SUPPORTING INFORMATION

Characterization of DNA Minor Groove Binding Alkylating Agents

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Chem. Res. Toxicol.

Details for the synthesis and characterization of compounds **1-11** (**see Figure 1**).

NMR and mass spectra of compounds **1-11**.

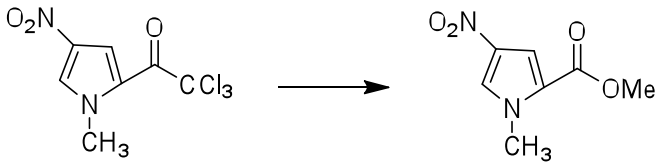
Figure S1. Sample HPLC trace of control calf thymus DNA and DNA treated with compound **7.**

Figure S2. Temperature-dependent UV melts of calf thymus DNA in the absence and presence of the minor groove binding compounds.

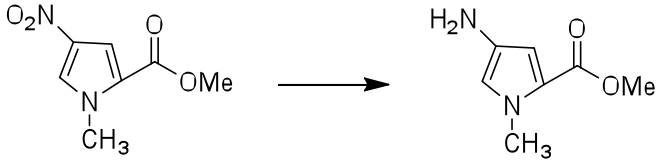
Figure S3. Temperature-dependent UV melts of poly-d(A-T)·poly-d(A-T) DNA in the absence and presence of the minor groove binding compounds.

Synthesis of 1: As previously described (reference #13)

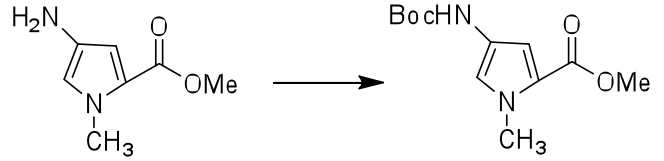
Synthesis of 2:



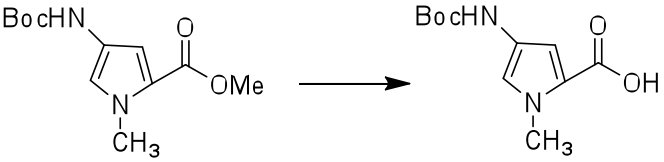
The synthesis of **2** followed previously reported method [Kumar, R., and Lown, J. W. (2003) Design, synthesis and *in vitro* cytotoxicity studies of novel pyrrolo[*2,1*][*1,4*] benzodiazepine-glycosylated pyrrole and imidazole polyamide conjugates. *Org. Biomol. Chem. 1*, 3327-3342.].



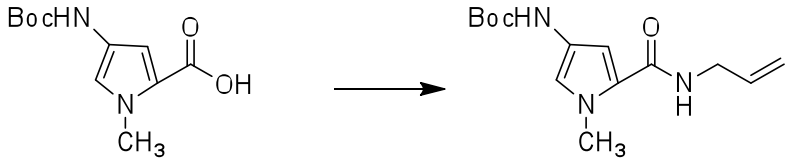
To a solution of methyl 1-methyl-4-nitro-*1H*-pyrrole-2-carboxylate (5.98 mmol, 1.1 g) in min amount of EtOAc (50 mL) and MeOH (350 mL) was added 10% Pd/C catalyst (389 mg) and the reaction mixture shaken in a Parr apparatus at 55 psi until complete disappearance of starting material (by TLC). The reaction mixture was filtered through a celite pad and solvents evaporated to dryness to afford the amine in quantitative yield (0.890 g, 96.73%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 3.67 (s, 3H), 3.70 (s, 3H), 3.90 (br, 2H), 6.21 (d, 1H, J = 2.34), 6.41 (d, 1H, J = 2.34).



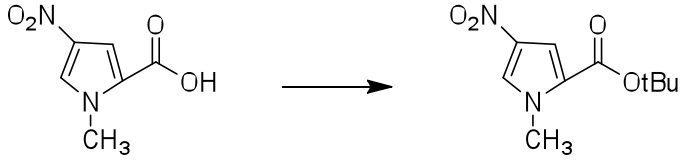
To a solution of methyl 4-amino-1-methyl-1H-pyrrole-2-carboxylate (5.778 mmol, 890 mg) in dry CH_2Cl_2 (40 mL) was added Et_3N (17.331 mmol, 2.4 mL). The reaction mixture was cooled to 0 ºC and Boc anhydride added (1.89 g, 8.67 mmol) in CH_2Cl_2 (15 mL). The reaction mixture was allowed to warm to room temperature and stirred for~ 18 h under N_2. The reaction mixture was diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with EtOAc. The organic layers were combined and dried over Na_2SO_4 and solvents evaporated to dryness. The residue was purified by silica gel column chromatography to yield the product (1.065 g, 72.55%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 1.44 (s, 9H), 3.70 (s, 3H), 3.78 (s, 3H), 6.61 (br, s, 1H), 7.10 (br, s, 1H), 9.12δ (s, br, 1H).



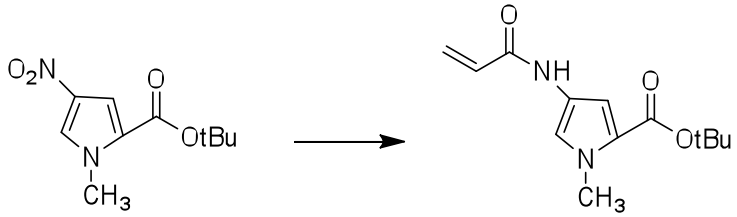
To a solution of methyl 4-((tert-butoxycarbonyl)amino)-1-methyl-*1H*-pyrrole-2-carboxylate (4.163 mmol,1.058 g) in MeOH (33 mL) was added solution of NaOH (826.54 mg in 33 mL of H_2O). The reaction mixture was refluxed at 65 ºC until complete disappearance of starting material (based on TLC). The MeOH was evaporated to minimum volume and the reaction mixture was cooled to 0 ºC with ice and acidified with Dowex 50WX4 ion exchange resin to pH 5-6. The resin beads were filtered and washed thoroughly with MeOH. The solvents were evaporated to dryness and the solid material obtained was then dried (908 mg, 90.8%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 1.43 (s, 9H), 3.76 (s, 3H), 6.24 (br, s, 1H), 6.70 (br, s, 1H), 8.80 (s, br, 1H).



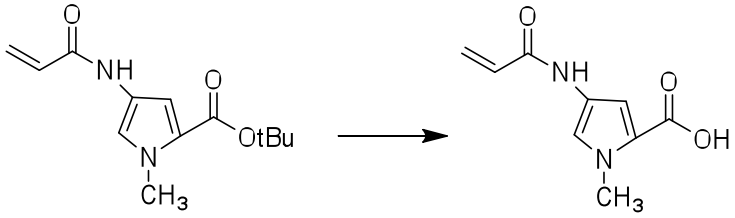
To a solution of 4-((tert-butoxycarbonyl)amino)-1-methyl-*1H*-pyrrole-2-carboxylic acid (3.721 mmol, 894 mg) and HOBT (5.582 mmol, 754 mg) in CH_2Cl_2 (20 mL) was added Et_3N (14.884 mmol, 2 mL). This was followed by the addition of EDC (7.442 mmol, 1.43 g) in CH_2Cl_2 (25 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled to 0 ºC and allyl amine (7.442 mmol, 557 µL) was added. The reaction mixture was allowed to come to room temperature and stirred for ~ 18 h. The white solid that precipitated was filtered off and the filtrate diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with EtOAc. The combined organic layers were dried over Na_2SO_4 and evaporated to dryness. The residue was purified by silica gel column chromatography to yield the product (854 mg, 82%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 1.44 (s, 9H), 3.75 (s, 3H), 3.76-3.78 (m, 2H), 5.04 (dd, 1H, J = 10.16 and 1.95), 5.11 (dd, 1H, J = 17.18 and 1.95), 5.79-5.87 (m, 1H), 6.66 (br, s, 1H), 6.84 (br, s, 1H), 8.14 (t, 1H, J = 5.47), 9.04 (s, br, 1H).



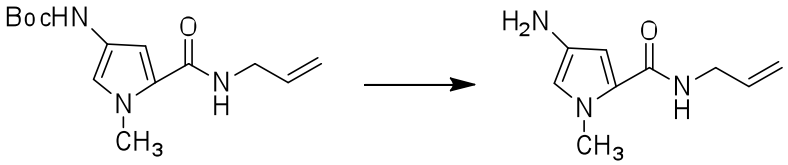
Synthesis followed previously published procedure [Wurtz, N. R., Turner, J. M., Baird, E. E., and Dervan, P. B. (2001) Fmoc solid phase synthesis of polyamides containing pyrrole and imidazole amino acids. *Org.Lett. 3*, 1201-1203.].



To a solution of tert-butyl 1-methyl-4-nitro-*1H*-pyrrole-2-carboxylate (6.188 mmol, 1.4 g) in MeOH (350 mL) was added 10% Pd-C (1 g) and the reaction mixture shaken in a Parr apparatus at 50 psi until complete disappearance of starting material (based on TLC). The reaction mixture was filtered through a celite pad and the solvents evaporated to give the amine (5.401 mmol, 1.06 g) that was dissolved in anhydrous THF (70 mL). To this was added diisopropylethylamine (16.203 mmol, 2.8 mL). The reaction mixture was cooled to -78 ºC and acryloyl chloride (8.102 mmol, 658 µL) was added dropwise at -78 ºC. The reaction mixture was maintained at -78 ºC in the dark until the disappearance of amine (based on TLC) and the reaction was then slowly allowed to warm to room temperature. THF was evaporated and H_2O added to the residue. The aqueous layer was extracted with CH_2Cl_2. The organic extracts are combined, dried over Na_2SO_4 and solvent evaporated to dryness. The compound was then isolated by silica gel column chromatography to yield the product (1.0388 g, 77%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 1.49 (s, 9H), 3.79 (s, 3H), 5.67 (dd, 1H, *J* = 10.16 and 2.34), 6.16 (dd, 1H, *J* = 17.19 and 2.34), 6.27-6.34 (m,1H), 6.71 (d,1H, *J* = 1.95), 7.34 (d, 1H, *J* = 1.95), 10.08 (br, s, 1H,-N*H*)

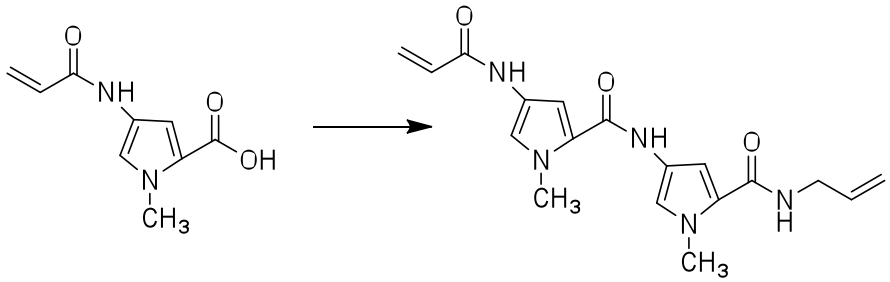


To a solution of tert-butyl 4-acrylamido-1-methyl-*1H*-pyrrole-2-carboxylate (4.12 mmol, 1.032 g) in CH_2Cl_2 (30 mL) was added 1M $TiCl_4$ solution (10.31 mmol, 10 mL) at 0 ºC. The reaction mixture was stirred at 0 ºC and slowly allowed to come to room temperature until complete disappearance of starting material. The reaction mixture was diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with EtOAc (4 x 50 mL). The organic solvents was dried over Na_2SO_4 and evaporated to dryness to give the product (782 mg, 97.62%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 3.81 (s, 3H), 5.67 (dd, 1H, *J* = 9.77 and 1.96), 6.17 (dd, 1H, *J* = 17.18 and 1.96), 6.29-6.35 (m, 1H), 6.71 (d, 1H, *J* = 1.95), 7.38 (d, 1H, *J* = 1.95), 10.09 (br, s),12.22 (br, s, 1H).

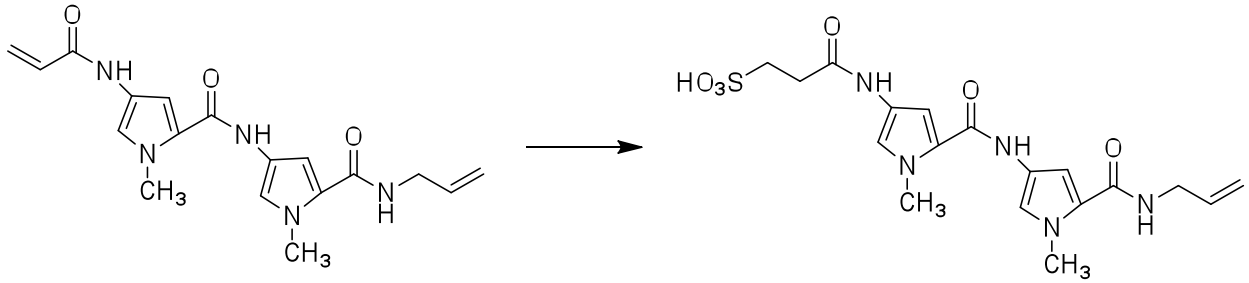


To a solution of tert-butyl (5-(allylcarbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamate (2.585 mmol, 722 mg,) in anhydrous CH_2Cl_2 (13 mL) was added 50% TFA:CH_2Cl_2 (38 mL) at 0 ºC such that the final concentration of TFA was around 40%. The reaction mixture was stirred under N_2 at 0 ºC until complete disappearance of starting material. The solvents were evaporated to dryness to give the amine, N-allyl-4-amino-1-methyl-*1H*-pyrrole-2-carboxamide in quantitative yields. ^{1}HNMR (400 MHz, DMSO-d_6) δ 3.80-3.83 (m, 2H), 3.84 (s, 3H), 5.07 (dd, 1H, *J* = 10.16 and

1.95), 5.13 (dd, 1H, *J* = 17.18 and 1.95), 5.81-5.91 (m, 1H), 6.81 (d, 1H, *J* = 1.95), 7.05 (d, 1H, *J* = 1.95), 8.357 (t, 1H, *J* = 5.7), 9.64 (s, br).

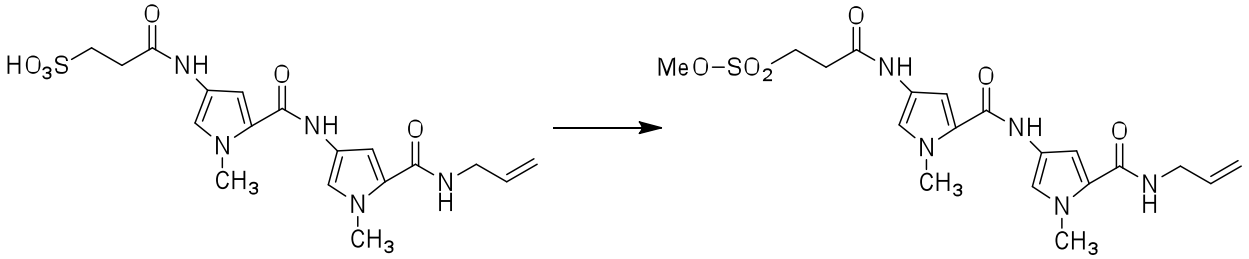


To a solution of 4-acrylamido-1-methyl-*1H*-pyrrole-2-carboxylic acid (1.293 mmol, 251 mg) and HOBT (1.94 mmol, 262 mg) in anhydrous CH_2Cl_2 (30 mL) was added Et_3N (5.172 mmol, 721 µL). This was followed by the addition of EDC (2.59 mmol, 496 mg) in CH_2Cl_2 (25 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled to 0 ºC and N-allyl-4-amino-1-methyl-*1H*-pyrrole-2-carboxamide (2.586 mmol, 0.496 g) added in CH_2Cl_2 (13 mL) containing Et_3N (0.6 mL). The reaction mixture was stirred under N_2 and at room temperature for 18 h and the reaction mixture diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and solvents evaporated to dryness. The residue was purified by silica gel column chromatography to get the product (444mg, 96%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 3.78-3.81 (m, 2H), 3.79 (s, 3H), 3.84 (s, 3H), 5.06 (dd, 1H, *J* = 10.16 and 1.95), 5.13 (dd, 1H, *J* = 17.18 and 1.95), 5.67 (dd, 1H, *J* = 9.76 and 1.95), 5.82-5.91 (m, 1H), 6.18 (dd, 1H, *J* = 16.79 and 1.95), 6.34-6.41 (m, 1H), 6.89 (d, 1H, *J* = 1.95), 6.92 (d, 1H, *J* = 1.95), 7.21 (d, 1H, *J* = 1.95), 7.27 (d, 1H, *J* = 1.95), 8.21 (t, 1H, *J* = 6.25), 9.91 (s, 1H), 10.11 (s, 1H).



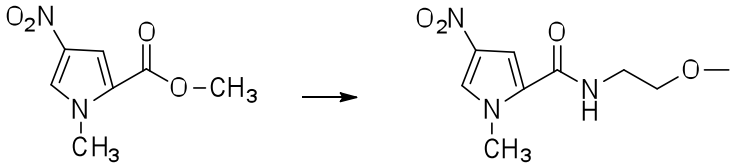
To a solution of 4-acrylamido-N-(5-(allylcarbamoyl)-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide (0.416 mmol, 148 mg) in EtOH: H_2O (4:1,10 mL) was added $NaHSO_3$ solution (0.833 mmol, 88 mg) in 1.2 mL of H_2O. The pH of the reaction mixture was then adjusted to 8.0 using a 5% NaOH solution. The reaction mixture was then heated to 80 ºC until complete disappearance of starting material (based on TLC). The reaction mixture was cooled to 0 ºC and conc, HCl added dropwise so that the pH was between 1 and 2. The solvents were evaporated to dryness and the solid obtained was treated with 1 N cold HCl solution and then centrifuged (4000 rpm, 10 min). The supernatant was decanted and the solid twice treated with 1 N cold HCl, centrifuged and the supernatant decanted. The solid obtained was then dried thoroughly to give the product (111 mg, 60%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 2.66-2.68 (m, 2H), 3.76-3.84 (m, 10H), 5.05 (dd, 1H, *J* = 10.55 and 1.56), 5.13 (dd, 1H, *J* = 17.18 and 1.56), 5.81-5.91 (m, 1H),

6.85 (d, 1H, *J* = 1.56), 6.88 (d, 1H, *J* = 1.95), 7.15 (d, 1H, *J* = 1.56), 7.20 (d, 1H, *J* = 1.95), 8.20 (t, 1H, *J* = 5.46), 9.87 (s, 1H), 9.97 (s, 1H).

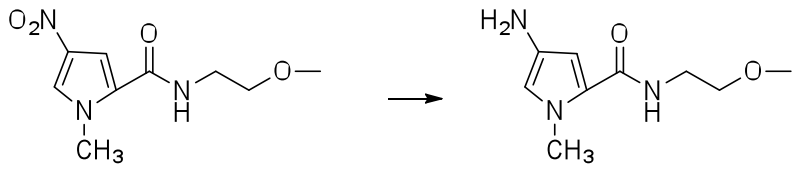


To a solution of 3-((5-((5-(allylcarbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)amino)-3-oxopropane-1-sulfonic acid (0.254 mmol, 111 mg) in dry dioxane (15 mL) was added 3-methyl-1-*p*-tolyltriaz-1-ene (1.522 mmol, 227 mg). The reaction was heated in an oil bath at 80 ºC till disappearance of starting material. The dioxane was evaporated to minimum volume and the residue was loaded onto a silica gel column deactivated with Et_3N. The product was eluted with EtOAc (88 mg, 76%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 2.73 (t, 2H, J = 7.03), 3.61 (t, 2H, J = 7.03), 3.77-3.82 (m, 5H), 3.83 (s, 3H), 3.86 (s, 3H), 5.06 (dd, 1H, *J* = 10.16 and 1.56), 5.13 (dd, 1H, *J* = 17.18 and 1.56), 5.83-5.91 (m, 1H), 6.87 (d, 1H, J = 1.95), 6.88 (d, 1H, J = 1.95), 7.17 (d, 1H, J = 1.95), 7.20 (d, 1H, J = 1.95), 8.20 (t, 1H, *J* = 5.47), 9.89 (s, 1H), 10.06 (s, 1H).
^{13}CNMR (150 MHz, DMSO-d_6) 29.85, 36.45, 36.62, 41.17, 44.50, 60.22, 104.32, 104.75, 115.14, 118.51, 118.63, 122.10, 122.47, 123.20, 123.32, 136.43, 158.77, 161.50, 166.03.
HRMS (ES+H) m/z calcd for $C_{19}H_{26}N_5O_6S$ (452.1604) Found (452.1591).

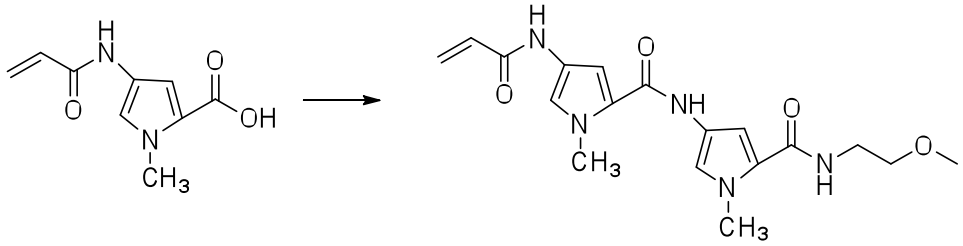
Synthesis of 3:



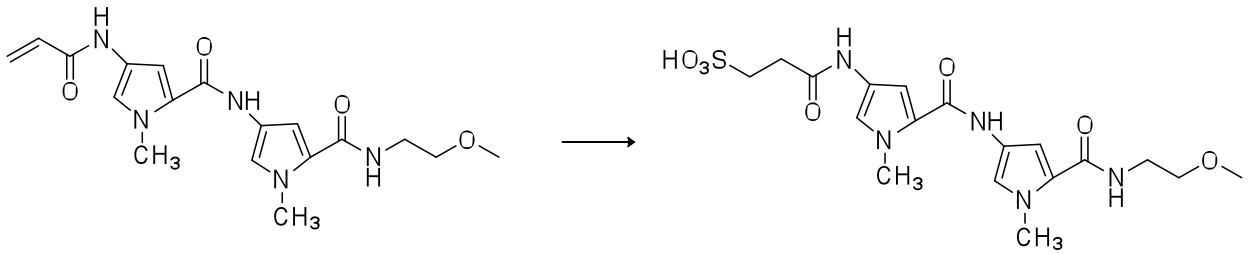
Synthesis followed previously reported method [Sabot, C., Kumar, K. A., Meunier, S., and Mioskowski, C. (2007) A convenient aminolysis of esters catalyzed by 1,5,7-triazabicyclo [4.4.0]dec-5-ene (TBD) under solvent-free conditions. *Tet. Lett. 48*, 3863-3866.].To methyl 1-methyl-4-nitro-*1H*-pyrrole-2-carboxylate (5.433 mmol, 1 g) was added 1,5,7-triazabicyclo-[*4.4.0*]dec-5-ene (TBD) (225 mg, 30 mol%) followed by 2-methoxyethylamine (10.866 mmol, 949 µL) under N_2 atmosphere. The reaction mixture was slowly warmed up to 75 ºC and stirred for 12 h. The reaction mixture was then cooled to room temperature and purified by silica gel column chromatography to yield the product (1.168g, 94.6%). ^{1}HNMR (600 MHz, $CDCl_3$) δ 3.41 (s, 3H), 3.53-3.55 (m, 2H), 3.57-3.60 (m, 2H), 3.99 (s, 3H), 6.326 (br, 1H), 7.09 (d, 1H, *J* = 1.8), 7.56 (d, 1H, *J* = 1.8).



To a solution of N-(2-methoxyethyl)-1-methyl-4-nitro-*1H*-pyrrole-2-carboxamide (5.109 mmol,1.16 g) in MeOH (320 mL) was added 10% Pd/C catalyst (330 mg) and the reaction mixture stirred in an atmosphere of H_2 at room temperature until complete disappearance of starting material (based on TLC). The reaction mixture was filtered through a celite pad and solvents evaporated to dryness to get the desired amine, 4-amino-N-(2-methoxyethyl)-1-methyl-*1H*-pyrrole-2-carboxamide in quantitative yield. ^{1}HNMR (600 MHz, DMSO-d_6) δ 3.24 (s, 3H), 3.26-3.29 (m, 2H), 3.36-3.38 (m, 2H), 3.67 (s, 3H), 4.09-4.126 (br, 2H), 6.18-6.19 (m, 2H), 7.72 (t, 1H, J = 6).

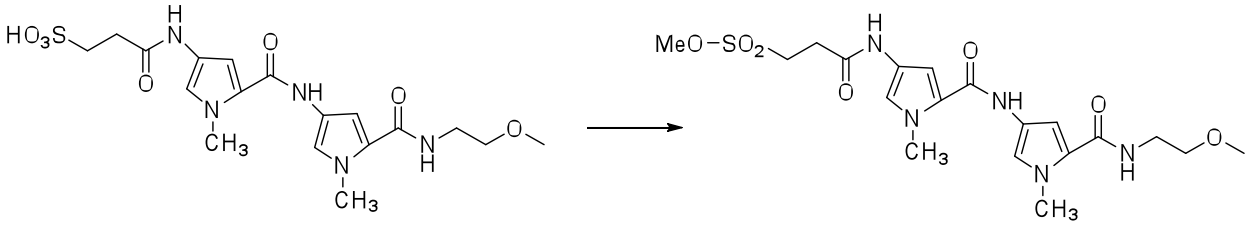


To a solution of 4-acrylamido-1-methyl-*1H*-pyrrole-2-carboxylic acid (1.416 mmol, 275 mg) and HOBT (2.124 mmol, 287 mg) under N_2 in CH_2Cl_2 (10mL) was added Et_3N (5.665 mmol, 789 µL). This was followed by the addition of EDC (2.832 mmol, 543 mg) in CH_2Cl_2 (20 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled to 0 ºC and 4-amino-N-(2-methoxyethyl)-1-methyl-*1H*-pyrrole-2-carboxamide (1.814 mmol, 385 mg) was added in CH_2Cl_2 (15 mL). The reaction mixture was stirred for about 18 h under N_2 and allowed to come to room temperature, diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4 and solvents evaporated to dryness. The residue was purified by silica gel column chromatography to get the product (365mg, 68.9%). ^{1}HNMR (600 MHz, $CDCl_3$) δ 3.38 (s, 3H), 3.55-3.56 (m, 2H), 3.58-3.61 (m, 2H), 3.87 (s, 3H), 3.90 (s, 3H), 5.75 (dd, 1H, J = 10.8 and 1.2), 6.27-6.32 (m, 1H), 6.42 (dd, 1H, J = 16.2 and 1.2), 6.53-6.57 (m, 2H), 7.14 (d, 1H, J = 1.2), 7.24 (d, 1H, J = 1.2), 7.36 (s, 1H, br), 7.87 (s, 1H, br).



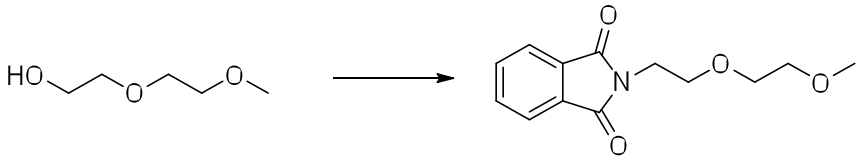
To a solution of 4-acrylamido-N-(5-((2-methoxyethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide (0.956 mmol, 357 mg) in EtOH:H_2O (4:1, 19 mL) was added $NaHSO_3$ solution (1.912 mmol, 203mg) in 2.9 mL of H_2O. The pH of the reaction mixture was

then adjusted to 8.0 using 5% NaOH solution. The reaction mixture was then heated to 80 ºC until complete disappearance of starting material (based on TLC). The reaction mixture was cooled to 0 ºC and conc. HCl added dropwise so that the pH was between 1 and 2. The solvents were evaporated to dryness and the solid obtained treated with 1 N cold HCl solution and then centrifuged (4000 rpm, 10 min). The supernatant was decanted and the solid was twice treated with 1 N cold HCl, centrifuged and the supernatant decanted. The solid obtained was then dried thoroughly to give the product (75 mg, 17%) ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.52-2.55 (m, 2H), 2.66-2.68 (m, 2H), 3.26 (s, 3H), 3.30-3.33 (m, 2H), 3.39-3.42 (m, 2H), 3.79 (s, 3H), 3.81 (s, 3H), 6.84-6.85 (m, 2H), 7.15 (d, 1H, *J* = 1.8), 7.19 (d, 1H, *J* = 1.2), 8.02 (t, 1H, *J* = 6), 9.86 (s, 1H), 9.97 (s, 1H).



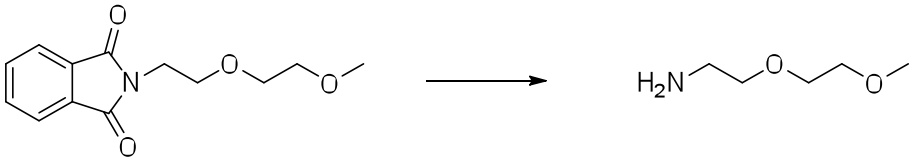
To a solution of 3-((5-((5-((2-methoxyethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)amino)-3-oxopropane-1-sulfonic acid (0.147 mmol, 67 mg) in dry dioxane (10 mL) was added 3-methyl-1-*p*-tolyltriaz-1-ene (1.522 mmol, 132 mg).The reaction was heated in an oil bath at 80 ºC until disappearance of starting material. The dioxane was evaporated to minimum volume and the residue was loaded onto a silica gel column deactivated with Et_3N. The product was eluted with sequential EtOAc and then with 2%MeOH:EtOAc to yield the product (34 mg, 49%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.73 (t, 2H, *J* = 7.2), 3.26 (s, 3H), 3.31-3.34 (m, 2H), 3.39-3.42 (m, 2H), 3.62 (t, 2H, *J* = 7.2), 3.79 (s, 3H), 3.83 (s, 3H), 3.86 (s, 3H), 6.85-6.86 (m, 2H), 7.17-7.19 (m, 2H), 8.02 (t, 1H, *J* = 5.4), 9.88 (s, 1H), 10.06 (s, 1H). HRMS (ES+Na) m/z calcd for $C_{19}H_{27}N_5O_7NaS$ (492.1529) Found (492.1537).

Synthesis of 4:

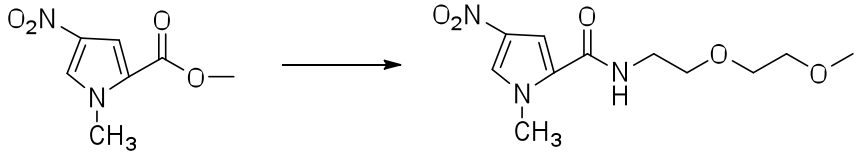


Prepared as previously reported [Dombi, K. L., Griesang, N., and Richert, C. (2002) Oligonucleotide arrays from aldehyde-bearing glass with coated background. *Synthesis 6*, 816–824.]. To a mixture of triphenyl phosphine (24 mmol, 6.3 g) and phthalimide (24 mmol, 3.53 g) in THF (100 mL) was added 2-(2-methoxyethoxy)ethanol (20 mmol, 2.35 mL). The reaction mixture was stirred at room temperature for 15 min and DIAD (24 mmol, 4.7 mL) was added dropwise. The reaction mixture was allowed to stir at room temperature under N_2 overnight. The reaction mixture was quenched with EtOH (40 mL) and solvents evaporated to dryness. The solid obtained was treated with 1:1 petroleum ether: EtOAc and stirred at 40 ºC for 1 h. The white residue was filtered off and washed with 1:1 petroleum ether: EtOAc (10 mL) and the

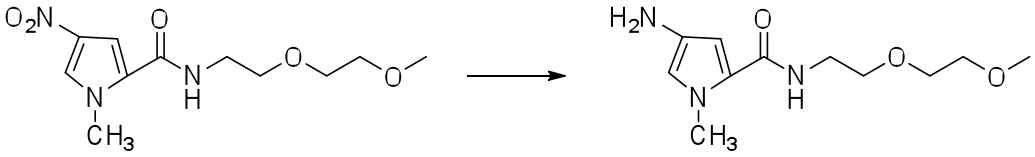
filtrate evaporated to dryness. The residue obtained was purified by silica gel column chromatography to yield product (2.47 g, 49%) ^{1}HNMR (600 MHz, $CDCl_3$) δ 3.32 (s, 3H), 3.49-3.51 (m, 2H), 3.65-3.66 (m, 2H), 3.76 (t, 2H, *J* = 5.4), 3.92 (t, 2H, *J* = 5.4), 7.71-7.73 (m, 2H), 7.85-7.86 (m, 2H).



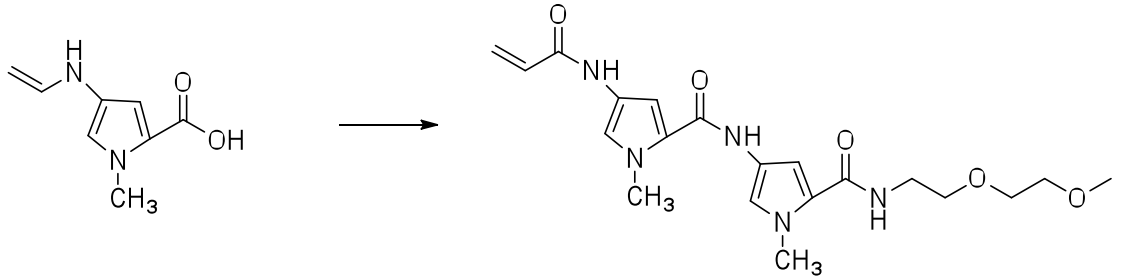
Compound was prepared as previously described [Dombi, K. L., Griesang, N., and Richert, C. (2002) Oligonucleotide arrays from aldehyde-bearing glass with coated background. *Synthesis 6*, 816–824.]. To a solution of 2-(2-(2-methoxyethoxy)ethyl)isoindoline-1,3-dione (9.49 mmol, 2.37 g) in EtOH (26 mL) was added hydrazine monohydrate (10.44 mmol, 506 µL). The resulting mixture was refluxed at 100 ºC for 5 h when a white precipitate formed. The slurry was allowed to cool and treated with conc. HCl (2.3 mL), followed by refluxing again for 1 h. The slurry was allowed to cool to room temperature and the white solid was filtered off. The filtrate was evaporated and the residue was taken up in H_2O (14 mL) and the pH of the solution adjusted to 11.0 with 1 N NaOH. The aqueous phase was saturated with NaCl and extracted with CH_2Cl_2. The organic extracts are dried over $MgSO_4$ and solvents evaporated. The residue was then distilled (Kugelrohr distillation) (0.5 Torr, heating chamber 190-195 ºC, compound distilled at 130 ºC) to yield product (0.682 g, 60%). ^{1}HNMR (600 MHz, $CDCl_3$) δ 2.88 (t, 2H, *J* = 5.4), 3.39 (s, 3H), 3.52 (t, 2H, *J* = 5.4), 3.55-3.57 (m, 2H), 3.61-3.63 (m, 2H).



