Supporting Information

Synthesis of 3-Acylindoles by Palladium-Catalyzed Acylation of Free (N-H) Indoles with Nitriles

Tao-Shan Jiang and Guan-Wu Wang*

CAS Key Laboratory of Soft Matter Chemistry, Hefei National Laboratory for Physical Sciences at Microscale, and Department of Chemistry, University of Science and Technology of China, Hefei, Anhui 230026, P. R. China

gwang@ustc.edu.cn

List of Contents

1. Experimental Reagents and Instruments

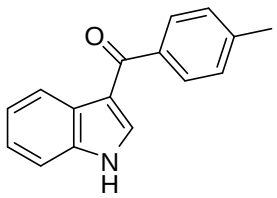
Unless otherwise noted, all reactions were carried out under air atmosphere, commercial materials and solvents were used without further purification. ^{1}H NMR and ^{13}C NMR spectra were measured on a 400 MHz spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz) using DMSO-d_6 as the solvent at room temperature. High-resolution mass spectra (HRMS) were recorded on a BRUKER VPEXII spectrometer with ESI mode.

Some of the products have been reported by other groups (**3aa**,[1] **3ad**,[2] **3af**,[2] **3ah**,[3] **3ai**,[1] **3am**,[4] **3cm**,[4] **3dm**,[4] **3em**,[5] **3fm**[6]**)**. These products were characterized by ^{1}H NMR spectra and confirmed by comparison with the authentic compounds.

2. Experimental Procedures and Spectral Data of Compounds 3

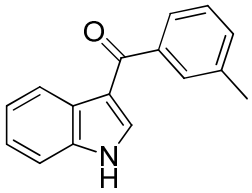
General Procedure for the Acylation of Indoles with Nitriles

A mixture of indole **1** (0.4 mmol), nitrile **2** (0.6 mmol, 1 mL if acetonitrile was used), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14,4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for the desired time. After the reaction was finished, the mixture was filtered by a silica gel plug with ethyl acetate (30 mL) as the eluent. The filtrate was washed with saturated brine (3×10 mL) and organic phase was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography on a silica gel using petroleum ether/EtOAc (4:1 to 1:1) as the eluent to give the desired product **3**.

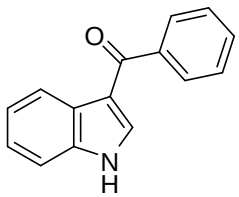


(1*H*-Indol-3-yl)(p-tolyl)methanone (3aa):[1] By following the general procedure, indole (46.8 mg, 0.4 mmol), 4-methylbenzonitrile (70.2 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1

mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (4:1 petroleum ether/EtOAc) to afford the title compound as a brown solid (70.6 mg, 75%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.04 (br, 1H), 8.26-8.24 (m, 1H), 7.94 (d, J = 2.8 Hz, 1H), 7.72 (d, J = 8.0 Hz, 2H), 7.54-7.52 (m, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.29-7.22 (m, 2H), 2.43 (s, 3H).

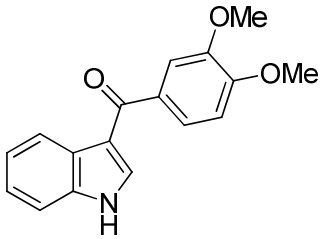


(1*H*-indol-3-yl)(m-tolyl)methanone (3ab): By following the general procedure, indole (46.8 mg, 0.4 mmol), 3-methylbenzonitrile (72.0 µL, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 µL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (4:1 petroleum ether/EtOAc) to afford the title compound as a grey solid (78.1 mg, 83%). m.p. 240 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (br, 1H), 8.26-8.23 (m, 1H), 7.91 (d, J = 2.4 Hz, 1H), 7.57-7.55 (m, 2H), 7.52-7.50 (m, 1H), 7.40-7.38 (m, 2H), 7.26-7.19 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.2, 140.7, 137.8, 136.8, 135.8, 131.7, 128.9, 128.3, 126.3, 125.7, 123.2, 121.9, 121.5, 115.2, 112.3, 21.0; IR (KBr) ν 3145, 2921, 1597, 1571, 1515, 1490, 1434, 1313, 1235, 1174, 1139, 936, 750, 642 cm^{-1}; HRMS (ESI) m/z [M+H^{+}] calcd for $C_{16}H_{14}ON$ 236.1070, found 236.1068.

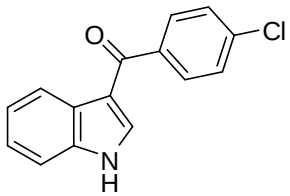


(1*H*-indol-3-yl)(phenyl)methanone (3ad):[2] By following the general procedure, indole (46.8 mg, 0.4 mmol), benzonitrile (61.3 µL, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg,

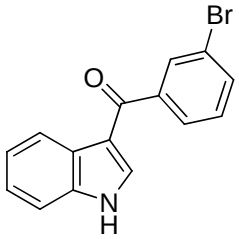
0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol) and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (4:1 petroleum ether/EtOAc) to afford the title compound as a brown solid (65.5 mg, 74%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.08 (br, 1H), 8.28-8.26 (m, 1H), 7.95 (d, J = 3.2 Hz, 1H), 7.82-7.80 (m, 2H), 7.65-7.61 (m, 1H), 7.58-7.53 (m, 3H), 7.31-7.24 (m, 2H).



(3,4-Dimethoxyphenyl)(1*H*-indol-3-yl)methanone (3ae): By following the general procedure, indole (46.8 mg, 0.4 mmol), 3,4-dimethoxybenzonitrile (97.9 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (1:1 petroleum ether/EtOAc) to afford the title compound as a brown solid (81.0 mg, 72%). m.p. 226 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 11.98 (br, 1H), 8.24-8.21 (m, 1H), 7.99 (d, J = 3.2 Hz, 1H), 7.53-7.50 (m, 1H), 7.45 (dd, J = 8.4, 2.0 Hz, 1H), 7.38 (d, J = 2.0 Hz, 1H), 7.27-7.19 (m, 2H), 7.08 (d, J = 8.4 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.8, 151.6, 148.5, 136.7, 134.9, 133.0, 126.5, 123.0, 122.5, 121.7, 121.5, 115.1, 112.2, 111.8, 110.9, 55.7, 55.6; IR (KBr) ν 3167, 2925, 1600, 1566, 1515, 1440, 1379, 1335, 1271, 1247, 1170, 1132, 1021, 836, 773, 741 cm^{-1}; HRMS (ESI) m/z [$M+H^+$] calcd for $C_{17}H_{16}O_3N$ 282.1125, found 282.1123.

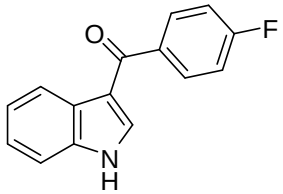


(4-Chlorophenyl)(1*H*-indol-3-yl)methanone (3af):[2] By following the general procedure, indole (46.8 mg, 0.4 mmol), 4-chlorobenzonitrile (82.6 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (4:1 petroleum ether/EtOAc) to afford the title compound as a brown solid (92.1 mg, 90%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.11 (br, 1H), 8.25-8.23 (m, 1H), 7.96 (s, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.53-7.51 (m, 1H), 7.28-7.21 (m, 2H).

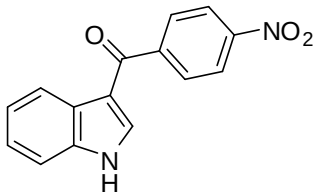


(3-Bromophenyl)(1*H*-indol-3-yl)methanone (3ag): By following the general procedure, indole (46.8 mg, 0.4 mmol), 3-bromobenzonitrile (109.2 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (4:1 petroleum ether/EtOAc) to afford the title compound as a grey solid (109.3 mg, 91%). m.p. 238 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 12.13 (br, 1H), 8.26-8.23 (m, 1H), 7.98 (d, J = 3.2 Hz, 1H), 7.89 (t, J = 1.6 Hz, 1H), 7.81-7.77 (m, 2H), 7.55-7.52 (m, 1H), 7.50 (t, J = 8.0 Hz, 1H), 7.30-7.23 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.2, 142.7, 136.8, 136.3, 133.7, 130.8, 130.7, 127.5, 126.2, 123.4, 122.2, 121.8, 121.5, 114.8, 112.4; IR (KBr) ν 3148, 2924, 1598, 1575, 1558, 1516, 1491, 1434, 1314, 1238, 1210,

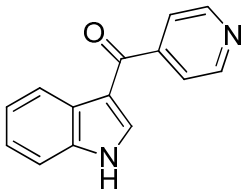
1143, 771, 748, 731 cm^{-1}; HRMS (ESI) m/z [$M+H^+$] calcd for $C_{15}H_{11}ON^{79}Br$ 300.0019, found 300.0019.



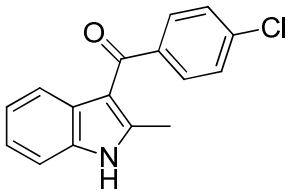
(4-Fluorophenyl)(1*H*-indol-3-yl)methanone (3ah):[3] By following the general procedure, indole (46.8 mg, 0.4 mmol), 4-fluorolbenzonitrile (72.7 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (4:1 petroleum ether/EtOAc) to afford the title compound as a grey solid (81.3 mg, 85%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.09 (br, 1H), 8.26-8.24 (m, 1H), 7.96 (d, J = 2.4 Hz, 1H), 7.90-7.85 (m, 2H), 7.54-7.52 (m, 1H), 7.39-7.33 (m, 2H), 7.29-7.22 (m, 2H).



(1*H*-indol-3-yl)(4-nitrophenyl)methanone (3ai):[1] By following the general procedure, indole (46.8 mg, 0.4 mmol), 4-nitrobenzonitrile (88.9 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (3:1 petroleum ether/EtOAc) to afford the title compound as a pale yellow solid (85.2 mg, 80%). ^1H NMR (400 MHz, DMSO-d_6) δ 12.24 (br, 1H), 8.38 (d, J = 8.8 Hz, 2H), 8.28-8.26 (m, 1H), 8.01 (d, J = 8.8 Hz, 2H), 7.99 (s, 1H), 7.56-7.54 (m, 1H), 7.32-7.26 (m, 2H).

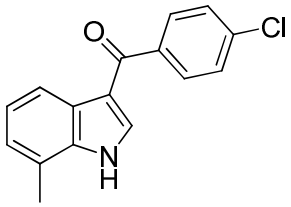


(1*H*-Indol-3-yl)(pyridin-4-yl)methanone (3aj): By following the general procedure, indole (46.8 mg, 0.4 mmol), isonicotinonitrile (62.5 mg, 0.6 mmol), $Pd(OAc)_2$ (8.8 mg, 0.04 mmol), 2,2'-bipyridine (7.5 mg, 0.048 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 48 h. After filtered, washed and dried, the crude product was purified by flash column chromatography (1:1 petroleum ether/EtOAc) to afford the title compound as a reddish brown solid (54.2 mg, 61%). m.p. 239 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 12.24 (br, 1H), 8.80-7.78 (m, 2H), 8.31-8.26 (m, 1H), 8.02 (d, J = 3.2 Hz, 1H), 7.71-7.69 (m, 2H), 7.58-7.53 (m, 1H), 7.33-7.27 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.6, 150.3 (2C), 147.1, 137.1, 137.0, 126.0, 123.7, 122.5, 122.2 (2C), 121.5, 114.7, 112.5; IR (KBr) v 3149, 3046, 2923, 1598, 1574, 1545, 1515, 1490, 1430, 1310, 1217, 1142, 899, 755, 719, 689, 636 cm^{-1}; HRMS (ESI) m/z [$M+H^+$] calcd for $C_{14}H_{11}ON_2$ 223.0866, found 223.0865.

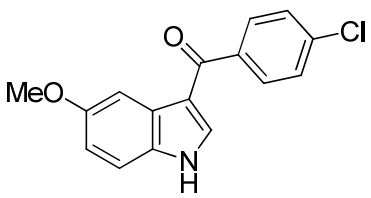


(4-Chlorophenyl)(2-methyl-1*H*-indol-3-yl)methanone (3bf): By following the general procedure, 2-methylindole (52.5 mg, 0.4 mmol), 4-chlorobenzonitrile (82.6 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 48 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (3:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (78.8 mg, 73%). m.p. 185 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 11.98 (br, 1H), 7.62 (d, J = 8.8 Hz, 2H), 7.56 (d, J = 8.8 Hz, 2H), 7.39 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.12 (m,

1H), 7.03 (m, 1H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.4, 144.8, 140.3, 135.9, 135.0, 130.1 (2C), 128.6 (2C), 127.2, 122.0, 121.2, 120.0, 112.3, 111.4, 14.3; IR (KBr) ν 3175, 3102, 1593, 1574, 1559, 1486, 1451, 1417, 1212, 1092, 962, 883, 825, 783, 744 cm^{-1}; HRMS (ESI) m/z [M+H$^+$] calcd for $C_{16}H_{13}ON^{35}Cl$ 270.0680, found 270.0678.

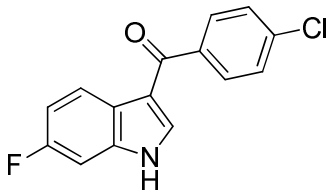


(4-Chlorophenyl)(7-methyl-1*H*-indol-3-yl)methanone (3cf): By following the general procedure, 7-methylindole (52.5 mg, 0.4 mmol), 4-chlorobenzonitrile (82.6 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed and dried, the crude product was purified by flash column chromatography (2:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (92.8 mg, 86%). m.p. 220 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (br, 1H), 8.07 (d, J = 8.0 Hz, 1H), 7.92 (d, J = 3.2 Hz, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.15 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 7.2 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.8, 139.3, 136.3, 135.9, 135.5, 130.3 (2C), 128.5 (2C), 126.0, 123.9, 122.3, 121.7, 119.0, 115.3, 16.7; IR (KBr) ν 3156, 2940, 2891, 1598, 1556, 1520, 1453, 1378, 1217, 1162, 1087, 1009, 891, 846, 785, 745 cm^{-1}; HRMS (ESI) m/z [M+H$^+$] calcd for $C_{16}H_{13}ON^{35}Cl$ 270.0680, found 270.0681.



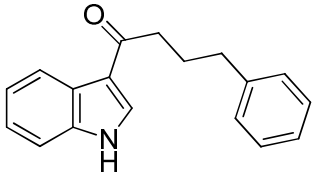
(4-Chlorophenyl)(5-methoxy-1*H*-indol-3-yl)methanone (3df): By following the

general procedure, 5-methoxyindole (58.9 mg, 0.4 mmol), 4-chlorobenzonitrile (82.6 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (3:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (88.0 mg, 77%). m.p. 219 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 12.02 (br, 1H), 7.91 (d, J = 3.2 Hz, 1H), 7.80 (d, J = 8.4 Hz, 2H), 7.78 (s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.8 Hz, 1H), 6.91 (dd, J = 8.8, 2.4 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.6, 155.7, 139.3, 136.1, 135.8, 131.6, 130.2 (2C), 128.5 (2C), 127.1, 114.7, 113.2, 113.1, 103.3, 55.4; IR (KBr) v 3180, 2938, 1624, 1594, 1559, 1511, 1468, 1429, 1275, 1217, 1174, 1068, 1018, 894, 845, 845, 810, 762, 696 cm^{-1}; HRMS (ESI) m/z [$M+H^+$] calcd for $C_{16}H_{13}O_2N^{35}Cl$ 286.0629, found 286.0627.

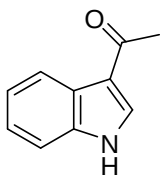


(4-Chlorophenyl)(6-fluoro-1*H*-indol-3-yl)methanone (3ef): By following the general procedure, 6-fluoroindole (54.1 mg, 0.4 mmol), 4-chlorobenzonitrile (82.6 mg, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^oC for 48 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (2:1 petroleum ether/EtOAc) to afford the title compound as a brown solid (82.5 mg, 75%). m.p. 251 ^oC; ^1H NMR (400 MHz, DMSO-d_6) δ 12.16 (br, 1H), 8.22 (dd, J = 8.8, 5.6 Hz, 1H), 7.98 (s, 1H), 7.30 (dd, J = 9.6, 2.4 Hz, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 7.32 (dd, J = 9.6, 2.4 Hz, 1H), 7.10 (ddd, J = 9.6, 8.8, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 188.6, 159.5 (d, $^1J_{C\text{-}F}$ = 237.4 Hz), 138.9, 136.8 (d, $^3J_{C\text{-}F}$ = 12.6 Hz), 136.7 (d, $^4J_{C\text{-}F}$ = 2.1 Hz), 136.1, 130.3 (2C), 128.6 (2C), 122.9, 122.7 (d,

$^{3}J_{C\text{-}F}$ = 10.0 Hz), 114.8, 110.4 (d, $^{2}J_{C\text{-}F}$ = 23.9 Hz), 98.6 (d, $^{2}J_{C\text{-}F}$ = 25.8 Hz); IR (KBr) *v* 3204, 2932, 1608, 1560, 1523, 1433, 1275, 1206, 1151, 1111, 1085, 1009, 950, 885, 841, 765, 724, 684 cm^{-1}; HRMS (ESI) m/z [M+H^+] calcd for $C_{15}H_{10}ON^{35}ClF$ 274.0430, found 274.0428.

