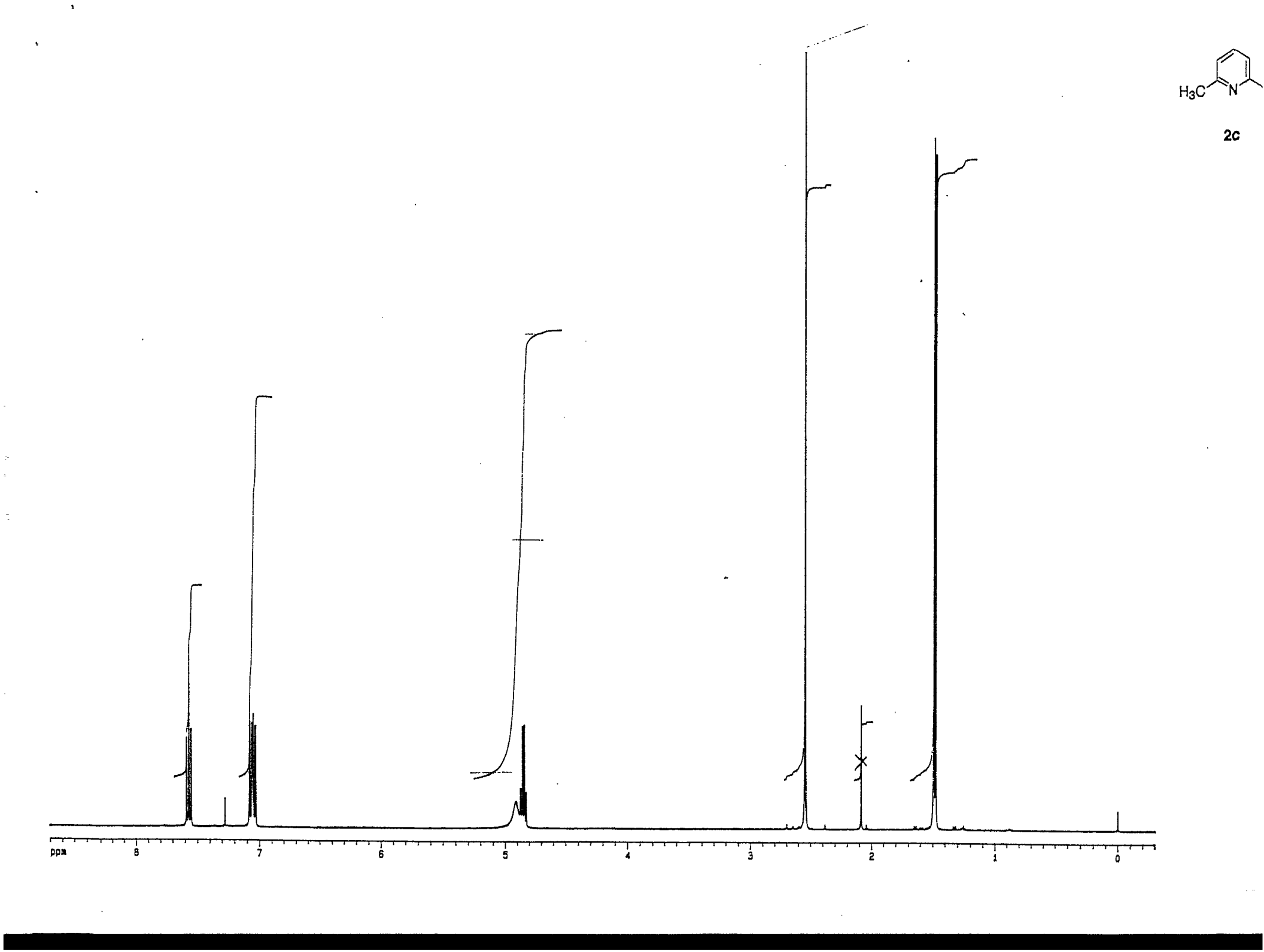
JOC The Journal of Organic Chemistry

J. Org. Chem., 1998, 63(8), 2481-2487, DOI:10.1021/jo971521g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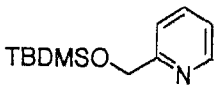

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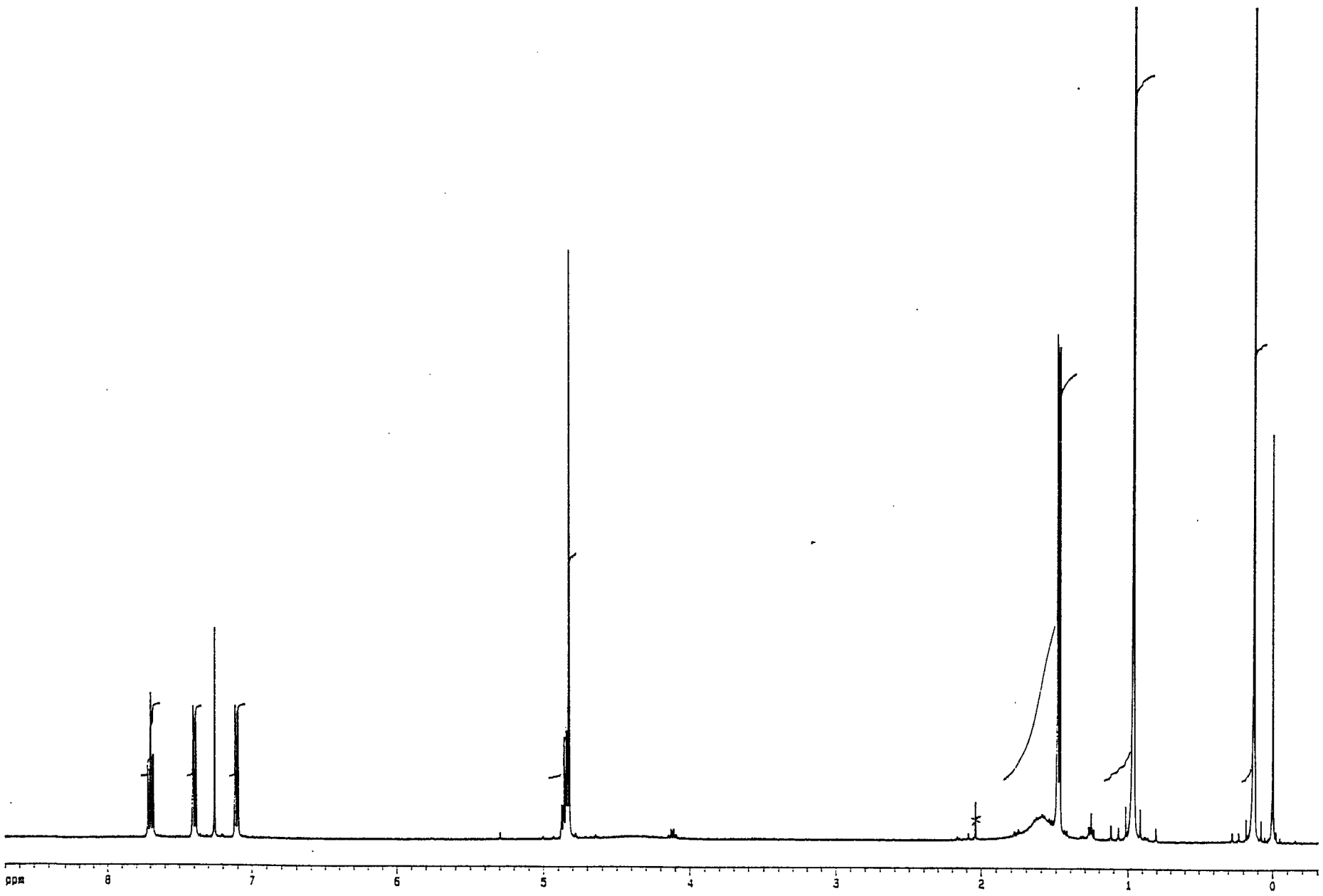

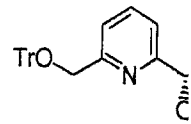

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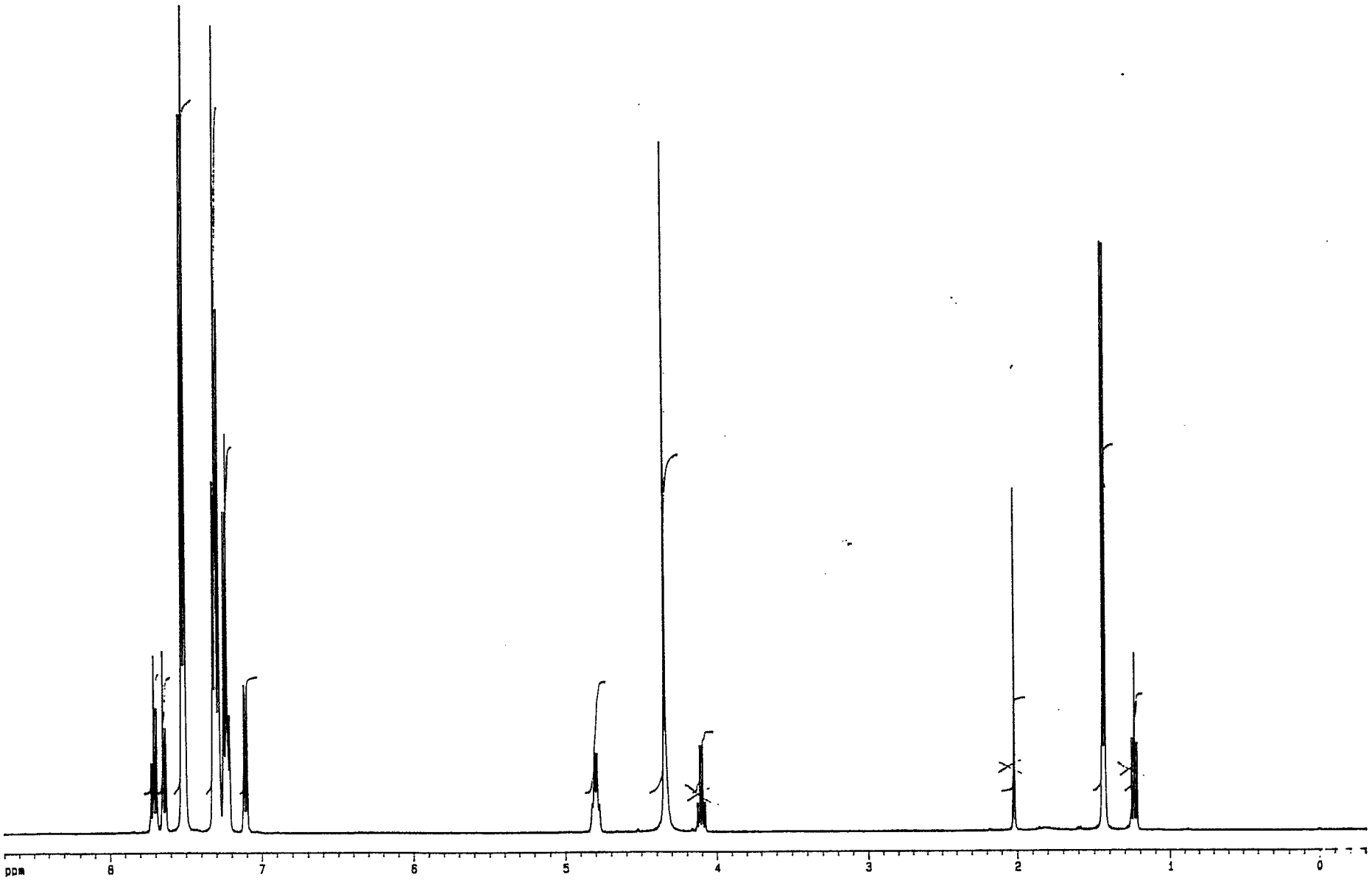

