Rh(III)-Catalyzed Regioselective Synthesis of Pyridines from Alkenes and α,β-Unsaturated Oxime Esters

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Supporting Information

General Methods

All reactions were carried out in oven-dried glassware under an atmosphere of argon with magnetic stirring. ACS grade acetic acid and 2,2,2-trifluoroethanol and reagent grade silver acetate were purchased from Sigma-Aldrich Co. and used without further purification. Dichloroethane was distilled from calcium hydride under an atmosphere of argon. Alkenes **2g**, **2j**, **2k**, **2o**, **2q**, **(*Z*)-6a** and **(*E*)-6a** were purchased from Sigma-Aldrich Co. and used without further purification. Methyl acetylacrylate **6c** was purchased from Tokyo Chemical Industry Co. and used without further purification. Alkenes **2n**, **2p** and **2r** were distilled and alkenes **2a-f**, **2h**, **2i**, **2l** and **2m** were distilled under reduced pressure prior to use. $[RhCp^*Cl_2]_2$ was prepared as previously reported.[1] Column chromatography was performed on Silicycle® Silica*Flash*® P60 (230-400 mesh). Thin layer chromatography was performed on Silicycle® 250μm silica gel 60A plates. Visualization was accomplished with UV light (254 nm) or potassium permanganate.

^{1}H NMR and ^{13}C NMR spectra were collected at ambient temperature in $CDCl_3$ on a Varian 400 MHz. Chemical shifts are expressed as parts per million (δ, ppm) and are referenced to 7.26 ($CHCl_3$) for ^{1}H NMR and 77.16 ($CDCl_3$) for ^{13}C NMR. Proton signal data uses the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and *J* = coupling constant. Mass spectra were obtained on a Fisons VG Autospec (HRMS) or an Agilent Technologies 6130 Quadropole Mass Spec (LRMS). Infrared spectra were collected on a Bruker Tensor 27 FT-IR spectrometer.

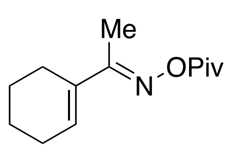
Regioisomeric ratios were determined by integration of ^{1}H NMR spectra of product mixtures collected with first relaxation delay (d1) = 15 seconds. The major product of the reaction of **1c** and **6c** was identified as **7cc** by ^{1}H-^{13}C HSQC and ^{1}H-^{13}C HMBC (p. S54).

Synthesis of Oxime Ester Precursors

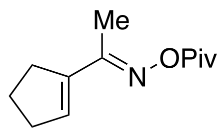
The α,β-unsaturated ketones corresponding to **1a**, **1b** and **1h** and to **1c** were purchased from Sigma-Aldrich Co. and Tokyo Chemical Industry Co., respectively. The precursors of **1d**-**1g** were obtained by methylenation of the appropriate ketones by the following procedure, adapted from the literature.[2] A solution of the ketone (20 mmol), aqueous formaldehyde (4.9 mL, 3 equiv) and morpholine (0.86 mL, 0.5 equiv) in 18 mL acetic acid was heated at 120 °C for 20 hours. After cooling, the mixture was neutralized with 3M NaOH and extracted with diethyl ether three times. The combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

General Procedure for Oxime Ester Synthesis

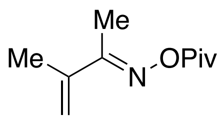
All *O*-pivaloyl oxime esters **1** were generated from the corresponding α,β-unsaturated ketones according to the following procedure, adapted from the literature.[3] Hydroxylamine hydrochloride (347 mg, 1.4 equiv) and Na_2CO_3 (742 mg, 1.4 equiv) were added to the enone (5 mmol) in 15 mL MeOH and the mixture was stirred at 65 °C for 1 hour (or room temperature for 4 hours in the case of **1h**). The solvent was removed *in vacuo* and the resulting residue was dissolved in 10 mL DCM and cooled to 0 °C. After the addition of Et_3N (1.74 mL, 2.5 equiv), a solution of pivaloyl chloride (1.23 mL, 2.0 equiv) in 5 mL DCM was added dropwise at 0 °C. The mixture was stirred at room temperature overnight and quenched with water. The aqueous layer was extracted with DCM three times and the combined organic layers were washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography.



