Allosteric Control of an Ionotropic Glutamate Receptor With an Optical Switch

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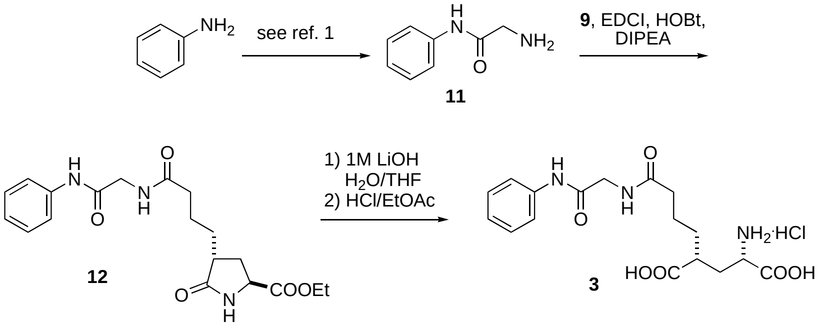
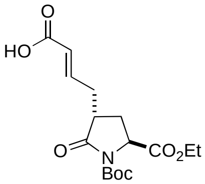
Supplementary Methods

General Information. All non-aqueous reactions were performed using flame- or oven-dried glassware under an atmosphere of dry nitrogen. Commercial reagents were used as received. Non-aqueous reagents were transferred under nitrogen with a syringe or cannula. Solutions were concentrated *in vacuo* on a Buchi rotary evaporator. Diisopropylethylamine (DIPEA) was distilled from calcium hydride prior to use. Tetrahydrofuran (THF) and methylene chloride (CH_2Cl_2) were passed through a column of activated alumina under N_2-pressure prior to use. All other reagents and solvents were used without further purification from commercial sources. Chromatographic purification of products was accomplished using flash column chromatography on ICN 60 32-64 mesh silica gel 63 (normal phase) or Waters Preparative C18 125 Å 55-105 μm silica gel (reversed phase), as indicated. Thin layer chromatography (TLC) was performed on EM Reagents 0.25 mm silica gel 60-F_{254} plates. Visualization of the developed chromatogram was performed using fluorescence quenching, $KMnO_4$, ceric ammonium molybdate (CAM), or iodine stains. IR spectra were measured with a Genesis FT-IR spectrometer by thin film or Avatar 370 FT-IR by attenuated total reflectance accessory. Optical rotations were measured using a Perkin-Elmer 241 Polarimeter at 25 ^{o}C and 589 nm. ^{1}H and ^{13}C NMR spectra were recorded in deuterated solvents on Bruker AVB-400, AVQ-400, or DRX-500 spectrometers and calibrated to the residual solvent peak. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, app = apparent, br = broad.

Scheme S1 Synthesis of tether model **3**.

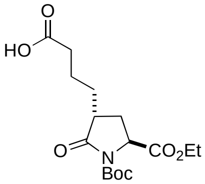


Unsaturated carboxylic acid **13**



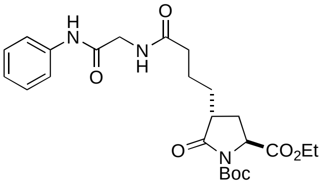
A solution of **8** (321 mg, 1.07 mmol) and freshly distilled acrylic acid (231 mg, 3.21 mmol) in CH_2Cl_2 (5.0 mL) was added directly to solid Grubbs' 2nd generation catalyst (43 mg, 0.025 mmol). The mixture was heated to reflux for 12 h. The reaction mixture was then concentrated and purified by normal phase chromatography (8.5:1.5 CH_2Cl_2:EtOAc with 1% AcOH) to yield **13** (317 mg, 92%) as a tan oil. Data for **13**: R_f 0.15 (5:4 hexanes:EtOAc with 1% AcOH); $[\alpha]_D = -21.8$ (*c* 1.0, in CH_2Cl_2); IR: 2981, 2937, 1788, 1742, 1717, 1653 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.98 (m, 1H), 5.90 (d, 1H, *J* = 15 Hz), 4.57 (d, 1H, *J* = 9 Hz), 4.24 (q, 2H, *J* = 7 Hz), 2.82 (m, 2H), 2.34 (m, 1H), 2.25 (m, 1H), 1.97 (m, 1H), 1.51 (s, 9H), 1.27 (t, 3H, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.4, 171.0, 149.2, 147.2, 123.3, 83.8, 61.8, 57.0, 40.6, 32.8, 28.1, 27.8, 20.7, 14.1; LRMS (ESI)$^-$ Calc for $C_{16}H_{22}NO_7$ $(M-H)^-$: 340.1. Found: 340.1.

Saturated carboxylic acid **9**



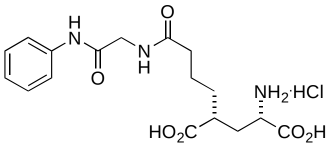
To a solution of **13** (80.0 mg, 0.234 mmol) in MeOH (10.0 mL) was added Pd/C (25 mg, 0.023 mmol). The resulting suspension was stirred at room temperature under a hydrogen atmosphere for 12 h. The suspension was then filtered through celite and concentrated to yield **9** (78 mg, 97%) as a tan oil. Data for **9**: R_f 0.15 (5:4 hexanes:EtOAc with 1% AcOH); $[\alpha]_D = -18.9$ (*c* 1.0, in CH_2Cl_2); IR: 2980, 2936, 1787, 1742, 1719 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.55 (d, 1H, *J* = 9 Hz), 4.24 (q, 2H, *J* = 7 Hz), 2.61 (m, 1H), 2.38 (m, 2H), 2.24 (m, 1H), 1.95 (m, 2H), 1.68 (m, 2H), 1.48 (s, 9H), 1.42 (m, 1H), 1.28 (t, 3H, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.7, 174.7, 171.2, 149.4, 83.5, 61.7, 57.1, 41.4, 33.6, 29.7, 28.4, 27.8, 21.9, 14.1; LRMS $(ESI)^-$ Calc for $C_{16}H_{24}NO_7$ $(M-H)^-$: 342.2. Found: 342.2.

Amide **12**



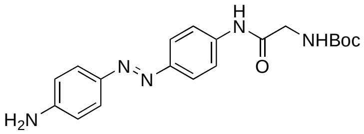
To a solution of **11** (83.7 mg, 0.316 mmol), 1-Hydroxy-benzotriazole hydrate (HOBt) (64.3 mg, 0.475 mmol), DIPEA (441 μL, 2.53 mmol), and *N*-Ethyl-*N*'-(3-dimethyldiaminopropyl)-carbodiimide · HCl (EDCI) (79.0 mg, 0.412 mmol) in CH_2Cl_2 (12.0 mL) was added a solution of **9** (130 mg, 0.380 mmol) in CH_2Cl_2 (5.0 mL). The mixture was stirred at room temperature for 12 h. The mixture was diluted with CH_2Cl_2 (60 mL) and washed with a saturated $NaHCO_3$ solution (2 × 100 mL) and brine (2 × 100 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. Purification by normal phase chromatography (95:5 CH_2Cl_2:MeOH) gave **12** (97 mg, 65%) as a white solid. Data for **12**: R_f 0.29 (95:5 CH_2Cl_2: MeOH); mp 57-59 °C; $[\alpha]_D = -14.4$ (*c* 1.0, in CH_2Cl_2); IR: 3324, 2980, 2936, 2359, 2251, 1784, 1744, 1716, 1653, 1601, 1547 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.83 (s, 1H), 7.50 (d, 2H, *J* = 8 Hz), 7.28 (t, 2H, *J* = 8 Hz), 7.06 (t, 2H, *J* = 7 Hz), 4.87 (d, 1H, 9Hz), 4.20 (q, 2H, *J* = 7 Hz), 4.08 (t, 2H, *J* = 5 Hz), 2.59 (m, 1H), 2.31 (m, 2H), 2.18 (m, 1H), 1.89 (m, 2H), 1.70 (m, 2H), 1.44 (s, 9H), 1.39 (m, 1H), 1.26 (t, 3H, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 175.3, 173.7, 171.2, 167.5, 149.3, 137.8, 128.9, 124.3, 120.0, 83.7, 61.7, 57.2, 44.4, 41.4, 35.7, 29.7, 28.3, 27.8, 22.8, 14.2; HRMS (FAB) Calc for $C_{24}H_{33}N_3O_7$ $(M)^+$: 475.231851. Found: 475.232400.

