Electronic Supplementary Information

Design and Synthesis of a Bivalent Probe Targeting the Putative Mu Opioid Receptor and Chemokine Receptor CXCR4 Heterodimer

Bethany A. Reinecke, Guifeng Kang, Yi Zheng, Samuel Obeng, Huijun Zhang, Dana E. Selley, Jing An, and Yan Zhang*

Experimental

Chemical Syntheses

All reagents were purchased from Sigma-Aldrich or as otherwise stated. Melting points were obtained with a Fisher Scientific micro melting point apparatus without further correction. All IR spectra were recorded on a Nicolet iS10 FT-IR Instrument. Proton (400 MHz) and carbon-13 (100 MHz) nuclear magnetic resonance (NMR) spectra were acquired at ambient temperature with tetramethylsilane as the internal standard on a Bruker Ultrashield 400 Plus spectrometer. HRMS (ESI) analysis was performed on Perkin Elmer AxION 2 TOF mass spectrometer. HPLC analysis of the final compounds was achieved on Varian ProStar 210 system on Microsorb-MV 100-5 C18 column (250 mm × 4.6 mm) at 254 nm eluting with acetonitrile (0.01% TFA):water, 40:60 – 0:100 (1 & 3) or 45:55 – 0:100 (2), at 0.65 mL/min over 30 min. TLC analyses were carried out on Analtech Uniplate F254 plates. Chromatographic purification was accomplished on silica gel columns (230~400 mesh, Merck). Yields were not maximized.

General procedure for amide coupling – On an ice-water bath, a solution of acid in DMF, was added EDCI (2 eq.), HOBt (2 eq.), 4Å molecular sieves, and TEA (4.0 eq.) under N_2 protection. After 30 minutes, a solution of amine (1.0 eq.) in DMF was added dropwise. The resultant mixture was allowed to warm up to room temperature. After reaction completion, the mixture was filtered through celite. Solvent was removed in vacuum and the product was purified using column chromatography or recrystallization.

6β-naltrexamine hydrochloride salt The title compound was prepared following the reported procedure[63] in 60% yield in two steps. ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.63 (s, 1H, exchangeable), 8.93 (brs, 1H, exchangeable), 8.56 (brs, 3H, exchangeable), 6.83 (d, J = 8.0 Hz,

1H), 6.66 (d, J = 8.0 Hz, 1H), 6.47 (brs, 1H), 4.71 (d, J = 7.2 Hz, 1H), 3.94 (d, J = 5.6 Hz, 1H), 3.35-3.27 (m, 2H), 3.06-3.00 (m, 2H), 2.92-2.87 (m, 1H), 2.78-2.74 (m, 1H), 2.46-2.44 (m, 2H), 2.01 (q, J = 12.8, 1H), 1.85 (d, J = 14.0 Hz, 1H), 1.79-1.75 (m, 1H), 1.44 (d, J = 8.8 Hz, 1H), 1.29 (td, J_1 = 13.6 Hz, J_2 = 2.4 Hz, 1H), 1.12-1.05 (m, 1H), 0.70-0.63 (m, 1H), 0.62-0.56 (m, 1H), 0.55-0.49 (m, 1H), 0.42-0.36 (m, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 141.62, 141.54, 129.06, 120.70, 119.83, 118.26, 88.08, 69.40, 61.28, 56.71, 52.35, 46.30, 45.62, 28.74, 27.14, 22.96, 21.39, 5.71, 5.08, 2.65.

3-(chloromethyl)-5,6-dihydro-6,6-dimethylimidazo[2,1-b]thiazole hydrochloride (5) A mixture of 4,4-dimethyl-imidazolidine-2-thione (500 mg, 3.84 mmol), 1,3-dichloroacetone (500 mg, 3.84 mmol), and acetonitrile (10 mL) was refluxed for 2 hr. The white precipitate was filtered off, dried, suspended in 1-methoxy-2-(2-methoxy-ethoxy)-ethane (5 mL), and subsequently heated at 145 °C for 2 hr. The precipitate was filtered off and washed with ether to give the hydrochloride product (571 mg, 56.3 %). ^{1}H NMR (400 MHz, DMSO-d_6/D_2O = 10:1): δ 7.07 (s, 1H), 4.85 (s, 2H), 4.22 (s, 2H), 1.50 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6/D_2O = 10:1): δ 168.38, 133.30, 111.16, 69.47, 57.92, 35.96, 27.47. IR v (Diamond, cm^{-1}) 3094, 2986, 2851, 2788, 1551, 1303, 1130. HRMS calc. m/z for [$C_8H_{11}ClN_2S$]: 202.0331, found: 203.0379 $(M+H)^+$.

***trans*-4-[(*tert*-butoxycarbonylamino)methyl]cyclohexanecarboxylic acid (6)** To a solution of *trans*-4-(aminomethyl)cyclohexane-1-carboxylic acid (500 mg, 3.18 mmol) and $NaHCO_3$ (600 mg, 7.14 mmol) in 10 mL water, added a solution of Boc_2O (834 mg, 3.82 mmol) in 1,4-dioxane (10 mL) at -5 °C. The pH was adjusted to 7-8 with additional $NaHCO_3$ (400 mg, 4.79 mmol). After stirred for 10 min, the solution was returned to room temperature and stirred for 24 hr. After 24 hr, 1,4-dioxane was removed under vacuum to give a white residue. The residue was extracted with

1:1 EtOAc/hexane system. The aqueous layer was cooled on ice bath and acidified to pH = 2 with HCl to give a white solid precipitate. The precipitate was filtered and washed with EtOAc to give the product (398 mg, 57%) ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 12.01 (s, 1H, exchangeable), 6.78 (t, *J* = 5.5 Hz, 1H, exchangeable), 2.76 (t, *J* = 6.4 Hz, 2H), 2.09 (tt, J_1 = 3.6 Hz, J_2 = 12.2 Hz, 1H), 1.88-1.86 (m, 2H), 1.70-1.68 (m, 2H), 1.37 (s, 9H), 1.32-1.18 (m, 3H), 0.91-0.81 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 176.66, 155.65, 77.20, 45.95, 42.60, 37.33, 29.32, 28.21. IR *v* (Diamond, cm^{-1}) 3366, 2924, 1686, 1522, 1251, 1166. HRMS calc. m/z for [$C_{13}H_{23}NO_4$]: 257.1627, found: 256.1551(M-H)$^-$.

(*tert*-butoxy-*N*-({*trans*-4-[(phenylmethoxy)carbonyl-amino]cyclohexyl}methyl) carboxamide (7) To a flask, **6** (250 mg, 0.971 mmol) was suspended in toluene (7 mL) and chilled in an ice-water bath under N_2. DPPA (267 mg, 0.971 mmol) and TEA (147 mg, 1.46 mmol) was added. The mixture was then warmed to room temperature and slowly heated to 80 °C. After 24 hr, the mixture was cooled to 35 ºC and benzyl alcohol (340 mg, 3.15 mmol) was added via syringe. The mixture was heated to 80 ºC and stirred for 24 hr. The reaction was concentrated in vacuum and the residue was treated with water (30 mL) and EtOAc (30 mL). The aqueous layer was extracted with EtOAc (30 mL). The combined organic layers were washed with concentrated HCl (25 mL), aqueous sodium bicarbonate (25 mL), and brine (25 mL), then dried over Na_2SO_4 and concentrated in vacuum to afford the white solid product (120 mg, 23.9%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 7.38-7.28 (m, 5H), 7.10 (d, *J* = 8.0 Hz, 1H, exchangeable), 6.75 (t, J = 5.6 Hz, 1H, exchangeable), 4.99 (s, 2H), 3.25-3.16 (m, *J* = 4.0 Hz, 1H), 2.75 (t, *J* = 6.4 Hz, 2H), 1.81-1.78 (m, 2H), 1.67-1.64 (m, 2H), 1.37 (s, 9H), 1.31-1.22 (m, 1H), 1.16-1.06 (m, 2H), 0.93-0.84 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d6*): δ 155.62, 155.18, 137.22, 128.21, 127.62, 127.59, 77.19, 64.92, 49.78, 45.74, 37.04, 32.03, 28.98, 28.19. IR *v* (Diamond, cm^{-1}) 3346, 2930, 1626, 1439, 1521, 1245, 1171.

HRMS calc. m/z for [$C_{20}H_{30}N_2O_4$]: 362.2206, found 385.2054 $(M+Na)^+$.

***tert*-butyl ((*trans*-4-aminocyclohexyl)methyl)carbamate (8)** A solution of **7** (100 mg, 0.276 mmol) in methanol (15 mL) was treated with Pd/C (10 mg, 10% wt). The resultant solution was reacted at 10 psi H_2 for 3 hr at room temperature. The reaction mixture was filtered through celite pad and washed with methanol to yield a white solid (84 mg, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.59 (s, 1H), 2.97-2.94 (m, 4H), 2.68-2.61 (m, 1H), 1.90-1.88 (m, 2H), 1.77-1.74 (m, 2H), 1.43 (s, 9H), 1.39-1.35 (m, 1H), 1.17-1.07 (m, 2H), 1.02-0.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.21, 79.22, 50.77, 46.61, 37.83, 35.56, 29.51, 28.58. IR *v* (Diamond, cm^{-1}) 3344, 2929, 2848, 1683, 1530, 1246, 1168. HRMS calc. m/z for [$C_{12}H_{24}N_2O_2$]: 228.1838, found: 229.1845 $(M+H)^+$.

Isothiocyanatocyclohexane (9) To a solution of cyclohexylamine (1.00g, 10.08 mmol), and triethylamine (3.36 g, 33.26 mmol) in 10 mL THF, carbon disulfide (767 mg, 10.08 mmol) was added in 40 min at 0 ºC. The resulted solution was stirred at room temperature for 2 hr. The mixture was cooled to 0 ºC and 4-toluene sulfonyl chloride (2.11g, 11.09 mmol) was added. The mixture was allowed to warm to room temperature and stirred for 2 hr. 1M Hydrochloric acid (20 mL) was then added. The mixture was extracted with hexane and Et_2O (1:1, 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuum. The resulting residue was purified by column chromatography to yield a clear oil (893 mg, 63%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 3.90 (m, *J* = 4.0 Hz, 1H), 1.89-1.83 (m, 2H), 1.60-1.57 (m, 4H), 1.44-1.34 (m, 4H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 128.39, 54.91, 32.42, 24.43, 22.59. IR *v* (Diamond, cm^{-1}) 2933, 2856, 2174, 2092, 2056, 1448, 1360, 1310, 1134.

tert-Butyl (((1r,4r)-4-(3-cyclohexylthioureido)cyclohexyl)methyl)carbamate (10) To a solution of **9** (100 mg, 0.71 mmol) in 10 mL CH_2Cl_2 was added **8** (162 mg, 0.71 mmol). After

stirring at room temperature for 24 hr, the solvent was removed in vacuum. The white residue was recrystallized using Et_2O to yield a white powder (189 mg, 72%). ^1H NMR (400 MHz, DMSO-*d*$_6$): δ 7.13 (t, *J* = 7.6 Hz, 2H, exchangeable), 6.80 (t, *J* = 5.65, 1H), 3.87 (bs, 2H), 2.76 (t, *J* = 6.4 Hz, 2H), 1.92-1.83 (m, 4H), 1.67-1.57 (m, 5H), 1.37 (m, 9H), 1.32-1.22 (s, 3H), 1.31-1.02 (m, 5H), 0.94-0.85 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 179.98, 155.61, 77.18, 52.02, 51.39, 45.69, 37.09, 32.24, 31.78, 28.96, 28.19, 25.12, 24.38. IR *v* (Diamond, cm^{-1}) 3374, 2936, 1685, 1556, 1406, 1297, 1152. HRMS calc. m/z for [$C_{19}H_{35}N_3O_2S$]: 369.2450, found: 392.2322 $(M+Na)^+$.

tert-Butyl (((1r,4r)-4-(((Z)-(cyclohexylamino)(((6,6-dimethyl-5,6-dihydroimidazo[2,1-b]thiazol-3-yl)methyl)thio)methylene)amino)cyclohexyl)methyl)carbamate (11) A solution of **10** (50 mg, 0.135 mmol) and **5** (32 mg, 0.135 mmol) in 3 mL acetonitrile was refluxed for 24 hr. The precipitate was filtered off and recrystallized from methanol/ether to give the product (43 mg, 51%). ^1H NMR (400 MHz, DMSO-*d*$_6$/D_2O = 10:1): δ 6.88 (s, 1H), 4.88 (s, 2H), 4.27 (s, 2H), 3.88 (s, 1H), 3.67 (s, 1H), 2.78 (m, 2H), 1.71-1.54 (m, 13H), 1.50 (s, 6H), 1.37 (s, 9H), 1.30-0.95 (m, 6H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$/D_2O = 10:1): δ 168.34, 160.32, 155.72, 131.36, 110.22, 77.40, 69.29, 58.15, 56.30, 53.34, 45.61,45.48, 40.08, 36.74, 32.07, 31.41, 30.96, 30.33, 28.51, 28.23, 28.04, 27.36, 24.51, 24.32. IR *v* (Diamond, cm^{-1}) 3333, 2929, 1698, 1610, 1499, 1250, 1172, 1027. HRMS calc. m/z for [$C_{27}H_{45}N_5O_2S_2$]: 535.3015, found: 536.2936 $(M+H)^+$.

aminomethyl-substituted IT1t (4) To a solution of **11** (500 mg, 0.821 mmol) in 10 mL CH_2Cl_2 was added TFA (1 mL). After being stirred for 0.5 hr, Et_2O (20 mL) was added. The precipitate

was filtered off and washed again with Et_2O to give a white solid as the trifluoroacetic acid salt (511 mg, 70.4 %). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 10.56 (s, 1H, exchangeable), 9.52 (s, 1H, exchangeable), 9.37 (s, 1H, exchangeable), 7.91 (s, 3H, exchangeable), 6.85 (s, 1H), 4.67 (s, 2H), 4.22 (s, 2H), 3.77-3.69 (m, 2H), 2.66 (m, 2H), 1.84-1.71 (m, 8H), 1.62-1.56 (m, 2H), 1.50 (s, 6H), 1.46-1.25 (m, 5H), 1.08-0.97 (m, 3H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 168.40, 160.50, 158.35, 131.27, 116.95, 110.24, 69.33, 58.03, 56.38, 55.76, 53.23, 52.86, 43.97, 43.85, 34.34, 32.07, 30.99, 30.01, 28.09, 27.86, 27.37, 24.55, 24.28. IR *v* (Diamond, cm^{-1}) 2936, 1669, 1607, 1556, 1451, 1310, 1126. HRMS calc. m/z for [$C_{22}H_{37}N_5S_2$]: 435.2490, found: 436.2321 $(M+H)^+$.

benzyl 6-aminohexylcarbamate (12) To a solution of 1,6-diaminohexane (2.32 g, 20 mmol) in CH_2Cl_2-MeOH (100 mL: 100 mL) was added a solution of CbzCl (3.08 g, 18 mmol) in CH_2Cl_2 (200 mL) dropwise over 8 hr while keeping the temperature below 0 °C. The mixture was stirred at the same temperature for another 16 hr before the solvent was removed under vacuum. The white residue was then dissolved in 100 mL water and acidified to pH = 2 using concentrated HCl. The resulting residue was then extracted using CH_2Cl_2 and stirred on ice. The organic solution was then basified using NaOH solution until pH = 12. The residue was then extracted again using CH_2Cl_2. The organic layer was dried with Na_2SO_4 and concentrated in vacuum to yield a white solid (2.03 g, 40.6 %) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36-7.34 (m, 4H), 7.33-7.29 (m, 1H), 5.10 (s, 2H), 4.72 (s, 1H, exchangeable), 3.19 (q, *J* = 6.8 Hz, 2H), 2.68 (t, *J* = 6.4 Hz, 2H), 1.55-1.48 (m, 2H), 1.45-1.41 (m, 2H), 1.35-1.32 (m, 4H), 1.26 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.55, 136.87, 128.66, 128.22, 66.76, 42.21, 41.20, 33.76, 30.13, 26.71, 26.65. IR *v* (Diamond, cm^{-1}) 3332, 2940, 2855, 1682, 1524, 1453, 1302, 1282, 1255, 1228, 1133, 1096, 1000. HRMS calc. m/z for [$C_{14}H_{22}N_2O_2$]: 250.1681, found: 251.1760 $(M+H)^+$.

3,12-dioxo-1-phenyl-2,14-dioxa-4,11-diazahexadecan-16-oic acid (13) To a stirring solution of **12** (6.09 g, 24.3 mmol) in 50 mL THF was added diglycolic anhydride (2.96 g, 25.5 mmol) in three portions. The resultant mixture was stirred at ambient temperature for 23 hr. After THF was removed under reduced pressure, the residue was crystallized by EtOAc–hexane to give a white solid (6.91g, 77%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 12.78 (s, 1H, exchangeable), 7.80 (bs, 1H, exchangeable), 7.40-7.28 (m, 5H), 7.19 (bs, 1H, exchangeable), 5.00 (s, 2H), 4.10 (s, 2H), 3.94 (s, 2H), 3.08 (q, *J* = 6.8 Hz, 2H), 2.98 (q, *J* = 6.8 Hz, 2H), 1.42-1.37 (m, 4H), 1.24 (br, 4H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 171.32, 168.45, 155.99, 137.26, 128.23, 127.61, 70.16, 67.88, 64.99, 38.00, 29.25, 28.97, 25.96, 25.84. IR *v* (Diamond, cm^{-1}) 3338, 3305, 2959, 2928, 1690, 1651, 1541, 1264, 1237, 1172, 1141, 1008. HRMS calc. m/z for [$C_{18}H_{26}N_2O_6$]: 366.1791, found: 389.1674 $(M+Na)^+$.

Benzyl (6-(2-(2-(((4R,4aS,7R,7aR)-3-(cyclopropylmethyl)-4a,9-dihydroxy-2,3,4,4a,5,6,7,7a-octahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinolin-7-yl)amino)-2-oxoethoxy)acetamido)hexyl)carbamate (14) The title compound was prepared according to the general amide coupling procedure by reacting **13** with 6β-naltrexamine hydrochloride salt in DMF. The resulting residue was dissolved in MeOH and 5 eq. of K_2CO_3 was added and stirred for 24 hr. After 24 hr, the K_2CO_3 was filtered out and the solution was concentrated to dryness to afford a brown solid. The solid was purified with column chromatography (CH_2Cl_2-MeOH, 30:1) and recrystallized with MeOH/Et_2O to afford an orange solid product (1.21 g, 72%) ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 9.2 Hz, 1H, exchangeable), 7.35-7.28 (m, 5H), 7.02 (t, *J* = 5.6 Hz, 1H, exchangeable), 6.71 (m, 1H), 6.55 (m, 1H), 5.09 (s, 2H), 4.95 (t, *J* = 5.6 Hz, 1H, exchangeable), 4.43 (d, *J* = 6.0 Hz, 1H), 4.11-3.99 (m, 4H), 3.31-3.24 (m, 2H), 3.21-3.17 (m, 2H),

3.09 (d, *J* = 6.0 Hz, 1H), 3.02 (d, *J* = 18.4 Hz, 1H), 2.64-2.58 (m, 2H), 2.40-2.30 (m, 2H), 2.23-2.14 (m, 2H), 1.84-1.74 (m, 1H), 1.66-1.60 (m, 1H), 1.53-1.45 (m, 7H), 1.35-1.34 (m, 4H), 1.14-1.11 (m, 1H), 0.85-0.75 (m, 1H), 0.55-0.50 (m, 2H), 0.14-0.10 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.82, 168.61, 156.78, 143.32, 139.61, 136.76, 130.75, 128.65, 128.23, 128.18, 124.76, 119.32, 117.89, 92.39, 77.36, 71.09, 71.06, 70.27, 66.81, 62.56, 59.54, 49.68, 47.37, 46.17, 44.03, 40.84, 38.85, 31.94, 30.00, 29.56, 29.17, 26.32, 26.11, 23.37, 22.77, 9.57, 4.12, 3.96. IR *v* (Diamond, cm^{-1}) 3297, 2929, 1651, 1538, 1505, 1454, 1323, 1239, 1126. HRMS calc. m/z for [$C_{38}H_{50}N_4O_8$]: 690.3629, found: 691.3459 $(M+H)^+$.

N-(6-aminohexyl)-2-(2-(((4R,4aS,7R,7aR)-3-(cyclopropylmethyl)-4a,9-dihydroxy-2,3,4,4a,5,6,7,7a-octahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinolin-7-yl)amino)-2-oxoethoxy)acetamide (15) A solution of **14** (250 mg, 0.36 mmol) in methanol (20 mL) was hydrogenated in the presence of 10% Pd/C (25 mg) under a H_2 atmosphere (10 psi) at room temperature for 3 hr. The mixture was filtered, and the filtrate was concentrated to a white foam (200 mg, 99%) ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 8.24 (d, *J* = 8.4 Hz, 1H, exchangeable), 8.05 (t, *J* = 5.2 Hz, 1H, exchangeable), 6.57 (m, 1H), 6.52 (m, 1H), 4.89 (brs, 1H, exchangeable), 4.59 (d, *J* = 7.6 Hz, 1H), 3.94 (m, 4H), 3.56-3.48 (m, 1H), 3.14 (m, *J* = 6.4 Hz, 2H), 3.01-2.94 (m, 2H), 2.60-2.56 (m, 2H), 2.38-2.28 (m, 2H), 2.15 (dt, J_1 = 4.4 Hz, J_2 = 12.0 Hz, 1H), 1.97 (dt, J_1 = 3.2 Hz, J_2 = 12.0 Hz, 1H), 1.84-1.75 (m, 1H), 1.46-1.44 (m, 4H), 1.33-1.23 (m, 9H), 0.87-0.79 (m, 1H), 0.48-0.46 (m, 2H), 0.11 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 168.36, 168.19, 142.06, 140.51, 131.20, 123,30, 118.32, 117.07, 90.43, 70.40, 70.35, 69.53, 61.72, 58.35, 50.62, 46.99, 43.64, 41.43, 38.09, 33.10, 30.25, 30.02, 29.15, 26.27, 26.05, 24.56, 22.13, 9.19, 3.62, 3.49. IR *v*

(Diamond, cm^{-1}) 3269, 2924, 1651, 1548, 1454, 1373, 1322, 1258, 1127, 1034. HRMS calc. m/z for [$C_{30}H_{44}N_4O_6$]: 556.3261, found: 557.3213 $(M+H)^+$.

