Experimental

Optical rotations were determined with a Perkin-Elmer 241 model polarimeter at the sodium D line at 23 °C. NMR spectra were recorded with JEOL JNM-GX270 and Varian Inova 300 and 500 and Bruker DRX-600 MHz spectrometers. Coupling constants are reported in Hz. LR and HRMS were obtained on either a micromass VG 70/70H or VG ZAB-E or autospec spectrometers and were measured in ES +ve mode unless otherwise indicated. TLC was performed on aluminium sheets precoated with silica gel 60 (HF_{254}, Merck) and spots visualized by UV and charring with sulphuric acid-ethanol (1:20). Flash column chromatography was carried out with silica gel 60 (0.040-0.630 mm, Merck) and employed a stepwise solvent polarity gradient correlated with TLC mobility unless otherwise stated. All analytical HPLC separations were performed using a Knauer Maxistar K1000 gradient pump and Knauer 4-channel degasser and a Knauer diode array detector DAP 2062. Semi-prep HPLC was carried out using a 2 Knauer ministar K500 gradient pump. Acetonitrile\water mixtures were used as eluant with a flow rate of 1mL\min (analytical scale) and 10mL\min (semi-preparative scale) The semi preparative column used was VYDAC C-18 rev phase (7µ, 250x20mm). Chromatography solvents used were ethyl acetate (Riedel-deHaen) and petroleum ether (BDH laboratory supplies), which is the fraction of light petroleum ether with boiling point 40-60 °C. All reaction solvents were dried and distilled before use.

Preparation of 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosylamine (1)

(i) *2,3,4,6-Tetra*-O-*acetyl-α-D-galactopyranosyl bromide*: β-D-Galactose pentaacetate (20 g, 51 mmol) was suspended in hydrogen bromide (30% in acetic acid, 50 mL). The reaction was stirred at 0 ºC. Analysis by TLC (EtOAc: Petroleum ether) showed that the reaction was complete after 4 h. Ice water (50 mL) was then added and the precipitate that formed was dissolved in ethyl acetate, washed with sodium bicarbonate (4 x 50 mL) and water (4 x 50 mL) and dried ($MgSO_4$). Excess solvent was removed to give the bromide as an orange oil. This intermediate was recrystallised from diethyl ether / petroleum ether to give a white solid (21.6 g) which was reacted immediately.

(ii) *2,3,4,6-Tetra*-O-*acetyl-β-D-galactopyranosyl azide:* 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide (2.1 g, 5.02 mmol), sodium azide (1.3 g, 26 mmol), tetrabutylammonium hydrogen phosphate (1.7 g, 5.02 mmol) were suspended in a two phase solution of CH_2Cl_2/$NaHCO_3$ (50:50). The reaction mixture was stirred at rt TLC analysis (EtOAc:Petroleum ether, 1:1) showed that the reaction was complete after 3 h. The organic layer was washed with water (3 x 50 mL) and aq. sodium bicarbonate (3 x 50 mL), dried ($MgSO_4$) and the excess solvent was removed and the residue was purified by silica gel chromatography (EtOAc:petroleum ether, 1:4) to yield the product as a white solid (1.5 g, 80%).

(iii) *2,3,4,6-Tetra*-O-*acetyl-β-D-galactopyranosylamine:* 2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosylazide (15.71 g, 42 mmol) was suspended in ethanol (200 mL) and Pd-C (1.18 g) was added. The reaction vessel was shaken under a hydrogen atmosphere at a pressure of 3 atm. Analysis by TLC (EtOAc : Petroleum ether, 1:1) showed that the reaction was complete after 24 h. The catalyst was filtered off and excess solvent was removed to give an orange oil (14.37 g). This oil was purified by silica gel chromatography (1:1 EtOAc:Pet) to give the amine **1**[1] as a white solid (9.96 g, 68%); $[\alpha]_D$ +29.5 (c 1.0, MeOH); mp 134-136 ^oC (Lit.[2] mp 139 ºC; $[\alpha]_D$ +26.7 (c 1.0, MeOH).

Preparation of 2

(i) 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosylamine (2.0 g, 5.76 mmol) and succinic anhydride (5.76 g, 57.6 mmol) were suspended in CH_2Cl_2 (50 mL) and DIPEA (1.0 mL, 5.76 mmol) was added and the reaction was allowed to stir at rt under N_2. More DIPEA (2.0 mL, 11.52 mmol) was added after 48 h and analysis by TLC (MeOH:EtOAc, 1:4) indicated that the reaction was complete after stirring for another 24 h. The reaction mixture was diluted with CH_2Cl_2 (50 mL), washed with 1M HCl (2 x 100 mL), dried ($MgSO_4$) and excess solvent was removed and the residue purified by silica gel chromatography (EtOAc:petroleum ether, 2:1) to give **2** as an off-white solid (1.45 g, 56%): R_f 0.37 (EtOAc); $[\alpha]_D$ +28 (c 0.5, $CHCl_3$); mp 57-60 ºC; ^{1}H-NMR δ (300MHz, $CDCl_3$) 6.90 (br s, 1H, CO_2H), 6.71 (d, 1H, J 9.0, NH), 5.28 (t, 1H, J 9.0, H-1), 5.44 (d, 1H, J 3.0, H-4), 5.16 (dd, 1H, J 3.0 and 9.0, H-3), 5.11 (t,1H, J 9.0, H-2,),

[1] Acetate migration onto the amino group can occur, the amine was usually stored in a freezer at 40 ºC.
[2] A. Bertho and J. Maier, *Justus Liebigs Ann. Chem.* **1932**, *50*, 498.

4.04-4.16 (overlapping signals, 3H, H-5,6a and 6b), 2.36-2.80 (ms, 4H, CH_2CH_2), 2.06, 2.05, 2.04, 2.00 (each s, each 3H, each CH_3); ^{13}C-NMR δ (300 MHz, $CDCl_3$) 176.6 (COOH), 172.3,171.5, 170.7, 170.2, 170.0 (each C=O), 78.4 (C-1), 72.3, 70.9, 68.3, 67.2 (C-2—5), 61.2 (C-6), 30.6, 28.6 (CH_2CH_2), 20.7 20.6 (each 2 signals, each CH_3); ν_{max}(KBr) 3051, 2981, 2693, 1787, 1666, 1599, 1538, 1371, 1227cm^{-1}; HRMS 470.1274 (M+Na), required 470.1274.

Preparation of 3

2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosylamine (0.78 g, 2.2 mmol), **2** (0.5 g, 1.12 mmol), formaldehyde (0.15 mL, 2.2 mmol) were suspended in methanol (25 mL) and the reaction mixture was stirred at rt for 1 h. Methyl isocyanoacetate (0.2 mL, 2.2 mmol) was then added and the reaction mixture was allowed to stir at rt Analysis by TLC (EtOAc) as eluant showed the reaction was complete after 24 h. Excess solvent was removed and the product (1.55 g) which was purified by silica gel chromatography (EtOAc) to give **3** as a white foam (0.5 g, 50%): R_f 0.075, (EtOAc); $[\alpha]_D$ +16 (c 0.5, $CHCl_3$); mp 100-102 ^oC; ^{1}H-NMR δ (300 MHz, $CDCl_3$) 7.19 (t, 1H, J 6.0, N*H*-CH_2), 6.69 (d, 1H, , J 9.5, N*H*-CH), 5.90 (d, 1H, J 9.0, CH-N*H*), 5.46 (d, 1H, J 1.5, H-4), 5.42 (d, 1H, J 3.0, H-4'), 5.25 (t, 1H, J 9.5, H-1), 4.95-5.19 (overlapping signals, 4H, H-2, 2', 3, 3'), 3.71-4.27 (overlapping signals, 10H, H-5, 5', 6a, 6a', 6b, 6b', NHCH_2CO-, NHCOCH_2N-) 3.76 (s, 3H, OCH_3), 2.49-2.67 (m's, 4H, CH_2CH_2CO-), 2.18, 2.13, 2.04, 2.03, 2.02, 2.00, 1.99, 1.98 (each s, each 3H, -$OCOCH_3$); ^{13}C-NMR δ ($CDCl_3$) 173.0, 171.8, 171.6, 170.5 (2 signals), 170.4, 170.3, 170.0 (2 signals), 169.8, 169.7 (each C=O), 80.4, 78.1 (C-1 and C-1'), 73.6, 72.4, 72.3, 70.9, 70.7, 68.1, 67.2, 67.1 (C-2-5 and C2'-5'), 61.6, 61.3 (C-6, C-6'), 52.6 (OCH_3), 47.5, 41.0, 31.0, 28.5 (each CH_2-), 21.0, 20.7, 20.6, 20.5 (each *C*H_3); ν_{max}(KBr) 3381, 2951, 2855, 1752, 1676, 1541, 1439, 1371, 1229, 1050 cm^{-1}; HRMS 928.2811 (M+Na), required 928.2811.

