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Supporting Information:

Applications of Aziridinium Ions. Selective Syntheses of α,β-Diamino Esters, α-Sulfanyl-β-amino Esters, β-Lactams and 1,5-Benzodiazepin-2-one

Tsung-Hsun Chuang and K. Barry Sharpless*

Department of Chemistry and the Skaggs Institute for Chemical Biology,

The Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA 92037

Experimental Section:

All commercially available chemicals were used without further purification. Reactions were monitored by TLC using pre-coated plates with a 0.2 mm layer of silica containing a fluorescent indicator (Merck Art. 5714-3). Melting points were obtained on a Thomas Hoover capillary melting apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX-400 or DRX-500 spectrometers. Chemical shifts are reported relative to $CHCl_3$ [δ_H 7.25, δ_C (central line) 77.0]. High resolution mass spectra (HRMS) were recorded by using fast atom bombardment (FAB) method in a *m*-nitrobenzyl alcohol matrix doped with NaI or CsI.

(2*R,3*R**)-Ethyl 2-hydroxy-3-morpholino-3-phenylpropionate (2a).** The epoxy ester **1** (15.3 g, 80.0 mmol) and morpholine (7.3 mL, 7.3 g, 80.0 mmol) were dissolved in ethanol (80 mL) and the mixture was heated at reflux (open to the atomosphere) for 12 h. The resulting mixture was cooled to ambient temperature and concentrated in *vacuo* to afford the crude product (21.4 g, 96%, an 87:13 mixture of **2a** and **3a**). Recrystallization from ether furnished the pure regioisomer **2a** (16.0 g, 72%) as a colorless crystalline solid. **2a**: Solid (diethyl ether), mp 89-91 °C (lit.* mp 88 °C); TLC (EtOAc/hexane (1:2)) R_f = 0.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14 (t, J = 7.2 Hz, 3 H), 2.40-2.45 (m, 2 H), 2.52-2.55 (m, 2 H), 3.09 (br s, 1 H), 3.54 (d, J = 4.4 Hz, 1 H), 3.67-3.69 (m, 4

H), 3.98-4.08 (m, 2 H), 4.72 (d, J = 4.4 Hz, 1 H), 7.24-7.29 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 51.4 (2 C), 61.4, 66.8 (2 C), 69.9, 72.1, 128.1 (2 C), 128.2, 129.1 (2 C), 135.4, 172.6; FAB-MS *m/z* (rel intensity) 280 (M^+ + 1, 35), 176 (100).

lit.* Tack, J. W.; Lehmann, J; Zymalkowski, F. *Arch. Pharm.* **1979**, *312*, 138

(2*R,3*R**)-Ethyl 2-hydroxy-3-(4-phenylpiperazino)-3-phenylpropionate (2b).** According to the procedure for the preparation of **2a**, a mixture of **2b** and **3b** (7.0 g, 99%, **2b**:**3b** = 87:13) was obtained by reaction of epoxy ester **1** (5.6 g, 20.0 mmol) and 1-phenylpiperazine (3.2 mL, 3.4 g, 21.0 mmol) in ethanol (20 mL). Recrystallization of the mixture from ether gave pure regioisomer **2b** (4.4 g, 62%). Solid (ether), mp 84-86 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.1; FAB-MS: *m/z* (rel intensity) 355 (M^+ + 1, 15), 251 (100); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, J = 7.2 Hz, 3 H), 2.60-2.66 (m, 2 H), 2.70-2.75 (m, 2 H), 3.11 (br s, 1 H), 3.18-3.20 (m, 4 H), 3.64 (d, J = 4.4 Hz, 1 H), 4.01-4.11 (m, 2 H), 4.80 (d, J = 4.4 Hz, 1 H), 6.82-6.90 (m, 3 H), 7.22-7.33 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 49.1 (2 C), 50.8 (2 C), 61.4, 70.3, 71.8, 115.9 (2 C), 119.7, 128.1 (2 C), 128.2 (2 C), 129.0, 129.1 (2 C), 135.6, 151.0, 172.6; FAB-MS *m/z* (rel intensity) 355 (M^+ + 1, 13), 251 (100); HRMS $[M + H]^+$ for $C_{21}H_{27}N_2O_3$: 355.2022, found 355.2028.

(2*R,3*R**)-Ethyl 3-diallylamino-2-hydroxy-3-phenylpropionate (2c).** According to the procedure for the preparation of **2a**, a mixture of **2c** and **3c** (27.1 g, 94%, **2c**:**3c** = 88:12) was obtained by reaction of epoxy ester **1** (19.2 g, 100.0 mmol) and diallylamine (12.9 mL, 10.2 g, 105.0 mmol) in ethanol (50 mL). Recrystallization of the mixture from ether gave pure regioisomer **2c** (18.0 g, 62%). **2c**: Solid (Et_2O), mp 72-73 °C; TLC ((EtOAc/hexane (2:1)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, J = 7.2 Hz, 3 H), 2.82 (br s, 1 H), 2.94 (dd, J = 14.4, 7.5

Hz, 2 H), 3.32 (dd, J = 14.4, 5.2 Hz, 2 H), 4.04 (d, J = 5.9 Hz, 1 H), 4.06-4.12 (m, 2 H), 4.74 (d, J = 5.9 Hz, 1 H), 5.12-5.16 (m, 4 H), 5.76-5.86 (m, 2 H), 7.28-7.31 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 52.8 (2 C), 61.3, 66.5, 71.3, 117.7 (2 C), 127.9, 128.1 (3 C), 129.2 (2 C), 135.4 (2 C), 173.1; MS *m/z* (rel intensity) 312 (M^+ + Na, 5), 290 (M^+ + 1, 100), 186 (7), 119 (18); HRMS $[M + H]^+$ for $C_{17}H_{24}NO_3$: 290.1751, found 290.1745.