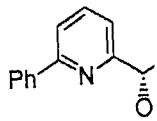

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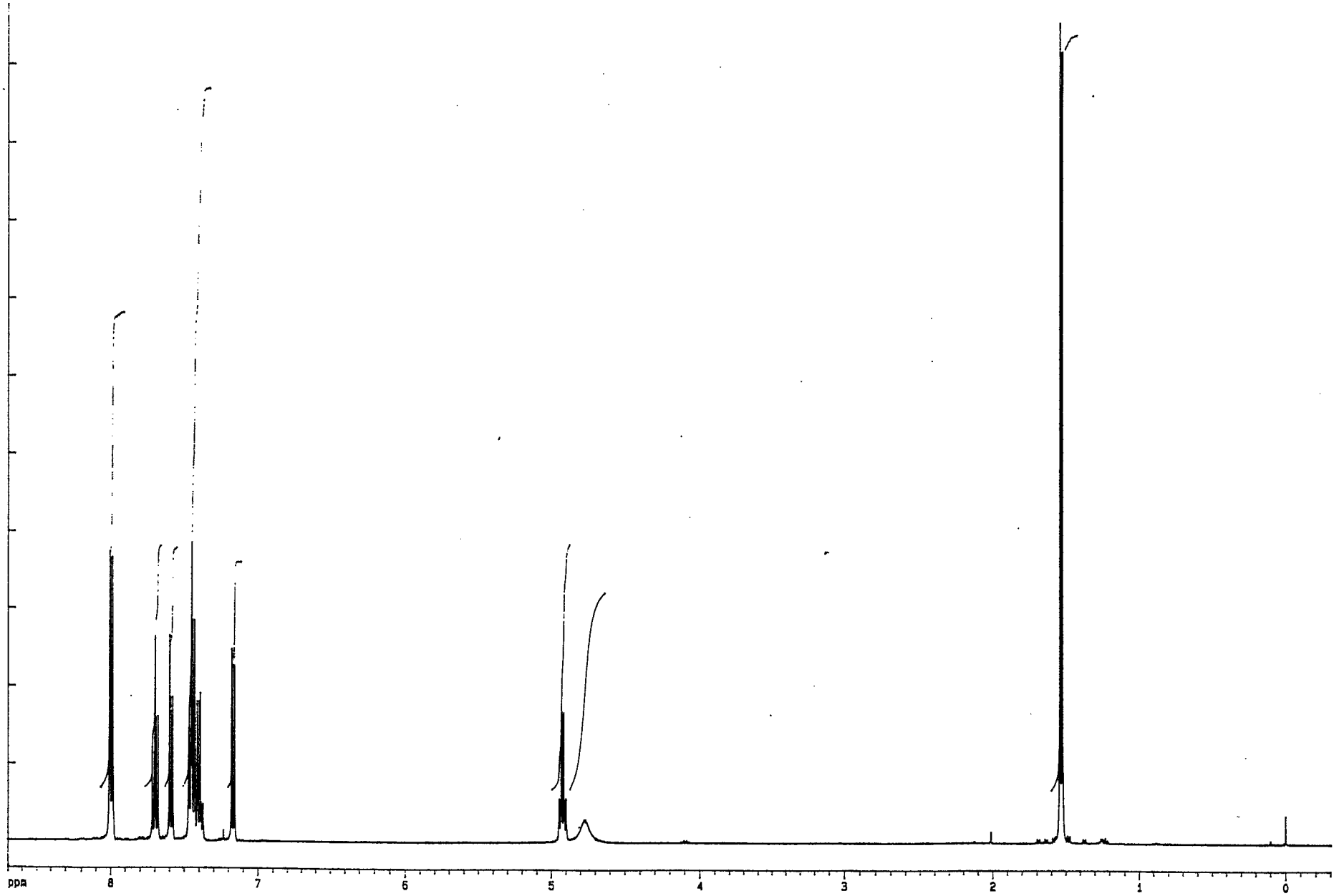
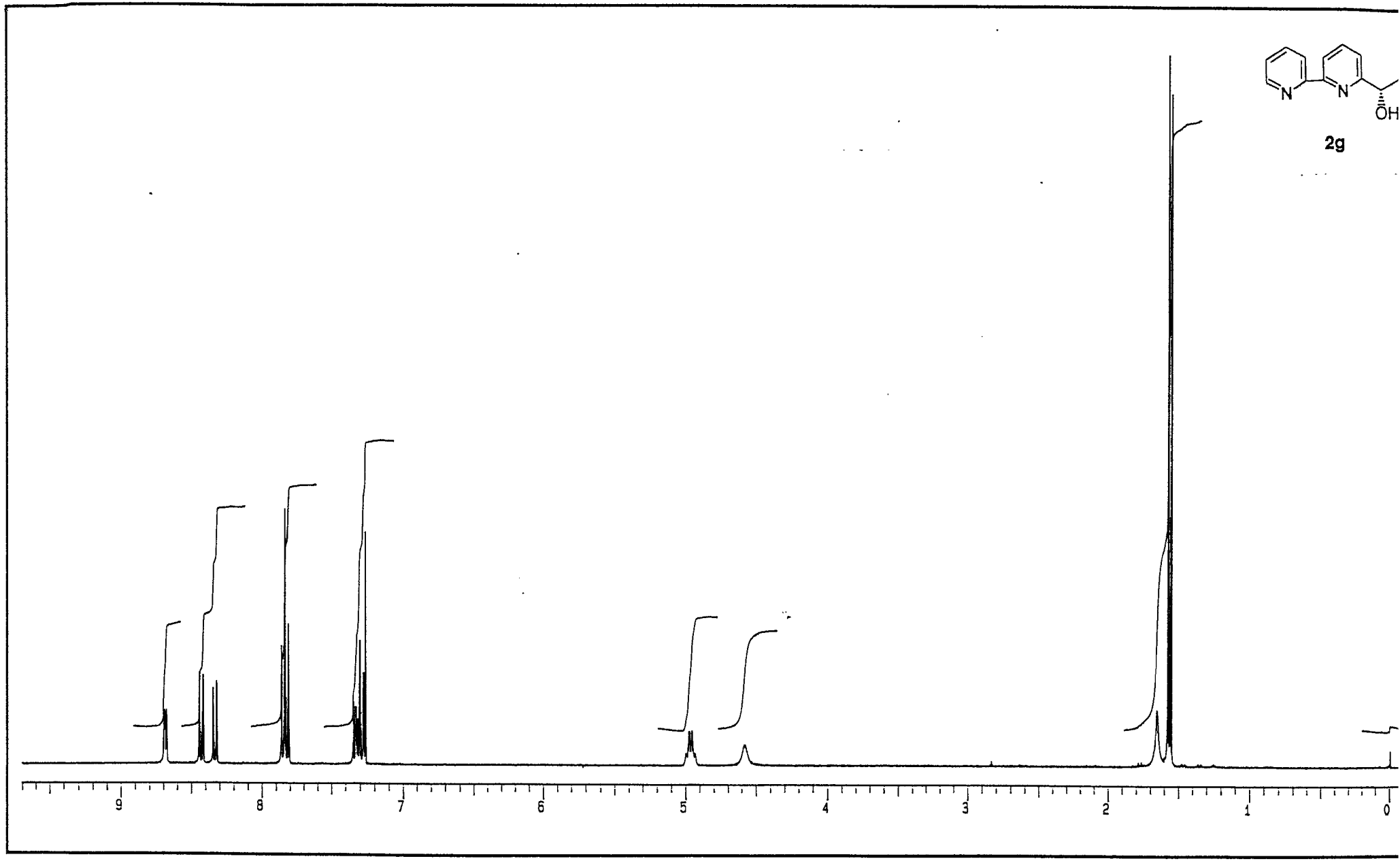




OBSERVE
Nucleus ____ Freq ____ MHz
Spec Width ____ Hz Offset ____ Hz
Acq Time ____ sec Delay ____ sec
Pulse Width ____ μsec Transients ____

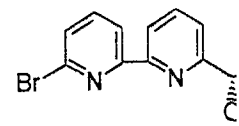
DECOUPLE
Nucleus ____ Offset ____ Hz
Mode ____ Power ____ db
Modulation Mode ____ Freq. ____ Hz
Pulse Width ____ μsec Power Mode ____

PLOT/PROCESSING
FN ____ K RE ____ sec CD ____ sec
LB ____ Hz AF ____ sec CCD ____
Width ____ Hz/ppm Start ____ Hz/ppm
Reference ____

EXPERIMENT
Pulse Sequence ____
Tube O.D. ____ mm
Temp. ____ °C
Solvent ____

SAMPLE

Number ____
File ____
Date ____
XL- ____



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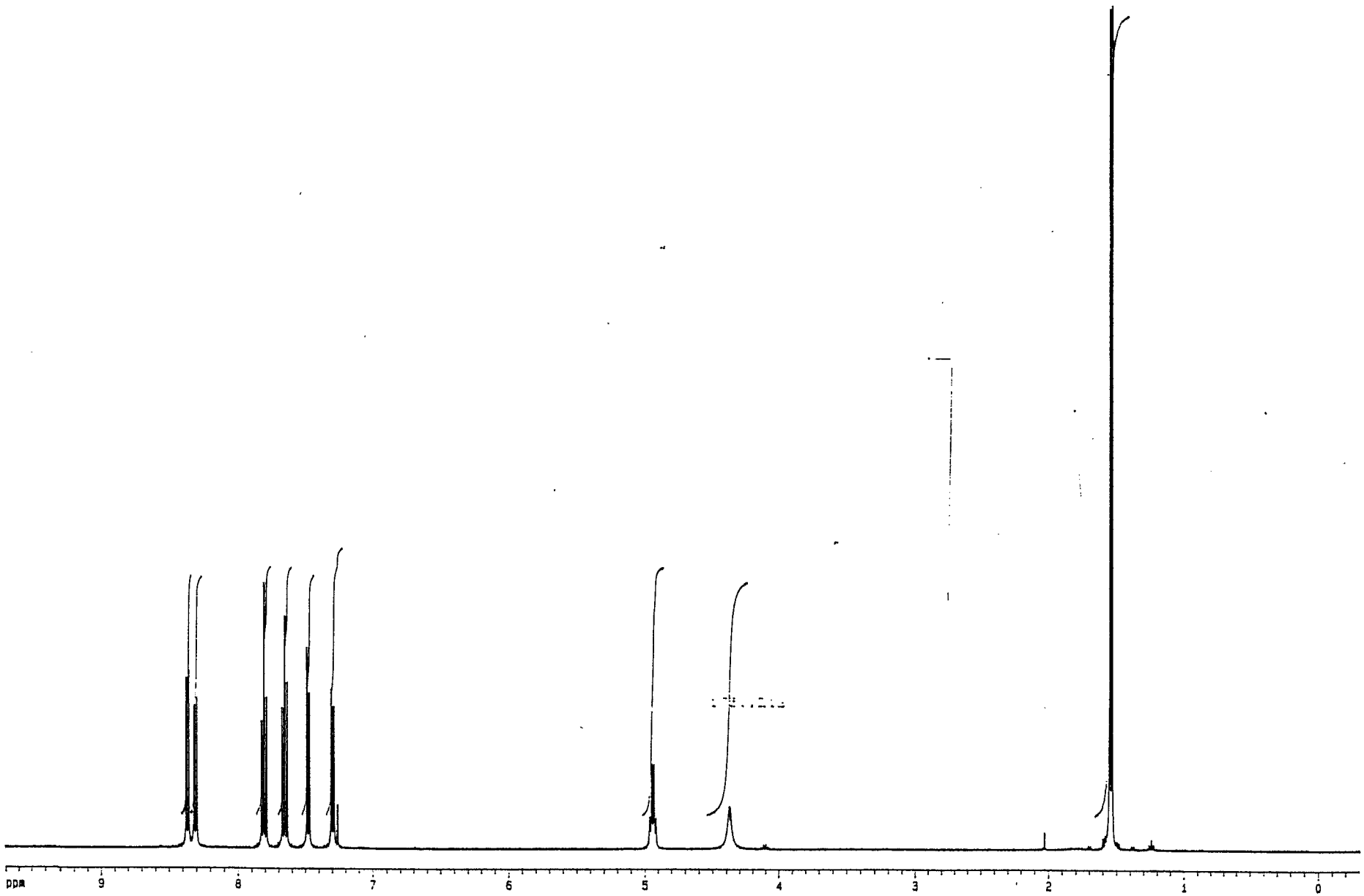
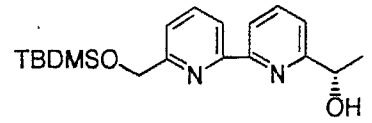




2i

OBSERVE: Nucleus ____ Freq ____ MHz; Spec Width ____ Hz; Offset ____ Hz; Acq Time ____ sec; Delay ____ sec; Pulse Width ____ μsec; Transients ____

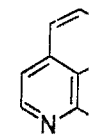
DECOUPLE: Nucleus ____ Offset ____ Hz; Mode ____ Power ____ db; Modulation: Mode ____ Freq. ____ Hz; Pulse Width ____ μsec; Power Mode ____

PLOT/PROCESSING: FN ____ K RE ____ sec CD ____ sec; LB ____ Hz AF ____ sec CCD ____; Width ____ Hz/ppm Start ____ Hz/ppm; Reference ____

