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SUPPORTING INFORMATION

Title: Mild and Ligand-Free Palladium-Catalyzed Cross-Couplings between Aryl Halides and Arylboronic Acids for the Synthesis of Biaryls and Heterocycle-Containing Biaryls

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Ref. No.: O200600879

(A) Typical Experimental Procedure for the Palladium-Catalyzed Suzuki-Miyaura Cross-Coupling Reaction. A mixture of aryl halide **1** (0.5 mmol), arylboronic acid **2** (0.6 mmol), $Pd(OAc)_2$ (1 mol-%), NaOMe (1 mol) and MeOH or EtOH (1 mL) was stirred at room temperature for the indicated time until complete consumption of starting material as monitored by TLC. After the mixture was filtered and evaporated, the residue was then purified by flash column chromatography (hexane or hexane/ethyl acetate) to afford the corresponding coupled product.

(B) Analytical data for 3─9, 11─18 and 20─27

4-Methoxy-biphenyl (3)[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.60─7.56 (m, 4H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.5, 1H), 7.02 (d, *J* = 9.0, 2H), 3.89 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.2, 140.9, 133.8, 128.7, 128.2, 126.8, 126.7, 114.2, 55.4.

LRMS (EI, 20 eV) *m/z* (%): 184 (M^+, 100).

4,4'-Dimethoxy-biphenyl (4)[1]

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.48 (d, *J* = 8.4 Hz, 4H), 6.95 (d, *J* = 8.87 Hz, 4H), 3.84 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 158.7, 133.5, 127.7, 114.1, 59.3.

LRMS (EI, 20 eV) *m/z* (%): 214 (M^+, 100).

4-Fluoro-4'-methoxy-biphenyl (5)[1]

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.50─7.45 (m, 4H), 7.09 (t, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.7 Hz, 2H), 3.83 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.7, 160.4, 159.0, 132.7, 128.2 (d, *J* = 9.3 Hz, 1C), 128.0, 115.5 (d, *J* = 28.2 Hz, 1C), 114.2, 55.3.

LRMS (EI, 20 eV) *m/z* (%): 202 (M^+, 100).

4-Nitro-biphenyl (6)[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.32 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 6.9 Hz, 2H), 7.55─7.48 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 147.6, 147.1, 138.8, 129.2, 128.9, 127.8, 127.4, 124.1.

LRMS (EI, 20 eV) *m/z* (%): 199 (M^+, 100).

4-Nitro--4'-methoxybiphenyl (7)[1]

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.25 (d, *J* = 9.0 Hz, 2H), 7.68 (d, *J* = 9.0 Hz, 2H), 7.57 (d, *J* = 9.0 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 160.4, 147.2, 146.5, 131.0, 128.5, 127.0, 124.1, 114.6, 55.4.

LRMS (EI, 20 eV) *m/z* (%): 229 (M^+, 100).

4-Nitro--4'-fluorobiphenyl (8)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 8.8 Hz, 2H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.59 (dd, *J* = 5.6 Hz, 5.6 Hz, 2H), 7.20 (t, *J* = 8.4 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.6, 162.1, 146.5, 134.9, 129.1 (d, *J* = 8.6 Hz, 1C), 127.6, 124.2, 116.2 (d, *J* = 21.7 Hz, 1C).

LRMS (EI, 20 eV) *m/z* (%): 217 (M^+, 100).

2-(4-Nitrophenyl)thiophene (9)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.23 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 9.6 Hz, 2H), 7.48 (d, *J* = 4.0 Hz, 1H), 7.44 (d, *J* = 5.2 Hz, 1H), 7.15 (t, *J* = 4.4 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.6, 141.6, 140.6, 128.7, 127.7, 126.0, 125.7, 124.4.

LRMS (EI, 20 eV) *m/z* (%): 205 (M^+, 100).

1-Biphenyl-4-yl-ethanone (11)[1]

^{1}H NMR (300 MHz, $CDCl_3$) δ: 8.04 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.50─7.40 (m, 3H), 2.64 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): δ 198.1, 146.1, 140.2, 136.2, 130.1, 129.2, 128.6, 127.6, 118.5, 27.0.

LRMS (EI, 20 eV) *m/z* (%): 196 (M^+, 100).

4-Phenylbenzonitrile (12)[1]

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.63 (d, *J* = 8.8 Hz, 2H), 7.52-7.44 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ: 146.7, 139.2, 132.6, 129.1, 128.7, 127.7, 127.2, 118.9, 111.0.

LRMS (EI, 20 eV) *m/z* (%): 179 (M^+, 100).

Methyl 2-phenyl-5-nitrobenzoate (13)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.69 (s, 1H), 8.37 (d, *J* = 8.8 Hz, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.44 (t, *J* = 6.8 Hz, 3H), 7.33 (d, *J* = 7.6 Hz, 2H), 3.72 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 166.9, 148.7, 146.7, 139.0, 132.0, 131.9, 128.5, 128.4, 128.0, 125.6, 125.1, 52.5.

LRMS (EI, 20 eV) *m/z* (%):259 (M^+, 12), 257 (M^+, 81), 226 (100).

Biphenyl (14)[1]

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.59 (d, *J* = 8.4 Hz, 4H), 7.43 (t, *J* = 7.2 Hz, 4H), 7.36 (t, *J* = 7.8 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ: 141.6, 129.1, 127.6, 127.5.

LRMS (EI, 20 eV) *m/z* (%): 154 (M^+, 100).

2-Phenylthiophene (15)[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.61─7.57 (m, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.29─7.23 (m, 2H), 7.05 (t, *J* = 4.0 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 144.4, 134.3, 128.8, 127.9, 127.4, 125.9, 124.7, 123.0.

LRMS (EI, 20 eV) *m/z* (%): 160 (M^+, 100).

4-Methyl-biphenyl (16)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (t, *J* = 7.6 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.42 (t, J = 7.6 Hz, 2H), 7.31 (t, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.1, 138.3, 137.0, 129.5, 128.7, 127.3, 127.2, 127.0, 21.1.

LRMS (EI, 20 eV) *m/z* (%): 168 (M^+, 100).

2-Methyl-biphenyl (17)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40 (t, *J* = 7.2 Hz, 2H), 7.32 (t, *J* = 6.8 Hz, 3H), 7.25-7.23 (m, 4H), 2.27 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.9, 135.3, 130.3, 129.8, 129.2, 128.0, 127.2, 126.7, 125.7, 125.6, 20.4.

LRMS (EI, 20 eV) *m/z* (%): 168 (M^+, 100).

3,5-Dimethyl-biphenyl (18)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, *J* = 8.4 Hz, 2H), 7.44─7.40 (m, 2H), 7.31─7.28 (m, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 9.2 Hz, 1H), 2.35 (s, 3H), 2.37 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 141.5, 138.1, 128.9, 128.7, 127.9, 127.2, 127.1, 125.1, 21.4.

LRMS (EI, 20 eV) *m/z* (%): 182 (M^+, 100).

2-Methoxy-5-phenylpyridine (20)

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (s, 1H), 7.79 (d, *J* = 2.8 Hz, 1H), 7.54─7.52 (m, 2H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.6, 145.0, 137.9, 137.4, 130.1, 128.9, 127.3, 126.7, 110.8, 53.5; LRMS (EI, 20 eV) *m/z* (%): 185 (M^+, 100); HRMS (EI) for $C_{12}H_{11}NO$ (M^+): calcd. 185.0841, found 185.0840.

2-Phenylpyridine (21)[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.59 (d, *J* = 4.8 Hz, 1H), 7.99 (d, *J* = 6.8 Hz, 2H), 7.78─7.71 (m, 2H), 7.48 (t, *J* = 8.8 Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.26─7.21 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.4, 149.6, 139.3, 136.7, 128.9, 128.7, 126.9, 122.1, 120.5.

LRMS (EI, 20 eV) *m/z* (%): 155 (M^+, 100).

3-Phenylpyridine (22)[5]

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.85 (s, 1H), 8.59 (d, *J* = 6.4 Hz, 1H), 7.88 (d, *J* = 12.0 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.49 (t, *J* = 7.2 Hz, 2H), 7.43─7.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.4, 148.3, 137.8, 136.6, 134.3, 129.0, 128.1, 127.1, 123.5; LRMS (EI, 20 eV) *m/z* (%): 155 (M^+, 100).

3-Phenylquinoline (23)[6]

Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.19 (s, 1H), 8.30 (s, 1H), 8.15 (d, *J* = 8.8 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.72 (d, *J* = 7.2 Hz, 3H), 7.60─7.51 (m, 3H), 7.44 (t, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 149.9, 147.3, 137.8, 133.8, 133.2, 129.4, 129.2, 129.1, 128.1, 128.0 (2C), 127.4, 127.0; LRMS (EI, 20 eV) *m/z* (%): 205 (M^+, 100).

2-Phenylpyrazine (24)[4]

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.04 (d, *J* = 1.6 Hz, 2H), 8.65 (s, 1H), 8.52 (d, *J* = 2.4 Hz, 1H), 8.02 (d, *J* = 8.0 Hz, 2H), 7.51(t, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 152.8, 144.2, 142.9, 142.2, 136.3, 129.9, 129.0, 126.9; LRMS (EI, 20 eV) *m/z* (%): 156 (M^+, 100).

2-(Thiophen-2-yl)pyrazine (25)[7]

Slight yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.96 (s, 1H), 8.51 (s, 1H), 8.40 (s, 1H), 7.69 (d, *J* = 4.0 Hz, 1H), 7.49 (d, *J* = 5.6 Hz, 1H), 7.16 (t, *J* = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.5, 143.9, 142.3, 141.3, 140.6, 129.0, 128.4, 125.7; LRMS (EI, 20 eV) *m/z* (%): 162 (M^+, 100).

2-(Pyridin-4-yl)pyrazine (26)

Slight yellow solid, m.p. 87.6-88.4 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.11 (s, 1H), 8.79 (d, *J* = 6.0 Hz, 2H), 8.72 (s, 1H), 8.64 (s, 1H), 7.93 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.7, 150.1, 144.7, 144.6, 143.5, 142.3, 120.9; LRMS (EI, 20 eV) *m/z* (%): 157 (M^+, 100); HRMS (EI) for $C_9H_7N_3$ (M^+): calcd. 157.0640, found 157.0640.

5-Phenylpyrimidine (27)[8]

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.21 (s, 1H), 8.96 (s, 2H), 7.58 (d, J = 8.8 Hz, 2H), 7.53 (t, J = 8.8 Hz, 2H), 7.47 (t, J = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.3, 154.8, 134.2, 134.1, 129.3, 128.9, 126.7; LRMS (EI, 20 eV) *m/z* (%): 156 (M^+, 100).

(C) References

(1) (a) Liu, D.; Gao, W.; Dai, Q. Zhang, X. *Org. Lett.* **2005**, *7*, 4907. (b) Thathagar, M. B. Beckers, J.; Rothenberg, G. *Adv. Synth. Chem.* **2003**, *345*, 979. (c) Venkatraman, S.; Li, C.-J. *Org. Lett.* **1999**, *1*, 1133. (d) Akiyama, R.; Kobayashi, S. *Angew. Chem. Int. Ed.* **2001**, *40*, 3469. (e) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020. (f) Bedford, R. B.; Limmert, M. E. *J. Org. Chem.* **2003**, *68*, 8669.

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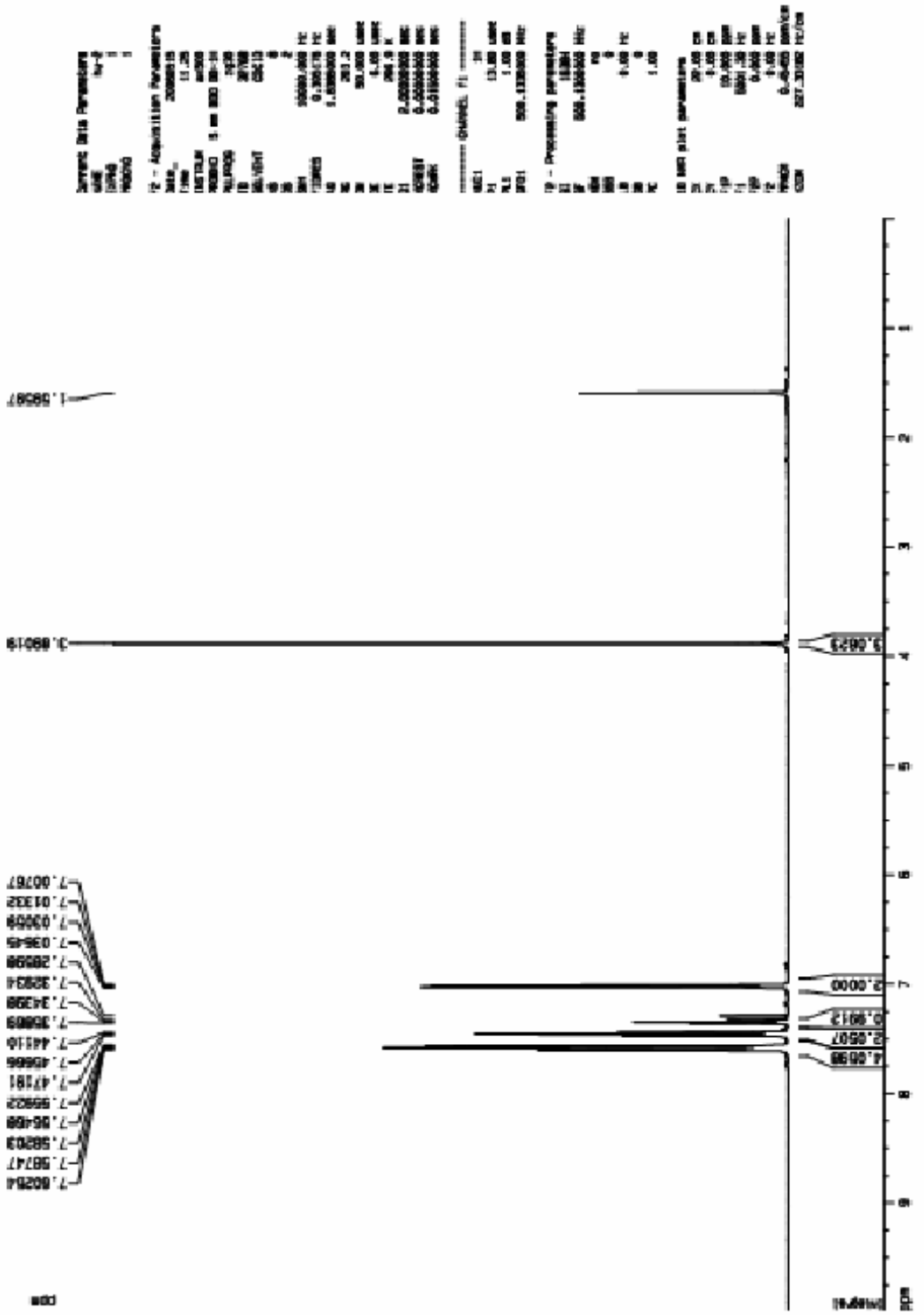
(8) Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302.

(D) Spectra

4-Methoxy-biphenyl (3)



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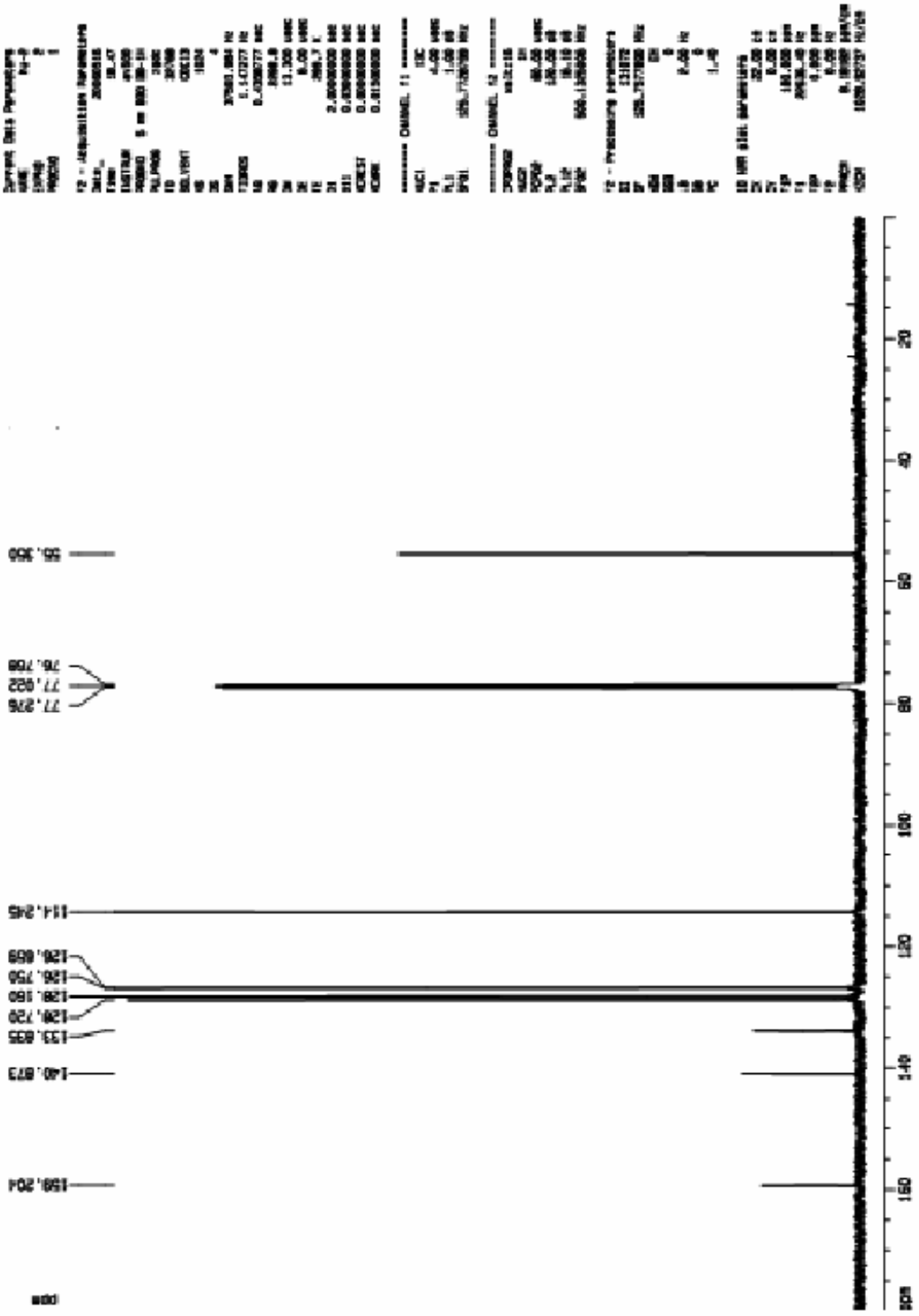
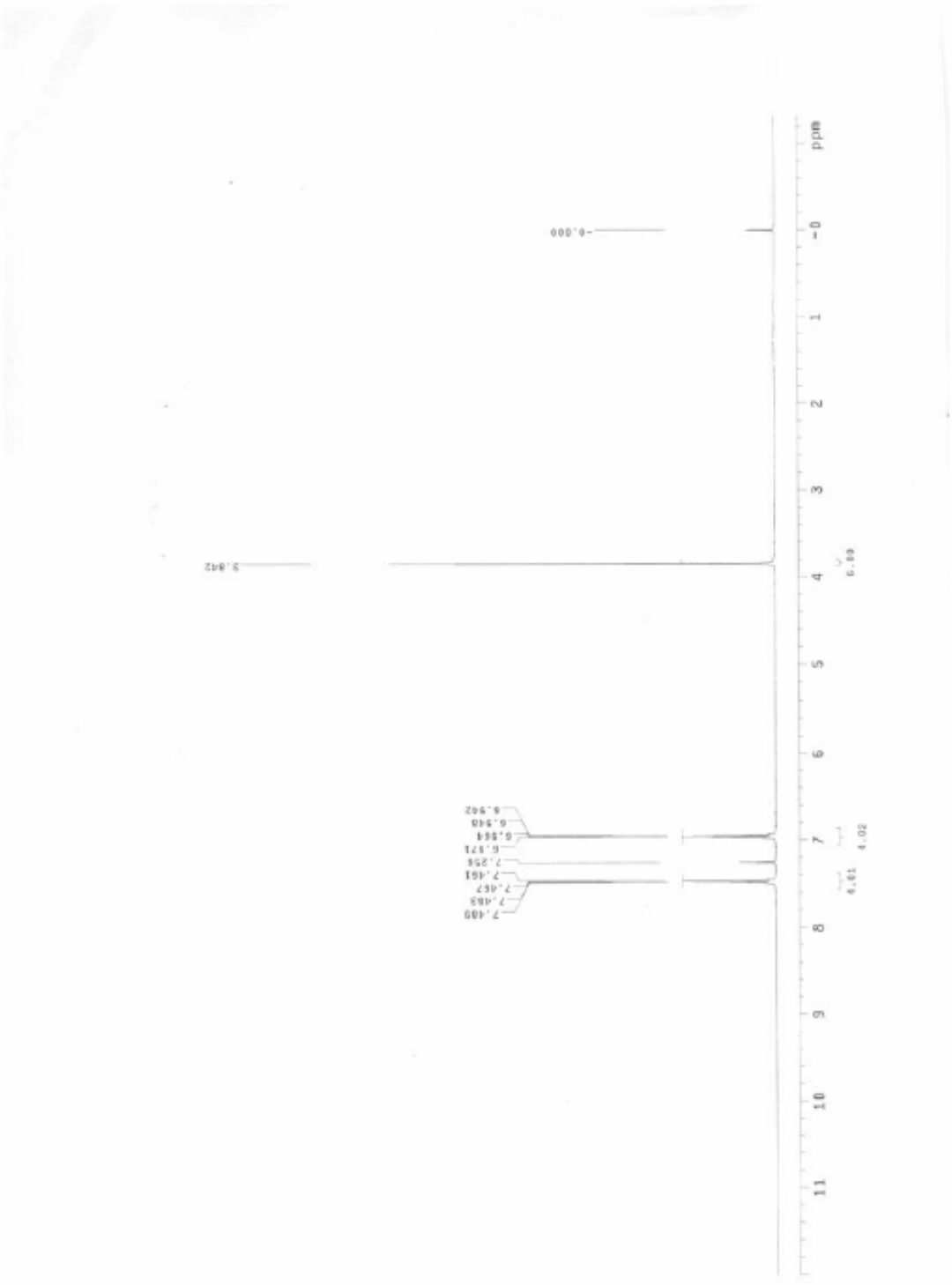
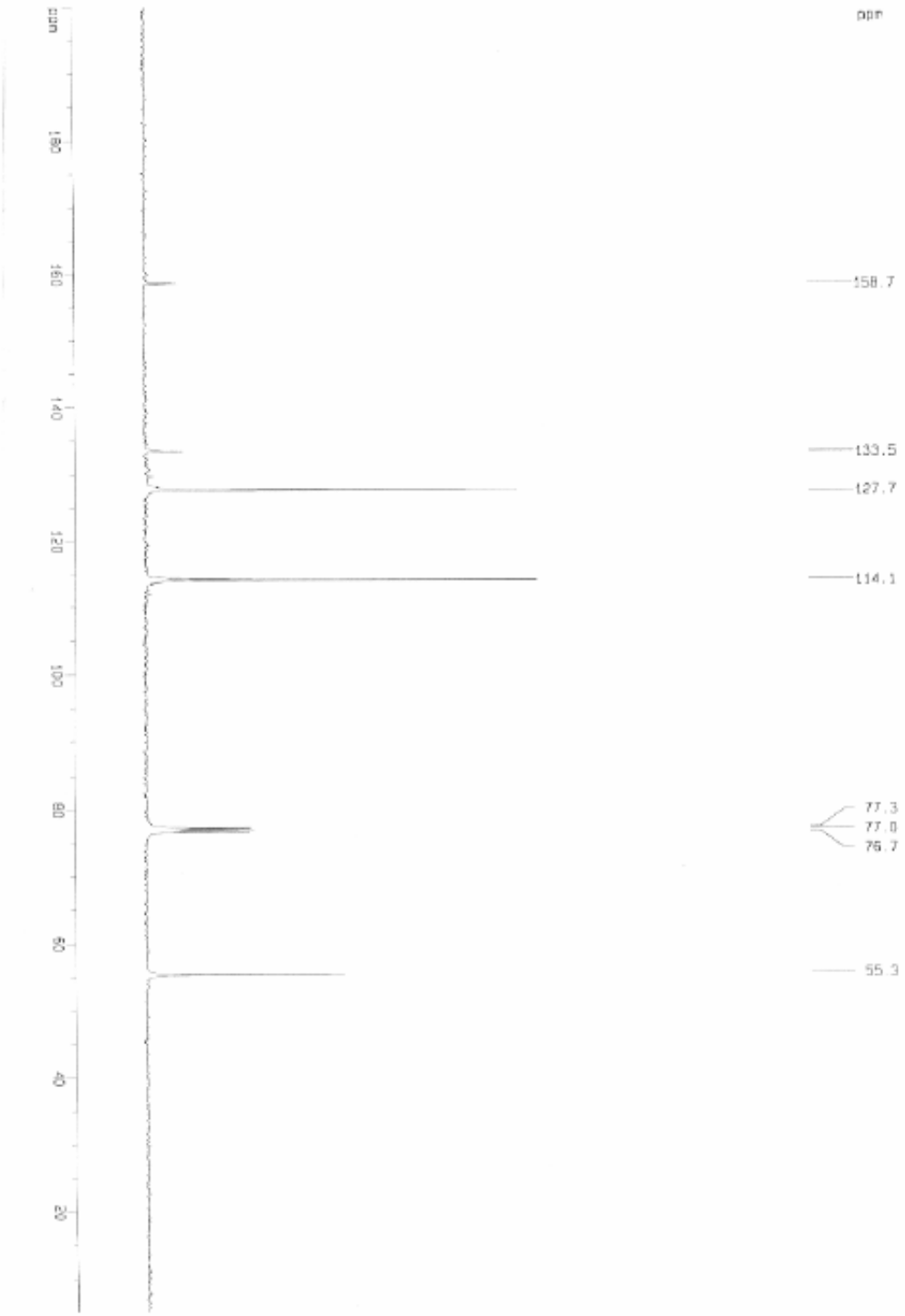


