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SUPPORTING INFORMATION

The biogenic amine transporter activity of vinylogous amphetamine analogs

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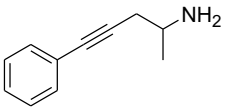
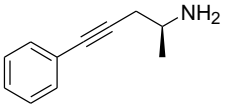
Synthetic Chemistry



1-Methyl-4-phenyl-but-3-ynylamine (4).
To a stirring solution of known alcohol **3** (432 mg, 2.70 mmol) in pyridine (1.7 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (1.03 g, 5.40 mmol) in pyridine (1 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water, and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as a brown oil contaminated with some unreacted starting material.

To a stirring solution of the crude tosylate (849 mg, 2.70 mmol) in DMF (9 mL) was added NaN_3 (702 mg, 10.8 mmol) and the suspension was allowed to stir vigorously overnight. The reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 258 mg (52% yield) of the azide as a clear oil.

To a stirring solution of the azide (158 mg, 0.853 mmol) in THF under N_2 (4.5 mL) was added PPh_3 (449 mg, 1.71 mmol). Water (0.53 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 10% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient) afforded 114 mg (84% yield) of amine **4** as a pale yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.42-7.39 (m, 2H), 7.29-7.27 (m, 3H), 3.24-3.14 (m, 1H), 2.56-2.37 (qd mixed with br. s, 4H), 1.21 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 131.6, 128.2, 127.8, 123.6, 87.1, 82.7, 46.4, 30.3, 22.7; MS (APCI) $(M+1)^+$ 160.2, found 160.1. The hydrochloride salt had mp 131-132°C; Anal. ($C_{11}H_{14}ClN$) C, H, N.

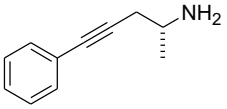


(1*S*)-1-Methyl-4-phenyl-but-3-ynylamine (*S*-4).
To a stirring solution of known alcohol ***R*-3** (580 mg, 3.62 mmol) in pyridine (2 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (1.38 g, 7.24 mmol) in pyridine (1.6 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded 949 mg (83% yield) of the crude tosylate as a white solid.

To a stirring solution of the crude tosylate (949 mg, 3.02 mmol) in DMF (10 mL) was added NaN_3 (787 mg, 12.1 mmol) and the suspension was allowed to stir vigorously overnight. The reaction mixture was

poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 490 mg (88% yield) of the azide as a clear oil.

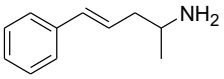
To a stirring solution of the azide (490 mg, 2.65 mmol) in THF (14 mL) under N_2 was added PPh_3 (1.39 g, 5.30 mmol). Water (1.7 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 10% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient) afforded 261 mg (62% yield) of amine ***S*-4** as a pale yellow oil. $[\alpha]^{20}_D$ +11.4 g/mL (*c* 0.0007, MeOH); ^{1}H NMR (CD_3OD, 300 MHz) δ 7.40-7.36 (m, 2H), 7.31-7.28 (m, 3H), 3.14-3.05 (m, 1H), 2.48-2.46 (m, 2H), 1.21 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 131.6, 128.2, 127.7, 123.7, 87.3, 82.6, 46.4, 30.7, 23.0; MS (APCI) $(M+1)^+$ 160.2, found 160.1. The hydrochloride salt had mp 141-142°C; Anal. ($C_{11}H_{14}ClN \cdot 0.2H_2O$) C, H, N.



(1*R*)-1-Methyl-4-phenyl-but-3-ynylamine (*R*-4).
To a stirring solution of known alcohol ***S*-3** (560 mg, 3.50 mmol) in pyridine (2 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (1.33 g, 7.00 mmol) in pyridine (1.5 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as a brown oil contaminated with some unreacted starting material.

To a stirring solution of the crude tosylate in DMF (11 mL) was added NaN_3 (826 mg, 12.7 mmol) and the suspension was allowed to stir vigorously overnight. The reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 370 mg (63% yield) of the azide as a clear oil.

