral HPLC with Daicel Chiralcel OD-H column.

*(S)-1,3-Diphenylprop-2-yn-1-ol (**5au**).* The experimental data are in accordance with those reported in the previous literature.[26] 99.2 mg (97% yield). $[\alpha]^{19}_{D}$ −1.8 (*c* 2.0, $CHCl_3$) for 75% ee [lit. $[\alpha]^{27}_{D}$ −2.4 (*c* 1.2, $CHCl_3$) for 86% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.29 (d, 1H, *J* = 6.1 Hz), 5.69 (d, 1H, *J* = 6.1 Hz), 7.28−7.48 (m, 8H), 7.61 (d, 2H, *J* = 7.3 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 65.1, 86.7, 88.7, 122.4, 126.7, 128.3, 128.4, 128.6, 128.7, 131.7, 140.6. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 14.5 min (*R*), t_R = 23.6 min (*S*).

*(S)-(−)-1-Phenylhept-2-yn-1-ol (**5av**).* The experimental data are in accordance with those reported in the previous literature.[26] 91.3 mg (99% yield). $[\alpha]^{24}_{D}$ −2.5 (*c* 1.0, $CHCl_3$) for 15% ee [lit. $[\alpha]^{25}_{D}$ −18.1 (*c* 1.3, $CHCl_3$) for 75% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.92 (t, 3H, *J* = 7.3 Hz), 1.40−1.57 (m, 4H), 2.06 (d, 1H, *J* = 6.1 Hz), 2.26−2.31 (m, 2H), 5.45 (d, 1H, *J* = 6.1 Hz), 7.30−7.40 (m, 3H), 7.55 (d, 2H, *J* = 7.0 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 13.7, 18.5, 22.0, 30.6, 64.9, 79.9, 87.7, 126.6, 128.2, 128.5, 141.3. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 8.9 min (*S*), t_R = 14.1 min (*R*).

*(−)-1-Phenylundec-2-yn-1-ol (**5aw**).* The experimental data are in accordance with those reported in the previous literature.[27] 112.2 mg (94% yield). $[\alpha]^{33}_{D}$ −2.5 (*c* 0.81, $CHCl_3$) for 21% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.88 (t, 3H, *J* = 6.7 Hz), 1.23−1.58 (m, 12H), 2.07 (d, 1H, *J* = 6.1 Hz), 2.24−2.29 (m, 2H), 5.44 (d, 1H, *J* = 6.1 Hz), 7.30−7.39 (m, 3H), 7.54 (d, 2H, *J* = 7.0 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 14.1, 18.8, 22.7, 28.6, 28.9, 29.1, 29.2, 31.8, 64.9, 79.9, 87.8, 126.6, 128.1, 128.5, 141.3. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 7.2 min (major), t_R = 11.3 min (minor).

*(S)-(−)-3-(1-Cyclohexenyl)-1-phenylprop-2-yn-1-ol (**5ax**).* The experimental data are in accordance with those reported in the previous literature.[8b] 96.0 mg (61% yield). $[\alpha]^{24}_{D}$ −2.8 (*c* 1.1, $CHCl_3$) for 61% ee [lit. $[\alpha]^{15}_{D}$ +6.7 (*c* 1.31, $CHCl_3$) for 95% ee, (*R*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.55−1.67 (m, 4H), 2.09−2.15 (m, 5H), 5.57 (d, 1H, *J* = 6.4 Hz), 6.15−6.17 (m, 1H), 7.30−7.40 (m, 3H), 7.55−7.57 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 21.4, 22.2, 25.6, 29.0, 65.0, 86.0, 88.6, 120.0, 126.7, 128.2, 128.5, 135.7, 141.0. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 11.9 min (major), t_R = 16.9 min (minor).

*(−)-4-(Benzyloxy)-1-phenylbut-2-yn-1-ol (**5ay**).* The experimental data are in accordance with those reported in the previous literature.[28] 121.9 mg (98% yield). $[\alpha]^{25}_{D}$ −4.8 (*c* 0.15, $CHCl_3$) for 42% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.23 (d, 1H, *J* = 5.8 Hz), 4.26 (s, 2H), 4.60 (s, 2H), 5.53 (d, 1H, *J* = 5.8 Hz), 7.28−7.41 (m, 8H), 7.54 (d, 2H, *J* = 7.3 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 57.4, 64.6, 71.8, 82.7, 86.3, 126.6, 127.9, 128.1, 128.2, 128.4, 128.6, 137.3, 140.4. HPLC: Daicel Chiralpak AD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 14.2 min (major), t_R = 16.3 min (minor).

*(S)-(−)-1-Phenyl-3-(trimethylsilyl)but-2-yn-1-ol (**5az**).* The experimental data are in accordance with those reported in the previous literature.[29] 91.3 mg (91% yield). $[\alpha]^{25}_{D}$ −11.6 (*c* 0.13, $CHCl_3$) for 44% ee [lit. $[\alpha]^{25}_{D}$ +11.2 (*c* 0.58, $CHCl_3$) for 52% ee, (*R*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 0.21 (s, 9H), 2.18 (d, 1H, *J* = 6.4 Hz), 5.46 (d, 1H, *J* = 6.4 Hz), 7.31−7.41 (m, 3H), 7.53−7.56 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ −0.2, 65.0, 91.6, 104.9, 126.7, 128.3, 128.6, 140.3. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 19:1, 1.0 mL/min, 254 nm, t_R = 4.6 min (*S*), t_R = 6.3 min (*R*).

