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Diastereoselective Alkynylation of *N*-*p*-Tolylsulfinylimines with Aluminum Acetylides†

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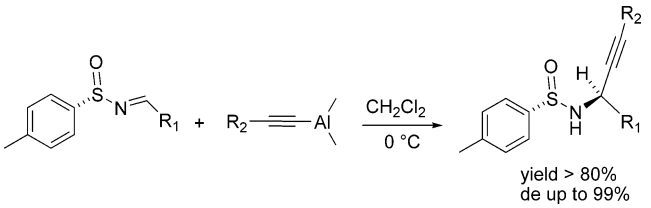
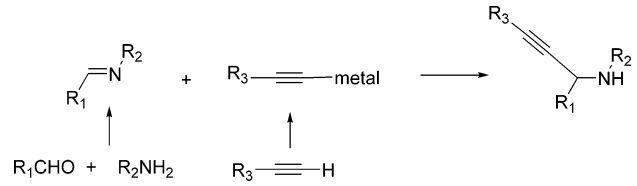


The addition of alkynyl dimethyl aluminum compounds onto *N*-*p*-tolylsulfinylimines was investigated. The reaction was proved to be totally regioselective, leading to propargylamines with high diastereoselectivity (up to 99% de). Addition of aluminum derivatives gave a reversal of diastereoselectivity compared to the addition reaction of lithium acetylide.

In recent years, the synthesis of propargyl amines via the alkynylation of imines and related derivatives has received a great deal of attention (Scheme 1).[1−5] Several procedures were described, including in situ preparation of the organometallic species[2] and one-pot Mannich-type reaction process.[3] These protocols have also been adapted for asymmetric synthesis by the use of asymmetric catalysts[4] or chiral auxiliaries[5] with various successes in terms of stereoselectivity. The use of more reactive electrophilic species such as iminiums,[4a] acyliminiums,[2b,e] tosylimines,[2a,c] and sulfinylimines[5] was also reported.

SCHEME 1



In the chiral auxiliary strategy, the use of chiral sulfinylimine appeared to be very attractive. This method[6] possesses several advantages such as the activation of imine function, the possible separation of diastereomers to give optically pure compounds, and the facile N−S bond cleavage. Furthermore, it was reported that the choice of the metal would have a profound effect on

† Dedicated to Prof. Henri-Philippe Husson on the occasion of his retirement.

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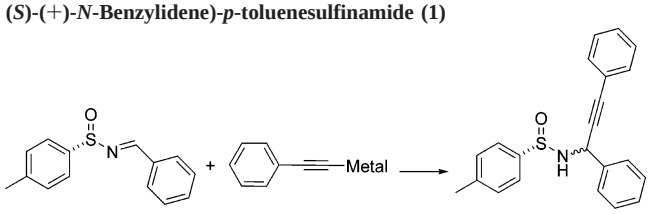
the diastereoselectivity, leading in some examples[7] to the reversal of the diastereofacial preference. Chiral sulfinylimines were largely studied in particular by F.A. Davis, who proposed the use of the *N*-*p*-tolylsulfinylimines,[8] and by J. Ellman, who developed the *N*-*tert*-butyl derivatives.[9] The latter compounds have the advantage to preclude the nucleophilic addition onto the sulfur atom, which is a classical side reaction observed with the tolylsulfinylimines.[10] Ellman has reported that, while lithium or magnesium derivatives gave poor results, these organometallics coupled with $AlMe_3$ used as Lewis acid gave better yield and diastereoselectivity.[11]

We have recently studied[12] the addition of acetylenic aluminum derivatives onto potential chiral *N*-arylsulfinyliminium ions. We observed that aluminum acetylenide derivatives gave a very clean and totally regioselective addition: no side products corresponding to the addition at the sulfur atom of the arylsulfoxide function was observed. Furthermore, the addition occurred with a very high diastereoselectivity. We thus suggested that these organometallic compounds could react regio- and diastereoselectively onto the *N*-tolylsulfinimines (Davis imines). The use of alane derivatives was not very often reported in the literature.[13] They only appeared in a few cases to be quite useful reagents for Michael-type addition.[13a,c,d] We want to describe herein the addition of aluminum acetylenides onto *p*-tolylsulfinylimines.