Preparation of 4

Compound **3** (0.15 g, 0.17 mmol) was suspended in methanol (5 mL) and then NaOMe in MeOH (0.1 mL of a 0.25 M solution) was added and the reaction mixture was stirred at rt (40 h). Amberlite (H^+) was added after the reaction was complete and the mixture was stirred for a few minutes and was then filtered and the solvent removed to give **4** as a yellow oil (91 mg, 97%). The product was further purified using silica gel chromatography (1:1 MeOH:EtOAc) and reverse phase HPLC (C-18 semi-preparative column, AcCN:H_2O gradient eluant, 1:99 to 100:0 after 40 min.) to give the desired compound as an off-white solid (retention time 7.75 min.): R_f 0.31 (MeOH); $[\alpha]_D$ -25 (c 0.02, MeOH); ^{1}H-NMR δ (600 MHz, D_2O, 20 ºC) 5.45 (d, 1H, J = 9.0, H-1, *Z*-isomer) 5.19 (d, 1H, J 8.0, H-1, *E*-isomer), 4.97 (d, 1H, J 9.0, H-1', E and Z-isomer), 3.70 (s, 3H, OCH_3), 3.50-4.40 (ms, 16H, H-2, 2', 3, 3', 4, 4', 5, 5', 6a, 6b, 6a', 6b', CH_2CONH-, $C\underline{H}_2NHCO$-), 2.89 (ms, 2H, CH_2CH_2CONH-), 2.6 (ms, 2H, CH_2CH_2CONH); ^{13}C-NMR δ (D_2O) 174.7, 175.3, 178.2, 178.9 (each *C*=O), 89.0 (C-1 E-isomer, (85.3 (C-1, Z-isomer), 82.5 (C-1'), 80.2, 79.4, 76.1, 75.4, 72.1, 71.4, 70.7 (C-2-5 and C-2'-5'), 63.8, 63.7 (C-6 and C-6'), 55.6 ($O\underline{C}H_3$), 47.4, 43.9, 32.9, 30.8 (CH_2CO-); ν_{max}(film) 3512, 2661, 2293, 2256, 1633, 1426, 1270, 1185cm^{-1}; HRMS 592.1966 (M+Na), required 592.1966.

Preparation of 5

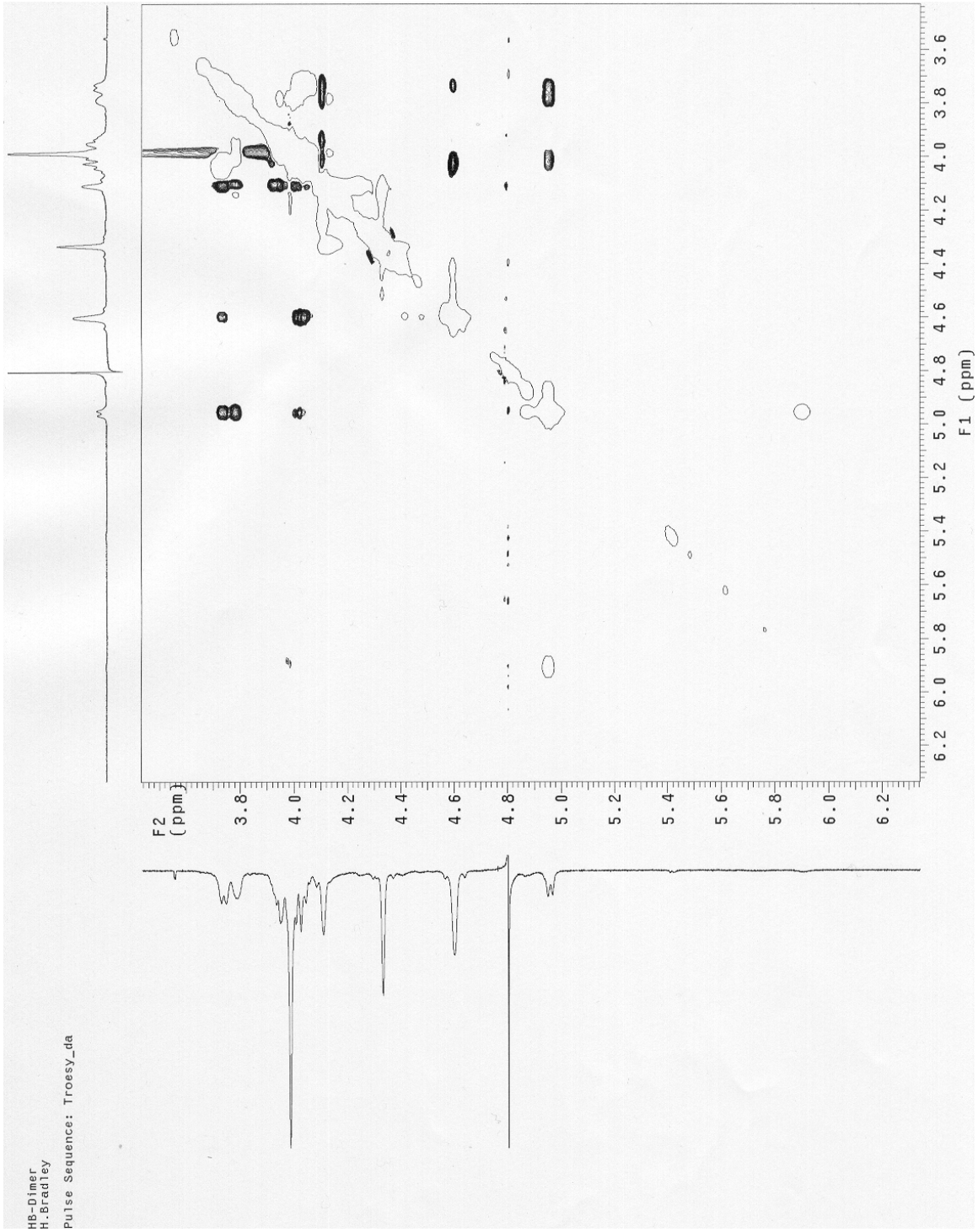
Terephthalic acid (0.2 g, 1.2 mmol), tetra-O-acetyl-β-D-galactopyranosylamine (0.84 g, 2.4 mmol) and formaldehyde (0.17 mL, 2.4 mmol) were suspended in methanol (20 mL) and stirred at rt for 1 h. Methyl isocyanoacetate (0.22 mL, 2.4 mmol) was then added and the reaction mixture was allowed to stir at rt. TLC analysis (EtOAc) showed that the reaction was complete after 48 h. The solvent was removed and the residue purified by silica gel chromatography (EtOAc) to give **5** as an off white foam (0.45 g, 34%): R_f 0.21 (EtOAc); mp 115-118 ºC; $[\alpha]_D$ +15 (c 0.02, $CHCl_3$); ^{1}H-NMR δ (270 MHz, C_5D_5N, 100 ºC) 8.16 (t, 2H, J 3.0, N*H*CH_2); 7.96 (s, 4H, aromatic H); 5.80-5.87 (overlapping signals, 6H, H-1,2,4), 6.05 (dd, 2H, J 3.5, 9.0, H-3), 3.90-4.60 (ms, 14H, H-5,6a,6b, methylenes), 3.72 (s, 6H, OMe), 2.16, 2.14, 2.09, 2.05 (each s, each 6H, OAc); ^{13}C-NMR δ (C_5D_5N, 100 ^{o}C) 171.8, 170.3, 169.9, 169.6, 169.4, 168.5 (each $\underline{C}$=O), 137.6 (s, aromatic C), 127.6 (d, aromatic CH), 73.6, 71.9, 68.1, 67.4 (C-2-5), 61.8 (C-6), 51.5

($O\underline{C}H_3$), 41.5 ($\underline{C}H_2$), 20.1, 20.0, 19.9, 19.6 (OAc); ν_{max}(film) 3058, 2333, 1749, 1667, 1536, 1439, 1371, 1224, 1055 cm^{-1}; MS 1105.4 (M+Na), requires 1105.3.