(2*R,3*R**)-Ethyl 3-dibenzylamino-2-hydroxy-3-phenylpropionate (2d).** According to the procedure for the preparation of **2a**, a mixture of **2d** and **3d** (19.0 g, 97%, **2d**:**3d** = 88:12) was obtained by reaction of epoxy ester **1** (9.6 g, 50.0 mmol) and dibenzylamine (10.6 mL, 10.8 g, 55.0 mmol) in ethanol (50 mL). Recrystallization of the mixture from ether gave pure regioisomer **2d** (12.1 g, 62%). **2d**: Solid (Et_2O), mp 114-115 °C; TLC ((EtOAc/hexane (2:1)) R_f = 0.5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, J = 7.3 Hz, 3 H), 2.52 (br s, 1 H), 3.30 (d, J = 13.9 Hz, 2 H), 3.95 (d, J = 13.9 Hz, 2 H), 4.09 (d, J = 6.9 Hz, 1 H), 4.20-4.24 (m, 2 H), 4.89 (br s, 1 H), 7.25-7.43 (m, 15 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 54.5 (2 C), 61.5, 65.4, 71.9, 126.9 (2 C), 127.8, 128.1 (2 C), 128.2 (4 C), 128.7 (4 C), 129.7 (2 C), 134.5, 139.2 (2 C), 173.3; HRMS $[M + H]^+$ for $C_{25}H_{28}NO_3$: 390.2064, found 390.2081.

(2*R,3*S**)-Ethyl 3-chloro-2-morpholino-3-phenylpropionate (4a).** To a cold (0 °C) stirred solution of **2a** and **3a** (15.6 g, 55.9 mmol) and Et_3N (8.5 mL, 6.2 g, 61.5 mmol) in CH_2Cl_2 (60 mL), the MsCl (4.7 mL, 7.1 g, 61.5 mmol) was added dropwise. After the addition was completed, the reaction was allowed to warm to room temperature (ice-bath removal) and stirred for 3 h. The resulting crude reaction mixture was concentrated and the residue was taken up in EtOAc (100 mL). The organic layer was washed with water (50 mL x 2), brine (25 mL x 2), dried over Na_2SO_4 and filtered. The filtrate was concentrated and recrystallized from CH_2Cl_2/hexane to give chloro

ester **4a** (16.0 g, 96%) as a colorless solid. **4a**: Solid (CH_2Cl_2/hexane), mp 66-67 °C; TLC (EtOAc/hexane (1:2)) R_f= 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 (t, J = 7.2 Hz, 3 H), 2.36-2.41 (m, 2 H), 2.58-2.63 (m, 2 H), 3.28-3.40 (m, 4 H), 3.69 (d, J = 10.8 Hz, 1 H), 4.00-4.33 (m, 2 H), 5.14 (d, J = 10.8 Hz, 1 H), 7.30-7.39 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 50.0 (2 C), 59.1, 60.8, 67.0 (2 C), 73.5, 127.7 (2 C), 128.3 (2 C), 128.5, 138.4, 168.5; FAB-MS *m/z* (rel intensity) 298 (M^+ + 1, 40), 262 (M^+ – Cl, 40), 172 (81); HRMS $[M + H]^+$ for $C_{15}H_{21}ClNO_3$: 298.1204, found 298.1196.

(2*R,3*S**)-Ethyl 3-chloro-3-phenyl-2-(4-phenylpiperazino)propionate (4b).** According to the procedure for the preparation of **4a**, **4b** (8.8 g, 99%) was obtained by reaction of **2b** and **3b** (8.4 g, 23.7 mmol), Et_3N (2.5 g, 3.5 mL, 25.0 mmol) and MsCl (2.9 g, 1.9 mL, 25.0 mmol) in CH_2Cl_2 (30 mL). **4b**: Solid (CH_2Cl_2/hexane), mp 82-84 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (t, J = 7.2 Hz, 3 H), 2.54-2.58 (m, 2 H), 2.77-2.89 (m, 6 H), 3.80 (d, J = 11.0 Hz, 1 H), 4.27-4.34 (m, 2 H), 5.20 (d, J = 11.0 Hz, 1 H), 6.78-6.82 (m, 3 H), 7.17-7.37 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 49.3 (2 C), 49.6 (2 C), 59.3, 60.8, 73.3, 115.9 (2 C), 119.7, 127.7 (2 C), 128.3 (2 C), 128.5, 128.9 (2 C), 138.5, 151.0, 168.6; FAB-MS: *m/z* (rel intensity) 373 (M^+, 0.1), 337 (M^+ – Cl, 100); HRMS $[M + H]^+$ for $C_{21}H_{26}ClN_2O_2$: 373.1677, found 373.1682.

(2*R,3*S**)-Ethyl 3-chloro-2-diallylamino-3-phenylpropionate (4c).** According to the procedure for the preparation of **4a**, **4c** was obtained by reaction of **2c** and **3c** (11.6 g, 40.0 mmol), Et_3N (4.5 g, 6.1 mL, 44.0 mmol) and MsCl (5.5 g, 3.7 mL, 48.0 mmol) in CH_2Cl_2 (40 mL). Recrystallization of the mixture from CH_2Cl_2/hexane gave pure regioisomer **4c** (12.3 g, 99%). **4c**: Solid (CH_2Cl_2/hexane), mp 50-51 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$)

δ 1.34 (t, J = 7.0 Hz, 3 H), 2.85 (dd, J = 12.9, 7.8 Hz, 2 H), 3.26 (br d, J = 12.9 Hz, 2 H), 3.98 (d, J = 10.5 Hz, 1 H), 4.24-4.33 (m, 2 H), 4.98-5.04 (m, 4 H), 5.17 (d, J = 10.5 Hz, 1 H), 5.20-5.40 (m, 2 H), 7.29-7.33 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 53.3 (2 C), 59.9, 60.6, 67.5, 117.9 (2 C), 128.1, 128.2 (2 C), 128.4 (2 C), 135.1, 138.6 (2 C), 172.0; MS *m/z* (rel intensity) 272 (M^+ – Cl, 100); HRMS $[M + H]^+$ for $C_{17}H_{22}NO_2$: 272.1645, found 272.1643.