The first experiments were done with the very classical and often used imine **1** derived from benzaldehyde and *N*-tolylsulfinamide.[14] Li or Mg acetylides were first checked as nucleophiles since their reaction was only reported with *tert*-butylsulfinimine but not with *p*-tolylsulfinimine. The reaction was conducted in two different solvents: CH_2Cl_2 and toluene. With both metals and in both solvents, a nice reaction occurred, leading to the sole C-alkynylated product **2** in good yield but with a quite poor diastereoselectivity (Table 1, entries 1−3). We checked the influence of $AlMe_3$ (as reported by Ellman onto *tert*-butylsulfinylketimines[11]) on the reaction of Li acetylide. Indeed, only a slightly better diastereoselectivity was obtained under these conditions (entries 4 and 5).

TABLE 1. Addition of Phenylacetylides to (*S*)-(+)-*N*-Benzylidene)-*p*-toluenesulfinamide (1)



entry	metal	solvent	conditions	yield (%)	dr[a]
1	MgBr	CH_2Cl_2	2 equiv, −78 °C to rt	65	65:35
2	MgBr	toluene	2 equiv, −78 °C to rt	51	51:49
3	Li	toluene	2 equiv, 0 °C	92	74:26
4	Li	CH_2Cl_2	2 equiv, −78 °C to rt + $AlMe_3$	86	76:24
5	Li	toluene	2 equiv, −78 °C to rt + $AlMe_3$	86	82:18
6	$Al(Me)_2$	CH_2Cl_2	2 equiv, rt	7	–
7	$Al(Me)_2$	toluene	2 equiv, rt	43	5:95
8	$Al(Me)_2$	CH_2Cl_2	4 equiv, 0 °C	86	0.5:99.5
9	$Al(Me)_2$	toluene	4 equiv, 0 °C	85	2:98

[a] Determined by HPLC (250 × 4.6 mm CN Exsil column) and ^1H NMR on the crude reaction mixture.

The addition of the organoaluminum derivatives was then tested. As already observed in our previous work,[12] the reaction needed 4 equiv of the organometallic species to occur cleanly and rapidly. By the use of 2 equiv of alane (entries 6 and 7), the reaction was very slow and gave poor yields (7% in CH_2Cl_2 and 43% in toluene), resulting in low conversion after 17 h at room temperature. The best results were obtained when 4 equiv of alane was used in CH_2Cl_2 at 0 °C for 3 h (entry 8). Under these conditions, the yield was excellent and the de was 99%. Furthermore, it is important to notice that, in this case, the major isomer corresponds to the minor isomer of the addition reaction of lithium acetylide. We can thus obtain, as will, the *R* or the *S* configuration for the major isomer with a de of 64 or 99%, respectively.

The absolute configuration of the new created center has been determined by transforming the amine **2a** into known acetamide **4**. The major isomer **2a** from the alane reaction was treated with an aqueous HCl solution in MeOH for 2 h followed by N-acetylation (Ac_2O, iPr_2NEt, CH_2Cl_2, 2 h) to give acetamine **3** in 82% yield (Scheme 2). The hydrogenation of the triple

