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Enantioselective Alkyne Addition to Aliphatic, Aromatic, and Vinyl Aldehydes Using Zn, ^{i}PrI, H_8BINOL, and $Ti(O^{i}Pr)_4$

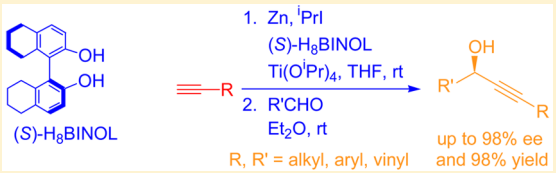
Wen-Cai Huang,[†,‡] Winnie Liu,[‡] Xue-Dan Wu,[‡] Jun Ying,[‡] and Lin Pu*[,‡]

[†]Department of Pharmaceutical and Bioengineering, School of Chemical Engineering, Sichuan University, Chengdu, China 610065

[‡]Department of Chemistry, University of Virginia, Charlottesville, Virginia 22904-4319, United States

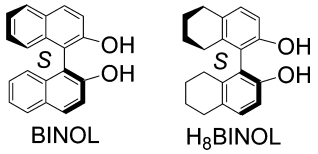
Supporting Information

ABSTRACT: A new catalytic system based on the readily available Zn, ^{i}PrI, H_8BINOL, and $Ti(O^{i}Pr)_4$ has been developed which avoids the use of pyrophoric $ZnEt_2$. It can effectively catalyze the reaction of various terminal alkynes with aromatic, aliphatic, and vinyl aldehydes to generate chiral propargylic alcohols at room temperature with up to 98% yield and 98% enantiomeric excess. This new system signifciantly expands the substrate scope of the previously reported system using Zn, EtI, BINOL, and $Ti(O^{i}Pr)_4$.



INTRODUCTION

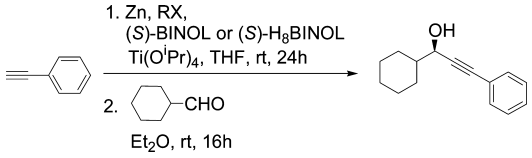
Over the past two decades, great progress has been made in the catalytic asymmetric alkyne addition to aldehydes to generate chiral propargylic alcohols, and a number of highly enantioselective catalysts have been developed.[1,2] Among these is the catalyst system of 1,1′-bi-2-naphthol (BINOL) in combination with $ZnEt_2$, $Ti(O^{i}Pr)_4$, and dicyclohexylamine developed in our laboratory which has exhibited high enantioselectivity and broad substrate scope.[3] Although this catalyst system is useful in the organic laboratory, because $ZnEt_2$ is spontaneously combustible upon exposure to air, its use presents important safety issues in transportation, storage, and operation when applied in large-scale industrial production. Recently, we discovered that using the easily manageable and inexpensive zinc powder in combination with EtI can replace $ZnEt_2$ in the presence of BINOL and $Ti(O^{i}Pr)_4$ to carry out the enantioselective alkyne addition to aromatic aldehydes with 90−96% enantiomeric excess (ee).[4] However, when this BINOL-based catalyst system is applied to the alkyne addition to aliphatic aldehydes, the enantioselectivity is much lower (*vide infra*). It would be highly desirable if this catalytic process could be applied to the reaction of other substrates such as aliphatic and vinyl aldehydes. Herein, we report our discovery that when octahydroBINOL (H_8BINOL) and ^{i}PrI are used in combination with Zn and $Ti(O^{i}Pr)_4$, it can promote the reaction of various alkynes with aliphatic, aromatic, and vinyl aldehydes under very mild conditions with excellent enantioselectivity.



RESULTS AND DISCUSSION

To explore the conditions for the alkyne addition to aliphatic aldehydes, we studied the reaction of phenylacetylene with cyclohexanecarboxaldehyde (Scheme 1). The reaction was

Scheme 1. Asymmetric Reaction of Phenylacetylene with Cyclohexanecarboxaldehyde



conducted at room temperature in two steps by first mixing Zn, an alkyl halide, a chiral ligand, and $Ti(O^{i}Pr)_4$ in THF and then adding an aldehyde and diethyl ether. We first tested the use of BINOL, $Ti(O^{i}Pr)_4$, and Zn in the presence of various alkyl halides, and the results are summarized in Table 1. As shown in entry 1, in the presence of Zn and EtI, the propargylic alcohol product was obtained in high yield (92%) but with only 69% ee. When a variety of other alkyl halides, including MeI, ^{i}PrI, benzyl bromide, allyl bromide, and 2-methylallyl bromide, were used, the enantioselectivities were found to be in the range of 49−77% ee (Table 1, entries 2−11). In entries 9−11, CuI was added to promote the reaction of the terminal alkynes. Although there was some improvement in enantioselectivity, it still did not meet the expectation.