4,4'-Dimethoxy-biphenyl (4)



4,4'-Dimethoxy-biphenyl (4)



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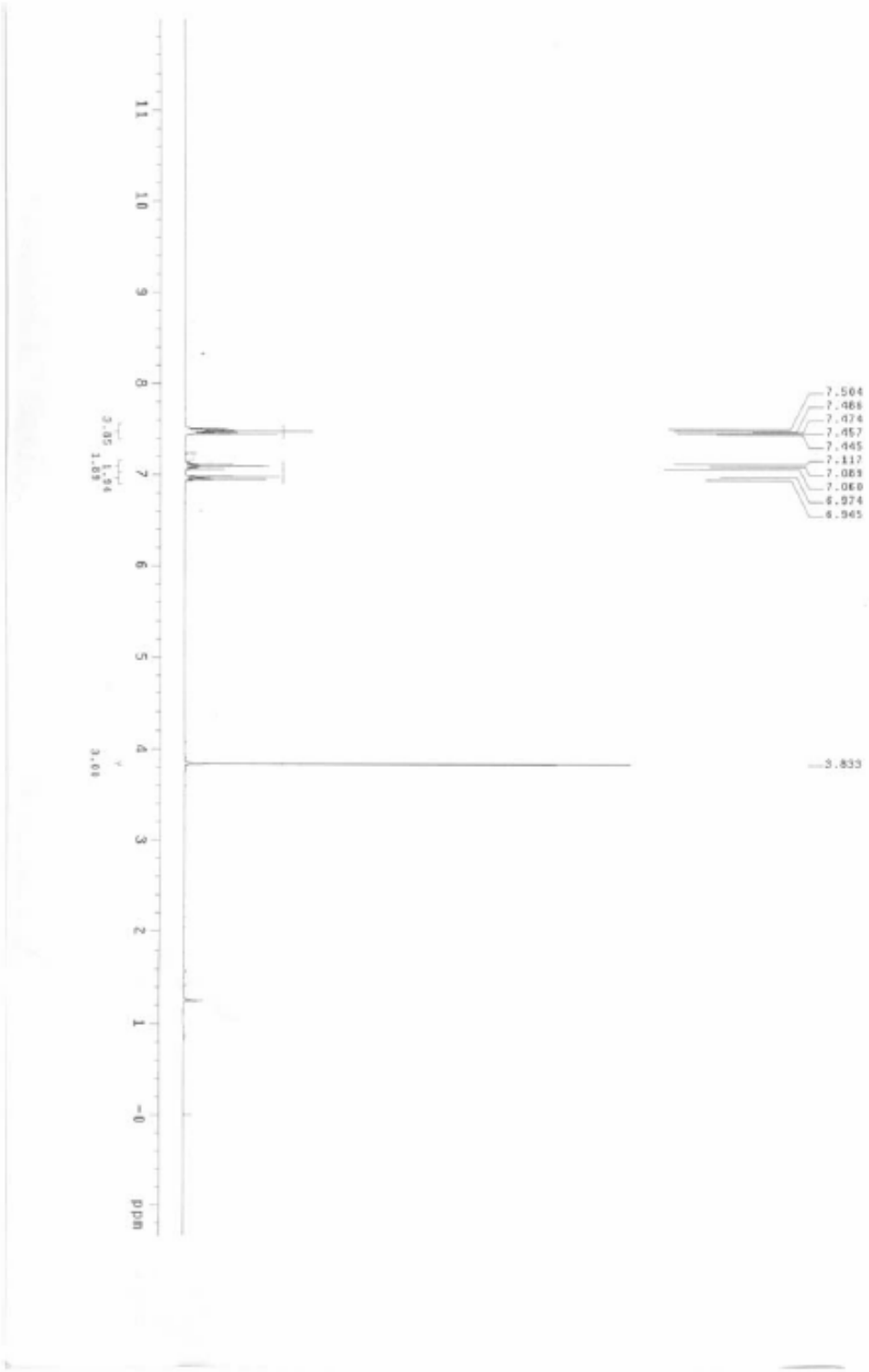

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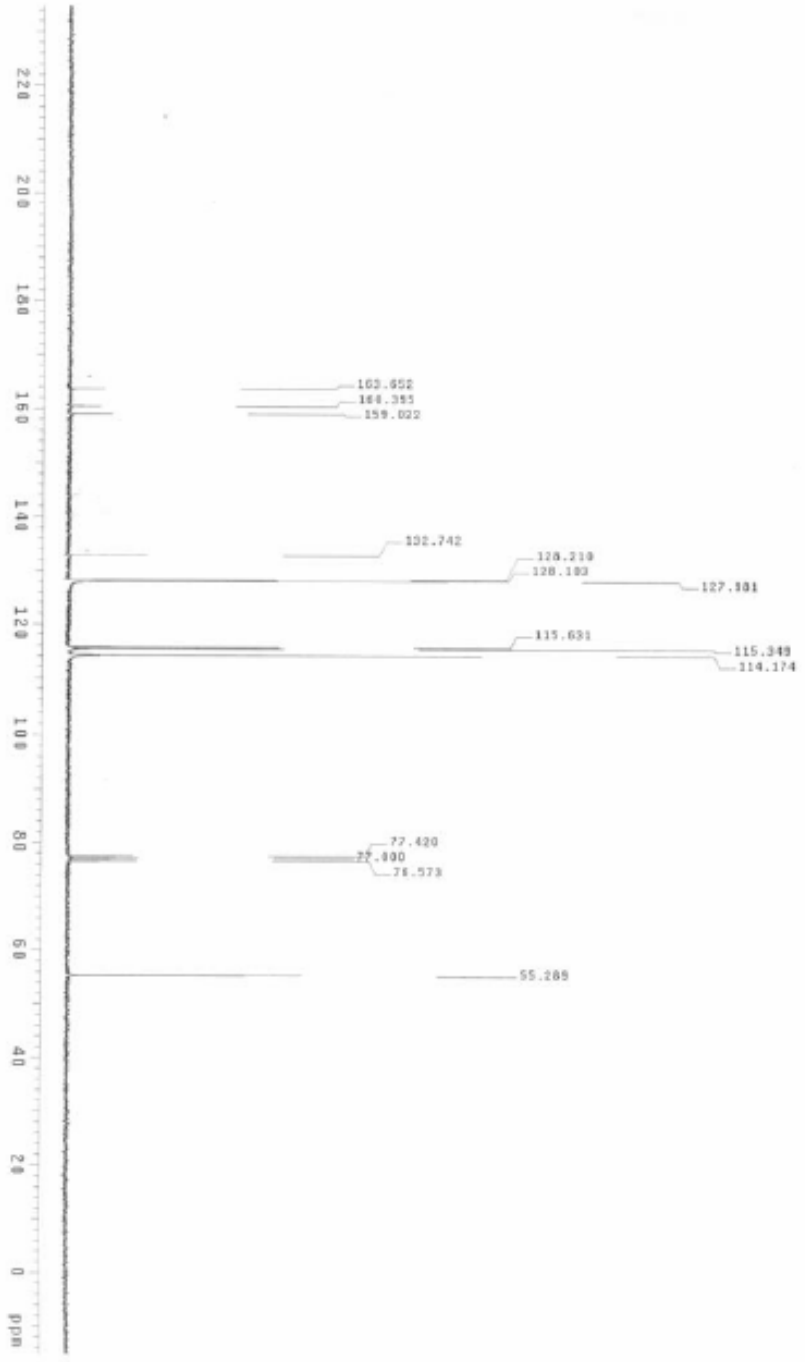

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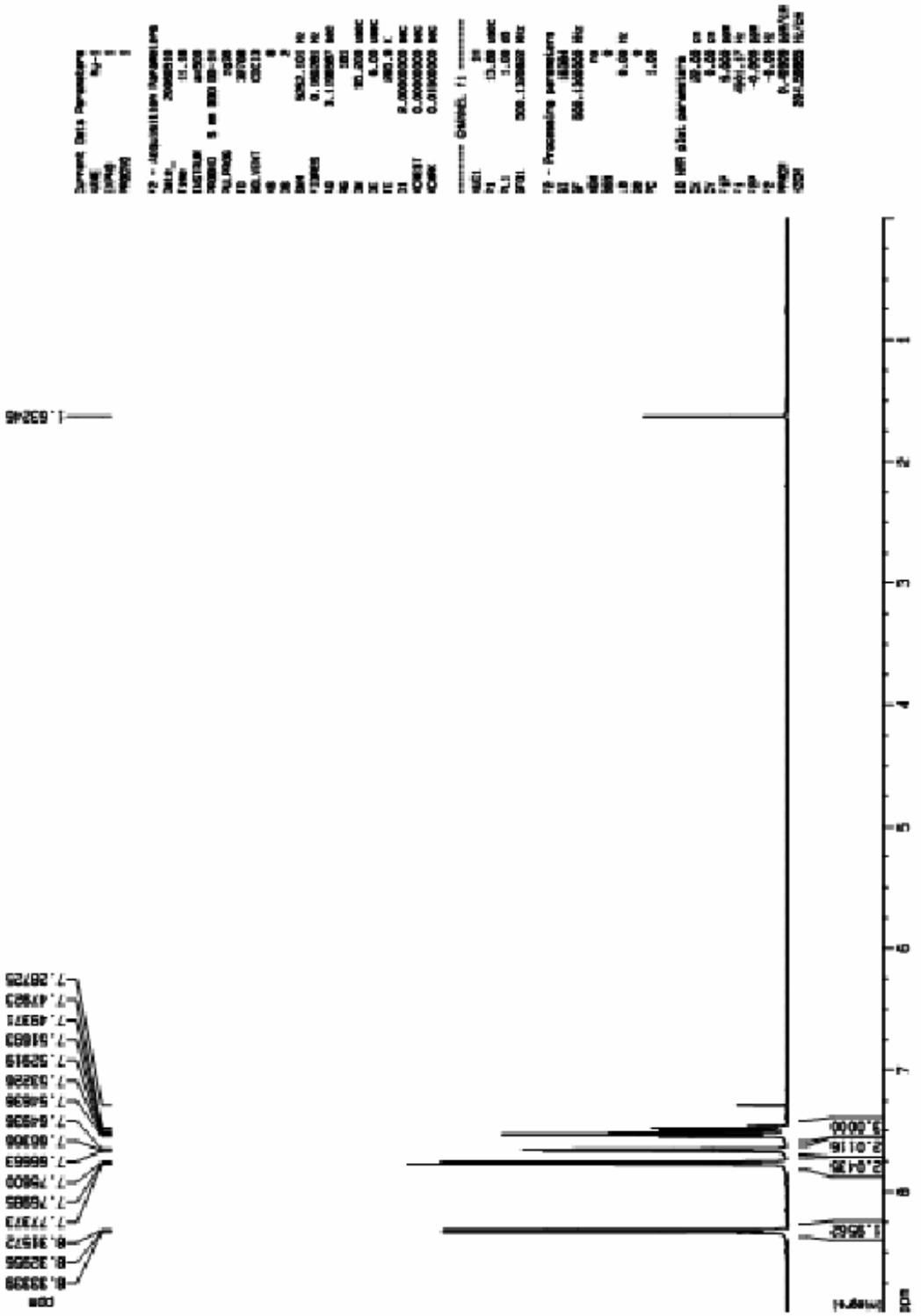

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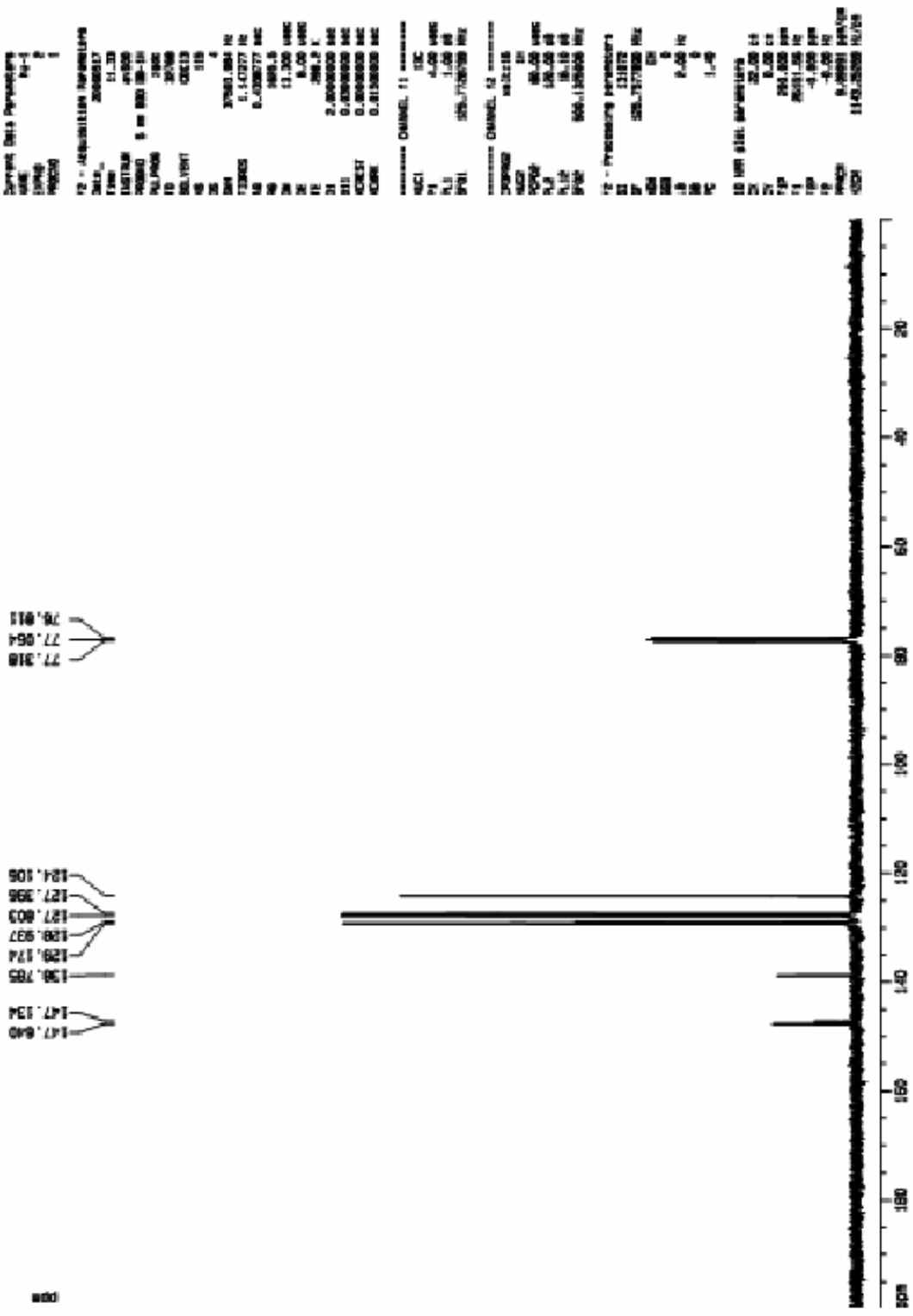