EXPERIMENT: Pulse Sequence ____; Tube O.D. ____ mm; Temp. ____ °C; Solvent ____

SAMPLE

Number ____; File ____; Date ____; XL- ____



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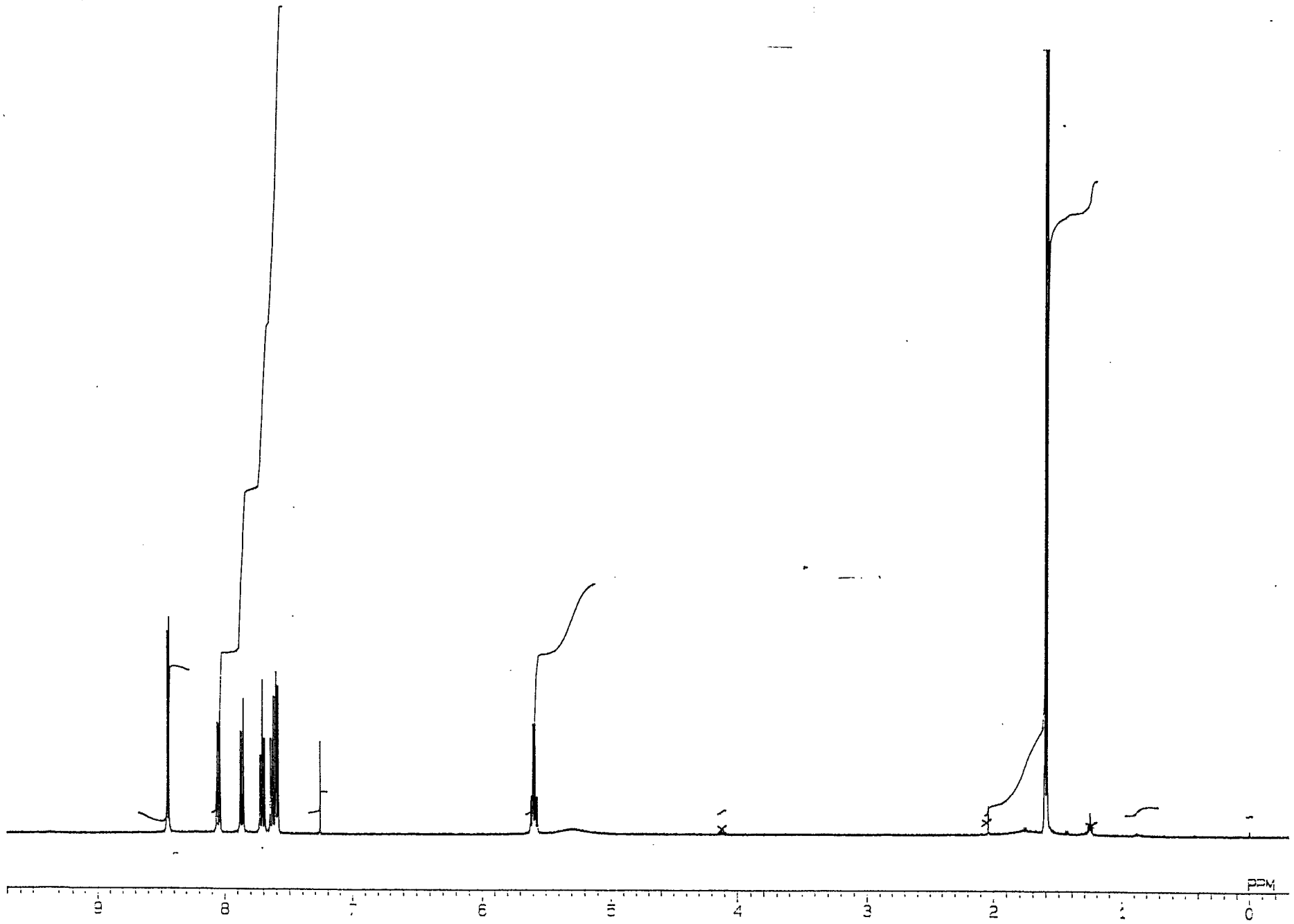

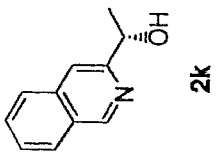

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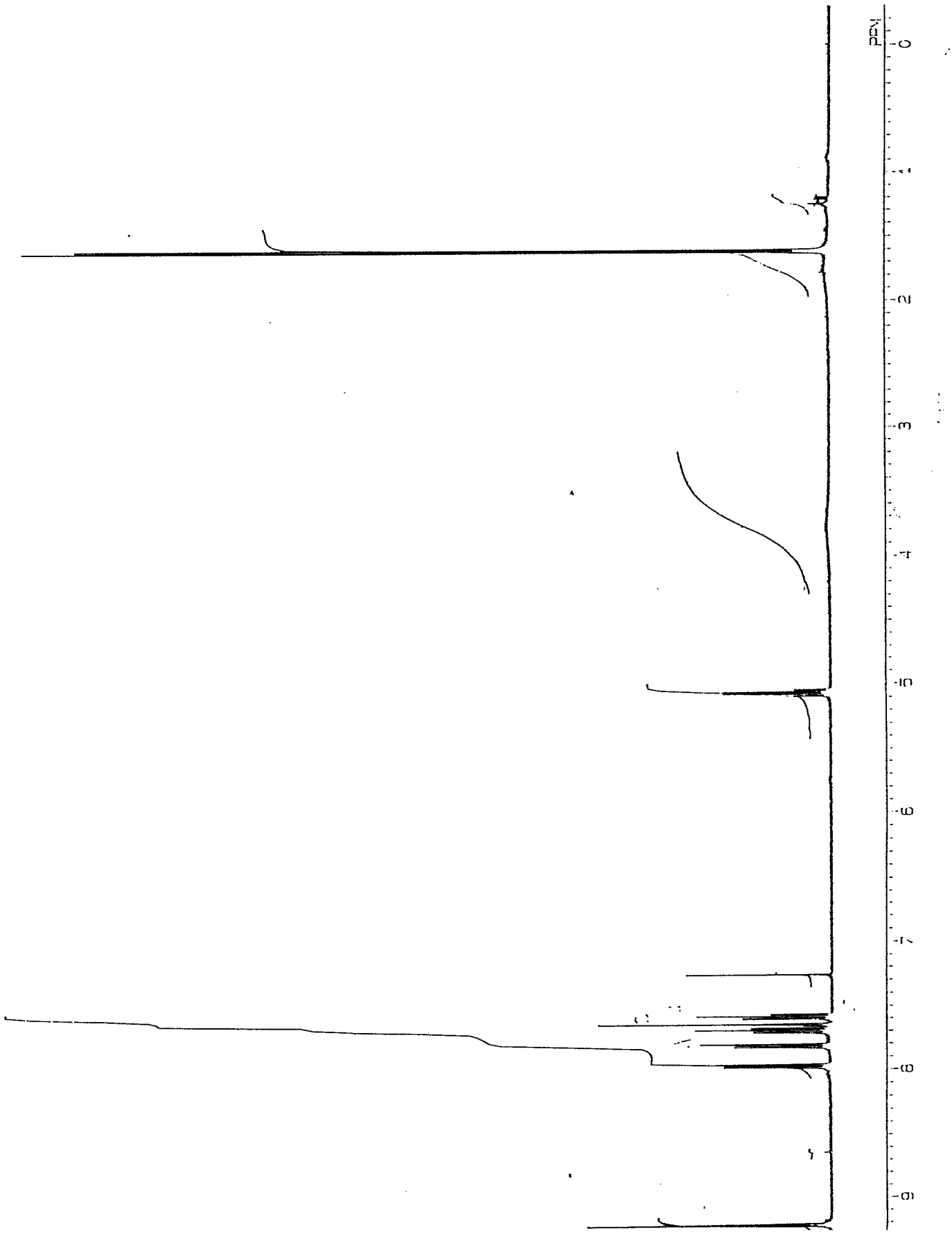

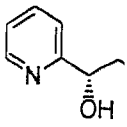

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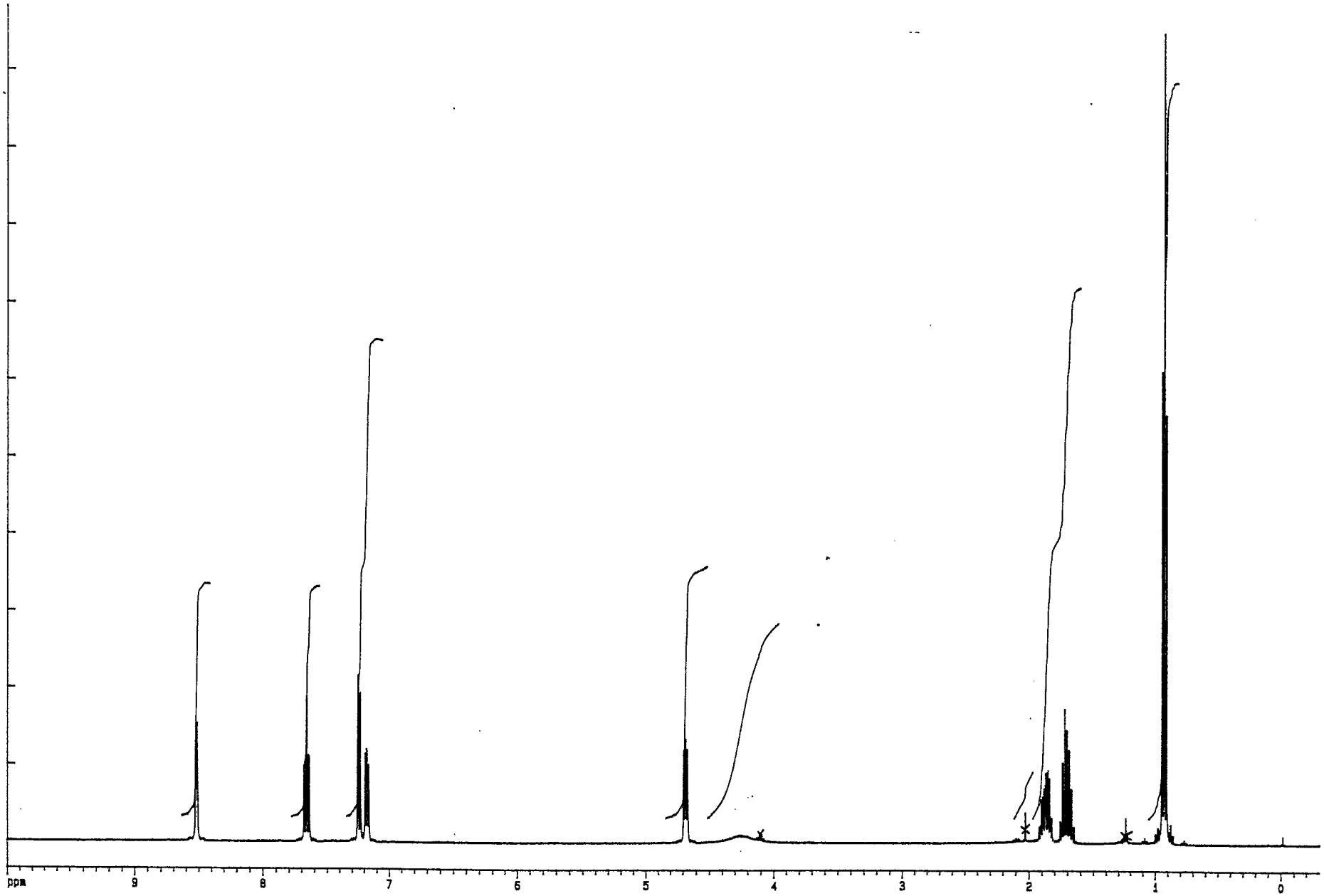

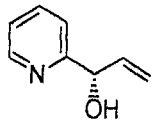

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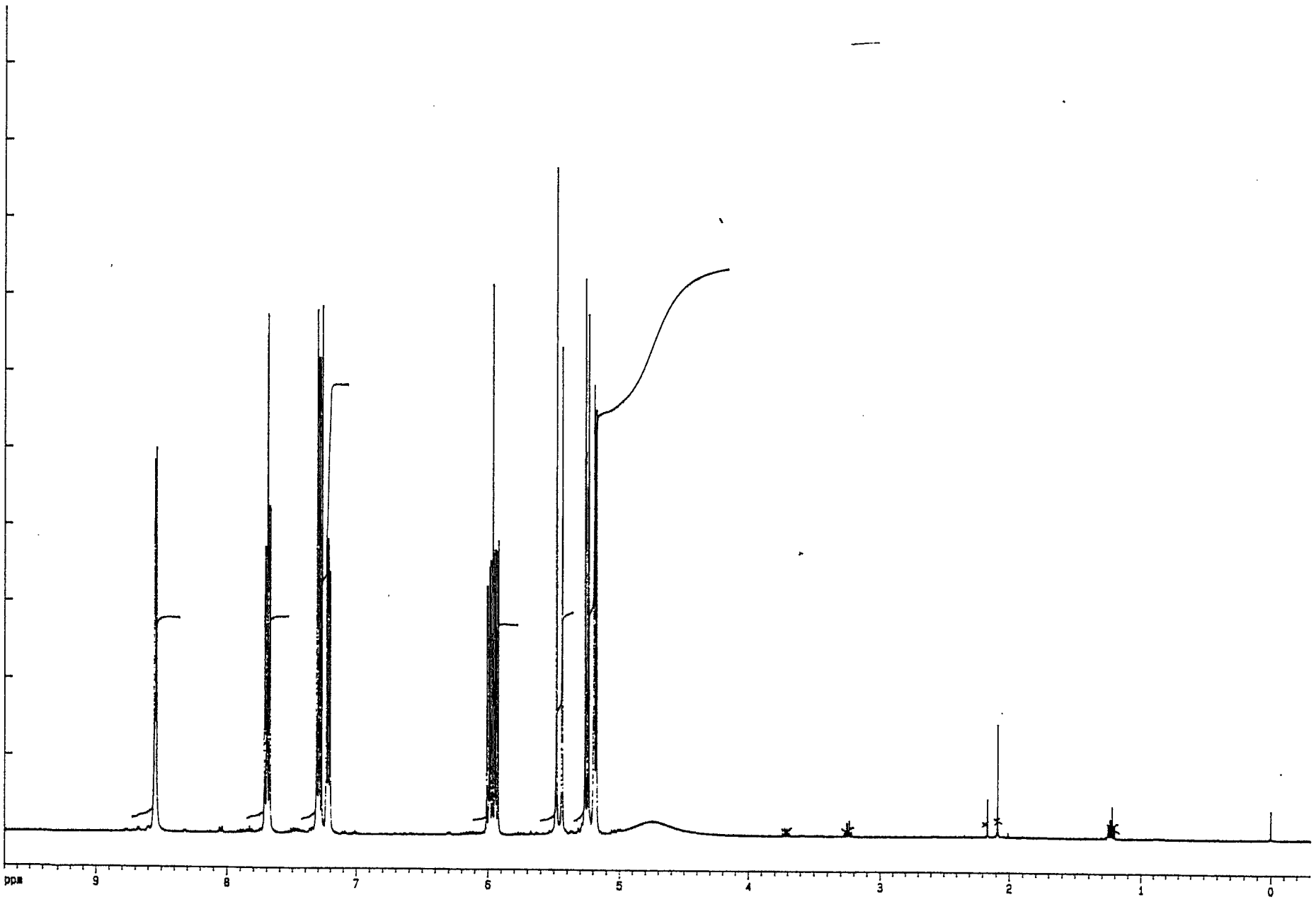