Tether model **3**



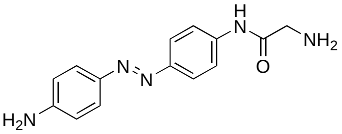
To a solution of **12** (96.0 mg, 0.200 mmol) in THF (2.0 mL) was added a 1.0 M aqueous solution of LiOH (2.0 mL). The mixture was stirred at 0 °C for 1 h and then acidified to pH 2 with a 1.0 M HCl solution and extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated to give an oily residue that was reacted with a saturated HCl solution in EtOAc for 2 h at room temperature. The resulting white solid was triturated with ethyl ether (3 × 20 mL) to yield **3** (68.5 mg, 85%). Data for **3**: mp 154-156 °C; $[\alpha]_D = -11.4$ (*c* 0.7, in H_2O); IR: 2933, 1709, 1598, 1544 cm^{-1}; ^1H NMR (D_2O, 500 MHz) δ 7.30 (m, 4H), 7.13 (m, 1H), 3.92 (s, 2H), 3.87 (m, 1H), 2.58 (m, 1H), 2.26 (m, 2H), 2.21 (m, 1H), 1.85 (m, 1H), 1.55 (m, 4H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 175.6, 172.4, 170.8, 167.9, 139.0, 128.7, 123.1, 119.1, 50.8, 42.7, 40.4, 35.0, 34.2, 31.2, 22.5; LRMS $(ESI)^-$ Calc for $C_{17}H_{22}N_3O_6$ $(M-H)^-$: 364.2. Found: 364.1.

N-Boc-glycine-amide **14**



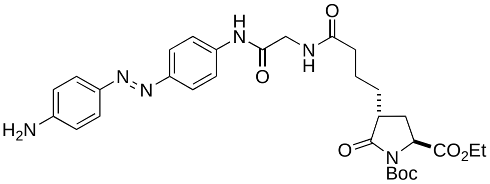
To a solution of azodianiline **5** (750 mg, 3.50 mmol), HOBt (135 mg, 5.25 mmol), DIPEA (2.40 mL, 14.0 mmol), and EDCI (872 mg, 4.55 mmol) in CH_2Cl_2 (100 mL) was added a solution of Boc-Gly-OH (674.0 mg, 3.85 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred at room temperature for 12 h. The mixture was diluted with CH_2Cl_2 (400 mL) and washed with a saturated $NaHCO_3$ solution (2 × 400 mL) and brine (2 × 400 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. Purification by normal phase chromatography (dry loaded, 10:0 → 7:3 CH_2Cl_2:EtOAc) gave **14** (581 mg, 66%) as an orange solid. Data for **14**: R_f 0.21 (95:5 CH_2Cl_2: MeOH); mp 184-185 °C; UV λ_{max} (MeOH): 391 nm; IR: 3306, 2424, 1705, 1673, 1602, 1531, 1501 cm^{-1}; ^1H NMR (MeOH-d_4, 400 MHz) δ 7.75 (d, 2H, *J* = 9 Hz), 7.68 (d, 4H, *J* = 9 Hz), 6.72 (d, 2H, *J* = 9 Hz), 3.88 (s, 2H), 1.46 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 168.5, 156.0, 152.4, 148.0, 142.8, 140.2, 124.8, 122.5, 119.3, 113.4, 78.1, 43.9, 28.2; HRMS (FAB) Calc for $C_{19}H_{24}N_5O_3$ $(MH)^+$: 370.187915. Found: 370.187140.

Glycine-amide **6**



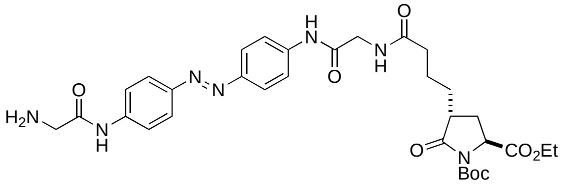
To a solution of **14** (565 mg, 1.53 mmol) in a 9:1 mixture of CH_2Cl_2:MeOH (50 mL) was added trifluoroacetic acid (50 mL). The mixture was stirred for 4 h at room temperature, concentrated, and triturated with diethyl ether (2 × 100 mL) to yield **6** (695 mg, 98%) as a purple solid. Data for **6**: mp >180 ^{o}C dec; UV λ_{max} (MeOH): 394 nm; IR: 2879, 2637, 1673, 1621, 1601, 1542, 1502 cm^{-1}; ^{1}H NMR (MeOH-*d*$_4$, 400 MHz) δ 7.81 (d, 2H, *J* = 9 Hz), 7.73 (m, 4H), 6.84 (d, 2H, *J* = 9 Hz), 3.89 (s, 2H); ^{13}C NMR (DMSO-*d*$_6$, 125 MHz) δ 165.6, 150.4, 149.5, 147.3, 140.9, 126.1, 124.1, 121.1, 117.5, 42.3; HRMS (FAB) Calc for $C_{14}H_{16}N_5O$ $(MH)^+$: 270.135485. Found: 270.135930.

Pyroglutamate **15**



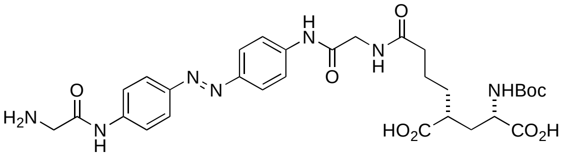
To a solution of **6** (180 mg, 0.387 mmol), HOBt (78.6 mg, 0.581 mmol), DIPEA (269 μL, 1.55 mmol), and EDCI (96.4 mg, 0.503 mmol) in CH_2Cl_2 (20 mL) was added a solution of **9** (159 mg, 0.465 mmol) in CH_2Cl_2 (5.0 mL). The mixture was stirred at room temperature for 12 h. The mixture was diluted with CH_2Cl_2 (250 mL) and washed with a saturated $NaHCO_3$ solution (2 × 200 mL) and brine (2 × 200 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. Purification by normal phase chromatography (97:3 → 95:5 CH_2Cl_2:MeOH) gave **15** (223 mg, 97%) as an orange solid. Data for **15**: R_f 0.32 (95:5 CH_2Cl_2: MeOH); mp 115-117 °C; $[\alpha]_D = -9.8$ (*c* 1.0, in CH_2Cl_2); UV λ_{max} ($CHCl_3$): 382 nm; IR: 3358, 2361, 1781, 1741, 1697, 1651, 1598, 1540 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.97 (s, 1H), 7.80 (d, 2H, *J* = 9 Hz), 7.76 (d, 2H, *J* = 9 Hz), 7.66 (d, 2H, *J* = 9 Hz), 7.03 (m, 1H), 6.72 (d, 2H, *J* = 9 Hz), 4.52 (dd, 1H, *J* = 9 Hz), 4.21 (q, 2H, *J* = 7 Hz), 4.12 (m, 2H), 4.07 (s-br, 2H), 2.67 (m, 1H), 2.33 (s, 2H), 2.26 (m, 1H), 1.94 (m, 2H), 1.74 (m, 3H), 1.46 (s, 9H), 1.27 (t, 3H, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.6, 173.7, 171.1, 167.6, 149.6, 149.2, 145.2, 139.3, 124.8, 123.1, 119.9, 114.5, 83.7, 61.7, 57.2, 44.3, 41.3, 35.6, 29.7, 28.1, 27.7, 22.7, 14.1; HRMS (FAB) Calc for $C_{30}H_{38}N_6O_7$ $(M)^+$: 594.280198. Found: 594.280490.

Amine **10**



To a solution of Fmoc-Gly-OH (600 mg, 2.02 mmol) and oxalyl chloride (1.2 mL of 2.0 M solution in THF, 2.4 mmol) in CH_2Cl_2 (6.0 mL) was added one drop of *N,N*-Dimethyl formamide (DMF). After stirring for 1 h at room temperature the mixture was concentrated. The resulting acid chloride was redissolved in THF (11.0 mL) and added via cannula to a solution of **15** (400 mg, 0.672 mmol), DIPEA (586 μL, 3.36 mmol), and 4-(Dimethylamino)-pyridine (DMAP) (8.2 mg, 0.067 mmol) in THF (26.0 mL). After stirring 10 min at 0 °C, the mixture was warmed to room temperature and stirred an additional 3 h. The mixture was then diluted with CH_2Cl_2 (150 mL) and washed with a saturated solution of $NaHCO_3$ (2 × 150 mL) and brine (2 × 150 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated. Purification by normal phase chromatography (90:10:0.6:0.6 CH_2Cl_2:MeOH:AcOH:H_2O) gave the Fmoc-glycine adduct as an orange solid that was sufficiently pure for further reaction. To a solution of this compound in DMF (20.0 mL) was added piperidine (200 μL, 2.02 mmol). After stirring for 6 h at room temperature, the mixture was concentrated and purified by reversed phase chromatography (4:1 → 2:3 0.1 % formic acid in H_2O:MeCN) to yield **10** (186 mg, 43%) as an orange solid. Data for **10**: mp >210 ^{o}C dec; $[\alpha]_D = -15.5$ (*c* 0.3, in MeOH); UV λ_{max} (MeOH): 365 nm; IR: 3280, 2981, 1781, 1690, 1593, 1546 cm^{-1}; ^{1}H NMR (MeOH-*d*$_4$, 500 MHz) δ 7.88 (m, 4H), 7.76 (m, 4H), 4.63 (d, 1H, *J* = 9 Hz), 4.24 (m, 2H), 4.03 (s, 2H), 3.85 (s, 2H), 2.64 (m, 1H), 2.34 (m, 2H), 2.28 (m, 1H), 2.08 (m, 1H), 1.89 (m, 1H), 1.72 (m, 2H), 1.47 (s, 9H), 1.42 (m, 1H), 1.29 (t, 3H, *J* = 7 Hz); ^{13}C NMR (MeOH-*d*$_4$, 100 MHz) δ 178.0, 176.5, 173.2, 170.1, 169.5, 151.0, 150.6, 150.3, 142.6, 141.9, 124.8, 124.7, 121.3, 121.1, 84.9, 63.0, 59.0, 45.9, 44.3, 42.8, 36.6, 31.1, 29.2, 28.3, 24.1, 14.7; HRMS (FAB) Calc for $C_{32}H_{41}N_7O_8$ $(M)^+$: 651.301662. Found: 651.304080.

