

Borane-Catalyzed Transfer Hydrogenations of Pyridines with Ammonia Borane

Qiwen Zhou,[†] Lanqiong Zhang,[†] Wei Meng,^{‡,§} Xiangqing Feng,^{‡,§} Jing Yang,^{*,†} and Haifeng Du^{*,‡,§}

[†] State Key Laboratory of Chemical Resource, Beijing Key Laboratory of Bioprocess, College of Life Science and Technology, Beijing University of Chemical Technology, Beijing 100029, China

[‡] Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

[§] University of Chinese Academy of Sciences, Beijing 100049, China

Supporting Information

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General information: All air-sensitive compounds were handled under an atmosphere of argon or in a nitrogen-filled glovebox. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AV 400 at ambient temperature with CDCl_3 as solvent and TMS as internal standard. Chemical shifts (δ) were given in ppm, referenced to the residual proton resonance of TMS (0), to the carbon resonance of the CDCl_3 (77.23). Coupling constants (J) were given in Hertz (Hz). IR spectrums were recorded on Perkin-Elmer-983 spectrometer. Column chromatography was performed on silica gel (200-300 mesh). All solvents were purified by conventional methods, distilled before use.

Representative procedure for hydrogenation of pyridines (Scheme 3, 5a): To a sealed tube (15 mL), were added 2,6-diphenylpyridine (**3a**) (0.0924 g, 0.40 mmol), $\text{B}(\text{C}_6\text{F}_5)_3$ (0.0205 g, 0.040 mmol), ammonia borane (0.0497 g, 1.6 mmol), and dry toluene (1.0 mL) in a nitrogen atmosphere glovebox. The resulting mixture was stirred at 120 °C for 6 h. After cooling to ambient temperature, the solvent was removed under reduced pressure. The crude residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (10/1) to petroleum ether/ethyl acetate/ Et_3N (5/1/0.1) as the eluent to give 2,6-diphenylpiperidine (**5a**) as a white solid (0.0768 g, 81% yield).

^{11}B NMR study on the reaction mixture: After the solvent of the reaction mixture was removed under reduced pressure, the crude residue was dissolved in C_6D_6 (2.0 mL). A ^{11}B NMR spectra is recorded on Bruker AV 400 at room temperature, and the

chemical shift is relative to Et₂O·BF₃ (0 ppm).

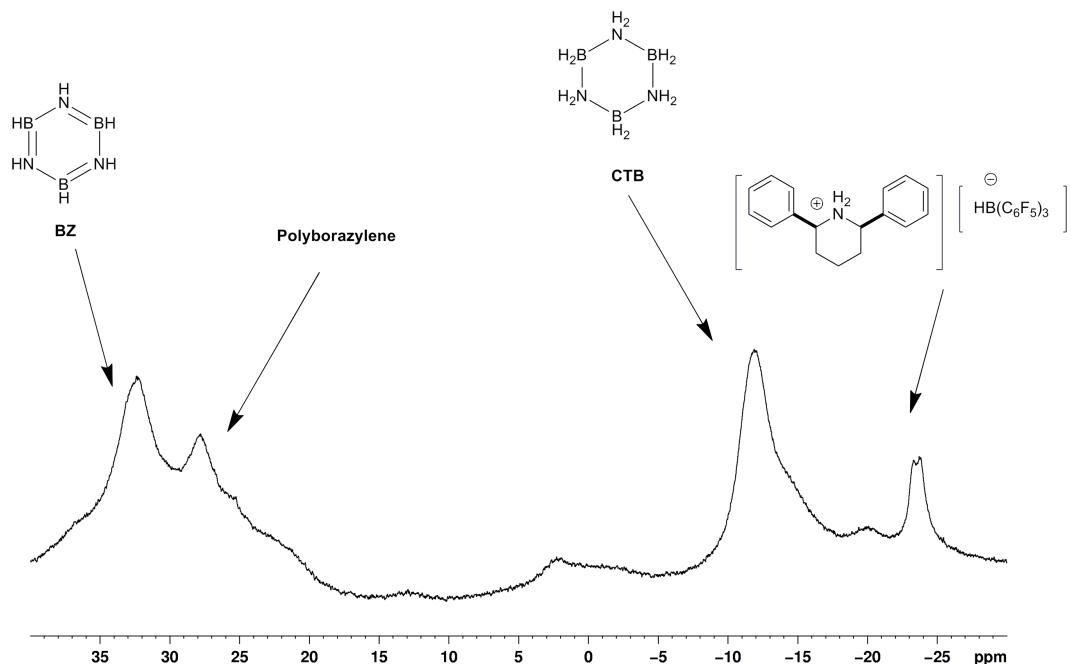
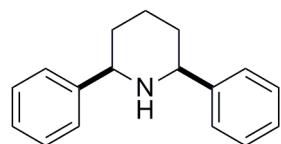
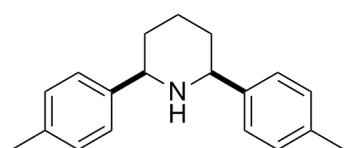


Figure S1



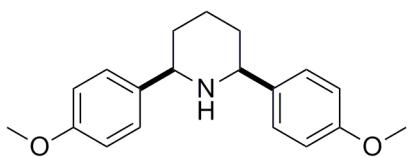
Cis-2,6-diphenylpiperidine (5a): 0.0765 g, 81% yield, *cis/trans* = 99/1, white solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.49 (d, *J* = 7.6 Hz, 4H), 7.40-7.32 (m, 4H), 7.30-7.24 (m, 2H), 3.88-3.82 (m, 2H), 2.06-1.96 (m, 1H), 1.90-1.82 (m, 3H), 1.76-1.49 (m, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 146.0, 128.5, 127.2, 126.9, 62.8, 34.9, 26.0.

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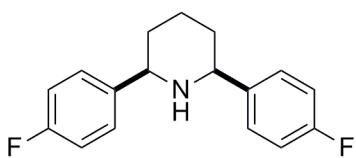
Cis-2,6-di(*p*-tolyl)piperidine (5b): 0.0806 g, 76% yield, *cis/trans* = 97/3, white solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.33 (d, *J* = 8.0 Hz, 4H), 7.11 (d, *J* = 8.0 Hz, 4H), 3.80-3.69 (m, 2H), 2.32 (s, 6H), 2.00-1.88 (m, 1H), 1.86-1.73 (m, 3H), 1.70-1.44 (m, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 143.2, 136.7, 129.2, 126.8, 62.6, 35.0, 26.1, 21.3.

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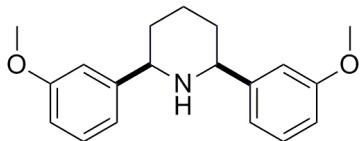
Cis-2,6-bis(4-methoxyphenyl)piperidine (5c): 0.0749 g, 63% yield, *cis/trans* = 99/1, white solid; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.35 (d, *J* = 8.4 Hz, 4H), 6.84 (d, *J* = 8.4 Hz, 4H), 3.70-3.70 (m, 8H), 2.00-1.88 (m, 1H), 1.88-1.69 (m, 3H), 1.66-1.40 (m, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 158.7, 138.3, 127.9, 113.8, 62.2, 55.4, 34.9, 26.0.

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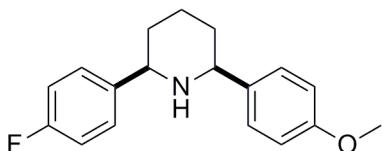
Cis-2,6-bis(4-fluorophenyl)piperidine (5d): 0.0930 g, 85% yield, *cis/trans* = 99/1, white solid, m.p. 179-181 °C; IR (film): 3268, 1514, 1465 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.29-7.16 (m, 4H), 6.98-6.83 (m, 4H), 4.03-3.91 (m, 2H), 2.12-2.00 (m, 3H), 1.99-1.70 (m, 4H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 162.6 (d, *J*_{C-F} = 247.0 Hz), 135.8 (d, *J*_{C-F} = 3.0 Hz), 129.0 (d, *J*_{C-F} = 9.0 Hz), 115.6 (d, *J*_{C-F} = 22.0 Hz),

68.9, 35.1, 24.0; HRMS (ESI) calcd. for $C_{17}H_{18}NF_2$ $[M+H]^+$: 274.1402, Found: 274.1402.



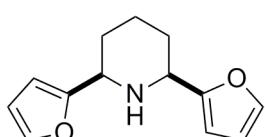
Cis-2,6-bis(3-methoxyphenyl)piperidine (5e): 0.0956 g, 80% yield, *cis/trans* = 99/1, colorless oil; 1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.29-7.19 (m, 2H), 7.09-6.98 (m, 4H), 6.83-6.75 (m, 2H), 3.91-3.82 (m, 8H), 1.99-1.94 (m, 1H), 1.86-1.74 (m, 3H), 1.67-1.46 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 159.8, 147.8, 129.5, 119.4, 112.6, 112.5, 62.7, 55.4, 35.0, 26.0.

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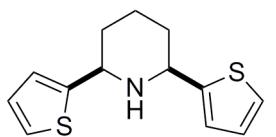
Cis-2-(4-fluorophenyl)-6-(4-methoxyphenyl)piperidine (5f): 0.0500 g, 88% yield, *cis/trans* = 97/3, colorless oil; 1H NMR (400 MHz, $CDCl_3$, ppm): δ 7.50-7.27 (m, 4H), 7.04-6.95 (m, 2H), 6.88 (d, J = 8.4 Hz, 2H), 3.81-3.69 (m, 5H), 2.02-1.93 (m, 1H), 1.89-1.73 (m, 3H), 1.71-1.42 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ 162.2 (d, J_{C-F} = 243.0 Hz), 158.8, 141.8 (d, J_{C-F} = 2.0 Hz), 138.1, 128.3 (d, J_{C-F} = 8.0 Hz), 128.0, 115.2 (d, J_{C-F} = 21.0 Hz), 113.9, 62.2, 62.1, 55.4, 35.1, 34.8, 25.9.

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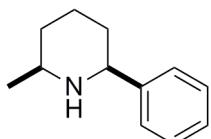


Cis-2,6-di(furan-2-yl)piperidine (5g): 0.0635 g, 73% yield, *cis/trans* = 97/3, colorless oil; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.37-7.28 (m, 2H), 6.32-6.25 (m, 2H), 6.20-6.14 (m, 2H), 3.94-3.85 (m, 2H), 2.21 (brs, 1H), 2.05-1.90 (m, 3H), 1.74-1.54 (m, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 157.2, 141.4, 110.1, 104.6, 55.0, 30.4, 24.5.

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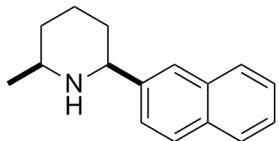
2,6-Di(thien-2-yl)piperidine (5h): 0.0757 g, 76% yield, *cis/trans* = 95/5, white solid, m.p. 55-62 °C; IR (film): 3304, 1593, 1438, 1289 cm⁻¹; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.24-7.15 (m, 2H), 6.98 (d, *J* = 3.2 Hz, 2H), 6.96-6.92 (m, 2H), 4.17-4.10 (m, 2H), 2.08 (brs, 1H), 2.02-1.95 (m, 3H), 1.69-1.55 (m, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 149.4, 126.5, 123.8, 123.0, 57.9, 35.4, 25.4; HRMS (ESI) calcd. for C₁₃H₁₆NS₂[M+H]⁺: 250.0724, Found: 250.0719.



Cis-2-methyl-6-phenylpiperidine (5i): 0.0567 g, 81% yield, *cis/trans* = 86/14, colorless oil; ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.28 (d, *J* = 7.2 Hz, 2H), 7.26-7.18 (m, 2H), 7.18-7.10 (m, 1H), 3.64-3.49 (m, 1H), 2.80-2.65 (m, 1H), 1.84-1.72 (m, 1H), 1.70-1.52 (m, 3H), 1.48-1.30 (m, 2H), 1.13-1.04 (m, 1H), 1.02 (d, *J* = 6.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃, ppm): δ 145.7, 128.5, 127.1, 126.9, 62.6, 53.3, 34.4,

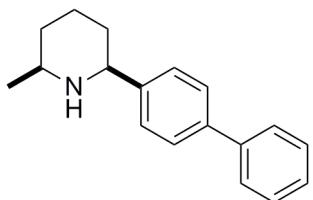
34.0, 25.5, 23.2.

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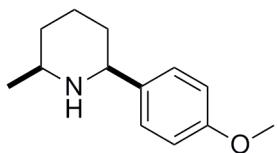
Cis-2-methyl-6-(naphthalen-2-yl)piperidine (5j): 0.0721 g, 80% yield, *cis/trans* = 99/1, white solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.85-7.73 (m, 4H), 7.52-7.46 (m, 1H), 7.46-7.37 (m, 2H), 3.86-3.73 (m, 1H), 2.90-2.74 (m, 1H), 1.97-1.75 (m, 2H), 1.74-1.61 (m, 2H), 1.60-1.43 (m, 2H), 1.28-1.16 (m, 1H), 1.13 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 143.2, 133.7, 132.9, 128.0, 127.9, 127.7, 126.0, 125.7, 125.6, 124.9, 62.7, 53.4, 34.6, 34.0, 25.6, 23.4.

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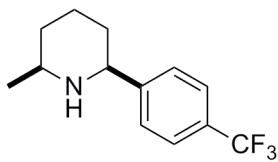
Cis-2-[(1,1'-biphenyl)-4-yl]-6-methylpiperidine (5k): 0.0885 g, 88% yield, *cis/trans* = 99/1, colorless oil; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.62-7.50 (m, 4H), 7.48-7.37 (m, 4H), 7.36-7.27 (m, 1H), 3.76-3.63 (m, 1H), 2.89-2.75 (m, 1H), 1.95-1.86 (m, 1H), 1.83-1.74 (m, 1H), 1.70-1.63 (m, 1H), 1.62-1.42 (m, 3H), 1.26-1.14 (m, 1H), 1.13 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 144.8, 141.2, 140.0, 128.8, 127.3, 127.2, 127.1, 62.3, 53.3, 34.5, 34.0, 25.5, 23.3.

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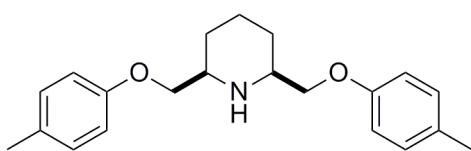
Cis-2-(4-methoxyphenyl)-6-methylpiperidine (5l): 0.0460 g, 56% yield, *cis/trans* = 99/1, colorless oil; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.29 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 3.79 (s, 3H), 3.67-3.57 (m, 1H), 2.91-2.69 (m, 1H), 1.92-1.81 (m, 1H), 1.79-1.56 (m, 3H), 1.56-1.34 (m, 2H), 1.30-1.10 (m, 1H), 1.10 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 158.8, 138.0, 128.0, 113.9, 62.0, 55.5, 53.4, 34.4, 34.0, 25.6, 23.3.

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Cis-2-methyl-6-[4-(trifluoromethyl)phenyl]piperidine (5m): 0.0797 g, 82% yield, *cis/trans* = 86/14, colorless oil; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.56 (d, J = 8.4 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 3.78-3.66 (m, 1H), 2.89-2.73 (m, 1H), 1.93-1.83 (m, 1H), 1.81-1.70 (m, 1H), 1.70-1.61 (m, 1H), 1.60-1.33 (m, 3H), 1.31-1.12 (m, 1H), 1.12 (d, J_{C-F} = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 149.8, 129.4 (q, J_{C-F} = 32.0 Hz), 127.2, 125.5 (q, J_{C-F} = 4.0 Hz), 123.1, 62.3, 53.2, 34.7, 33.9, 25.5, 23.2.

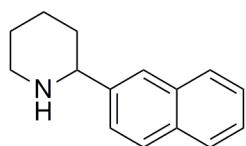
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Cis-2,6-bis[(p-tolyloxy)methyl]piperidine (5n): 0.1044 g, 80% yield, *cis/trans* =

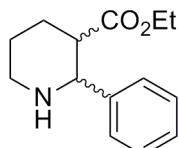
99/1, white solid; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.06 (d, $J = 8.4$ Hz, 4H), 6.81 (d, $J = 8.4$ Hz, 4H), 3.94-3.85 (m, 2H), 3.84-3.75 (m, 2H), 3.12-2.99 (m, 2H), 2.64 (brs, 1H), 2.27 (s, 6H), 1.93-1.83 (m, 1H), 1.77-1.63 (m, 2H), 1.56-1.39 (m, 1H), 1.30-1.13 (m, 2H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 157.0, 130.2, 130.0, 114.7, 73.0, 55.6, 28.7, 24.0, 20.7.

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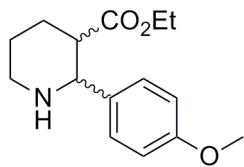
2-(Naphthalen-2-yl)piperidine (5o): 0.0372 g, 44% yield, white solid, m.p. 42-44 °C; IR (film): 3321, 1633, 1601, 1440, 1316, 1107 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.90-7.75 (m, 4H), 7.53-7.48 (m, 1H), 7.48-7.42 (m, 2H) 3.83-3.69 (m, 1H), 3.33-3.20 (m, 1H), 2.93-2.79 (m, 1H), 2.00-1.82 (m, 3H), 1.78-1.68 (m, 1H), 1.70-1.50 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 143.3, 133.8, 133.0, 128.2, 128.1, 127.8, 126.1, 125.7, 124.9, 62.6, 48.1, 35.3, 26.2, 25.7.

