Water mediated construction of trisubstituted pyrazoles/isoxazoles library using ketene dithioacetals

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Experimental section: ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded in DMSO and $CDCl_3$, and TMS was used as an internal reference on a Bruker AVANCE II spectrometer. Mass spectra were determined using direct inlet probe on a GCMS-QP2010 mass spectrometer. IR spectra were recorded on KBr discs, using FTIR-8400 spectrophotometer. Purity was determined on Waters Acquity UPLC with PDA Detector using Acquity BEH C18 50 × 2.1, 1.7um column at 254 nm. Melting points were measured in open capillaries and are uncorrected. Chemicals were supplied by E. Merck (Germany), Loba Chemie (India) and S. D. Fine Chemicals (India) and used without further purification unless otherwise stated. The solvents were analytical grade and demineralized water was used. Analytical thin layer chromatography (TLC) was performed on Silica Gel 60 F_{254} precoated plates.

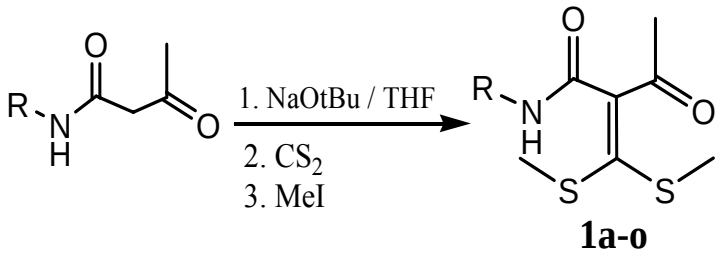
Gradient Program for UPLC

Mobile Phase: **A** - 5 mM Ammonium dihydrogenphosphate pH = 2.5,
B – Acetonitrile

Entry	Time	Flow	%A	%B
1	Initial	0.2 ml	95	05
2	4.0 min	0.2 ml	05	95
3	4.1 min	0.2 ml	95	05
4	5.0 min	0.2 ml	95	05

General procedure for the synthesis of various *α*-acylketene dithioacetals 1a-o.

To a well-stirred suspension of sodium *tert*-butoxide (2.88 g, 30 mmol) in THF (15 mL) at 0 ºC was added CS_2 (0.9 mL, 15 mmol) diluted with 10 mL THF along with *N*-(aryl)-3-oxobutanamide (15 mmol) over a period of 30 min. After completion of the addition, the reaction mixture was stirred at 0 ºC for 1.0 h. Appearance of reddish solid in the reaction medium indicated the formation of disodium salt. To this reaction, a solution of methyl iodide (1.86 mL, 30 mmol) in THF (5 mL) was added dropwise within 15 min at 0 ºC. The mixture was allowed to warm to room temperature and stirred for 5 h, and then poured onto crushed ice (100 g) under stirring. The separated solid was collected by filtration, washed with water (2 × 100 mL), dried in *vacuo* and crystallized from chloroform to furnish the analytically pure products in excellent yield.



1a-o

2-(bis(methylthio)methylene)-3-oxo-*N*-phenylbutanamide 1a

Yellow solid; R_f 0.67 (8:2 hexane-EtOAc); yield 99%; m.p.103-105 °C; ^{1}H NMR: δ 1.91 (s, 3H), 2.45 (s, 6H), 7.06-7.71 (m, 5H), 8.73 (s, 1H); IR (KBr, cm^{-1}) 3349, 1674, 1662, 1529, 1307; MS (*m/z*): 281 (M + H); Anal. Calcd for $C_{13}H_{15}NO_2S_2$: C, 55.49; H, 5.37; N, 4.98; Found: C, 55.35; H, 5.24; N, 4.89.

2-(bis(methylthio)methylene)-3-oxo-*N*-p-tolylbutanamide 1b

Yellow solid; R_f 0.61 (8:2 hexane-EtOAc); yield 97%; m.p.108-110 °C; ^{1}H NMR: δ 1.57 (s, 3H), 1.87 (s, 3H), 2.44 (s, 6H), 6.99-7.03 (m, 2H), 7.51-7.54 (m, 2H), 8.24 (s, 1H); IR (KBr,

cm^{-1}) 3369, 1672, 1662, 1529, 1315; MS (*m/z*): 295 (M + H); Anal. Calcd for $C_{14}H_{19}NO_2S_2$: C, 56.92; H, 5.80; N, 4.74; Found: C, 56.77; H, 5.74; N, 4.59.

2-(bis(methylthio)methylene)-*N*-(4-methoxyphenyl)-3-oxobutanamide 1c

Yellow solid; R_f 0.65 (8:2 hexane-EtOAc); yield 96%; m.p.111-113 °C; ^{1}H NMR δ: 1.85 (s, 3H), 2.44 (s, 6H), 3.75 (s, 3H), 7.01-7.05 (m, 2H), 7.84-7.89 (m, 2H), 8.38 (s, 1H); IR (KBr, cm^{-1}) 3299, 1676, 1599, 1533, 1307; MS (*m/z*): 311 (M + H); Anal. Calcd for $C_{14}H_{17}NO_3S_2$: C, 53.99; H, 5.50; N, 4.50; Found: C, 53.75; H, 5.44; N, 4.39.

2-(bis(methylthio)methylene)-*N*-(4-fluorophenyl)-3-oxobutanamide 1d

Reddish brown solid; R_f 0.59 (8:2 hexane-EtOAc); yield 97%; m.p.128-130 °C; ^{1}H NMR: δ 1.84 (s, 3H), 2.44 (s, 6H), 6.97-7.02 (m, 2H), 7.48-7.51 (m, 2H), 8.58 (s, 1H); IR (KBr, cm^{-1}) 3285, 1654, 1632, 1519, 1297; MS (*m/z*): 299 (M + H); Anal. Calcd for $C_{13}H_{14}FNO_2S_2$: C, 52.15; H, 4.71; N, 6.35; Found: C, 52.05; H, 4.64; N, 6.39.

2-(bis(methylthio)methylene)-*N*-(2-methoxyphenyl)-3-oxobutanamide 1e

Yellowish solid; R_f 0.66 (8:2 hexane-EtOAc); yield 97%; m.p. 112-114 ºC; ^{1}H NMR: δ 1.91 (s, 3H), 2.48 (s, 6H), 3.77 (s, 3H), 7.09-7.16 (m, 2H), 7.25-7.44 (m, 2H), 9.11 (s, 1H); IR (KBr, cm^{-1}) 3327, 1645, 1589, 1533, 1489, 1417, 1313, 1254, 1202, 1091, 831; MS (*m/z*): 311 (M + H); Anal. Calcd for $C_{14}H_{17}NO_3S_2$: C, 53.99; H, 5.50; N, 4.50; Found: C, 53.02; H, 5.39; N, 4.41.

2-(bis(methylthio)methylene)-3-oxo-*N*-o-tolylbutanamide 1f

Yellowish solid; R_f 0.63 (8:2 hexane-EtOAc); yield 97%; m.p. 105-107 ºC; ^{1}H NMR: δ 1.55 (s, 3H), 1.89 (s, 3H), 2.46 (s, 6H), 7.01-7.06 (m, 2H), 7.52-7.55 (m, 2H), 8.87 (s, 1H); IR (KBr, cm-1) 3227, 1640, 1599, 1543, 1486, 1397, 1322, 1264, 1223, 1191, 831; MS (m/z): 295 (M + H); Anal. Calcd for $C_{14}H_{19}NO_2S_2$: C, 56.92; H, 5.80; N, 4.74; Found: C, 56.79; H, 5.71; N, 4.60.

2-(bis(methylthio)methylene)-*N*-(4-chlorophenyl)-3-oxobutanamide 1g

Yellowish solid; R_f 0.63 (8:2 hexane-EtOAc); yield 95%; m.p. 153-155 ºC; ^{1}H NMR: δ 1.86 (s, 3H), 2.44 (s, 6H), 7.14-7.29 (m, 2H), 7.32-7.57 (m, 2H), 9.06 (s, 1H); IR (KBr, cm-^{1}) 3274, 1652, 1551, 1492, 1092, 826; MS (m/z): 315 (M + H); Anal. Calcd for $C_{13}H_{14}ClNO_2S_2$: C, 49.44; H, 4.47; N, 4.43; Found: C, 49.17; H, 4.32; N, 4.37.

2-(bis(methylthio)methylene)-*N*-(4-ethylphenyl)-3-oxobutanamide 1h

Yellowish solid; R_f 0.67 (8:2 hexane-EtOAc); yield 97%; m.p. 139-141 ºC; ^{1}H NMR: δ 1.11-1.14 (t, 3H), 1.85 (s, 3H), 2.44 (s, 6H), 2.48-2.52 (q, 2H), 6.98-7.04 (m, 2H), 7.42-7.57 (m, 2H), 8.96 (s, 1H); IR (KBr, cm-^{1}) 3354, 1664, 15451, 1462, 1101, 846. MS (*m/z*): 309 (M + H); Anal. Calcd for $C_{15}H_{19}NO_2S_2$: C, 58.22; H, 6.19; N, 4.53; Found: C, 58.07; H, 6.02; N, 4.57.

2-(bis(methylthio)methylene)-*N*-(4-nitrophenyl)-3-oxobutanamide 1i

Pale yellow solid; R_f 0.71 (8:2 hexane-EtOAc); yield 97%; m.p. 138-140 ºC; ^{1}H NMR: δ 1.91 (s, 3H), 2.48 (s, 6H), 8.09-8.15 (m, 2H), 8.32-8.45 (m, 2H), 8.85 (s, 1H); IR (KBr, cm^{-1}) 3257, 1655, 1599, 1563, 1519, 1457, 1323, 1212, 1181, 861; MS (*m/z*): 326 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_4S_2$: C, 47.84; H, 4.32; N, 8.58; Found: C, 47.69; H, 4.34; N, 8.60.

2-(bis(methylthio)methylene)-*N*-(3-chloro-4-fluorophenyl)-3-oxobutanamide 1j

Yellowish solid; R_f 0.63 (8:2 hexane-EtOAc); yield 95%; m.p. 144-146 ºC; ^{1}H NMR: δ 1.92 (s, 3H), 2.51 (s, 6H), 7.14-7.30 (m, 2H), 7.36-7.45 (m, 1H), 9.16 (s, 1H); IR (KBr, cm-^{1}) 3354, 1657, 1561, 1512, 1112, 826; MS (*m/z*): 333 (M + H); Anal. Calcd for $C_{13}H_{13}ClFNO_2S_2$: C, 46.77; H, 3.93; N, 4.20; Found: C, 46.58; H, 4.04; N, 4.27.

2-(bis(methylthio)methylene)-*N*-(5-chloro-2-methoxyphenyl)-3-oxobutanamide 1k

Yellowish solid; R_f 0.64 (8:2 hexane-EtOAc); yield 94%; m.p. 136-138 ºC; ^{1}H NMR: δ 1.84 (s, 3H), 2.44 (s, 6H), 3.67 (s, 3H), 6.99-7.16 (m, 2H), 7.35-7.42 (m, 1H), 9.24 (s, 1H); IR (KBr, cm^{-1}) 3297, 1645, 1569, 1513, 1502, 1467, 1293, 1254, 1201, 1091, 831; MS (*m/z*):

345 (M + H); Anal. Calcd for $C_{14}H_{16}ClNO_3S_2$: C, 48.62; H, 4.66; N, 4.05; Found: C, 48.55; H, 4.54; N, 3.99.

2-(bis(methylthio)methylene)-*N*-(2,5-dichlorophenyl)-3-oxobutanamide 1l

Yellowish solid; R_f 0.64 (8:2 hexane-EtOAc); yield 94%, m.p; 158-160 ºC; ^{1}H NMR: δ 1.74 (s, 3H), 2.39 (s, 6H), 6.99-7.05 (m, 2H), 7.25-7.36 (m, 1H), 9.19 (s, 1H); IR (KBr, cm^{-1}) 3387, 1675, 1619, 1583, 1519, 1415, 1326, 1284, 1202, 1191, 811; MS (*m/z*): 350 (M + H); Anal. Calcd for $C_{13}H_{13}Cl_2NO_2S_2$: C, 44.58; H, 3.74; N, 4.00; Found: C, 44.45; H, 3.59; N, 4.09.

2-(bis(methylthio)methylene)-*N*-(2,5-dimethylphenyl)-3-oxobutanamide 1m

Pale yellow solid; R_f 0.62 (8:2 hexane-EtOAc); yield 97%; m.p. 125-127 ºC; ^{1}H NMR: δ 1.65 (s, 6H), 1.97 (s, 3H), 2.48 (s, 6H), 6.88-7.03 (m, 2H), 7.12-7.16 (t, 1H), 9.07 (s, 1H); IR (KBr, cm-^{1}) 3327, 1678, 1602, 1565, 1501, 1499, 1352, 1284, 1214, 1187, 811; MS (*m/z*): 309 (M + H); Anal. Calcd for $C_{15}H_{19}NO_2S_2$: C, 58.22; H, 6.19; N, 4.53; Found: C, 58.15; H, 6.04; N, 4.39.

2-(bis(methylthio)methylene)-*N*-(4-chloro-2-methylphenyl)-3-oxobutanamide 1n

Yellowish solid; R_f 0.67 (8:2 hexane-EtOAc); yield 94%; m.p. 148-150 ºC; ^{1}H NMR: δ 1.85 (s, 3H), 1.96 (s, 3H), 2.46 (s, 6H), 7.01-7.33 (m, 3H), 8.98 (s, 1H); IR (KBr, cm-^{1}) 3398, 1676, 1592, 1555, 1503, 1489, 1312, 1287, 1214, 811; MS (*m/z*): 330 (M + H); Anal. Calcd for $C_{14}H_{16}ClNO_2S_2$: C, 50.98; H, 4.89; N, 4.25; Found: C, 50.85; H, 4.74; N, 4.19.

2-(bis(methylthio)methylene)-*N*-(3,4-difluorophenyl)-3-oxobutanamide 1o

Yellowish solid; R_f 0.64 (8:2 hexane-EtOAc); yield 93%; m.p. 132-134 ºC; ^{1}H NMR: δ 1.84 (s, 3H), 2.43 (s, 6H), 7.01-7.13 (m, 1H), 7.22-7.37 (m, 2H), 8.26 (s, 1H); IR (KBr, cm-^{1}) 3384, 1672, 1561, 1472, 1192, 817; MS (*m/z*): 317 (M + H); Anal. Calcd for $C_{13}H_{13}F_2NO_2S_2$: C, 49.20; H, 4.13; N, 4.41; Found: C, 49.04; H, 4.23; N, 4.32.

General procedure for the synthesis of trisubstituted pyrazoles 4a-o.

To a suspension of various *α*-acylketene dithioacetals **1a-o** (10 mmol) in water (25 mL), hydrazine hydrate 80% (1 mL, 20 mmol) was added and the reaction mixture was refluxed for appropriate time (Table 2) with constant stirring. After completion of the reaction, the reaction mixture was cooled to room temperature and add cold water (50 mL). The separated solid was filtered, washed with water (2 × 50 mL), dried and crystallized from methanol to afford analytically pure products which were used for next step without further purification.

3-methyl-5-(methylthio)-*N*-phenyl-1*H*-pyrazole-4-carboxamide 4a

white solid; R_f 0.41 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.52 (s, 3H), 2.63 (s, 3H), 7.11 (t, J = 7.58 Hz, 1H), 7.33 (t, 8.03 Hz, 2H), 7.69 (d, J = 7.7 Hz, 2H), 9.58 (s, 1H), 10.26 (s, 1H); ^{13}C NMR: δ 12.72, 16.42, 85.54, 120.38, 132.61, 138.99, 140.22, 146.22, 153.93, 167.05; MS (*m/z*): 247 (M + H); Anal. Calcd for $C_{12}H_{13}N_3OS$: C, 58.28; H, 5.30; N, 16.99; Found: C, 58.14; H, 5.13; N, 16.82.

***N*-(4-methylphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4b**

white solid; R_f 0.39 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.87 (s, 3H), 2.52 (s, 3H), 2.65 (s, 3H), 7.11 (d, J=8.4 Hz, 2H), 7.55 (d, J=8.5 Hz, 2H), 9.19 (s, 1H), 10.08 (s, 1H); ^{13}C NMR: δ 12.72, 15.29, 19.96, 83.14, 121.06, 121.67, 130.58, 137.99, 140.56, 145.99, 157.83, 162.56; MS (*m/z*): 261 (M + H); Anal. Calcd for $C_{13}H_{15}N_3OS$: C, 59.74; H, 5.79; N, 16.08; Found: C, 59.63; H, 5.63; N, 16.12.

***N*-(4-methoxyphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4c**

white solid; R_f 0.43 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 2.64 (s, 3H), 3.92 (s, 3H), 6.92 (d, J = 8 Hz, 1H), 6.99 (t, J = 8 Hz, 1H), 7.06 (t, J = 7.58 Hz, 1H), 8.48 (dd, J = 8 Hz, 1H), 9.62 (s, 1H), 10.31 (s, 1H); ^{13}C NMR: δ 12.82, 15.38, 54.50, 83.84, 121. 21, 122.26,

133.54, 139.14, 140.18, 146.33, 154.03, 165.15; MS (*m/z*): 277 (M + H); Anal. Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15; Found: C, 56.26; H, 5.33; N, 15.08.

***N*-(4-fluorophenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4d**

white solid; R_f 0.45 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.52 (s, 3H), 2.65 (s, 3H), 7.28-7.31 (m, 2H), 7.49-7.52 (m, 2H), 9.18 (s, 1H), 10.46 (s, 1H); ^{13}C NMR: δ 13.05, 15.98, 84.44, 121.38, 122.42, 137.99, 141.03, 145.34, 156.83, 166.05; MS (*m/z*): 265 (M + H); Anal. Calcd for $C_{12}H_{12}FN_3OS$: C, 54.33; H, 4.56; N, 15.84; Found: C, 54.34; H, 4.23; N, 15.69.

***N*-(2-methoxyphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4e**

white solid; R_f 0.40 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 2.68 (s, 3H), 3.68 (s, 1H), 6.82-6.85 (t, 1H), 7.12-7.16 (q, 2H), 7.61 (d, *J*=7.2 Hz, 2H), 9.23 (s, 1H), 10.35 (s, 1H); ^{13}C NMR: δ 13.12, 16.42, 58.23, 86.12, 114.23. 119.45, 120.38, 122.65, 142.61, 144.56, 145.15, 155.27, 166.15; MS (*m/z*): 277 (M + H); Anal. Calcd for $C_{13}H_{15}N_3O_2S$: C, 56.30; H, 5.45; N, 15.15; Found: C, 56.24; H, 5.35; N, 15.06.

***N*-(2-methylphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4f**

white solid; R_f 0.41 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.77 (s, 3H), 2.55 (s, 3H), 2.66 (s, 3H), 7.02-7.07 (q, 1H), 7.31-7.39 (m, 2H), 7.82 (d, *J*=7.4 Hz, 1H) 9.21 (s, 1H), 10.33 (s, 1H); ^{13}C NMR: δ 12.88, 15.08, 19.78, 84.44, 119.38, 127.35, 132.45, 138.54, 146.22, 155.63, 167.15; MS (*m/z*): 261 (M + H); Anal. Calcd for $C_{13}H_{15}N_3OS$: C, 59.74; H, 5.79; N, 16.08; Found: C, 59.61; H, 5.63; N, 16.11.

***N*-(4-chlorophenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4g**

white solid; R_f 0.45 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.56 (s, 3H), 2.67 (s, 3H), 7.16-7.27 (m, 2H), 7.38-7.44 (m, 2H), 9.38 (s, 1H), 10.46 (s, 1H); ^{13}C NMR: δ 12.62, 15.65, 85.34, 121.18, 131.57, 138.19, 140.98, 141.65, 154.65, 166.87; MS (*m/z*): 281 (M + H); Anal. Calcd for $C_{12}H_{12}ClN_3OS$: C, 51.15; H, 4.29; N, 14.91; Found: C, 51.03; H, 4.13; N, 14.79.

***N*-(4-ethylphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4h**

white solid; R_f 0.49 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.13-1.16 (t, 3H), 2.50-2.54 (q, 2H), 2.56 (s, 3H), 2.66 (s, 3H), 7.06-7.12 (q, 2H), 7.31 (t, *J*=8.2 Hz, 2H), 9.54 (s, 1H), 10.68 (s, 1H); ^{13}C NMR: δ 12.74, 16.47, 19.65, 27.68, 86.02, 119.63, 120.38, 132.61, 133.59, 141.25, 145.61, 154.84, 167.65; MS (*m/z*): 275 (M + H); Anal. Calcd for $C_{14}H_{17}N_3OS$: C, 61.07; H, 6.22; N, 15.26; Found: C, 61.14; H, 6.13; N, 15.22.

***N*-(4-nitrophenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4i**

white solid; R_f 0.48 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 2.63 (s, 3H), 8.02-8.12 (m, 2H), 8.33-8.52 (m, 2H), 9.46 (s, 1H), 10.68 (s, 1H); ^{13}C NMR: δ 12.56, 15.21, 81.64, 120.18, 124.89, 141.61, 142.53, 144.74, 149.22, 155.65, 166.85; MS (*m/z*): 292 (M + H); Anal. Calcd for $C_{12}H_{12}N_4O_3S$: C, 49.31; H, 4.14; N, 19.17; Found: C, 49.14; H, 4.13; N, 19.02.

***N*-(3-chloro-4-fluorophenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4j**

white solid; R_f 0.44 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.51 (s, 3H), 2.68 (s, 3H), 7.20 (t, 1H), 7.47 (d, *J*=7.9 Hz, 1H), 8.01- 8.06 (q, 1H), 9.38 (s, 1H), 10.66 (s, 1H); ^{13}C NMR: δ 12.68, 15.42, 84.54, 118.25, 119.54, 120.38, 121.41, 136.99, 140.22, 143.22, 155.93, 167.54; MS (*m/z*): 299 (M + H); Anal. Calcd for $C_{12}H_{11}ClFN_3OS$: C, 48.08; H, 3.70; N, 14.02; Found: C, 47.94; H, 3.59; N, 14.12.

***N*-(5-chloro-2-methoxyphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4k**

white solid; R_f 0.41 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.53 (s, 3H), 2.62 (s, 3H), 3.78 (s, 3H), 7.13-7.17 (t, 1H), 7.31-7.37 (t, 1H), 8.21 (d, *J*=8.9 Hz, 1H), 9.58 (s, 1H), 10.86 (s, 1H); ^{13}C NMR: δ 12.72, 16.62, 55.27, 84.54, 117.41, 120.38, 122.61. 131.51, 139.50, 141.25, 156.47, 166.78; MS (*m/z*): 311 (M + H); Anal. Calcd for $C_{13}H_{14}ClN_3O_2S$: C, 50.08; H, 4.53; N, 13.48; Found: C, 50.04; H, 4.33; N, 13.33.

***N*-(2,5-dichlorophenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4l**

white solid; R_f 0.39 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.56 (s, 3H), 2.71 (s, 3H), 6.98-7.03 (q, 1H), 7.32 (d, *J*=7.9 Hz, 1H), 7.81-7.85 (q, 1H), 9.86 (s, 1H), 10.88 (s, 1H); ^{13}C NMR: δ 13.51, 17.42, 85.48, 120.14, 126.34, 132.66, 136.54, 142.67, 146.26, 157.41, 168.47; MS (*m/z*): 316 (M + H); Anal. Calcd for $C_{12}H_{11}Cl_2N_3OS$: C, 45.58; H, 3.51; N, 13.29; Found: C, 45.44; H, 3.43; N, 13.12.

***N*-(2,5-dimethylphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4m**

white solid; R_f 0.43 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.72 (s, 6H), 2.54 (s, 6H), 2.64 (s, 1H), 6.93-6.98 (q, 1H), 7.12-7.16 (t, 1H), 7.62 (d, *J*=7.56 Hz, 1H), 9.58 (s, 1H), 10.66 (s, 1H); ^{13}C NMR: δ 12.84, 16.54, 19.84, 21.65, 85.42, 126.74, 128.79, 131.24, 132.61, 138.74, 142.12, 146.34, 155.87, 169.51; MS (*m/z*): 275 (M + H); Anal. Calcd for $C_{14}H_{17}N_3OS$: C, 61.07; H, 6.22; N, 15.26; Found: C, 59.94; H, 6.13; N, 15.33.

***N*-(4-chloro-2-methylphenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4n**

white solid; R_f 0.46 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.49 (s, 3H), 2.55 (s, 3H), 2.68 (s, 1H), 6.97 (d, *J*=7.58 Hz, 1H), 7.42-7.547 (t, 1H), 7.77-7.80 (q, 1H) 9.76 (s, 1H), 10.88 (s, 1H); ^{13}C NMR: δ 12.78, 16.08, 19.16, 85.44, 121.98, 127.43, 131.61, 132.04, 138.45, 142.27, 146.98, 154.17, 166.85; MS (*m/z*): 295 (M + H); Anal. Calcd for $C_{13}H_{14}ClN_3OS$: C, 52.79; H, 4.77; N, 14.21; Found: C, 52.68; H, 4.64; N, 14.12.

***N*-(3,4-difluorophenyl)-3-methyl-5-(methylthio)-1*H*-pyrazole-4-carboxamide 4o**

white solid; R_f 0.48 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.53 (s, 3H), 2.65 (s, 3H), 6.96 (d, *J*=8.1 Hz, 1H), 7.68-7.72 (q, 1H), 7.89-7.93 (t, 1H), 9.76 (s, 1H), 10.76 (s, 1H); ^{13}C NMR: δ 13.02, 15.82, 83.54, 119.13, 123.67, 123.54, 126.84, 127.10, 138.61, 139.23, 146.87, 153.83, 158.61, 165.24; MS (*m/z*): 283 (M + H); Anal. Calcd for $C_{12}H_{11}F_2N_3OS$: C, 50.88; H, 3.91; N, 14.83; Found: C, 50.69; H, 3.83; N, 14.76.

General procedure for the synthesis of trisubstituted isoxzoles 5a-o.

To a well stirred solution of hydroxyl amine hydrochloride (1.04 g, 15 mmol), potassium hydroxide (0.84 g, 15 mmol) in water (25 mL) was added suspension of various AKDTAs **1a-o** and refluxed the resulting mixture for appropriate time (Table 2) with constant stirring. After completion of the reaction, the reaction mixture was allowed to come to room temperature and add cold water (50 mL). The separated suspension was filtered, washed with water (2 × 50 mL), dried and crystallized from methanol to afford analytically pure products which were used for next step without further purification.

3-methyl-5-(methylthio)-*N*-phenylisoxazole-4-carboxamide 5a

white solid; R_f 0.53 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.49(s, 3H), 2.57 (s, 3H), 7.03-7.08 (t, 1H), 7.27-7.31 (t, 2H), 7.56-7.59 (d, J = 7.66 Hz, 2H), 9.24 (s, 1H); ^{13}C NMR: δ 14.77, 21.97, 101.08, 120.18, 122.38, 132.61, 132.99, 140.22, 155.75, 165.65; MS (*m/z*): 248 (M + H); Anal. Calcd for $C_{12}H_{12}N_2O_2S$: C, 58.05; H, 4.87; N, 11.28; Found: C, 57.90; H, 4.76; N, 11.15.

***N*-(4-methylphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5b**

white solid; R_f 0.51 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.33 (s, 3H), 2.55 (s, 3H), 2.63 (s, 3H), 7.16 (d, J= 9.6 Hz, 2H), 7.53 (d, J=9.2 Hz, 2H), 9.19 (s, 1H); ^{13}C NMR: δ 14.72, 21.29, 22.96, 99.82, 122.65, 122.66, 130.24, 137.71, 156.49, 164.87; MS (*m/z*): 262 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; Found: C, 59.36; H, 5.23; N, 10.54.

***N*-(4-methoxyphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5c**

white solid; R_f 0.56 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.55 (s, 3H), 2.64 (s, 3H), 3.93 (s, 3H), 6.95 (d, J=8.27 Hz, 2H), 7.76 (d, J=7.56 Hz, 1H), 9.59 (s, 1H); ^{13}C NMR: δ 14.84, 20.36, 56.81, 101.98, 121.11, 122.32, 131.54, 139.56, 155.01, 164.74; MS (*m/z*): 278 (M + H);

Anal. Calcd for $C_{13}H_{14}N_2O_3S$: C, 56.10; H, 5.07; N, 10.07; Found: C, 56.06; H, 4.93; N, 10.09.

***N*-(4-fluorophenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5d**

white solid; R_f 0.59 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.53 (s, 3H), 2.66 (s, 3H), 7.26-7.29 (m, 2H), 7.59-7.62 (m, 2H), 9.39 (s, 1H); ^{13}C NMR: δ 13.89, 21.98, 101.59, 121.01, 121.61, 123.57, 136.57, 141.45, 155.13, 165.47; MS (*m/z*): 266 (M + H); Anal. Calcd for $C_{12}H_{11}FN_2O_2S$: C, 54.13; H, 4.16; N, 10.52; Found: C, 54.01; H, 4.08; N, 10.69.

***N*-(2-methoxyphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5e**

white solid; R_f 0.51 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.50 (s, 3H), 2.58 (s, 3H), 3.75 (s, 1H), 7.01- 7.07 (t, 1H), 7.21-7.34 (m, 2H), 7.81 (d, *J*=7.84 Hz, 1H), 9.67 (s, 1H); ^{13}C NMR: δ 14.85, 19.64, 57.02, 101.54. 110.45, 122.48, 122.55, 144.61, 155.27, 166.15; MS (*m/z*): 278 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_3S$: C, 56.10; H, 5.07; N, 10.07; Found: C, 56.14; H, 4.95; N, 9.93.

***N*-(2-methylphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5f**

white solid; R_f 0.52 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.77 (s, 3H), 2.55 (s, 3H), 2.67 (s, 3H), 7.11-7.13 (t, 1H), 7.49-7.61 (m, 2H), 7.81 (d, *J*=7.62 Hz, 1H) 9.81 (s, 1H); ^{13}C NMR: δ 14.08, 19.78, 22.44, 101.20, 119.45, 127.74, 132.51, 137.94, 155.45, 167.59; MS (*m/z*): 262 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_2S$: C, 59.52; H, 5.38; N, 10.68; Found: C, 59.45; H, 5.23; N, 10.54.

***N*-(4-chlorophenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5g**

white solid; R_f 0.56 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.52 (s, 3H), 2.59 (s, 3H), 7.21-7.35 (m, 2H), 7.39-7.44 (m, 2H), 9.43 (s, 1H); ^{13}C NMR: δ 14.65, 22.38, 101.45, 120.08, 121.03, 131.63, 138.72, 153.47, 154.71, 165.67; MS (*m/z*): 282 (M + H); Anal. Calcd for $C_{12}H_{11}ClN_2O_2S$: C, 50.98; H, 3.92; N, 9.91; Found: C, 50.83; H, 4.03; N, 9.85.

***N*-(4-ethylphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5h**

white solid; R_f 0.62 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.14-1.16 (t, 3H), 2.50-2.54 (q, 2H), 2.57 (s, 3H), 2.64 (s, 3H), 7.11-7.18 (m, 2H), 7.28-7.38 (q, 2H), 9.54 (s, 1H); ^{13}C NMR: δ 14.74, 15.47, 21.85, 28.68, 99.82, 119.27, 120.43, 132.46, 136.19, 145.18, 155.14, 166.85; MS (*m/z*): 276 (M + H); Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14; Found: C, 60.74; H, 5.73; N, 10.21.

***N*-(4-nitrophenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5i**

white solid; R_f 0.61 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.51 (s, 3H), 2.62 (s, 3H), 8.06-8.17 (m, 2H), 8.38-8.59 (m, 2H), 9.46 (s, 1H); ^{13}C NMR: δ 14.67, 21.81, 101.71, 120.48, 125.89, 141.31, 144.34, 154.89, 167.05; MS (*m/z*): 293 (M + H); Anal. Calcd for $C_{12}H_{11}N_3O_4S$: C, 49.14; H, 3.78; N, 14.33; Found: C, 49.18; H, 3.63; N, 14.11.

***N*-(3-chloro-4-fluorophenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5j**

white solid; R_f 0.54 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.51 (s, 3H), 2.59 (s, 3H), 7.24 (d, *J*=7.82 Hz, 1H), 7.52 (d, *J*=7.56 Hz, 1H), 7.89-7.93 (t, 1H), 9.52 (s, 1H); ^{13}C NMR: δ 14.78, 21.82, 101.61, 119.48, 119.54, 120.18, 121.24, 137.59, 143.58, 154.27, 167.42; MS (*m/z*): 300 (M + H); Anal. Calcd for $C_{12}H_{10}ClFN_2O_2S$: C, 47.93; H, 3.35; N, 9.32; Found: C, 47.82; H, 3.29; N, 9.24.

***N*-(5-chloro-2-methoxyphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5k**

white solid; R_f 0.53 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.48 (s, 3H), 2.57 (s, 3H), 3.81 (s, 1H), 7.18-7.21 (q, 1H), 7.29-7.32 (t, 1H), 8.11 (d, *J*=8.2 Hz, 1H), 9.58 (s, 1H); ^{13}C NMR: δ 14.72, 21.92, 55.57, 99.78, 116.18, 120.57, 122.29, 124.81, 132.49, 141.37, 156.47, 166.58; MS (*m/z*): 312 (M + H); Anal. Calcd for $C_{13}H_{13}ClN_2O_3S$: C, 49.92; H, 4.19; N, 8.96; Found: C, 50.04; H, 4.06; N, 8.78.

N-(2,5-dichlorophenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5l

white solid; R_f 0.51 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.55 (s, 3H), 2.68 (s, 3H), 7.03-7.09 (q, 1H), 7.37 (d, *J*=7.58 Hz, 1H), 7.78-7.81 (t, 1H), 9.79 (s, 1H); ^{13}C NMR: δ 14.51, 21.42,

101.48, 120.14, 125.14, 132.29, 136.78, 142.56, 157.11, 168.47; MS (*m/z*): 317 (M + H); Anal. Calcd for $C_{12}H_{10}Cl_2N_2O_2S$: C, 45.44; H, 3.18; N, 8.83; Found: C, 45.39; H, 3.13; N, 8.72.

***N*-(2,5-dimethylphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5m**

white solid; R_f 0.54 (7:3 hexane-EtOAc); ^{1}H NMR: δ 1.72 (s, 6H), 2.51 (s, 6H), 2.59 (s, 1H), 6.95-7.99 (t, 1H), 7.21-7.25 (q, 1H), 7.82 (d, *J*=8.1 Hz, 1H), 9.60 (s, 1H); ^{13}C NMR: δ 14.84, 17.54, 19.94, 21.95, 101.42, 120.71, 122.49, 126.31, 128.27, 131.24, 138.74, 140.32, 155.85, 168.91; MS (*m/z*): 276 (M + H); Anal. Calcd for $C_{14}H_{16}N_2O_2S$: C, 60.85; H, 5.84; N, 10.14 Found: C, 60.74; H, 5.64; N, 10.07.

***N*-(4-chloro-2-methylphenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5n**

white solid; R_f 0.56 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.49 (s, 3H), 2.51 (s, 3H), 2.63 (s, 1H), 7.08-7.15 (t, 1H), 7.51 (d, *J*=7.57 Hz, 1H), 8.01 (t, 1H), 9.76 (s, 1H); ^{13}C NMR: δ 14.78, 19.16, 21.86, 99.65, 121.41, 127.87, 131.45, 132.72, 137.45, 155.77, 166.78; MS (*m/z*): 296 (M + H); Anal. Calcd for $C_{13}H_{13}ClN_2O_2S$: C, 52.61; H, 4.42; N, 9.44; Found: C, 52.58; H, 4.34; N, 9.30.

***N*-(3,4-difluorophenyl)-3-methyl-5-(methylthio)isoxazole-4-carboxamide 5o**

white solid; R_f 0.60 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.53 (s, 3H), 2.63 (s, 3H), 7.05-7.14 (t, 1H), 7.32 (d, *J*=7.62 Hz, 1H) 7.84- 7.87 (t, 1H), 9.86 (s, 1H); ^{13}C NMR: δ 14.02, 20.82, 101.54, 111.27, 119.01, 122.37, 123.54, 123.87, 137.10, 139.23, 149.88, 157.83, 158.29, 166.14; MS (*m/z*): 284 (M + H); Anal. Calcd for $C_{12}H_{10}F_2N_2O_2S$: C, 50.70; H, 3.55; N, 9.85; Found: C, 50.59; H, 3.47; N, 9.72.

General procedure for the oxidation of sulfide to sulfones 6/7a-o.

The appropriate sulfide **4/5a-o** (6 mmol) in water (15 mL) was added sodium per borate (2.79 g, 18 mmol) and the resulting mixture was heated to reflux for appropriate time (Table 4). The mixture was cooled to room temperature and extracted with ethyl acetate (2 × 15 mL). The organic layer was washed with water (2× 20 mL) and dried over magnesium sulphate. The solvent was evaporated at r.t and product was isolated by crystallization technique in excellent yield.

3-methyl-5-(methylsulfonyl)-*N*-phenyl-1*H*-pyrazole-4-carboxamide 6a

white solid; R_f 0.32 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 3.63 (s, 3H), 7.11-7.15 (t, 1H), 7.68-7.73 (m, 2H), 7.83 (d, *J*=8.1 Hz, 2H), 9.60 (s, 1H), 12.86 (s, 1H); ^{13}C NMR: δ 12.32, 46.92, 111.51, 121.38, 132.86, 138.57, 143.02, 154.13, 162.55; MS (*m/z*): 279 (M + 23); Anal. Calcd for $C_{12}H_{13}N_3O_3S$: C, 51.60; H, 4.69; N, 15.05; Found: C, 51.48; H, 4.56; N, 15.12.