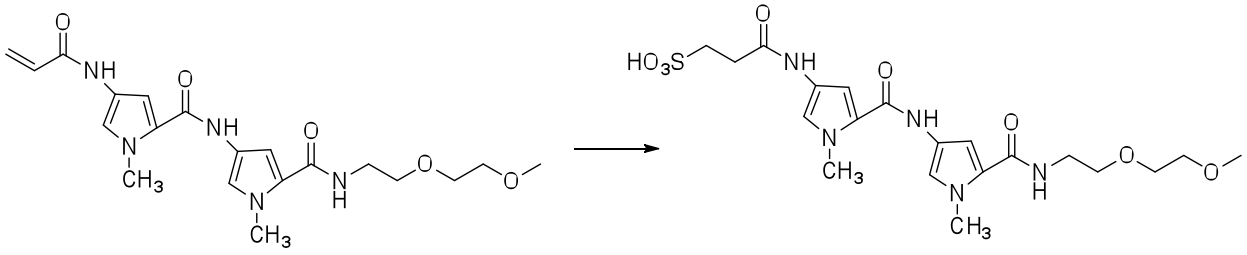
To methyl 1-methyl-4-nitro-*1H*-pyrrole-2-carboxylate (2.861 mmol, 0.527 g) was added 1,5,7-triazabicyclo[*4.4.0*]dec-5-ene (118 mg, 30 mol%) followed by 2-(2-methoxyethoxy)ethanamine (5.723 mmol, 628 mg) under N_2 atmosphere. The reaction mixture was slowly warmed up to 75 ºC and stirred for 12 h. The reaction mixture was cooled to room temperature and purified by silica gel column chromatography to yield product (0.430 g, 55%). ^{1}HNMR (600 MHz, $CDCl_3$) δ 3.45 (s, 3H), 3.58-3.61 (m, 4H), 3.66-3.69 (m, 4H), 3.99 (s, 3H), 6.71 (s, br), 7.13 (d, 1H, *J* = 1.2), 7.55 (d, 1H, *J* = 1.2).



To a solution of N-(2-(2-methoxyethoxy)ethyl)-1-methyl-4-nitro-*1H*-pyrrole-2-carboxamide (1.452 mmol, 0.394 g) in MeOH (3 8mL) was added 10% Pd/C catalyst (67 mg) and the reaction mixture stirred in an atmosphere of H_2 at room temperature until complete disappearance of starting material (based on TLC). The reaction mixture was filtered through a celite pad and solvents evaporated to dryness to afford 4-amino-N-(2-(2-methoxyethoxy)ethyl)-1-methyl-*1H*-pyrrole-2-carboxamide in quantitative yield. ^{1}HNMR (600 MHz, $CDCl_3$) δ 3.41 (s, 3H), 3.55-3.58 (m, 4H), 3.61-3.65 (m, 4H), 3.83 (s, 3H), 6.13 (d, 1H, *J* = 2.4), 6.29-6.32 (m, 2H).

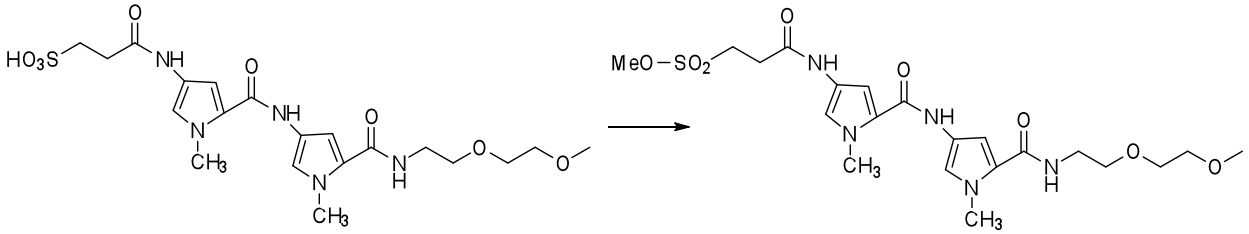


To a solution of 4-acrylamido-1-methyl-*1H*-pyrrole-2-carboxylic acid (1.128 mmol, 219 mg) and HOBT (1.692 mmol, 229 mg) under N_2 in CH_2Cl_2 (20 mL) was added Et_3N (4.511 mmol, 629 µL), followed by the addition of EDC (2.256 mmol, 432 mg) in CH_2Cl_2 (20 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled to 0 ºC and 4-amino-N-(2-(2-methoxyethoxy)ethyl)-1-methyl-*1H*-pyrrole-2-carboxamide (1.450 mmol, 350 mg) added in CH_2Cl_2 (15 mL). The reaction mixture was stirred for about 18 h under N_2, allowed to come to room temperature and then diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and solvents evaporated to dryness. The residue was purified by silica gel column chromatography to give product (339 mg, 72%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 3.29-3.32 (m, 2H), 3.33 (s, 3H), 3.43-3.45 (m, 2H), 3.48 (t, 2H, *J* = 6), 3.52-3.54 (m, 2H), 3.79 (s, 3H), 3.83 (s, 3H), 5.67 (dd, 1H *J* = 10.2 and 1.8), 6.18 (dd, 1H, *J* = 16.8 and 1.8), 6.35-6.39 (m, 1H), 6.85 (d, 1H, *J* = 1.8), 6.91 (d, 1H, *J* = 1.8), 7.19 (d, 1H, *J* = 1.8), 7.27 (d, 1H, *J* = 1.8), 8.02 (t, 1H, *J* = 6), 9.91 (s, 1H), 10.11 (s, 1H).



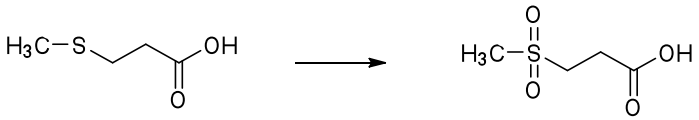
To a solution of 4-acrylamido-N-(5-((2-(2-methoxyethoxy)ethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide (0.099 mmol, 41.7 mg) in EtOH:H_2O (4:1, 1.9 mL) was added $NaHSO_3$ solution (0.199 mmol, 21.1 mg) in 0.3 mL of H_2O. The pH of the reaction mixture was then adjusted to 8.0 with using 5% NaOH solution. The reaction mixture was then heated to 80 ºC until complete disappearance of starting material (based on TLC). The reaction mixture was cooled to 0 ºC and conc. HCl added dropwise so that the pH remained

between 1 and 2. The solvents were evaporated to dryness to yield the product (44 mg, 88%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.53-2.56 (m, 2H), 2.67-2.69 (m, 2H), 3.25 (s, 3H), 3.29-3.32 (m, 2H), 3.43-3.46 (m, 2H), 3.46-3.49 (m, 2H), 3.52-3.53 (m, 2H), 3.79 (s, 3H), 3.81 (s, 3H), 6.84-6.86 (m, 2H), 7.15 (s, 1H), 7.19 (s, 1H), 8.01 (t, 1H, *J* = 5.4), 9.87 (s, 1H), 9.98 (s, 1H).

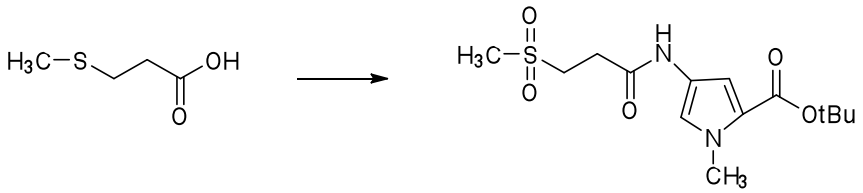


To a solution of 3-((5-((5-((2-(2-methoxyethoxy)ethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)amino)-3-oxopropane-1-sulfonic (0.0372 mmol, 18.6 mg) in dry dioxane (5 mL) was added 3-methyl-1-*p*-tolyltriaz-1-ene (0.149 mmol, 23 mg).The reaction was heated in an oil bath at 80 ºC for 1 h, then another 20 mg of 3-methyl-1-*p*-tolyltriaz-1-ene was added and the reaction heated for another 30 min. The dioxane was evaporated to minimum volume and the residue was loaded onto a silica gel column deactivated with Et_3N. The product was sequentially eluted with EtOAc and then 5% MeOH:EtOAc to yield product (15mg, 78%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.50-2.53 (m, 2H), 2.73 (t, 2H, *J* = 7.2), 3.24 (s, 3H), 3.43-3.4 (m, 2H), 3.47 (t, 2H, *J* = 6.6), 3.52-3.54 (m, 2H), 3.62 (t, 2H, *J* = 7.2), 3.79 (s, 3H), 3.81 (s, 3H), 3.86 (s, 3H), 6.85 (d, 1H, *J* = 1.8), 6.87 (d, 1H, *J* = 1.8), 7.17 (d, 1H, *J* = 1.8), 7.19 (d, 1H, *J* = 1.8), 8.01 (t, 1H, *J* = 5.4), 9.88 (s, 1H), 10.06 (s, 1H). HRMS (ES+Na) m/z calcd for $C_{21}H_{31}N_5O_8NaS$ (536.1791) Found (536.1765).

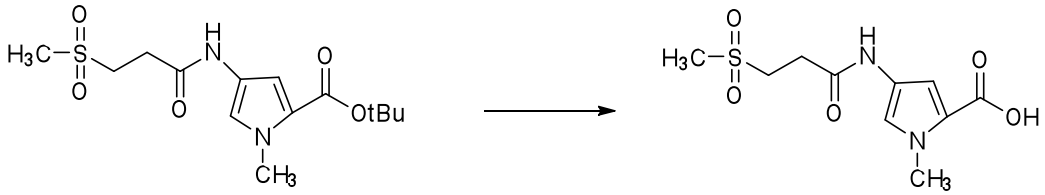
Synthesis of 5:



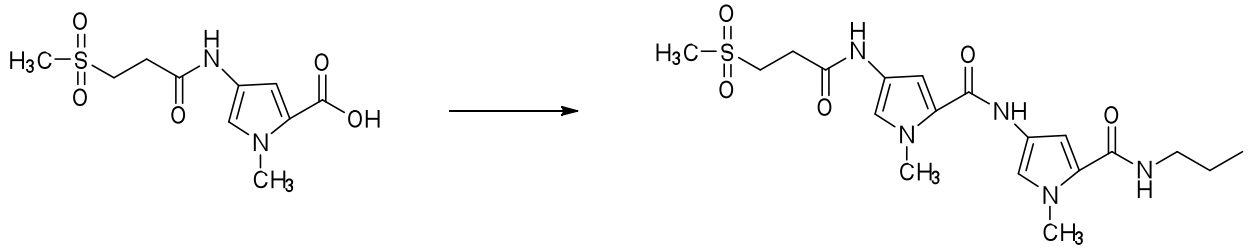
Prepared as previously described [Truce, W. E., and Knospe, R. H. (1955) The preparation of 0-keto sulfones by the Claisen condensation. *J. Am. Chem. Soc. 77*, 5063-5067.]. To a solution of 3-(methylthio)propionic acid (6.241 mmol, 0.65 mL) in a 1:1 mixture of AcOH:Ac_2O (6 mL) was added 35% H_2O_2 (3 mL) and the reaction was stirred at room temperature for 48 h and the excess of peroxide quenched by addition of a trace amount of MnO_2 under N_2. The solvent was removed by distillation to give a white solid in quantitative yield. ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.68 (t, 2H, *J* = 7.8) 3.00 (s, 3H), 3.33 (t, 2H, *J* = 7.8), 12.56 (s, br, 1H).



To a solution of 3-(methylthio)propanoic acid (1.045 mmol, 159 mg) and HOBT (1.484 mmol, 200 mg) in CH_2Cl_2 (15 mL) was added Et_3N (3.956 mmol, 0.551 mL), followed by the addition of EDC (1.978 mmol, 0.379 g) in CH_2Cl_2 (15 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled to 0 ºC and tert-butyl 4-amino-1-methyl-*1H*-pyrrole-2-carboxylate (1.484 mmol) added. The reaction mixture was allowed to warm to room temperature and stirred for about 18 h and then diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with CH_2Cl_2 and the organic layer dried over Na_2SO_4 and evaporated to dryness. The residue was purified by silica gel column chromatography to yield product (282 mg, 81.7%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 1.49 (s, 9H), 2.69 (t, 2H, *J* = 7.8), 3.00 (s, 3H), 3.39 (t, 2H, *J* = 7.8), 3.78 (s, 3H), 6.65 (d, 1H, *J* = 1.96), 7.23 (d, 1H, *J* = 1.96), 10.03 (s, br, 1H).



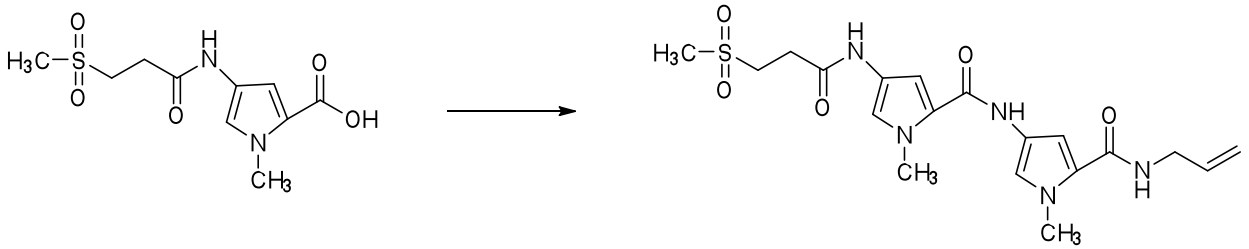
To a solution of tert-butyl 1-methyl-4-(3-(methylsulfonyl)propanamido)-*1H*-pyrrole-2-carboxylate (0.847 mmol, 0.280 g) in CH_2Cl_2 (27 mL) was added 1M $TiCl_4$ solution (1.694 mmol, 1.7 mL) at 0 ºC. The reaction mixture was stirred at 0 ºC and slowly allowed to come to room temperature until complete disappearance of starting material. The reaction mixture was diluted with CH_2Cl_2 and washed with H_2O. The aqueous layer was extracted thoroughly with EtOAc (4 x 50 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated to give a quantitative yield of the acid product. ^{1}HNMR (400 MHz, DMSO-d_6) δ 2.70 (t, 2H, *J* = 7.8), 3.0 (s, 3H), 3.39 (t, 2H, *J* = 7.8), 3.79 (s, 3H), 6.66 (d, 1H *J* = 1.95), 7.28 (d, 1H, *J* = 1.95), 10.08 (s, br, 1H).



To a solution of 1-methyl-4-(3-(methylsulfonyl)propanamido)-*1H*-pyrrole-2-carboxylic acid (0.551 mmol, 151 mg) and HOBT (0.765 mmol, 103 mg) in anhydrous DMF (2 mL) was added

Et_3N (2.042 mmol, 0.285 mL) followed by the addition of EDC (1.02 mmol, 0.196 g) in CH_2Cl_2 (15 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and the reaction mixture cooled to 0 ºC and 4-amino-1-methyl-N-propyl-*1H*-pyrrole-2-carboxamide (0.765 mmol) was added in CH_2Cl_2 (10 mL) and Et_3N (100 µL). The reaction mixture was allowed to come to room temperature and stirred for about 18 h and the solvent removed. The residue was purified by silica gel column chromatography to yield product (111 mg, 46%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 0.863 (t, 3H, *J* = 7.42), 1.44-1.51 (m, 2H), 2.73 (t, 2H, *J* = 7.8), 3.01 (s, 3H), 3.09-3.14 (m, 2H) 3.40 (t, 2H, *J* = 7.8), 3.79 (s, 3H), 3.83 (s, 3H), 6.84 (d, 1H, *J* = 1.95), 6.86 (d, 1H, *J* = 1.95), 7.16-7.17 (m, 2H,), 8.0 (t, 1H, *J* = 6.25), 9.86 (s, br, 1H), 10.06 (s, br, 1H). ^{13}CNMR (150MHz, DMSOd_6) δ 11.91, 23.05, 28.68, 36.37, 36.61, 40.65, 40.91, 50.24, 104.31, 104.56, 118.20, 118.62, 122.15, 122.42, 123.33, 123.56, 158.76, 161.68, 166.55. HRMS (ES+Na) m/z calcd for $C_{19}H_{27}N_5O_5NaS$ (460.163) Found (460.162).

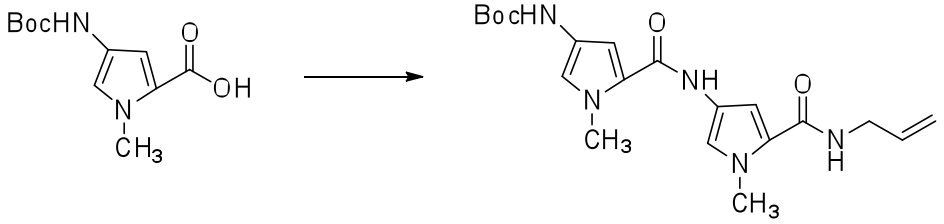
Synthesis of 6:



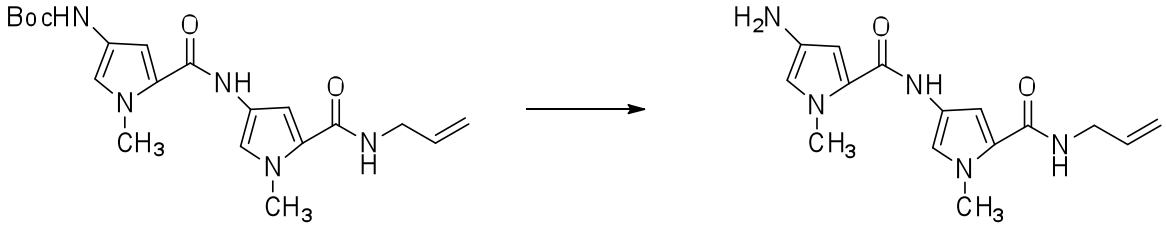
To a solution of 1-methyl-4-(3-(methylsulfonyl)propanamido)-*1H*-pyrrole-2-carboxylic acid (0.193 mmol, 53 mg) and HOBT (0.289 mmol, 39 mg) in anhydrous CH_2Cl_2 (10 mL) was added Et_3N (0.773 mmol, 0.108 mL) followed by the addition of EDC (0.386 mmol, 74 mg) in CH_2Cl_2 (15 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and the reaction mixture cooled to 0 ºC and N-allyl-4-amino-1-methyl-*1H*-pyrrole-2-carboxamide (0.289 mmol) added in CH_2Cl_2 (10 mL) and Et_3N (100 µL). The reaction mixture was allowed to come to room temperature and stirred for about 18 h and diluted with H_2O and extracted with CH_2Cl_2. The organic solvents were dried over Na_2SO_4, the solvent evaporated and the residue purified by silica gel column chromatography to yield product (26 mg, 31%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 2.73 (t, 2H, *J* = 7.80), 3.01 (s, 3H), 3.38-3.42 (m, 2H), 3.76-3.80 (m, 5H), 3.82 (s, 3H), 5.05 (dd, 1H, *J* = 10.15 and 1.56), 5.13 (dd, 1H, *J* = 17.18 and 1.56), 5.81-5.90 (m, 1H) 6.86 (d, 1H, *J* = 1.95), 6.88 (d, 1H, *J* = 1.95), 7.16 (d, 1H, *J* = 1.95), 7.20 (d, 1H, *J* = 1.95), 8.20 (t, 1H, *J* = 7.68), 9.88 (s, br, 1H), 10.06 (s, br, 1H). ^{13}CNMR (150 MHz, DMSO-d_6) δ 28.68, 36.45, 36.60, 40.91, 41.18, 50.24, 104.32, 104.74, 115.15, 118.52, 118.63, 122.15, 122.48, 123.21, 123.31δ, 136.44, 158.78, 161.50, 166.55. HRMS (ES+Na) m/z calcd for $C_{19}H_{25}N_5O_5NaS$ (458.147) Found (458.145).

Synthesis of 7: see experimental in manuscript

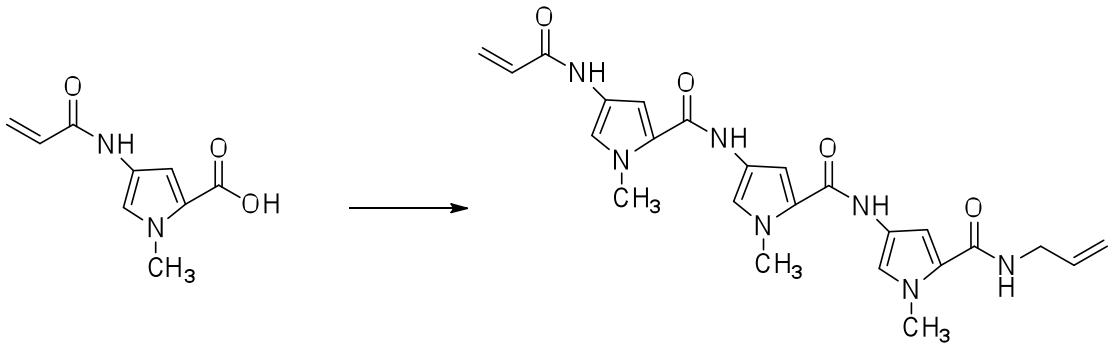
Synthesis of 8:



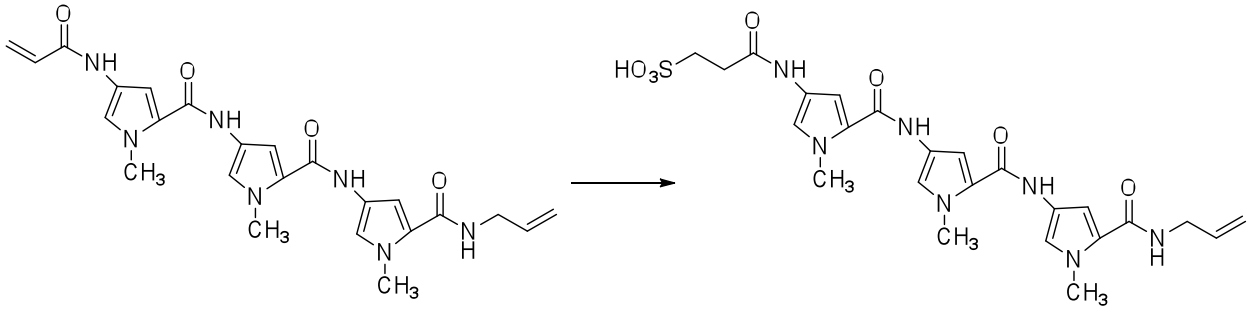
To a solution of 4-((tert-butoxycarbonyl) amino)-1-methyl-*1H*-pyrrole-2-carboxylic acid (2.805 mmol, 674 mg) and HOBT (4.208 mmol, 569 mg) in anhydrous CH_2Cl_2 (20 mL) was added Et_3N (11.221 mmol, 1.56 mL) followed by the addition of EDC (5.61 mmol, 1.075 g) in CH_2Cl_2 (25 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled to 0 ºC and N-allyl-4-amino-1-methyl-*1H*-pyrrole-2-carboxamide (5.61 mmol added in CH_2Cl_2 (15 mL) and Et_3N (1 mL). The reaction mixture was allowed to come to room temperature and stirred for about 18 h and then the reaction was diluted with H_2O and extracted with CH_2Cl_2. The combined organic solvents were dried over Na_2SO_4 and evaporated. The residue was purified by silica gel column chromatography to yield product (1.011 g, 89%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 1.45 (s, 9H), 3.74-3.84 (m, 8H), 5.05 (dd, 1H, *J* = 8.59 and 1.56), 5.13 (dd, 1H, *J* = 15.23 and 1.56), 5.81-5.91 (m, 1H), 6.82 (br, s, 1H), 6.86-6.92 (m, 2H), 7.18 (d, 1H, *J* = 1.95), 8.18 (t, 1H, *J* = 6.25), 9.09 (s, 1H), 9.83 (s, 1H).



To a solution of tert-butyl (5-((5-(allylcarbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-carbamoyl)-1-methyl-1H-pyrrol-3-yl) carbamate (2.391 mmol, 960 mg,) in anhydrous CH_2Cl_2 (12 mL) was added 50% TFA: dichloromethane (34mL) at 0 ºC such that the final concentration of TFA was ~40%. The reaction mixture was stirred under N_2 and at 0 ºC until complete disappearance of starting material. The solvents were evaporated to dryness to give the N-allyl-4-(4-amino-1-methyl-*1H*-pyrrole-2-carboxamido)-1-methyl-*1H*-pyrrole-2-carboxamide product in quantitative yield. ^{1}HNMR (400 MHz, DMSO-d_6) δ 3.78-3.82 (m, 5H), 3.89 (s, 3H), 5.06 (dd, 1H, *J* = 10.16 and 1.95), 5.13 (dd, 1H, *J* = 15.23 and 1.95), 5.82-5.91 (m, 1H), 6.88 (d, 1H, *J* = 1.95), 6.94 (d, 1H, *J* = 1.95), 7.11 (d, 1H, *J* = 1.95), 7.21 (d, 1H, *J* = 1.95), 8.22 (t, 1H, *J* = 6.25), 9.71 (s, br, 2H), 10.00 (s,1H).

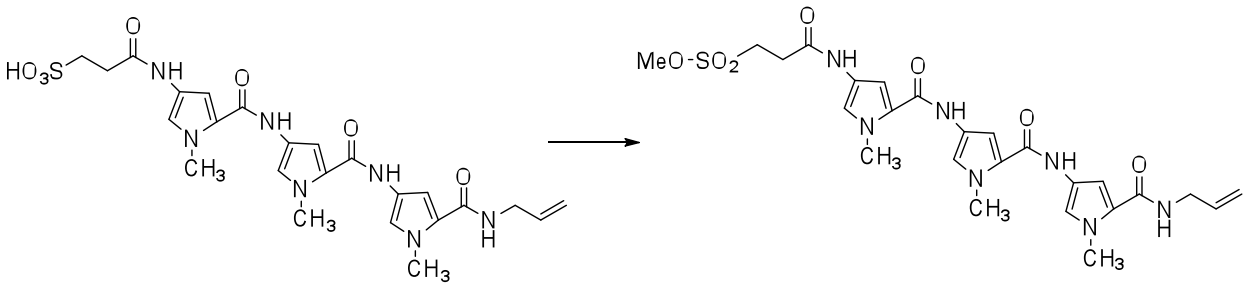


To a solution of 4-acrylamido-1-methyl-*1H*-pyrrole-2-carboxylic acid (1.545 mmol, 300 mg) and HOBT (2.318 mmol, 313 mg) in anhydrous CH_2Cl_2 (25 mL) was added Et_3N (6.18 mmol, 0.861 mL) followed by the addition of EDC (3.09 mmol, 0.592 g) in CH_2Cl_2 (20 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h, cooled to 0 ºC and N-allyl-4-(4-amino-1-methyl-*1H*-pyrrole-2-carboxamido)-1-methyl-*1H*-pyrrole-2-carboxamide (2.39 mmol) added in CH_2Cl_2 (10 mL) and Et_3N (1 mL). The reaction mixture was allowed to come to room temperature, stirred for 18 h and then diluted with H_2O and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and evaporated and the residue purified by silica gel column chromatography to give product (0.555 g, 75%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 3.77-3.82 (m, 5H), 3.847 (s, 3H), 3.854 (s, 3H), 5.06 (dd, 1H, *J* = 10.16 and 1.56Hz), 5.13 (dd, 1H, *J* = 15.23 and 1.56), 5.67 (dd, 1H, *J* = 10.16 and 1.95), 5.82-5.91 (m, 1H), 6.19 (dd, 1H, *J* = 17.19 and 1.95), 6.34-6.41 (m, 1H), 6.90 (d, 1H, *J* = 1.56), 6.94 (d, 1H, *J* = 1.95), 7.04 (d, 1H, *J* = 1.95), 7.21 (d, 1H, *J* = 1.56), 7.25 (d, 1H, *J* = 1.95), 7.28 (d, 1H, *J* = 1.95), 8.21 (t, 1H, *J* = 6.25), 9.91 (s, 1H), 9.96 (s, 1H), 10.117 (s, 1H).



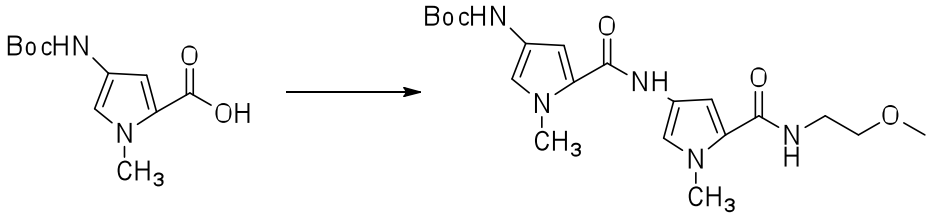
To a solution of 4-acrylamido-N-(5-((5-(allylcarbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide (1.114 mmol, 532 mg) in EtOH:H_2O (4:1, 24 mL) was added $NaHSO_3$ solution (2.228 mmol, 236 mg) in 3.2 mL of H_2O. The pH of the reaction mixture was then adjusted to 8.0 using 5% NaOH solution. The reaction mixture was then heated at 80 ºC until complete disappearance of starting material (based on TLC). The reaction mixture was cooled to 0 ºC and conc. HCl added dropwise so that the pH remained between 1 and 2. The solvent were evaporated to dryness and the solid residue treated with 1 N cold HCl solution and then centrifuged (4000 rpm, 10 min).The supernatant was decanted and the solid was twice treated with 1 N cold HCl, centrifuged and the supernatant decanted. The solid obtained was then dried thoroughly to give product (550 mg, 88%). ^{1}HNMR

(400 MHz, DMSO-d_6) δ 2.53-2.57 (m, 2H), 2.66-2.70 (m, 2H), 3.75-3.87(m, 11H), 5.06 (dd, 1H, *J* = 10.16 and 1.56), 5.13 (dd, 1H, *J* = 17.18 and 1.56), 5.82-5.91 (m, 1H), 6.87 (d, 1H, *J* = 1.56), 6.90 (d, 1H, *J* = 1.56), 7.03 (d, 1H, *J* = 1.56), 7.15 (d, 1H, *J* = 1.56), 7.21 (d, 1H, *J* = 1.56), 7.25 (d, 1H, *J* = 1.56) 8.20 (t, 1H, *J* = 6.25), 9.91 (s, 2H), 9.97 (s, 1H).



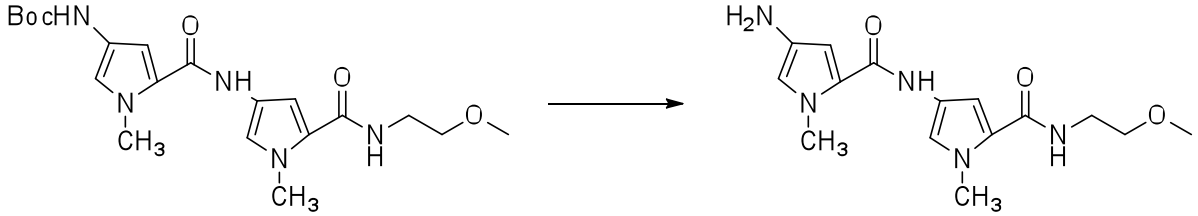
To a solution of 3-((5-((5-((5-(allylcarbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)amino)-3-oxopropane-1-sulfonic acid (0.947 mmol, 530 mg) in dry dioxane (53 mL) was added 3-methyl-1-*p*-tolyltriaz-1-ene (5.683 mmol, 848 mg).The reaction was heated in an oil bath at 80 ºC for about 1 h and then the dioxane evaporated to minimum volume and the residue loaded onto a silica gel column deactivated with Et_3N. The product was eluted in EtOAc (159 mg, 29%). ^{1}HNMR (400 MHz, DMSO-d_6) δ 2.74 (t, 2H, J = 7.03), 3.62 (t, 2H, J = 7.03), 3.77-3.82 (m, 5H), 3.83-3.86 (s, br, 6H), 3.87 (s, 3H), 5.06 (dd, 1H, *J* = 10.16 and 1.56), 5.13 (dd, 1H, *J* = 17.18 and 1.56), 5.82-5.91 (m, 1H), 6.89 (d, 1H, J = 1.95), 6.90 (d, 1H, J = 1.56), 7.04 (d, 1H, J = 1.95), 7.18 (d, 1H, J = 1.56), 7.21 (d, 1H, J = 1.95), 7.25 (d, 1H, J = 1.95), 8.20 (t, 1H, *J* = 6.25), 9.91 (s, 1H), 9.93 (s, 1H), 10.07 (s, 1H). ^{13}CNMR (150 MHz, DMSO-d_6) δ 29.84, 36.44, 36.57, 36.63, 41.18, 44.50, 57.38, 104.37, 104.80, 105.15, 115.16, 118.45, 118.65, 118.94, 122.12, 122.53, 123.62, 123.20, 123.23, 123.33, 136.45, 158, 158.93, 161.53, 166.05. HRMS (ES+H) m/z calcd for $C_{25}H_{32}N_7O_7S$ (574.2084) Found (574.2072).