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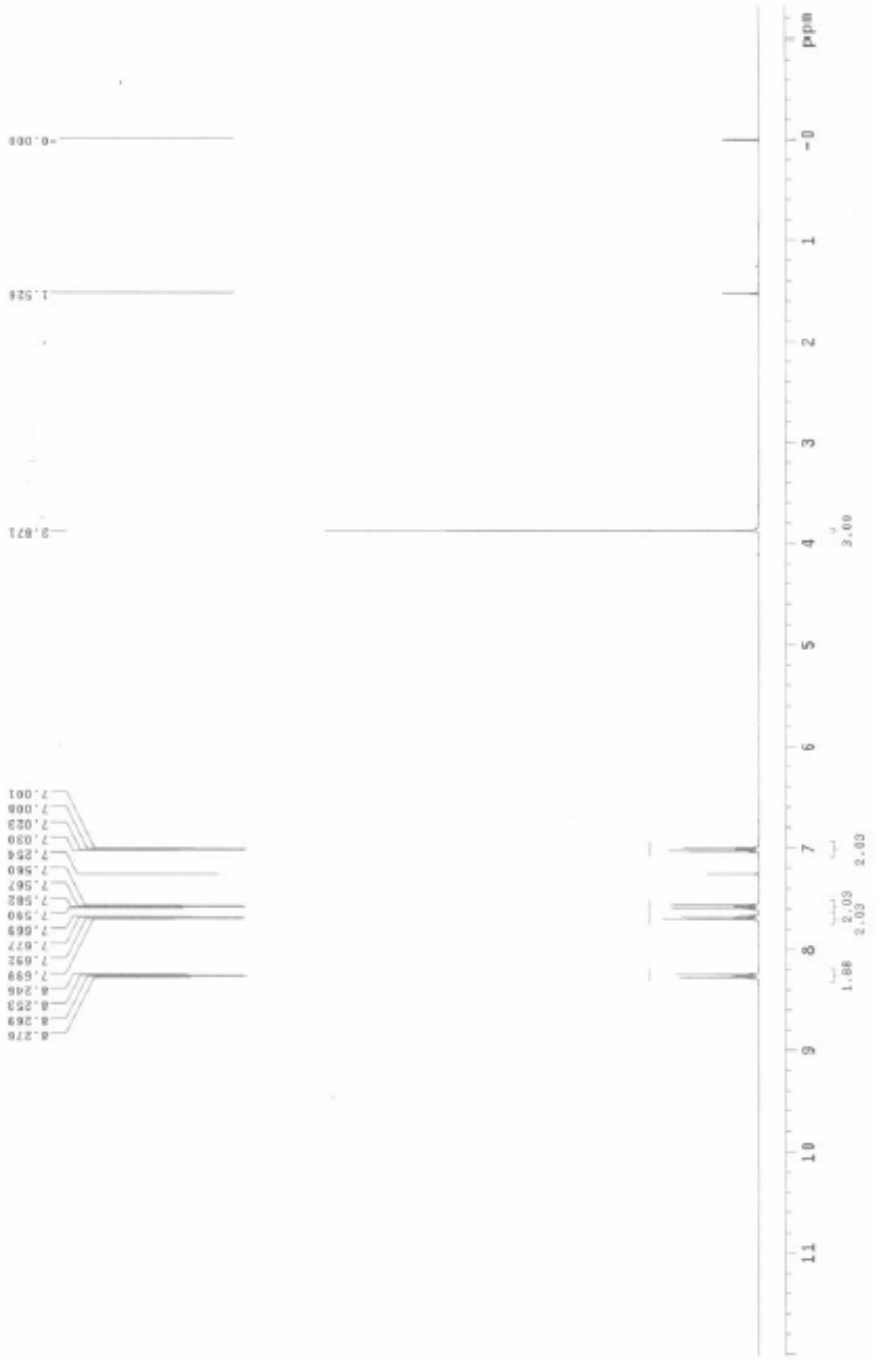

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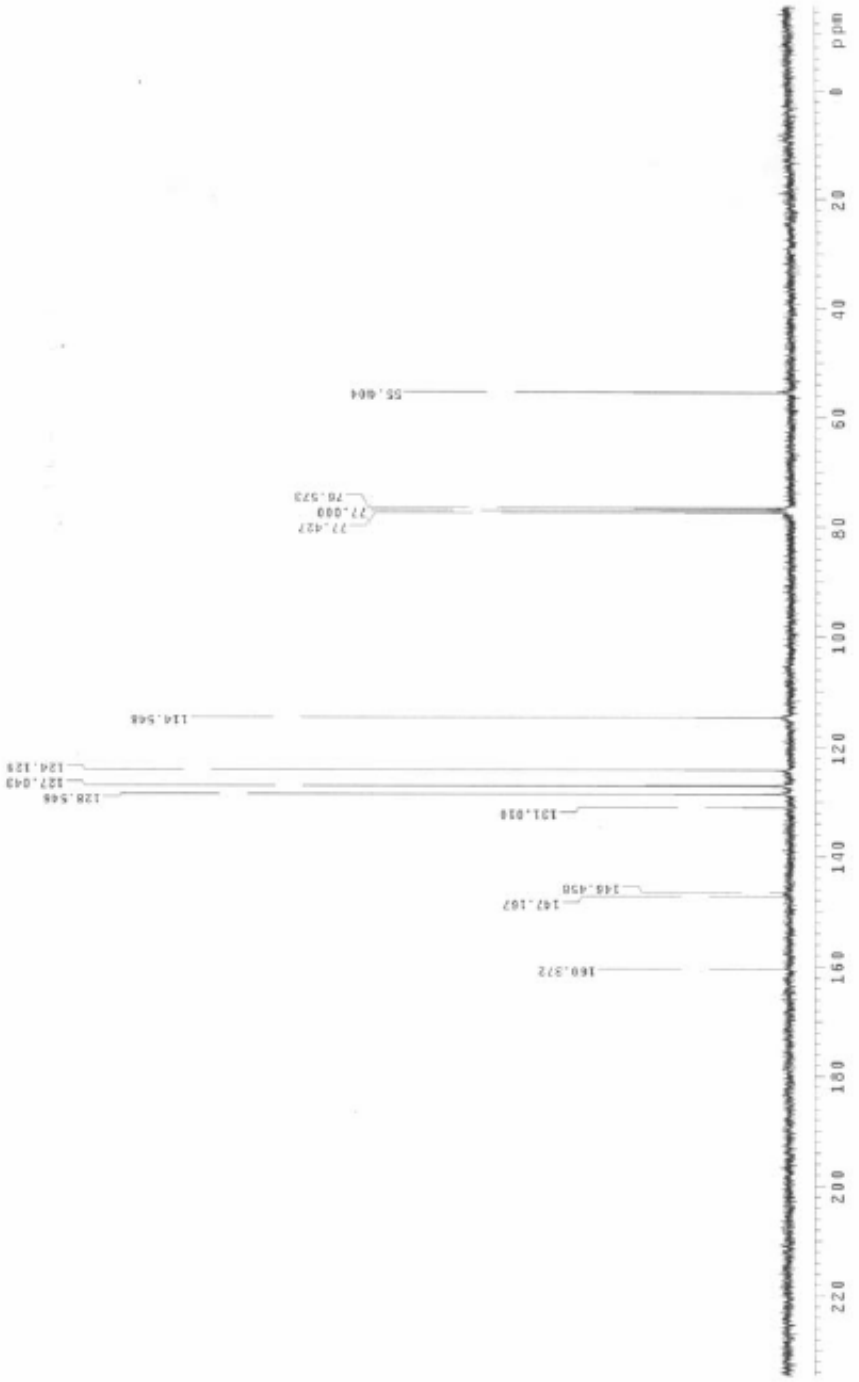
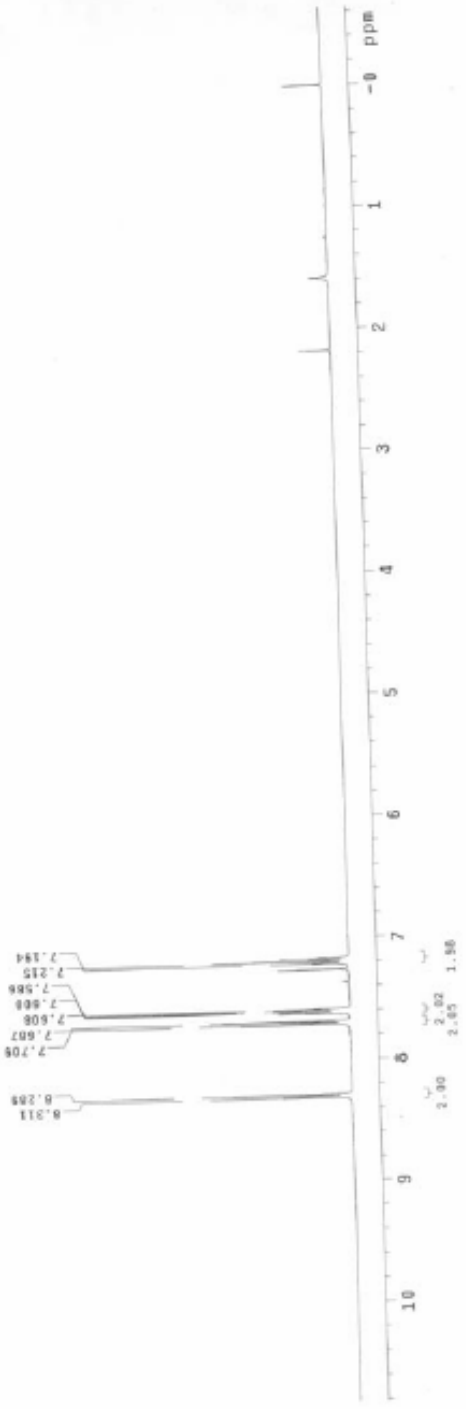


4-Nitro--4'-flurobiphenyl (8)



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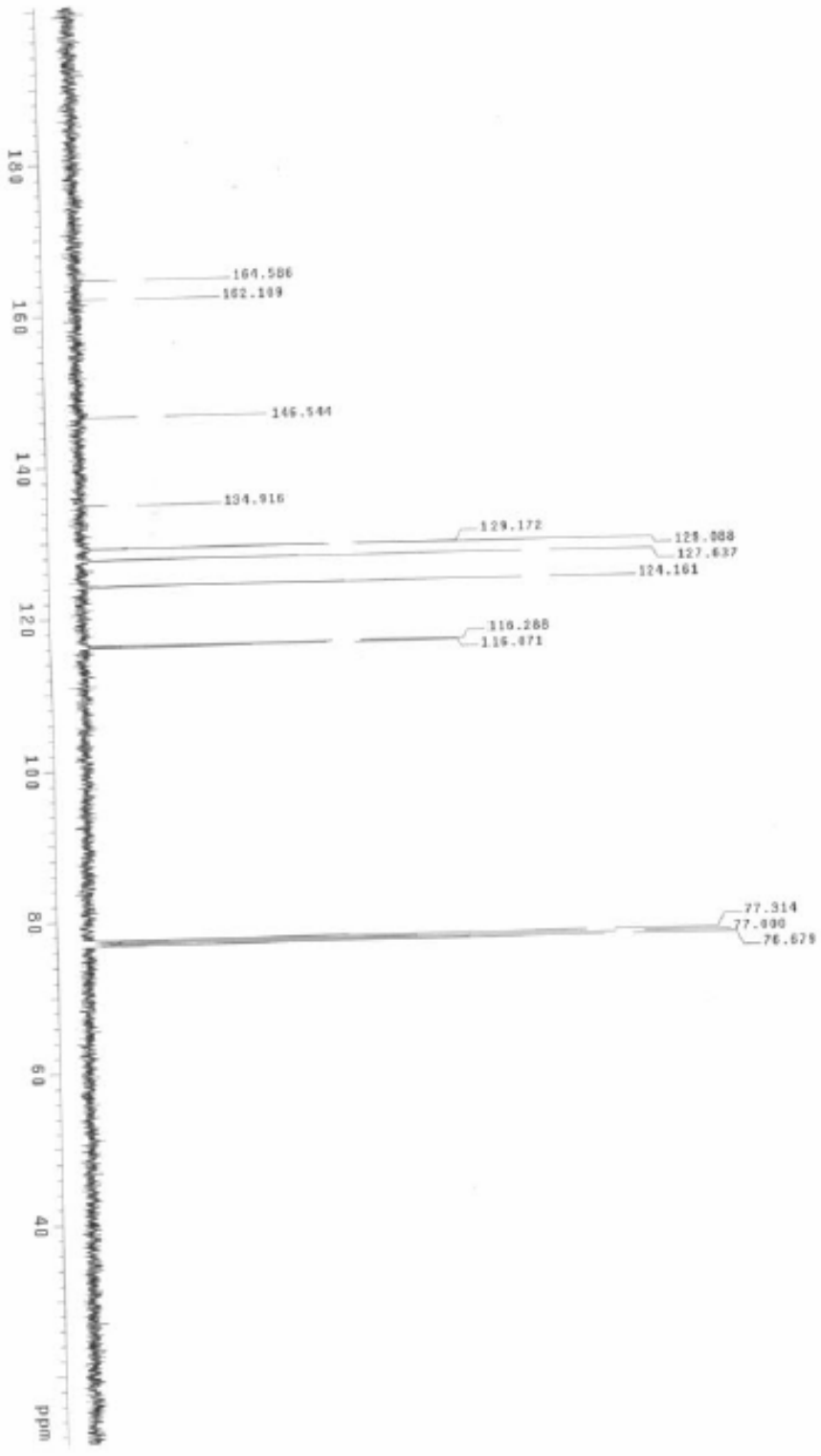
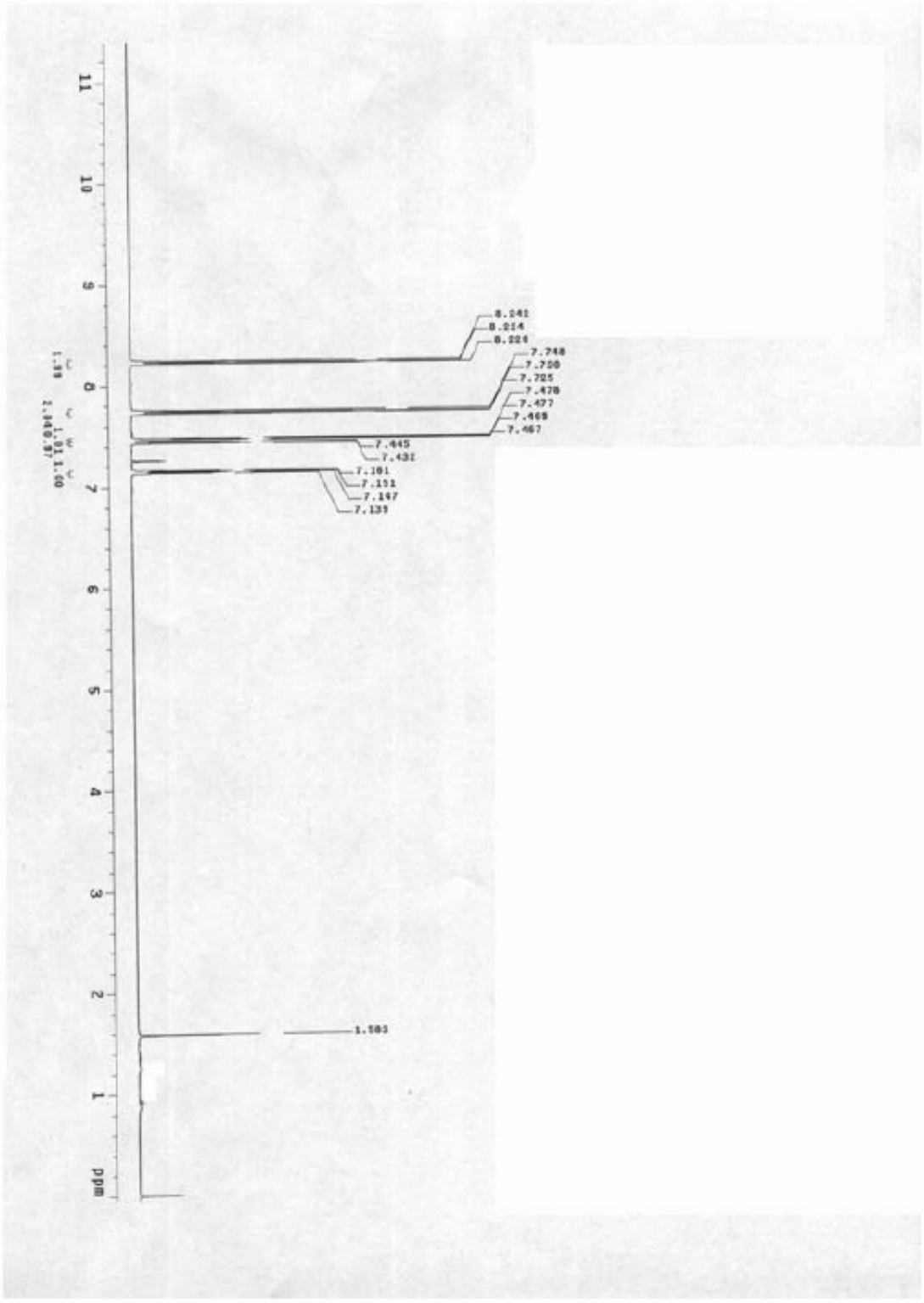
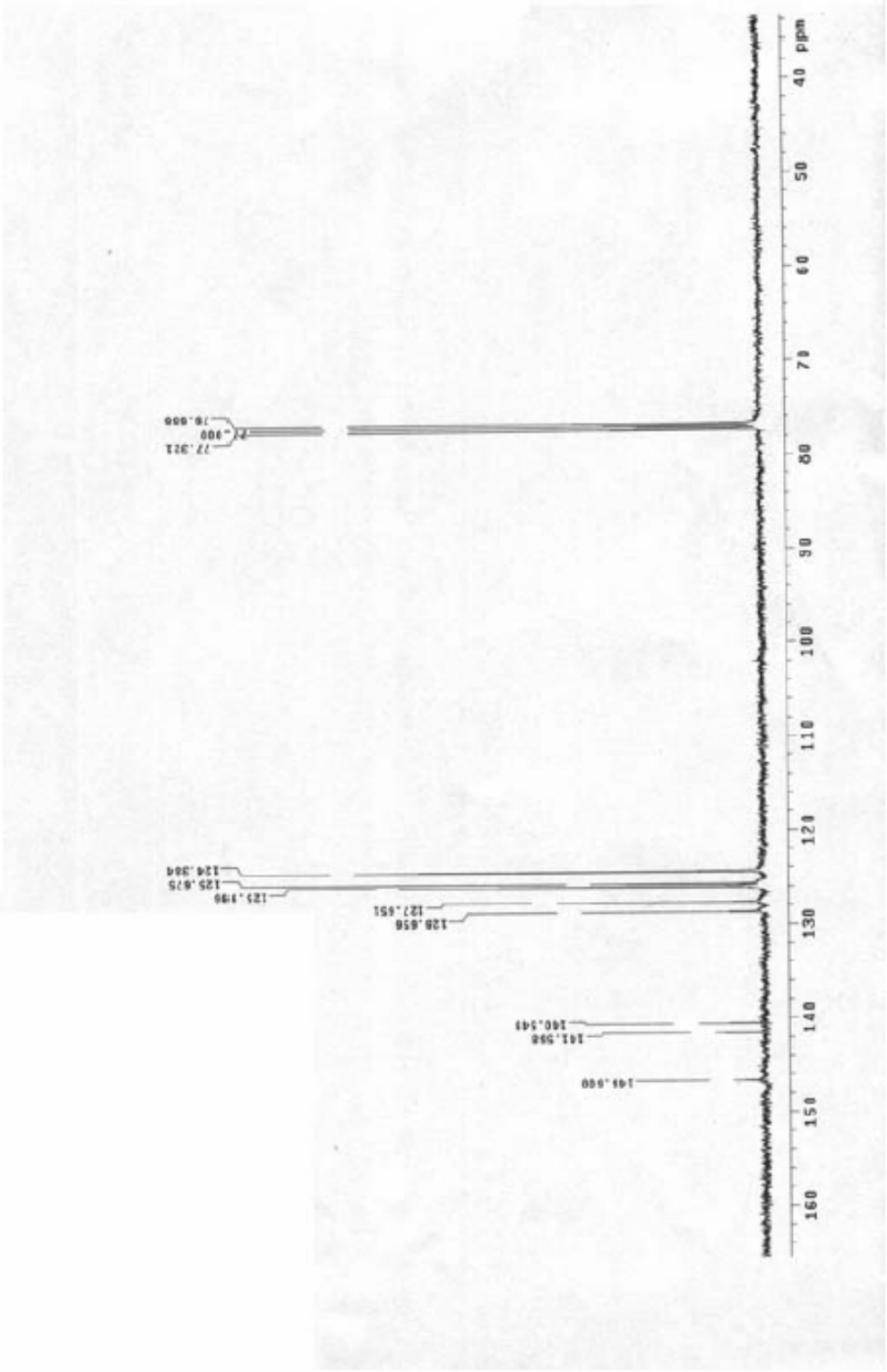