18-(((4R,4aS,7R,7aR)-3-(cyclopropylmethyl)-4a,9-dihydroxy-2,3,4,4a,5,6,7,7a-octahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinolin-7-yl)amino)-5,14,18-trioxo-3,16-dioxa-6,13-diazaoctadecanoic acid (16) Diglycolic anhydride (125 mg, 1.08 mmol) was added to the solution of **15** (600 mg, 1.08 mmol) in DMF (5 mL). The resultant mixture was stirred at ambient temperature for 3 hr. After removal of DMF under reduced pressure, the residue was recrystallized by MeOH/Et_2O to give a white solid (586 mg, 80%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 8.70 (br, 1H, exchangeable), 8.36 (d, *J* = 8.4 Hz, 1H, exchangeable), 8.20 (br, 1H, exchangeable), 6.62 (m, 1H), 6.53 (m, 1H), 4.66 (d, *J* = 7.6 Hz, 1H), 3.95 -3.93 (m, 8H), 3.56-3.48 (m, 1H), 3.15-3.00 (m, 6H), 2.70-2.60 (m, 2H), 2.55-2.52 (m, 1H), 2.43-2.39 (m, 1H), 2.20 (dt, J_1 = 4.0 Hz, J_2 = 12.0 Hz, 1H), 2.09-2.02 (m, 1H), 1.87-1.78 (m, 1H), 1.50-1.33 (m, 6H), 1.29-1.24 (m, 6H), 0.90-0.87 (m, 1H), 0.49 (m, *J* = 7.2 Hz, 2H), 0.17-0.16 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d6*): δ 168.37, 168.16, 142.04, 140.61, 130.97, 122.84, 118.37, 117.13, 90.31, 70.35, 70.31, 69.51, 61.71, 58.10, 50.56, 46.75, 44.00, 37.96, 29.96, 29.76, 28.94, 28.88, 25.90, 25.87, 24.39, 22.25, 8.62, 3.75, 3.78. IR *v* (Diamond, cm^{-1}) 2931, 1651, 1599, 1504, 1432, 1393, 1253, 1126, 1034. HRMS calc. m/z for [$C_{34}H_{48}N_4O_{10}$]: 672.3370, found: 673.3519 $(M+H)^+$.

2-(2-(methylamino)-2-oxoethoxy)acetic acid (17) To a cooled 2M solution of methylamine in THF (10 mL), diglycolic anhydride (2.00 g, 17.2 mmol) was added. The resulted solution was stirred for 5 min on ice bath and then allowed to continue at ambient temperature for 24 hr. The resulting yellow oil was concentrated under vacuum and recrystallized using MeOH-Et_2O to yield

an off white solid (1.704g, 67%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.07 (s, 1H, exchangeable), 4.00 (s, 2H), 3.92 (s, 2H), 2.62 (d, J = 4.72 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.28, 169.08, 70.13, 67.83, 25.11. IR v (Diamond, cm^{-1}) 3387, 2919, 2524, 1707, 1627, 1258, 1203, 1130, 1084. HRMS calc. m/z for [$C_5H_9NO_4$]: 147.0532, found: 146.4232 $(M-H)^-$.

benzyl (6-(2-(2-(methylamino)-2-oxoethoxy)acetamido)hexyl)carbamate (18) The title compound was prepared according to the general amide coupling procedure by reacting acid **17** with amine **12**. The residue was then purified using column chromatography (CH_2Cl_2-MeOH, 20:1) to afford the product (2.79 g, 50%) ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.97 (m, 2H, exchangeable), 7.35 (m, 5H), 7.27 (m, 1H, exchangeable), 5.00 (s, 2H), 3.93 (m, 4H), 3.12 (m, 2H), 2.98 (m, 2H), 2.66 (d, J = 4.68 Hz, 3H), 2.51 (m, 2H), 1.40 (m, 4H), 1.26 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.87, 168.27, 156.06, 137.32, 128.28, 128.08, 127.66, 127.62, 70.32, 65.05, 40.22, 40.01, 39.80, 39.59, 39.38, 39.17, 38.96, 38.06, 29.53, 29.31, 29.15, 26.04, 25.89, 25.06. IR v (Diamond, cm^{-1}) 3337, 2924, 2855, 1690, 1652, 1543, 1454, 1435, 1407, 1367, 1279, 1148, 1124, 1059. HRMS calc. m/z for [$C_{19}H_{29}N_3O_5$]: 379.2107, found: 402.2018 $(M+Na)^+$.

***N*-(6-aminohexyl)-2-(2-(methylamino)-2-oxoethoxy)acetamide (19)** A solution of **18** (400 mg, 1.21 mmol) and Pd/C (40 mg, 10%) in 25 mL MeOH was shaken at 60 psi of H_2. After 24 hr the solution was filtered through celite and concentrated under vacuum. The residue was recrystallized using MeOH:Et_2OH to afford a white solid (258 mg, 100%) ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.00 (br, 2H, exchangeable), 3.90 (m, 4H), 3.13-3.08 (m, 2H), 2.65 (d, J = 4.68 Hz, 3H), 2.54-2.52 (m, 1H), 1.44-1.39 (m, 2H), 1.35-1.31 (m, 2H), 1.26 (m, 4H) ^{13}C NMR (100 MHz, DMSO-d_6): δ 70.29, 48.55, 41.32, 40.19, 39.98, 39.77, 39.56, 39.36, 39.15, 38.94, 38.07, 32.79, 29.21, 26.27,

26.04, 25.06. IR *v* (Diamond, cm^{-1}) 3318, 2924, 2855, 1652, 1548, 1432, 1338, 1124, 1004. HRMS calc. m/z for [$C_{11}H_{23}N_3O_3$]: 245.1739, found: 246.1798 $(M+H)^+$.

3,7,16-trioxo-5,18-dioxa-2,8,15-triazaicosan-20-oic acid (20) To a 25 mL flask added **19** (188 mg, 0.770 mmol), diglycolic anhydride (95 mg, 0.880 mmol), and 3 mL CH_2Cl_2. After 24 hr of stirring at ambient temperature, the solution was concentrated under vacuum to afford a faint yellow oil. Recrystallization using MeOH:Et_2OH afforded a faint yellow solid (157 mg, 56%) ^1H NMR (400 MHz, DMSO-d_6): δ 7.99 (m, 2H, exchangeable), 7.82 (m, 1H, exchangeable), 4.10 (s, 2H), 3.94 (s, 2H), 3.90(s, 4H), 3.13-3.06 (m, 4H), 2.65 (d, J = 4.68 Hz, 3H), 1.42 (m, 4H), 1.25 (m, 4H) ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.31, 168.81, 168.47, 168.20, 70.23, 70.15, 67.87, 40.13, 39.92, 39.71, 39.50, 39.30, 39.09, 38.88, 37.97, 37.96, 29.07, 28.94, 25.96, 25.94, 25.00. IR *v* (Diamond, cm^{-1}) 3310, 2930, 1651, 1538, 1469, 1417, 1362, 1338, 1124, 1036. HRMS calc. m/z for [$C_{15}H_{27}N_3O_7$]: 361.1849, found: 384.1774 $(M+Na)^+$.

Bivalent ligand (1) The title compound was prepared according to the general amide coupling procedure by reacting **16** with the aminomethyl-substituted It1t **4** in DMF. The resulting crude residue was purified using column chromatography (CH_2Cl_2-MeOH, 10:1) to afford the product (104 mg, 38%). ^1H NMR (400 MHz, DMSO-d_6) δ 9.01 (m, 1H, exchangeable), 8.21 (m, 1H, exchangeable), 8.19-8.01 (m, exchangeable, 3H), 6.58 (m, 1H), 6.52 (m, 1H), 4.59 (d, J = 7.80 Hz, 1H), 3.94 (m, 8H), 3.29 (s, 14H), 3.16 (m, 6H), 3.01 (m, 3H), 2.94 (m, 2H) 2.84 (m, 2H), 2.69 (m, 3H) 2.57 (m, 3H) 2.33 (m, 3H), 2.18-2.11 (m, 1H), 2.00-1.95 (m, 1H), 1.69 (m, 6H), 1.46 (m, 9H) 1.27 (m, 10H), 1.20 (m, 9H), 1.00-0.90 (m, 2H), 0.82 (m, 2H), 0.47 (m, 2H) 0.14 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 169.31, 168.50, 168.38, 168.24, 141.00, 141.10, 119.05, 117.71, 89.72, 83.47, 70.31, 69.58, 63.36, 61.65, 55.65, 55.42, 50.26, 45.73, 43.89, 43.03, 40.09, 39.88,

39.68, 39.47, 39.26, 39.05, 38.84, 38.00, 36.64, 33.85, 33.64, 33.23, 30.17, 29.42, 29.06, 28.61, 28.37, 27.67, 27.41, 26.09, 25.96, 25.43, 24.97, 23.74, 23.61, 22.77. IR *v* (Diamond, cm^{-1}) 3611, 3451, 3252, 3003, 1657, 1553, 1501, 1466, 1430, 1361, 1202, 1188, 1128, 1059. HRMS calc. m/z for $[C_{56}H_{83}N_9O_9S_2]$: 1089.5755, found: 1090.5825 $(M+H)^+$.

MOR Monovalent Control (2) The title compound was prepared according to the general amide coupling procedure by reacting **20** with 6β-naltrexamine hydrochloride salt. After starting material was consumed, the reaction mixture was filtered through celite and concentrated under vacuum. The resulting residue was dissolved in 5 mL MeOH and stirred at room temperature with K_2CO_3 (120 mg, 0.875 mmol). After 24 hr, K_2CO_3 was filtered out and the filtrate was concentrated to dryness to afford a brown solid. The residue was then purified using column chromatography (CH_2Cl_2-MeOH, 5:1) to afford the product (45 mg, 19%). ^{1}H NMR (400 MHz, DMSO-*d*$_6$): δ 9.01 (brs, 1H, exchangeable), 8.21 (d, *J* = 8.4 Hz, 1H, exchangeable), 8.03-7.96 (m, 3H, exchangeable), 6.58 (m, 1H), 6.52 (m, 1H), 4.88 (brs, 1H, exchangeable), 4.59 (d, *J* = 7.6 Hz, 1H), 3.95 (s, 2H), 3.93 (s, 2H), 3.91 (s, 4H), 3.56-3.48 (m, 1H), 3.17-3.09 (m, 4H), 3.01-2.95 (m, 2H), 2.65 (d, *J* = 4.4 Hz, 3H), 2.62-2.57 (m, 2H), 2.38-2.28 (m, 2H), 2.19-2.11 (m, 1H), 2.01-1.94 (m, 1H), 1.83-1.74 (m, 1H), 1.46-1.44 (m, 6H), 1.32-1.23 (m, 6H), 0.87-0.81 (m, 1H), 0.48-0.46 (m, 2H), 0.12-0.11 (m, 2H). ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 168.80, 168.33, 168.22, 168.14, 142.02, 140.35, 131.22, 123.40, 118.28, 116.98, 90.43, 70.36, 70.31, 70.24, 69.51, 61.71, 58.34, 50.60, 46.97, 43.62, 38.01, 37.97, 30.24, 29.99, 29.10, 25.98, 25.01, 24.51, 22.13, 9.16, 3.59, 3.46. IR *v* (Diamond, cm^{-1}) 3288, 2929, 1651, 1548, 1504, 1454, 1323, 1239, 1185, 1124, 1035. HRMS calc. m/z for $[C_{35}H_{51}N_5O_9]$: 685.3687, found: 686.3595 $(M+H)^+$.

CXCR4 Monovalent Control (3) The title compound was prepared according to the general amide coupling procedure by reacting **20** with the aminomethyl-substituted It1t **4**. The residue was then purified using column chromatography (CH_2Cl_2-MeOH, 30:1) to afford the product (47 mg, 11%) ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.03-7.95 (m, 4H, exchangeable), 3.92-3.86 (m, 8H), 3.71 (s, 2H), 3.69-3.66 (m, 1H, exchangeable), 3.36-3.12 (m, 2H), 3.15-3.07 (m, 4H), 2.99-2.95 (m, 2H), 2.93-2.87 (m, 2H), 2.83 (m, 2H), 2.65 (d, J = 4.6 Hz, 3H), 1.72-1.40 (m, 4H), 1.36-1.26 (m, 3H), 1.20-1.19 (m, 5H), 1.06-1.02 (m, 8H), 1.00-0.98 (d, J = 5.8 Hz, 6H), 0.90-0.79 (m, 3H) ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.90, 168.58, 168.48, 168.30, 148.75, 84.48, 74.29, 70.27, 70.15, 55.51, 54.79, 40.00, 39.79, 39.58, 39.37, 39.16, 38.95, 38.74, 37.87, 36.86, 33.74, 33.32, 29.07, 28.91, 25.97, 24.93, 23.67. IR v (Diamond, cm^{-1}) 3289, 2924, 2850, 2359, 2161, 2027, 1651, 1544, 1435, 1363, 1120, 1031. HRMS calc. m/z for [$C_{37}H_{62}N_8O_6S_2$]: 778.4234, found: 779.4079 $(M+H)^+$.

Radioligand Binding Assay

The competition-binding assay was conducted to determine the affinity of the bivalent compound and its monovalent control at the mu opioid receptor (MOR) using monoclonal mouse opioid receptor expressed in Chinese hamster ovary (CHO) cell lines. MOR-CHO cells were cultured and maintained in DMEM (90%), and fetal bovine serum 10% (v/v). [^{3}H]naloxone ([^{3}H]NLX) was used to label the MOR and a saturation assay was conducted to determine the K_d and B_{max} values for [^{3}H]NLX at the MOR, which were measured as 1.81 ± 0.16 nM and 2.47 ± 0.20 pmol/mg, respectively. To determine the binding affinity of test compounds, 30 μg of membrane protein was incubated with [^{3}H]NLX in the presence of different concentrations of test compounds in TME buffer (50 mM Tris, 3 mM $MgCl_2$, and 0.2 mM EGTA, pH 7.7) for 1.5

h at 30 °C. The bound radioligand was separated by filtration using the Brandel harvester. Specific (i.e., opioid receptor-related) binding at the KOR was determined as the difference in binding obtained in the absence and presence of 5 μM naltrexone. The IC_{50} values were determined and converted to K_i values using the Cheng–Prusoff equation.

Antibody Binding Assays

CHO-CXCR4 cells were maintained in RPMI1640 medium supplemented with 10% (v/v) FBS, 100 units/mL penicillin, 100 mg/mL streptomycin and 2 mM L-glutamine, and 400 μg/mL geneticin. Following trypsinization, CHO-CXCR4 cells were washed twice with FACS buffer (0.5% BSA, 0.05% sodium azide in PBS). 5×105 cells per well with primary antibody (1:2000, mouse anti-human CD184 antibody, BD Biosciences, USA) were seeded in 96-well v-bottom plates at the presence of various concentrations of compounds. After incubation for 40 min on ice, cells were washed twice with FACS buffer, and then incubated with secondary antibody (1:1000, anti-mouse IgG-FITC antibody, Sigma, USA) for 30 min on ice. Cells were washed twice again and re-suspended with FACS buffer. The fluorescence (excitation 485/emission 528) was recorded using a Synergy II plate reader. IC_{50}s were calculated by GraphPad Prism from at least three independent experiments.

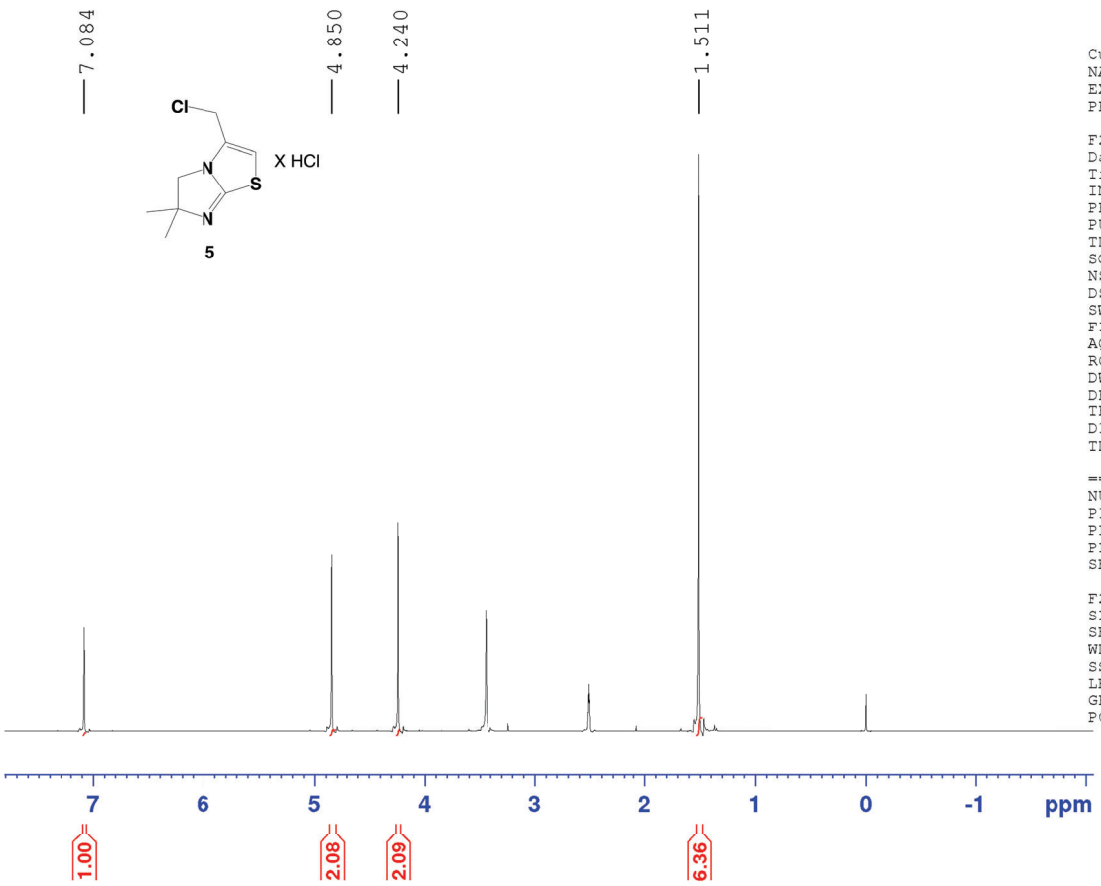
Calcium Mobilization Assays

The ligands were first tested with various concentrations (0.3 nM to 3 μM) for possible agonist activity in either MOR-CHO or CXCR4-HOS cells. The protocol was the same for the antagonism study for both MOR and CXCR4 cell types, except for the addition of an agonist (either DAMGO or SDF-1).

CXCR4-HOS cells were cultured and maintained in DMEM (90%), fetal bovine serum 10% (v/v), and supplemented with 1.0 μg/ml puromycin. MOR-CHO cells were cultured and maintained in DMEM (90%), and fetal bovine serum 10% (v/v).

Either CXCR4-HOS or MOR-CHO cells were transfected with Gqi5 pcDNA1 (Addgene, Cat# 24501) using Lipofectamine 2000 (Invitrogen) according to the manufacturer's recommended procedure. Cells were incubated for 4 hr at 37 °C and 5% CO_2 and then trypsinized and transferred to a clear bottom, black 96-well plate (Greiner Bio-one) at $3x10^6$ cells per well in their respective growth media and incubated until confluent. 48 hours after transfection the growth media was decanted and cells were then incubated with 50 μL of fluo-4 AM loading buffer [24 μL 2 mM fluo-4 AM solution (Invitrogen), 12 μL 250 mM probenecid, in 6 mL assay buffer (HBSS–HEPES–Ca–Mg-probenecid)] for 45 min. Loading buffer was then decanted and cells were incubated for an additional 15 min in 20 μL of each compound in varying concentrations and 60 μL assay buffer. Ca^{2+} concentrations were monitored by RFU for 90 seconds right after addition of 20 μL of agonist (DAMGO or SDF-1) to each well in the microplate reader (FlexStation3, Molecular Devices). Peak values were obtained using SoftMaxPro software (Molecular Devices) and non-linear regression curves were generated using Prism (GraphPad) to calculate IC_{50} values. All doses were tested with triplicates. All experiments were repeated at least 4 times to obtain standard error values.

Apr.23,2015
PROTON DMSO /opt/topspin Kang.g 42



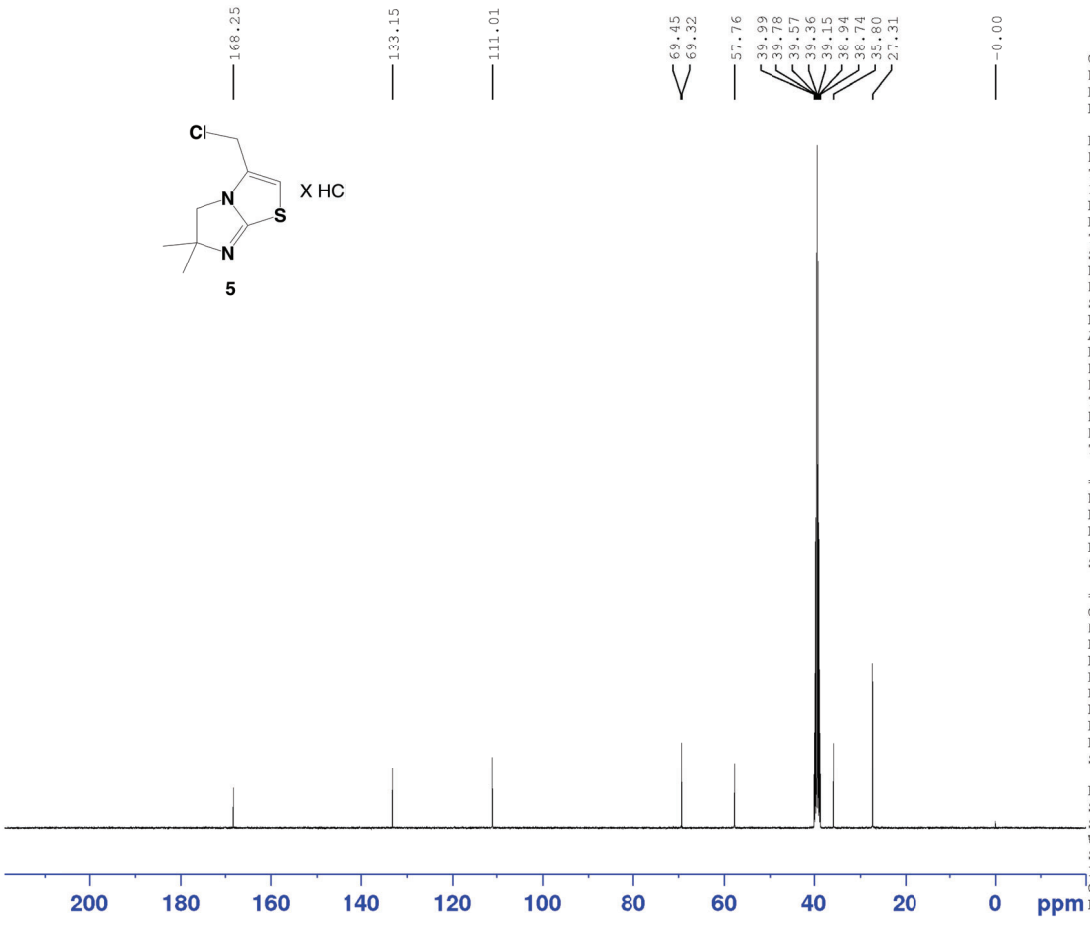
Current Data Parameters
NAME GK-II-42
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150423
Time 17.53
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1299984 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Apr.23,2015
C13C?D DMSO /opt/topspin Kang.g 42



Current Data Parameters

NAME	GK-II-42_C
EXPNO	10
PROCNO	1

F2 - Acquisition Parameters

Date_	20150423
Time	23.02
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	DMSO
NS	4096
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	301.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

