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Copper(I) Halide Promoted Diastereoselective Synthesis of Chiral Propargylamines and Chiral Allenes using 2-Dialkylaminomethylpyrrolidine, Aldehydes, and 1-Alkynes

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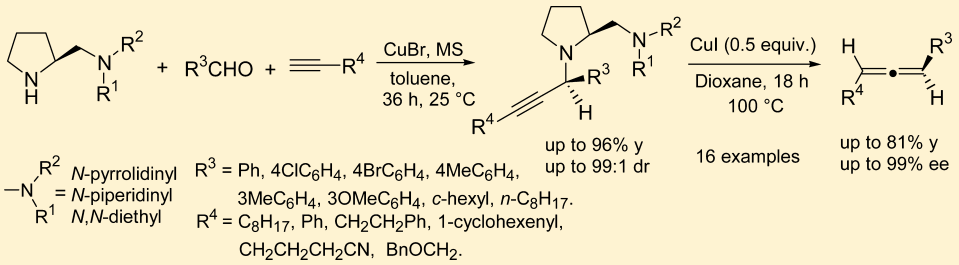
Supporting Information



ABSTRACT: Copper bromide promoted reactions of aldehydes, 1-alkynes, and chiral 2-dialkylaminomethylpyrrolidine at 25 °C give the corresponding chiral propargylamine derivatives in up to 96% yield and 99:1 dr that are readily converted to the corresponding disubstitued chiral allenes in up to 81% yield and 99% ee upon reaction with CuI in dioxane at 100 °C.

INTRODUCTION

Chiral propargylamines are useful synthons for synthesis of biological active skeletons, natural products, and polyfunctional amino derivatives.[1−4] Copper−chiral ligand catalyzed enantioselective propargylamines have been accessed using the chiral auxiliaries quinap,[5−8] pinap,[9−11] pybox,[12−15] and binam diimine.[16,17] Also, chiral amino acid promoted enantioselective synthesis of propargylamines has been reported.[18−20] Recently, Che et al. reported the chiral prolinol derived propargylamines using gold(III) salen complexes.[21,22] The chiral allene structural motifs are also present in several biologically active natural products and pharmaceuticals.[23−25] Also, chiral allenes are versatile synthons with the potential to provide excellent axis-to-center chirality transfer in organic synthesis.[23,26,27]

Over the years, several synthetic methods were developed to access allenes.[28−35] Recently, zinc halide promoted conversion of 1-alkynes, aldehydes, and morpholine to racemic 1,3-disubstituted allenes[36] and to enantiopure allenes using certain chiral cyclic secondary amines were reported.[37] Also, a two-step synthesis involving preparation of chiral propargylamines and conversion to chiral allenes in a ZnI_2-promoted reaction was reported.[38] Copper(I) bromide promoted reactions of 1-alkynes, paraformaldehyde, or substituted aldehydes and diisopropylamine or *N*,*N*-dicyclohexylamine were reported to give 1-substituted allenes[39−41] or racemic 1,3-disubstituted allenes.[42,43] Herein, we report the results of detailed studies on the CuBr-promoted diastereoselective synthesis of chiral propargylamines (**4**−**6**) using 1-alkynes, aldehydes, and 2-dialkylaminomethylpyrrolidines (**1**−**3**) and their conversion to chiral allenes **7** in a CuI-promoted reaction (Figure 1).

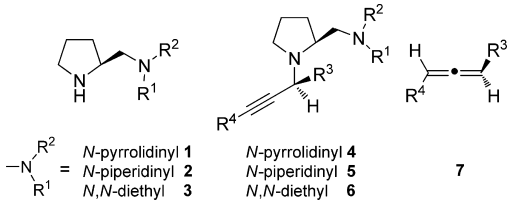


Figure 1. Chiral 2-dialkylaminomethylpyrrolidine derivatives, propargylamines, and allenes.

RESULTS AND DISCUSSION

Recently, we have reported that the chiral (2*S*)-phenylpyrrolidine (**10**) and (*S*)-diphenypyrrolidinemethanol (**11**; (*S*)-DPP) gave the chiral (*R*)-allene **7** in 66% and 98% ee, respectively, in a ZnX_2-promoted one-pot, three-component allene transformation (Scheme 1).[37]

Presumably, better selectivity is observed in the case of (*S*)-DPP (**11**) due to coordination of the hydroxyl group with the $ZnBr_2$ during the formation of the chiral propargylamine intermediate and also during the conversion of the propargylamine into the chiral allene.[37] It was of interest to us to examine the use of the readily accessible and commercially available (*S*)-2-(1-pyrrolidinylmethyl)pyrrolidine (**1**) in this one-pot, three-component chiral allene transformation using ZnI_2. We have observed that in this reaction the (*R*)-allene **7aa** was obtained with 94% ee but only in 4% yield in addition to the corresponding propargylamine intermediate **4aa** (88% yield, 96:4 dr).

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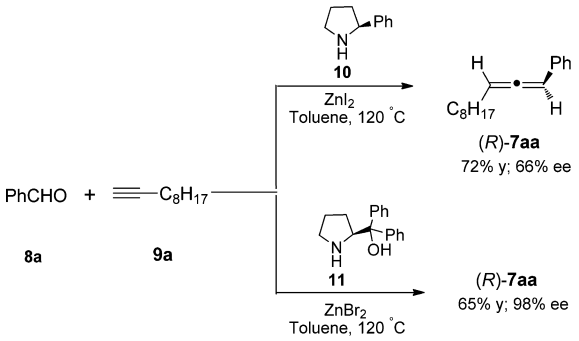
Scheme 1. Chiral Allene Transformation Using 1-Decyne, Benzaldehyde, and Pyrrolidine Derivatives Promoted by ZnX_2



We have also examined the other proline diamines (*S*)-2-(piperidinomethyl)pyrrolidine (**2**) and (*S*)-2-(diethylaminomethyl)-pyrrolidine (**3**) in this reaction. Whereas the chiral diamine **2** gave the (*R*)-allene **7aa** in 7% yield with 94% ee in addition to the corresponding propargylamine derivative **5** with 82% yield and 96:4 dr, the chiral diamine **3** gave the chiral allene **7aa** in 11% yield with 90% ee along with the propargylamine derivative **6** in 50% yield and 90:10 dr (Scheme 2).

This ZnI_2-promoted three-component coupling gave the corresponding chiral propargylamine derivatives in reasonable yields and diastereoselectivity but requires refluxing toluene. Fortunately, the relatively inexpensive CuBr catalyzes this reaction and various chiral propargylamines (**4aa**−**4fh**) are readily accessed using different substrates of aldehydes and alkynes at 25 °C (Table 1). The chiral propargylamines were obtained with good yields (75−96%) and diastereoselectivities (96:4−99:1 dr).

To study the structural effects of the diamine derivatives in this transformation, we have used the diamines **2** and **3**, containing piperidine and diethylamine moieties. The corresponding propargylamines **5** and **6** were prepared using CuBr (20 mol %), benzaldehyde (**8a**) and 1-decyne (**9a**) with up to 84% yield (99:1 dr) and 68% yield (98:2 dr), respectively. The absolute configurations of propargylamines **4**−**6** were assigned by comparison with the data reported for the propargylamine **6ba**.[22] We have observed that the reaction of the chiral diamine **1** with ethyl propiolate gave the Michael adduct **12** in 88% yield in 15 min at 25 °C.[44] When the reaction was carried out with the propargyl alcohol under these conditions, only a complex mixture of unidentified products was obtained. The corresponding benzoyl ester leads to the formation of the *N*-benzoyl derivative of the diamine **1**. However, when the reaction was carried out with propargyl benzyl ether, the corresponding chiral propargylamines (**4fa**−**fh**) were obtained (Table 1).