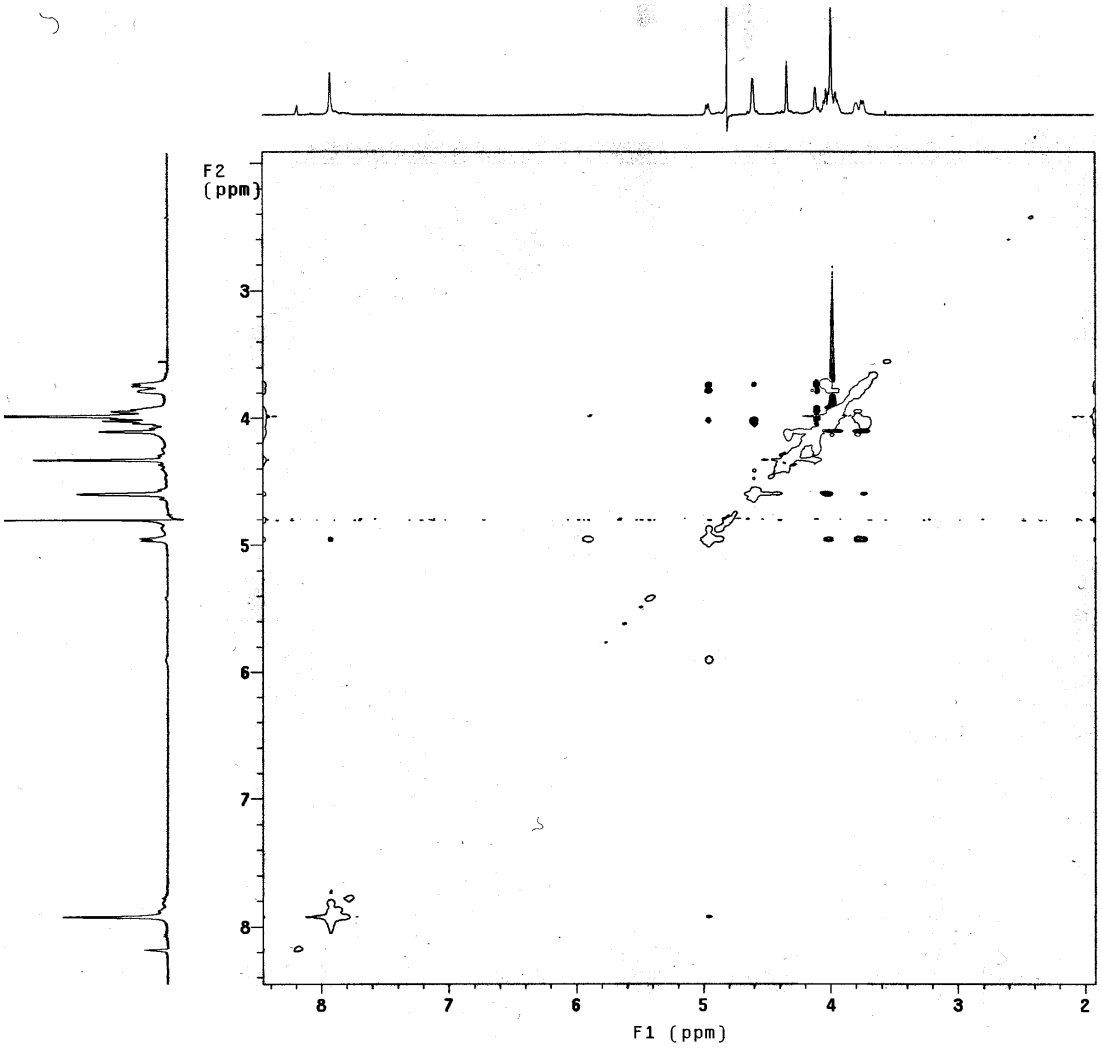
Preparation of 6.

Compound **5** (72 mg, 0.067 mmol) was suspended in MeOH (5 mL) and NaOMe in MeOH (0.1 mL of a 0.25 M solution) was then added. TLC analysis (MeOH) showed that the reaction was complete after 1 h. Amberlite (H^+) was added and after a five minutes, the reaction mixture was filtered and excess solvent removed on a rotary evaporator to give **6** as a yellow oil (48 mg, 98%). The compound was further purified by reverse phase HPLC (C-18 semi-preparative column, AcCN:H_2O, 1:99 to 5:95 gradient elution over 1 h) and after lyophilisation was a white solid (retention time, 11.5 min); R_f 0.48 (MeOH); $[\alpha]_D$ +262.5 (c 0.008, MeOH); ^{1}H-NMR δ (500 MHz, D_2O, 10 ºC) 7.40-7.60 (ms, 4H, aromatic-H), 5.58 (d, 1H, J 9.0, H-1 (E/Z isomer), 4.61 (d, 2H, J 9.0, H-1 (E/E isomer)) 4.60 (d, 1H, J 9.0, H-1 (E/Z isomer), 4.22 (AB d, 4H, J 16.5, $NC\underline{H}_2CONHCH_2$), 3.92 (AB d, 4H, J 17.5, $NCH_2CONHC\underline{H}_2$), 3.92 (d, 2H, J 3.0, H-4), 3.69 (t, 2H, J 9.0, H-2), 3.51-3.71 (overlapping signals, 10H, H-6a, 6b, OCH_3), 3.42 (dd, 2H, J 8.0, 3.5, H-5), 3.39 (dd, 2H, J 3.0, 9.0); ^{13}C-NMR δ (D_2O) 174.6, 172.3 (2 signals, each C=O), 136.4 (s, aromatic C), 128.0 (d, aromatic CH), 88.5 (C-1, *EE* isomer), 83.5 (C-1, *ZE* isomer), 77.8, 73.0, 69.0, 68.1 (C-2-5), 61.5 (C-6), 53.2 (OCH_3), 45.3, 41.8 (each CH_2); ν_{max}(film) 3383, 3045, 2356, 1620, 1421, 1255, 1109, 725cm^{-1}; HRMS 769.2392 (M+Na), required 769.2392.