NUC1	13C
P1	8.50 usec
PL1	-1.70 dB
PL1W	55.73028564 W
SFO1	100.6228298 MHz

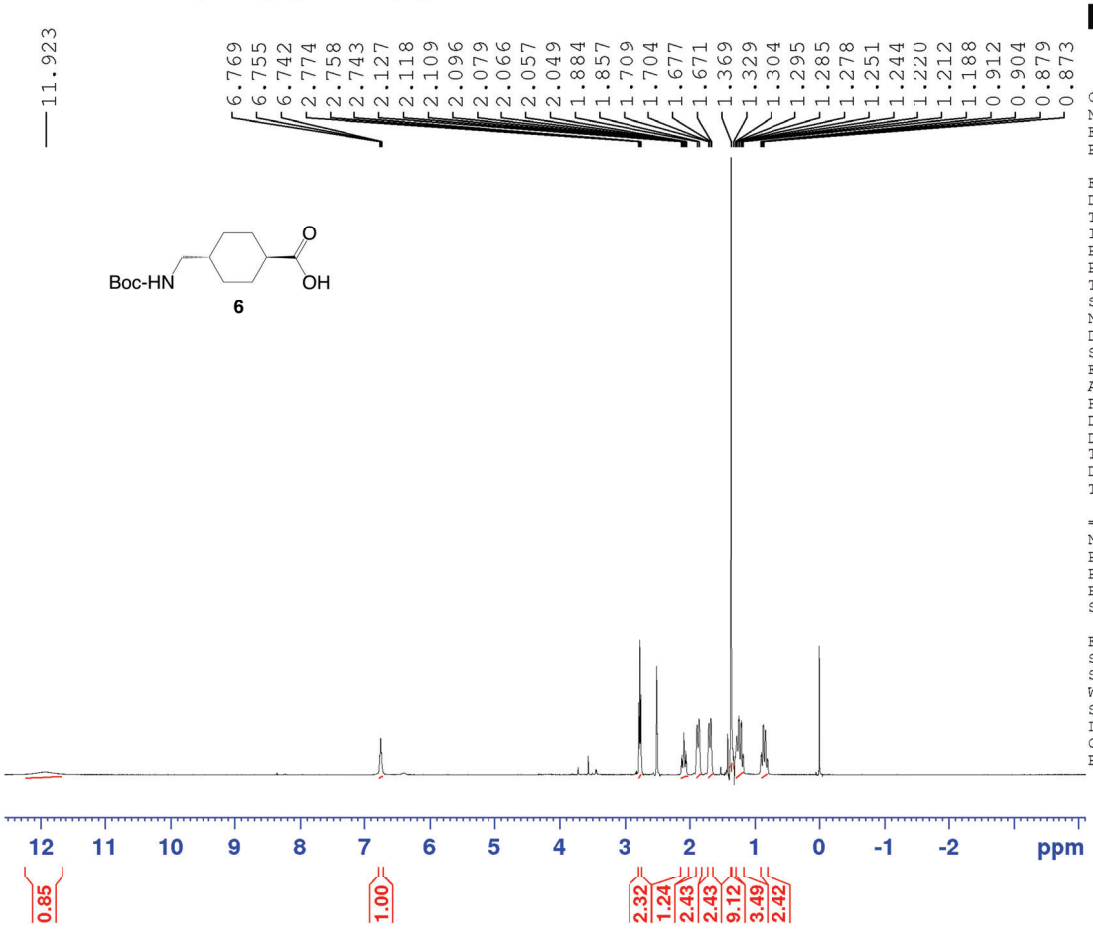
======== CHANNEL f2 ========

CPDPRG[2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	14.50 dB
PL13	14.50 dB
PL2W	15.12807274 W
PL12W	0.33867535 W
PL13W	0.33867535 W
SFO2	400.1316005 MHz

F2 - Processing parameters

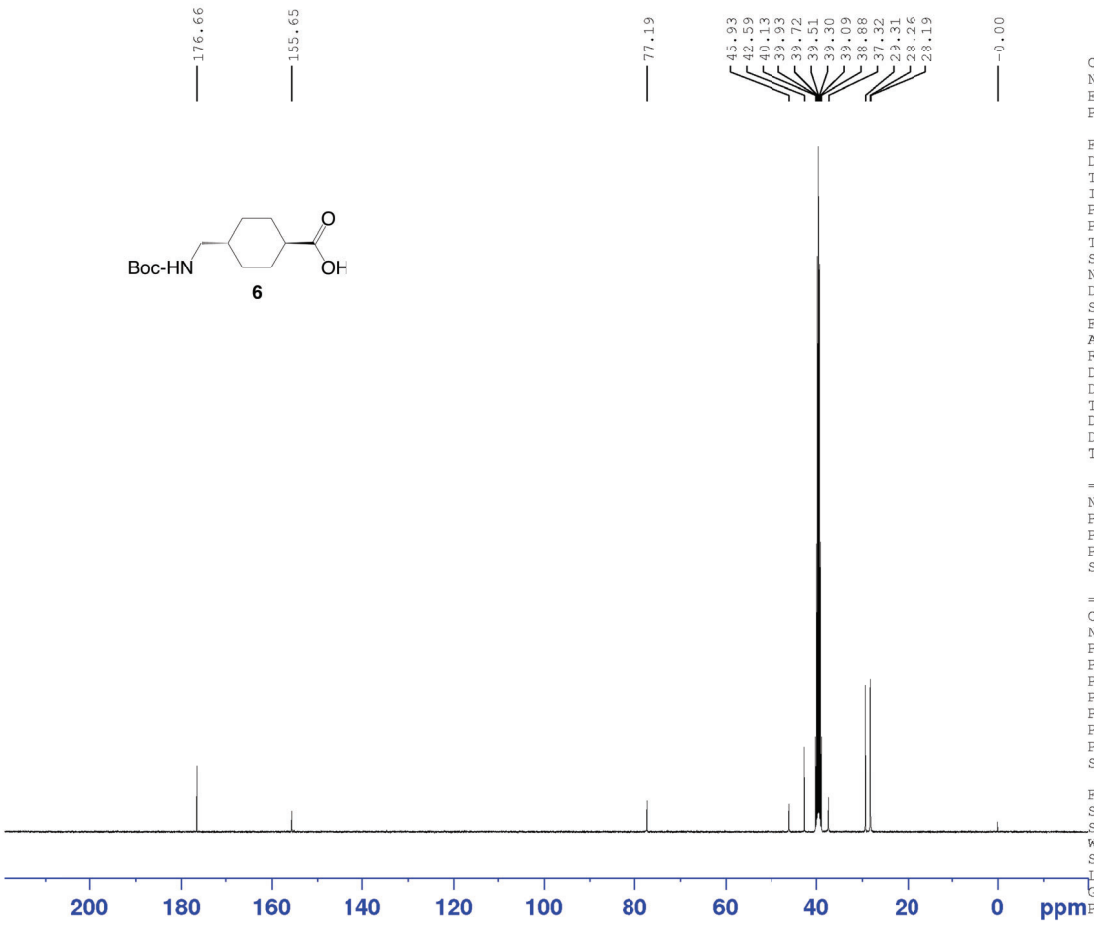
SI	32768
SF	100.6128258 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

May 27,2015
PROTON DMSO /opt/topspin Kang.g 27




```
Current Data Parameters
NAME                  GK-II-27
EXPNO                       10
PROCNO                       1

F2 - Acquisition Parameters
Date_               20150527
Time                   16.49
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                 zg30
TD                     65536
SOLVENT                 DMSO
NS                         8
DS                         2
SWH                 8223.685 Hz
FIDRES              0.125483 Hz
AQ                  3.9845889 sec
RG                       144
DW                    60.800 usec
DE                     6.50 usec
TE                    303.4 K
D1                 1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     12.00 usec
PL1                    -2.00 dB
PL1W             15.12807274 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                     32768
SF               400.1300045 MHz
WDW                       EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

May 27,2015
C13C?D DMSO /opt/topspin Kang.g 27



Current Data Parameters
NAME GK-II-27_C
EXPNO 10
PROCNO 1

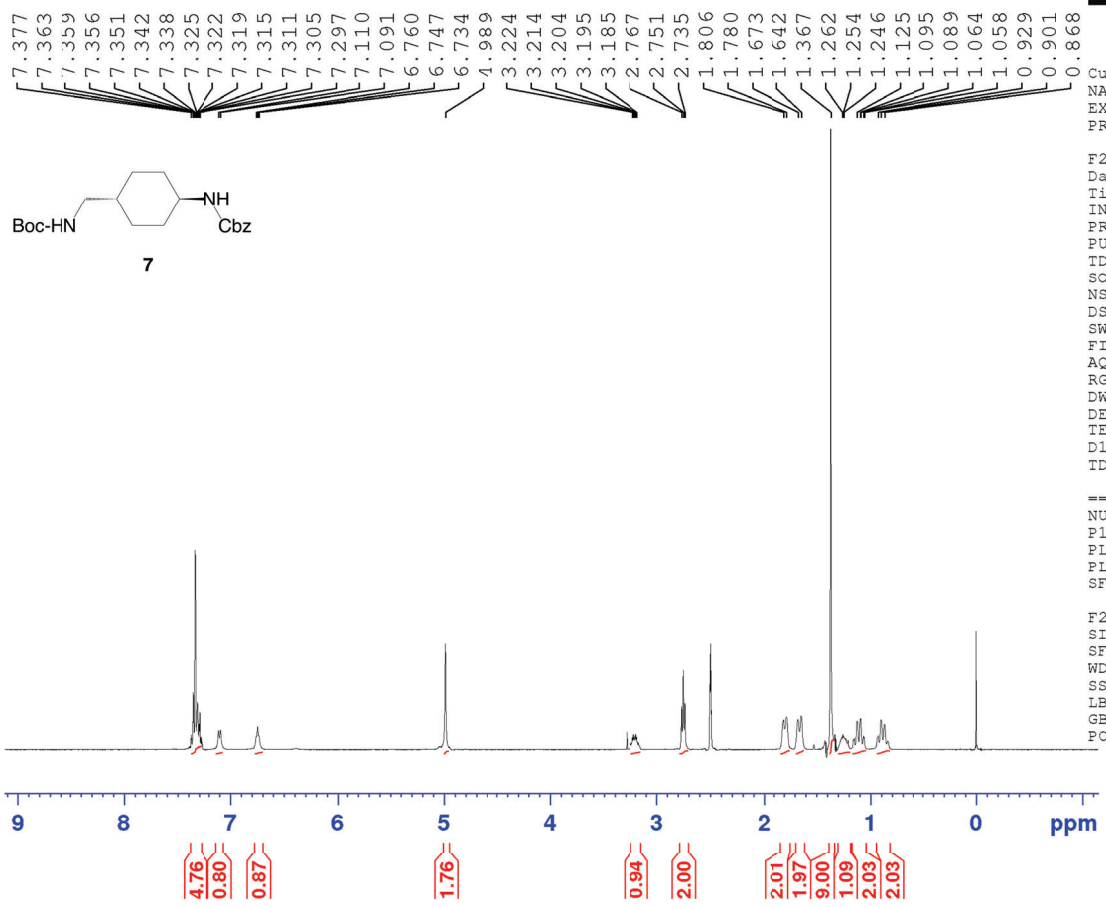
F2 - Acquisition Parameters
Date_ 20150528
Time 22.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 5120
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 305.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128250 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

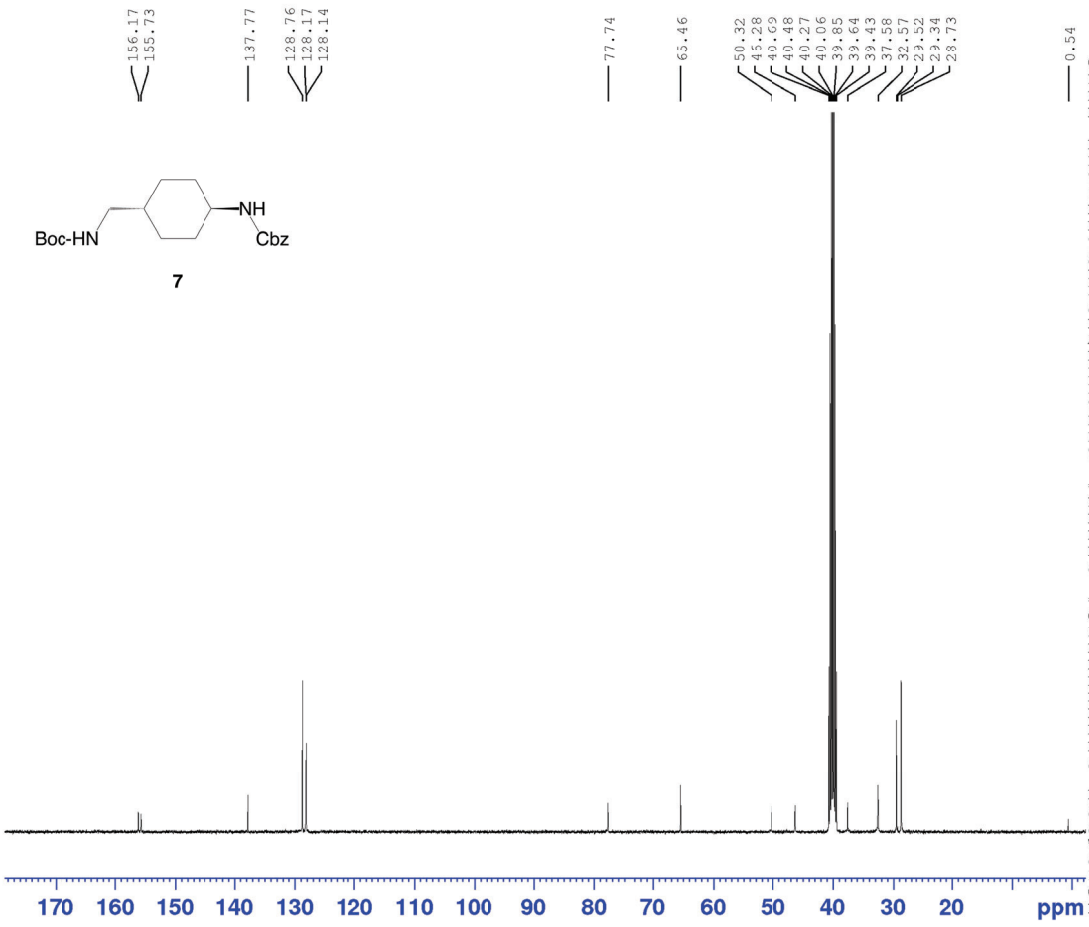
Apr.05,2015
PROTON DMSO /opt/topspin Kang.g 60



BRUKER

```
Current Data Parameters
NAME      GK-II-30a_DMSO
EXPNO                 30
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150405
Time               18.01
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                     8
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   181
DW                60.800 usec
DE                 6.50 usec
TE                304.6 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -2.00 dB
PL1W        15.12807274 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300049 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

Apr.05,2015
C13CPD DMSO /opt/topspin Kang.g 60



BRUKER

Current Data Parameters
NAME GK-II-30a_DMSO_C
EXPNO 10
PROCNO 1

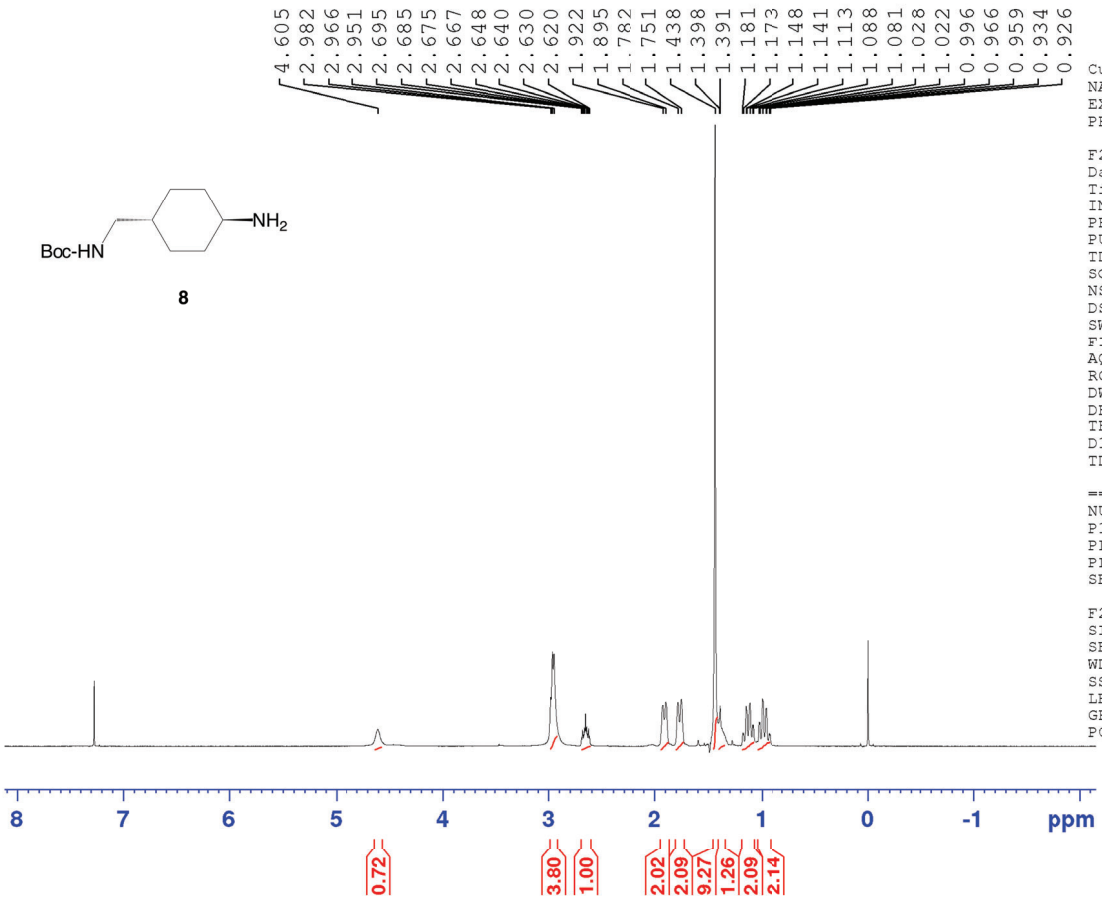
F2 - Acquisition Parameters
Date_ 20150407
Time 0.05
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 5120
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 305.7 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127711 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

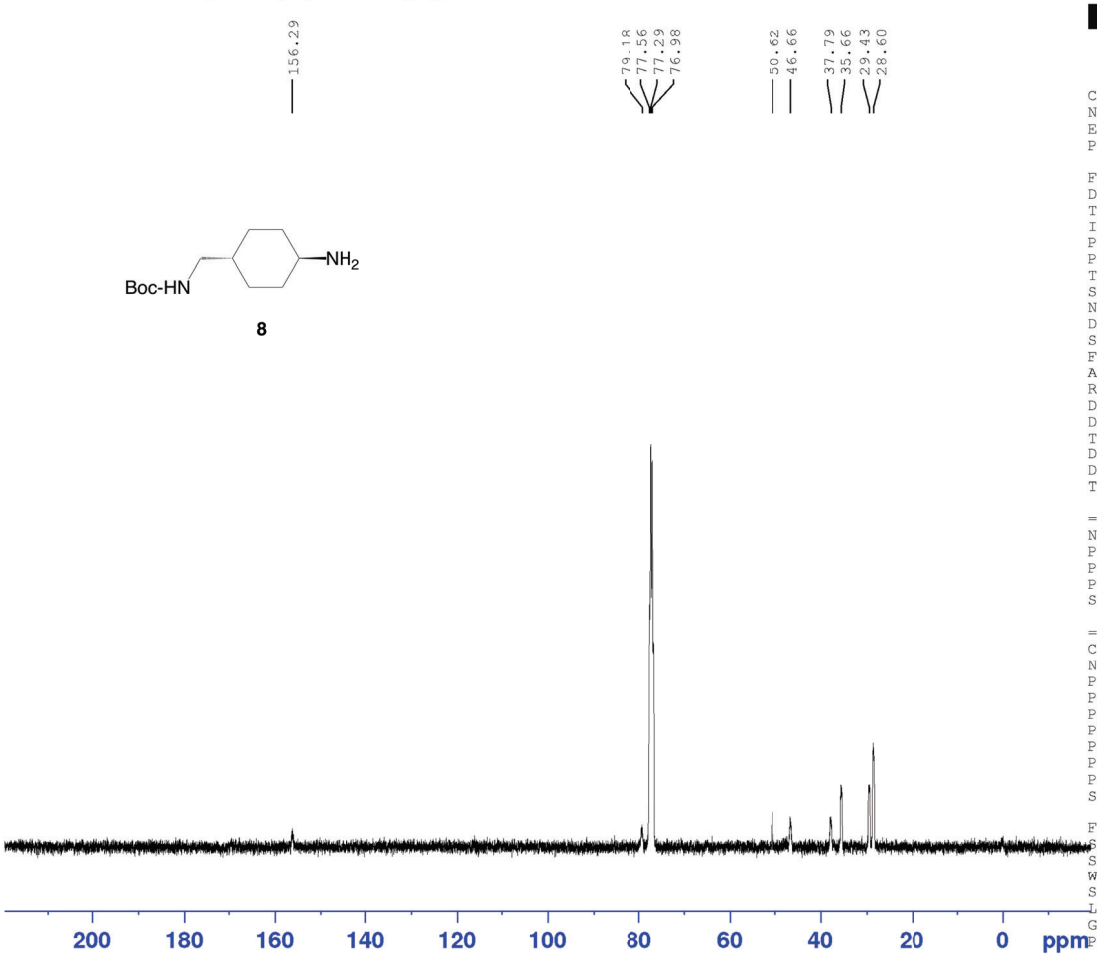
May 28,2015
PROTON CDCl3 /opt/topspin Kang.g 56



BRUKER

```
Current Data Parameters
NAME      GK-II-33_CDCl3
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150528
Time               16.48
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   114
DW                60.800 usec
DE                 6.50 usec
TE                302.7 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -2.00 dB
PL1W        15.12807274 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300052 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

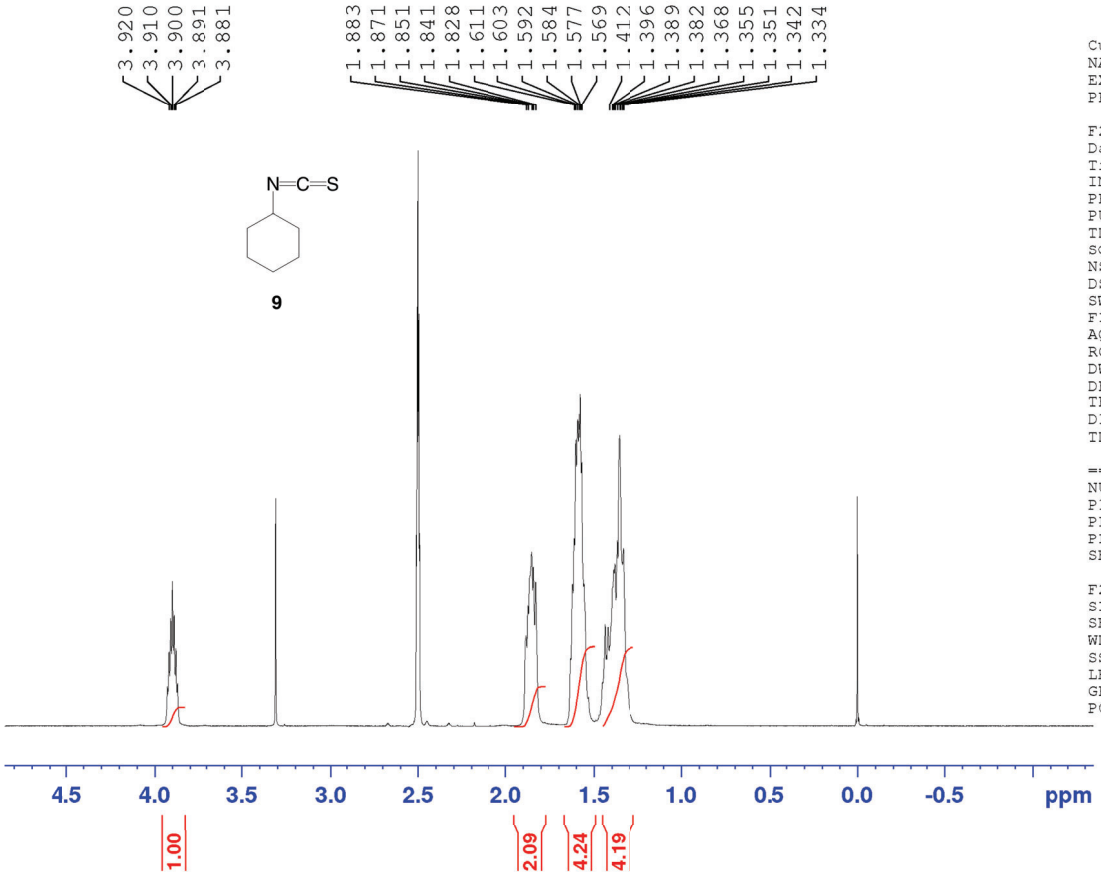
May 29,2015
C13C?D CDCl3 /opt/topspin Kang.g 26



BRUKER