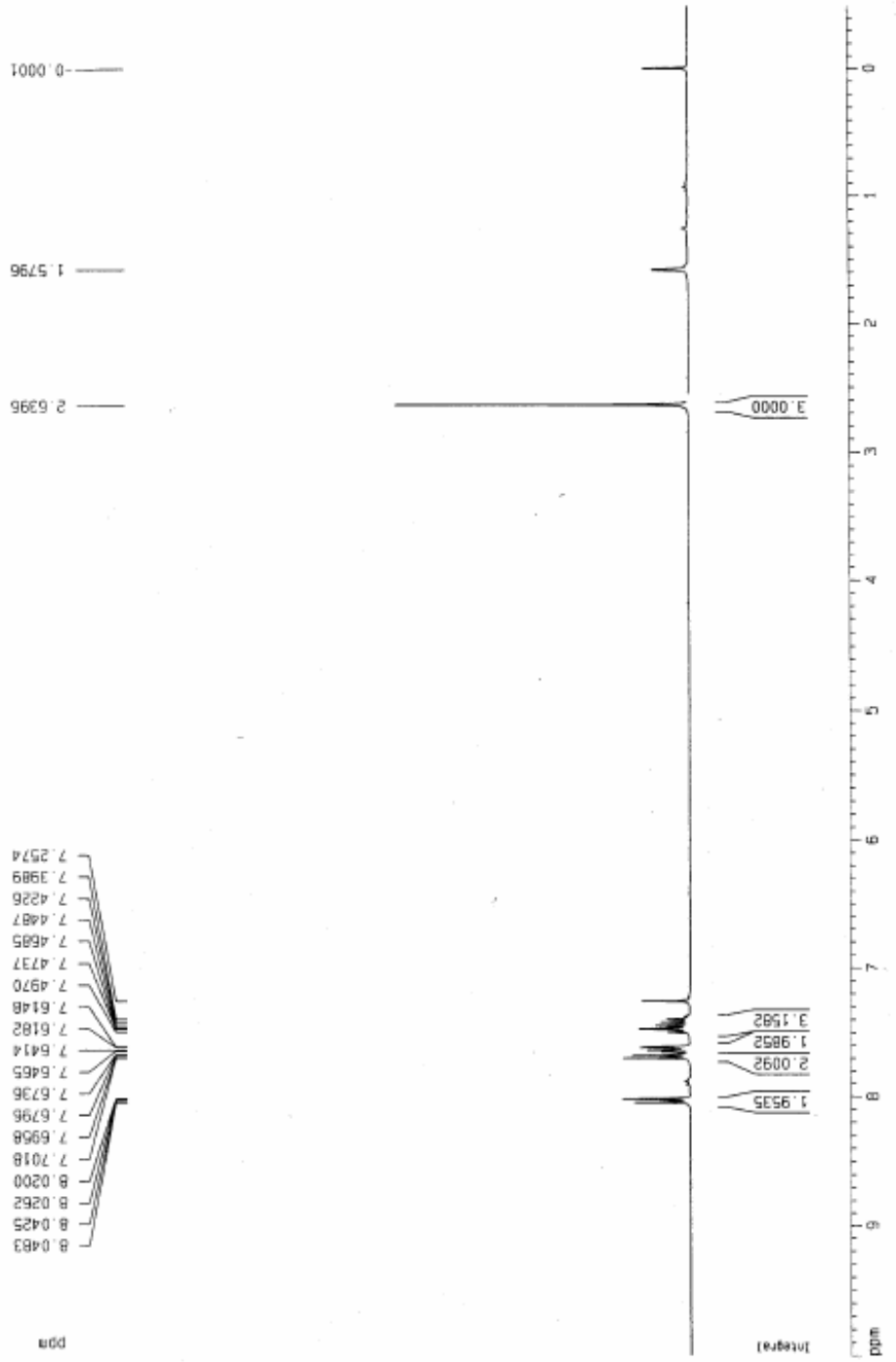
2-(4-nitrophenyl)thiophene (9)



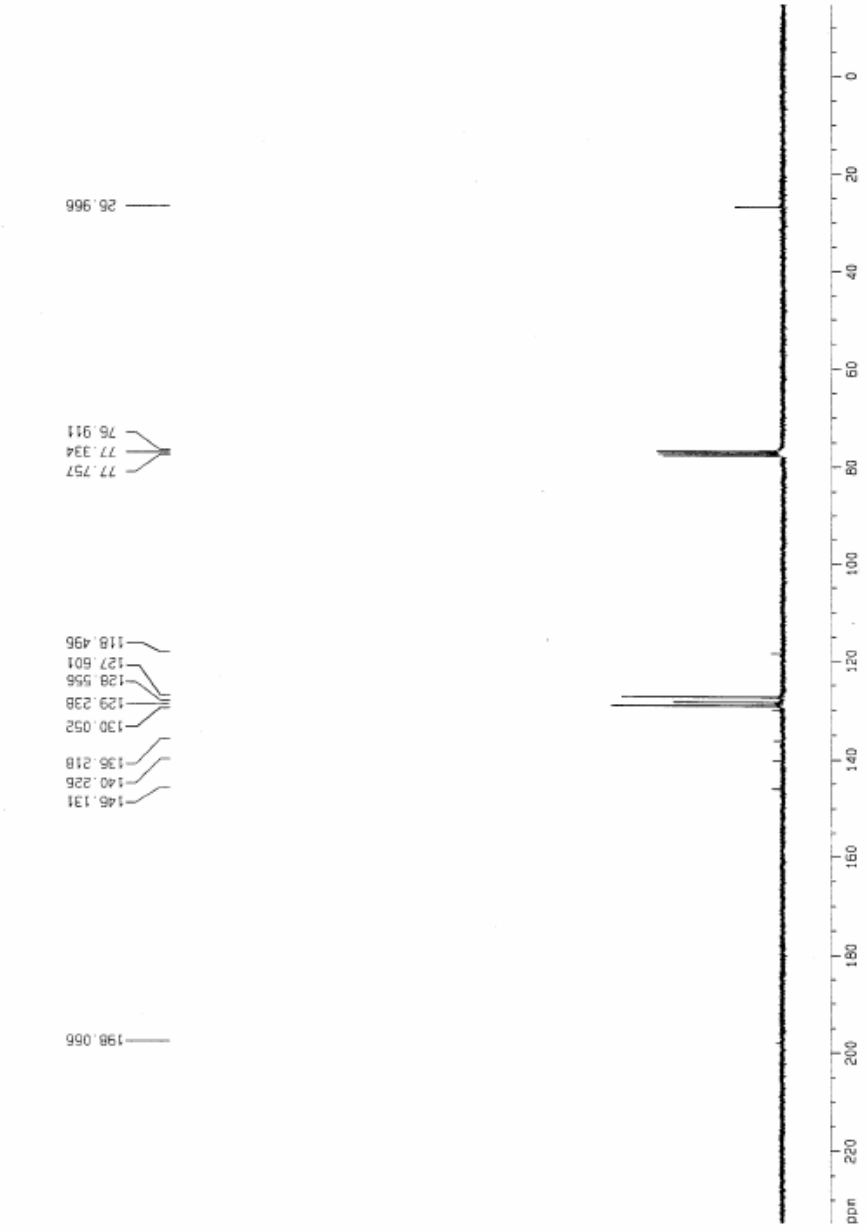
2-(4-nitrophenyl)thiophene (9)



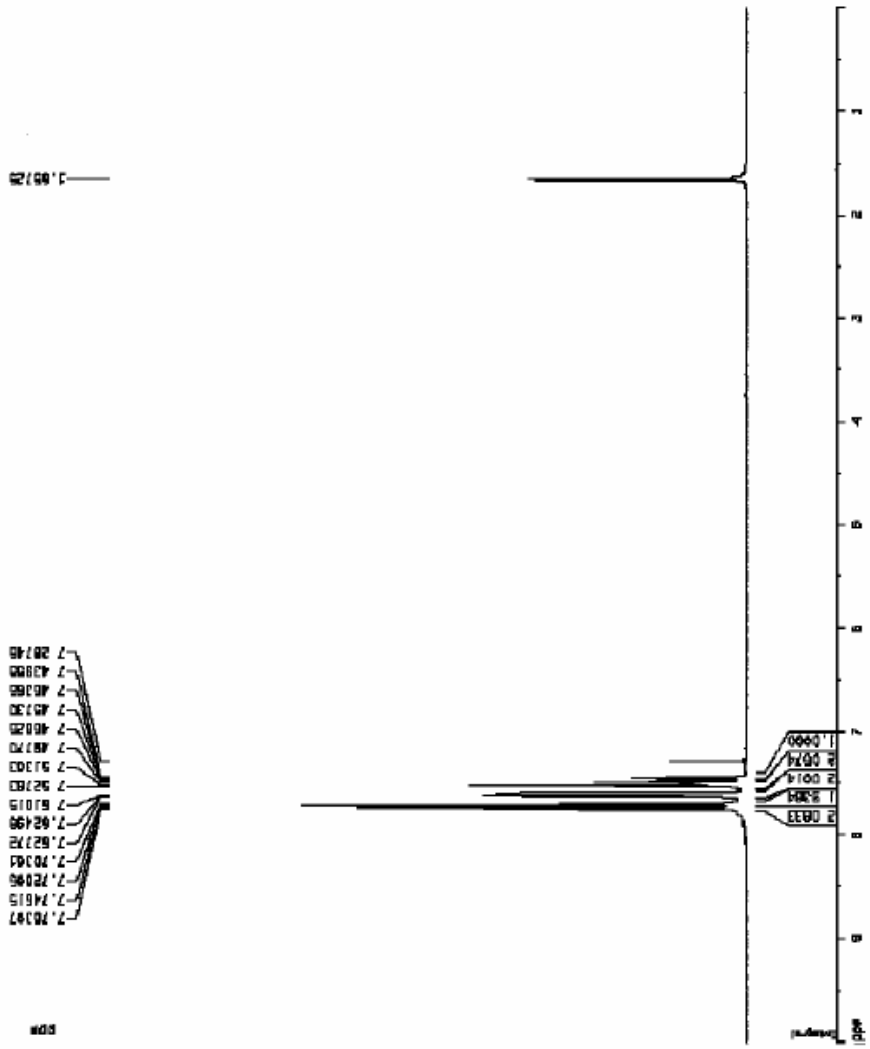
1-Biphenyl-4-yl-ethanone (11)



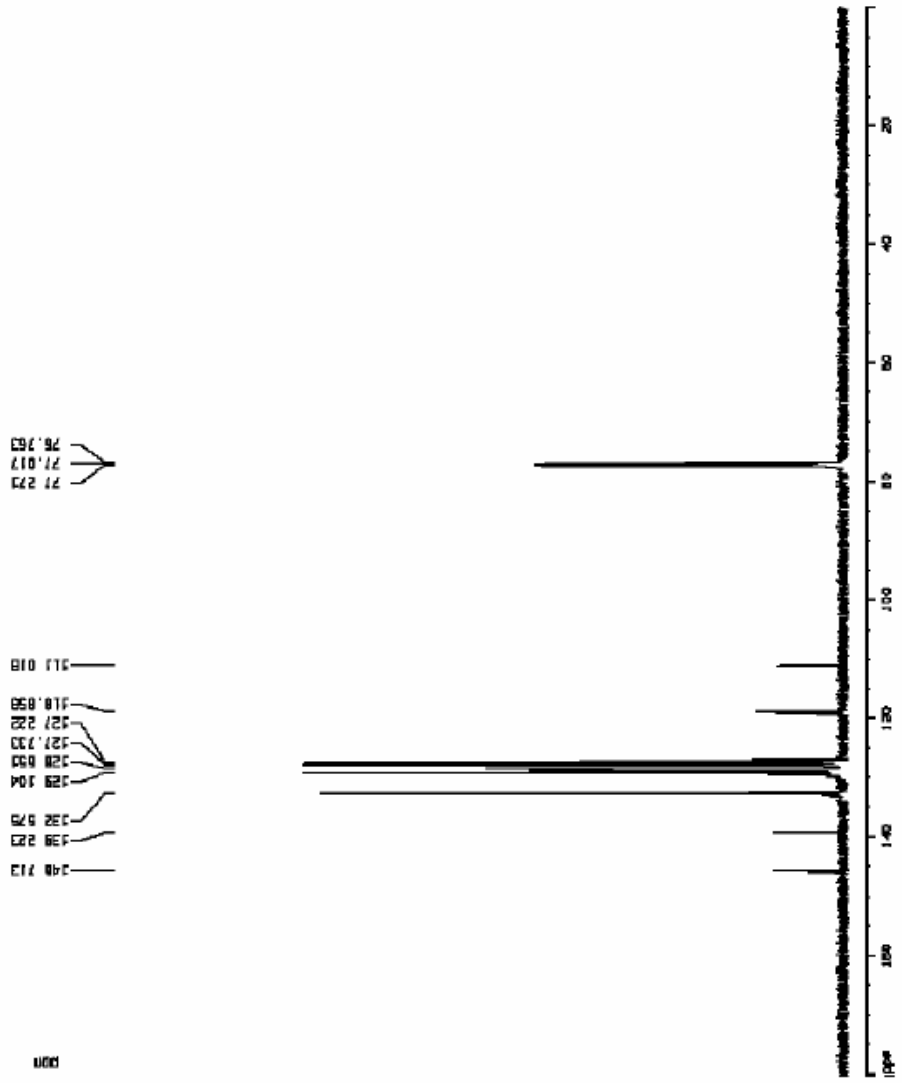
1-Biphenyl-4-yl-ethanone (11)



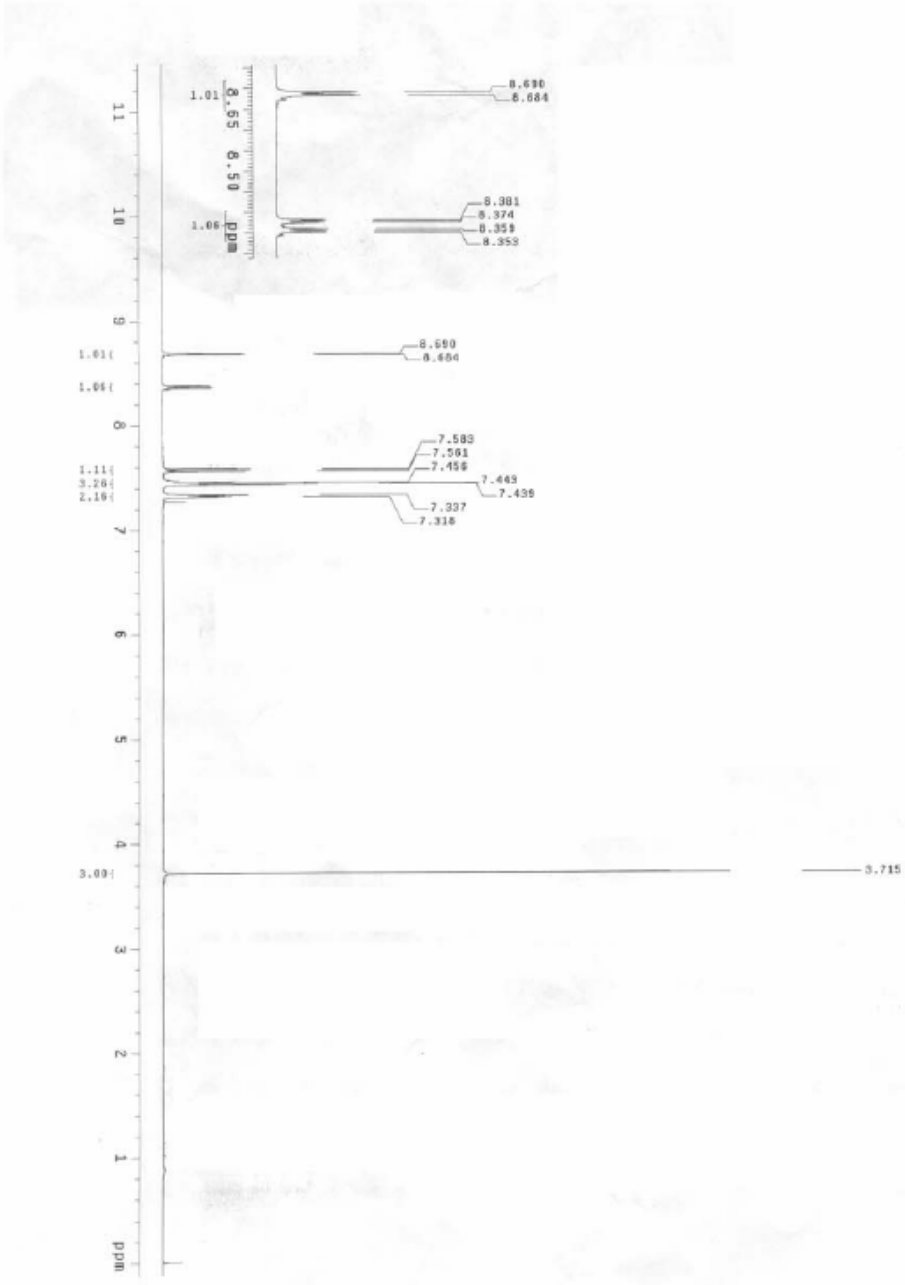
4-Phenylbenzonitrile (12)



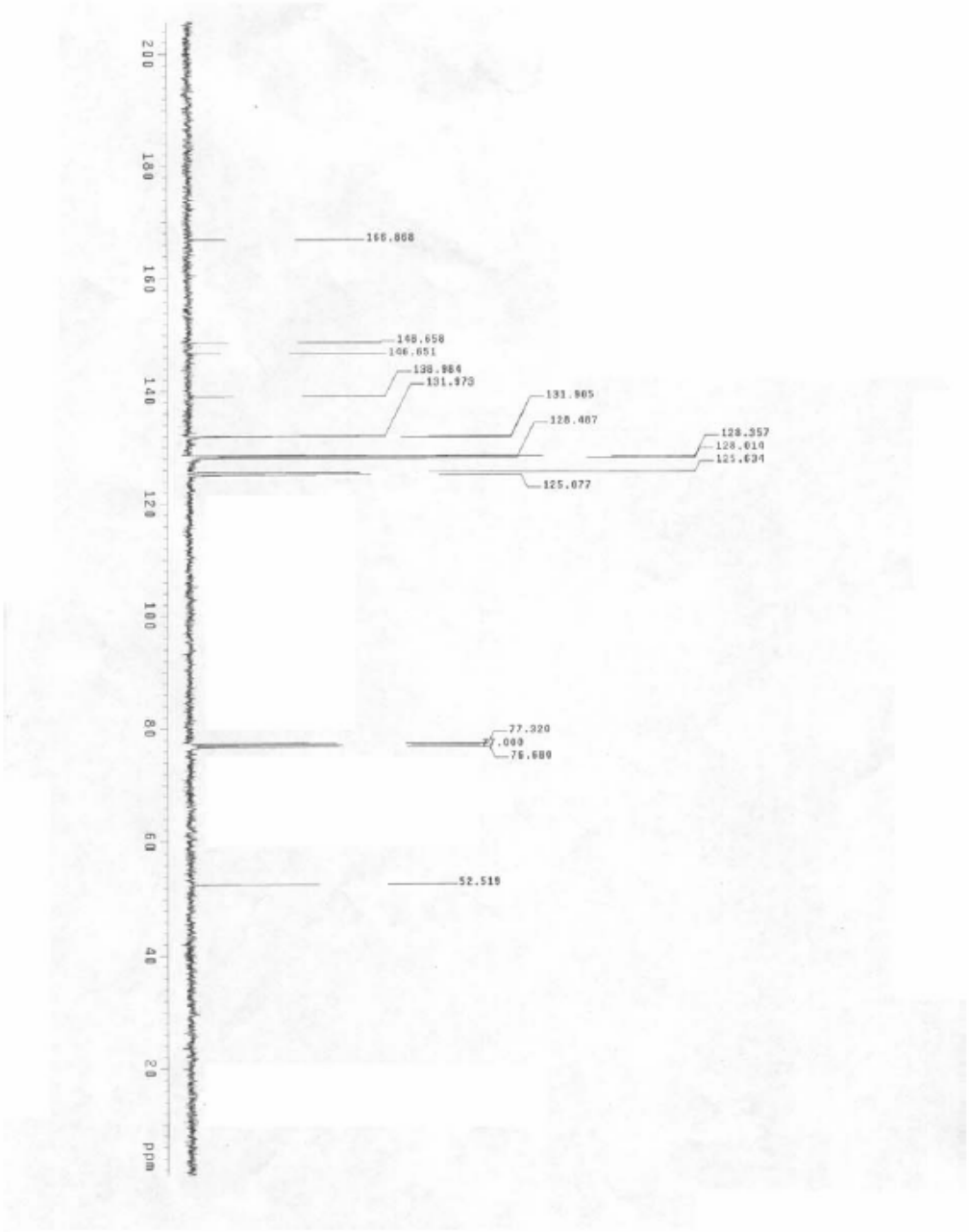
4-Phenylbenzonitrile (12)



Methyl 2-phenyl-5-nitrobenzoate (13)



