Supporting Information

Intramolecular 1,5-H transfer reaction of aryl iodides through visible-light photoredox catalysis: a concise method for the synthesis of the natural product scaffolds

Jian-Qiang Chen, Yun-Long Wei, Guo-Qiang Xu, Yong-Min Liang and Peng-Fei Xu*

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, P.R. China.

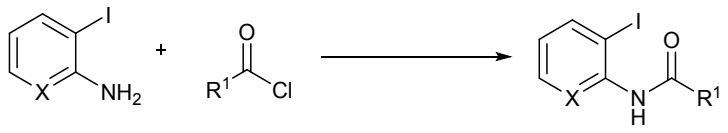
Corresponding author: xupf@lzu.edu.cn

Contents

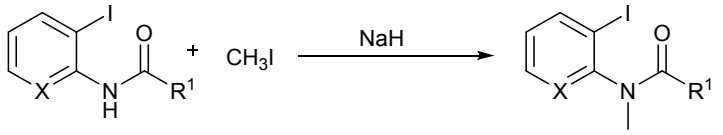
1. General information

All glassware was thoroughly oven-dried. Chemicals and solvents were either purchased from commercial suppliers or purified by standard techniques. Thin-layer chromatography plates were visualized by exposure to ultraviolet light and/or staining with phosphomolybdic acid followed by heating on a hot plate. Flash chromatography was carried out using silica gel (200−300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AM-400 (400 MHz). The spectra were recorded in deuterochloroform ($CDCl_3$) as solvent at room temperature, ^{1}H and ^{13}C NMR chemical shifts are reported in ppm relative to the residual solvent peak. The residual solvent signals were used as references and the chemical shifts were converted to the TMS scale ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.0 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet, br = broad), integration, coupling constant (Hz) and assignment. Data for ^{13}C NMR are reported as chemical shift. IR spectra were recorded using Nicolet NEXUS 670 FT-IR instrument and are reported in wave numbers (cm^{-1}). HRMS were performed on a Bruker Apex II mass instrument (ESI).

2. General preparation of substrates[1]

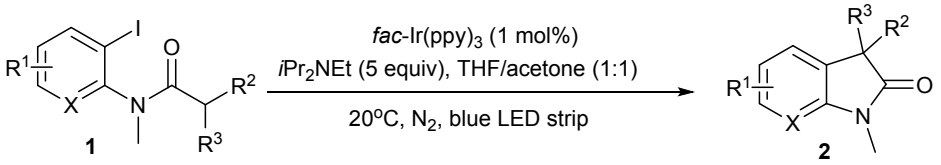


To a stirred, cooled (0−5℃) solution of 2-iodoaniline (2.190 g, 10 mmol) and Et_3N (1.113 g, 1.55 ml, 11 mmol) in 20 ml of dry THF a solution of an appropriate acyl chloride (10 mmol) in 5 ml of dry THF was added dropwise within 10 min. Then the ice bath was removed and the mixture was stirred vigorously for 30 min at room temperature. After solid $Et_3N{\cdot}HCl$ was filtered off and washed with THF (3 x 5 ml), the resulting organic fractions were combined and THF was removed under reduced pressure to yield crude amides. Recrystallization from hexane/$CHCl_3$ and drying in vacuum afforded analytically pure compounds.



To a stirred suspension of NaH (0.132 g; 5.5 mmol) in 5 ml of dry THF at 0°C, the respective amide (5 mmol) dissolved in 10 ml of THF was added dropwise within 10 min. The reaction mixture was stirred until the solution became clear (30 min, hydrogen gas evolved), and the solution of MeI (0.9226 g; 0.405 ml; 6.5 mmol) in 5 ml of THF was added dropwise within 10 min. The solution was warmed up to room temperature and stirred for 3 h. Then the reaction mixture was quenched with water (30 ml). The resulting solution was extracted with ethyl acetate (3 x 20 ml). Combined organic layers were washed with brine (1 x 20 ml) and dried over Na_2SO_4. Ethyl acetate was removed under reduced pressure to give crude products. Recrystallization from hexane or hexane/$CHCl_3$ and drying in vacuum afforded analytically pure compounds.

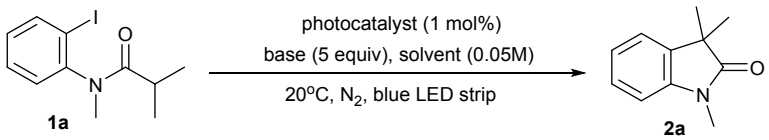
3. General procedure for intramolecular 1,5-HAT reaction



o-anilide aryl iodide **1** (0.2 mmol) and DIPEA (1.0 mmol) were added to a solution of photocatalyst *fac*-Ir(ppy)$_3$ (1 mol%) in dry THF/acetone (1:1) (4mL) at room temperature. The heterogenous mixture was degassed by three cycles of freeze-pump-thaw and then placed in the irradiation apparatus equipped with a 25 W blue light-emitting diode (LED) strip. The resulting mixture was stirred at 20^{o}C until the starting material was completely consumed as monitored by TLC. Upon completion of the reaction, the reaction mixture was concentrated under reduced pressure, and the resulting crude mixture was purified by flash column chromatography on silica gel, which furnished the title compounds as described. (Attention: THF should be purified by standard techniques before using)

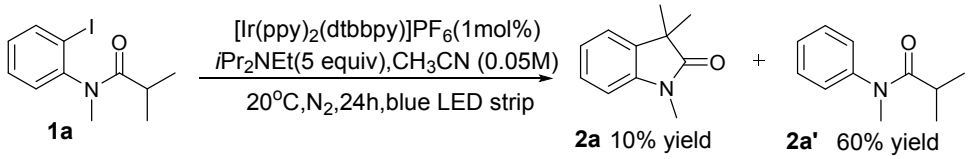
4. Initial studies and reaction optimization

Table 1 Screening of catalysts, bases, and solvents for 1,5-HAT reaction of **1a**



Entry	Photocatalyst	Base	Solvent	Light	Time	Yield(%)[a]
1	$Ru(bpy)_3Cl_2$	iPr_2NEt	MeCN	blue LED	24h	0
2	*fac*-Ir(ppy)$_3$	iPr_2NEt	MeCN	blue LED	24h	37
3	$[Ir(ppy)_2(dtbbpy)]PF_6$	iPr_2NEt	MeCN	blue LED	24h	10
4	*fac*-Ir(ppy)$_3$	Et_3N	$MeCN/CH_2Cl_2$(1:1)	blue LED	24h	46
5	*fac*-Ir(ppy)$_3$	iPr_2NEt	$MeCN/CH_2Cl_2$(1:1)	blue LED	24h	57
6	*fac*-Ir(ppy)$_3$	Bu_3N	$MeCN/CH_2Cl_2$(1:1)	blue LED	24h	49
7	*fac*-Ir(ppy)$_3$	iBu_3N	$MeCN/CH_2Cl_2$(1:1)	blue LED	24h	52
8	*fac*-Ir(ppy)$_3$	K_2HPO_4	DMSO	blue LED	24h	0
9	*fac*-Ir(ppy)$_3$	iPr_2NEt	CH_2Cl_2	blue LED	24h	51
10	*fac*-Ir(ppy)$_3$	iPr_2NEt	DCE	blue LED	36h	36
11	*fac*-Ir(ppy)$_3$	iPr_2NEt	DMA	blue LED	36h	34
12	*fac*-Ir(ppy)$_3$	iPr_2NEt	THF	blue LED	7d	78
13	*fac*-Ir(ppy)$_3$	iPr_2NEt	Toluene	blue LED	7d	61
14	*fac*-Ir(ppy)$_3$	iPr_2NEt	DMSO	blue LED	12h	44
15	*fac*-Ir(ppy)$_3$	iPr_2NEt	Acetone	blue LED	36h	67
16	*fac*-Ir(ppy)$_3$	iPr_2NEt	MeOH	blue LED	36h	46
17	*fac*-Ir(ppy)$_3$	iPr_2NEt	$CHCl_3$	blue LED	36h	0
18	*fac*-Ir(ppy)$_3$	iPr_2NEt	DMF	blue LED	12h	51
19	*fac*-Ir(ppy)$_3$	iPr_2NEt	EA	blue LED	5d	46
20	*fac*-Ir(ppy)$_3$	iPr_2NEt	THF/H_2O(7:1)	blue LED	60h	82
21	*fac*-Ir(ppy)$_3$	iPr_2NEt	THF/Acetone(1:1)	blue LED	60h	87
22	*fac*-Ir(ppy)$_3$	Et_3N	THF/Acetone(1:1)	blue LED	60h	75
23	*fac*-Ir(ppy)$_3$	Bu_3N	THF/Acetone(1:1)	blue LED	60h	77
24	*fac*-Ir(ppy)$_3$	2,6-lutidine	THF/Acetone(1:1)	blue LED	60h	0
25	*fac*-Ir(ppy)$_3$	K_2HPO_4	THF/Acetone(1:1)	blue LED	60h	0
26	*fac*-Ir(ppy)$_3$	-	THF/Acetone(1:1)	blue LED	60h	0
27	*fac*-Ir(ppy)$_3$	iPr_2NEt	THF/Acetone(1:1)	-	60h	0
28	-	iPr_2NEt	THF/Acetone(1:1)	blue LED	60h	0

[a] Isolated yield.



when $[Ir(ppy)_2(dtbbpy)]PF_6$ was used instead of *fac*-Ir(ppy)$_3$, the yield of the product was decreased to 10%.

5. Devices for the photocatalytic reactions

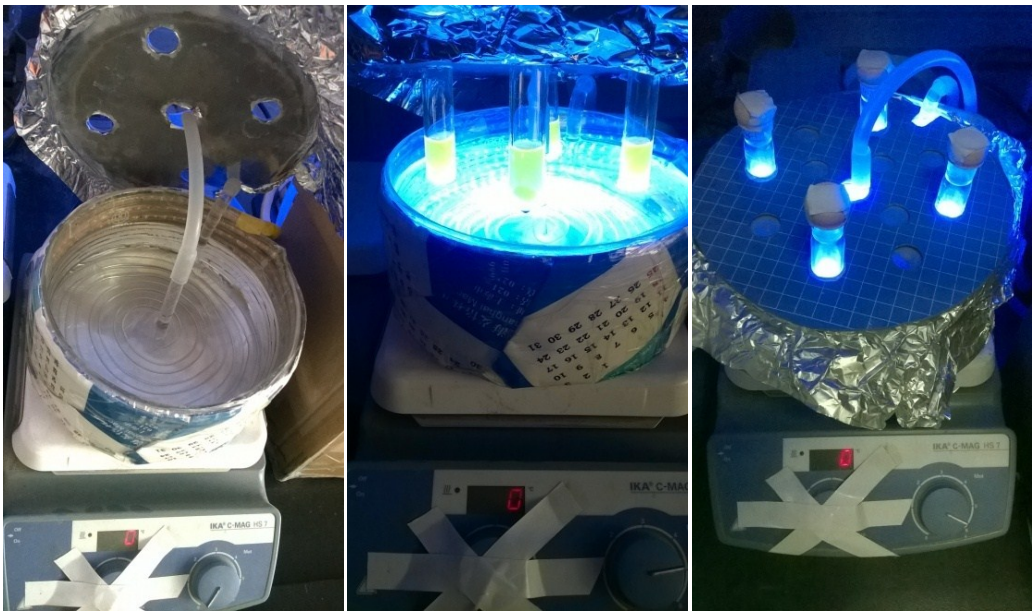
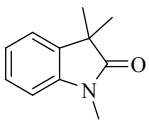


Figure 1.Devices for the photocatalytic reactions

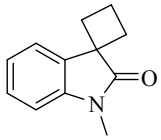
6. Characterization of products

1,3,3-trimethylindolin-2-one (2a)



Colorless oil; 87% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.37 (s, 6H), 3.22 (s, 3H), 6.85 (d, *J* = 7.8 Hz, 1H), 7.06 (m, 1H), 7.21 (dd, *J* = 7.4, 0.7 Hz, 1H), 7.24−7.28 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.3, 26.2, 44.2, 108.0, 122.2, 122.4, 127.6, 135.8, 142.6, 181.4; IR (KBr, cm^{-1}): 3504, 2967, 2927, 1710, 1613, 1493, 1472, 1382, 1348, 1247, 1125,757, 562. HRMS (ESI) for $C_{11}H_{13}NO$ $[M+H]^+$calcd.176.1070, found 176.1067.

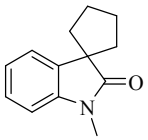
1'-methylspiro[cyclobutane-1,3'-indolin]-2'-one (2b)



Colorless oil; 67% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 2.23−2.37 (m, 4H), 2.61−2.69(m, 2H), 3.18 (s, 3H), 6.78 (d, *J* = 7.8 Hz, 1H), 7.07−7.11 (m, 1H), 7.23−7.28 (m, 1H), 7.51 (dd, *J* = 7.3, 0.7 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 16.7, 26.1,31.3, 48.1, 107.6, 122.2,

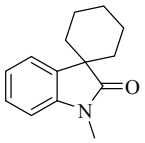
122.5, 127.8, 134.4, 143.0, 180.2; IR (KBr, cm^{-1}): 3401, 2936, 1705, 1639, 1614, 1469, 1375, 1349, 1267, 1101, 1006,740, 543. HRMS (ESI) for $C_{12}H_{13}NO$ $[M+H]^+$ calcd.188.1070, found 188.1067.

1'-methylspiro[cyclopentane-1,3'-indolin]-2'-one (2c)



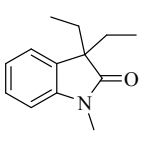
Colorless oil; 93% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.80−1.86 (m, 2H), 1.86−2.18 (m, 6H), 3.21 (s, 3H), 6.82 (d, *J* = 7.8 Hz, 1H), 7.02−7.06 (m, 1H), 7.20 (d, *J* = 7.4 Hz, 1H), 7.22−7.26 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 26.2, 26.6, 38.3, 53.9, 107.7, 122.2, 122.5, 127.3, 136.9, 142.9, 181.9; IR (KBr, cm^{-1}): 3405, 2954, 2867, 1709, 1656, 1612, 1468, 1375, 1347, 1264, 1124, 1077, 968, 745, 543. HRMS (ESI) for $C_{13}H_{16}NO$ $[M+H]^+$ calcd.202.1226, found 202.1224.

1'-methylspiro[cyclohexane-1,3'-indolin]-2'-one (2d)



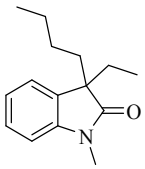
Colorless oil; 90% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.56−1.59 (m, 2H), 1.61−1.79 (m, 4H), 1.81−1.88 (m, 2H), 1.92−1.98 (m, 2H),3.20 (s,3H), 6.84 (d, *J* = 7.7 Hz, 1H), 7.02−7.06 (m, 1H), 7.25−7.27 (m, 1H), 7.25 (d, *J* = 7.4 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 21.2, 25.2,26.1,33.0, 47.4, 107.8, 121.9, 123.8, 127.4, 135.4, 142.8, 180.7; IR (KBr, cm^{-1}): 3399, 3053, 2931, 2851, 1709, 1612, 1492, 1470, 1377, 1350, 1252, 1081, 1006,744, 543. HRMS (ESI) for $C_{14}H_{18}NO$ $[M+H]^+$ calcd.216.1383, found 216.1379.

3,3-diethyl-1-methylindolin-2-one (2e)



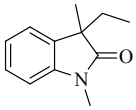
Colorless oil; 87% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.56 (t, *J* = 7.4 Hz, 6H), 1.74−1.83 (m, 2H), 1.88−1.97 (m, 2H), 3.20 (s, 3H), 6.84 (d, *J* = 7.8 Hz, 1H), 7.05−7.09 (m, 1H), 7.12−7.14 (m, 1H), 7.24−7.29 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 8.6, 25.9, 30.6, 54.3, 107.6, 122.3, 122.7, 127.6, 132.0, 144.4, 180.0; IR (KBr, cm^{-1}): 3407, 3054, 2966, 2929, 1709, 1612, 1493, 1468, 1377, 1338, 1254, 1124, 1079, 1021, 749, 546. HRMS (ESI) for $C_{13}H_{18}NO$ $[M+H]^+$ calcd.204.1383, found 204.1380.

3-ethyl-1-methyl-3-propylindolin-2-one (2f)



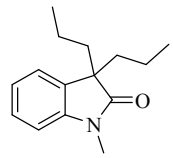
Colorless oil; 89% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.55 (t, *J* = 7.4 Hz, 3H), 0.72−0.84 (m, 4H), 0.89−0.97 (m, 1H),1.14−1.21 (m, 2H), 1.70−1.82 (m, 2H), 1.84−1.94 (m, 2H), 3.21 (s, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 7.05−7.09 (m, 1H), 7.12−7.14 (m, 1H), 7.24−7.28 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 8.5, 13.8, 22.9, 25.9, 26.4, 31.0, 37.5, 53.7, 107.6, 122.3, 122.6, 127.5, 132.4, 144.2, 180.2; IR (KBr, cm^{-1}): 3409, 3055, 2960, 2933, 2875, 1716, 1613, 1493, 1469, 1377, 1350, 1252, 1123, 1075, 1021, 750, 542. HRMS (ESI) for $C_{13}H_{18}NO$ $[M+H]^+$calcd.232.1696, found 232.1693.

3-ethyl-1,3-dimethylindolin-2-one (2g)



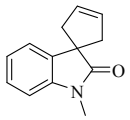
Colorless oil; 83% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.59 (t, *J* = 7.4 Hz, 3H), 1.35 (s, 3H), 1.73−1.82 (m, 1H), 1.89−1.97 (m, 1H), 3.21 (s, 3H), 6.84 (d, *J* = 7.8 Hz, 1H), 7.05−7.09 (m, 1H), 7.16−7.18 (m, 1H), 7.24−7.28 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 8.8, 23.3, 26.0, 31.4, 48.9, 107.8, 122.4, 122.5, 127.6, 133.9, 143.5, 180.7; IR (KBr, cm^{-1}): 3409, 3055, 2966, 2928, 2877, 1713, 1613, 1493, 1471, 1378, 1349, 1258, 1124, 1078, 1017, 751, 549. HRMS (ESI) for $C_{13}H_{18}NO$ $[M+H]^+$ calcd.190.1226, found 190.1223.

1-methyl-3,3-dipropylindolin-2-one (2h)



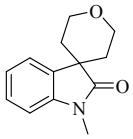
Colorless oil; 67% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.76 (t, *J* = 6.9 Hz, 3H), 0.79−0.85 (m, 2H), 0.94−1.03 (m, 2H), 1.67−1.74 (m, 2H), 1.82−1.90 (m, 2H), 3.20 (s, 3H), 6.82 (d, *J* = 7.8 Hz, 1H), 7.04−7.08 (m, 1H), 7.13−7.15(m, 1H), 7.23−7.27 (m,1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 14.1, 17.5, 25.9, 40.3, 53.3, 107.6, 122.3, 122.6, 127.4, 132.8, 144.0, 180.3; IR (KBr, cm^{-1}): 3409, 3054, 2958, 2933, 2873, 1711, 1613, 1493, 1467, 1378, 1347, 1248, 1126, 1076, 1019, 747, 543. HRMS (ESI) for $C_{15}H_{22}NO$ $[M+H]^+$calcd. 232.1696, found 232.1692.

1'-methylspiro[cyclopent[3]ene-1,3'-indolin]-2'-one (2i)



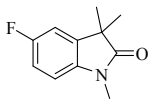
Yellow oil; 65% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 2.59 (d, *J* = 14.6 Hz, 2H), 3.00 (d, *J* = 14.7 Hz, 2H), 3.22 (s, 3H), 5.84 (s, 1H), 6.82 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.00−7.04 (m, 1H), 7.23−7.27 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 26.3, 44.9, 52.1, 107.7, 121.6, 122.8, 127.6, 128.9, 137.4, 142.6, 181.4; IR (KBr, cm^{-1}): 3398, 2918, 2839, 1708, 1611, 1494, 1470, 1378, 1346, 1266, 1185, 1085, 1029, 756, 689, 542, 470. HRMS (ESI) for $C_{13}H_{14}NO$ $[M+H]^+$calcd. 200.1070, found 200.1067.

1-methyl-2',3',5',6'-tetrahydrospiro[indoline-3,4'-pyran]-2-one (2j)



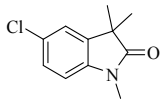
White solid; 70% yield; mp 85−86℃； **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.86 (t, *J* = 6.0 Hz, 4H), 3.21 (s, 3H), 3.90−3.95 (m, 2H) , 4.23−4.29 (m, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 7.06−7.10 (m, 1H), 7.28−7.32(m, 1H), 7.38 (d, *J* = 7.4 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 26.0, 32.9, 44.2, 62.9, 108.0, 122.4, 123.0, 127.9, 134.0, 142.7, 179.6; IR (KBr, cm^{-1}): 3398, 2946, 2861, 1703, 1611, 1477, 1458, 1371, 1348, 1245, 1103, 1076, 1023, 1006, 836, 760, 751, 695, 538, 490. HRMS (ESI) for $C_{13}H_{16}NO_2$ $[M+H]^+$calcd. 218.1176, found 218.1172.

5-fluoro-1,3,3-trimethylindolin-2-one (2k)



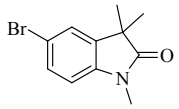
White solid; 87% yield; mp 81−83℃； **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.37 (s, 6H), 3.20 (s, 3H), 6.76 (dd, *J* = 9.2, 4.1 Hz, 1H), 6.93-6.98 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.3, 26.3, 44.6 (d, *J* = 1.8 Hz), 108.3 (d, *J* = 8.1 Hz), 110.5 (d, *J* = 24.3 Hz), 113.7 (d, *J* = 23.3 Hz), 137.5 (d, *J* = 7.8 Hz), 138.5 (d, *J* = 1.8 Hz), 159.4 (d, *J* = 239 Hz), 180.9; IR (KBr, cm^{-1}): 3387, 3067, 2968, 2925, 2866, 1700, 1620, 1501, 1485, 1460, 1353, 1275, 1187, 1114, 1045, 886, 818, 696, 616, 559, 467. HRMS (ESI) for $C_{11}H_{13}FNO$ $[M+H]^+$calcd. 194.0976, found 194.0973.

5-chloro-1,3,3-trimethylindolin-2-one (2l)



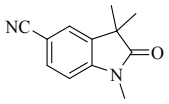
White solid; 82% yield; mp 86−87℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.37 (s, 6H), 3.20 (s, 3H), 6.76 (d, *J* = 8.2 Hz, 1H), 7.18 (d, *J* = 2.0 Hz, 1H), 7.23(dd, *J* = 8.2 2.0 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.3, 26.3, 44.4, 108.9, 122.9, 127.6, 127.9, 137.5, 141.2, 180.8; IR (KBr, cm^{-1}): 3395, 2976, 2930, 2866, 1706, 1610, 1490, 1467, 1426, 1345, 1266, 1242, 1125, 1087, 813, 587, 543, 468. HRMS (ESI) for $C_{11}H_{13}ClNO$ $[M+H]^+$ calcd. 210.0680, found 210.0677.

5-bromo-1,3,3-trimethylindolin-2-one (2m)



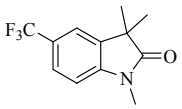
White solid; 80% yield; mp 102−104℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.29 (s, 6H), 3.12 (s, 3H), 6.65 (d, *J* = 8.2 Hz, 1H), 7.23 (d, *J* = 1.9Hz, 1H), 7.23(dd, *J* = 8.2, 1.9 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.3, 26.3, 44.4, 109.5, 115.2, 125.7, 130.5, 137.9, 141.7, 180.7; IR (KBr, cm^{-1}): 3398, 2966, 2925, 2863, 1716, 1606, 1488, 1468, 1415, 1361, 1342, 1264, 1242, 1126, 1077, 814, 560, 532, 463. HRMS (ESI) for $C_{11}H_{13}BrNO$ $[M+H]^+$calcd. 254.0175, found 254.0171.

1,3,3-trimethyl-2-oxoindoline-5-carbonitrile (2n)



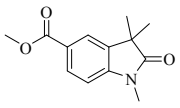
Light yellow solid; 89% yield; mp 131−132℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.40 (s, 6H), 3.26 (s, 3H), 6.93 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 1.4Hz, 1H), 7.61(dd, *J* = 8.1, 1.4Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.2, 26.4, 44.0, 105.6, 108.5, 119.3, 125.7, 133.2, 136.7, 146.6, 180.9; IR (KBr, cm^{-1}): 3414, 2973, 2947, 2217, 1712, 1615, 1492, 1462, 1365, 1343, 1283, 1241, 1177, 1118, 1060, 1040, 826, 610, 559, 492. HRMS (ESI) for $C_{12}H_{13}N_2O$ $[M+H]^+$calcd. 201.1022, found 201.1018.

1,3,3-trimethyl-5-(trifluoromethyl)indolin-2-one (2o)



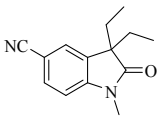
Light yellow solid; 92% yield; mp 37−39℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.40 (s, 6H), 3.25 (s, 3H), 6.92 (d, *J* = 8.2 Hz, 1H), 7.43 (d, *J* = 1.0 Hz, 1H), 7.55(dd, *J* = 8.2, 1.0 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.1, 26.4, 44.2, 107.7, 119.3 (q, *J* = 3.6 Hz), 124.5 (q, *J* = 270 Hz), 124.7 (q, *J* = 32.3 Hz), 125.5 (q, *J* = 3.9 Hz), 136.3, 145.7, 181.2; IR (KBr, cm^{-1}): 3424, 2973,2930,1721, 1624, 1503, 1467, 1384, 1327, 1261, 1158, 1116, 1076, 1053, 890, 835, 707, 653, 562, 536, 474. HRMS (ESI) for $C_{12}H_{13}F_3NO$ $[M+H]^+$calcd. 244.0944, found 244.0940.

methyl 1,3,3-trimethyl-2-oxoindoline-5-carboxylate (2p)



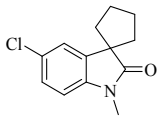
White solid; 90% yield; mp 96−97℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.40 (s, 6H), 3.26 (s, 3H), 3.92 (s, 3H), 6.89 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 1.6 Hz, 1H), 8.02(dd, *J* = 8.2, 1.6 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.2, 26.3, 43.9, 51.9, 107.5, 123.5, 124.3, 130.4, 135.6, 146.8, 166.9, 181.5; IR (KBr, cm^{-1}): 3409, 2978, 2947, 1709, 1616, 1496, 1456, 1363, 1290,1242, 1192, 1106, 1062, 938, 834, 773, 710, 561, 544, 472. HRMS (ESI) for $C_{13}H_{16}NO_3$ $[M+H]^+$calcd. 234.1125, found 234.1119.

3,3-diethyl-1-methyl-2-oxoindoline-5-carbonitrile (2q)



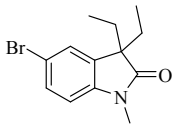
Light yellow solid; 88% yield; mp 60−62℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.57 (t, *J* = 7.5 Hz, 6H), 1.75−1.85 (m, 2H), 1.91−2.00 (m, 2H), 3.25 (s, 3H), 6.92 (d, *J* = 8.1 Hz, 1H), 7.40 (d, *J* = 1.4 Hz, 1H), 7.62(dd, *J* = 8.1, 1.4 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= 8.5, 26.2, 30.5, 54.3, 105.5, 108.1, 119.4, 126.0, 133.1, 133.2, 148.2, 179.7; IR (KBr, cm^{-1}): 3416, 2963, 2928, 2878, 2218, 1719, 1612, 1495, 1460, 1359, 1262, 1122, 1069, 940, 836, 539, 513. HRMS (ESI) for $C_{14}H_{17}N_2O$ $[M+H]^+$calcd. 229.1335, found 229.1331.

5'-chloro-1'-methylspiro[cyclopentane-1,3'-indolin]-2'-one (2r)



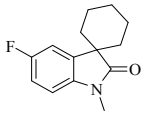
White solid; 82% yield; mp 70−71℃； **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.80−1.85 (m, 2H), 1.93−1.99 (m, 2H), 2.04−2.18 (m, 4H), 3.19 (s, 3H), 6.73 (d, *J* = 8.2 Hz, 1H), 7.16 (d, *J* = 2.1 Hz, 1H), 7.21(dd, *J* = 8.2, 2.1 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 26.3, 26.6, 38.3, 54.1, 108.5, 122.8, 127.1, 127.7, 138.5, 141.4, 181.4; IR (KBr, cm^{-1}): 3405, 2947, 2872, 1705, 1610, 1490, 1469, 1429, 1365, 1346, 1274, 1246, 1039, 1067, 971, 879, 844, 806, 545, 460. HRMS (ESI) for $C_{13}H_{15}ClNO$ $[M+H]^+$calcd. 236.0837, found 236.0832.

5-bromo-3,3-diethyl-1-methylindolin-2-one (2s)



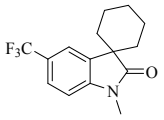
White solid; 86% yield; mp 74−75℃； **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.57 (t, *J* = 7.4 Hz, 6H), 1.71−1.80 (m, 2H), 1.88−1.97 (m, 2H), 3.20(s, 3H), 6.72 (d, *J* = 8.2 Hz, 1H), 7.25 (d, *J* = 1.9 Hz, 1H), 7.39(dd, *J* = 8.2, 1.9 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 8.6, 26.0, 30.6, 54.6, 109.3, 115.1, 125.9, 130.4, 134.2, 143.4, 179.4; IR (KBr, cm^{-1}): 3401, 3057, 3042, 2960, 2932, 2874, 1706, 1604, 1481, 1457, 1429, 1365, 1331, 1269, 1253, 1125, 1084, 905, 806, 774, 540, 489. HRMS (ESI) for $C_{13}H_{17}BrNO$ $[M+H]^+$calcd. 282.0488, found 282.0482.

5'-fluoro-1'-methylspiro[cyclohexane-1,3'-indolin]-2'-one (2t)



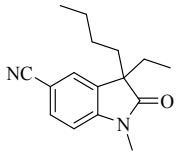
Light yellow oil; 80% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.51−1.57 (m, 2H), 1.61−1.75 (m, 4H), 1.82−1.88 (m, 2H), 1.92−1.98 (m, 2H), 3.19 (s, 3H), 6.75 (dd, *J* = 8.5, 4.3 Hz, 1H), 6.95−7.00 (m, 1H), 7.20 (dd, *J* = 8.5, 2.5 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 21.1, 25.0, 26.2, 32.8, 47.9 (d, *J* = 1.3 Hz), 108.1 (d, *J* = 8.1 Hz), 112.1 (d, *J* = 24.8 Hz), 113.4 (d, *J* = 23.2 Hz), 136.9 (d, *J* = 7.6 Hz), 138.7 (d, *J* = 1.4 Hz), 158.8 (d, *J* = 238 Hz), 180.3; IR (KBr, cm^{-1}): 3403, 3060, 2933, 2856, 1709, 1620, 1495, 1470, 1446, 1352, 1276, 1137, 1097, 1006, 932, 869, 809, 760, 702, 643, 560, 483. HRMS (ESI) for $C_{14}H_{17}FNO$ $[M+H]^+$calcd. 234.1289, found 234.1282.

1'-methyl-5'-(trifluoromethyl)spiro[cyclohexane-1,3'-indolin]-2'-one (2u)



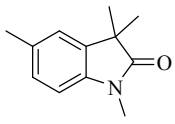
White solid; 92% yield; mp 37−39℃; **H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.56−1.62 (m, 2H), 1.67−1.75 (m, 4H), 1.82−1.88 (m, 2H), 1.97−2.01 (m, 2H), 3.23(s, 3H), 6.91 (d, *J* = 8.2 Hz, 1H), 7.56 (dd, *J* = 8.2, 0.6 Hz, 1H), 7.64(s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 21.0, 25.0, 26.3, 32.9, 47.3, 107.5, 120.5 (q, *J* = 3.6 Hz), 124.1 (q, *J* = 32.1 Hz), 124.5 (q, *J* = 270 Hz), 125.2 (q, *J* = 4.1 Hz), 135.8, 145.8, 180.5; IR (KBr, cm^{-1}): 3424, 3083, 2972, 2930, 1721, 1624, 1503, 1467, 1384, 1327, 1297, 1261, 1116, 1076, 1054, 890, 835, 707, 653, 562, 536, 474. HRMS (ESI) for $C_{12}H_{13}F_3NO$ $[M+H]^+$calcd. 244.0944, found 244.0940.

3-butyl-3-ethyl-1-methyl-2-oxoindoline-5-carbonitrile (2v)



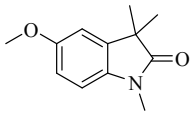
Light yellow oil; 86% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 0.55 (t, *J* = 7.4 Hz, 3H), 0.72−0.84 (m, 4H), 0.89−0.97 (m, 1H), 1.14−1.21 (m, 2H), 1.70−1.82 (m, 2H), 1.84−1.94 (m, 2H), 3.21 (s, 3H), 6.83 (d, *J* = 7.8 Hz, 1H), 7.05−7.09 (m, 1H), 7.12−7.14 (m, 1H), 7.24−7.28 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 8.5, 13.8, 22.9, 25.9, 26.4, 31.0, 37.5, 53.7, 107.6, 122.3, 122.6, 127.5, 132.4, 144.2, 180,2; IR (KBr, cm^{-1}): 3513, 3432, 2962, 2934, 2875, 2223, 1721, 1614, 1592, 1493, 1460, 1371, 1348, 1254, 1173, 1123, 1068, 822, 737, 569, 521, 508. HRMS (ESI) for $C_{16}H_{20}NO$ $[M+Na]^+$calcd. 279.1468, found 279.1462.

1,3,3,5-tetramethylindolin-2-one (2w)



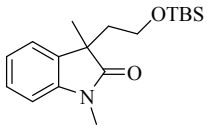
White solid; 70% yield; mp 54−56℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.35 (s, 6H), 2.34 (s, 3H), 3.19 (s, 3H), 6.73 (d, *J* = 7.8 Hz, 1H), 7.02−7.06 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 21.1, 24.4, 26.2, 44.2, 107.7, 123.1, 127.8, 132.0, 135.9, 140.3, 181.3; IR (KBr, cm^{-1}): 3400, 2961, 2925, 2863, 1710, 1620, 1603, 1505, 1458, 1380, 1349, 1348, 1244, 1133, 1117, 1066, 1045, 882, 800, 617, 555, 465. HRMS (ESI) for $C_{12}H_{16}NO$ $[M+H]^+$calcd. 190.1226, found 190.1223.

5-methoxy-1,3,3-trimethylindolin-2-one (2x)



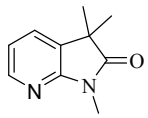
Colorless oil; 77% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.36 (s, 6H), 3.19 (s, 3H), 3.81 (s, 3H), 6.73−6.80 (m, 2H), 6.83 (d, *J* = 2.3 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 24.4, 26.2, 44.6, 55.8, 108.2, 110.0, 111.5, 136.1, 137.2, 156.0, 181.0; IR (KBr, cm^{-1}): 3487, 2966, 2929, 2867, 1708, 1662, 1602, 1500, 1472, 1436, 1383, 1356, 1289, 1220, 1120, 1048, 1028, 882, 805, 697, 558, 463. HRMS (ESI) for $C_{12}H_{16}NO_2$ $[M+H]^+$calcd. 206.1176, found 206.1171.

3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1,3-dimethylindolin-2-one (2y)



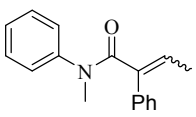
Colorless oil; 64% yield; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= −0.13 (s, 6H), 0.77 (s, 9H), 1.36(s, 3H), 1.94−2.00(m, 1H), 2.20−2.27 (m, 1H), 3.19 (s, 3H), 3.36 (t, *J* = 6.7 Hz, 2H), 6.82 (d, *J* = 7.8 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.25 (t, *J* = 7.7 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= −5.7, −5.6, 18.1, 24.8, 25.8, 26.2, 40.3, 46.5, 59.5, 107.8, 122.2, 122.7, 127.6, 133.7, 143.3, 180.4; IR (KBr, cm^{-1}): 3426, 2954, 2928, 2856, 1719, 1614, 1494, 1471, 1377, 1348, 1253, 1110, 835, 752. HRMS (ESI) for $C_{18}H_{30}NO_2Si$ $[M+H]^+$calcd. 320.2040, found 320.2033.

1,3,3-trimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one (2z)



Yellow oil; 65% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.40 (s, 6H), 3.31 (s, 3H), 6.96 (dd, *J* = 7.2, 5.3 Hz, 1H), 7.43 (dd, *J* = 7.2, 1.5 Hz, 1H), 8.18 (dd, *J* = 5.3, 1.5 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 23.8, 25.3, 118.0, 129.5, 130.0, 146.5, 156.2, 180.8; IR (KBr, cm^{-1}): 3425, 2971, 2932, 2870, 1720, 1608, 1595, 1471, 1360, 1258, 1143, 1046, 939, 803, 782, 559, 497. HRMS (ESI) for $C_{10}H_{13}N_2O$ $[M+H]^+$calcd.177.1022, found 177.1025.

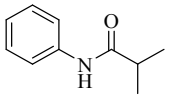
(E)-N-methyl-N,2-diphenylbut-2-enamide (2aa)



Colorless oil; 20% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.63 (d, *J* = 7.1 Hz, 3H), 3.29 (s, 3H), 6.25 (q, *J* = 7.1 Hz, 1H),

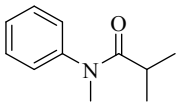
6.80−6.84 (m, 4H), 7.10−7.12 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 14.4, 37.9, 126.4, 126.7, 127.3, 127.7, 128.7, 128.7, 131.6, 135.7, 139.3, 144.1, 171.8; IR (KBr, cm^{-1}): 3390, 3057, 2963, 2932, 1720, 1650, 1595, 1495, 1455, 1382, 1367, 1267, 1134, 1075, 766, 737, 700, 553. HRMS (ESI) for $C_{17}H_{18}NO$ $[M+H]^+$calcd. 252.1383, found 252.1386

N-phenylisobutyramide (2ab)



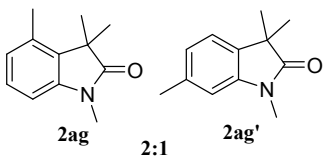
White solid; 95% yield; mp 98−99℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.21 (d, *J* = 1.4 Hz, 3H), 1.23 (d, *J* = 1.4 Hz, 3H), 2.52 (m, 1H), 7.08 (t, *J* = 7.3 Hz, 1H), 7.28 (t, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.58−7.80 (br, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 19.6, 36.5, 119.9, 124.0, 128.8, 138.1, 175.6; IR (KBr, cm^{-1}): 3302, 3263, 2969, 2931, 1662, 1600, 1549, 1490, 1442, 1386, 1310, 1252, 1204, 1099, 942, 883, 761, 734,694, 589, 510. HRMS (ESI) for $C_{10}H_{14}NO$ $[M+H]^+$calcd. 164.1070, found 164.1067.

N-methyl-N-phenylisobutyramide (2a')



White solid; 60% yield; mp 98−99℃; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.03 (d, *J* = 6.7 Hz, 6H), 2.51 (m, 1H), 3.25 (s, 3H), 7.19 (dd, *J* = 8.3, 1.4 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 2H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 19.6, 30.9, 37.4, 127.2, 127.6, 129.7, 144.3, 177.4; IR (KBr, cm^{-1}): 3442, 3054, 2962, 2933, 2870, 1652, 1595, 1496, 1471, 1420, 1387, 1268, 1117, 1039, 783, 708, 572, 411. HRMS (ESI) for $C_{11}H_{16}NO$ $[M+H]^+$calcd. 178.1226, found 178.1222.

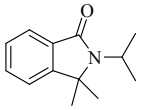
1,3,3,4-tetramethylindolin-2-one (2ag);1,3,3,6-tetramethylindolin-2-one (2ag')



White solid; 71% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.35 (s, 3H), 1.45 (s, 6H), 2.38 (s, 1.5H), 2.40 (s, 3H), 3.20 (d, 4.7H), 6.67 (s, 0.5H), 6.69 (d, *J* = 7.8 Hz,

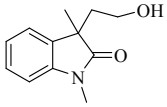
1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.87 (dd, *J* = 7.5, 0.6 Hz, 0.5H), 7.08 (d, *J* = 7.5 Hz, 0.5H), 7.16 (t, *J* = 7.8 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 18.1, 21.7, 22.4, 24.5, 26.1, 26.3, 43.9, 45.0, 105.8, 109.0, 122.0, 122.9, 125.0, 127.4, 132.6, 133.0, 134.0, 137.7, 142.7, 142.9, 181.4, 181.7; IR (KBr, cm^{-1}): 3396, 2979, 2965, 2928, 1712, 1608, 1598, 1468, 1442, 1381, 1331, 1300, 1243, 1073, 1047, 954, 826, 786, 760, 600, 560, 474. HRMS (ESI) for $C_{12}H_{16}NO$ $[M+H]^+$calcd. 190.1226, found 190.1222.