(2*R,3*S**)-Ethyl 3-chloro-2-dibenzylamino-3-phenylpropionate (4d).** According to the procedure for the preparation of **4a**, **4d** was obtained by reaction of **2d** and **3d** (9.7 g, 25.0 mmol), Et_3N (2.8 g, 3.8 mL, 27.5 mmol) and MsCl (3.4 g, 2.3 mL, 30.0 mmol) in CH_2Cl_2 (50 mL). Recrystallization of the mixture from ether gave pure regioisomer **4d** (9.6 g, 94%). **4d**: Solid (ether), mp 79-80 °C; TLC ((EtOAc/hexane (1:9)) R_f = 0.5; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.44 (t, J = 7.0 Hz, 3 H), 3.28 (d, J = 13.6 Hz, 2 H), 3.79 (d, J = 13.6 Hz, 2 H), 3.92 (d, J = 11.0 Hz, 1 H), 4.35-4.47 (m, 2 H), 5.27 (d, J = 11.0 Hz, 1 H), 6.88-7.38 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 54.5 (2 C), 60.0, 60.7, 66.5, 127.1 (2 C), 128.0 (4 C), 128.3 (2 C), 128.6, 128.7 (2 C), 129.0 (4 C), 137.9 (3 C), 169.3; MS *m/z* (rel intensity) 372 (M^+ – Cl, 20); HRMS $[M + H]^+$ for $C_{25}H_{27}ClNO_2$: 408.1725, found 408.1712.

General Procedure for the Reaction of Chloro Esters 4 with Nucleophiles. (eq. 1, Table 2). To a stirred suspension of chloro ester **4** (1.0 mmol) and K_2CO_3 (138 mg, 1.0 mmol) in CH_3CN (2 mL), the nucleophile (1.2 mmol) was added at room temperature and the mixture was heated at 60 °C (open to air) for 12 h. The resulting mixture was then cooled to ambient temperature, filtered through a short plug of silica gel (3 cm in a pipette), which was washed with 10 mL of EtOAc. The combined filtrates were concentrated to give the products as the indicated (Table 2) mixture of regioisomers **5** and **6**. Product mixtures d, e, g, m, n, o, and p remained as oils, whereas a, b, c, f, h, i, j, k, l, q and r crystallized. Recrystallization of these latter product mixtures from

CH_2Cl_2/hexane or ether gave regioisomerically pure samples of **5a-c**, **5f**, **5h**, **5i**, **5j**, **5k**, **5l**, **5q** and **5r**.

(2*S,3*S**)-Ethyl 3-[(1,1-dimethylethyl)amino]-2-morpholino-3-phenylpropionate (5a):** As described in the general procedure, **5a** and **6a** (280.0 mg, 84%) were obtained from **4a** (297.0 mg) and **13** (87.7 mg). **5a**: Solid (CH_2Cl_2/hexane), mp 69-70 °C; TLC (EtOAc/hexane (1:2)) R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (s, 9 H), 1.27 (t, J = 7.0 Hz, 3 H), 2.37-2.42 (m, 2 H), 2.59-2.64 (m, 2 H), 3.26-3.29 (m, 2 H), 3.12 (d, J = 10.5 Hz, 1 H), 3.27-3.39 (m, 4 H), 4.09-4.20 (m, 3 H), 7.16-7.27 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 30.4 (3 C), 50.3 (2 C), 51.0, 55.9, 59.9, 67.2 (2 C), 75.3, 126.5, 127.1 (2 C), 128.0 (2 C), 145.1, 170.5; FAB-MS *m/z* (rel intensity) 335 (M^+ + 1, 23), 162 (100); HRMS $[M + H]^+$ for $C_{19}H_{31}N_2O_3$: 335.2335, found 335.2330.

(2*S,3*S**)-Ethyl 3-[4-(4-fluorophenyl)piperazino]-2-morpholino-3-phenylpropionate (5b).** As described in the general procedure, **5b** and **6b** (366.0 mg, 83%) were obtained from **4a** (297.0 mg) and **14** (216.2 mg). **5b:** Solid, mp 241-242 °C; TLC ((EtOAc/hexane (1:4)) R_f = 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32 (t, J = 7.0 Hz, 3 H), 2.30-2.40 (m, 2 H), 2.49-2.54 (m, 2 H), 2.59-2.64 (m, 2 H), 2.68-2.73 (m, 2 H), 2.92-3.05 (m, 4 H), 3.27-3.32 (m, 2 H), 3.42-3.47 (m, 2 H), 3.89 (d, J = 11.8 Hz, 1 H), 4.13 (d, J = 11.8 Hz, 1 H), 4.22-4.24 (m, 2 H), 6.73-6.77 (m, 2 H), 6.86-6.89 (m, 2 H), 6.91-7.15 (m, 2 H), 7.24-7.40 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 49.4 (2 C), 49.6 (2 C), 50.6 (2 C), 59.9, 67.2 (2 C), 67.3, 67.9, 115.2, 115.4, 117.6, 117.7, 127.4, 127.6 (2 C), 129.3 (2 C), 133.1, 148.8, 158.2, 170.9; FAB-MS *m/z* (rel intensity) 442 (M^+ + 1, 25), 269 (100); HRMS $[M + H]^+$ for $C_{25}H_{33}N_3O_3$: 442.2506, found 442.2514.