Synthesis of 9:

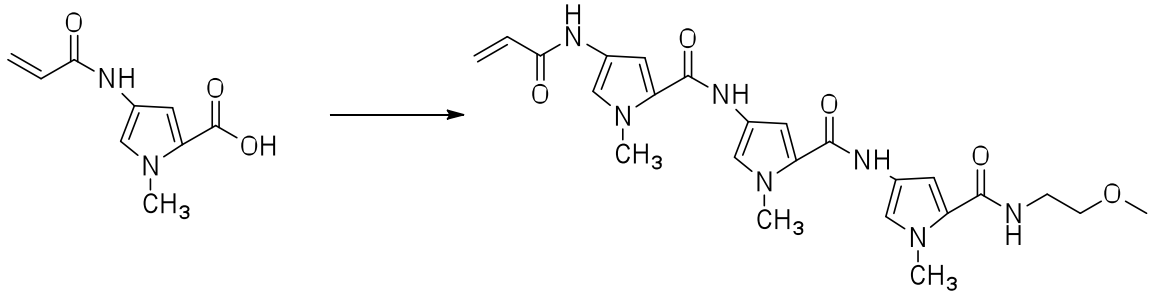


To a solution of 4-((tert-butoxycarbonyl)amino)-1-methyl-*1H*-pyrrole-2-carboxylic acid (3.90 mmol, 937 mg) and HOBT (5.85 mmol, 790 mg) in anhydrous CH_2Cl_2 (25mL) was added Et_3N (15.60 mmol, 2.17 mL) followed by the addition of EDC (7.80 mmol, 1.495 g) in CH_2Cl_2 (25mL). The reaction mixture was stirred under N_2 at room temperature for 1 h and then cooled

to 0 ºC and 4-amino-N-(2-methoxyethyl)-1-methyl-*1H*-pyrrole-2-carboxamide (5.07 mmol) added in CH_2Cl_2 (30 mL). The reaction mixture was allowed to warm to room temperature and stirred for 18h, diluted with H_2O and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and evaporated, and the residue purified by silica gel column chromatography to yield product (1.141 g, 69%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 1.45 (s, 9H), 3.26 (s, 3H), 3.30-3.32 (m, 2H), 3.39-3.42 (m, 2H,), 3.78 (s,3H), 3.79δ (s, 3H), 6.81 (s, 1H), 6.86 (d, 1H, *J* = 1.26Hz), 6.88 (s, 1H), 7.16 (d, 1H, *J* = 1.2), 7.99 (t, 1H, *J* = 5.4), 9.09 (s, 1H), 9.80 (s, 1H).

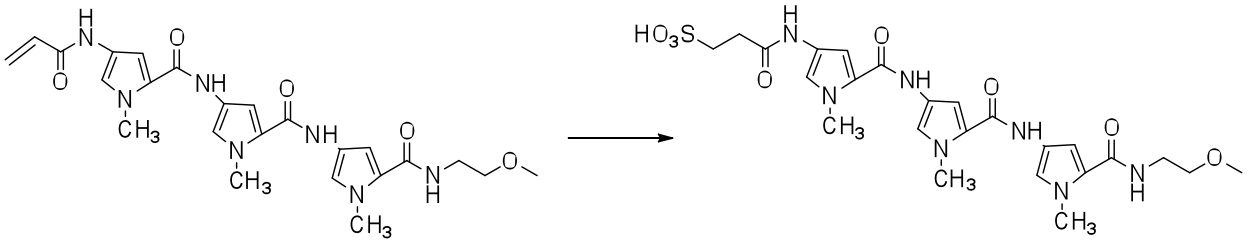


To a solution of tert-butyl (5-((5-((2-methoxyethyl) carbamoyl)-1-methyl-*1H*-pyrrol-3-yl) carbamoyl)-1-methyl-*1H*-pyrrol-3-yl) carbamate (2.625 mmol, 1.101 g,) in anhydrous CH_2Cl_2 (13 mL) was added 50%TFA:CH_2Cl_2 (40 mL) at 0 ºC such that the final concentration of TFA was around 40%. The reaction mixture was stirred under N_2 at 0 ºC until complete disappearance of starting material. The solvent was removed to give 4-amino-N-(5-((2-methoxyethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide in quantitative yield. ^{1}HNMR (600 MHz, DMSO-d_6) δ 3.26 (s, 3H), 3.31-3.34 (m, 2H), 3.39-3.42 (m, 2H), 3.80 (s,3H), 3.89 (s,3H), 6.86 (d, 1H, *J* = 1.8), 6.94 (d, 1H, *J* = 1.8), 7.11 (d, 1H, *J* = 1.8), 7.19 (d, 1H, *J* = 1.8), 8.04 (t, 1H, *J* = 5.4), 9.73 (s, br ,2H), 9.99 (s, 1H).

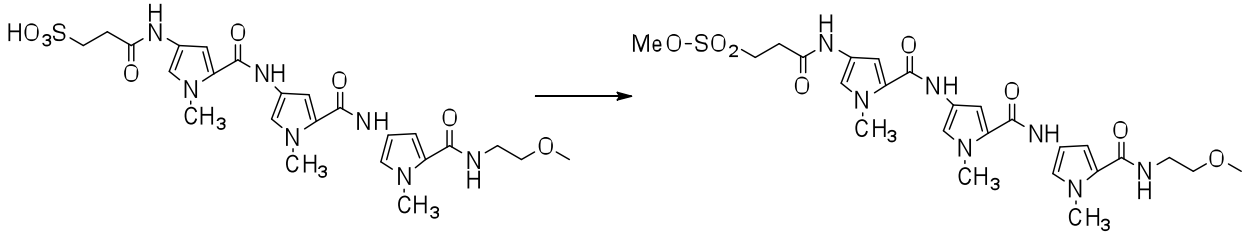


To a solution of 4-acrylamido-1-methyl-*1H*-pyrrole-2-carboxylic acid (2.059 mmol, 400 mg) and HOBT (3.086 mmol, 417 mg) in anhydrous CH_2Cl_2 (40 mL) was added Et_3N (8.24 mmol, 1.15 mL) followed by the addition of EDC (4.12 mmol, 0.789 g) in CH_2Cl_2 (30 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h, cooled to 0 ºC and 4-amino-N-(5-((2-methoxyethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide (2.68 mmol) added in CH_2Cl_2 (30 mL) and Et_3N (0.5 mL). The reaction mixture was allowed to come to room temperature and stirred for about 18h, diluted with H_2O and sequentially extracted with CH_2Cl_2, EtOAc and MeOH. The organic extracts were dried over Na_2SO_4, evaporated and the residue purified by silica gel column chromatography to yield yellow product (0.720 g, 70%) that

was washed with hot EtOH to give white product. ^{1}HNMR (600 MHz, DMSO-d_6) δ 3.26 (s, 3H), 3.31-3.34 (m, 2H), 3.40-3.42 (m, 2H), 3.80 (s, 3H), 3.846 (s, 3H), 3.85 (s, 3H), 5.67 (dd,1H, *J* = 10.2 and 1.8), 6.19 (dd,1H, *J* = 17.4 and 1.8), 6.35-6.39 (m,1H), 6.88 (d, 1H, *J* = 1.2), 6.94 (d, 1H, *J* = 1.8), 7.04 (d, 1H, *J* = 1.8), 7.19 (d, 1H, *J* = 1.8), 7.25 (d, 1H, *J* = 1.8), 7.28 (d, 1H, *J* = 1.8), 8.02 (t, 1H, *J* = 5.4), 9.91 (s, 1H), 9.95 (s, 1H), 10.11 (s, 1H).



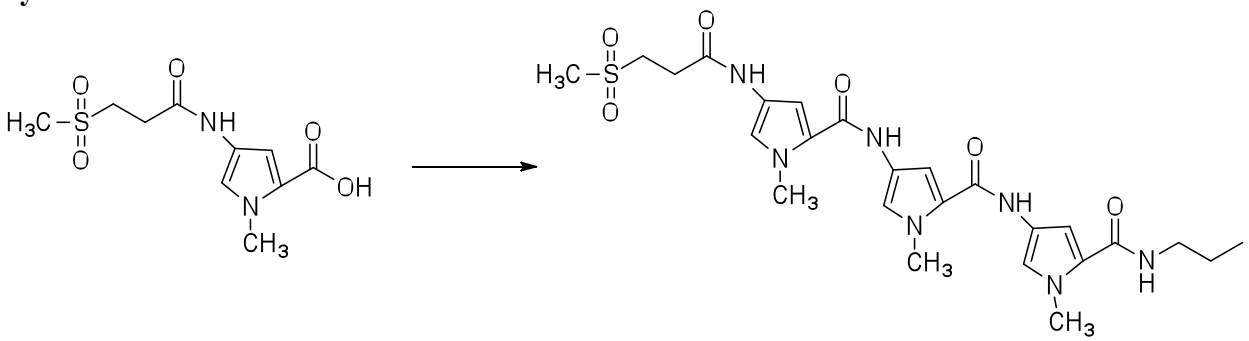
To a solution of 4-acrylamido-N-(5-((5-((2-methoxyethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)-1-methyl-*1H*-pyrrole-2-carboxamide (0.0787 mmol, 39 mg) in EtOH:H_2O (4:1, 2 mL) was added $NaHSO_3$ solution (0.157 mmol, 16.7 mg) in 0.242 mL of H_2O. The pH of the reaction mixture was then adjusted to 8.0 using 5% NaOH solution. The reaction mixture was then heat at 80 ºC until complete disappearance of starting material (based on TLC). The reaction mixture was cooled to 0 ºC and conc. HCl was added dropwise so that the pH was between 1 and 2. The solvent was then evaporated to dryness and the solid residue was then treated with 1 N cold HCl solution and then centrifuged (4000 rpm, 10 min).The supernatant was decanted and the solid was twice treated with 1 N cold HCl, centrifuged and the supernatant decanted. The solid obtained was then dried thoroughly to give product (38mg, 83%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.52-2.54 (m, 2H), 2.65-2.68 (m, 2H), 3.26 (s, 3H), 3.31-3.34 (m, 2H), 3.41 (t, 2H, *J* = 6), 3.80 (s, 3H), 3.83 (s, 3H), 3.84 (s, 3H), 6.87 (d, 2H, *J* = 1.2), 7.02 (d, 1H, *J* = 1.2), 7.15 (d, 1H, *J* = 1.2), 7.19 (d, 1H, *J* = 1.8), 7.24(d, 1H, *J* = 1.8), 8.02 (t, 1H, *J* = 5.4), 9.90 (s, 1H), 9.91 (s, 1H), 9.98 (s, 1H). HRMS (EI^+) m/z calcd for $C_{24}H_{31}N_7O_8S$ (577.61) Found (577.20).



To a solution of 3-((5-((5-((5-((2-methoxyethyl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)carbamoyl)-1-methyl-*1H*-pyrrol-3-yl)amino)-3-oxopropane-1-sulfonic acid (0.0658 mmol, 38 mg) in dry dioxane (5 mL) was added 3-methyl-1-*p*-tolyltriaz-1-ene (0.263 mmol, 39.2 mg).The reaction was heated in an oil bath at 80 ºC for about 1h and the dioxane reduced to a minimum volume and then loaded onto a silica gel column deactivated with Et_3N. The product was sequentially eluted in EtOAc to 5% MeOH:EtOAc (4

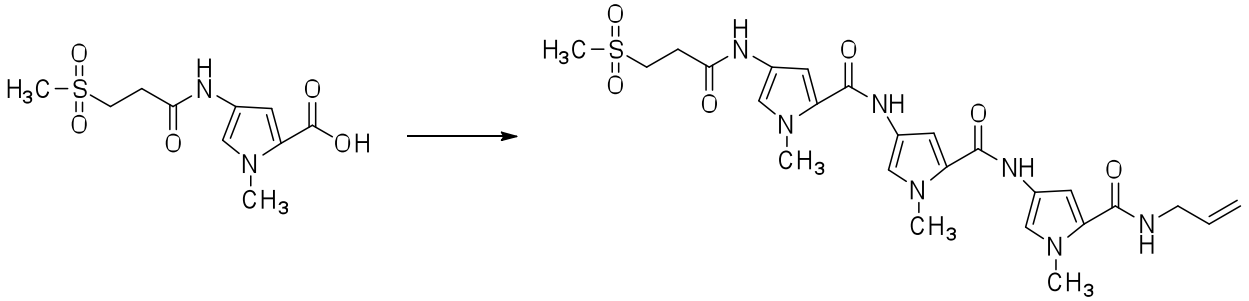
mg, 10%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.52-2.56 (m, 2H), 2.74 (t, 2H, *J* = 7.2), 3.27 (s, 3H), 3.39-3.43 (m, 2H), 3.62 (t, 2H, *J* = 7.2), 3.78 (s, 3H), 3.841 (s, 3H), 3.843(s, 3H), 3.87(s,3H), 6.87 (d, 2H, *J* = 1.8), 6.89(d,1H, *J* = 1.8), 7.03 (d, 1H, *J* = 1.8), 7.17 (d, 1H, *J* = 1.2), 7.19 (d, 1H, *J* = 1.8), 7.24(d, 1H, *J* = 1.8), 8.02 (t, 1H, *J* = 5.4), 9.89 (s, 1H), 9.92 (s, 1H), 10.07 (s, 1H).

Synthesis of 10:



To a solution of 1-methyl-4-(3-(methylsulfonyl)propanamido)-*1H*-pyrrole-2-carboxylic acid (0.397 mmol, 109 mg) and HOBT (0.548 mmol, 74 mg) in anhydrous DMF (2.5 mL) was added Et_3N (1.46 mmol, 0.203 mL). This was followed by the addition of EDC (0.73 mmol, 0.140 g) in CH_2Cl_2 (15 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h, cooled to 0 ºC and amine, **f** (0.548 mmol) was added in CH_2Cl_2 (10 mL) and Et_3N (0.1 mL). The reaction mixture was allowed to come to room temperature and stirred for about 18 h, solvent removed and the residue purified by silica gel column chromatography to yield product (66 mg, 30%). The product had a yellow color and was treated with hot EtOH to yield a white solid ethanol when a white solid product. ^{1}HNMR (400 MHz, DMSO-d_6) δ 0.867 (t, 3H, *J* = 7.42), 1.442-1.532 (m, 2H) 2.73 (t, 2H, *J* = 7.8), 3.01(s, 3H), 3.10-3.15 (m, 2H) 3.41 (t, 2H, *J* = 7.8), 3.79 (s, 3H), 3.84 (s, br 6H), 6.86 (d, 1H, *J* = 1.95), 6.89 (d, 1H, *J* = 1.95), 7.03 (d, 1H, *J* = 1.95), 7.16-7.18 (m, 2H) 7.24 (d, 1H, *J* = 1.97), 8.0 (t, 1H, *J* = 5.86), 9.89 (s, br, 1H), 9.93 (s, br, 1H), 10.07 (s, br, 1H). ^{13}CNMR (150 MHz, DMSO-d_6) δ 11.92, 23.07, 28.69, 36.36, 36.57, 36.61, 40.66, 40.91, 50.24, 104.39, 104.58, 105.13, 118.15, 118.67, 118.93, 122.17, 122.56, 123.25, 123.33, 123.56, 158.83, 158.91, 161.71, 166.57. HRMS (ES+H) m/z calcd for $C_{25}H_{34}N_7O_6S$ (560.229) Found (560.224).

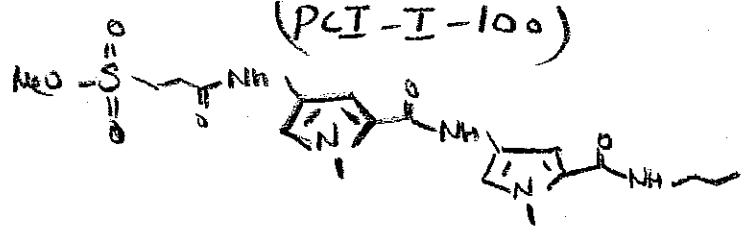
Synthesis of 11:



To a solution of 1-methyl-4-(3-(methylsulfonyl)propanamido)-*1H*-pyrrole-2-carboxylic acid (0.390 mmol, 107 mg) and HOBT (0.518 mmol, 70 mg) in anhydrous DMF (2 mL) was added

Et_3N (1.38 mmol, 0.192 mL) followed by the addition of EDC (0.69 mmol, 133 mg) in CH_2Cl_2 (10 mL). The reaction mixture was stirred under N_2 at room temperature for 1 h, cooled to 0 ºC and N-allyl-4-(4-amino-1-methyl-*1H*-pyrrole-2-carboxamido)-1-methyl-*1H*-pyrrole-2-carboxamide (0.518 mmol) added in CH_2Cl_2 (10 mL) and Et_3N (0.10 mL). The reaction mixture was allowed to come to room temperature, stirred for about 18 h and the solvent evaporated. The residue was purified by silica gel column chromatography to yield product (19 mg, 8.7%). ^{1}HNMR (600 MHz, DMSO-d_6) δ 2.73 (t, 2H, *J* = 7.8), 3.01 (s, 3H), 3.41 (t, 2H, *J* = 7.8), 3.78-3.82 (m, 5H), 3.84 (s, 3H), 3.85(s, 3H), 5.06 (dd, 1H, *J* = 10.80 and 1.80), 5.14 (dd, 1H, *J* = 17.40 and 1.80), 5.84-5.90 (m, 1H) 6.89(d, 1H, *J* = 1.2), 6.90 (d, 1H, *J* = 1.2), 7.04 (d, 1H, *J* = 1.2), 7.17 (d, 1H, *J* = 1.2), 7.21 (d, 1H, *J* = 1.2), 7.24 (d, 1H, *J* = 1.2), 8.19(t, 1H, *J* = 5.4), 9.90(s, br, 1H), 9.92 (s, br, 1H), 10.05 (s, br, 1H). ^{13}CNMR (150 MHz, DMSO-d_6) δ 28.69, 36.45, 36.57, 36.62, 40.91, 41.19, 50.24, 104.39, 104.78, 105.16, 115.16, 118.47, 118.67, 118.94, 122.17, 122.54, 122.62, 123.21, 123.24, 123.32, 136.45, 158.83, 158.94, 161.54, 166.57. HRMS (ES+H) m/z calcd for $C_{25}H_{32}N_7O_6S$ (558.213) Found (558.214).