2-isopropyl-3,3-dimethylisoindolin-1-one (1af)



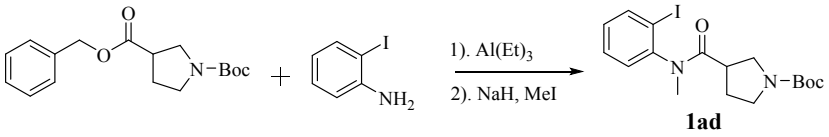
White solid; 53% yield; **^{1}H NMR (400 MHz, $CDCl_3$)** δ (ppm) = 1.28 (s, 6H), 1.56 (s, *J* = 6.9 Hz, 6H), 3.65 (m, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.5 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 20.5, 25.4, 44.5, 63.2, 120.5, 123.1, 127.8, 131.2, 132.0, 151.1, 167.2; IR (KBr, cm^{-1}): 3424, 2970, 2932, 2874, 1647, 1578, 1471, 1428, 1389, 1280, 1128, 1051, 1019, 769, 727. HRMS (ESI) for $C_{13}H_{17}NONa$ $[M+Na]^+$calcd. 226.1202, found 226.1202.

3-(2-hydroxyethyl)-1,3-dimethylindolin-2-one (**2ae**)



Colorless oil**;** 88% yield; **^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= 1.41 (s, 3H), 1.96−2.02 (m, 1H), 2.13−2.19 (m, 1H), 2.62 (br, 1H), 3.22 (s, 3H), 3.41−3.47 (m, 1H), 3.61−3.67 (m, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.18 (d, *J* = 7.0Hz, 1H), 7.29 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm) = 23.5, 26.3, 40.0, 46.9, 59.2, 108.3, 122.4, 122.7, 127.9, 134.0, 142.8, 181.5; IR (KBr, cm^{-1}): 3417, 3055, 2968, 2925, 1703, 1613, 1493, 1471, 1453, 1379, 1352, 1265, 1126, 1105, 1043, 737, 701. HRMS (ESI) for $C_{12}H_{15}NO_2Na$ $[M+Na]^+$calcd. 228.0995, found 228.0995.

7. Synthesis of the (±)-coerulescine scaffold



1ad

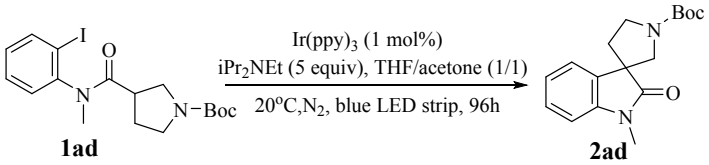
A solution of triethylaluminum in toluene (1.0 M, 2.5 ml, 2.5 mmol, 2.5 equiv.) was added to a solution of 2-iodoaniline (0.219 g, 1.0 mmol, 1 equiv.) in toluene (3 ml) at 0°C under inert atmosphere. The mixture was then warmed to room temperature. After stirring for 3h, a solution of benzyl 1-tert-{butyloxycarbonyl}-pyrrolidine-3-car

-boxylate (0.305 g, 1.0 mmol, 1 equiv.) in toluene (3 ml) was added, and the mixture was heated at 80°C for 12 h. On completion of the reaction, a saturated aqueous solution of ammonium chloride and a few drops of hydrochloric acid (2M) were added. The mixture was washed with a solution of sodium hydroxide (2M), and extracted with diethyl ether, and the combined organic phase was dried over sodium sulfate. The product was purified by column chromatography (70:30, hexanes-ethyl acetate) giving tert-butyl-3-((2-iodophenyl)carbamoyl)pyrrolidine-1-carboxylate as a white powder.[2,4]

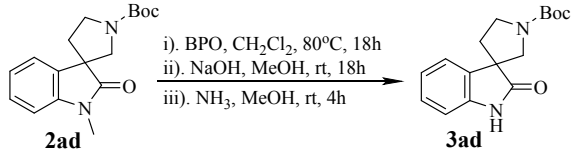
To a stirred suspension of NaH (0.027 g; 1.1 mmol) in 1 ml of dry THF at 0°C, the tert-butyl-3-((2-iodophenyl)carbamoyl)pyrrolidine-1-carboxylate (1 mmol) dissolved in 2 ml of THF was added dropwise within 10 min. The reaction mixture was stirred until the solution became clear (30 min, hydrogen gas evolved), and the solution of MeI (0.22 g; 1.5 mmol) in 1 ml of THF was added dropwise within 10 min. The solution was warmed up to room temperature and stirred for 3 h. Then the reaction mixture was quenched with water (5 ml). The resulting solution was extracted with ethyl acetate (3 x 5 ml). Combined organic layers were washed with brine (1 x 4 ml) and dried over Na_2SO_4. Ethyl acetate was removed under reduced pressure to give crude products. The product was purified by column chromatography (7:3, hexanes-ethyl acetate) giving tert-butyl-3-((2-iodophenyl)(methyl)carbamoyl)py

-rrolidine-1-carboxylate **1ad** as a pale oil (0.38 g, 88% over 2 steps); **^{1}H NMR (400**

MHz, $CDCl_3$): δ(ppm)= 1.42 (2 x s, 9H), 1.95−2.02 (m, 1H), 2.09 (br ,1H), 2.62−2.70 (m, 1H), 3.05-3.14 (m, 1H), 3.19 (s, 3H), 3.31−3.36 (m, 1H), 3.51-3.62 (m, 2H), 7.11−7.55 (m, 1H), 7.26−7.30 (m, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ (ppm)= 28.4, 36.2, 36.2, 45.4, 45.5, 49.1, 79.1, 79.1, 99.7, 99.8, 128.8, 128.8, 129.0, 129.8, 130.0, 130.1, 130.1, 140.2, 140.3, 145.5, 154.1, 154.1, 172.2, 172.3; IR (KBr, cm^{-1}): 3315, 2974, 2931, 2884, 2372, 1688, 1663, 1578, 1470, 1409, 1386, 1250, 1169, 1125, 1019, 875, 771, 728, 552. HRMS (ESI) for $C_{17}H_{23}N_2O_3INa$ $[M+Na]^+$calcd. 453.0646, found 453.0657.



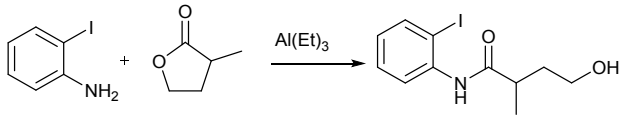
The title compound **2ad** was prepared according to the general method described above and purified by flash column chromatography (2:1, hexanes-ethyl acetate) in 65% yield. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= 1.48 (2 x s, 9H), 2.03 (br, 1H), 2.38−2.45 (m ,1H), 3.24 (s, 3H), 3.52−3.86 (m, 4H), 6.88 (d, J = 7.7 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 7.4 (br, 1H), 7.32 (t, J = 7.6 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= 26.4, 28.4, 35.4, 36.2, 45.2, 45.4, 51.9, 52.8, 53.8, 54.3, 79.7, 108.2, 122.3, 122.9, 128.3, 142.7, 154.3, 177.2; IR (KBr, cm^{-1}): 3414, 3056, 2975, 2934, 2885, 1717, 1696, 1614, 1494, 1472, 1402, 1375, 1350, 1254, 1171, 1124, 1022, 988, 882, 752, 544,463. HRMS (ESI) for $C_{17}H_{22}N_2O_3Na$ $[M+Na]^+$calcd. 325.1523, found 325.1531.



A solution of **2ad** (60.4 mg, 0.2 mmol) and benzoyl peroxide (96.8 mg, 0.4 mmol) in CH_2Cl_2 (1 mL) in a sealed tube was heated slowly to 80 °C. After stirring for 18 h, the reaction mixture was cooled to rt and the solvent was evaporated. The residue was dissolved in MeOH (1 mL), NaOH (29.2 mg, 0.8 mmol) was added and the reaction

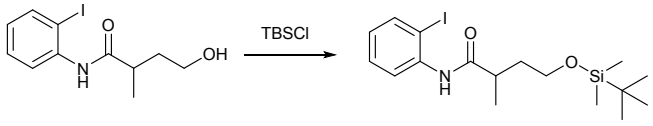
mixture was stirred for 18 h at rt. Then the slurry was poured onto saturated aqueous NH_4Cl (1 mL) and extracted with CH_2Cl_2 (3 x 2 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. The residue was dissolved in a saturated methanolic NH_3 solution (0.5 mL) and stirred for 4 h at rt. The solvent was evaporated and the residue chromatographed to give **3ad** as a pale oil (25 mg, 43%);[3] **^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= 1.49 (2 x s, 9H), 2.04−2.14 (m, 1H), 2.39−2.46 (m ,1H), 3.55−3.91 (m, 4H), 6.97 (t, *J* = 6.3 Hz, 1H), 7.06 (t, *J* = 7.3 Hz, 1H), 7.16−7.26 (m, 2H), 9.19 (2 x s, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= 28.4, 28.5, 35.5, 36.3, 45.2, 45.4, 52.4, 53.3, 53.8, 54.3, 79.8, 110.1, 122.7, 122.9, 128.4, 132.6, 133.0, 140.1, 140.2, 154.4, 180.1, 180.4; IR (KBr, cm^{-1}): 3248, 2977, 2932, 2887, 1719, 1700, 1621, 1472, 1404, 1367, 1345, 1228, 1172, 1130, 879, 751, 737, 702, 674, 636. HRMS (ESI) for $C_{16}H_{20}N_2O_3Na$ $[M+Na]^+$calcd. 311.1366, found 311.1357.

8. Synthesis of the (±) - physovenine scaffold

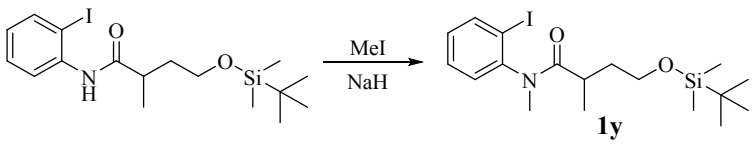


A solution of triethylaluminum in toluene (1.0 M, 10 ml, 10 mmol, 2.5 equiv.) was added to a solution of 2-iodoaniline (0.876 g, 4.0 mmol, 1 equiv.) in toluene (15 ml) at 0^{o}C under inert atmosphere. The mixture was then warmed to room temperature. After stirring for 3h, a solution of 3-methyldihydrofuran-2(3H)-one (0.40 g, 4.0 mmol, 1 equiv.) in toluene (15 ml) was added, and the mixture was heated at 80^{o}C for 12 h. On completion of the reaction, a saturated aqueous solution of ammonium chloride and a few drops of hydrochloric acid (2M) were added. The mixture was washed with a solution of sodium hydroxide (2M), and extracted with diethyl ether, and the combined organic phase was dried over sodium sulfate and concentrated. The product was purified by column chromatography (1:1,

dichloromethane-ethyl acetate) giving the product as a white powder (1.13 g, 89%).[2,4]



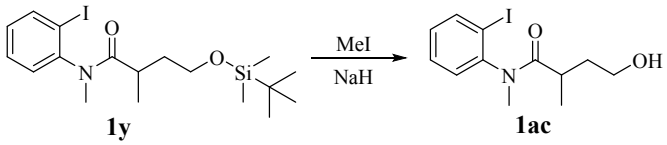
To a reaction flask containing the 4-hydroxy-N-(2-iodophenyl)-2-methylbutanam -ide (0.64 g, 2 mmol) and imidazole (0.2 g, 3 mmol) was added CH_2Cl_2 (3 mL). The solution was cooled to 0°C in an ice bath before adding TBSCl (0.34 g, 2.2 mmol). The reaction was allowed to warm to room temperature overnight (12 h) and a white precipitate emerged. The reaction was diluted with CH_2Cl_2 (3 mL) and quenched with saturated NH_4Cl solution. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layers were washed with saturated $NaHCO_3$ solution, water, and brine; dried over sodium sulfate; and concentrated. The resulting crude mixture was purified by flash column chromatography (4:1, hexanes-ethyl acetate) giving the product as a pale oil (0.85 g, 95%).[5] **^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= 0.04 (2 x s, 6H), 0.88 (s, 9H), 1.28 (d, *J* = 6.9 Hz, 3H), 1.64−1.72 (m, 1H), 1.95−2.03 (m, 1H), 2.65−2.73 (m, 1H), 3.70 (t, *J* = 6.0 Hz, 2H), 6.81 (m, 1H), 7.31 (m, 1H), 7.59 (br, 1H), 7.75 (dd, *J* = 8.0, 1.4 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= -5.4, -5.3, 17.7, 18.2, 25.9, 37.0, 38.7, 60.4, 90.0, 122.0, 125.7, 129.1, 138.2, 138.6, 174.6; IR (KBr, cm^{-1}): 3388, 3278, 2955, 2930, 2856, 1671, 1584, 1516, 1462, 1431, 1387, 1288, 1255, 1176, 1102, 1014, 903, 835, 776, 749, 665, 649. HRMS (ESI) for $C_{17}H_{28}NO_2INa$ $[M+Na]^+$calcd. 456.0826, found 456.0820.



1y

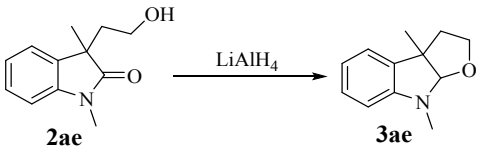
The title compound **1y** was prepared according to the general method described above and purified by flash column chromatography (6:1, hexanes-ethyl acetate) in 98% yield. Colorless oil**; ^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= -0.06− -0.03 (m, 6H), 0.78 (2 x s, 9H), 1.06 (4 x s, 3H), 1.44−1.58 (m, 1H), 1.79−1.05 (m, 1H), 2.25−2.40 (m, 1H), 3.17 (2 x s, 3H), 3.52−3.58 (m, 2H), 7.04−7.09 (m, 1H), 7.26−7.32 (m, 1H),

7.38−7.44 (m, 1H), 7.91−7.94 (m, 1H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= -5.5, -5.4, -5.3, 17.1, 17.2, 18.1, 18.2, 25.9, 33.4, 33.5, 36.1, 36.2, 36.3, 37.0, 60.4, 60.6, 99.5, 99.8, 128.8, 129.4, 129.6, 129.6, 129.6, 129.7, 140.1, 140.3, 146.1, 176.5, 176.7; IR (KBr, cm^{-1}): 3413, 2930, 2857, 2372, 1647, 1578, 1468, 1429, 1388, 1280, 1252, 1112, 1051, 1020, 878, 836, 772, 726, 666, 575. HRMS (ESI) for $C_{18}H_{30}NO_2INa$ $[M+Na]^+$calcd. 470.0983, found 470.0999.



1y **1ac**

To a solution of the silyl ether (447 mg, 1 mmol) in THF (5 mL) at 0°C was added TBAF (1.0 M in THF, 1.2 mL, 1.2 mmol). The reaction mixture was stirred at room temperature for 4 h and quenched by saturated NH_4Cl solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with water and brine, dried, and concentrated. The residue was purified by flash chromatography (EtOAc). The alcohol as a colorless oil which solidified upon standing (318 mg, 96%).



2ae **3ae**

To a solution of the oxindole-3- ethanol (41 mg, 0.2 mmol) in dry THF (4 mL) at 0°C was added LAH (31 mg, 0.8 mmol). The reaction mixture was stirred at this temperature for 40 min and quenched by saturated $NaHCO_3$ (5 mL) solution. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine, dried, and concentrated. The residue was purified by flash chromatography (EtOAc) gave **3ae** (15.1 mg, 80%) as a slightly white solid:[6] **^{1}H NMR (400 MHz, $CDCl_3$)**: δ(ppm)= 1.46 (s, 3H), 2.00–2.15 (m, 2H), 2.92 (s, 3H), 3.42–3.48 (m, 1H), 3.92–3.96 (m, 1H), 5.06 (s, 1H), 6.36 (d, *J* = 7.8 Hz, 1H), 6.67 (m, 1H), 7.04 (d, *J* = 6.9 Hz, 1H), 7.07–7.12 (m, 1H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ(ppm)= 24.7, 30.9, 41.7, 52.3, 67.3, 104.8, 104.9, 117.3, 122.4, 128.1, 134.4,

150.4；IR (KBr, cm^{-1}): 2959, 2926, 2866, 1608, 1494, 1448, 1388, 1301, 1216, 124, 1033, 1011, 918, 740. HRMS (ESI) for $C_{12}H_{15}NONa$ $[M+Na]^+$calcd. 212.1046, found 212.1041.

References:

1 U. Ladziata, A. Y. Koposov, K. Y. Lo, J. Willging, V. N. Nemykin and V. V. Zhdankin, *Angew. Chem. Int. Ed.*, 2005, **44**, 7127.

2 J. A. Murphy , R. Tripoli, T. A. Khan , and Umesh W. Mali, *Org. Lett.,* 2005, **7**, 3287.

3 W. G. B. van Henegouwen, R. M. Fieseler, F. P. J. T. Rutjes, and H. Hiemstra, *J. Org. Chem.*, 2000, **65**, 8317.

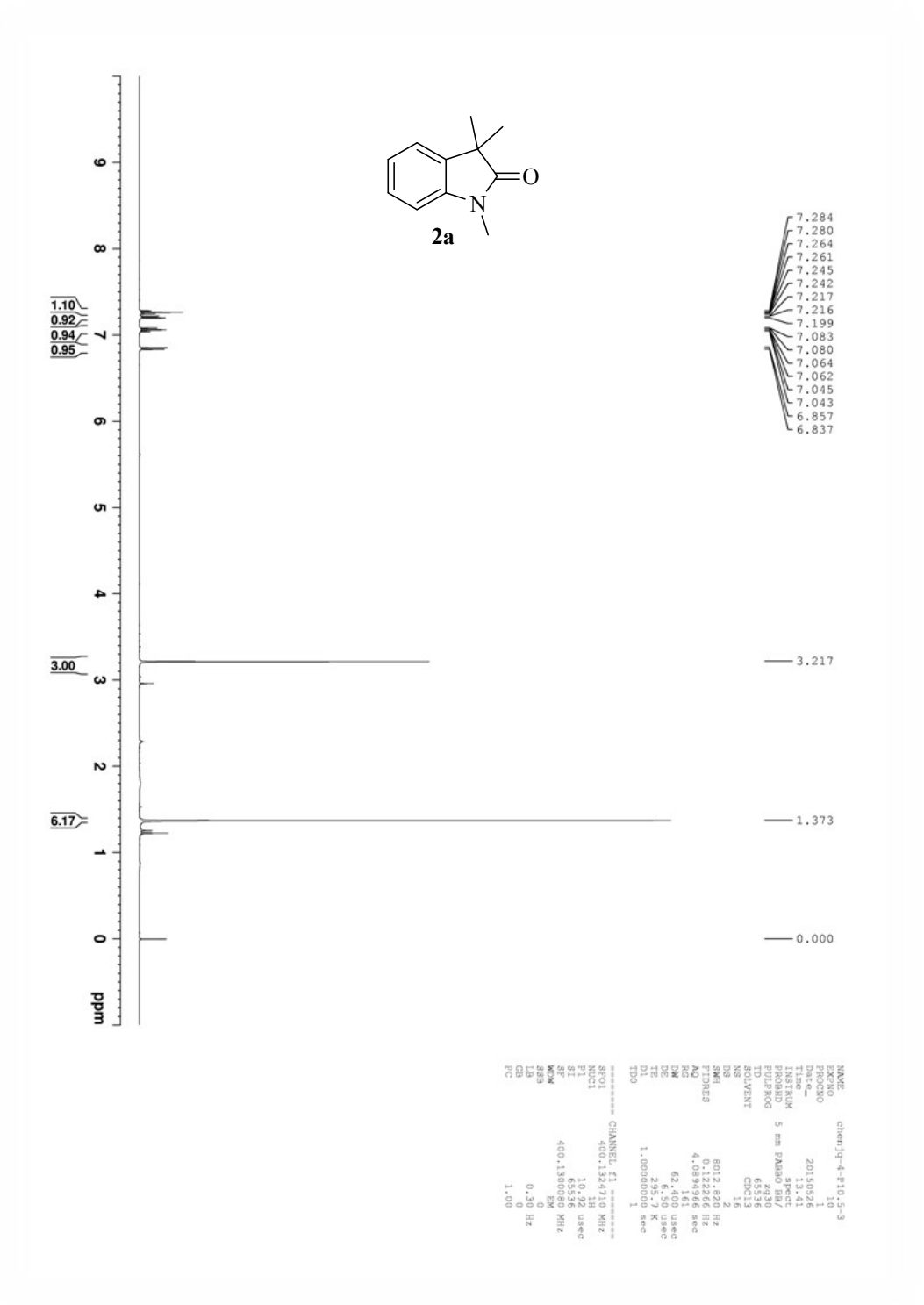
4 T. Y. Zhang and H. Zhang, *Tetrahedron Letters,* 2002, **43**, 1363.

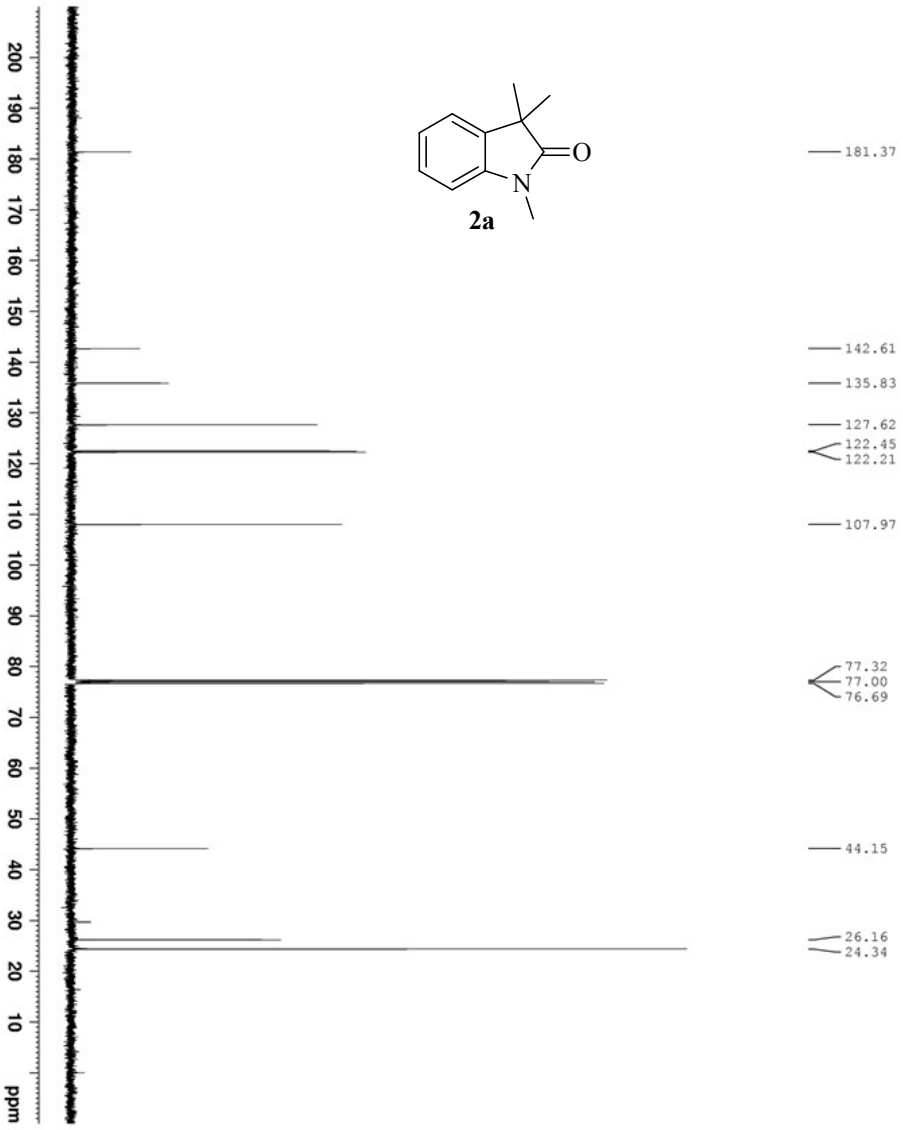
5 K. Kong, J. A. Enquist, J. M. E. McCallum, G. M. Smith, T. Matsumaru, E. Menhaji-Klotz, and J. L. Wood, *J. Am. Chem. Soc.*, 2013, **135**, 10890.

6 B. Zhou, W. Hou, Y. Yang, H. Feng, and Y. Li, *Org. Lett.,* 2014, **16**, 1322.

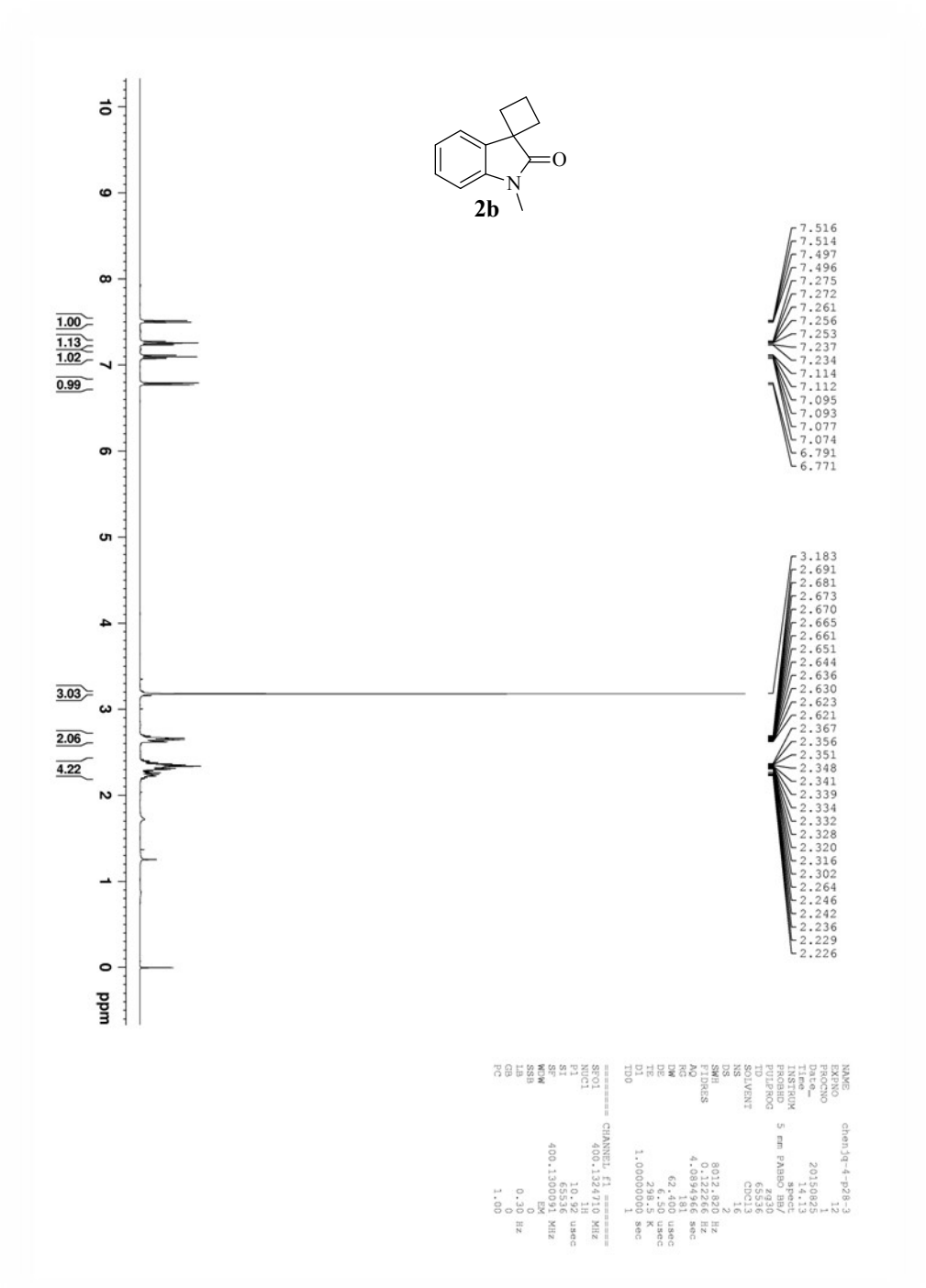
9. NMR spectra of compounds

1,3,3-trimethylindolin-2-one (**2a**)



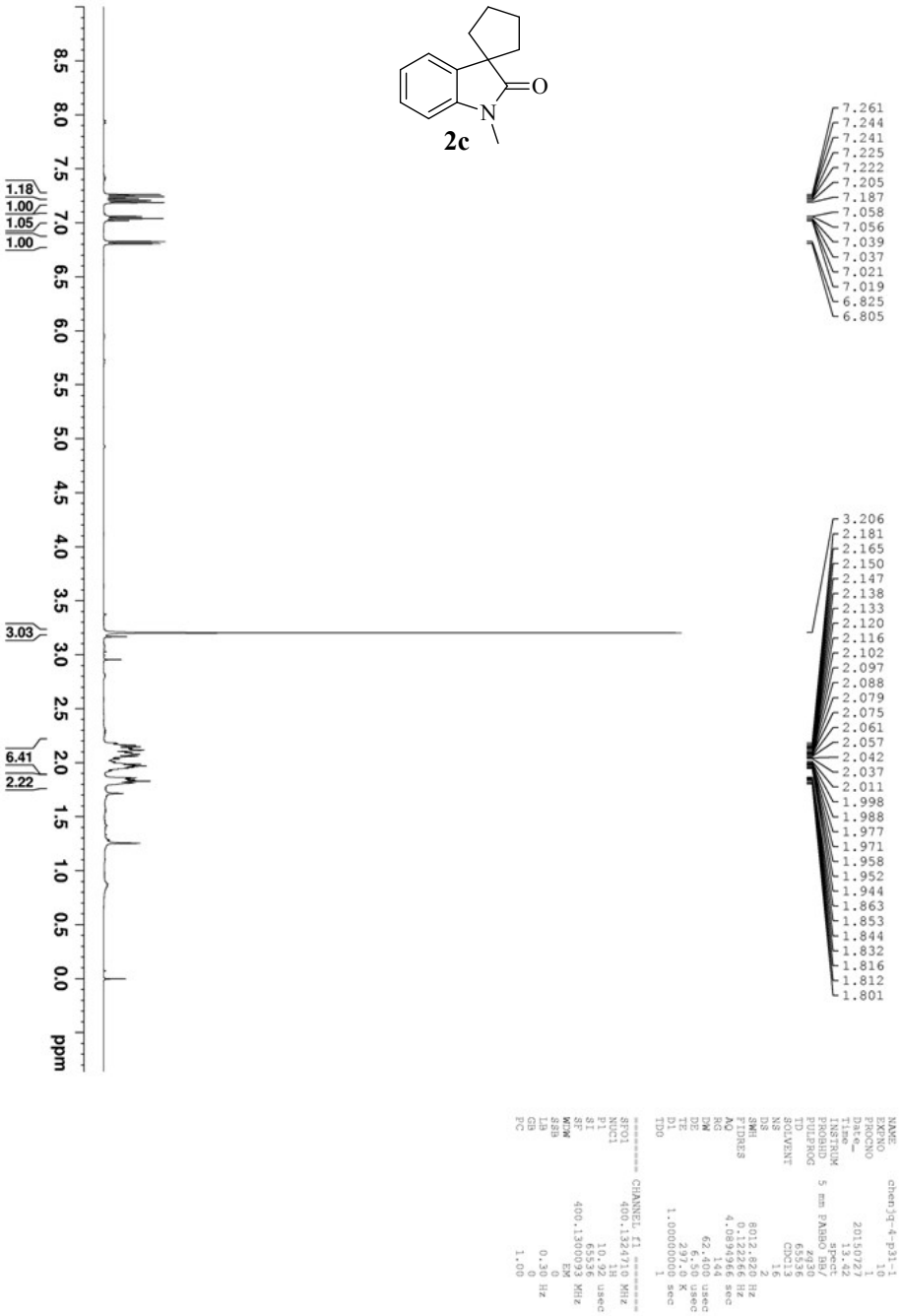

O
N
2a
181.37
142.61
135.83
127.62
122.45
122.21
107.97
77.32
77.00
76.69
44.15
26.16
24.34
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

1'-methylspiro[cyclobutane-1,3'-indolin]-2'-one (**2b**)




O
N
2b
180.19
142.98
134.39
127.77
122.52
122.22
107.59
77.34
77.02
76.71
48.14
31.29
26.12
16.77
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

1'-methylspiro[cyclopentane-1,3'-indolin]-2'-one (**2c**)

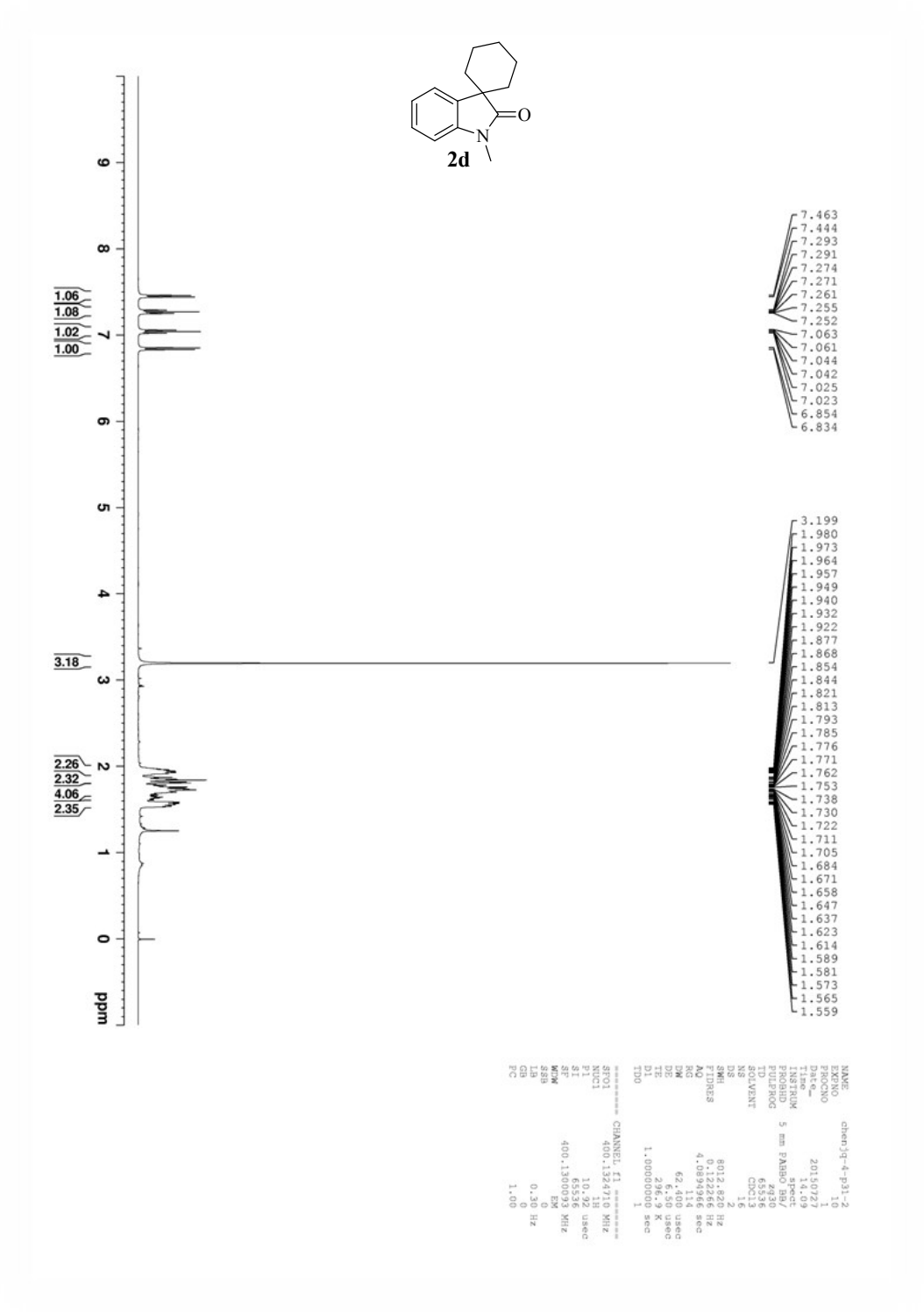


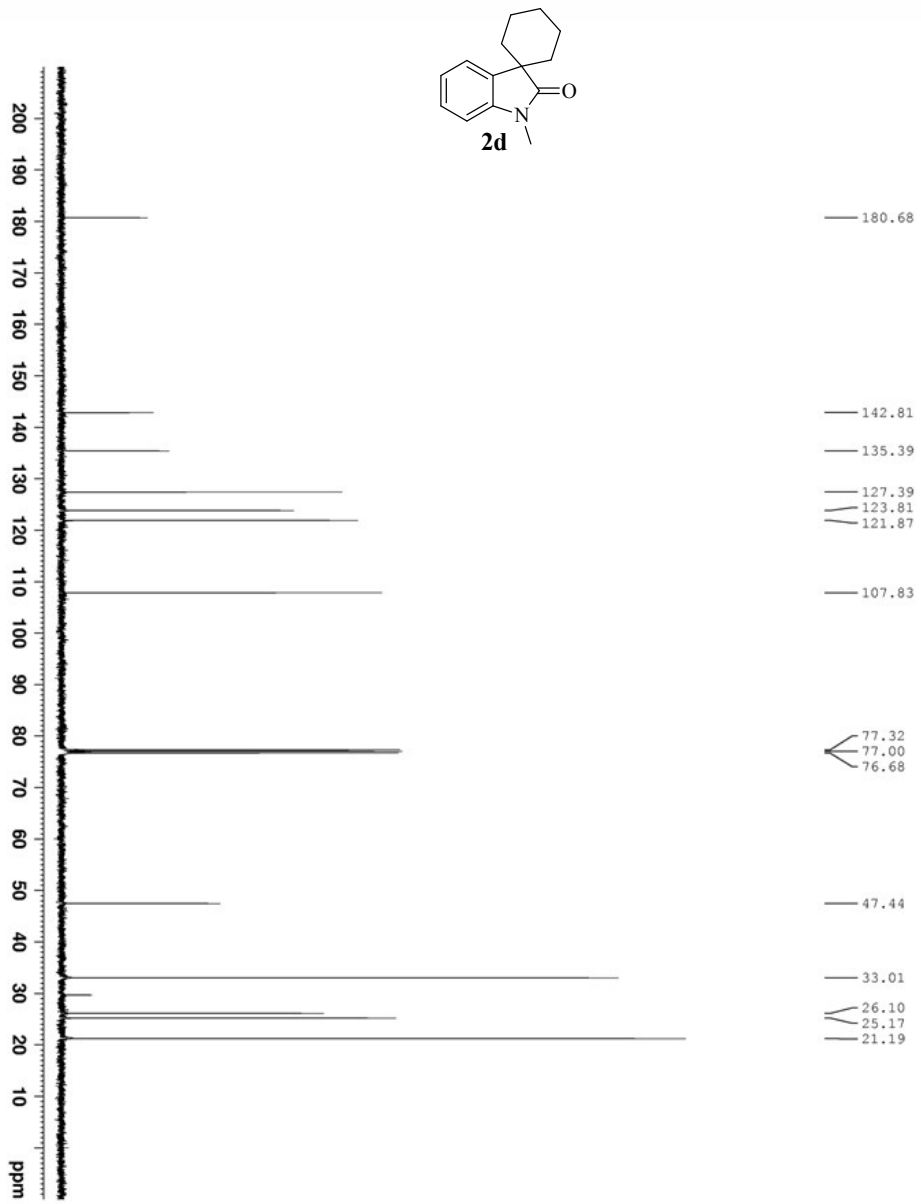

O
N

2c

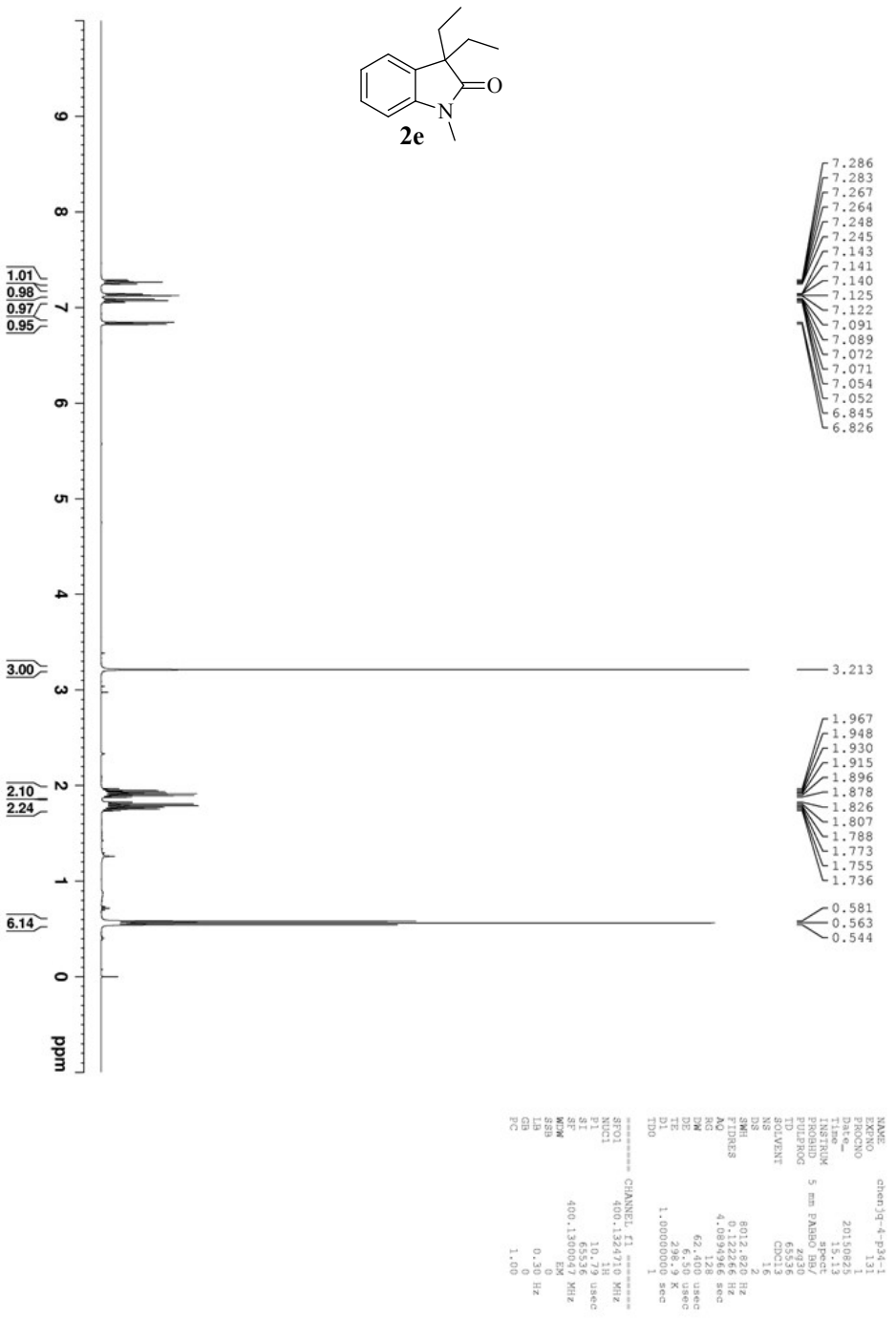
181.90
142.90
136.85
127.30
122.47
122.18
107.65
77.32
77.00
76.68
53.89
38.30
26.60
26.20
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