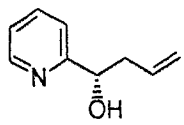

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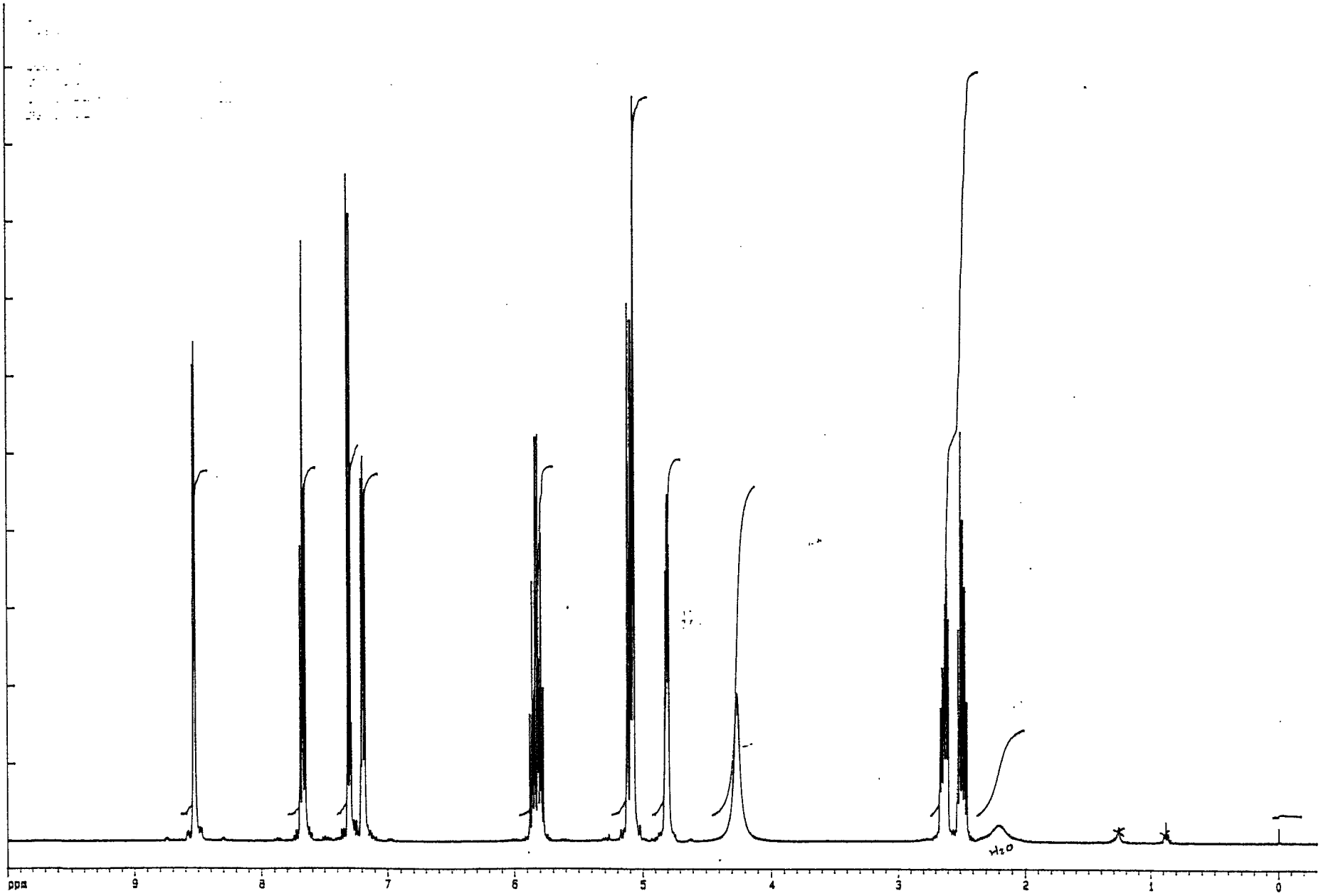

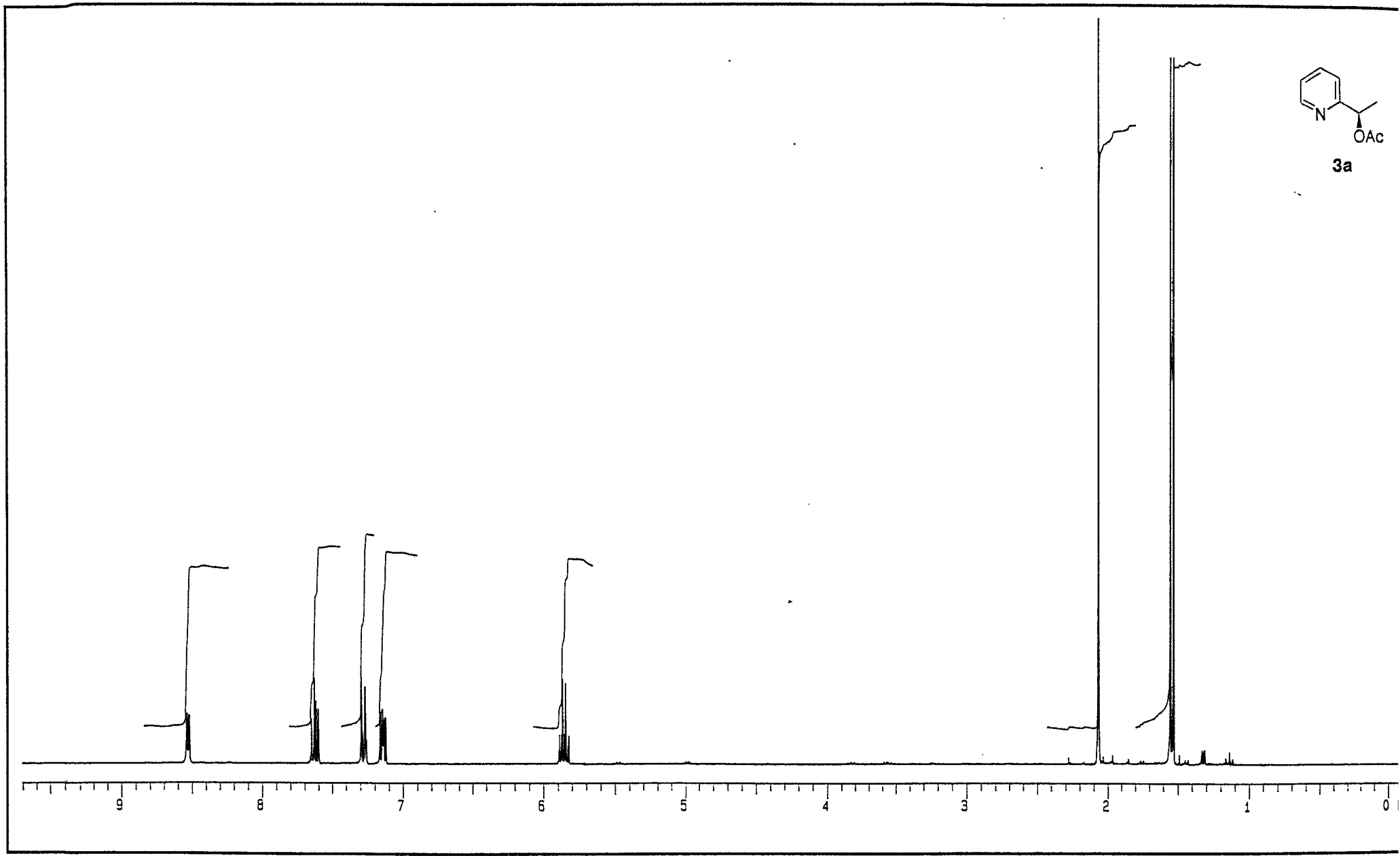

OBSERVE
Nucleus _____ Freq _____ MHz
Spec Width _____ Hz Offset _____ Hz
Acq Time _____ sec Delay _____ sec
Pulse Width _____ μsec Transients _____

DECOUPLE
Nucleus _____ Offset _____ Hz
Mode _____ Power _____ db
Modulation Mode _____ Freq _____ Hz
Pulse Width _____ μsec Power Mode _____

PLOT/PROCESSING
FN _____ K RE _____ sec CD _____ sec
LB _____ Hz AF _____ sec CCD _____
Width _____ Hz/ppm Start _____ Hz/ppm
Reference _____

EXPERIMENT
Pulse Sequence _____
Tube O.D. _____ mm
Temp. _____ °C
Solvent _____

SAMPLE

Number _____
File _____
Date _____
XL _____

INDEX	FREQ	PPM	INTENSITY
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03	2255.45	7.516	39.999
04	2221.34	7.403	30.216
05	2213.64	7.377	22.276
06	2212.61	7.374	20.017
07	2193.56	7.310	30.790
08	2187.82	7.291	8.309
09	2185.58	7.284	24.092
10	1767.01	5.889	8.019
11	1760.36	5.866	25.379
12	1753.70	5.844	25.707
13	1747.05	5.822	8.252
14	641.88	2.139	8.348
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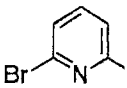


3b

OBSERVE: Nucleus ____ Freq ____ MHz; Spec. Width ____ Hz Offset ____ Hz; Acq. Time ____ sec Delay ____ sec; Pulse Width ____ μsec Transients ____

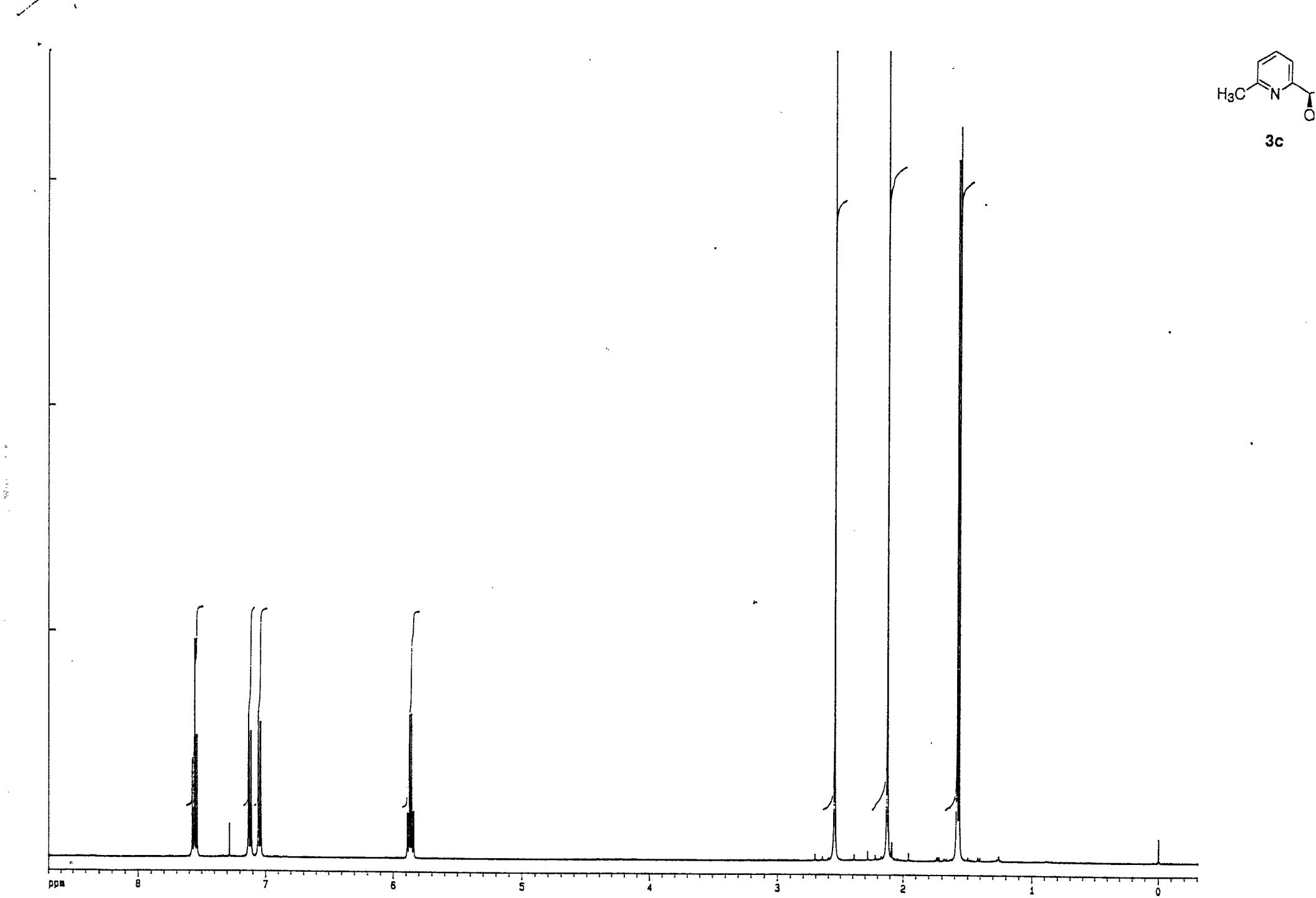
DECOUPLE: Nucleus ____ Offset ____ Hz; Mode ____ Power ____ db; Modulation Mode ____ Freq. ____ Hz; Pulse Width ____ μsec Power Mode ____