(2*S,3*S**)-Ethyl 2-morpholino-3-phenyl-3-piperazinopropionate (5c).** As described in the general procedure, **5c** and **6c** (257.0 mg, 74%) were obtained from **4a** (297.0 mg) and **15** (560.0

mg, 4 mmol). **5c:** Solid (EtOH), mp 97-99 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.05; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (t, J = 7.3 Hz, 3 H), 2.05-2.20 (m, 2 H), 2.46-2.77 (m, 11 H), 3.25-3.30 (m, 2 H), 3.40-3.45 (m, 2 H), 3.84 (d, J = 11.8 Hz, 1 H), 4.01 (d, J = 11.8 Hz, 1 H), 4.25 (q, J = 7.2 Hz, 2 H), 7.08-7.10 (m, 2 H), 7.25-7.32 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 46.5 (2 C), 49.6 (2 C), 50.2 (2 C), 59.8, 67.2 (2 C), 67.7, 68.0, 127.2, 127.5 (2 C), 129.3 (2 C), 133.4, 171.0; FAB-MS *m/z* (rel intensity) 348 (M^+ + 1, 100), 262 (52); HRMS $[M + H]^+$ for $C_{19}H_{30}N_3O_3$: 348.2287, found 348.2284.

(2*S,3*S**)-Ethyl 2-morpholino-3-phenyl-3-(2-propynylamino)propionate (5d).** As described in the general procedure, **5d** (278.0 mg, 88%) was obtained from **4a** (297.0 mg) and **16** (66.0 mg). **5d:** An oil; TLC ((EtOAc/hexane (1:2)) R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, J = 7.2 Hz, 3 H), 2.14 (br s, 1 H), 2.44-2.49 (m, 2 H), 2.58-2.63 (m, 2 H), 3.06 (dd, J = 17.2, 2.4 Hz, 1 H), 3.25 (d, J = 8.6 Hz, 1 H), 3.36 (dd, J = 17.2, 2.4 Hz, 1 H), 3.46-3.48 (m, 4 H), 4.03-4.08 (m, 3 H), 4.25 (d, J = 8.6 Hz, 1 H), 7.25-7.30 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 35.6, 50.5 (2 C), 59.2, 60.3, 67.0 (2 C), 71.3, 73.5, 81.7, 127.4, 127.8 (2 C), 128.2 (2 C), 139.5, 170.3; FAB-MS *m/z* (rel intensity) 317 (M^+ + 1, 100), 144 (45); HRMS $[M + H]^+$ for $C_{18}H_{25}N_2O_3$: 317.1865, found 317.1863.

(2*S,3*S**)-Ethyl 3-(3-ethynylanilino)-2-morpholino-3-phenylpropionate (5e).** As described in the general procedure, **5e** and **6e** (309.9 mg, 82%) were obtained from **4a** (297.0 mg) and **17** (117.0 mg). **5e:** An oil; TLC ((EtOAc/hexane (1:2)) R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.2 Hz, 3 H), 2.51-2.59 (m, 4 H), 3.01 (s, 1 H), 3.29 (d, J = 5.9 Hz, 1 H), 3.65-3.68 (m, 4 H), 3.81-3.95 (m, 2 H), 4.72 (d, J = 5.9 Hz, 1 H), 6.49-7.30 (m, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 50.9 (2 C), 56.0, 60.5, 66.6 (2 C), 73.7, 76.3, 84.0, 113.9, 116.2, 121.2, 122.4, 126.6 (2 C),

127.5, 128.4 (2 C), 128.8, 138.9, 146.7, 170.2; FAB-MS *m/z* (rel intensity) 379 (M^+ + 1, 31), 206 (100); HRMS $[M + H]^+$ for $C_{23}H_{27}N_2O_3$: 379.2022, found 379.2018.

(2*S,3*S**)-Ethyl 2-morpholino-3-phenyl-3-pyrazolopropionate (5f).** As described in the general procedure, **5f** and **6f** (237.0 mg, 72%) were obtained from **4a** (297.0 mg) and **18** (68.0 mg). **5f:** Solid (EtOAc/hexane), mp 122-123 °C; TLC ((EtOAc/Hexane (1:2)) R_f = 0.3; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (t, *J* = 7.2 Hz, 3 H), 2.41-2.46 (m, 2 H), 2.74-2.79 (m, 2 H), 3.38-3.48 (m, 4 H), 4.03-4.14 (m, 2 H), 4.39 (d, *J* = 11.3 Hz, 1 H), 5.57 (d, *J* = 11.3 Hz, 1 H), 6.17 (dd, *J* = 2.2, 1.9 Hz, 1 H), 7.25-7.39 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 50.2 (2 C), 60.5, 63.5, 67.1 (2 C), 70.4, 105.5, 127.7 (2 C), 127.9, 128.1 (2 C), 129.8, 138.3, 139.3, 168.8; MS *m/z* (rel intensity) 330 (M^+ + 1, 10), 262 (100), 176; HRMS $[M + H]^+$ for $C_{18}H_{24}N_3O_3$: 330.1818, found 330.1814.