1'-methylspiro[cyclohexane-1,3'-indolin]-2'-one (**2d**)



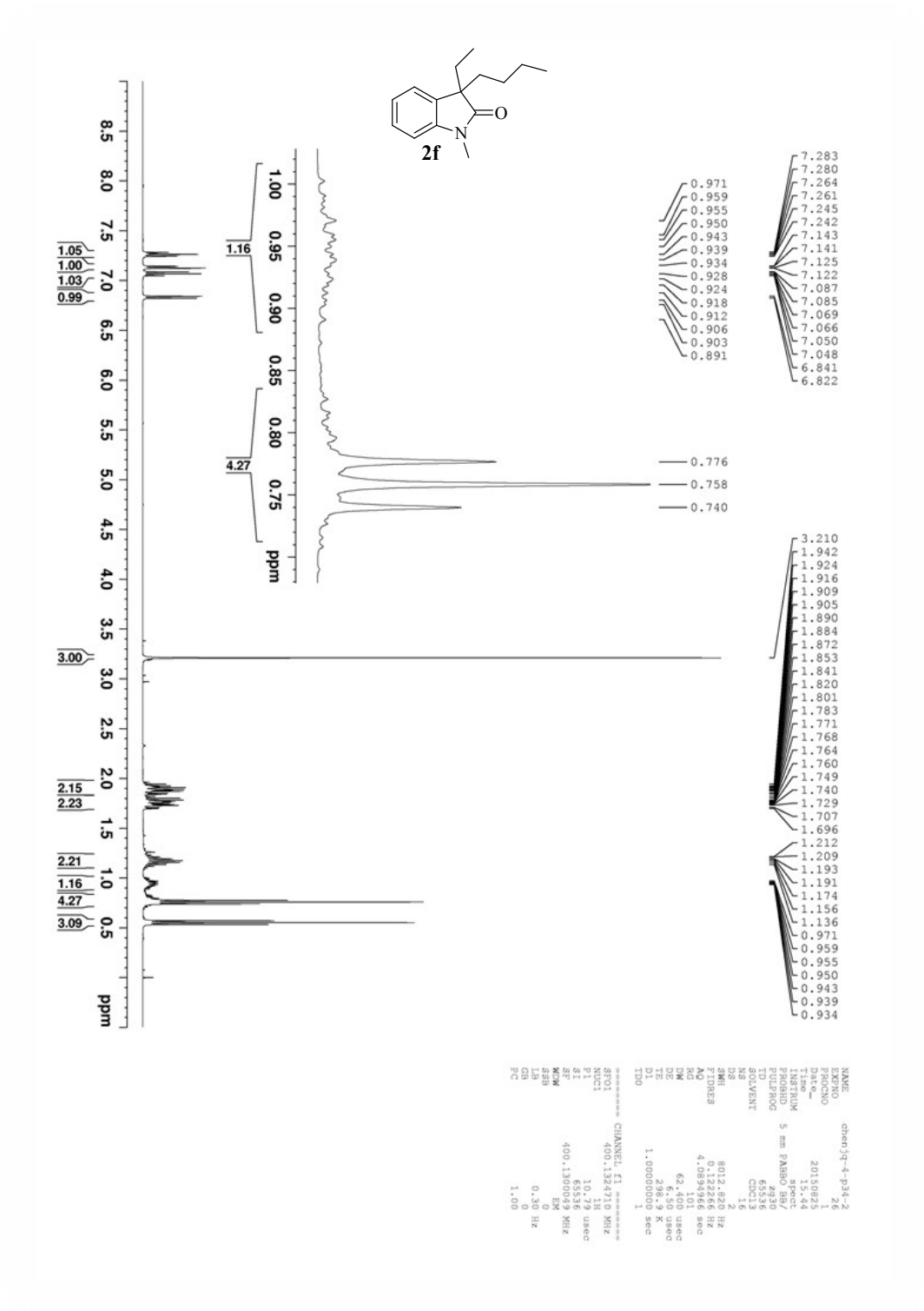

O
N
2d
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
180.68
142.81
135.39
127.39
123.81
121.87
107.83
77.32
77.00
76.68
47.44
33.01
26.10
25.17
21.19

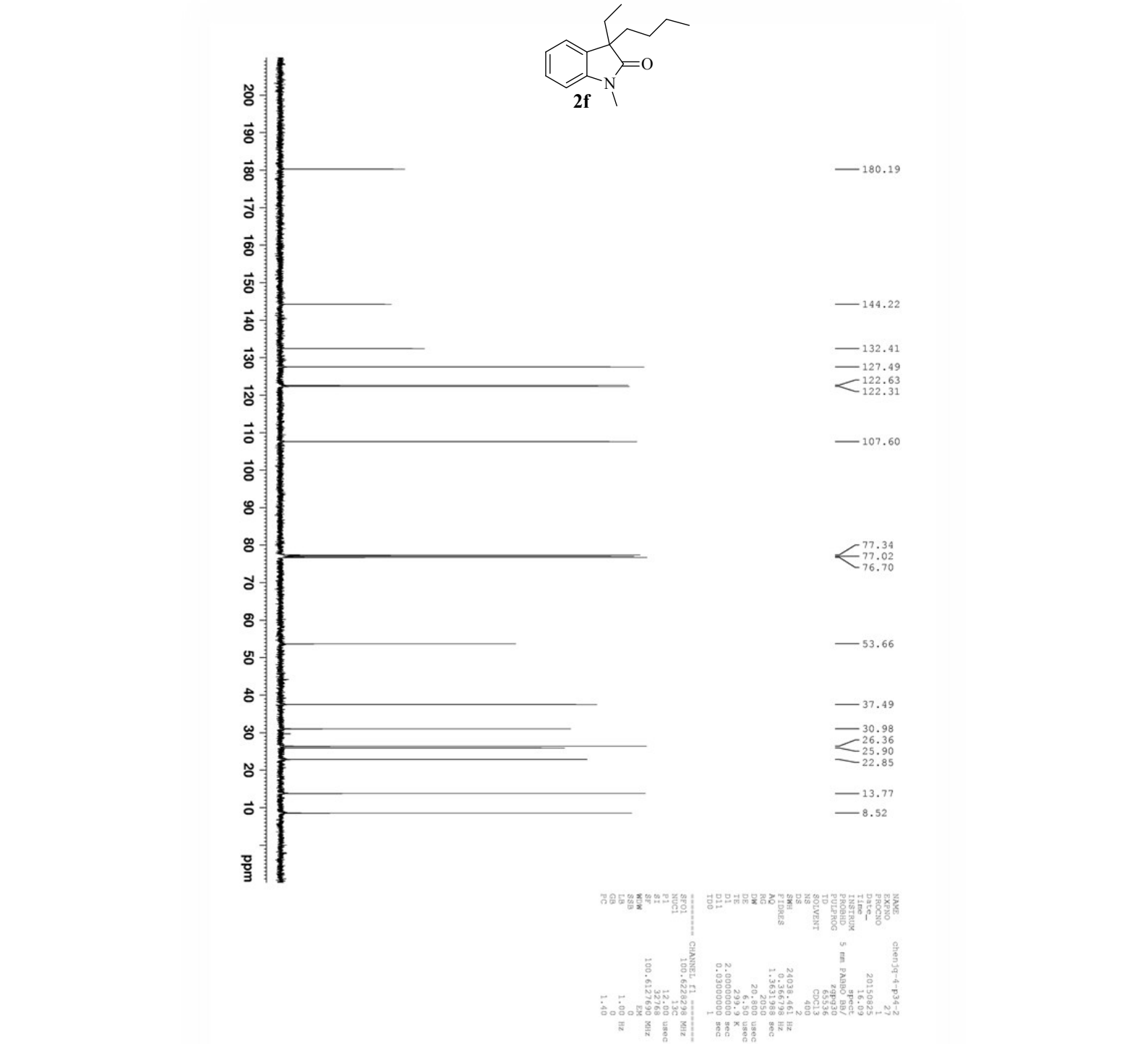
3,3-diethyl-1-methylindolin-2-one (**2e**)



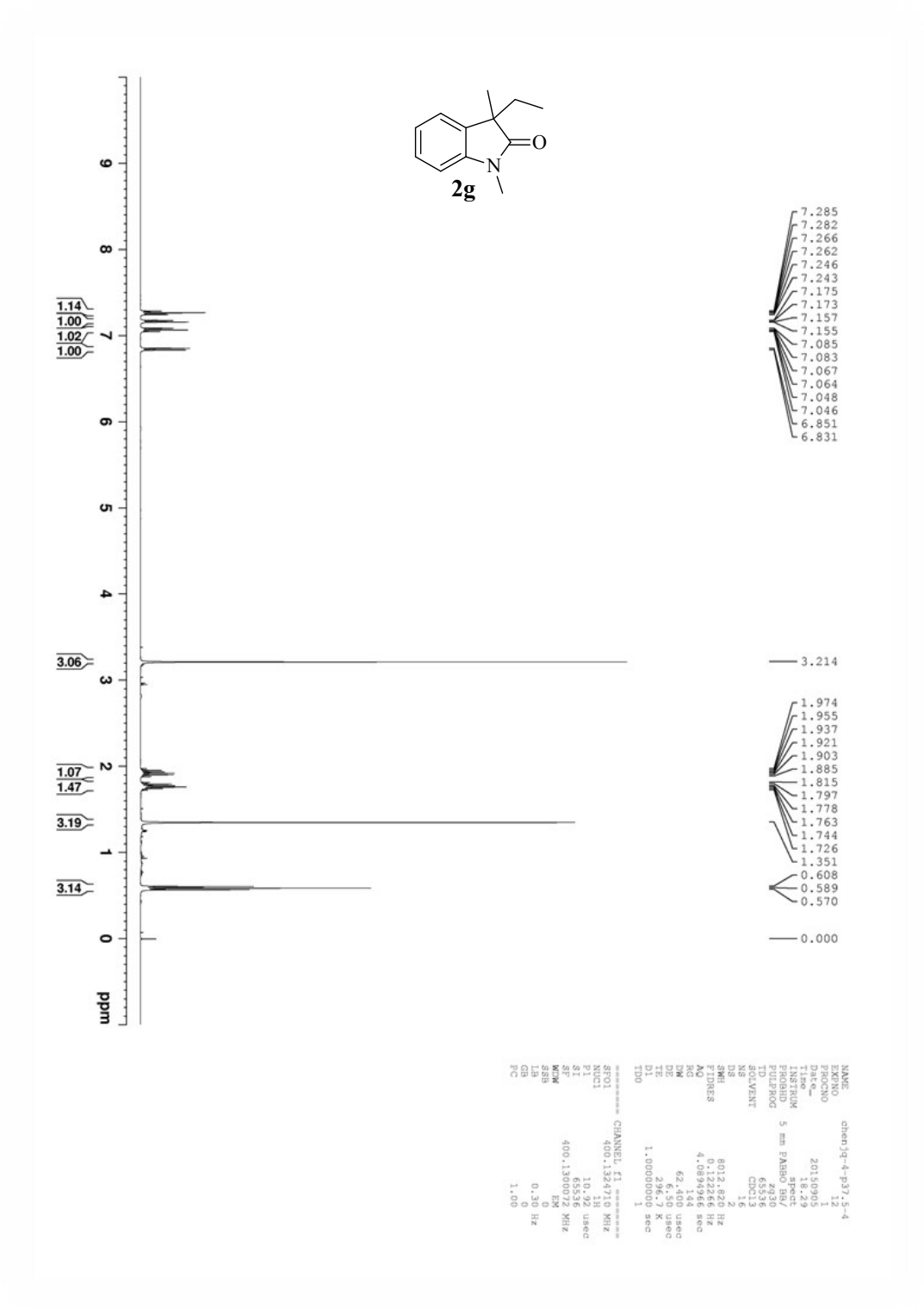

2e
O
N
180.06
144.38
132.02
127.55
122.68
122.32
107.60
77.34
77.02
76.70
54.30
30.59
25.88
8.63
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

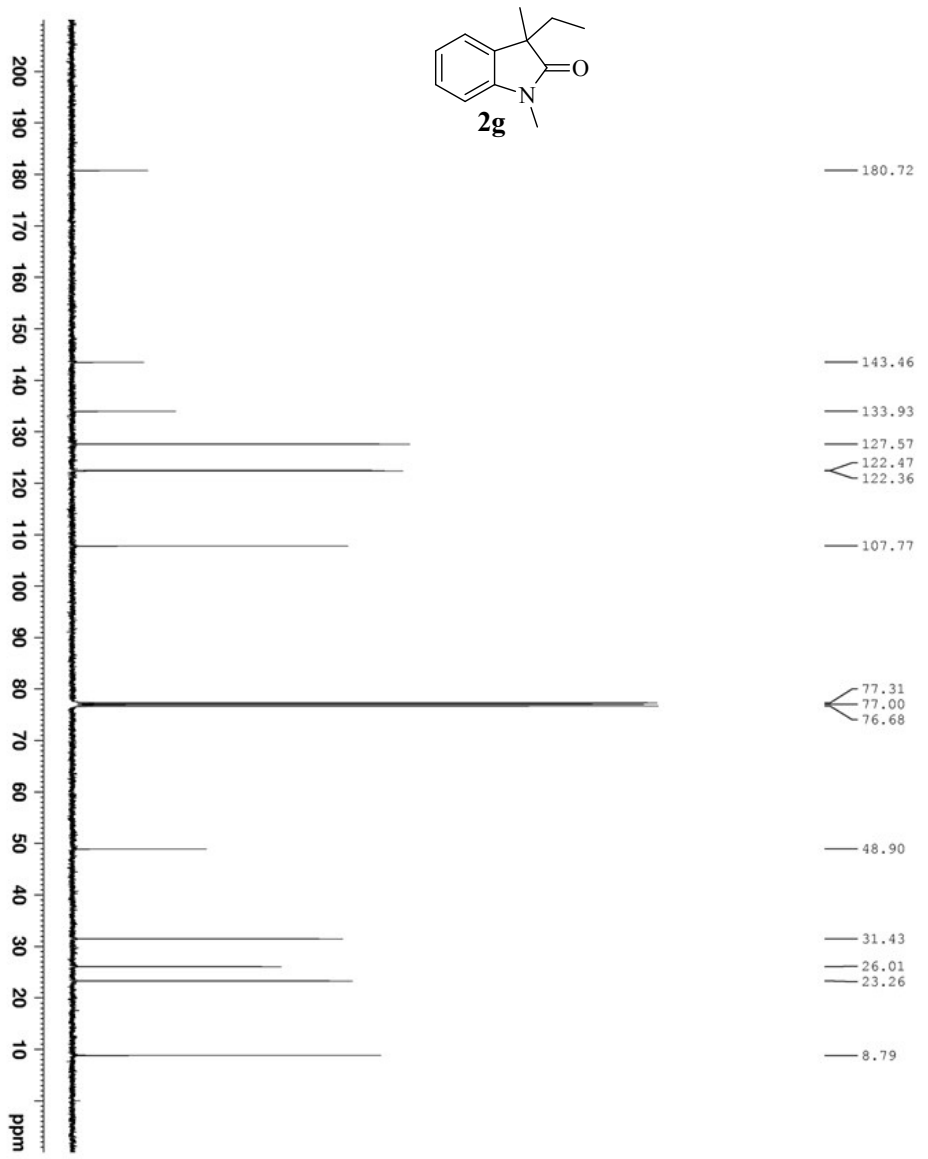
3-butyl-3-ethyl-1-methylindolin-2-one (**2f**)



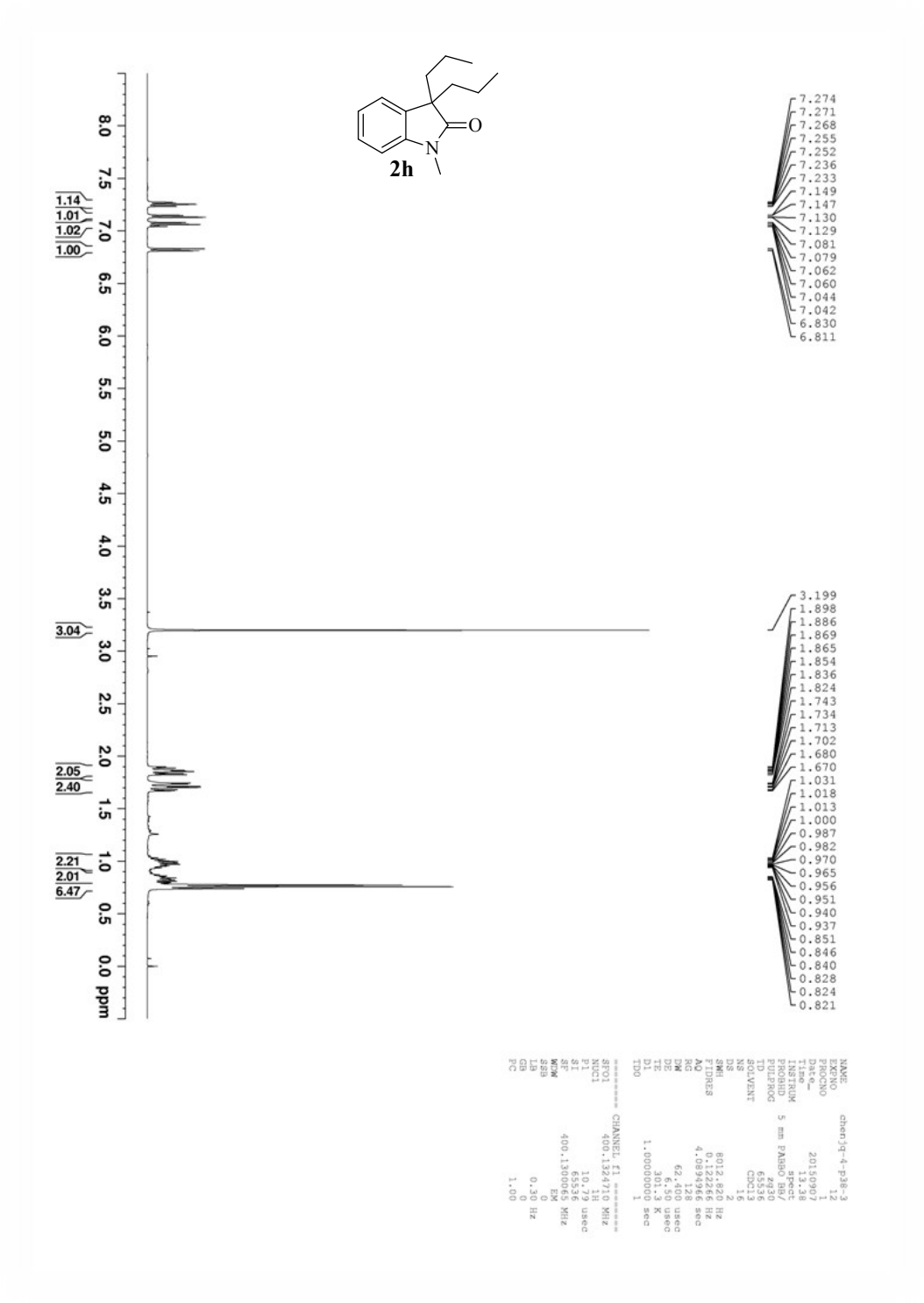

O
N
2f
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
180.19
144.22
132.41
127.49
122.63
122.31
107.60
77.34
77.02
76.70
53.66
37.49
30.98
26.36
25.90
22.85
13.77
8.52
NAME chen3g-4-p34-2
EXPNO 27
PROCNO 1
Date_ 20150921
Time 16.05
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 400
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 293.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6228298 MHz
NUC1 13C
P1 12.00 usec
PL1 1.00 dB
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

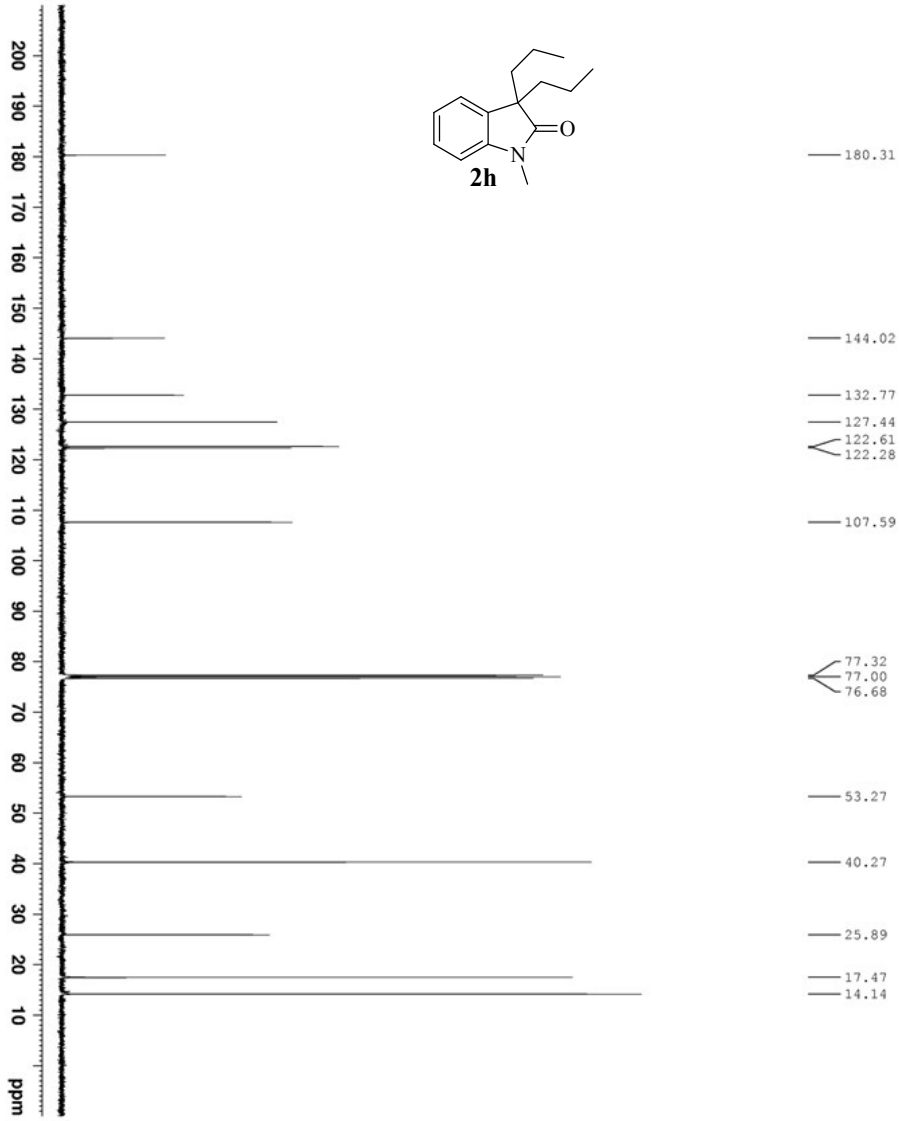
3-ethyl-1,3-dimethylindolin-2-one (**2g**)



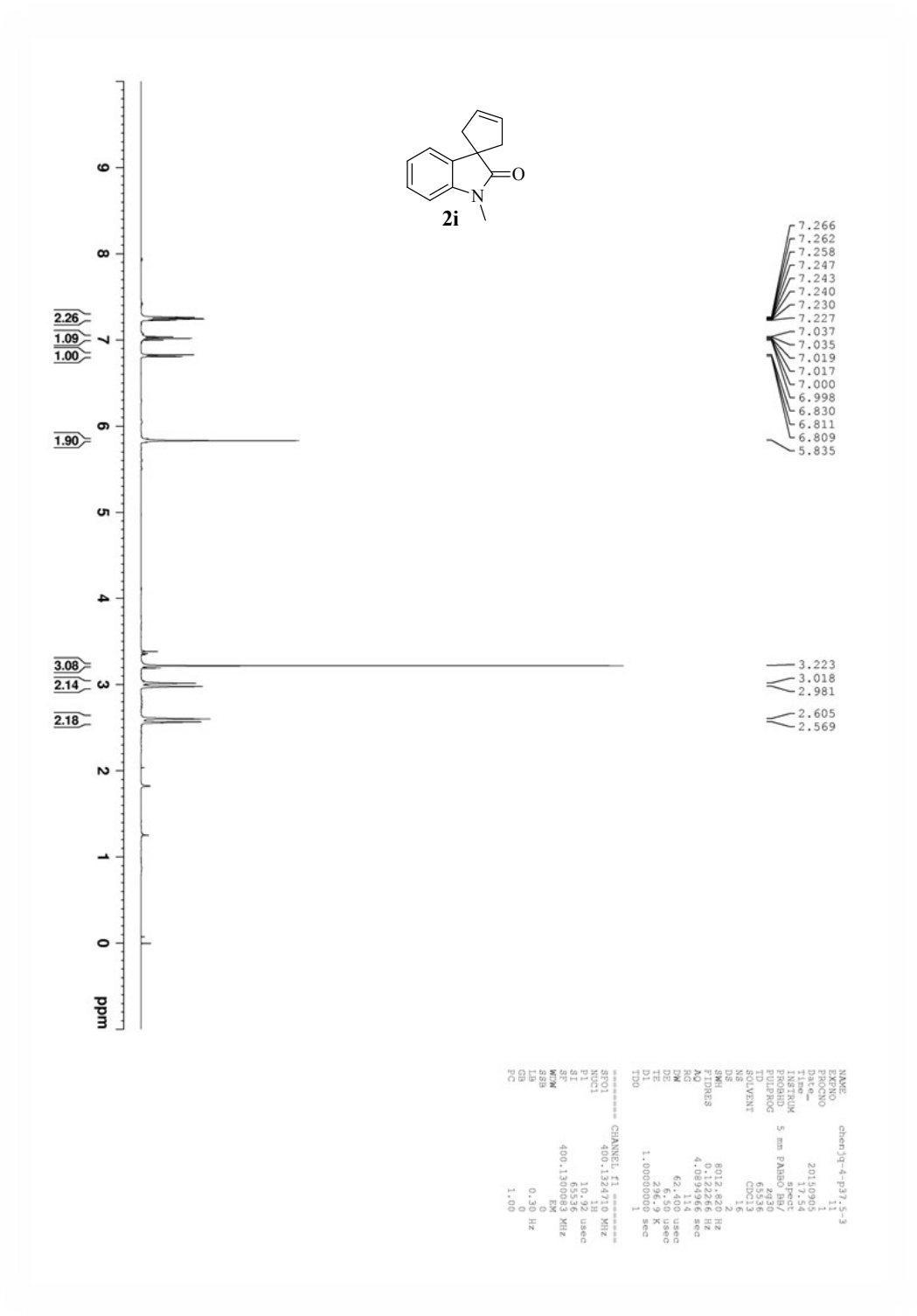

O
N
2g
180.72
143.46
133.93
127.57
122.47
122.36
107.77
77.31
77.00
76.68
48.90
31.43
26.01
23.26
8.79
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

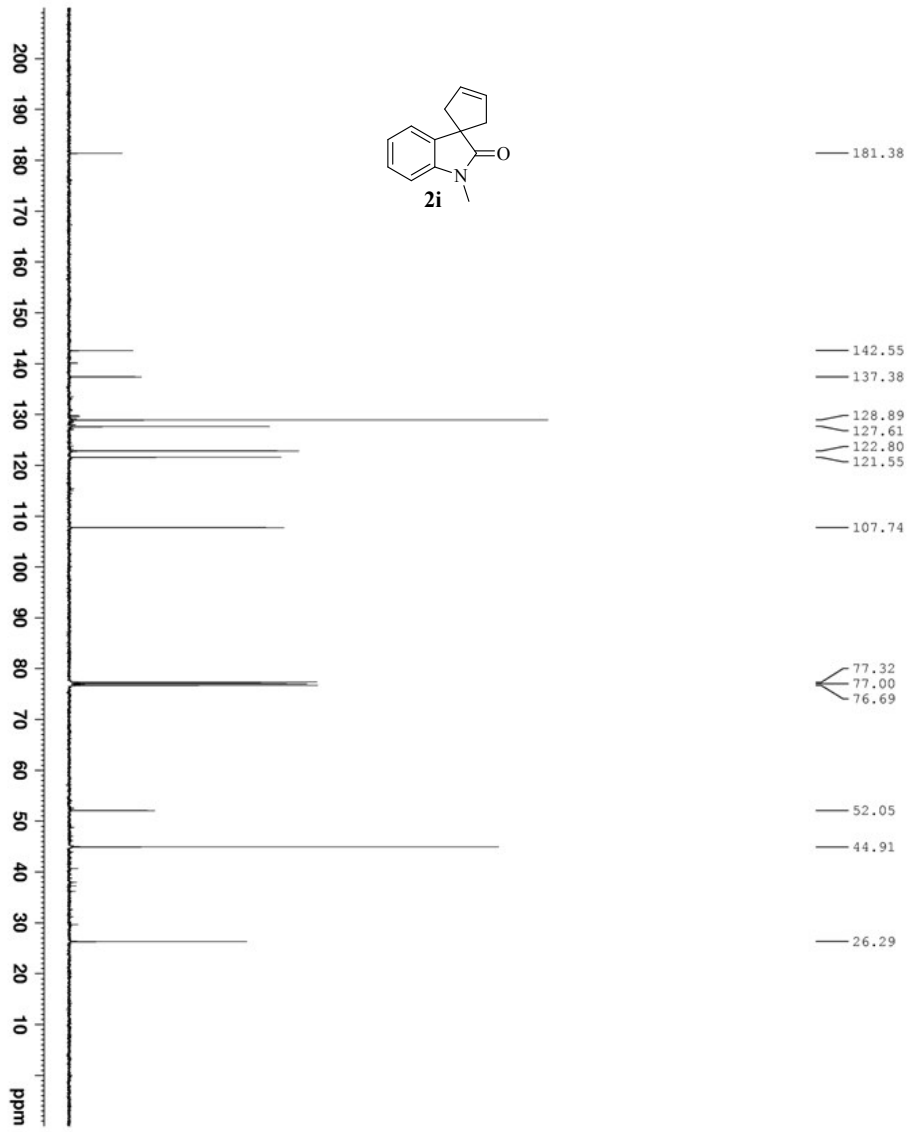
1-methyl-3,3-dipropylindolin-2-one (**2h**)



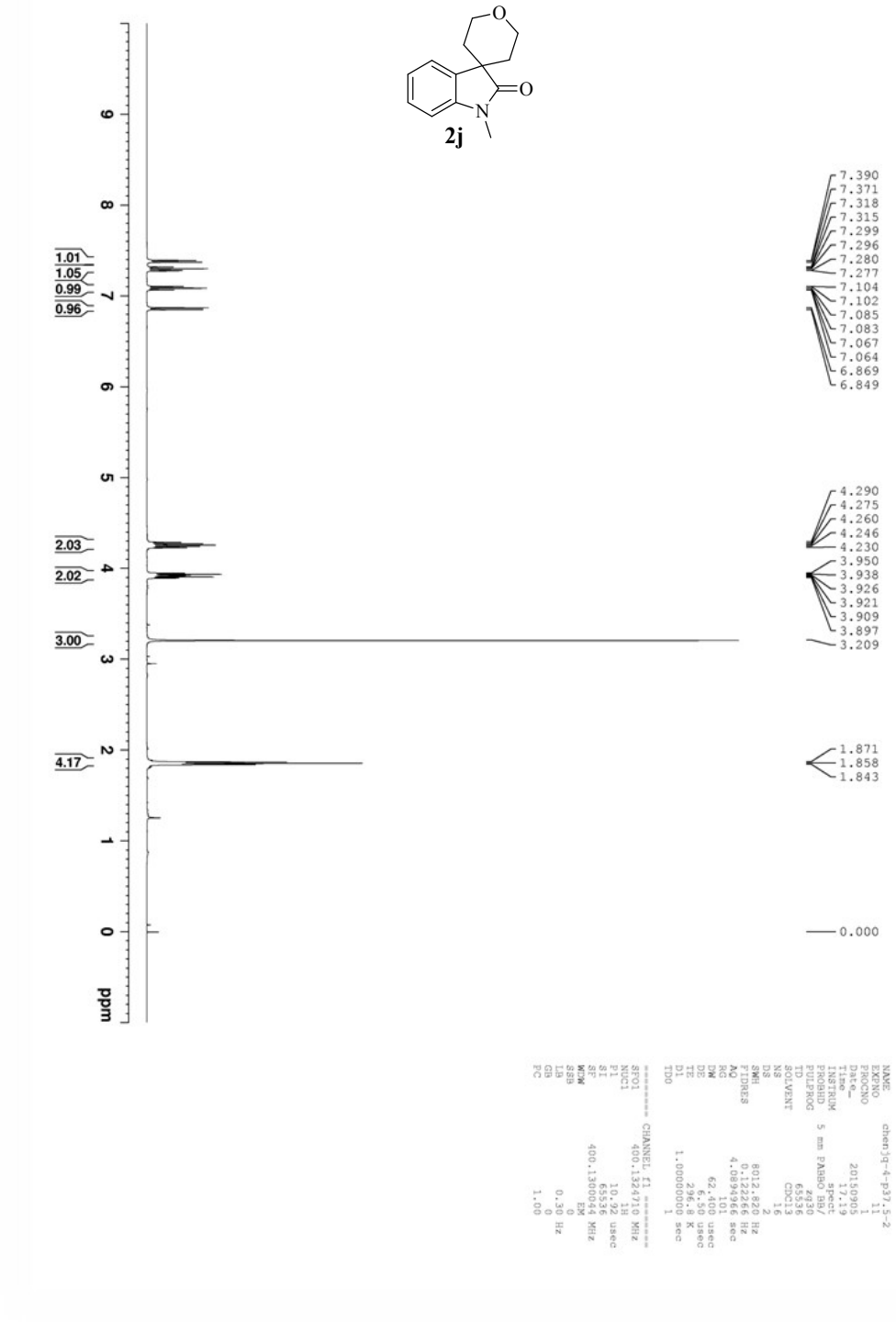

2h
180.31
144.02
132.77
127.44
122.61
122.28
107.59
77.32
77.00
76.68
53.27
40.27
25.89
17.47
14.14
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

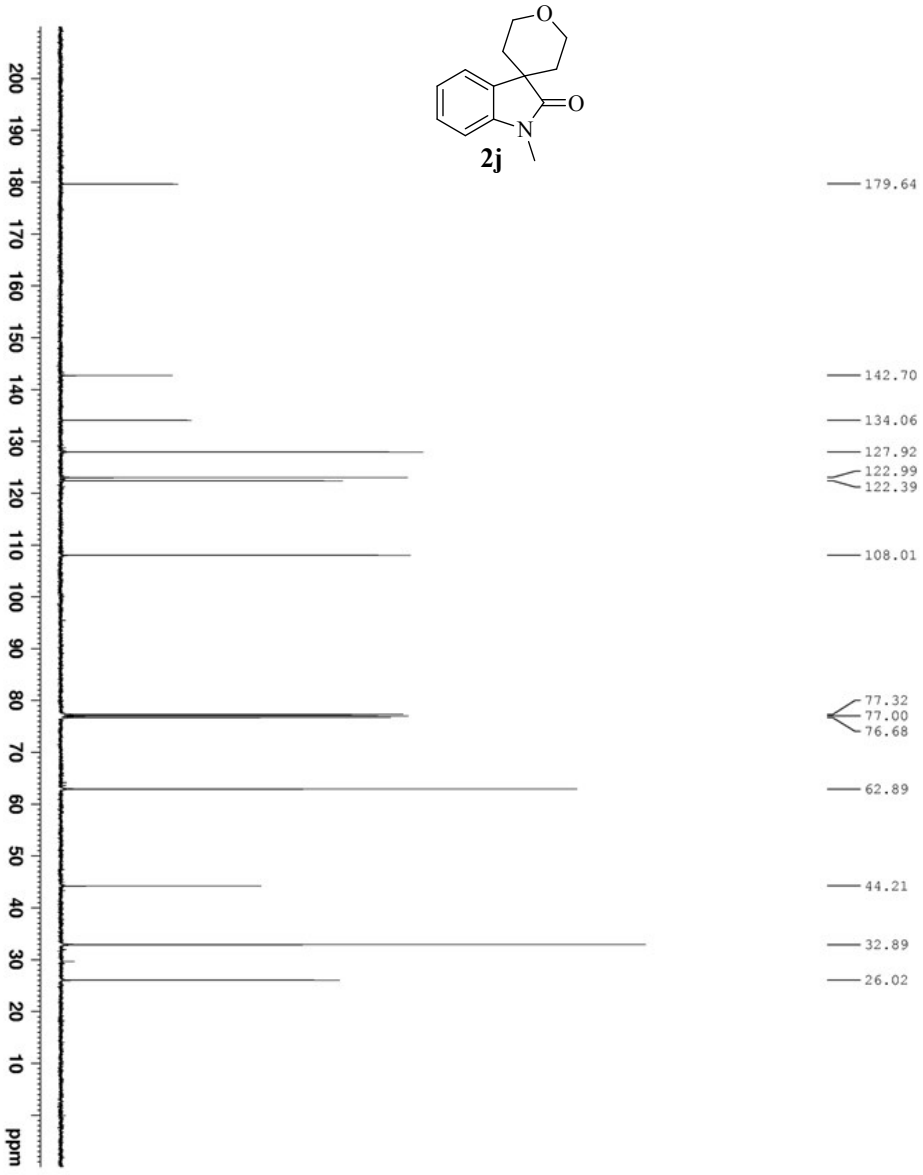
1'-methylspiro[cyclopent[3]ene-1,3'-indolin]-2'-one (**2i**)



