An straightforward entry to new pyrazolo-fused dibenzo[1.4]diazepines

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Supporting Information

1. General remarks.

All reagents were purchased and used as received except when indicated. Chemical shifts (δ) are given in ppm downfield from Me_4Si and refer as internal standard to the residual solvent (unless indicated) $CDCl_3$: (δ = 7.26 for ^{1}H and 77.00 for ^{13}C). Coupling constants, *J*, are reported in hertz (Hz). Melting points were determined in a capillary tube and are uncorrected. TLC was carried out on SiO_2, and the spots were located with UV light. Flash chromatography was carried out on SiO_2. Drying of organic extracts during work-up of reactions was performed over anhydrous Na_2SO_4. Evaporation of solvents was accomplished with a rotary evaporator.

2. Synthesis of enaminones 3. General procedure.[1] DMFDA (34.6 mmol) was added to a solution of acetophenone (24.7 mmol) in dry toluene (18 mL) under argon. The reaction mixture was heated to 110ºC until TLC showed the completion of the reaction (1-2 days). After cooling, the solvent was evaporated under reduced pressure and the so-obtained residue was purified by crystallization.

***(E)*-3-(*N,N*-Dimethylamino)-1-(2-nitrophenyl)-2-propen-1-one (3a)** 95% orange prisms**.** m.p.: 124-127^{o}C (EtOAc) Lit.[2] 127-130^{o}C (toluene).

***(E)*-3-(*N,N*-Dimethylamino)-1-(4,5-dimethoxy-2-nitrophenyl)-2-propen-1-one (3b).** 92% yellowish powder**.** m.p. 142-145^{o}C (EtOAc). ^{1}H NMR: (250 MHz, $CDCl_3$) δ : 2.84 (3H, bs), 3.07 (3H, bs), 3.95 (3H, s), 3.96 (3H, s), 5.19 (1H, d, *J* 12.7), 6.83 (1H, s), 7.58 (1H, s). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 36.9, 44.8, 56.1, 56.2, 96.5, 106.7, 109.9, 132.7, 138.8, 148.2, 152.8, 154.4, 188.9. IR: 1637, 1519, 1360, 1305. HRMS: Calcd for $C_{13}H_{16}N_2O_5$ 280.1059; found 280.1058

***(E)*-3-(*N,N*-Dimethylamino)-1-(4,5-methylenedioxy-2-nitrophenyl)-2-propen-1-one (3c).** 84% orange powder. m. p. 165-168^{o}C (EtOAc). ^{1}H NMR: (250 MHz, $CDCl_3$) δ : 2.83 (3H, bs), 3.07 (3H, bs), 5.17 (1H, d, *J* 12.3), 6.11 (2H, s), 6.80 (1H, s), 7.46 (1H, s). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 37.2, 44.7, 95.6, 103.0, 104.9, 107.8, 135.4, 141.3, 147.8, 151.6, 154.5, 188.4. IR: 1519, 1330. HRMS: Calcd for $C_{12}H_{12}N_2O_5$ 264,0746; found 264,0747

***(E)*-1-(2-Bromophenyl)-3-(*N,N*-dimethylamino)-2-propen-1-one (3d).**[3] 90% yellowish oil. ^{1}H NMR: (250 MHz, $CDCl_3$) δ : 2.78 (3H, bs), 2.97 (3H, bs), 5.21 (1H, d, *J* 12.7), 7.08-7.15 (1H, m), 7.20-7.25 (2H, m), 7.45-7.49 (1H, m). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 37.0, 44.9, 95.6, 119.0, 126.8, 128.3, 129.6, 132.7, 143.0, 155.1, 191.0. IR: 1645.

3. Synthesis of hydrazines 4. General procedure.[4] Commercially available bromoaniline (8.1 mmol) was added at 0ºC to a vigorously stirred aqueous solution of HCl (35%, 2.9 ml). To the so-obtained acid suspension, a solution of $NaNO_2$ (15.7 mmol) in H_2O (1.8 mL) and a solution of $SnCl_2$ (19.8 mmol) in HCl 6 M (8.2 mL) were added. The reaction crude was stirred at room temperature for 24 hours and the mixture was basified with NaOH 12 M. The aqueous phase was extracted with Et_2O (3 x 25 mL), the

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[1] SanMartin, R.; Martínez de Marigorta, E.; Domínguez, E. *Tetrahedron* **1994**, *50*, 2255-2264.

[2] Paradkar, V. M.; Latham, T. B.; Krishnaswami, A. *J. Heterocycl. Chem.* **1993**, *30*, 1497-1500.

[3] Boyd, D. B.; Lifer, S. L.; Marshall. W. S.; Palkowitz, A. D.; Pfeifer, W.; Reel, J. K.; Simon, R. L.; Steinberg, M. I.; Thrasher, K. J.; *et al.* (Lilly, Eli and Co.) EP 19931215, 1993 (C. A. 122: 290852).

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combined organic extracts were dried over anhydrous sodium sulfate and concentrated in vacuo. A saturated solution of HCl in Et_2O was added dropwise. The hydrochloride was filtered and recrystallized from Et_2O.

2-Bromo-4,6-difluorophenylhydrazine hydrochloride (4b). m.p. 155-160°C (dec.). ^{1}H NMR: (250 MHz, $CDCl_3$) δ**:** 3.90 (2H, bs), 5.20 (1H, bs), 6.80-6.89 (1H, m), 7.05-7.10 (1H, m). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 104.5 (dd, *J* 25.1, *J* 25.1), 114.3 (dd, *J* 12.6, *J* 5.4), 115.4 (dd, *J* 25.1, *J* 3.6), 134.3 (d, *J* 10.8), 154.3 (dd, *J* 249.5, *J* 12.6), 157.0 (dd, *J* 246.8, *J* 12.6). IR: 3366, 2614. HRMS: Calcd for $C_6H_6BrClF_2N_2$ 257,9371; found 257,9371

2-Bromo-4-methylphenylhydrazine hydrochloride (4c). m.p. 172-173°C (Et^2O)**.** ^{1}H NMR: (250 MHz, $CDCl_3$) δ**:** 2.25 (3H, s), 3.57 (2H, bs), 5.58 (1H, bs), 6.97 (1H, d, *J* 8.3), 7.06-7.09 (1H, m), 7.25 (1H, s). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 20.1, 107.8, 112.2, 128.9, 129. 4, 132.7, 145.3. IR**:** 3366, 2602. HRMS: Calcd for $C_7H_{10}BrClN_2$ 235,9716; found 235,9713

2-Bromo-5-methylphenylhydrazine hydrochloride (4d). 93%, brownish podwer. m.p. 168-169°C (Et_2O). ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.31 (3H, s), 3.58 (2H, bs), 5.65 (1H, bs), 6.50 (1H, d, *J* 7.9), 6.90 (1H, s), 7.28 (1H, d, *J* 7.5).^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 21.5, 104.7, 112.9, 120.5, 132.0, 138.5, 147.1. HRMS: Calcd for $C_7H_{10}BrClN_2$ 235,9716; found 235,9718

4. Synthesis of pyrazoles 5. General procedure.[5] Hydrazine hydrochloride **4** (2.7 mmol) was added to a solution of enaminoketone **3** (2.4 mmol) in MeOH (25 mL). Next, H_2O (8 mL) was added and the resulting mixture was heated to 135ºC for 2 hours. After cooling, the suspension was diluted with EtOAc (20 mL), and the solvent was evaporated under reduced pressure. The so-obtained residue was purified by flash chromatography on silicagel with EtOAc/Hexanes as eluent.

1-(2-Bromophenyl)-5-(2-nitrophenyl)pyrazole (5a). 94% brownish podwer. m.p. 116-120°C (EtOH). ^{1}H NMR (250 MHz, $CDCl_3$) δ : 6.50 (1H, d, *J* 2.0), 7.18-7.40 (3H, m), 7.43-7.57 (4H, m), 7.80 (1H, d, *J* 1.6), 7.82-7.85 (1H, m). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 107.4, 121.6, 124.0, 124.6, 128.0, 129.8, 130.5, 132.4, 132.7, 133.1, 138.1, 139.4, 140.2, 148.5. IR: 1525, 1349. HRMS: Calcd for $C_{15}H_{10}BrN_3O_2$ 342.9956; found 342.9949.

1-(2-Bromo-4.6-difluorophenyl)-5-(2-nitrophenyl)pyrazole (5b). 95% brownish podwer. m.p. 109-111°C (Et_2O). ^{1}H NMR (250 MHz, $CDCl_3$) δ : 6.62 (1H, d, *J* 1.6), 6.79-6.87 (1H, m), 7.13-7.18 (1H, m), 7.35-7.39

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(1H, m), 7.48-7.53 (2H, m), 7.82-7.85 (1H, m), 7.84 (1H, d, *J* 2.0). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 104.3 (dd, *J* 25.1, *J* 25.1), 108.9, 116.5 (dd, *J* 25.1, *J* 3.6), 123.6, 124.0 (dd, *J* 14.4, *J* 3.6), 124.3, 124.5 (d, *J* 12.6), 130.1, 132.1, 132.2, 140.0, 141.5, 148.8, 158.8 (dd, *J* 258.5, *J* 12.6), 162.4 (dd, *J* 256.7, 12.6). IR: 1610, 1529, 1351. HRMS: Calcd for $C_{15}H_8BrF_2N_3O_2$ 378.9768; found 378.9760.

1-(2-Bromo-4-methylphenyl)-5-(2-nitrophenyl)pyrazole (5c). 68% yellow podwer m.p. 132-134°C (Et_2O). ^{1}H NMR (250 MHz, $CDCl_3$) δ : 2.26 (3H, s), 6.45 (1H, d, *J* 1.6), 7.02-7.05 (1H, m), 7.22 (1H, d, *J* 8.3), 7.32 (1H, s), 7.39-7.53 (3H, m), 7.74 (1H, d, *J* 2.0), 7.77-7.81 (1H, m). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 20.7, 107.3, 121.3, 124.0, 124.8, 128.8, 129.4, 129.7, 132.4, 132.8, 133.4, 135.5, 139.4, 140.3, 141.0, 148.6. IR: 1637, 1525, 1349. HRMS: Calcd for $C_{16}H_{12}BrN_3O_2$ 357.0113; found 357.0109.

1-(2-Bromo-5-methylphenyl)-5-(2-nitrophenyl)pyrazole (5d). 83% brownish podwer. m.p. 123-124°C (Et_2O). ^{1}H NMR (250 MHz, $CDCl_3$) δ :2.16 (3H, s), 6.44 (1H, d, *J* 2.0), 6.91-6.95 (1H, m), 7.15 (1H, d, *J* 2.0), 7.28 (1H, d, *J* 8.3) 7.35-7.47 (3H, m), 7.70 (1H, d, *J* 1.6), 7.71-7.74 (1H, m). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 20.3, 107.2, 117.9, 123.8, 124.5, 129.6, 130.3, 131.2, 132.3, 132.4, 132.6, 137.6, 138.4, 139.3, 140.2, 148.4. IR: 1530, 1349. HRMS: Calcd for $C_{16}H_{12}BrN_3O_2$ 357.0113; found 357.0115.

1-(2-Bromophenyl)-5-(4,5-dimethoxy-2-nitrophenyl)pyrazole (5e). 97% yellow podwer m.p. 155-159 °C (MeOH). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 3.81 (3H, s), 3.86 (3H, s), 6.63 (1H, d, *J* 2.0), 6.85 (1H, s), 7.14-7.35 (3H, m), 7.44 (1H, s), 7.52 (1H, dd, *J* 7.5, *J* 1.6), 7.75 (1H, d, *J* 1.6). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 56.3, 56.4, 107.0, 107.4 , 114.2, 119.1, 122.1, 128.2, 130.1, 130.7, 133.1, 138.6, 140.2, 140.5, 141.2, 149.0, 152.0. IR: 1514, 1310. HRMS: Calcd for**:** $C_{17}H_{14}BrN_3O_4$ 403.0168; found 403.0153.

1-(2-Bromophenyl)-5-(4,5-methylenedioxy-2-nitrophenyl)pyrazole (5f). 96% yellow podwer m.p. 167-170 °C (40% EtOAc/Hexanes). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 6.11 (2H, s), 6.43 (1H, d, *J* 1.6), 6.87 (1H, s), 7.20-7.42 (4H, m), 7.57 (1H, dd, *J* 7.9, *J* 1.6), 7.78 (1H, d, *J* 1.6). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 103.3, 105.3, 107.2, 111.6, 121.1, 121.9, 128.2, 130.0, 130.7, 133.2, 138.4, 139.9, 140.6, 143.0, 148.5, 151.0. IR: 1519, 1331. HRMS: Calcd for $C_{16}H_{10}BrN_3O_4$ 386.9855; found 386.9859

1-(2-Bromo-4.6-difluorophenyl)-5-(4,5-methylenedioxy-2-nitrophenyl)pyrazole (5g). 88% yellow podwer m.p. 170-171 °C (MeOH). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 6.09 (2H, s), 6.52 (1H, d, *J* 2.0), 6.75 (1H, s), 6.80-6.89 (1H, m), 7.13-7.19 (1H, m), 7.34 (1H, s), 7.79 (1H, d, *J* 1.6). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 103.3, 104.3 (dd, *J* 25.1, *J* 25.1), 105.4, 108.6, 110.9, 116.6 (dd, *J* 25.1, *J* 3.6), 119.5, 123.9 (dd, *J* 16.2, *J* 5.4), 124.4 (d, *J* 12.6), 140.4, 141.4, 143.0, 148.6, 150.8, 158.9 (dd, *J* 258.5, *J* 14.4), 162.3 (dd, *J* 256.7, *J* 12.6). IR: 1608, 1525, 1337. HRMS: Calcd for $C_{16}H_8BrF_2N_3O_4$ 422.9666; found 422.9652.

1-(2-Bromo-5-methylphenyl)-5-(4,5-methylendioxy-2-nitrophenyl)pyrazole (5h). 81% yellow podwer m.p. 155-156 ^{o}C (MeOH). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 2.23 (3H, s), 6.05 (2H, s), 6.38 (1H, d, *J* 2.0), 6.85 (1H, s), 7.00 (1H, dd, *J* 8.3, *J* 1.6), 7.18 (1H, d, *J* 1.6), 7.30 (1H, s), 7.35 (1H, d, *J* 8.3), 7.71 (1H, d, *J* 2.0). ^{13}C NMR (63 MHz, $CDCl_3$)**:** δ 20.5, 103.2, 105.1, 107.0, 111.4, 121.0, 130.4, 131.4, 132.5, 137.9, 138.6, 139.8, 140.3, 143.0, 148.3, 150.8. IR: 1525, 1337. HRMS: Calcd for $C_{17}H_{12}BrN_3O_4$ 401.0011; found 401.0012.

5. Synthesis of pyrazoles 2. General procedure. Acetic acid (a 20% aqueous solution, 0.1 mL) was added onto a vigorously stirred suspensión of nitro derivative 5 (0.1 mmol) and iron poder (1.2 mmol) in EtOH (2 mL) at room temperature. The stirred mixture was refluxed for 3h, and then allowed to cool to r.t. EtOAc (10 mL) was added and this crude was filtered over Celite. The filtrate was washed with a saturated aqueous solution of $NaHCO_3$ (3 x 5 mL) and with H_2O (3 x 5 mL), dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was purified by flash column chromatography using 30% EtOAc/hexanes as eluent

5-(2-Aminophenyl)-1-(2-bromophenyl)pyrazole (2a). 98%, white powder, m.p. 112-115^{o}C (Et_2O). ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 3.93 (2H, bs), 6.52-6.80 (2H, m), 6.59 (1H, d, *J* 1.6, H-4), 6.83 (1H, dd, *J* 7.5, *J* 1.2, H_{arom}), 7.03-7.09 (1H, m, H_{arom}), 7.17-7.38 (3H, m, H_{arom}), 7.58 (1H, dd, *J* 7.5, *J* 1.2), 7.83 (1H, d, *J* 1.6). ^{13}C-RMN(63 MHz, $CDCl_3$) δ: 106.9, 114.7, 115.3, 117.6, 121.9, 127.7, 129.7, 130.0, 130.5, 133.2, 139.0, 140.4, 141.0, 144.7; IR: 3460, 3342, 1619; MS (EI) m/z (%): 315 (M^++2, 22), 313 (M^+, 20), 235 (17), 234 (100), 233 (15), 207 (25), 206 (20), 205 (13), 204 (13), 180 (18), 117 (20), 103 (17), 90 (15), 89 (12), 77 (17). HRMS: Calcd for $C_{15}H_{12}BrN_3$ 313.0215; found 313.0216.

5-(2-Aminophenyl)-1-(2-bromo-4,6-difluorophenyl)pyrazole (2b). 98%, brownish powder, 82-83^{o}C (40% hexanes/EtOAc). ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 3.95 (2H, bs), 6.55-6.67 (2H, m), 6.60 (1H, d, *J* 1.6), 6.79-6.87 (1H. m), 6.89-6.92 (1H, m), 7.04-7.10 (1H, m), 7.13-7.18 (1H, m), 7.87 (1H, d, *J* 1.6); ^{13}C-RMN(63 MHz, $CDCl_3$) δ: 104.1 (dd, *J* 25.1, *J* 25.1), 107.2, 113.7, 115.4, 116.2 (dd, *J* 25.1, *J* 3.6), 117.6, 124.7 (d, *J* 10.8) , 124.9 (dd, *J* 10.8, *J* 5.4), 129.9, 130.1, 141.6, 142.3, 144.9, 159.1 (dd, *J* 256.7, *J* 14.4), 162.1 (dd, *J* 254.9, *J* 14.4); IR: 3466, 3373, 1617; MS (EI) m/z (%): 352 (11), 351 (M^++2, 62), 350 (13), 349 (M^+, 64), 271 (17), 270 (100), 269 (15), 243 (33), 242 (29), 241 (17), 240 (14), 223 (17), 222 (10), 216 (31), 135 (13), 131 (22), 130 (15), 126 (18), 121 (27), 118 (12), 117 (28), 116 (13), 115 (13), 112 (28), 104 (24), 102 (15), 92 (18), 91 (12), 90 (24), 89 (29), 78 (16), 77 (45). HRMS: Calcd for $C_{15}H_{10}BrF_2N_3$ 349.0026; found 349.0022.

5-(2-Aminophenyl)-1-(2-bromo-4-methylphenyl)pyrazole (2c). 98%, brownish powder, m.p. 113-116^{o}C (50% hexanes/EtOAc). ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 2.28 (3H, s,), 3.96 (2H, bs), 6.54-6.57 (2H, m, H-4), 6.61-6.64 (1H, m), 6.84-6.87 (1H, m), 7.00-7.07 (1H, m), 7.21-7.26 (2H, m), 7.37 (1H, s), 7.80 (1H, d, *J* 1.2); ^{13}C-RMN(63 MHz, $CDCl_3$) δ: 20.7, 106.7, 114.7, 115.2, 117.4, 121.4, 128.4, 129.1, 129.5, 130.5, 133.5, 136.4, 140.2, 140.4, 141.0, 144.7; IR: 3460, 3342, 1619; MS (EI) m/z (%): 329 (M^++2, 19), 327 (M^+, 18), 248 (100), 247 (11), 233

(17), 221 (14), 220 (10), 206 (21), 204 (13), 194 (18), 124 (19), 104 (14), 103 (15), 90 (25), 89 (29), 77 (26). HRMS: Calcd for $C_{16}H_{14}BrN_3$ 327.0371; found 327.0374.

5-(2-Aminophenyl)-1-(2-bromo-5-methylphenyl)pyrazole (2d). 98%, brownish powder, m.p. 101-102°C (50% hexanes/EtOAc). ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 2.21 (3H, s), 4.02 (2H, bs), 6.48-6.54 (1H, m), 6.56 (1H, d, *J* 1.2), 6.59-6.62 (1H, m), 6.81-6.84 (1H, m), 6.93-7.03 (2H, m), 7.21 (1H, s), 7.35-7.38 (1H, m), 7.79 (1H, d, *J* 1.2); ^{13}C-RMN(63 MHz, $CDCl_3$) δ: 20.3, 106.5, 114.4, 115.1, 117.2, 118.1, 129.4, 130.0, 130.1, 130.7, 132.5, 137.8, 138.5, 140.1, 140.8, 144.6; IR3472, 3389, 1616. MS (EI) m/z (%): 329 (M^++2, 11), 327 (M^+, 13), 249 (19), 248 (100), 247 (11), 233 (17), 221 (12), 220 (10), 206 (18), 205 (11), 204 (13), 194 (16), 124 (14), 104 (11), 103 (13), 90 (21), 89 (23), 77 (25).). HRMS: Calcd for $C_{16}H_{14}BrN_3$ 327.0371; found 327.0375.

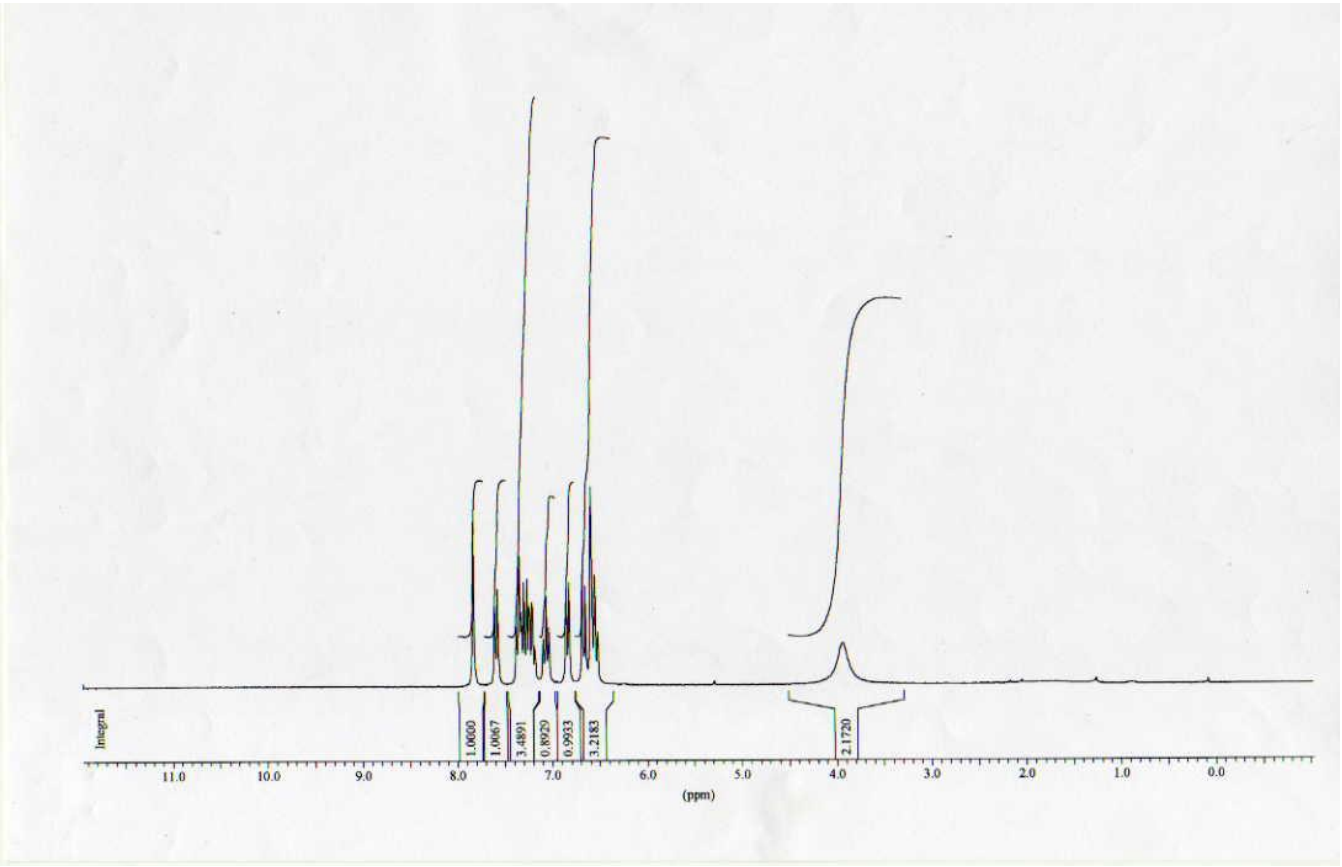
5-(2-Amino-4.5-dimethoxyphenyl)-1-(2-bromophenyl)pyrazole (2e). 92%, white powder; m.p. 128-131°C (hexanes). ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 3.53 (3H, s), 3.80 (3H, s), 3.89 (1H, bs), 6.30 (1H, s), 6.38 (1H, s), 6.62 (1H, d, *J* 1.6), 7.22-7.44 (3H, m), 7.63 (1H, dd, *J* 7.9, *J* 1.2), 7.86 (1H, d, *J* 2.0); ^{13}C-RMN(63 MHz, $CDCl_3$) δ: 55.5, 55.9, 100.0, 105.7, 106.6, 113.6, 122.2, 127.8, 129.8, 130.1, 133.2, 139.1, 139.3, 140.4, 141.1, 141.2, 150.1. IR: 3448, 3354, 1619. MS (EI) m/z (%): 376 (18), 375 (M^++2, 83), 374 (19), 373 (M^+, 100), 360 (30), 358 (32), 294 (11), 278 (12), 263 (20), 250 (32), 236 (75), 181 (11), 132 (13), 90 (11), 77 (12). HRMS: Calcd for $C_{17}H_{16}BrN_3O_2$ 373.0426; found 373.0414.