2D ROESY (500 MHz, D_2O, 40 °C) of 6



2D ROESY (500 MHz, D_2O, 40 ºC) of 6



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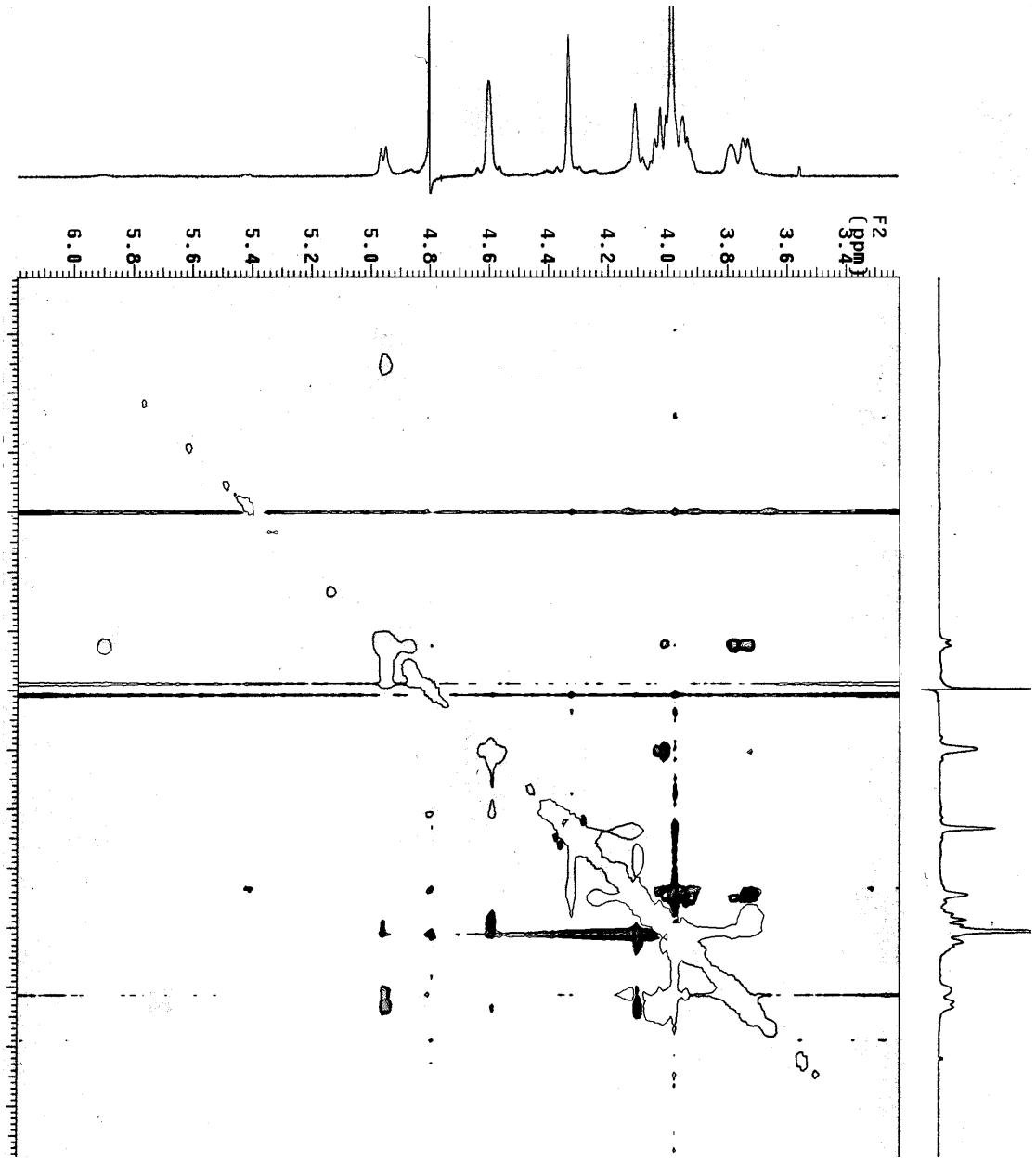
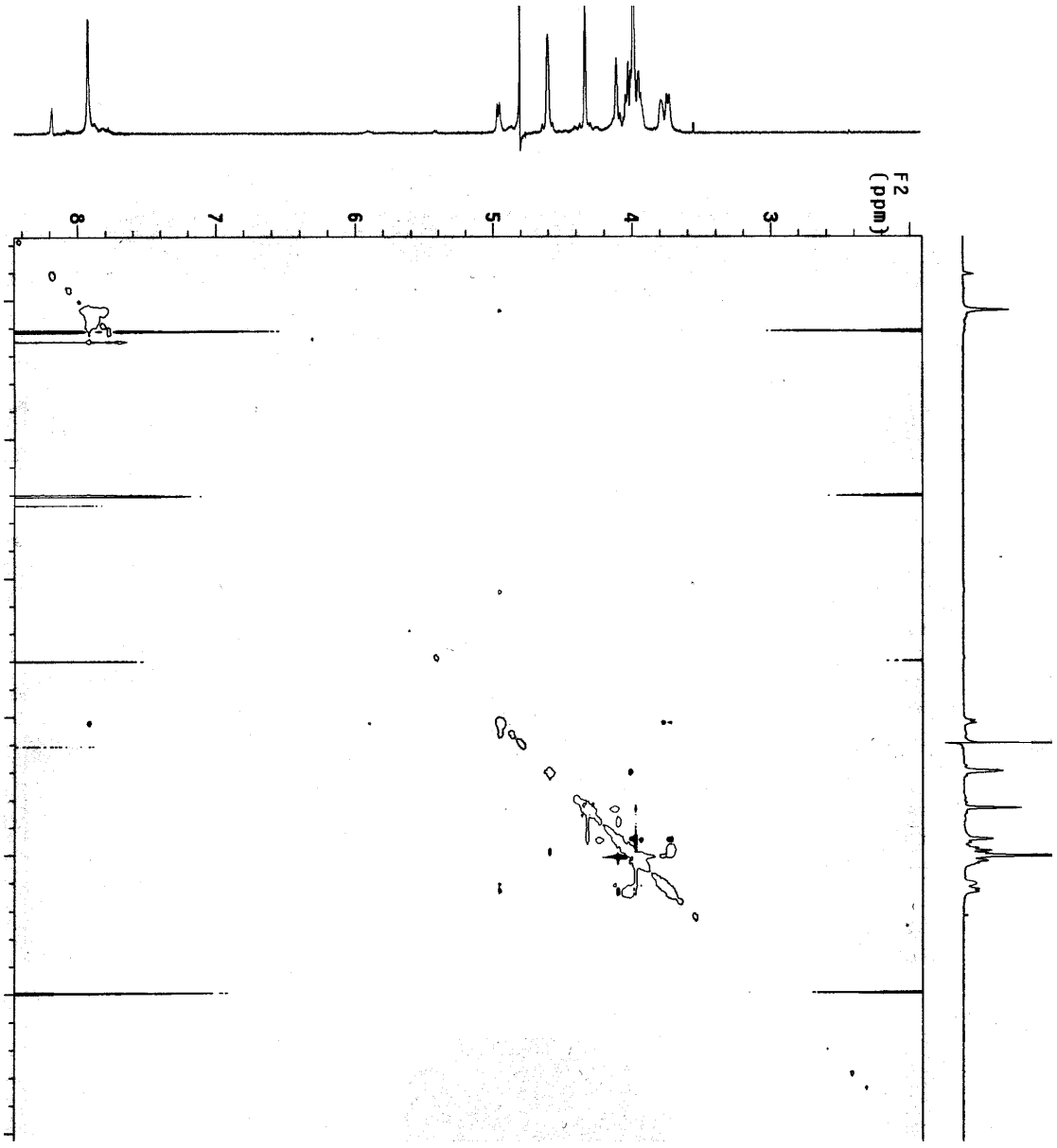
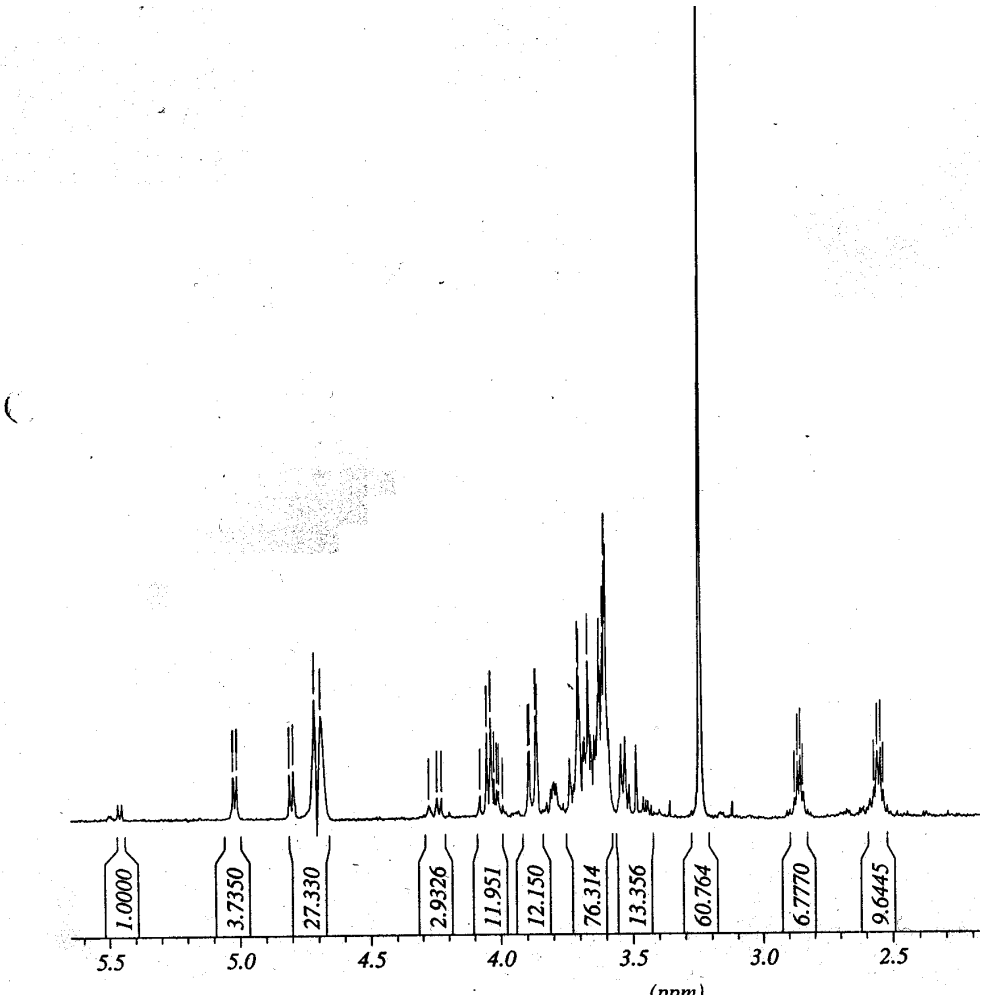