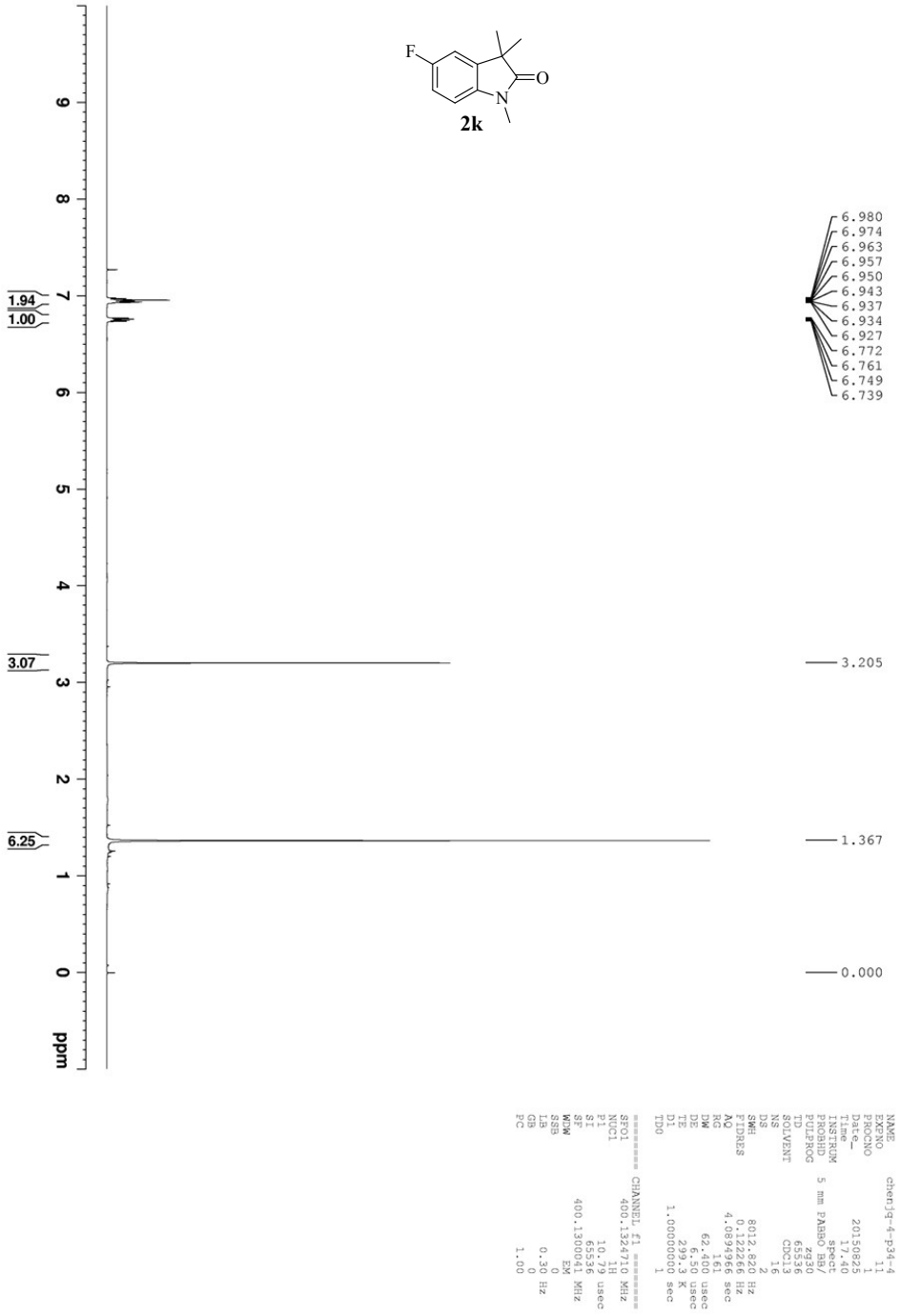

O
N
2i
181.38
142.55
137.38
128.89
127.61
122.80
121.55
107.74
77.32
77.00
76.69
52.05
44.91
26.29
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

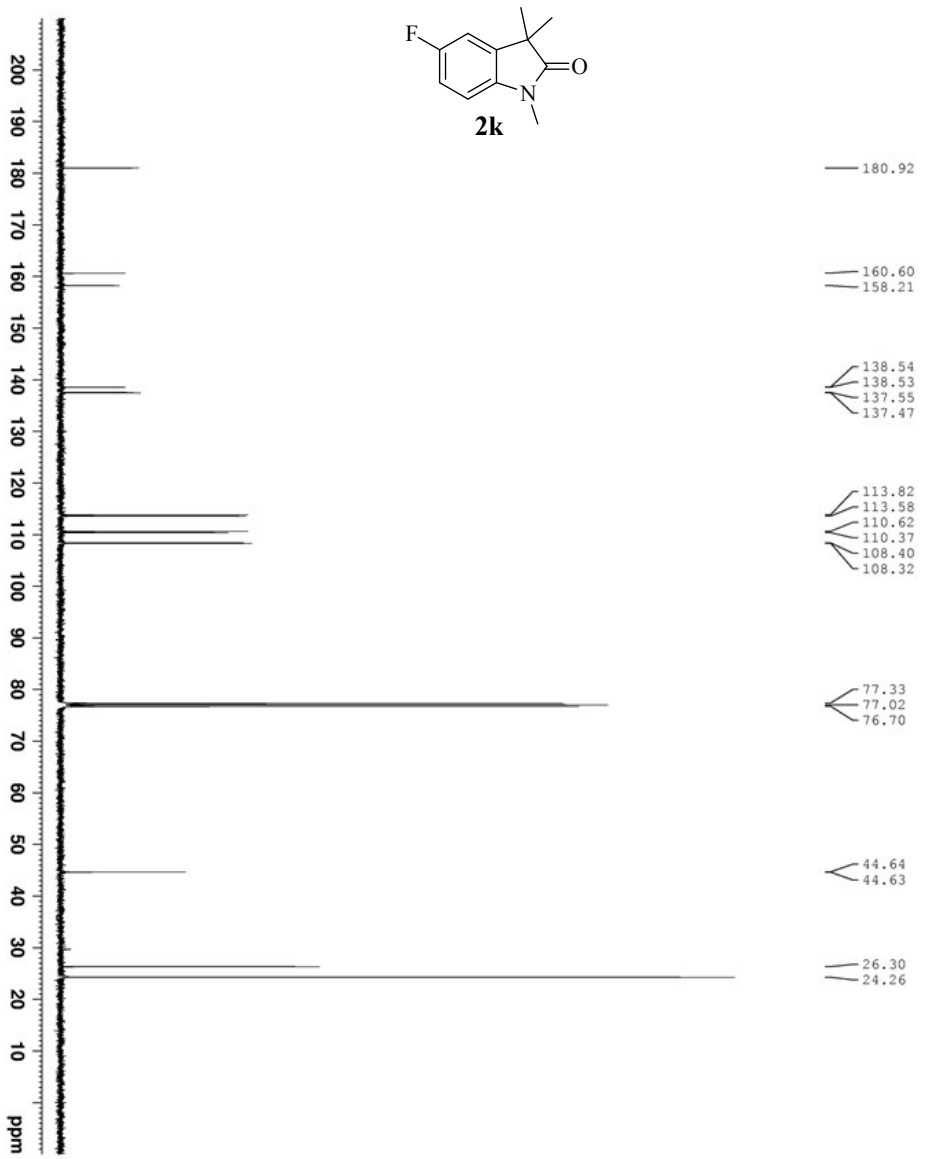
1-methyl-2',3',5',6'-tetrahydrospiro[indoline-3,4'-pyran]-2-one (**2j**)




O
O
N
2j
179.64
142.70
134.06
127.92
122.99
122.39
108.01
77.32
77.00
76.68
62.89
44.21
32.89
26.02
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

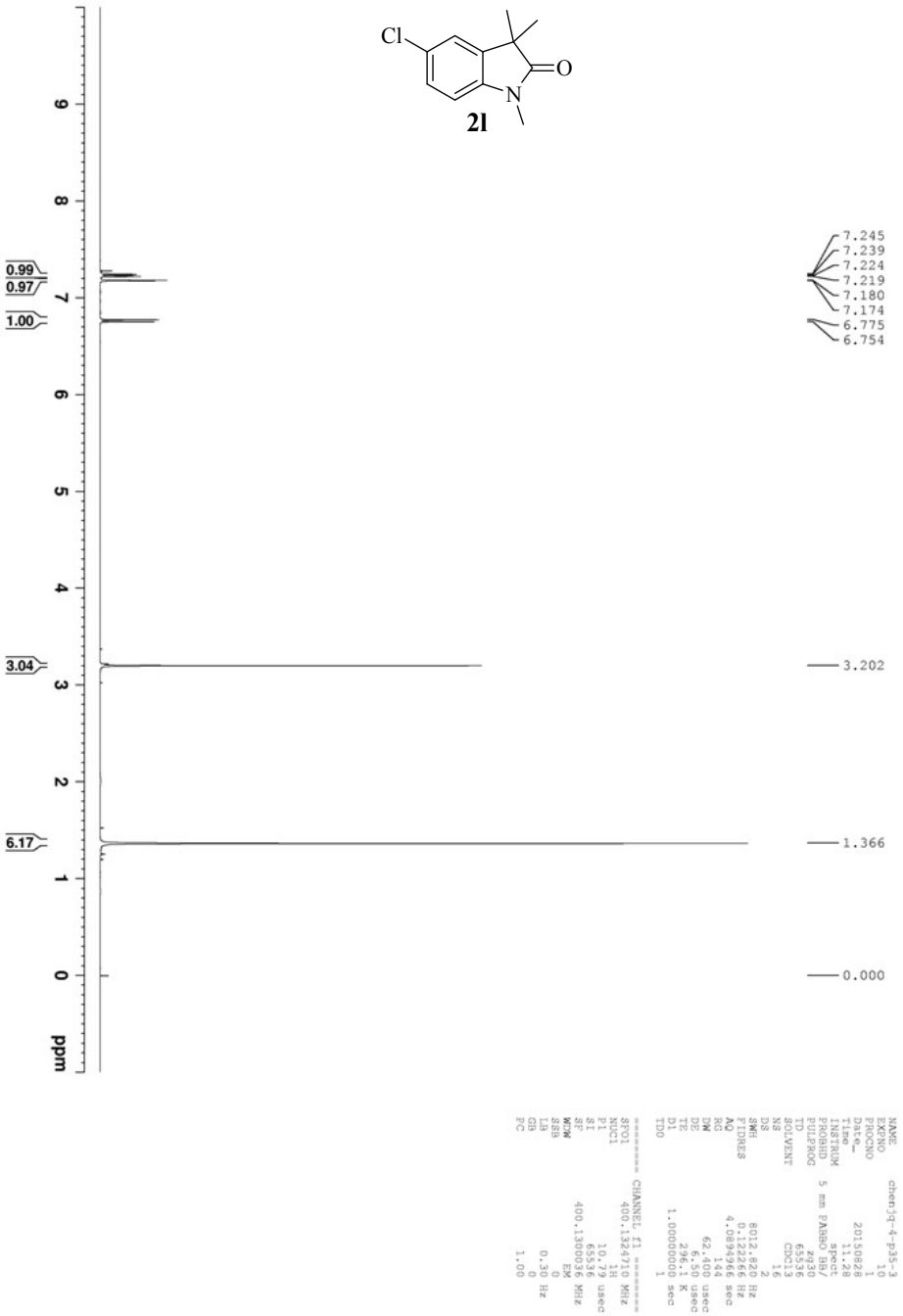
5-fluoro-1,3,3-trimethylindolin-2-one (**2k**)

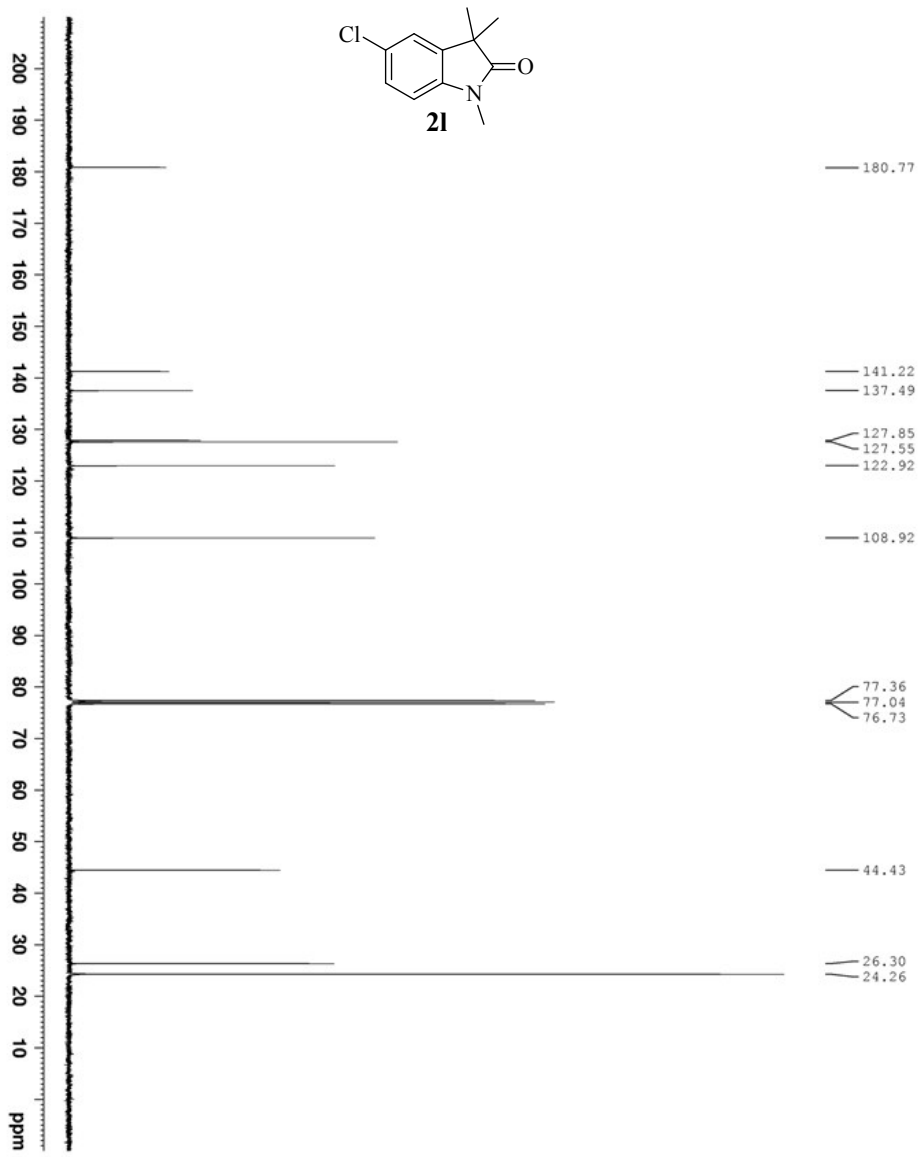




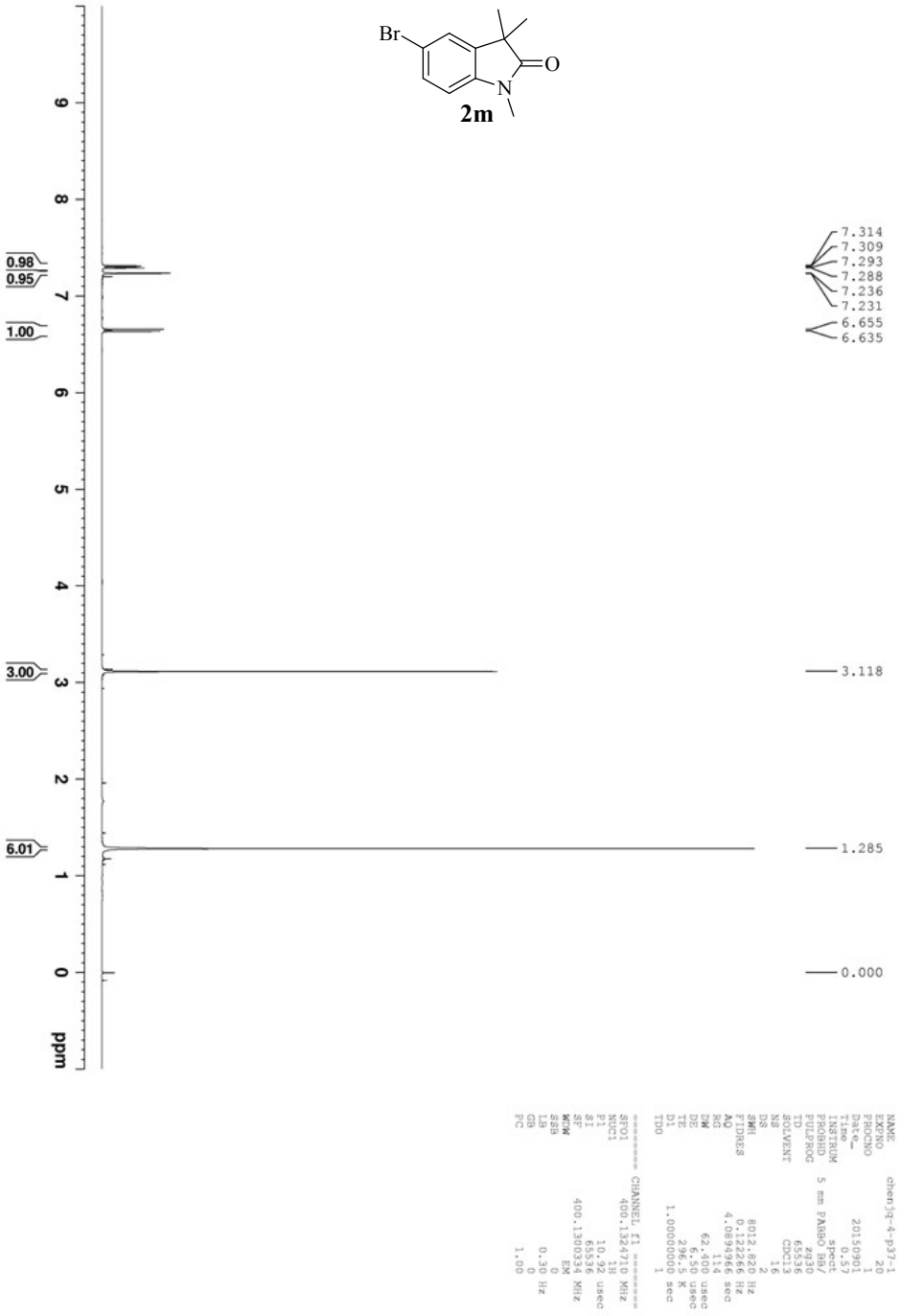
NAME chenjq-4-p34-4
EXPNO 13
PROCNO 1
Date_ 20150825
Time 19.02
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 400
DS 2
SWH 24038.461 Hz
FIDRES 0.366796 Hz
AQ 1.3631988 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 300.5 K
D1 2.0000000 sec
D11 0.0300000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.622898 MHz
NUC1 13C
P1 12.00 usec
PL1 32.00 dB
SF 100.612690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

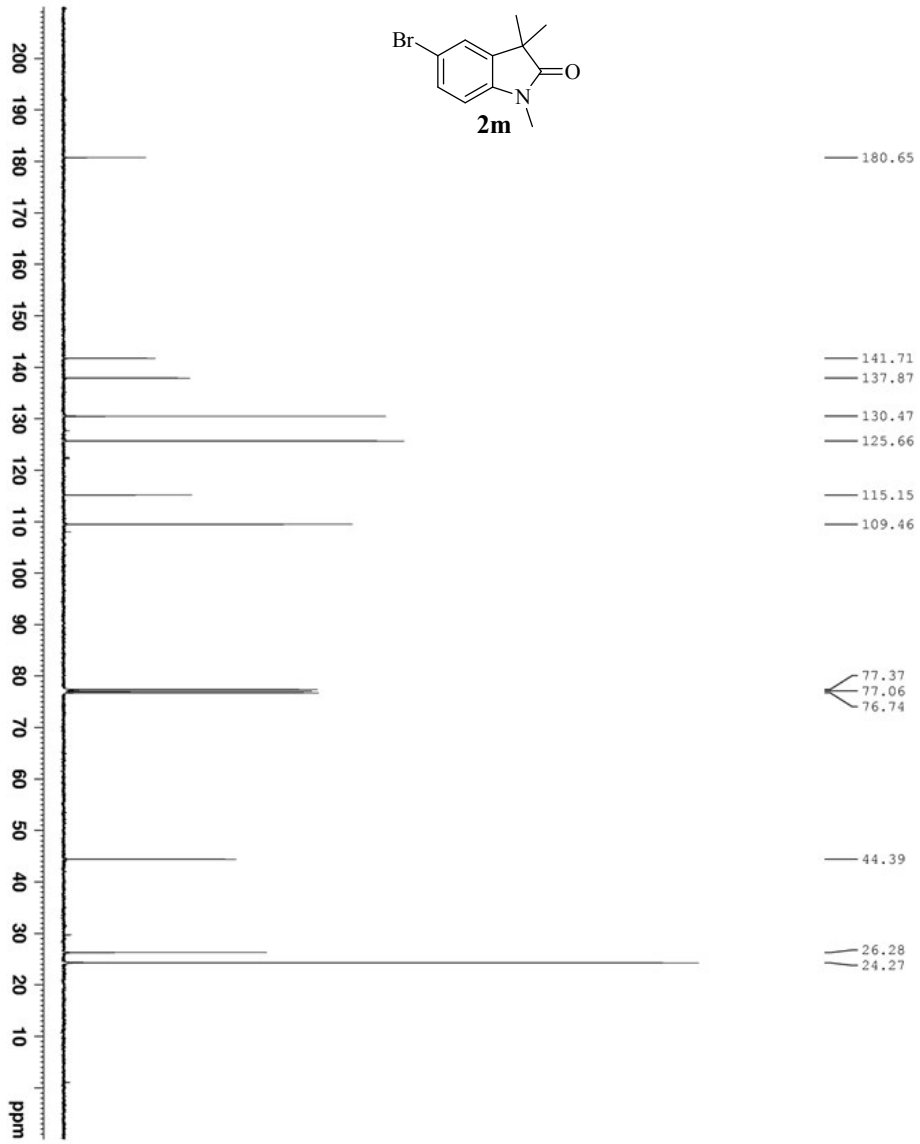
5-chloro-1,3,3-trimethylindolin-2-one (**2l**)



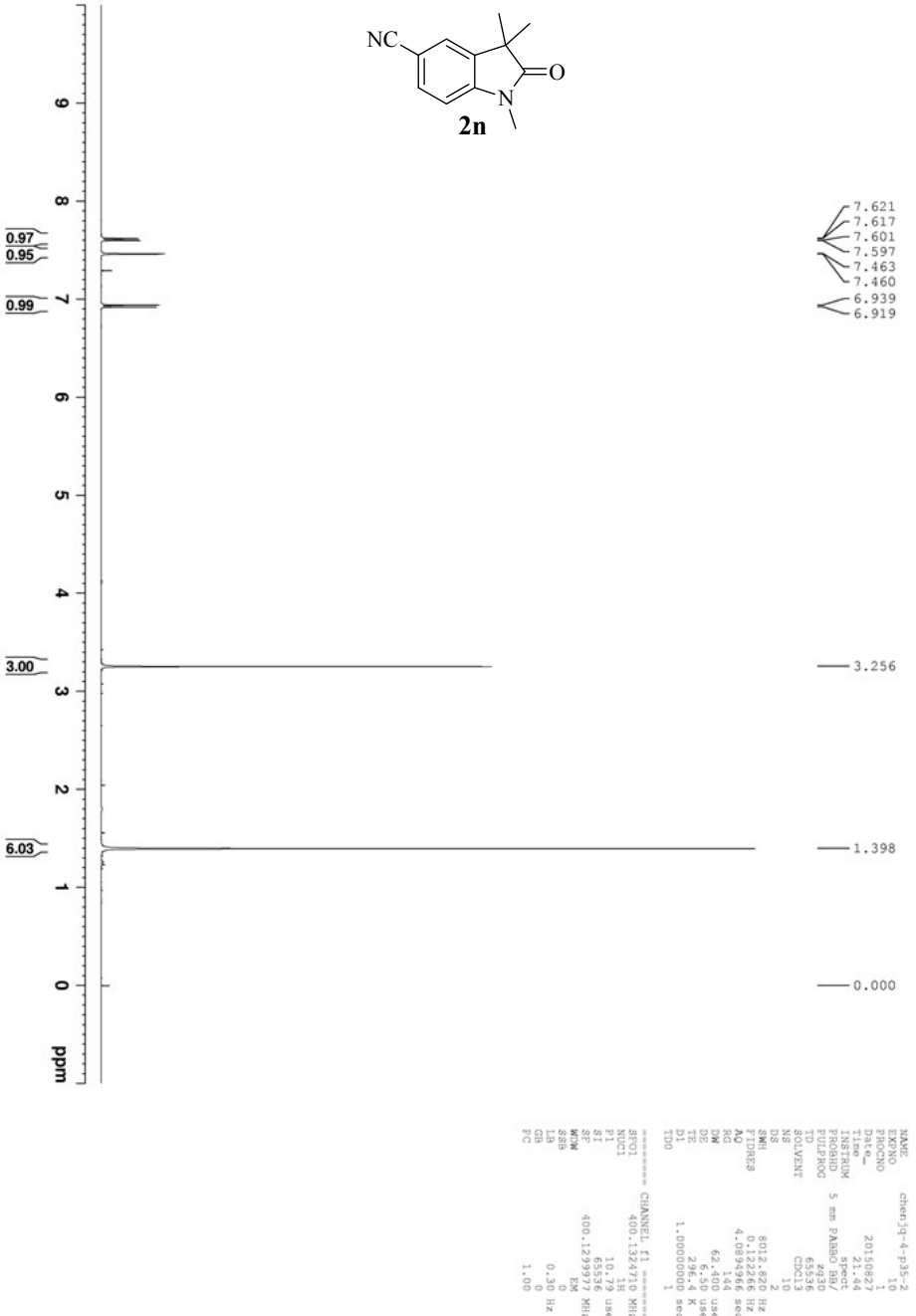

Cl
O
N
2l
180.77
141.22
137.49
127.85
127.55
122.92
108.92
77.36
77.04
76.73
44.43
26.30
24.26
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

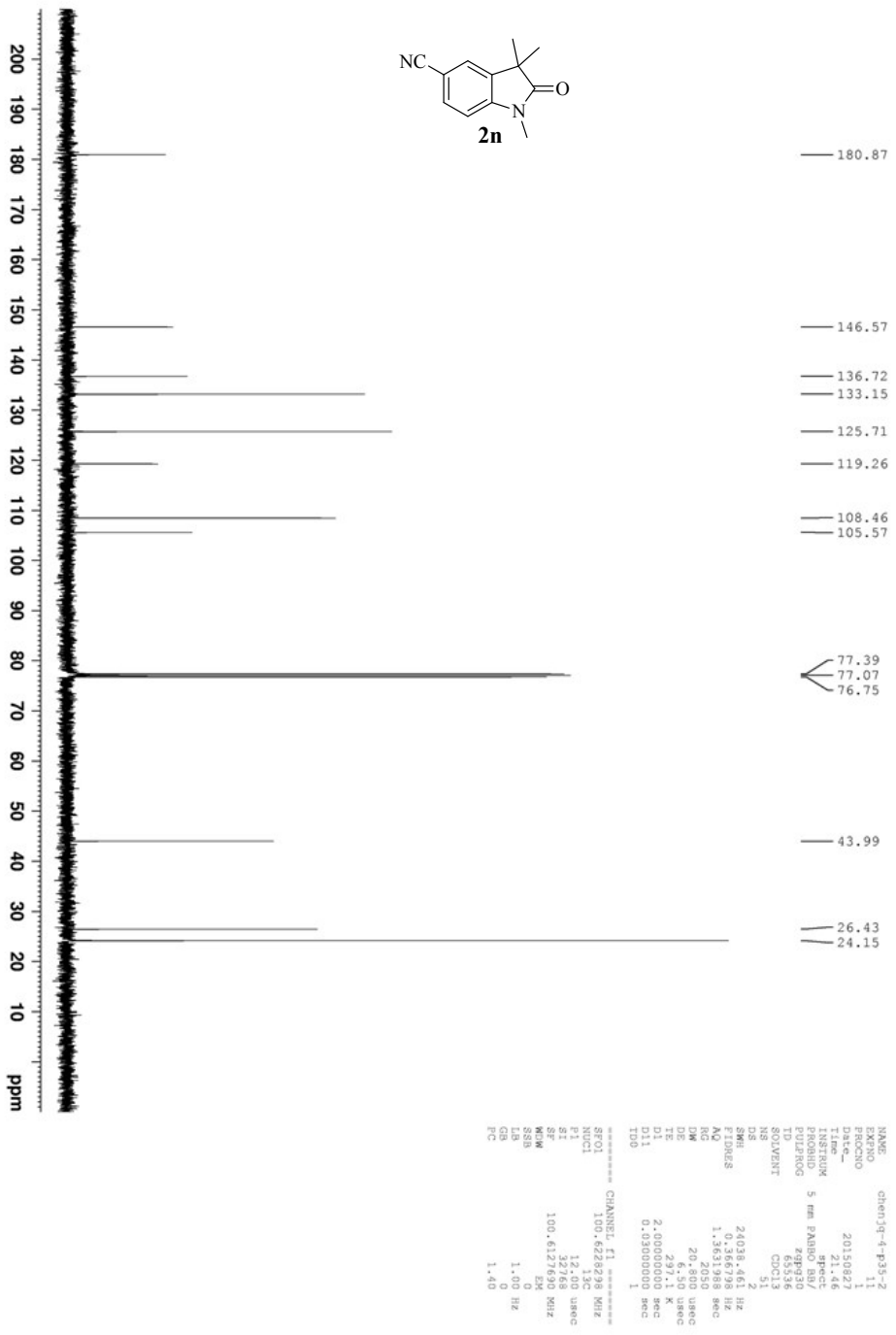
5-bromo-1,3,3-trimethylindolin-2-one (**2m**)



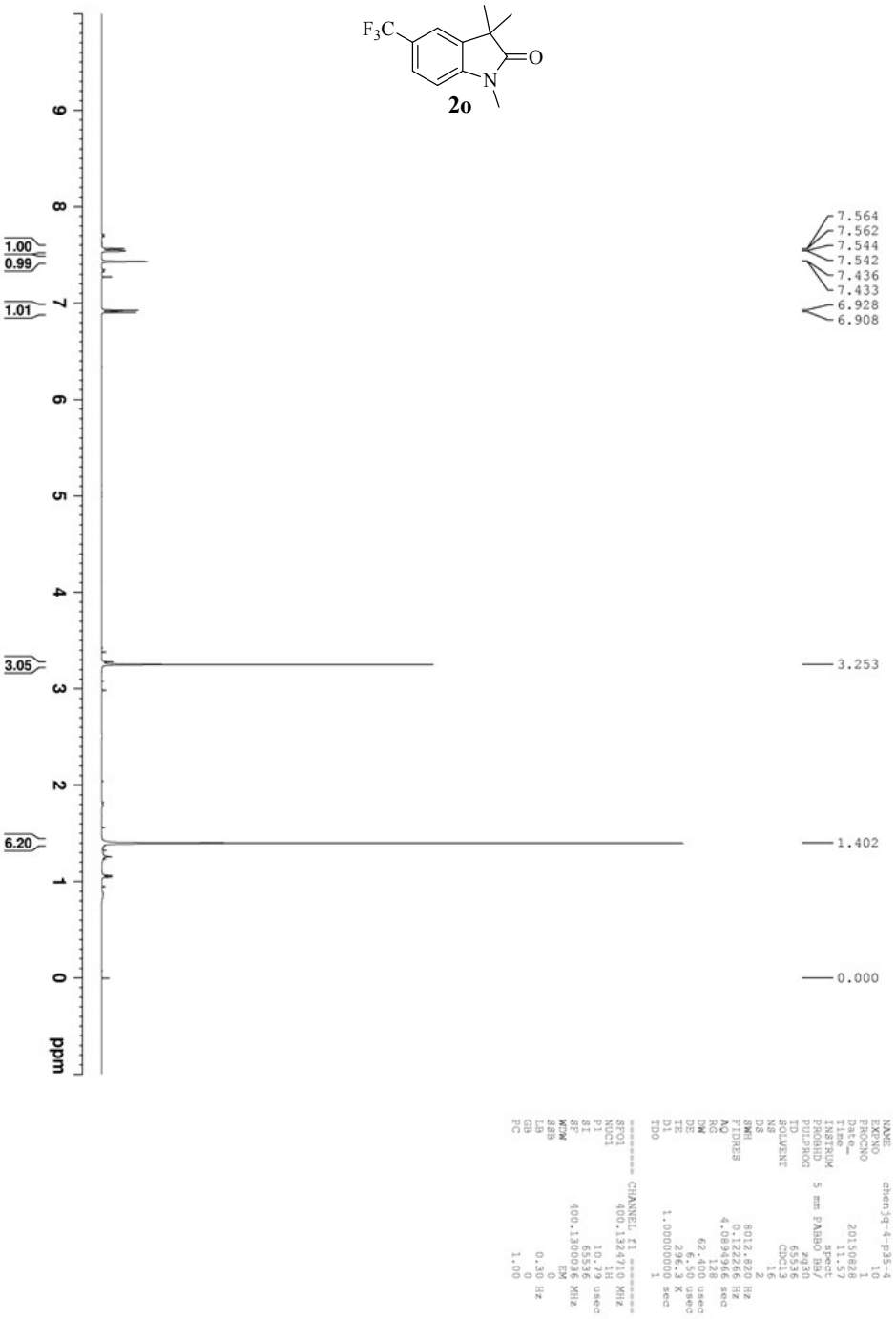

Br
O
N
2m
180.65
141.71
137.87
130.47
125.66
115.15
109.46
77.37
77.06
76.74
44.39
26.28
24.27
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

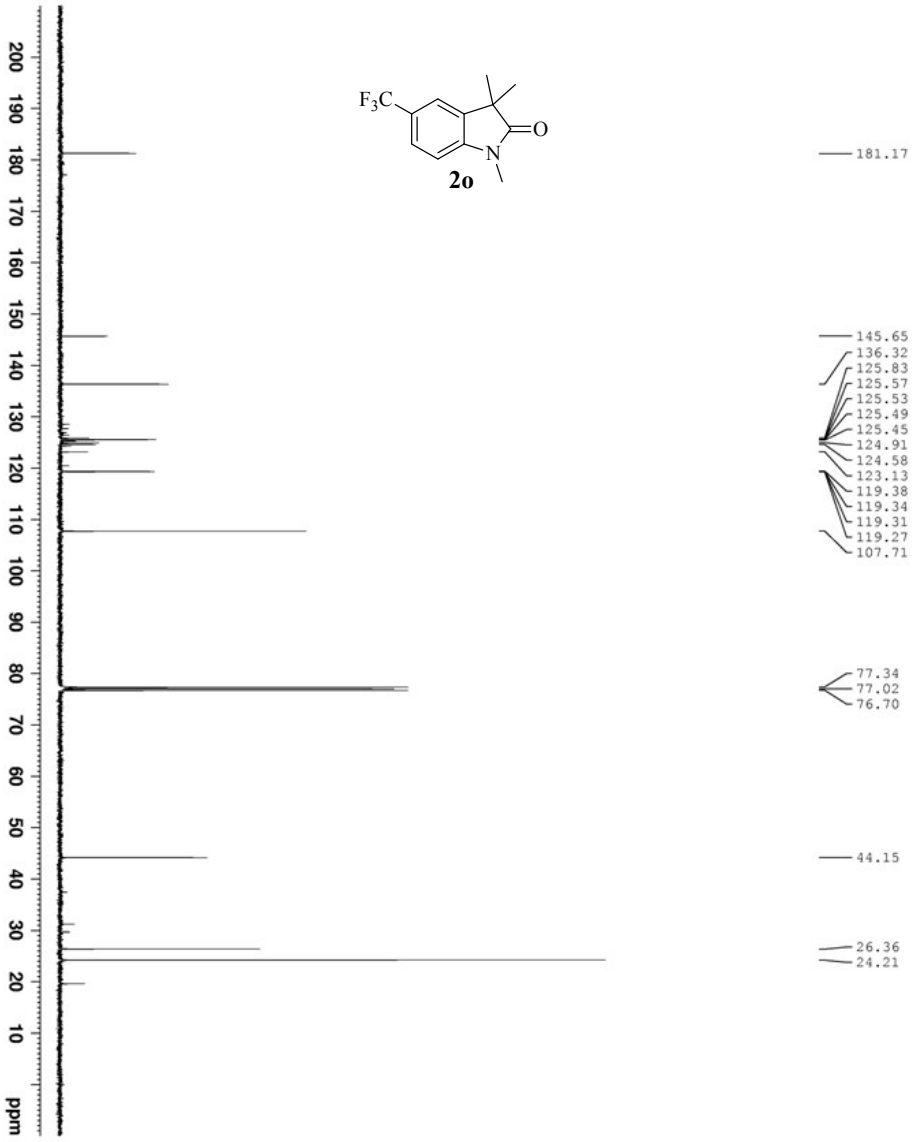
1,3,3-trimethyl-2-oxoindoline-5-carbonitrile (**2n**)



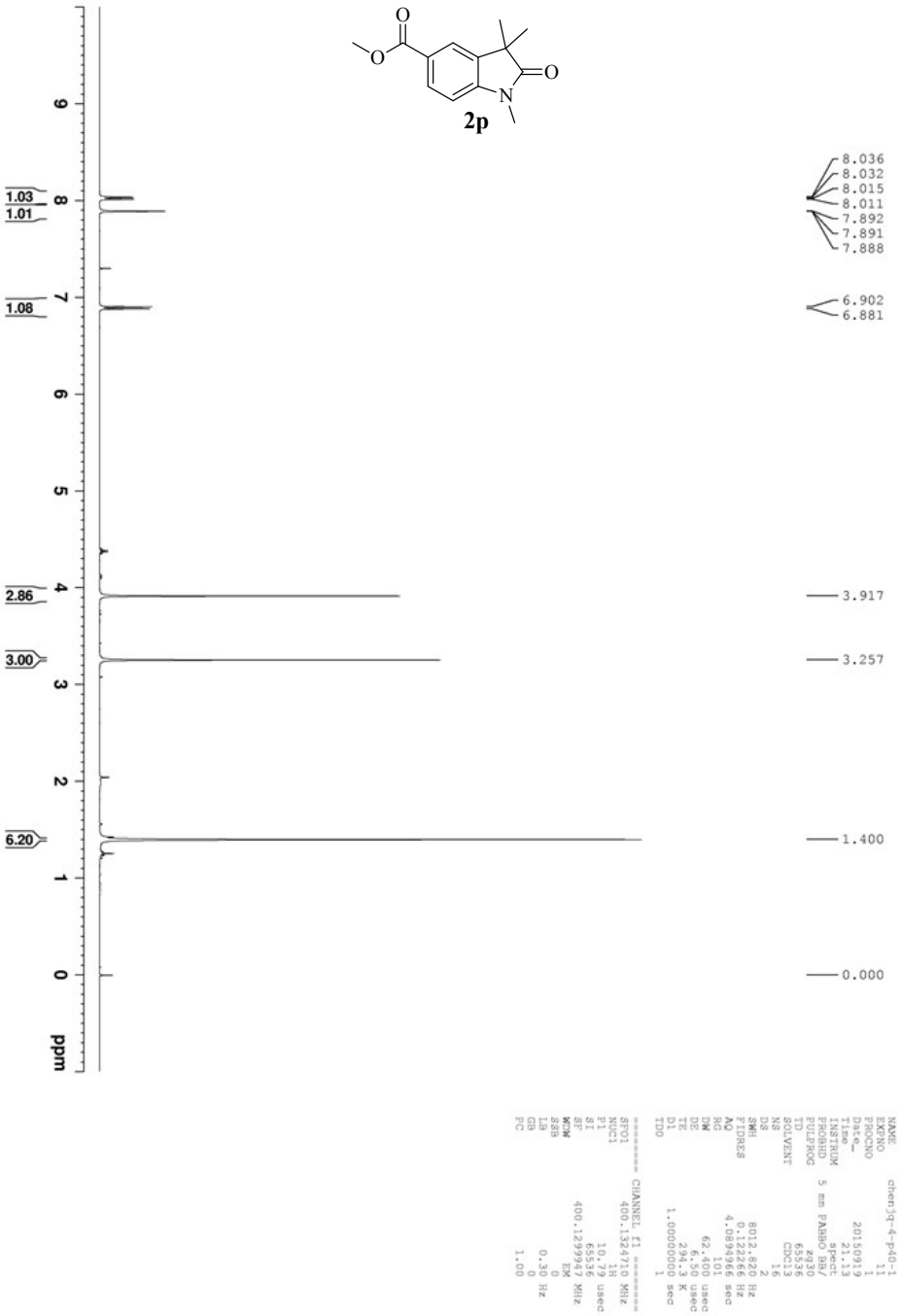

NC
O
N
2n
180.87
146.57
136.72
133.15
125.71
119.26
108.46
105.57
77.39
77.07
76.75
43.99
26.43
24.15
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