```
Current Data Parameters
NAME      GK-II-33_CDCl3_C
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_              20150601
Time                   5.51
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    5120
DS                       4
SWH              24038.461 Hz
FIDRES           0.366798 Hz
AQ               1.3631488 sec
RG                     203
DW                20.800 usec
DE                 6.50 usec
TE                 303.8 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                  8.50 usec
PL1                -1.70 dB
PL1W         55.73028564 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                -2.00 dB
PL12               14.50 dB
PL13               14.50 dB
PL2W         15.12807274 W
PL12W         0.33867535 W
PL13W         0.33867535 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                   32768
SF           100.6127690 MHz
WDW                     EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

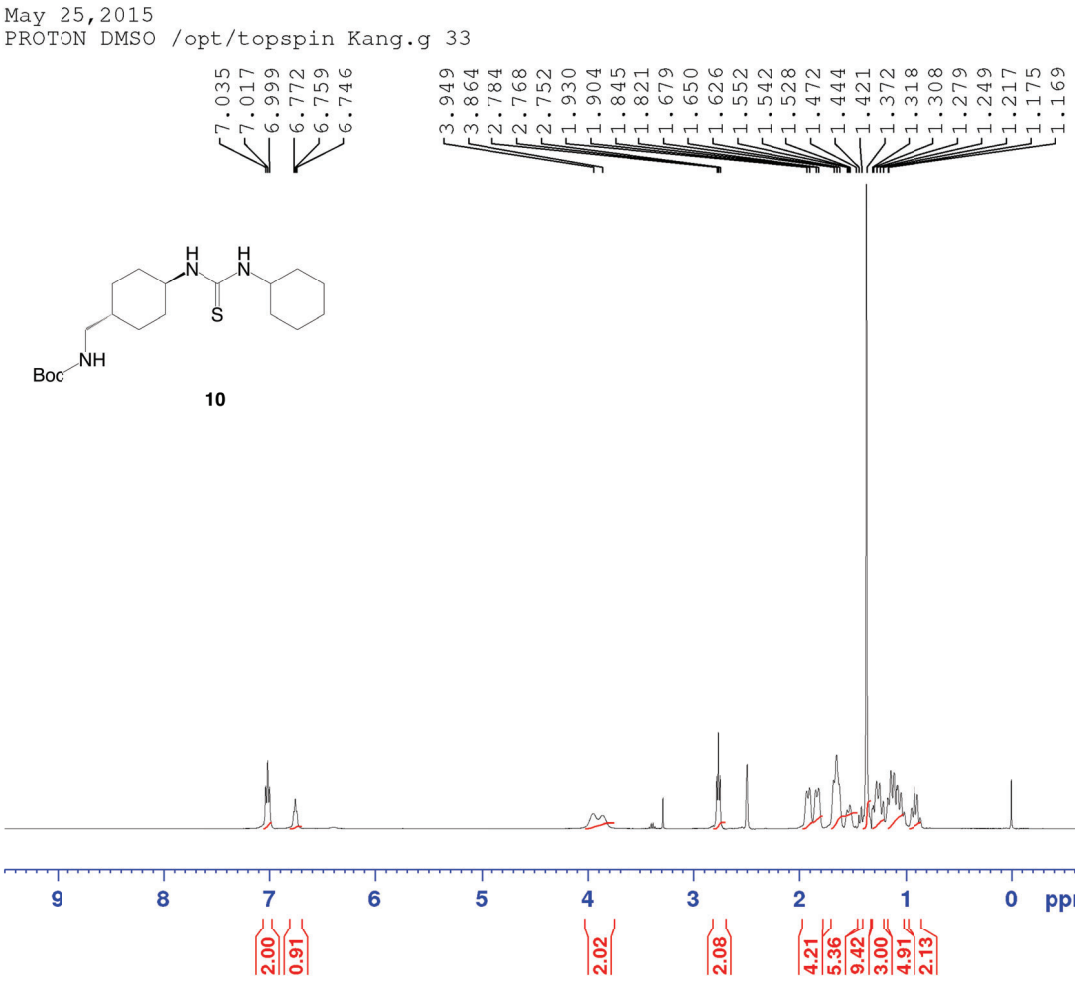
Jan.21,2015
PROTON DMSO /opt/topspin Kang.g 16



BRUKER

```
Current Data Parameters
NAME                  GK-I-71
EXPNO                      10
PROCNO                      1

F2 - Acquisition Parameters
Date_               20150121
Time                   10.10
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT                DMSO
NS                       32
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9845889 sec
RG                       203
DW                    60.800 usec
DE                     6.50 usec
TE                    298.2 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                     12.00 usec
PL1                    -2.00 dB
PL1W            15.12807274 W
SFO1            400.1324710 MHz

F2 - Processing parameters
SI                        32768
SF              400.1300045 MHz
WDW                        EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```

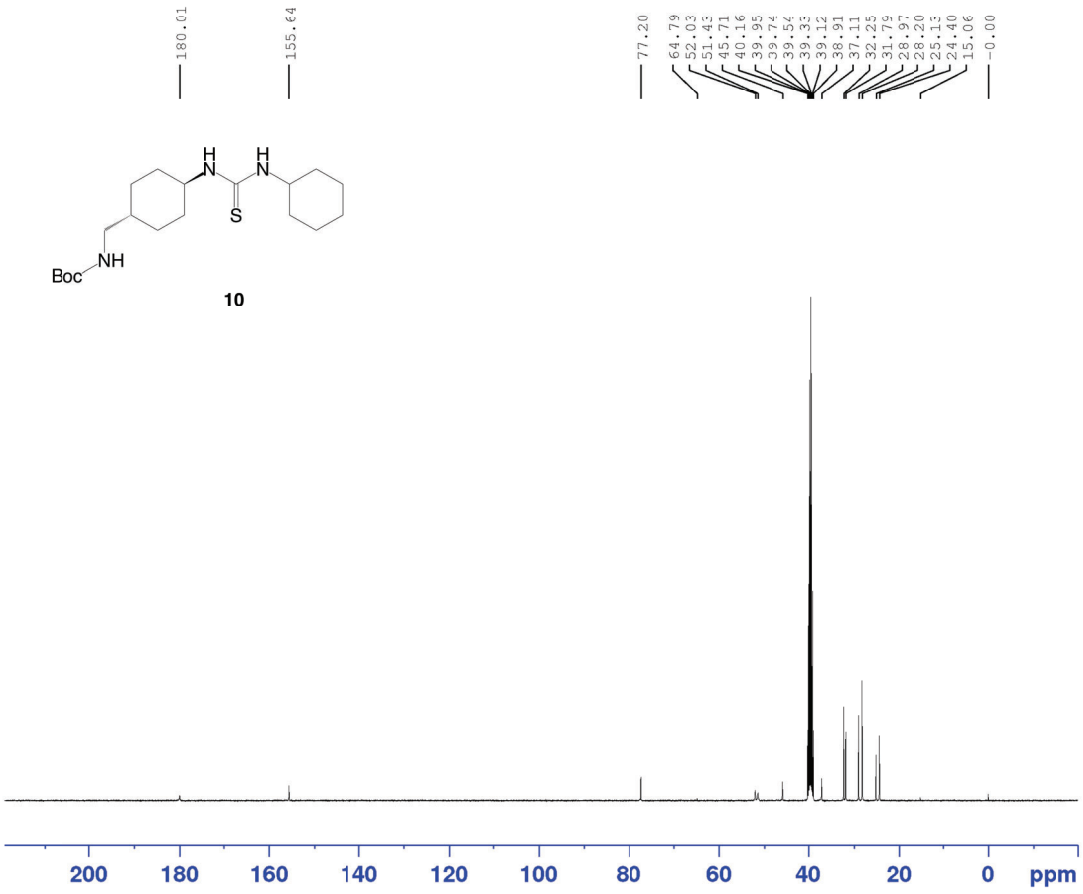
May 25,2015
PROTON DMSO /opt/topspin Kang.g 33



BRUKER

```
Current Data Parameters
NAME      GK-I-73b_DMSOb
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150525
Time               19.49
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                  90.5
DW                60.800 usec
DE                 6.50 usec
TE                305.1 K
D1            1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -2.00 dB
PL1W        15.12807274 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300045 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

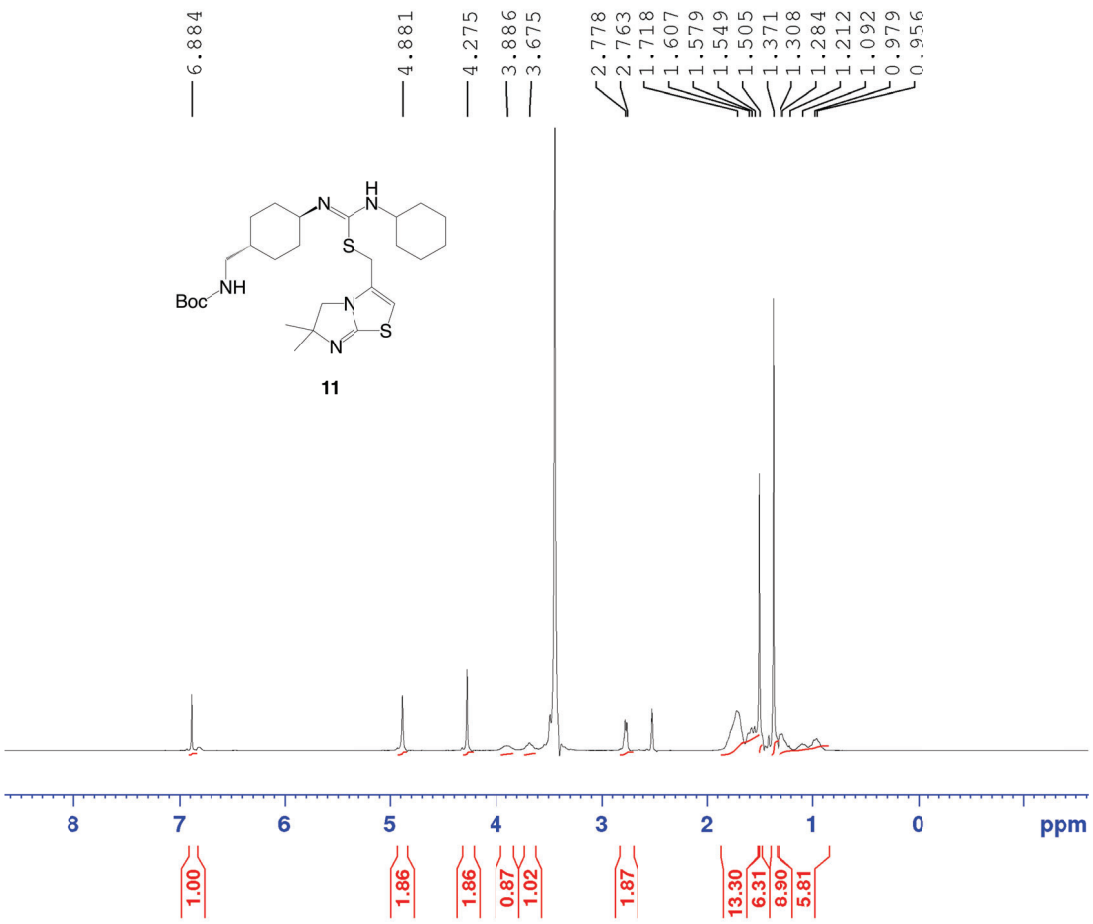
May 25,2015
C13CPD DMSO /opt/topspin Kang.g 33



10

```
Current Data Parameters
NAME      GK-I-73b_DMSOb_C
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_              20150526
Time                   0.48
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT                DMSO
NS                     5120
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631488 sec
RG                      203
DW                   20.800 usec
DE                    6.50 usec
TE                   306.9 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    8.50 usec
PL1                  -1.70 dB
PL1W          55.73028564 W
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2           waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                  -2.00 dB
PL12                 14.50 dB
PL13                 14.50 dB
PL2W          15.12807274 W
PL12W          0.33867535 W
PL13W          0.33867535 W
SFO2         400.1316005 MHz

F2 - Processing parameters
SI                    32768
SF           100.6128250 MHz
WDW                      EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.40
```

Mar.17,2015
PROTON DMSO /opt/topspin Kang.g 29

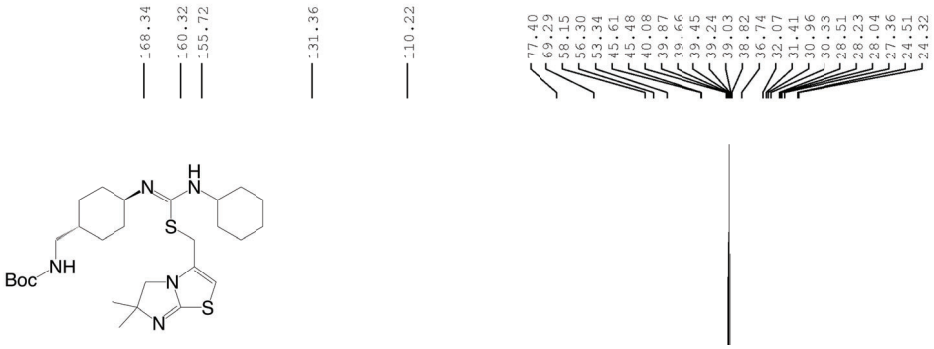


11

BRUKER

```
Current Data Parameters
NAME                  GK-II-19b
EXPNO                        10
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20150317
Time                      17.11
INSTRUM                   spect
PROBHD     5 mm PABBO BB-
PULPROG                   zg30
TD                       65536
SOLVENT                   DMSO
NS                           8
DS                           2
SWH                   8223.685 Hz
FIDRES                0.125483 Hz
AQ                    3.9845889 sec
RG                        80.6
DW                       60.800 usec
DE                        6.50 usec
TE                       303.2 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                         1H
P1                       12.00 usec
PL1                      -2.00 dB
PL1W             15.12807274 W
SFO1             400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF                400.1300000 MHz
WDW                         EM
SSB             0
LB                        0.30 Hz
GB              0
PC                        1.00
```

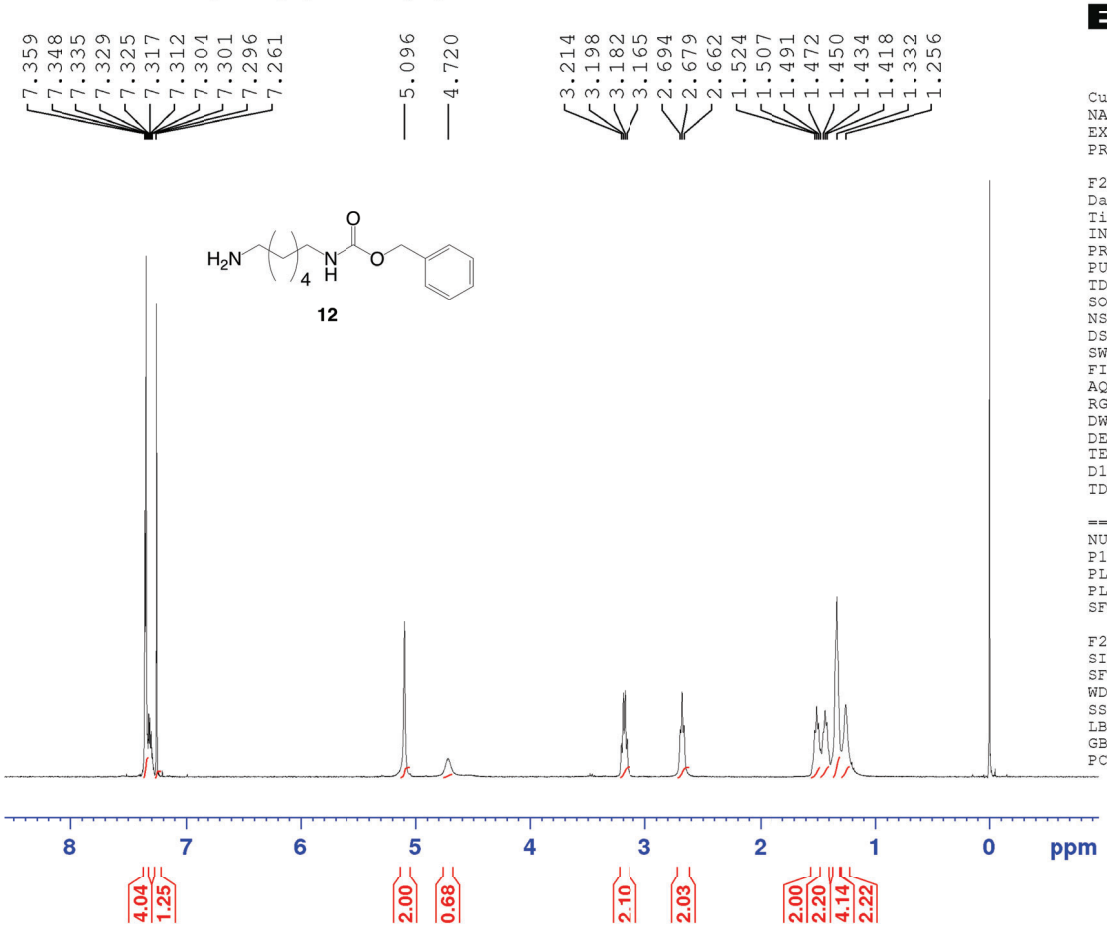
Mar.17,2015
C13C?D DMSO /opt/topspin Kang.g 29



Current Data Parameters
NAME GK-II-19b_C
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150319
Time 1.54
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS
DS
SWH
FIDRES

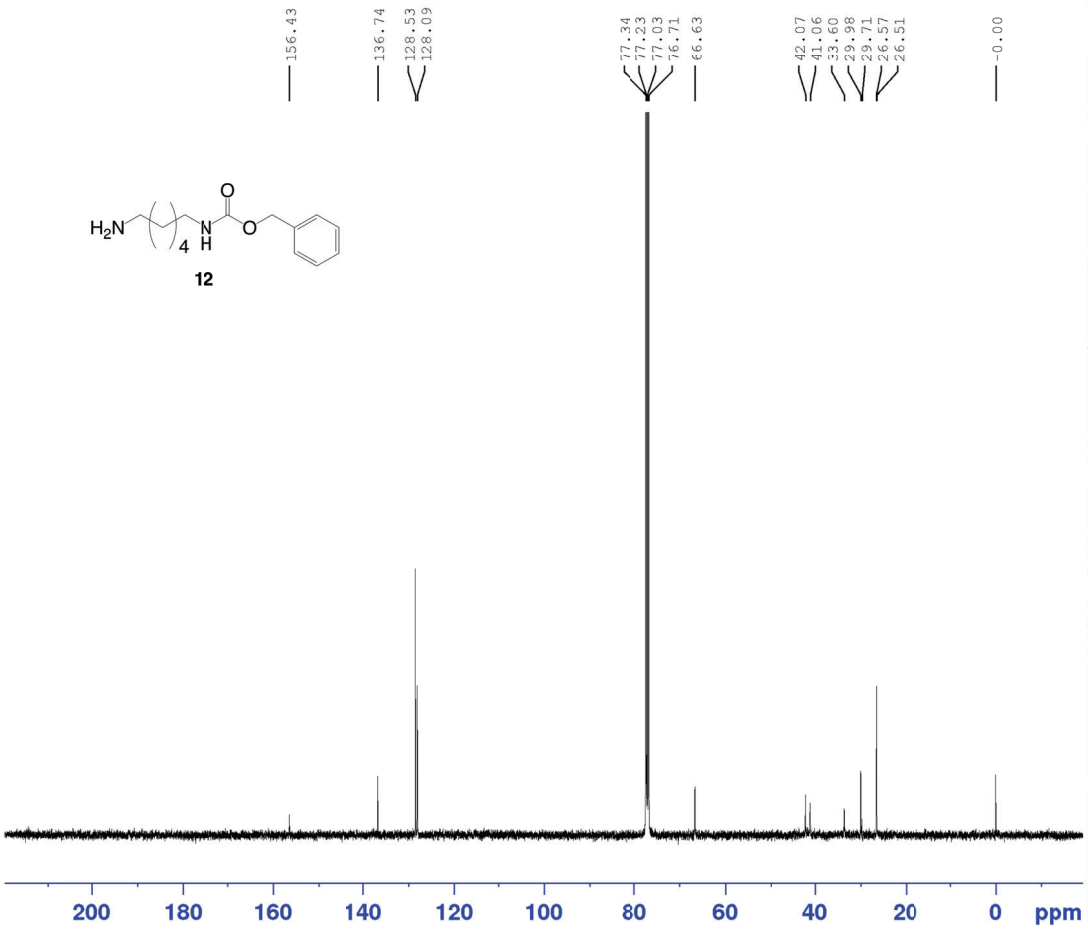
Apr.02,2015
PROTON CDCl3 /opt/topspin Kang.g 59



BRUKER

```
Current Data Parameters
NAME            GK-II-29
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150402
Time               16.54
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9845889 sec
RG                   203
DW                60.800 usec
DE                 6.50 usec
TE                306.5 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -2.00 dB
PL1W        15.12807274 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1300115 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

Apr.12,2015
C13C?D CDCl3 /opt/topspin Kang.g 29

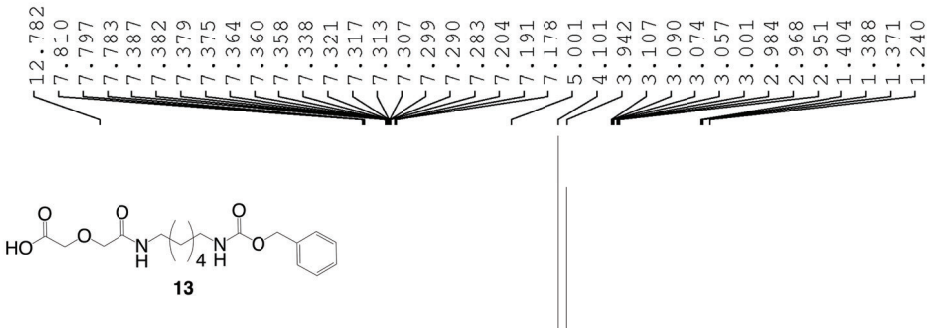


12

BRUKER

```
Current Data Parameters
NAME          GK-II-29_C
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150413
Time              23.03
INSTRUM           spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD                65536
SOLVENT           CDCl3
NS                 5210
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  203
DW               20.800 usec
DE                6.50 usec
TE                304.4 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 8.50 usec
PL1               -1.70 dB
PL1W        55.73028564 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2              80.00 usec
PL2                -2.00 dB
PL12               14.50 dB
PL13               14.50 dB
PL2W        15.12807274 W
PL12W        0.33867535 W
PL13W        0.33867535 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF         100.6127655 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