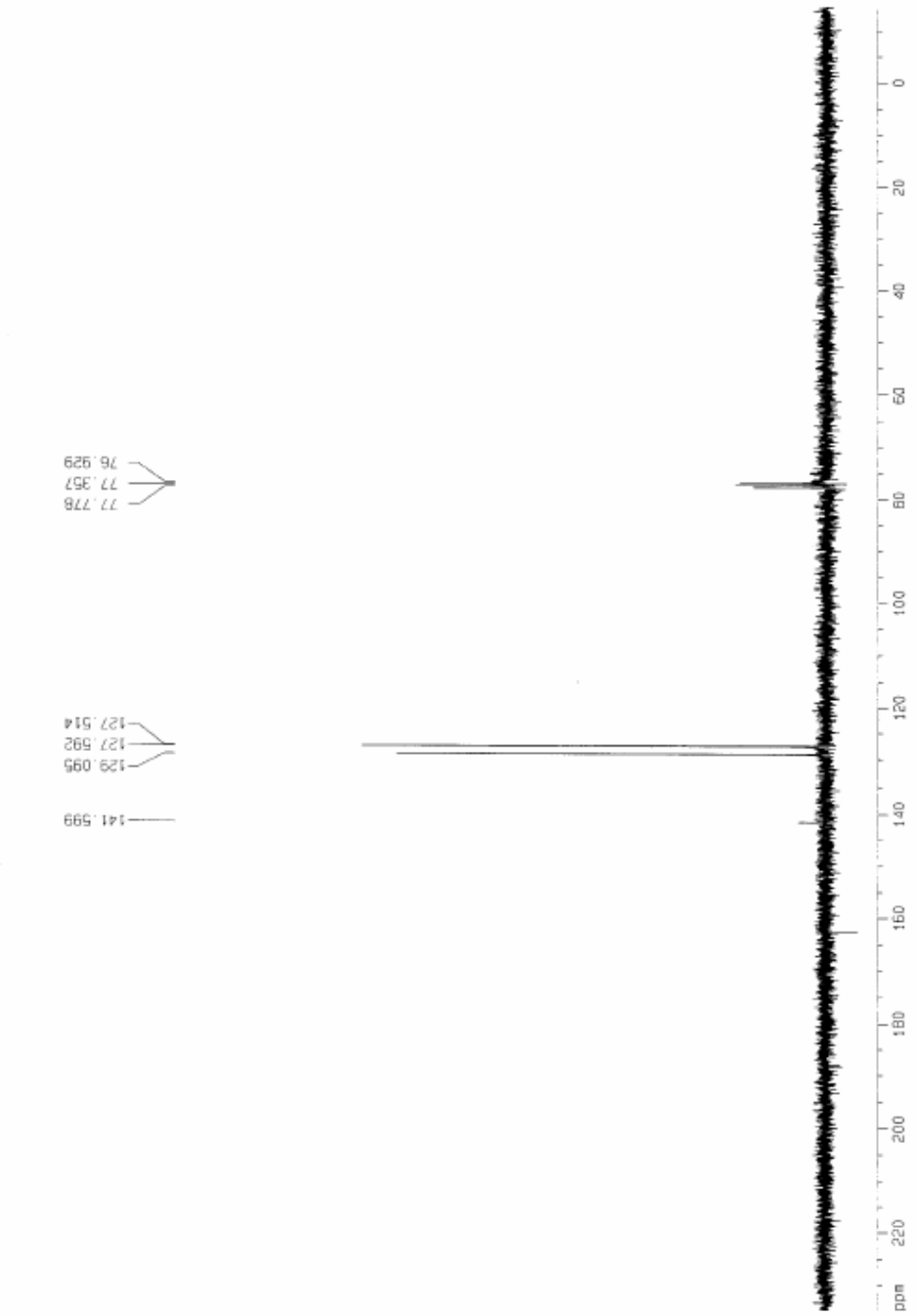
Methyl 2-phenyl-5-nitrobenzoate (13)



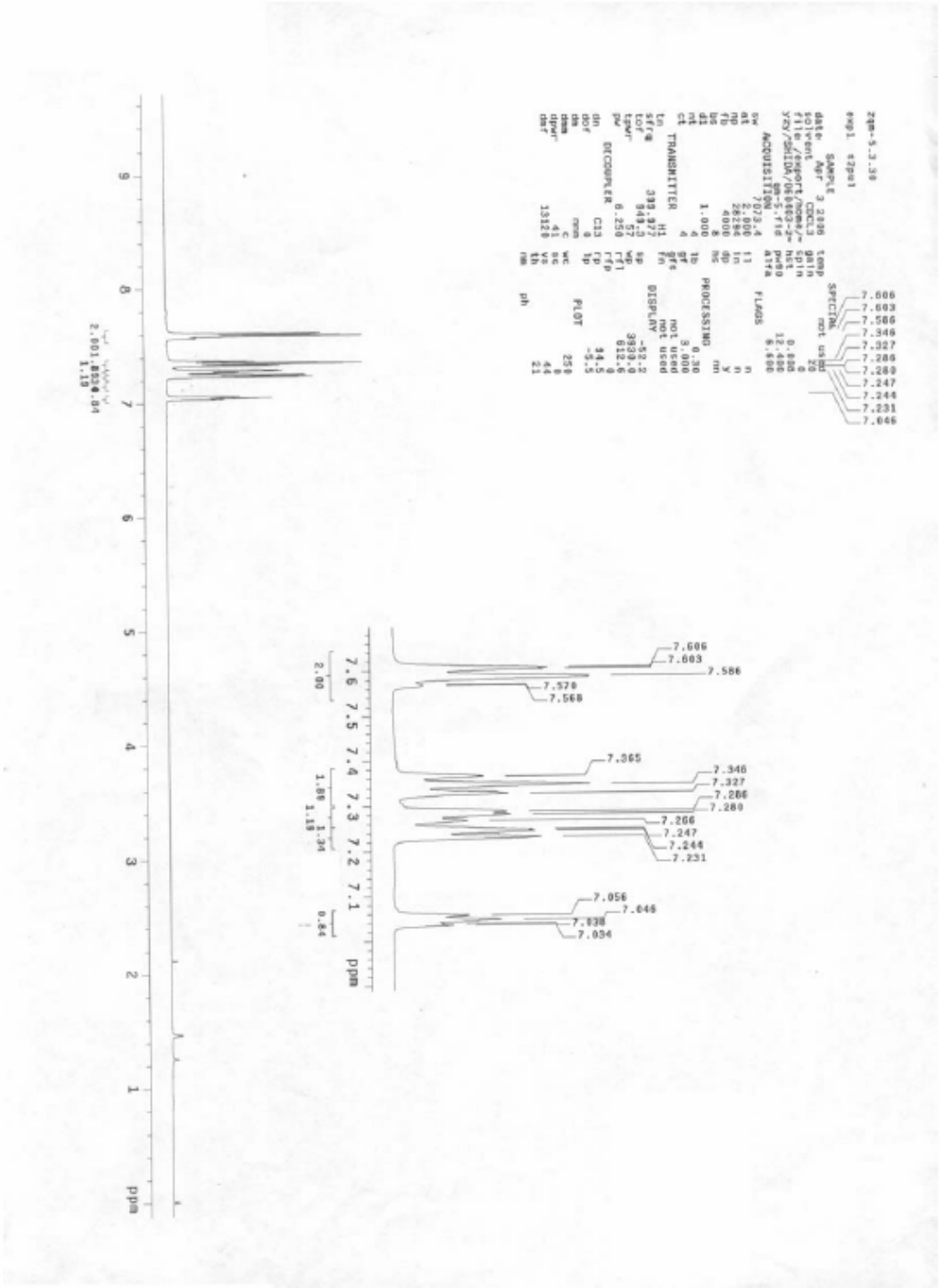
Biphenyl (14)

0.0001
1.5114
7.2305
7.3122
7.3292
7.3366
7.3438
7.3566
7.3608
7.3649
7.4088
7.4296
7.4344
7.4524
7.4581
7.5782
7.5959
7.6021
7.6069
2.0337
4.0351
4.0000
ppm
Integral

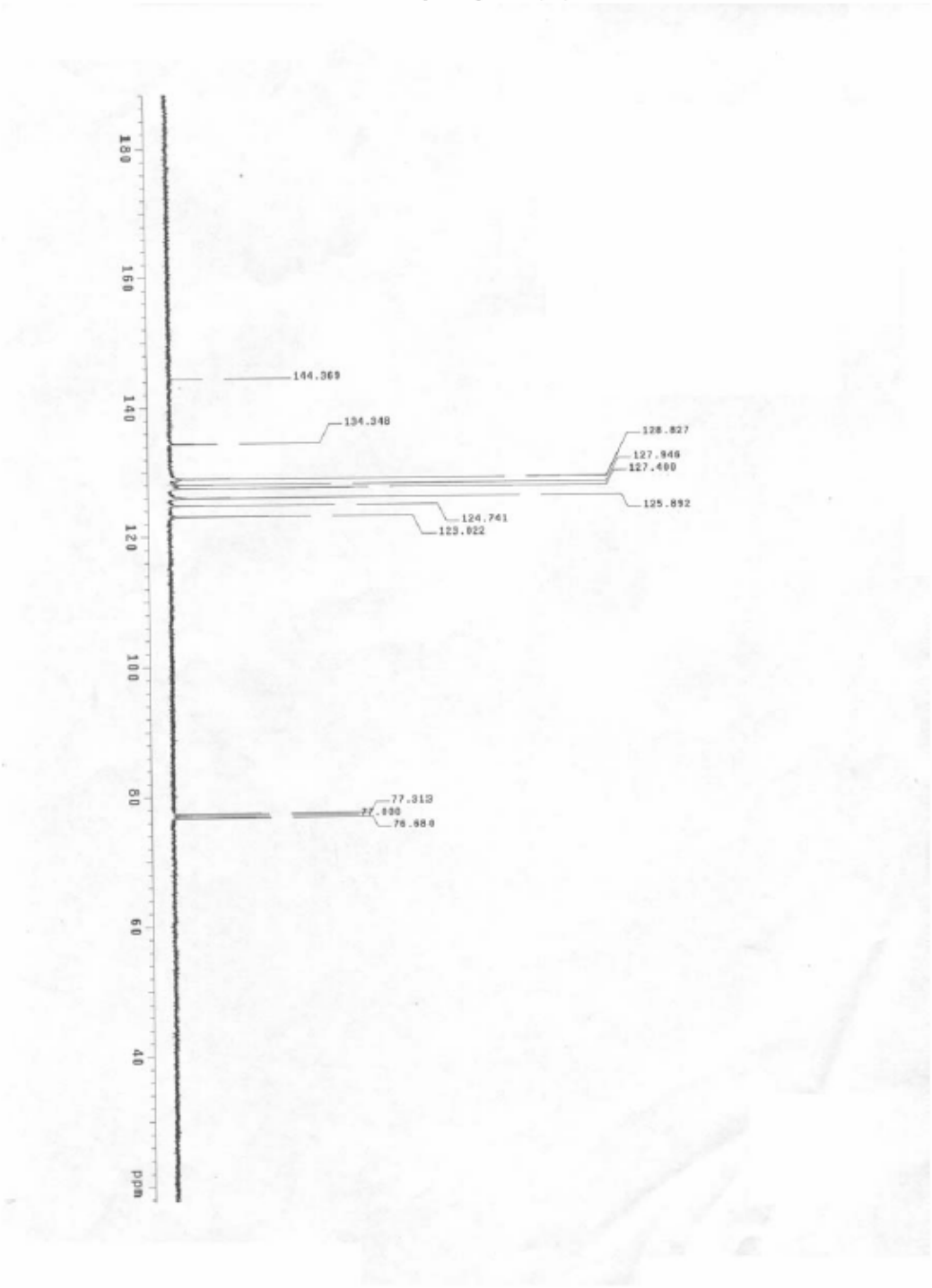
Biphenyl (14)


77.778
77.357
76.929
127.514
127.592
129.095
141.599
0
20
40
60
80
100
120
140
160
180
200
220
ppm

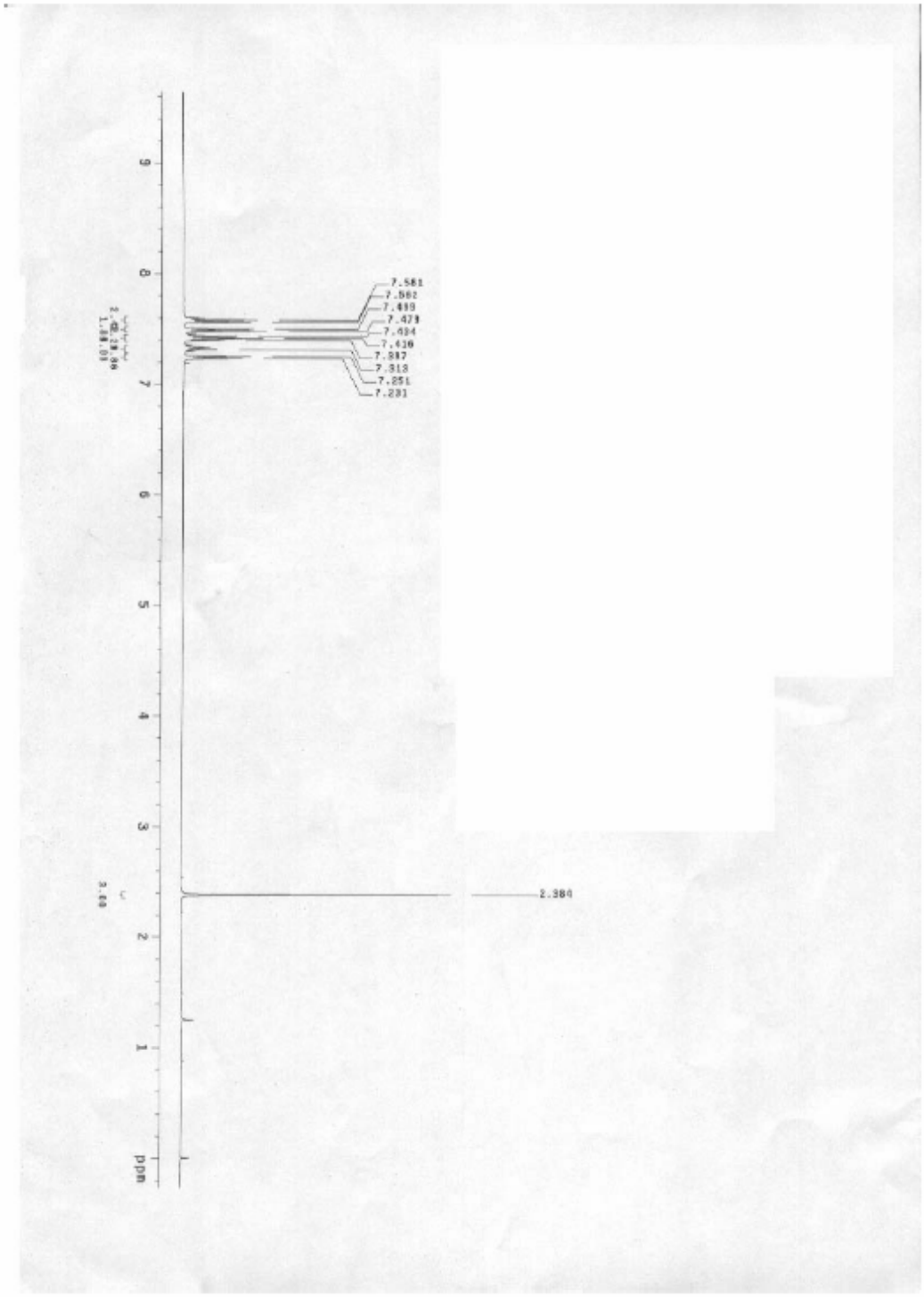
2-Phenylthiophene (15)



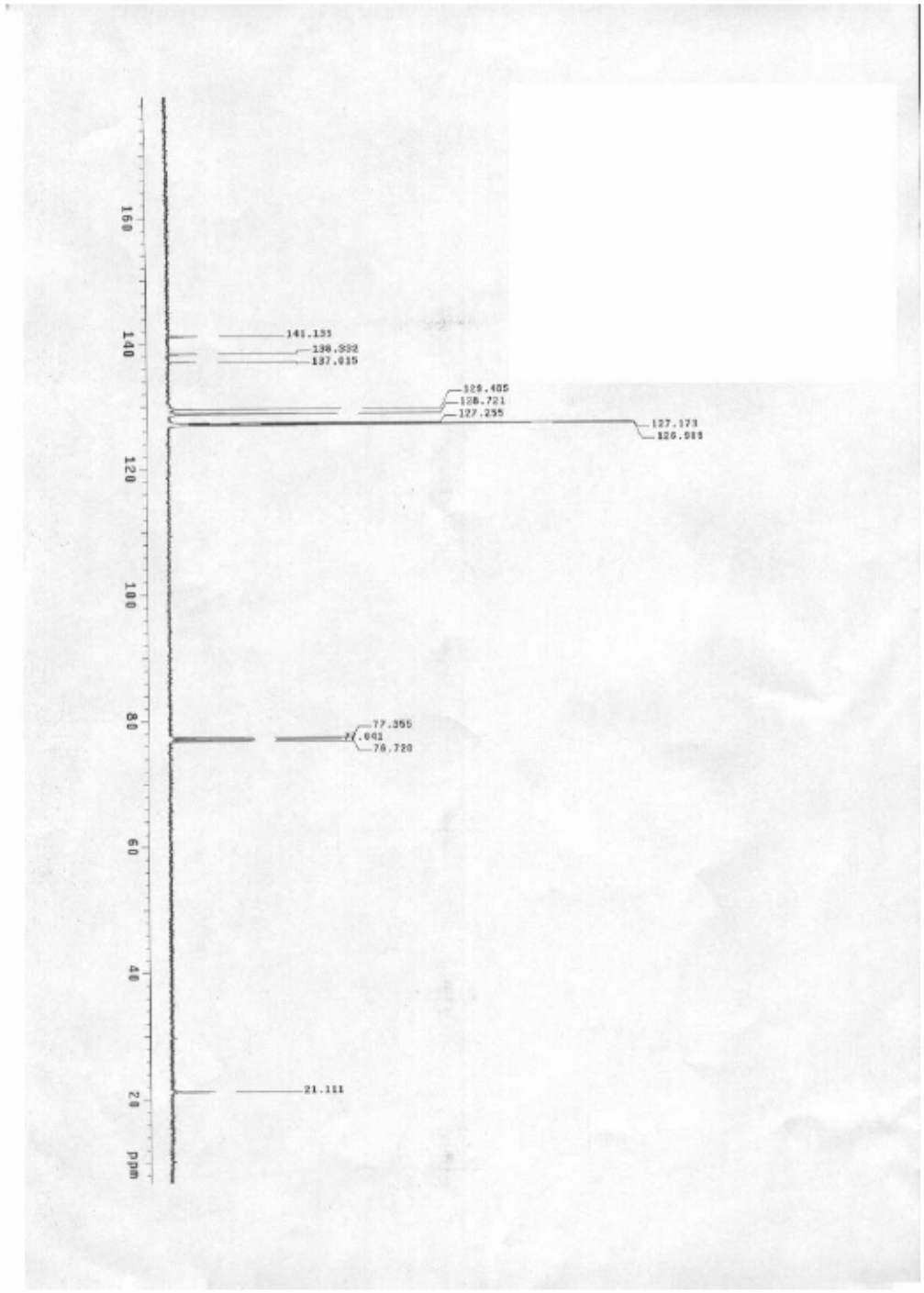
2-Phenylthiophene (15)



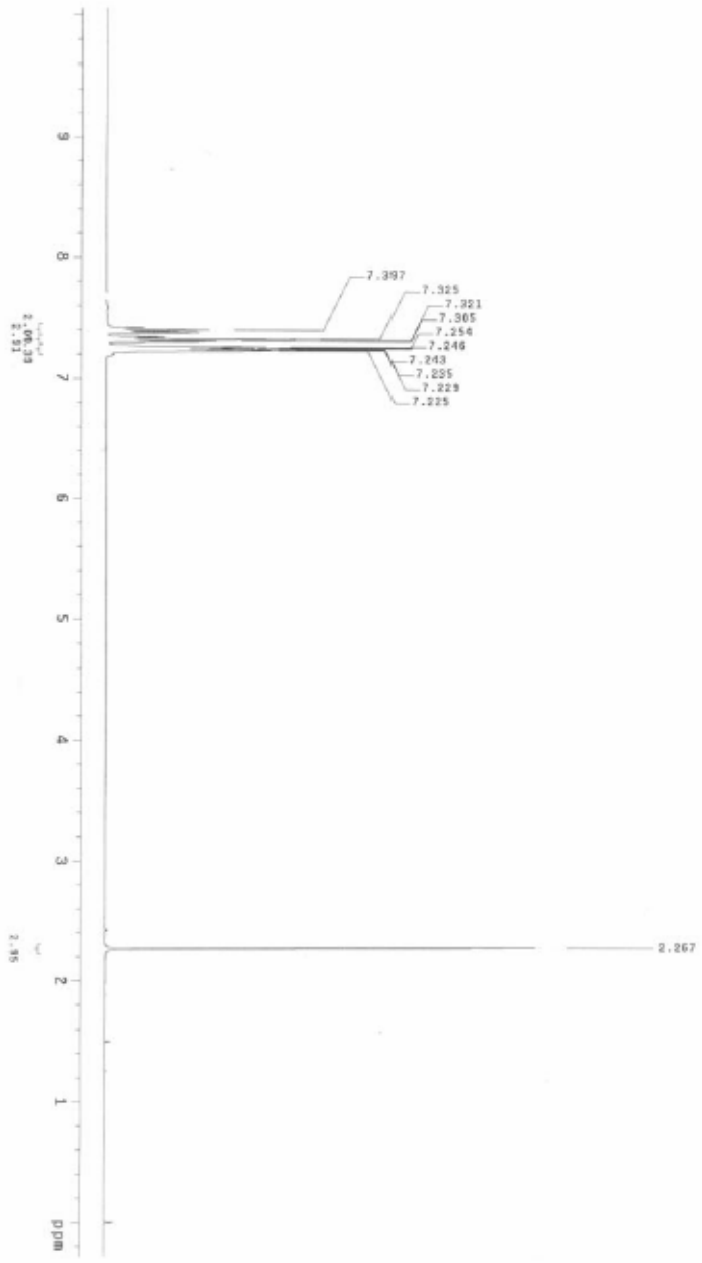
4-Methyl-biphenyl (16)