5-(2-Amino-4,5-methylenedioxyphenyl)-1-(2-bromophenyl)pyrazole (2f). 93%, brownish powder; m.p. 118-121°C (hexanes); ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 3.72 (2H, bs), 5.78 (2H, s), 6.23 (1H, s), 6.33 (1H, s), 6.51 (1H, d, *J* 1.6), 7.19-7.37 (3H, m), 7.58-7.61 (1H, m), 7.79 (1H, d, *J* 1.6) ; ^{13}C-RMN (63 MHz, $CDCl_3$) δ: 97.3, 100.6, 106.1, 107.1, 109.5, 121.8, 127.8, 129.6, 130.1, 133.2, 138.9, 139.7, 140.4, 140.4, 141.1, 148.6; MS (EI) m/z (%): 360 (19), 359 (M^++2, 91), 358 (20), 357 (M^+, 100), 278 (30), 277 (11), 262 (42), 248 (37), 221 (18), 220 (69), 193 (13), 192 (16), 139 (13), 110 (25). HRMS: Calcd for $C_{16}H_{12}BrN_3O_2$ 357.0113; found 313.0111.

5-(2-Amino-4,5-methylenedioxyphenyl)-1-(2-bromo-4.6-difluorophenyl)pyrazole (2g). 98%, brownish powder; m.p. 141-143°C (40% hexanes/EtOAc); ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 3.74 (2H, bs), 5.75 (2H, s), 6.20 (1H, s), 6.37 (1H, s), 6.50 (1H, d, *J* 1.2), 6.81-6.89 (1H, m), 7.14-7.17 (1H, m), 7.80 (1H, d, *J* 1.6); ^{13}C-RMN (63 MHz, $CDCl_3$) δ: 97.3, 100.6, 104.1 (dd, *J* 25.1, *J* 25.1, 105,0, 107.4, 108.8, 116.2 (dd, *J* 25.1, *J* 3.6), 124.6 (d, *J* 12.6), 124.7.124.8 (m), 139.6, 140.6, 141.5, 142.2, 148.9, 158.9 (dd, *J* 256.7, *J* 14.4), 162.0 (dd, *J* 254.9, *J* 12.6); IR: 3446, 3365, 1613. MS (EI) m/z (%): 396 (17), 395 (M^++2, 100), 394 (19), 393 (M^+, 100), 298 (18), 284 (19), 257 (16), 256 (62), 229 (15), 228 (13), 202 (12), 175 (10), 161 (10), 157 (10), 128 (22), 114 (13), 112 (24), 104 (10), 103 (10), 91 (14), 90 (12), 89 (14), 77 (12). HRMS: Calcd for $C_{16}H_{10}BrF_2N_3O_2$ 392.9924; found 392.9925.

5-(2-Amino-4,5-methylenedioxyphenyl)-1-(2-bromo-5-methylphenyl)pyrazole (2h). 77%, brownish powder; m.p. 188-190^{o}C (MeOH) ; ^{1}H-RMN (250 MHz, $CDCl_3$) δ: 2.27 (3H, s), 3.78 (2H, bs), 5.76 (2H, s), 6.22 (1H, s), 6.31 (1H, s), 6.50 (1H, d, *J* 2.0), 7.01 (1H, dd, *J* 7.9, *J* 1.6), 7.20 (1H, d, *J* 1.6,), 7.42 (1H, d, *J* 8.3), 7.76 (1H, d, *J* 1.6) ; ^{13}C-RMN (63 MHz, $CDCl_3$) δ: 20.7, 97.4, 100.7, 106.4, 107.0, 109.5 118.3, 130.3, 131.1, 132.8, 138.2, 138.7, 139.7, 140.4, 141.1, 148.6; IR: 3436, 3342, 1619. MS (EI) m/z (%): 374 (18), 373 (M^++2, 92), 372 (20), 371 (M^+, 90), 293 (12), 292 (60), 291 (13), 277 (18), 276 (65), 263 (12), 262 (41), 235 (24), 234 (100), 207 (15), 206 (12), 205 (10), 192 (14), 146 (23), 131 (17), 117 (83), 104 (22), 103 (44), 102 (15), 91 (10), 90 (52), 89 (52), 78 (18), 77 (31). . HRMS: Calcd for $C_{17}H_{14}BrN_3O_2$ 371.1269; found 371.1262.

2a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0.9933
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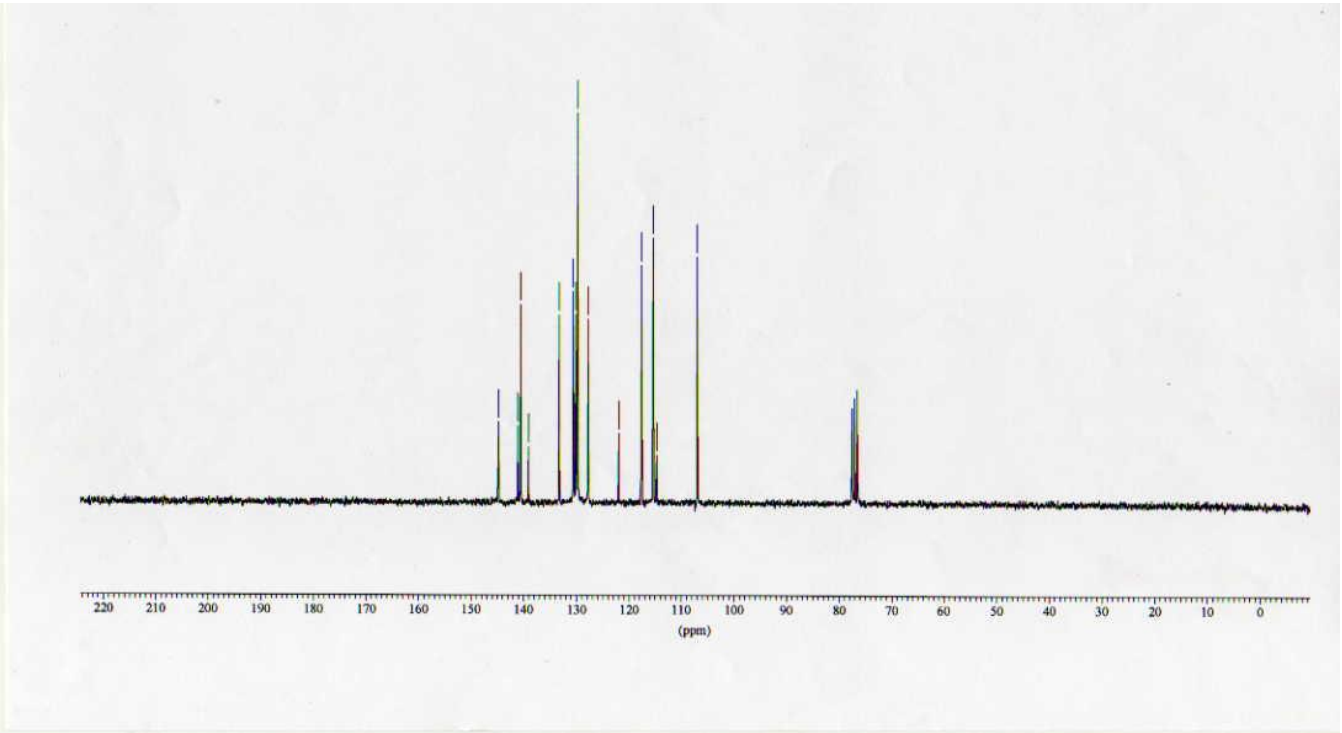
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)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80
70
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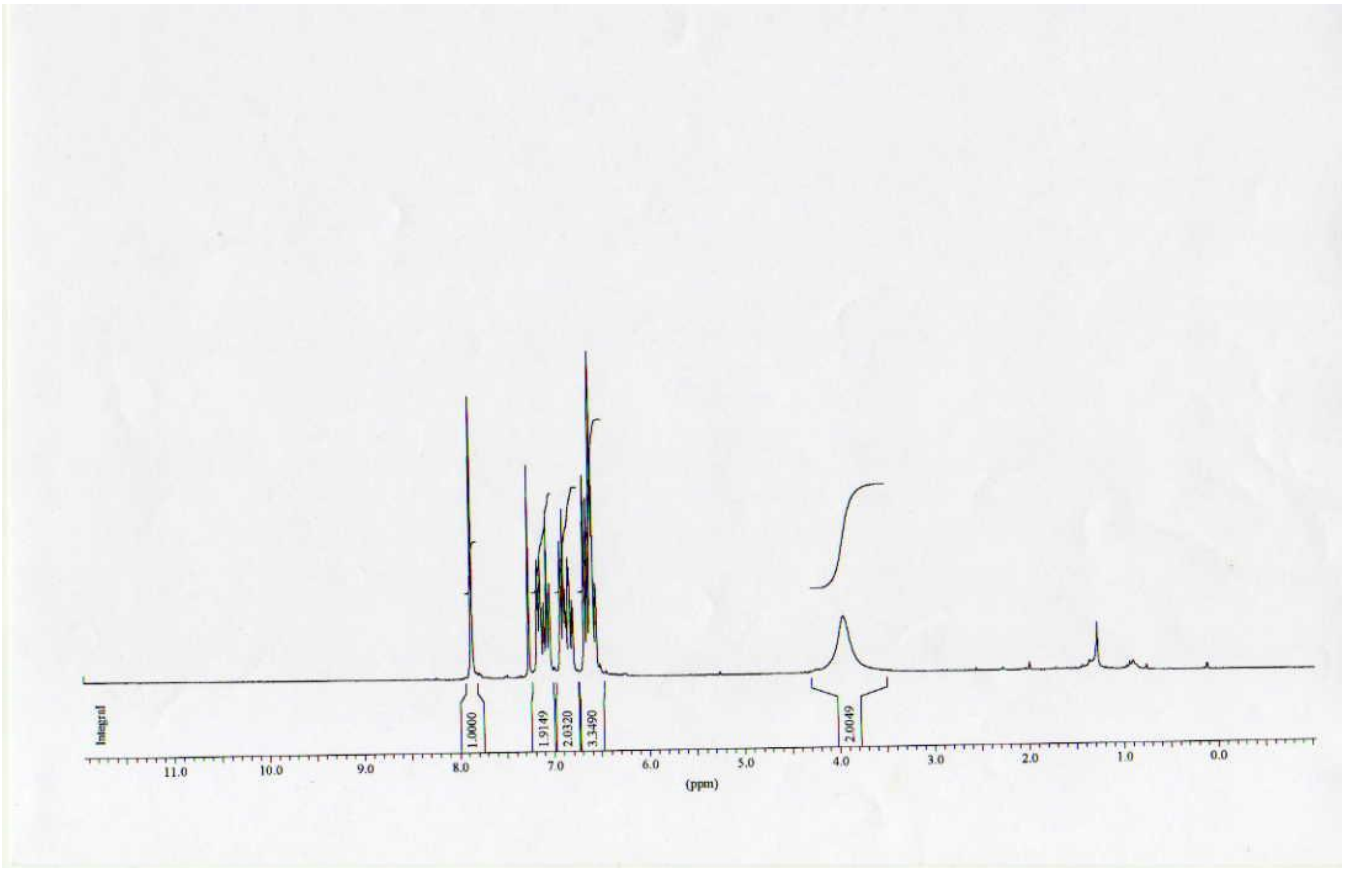
30
20
10
0
(ppm)

2b


Integral
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3.3490
2.0049
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3.0
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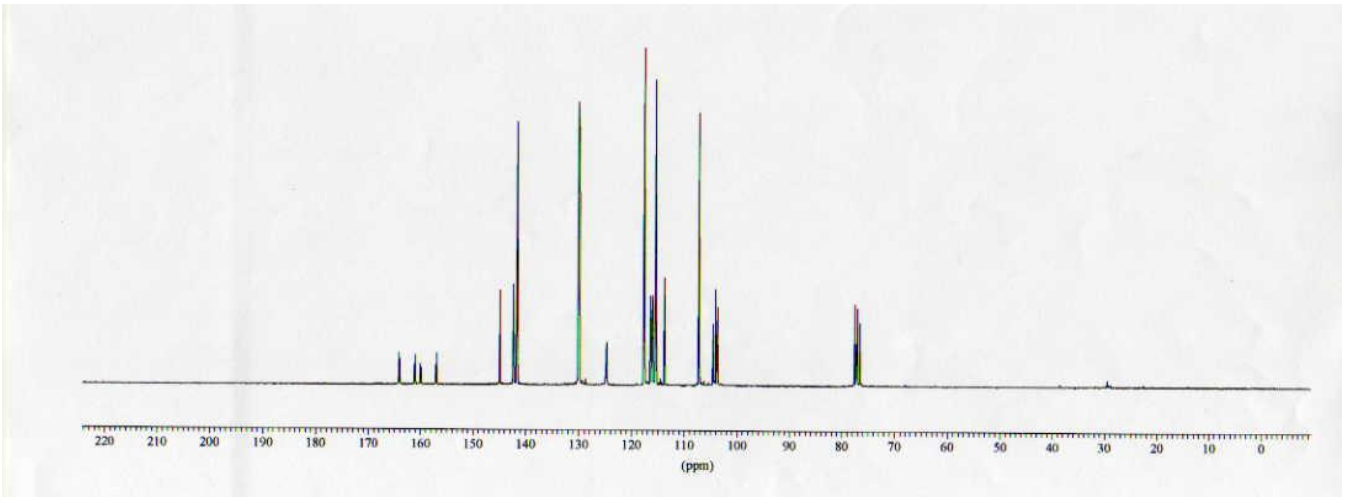
1.0
0.0
(ppm)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210
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120
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100
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80
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60
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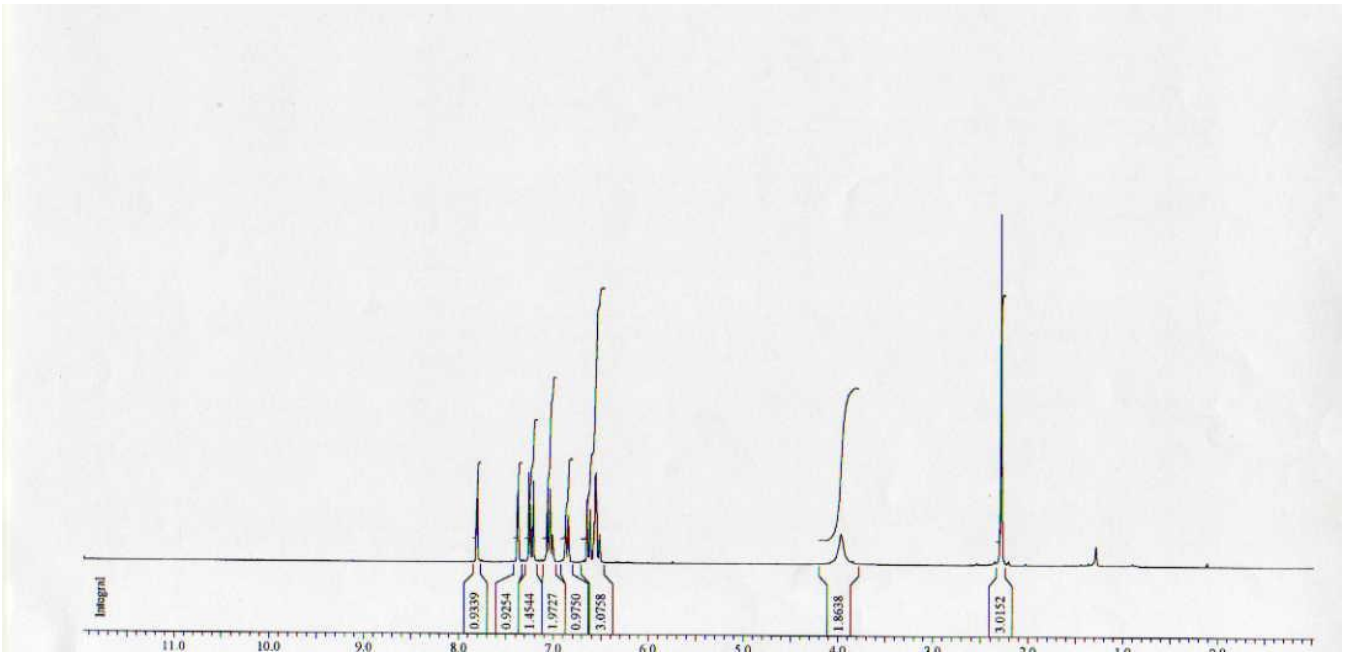
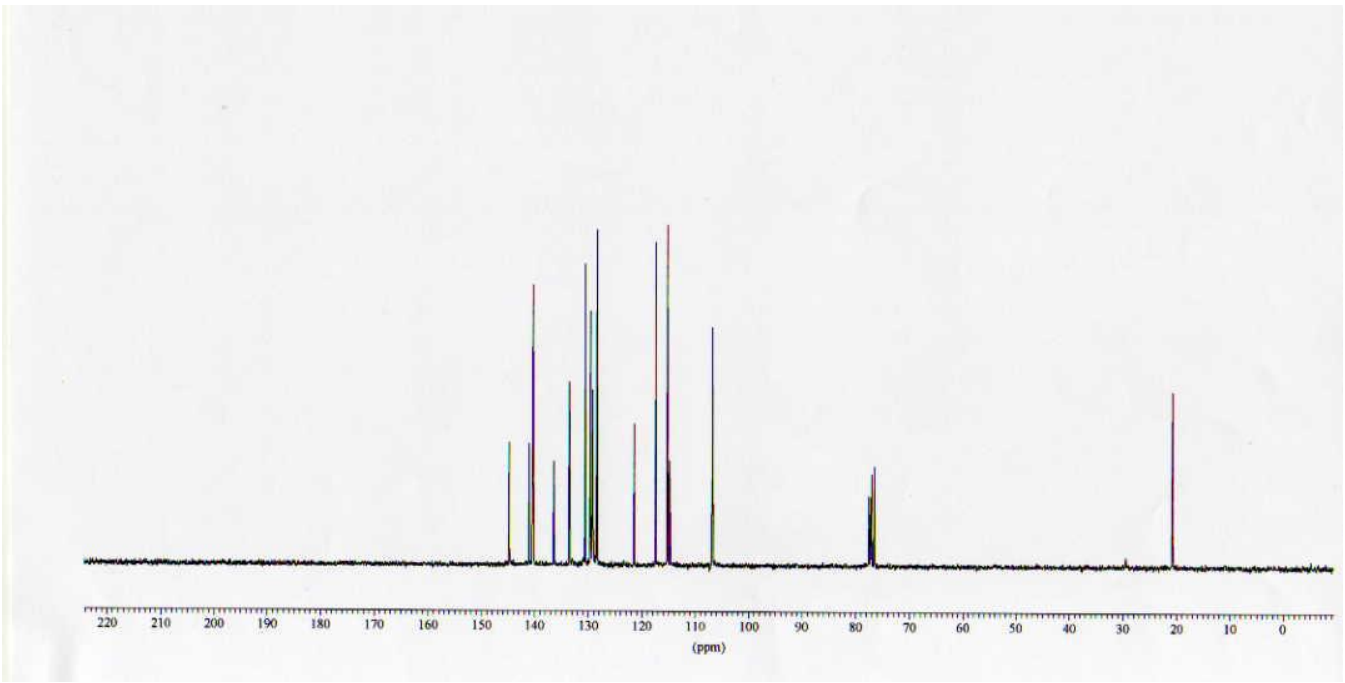
40
30
20
10
0
(ppm)

2c


Integral
0.9339
0.9254
1.4544
1.9727
0.9750
3.0758
1.8638
3.0152
11.0
10.0
9.0
8.0
7.0
6.0
5.0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210
200
190
180
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120
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100
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70
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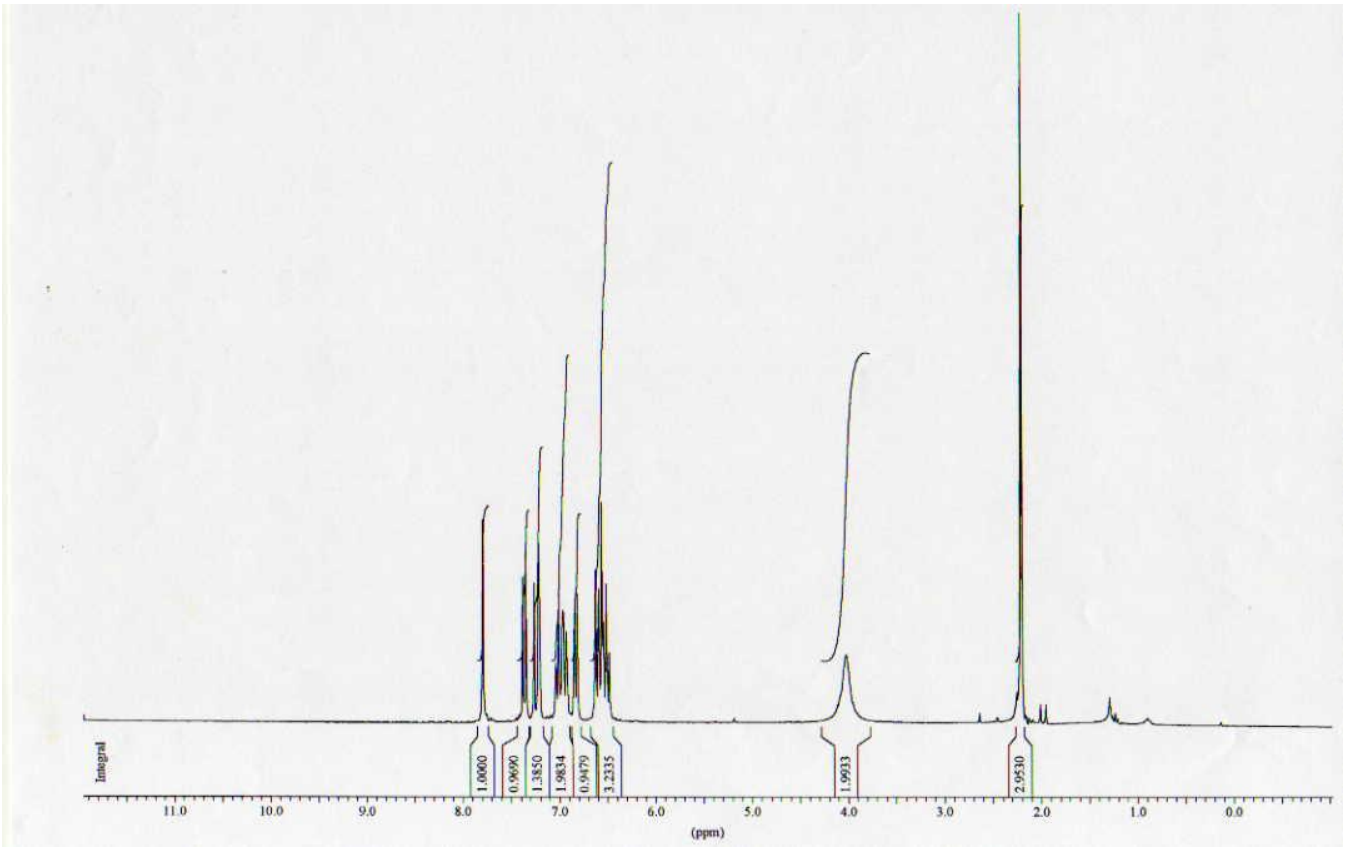
40
30
20
10
0
(ppm)