Apr.07,2015
PROTON DMSO /opt/topspin Kang.g 33

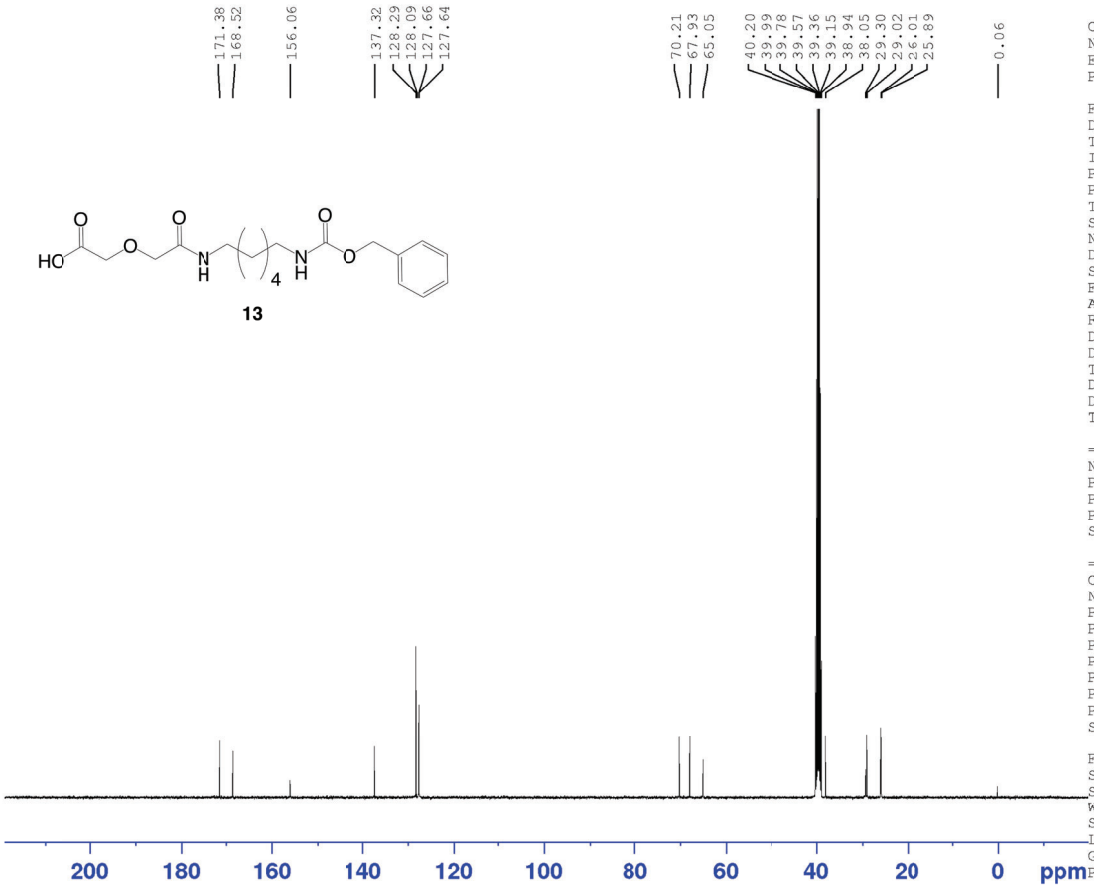


13

Current Data Parameters
NAME GK-II-31
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150407
Time 17.27
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 8223.685 H
FIDRES 0.125483 H

Apr.07,2015
C13CPD DMSO /opt/topspin Kang.g 33



13

BRUKER

Current Data Parameters
NAME GK-II-31_C
EXPNO 10
PROCNO 1

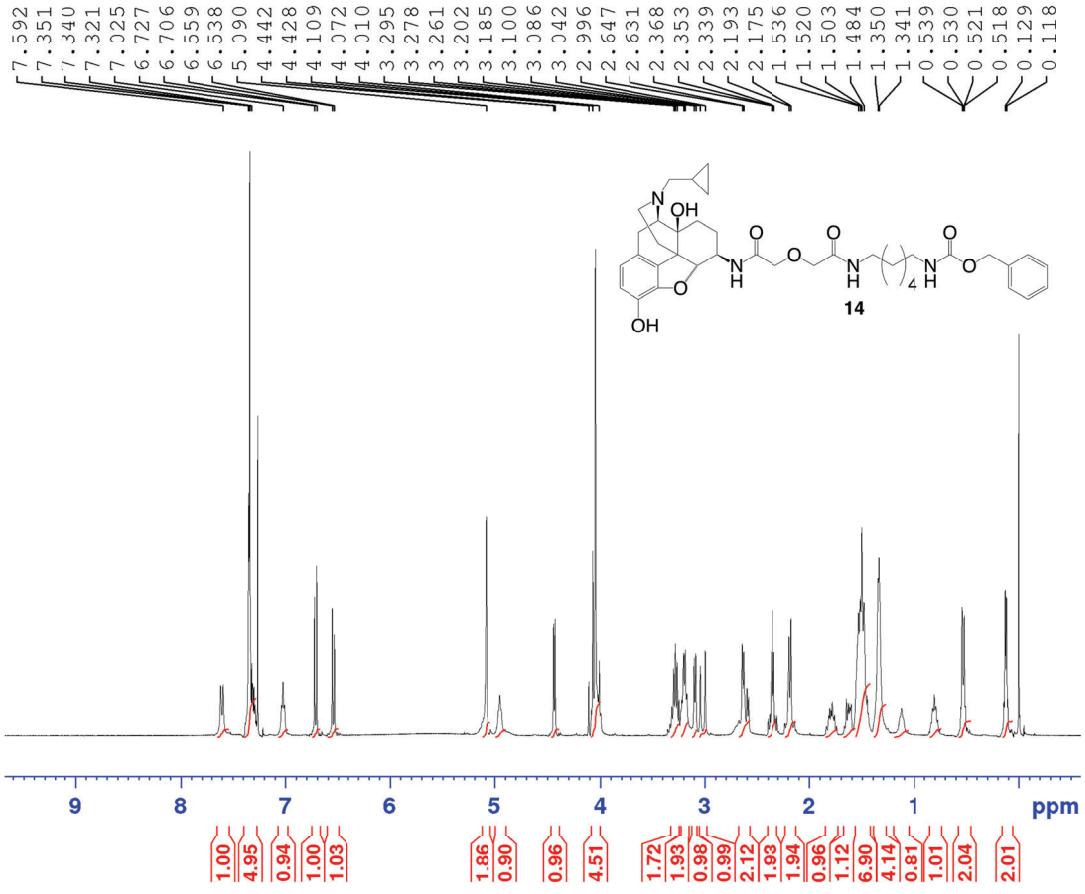
F2 - Acquisition Parameters
Date_ 20150408
Time 22.02
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 4096
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 305.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

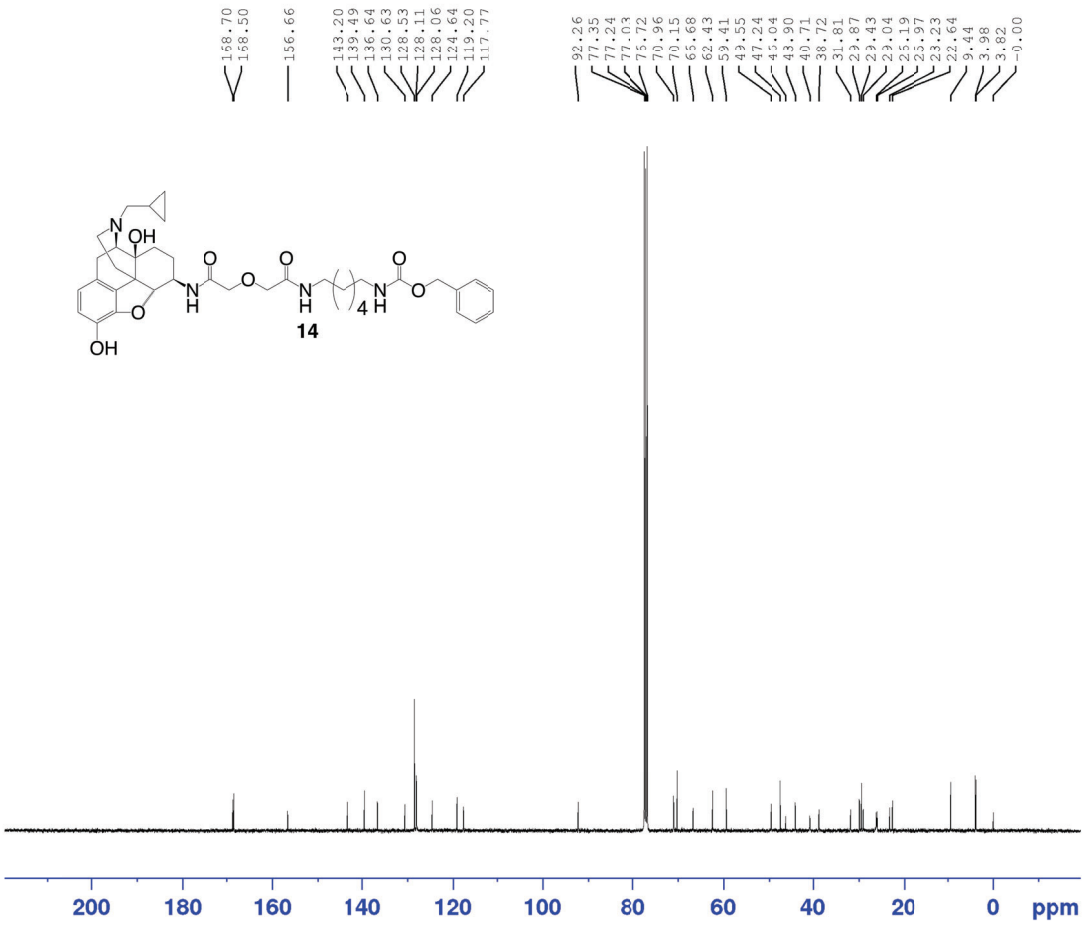
Apr.25,2015
PROTON CDCl3 /opt/topspin Kang.g 58



BRUKER

```
Current Data Parameters
NAME                  GK-II-34a
EXPNO                        10
PROCNO                        1

F2 - Acquisition Parameters
Date_                 20150425
Time                     16.31
INSTRUM                  spect
PROBHD    5 mm PABBO BB-
PULPROG                   zg30
TD                       65536
SOLVENT                  CDCl3
NS                          16
DS                           2
SWH                   8223.685 Hz
FIDRES                0.125483 Hz
AQ                    3.9845889 sec
RG                         181
DW                      60.800 usec
DE                       6.50 usec
TE                      298.4 K
D1                    1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                        1H
P1                       12.00 usec
PL1                      -2.00 dB
PL1W                15.12807274 W
SFO1                400.1324710 MHz

F2 - Processing parameters
SI                       32768
SF                  400.1300087 MHz
WDW                         EM
SSB                  0
LB                       0.30 Hz
GB                   0
PC                       1.00
```

Apr.25,2015
C13C?D CDCl3 /opt/topspin Kang.g 58



14

BRUKER

Current Data Parameters
NAME GK-II-34a_C
EXPNO 10
PROCNO 1

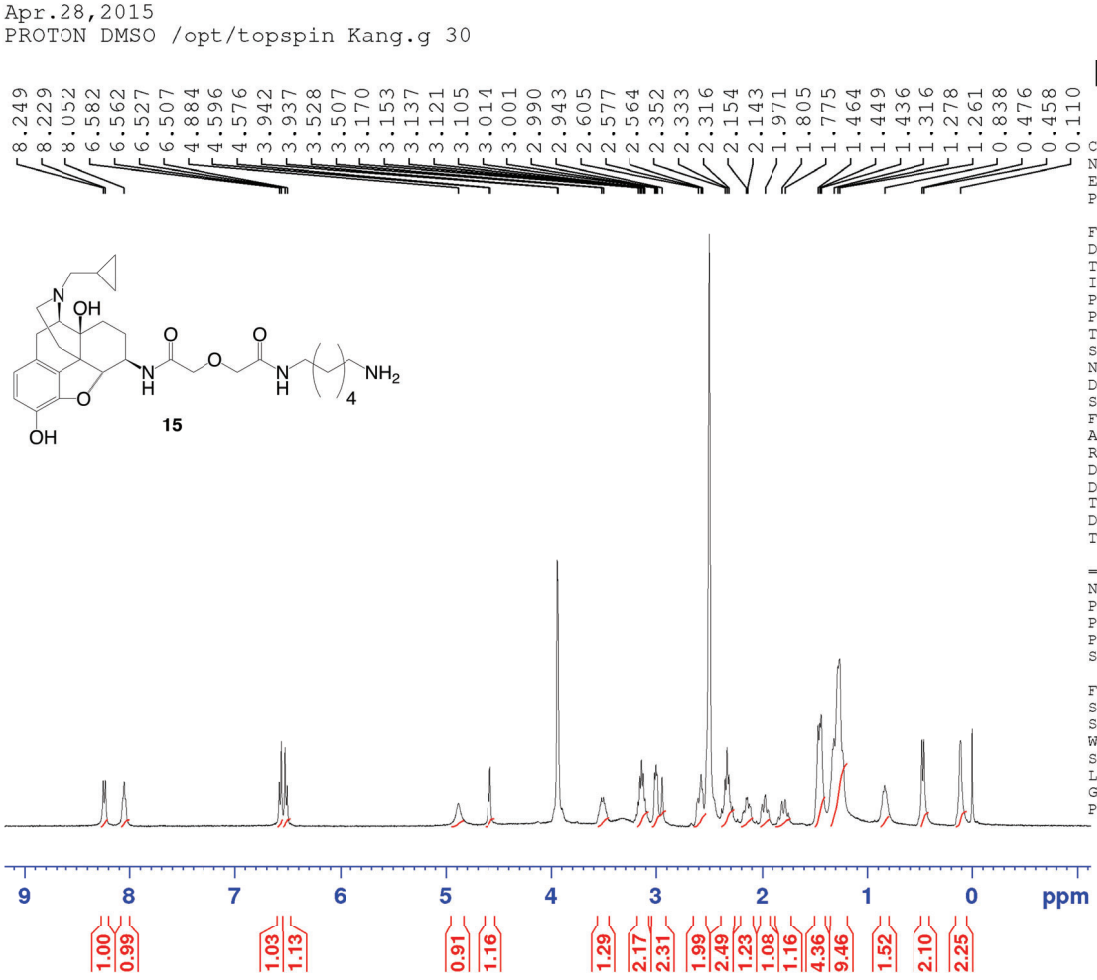
F2 - Acquisition Parameters
Date_ 20150426
Time 7.50
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4096
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 302.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6127670 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Apr.28,2015
PROTON DMSO /opt/topspin Kang.g 30



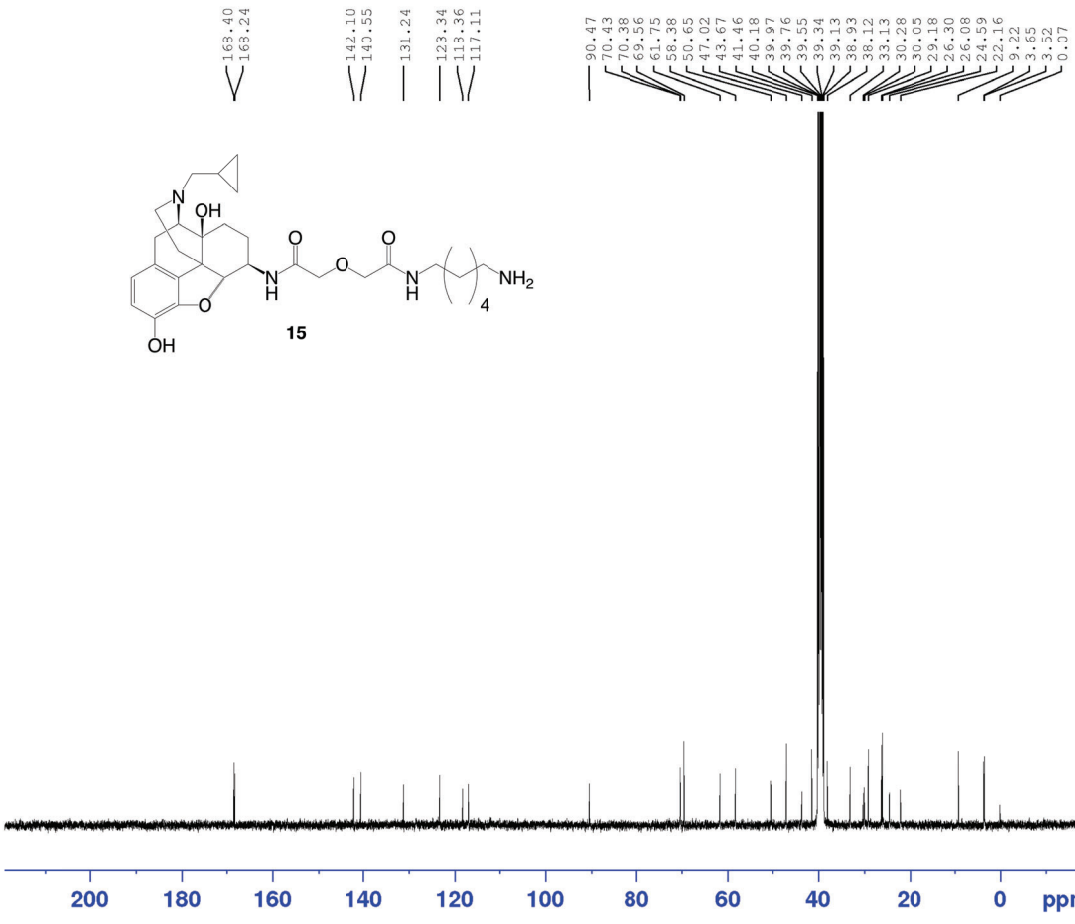
Current Data Parameters
NAME GK-II-40a
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150428
Time 9.06
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 299.6 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300043 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Apr.28,2015
C13CPD DMSO /opt/topspin Kang.g 30



BRUKER

Current Data Parameters
NAME GK-II-40a_C
EXPNO 10
PROCNO 1

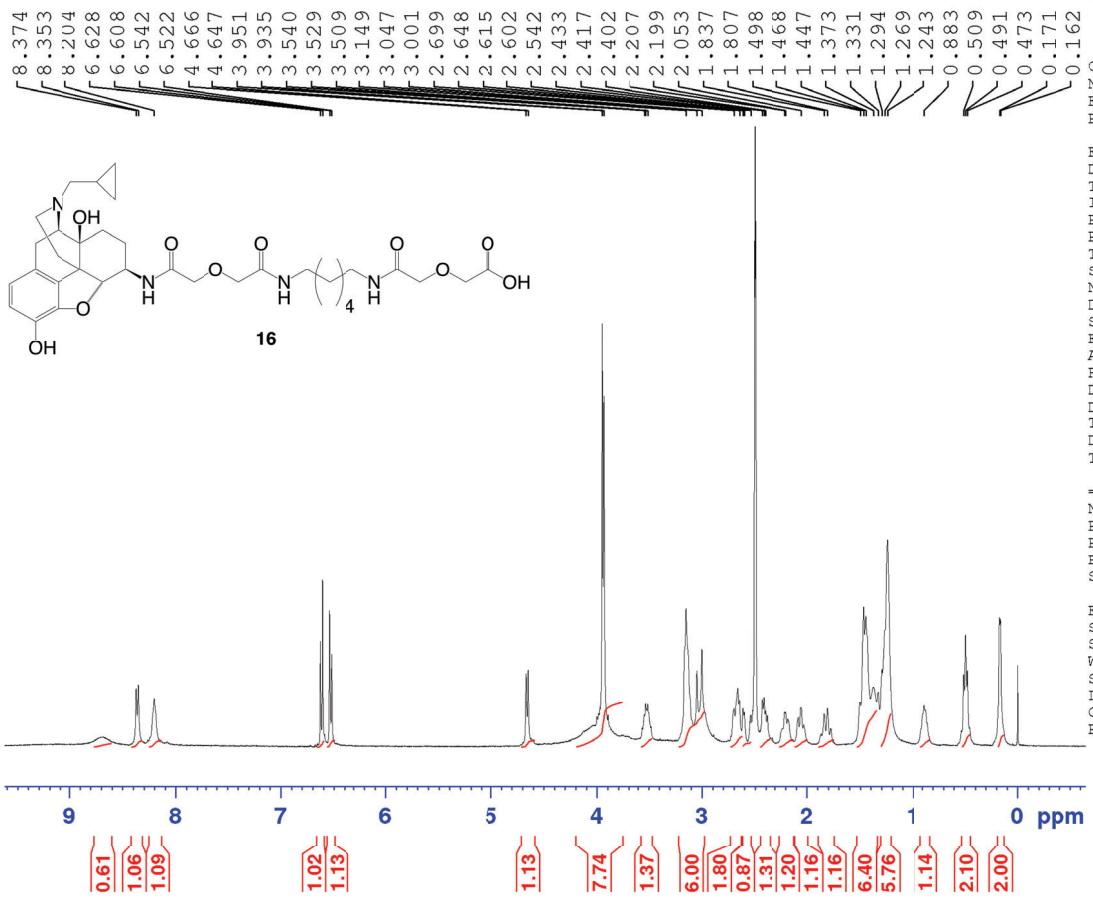
F2 - Acquisition Parameters
Date_ 20150429
Time 7.51
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 10240
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 301.8 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

May 08, 2015
PROTON DMSO /opt/topspin Kang.g 37



BRUKER

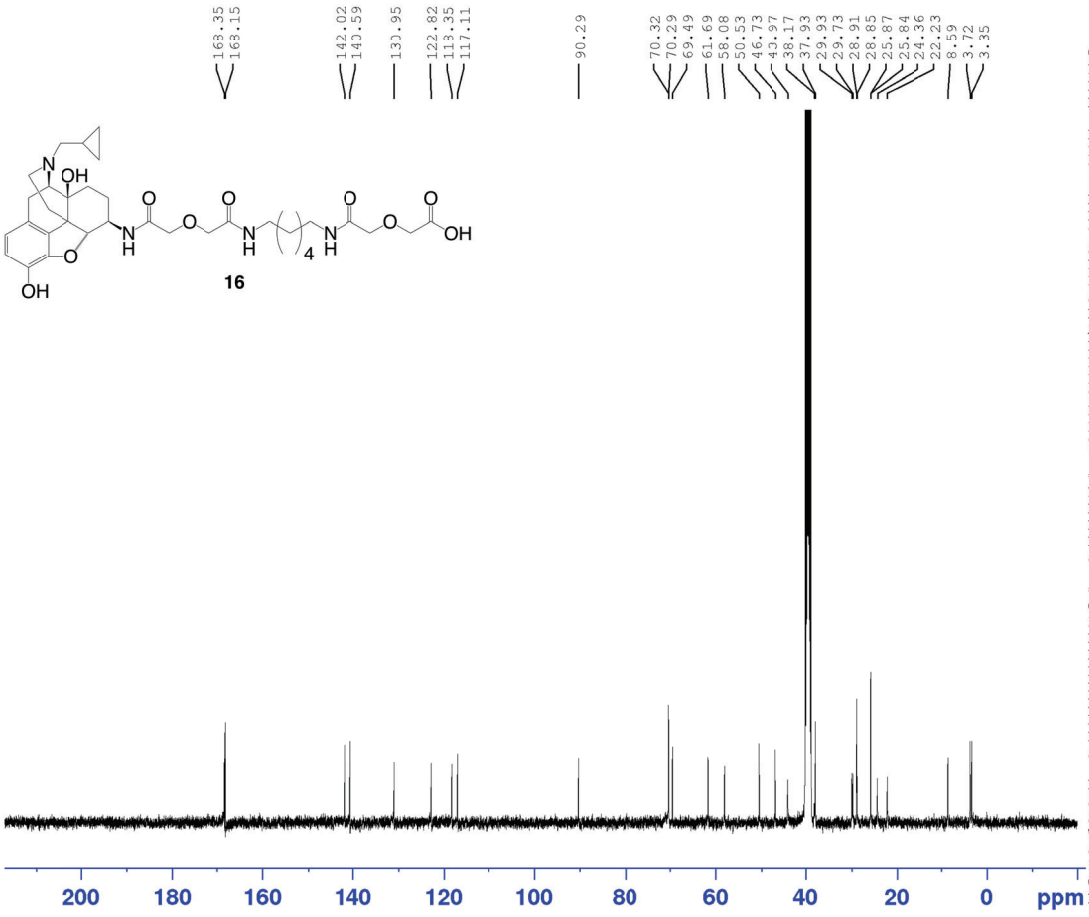
Current Data Parameters
NAME GK-II-47c
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150508
Time 15.27
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 301.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300041 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