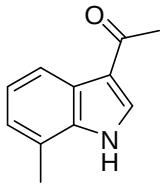


1-(1*H*-indol-3-yl)-4-phenylbutan-1-one (3al): By following the general procedure, indole (46.8 mg, 0.4 mmol), 4-phenylbutanenitrile (89.5 μL, 0.6 mmol), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (3:1 petroleum ether/EtOAc) to afford the title compound as a brown solid (52.5 mg, 50%). m.p. 190 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (br, 1H), 8.26 (d, *J* = 3.2 Hz, 1H), 8.21-8.19 (m, 1H), 7.48-7.45 (m, 1H), 7.31-7.27 (m, 2H), 7.23-7.15 (m, 5H), 2.88 (t, *J* = 7.6 Hz, 2H), 2.68-2.64 (m, 2H), 1.99-1.93 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.1, 142.0, 136.7, 133.7, 128.4 (2C), 128.3 (2C), 125.8, 125.4, 122.7, 121.7, 121.4, 116.4, 112.1, 38.3, 34.9, 26.7; IR (KBr) *v* 3175, 2927, 1619, 1577, 1521, 1492, 1440, 1309, 1238, 1146, 944, 749, 700 cm^{-1}; HRMS (ESI) m/z [M+H^+] calcd for $C_{18}H_{18}ON$ 264.1383, found 264.1382.

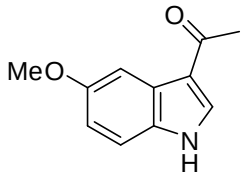


1-(1*H*-indol-3-yl)ethanone (3am):[4] By following the general procedure, indole (46.8 mg, 0.4 mmol), acetonitrile (1 mL), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O

(14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (1:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (60.5 mg, 95%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (br, 1H), 8.28 (d, J = 2.0 Hz, 1H), 8.18-8.16 (m, 1H), 7.47-7.45 (m, 1H), 7.22-7.14 (m, 2H), 2.44 (s, 3H).

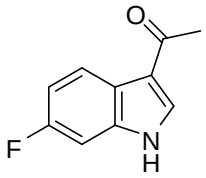


1-(7-Methyl-1*H*-indol-3-yl)ethanone (3cm):[5] By following the general procedure, 7-methylindole (52.5 mg, 0.4 mmol), acetonitrile (1 mL), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (2:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (64.6 mg, 93%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (br, 1H), 8.29 (d, J = 3.2 Hz, 1H), 8.01 (d, J = 8.0 Hz, 1H), 7.08 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 2.50 (s, 3H), 2.46 (s, 3H).

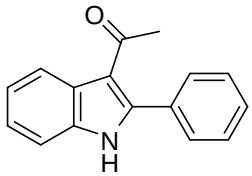


1-(5-Methoxy-1*H*-indol-3-yl)ethanone (3dm):[4] By following the general procedure, 5-methoxyindole (58.9 mg, 0.4 mmol), acetonitrile (1 mL), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (2:1 petroleum ether/EtOAc) to afford the title

compound as a off-white solid (66.5 mg, 88%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.79 (br, 1H), 8.24 (d, J = 3.2 Hz, 1H), 7.70 (d, J = 2.4 Hz, 1H), 7.37 (d, J = 8.8 Hz, 1H), 6.85 (dd, J = 8.8, 2.4 Hz, 1H), 3.79 (s, 3H), 2.44 (s, 3H).



1-(6-Fluoro-1*H*-indol-3-yl)ethanone (3em):[5] By following the general procedure, 6-fluoroindole (54.1 mg, 0.4 mmol), acetonitrile (1 mL), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 36 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (2:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (53.9 mg, 76%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.96 (br, 1H), 8.32 (s, 1H), 8.16 (dd, J = 8.8, 6.0 Hz, 1H), 7.26 (dd, J = 10.0, 2.0 Hz, 1H), 7.07-7.02 (m, 1H), 2.45 (s, 3H).



1-(2-Phenyl-1*H*-indol-3-yl)ethanone (3fm):[6] By following the general procedure, 2-phenyl-1*H*-indole (77.3 mg, 0.4 mmol), acetonitrile (1 mL), $Pd(OAc)_2$ (4.4 mg, 0.02 mmol), 2,2'-bipyridine (3.7 mg, 0.024 mmol), D-(+)-camphorsulfonic acid (139.4 mg, 0.6 mmol), and H_2O (14.4 μL, 0.8 mmol) in *N*-methylacetamide (1 mL) was stirred at 120 ^{o}C for 48 h. After filtered, washed, and dried, the crude product was purified by flash column chromatography (3:1 petroleum ether/EtOAc) to afford the title compound as a off-white solid (86.6 mg, 92%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (br, 1H), 8.21-8.19 (m, 1H), 7.65-7.62 (m, 2H), 7.56-7.54 (m, 3H), 7.43-7.41 (m, 1H), 7.24-7.17 (m, 2H), 2.07 (s, 3H).

3. References

(1) Katritzky, A. R.; Suzuki, K.; Singh, S. K.; He, H. Y. *J. Org. Chem.* **2003**, *68*, 5720.

(2) Guchhait, S. K.; Kashyap, M.; Kamble, H. *J. Org. Chem.* **2011**, *76*, 4753.

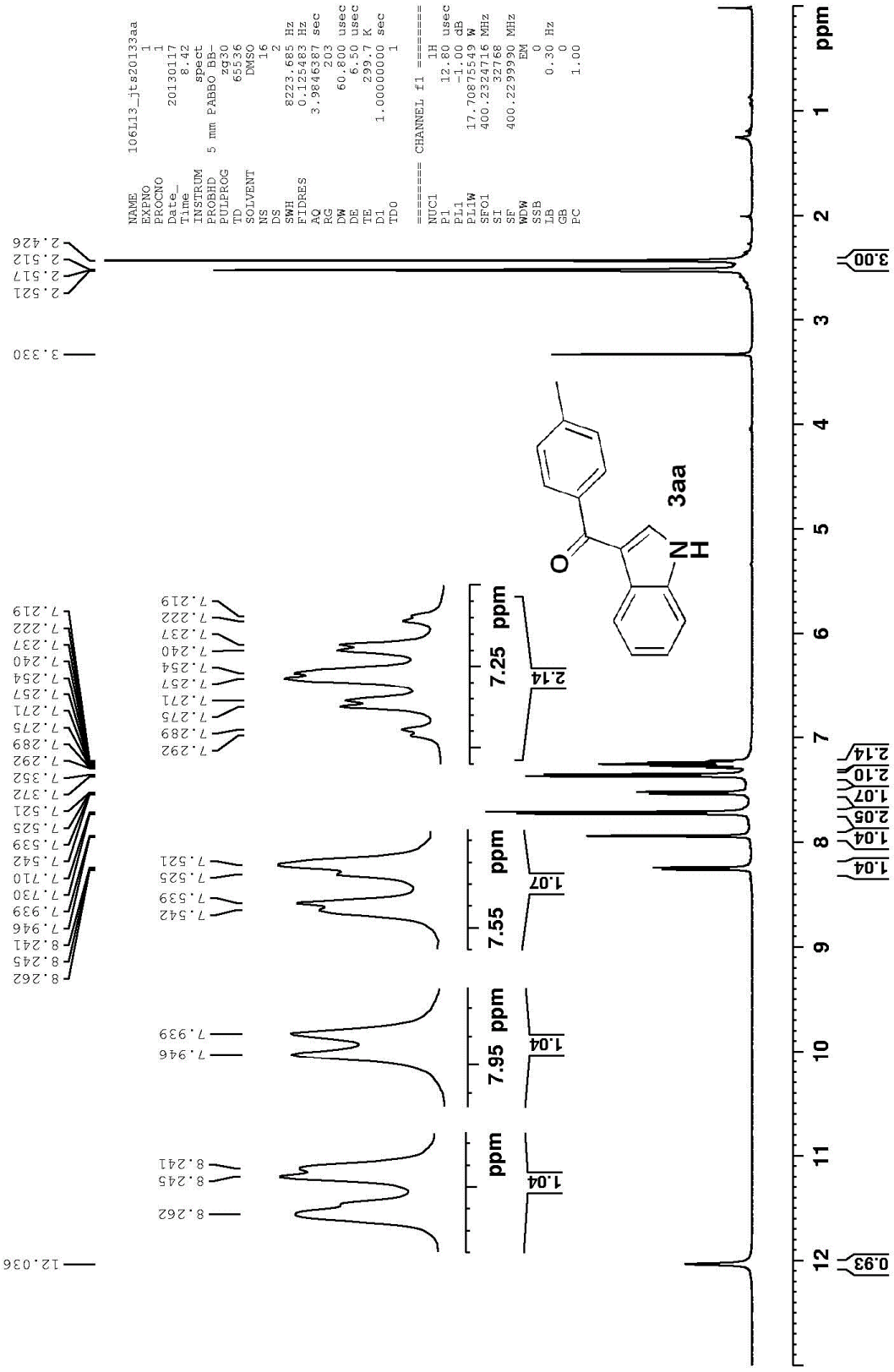
(3) Yang, C. X.; Patel, H. H.; Ku, Y. Y.; Shah, R.; Sawick, D. *Synth. Commun.* **1997**, *27*, 2125.

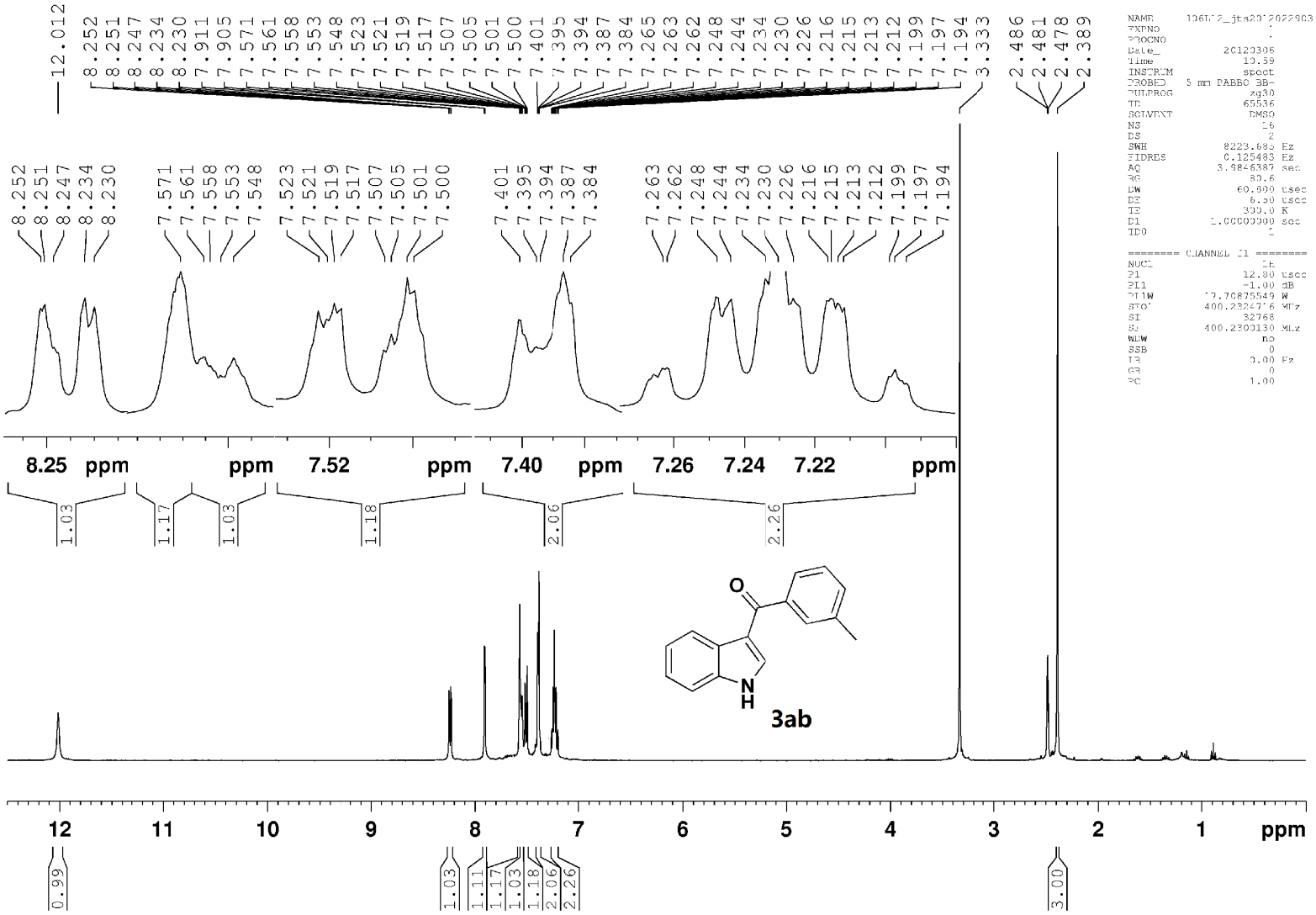
(4) Okauchi, T.; Itonaga, M.; Minami, T.; Owa, T.; Kitoh, K.; Yoshino, H. *Org. Lett.* **2000**, *2*, 1485.

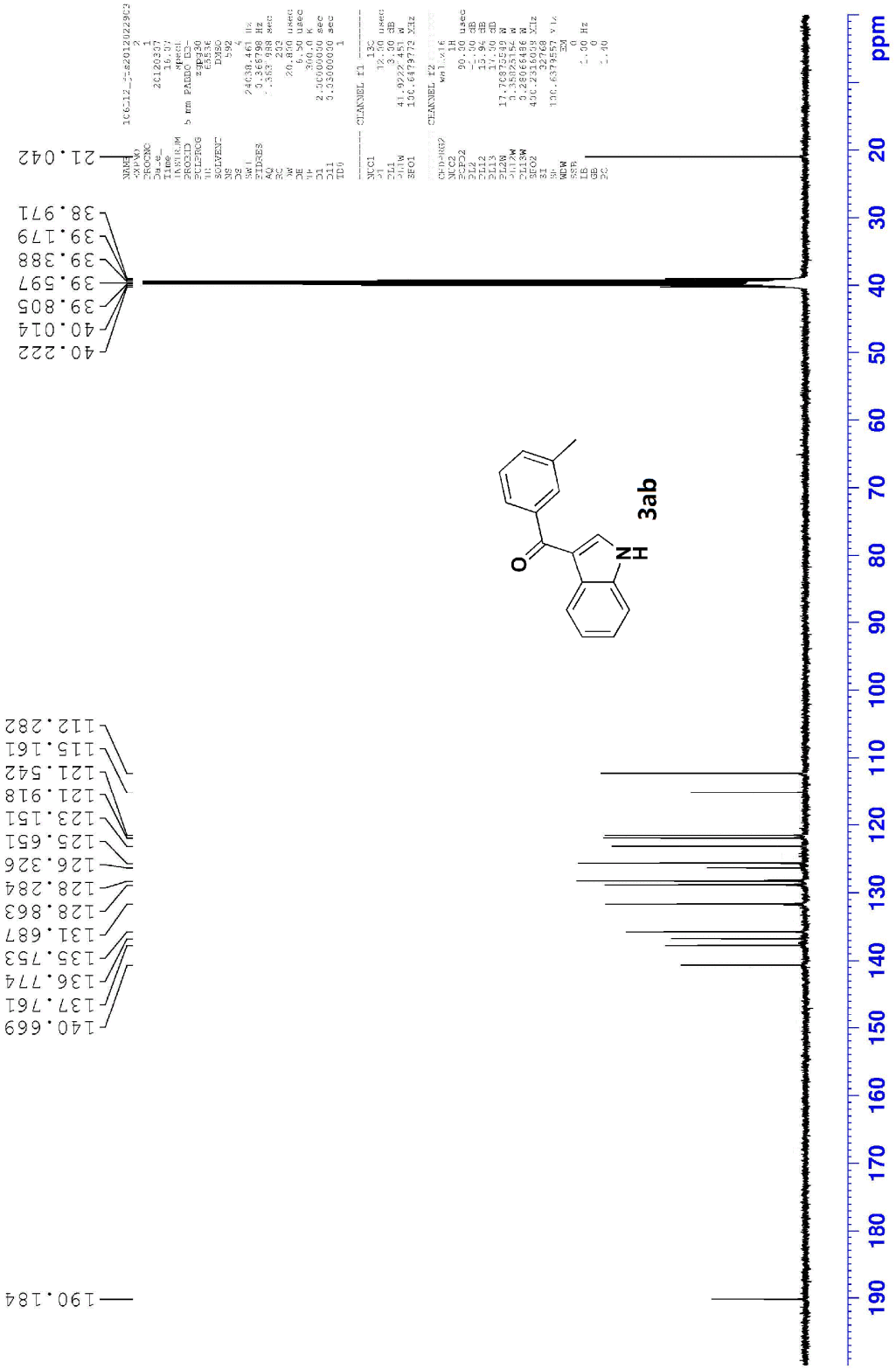
(5) Zhang, F.; Zhao, Y.; Sun, L.; Ding, L.; Gu, Y.; Gong, P. *Eur. J. Med. Chem.* **2011**, *46*, 3149.