PLOT/PROCESSING: FN ____ X RE ____ sec CD ____ sec; LB ____ Hz AF ____ sec CCD ____; Width ____ Hz/ppm Start ____ Hz/ppm; Reference ____

EXPERIMENT: Pulse Sequence ____; Tube O.D. ____ mm; Temp. ____ °C; Solvent ____

SAMPLE

Number ____; File ____; Date ____; XL ____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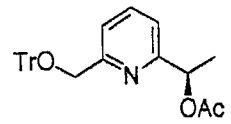
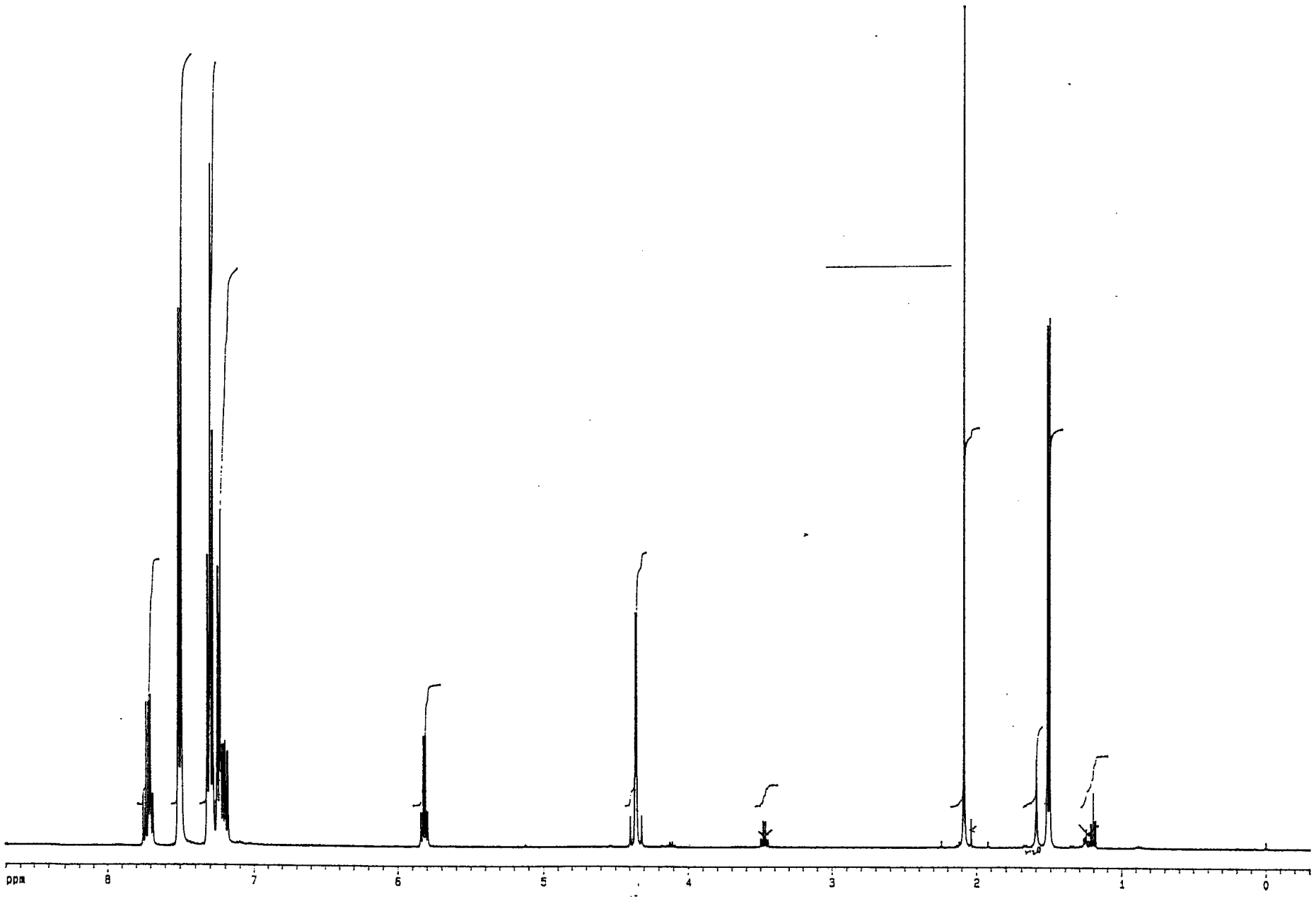
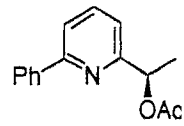


3e





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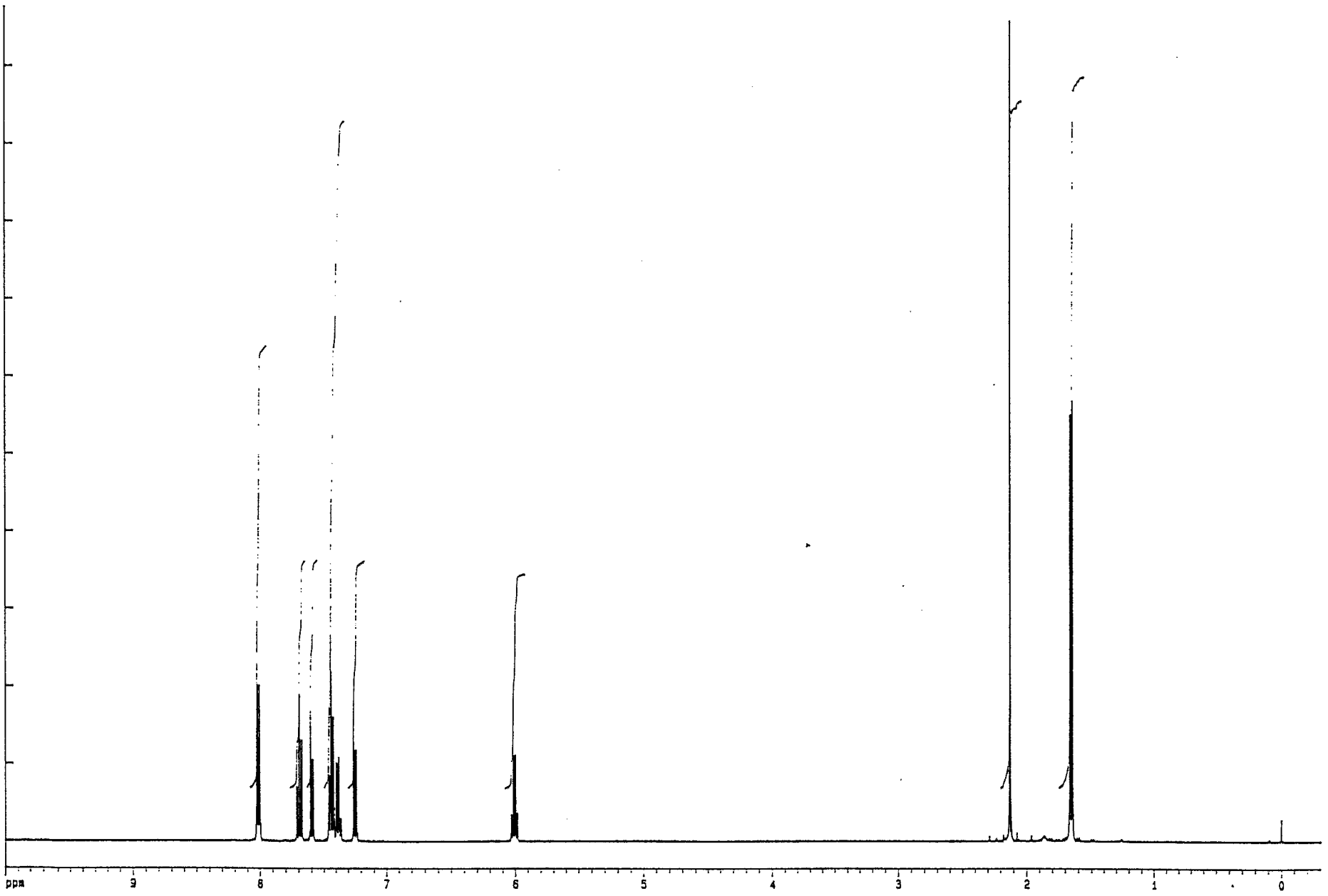

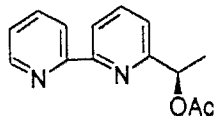

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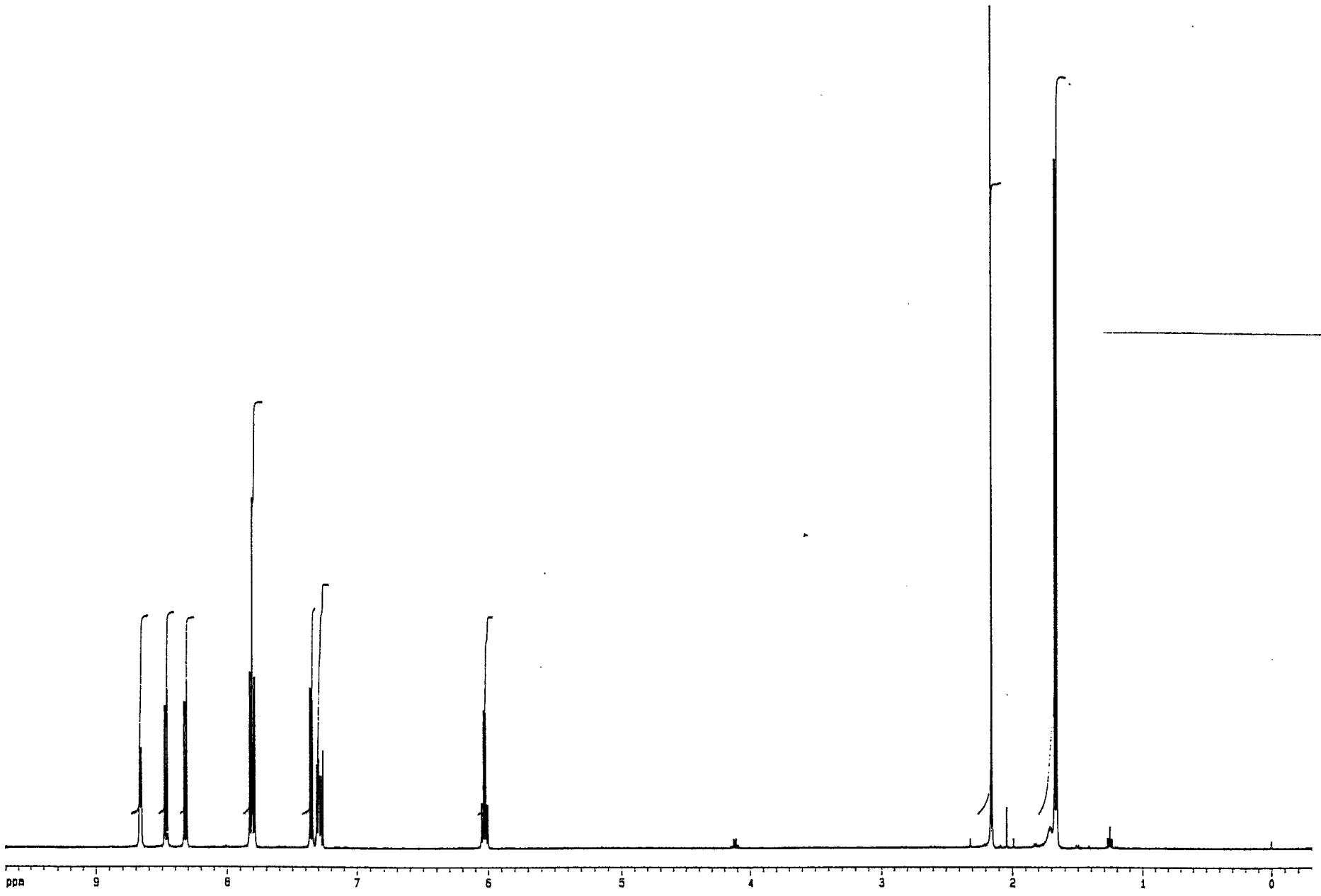