A mechanism outlined in Scheme 3 can be considered for this transformation on the basis of previous reports on reactions of CuBr amine phosphine complexes.[6] Probably, the chiral diamine **1** would initially form the dimeric copper complex **13** on reaction with CuBr,[5,45] which would then react with 1-alkyne to give the intermediate complex **14**. This could react with the intermediate aminal **15**, formed in situ by the reaction of chiral diamine and aldehyde. The intermediate **16** formed in this way would then deliver the alkynyl group from the bottom face of the iminium group, leading to an *S* stereogenic center at the propargylamine product **4**.

We then turned our attention toward conversion of the chiral propargylamines obtained this way into the chiral allene **7** using various metal salts in different solvents. We have observed that the reaction of the propargylamine derivative **4aa** with ZnI_2 gave the (*R*)-allene **7aa** in 98% ee but only in 8% yield. The unreacted propargylamine **4aa** was recovered in 70% yield after the reaction (Table 2, entry 1). The same reaction in dioxane gave the (*R*)-allene in only 10% yield but with 86% ee. We have examined the use of $AgNO_3$ in this conversion, as it was reported to give the chiral allenes with high enantioselectivities using the corresponding propargylamine derivatives prepared with (*S*)-prolinol.[46] However, in this run also the (*R*)-allene **7aa** was obtained only in 14% yield and 99% ee (Table 2, entry 3).

The use of CuI (0.5 equiv) gave better results. Whereas (*R*)-allene in 76−92% ee with 18−35% yield was observed in reactions in toluene, when the reaction was carried out in dioxane at 100 °C for 18 h using CuI (0.25 equiv), the (*R*)-allene was obtained in 33% yield with 99% ee (Table 2, entry 6). When the same reaction reaction was carried out using more CuI (0.5 equiv), the yield was improved to 62% with 99% ee (Table 2, entry 7). Further increases in the amount of CuI did not improve yields (Table 2, entries 9 and 10). We have also observed that the use of other copper halides, CuCl and CuBr, led to lower yields (22−30%) and enantioselectivities (90−92% ee) (Table 2, entries 11 and 12). The reason for the higher yields and selectivity obtained using the CuI−dioxane system is not clear. However, such observations have been observed in other transformations using the CuI−dioxane system by previous workers.[42,43,47]

The propargylamines **5** and **6** gave the chiral (*R*)-allene **7aa** in 54% yield and 99% ee and 42% yield and 96% ee, respectively, under these conditions (Table 2, entries 13 and 14). Clearly, the chiral diamine containing pyrrolidine moiety **4aa** gave better results in comparison to the propargylamine containing diethylamine and piperidine amine moieties.

We then carried out the reaction of other propargylamine derivatives **4ab**−**fh** using CuI (0.5 equiv) at 100 °C, which gave optimum results using **7aa** (Table 2, entry 7). The propargylamines **4ab**−**af** were converted to the corresponding chiral allenes **7ab**−**af** in 59−68% yields with good enantioselectivities (94−98% ee, Table 3). The propargylamine (**4ba**) prepared

Scheme 2. Chiral Allene Transformation Using 1-Decyne, Benzaldehyde, and (*S*)-2-Dialkylaminomethylpyrrolidine Promoted by ZnI_2

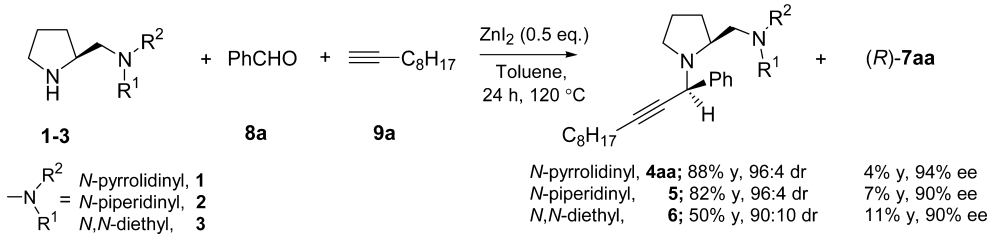


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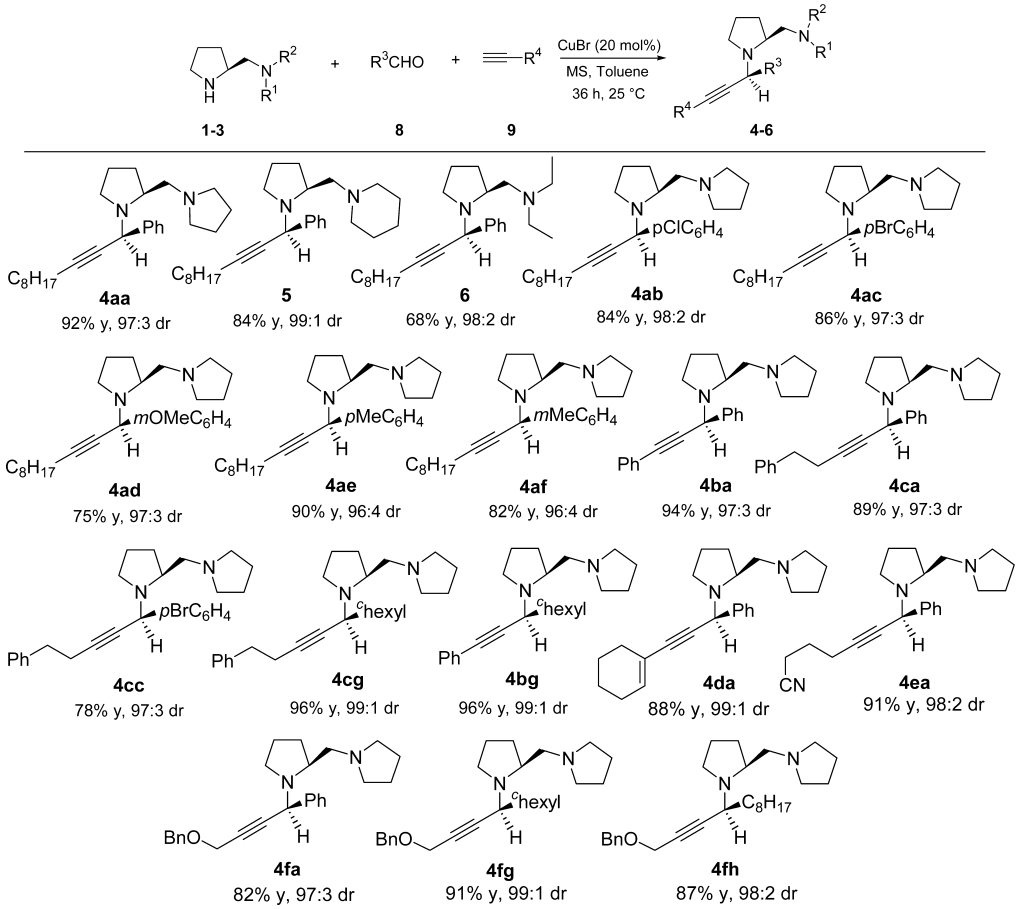
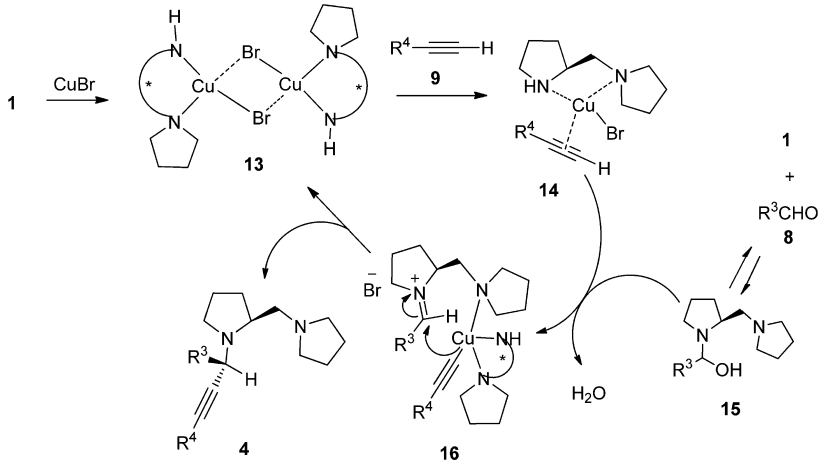
Table 1. Diastereoselective Synthesis of Propargylamines Using Chiral Amine, Aldehyde, and 1-Alkyne and Copper Bromide[a−c]