***N*-(4-methylphenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6b**

white solid; R_f 0.35 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.37 (s, 3H), 2.58 (s, 3H), 3.66 (s, 3H), 7.22-7.28 (t, 2H), 7.61 (d, *J*=7.5 Hz, 1H), 7.63 (*J*=7.8 Hz. 1H), 9.79 (s, 1H), 12.97 (s, 1H); ^{13}C NMR: δ 12.37, 18.26, 46.89, 114.64, 120.03, 121.60, 129.51, 134.27, 136.27, 138.93, 146.66, 158.36, 161.09; MS (*m/z*): 293 (M + H); Anal. Calcd for $C_{13}H_{15}N_3O_3S$: C, 53.23; H, 5.15; N, 14.32; Found: C, 53.08; H, 5.13; N, 14.19.

***N*-(4-methoxyphenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6c**

white solid; R_f 0.29 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.55 (s, 3H), 3.84 (s, 3H), 3.93 (s, 3H), 7.09 (d, *J* = 7.68 Hz, 2H), 7.93-8.08 (q, 2H), 9.33 (s, 1H), 12.31 (s, 1H); ^{13}C NMR: δ 12.79, 46.98, 55.90, 110.84, 120.12, 122.54, 139.24, 147.58, 153.87, 163.05; MS (*m/z*): 309 (M +

H); Anal. Calcd for $C_{13}H_{15}N_3O_4S$: C, 50.48; H, 4.89; N, 13.58; Found: C, 50.36; H, 4.73; N, 13.45.

_N_-(4-fluorophenyl)-3-methyl-5-(methylsulfonyl)-1_H_-pyrazole-4-carboxamide 6d

white solid; R_f 0.37 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 3.68 (s, 3H), 7.31-7.35 (t, 2H), 7.89-7.93 (q, 2H), 9.89 (s, 1H), 12.96 (s, 1H); ^{13}C NMR: δ 12.99, 46.98, 114.44, 121.88, 122.75, 136.57, 142.14, 142.44, 156.53, 165.41; MS (*m/z*): 297 (M + H); Anal. Calcd for $C_{12}H_{12}FN_3O_3S$: C, 48.48; H, 4.07; N, 14.13; Found: C, 48.34; H, 3.93; N, 14.03.

_N_-(2-methoxyphenyl)-3-methyl-5-(methylsulfonyl)-1_H_-pyrazole-4-carboxamide 6e

white solid; R_f 0.37 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 3.78 (s, 3H), 3.84 (s, 1H), 6.88 (d, *J*=9.1 Hz, 1H), 7.09-7.15 (m, 2H), 7.67 (d, *J*=8.5 Hz, 1H), 9.64 (s, 1H), 13.05 (s, 1H); ^{13}C NMR: δ 12.50, 46.98, 55.87, 110.27, 114.64. 120.43, 121.10, 123.60, 128.13, 138.03, 148.62, 153.12, 161.19; MS (*m/z*): 309 (M + H); Anal. Calcd for $C_{13}H_{15}N_3O_4S$: C, 50.48; H, 4.89; N, 13.58; Found: C, 50.38; H, 4.79; N, 13.44.

_N_-(2-methylphenyl)-3-methyl-5-(methylsulfonyl)-1_H_-pyrazole-4-carboxamide 6f

white solid; R_f 0.38 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.07 (s, 3H), 2.58 (s, 3H), 3.66 (s, 3H), 7.02 (d, *J*=7.34 Hz, 1H), 7.18-7.31 (m, 2H), 7.94 (t, 1H), 9.58 (s, 1H), 12.97 (s, 1H); ^{13}C NMR: δ 12.43, 18.24, 46.82, 114.58, 120.11, 121.78, 129.11, 134.07, 136.57, 139.01, 146.24, 158.87, 161.56; MS (*m/z*): 293 (M + H); Anal. Calcd for $C_{13}H_{15}N_3O_3S$: C, 53.23; H, 5.15; N, 14.32; Found: C, 53.11; H, 5.09; N, 14.21.

_N_-(4-chlorophenyl)-3-methyl-5-(methysulfonyl)-1_H_-pyrazole-4-carboxamide 6g

white solid; R_f 0.35 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.55 (s, 3H), 3.81 (s, 3H), 7.26-7.31 (m, 2H), 7.59-7.65 (m, 2H), 9.78 (s, 1H), 13.15 (s, 1H); ^{13}C NMR: δ 12.62, 46.95, 114.34, 121.28, 131.27, 139.19, 141.78, 141.95, 155.45, 161.87; MS (*m/z*): 313 (M + H); Anal. Calcd for $C_{12}H_{12}ClN_3O_3S$: C, 45.94; H, 3.85; N, 13.39; Found: C, 45.83; H, 3.74; N, 13.27.

***N*-(4-ethylphenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6h**

white solid; R_f 0.29 (6:4 hexane-EtOAc); ^{1}H NMR: δ 1.15-1.17 (t, 3H), 2.48-2.53 (q, 2H), 2.58 (s, 3H), 3.91 (s, 3H), 7.19 (d, *J*=7.8 Hz, 2H), 7.43-7.49 (m, 2H), 9.84 (s, 1H), 13.25 (s, 1H); ^{13}C NMR: δ 12.56, 18.77, 22.65, 46.68, 114.65, 119.13, 120.48, 131.72, 136.27, 141.55, 145.57, 155.01, 162.13; MS (*m/z*): 307 (M + H); Anal. Calcd for $C_{14}H_{17}N_3O_3S$: C, 54.71; H, 5.57; N, 13.67; Found: C, 54.64; H, 5.46; N, 13.54.

***N*-(4-nitrophenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6i**

white solid; R_f 0.32 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 3.92 (s, 3H), 8.02-8.11 (d, *J*=7.4 Hz, 2H), 8.34-8.50 (t, 2H), 9.76 (s, 1H), 12.78 (s, 1H); ^{13}C NMR: δ 12.66, 46.56, 114.64, 120.14, 125.25, 142.23, 144.57, 145.22, 154.35, 161.85; MS (*m/z*): 324 (M + H); Anal. Calcd for $C_{12}H_{12}N_4O_5S$: C, 44.44; H, 3.73; N, 17.28; Found: C, 44.32; H, 3.34; N, 17.20.

***N*-(3-chloro-4-fluorophenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6j**

white solid; R_f 0.29 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.53 (s, 3H), 3.64 (s, 3H), 7.12-7.16 (t, 1H), 7.46-7.49 (m, 1H), 7.96-7.98 (q, 1H), 9.61 (s, 1H), 12.97 (s, 1H); ^{13}C NMR: δ 12.58, 46.42, 114.54, 118.38, 119.81, 120.48, 121.41, 135.79, 141.12, 154.73, 162.97; MS (*m/z*): 331 (M + H); Anal. Calcd for $C_{12}H_{11}ClFN_3O_3S$: C, 43.45; H, 3.34; N, 12.67; Found: C, 43.34; H, 3.29; N, 12.58.

***N*-(5-chloro-2-methoxyphenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6k**

white solid; R_f 0.31 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.55 (s, 3H), 3.69 (s, 3H), 3.84 (s, 3H), 7.11-7.26 (m, 2H), 8.29 (d, *J*=7.9 Hz, 1H), 9.71 (s, 1H), 12.96 (s, 1H); ^{13}C NMR: δ 12.62, 46.82, 55.85, 114.72, 117.82, 120.18, 122.37. 131.51, 139.50, 143.45, 156.57, 163.18; MS

(*m/z*): 343 (M + H); Anal. Calcd for $C_{13}H_{14}ClN_3O_4S$: C, 45.42; H, 4.10; N, 12.22; Found: C, 45.34; H, 4.03; N, 12.13.

***N*-(2,5-dichlorophenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6l**

white solid; R_f 0.29 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.54 (s, 3H), 3.67 (s, 3H), 7.01 (d, *J*=7.9 Hz, 1H), 7.41-7.45 (t, 1H), 8.10-8.16 (t, 1H), 9.86 (s, 1H), 13.37 (s, 1H); ^{13}C NMR: δ 12.78, 46.78, 114.28, 120.14, 126.24, 132.41, 136.54, 140.57, 142.87, 153.11, 162.39; MS (*m/z*): 348 (M + H); Anal. Calcd for $C_{12}H_{11}Cl_2N_3O_3S$: C, 41.39; H, 3.18; N, 12.07; Found: C, 41.26; H, 3.04; N, 11.95.

***N*-(2,5-dimethylphenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6m**

white solid; R_f 0.33 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.33 (d, *J* = 7.6 Hz, 6H), 2.58 (s, 3H), 3.84 (s, 3H), 6.84-6.87 (q, 1H), 7.08 (d, *J* = 7.68 Hz, 1H), 7.68 (d, *J* = 1.28 Hz, 1H), 9.03 (s, 1H), 12.94 (s, 1H); ^{13}C NMR: δ 12.64, 18.94, 22.34, 46.85, 113.98, 122.57, 126.22, 128.34, 132.84, 135.78, 138.49, 142.89, 153.32, 162.71; MS (*m/z*): 307 (M + H); Anal. Calcd for $C_{14}H_{17}N_3O_3S$: C, 54.71; H, 5.57; N, 13.67; Found: C, 54.64; H, 5.44; N, 13.58.

***N*-(4-chloro-2-methylphenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6n**

white solid; R_f 0.32 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.44 (s, 3H), 2.54 (s, 3H), 3.68 (s, 3H), 6.89 (d, *J*=8.2 Hz, 1H), 7.33 (d, *J*=7.9 Hz, 1H), 7.89-7.93 (t, 1H), 9.75 (s, 1H), 12.98 (s, 1H); ^{13}C NMR: δ 12.68, 18.88, 46.76, 113.24, 120.12, 129.71, 131.61, 132.54, 137.55, 141.27, 155.07, 163.08; MS (*m/z*): 327 (M + H); Anal. Calcd for $C_{13}H_{14}ClN_3O_3S$: C, 47.64; H, 4.30; N, 12.82; Found: C, 47.51; H, 4.17; N, 12.69.

***N*-(3,4-difluorophenyl)-3-methyl-5-(methylsulfonyl)-1*H*-pyrazole-4-carboxamide 6o**

white solid; R_f 0.31 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.53 (s, 3H), 3.78 (s, 3H), 7.01-7.07 (t, 1H), 7.31-7.37 (q, 1H), 7.89- 7.92 (q, 1H), 9.73 (s, 1H), 13.06 (s, 1H); ^{13}C NMR: δ 13.01, 46.99, 110.37, 113.84, 120.63, 122.77, 123.54, 138.41, 139.23, 145.57, 149.89, 154.12,

157.11, 163.67; MS (*m/z*): 315 (M + H); Anal. Calcd for $C_{12}H_{11}F_2N_3O_3S$: C, 45.71; H, 3.52; N, 13.33; Found: C, 45.59; H, 3.38; N, 13.21.

3-methyl-5-(methylsulfonyl)-*N*-phenylisoxazole-4-carboxamide 7a

white solid; R_f 0.31 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.69(s, 3H), 3..33 (s, 3H), 7.09-7.15 (q, 1H), 7.66-7.73 (t, 2H), 7.75-7.97 (t, 2H), 9.88 (s, 1H); ^{13}C NMR: δ 12.47, 40.97, 111.18, 121.41, 122.76, 132.52, 132.24, 140.19, 159.75, 169.74; MS (*m/z*): 280 (M + H); Anal. Calcd for $C_{12}H_{12}N_2O_4S$: C, 51.42; H, 4.32; N, 9.99; Found: C, 51.29; H, 4.24; N, 9.89.

***N*-(4-methylphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7b**

white solid; R_f 0.33 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.32 (s, 3H), 2.69 (s, 3H), 3.32 (s, 3H), 7.13-7.16 (q, 2H), 7.52-7.56 (t, 2H), 9.79 (s, 1H); ^{13}C NMR: δ 12.43, 25.99, 40.59, 111.38, 124.74, 124.95, 132.59, 137.43, 138.16, 138.24, 142.32, 159.47, 159.98, 169.05, 169.96; MS (*m/z*): 294 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_4S$: C, 53.05; H, 4.79; N, 9.52; Found: C, 53.06; H, 4.65; N, 9.44.

***N*-(4-methoxyphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7c**

white solid; R_f 0.32 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.57 (s, 3H), 2.68 (s, 3H), 3.42 (s, 3H), 6.91 (d, *J*=7.52 Hz, 2H), 7.82-7.87 (t, 1H), 8.21 (d, *J*=7.82 Hz, 1H), 9.72 (s, 1H); ^{13}C NMR: δ 12.53, 40.85, 58.43, 112.02, 120.59, 122.36, 139.46, 155.76, 161.27, 169.38; MS (*m/z*): 310 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_5S$: C, 50.31; H, 4.55; N, 9.03; Found: C, 50.27; H, 4.43; N, 9.09.

***N*-(4-fluorophenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7d**

white solid; R_f 0.36 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.83 (s, 3H), 3.33 (s, 3H), 7.19-7.23 (t, 2H), 7.34-7.43 (q, 2H), 9.89 (s, 1H); ^{13}C NMR: δ 12.42, 40.58, 111.99, 118.36, 121.01, 121.61, 123.57, 136.77, 143.72, 160.13, 169.87; MS (*m/z*): 298 (M + H); Anal. Calcd for $C_{12}H_{11}FN_2O_4S$: C, 48.32; H, 3.72; N, 9.39; Found: C, 48.21; H, 3.60; N, 9.31.

***N*-(2-methoxyphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7e**

white solid; R_f 0.34 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.71 (s, 3H), 3.34 (s, 3H), 3.85 (s, 1H), 6.76-6.80 (t, 1H), 7.08-7.17 (m, 2H), 7.42 (d, *J*=7.6 Hz, 1H), 9.87 (s, 1H); ^{13}C NMR: δ 12.46, 40.64, 56.82, 111.67. 113.71, 121.37, 122.48, 144.61, 161.51, 169.27; MS (*m/z*): 310 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_5S$: C, 50.31; H, 4.55; N, 9.03; Found: C, 50.29; H, 4.44; N, 9.07.

***N*-(2-methylphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7f**

white solid; R_f 0.31 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.33 (s, 3H), 2.71 (s, 3H), 3.38 (s, 3H), 6.99-7.04 (q, 1H), 7.12-7.28 (m, 2H), 8.21-8.25 (t, 1H), 9.79 (s, 1H); ^{13}C NMR: δ 12.58, 25.78, 40.49, 110.18, 120.81, 122.31, 124.21, 124.95, 159.76, 169.68; MS (*m/z*): 294 (M + H); Anal. Calcd for $C_{13}H_{14}N_2O_4S$: C, 53.05; H, 4.79; N, 9.52; Found: C, 53.03; H, 4.67; N, 9.45.

***N*-(4-chlorophenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7g**

white solid; R_f 0.31 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.68 (s, 3H), 3.29 (s, 3H), 7.34-7.39 (m, 2H), 7.78-7.83 (m, 2H), 9.76 (s, 1H); ^{13}C NMR: δ 12.55, 40.38, 111.52, 121.18, 121.63, 130.54, 131.63, 139.48, 159.82, 169.67; MS (*m/z*): 314 (M + H); Anal. Calcd for $C_{12}H_{11}ClN_2O_4S$: C, 45.79; H, 3.52; N, 8.90; Found: C, 45.71; H, 3.43; N, 8.82.

***N*-(4-ethylphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7h**

white solid; R_f 0.33 (6:4 hexane-EtOAc); ^{1}H NMR: δ 1.18-1.21 (t, 3H), 2.59-2.63 (q, 2H), 2.67 (s, 3H), 3.34 (s, 3H), 7.17-7.20 (t, 2H), 7.38-7.42 (t, 2H), 9.84 (s, 1H); ^{13}C NMR: δ 12.45, 18.17, 27.24, 40.68, 111.41, 119.27, 120.14, 131.38, 134.81, 146.64, 159.51, 169.88; MS (*m/z*): 308 (M + H); Anal. Calcd for $C_{14}H_{16}N_2O_4S$: C, 54.53; H, 5.23; N, 9.08; Found: C, 54.41; H, 5.11; N, 8.98.

***N*-(4-nitrophenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7i**

white solid; R_f 0.32 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.58 (s, 3H), 3.41 (s, 3H), 8.13-8.19 (d, *J*=7.8 Hz, 2H), 8.42-8.51 (q, 2H), 9.76 (s, 1H); ^{13}C NMR: δ 13.24, 40.41, 113.38, 125.51,

127.43, 132.39, 135.06, 136.40, 141.56, 144.50, 164.49, 171.75; MS (*m/z*): 325 (M + H); Anal. Calcd for $C_{12}H_{11}N_3O_6S$: C, 44.31; H, 3.41; N, 12.92; Found: C, 44.20; H, 3.29; N, 12.81.

***N*-(3-chloro-4-fluorophenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7j**

white solid; R_f 0.54 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.51 (s, 3H), 2.59 (s, 3H), 7.15-7.19 (t, 1H), 7.45-7.48 (q, 1H), 8.05-8.09 (q, 1H), 9.82 (s, 1H); ^{13}C NMR: δ 13.18, 40.52, 111.61, 119.23, 119.31, 120.56, 122.47, 137.61, 148.18, 159.27, 169.42; MS (*m/z*): 332 (M + H); Anal. Calcd for $C_{12}H_{10}ClFN_2O_4S$: C, 43.32; H, 3.03; N, 8.42; Found: C, 43.19; H, 2.90; N, 8.44.

***N*-(5-chloro-2-methoxyphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7k**

white solid; R_f 0.34 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.68 (s, 3H), 3.37 (s, 3H), 3.87 (s, 1H), 7.19-7.25 (m, 2H), 8.32 (d, *J*= 8 Hz, 1H), 9.78 (s, 1H); ^{13}C NMR: δ 12.92, 40.91, 56.21, 111.91, 115.53, 120.41, 122.84, 125.17, 131.49, 132.54, 143.37, 161.47, 169.58; MS (*m/z*): 344 (M + H); Anal. Calcd for $C_{13}H_{13}ClN_2O_5S$: C, 45.29; H, 3.80; N, 8.13; Found: C, 45.16; H, 3.71; N, 8.08.

***N*-(2,5-dichlorophenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7l**

white solid; R_f 0.51 (7:3 hexane-EtOAc); ^{1}H NMR: δ 2.73 (s, 3H), 3.28 (s, 3H), 7.03 (d, *J*= 7.8 Hz, 1H), 7.33-7.38 (q, 1H), 8.01-8.06 (t, 1H), 9.79 (s, 1H); ^{13}C NMR: δ 12.69, 40.42, 111.51, 119.34, 120.44, 126.04, 133.56, 137.27, 138.91, 159.83, 169.57; MS (*m/z*): 349 (M + H); Anal. Calcd for $C_{12}H_{10}Cl_2N_2O_4S$: C, 41.28; H, 2.89; N, 8.02; Found: C, 41.19; H, 2.76; N, 7.92.

***N*-(2,5-dimethylphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7m**

white solid; R_f 0.31 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.22 (s, 6H), 2.58 (s, 6H), 3.49 (s, 1H), 6.95-6.98 (d, *J*=7.64 Hz, 1H), 7.18-7.20 (t, 1H) 7.38-7.41 (t, 1H), 9.76 (s, 1H); ^{13}C NMR: δ 12.84, 23.94, 25.11, 41.35, 111.42, 119.71, 122.64, 126.48, 128.07, 131.24, 138.74, 159.57,

169.43; MS (*m/z*): 308 (M + H); Anal. Calcd for $C_{14}H_{16}N_2O_4S$: C, 54.53; H, 5.23; N, 9.08 Found: C, 54.44; H, 5.10; N, 8.97.

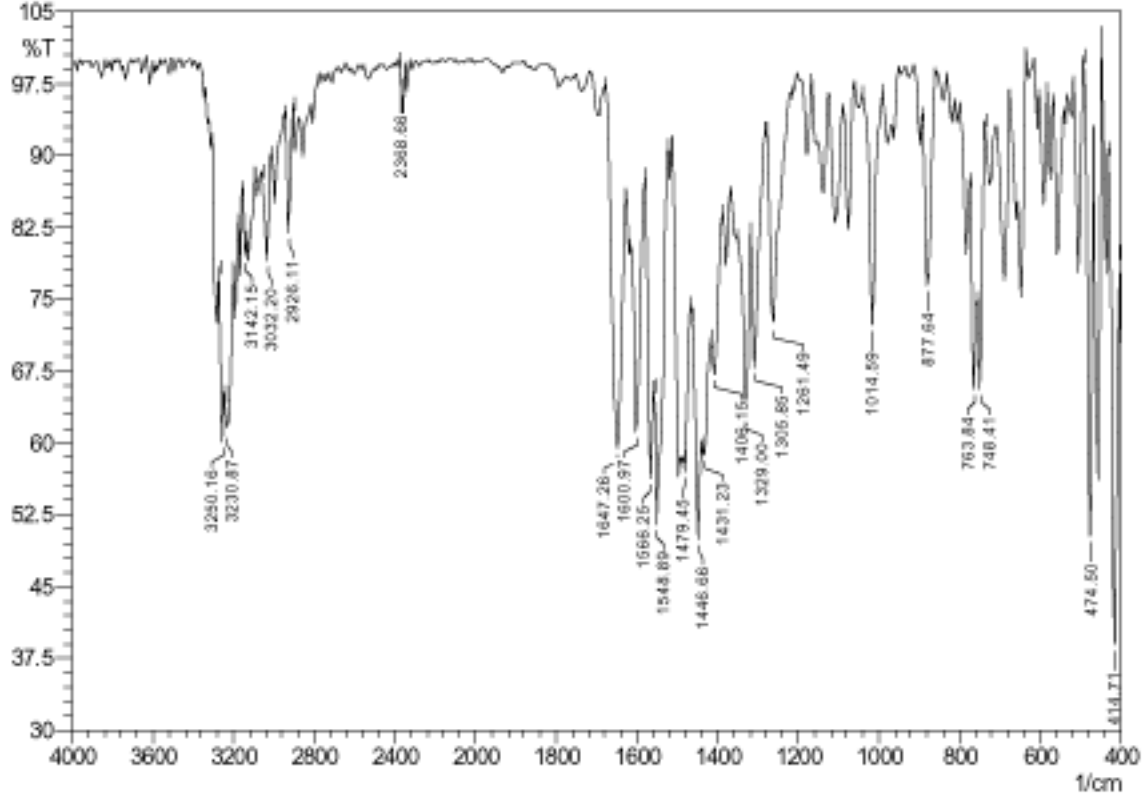
***N*-(4-chloro-2-methylphenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7n**

white solid; R_f 0.34 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.32 (s, 3H), 2.61 (s, 3H), 3.63 (s, 1H), 6.99-7.02 (t, 1H), 7.28-7.32 (q, 1H), 7.88-7.91 (d, J=8.1 Hz, 1H), 9.76 (s, 1H); ^{13}C NMR: δ 12.78, 24.35, 41.37, 111.94, 120.73, 126.34, 130.71, 133.71, 136.96, 162.77, 170.24; MS (*m/z*): 328 (M + H); Anal. Calcd for $C_{13}H_{13}ClN_2O_4S$: C, 47.49; H, 3.99; N, 8.52; Found: C, 47.38; H, 3.87; N, 8.39.

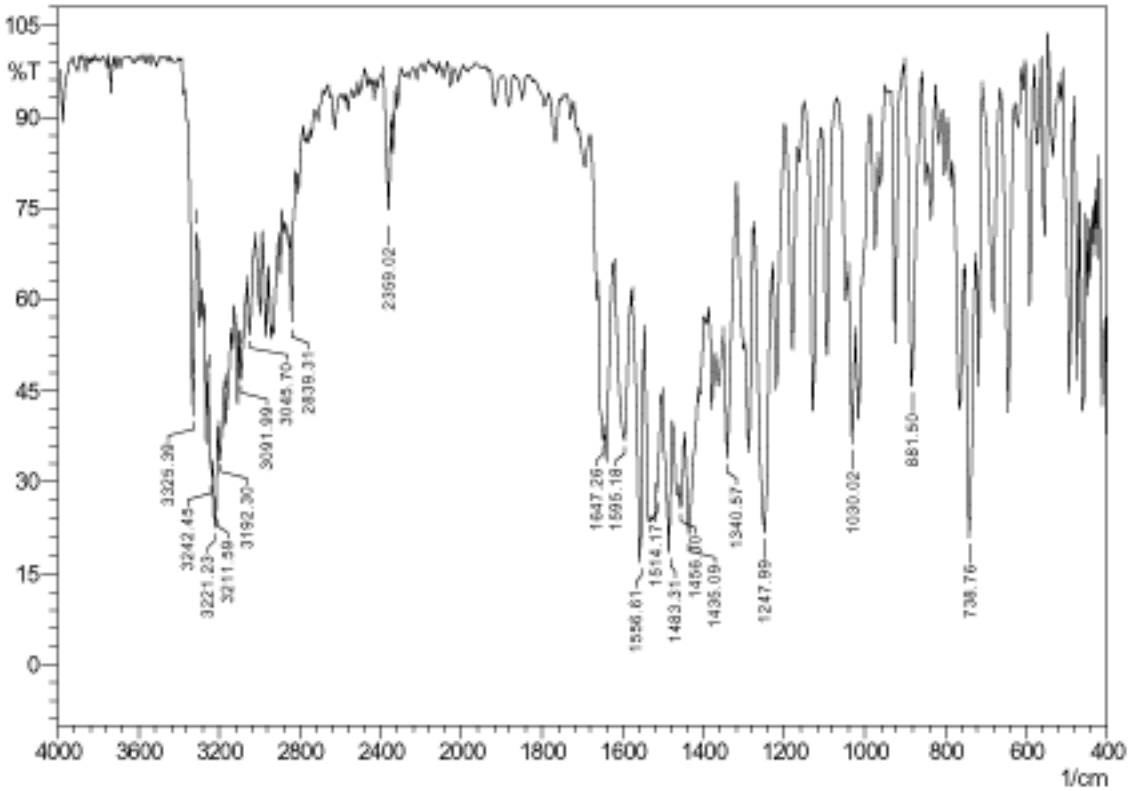
***N*-(3,4-difluorophenyl)-3-methyl-5-(methylsulfonyl)isoxazole-4-carboxamide 7o**

white solid; R_f 0.32 (6:4 hexane-EtOAc); ^{1}H NMR: δ 2.68 (s, 3H), 3.33 (s, 3H), 7.05-7.11 (t, 1H), 7.31-7.37 (q, 1H), 7.98-8.01 (q, 1H), 9.81 (s, 1H); ^{13}C NMR: δ 13.21, 40.42, 111.54, 111.97, 119.01, 122.37, 123.54, 123.87, 137.10, 138.11, 140.94, 148.43, 158.61, 162.87, 171.84; MS (*m/z*): 316 (M + H); Anal. Calcd for $C_{12}H_{10}F_2N_2O_4S$: C, 45.57; H, 3.19; N, 8.86; Found: C, 45.44; H, 3.07; N, 8.72.