H_8BINOL is a readily accessible chiral compound which has found applications in many asymmetric processes.[5] It can be easily prepared from the partial hydrogenation of BINOL and is also commercially available. To improve the enantioselectivity for the asymmetric alkyne addition to the aliphatic aldehyde, we

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Table 1. Conditions for the Reaction of Phenylacetylene with Cyclohexanecarboxaldehyde in the Presence of (*S*)-BINOL[a]

entry	chiral ligand[b]	Zn (equiv)	RX (equiv)	alkyne (equiv)	isolated yield (%)	ee (%)
1	(*S*)-BINOL	6	EtI, 12	4	92	69
2	(*S*)-BINOL	6	MeI, 12	4	79	77
3	(*S*)-BINOL	6	^{i}PrI, 12	4	81	71
4	(*S*)-BINOL	6	BnBr, 6	4	73	71
5	(*S*)-BINOL	6	2-Me-allyl-Br, 6	4	90	51
6	(*S*)-BINOL	6	allyl-Br, 6	4	93	77
7	(*S*)-BINOL	10	allyl-Br, 10	9	86	48
8	(*S*)-BINOL	3	allyl-Br, 3	2	81	49
9[c]	(*S*)-BINOL	6	EtI, 12	4	95	77
10[c]	(*S*)-BINOL	6	BnBr, 6	4	83	74
11[c]	(*S*)-BINOL	6	allyl-Br, 6	4	95	49

[a]THF (1 mL) was used in the first step, and diethyl ether (10 mL) was used in the second step. [b]0.4 equiv of ligand was used. [c]0.1 equiv of CuI was used as additive.

tested the use of (*S*)-H_8BINOL in place of (*S*)-BINOL for the reaction of phenylacetylene with cyclohexanecarboxaldehyde. The results are summarized in Table 2. As shown in entry 1, in

Table 2. Conditions for the Reaction of Phenylacetylene with Cyclohexanecarboxaldehyde in the Presence of (*S*)-H_8BINOL[a]

entry	chiral ligand[b]	Zn (equiv)	RX (equiv)	alkyne (equiv)	isolated yield (%)	ee (%)
1	(*S*)-H_8BINOL	6	EtI, 12	4	93	84
2	(*S*)-H_8BINOL	6	BnBr, 6	4	92	74
3	(*S*)-H_8BINOL	6	allyl-Br, 6	4	93	64
4	(*S*)-H_8BINOL	6	CH_3I, 12	4	54	63
5	(*S*)-H_8BINOL	6	^{i}PrI, 12	4	86	92
6	**(*S*)-H_8BINOL**	**6**	**^{i}PrI, 8**	**4**	**98**	**92**
7	(*S*)-H_8BINOL	4	^{i}PrI, 6	3	86	88
8[c]	(*S*)-H_8BINOL	6	^{i}PrI, 8	4	98	90
9[d]	(*S*)-H_8BINOL	6	^{i}PrI, 8	4	95	89

[a]THF (1 mL) was used in the first step, and diethyl ether (10 mL) was used in the second step. [b]0.4 equiv of ligand was used. [c]Reaction time was 16 h + 8 h. [d]Reaction time was 8 h + 16 h.

the presence of (*S*)-H_8BINOL, Zn, EtI, and Ti(O^{i}Pr)$_4$, the reaction of phenylacetylene with cyclohexanecarboxaldehyde gave high yield (93%) and significantly improved enantioselectivity (84% ee). Encouraged by this result, we explored the use of other alkyl halides for this reaction. Although alkyl halides such as MeI, benzyl bromide, and allyl bromide were found to give lower enantioselectivity than EtI (entries 2–4), we were delighted to find that when ^{i}PrI was used in place of EtI, up to 92% ee was achieved for the reaction (entry 5). When the amount of ^{i}PrI was reduced from 12 equiv to 8 equiv, the yield was increased to 98% while the high enantioselectivity was maintained (entry 6). Further decreasing the amount of the reagents led to reduced yield and enantioselectivity (entry 7). Shortening the reaction time gave slightly lower enantioselectivity (entries 8 and 9). Thus, we have identified the conditions in entry 6 as the optimized conditions.

