Iron Catalyzed Cycloaddition of Alkynenitriles and Alkynes

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SUPPORTING INFORMATION

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General Experimental:

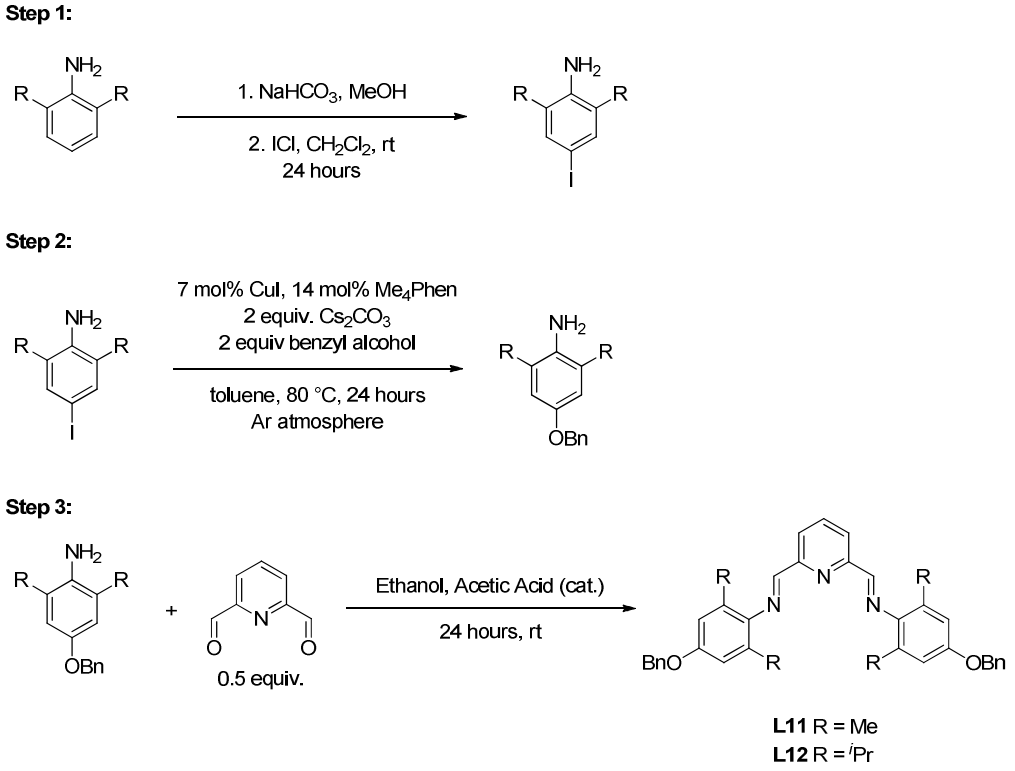
All reactions were conducted under an atmosphere of N_2 using standard Schlenk techniques or in a N_2 filled glove-box unless otherwise noted. Toluene was dried over neutral alumina under N_2 using a Grubbs type solvent purification system. Dimethyl formamide was purchased from Sigma Aldrich in a sure-seal® bottle. THF was freshly distilled from Na/benzophenone. Iron acetate (99.995% purity) was purchased from Sigma Aldrich. Cyanoalkynes **1a**,[1a] **1b**,[1a] **1i**,[1b] and **1j**,[2] were prepared by known literature procedures.

^{1}H and ^{13}C Nuclear Magnetic Resonance spectra of pure compounds were acquired at 400 and 100 MHz, respectively unless otherwise noted. All spectra are referenced to residual proteated $CHCl_3$ via a singlet at 7.27 ppm for ^{1}H and to the center line of a triplet at 77.26 ppm for ^{13}C. The abbreviations s, d, dd, dt, dq, t, q, and quint stand for singlet, doublet, doublet of doublets, doublet of triplets, doublet of quartets, triplet, quartet, and quintet, in that order. All ^{13}C NMR spectra are proton decoupled. Gas Chromatography was performed using the following conditions: initial oven temperature: 100 ºC; temperature ramp rate 10 ºC/min.; final temperature: 300 ºC held for 12 minutes; detector temperature: 250 ºC.

Ligand Syntheses

Ligands **L1-L6**[4a] and **L7-L10**[4b] were synthesized by the reported methods.

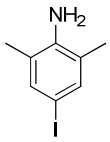
Ligands **L11** and **L12** were synthesized as follows:



Step 1 (general procedure):

Adapted from the literature procedure.[5a] To a stirring mixture of 2,6-substituted aniline and $NaHCO_3$ (3 equiv) in methanol, a solution of iodinemonochloride (1.1 equiv) in CH_2Cl_2 was added dropwise over 1 hour. The reaction was stirred at room temperature for 24 hours. Solids were filtered from the mixture and rinsed with diethyl ether. The filtrate was reduced *in vacuo* to a dark red oil to which a 300 mL solution of saturated sodium thiosulfate was added. The solution was stirred for 10 minutes then extracted with 3 x 200 mL portions of diethyl ether. The organic extracts were dried with Na_2SO_4 and reduced *in vacuo*.

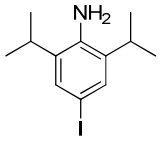
Synthesis of 4-iodo-2,6-dimethylaniline



4-iodo-2,6-dimethylaniline was prepared using the Step 1 general procedure with 2,6-dimethylaniline (10.0 g, 83 mmol), iodinemonochloride (14.7 g, 91 mmol), sodium bicarbonate (20.8 g, 248 mmol) of sodium bicarbonate. The reaction was stirred at

room temperature with 115 mL of methanol and 90 mL of dichloromethane to yield **4-iodo-2,6-dimethylaniline** (19.2g, 93%) as a dark red oil. Spectral data matches the reported values.[5b]

Synthesis of 4-iodo-2,6-diisopropylaniline

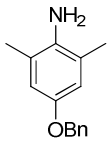


4-iodo-2,6-diisopropylaniline was prepared using the Step 1 general procedure with 2,6 diisopropylaniline (10.0 g, 56 mmol), iodinemonochloride (10.1 g, 62 mmol), sodium bicarbonate (14.2 g, 169 mmol). The reaction was stirred at room temperature with 80 mL of methanol and 60 mL of dichloromethane to yield **4-iodo-2,6-diisopropylaniline** (16.8 g, 93%) as a dark red oil. Spectral data matches the reported values. [5c]

Step 2 (general procedure):

Adapted from the literature procedure.[5c] In a nitrogen glove box, a 20 mL scintillation vial was filled with CuI (7 mol%) 3,4,7,8-tetramethyl-1,10-phenanthroline (Me_4Phen, 14 mol%), Cs_2CO_3 (2.0 equiv), and 4-iodo-2,6-dialkyl aniline (1.0 equiv). The vial was sealed with a rubber septum, removed from the glove box then evacuated and backfilled with Argon three times. Toluene was added and the mixture was stirred at 80 °C for 20 minutes. Benzyl alcohol (2.0 equiv) was added and the rubber septum was quickly replaced with a vial cap. The reaction was stirred for 24 hours at 80 °C then cooled to room temperature, filtered through a silica gel plug, and flushed with 150 mL of ethyl acetate. The resulting solution was reduced *in vacuo* and purified using silica gel flash chromatography with 10% ethyl acetate in hexanes.

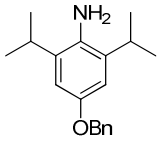
Synthesis of 4-(benzyloxy)-2,6-dimethylaniline



4-(benzyloxy)-2,6-dimethylaniline was prepared using the Step 2 general procedure with CuI (57.8 mg, 0.30 mmol), Me_4Phen (143.5 mg, 0.61 mmol), cesium carbonate (1.56 g, 8.1 mmol), 4-iodo-2,6-dimethylaniline (1.0 g, 4.0 mmol), and benzyl alcohol (875.3 mg, 8.1 mmol). The reaction was run for 24 hours at 80 °C in 1.9 mL of toluene to yield **4-(benzyloxy)-2,6-dimethylaniline** (362.9 mg, 40%) as a blue solid. Mp: 71-73 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.48-7.33 (m, 5H), 6.68 (s, 2H), 5.01 (s, 2H), 3.35 (s, 2H), 2.20 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 151.5, 137.9, 136.9, 128.7, 127.9, 127.7, 123.4, 115.2, 70.9, 18.2. IR (cm^{-1}) 3450, 3375, 3032, 2969, 2908, 2735, 1602, 1489, 1380, 1328, 1298, 1242,

1150, 1054, 856, 738, 698. HRMS (ESI) calcd for $C_{15}H_{17}NO$ $[M+H]^+$ 228.1388, found 228.1385.

Synthesis of 4-(benzyloxy)-2,6-diisopropylaniline

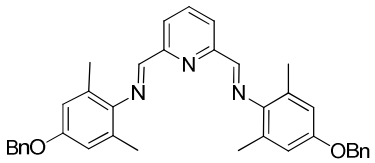


4-(benzyloxy)-2,6-diisopropylaniline was prepared using the Step 2 general procedure with CuI (57.8 mg, 0.30 mmol), Me_4Phen (143.5 mg, 0.61 mmol), cesium carbonate (1.56 g, 8.1 mmol), 4-iodo-2,6-diisopropylaniline (1.0 g, 4.0 mmol), and benzyl alcohol (875.3 mg, 8.1 mmol). The reaction was run for 24 hours at 80 ° in 1.9 mL of toluene to yield **4-(benzyloxy)-2,6-diisopropylaniline** (948.9 mg, 84%) as a dark red oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.48-7.27 (m, 5H), 6.74 (s, 2H), 3.48 (s, 2H), 3.01-2.94 (m, 2H), 1.28 (d, J = 6.8, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 152.4, 138.0, 134.5, 134.4, 128.7, 128.01, 127.96, 110.1, 71.0, 28.4, 22.7. IR (cm^{-1}) 3382, 2960, 1599, 1463, 1347, 1218, 1175, 1100, 1027, 737, 696. HRMS (ESI) calcd for $C_{19}H_{26}NO$ $[M+H]^+$ 284.2014, found 284.2013.

Step 3 (general procedure):

Adapted from the literature procedure[5a] 4-benzyloxy-2,6-dialkyl aniline (2.0 equiv.) and 2,6-pyridinedicarboxaldehyde (1.0 equiv) and a catalytic amount glacial acetic acid were stirred in 100% ethanol overnight at room temperature. The mixture was cooled to 0 °C, filtered, and rinsed with cold 100% ethanol.

Synthesis of (*N*,*N*'E,*N*,*N*'E)-N,N'-(pyridine-2,6-diylbis(methanylylidene))bis(4-(benzyloxy)-2,6-dimethylaniline) (L11)

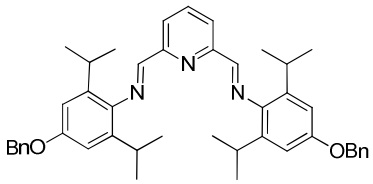


L11

Coumpound **L11** was prepared using the Step 3 general procedure with 4-(benzyloxy)-2,6-dimethylaniline (194.6 mg, 0.86 mmol), 2,6-pyridinedicarboxaldehyde (57.8 mg, 0.43 mmol), and 5 drops of glacial acetic acid. The reaction was run at room temperature in 10 mL of 100% ethanol yielding **L11** (108.0 mg, 45.6%) as a yellow solid. Mp: 174-177 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.40 (s, 2H), 8.38 (d, *J* = 8.0 2H), 7.97 (t, *J* = 7.8, 1H), 7.47-7.33 (m, 10H), 7.76 (s, 4H), 5.06 (s, 4H), 2.20 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ

(ppm). IR (cm^{-1}) 3087, 2970, 2948, 1602, 1584, 1480, 1455, 1379, 1332, 1312, 1198, 1052, 738, 698. HRMS (ESI) calcd for $C_{37}H_{35}N_3O_2$ $[M+H]^+$ 576.2627, found 576.2633.

Synthesis of (*N*,*N*'E,*N*,*N*'E)-N,N'-(pyridine-2,6-diylbis(methanylylidene))bis(4-(benzyloxy)-2,6-diisopropylaniline) (L12)

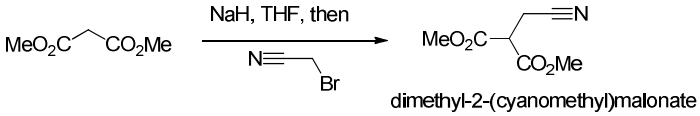


L12

Coumpound **L12** was prepared using the Step 3 general procedure with 4-(benzyloxy)-2,6-diisopropylaniline (2.35 g, 8.3 mmol), 2,6-pyridinedicarboxaldehyde (599.5 mg, 4.1 mmol), and 10 drops of glacial acetic acid. The reaction was run at room temperature in 10 mL of 100% ethanol to yield **L12** (2.48 g, 85%) as a yellow solid. M.p. 170-173 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 8.40-8.38 (m, 4H), 7.99 (t, *J* = 8.0, 1H), 7.51-7.28 (m, 10H), 6.83 (s, 4H), 5.08 (s, 4H), 3.07-2.98 (m, 4H), 1.18 (d, *J* = 7.2, 24H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 163.4, 156.3, 154.8, 142.4, 139.1, 137.6, 137.5, 128.1, 128.2, 128.0, 122.8, 109.9, 70.5, 28.4, 23.7. IR (cm^{-1}) 3391, 2961, 2869, 1637, 1600, 1458, 1326, 1190, 1026, 736. HRMS (ESI) calcd for $C_{45}H_{51}N_3O_2$ $[M+H]^+$ 688.3879, found 688.3882.

Alkynenitrile Syntheses

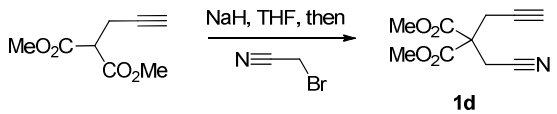
Synthesis of dimethyl-2-(cyanomethyl)malonate:



dimethyl-2-(cyanomethyl)malonate

To a stirring suspension of NaH (1.8 g, 75.7 mmol) in 150 ml THF was added dimethylmalonate (10 g, 75.7 mmol) under N_2 counter-flow. The resulting solution was stirred at room temperature for 1 h after which time bromoacetonitrile (5.0 g, 42.1 mmol) was added. The mixture was stirred at room temperature for 24 h at which time the solution was quenched with 100 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (20% EtOAc/hexanes) to yield **dimethyl-2-(cyanomethyl)malonate** (4.1 g, 57%) as a pale yellow oil. ^{1}H NMR (400 MHz, CDCl3) δ (ppm) 3.78 (s, 6H), 3.73 (t, *J*= 8.8 Hz, 1H), 2.89 (d, *J*= 7.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 167, 116.8, 53.5, 47.8, 17.1

Synthesis of dimethyl 2-(cyanomethyl)-2-(prop-2-yn-1-yl)malonate (1d)

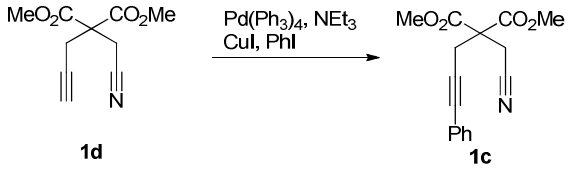


dimethyl-2-(prop-2-yn-1-yl)malonate **1d**

Dimethyl-2-(prop-2-yn-1-yl)malonate was prepared by known literature procedure.[7]

To a stirring suspension of NaH (0.21 g, 8.82 mmol) in 50 ml THF was added dimethyl-2-(prop-2-yn-1-yl)malonate (1.0g, 5.88 mmol) under N_2 counter-flow. The resulting solution was stirred at room temperature for 1 h after which time bromoacetonitrile (1.0 g, 8.82 mmol) was added. A reflux condenser was attached and the mixture was stirred at reflux for 8-12 h at which time GC analysis showed no starting material. The solution was cooled to room temperature and quenched with 100 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (10% EtOAc/hexanes then 12% EtOAc/hexanes) to yield **1d** (0.6 g, 49%) as pale yellow oil. ^1H (400 MHz, $CDCl_3$): 3.83 (s, 6H), 3.17 (s, 2H), 3.03 (d, *J*= 2.8Hz, 2H), 2.13 (t, *J*= 2.8Hz, 1H). ^{13}C (100 MHz, $CDCl_3$) δ (ppm) 168.3, 116.4, 81.0, 71.8, 53.9, 24.2, 22.1, 3.7. IR (cm^{-1}) 3288, 2960, 2253, 1743, 1483, 1327, 1217, 971, 892. HRMS calculated for $C_{10}H_{11}NO_4Na$ 232.0586, found 232.0592.

Synthesis of dimethyl-2-(cyanomethyl)-2-(3-phenylprop-2-yn-1-yl)malonate (1c)

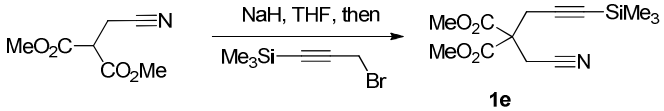


1d **1c**

$Pd(PPh_3)_2Cl_2$ (28.4 mg, 0.04 mmol) and CuI (27.7 mg, 0.14 mmol) were added to a solution of **1d** (3.0 g, 14.5 mmol) in Et_3N (17 mL). To the mixture was added a solution of phenyl iodide (1.6 g, 8.1 mmol). The resulting mixture was stirred at 50 °C for 6h. The reaction was quenched by the addition of water and extracted with Et_2O. The organic layer was washed with saturated aqueous NH_4Cl, and the water layer was extracted with Et_2O. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified on a silica

gel column chromatography (10% EtOAc/Hexanes), which furnished **1c** (1.2 g, 52% yield) as a dark brownish yellow oil. ^{1}H (400 MHz, $CDCl_3$): δ (ppm) 7.34 (m, 5H), 3.85 (s, 6H), 3.25 (s, 2H) 3.22 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 168.1, 132.0, 128.7, 128.5, 122.6, 116.2, 85.2, 82.3, 55.5, 54.0, 24.7, 22.3. IR (cm^{-1}) 2957, 2253, 1743, 1438, 1295, 1215, 1030. HRMS (ESI) calculated for $C_{16}H_{15}NO_4Na$ $(M+Na)^+$ 308.0899, observed 308.0895.

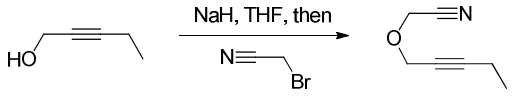
Synthesis of dimethyl 2-(cyanomethyl)-2-(3-(trimethylsilyl)prop-2-yn-1-yl)malonate (1e)



1e

To a stirring suspension of NaH (0.12 g, 4.82 mmol) in 30 ml THF was added dimethyl-2-(cyanomethyl)malonate (0.55 mg, 3.21 mmol) under N_2. The resulting solution was stirred at room temperature for 1 h after which time (3-bromoprop-1-yn-1-yl)trimethylsilane (0.50 g, 4.82 mmol) was added. A reflux condenser was attached and the mixture was stirred at reflux for 12 h at which time GC analysis showed no starting material. The solution was cooled to room temperature and quenched with 70 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 70 mL). The combined organics were washed with brine (100 mL), dried over anhydrous magnesium sulfate, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (20% EtOAc/hexanes) to yield **1e** (0.79 g, 87%) as a colorless solid. Mp: 34-36 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.82 (s, 6H), 3.14 (s, 2H), 3.03 (s, 2H), 0.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 167.9, 116.2, 99.1, 90.5, 55.4, 53.9, 25.4, 22.1, 0.1. IR (cm^{-1}): 2960, 2902, 2253, 2181, 1746, 1437, 1322, 1294, 1028, 847. HRMS calculated for $C_{13}H_{19}NO_4NaSi$ 304.0981, found 304.0977.

Synthesis of 2-(pent-2-yn-1-yloxy)acetonitrile (1f)

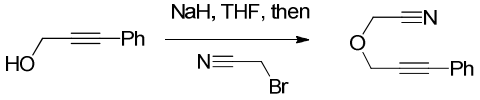


1f

To a stirring suspension of NaH (0.7 g, 30.9 mmol) in 25 ml THF was added pent-2-yn-1-ol (2.0 g, 23.8 mmol) under N_2 counter-flow in two portions. The resulting solution was stirred at room temperature for 1 h after which time bromoacetonitrile (3.7 g, 30.9 mmol) was added. The

reaction mixture was stirred at room temperature for 8-12 h at which time GC analysis showed no starting material. The solution was cooled and quenched with 100 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (10% EtOAc/hexanes) to yield **1f** (1.2 g, 42%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 4.34 (s, 2H), 4.28 (t, *J*= 4.4 Hz, 2H), 2.25 (m, 2H), 1.15 (t, *J*= 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 115.9, 91.3, 72.8, 58.9, 54.0, 13.7, 12.5. IR (cm^{-1}) 2980, 2919, 2292, 1452, 1320, 1140, 1092, 902. HRMS (ESI) calcd for $C_{21}H_{24}NO_5$ $[M+H]^+$ 124.0762, found 124.0776.

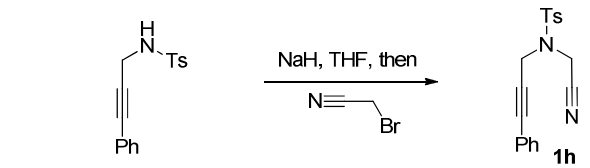
Synthesis of 2-((3-phenylprop-2-yn-1-yl)oxy)acetonitrile (1g)



1g

To a stirring suspension of NaH (0.3 g, 9.1 mmol) in 50 ml THF was added 3-phenylprop-2-yn-1-ol (2.0 g, 7.57 mmol) under N_2 counter-flow. The resulting solution was stirred at room temperature for 1 h after which time bromoacetonitrile (1.1 g, 9.1 mmol) was added. The mixture was stirred at room temperature for 12 h at which time GC analysis showed no starting material. The solution was cooled and quenched with 100 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (20% EtOAc/hexanes) to yield **1g** (1.2 g, 92%) as pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.49 (m, 2H), 7.36 (m, 3H), 4.55 (s, 2H), 4.43 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 132.0, 129.2, 128.6, 121.9, 115.9, 88.8, 82.3, 59.1, 54.3. IR cm^{-1} 3060, 2908, 2857, 2242, 1964, 1598, 1490, 1350, 1249, 1093, 902, 759, 692. HRMS (ESI) calcd for $C_{11}H_{10}NO$ $[M+H]^+$ 172.0762, found 172.0728.

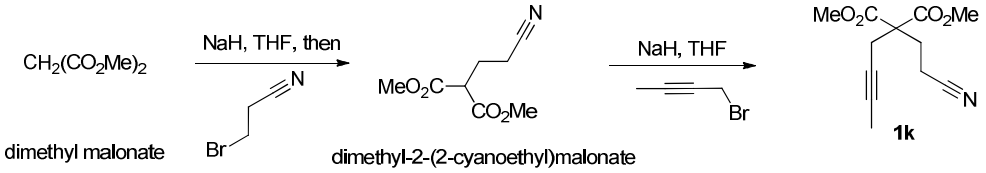
Synthesis of *N*-(cyanomethyl)-4-methyl-*N*-(3-phenylprop-2-yn-1yl)benzenesulfonamide (1h)



4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide

To a stirring suspension of NaH (0.05 g, 1.9 mmol) in 20 ml THF was added 4-methyl-*N*-(3-phenylprop-2-yn-1-yl)benzenesulfonamide [9] (0.5 g, 1.7 mmol) under N_2. The resulting solution was stirred at room temperature for 1 h after which time bromoacetonitrile (0.2 g, 1.9 mmol) was added. A reflux condenser was attached and the mixture was stirred at reflux for 12 h at which time GC analysis showed no starting material. The solution was cooled to room temperature and quenched with 100 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (30% EtOAc/hexanes) to yield **1h** (0.34 g, 60%) as a colorless solid. Mp: 97-99 °C. ^{1}H (400 MHz, $CDCl_3$): δ (ppm) 7.78 (d, *J*= 8Hz, 2H), 4.28 (t, *J*= 4.4 Hz, 2H), 2.25 (m, 2H), 1.15 (t, *J*= 7.6 Hz, 3H). ^{13}C (100 MHz, $CDCl_3$) δ (ppm) 145.2, 134.3, 131.9, 130.3, 129.2, 128.5, 128.1, 121.8, 113.8, 87.6, 80.1, 38.8, 35.4, 21.8. IR (cm^{-1}) 2958, 2253, 1744, 1438, 1215, 1072, 759. HRMS (ESI) calculated for $C_{18}H_{16}N_2O_2NaS$ (M+Na) 347.0830, observed: 347.0835.

Synthesis of dimethyl-2-(but-2-yn-1-yl)-2-(2-cyanoethyl)malonate (1k)



dimethyl malonate

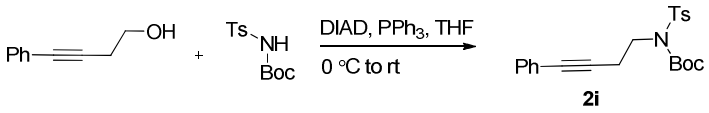
dimethyl-2-(2-cyanoethyl)malonate

To a stirring suspension of NaH (0.24 g, 10.1 mmol) in 100 ml THF was added dimethyl malonate (2.00 g, 15.14 mmol) under N_2. The resulting solution was stirred at room temperature for 1 h after which time bromopropionitrile (1.35 g, 10.1 mmol) was added. A reflux condenser was attached and the mixture was stirred at reflux for 12 h at which time the solution was cooled to room temperature and quenched with 100 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 100 mL). The combined organics were washed with brine (100 mL), dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (40% EtOAc/hexanes)

to yield dimethyl-2-(2-cyanoethyl)malonate (1.2 g, 64%) as a pale yellow oil. Spectral data was compared with known literature values.[10]

To a stirring suspension of NaH (0.16 g, 6.5 mmol) in 50 ml THF was added dimethyl-2-(2-cyanoethyl)malonate (1g, 5.4 mmol) under N_2. The resulting solution was stirred at room temperature for 1 h after which time 1-bromo-2-butyne (0.86 g, 6.5 mmol) was added. A reflux condenser was attached and the mixture was stirred at reflux for 12 h at which time the solution was cooled to room temperature and quenched with 50 mL of a saturated NH_4Cl solution. The layers were separated and aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organics were washed with brine (50 mL), dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The resulting crude yellow oil was purified by flash column chromatography (40% EtOAc/hexanes) to yield **1k** (0.6 g, 50%) as a colorless solid. Mp: 62-63 °C. ^{1}H (400 MHz, $CDCl_3$): δ (ppm) 3.78 (s, 6H), 2.79 (q, *J*= 2.4, 2.8 Hz, 2H), 2.44 (m, 4H), 1.77 (t, *J*= 2.4, 2.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.0, 119.2, 80.3, 72.4, 56.2, 53.3, 28.9, 24.2, 13.2, 3.7. IR (cm^{-1}) 2957, 2249, 1736, 1441, 1340, 1209. HRMS $C_{12}H_{15}NO_4Na$ calculated: 260.0899, observed 260.0898.

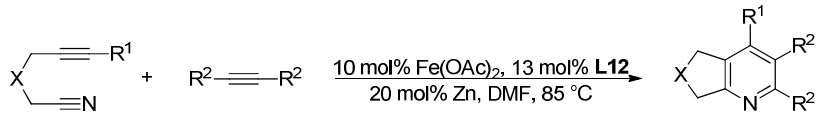
Synthesis of tert-butyl(4-phenylbut-3-yn-1-yl)tosylcarbamate (2i)



2i

Under N_2, diisopropylazodicarboxylate (1.7 ml, 8.92 mmol, 1.1 equiv) was added to a solution of *N*-(tert-butyoxycarbonyl)-*p*-toluenesulfonamide (2.2 g, 8.1 mmol, 1 equiv), triphenylphosphine (8.9 g, 1.3 mmol, 1.1 equiv) and 4-phenylbut-3-yn-1-ol [11] (1.3 g, 8.92 mmol, 1.1 equiv) in a dropwise fashion at 0 °C. The reaction mixture was then stirred at room temperature for 15 h. The solvent was removed under reduced pressure. Hexanes (100 ml) were added to the resultant yellow mixture and the white precipitate was filtered. The solid was pre-absorbed on silica gel and purified by flash column chromatography (20% EtOAc and Hexanes) affording the product **2i** as a white solid (3.1 g, 96%). Mp: 98-99 °C. ^{1}H (400 MHz, $CDCl_3$) δ (ppm) 7.84 (d, *J*= 6.8 Hz, 2H), 7.38 (m, 2H), 7.28 (m, 5H), 4.10 (t, *J*= 7.2 Hz, 2H), 2.89 (t, *J*= 8 Hz, 2H), 2.43 (s, 3H), 1.35 (s, 9H). ^{13}C (100 MHz, $CDCl_3$) δ ppm 151.1, 144.4, 137.6, 131.9, 129.5, 128.4, 128.2, 128.1, 123.7, 86.3, 84.7, 82.8, 45.6, 28.1, 21.8, 21.1. IR (in cm^{-1}): 3058, 2980, 2932, 1739, 1598,

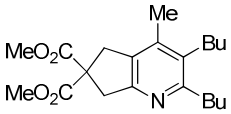
1357, 1287, 1162, 970, 846, 693. HRMS (ESI) calculated for m/z $C_{22}H_{25}NO_4NaS$ $(M+Na)^+$ 422.1402, observed 422.1403.



General Procedure for Cycloaddition:

In a nitrogen filled glove box, a solution of alkynenitrile (>1.0 M in DMF) was added to a vial containing 10 mol% $Fe(OAc)_2$ and 13 mol% **L12**. Additional DMF was added to make the final concentration of cyanoalkyne 0.4 M (accounting for alkyne volume). The mixture was stirred for 10 minutes then 1 equiv of alkyne and 20 mol% of zinc dust was added. The vial was capped and removed from the glove box then stirred at 85 °C for the indicated period of time. The crude mixture was purified via silica gel flash chromatography.

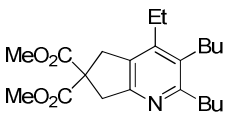
Synthesis of dimethyl-2,3-dibutyl-4-methyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3a)



3a

Compound **3a** was prepared using the general procedure with **1a** (51.3 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 μL of *N*,*N*-dimethylformamide. The reaction was stirred at 85 °C for 2 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3a** (58.2 mg, 70%) as a viscous, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.75 (s, 6H), 3.70 (s, 2H), 3.64 (s, 2H), 2.72 (t, *J* = 8 Hz, 2H), 2.56, (t, *J* = 8 Hz, 2H), 2.19 (s, 3H), 1.62 (m, 2H), 1.42 (m, 2H), 0.93 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.4, 159.8, 156.6, 141.6, 123.3, 130.3, 57.7, 53.2, 42.2, 38.1, 35.6, 33.0, 32.5, 28.4, 23.4, 23.3, 15.9, 14.2, 14.1. IR (cm^{-1}) 3476, 2963, 2019, 1736, 1582, 1438, 1380, 1241, 1071, 963, 863, 818, 737. HRMS (ESI) calcd for $C_{21}H_{32}NO_4$ $[M+H]^+$ 362.2331, found 362.2338.

Synthesis of dimethyl-2,3-dibutyl-4-ethyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3b)

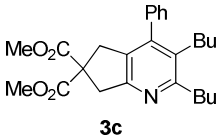


3b

Compound **3b** was prepared using the general procedure with **1a** (81.8 mg, 0.23 mmol), **2a** (47.7 mg, 0.35 mmol), $Fe(OAc)_2$ (6.0 mg, 3.5 x 10^{-2} mmol),

L12 (29.9 mg, 4.5 x 10^{-2} mmol), and zinc (4.5 mg, 6.9 x 10^{-2} mmol) in 800 µL of dimethylformamide. The reaction was stirred at 85 °C for 4 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3b** (102.9 mg, 86%) as a viscous, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.75 (s, 6H), 3.63 (s, 2H), 3.51 (s, 2H), 2.76 (q, *J* = 7.6, 7.6, 7.6 Hz, 2H), 2.62 (q, *J* = 7.2, 7.2, 7.2 Hz, 2H), 2.20 (s, 3H), 1.24 (t, *J* = 7.6, 7.6 Hz, 3H), 1.10 (t, *J* = 7.6, 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.3, 160.4, 157.1, 147.4, 131.4, 129.7, 58.1, 53.2, 42.0, 37.5, 42.0, 37.5, 35.5, 33.7, 33.0, 27.9, 23.5, 23.4, 23.3, 14.2, 14.04, 13.98. IR (cm^{-1}) 3476, 2958, 1744, 1580, 1437, 1408, 1378, 1253, 1104, 1070, 964, 905, 865, 736. HRMS (ESI) calcd for $C_{22}H_{34}NO_4$ $[M+H]^+$ 376.2488, found 376.2497.

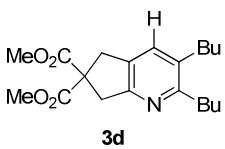
Synthesis of dimethyl-2,3-dibutyl-4-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3c)



3c

Compound **3c** was prepared using the general procedure with **1c** (98.4 mg, 0.35 mmol), **2a** (47.7 mg, 0.35 mmol), $Fe(OAc)_2$ (6.0 mg, 3.5 x 10^{-2} mmol), **L12** (29.9 mg, 4.5 x 10^{-2} mmol), and zinc (4.5 mg, 6.9 x 10^{-2} mmol) in 800 µL of *N*,*N*-dimethylformamide. The reaction was stirred at 85 °C for 4 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3c** (136.6 mg, 75%) as a viscous yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.42 (t, *J* = 8Hz, 2H), 7.36 (d, *J* = 7.2, 1H), 7.17 (d, *J* = 8 Hz, 2H), 3.71 (s, 6H), 3.22 (s, 2H), 2.78 (t, *J* = 10 Hz, 2H), 2.41 (t, *J* = 8 Hz, 2H), 1.70 (q, *J* = 7.2 Hz, 8 Hz, 2H), 1.46 (sext, *J* = 7.2 Hz, 7.2 Hz, 2H), 1.28 (q, *J* = 6.8 Hz, 8 Hz, 2H), 1.15 (q, *J* = 7.2 Hz, 7.2 Hz, 7.2 Hz, 2H), 0.96 (t, *J* = 7.2, 3H), 0.71 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.1, 160.6, 156.9, 146.8, 138.2, 131.6, 129.7, 128.6, 128.2, 127.7, 57.9, 42.3, 38.4, 35.4, 33.2, 32.9, 28.6, 23.3, 22.9, 14.2, 13.7. IR (cm^{-1}) 2956, 2869, 1783, 1576, 1490, 1437, 1273, 1198, 1073, 964, 739. HRMS (ESI) calcd for $C_{26}H_{34}NO_4$ $[M+H]^+$ 424.2488, found 424.2484.

Synthesis of dimethyl 2,3-dibutyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3d)

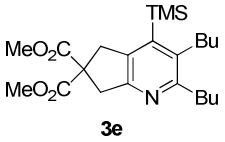


3d

Compound **3d** was prepared using the general procedure with **1d** (32.8 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 µL

of N,N-dimethylformamide. The reaction was stirred at 85 °C for 26 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3d** (24.0 mg, 30%) as a viscous yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.23 (s, 1H), 3.76 (s, 6H), 3.65 (s, 2H), 3.54, (s, 2H), 2.76 (t, *J* = 8 Hz, 2H), 2.56 (t, *J* =8 Hz, 2H), 1.63 (m, 4H), 1.53 (m, 4H), 1.42 (m, 4H), 0.95 (td, *J* = 7.2 Hz, 1.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.2, 159.7, 157.7, 133.8, 133.2, 130.6, 58.4, 53.3, 41.9, 38.5, 35.0, 33.4, 32.6, 32.2, 30.6, 23.3, 22.9, 14.24, 14.17. IR (cm^{-1}) 3286, 2958, 2868, 1737, 1603, 1572, 1437, 1379, 1249, 1072, 969, 853, 654. HRMS (ESI) calcd for $C_{26}H_{34}NO_4$ $[M+H]^+$ 348.2175, found 348.2176.

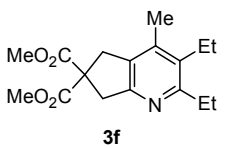
Synthesis of dimethyl 2,3-dibutyl-4-(trimethylsilyl)-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3e)



3e

Compound **3e** was prepared using the general procedure with **1e** (64.7 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 μL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 26 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3e** (55.0 mg, 57%) as a viscous, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.75 (s, 6H), 3.60 (s, 4H), 2.72 (t, *J* = 8 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H, 1.64 (m, 4H), 1.42 (m, 4H), 0.96 (m, 6H), 0.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.3, 159.3, 156.5, 144.4, 138.8, 136.0, 58.3, 53.2, 41.3, 41.0, 35.4, 35.3, 33.0, 32.2, 29.9, 23.4, 23.3, 14.2, 14.1, 2.4. IR (cm^{-1}) 3476, 2957, 2870, 2179, 1739, 1556, 1436, 1376, 1253, 1200, 1167, 1072, 1049, 965, 877, 843, 762, 695, 633. HRMS (ESI) calcd for $C_{23}H_{38}NO_4$ $[M+H]^+$ 420.2570, found 420.2579.

Synthesis of dimethyl 2,3-diethyl-4-methyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3f)

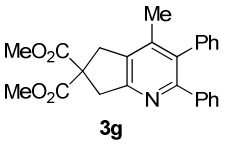


3f

Compound **3f** was prepared using the general procedure with **1a** (100.0 mg, 0.45 mmol), **2b** (36.8 mg, 0.45 mmol), $Fe(OAc)_2$ (7.8 mg, 4.5 x 10^{-2} mmol), **L12** (38.8 mg, 5.8 x 10^{-2} mmol), and zinc (5.9 mg, 9.0 x 10^{-2} mmol) in 1.0 mL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 6 hours and the resulting

brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3f** (97.0 mg, 71%) as a viscous, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 3.77 (s, 6H), 3.65 (s, 2H), 3.52 (s, 2H), 2.78 (q, *J* = 7.8 Hz, 7.5, Hz, 7.5 Hz, 2H), 2.64 (q, *J* = 7.5 Hz, 7.5 Hz, 7.5 Hz, 2H), 2.21 (s, 3H), 1.29-1.23 (m, 3H), 1.11 (t, *J* = 7.5 Hz, 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 172.3, 160.6. 156.7, 141.6, 133.4, 130.5, 57.7, 53.2, 42.2, 38.1, 28.7, 21.6, 15.6, 14.9, 14.5. IR (cm^{-1}) 2965, 1737, 1584, 1437, 1377, 1259, 1071, 961, 928, 864, 820, 733. HRMS (ESI) calcd for $C_{17}H_{24}NO_4$ $[M+H]^+$ 306.1705, found 306.1707.

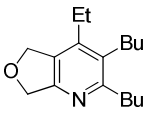
Synthesis of dimethyl-4-methyl-2,3-diphenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3g)



3g

Compound **3g** was prepared using the general procedure with **1a** (100.0 mg, 0.45 mmol), **2c** (159.7 mg, 0.90 mmol), $Fe(OAc)_2$ (7.8 mg, 4.5 x 10^{-2} mmol), **L12** (38.8 mg, 5.8 x 10^{-2} mmol), and zinc (5.9 mg, 9.0 x 10^{-2} mmol) in 1.1 mL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 6 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3g** (88.0 mg, 54%) as a viscous, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.27-7.02 (m, 10H), 3.82 (s, 8H), 3.65 (s, 2H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm). IR (cm^{-1}) 3057, 2854, 1737, 1601, 1554, 1495, 1432, 1400, 1266, 1201, 1121, 1073, 908, 862, 819, 797, 771, 736, 701, 574. HRMS (ESI) calcd for $C_{25}H_{24}NO_4$ $[M+H]^+$ 402.1705, found 402.1700.

Synthesis of 2,3-dibutyl-4-ethyl-5,7-dihydrofuro[3,4-b]pyridine (3h)

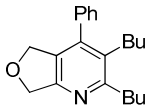


3h

Compound **3h** was prepared using the general procedure with **1f** (28.3 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 µL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 26 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3h** (24.7 mg, 41%) as a yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 5.13 (s, 2H), 5.02 (s, 2H), 2.77, (t, *J* = 8.4 Hz, 8.1 Hz, 2H), 2.64-2.50 (m, 4H), 1.71-1.6 (m, 2H), 1.50-1.41 (m, 6H), 1.15 (t, *J* = 7.8 Hz, 7.8 Hz, 3H), 1.00-0.929 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 160.9, 156.9, 145.2, 131.6, 128.7, 73.4, 71.9, 35.4, 33.7, 32.8, 27.6, 23.7, 23.4,

23.2, 14.1, 14.02, 13.97. IR (cm^{-1}) 2959, 1768, 1583, 1462, 1406, 1376, 1304, 1186, 1104, 1049, 903, 795, 742. HRMS (ESI) calcd for $C_{17}H_{28}NO$ $[M+H]^+$ 262.2171, found 262.2173.

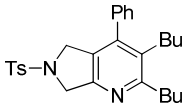
Synthesis of 2,3-dibutyl-4-phenyl-5,7-dihydrofuro[3,4-b]pyridine (3i)



3i

Compound **3i** was prepared using the general procedure with **1g** (39.4 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 µL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 4 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3i** (37.8 mg, 45%) as a colorless solid. Mp 49-50 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.41 (m, 3H), 7.19 (m, 2H), 5.1 (s, 2H), 4.8 (s, 2H), 2.85 (t, *J* = 8.0 Hz, 8.0 Hz, 2H), 2.49 (t, *J* = 8.0 Hz, 8.4 Hz, 2H), 1.74 (m, 2H), 1.45 (sext, *J* = 7.2 Hz, 7.2 Hz, 7.2 Hz, 2H), 1.34 (m, 2H), 1.18 (sext, *J* = 7.2, 7.2 Hz, 7.2 Hz, 2H), 0.98 (t, *J* = 7.6 Hz, 7.6 Hz, 3H), 0.74 (t, *J* = 7.2 Hz, 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.3, 156.9, 144.5, 137.9, 131.9, 129.0, 128.8, 128.1, 128.0, 73.8, 72.6, 35.5, 33.4, 32.9, 28.4, 23.3, 23.0, 14.2, 13.7. IR (cm^{-1}) 3058, 2957, 1952, 1780, 1581, 1497, 1463, 1399, 1289, 1257, 1181, 1101, 1042, 999, 900, 849, 748, 704, 647. HRMS (ESI) calcd for $C_{21}H_{28}NO$ $[M+H]^+$ 310.2171, found 310.2171.

Synthesis of 2,3-dibutyl-4-phenyl-6-tosyl-6,7-dihydro-5H-pyrrolo[3,4-b]pyridine (3j)

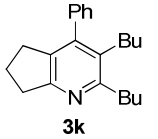


3j

Compound **3j** was prepared using the general procedure with **1h** (74.6 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 µL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 4 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3j** (43.5 mg, 41%) as a colorless solid. Mp 158-160 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.71 (d, *J*= 8Hz, 2H), 7.43 (q, *J*= 6.0, 7.2, 8.0 Hz, 4H), 7.29 (d, *J*= 8.4 Hz, 2H), 7.10 (dd, J= 18.4, 0.8 Hz, 2H), 4.63 (s, 2H), 4.28 (s, 2H), 2.78 (t, *J*= 7.6, 8.4 Hz, 2H), 2.41 (t, *J*= 10.4, 5.6 Hz, 5H), 1.68 (q, *J*= 6.8, 8.4, 7.6 Hz, 2H), 1.43 (sext, *J*= 7.6, 7.2, 7.6, 7.2 Hz, 2H), 1.26 (q, *J*= 7.2, 8.4, 7.2 Hz, 2H), 0.96 (t, *J*= 7.2, 7.2, 3H), 0.71 (t, *J*= 7.2, 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.8, 153.3, 145.7, 143.9, 137.2, 134.0, 132.7, 130.0, 129.0, 128.3, 127.9, 127.8, 126.7, 54.5, 52.4, 35.4, 33.2, 32.7, 28.5, 23.2, 23.0, 21.7, 14.2, 13.7. IR (cm^{-1}) 3064,

2957, 2926, 2860, 1725, 1494, 1212, 1097, 1061, 966, 740. HRMS (ESI) calcd for $C_{28}H_{35}N_2O_2$ $[M+H]^+$ 463.2419, found 463.2426.

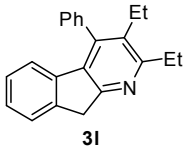
Synthesis of 2,3-dibutyl-4-phenyl-6,7-dihydro-5H-cyclopenta[b]pyridine (3k)



3k

Compound **3k** was prepared using the general procedure with **1i** (38.9 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 µL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 4 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3k** (54.3 mg, 65%) as a yellow viscous oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ (ppm) 7.46-7.39 (m, 3H), 7.19 (dd, *J* = 1.5 Hz, 6.6 Hz, 1.2 Hz, 2H), 5.09 (s, 2H), 4.84 (s, 2H), 2.85 (t, *J* = 7.8 Hz, 8.1 Hz, 2H), 2.49 (t, *J* = 7.5 Hz, 8.4 Hz, 2H), 1.79 (m, 2H), 1.48 (sext, 7.5 Hz, 7.2 Hz, 7.8 Hz, 8.7 Hz, 6.0 Hz, 2H), 1.38-1.12 (m, 6H), 0.98 (t, *J* = 7.2 Hz, 7.8 Hz, 3H), 0.74 (t, *J* = 7.2 Hz, 7.5 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 161.6, 159.1, 146.7, 139.0, 133.2, 130.3, 128.5, 128.32, 128.25, 127.3, 35.5, 34.7, 33.3, 33.1, 30.4, 28.6, 23.3, 23.0, 22.9, 14.2, 13.6. IR (cm^{-1}) 3057, 3029, 2959, 1950, 1725, 1573, 1496, 1462, 1393, 1338, 1243, 1178, 1104, 1073, 1028, 964, 916, 846, 739, 703, 619. HRMS (ESI) calcd for $C_{22}H_{30}N$ $[M+H]^+$ 308.2378, found 308.2384.

2,3-diethyl-4-phenyl-9H-indeno[2,1-b]pyridine (3l)

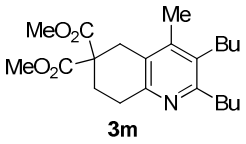


3l

Compound **3l** was prepared using the general procedure with **1j** (50.0 mg, 0.23 mmol), **2b** (18.9 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 552 µL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 2 hours. To the resulting brown mixture, 5 mL of dichloromethane, 5 mL of acetone and 10 mL of 6M HCl was added. The solution was stirred for 2 hours. The aqueous layer was extracted with 3 x 25 mL portions of dichloromethane and the organic layer was collected and concentrated *in vacuo*. The resulting greenish-yellow oil was dissolved in minimal dichloromethane and loaded onto a silica plug. The silica plug was then washed with 100 mL of ethyl acetate and the resulting filtrate was discarded. A 100 mL solution of 1% acetic acid in ethyl acetate was passed through the plug which was also discarded. A 100 mL of 1% NEt_3 solution in ethyl acetate was run through the

plug, collected, concentrated *in vacuo*, and further purified by column with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3l** (44.2 mg, 64%) as a yellow solid. Mp: 118-122 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 7.56-7.50 (m, 4H), 7.31 (d, *J* = 2.0 Hz, 2H), 7.19 (t, *J* = 7.5 Hz, 8.0 Hz, 1H), 6.15 (d, *J* = 8.0 Hz, 1H), 3.99 (s, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ (ppm) 161.4, 159.9, 144.5, 141.8, 140.2, 138.4, 132.9, 131.1, 129.2, 128.6, 128.1, 126.7, 125.1, 122.7, 38.7, 28.8, 22.2, 15.8, 15.0. IR (cm^{-1}). HRMS (ESI) calcd for $C_{22}H_{22}N$ $[M+H]^+$ 300.1752, found 300.1746.

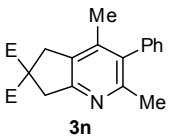
Synthesis of dimethyl 2,3-dibutyl-4-methyl-7,8-dihydroquinoline-6,6(5H)-dicarboxylate (3m)



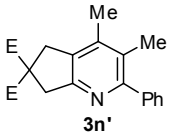
3m

Compound **3m** was prepared using the general procedure with **1k** (54.6 mg, 0.23 mmol), **2a** (32.8 mg, 0.23 mmol), $Fe(OAc)_2$ (4.0 mg, 2.3 x 10^{-2} mmol), **L12** (20 mg, 3.1 x 10^{-2} mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 533 μL of N,N-dimethylformamide. The reaction was stirred at 85 °C for 24 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% ethyl acetate in hexanes to yield **3m** (34.5 mg, 40%) as yellow viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 3.74 (s, 6H), 3.12 (s, 2H), 2.86 (t, *J*= 6.5, 6.5 Hz, 2H), 2.70 (t, *J*= 8.5, 8.0 Hz, 2H), 2.59 (t, *J*= 8 Hz, 2H), 2.37 (t, *J*= 7.0, 6.0 Hz, 2H), 2.19 (s, 3H), 1.62 (m, 2H), 1.44 (m, 6H), 0.96 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 171.8, 157.4, 150.4, 131.6, 127.7, 124.8, 53.7, 52.8, 35.5, 32.6, 32.3, 32.0, 29.5, 28.5, 27.7, 23.3, 23.1, 14.6, 14.0, 13.8. IR (cm^{-1}) 2957, 2870, 1738, 1665, 1571, 1438, 1332, 1242, 1169, 1084, 1027, 976, 858, 792, 737, 700. HRMS (ESI) calcd for $C_{22}H_{34}NO_4$ $[M+H]^+$ 376.2488, found 376.2486.

Synthesis of Dimethyl-2,4-dimethyl-3-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3n) and dimethyl-3,4-dimethyl-2-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3n'):



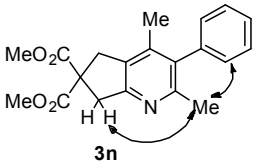
3n



3n'

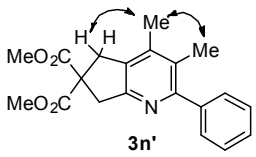
Compounds **3n** and **3n'** were prepared using the general procedure with **1a** (100 mg, 0.45 mmol) and **2e** (52 mg, 0.45 mmol), 10 mol% $Fe(OAc)_2$ (7.80 mg, 4.5x10^{-2} mmol), 13 mol% of **L12** (39.7 mg, 5.9x10^{-2} mmol), and zinc (5.9 mg, 9.0 x 10^{-2} mmol) in *N*,*N*-dimethylformamide. After 6h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes then

20% ethyl acetate in hexanes to afford 3m and 3m' in a 1.2:1.0::**3n**:**3n'** as yellowish oils (105.3 mg, 69% yield).