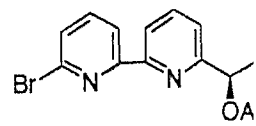

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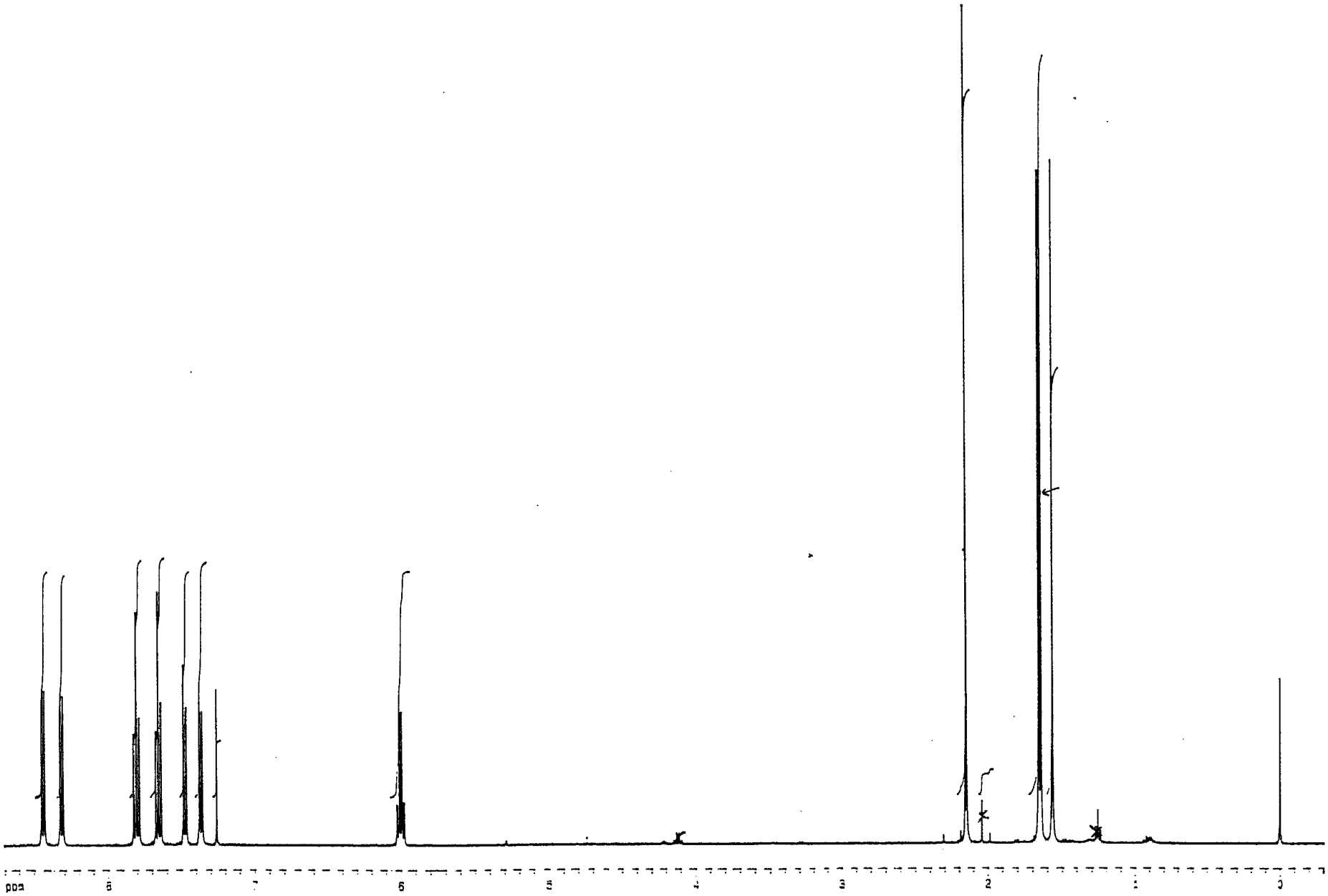
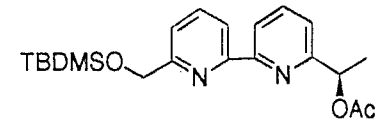
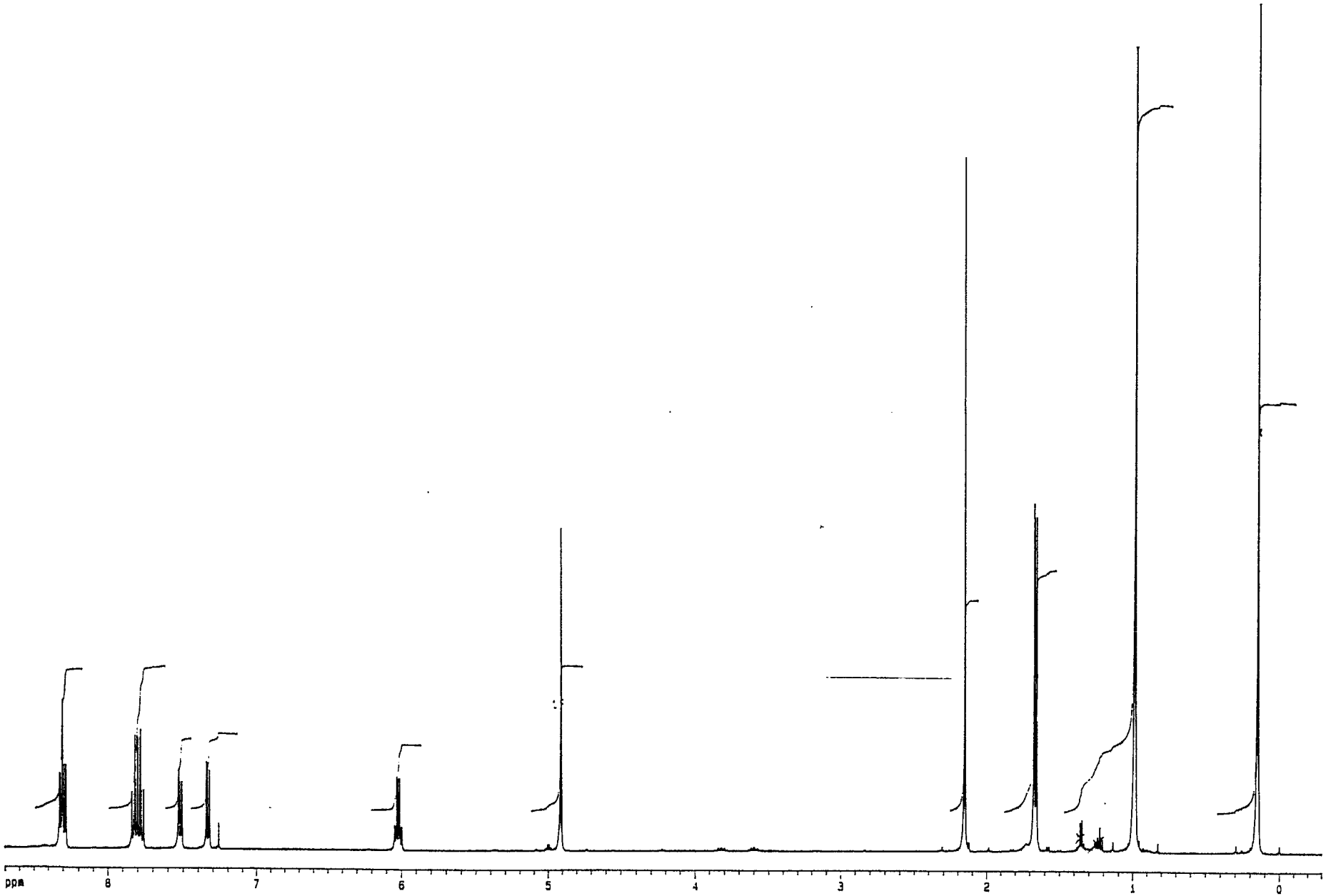
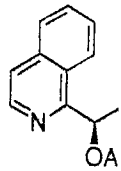




3i





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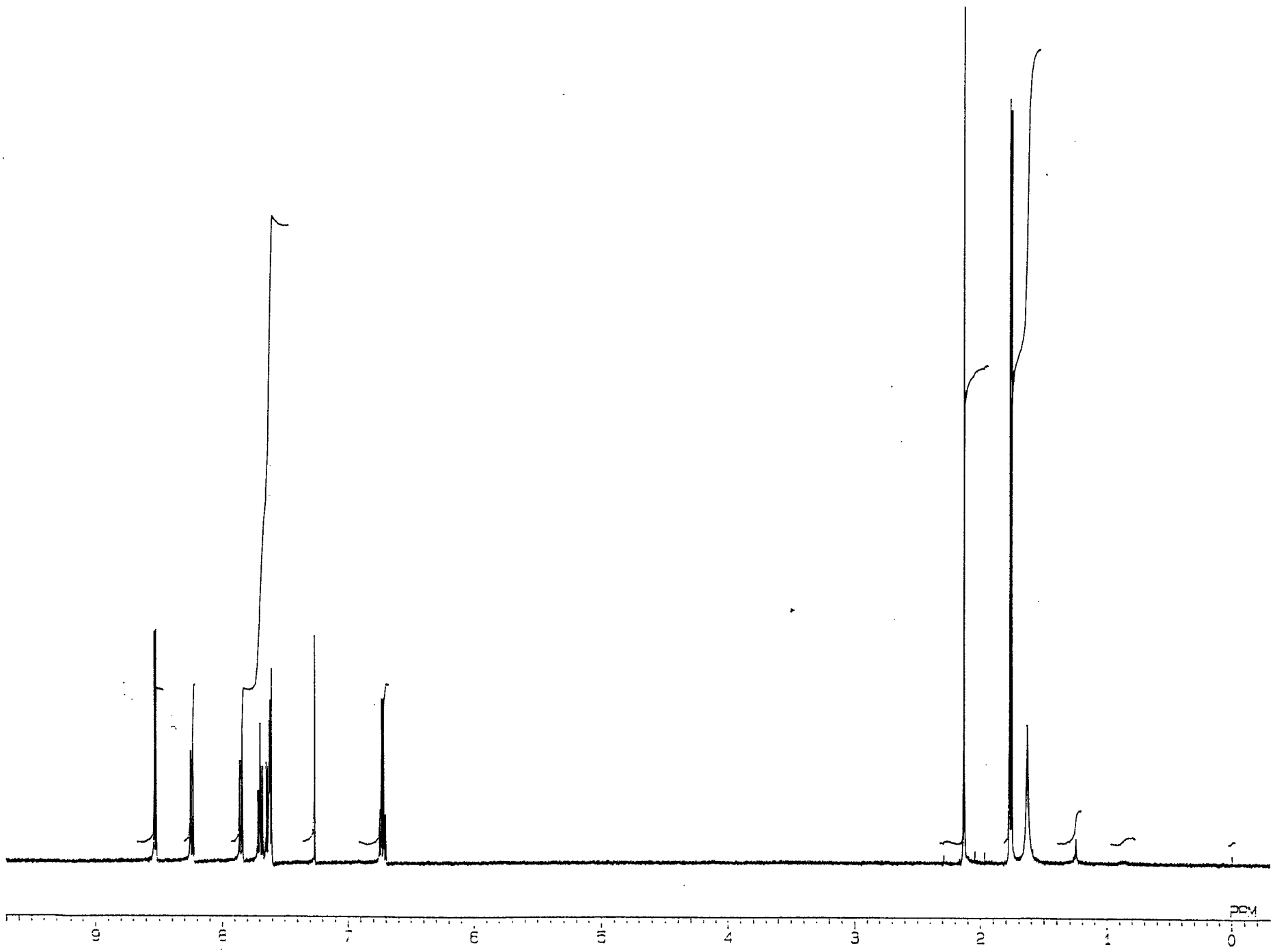