[a]The reactions were carried out by taking amine **1**−**3** (2.0 mmol), 1-alkyne (2.2 mmol), and aldehyde (2.0 mmol) in toluene (3 mL) with CuBr (0.4 mmol) and MS (1.0 g, 4 Å) at 25 °C for 36 h. [b]dr ratio based on crude ^{1}H NMR. [c]Isolated yield.

Scheme 3. Tentative Mechanism for Copper-Catalyzed Propargylamine Formation



from phenylacetylene (**9b**) and benzaldehyde (**8a**) gave the chiral allene **7ba** in 56% yield and 85% ee. The other propargylamines **4ca**−**fh** prepared from different alkynes and aldehydes afforded the corresponding chiral allenes **7ca**−**fh** in 58−81% yields with good enantioselectivities (94−99%, Table 3).

The mechanism outlined in Scheme 4 may be considered for this transformation.[43,48] The triple bond of propargylamine **4** would complex with CuI to give the intermediate **18**, which could undergo a 1,5-hydride shift to give the alkenyl copper species **19**. Antiperiplanar elimination of the CuI and the imine would then give the chiral allene (*R*)-**7**. A similar mechanism was previously proposed for the Ag(I)-catalyzed conversion of a chiral propargylamino alcohol to chiral allenes (Scheme 4). The optimum results obtained using dioxane may be due to its interaction with CuI in the transition states for the formation of the intermediate **18**, **19**, and allene (*R*)-**7**.

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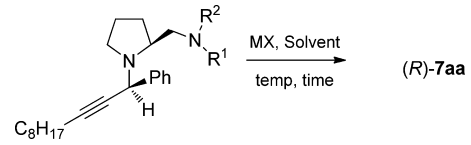
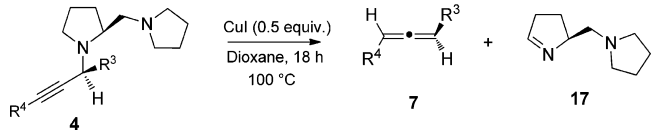
Table 2. Reaction of Propargylamines 4aa, 5, and 6 with ZnI_2, $AgNO_3$, and CuX[a]

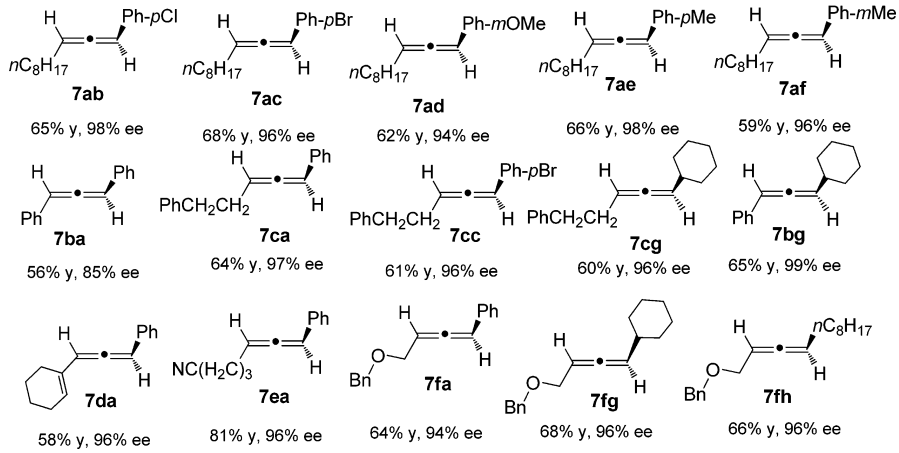


entry	diamine	solvent	temp (°C)	MX	amt of MX (equiv)	time (h)	yield (%)[b]	ee (%)[c]
1	**4aa**	toluene	120	ZnI_2	0.5	24	8	98
2	**4aa**	dioxane	100	ZnI_2	0.5	18	10	86
3	**4aa**	CH_3CN	50	$AgNO_3$	0.5	24	14	99
4	**4aa**	toluene	120	CuI	0.5	2	18	92
5	**4aa**	toluene	120	CuI	0.5	5	35	76
6	**4aa**	dioxane	100	CuI	0.25	18	33	99
7	**4aa**	dioxane	100	CuI	0.5	18	62	99
8	**4aa**	dioxane	100	CuI	0.5	24	68	98
9	**4aa**	dioxane	100	CuI	0.75	18	65	99
10	**4aa**	dioxane	100	CuI	1.0	18	70	98
11	**4aa**	dioxane	100	CuCl	0.5	18	22	92
12	**4aa**	dioxane	100	CuBr	0.5	18	30	90
13	**5**	dioxane	100	CuI	0.5	18	54	99
14	**6**	dioxane	100	CuI	0.5	18	42	96

[a]The reactions were carried out by taking up amines **4aa**, **5**, and **6** (0.5 mmol) in solvent (2 mL). [b]Isolated yields. [c]The % ee was confirmed by HPLC analysis on Chiralcel OD-H.

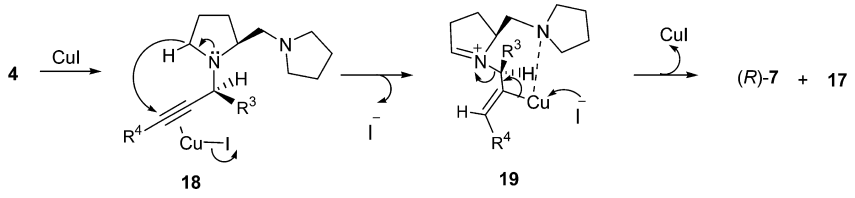
Table 3. Copper Iodide Promoted Chiral Allene Transformation Using Corresponding Propargylamines[a–c]





[a]The reactions were carried out by taking up amines **4** (0.5 mmol) and CuI (0.25 mmol) in dioxane (2 mL). [b]Isolated yield. [c]The % ee was confirmed by HPLC analysis on Chiralcel OD-H, OB-H and OJ-H columns.

Scheme 4. Tentative Mechanism for Copper(I)-Catalyzed Allene Formation



We have made efforts to isolate the imine byproduct **17** but were not successful. However, we have observed that the imine intermediate **17** formed during the reaction could be readily converted back to the starting (*S*)-2-(1-pyrrolidinylmethyl)pyrrolidine

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1 by reduction in situ using $NaBH_4$/MeOH in 61% yield without loss of its optical purity (eq 1).

$$\mathbf{4aa} \xrightarrow[\text{dioxane, 18 h}]{\text{CuI (0.5 equiv)}} (R)\text{-}\mathbf{7aa} + [\mathbf{17}] \xrightarrow[0-25\ ^\circ\text{C, 2 h}]{NaBH_4/\text{MeOH}} \underset{61\%\text{ y, 99\% ee}}{\mathbf{1}} \quad (1)$$

We have also examined the utility of chiral diamine **1** in a one-pot chiral allene transformation using CuBr for the preparation of a propargylamine derivative followed by addition of CuI (in dioxane) for chiral (*R*)-allene formation. In this case, we have obtained the chiral (*R*)-allene **7aa** with 48% yield and 90% ee.