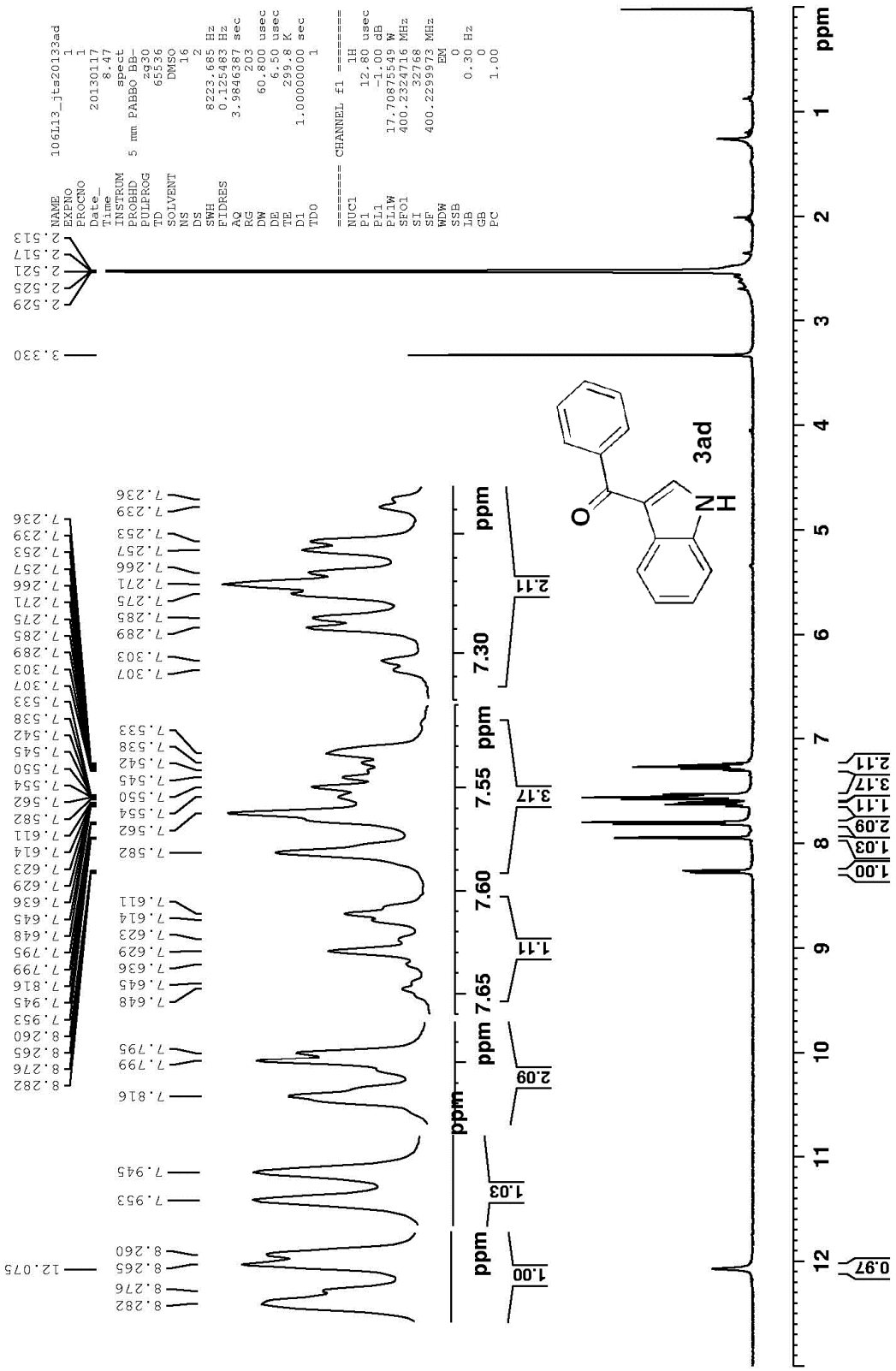
(6) Kim, T.; Kim, K. *Tetrahedron Lett.* **2010**, *51*, 868.

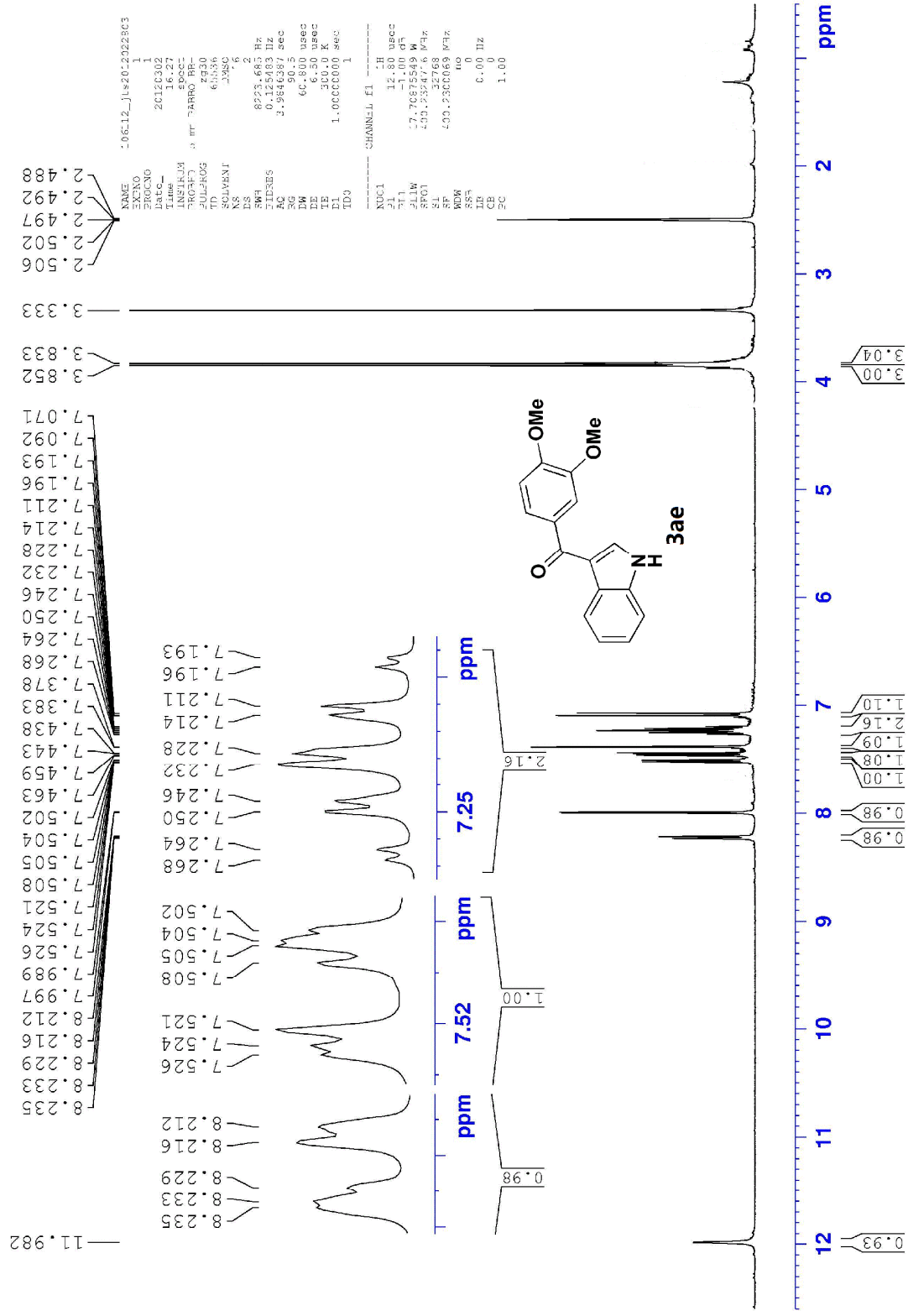
4 NMR Spectra of Compounds 3

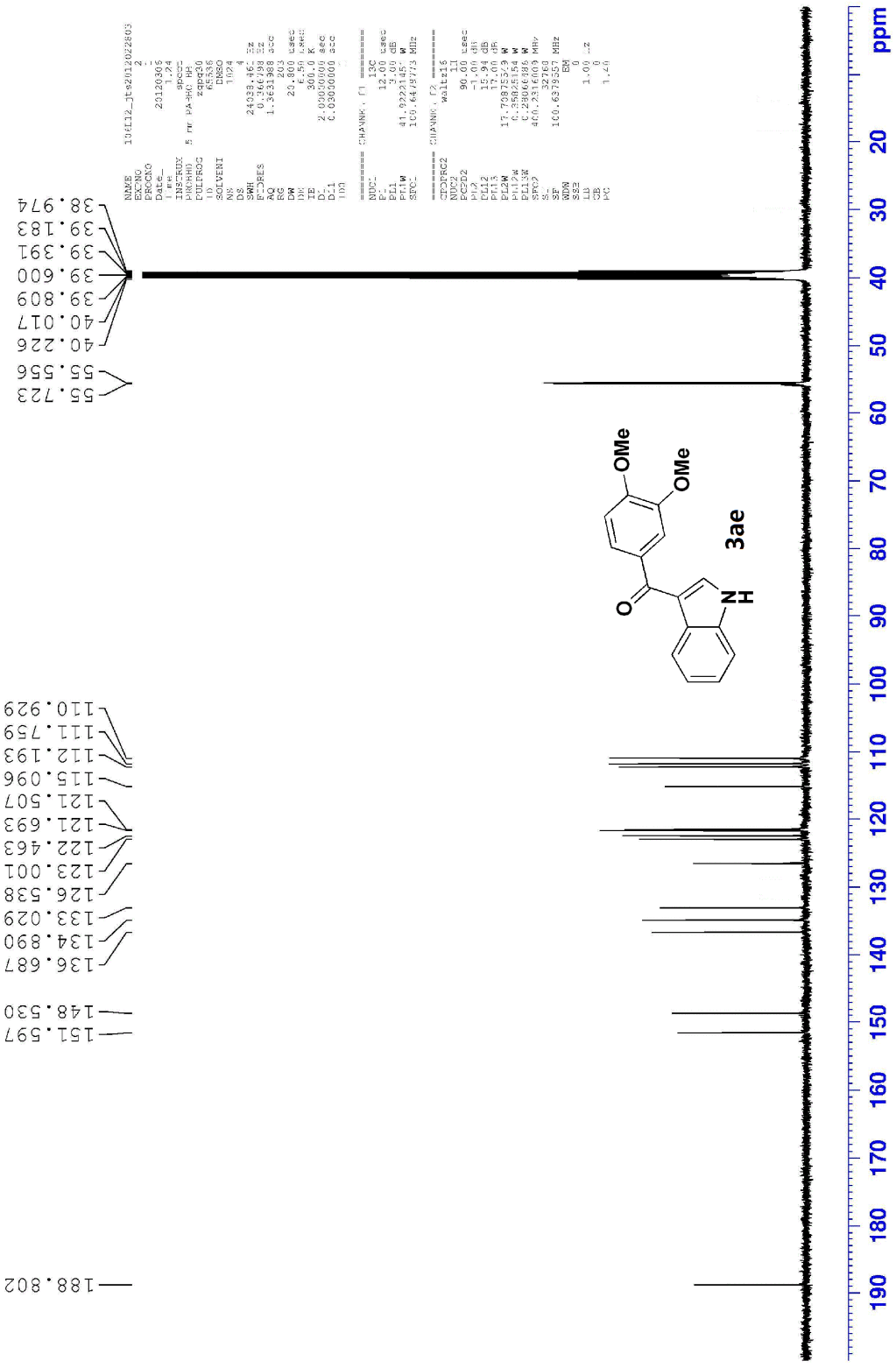


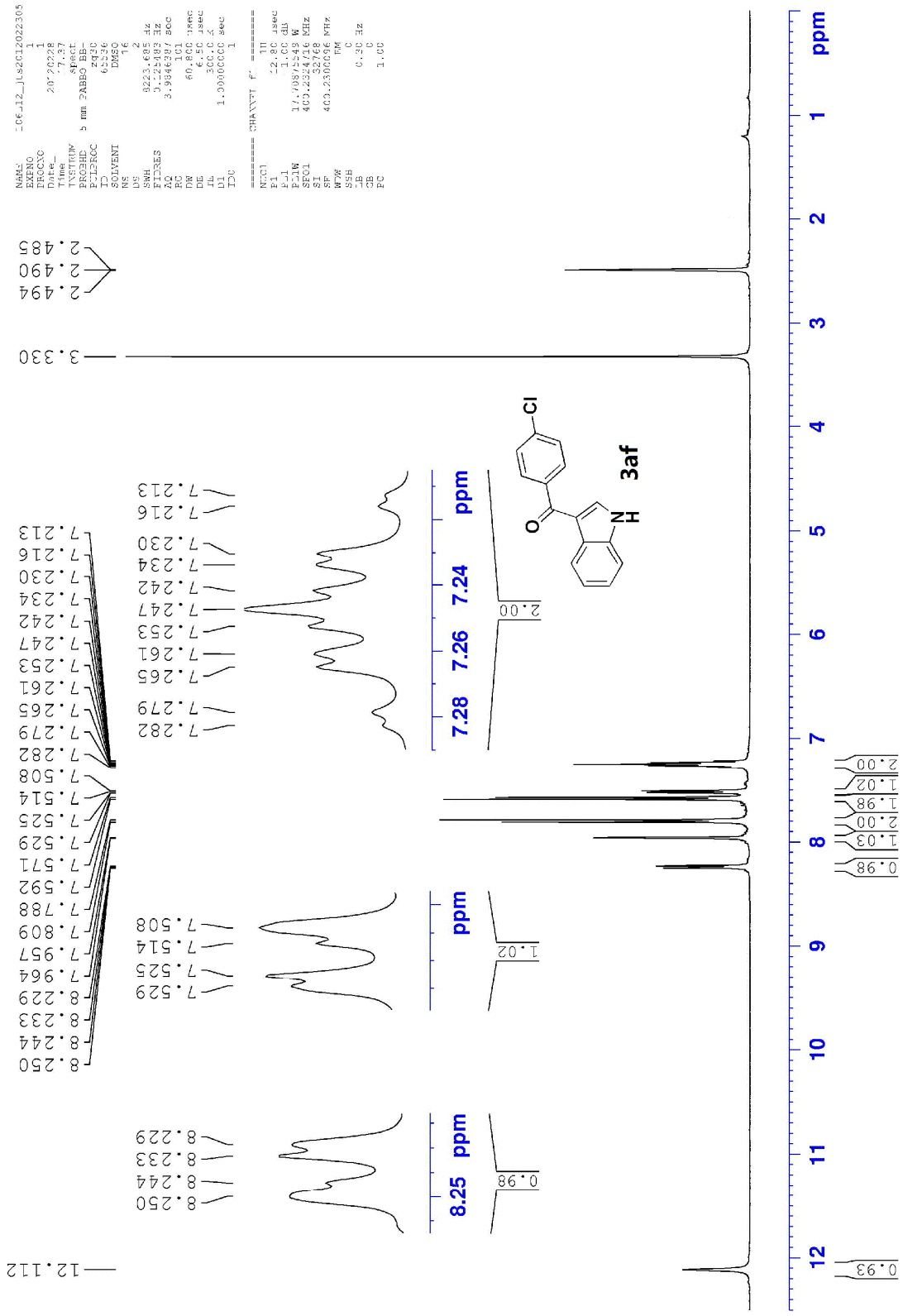

12.012
8.252
8.251
8.247
8.234
8.230
7.911
7.905
7.571
7.561
7.558
7.553
7.548
7.523
7.521
7.519
7.517
7.507
7.505
7.501
7.500
7.401
7.395
7.394
7.387
7.384
7.263
7.262
7.248
7.244
7.234
7.230
7.226
7.216
7.215
7.213
7.212
7.199
7.197
7.194
3.333
2.486
2.481
2.478
2.389
8.25 ppm
7.52 ppm
7.40 ppm
7.26 7.24 7.22 ppm
1.03
1.17
1.03
1.18
2.06
2.26
O
N
H
3ab
12 11 10 9 8 7 6 5 4 3 2 1 ppm
0.99
1.03
1.11
1.17
1.03
1.18
2.06
2.26
3.00
NAME 106L12_jts20120229_03
EXPNO 1
PROCNO 1
Date_ 20120306
Time 10.59
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846587 sec
RG 80.6
DW 60.800 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.80 usec
PL1 -1.00 dB
PL1W 17.70875549 W
SFO1 400.2324716 MHz
SI 32768
SF 400.2300130 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