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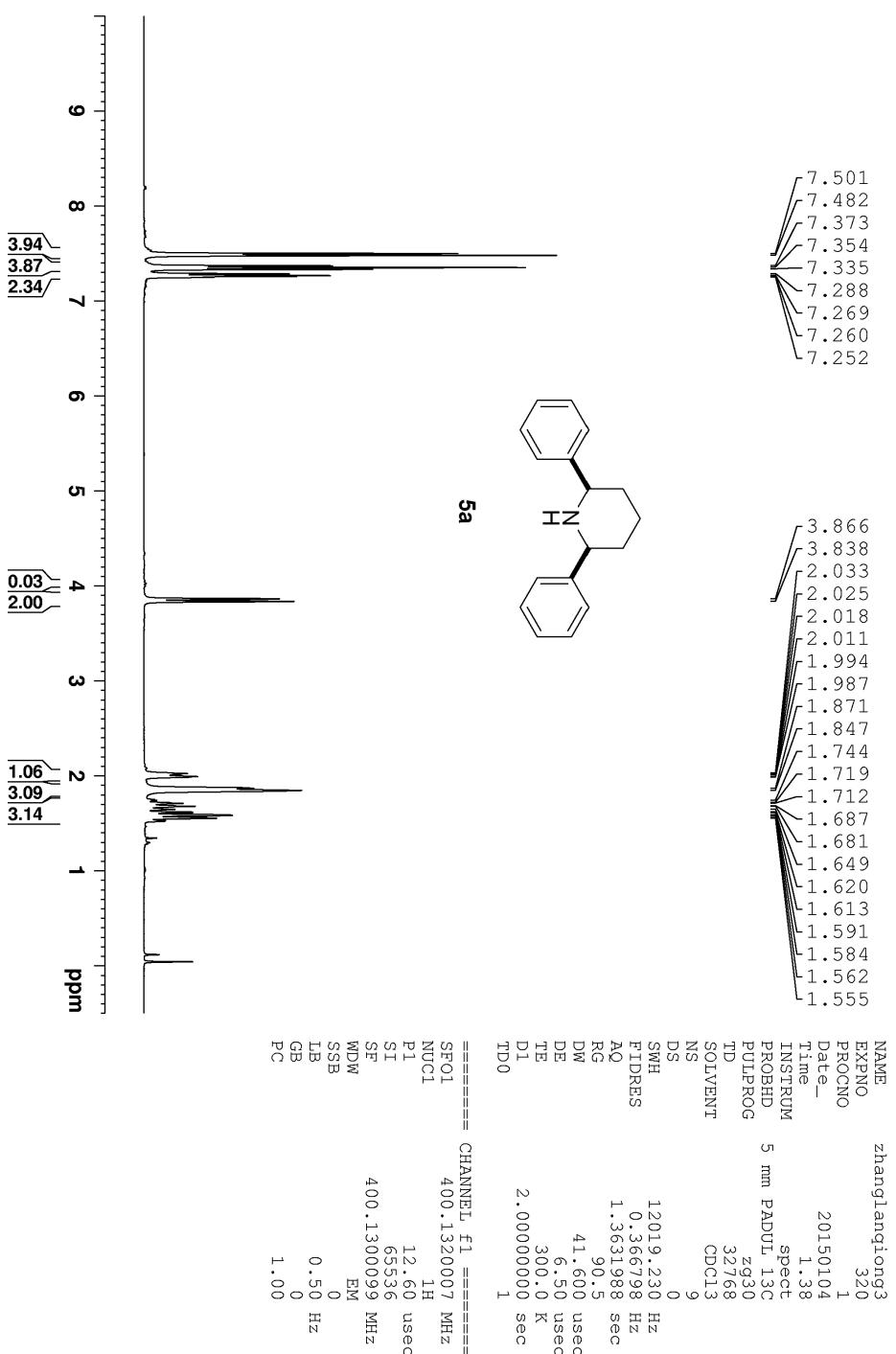


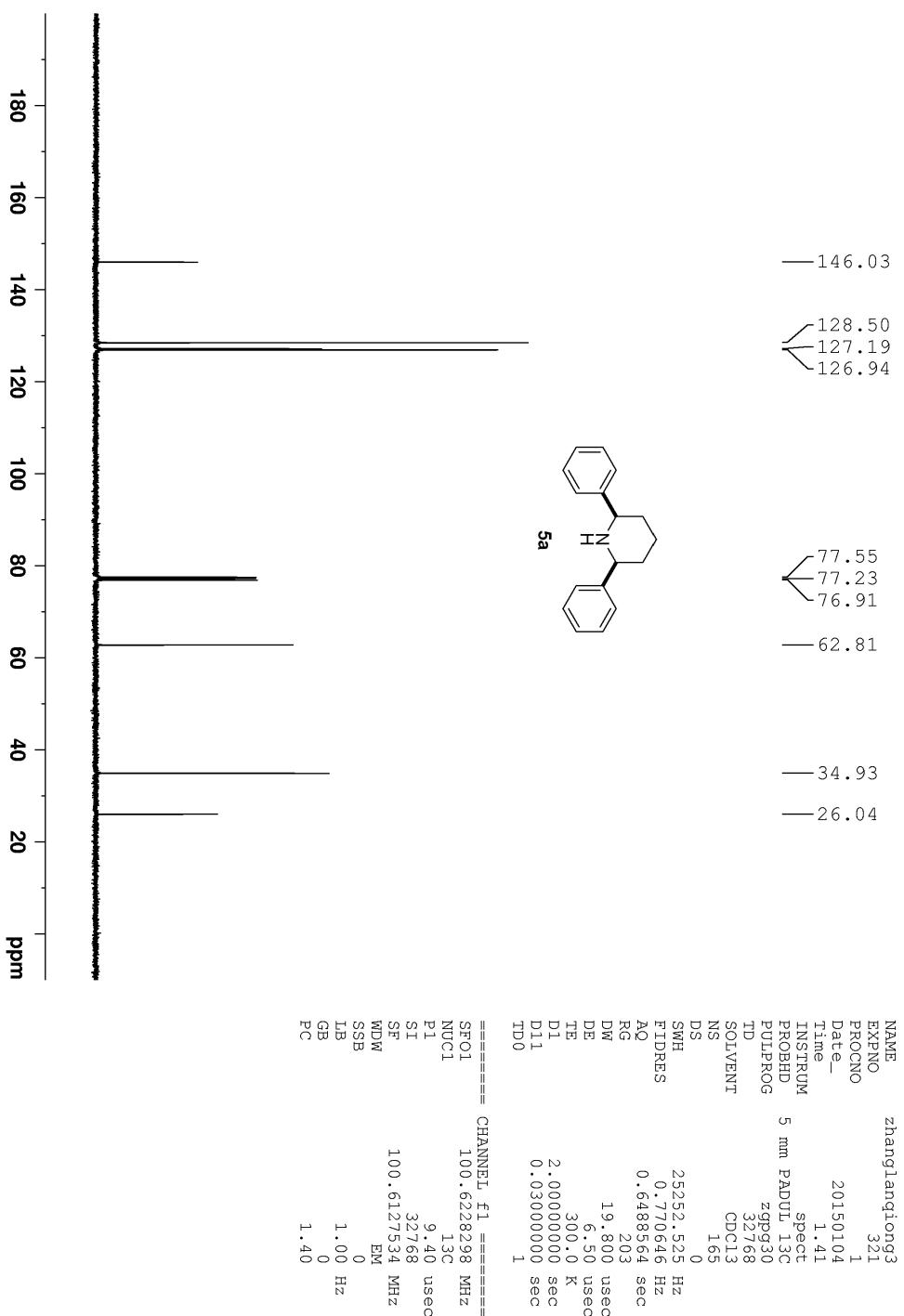
Ethyl 2-phenylpiperidine-3-carboxylate (5p): 0.0411 g, 44% yield, *cis/trans* = 67/33, yellow oil; IR (film): 3359, 1724, 1655, 1633, 1175 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.48-7.15 (m, 5H), 4.04-3.69 (m, 3H), 3.39-3.23 (m, 0.67H) (*cis*

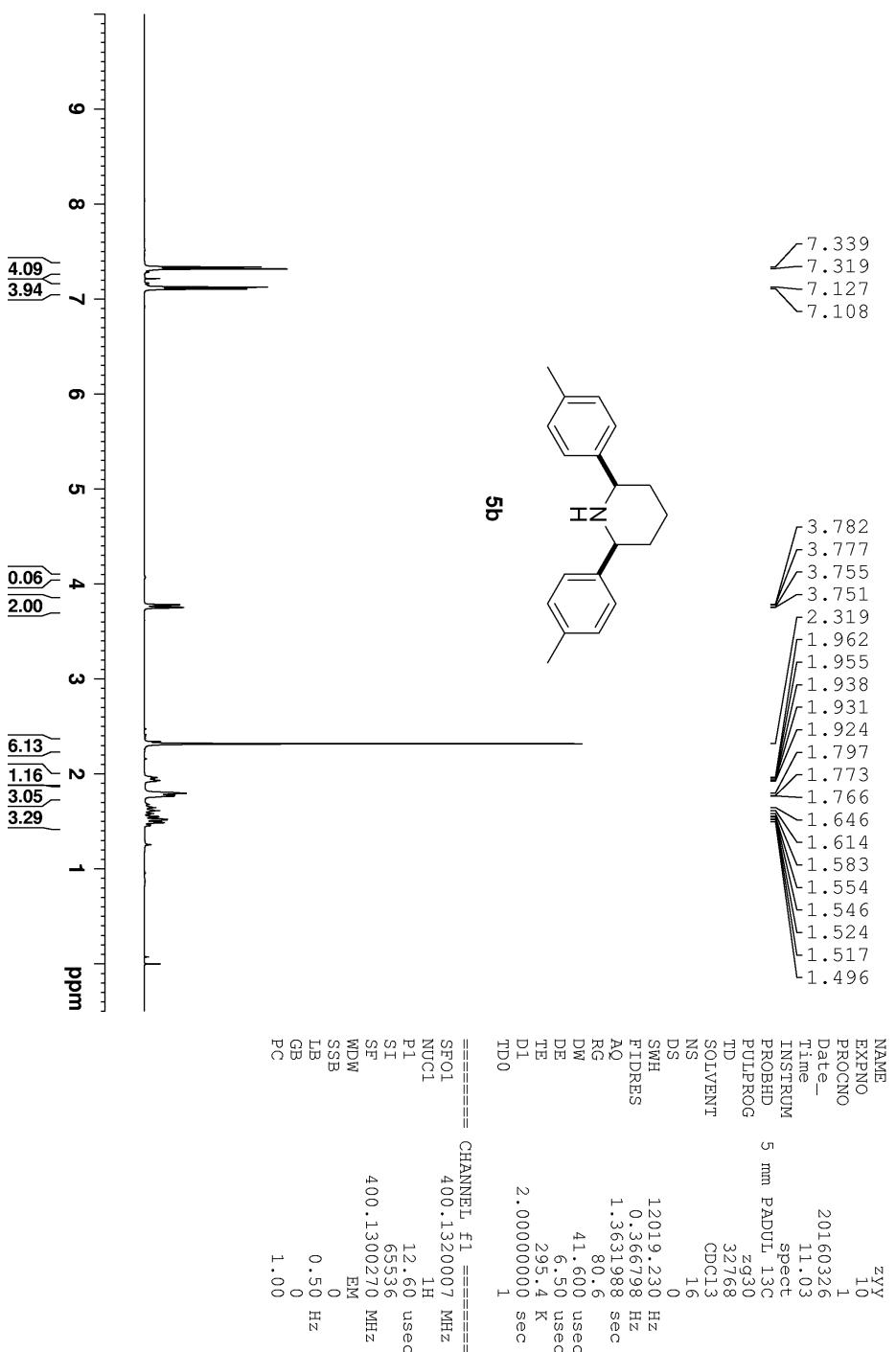
isomer), 3.23-3.13 (m, 0.33H) (*trans* isomer), 3.04-2.56 (m, 3H), 2.22-2.04 (m, 1H), 2.00-1.45 (m, 3H), 1.02-0.86 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 173.7, 142.2, 128.5, 128.2, 127.9, 127.8, 126.9, 126.2, 64.3, 61.2, 60.1, 59.9, 50.5, 47.2, 47.1, 44.6, 28.9, 28.0, 25.1, 22.1, 14.1; HRMS (ESI) calcd. for $\text{C}_{14}\text{H}_{20}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 234.1494, Found: 234.1486.

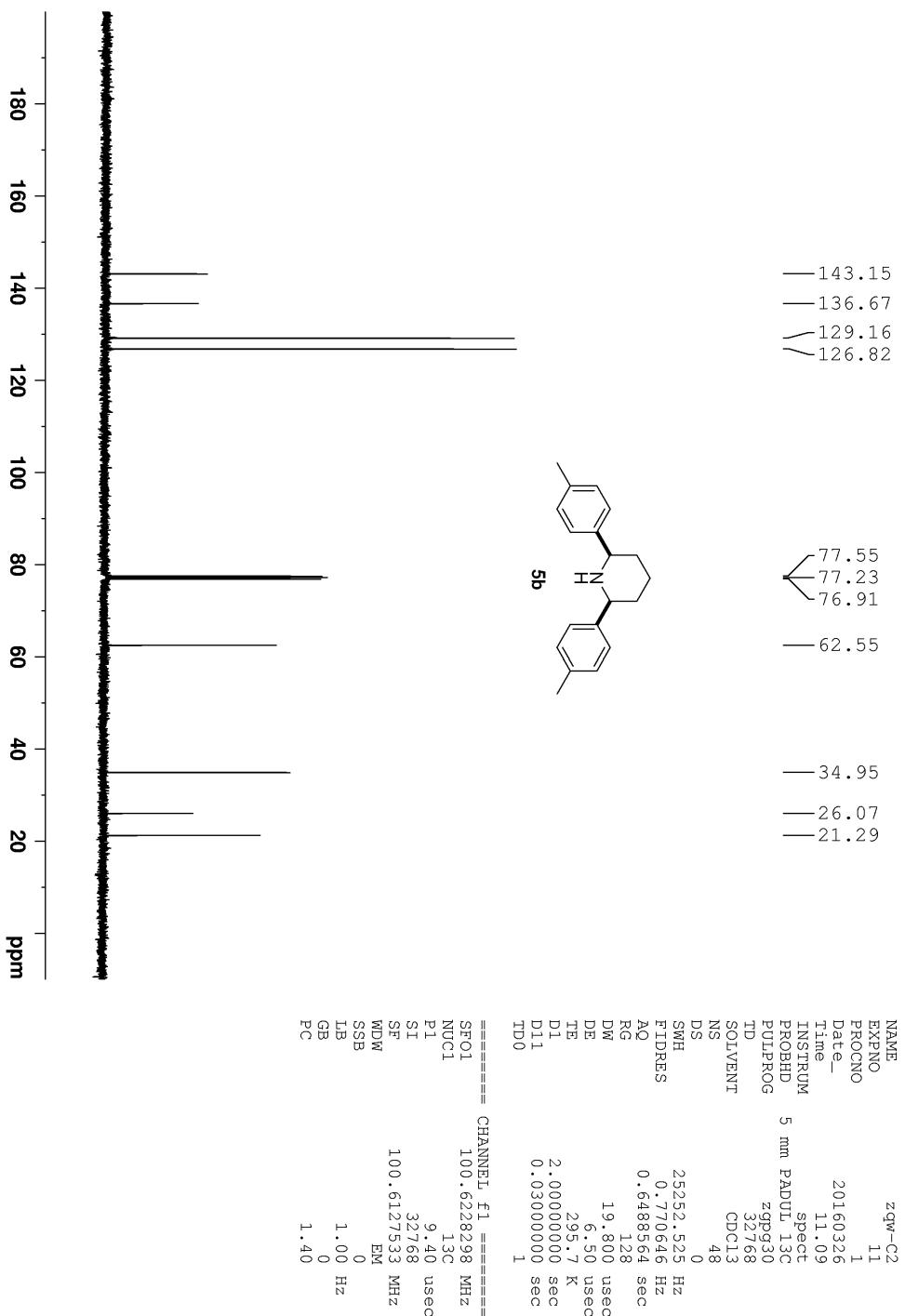


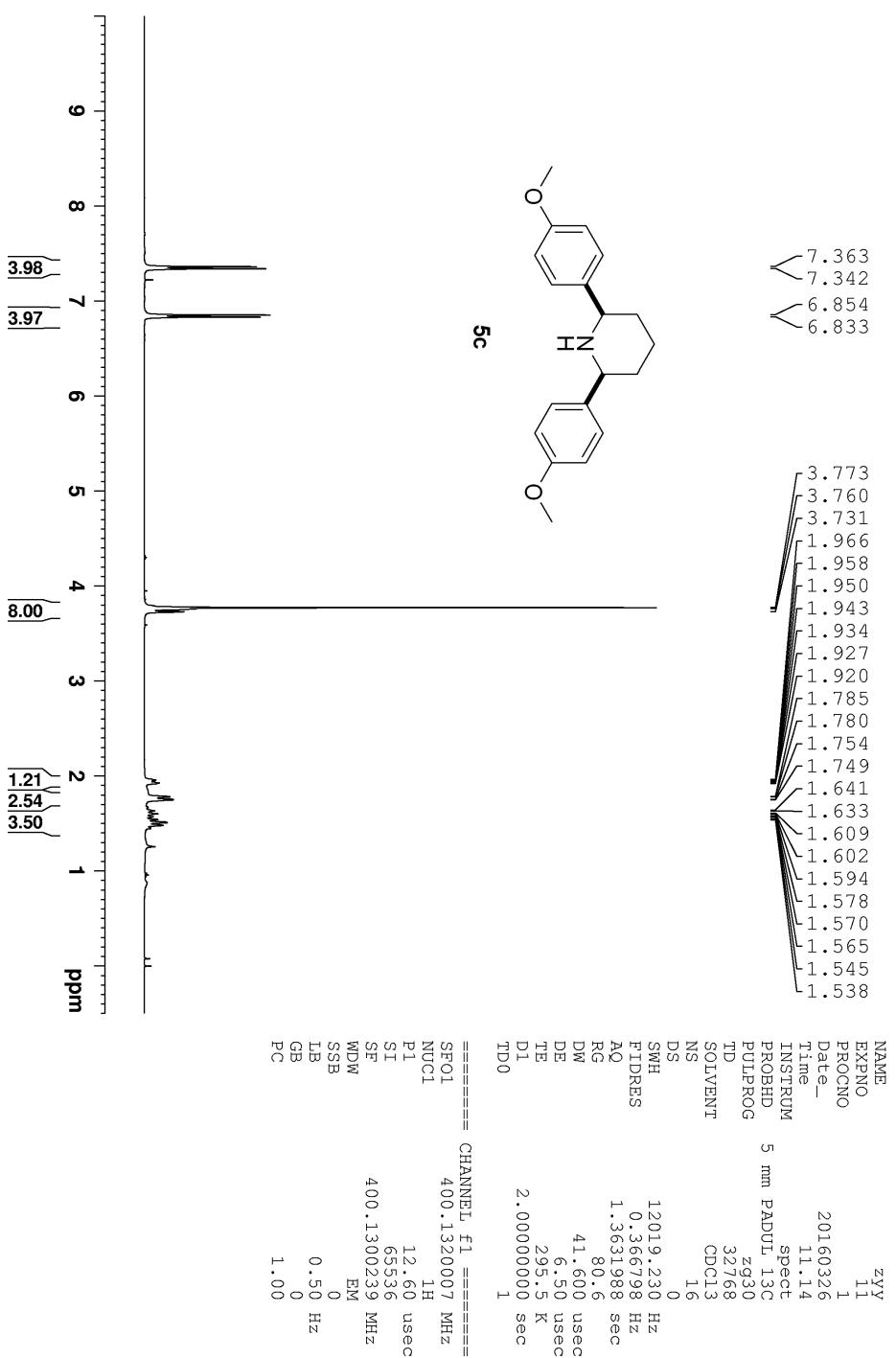
Ethyl 2-(4-methoxyphenyl)piperidine-3-carboxylate (5q): 0.0558 g, 53% yield, *cis/trans* = 70/30, yellow oil; IR (film): 3322, 1720, 1514, 1247, 1177 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.39-7.10 (m, 2H), 6.96-6.74 (m, 2H), 3.98-3.82 (m, 3H), 3.77 (s, 3H), 3.40-3.21 (m, 0.7H) (*cis* isomer), 3.21-3.09 (m, 0.3H) (*trans* isomer), 2.99-2.55 (m, 3H), 2.26-1.60 (m, 4H), 1.59-1.43 (m, 1H), 1.12-0.90 (m, 3H); ^{13}C NMR (100 MHz, CDCl_3 , ppm): δ 173.8, 158.5, 134.4, 128.9, 127.3, 113.8, 113.6, 63.5, 60.7, 60.1, 59.9, 55.4, 50.5, 47.2, 47.1, 44.6, 29.0, 27.8, 25.0, 22.1, 14.2; HRMS (ESI) calcd. for $\text{C}_{15}\text{H}_{22}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 264.1600, Found: 264.1594.