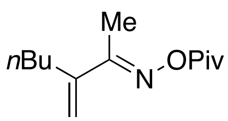
(*E*)-1-(cyclohex-1-en-1-yl)ethanone *O*-pivaloyl oxime (1a). White solid. R_f = 0.25 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (m, 1H), 2.40 (m, 2H), 2.20 (m, 2H), 2.07 (s, 3H), 1.63 (m, 4H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 164.1, 134.6, 133.5, 38.9, 27.4, 26.3, 24.6, 22.2, 22.0, 12.0. IR (NaCl, thin film) ν 2936, 1759, 1638, 1590, 1480, 1294, 1114, 917, 804 cm^{-1}. HRMS (ESI) *m/z* [2M+Na] calcd 469.3042, found 469.3046.



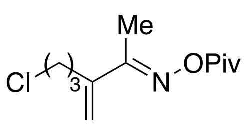
(*E*)-1-(cyclopent-1-en-1-yl)ethanone *O*-pivaloyl oxime (1b). Colorless liquid. R_f = 0.33 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.35 (m, 1H), 2.68 (m, 2H), 2.48 (m, 2H), 2.14 (s, 3H), 1.94 (m, 2H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 161.1, 140.8, 138.0, 39.0, 33.4, 31.5, 27.4, 23.4, 13.3. IR (NaCl, thin film) ν 2971, 1760, 1480, 1272, 1113, 891 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 210.1494, found 210.1495.



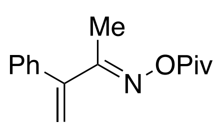
(*E*)-3-methylbut-3-en-2-one *O*-pivaloyl oxime (1c). Colorless liquid. R_f = 0.43 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.54 (m, 1H), 5.43 (m, 1H), 2.12 (s, 3H), 2.05 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 163.7, 141.0, 120.6, 38.9, 27.4, 19.3, 12.2. IR (NaCl, thin film) ν 2976, 1762, 1480, 1270, 1108, 921 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 184.1338, found 184.1331.



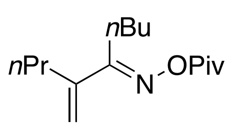
(*E*)-3-methyleneheptan-2-one *O*-pivaloyl oxime (1d). Colorless liquid. R_f = 0.45 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (s, 1H), 5.38 (m, 1H), 2.44 (td, *J* = 7.6, 1.2 Hz, 2H), 2.10 (s, 3H), 1.50 (m, 2H), 1.34 (m, 2H), 1.30 (s, 9H), 0.90 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 163.5, 145.4, 119.1, 38.9, 32.0, 30.6, 27.4, 22.6, 14.1, 12.8. IR (NaCl, thin film) ν 2960, 1763, 1480, 1270, 1107, 920 cm^{-1}. HRMS (ESI) *m/z* [M+Na] calcd 248.1626, found 248.1622.



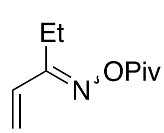
(*E*)-6-chloro-3-methylenehexan-2-one *O*-pivaloyl oxime (1e). Colorless liquid. R_f = 0.33 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (s, 1H), 5.49 (m, 1H), 3.55 (t, *J* = 6.4 Hz, 2H), 2.62 (td, *J* = 7.6, 1.2 Hz, 2H), 2.12 (s, 3H), 2.04 (m, 2H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 162.7, 143.6, 120.9, 44.7, 39.0, 31.4, 30.0, 27.4, 12.6. IR (NaCl, thin film) ν 2971, 1761, 1480, 1270, 1106, 1027, 921 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 246.1, found 246.1.



(*E*)-3-phenylbut-3-en-2-one *O*-pivaloyl oxime (1f). White solid. R_f = 0.26 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 5.70 (d, *J* = 0.8 Hz, 1H), 5.58 (d, *J* = 0.4 Hz, 1H), 2.09 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 165.4, 145.2, 137.5, 128.6, 128.4, 127.9, 119.4, 39.0, 27.5, 15.6. IR (NaCl, thin film) ν 2980, 1752, 1584, 1367, 1267, 1110, 1031, 947, 896, 776, 695 cm^{-1}. HRMS (ESI) *m/z* [M+Na] calcd 268.1313, found 268.1312.

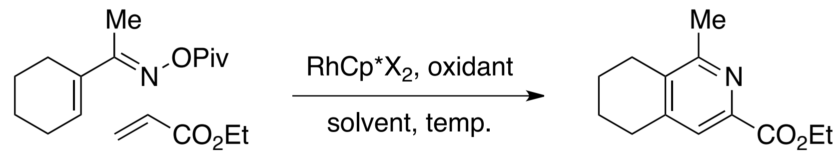


(*E*)-4-methylenenonan-5-one *O*-pivaloyl oxime (1g). Colorless liquid. R_f = 0.26 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (s, 1H), 5.38 (m, 1H), 2.55 (t, *J* = 8.0 Hz, 2H), 2.40 (td, *J* = 7.2, 1.2 Hz, 2H), 1.57-1.35 (m, 6H), 1.29 (s, 9H), 0.92 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 167.3, 144.2, 119.1, 38.9, 34.7, 29.5, 27.4, 26.8, 23.1, 21.5, 13.9. IR (NaCl, thin film) ν 2962, 1763, 1462, 1110, 1026, 916 cm^{-1}. HRMS (ESI) *m/z* [M+Na] calcd 276.1939, found 276.1935.