SCHEME 2

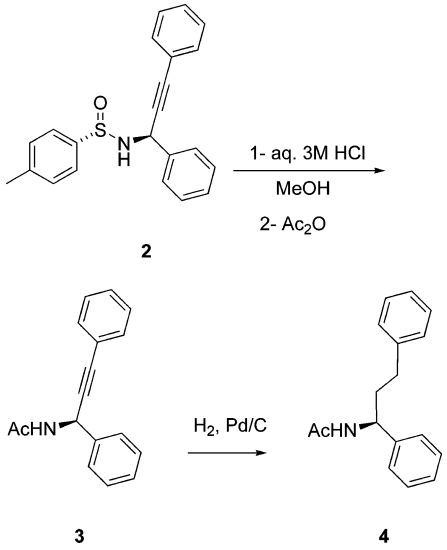


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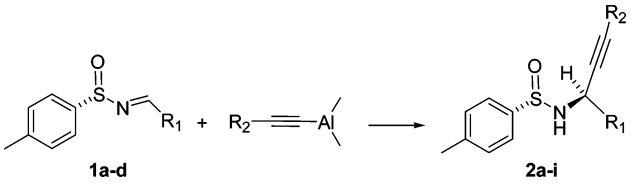
TABLE 2. Addition of Various Aluminum Acetylides to *p*-Tolylsulfylimines (1)



a R_1 = Ph
b R_1= 4-Br-C_6H_4
c R_1= n-Pr
d R_1= t-Bu
e R_1= 2,4-diOMe-C_6H_3

entry	R_1	R_2	conditions	compound	yield (%)	dr[a]
1	Ph	Ph	0 °C, 3h	**2a**	85	99.5:0.5
2		1-cyclohexenyl	0 °C, 3h	**2b**	84	99.5:0.5
3		$(CH_2)_2CH_2Cl$	0 °C, 3 h, then rt 15 h	**2c**	85	96:4
4		$(CH_2)_4CH_3$	0 °C, 2 h, then rt 2 h	**2d**	83	96:4
5		$(CH_2)_2CH(CH_3)_2$	0 °C, 3 h, then rt 3 h	**2e**	86	93:7
6	4-Br−C_6H_4	Ph	0 °C, 2 h, then rt 2 h	**2f**	84	95:5
7	*n*-Pr	Ph	0 °C, 2 h	**2g**	88	96:4
8	*n*-Pr	$(CH_2)_2CH_2Cl$	0 °C, 2 h	**2h**	81	94:6
9	*t*-Bu	Ph	rt, 18 h	**2i**	23	90:10
10	2,4-diOMe−C_6H_3	Ph	rt, 2 h	**2j**	83	84:16

[a] Determined by HPLC (250 × 4.6 mm CN Exsil column or Kromasil modulo-Cart C18) and ^{1}H NMR on the crude reaction mixture.

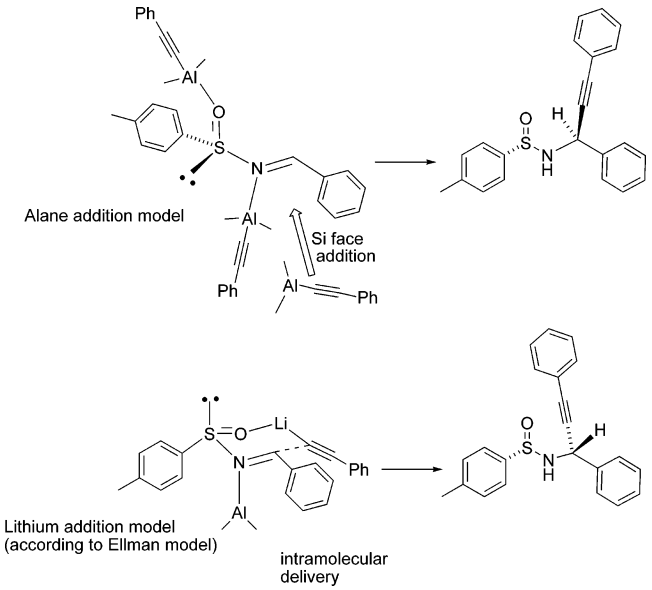


FIGURE 1. Proposed models for the diastereoselective addition of aluminum and lithium acetylides.

bond furnished the acetamide **4** in 81% yield. The acetamide **4** exhibited a rotation of $[\alpha]_D = -48$ (*c* 0.6, MeOH), which allowed us to assign the configuration of the chiral center of this compound as *S*. The *R* enantiomer has been described to have a rotation of $[\alpha]_D = +53$ (*c* 0.02, MeOH)[15]