To a stirring solution of the azide (370 mg, 2.00 mmol) in THF (11 mL) under N_2 was added PPh_3 (1.05 g, 4.00 mmol). Water (1.3 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 10% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient) afforded 213 mg (67% yield) of amine ***R*-4** as a pale yellow oil. $[\alpha]^{20}_D$ -4.2 g/mL (*c* 0.0050, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.43-7.40 (m, 2H), 7.29-7.27 (m, 3H), 3.24-3.14 (m, 1H), 2.44 (qd, J = 54.0, 42.0, 24.0, 6.0 Hz, 2H), 1.81 (br. s, 2H), 1.22 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 131.6, 128.2, 127.7, 123.7, 87.3, 82.6, 46.5, 30.6, 23.0; MS (APCI) $(M+1)^+$ 160.2, found 160.0. The hydrochloride salt had mp 143-144°C; Anal. ($C_{11}H_{14}ClN$) C, H, N.

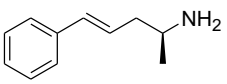


(3*E*)-1-Methyl-4-phenyl-but-3-enylamine (6).
To a stirring solution of LAH (12.5 mL, 1M in THF, 12.5 mmol) in dry THF (15 mL) at 0°C under N_2 was slowly added alcohol **3a** (500 mg, 3.12 mmol) in dry THF (3 mL). CAUTION: Bubbling results due to H_2 gas evolution. After the bubbling ceased, the reaction mixture was slowly warmed to room temperature and then refluxed for 5 h. After cooling to room temperature, then to 0°C, the reaction mixture was carefully quenched with the successive addition of 0.47 mL H_2O, 0.47 mL 3 M aqueous HCl, 1.4 mL H_2O, and 1.4 mL 3 M aqueous HCl. CAUTION: Vigorous exotherm and bubbling results due to H_2 gas evolution. After the bubbling ceased, the quenched reaction mixture was slowly warmed to room temperature, stirred for 30 min, and transferred to a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, water, and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded 446 mg (88% yield) of the crude (*E*)-olefin **5** as a clear oil.

To a stirring solution of the (*E*)-olefin **5** (738 mg, 4.55 mmol) in pyridine (3 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (1.73 g, 9.10 mmol) in pyridine (1.6 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as a brown oil contaminated with some unreacted starting material.

To a stirring solution of the crude tosylate in DMF (15 mL) was added NaN_3 (1.18 g, 18.2 mmol) and the suspension was allowed to stir vigorously overnight. The reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 640 mg (75% yield) of the azide as a clear oil.

To a stirring solution of the azide (640 mg, 3.42 mmol) in THF (18 mL) under N_2 was added PPh_3 (1.79 g, 6.84 mmol). Water (2.1 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 10% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient) afforded 404 mg (73% yield) of amine **6** as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.17 (m, 5H), 6.44 (d, J = 15.0 Hz, 1H), 6.23-6.13 (m, 1H), 3.09-2.98 (m, 1H), 2.34-2.25 (m, 1H), 2.23-2.13 (m, 1H), 1.83 (br. s, 2H), 1.12 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 137.5, 132.5, 128.5, 127.4, 127.1, 126.1, 46.9, 43.6, 23.4; MS (APCI) $(M+1)^+$ 162.2, found 162.2. The hydrochloride salt had mp 147-148°C; Anal. ($C_{11}H_{16}ClN \cdot 0.1H_2O$) C, H, N.



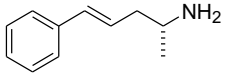
(1*S*,3*E*)-1-Methyl-4-phenyl-but-3-enylamine (*S*-6).
To a stirring solution of LAH (12.5 mL, 1M in THF, 12.5 mmol) in dry THF (15 mL) at 0°C under N_2 was slowly added alcohol ***R*-3** (500 mg, 3.12 mmol) in dry THF (3 mL). CAUTION: Bubbling results due to H_2 gas evolution. After the bubbling ceased, the reaction mixture was slowly warmed to room temperature and then refluxed for 5 h. After cooling to room temperature, then to 0°C, the reaction mixture was

carefully quenched with the successive addition of 0.47 mL H_2O, 0.47 mL 3 M aqueous HCl, 1.4 mL H_2O, and 1.4 mL 3 M aqueous HCl. CAUTION: Vigorous exotherm and bubbling results due to H_2 gas evolution. After the bubbling ceased, the quenched reaction mixture was slowly warmed to room temperature, stirred for 30 min, and transferred to a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, water, and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded 417 mg (82% yield) of the crude (*E*)-olefin ***R*-5** as a clear oil.