NMR Spectra of Compounds



COMPOUND 1

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expi  s2pul

      SAMPLE              SPECIAL
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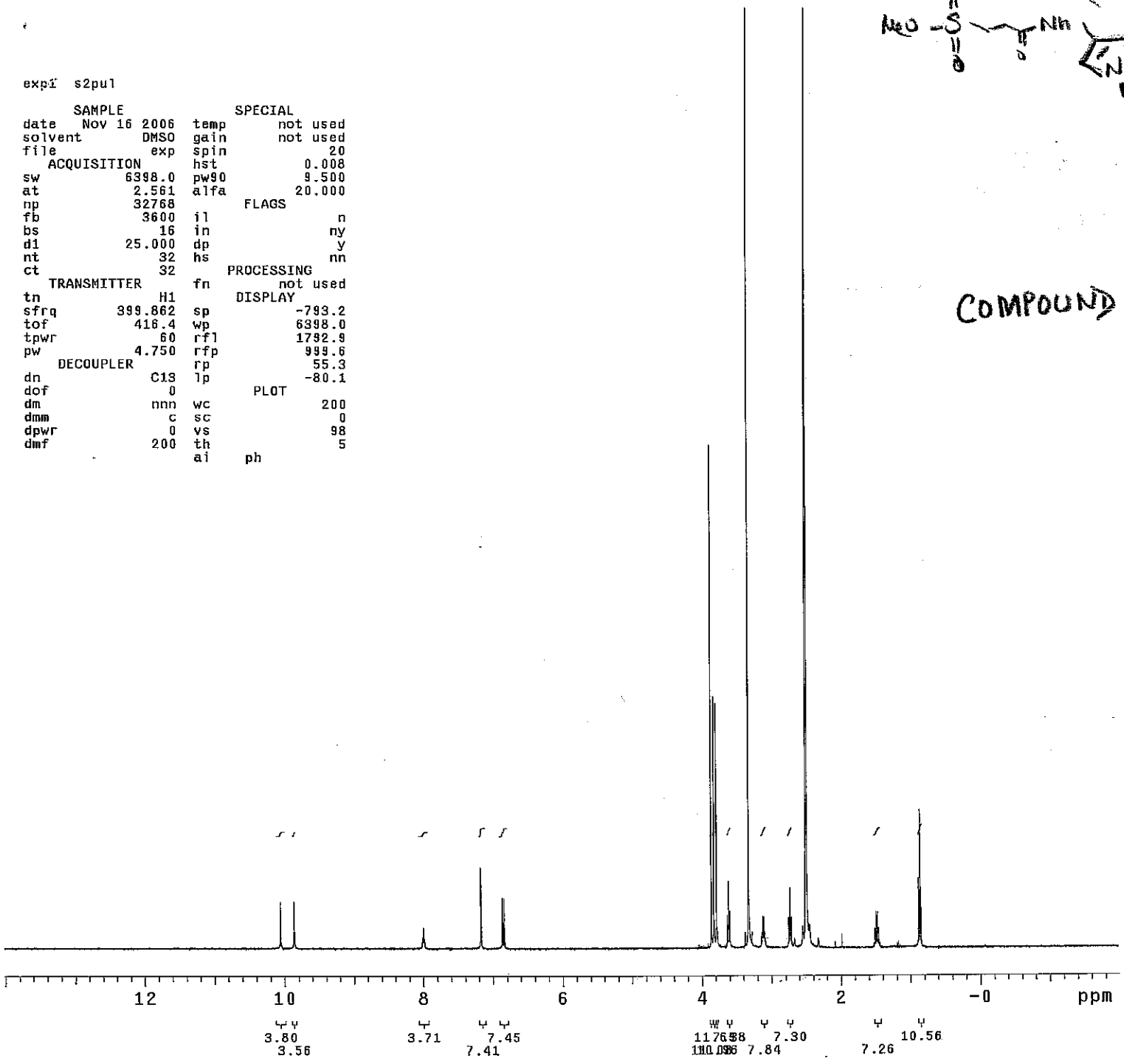
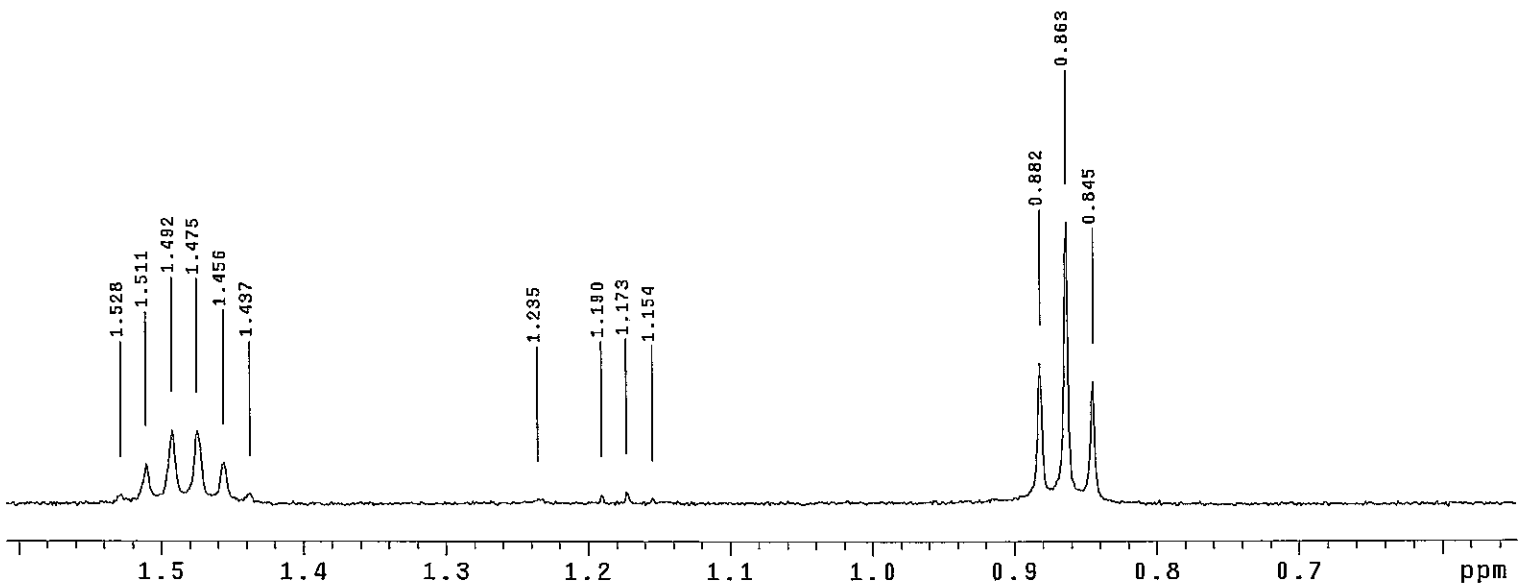
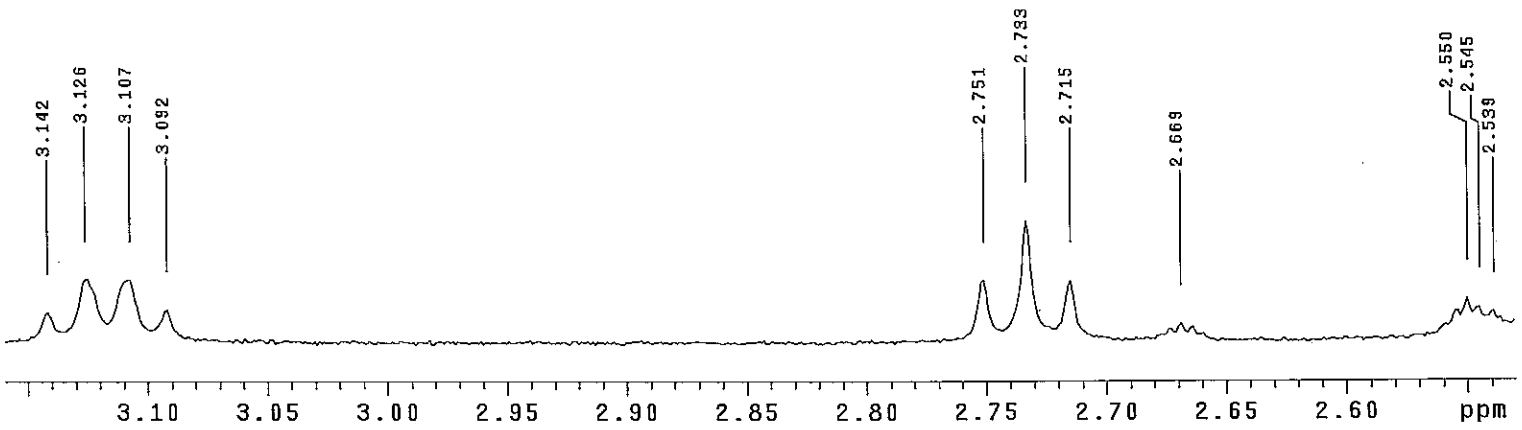
solvent        DMSO  gain       not used
file            exp  spin             20
   ACQUISITION       hst           0.008
sw            6398.0  pw90          9.500
at             2.561  alfa         20.000
np             32768        FLAGS
fb              3600  il                n
bs                16  in               ny
d1            25.000  dp                y
nt                32  hs               nn
ct                32      PROCESSING
   TRANSMITTER        fn       not used
tn                H1       DISPLAY
sfrq         399.862  sp           -793.2
tof            416.4  wp           6398.0
tpwr              60  rfl          1792.9
pw             4.750  rfp           999.6
    DECOUPLER         rp            55.3
dn              C13   lp           -80.1
dof               0          PLOT
dm              nnn   wc             200
dmm               c   sc               0
dpwr              0   vs              98
dmf             200   th               5
                      ai     ph
```



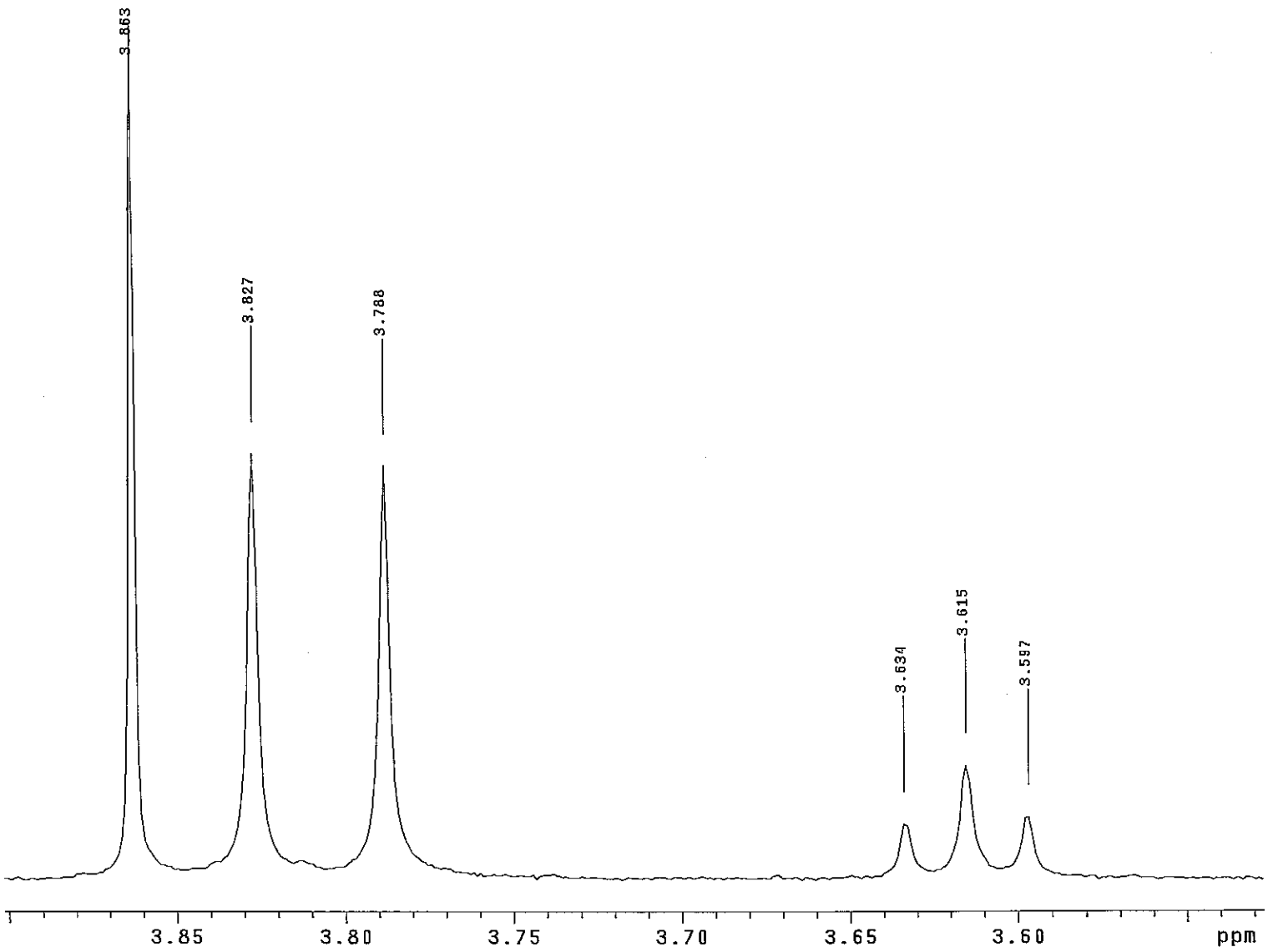
COMPOUND 1


1.528
1.511
1.492
1.475
1.456
1.437
1.235
1.180
1.173
1.154
0.882
0.863
0.845
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
ppm

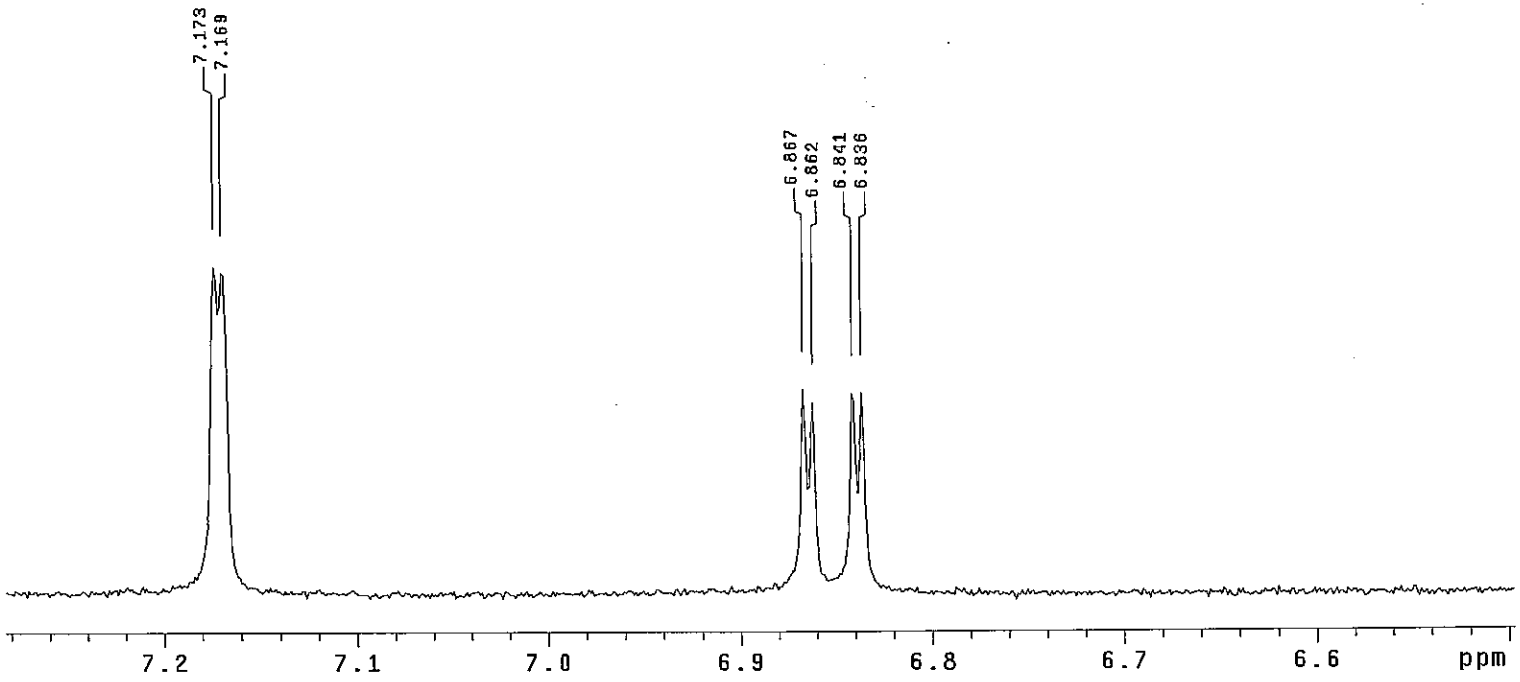
COMPOUND 1


3.142
3.126
3.107
3.092
2.751
2.733
2.715
2.669
2.550
2.545
2.539
3.10
3.05
3.00
2.95
2.90
2.85
2.80
2.75
2.70
2.65
2.60
ppm

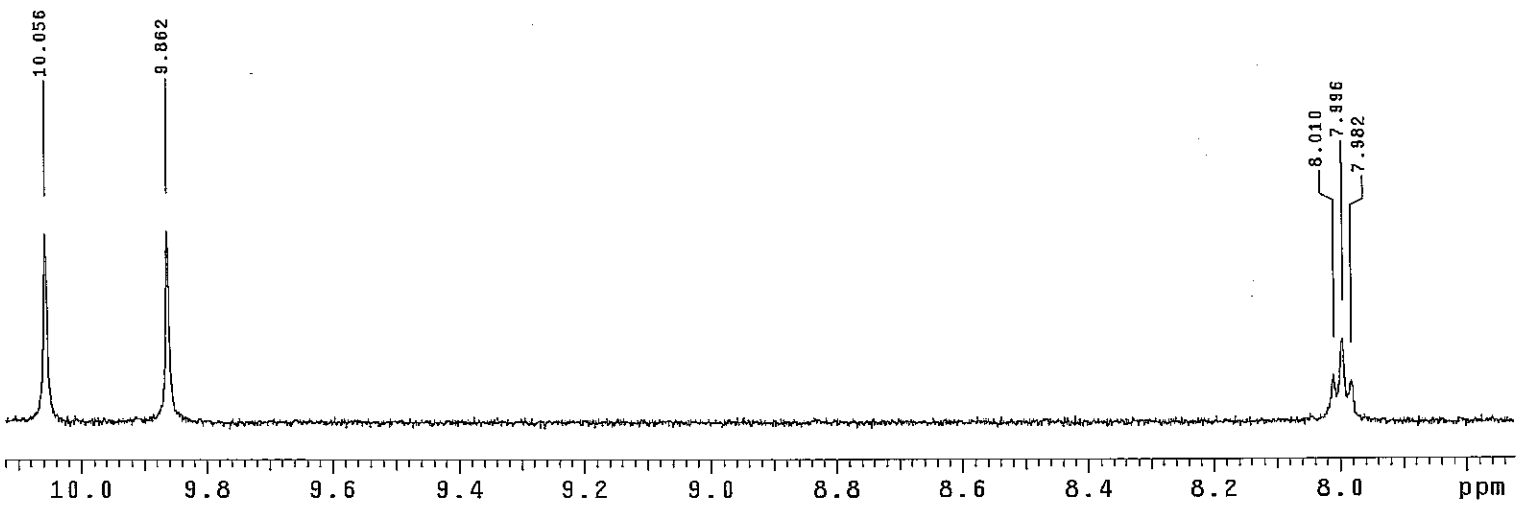
COMPOUND 1



COMPOUND 1

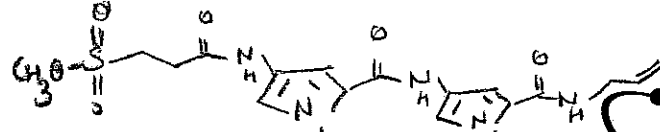


COMPOUND 1



PCI-II-439

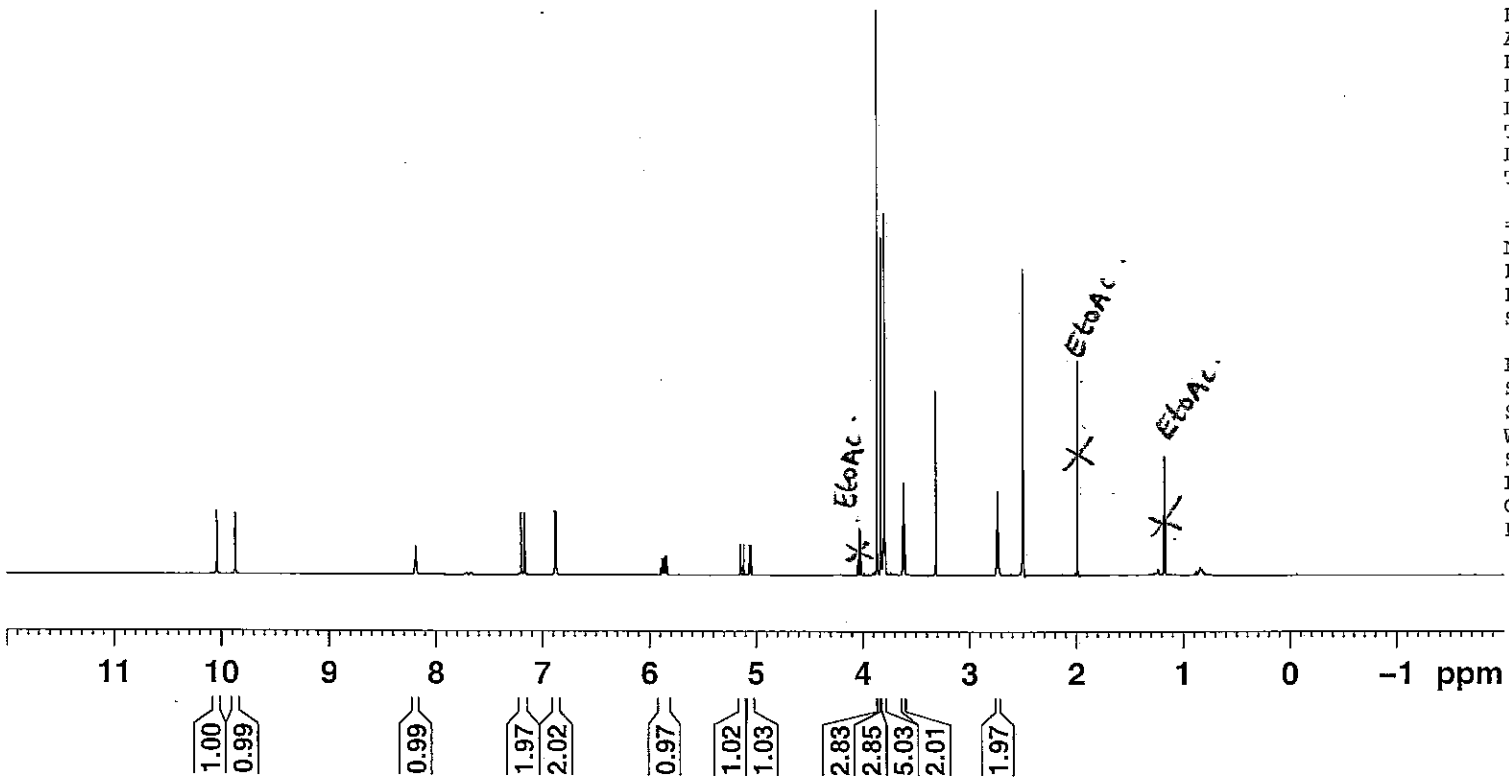
PCI-II-439



BRUKER

10.044 9.871 8.198 8.188 8.202 7.199 7.170 7.167 6.886 6.883 6.871 6.868 5.885 5.877 5.868 5.856 5.848 5.839 5.148 5.145 5.120 5.117 5.065 5.063 5.048 5.045 4.046 4.034 4.022 4.011 3.865 3.830 3.799 3.627 3.615 3.603 3.316 2.748 2.736 2.724 1.988 1.186 1.174 1.162

COMPOUND 2



Current Data Parameters

NAME	PCI-II-439
EXPNO	20
PROCNO	1

F2 - Acquisition Parameters

Date_	20071126
Time	22.01
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	16
DS	2
SWH	12376.237 Hz
FIDRES	0.188846 Hz
AQ	2.6477449 sec
RG	7.1
DW	40.400 usec
DE	6.00 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1

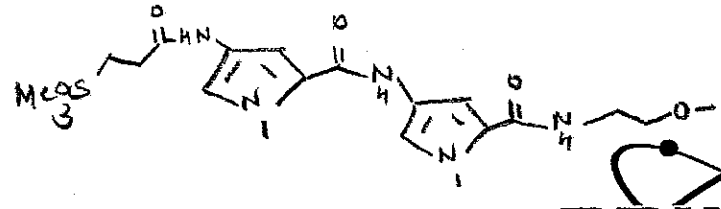
======== CHANNEL f1 ========

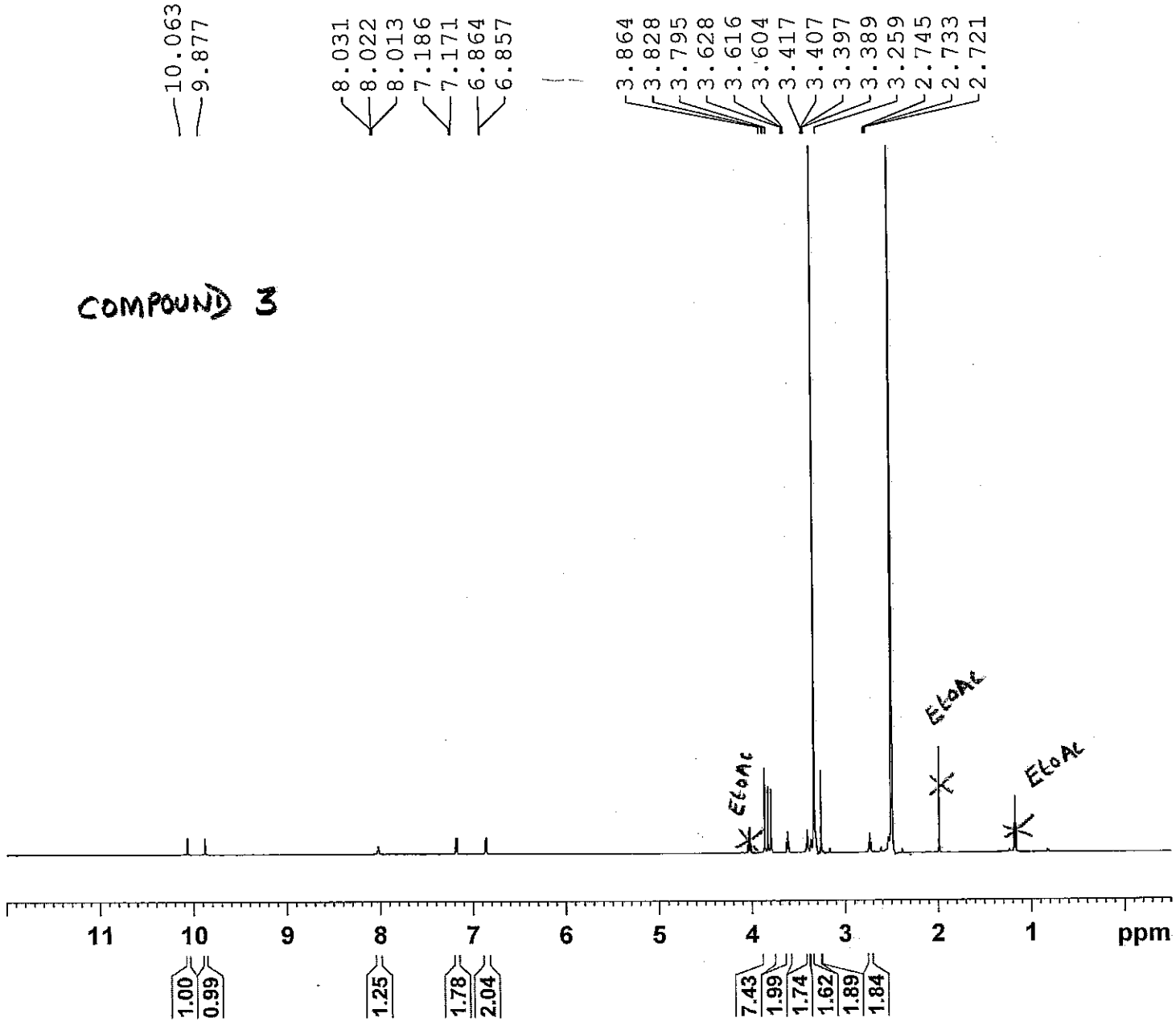
NUC1	1H
P1	8.00 usec
PL1	4.10 dB
SFO1	600.1337060 MHz

F2 - Processing parameters

SI	32768
SF	600.1300072 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

PCI-III-605

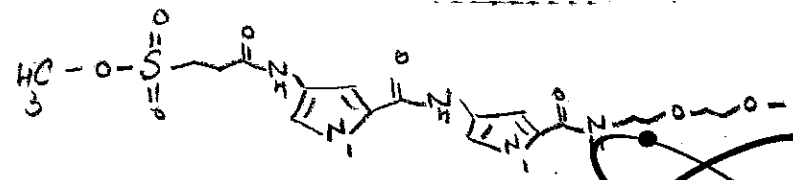


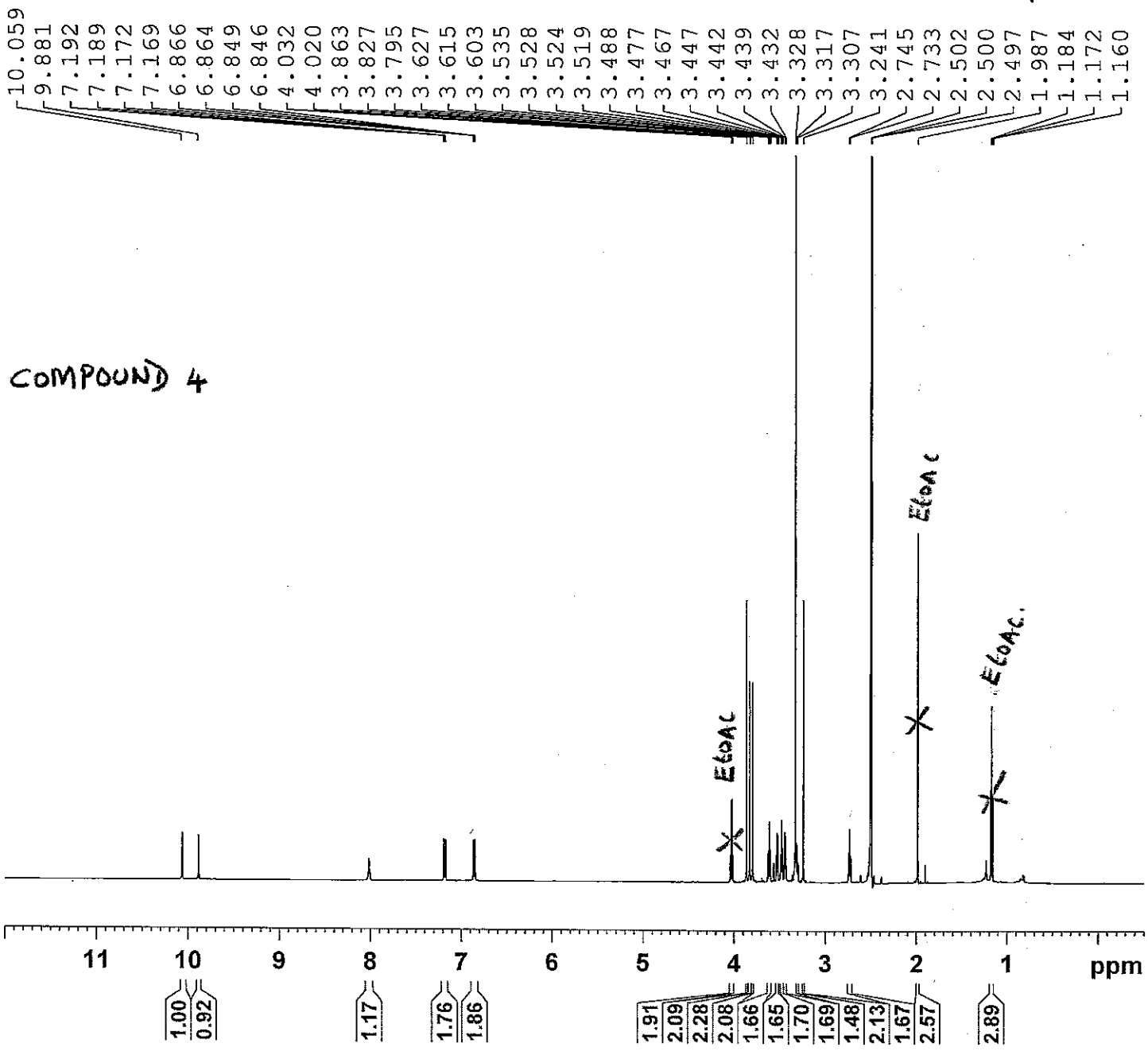


BRUKER

NAME	PCI-III-605	
EXPNO	1	
PROCNO	1	
Date_	20080820	
Time	20.47	
INSTRUM	spect	
PROBHD	5 mm CPTCI 1H-	
PULPROG	zg30	
TD	65536	
SOLVENT	DMSO	
NS	16	
DS	2	
SWH	12376.237	Hz
FIDRES	0.188846	Hz
AQ	2.6477449	sec
RG	362	
DW	40.400	usec
DE	6.50	usec
TE	298.0	K
D1	1.00000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	1H	
P1	8.00	usec
PL1	4.00	dB
PL1W	7.00000000	W
SFO1	600.1337060	MHz
SI	32768	
SF	600.1299994	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	

PCI-III-659





BRUKER

NAME	PCI-III-659
EXPNO	1
PROCNO	1
Date_	20081117
Time	21.32
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	16
DS	2
SWH	12376.237 Hz
FIDRES	0.188846 Hz
AQ	2.6477449 sec
RG	362
DW	40.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	8.00 usec
PL1	4.00 dB
PL1W	7.00000000 W
SFO1	600.1337060 MHz
SI	32768
SF	600.1300007 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

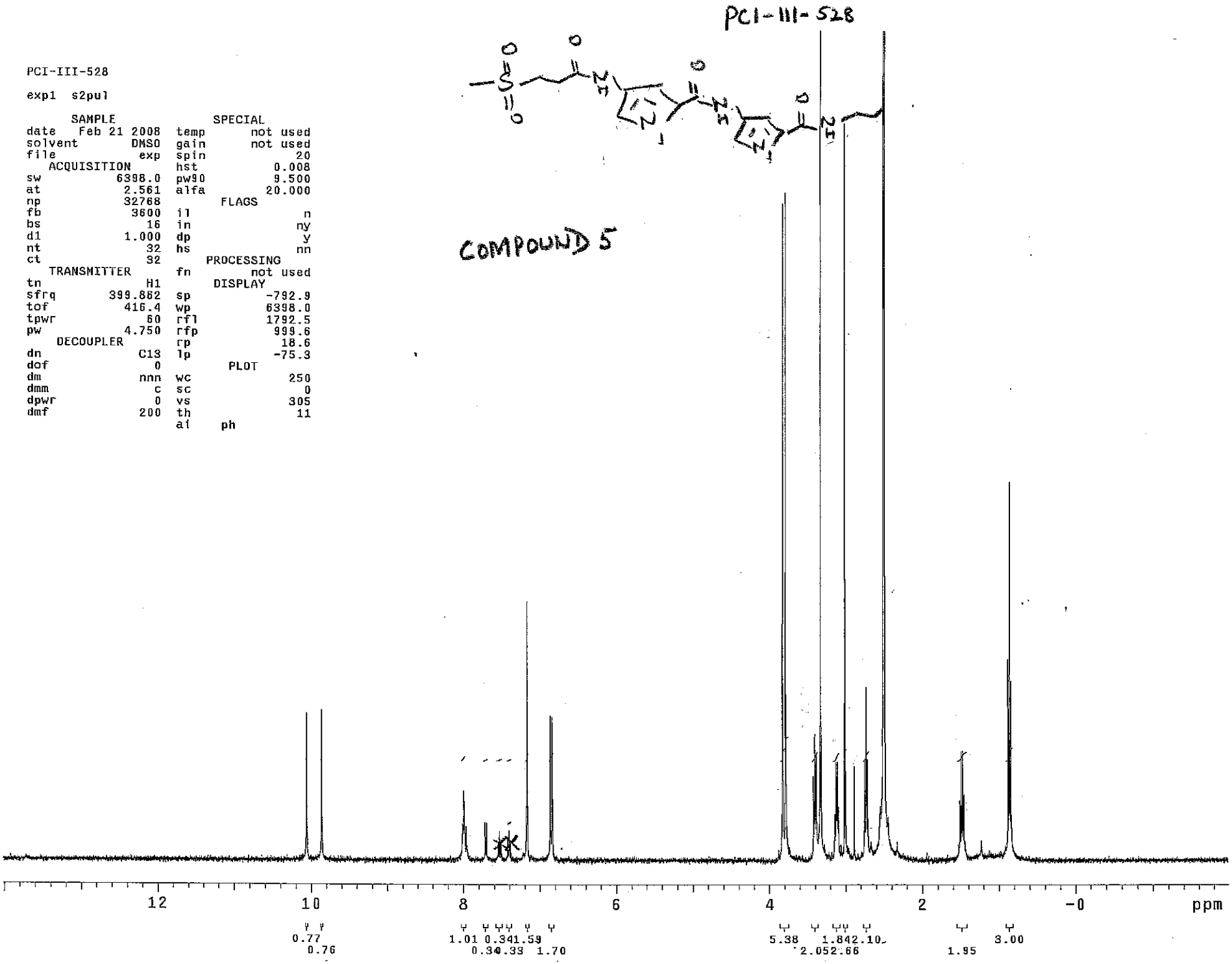
PCI-III-528

exp1 s2pul