*(S)-(−)-1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-ol (**5bu**).* The experimental data are in accordance with those reported in the previous literature.[26] 97.7 mg (99% yield). $[\alpha]^{24}_{D}$ −8.8 (*c* 1.2, $CHCl_3$) for 75% ee [lit. $[\alpha]^{27}_{D}$ −4.2 (*c* 1.7, $CHCl_3$) for 80% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.21 (d, 1H, *J* = 6.1 Hz), 3.83 (s, 3H), 5.64 (d, 1H, *J* = 6.1 Hz), 6.91−6.94 (m, 2H), 7.28−7.32 (m, 3H), 7.45−7.48 (m, 2H), 7.52−7.56 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 55.3, 64.8, 86.5, 88.9, 114.0, 122.5, 128.2, 128.3, 128.6, 131.7, 133.0, 159.8. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 4:1, 1.0 mL/min, 254 nm, t_R = 8.6 min (*R*), t_R = 13.6 min (*S*).

*(S)-(−)-1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-ol (**5cu**).* The experimental data are in accordance with those reported in the previous literature.[26] 116.4 mg (98% yield). $[\alpha]^{22}_{D}$ −5.9 (*c* 0.98, $CHCl_3$) for 71% ee [lit. $[\alpha]^{27}_{D}$ −7.9 (*c* 1.4, $CHCl_3$) for 84% ee, (*S*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.33 (d, 1H, *J* = 6.1 Hz), 5.66 (d, 1H, *J* = 6.1 Hz), 7.29−7.58 (m, 9H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 64.4, 87.0, 88.2, 122.1, 128.1, 128.3, 128.8, 131.7, 134.2, 139.1. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 9.5 min (*R*), t_R = 28.3 min (*S*).

*(S)-(+)-1-(2-Naphthyl)-3-phenylprop-2-yn-1-ol (**5du**).* The experimental data are in accordance with those reported in the previous literature.[30] 124.3 mg (98% yield). $[\alpha]^{18}_{D}$ +7.0 (*c* 1.6, $CHCl_3$), 65% ee [lit. $[\alpha]^{27}_{D}$ −7.8 (*c* 0.5, $CHCl_3$) for 87% ee, (*R*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): 2.35 (d, 1H, *J* = 6.1 Hz), 5.86 (d, 1H, *J* = 6.1 Hz), 7.32−7.33 (m, 3H), 7.48−7.51 (m, 4H), 7.71−7.73 (m, 1H), 7.84−7.89 (m, 3H), 8.04 (s, 1H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 65.3, 87.0, 88.6, 122.4, 124.6, 125.5, 126.3, 127.7, 128.2, 128.3, 128.61, 128.64, 131.8, 133.2, 133.3, 138.0. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 4:1, 1.0 mL/min, 254 nm, t_R = 9.6 min (*R*), t_R = 23.5 min (*S*).

*(−)-3-Phenyl-1-(3,4,5-trimethoxyphenyl)prop-2-yn-1-ol (**5eu**).* The experimental data are in accordance with those reported in the previous literature.[31] 139.4 mg (95% yield). $[\alpha]^{19}_{D}$ −6.1 (*c* 1.3, $CHCl_3$) for 82% ee. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.26 (d, 1H, *J* = 6.1 Hz), 3.86 (s, 3H), 3.91 (s, 6H), 5.64 (d, 1H, *J* = 6.1 Hz), 6.87 (s, 2H), 7.33−7.36 (m, 3H), 7.47−7.49 (m, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 56.2, 60.9, 65.3, 86.7, 88.5, 103.8, 128.4, 128.7, 131.7, 136.2, 153.4. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 2:1, 1.0 mL/min, 254 nm, t_R = 7.0 min (minor), t_R = 15.9 min (major).

*(S)-(+)-1-Cyclohexyl-3-phenylprop-2-yn-1-ol (**5fu**).* The experimental data are in accordance with those reported in the previous literature.[8b] 79.6 mg (90% yield). $[\alpha]^{19}_{D}$ +6.9 (*c* 1.2, $CHCl_3$) for 58% ee [lit. $[\alpha]^{25}_{D}$ −11.4 (*c* 3.17, $CHCl_3$) for 97% ee, (*R*)]. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.08−1.32 (m, 5H), 1.60−1.99 (m, 7H), 4.38 (t, 1H, *J* = 5.8 Hz), 7.28−7.32 (m, 3H), 7.41−7.47 (m, 2H). ^{13}C{^{1}H}

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NMR ($CDCl_3$, 125 MHz): δ 25.9, 26.4, 28.2, 28.7, 44.3, 67.7, 85.7, 89.2, 122.8, 128.27, 128.32, 131.7. HPLC: Daicel Chiralcel OD-H, hexane/IPA = 9:1, 1.0 mL/min, 254 nm, t_R = 5.9 min (*R*), t_R = 10.8 min (*S*).

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H and ^{13}C NMR spectra and HPLC profiles. This material is available free of charge via the Internet at http://pubs.acs.org/.

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Notes

The authors declare no competing financial interest.

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