CONCLUSION

We have developed a CuBr-promoted method for diastereoselective synthesis of chiral propargylamine derivatives using (2*S*)-dialkylaminomethylpyrrolidine and transformed them into chiral (*R*)-allenes using copper iodide. Since the chiral propargylamines were obtained in good yields and excellent diastereoselectivities and the chiral allenes synthesized were in high enantiomeric purities, the methods described here have considerable potential for further exploitations in synthesis.

EXPERIMENTAL SECTION

General Information. Chiral proline diamine derivatives **1**–**3** were synthesized by following the literature reports.[49] CuBr and CuI were purchased from Sigma Aldrich and used without any further purification. Toluene and dioxane were dried on sodium benzophenone ketyl and stored on sodium wire.

General Procedure for Synthesis of (2*S*)-Dialkylaminomethylpyrrolidine-Derived Chiral Propargylamines. In an oven-dried 10 mL flask, copper(I) bromide (57 mg, 20 mol %) and chiral diamine **1**–**3** (2 mmol) in dry toluene (3 mL) were added. Freshly distilled aldehyde **8** (2 mmol), 4 Å MS (1.0 g), and 1-alkyne **9** (2.2 mmol) were added, and the mixture was stirred at 25 °C for 36 h. The 4 Å MS was removed by filtration and washed with Et_2O. The crude product was concentrated in vacuo and purified by chromatography on basic alumina. The product was eluted in a 98/2 mixture of hexane and ethyl acetate.

*(S)-1-((S)-1-Phenylundec-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)-pyrrolidine (**4aa**).* Light yellow oil. Yield: 0.70 g (92%). IR (neat): 3061, 3028, 2928, 1601, 1493, 1450, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.6 Hz, 2H), 7.31–7.23 (m, 3H), 5.20 (s, 1H), 3.10–3.03 (m, 1H), 2.69 (dd, J = 11.9, 5.0 Hz, 1H), 2.62–2.44 (m, 6H), 2.34–2.30 (m, 2H), 2.01–1.94 (m, 1H), 1.81–1.77 (m, 5H), 1.69–1.54 (m, 5H), 1.48–1.44 (m, 2H), 1.31–1.29 (m, 8H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 128.2, 127.9, 126.9, 87.6, 76.1, 62.3, 59.5, 56.5, 54.9, 47.5, 31.8, 30.6, 29.3, 29.1, 28.9, 23.5, 22.7, 22.7, 18.8, 14.1. $[\alpha]_D^{25}$ = −89.3° (c = 0.68, $CHCl_3$). LCMS (m/z): 381 (M + 1). Anal. Calcd for $C_{26}H_{40}N_2$: C, 82.05; H, 10.59; N, 7.36. Found: C, 82.15; H, 10.59; N, 7.31.

*(S)-1-((S)-1-(4-Chlorophenyl)undec-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4ab**).* Light yellow oil. Yield: 0.70 g (84%). IR (neat): 2928, 2785, 1487, 1460, 1089, 1016 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.3 Hz, 2H), 5.21 (s, 1H), 3.10–3.05 (m, 1H), 2.70 (dd, J = 11.9, 5.4 Hz, 1H), 2.60–2.47 (m, 7H), 2.32 (t, J = 6.8 Hz, 2H), 1.99–1.94 (m, 1H), 1.77 (bs, 4H), 1.68–1.53 (m, 5H), 1.47–1.45 (m, 2H), 1.29 (s, 8H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.3, 132.6, 129.5, 128.0, 88.0, 75.8, 62.4, 59.4, 55.9, 54.9, 47.5, 31.9, 30.6, 29.3, 29.1, 28.9, 23.5, 22.7, 22.6, 18.8, 14.1. $[\alpha]_D^{25}$ = −79.5° (c = 0.75, $CHCl_3$). LCMS (m/z): 415 (M + 1). Anal. Calcd for $C_{26}H_{39}ClN_2$: C, 75.24; H, 9.47; N, 6.75. Found: C, 75.11; H, 9.56; N, 6.68.

*(S)-1-((S)-1-(4-Bromophenyl)undec-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4ac**).* Yellow oil. Yield: 0.79 g (86%). IR (neat): 3435, 2926, 2858, 1658, 1587, 1483, 1012, 856, 723 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.47–7.41 (m, 4H), 5.18 (s, 1H), 3.07–3.03 (m, 1H), 2.68 (dd, J = 11.9, 5.2 Hz, 1H), 2.58–2.46 (m, 6H), 2.31 (t, J = 6.7 Hz, 2H), 1.99–1.93 (m, 2H), 1.77 (s, 4H), 1.68–1.53 (m, 5H), 1.46–1.44 (m, 2H), 1.29 (s, 8H), 0.88 (t, J = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.8, 130.9, 129.9, 120.7, 88.1, 75.6, 62.3, 59.4, 55.9, 54.9, 47.4, 31.8, 30.6, 29.3, 29.1, 28.9, 23.5, 22.7, 22.6, 18.7, 14.1. $[\alpha]_D^{25}$ = −64.6° (c = 0.85, $CHCl_3$). LCMS (m/z): 461 (M + 2). Anal. Calcd for $C_{26}H_{39}BrN_2$: C, 67.96; H, 8.55; N, 6.10. Found: C, 67.85; H, 8.51; N, 6.15.

*(S)-1-((S)-1-(3-Methoxyphenyl)-3-phenylprop-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4ad**).* Yellow oil. Yield: 0.62 g (75%). IR (neat): 2925, 2448, 2777, 1599, 1484, 1314, 1424, 1045, 755, 689 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.23 (d, J = 8.0 Hz, 1H), 7.18–7.17 (m, 2H), 6.78 (d, J = 8.1 Hz, 1H), 5.18 (s, 1H), 3.82 (s, 3H), 3.08–3.04 (m, 1H), 2.68 (dd, J = 12.0, 5.3 Hz, 1H), 2.62–2.47 (m, 6H), 2.31 (t, J = 6.8 Hz, 2H), 1.99–1.97 (m, 1H), 1.77 (s, 4H), 1.68–1.53 (m, 6H), 1.45–1.44 (m, 2H), 1.29 (bs, 8H), 0.89 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.4, 142.4, 128.9, 120.7, 114.0, 112.1, 87.5, 76.2, 62.4, 59.5, 56.4, 55.1, 55.0, 47.6, 31.9, 30.6, 29.3, 29.2, 28.9, 23.5, 22.8, 22.7, 18.8, 14.1. $[\alpha]_D^{25}$ = −82.1° (c = 1.03, $CHCl_3$). LCMS (m/z): 409 (M − 1). Anal. Calcd for $C_{25}H_{42}N_2O$: C, 78.97; H, 10.31; N, 6.82. Found: C, 78.85; H, 10.38; N, 6.73.