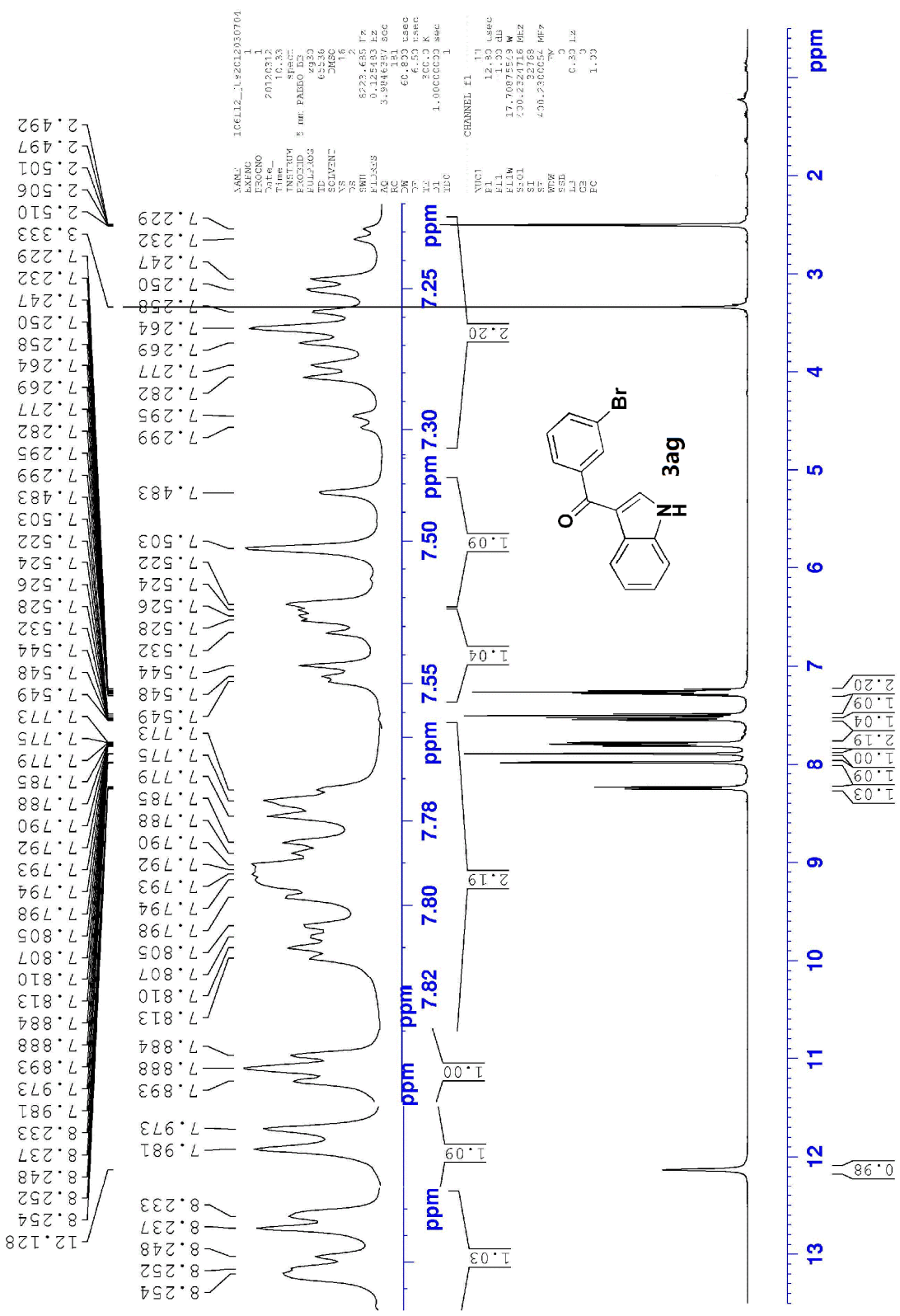

21.042
38.971
39.179
39.388
39.597
39.805
40.014
40.222
112.282
115.161
121.542
121.918
123.151
125.651
126.326
128.284
128.863
131.687
135.753
136.774
137.761
140.669
190.184
3ab
O
N
H
ppm

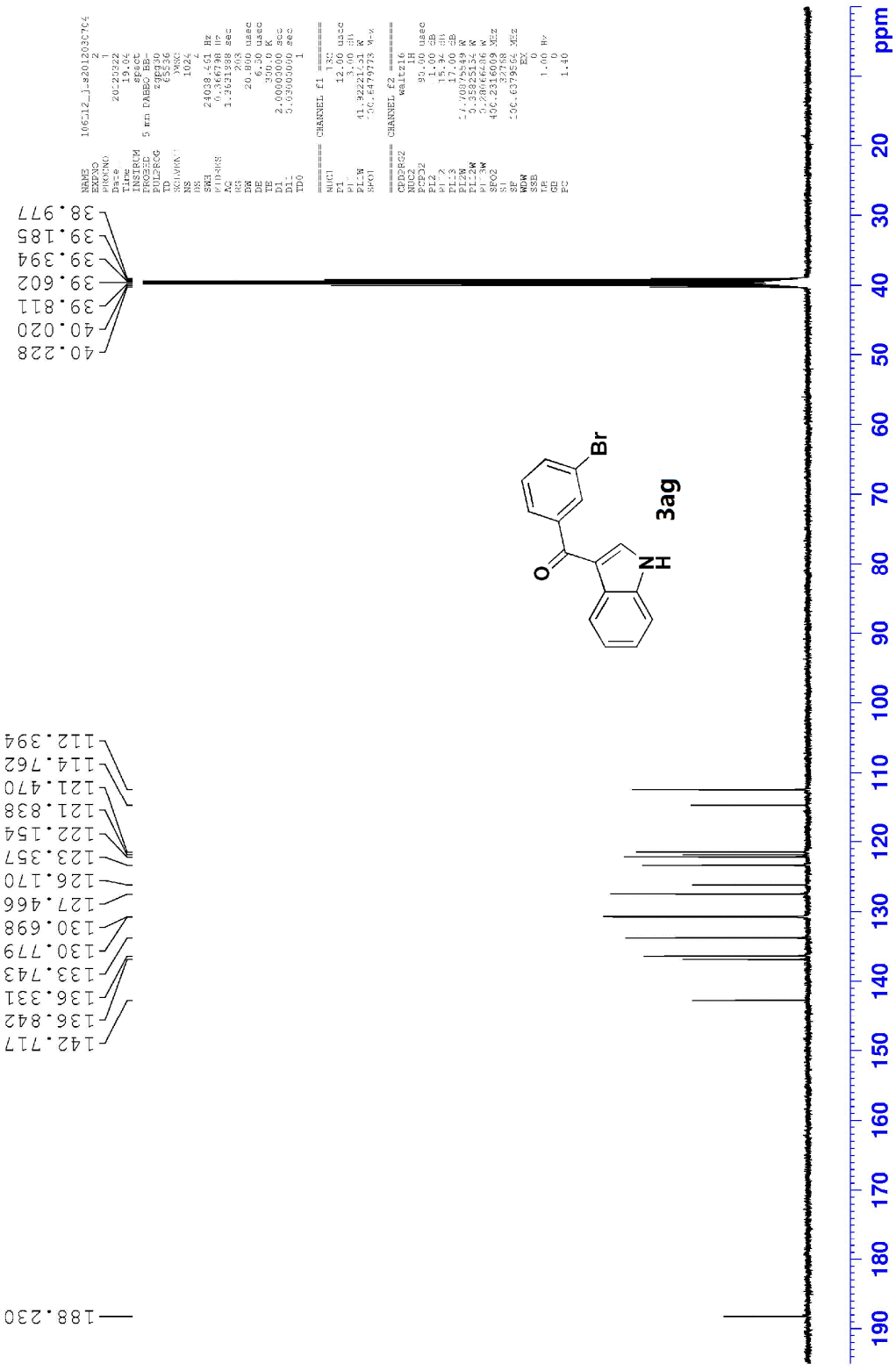

NAME 106l13_jta20133ad
EXPNO 1
PROCNO 1
Date_ 20130117
Time 8.47
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 299.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.80 usec
PL1 -1.00 dB
PL1W 17.70875549 W
SFO1 400.2324716 MHz
SI 32768
SF 400.2299973 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3ad
ppm
1.00
1.03
2.09
1.11
3.17
2.11
0.97