3n

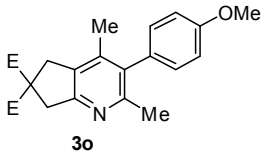
3n: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.41 (d, *J*= 8.4Hz, 2H), 7.34 (m, 1H), 7.41 (m, 2H), 3.78 (s, 6H), 3.71 (s, 2H), 3.55 (s, 2H), 2.21 (s, 3H), 1.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.2, 158.2, 155.5, 141.7, 139.1, 135.5, 130.1, 129.3, 128.8, 127.4, 127.4, 57.8, 53.3, 42.2, 37.8, 23.7, 17.1. IR (cm^{-1}) 3472, 2954, 1737, 1575, 1437, 1273, 1071, 868, 705. nOe correation of the methyl group and the phenyl ring and between the methyl and the methylene on the 5-membered ring. HRMS (ESI) calcd for $C_{20}H_{22}NO_4$ $[M+H]^+$ 340.1549, found 340.1552.



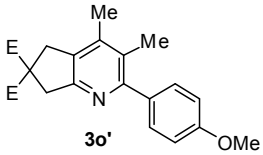
3n'

3n': ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.41 (d, *J*= 4Hz, 4H), 7.36 (d, t, *J*= 4.4Hz, 1H), 3.78 (s, 6H), 3.72 (s, 2H), 3.6 (s, 2H), 2.25 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.2, 158.4, 157.1, 142.8, 141.5, 131.3, 129.3, 128.3, 127.9, 127.7, 57.9, 53.3, 42.2, 37.9, 16.5, 16.4. IR (cm^{-1}) 3055, 2955, 1736, 1575, 1436, 1269, 1073, 738, 703. nOe corelation between the 2 methyl groups and the methyl group with the methylene on the 5-membered ring. HRMS (ESI) calcd for $C_{20}H_{22}NO_4$ $[M+H]^+$ 340.1549, found 340.1553.

Synthesis of dimethyl-3-(4-methoxyphenyl)-2,4-dimethyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3o) and dimethyl-2-(4-methoxyphenyl)-3,4-dimethyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3o')

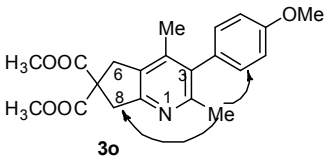


3o



3o'

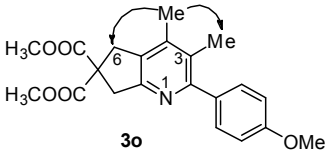
Compounds **3o** and **3o'** were prepared using the general procedure with **1a** (100 mg, 0.45 mmol) and **2f** (65 mg, 0.45 mmol), 10 mol% $Fe(OAc)_2$ (7.80 mg, $4.5x10^{-2}$ mmoles), 13 mol% of **L12** (39.7 mg, $5.9x10^{-2}$ mmol), and zinc (5.9 mg, 9.0 x 10^{-2} mmol) in *N*,*N*-dimethylformamide. After 6h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes then 20% ethyl acetate in hexanes and finally 30% ethyl acetate and hexanes to afford **3o** and **3o'** in a 3:2::**3o**:**3o'** as oils (65.2 mg, 39% yield).



3o

3o: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.02 (d, *J*= 8.8Hz, 2H), 6.96 (d, *J*= 8.4Hz 2H), 7.41 (m, 2H), 3.86 (s, 3H), 3.79 (s, 6H), 3.72 (s, 2H), 3.55 (s, 2H), 2.23 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz,

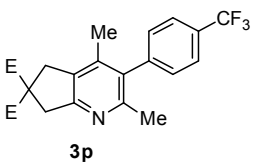
$CDCl_3$) δ (ppm) 172.3, 158.9, 158.0, 156.0, 142.3, 135.1, 131.2, 130.5, 130.2, 114.3, 57.9, 55.5, 53.3, 42.2, 37.9, 23.8, 17.2. IR (cm^{-1}): 3053, 2956, 2842, 1736, 1515, 1269, 1246, 1071, 838, 737. nOe corelation between the methyl group and phenyl ring. HRMS (ESI) calcd for $C_{19}H_{21}N_2O_4$ $[M+H]^+$ 370.1654, found 370.1660



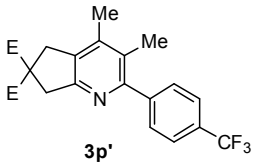
3o

3o': ^1H NMR (400 MHz, $CDCl_3$) δ ppm 7.37 (d, *J*= 8.8Hz, 2H), 6.95 (d, t, *J*= 8.8Hz, 2H), 3.84 (s, 3H), 3.78 (s, 6H), 3.71 (s, 2H), 3.59 (s, 2H), 2.25 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.3, 159.3, 158.1, 157.1, 142.8, 134.2, 130.9, 130.6, 127.9, 113.8, 58.0, 55.5, 53.3, 42.2, 38.0, 16.6, 16.5. IR (cm^{-1}): 2955, 2840, 1736, 1608, 1437, 1247, 1107, 1071, 839, 765. nOe correation between the two methyl groups and the methylene on the 5-membered ring. HRMS (ESI) calcd for $C_{21}H_{24}NO_5$ $[M+H]^+$ 370.1654, found 370.1660

Synthesis of dimethyl-2,4-dimethyl-3-(4-(trifluoromethyl)phenyl)-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3p) and dimethyl-3,4-dimethyl-2-(4-(trifluoromethyl)phenyl)-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3p')

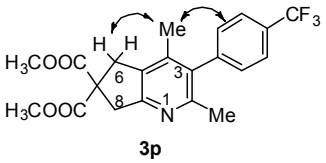


3p



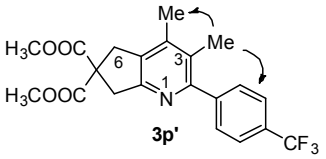
3p'

Compounds **3p** and **3p'** were prepared using the general procedure with **1a** (100 mg, 0.45 mmol) and **2g** (65 mg, 0.45 mmol), 10 mol% $Fe(OAc)_2$ (7.80 mg, $4.5x10^{-2}$ mmol), 13 mol% of **L12** (39.7 mg, $5.9x10^{-2}$ mmol), and zinc (5.9 mg, 9.0 x 10^{-2} mmol) in DMF. After 4h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes then 20% ethyl acetate in hexanes, and finally 30% ethyl acetate in hexanes to afford **3p** and **3p'** in a 4:1::**3p**:**3p'** as yellowish oils (63.7 mg, 39%).



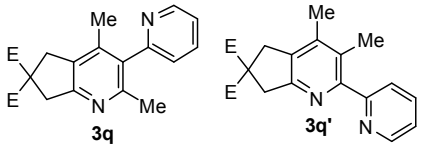
3p

3p: ^1H NMR (400 MHz, $CDCl_3$)δ ppm 7.02 (d, *J*= 8.8Hz, 2H), 6.96 (d, *J*= 8.4Hz 2H), 7.41 (m, 2H), 3.86 (s, 3H), 3.79 (s, 6H), 3.72 (s, 2H), 3.55 (s, 2H), 2.23 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.2, 158.9, 158.0, 156.0, 142.3, 135.1, 131.2, 130.5, 130.2, 114.3, 57.9, 55.5, 53.3, 42.2, 37.9, 23.8, 17.2. IR (cm^{-1}): 2956, 2927, 2856, 1737, 1615, 1438, 1325, 1167, 1126, 1067, 848. nOe correaltion between the methyl and the methylene, and also the methyl group with the phenyl ring. HRMS (ESI) calcd for $C_{21}H_{21}NO_4F_3$ $[M+H]^+$ 408.1423, found 408.1425.

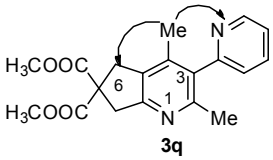


3p': ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.69 (d, *J*= 8Hz, 2H), 7.25 (d, *J*= 8Hz, 2H), 3.78 (s, 6H), 3.71 (s, 2H), 3.55 (s, 2H), 2.19 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.1, 159.0, 155.2, 143.1, 141.5, 134.0, 130.3, 130.0, 126.0, 125.9, 57.8, 53.4, 42.3, 37.8, 23.8, 17.1. nOe correation between the methyl group and the phenyl and also between the 2 methyl groups. IR (CH_2Cl_2, cm^{-1}): HRMS (ESI) calcd for $C_{19}H_{21}N_2O_4$ $[M+H]^+$ 370.16, found 370.1660

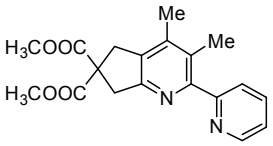
Synthesis of dimethyl-2,4-dimethyl-3-(pyridin-2-yl)-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3q) and dimethyl-3,4-dimethyl-2-(pyridin-2-yl)-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3q')



Compounds **3q** and **3q'** were prepared using the general procedure with **1a** (50 mg, 0.22 mmol) and **2g** (39.4 mg, 0.22 mmol) with 10 mol% $Fe(OAc)_2$ (3.89 mg, $2.2x10^{-2}$ mmol), 13 mol% of **L12** (19.83 mg, $2.9x10^{-2}$ mmol), and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in DMF. After 5h the crude reaction mixture was purified via flash column chromatography using using 50% EtOAc in hexanes then 2% dichloromethane in methanol, and finally 5% dichloromethane in methanol to afford **3q** and **3q'** in a 7:3::**3q**:**3q'** as yellowish oils (42.7 mg, 56%).

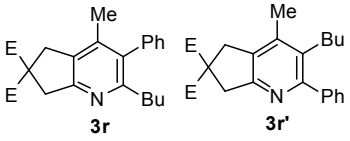


3q: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 8.80 (s, 1H), 7.70 (dt, *J*= 8Hz. 1.2Hz, 1H), 7.28 (m, 1H), 7.21 (d, *J*= 7.6 Hz, 1H), 3.77 (s, 6H), 3.70 (s, 2H), 3.54 (s, 2H), 2.22 (s, 3H), 1.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.1, 159.2, 158.3, 155.4, 150.1, 141.7, 136.8, 134.2, 130.3, 124.9, 122.4, 58.0, 53.3, 42.2, 37.7, 23.3, 16.7. IR (cm^{-1}): 2954, 2924, 2851, 1736, 1588, 1434, 1274, 1071, 964, 823. nOe corelation between the methyl group and the pyridyl ring and also with the methylene protons on the 5 membered ring. HRMS (ESI) calcd for $C_{19}H_{21}N_2O_4$ $[M+H]^+$ 341.1517, found 341.1511.

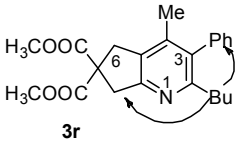


3q': ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.70 (s, 1H), 7.79 (t, *J*= 7.6Hz, 1H), 7.60 (d, *J*= 7.6Hz, 1H), 7.28 (m, 1H), 3.78 (s, 6H), 3.73 (s, 2H), 3.61 (s, 2H), 2.26 (d, *J*= 4Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 172.2, 159.8, 157.3, 156.4, 149.0, 143.4, 136.7, 132.4, 129.0, 124.6, 122.6, 58.1, 53.4, 42.2, 38.0, 16.5, 15.9. IR (cm^{-1}): 2954, 2924, 2853, 1736, 1585, 1436, 1276, 1072, 964. HRMS (ESI) calcd for $C_{19}H_{21}N_2O_4$ $[M+H]^+$ 341.1501, found 341.1505

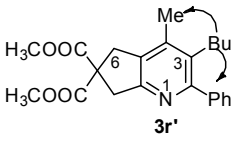
Synthesis of dimethyl-2-butyl-4-methyl-3-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3r) and dimethyl-3-butyl-4-methyl-2-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3r')



Compounds **3r** and **3r'** were prepared using the general procedure with **1a** (50 mg, 0.22 mmol) and **2i** (26.2 mg, 0.22 mmol), 10 mol% $Fe(OAc)_2$ (3.89 mg, $2.2x10^{-2}$ mmol), 13 mol% of **L12** (19.83 mg, $2.9x10^{-2}$ mmol) catalyst, and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in DMF. After 16h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes and then 20% EtOAc in hexanes to afford **3q** and **3q'** in a 3:2::**3r**:**3r'** as oils (45.2 mg, 53%).

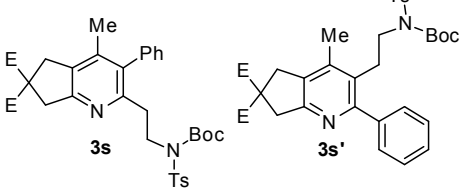


3r: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.36 (m, 5H), 3.76 (s, 6H), 3.71 (s, 2H), 3.60 (s, 2H), 2.53 (t, *J*= 8.4Hz, 2H), 2.29 (s, 3H), 1.35 (s, 2H), 1.21 (sext, *J*= 7.2 Hz, 2H), 0.77 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.3, 159.0, 156.8, 142.3, 141.8, 132.9, 131.8, 128.9, 128.2, 127.6, 57.8, 53.3, 42.2, 38.1, 32.5, 29.0, 23.0, 16.0, 13.8. IR (cm^{-1}): 2956, 2860, 1737, 1574, 1437, 1273, 1071, 736, 705. HRMS (ESI) calcd for $C_{23}H_{27}NO_4$ $[M+H]^+$ 382.2018, found 382.2022



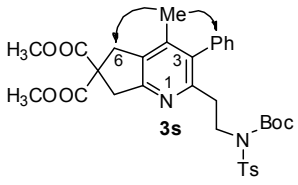
3r': ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.39 (m, 3H), 7.60 (td, J_1= 6.8 Hz, J_2= 1.6 Hz, J_3= 1.2 Hz, 2H) 3.80 (s, 6H), 3.74 (s, 2H), 3.56 (s, 2H), 2.45 (t, J_1= 8.4Hz, J_2= 7.6 Hz, 2H), 1.91 (s, 3H), 1.76 (sext, J_1= 7.6 Hz, J_2= 7.2 Hz, J_3= 7.2 Hz, 2H), 0.73 (t, J_1= 7.6 Hz, J_2= 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.2, 159.7, 158.4, 141.9, 139.0, 135.0, 129.9., 129.0, 128.6, 127.4, 57.7, 53.3, 42.4, 38.0, 36.1, 32.6, 22.9, 17.2, 14.0. IR (cm^{-1}): 2956, 2870, 1737, 1436, 1274, 1071, 961, 862, 735, 702. HRMS (ESI) calcd for $C_{23}H_{28}NO_4$ $[M+H]^+$ 382.2018, found 382.2032.

Synthesis of dimethyl 2-(2-(N-(tert-butoxycarbonyl)-4-methylphenylsulfonamido)ethyl)-4-methyl-3-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3s), and dimethyl 3-(2-(N-(tert-butoxycarbonyl)-4-methylphenylsulfonamido)ethyl)-4-methyl-2-phenyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3s')

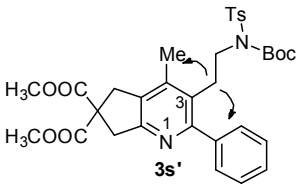


Compounds **3s** and **3s'** were prepared using the general procedure with **1a** (50 mg, 0.22 mmol), **2i** (26.2 mg, 0.22 mmol), 10 mol% $Fe(OAc)_2$ (3.89 mg, $2.2x10^{-2}$ mmol), 13 mol% of **L12** (19.83 mg, $2.9x10^{-2}$ mmol) catalyst, and zinc

(3.0 mg, 4.6 x 10^{-2} mmol) in DMF. After 16h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes, then 20% EtOAc in hexanes and finally 40% EtOAc in hexanes to afford **3s** and **3s'** in a 3:2::**3s**:**3s'** as yellowish oils (61.8 mg, 44%).

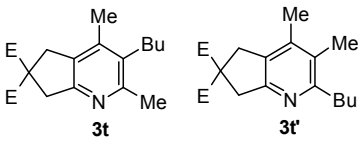


3s: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.52 (d, J= 8.4 Hz, 2H), 7.44 (m, 4H), 7.39 (m, 1H), 7.21 (d, *J*= 8.14 Hz, 2H), 3.80 (s, 6H), 3.74 (s, 2H), 3.61 (s, 2H), 3.03 (t, *J*= 8.4, 8.0 Hz, 2H), 2.42 (d, *J*= 8.4 Hz, 6H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.2, 160.0, 158.0, 151.0, 144.3, 143.6, 141.3, 137.5, 132.1, 129.4, 129.1, 128.6, 128.2, 128.1, 127.9, 84.6, 57.8, 53.4, 46.1, 42.3, 38.1, 30.1, 28.1, 21.8, 16.3. nOe correlation between the methyl group and the phenyl ring and also the methyl group and the methylene protons on the 5 membered ring. IR (cm^{-1}): 2956, 1734, 1575, 1437, 1400, 1278, 1159, 1090, 969, 736. HRMS (ESI) calcd for $C_{33}H_{38}N_2O_8SNa$ $[M+Na]^+$ 645.2247, found 645.2264.



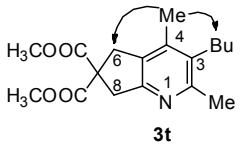
3s': ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.61(d, J=8.4 Hz, 2H), 7.45 (t, *J*=7.2 Hz, 2H), 7.39 (d, J=7.2 Hz, 2H), 7.20 (d, J=7.6, 2H), 7.13 (d, *J*=7.6 Hz, 2H), 4.12 (t, *J*=7.6 Hz, 2H), 3.80 (s, 6H), 3.72 (s, 2H), 3.57 (s, 2H), 2.86 (t, *J*= 7.2 Hz, 2H), 2.41 (s, 3H), 1.92 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.3, 158.7, 155.6, 151.0, 144.0, 141.7, 138.5, 137.7, 135.6, 130.4, 129.6, 129.2, 128.9, 128.1, 127.5, 84.0, 57.8, 53.3, 46.8, 42.2, 37.9, 35.8, 28.0, 21.8, 17.2. nOe corelation between the methylene on the side chain with the phenyl and also the methyl group. IR (cm^{-1}): 2956, 1734, 1596, 1439, 1400, 1277, 1159, 1088, 970, 735. HRMS (ESI) calcd for $C_{33}H_{38}N_2O_8SNa$ $[M+Na]^+$ 645.2247, found 645.2254.

Synthesis of dimethyl-3-butyl-2,4-dimethyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3t) and dimethyl-2-butyl-3,4-dimethyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3t')



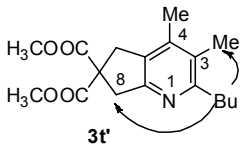
Compounds **3t** and **3t'** were prepared using the general procedure with **1a** (50 mg, 0.22 mmol) and **2j** (28.9 mg, 0.22 mmol), 10 mol% $Fe(OAc)_2$ (3.89 mg, 2.2x10^{-2} mmol) and 13 mol% of **L12** (19.83 mg, 2.9x10^{-2} mmol) catalyst, and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 0.53 ml DMF. After 16h the crude reaction mixture was purified via flash column chromatography using 100 ml

hexanes, then 20% EtOAc in hexanes and finally 30% EtOAc in hexanes to afford **3t** and **3t'** in a 1:1::**3t**:**3t'** as oils (44.3 mg, 62%).



3t

3t: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.76 (s, 3H), 3.63 (s, 2H), 3.51 (s, 2H), 2.57 (t, *J*= 8Hz, 2H), 2.50 (s, 3H), 2.20 (s, 3H), 1.42 9m, 4H), 0.96 (t, *J*= 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.3, 156.4, 155.7, 141.4, 133.0, 130.6, 57.9, 53.3, 42.2, 38.1, 31.6, 28.9, 23.3, 22.8, 15.8, 14.1. IR (cm^{-1}) 2956, 2869, 1737, 1586, 1437, 1274, 1070, 961, 736. nOe correlation between the methyl group and the butyl group and also the methyl group with the methylene protons on the 5 membered ring. HRMS (ESI) calcd for $C_{18}H_{26}NO_4$ $[M+H]^+$ 320.1862, found 320.1867

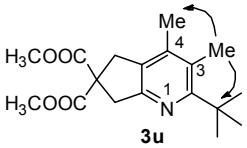


3t'

3t': ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.76 (s, 6H), 3.65 (s, 2H), 3.52 (s, 2H), 2.76 (t, J= 8.4 , 8.0Hz, 2H), 2.17 (d, J= 3.6 Hz, 6H), 1.60 (m, 2H), 1.43 (sextet, J= 7.6, 7.2, 2H), 0.94 (t, *J*= 7.2 Hz, 3H) . ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.3, 159.8, 156.5, 142.0, 130.1, 127.6, 57.9, 53.3, 42.2, 38.0, 36.5, 32.0, 23.2, 16.5, 14.5, 14.2. IR (cm^{-1}) 2956, 1737, 1583, 1436, 1378, 1273, 1199, 1163, 1103, 1071, 962, 863, 735. nOe correation between the methylene of the butyl group and the methyl group. HRMS (ESI) calcd for $C_{18}H_{25}NO_4$ $[M+H]^+$ 320.1862, found 320.1866.

Synthesis of dimethyl-2-(tert-butyl)-3,4-dimethyl-5H-cyclopenta[b]pyridine-6,6(7H)-dicarboxylate (3u)

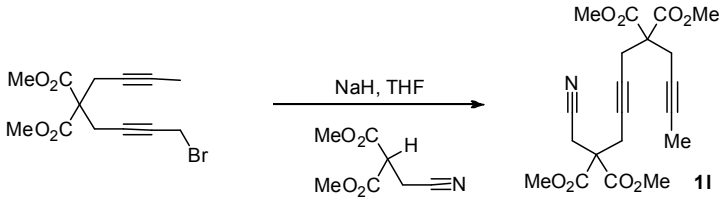
Compound **3u** was prepared using the general procedure with **1a** (50 mg, 0.22 mmol) and **2j** (28.9 mg, 0.22 mmol), 10 mol% $Fe(OAc)_2$ (3.89 mg, $2.2x10^{-2}$mmoles), 13 mol% of **L12** (19.83 mg, $2.9x10^{-2}$mmoles) catalyst, and zinc (3.0 mg, 4.6 x 10^{-2} mmol) in 0.53 ml DMF. After 16h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes, then 20% EtOAc in hexanes and finally 30% EtOAc in hexanes to afford **3u** as a single product as an oil (44.3 mg, 26%).



3u

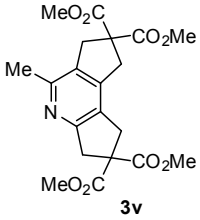
3u: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.78 (s, 6H), 3.66 (s, 2H), 3.53 (s, 2H), 2.35 (s, 2H), 2.16 (s, 3H), 1.43 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.5, 165.0, 155.2, 142.9, 129.7, 128.7, 128.0, 57.7, 53.2, 42.4, 38.8, 38.1, 30.6, 24.4, 23.7, 22.7, 17.1, 16.7. nOe correlation between the 2 methyl groups and one methyl group with the *t*-butyl group. IR (cm^{-1}): 2956, 2900, 1731, 1638, 1438, 1273, 1199, 1071, 961, 737, 701. HRMS (ESI) calcd for $C_{18}H_{26}NO_4$ $[M+H]^+$ 320.1862, found 320.1861.

Synthesis of tetramethyl 1-cyanoundeca-4,9-diyne-2,2,7,7-tetracarboxylate (1l)



Dimethyl 2-(4-bromobut-2-yn-1-yl)-2-(but-2-yn-1-yl)malonate[12] was then added to a solution of NaH (92 mg, 3.85 mmol), THF (40 ml), and dimethyl-2-(cyanomethyl)malonate (0.6 g, 3.5 mmol) which was previously stirred at room temperature for 1 hour. After the addition was complete the reaction mixture was refluxed for 12-15 hours. Completion of the reaction was monitored by gas chromatography. The reaction was later quenched by addition of 50 ml saturated ammonium chloride and distilled water 20 ml and extracted with diethyl ether (3x100 ml). All organic layers were washed with brine and then dried over magnesium sulfate. The organic layers were concentrated *in vacuo* to afford a crude oil. The crude oil was then purified by column chromatography using silica gel to afford **1l** (1.2 g, 86%) as yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.81 (s, 6H), 3.75 (s, 6H), 3.12 (s, 2H), 2.98 (t, *J*= 2 Hz, 2H), 2.93 (t, *J*= 2.4 Hz, 2H), 2.84 (q, *J*=2.4 Hz, 2H), 1.75 (t, *J*= 2.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 169.6, 168.1, 116.3, 79.7, 79.5, 723.0, 56.9, 55.3, 53.9, 53.2, 24.1, 23.2, 23.1, 22.0, 3.7. IR (cm^{-1}): 2958, 2848, 2251, 1741, 1437, 1294, 1214, 1056, 952, 819. HRMS (ESI) calcd for $C_{20}H_{23}NO_8Na$ $[M+Na]^+$ 428.1321, found 428.1328.

Synthesis of tetramethyl-5-methyl-dicyclopenta[b,d]pyridine-2,2,7,7(1H,3H,6H,8H)-tetracarboxylate (3v)

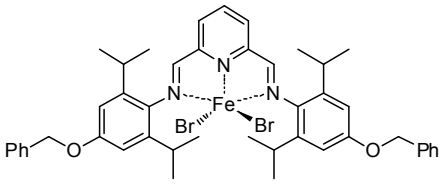


The general procedure was used with **1l** (50 mg, 0.12 mmol) with 20 mol% $Fe(OAc)_2$ (4.3 mg, 3.2x10^{-2} mmoles) and 32 mol% of **L12** (21.4 mg, 2.5 x10^{-2} mmoles), and zinc dust (3.2 mg, 4.9 x10^{-2}) in 0.4 ml DMF. After 24h the crude reaction mixture was purified via flash column chromatography using 100 ml hexanes, then 30% EtOAc in hexanes and finally 50% EtOAc in hexanes to afford **3v** as yellowish oil (37 mg, 74%).

3v: ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.76 (s, 6H), 3.75 (s, 6H), 3.62 (s, 2H), 3.52 (s, 2H), 3.49 (s, 2H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 172.1, 171.9, 159.3, 152.9, 145.5, 132.7, 126.8, 59.8, 58.3, 53.4, 41.8, 39.4, 39.1, 37.1, 22.0. IR (cm^{-1}): 2955, 2850, 1736,

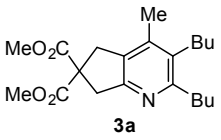
1592, 1434, 1266, 1200, 1068, 961, 860, 737. HRMS (ESI) calcd for $C_{20}H_{24}NO_4$ $[M+H]^+$ 406.1502, found 406.1502.

Synthesis of $FeBr_2$ and L12 complex



The $FeBr_2$ and L12 complex was prepared by a previous reported method[13] using $FeBr_2$ (20 mg, 9.2 x10^{-2} mmol) **L12** (61.8 mg, 9.2 x10^{-2} mmol) in THF in the glove box. The reaction mixture was stirred for 3 hours and then filtered over celite. Removal of THF in *vacuo* afforded the complex as a dark green solid.

^{1}H NMR (300 MHz, CD_2Cl_2) (All peaks appeared broad) δ (ppm) 59.5 (2H), 14.02 (4H), 7.55 (17H), 0.34 (28H), 3.62 (s, 2H), 3.52 (s, 2H), 3.49 (s, 2H), 2.42 (s, 3H). Crystals were grown by slow diffusion of diethyl ether from dichloromethane. Based on the preliminary crystal structure analysis, we found that the iron is coordinated to the 3 nitrogens of **L12**. The crystal system is triclinic A= 8.8401 Å, B= 9.9680 Å, C= 27.2923 Å, α= 90.91°, β= 94.59°, γ= 113.99°. Unit cell volume= 2194.98 Å^3, Space group= P$\bar{1}$. Disorder in the *p*-substituted benzyloxy region was also observed.



3a

Compound **3a** was prepared using **1a** (51.3 mg**,** 0.23 mmol) **2a** (32.8 mg, 0.23 mmol), $FeBr_2$-L12 complex (20.3 mg, 2.3x 10^{-2} mmol), and zinc (30 mg, 4.6x10^{-2} mmol) in 533μL of *N*,*N*-dimethyl formamide. The reaction was stirred at 85 °C for 2 hours and the resulting brown mixture was purified with silica gel flash chromatography using 10% EtOAc in hexanes to yield **3a** (48 mg, 58%) as a viscous yellow oil (characterization reported above).

References:

(1) (a) Miura, T.; Nakazawa. H.; Murakami, M. *Chem*. *Commun*. **2005**, 2855-2856. (b) Eckhardt, M.; Fu, G. C. *J*. *Am*. *Chem*. *Soc*. **2003**, *125*, 13642-13643.

(2) Shen, H.; Xie, Z. *J*. *Am*. *Chem*. *Soc*. **2010**, 132, 11473-11480.

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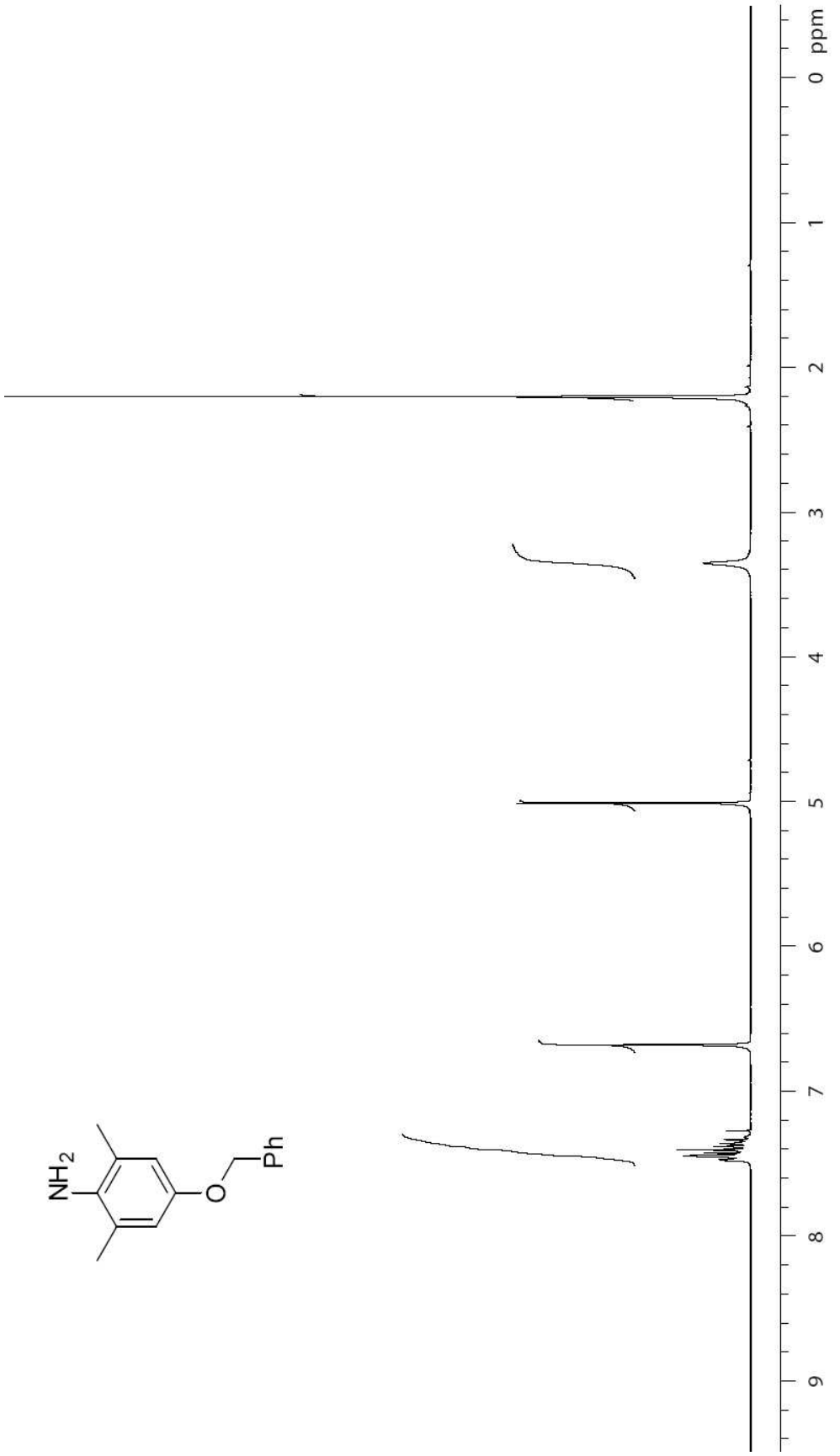
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O
Ph
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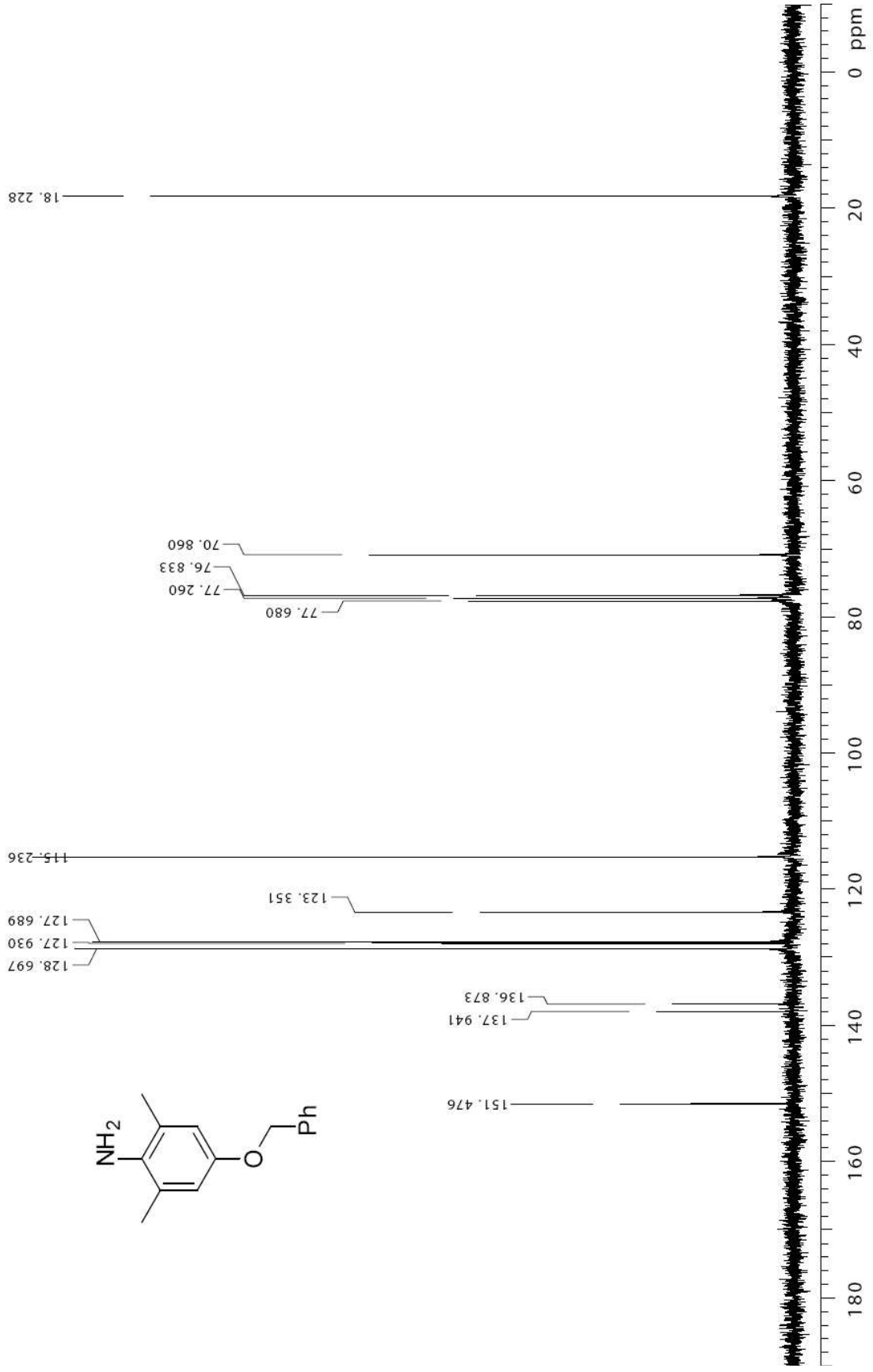
1
2
3
4
5
6
7
8
9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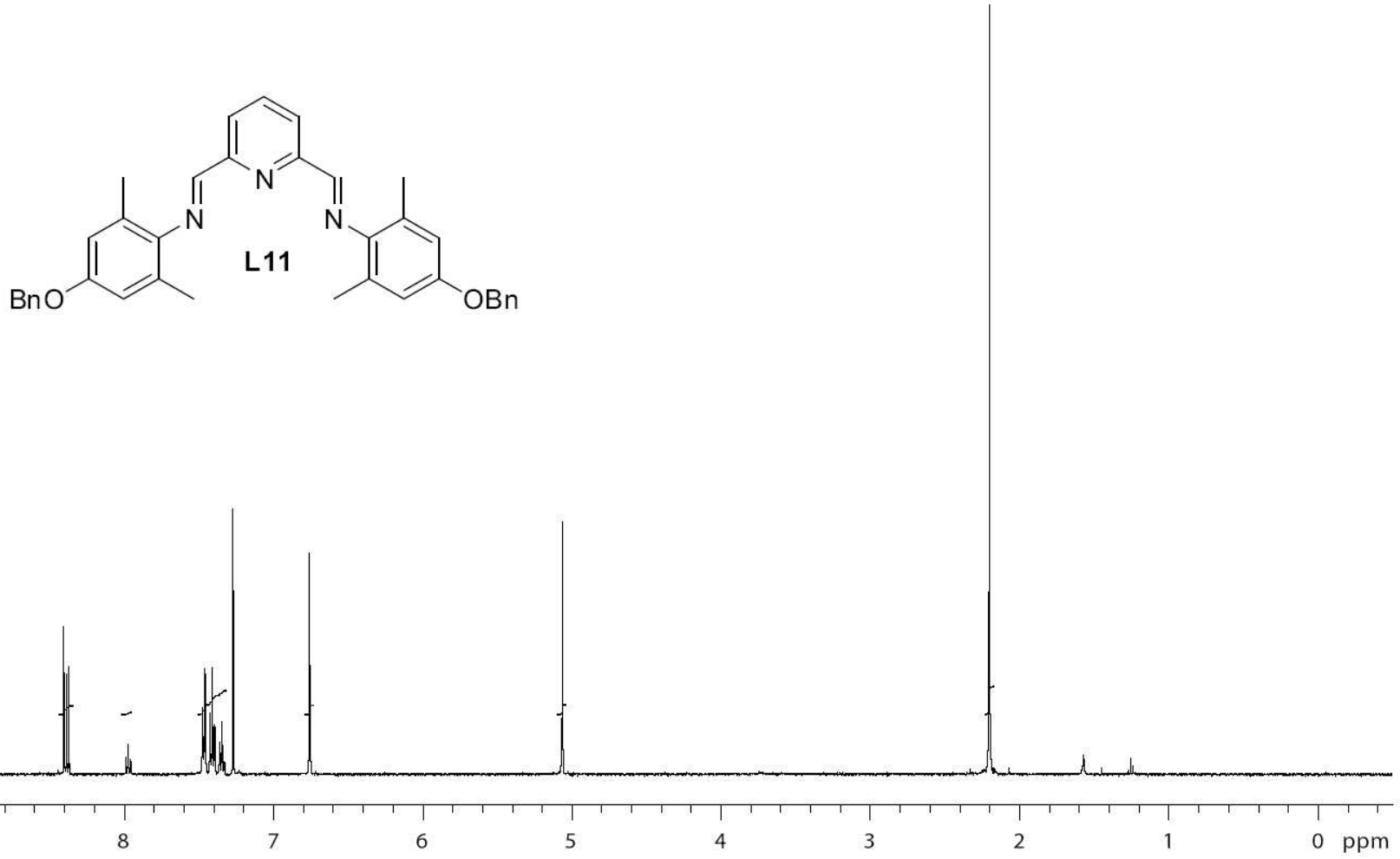
70.860
76.833
77.260
77.680
115.236
123.351
127.689
127.930
128.697
136.873
137.941
151.476
NH2
O
Ph
0 ppm
20
40
60
80
100
120
140
160
180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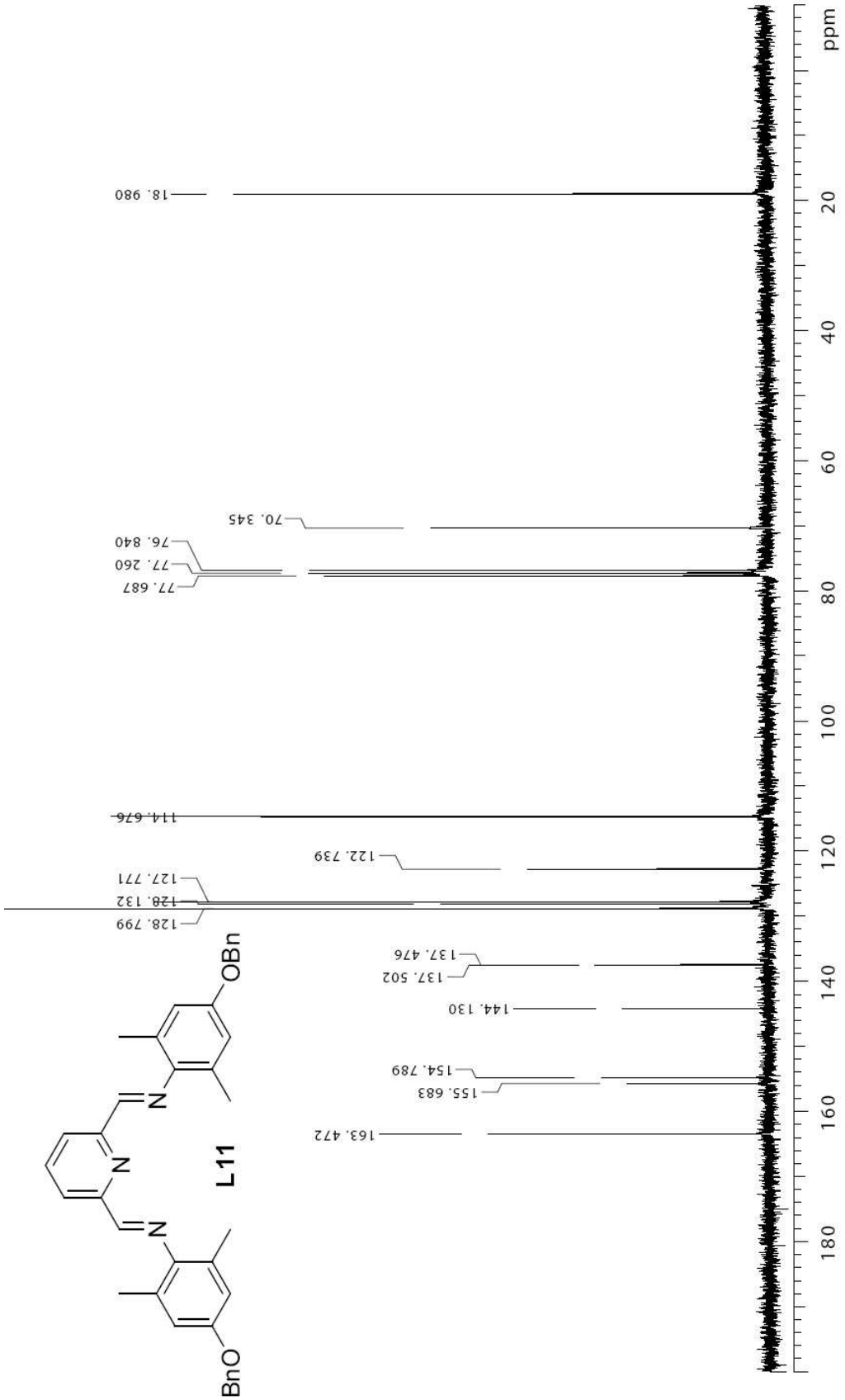
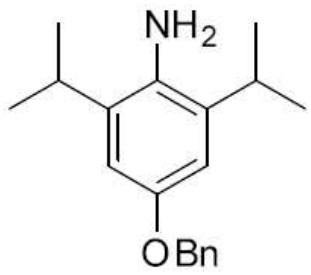
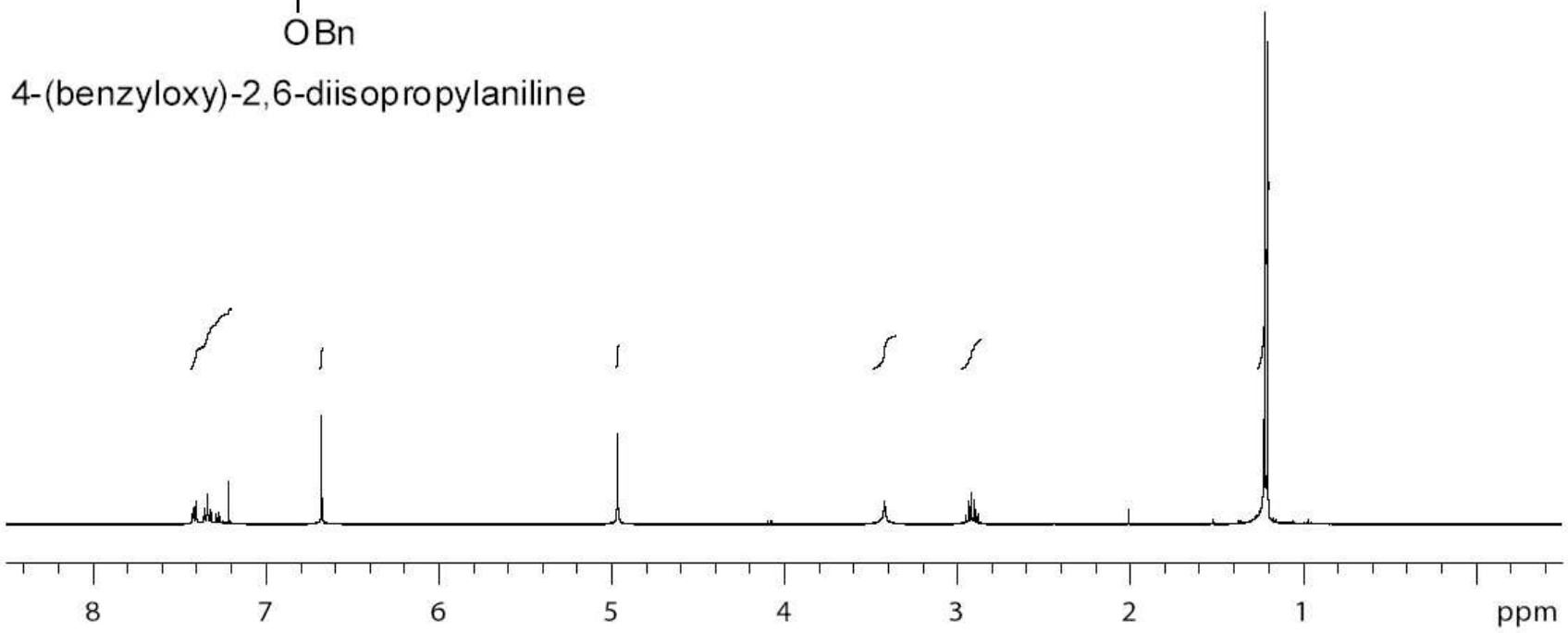
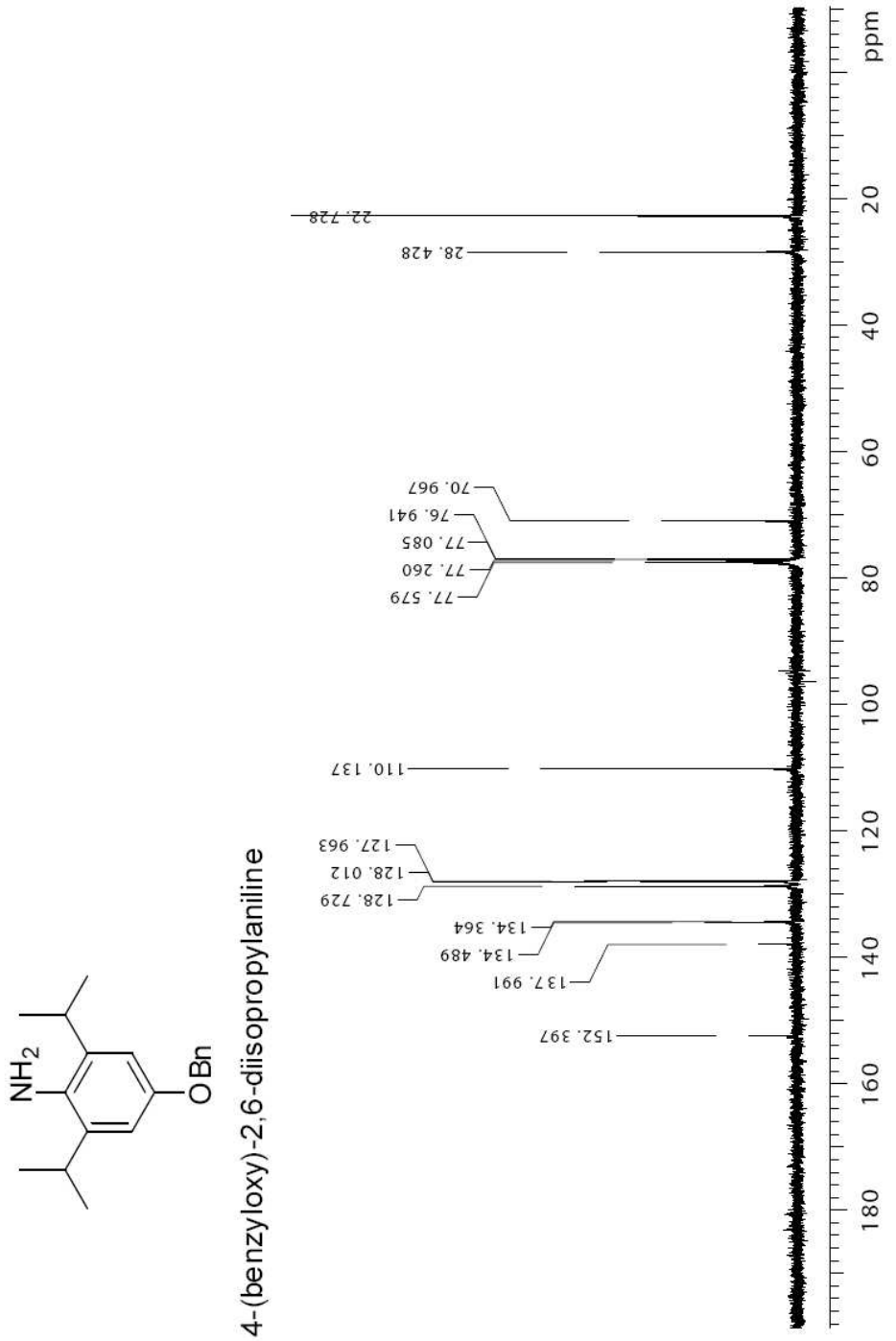
N
N
L11
BnO
OBn
9
8
7
6
5
4
3
2
1
0 ppm


ppm
20
40
60
80
100
120
140
160
180
18.980
70.345
76.840
77.260
77.687
114.676
122.739
127.771
128.132
128.799
137.476
137.502
144.130
154.789
155.683
163.472
L11
OBn
BnO
N
N
N