The reversal of the diastereoselectivity could be tentatively explained by the models shown in Figure 1. The configuration of the new created center obtained with the lithium (or magnesium) acetylide could be explained by the model proposed by Ellman,[11a] in which the nitrogen was chelated by $AlMe_3$ and a sulfinyl-directed alkynyl transfer was occurring. In the case of the alane addition, the observed configuration of the propargylic amines as well as the necessity to use several equivalents (4 equiv was optimum) of aluminum reagent was consistent with the "alane model" shown in Figure 1. In this model, we proposed that both the nitrogen and the oxygen of sulfinimines were chelated by two different molecules of the organoaluminum reagent. An antiperiplanar disposition of these groups should result and explain the addition of a third reagent molecule on the less hindered Si face. The use of 4 equiv of alane in Michael addition of aluminum reagent to δ-sulfinyl-α,β-unsaturated carbonyl systems was also reported by Carreño,[13b,c] who proposed a mechanism involving complexation with 3 equiv of aluminum reagent.

We thus investigated the addition of different alanes to a variety of *N*-tolylsulfinylimines in order to check the generality, the efficiency, and the diastereoselectivity of this process of preparation of propargylamines.

With imine **1** derived from benzaldehyde, a variety of alanes have been tested (Table 2, entries 1−5) and shown to give a highly diastereoselective addition. Substituted aryl and some aliphatic imines were tested (entries 6−10) and were shown to give the reaction in excellent yield (excepted for compound **2i**, entry 9) and with very high diastereoselectivity (excepted for compound **2j**, entry 10).

In conclusion, the addition of aluminum acetylides onto *p*-tolylsulfylimines was proved to occur cleanly with a total regioselectivity and in very good yield, opening the way to various chiral propargylamines. The diastereoselectivity of the reaction was excellent (up to 99%) and opposite of the diastereoselectivity obtained with lithium acetylides.

Experimental Section

General Experimental Procedure for the Preparation of Alkynylalanes: The alkynylalanes were prepared as described,[13j] and the obtained *n*-heptane solution was used as it stands. The

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concentration of this solution can be established by NMR analysis after reaction with benzaldehyde in toluene. In all cases, the theoretical concentration was confirmed.

General Experimental Procedure for the Preparation of Imines 1a−e: The procedure described by Davis[14,16] was used in all cases. Imines **1a−d** are known compounds.[14,16]

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-2,4-dimethoxybenzylideneamine (1e): White solid (1.52 mmol, 0.460 g, 76%); mp = 76 °C; $[\alpha]^{22}_D$ +158.1 (*c* 1.02, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.40 (s, 3H), 3.85 (s, 3H), 3.87 (s, 3H), 6.44 (d, 1H, *J* = 2.31 Hz), 6.52 (m, 1H), 7.30 (d, 2H, *J* = 8.47 Hz), 7.64 (d, 2H, *J* = 8.20 Hz), 7.95 (d, 1H, *J* = 8.71 Hz), 9.15 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.4, 55.6, 97.7, 105.9, 116.1, 124.9, 129.7, 130.1, 141.4, 142.9, 156.0, 161.4, 164.9; MS *m*/*z* 326 (M + Na), 342 (M + K). Anal. Calcd for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65; N, 4.62. Found: C, 63.15; H, 5.62; N, 4.51. IR (neat): 3451, 3030, 2999, 2972, 2840, 1587 cm^{-1}.