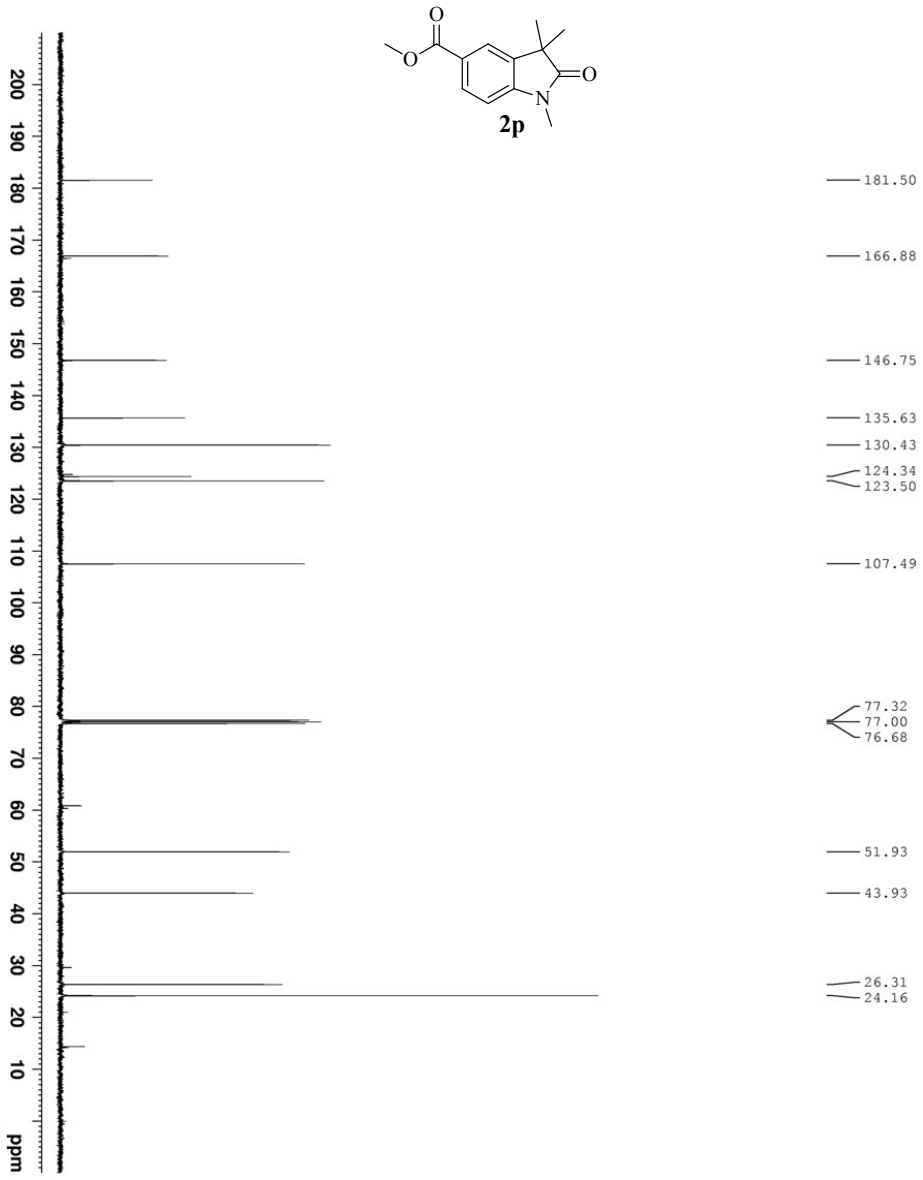
1,3,3-trimethyl-5-(trifluoromethyl)indolin-2-one (**2o**)



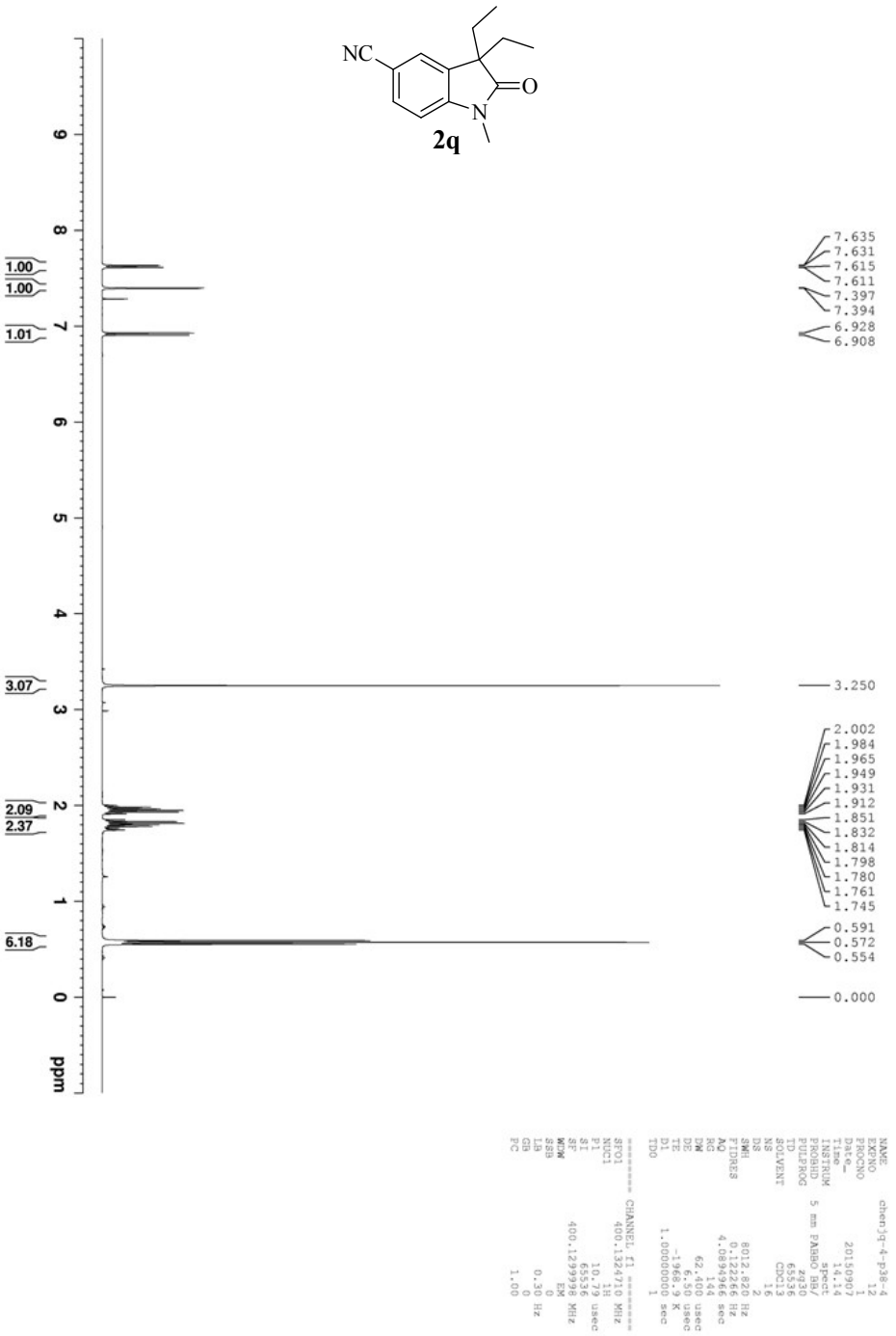

F3C
O
N
2o
181.17
145.65
136.32
125.83
125.57
125.53
125.49
125.45
124.91
124.58
123.13
119.38
119.34
119.31
119.27
107.71
77.34
77.02
76.70
44.15
26.36
24.21
ppm

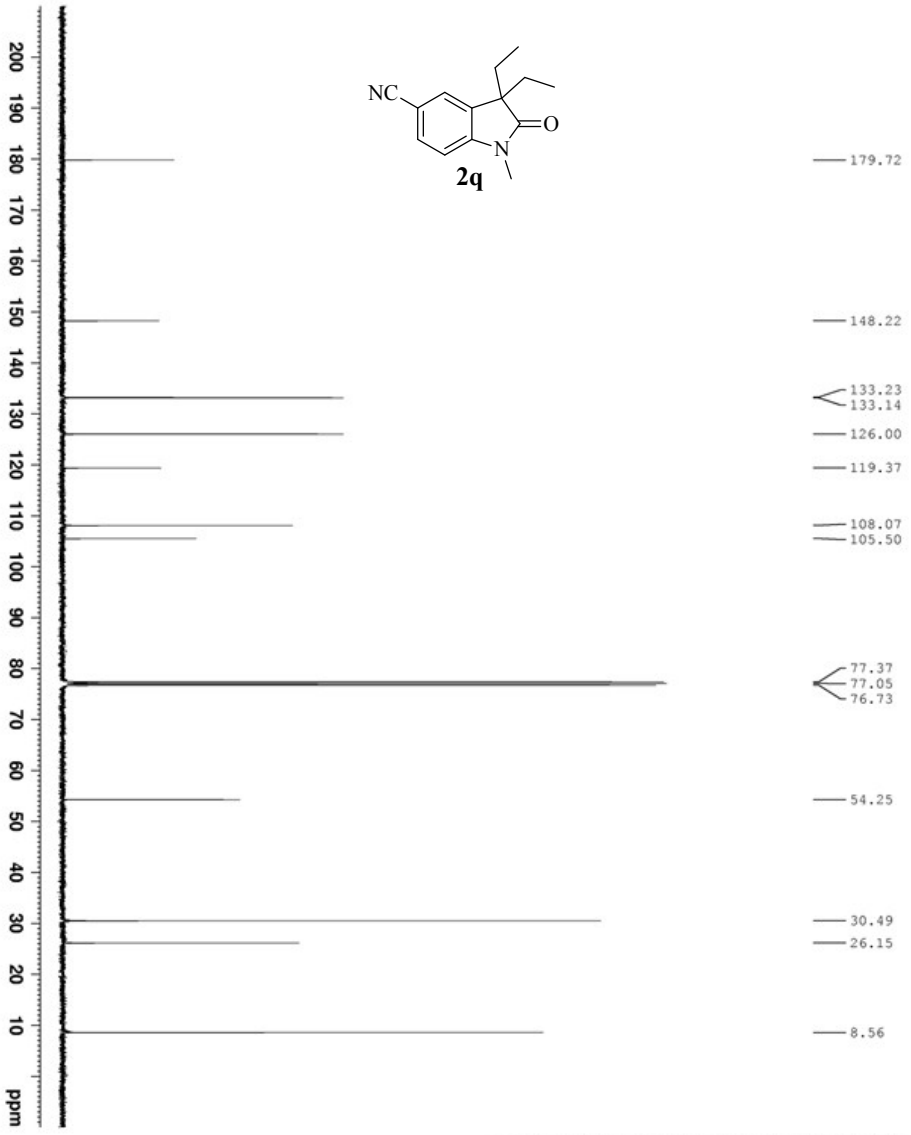
methyl 1,3,3-trimethyl-2-oxoindoline-5-carboxylate (**2p**)



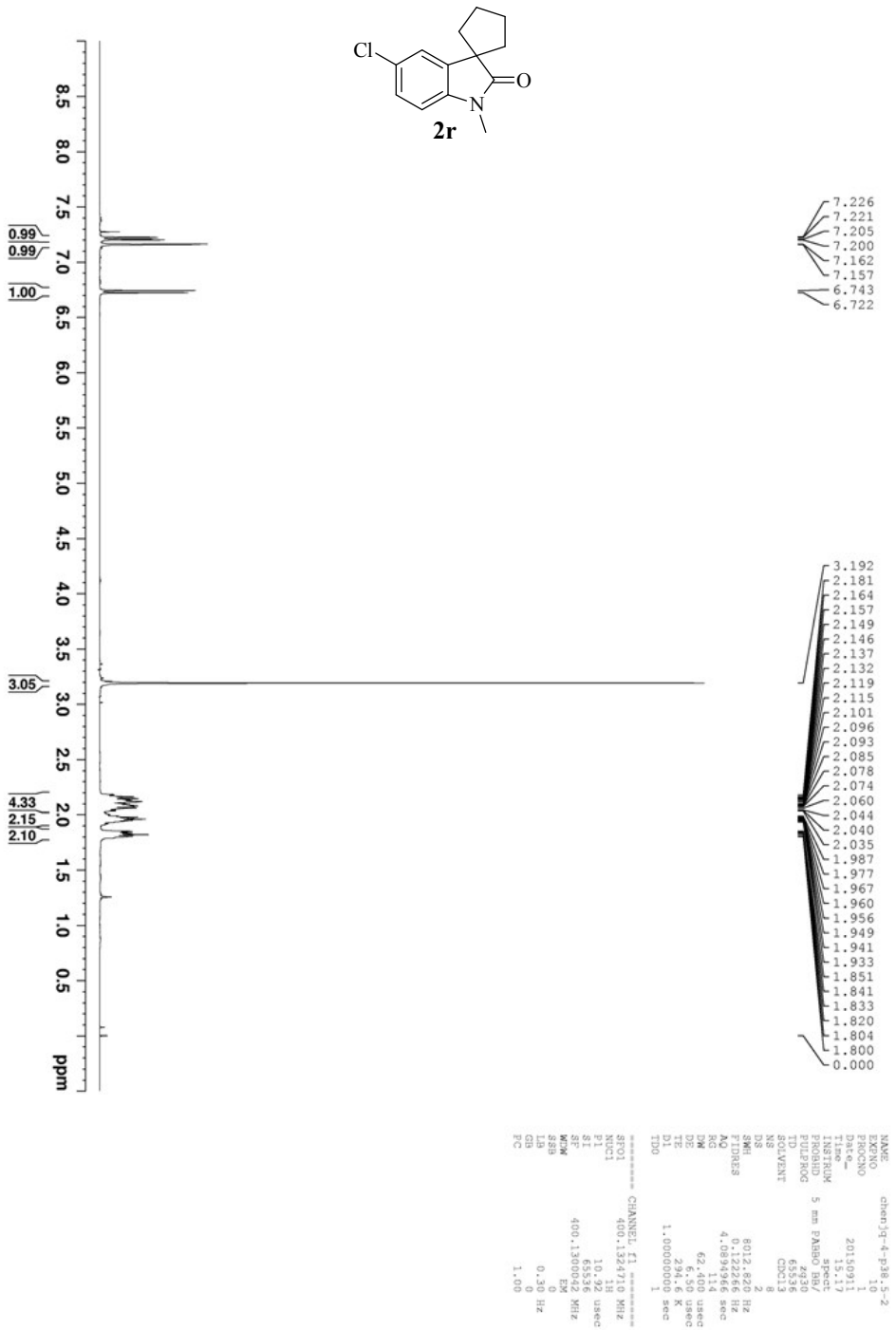

2p
181.50
166.88
146.75
135.63
130.43
124.34
123.50
107.49
77.32
77.00
76.68
51.93
43.93
26.31
24.16
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

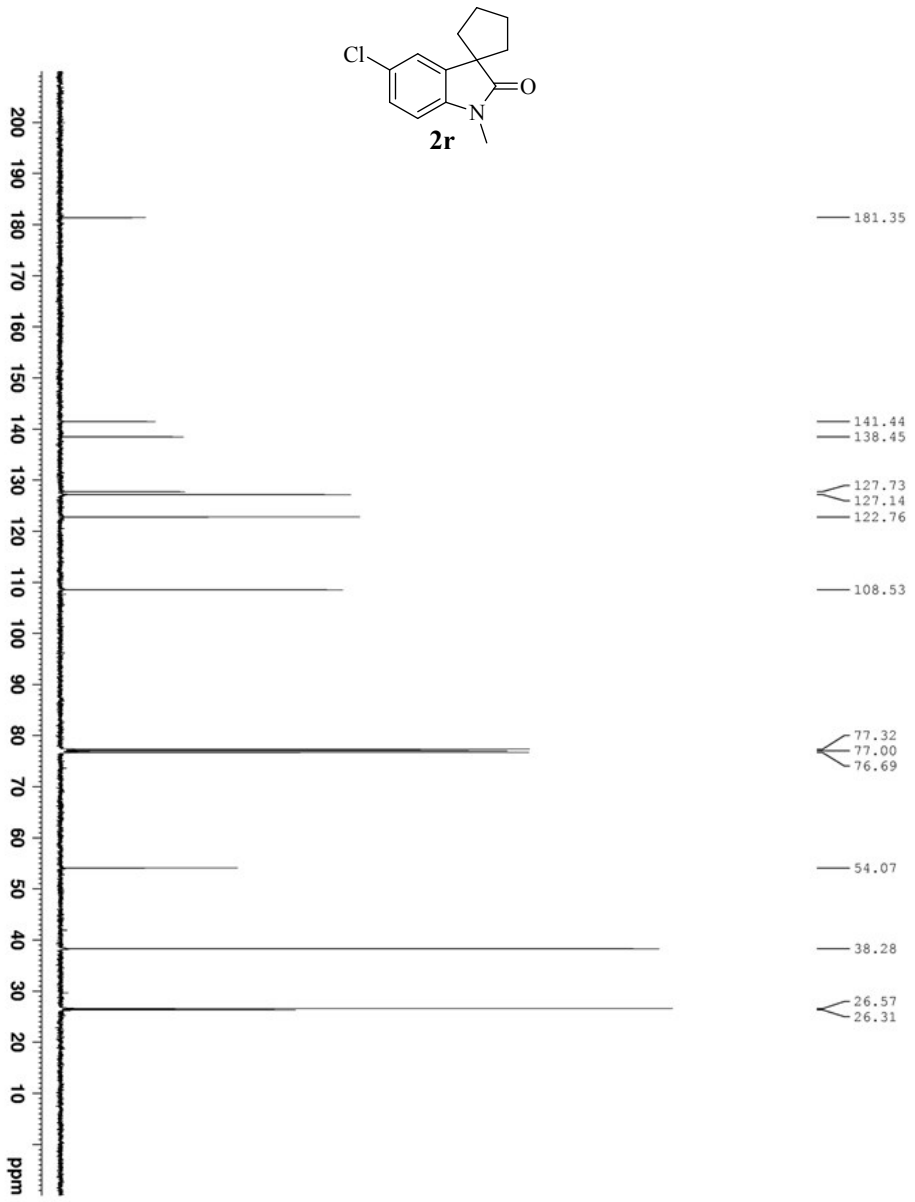
3,3-diethyl-1-methyl-2-oxoindoline-5-carbonitrile (**2q**)



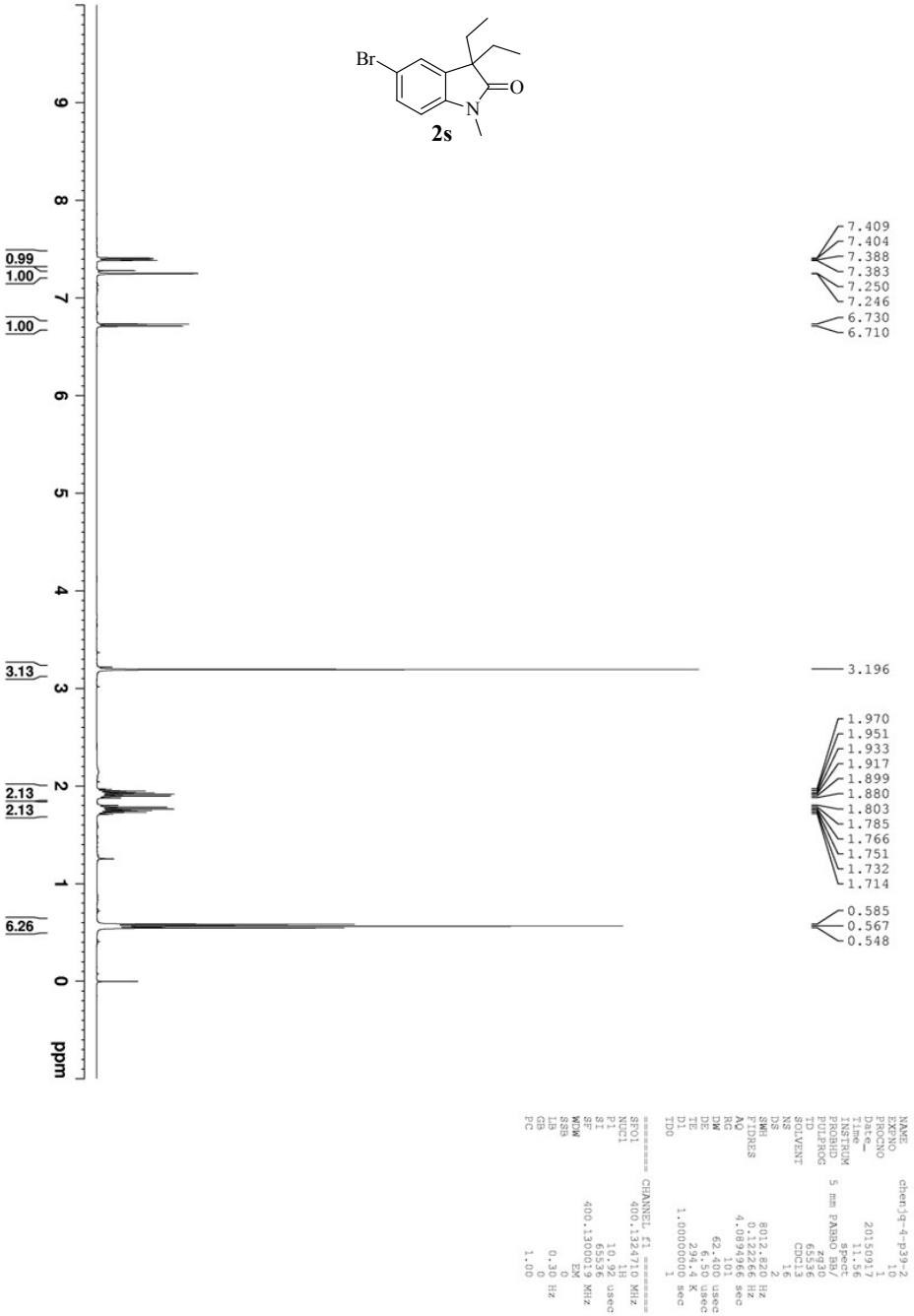

NC
O
N
2q
179.72
148.22
133.23
133.14
126.00
119.37
108.07
105.50
77.37
77.05
76.73
54.25
30.49
26.15
8.56
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

5'-chloro-1'-methylspiro[cyclopentane-1,3'-indolin]-2'-one (**2r**)



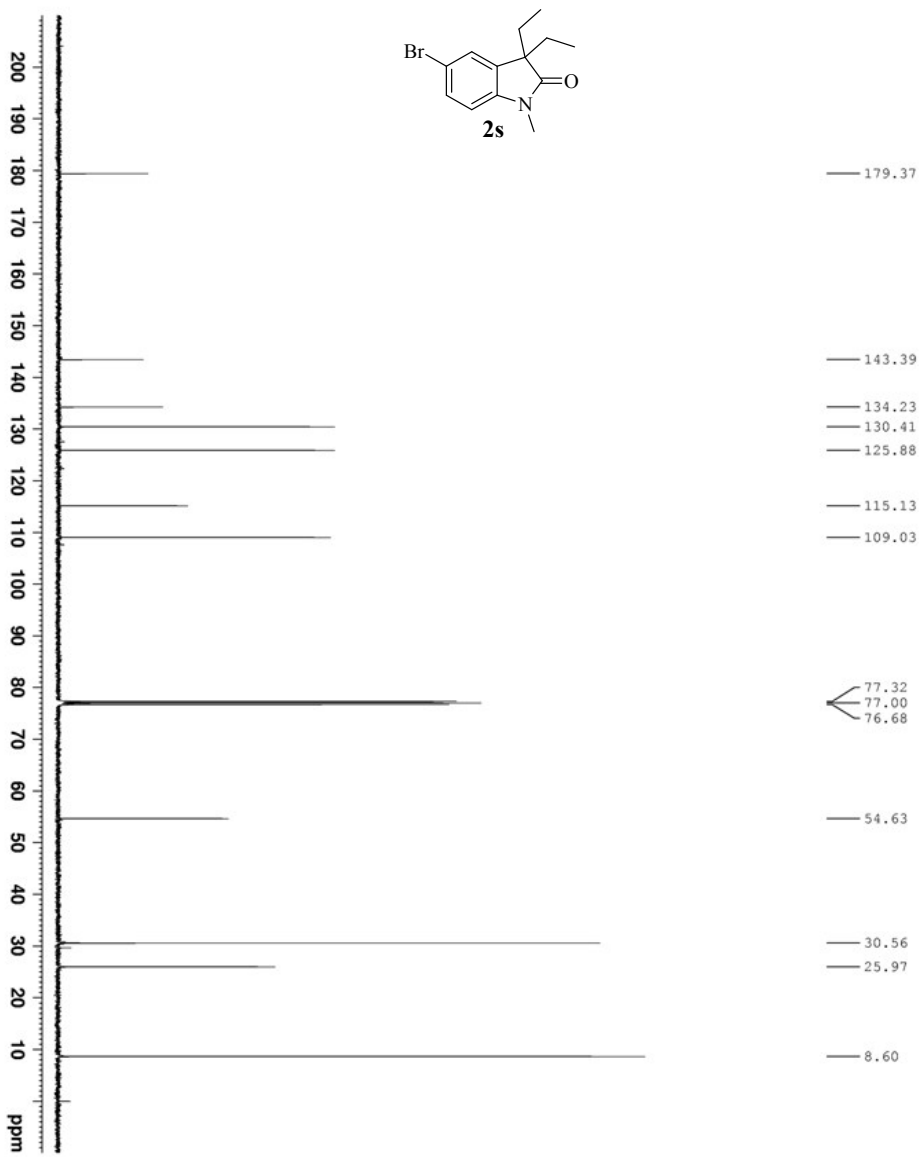

Cl
O
N
2r
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
181.35
141.44
138.45
127.73
127.14
122.76
108.53
77.32
77.00
76.69
54.07
38.28
26.57
26.31

5-bromo-3,3-diethyl-1-methylindolin-2-one (**2s**)

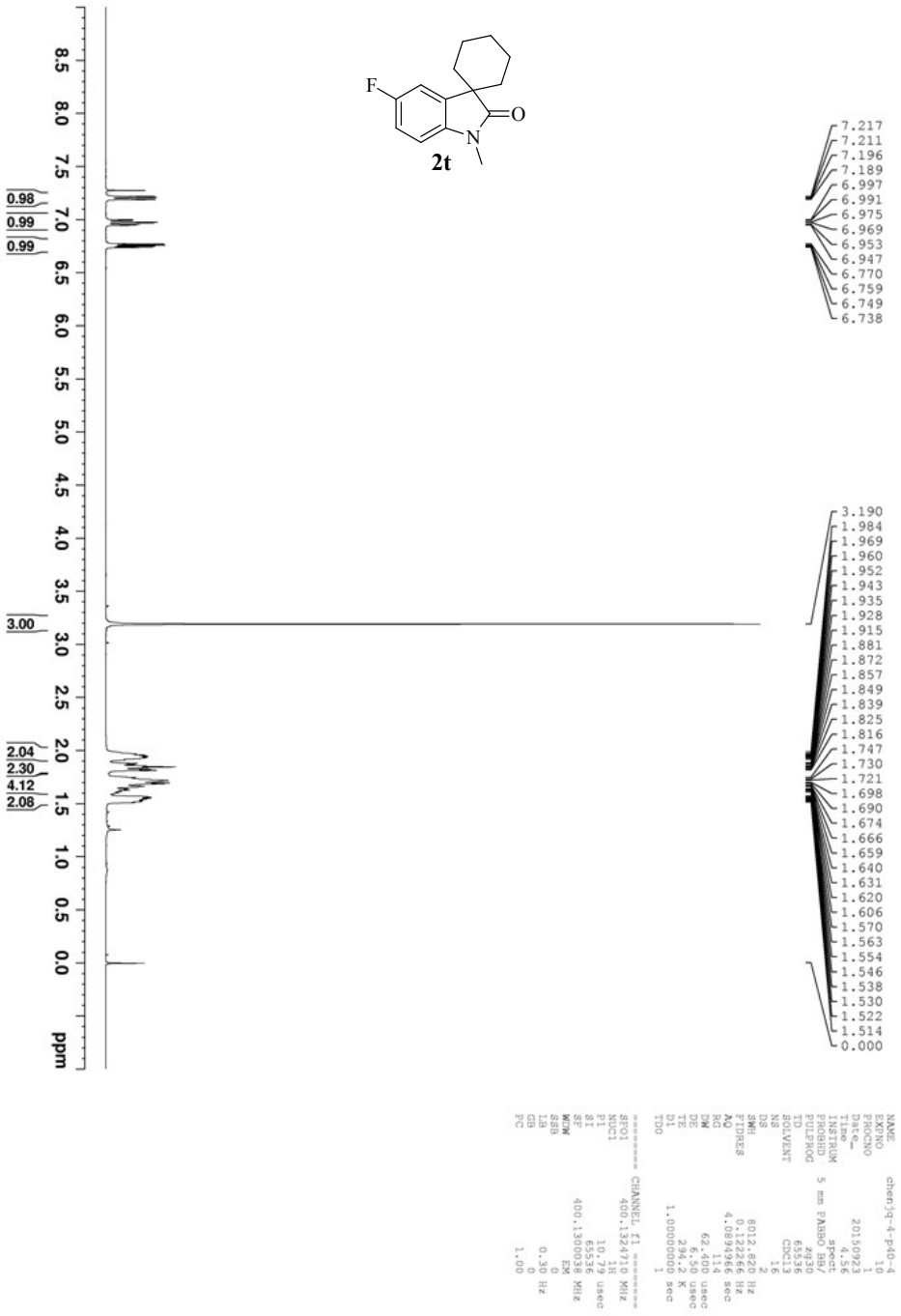


NAME chenjq-4-p39-2
EXPNO 10
PROCNO 1
Date_ 20150917
Time 11.56
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122766 Hz
AQ 4.0894966 sec
RG 101
DW 62.400 usec
DE 6.50 usec
TE 296.0 K
D1 1.0000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.45 usec
SI 65536
SF 400.1300019 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

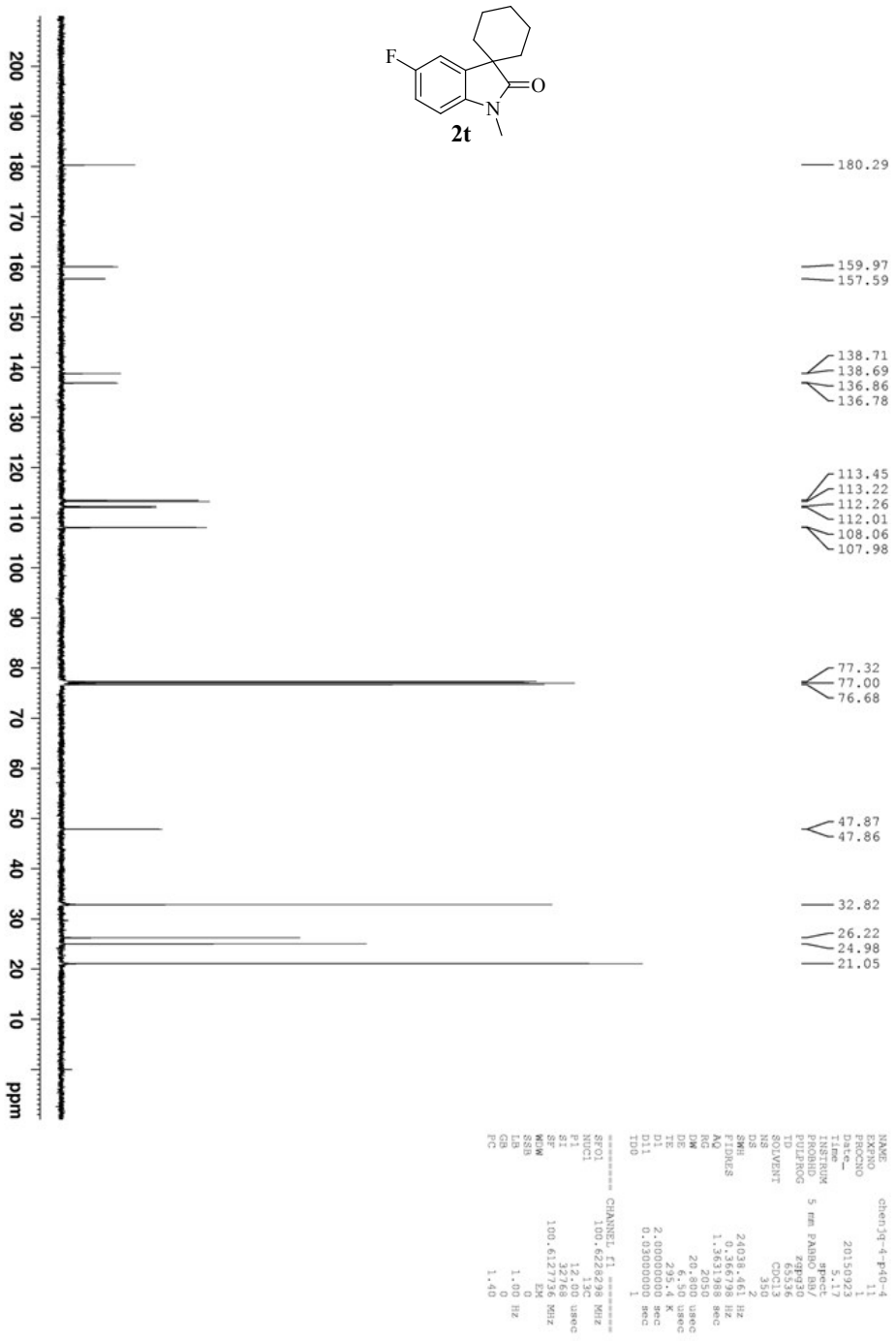

Br
O
N
2s
179.37
143.39
134.23
130.41
125.88
115.13
109.03
77.32
77.00
76.68
54.63
30.56
25.97
8.60
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

5'-fluoro-1'-methylspiro[cyclohexane-1,3'-indolin]-2'-one (**2t**)

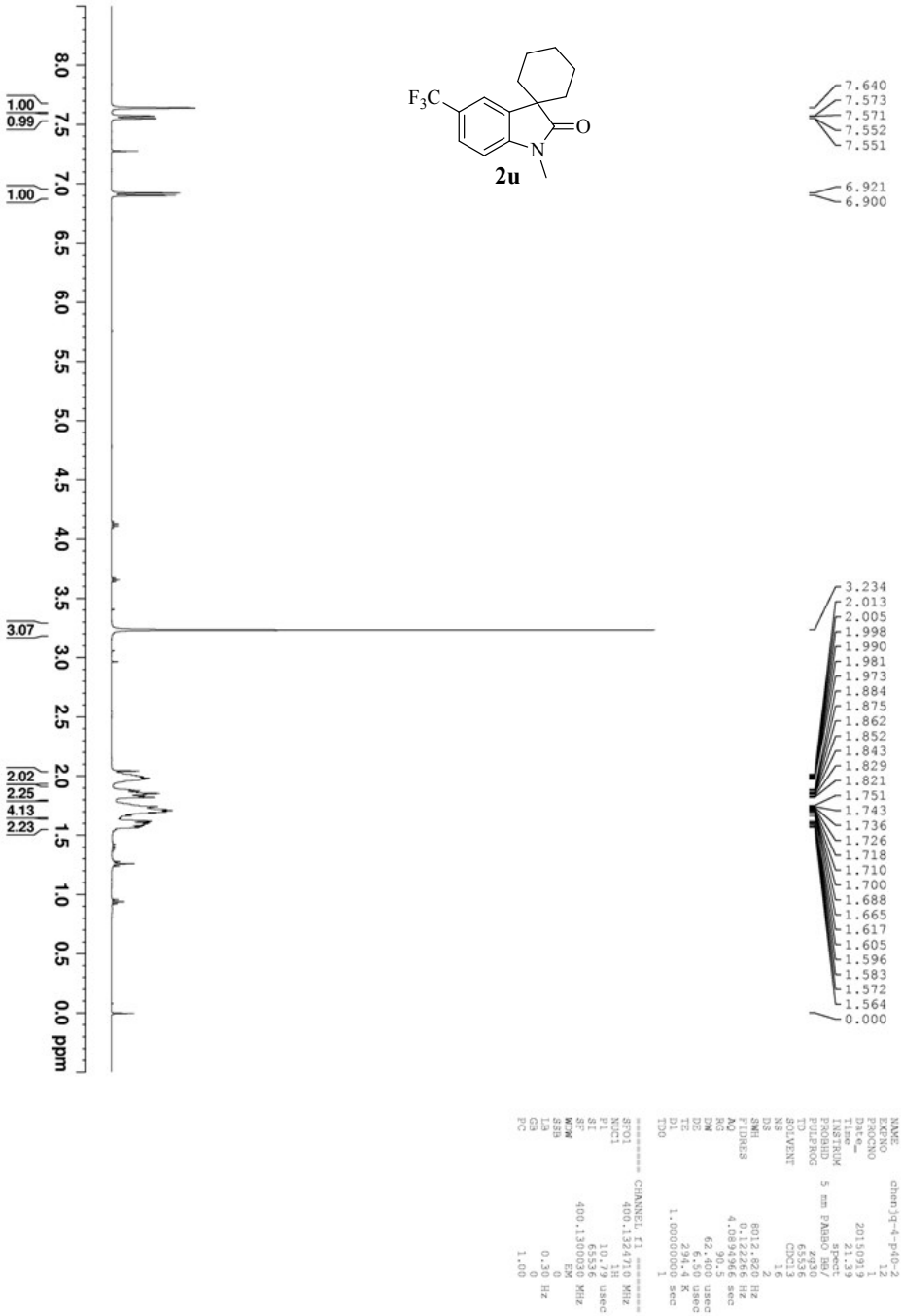


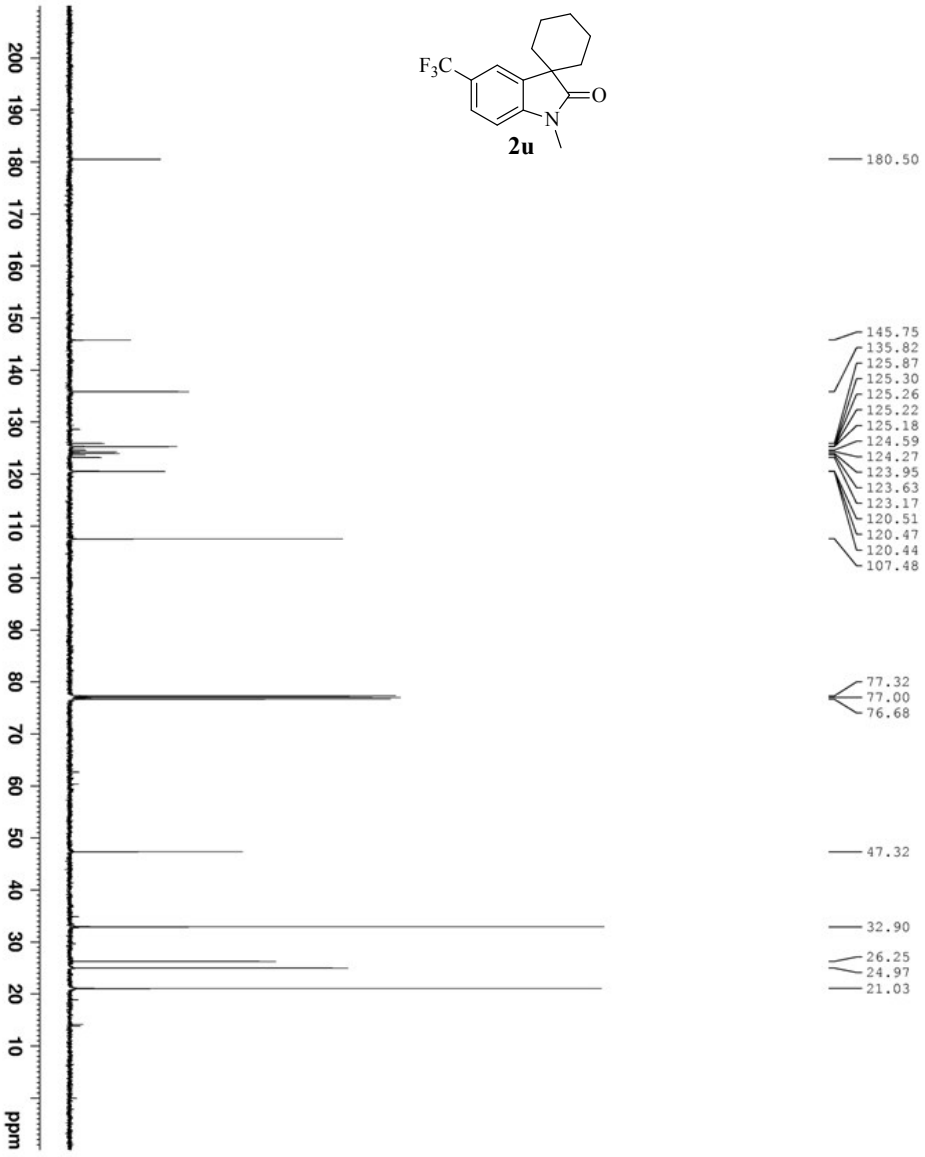
NAME chen3q-4-p40-4
EXPNO 10
PROCNO 1
Date_ 20150923
Time 9.56
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 2
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894966 sec
RG 114
DW 62.400 usec
DE 6.50 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.79 usec
SI 65536
SF 400.1300038 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