4-(benzyloxy)-2,6-diisopropylaniline

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OBn
4-(benzyloxy)-2,6-diisopropylaniline
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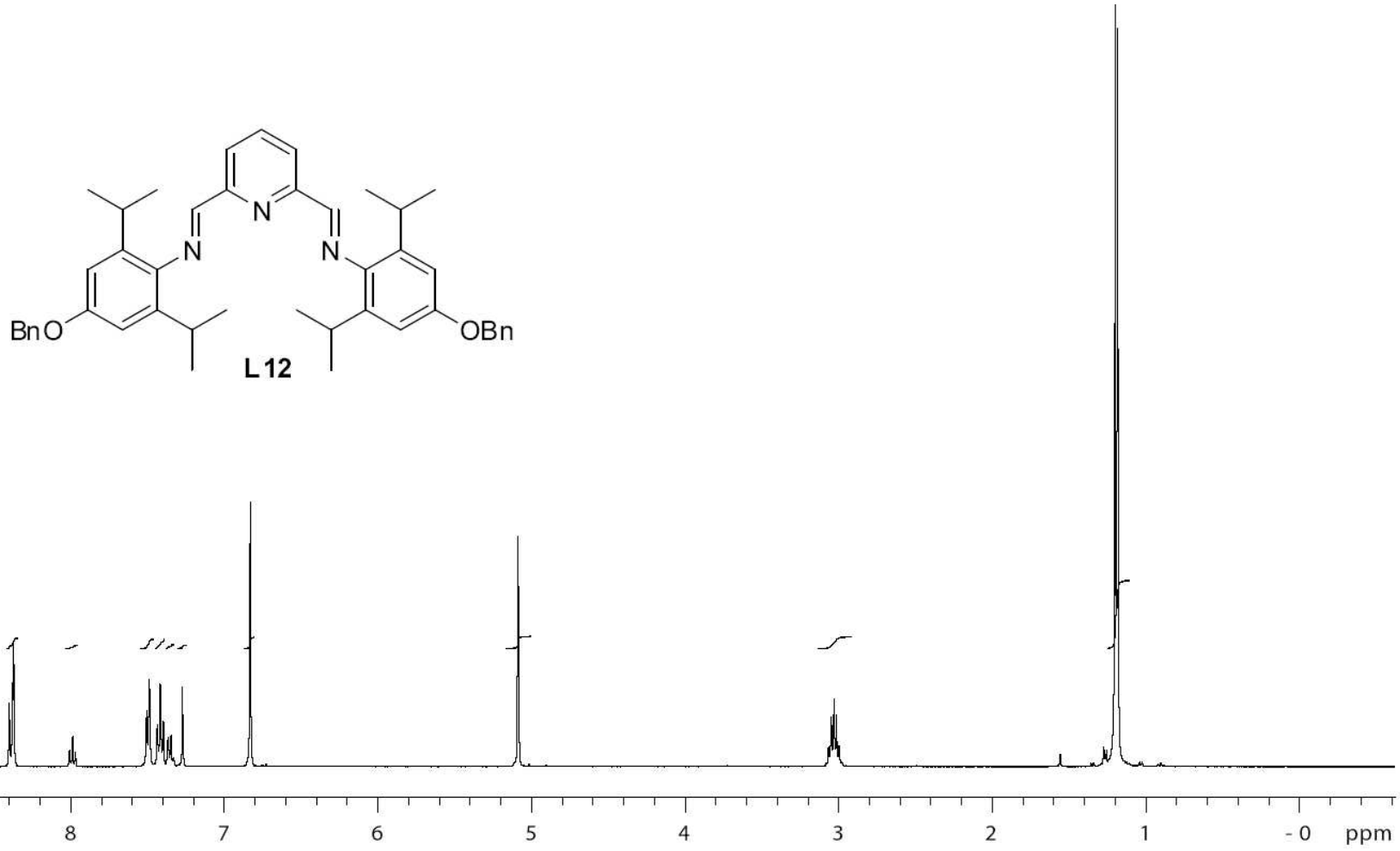
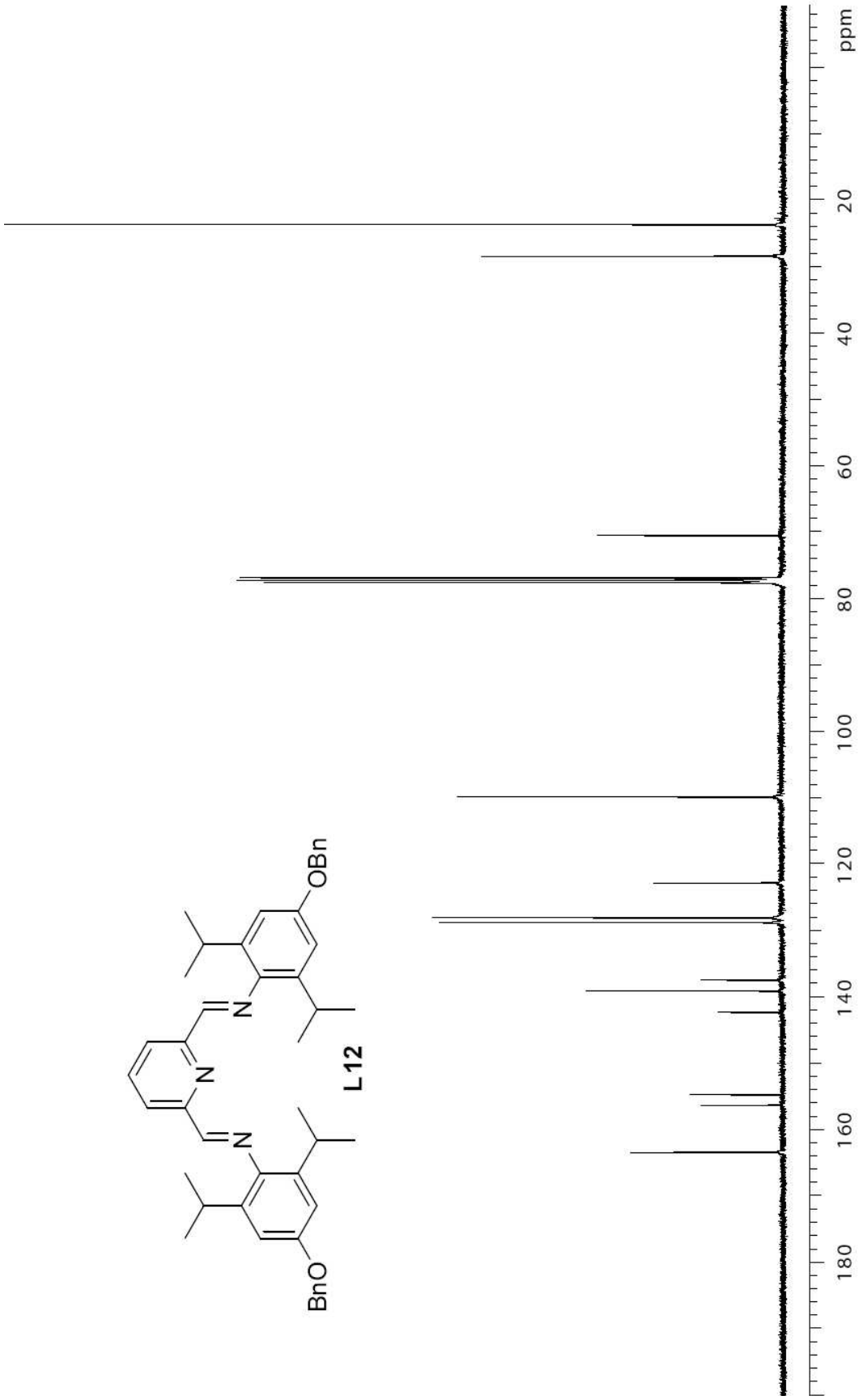
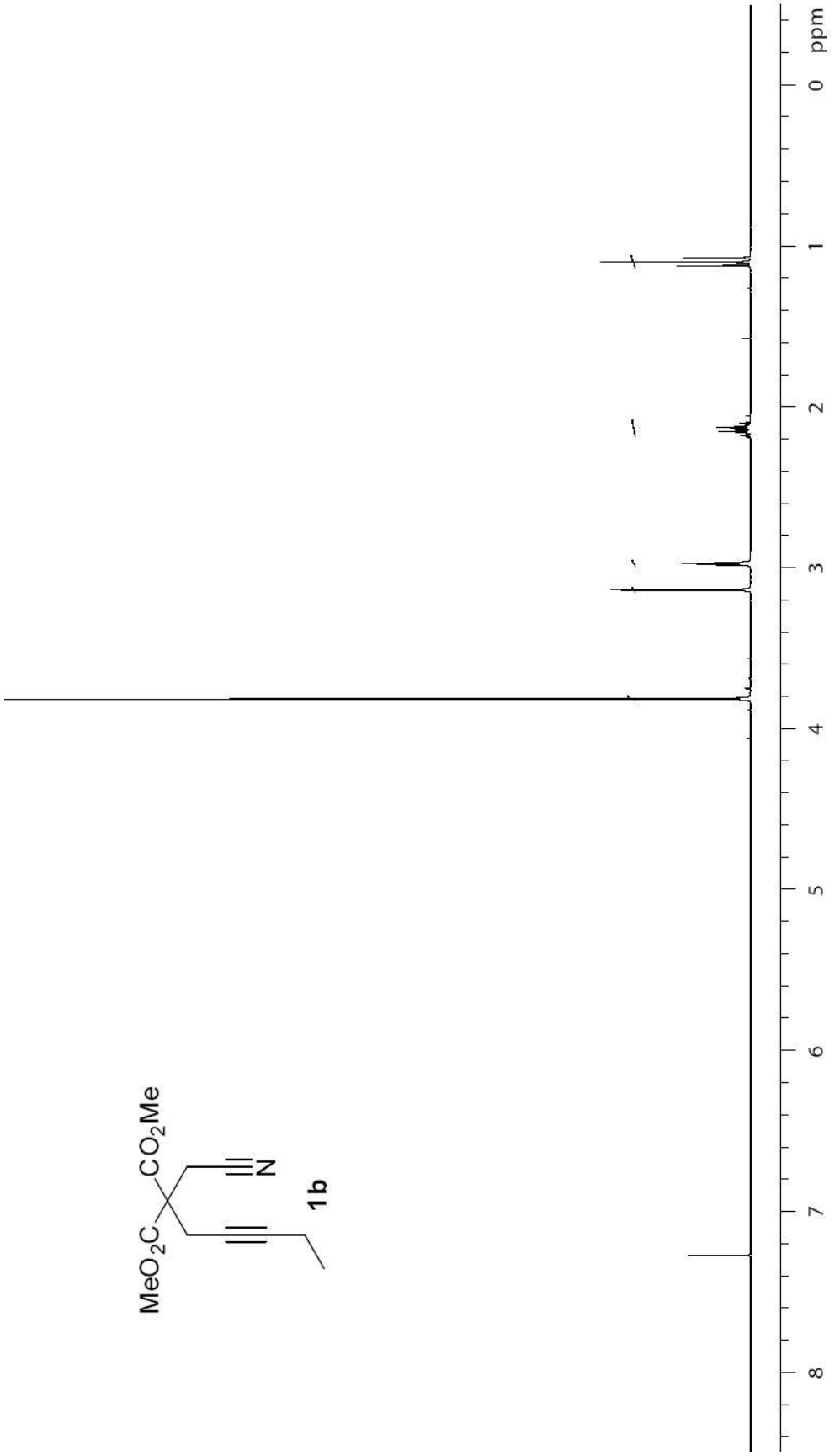
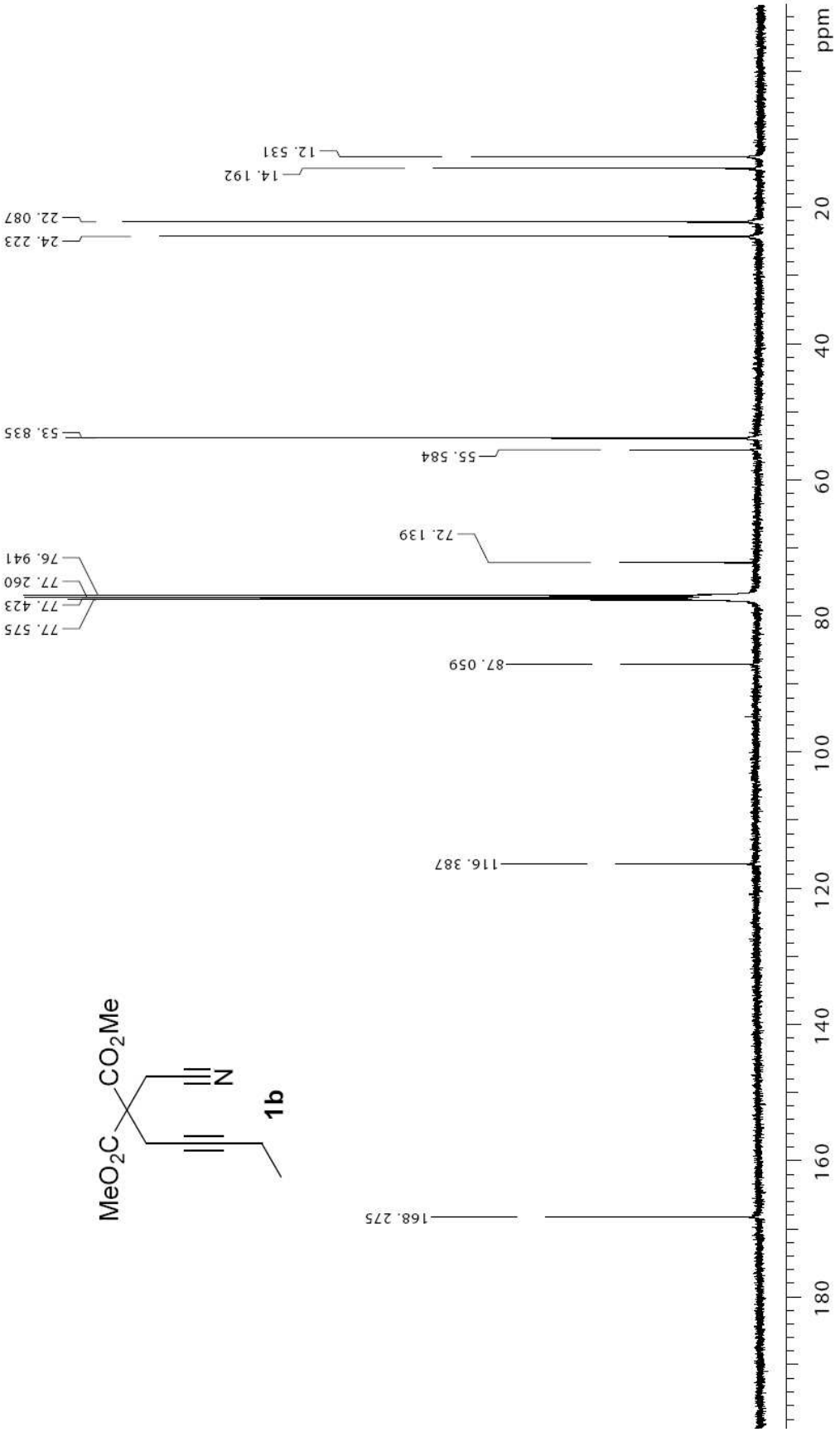
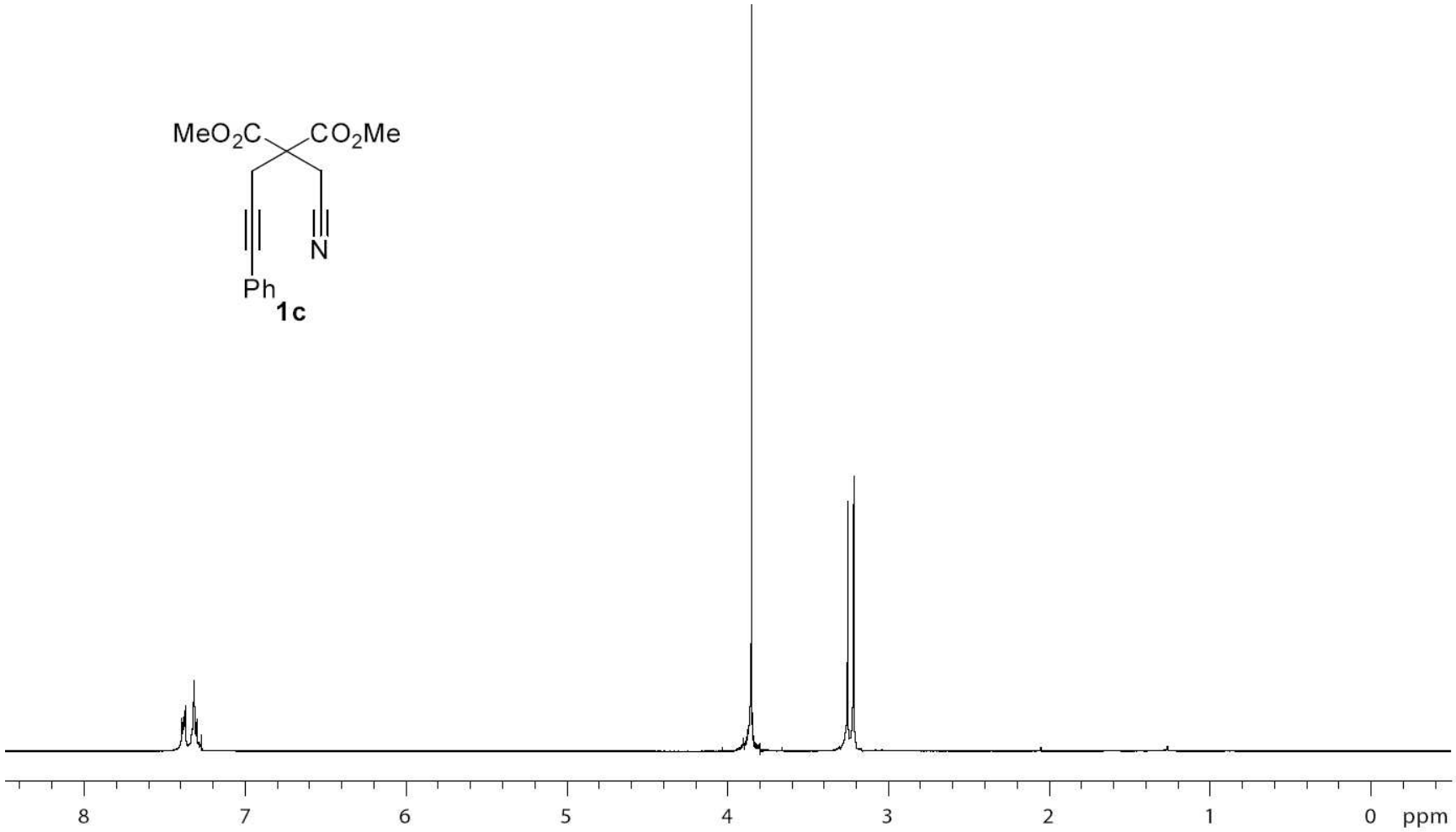
28.428
70.967
76.941
77.085
77.260
77.579
110.137
127.963
128.012
128.729
134.364
134.489
137.991
152.397
ppm
20
40
60
80
100
120
140
160
180

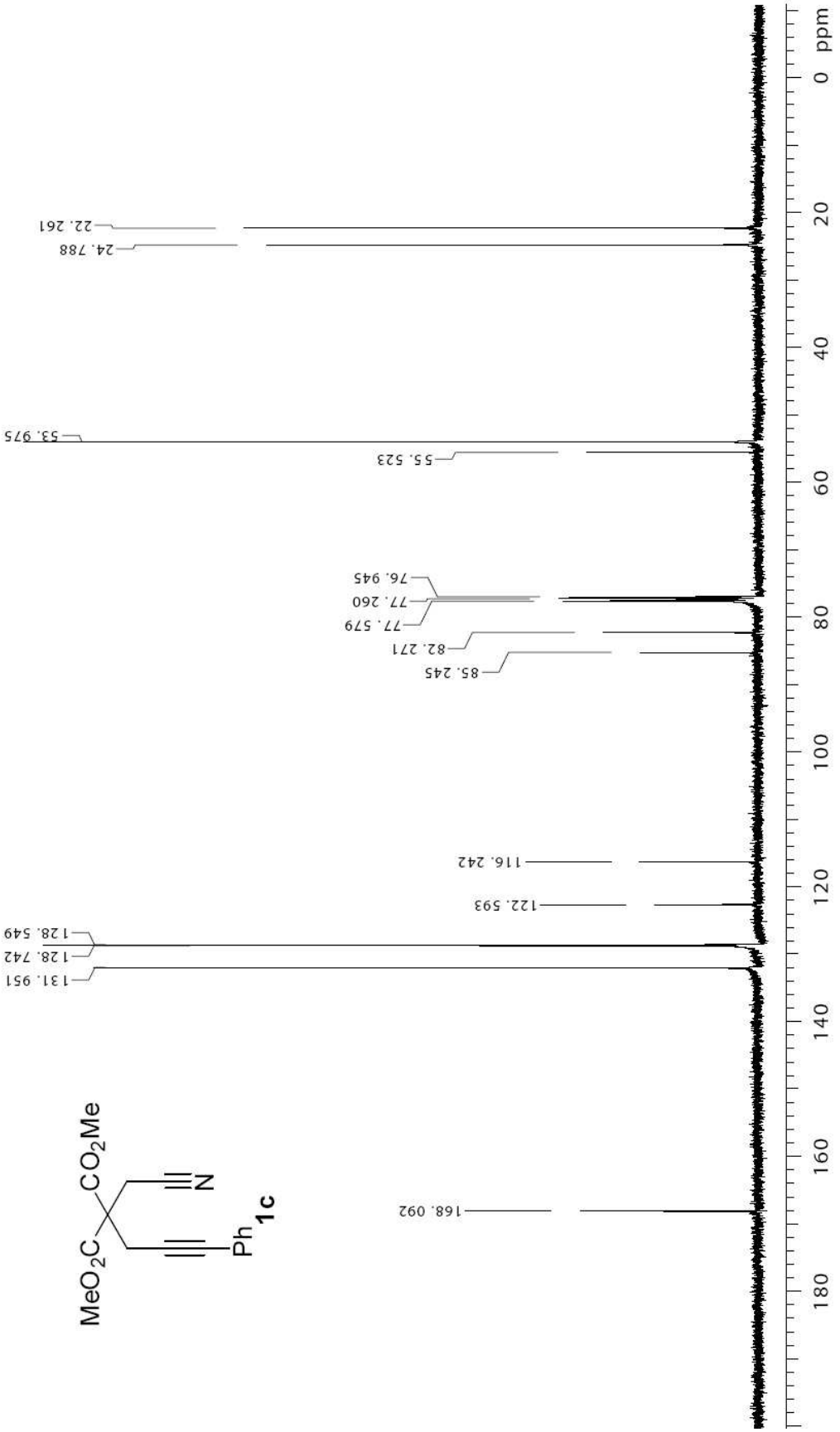

BnO
N
N
N
OBn
L12
8
7
6
5
4
3
2
1
- 0
ppm


OBn
N
N
N
BnO
L12
ppm
20
40
60
80
100
120
140
160
180


MeO2C
CO2Me
N
1b
8
7
6
5
4
3
2
1
0
ppm


MeO2C
CO2Me
N
1b
168.275
116.387
87.059
77.575
77.423
77.260
76.941
72.139
55.584
53.835
24.223
22.087
14.192
12.531
ppm
180
160
140
120
100
80
60
40
20


MeO2C
CO2Me
N
Ph
1c
8
7
6
5
4
3
2
1
0
ppm


MeO2C
CO2Me
N
Ph
1c
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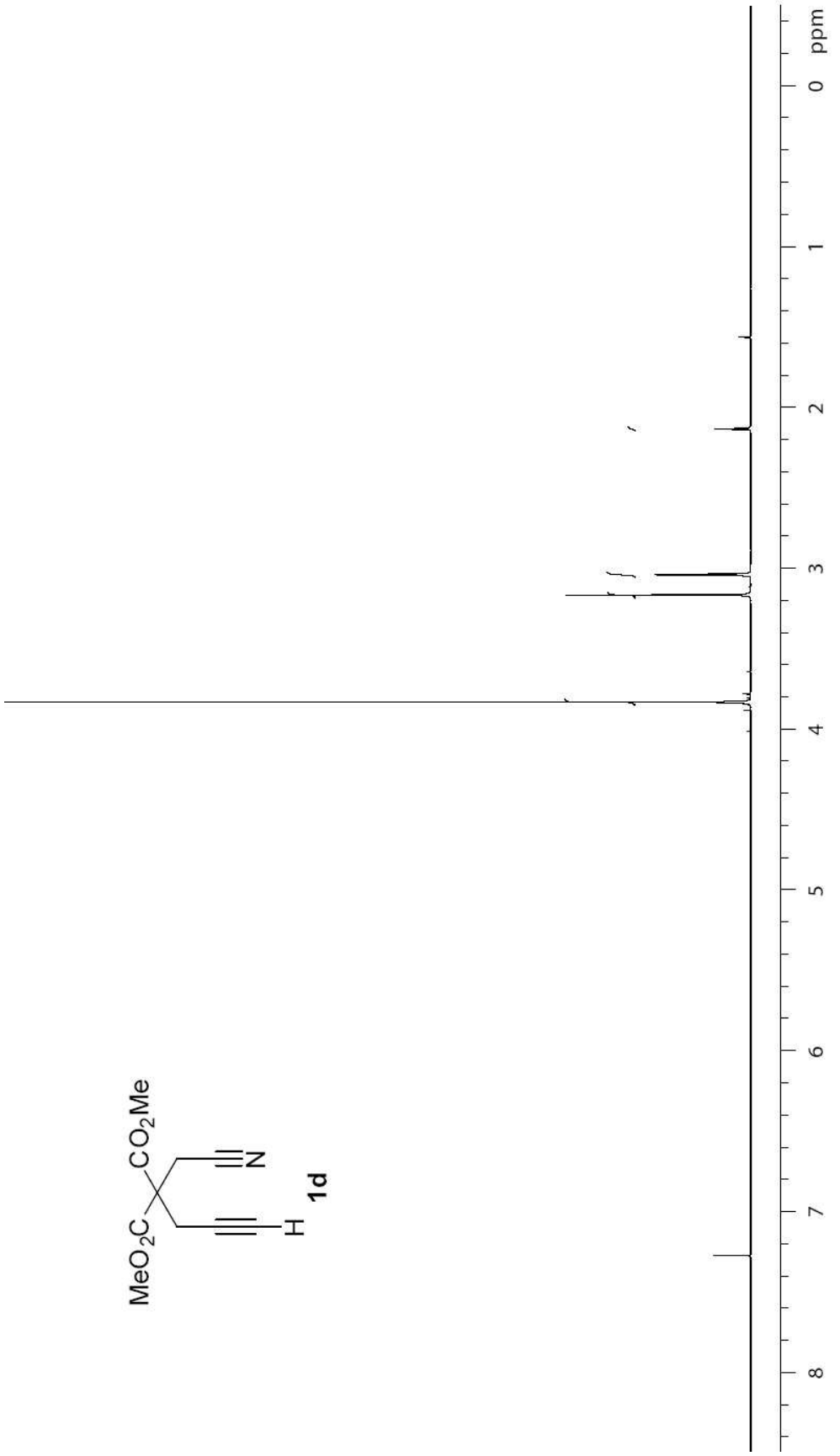
131.951
128.742
128.549
122.593
116.242
85.245
82.271
77.579
77.260
76.945
55.523
53.975
24.788
22.261
0 ppm
20
40
60
80
100
120
140
160
180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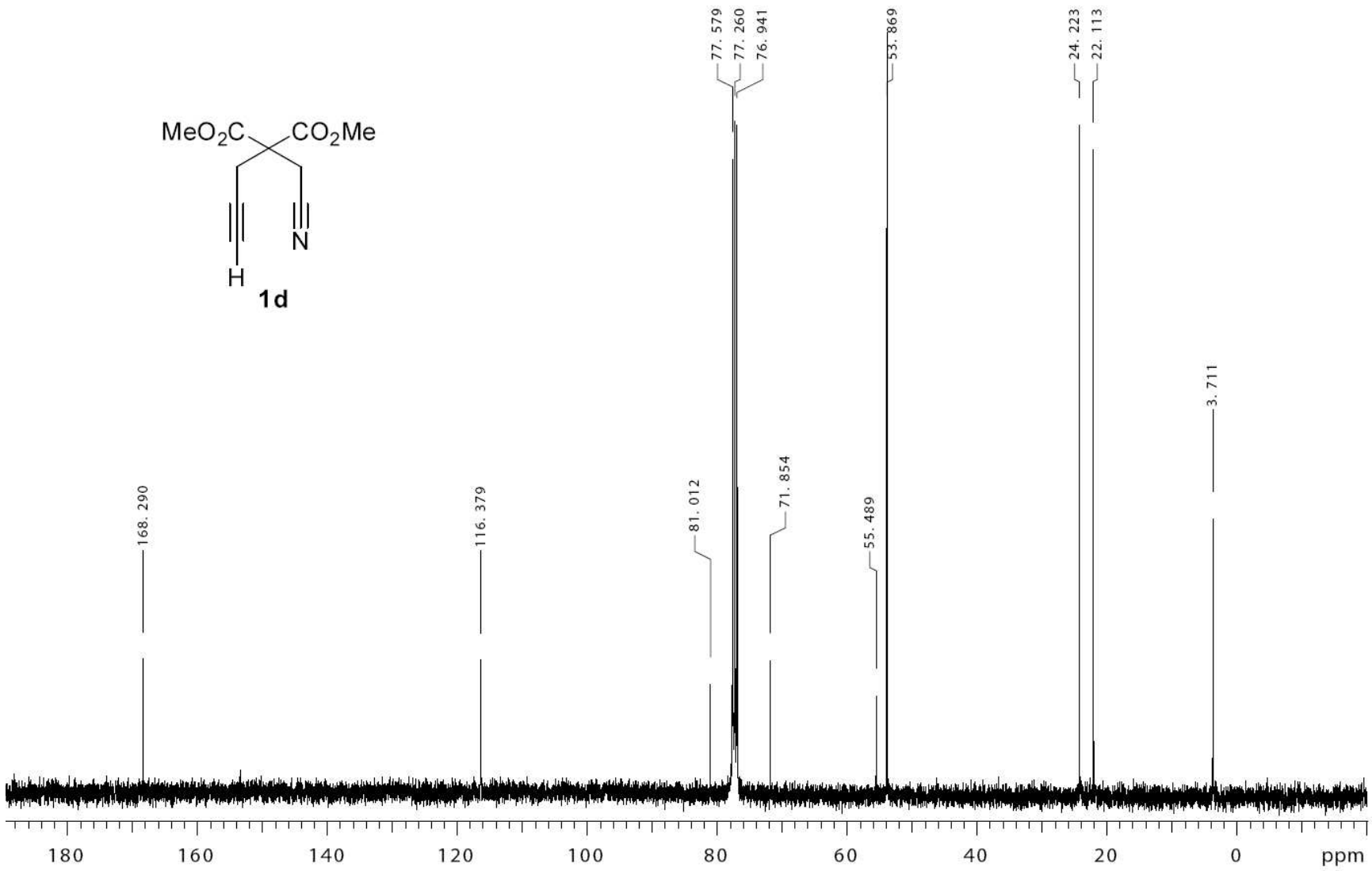
CO2Me
N
H
1d
0
1
2
3
4
5
6
7
8
ppm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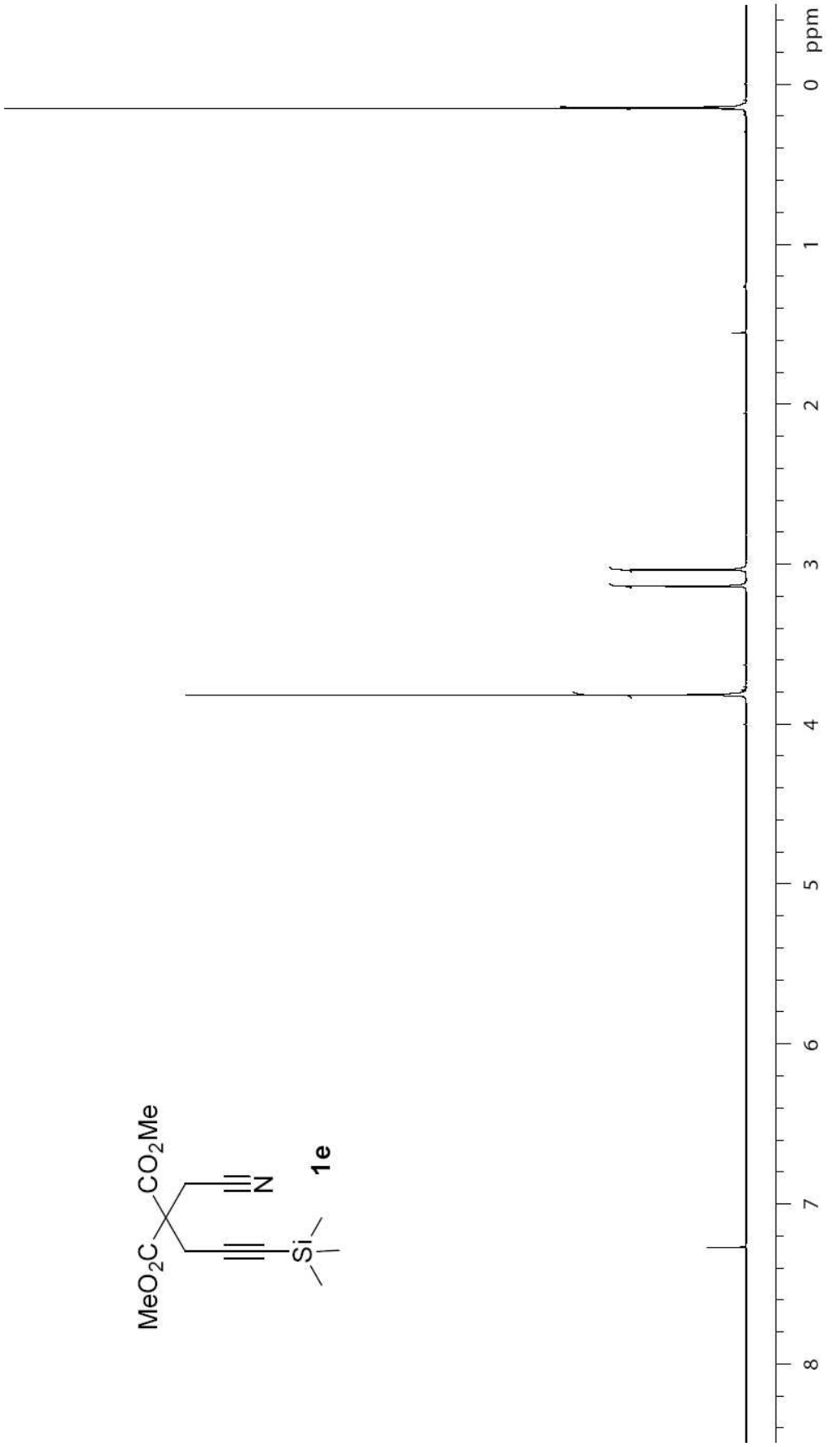
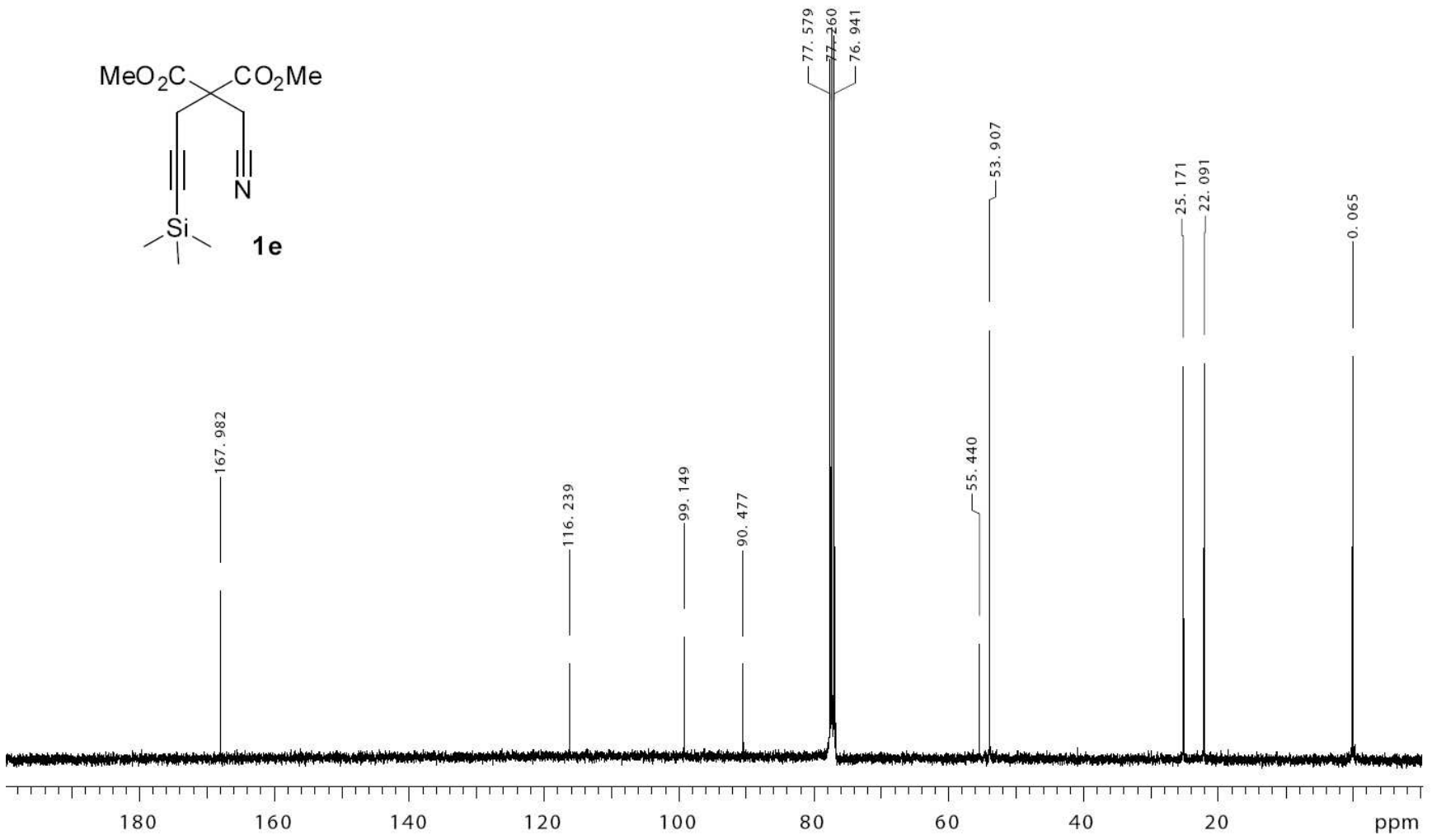
CO2Me
N
H
1d
168.290
116.379
81.012
77.579
77.260
76.941
71.854
55.489
53.869
24.223
22.113
3.711
180
160
140
120
100
80
60
40
20
0
ppm


MeO2C
CO2Me
N
Si
1e
ppm
0
1
2
3
4
5
6
7
8


MeO2C
CO2Me
N
Si
1e
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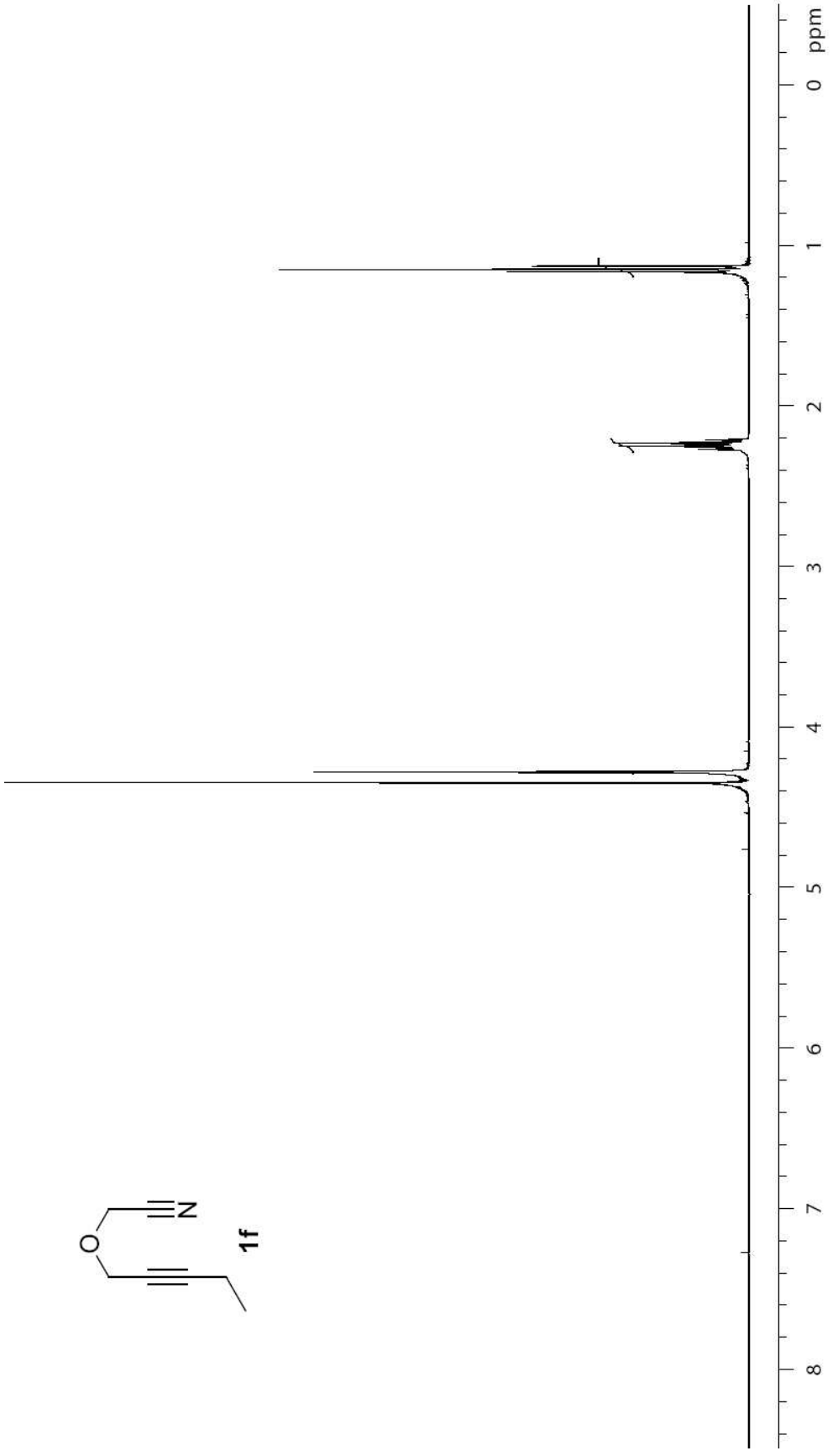
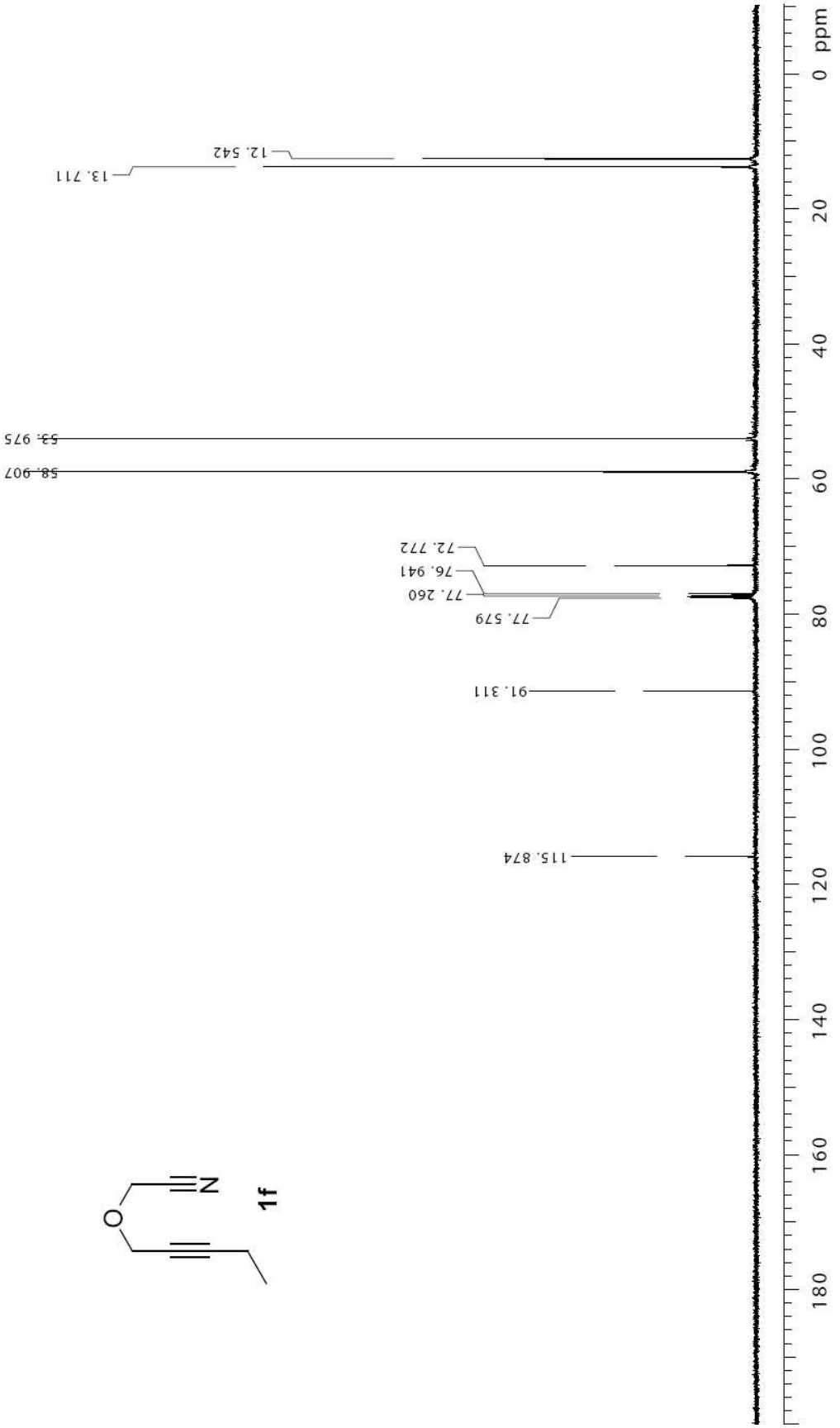
116.239
99.149
90.477
77.579
77.260
76.941
55.440
53.907
25.171
22.091
0.065
180
160
140
120
100
80
60
40
20
ppm