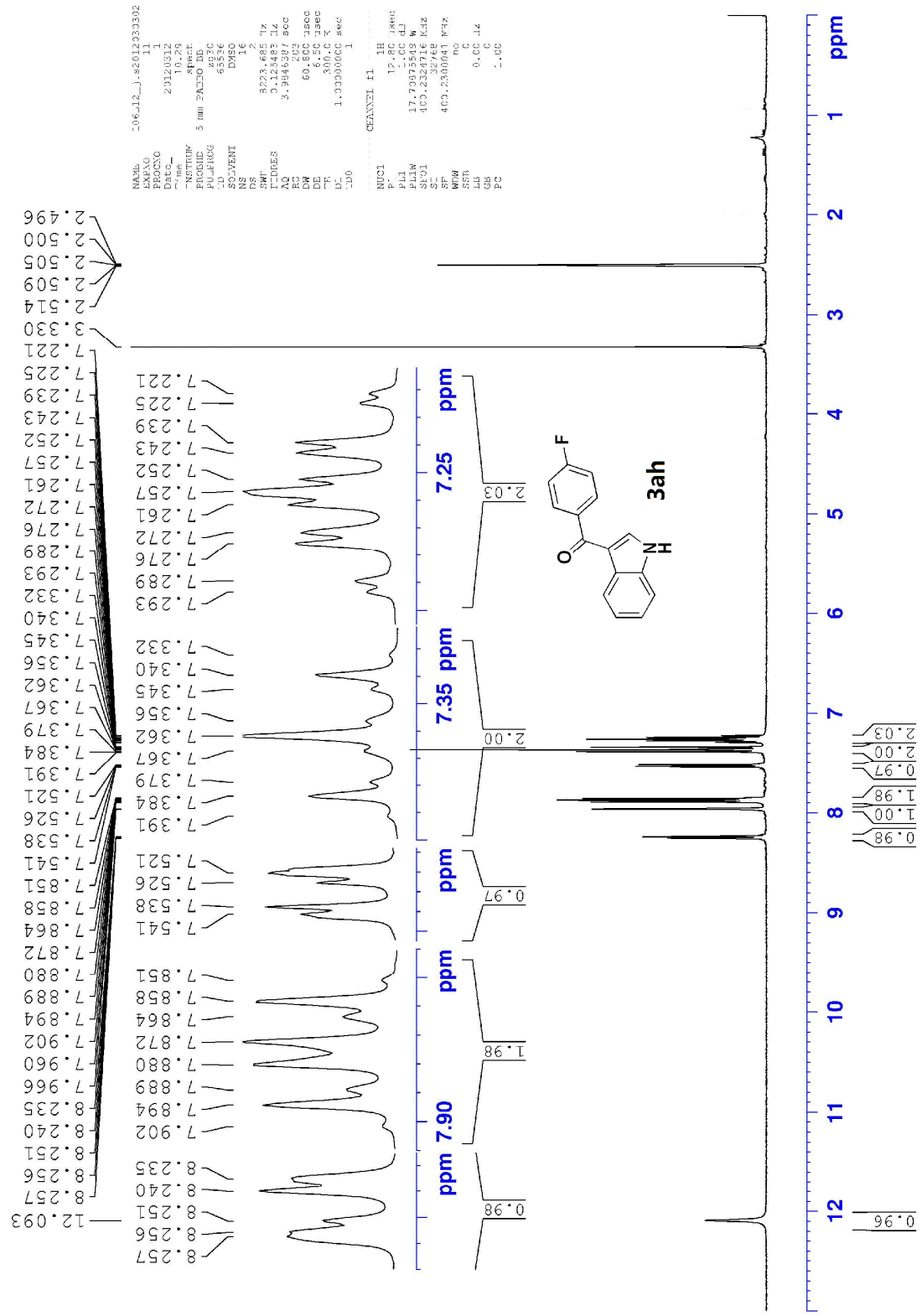

OMe
OMe
O
N
H
3ae
ppm
7.25
7.52
2.16
1.00
0.98

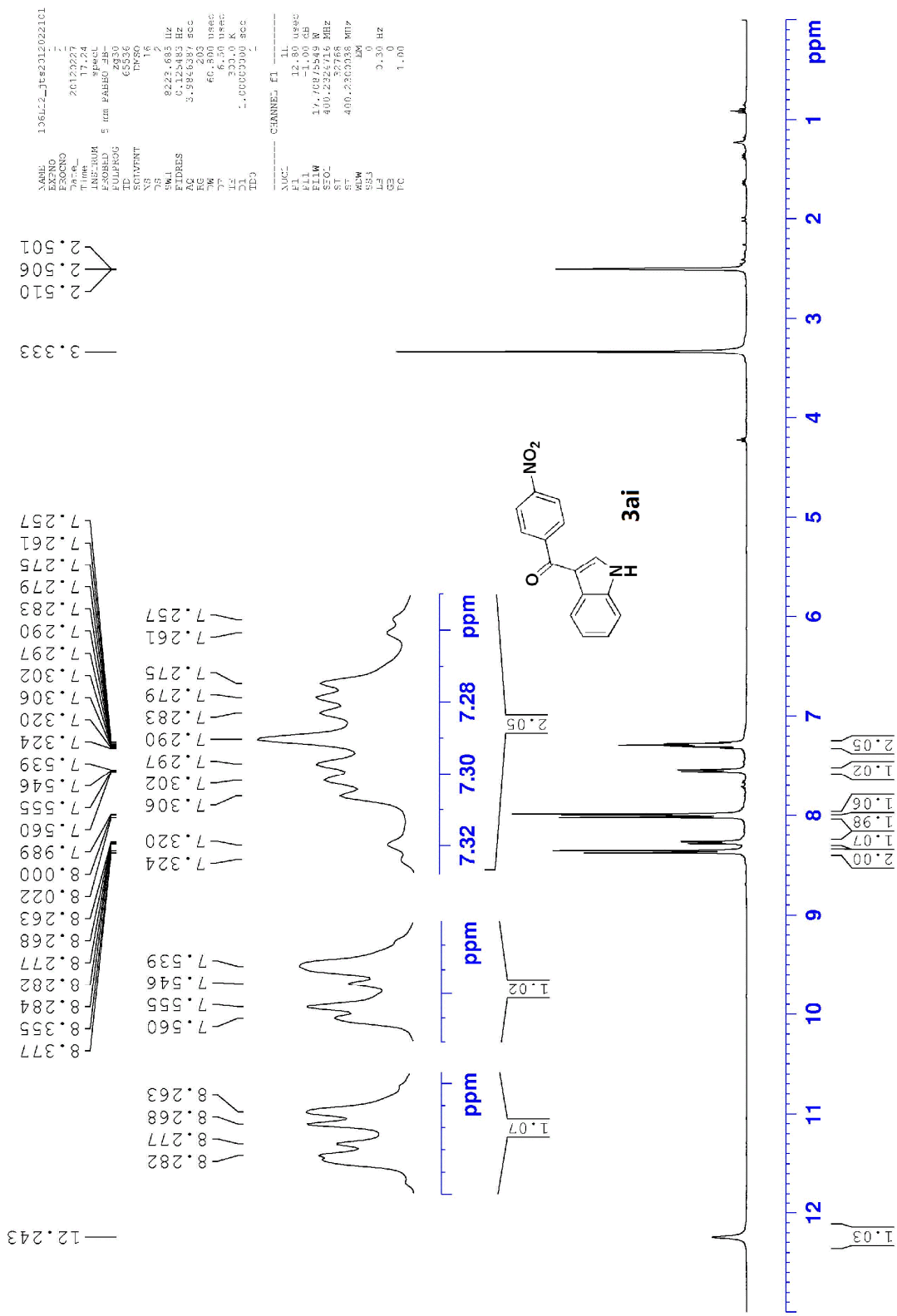

OMe
OMe
O
N
H
3ae
ppm

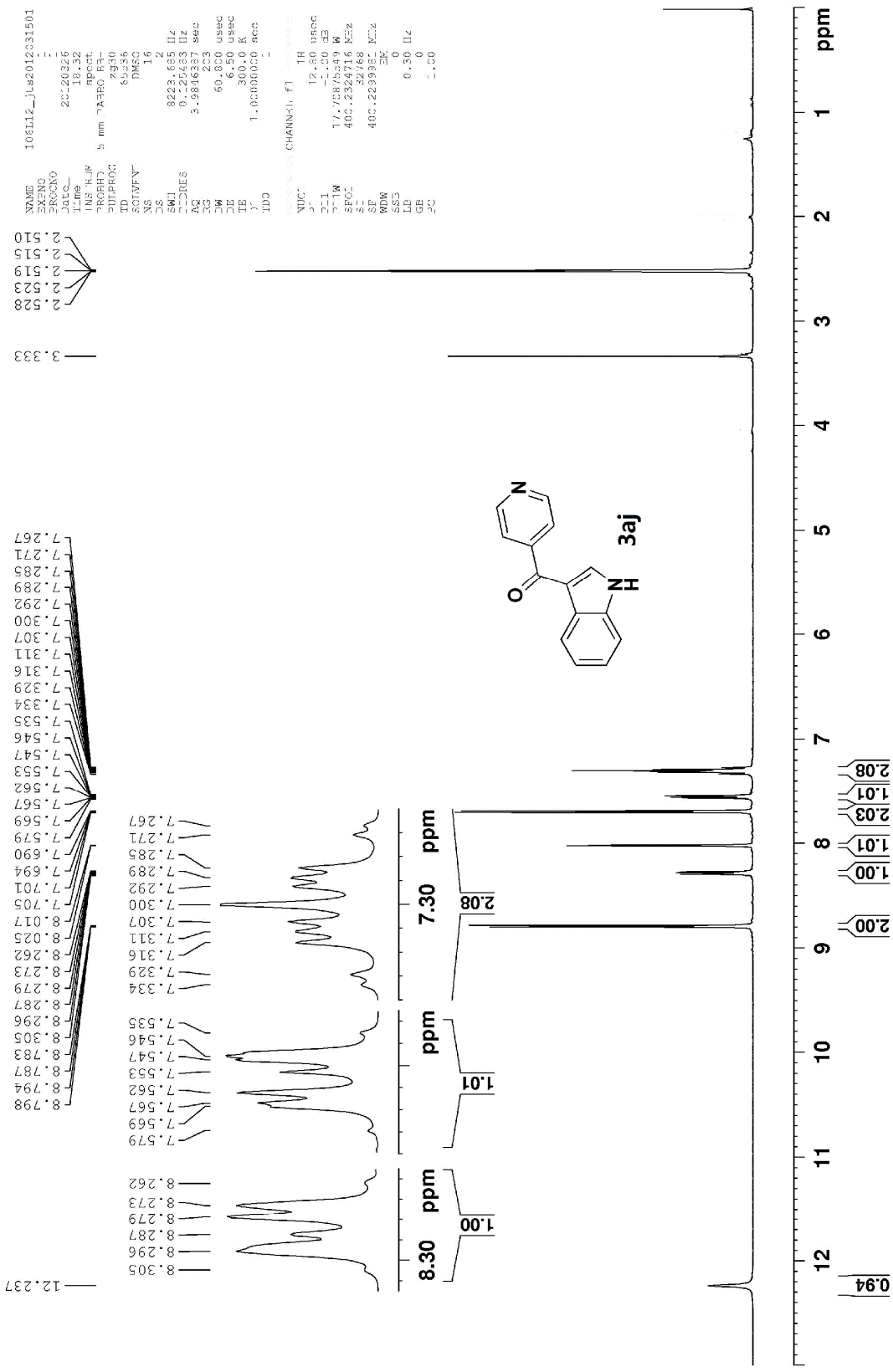

3af
ppm

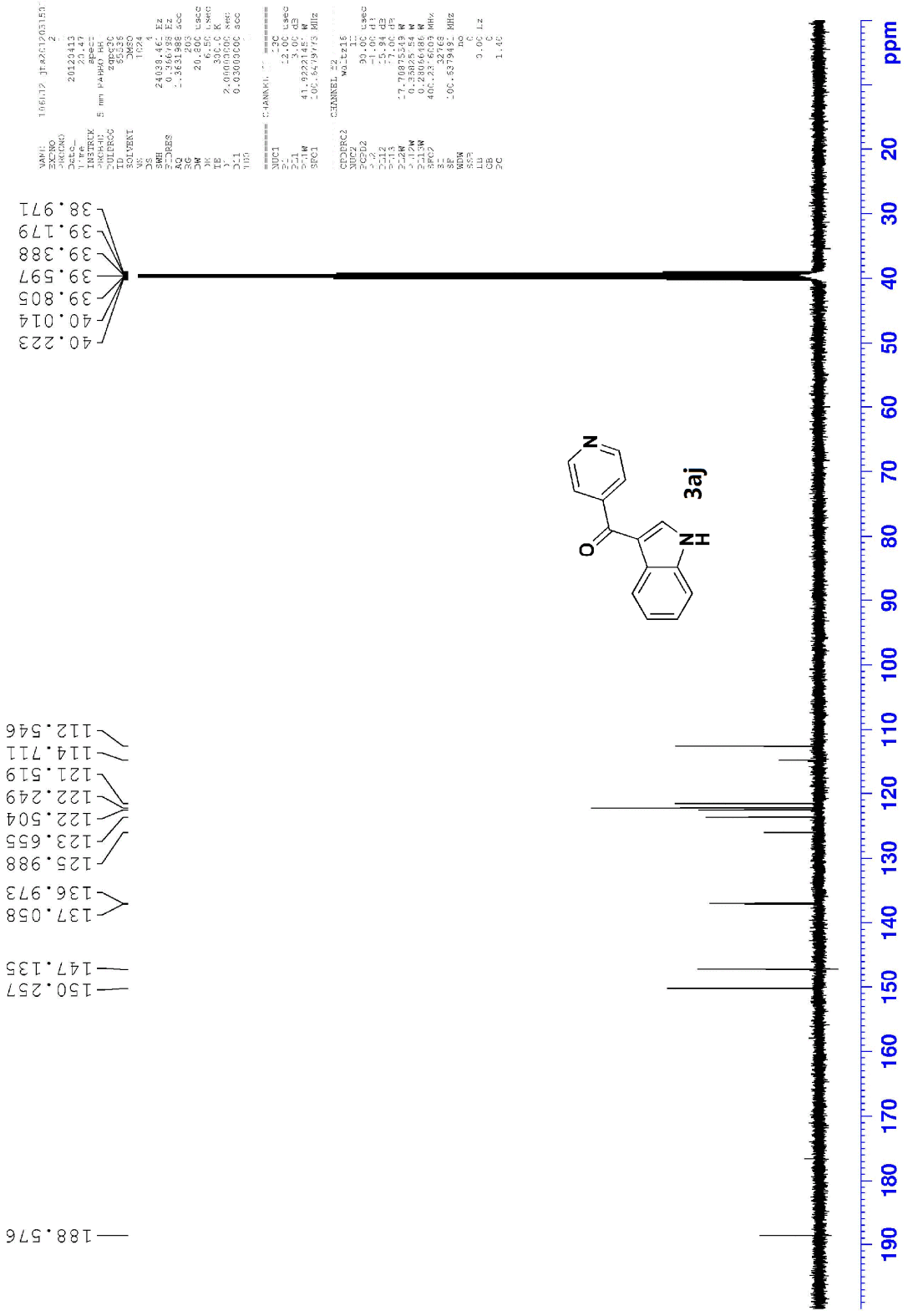

Br
O
N
H
3ag

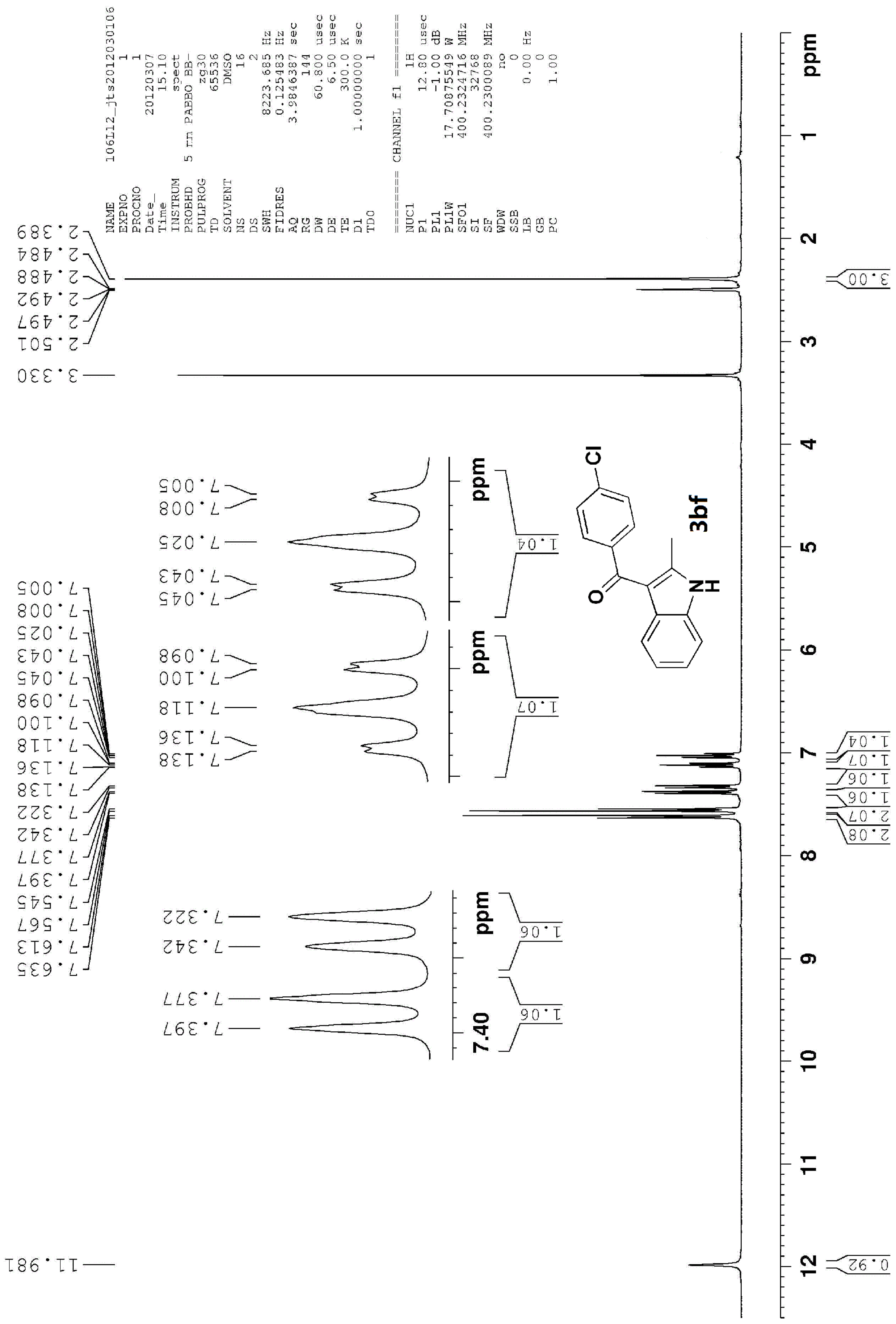

Br
O
N
H
3ag
ppm

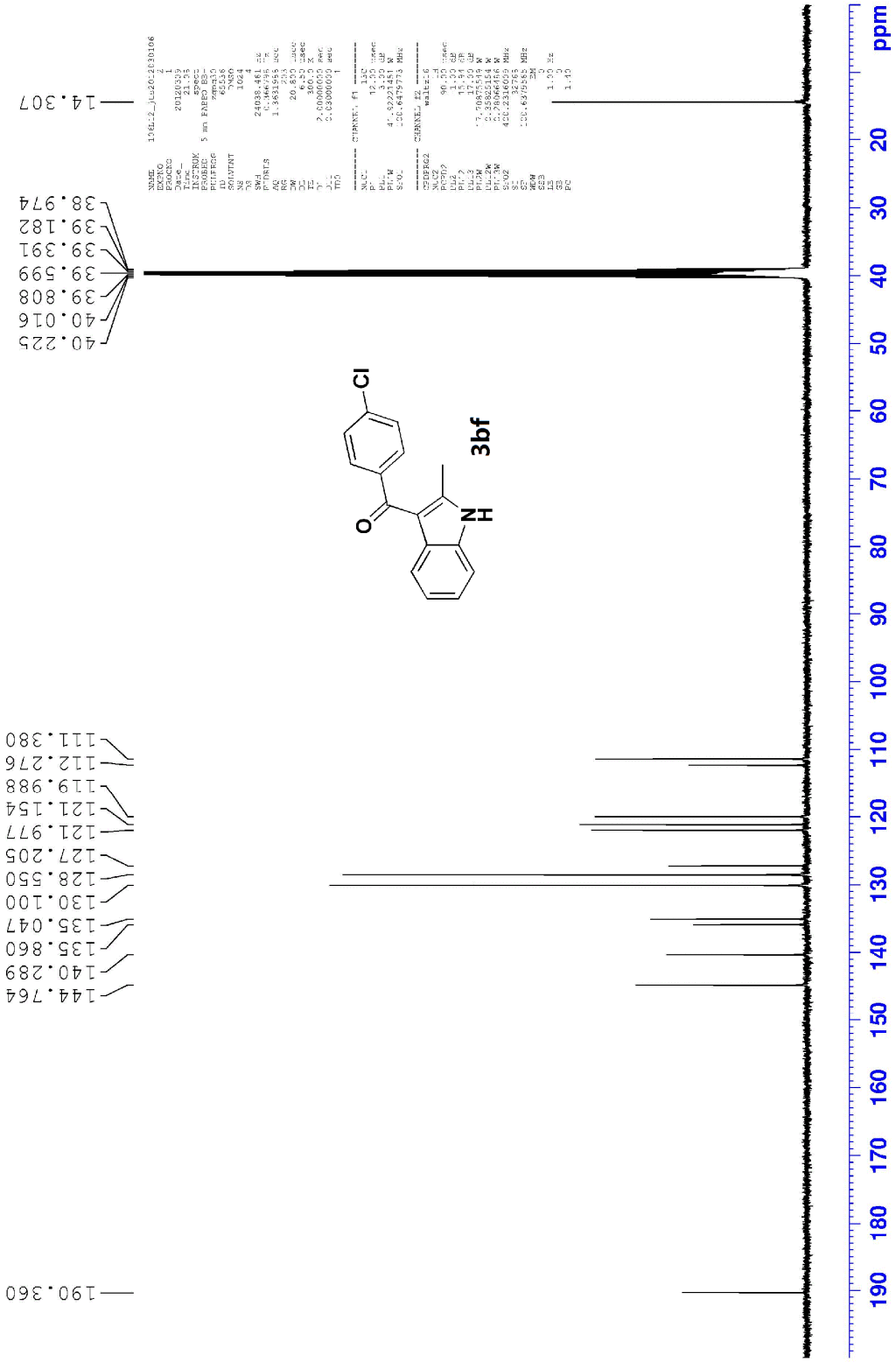

F
O
N
H
3ah
7.25 ppm
7.35 ppm
7.90 ppm
ppm

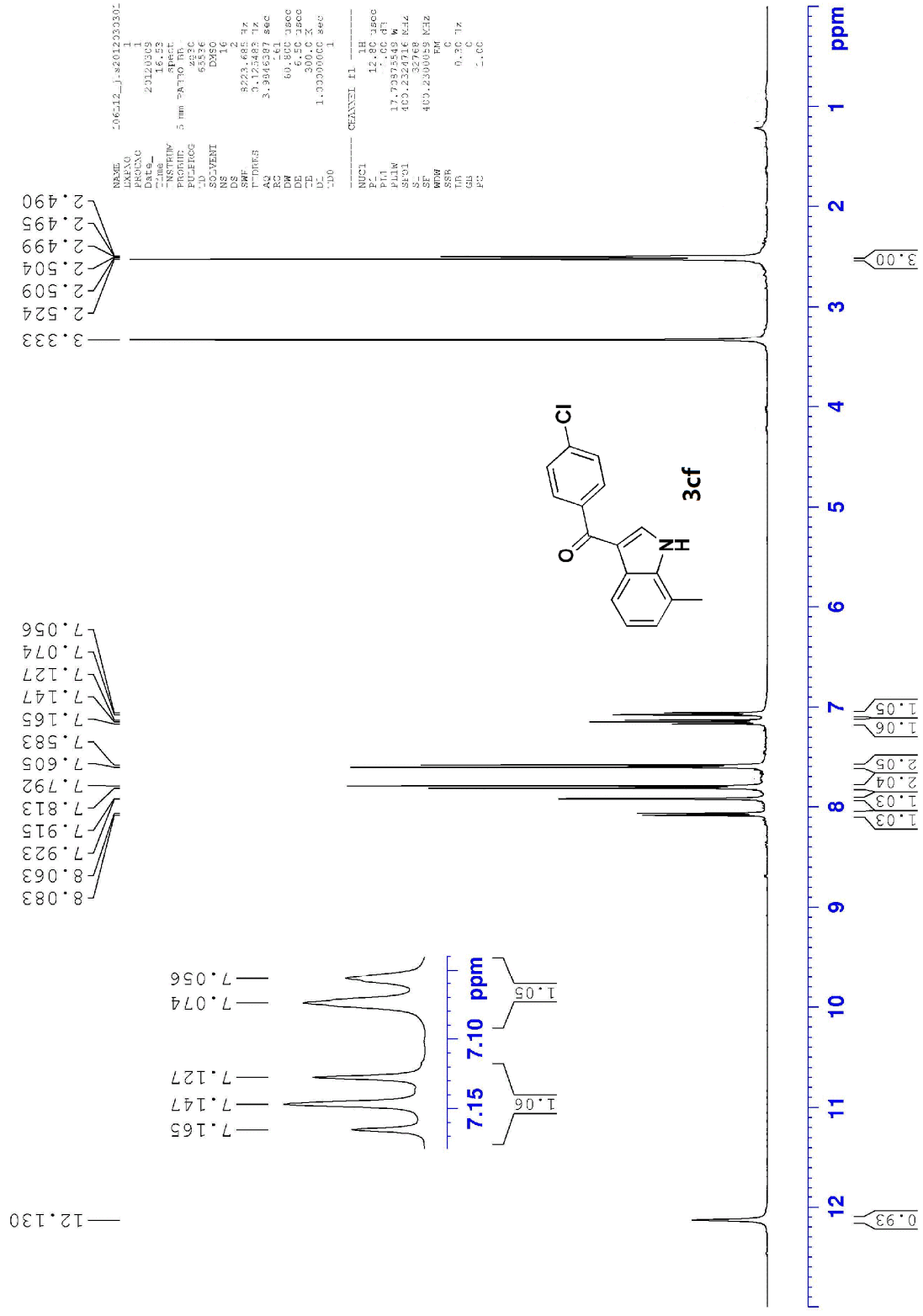

NO2
O
N
H
3ai

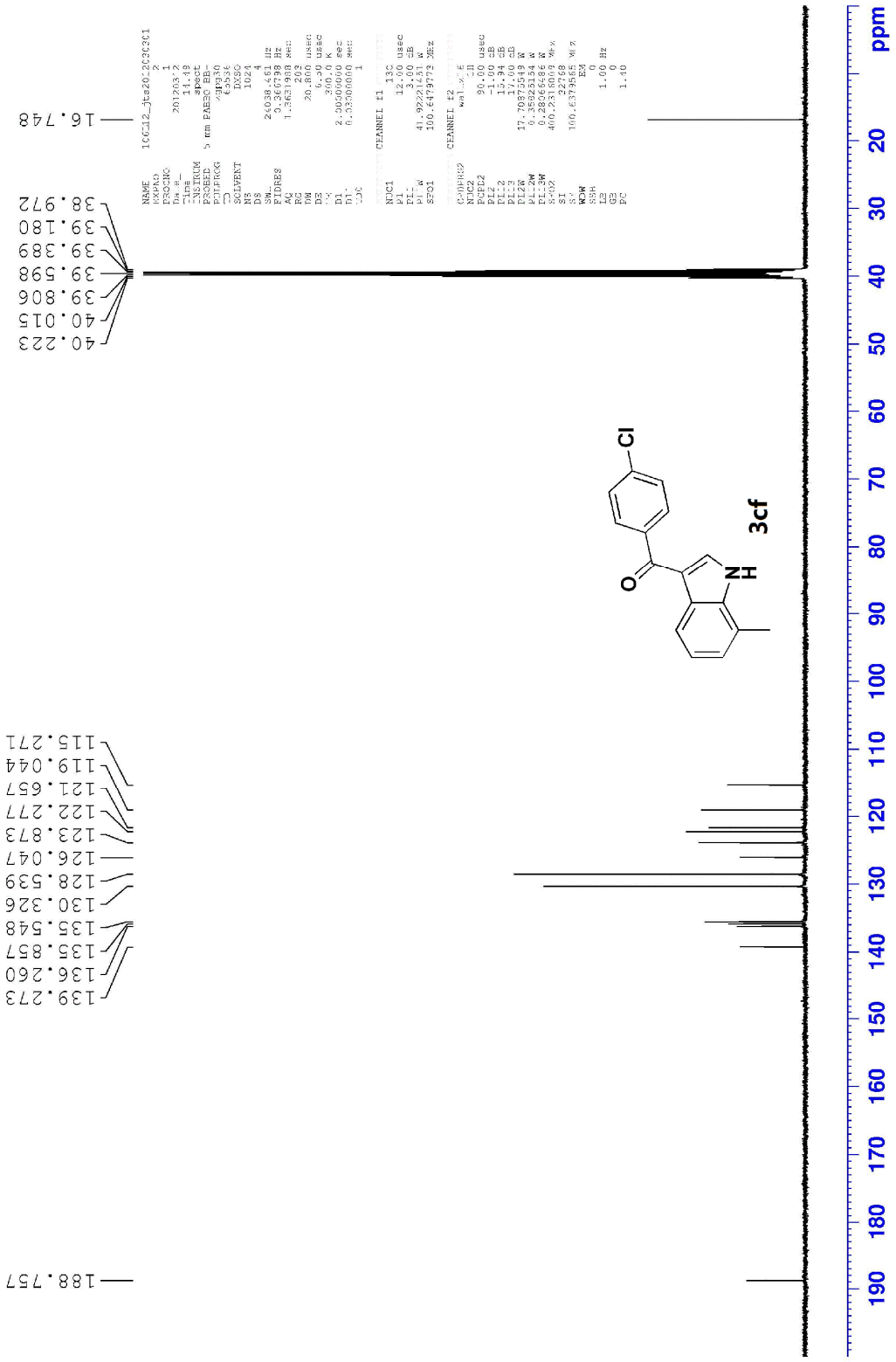