(2*S,3*S**)-Ethyl 3-(2-aminoanilino)-2-morpholino-3-phenylpropionate (5g).** As described in the general procedure, **5g** (324.5 mg, 83%) was obtained from **4a** (297.0 mg) and **19** (434.0 mg, 4 mmol). **5g:** An oil; TLC ((EtOAc/hexane (1:2)) R_f = 0.05; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (t, *J* = 7.3 Hz, 3 H), 2.55-2.58 (m, 4 H), 3.36 (d, *J* = 6.4 Hz, 1 H), 3.62-3.63 (m, 4 H), 3.88-4.02 (m, 2 H), 4.73 (d, *J* = 6.4 Hz, 1 H), 6.25 (dd, *J* = 7.8, 1.3 Hz, 1 H), 6.53-6.70 (m, 3 H), 7.22-7.23 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 50.9 (2 C), 56.5, 60.5, 66.9 (2 C), 73.9, 114.0, 116.2, 119.1, 119.9, 126.8 (2 C), 127.4, 128.3 (2 C), 135.2, 135.5, 139.6, 170.4; MS *m/z* (rel intensity) 356 (M^+ + 1, 11), 248 (100), 197 (10), 160 (14); HRMS $[M + Na]^+$ for $C_{21}H_{27}N_3NaO_3$: 392.1950, found 392.1960.

(2*S,3*S**)-Ethyl 3-(2-hydroxyanilino)-2-morpholino-3-phenylpropionate (5h).** As described in the general procedure, **5h** (251.0 mg, 68%) was obtained from **4a** (297.0 mg) and **20** (131.0 mg).

5h: Solid (EtOAc/hexane), mp 114-115 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.3; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.07 (t, J = 7.0 Hz, 3 H), 2.37-2.41 (m, 2 H), 2.58-2.62 (m, 2 H), 3.30-3.38 (m, 4 H), 3.60 (d, J = 8.8 Hz, 1 H), 3.94-4.08 (m, 2 H), 4.80 (dd, J = 8.8, 8.8 Hz, 1 H), 5.32 (d, J = 8.8 Hz, 1 H), 6.32-6.61 (m, 4 H), 7.15-7.42 (m, 5 H), 9.24 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 51.0 (2 C), 58.3, 60.9, 66.7 (2 C), 73.5, 115.1, 116.6, 120.0, 120.6, 126.8 (2 C), 127.4, 128.4 (2 C), 135.1, 139.7, 146.4, 170.9; MS *m/z* (rel intensity) 371 (M^+ + 1, 9), 262 (100), 198 (2), 174 (4); HRMS $[M + H]^+$ for $C_{21}H_{27}N_2O_4$: 371.1971, found 371.1965.

(2*R,3*R**)-Ethyl 3-morpholino-2-phenylsulfanyl-3-phenylpropionate (5i).** As described in the general procedure, **5i** and **6i** (367.3 mg, 99%) were obtained from **4a** (297.0 mg) and **21** (132.2 mg). **5i:** Solid (CH_2Cl_2/hexane), mp 63-65 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J = 7.2 Hz, 3 H), 2.15-2.30 (m, 2 H), 2.46-2.60 (m, 2 H), 3.52-3.60 (m, 4 H), 3.96 (d, J = 12.4 Hz, 1 H), 4.18-4.23 (m, 2 H), 4.28 (d, J = 12.4 Hz, 1 H), 7.07-7.27 (m, 10 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 49.5 (2 C), 52.7, 61.0, 67.2 (2 C), 70.6, 127.4, 127.8, 128.0 (2 C), 128.7 (2 C), 129.0, 129.2 (2 C), 132.3, 133.0 (2 C), 171.6; MS *m/z* (rel intensity) 372 (M^+ + 1, 25), 285 (25), 262 (12), 211 (100); HRMS $[M + H]^+$ for $C_{21}H_{26}NO_3S$: 372.1633, found 372.1628.

(2*R,3*R**)-Ethyl 2-[(1,1-dimethylethyl)sulfanyl]-3-morpholino-3-phenylpropionate (5j).** As described in the general procedure, **5j** and **6j** (347.5 mg, 99%) were obtained from **4a** (297.0 mg) and **22** (108.2 mg). **5j:** Solid (CH_2Cl_2/hexane), mp 118-119 °C; TLC ((EtOAc/hexane (1:2)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (S, 9 H), 1.34 (t, J = 7.0 Hz, 3 H), 2.10-2.28 (m, 2 H), 2.46-2.58 (m, 2 H), 3.51-3.61 (m, 4 H), 3.77 (d, J = 12.4 Hz, 1 H), 4.05 (d, J = 12.4 Hz, 1 H), 4.19-4.35 (m, 2 H), 7.08-7.36 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 30.9 (3 C), 31.5, 43.9,

46.9, 67.2 (2 C), 70.7, 127.8 (3 C), 129.0 (2 C), 132.7, 173.8; MS *m/z* (rel intensity) 352 (M^+ + 1, 60), 262 (30), 209 (2 C), 135 (7); HRMS $[M + H]^+$ for $C_{19}H_{30}NO_3S$: 352.1946, found 352.1942.

(2*S,3*S**)-Ethyl 3-butylamino-3-phenyl-2-(4-phenylpiperazino)propionate (5k).** As described in the general procedure, **5k** and **6k** (355.8 mg, 87%) were obtained from **4b** (373.0 mg) and **8** (87.7 mg). **5k:** Solid (EtOAc/hexane), mp 71-73 °C; TLC ((EtOAc/hexane (1:4)) R_f = 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.2 Hz, 3 H), 1.26-1.36 (m, 7 H), 2.34-2.48 (m, 2 H), 2.56-2.61 (m, 2 H), 2.77-2.94 (m, 6 H), 3.38 (d, *J* = 9.7 Hz, 1 H), 4.00 (d, *J* = 9.7 Hz, 1 H), 4.18-4.22 (m, 2 H), 6.79-6.83 (m, 3 H), 7.17-7.28 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 14.5, 20.2, 32.0, 47.1, 49.3 (2 C), 49.8 (2 C), 60.2, 61.5, 73.2, 115.8 (2 C), 119.5, 127.0, 127.5 (2 C), 128.0 (2 C), 128.9 (2 C), 141.4, 151.2, 170.8; FAB-MS *m/z* (rel intensity) 410 (M^+ + 1, 100), 162 (93); HRMS $[M + H]^+$ for $C_{25}H_{36}N_3O_2$: 410.2808, found 410.2816.