N
O
1f
8
7
6
5
4
3
2
1
0
ppm


1f
N
O
0 ppm
20
40
60
80
100
120
140
160
180
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13.711
53.975
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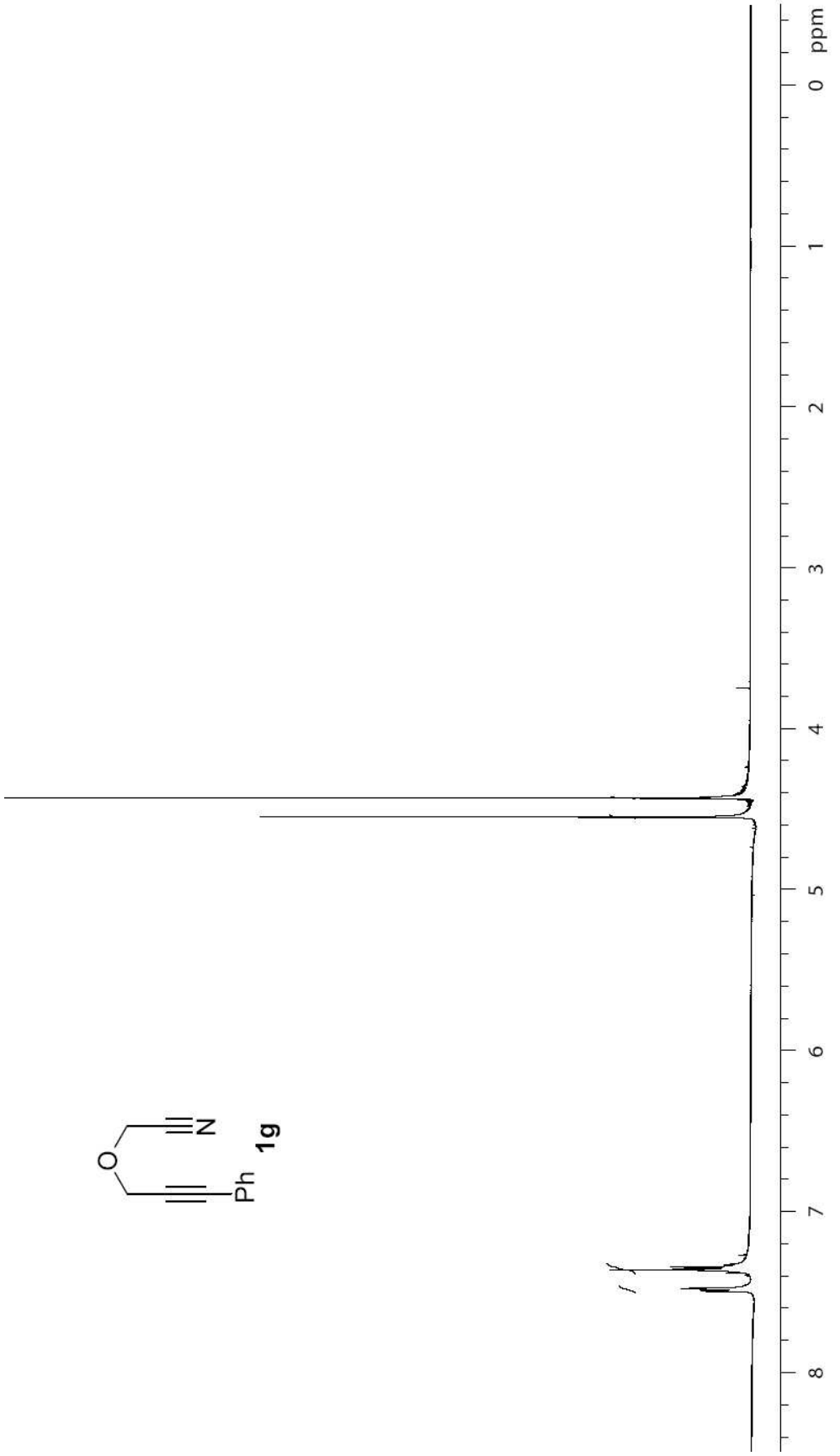
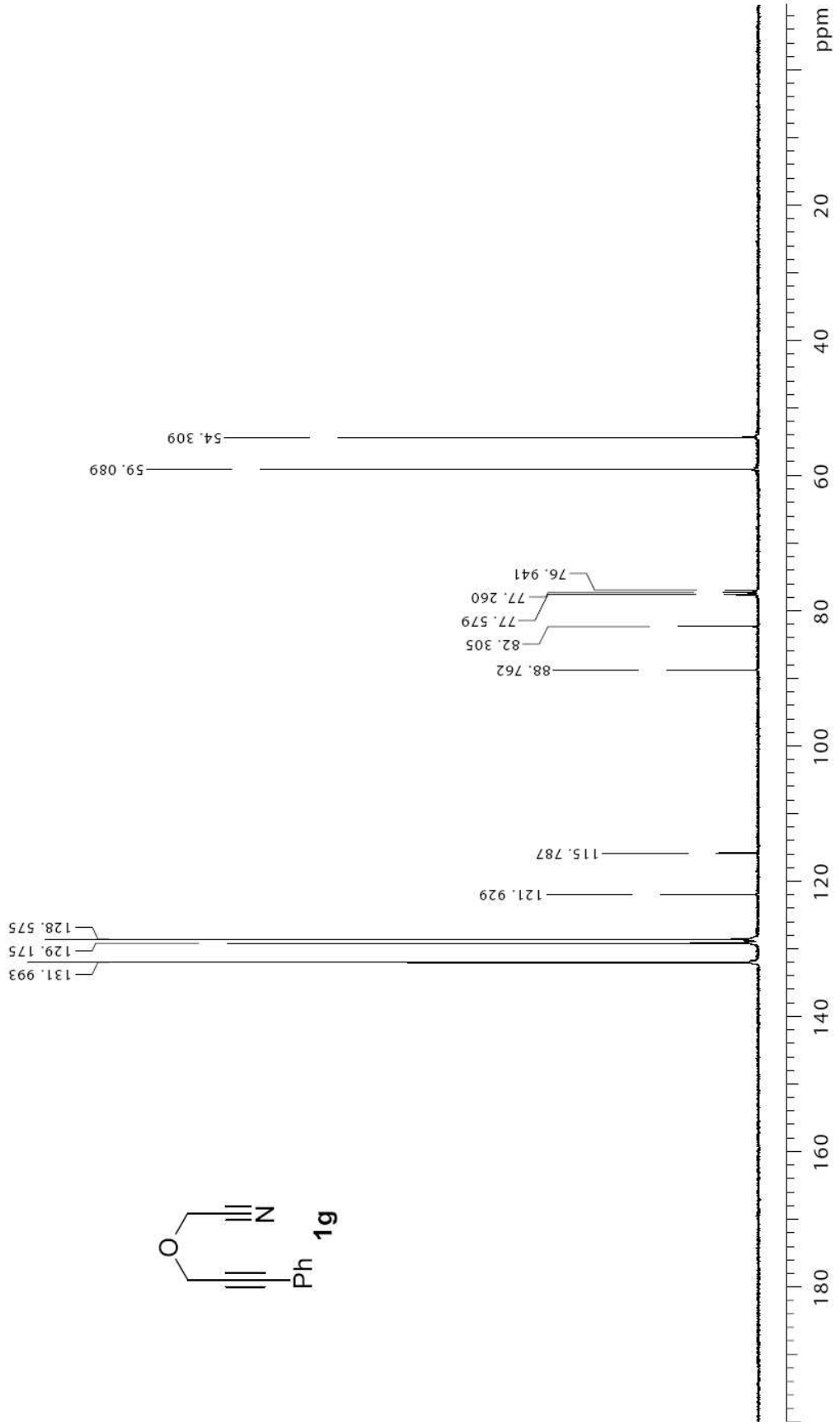
76.941
77.260
77.579
91.311
115.874


O
N
Ph
1g
8
7
6
5
4
3
2
1
0
ppm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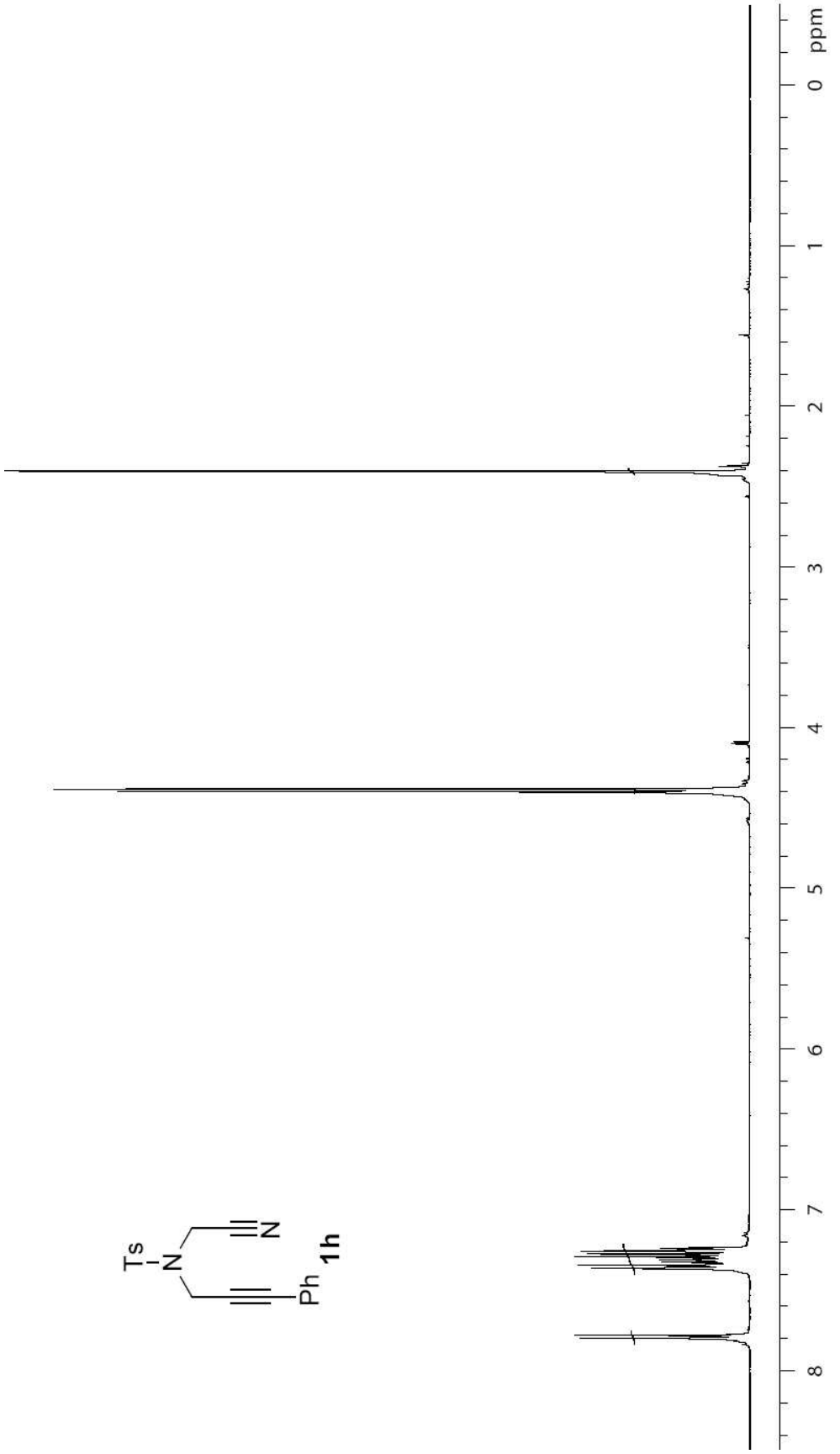
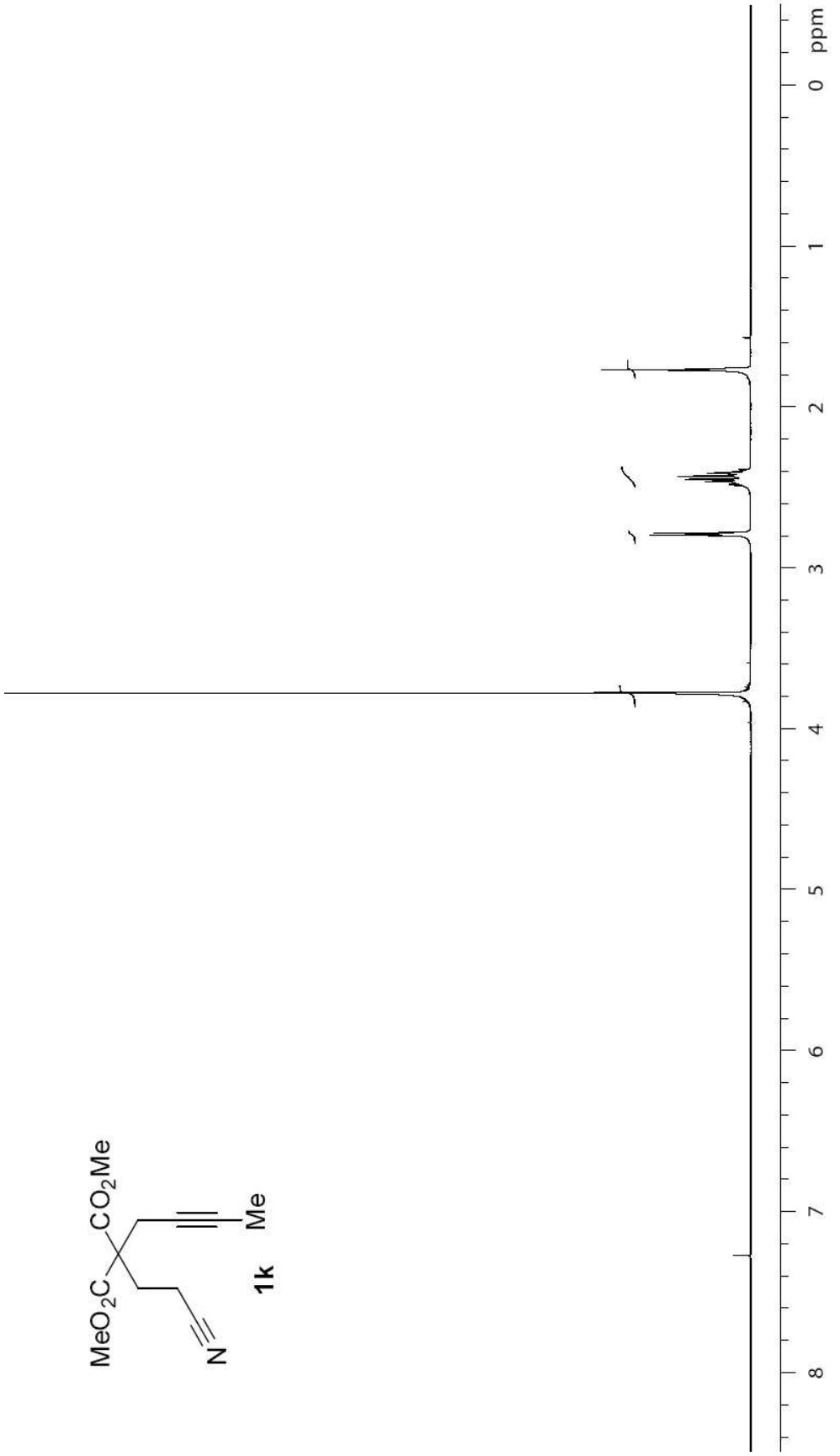
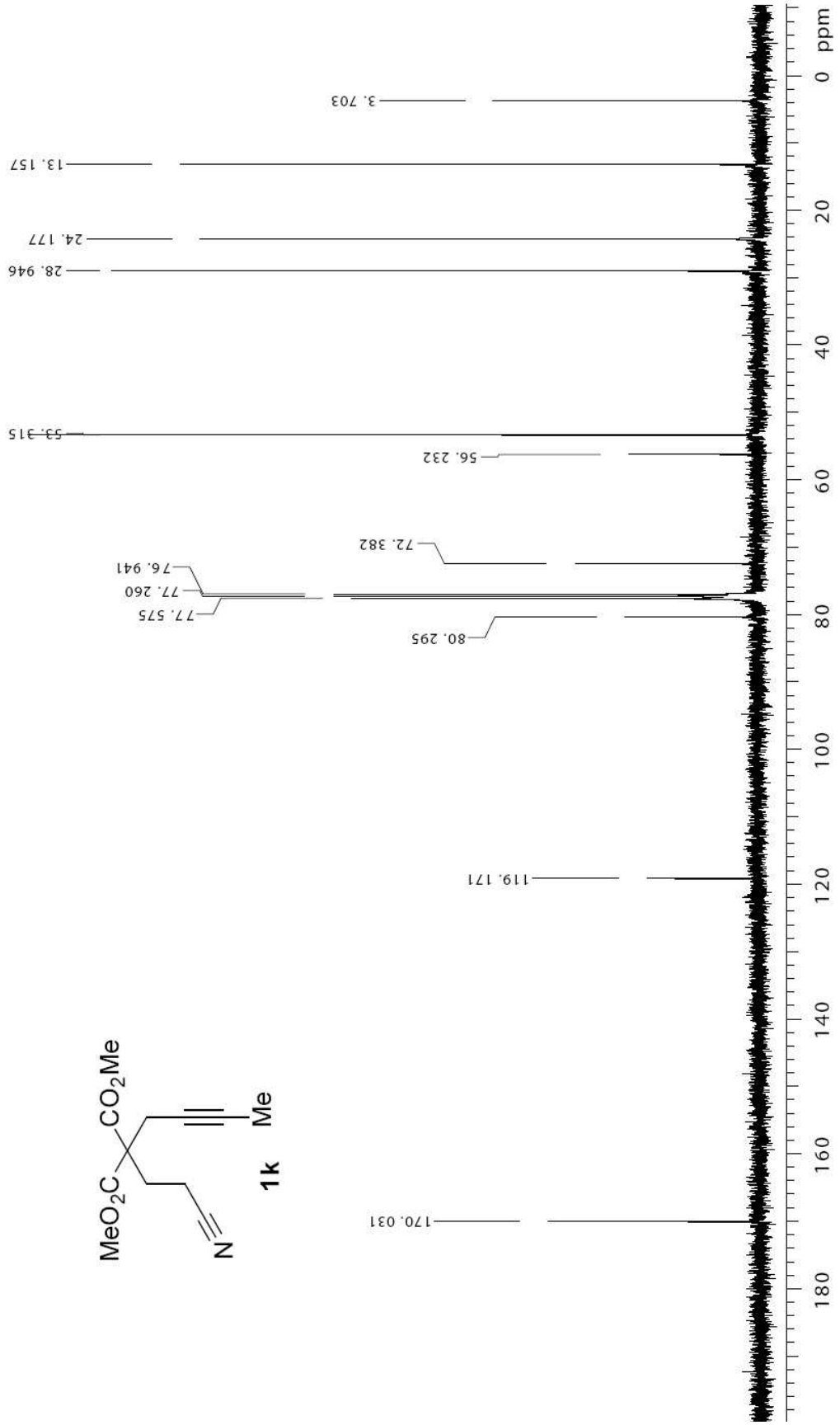
129.175
128.575
121.929
115.787
88.762
82.305
77.579
77.260
76.941
59.089
54.309
ppm
20
40
60
80
100
120
140
160
180
O
N
Ph
1g


Ts
N
N
Ph
1h
ppm
0
1
2
3
4
5
6
7
8

21.814
35.440
38.831
76.945
77.260
77.579
80.060
87.586
113.856
121.758
128.146
128.537
129.201
130.313
131.944
134.296
145.217
ppm
20
40
60
80
100
120
140
160
180
Ts
N
Ph
1h


MeO2C
CO2Me
Me
N
1k
0
1
2
3
4
5
6
7
8
ppm


MeO2C
CO2Me
Me
N
1k
170.031
119.171
80.295
77.575
77.260
76.941
72.382
56.232
53.315
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24.177
13.157
3.703
0 ppm
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40
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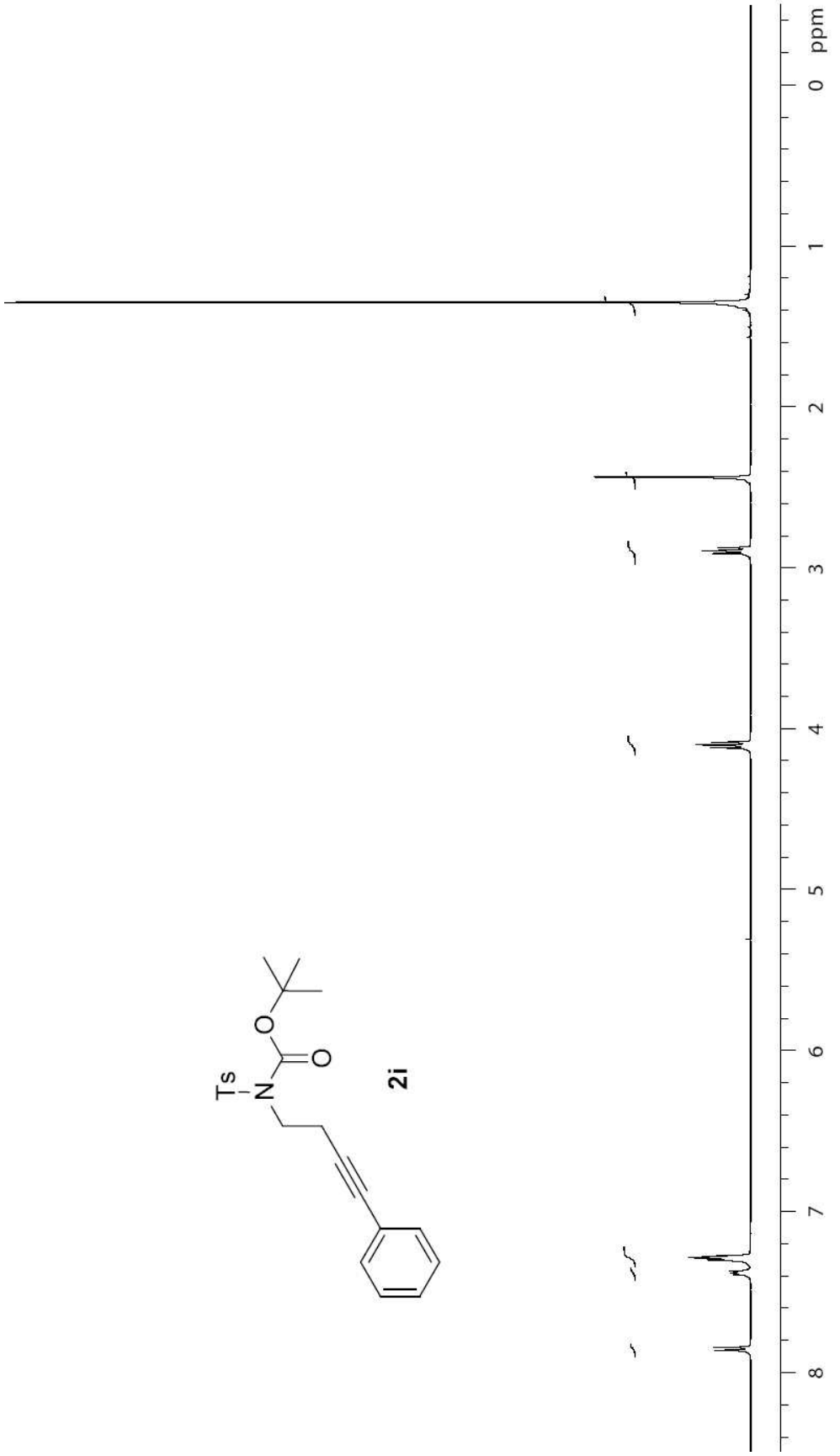
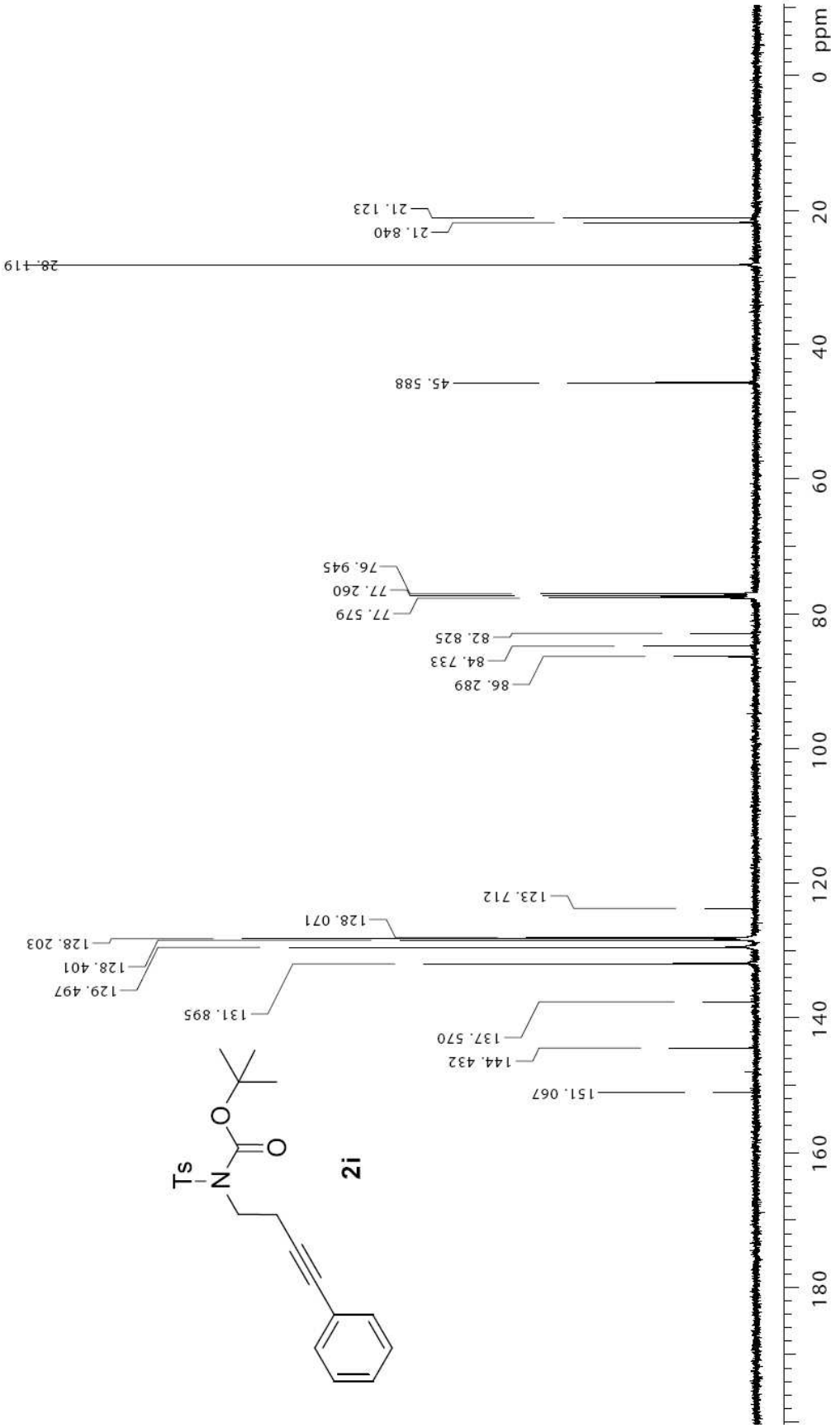
100
120
140
160
180


Ts
N
O
O
O
2i
8
7
6
5
4
3
2
1
0
ppm


Ts
N
O
O
O
2i
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144.432
137.570
131.895
129.497
128.401
128.203
128.071
123.712
86.289
84.733
82.825
77.579
77.260
76.945
45.588
28.119
21.840
21.123
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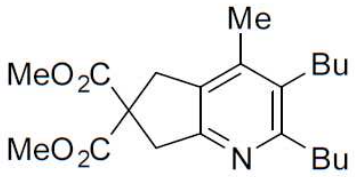
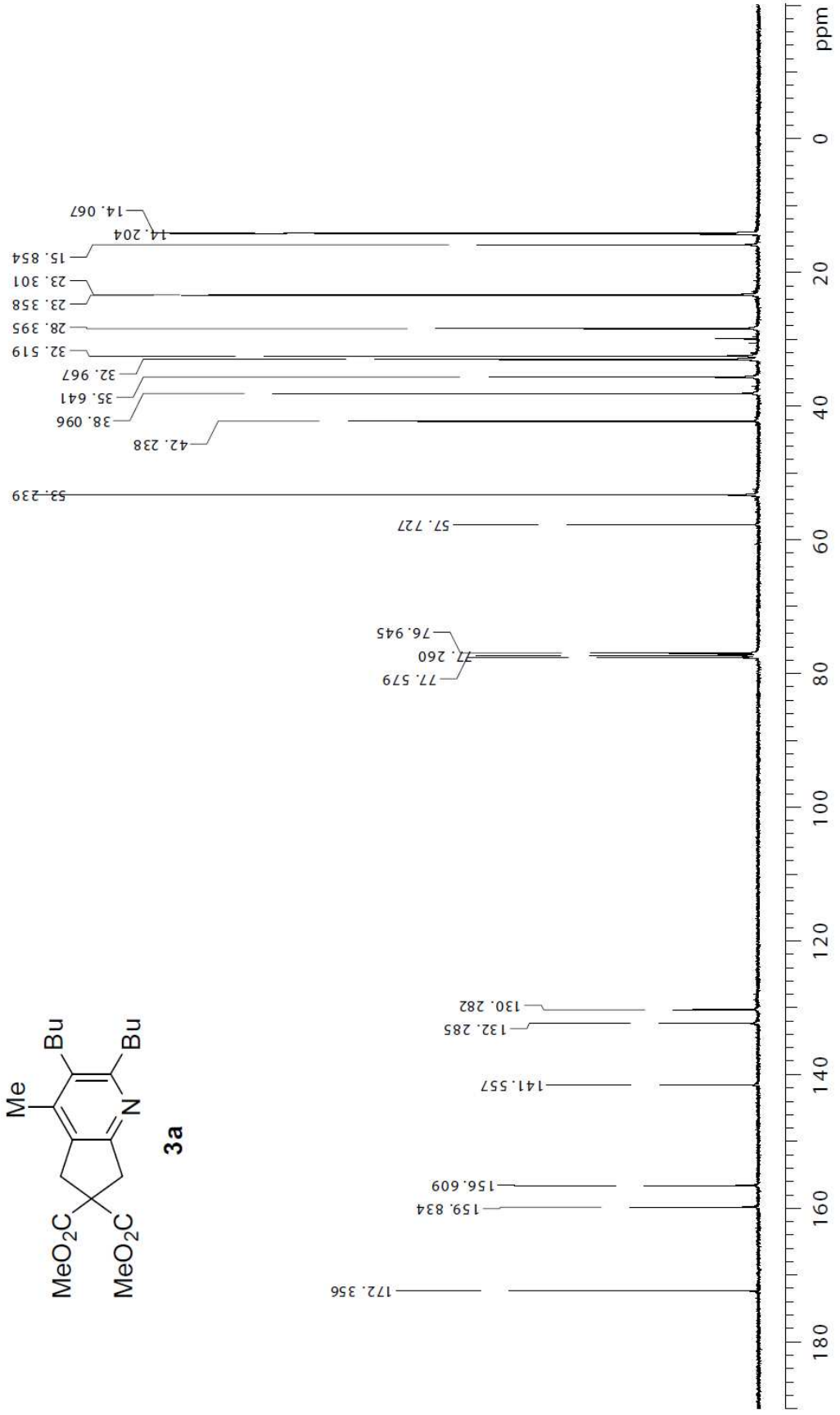
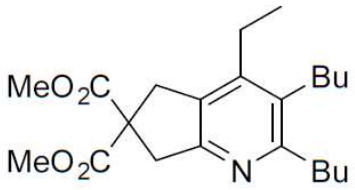
20
40
60
80
100
120
140
160
180
ppm

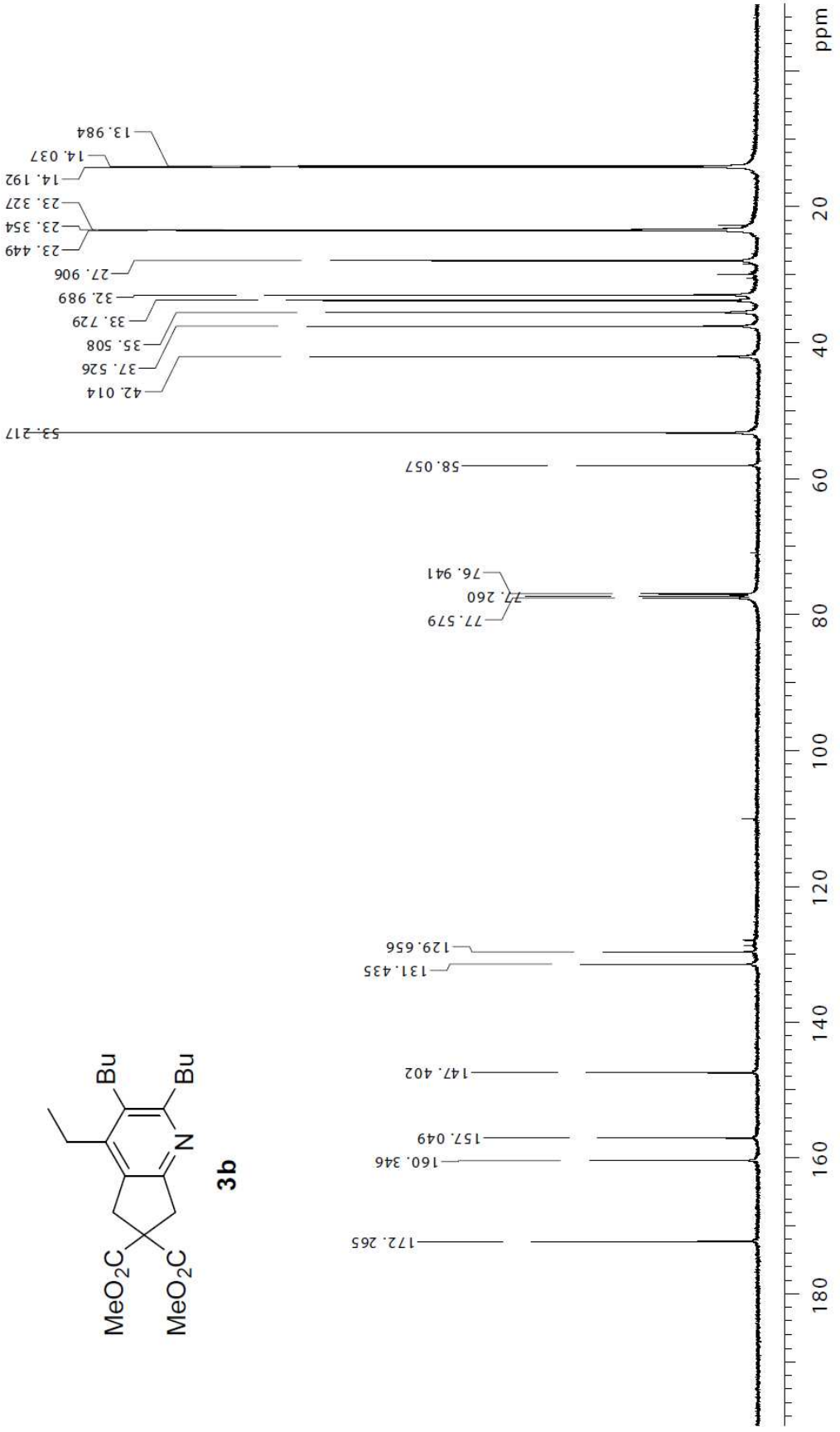


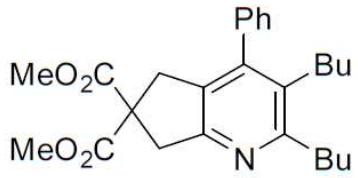
3a


Me
Bu
Bu
N
MeO2C
MeO2C
3a
172.356
159.834
156.609
141.557
132.285
130.282
77.579
77.260
76.945
57.727
53.239
42.238
38.096
35.641
32.967
32.519
28.395
23.358
23.301
15.854
14.204
14.067
ppm
0
20
40
60
80
100
120
140
160
180

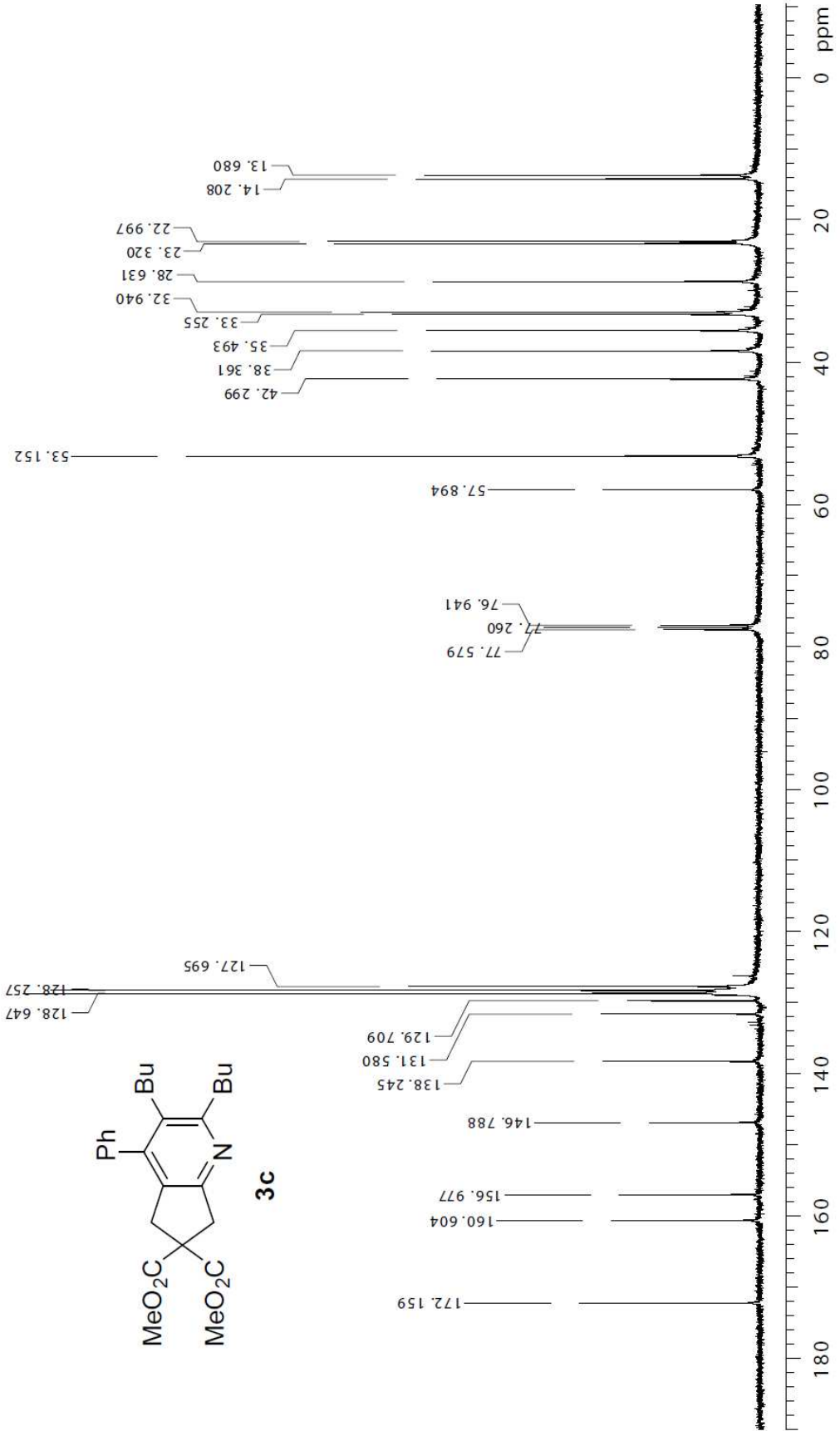


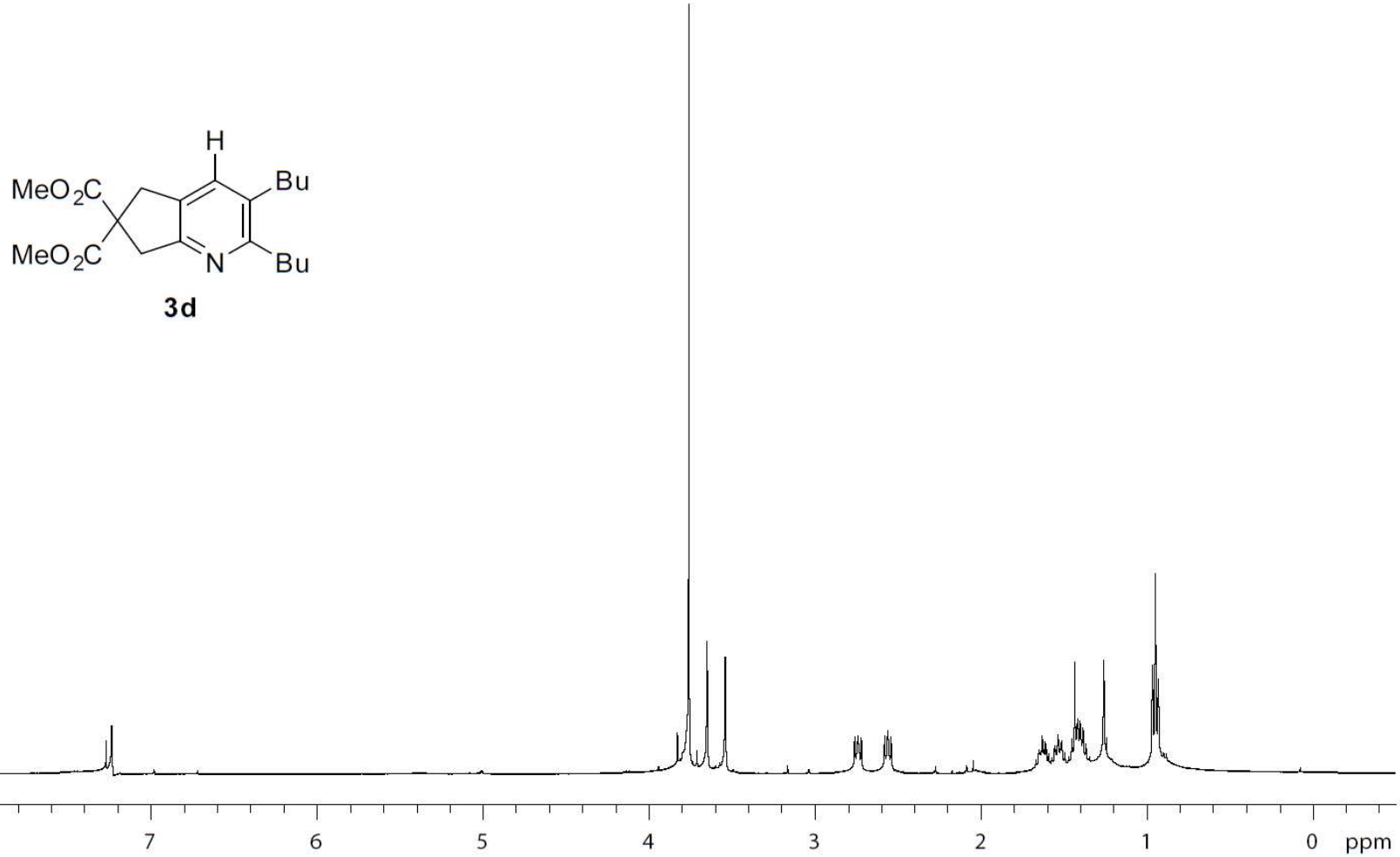
3b

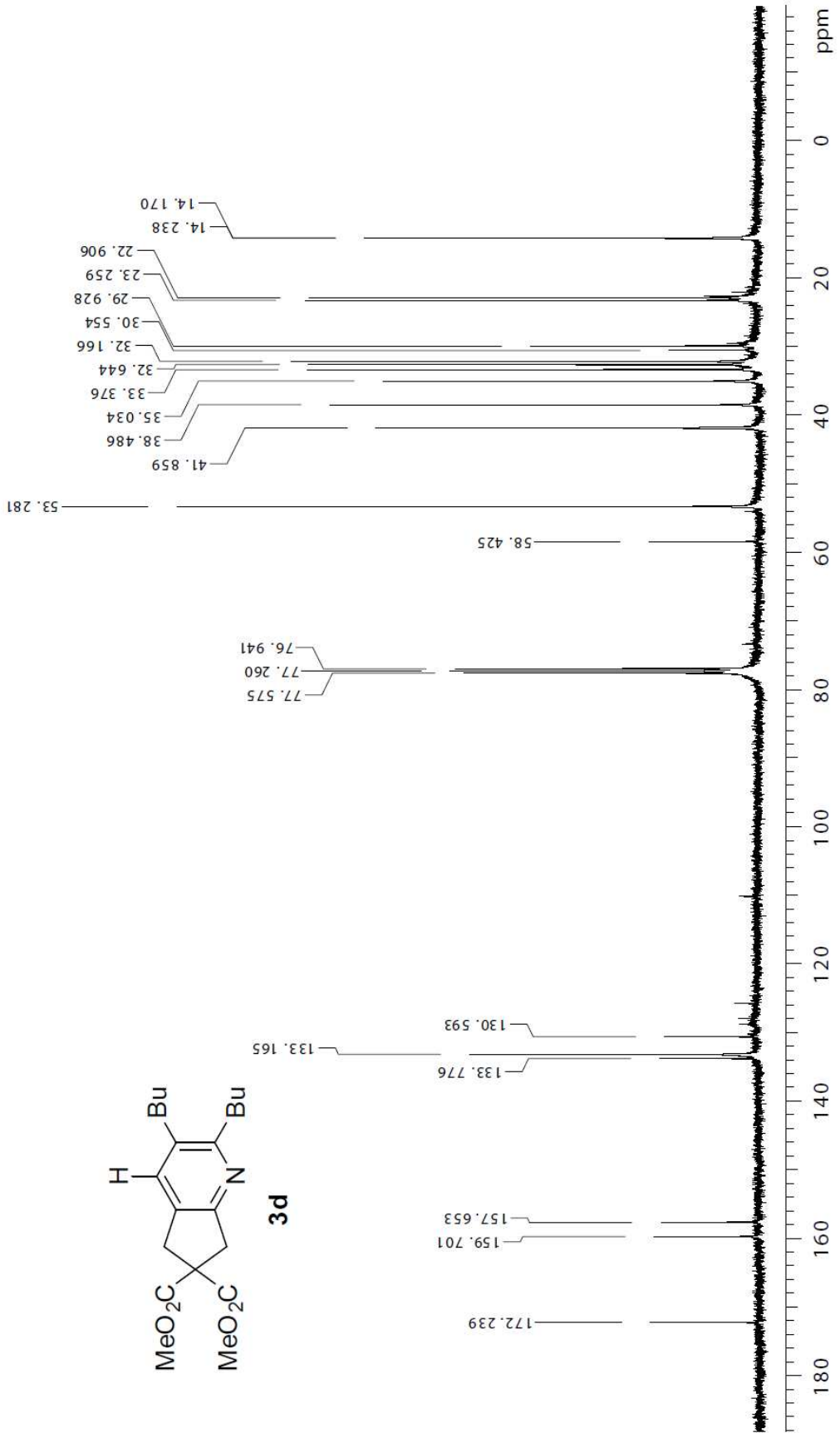

Bu
Bu
N
MeO2C
MeO2C
3b
172.265
160.346
157.049
147.402
131.435
129.656
77.579
77.260
76.941
58.057
53.217
42.014
37.526
35.508
33.729
32.989
27.906
23.449
23.354
23.327
14.192
14.037
13.984
ppm
180
160
140
120
100
80
60
40
20

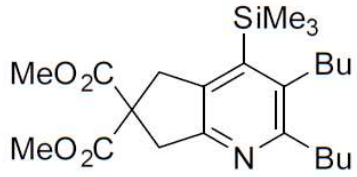


3c


172.159
160.604
156.977
146.788
138.245
131.580
129.709
128.647
128.257
127.695
77.579
77.260
76.941
57.894
53.152
42.299
38.361
35.493
33.255
32.940
28.631
23.320
22.997
14.208
13.680
0 ppm
20
40
60
80
100
120
140
160
180
Ph
Bu
Bu
N
MeO2C
MeO2C
3c


H
MeO2C
MeO2C
Bu
Bu
N
3d
8
7
6
5
4
3
2
1
0
ppm


ppm
0
20
40
60
80
100
120
140
160
180
172.239
159.701
157.653
133.776
133.165
130.593
77.575
77.260
76.941
58.425
53.281
41.859
38.486
35.034
33.376
32.644
32.166
30.554
29.928
23.259
22.906
14.238
14.170
Bu
Bu
H
N
MeO2C
MeO2C
3d



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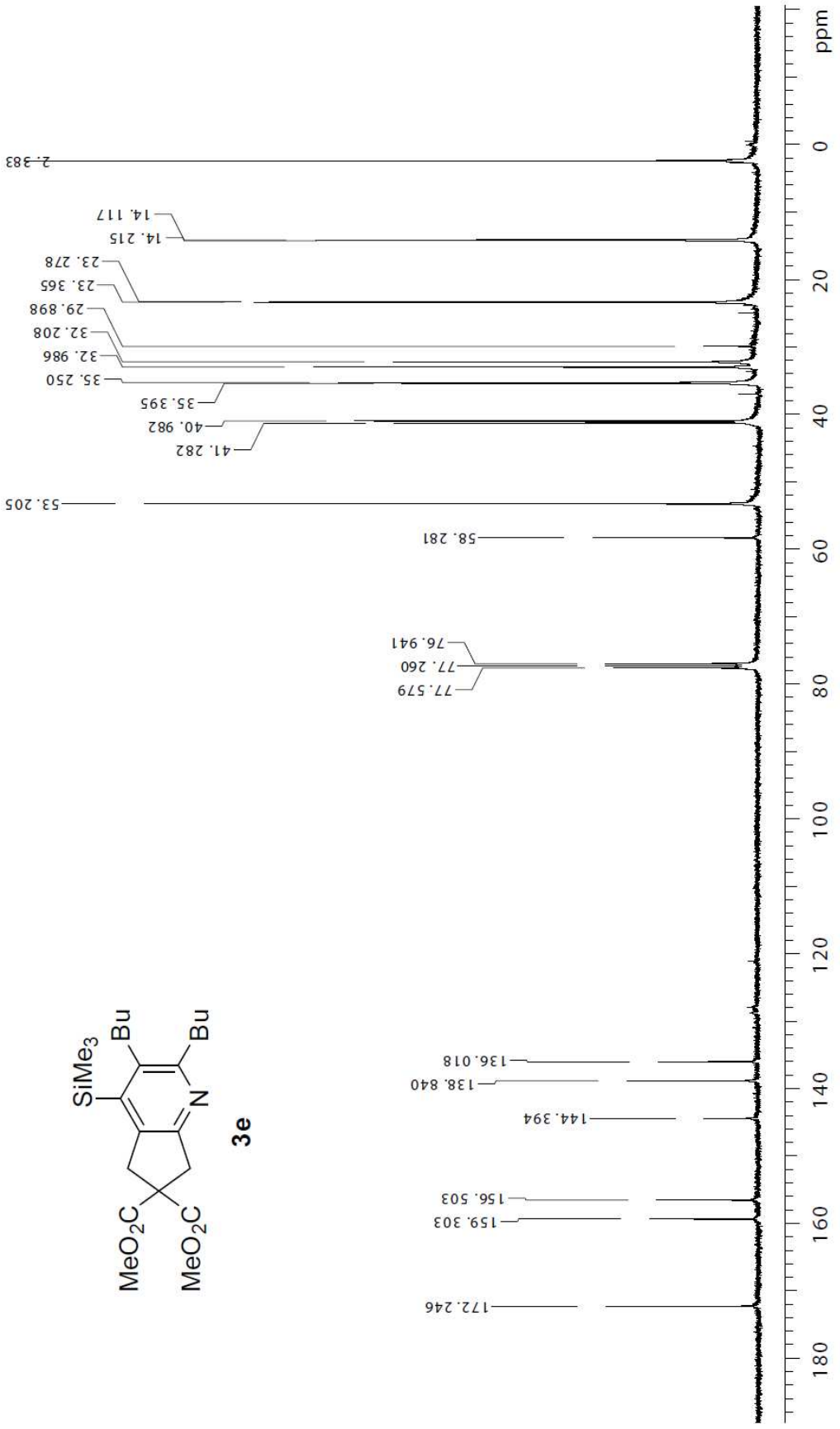
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60
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140
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180
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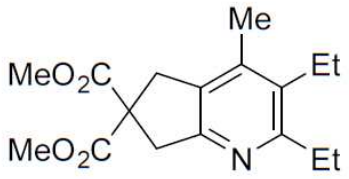
14.215
23.278
23.365
29.898
32.208
32.986
35.250
35.395
40.982
41.282
53.205
58.281
76.941
77.260
77.579
136.018
138.840
144.394
156.503
159.303
172.246
SiMe3
Bu
Bu
N
MeO2C
MeO2C
3e