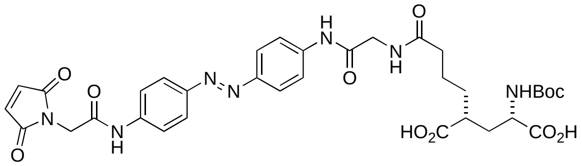
Amino acid **16**



To a solution of **10** (180 mg, 0.276 mmol) in THF (10.0 mL) at 0 ^{o}C was added 1.0 M LiOH (10.0 mL). After stirring for 1 h, the mixture was acidified to pH 2 with 1 M

HCl, THF was removed *in vacuo*, and the mixture was purified by reversed pahse chromatography (5:0 → 4:1 0.1% formic acid in H_2O:MeCN) to yield **16** (143 mg, 80%) as a yellow solid. Data for **16**: mp >230 °C dec; $[\alpha]_D = -15.9$ (*c* 0.1, in DMSO); UV λ_{max} (DMSO): 379 nm; IR: 2981, 1690, 1660, 1595, 1546, 1500 cm^{-1}; ^1H NMR (MeOH-d_4, 500 MHz) δ 7.87 (m, 4H), 7.76 (m, 4H), 4.07 (m, 1H), 4.03 (d, 2H, *J* = 5 Hz), 3.88 (s, 2H), 2.55 (m, 1H), 2.32 (m, 2H), 2.20 (m, 1H), 1.70 (m, 4H), 1.59 (m, 1H), 1.42 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 176.4, 174.2, 172.5, 168.5, 163.8, 155.4, 147.8, 147.6, 141.7, 141.2, 123.5, 123.4, 119.3, 79.2, 77.9, 52.5, 44.0, 42.9, 41.6, 35.0, 32.0, 28.2, 23.0; LRMS $(ESI)^-$ Calc for $C_{30}H_{38}N_7O_9$ $(M-H)^-$: 640.3. Found: 640.2.

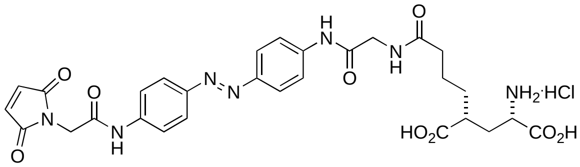
Maleimide **17**



To a solution of **16** (53 mg, 0.082 mmol) in a saturated solution of $NaHCO_3$ (3.5 mL) was added finely ground *N*-methoxycarbonylmaleimide (105 mg, 0.677 mmol) under vigorous stirring. After 30 min at 0 °C, the mixture was diluted with THF (3.5 mL) and warmed to room temperature. After 1 h, the mixture was acidified to pH 1-2 with an aqueous aolution of 1.0 M H_2SO_4 and extracted with EtOAc (2 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Purification by normal phase chromatography (90:10:0.6:0.6 CH_2Cl_2:MeOH:AcOH:H_2O) gave **17** (42 mg, 71%) as a yellow solid. Data for **17**: R_f 0.20 (90:10:0.6:0.6 CH_2Cl_2:MeOH:AcOH:H_2O); mp >230 °C dec; $[\alpha]_D = -14.0$ (*c* 0.1, in MeOH); UV λ_{max}

(MeOH): 365 nm; IR: 3249, 3186, 2928, 1753, 1708, 1687, 1651, 1520 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 10.61 (s, 1H), 10.31 (s, 1H), 8.19 (m, 1H), 7.84 (d, 4H, *J* = 9 Hz), 7.79 (d, 2H, *J* = 9 Hz), 7.75 (d, 2H, *J* = 9 Hz), 7.16 (s, 2H), 7.10 (d, 2H, *J* = 8 Hz), 4.32 (s, 2H), 3.82 (m, 1H), 3.64 (s, 2H), 2.35 (m, 1H), 2.15 (m, 2H), 1.93 (m, 1H), 1.59 (m, 1H), 1.49 (m, 3H), 1.42 (m, 1H), 1.36 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 176.1, 174.2, 172.5, 170.7, 168.4, 166.6, 155.7, 147.9, 147.6, 141.7, 141.1, 135.0, 123.5, 123.4, 119.5, 119.3, 78.0, 52.4, 42.8, 41.4, 40.5, 45.0, 32.8, 32.1, 28.2, 22.9; LRMS (ESI)$^-$ Calc for $C_{34}H_{38}N_7O_{11}$ (M-H)$^-$: 720.3. Found: 720.3.