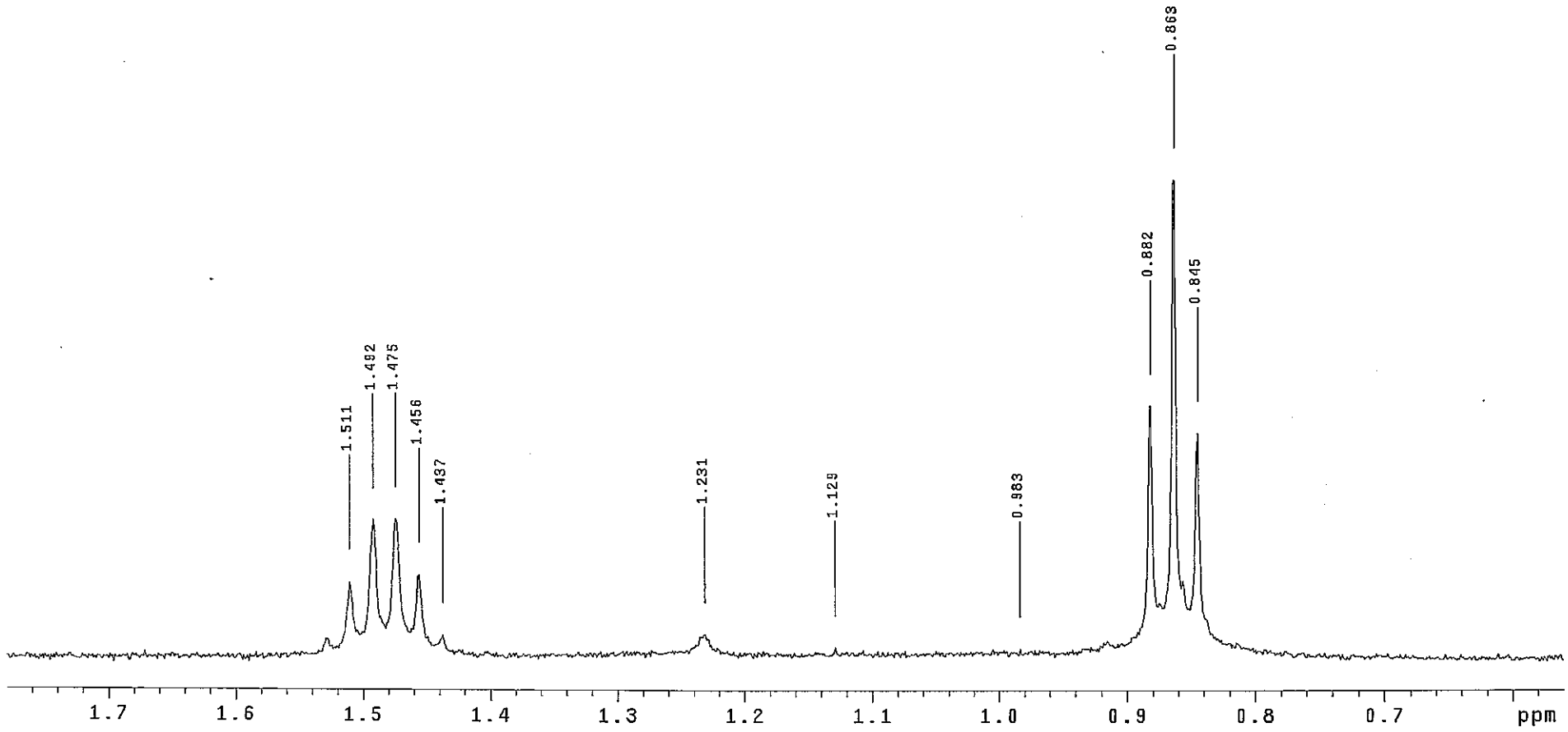
SAMPLE		SPECIAL	
date	Feb 21 2008	temp	not used
solvent	DMSO	gain	not used
file	exp	spin	20
ACQUISITION		hst	0.008
sw	6398.0	pw90	9.500
at	2.561	alfa	20.000
np	32768	FLAGS	
fb	3600	il	n
bs	16	in	ny
d1	1.000	dp	y
nt	32	hs	nn
ct	32	PROCESSING	
TRANSMITTER		fn	not used
tn	H1	DISPLAY	
sfrq	399.862	sp	-792.9
tof	416.4	wp	6398.0
tpwr	60	rfl	1792.5
pw	4.750	rfp	999.6
DECOUPLER		rp	18.6
dn	C13	lp	-75.3
dof	0	PLOT	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	0	vs	305
dmf	200	th	11
		ai	ph

PCI-III-528

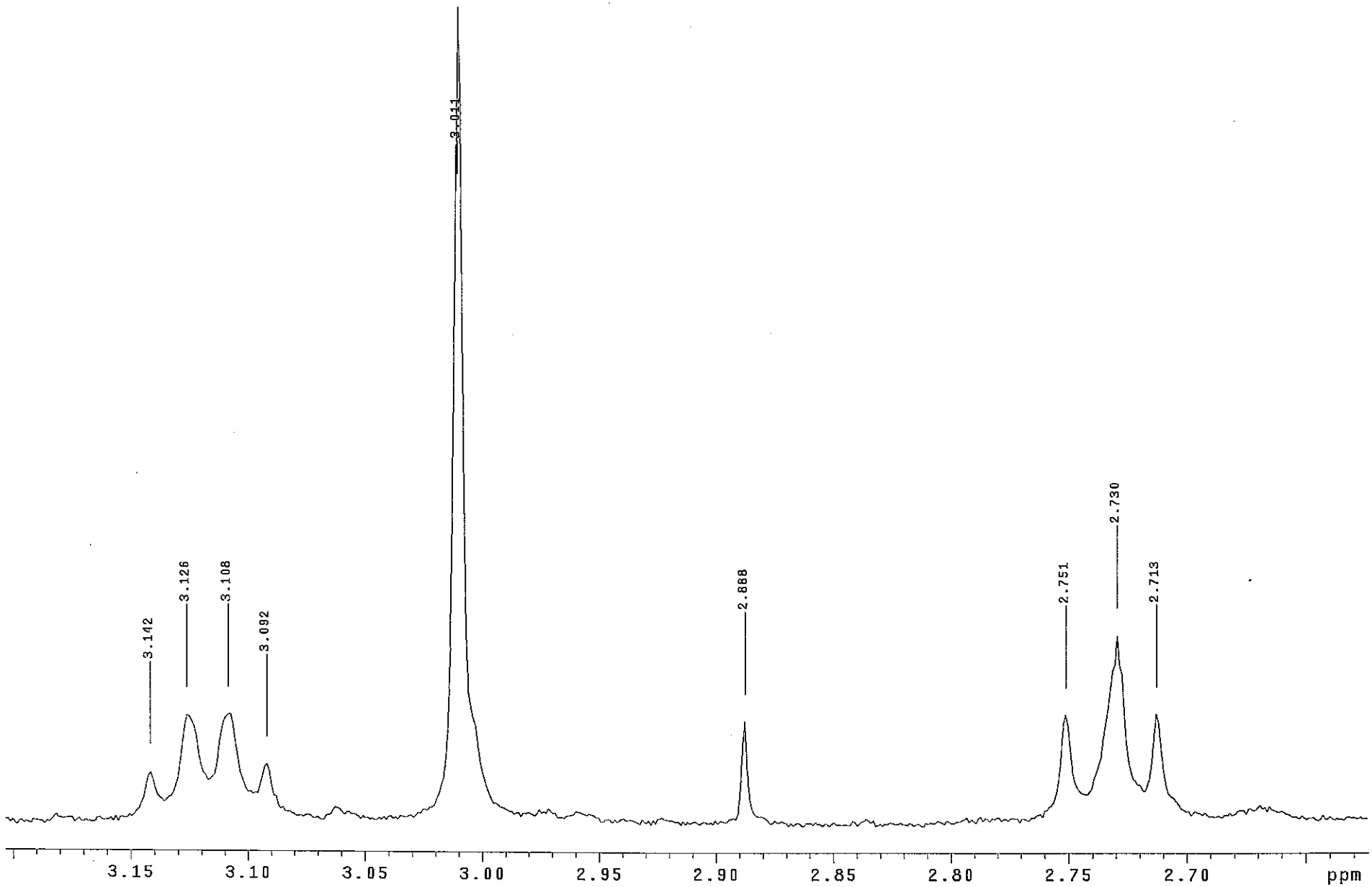
COMPOUND 5



COMPOUND 5

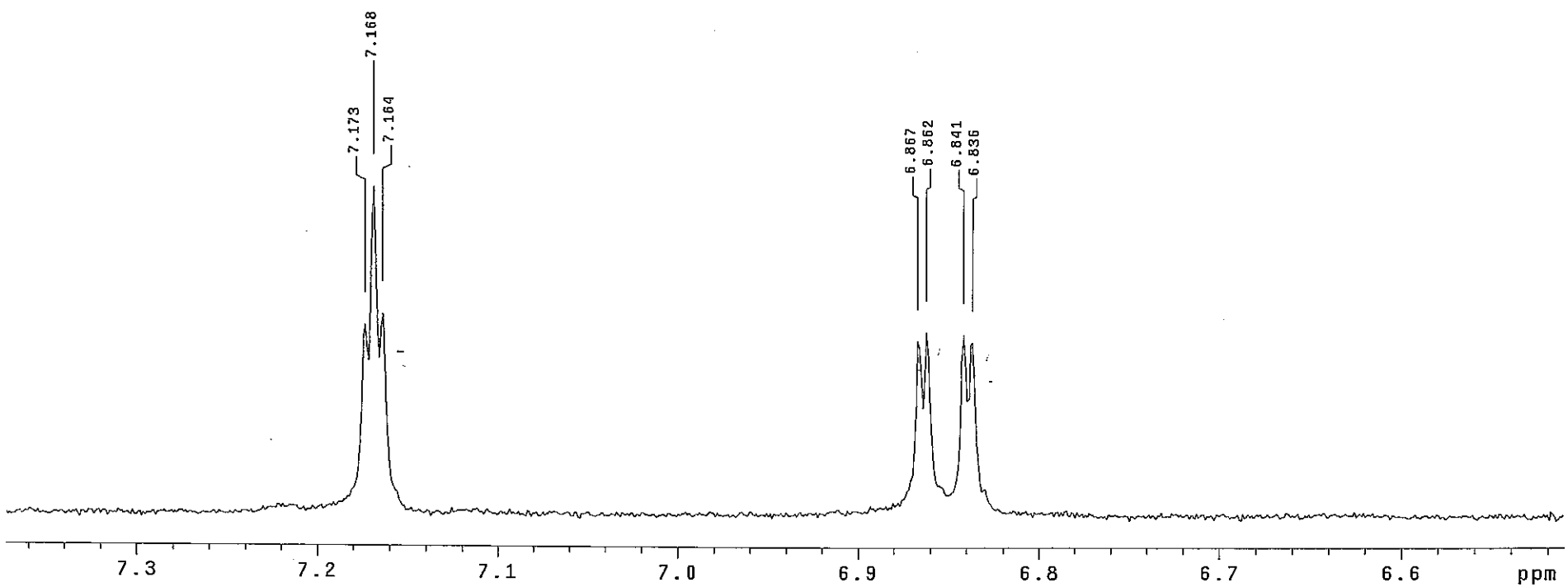

1.511
1.492
1.475
1.456
1.437
1.231
1.129
0.983
0.882
0.863
0.845
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
ppm

COMPOUND 5


3.142
3.126
3.108
3.092
3.011
2.888
2.751
2.730
2.713
3.15
3.10
3.05
3.00
2.95
2.90
2.85
2.80
2.75
2.70
ppm

COMPOUND 5

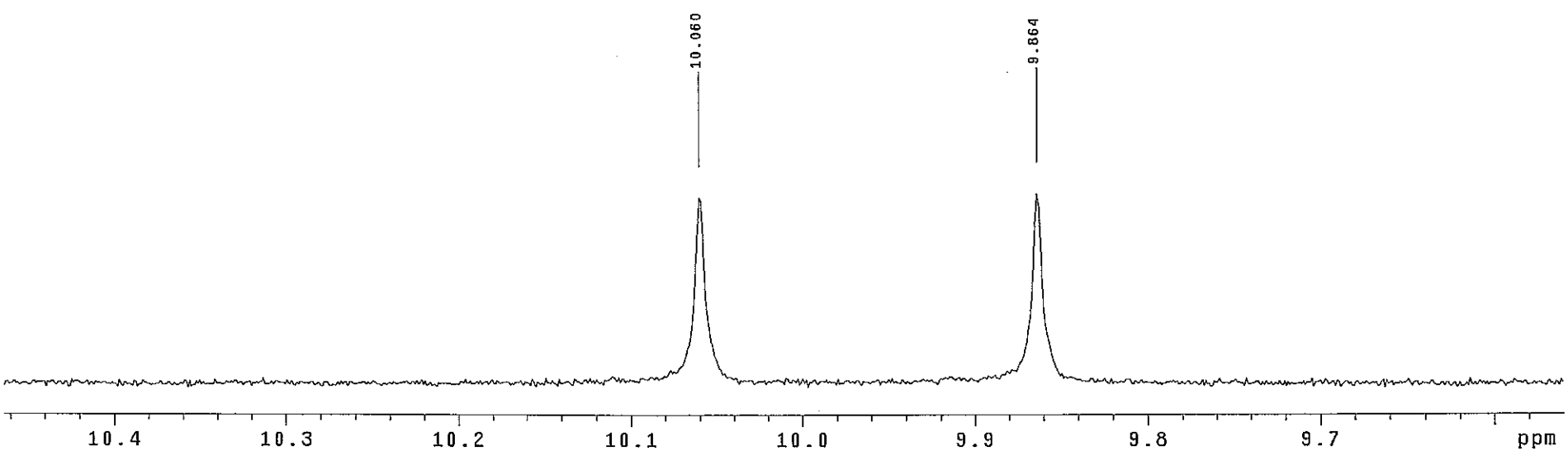
COMPOUND 5



8.012
7.997
7.983
7.964
7.720
7.699
7.531
7.405
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
ppm

COMPOUND 5

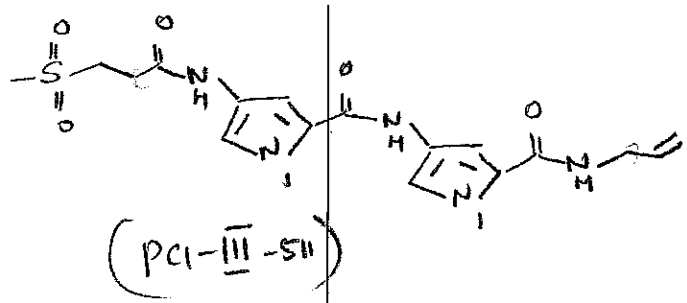
COMPOUND 5



PCI-III-511

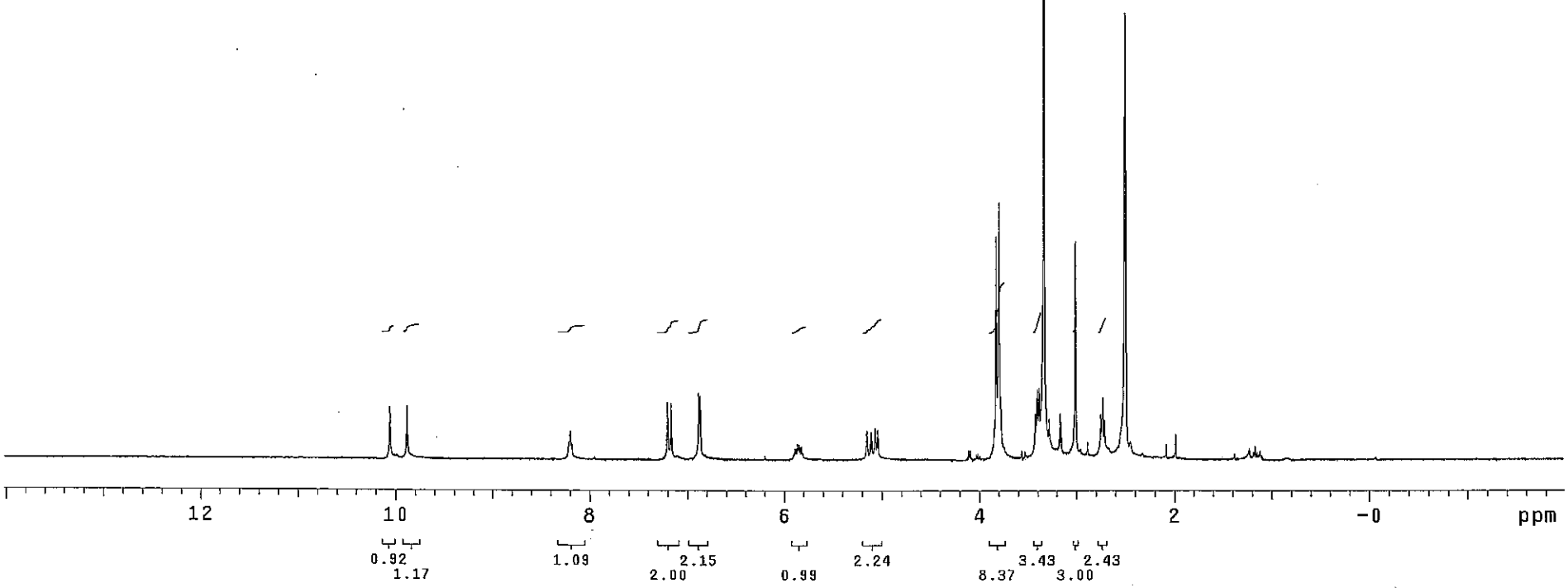
exp1 s2pul

SAMPLE		SPECIAL	
date	Feb 8 2008	temp	not used
solvent	DMSO	gain	not used
file	exp	spin	20
ACQUISITION		hst	0.008
sw	6398.0	pw90	9.500
at	2.561	alfa	20.000
np	32768	FLAGS	
fb	3600	il	n
bs	16	in	ny
d1	1.000	dp	y
nt	32	hs	nn
ct	32	PROCESSING	
TRANSMITTER		fn	not used
tn	H1	DISPLAY	
sfrq	399.862	sp	-793.6
tof	416.4	wp	6398.0
tpwr	60	rfl	1793.3
pw	4.750	rfp	999.6
DECOUPLER		rp	31.6
dn	C13	lp	-121.2
dof	0	PLOT	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	0	vs	127
dmf	200	th	2
		ai	ph

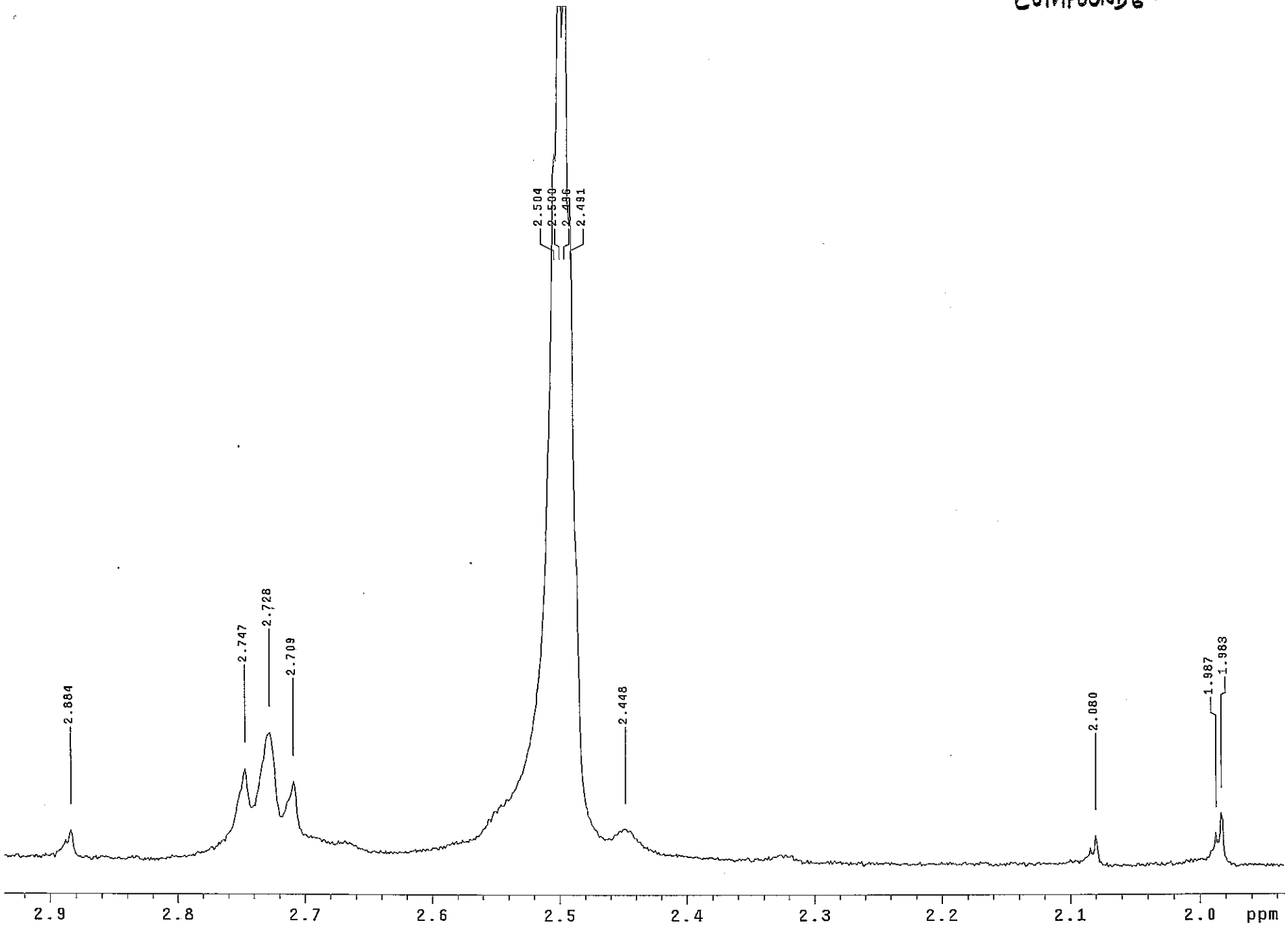


(PCI-III-511)

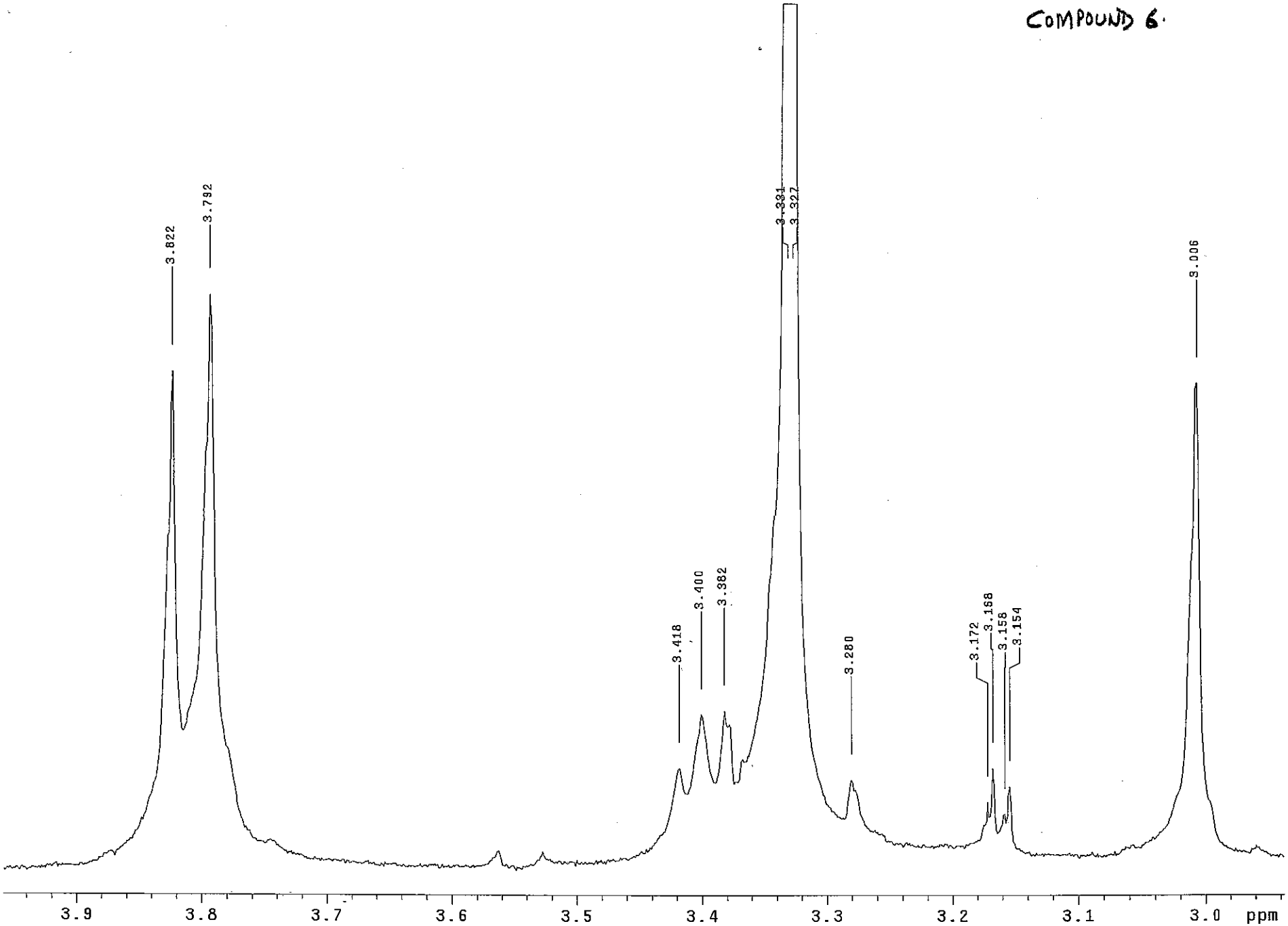
COMPOUND 6.



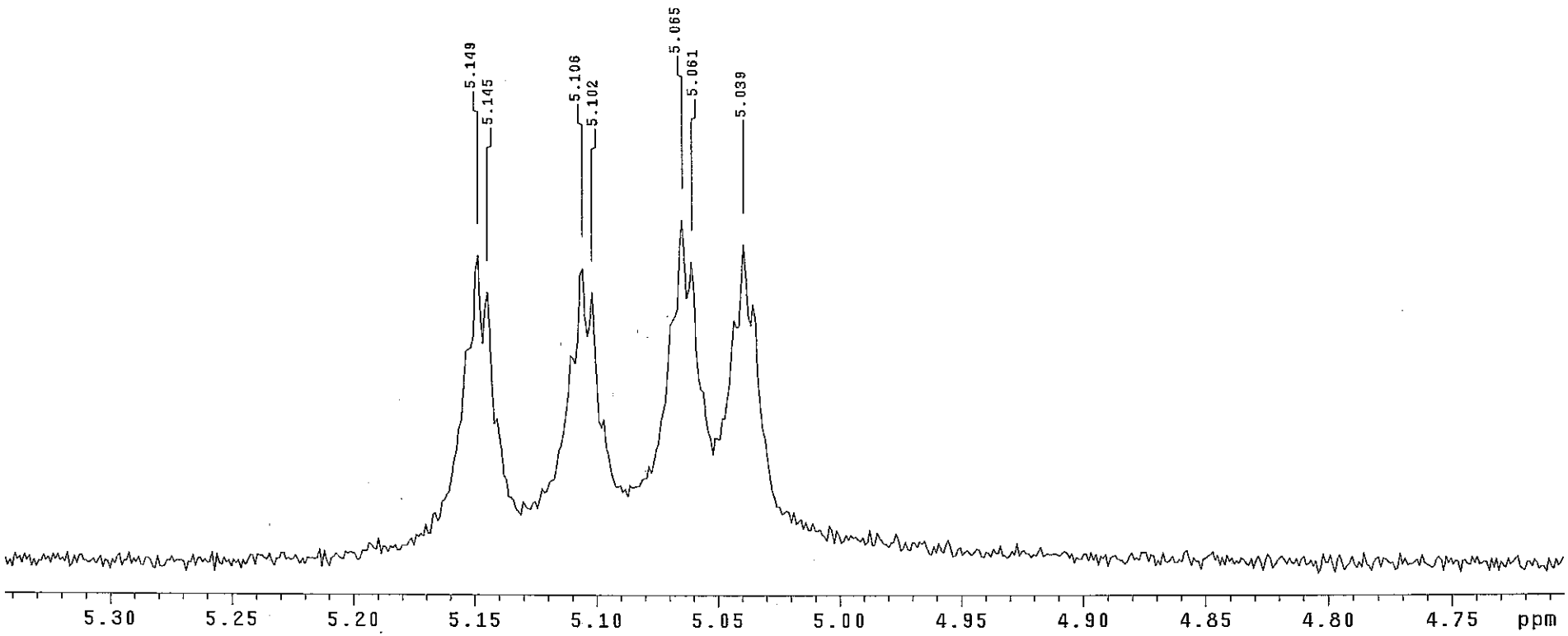
COMPOUND 6.


2.884
2.747
2.728
2.709
2.504
2.500
2.496
2.491
2.448
2.080
1.987
1.983
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
ppm

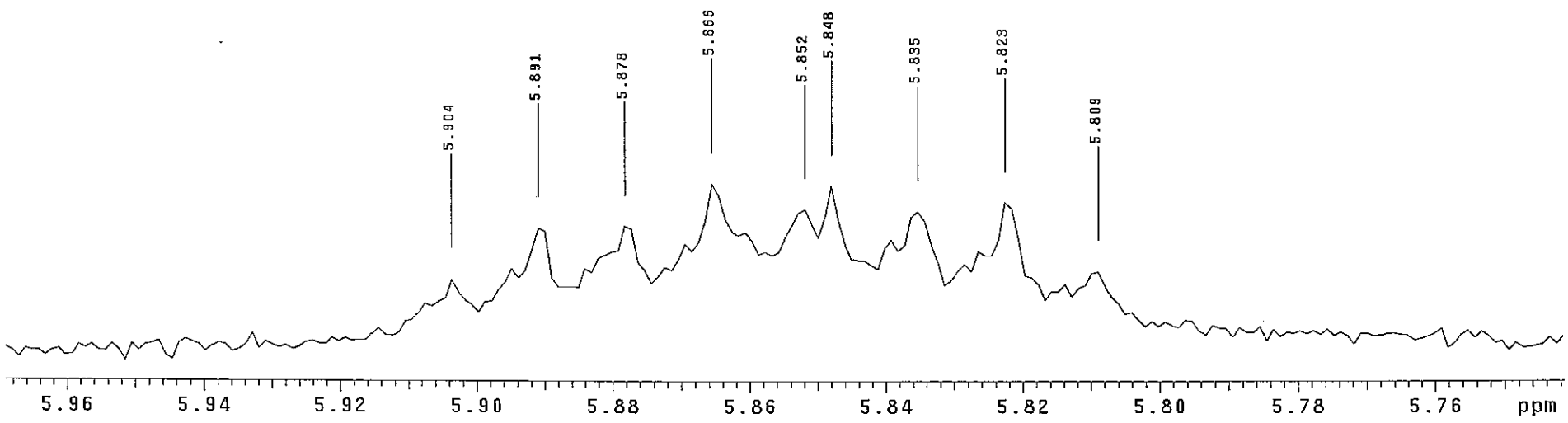
COMPOUND 6.


3.822
3.792
3.418
3.400
3.382
3.331
3.322
3.280
3.172
3.168
3.158
3.154
3.006
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
ppm

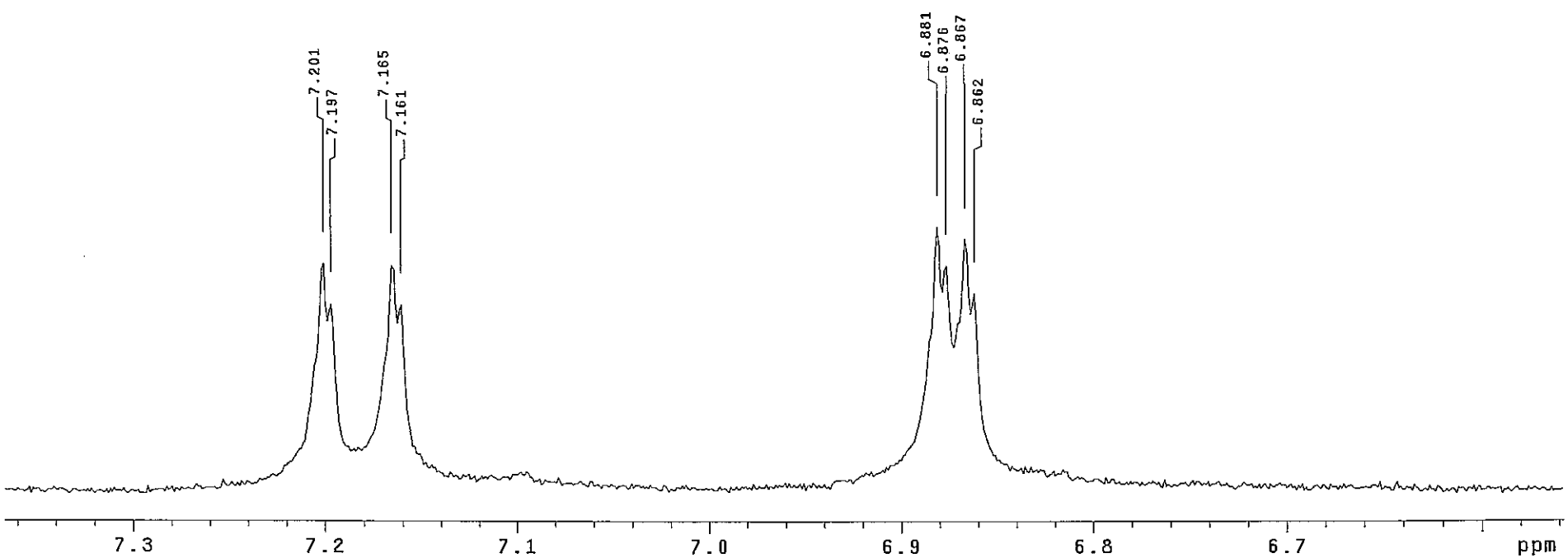
COMPOUND 6


5.149
5.145
5.106
5.102
5.065
5.061
5.039
5.30
5.25
5.20
5.15
5.10
5.05
5.00
4.95
4.90
4.85
4.80
4.75
ppm

COMPOUND 6.


5.904
5.891
5.878
5.866
5.852
5.848
5.835
5.823
5.809
5.96
5.94
5.92
5.90
5.88
5.86
5.84
5.82
5.80
5.78
5.76
ppm

COMPOUND 6.

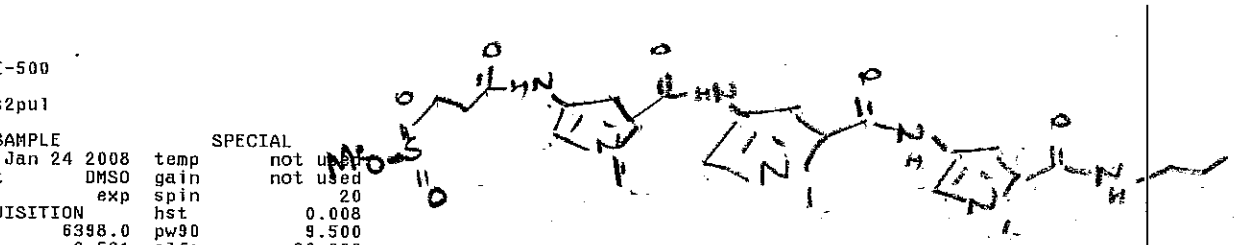


COMPOUND 6.

PCI-III-500

exp1 s2pul

SAMPLE		SPECIAL	
date	Jan 24 2008	temp	not used
solvent	DMSO	gain	not used
file	exp	spin	20
ACQUISITION		hst	0.008
sw	6398.0	pw90	9.500
at	2.561	alfa	20.000
np	32768	**FLAGS**	
fb	3600	il	n
bs	16	in	ny
d1	1.000	dp	y
nt	32	hs	nn
ct	32	**PROCESSING**	
TRANSMITTER		fn	not used
tn	H1	**DISPLAY**	
sfrq	399.862	sp	-792.9
tof	416.4	wp	6398.0
tpwr	60	rfl	1792.5
pw	4.750	rfp	999.6
DECOUPLER		rp	23.3
dn	C13	lp	-85.2
dof	0	**PLOT**	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	0	vs	385
dmf	200	th	10
		ai	ph



COMPOUND 7

EtOAc

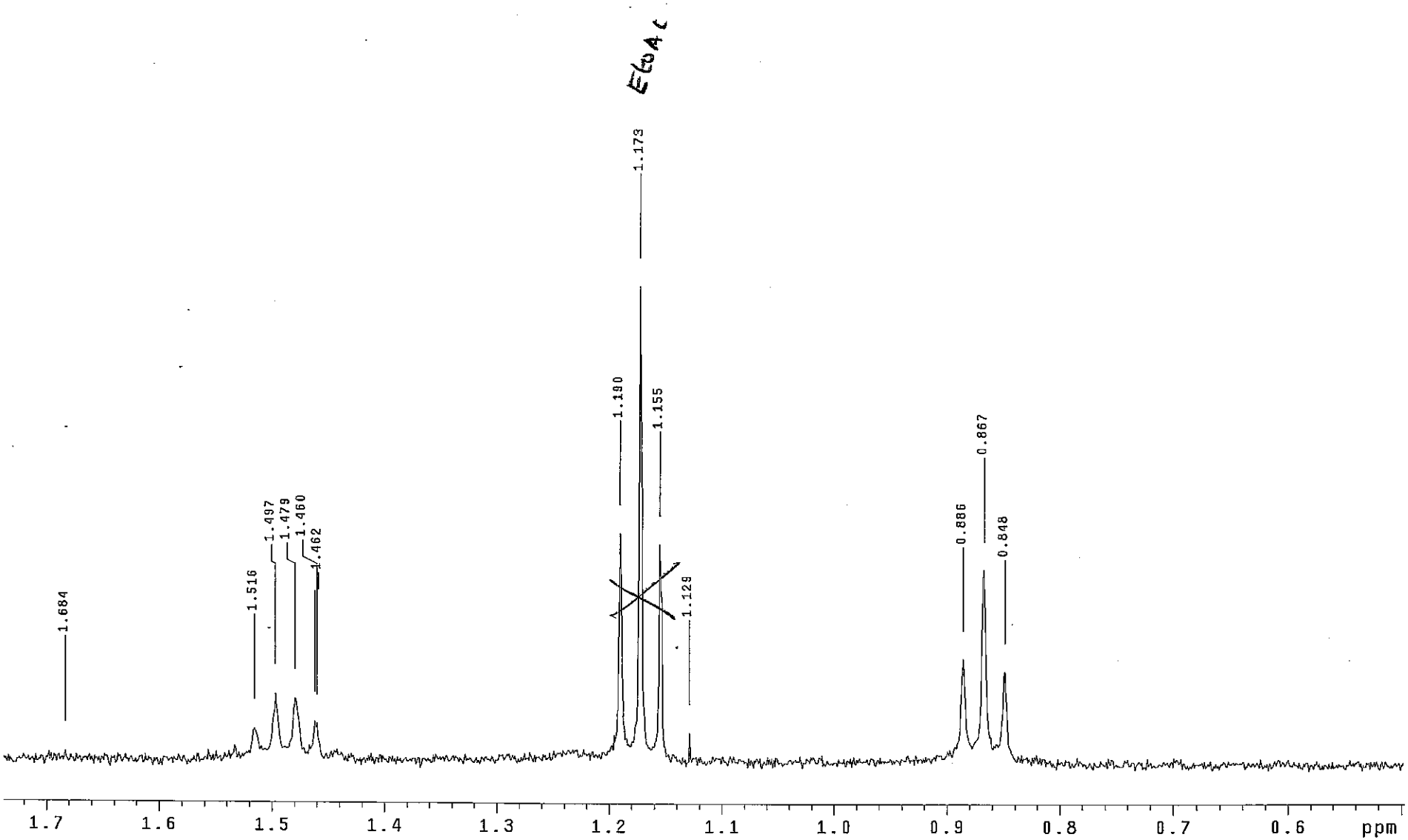
EtOAc

EtOAc

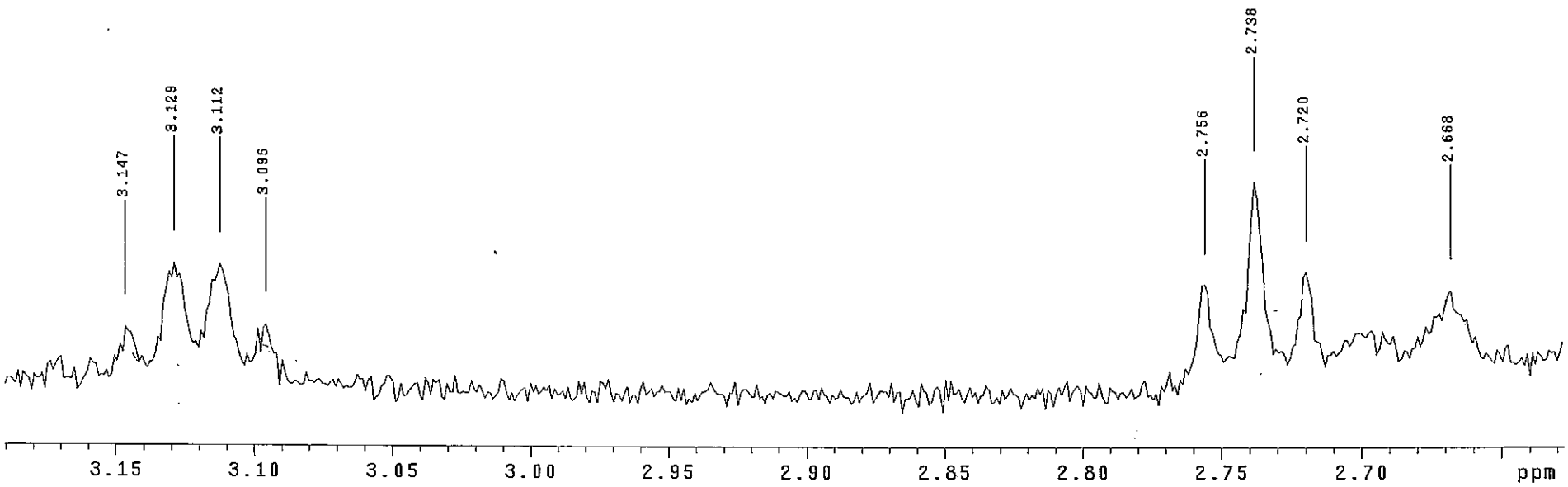
12 10 8 6 4 2 -0 ppm

0.6165 0.65 | 0.79 | 2.32 1.55 0.71 | 2.00 9.73 | 2.38 | 2.16 | 2.65 | 3.00

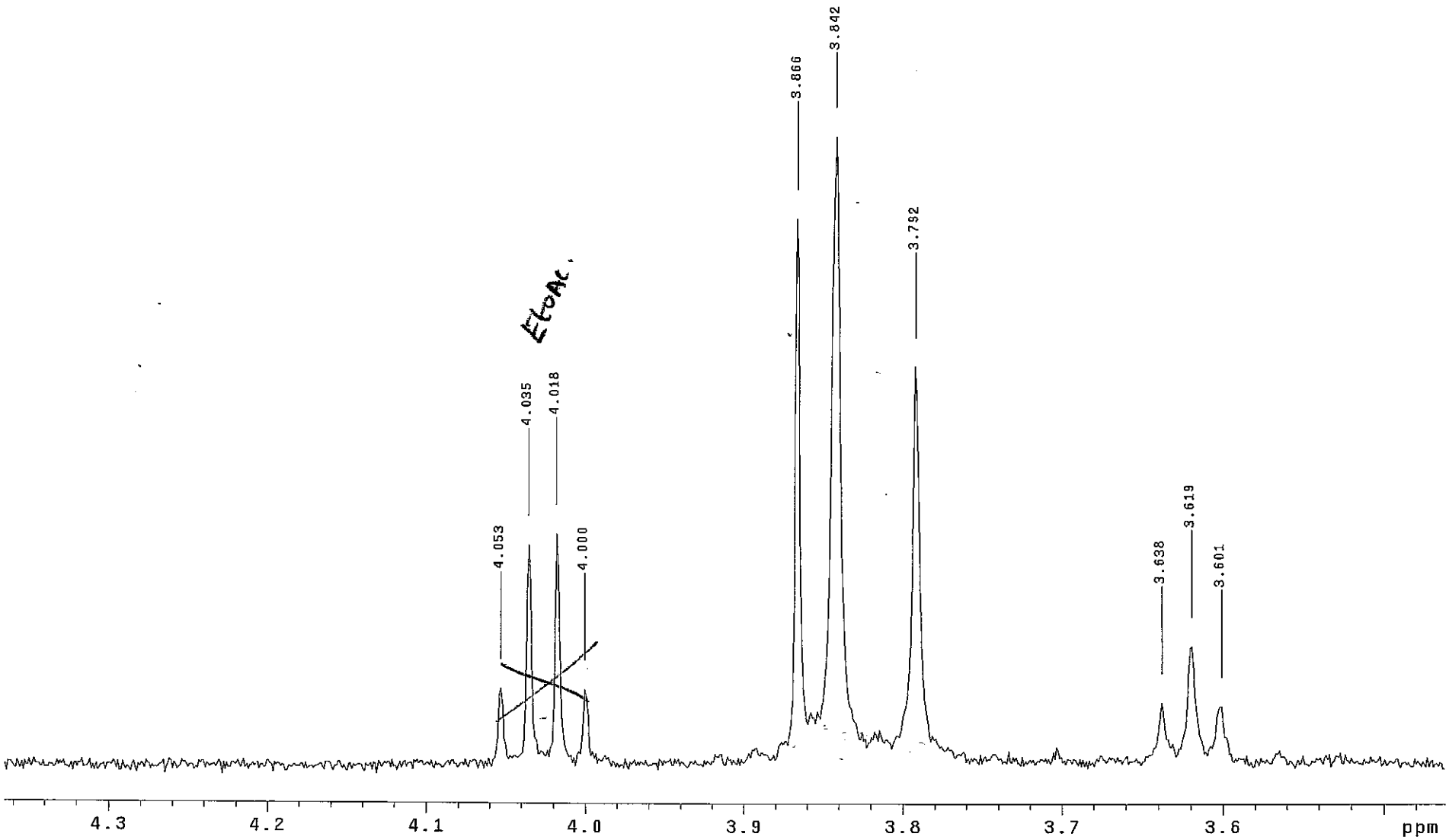
COMPOUND 7


EtOAc
1.684
1.516
1.497
1.479
1.460
1.462
1.190
1.173
1.155
1.128
0.886
0.867
0.848
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
ppm

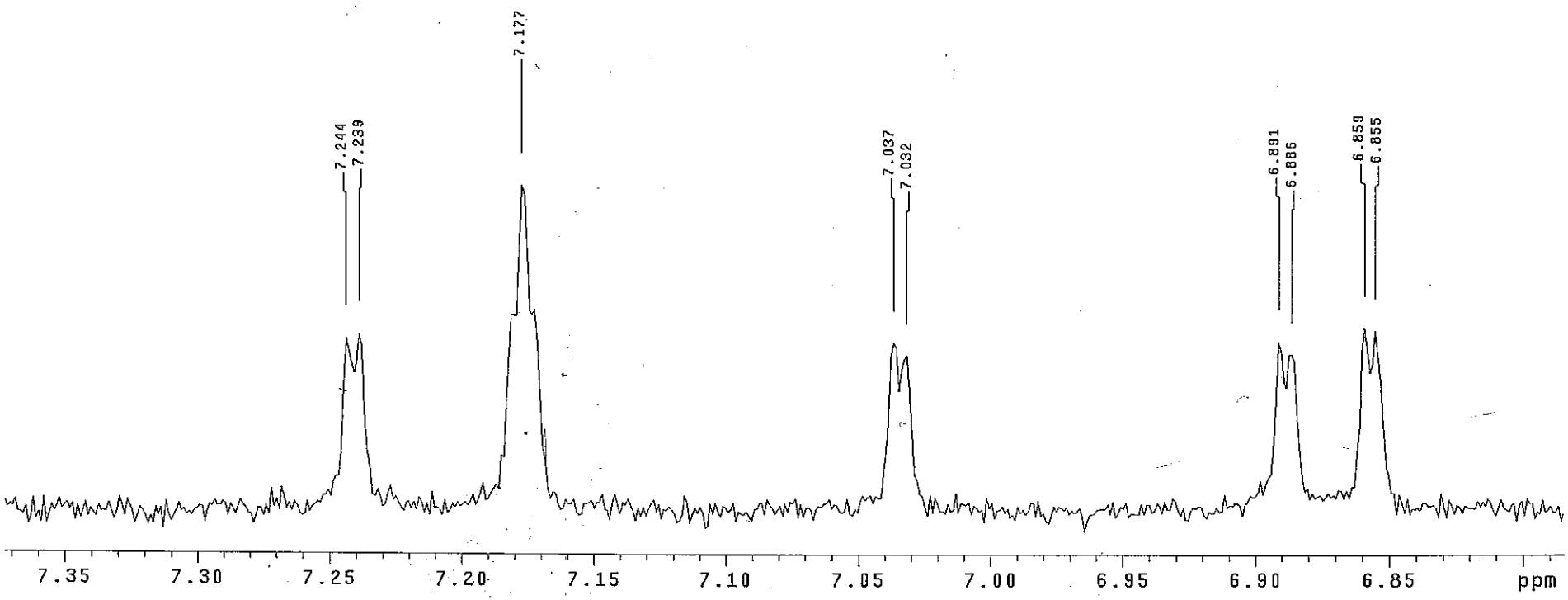
COMPOUND 7


3.147
3.129
3.112
3.096
2.756
2.738
2.720
2.668
3.15
3.10
3.05
3.00
2.95
2.90
2.85
2.80
2.75
2.70
ppm

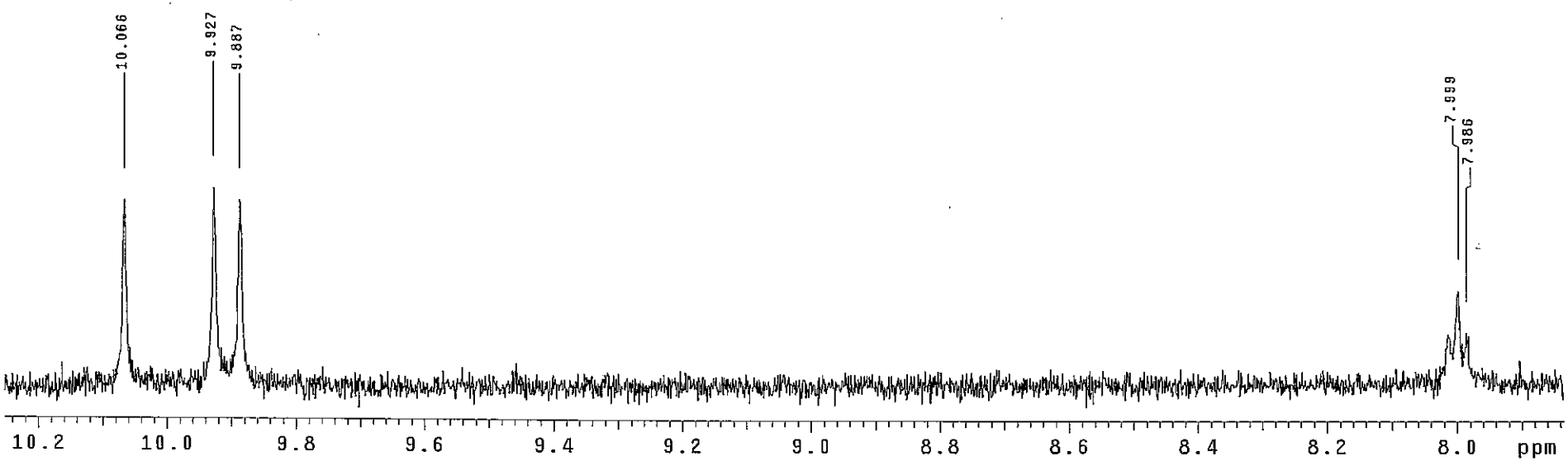
COMPOUND 7


4.053
4.035
4.018
4.000
3.866
3.842
3.792
3.638
3.619
3.601
EtOAc
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