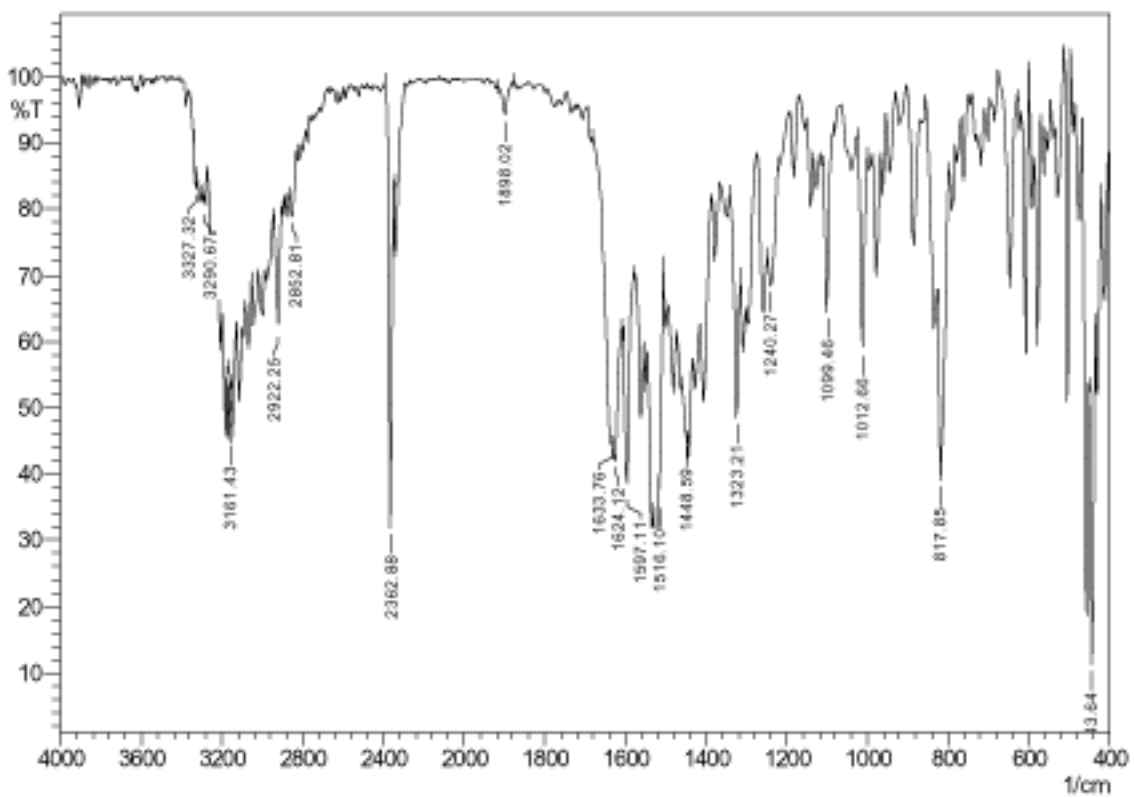
IR Spectrum of compound 6a



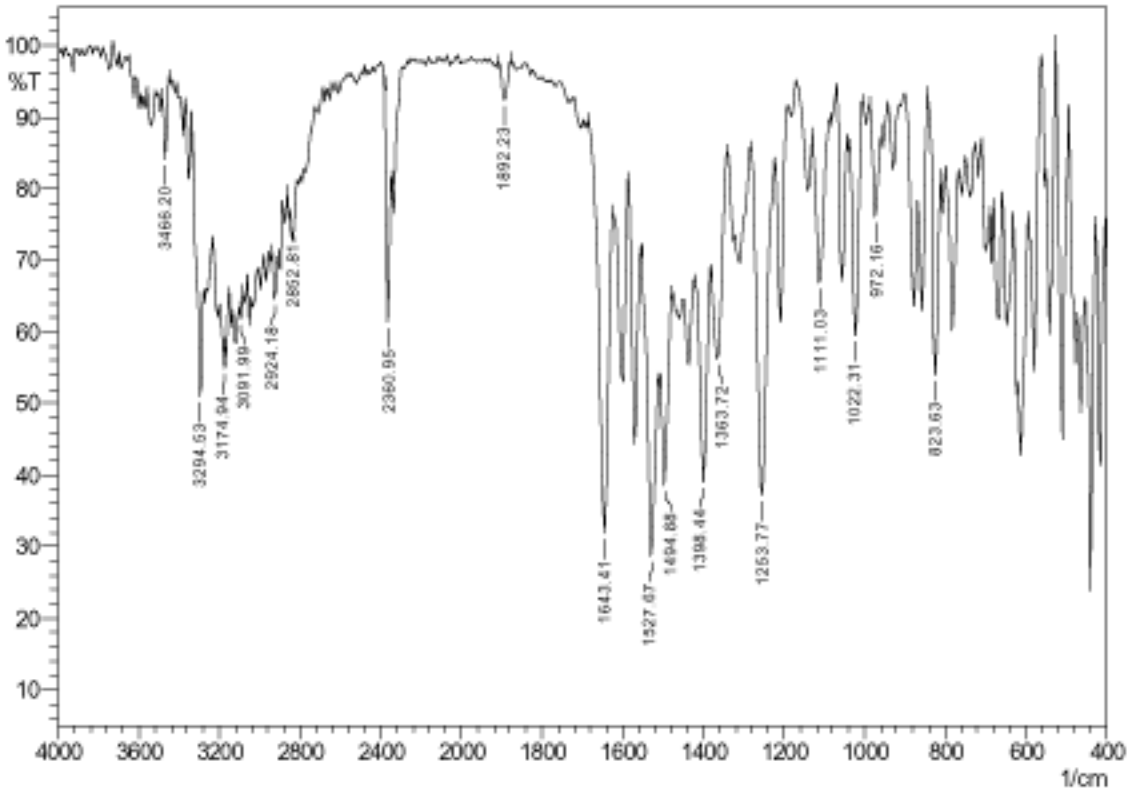
IR Spectrum of compound 6b



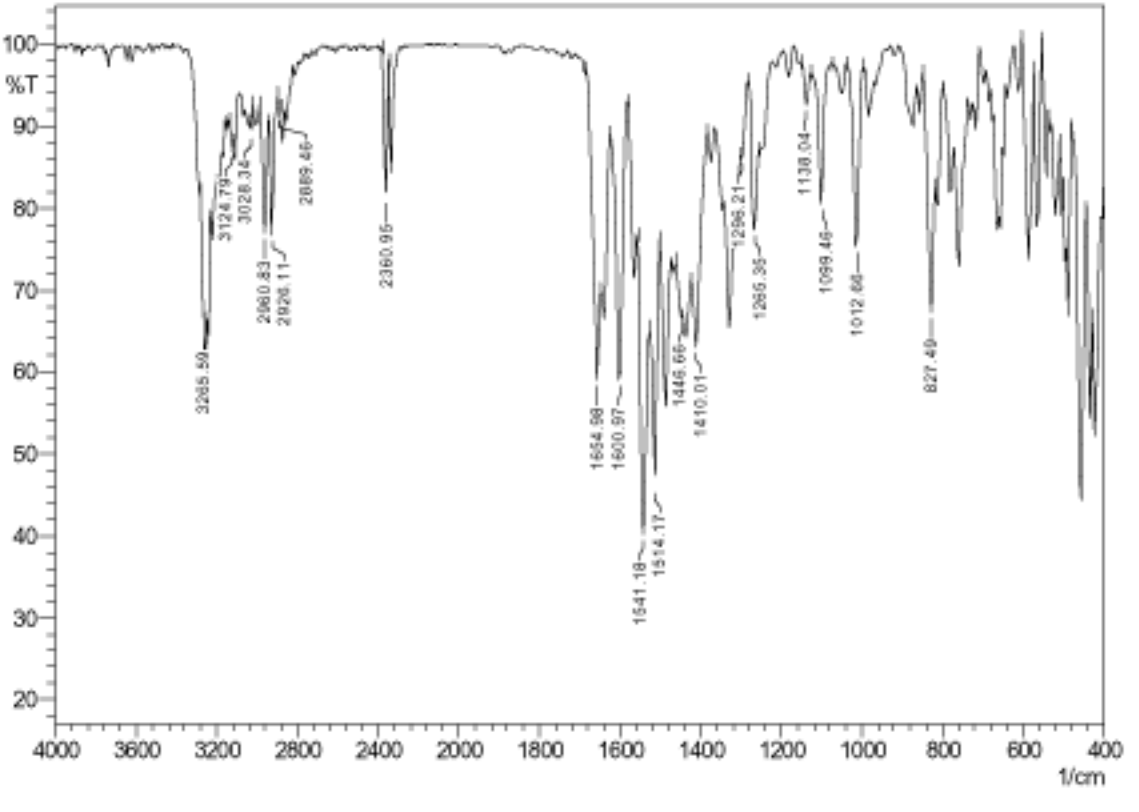
IR Spectrum of compound 6c



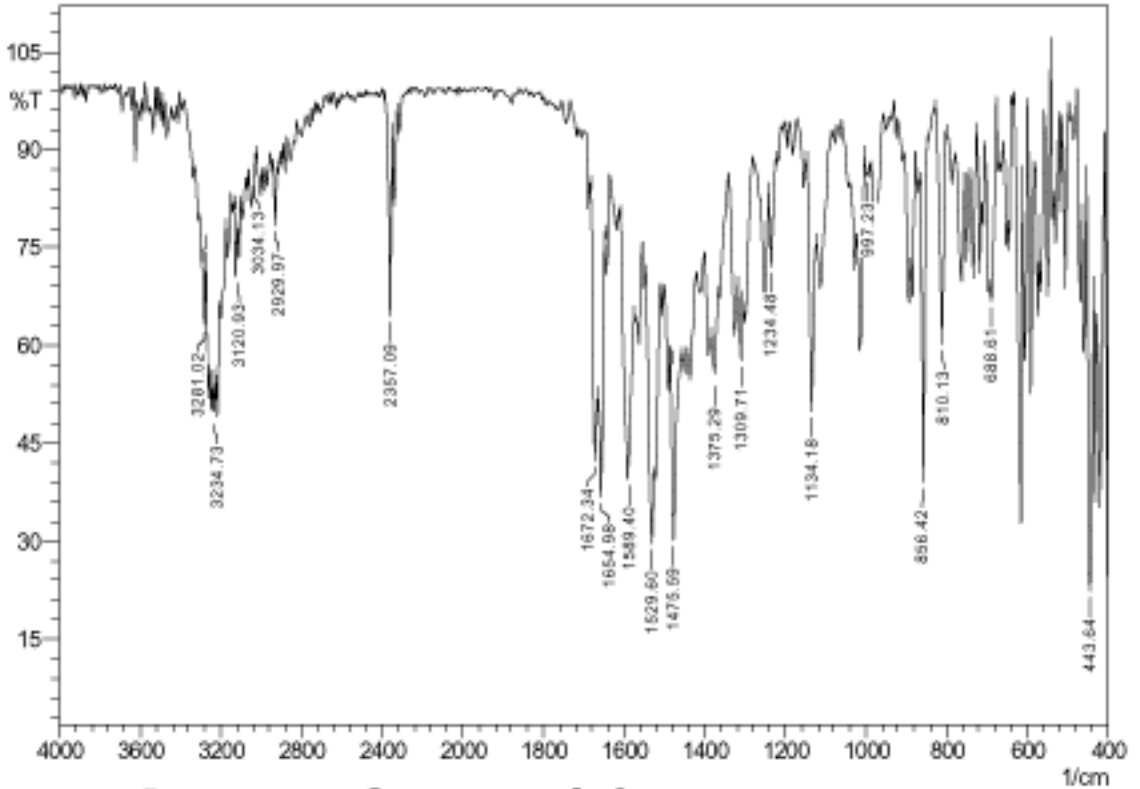
IR Spectrum of compound 6d



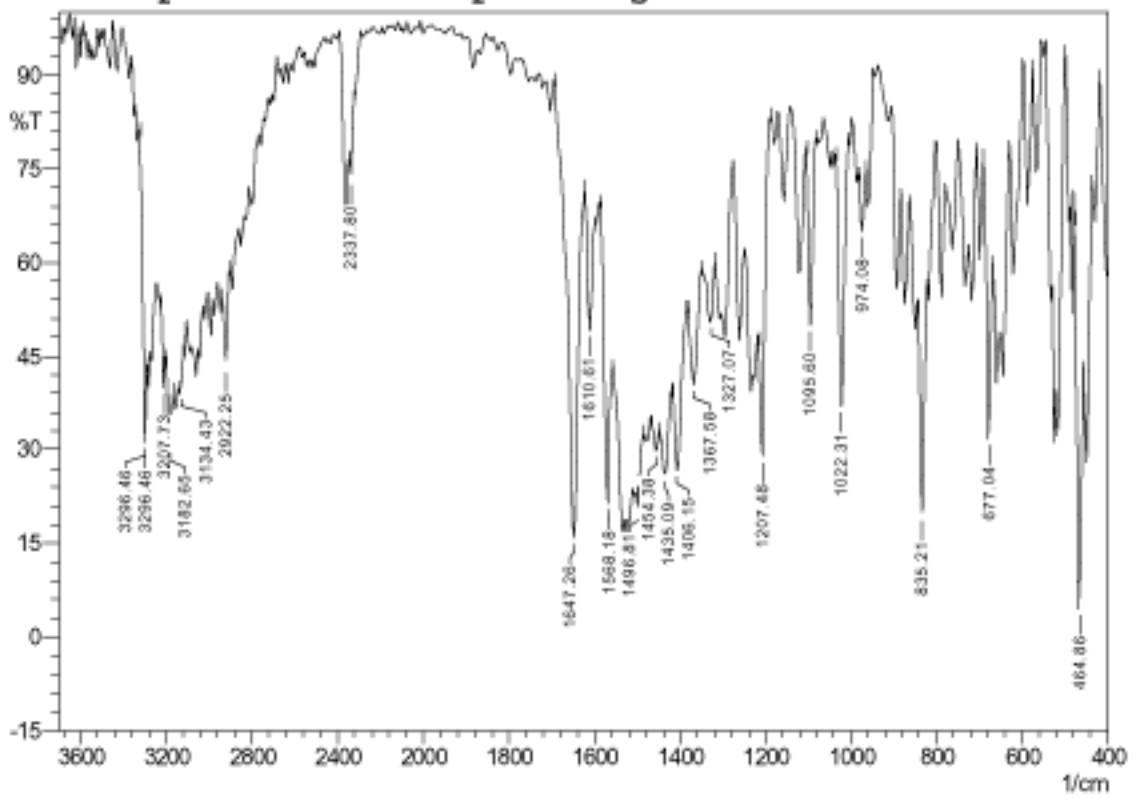
IR Spectrum of compound 6e



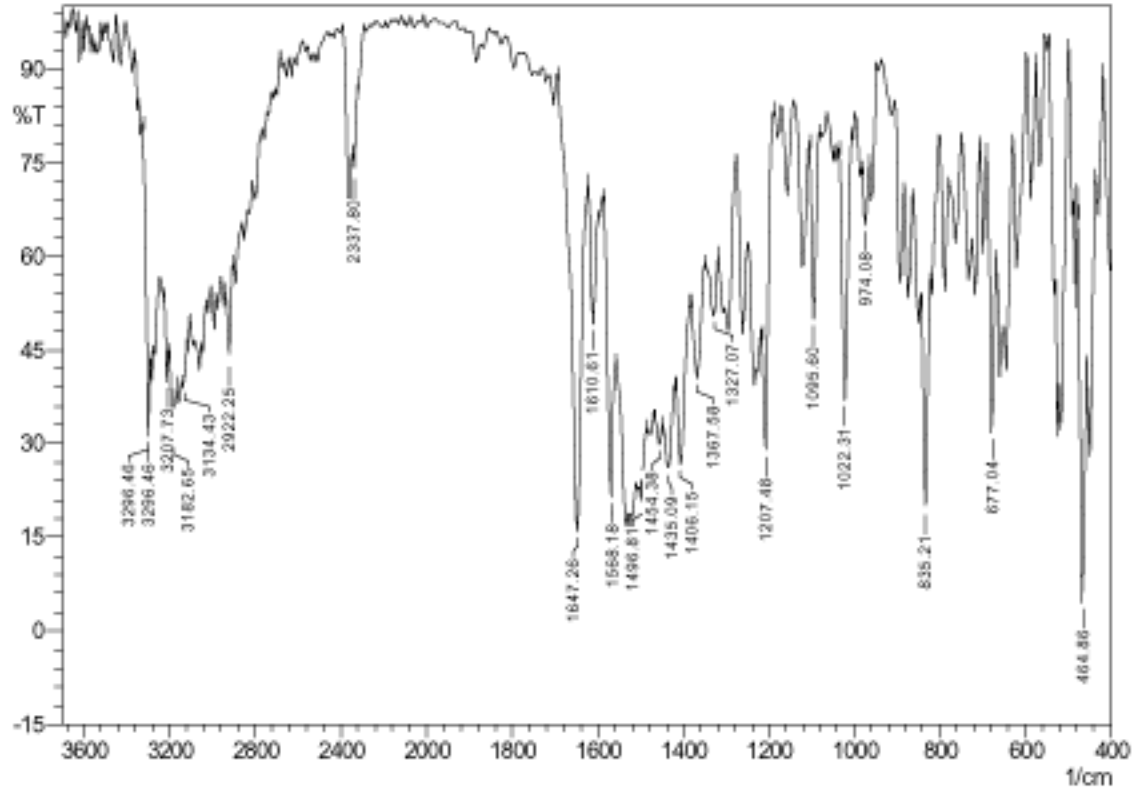
IR Spectrum of compound 6f



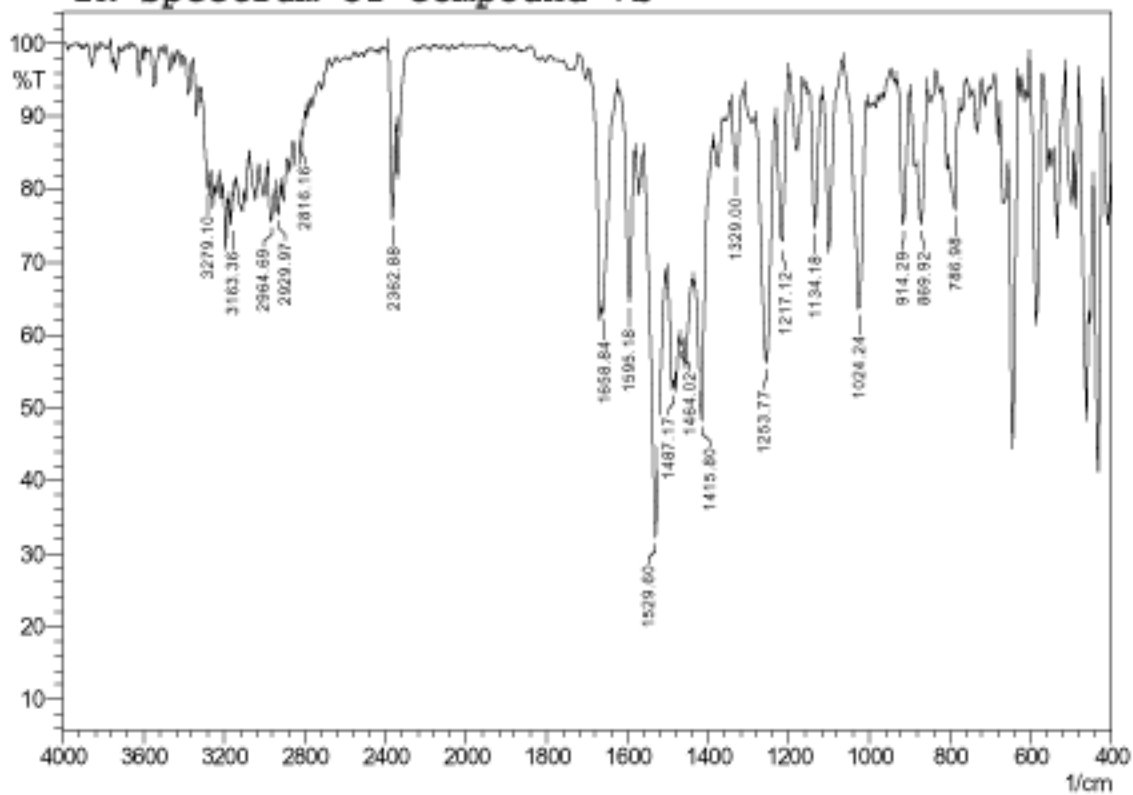
IR Spectrum of compound 6g



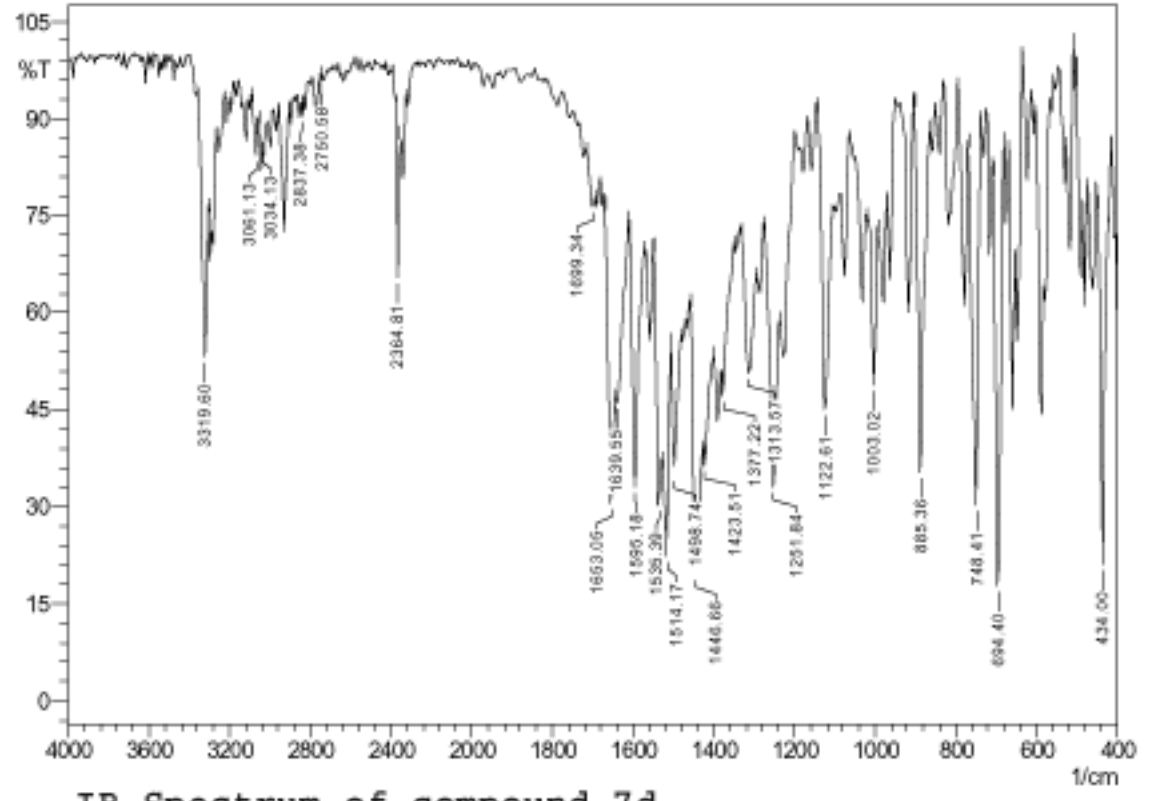
IR Spectrum of compound 7a



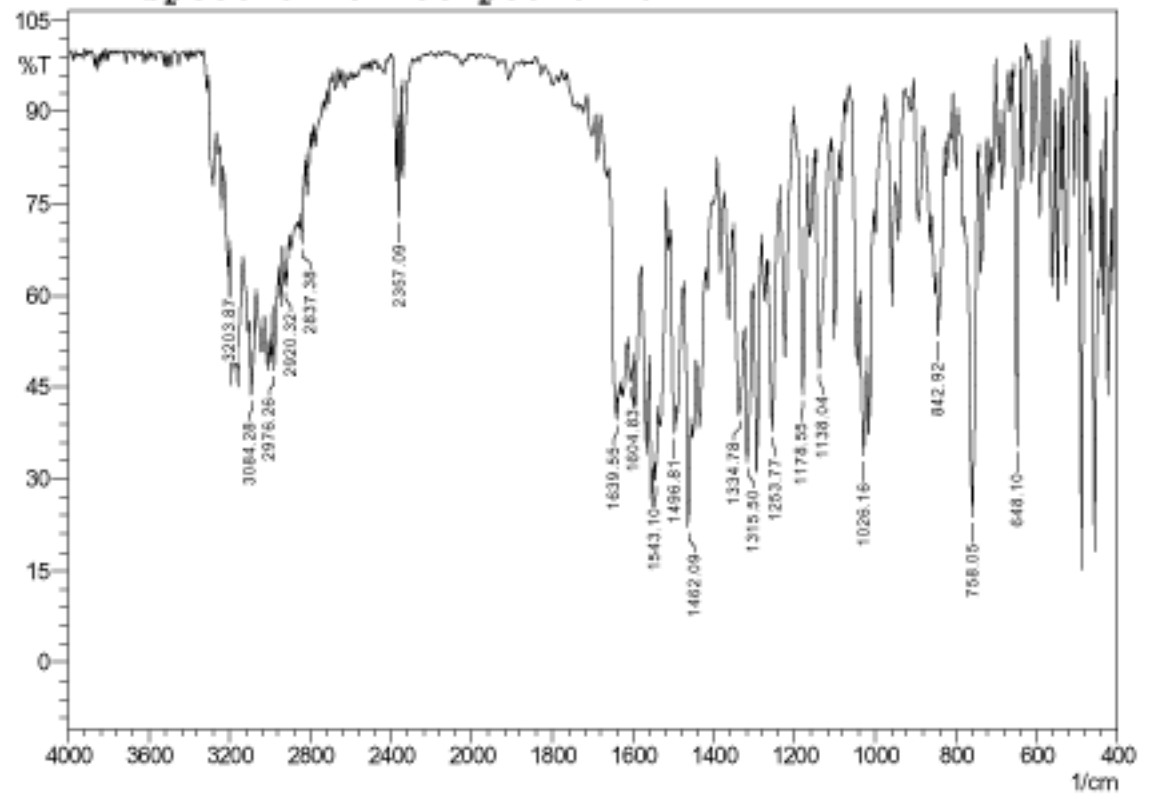
IR Spectrum of compound 7b



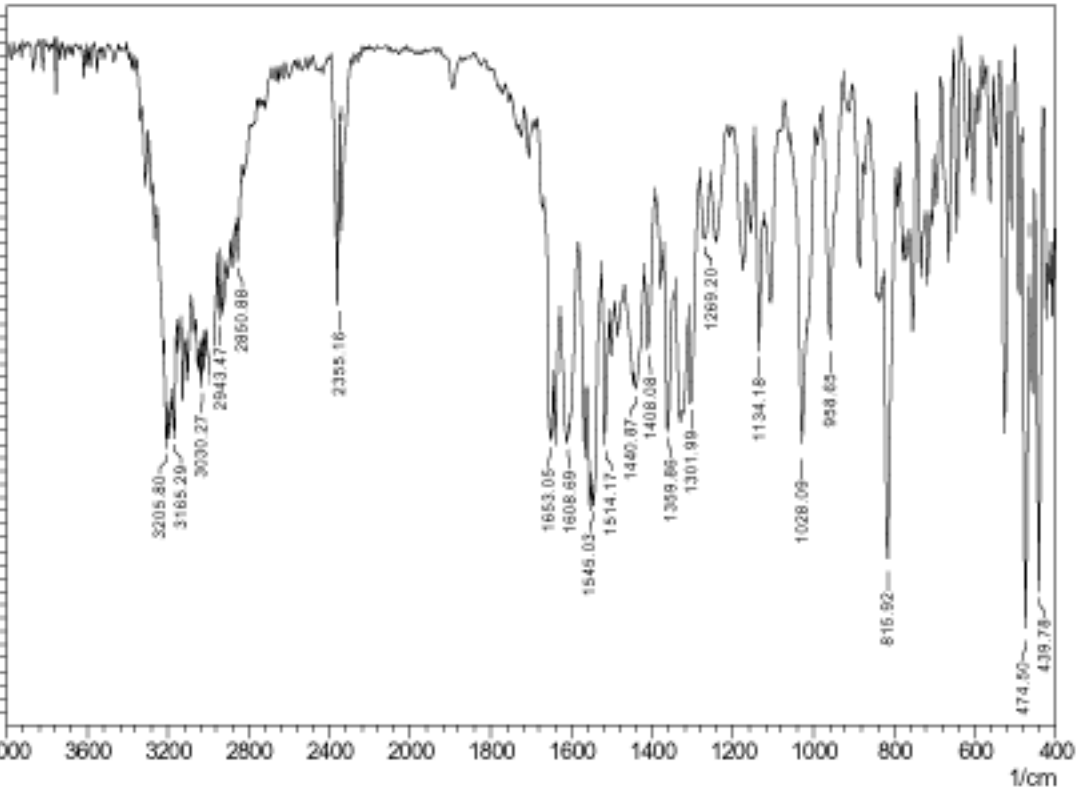
IR Spectrum of compound 7c



IR Spectrum of compound 7d



IR Spectrum of compound 7e



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Sample Information

Mass spectrum of compound 1a

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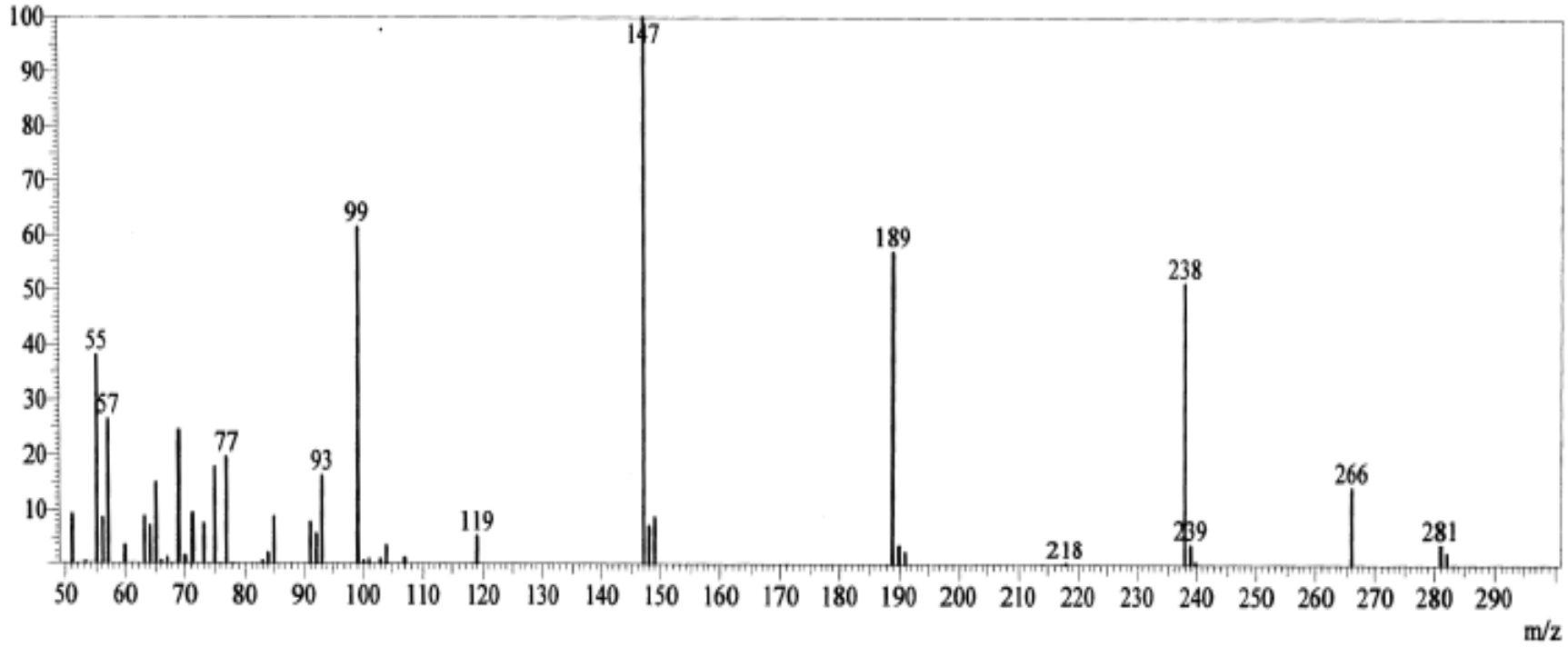
BG Mode:None



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Sample Information

Mass spectrum of compound 1j

Line#:1 R.Time:3.8(Scan#:423)
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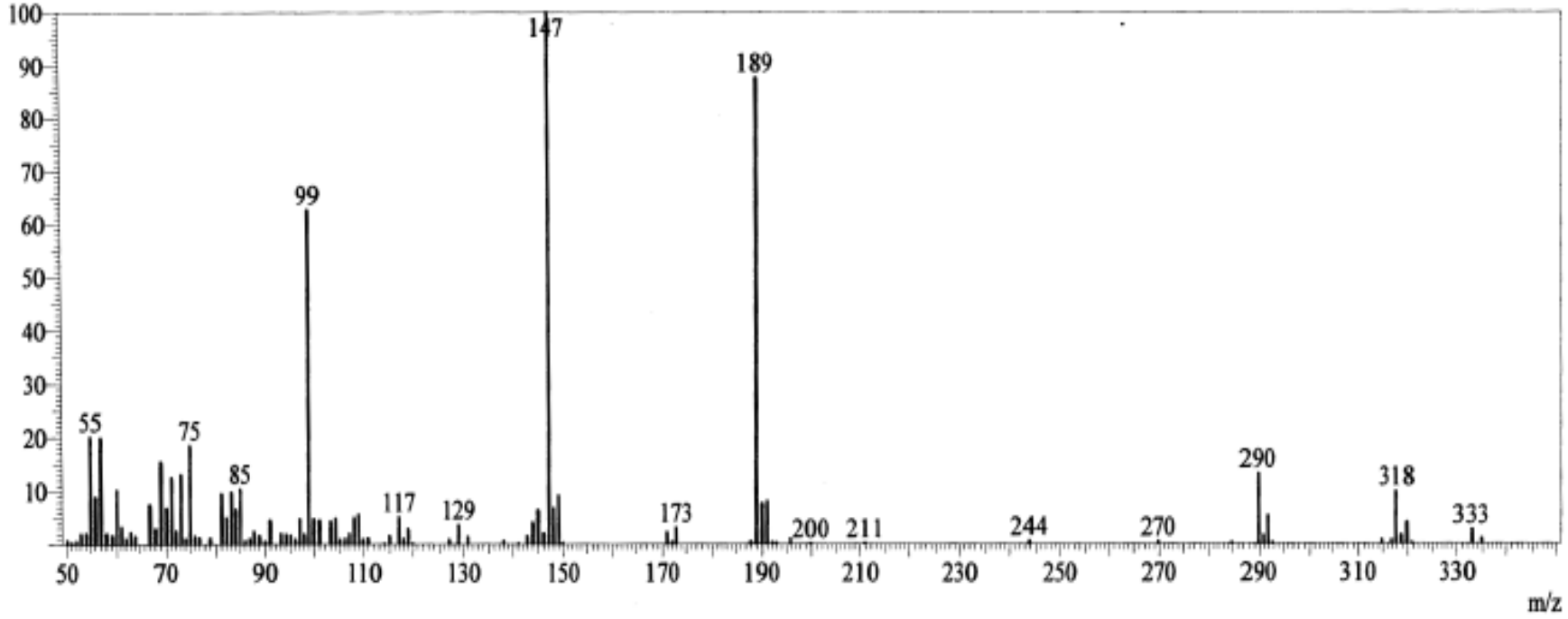

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Sample Information

Mass spectrum of compound 11

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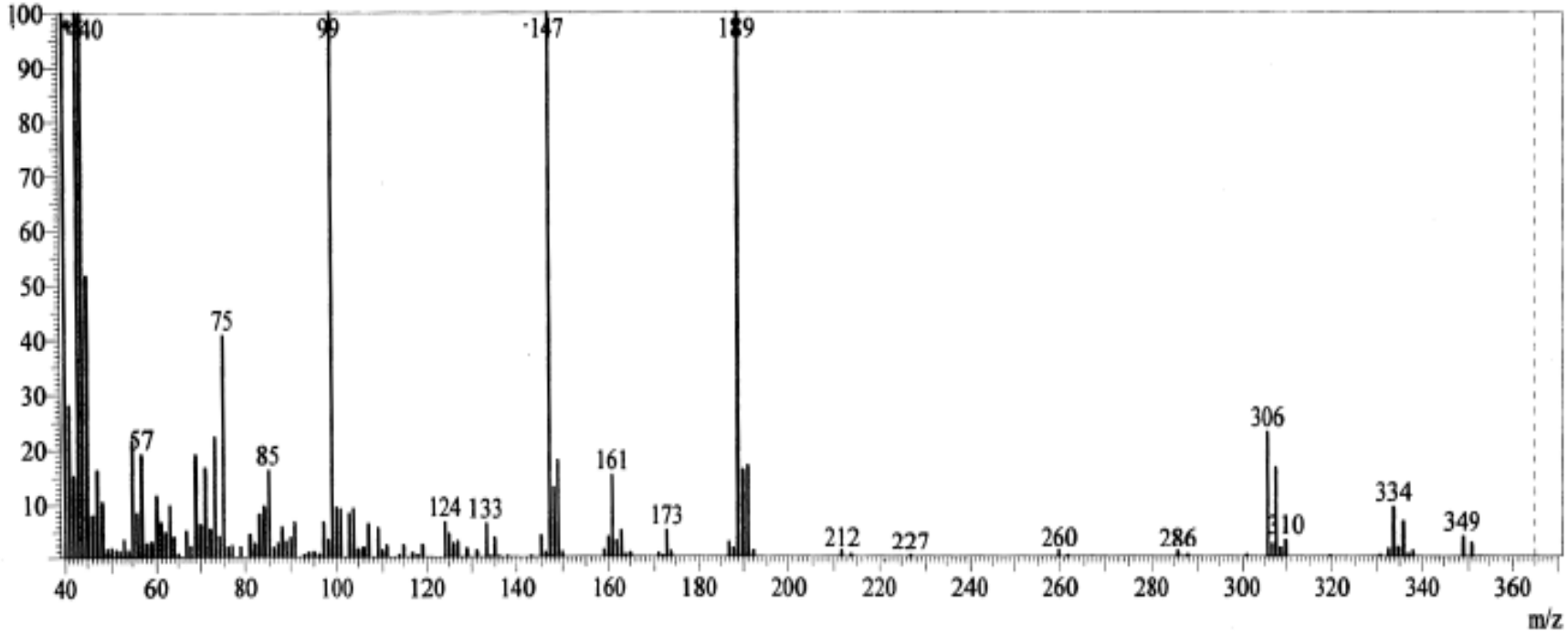

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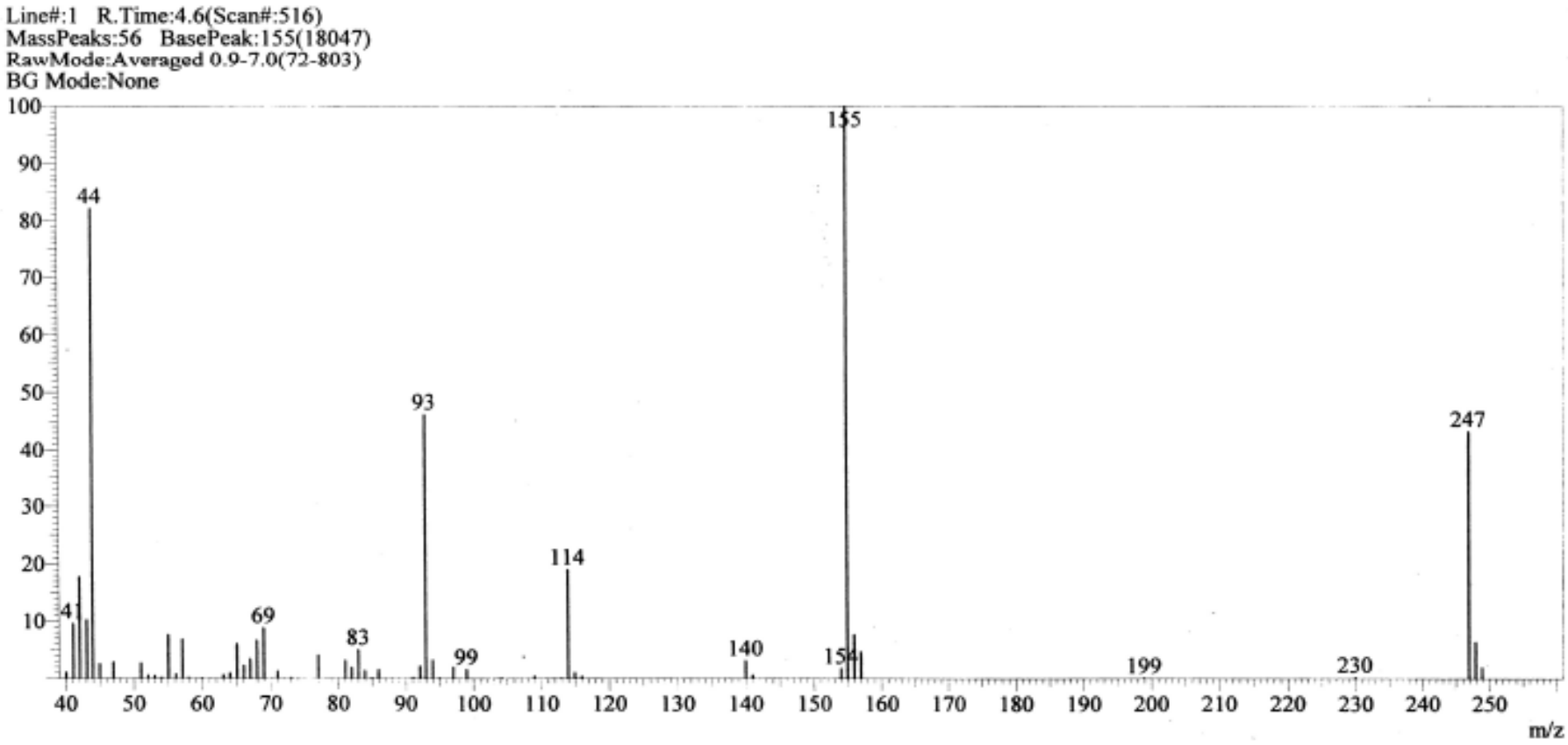
Sample Information

Mass spectrum of compound 4a



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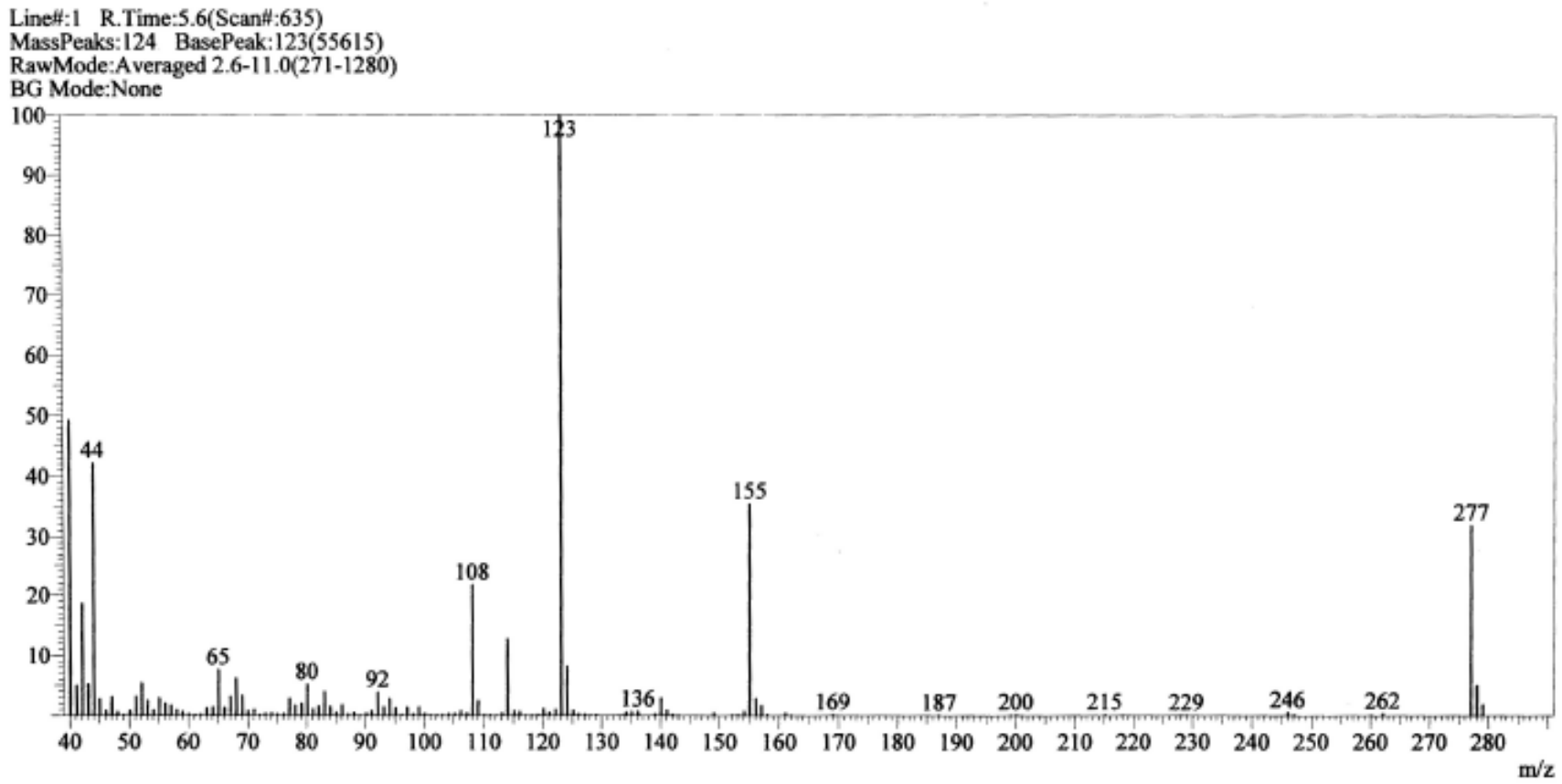
Sample Information