We have applied the conditions in entry 6 of Table 2 to the asymmetric reaction of phenylacetylene with other aliphatic aldehydes. The results of these reactions and the structures of the products are shown in Figure 1. These results demonstrate that the addition of the alkyne to both secondary and primary alkyl aldehydes in the presence of the new H_8BINOL-Zn-^{i}PrI-Ti(O^{i}Pr)$_4$ catalyst system gave excellent enantioselectivities

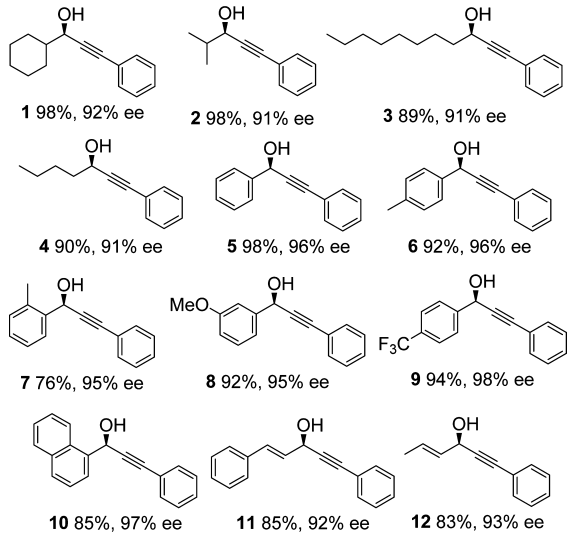

Figure 1. Products for the reaction of phenylacetylene with a variety of aldehydes in the presence of Zn, ^{i}PrI, (*S*)-H_8BINOL, and Ti(O^{i}Pr)$_4$.

(91–92% ee) and high yields (89–98%) at room temperature. We also studied the reaction of phenylacetylene with various aromatic and vinyl aldehydes under the same conditions. As the results listed in Figure 1 show, excellent enantioselectivity and high yield are generally observed for a broad range of aldehydes.

We have further extended the application of the Zn-^{i}PrI-H_8BINOL-Ti(O^{i}Pr)$_4$ catalyst system to the reaction of various alkynes with various aldehydes, and the results are summarized in Table 3. For the reactions of 1-hexyne and 4-phenylbutyne, the first step was conducted at 45 °C and the second step at room temperature. Under these conditions, the vinyl and alkyl alkynes reacted with a variety of aldehydes to give good yields and high enantioselectivities.

CONCLUSIONS

We have discovered that the substrate scope of a previously reported catalytic asymmetric alkyne addition to aldehydes processes can be greatly expanded by using H_8BINOL and ^{i}PrI in place of BINOL and EtI. We have demonstrated that this new catalyst system can carry out the alkyne addition to aliphatic aldehydes with high enantioselectivity at room temperature. In addition, the new catalyst system can also promote the enantioselective reaction of a variety of alkynes

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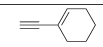
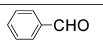
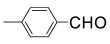
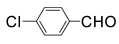
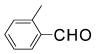
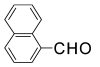
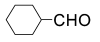
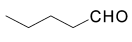
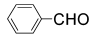
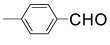
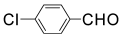
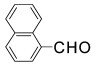
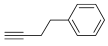
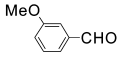
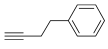
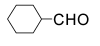
Table 3. Addition of Alkynes to Aldehydes in the Presence of Zn, ^{i}PrI, (*S*)-H_8BINOL, and Ti($O^{i}Pr$)$_4$[a]

entry	alkyne	aldehyde	isolated yield (%)	ee (%)
1			90	96
2			78	95
3			95	89
4			88	91
5			86	95
6			88	85
7			85	88
8			83	90
9			84	91
10			66	91
11			68	92
12			77	96
13			82	86

[a]First step: Zn (3 mmol, 6 equiv), (*S*)-H_8BINOL (0.2 mmol, 0.4 equiv), ^{i}PrI (4 mmol, 8 equiv), an alkyne (2 mmol, 4 equiv), THF (1 mL), Ti($O^{i}Pr$)$_4$ (1 equiv), and 24 h at room temperature for 1-ethynylcyclohexene and 45 °C for 1-hexyne or 4-phenylbutyne. Second step: Et_2O (10 mL), an aldehyde (0.5 mmol), and 16 h at room temperature.

with a broad range of aldehydes. This process avoids the use of the pyrophoric $ZnEt_2$ and is useful in practice for the synthesis of structurally diverse chiral propargylic alcohols.