ppm

COMPOUND 7


7.244
7.239
7.177
7.037
7.032
6.891
6.886
6.859
6.855
7.35
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
6.90
6.85
ppm

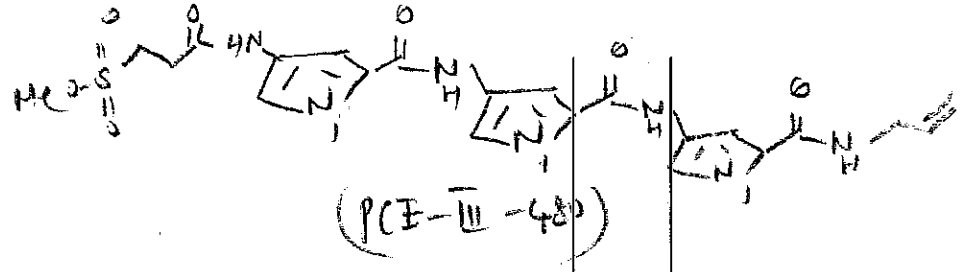
COMPOUND 7


10.066
9.927
9.887
7.999
7.986
10.2
10.0
9.8
9.6
9.4
9.2
9.0
8.8
8.6
8.4
8.2
8.0
ppm

PCI-III-480

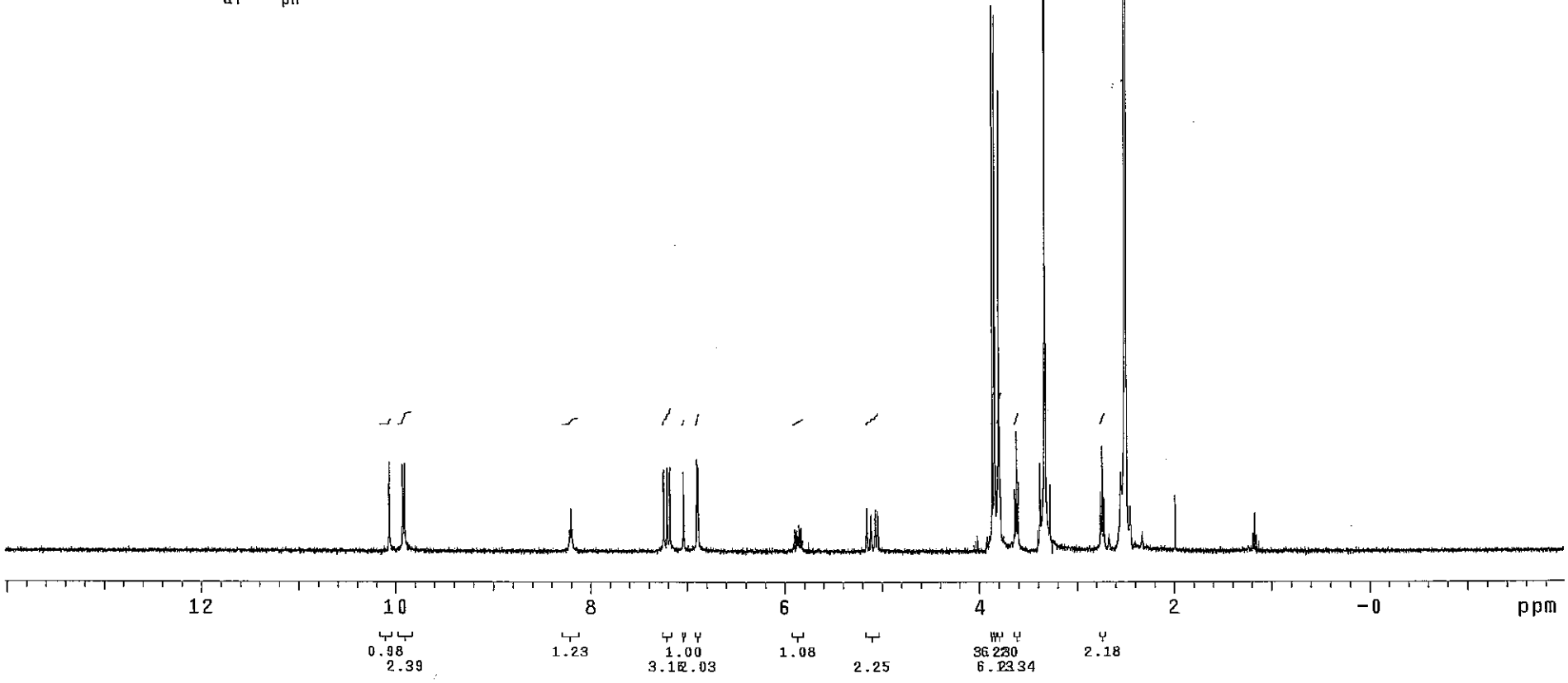
exp1 s2pul

SAMPLE		SPECIAL	
date	Dec 28 2007	temp	not used
solvent	DMSO	gain	not used
file	exp	spin	20
ACQUISITION		hst	0.008
sw	6398.0	pw90	9.500
at	2.561	alfa	20.000
np	32768	FLAGS	
fb	3600	il	n
bs	16	in	ny
d1	1.000	dp	y
nt	32	hs	nn
ct	32	PROCESSING	
TRANSMITTER		fn	not used
tn	H1	DISPLAY	
sfrq	399.862	sp	-792.9
tof	416.4	wp	6398.0
tpwr	60	rfl	1792.5
pw	4.750	rfp	999.6
DECOUPLER		rp	32.6
dn	C13	lp	-101.3
dof	0	PLOT	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	0	vs	225
dmf	200	th	1
		ai	ph

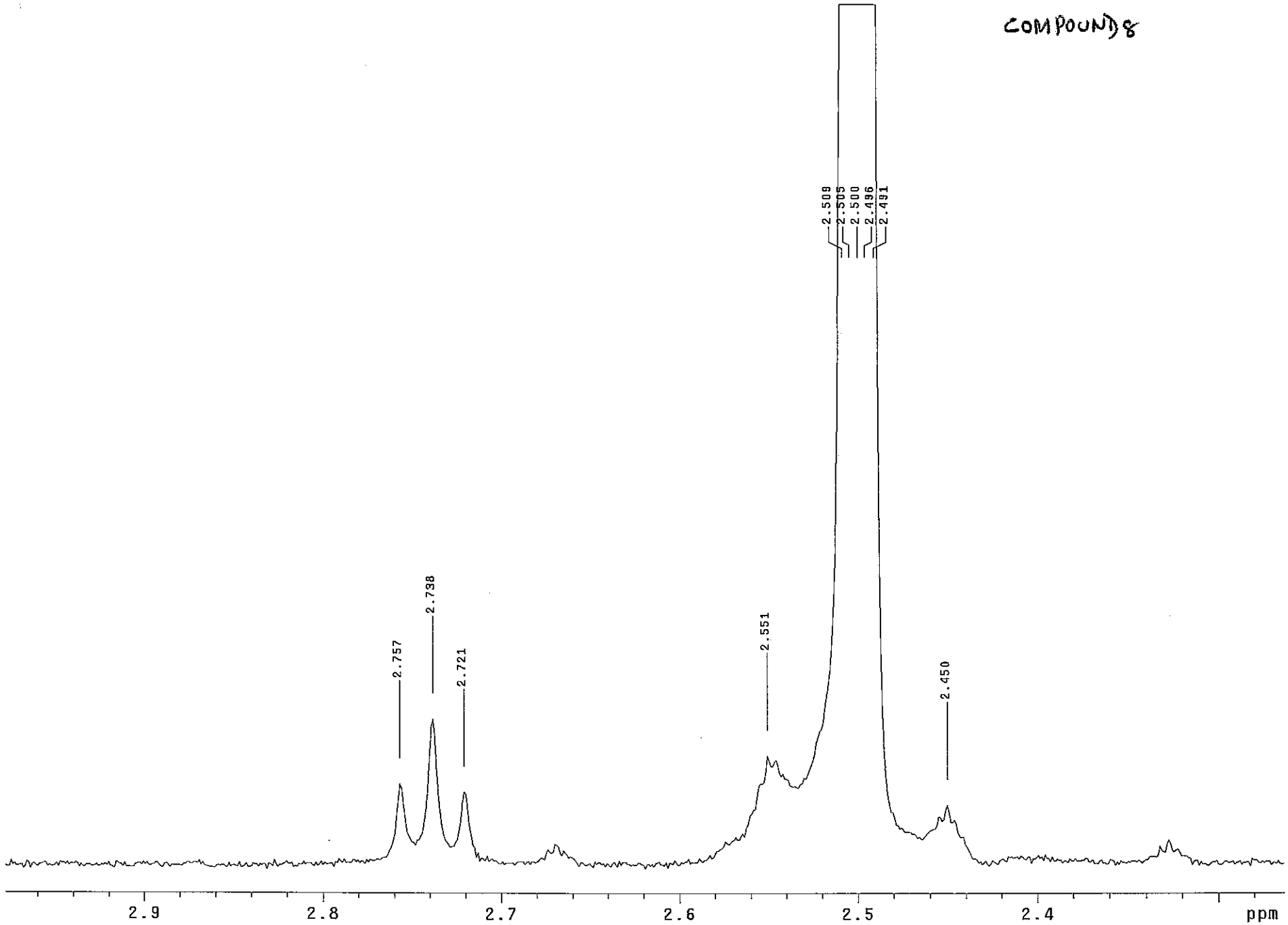


(PCI-III-480)

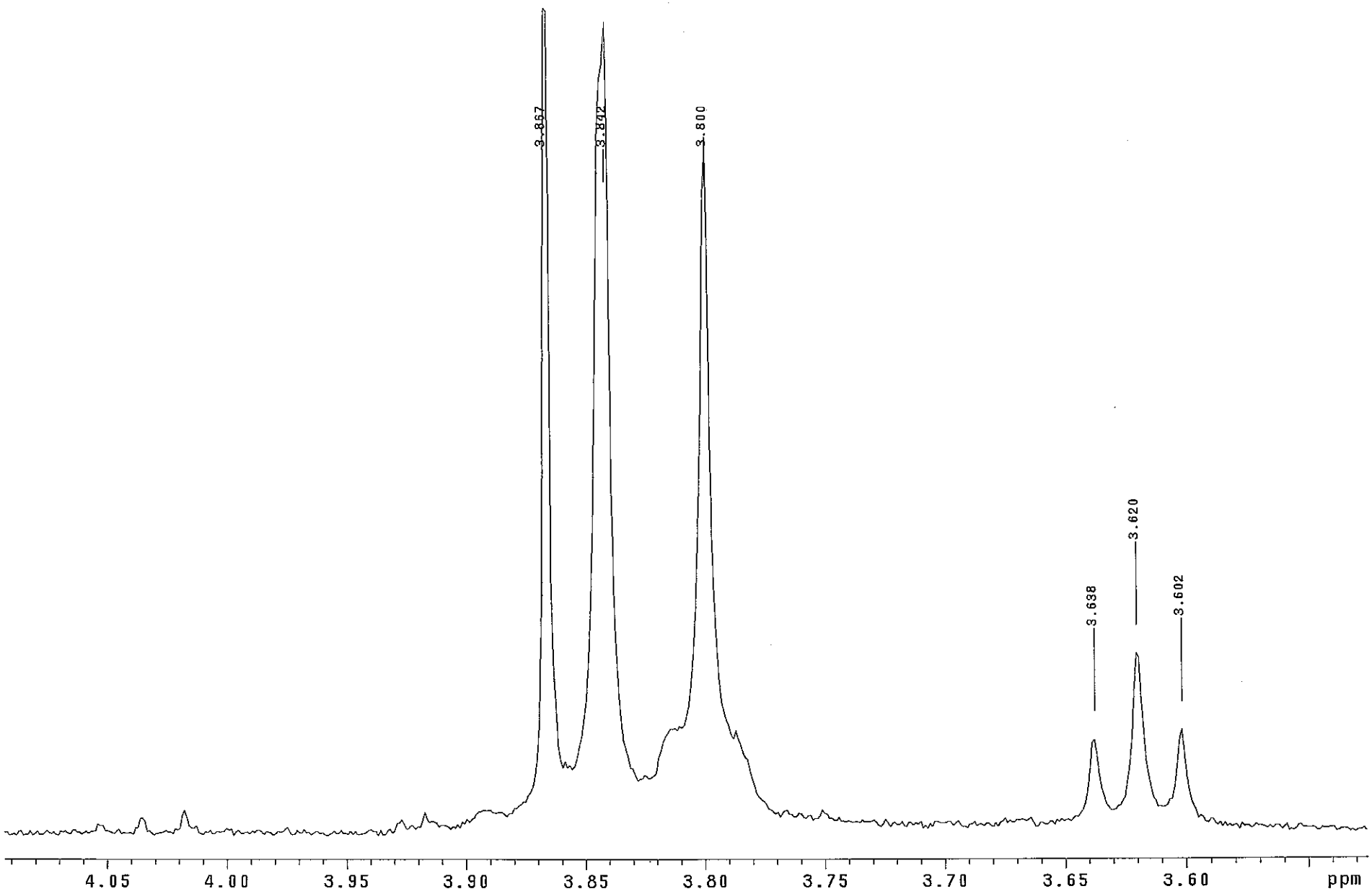
COMPOUND 8



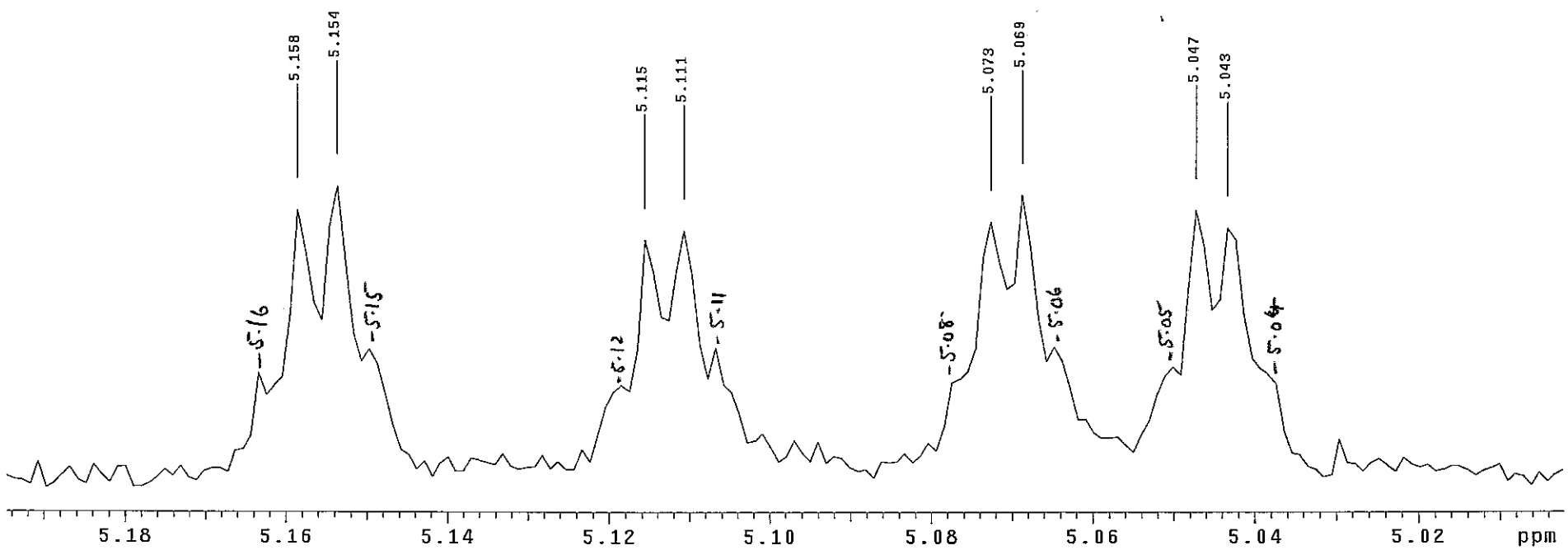
COMPOUND 8


2.509
2.505
2.500
2.496
2.491
2.757
2.738
2.721
2.551
2.450
2.9
2.8
2.7
2.6
2.5
2.4
ppm

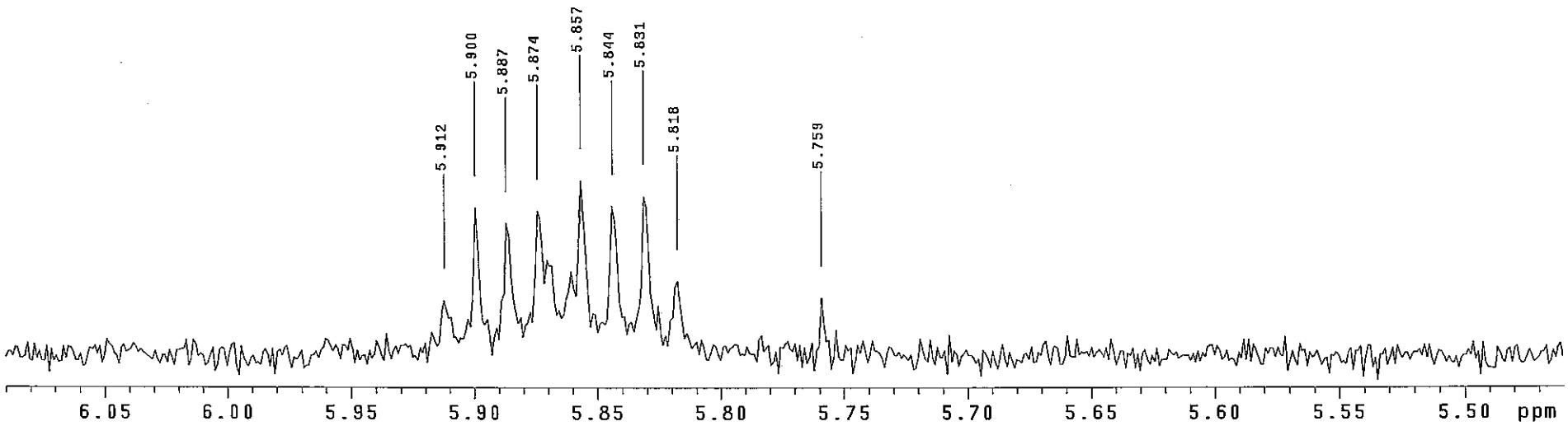
COMPOUND 8.


3.867
3.842
3.800
3.638
3.620
3.602
4.05
4.00
3.95
3.90
3.85
3.80
3.75
3.70
3.65
3.60
ppm

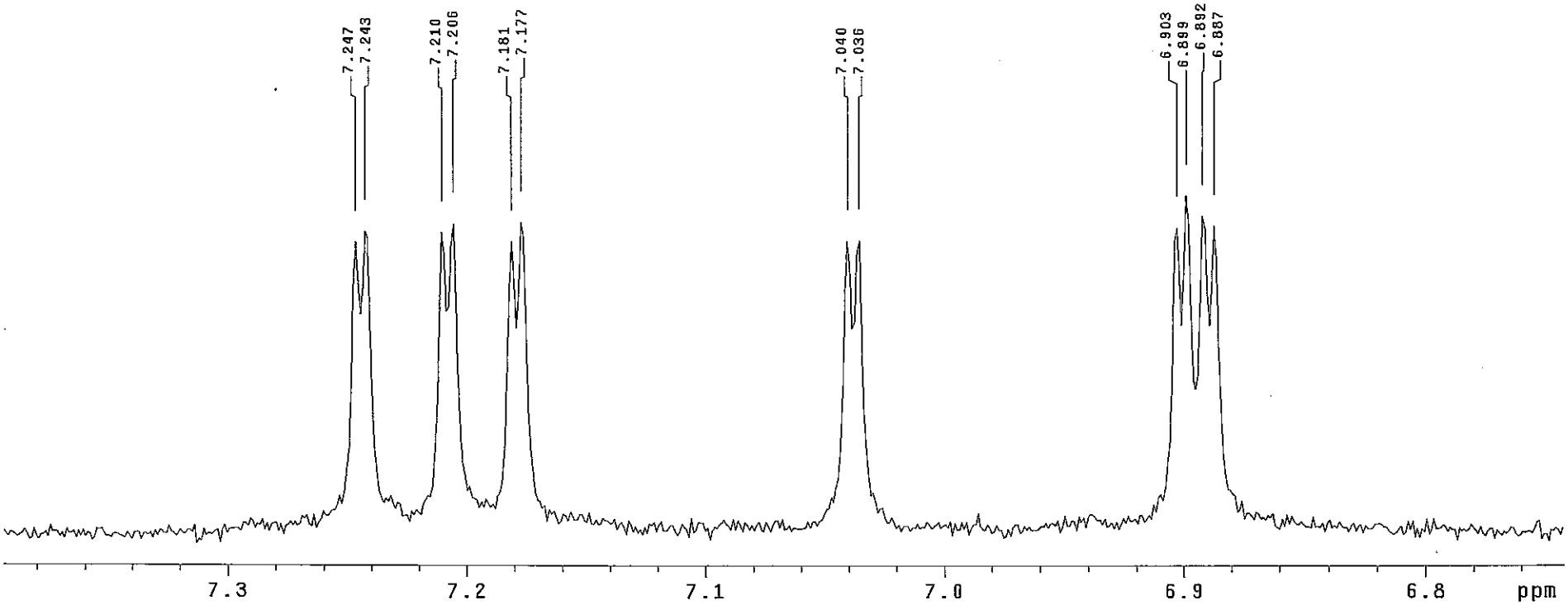
COMPOUND 8


5.158
5.154
5.115
5.111
5.073
5.069
5.047
5.043
5.18
5.16
5.14
5.12
5.10
5.08
5.06
5.04
5.02
ppm

COMPOUND 8


5.912
5.900
5.887
5.874
5.857
5.844
5.831
5.818
5.759
6.05
6.00
5.95
5.90
5.85
5.80
5.75
5.70
5.65
5.60
5.55
5.50
ppm

COMPOUND 8.

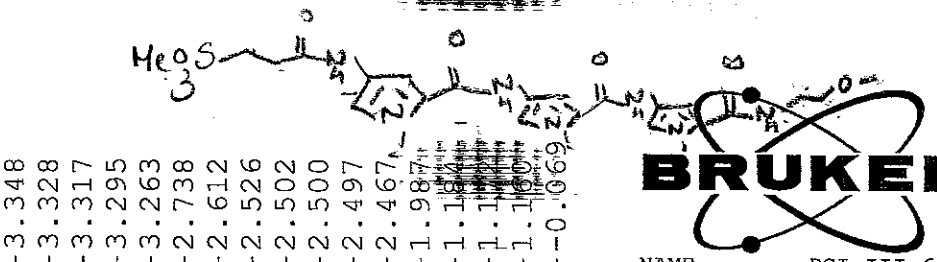

7.247
7.243
7.210
7.206
7.181
7.177
7.040
7.036
6.903
6.899
6.892
6.887
7.3
7.2
7.1
7.0
6.9
6.8
ppm

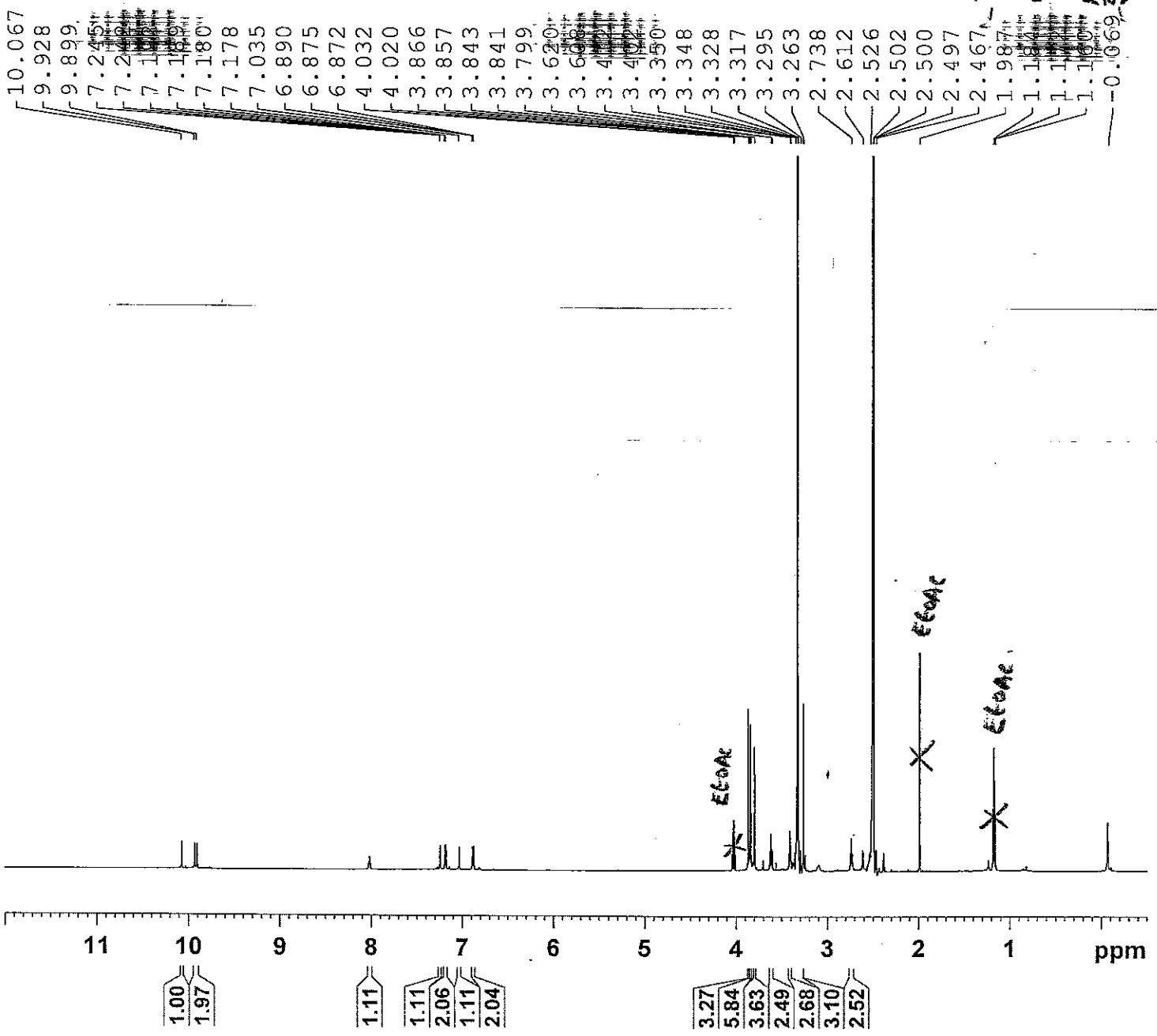
10.066
9.927
9.908
8.217
8.204
8.188
10.2
10.0
9.8
9.6
9.4
9.2
9.0
8.8
8.6
8.4
8.2
ppm

COMPOUND 8

PCI-III-683

COMPOUND 9



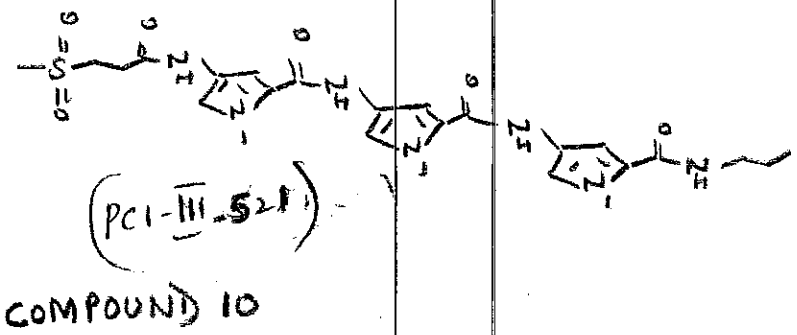


NAME	PCI-III-683
EXPNO	2
PROCNO	1
Date_	20081218
Time	21.09
INSTRUM	spect
PROBHD	5 mm CPTCI 1H-
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	16
DS	2
SWH	12376.237 Hz
FIDRES	0.188846 Hz
AQ	2.6477449 sec
RG	456.1
DW	40.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	8.00 usec
PL1	4.00 dB
PL1W	7.00000000 W
SFO1	600.1337060 MHz
SI	32768
SF	600.1300008 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

PCI-III-521,mon

exp1 s2pul

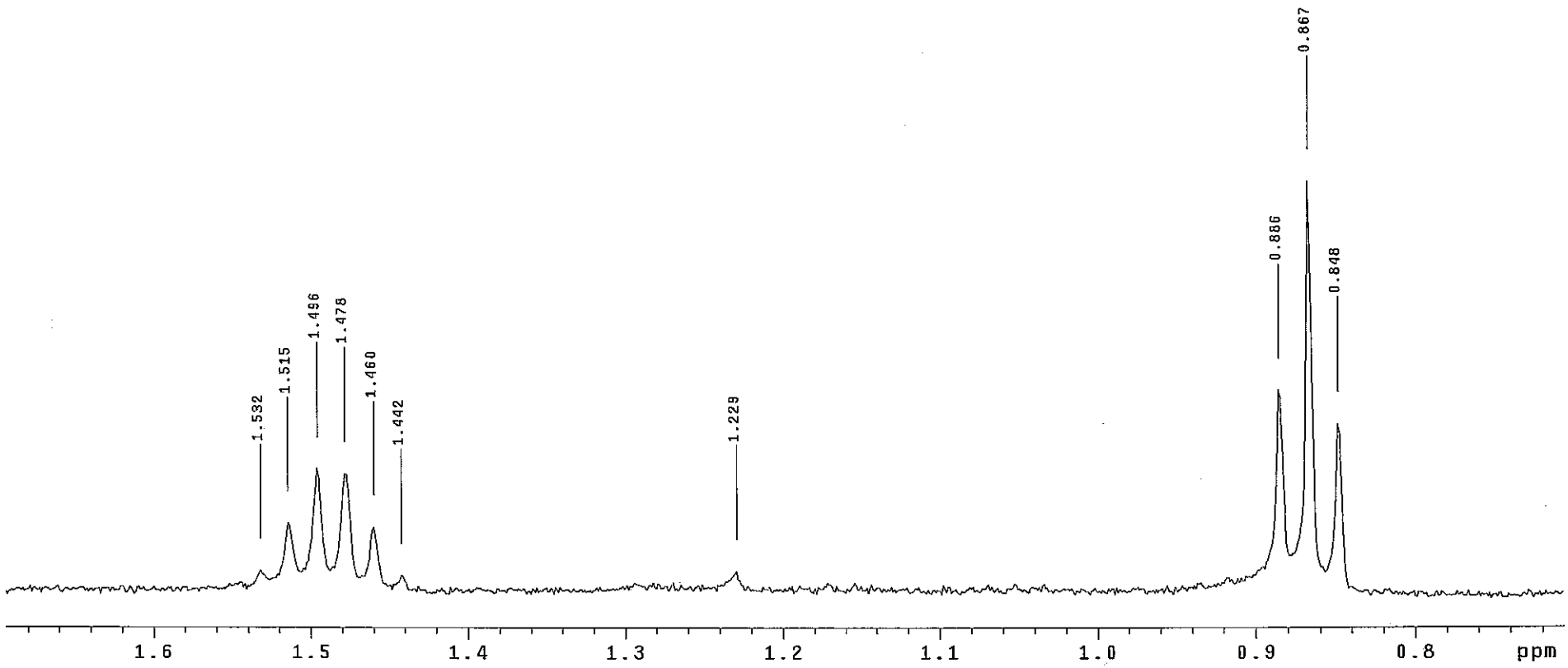
SAMPLE		SPECIAL	
date	Feb 18 2008	temp	not used
solvent	DMSO	gain	not used
file	exp	spin	20
ACQUISITION		hst	0.008
sw	6398.0	pw90	9.500
at	2.561	alfa	20.000
np	32768	**FLAGS**	
fb	3600	il	n
bs	16	in	ny
d1	1.000	dp	y
nt	1000	hs	nn
ct	416	**PROCESSING**	
TRANSMITTER		fn	not used
tn	H1	**DISPLAY**	
sfrq	399.862	sp	-793.2
tof	416.4	wp	6398.0
tpwr	60	rfl	1792.9
pw	4.750	rfp	999.6
DECOUPLER		rp	34.2
dn	C13	lp	-106.8
dof	0	**PLOT**	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	0	vs	297
dmf	200	th	2
		ai	ph

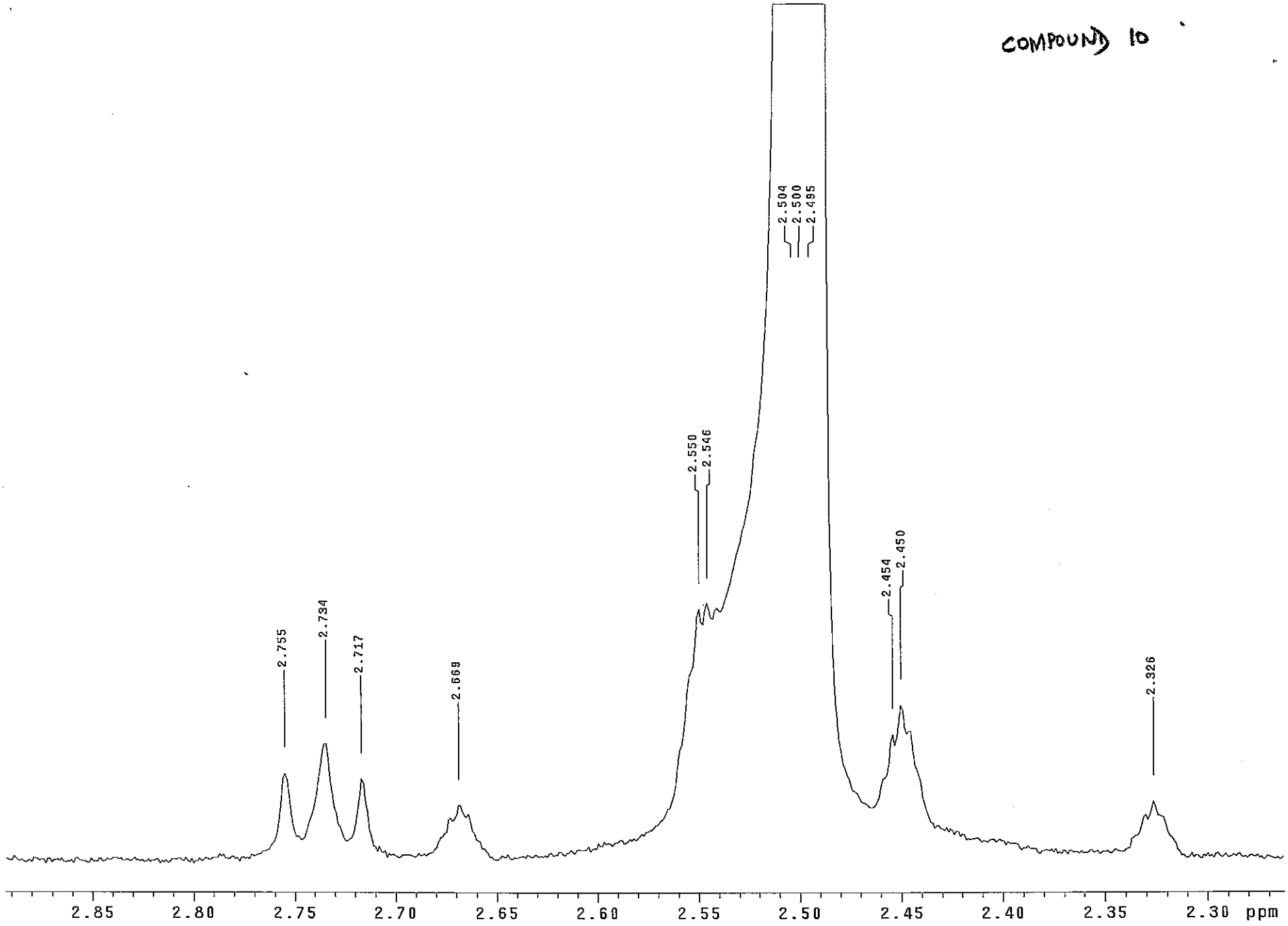


(PCI-III-521)

COMPOUND 10

COMPOUND 10

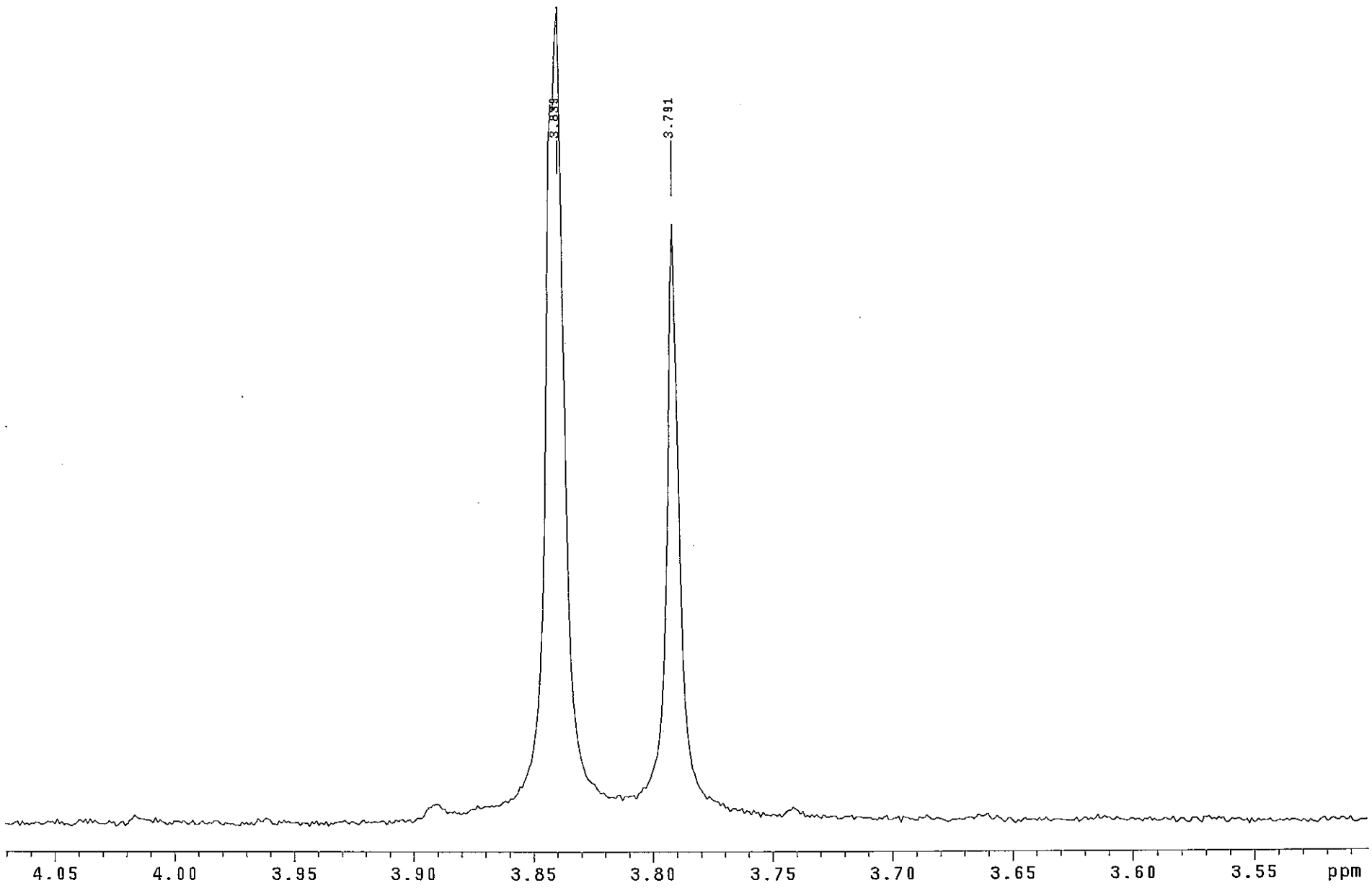

1.532
1.515
1.496
1.478
1.460
1.442
1.229
0.886
0.867
0.848
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm


COMPOUND 10
2.755
2.734
2.717
2.669
2.550
2.546
2.504
2.500
2.495
2.454
2.450
2.326
2.85
2.80
2.75
2.70
2.65
2.60
2.55
2.50
2.45
2.40
2.35
2.30
ppm

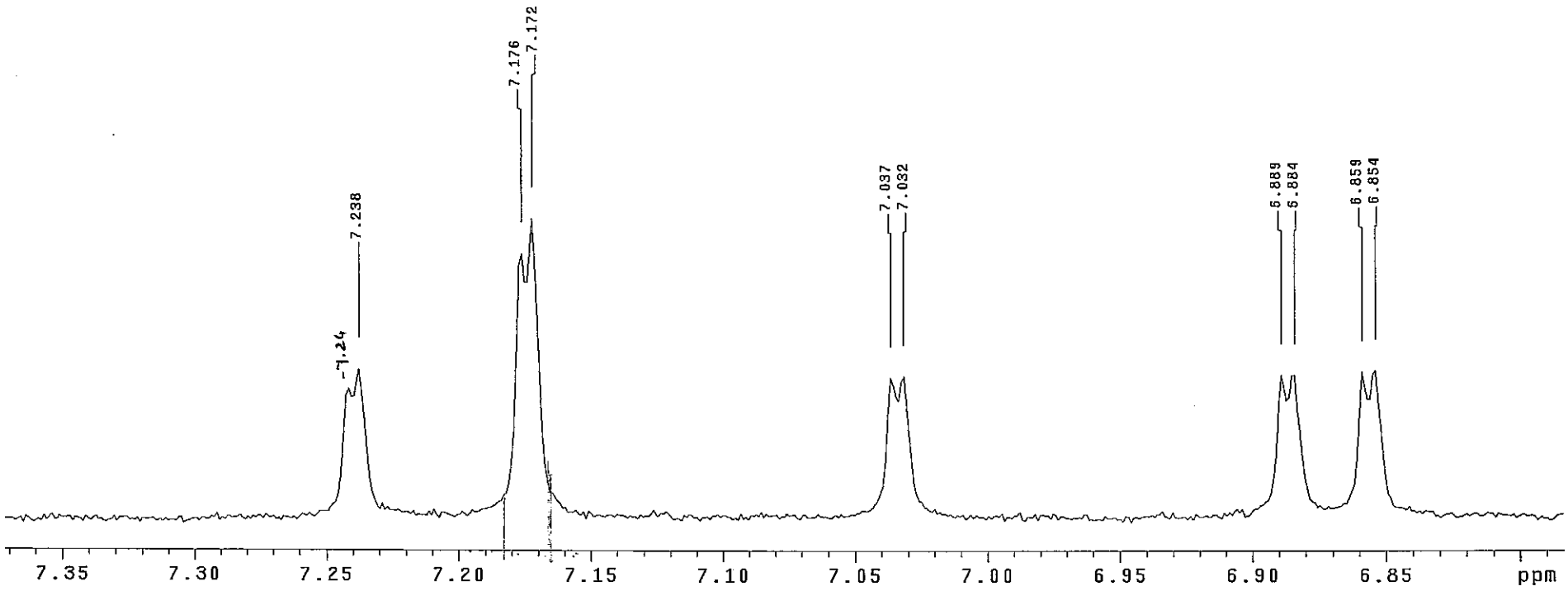
3.426
3.406
3.387
3.379
3.328
3.278
3.145
3.129
3.111
3.096
3.014
3.5
3.4
3.3
3.2
3.1
3.0
ppm

Compound 10

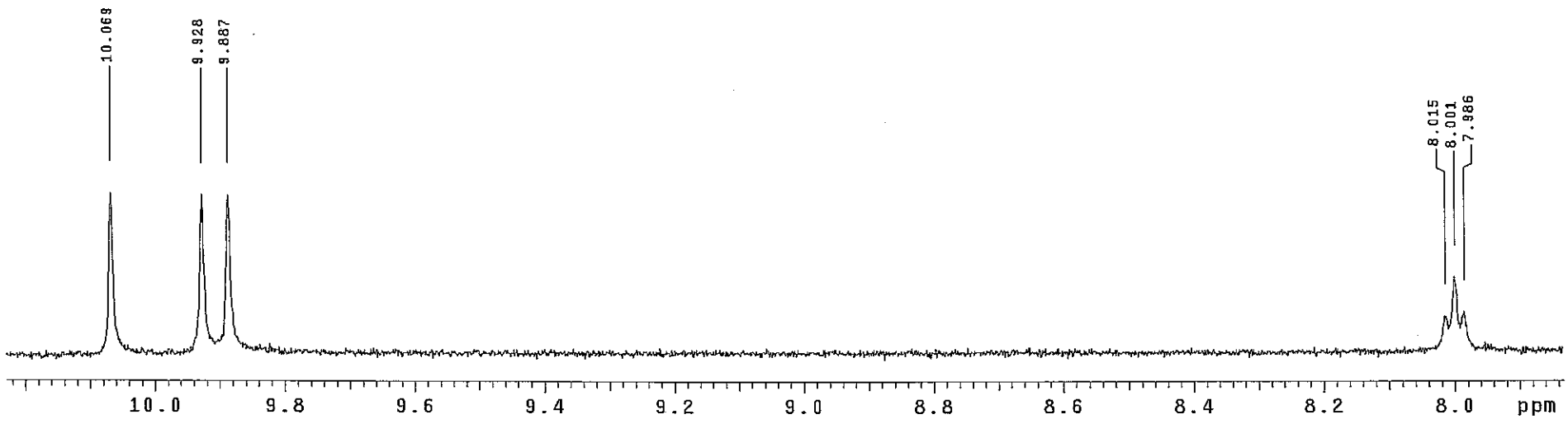
COMPOUND 10



COMPOUND 10


7.238
7.176
7.172
7.037
7.032
6.889
6.884
6.859
6.854
7.35
7.30
7.25
7.20
7.15
7.10
7.05
7.00
6.95
6.90
6.85
ppm

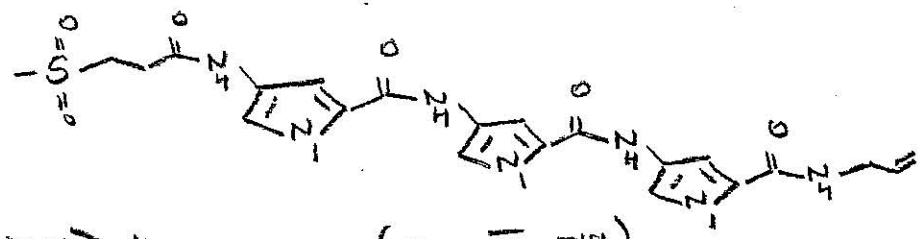
COMPOUND 10


10.069
9.928
9.887
8.015
8.001
7.986
10.0
9.8
9.6
9.4
9.2
9.0
8.8
8.6
8.4
8.2
8.0
ppm

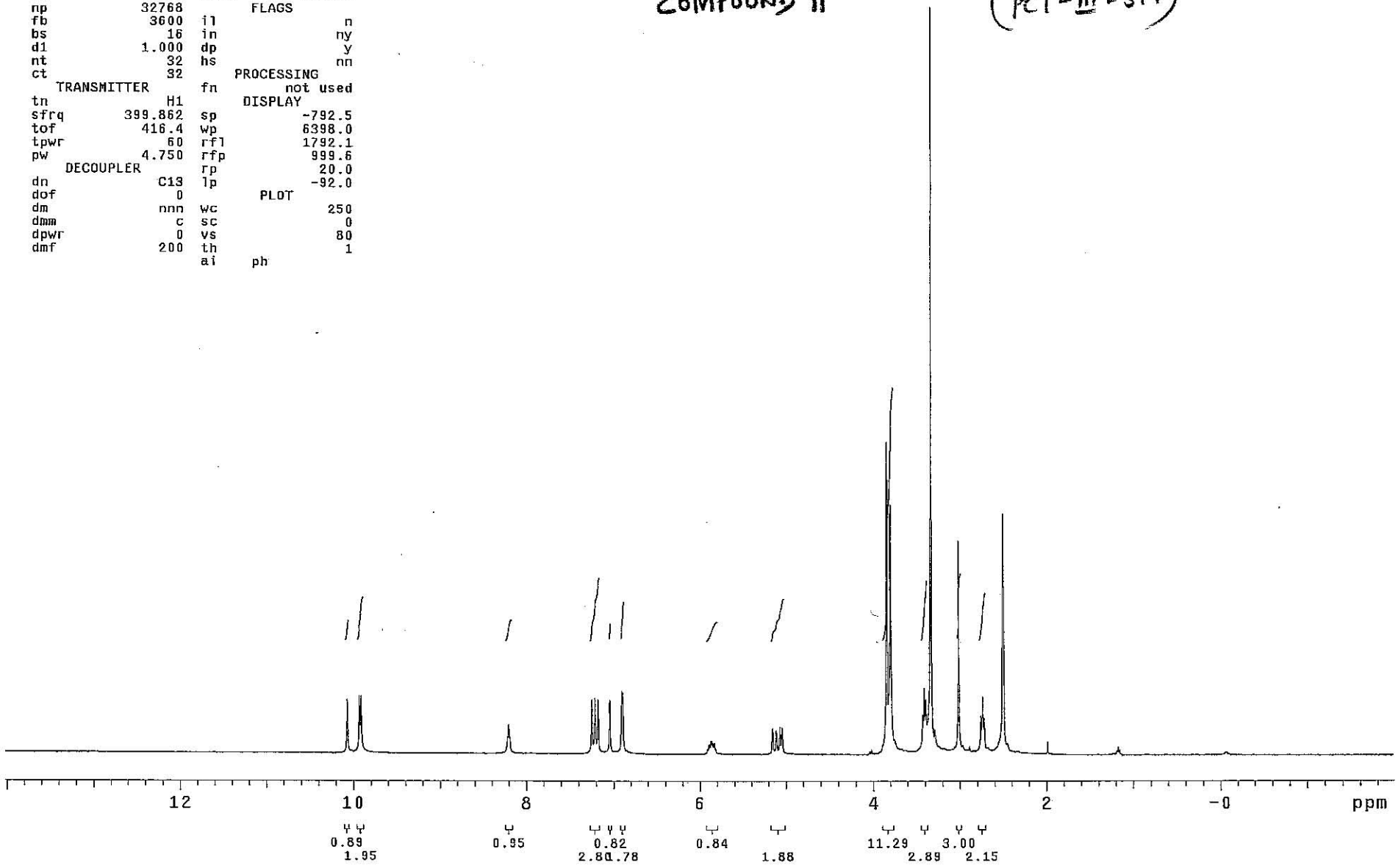
PCI-III-517