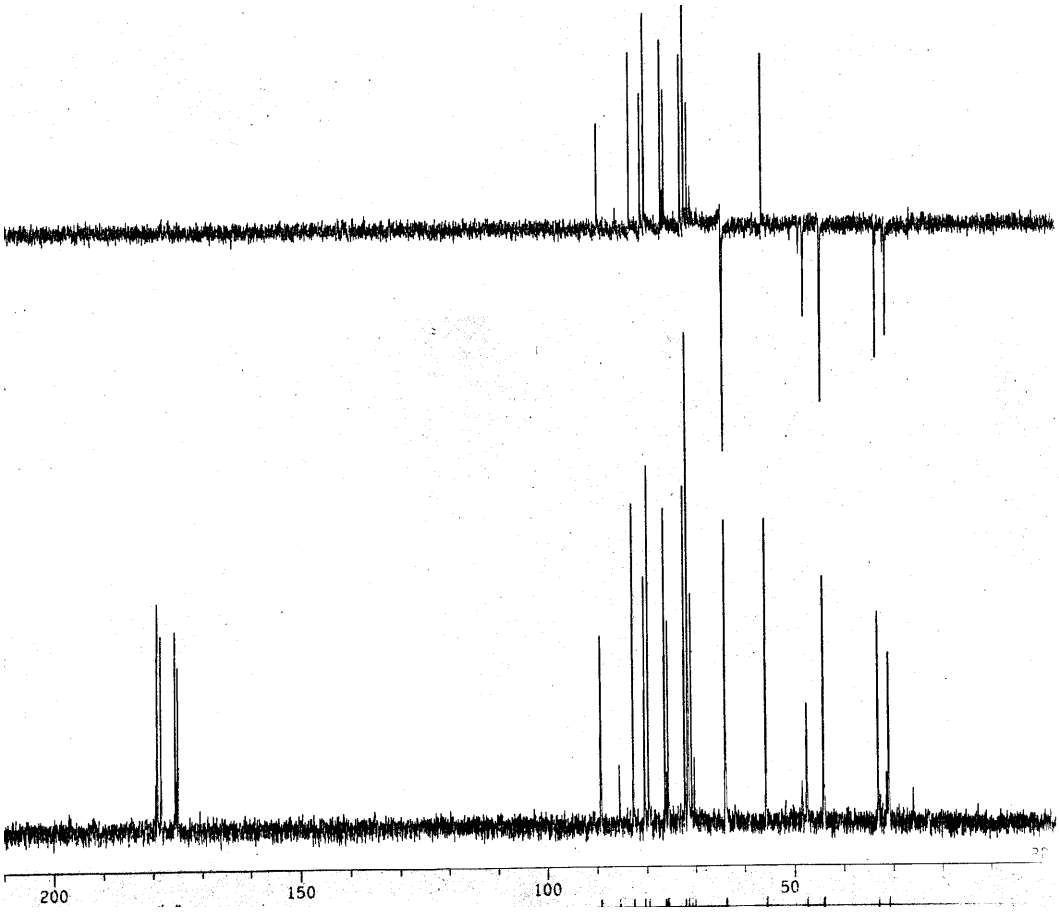
2D NOESY (500 MHz, D_2O, 40 ºC) for 6



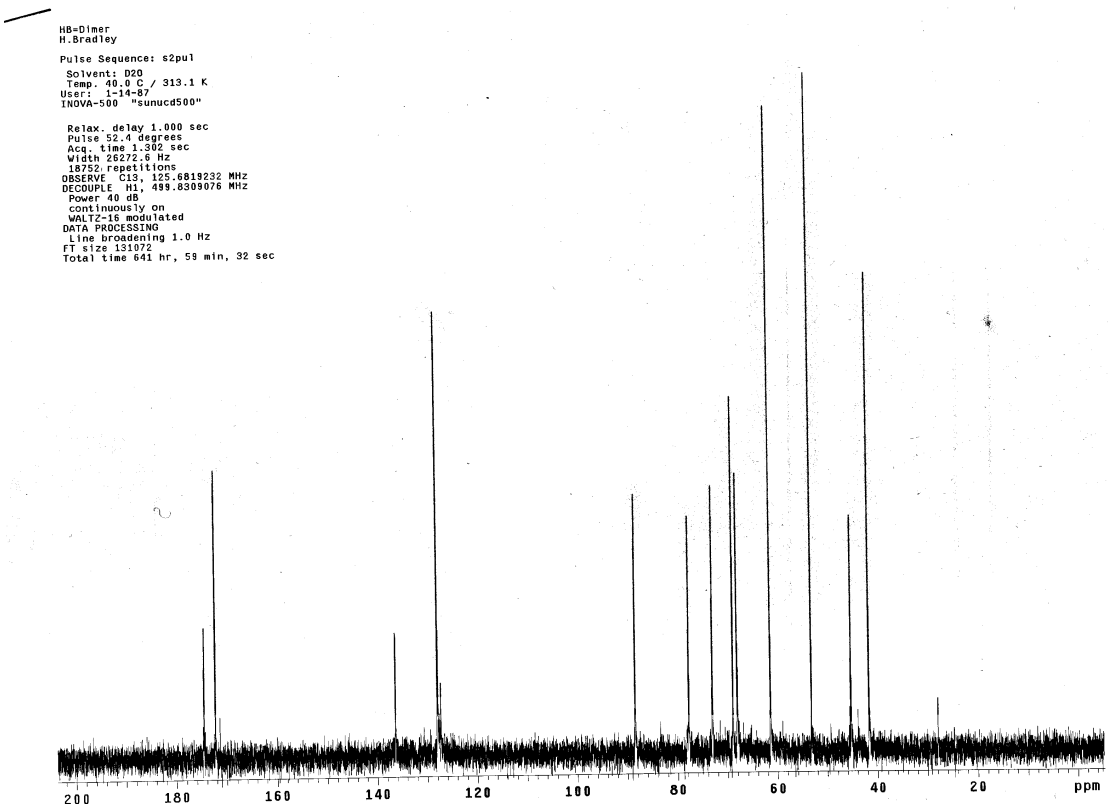
1H-NMR (600 MHz) of 4



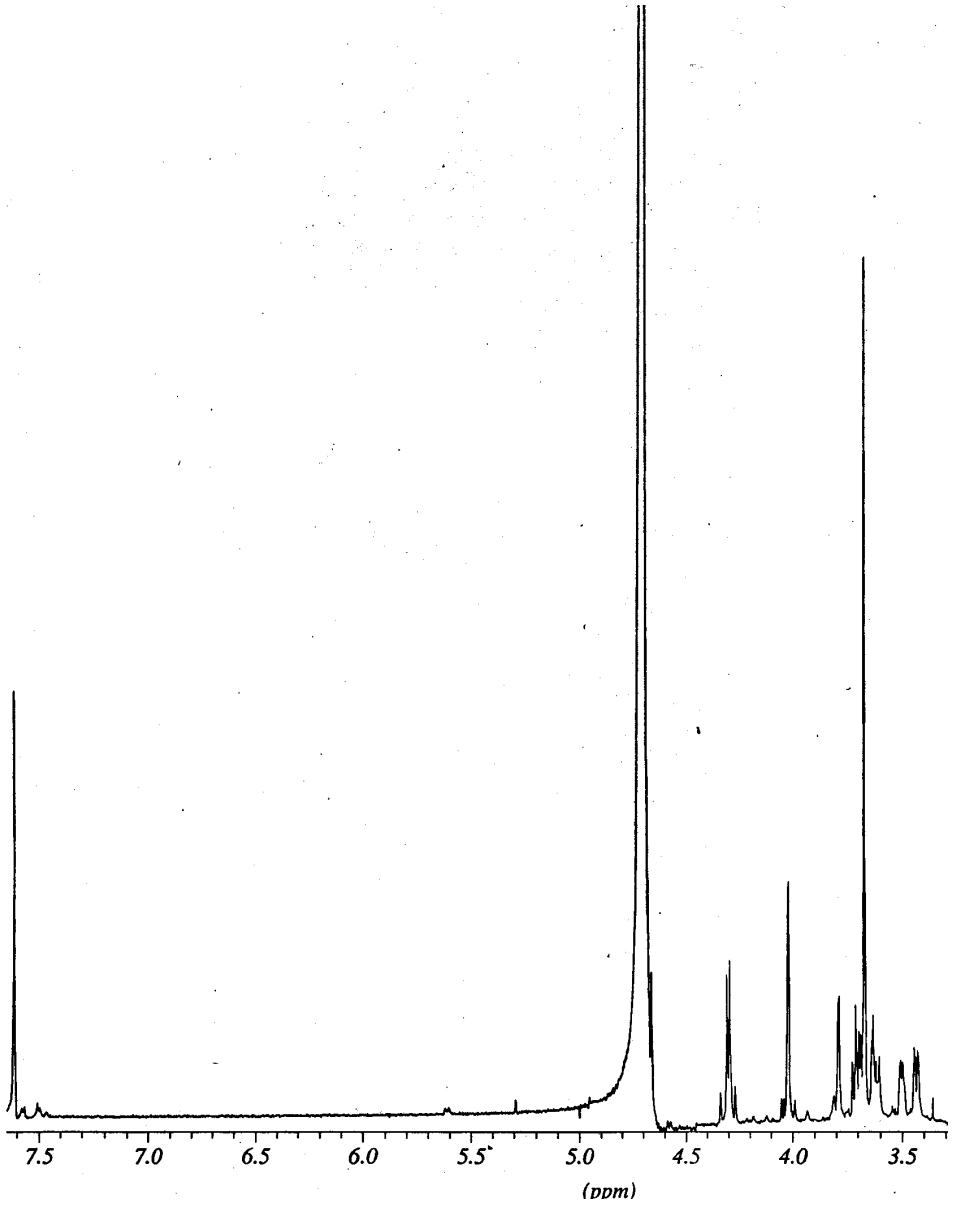
^{13}C-NMR and DEPT of 4