To a stirring solution of the (*E*)-olefin ***R*-5** (417 mg, 2.57 mmol) in pyridine (2 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (980 mg, 5.14 mmol) in pyridine (1 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as a brown oil contaminated with some unreacted starting material.

To a stirring solution of the crude tosylate in DMF (8.6 mL) was added NaN_3 (670 mg, 10.3 mmol) and the suspension was allowed to stir vigorously overnight. The reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 440 mg (91% yield) of the azide as a clear oil.

To a stirring solution of the azide (440 mg, 2.35 mmol) in THF (12 mL) under N_2 was added PPh_3 (1.23 g, 4.70 mmol). Water (1.5 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 10% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient) afforded 190 mg (50% yield) of amine ***S*-6** as a clear oil. $[\alpha]^{20}_D$ +24.1 g/mL (*c* 0.0039, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37-7.17 (m, 5H), 6.45 (d, J = 15.0 Hz, 1H), 6.26-6.13 (m, 1H), 3.09-3.01 (m, 1H), 2.34-2.25 (m, 1H), 2.23-2.13 (m, 1H), 1.80 (br. s, 2H), 1.12 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 137.5, 132.5, 128.5, 127.4, 127.1, 126.1, 46.9, 43.6, 23.4; MS (APCI) $(M+1)^+$ 162.2, found 162.3. The hydrochloride salt had mp 172-173°C; Anal. ($C_{11}H_{16}ClN$) C, H, N.

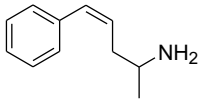


(1*S*,3*E*)-1-Methyl-4-phenyl-but-3-enylamine (*R*-6).
To a stirring solution of LAH (12.5 mL, 1M in THF, 12.5 mmol) in dry THF (15 mL) at 0°C under N_2 was slowly added alcohol ***S*-3** (500 mg, 3.12 mmol) in dry THF (3 mL). CAUTION: Bubbling results due to H_2 gas evolution. After the bubbling ceased, the reaction mixture was slowly warmed to room temperature and then refluxed for 5 h. After cooling to room temperature, then to 0°C, the reaction mixture was carefully quenched with the successive addition of 0.47 mL H_2O, 0.47 mL 3 M aqueous HCl, 1.4 mL H_2O, and 1.4 mL 3 M aqueous HCl. CAUTION: Vigorous exotherm and bubbling results due to H_2 gas evolution. After the bubbling ceased, the quenched reaction mixture was slowly warmed to room temperature, stirred for 30 min, and transferred to a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, water, and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded 500 mg (99% yield) of the crude (*E*)-olefin ***S*-5** as a white solid.

To a stirring solution of the (*E*)-olefin ***S*-5** (500 mg, 3.08 mmol) in pyridine (2.1 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (1.17 g, 6.16 mmol) in pyridine (1 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water, and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as a brown oil contaminated with some unreacted starting material.

To a stirring solution of the crude tosylate in DMF (10 mL) was added NaN_3 (800 mg, 12.3 mmol) and the suspension was allowed to stir vigorously overnight. The reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 370 mg (64% yield) of the azide as a clear oil.

To a stirring solution of the azide (370 mg, 1.98 mmol) in THF (10 mL) under N_2 was added PPh_3 (1.04 g, 3.96 mmol). Water (1.2 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 10% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient) afforded 146 mg (46% yield) of amine ***R*-6** as a clear oil. $[\alpha]^{20}_D$ -5.7 g/mL (*c* 0.0021, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.20 (m, 5H), 6.45 (d, J = 15.0 Hz, 1H), 6.24-6.16 (m, 1H), 3.12-3.01 (m, 1H), 2.37-2.17 (br. m, 4H), 1.15 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 137.4, 132.7, 128.5, 127.2, 126.1, 47.0, 43.3, 23.1; MS (APCI) $(M+1)^+$ 162.2, found 162.2. The hydrochloride salt had mp 172-174°C; Anal. ($C_{11}H_{16}ClN \cdot 0.1H_2O$) C, H, N.