May 07,2015
C13CPD DMSO /opt/topspin Kang.g 37



16

BRUKER

Current Data Parameters
NAME GK-II-47b_C
EXPNO 10
PROCNO 1

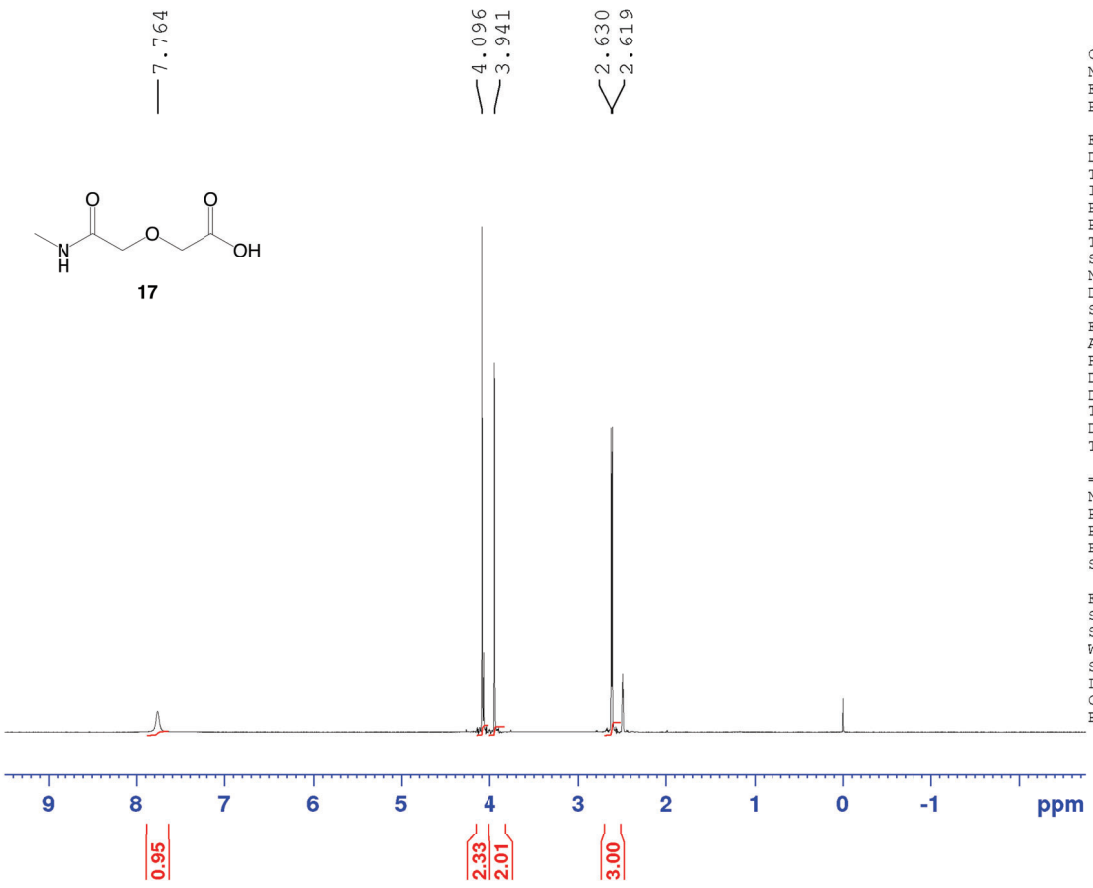
F2 - Acquisition Parameters
Date_ 20150508
Time 6.43
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 8192
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 302.8 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128279 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Jun 10,2015
PROTON DMSO /opt/topspin Kang.g 1



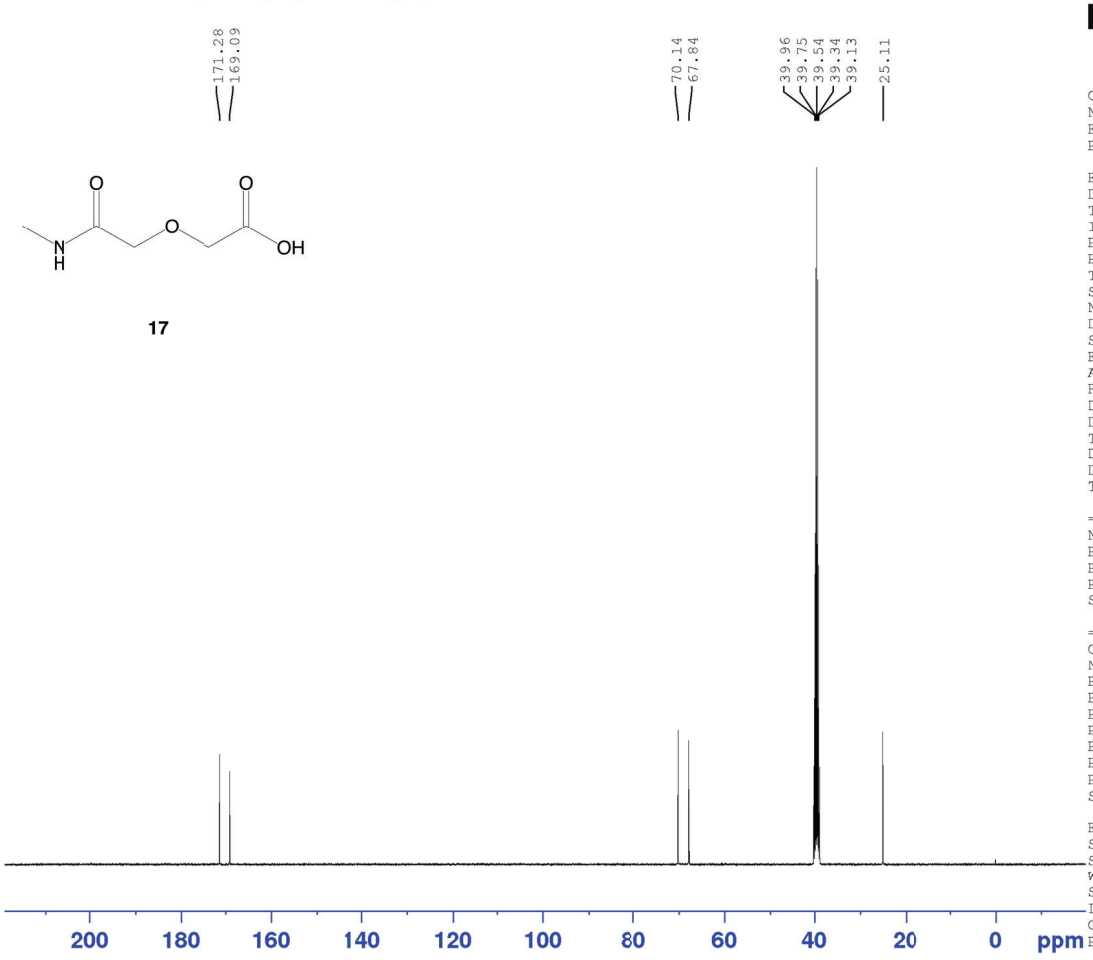
Current Data Parameters
NAME GK-II-54a
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150610
Time 17.09
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 181
DW 60.800 usec
DE 6.50 usec
TE 302.4 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300039 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

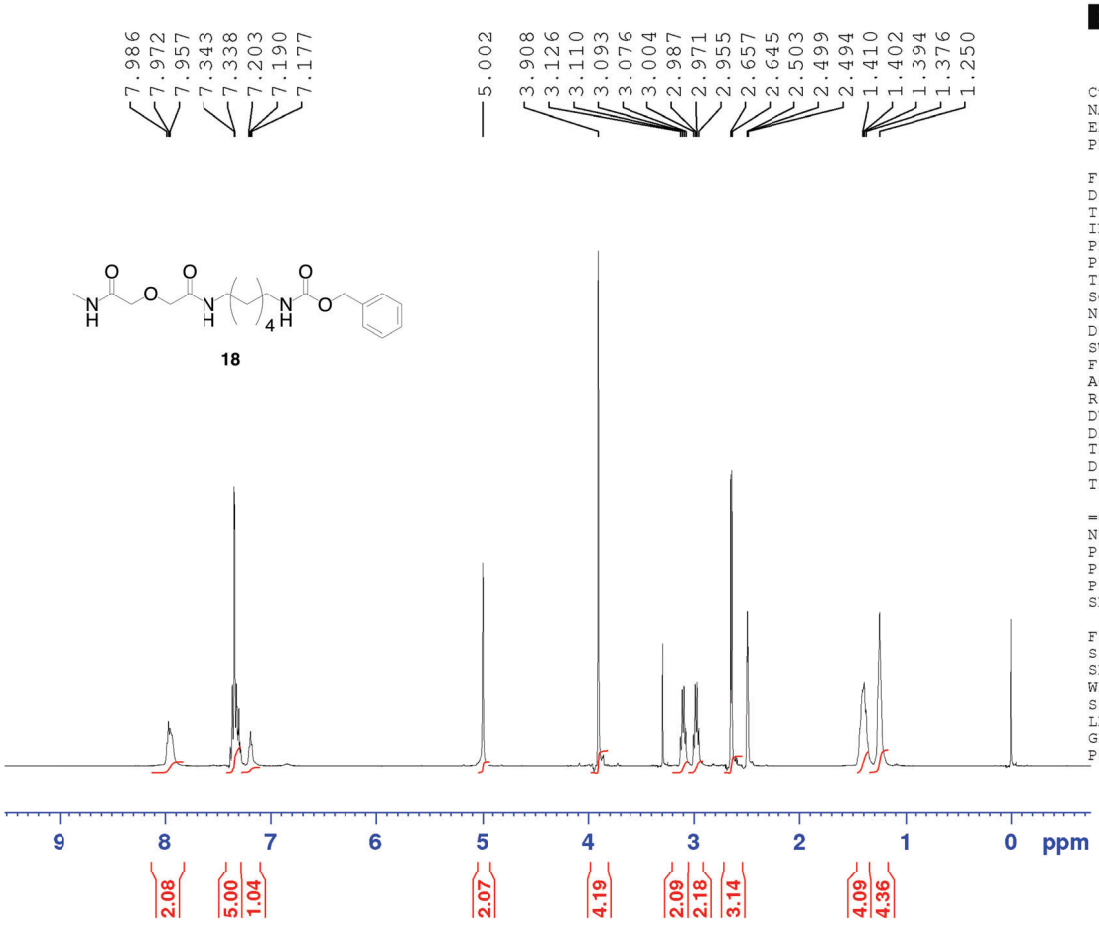
Jun 10,2015
C13C?D DMSO /opt/topspin Kang.g 1



17

```
Current Data Parameters
NAME         GK-II-54a_C
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150611
Time                1.52
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                  4096
DS                     4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                304.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  8.50 usec
PL1                -1.70 dB
PL1W        55.73028564 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                 1H
PCPD2              80.00 usec
PL2                -2.00 dB
PL12               14.50 dB
PL13               14.50 dB
PL2W        15.12807274 W
PL12W        0.33867535 W
PL13W        0.33867535 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF         100.6128193 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```

Jun 22,2015
PROTON DMSO /opt/topspin Kang.g 17



18

BRUKER

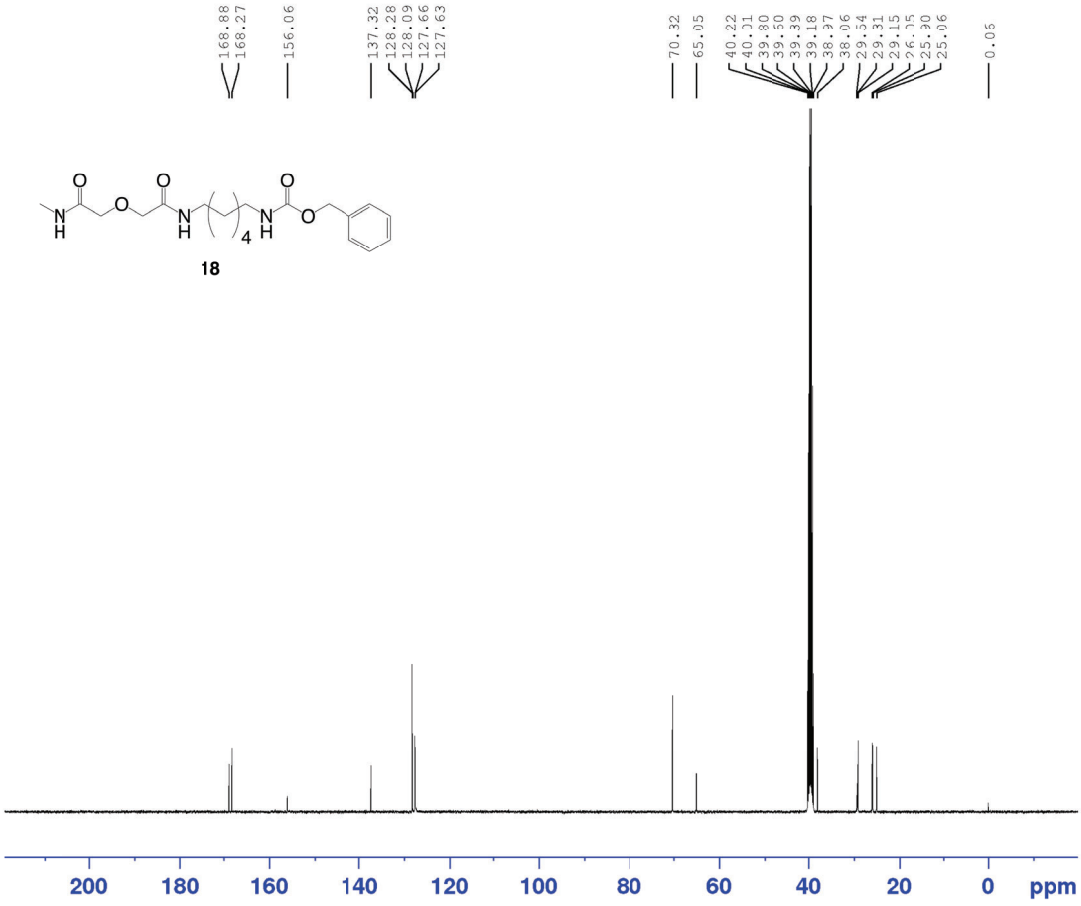
Current Data Parameters
NAME GK-II-57b
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150622
Time 14.54
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 161
DW 60.800 usec
DE 6.50 usec
TE 304.9 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300055 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Jun.22,2015
C13CPD DMSO /opt/topspin Kang.g 17



18

Current Data Parameters
NAME GK-II-57b_C
EXPNO 10
PROCNO 1

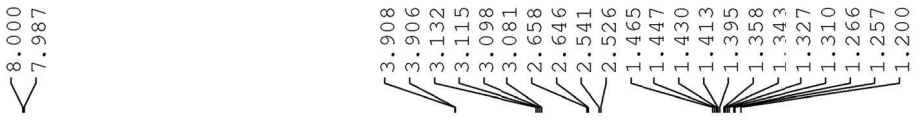
F2 - Acquisition Parameters
Date_ 20150623
Time 22.56
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 5120
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 308.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

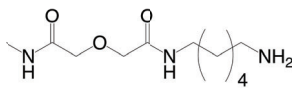
======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

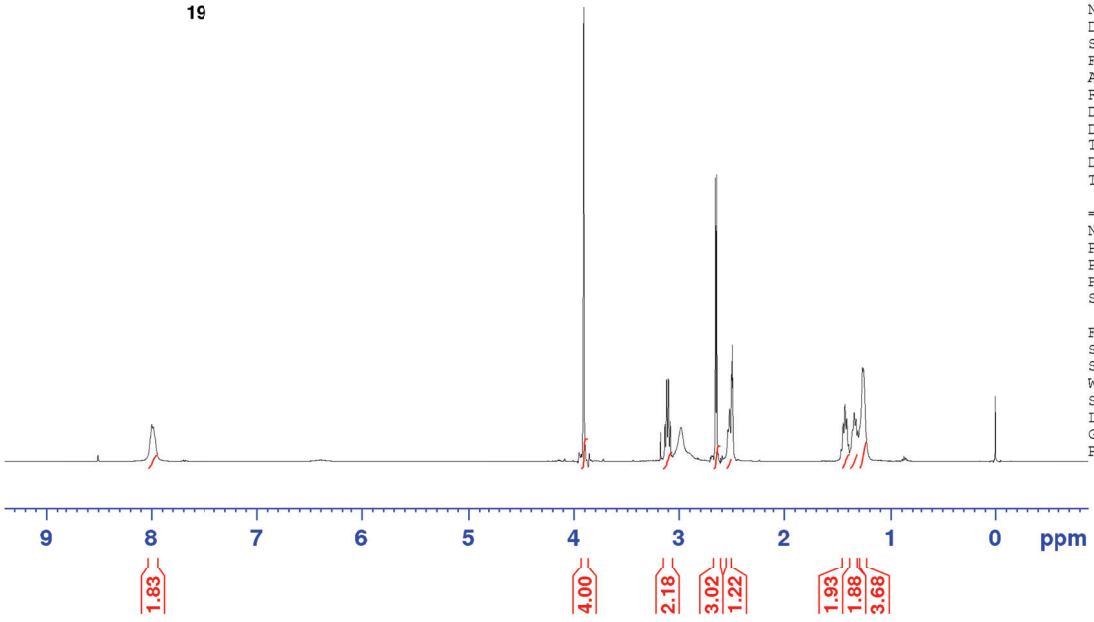
F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Jun.25,2015
PROTON DMSO /opt/topspin Kang.g 22





19



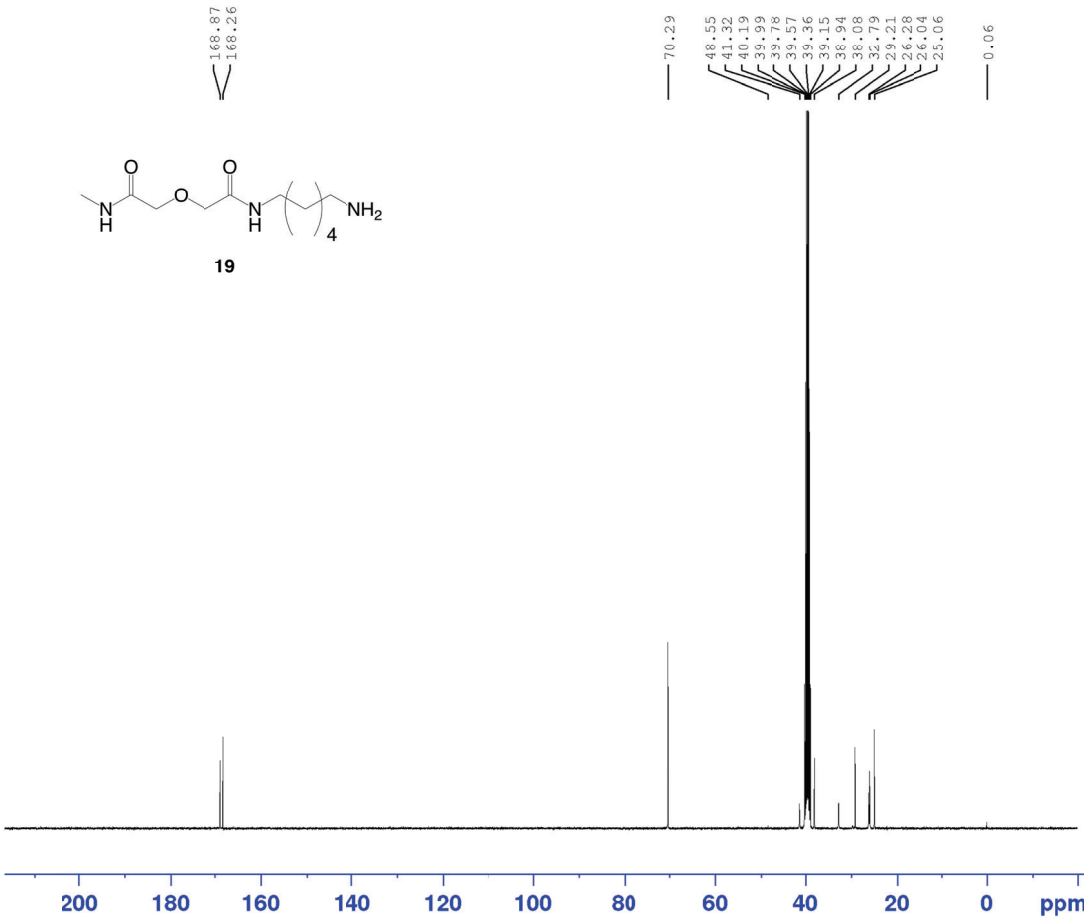
Current Data Parameters
NAME GK-II-62
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150625
Time 17.26
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 161
DW 60.800 usec
DE 6.50 usec
TE 304.4 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300047 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Jun.25,2015
C13CPD DMSO /opt/topspin Kang.g 22



BRUKER

Current Data Parameters
NAME GK-II-62
EXPNO 20
PROCNO 1

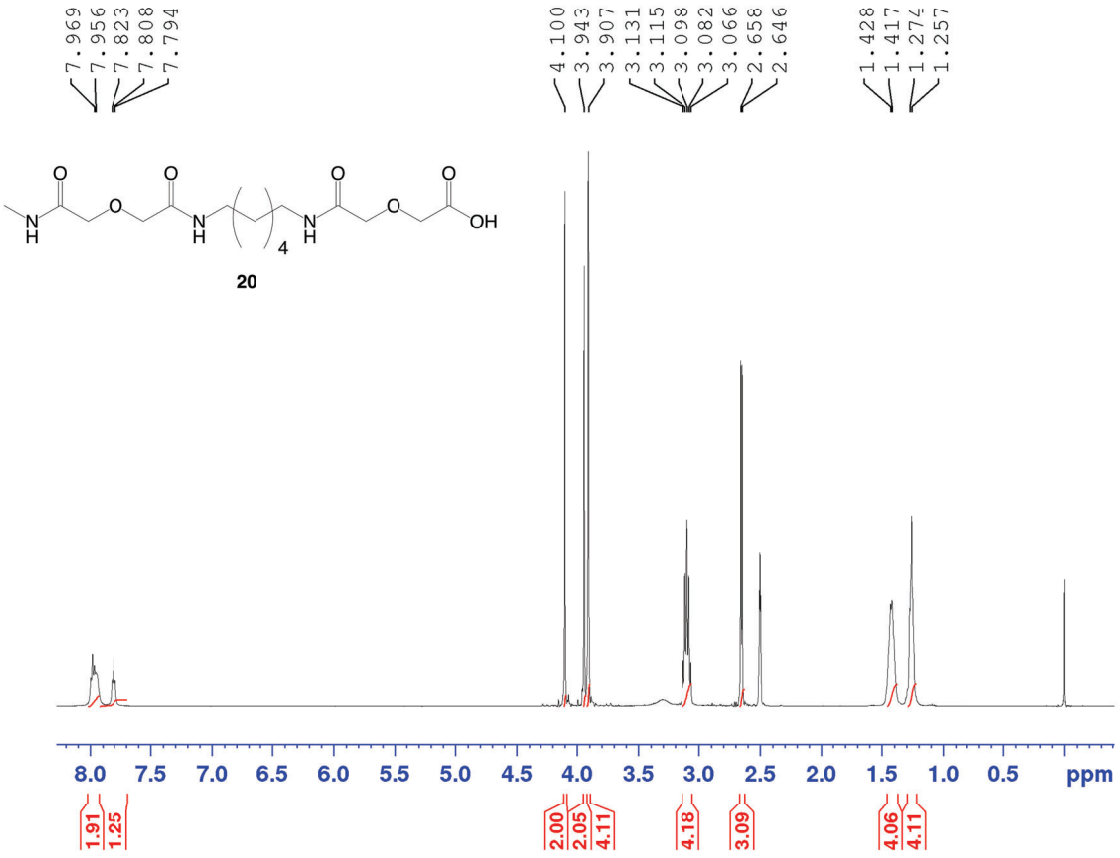
F2 - Acquisition Parameters
Date_ 20150626
Time 7.53
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 7168
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 304.8 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

Jul.01,2015
PROTON DMSO /opt/topspin Kang.g 33



20

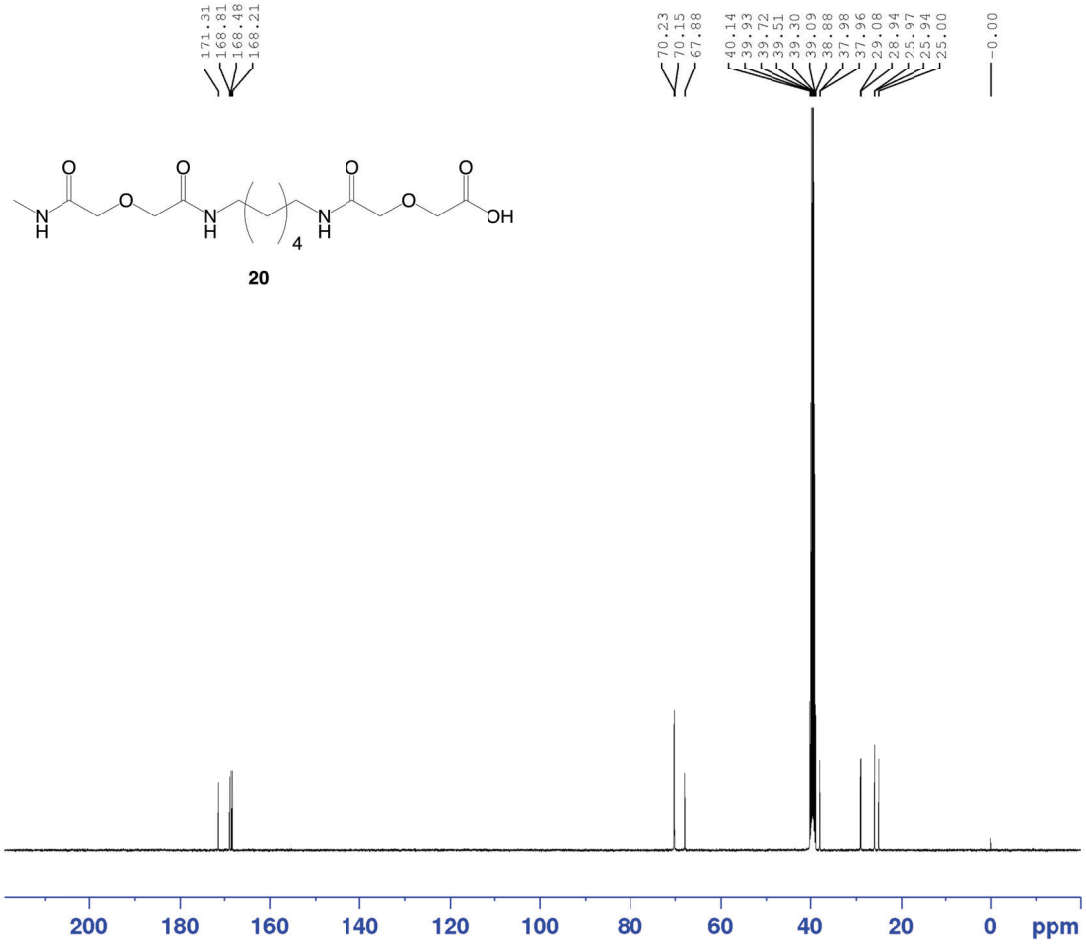
Current Data Parameters
NAME GK-II-63
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150701
Time 17.18
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 161
DW 60.800 usec
DE 6.50 usec
TE 304.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300047 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Jul.1,2015
C13CPD DMSO /opt/topspin Kang.g 33

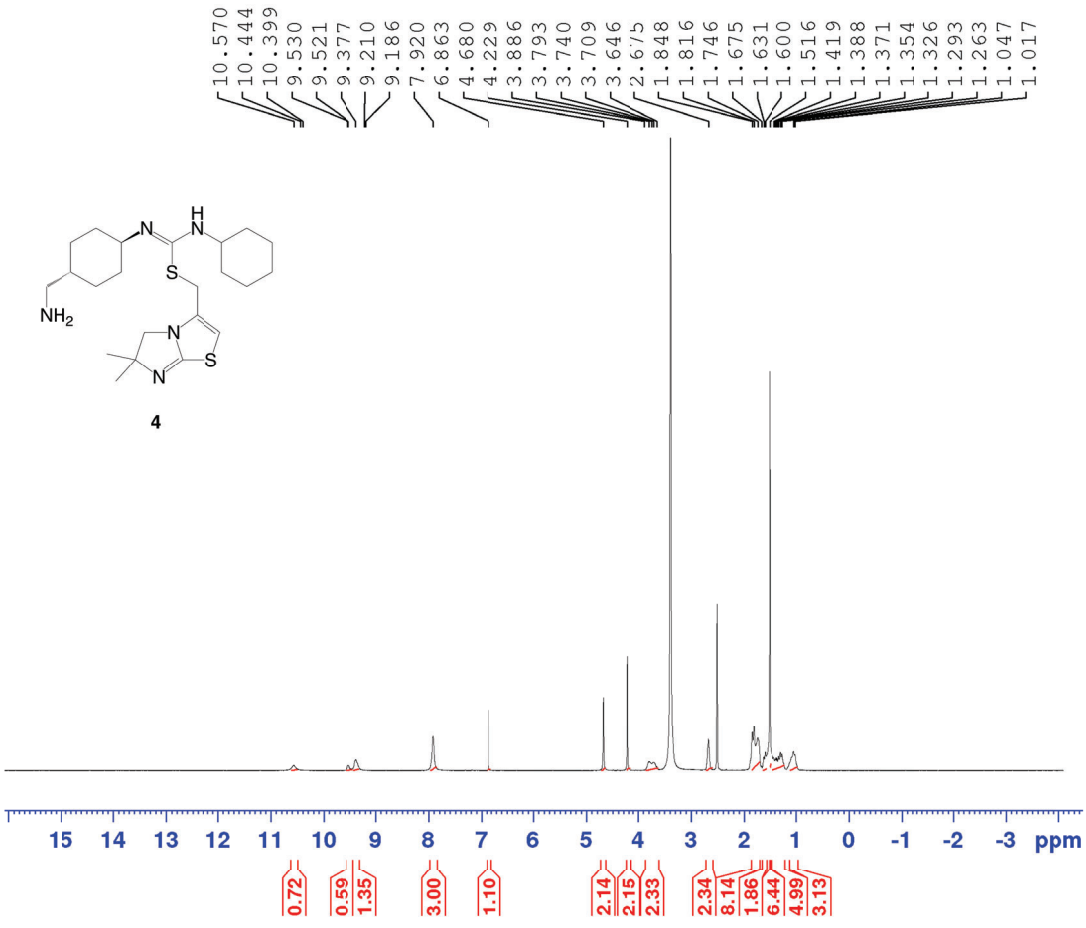


20

BRUKER