Mass spectrum of compound 4e



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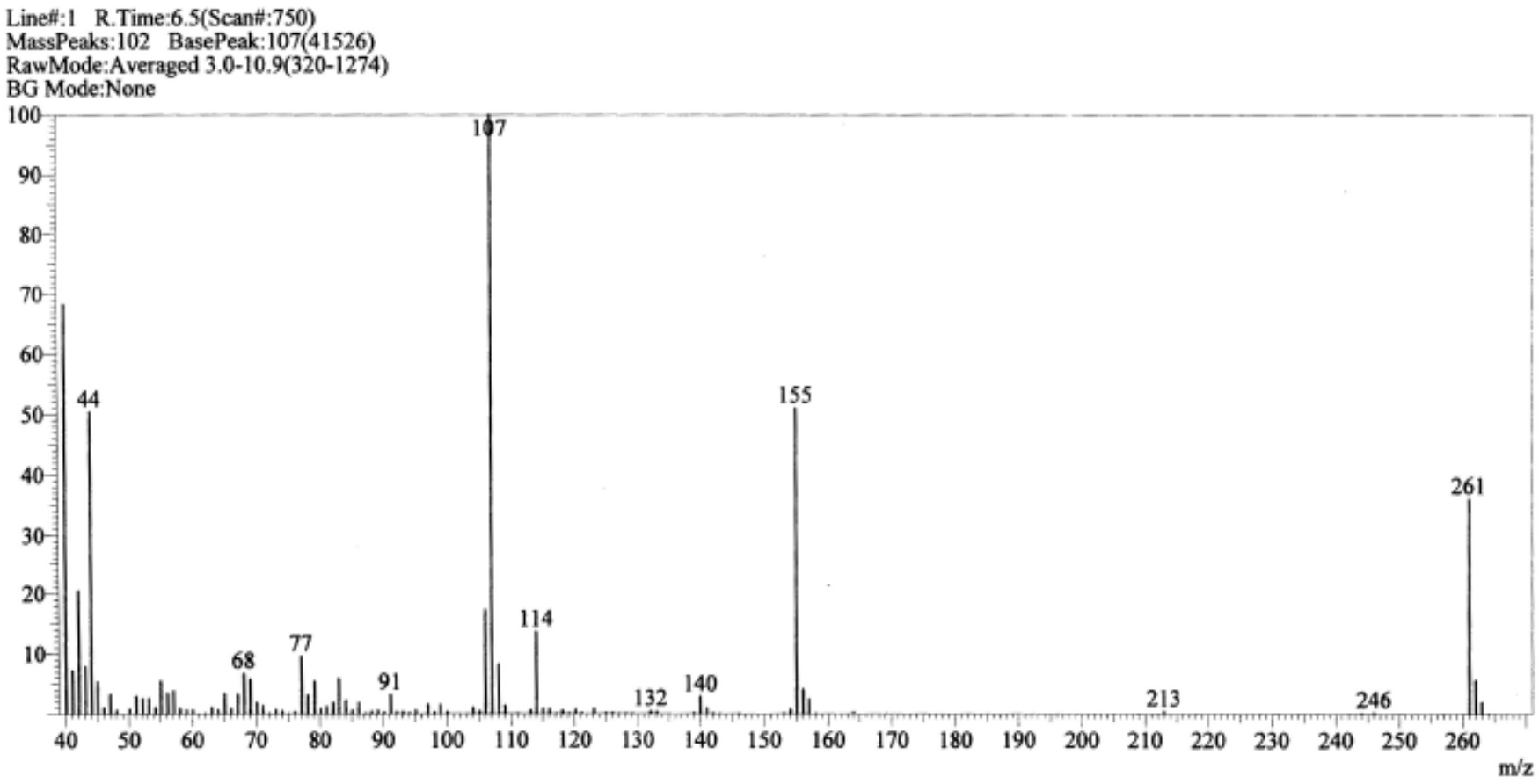
Sample Information

Mass spectrum of compound 4f



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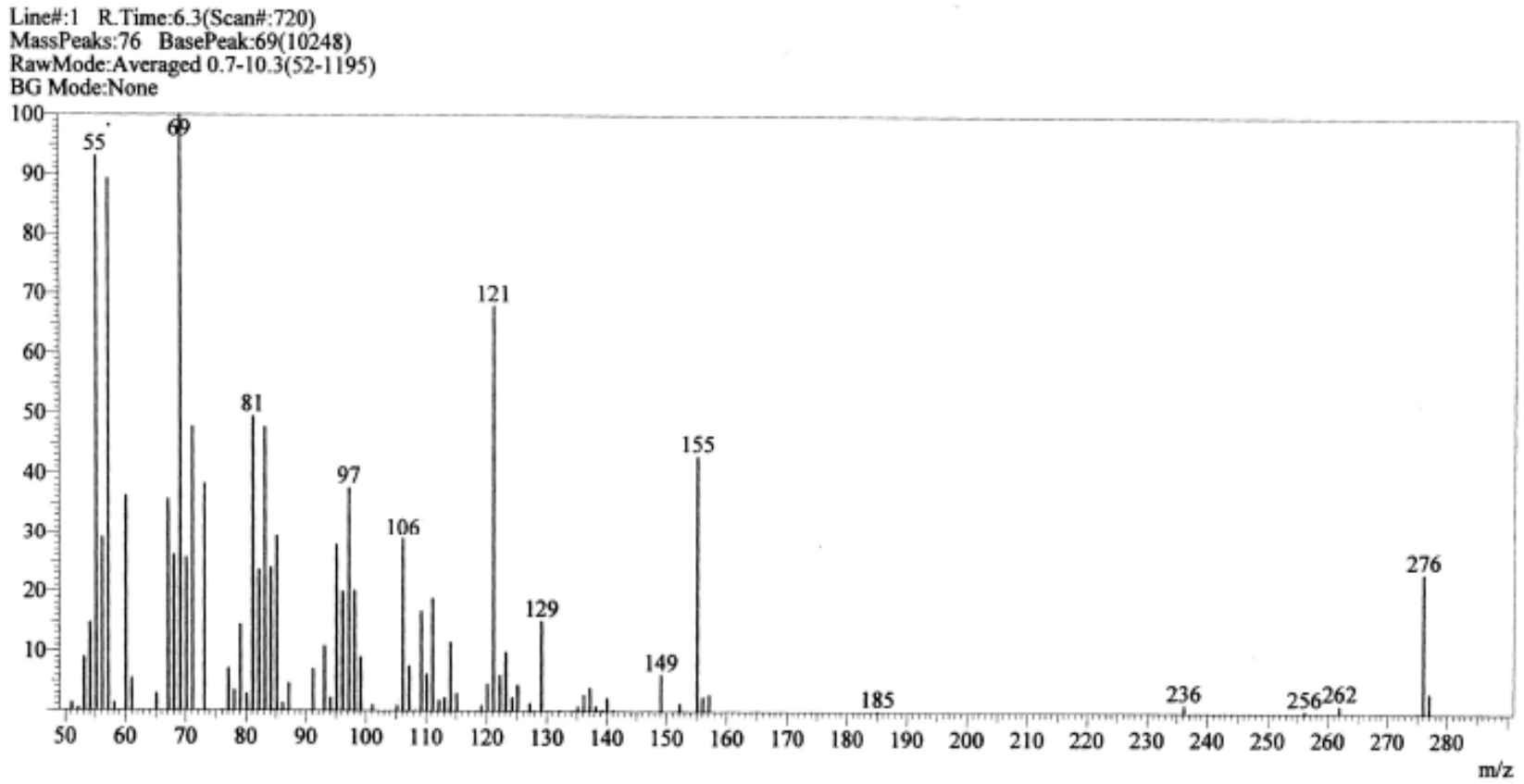
RAJKOT-360005

Sample Information

Mass spectrum of compound 5h



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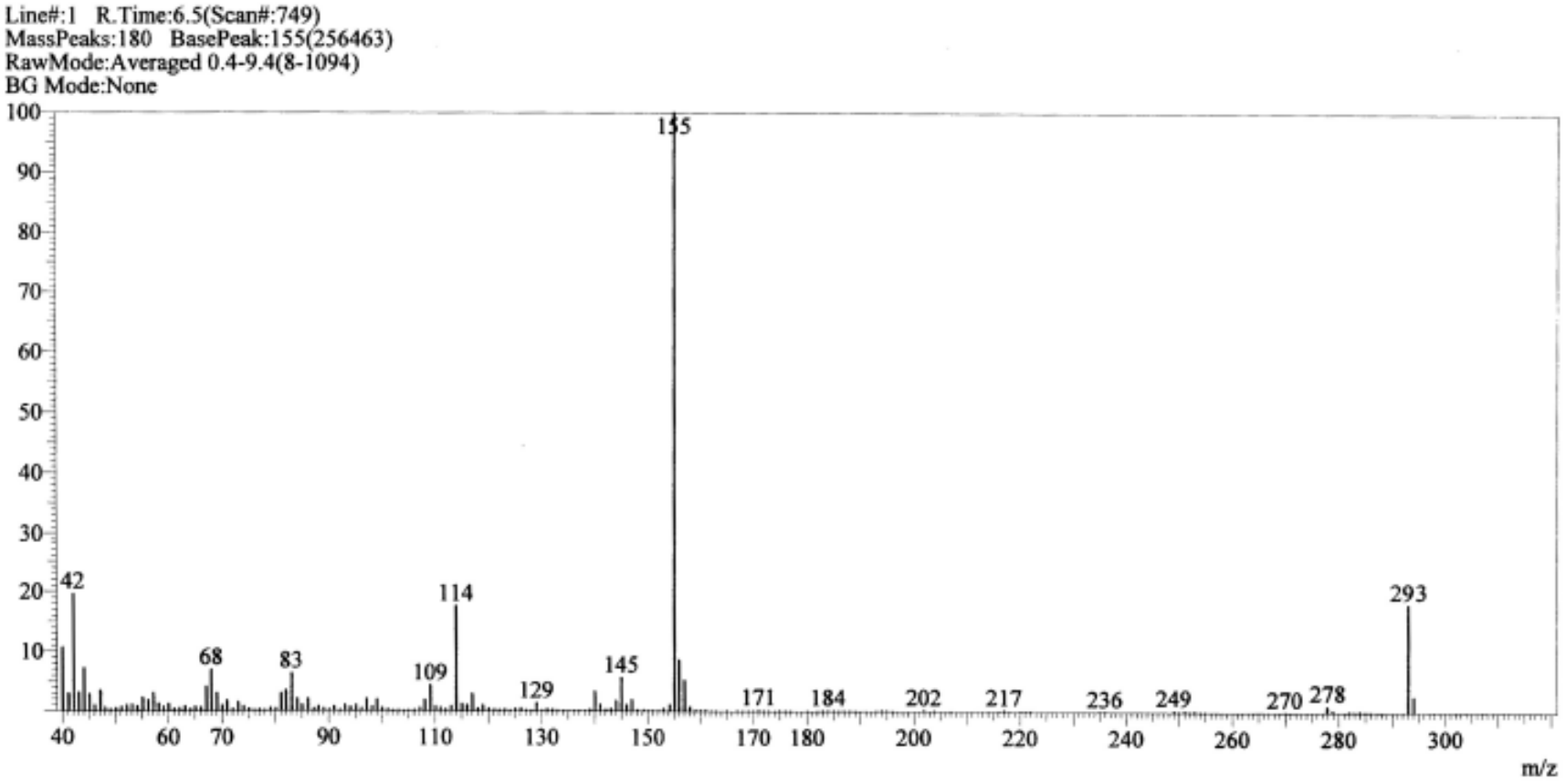
RAJKOT-360005

Sample Information

Mass spectrum of compound 5i



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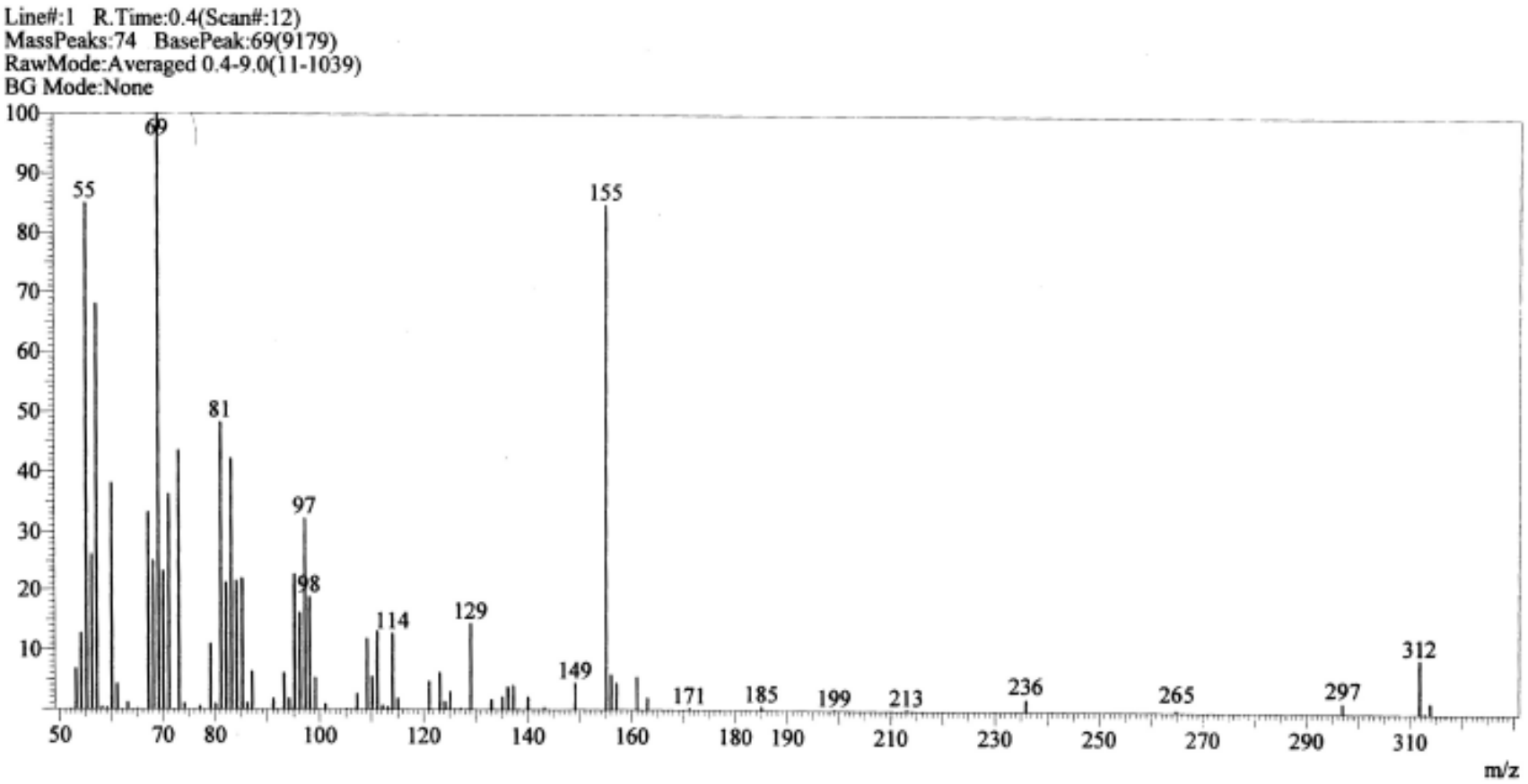
RAJKOT-360005

Sample Information

Mass spectrum of compound 5k



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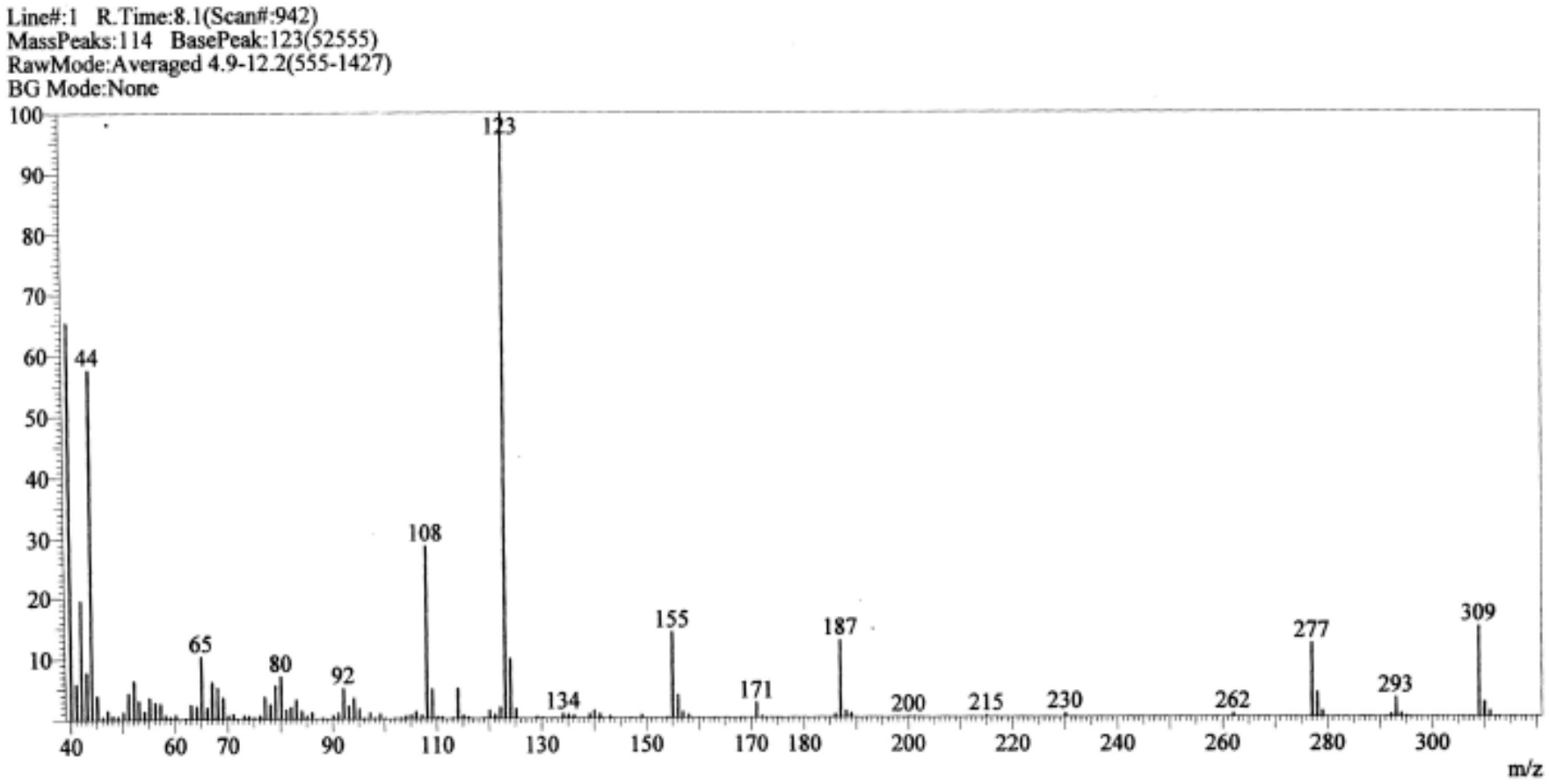
RAJKOT-360005

Sample Information

Mass spectrum of compound 6c



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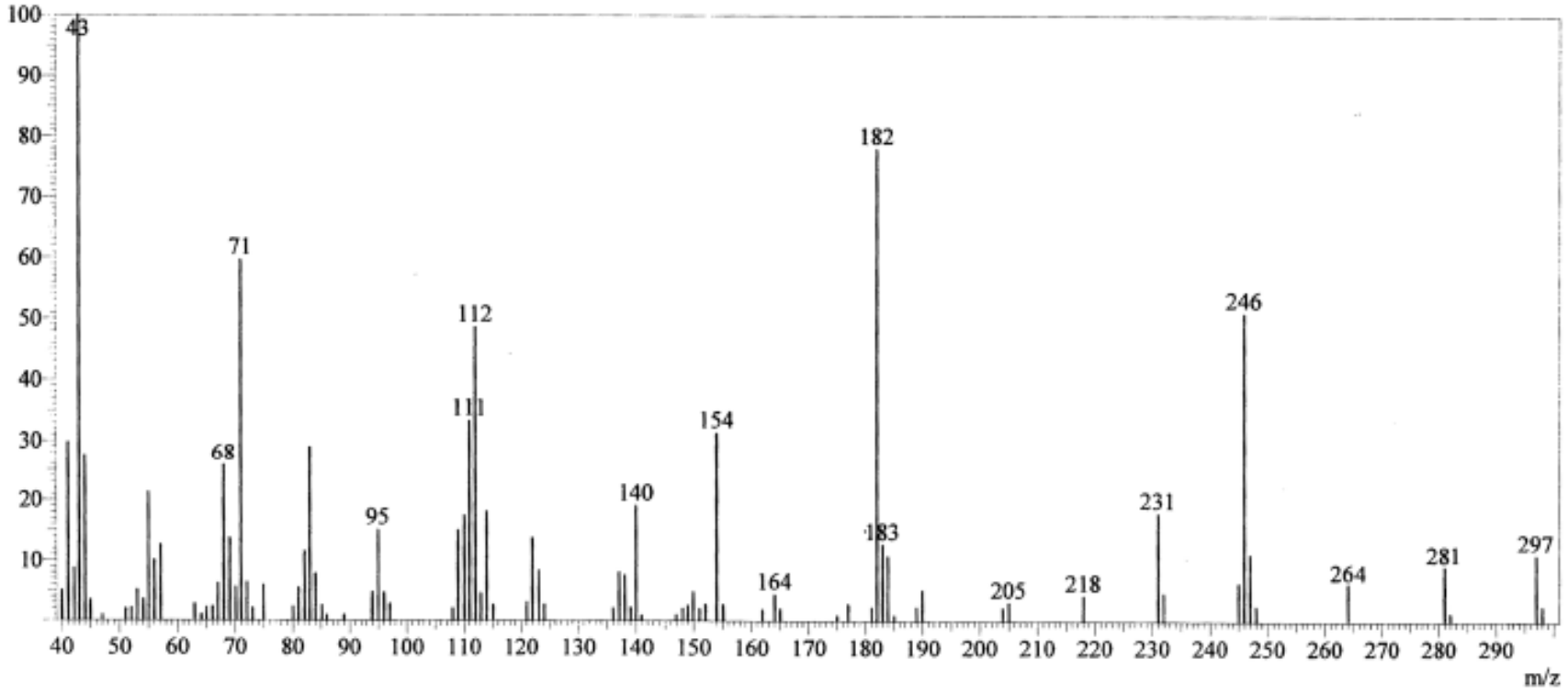
RAJKOT-360005

Sample Information

Mass spectrum of compound 6d

Line#:1 R.Time:1.6(Scan#:159)
MassPeaks:89 BasePeak:43(57797)
RawMode:Averaged 1.6-1.6(159-160)
BG Mode:None



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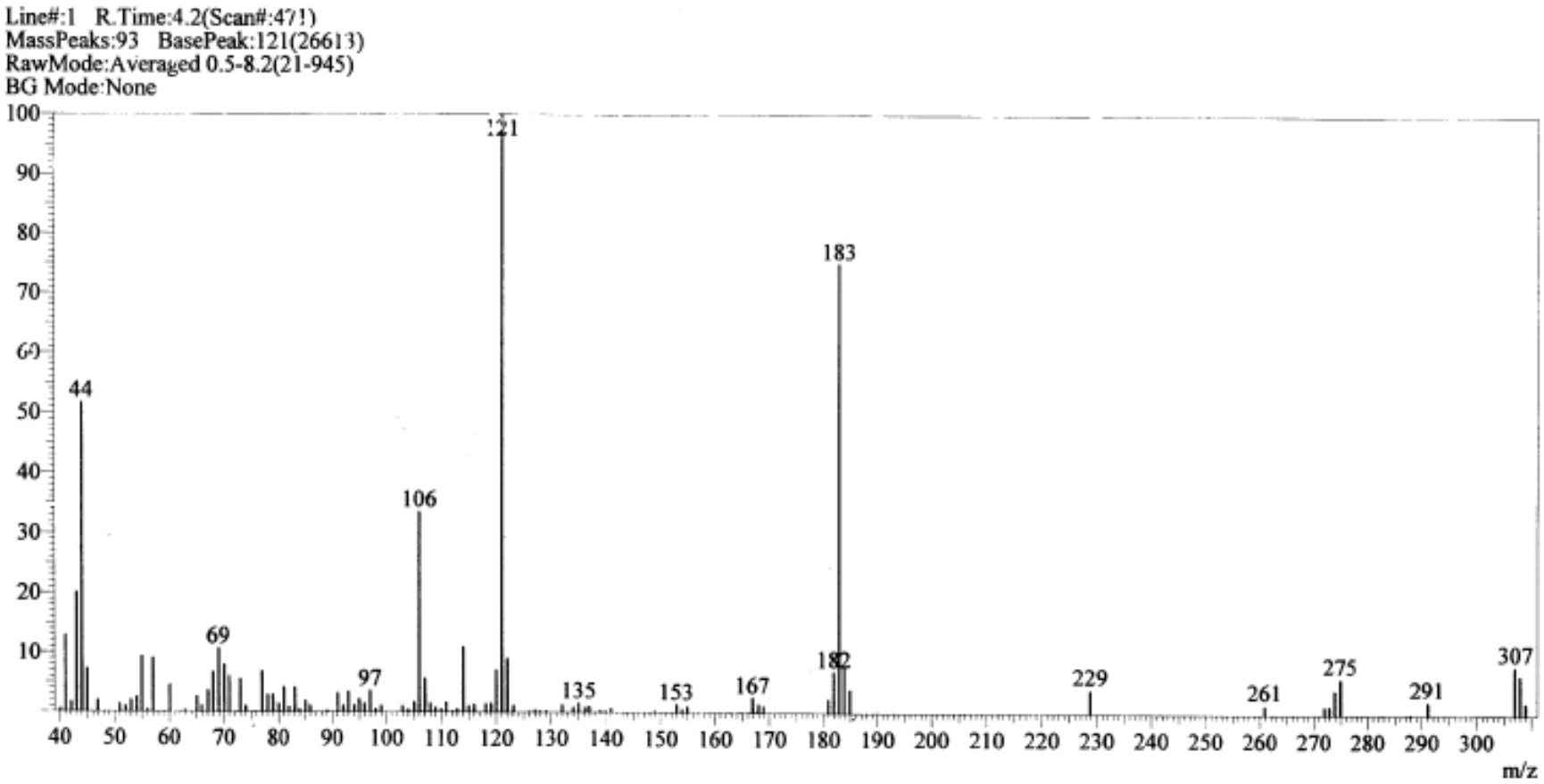
RAJKOT-360005

Sample Information

Mass spectrum of compound 6h



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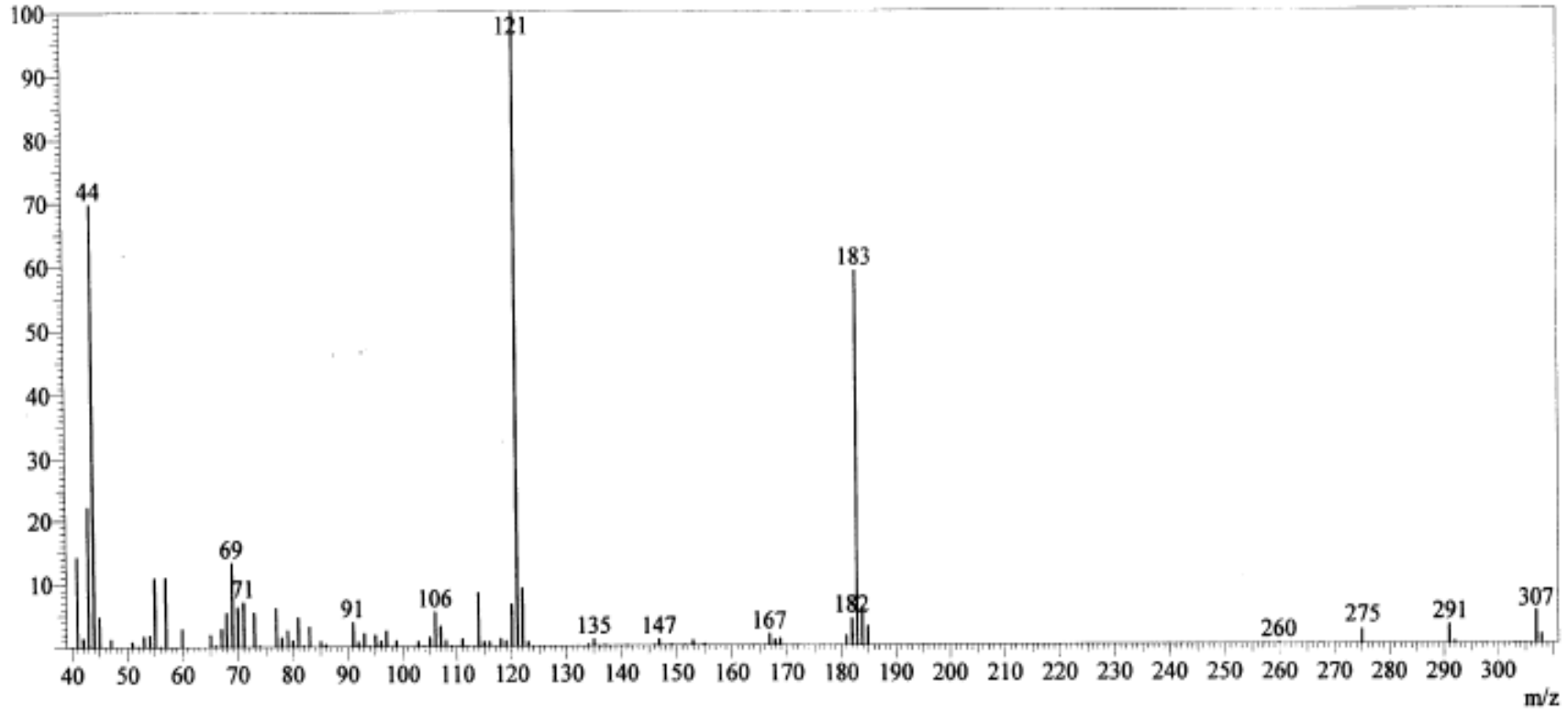
RAJKOT-360005

Sample Information

Mass spectrum of compound 6m

Line#:1 R.Time:4.4(Scan#:496)
MassPeaks:80 BasePeak:121(18693)
RawMode:Averaged 0.4-6.4(10-731)
BG Mode:None



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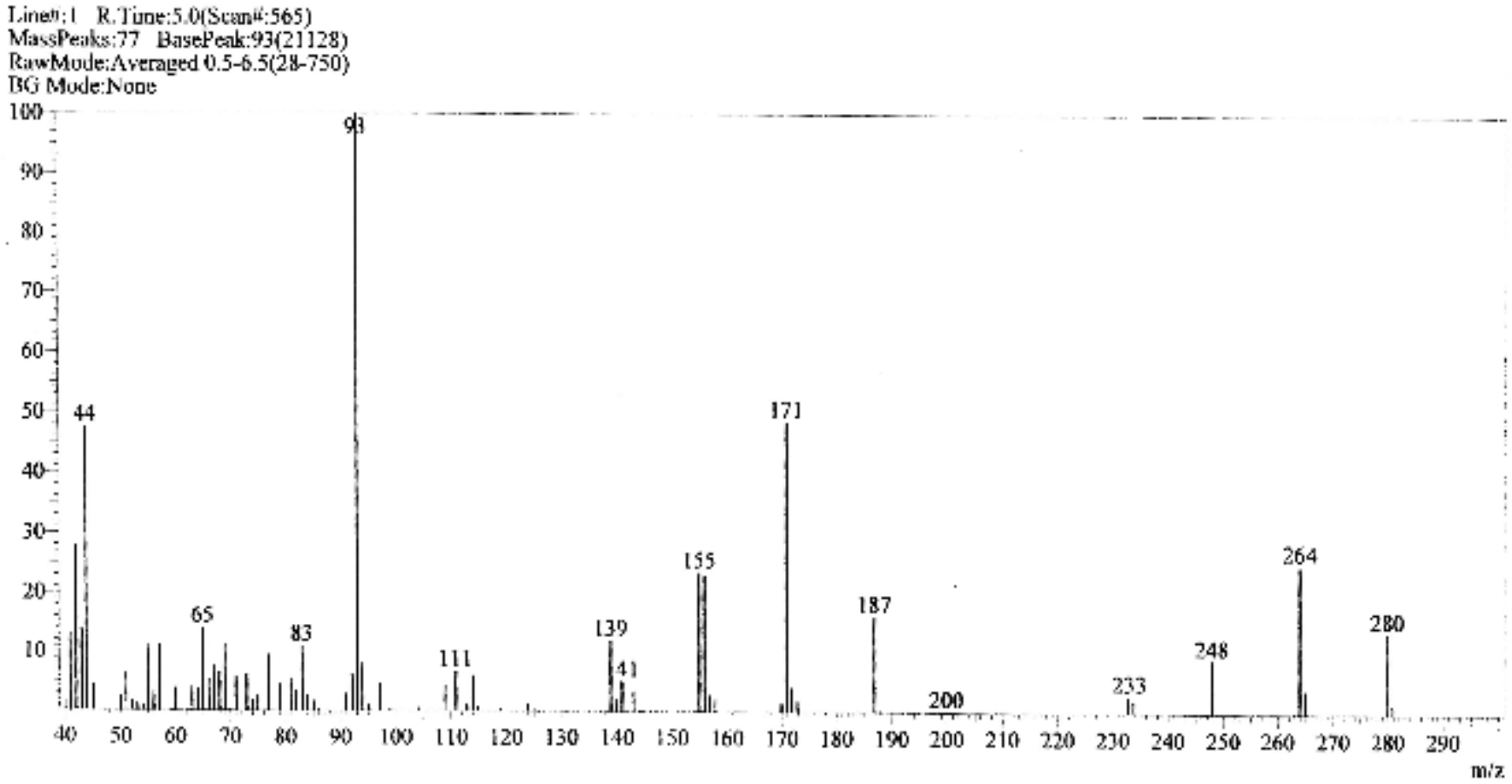
RAJKOT-360005

Sample Information

Mass spectrum of compound 7a



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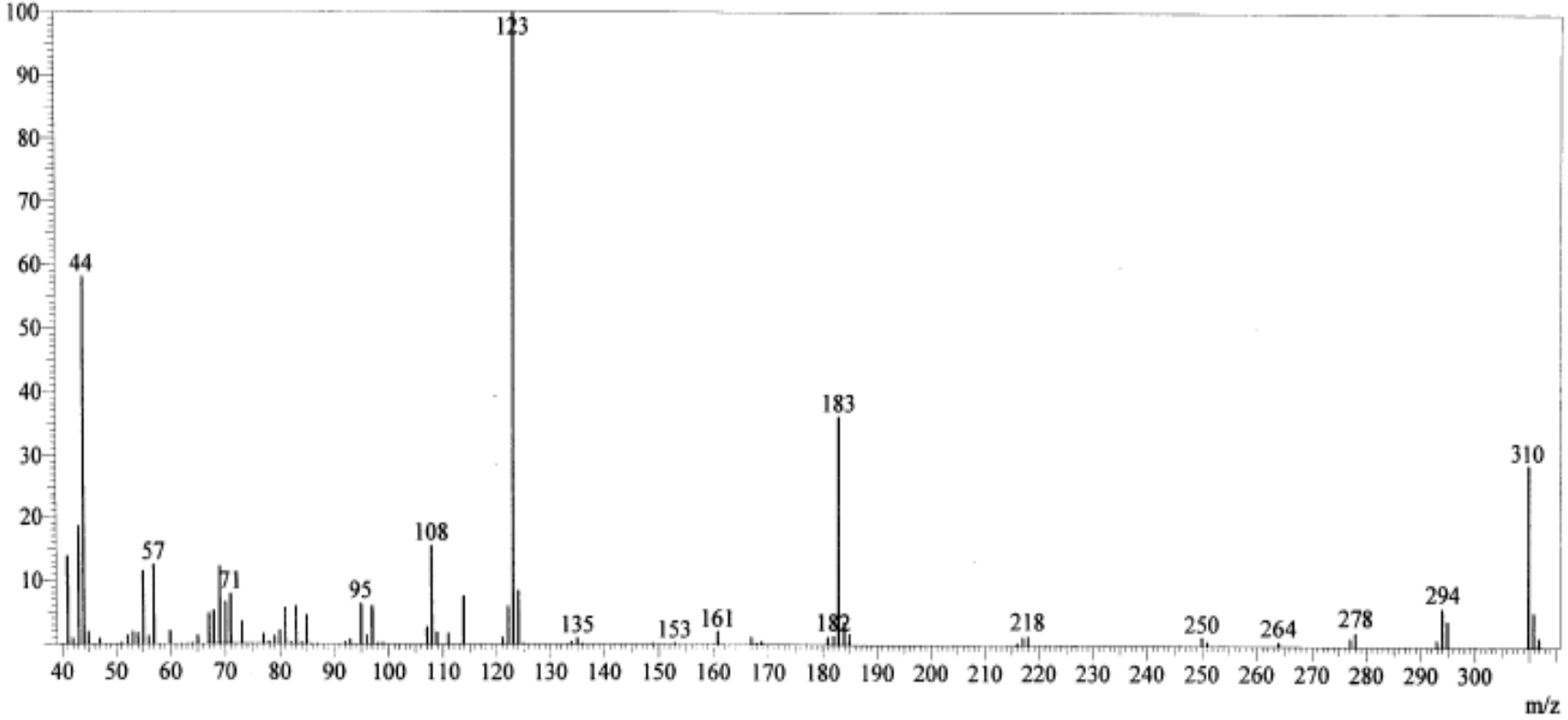
RAJKOT-360005

Sample Information

Mass spectrum of compound 7c

Line#:1 R.Time:4.3(Scan#:479)
MassPeaks:67 BasePeak:123(23980)
RawMode:Averaged 0.6-6.3(35-726)
BG Mode:None