General Experimental Procedure for the Synthesis of Compounds 2a−j: To a solution of **1a−e** (0.411 mmol) in anhydrous dichloromethane (2 mL) was added at 0 °C alkynylalane[13i,j] (1.64 mmol). The reaction was monitored by HPLC (Exsil CN; 100 Å; 5 μm; 250 × 4.6 mm; wavelength 254 nm; flow rate 2 mL/min; in *n*-heptane/ethyl acetate) or TLC in diethyl ether/*n*-heptane 6/4 and quenched by addition of 3 mL of a 2 M La Rochelle's salt solution. After 15 min at room temperature, the product was extracted with dichloromethane, and the organic layer was washed successively with water and brine. After drying, the organic layer was evaporated under reduced pressure, and the oily residue was purified by column chromatography on silica gel neutralized with triethylamine. The major diastereomer was isolated and characterized.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-1,3-diphenylprop-2-ynylamine (2a): After 3 h at 0 °C, the product was obtained as a white solid (0.35 mmol, 0.12 g, 85%); mp = 101 °C; $[\alpha]^{22}_D$ −95.0 (*c* 0.72, $CHCl_3$); R_f = 0.18 (diethyl ether/*n*-heptane 6/4); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 8.5 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.41 (s, 3H), 4.58 (d, 1H, *J* = 5.43 Hz), 5.49 (d, 1H, *J* = 5.46 Hz), 7.34 (m, 8H), 7.45 (m, 4H), 7.65 (d, 2H, *J* = 8.21 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.4, 49.0, 86.8, 87.5, 122.5, 122.8, 127.6, 128.3, 128.6, 128.7, 129.6, 131.8, 139.1, 141.3, 141.6; MS *m*/*z* 368 (M + Na). Anal. Calcd for $C_{22}H_{19}NSO$: C, 76.42; H, 5.50; N, 4.05. Found: C, 76.23; H, 5.83; N, 3.89.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-3-cyclohex-1-enyl-1-phenylprop-2-ynylamine (2b): After 3 h at 0 °C, the product was obtained as a white solid (0.345 mmol, 0.12 g, 84%); mp = 106 °C; $[\alpha]^{22}_D$ −96.6 (*c* 0.93, $CHCl_3$); R_f = 0.24 (diethyl ether/*n*-heptane 6/4); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 6.6 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.63 (m, 4H), 2.14 (m, 4H), 2.39 (s, 3H), 4.51 (d, 1H, *J* = 5.34 Hz), 5.37 (d, 1H, *J* = 5.34 Hz), 6.19 (m, 1H), 7.28 (m, 5H), 7.39 (m, 2H), 7.62 (d, 2H, *J* = 8.23 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.4, 21.5, 22.2, 25.6, 29.1, 49.1, 84.7, 88.7, 120.1, 125.8, 127.5, 128.1, 128.6, 129.5, 135.7, 139.5, 141.4; MS *m*/*z* 372 (M + Na). Anal. Calcd for $C_{22}H_{23}NSO$: C, 75.64; H, 6.59; N, 4.01. Found: C, 75.23; H, 6.58; N, 3.77.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-6-chloro-1-phenylhex-2-ynylamine (2c): After 3 h at 0 °C and overnight at room temperature, the product was obtained as a white solid (0.35 mmol, 0.12 g, 85%); mp = 64 °C; $[\alpha]^{22}_D$ −88.5 (*c* 0.87, $CHCl_3$); R_f = 0.19 (diethyl ether/*n*-heptane 6/4); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 8.1 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.04 (q, 2H, *J* = 6.49 Hz), 2.40 (s, 3H), 2.5 (td, 2H, *J* = 2.16 Hz, *J* = 6.84 Hz), 3.70 (t, 2H, *J* = 6.39 Hz), 4.49 (d, 1H, *J* = 5.40 Hz), 5.21 (m, 1H), 7.33 (m, 7H), 7.62 (d, 2H, *J* = 8.20 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 16.4, 21.4, 31.2, 43.7, 48.4, 79.6, 85.7, 125.8, 127.4, 128.2, 128.7, 129.5, 139.4, 141.3, 141.5; MS *m*/*z* 368 (M + Na), 370 (M + 1 + Na). Anal. Calcd for $C_{19}H_{20}ClNSO$: C, 65.99; H, 5.78; N, 4.05. Found: C, 66.01; H, 5.76; N, 4.28.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-1-phenyloct-2-ynylamine (2d): After 2 h at 0 °C and 2 h at room temperature, the product was obtained as a white solid (0.341 mmol, 0.11 g, 83%); mp = 60 °C; $[\alpha]^{22}_D$ −85.7 (*c* 0.93, $CHCl_3$); R_f = 0.27 (diethyl ether/*n*-heptane 6/4); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 5.8 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.92 (t, 3H, *J* = 6.99 Hz), 1.41 (m, 4H), 1.56 (m, 2H), 2.30 (td, 2H, *J* = 2.11 Hz, *J* = 7.03 Hz), 2.40 (s, 3H), 4.40 (d, 1H, *J* = 5.19 Hz), 5.25 (m, 1H), 7.33 (m, 7H), 7.62 (d, 2H, *J* = 8.20 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 14.0, 18.9, 21.3, 22.2, 28.3, 31.1, 48.7, 78.3, 87.9, 125.7, 127.5, 128.0, 128.6, 129.5, 139.7, 141.4, 141.5; MS *m*/*z* 362 (M + Na). Anal. Calcd for $C_{21}H_{25}NSO$: C, 74.23; H, 7.36; N, 4.12. Found: C, 74.41; H, 7.52; N, 4.06.