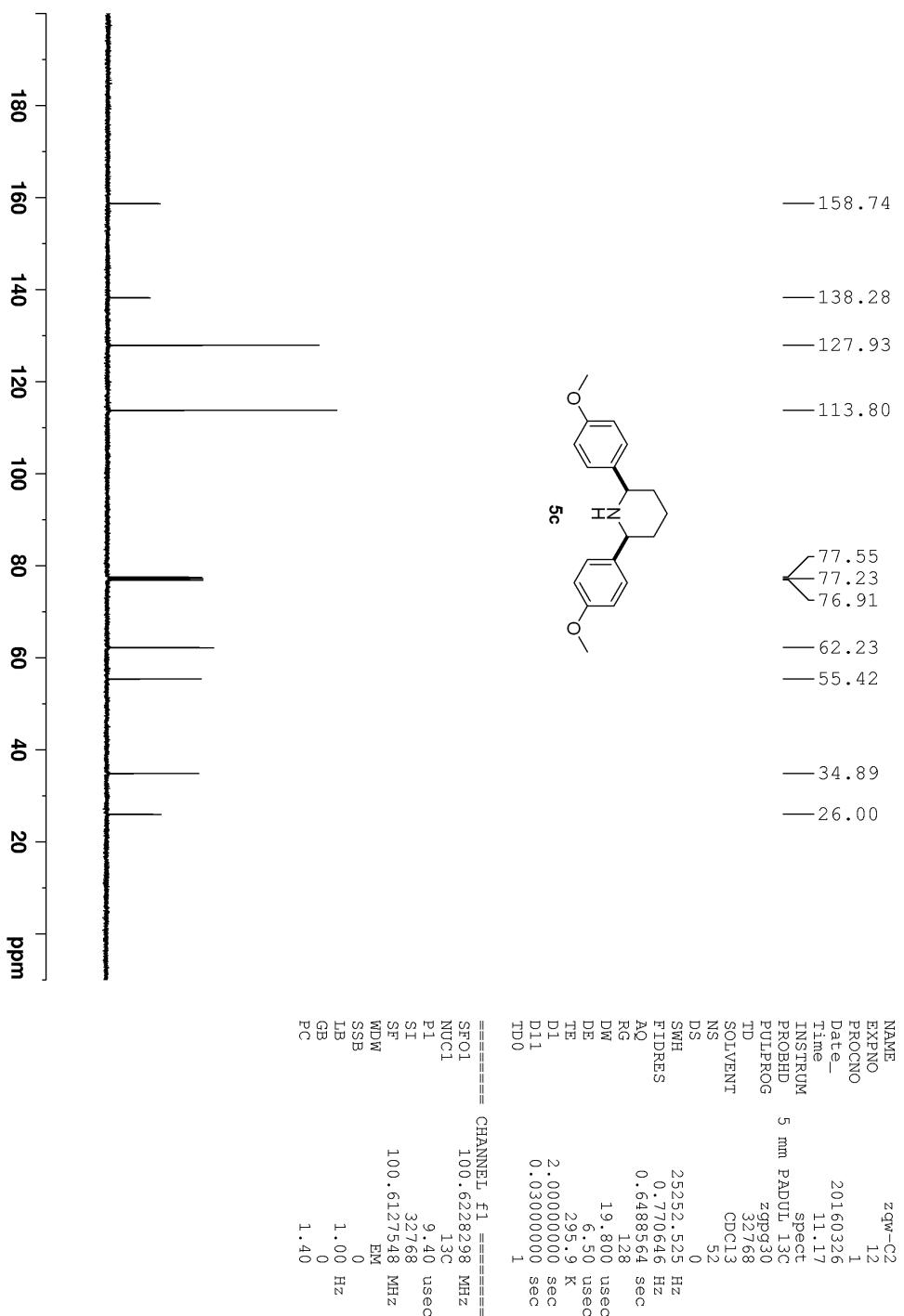


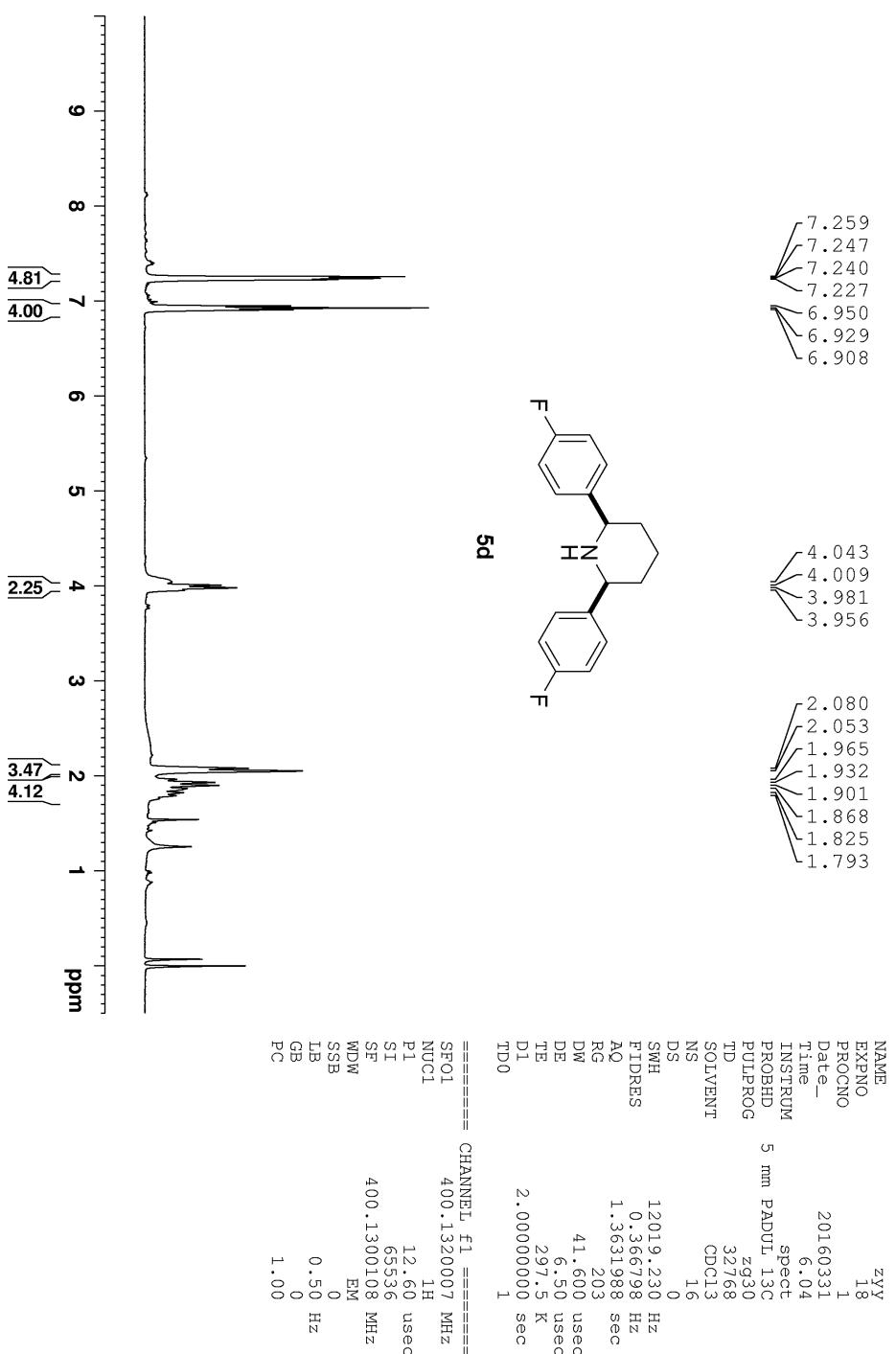


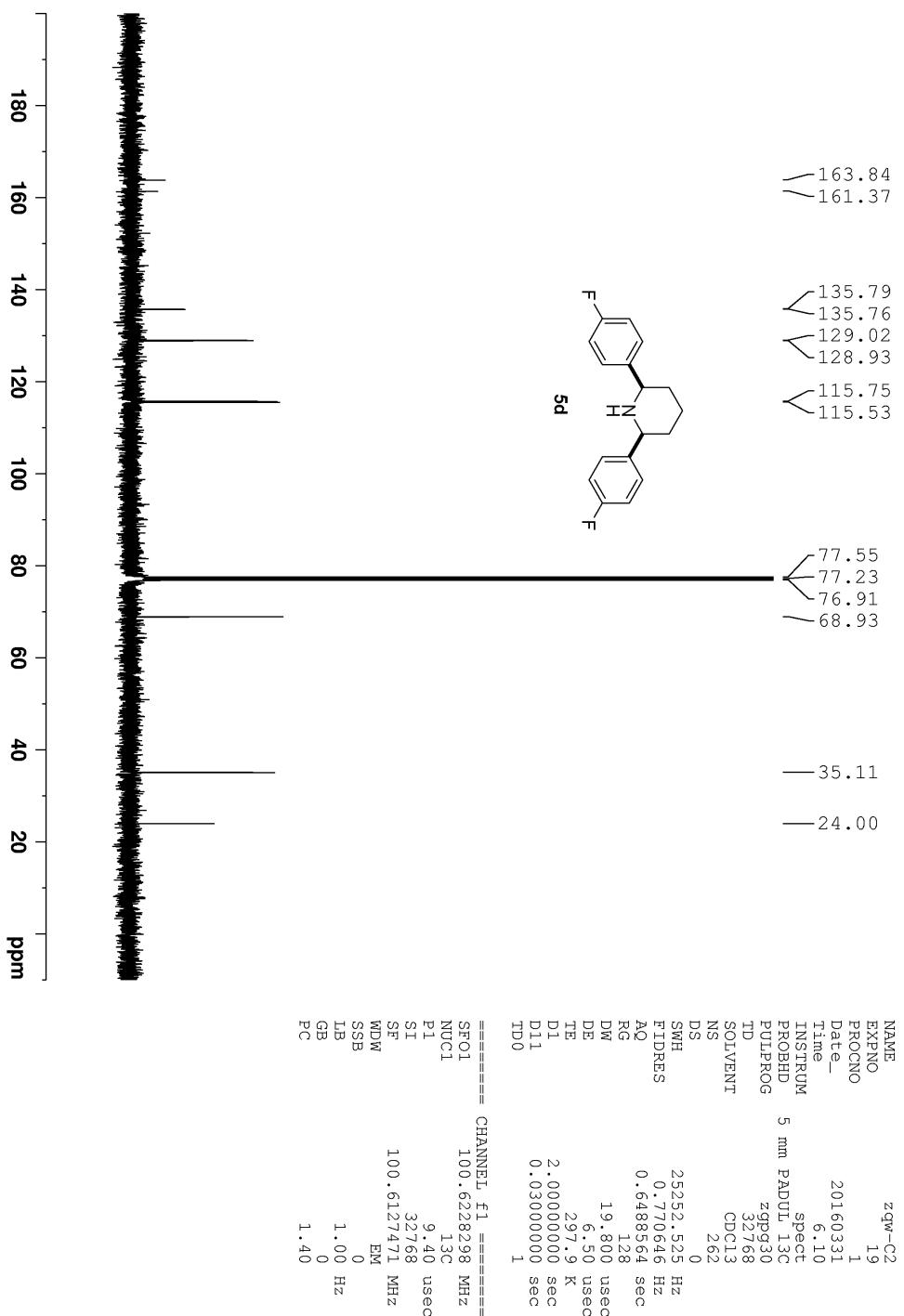


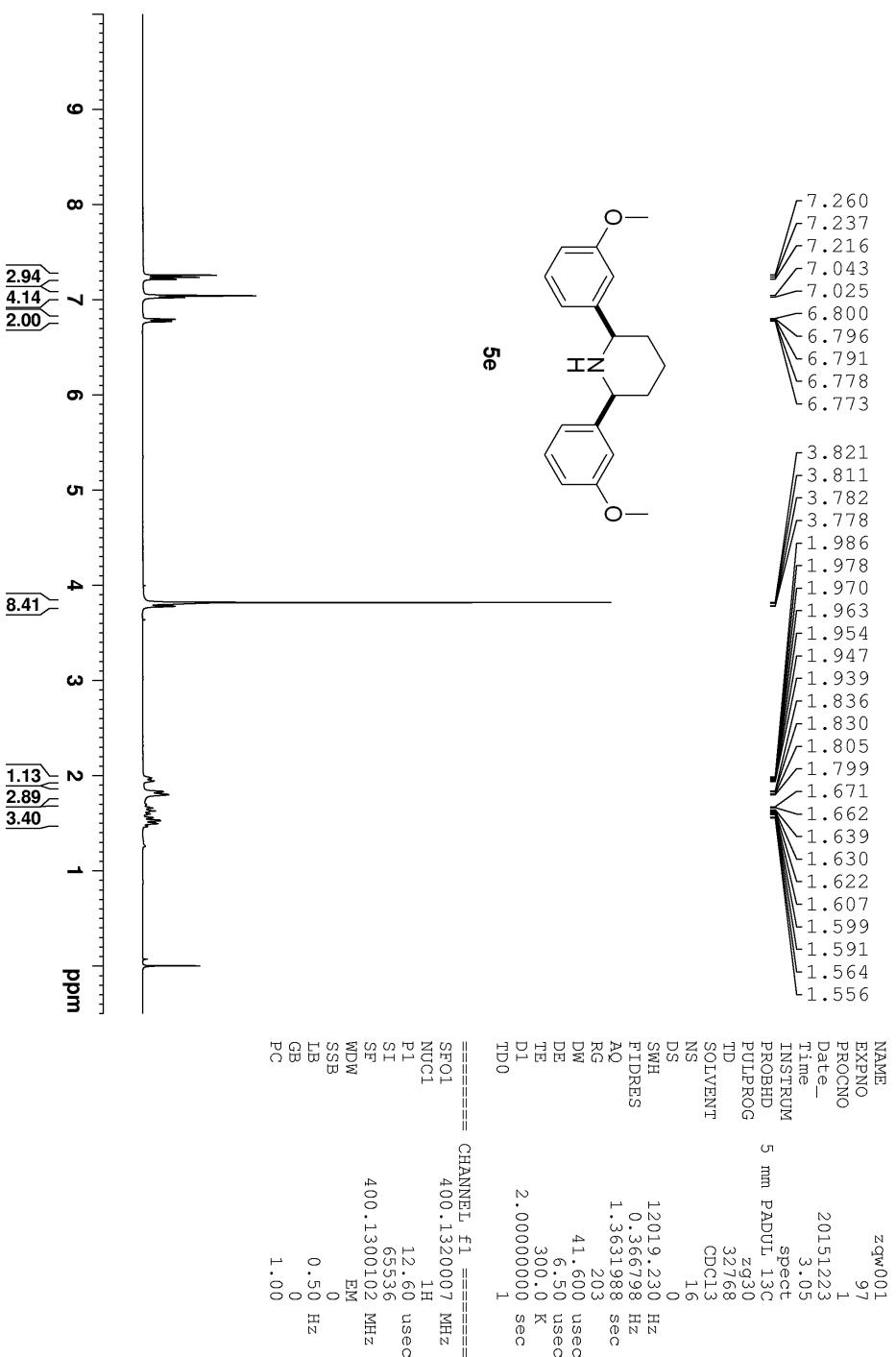


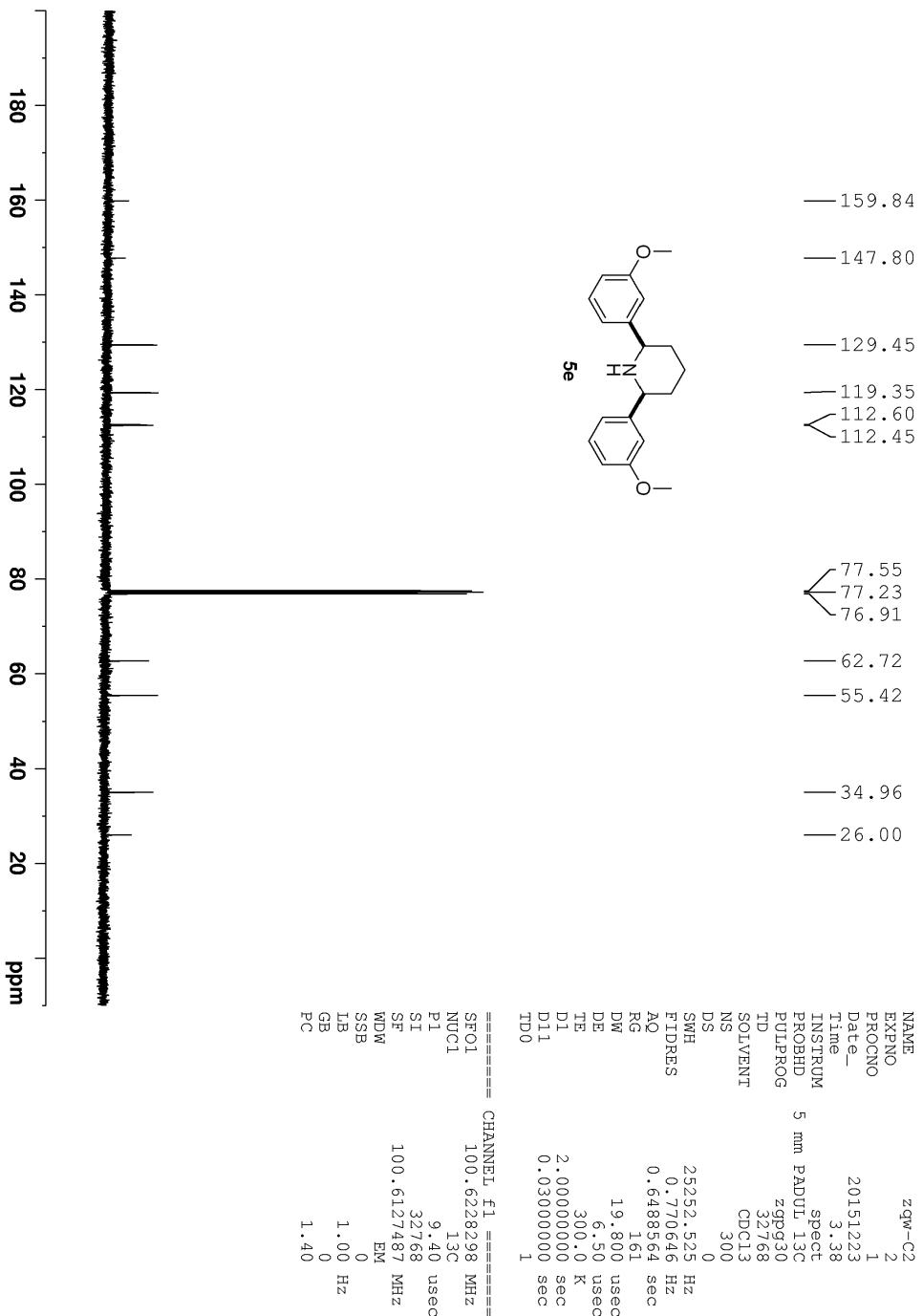


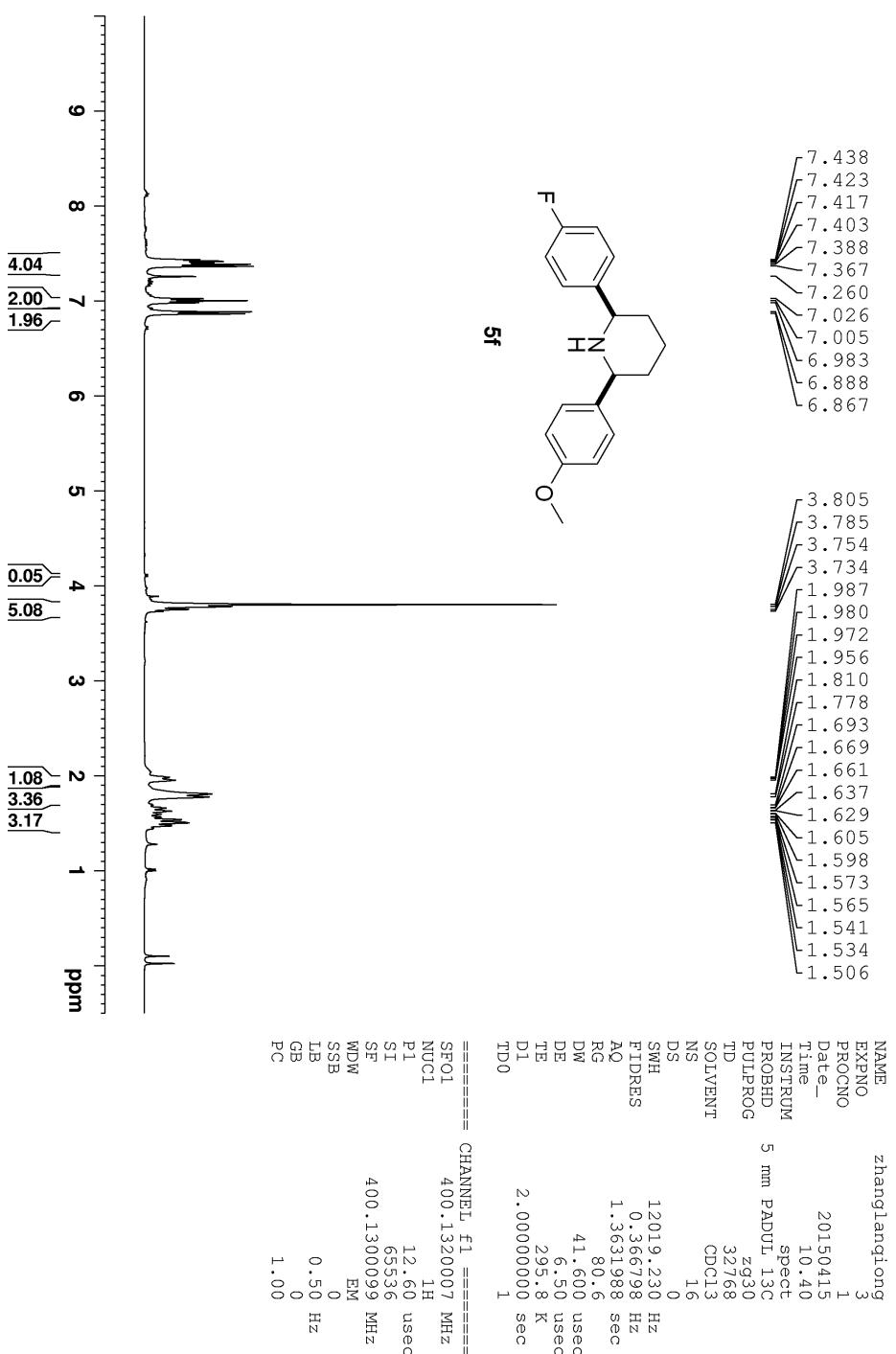


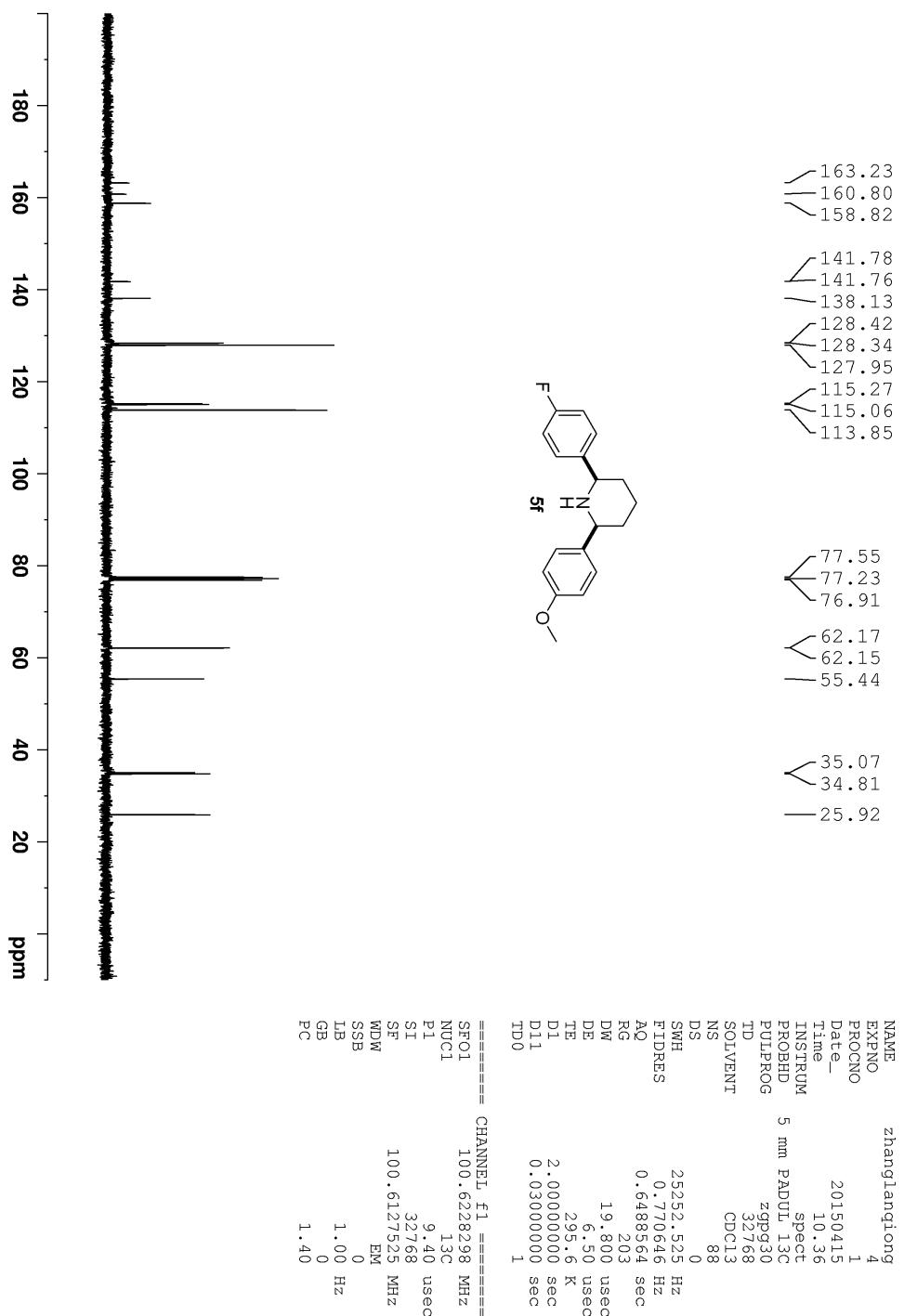


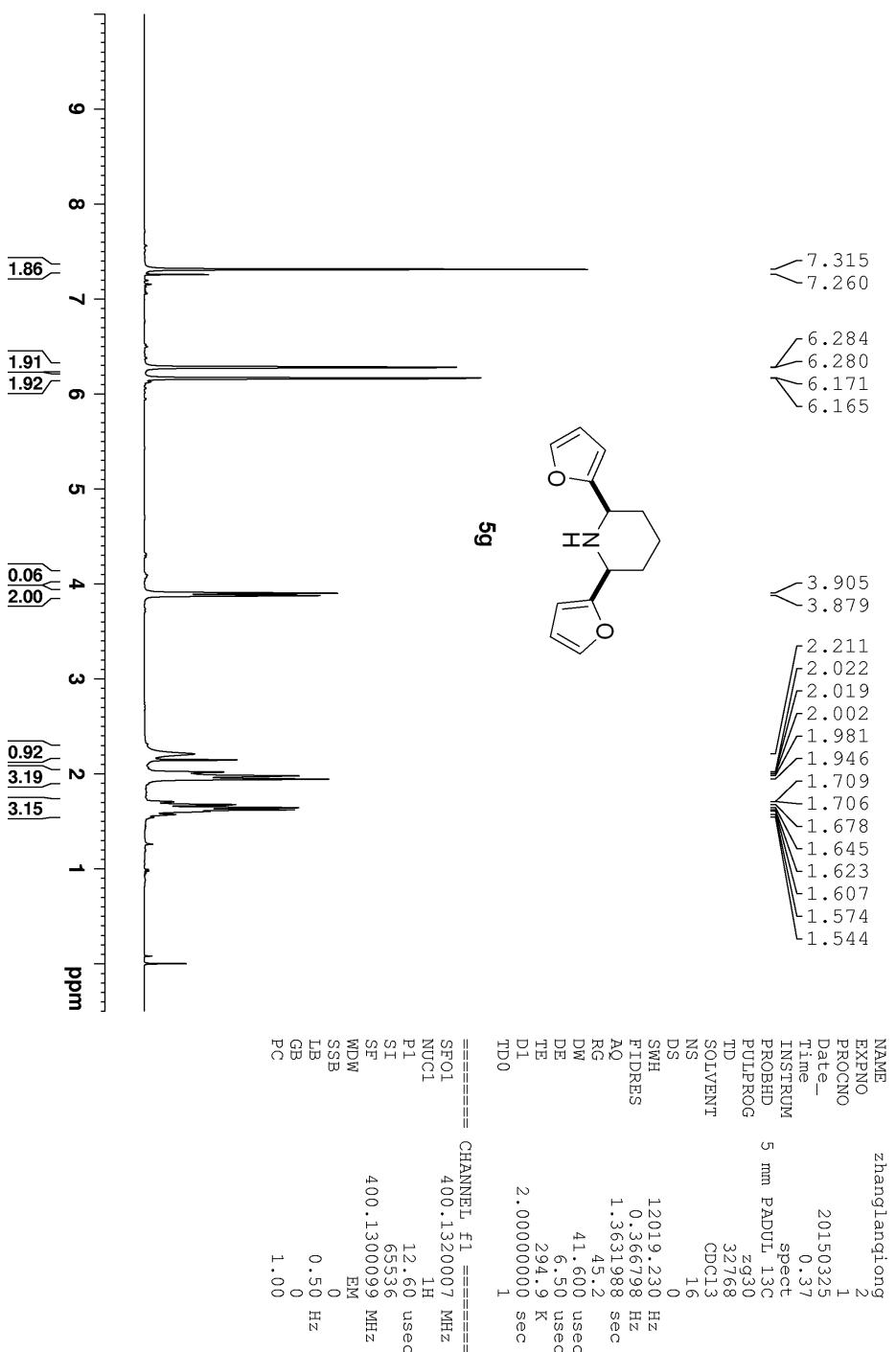


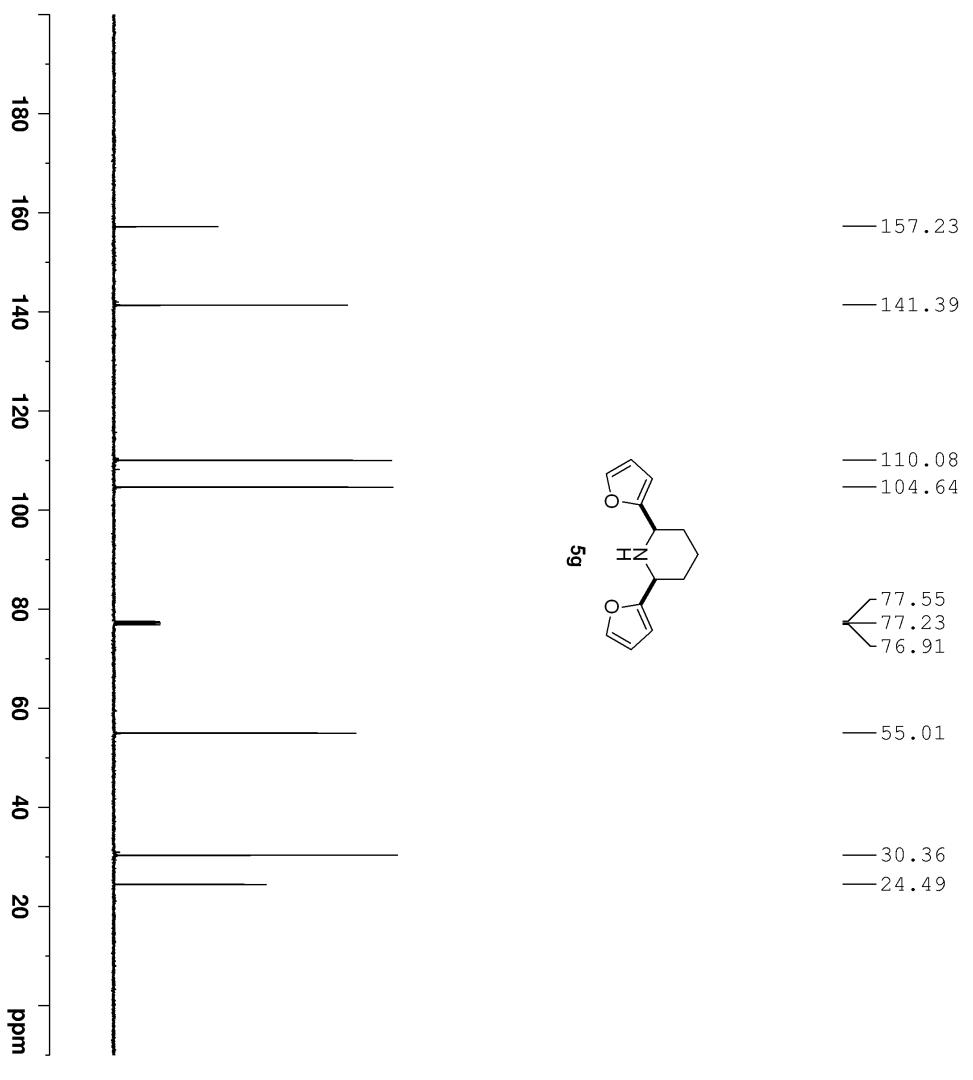










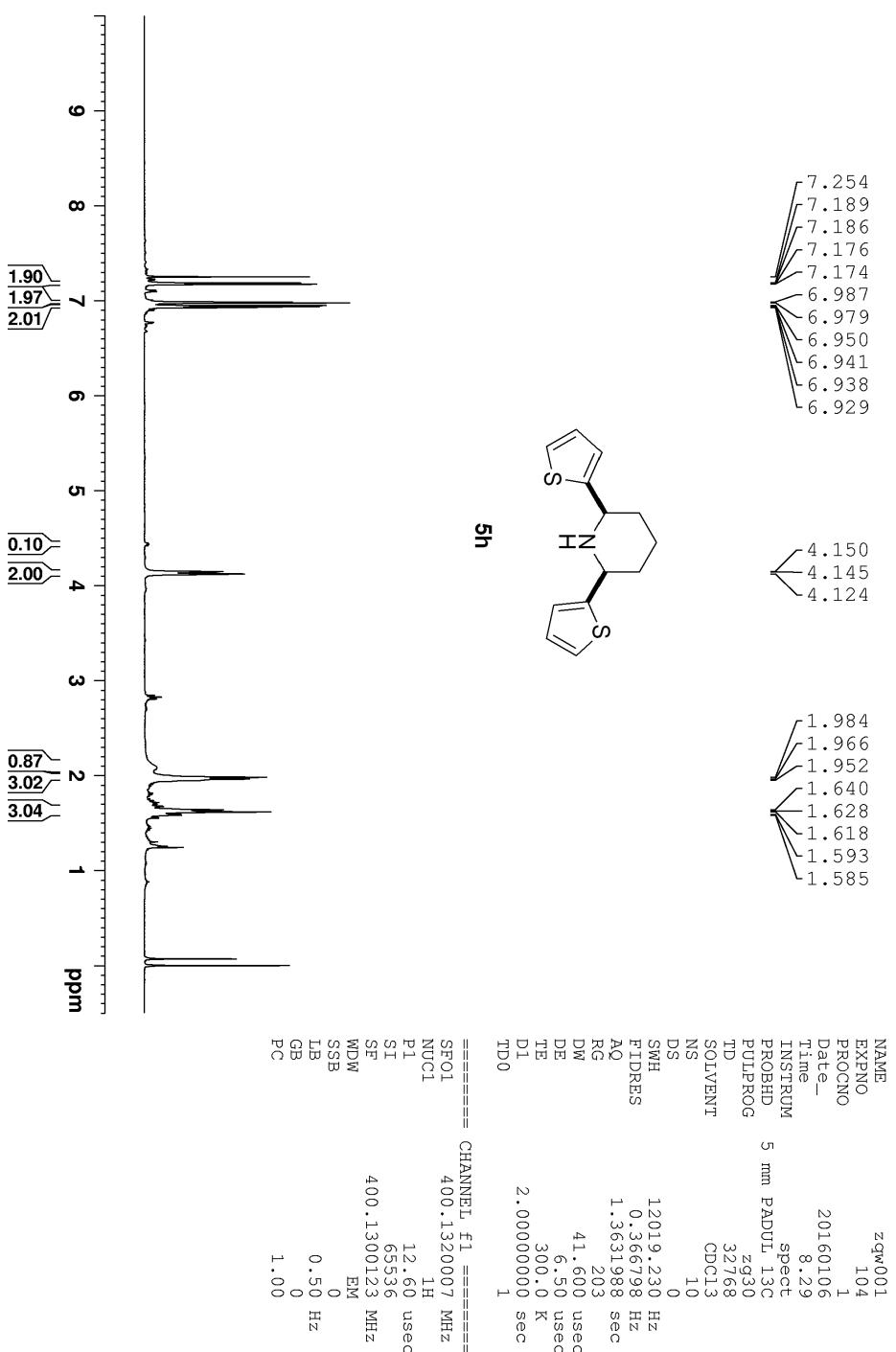


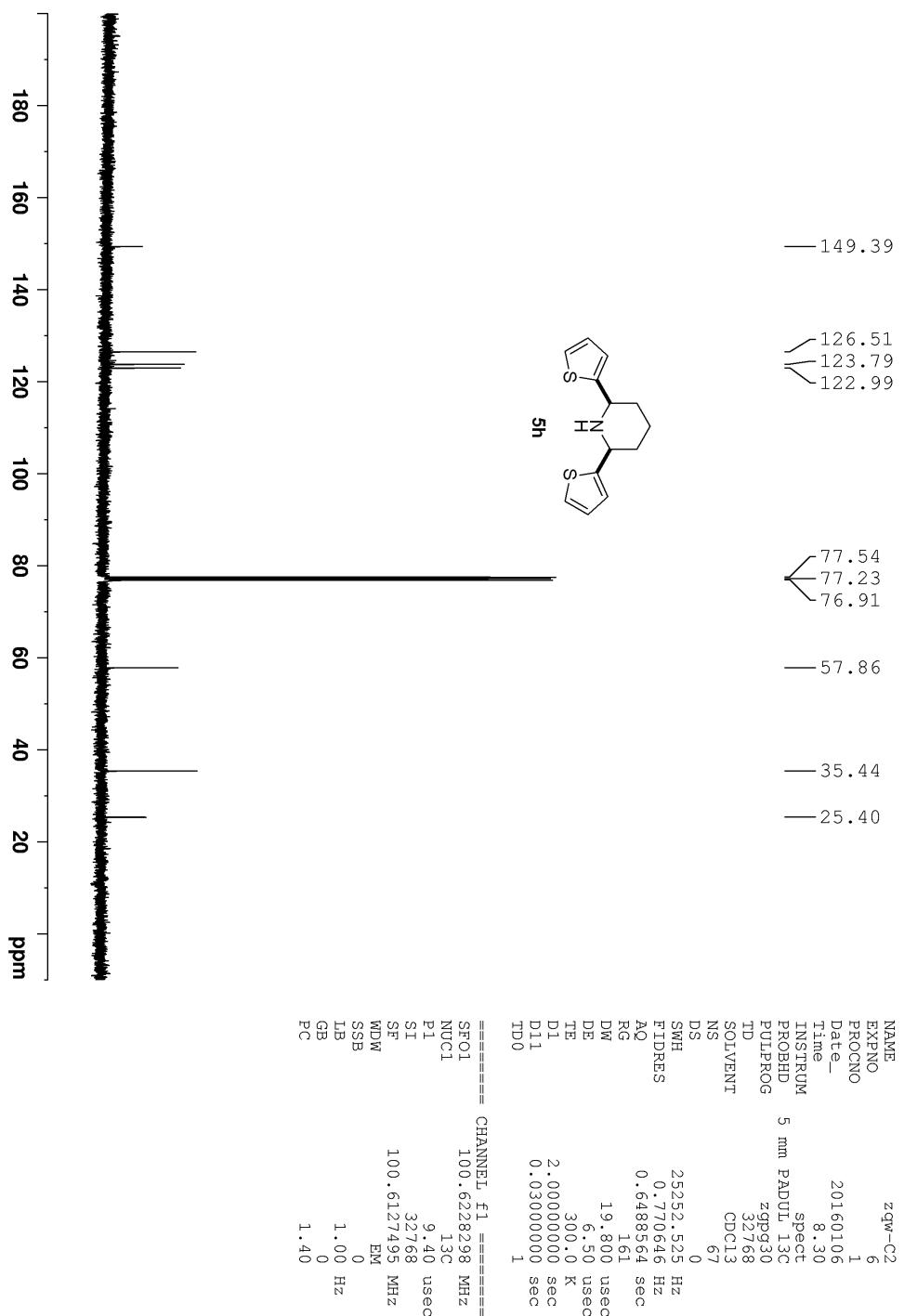