EXPERIMENTAL SECTION

Typical Experimental Procedure for the Use of the H_8BINOL-Zn-^{i}PrI-Ti($O^{i}Pr$)$_4$ Catalyst System in the Asymmetric Alkyne Addition to Aldehydes. To a flame-dried 25 mL flask was added Zn powder (3 mmol, 6 equiv) and (*S*)-H_8BINOL (0.2 mmol, 0.4 equiv). Then an alkyne (2 mmol, 4 equiv), THF (1 mL, dry), ^{i}PrI (4 mmol, 8 equiv), and Ti($O^{i}Pr$)$_4$ (1 equiv) were added via syringe under nitrogen. After the mixture was stirred at room temperature for 24 h, diethyl ether (10 mL, dry) was added followed by an aldehyde (0.5 mmol) and the stirring was continued for 16 h. Saturated ammonia chloride solution (5 mL) was then added to quench the reaction. After extraction with methylene chloride (2 × 10 mL) and concentration under vacuum, the residue was purified by column chromatography on silica gel with hexane and 5−10% ethyl acetate as the eluent to afford the pure product. The ee value was determined by HPLC equipped with a chiral column.

Characterizations of the Chiral Propargylic Alcohols in Figure 1. *(R)-1-Cyclohexyl-3-phenylprop-2-yn-1-ol (**1**).* Colorless oil, 105 mg, 98% yield; 92% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 7.5 min and t_{minor} = 17.4 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38−7.37 (m, 2H), 7.25−7.19 (m, 3H), 4.32 (t, J = 6.0 Hz, 1H), 1.88−1.05 (m, 12H). These data are consistent with those reported in ref 6.

*(R)-4-Methyl-1-phenylpent-1-yn-3-ol (**2**).* Colorless oil, 85 mg, 98% yield; 91% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 7.1 min and t_{minor} = 13.5 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37−7.36 (m, 2H), 7.24−7.19 (m, 3H), 4.33 (t, J = 6.0 Hz, 1H), 1.93−1.88 (m, 1H), 1.77 (d, J = 6.0 Hz, 2H), 1.00 (dd, J = 6.0, 6.6 Hz, 6H). These data are consistent with those reported in ref 6.

*(R)-1-Phenylundec-1-yn-3-ol (**3**).* Colorless oil, 109 mg, 89% yield; 91% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 7.2 min and t_{minor} = 19.8 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.36−7.35 (m, 2H), 7.24−7.19 (m, 3H), 4.52 (q, J = 6.6 Hz, 1H), 1.78−1.68 (m, 3H), 1.45−1.41 (m, 2H), 1.24−1.19 (m, 10H), 0.81 (t, J = 6.6 Hz, 3H). These data are consistent with those reported in ref 6.

*(R)-1-Phenylhept-1-yn-3-ol (**4**).* Colorless oil, 85 mg, 90% yield; 91% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 6.7 min and t_{minor} = 18.7 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.37−7.36 (m, 2H), 7.24−7.19 (m, 3H), 4.52 (q, J = 6.0 Hz, 1H), 1.80−1.69 (m, 3H), 1.50−1.30 (m, 4H), 0.87 (t, J = 7.2 Hz, 3H). These data are consistent with those reported in ref 7.

*(R)-1,3-Diphenylprop-2-yn-1-ol (**5**).* Colorless oil, 102 mg, 98% yield; 96% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 15.1 min and t_{minor} = 30.7 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54 (d, J = 7.8 Hz, 2H), 7.33−7.17 (m, 8H), 5.62 (d, J = 6.0 Hz, 1H), 2.18 (d, J = 6.0 Hz, 1H). These data are consistent with those reported in ref 4.

*(R)-3-Phenyl-1-(p-tolyl)prop-2-yn-1-ol (**6**).* White solid, 102 mg, 92% yield; 96% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 11.1 min and t_{minor} = 25.3 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43−7.38 (m, 4H), 7.24−7.13 (m, 5H), 5.57 (s, 1H), 2.29 (s, 3H), 2.16 (s, 1H). These data are consistent with those reported in ref 4.