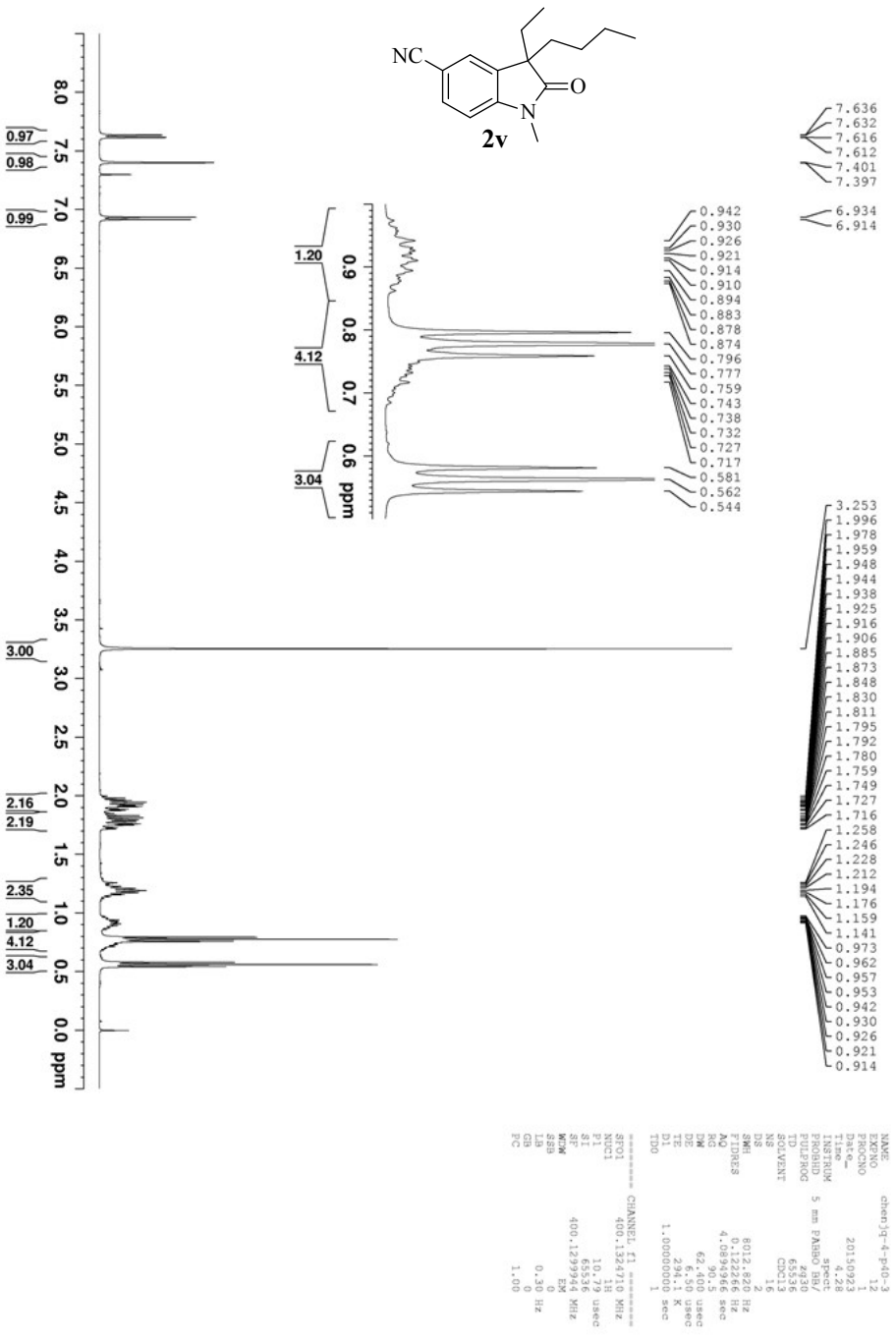

F
O
N
2t
180.29
159.97
157.59
138.71
138.69
136.86
136.78
113.45
113.22
112.26
112.01
108.06
107.98
77.32
77.00
76.68
47.87
47.86
32.82
26.22
24.98
21.05
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

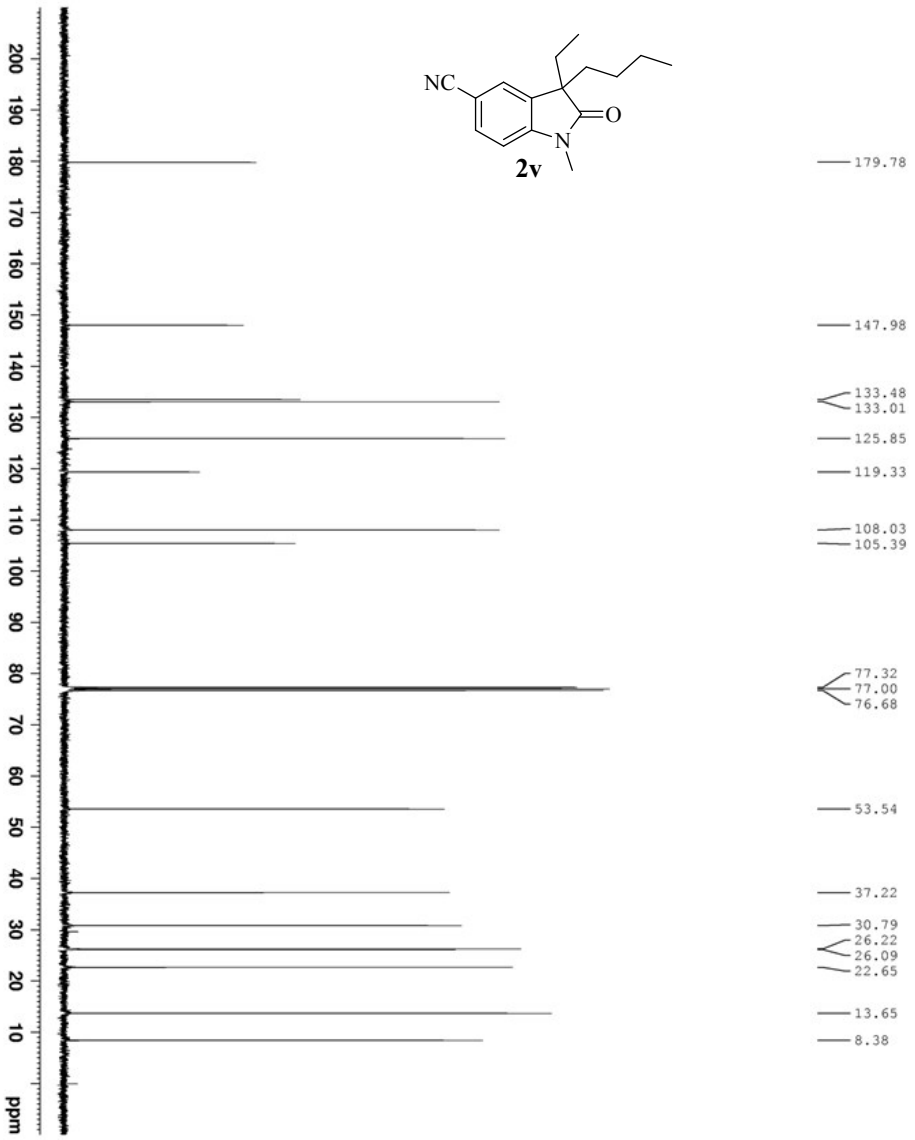
1'-methyl-5'-(trifluoromethyl)spiro[cyclohexane-1,3'-indolin]-2'-one (**2u**)



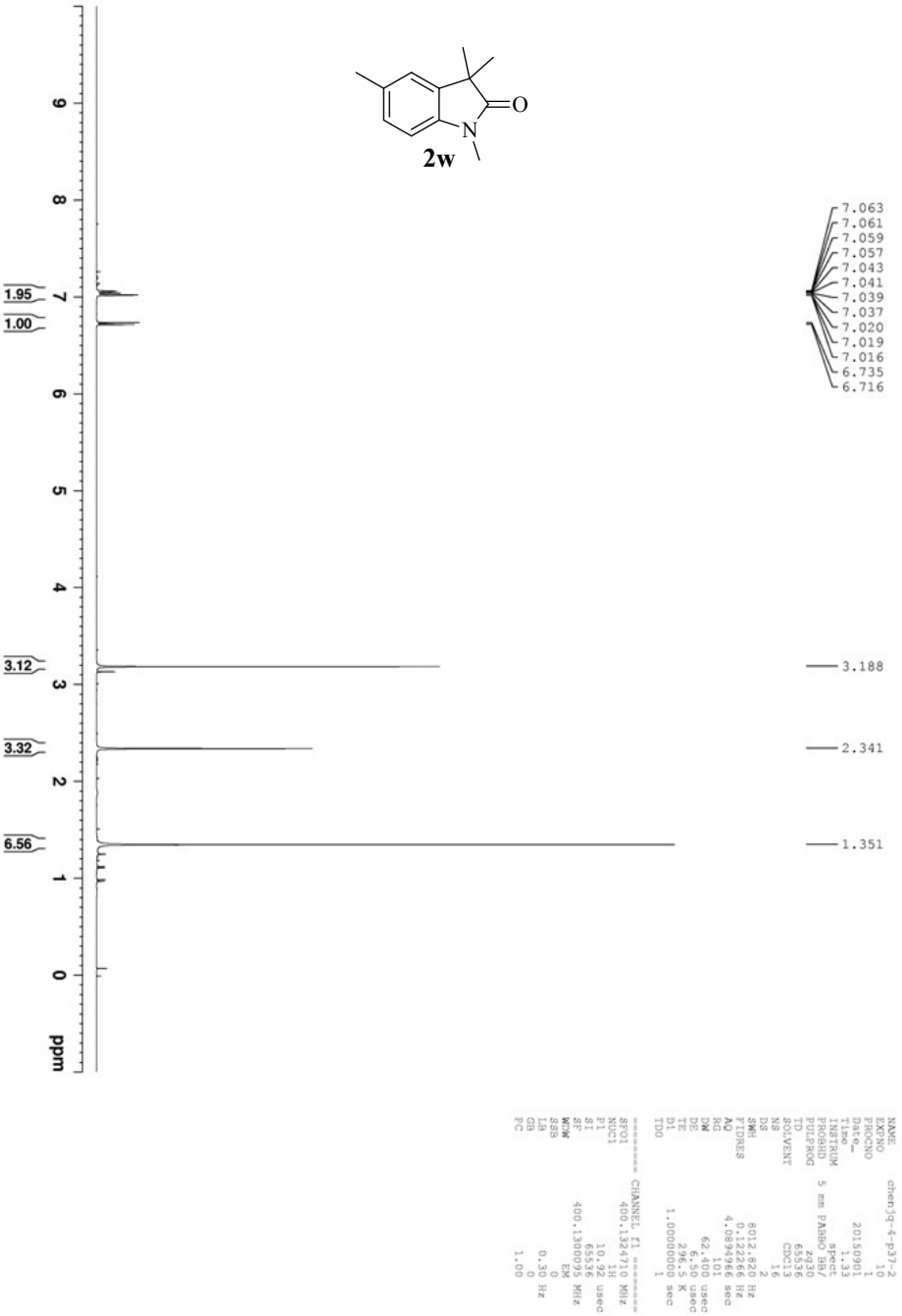

F3C
O
N
2u
180.50
145.75
135.82
125.87
125.30
125.26
125.22
125.18
124.59
124.27
123.95
123.63
123.17
120.51
120.47
120.44
107.48
77.32
77.00
76.68
47.32
32.90
26.25
24.97
21.03
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
NAME chen3q-4-p40-2
EXPNO 13
PROCNO 1
Date_ 20150919
Time 21.58
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 312
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 295.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6228298 MHz
NUC1 13C
P1 12.30 usec
PL1 32768.00 dB
SF 100.6127722 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

3-butyl-3-ethyl-1-methyl-2-oxoindoline-5-carbonitrile (**2v**)



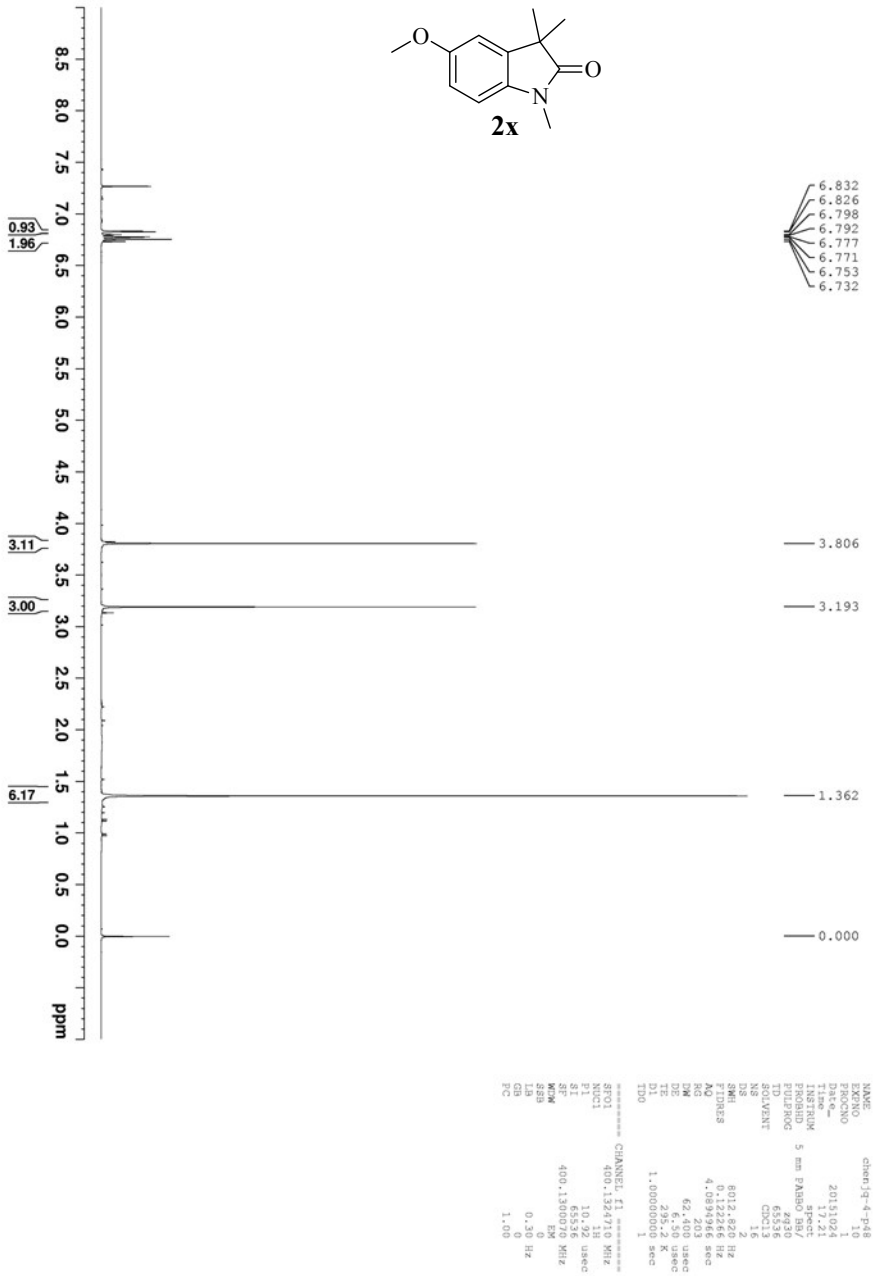

NC
O
N
2v
179.78
147.98
133.48
133.01
125.85
119.33
108.03
105.39
77.32
77.00
76.68
53.54
37.22
30.79
26.22
26.09
22.65
13.65
8.38
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

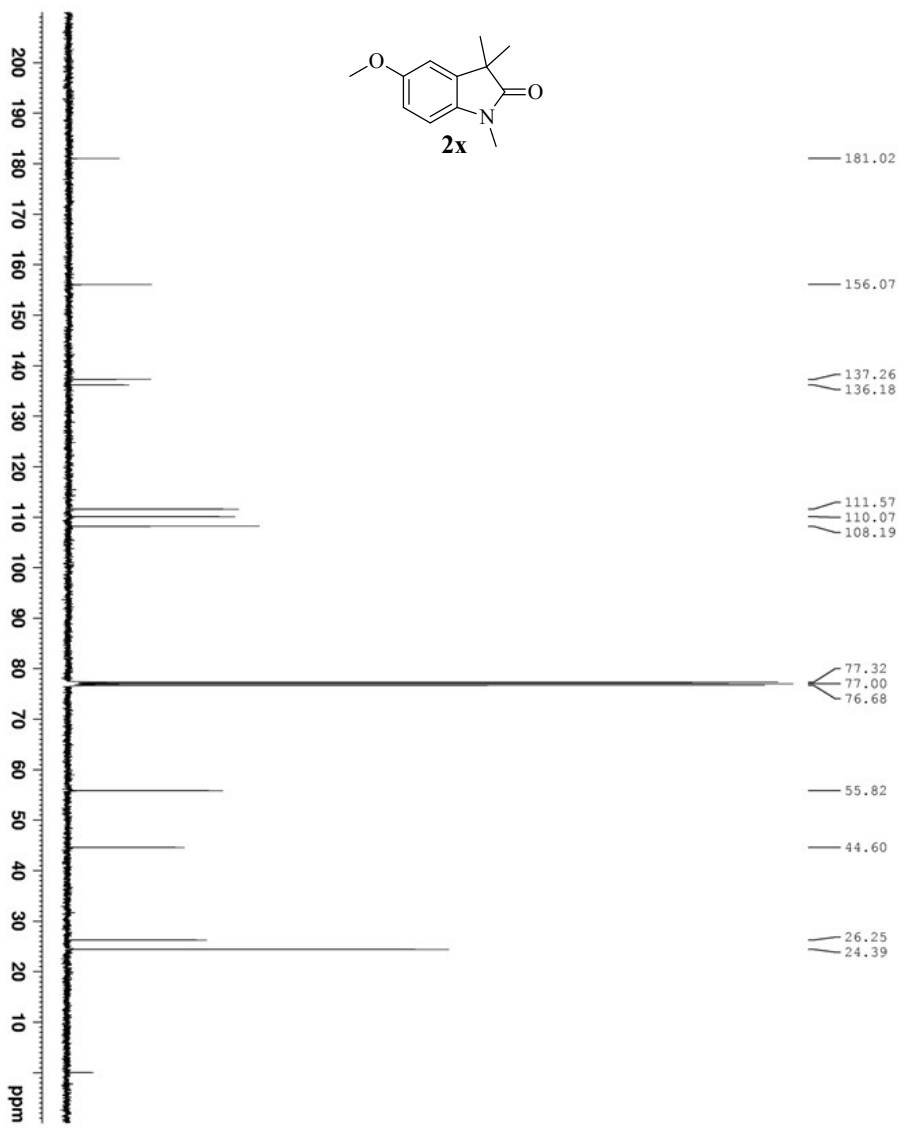
1,3,3,5-tetramethylindolin-2-one (**2w**)



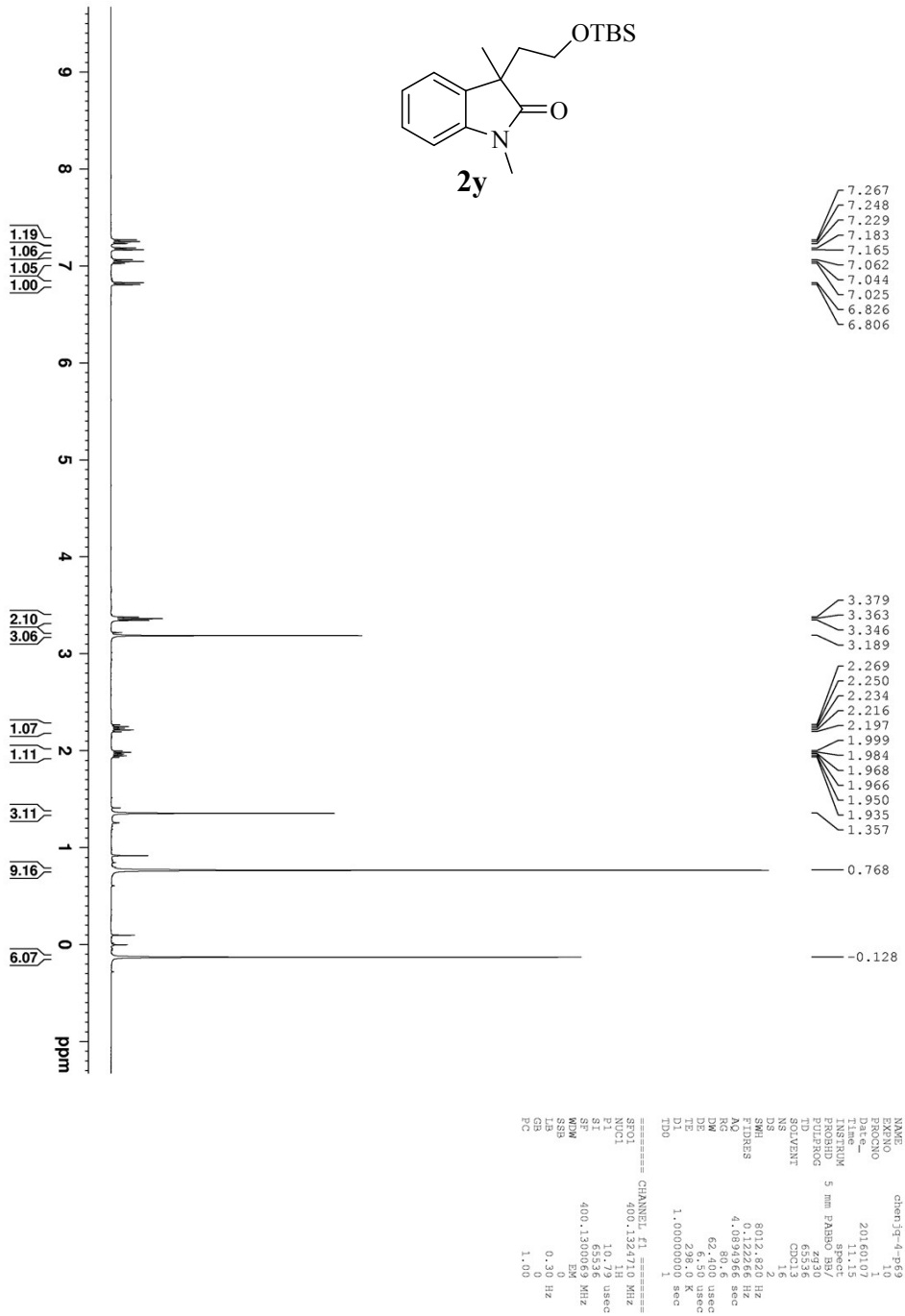

2w
181.33
140.27
135.91
131.96
127.82
123.14
107.71
77.36
77.05
76.73
44.21
26.20
24.41
21.10
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
NAME chem3q-4-p37-2
EXPNO 11
PROCNO 1
Date_ 20150901
Time 12.02
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 500
DS 2
SWH 24038.461 Hz
FIDRES 0.366796 Hz
AQ 1.3631988 sec
RG 1030
DW 20.800 usec
DE 6.50 usec
TE 297.4 K
D1 2.0000000 sec
D11 0.0300000 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 14.70 usec
PL1 -3.27 dB
SFO1 100.6127690 MHz
EM 0
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

5-methoxy-1,3,3-trimethylindolin-2-one (**2x**)



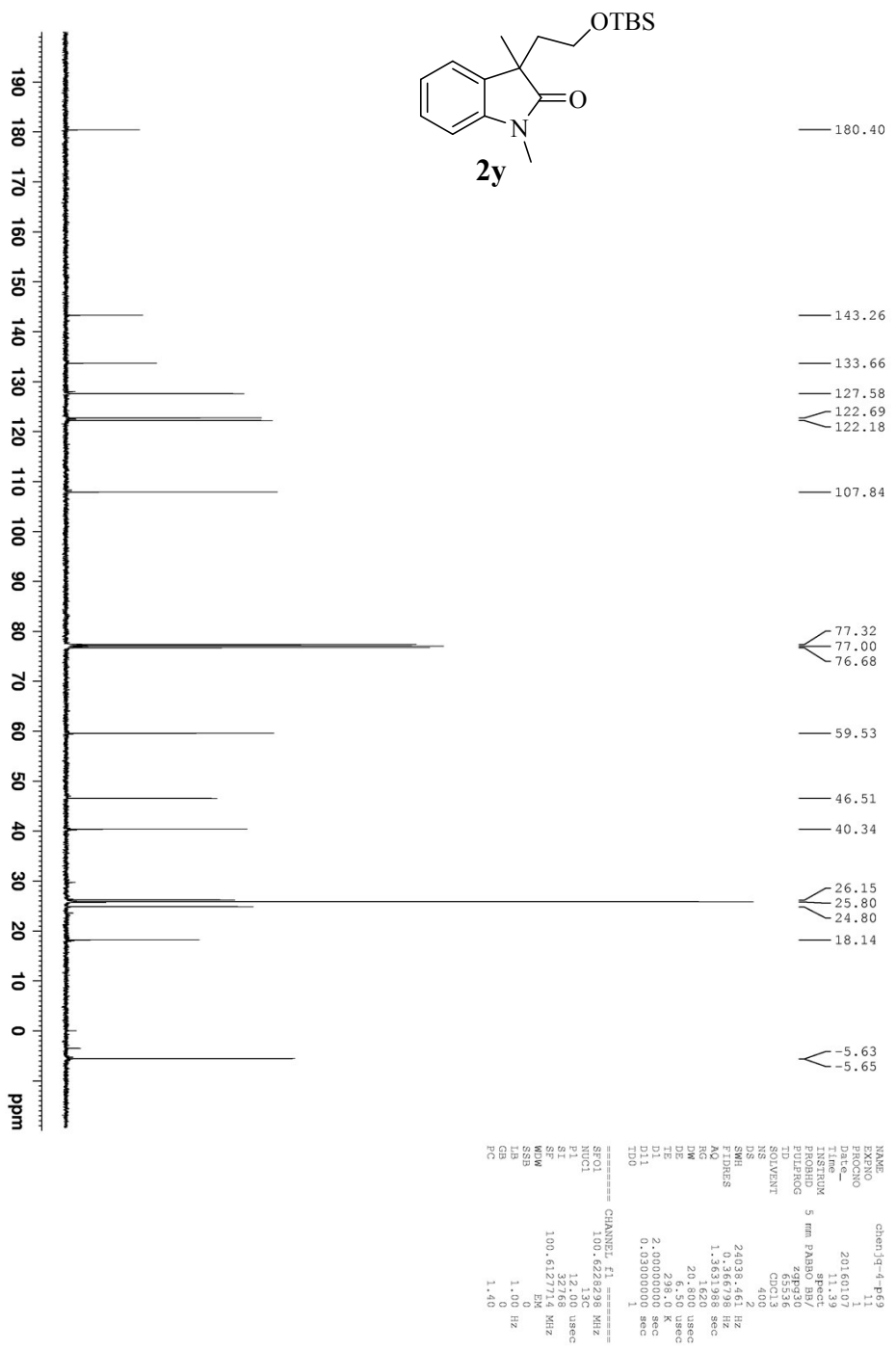

2x
181.02
156.07
137.26
136.18
111.57
110.07
108.19
77.32
77.00
76.68
55.82
44.60
26.25
24.39
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

3-(2-((tert-butyldimethylsilyl)oxy)ethyl)-1,3-dimethylindolin-2-one (**2y**)

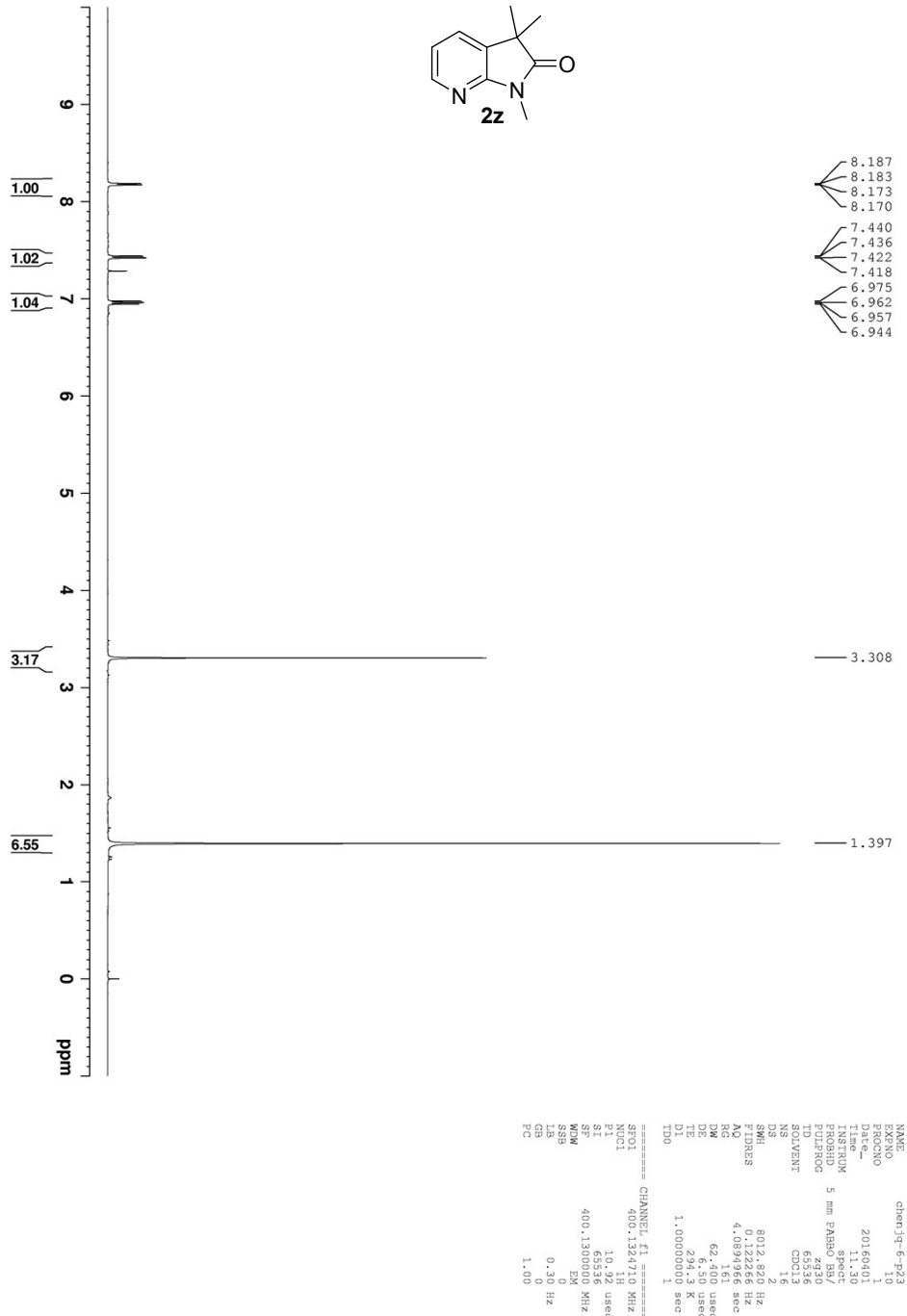


NAME chen3q-4-p69
EXPNO 10
PROCNO 1
Date_ 20160107
Time 11.15
INSTRUM spect
PROBHD 5 mm PABBO BB/7
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122868 Hz
AQ 4.089496 sec
RG 80.6
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.79 usec
SI 65536
SF 400.1300069 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

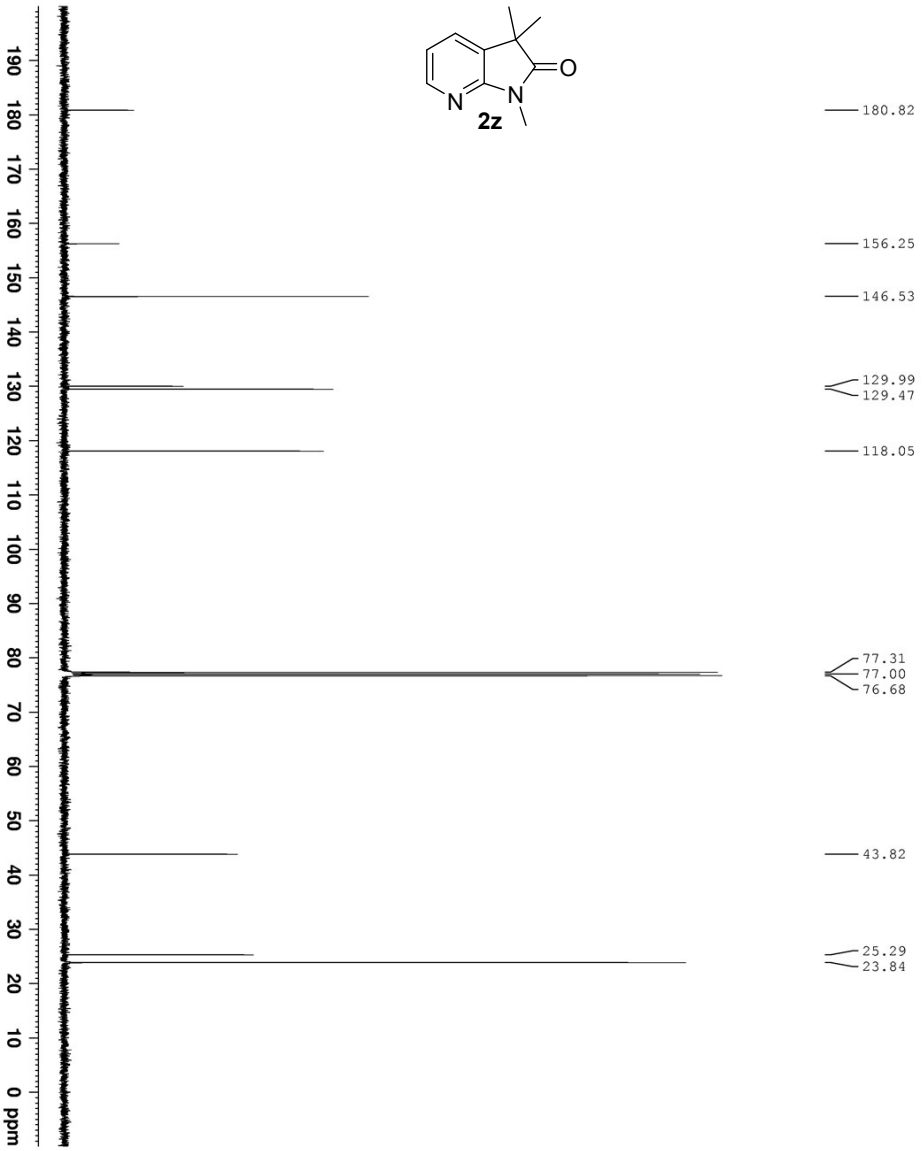

OTBS
O
N
2y
180.40
143.26
133.66
127.58
122.69
122.18
107.84
77.32
77.00
76.68
59.53
46.51
40.34
26.15
25.80
24.80
18.14
-5.63
-5.65
ppm

1,3,3-trimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one (**2z**)



NAME chen3q-6-p23
EXPNO 10
PROCNO 1
Date_ 20160401
Time 11.30
INSTRUM spect
PROBHD 5 mm PABBO BB/7
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122268 Hz
AQ 4.089496 sec
RG 161
DW 62.400 usec
DE 6.50 usec
TE 294.3 K
D1 1.00000000 sec
TD0 1

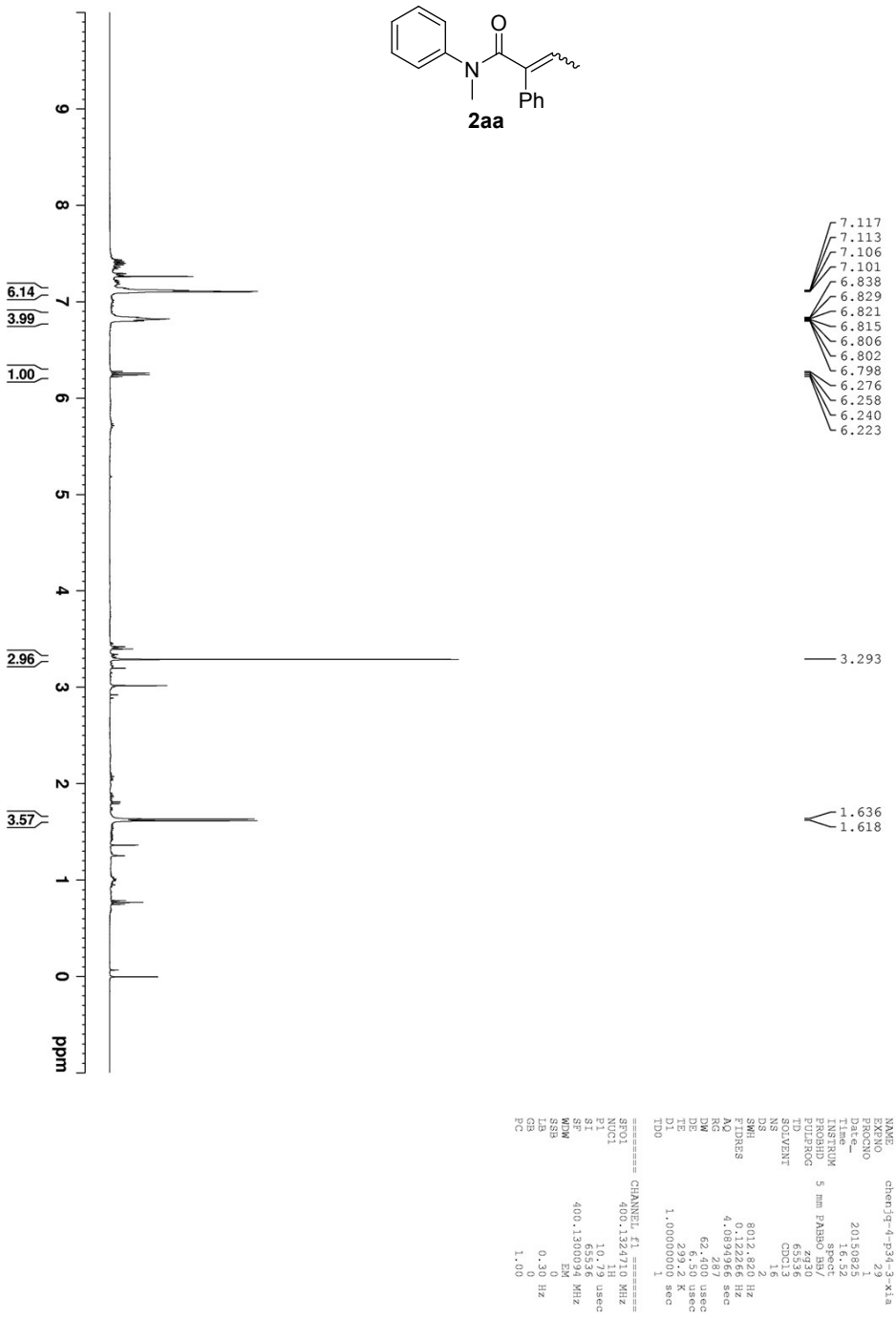
======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.92 usec
SI 65536
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



NAME chenjq-6-p23-C
EXPNO 10
PROCNO 1
Date_ 20160401
Time 19.21
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 350
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.363188 sec
RG 2050
DW 20.800 usec
DE 6.50 usec
TE 296.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

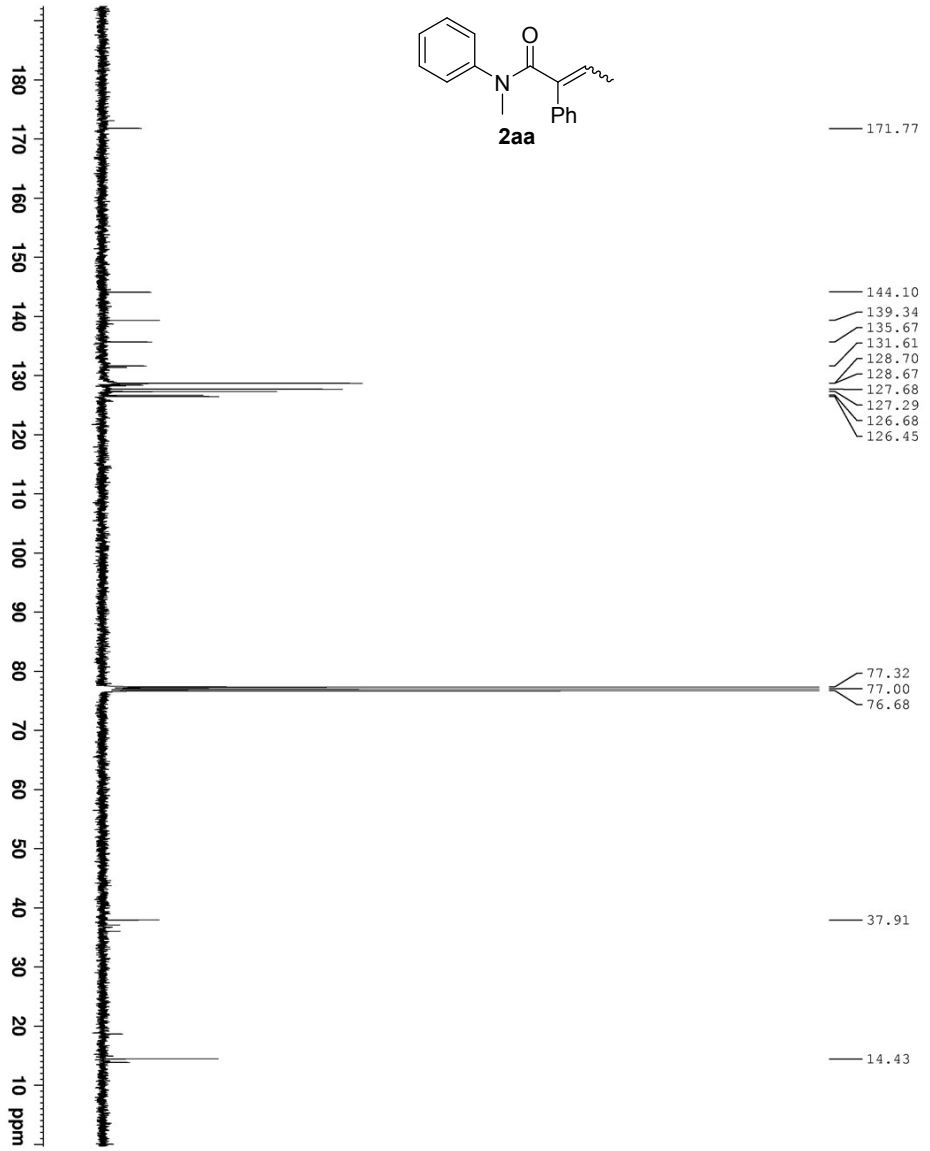
======== CHANNEL f1 ========
SFO1 100.622898 MHz
NUC1 13C
P1 12.00 usec
SF 100.612772 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