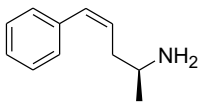


(3*Z*)-1-Methyl-4-phenyl-but-3-enylamine (8).
A mixture of alcohol **3** (900 mg, 5.62 mmol), Lindlar's catalyst (720 mg, 80 wt. %), and quinoline (9 mL, 76.4 mmol) in MeOH (250 mL) in a Paar bottle was shaken in a Paar hydrogenator at 43 psi for 3 h. The mixture was filtered through Celite, washed with MeOH and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and 10% aqueous HCl. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed twice with 10% aqueous HCl and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude (*Z*)-olefin **7** contaminated with ~10% of the fully saturated compound as a brown oil.

To a stirring solution of the crude (*Z*)-olefin **7** in pyridine (2 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (2.14 g, 11.2 mL) in pyridine (4 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded 1.74 g (97% yield) of the crude tosylate as an orange oil.

To a stirring solution of the crude tosylate (1.74 g, 5.50 mmol) in DMF (18 mL) was added NaN_3 (1.43 g, 22.0 mmol). After stirring overnight, the reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded the azide as a clear oil which was used without any further purification.

To a stirring solution of the azide in THF (29 mL) under N_2 was added PPh_3 (2.89 g, 11.0 mmol). Water (3.4 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient, then 100% MeOH) afforded 367 mg (41% yield) of amine **8** as a pale yellow oil. The hydrochloride salt had mp 115-117°C; ^{1}H NMR (CD_3OD, 300 MHz) δ 7.38-7.25 (m, 5H), 6.69 (d, J = 12.0 Hz, 1H), 5.71-5.63 (m, 1H), 3.44-3.38 (m, 1H), 2.78-2.57 (m, 2H), 1.29 (d, J = 6.0 Hz, 3H); ^{13}C NMR (CD_3OD, 75 MHz) ppm 138.1, 134.1, 129.8, 129.6, 128.3, 127.4, 126.5, 49.2, 34.6, 18.5; MS (ESI) $(M+1)^+$ 162.2, found 162.2 (free base); Anal. ($C_{11}H_{16}ClN$) C, H, N.



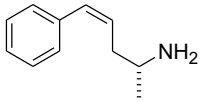
(1*S*,3*Z*)-1-Methyl-4-phenyl-but-3-enylamine (*S*-8).
A mixture of alcohol ***R*-3** (350 mg, 2.18 mmol), Lindlar's catalyst (280 mg, 80 wt. %), and quinoline (3.5 mL, 29.6 mmol) in MeOH (200 mL) in a Paar bottle was shaken in a Paar hydrogenator at 43 psi for 3 h. The mixture was filtered through Celite, washed with MeOH and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and 10% aqueous HCl. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed twice with 10% aqueous HCl and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude (*Z*)-olefin ***R*-7** contaminated with ~10% of the fully saturated compound as a brown oil.

To a stirring solution of the crude (*Z*)-olefin ***R*-7** in pyridine (1 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (831 mg, 4.36 mmol) in pyridine (1 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water, and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as an orange oil.

To a stirring solution of the crude tosylate in DMF (3.7 mL) was added NaN_3 (291 mg, 4.48 mmol). After stirring overnight, the reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded the azide as a clear oil which was used without any further purification.

To a stirring solution of the azide in THF (5.9 mL) under N_2 was added PPh_3 (588 mg, 2.24 mmol). Water (0.7 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory

funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient, then 100% MeOH) afforded 118 mg (65% yield) of amine ***S*-8** as a clear thick oil. The hydrochloride salt had mp 83-84°C; $[\alpha]^{20}_D$ -27.9 g/mL (*c* 0.0014, MeOH); ^{1}H NMR (CD_3OD, 300 MHz) δ 7.38-7.23 (m, 5H), 6.69 (d, J = 12.0 Hz, 1H), 5.71-5.63 (m, 1H), 3.44-3.33 (m, 1H), 2.77-2.56 (m, 2H), 1.29 (d, J = 6.0 Hz, 3H); ^{13}C NMR (CD_3OD, 75 MHz) ppm 138.1, 134.1, 129.8, 129.5, 128.3, 126.5, 49.2, 34.6, 18.5; MS (ESI) $(M+1)^+$ 162.2, found 162.4; Anal. ($C_{11}H_{16}ClN \cdot 0.45H_2O$) C, H, N.