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-6-methyl-1-phenylhept-2-ynylamine (2e): After 2 h at 0 °C and 3 h at room temperature, the product was obtained as a white solid (0.353 mmol, 0.12 g, 86%); mp = 58 °C; $[\alpha]^{22}_D$ −90.4 (*c* 1.15, $CHCl_3$); R_f = 0.36 (diethyl ether/*n*-heptane 6/4); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 8.9 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.92 (d, 6H, *J* = 6.63 Hz), 1.46 (q, 2H, *J* = 7.28 Hz), 1.73 (m, 1H, *J* = 6.70 Hz), 2.30 (td, 2H, *J* = 2.10 Hz, *J* = 7.46 Hz), 2.39 (s, 3H), 4.44 (d, 1H, *J* = 5.17 Hz), 5.24 (m, 1H), 7.33 (m, 7H), 7.62 (d, 2H, *J* = 8.22 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 16.9, 21.4, 22.2, 27.3, 37.5, 48.7, 78.2, 87.9, 125.8, 127.5, 128.0, 128.6, 129.5, 139.7, 141.4, 141.5; MS *m*/*z* 362 (M + Na). Anal. Calcd for $C_{21}H_{25}NSO$: C, 74.23; H, 7.36; N, 4.12. Found: C, 74.33; H, 7.45; N, 3.82.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-1-(4-bromophenyl)-3-phenylprop-2-ynylamine (2f): After 2 h at 0 °C and 2 h at room temperature, the product was obtained as a white solid (0.345 mmol, 0.146 g, 84%); mp = 104−106 °C; $[\alpha]^{23}_D$ +42.6 (*c* 1.00, $CHCl_3$); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 8.45 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.41 (s, 3H), 4.59 (d, 1H, *J* = 5.60 Hz), 5.44 (d, 1H, *J* = 5.48 Hz), 7.25−7.62 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.4, 47.9, 87.0, 87.1, 122.2, 125.8, 128.3, 128.7, 129.3, 129.6, 131.7, 131.8, 138.3, 140.9, 141.7; MS *m*/*z* 448 (M + Na), 464 (M + K). Anal. Calcd for $C_{22}H_{18}BrNSO$: C, 62.27; H, 4.28; N, 3.30. Found: C, 62.07; H, 4.52; N, 3.04. IR (neat): 3448, 3221, 3050, 2923, 2346 cm^{-1}.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-1-phenylethynylbutylamine (2g): After 2 h at 0 °C, the product was obtained as a white solid (0.362 mmol, 0.112 g, 88%); mp = 57−60 °C; $[\alpha]^{23}_D$ +144.7 (*c* 0.96, $CHCl_3$); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 8.56 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.91 (t, 3H, *J* = 7.30 Hz), 1.44−1.54 (m, 2H), 1.66−1.73 (m, 2H), 2.40 (s, 3H), 4.30−4.42 (m, 2H), 7.29−7.36 (m, 5H), 7.43−7.50 (m, 2H), 7.66 (d, 2H, *J* = 8.22 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 13.6, 18.9, 21.4, 39.4, 45.9, 85.0, 88.8, 122.8, 125.7, 128.2, 128.3, 129.6, 131.8, 141.4, 141.8; MS *m*/*z* 334 (M + Na), 350 (M + K); HRMS calcd for $C_{19}H_{21}NOS$ + Na, 334.1237; found, 334.1242. Anal. Calcd for $C_{19}H_{21}NOS$ + 0.5 H_2O: C, 71.21; H, 6.61; N, 4.37. Found: C, 71.17; H, 6.82; N, 4.05. IR (neat): 3448, 3170, 3060,2955, 2936, 2869, 2336 cm^{-1}.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-6-chloro-1-propylhex-2-ynylamine (2h): After 2 h at 0 °C, the product was obtained as a white solid (0.333 mmol, 0.104 g, 81%); mp < 50 °C; $[\alpha]^{23}_D$ +113.8 (*c* 0.95, $CHCl_3$); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 8.65 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.87 (t, 3H, *J* = 7.29 Hz), 1.36−1.49 (m, 2H), 1.52−1.62 (m, 2H), 1.99 (qt, 2H, *J* = 6.71 Hz), 2.41−2.49 (m, 5H), 3.62 (t, 2H, *J* = 6.36 Hz), 4.03−4.20 (m, 2H), 7.31 (d, 2H, *J* = 7.99 Hz), 7.62 (d, 2H, *J* = 8.23 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 13.5, 16.2, 18.8, 21.4, 31.3, 39.5, 43.7, 45.2, 80.7, 83.5, 125.7, 129.5, 141.4, 141.8; MS *m*/*z* 334 (M + Na), 350 (M + K). Anal. Calcd for $C_{16}H_{22}ClNSO$: C, 61.62; H, 7.11; N, 4.49. Found: C, 61.75; H, 7.18; N, 4.29. HRMS (M + Na) calcd, 334.1004 (M + Na); found, 334.1008. IR (neat): 3390, 3053, 2985, 2962, 2306 cm^{-1}.