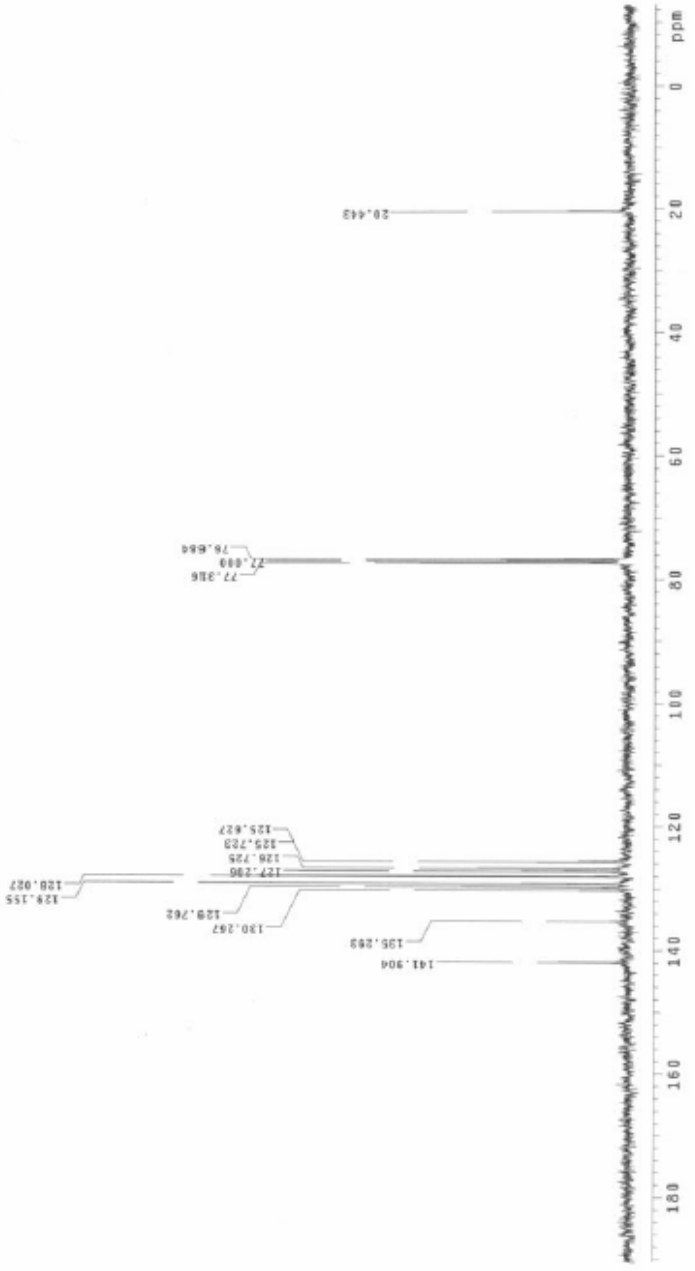
4-Methyl-biphenyl (16)



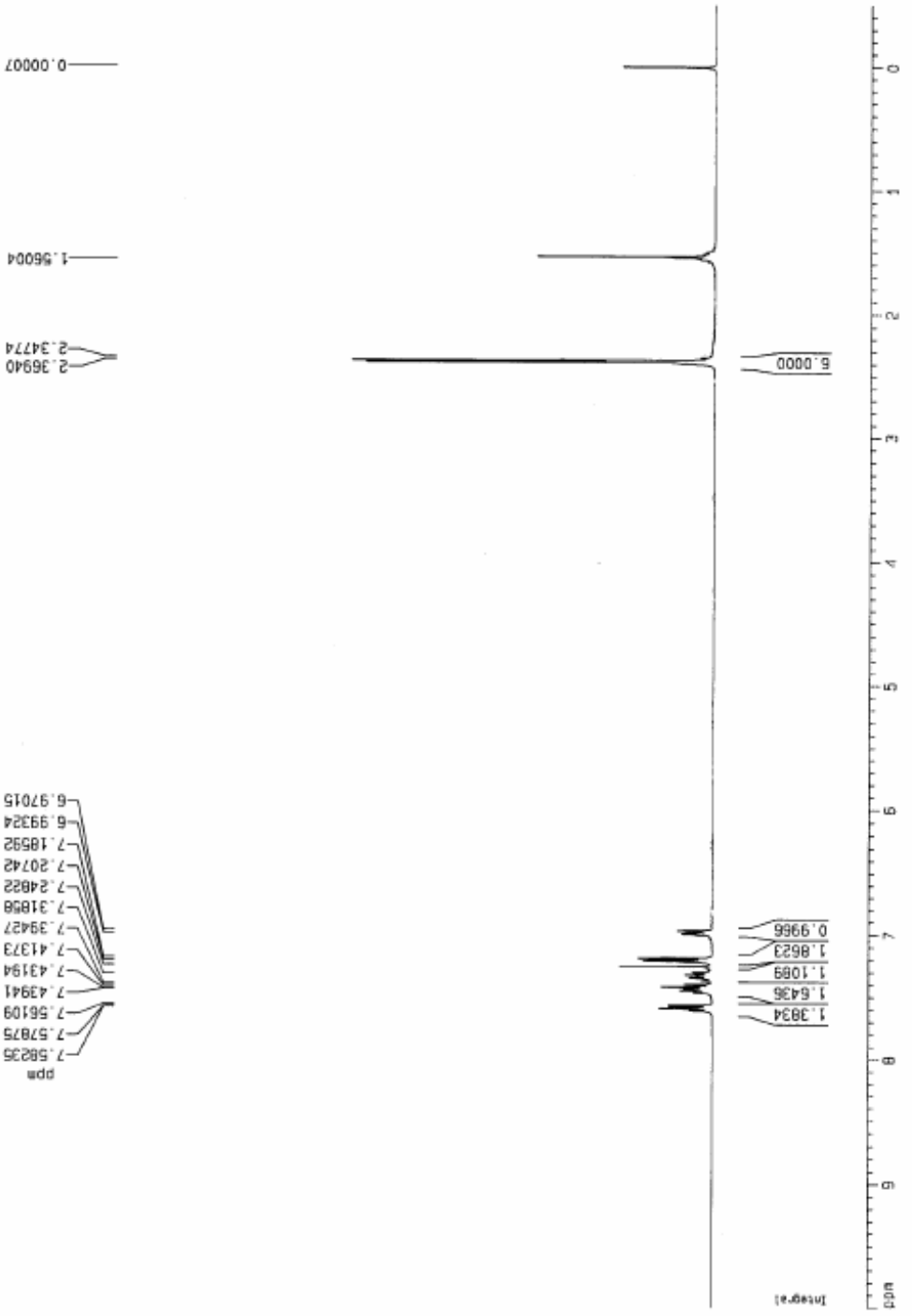
2-Methyl-biphenyl (17)



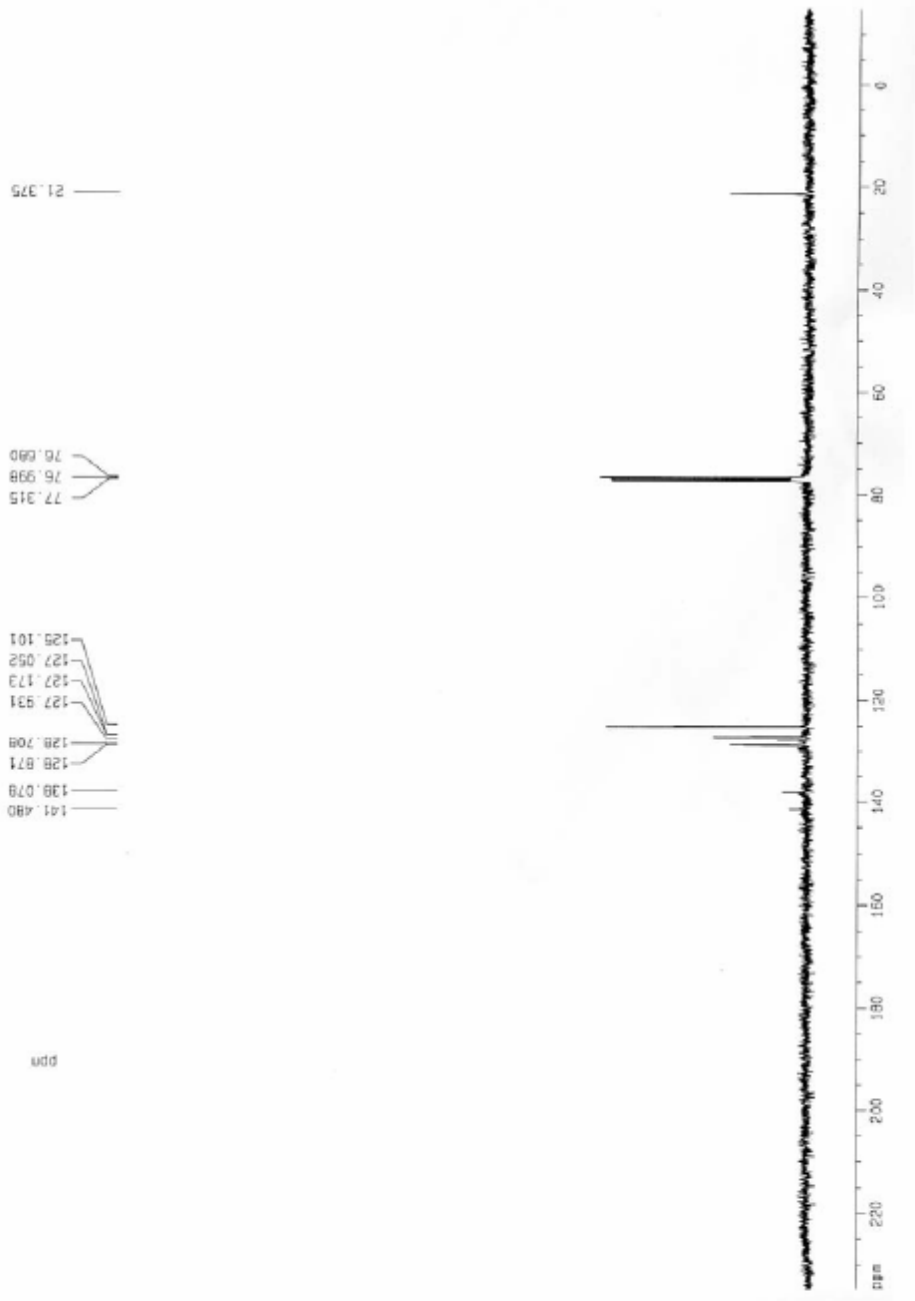
2-Methyl-biphenyl (17)



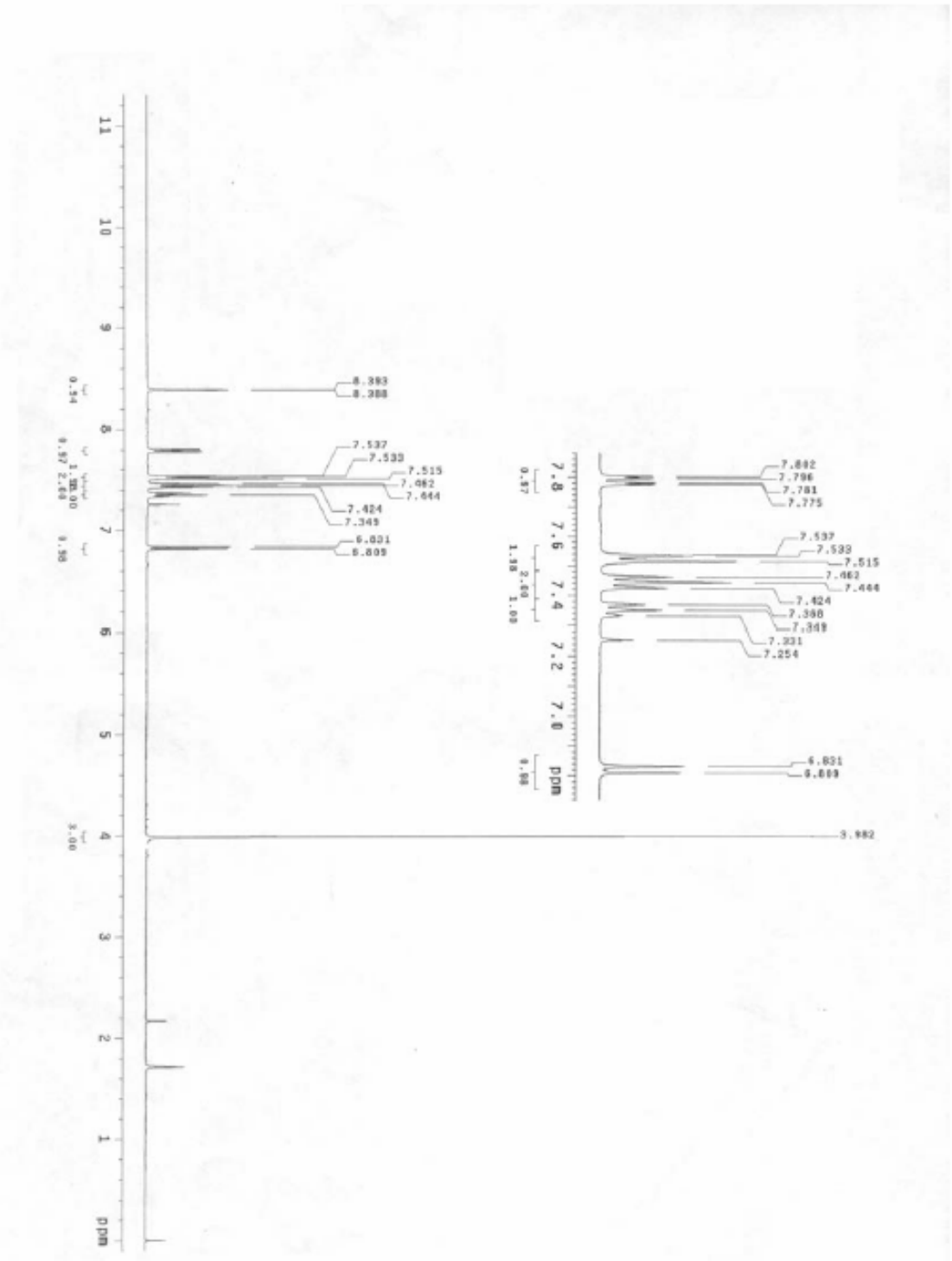
3,5-Dimethyl-biphenyl (18)



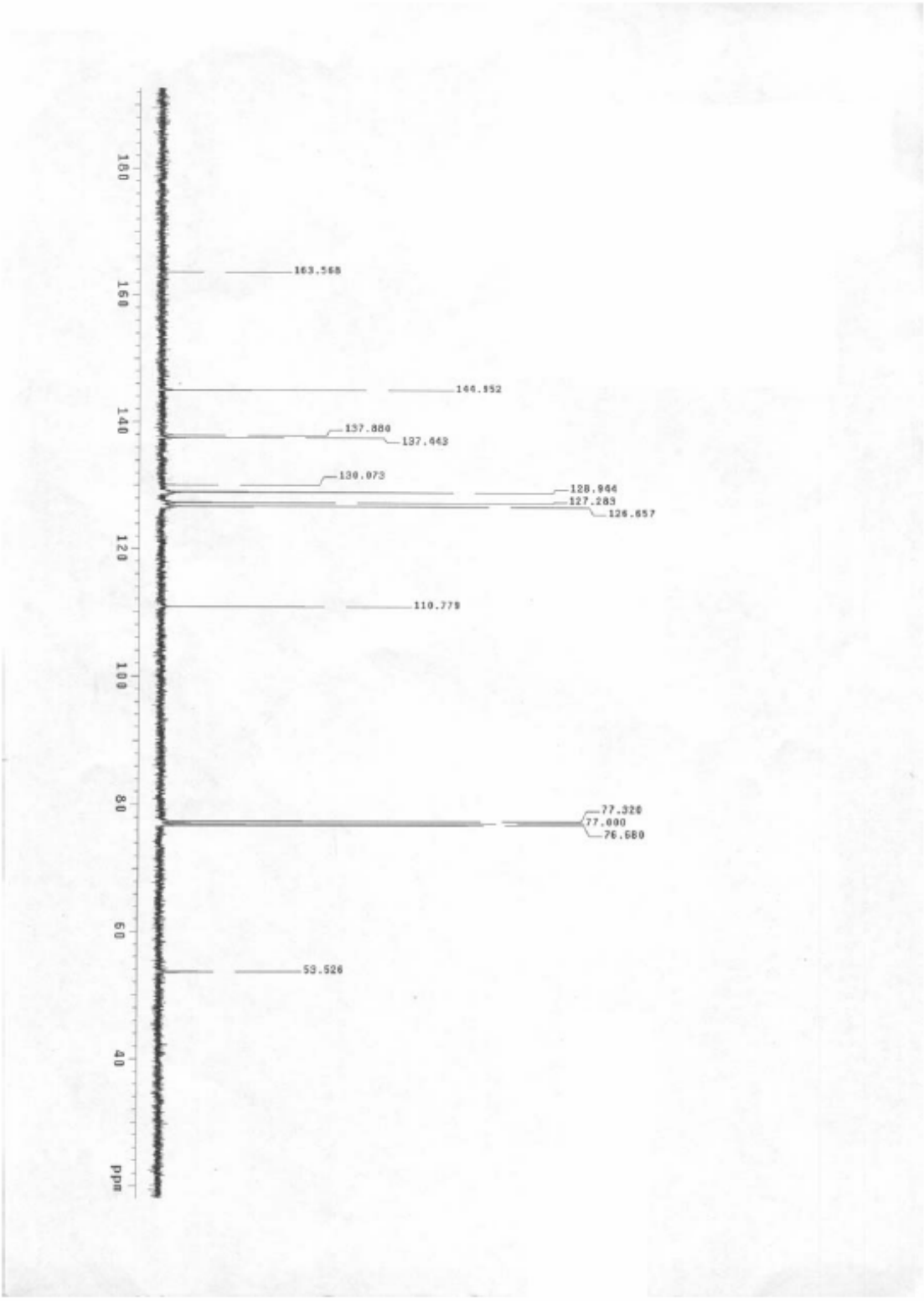
3,5-Dimethyl-biphenyl (18)



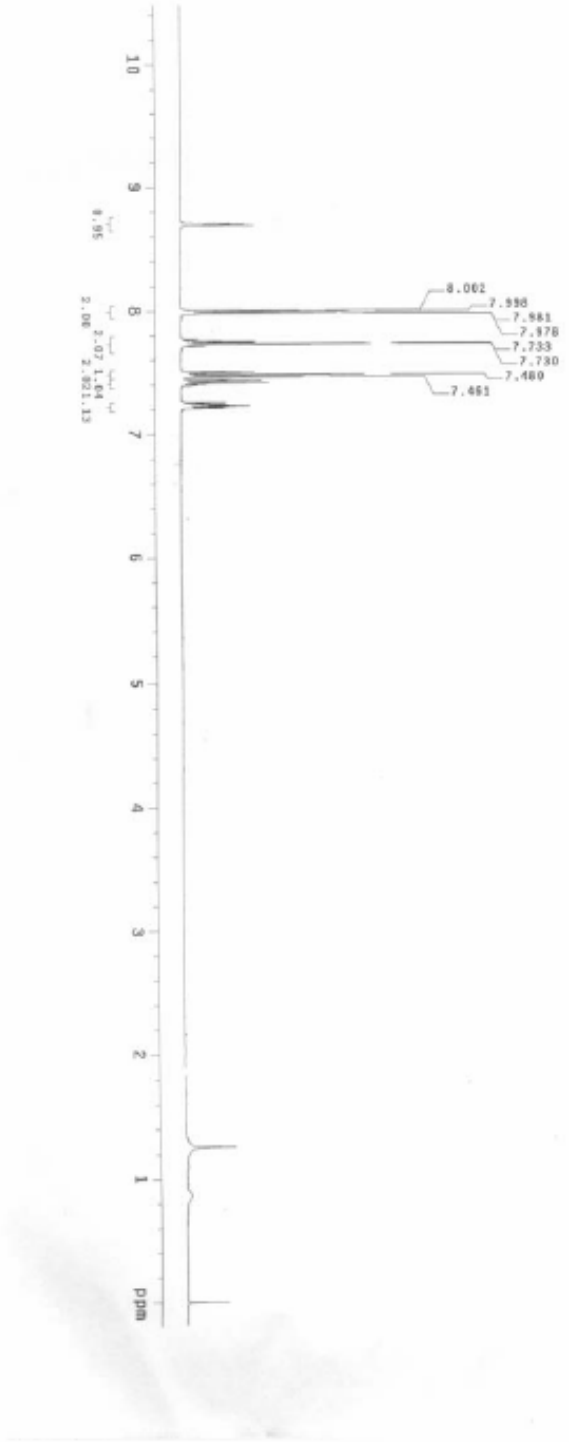
2-Methoxy-5-phenylpyridine (20)