*(S)-2-(Pyrrolidin-1-ylmethyl)-1-((S)-1-(p-tolyl)undec-2-yn-1-yl)-pyrrolidine (**4ae**).* Light yellow oil. Yield: 0.71 g (90%). IR (neat): 2928, 2858, 2791, 1510, 1460, 1350, 1141, 831, 765 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.47 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 7.8 Hz, 2H), 5.17 (s, 1H), 3.09–3.06 (m, 1H), 2.70 (dd, J = 11.9, 5.0 Hz, 1H), 2.62–2.46 (m, 7H), 2.34–2.30 (m, 5H), 2.02–1.96 (m, 1H), 1.78 (s, 4H), 1.69–1.55 (m, 5H), 1.49–1.48 (m, 2H), 1.31 (s, 8H), 0.91 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 136.5, 128.6, 128.1, 87.4, 76.4, 62.3, 59.5, 56.2, 54.9, 47.6, 31.9, 30.7, 29.3, 29.2, 29.1, 28.9, 23.5, 22.8, 22.7, 21.1, 18.8, 14.1. $[\alpha]_D^{25}$ = −81.9° (c = 1.19, $CHCl_3$). LCMS (m/z): 395 (M + 1). Anal. Calcd for $C_{27}H_{42}N_2$: C, 82.17; H, 10.73; N, 7.10. Found: C, 82.21; H, 10.81; N, 7.03.

*(S)-2-(Pyrrolidin-1-ylmethyl)-1-((S)-1-(m-tolyl)undec-2-yn-1-yl)-pyrrolidine (**4af**).* Light yellow oil. Yield: 0.65 g (82%). IR (neat): 2926, 2858, 2785, 1608, 1460, 1143, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.37 (m, 2H), 7.21 (t, J = 7.4 Hz, 1H), 7.05 (d, J = 7.3 Hz, 1H), 5.15 (s, 1H), 3.08–3.05 (m, 1H), 2.69 (dd, J = 11.9, 4.9 Hz, 1H), 2.63–2.46 (m, 7H), 2.39–2.30 (m, 5H), 2.02–1.97 (m, 1H), 1.78 (s, 4H), 1.70–1.54 (m, 5H), 1.49–1.47 (m, 2H), 1.31–1.30 (m, 8H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.5, 137.5, 128.9, 127.9, 127.7, 125.3, 87.5, 76.3, 62.3, 59.6, 56.5, 55.0, 47.6, 31.9, 30.7, 29.3, 29.2, 28.9, 23.5, 22.73, 22.70, 21.5, 18.8, 14.1. $[\alpha]_D^{25}$ = −80.2° (c = 0.7, $CHCl_3$). LCMS (m/z): 395 (M + 1). Anal. Calcd for $C_{27}H_{42}N_2$: C, 82.17; H, 10.73; N, 7.10. Found: C, 82.06; H, 10.65; N, 7.18.

*(S)-1-((S)-1,3-Diphenylprop-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)-pyrrolidine (**4ba**).*[22] Yellow oil. Yield: 0.65 g (94%). IR (neat): 3437, 3061, 3030, 1599, 1489, 1448, 756, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 7.6 Hz, 2H), 7.54–7.52 (m, 2H), 7.38–7.28 (m, 6H), 5.57 (s, 1H), 3.23–3.18 (m, 1H), 2.79 (dd, J = 12.0, 5.6 Hz, 1H), 2.73 (t, J = 8.6 Hz, 1H), 2.65–2.52 (m, 6H), 2.05–2.0 (m, 1H), 1.79 (s, 4H), 1.74–1.62 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 131.9, 128.4, 128.25, 128.20, 128.1, 127.3, 123.5, 87.6, 86.5, 62.3, 59.5, 57.0, 54.9, 47.9, 30.8, 23.6, 22.9. $[\alpha]_D^{25}$ = −120.8° (c = 0.91, $CHCl_3$). LCMS (m/z): 346 (M + 1). Anal. Calcd for $C_{24}H_{28}N_2$: C, 83.68; H, 8.19; N, 8.13. Found: C, 83.56; H, 8.12; N, 8.25.

*(S)-1-((S)-1,5-Diphenylpent-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)-pyrrolidine (**4ca**).* Yellow oil. Yield: 0.66 g (89%). IR (neat): 3057, 3030, 2964, 1600, 1490, 1441, 695 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, J = 7.3 Hz, 2H), 7.35–7.24 (m, 8H), 5.21 (s, 1H), 3.04–2.97 (m, 1H), 2.93 (t, J = 7.3 Hz, 2H), 2.71–2.66 (m, 3H), 2.58–2.42 (m, 8H), 1.98–1.91 (m, 1H), 1.79 (bs, 4H), 1.67–1.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 140.5, 128.6, 128.4, 128.2, 128.0, 127.0, 126.2, 86.7, 62.4, 59.5, 56.4, 55.0, 47.5, 35.4, 30.6, 23.5, 22.7, 20.8. $[\alpha]_D^{25}$ = −87.7° (c = 0.12, $CHCl_3$). LCMS (m/z): 373 (M + 1). Anal. Calcd for $C_{26}H_{32}N_2$: C, 83.82; H, 8.66; N, 7.52. Found: C, 83.91; H, 8.72; N, 7.45.

*(S)-1-((S)-1-(4-Bromophenyl)-5-phenylpent-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4cc**).* Yellow oil. Yield: 0.70 g (78%). IR

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(neat): 3030, 2962, 2868, 2789, 1604, 1485, 1010, 744, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.41−7.22 (m, 9H), 5.16 (s, 1H), 2.98−2.95 (m, 1H), 2.90 (t, J = 7.2 Hz, 2H), 2.69−2.64 (m, 3H), 2.58−2.43 (m, 6H), 2.39−2.34 (m, 1H), 1.94−1.89 (m, 1H), 1.79−1.75 (m, 4H), 1.63−1.55 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.6, 139.6, 130.1, 129.9, 128.6, 128.4, 126.3, 120.7, 87.1, 76.6, 62.4, 59.3, 55.9, 55.0, 47.4, 35.3, 30.5, 23.5, 22.7, 20.7. $[\alpha]_D^{25}$ = −56.6° (c = 0.1, $CHCl_3$). LCMS (m/z): 451(M + 1). Anal. Calcd for $C_{26}H_{31}BrN_2$: C, 69.17; H, 6.92; N, 6.21. Found: C, 69.05; H, 6.87; N, 6.28.

*(S)-1-((R)-1-Cyclohexyl-5-phenylpent-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4cg**).* Yellow oil. Yield: 0.73 g (96%). IR (neat): 3063, 3028, 2922, 2851, 2785, 1670, 1604, 1496, 1450, 744, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.32−7.20 (m, 5H), 3.30 (d, J = 10.0 Hz, 1H), 2.85−2.80 (m, 3H), 2.70−2.66 (m, 1H), 2.57−2.48 (m, 7H), 2.43−2.32 (m, 2H), 1.97−1.96 (m, 2H), 1.89−1.85 (m, 1H), 1.76−1.55 (m, 10H), 1.34−1.14 (m, 4H), 0.93−0.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 128.5, 128.2, 126.1, 84.4, 78.8, 62.1, 59.9, 58.6, 54.9, 46.8, 41.3, 35.7, 31.4, 30.5, 30.4, 26.9, 26.2, 26.0, 23.5, 23.3, 20.8. $[\alpha]_D^{25}$ = −94.0° (c = 1.02, $CHCl_3$). LCMS (m/z): 380 (M + 1). Anal. Calcd for $C_{26}H_{38}N_2$: C, 82.48; H, 10.12; N, 7.40. Found: C, 82.36; H, 10.18; N, 7.31.