2d


Integral
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0.9690
1.3850
1.9834
0.9479
3.2335
1.9933
2.9530
11.0
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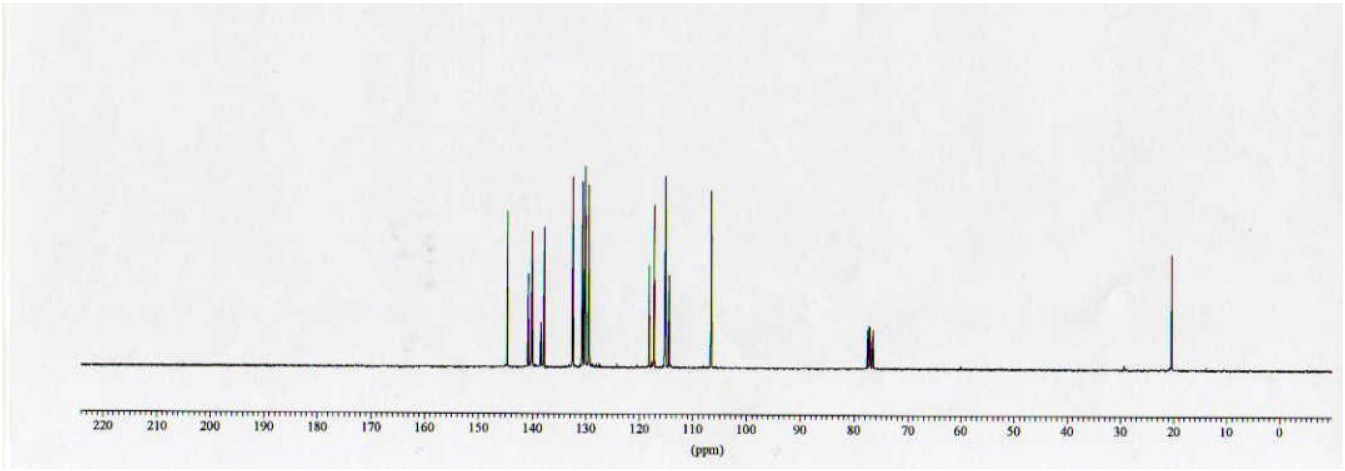
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)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210
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190
180
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120
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100
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80
70
60
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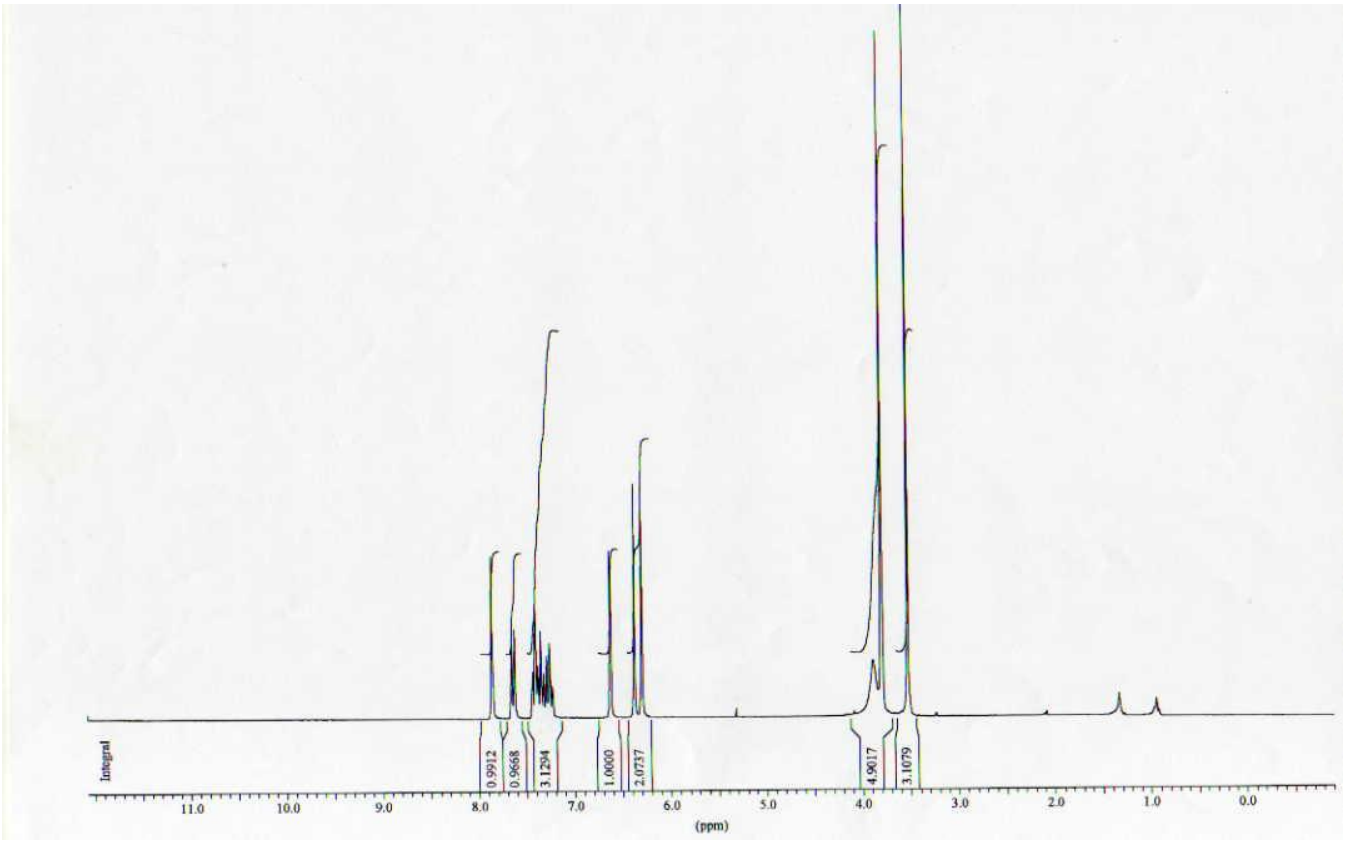
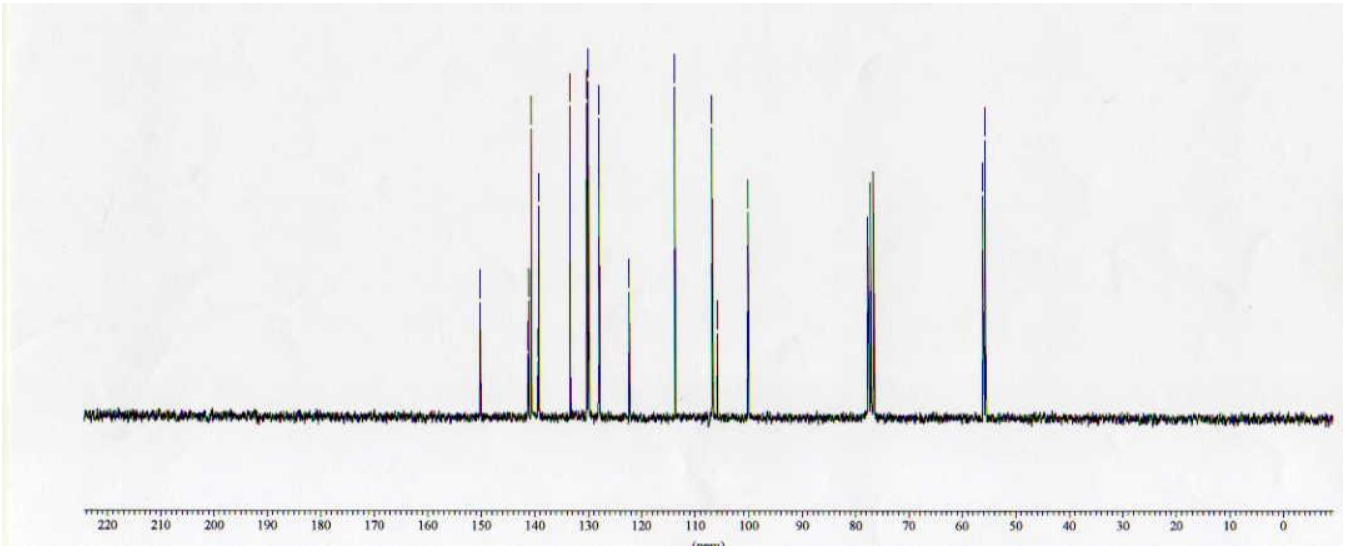
40
30
20
10
0
(ppm)

2e


Integral
0.9912
0.9668
3.1294
1.0000
2.0737
4.9017
3.1079
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)


220
210
200
190
180
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100
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80
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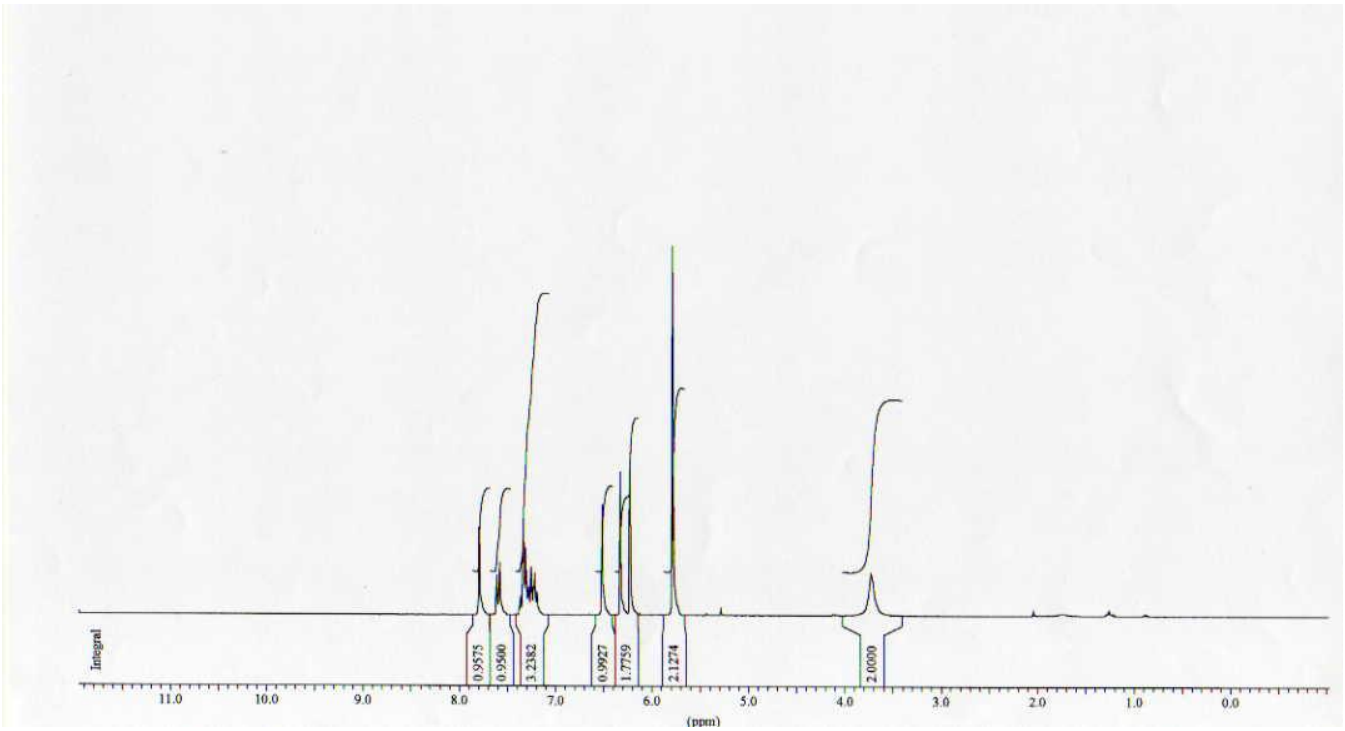
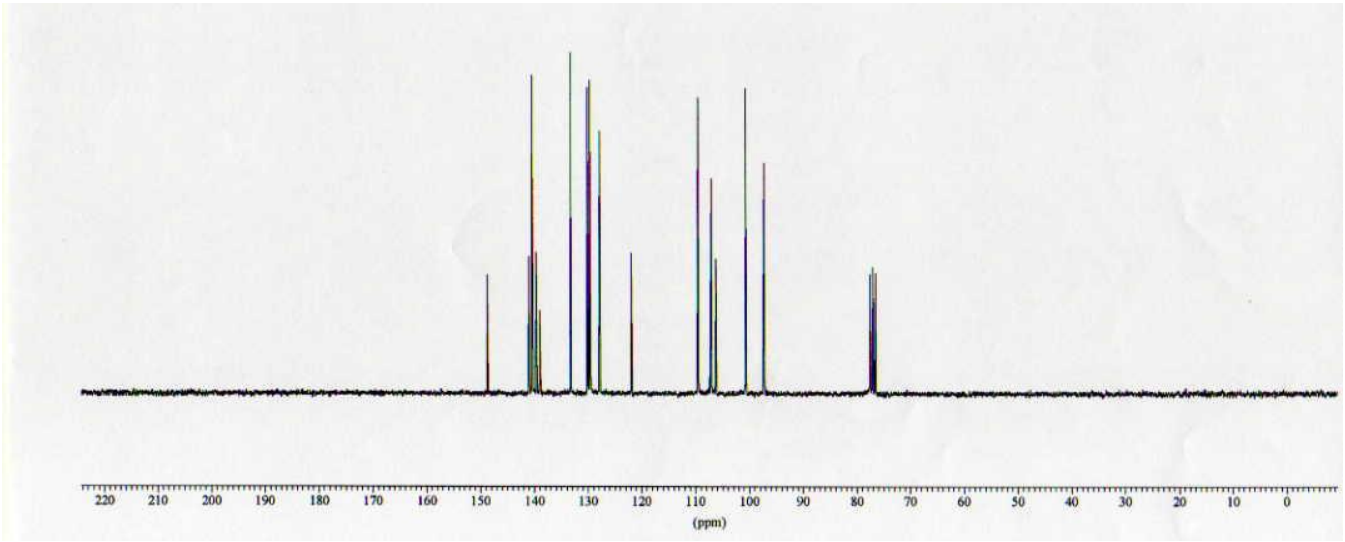
60
50
40
30
20
10
0

2f


Integral
0.9575
0.9560
3.2382
0.9927
1.7759
2.1274
2.0000
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)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210
200
190
180
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120
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100
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80
70
60
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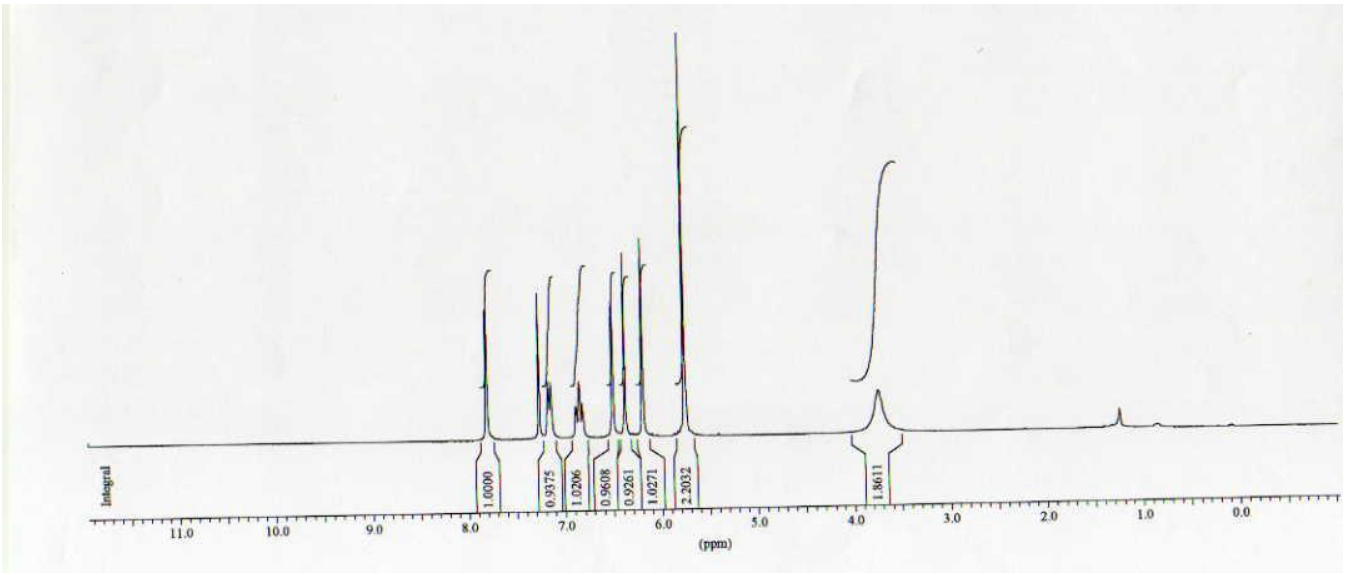
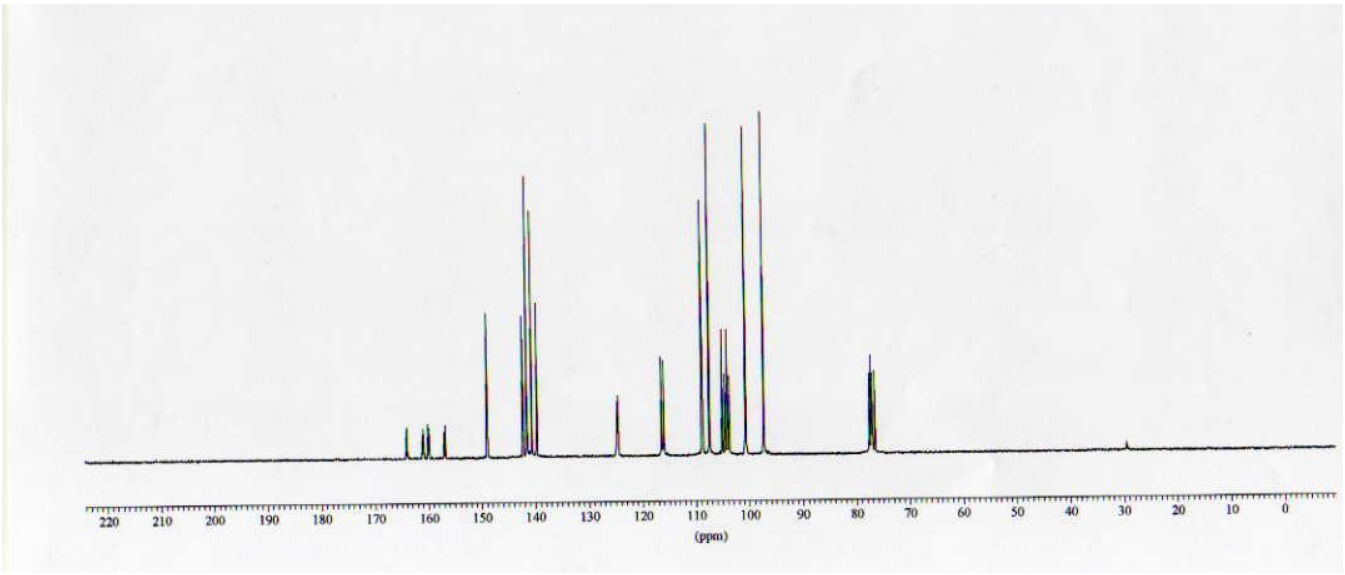
40
30
20
10
0
(ppm)

2g


Integral
1.0000
0.9375
1.0206
0.9608
0.9261
1.0271
2.2032
1.8611
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)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180
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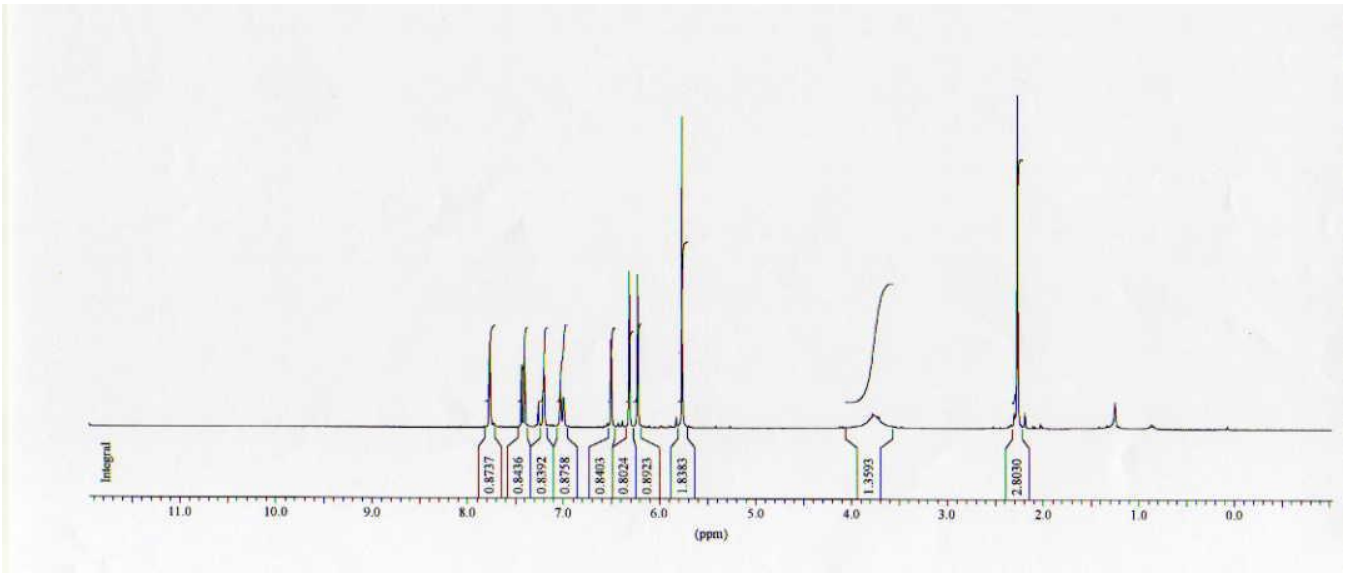
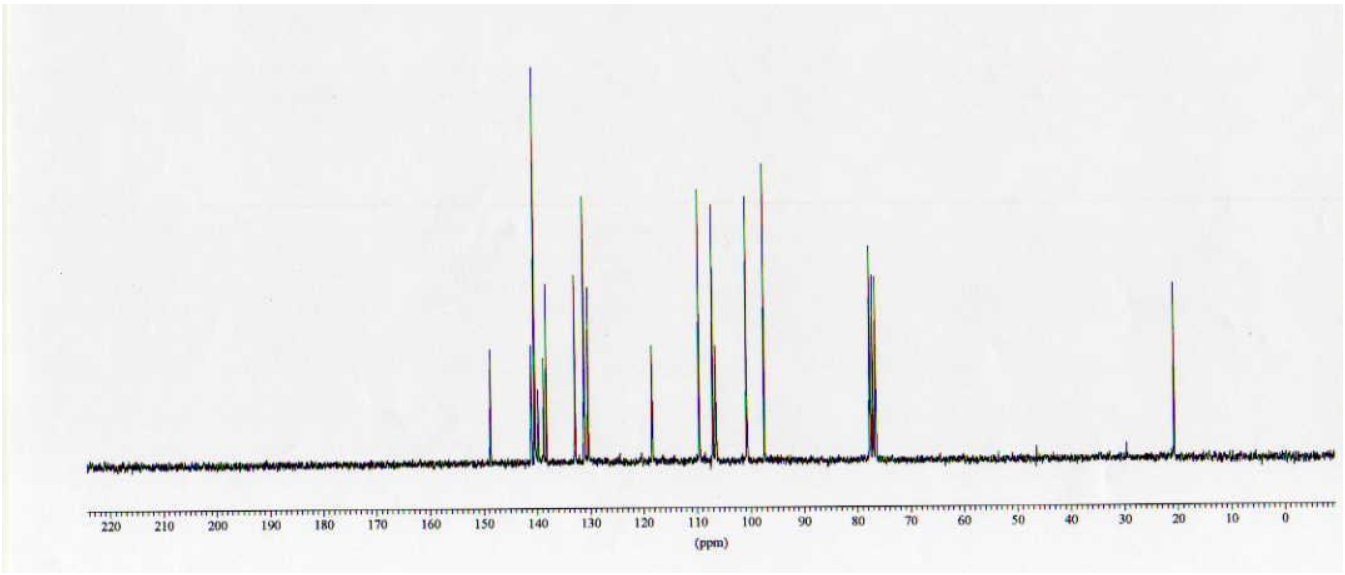
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

2h


Integral
0.8737
0.8436
0.8392
0.8758
0.8403
0.8024
0.8923
1.8383
1.3593
2.8030
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)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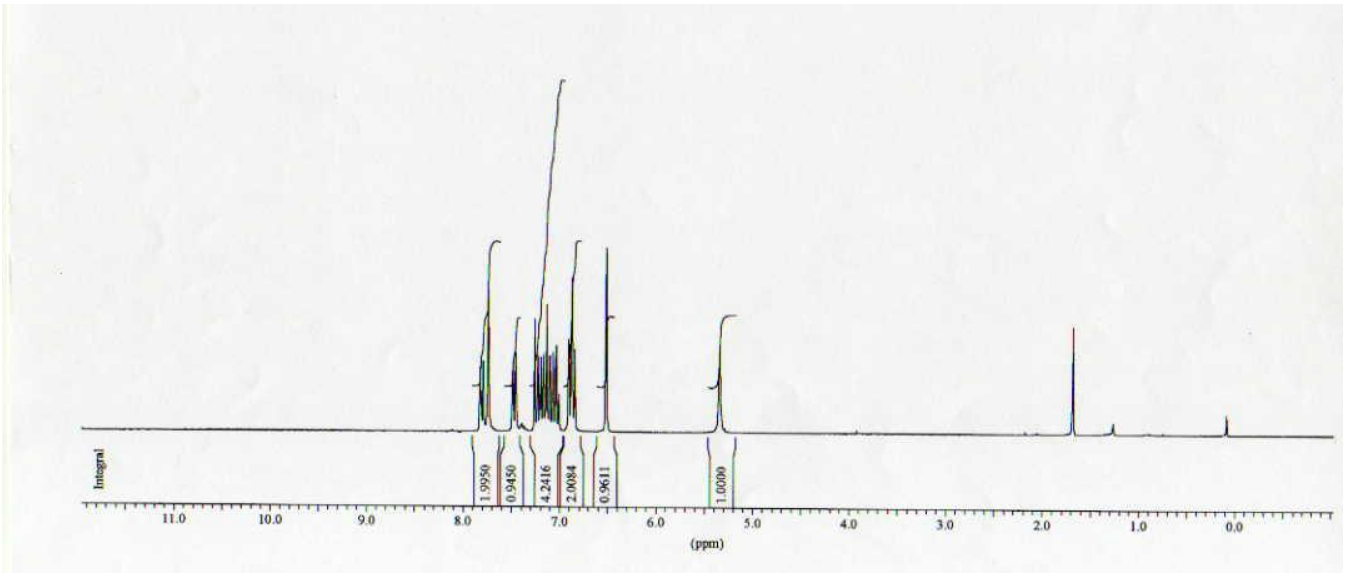
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