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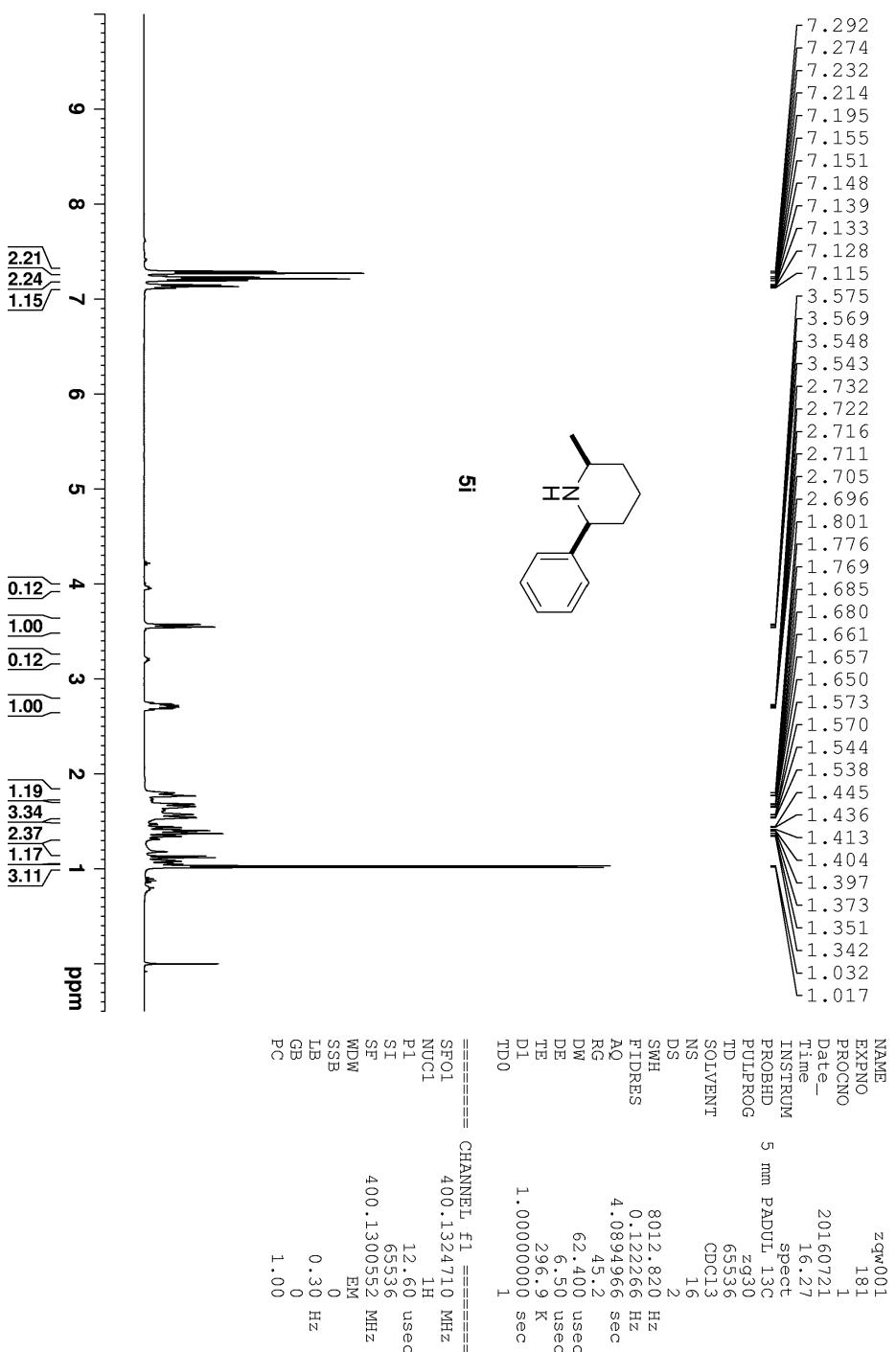
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NAME          zhanglanqiong
EXPNO         1
PROCNO        1
Date_        20150325
Time         0.38
INSTRUM      spect
PROBID       5 mm PADUL 13C
PULPROG     zgppg30
TD           33768
SOLVENT      CDCl3
NS            110
DS             0
SWH         25252.525 Hz
FIDRES      0.6488564 sec
AQ            203
RG            1.9800 usec
DW            6.50 usec