exp1 s2pul

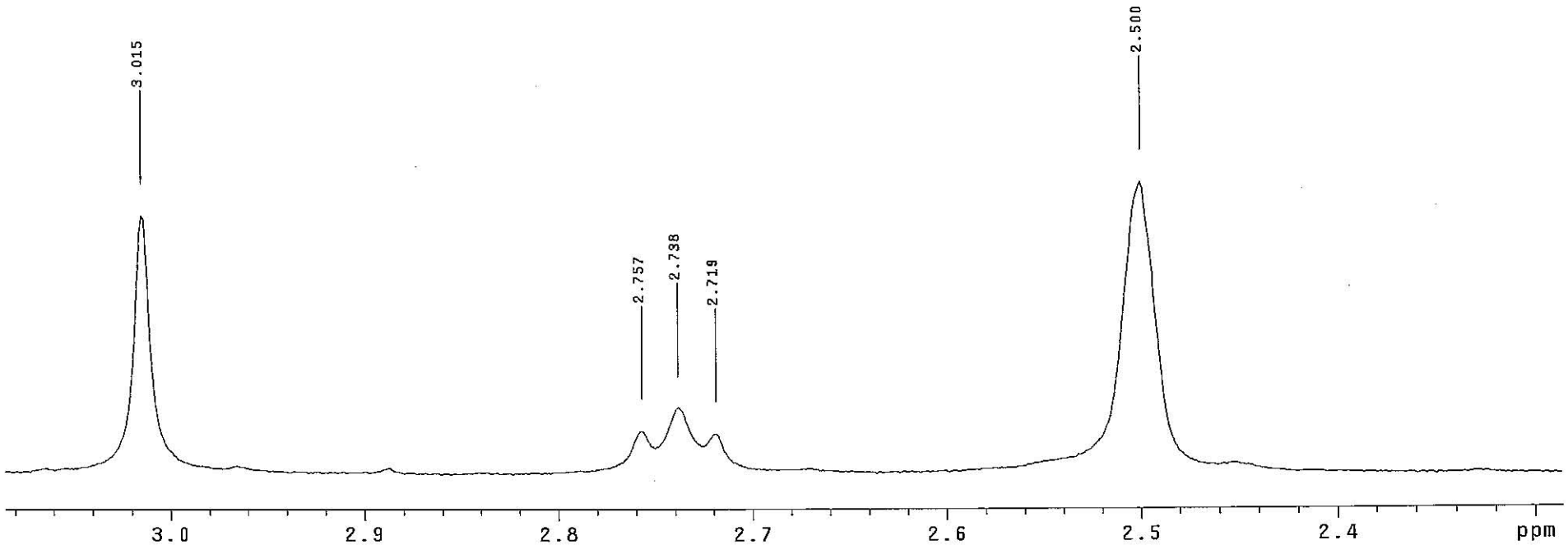
SAMPLE		SPECIAL	
date	Feb 13 2008	temp	not used
solvent	DMSO	gain	not used
file	exp	spin	20
ACQUISITION		hst	0.008
sw	6398.0	pw90	9.500
at	2.561	alfa	20.000
np	32768	FLAGS	
fb	3600	il	n
bs	16	in	ny
d1	1.000	dp	y
nt	32	hs	nn
ct	32	PROCESSING	
TRANSMITTER		fn	not used
tn	H1	DISPLAY	
sfrq	399.862	sp	-792.5
tof	416.4	wp	6398.0
tpwr	60	rfl	1792.1
pw	4.750	rfp	999.6
DECOUPLER		rp	20.0
dn	C13	lp	-92.0
dof	0	PLOT	
dm	nnn	wc	250
dmm	c	sc	0
dpwr	0	vs	80
dmf	200	th	1
		ai ph	



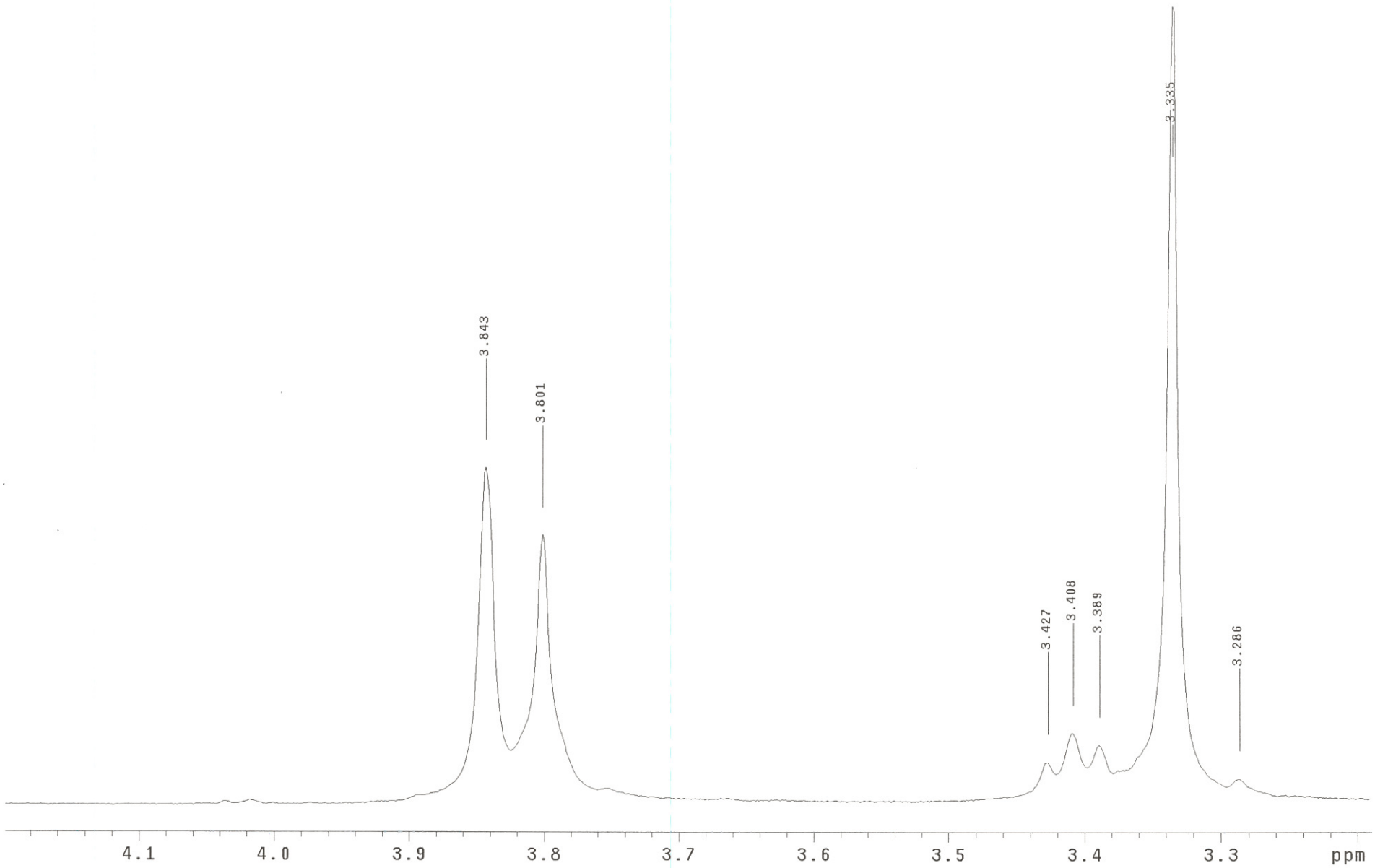
COMPOUND II (PCI-III-517)



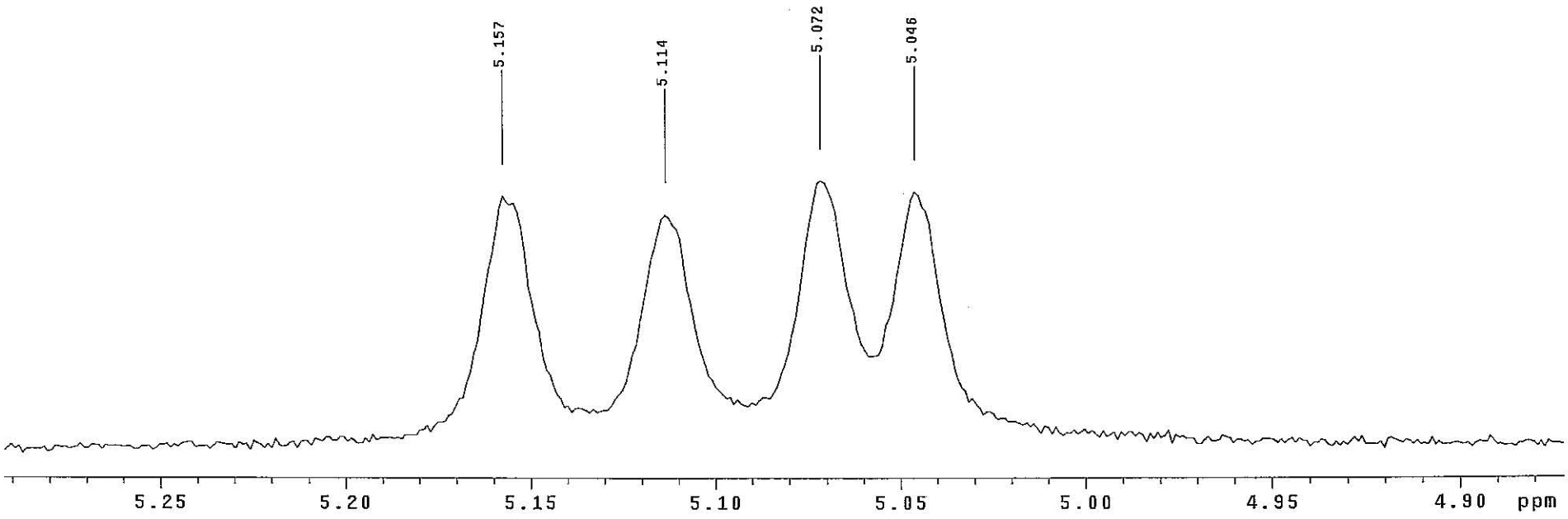
COMPOUND 11



COMPOUND 11



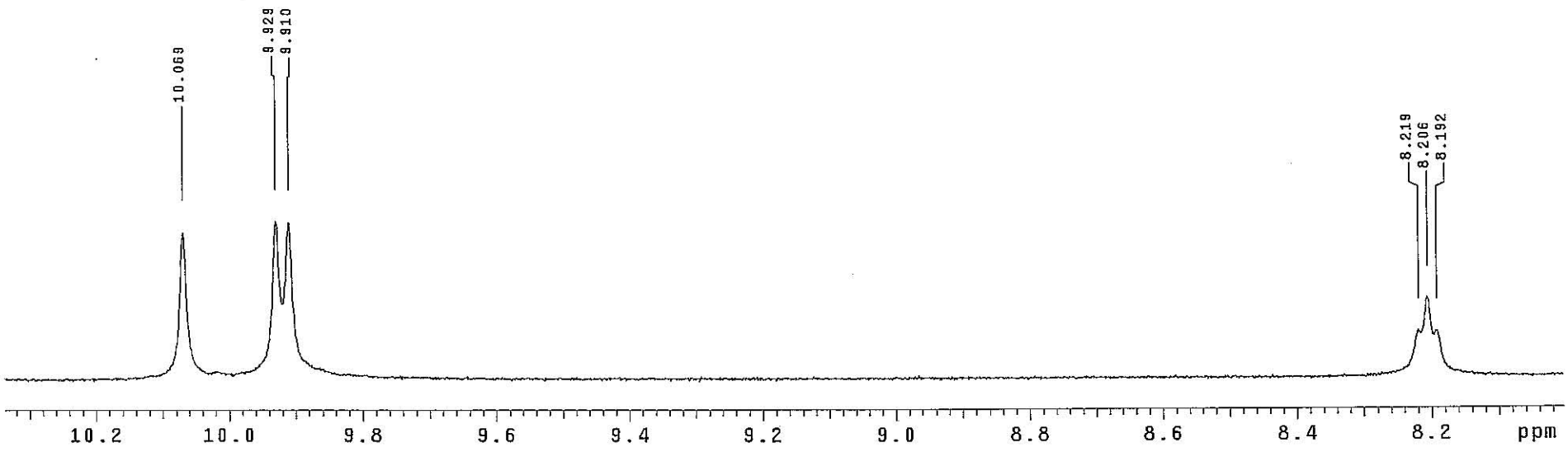
COMPOUND 11



COMPOUND 11

COMPOUND 11

COMPOUND 11


10.069
9.929
9.910
8.219
8.206
8.192
10.2
10.0
9.8
9.6
9.4
9.2
9.0
8.8
8.6
8.4
8.2
ppm

Mass Spectra of Compounds

Elemental Composition Report

Single Mass Analysis

Tolerance = 5000.0 PPM / DBE: min = -1.5, max = 100.0

Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

(PCI-II-439)

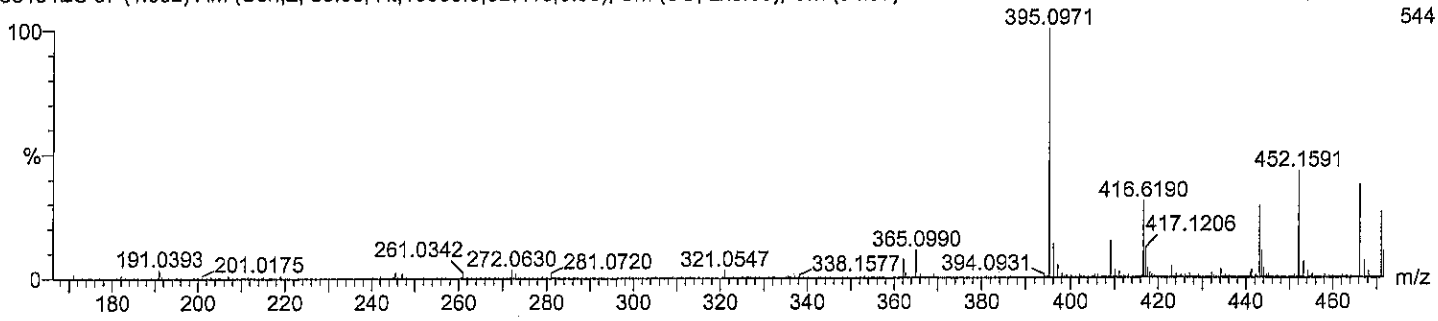
Monoisotopic Mass, Odd and Even Electron Ions

82 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

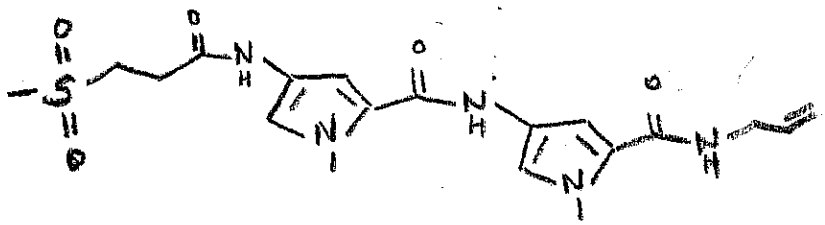
IYER/GOLD
PC-II-439
58104ES 57 (1.092) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (52:57)

Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

03-Jan-2008
11:00:48
TOF MS ES+
544

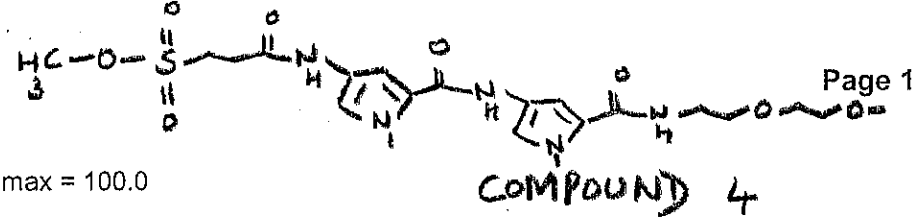


Minimum:				-1.5		
Maximum:		200.0	5000.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
452.1591	452.1604	-1.2	-2.7	9.5	1	C19 H26 N5 O6 S



COMPOUND 2

Elemental Composition Report



COMPOUND 4

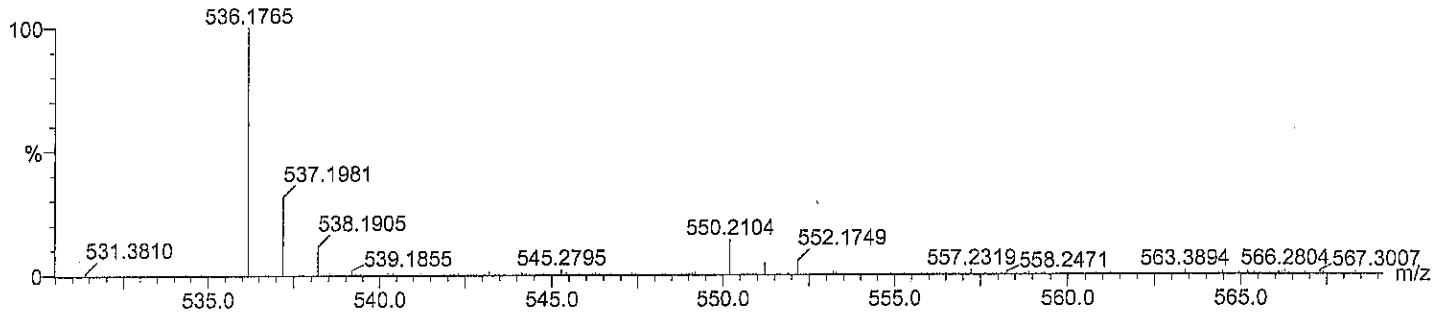
Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 100.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
330 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-24 H: 0-35 N: 0-6 O: 0-10 23Na: 0-1 S: 0-1

IYER PCI-III-659 GOLD
62589ES 187 (3.525) AM (Cen,5, 80.00, Ar,5000.0,527.16,0.00); Sm (Mn, 2x3.00)

TOF MS ES+
5.34e+003



Minimum:				-1.5							
Maximum:		5.0	20.0	100.0							
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula					
536.1765	536.1757	0.8	1.5	13.5	76.6	C24	H27	N5	O8	23Na	
	536.1791	-2.6	-4.8	8.5	23.3	C21	H31	N5	O8	23Na	S
	536.1815	-5.0	-9.3	11.5	9.9	C23	H30	N5	O8	S	
	536.1703	6.2	11.6	11.5	17.0	C24	H30	N3	O9	S	
	536.1679	8.6	16.0	8.5	32.4	C22	H31	N3	O9	23Na	S

Elemental Composition Report

COMPOUND 5

Single Mass Analysis

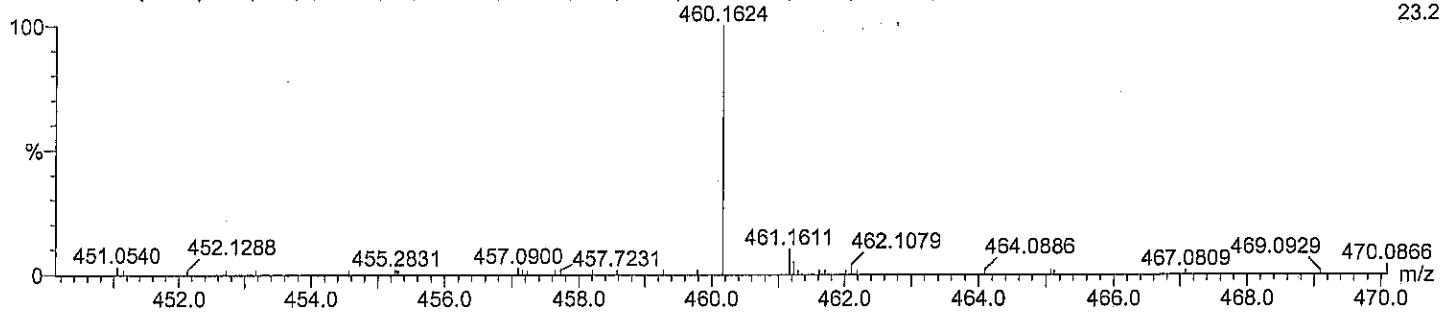
Tolerance = 500.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
141 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

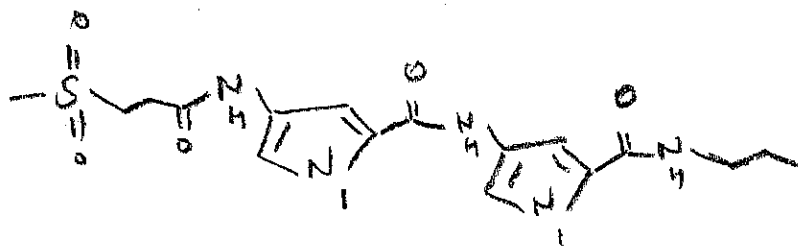
IYEU/GOLD
PCI-III-528
58536ES 119 (2.263) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (119:150)

Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

27-Feb-2008
10:40:18
TOF MS ES+
23.2



Minimum:				-1.5		
Maximum:		200.0	500.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
460.1624	460.1631	-0.6	-1.3	8.5	1	C19 H27 N5 O5 Na S



Single Mass Analysis

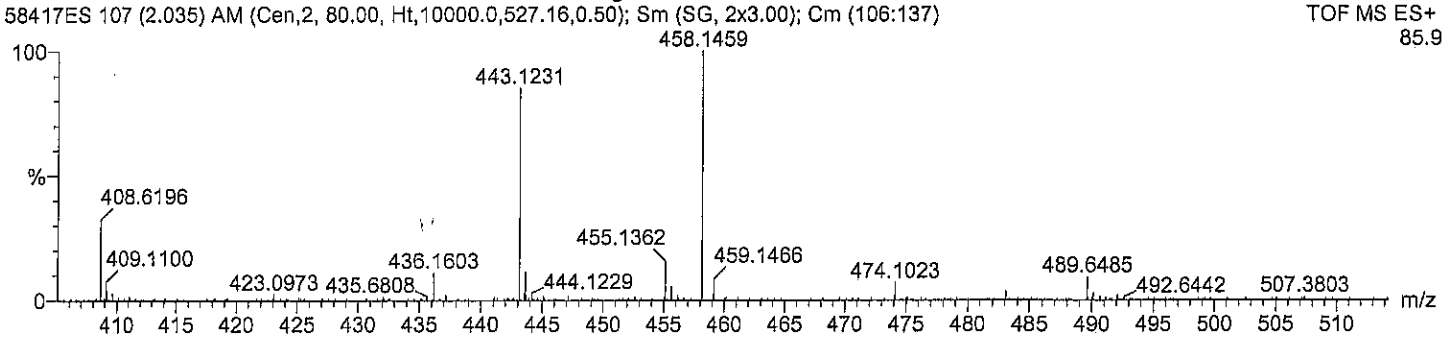
Tolerance = 300.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
141 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

IYER/GOLD
PC1-3-511
58417ES 107 (2.035) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (106:137)

Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

12-Feb-2008
09:52:50
TOF MS ES+
85.9



Minimum:				-1.5		
Maximum:		200.0	300.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
458.1459	458.1474	-1.5	-3.3	9.5	1	C19 H25 N5 O5 Na S

COMPOUND 6

Elemental Composition Report

Single Mass Analysis

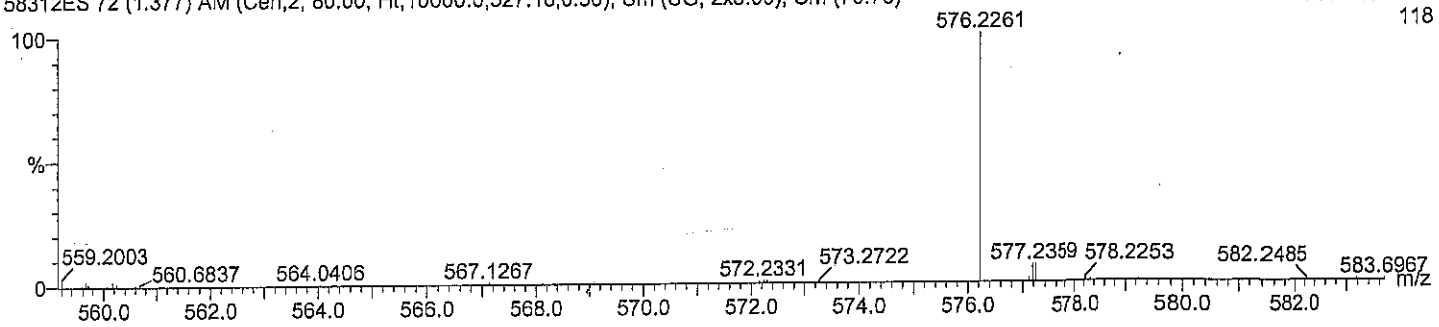
Tolerance = 200.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
122 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