1a


Integral
1.9950
0.9450
4.2416
2.0084
0.9611
1.0000
11.0
10.0
9.0
8.0
7.0
6.0
5.0
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3.0
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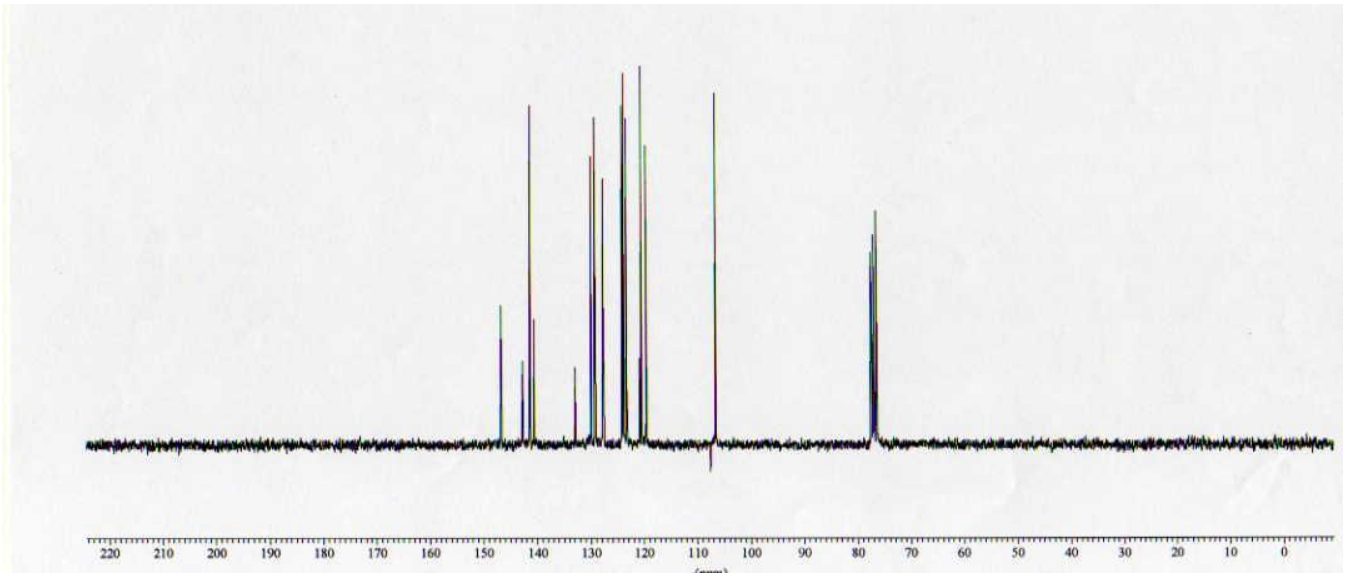
(ppm)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80
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60
50
40
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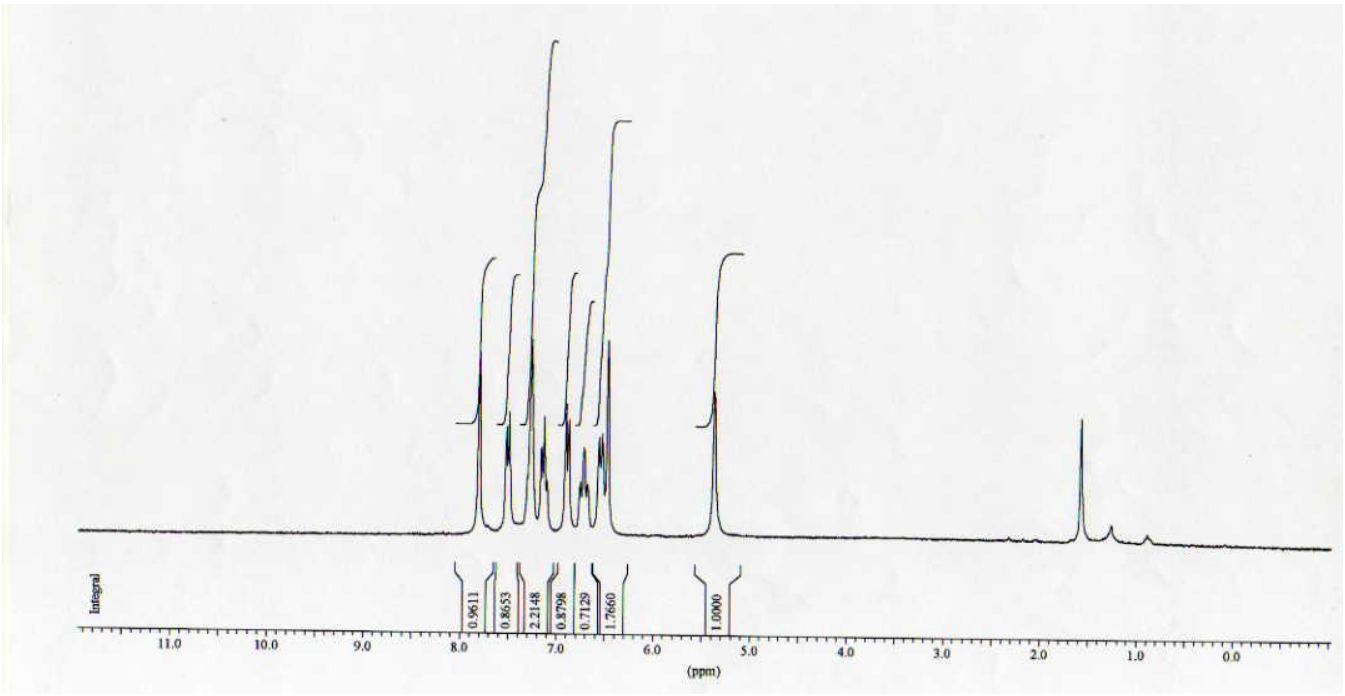
20
10
0

1b


Integral
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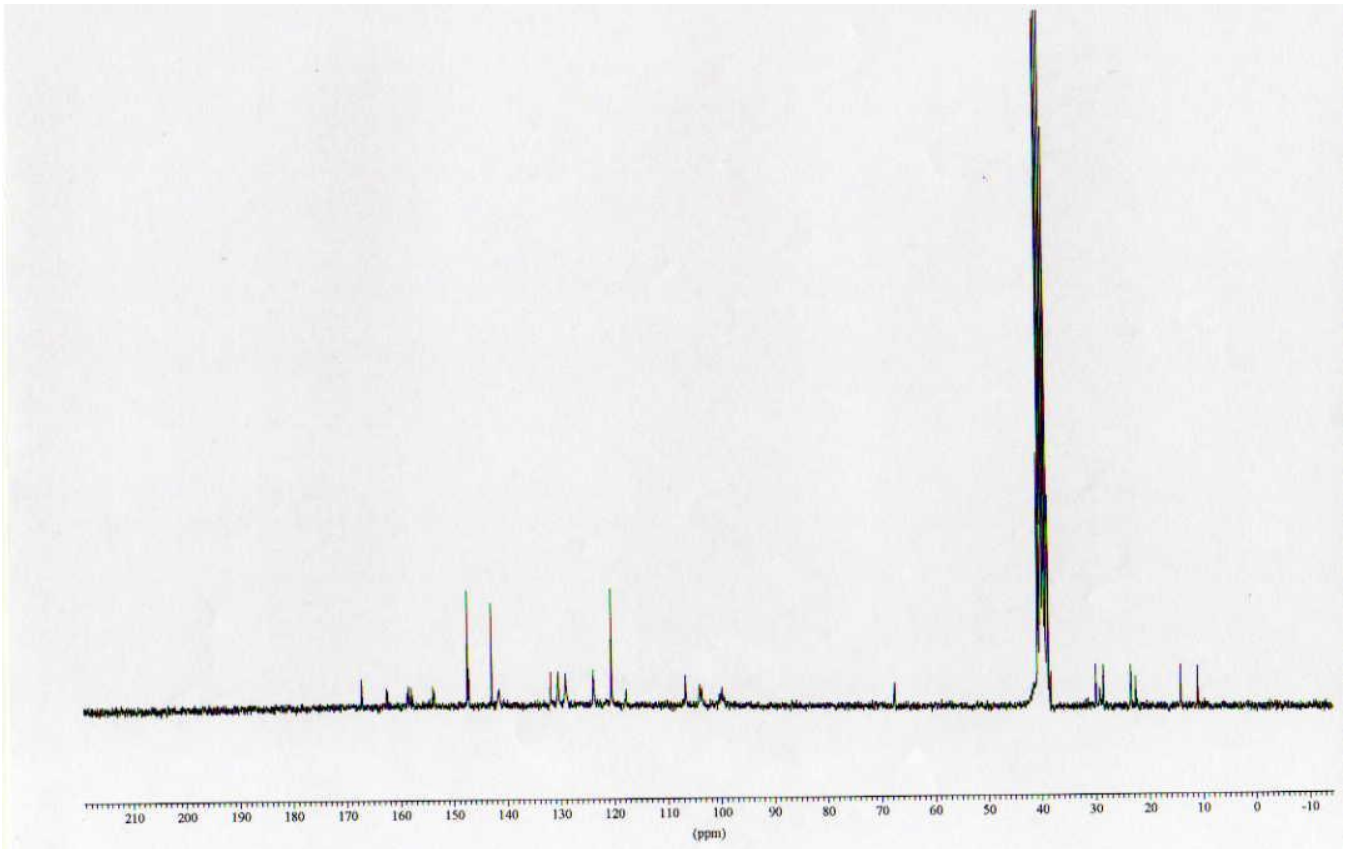
0.8653
2.2148
0.8798
0.7129
1.7660
1.0000
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)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200
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60
50
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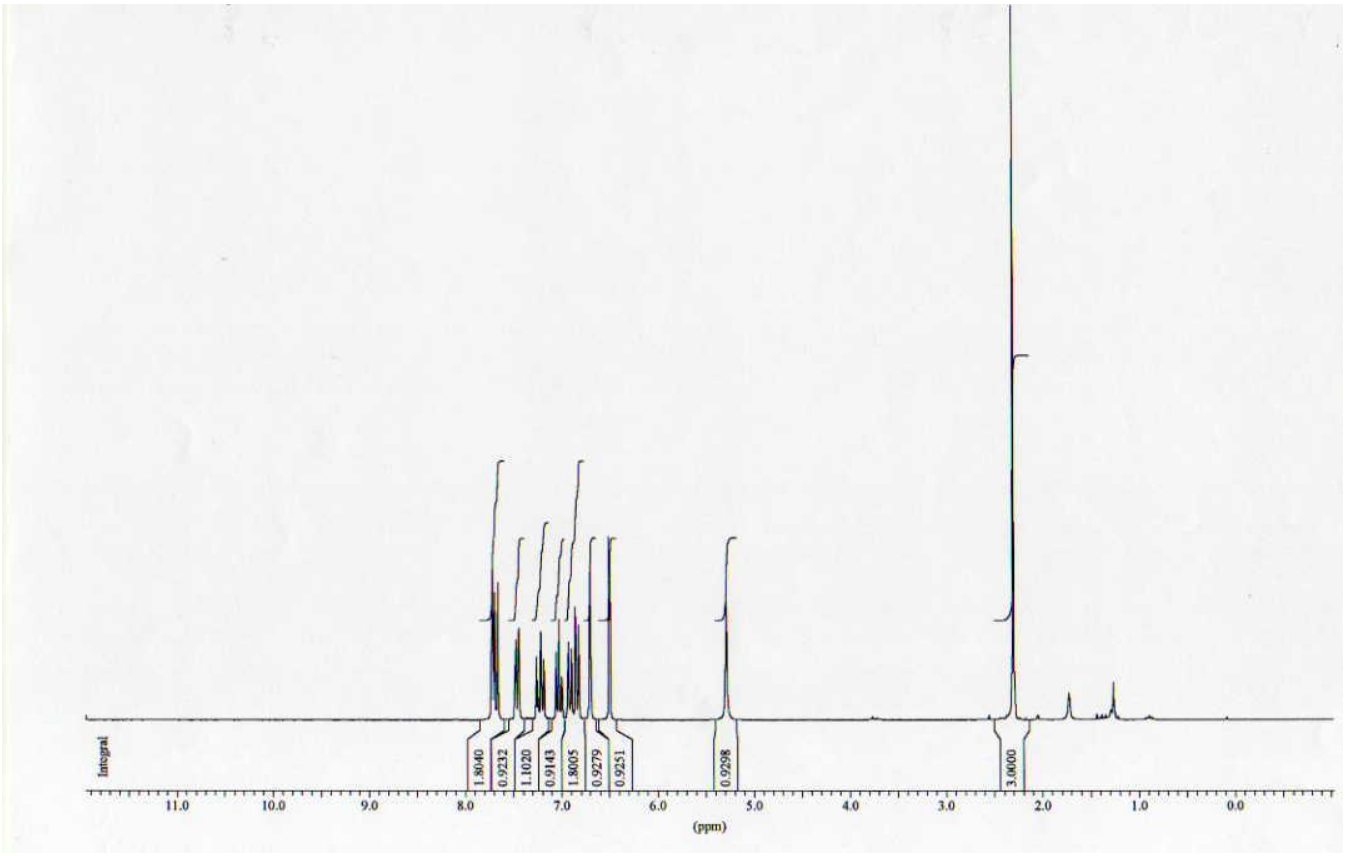
30
20
10
0
-10
(ppm)

1c


Integral
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1.1020
0.9143
1.8005
0.9279
0.9251
0.9298
3.0000
11.0
10.0
9.0
8.0
7.0
6.0
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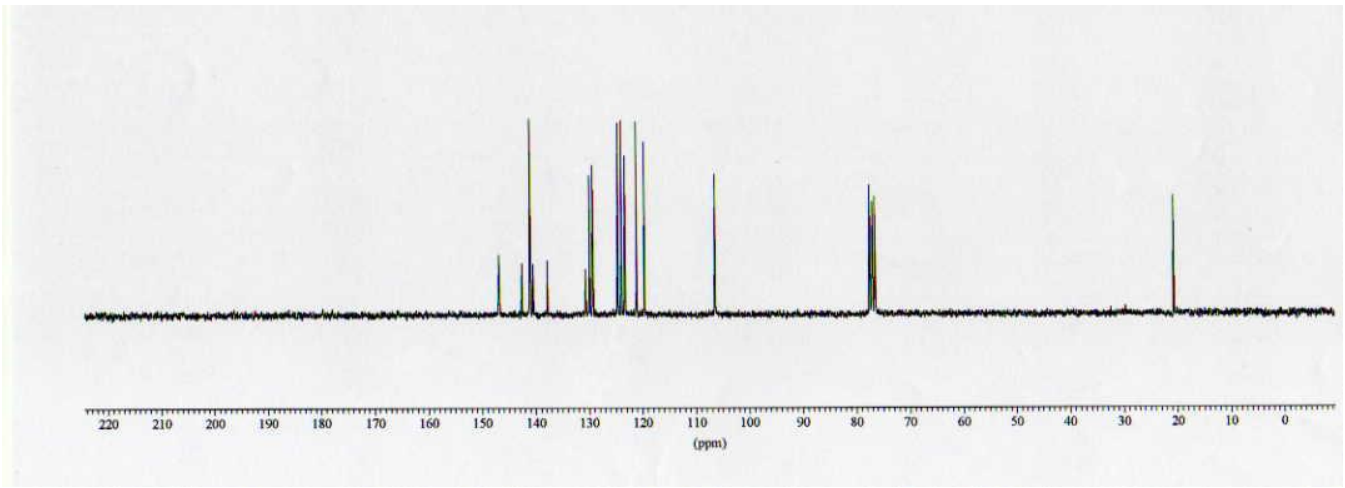
4.0
3.0
2.0
1.0
0.0
(ppm)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180
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40
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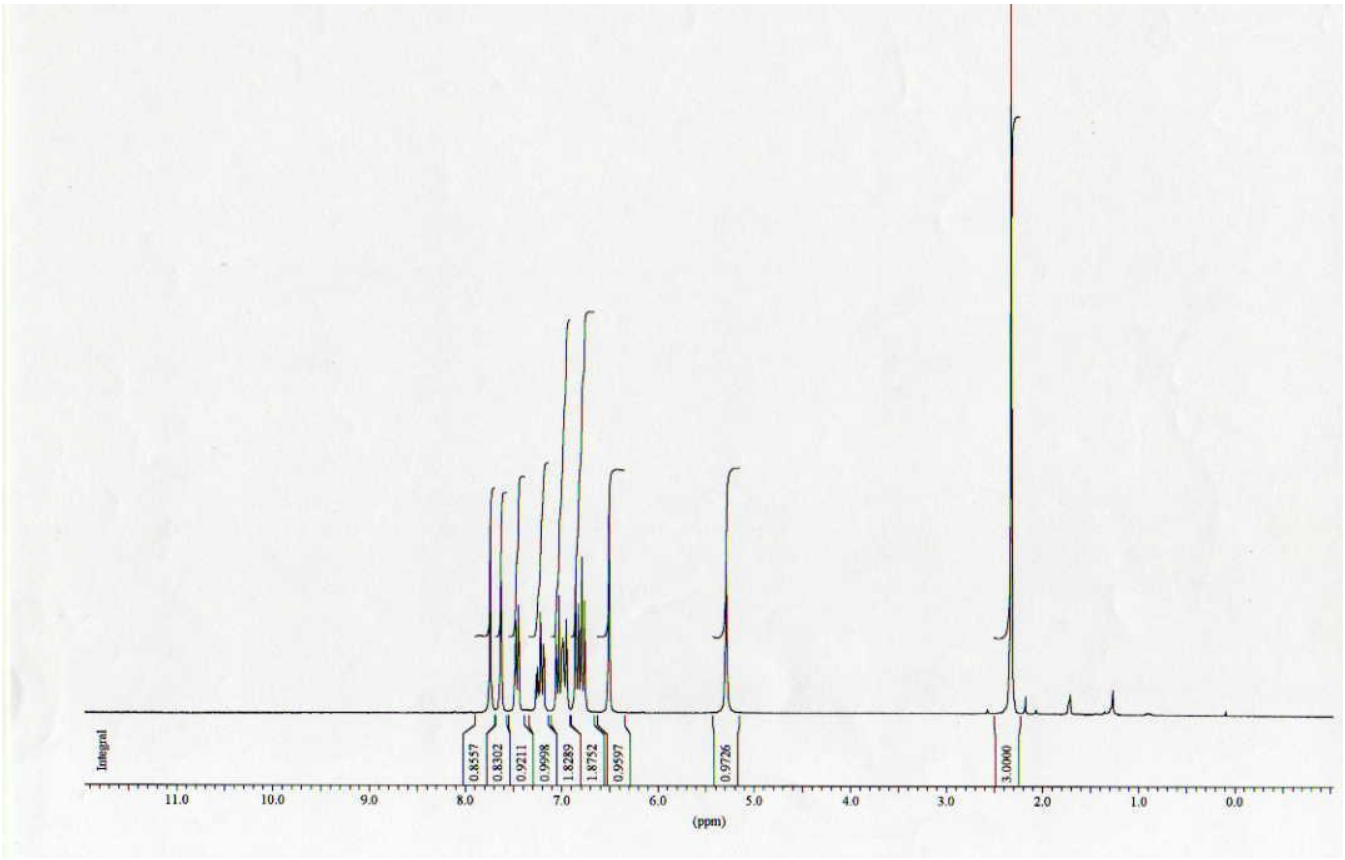
0
(ppm)

1d


Integral
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0.9211
0.9998
1.8289
1.8752
0.9597
0.9726
3.0000
11.0
10.0
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7.0
6.0
5.0
4.0
3.0
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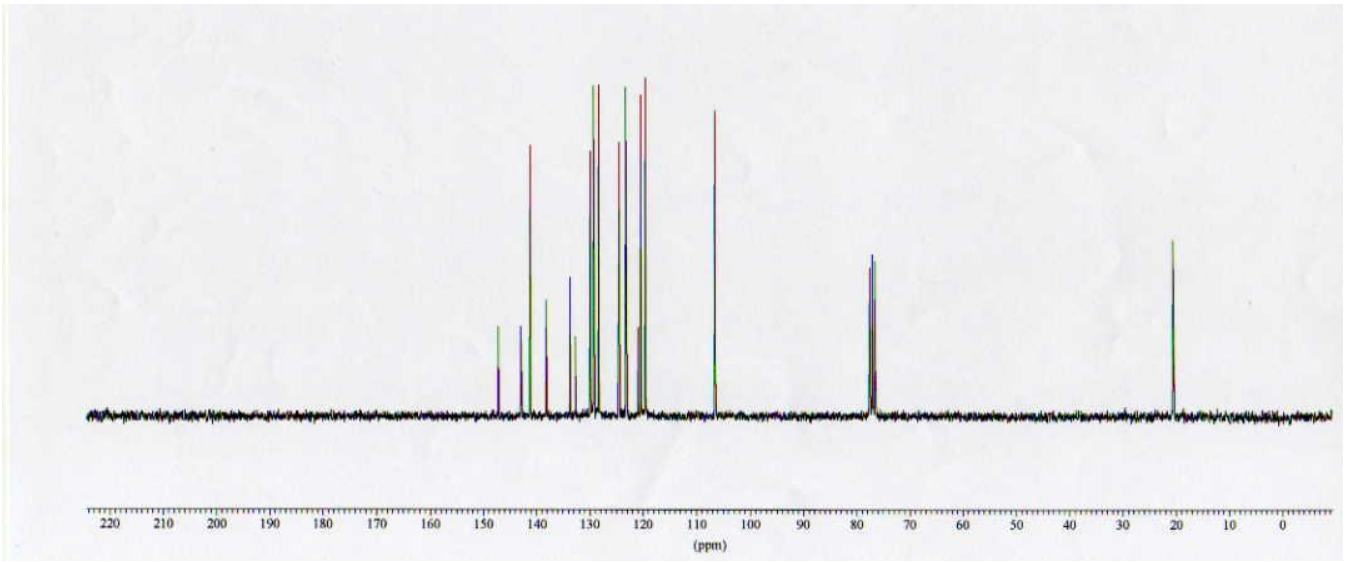
(ppm)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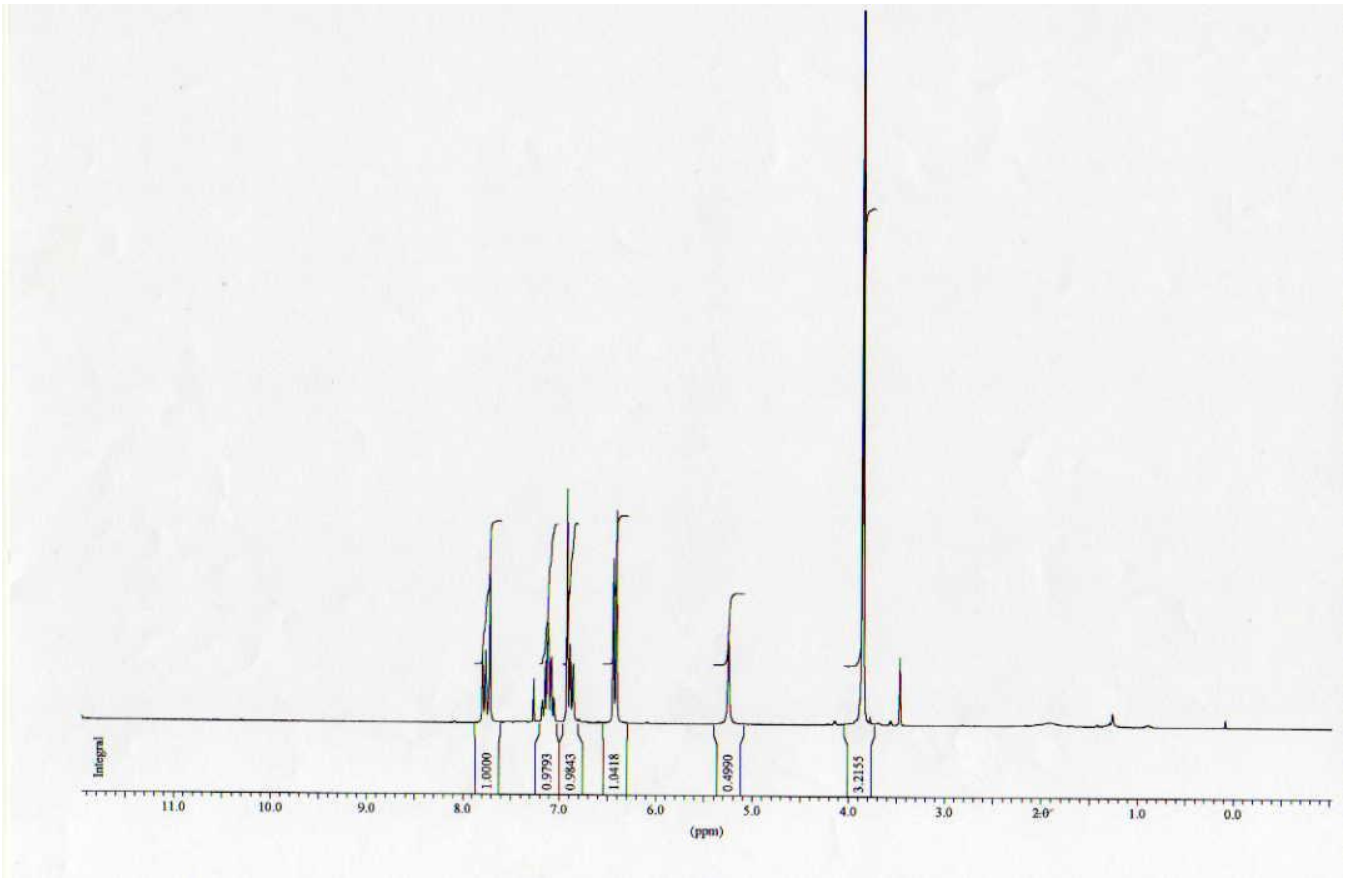
0
(ppm)