DE            2.00 usec
TE            235.0 K
D1           2.0000000 sec
D11          0.03000000 sec
TD0           1

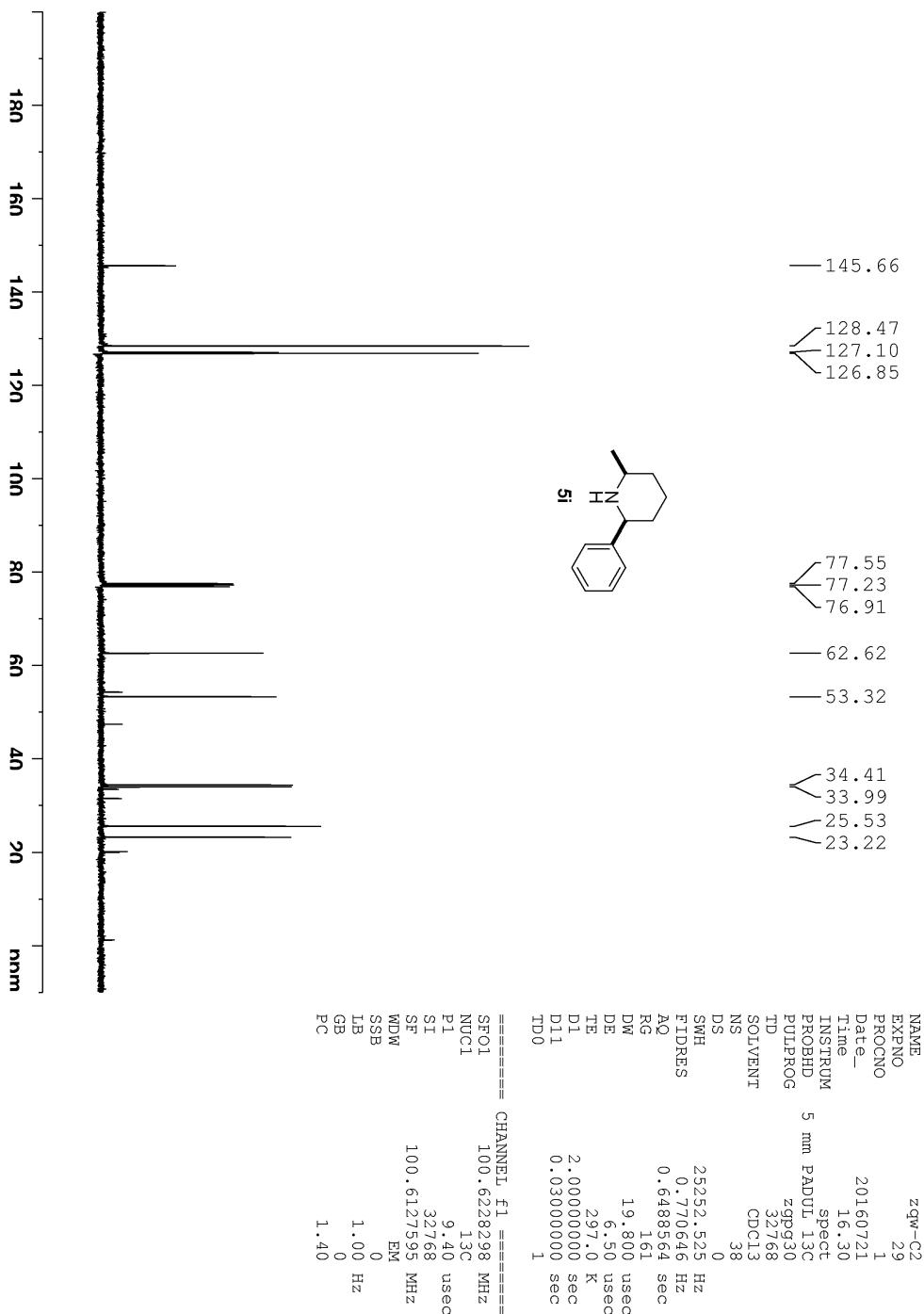
===== CHANNEL f1 =====
SFO1        100.6228298 MHz
NUC1         13C
P1           9.40 usec
SI            32768
SF          100.6127610 MHz
WDW
SSB
LB            0 Hz
GB           1.00 Hz
PC           1.40

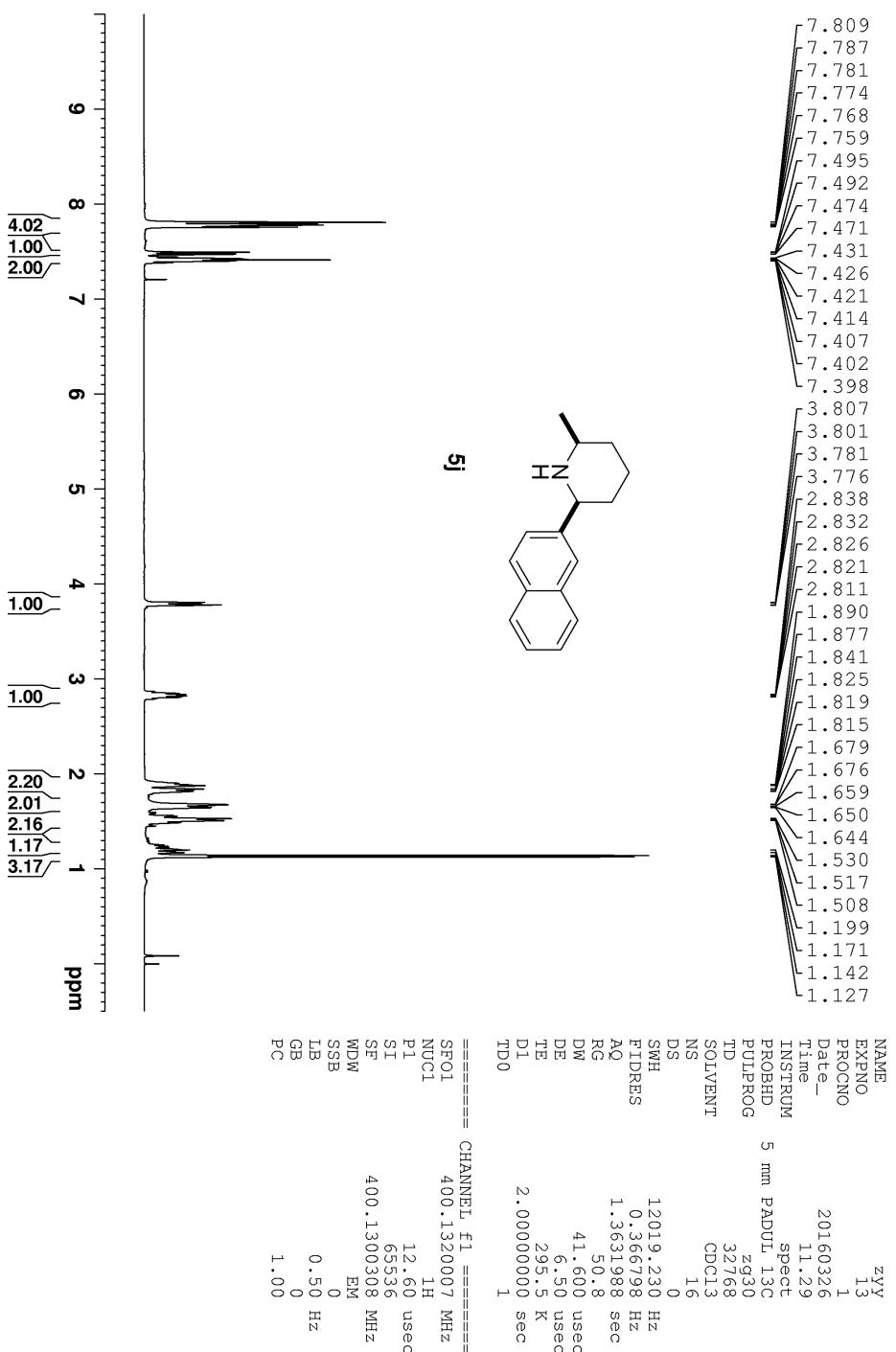
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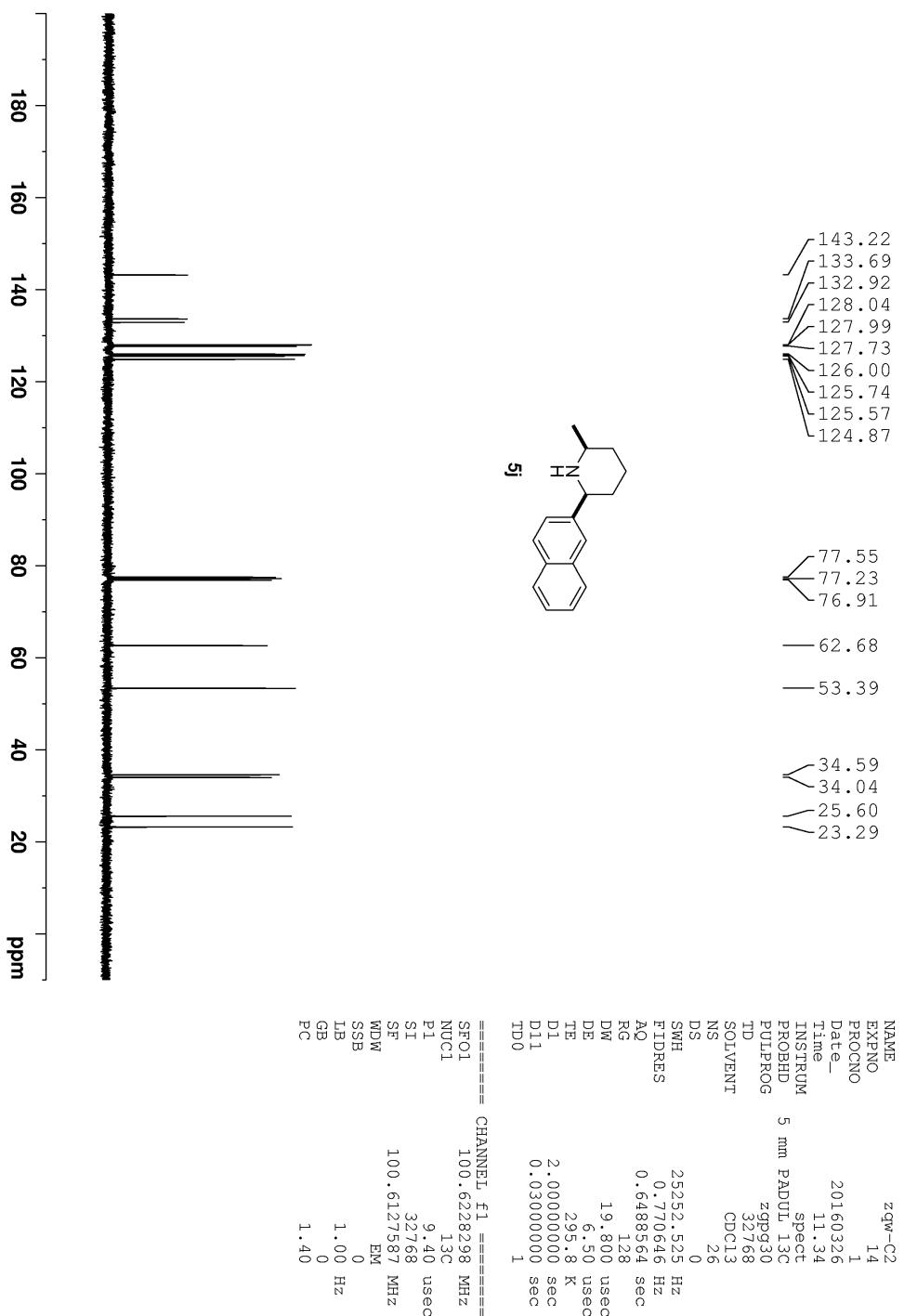