3aj
8.30 ppm
7.30 ppm
ppm

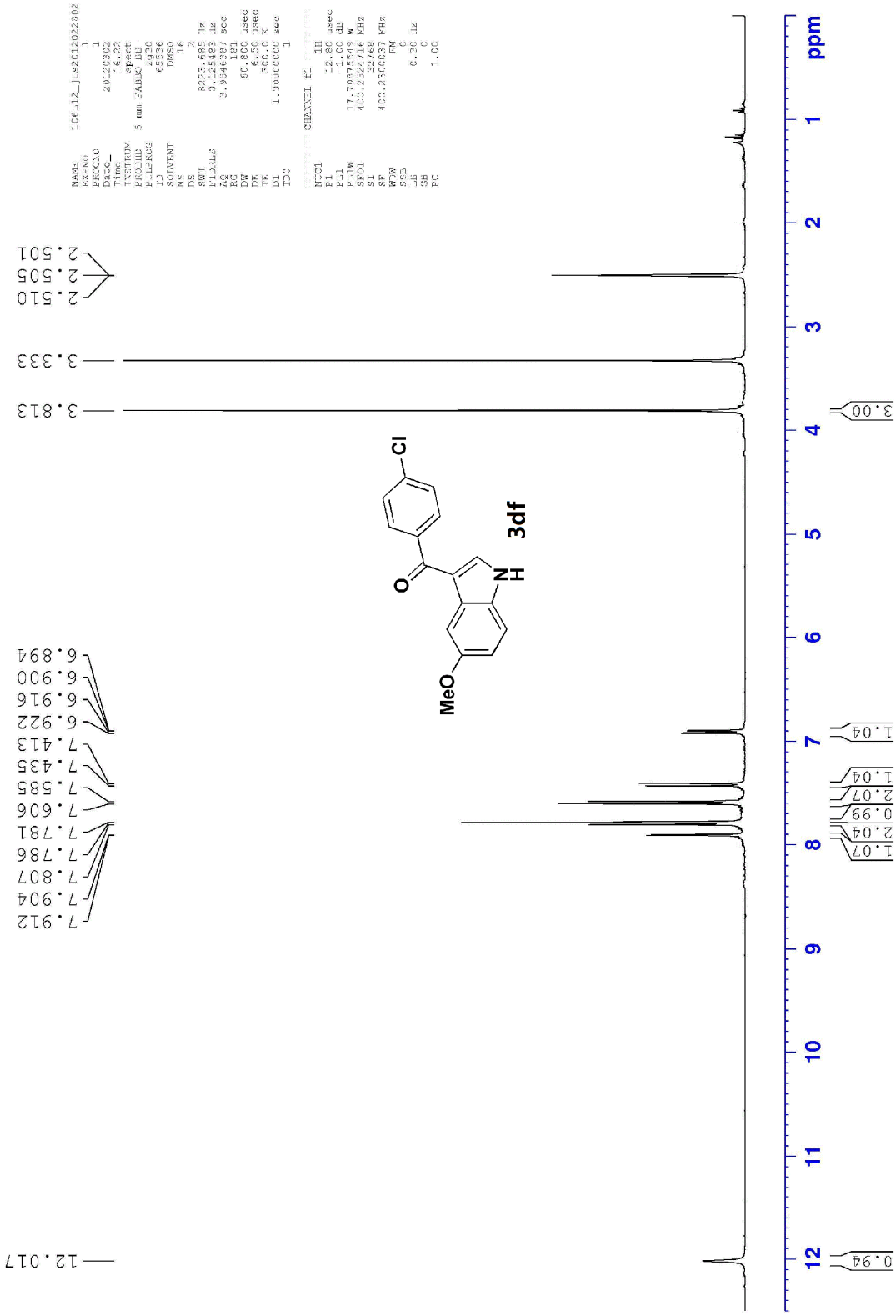

38.971
39.179
39.388
39.597
39.805
40.014
40.223
112.546
114.711
121.519
122.249
122.504
123.655
125.988
136.973
137.058
147.135
150.257
188.576
3aj
ppm

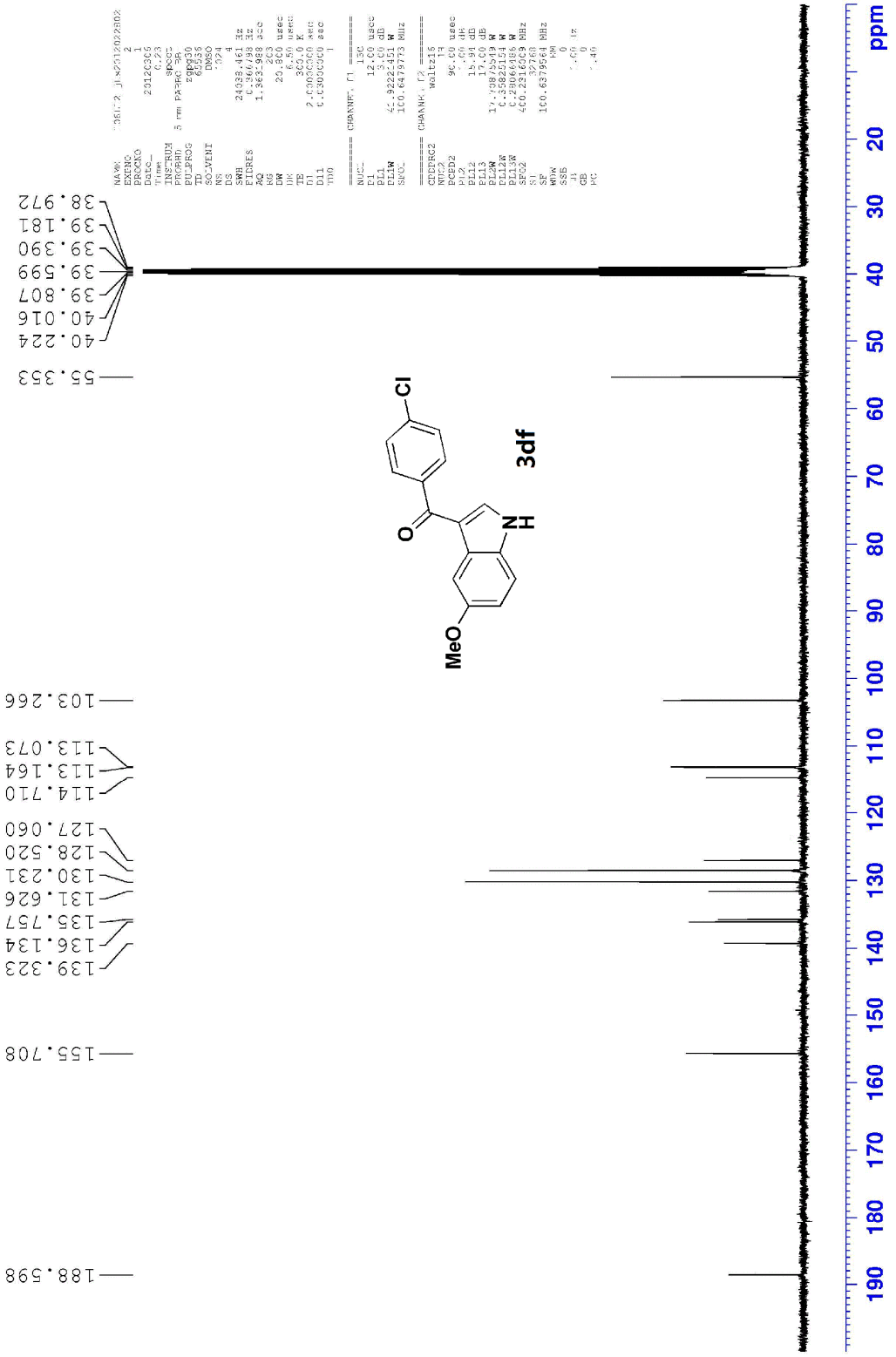

3bf

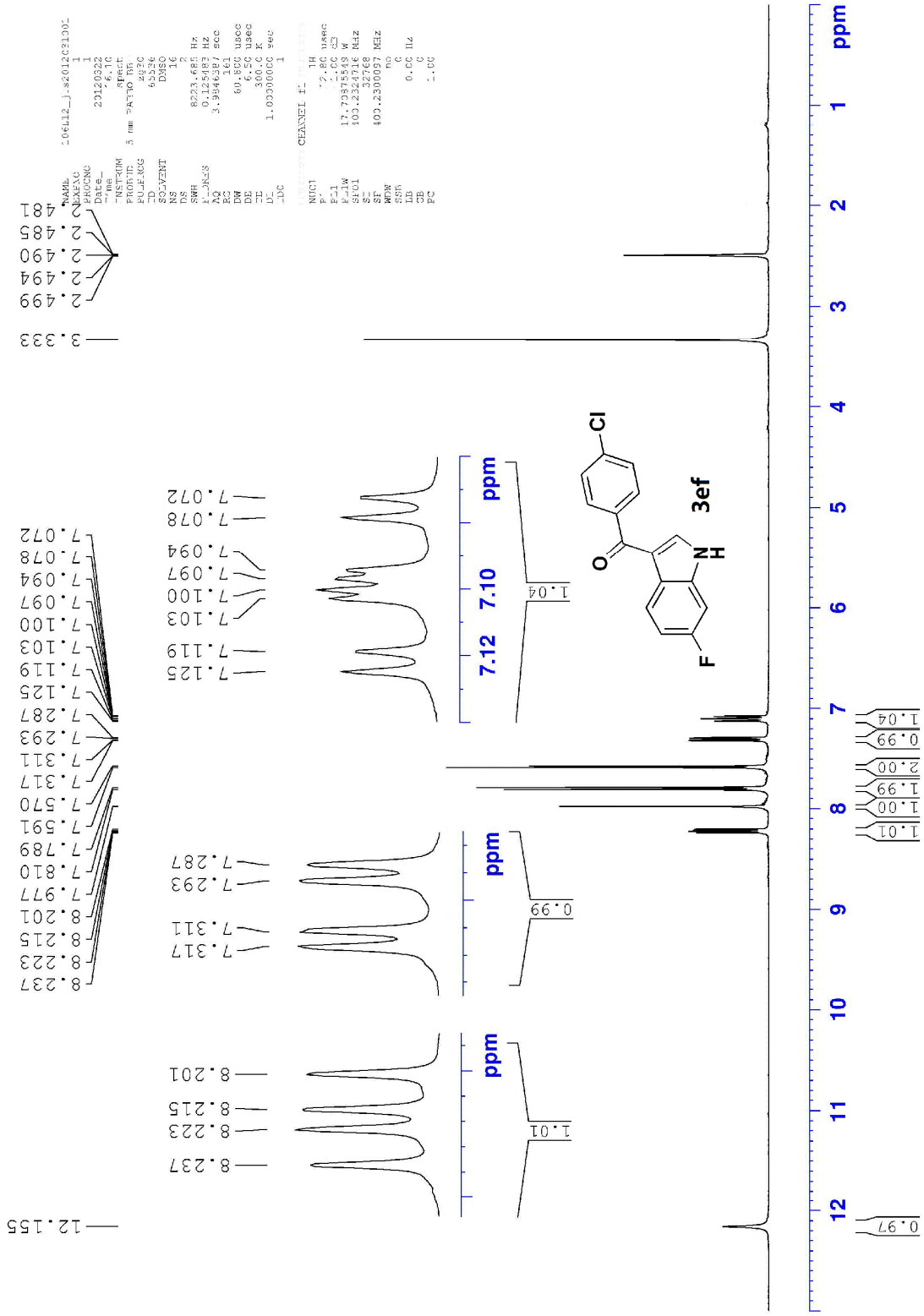

14.307
38.974
39.182
39.391
39.599
39.808
40.016
40.225
111.380
112.276
119.988
121.154
121.977
127.205
128.550
130.100
135.047
135.860
140.289
144.764
190.360
ppm
3bf
Cl
O
N
H