*(S)-1-((R)-1-Cyclohexyl-3-phenylprop-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4bg**).* Yellow oil. Yield: 0.67 g (96%). IR (neat): 3435, 2924, 2787, 1599, 1489, 1446, 754, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.43−7.41 (m, 2H), 7.31−7.27 (m, 3H), 3.61 (d, J = 10.0 Hz, 1H), 3.03−2.96 (m, 1H), 2.84−2.79 (m, 1H), 2.72 (q, J = 8.4 Hz, 1H), 2.53−2.37 (m, 6H), 2.12−1.92 (m, 3H), 1.76−1.48 (m, 13H), 1.30−1.19 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 131.7, 128.2, 127.6, 123.9, 88.5, 85.6, 62.1, 60.2, 59.1, 55.0, 47.2, 41.3, 31.5, 30.6, 30.5, 26.9, 26.2, 26.0, 23.6, 23.5. $[\alpha]_D^{25}$ = −142.1° (c = 0.83, $CHCl_3$). LCMS (m/z): 352 (M + 1). Anal. Calcd for $C_{24}H_{34}N_2$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.15; H, 9.86; N, 7.91.

*(S)-1-((S)-3-(Cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4da**).* Light yellow oil. Yield: 0.61 g (88%). IR (neat): 3061, 3028, 2930, 2785, 1491, 1448, 1136, 702 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.5 Hz, 2H), 7.34−7.21 (m, 4H), 6.16−6.14 (m, 1H), 5.37 (s, 1H), 3.12−3.07 (m, 1H), 2.72 (dd, J = 12.0, 5.4 Hz, 1H), 2.65−2.47 (m, 6H), 2.22−2.11 (m, 4H), 2.01−1.96 (m, 1H), 1.77−1.58 (m, 11H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.4, 134.0, 128.2, 128.0, 127.0, 120.8, 89.4, 83.3, 62.4, 59.6, 56.9, 55.0, 47.7, 30.6, 29.8, 25.6, 23.6, 22.8, 22.4, 21.6. $[\alpha]_D^{25}$ = −115.6° (c = 1.18, $CHCl_3$). LCMS (m/z): 350 (M + 1). Anal. Calcd for $C_{24}H_{32}N_2$: C, 82.71; H, 9.25; N, 8.04. Found: C, 82.65; H, 9.21; N, 8.12.

*(S)-7-Phenyl-7-((S)-2-(pyrrolidin-1-ylmethyl)pyrrolidin-1-yl)hept-5-ynenitrile (**4ea**).* Yellow oil. Yield: 0.61 g (91%). IR (neat): 3059, 3030, 2922, 2868, 2797, 2247, 1493, 1450, 702, 665 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (d, J = 7.4 Hz, 2H), 7.35−7.31 (m, 2H), 7.25−7.23 (m, 1H), 5.27 (s, 1H), 3.04−2.99 (m, 1H), 2.71 (dd, J = 12.0, 5.4 Hz, 1H), 2.57−2.48 (m, 11H), 1.98−1.90 (m, 3H), 1.77 (s, 4H), 1.68−1.61 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.1, 128.1, 128.0, 127.2, 119.1, 84.4, 78.6, 62.3, 59.6, 56.4, 55.0, 47.8, 30.6, 25.0, 23.5, 22.8, 18.0, 16.2. $[\alpha]_D^{25}$ = −104.2° (c = 0.96, $CHCl_3$). LCMS (m/z): 336 (M + 1). Anal. Calcd for $C_{22}H_{29}N_3$: C, 78.76; H, 8.71; N, 12.53. Found: C, 78.85; H, 8.65; N, 12.45.

*(S)-1-((S)-4-(Benzyloxy)-1-phenylbut-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4fa**).* Yellow oil. Yield: 0.64 g (82%). IR (neat): 3061, 3030, 2962, 1602, 1493, 1452, 1201 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 7.4 Hz, 2H), 7.41−7.28 (m, 8H), 5.42 (s, 1H), 4.70 (s, 2H), 4.37 (s, 2H), 3.14−3.11 (m, 1H), 2.75 (dd, J = 5.5, 5.5 Hz, 1H), 2.67−2.51 (m, 7H), 2.03−1.99 (m, 1H), 1.79−1.62 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.9, 137.7, 128.5, 128.2, 127.9, 127.3, 83.5, 83.2, 71.3, 62.5, 59.5, 57.6, 56.6, 55.0, 47.9, 30.6, 23.6, 22.8. $[\alpha]_D^{25}$ = −86.2° (c = 0.6, $CHCl_3$). LCMS (m/z): 389 (M + 1). Anal. Calcd for $C_{26}H_{32}N_2O$: C, 80.37; H, 8.30; N, 7.21. Found: C, 80.25; H, 8.36; N, 7.13.

*(S)-1-((S)-4-(Benzyloxy)-1-cyclohexylbut-2-yn-1-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4fg**).* Yellow oil. Yield: 0.72 g (91%). IR (neat): 3065, 3030, 2928, 1450, 1352 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.29 (m, 5H), 4.62 (s, 2H), 4.24 (d, J = 1.6 Hz, 2H), 3.46 (d, J = 9.9 Hz, 1H), 2.93−2.90 (m, 1H), 2.79−2.74 (m, 1H), 2.64−2.62 (m, 1H), 2.51−2.34 (m, 6H), 2.06−1.88 (m, 2H), 1.75−1.59 (m, 12H), 1.31−1.20 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.7, 128.4, 128.1, 127.8, 85.2, 80.9, 71.0, 62.1, 60.1, 58.6, 57.5, 55.0, 47.1, 41.1, 31.4, 30.5, 30.4, 26.8, 26.1, 25.9, 23.5, 23.3. $[\alpha]_D^{25}$ = −101.9° (c = 0.71, $CHCl_3$). LCMS (m/z): 395 (M + 1). Anal. Calcd for $C_{26}H_{38}N_2O$: C, 79.14; H, 9.71; N, 7.10. Found: C, 79.25; H, 9.63; N, 7.18.

*(S)-1-((S)-1-(Benzyloxy)dodec-2-yn-4-yl)-2-(pyrrolidin-1-ylmethyl)pyrrolidine (**4fh**).* Yellow oil. Yield: 0.74 g (87%). IR (neat): 3027, 2925, 2854, 1455, 1350, 1073, 734, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.30 (m, 5H), 4.62 (s, 2H), 4.23 (s, 2H), 3.88 (t, J = 7.4 Hz, 1H), 2.95−2.86 (m, 2H), 2.64 (q, J = 8.6 Hz, 1H), 2.51 (s, 5H), 2.43−2.38 (m, 1H), 1.98−1.93 (m, 1H), 1.75 (s, 6H), 1.65−1.60 (m, 3H), 1.50−1.41 (m, 2H), 1.29−1.27 (m, 10H), 0.88 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.6, 128.4, 128.1, 127.8, 85.8, 80.4, 71.1, 62.1, 60.0, 57.5, 55.0, 52.8, 47.4, 35.2, 31.9, 30.5, 29.5, 29.3, 26.8, 23.5, 22.9, 22.7, 14.2. $[\alpha]_D^{25}$ = −66.5° (c = 1.22, $CHCl_3$). LCMS (m/z): 425 (M + 1). Anal. Calcd for $C_{28}H_{44}N_2O$: C, 79.19; H, 10.44; N, 6.60. Found: C, 79.32; H, 10.38; N, 6.75.