1e


Integral
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0.4990
3.2155
11.0
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7.0
6.0
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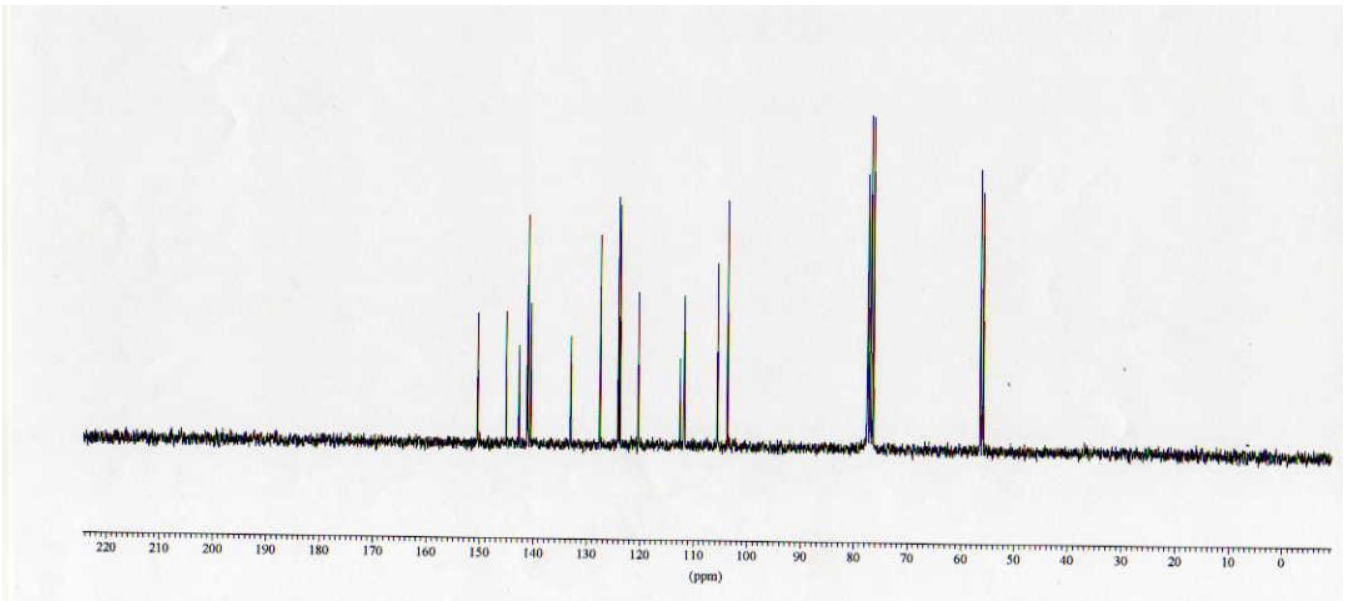
4.0
3.0
2.0
1.0
0.0
(ppm)


220
210
200
190
180
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120
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100
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80
70
60
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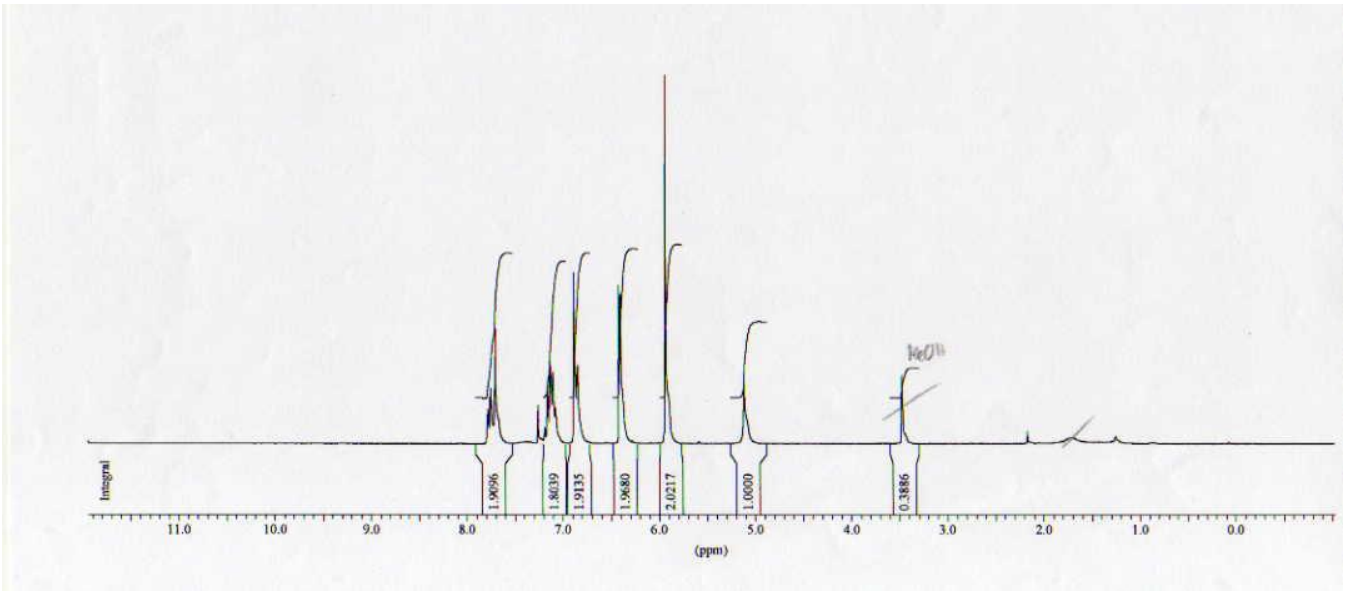
40
30
20
10
0
(ppm)

1f


Integral
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1.9135
1.9680
2.0217
1.0000
0.3886
11.0
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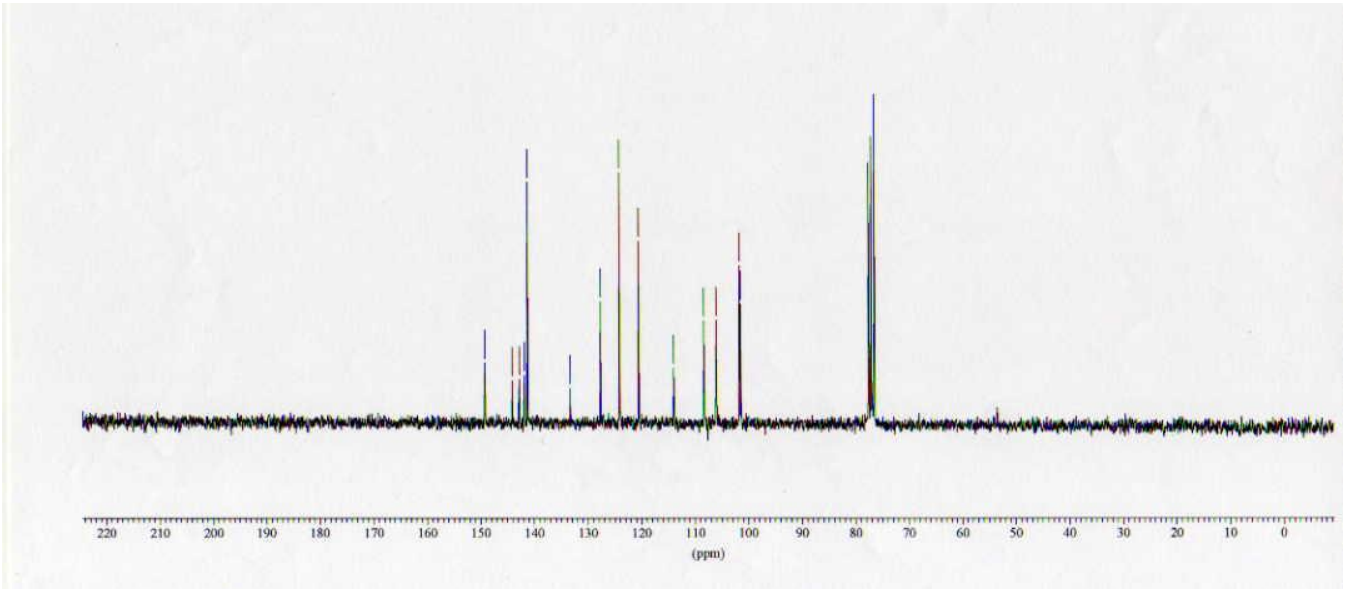
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)


220
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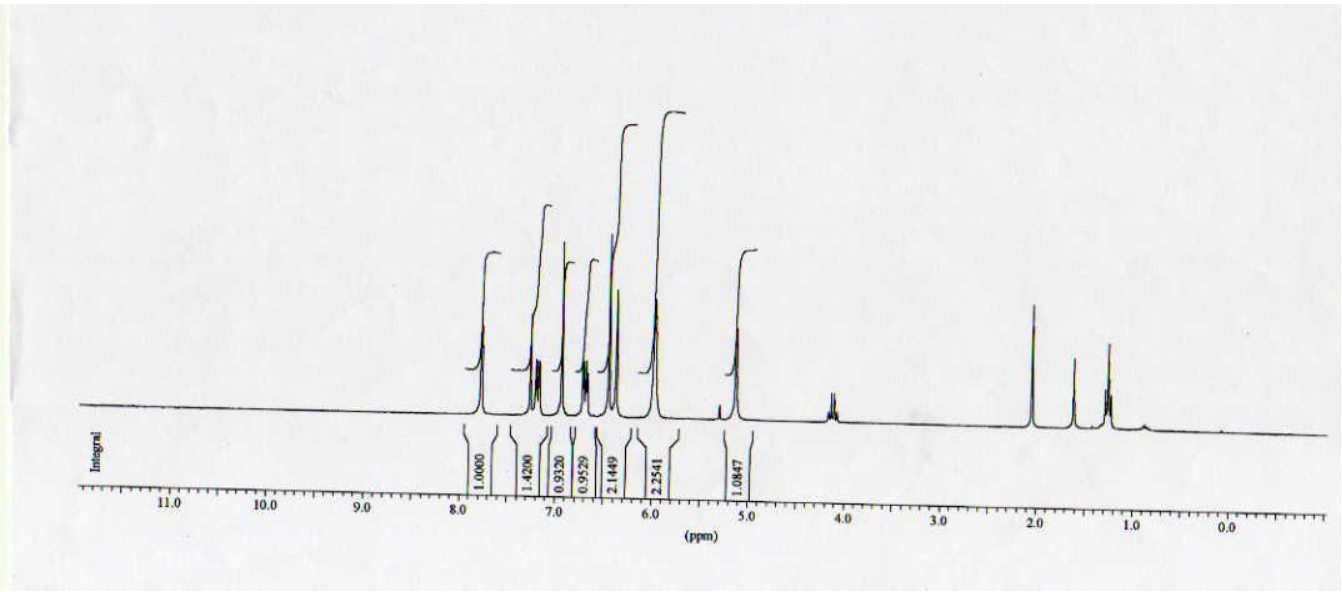
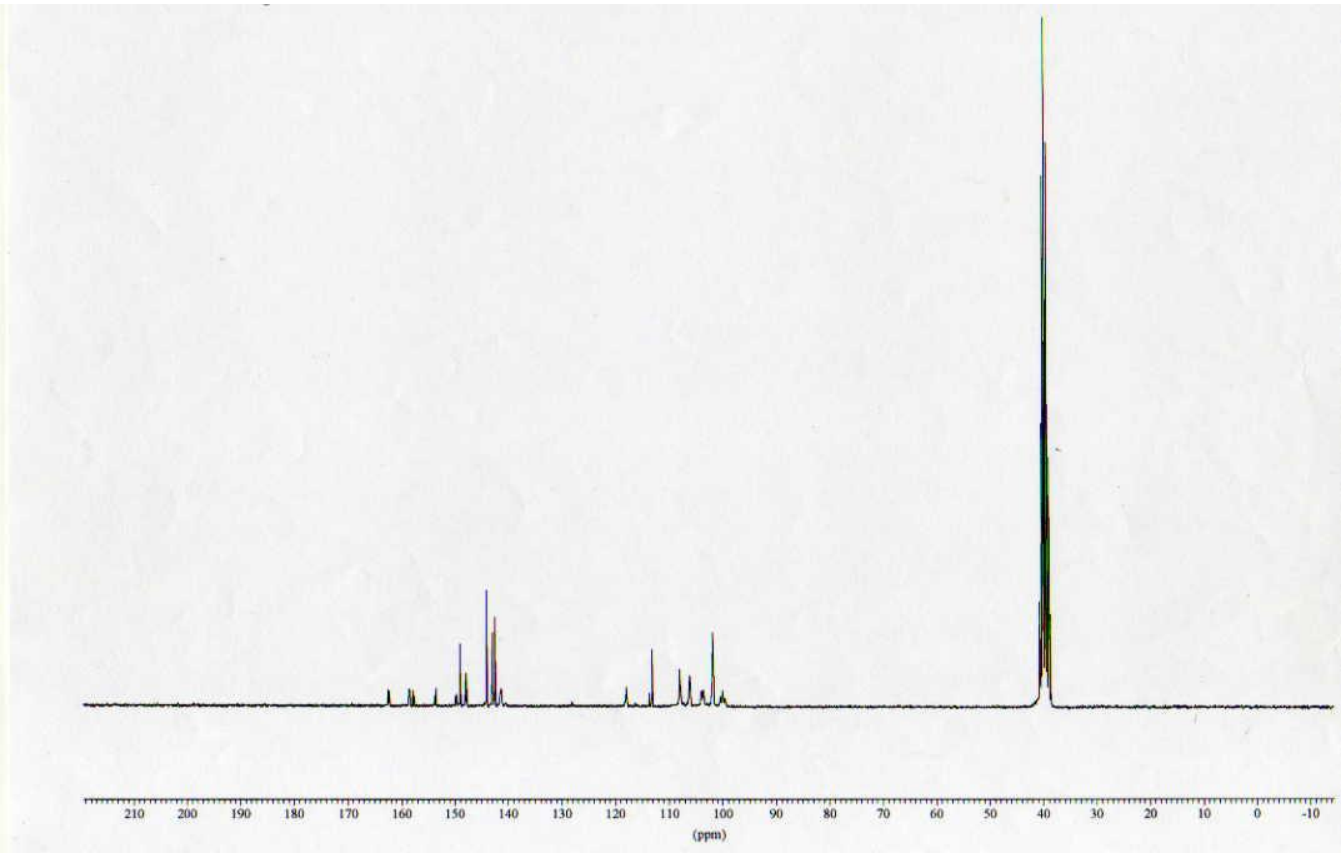
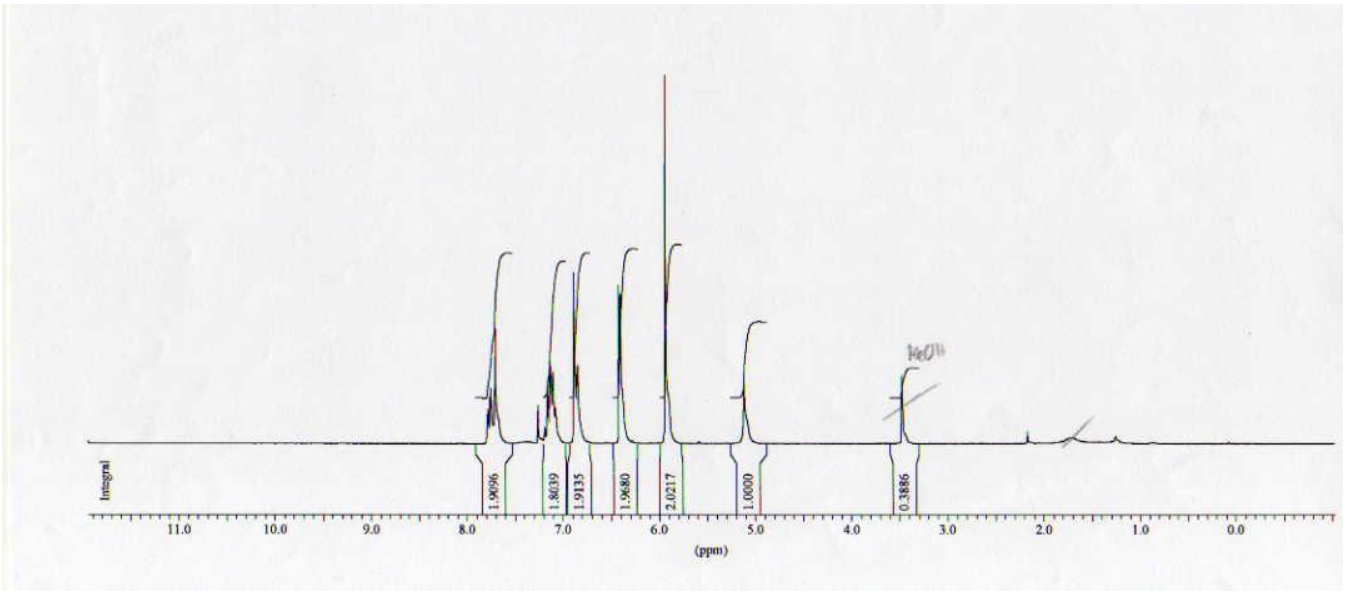
40
30
20
10
0
(ppm)

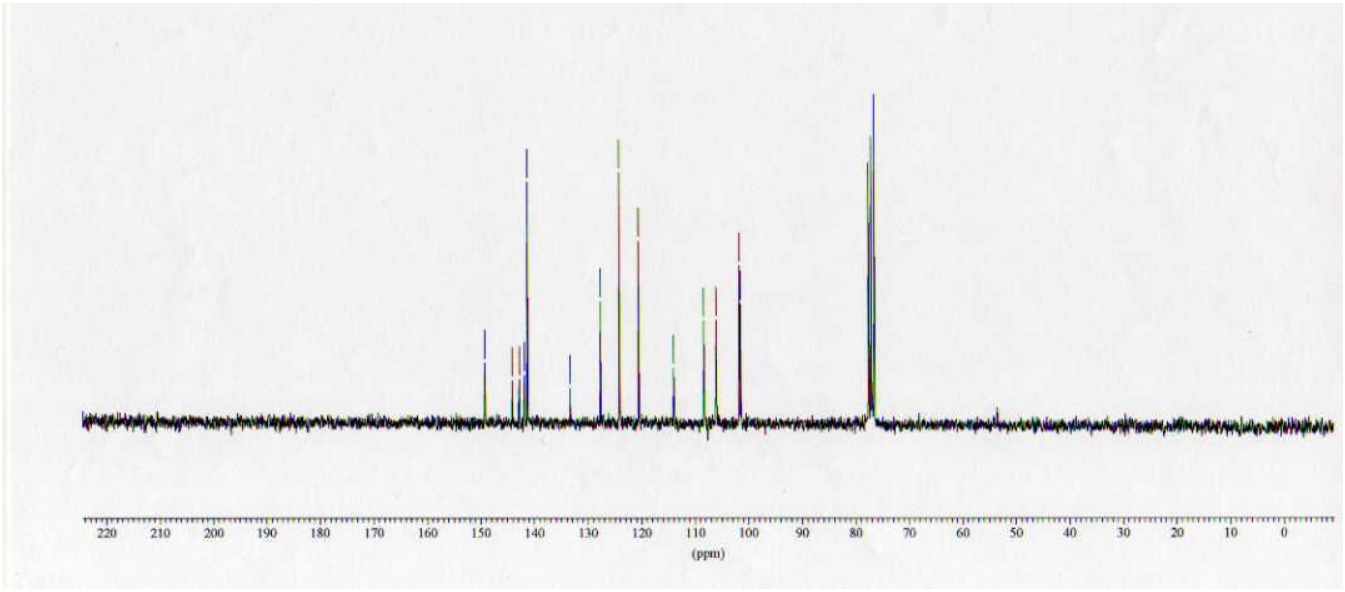
1g


Integral
1.0000
1.4200
0.9320
0.9529
2.1449
2.2541
1.0847
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

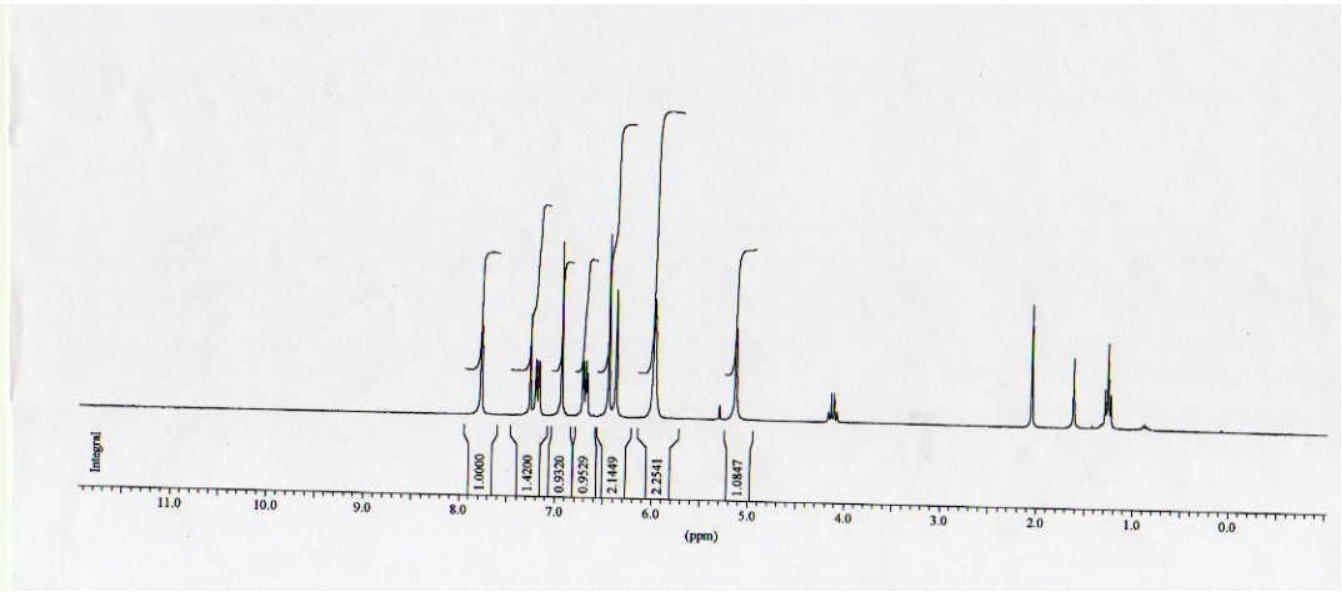

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
(ppm)

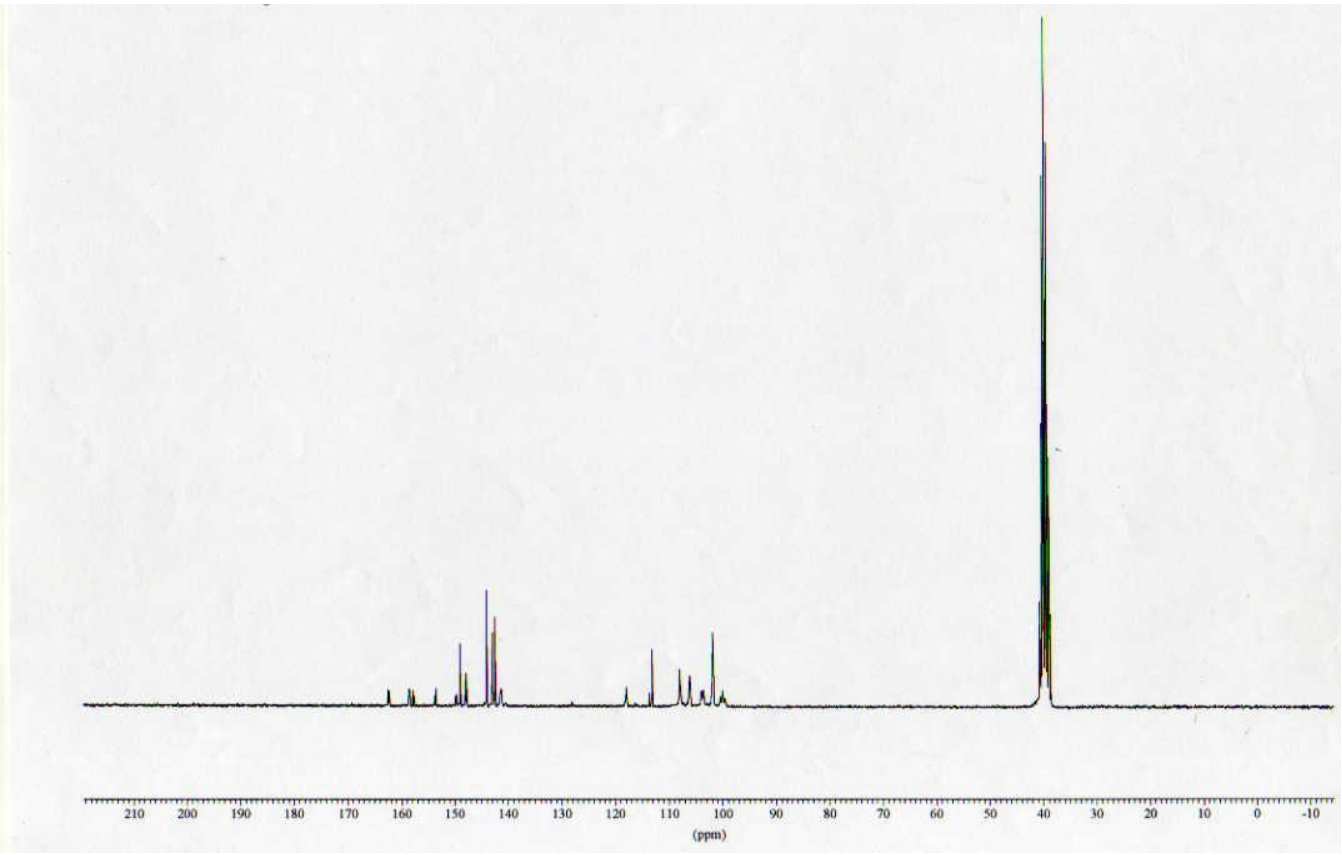
1f


Integral
1.9096
1.8039
1.9135
1.9680
2.0217
1.0000
0.3886
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