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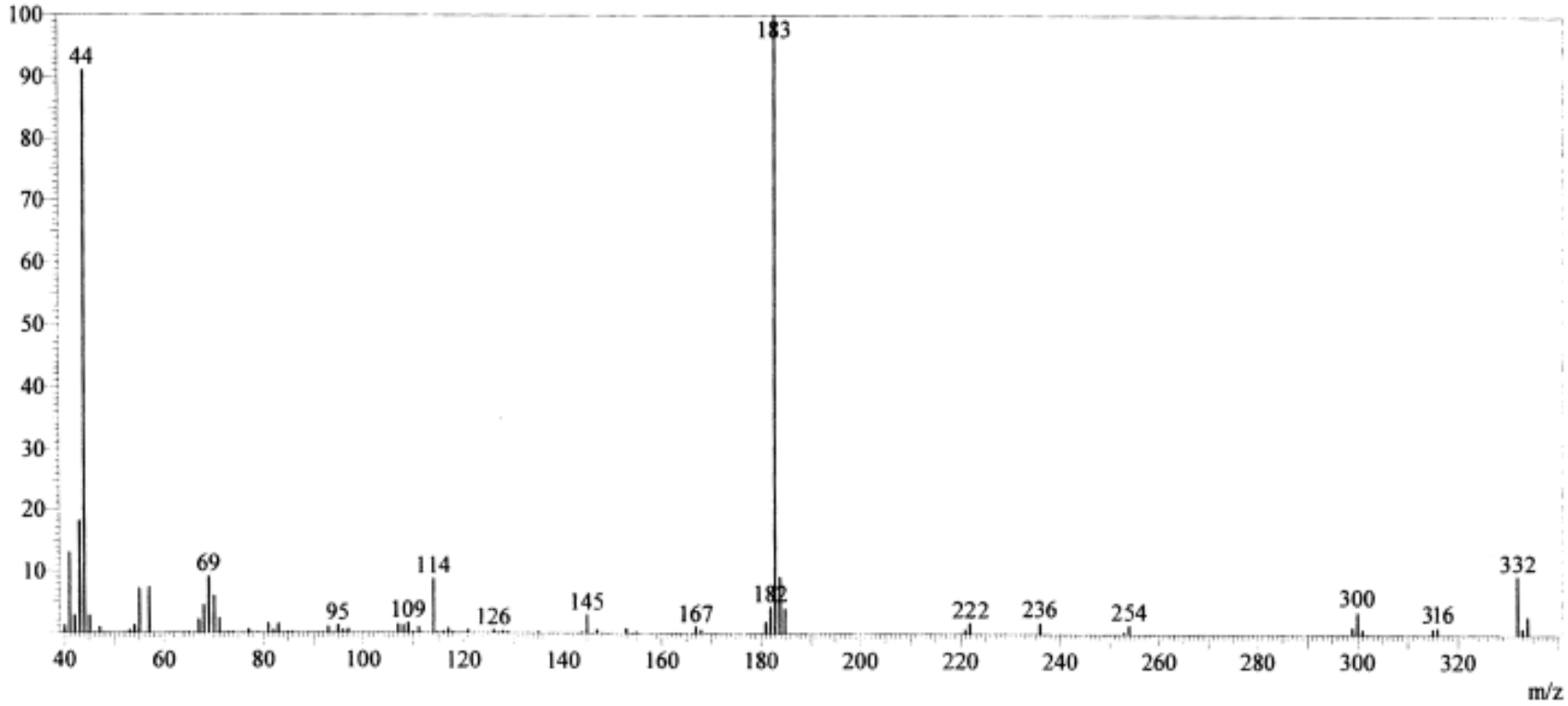
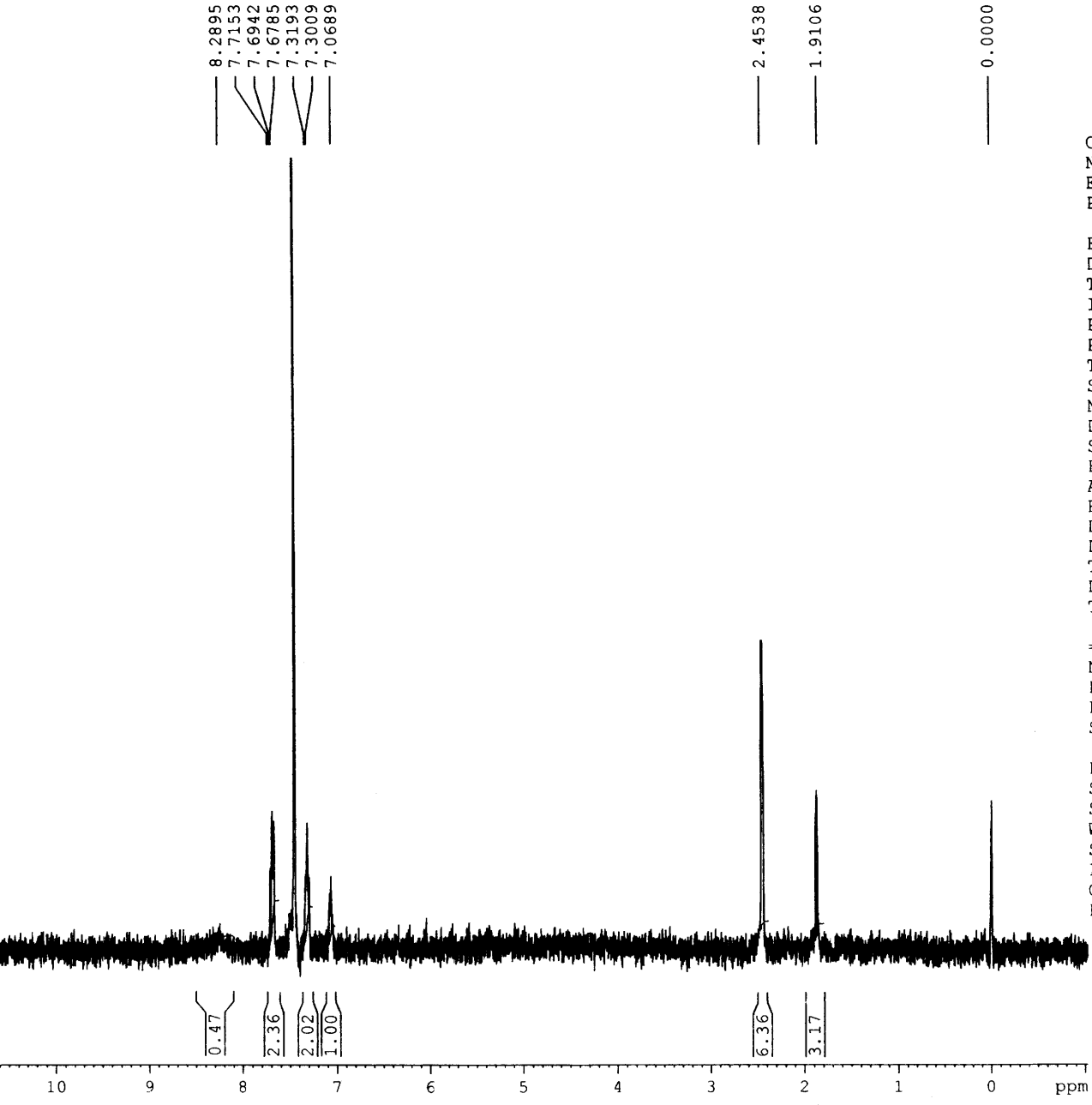
Sample Information

Mass spectrum of compound 7j

Line#:1 R.Time:5.2(Scan#:588)
MassPeaks:60 BasePeak:183(17765)
RawMode:Averaged 0.4-8.3(8-957)
BG Mode:None



^{1}H NMR Spectrum of compound 1a



BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

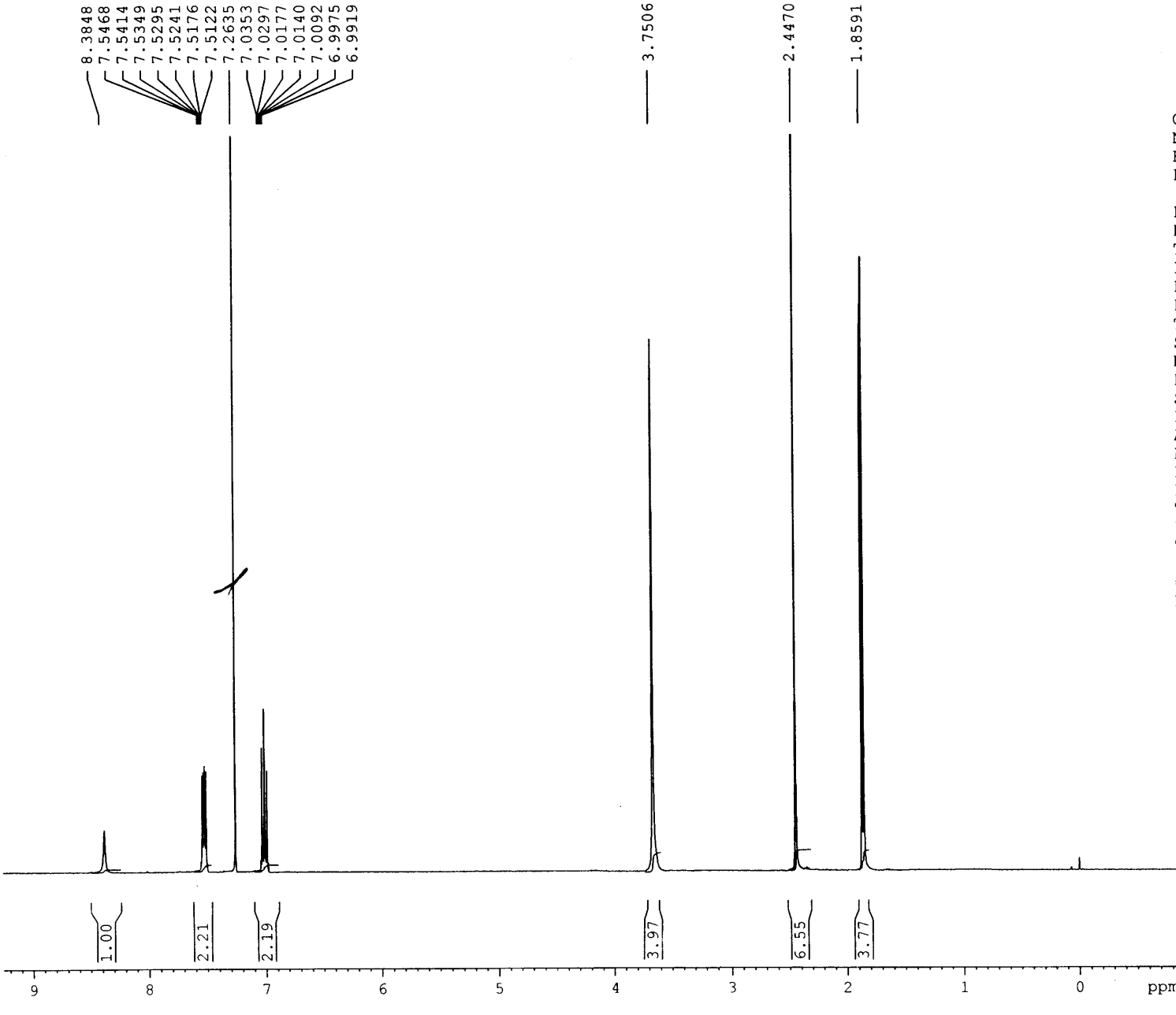
Current Data Parameters	
NAME	Oct30-2008
EXPNO	90
PROCNO	1

F2 - Acquisition Parameters	
Date_	20081030
Time	15.11
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12019.230 Hz
FIDRES	0.183399 Hz
AQ	2.7263477 sec
RG	575
DW	41.600 usec
DE	6.00 usec
TE	294.7 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========	
NUC1	1H
P1	10.90 usec
PL1	-3.00 dB
SFO1	400.1324008 MHz

F2 - Processing parameters	
SI	32768
SF	400.1280310 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

^{1}H NMR Spectrum of compound 1c



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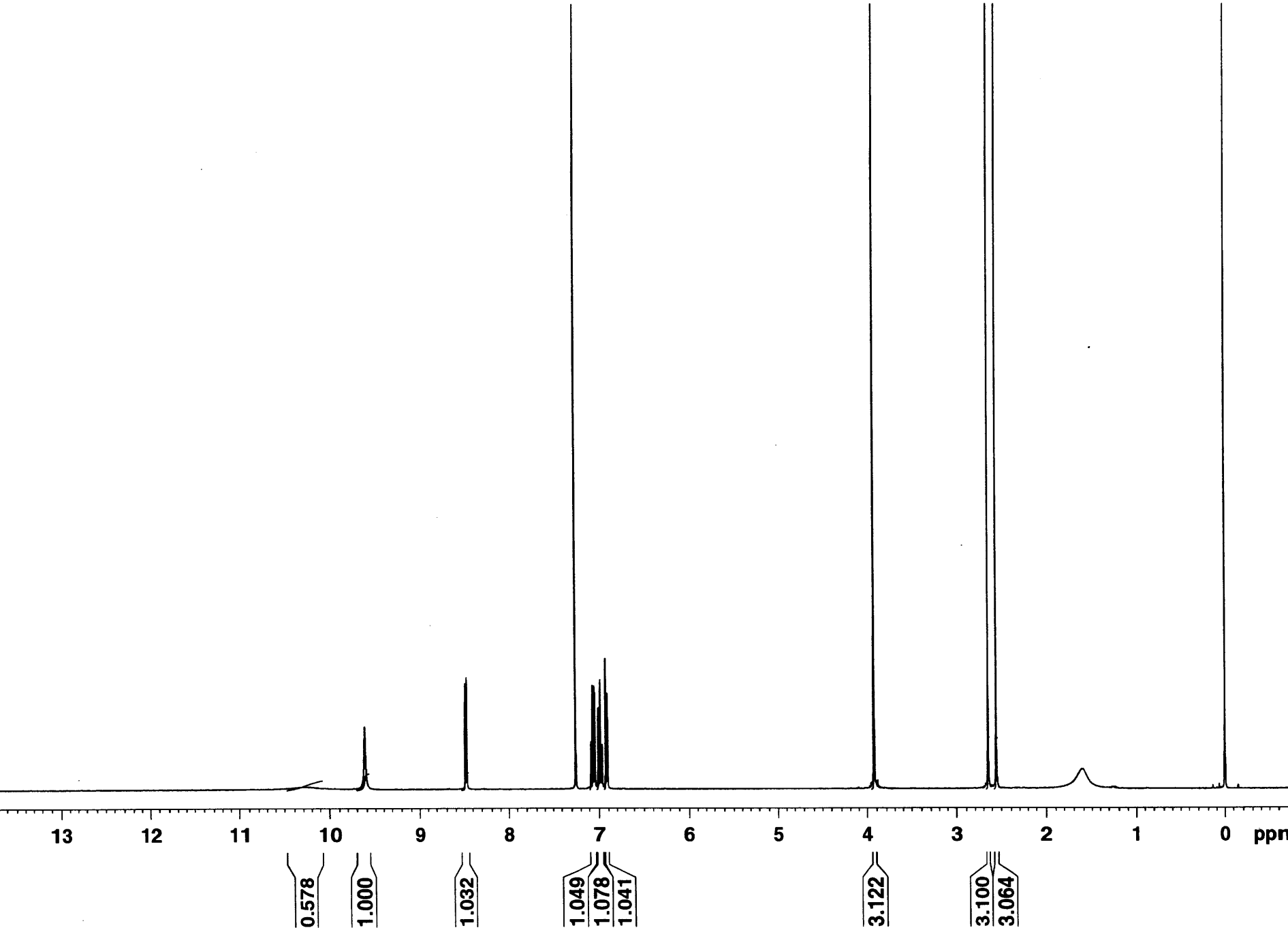
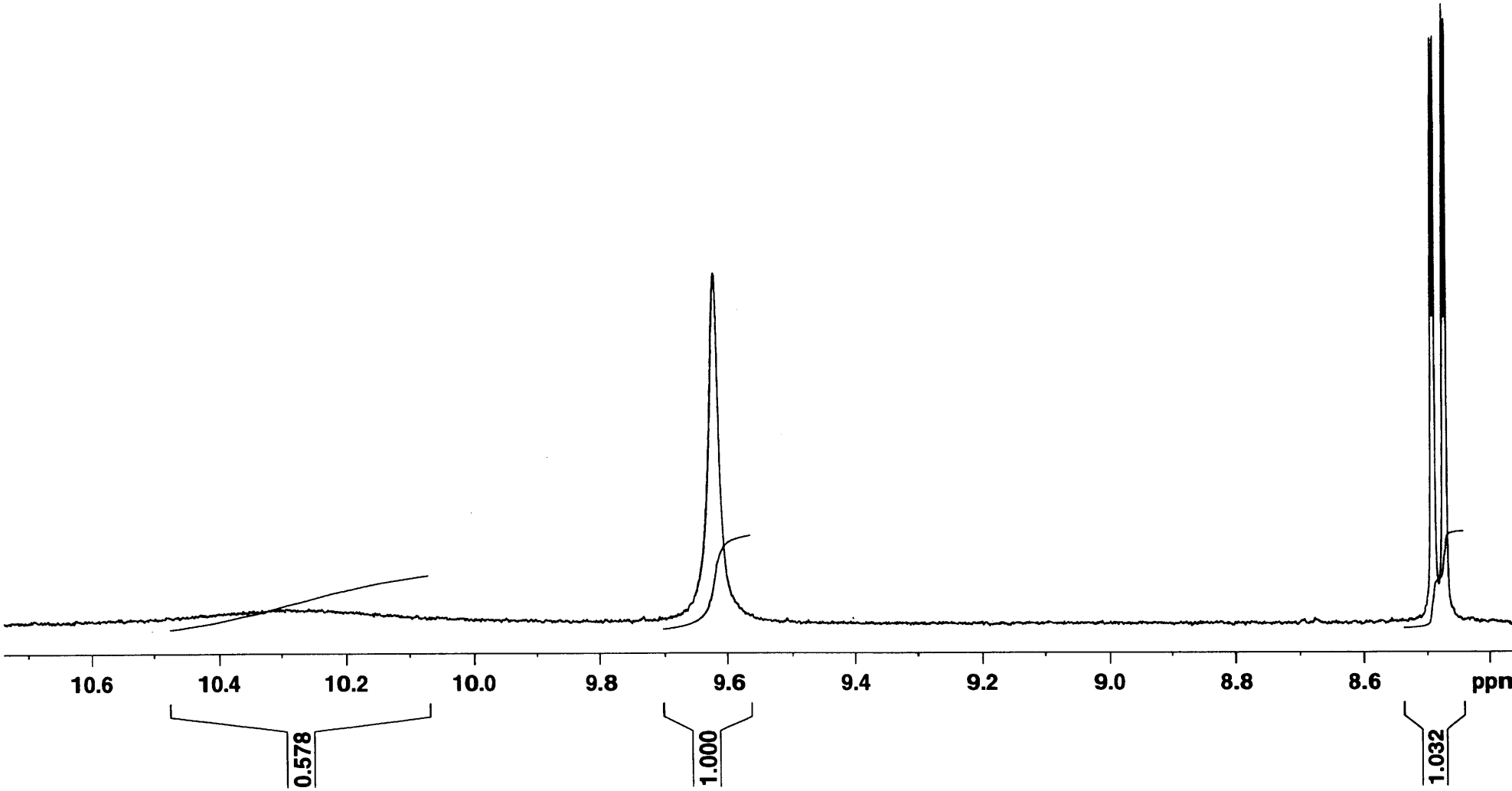
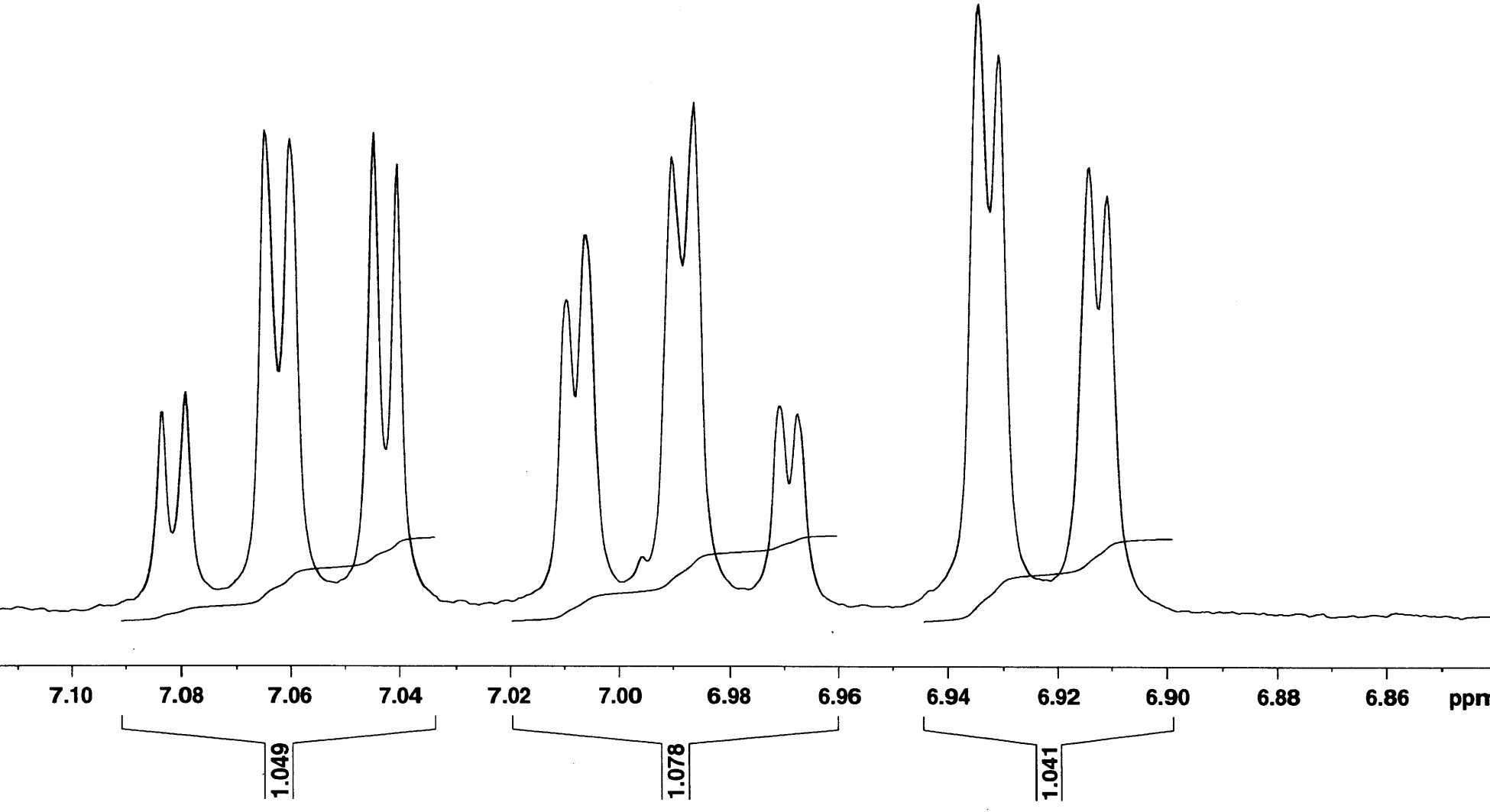
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

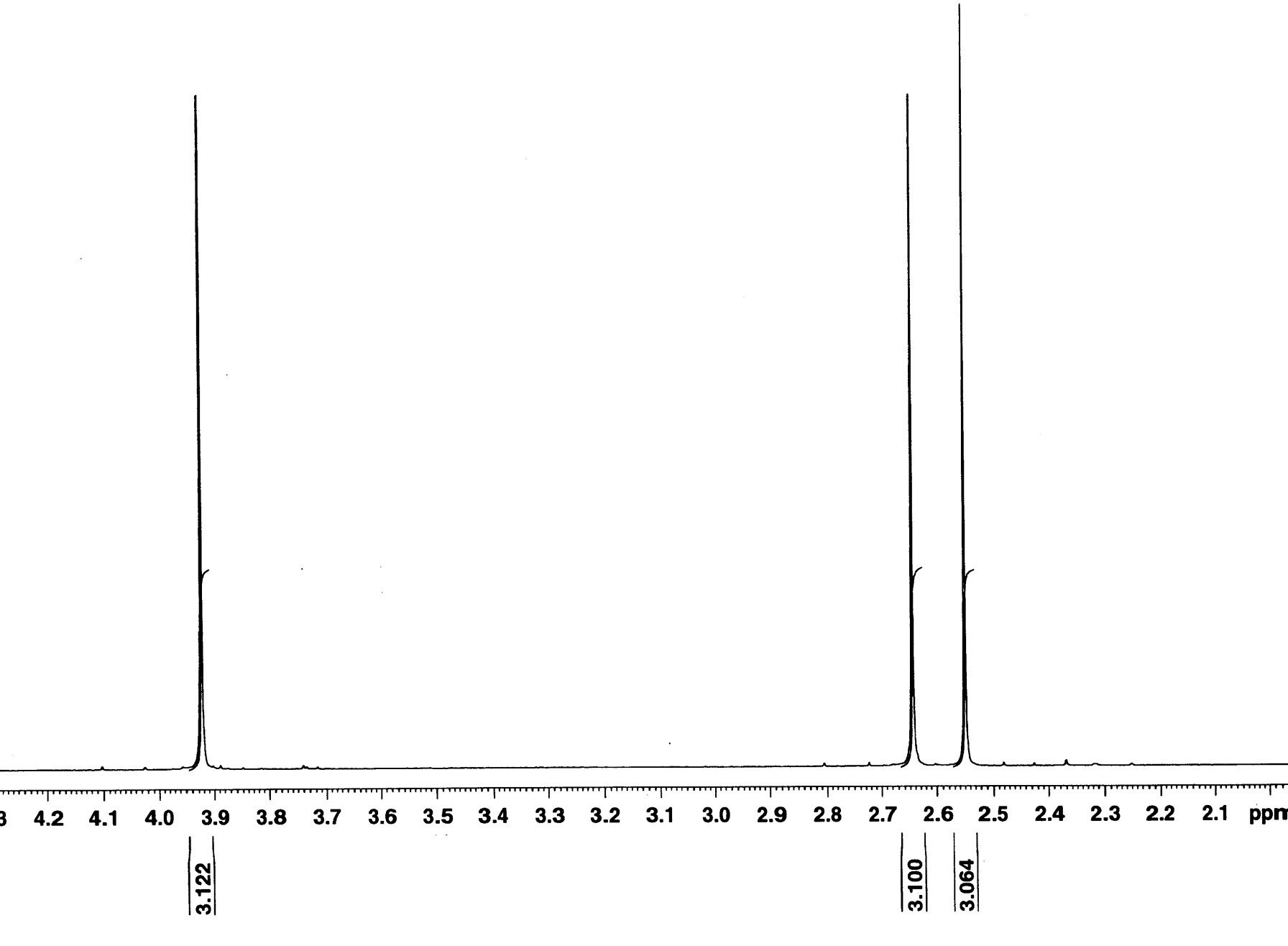
Current Data Parameters	
NAME	Feb09-2009
EXPNO	350
PROCNO	1
F2 - Acquisition Paramete	
Date_	20090210
Time	12.09
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12019.230 H
FIDRES	0.183399 H
AQ	2.7263477 s
RG	456
DW	41.600 u
DE	6.00 u
TE	295.5 K
D1	1.00000000 s
TD0	1
======== CHANNEL f1 =====	
NUC1	1H
P1	10.90 u
PL1	-3.00 d
SFO1	400.1324008 M
F2 - Processing parameter	
SI	32768
SF	400.1300083 M
WDW	EM
SSB	0
LB	0.30 H
GB	0
PC	1.00

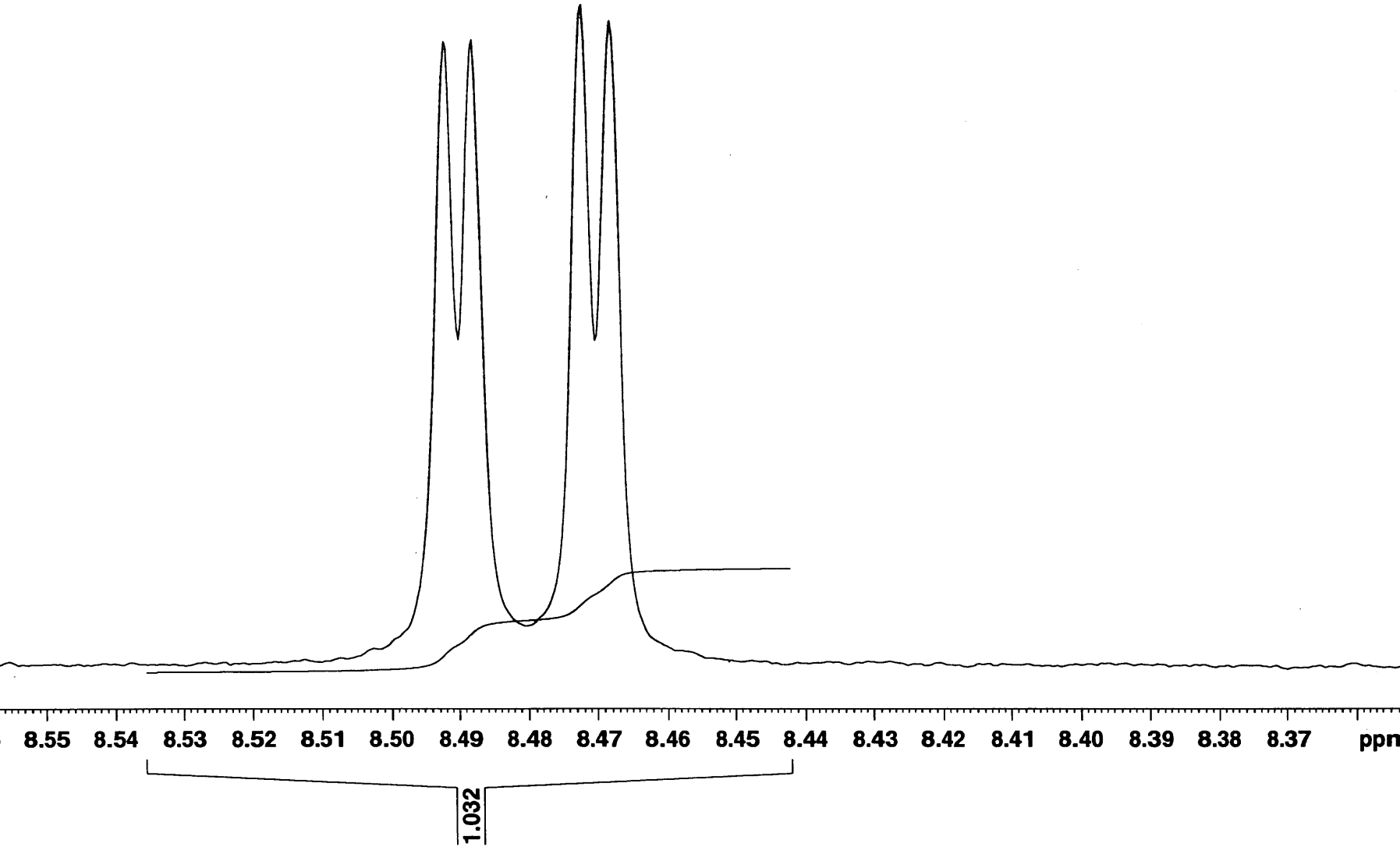
^{1}H NMR Spectrum of Compound 4c




10.6
10.4
10.2
10.0
9.8
9.6
9.4
9.2
9.0
8.8
8.6
ppm
0.578
1.000
1.032

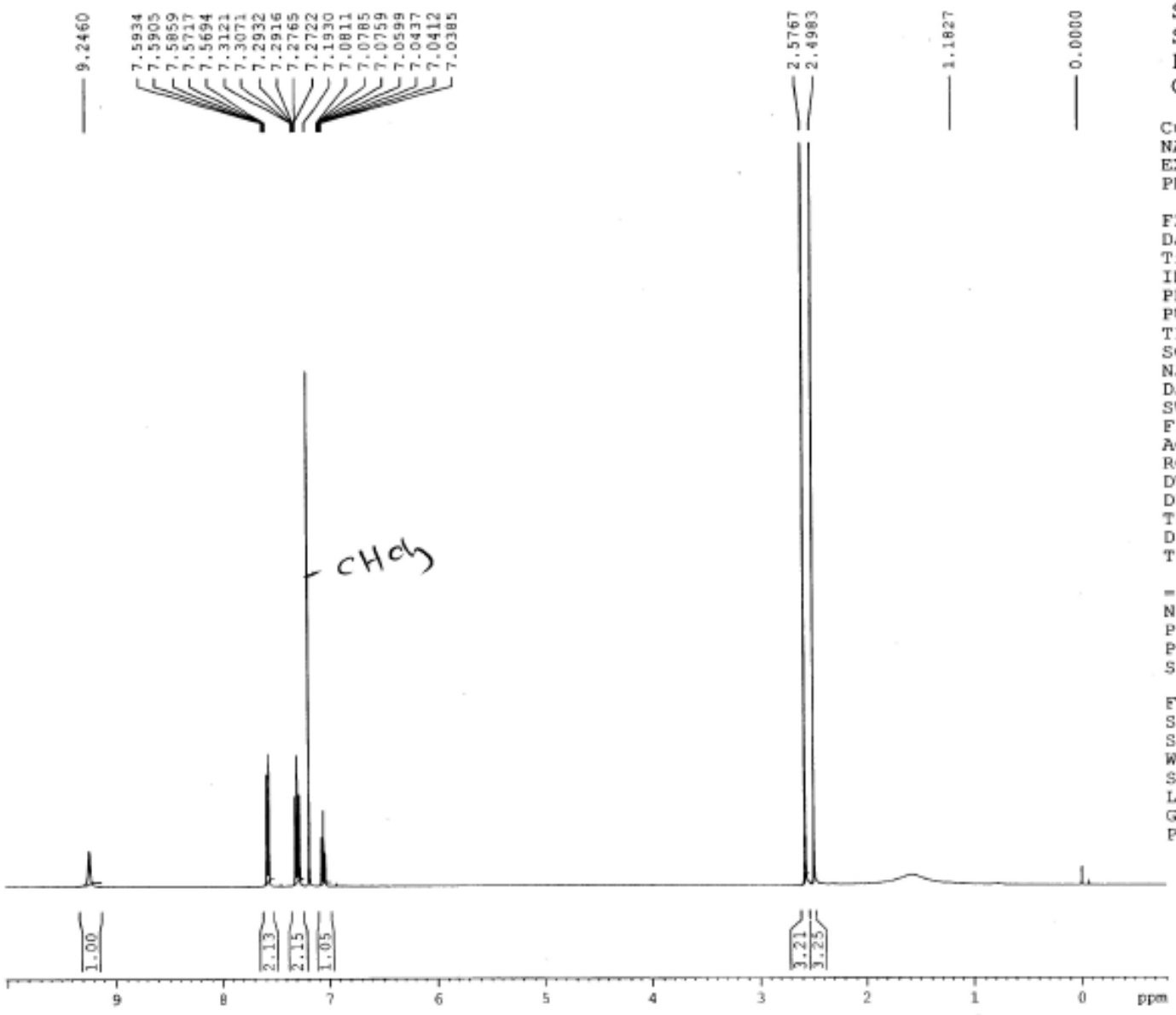

7.10
7.08
7.06
7.04
7.02
7.00
6.98
6.96
6.94
6.92
6.90
6.88
6.86
ppm
1.049
1.078
1.041


4.2
4.1
4.0
3.9
3.8
3.7
3.6
3.5
3.4
3.3
3.2
3.1
3.0
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
ppm
3.122
3.100
3.064


8.55
8.54
8.53
8.52
8.51
8.50
8.49
8.48
8.47
8.46
8.45
8.44
8.43
8.42
8.41
8.40
8.39
8.38
8.37
ppm
1.032

Peak	ν(F1) [ppm]	ν(F1) [Hz]	Intensity [rel]
1	9.6206	3850.4529	0.59
2	8.4921	3398.7934	0.99
3	8.4879	3397.1124	0.99
4	8.4722	3390.8288	1.04
5	8.4680	3389.1478	1.02
6	7.2598	2905.5899	7.62
7	7.0834	2834.9893	0.41
8	7.0792	2833.3084	0.45
9	7.0643	2827.3449	0.97
10	7.0600	2825.6239	0.95
11	7.0447	2819.5004	0.96
12	7.0403	2817.7394	0.90
13	7.0095	2805.4123	0.63
14	7.0059	2803.9715	0.76
15	6.9958	2799.9292	0.12
16	6.9900	2797.6078	0.91
17	6.9864	2796.1670	1.02
18	6.9708	2789.9234	0.42
19	6.9673	2788.5226	0.40
20	6.9344	2775.3551	1.22
21	6.9308	2773.9142	1.12
22	6.9144	2767.3505	0.90
23	6.9108	2765.9096	0.84
24	3.9238	1570.4226	13.23
25	3.4928	1397.9234	0.45
26	2.6451	1058.6484	13.29
27	2.5496	1020.4265	15.00
28	1.6106	644.6105	0.19
29	0.0081	3.2419	0.34
30	0.0000	0.0000	9.39
31	-0.0081	-3.2419	0.30
32	10.3176	4129.4133	0.02