```
Current Data Parameters
NAME          GK-II-63_C
EXPNO                 10
PROCNO                 1

F2 - Acquisition Parameters
Date_           20150702
Time                1.51
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG          zgpg30
TD                65536
SOLVENT             DMSO
NS                  8192
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631488 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                308.5 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                  8.50 usec
PL1                -1.70 dB
PL1W         55.73028564 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                 1H
PCPD2              80.00 usec
PL2                -2.00 dB
PL12               14.50 dB
PL13               14.50 dB
PL2W         15.12807274 W
PL12W         0.33867535 W
PL13W         0.33867535 W
SFO2        400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF          100.6128256 MHz
WDW                   EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

Mar.22,2015
PROTON DMSO /opt/topspin Kang.g 15



4

BRUKER

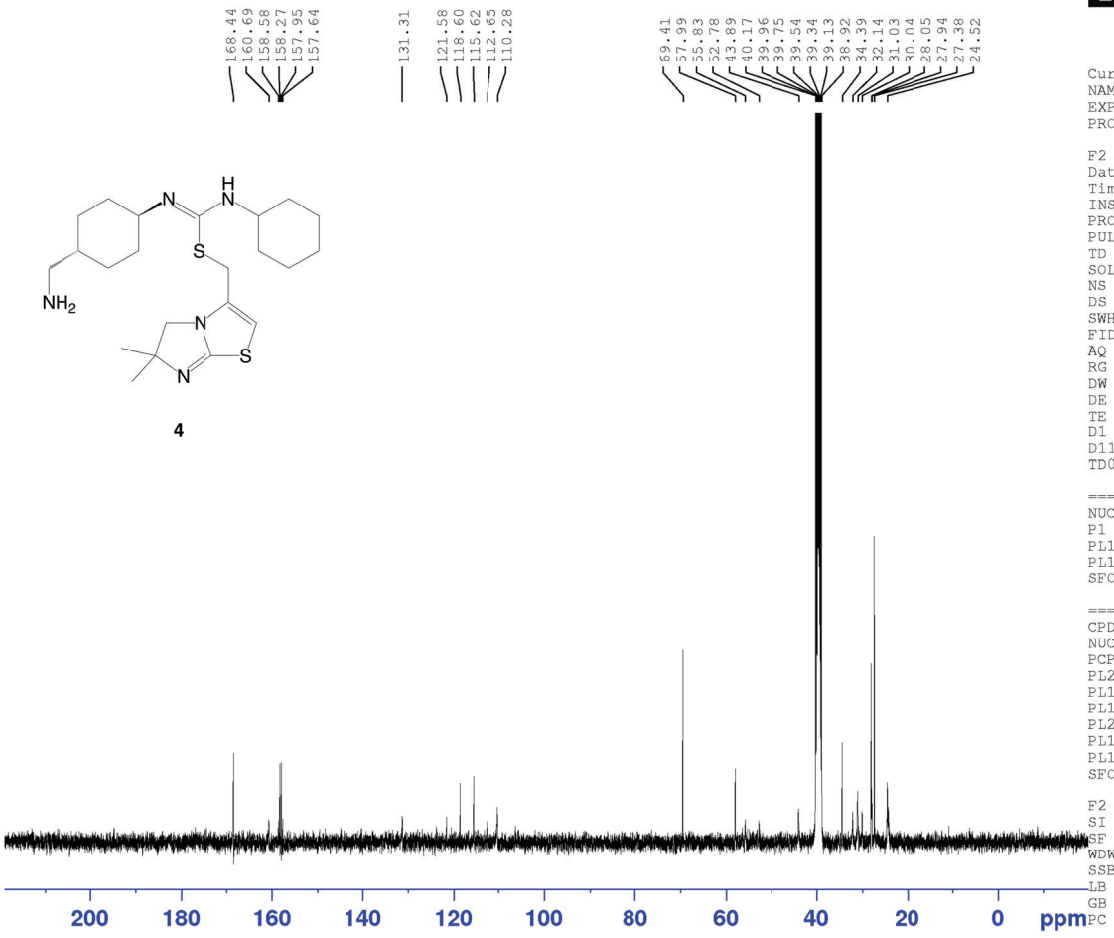
Current Data Parameters
NAME GK-II-25b
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150322
Time 13.06
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 303.3 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

Mar.22,2015
C13C?D DMSO /opt/topspin Kang.g 45



4

BRUKER

Current Data Parameters
NAME GK-II-25b_C
EXPNO 10
PROCNO 1

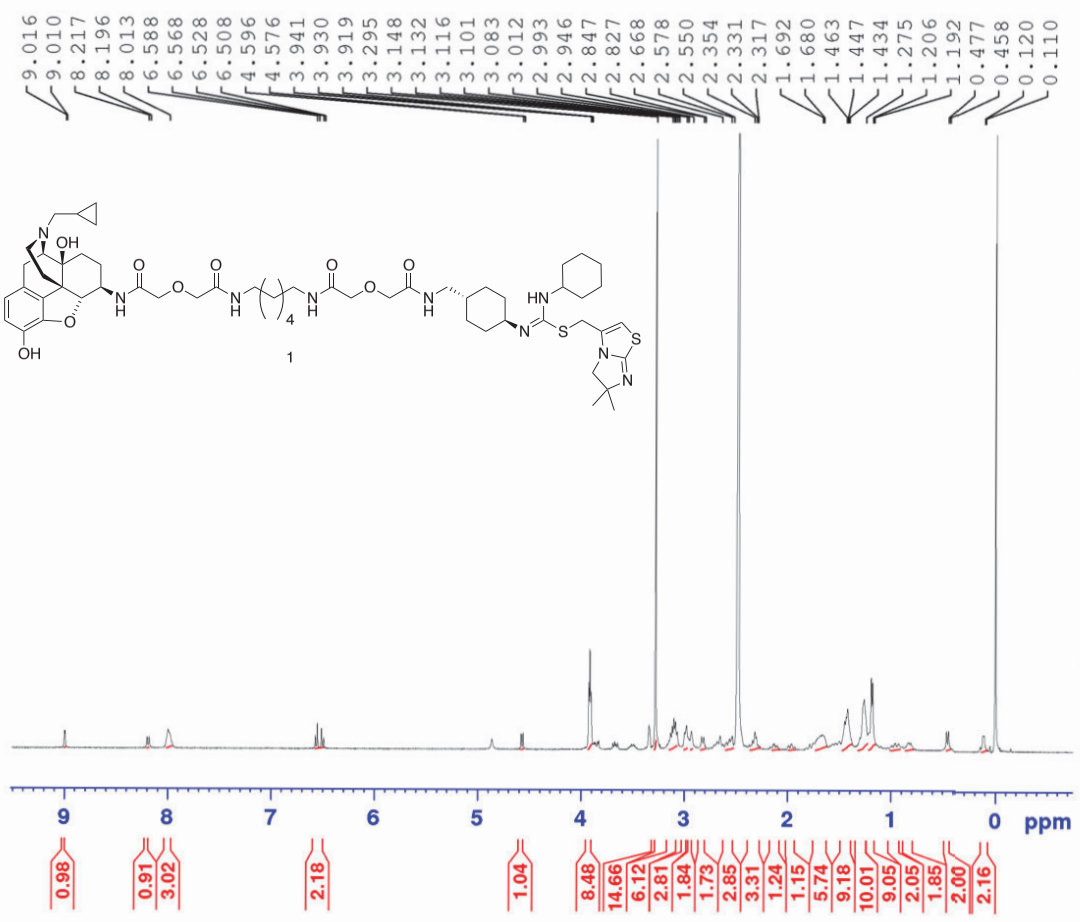
F2 - Acquisition Parameters
Date_ 20150324
Time 1.52
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 8192
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 304.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128193 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

May 26,2015
PROTON DMSO /opt/topspin Kang.g 50



Current Data Parameters

NAME	GK-II-50e
EXPNO	10
PROCNO	1

F2 - Acquisition Parameters

Date_	20150526
Time	9.17
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	128
DS	2
SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9845889 sec
RG	203
DW	60.800 usec
DE	6.50 usec
TE	302.2 K
D1	1.00000000 sec
TD0	1

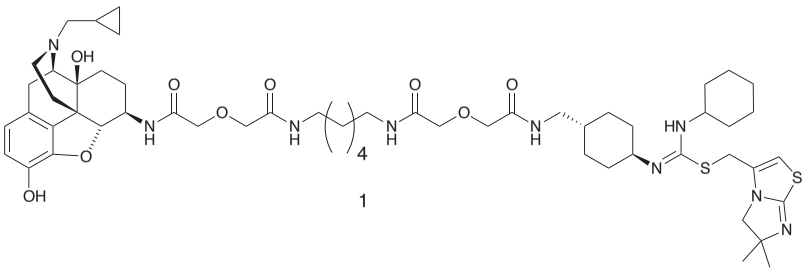
======== CHANNEL f1 ========

NUC1	1H
P1	12.00 usec
PL1	-2.00 dB
PL1W	15.12807274 W
SFO1	400.1324710 MHz

F2 - Processing parameters

SI	32768
SF	400.1300050 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

May 14,2015
C13CPD DMSO /opt/topspin Kang.g 10

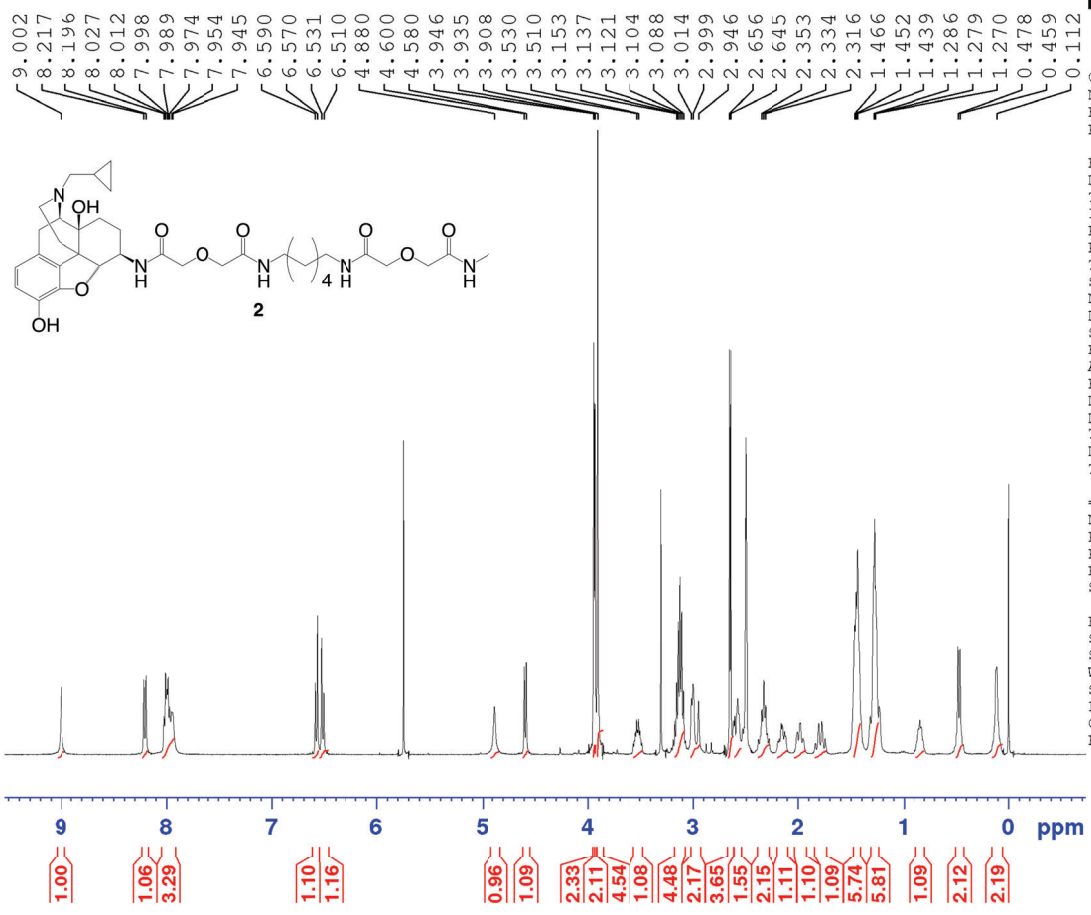


1

BRUKER

```
Current Data Parameters
NAME                 GK-II-50a_C
EXPNO                         10
PROCNO                         1

F2 - Acquisition Parameters
Date_                   20150516
Time                        1.51
INSTRUM                    spect
PROBHD    5 mm PABBO BB-
PULPROG                 zgpg30
TD                         65536
SOLVENT                    DMSO
NS                         8192
DS                            4
SWH                  24038.461 Hz
FIDRES                0.366798 Hz
AQ                    1.3631488 sec
RG                          203
DW                       20.800 usec
DE                        6.50 usec
TE                       301.7 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                        13C
P1                        8.50 usec
PL1                      -1.70 dB
PL1W                55.73028564 W
SFO1                100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2                waltz16
NUC2                        1H
PCPD2                    80.00 usec
PL2                      -2.00 dB
PL12                     14.50 dB
PL13                     14.50 dB
PL2W                15.12807274 W
PL12W                0.33867535 W
PL13W                0.33867535 W
SFO2                400.1316005 MHz

F2 - Processing parameters
SI                          32768
SF                  100.6128271 MHz
WDW                            EM
SSB                 0
LB                       1.00 Hz
GB                  0
PC                       1.40
```