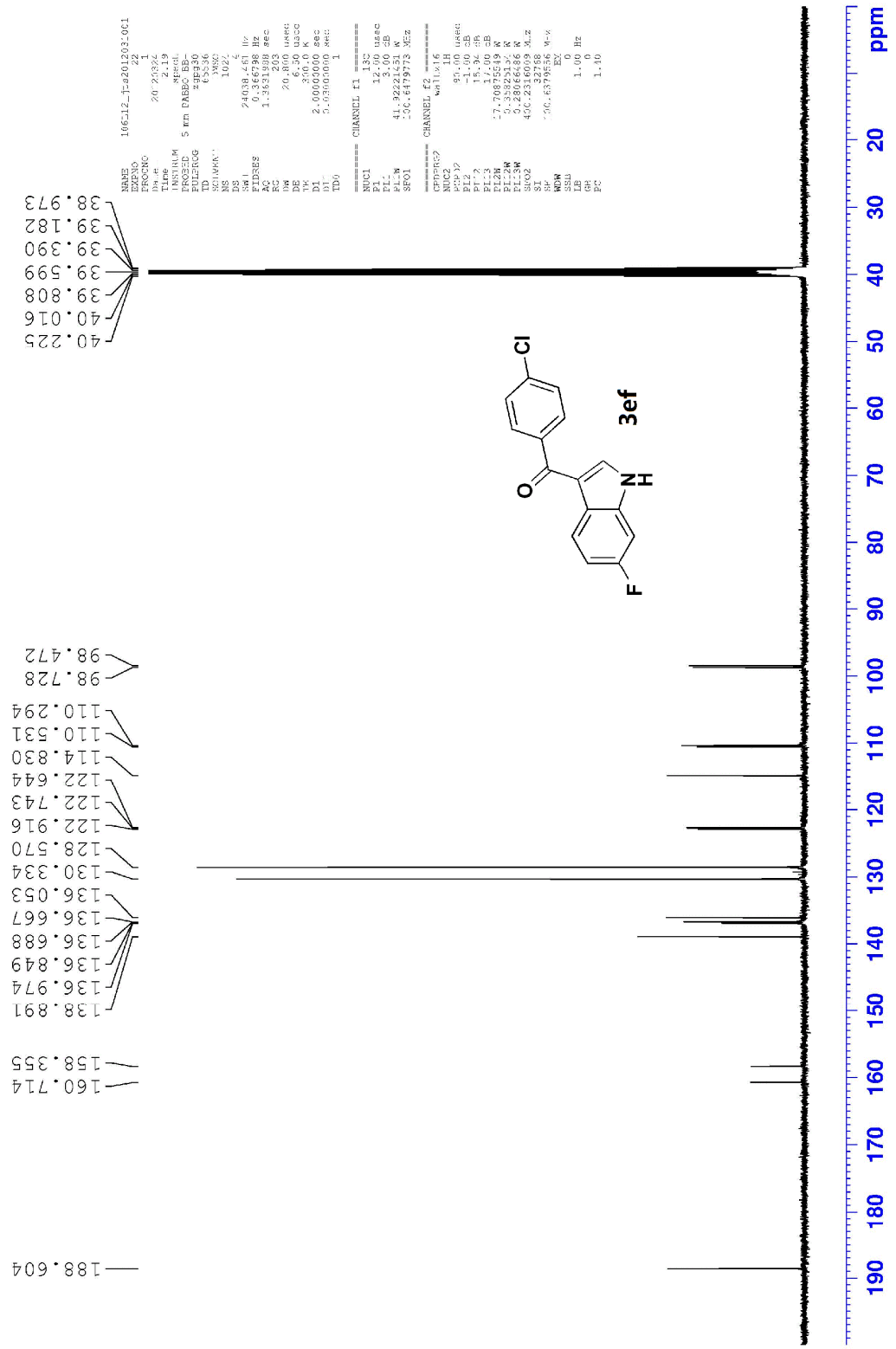

3cf
ppm
7.15
7.10
ppm

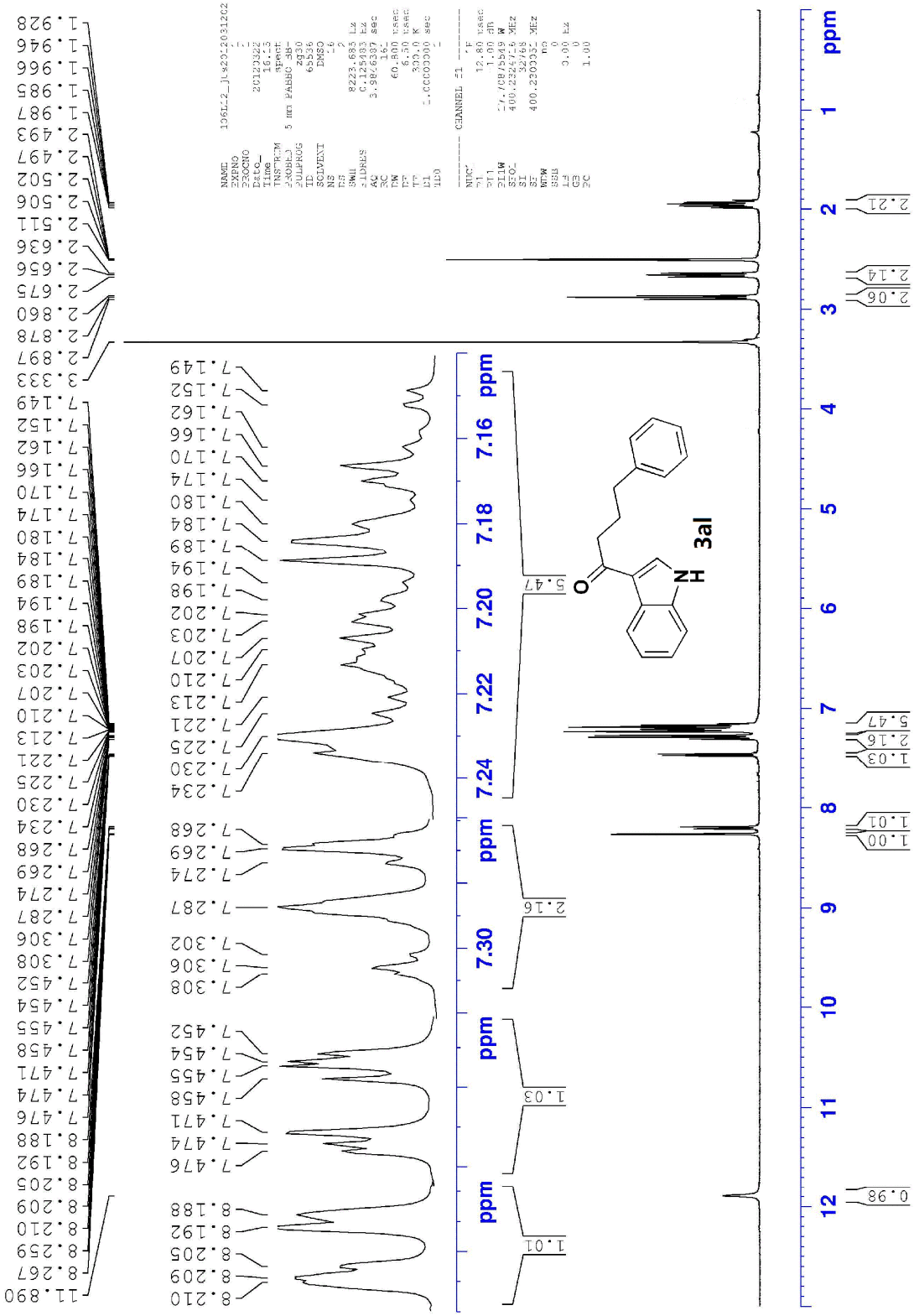

188.757
139.273
136.260
135.857
135.548
130.326
128.539
126.047
123.873
122.277
121.657
119.044
115.271
40.223
40.015
39.806
39.598
39.389
39.180
38.972
16.748
ppm
3cf
Cl
O
N
H

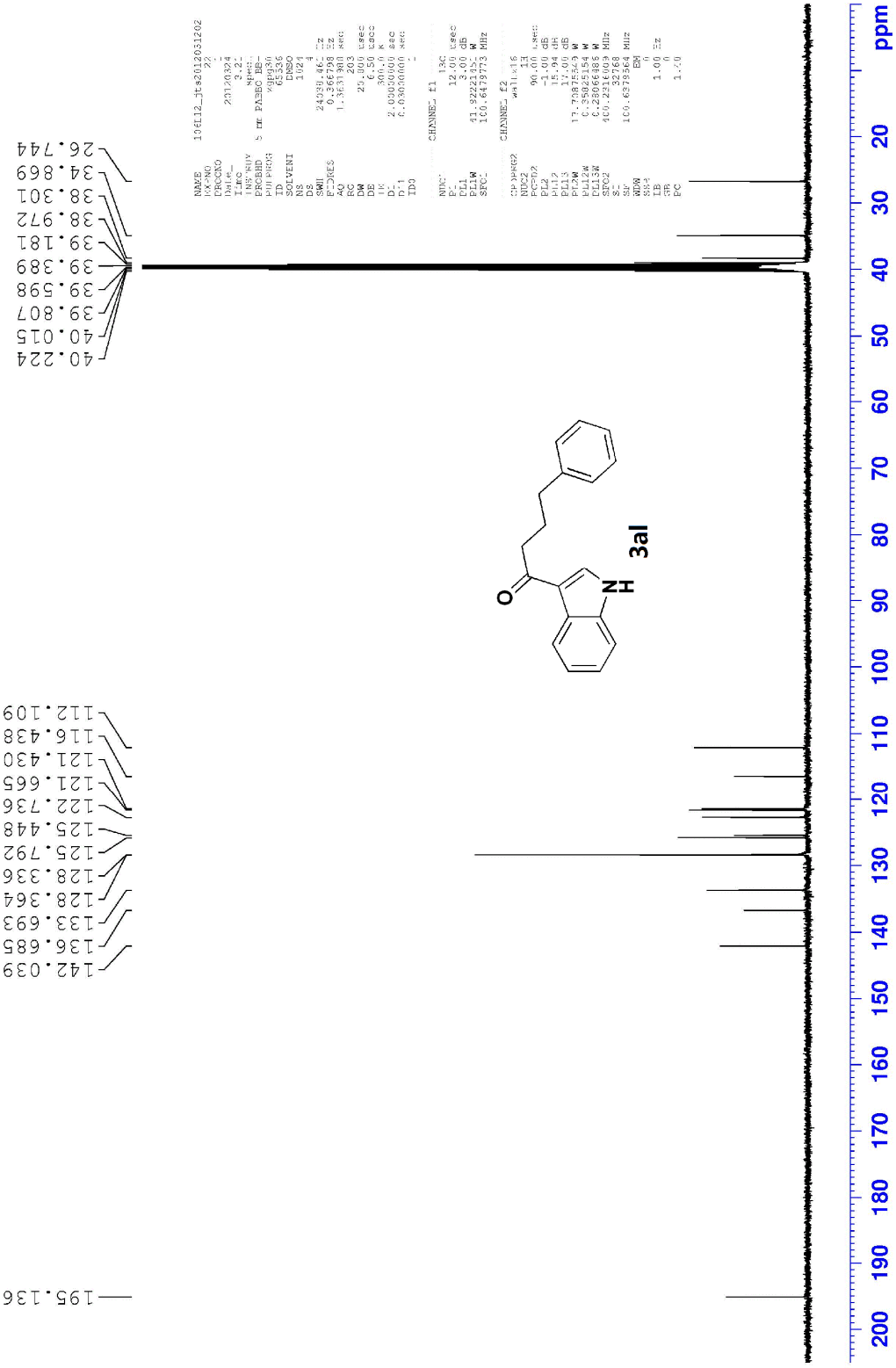

Cl
O
N
H
MeO
3df
12.017
7.912
7.904
7.807
7.786
7.781
7.606
7.585
7.435
7.413
6.922
6.916
6.900
6.894
3.813
3.333
2.510
2.505
2.501
0.94
1.07
2.04
0.99
2.07
1.04
1.04
3.00
ppm

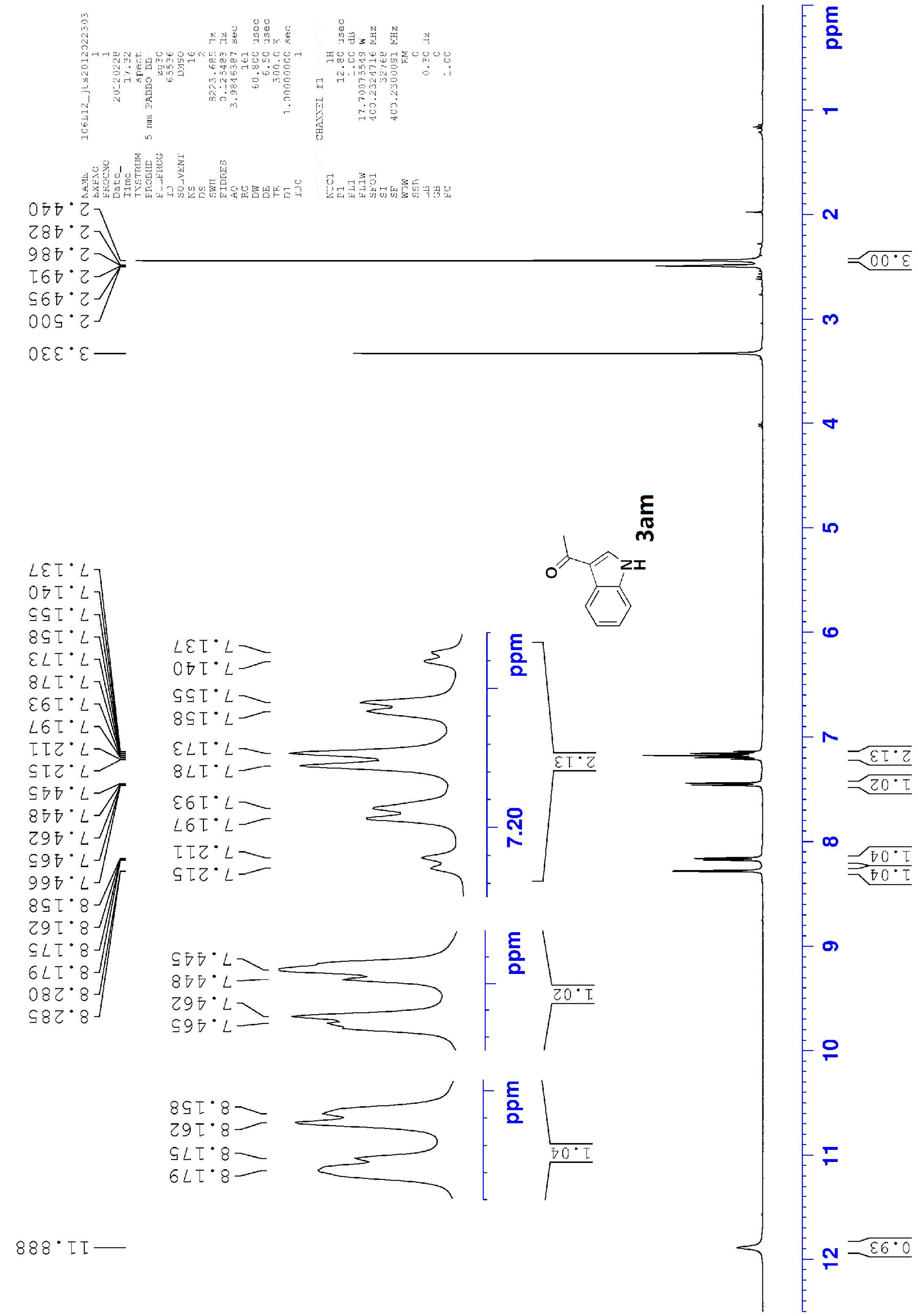

3df
Cl
O
N
H
MeO
188.598
155.708
139.323
136.134
135.757
131.626
130.231
128.520
127.060
114.710
113.164
113.073
103.266
55.353
40.224
40.016
39.807
39.599
39.390
39.181
38.972
ppm