IYER/COLD
PCI-III-500
58312ES 72 (1.377) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (70:76)

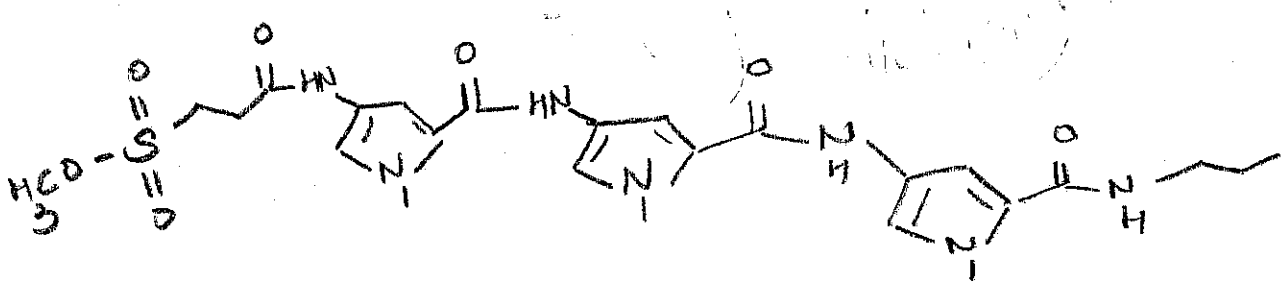
Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

30-Jan-2008
10:07:02
TOF MS ES+
118



Minimum:				-1.5		
Maximum:		200.0	200.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
576.2261	576.2240	2.1	3.6	12.5	1	C25 H34 N7 O7 S

COMPOUND 7



PCI-III-480

Elemental Composition Report

Single Mass Analysis

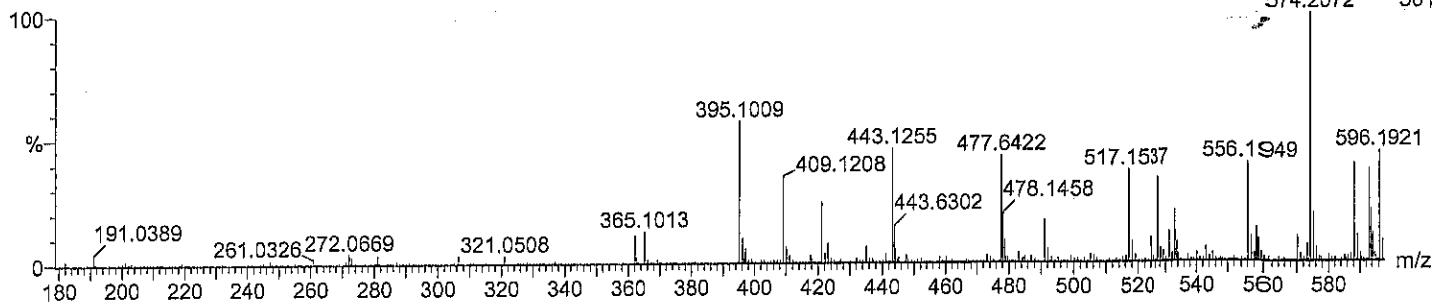
Tolerance = 5000.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
122 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

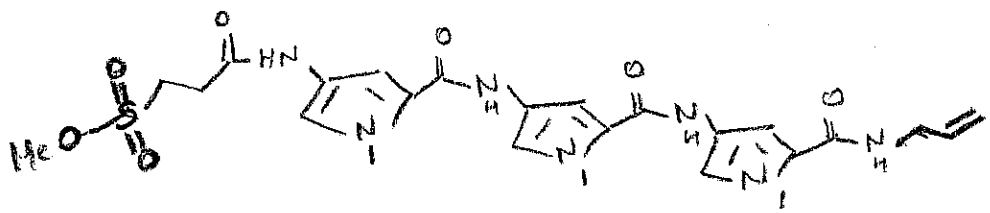
IYER/GOLD
PCI-III-480
58103ES 98 (1.868) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (98:105)

Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

03-Jan-2008
10:51:42
TOF MS ES+



Minimum:				-1.5		
Maximum:		200.0	5000.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
574.2072	574.2084	-1.2	-2.1	13.5	1	C25 H32 N7 O7 S



COMPOUND 8.

(PCI-III-521)

Elemental Composition Report

Single Mass Analysis

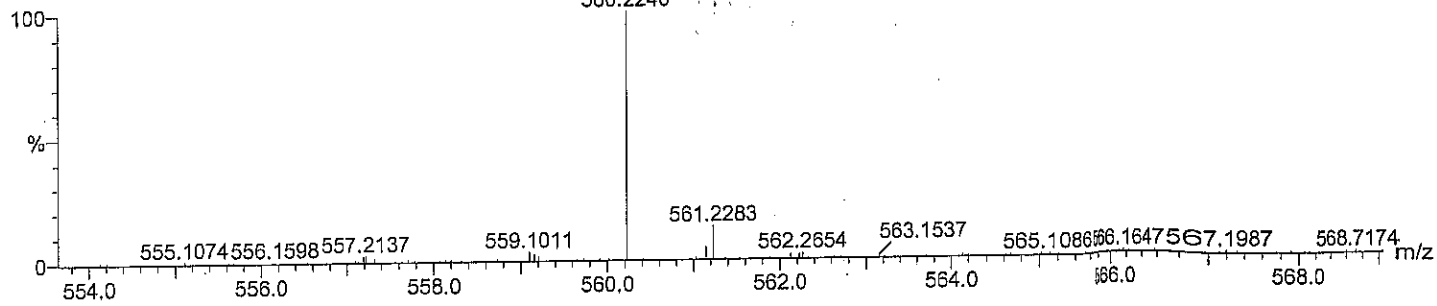
Tolerance = 500.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
106 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

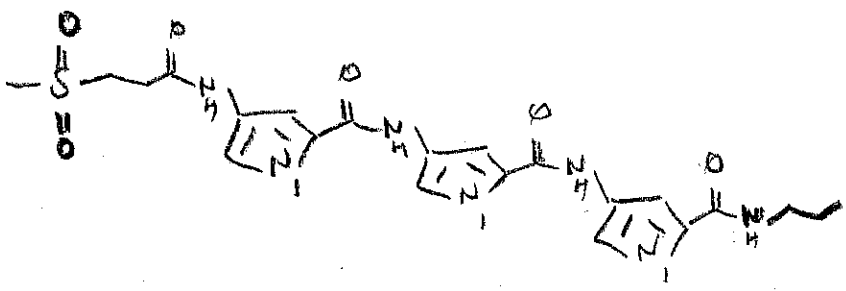
IYEU/GOLD
PCI-III-521
58494ES 80 (1.517) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (80:122)

Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

21-Feb-2008
10:11:18
TOF MS ES+
120

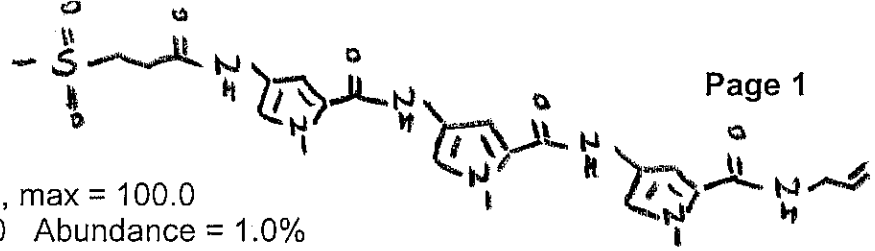


Minimum:				-1.5		
Maximum:		200.0	500.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
560.2240	560.2291	-5.1	-9.2	12.5	1	C25 H34 N7 O6 S



COMPOUND 10

Elemental Composition Report



Single Mass Analysis

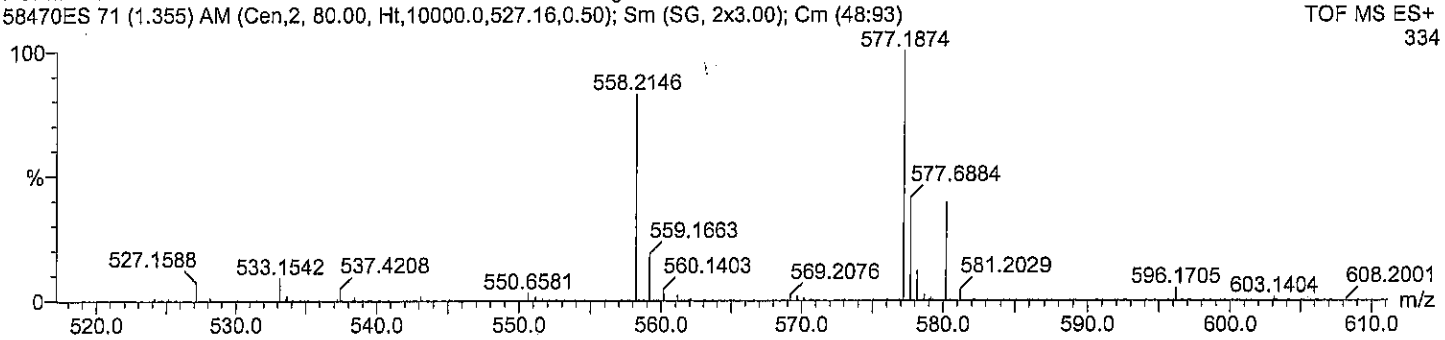
Tolerance = 500.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
106 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

IYER/GOLD
PCI-III-517
58470ES 71 (1.355) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x3.00); Cm (48:93)

Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

15-Feb-2008
11:05:22
TOF MS ES+
334



Minimum:				-1.5		
Maximum:		200.0	500.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
558.2146	558.2135	1.1	2.0	13.5	1	C25 H32 N7 O6 S

COMPOUND 11

Elemental Composition Report

Single Mass Analysis

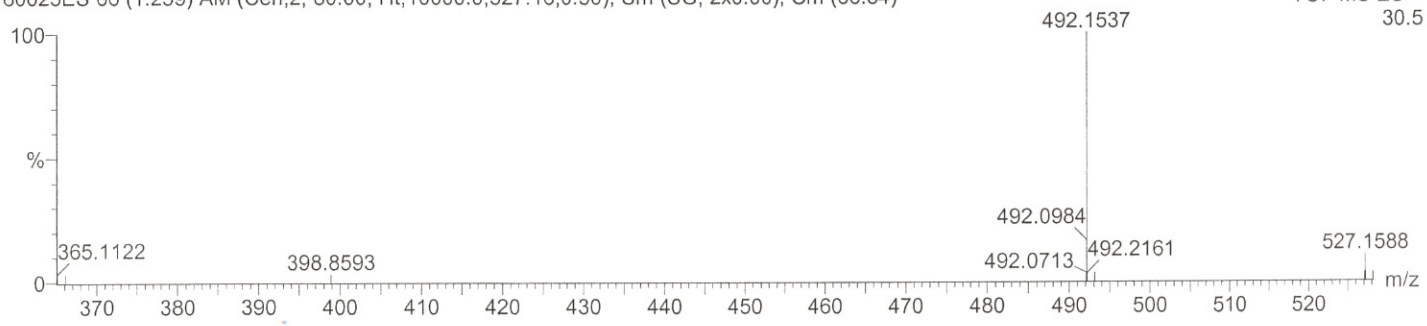
Tolerance = 1000.0 PPM / DBE: min = -1.5, max = 100.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

Monoisotopic Mass, Odd and Even Electron Ions
189 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

IYER/GOLD
PCI-3-609
60025ES 66 (1.259) AM (Cen,2, 80.00, Ht,10000.0,527.16,0.50); Sm (SG, 2x0.00); Cm (66:84)

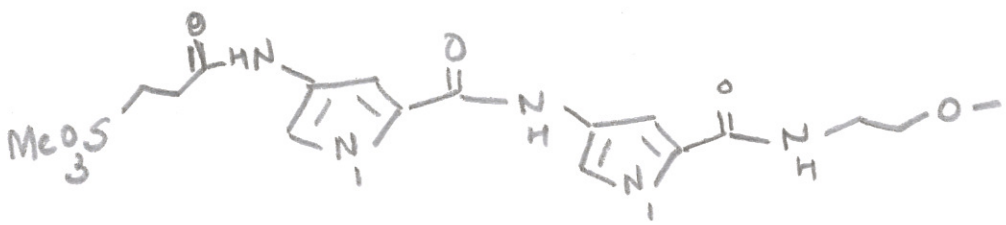
Q-Tof - Dept. of Chemistry U. of Pitt
Acknowledge NIH Grant: 1S10RR017977-01

26-Aug-2008
10:14:02
TOF MS ES+
30.5



Minimum:				-1.5		
Maximum:		200.0	1000.0	100.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
492.1537	492.1529	0.9	1.7	8.5	1	C19 H27 N5 O7 Na S

COMPOUND 3



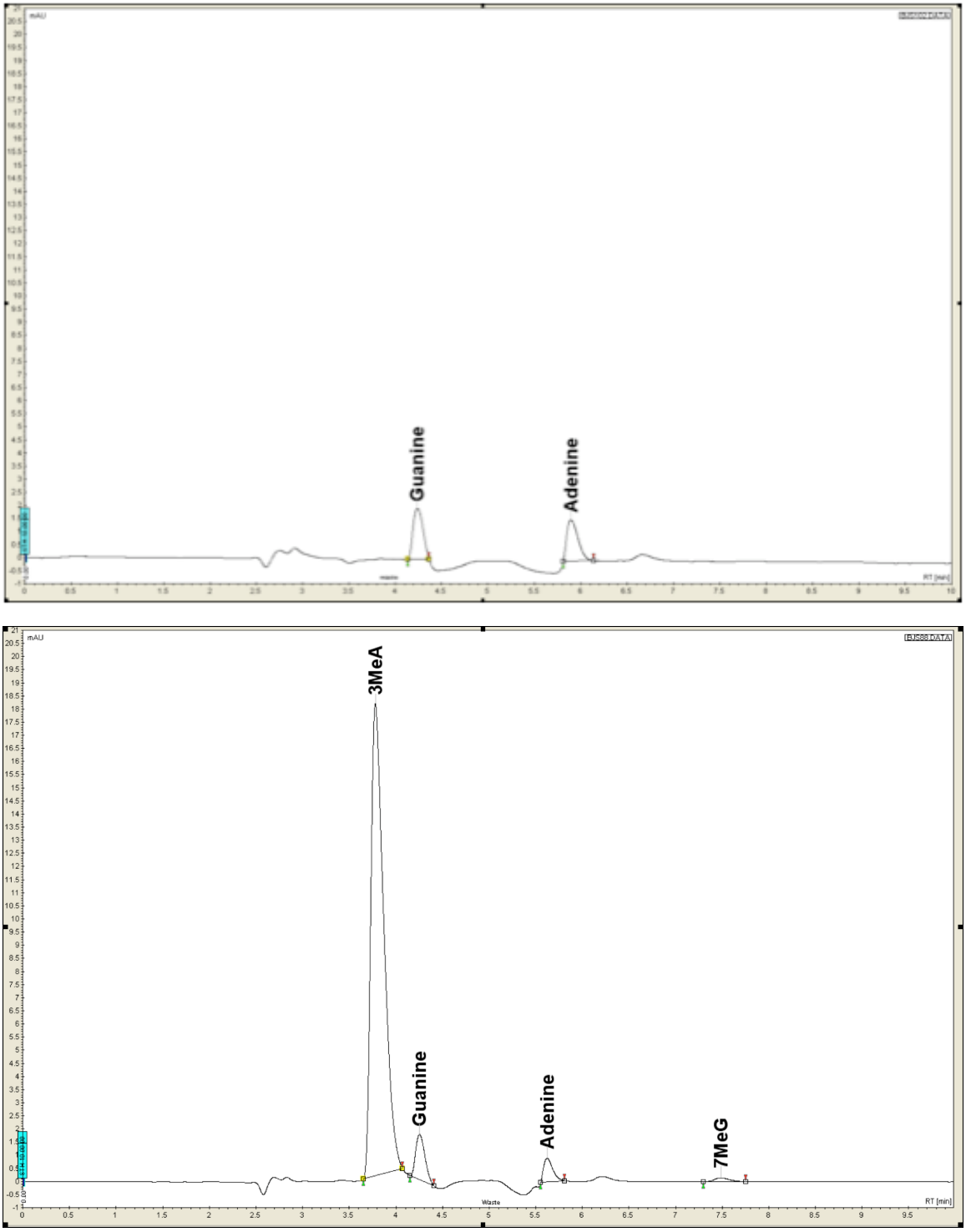


Figure S1. HPLC trace of untreated calf thymus DNA (top) and DNA treated with compound **7**.

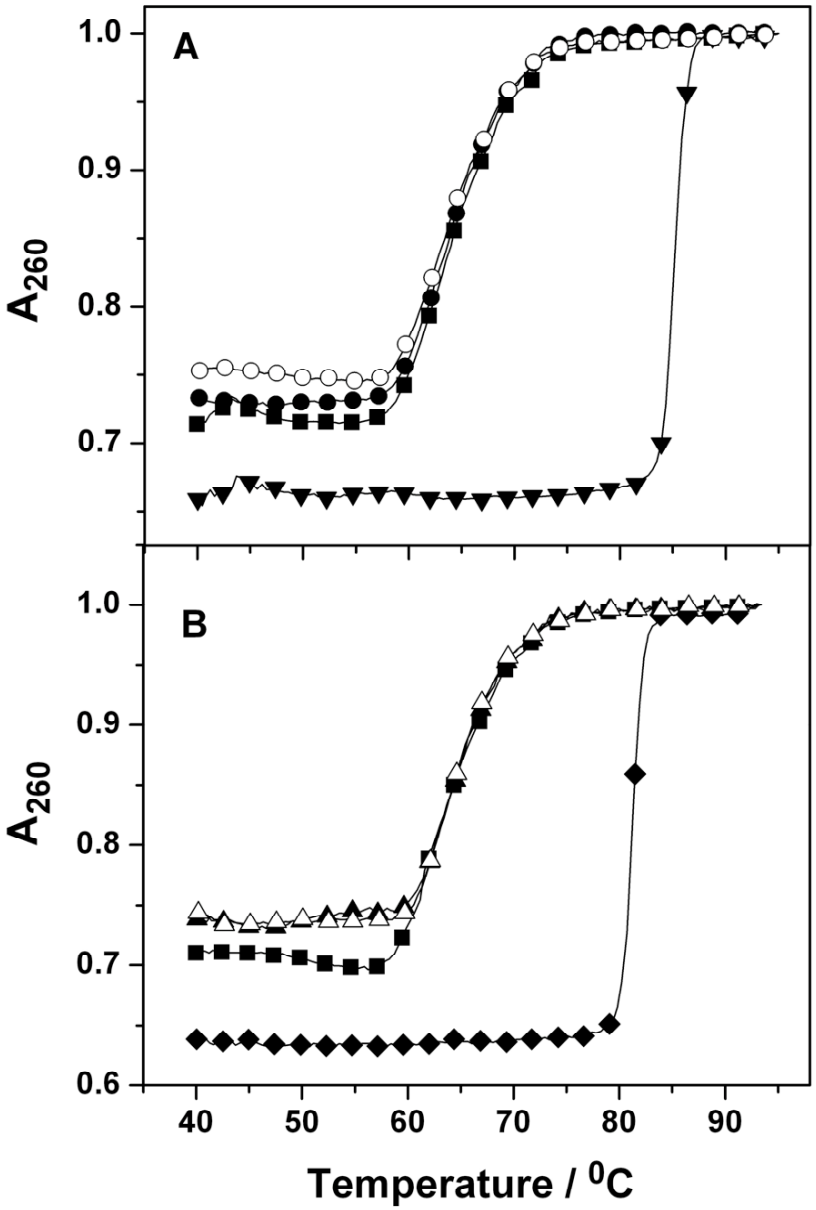


Figure S2. UV melting curves of calf thymus DNA (~ 76 μM) in the absence (■) and presence of 1:1 complex of (**A**) compound **5** (●), compound **6** (o) and netropsin (▼) and (**B**) compound **10** (▲), compound **11** (Δ) and distamycin (◆) in 10% ethanol-phosphate buffer, pH 7 at 260 nm.

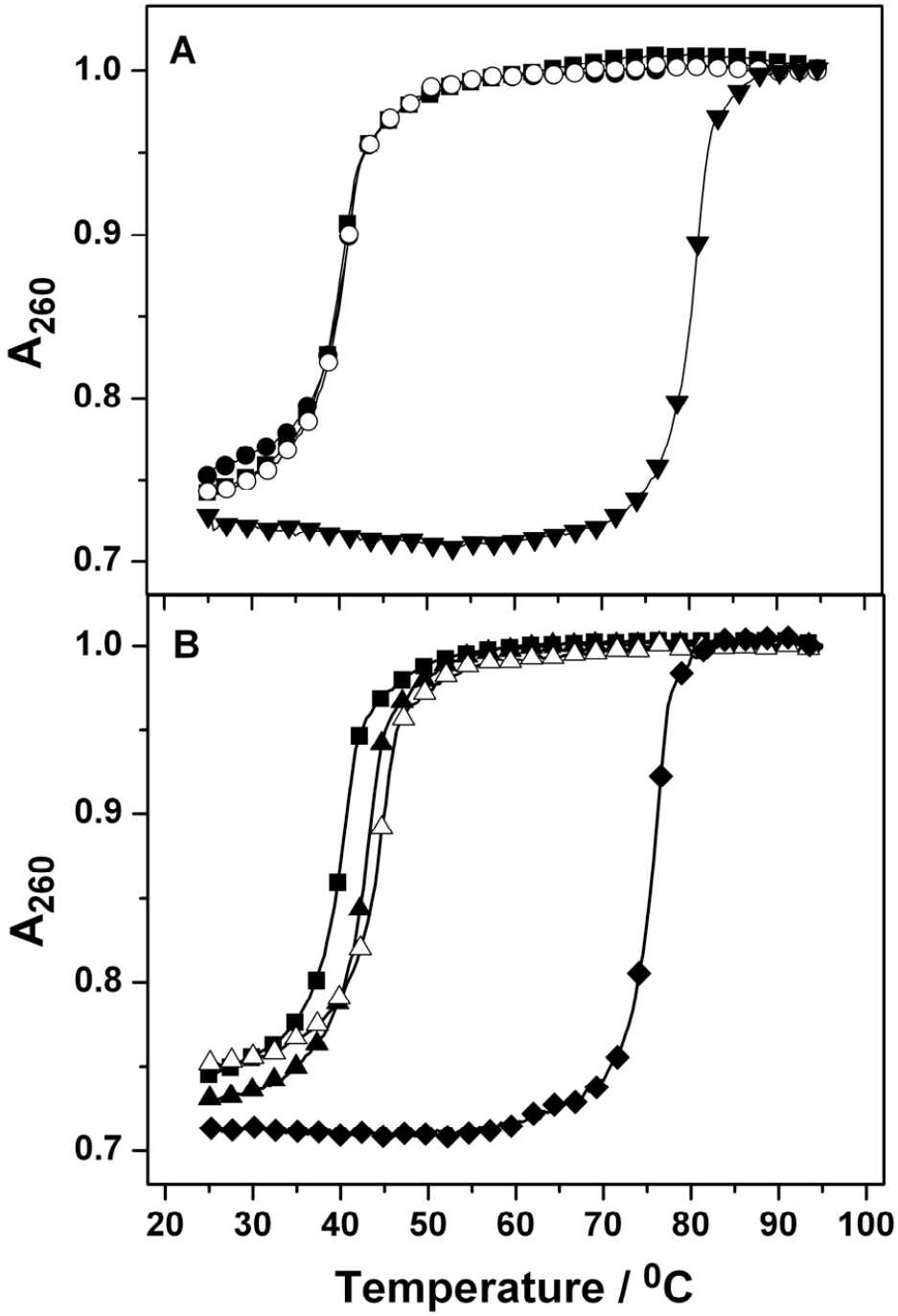


Figure S3. UV melting curves of poly-d(A-T) · poly-d(A-T) ~ 76 μM, in the absence (■) and presence of 1:1 complex of (**A**) compound 1 (●), compound 2 (o) and netropsin (▼) and (**B**) compound 3 (▲), compound 4 (Δ) and distamycin (◆) in 10% EtOH-phosphate buffer, pH 7 at 260 nm.