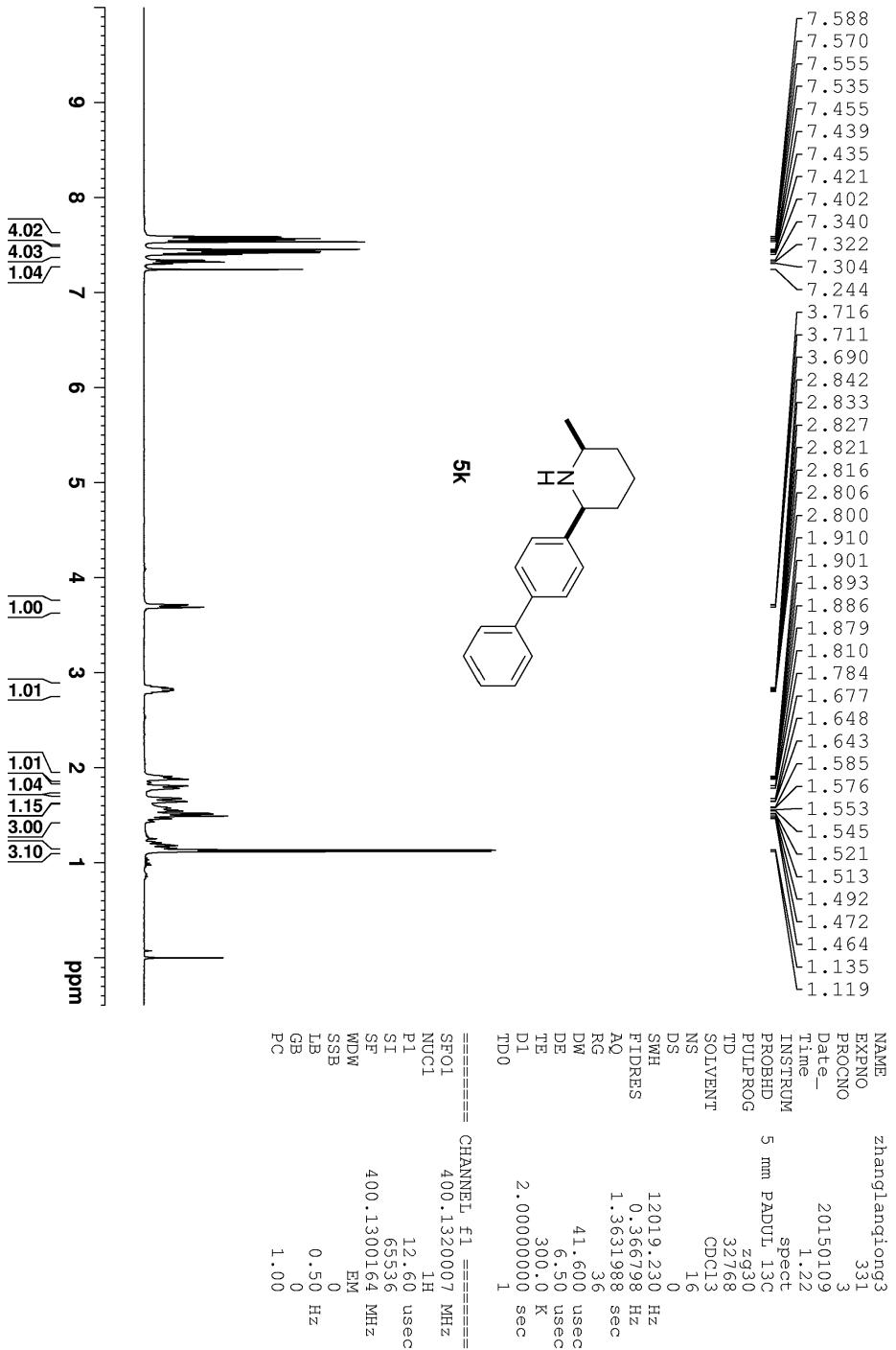


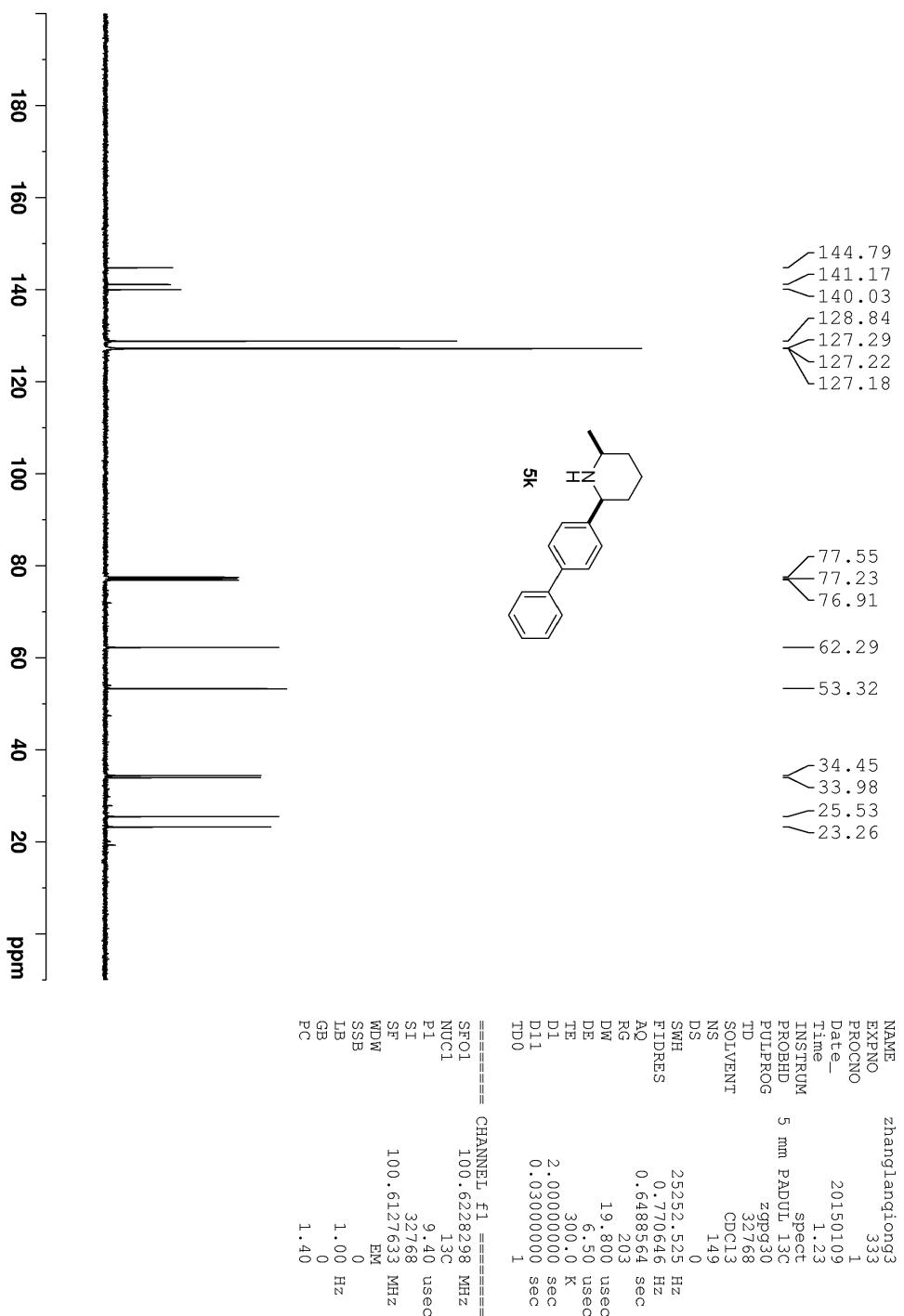


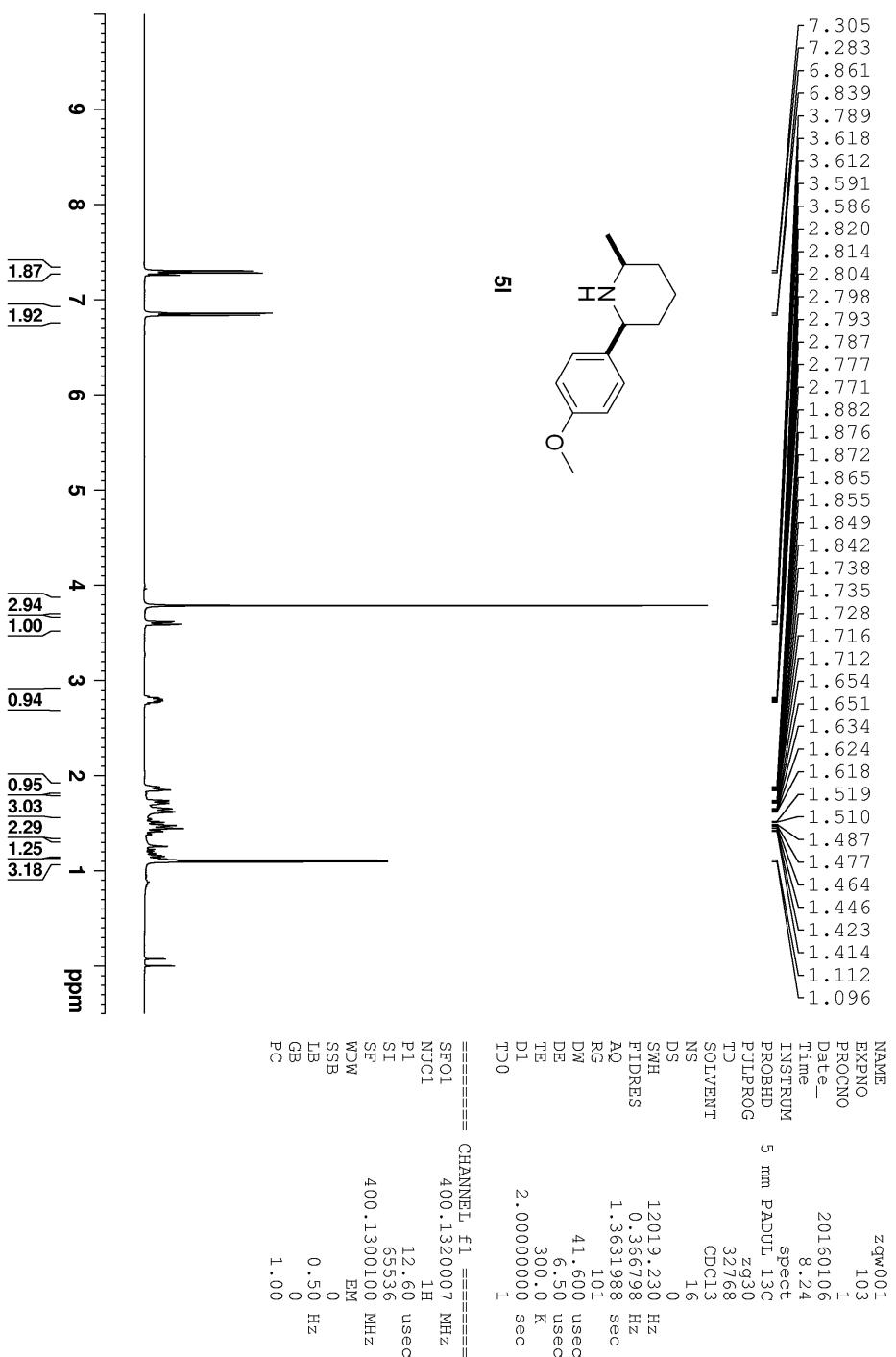


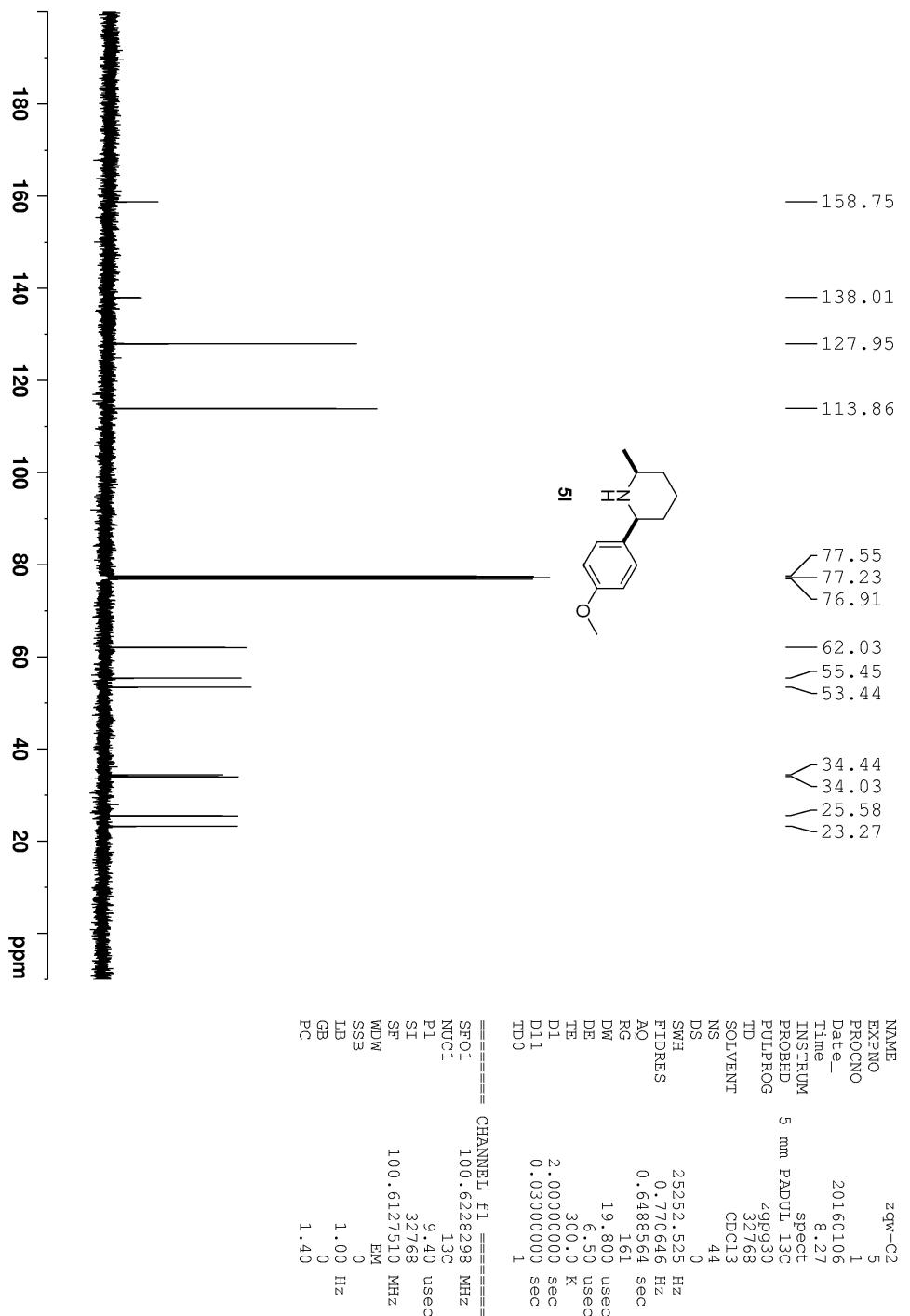


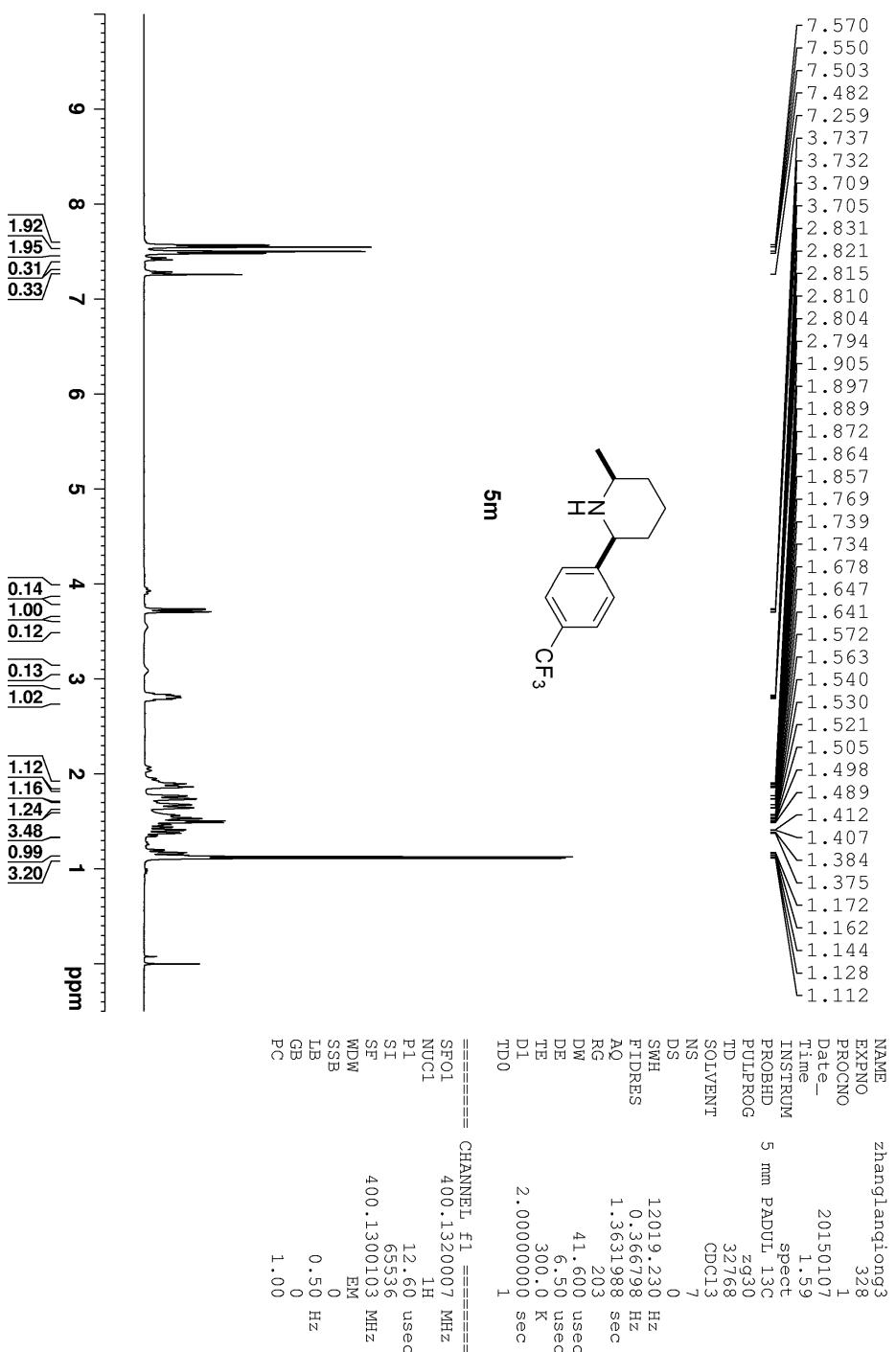


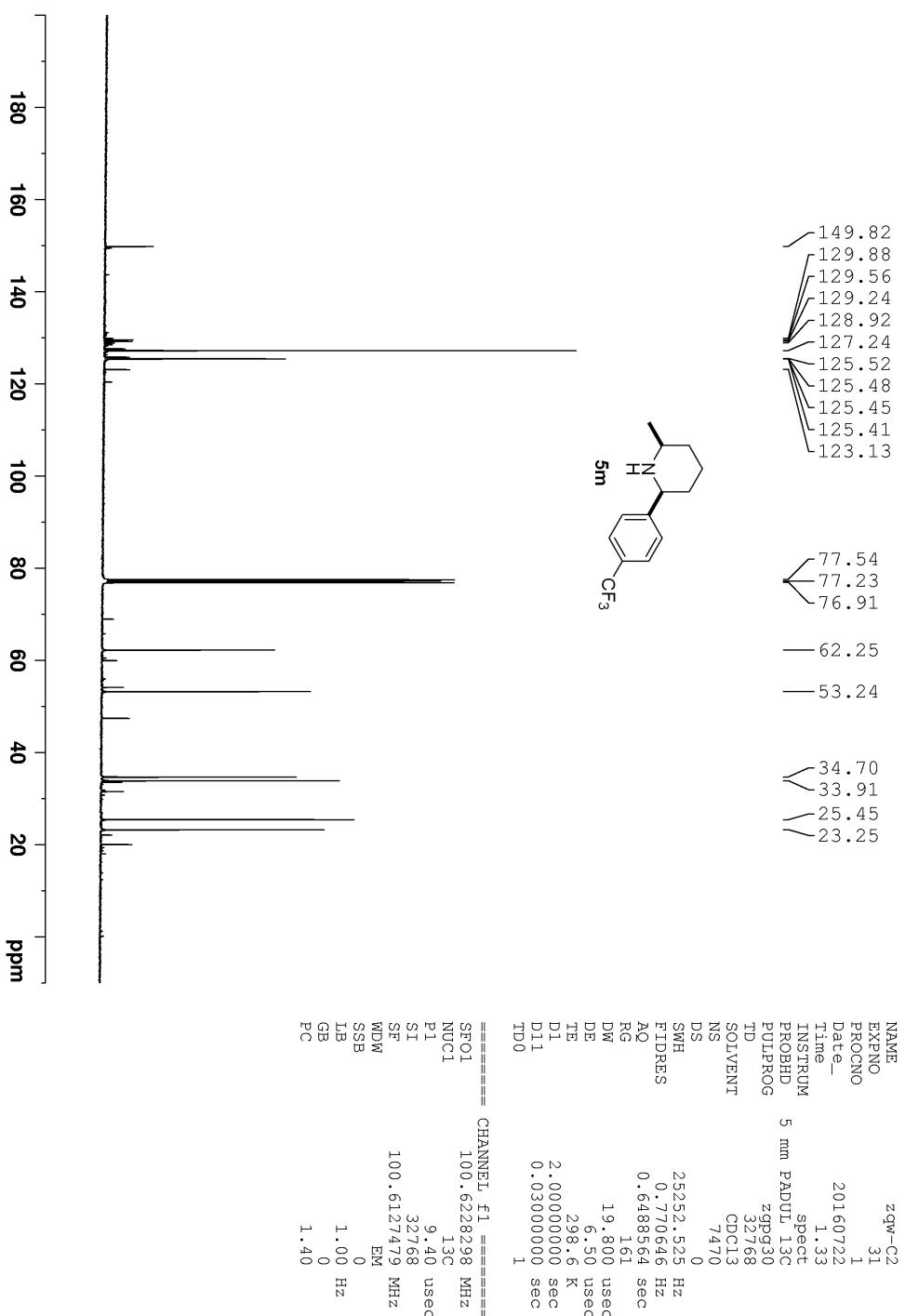


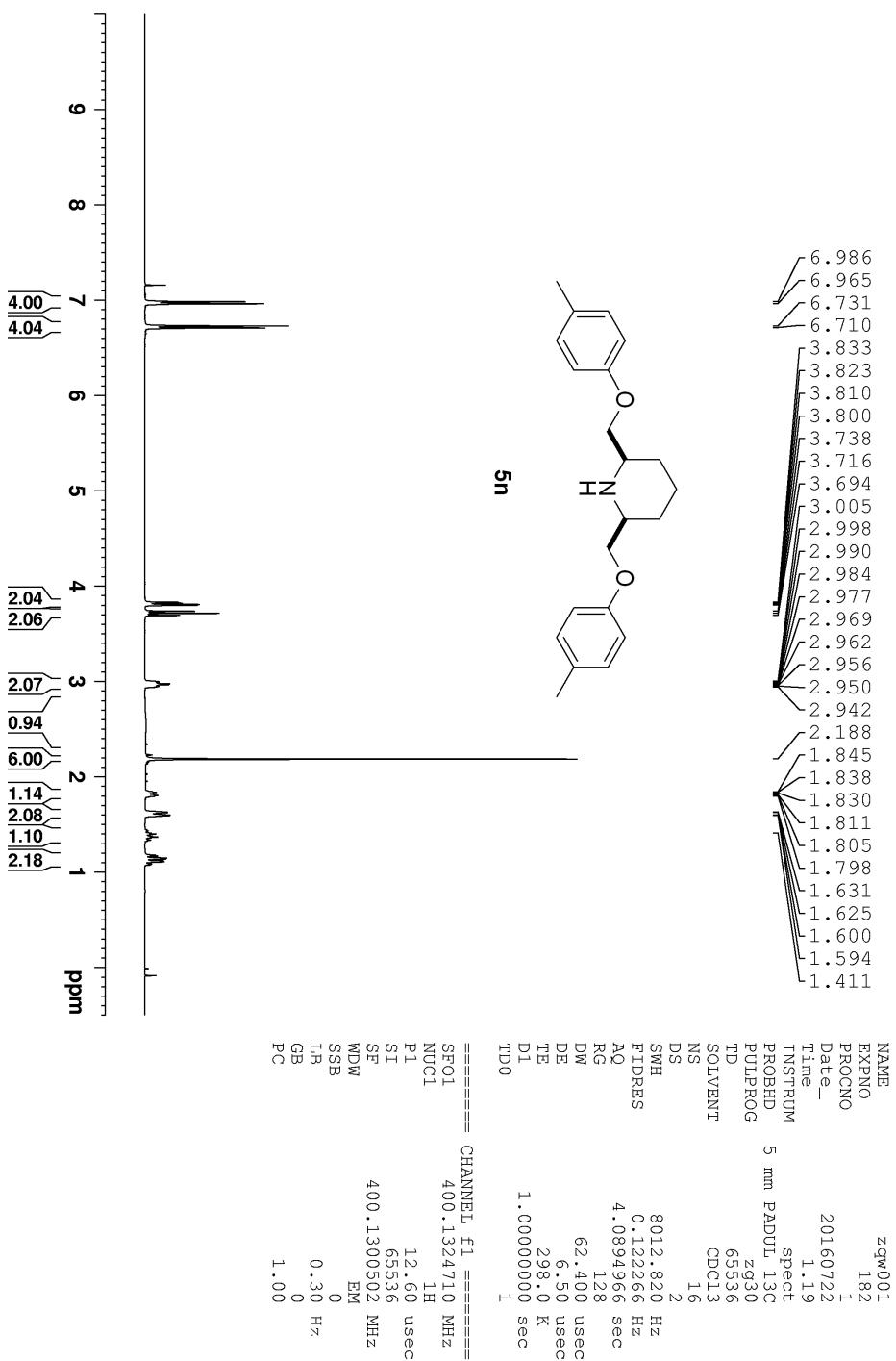


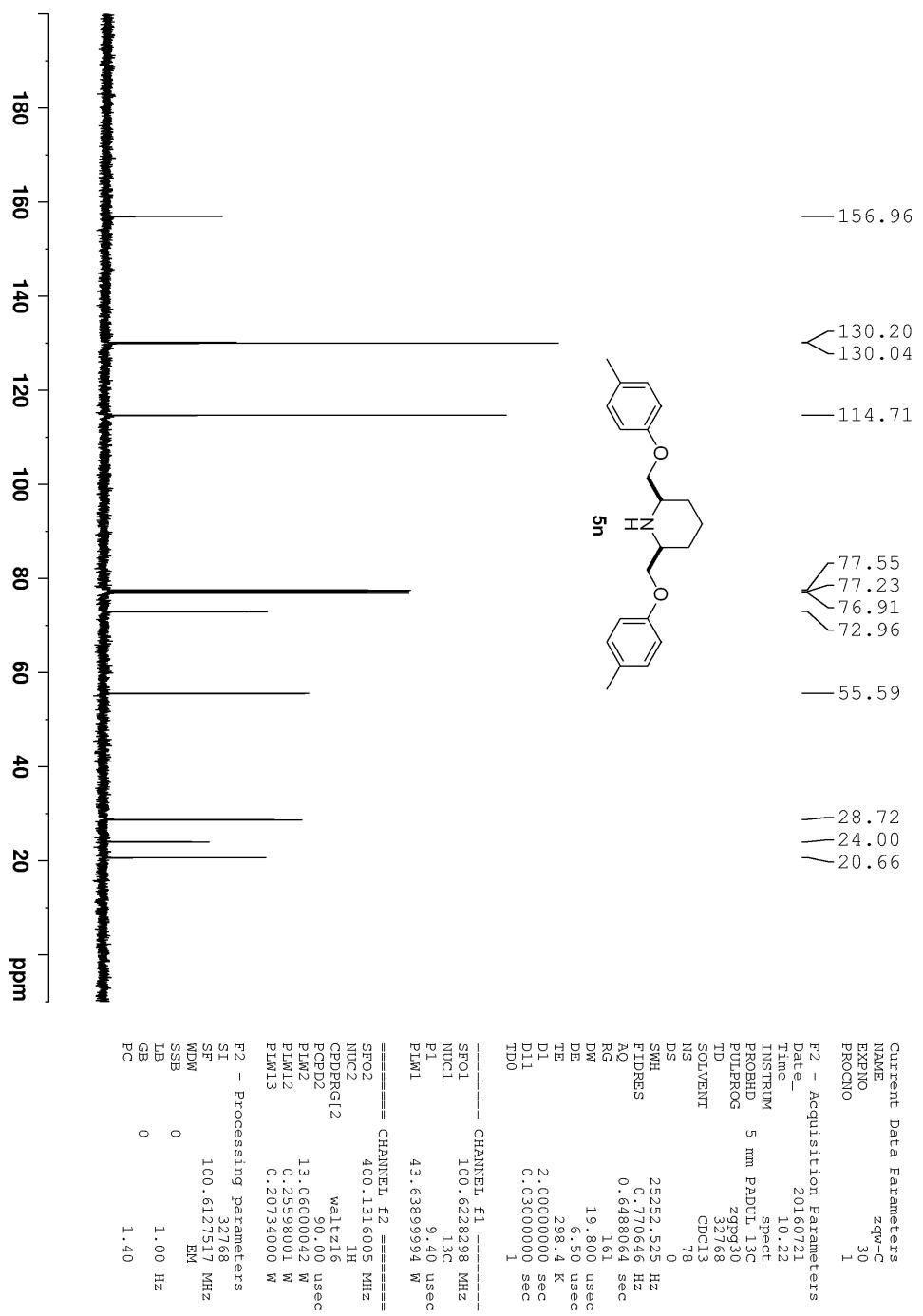


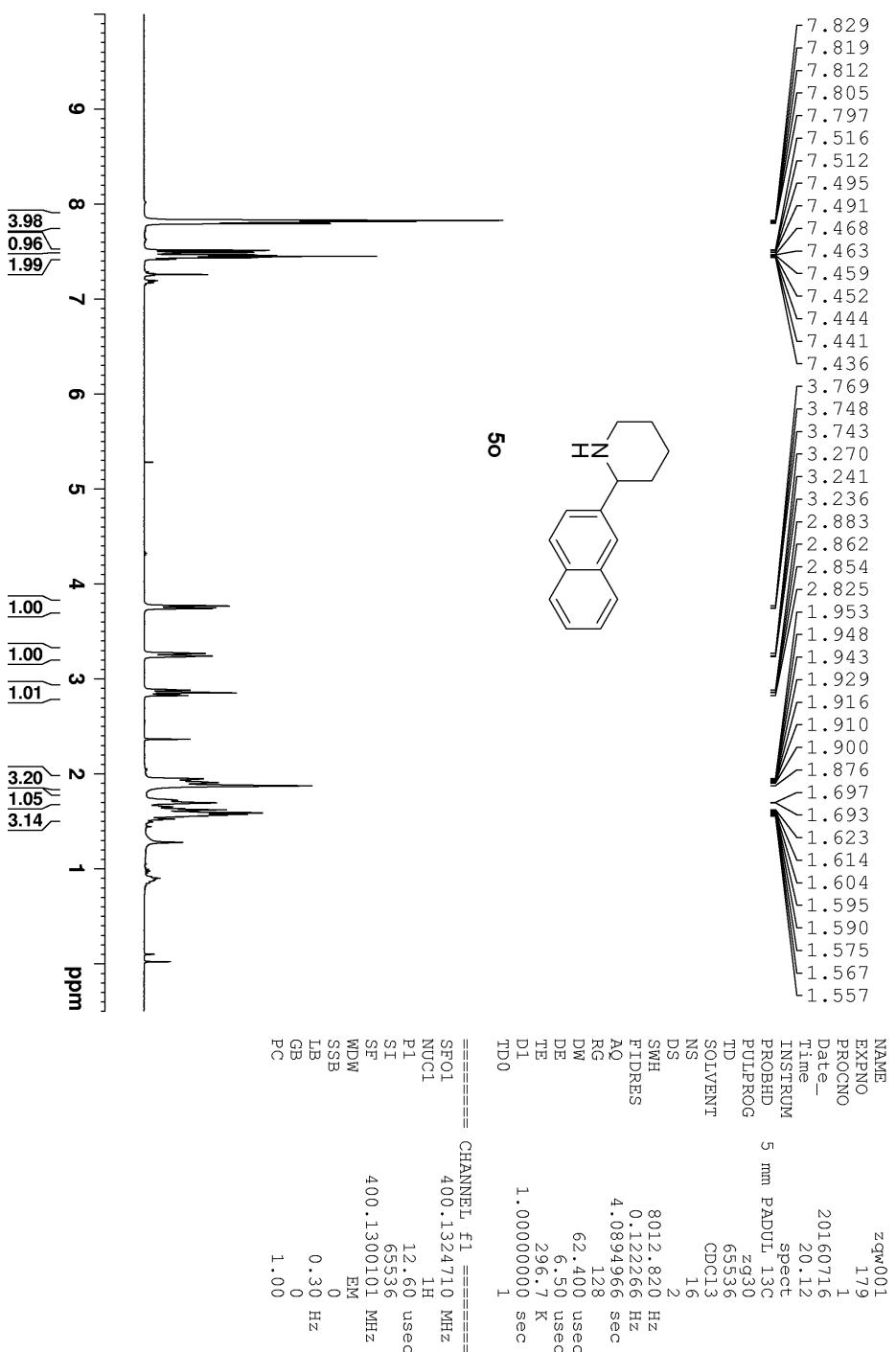


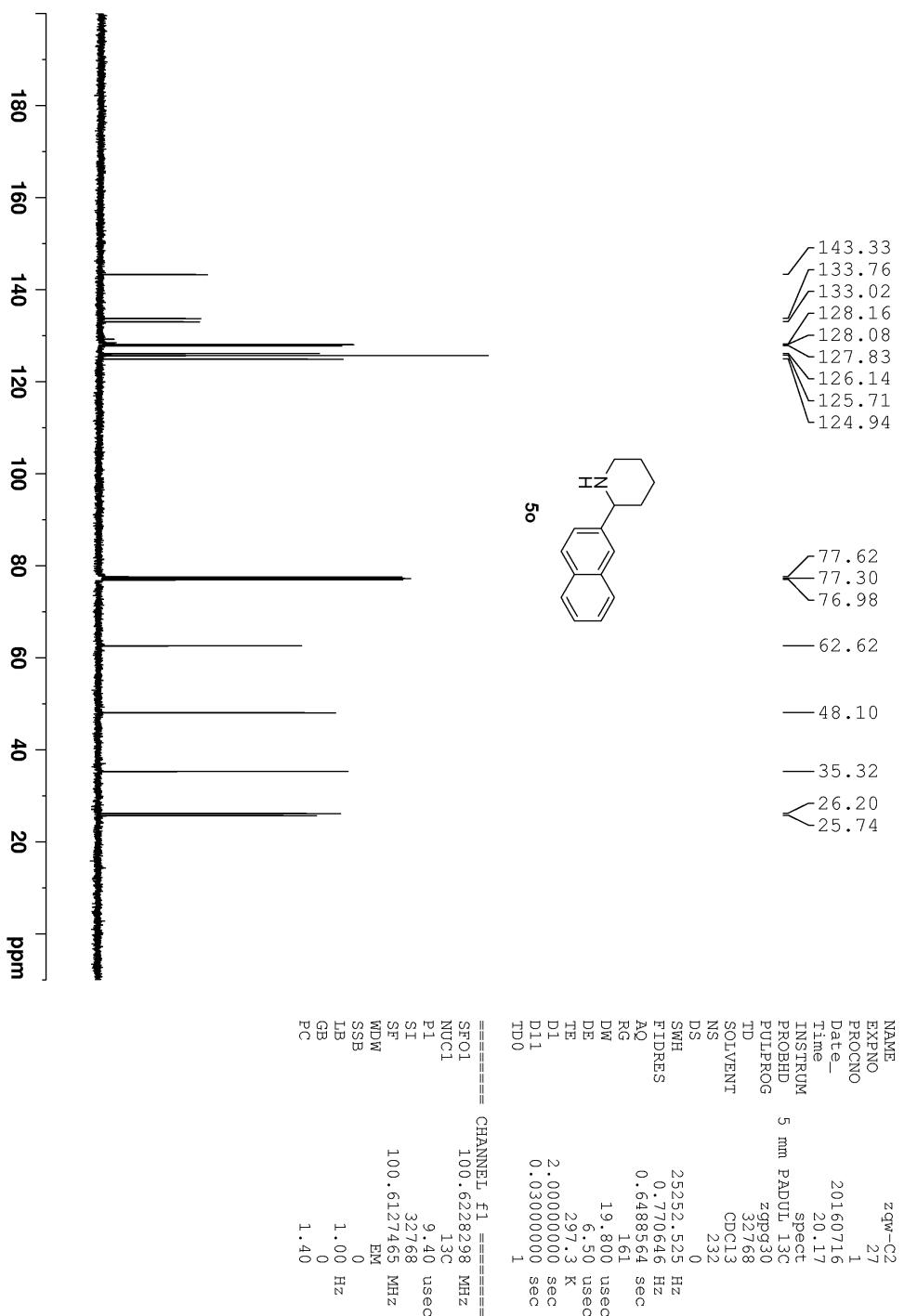


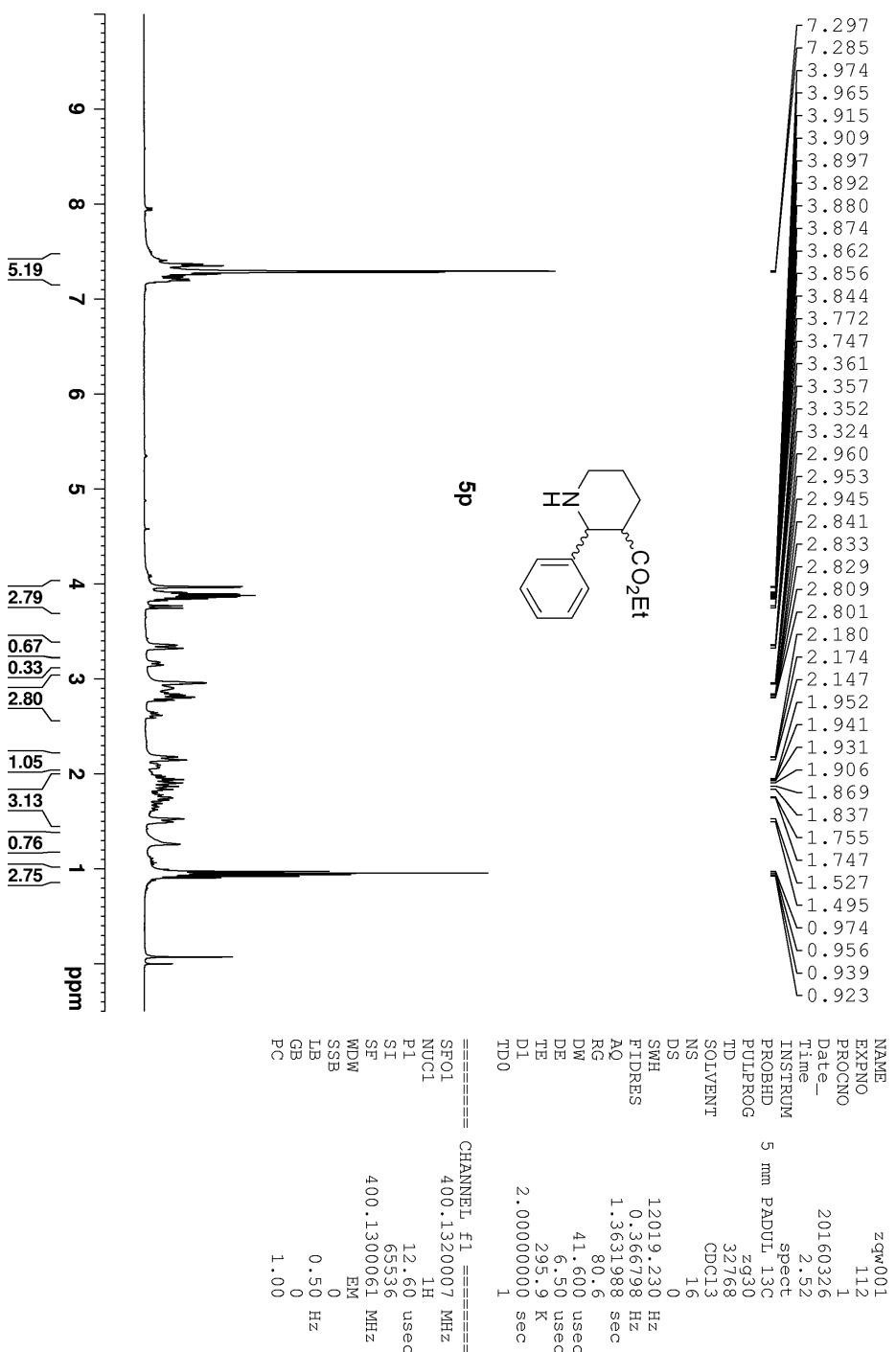