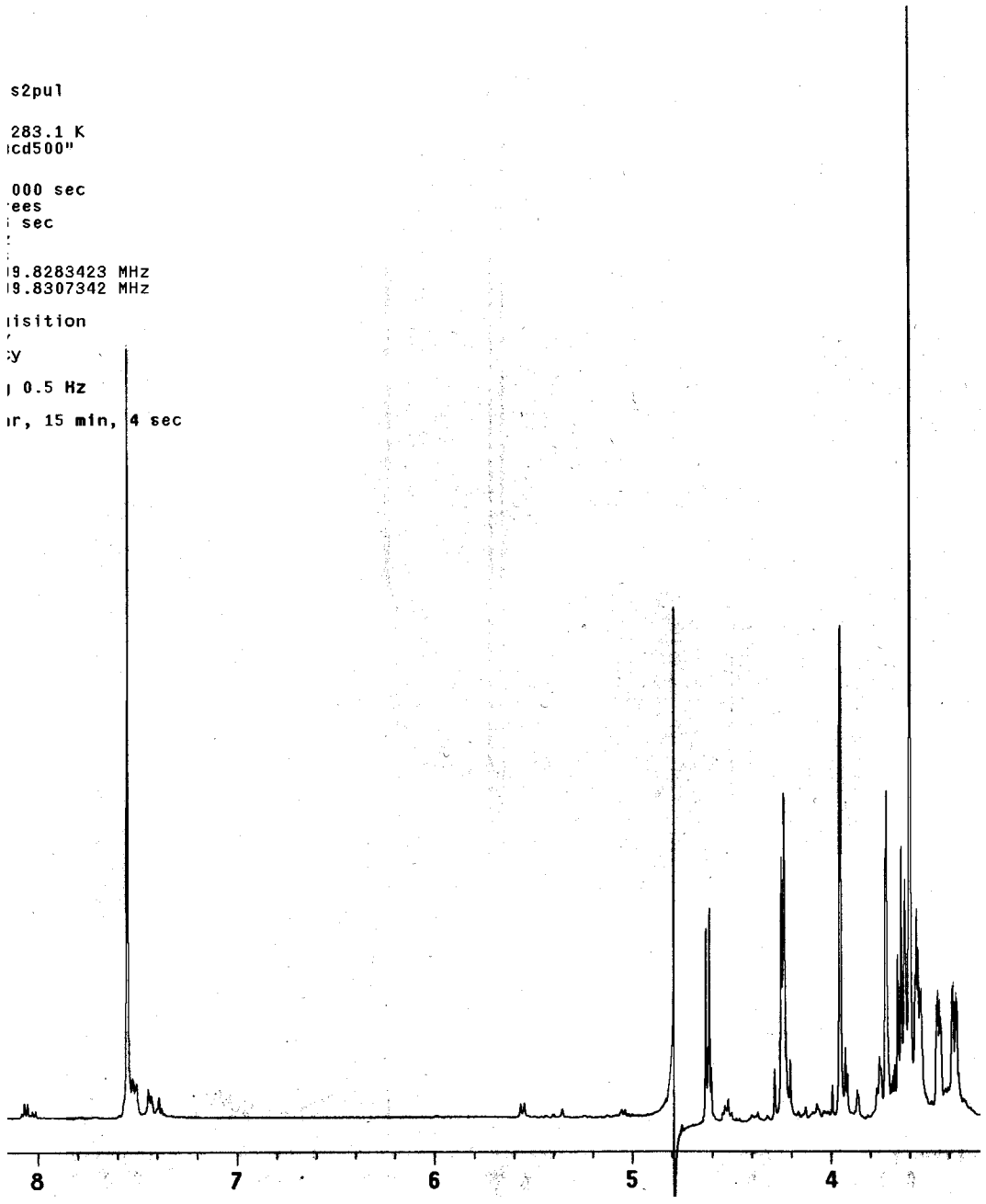
^{13}C-NMR spectrum of 6



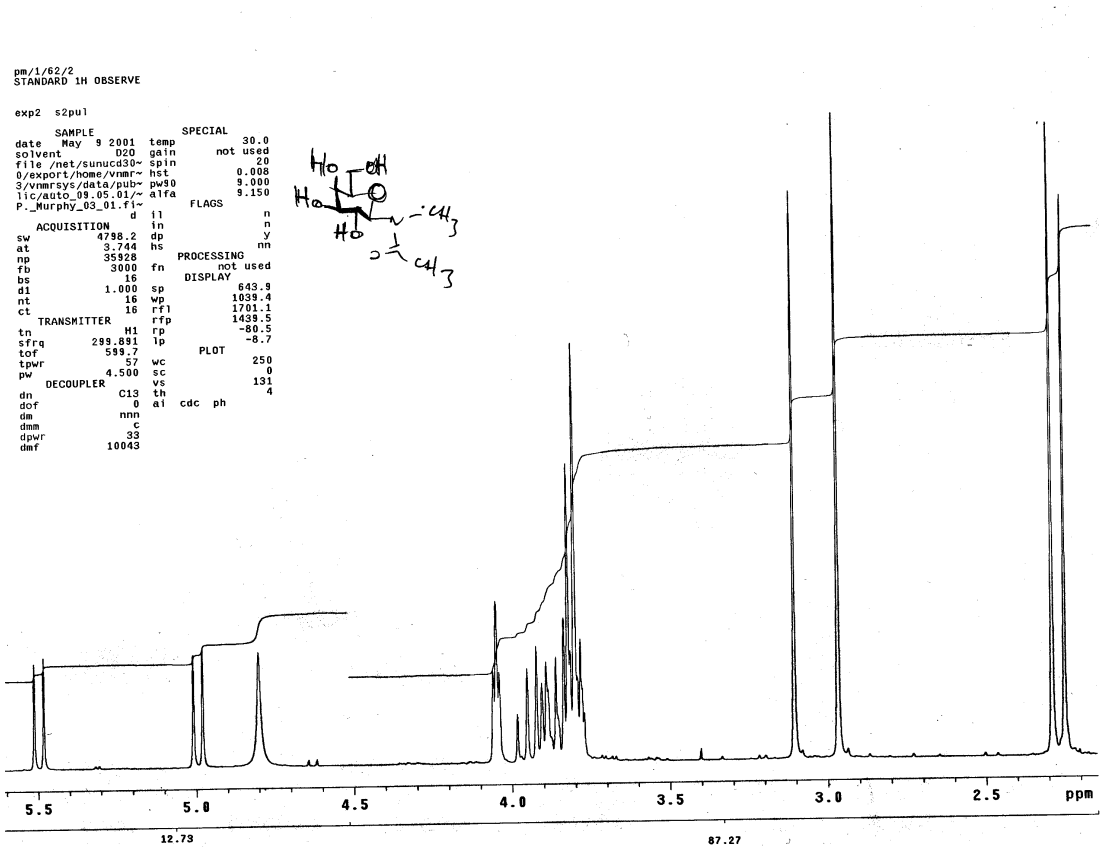
^{1}H-NMR (600 MHz, 20 °C) of 6



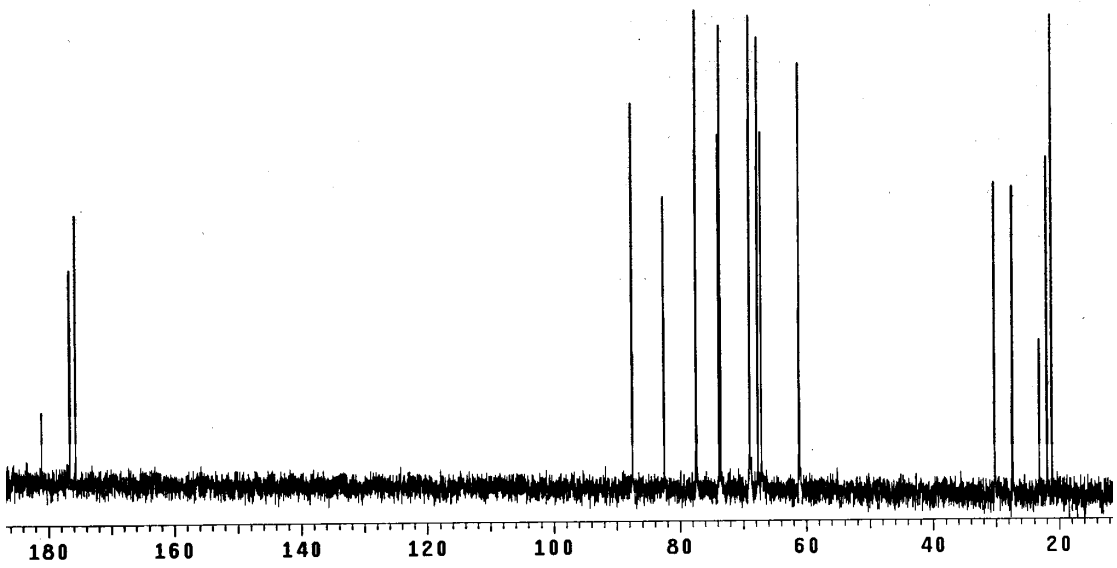
^{1}H-NMR (500 MHz, D_2O, 10 °C)