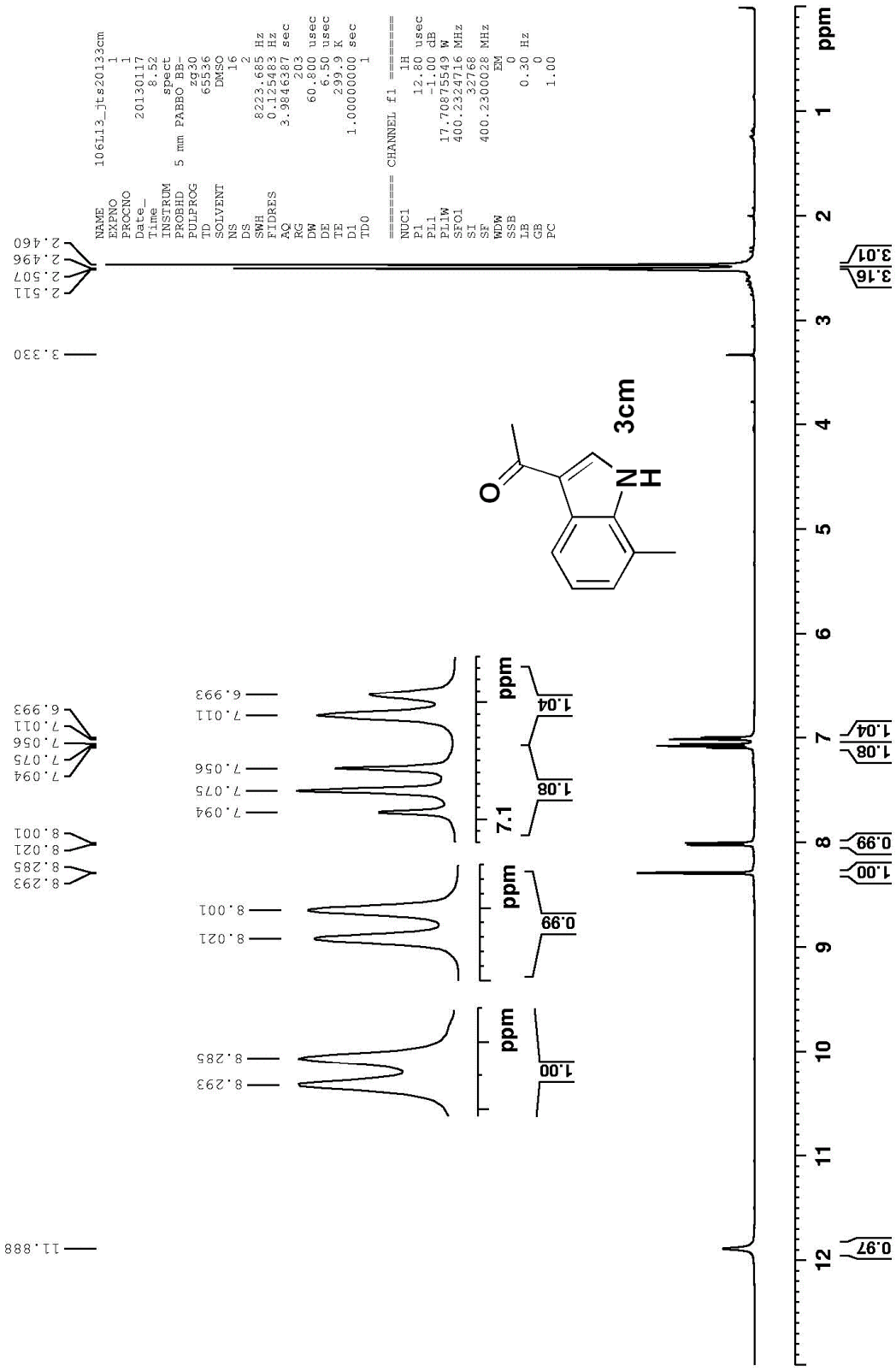

3ef
Cl
O
N
H
F
7.12
7.10
ppm
1.04
0.99
1.01
2.00
1.99
1.00
1.01
0.97

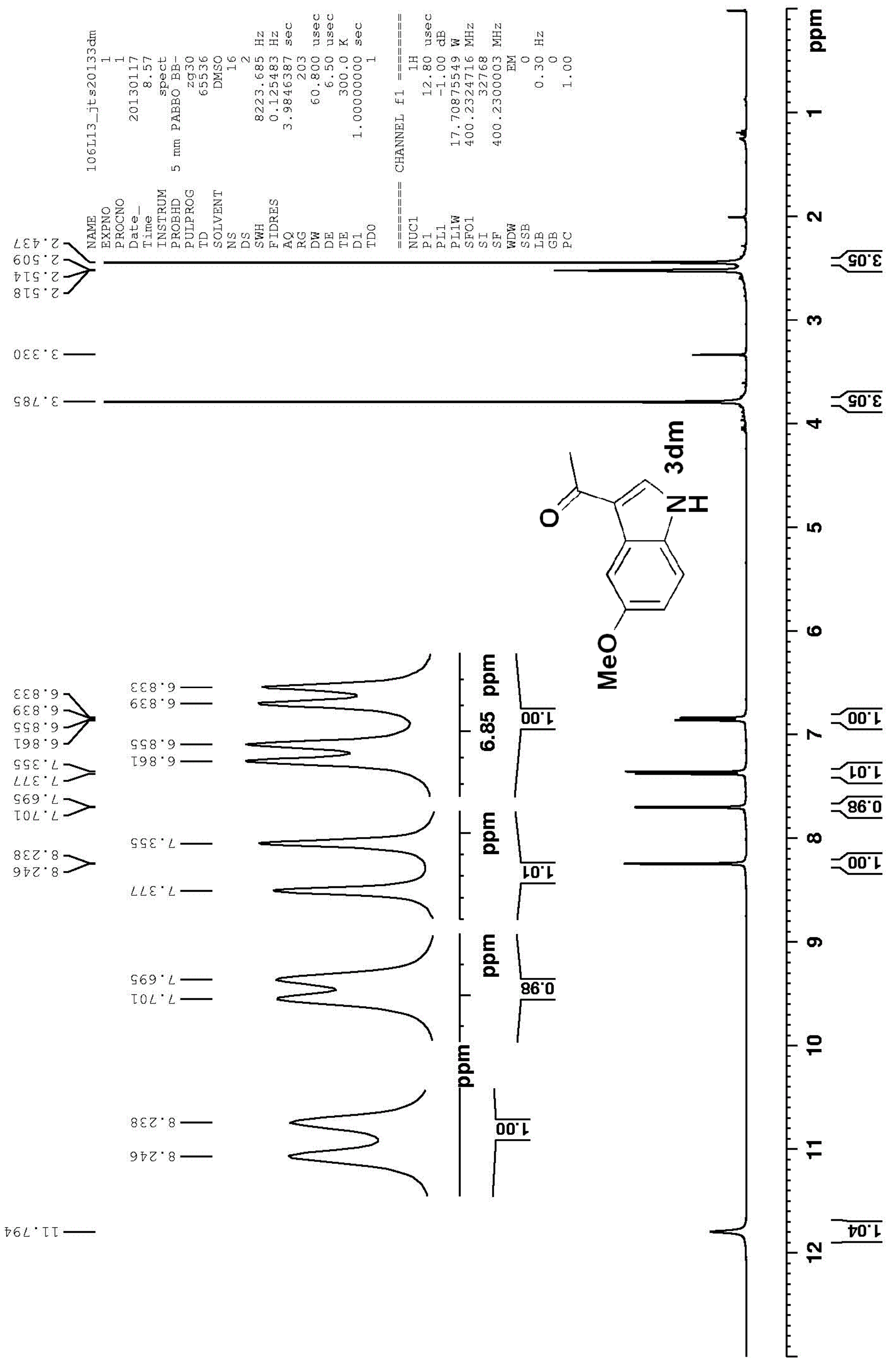

38.973
39.182
39.390
39.599
39.808
40.016
40.225
98.472
98.728
110.294
110.531
114.830
122.644
122.743
122.916
128.570
130.334
136.053
136.667
136.688
136.849
136.974
138.891
158.355
160.714
188.604
Cl
O
N
H
F
3ef
ppm

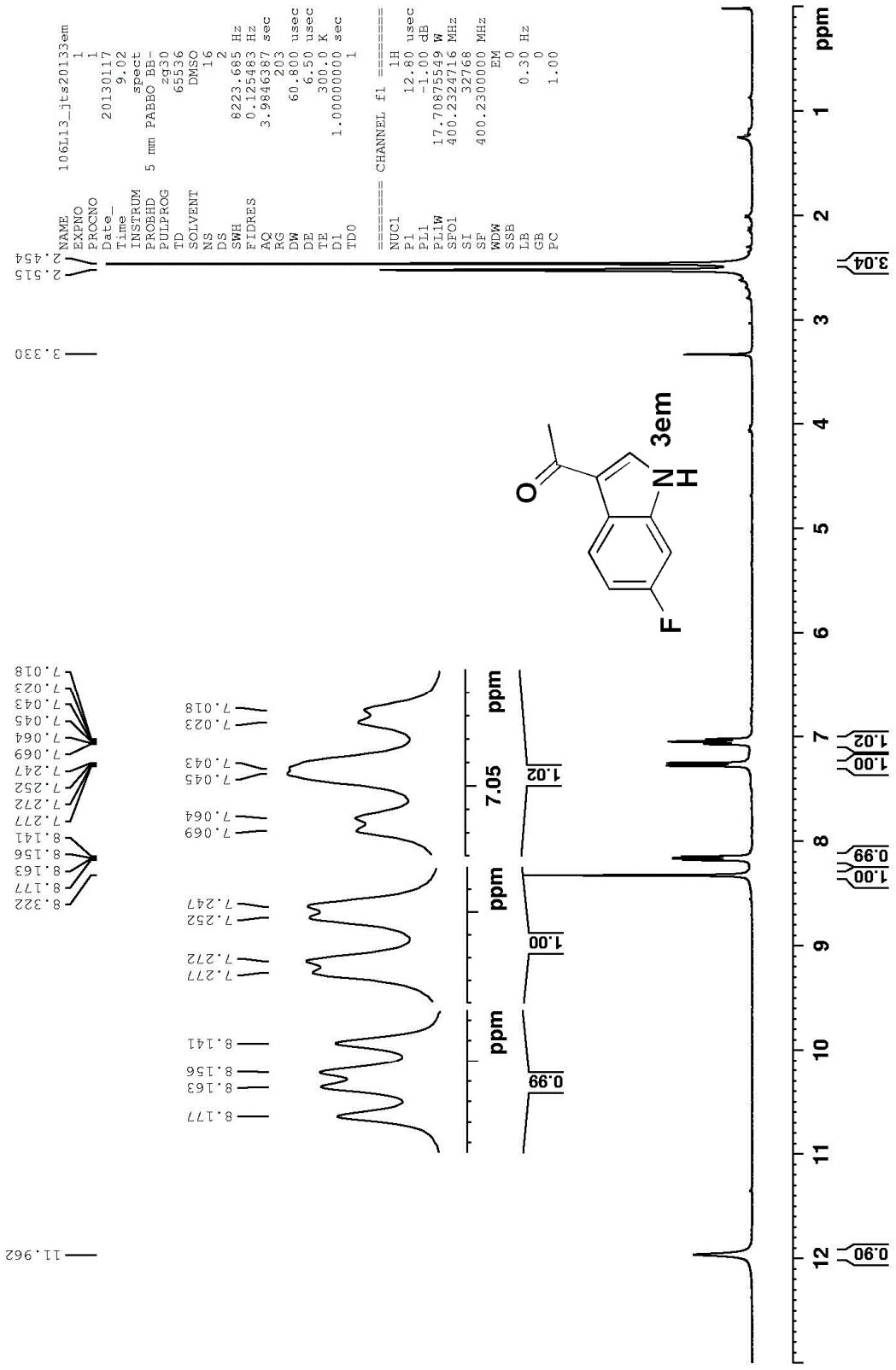

3al

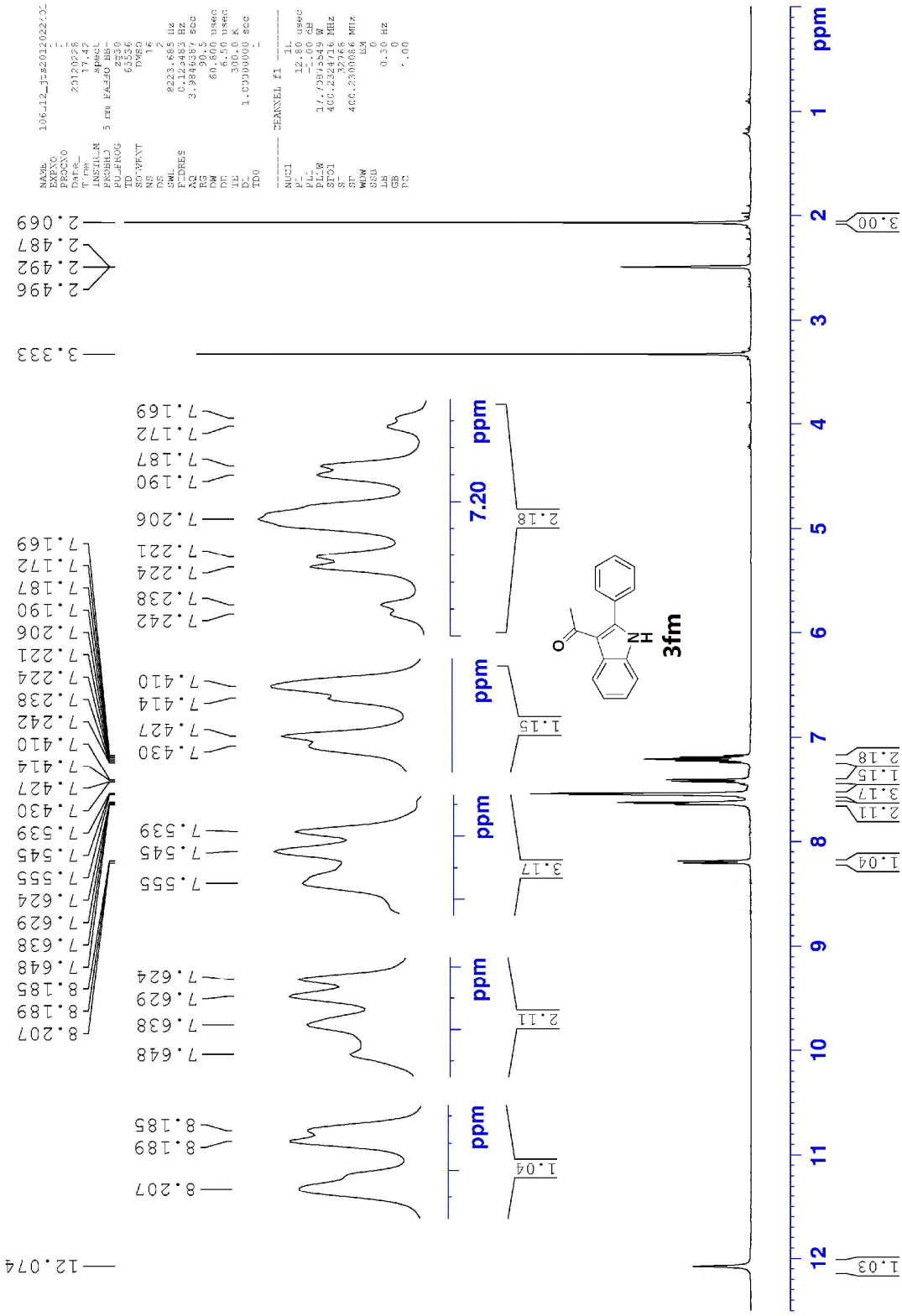

26.744
34.869
38.301
38.972
39.181
39.389
39.598
39.807
40.015
40.224
112.109
116.438
121.430
121.665
122.736
125.448
125.792
128.336
128.364
133.693
136.685
142.039
195.136
3al
O
N
H
ppm


3am
2.440
2.482
2.486
2.491
2.495
2.500
3.330
7.137
7.140
7.155
7.158
7.173
7.178
7.193
7.197
7.211
7.215
7.445
7.448
7.462
7.465
7.466
8.158
8.162
8.175
8.179
8.280
8.285
11.888
3.00
2.13
1.02
1.04
1.04
0.93
7.20
ppm


3cm
O
N
H
ppm
1.00
0.99
1.08
1.04
7.1
0.97
3.01
3.16
11.888
8.293
8.285
8.021
8.001
7.094
7.075
7.056
7.011
6.993
3.330
2.511
2.507
2.496
2.460


3dm
MeO
O
N
H
NAME 106L13_jts20133dm
EXPNO 1
PROCNO 1
Date_ 20130117
Time 8.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.80 usec
PL1 -1.00 dB
PL1W 17.70875549 W
SFO1 400.2324716 MHz
SI 32768
SF 400.2300003 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
2.437
2.509
2.514
2.518
3.330
3.785
6.833
6.839
6.855
6.861
7.355
7.377
7.695
7.701
8.238
8.246
11.794
6.85 ppm
ppm
1.00
1.01
0.98
3.05
1.04


3em
F
O
N
H
ppm
7.05
1.02
1.00
0.99
3.04
0.90


3fm
7.20
ppm
12.074
8.207
8.189
8.185
7.648
7.638
7.629
7.624
7.555
7.545
7.539
7.430
7.427
7.414
7.410
7.242
7.238
7.224
7.221
7.206
7.190
7.187
7.172
7.169
3.333
2.496
2.492
2.487
2.069
1.03
1.04
2.11
3.17
1.15
2.18
3.00