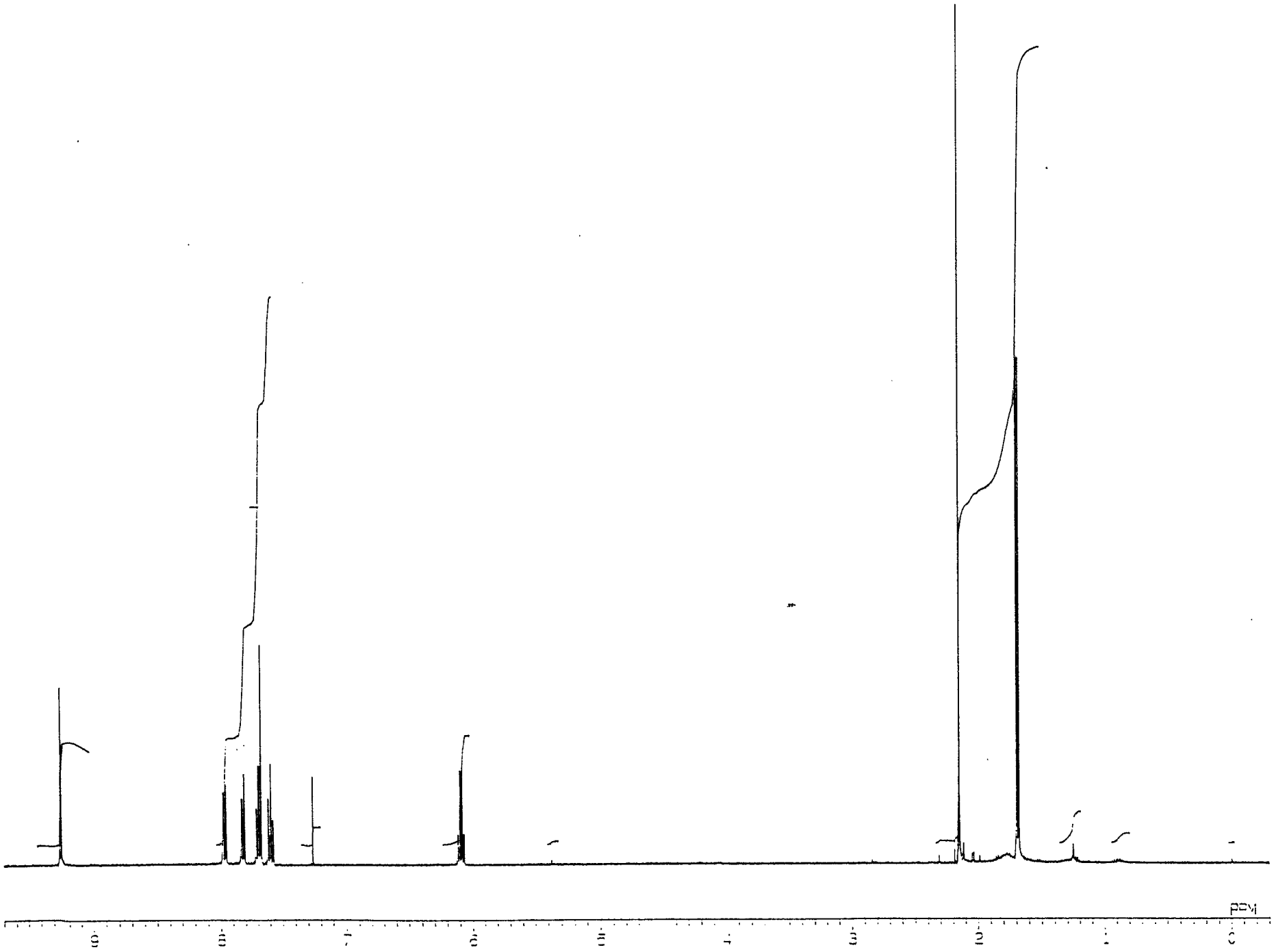
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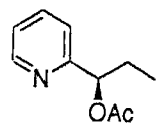
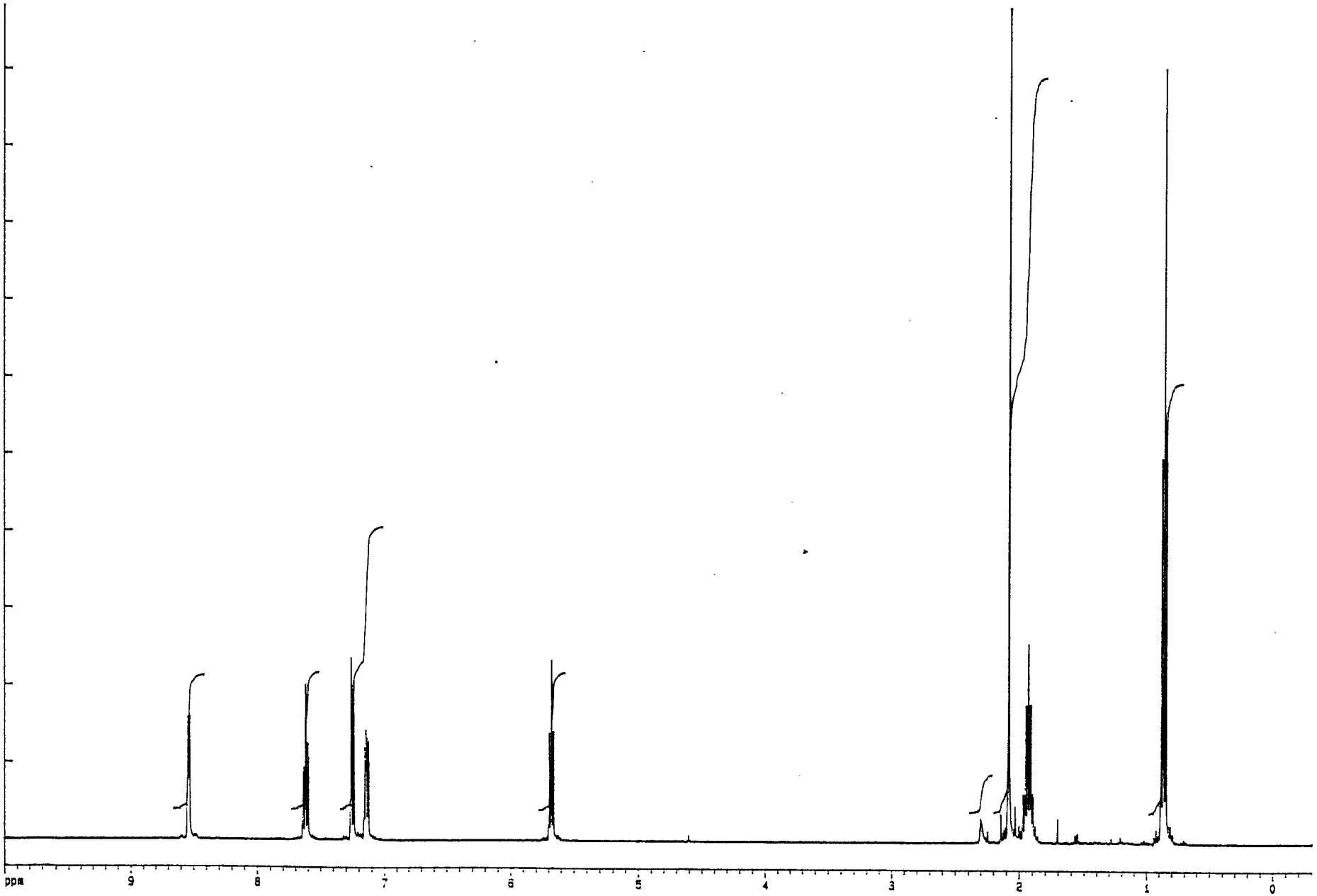
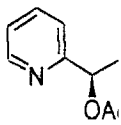
ppm



3l





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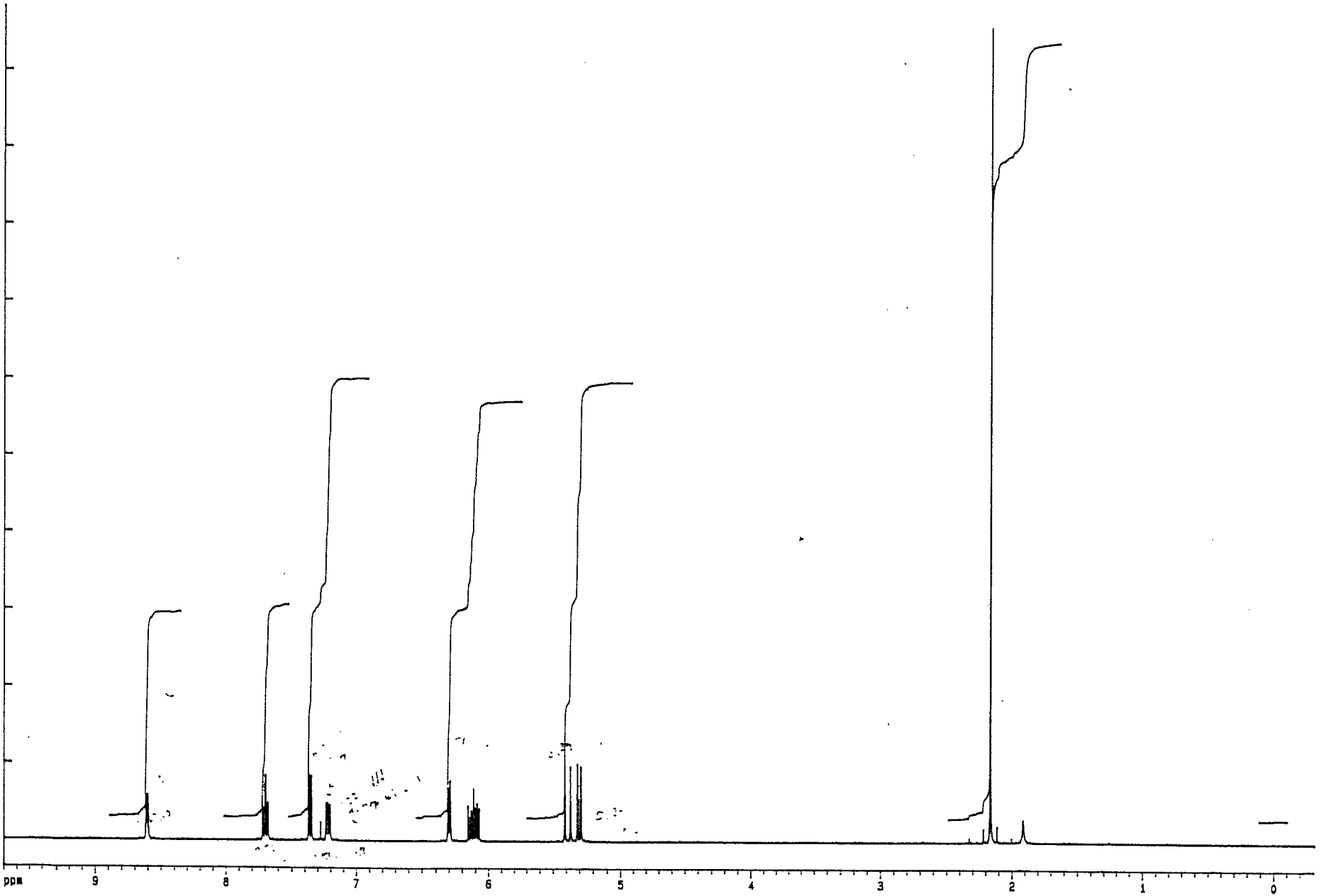

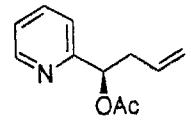

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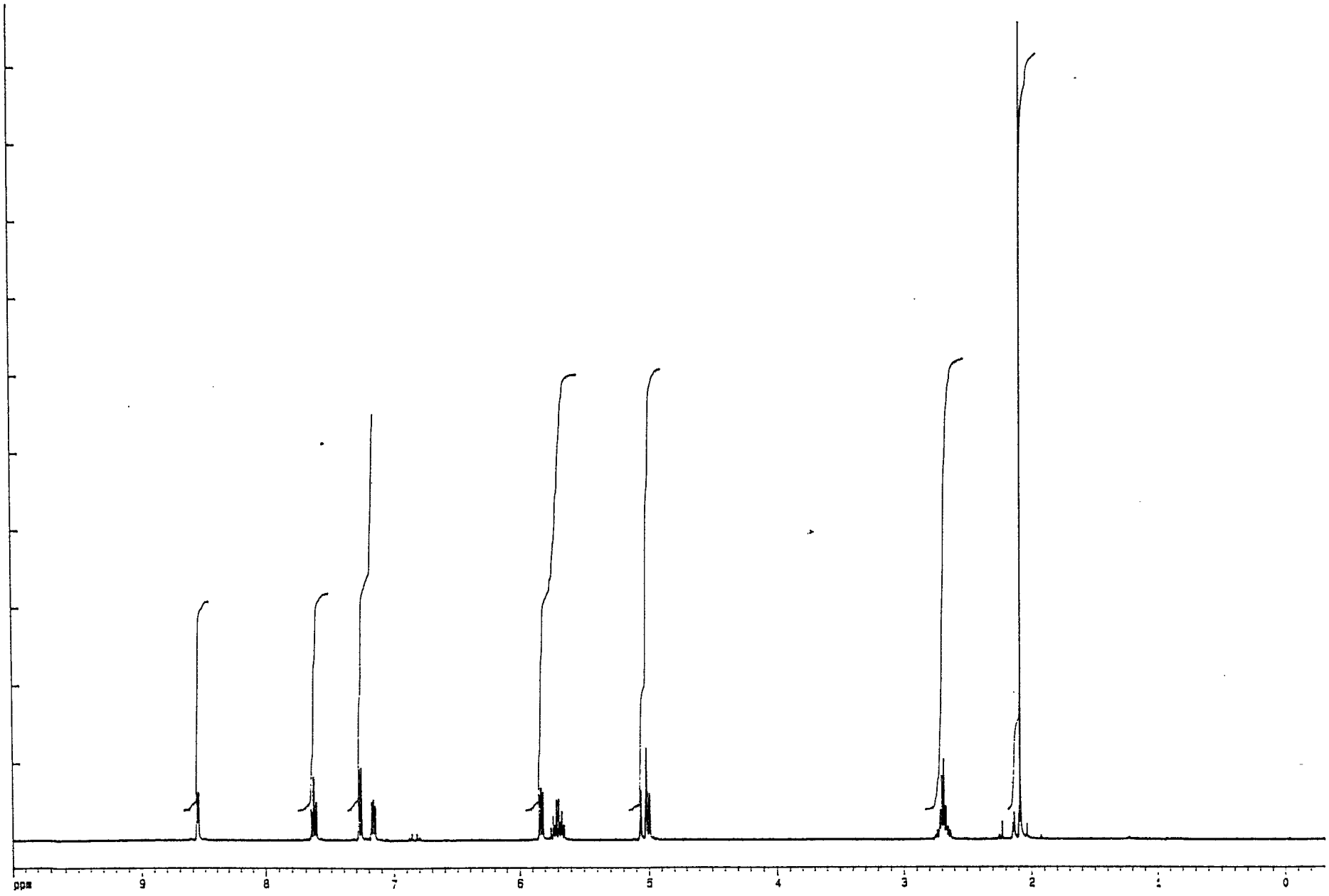