*(S)-3-Phenyl-1-(o-tolyl)prop-2-yn-1-ol (**7**).* Colorless oil, 84 mg, 76% yield; 95% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 12.0 min and t_{minor} = 29.5 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.72−7.71 (m, 1H), 7.45−7.44 (m, 2H), 7.31−7.20 (m, 6H), 5.83 (s, 1H), 2.49 (s, 3H), 2.17 (s, 1H). These data are consistent with those reported in ref 4.

*(R)-1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-ol (**8**).* Colorless oil, 110 mg, 92% yield; 95% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 22.0 min and t_{minor} = 38.3 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42−7.38 (m, 2H), 7.24−7.22 (m, 4H), 7.12−7.10 (m, 2H), 6.82−6.80 (m, 1H), 5.59 (d, J = 6.0 Hz, 1H), 3.76 (s, 3H), 2.21 (d, J = 6.6 Hz, 1H). These data are consistent with those reported in ref 8.

*(R)-3-Phenyl-1-(4-(trifluoromethyl)phenyl)prop-2-yn-1-ol (**9**).* Colorless oil, 130 mg, 94% yield; 98% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 10.2 min and t_{minor} = 15.5 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.65−7.56 (m, 4H), 7.37−7.16 (m, 5H), 5.65 (d, J = 6.0 Hz, 1H), 2.27 (d, J = 6.0 Hz, 1H). These data are consistent with those reported in ref 4.

*(S)-1-(Naphthalen-1-yl)-3-phenylprop-2-yn-1-ol (**10**).* Colorless oil, 110 mg, 85% yield; 97% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 18.8 min and t_{minor} = 46.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.37 (d, J = 8.4 Hz, 1H), 7.93−7.85 (m, 3H), 7.59−7.46 (m, 5H), 7.33−7.29 (m, 3H), 6.35 (d, J = 6.0 Hz, 1H), 2.38 (d, J = 6.0 Hz, 1H). These data are consistent with those reported in ref 4.

*(R,E)-1,5-Diphenylpent-1-en-4-yn-3-ol (**11**).* White solid, 100 mg, 85% yield; 92% ee determined by HPLC analysis (OD column, 20% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 11.3 min and t_{minor} = 34.2 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39−7.14 (m, 10H), 6.77−6.73 (m, 1H), 6.33−6.27 (m, 1H), 5.19 (s, 1H), 2.00 (s, 1H). These data are consistent with those reported in ref 6.

*(R,E)-1-Phenylhex-4-en-1-yn-3-ol (**12**).* White solid, 71 mg, 83% yield; 93% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 8.3 min and t_{minor}

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= 30.0 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.38−7.37 (m, 2H), 7.24−7.18 (m, 3H), 5.93−5.88 (m, 1H), 5.66−5.63 (m, 1H), 4.98 (s, 1H), 1.85 (s, 1H), 1.69 (d, J = 6.6 Hz, 1H). These data are consistent with those reported in ref 6.

Characterizations of the Chiral Propargylic Alcohols in Table 3. *(R)-3-(Cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-ol (Entry 1).* Colorless oil, 96 mg, 90% yield; 96% ee determined by HPLC analysis (OD-H column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 17.2 min and t_{minor} = 11.8 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.54 (d, J = 7.8 Hz, 2H), δ 7.36−7.24 (m, 3H), 6.15−6.14 (m, 1H), 5.55 (s, 1H), 2.14−2.08 (m, 4H), 1.63−1.55 (m, 4H). These data are consistent with those reported in ref 9.

(R)-3-Cyclohexenyl-1-p-tolylprop-2-yn-1-ol (Entry 2). Colorless oil, 88 mg, 78% yield; 95% ee determined by HPLC analysis (OD-H column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 17.1 min and t_{minor} = 10.8 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42 (d, J = 6.6 Hz, 2H), 7.17 (d, J = 6.0 Hz, 2H), 6.14 (s, 1H), 5.52 (s, 1H), 2.34 (s, 3H), 2.08−2.07 (m, 4H), 1.63−1.54 (m, 4H). These data are consistent with those reported in ref 9.