Aug.23,2015
PROTON DMSO /opt/topspin Kang.g 2



BRUKER

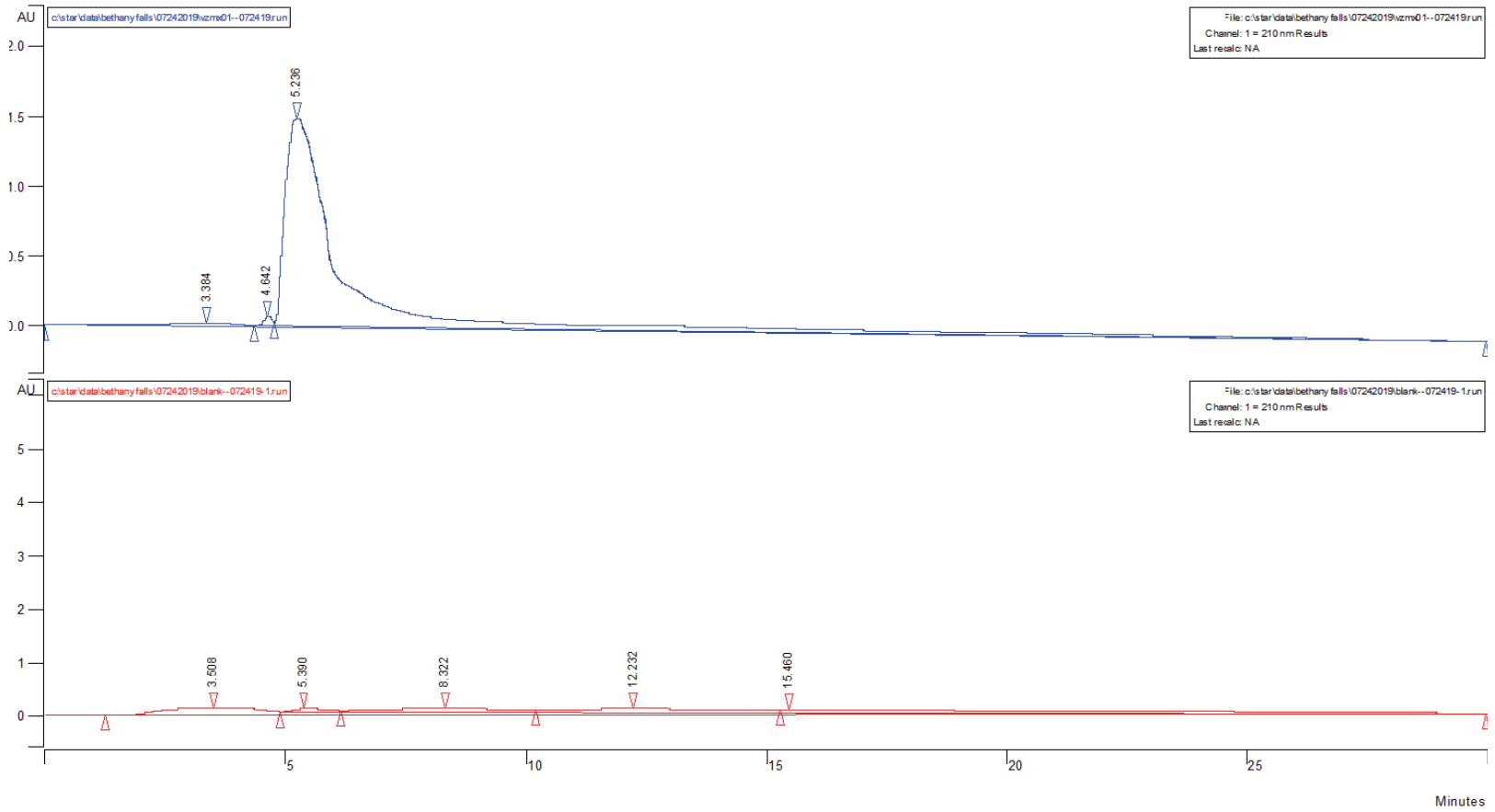
Current Data Parameters
NAME GK-II-82
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20150823
Time 16.37
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 161
DW 60.800 usec
DE 6.50 usec
TE 303.0 K
D1 1.00000000 sec
TD0 1

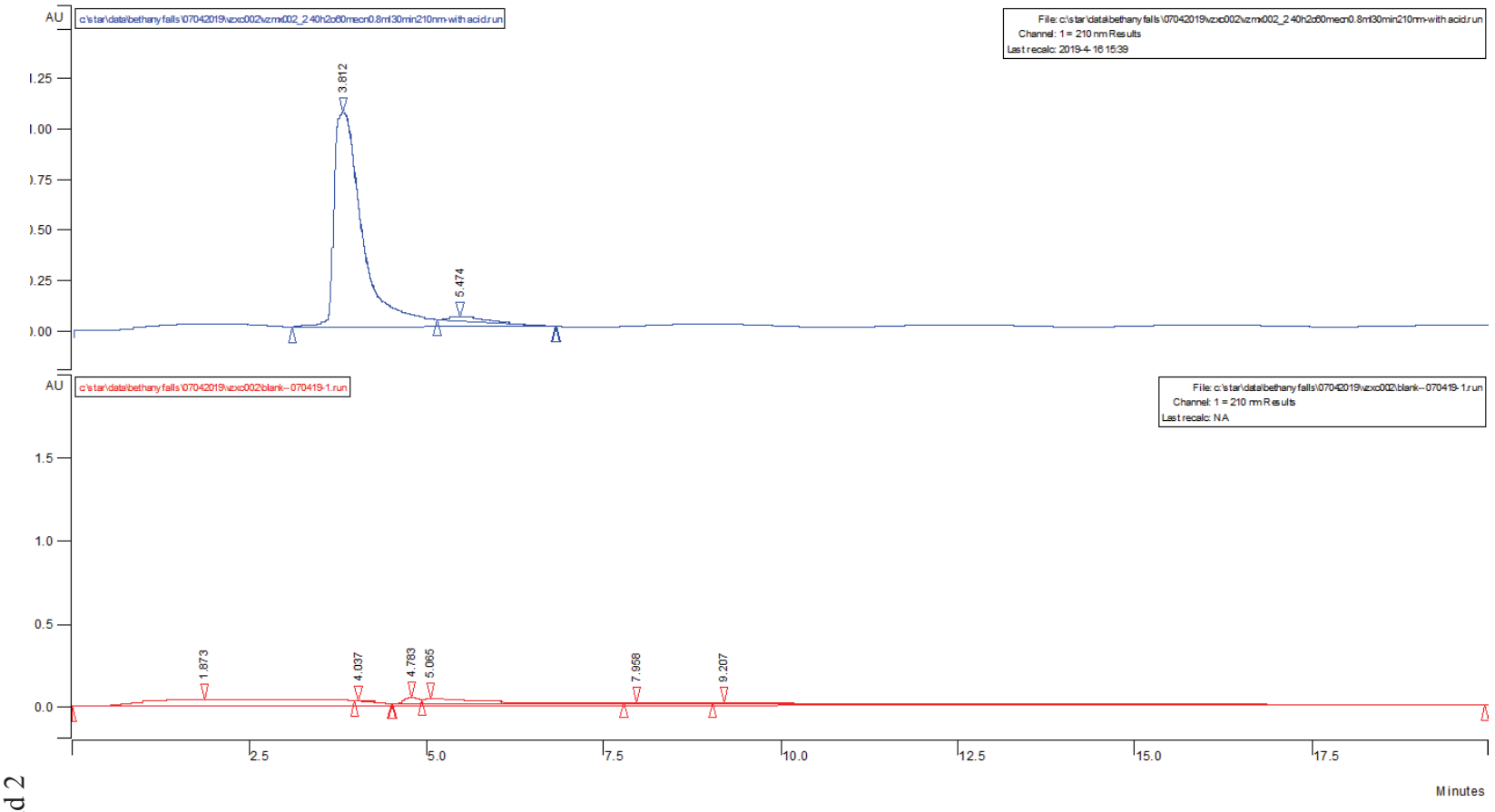
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300044 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

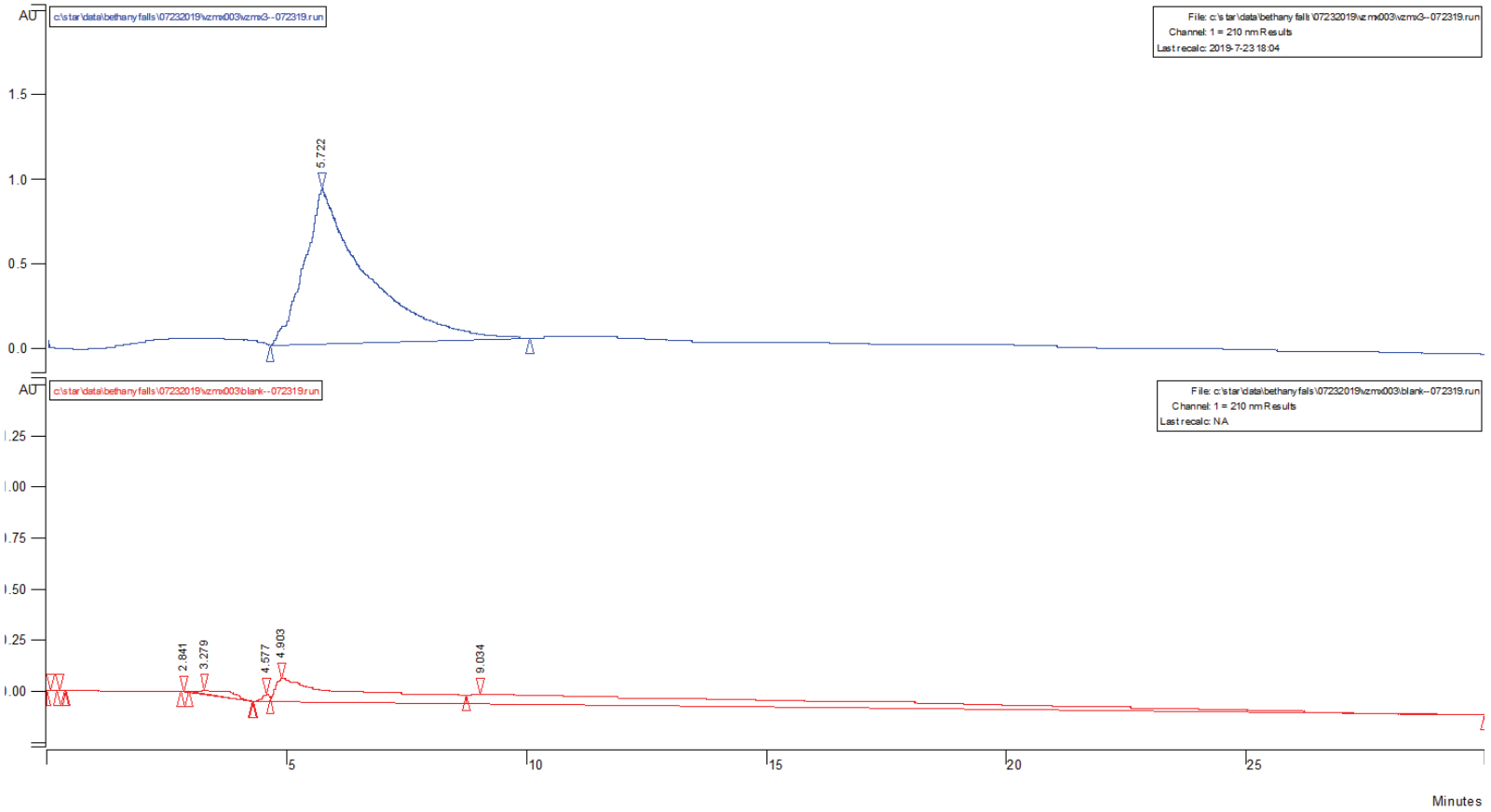
Compound 1


AU
c:\star\data\bethany falls\07242019\vzms01--072419r.run
File: c:\star\data\bethany falls\07242019\vzms01--072419r.run
Channel: 1 = 210 nm Results
Last recalc: NA
5.236
3.384
4.642
AU
c:\star\data\bethany falls\07242019\blank--072419-1r.run
File: c:\star\data\bethany falls\07242019\blank--072419-1r.run
Channel: 1 = 210 nm Results
Last recalc: NA
3.508
5.390
8.322
12.232
15.460
Minutes

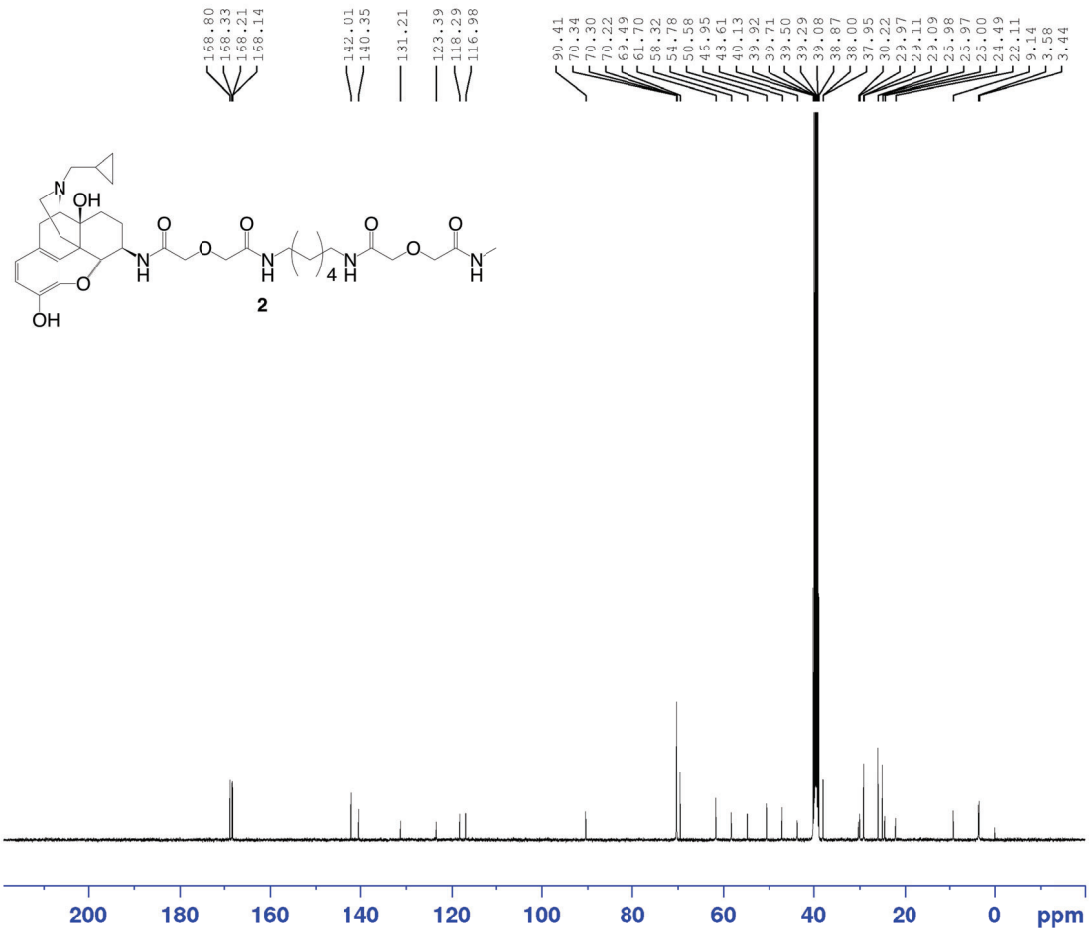
Compound 2


AU
c:\star\data\bethany falls\07042019\wzxc002\wzmx002_2 40h2o60mecn0.8ml30min210nm-with acid.r un
File: c:\star\data\bethany falls\07042019\wzxc002\wzmx002_2 40h2o60mecn0.8ml30min210nm-with acid.r un
Channel: 1 = 210 nm Results
Last recalc: 2019-4-16 15:39
3.812
5.474
AU
c:\star\data\bethany falls\07042019\wzxc002\blank--070419-1.run
File: c:\star\data\bethany falls\07042019\wzxc002\blank--070419-1.run
Channel: 1 = 210 nm Results
Last recalc: NA
1.873
4.037
4.783
5.065
7.958
9.207
2.5
5.0
7.5
10.0
12.5
15.0
17.5
Minutes

Compound 3


AU
c:\star\data\bethany falls\07232019\vzmx003\vzmx3--072319.run
File: c:\star\data\bethany falls\07232019\vzmx003\vzmx3--072319.run
Channel: 1 = 210 nm Results
Last recalc: 2019-7-23 18:04
1.5
1.0
0.5
0.0
5.722
AU
c:\star\data\bethany falls\07232019\vzmx003\blank--072319.run
File: c:\star\data\bethany falls\07232019\vzmx003\blank--072319.run
Channel: 1 = 210 nm Results
Last recalc: NA
.25
.00
.75
.50
.25
.00
2.841
3.279
4.577
4.903
9.034
5
10
15
20
25
Minutes

Aug.23,2015
C13CPD DMSO /opt/topspin Kang.g 2



BRUKER

Current Data Parameters
NAME GK-II-82_C
EXPNO 10
PROCNO 1

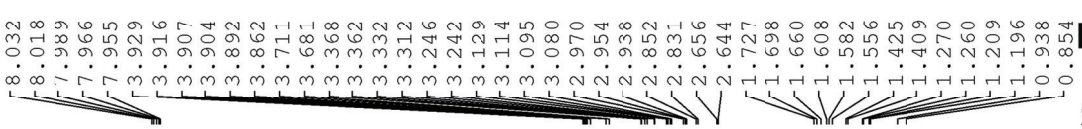
F2 - Acquisition Parameters
Date_ 20150823
Time 19.11
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 10240
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 304.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

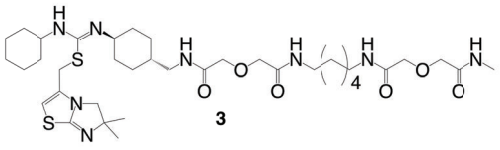
======== CHANNEL f1 ========
NUC1 13C
P1 8.50 usec
PL1 -1.70 dB
PL1W 55.73028564 W
SFO1 100.6228298 MHz

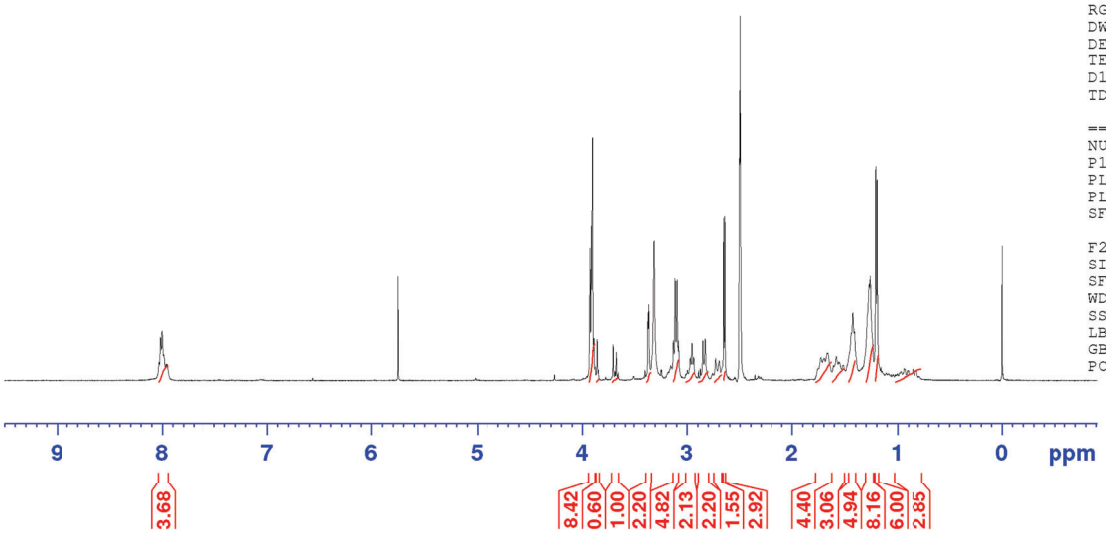
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.50 dB
PL13 14.50 dB
PL2W 15.12807274 W
PL12W 0.33867535 W
PL13W 0.33867535 W
SFO2 400.1316005 MHz

F2 - Processing parameters
SI 32768
SF 100.6128261 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

PROTON DMSO /opt/topspin Falls.B 43







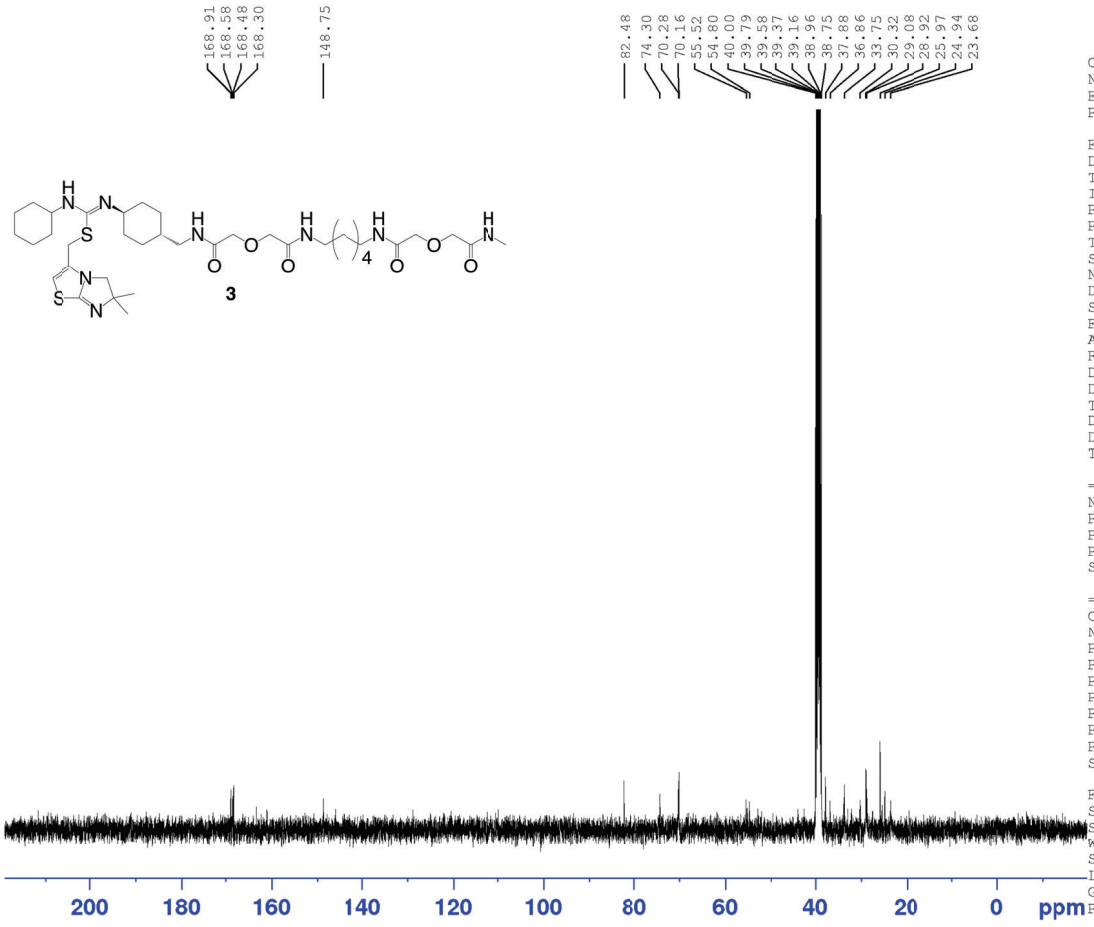
Current Data Parameters
NAME Bf-II-it1tmono
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20171107
Time 10.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 299.8 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -2.00 dB
PL1W 15.12807274 W
SFO1 400.1324710 MHz

F2 - Processing parameters
SI 32768
SF 400.1300022 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

C13C?D DMSO /opt/topspin Falls.B 41



BRUKER

```
Current Data Parameters
NAME      Bf-II-it1tmono
EXPNO                 60
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171114
Time               19.02
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG         zgpg30
TD                65536
SOLVENT            DMSO
NS                 1024
DS                    4
SWH           24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631488 sec
RG                  203
DW               20.800 usec
DE                6.50 usec
TE                300.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 8.50 usec
PL1               -1.70 dB
PL1W       55.73028564 W
SFO1       100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG[2         waltz16
NUC2                1H
PCPD2              80.00 usec
PL2                -2.00 dB
PL12               14.50 dB
PL13               14.50 dB
PL2W       15.12807274 W
PL12W       0.33867535 W
PL13W       0.33867535 W
SFO2       400.1316005 MHz

F2 - Processing parameters
SI                 32768
SF         100.6128193 MHz
WDW                   EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```