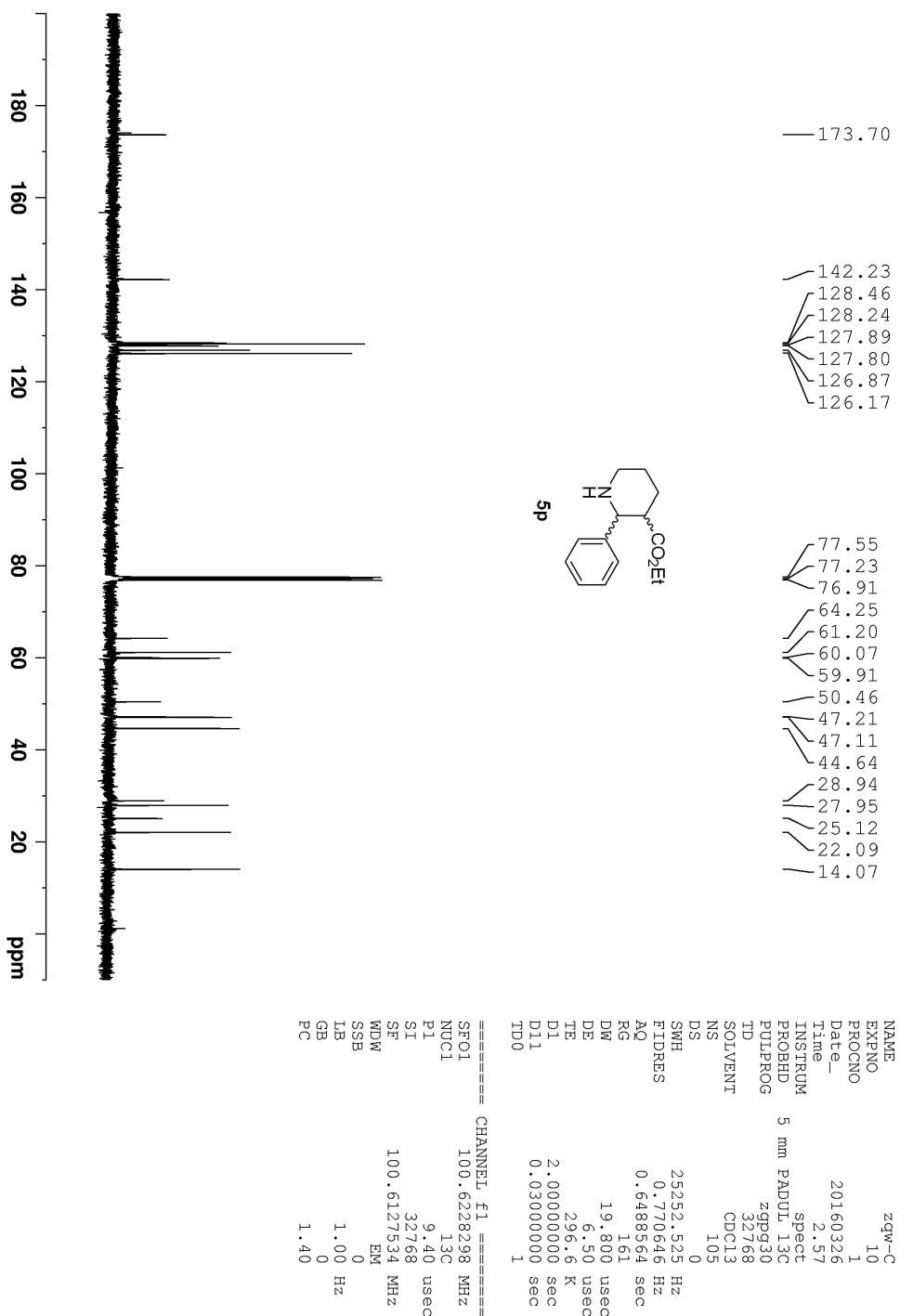


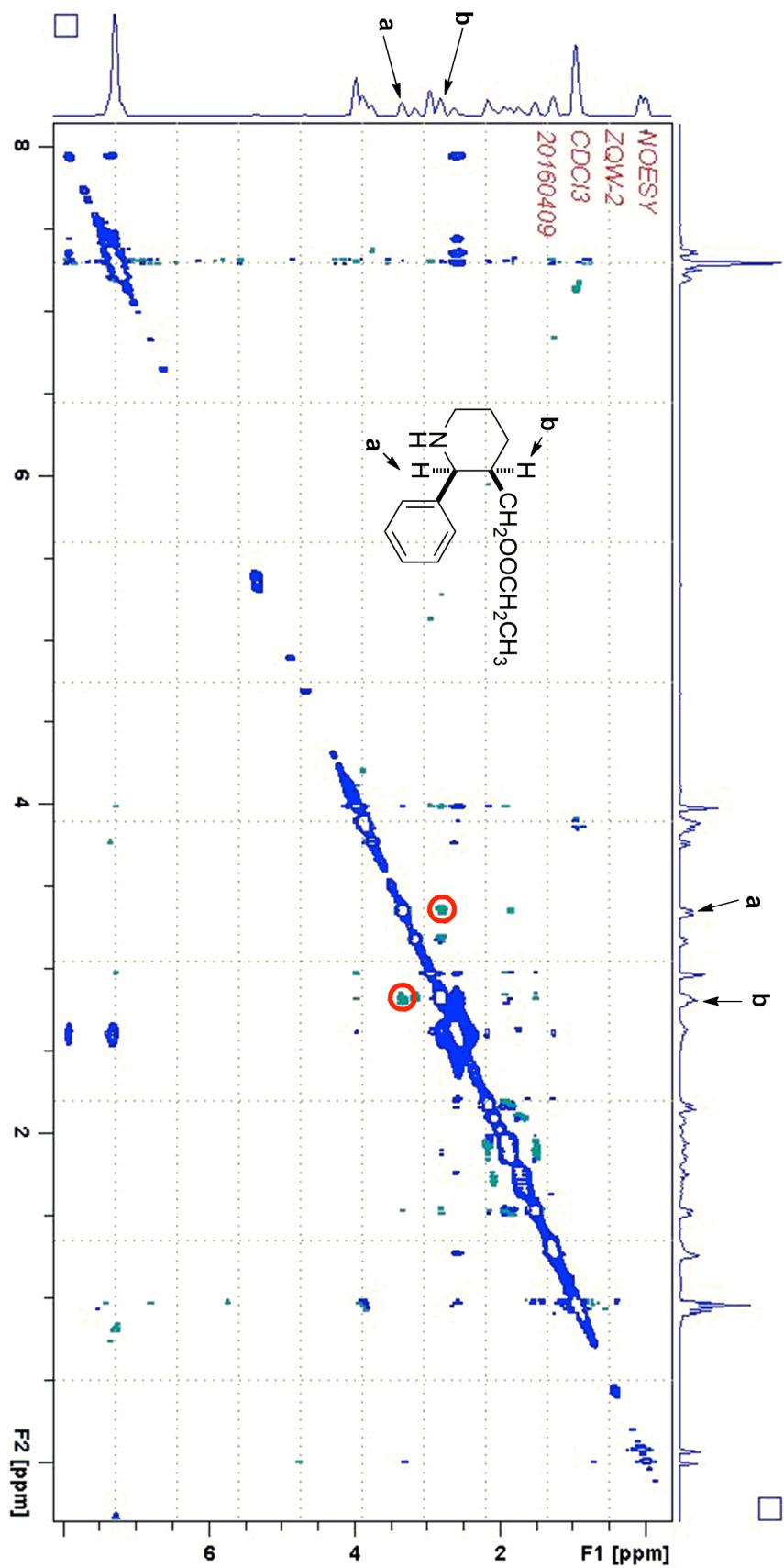


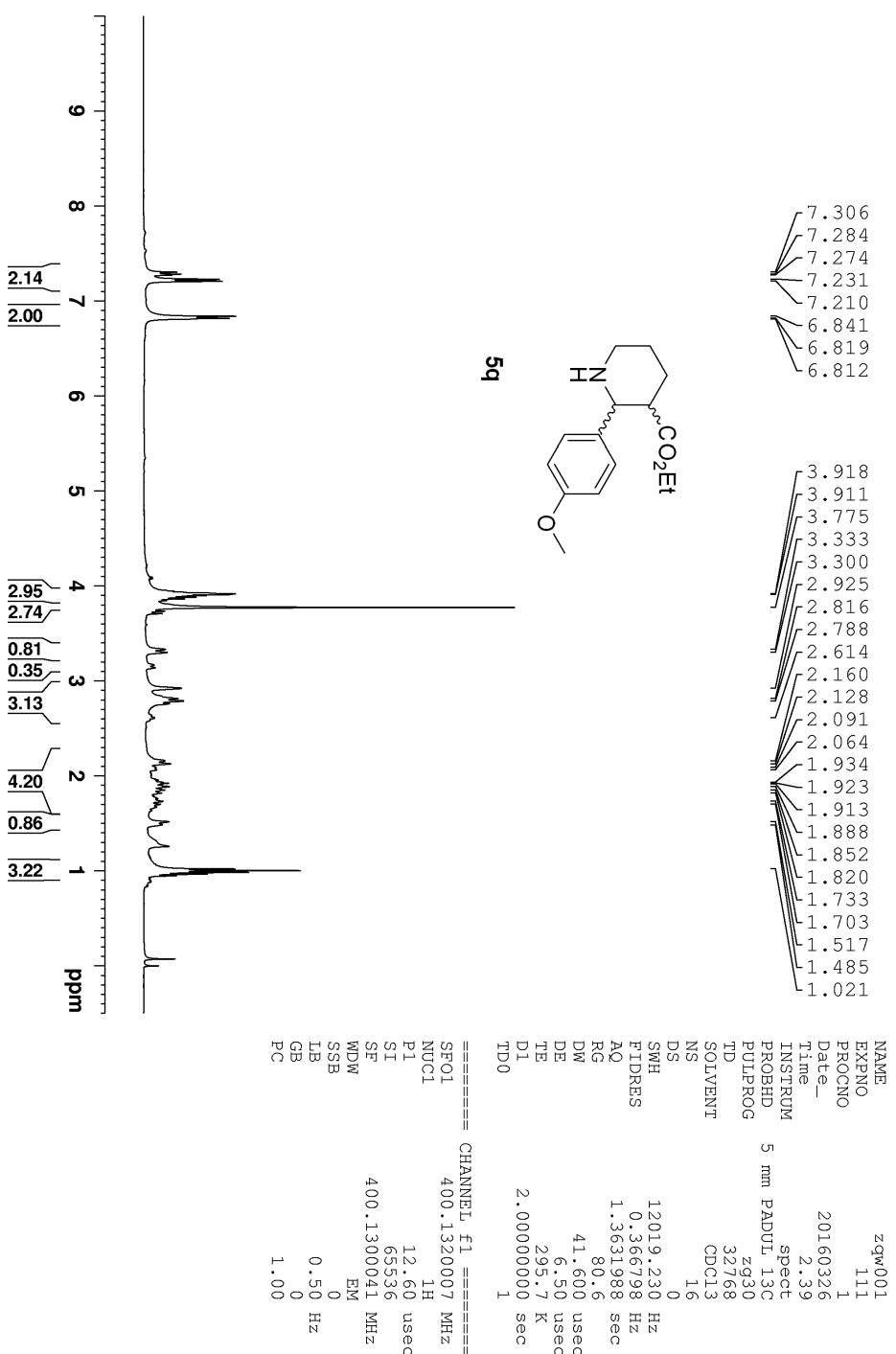


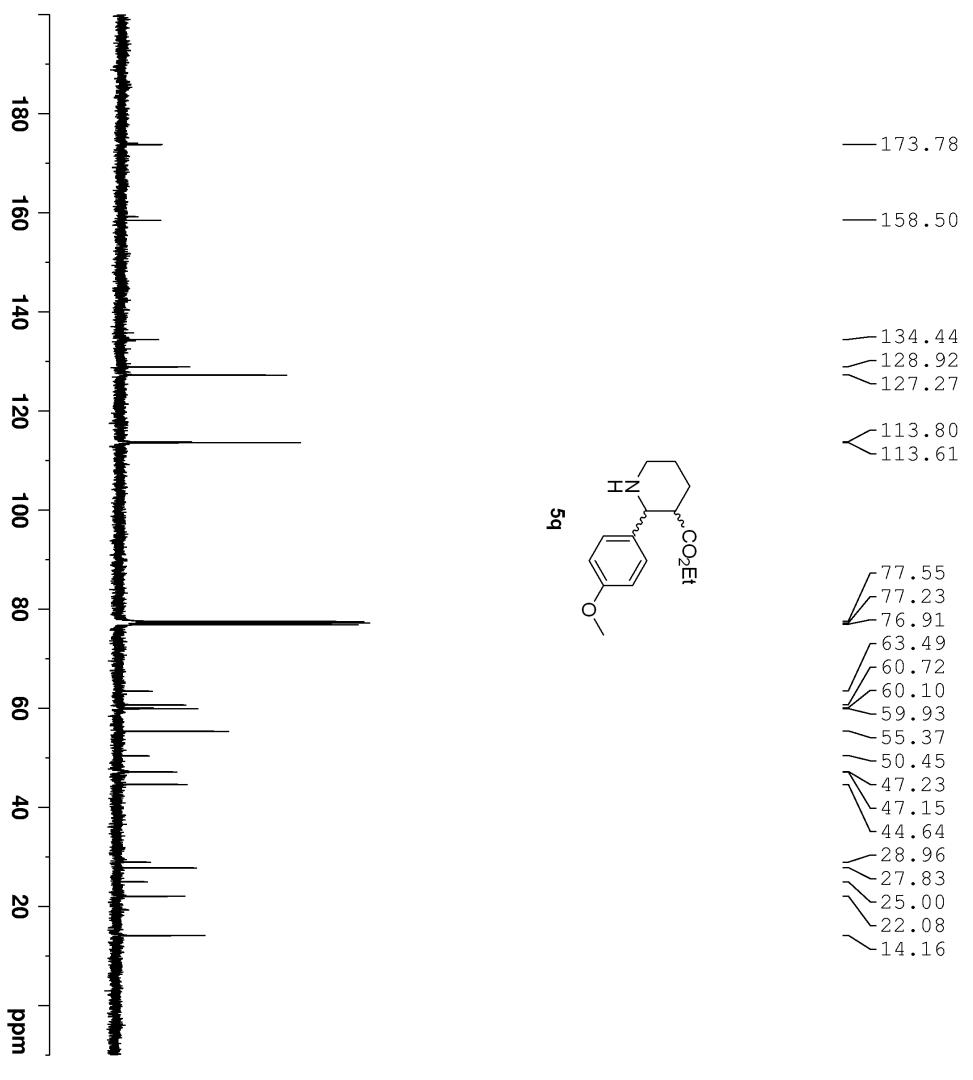












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=====
NAME          zqw-C
EXPNO         9
PROCNO        1
Date_        20160326
Time         2.46
INSTRUM      spect
PROBID       5 mm PADUL 13C
PULPROG     zg3g30
TD           33768
SOLVENT      CDCl3
NS            108
DS             0
SWH          25252.525 Hz
FIDRES      0.770646 Hz
AQ            0.6488564 sec
RG            161
DW            1.9800 usec
DE            6.50 usec
TE            296.4 K
TEUN        2.0000000 sec
D1           0.0300000 sec
D11          1
TDO          1

===== CHANNEL f1 =====
SFO1        100.6228298 MHz
NUC1         13C
P1           9.40 usec
SI            32768
SF          100.6127525 MHz
WDW
SSB           0
LB           1.00 Hz
GB           0
PC           1.40

```