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(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-1-*tert*-butyl-3-phenylprop-2-ynylamine (2i): After 18 h at room temperature, the product was obtained as a clear oil (0.0945 mmol, 0.030 g, 23%); $[\alpha]^{23}_D$ +147.9 (*c* 0.76, $CHCl_3$); HPLC analysis, *n*-heptane/ethyl acetate = 8:2; t_r = 7.16 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 0.99 (s, 9H), 2.42 (s, 3H), 3.97 (d, 1H, J = 7.36 Hz), 4.26 (d, 1H, J = 7.00 Hz), 7.29−7.36 (m, 5H), 7.45−7.51 (m, 2H), 7.67 (d, 2H, J = 8.14 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.4, 26.1, 35.7, 55.9, 86.1, 87.7, 122.9, 125.8, 128.2, 129.5, 131.7, 141.4, 142.1; MS *m*/*z* 348 (M + Na), 364 (M + K); HRMS calcd for $C_{20}H_{23}NSO$ + Na, 348.1393; found, 348.1398. IR (neat): 3190, 3048, 2960, 2927, 2859, 2354 cm^{-1}.

(S_S,*R*)-*N*-(*p*-Toluenesulfinyl)-1-(2,4-dimethoxyphenyl)-3-phenylprop-2-ynylamine (2j): After 2 h at room temperature, the product was obtained as a pale yellow oil (0.341 mmol, 0.137 g, 83%); $[\alpha]^{22}_D$ +41.5 (*c* 0.95, $CHCl_3$); HPLC analysis, Kromasil Modulo-Cart C_{18}; 5 μm; 250 × 4.6 mm; wavelength 254 nm; flow rate 1 mL/min, MeOH/H_2O = 78:22; t_r = 11.4 min; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.39 (s, 3H), 3.79 (s, 3H), 3.82 (s, 3H), 4.67 (d, 1H, J = 5.15 Hz), 5.77 (d, 1H, J = 5.16 Hz), 6.42 (d, 1H, J = 2.35 Hz), 6.50 (dd, 1H, J = 2.3 Hz, J = 8.35 Hz), 7.23−7.42 (m, 5H), 7.49−7.56 (m, 3H), 7.63 (d, 2H, J = 8.22 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 21.4, 44.6, 55.5, 86.3, 87.5, 98.6, 104.5, 119.9, 122.9, 125.8, 128.2, 128.4, 129.4, 129.5, 131.8, 141.2, 142.1, 157.3, 161.1; MS *m*/*z* 428 (M + Na), 444 (M + K); HRMS calcd for $C_{24}H_{23}NO_3S$ + Na, 428.1291; found, 428.1296. IR (neat): 3459, 3206, 3050, 2957, 2932, 2836, 2360 cm^{-1}.