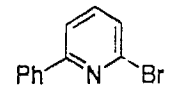

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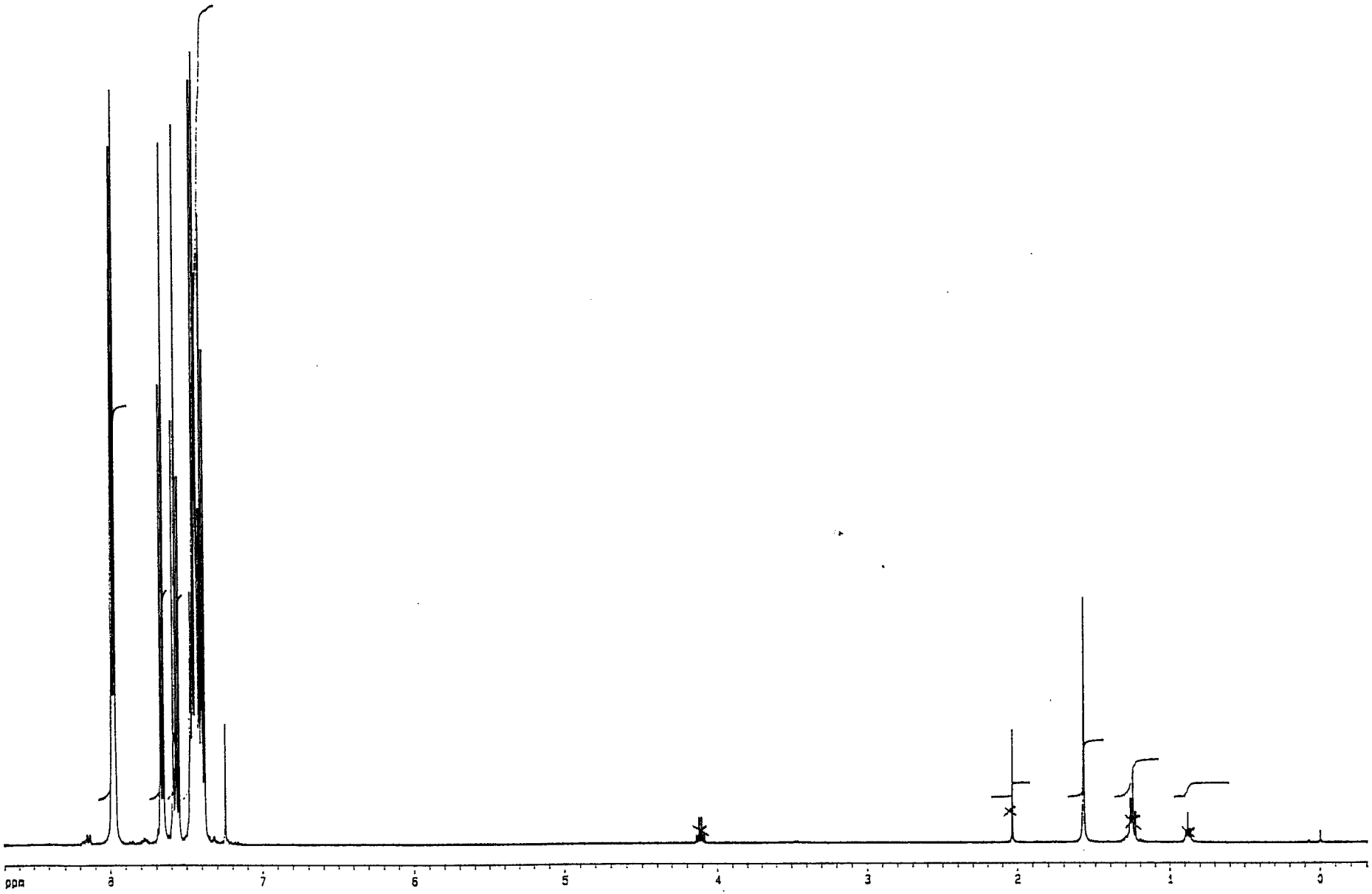

INDEX	FREQ	PPM	INTENSITY
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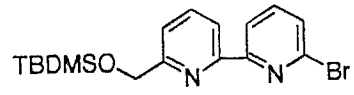
02	2503.83	8.344	65.670
03	2480.14	8.265	42.299
04	2472.45	8.239	45.557
05	2355.36	7.849	46.902
06	2347.61	7.823	90.502
07	2338.73	7.797	47.535
08	2299.62	7.663	43.315
09	2291.81	7.637	115.425
10	2284.05	7.612	75.800
11	2266.96	7.555	51.399
12	2259.33	7.529	42.782
13	2243.40	7.476	76.491
14	2235.89	7.451	49.542
15	2178.56	7.260	46.474
16	1468.14	4.893	254.594
17	293.38	0.979	1.86E 3
18	290.39	0.968	90.021
19	46.62	0.155	52.055
20	43.51	0.145	1.18E 3
21	40.45	0.135	30.298



1i

OBSERVE: Nucleus ____ Freq ____ MHz; Spec Width ____ Hz Offset ____ Hz; Acq Time ____ sec Delay ____ sec; Pulse Width ____ μsec Transients ____

DECOUPLE: Nucleus ____ Offset ____ Hz; Mode ____ Power ____ db; Modulation Mode ____ Freq. ____ Hz; Pulse Width ____ μsec Power Mode ____

PLOT/PROCESSING: FN ____ K RE ____ sec CD ____ sec; LB ____ Hz AF ____ sec CCD ____; Width ____ Hz/ppm Start ____ Hz/ppm; Reference ____

EXPERIMENT: Pulse Sequence ____ SAMPLE; Tube O.D. ____ mm; Temp. ____ °C; Solvent ____

Number ____; Pw ____; Date ____; XL ____

Preparation of 2-Bromo-6-phenylpyridine (1f). A mixture of 2,6-dibromopyridine (1.0 g, 4.22 mmol) and phenylboronic acid (412 mg, 3.38 mmol) and Na_2CO_3 (895 mg, 8.44 mmol) in a mixture of ethanol, toluene and water (40 mL, 2:1:1 ratio) was degassed, and to this mixture, $Pd(PPh_3)_4$ (146 mg, 0.127 mmol) was added. Then, the mixture was heated at 85°C under an Ar atmosphere for 12 hr. After cooling, sat. Na_2CO_3 (2.5 mL) and 28% ammonia in water (2.5 mL) were added and the mixture was extracted with dichloromethane (200 mL). The organic layer was washed with water, and brine, and dried over $MgSO_4$. Evaporation of the solvent and purification of the resulted residue by column chromatography on silica gel eluted with 10% EtOAc in hexane, afforded almost pure product, which was further purified by HPLC gave pure **1f** (508 mg) in 64% yield. Colorless crystals; mp 49-50°C (hexane), *Rf* = 0.43 (5% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (2H, dd, *J* = 7.9 and 1.1 Hz), 7.66 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.57 (1H, t, *J* = 7.7 Hz), 7.41-7.48 (3H, m), 7.39 (1H, dd, *J* = 7.7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 142.2, 138.9, 137.6, 129.6, 128.8, 127.0, 126.3, 118.9; MS (EI) *m/z* (rel intensity) 235 and 233 (M^+, 60 and 62), 154 (base), 127 (57). Anal. Calcd for $C_{11}H_8NBr$: C, 56.44; H, 3.44; N, 5.98. Found: C, 56.50; H, 3.43; N, 6.04.

Preparation of 6-Bromo-6'-[(*tert*-butyldimethylsilyl)oxymethyl]-2,2'-bipyridine (1i). To an solution of 2,6-dibromopyridine(474 mg, 2 mmol) in hexane, ether, and THF (16 mL, 1:2:1), was added *n*-BuLi (1.28 mL, 1.56M in hexane solution) dropwise at -78°C. After stirring for 5 min, the mixture was quenched with a THF solution of ethyl 2-{[6-(*tert*-butyldimethylsilyl)oxymethyl]-pyridyl} sulfoxide (499 mg, 1.67 mmol) in at -78°C. The mixture was stirred for an additional 15 min at the same temperature and allowed to warm up to room temperature. The reaction mixture was diluted with 10% EtOAc in hexane (100 mL), and washed with water and brine. The organic layer was dried over $MgSO_4$, and condensed. The crude mixture was purified by chromatography on silica gel eluted with 10% EtOAc in hexane to give **1i** (494 mg) in 78% yield. Colorless crystals, mp 79-80 °C (hexane); *Rf* = 0.38 (5% EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (1H, dd, *J* = 7.7 and 1.1 Hz), 8.26 (1H, d, *J* = 7.8 Hz), 7.83 (1H, t, *J* = 7.7 Hz), 7.65 (1H, t, *J* = 7.8 Hz), 7.54 (1H, d, *J* = 7.8 Hz), 7.47 (1H, dd, *J* = 7.7 and 1.1 Hz), 4.89 (2H, s), 0.98 (9H, s), 0.14 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0, 157.5, 153.3, 141.5, 139.1, 137.5, 127.8, 120.6, 119.7, 119.6, 66.2, 25.9, 18.4, -5.3; MS (EI) *m/z* (rel intensity) 323 (M^+-57, base), 321 (97), 227 (9). Anal. Calcd for $C_{17}H_{23}N_2OBrSi$: C, 53.82; H, 6.11; N, 7.38. Found: C, 53.94; H, 6.19; N, 7.44.

2-Acetyl-6-bromopyridine. Colorless crystals, mp 50-51°C (hexane); *Rf* = 0.35 (10 % EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (1H, dd, *J* = 7.7 and 1.1 Hz), 7.70 (1H, t, *J* = 7.7 Hz), 7.66 (1H, dd, *J* = 7.7 and 1.1 Hz), 2.71 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.5, 154.2, 141.2, 139.1, 131.7, 120.3, 25.6; IR (film) 1690 cm^{-1}; MS (FAB) *m/z* 200 and 202 (MH^+); HRMS (FAB) *m/z* Calcd for C_7H_7BrNO: MH^+, 199.9711 and 201.9691. Found: *m/z* 199.9631 and 201.9688.

2-Acetyl-6-methylpyridine. Oil; *Rf* = 0.30 (10 % EtOAc in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (1H, d, *J* = 7.7 Hz), 7.69 (1H, t, *J* = 7.7 Hz), 7.31 (1H, d, *J* = 7.7 Hz), 2.71 (3H, s), 2.61 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.6, 158.0, 153.2, 136.8, 126.6, 118.7, 25.7, 24.4; MS (EI) *m/z* (rel intensity) 135 (M^+, 84). HRMS Calcd for C_8H_9NO: M^+, 135.0684. Found: *m/z* 135.0677.

2-Acetyl-6-(*tert*-butyldimethylsilyl)oxymethylpyridine. Oil; *Rf* = 0.42 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (1H, d, *J* = 7.7 Hz), 7.83 (1H, t, *J* = 7.7 Hz), 7.67 (1H, d, *J* = 7.7 Hz), 4.87 (2H, s), 2.69 (3H, s), 0.97 (9H, s), 0.14 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 160.9, 152.6, 137.2, 123.5, 119.7, 66.0, 25.9, 25.6, 18.3, -5.4; IR (film) 1700 cm^{-1}; MS (FAB) *m/z* (rel intensity) 266 (MH^+, 50). HRMS Calcd for $C_{14}H_{24}NO_2Si$: MH^+, 266.1576. Found: *m/z* 266.1575.

2-Acetyl-6-phenylpyridine. Colorless crystals, mp 75-76 °C (hexane), *Rf* = 0.33 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (2H, dm, *J* = 7.1 Hz), 7.97 (1H, dd, *J* = 7.6 and 1.4 Hz), 7.92 (1H, dd, *J* = 7.6 and 1.4 Hz), 7.88 (1H, t, *J* = 7.6 Hz), 7.51 (2H, tm, *J* = 7.1 Hz), 7.45 (1H, tm, *J* = 7.1 Hz), 2.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 156.4, 153.4, 138.4, 137.6, 129.4, 128.8, 126.9, 123.4, 119.7, 25.7; IR (film) 1695 cm^{-1}; MS (EI) *m/z* (rel intensity,) 197 (M^+, base), 169 (49), 155 (81), 154 (69), 127 (33). HRMS Calcd for $C_{13}H_{11}NO$: M^+, 197.0841. Found: *m/z* 197.0825.

6-Acetyl-2,2'-bipyridine. Colorless crystals, mp 73-74 °C (hexane), *Rf* = 0.30 (10% EtOAc in hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (1H, dm, *J* = 4.9 Hz), 8.63(1H, dd, *J* = 7.7 and 1.2 Hz), 8.54 (1H, dm, *J* = 7.8 Hz), 8.06 (1H, dd, *J* = 7.7 and 1.2 Hz), 7.96 (1H, t, *J* = 7.7 Hz), 7.87 (1H, td, *J* = 7.8 and 1.2 Hz), 7.36 (1H, ddd, *J* = 7.8, 4.8 and 1.2 Hz), 2.83 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.2, 155.4, 155.4, 152.9, 149.2, 137.8, 137.0, 124.3, 124.1, 121.4, 121.1, 25.7; IR (KBr) 1695 cm^{-1}; MS (EI) *m/z* (rel intensity) 198 (M^+, base), 171 (23), 156 (77), 155 (64); HRMS Calcd for $C_{12}H_{10}N_2O$: M^+, 198.0793. Found: *m/z* 198.0780. Anal.

Calcd for $C_{12}H_{10}N_2O$: C, 72.71; H, 5.08; N, 14.13. Found: C, 72.57; H, 5.05; N, 14.20.

6-Acetyl-6'-[(*tert*-butyldimethylsilyl)oxymethyl]-2,2'-bipyridine. Colorless crystals, mp 54-56 °C (hexane), *Rf* = 0.41 (10% EtOAc in hexane); ^1H NMR (300 MHz, $CDCl_3$) δ 8.61 (1H, dd, *J* = 7.8 and 1.1 Hz), 8.38 (1H, d, *J* = 7.7 Hz), 8.04 (1H, dd, *J* = 7.8 and 1.1 Hz), 7.94 (1H, t, *J* = 7.7 Hz), 7.88 (1H, t, *J* = 7.8 Hz), 7.58 (1H, d, *J* = 7.7 Hz), 4.93 (2H, s), 2.84 (3H, s), 0.99 (9H, s), 0.16 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.4, 161.0, 155.5, 154.2, 152.9, 137.7, 137.5, 124.3, 121.3, 120.5, 119.1, 66.2, 25.9, 25.7, 18.4, -5.3; IR (KBr) 1700 cm^{-1}; MS (EI) *m/z* (rel intensity) 327 (M^+-15, 3), 270 (42), 255 (9), 227 (6). Anal. Calcd for $C_{19}H_{26}N_2O_2Si$: C, 66.63; H, 7.65; N, 8.18. Found: C, 66.33; H, 7.70; N, 8.18.