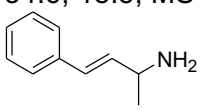


(1*R*,3*Z*)-1-Methyl-4-phenyl-but-3-enylamine (*R*-8).
A mixture of alcohol ***S*-3** (350 mg, 2.18 mmol), Lindlar's catalyst (280 mg, 80 wt. %), and quinoline (3.5 mL, 29.6 mmol) in MeOH (200 mL) in a Paar bottle was shaken in a Paar hydrogenator at 43 psi for 3 h. The mixture was filtered through Celite, washed with MeOH and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and 10% aqueous HCl. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed twice with 10% aqueous HCl and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude (Z)-olefin ***S*-7** contaminated with ~10% of the fully saturated compound as a brown oil.

To a stirring solution of the crude (Z)-olefin ***S*-7** in pyridine (1 mL) at 0°C under N_2 was slowly added p-toluenesulfonyl chloride (831 mg, 4.36 mmol) in pyridine (1 mL). The reaction mixture was allowed to warm to room temperature slowly and then stirred overnight. The reaction mixture was poured into an Erlenmeyer flask containing ice and 10% aqueous HCl, using CH_2Cl_2 to aid in the transfer, and stirred until it reached room temperature. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed three times with 10% aqueous HCl, once with water, and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude tosylate as an orange oil.

To a stirring solution of the crude tosylate in DMF (3.7 mL) was added NaN_3 (291 mg, 4.48 mmol). After stirring overnight, the reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded the azide as a clear oil which was used without any further purification.

To a stirring solution of the azide in THF (5.9 mL) under N_2 was added PPh_3 (588 mg, 2.24 mmol). Water (0.7 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient, then 100% MeOH) afforded 102 mg (56% yield) of amine ***R*-8** as a clear thick oil. The hydrochloride salt had mp 83-84°C; $[\alpha]^{20}_D$ +20 g/mL (*c* 0.00085, MeOH); ^{1}H NMR (CD_3OD, 300 MHz) δ 7.38-7.22 (m, 5H), 6.69 (d, J = 12.0 Hz, 1H), 5.71-5.63 (m, 1H), 3.44-3.33 (m, 1H), 2.77-2.56 (m, 2H), 1.29 (d, J = 6.0 Hz, 3H); ^{13}C NMR (CD_3OD, 75 MHz) ppm 138.1, 134.1, 129.8, 129.5, 128.3, 126.5, 49.2, 34.6, 18.5; MS (ESI) $(M+1)^+$ 162.2, found 162.2 (free base); Anal. ($C_{11}H_{16}ClN \cdot 0.5H_2O$) C, H, N.

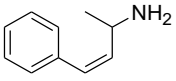


(2*E*)-1-Methyl-3-phenyl-prop-2-enylamine (10).
To a stirring solution of LAH (13.7 mL, 1M in THF, 13.7 mmol) in dry THF (17 mL) at 0°C under N_2 was slowly added alcohol **9** (500 mg, 3.42 mmol) in dry THF (3 mL). CAUTION: Bubbling results due to H_2 gas evolution. After the bubbling ceased, the reaction mixture was slowly warmed to room temperature and then refluxed for 5 h. After cooling to room temperature, then to 0°C, the reaction mixture was carefully quenched with the successive addition of 0.52 mL H_2O, 0.52 mL 3 M aqueous HCl, 1.6 mL H_2O, and 1.6 mL 3 M aqueous HCl. CAUTION: Vigorous exotherm and bubbling results due to H_2 gas evolution. After the bubbling ceased, the quenched reaction mixture was slowly warmed to room temperature, stirred for 30 min, and transferred to a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with saturated aqueous $NaHCO_3$, water, and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude (*E*)-olefin as a clear oil.

To a stirring solution of the crude (*E*)-olefin in CH_2Cl_2 (34 mL) at 0°C under N_2 was added NEt_3 (0.95 mL, 6.84 mmol) and MsCl (0.40 mL, 5.13 mmol). The reaction mixture was stirred at 0°C for 1 h and then at room temperature for 1 h after which it was quenched with saturated aqueous $NaHCO_3$ and diluted with water and CH_2Cl_2. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude mesylate as a brown oil which was used without any purification.