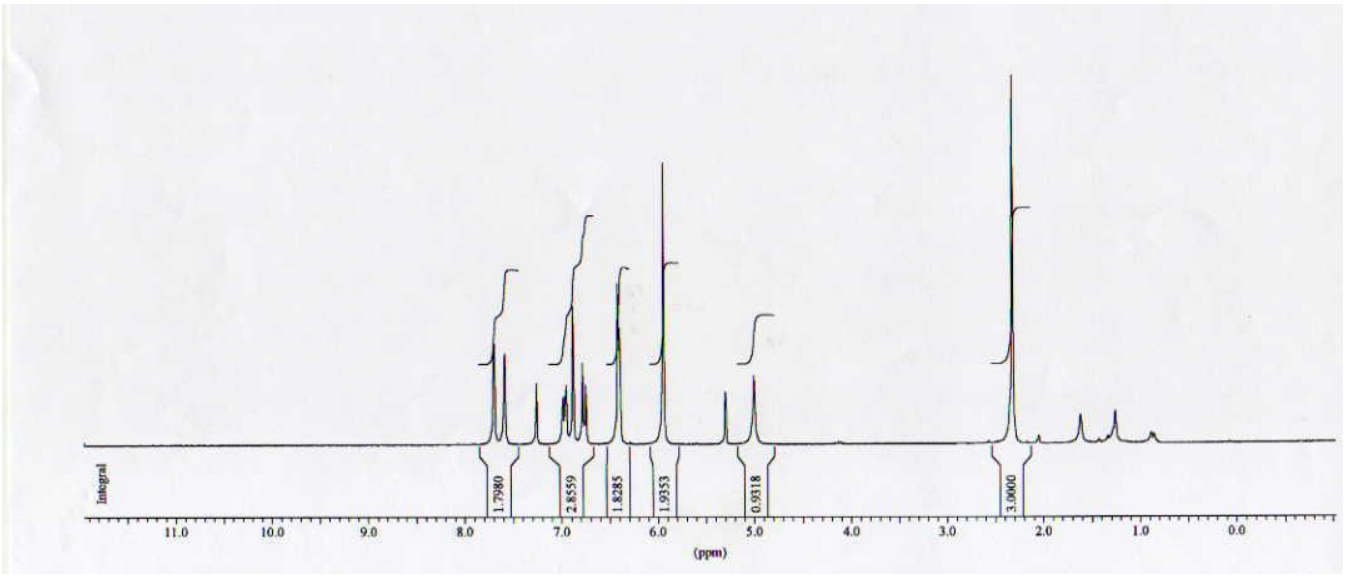

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

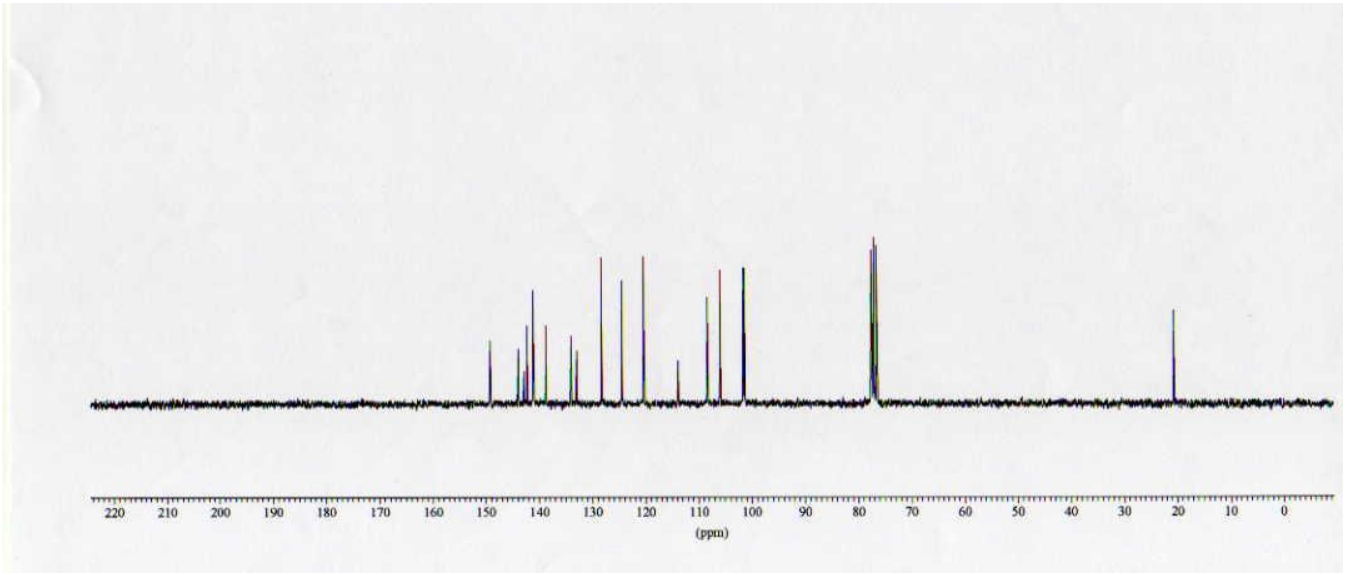
1g


Integral
1.0000
1.4200
0.9320
0.9529
2.1449
2.2541
1.0847
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

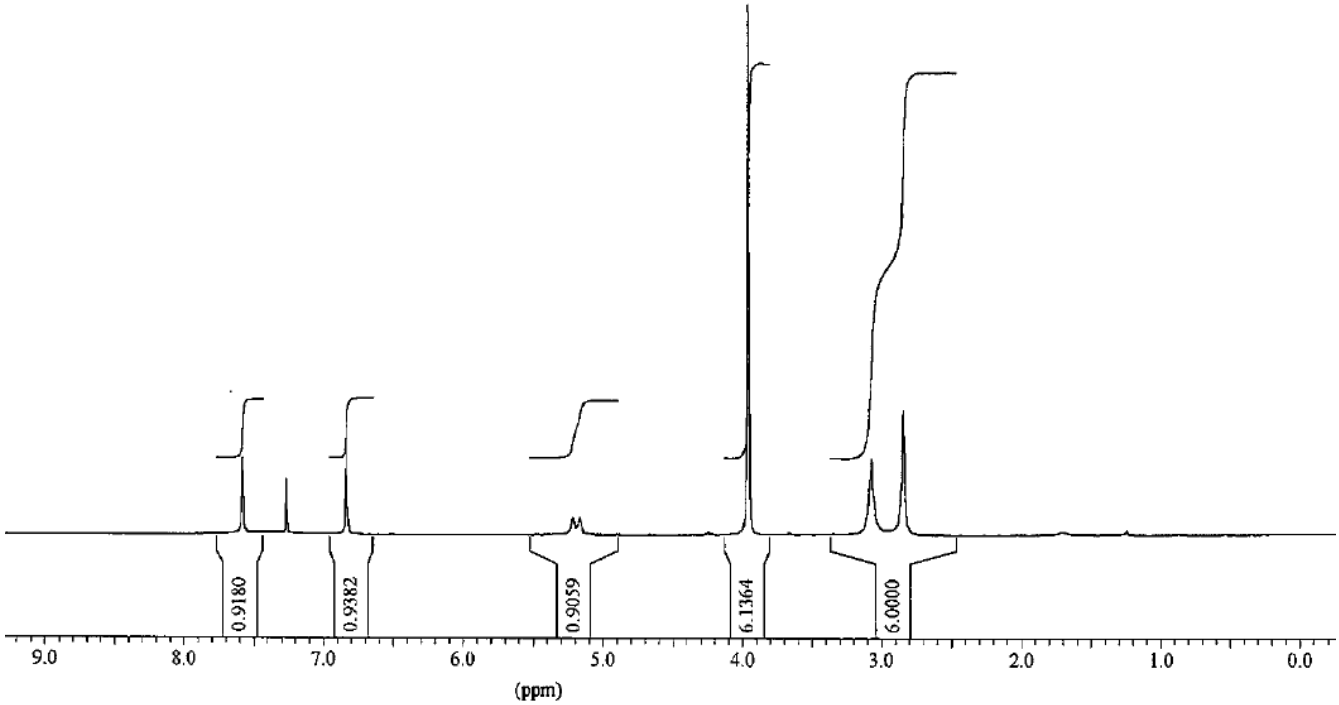

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
(ppm)

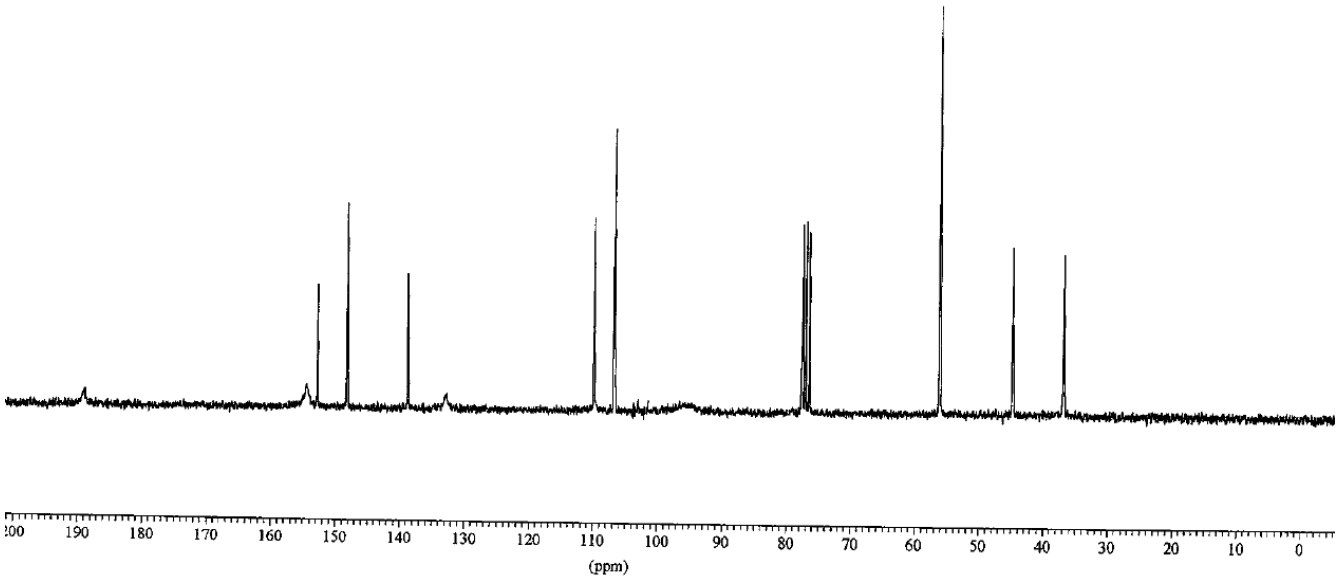
1h


Integral
1.7980
2.8559
1.8285
1.9353
0.9318
3.0000
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

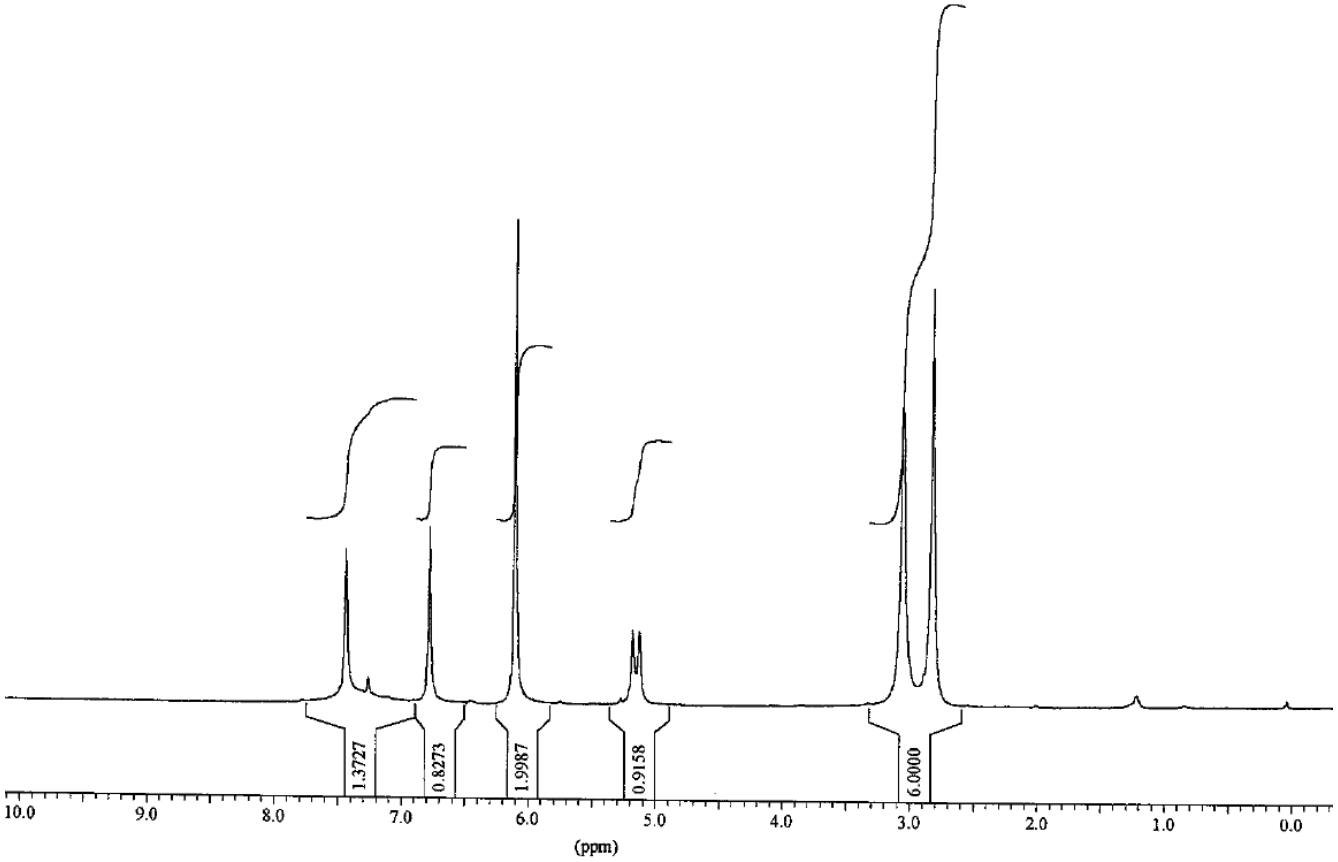

220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

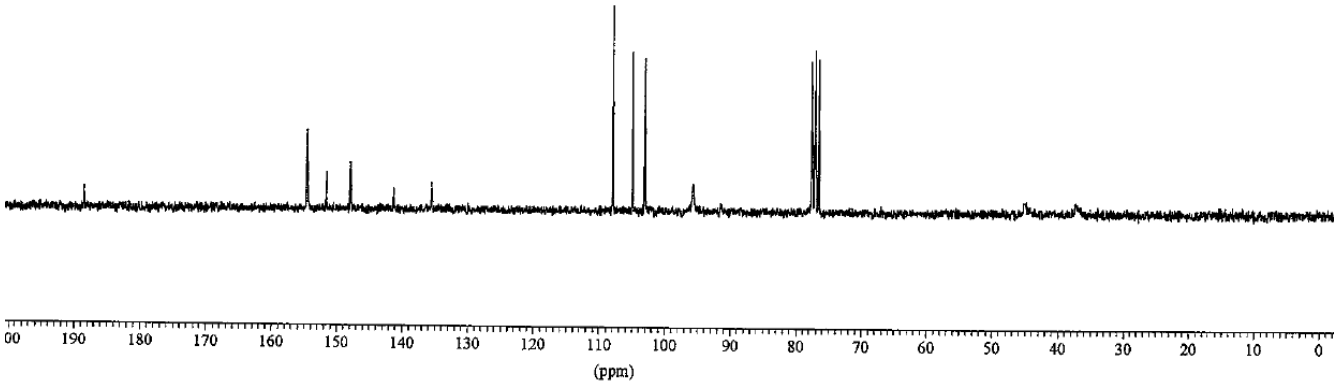
3b


0.9180
0.9382
0.9059
6.1364
6.0000
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

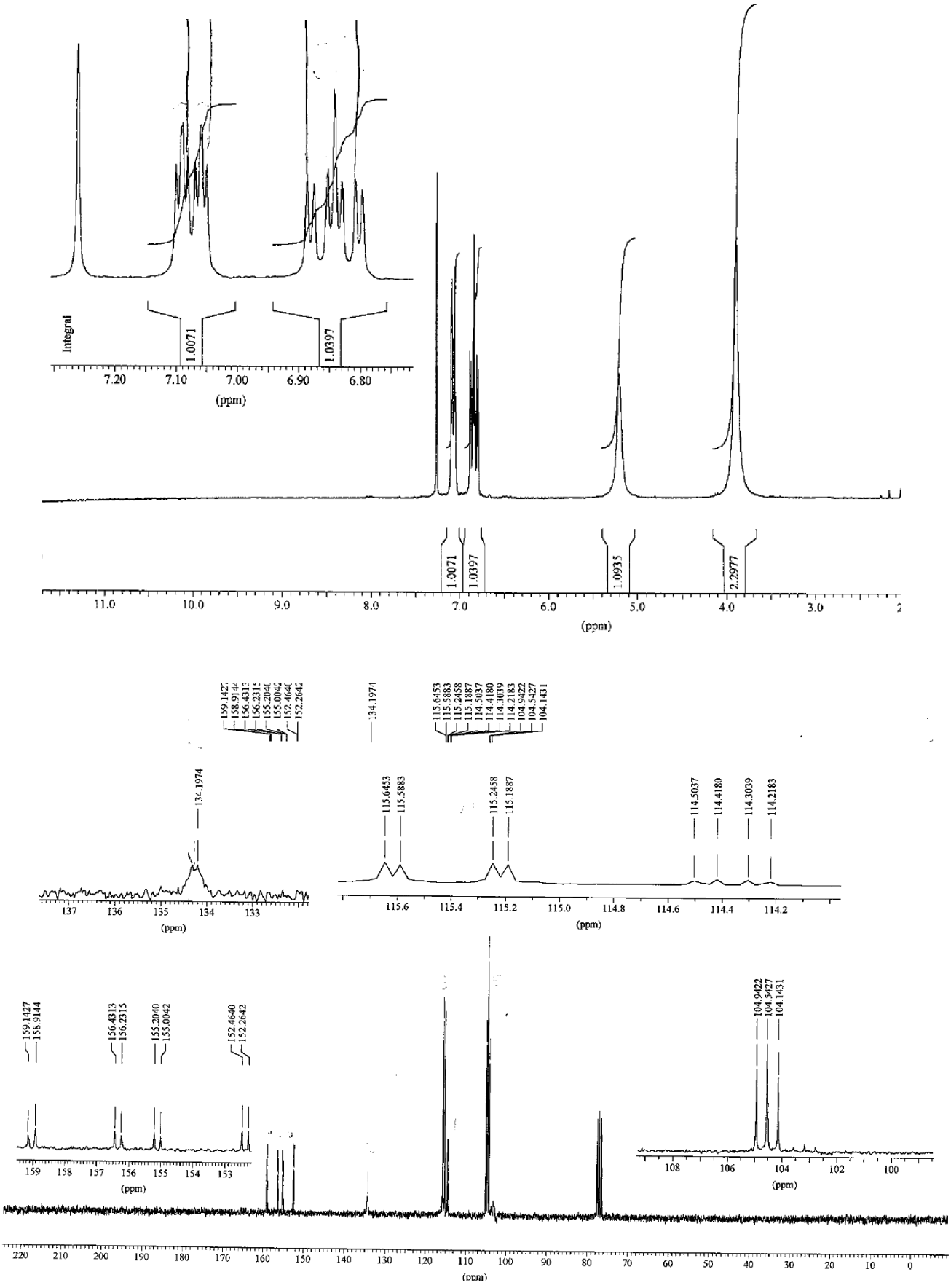

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

3c

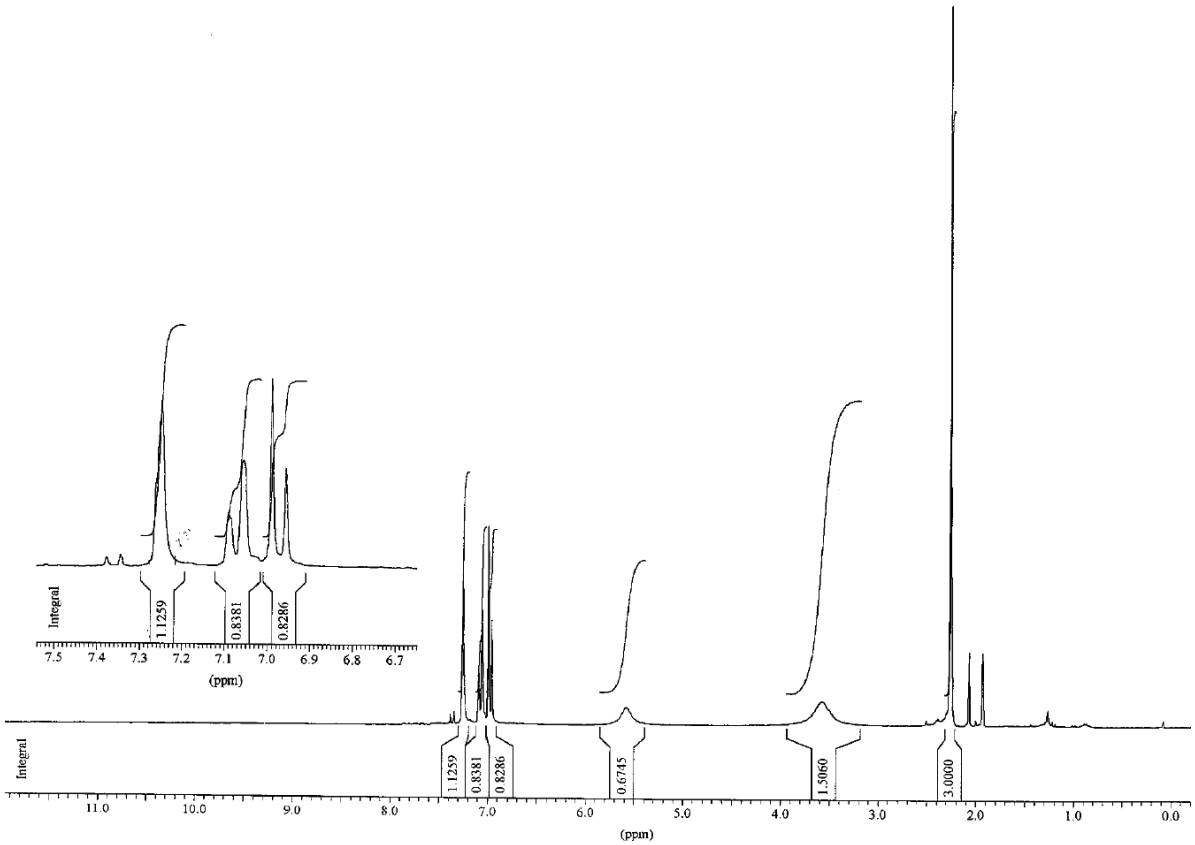

1.3727
0.8273
1.9987
0.9158
6.0000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