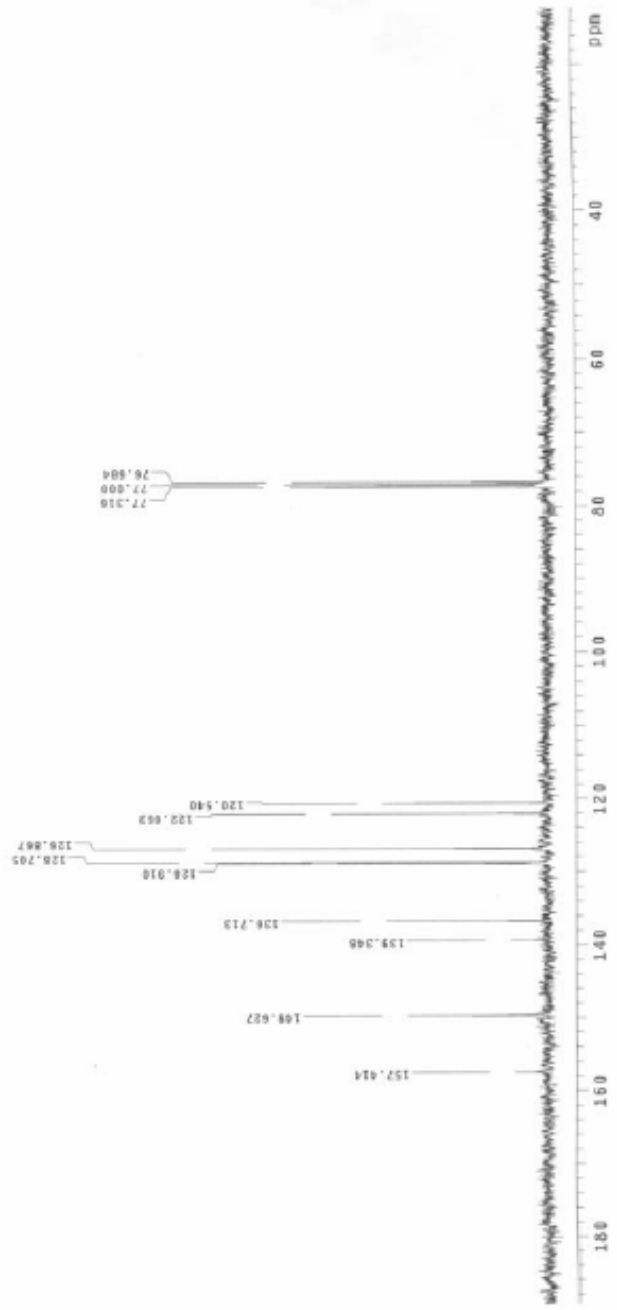
2-Methoxy-5-phenylpyridine (20)



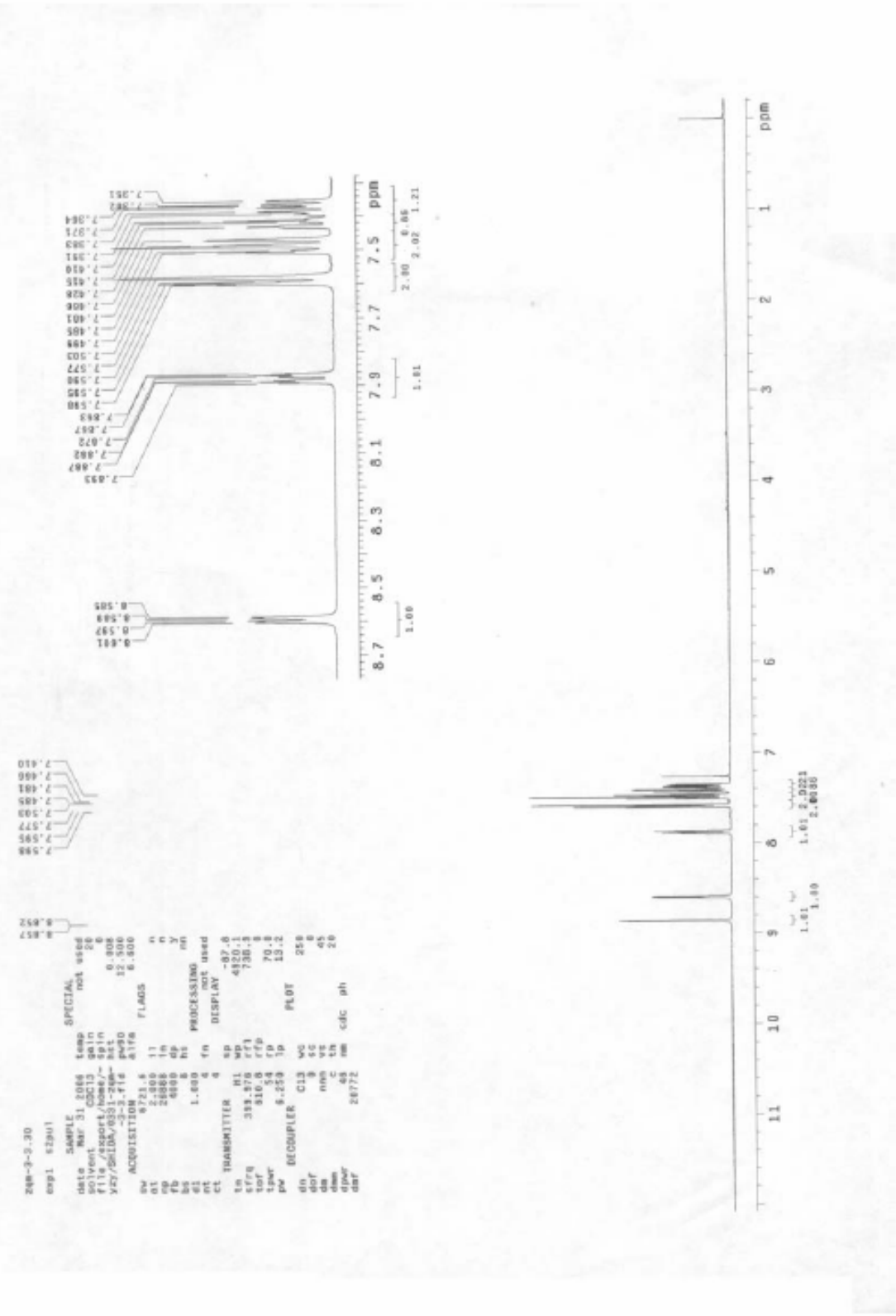
2-Phenylpyridine (21)



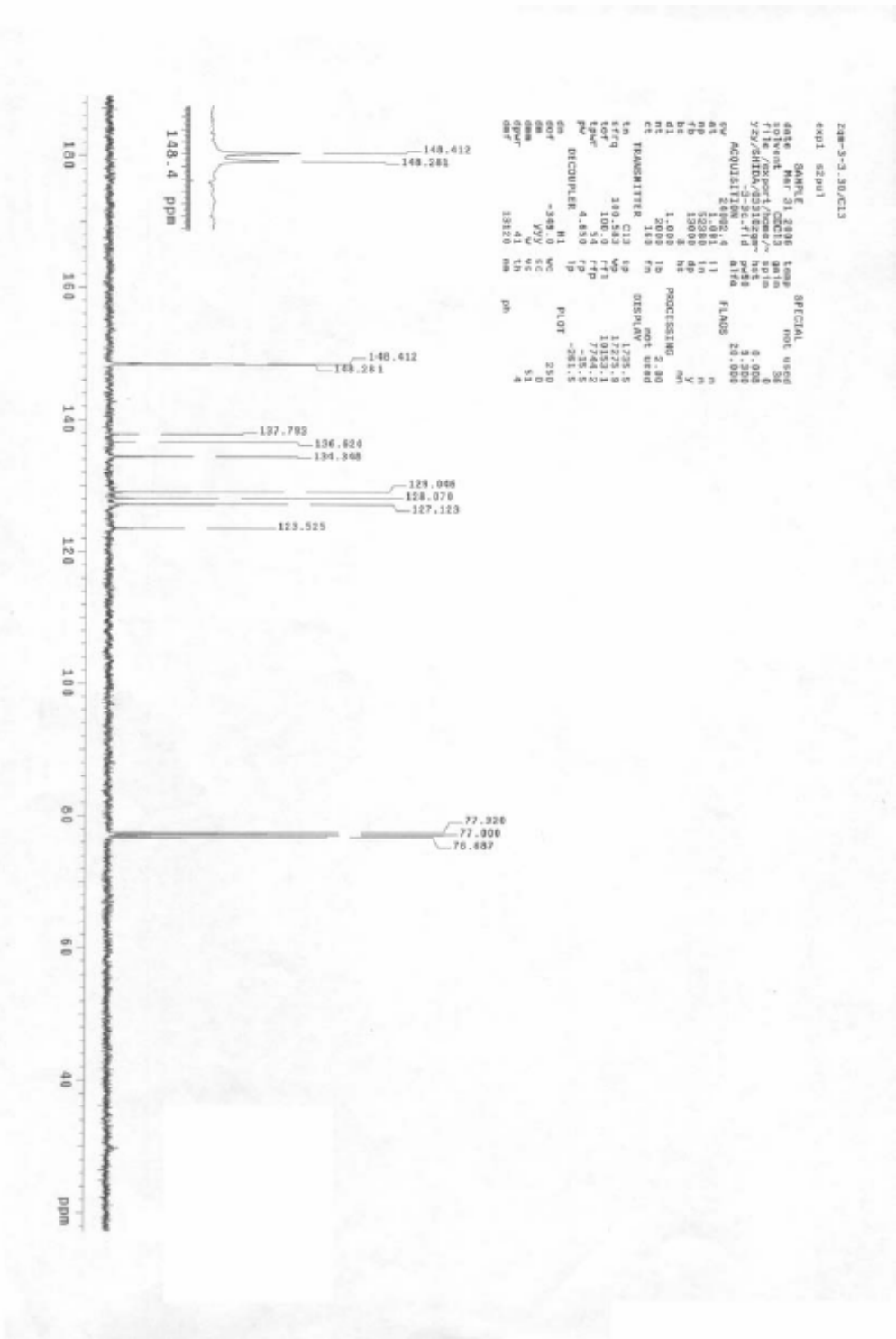
2-Phenylpyridine (21)



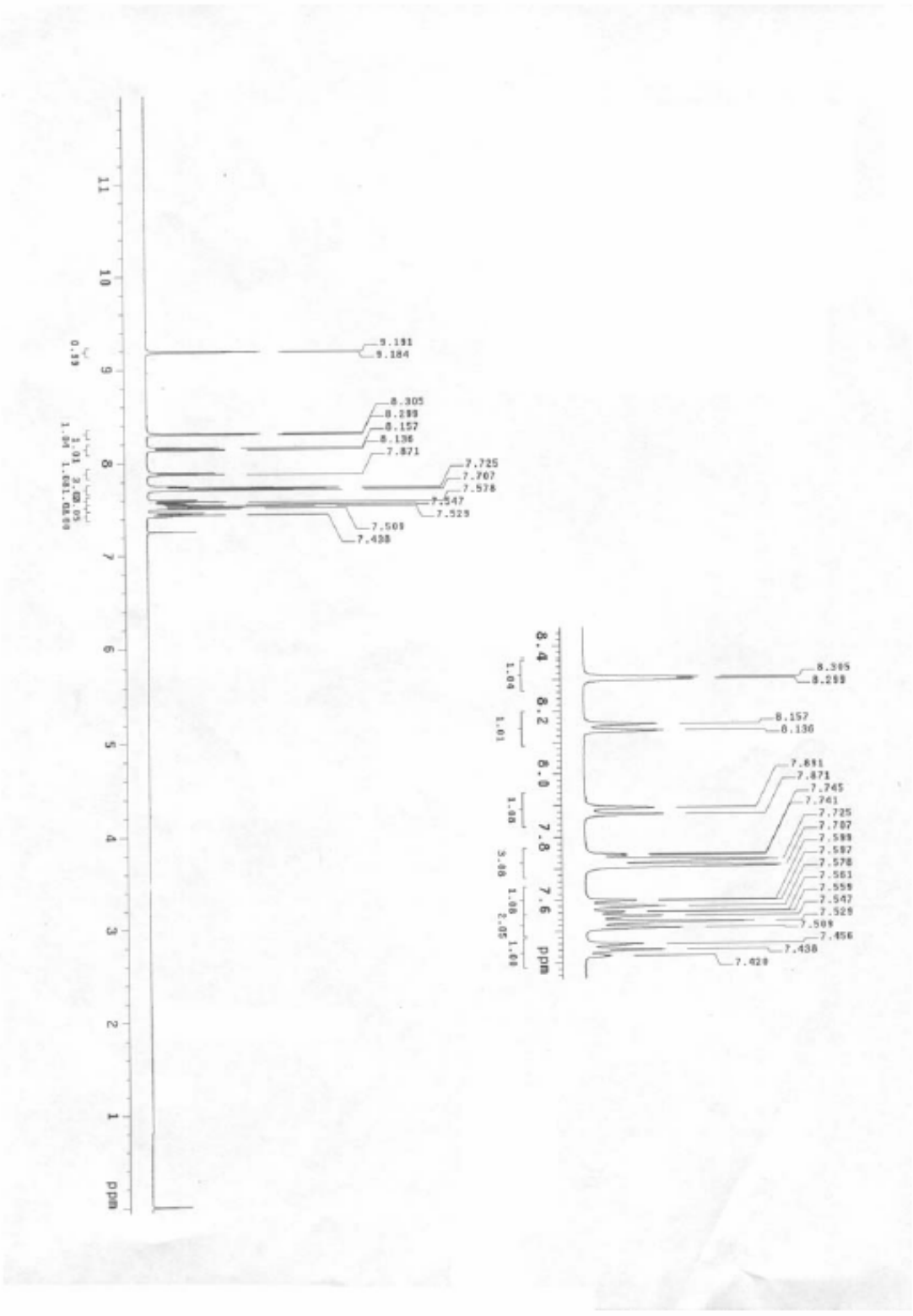
3-Phenylpyridine (22)



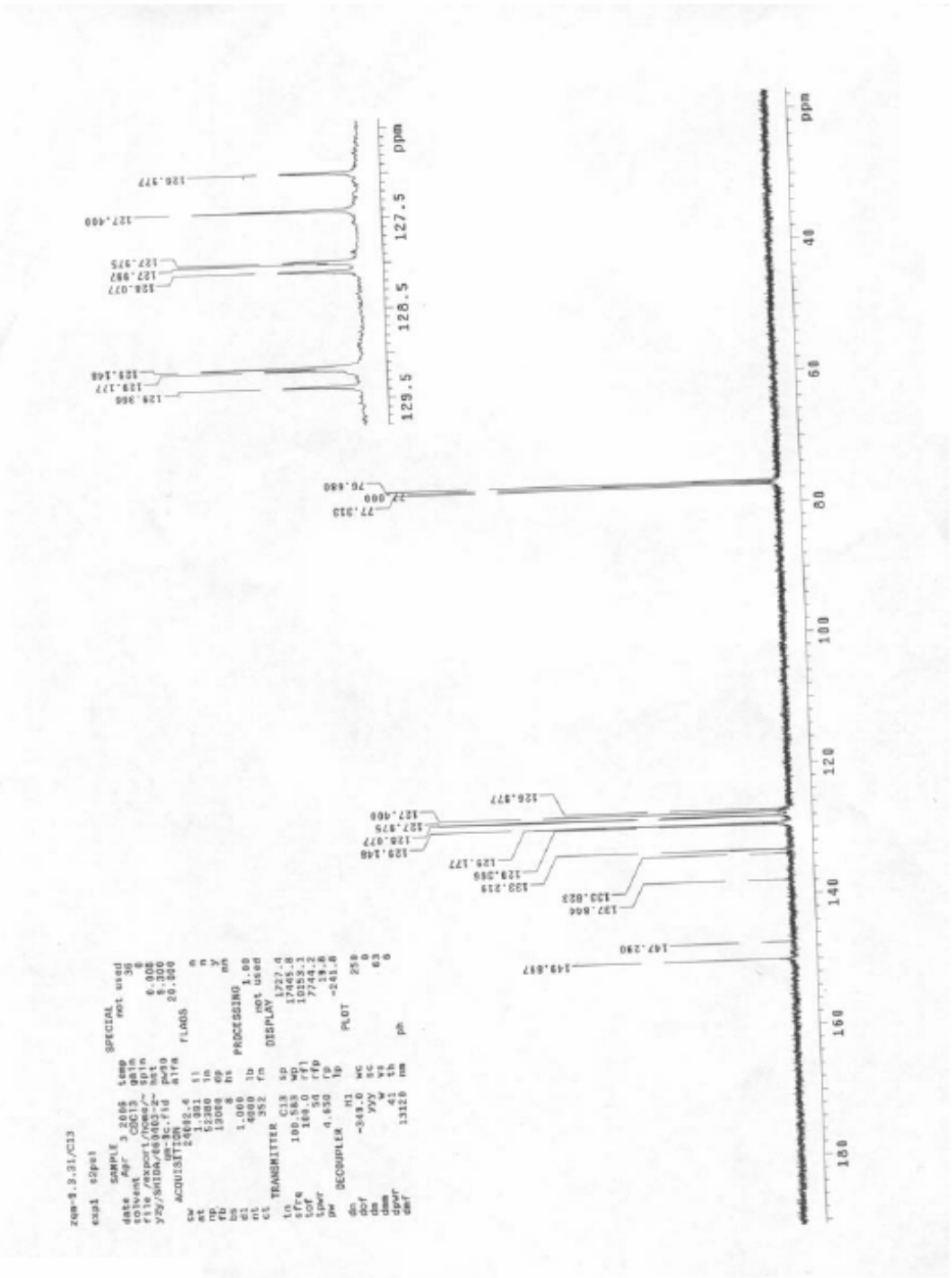
3-Phenylpyridine (22)



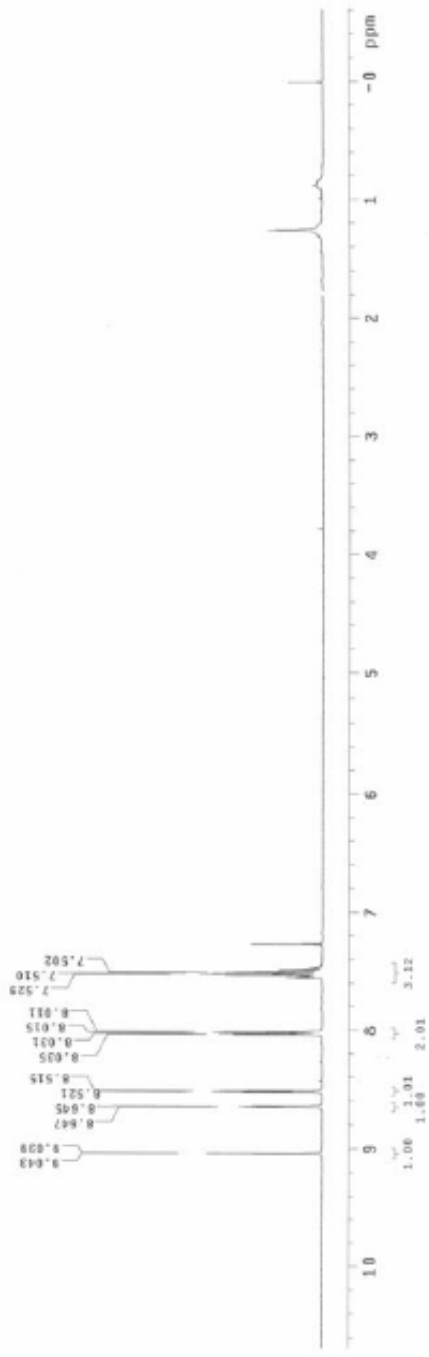
3-Phenylquinoline (23)