BD-64-006 1 fr 78-105
CDCl 3, 03-04-2010

Pulse Sequence: s2pul



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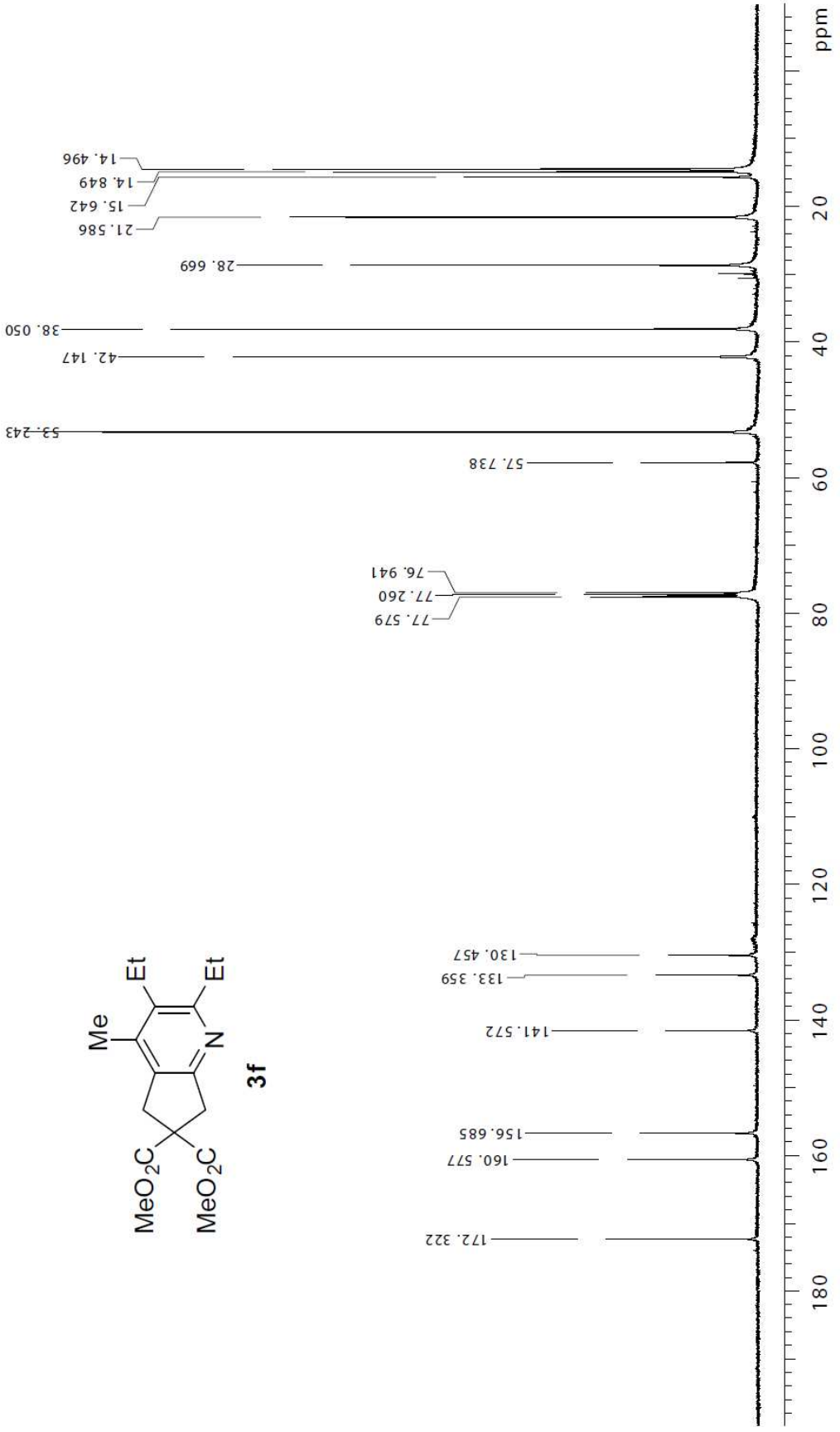
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160
180
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28.669
38.050
42.147
53.243
57.738
76.941
77.260
77.579
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141.572
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160.577
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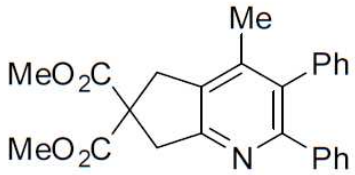
Et
Et
Me
N
MeO2C
MeO2C
3f



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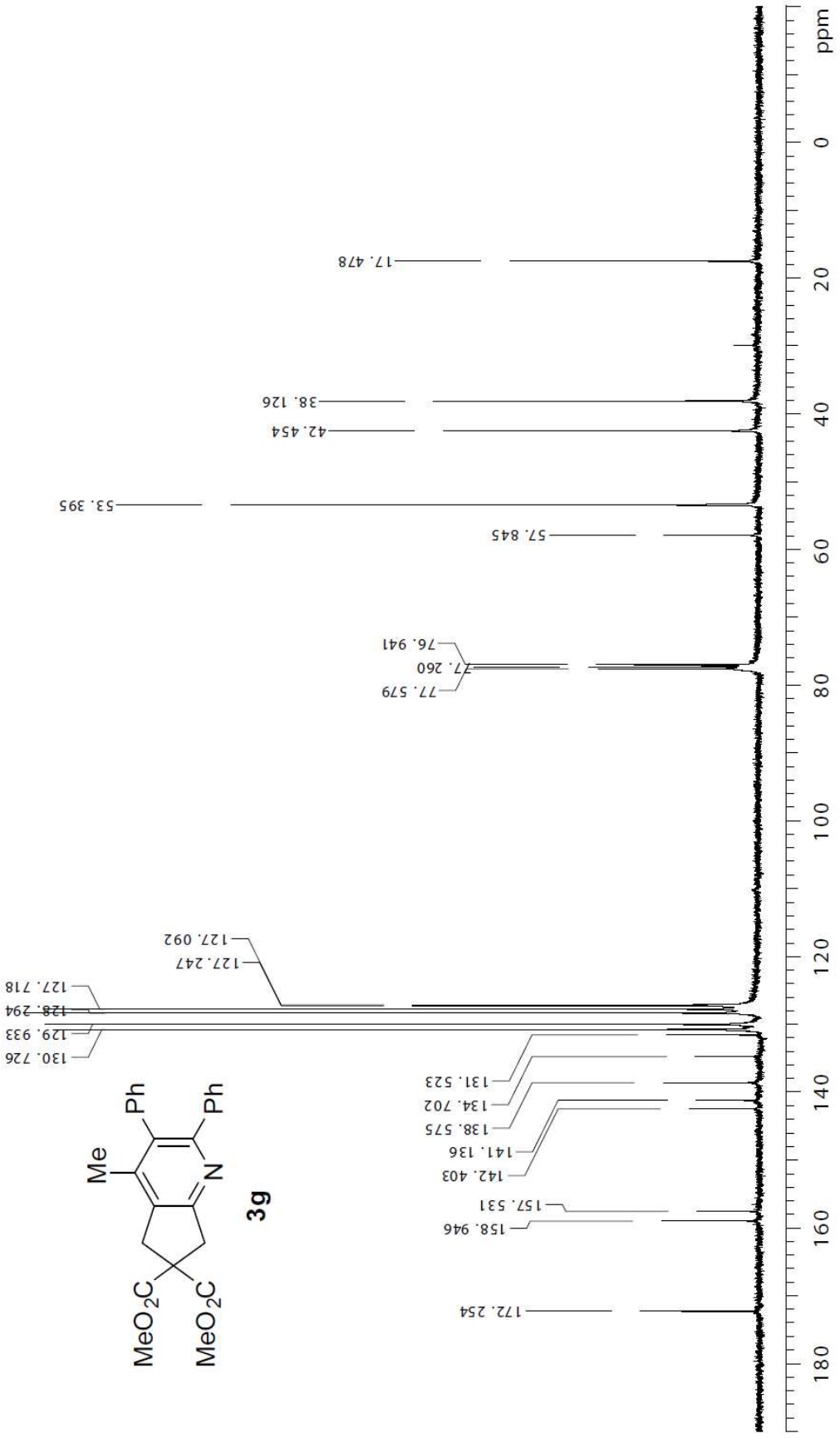
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Ph
Me
N
MeO2C
MeO2C
3g
ppm
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140
160
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38.126
42.454
53.395
57.845
76.941
77.260
77.579
127.092
127.247
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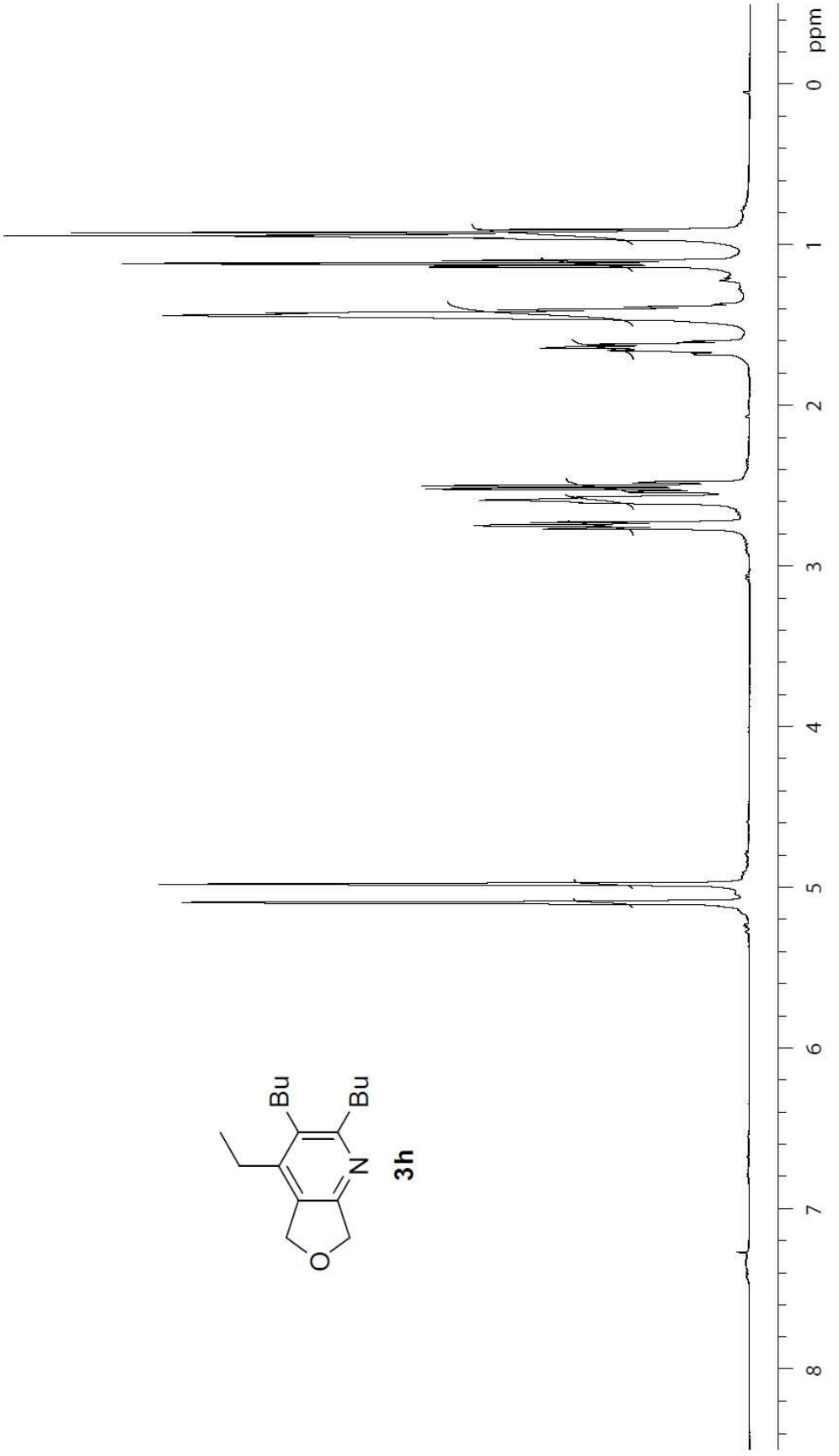
158.946
172.254


Bu
Bu
N
O
3h
ppm
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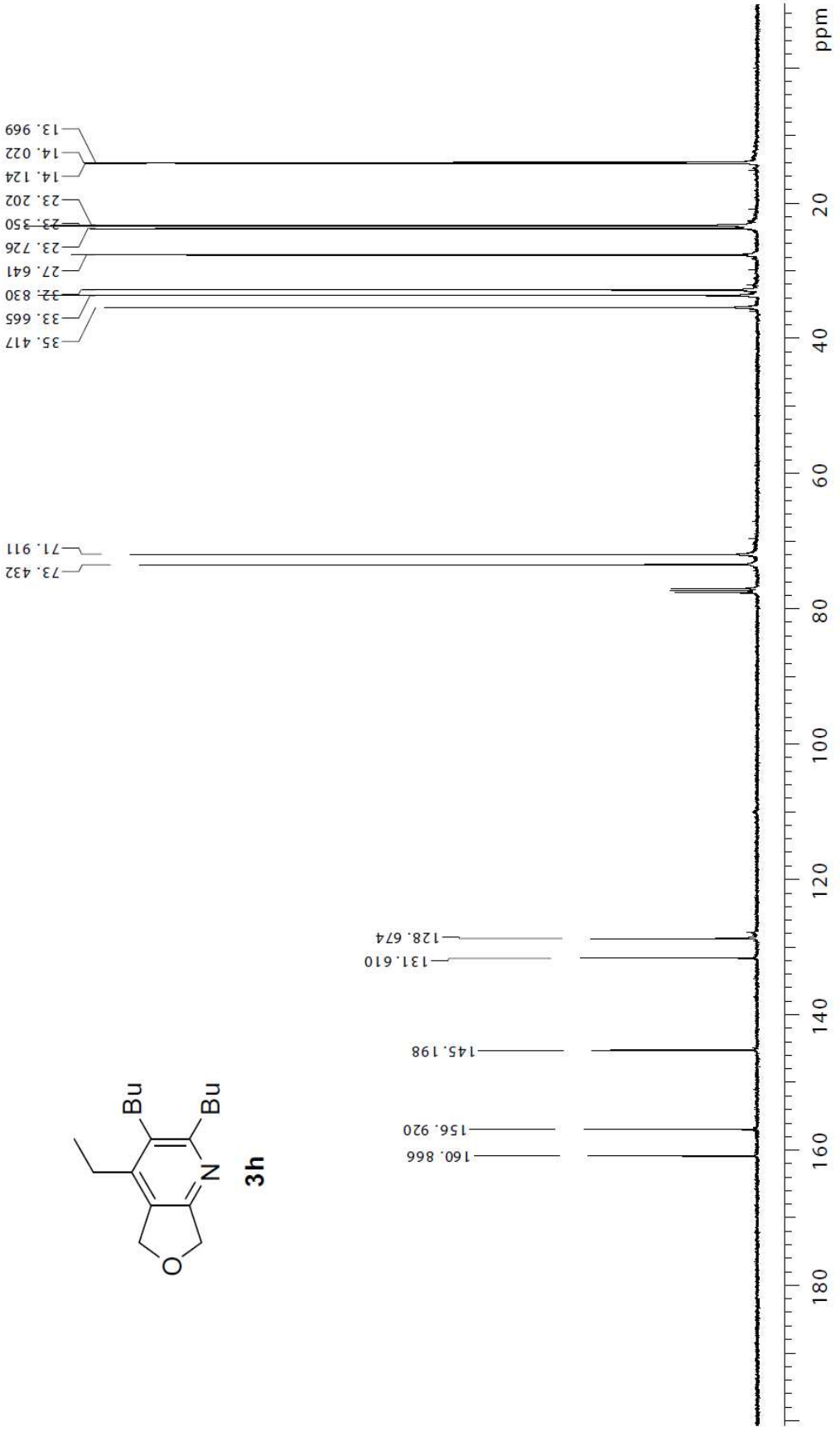
8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160
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23.350
23.726
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32.830
33.665
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145.198
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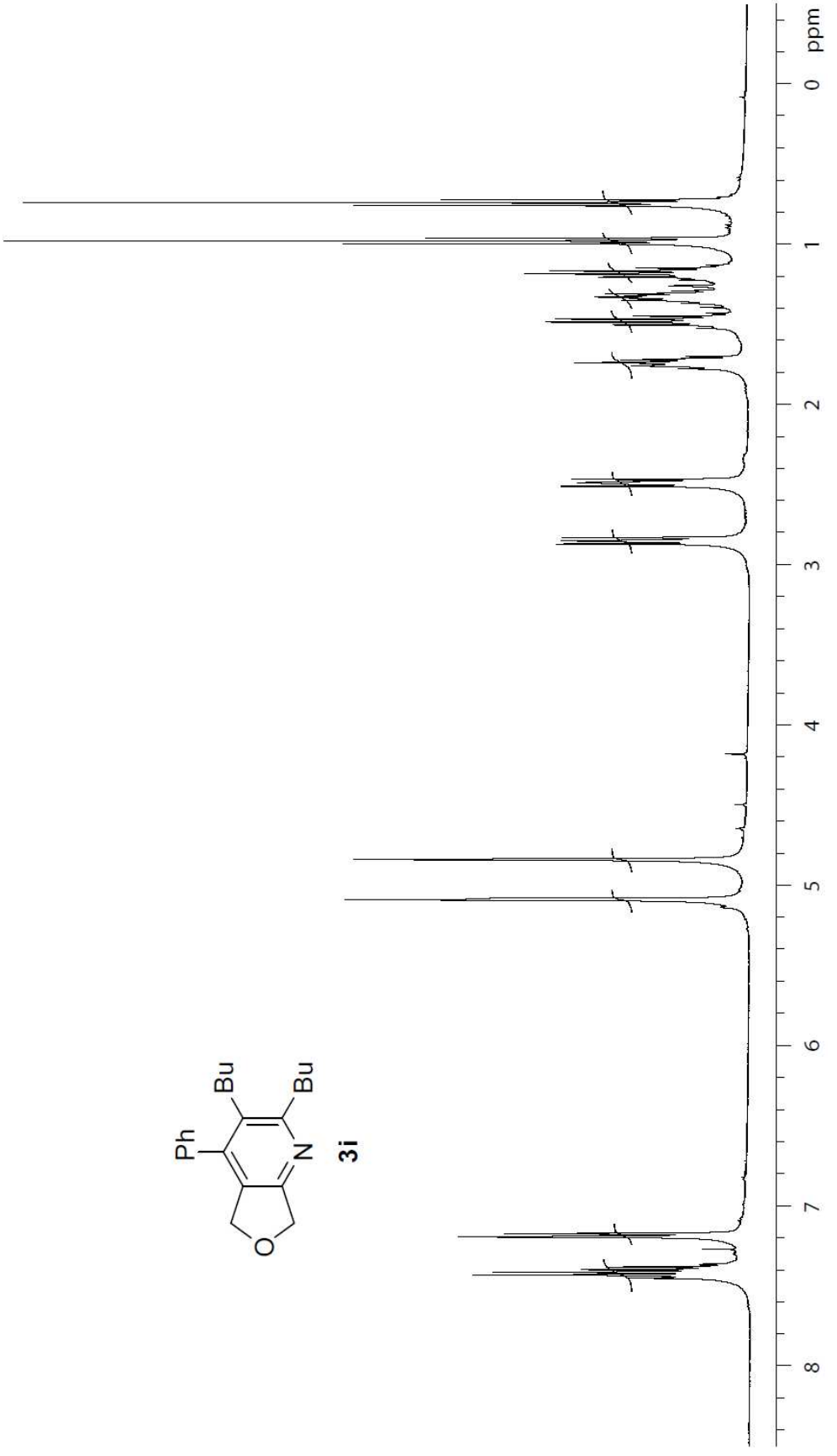
Bu
Bu
N
O
3h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Bu
Bu
N
O
3i
8
7
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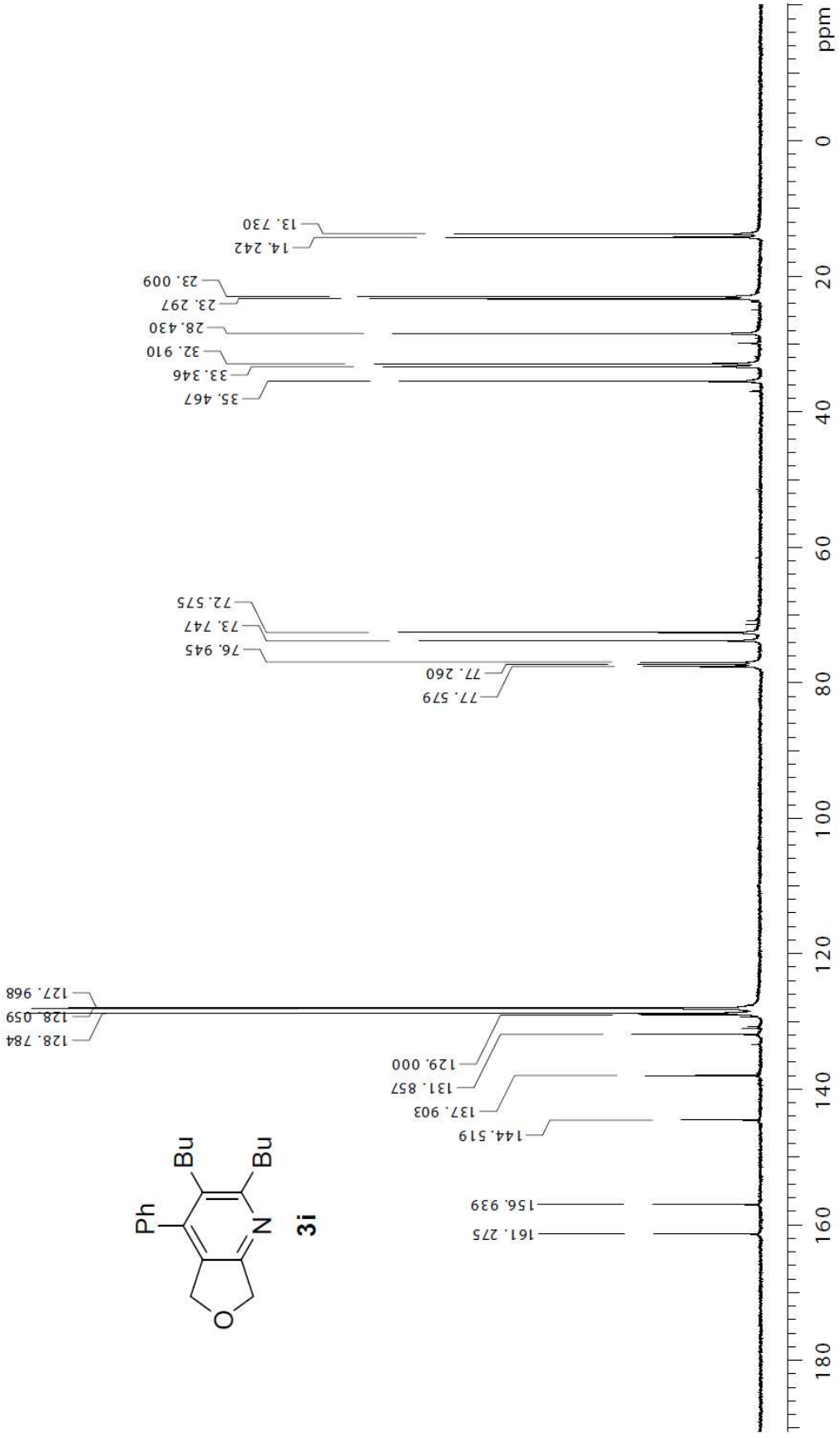
1
0
ppm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140
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180
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23.297
28.430
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73.747
76.945
77.260
77.579
127.968
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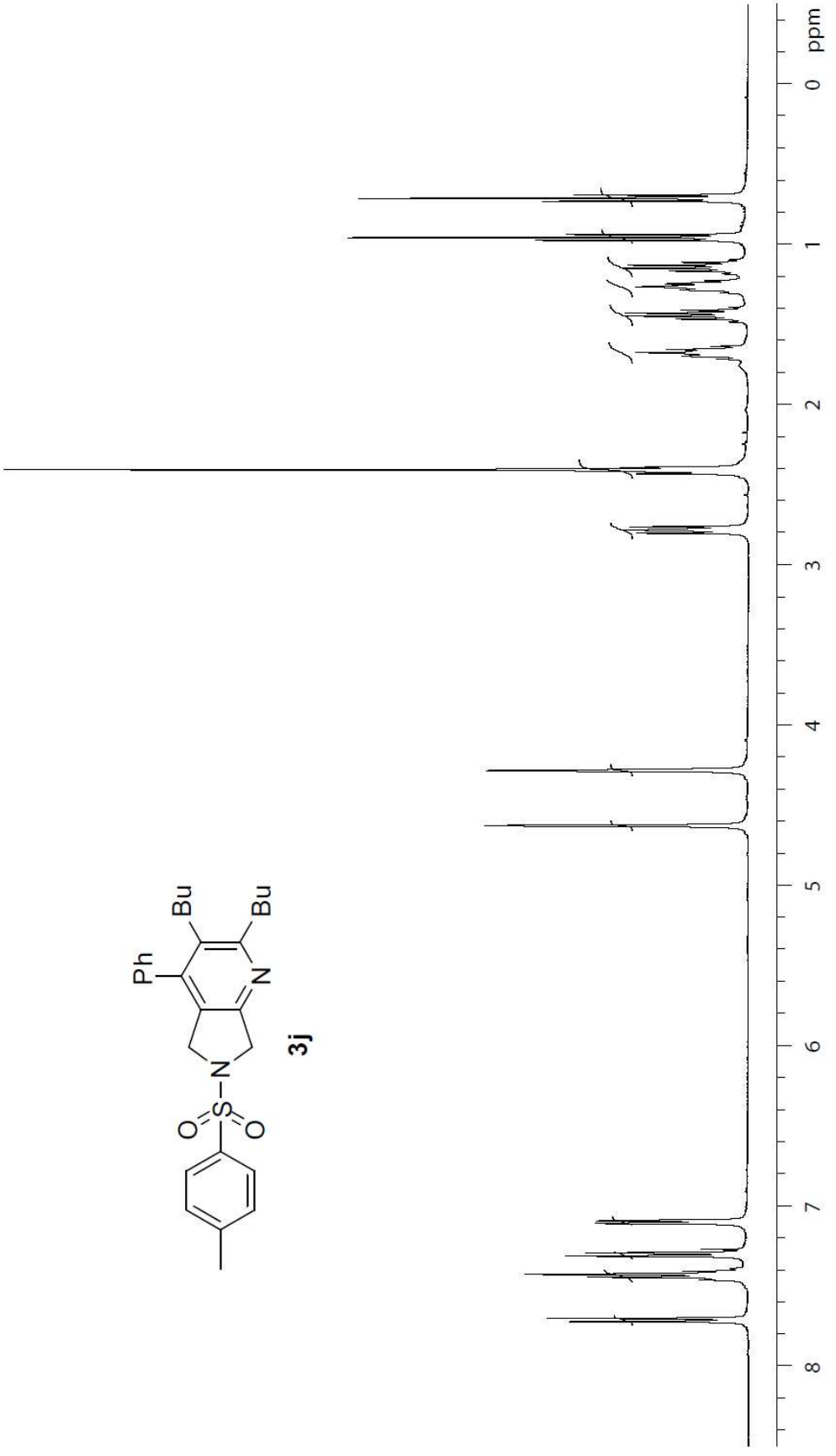
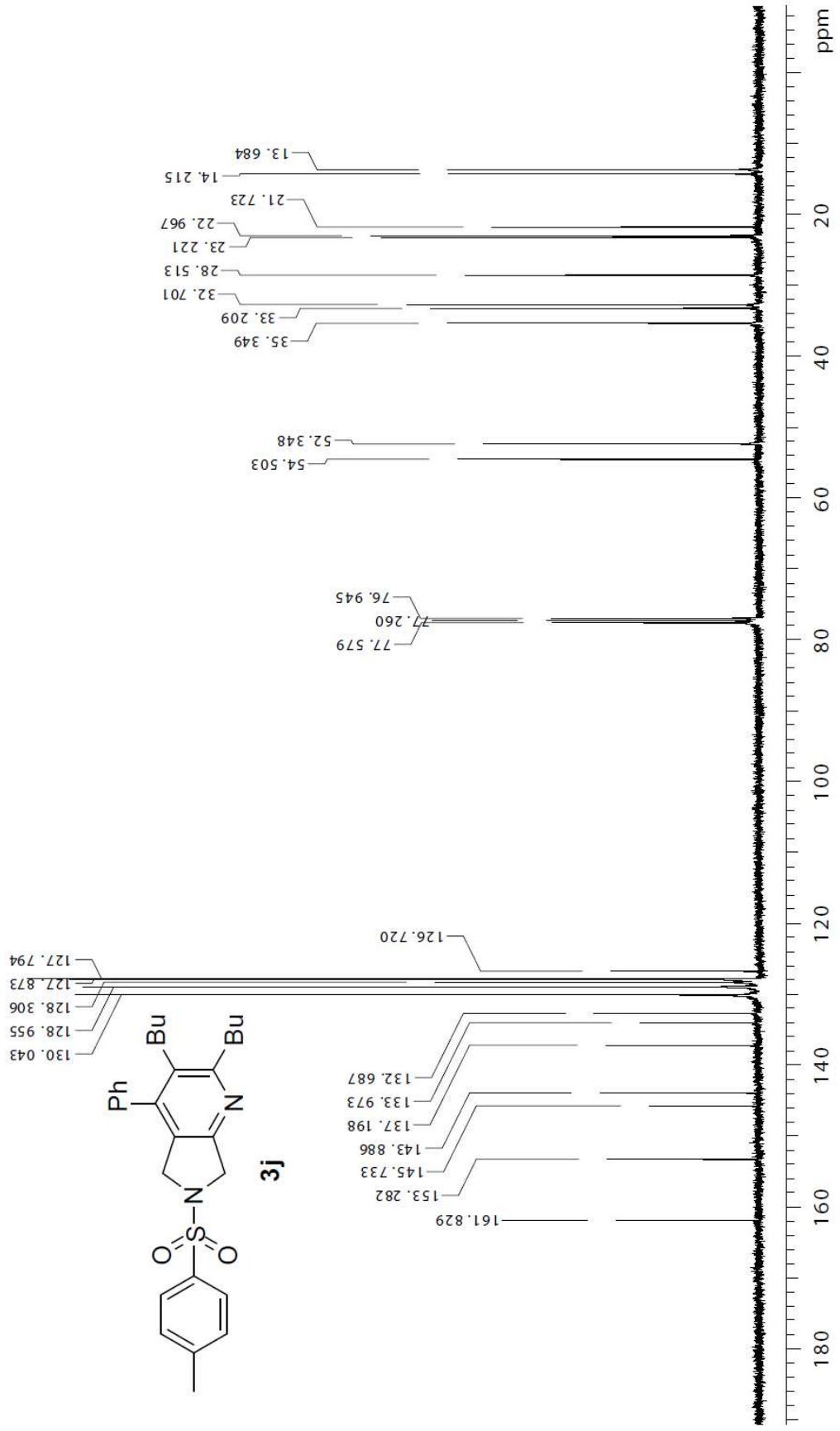
156.939
161.275
Bu
Bu
Ph
N
O
3i


Bu
Bu
Ph
N
N
S
O
O
3j
ppm
0
1
2
3
4
5
6
7
8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80
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120
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160
180
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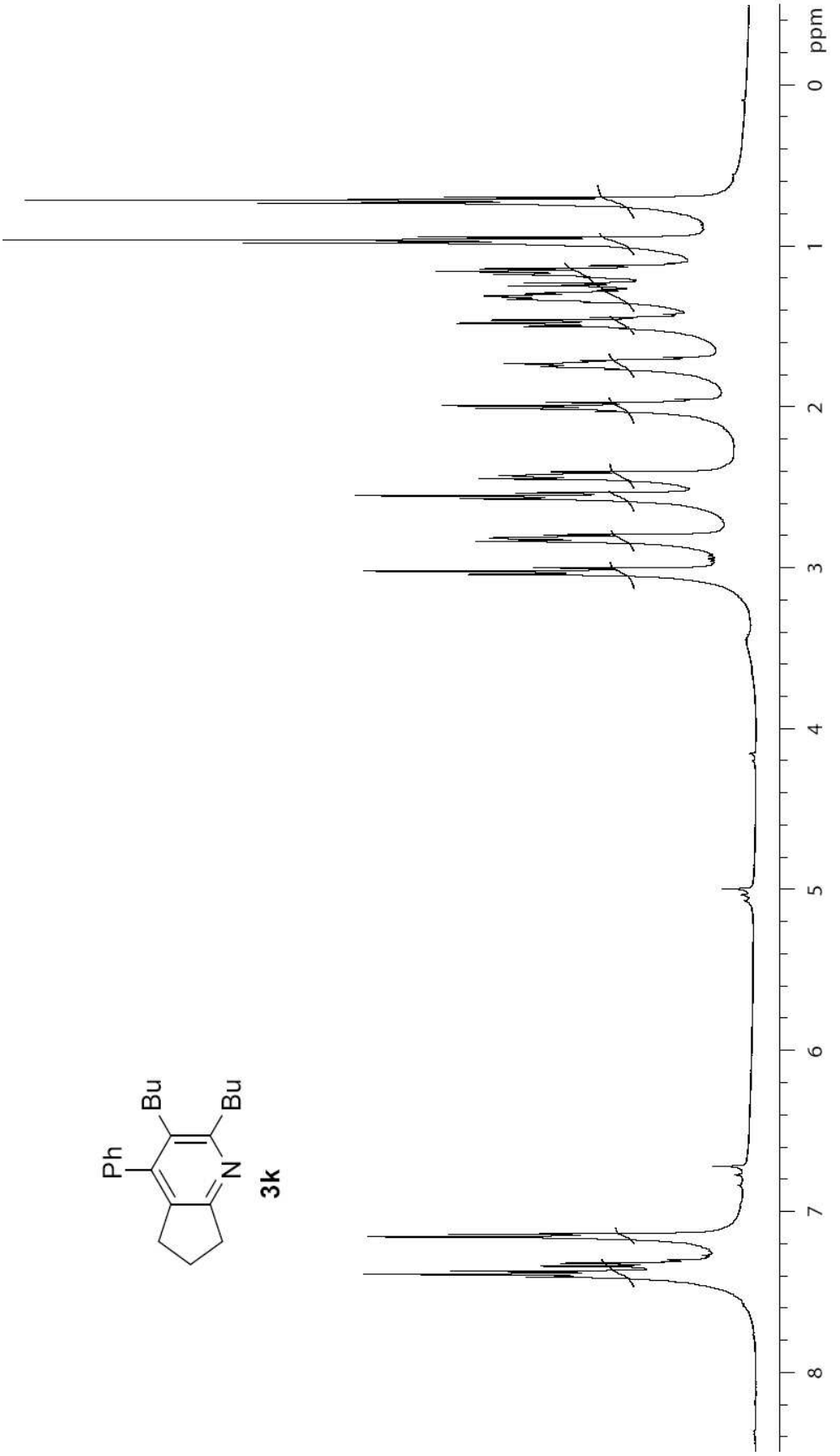
22.967
23.221
28.513
32.701
33.209
35.349
52.348
54.503
76.945
77.260
77.579
126.720
130.043
128.955
128.306
127.873
127.794
132.687
133.973
137.198
143.886
145.733
153.282
161.829
Bu
Bu
Ph
N
N
S
O
O
3j


Ph
Bu
Bu
N
3k
ppm
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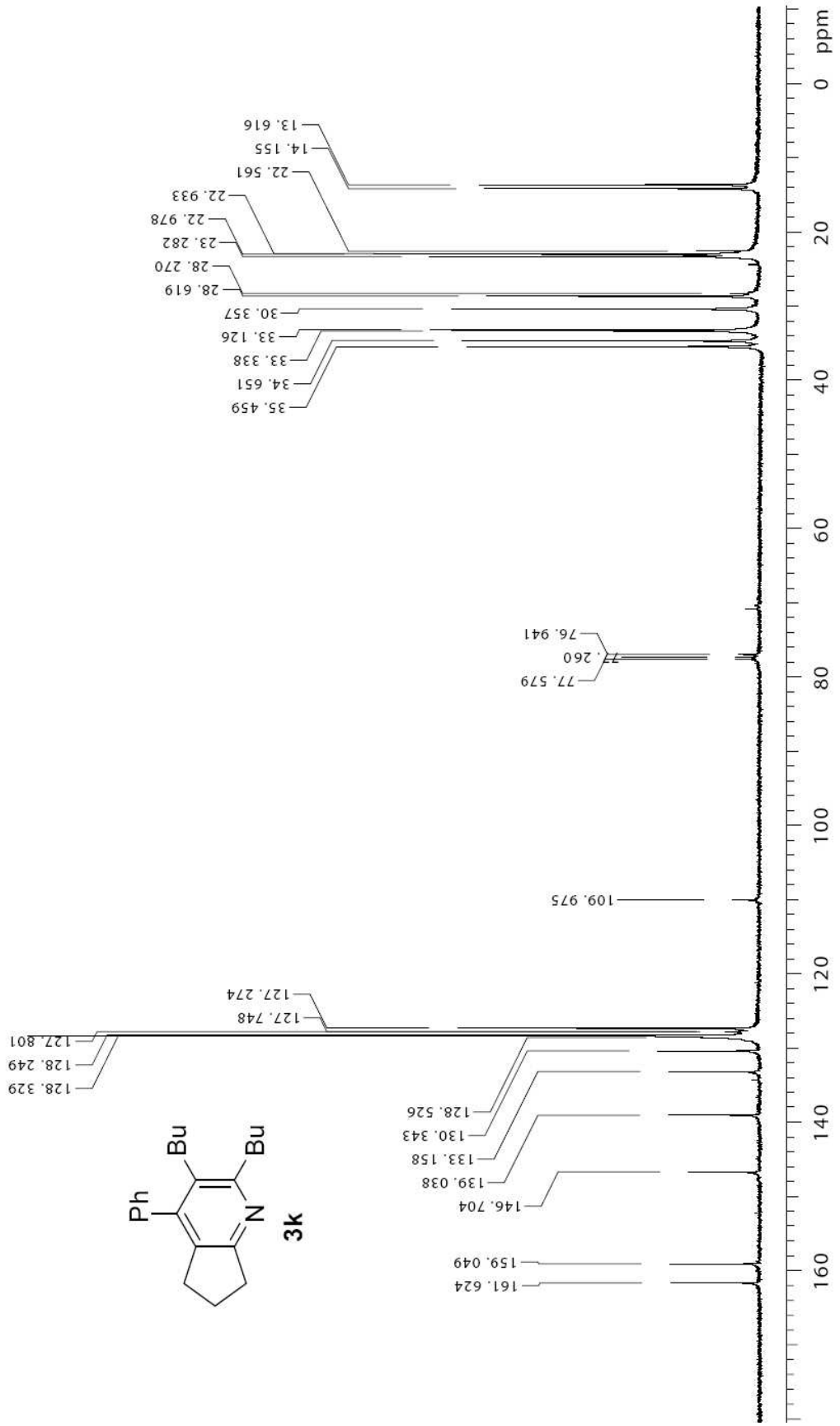
1
2
3
4
5
6
7
8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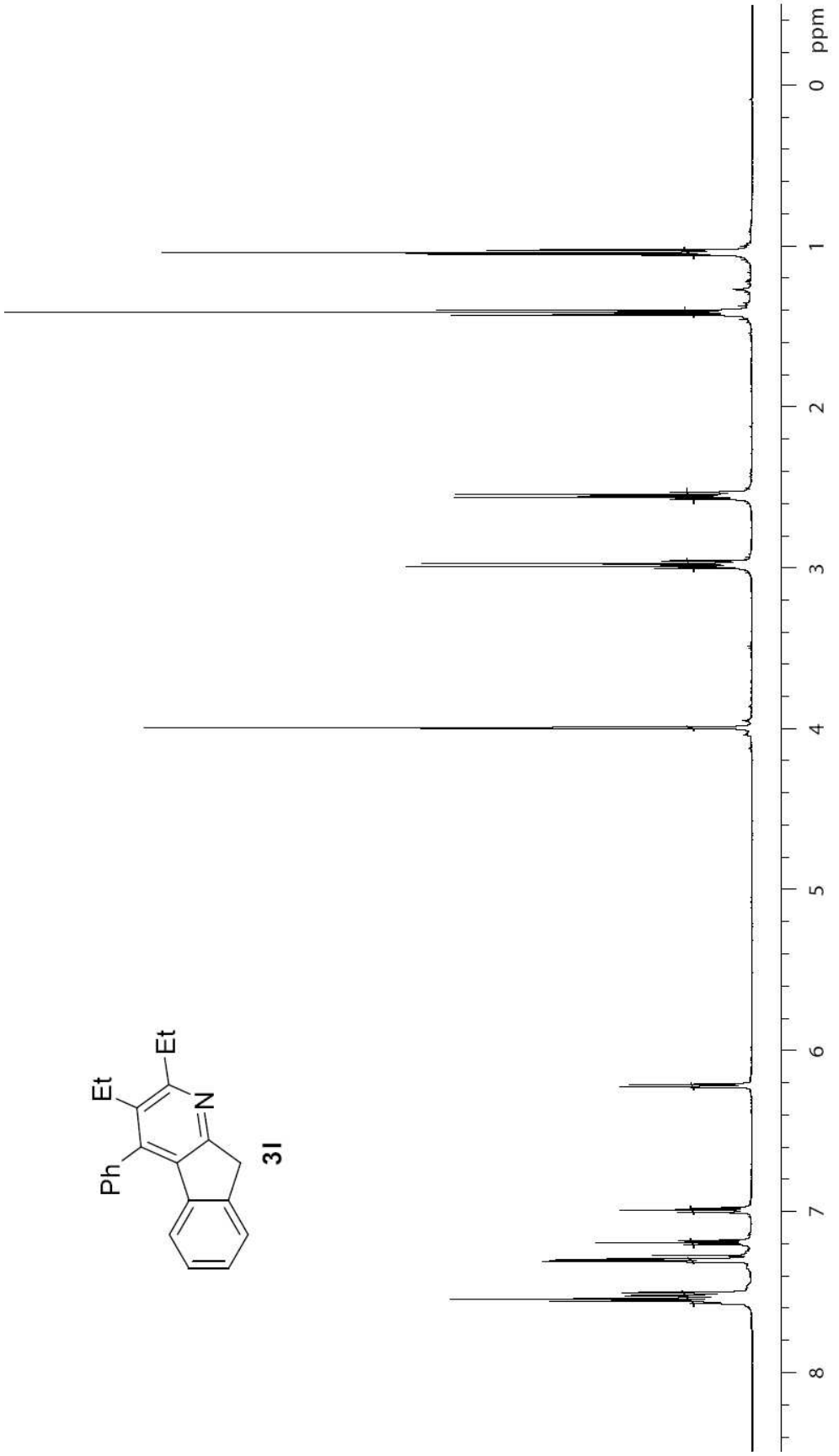
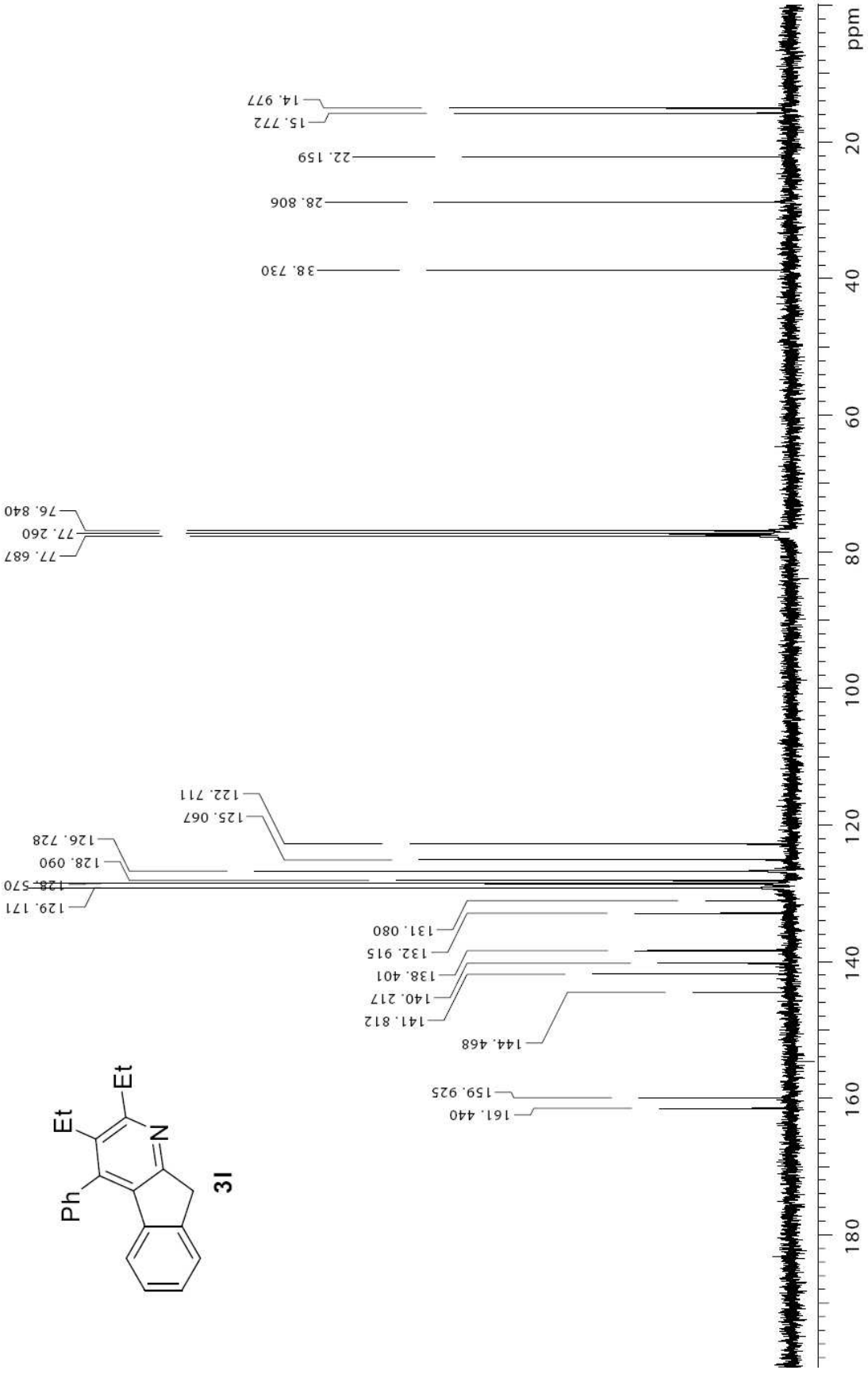
22.978
23.282
28.270
28.619
30.357
33.126
33.338
34.651
35.459
76.941
77.260
77.579
109.975
127.274
127.748
127.801
128.249
128.329
128.526
130.343
133.158
139.038
146.704
159.049
161.624
Bu
Bu
Ph
N
3k
0
20
40
60
80
100
120
140
160
ppm


Et
Et
Ph
N
3l
8
7
6
5
4
3
2
1
0
ppm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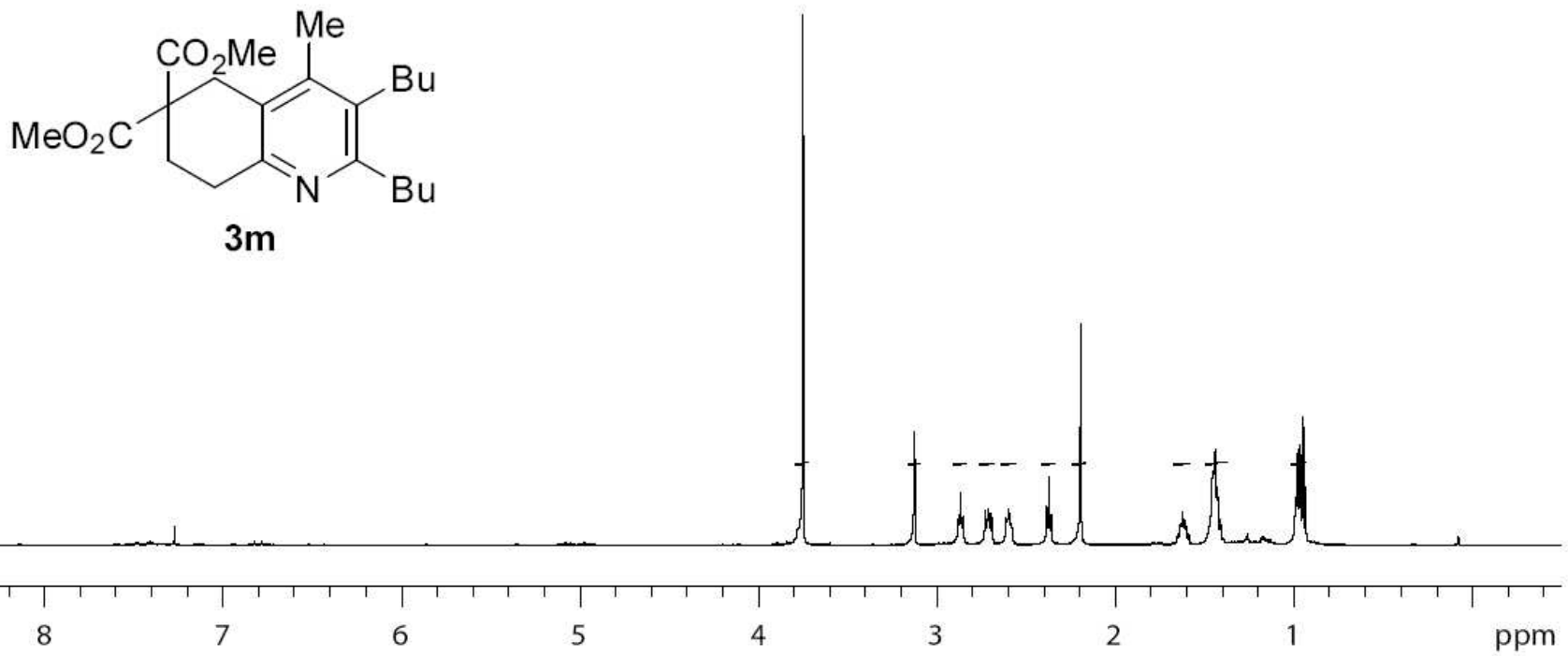
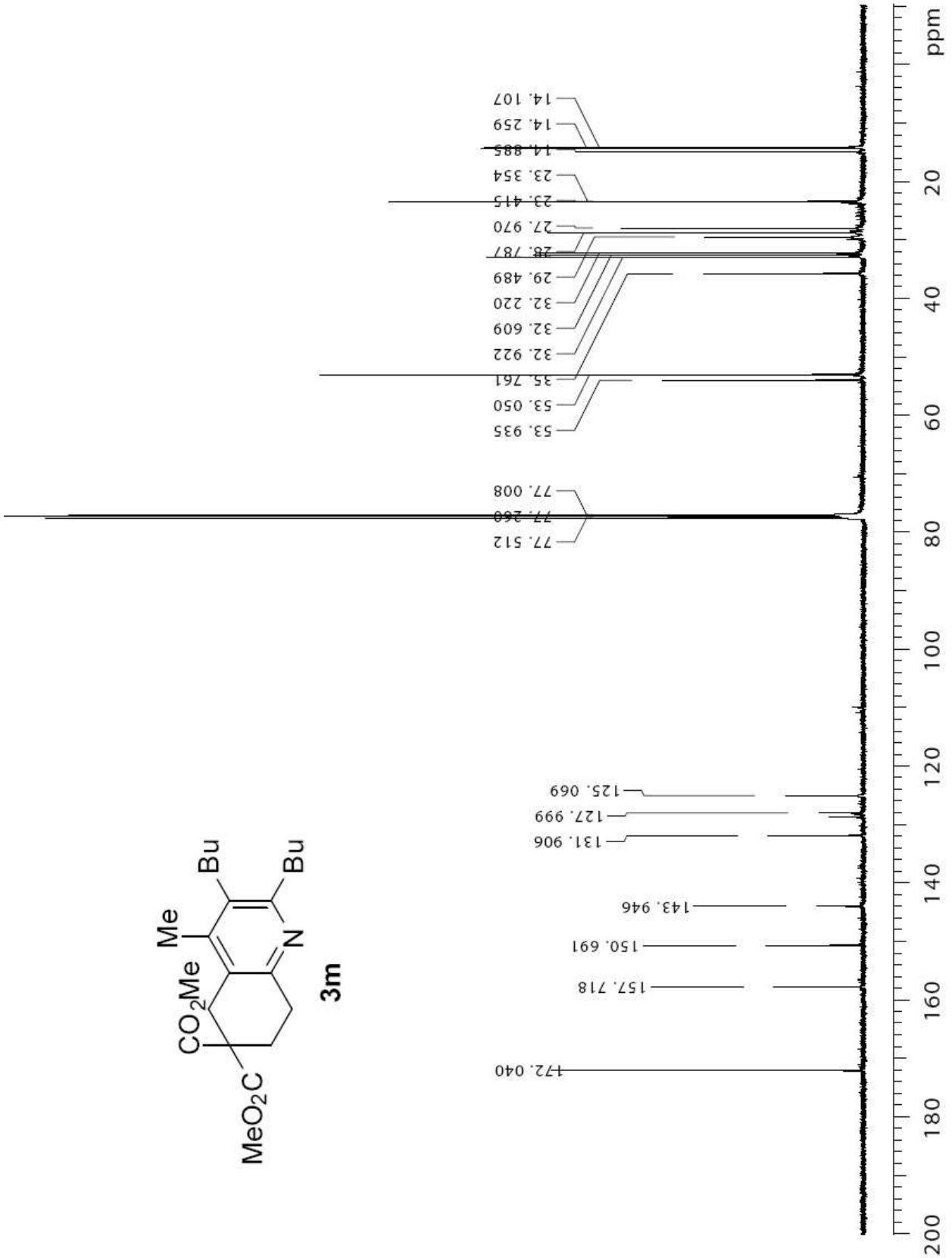
22.159
28.806
38.730
76.840
77.260
77.687
122.711
125.067
126.728
128.090
128.570
129.171
131.080
132.915
138.401
140.217
141.812
144.468
159.925
161.440
ppm
20
40
60
80
100
120
140
160
180
Et
Et
N
Ph
3l