(2*S,3*S**)-Ethyl 3-[(1,1-dimethylethyl)amino]-3-phenyl-2-(4-phenylpiperazino)propionate (5l).** As described in the general procedure, **5l** and **6l** (368.0 mg, 90%) were obtained from **4b** (373.0 mg) and **13** (87.7 mg). **5l:** Solid (EtOAc/hexane), mp 42-44 °C; TLC ((EtOAc/hexane (1:4)) R_f = 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 9 H), 1.31 (t, *J* = 7.0 Hz, 3 H), 2.55-2.59 (m, 2 H), 2.78-2.90 (m, 6 H), 3.25 (d, *J* = 10.2 Hz, 1 H), 4.15-4.20 (m, 3 H), 6.79-6.81 (m, 3 H), 7.17-7.23 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 30.4 (3 C), 49.3 (2 C), 49.7 (2 C), 51.2, 56.1, 59.9, 74.9, 115.8 (2 C), 119.4, 126.5, 127.1 (2 C), 127.9 (2 C), 128.8 (2 C), 145.1, 151.3, 170.5; FAB-MS *m/z* (rel intensity) 410 (M^+ + 1, 100), 337 (20), 249 (28), 162 (93); HRMS $[M + H]^+$ for $C_{25}H_{36}N_3O_2$: 410.2808, found 410.2820.

(2*S,3*S**)-Ethyl 3-phenyl-2-(4-phenylpiperazino)-3-(2-propynylamino)propionate (5m).** As described in the general procedure, **5m** and **6m** (375.4 mg, 96%) were obtained from **4b** (373.0 mg) and **16** (66.0 mg). **5m:** An oil; TLC ((EtOAc/hexane (1:4)) R_f = 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, *J* = 7.2 Hz, 3 H), 1.90 (br s, 1 H), 2.18 (t, *J* = 2.4 Hz, 1 H), 2.60-2.65 (m, 2 H), 2.78-2.83 (m, 2 H), 2.95-2.98 (m, 4 H), 3.10 (dd, *J* = 17.0, 2.4 Hz, 1 H), 3.36 (d, *J* = 8.6 Hz, 1 H), 3.39 (dd, *J* = 17.0, 2.4 Hz, 1 H), 4.08-4.18 (m, 2 H), 4.31 (d, *J* = 8.6 Hz, 1 H), 6.81-6.85 (m, 3 H), 7.19-7.30 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 35.6, 49.2 (2 C), 50.0 (2 C), 59.5, 60.3, 71.3, 81.7, 115.8 (2 C), 119.5, 127.3, 127.8 (2 C), 128.1 (2 C), 128.9 (2 C), 139.6, 151.1, 170.4; FAB-MS *m/z* (rel intensity) 392 (M^+ + 1, 35), 337 (24), 249 (22), 144 (100); HRMS $[M + H]^+$ for $C_{24}H_{30}N_3O_2$: 392.2338, found 392.2334.

(2*S,3*S**)-Ethyl 3-butylamino-2-diallylamino-3-phenylpropionate (5n).** As described in the general procedure, **5n** (340.5 mg, 99%) was obtained from **4c** (308.0 mg) and **8** (87.7 mg). **5n:** An oil; TLC ((EtOAc/hexane (1:2)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.2 Hz, 3 H), 1.19-1.33 (m, 7 H), 2.32-2.40 (m, 2 H), 2.82 (dd, *J* = 14.4, 8.3 Hz, 2 H), 3.29 (br d, *J* = 14.4 Hz, 2 H), 3.59 (d, *J* = 10.5 Hz, 1 H), 3.93 (d, *J* = 10.5 Hz, 1 H), 4.16-4.26 (m, 2 H), 4.94-4.98 (m, 4 H), 5.28-5.38 (m, 2 H), 7.19-7.29 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 14.5, 20.2, 32.0, 47.1, 53.4 (2 C), 60.0, 62.4, 67.0, 117.0 (2 C), 126.9, 127.8 (2 C), 128.0 (2 C), 129.1, 136.1 (2 C), 172.0; MS *m/z* (rel intensity) 345 (M^+ + 1, 56), 272 (100), 248 (13), 184 (82), 162 (27); HRMS $[M + H]^+$ for $C_{21}H_{33}N_2O_2$: 345.2542, found 345.2537.

(2*S,3*S**)-Ethyl 2-diallylamino-3-[(1,1-dimethylethyl)amino]-3-phenylpropionate (5o).** As described in the general procedure, **5o** and **6o** (340.5 mg, 99%) were obtained from **4c** (308.0 mg) and **13** (87.7 mg). **5o:** An oil; TLC ((EtOAc/hexane (1:2)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ

0.88 (s, 9 H), 1.31 (t, J = 7.2 Hz, 3 H), 2.77 (dd, J = 14.5, 8.1 Hz, 2 H), 3.29 (br d, J = 14.5 Hz, 2 H), 3.42 (d, J = 10.5 Hz, 1 H), 4.09-4.25 (m, 3 H), 4.91-4.95 (m, 4 H), 5.26-5.36 (m, 2 H), 7.16-7.31 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.6, 30.4 (3 C), 51.2, 53.2 (2 C), 56.8, 59.7, 68.9, 116.8 (2 C), 126.4, 127.5 (2 C), 127.8 (2 C), 135.3, 136.3 (2 C), 171.6; MS *m/z* (rel intensity) 345 (M^+ + 1, 62), 272 (100), 184 (51), 162 (38); HRMS $[M + H]^+$ for $C_{21}H_{33}N_2O_2$: 345.2542, found 345.2540.