To a stirring solution of the crude mesylate in DMF (11 mL) was added NaN_3 (891 mg, 13.7 mmol). After stirring overnight, the reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 570 mg (96% yield) of the azide as a clear oil.

To a stirring solution of the azide (570 mg, 3.29 mmol) in THF (17.3 mL) under N_2 was added PPh_3 (1.73 g, 6.58 mmol). Water (2.1 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient, then 100% MeOH) afforded 70 mg (14% yield) of amine **11** as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.38-7.20 (m, 5H), 6.48 (d, J = 18.0 Hz, 1H), 6.20 (dd, J = 15.0, 6.0 Hz, 1H), 3.72-3.64 (m, 1H), 2.00 (br. s, 2H), 1.26 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) ppm 135.7, 128.5, 128.2, 127.3, 126.3, 49.3, 23.7; MS (ESI) $(M+1)^+$ 148.2, found 146.2. The hydrochloride salt had mp 151-152°C; Anal. ($C_{10}H_{14}ClN$) C, H, N.



(2*Z*)-1-Methyl-3-phenyl-prop-2-enylamine (11).
A mixture of alcohol **9** (100 mg, 0.684 mmol), Lindlar's catalyst (80 mg, 80 wt. %), and quinoline (1.1 mL, 9.31 mmol) in MeOH (100 mL) in a Paar bottle was shaken in a Paar hydrogenator at 43 psi for 4 h. The mixture was filtered through Celite and then concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and 10% aqueous HCl. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed twice with 10% aqueous HCl and once with brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude (*Z*)-olefin contaminated with ~10% of the fully saturated compound as a brown oil.

To a stirring solution of the crude (*Z*)-olefin in CH_2Cl_2 (6.8 mL) at 0°C under N_2 was added NEt_3 (0.19 mL, 1.36 mmol) and MsCl (0.16 mL, 2.04 mmol). The reaction mixture was stirred at 0°C for 1 h and then at room temperature for 1 h after which it was quenched with saturated aqueous $NaHCO_3$ and diluted with water and CH_2Cl_2. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with CH_2Cl_2 and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure afforded the crude mesylate as a brown oil which was used without any purification.

To a stirring solution of the crude mesylate in DMF (2.3 mL) was added NaN_3 (177 mg, 2.73 mmol). After stirring overnight, the reaction mixture was poured onto water and ether and stirred for 20 min. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with ether and the combined organic extracts were washed with water twice and brine once, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% EtOAc/hexanes) afforded 118 mg (100% yield) of the azide as a clear oil.

To a stirring solution of the azide (118 mg, 0.682 mmol) in THF (3.6 mL) under N_2 was added PPh_3 (357 mg, 1.36 mmol). Water (0.43 mL) was then added dropwise and the reaction mixture was stirred overnight. The reaction mixture was diluted with ethyl acetate and water. The biphasic mixture was partitioned in a separatory funnel. The aqueous layer was extracted twice with EtOAc and the combined organic extracts were washed with water and brine, dried over Na_2SO_4, and filtered. Concentration under reduced pressure followed by flash chromatography on silica gel (elution with 5% MeOH/CH_2Cl_2 to 20% MeOH/CH_2Cl_2 gradient, then 100% MeOH) afforded 46.2 mg (46% yield) of amine **12** as a clear oil. The hydrochloride salt had mp 149-151°C; ^{1}H NMR (CD_3OD, 300 MHz) δ 7.48-7.45 (m, 2H), 7.37-7.28 (m, 3H), 6.77 (d, J = 15.0 Hz, 1H), 6.26 (dd, J = 15.0, 6.0 Hz, 1H), 4.11-4.02 (m, 1H), 1.50 (d, J = 9.0 Hz, 3H); ^{13}C NMR (CD_3OD, 75 MHz) ppm 137.1, 135.5, 129.8, 129.6, 127.8, 126.9, 50.7, 19.6; MS (APCI) $(M+1)^+$ 148.2, found 146.3 (free base); Anal. ($C_{10}H_{14}ClN$) C, H, N.