Me
CO2Me
Bu
MeO2C
N
Bu
3m
8
7
6
5
4
3
2
1
ppm


Bu
Bu
Me
N
CO2Me
MeO2C
3m
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157.718
150.691
143.946
131.906
127.999
125.069
77.512
77.260
77.008
53.935
53.050
35.761
32.922
32.609
32.220
29.489
28.787
27.970
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14.885
14.259
14.107
ppm
200
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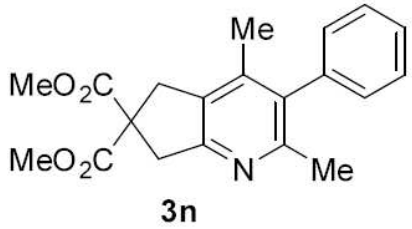
160
140
120
100
80
60
40
20



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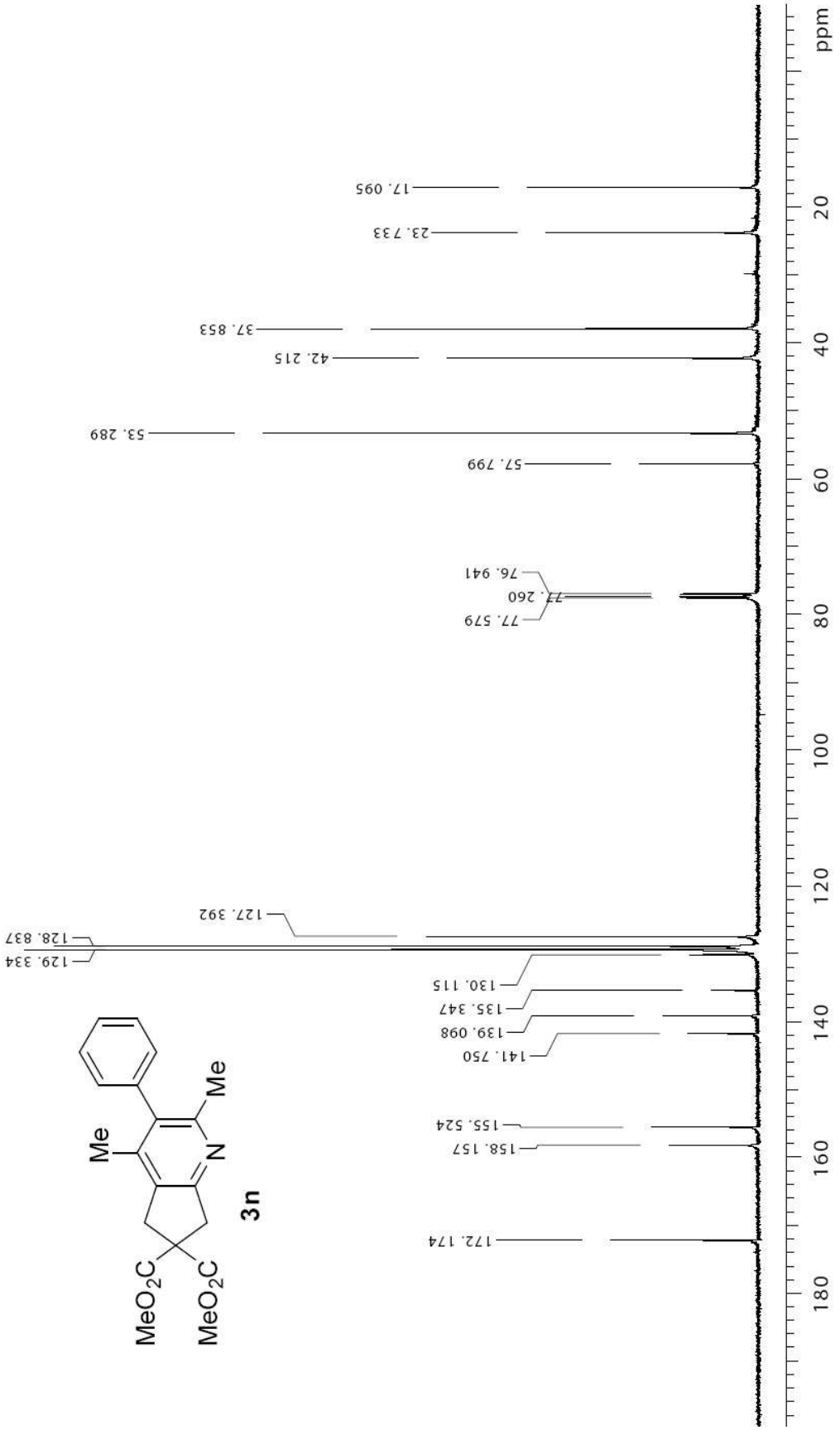
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80
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120
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160
180
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42.215
53.289
57.799
76.941
77.260
77.579
127.392
128.837
129.334
130.115
135.347
139.098
141.750
155.524
158.157
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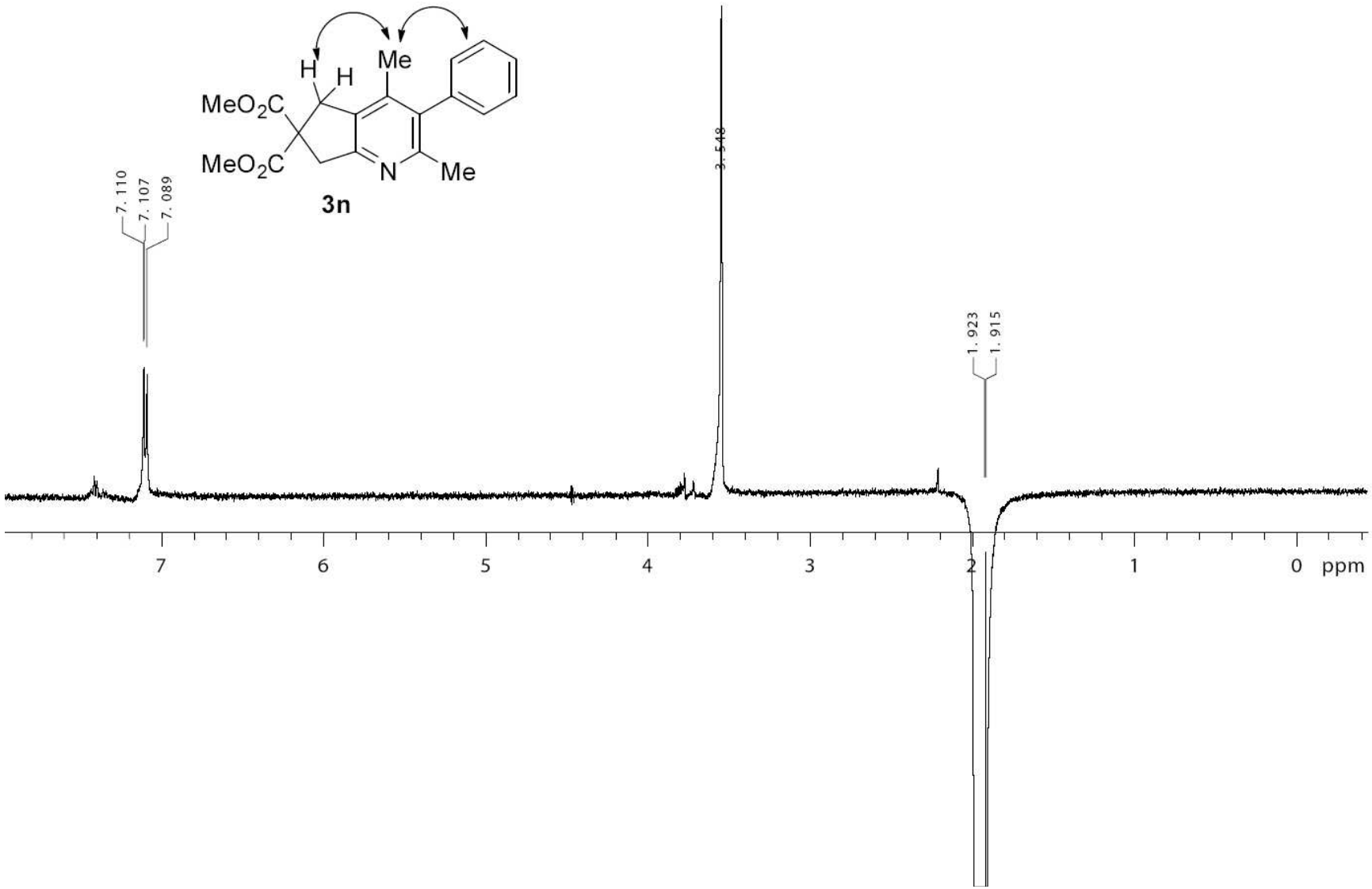
Me
Me
N
MeO2C
MeO2C
3n


H
H
Me
MeO2C
MeO2C
N
Me
3n
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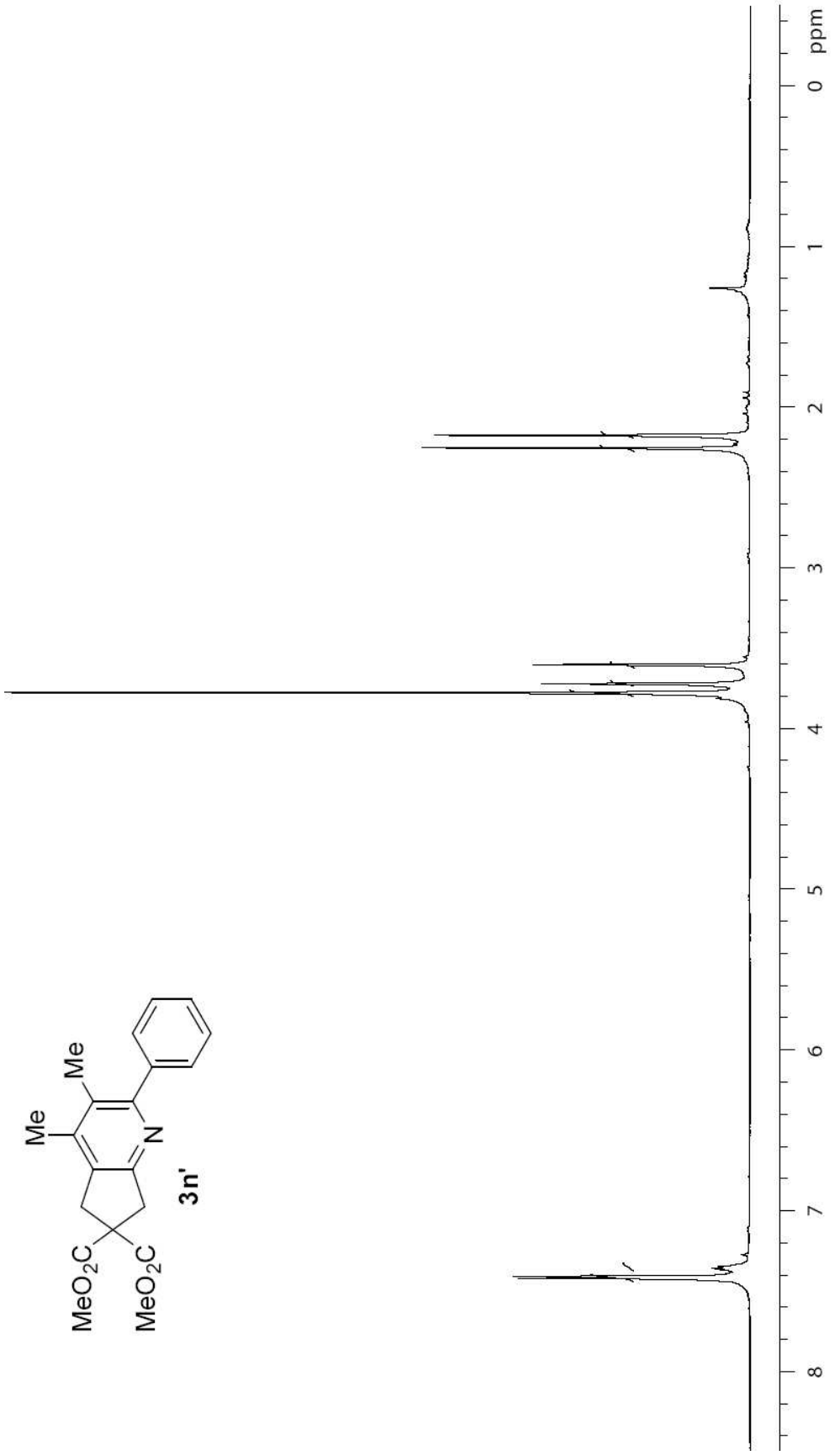
7.107
7.089
3.548
1.923
1.915
7
6
5
4
3
2
1
0
ppm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Me
N
MeO2C
MeO2C
3n'
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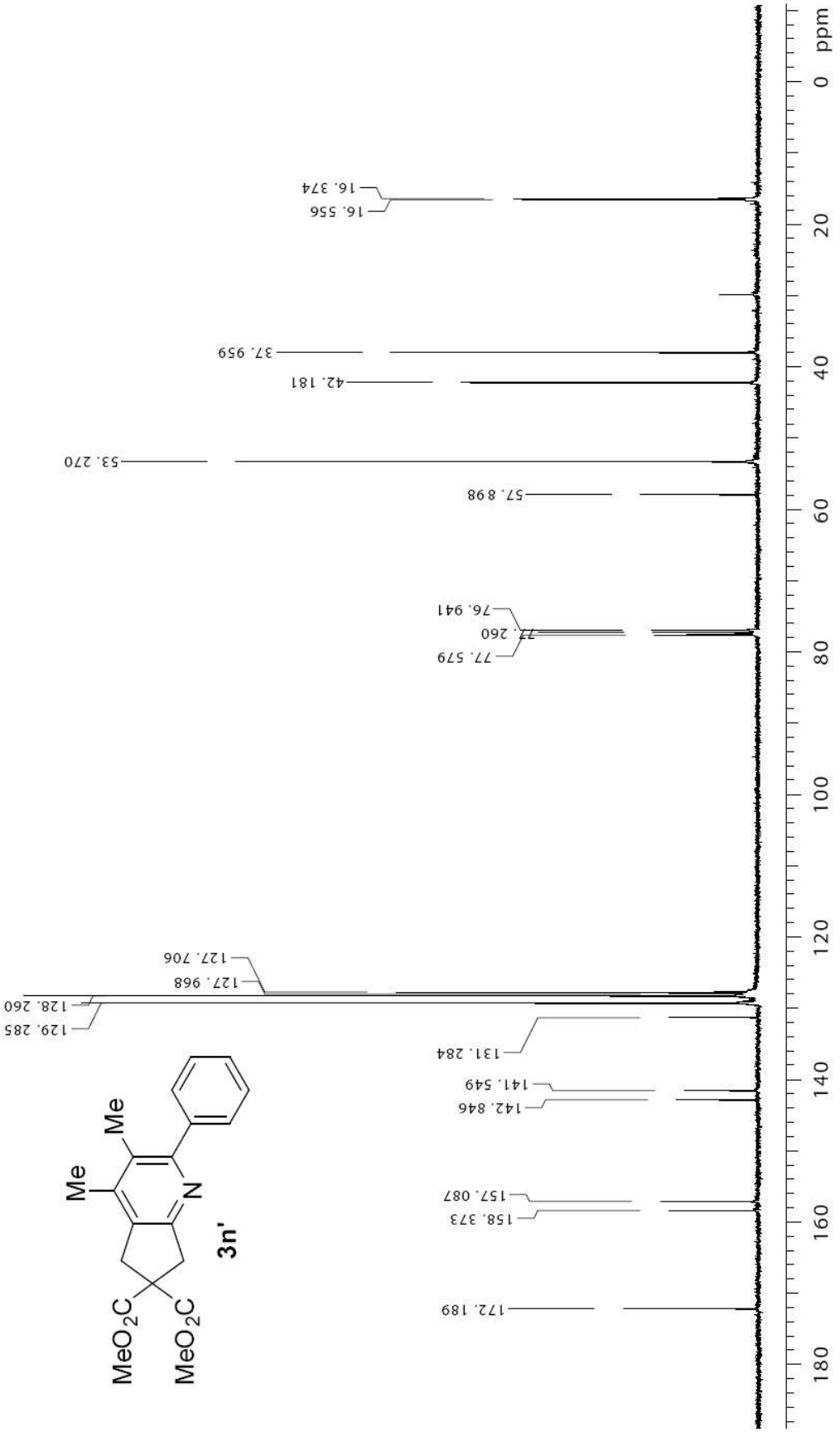
7
6
5
4
3
2
1
0
ppm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140
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180
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42.181
53.270
57.898
76.941
77.260
77.579
127.706
127.968
128.260
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131.284
141.549
142.846
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158.373
172.189
Me
Me
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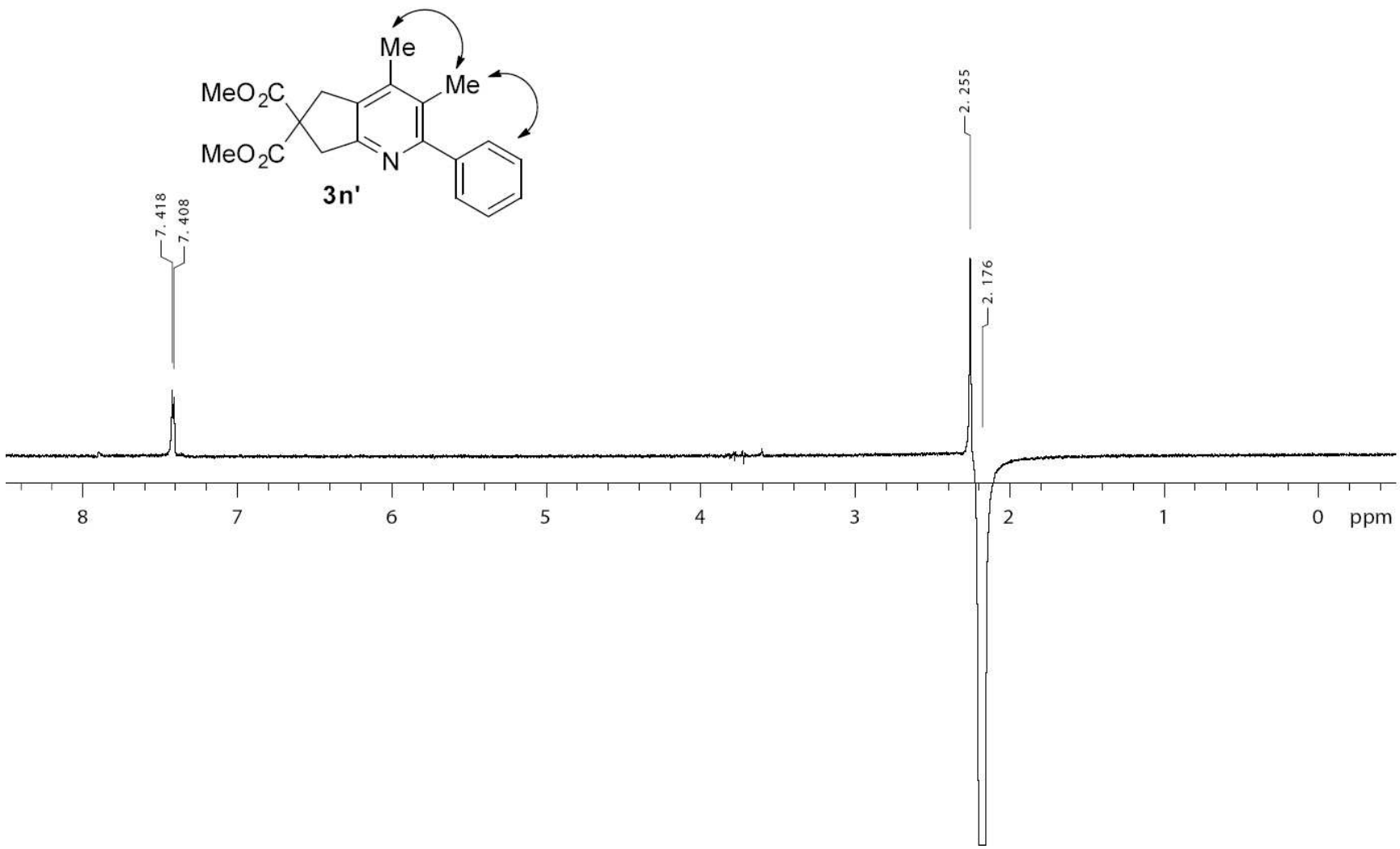
MeO2C
MeO2C
3n'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Me
MeO2C
MeO2C
N
3n'
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2.176
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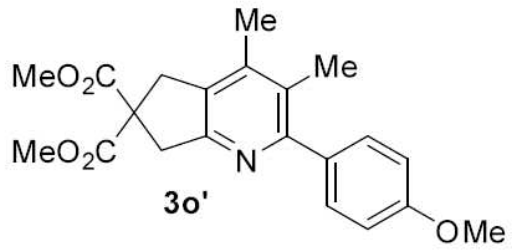
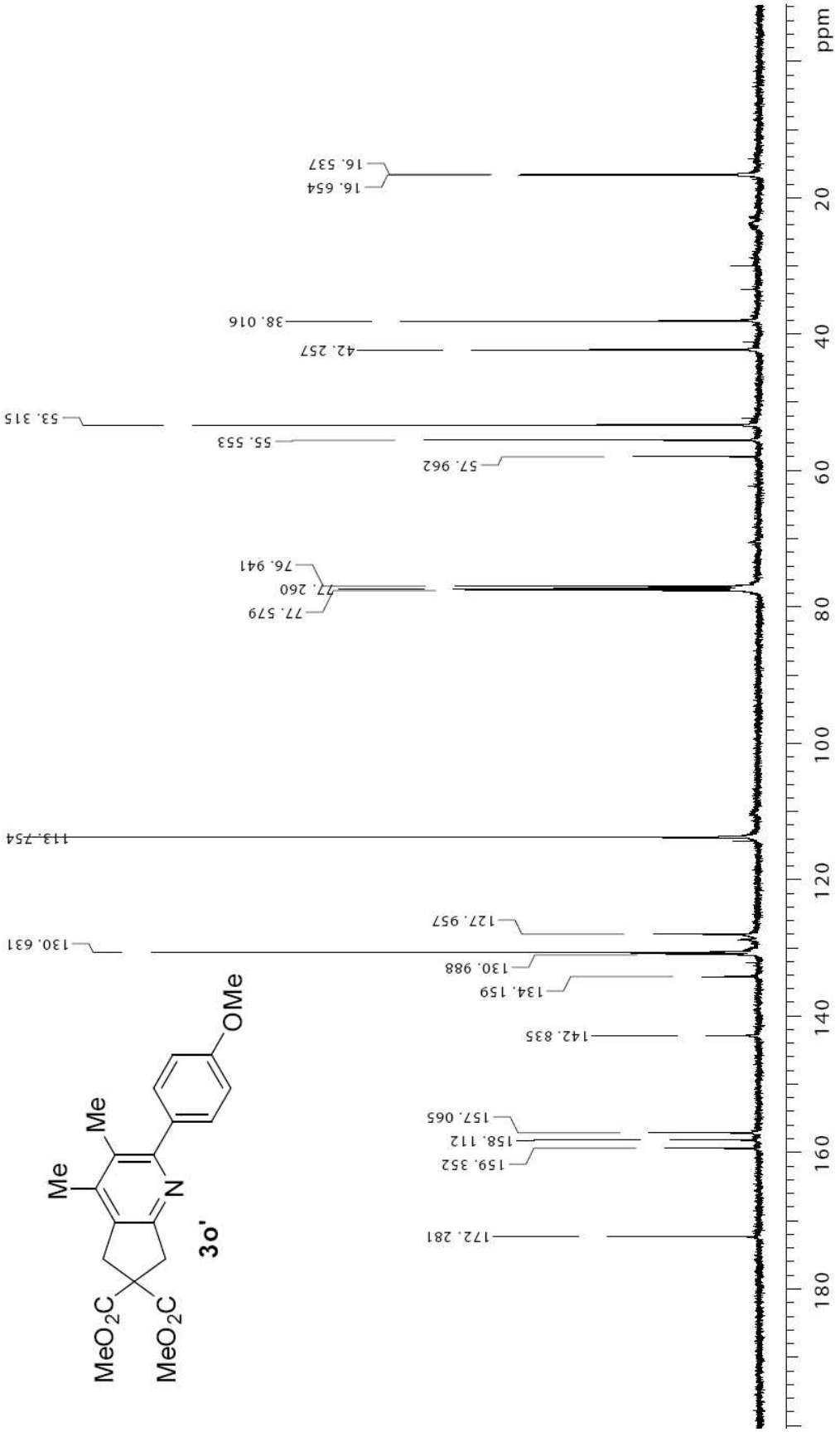
7
6
5
4
3
2
1
0
ppm



3o'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80
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120
140
160
180
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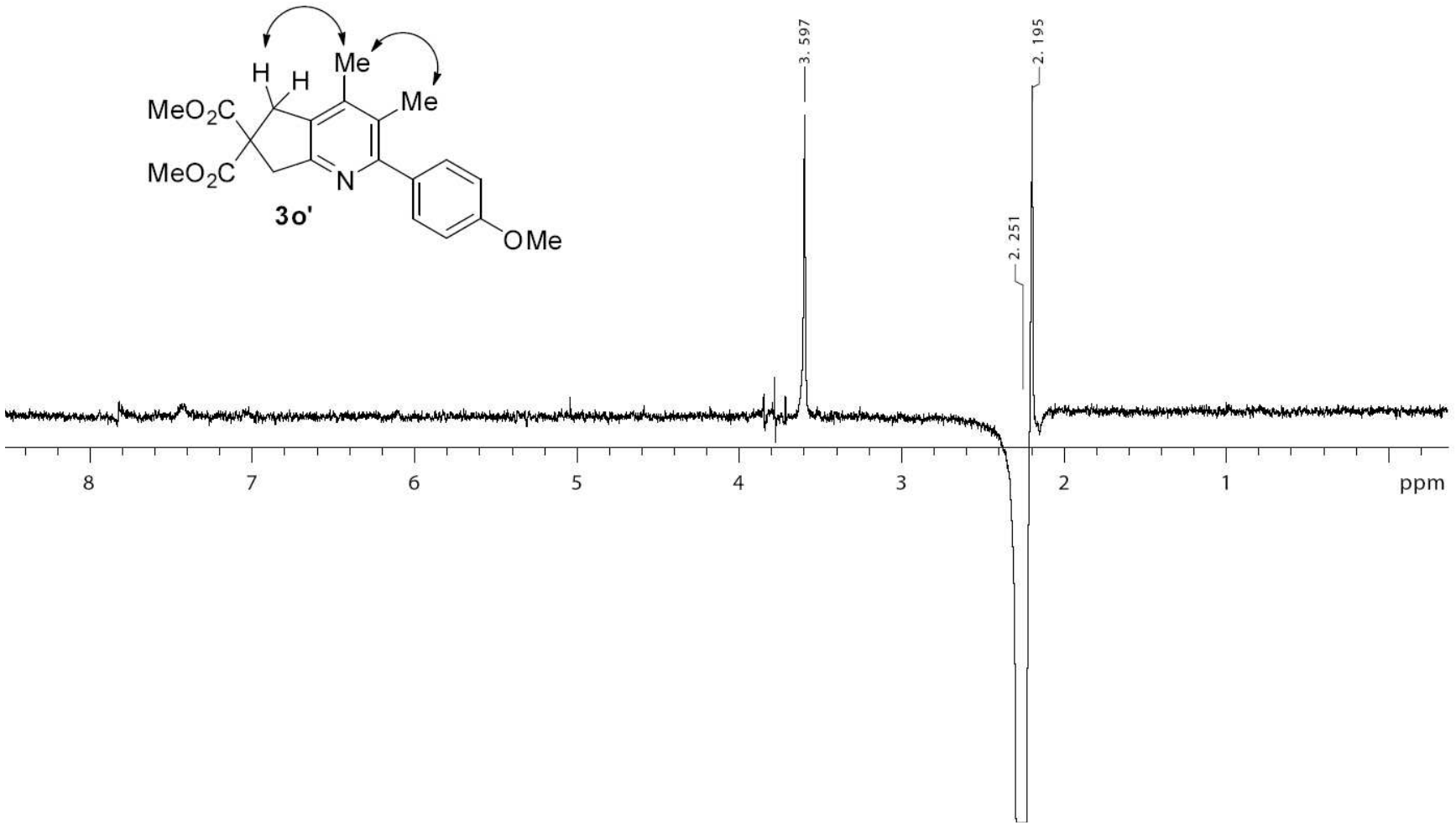
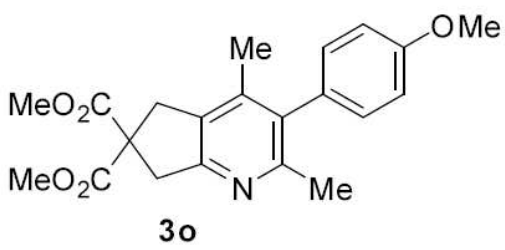
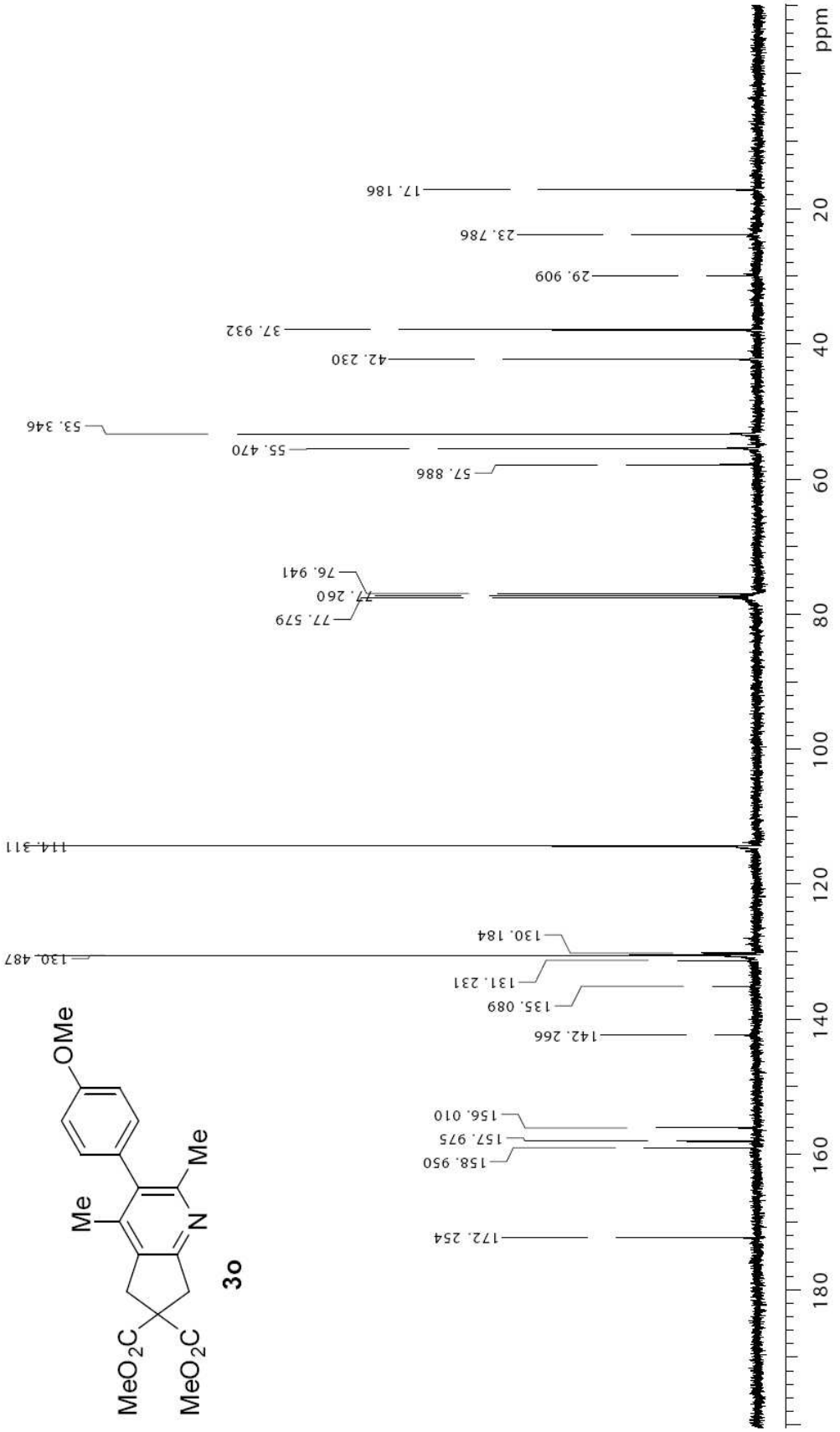
53.315
55.553
57.962
76.941
77.260
77.579
113.754
127.957
130.631
130.988
134.159
142.835
157.065
158.112
159.352
172.281
OMe
Me
Me
N
MeO2C
MeO2C
3o'


H
H
Me
Me
MeO2C
MeO2C
N
OMe
3o'
3. 597
2. 251
2. 195
8
7
6
5
4
3
2
1
ppm



3o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140
160
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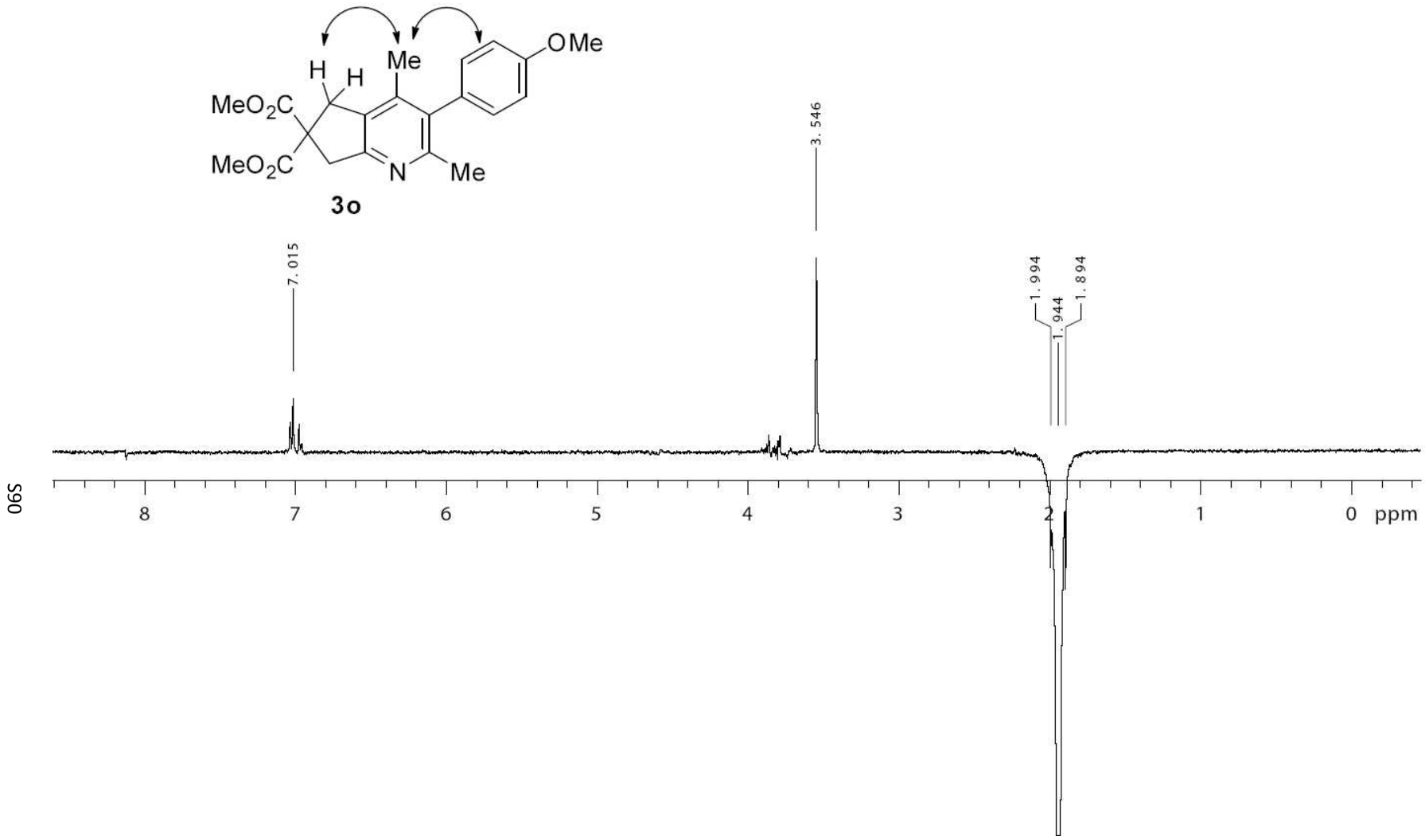
37.932
42.230
53.346
55.470
57.886
76.941
77.260
77.579
114.311
130.184
130.487
131.231
135.089
142.266
156.010
157.975
158.950
172.254
OMe
Me
Me
N
MeO2C
MeO2C
3o


OMe
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H
Me
MeO2C
MeO2C
N
Me
3o
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1.894
8
7
6
5
4
3
2
1
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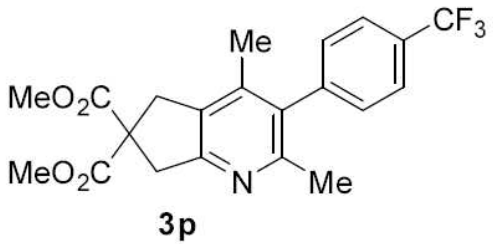
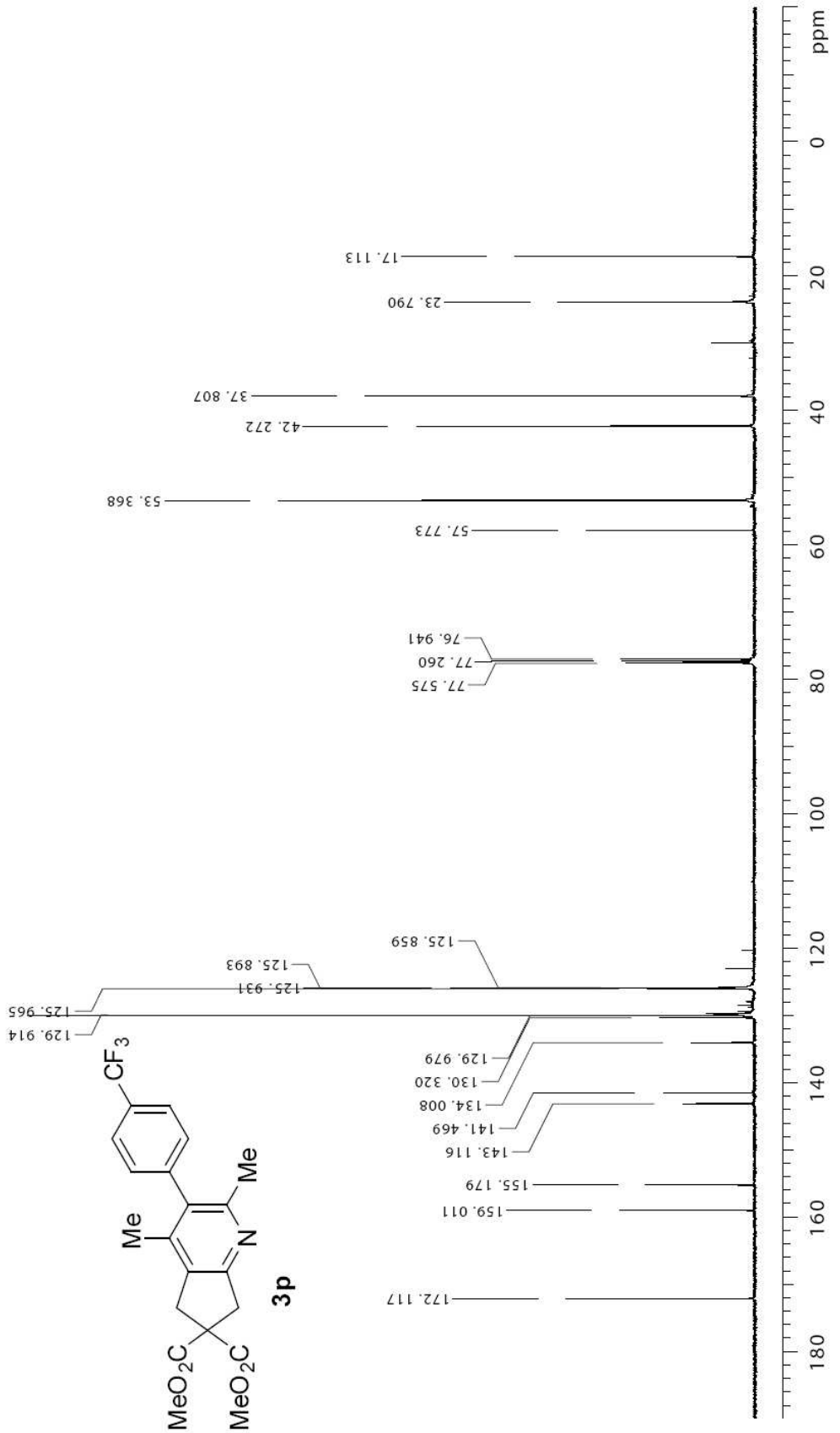


3p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80
100
120
140
160
180
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37.807
42.272
53.368
57.773
76.941
77.260
77.575
125.859
125.893
125.931
125.965
129.914
129.979
130.320
134.008
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143.116
155.179
159.011
172.117
CF3
Me
Me
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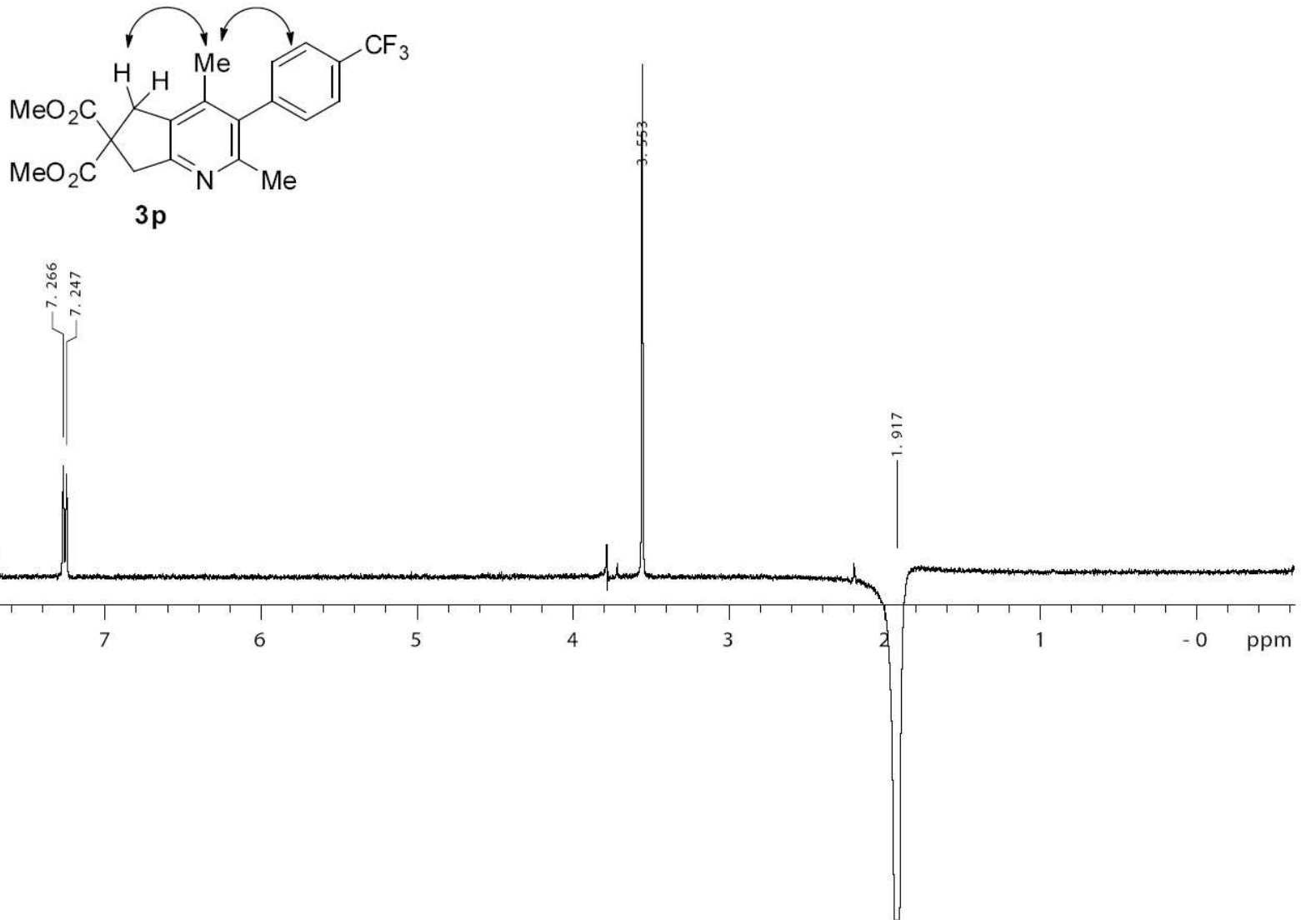
MeO2C
MeO2C
3p