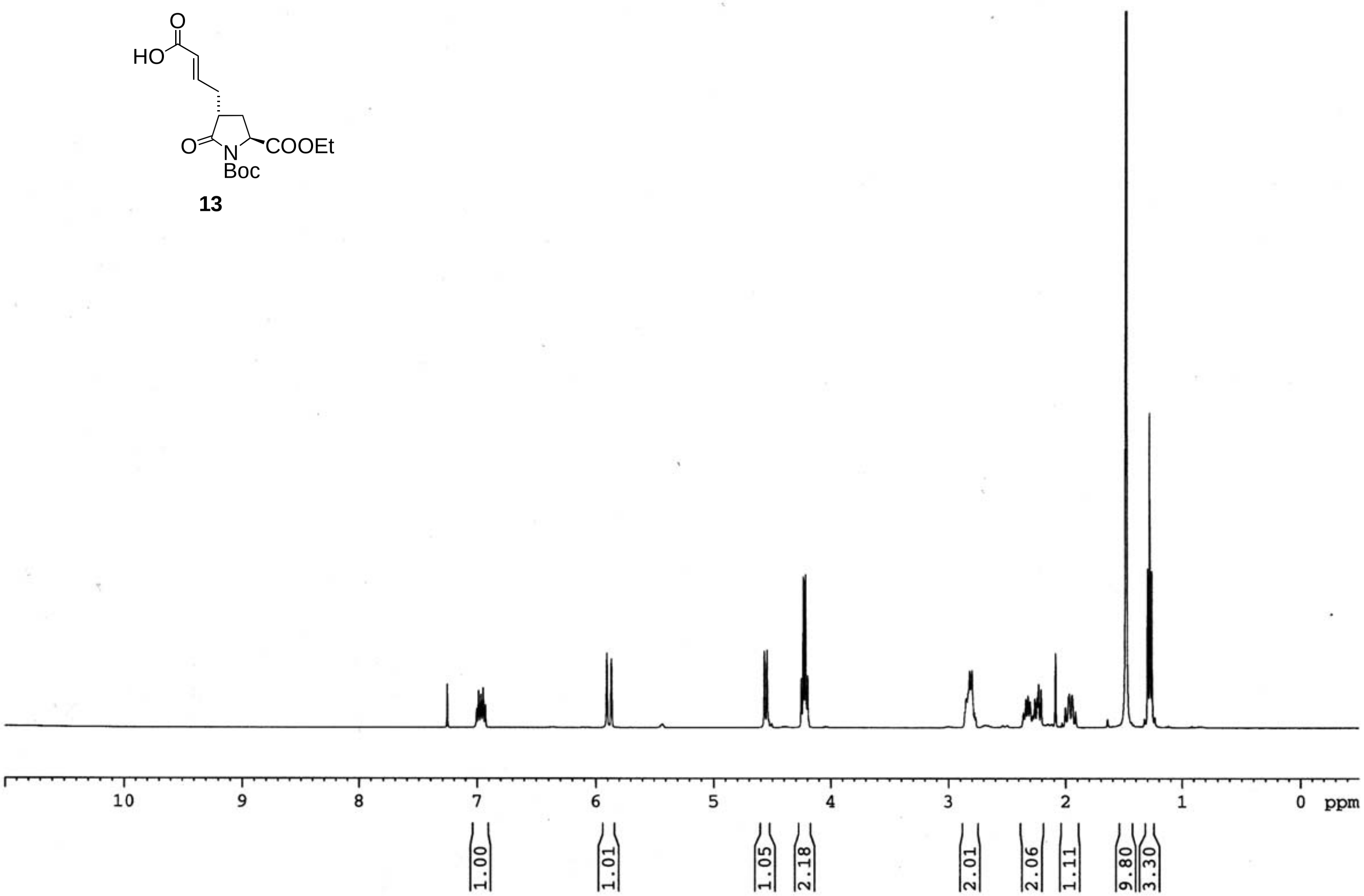
MAG **4**



To a flask containing solid **17** (38 mg, 0.053 mmol) was added a saturated HCl solution in EtOAc (25.0 mL). After stirring at room temperature for 2 h, the resulting purple solid was triturated with ethyl ether (2 × 40 mL) to yield **4** (30 mg, 87%). Data for **4**: mp >230 °C dec; $[\alpha]_D$ = –19.5 (*c* 0.7, in DMSO); UV λ_{max} (10% DMSO in H_2O): 363 nm; IR: 3279, 3052, 2935, 2362, 1922, 1709, 1598, 1538 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 10.70 (s, 1H), 10.39 (s, 1H), 8.23 (m, 1H), 7.84 (d, 4H, *J* = 8 Hz), 7.79 (d, 2H, *J* = 9 Hz), 7.76 (d, 2H, *J* = 9 Hz), 7.16 (s, 2H), 4.32 (s, 2H), 3.91 (d, 2H, *J* = 6 Hz), 3.81 (m, 1H), 2.89 (m, 1H), 