^{1}H NMR Spectrum of Compound 5a



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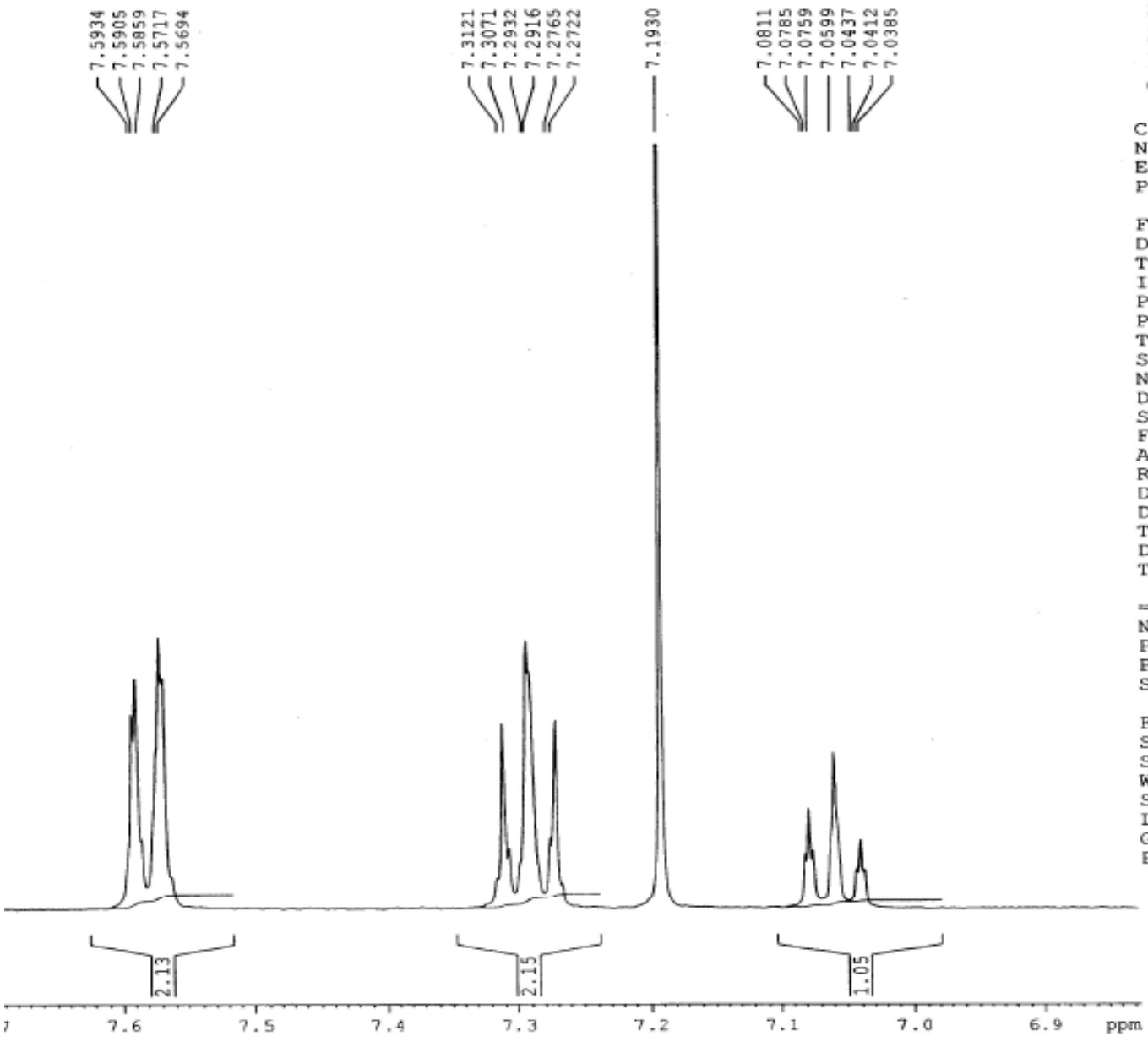
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

Current Data Parameters	
NAME	Feb09-2009
EXPNO	280
PROCNO	1
F2 - Acquisition Paramete	
Date_	20090210
Time	10.32
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12019.230 H
FIDRES	0.183399 H
AQ	2.7263477 s
RG	512
DW	41.600 u
DE	6.00 u
TE	295.2 K
D1	1.00000000 s
TD0	1
======== CHANNEL f1 ======	
NUC1	1H
P1	10.90 u
PL1	-3.00 d
SFO1	400.1324008 M
F2 - Processing parameter	
SI	32768
SF	400.1300365 M
WDW	EM
SSB	0
LB	0.30 H
GB	0
PC	1.00



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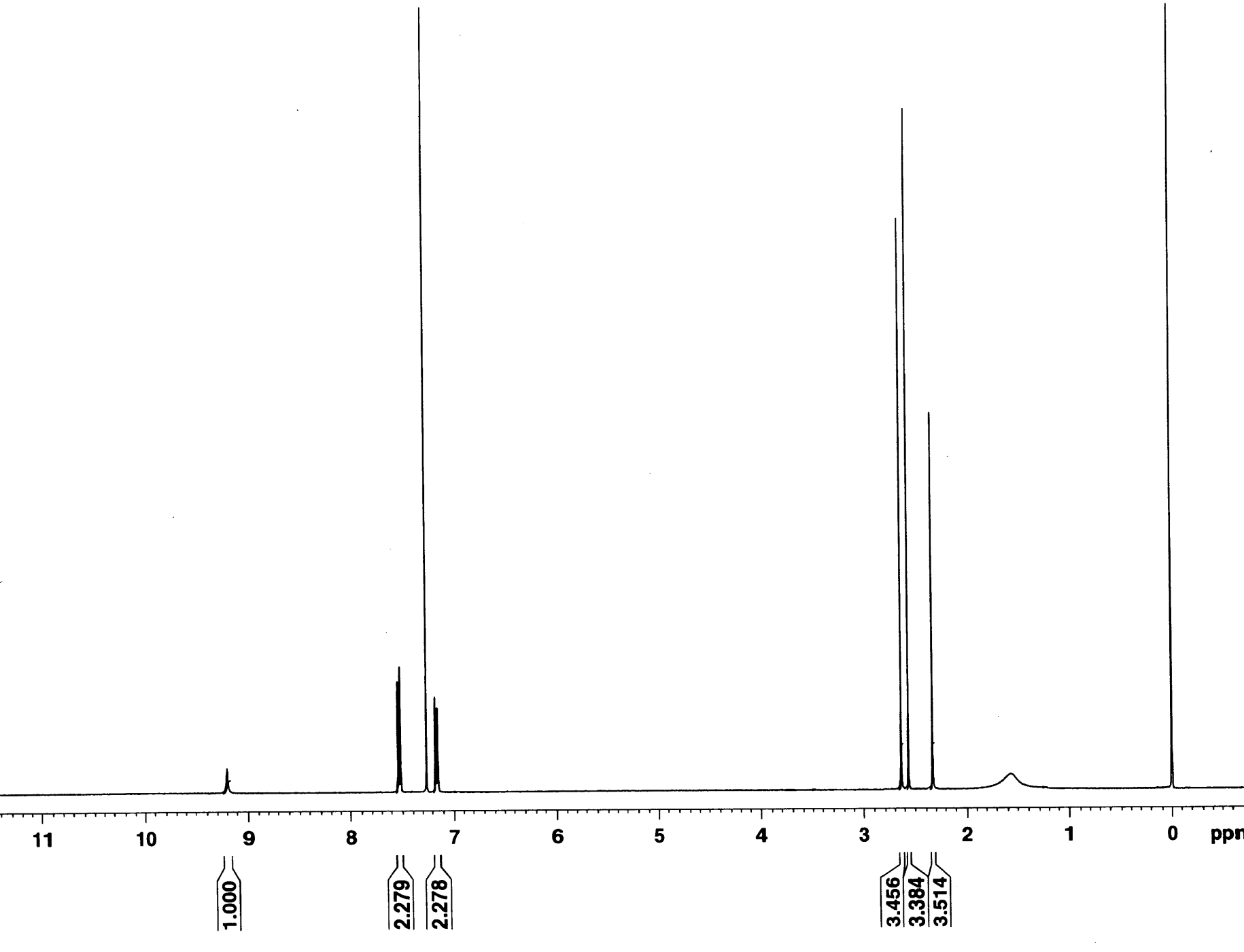
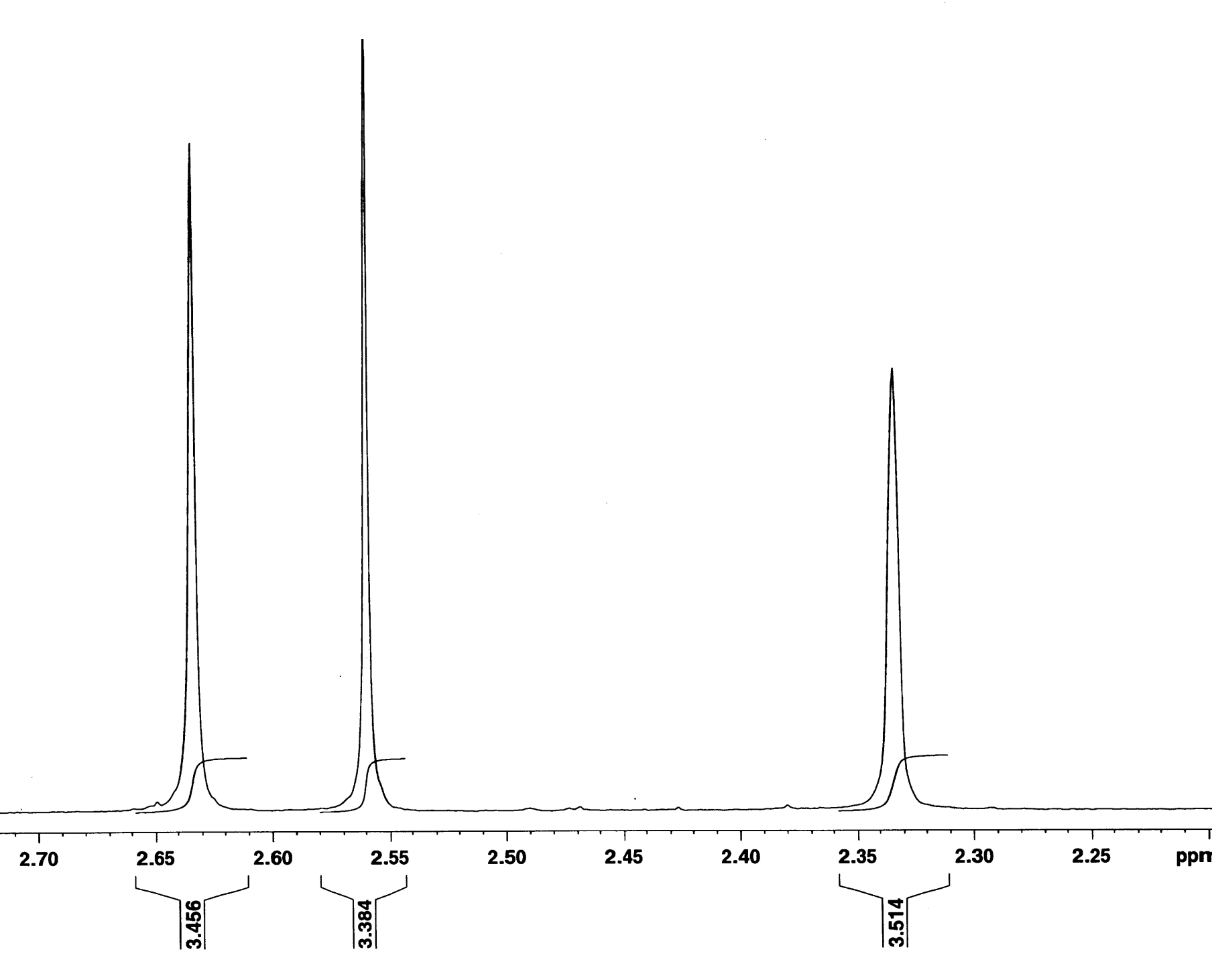
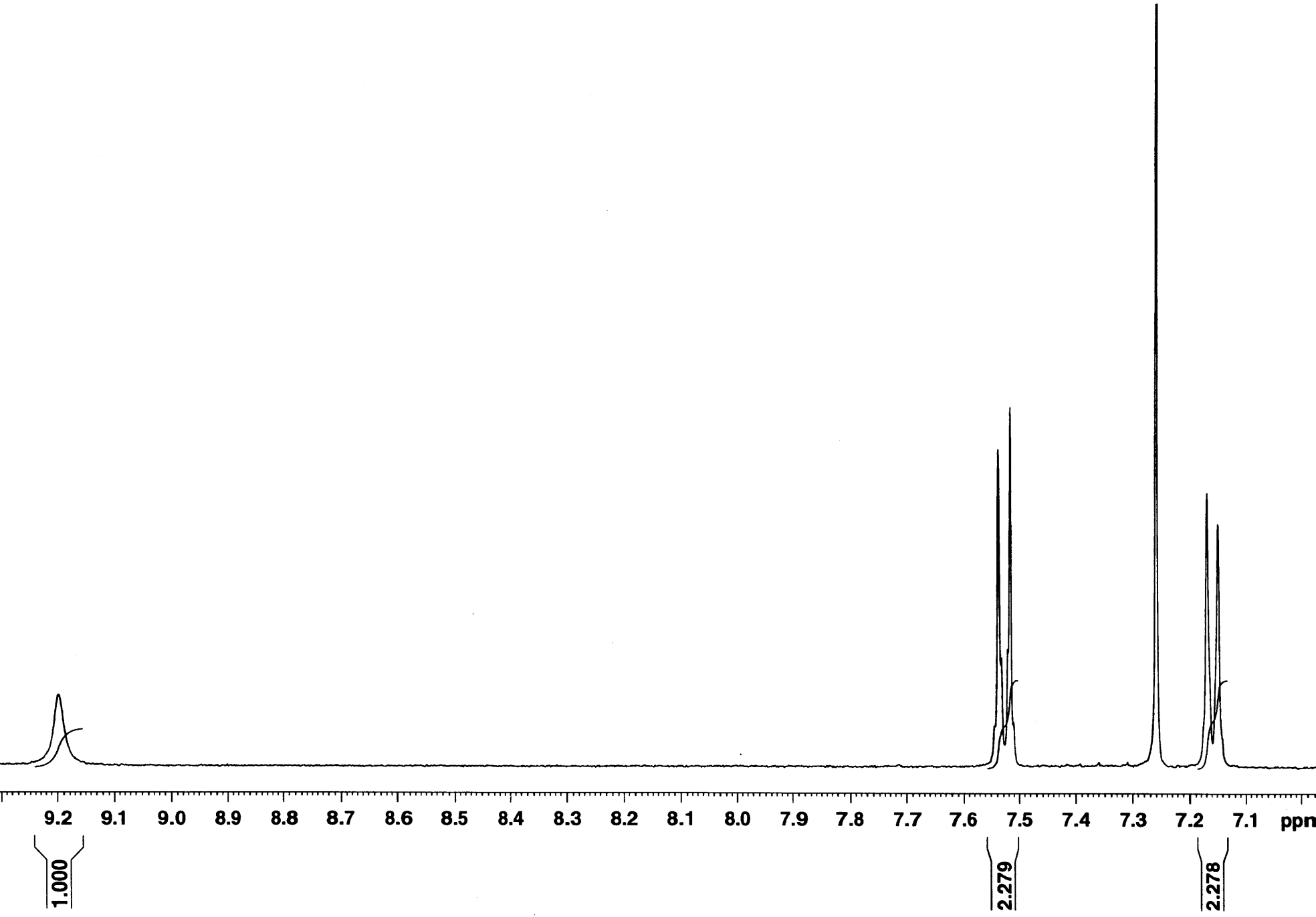
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

Current Data Parameters	
NAME	Feb09-2009
EXPNO	280
PROCNO	1
F2 - Acquisition Paramete	
Date_	20090210
Time	10.32
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDC13
NS	16
DS	2
SWH	12019.230 H
FIDRES	0.183399 H
AQ	2.7263477 s
RG	512
DW	41.600 u
DE	6.00 u
TE	295.2 K
D1	1.00000000 s
TD0	1
======== CHANNEL f1 =====	
NUC1	1H
P1	10.90 u
PL1	-3.00 d
SFO1	400.1324008 M
F2 - Processing parameter	
SI	32768
SF	400.1300365 M
WDW	EM
SSB	0
LB	0.30 H
GB	0
PC	1.00

^{1}H NMR Spectrum of compound 5b

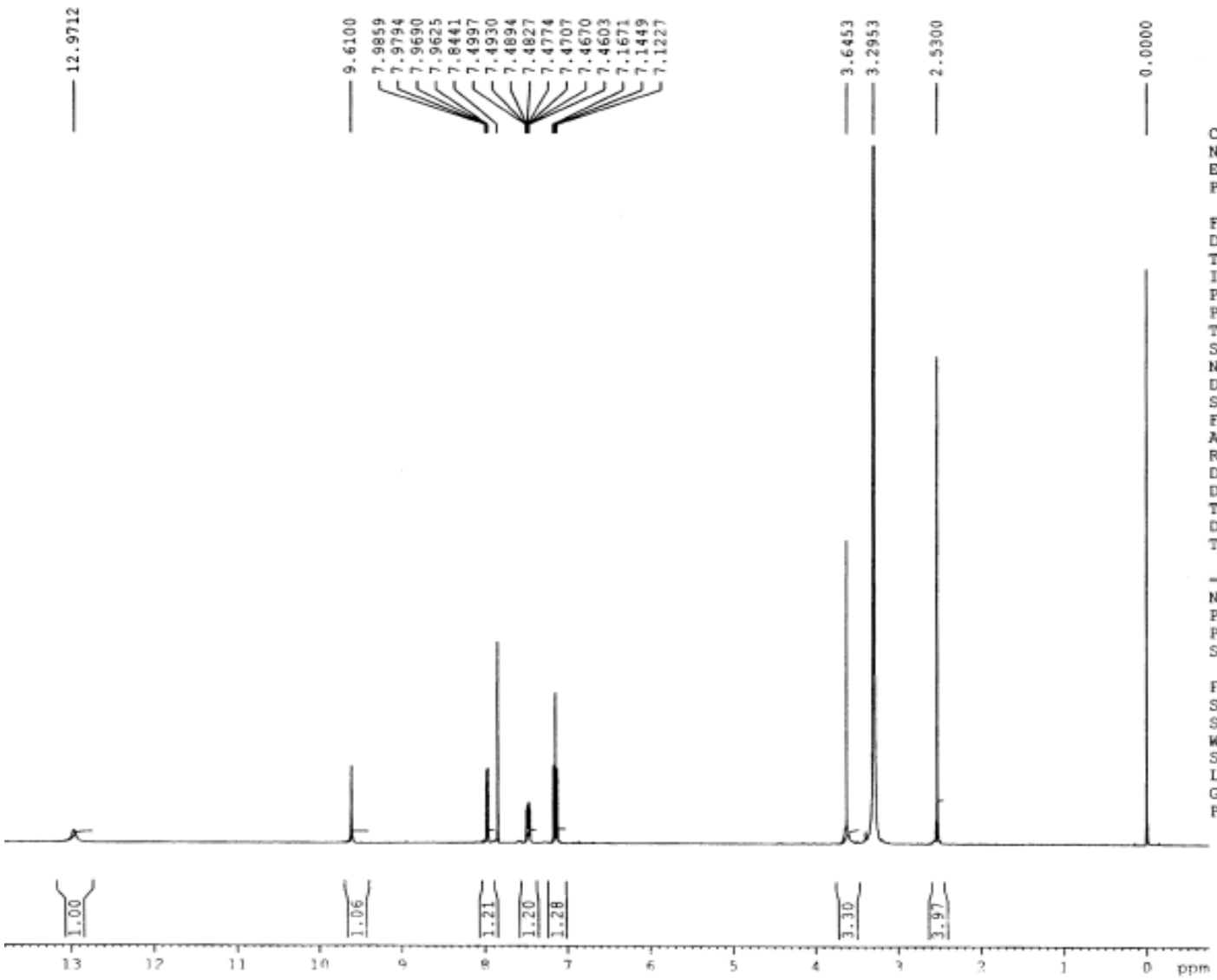



2.70
2.65
2.60
2.55
2.50
2.45
2.40
2.35
2.30
2.25
ppm
3.456
3.384
3.514


9.2
9.1
9.0
8.9
8.8
8.7
8.6
8.5
8.4
8.3
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
7.1
ppn
1.000
2.279
2.278

Peak	ν(F1) [ppm]	ν(F1) [Hz]	Intensity [rel]
1	9.1976	3681.1556	0.30
2	7.5376	3016.7738	1.37
3	7.5330	3014.9327	0.47
4	7.5212	3010.2100	0.51
5	7.5166	3008.3690	1.54
6	7.5105	3005.9276	0.19
7	7.2596	2905.5099	11.23
8	7.1686	2869.0889	1.17
9	7.1482	2860.9242	1.05
10	3.7326	1493.8986	0.17
11	3.7151	1486.8945	0.17
12	3.4910	1397.2030	1.14
13	2.6337	1054.0858	7.00
14	2.5594	1024.3487	8.64
15	2.3340	934.1369	4.63
16	1.5726	629.4017	0.19
17	1.2624	505.2504	0.22
18	1.2449	498.2464	0.39
19	1.2274	491.2423	0.19
20	0.0082	3.2819	0.49
21	0.0001	0.0400	15.00
22	-0.0080	-3.2018	0.43

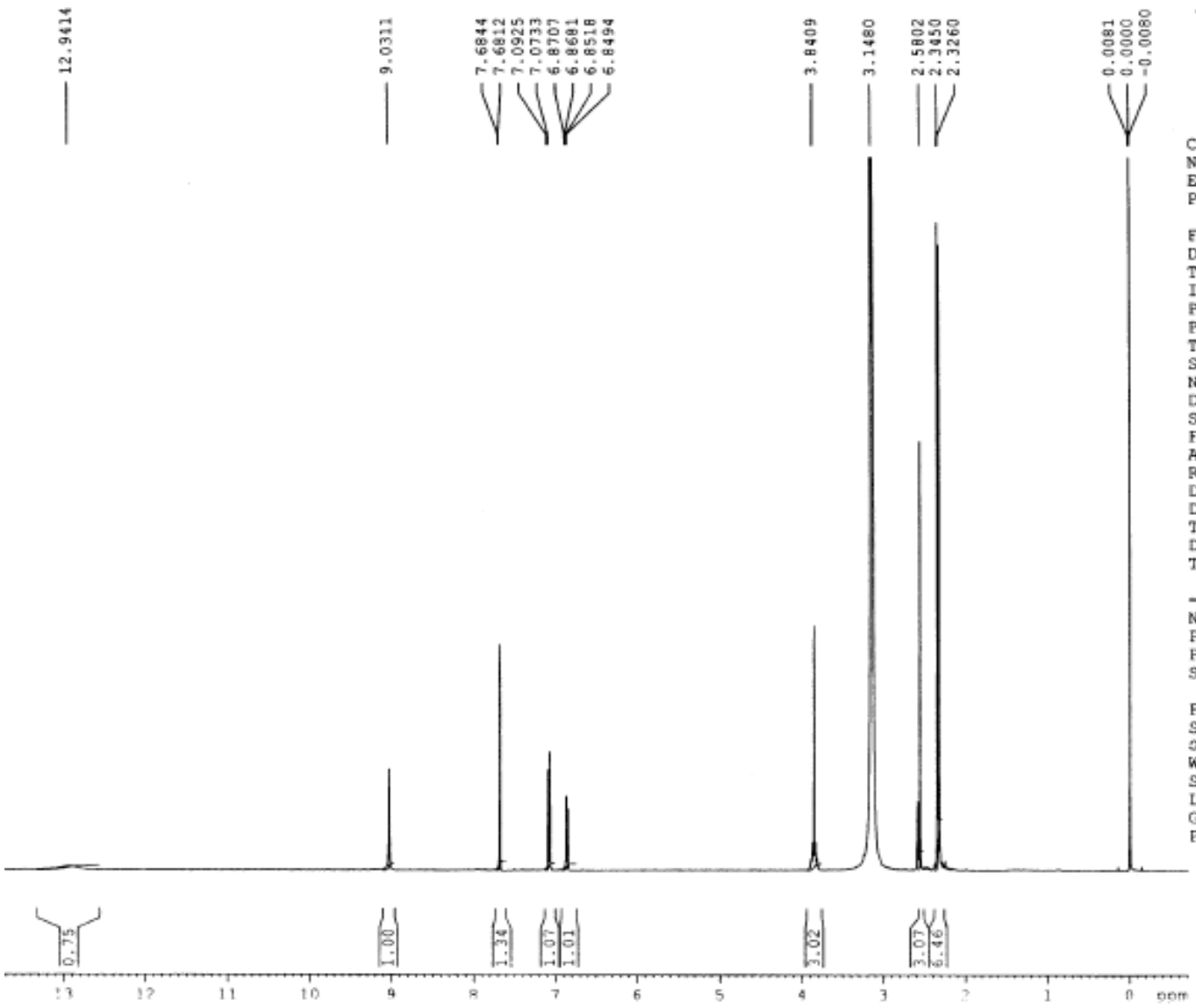
^{1}H NMR Spectrum of compound 6j



BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

Current Data Parameters	
NAME	Jan24-2009
EXPNO	390
PROCNO	1
F2 - Acquisition Paramete	
Date_	20090124
Time	23.50
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	DMSO
NS	16
DS	2
SWH	12019.230 H
FIDRES	0.183399 H
AQ	2.7263477 s
RG	256
DW	41.600 u
DE	6.00 u
TE	295.6 K
D1	1.00000000 s
TD0	1
======== CHANNEL f1 =====	
NUC1	1H
P1	10.90 u
PL1	-3.00 d
SFO1	400.1324008 M
F2 - Processing parameter	
SI	32768
SF	400.1299722 M
WDW	EM
SSB	0
LB	0.30 H
GB	0
PC	1.00

^{1}H NMR Spectrum of compound 6m



BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

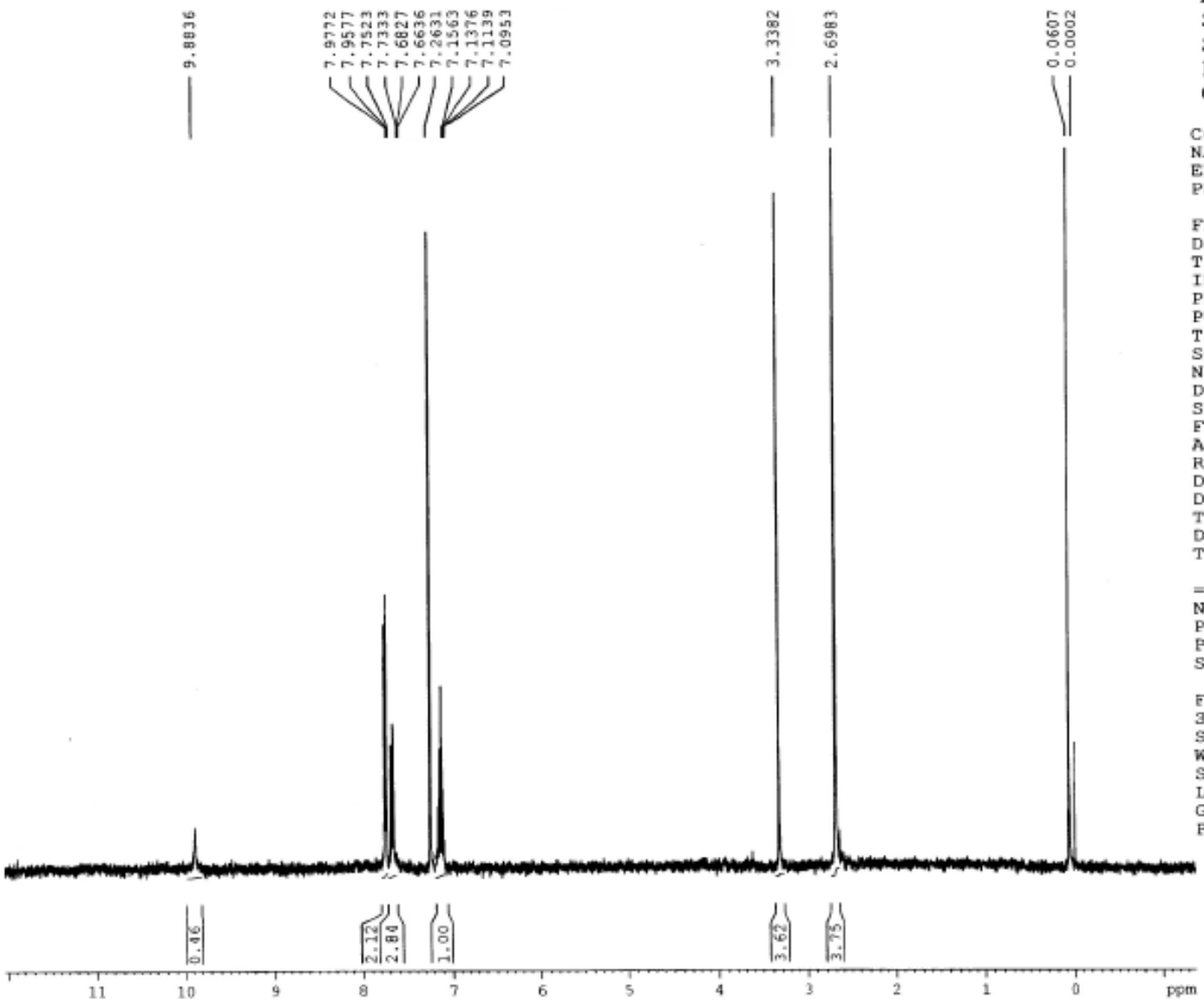
Current Data Parameters	
NAME	Jan24-2009
EXPNO	380
PROCNO	1

F2 - Acquisition Parameters		
Date_	20090124	
Time	23.43	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zg30	
TD	65536	
SOLVENT	DMSO	
NS	16	
DS	2	
SWH	12019.230	Hz
FIDRES	0.183399	Hz
AQ	2.7263477	sec
RG	362	
DW	41.600	usec
DE	6.00	usec
TE	295.6	K
D1	1.00000000	sec
TD0	1	

-------- CHANNEL f1 --------		
NUC1	1H	
P1	10.90	usec
PL1	-3.00	dB
SFO1	400.1324008	MHz

F2 - Processing parameters		
SI	32768	
SF	400.1299006	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	

^{1}H NMR Spectrum of compound 7a



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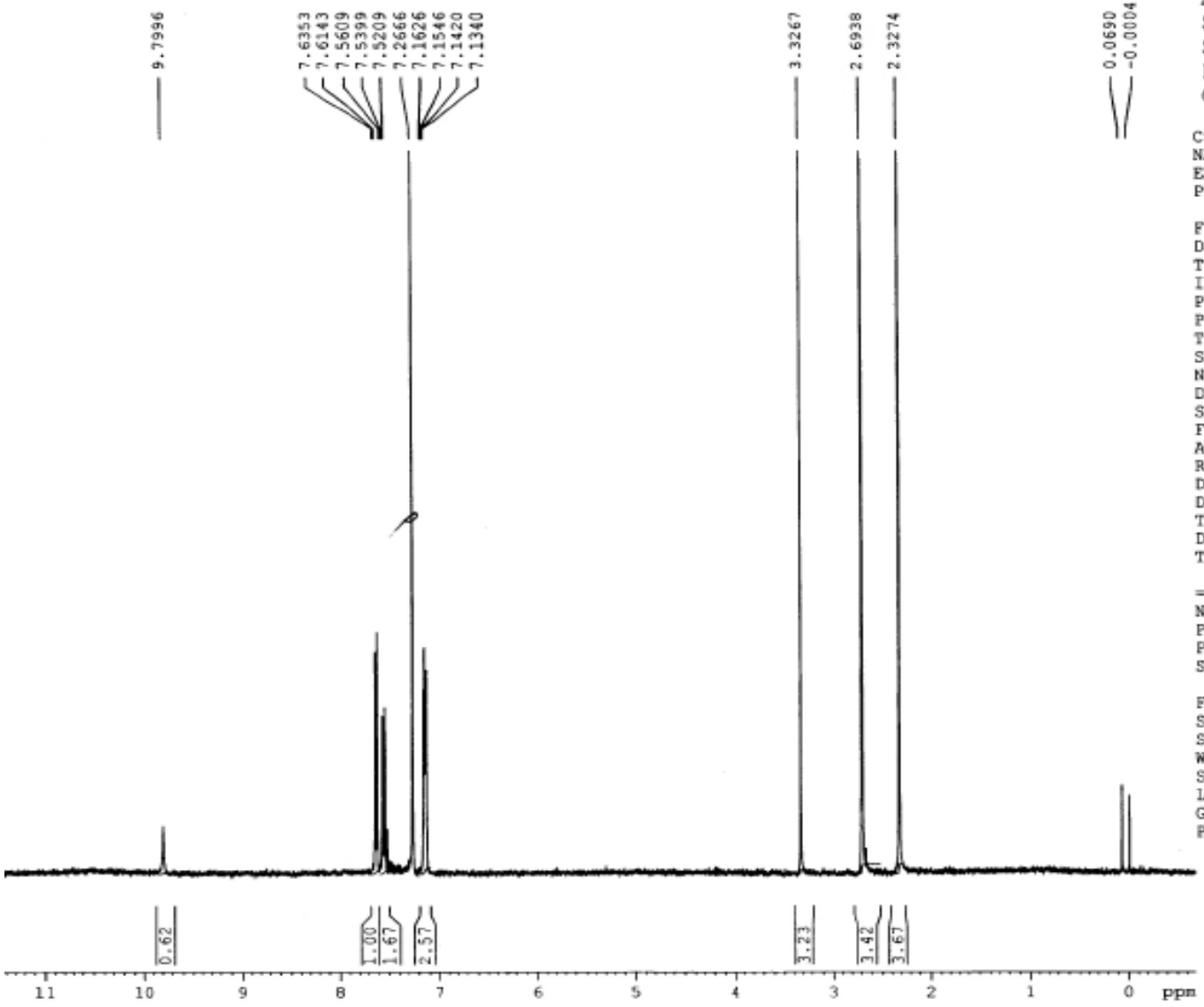
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

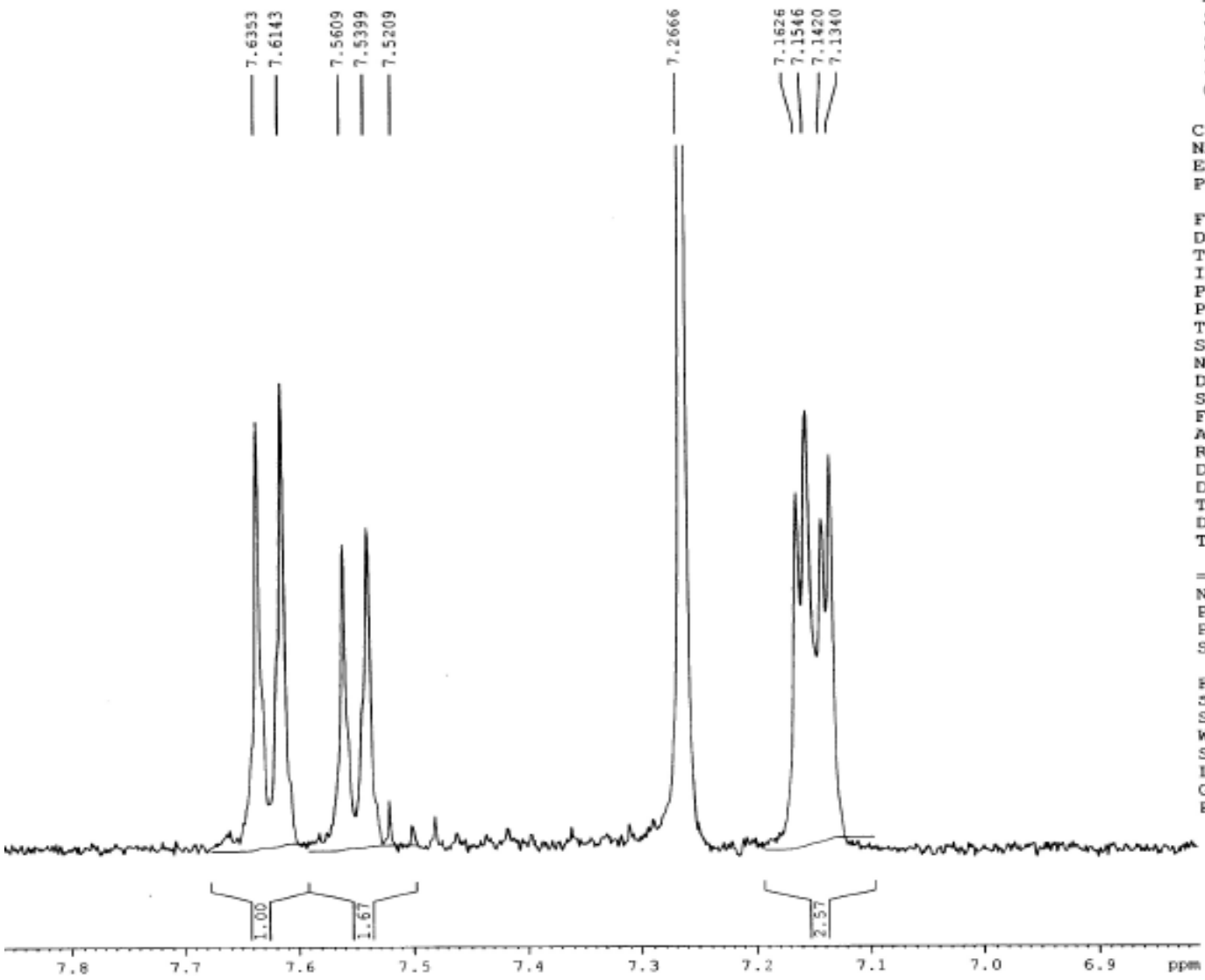
Current Data Parameters	
NAME	Feb09-2009
EXPNO	290
PROCNO	1
F2 - Acquisition Paramete	
Date_	20090210
Time	10.44
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12019.230 H
FIDRES	0.183399 H
AQ	2.7263477 s
RG	512
DW	41.600 u
DE	6.00 u
TE	295.2 K
D1	1.00000000 s
TD0	1
======== CHANNEL f1 =====	
NUC1	1H
P1	10.90 u
PL1	-3.00 d
SFO1	400.1324008 M
F2 - Processing parameter	
SI	32760
SF	400.1300084 M
WDW	EM
SSB	0
LB	0.30 H
GB	0
PC	1.00