H
H
Me
CF3
MeO2C
MeO2C
N
Me
3p
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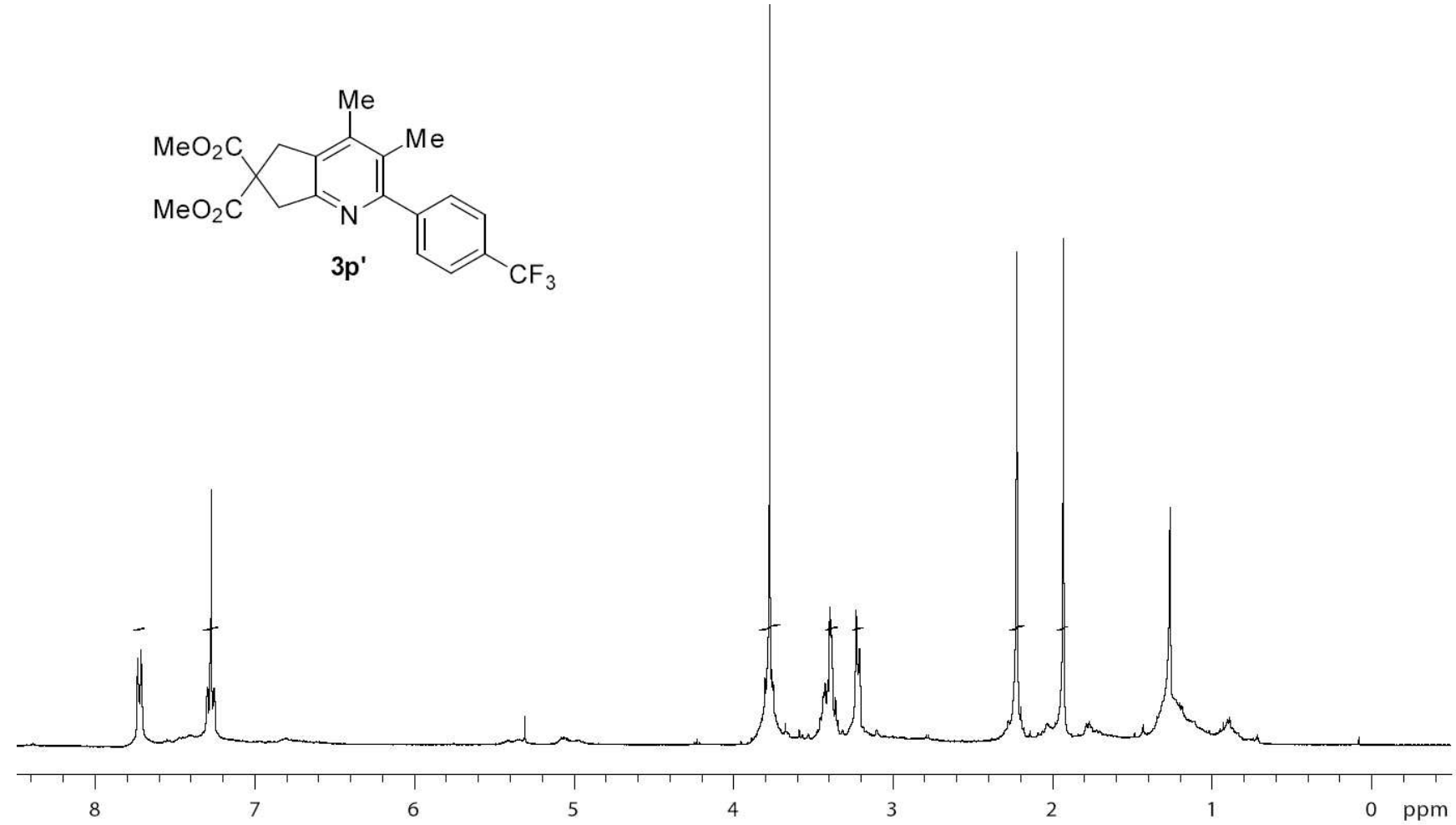
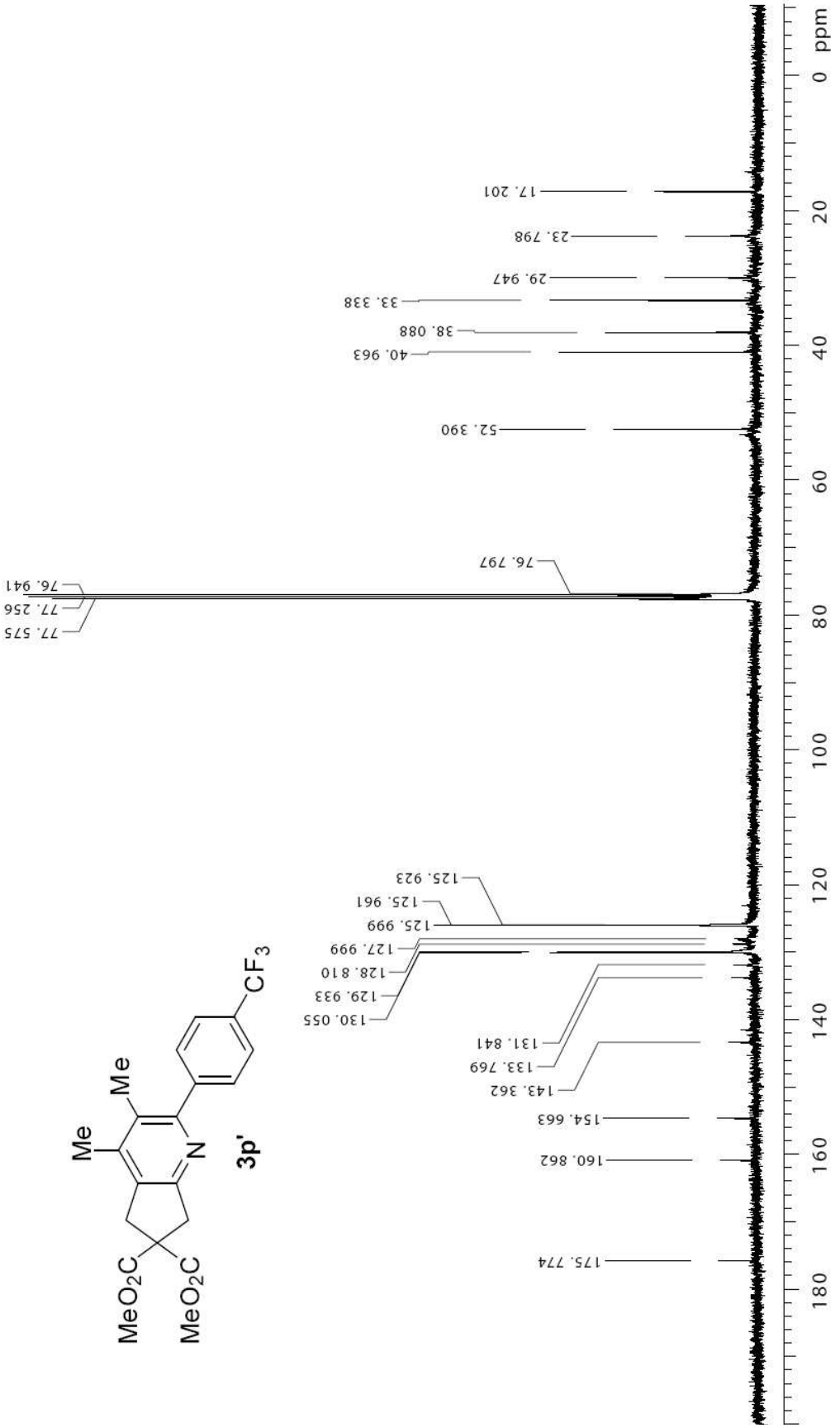
7.247
3.553
1.917
8
7
6
5
4
3
2
1
-0
ppm


Me
Me
MeO2C
MeO2C
N
CF3
3p'
8
7
6
5
4
3
2
1
0
ppm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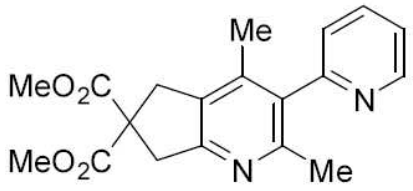
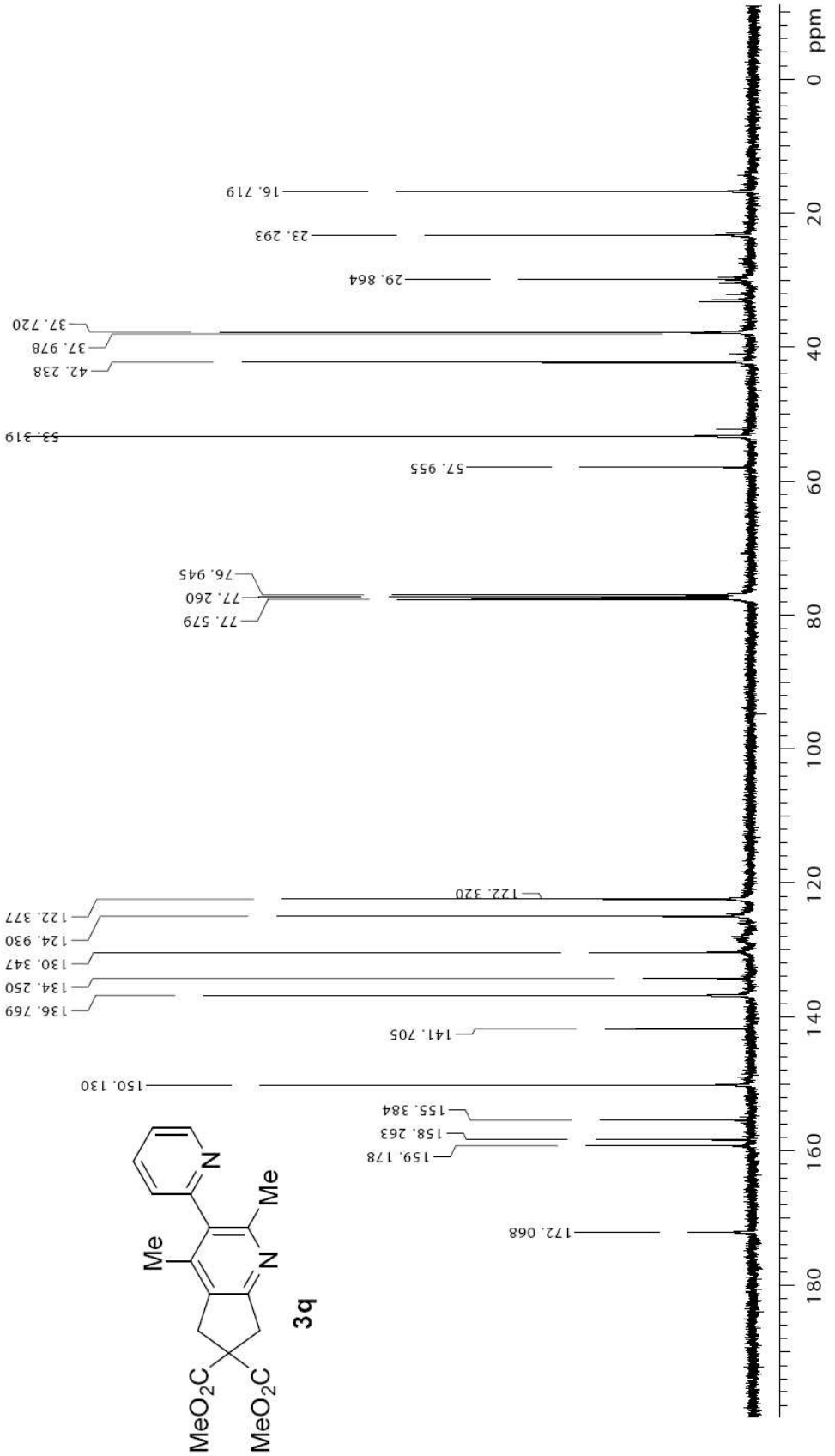
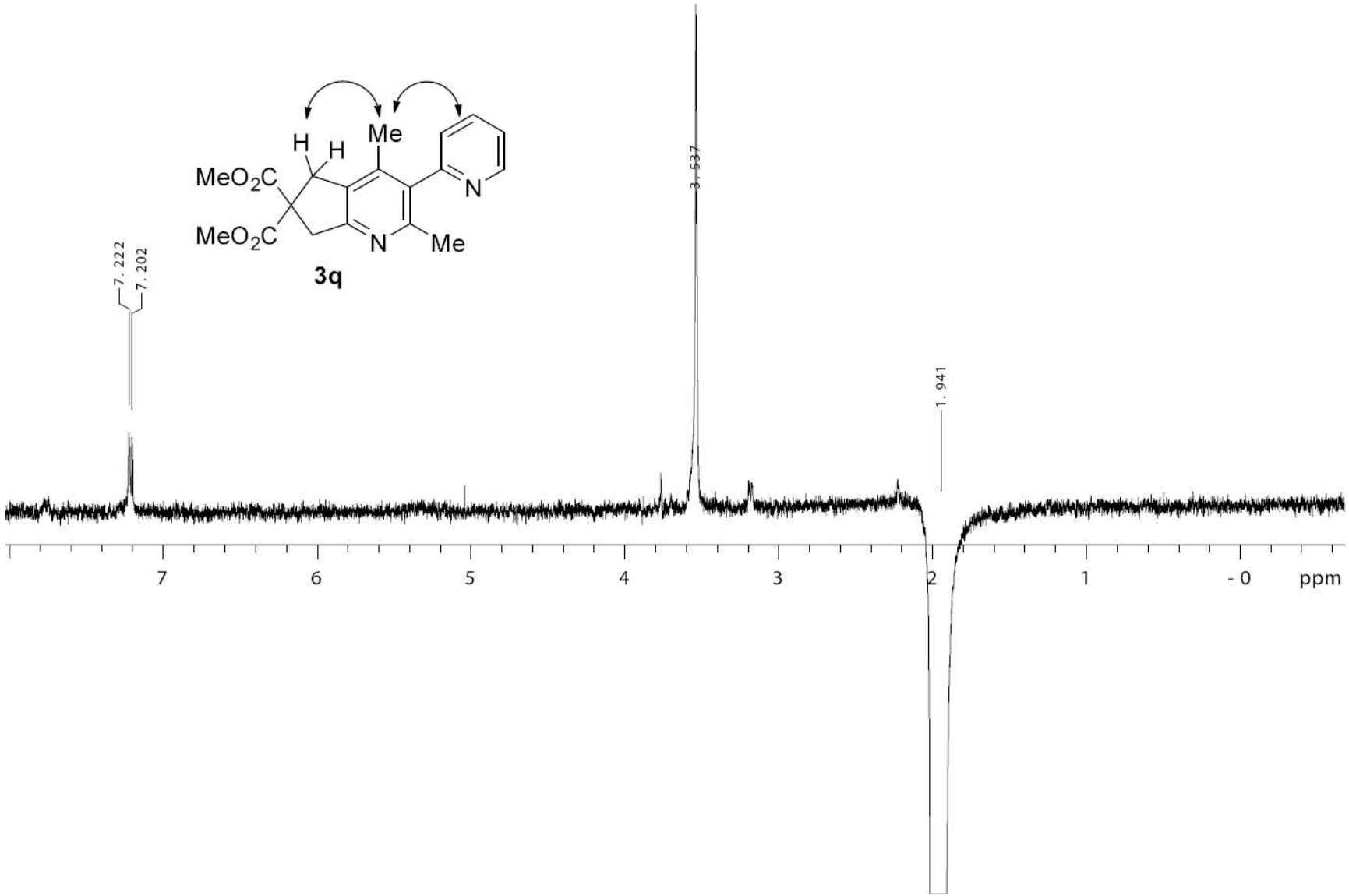
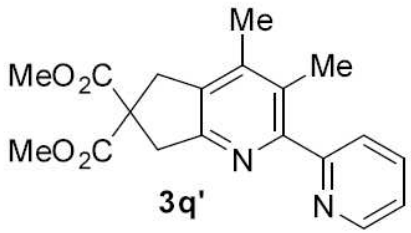
154.663
143.362
133.769
131.841
130.055
129.933
128.810
127.999
125.999
125.961
125.923
77.575
77.256
76.941
76.797
52.390
40.963
38.088
33.338
29.947
23.798
17.201
0 ppm
20
40
60
80
100
120
140
160
180
Me
Me
N
CF3
MeO2C
MeO2C
3p'



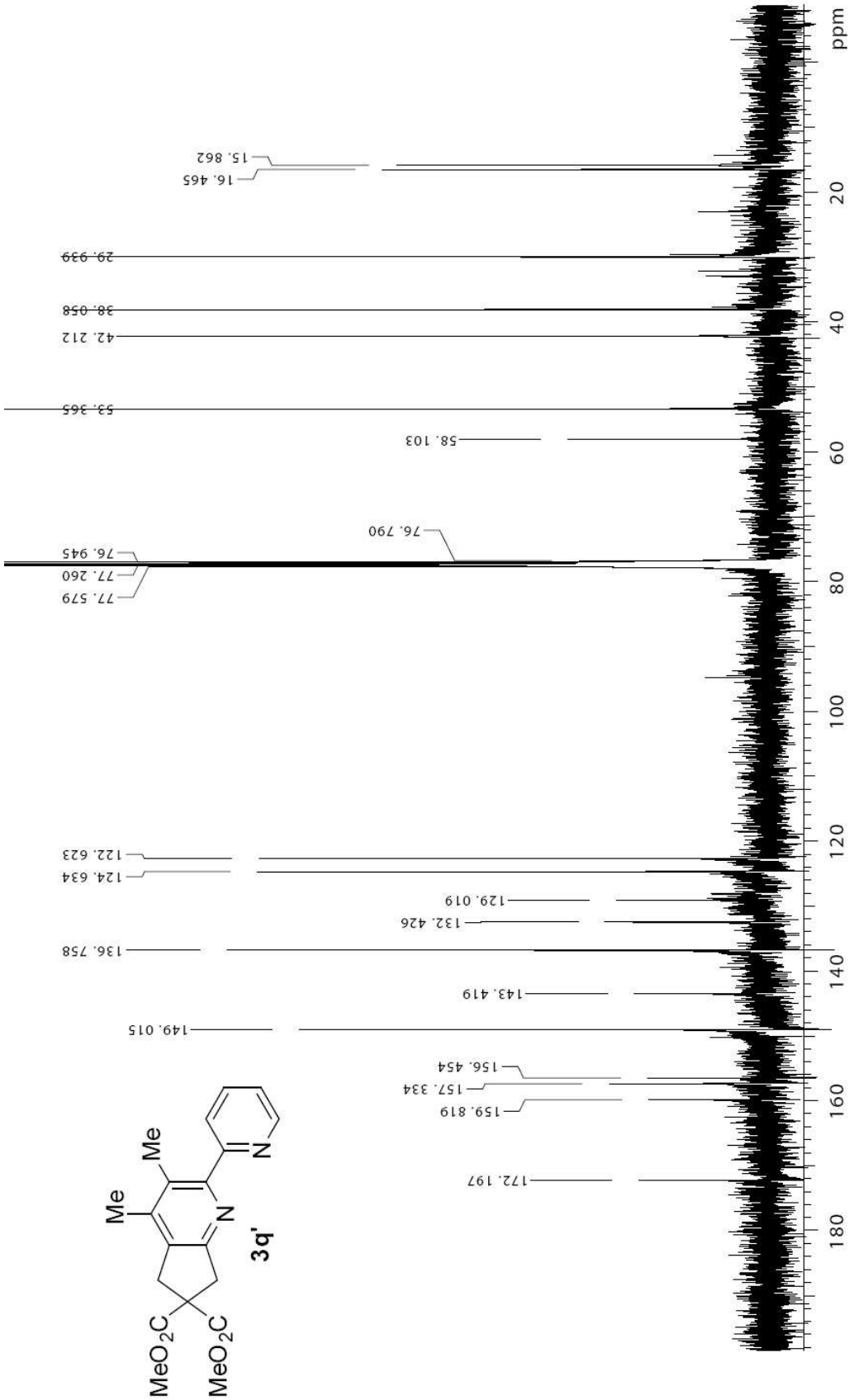
3q

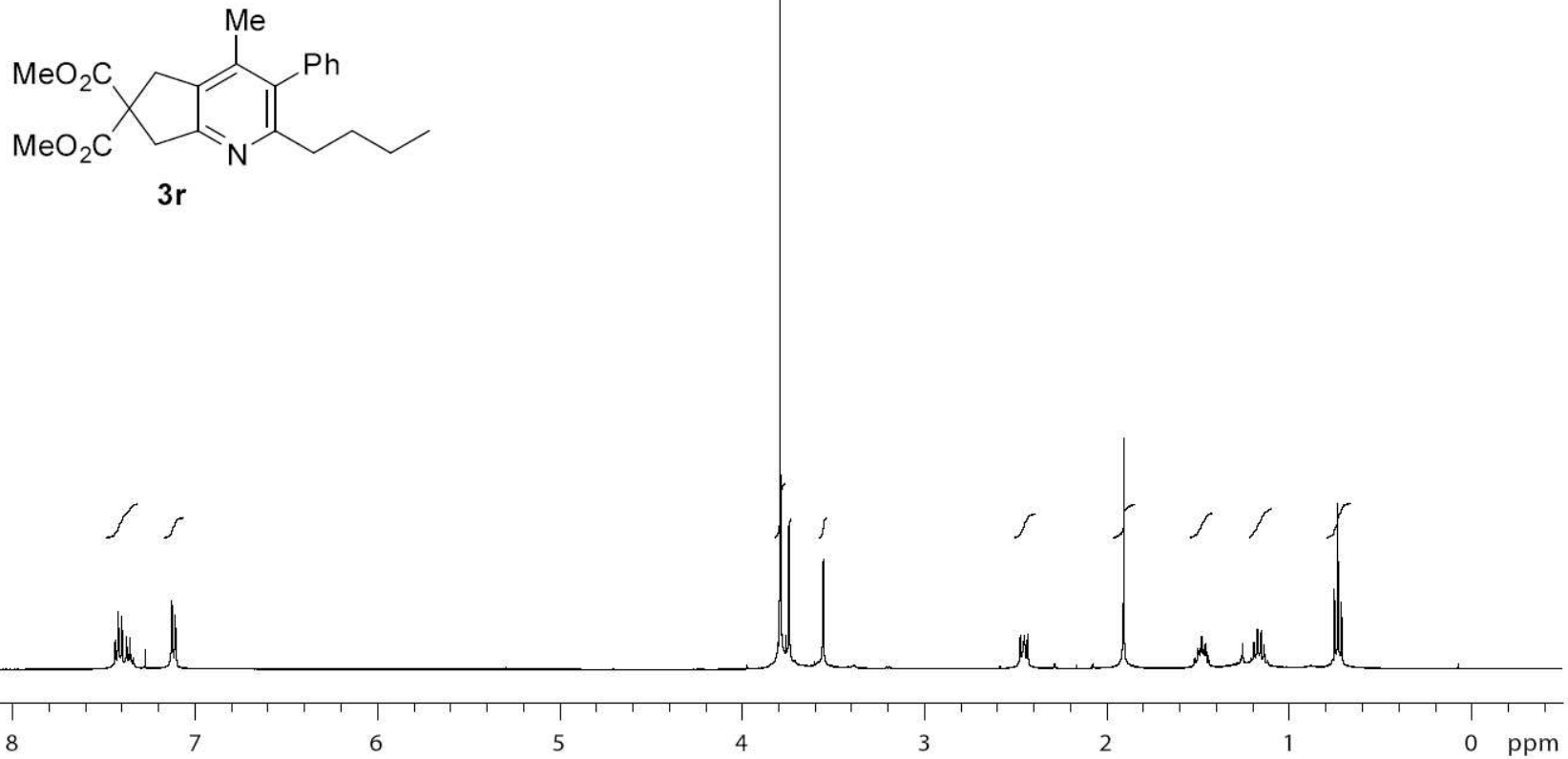

ppm
0
20
40
60
80
100
120
140
160
180
172.068
159.178
158.263
155.384
150.130
141.705
136.769
134.250
130.347
124.930
122.377
122.320
77.579
77.260
76.945
57.955
53.319
42.238
37.978
37.720
29.864
23.293
16.719
Me
Me
N
N
MeO2C
MeO2C
3q

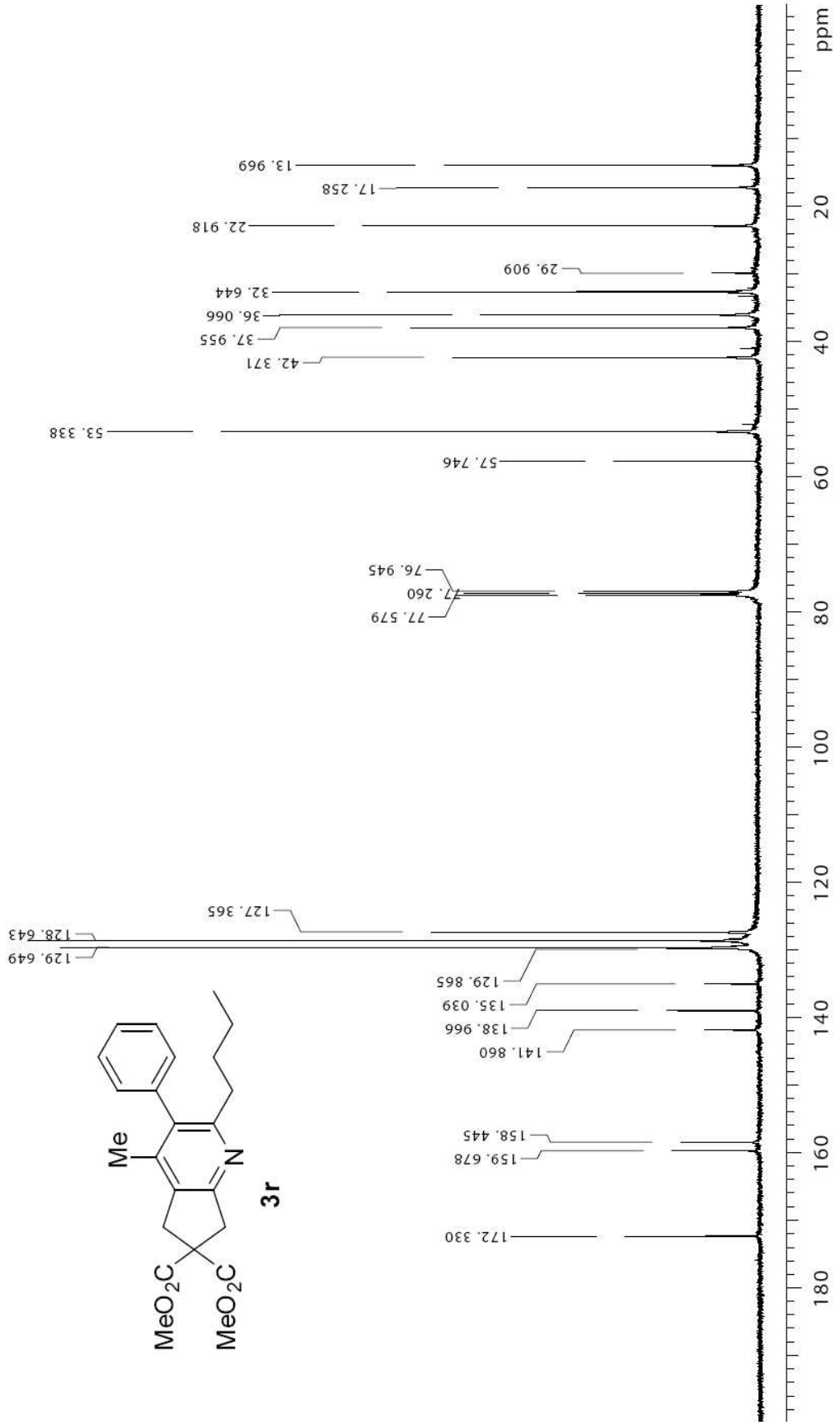

H
H
Me
MeO2C
MeO2C
N
N
Me
3q
7.222
7.202
3.537
1.941
7
6
5
4
3
2
1
- 0
ppm

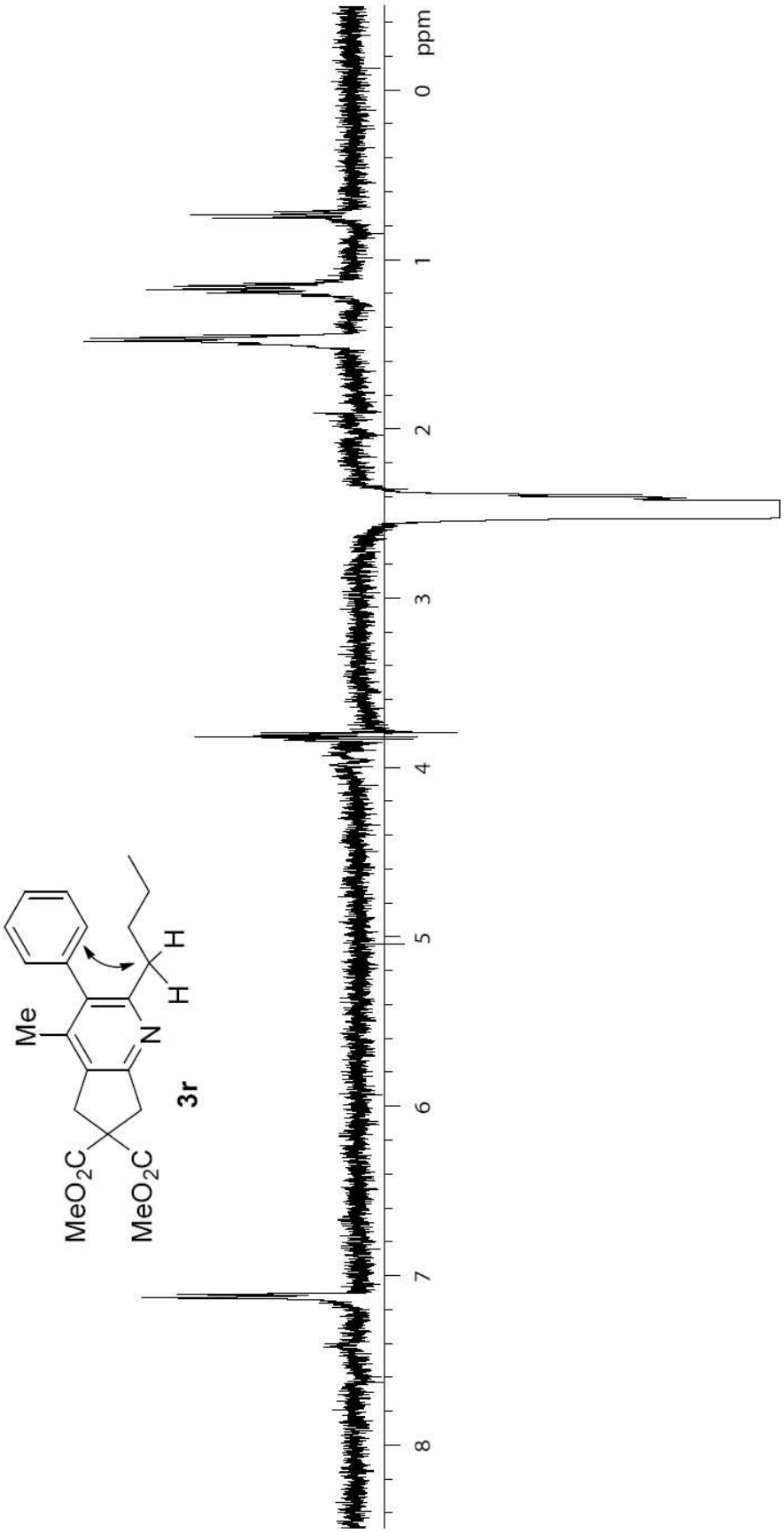


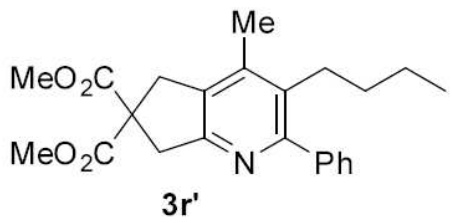
3q'


15.862
16.465
29.939
38.058
42.212
53.365
58.103
76.790
76.945
77.260
77.579
122.623
124.634
129.019
132.426
136.758
143.419
149.015
156.454
157.334
159.819
172.197
ppm
20
40
60
80
100
120
140
160
180
Me
Me
N
N
MeO2C
MeO2C
3q'

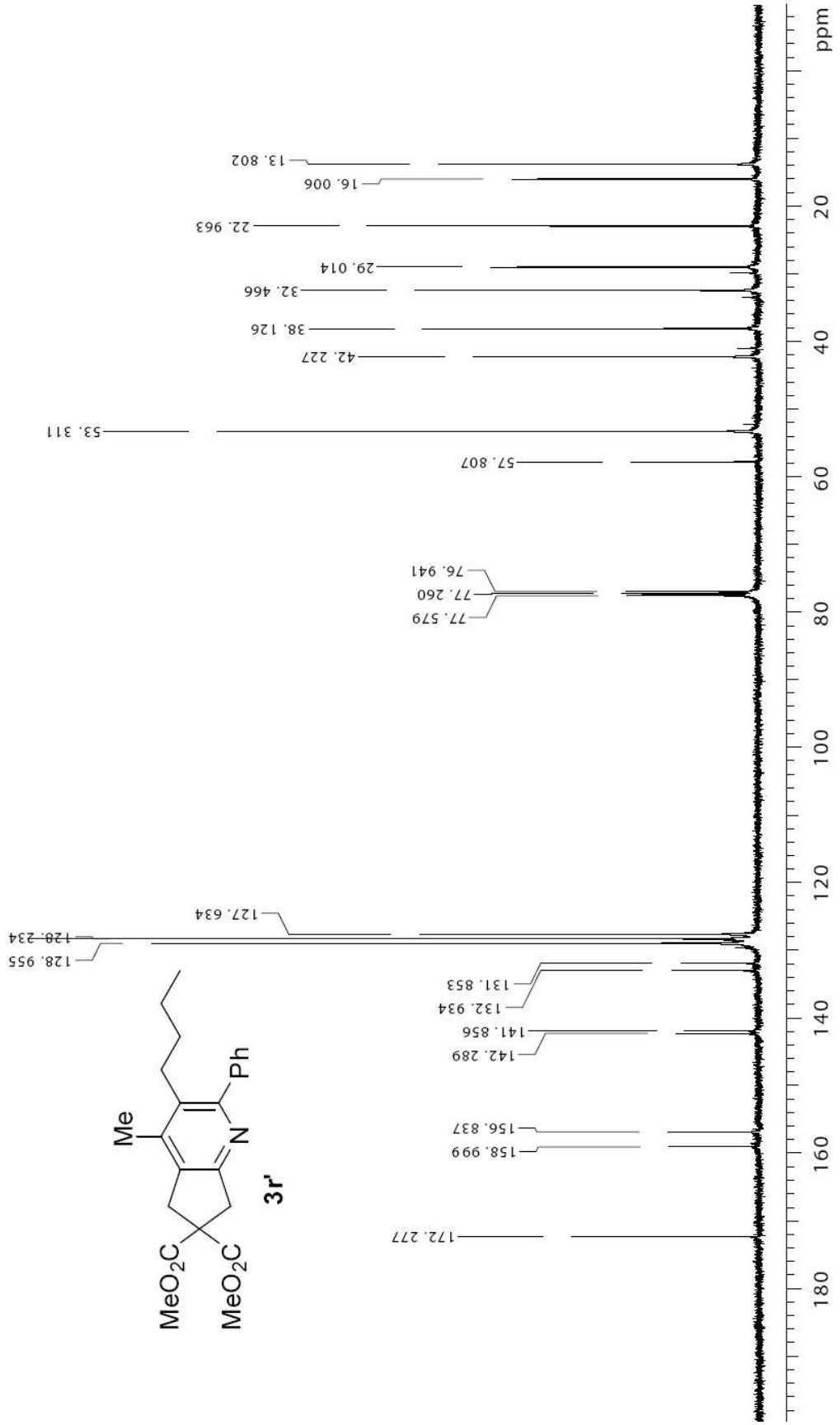

Me
Ph
MeO2C
MeO2C
N
3r
8
7
6
5
4
3
2
1
0
ppm

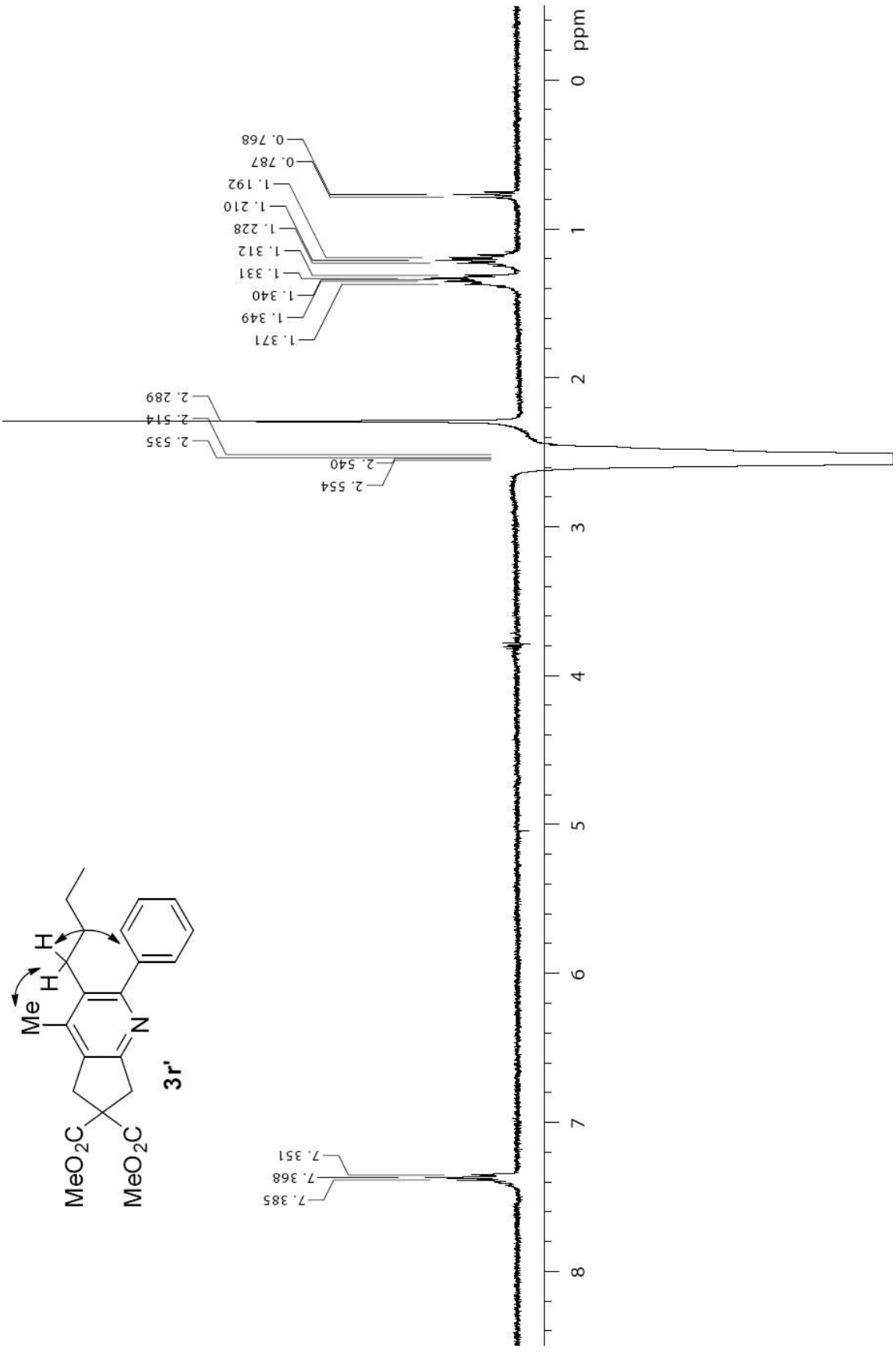

13.969
17.258
22.918
29.909
32.644
36.066
37.955
42.371
53.338
57.746
76.945
77.260
77.579
127.365
128.643
129.649
129.865
135.039
138.966
141.860
158.445
159.678
172.330
ppm
20
40
60
80
100
120
140
160
180
Me
N
MeO2C
MeO2C
3r

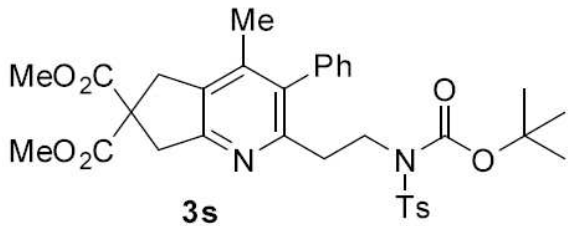

Me
H
H
N
MeO2C
MeO2C
3r
ppm
0
1
2
3
4
5
6
7
8



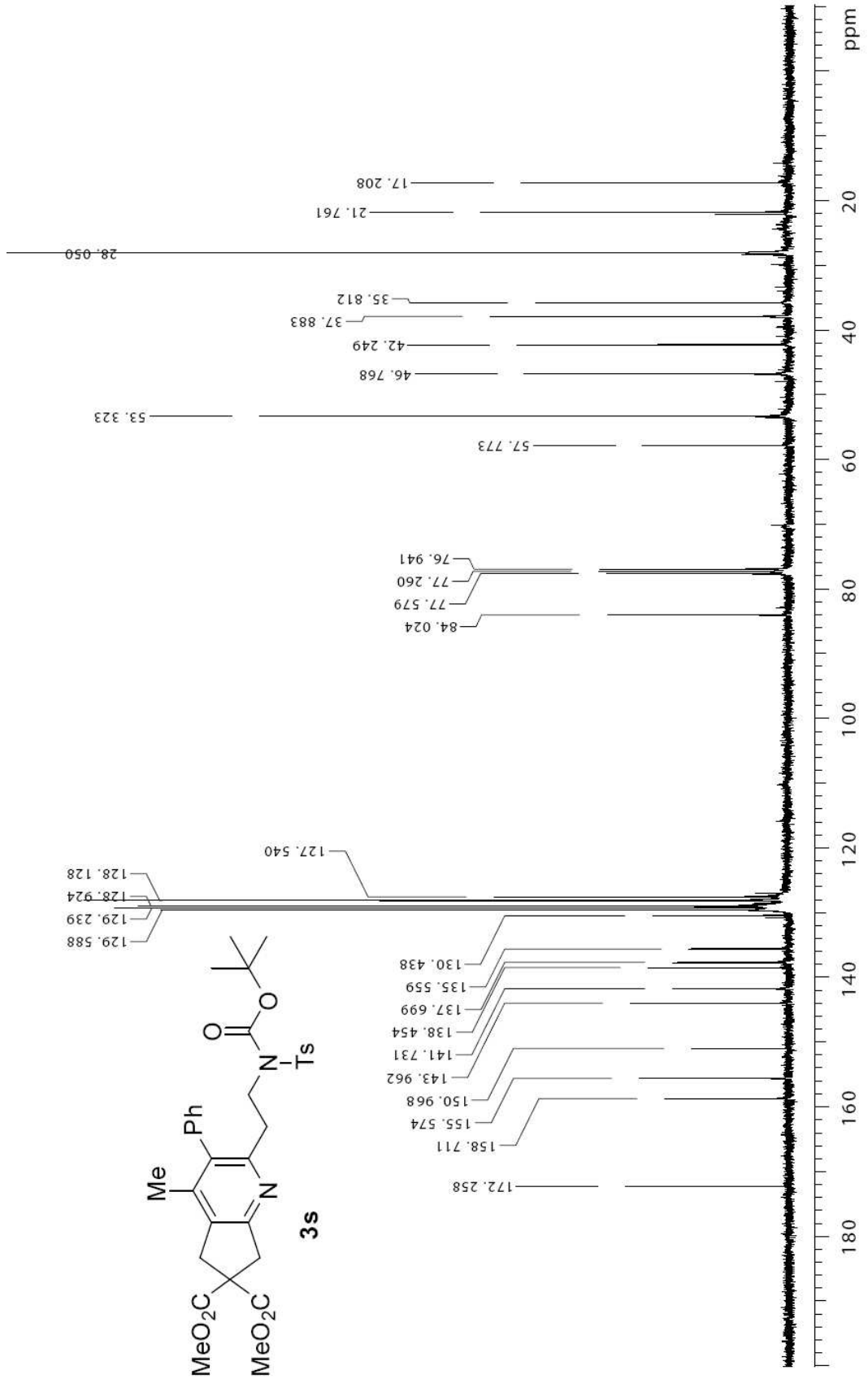
3r'

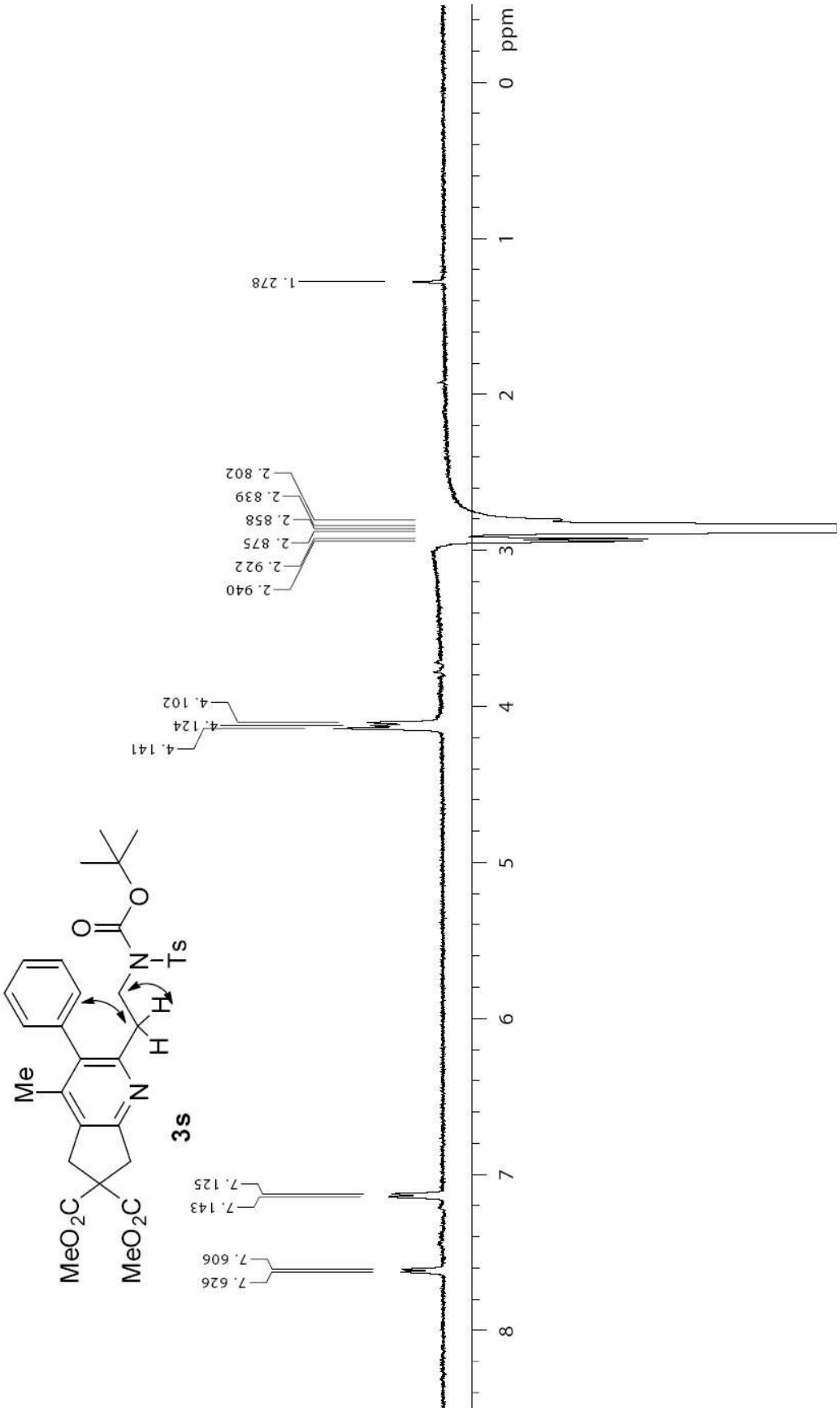

ppm
20
40
60
80
100
120
140
160
180
13.802
16.006
22.963
29.014
32.466
38.126
42.227
53.311
57.807
76.941
77.260
77.579
127.634
128.234
128.955
131.853
132.934
141.856
142.289
156.837
158.999
172.277
Me
Ph
N
MeO2C
MeO2C
3r'

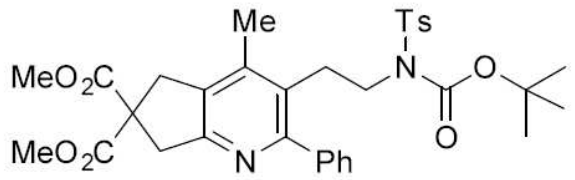

0. 768
0. 787
1. 192
1. 210
1. 228
1. 312
1. 331
1. 340
1. 349
1. 371
2. 289
2. 514
2. 535
2. 540
2. 554
7. 351
7. 368
7. 385
ppm
0
1
2
3
4
5
6
7
8
Me
H
H
N
MeO2C
MeO2C
3r'