(2*S,3*S**)-Ethyl 2-diallylamino-3-phenyl-3-(2-propynylamino)propionate (5p).** As described in the general procedure, **5p** and **6p** (319.5 mg, 98%) were obtained from **4c** (308.0 mg) and **16** (66.0 mg). **5p:** An oil; TLC ((EtOAc/hexane (1:2)) R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (t, J = 7.0 Hz, 3 H), 1.90 (br s, 1 H), 2.16 (t, J = 2.4 Hz, 1 H), 2.86 (dd, J = 14.3, 8.3 Hz, 2 H), 3.04 (dd, J = 16.7, 2.4 Hz, 1 H), 3.24-3.31 (m, 3 H), 3.65 (d, J = 9.7 Hz, 1 H), 4.16-4.28 (m, 3 H), 4.95-4.99 (m, 4 H), 5.28-5.38 (m, 2 H), 7.23-7.32 (m, 5 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.5, 35.9, 53.5 (2 C), 60.3, 60.8, 66.6, 71.4, 87.8, 117.2 (2 C), 127.4, 127.9 (2 C), 128.5 (2 C), 135.9 (2 C), 140.0, 171.8; MS *m/z* (rel intensity) 327 (M^+ + 1, 12), 272 (100), 184 (22); HRMS $[M + H]^+$ for $C_{20}H_{27}N_2O_2$: 327.2073, found 327.2068.

(2*S,3*S**)-Ethyl 3-anilino-2-dibenzylamino-3-phenylpropionate (5q).** As described in the general procedure, **5q** and **6q** (445.4 mg, 99%) were obtained from **4d** (407.0 mg) and **11** (111.7 mg). **5q:** Solid (EtOAc/hexane), mp 112-114 °C; TLC ((EtOAc/hexane (1:9)) R_f = 0.4;^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, J = 7.0 Hz, 3 H), 3.41 (d, J = 13.8 Hz, 2 H), 3.65 (d, J = 10.0 Hz, 1 H), 3.94 (d, J = 13.8 Hz, 2 H), 4.15-4.25 (m, 2 H), 4.95 (d, J = 10.0 Hz, 1 H), 6.51-6.57 (m, 3 H), 6.97-7.21 (m, 17 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.4, 54.6 (2 C), 57.7, 60.3, 66.1, 114.0 (2 C),

117.8, 126.9 (2 C), 127.3, 127.6 (2 C), 127.9 (4 C), 128.1 (2 C), 128.8 (4 C), 128.9 (2 C), 138.5 (2 C), 140.0, 146.5, 170.5; HRMS $[M + H]^+$ for $C_{31}H_{33}N_2O_2$: 465.2542, found 465.2537.

(2*S,3*S**)-Ethyl 2-dibenzylamino-3-[(1,1-dimethylethyl)amino]-3-phenylpropionate (5r).** As described in the general procedure, **5r** and **6r** (426.2 mg, 96%) were obtained from **4d** (407.0 mg) and **13** (87.7 mg). **5r:** Solid (EtOAc/hexane), mp 87-89 °C; TLC ((EtOAc/hexane (1:9)) R_f = 0.4;^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 9 H), 1.39 (t, J = 7.0 Hz, 3 H), 3.27 (d, J = 13.8 Hz, 2 H), 3.37 (d, J = 10.8 Hz, 1 H), 3.87 (d, J = 13.8 Hz, 2 H), 4.24-4.30 (m, 3 H), 6.85-6.88 (m, 4 H), 6.98-7.26 (m, 11 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.7, 30.3 (3 C), 51.2, 54.5 (2 C), 56.5, 59.7, 67.9, 126.7 (3 C), 127.8 (5 C), 128.0 (3 C), 128.8 (4 C), 138.9 (2 C), 144.5, 171.2.1; MS *m/z* (rel intensity) 445 (M^+ + 1, 100), 372 (45), 284 (50), 162 (7); HRMS $[M + H]^+$ for $C_{29}H_{37}N_2O_2$: 445.2855, found 445.2852.

(3*S,4*S**)-*N*-Butyl-3-morpholino-4-phenylazetidin-2-one (24a).** To a cold (0 °C) solution of **5a** (0.1 g, 0.3 mmol) in THF (2 mL) was added MeMgBr (0.2 mL of 3.0 M solution in ether, 0.6 mmol) dropwise. The resulting solution was stirred at room temperature for 24 h and then quenched by the addition of saturated aqueous NH_4Cl (1 mL). The mixture was extracted with CH_2Cl_2 (10 mL x 2) and the combined organic layers was washed with water (5 mL x 2), brine (5 mL x 2), dried over Na_2SO_4, and concentrated. The residue was filtered through a short plug of silica gel (2 cm in a pipette), which was washed with 10 mL of EtOAc. The combined filtrates were concentrated to give azetidin-2-one **24a** (80.0 mg, 88%). **24a:** Solid (EtOAc/hexane), mp 86-88 °C; TLC ((EtOAc/hexane (1:1)) R_f = 0.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (m, 9 H), 2.60-2.70 (m, 4 H), 3.55 (d, J = 1.8 Hz, 1 H), 3.71-3.73 (m, 4 H), 4.64 (d, J = 1.8 Hz, 1 H), 7.28-7.35 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0 (3 C), 50.3 (2 C), 54.6, 56.8, 66.4 (2 C), 80.1, 126.1

(2 C), 128.0, 128.8 (2 C), 140.2, 167.1; MS *m/z* (rel intensity) 311 (M^+ + Na, 21), 289 (M^+ + 1, 100), 162 (7); HRMS $[M + H]^+$ for $C_{17}H_{25}N_2O_2$: 289.1916, found 289.1918.