*1-(((S)-1-((S)-1-Phenylundec-2-yn-1-yl)pyrrolidin-2-yl)methyl)-piperidine (**5**).* Light yellow oil. Yield: 0.66 g (84%). IR (neat): 3061, 3028, 1726, 1602, 1493, 1450, 1124, 725, 700 cm^{-1}. ^1H NMR: (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.4 Hz, 2H), 7.33−7.21 (m, 3H), 5.42 (s, 1H), 3.13−3.08 (m, 1H), 2.62 (dd, J = 17.2, 8.6 Hz, 1H), 2.65−2.30 (m, 8H), 2.17 (s, 1H), 1.94−1.88 (m, 1H), 1.65−1.43 (m, 13H), 1.30 (s, 8H), 0.89−0.88 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 128.2, 127.9, 126.9, 87.4, 76.4, 65.8, 57.4, 56.6, 55.4, 47.7, 31.9, 30.6, 29.3, 29.2, 29.1, 28.9, 26.2, 24.6, 22.73, 22.7, 18.8, 14.1. $[\alpha]_D^{25}$ = −76.0° (c = 0.81, $CHCl_3$). LCMS (m/z): 396 (M + 1). Anal. Calcd for $C_{27}H_{42}N_2$: C, 82.17; H, 10.73; N, 7.10. Found: C, 82.35; H, 10.62; N, 7.18.

*N-Ethyl-N-((S)-1-((S)-1-phenylundec-2-yn-1-yl)pyrrolidin-2-yl)-methyl)ethanamine (**6**).* Yellow oil. Yield: 0.52 g (68%). IR (neat): 3061, 2959, 2928, 1493, 1450, 1383, 1327, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J = 7.4 Hz, 2H), 7.33−7.23 (m, 3H), 5.33 (s, 1H), 3.08−3.06 (m, 1H), 2.61−2.41 (m, 8H), 2.33−2.30 (m, 2H), 1.98−1.91 (m, 1H), 1.66−1.54 (m, 5H), 1.47−1.46 (m, 2H), 1.29 (s, 8H), 1.06 (t, J = 6.9 Hz, 6H), 0.89 (t, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.8, 128.2, 127.9, 126.9, 87.5, 76.3, 59.5, 58.4, 56.6, 48.0, 47.9, 31.9, 30.6, 29.4, 29.3, 29.0, 22.8, 22.6, 18.8, 14.2, 12.1. $[\alpha]_D^{25}$ = −89.3° (c = 1.15, $CHCl_3$). LCMS (m/z): 383 (M + 1). Anal. Calcd for $C_{26}H_{42}N_2$: C, 81.61; H, 11.06; N, 7.32. Found: C, 81.49; H, 11.15; N, 7.21.

General Procedure for Synthesis of Chiral Allenes from Chiral Proline Derived Propargylamines. The chiral propargylamine (0.5 mmol) was added to a stirred suspension of CuI (48 mg, 0.25 mmol) in dry dioxane (2 mL), and the contents were refluxed for 18 h at 100 °C under a nitrogen atmosphere. Dioxane was removed under reduced pressure, and the crude product was purified on silica gel (100−200) using hexane as eluent to isolate the chiral allene **7**. Characterization data of the chiral allenes **7aa**−**ea** were identical with our previously reported data.[40]

*(R)-(4-(Benzyloxy)buta-1,2-dien-1-yl)benzene (**7fa**).* Colorless liquid. Yield: 0.076 g (64%). IR (neat): 3063, 3032, 1952, 1726, 1599, 1494, 1454 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36−7.20 (m, 10H), 6.29−6.26 (m, 1H), 5.73 (q, J = 6.6 Hz, 1H), 4.63−4.56 (m, 2H), 4.19 (dd, J = 6.7, 2.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.1, 138.1, 133.9, 128.7, 128.4, 127.9, 127.7, 127.1, 126.9, 95.6, 92.6, 72.0, 67.9. $[\alpha]_D^{25}$ = −116.5° (c = 0.55, $CHCl_3$). LCMS (m/z): 237 (M + 1). Anal. Calcd for $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.18; H, 6.91. HPLC: 94% ee (Daicel Chiralcel OJ-H, hexane/^{i}PrOH 99/1, flow rate 1.0 mL/min, 254 nm, $t_R(R)$ = 31.9 min, $t_R(S)$ = 34.7 min).

*(R)-(((4-Cyclohexylbuta-2,3-dien-1-yl)oxy)methyl)benzene (**7fg**).* Colorless liquid. Yield: 0.082 g (68%). IR (neat): 3030, 2926, 2851, 1961, 1450, 1095 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.37−7.30 (m, 5H), 5.32−5.23 (m, 2H), 4.56 (s, 2H), 4.07 (dd, J = 6.8, 2.2 Hz, 2H), 2.04−2.00 (m, 1H), 1.79−1.64 (m, 6H), 1.35−1.11 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0, 138.3, 128.4, 127.8, 127.6, 98.0, 89.3, 71.6, 68.8, 37.0, 33.07, 33.03, 26.1, 25.9. $[\alpha]_D^{25}$ = −39.7° (c = 0.58, $CHCl_3$). LCMS (m/z): 243 (M + 1). HPLC: 94% ee (Daicel

Chiralcel OB-H, hexane/^{i}PrOH 99/1, flow rate 0.5 mL/min, 215 nm, $t_R(R)$ = 10.2 min, $t_R(S)$ = 11.2 min). Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.15; H, 9.21.

(R)-((Dodeca-2,3-dien-1-yloxy)methyl)benzene (7fh). Colorless liquid. Yield: 0.090 g (66%). IR (neat): 3058, 3032, 2925, 2856, 1961, 1453, 1096, 734, 687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38−7.28 (m, 5H), 5.25−5.20 (m, 2H), 4.55 (s, 2H), 4.06 (dd, J = 6.6, 2.4 Hz, 2H), 2.04−2.0 (m, 2H), 1.44−1.27 (m, 12H), 0.89 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 205.1, 138.3, 128.4, 127.9, 127.6, 92.0, 88.3, 71.6, 68.7, 31.9, 29.4, 29.3, 29.15, 29.10, 28.6, 22.7, 14.1. $[\alpha]_D^{25}$ = −15.3° (c = 0.4, $CHCl_3$). LCMS (m/z): 273 (M + 1). HPLC: 96% ee (Daicel Chiralcel OB-H, hexane/^{i}PrOH 100/0, flow rate 0.5 mL/min, 215 nm, $t_R(R)$= 15.2 min, $t_R(S)$= 17.0 min). Anal. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.65; H, 10.26.

Reduction of the Imine Intermediate 17 Present in the Product Mixture. The procedure for the synthesis of chiral allenes from chiral propargylamine (0.5 mmol, 0.190 g was followed, and this crude mixture was cooled to 0 °C. Methanol (3 mL) and $NaBH_4$ (0.6 mmol, 0.023 g) were added, and the mixture was stirred further for 2 h at 25 °C. The mixture was then chromatographed on a silica gel (100−200 mesh) column to isolate the allene (*R*)-7 using *n*-hexane as eluent (yield 0.07 g, 62% y, 99% ee). The chiral diamine **1** was recovered using $CHCl_3$/MeOH (90/10) as eluent without change in its enantiomeric purity. Yield: 0.047 g (61%). $[\alpha]_D^{25}$ = +8.4° (c = 0.94, EtOH) (lit.[50] $[\alpha]_D^{25}$ = +8.5° (c = 2.4, EtOH)).

Procedure for the Synthesis of (*S,E*)-Ethyl 3-(2-(Pyrrolidin-1-ylmethyl)pyrrolidin-1-yl)acrylate (12). To the chiral diamine **1** (0.31 g, 2.0 mmol) in dry toluene (3 mL) was added ethyl propiolate (0.2 g, 2.0 mmol) at 25 °C slowly, and the mixture was stirred further for 15 min. Toluene was removed under reduced pressure, and the crude product was purified on basic alumina. The enamine adduct **8** was eluted using hexane/ethyl acetate (80/20).