2.16 (m, 2H), 2.13 (m, 1H), 2.77 (m, 1H), 1.53 (m, 4H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 175.5, 172.4, 170.9, 170.7, 168.4, 165.3, 147.8, 147.6, 141.7, 141.1, 135.0, 123.5, 123.4, 119.4, 119.3, 64.9, 50.8, 42.7, 34.9, 31.7, 31.2, 22.4, 15.2; HRMS $(ESI)^+$ Calc for $C_{29}H_{32}N_7O_9$ $(MH)^+$: 622.2262. Found: 622.2268.

Supplementary References:

1. Nakane, M. et al. 7-Oxabicyclo[2.2.1]Heptyl Carboxylic-Acids as Thromboxane-A2 Antagonists - Aza Omega-Chain Analogs. *J. of Med. Chem.* **33**, 2465-2476 (1990).



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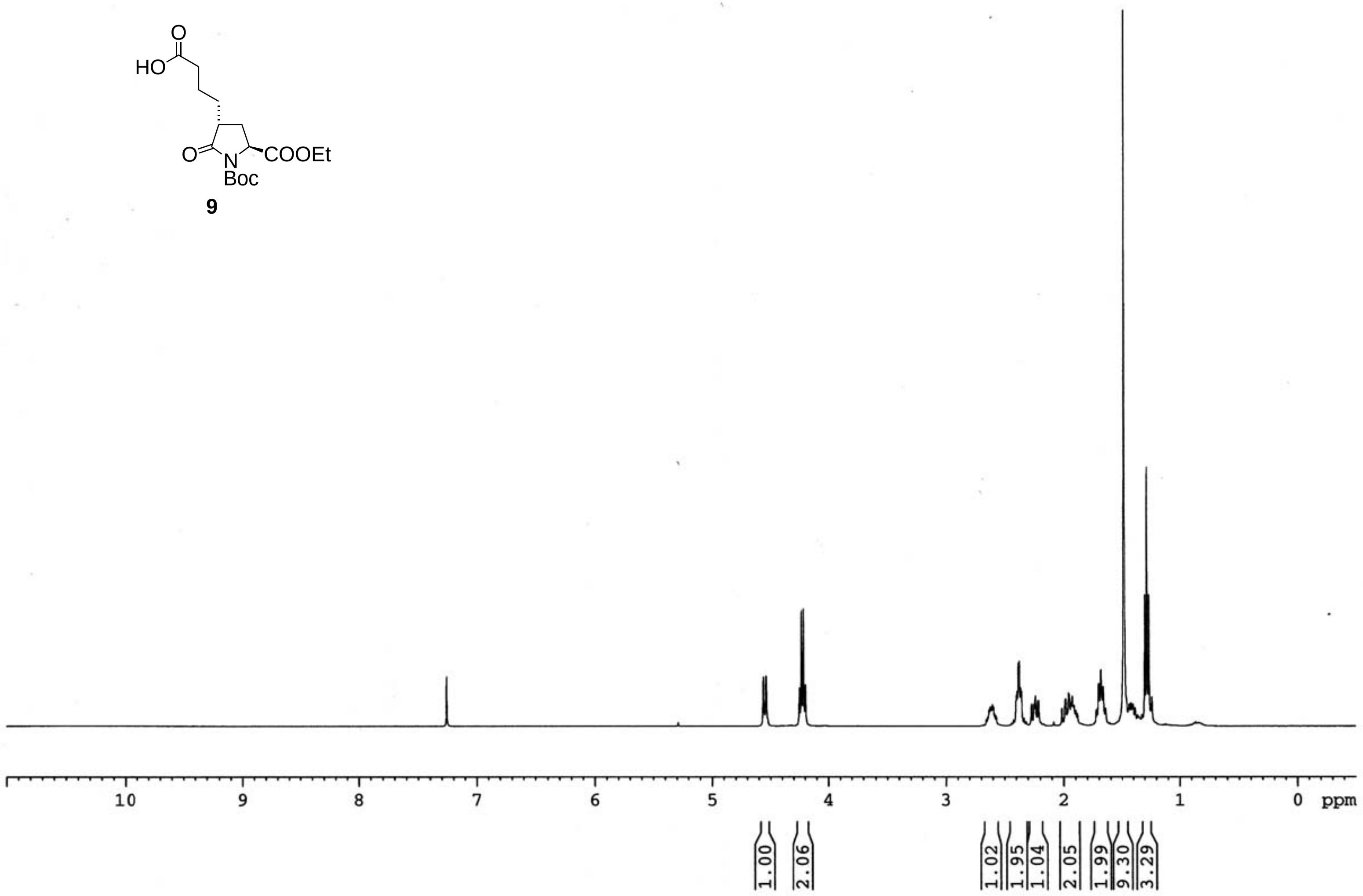
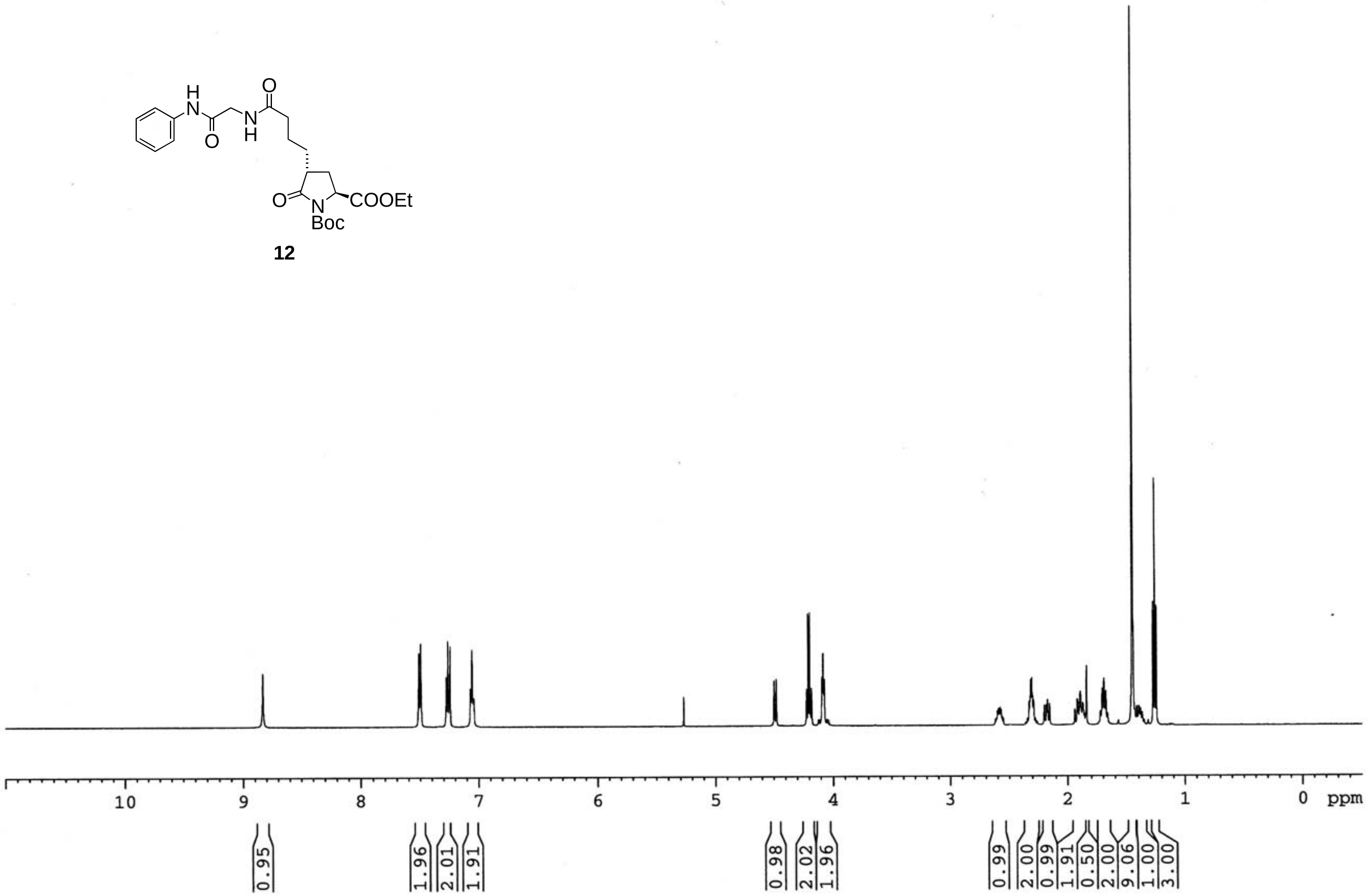
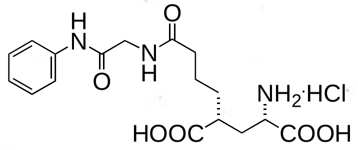
9.80
3.30