(R)-1-(4-Chlorophenyl)-3-(cyclohex-1-en-1-yl)prop-2-yn-1-ol (Entry 3). White solid, 117 mg, 95% yield; 89% ee determined by HPLC analysis (AD-H column, 4% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 23.8 min and t_{minor} = 21.7 min. $[\alpha]^{22}_D$ = 10.1 (c = 1.15, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.39 (d, J = 7.2 Hz, 2H), 7.25 (d, J = 7.2 Hz, 2H), 6.07 (s, 1H), 5.45 (s, 1H), 2.13−2.00 (m, 4H), 1.55−1.49 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 139.7, 136.3, 134.2, 128.9, 128.3, 120.1, 89.1, 85.8, 64.6, 29.2, 25.8, 22.4, 21.6. HRMS (M^+) for $C_{15}H_{15}OCl$. Calcd: 246.0811. Found: 246.0812.

(S)-3-(Cyclohex-1-en-1-yl)-1-(o-tolyl)prop-2-yn-1-ol (Entry 4). Colorless oil, 100 mg, 88% yield; 91% ee determined by HPLC analysis (AD-H column, 5% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 14.5 min and t_{minor} = 11.8 min. $[\alpha]^{22}_D$ = −5.0 (c = 1.02, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.67 (s, 1H), 7.27−7.19 (m, 3H), 6.16 (s, 1H), 5.73 (s, 1H), 2.47 (s, 3H), 2.16−2.10 (m, 4H), 1.65−1.59 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 138.9, 136.2, 135.8, 130.9, 128.5, 126.7, 126.4, 120.3, 88.6, 86.0, 63.1, 29.3, 25.8, 22.4, 21.7, 19.2. HRMS (M^+) for $C_{16}H_{18}O$. Calcd: 226.1358. Found: 226.1362.

(S)-3-(Cyclohex-1-en-1-yl)-1-(naphthalen-1-yl)prop-2-yn-1-ol (Entry 5). Colorless oil, 113 mg, 86% yield; 95% ee determined by HPLC analysis (OB-H column, 10% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 22.0 min and t_{minor} = 12.0 min. $[\alpha]^{22}_D$ = −10.3 (c = 1.10, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.31 (d, J = 8.4 Hz, 1H), 7.85−7.81 (m, 3H), 7.56−7.45 (m, 3H), 6.22 (s, 1H), 6.16 (s, 1H), 2.31−2.30 (m, 1H), 2.15−2.08 (m, 4H), 1.62−1.56 (m, 4H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 136.2, 136.0, 134.2, 130.8, 129.5, 128.9, 126.5, 126.0, 125.4, 124.8, 124.3, 120.3, 89.5, 86.0, 63.6, 29.3, 25.8, 22.4, 21.7. HRMS (M^+) for $C_{19}H_{18}O$. Calcd: 262.1358. Found: 262.1360.

(R)-3-(Cyclohex-1-en-1-yl)-1-cyclohexylprop-2-yn-1-ol (Entry 6). Colorless oil, 96 mg, 88% yield; 85% ee determined by HPLC analysis (OD-H column, 1.5% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 50.1 min and t_{minor} = 82.7 min. $[\alpha]^{22}_D$ = −6.6 (c = 1.00, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.08 (s, 1H), 4.24−4.23 (m, 1H), 2.10−2.06 (m, 4H), 1.85−1.50 (m, 10H), 1.27−1.01 (m, 5H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 135.2, 120.4, 87.7, 86.7, 67.9, 44.6, 29.5, 28.8, 28.4, 26.6, 26.2, 26.1, 25.8, 22.5, 21.7. HRMS (M^+) for $C_{15}H_{22}O$. Calcd: 218.1671. Found: 218.1672.

(R)-1-(Cyclohex-1-en-1-yl)hept-1-yn-3-ol (Entry 7). Colorless oil, 82 mg, 85% yield; 88% ee determined by HPLC analysis (OB-H column, 1% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 34.6 min and t_{minor} = 26.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.07 (s, 1H), 4.45 (s, 1H), 2.07−1.18 (m, 15H), 0.89 (t, J = 7.2 Hz, 3H). These data are consistent with those reported in ref 10.

(R)-1-Phenylhept-2-yn-1-ol (Entry 8). Colorless oil, 78 mg, 83% yield; 90% ee determined by HPLC analysis (AD-H column, 10% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 7.8 min and t_{minor} = 6.9 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.40−7.39 (m, 2H), 7.24−7.11 (m, 3H), 5.30 (d, J = 4.8 Hz,1H), 2.13 (t, J = 7.2 Hz, 2H), 1.97 (dd, J = 6.0, 1.2 Hz, 1H), 1.43−1.36 (m, 2H), 1.30−1.25 (m, 2H), 0.77 (td, J = 7.2, 1.2 Hz, 3H). These data are consistent with those reported in ref 3c.