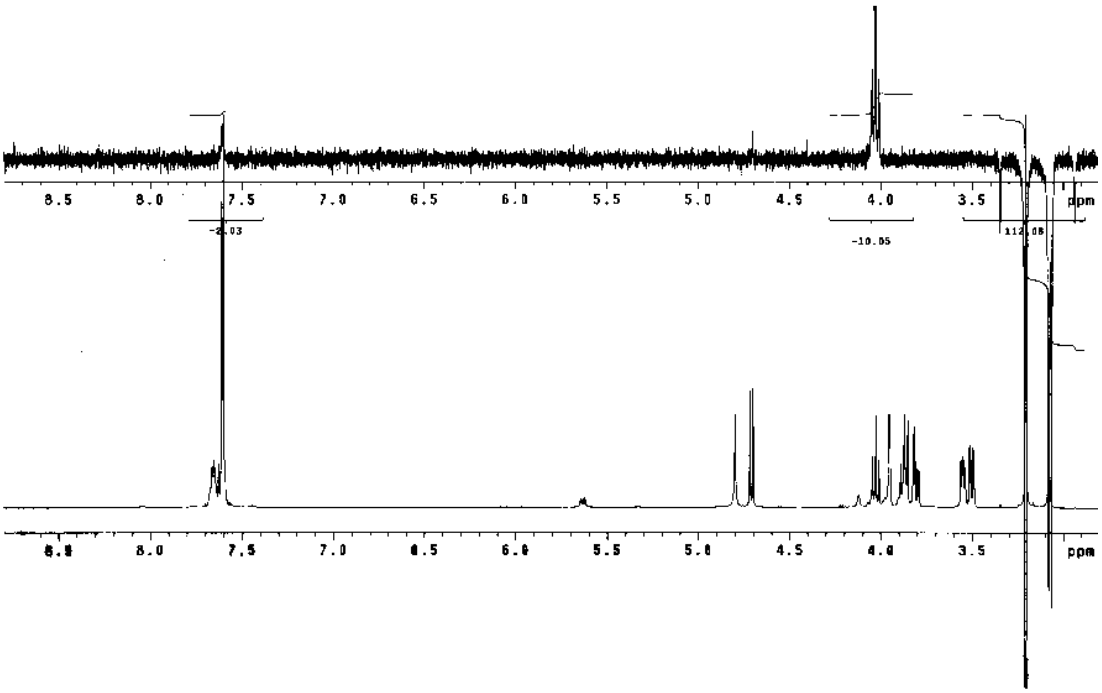
1H-NMR (300 MHz, D_2O) of 7



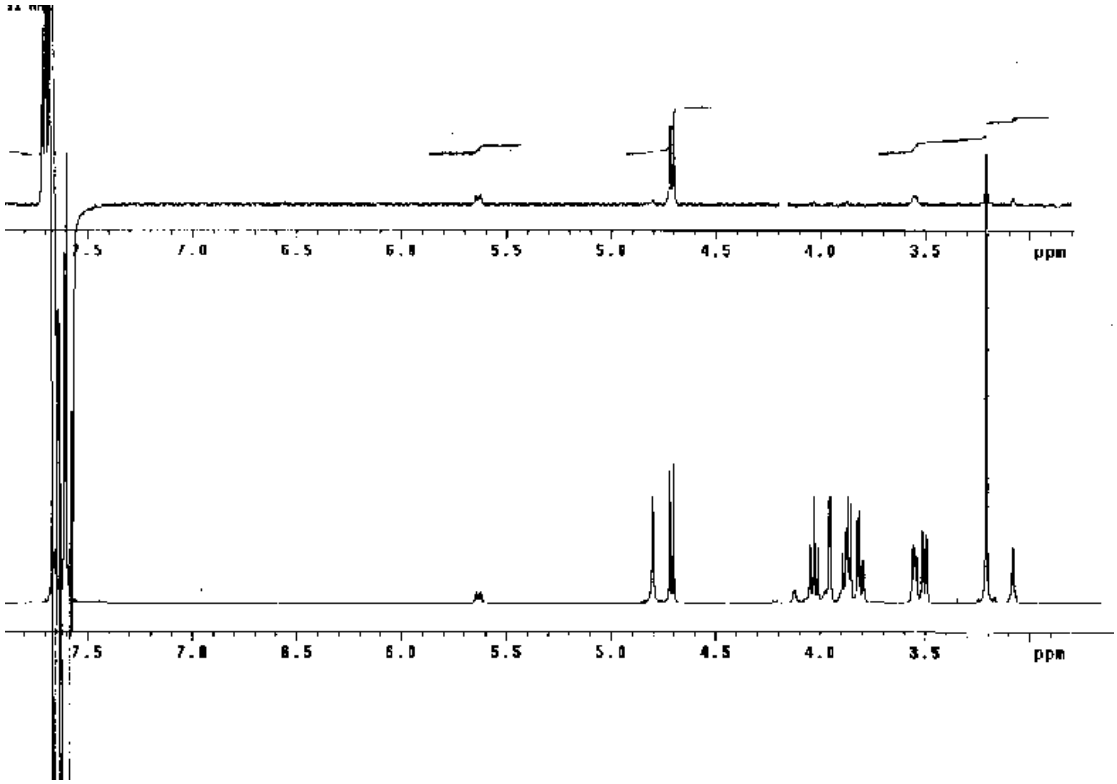
^{13}C-NMR of 7



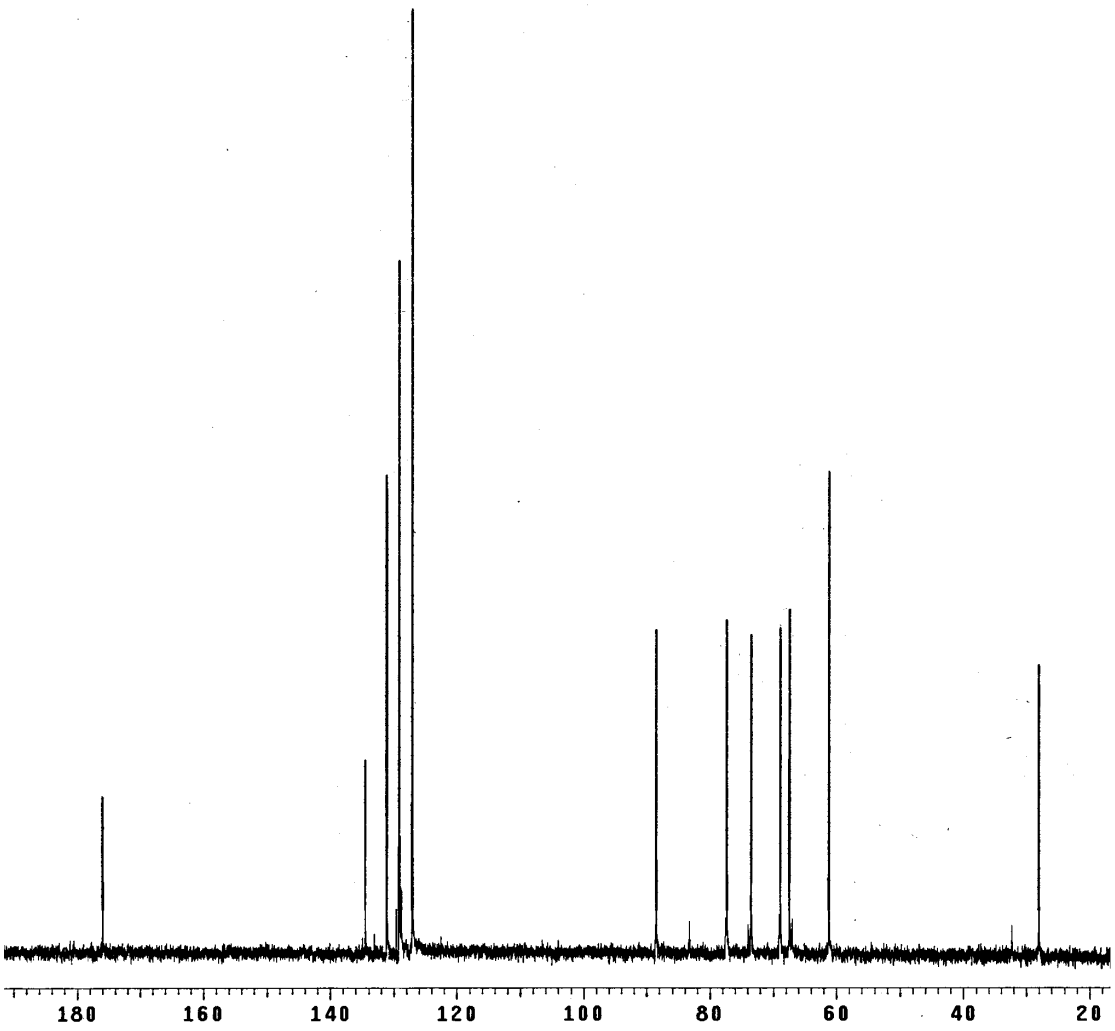
1D-NOE of 8 (irradiation of methyl signal)