HO
O
O
N
Boc
COOEt
9
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.06
1.02
1.95
1.04
2.05
1.99
9.30
3.29

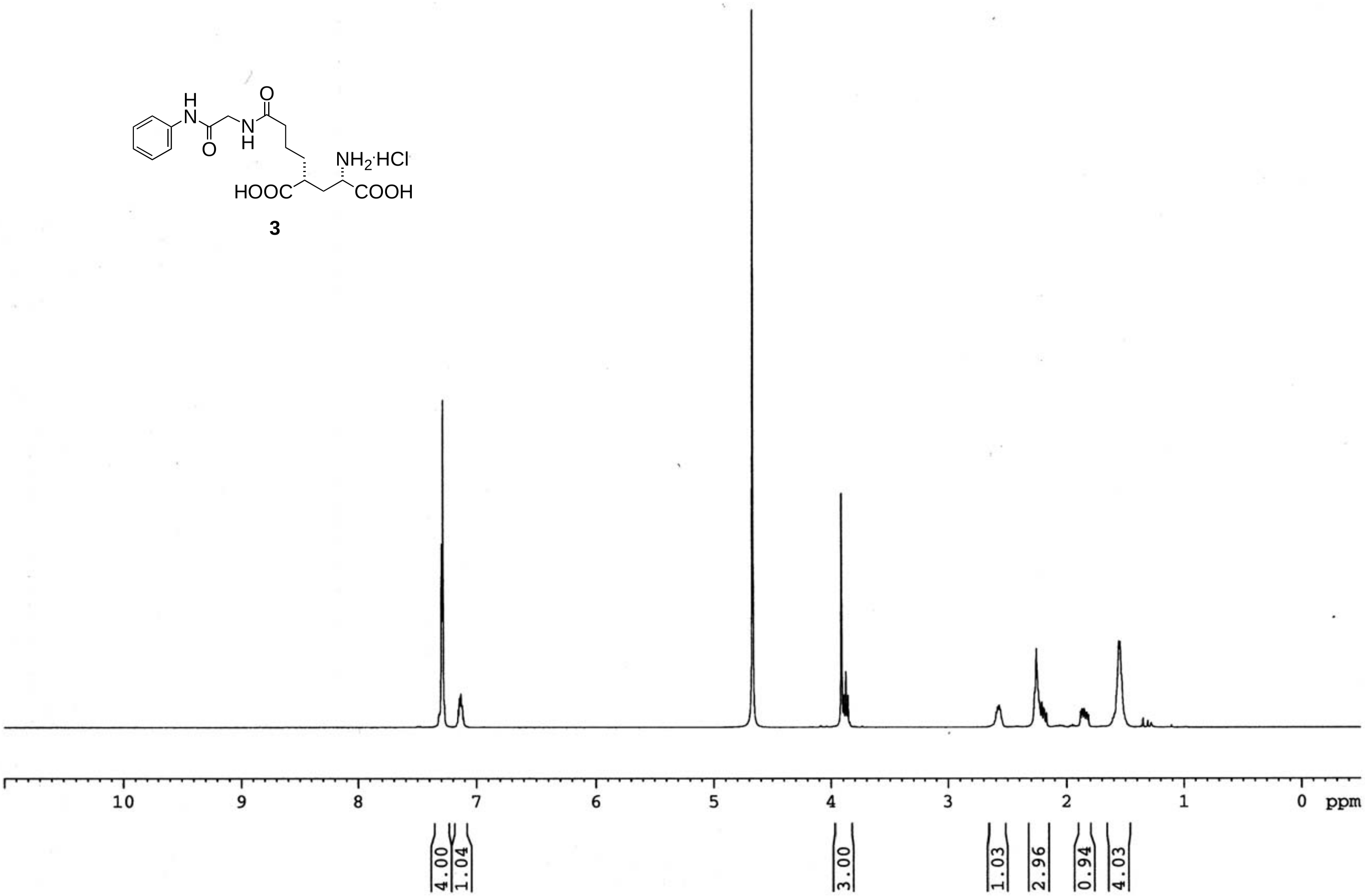


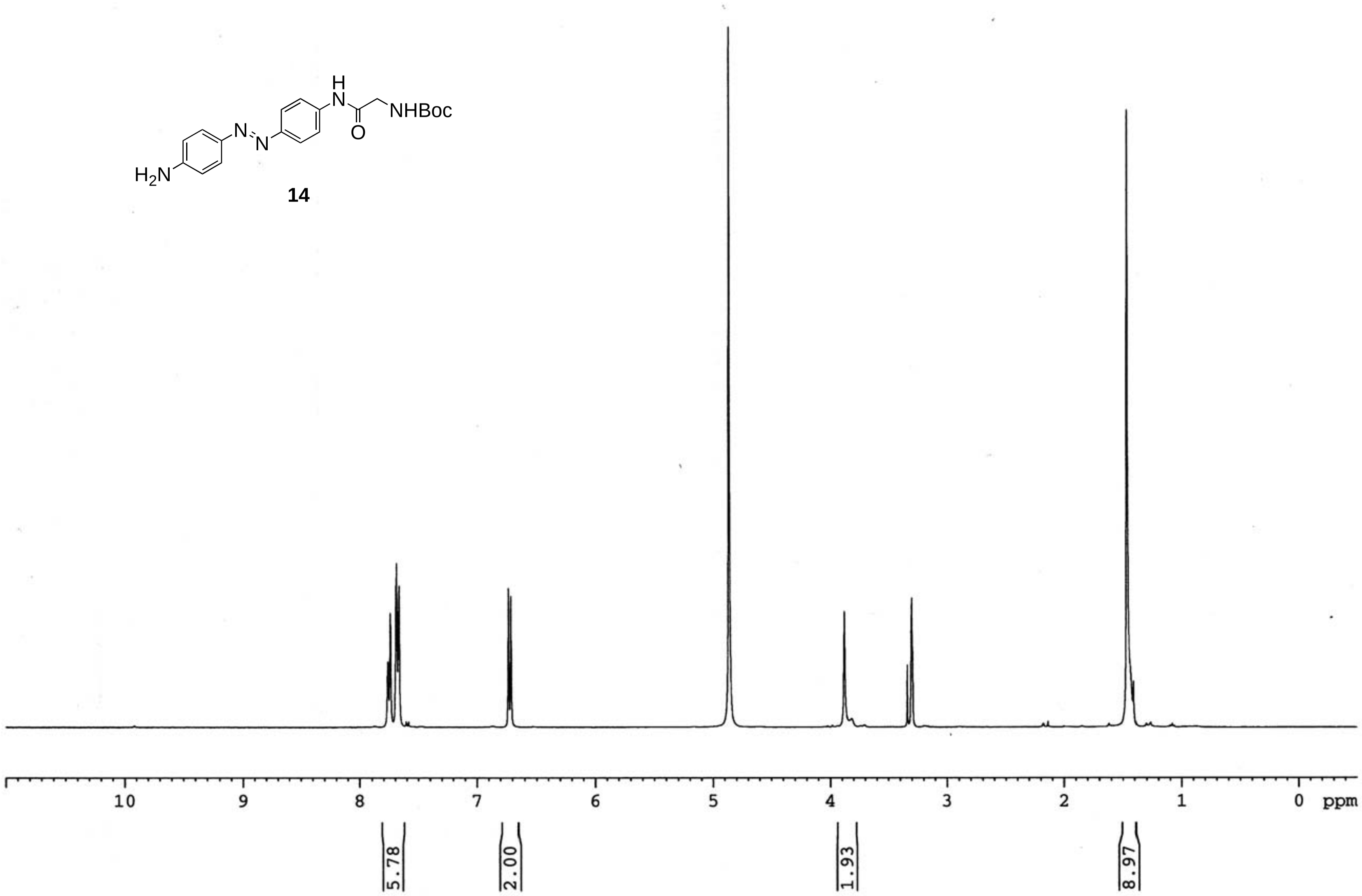
12

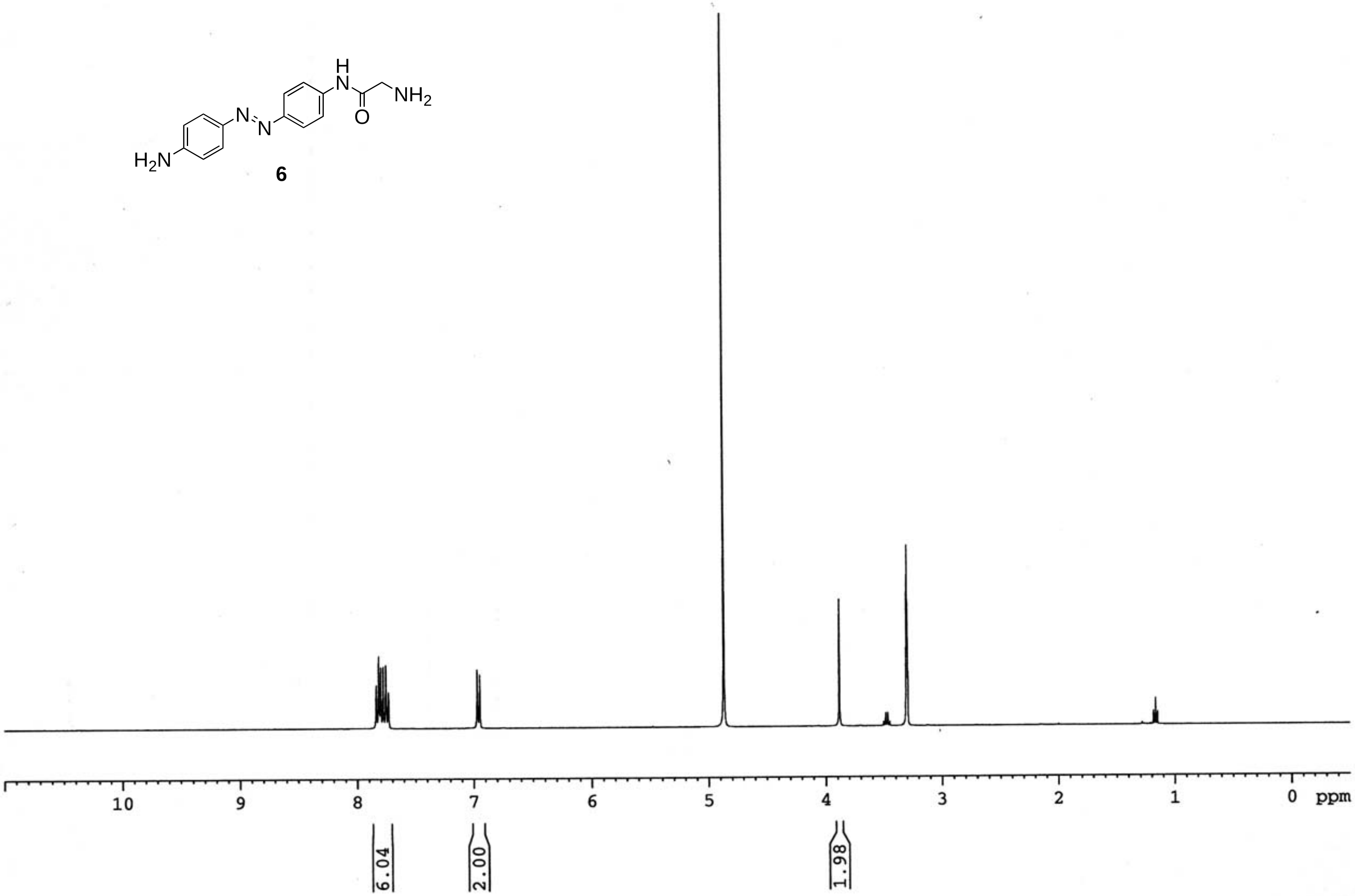
10
9
8
7
6
5
4
3
2
1
0
ppm
0.95
1.96
2.01
1.91
0.98
2.02
1.96
0.99
2.00
0.99
1.91
0.50
2.00
9.06
1.00
3.00