N-methyl-N,2-diphenylbut-2-enamide (**2aa**)

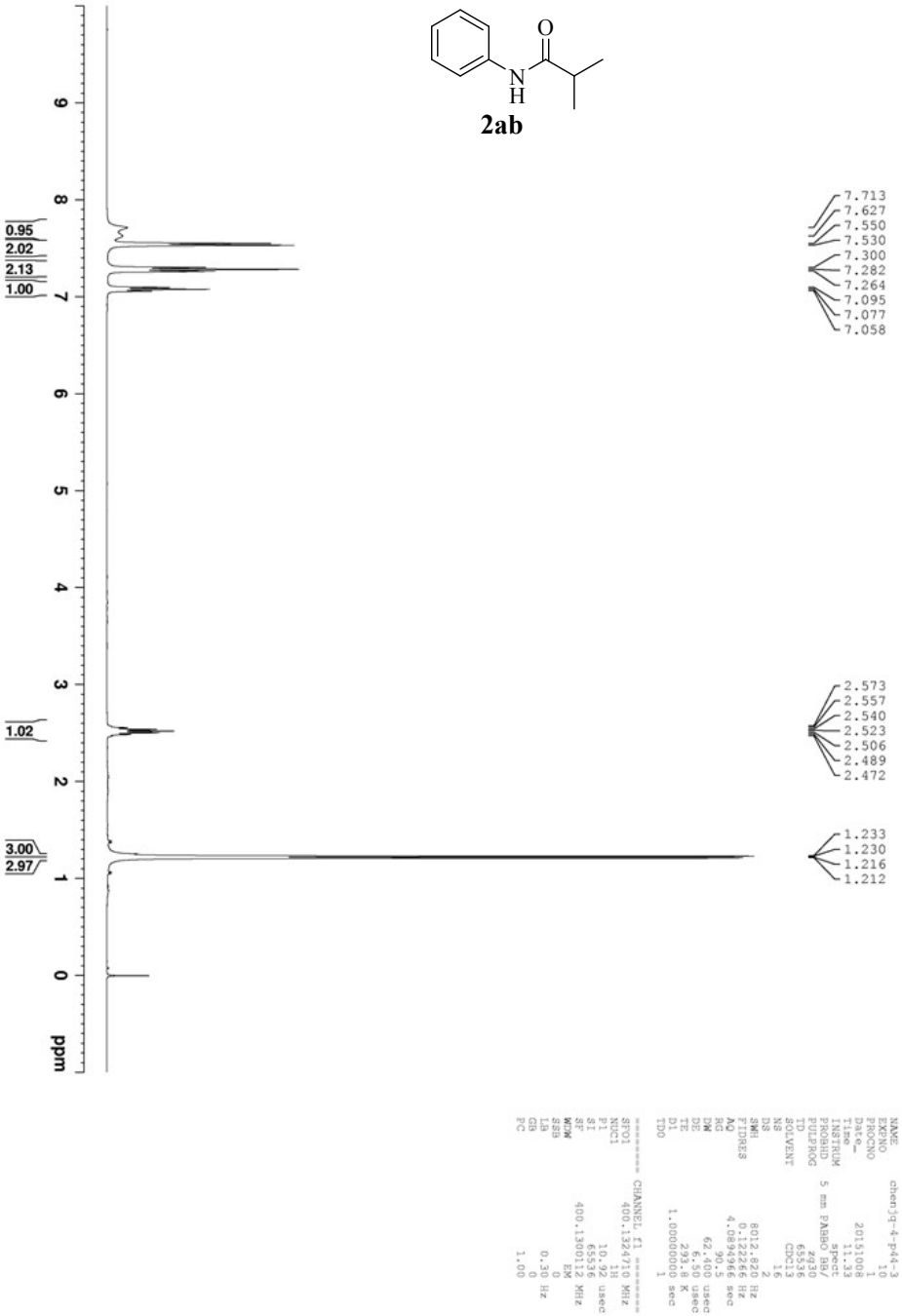


NAME chemjq-4-p34-3-xia
EXPNO 29
PROCNO 1
Date_ 20150825
Time 16.52
INSTRUM spect
PROBHD 5 mm PABBO BB/7
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122260 Hz
AQ 4.089496 sec
RG 287
DW 62.400 usec
DE 6.50 usec
TE 299.2 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.79 usec
SI 65536
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

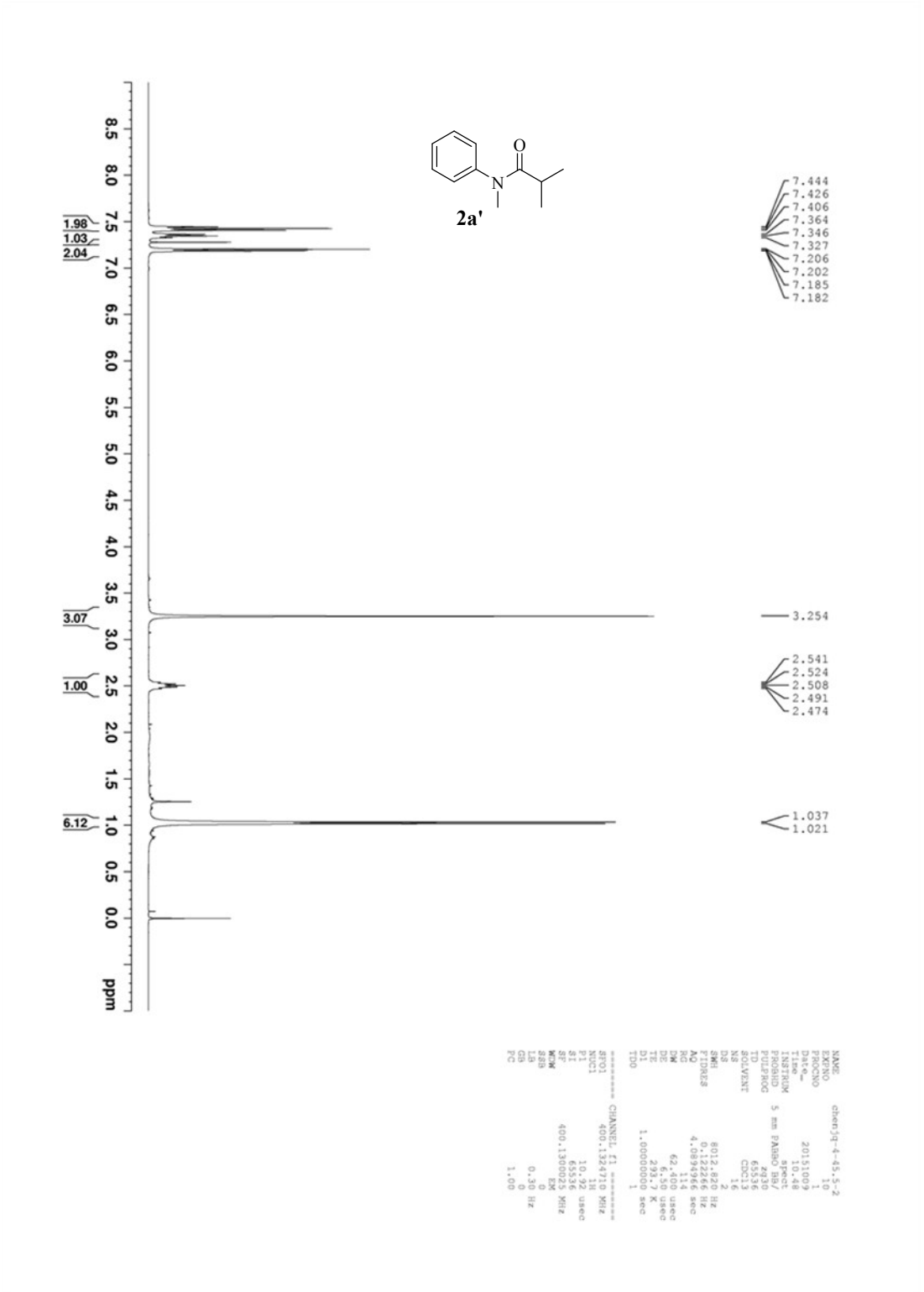

O
N
Ph
2aa
171.77
144.10
139.34
135.67
131.61
128.70
128.67
127.68
127.29
126.68
126.45
77.32
77.00
76.68
37.91
14.43
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
NAME chenjq-4-p36-3-xia
EXPNO 30
PROCNO 1
Date_ 20150825
Time 17.33
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 700
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631968 sec
RG 20.800
DW 20.800 usec
DE 6.50 usec
TE 300.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6228298 MHz
NUC1 13C
P1 12.00 usec
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

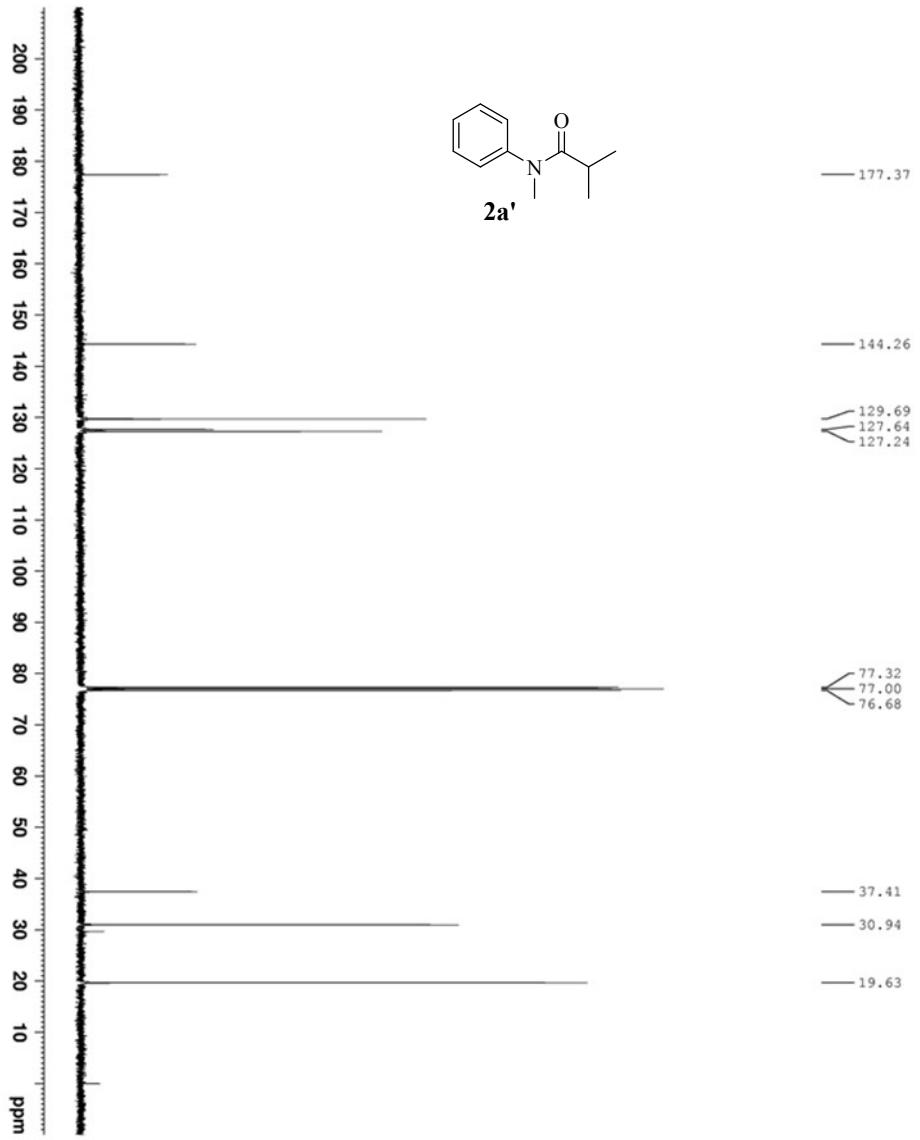
N-phenylisobutyramide (**2ab**)



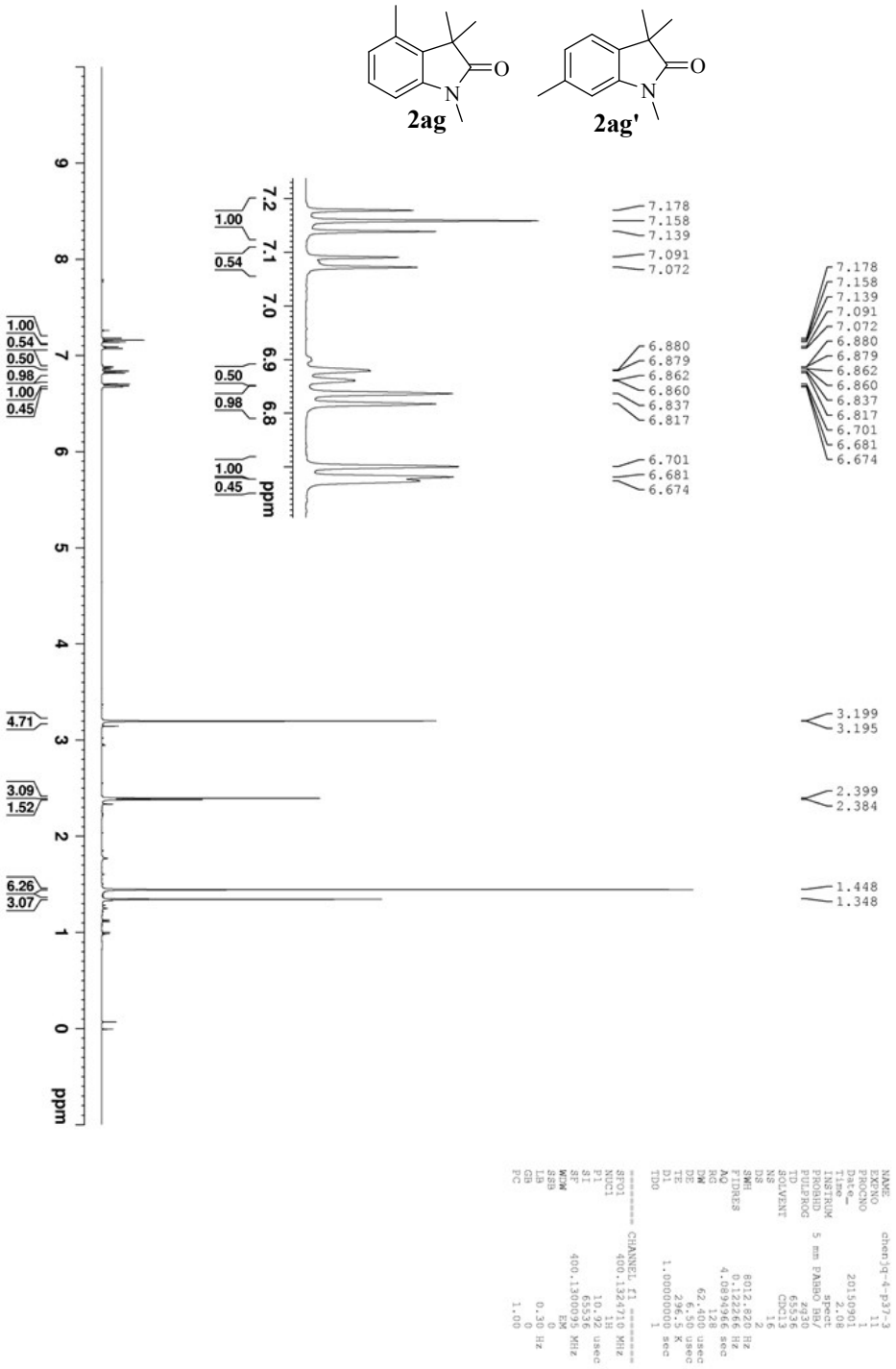

O
N
H
2ab
175.62
138.11
128.83
124.03
119.93
77.32
77.00
76.68
36.46
19.55
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

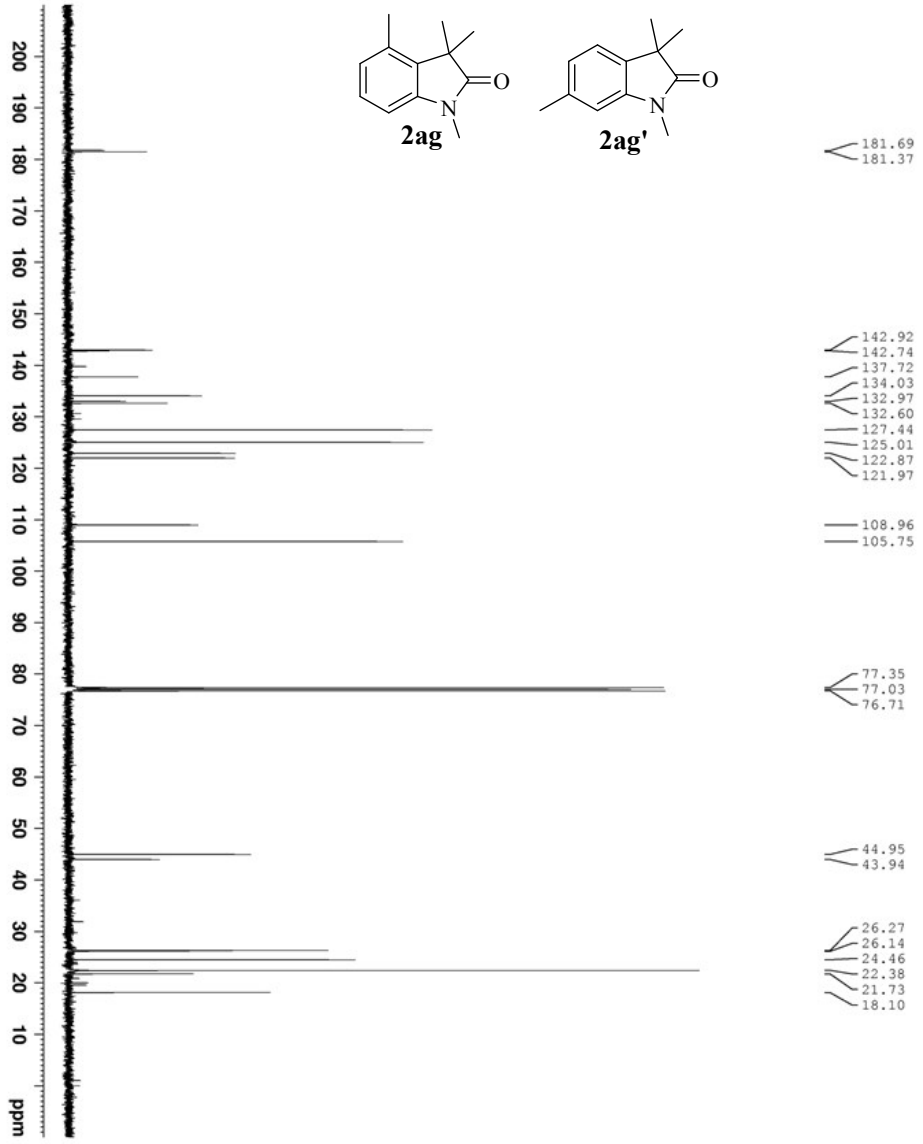
N-methyl-N-phenylisobutyramide (**2a'**)



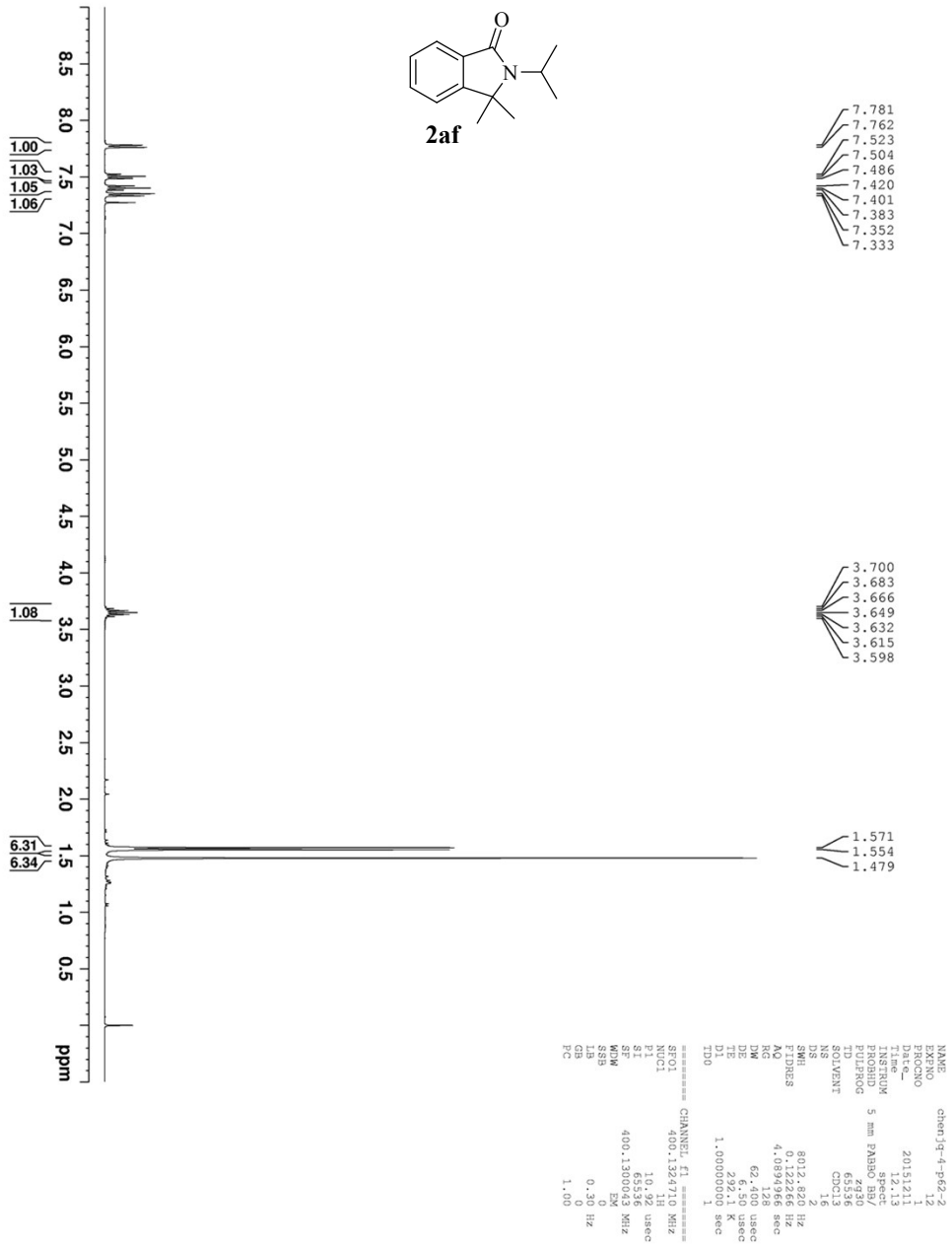

O
N
2a'
177.37
144.26
129.69
127.64
127.24
77.32
77.00
76.68
37.41
30.94
19.63
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

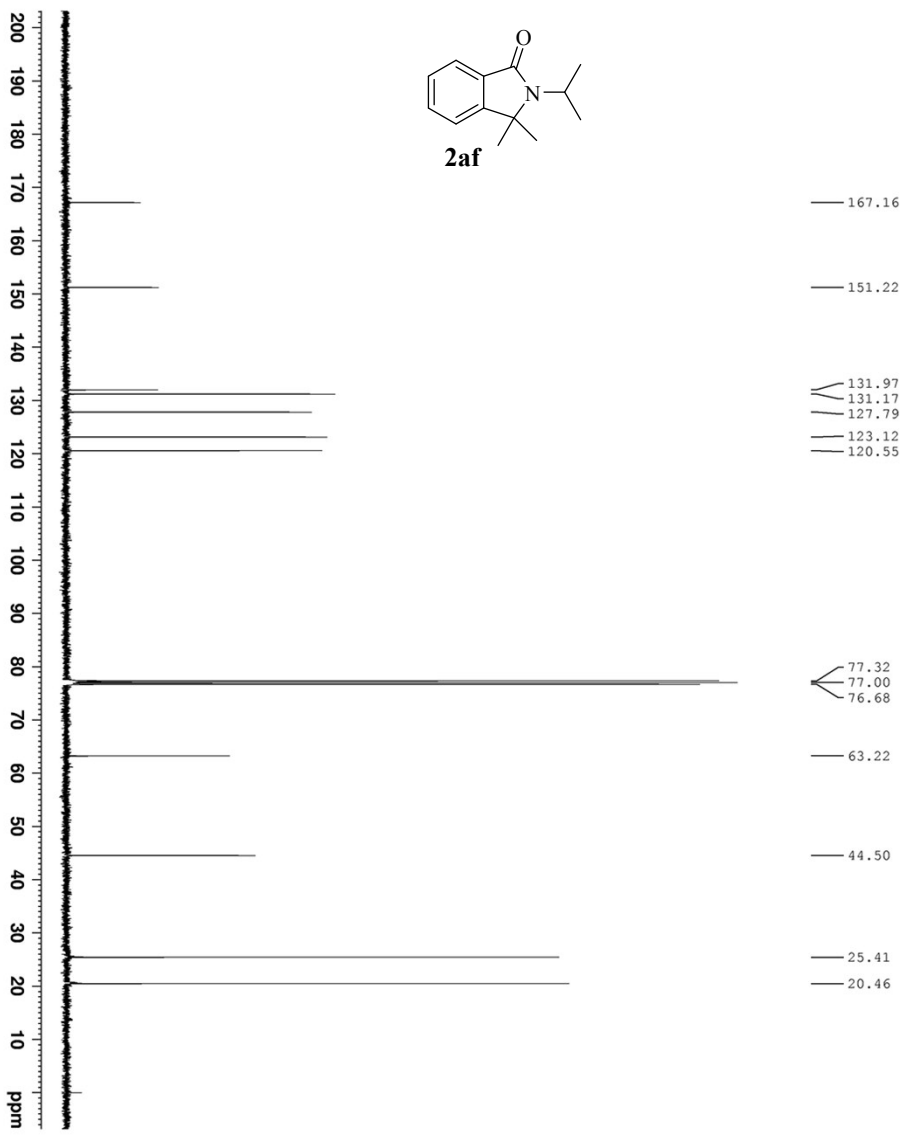
1,3,3,4-tetramethylindolin-2-one (**2ag**) and 1,3,3,6-tetramethylindolin-2-one (**2ag'**)



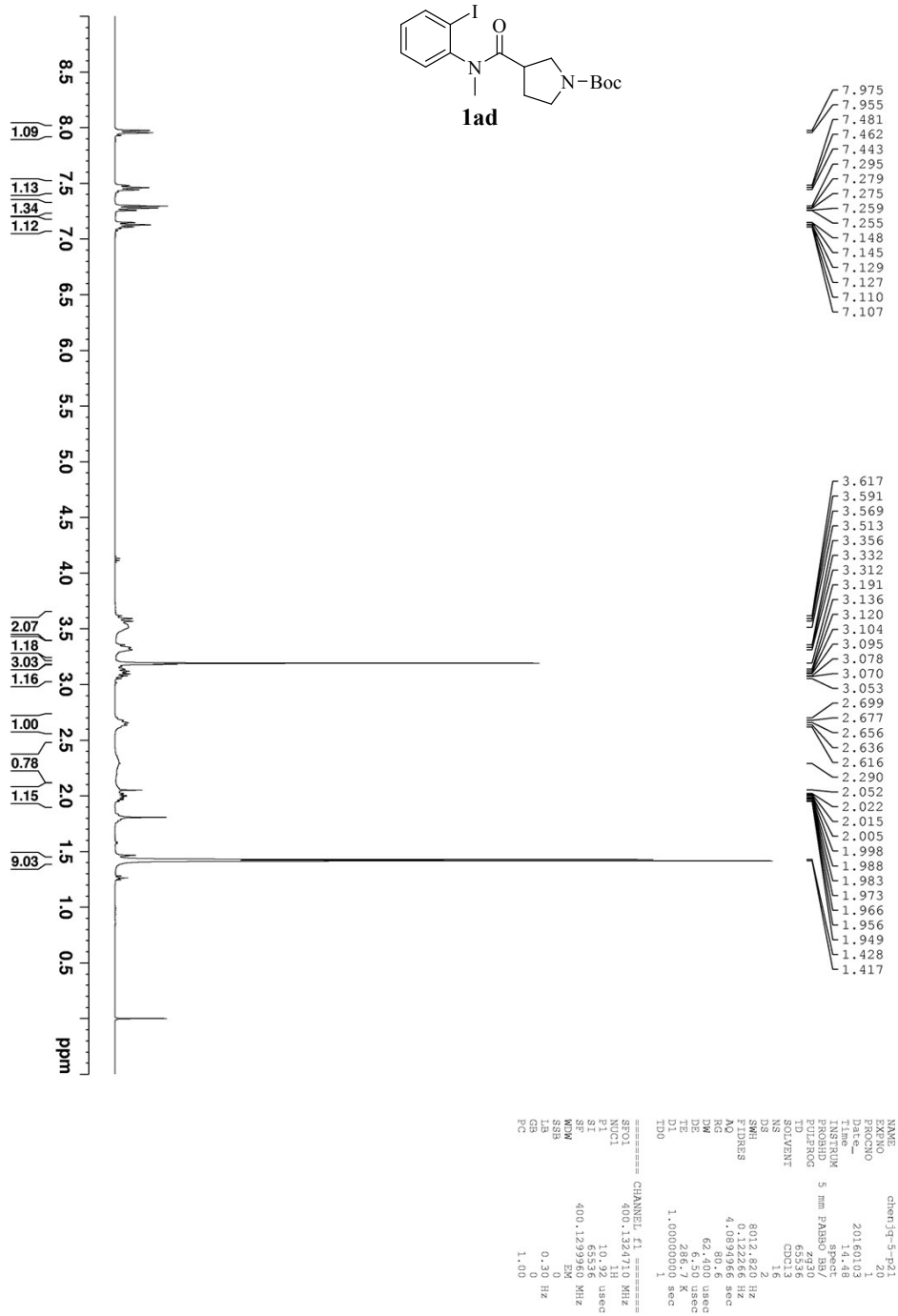

2ag
2ag'
181.69
181.37
142.92
142.74
137.72
134.03
132.97
132.60
127.44
125.01
122.87
121.97
108.96
105.75
77.35
77.03
76.71
44.95
43.94
26.27
26.14
24.46
22.38
21.73
18.10
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

2-isopropyl-3,3-dimethylisoindolin-1-one (**2af**)



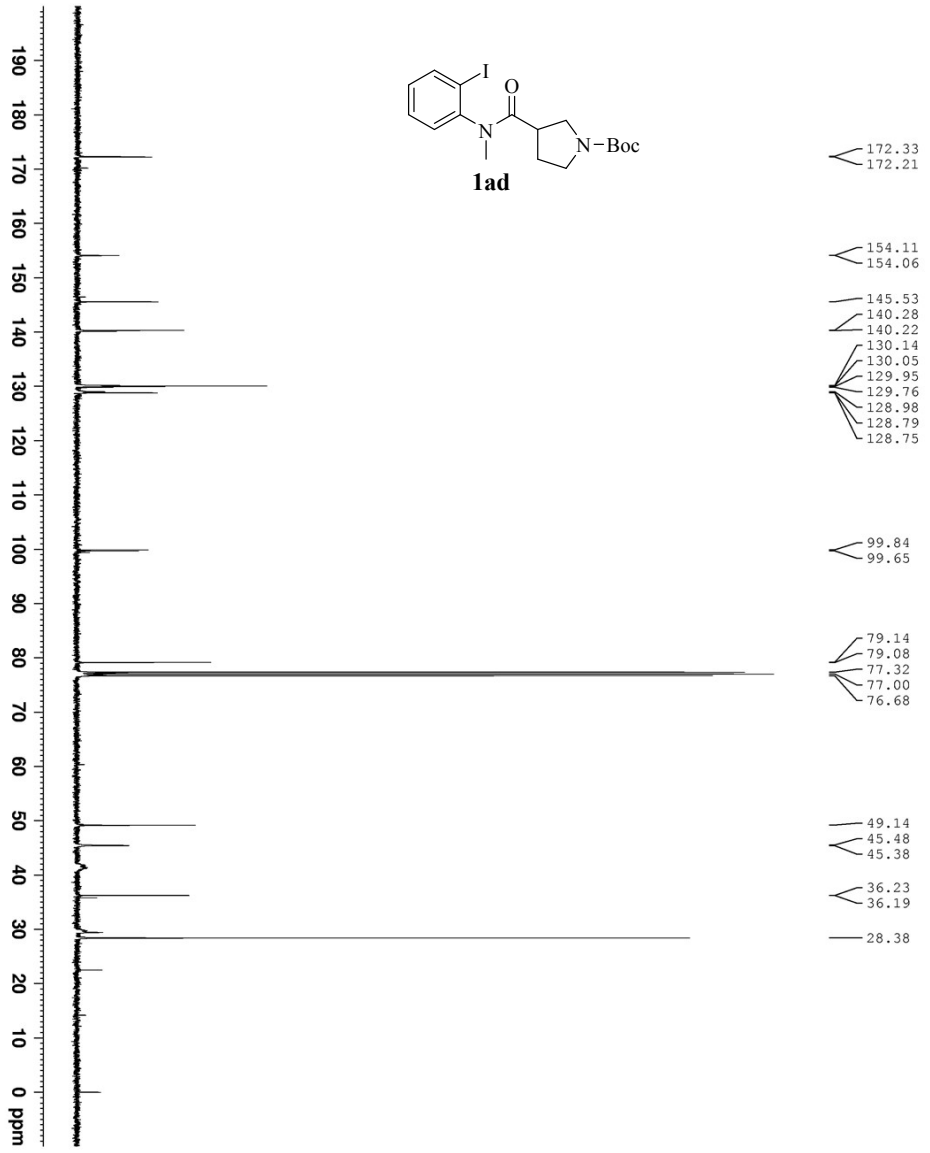

O
N
2af
167.16
151.22
131.97
131.17
127.79
123.12
120.55
77.32
77.00
76.68
63.22
44.50
25.41
20.46
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
NAME chenjq-4-
EXPNO 201
PROCNO
Date_
Time
INSTRUM
PROBHD 5 mm PABB
PULPROG z
TD
SOLVENT
NS
DS
SWH 2403
FIDRES 0.3
AQ 1.36
RG
DW 2
DE
TE
D1 2.000
D11 0.030
TD0
========== CHANNEL f
SFO1 100.62
NUC1
P1
SI
SF 100.61
WDW
SSB
LB
GB
PC

tert-butyl 3-((2-iodophenyl)(methyl)carbamoyl)pyrrolidine-1-carboxylate (**1ad**)

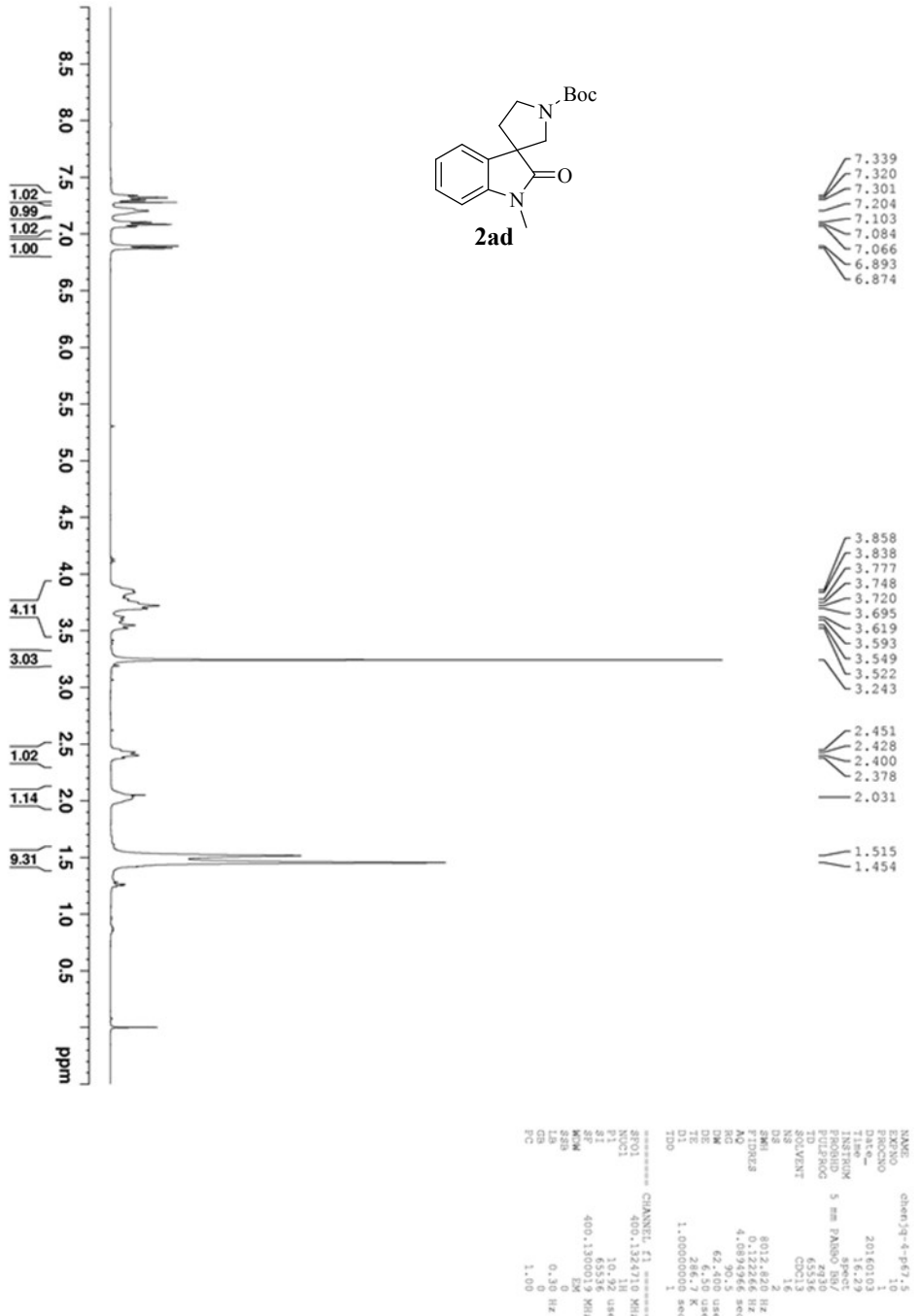


NAME chen1q-5-p21
EXPNO 20
PROCNO 1
Date_ 20160103
Time 14.48
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.089496 sec
RG 80.6
DW 62.400 usec
DE 6.50 usec
TE 286.7 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.92 usec
SI 65536
SF 400.1299960 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