^{1}H NMR Spectrum of compound 7b



BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

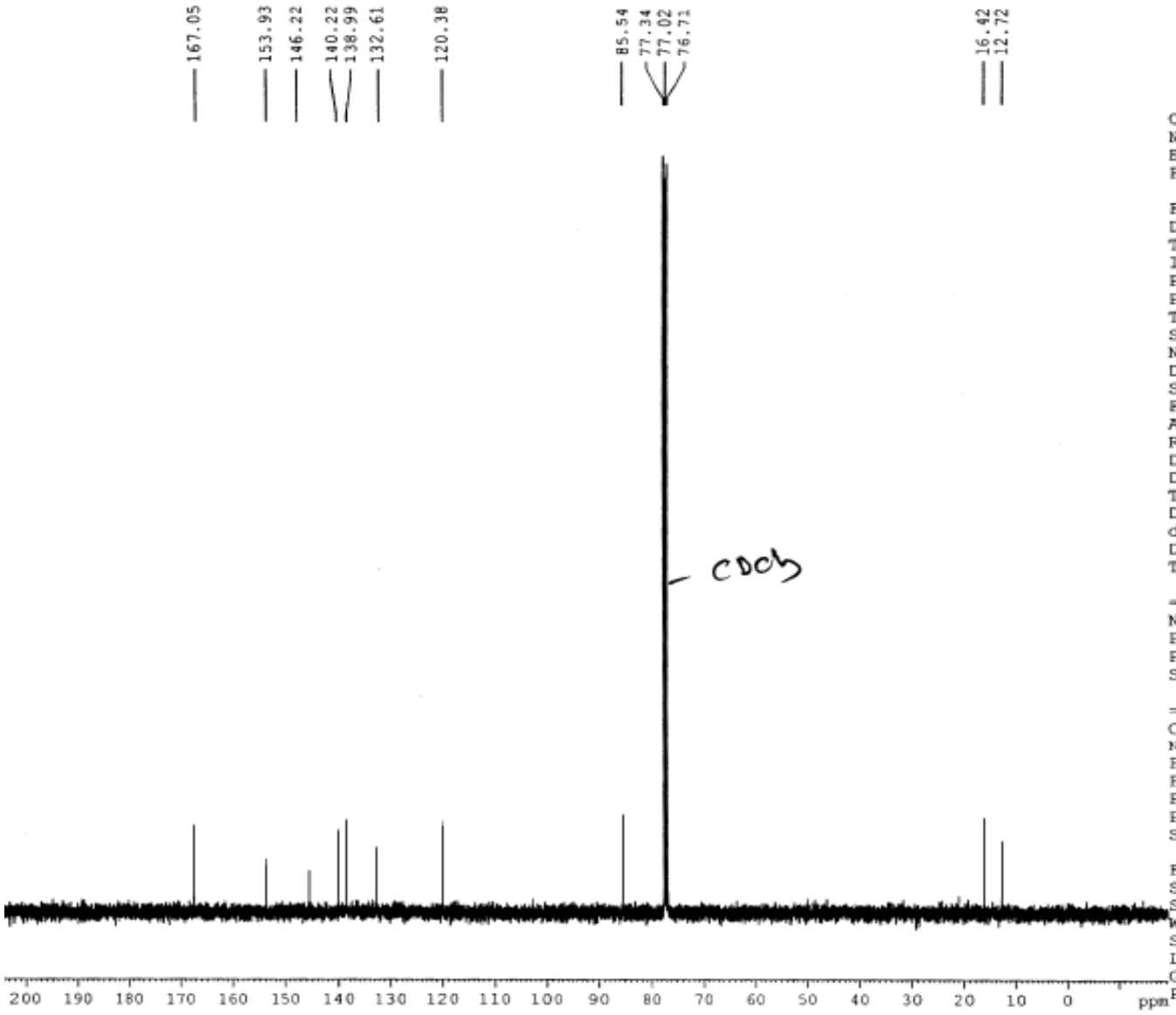
Current Data Parameters		
NAME	Feb09-2009	
EXPNO	300	
PROCNO	1	
F2 - Acquisition Parameters		
Date_	20090210	
Time	11.01	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zg30	
TD	65536	
SOLVENT	CDCl3	
NS	16	
DS	2	
SWH	12019.230	Hz
FIDRES	0.183399	Hz
AQ	2.7263477	sec
RG	575	
DW	41.600	usec
DE	6.00	usec
TE	295.3	K
D1	1.00000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	1H	
P1	10.90	usec
PL1	-3.00	dB
SFO1	400.1324008	MHz
F2 - Processing parameters		
SI	32768	
SF	400.1300087	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	



BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

Current Data Parameters	
NAME	Feb09-2009
EXPNO	300
PROCNO	1
F2 - Acquisition Paramet	
Date_	20090210
Time	11.01
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	12019.230
FIDRES	0.183399
AQ	2.7263477
RG	575
DW	41.600
DE	6.00
TE	295.3
D1	1.00000000
TD0	1
======== CHANNEL f1 ====	
NUC1	1H
P1	10.90
PL1	-3.00
SFO1	400.1324008
F2 - Processing paramete	
SI	32768
SF	400.1300087
WDW	EM
SSB	0
LB	0.30
GB	0
PC	1.00

^{13}C NMR Spectrum of compound 4a



BRUKER
AVANCE II 400 NMR
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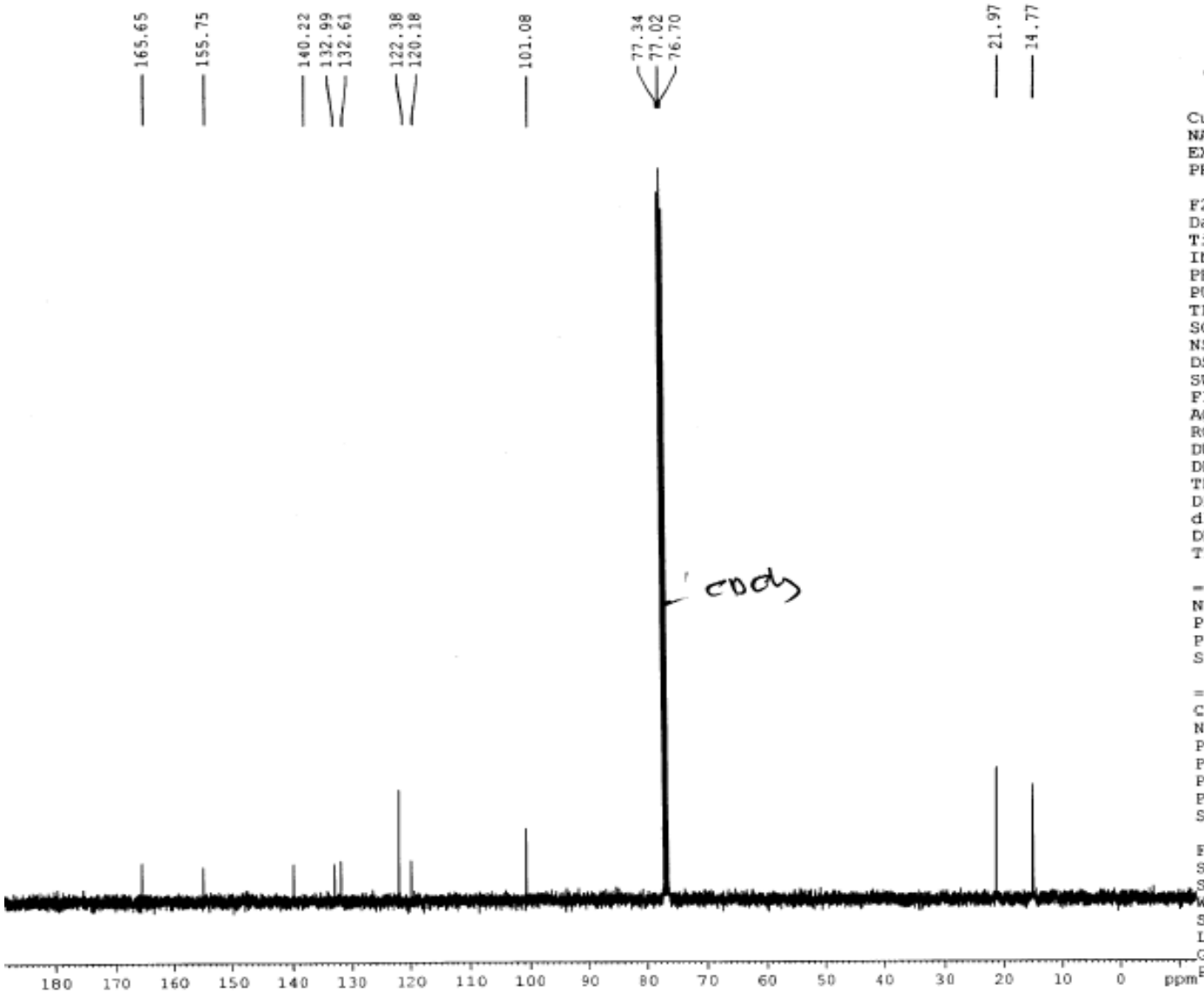
Current Data Parameters	
NAME	Feb09-2009
EXPNO	301
PROCNO	1
F2 - Acquisition Parameter	
Date_	20090210
Time	11.13
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	176
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	1030
DW	20.800 us
DE	6.00 us
TE	296.0 K
D1	2.00000000 sec
d11	0.03000000 sec
DELTA	1.89999998 sec
TDO	1
======== CHANNEL f1 ======	
NUC1	13C
P1	9.60 us
PL1	-2.00 dB
SFO1	100.6228298 MHz
======== CHANNEL f2 ======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 us
PL2	-3.00 dB
PL12	14.31 dB
PL13	18.00 dB
SFO2	400.1316005 MHz
F2 - Processing parameters	
SI	32768
SF	100.6127690 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

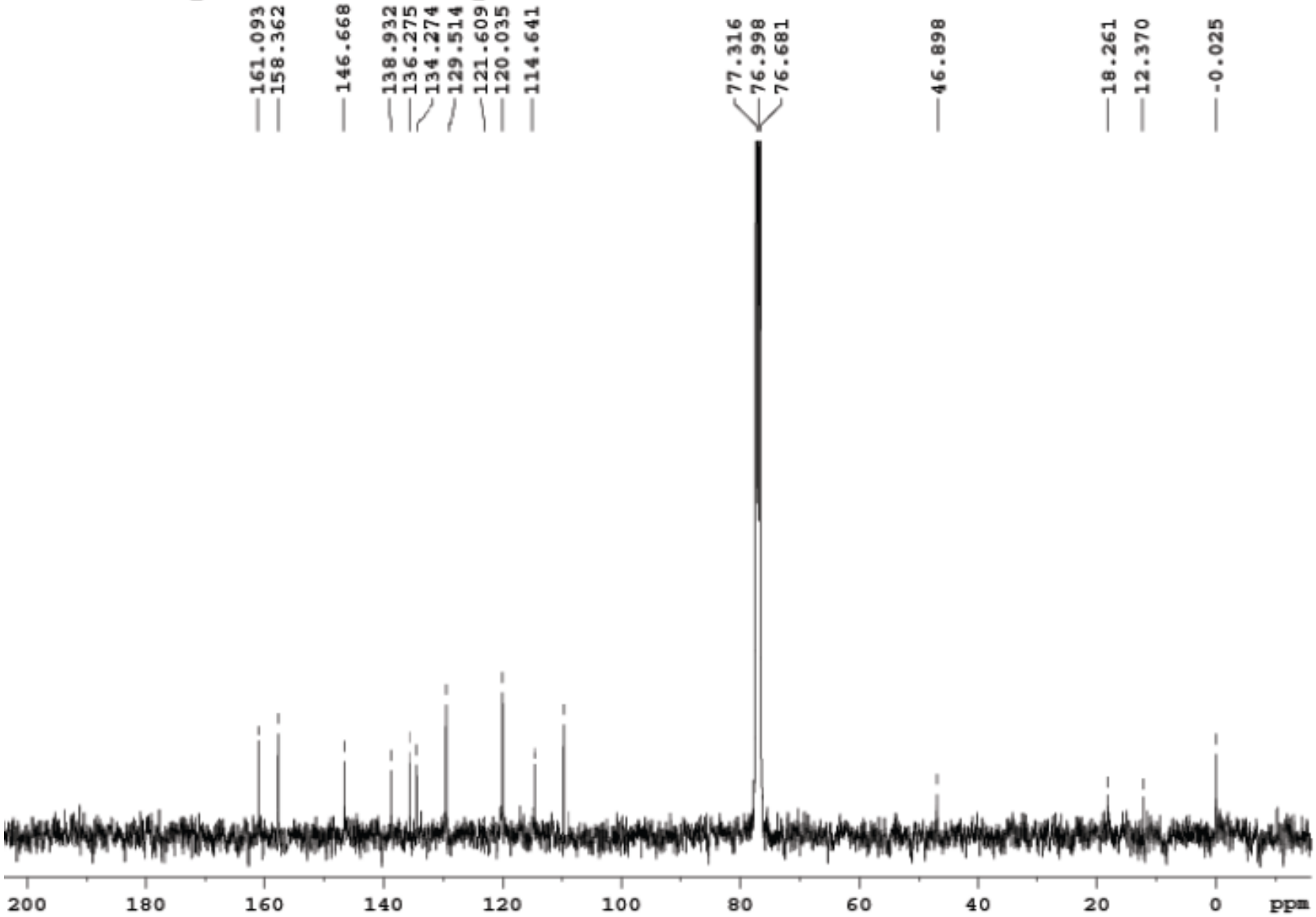
^{13}C NMR Spectrum of compound 5a

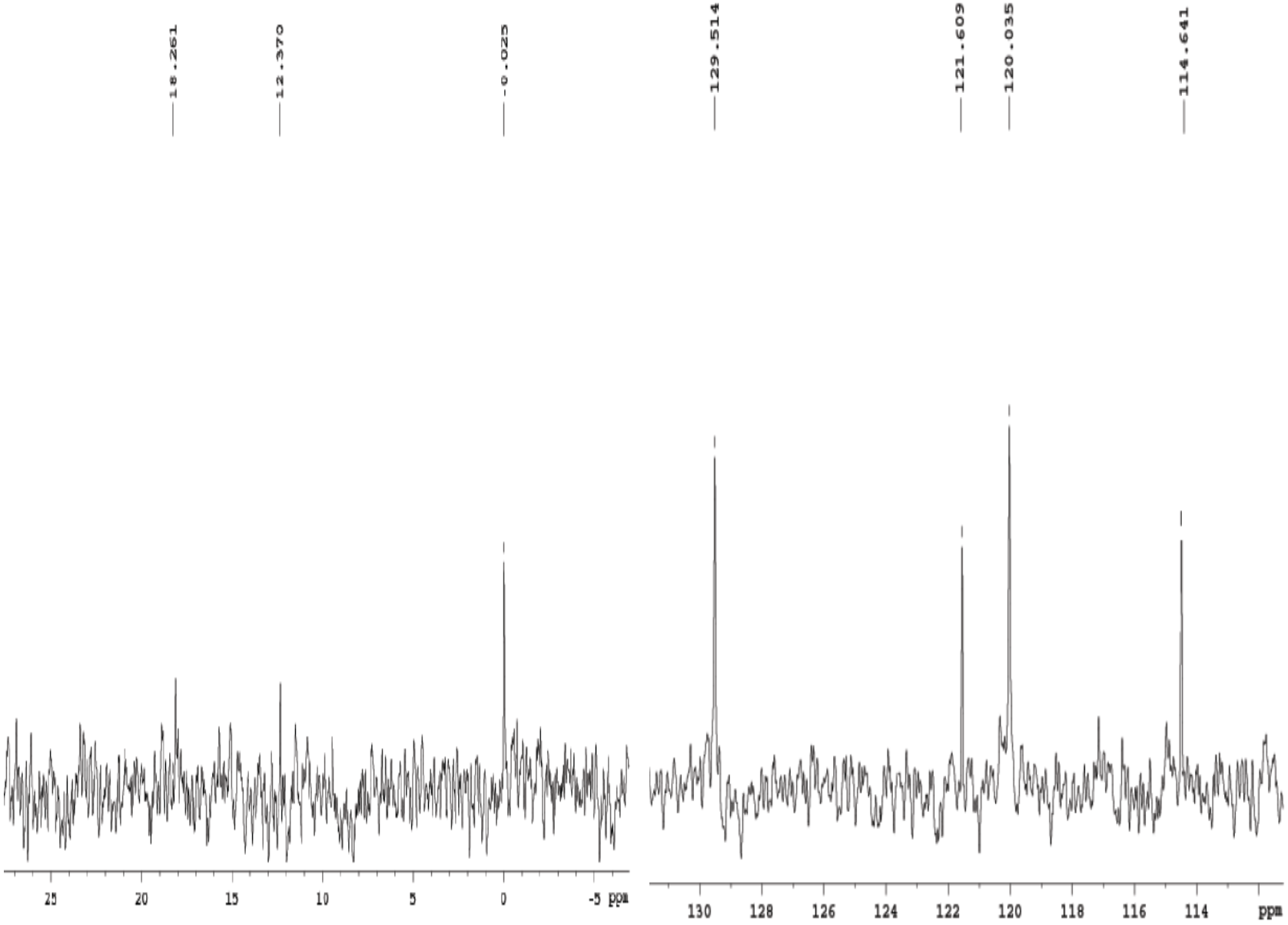


BRUKER
AVANCE II 400 NMR
Spectrometer
SAIF
Panjab University
Chandigarh

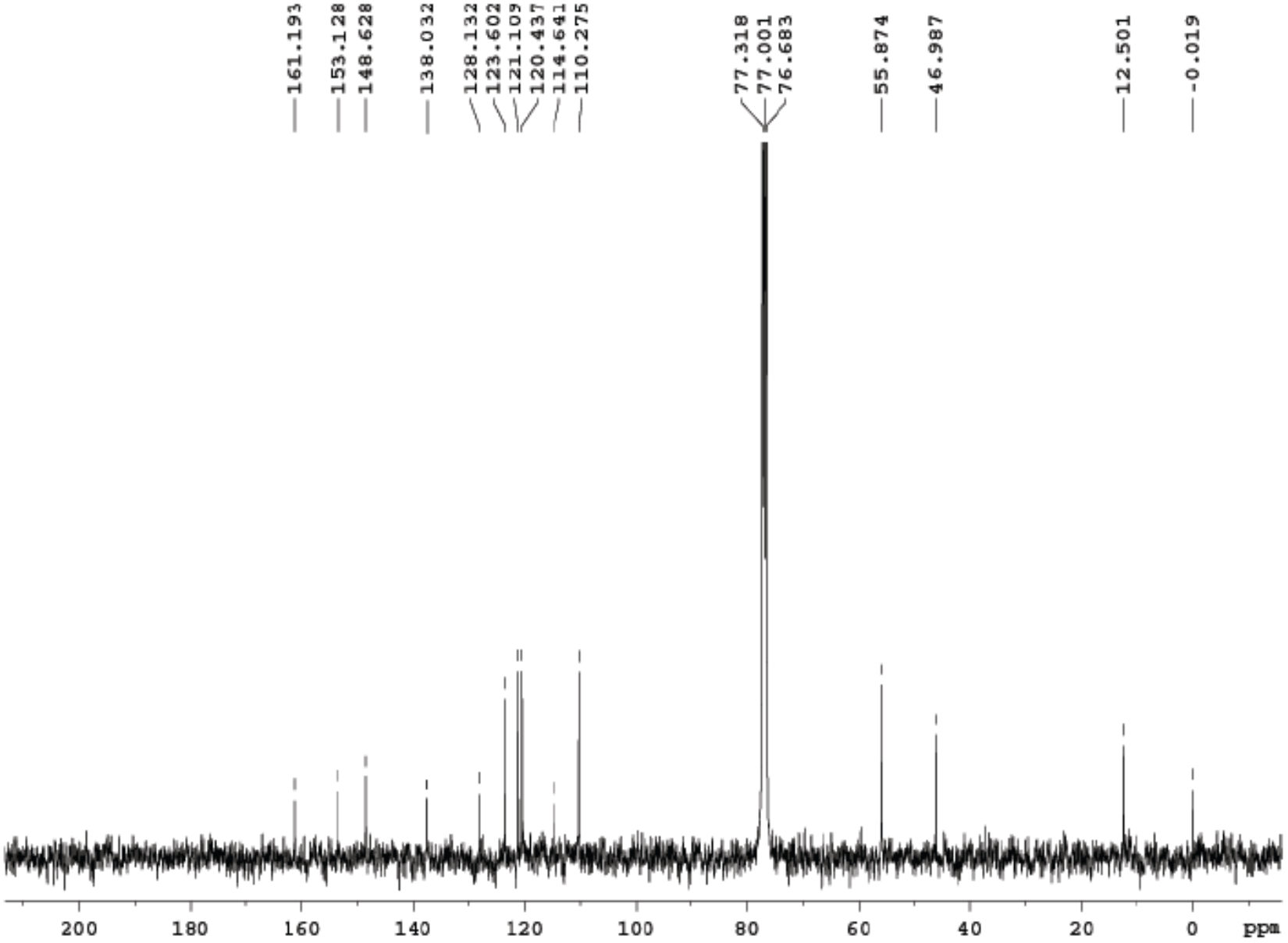
Current Data Parameters	
NAME	Feb09-2009
EXPNO	311
PROCNO	1
F2 - Acquisition Paramete	
Date_	20090210
Time	11.33
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	200
DS	4
SWH	24038.461 H
FIDRES	0.366798 H
AQ	1.3631988 s
RG	1030
DW	20.800 u
DE	6.00 u
TE	296.1 K
D1	2.00000000 s
d11	0.03000000 s
DELTA	1.89999998 s
TDO	1
======== CHANNEL f1 ====	
NUC1	13C
P1	9.60 u
PL1	-2.00 d
SFO1	100.6228298 M
======== CHANNEL f2 ====	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 u
PL2	-3.00 d
PL12	14.31 d
PL13	18.00 d
SFO2	400.1316005 M
F2 - Processing paramete	
SI	32768
SF	100.6127690 M
WDW	EM
SSB	0
LB	1.00 H
GB	0
PC	1.40

^{13}C NMR Spectrum of compound 6b



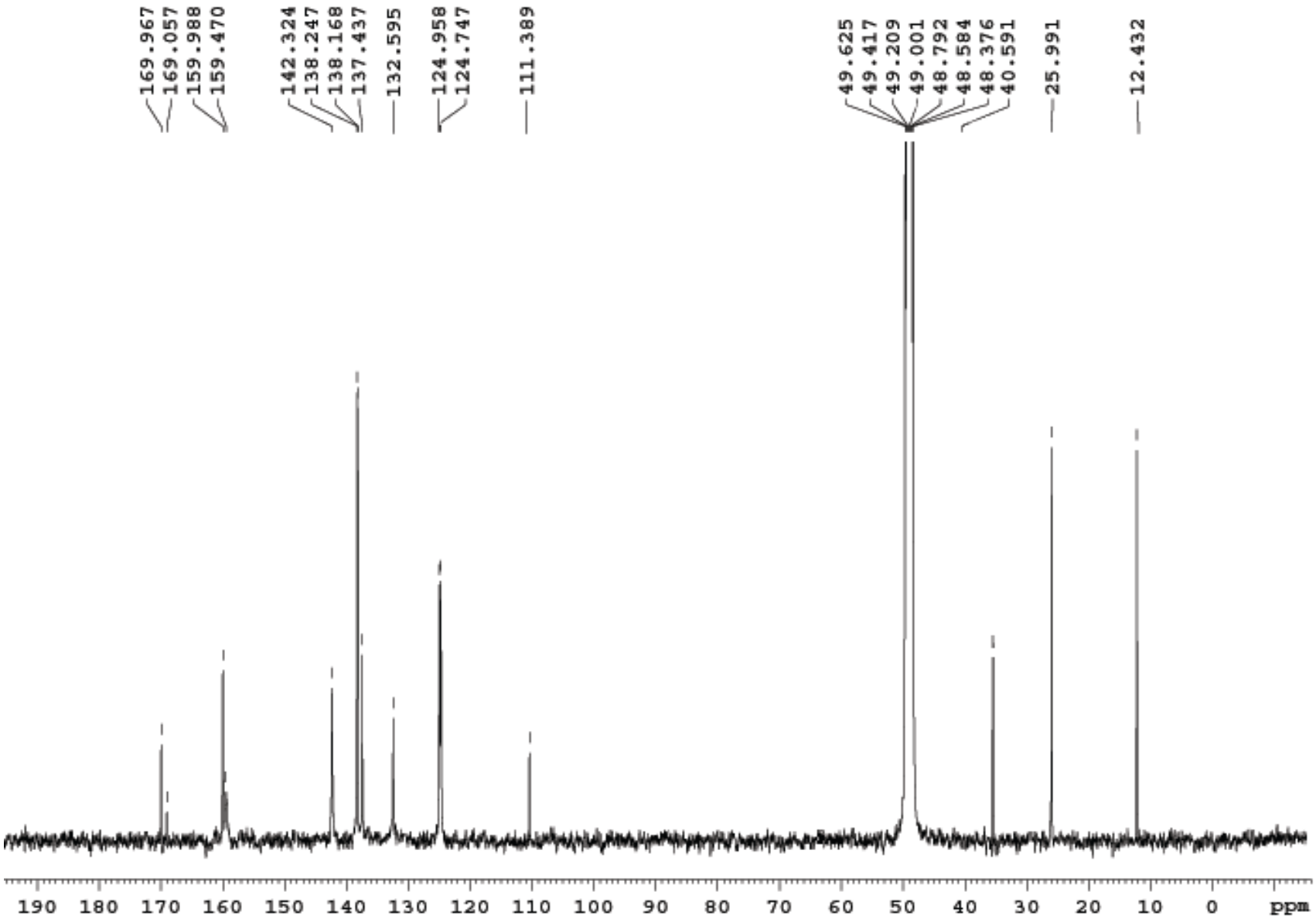

18.261
12.370
-0.025
129.514
121.609
120.035
114.641
25
20
15
10
5
0
-5 ppm
130
128
126
124
122
120
118
116
114
ppm

^{13}C NMR Spectrum of compound 6e

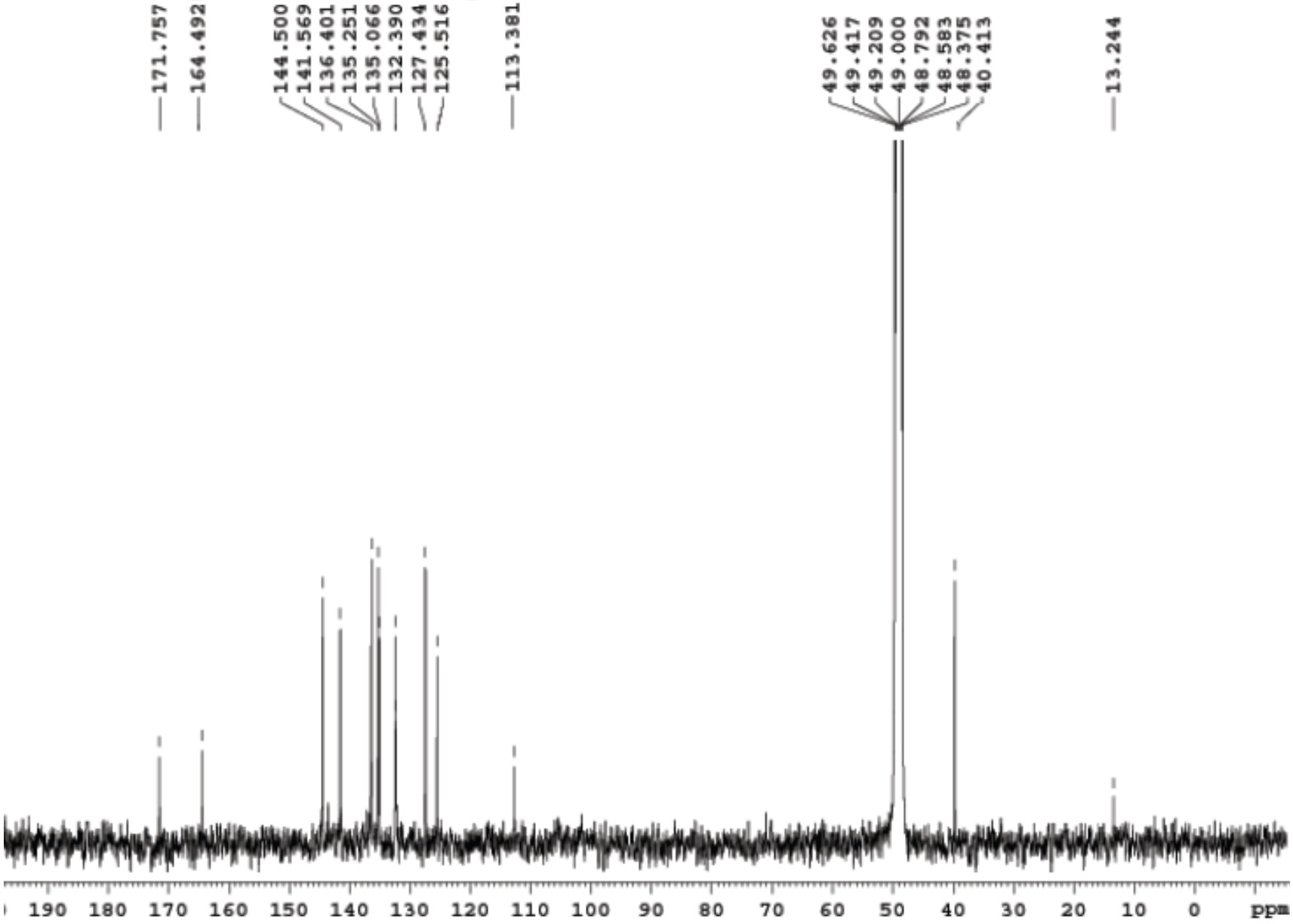


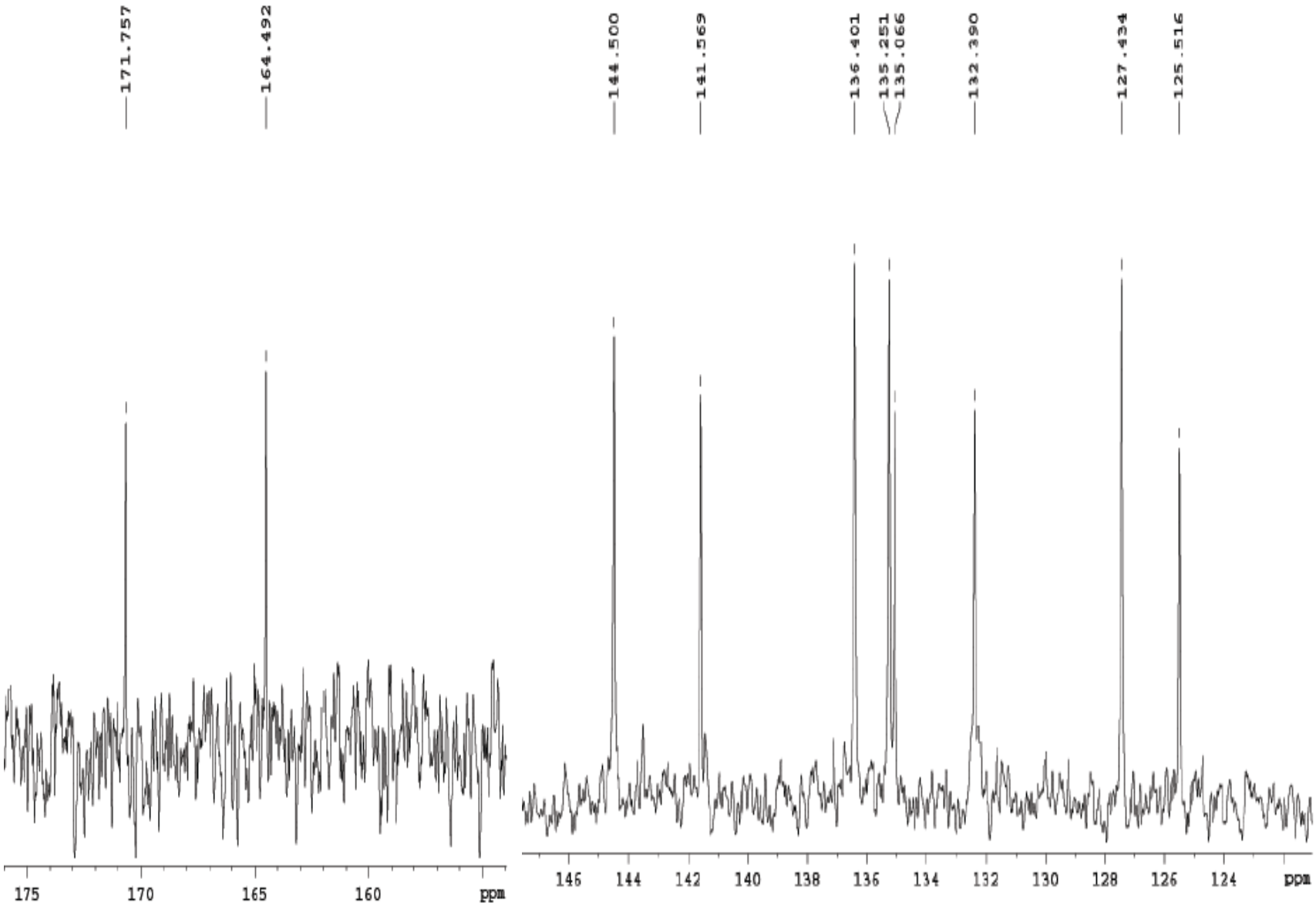
MS-C
161.193
153.128
148.628
138.032
128.132
123.602
121.109
120.437
114.641
110.275
55.874
46.987
12.501
-0.019
160
155
150
145
140
135
130
125
120
115
110
105
ppm
60
55
50
45
40
35
30
25
20
15
10
5
0
ppm

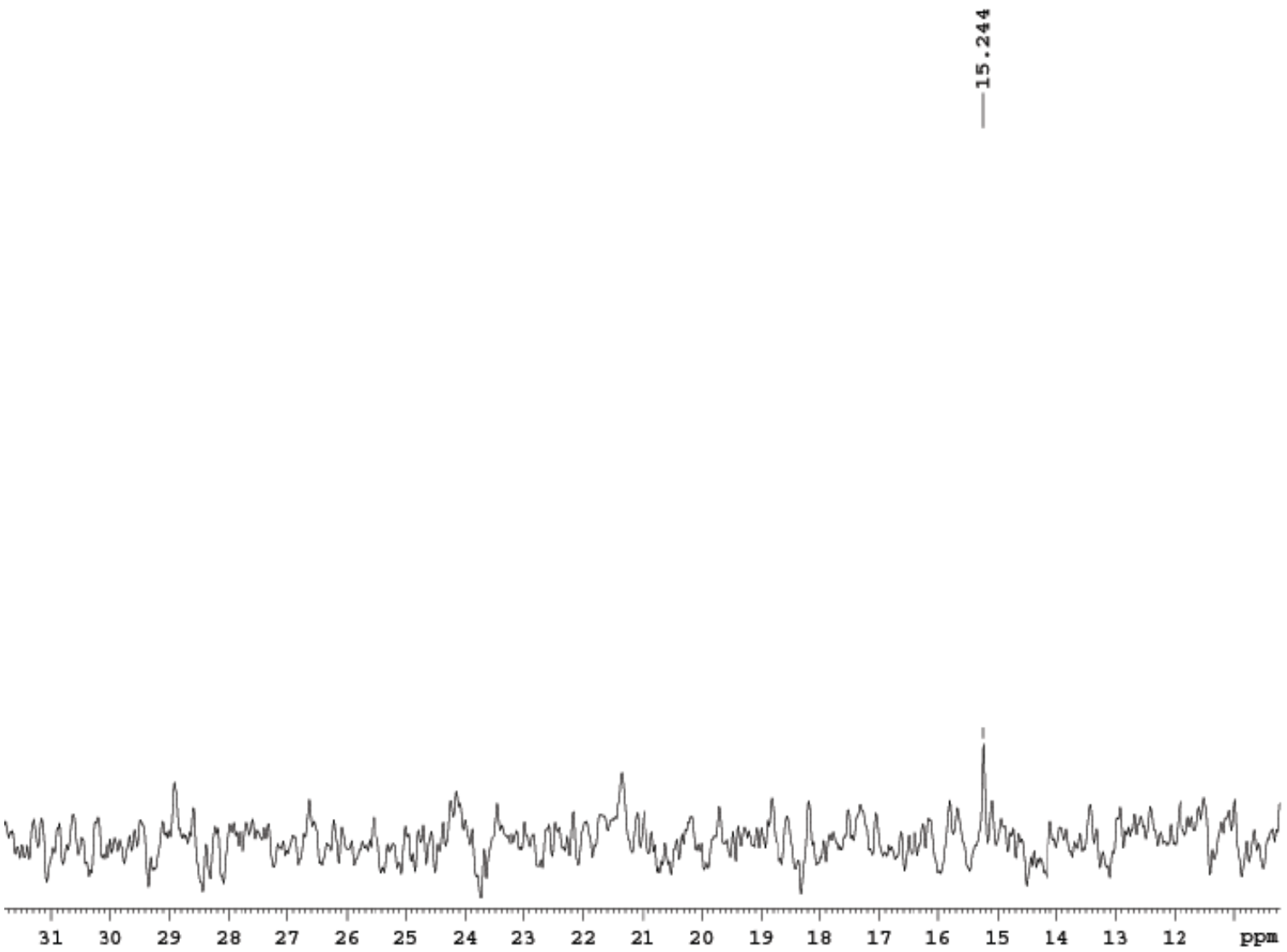
^{13}C NMR Spectrum of compound 7b



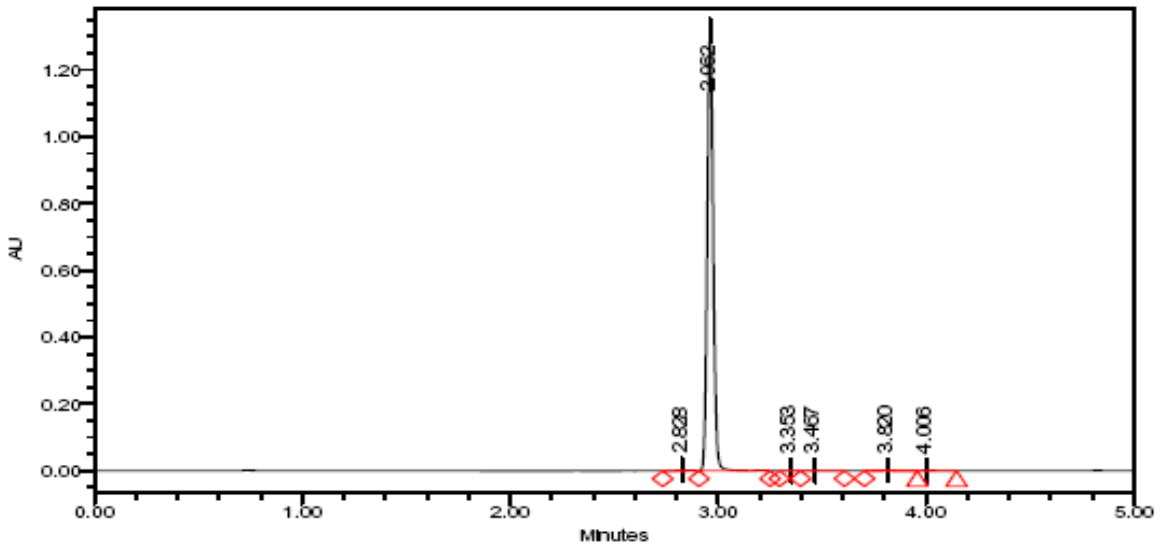
^{13}C NMR Spectrum of compound 7i




171.757
164.492
144.500
141.569
136.401
135.251
135.066
132.390
127.434
125.516
175
170
165
160
ppm
146
144
142
140
138
136
134
132
130
128
126
124
ppm