(3*S,4*S**) 3-Morpholino-4-phenyl-*N*-(2-propynyl)azetidin-2-one (24b).** According to the procedure for the preparation of **24a**, **24b** (121.0 mg, 90%) was obtained by reaction of **5d** (158.0 mg, 0.5 mmol) and MeMgBr (0.4 mL of 3.0 M solution in ether, 1.2 mmol) in THF (2 mL). **24b:** An oil; TLC ((EtOAc/hexane (1:1)) R_f = 0.2; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (t, *J* = 2.5 Hz, 1 H), 2.65-2.75 (m, 4 H), 3.08 (d, *J* = 1.9 Hz, 1 H), 3.56 (dd, *J* = 17.8, 2.5 Hz, 1 H), 3.72-3.77 (m, 4 H), 4.38 (dd, *J* = 17.8, 2.5 Hz, 1 H), 4.80 (d, *J* = 1.9 Hz, 1 H), 7.28-7.36 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.6, 50.3 (2 C), 57.4, 66.4 (2 C), 72.6, 76.2, 81.8, 126.2 (2 C), 128.4, 129.0 (2 C), 136.7, 166.6; MS *m/z* (rel intensity) 293 (M^+ + Na, 28), 271 (M^+ + 1, 18), 144 (100), 128 (6); HRMS $[M + H]^+$ for $C_{16}H_{19}N_2O_2$: 271.1446, found 271.1457.

(3*S,4*S**)-*N*-Butyl-4-phenyl-3-(4-phenylpiperazino)azetidin-2-one (24c).** According to the procedure for the preparation of **24a**, **24c** (180.0 mg, 99%) was obtained by reaction of **5m** (205.0 mg, 0.5 mmol) and MeMgBr (0.3 mL of 3.0 M solution in ether, 0.9 mmol) in THF (2 mL). **24c:** Solid (EtOAc/hexane), mp 78-80 °C; TLC ((EtOAc/hexane (1:1)) R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.2 Hz, 3 H), 1.23-1.48 (m, 4 H), 2.78-2.86 (s, 5 H), 3.21-3.23 (m, 4 H), 3.50-3.57 (m, 1 H), 3.78 (d, *J* = 1.6 Hz, 1 H), 4.69 (d, *J* = 1.6 Hz, 1 H), 6.86-7.39 (m, 10 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 20.0, 29.5, 39.8, 48.8 (2 C), 49.9 (2 C), 57.4, 81.5, 116.1 (2 C), 119.8, 126.1 (2 C), 128.0, 129.0 (4 C), 137.3, 151.0, 167.0; MS *m/z* (rel intensity) 386 (M^+ + Na, 32), 364 (M^+ + 1, 100), 162 (15); HRMS $[M + H]^+$ for $C_{23}H_{30}N_3O$: 364.2389, found 364.2406.

(3*S,4*S**)-2-Morpholino-3-phenyl-1,5-benzodiazepin-2-one (25).** Method 1: To a cold (0 °C) solution of **5a** (120.0 mg, 0.3 mmol) in THF (2 mL) was added MeMgBr (0.2 mL of 3.0 M solution in ether, 0.6 mmol) dropwise. The resulting solution was stirred at room temperature for 24 h and then quenched by the addition of saturated aqueous NH_4Cl (1 mL). The mixture was extracted with CH_2Cl_2 (10 mL x 2) and the combined organic layers was washed with water (5 mL x 2), brine (5 mL x 2), dried over Na_2SO_4, and concentrated. The residue was filtered through a short plug of silica gel (2 cm in a pipette), which was washed with 10 mL of EtOAc. The combined filtrates were concentrated and the residue was rescrystallized from EtOAc/hexane to give **25** (75.0 mg, 73%). Method 2: Sodium hydride (80.0 mg, 2.0 mmol, 60% dispersion in mineral oil) was added to a 2 mL of DMSO solution at 0 °C under Ar. The resulting mixture was warmed to room temperature (ice bath removal) and **5g** (0.3 g, 0.8 mmol) in DMSO (1 mL) was added. After stirring at room temperature for1 h, the mixture was poured into an ice water (5 mL). The mixture was acidified by HOAc and extracted with CH_2Cl_2 (10 mL x 3). The combined extracts were washed with brine (10 mL x 3), dried over Na_2SO_4, and concentrated. The residue was rescrystallized from EtOAc/hexane to give **25** (195.0 mg, 60%). **25:** Solid (EtOAc/hexane), mp 165-167 °C; TLC ((EtOAc/hexane (2:1)) R_f = 0.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.70-2.72 (m, 4 H), 3.40-3.42 (m, 4 H), 3.63 (d, J = 8.6 Hz, 1 H), 4.81 (d, J = 8.6 Hz, 1 H), 6.68-6.98 (m, 4 H), 7.25-7.33 (m, 5 H), 8.01 (br s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.2 (2 C), 63.5, 67.1 (2 C), 72.0, 120.3, 121.1, 121.3, 125.3, 126.5 (2 C), 127.0, 127.9, 128.6 (2 C), 138.7, 142.1, 171.9; HRMS $[M + Na]^+$ for $C_{19}H_{21}N_3NaO_2$: 346.1531, found 346.1535.