Pent-1-en-3-one *O*-pivaloyl oxime (1h). Pale yellow liquid, 5.1:1 mixture of isomers. R_f = 0.46 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.9 (dd, *J* = 18.0, 11.2 Hz, 1H), 6.52 (dd, *J* = 18.0, 11.2 Hz, 1H), 5.80 (dd, *J* = 18.0, 0.8 Hz, 1H), 5.79 (d, *J* = 18.0 Hz, 1H), 5.67 (dd, *J* = 11.2, 0.8 Hz, 1H), 5.64 (d, *J* = 10.8 Hz, 1H), 2.56 (m, 2H), 1.29 (s, 9H), 1.28 (s, 9H), 1.20 (t, *J* = 7.6 Hz, 3H), 1.13 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 167.5, 164.4, 132.2, 125.3, 125.2, 122.7, 38.9, 27.4, 27.3, 24.1, 18.9, 12.3, 11.4. IR (NaCl, thin film) ν 2977, 1762, 1481, 1271, 1110, 1027, 899 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 184.1, found 184.2.

Reaction Optimization[a]



1a 2a 3aa

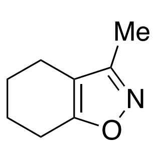
entry	solvent	temp. (°C)	oxidant	yield **3aa** (%)[b]
1	TFE	74	AgOAc	30[c]
2	EtOH	90	AgOAc	<5
3	*t*AmOH	90	AgOAc	0
4	MeCN	90	AgOAc	<5
5	PhMe	110	AgOAc	0
6	dioxane	110	AgOAc	0
7	acetone	68	AgOAc	<5
8	THF	68	AgOAc	0
9	*i*PrOH	68	AgOAc	0
10	HFIP	68	AgOAc	20
11	DCE	85	AgOAc	<5
12	DCE/AcOH (20:1)	85	AgOAc	25
13	DCE/AcOH (10:1)	85	AgOAc	35
14	DCE/AcOH (2:1)	85	AgOAc	45
15	AcOH	85	AgOAc	35
16[d]	DCE/AcOH (2:1)	85	AgOAc	65
17	DCE/AcOH (2:1)	85	$Cu(OAc)_2 \cdot H_2O$	0
18	DCE/AcOH (2:1)	85	CAN	0
19	DCE/AcOH (2:1)	85	benzoquinone	0
20	DCE/AcOH (2:1)	85	anthraquinone	10
21	DCE/AcOH (2:1)	85	NMO	10
22	DCE/AcOH (2:1)	85	TEMPO	20

[a]Conditions: 1.2 equiv **2a**, 2.1 equiv oxidant (1.05 equiv 2 e^- oxidants). Entries 1-16: $[RhCp^*Cl_2]_2$ (2.5 mol %), 0.15M solution. Entries 17-22: $RhCp^*(OAc)_2$ (5 mol %), 0.3M solution. [b]Determined by ^1H NMR. [c]~4:1 mixture of Et and CH_2CF_3 esters. [d]0.3M solution.

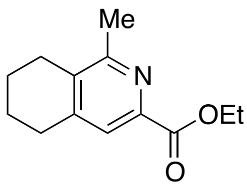
General Procedure for Pyridine Synthesis

A 0.5 dram vial was charged with oxime ester **1** (0.21 mmol) and AgOAc (73.6 mg, 2.1 equiv) and a solution of $[RhCp^*Cl_2]_2$ (3.3 mg, 0.025 equiv) and alkene **2** (0.252 mmol, 1.2 equiv) in 0.7 mL 2:1 DCE/AcOH was added. The vial was flushed with argon, sealed and heated at 85 °C in an aluminum heating block for 14 hours. The solids were filtered and the mixture was diluted with DCM and washed with 15% Na_2CO_3. The aqueous layer was extracted twice with DCM and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography.