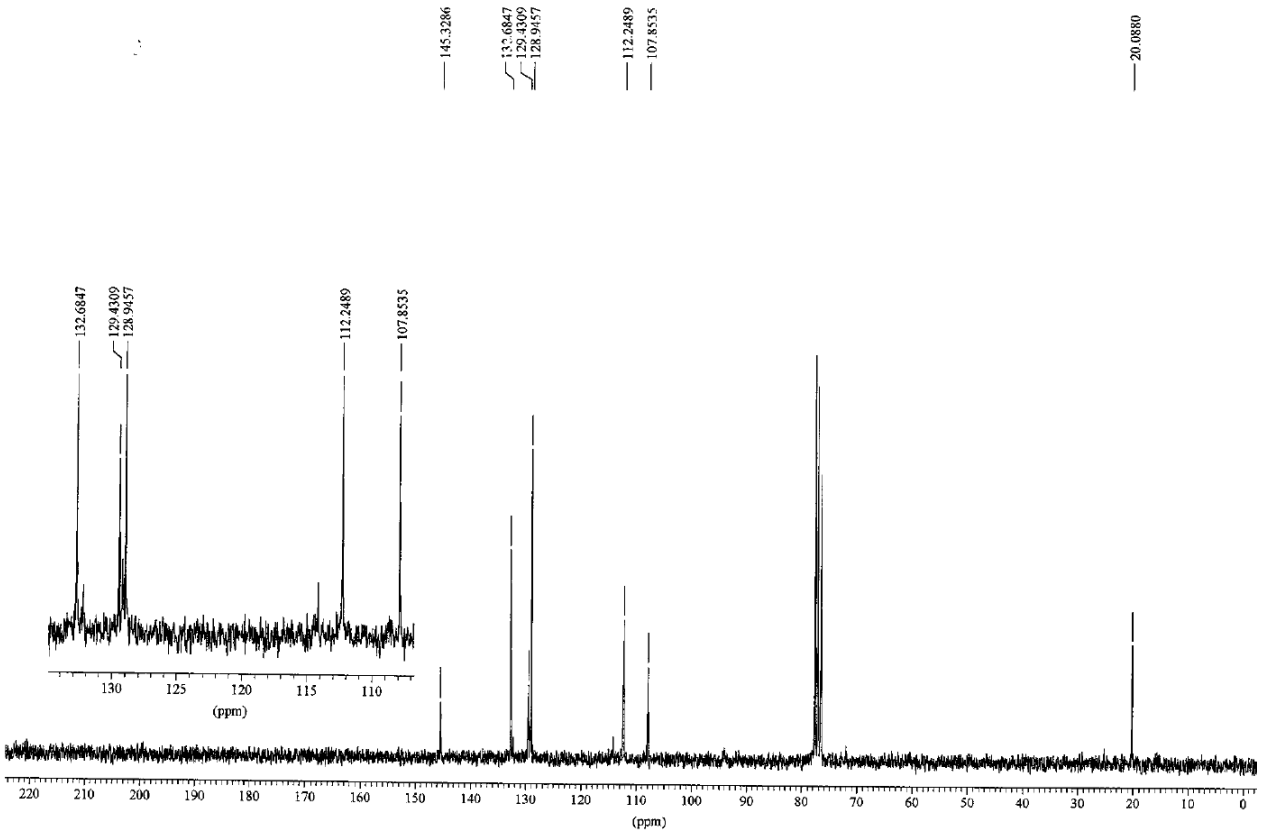

190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

4b

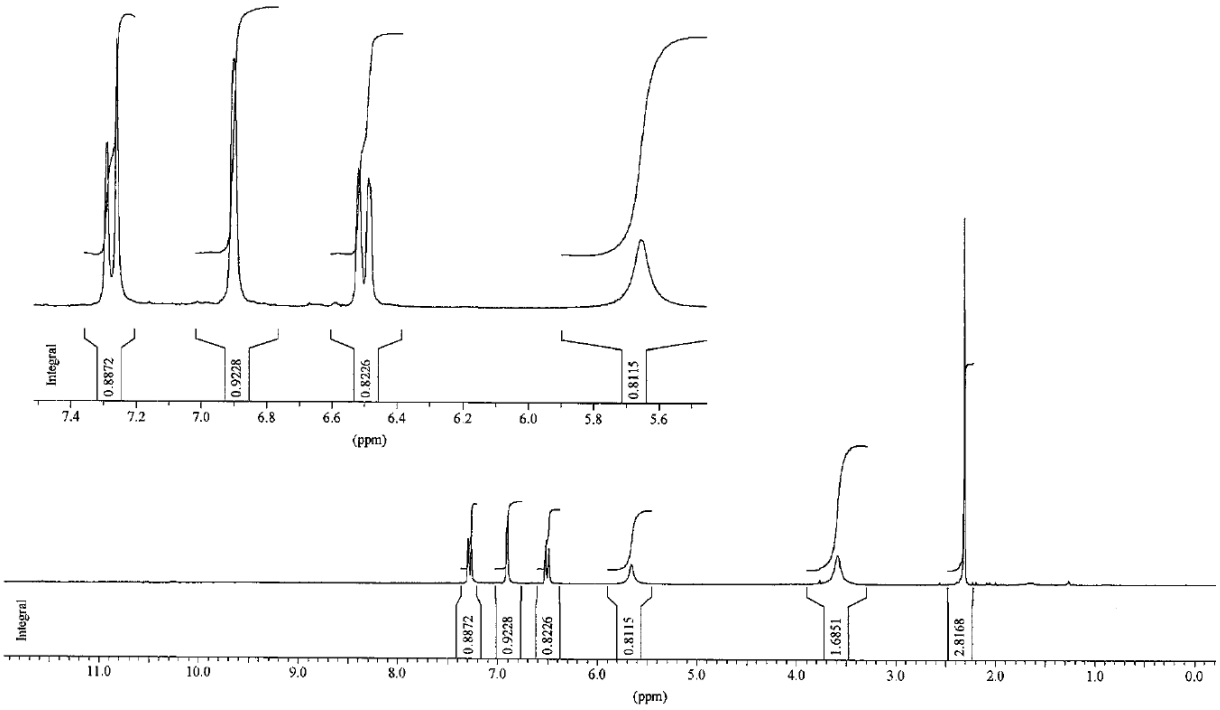

Integral
1.0071
1.0397
(ppm)
1.0071
1.0397
1.0935
2.2977
(ppm)
159.1427
158.9144
156.4313
156.2315
155.2040
155.0042
152.4640
152.2642
134.1974
115.6453
115.5883
115.2458
115.1887
114.5037
114.4180
114.3039
114.2183
104.9422
104.5427
104.1431
(ppm)
(ppm)
(ppm)
(ppm)

4c

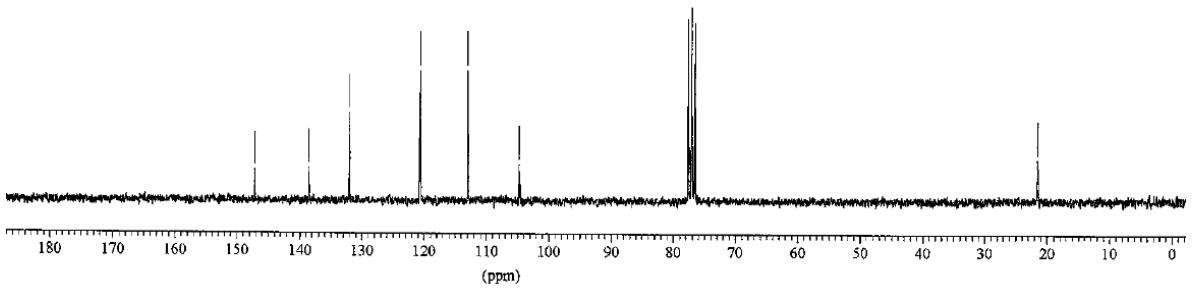

Integral
1.1259
0.8381
0.8286
(ppm)
Integral
1.1259
0.8381
0.8286
0.6745
1.5060
3.0000
(ppm)


145.3286
132.6847
129.4309
128.9457
112.2489
107.8535
20.0880
132.6847
129.4309
128.9457
112.2489
107.8535
(ppm)
(ppm)

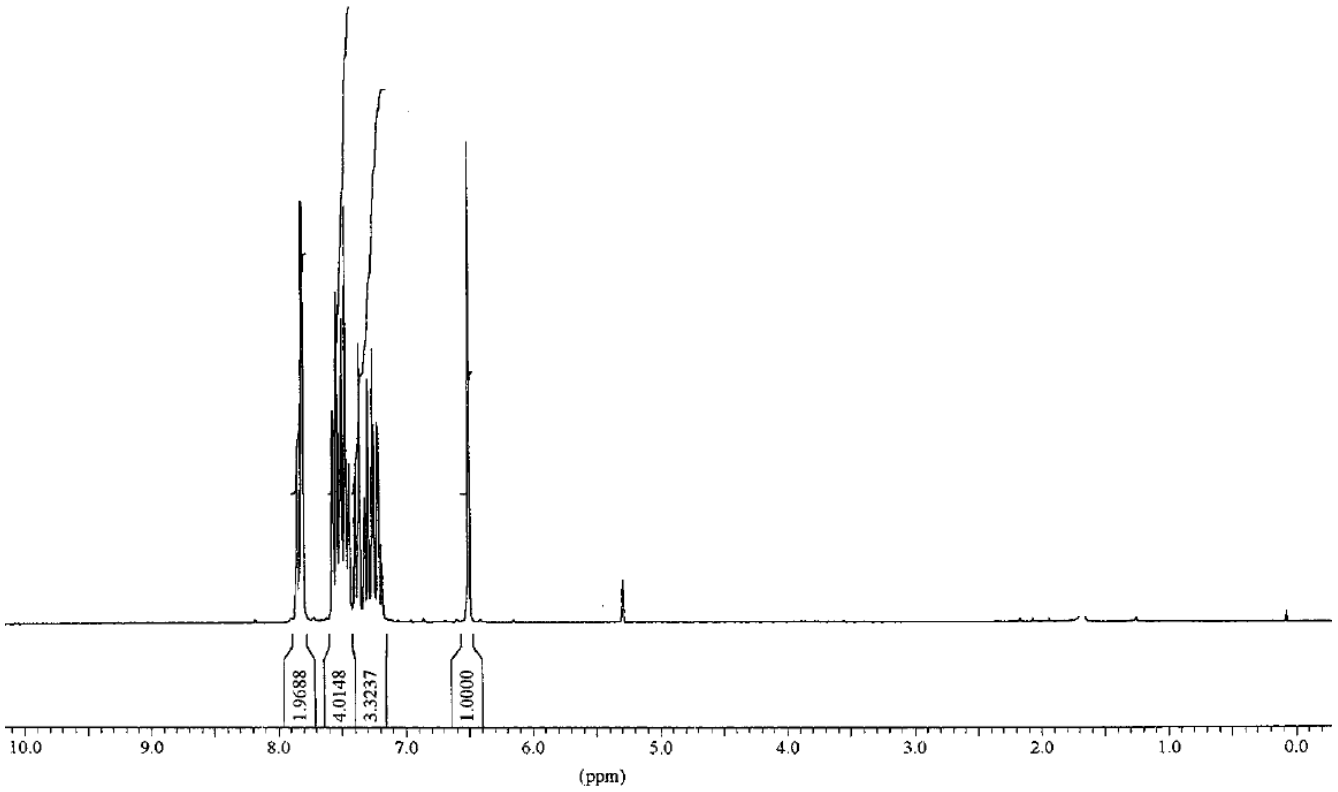
4d

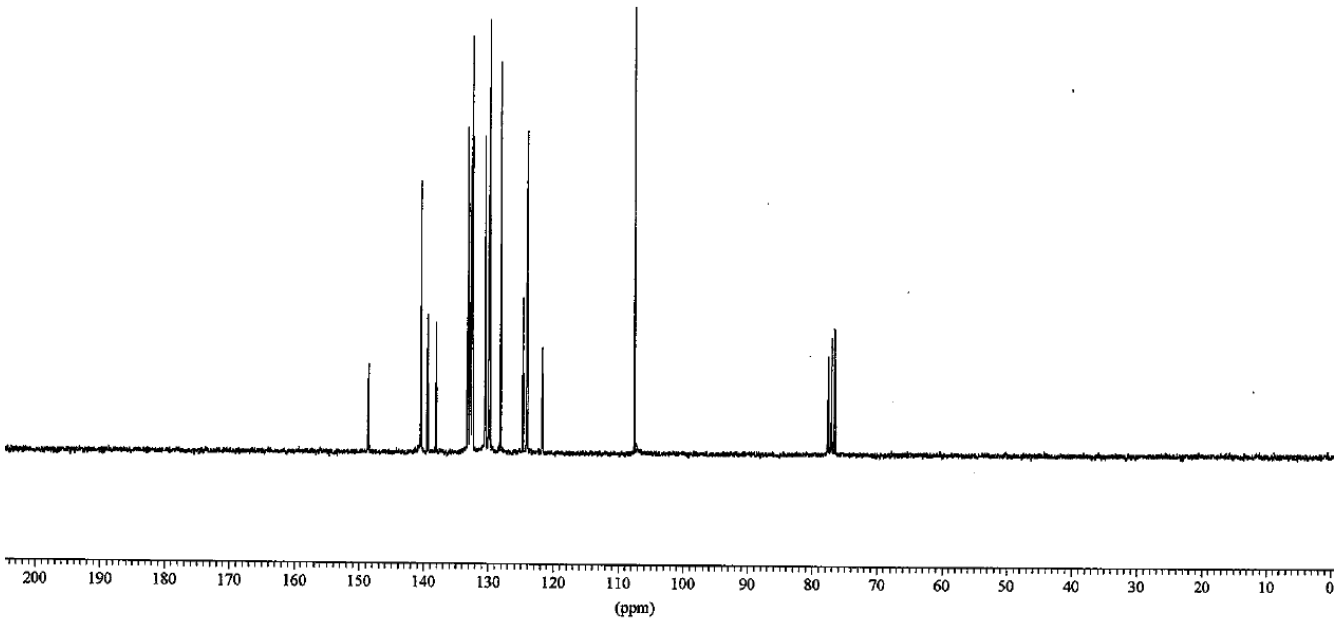

Integral
0.8872
0.9228
0.8226
0.8115
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
(ppm)
Integral
0.8872
0.9228
0.8226
0.8115
1.6851
2.8168
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)


147.1267
138.5072
131.9997
120.5545
112.9053
104.6568
21.4580

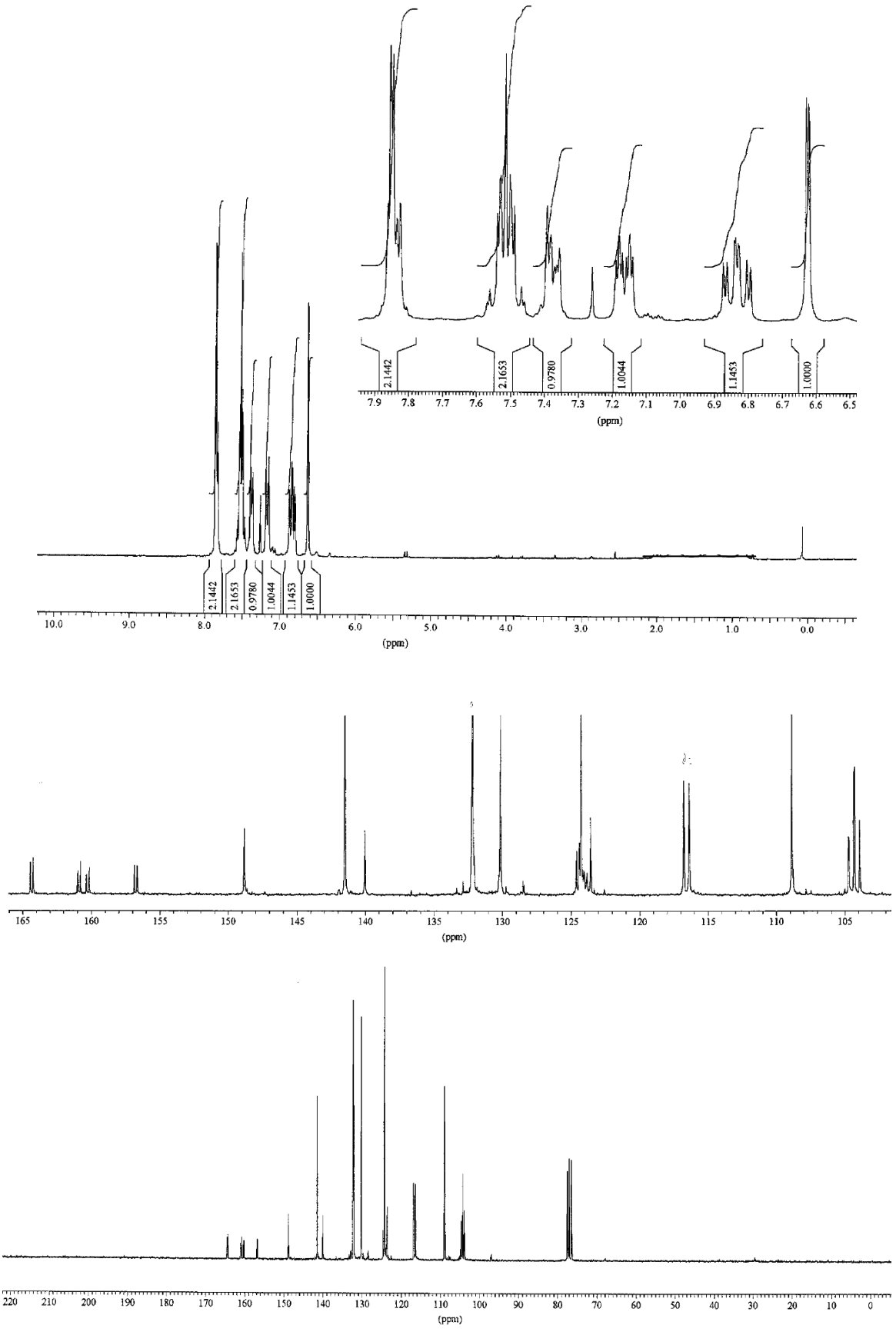

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

5a

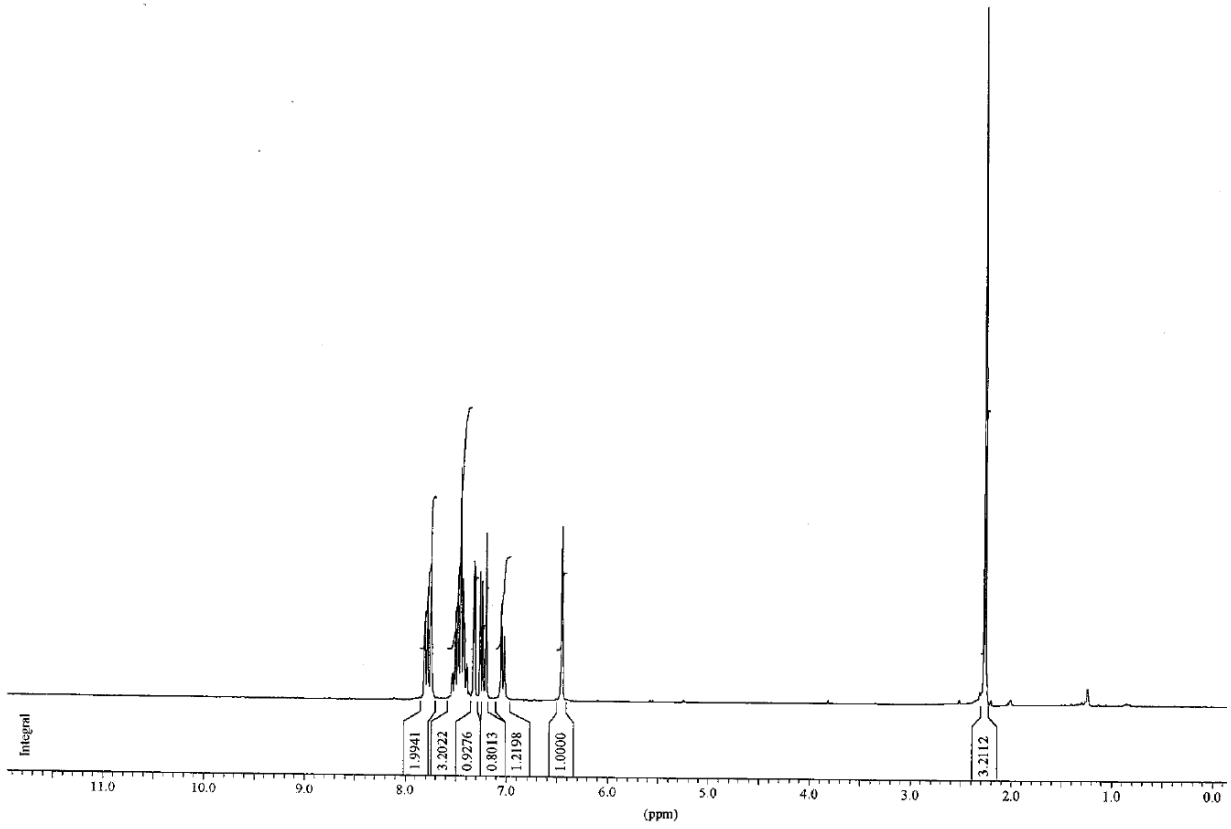

1.9688
4.0148
3.3237
1.0000
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

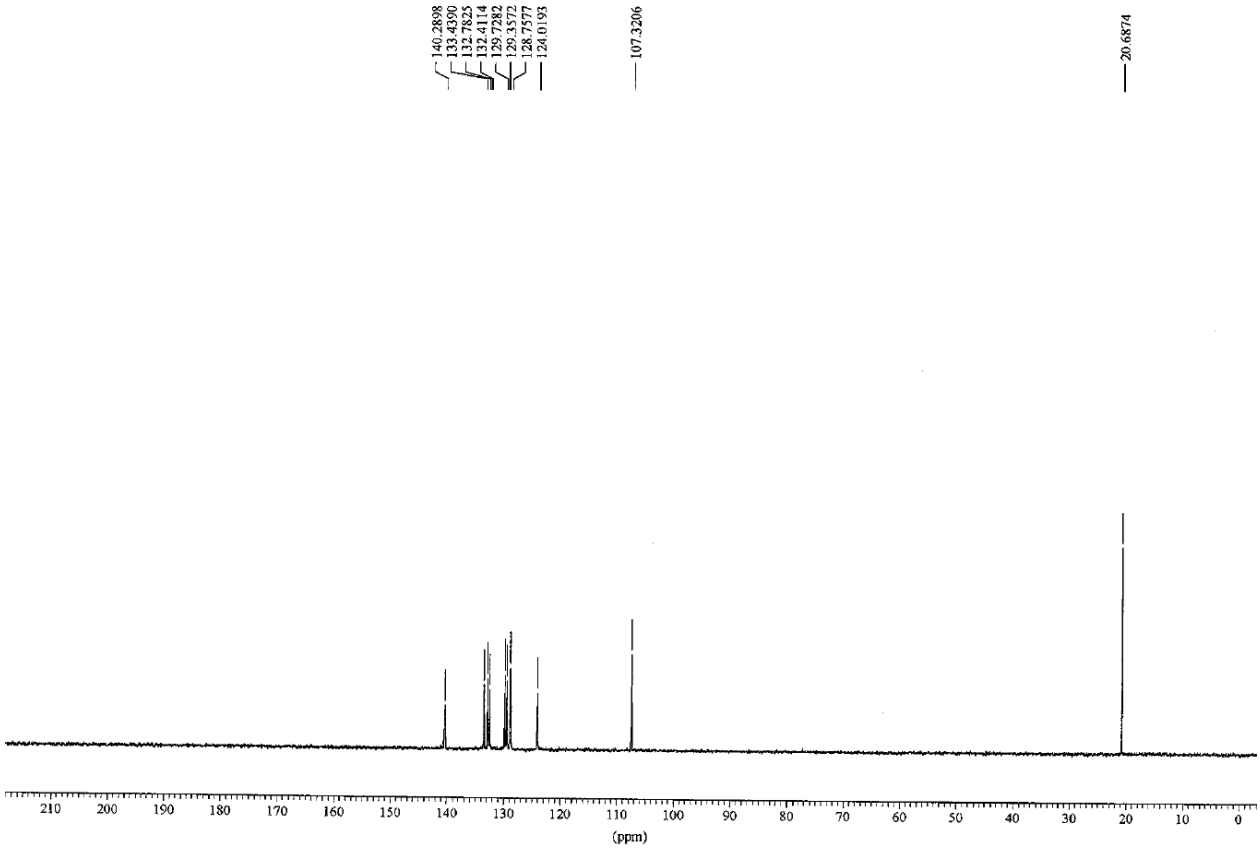

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

5b

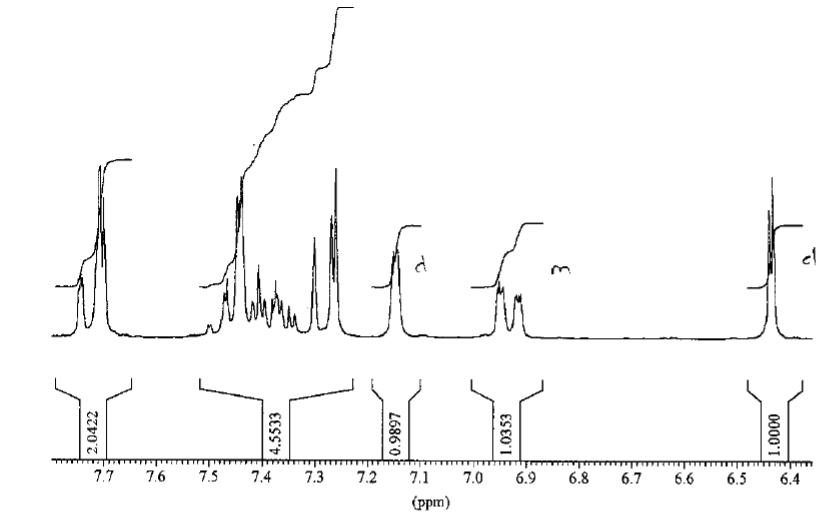


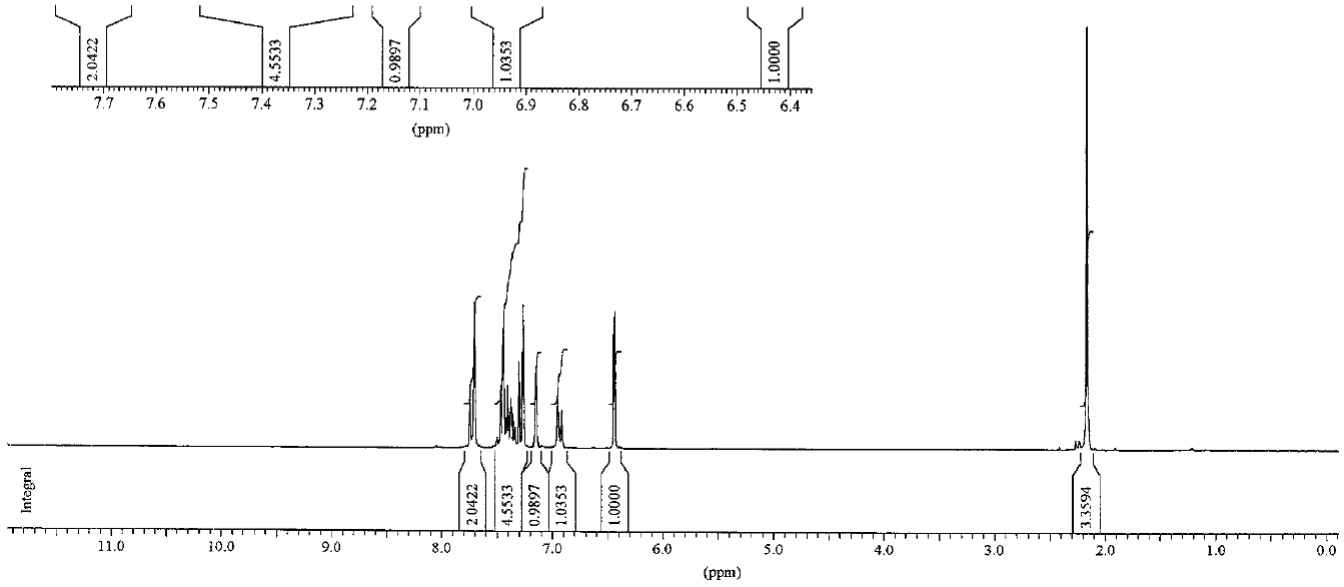
5c

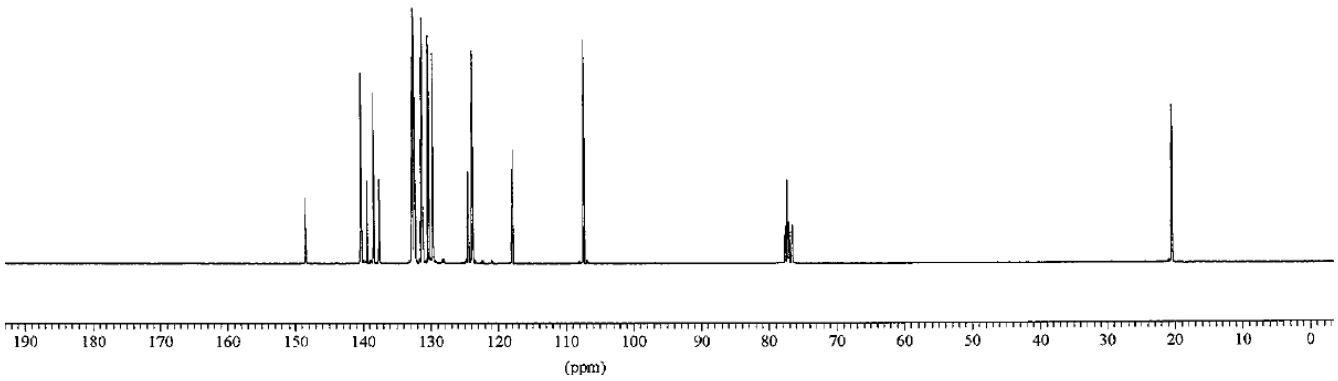

Integral
1.9941
3.2022
0.9276
0.8013
1.2198
1.0000
3.2112
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)