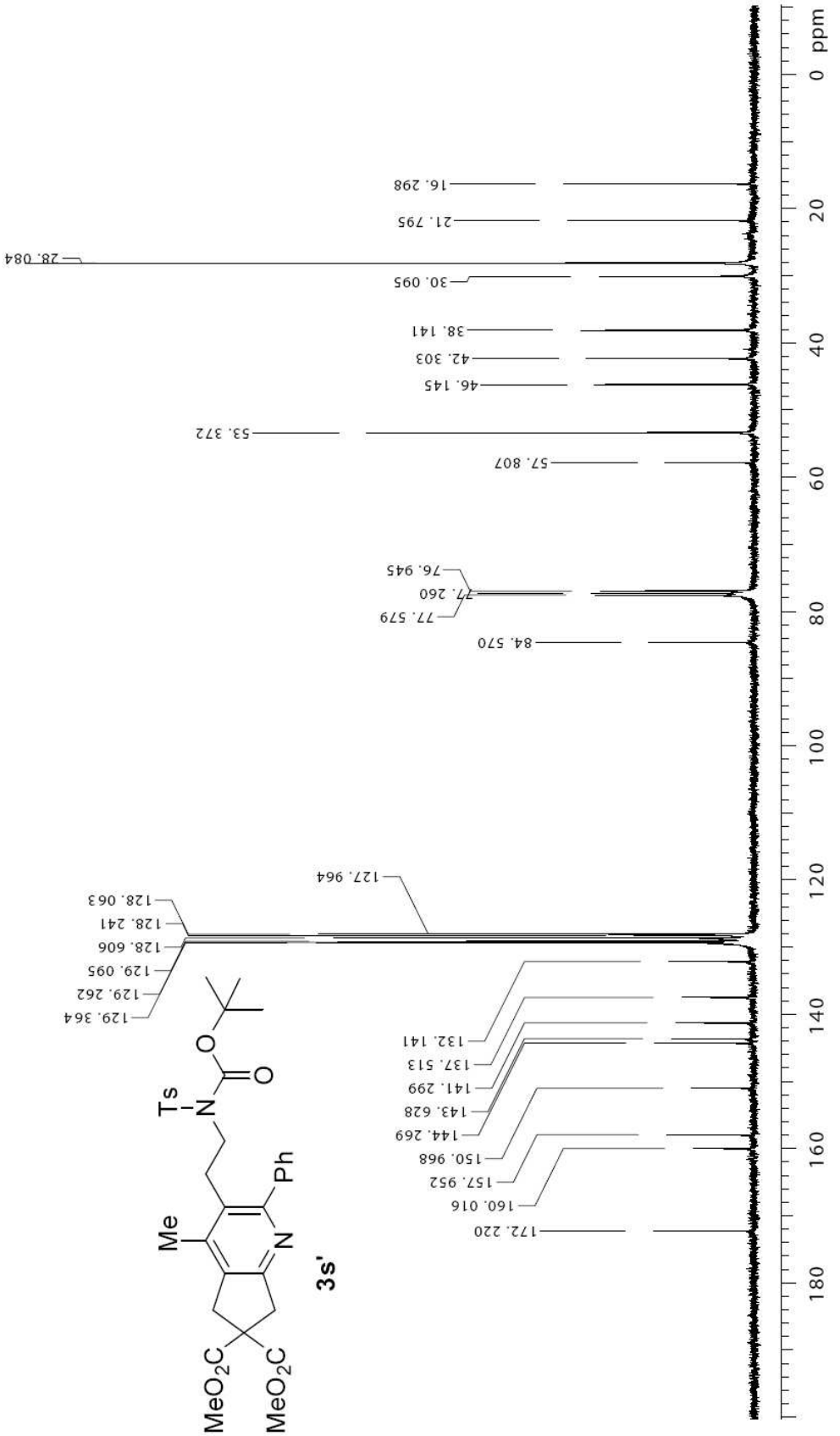
3s

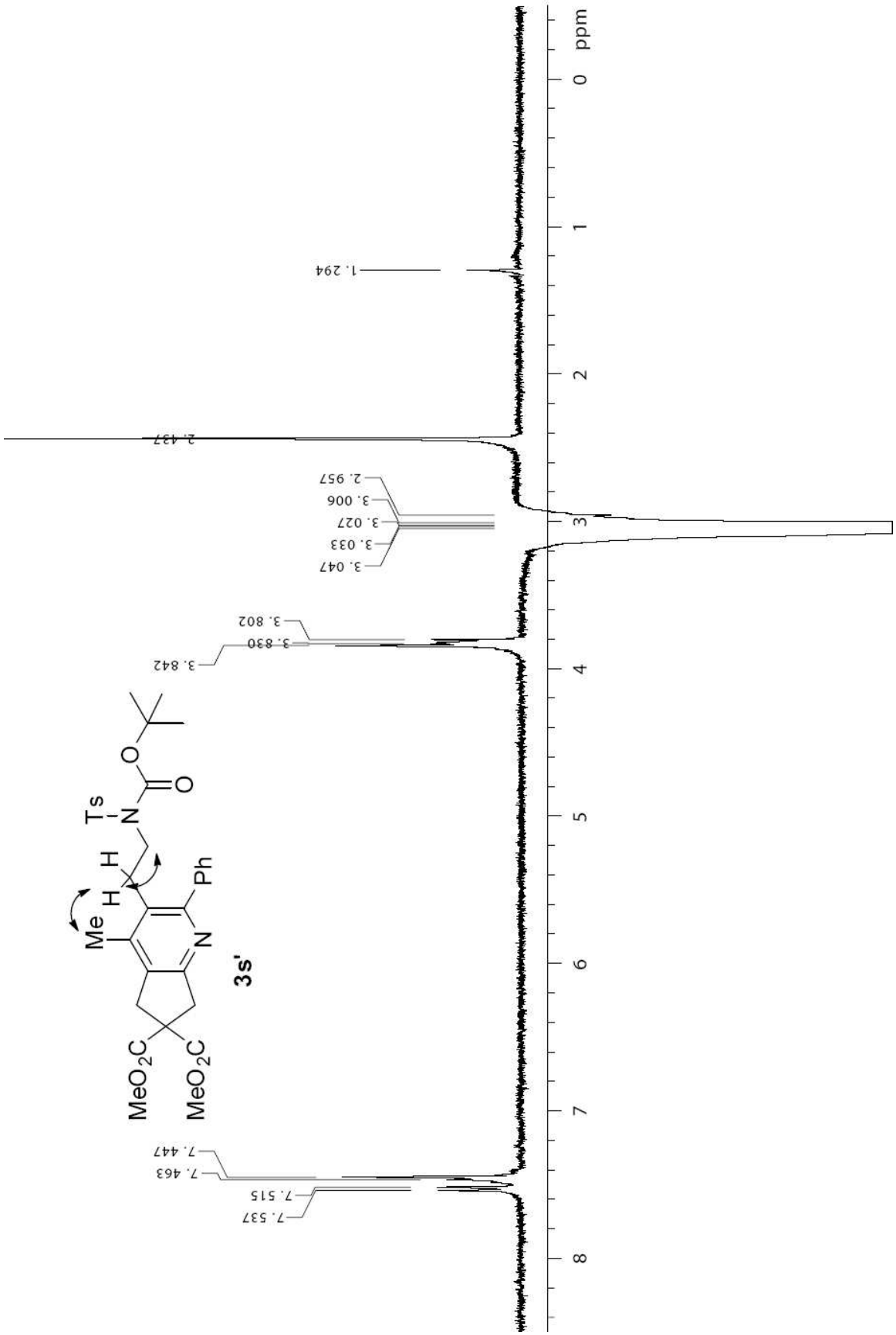

ppm
20
40
60
80
100
120
140
160
180
17.208
21.761
28.050
35.812
37.883
42.249
46.768
53.323
57.773
76.941
77.260
77.579
84.024
127.540
128.128
128.924
129.239
129.588
130.438
135.559
137.699
138.454
141.731
143.962
150.968
155.574
158.711
172.258
Me
Ph
N
Ts
O
O
MeO2C
MeO2C
3s

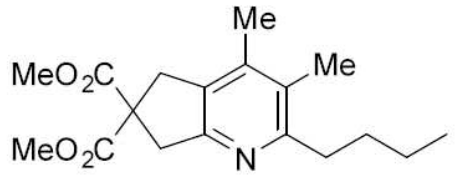

ppm
0
1
2
3
4
5
6
7
8
1.278
2.802
2.839
2.858
2.875
2.922
2.940
4.102
4.124
4.141
7.125
7.143
7.606
7.626
3s
Me
MeO2C
MeO2C
N
H
H
N
Ts
O
O



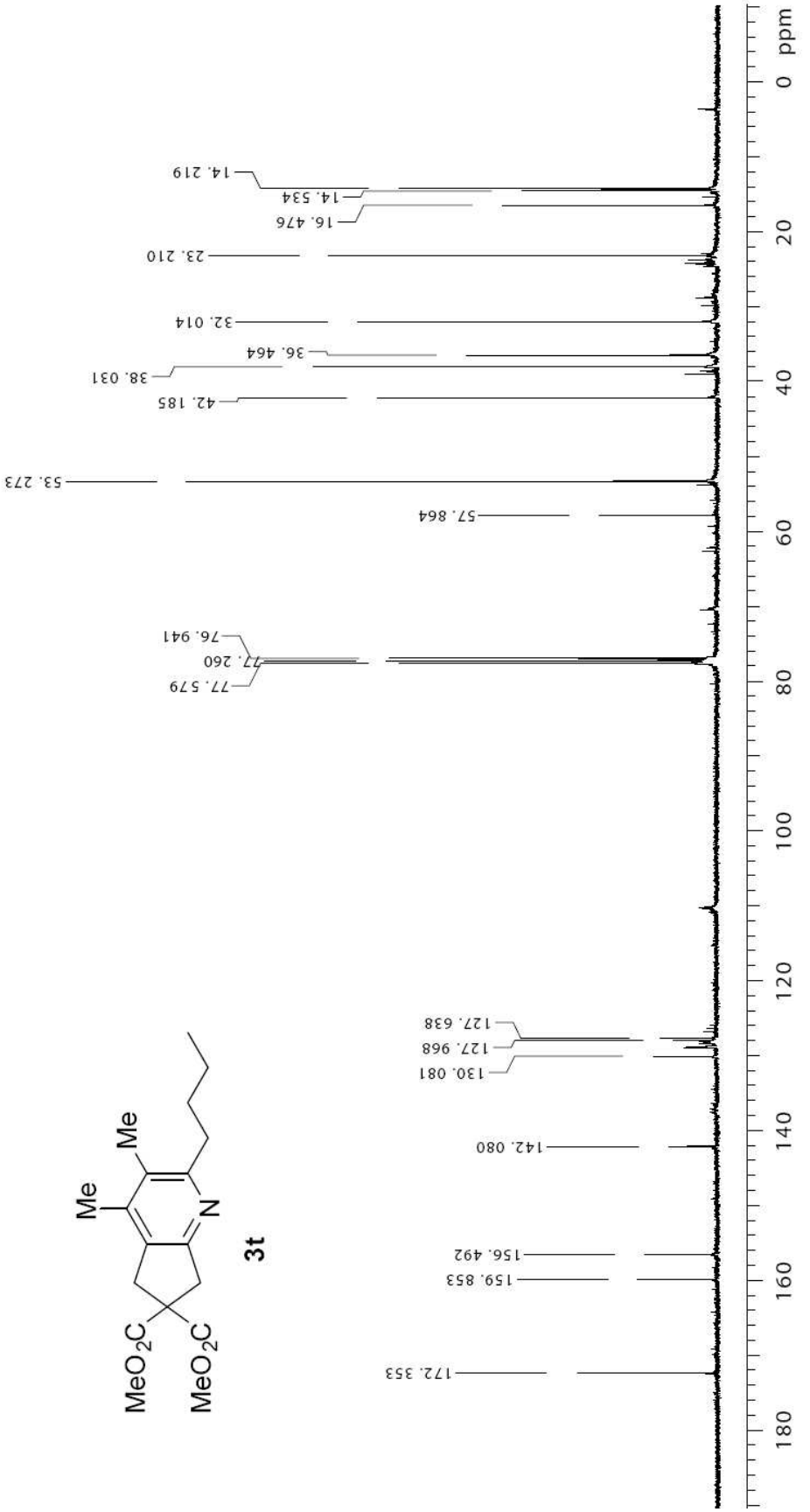
3s'

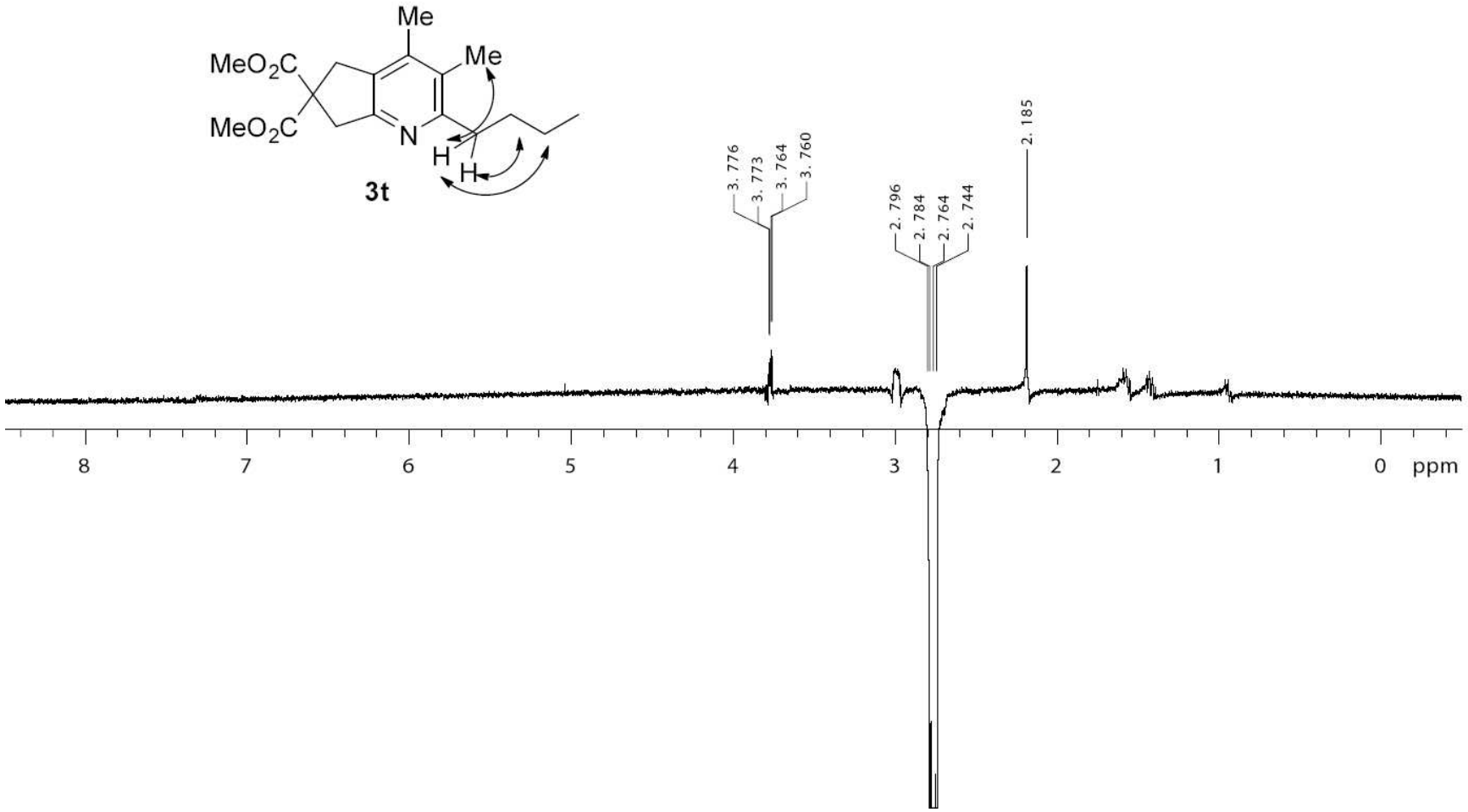

0 ppm
20
40
60
80
100
120
140
160
180
16.298
21.795
28.084
30.095
38.141
42.303
46.145
53.372
57.807
76.945
77.260
77.579
84.570
127.964
128.063
128.241
128.606
129.095
129.262
129.364
132.141
137.513
141.299
143.628
144.269
150.968
157.952
160.016
172.220
Me
Ph
Ts
N
O
O
O
N
MeO2C
MeO2C
3s'

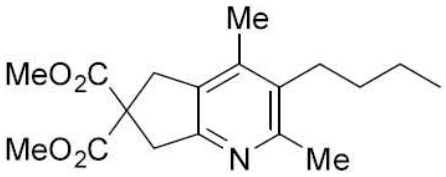

7.537
7.515
7.463
7.447
3.842
3.830
3.802
3.047
3.033
3.027
3.006
2.957
2.437
1.294
3s'
Me
H
H
Ph
N
Ts
O
O
O
MeO2C
MeO2C
ppm
0
1
2
3
4
5
6
7
8



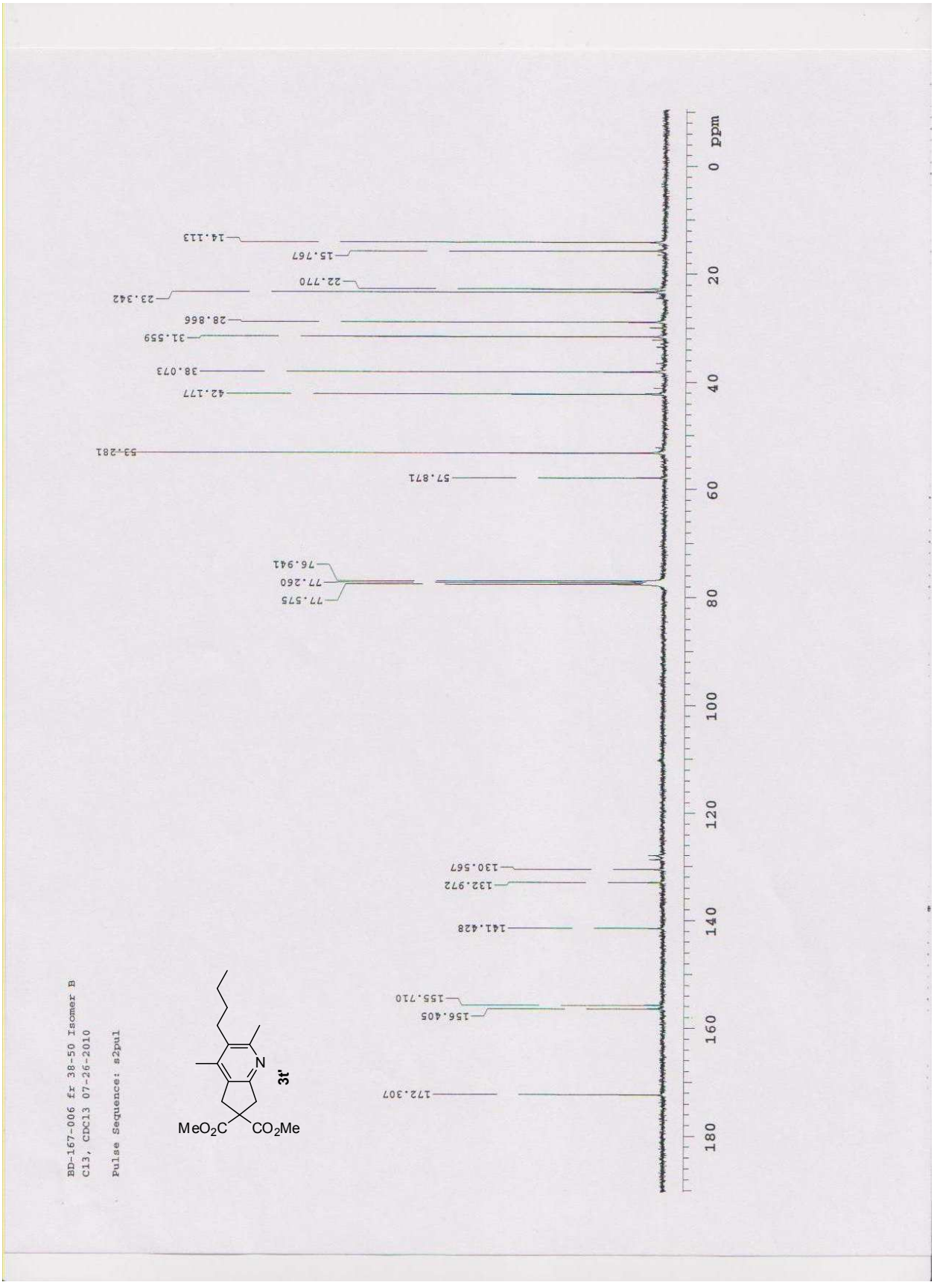
3t

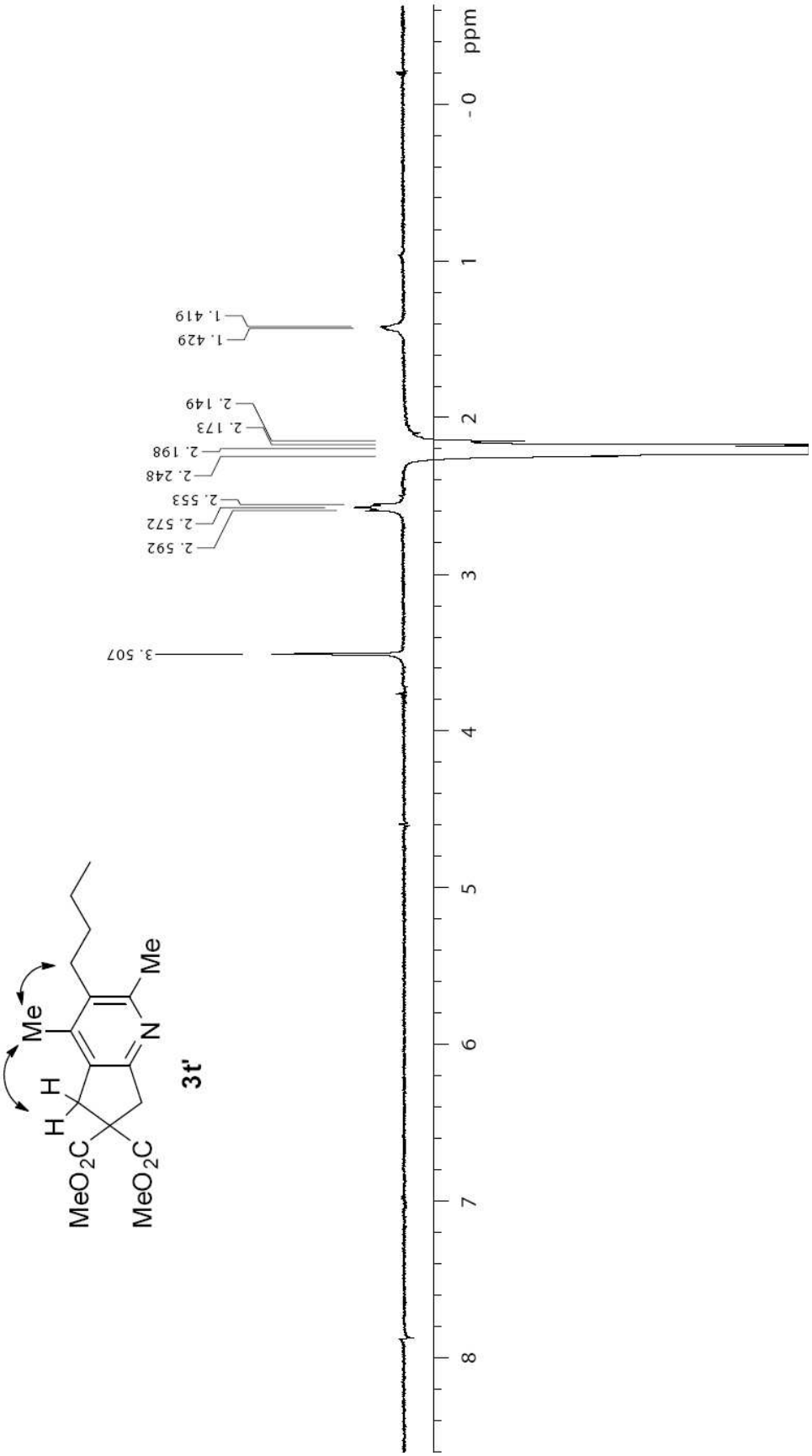

14.219
14.534
16.476
23.210
32.014
36.464
38.031
42.185
53.273
57.864
76.941
77.260
77.579
127.638
127.968
130.081
142.080
156.492
159.853
172.353
0 ppm
20
40
60
80
100
120
140
160
180
Me
Me
N
MeO2C
MeO2C
3t

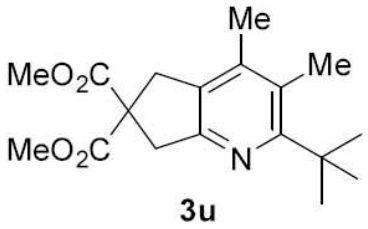

Me
MeO2C
Me
MeO2C
N
H
H
3t
3. 776
3. 773
3. 764
3. 760
2. 796
2. 784
2. 764
2. 744
2. 185
8
7
6
5
4
3
2
1
0
ppm



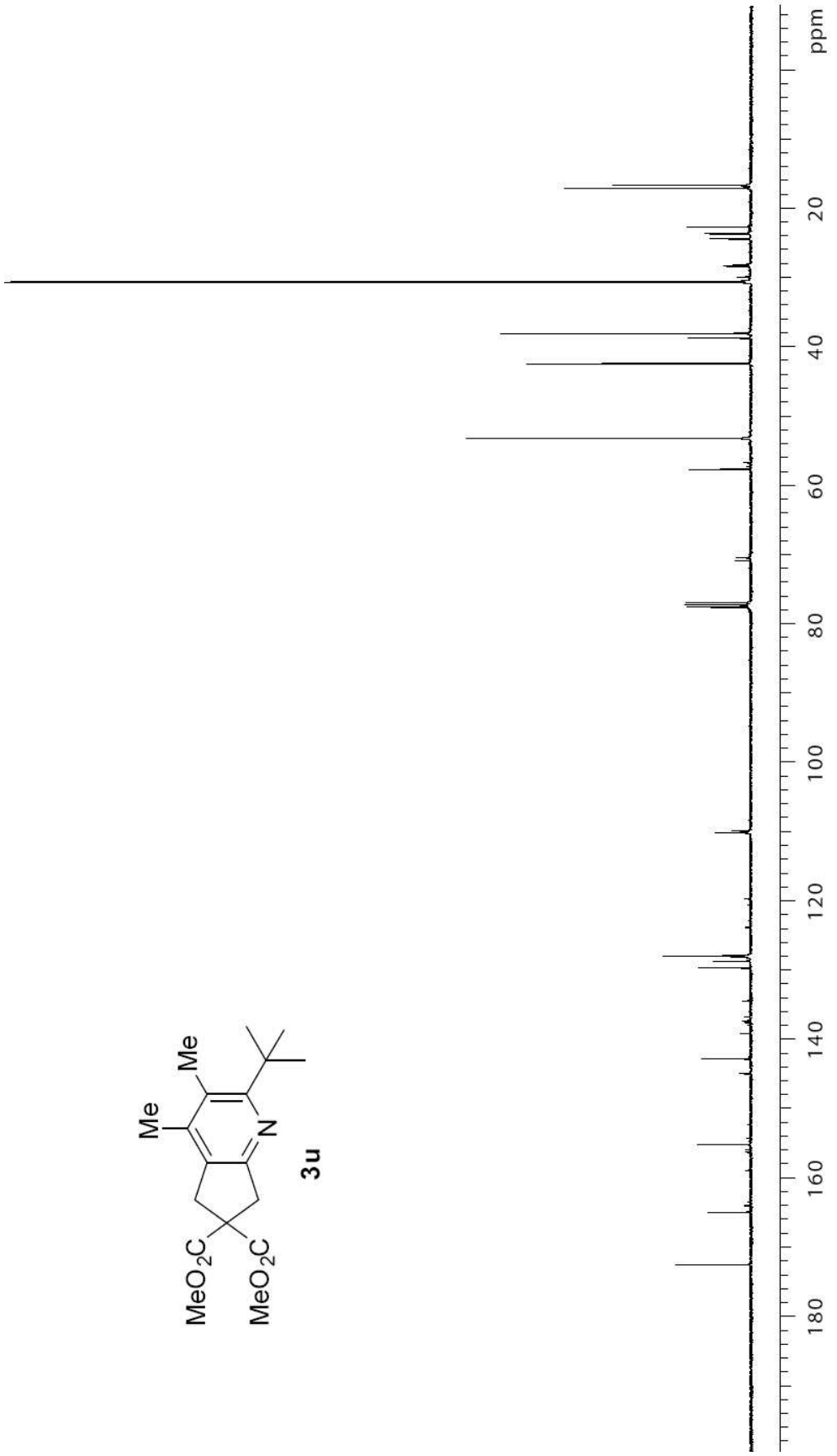
3t'

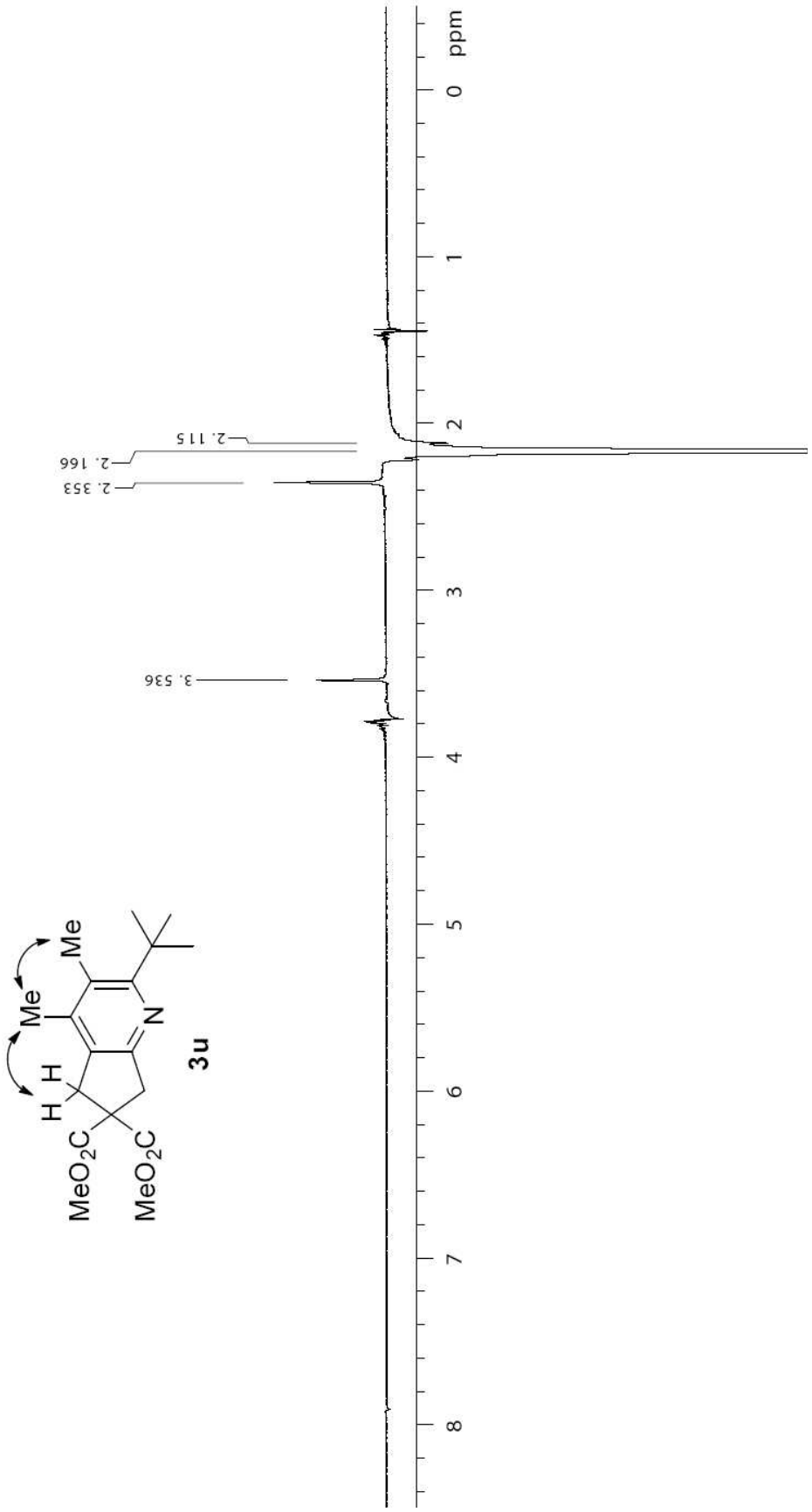

BD-167-006 fr 38-50 Isomer B
C13, CDCl3 07-26-2010
Pulse Sequence: s2pul
3t'
MeO2C
CO2Me
N
172.307
156.405
155.710
141.428
132.972
130.567
77.575
77.260
76.941
57.871
53.281
42.177
38.073
31.559
28.866
23.342
22.770
15.767
14.113
ppm

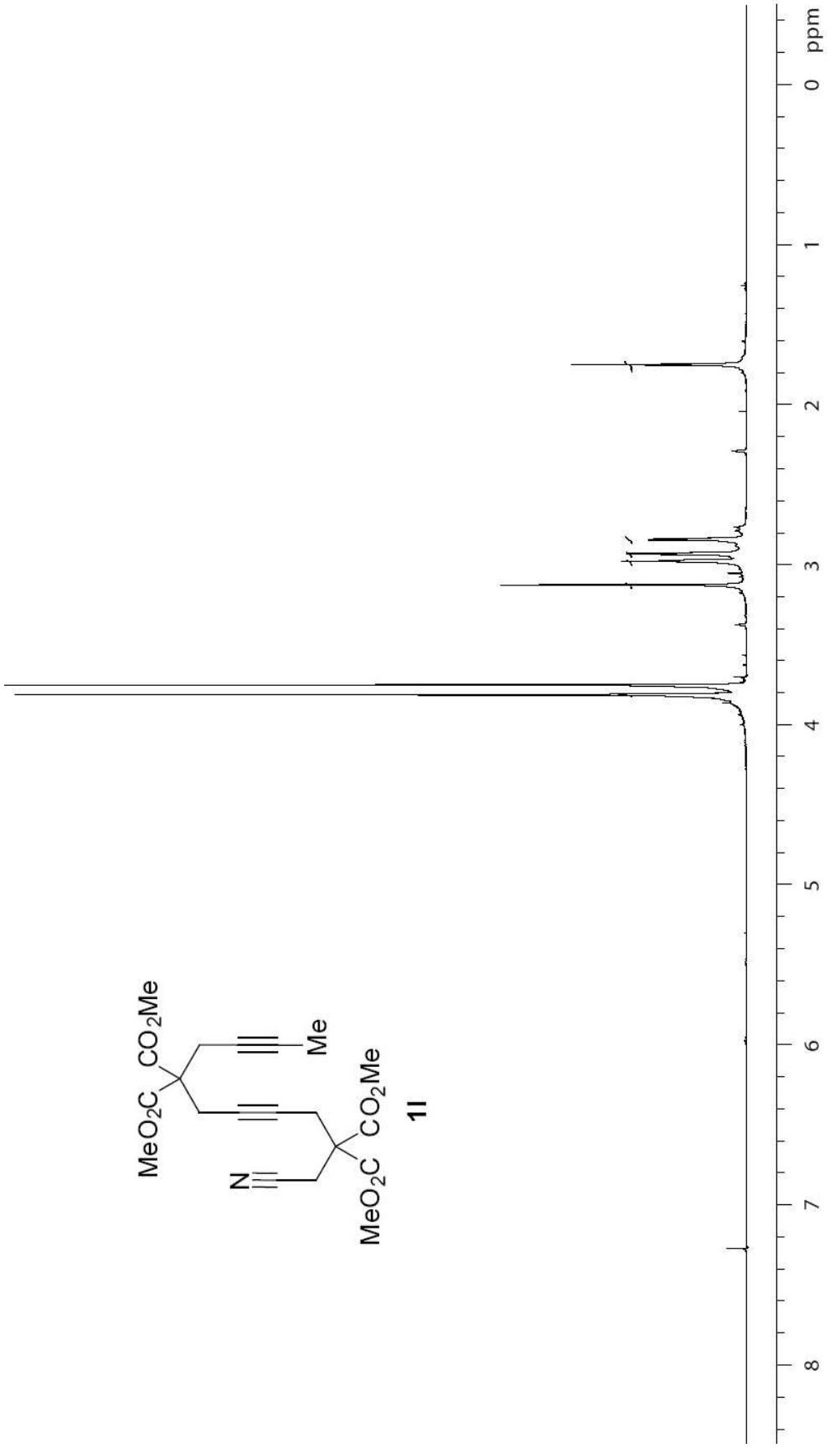

1.419
1.429
2.149
2.173
2.198
2.248
2.553
2.572
2.592
3.507
ppm
- 0
1
2
3
4
5
6
7
8
Me
Me
N
H
H
MeO2C
MeO2C
3t'

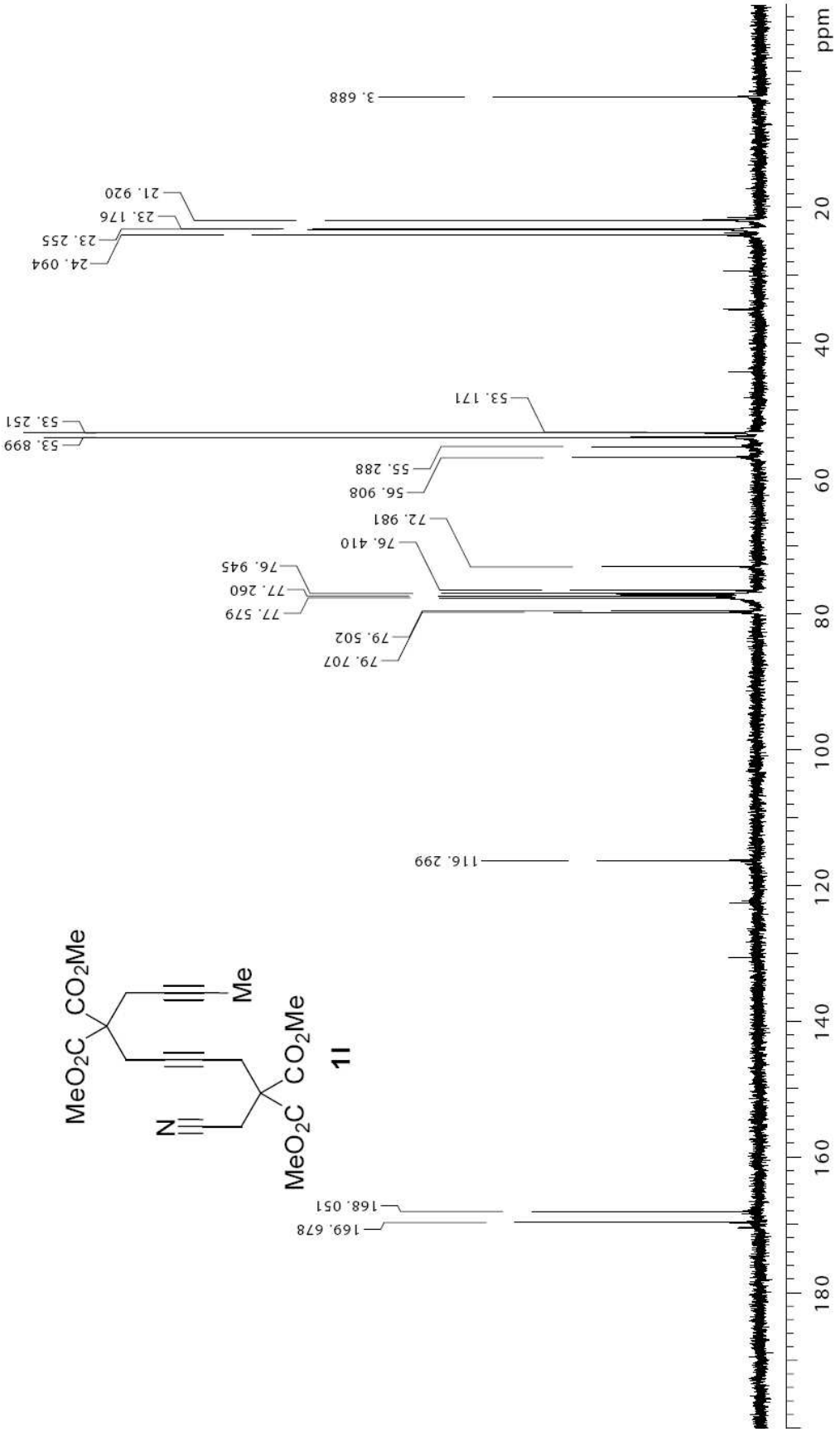


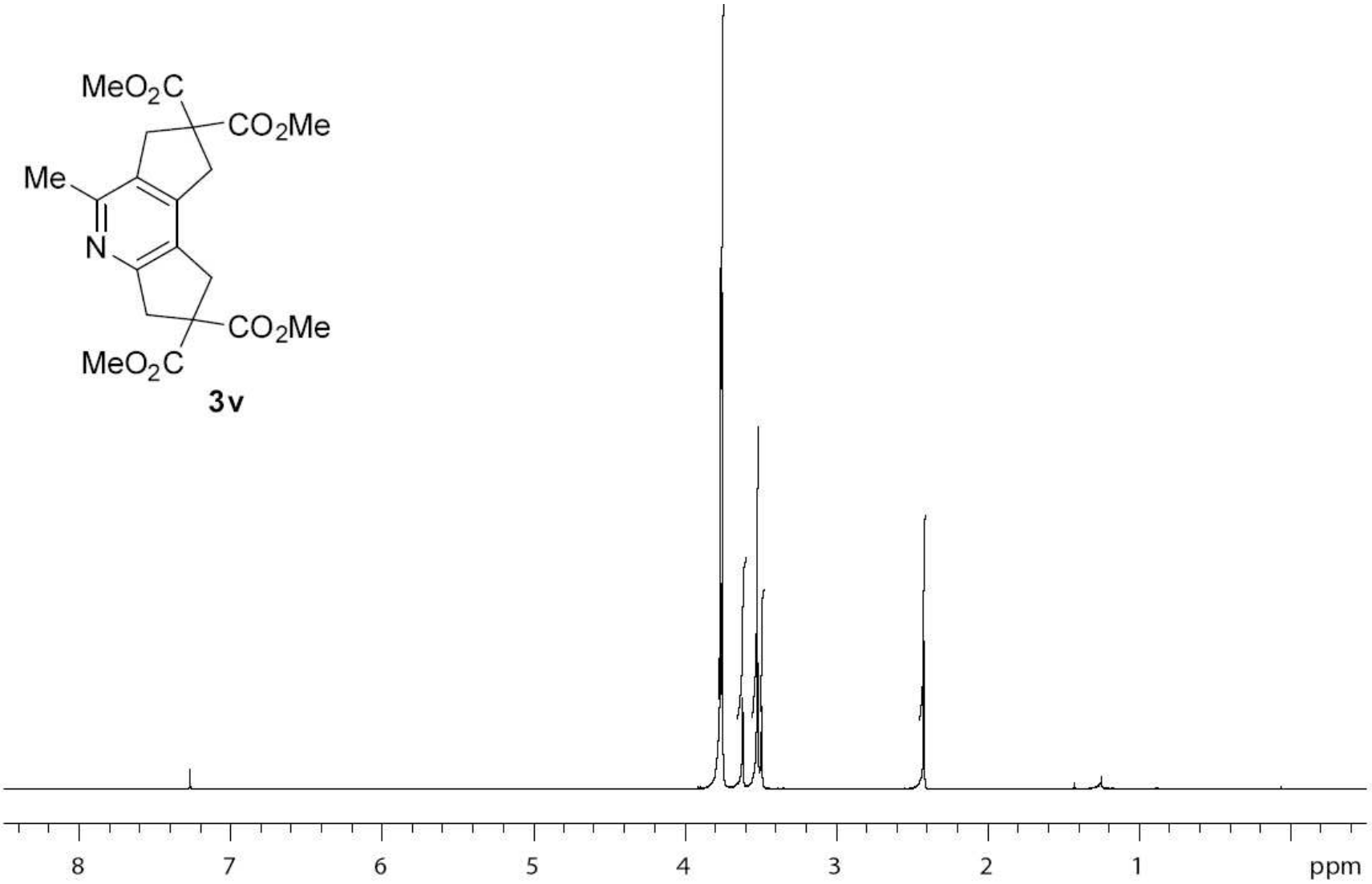
3u

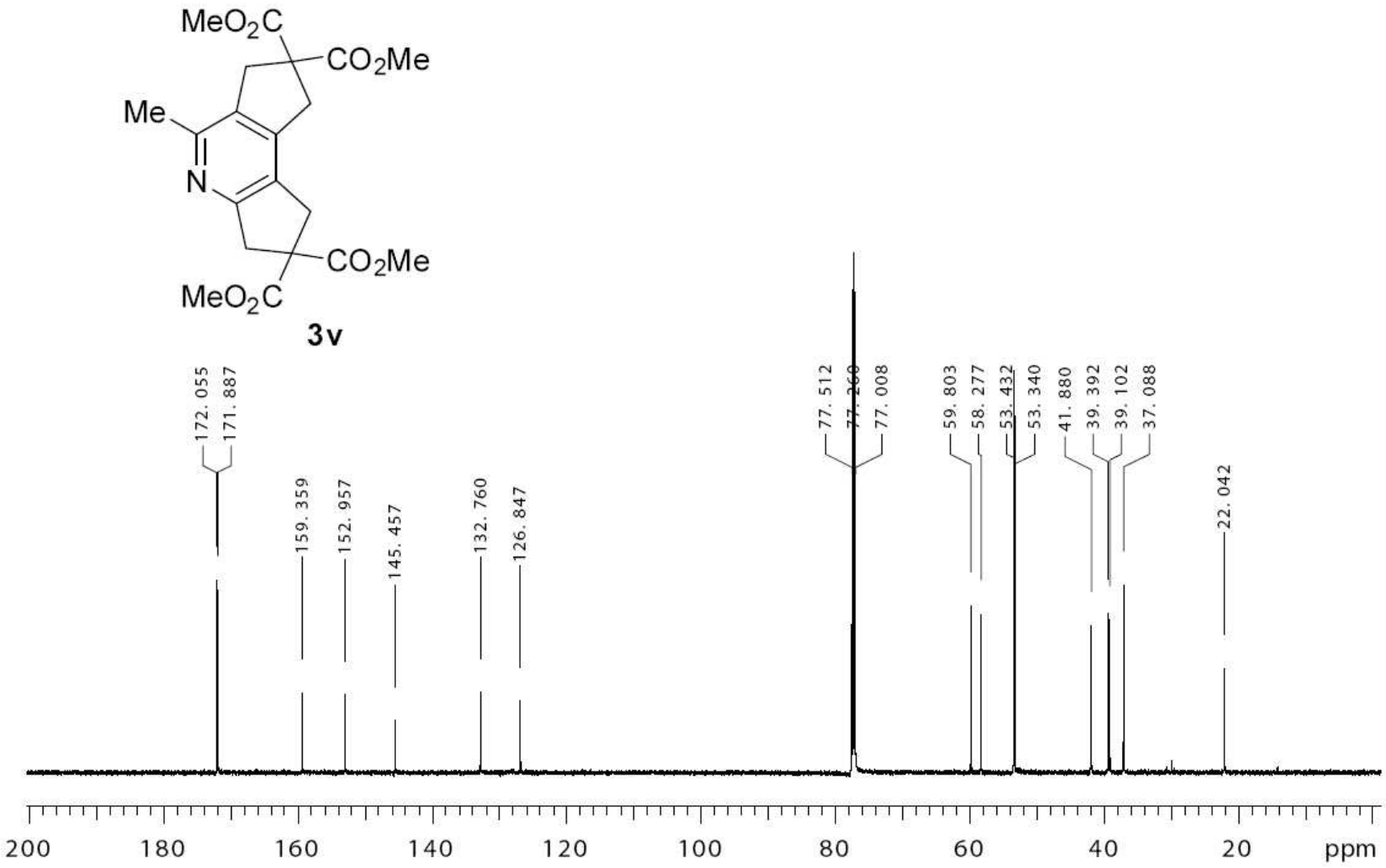

Me
Me
N
MeO2C
MeO2C
3u
ppm
20
40
60
80
100
120
140
160
180

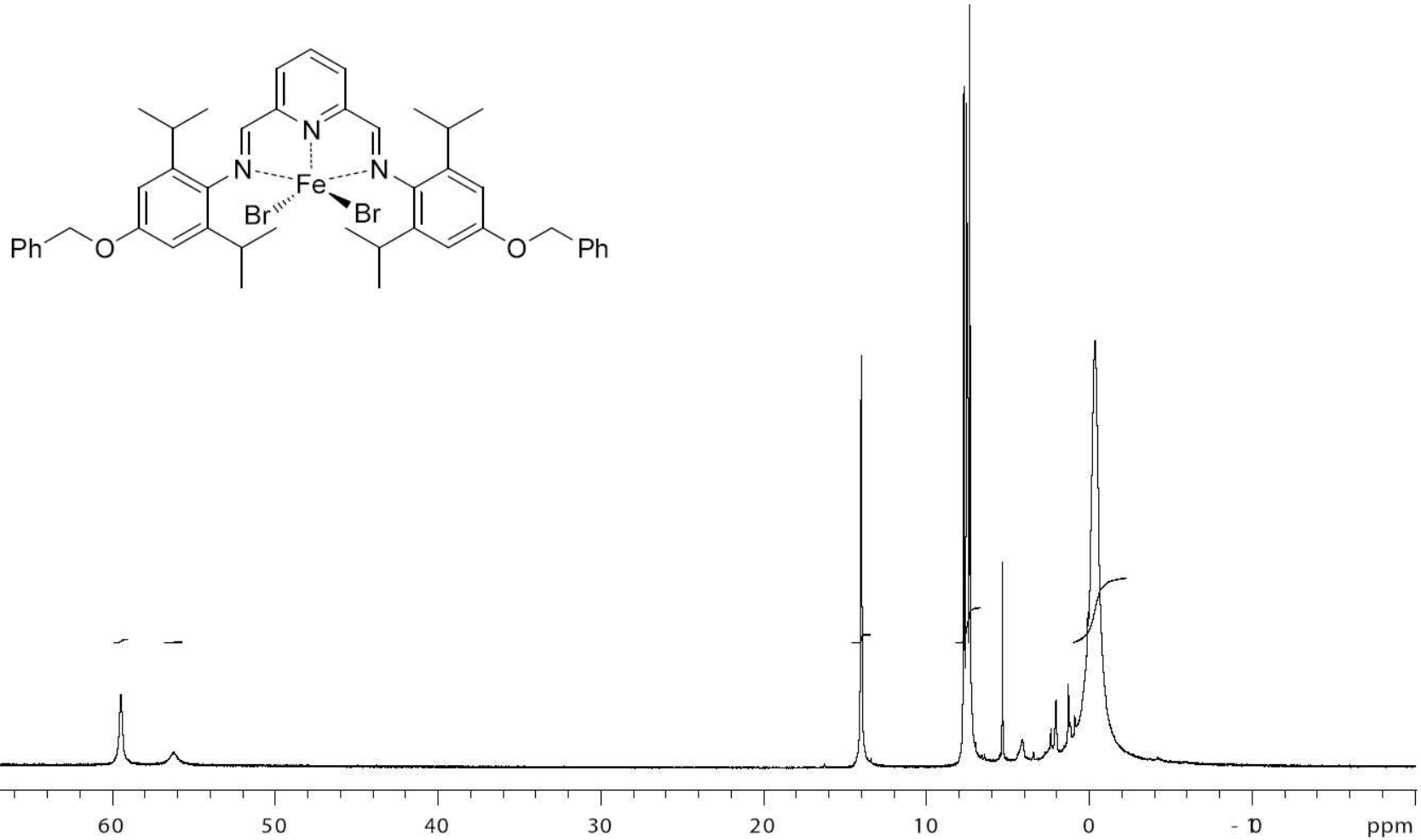

ppm
0
1
2
3
4
5
6
7
8
2.115
2.166
2.353
3.536
Me
Me
N
H
H
MeO2C
MeO2C
3u


MeO2C CO2Me
Me
N
MeO2C CO2Me
1l
8
7
6
5
4
3
2
1
0
ppm


MeO2C
CO2Me
Me
N
MeO2C
CO2Me
11
ppm
20
40
60
80
100
120
140
160
180
3.688
21.920
23.176
23.255
24.094
53.171
53.251
53.899
55.288
56.908
72.981
76.410
76.945
77.260
77.579
79.502
79.707
116.299
168.051
169.678


MeO2C
CO2Me
Me
N
CO2Me
MeO2C
3v
8
7
6
5
4
3
2
1
ppm


MeO2C
CO2Me
Me
N
CO2Me
MeO2C
3v
172.055
171.887
159.359
152.957
145.457
132.760
126.847
77.512
77.260
77.008
59.803
58.277
53.432
53.340
41.880
39.392
39.102
37.088
22.042
200
180
160
140
120
100
80
60
40
20
ppm


N
N
N
Fe
Br
Br
Ph
O
O
Ph
60
50
40
30
20
10
0
ppm