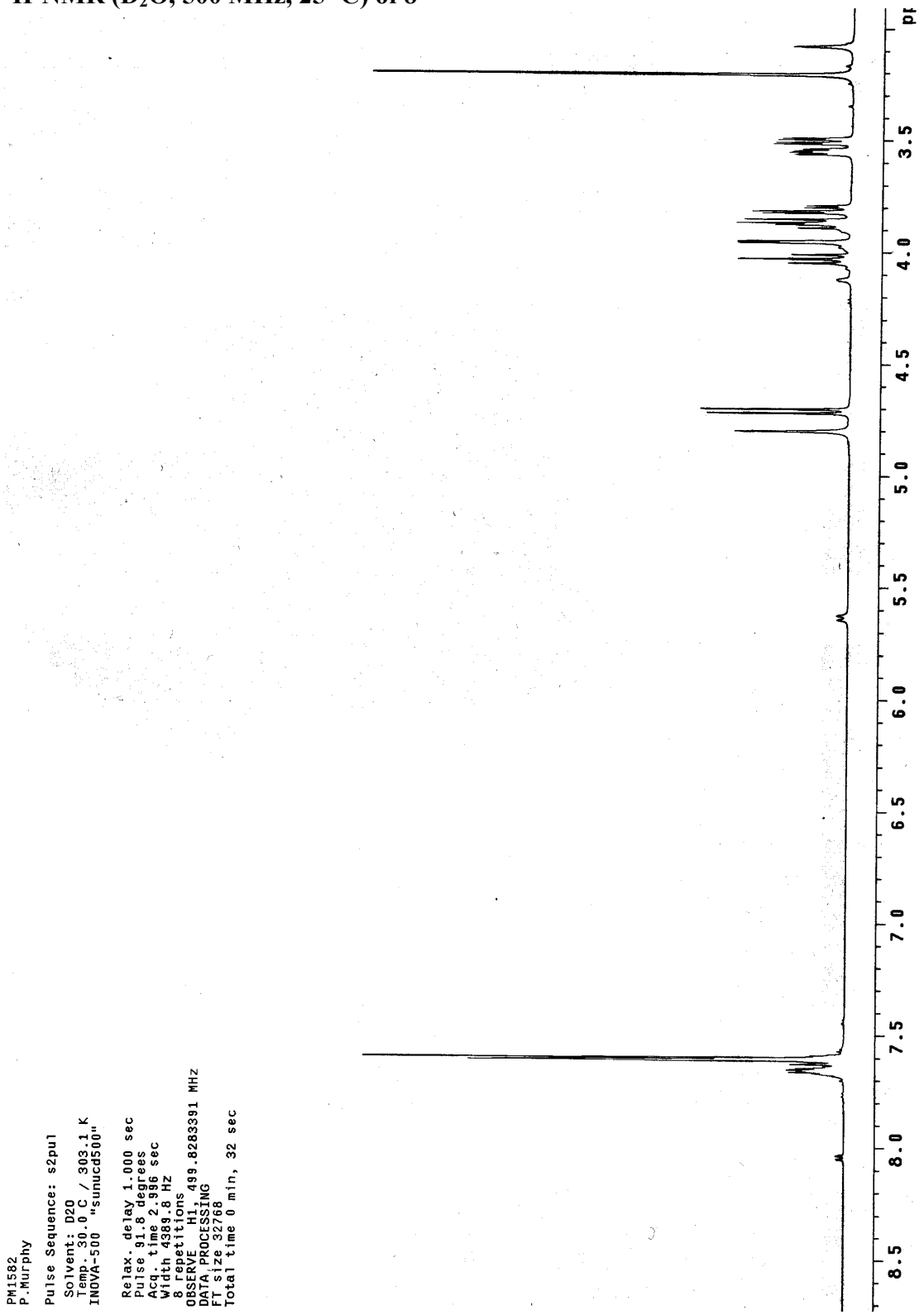
1D NOE of 8 (irradiation of aromatic signal)



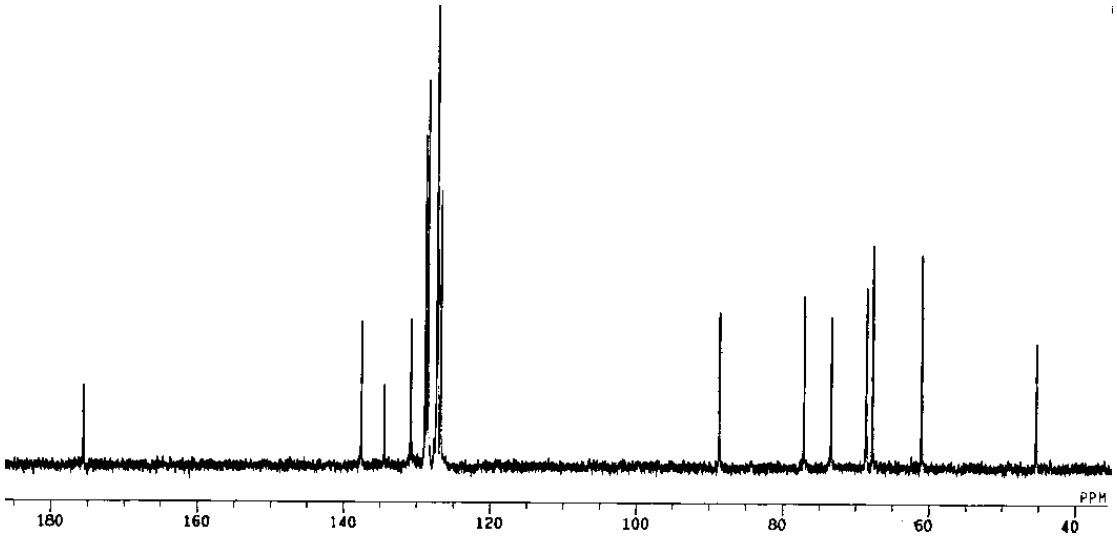
^{13}C-NMR of 8



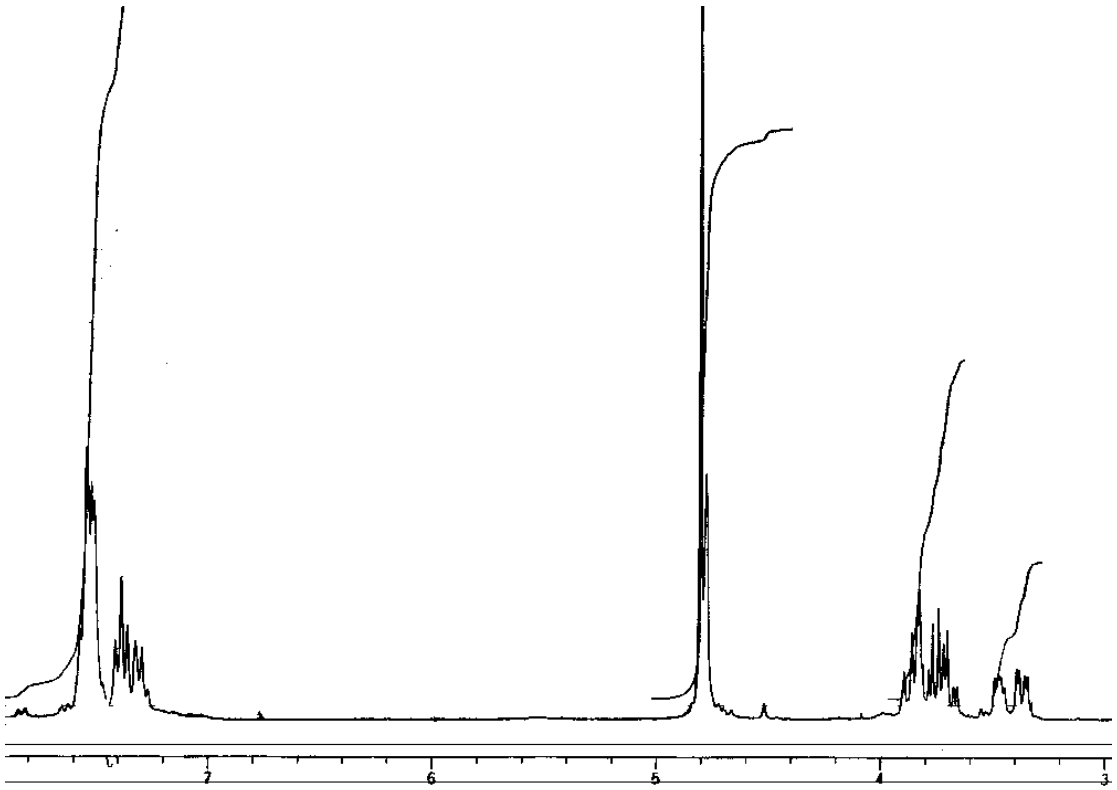
^{1}H-NMR (D_2O, 500 MHz, 25 °C) of 8



^{13}C-NMR of 9

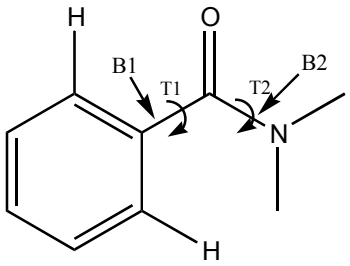


1H-NMR of 9 (270 MHz, D_2O, 20 ºC)



Statistical Data on X-ray structures from Cambridge Crystallographic Database Centre.

Search Fragment



N = No of Structures