H
N
O
N
H
O
NH2·HCl
HOOC
COOH

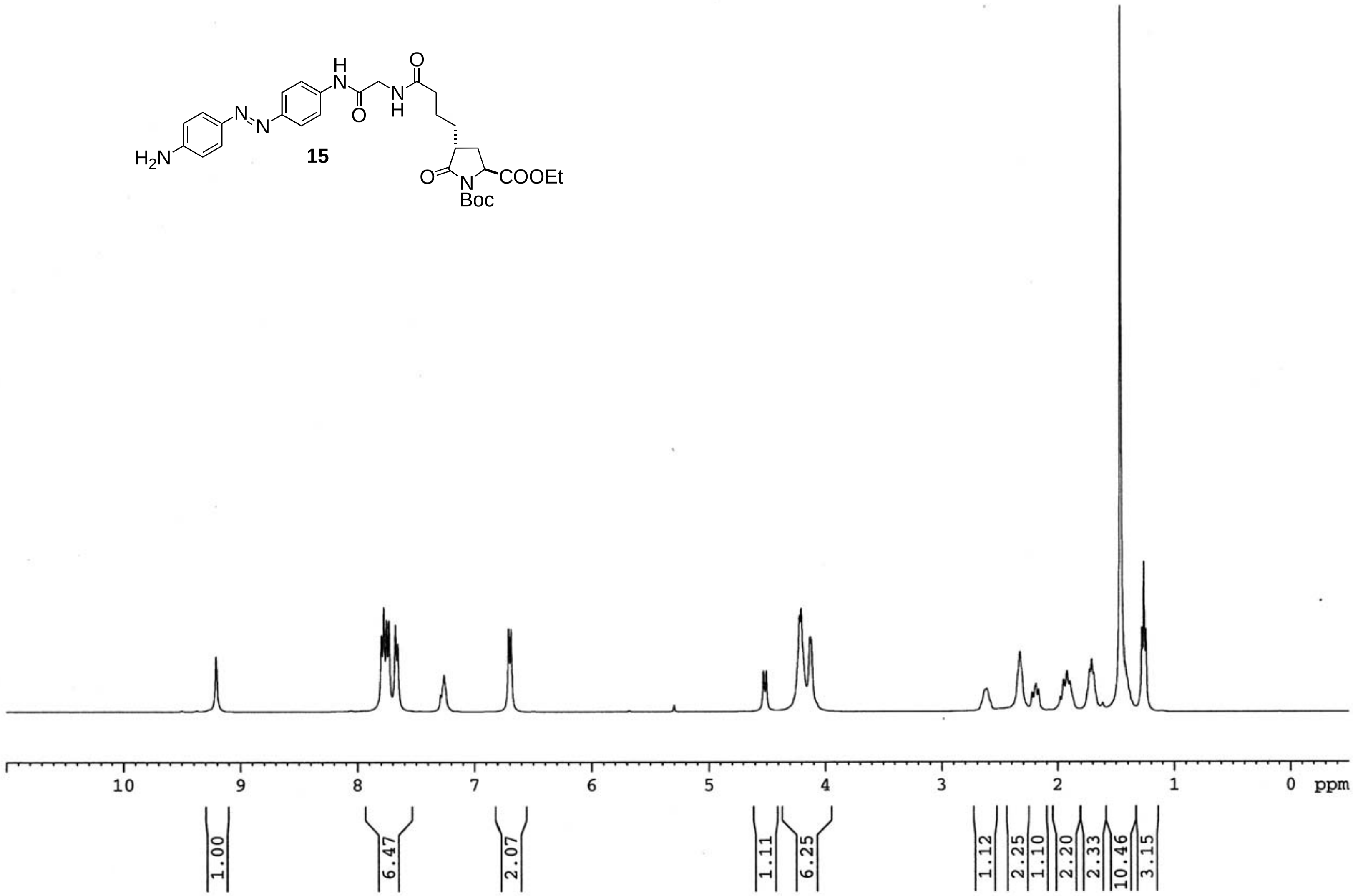
3


10
9
8
7
6
5
4
3
2
1
0
ppm
4.00
1.04
3.00
1.03
2.96
0.94
4.03


14

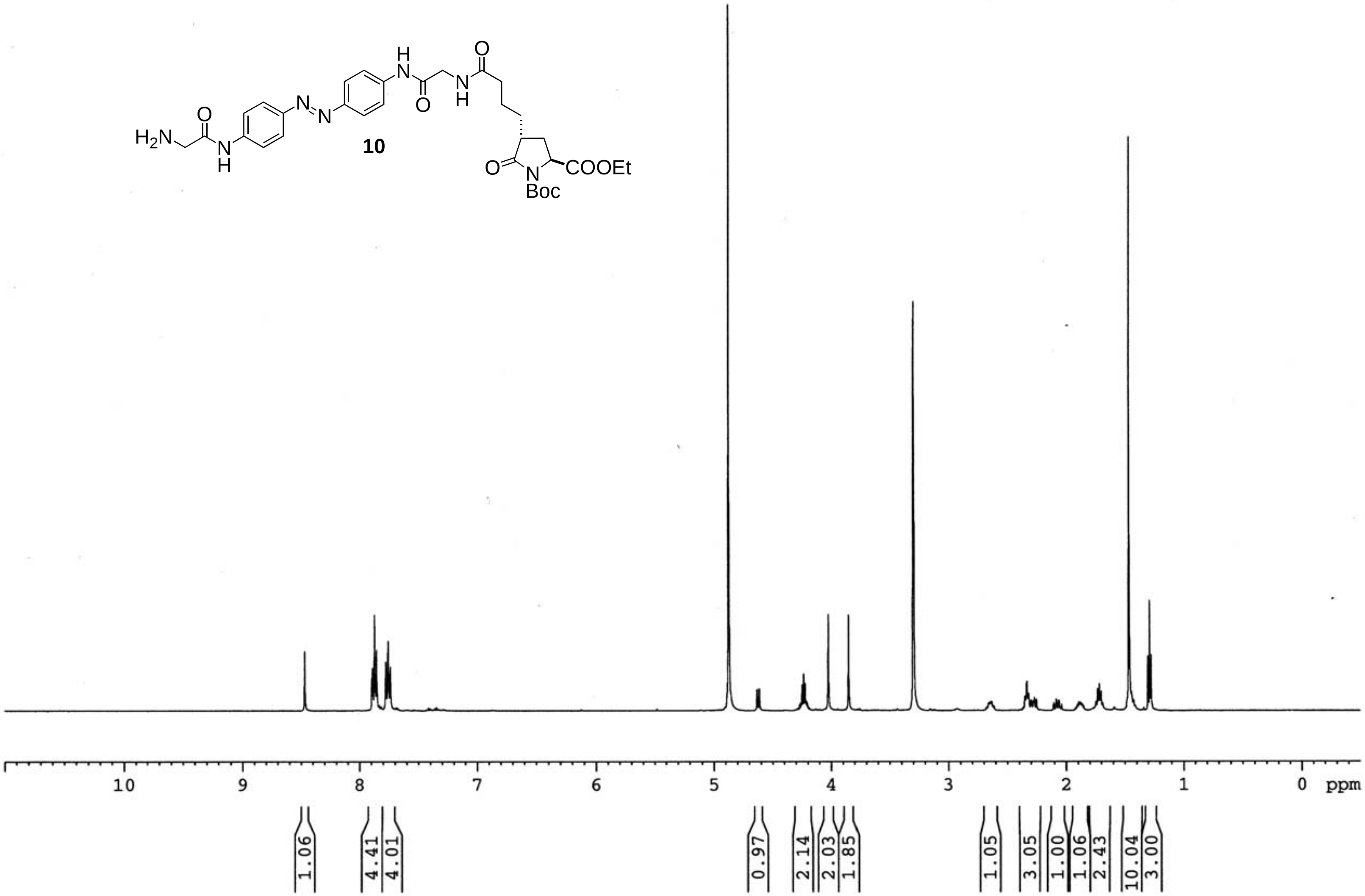


6



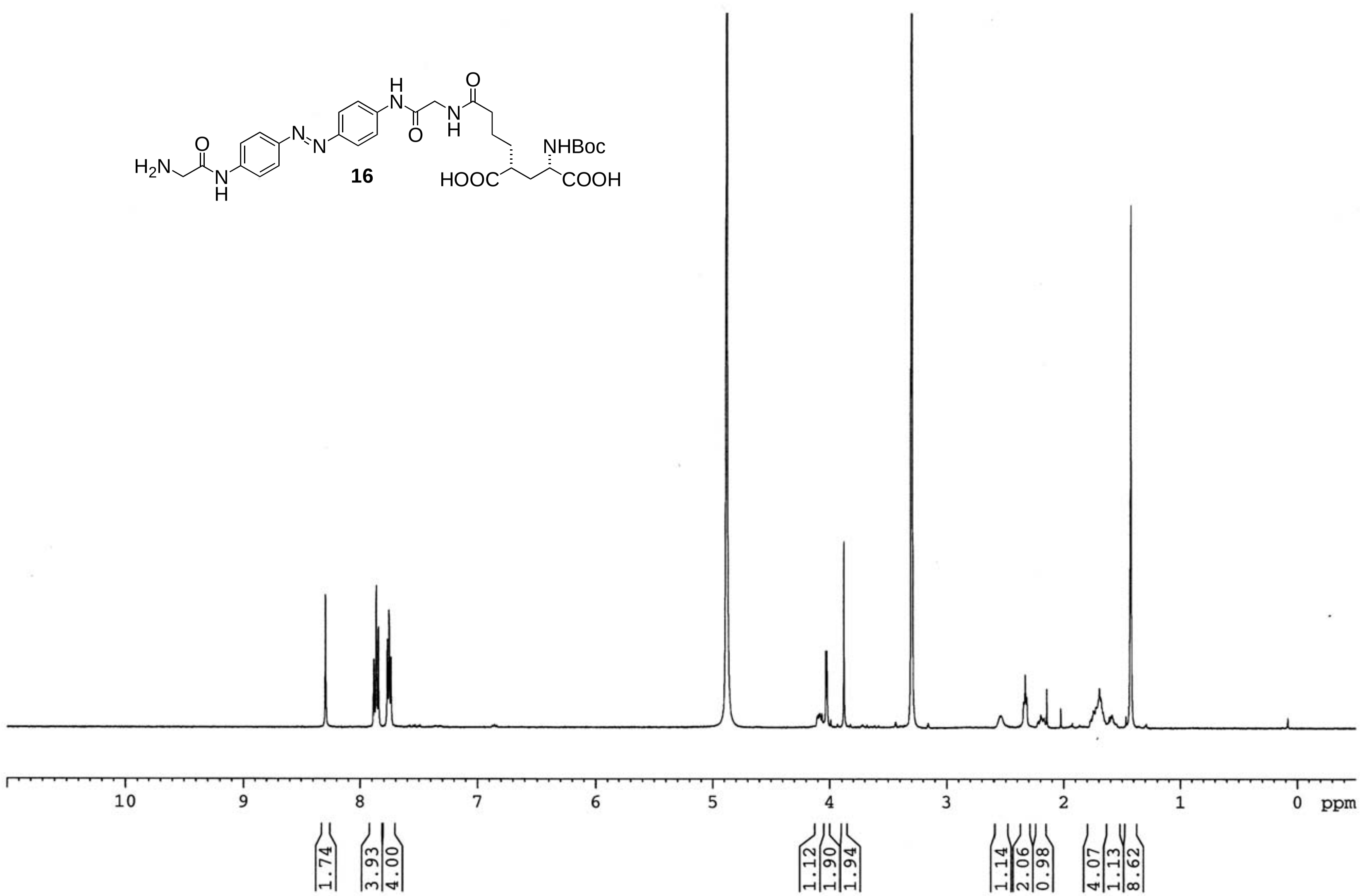
15

H2N
N
N
H
N
O
O
N
H
O
N
Boc
COOEt
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
6.47
2.07
1.11
6.25
1.12
2.25
1.10
2.20
2.33
10.46
3.15