140.2898
133.4390
132.7825
132.4114
129.7282
129.3572
128.7577
124.0193
107.3206
20.6874
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

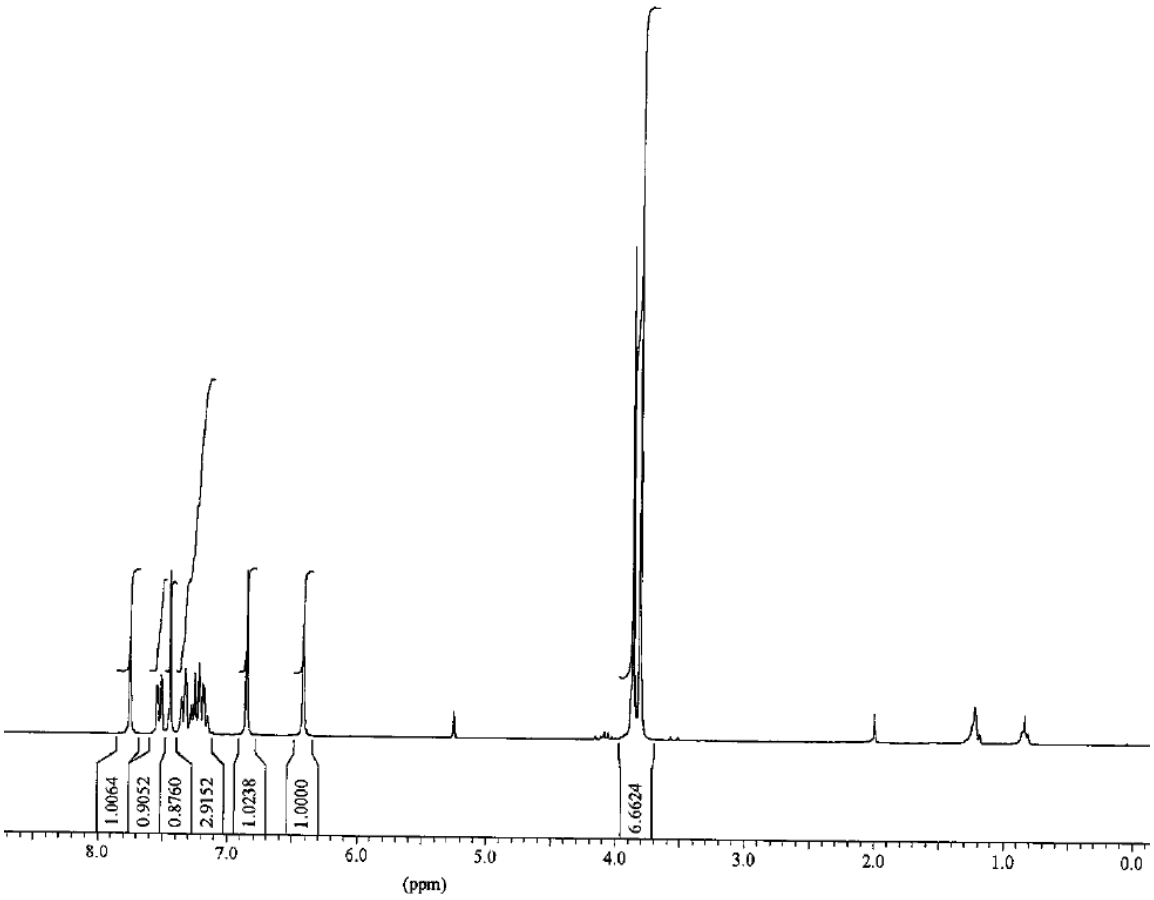
5d

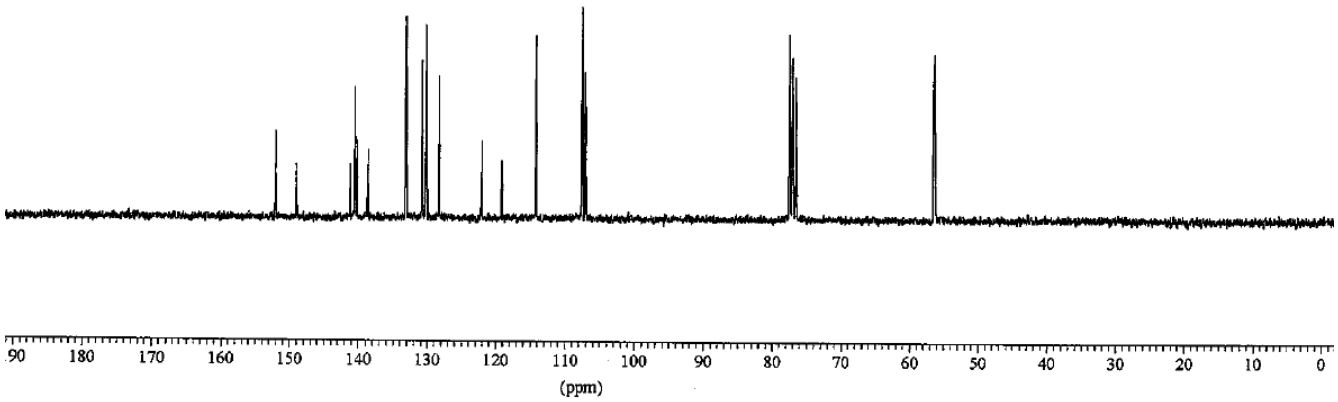

d
m
d1
2.0422
4.5533
0.9897
1.0353
1.0000
(ppm)


Integral
2.0422
4.5533
0.9897
1.0353
1.0000
3.3594
(ppm)

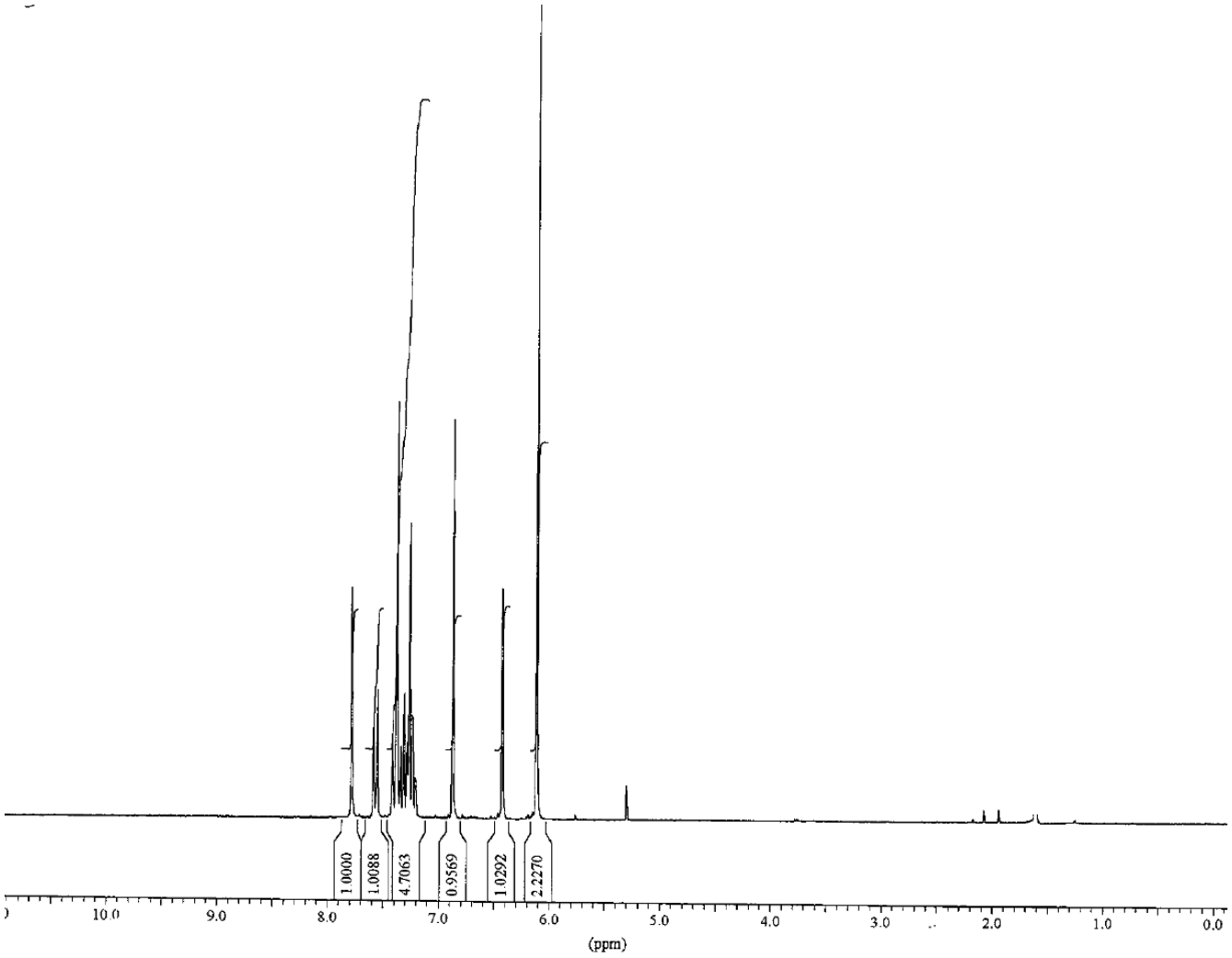

(ppm)

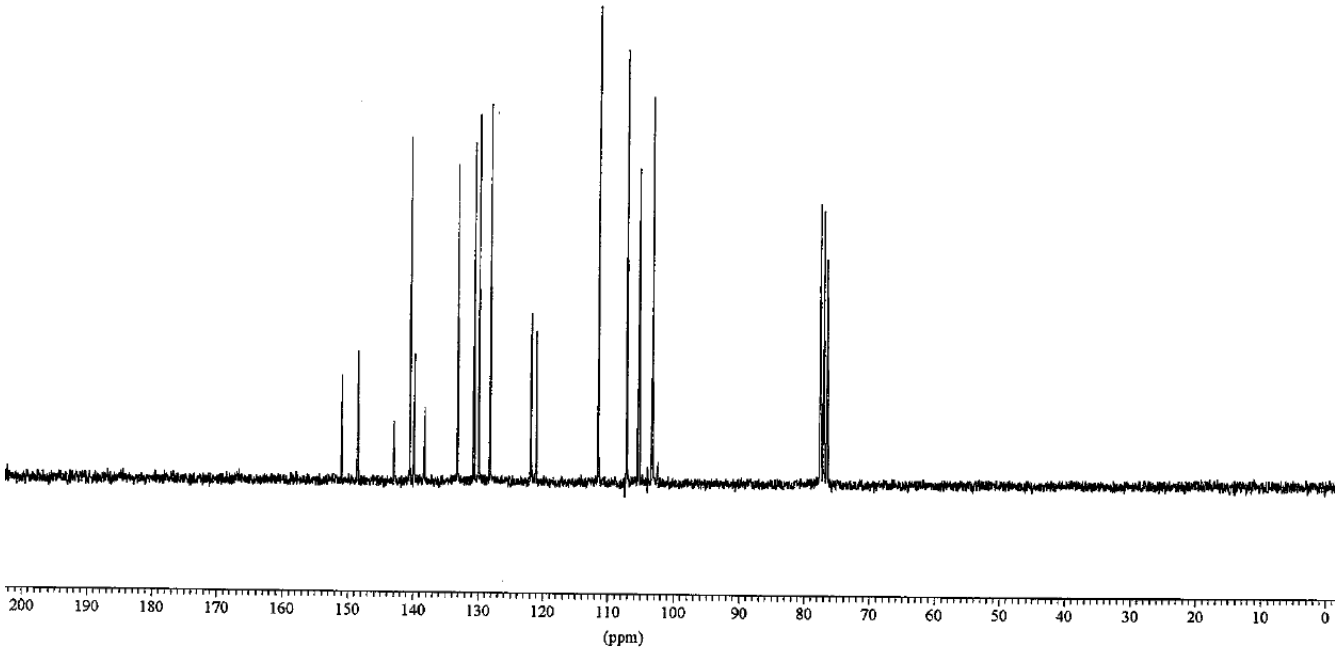
5e


1.0064
0.9052
0.8760
2.9152
1.0238
1.0000
6.6624
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

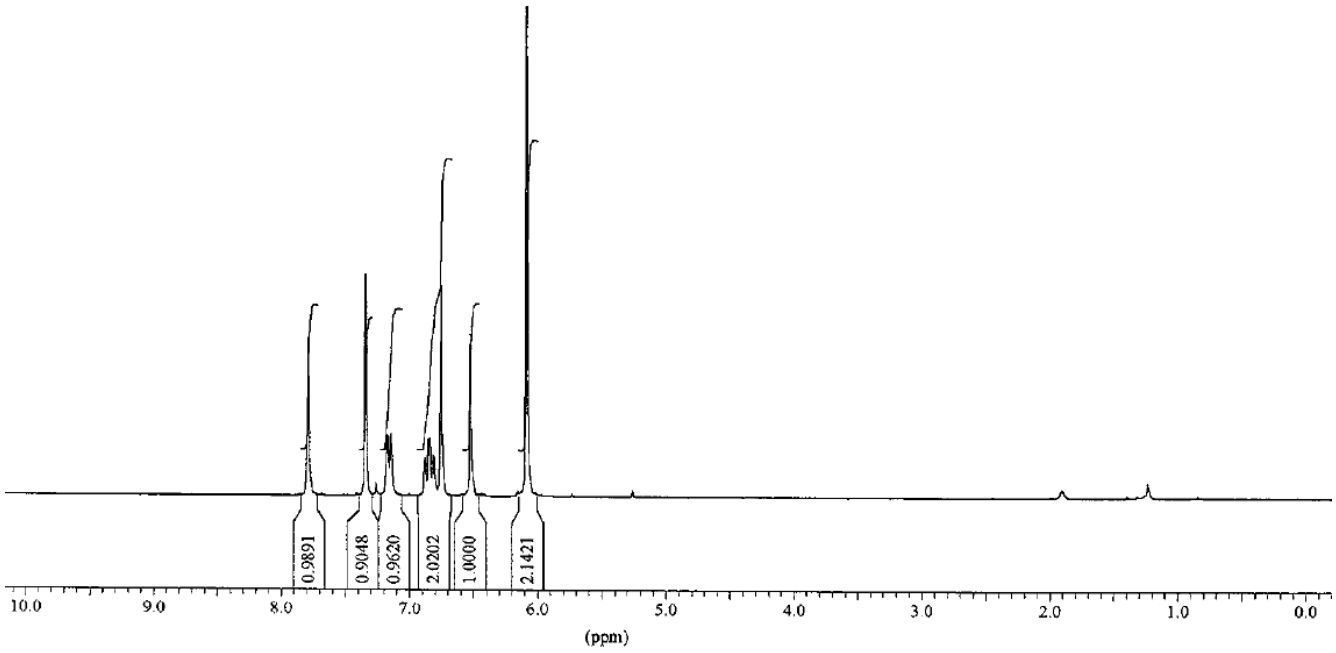

90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

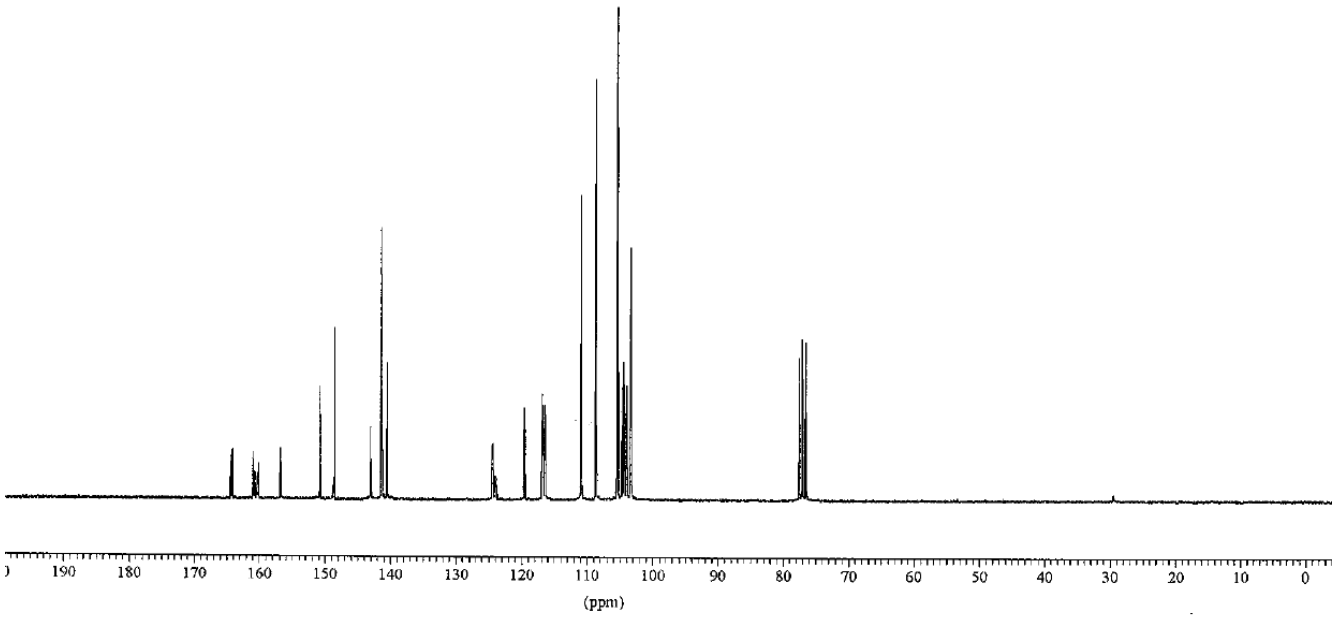
5f


1.0000
1.0088
4.7063
0.9569
1.0292
2.2270
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)

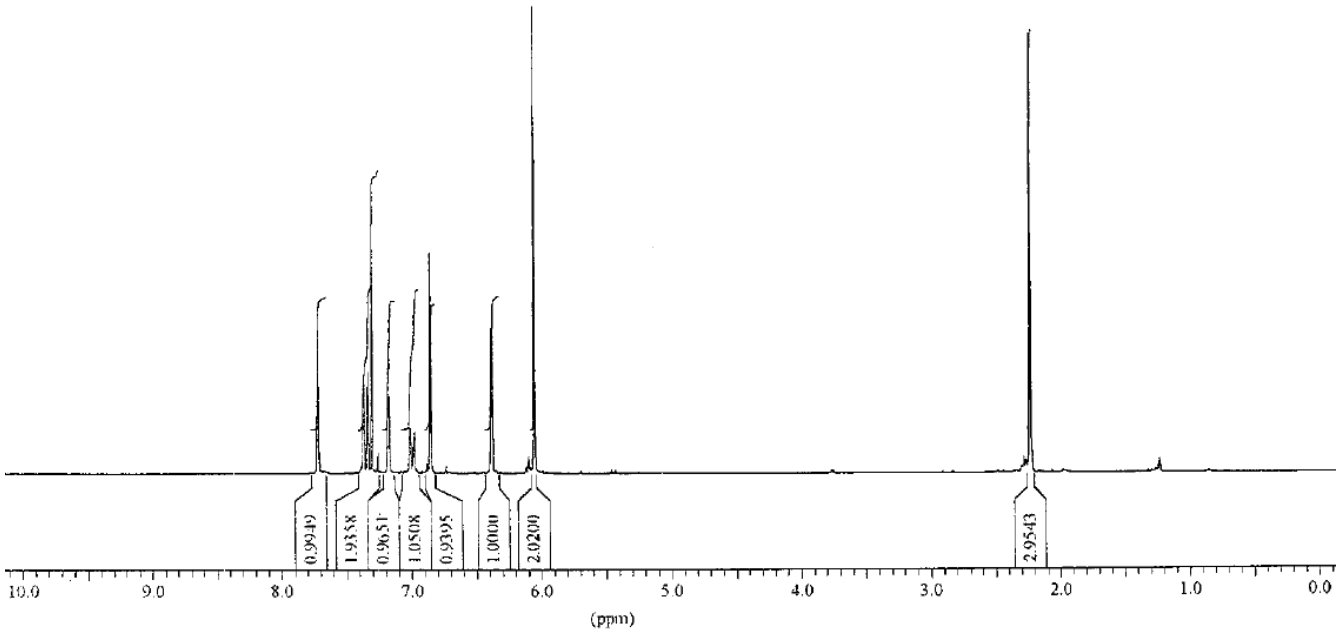

200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

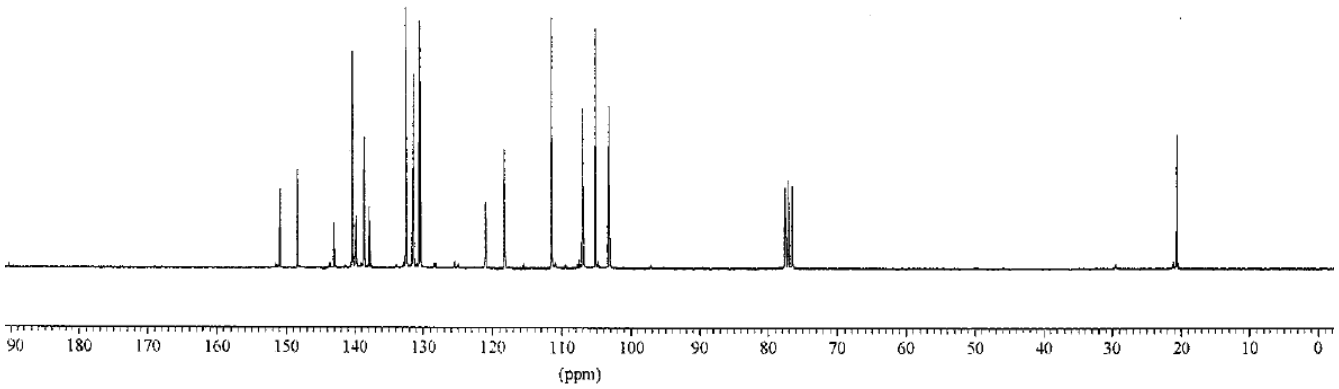
5g


0.9891
0.9048
0.9620
2.0202
1.0000
2.1421
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)


190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)

5h


0.9949
1.9358
0.9651
1.0508
0.9395
1.0000
2.0200
2.9543
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
(ppm)


90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
(ppm)