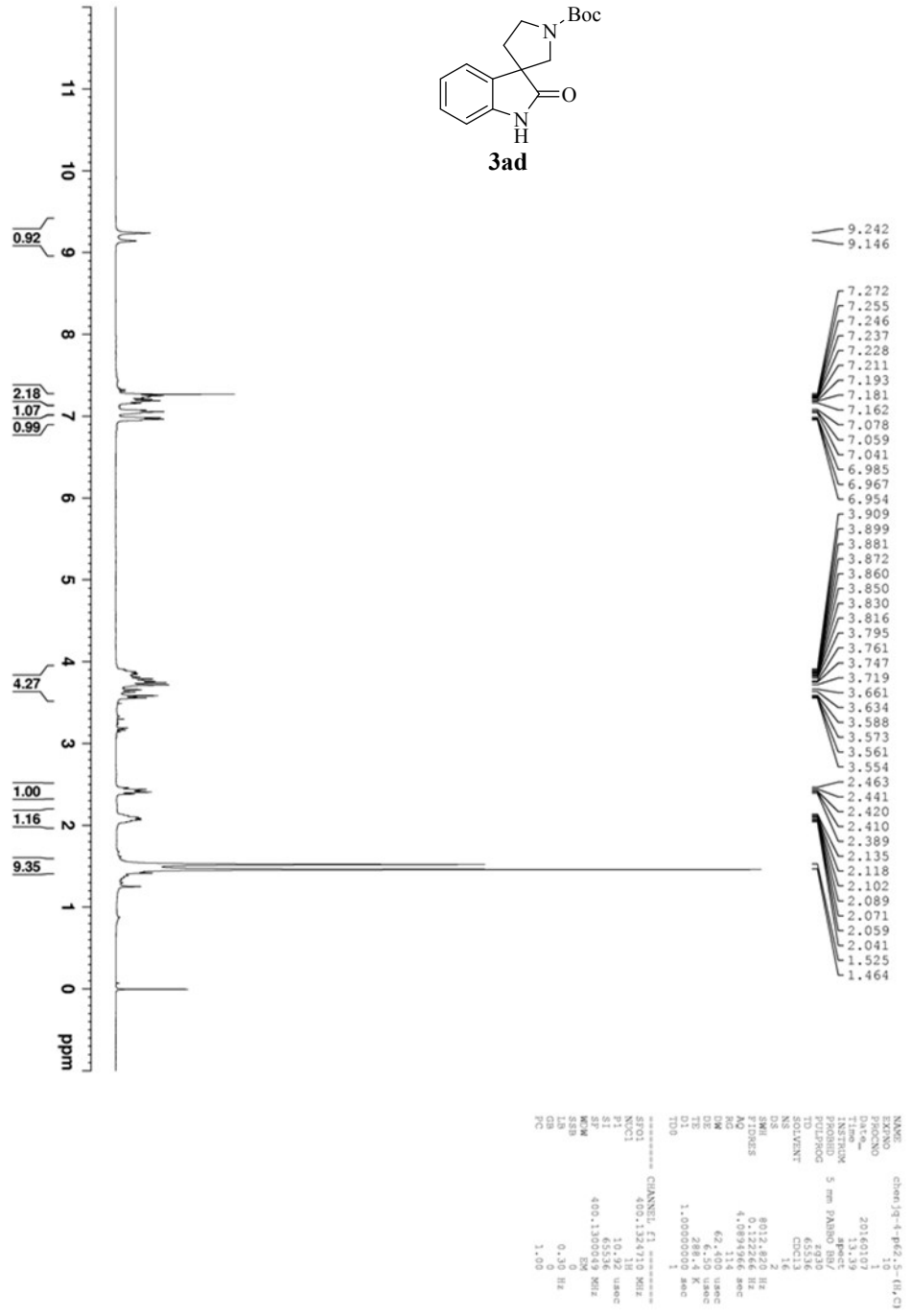

I
O
N
N−Boc
1ad
172.33
172.21
154.11
154.06
145.53
140.28
140.22
130.14
130.05
129.95
129.76
128.98
128.79
128.75
99.84
99.65
79.14
79.08
77.32
77.00
76.68
49.14
45.48
45.38
36.23
36.19
28.38
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
NAME chenjq-5-p21
EXPNO 21
PROCNO 1
Date_ 20160103
Time 15.15
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 460
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631968 sec
RG 287.7
DW 20.800 usec
DE 6.50 usec
TE 287.7 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6228298 MHz
NUC1 13C
P1 14.70 usec
SI 32768
SF 100.6127788 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

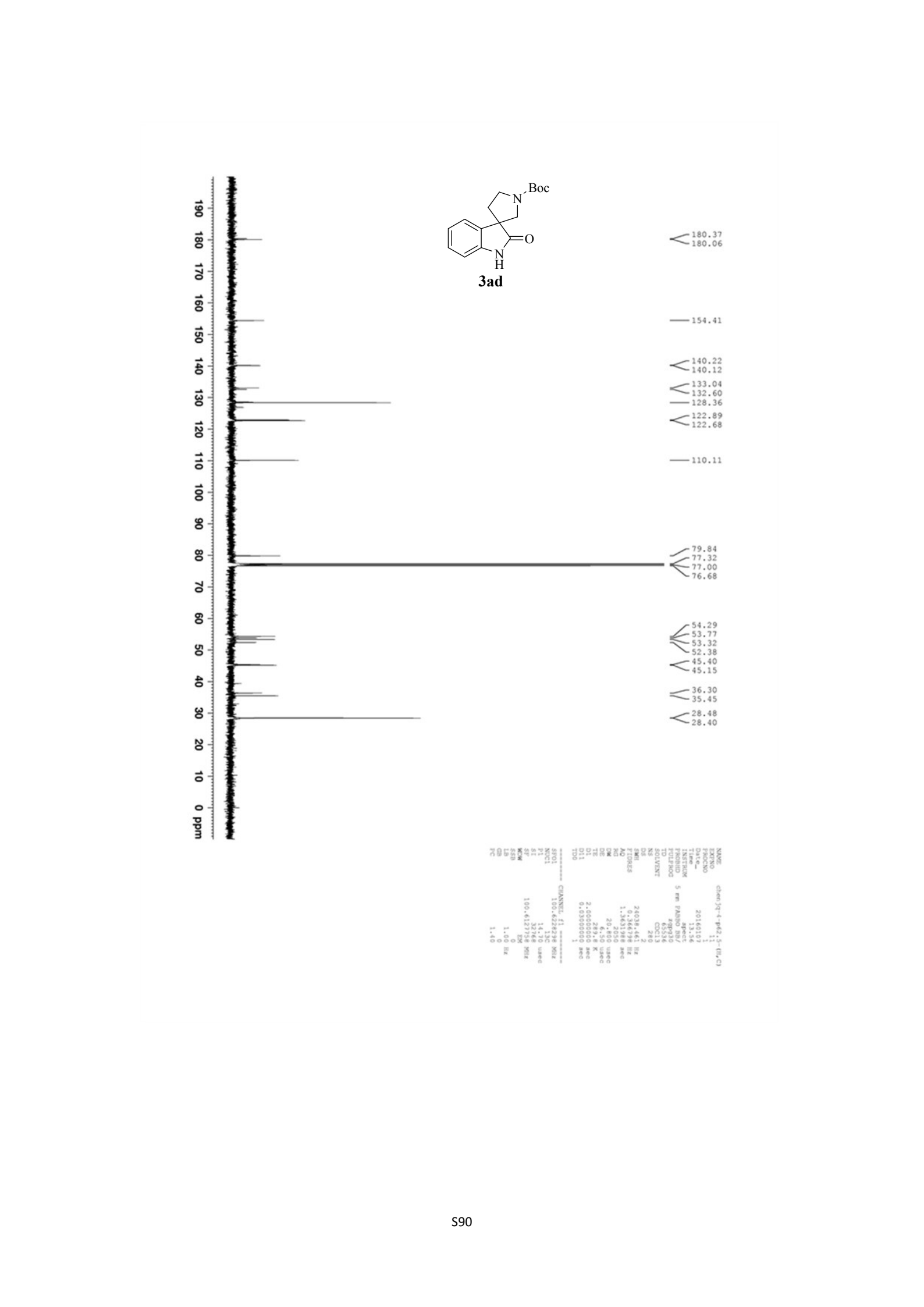
tert-butyl 1-methyl-2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate (**2ad**)



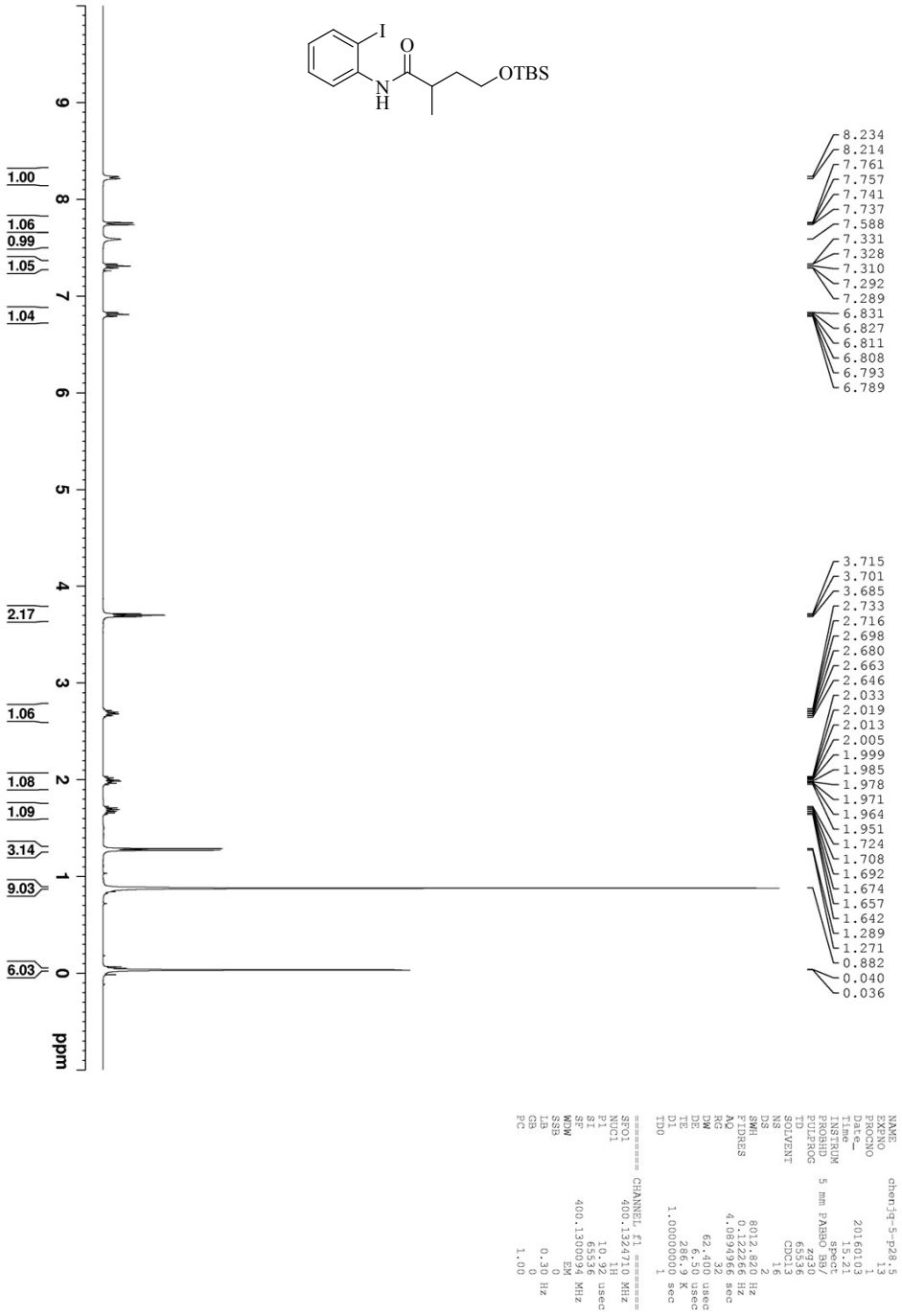

Boc
N
O
N
2ad
177.20
154.32
142.70
128.32
122.93
122.34
108.18
79.68
54.34
53.82
52.84
51.88
45.37
45.15
36.23
35.38
28.38
26.36
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

tert-butyl 2-oxospiro[indoline-3,3'-pyrrolidine]-1'-carboxylate (**3ad**)



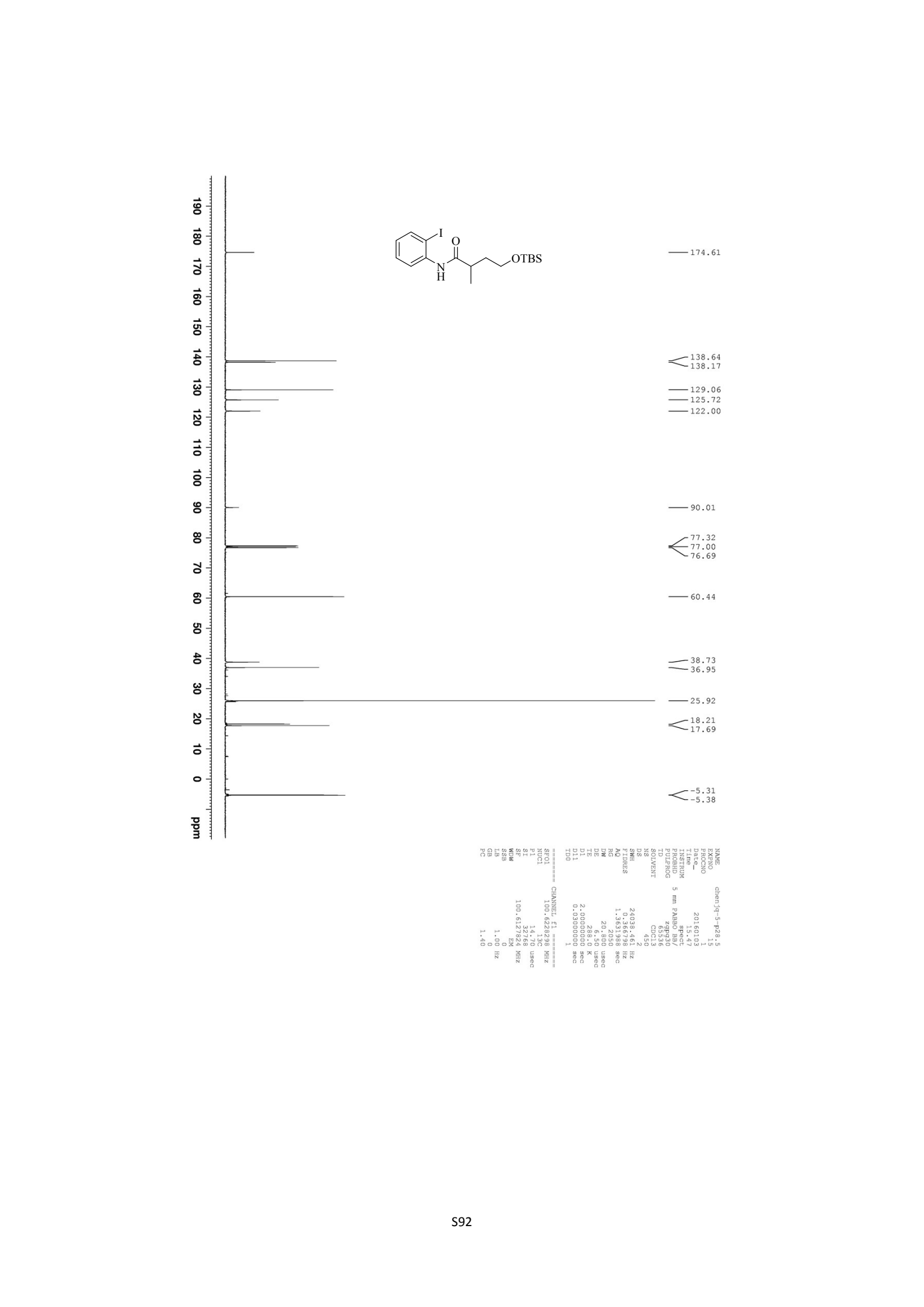

Boc
N
O
N
H
3ad
180.37
180.06
154.41
140.22
140.12
133.04
132.60
128.36
122.89
122.68
110.11
79.84
77.32
77.00
76.68
54.29
53.77
53.32
52.38
45.40
45.15
36.30
35.45
28.48
28.40
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

4-((tert-butyldimethylsilyl)oxy)-N-(2-iodophenyl)-2-methylbutanamide

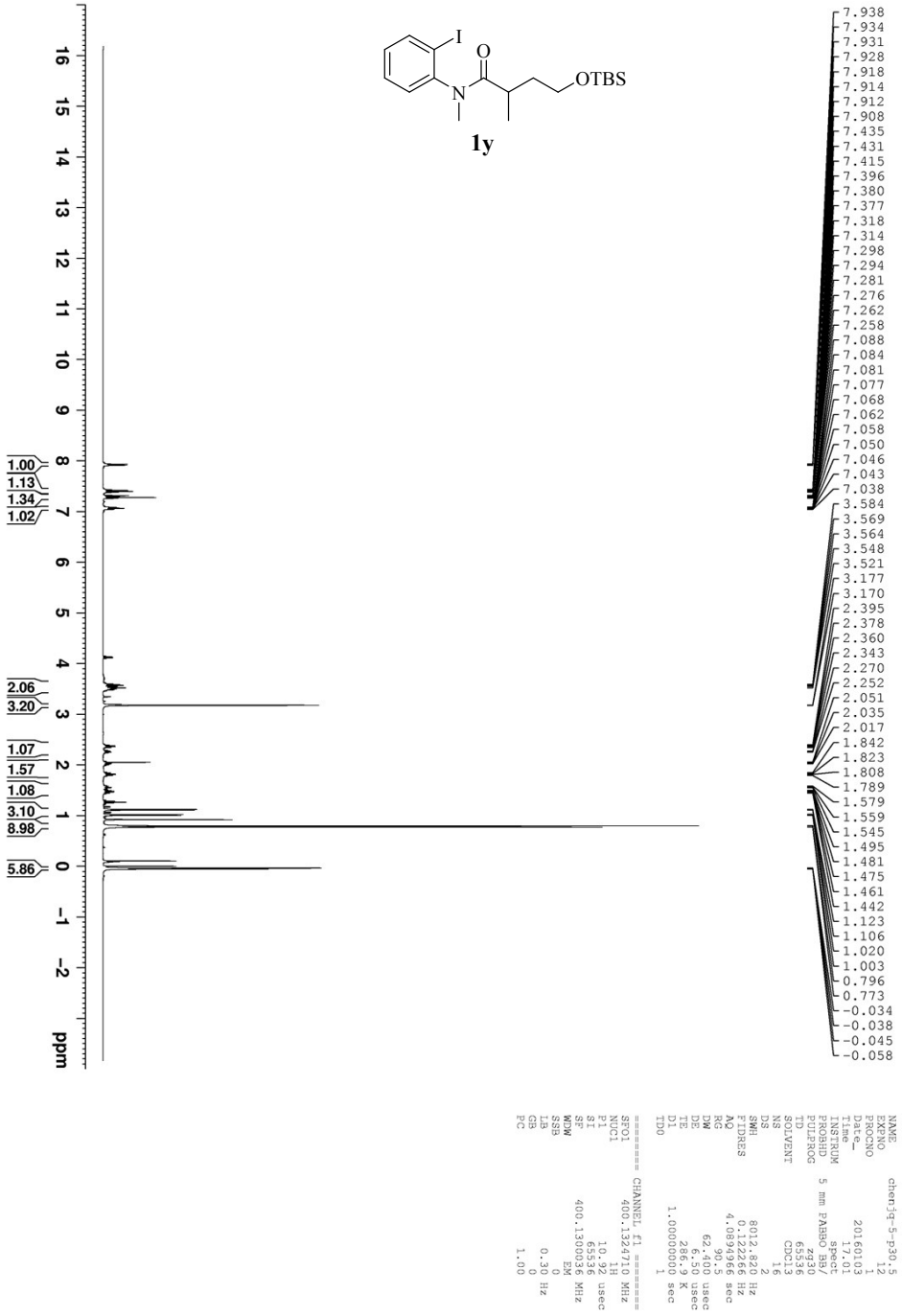


NAME chemjq-5-p28.5
EXPNO 13
PROCNO 1
Date_ 20160103
Time 15.21
INSTRUM 5 mm PABBO BB/F
PROBHD
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122966 Hz
AQ 4.089396 sec
RG 32
DW 62.400 usec
DE 6.50 usec
TE 286.9 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.92 usec
SI 65536
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

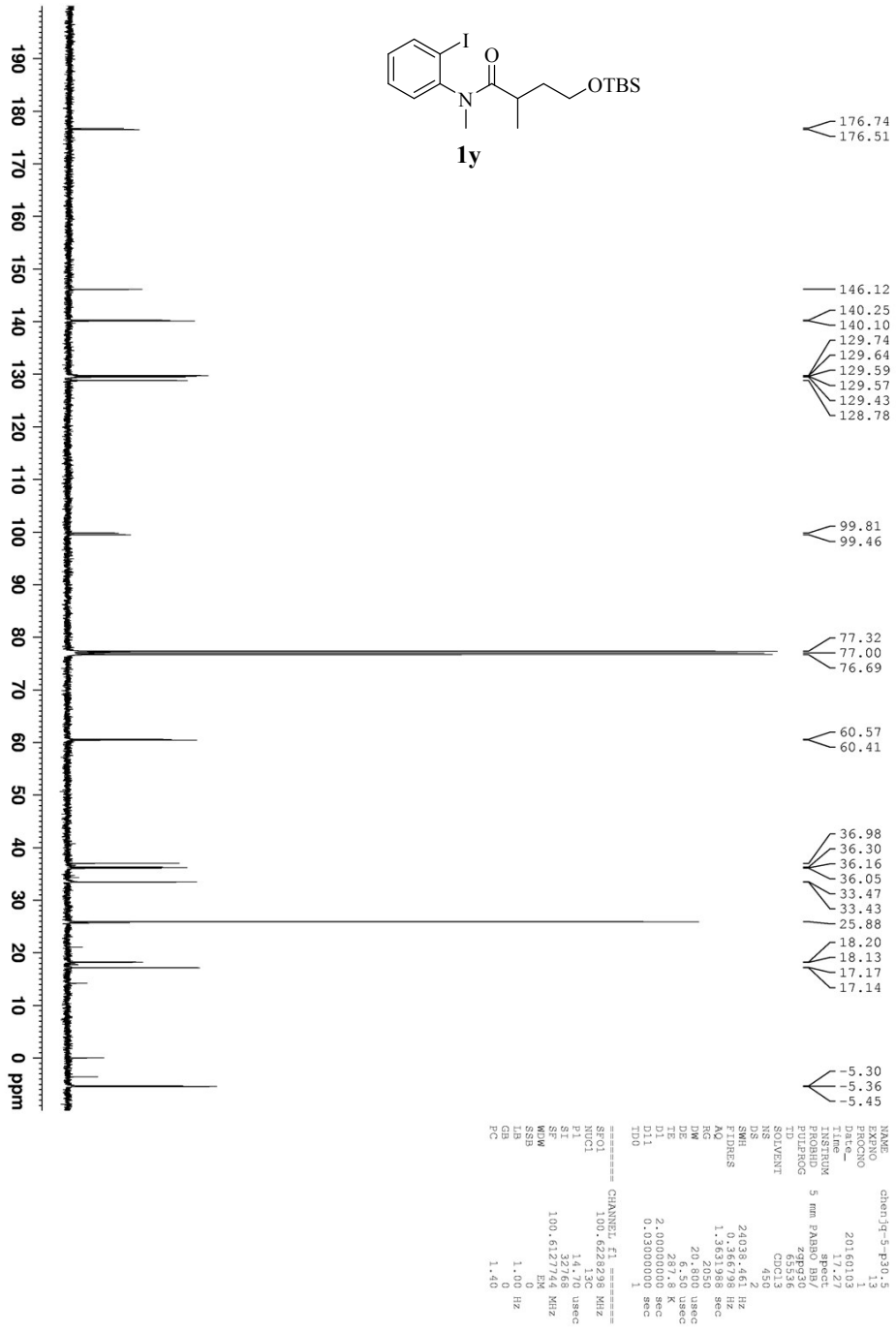

I
O
N
H
OTBS
174.61
138.64
138.17
129.06
125.72
122.00
90.01
77.32
77.00
76.69
60.44
38.73
36.95
25.92
18.21
17.69
-5.31
-5.38
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
NAME chenjg-5-p28.5
EXPNO 15
PROCNO 1
Date_ 20160103
Time 15.47
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 450
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631968 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 288.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6228298 MHz
NUC1 13C
P1 14.70 usec
SI 32768
SF 100.6127824 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

4-((tert-butyldimethylsilyl)oxy)-N-(2-iodophenyl)-N,2-dimethylbutanamide (**1y**)



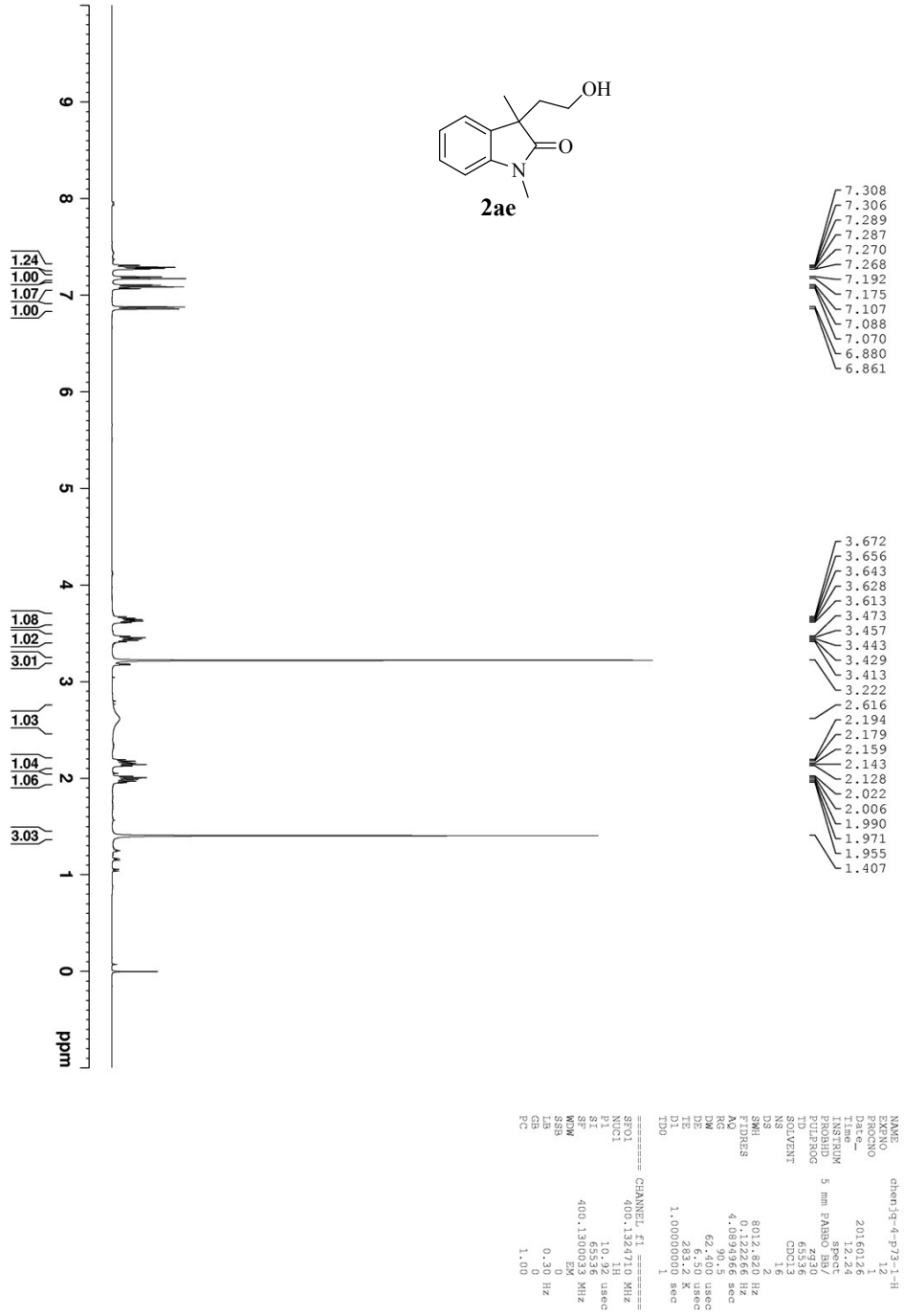
NAME chenjq-5-p30.5
EXPNO 12
PROCNO 1
Date_ 20160103
Time 17.01
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122906 Hz
AQ 4.089496 sec
RG 90.5
DW 62.400 usec
DE 6.50 usec
TE 286.9 K
D1 1.00000000 sec
TD0 1

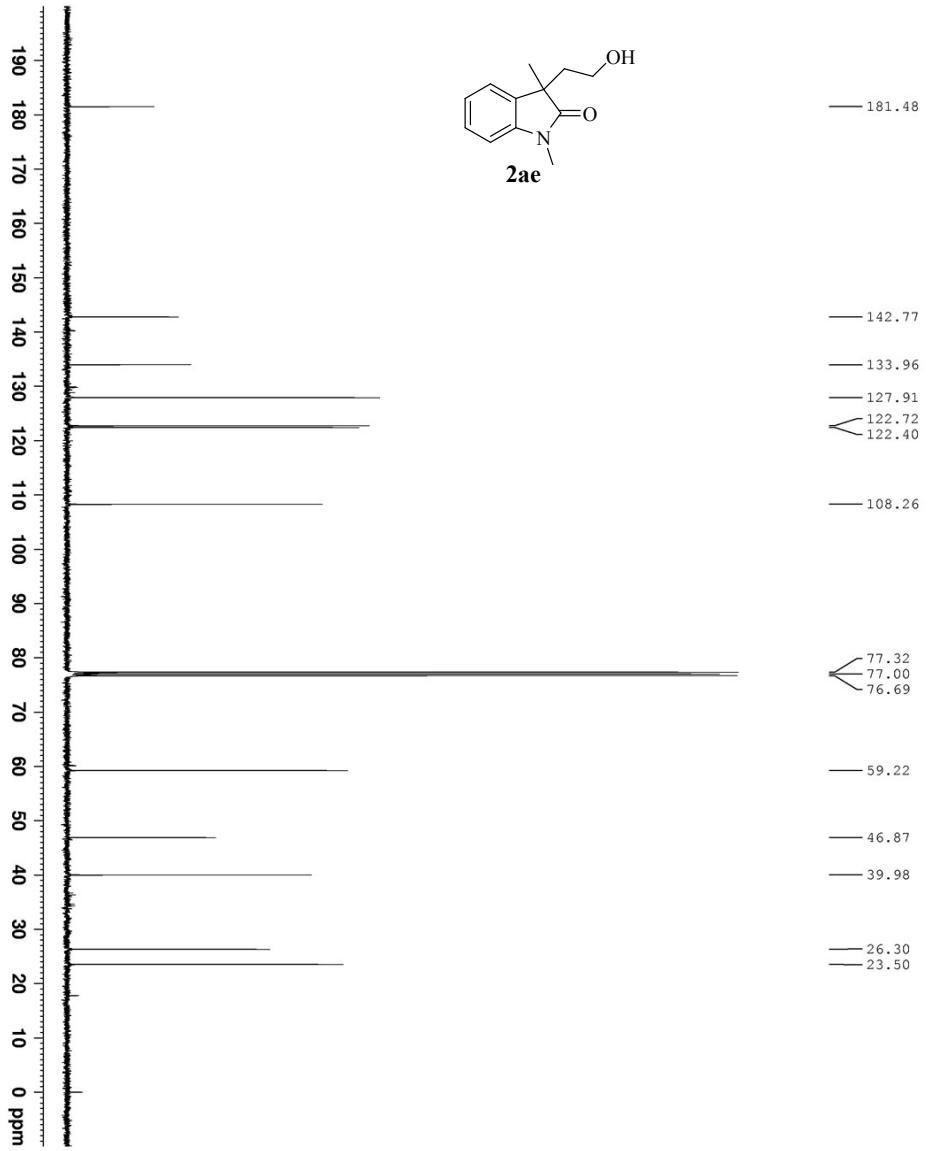
======== CHANNEL f1 ========
SFO1 400.1324710 MHz
NUC1 1H
P1 10.92 usec
SI 65536
SF 400.1300036 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


I
O
N
OTBS
1y
176.74
176.51
146.12
140.25
140.10
129.74
129.64
129.59
129.57
129.43
128.78
99.81
99.46
77.32
77.00
76.69
60.57
60.41
36.98
36.30
36.16
36.05
33.47
33.43
25.88
18.20
18.13
17.17
17.14
-5.30
-5.36
-5.45
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

]

3-(2-hydroxyethyl)-1,3-dimethylindolin-2-one (**2ae**)

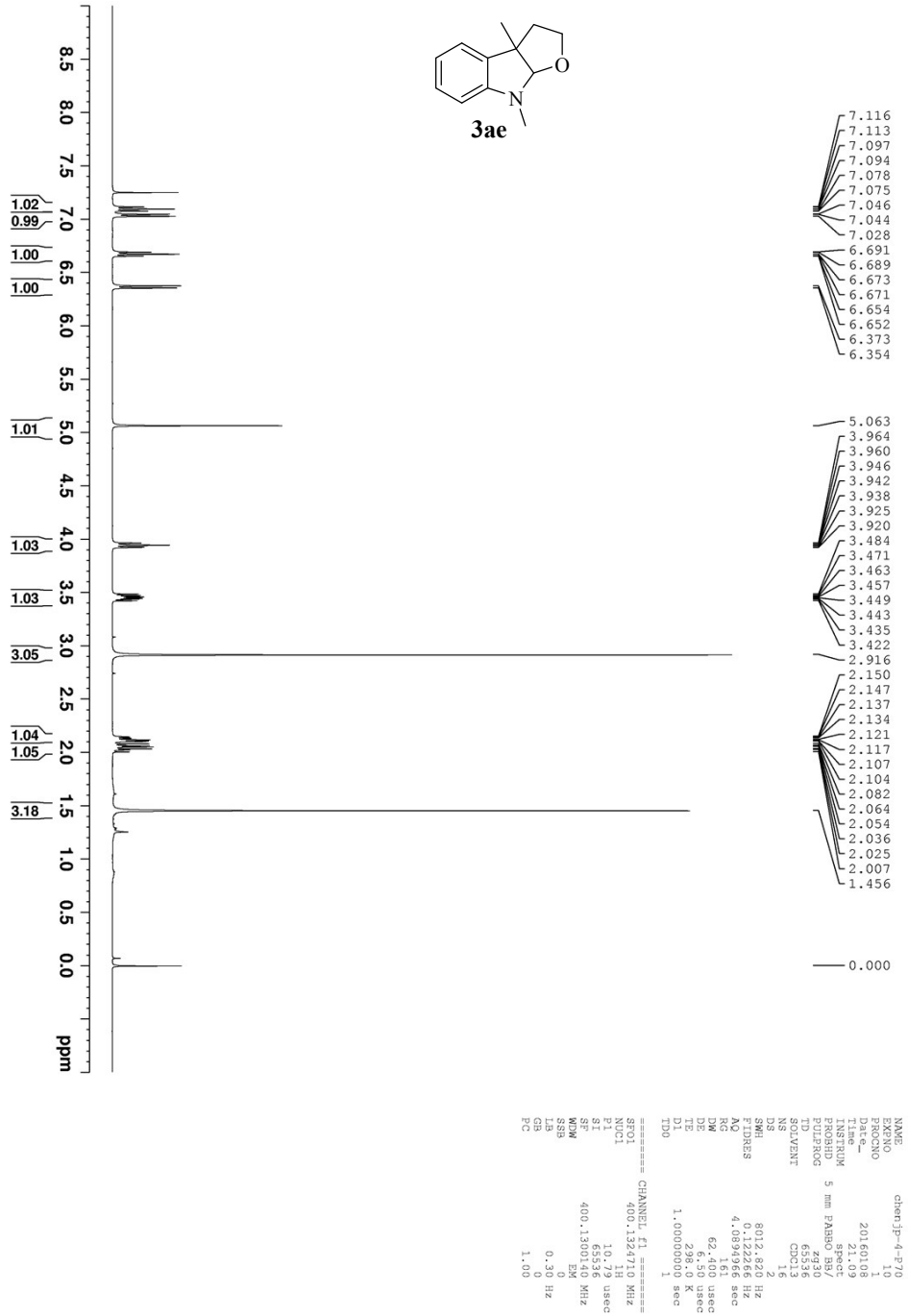


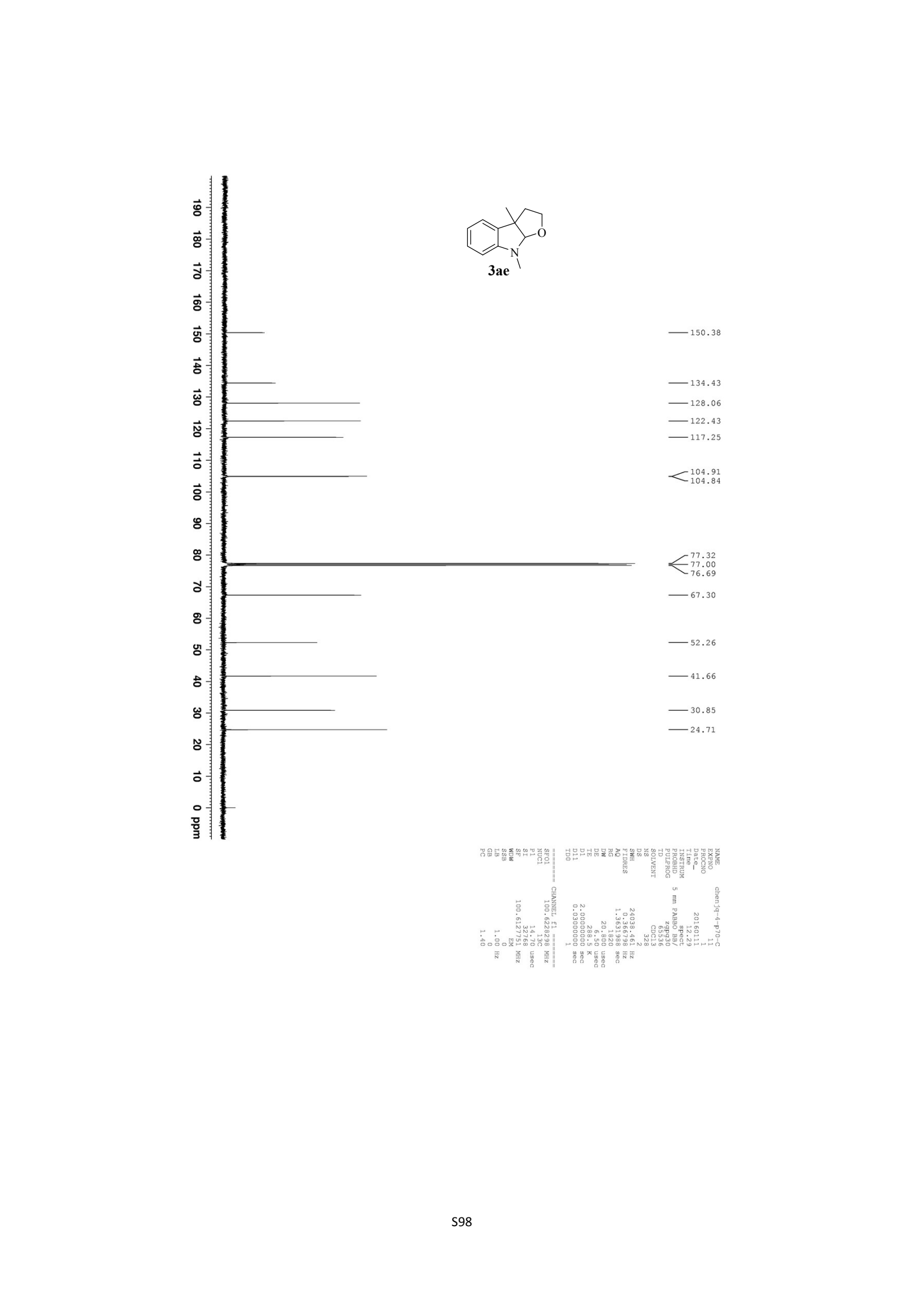



```
NAME                 chenjg-p73-1-c
EXPNO                          11
PROCNO                          1
Date_                    20160126
Time                        20.29
INSTRUM                      spect
PROBHD     5 mm PABBO BB/
PULPROG                  zgpg30
TD                          65536
SOLVENT                     CDCl3
NS                            400
DS                              2
SWH                     24038.461 Hz
FIDRES                   0.366798 Hz
AQ                       1.363008 sec
RG                           203
DW                        20.800 usec
DE                         6.50 usec
TE                        285.5 K
D1                      2.00000000 sec
D11                     0.03000000 sec
TD0                             1

======== CHANNEL f1 ========
SFO1            100.6228298 MHz
NUC1                        13C
P1                        14.70 usec
SI                         32768
SF              100.6127788 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.40
```

3a,8-dimethyl-3,3a,8,8a-tetrahydro-2H-furo[2,3-b]indole (**3ae**)




3ae
150.38
134.43
128.06
122.43
117.25
104.91
104.84
77.32
77.00
76.69
67.30
52.26
41.66
30.85
24.71
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
NAME chenjq-4-p70-C
EXPNO 11
PROCNO 1
Date_ 20160111
Time 12.29
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 328
DS 2
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.363198 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 288.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 100.6228298 MHz
NUC1 13C
P1 14.70 usec
SI 32768
SF 100.6127751 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40