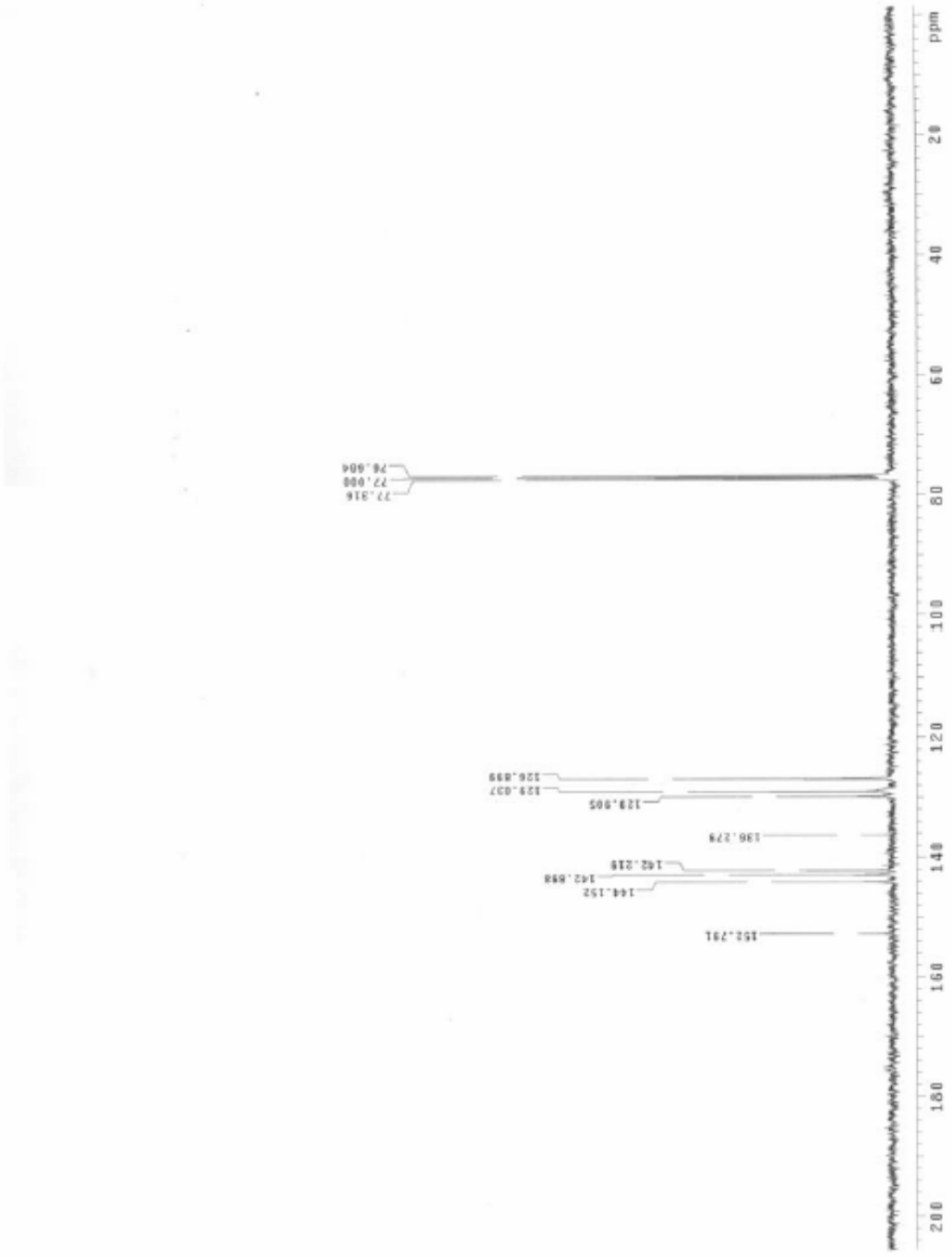
3-Phenylquinoline (23)



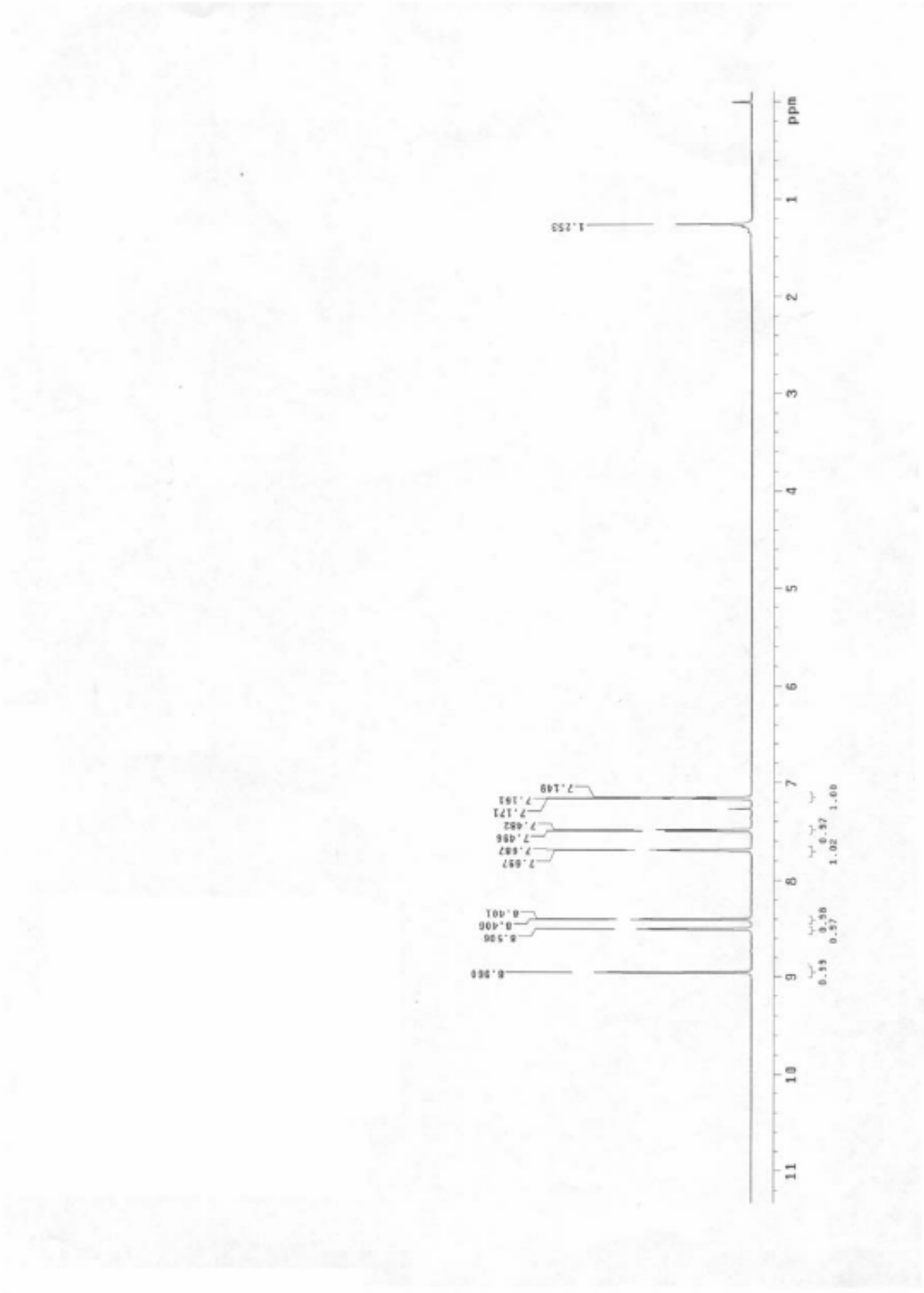
2-Phenylpyrazine (24)



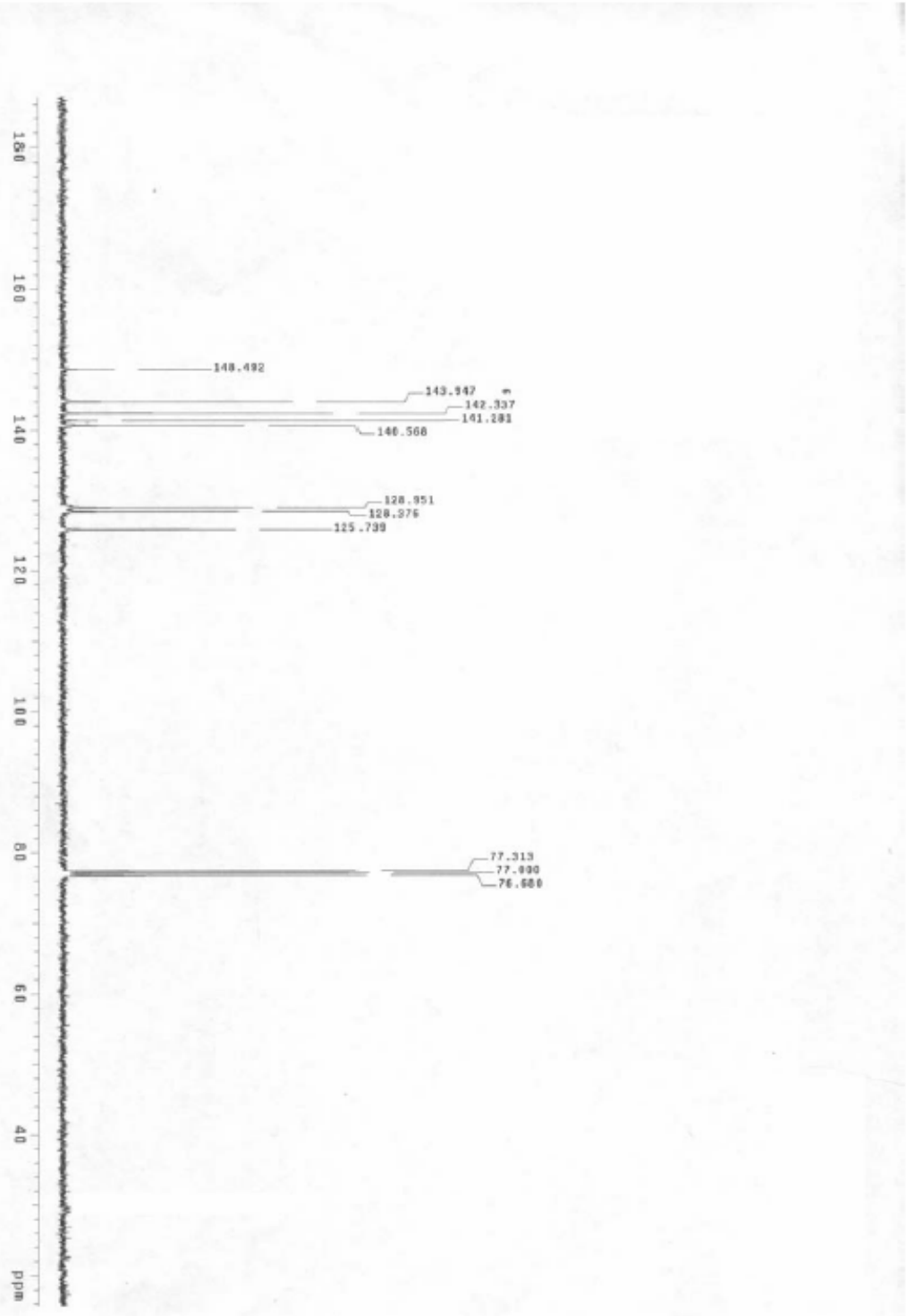
2-Phenylpyrazine (24)



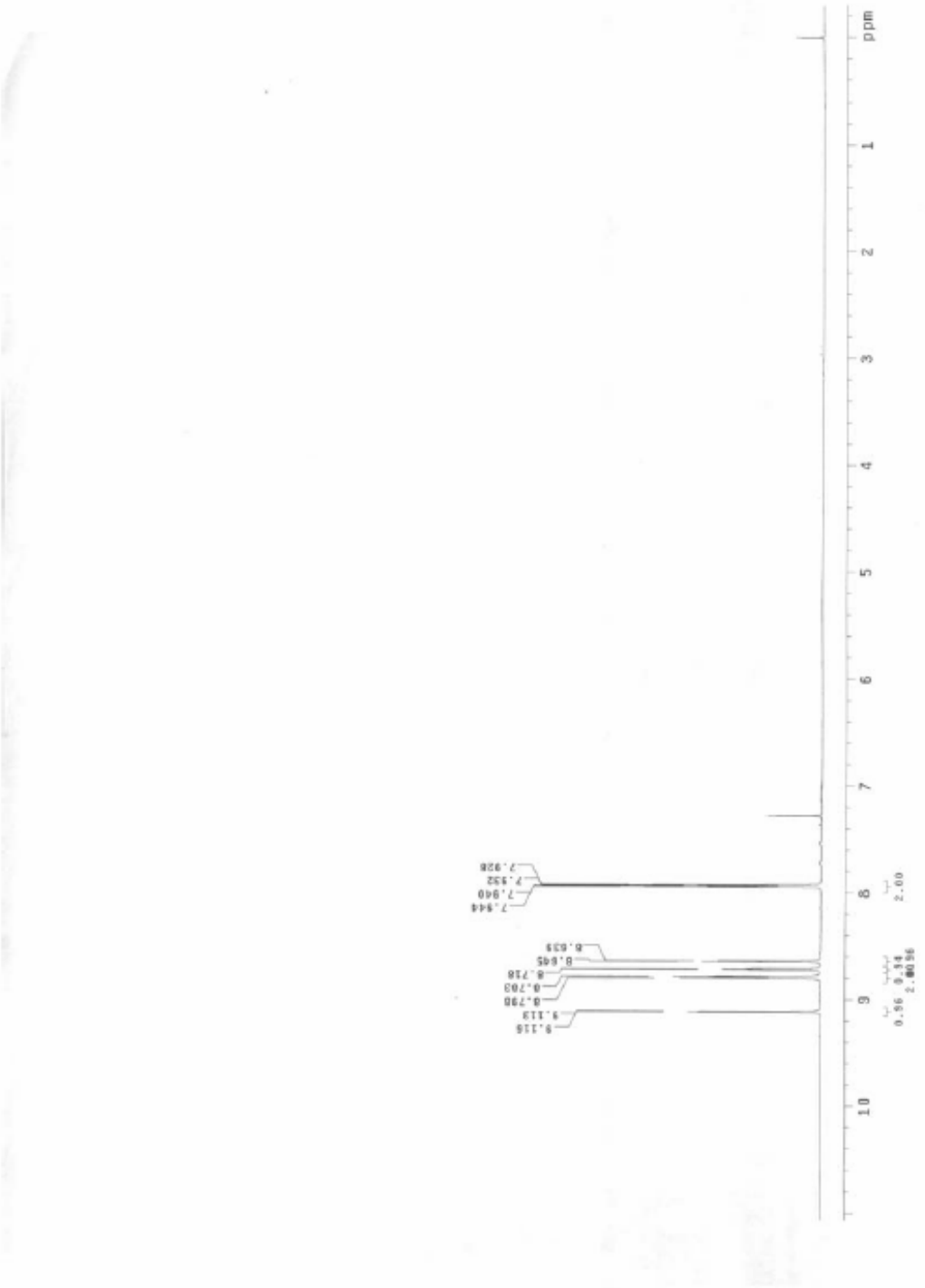
2-(Thiophen-2-yl)pyrazine (25)



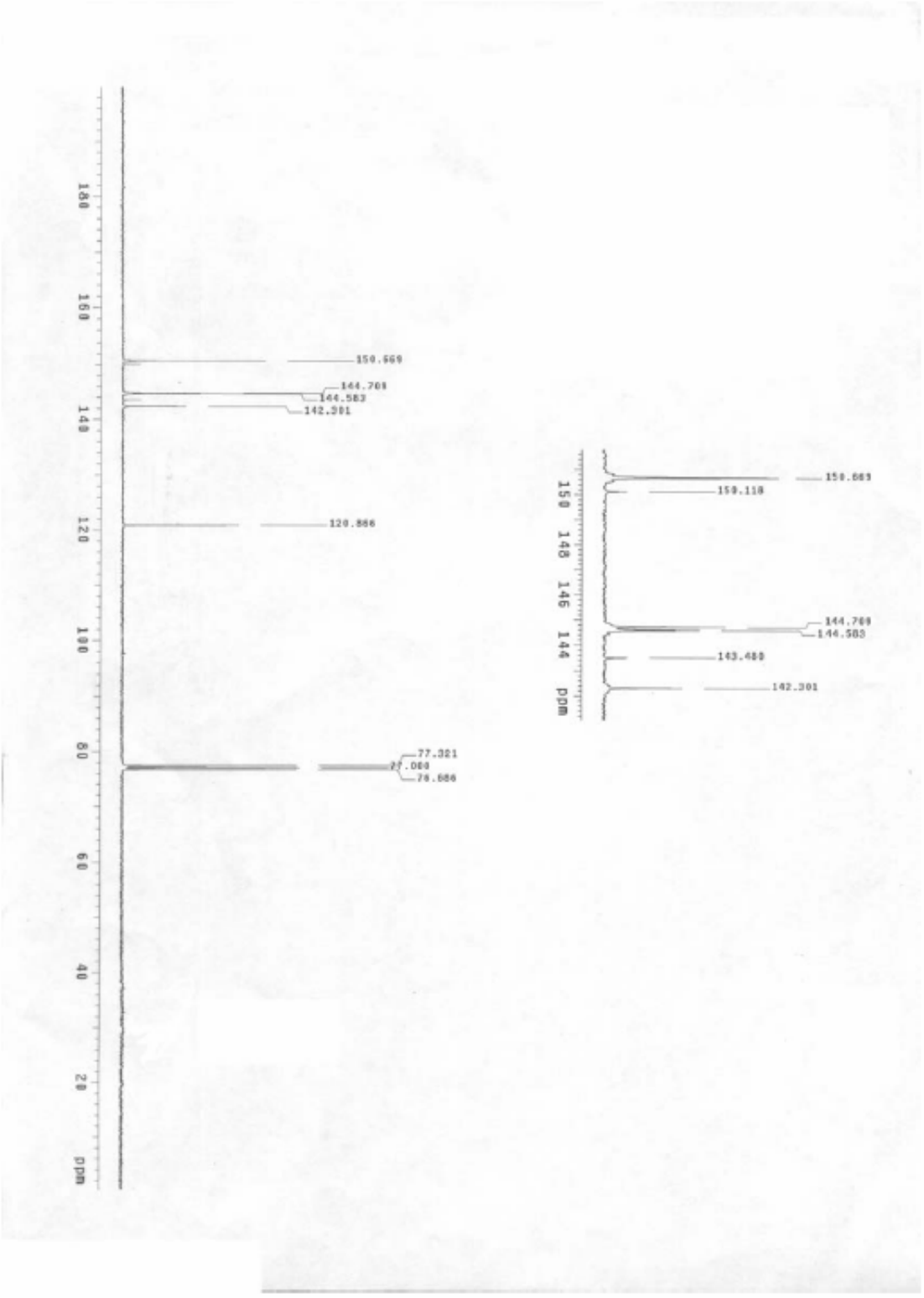
2-(Thiophen-2-yl)pyrazine (25)



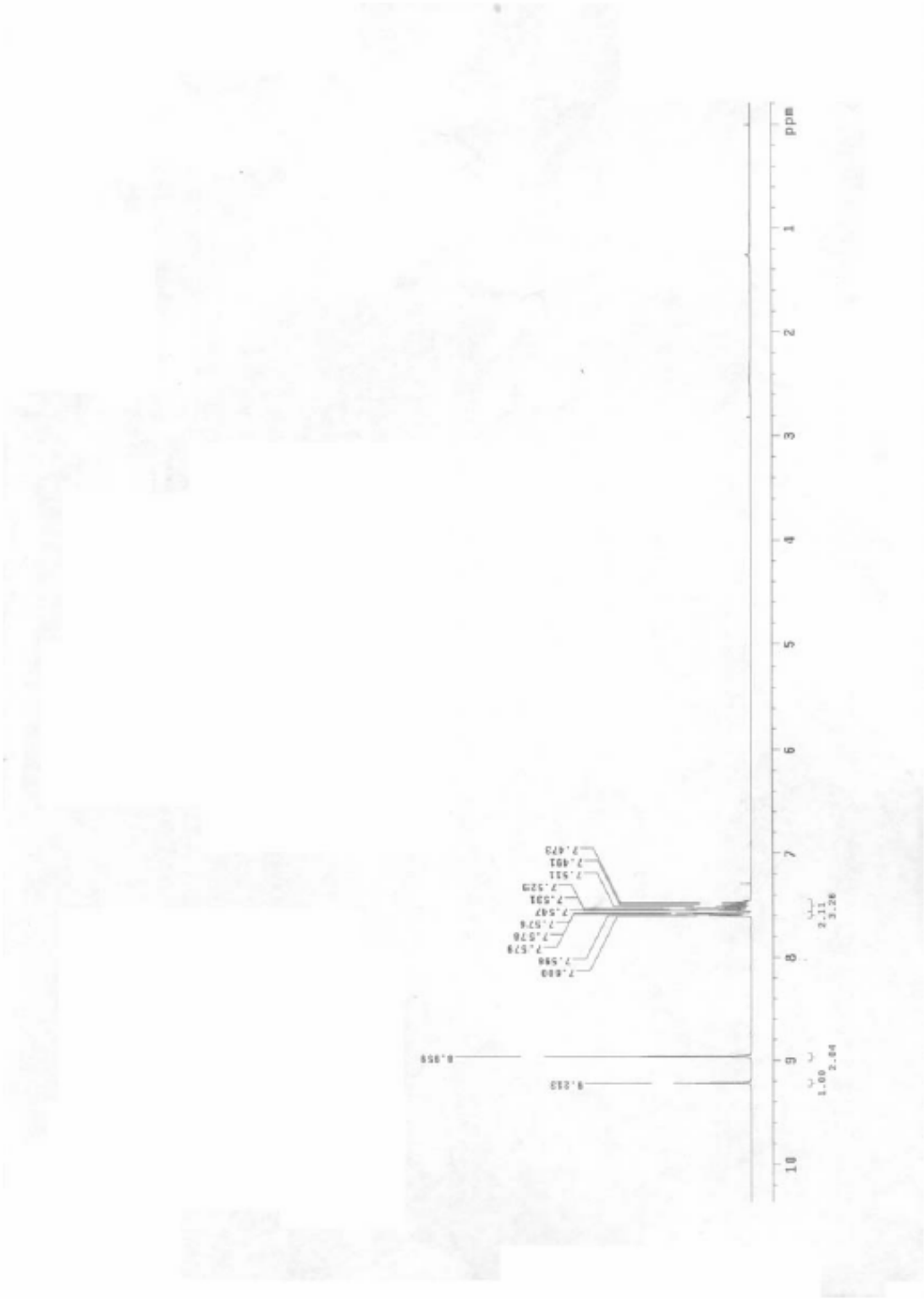
2-(Pyridin-4-yl)pyrazine (26)



2-(Pyridin-4-yl)pyrazine (26)



5-Phenylpyrimidine (27)



5-Phenylpyrimidine (27)