***N*-((*R*)-1.3-Diphenylprop-2-ynyl)acetamide (3).** To a solution of compound **2a** (0.069 g, 0.2 mmol) in 1 mL of methanol at 0 °C was added an aqueous solution of 3 M HCl solution (0.2 mL, 3 equiv). The reaction mixture was stirred for 30 min at 0 °C and 1.5 h at room temperature. The solvent was removed under reduced pressure, and the residue was dissolved in 2 mL of dichloromethane. To this solution stirred at 0 °C were added successively diisopropylethylamine (70 μL, 0.4 mmol, 2 equiv) and acetic anhydride (60 μL, 0.6 mmol, 3 equiv). After 30 min at 0 °C and 2 h at room temperature, the resulting solution was extracted with water, and the organic layer was dried over magnesium sulfate. The solvent was removed under reduced pressure, and the product was used in the next step without purification: white solid (0.164 mmol, 0.041 g, 82%); mp = 174 °C; $[\alpha]^{22}_D$ +36.1 (*c* 0.82, $CHCl_3$); R_f = 0.7 (dichloromethane/methanol 9/1); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 2.05 (s, 3H), 6.27 (s, 2H), 7.35 (m, 6H), 7.40 (m, 2H), 7.61 (d, 2H, J = 8.14 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 23.3, 45.2, 84.8, 87.0, 122.5, 127.1, 128.2, 128.3, 128.6, 128.7, 128.8, 131.8, 139.1, 168.9.

***N*-((*S*)-1.3-Diphenylpropyl)acetamide (4).** Compound **3** (0.040 g, 0.16 mmol) in methanol (1 mL) was hydrogenolyzed in the presence of 10% Pd/C at atmospheric pressure and room temperature for 2 h. The mixture was filtered through Celite 545, and the filtrate was concentrated in vacuo. The product was characterized without purification: white solid (0.144 mmol, 0.036 g, 90%); mp = 112 °C; $[\alpha]^{22}_D$ −48.0 (*c* 0.64, MeOH); $[\alpha]^{22}_D$ +53 (*c* 0.021, MeOH);[15] R_f = 0.44 (diethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm) 1.95 (s, 3H), 2.15 (m, 2H), 2.64 (m, 2H), 5.06 (q, 1H, J = 7.47 Hz), 6.06 (d, 1H, J = 8.32 Hz), 7.27 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm) 23.4, 32.6, 37.7, 53.4, 126.0, 126.7, 127.5, 128.3, 128.5, 128.8, 141.4, 142.1, 169.3; MS *m*/*z* 276 (M + Na). Anal. Calcd for $C_{17}H_{19}NO$: C, 80.63; H, 7.51; N, 5.53. Found: C, 80.38; H, 7.46; N, 5.28.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra of compounds **1e, 2a**−**i**, **3**, and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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