(R)-1-(p-Tolyl)hept-2-yn-1-ol (Entry 9). Colorless oil, 85 mg, 84% yield; 91% ee determined by HPLC analysis (AD-H column, 10% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 8.5 min and t_{minor} = 7.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.42−7.40 (m, 2H), 7.24−7.16 (m, 2H), 5.40 (d, J = 6.0 Hz, 1H), 2.34 (s, 3H), 2.27−2.24 (m, 2H), 2.03−2.02 (m, 1H), 1.55−1.49 (m, 2H), 1.44−1.38 (m, 2H), 0.90 (td, J = 7.2, 1.2 Hz, 3H). These data are consistent with those reported in ref 3c.

(R)-1-(4-Chlorophenyl)hept-2-yn-1-ol (Entry 10). Colorless oil, 73 mg, 66% yield; 91% ee determined by HPLC analysis (AD-H column, 10% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 8.2 min and t_{minor} = 6.9 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47−7.44 (m, 2H), 7.34−7.25 (m, 2H), 5.41 (s, 1H), 2.28−2.23 (m, 2H), 2.11−2.08 (m, 1H), 1.54−1.40 (m, 4H), 0.93−0.88 (m, 3H). These data are consistent with those reported in ref 3c.

(S)-1-(Naphthalen-1-yl)hept-2-yn-1-ol (Entry 11). Colorless oil, 81 mg, 68% yield; 92% ee determined by HPLC analysis (AD-H column, 10% IPA in hexane, 1 mL/min, 254 nm). Retention time: t_{major} = 13.7 min and t_{minor} = 8.8 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.30 (d, J = 8.4 Hz, 1H), 7.87−7.81 (m, 3H), 7.55−7.44 (m, 3H), 6.11 (d, J = 6.0 Hz, 1H), 2.28 (dt, J = 7.2, 1.8 Hz, 2H), 2.21 (d, J = 6.0 Hz, 1H), 1.55−1.50 (m, 2H), 1.44−1.38 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H). These data are consistent with those reported in ref 3c.

(R)-1-(3-Methoxyphenyl)-5-phenylpent-2-yn-1-ol (Entry 12). Colorless oil, 103 mg, 77% yield; 96% ee determined by HPLC analysis (AD-H column, 10% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 14.3 min and t_{minor} = 12.8 min. $[\alpha]^{22}_D$ = 17.5 (c = 0.99, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.28−7.24 (m, 3H), 7.20−7.19 (m, 3H), 7.05−7.03 (m, 2H), 6.84 (d, J = 7.8 Hz, 1H), 5.39 (d, J = 5.4 Hz, 1H), 3.79 (s, 3H), 2.84 (t, J = 7.8 Hz, 2H), 2.56 (t, J = 7.8 Hz, 2H), 2.04 (d, J = 6.0 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 159.9, 142.8, 140.7, 129.8, 128.7, 128.6, 126.5, 119.1, 114.1, 112.2, 86.9, 80.9, 64.9, 55.5, 35.1, 21.2. HRMS (M^+) for $C_{18}H_{18}O_2$. Calcd: 266.1307. Found: 266.1310.

(R)-1-Cyclohexyl-5-phenylpent-2-yn-1-ol (Entry 13). Colorless oil, 99 mg, 82% yield; 86% ee determined by HPLC analysis (OD column, 10% IPA in hexane, 1 mL/min, 220 nm). Retention time: t_{major} = 8.9 min and t_{minor} = 24.1 min. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.33−7.23 (m, 5H), 4.15−4.12 (m, 1H), 2.86 (t, J = 7.8 Hz, 2H), 2.55 (td, J = 7.8, 1.8 Hz, 2H), 1.83−1.76 (m, 4H), 1.70−1.66 (m, 2H), 1.53−1.46 (m, 1H), 0.99−1.29 (m, 5H). These data are consistent with those reported in ref 2a.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02185.

NMR spectra and HPLC plots of the propargylic alcohol products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: lp6n@virginia.edu

Notes

The authors declare no competing financial interest.

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