Yield: 0.44 g (88%). IR (neat): 3503, 2972, 2791, 1685, 1608, 1460, 787, 733 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, J = 12.0 Hz, 1H), 4.47 (d, J = 12.8 Hz, 1H), 4.09 (q, J = 8.0 Hz, 2H), 3.64−3.62 (m, 1H), 3.18−3.11 (m, 2H), 2.53−2.42 (m, 6H), 1.96−1.74 (m, 8H), 1.23 (t, J = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 148.6, 84.9, 60.6, 58.7, 54.6, 29.6, 23.5, 23.2, 14.7. $[\alpha]_D^{25}$ = −43.9° (c = 0.58, $CHCl_3$). LCMS (m/z): 253 (M + 1). Anal. Calcd for $C_{14}H_{24}N_2O_2$: C, 66.63; H, 9.59; N, 11.10. Found: C, 66.51; H, 9.52; N, 11.21.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text giving a representative procedure for the preparation of racemic allenes and figures giving ^{1}H and ^{13}C NMR spectra of the products and HPLC analysis 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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■ REFERENCES

(1) Konishi, M.; Ohkuma, H.; Tsuno, T.; Oki, T. *J. Am. Chem. Soc.* **1990**, *112*, 3715.
(2) Huffman, M. A.; Yasuda, N.; DeCamp, A. E.; Grabowski, E. J. J. *J. Org. Chem.* **1995**, *60*, 1590.
(3) Kauffman, G. S.; Harris, G. D.; Dorow, R. L.; Stone, B. R. P.; Parsons, R. L.; Pesti, J. A., Jr.; Magnus, N. A.; Fortunak, J. M.; Confalone, P. N.; Nugent, W. A. *Org. Lett.* **2000**, *2*, 3119.
(4) Trost, B. M.; Chung, C. K.; Pinkerton, A. B. *Angew. Chem., Int. Ed.* **2004**, *43*, 4327.
(5) Koradin, C.; Polborn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2002**, *41*, 2535.
(6) Gommermann, N.; Koradin, C.; Polborn, K.; Knochel, P. *Angew. Chem., Int. Ed.* **2003**, *42*, 5763.
(7) Koradin, C.; Gommermann, N.; Polborn, K.; Knochel, P. *Chem. Eur. J.* **2003**, *9*, 2797.
(8) Gommermann, N.; Knochel, P. *Chem. Eur. J.* **2006**, *12*, 4380.
(9) Knöpfel, T. F.; Aschwanden, P.; Ichikawa, T.; Watanabe, T.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 5971.
(10) Aschwanden, P.; Stephenson, C. R. J.; Carreira, E. M. *Org. Lett.* **2006**, *8*, 2437.
(11) Zarotti, P.; Knöpfel, T. F.; Aschwanden, P.; Carreira, E. M. *ACS Catal.* **2012**, *2*, 1232.
(12) Wei, C.; Li, C.-J. *J. Am. Chem. Soc.* **2002**, *124*, 5638.
(13) Singh, V. K.; Bisai, A. *Org. Lett.* **2006**, *8*, 2405.
(14) Panera, M.; Diez, J.; Merino, I.; Rubio, E.; Gamasa, M. P. *Inorg. Chem.* **2009**, *48*, 11147.
(15) Nakamura, S.; Ohara, M.; Makamura, Y.; Shinbata, N.; Toru, T. *Chem. Eur. J.* **2010**, *16*, 2360.
(16) Benadlia, M.; Negri, D.; Anna, G. D. *Tetrahedron Lett.* **2004**, *45*, 8705.
(17) Colombo, F.; Benaglia, M.; Orlandi, S.; Usuelli, F.; Celentano, G. *J. Org. Chem.* **2006**, *71*, 2064.
(18) Akullian, L. C.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2003**, *42*, 4244.
(19) Traverse, J. F.; Hoveyda, A. H.; Snapper, M. L. *Org. Lett.* **2003**, *5*, 3273.
(20) Lu, Y.; Johnstone, T. C.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2009**, *131*, 11284.
(21) Lo, V. K.-Y.; Liu, Y.; Wong, M.-K.; Che, C.-M. *Org. Lett.* **2006**, *8*, 1529.
(22) Lo, V. K-Y.; Kung, K. K-Y.; Wong, M.-K.; Che, C.-M. *J. Organomet. Chem.* **2009**, *694*, 583.
(23) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Eds.; Wiley-VCH: Weinheim, Germany, 2004.
(24) Hoffmann-Röder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196.
(25) Yu, S.; Ma, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 2.
(26) Bates, R. W.; Satcharoen, V. *Chem. Soc. Rev.* **2002**, *31*, 12.
(27) Ma, S. *Chem. Rev.* **2005**, *105*, 2829.
(28) Rona, P.; Crabbé, P. *J. Am. Chem. Soc.* **1969**, *91*, 3289.
(29) Alexakis, A.; Marek, I.; Mangeney, P.; Normant, J. F. *J. Am. Chem. Soc.* **1990**, *112*, 8042.
(30) Krause, N.; Hoffmann-Röder, A. *Tetrahedron* **2004**, *60*, 11671.
(31) Karunakar, G. V.; Periasamy, M. *J. Org. Chem.* **2006**, *71*, 7463.
(32) Liu, H.; Leow, D.; Huang, K.-W.; Tan, C.-H. *J. Am. Chem. Soc.* **2009**, *131*, 7212.
(33) Ogasawara, M. *Tetrahedron: Asymmetry* **2009**, *20*, 259.
(34) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. *Org. Lett.* **2011**, *13*, 6312.
(35) Yu, S.; Ma, S. *Chem. Commun.* **2011**, *47*, 5384.
(36) Kuang, J.; Ma, S. *J. Am. Chem. Soc.* **2010**, *132*, 1786.
(37) Periasamy, M.; Sanjeevakumar, N.; Dalai, M.; Gurubrahamam, R.; Reddy, P. O. *Org. Lett.* **2012**, *14*, 2932.
(38) Ye, J.; Li, S.; Chen, B.; Fan, W.; Kuang, J.; Liu, J.; Liu, Y.; Miao, B.; Wan, B.; Wang, Y.; Xie, X.; Yu, Q.; Yuan, W.; Ma, S. *Org. Lett.* **2012**, *14*, 1346.
(39) Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859.
(40) Searles, S.; Li, Y.; Nassim, B.; Lopes, M.-T. R.; Tran, P. T.; Crabbé, P. *J. Chem. Soc., Perkin Trans. 1* **1984**, 747.
(41) Kuang, J.; Ma, S. *J. Org. Chem.* **2009**, *74*, 1763.
(42) Kitagaki, S.; Komizu, M.; Mukai, C. *Synlett* **2011**, *8*, 1129.
(43) Kuang, J.; Luo, H.; Ma, S. *Adv. Synth. Catal.* **2012**, *354*, 933.

(44) See the Experimental Section and Supporting Information.
(45) Harutyunyan, S. R.; Lopez, F.; Browne, W. R.; Correa, A.; Pena, D.; Badorrey, R.; Meetsma, A.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2006**, *128*, 9103.
(46) Lo, V. K.-Y.; Zhou, C.-Y.; Wong, M.-K.; Che, C.-M. *Chem. Commun.* **2010**, *46*, 213.
(47) Klapars, A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 14844.
(48) Liao, C.; Li, B.; Wang, J.; Wang, Y. *Chin. J. Chem.* **2012**, *30*, 951.
(49) Asami, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 721.
(50) Sone, T.; Hiroi, K.; Yamada, S. *Chem. Pharm. Bull.* **1973**, *21*, 2331.