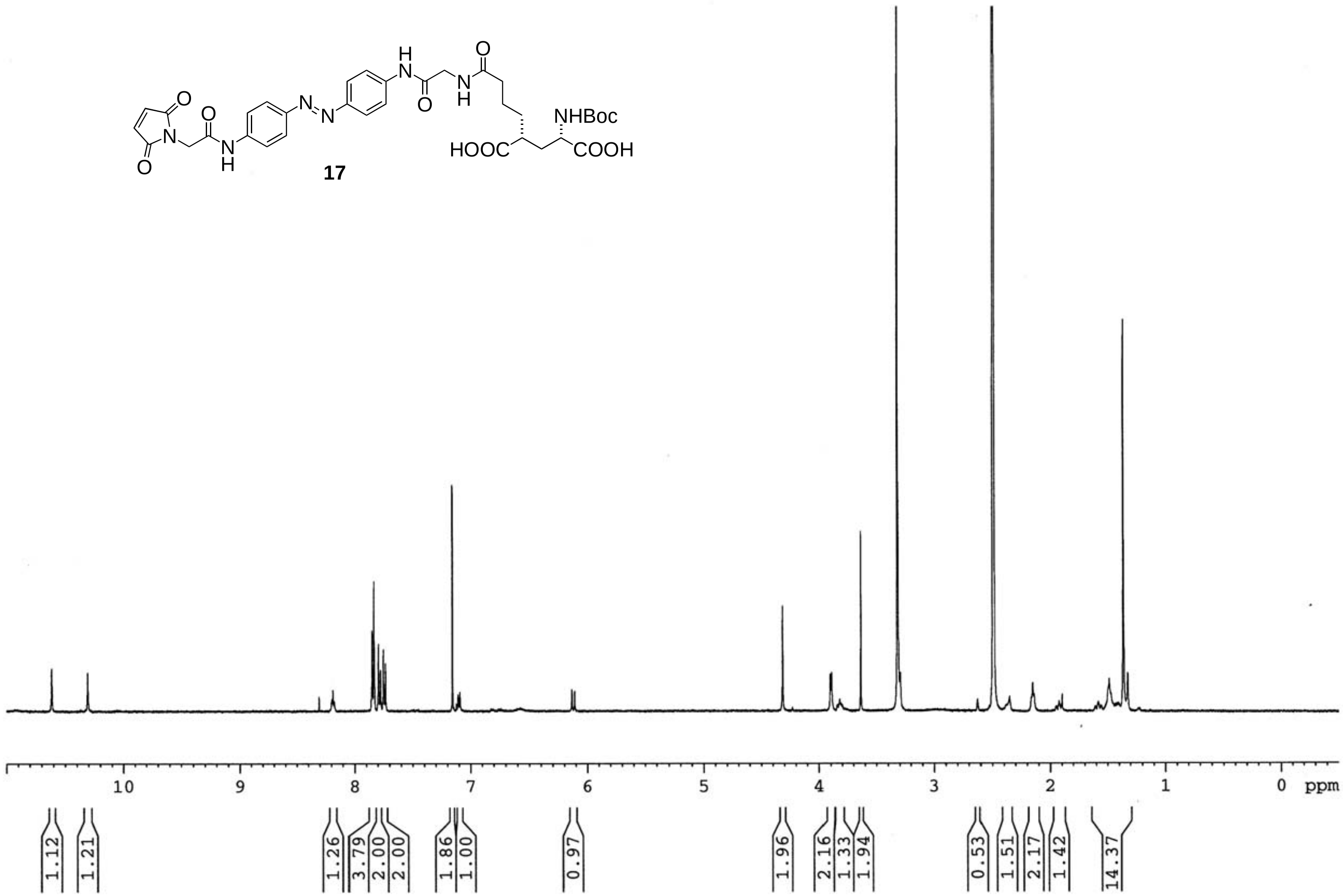
10

H2N
O
N
H
N
N
H
N
O
N
H
O
O
N
Boc
COOEt
10
9
8
7
6
5
4
3
2
1
0
ppm
1.06
4.41
4.01
0.97
2.14
2.03
1.85
1.05
3.05
1.00
1.06
2.43
10.04
3.00

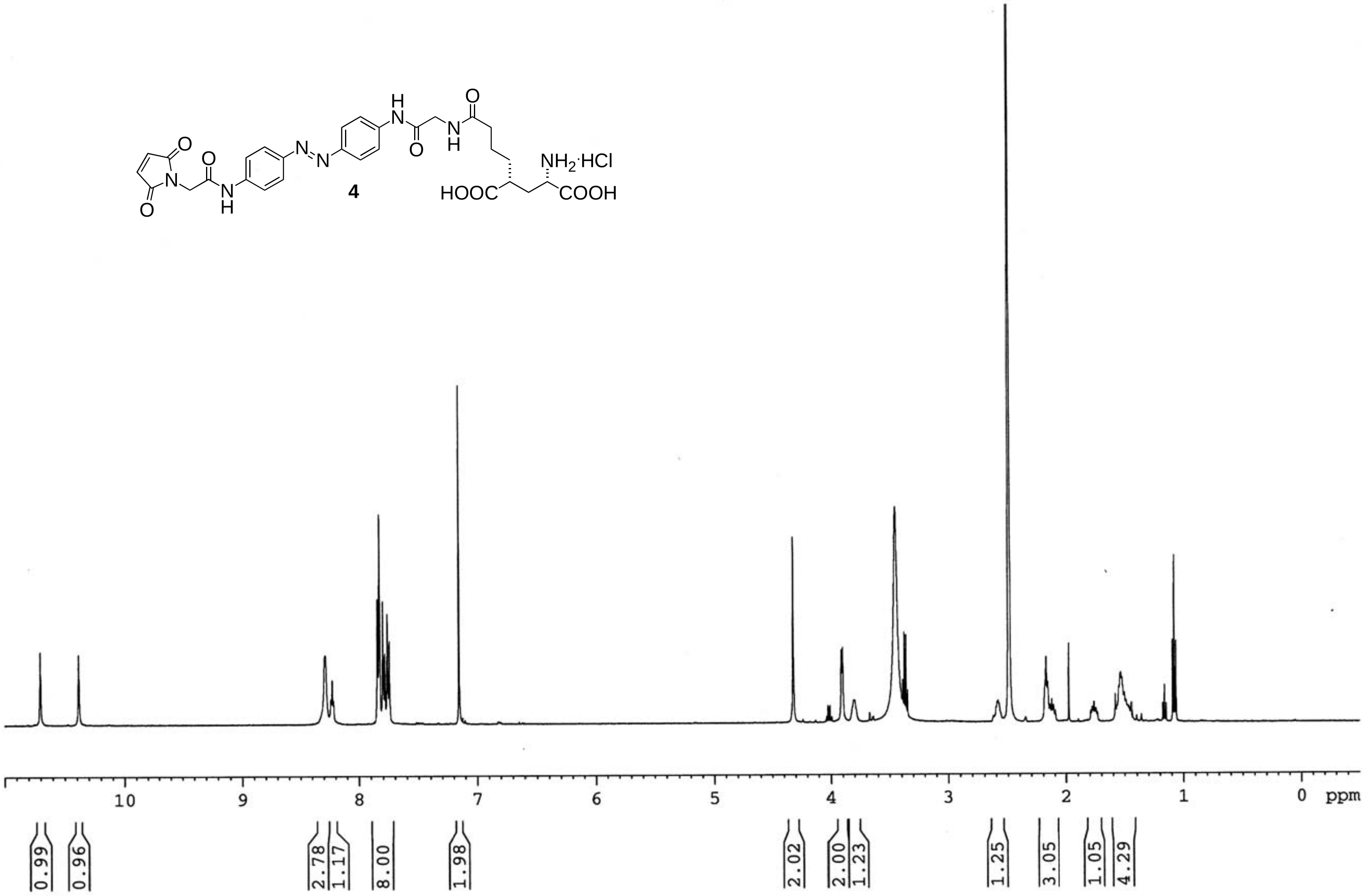


16

H2N
O
N
H
N
N
H
N
O
N
H
O
NHBoc
HOOC
COOH
10
9
8
7
6
5
4
3
2
1
0
ppm
1.74
3.93
4.00
1.12
1.90
1.94
1.14
2.06
0.98
4.07
1.13
8.62



17
10
9
8
7
6
5
4
3
2
1
0
ppm
1.12
1.21
1.26
3.79
2.00
2.00
1.86
1.00
0.97
1.96
2.16
1.33
1.94
0.53
1.51
2.17
1.42
14.37


4

NH2·HCl
HOOC
COOH
10
9
8
7
6
5
4
3
2
1
0
ppm
0.99
0.96
2.78
1.17
8.00
1.98
2.02
2.00
1.23
1.25
3.05
1.05
4.29