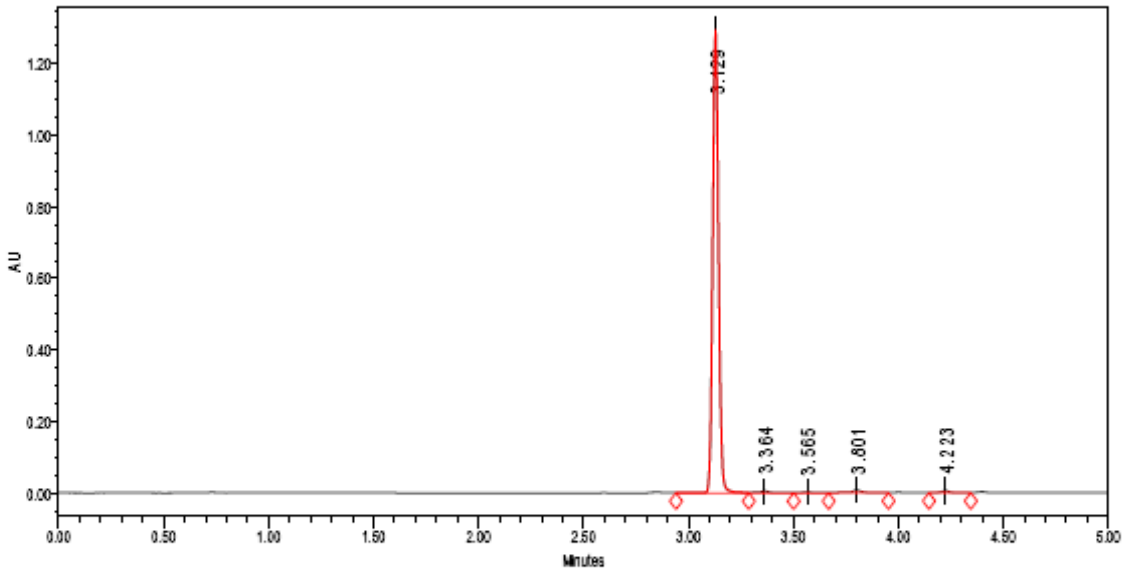

15.244
31
30
29
28
27
26
25
24
23
22
21
20
19
18
17
16
15
14
13
12
ppm

UPLC Purity of compound 6a



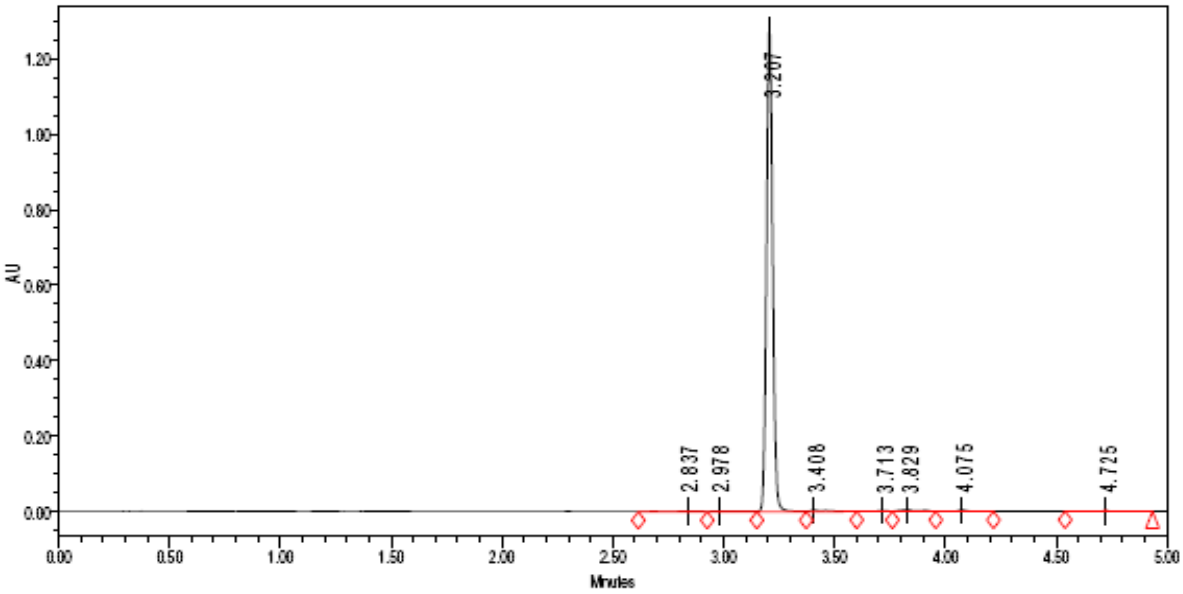
	Name	Retention Time	Area	% Area	Height
1		2.828	10982	0.41	1867
2		2.962	2628764	98.92	1318353
3		3.353	2527	0.10	614
4		3.467	4445	0.17	701
5		3.820	7621	0.29	1108
6		4.006	3109	0.12	761

UPLC Purity of compound 6c



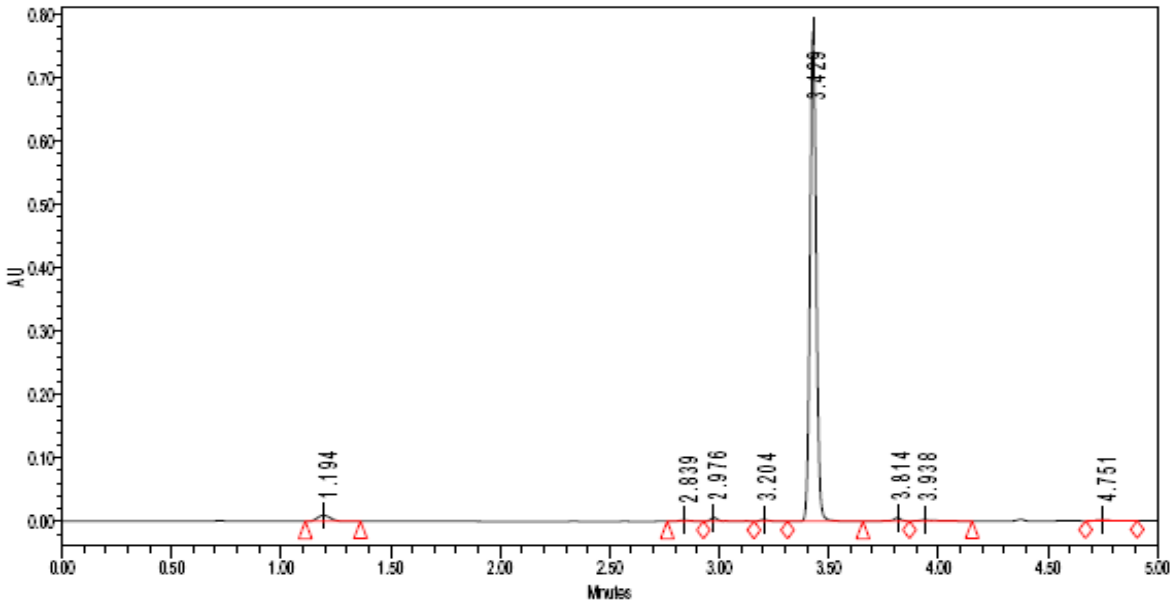
	Name	Retention Time	Area	% Area	Height
1		3.129	2509476	97.16	1295491
2		3.364	21663	0.84	5459
3		3.565	8321	0.32	2037
4		3.801	27616	1.07	7608
5		4.223	15761	0.61	5816

UPLC Purity of compound 6e



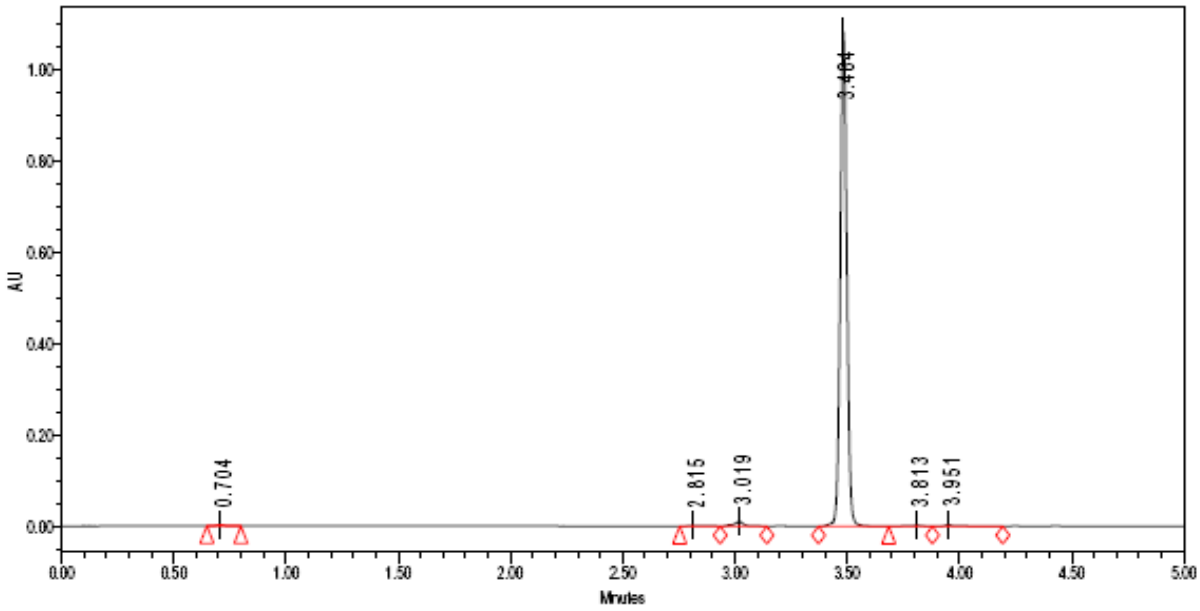
	Name	Retention Time	Area	% Area	Height
1		2.837	11029	0.43	1605
2		2.978	7921	0.31	1138
3		3.207	2470828	97.06	1275692
4		3.408	21462	0.83	3829
5		3.713	10806	0.42	2467
6		3.829	25792	1.00	3917
7		4.075	16754	0.65	3861
8		4.725	7620	0.30	921

UPLC Purity of compound 6g



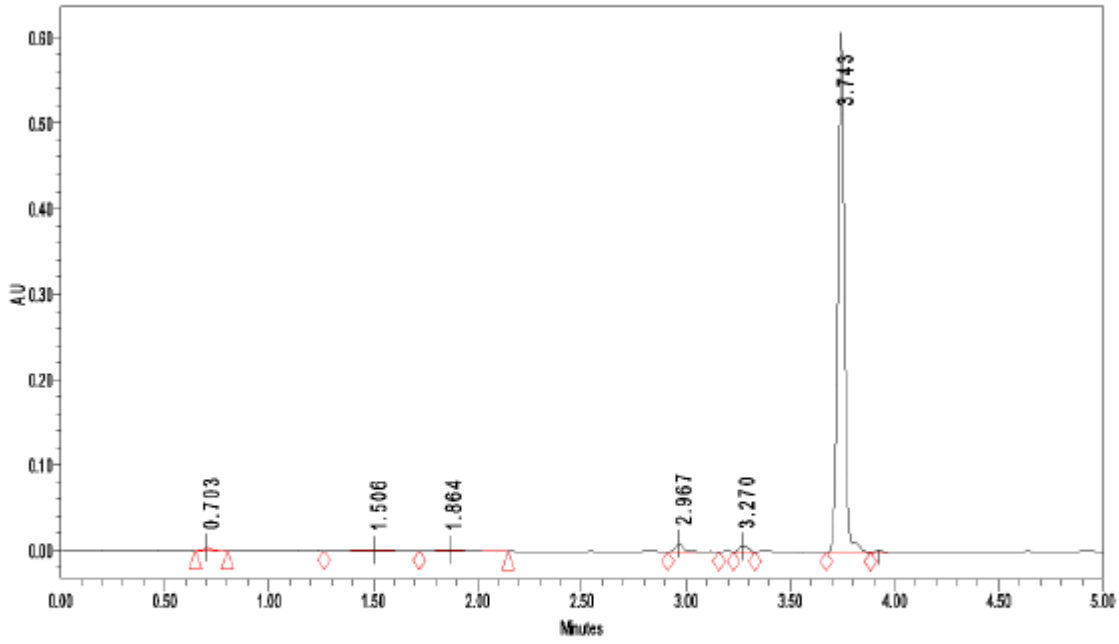
	Name	Retention Time	Area	% Area	Height
1		1.194	37676	2.32	9217
2		2.839	6686	0.41	1542
3		2.976	16516	1.02	6036
4		3.204	8066	0.50	2703
5		3.429	1525145	95.75	773238
6		3.814	14248	0.88	5257
7		3.938	11661	0.72	2339
8		4.751	6879	0.42	1252

UPLC Purity of compound 6i



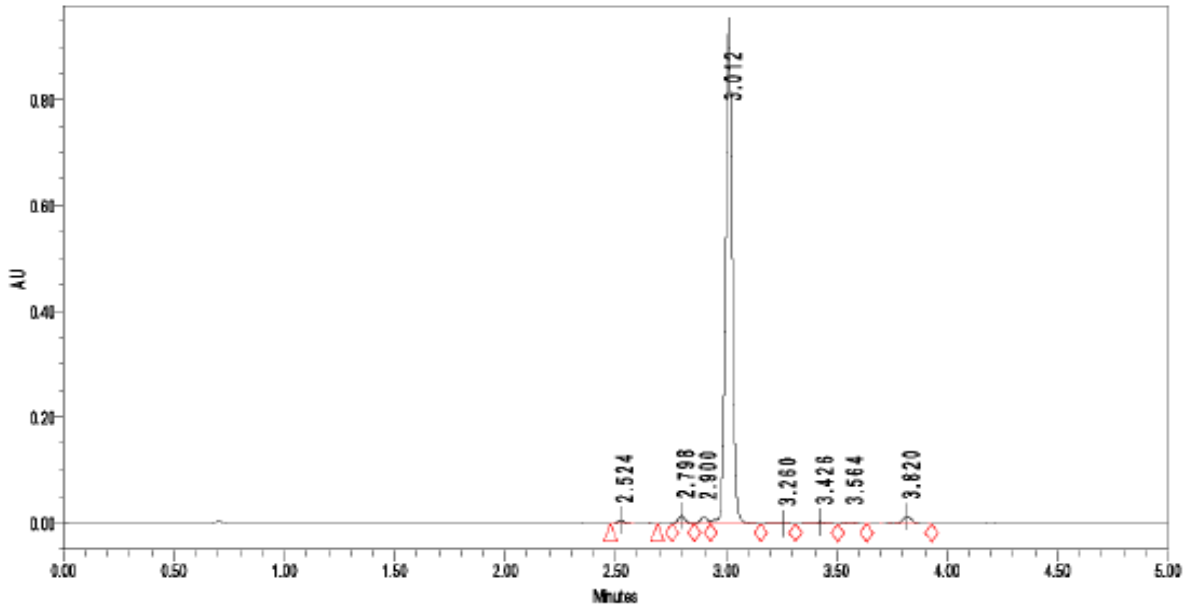
	Name	Retention Time	Area	% Area	Height
1		0.704	4834	0.21	1798
2		2.815	8076	0.36	1390
3		3.019	33664	1.48	10297
4		3.484	2206538	97.04	1082902
5		3.813	8359	0.37	2040
6		3.951	12287	0.54	2897

UPLC Purity of compound 6k



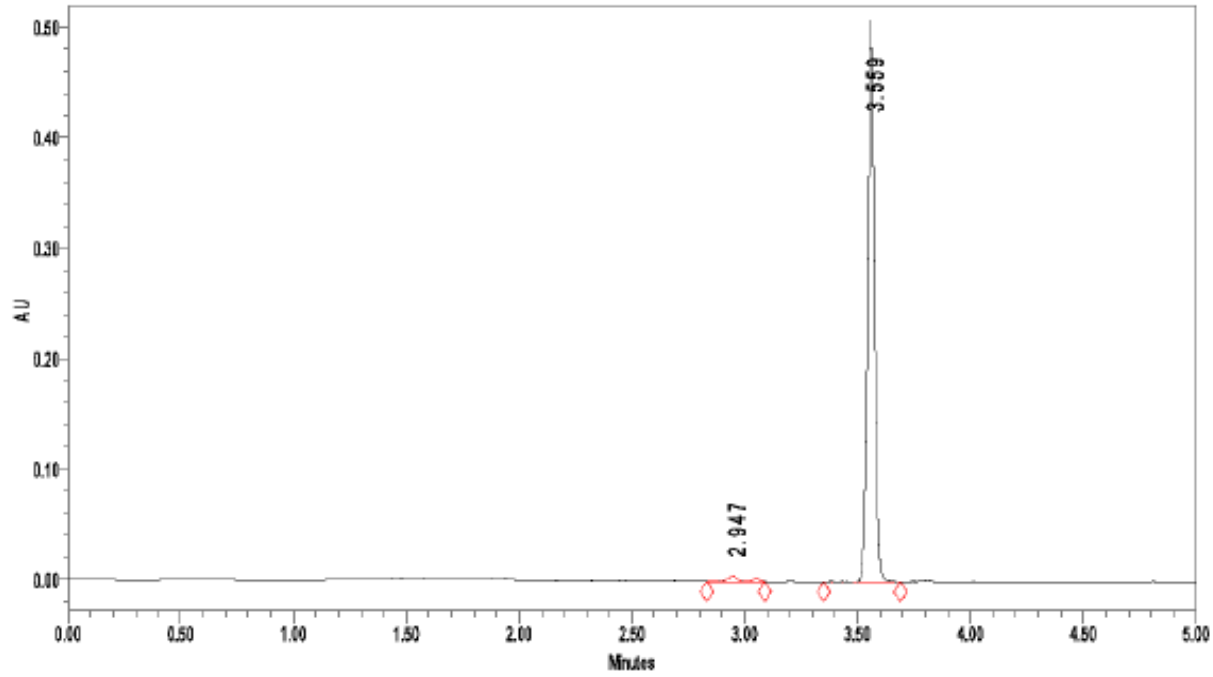
	Name	Retention Time	Area	% Area	Height
1		0.703	7353	0.47	3287
2		1.506	18502	1.19	997
3		1.864	18143	1.17	1693
4		2.967	30707	1.97	10064
5		3.270	22049	1.30	6499
6		3.743	1352831	93.90	608785

UPLC Purity of compound 6m



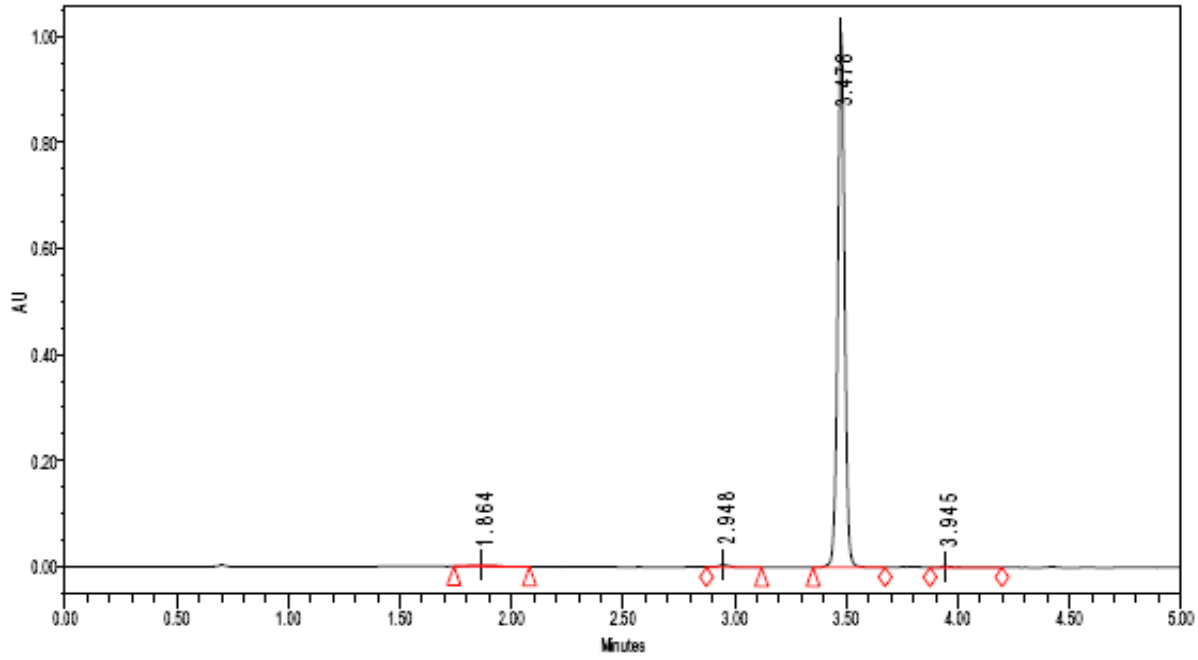
	Name	Retention Time	Area	% Area	Height
1		2.524	15032	0.67	6832
2		2.798	34450	1.54	15781
3		2.900	28796	1.29	12931
4		3.012	2072120	95.91	933919
5		3.260	7365	0.33	1147
6		3.426	15075	0.67	4056
7		3.564	11710	0.52	3949
8		3.820	45904	2.05	14777

UPLC Purity of compound 7b



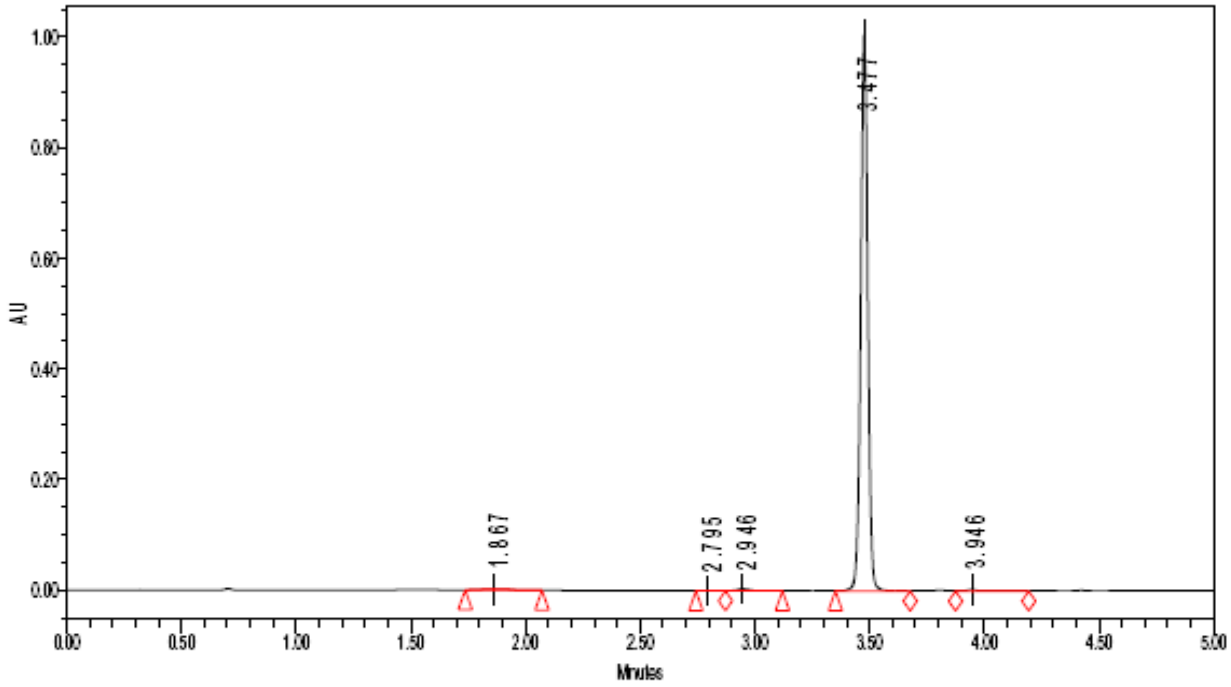
	Name	Retention Time	Area	% Area	Height
1		2.947	24171	2.03	5381
2		3.559	1084608	97.97	495881

UPLC Purity of compound 7d



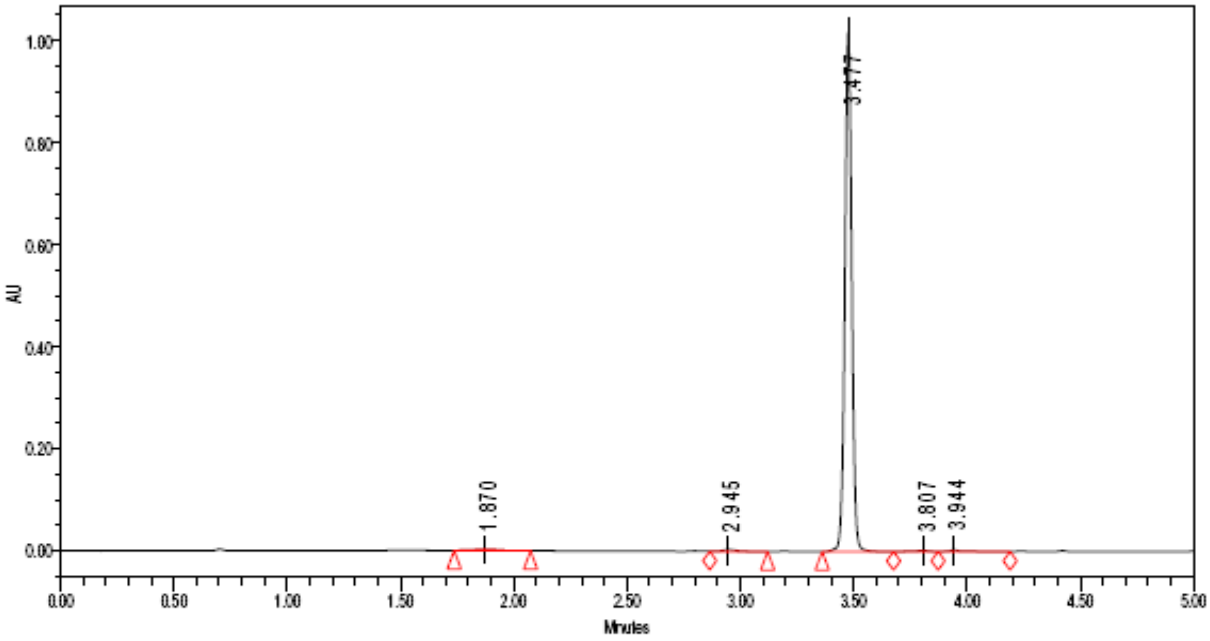
	Name	Retention Time	Area	% Area	Height
1		1.864	15050	0.68	1918
2		2.948	17312	0.78	4646
3		3.478	2176169	97.98	1008751
4		3.945	12458	0.56	2765

UPLC Purity of compound 7f



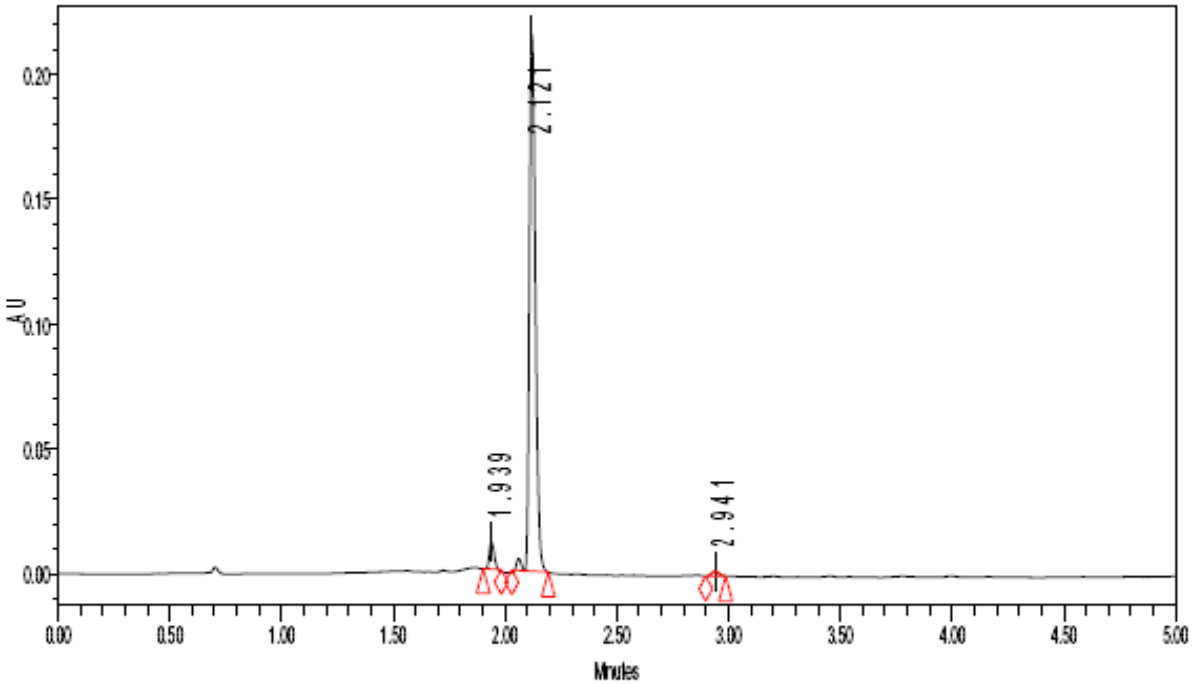
	Name	Retention Time	Area	% Area	Height
1		1.867	15602	0.71	1959
2		2.795	3319	0.15	853
3		2.946	15750	0.72	3957
4		3.477	2151558	97.84	1006411
5		3.946	12760	0.58	2775

UPLC Purity of compound 7h



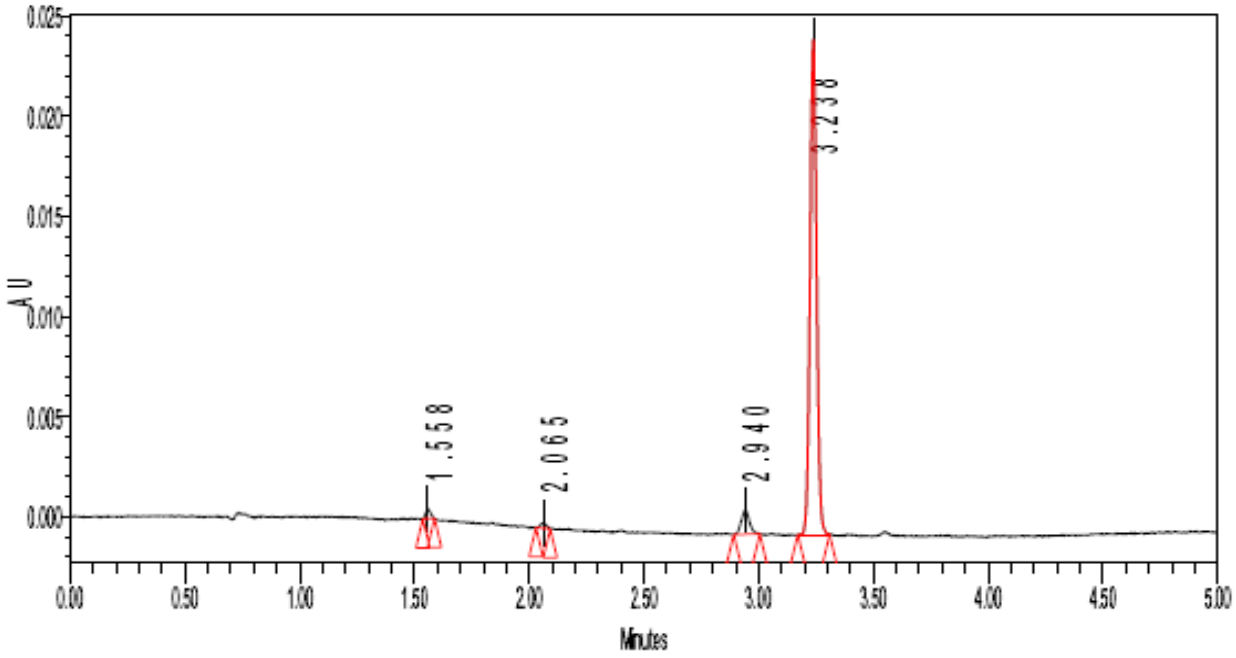
	Name	Retention Time	Area	% Area	Height
1		1.870	15684	0.71	1981
2		2.945	14701	0.66	3394
3		3.477	2166318	97.68	1018436
4		3.807	8425	0.38	1909
5		3.944	12685	0.57	2792

UPLC Purity of compound 7j



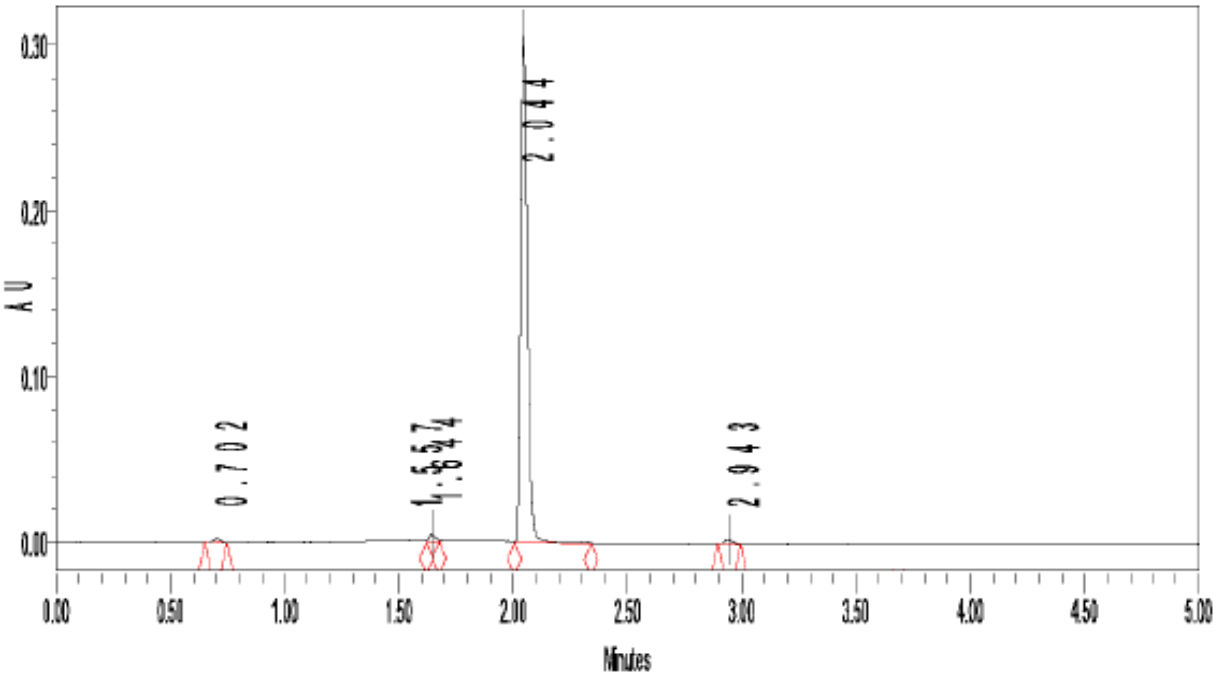
	Name	Retention Time	Area	% Area	Height
1		1.939	9982	1.01	1167
2		2.121	648764	98.47	221353
3		2.941	2874	0.52	414

UPLC Purity of compound 7l



	Name	Retention Time	Area	% Area	Height
1		1.558	688	1.29	488
2		2.065	430	0.81	243
3		2.940	2933	5.52	1186
4		3.238	49104	92.38	24725

UPLC Purity of compound 7n



	Name	Retention Time	Area	% Area	Height
1		0.702	4126	0.59	2375
2		1.557	8594	1.23	937
3		1.644	8964	1.28	4776
4		2.044	641848	96.07	308205
5		2.943	5811	0.83	2498