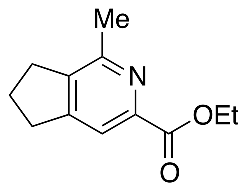
Compound **3cf** was previously characterized by Ogoshi and coworkers.[4] Compounds **3cp** and **5cp** were previously characterized by Ellman and coworkers.[5]



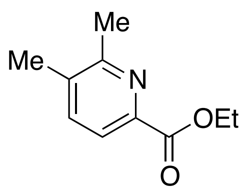
3-Methyl-4,5,6,7-tetrahydrobenzo[*d*]isoxazole (4). Colorless viscous liquid. R_f = 0.34 (10:1 hexanes/EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 2.64 (tt, J = 6.4, 1.6 Hz, 2H), 2.33 (tt, J = 6.0, 1.6 Hz, 2H), 2.19 (s, 3H), 1.86-1.71 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 158.3, 112.1, 22.7, 22.6, 22.3, 19.3, 10.1. IR (NaCl, thin film) ν 2938, 2856, 1642, 1466, 1321, 1201, 869, 740 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 138.1, found 138.2.



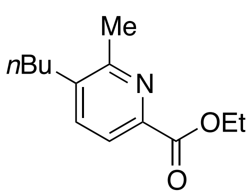
Ethyl 1-methyl-5,6,7,8-tetrahydroisoquinoline-3-carboxylate (3aa). Pale yellow viscous liquid. R_f = 0.13 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 4.44 (q, J = 7.2 Hz, 2H), 2.79 (t, J = 6.0 Hz), 2.66 (t, J = 6.4 Hz, 2H), 2.53 (s, 3H), 1.87 (m, 2H), 1.76 (m, 2H), 1.42 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 157.8, 147.0, 144.1, 135.4, 124.0, 61.8, 29.6, 26.4, 22.8, 22.6, 22.0, 14.5. IR (NaCl, thin film) ν 2944, 1708, 1589, 1372, 1317, 1261, 1212, 1028, 789 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 220.1338, found 220.1339.



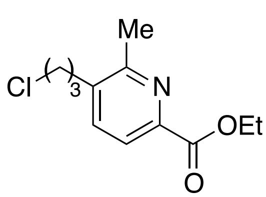
Ethyl 1-methyl-6,7-dihydro-5*H*-cyclopenta[*c*]pyridine-3-carboxylate (3ba). Pale yellow viscous liquid. R_f = 0.12 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 4.44 (q, J = 7.2 Hz, 2H), 2.97 (t, J = 7.6 Hz, 2H), 2.91 (t, J = 7.2 Hz, 2H), 2.55 (s, 3H), 2.14 (dd, J = 7.6, 7.6 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 154.5, 146.0, 142.5, 119.6, 61.8, 33.0, 31.0, 24.3, 22.4, 14.5. IR (NaCl, thin film) ν 2960, 1716, 1594, 1376, 1329, 1224, 1030, 791 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 206.1181, found 206.1175.



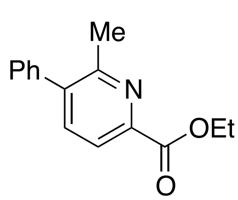
Ethyl 5,6-dimethylpicolinate (3ca). Pale yellow viscous liquid. R_f = 0.15 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 7.6 Hz, 1H), 4.43 (q, J = 7.2 Hz, 2H), 2.57 (s, 3H), 2.32 (s, 3H), 1.40 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 157.9, 145.4, 137.7, 135.9, 123.0, 61.8, 23.0, 19.5, 14.4. IR (NaCl, thin film) ν 2983, 1716, 1460, 1369, 1312, 1249, 1188, 1135, 1025, 783, 718 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 180.1025, found 180.1025.



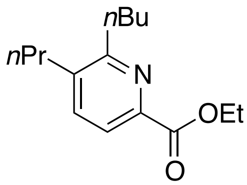
Ethyl 5-butyl-6-methylpicolinate (3da). Yellow viscous liquid. R_f = 0.26 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 4.44 (q, J = 7.2 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), 2.61 (s, 3H), 1.56 (m, 2H), 1.43-1.34 (m, 5H), 0.94 (t, J = 5.4, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 157.4, 145.3, 140.3, 136.9, 123.0, 61.8, 32.6, 31.7, 22.6, 22.5, 14.4, 14.0. IR (NaCl, thin film) ν 2959, 1717, 1574, 1458, 1369, 1313, 1180, 1138, 1028 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 222.1494, found 222.1489.



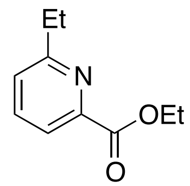
Ethyl 5-(3-chloropropyl)-6-methylpicolinate (3ea). Pale yellow viscous liquid. R_f = 0.17 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.56 (d, J = 8.0 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 3.56 (t, J = 6.0 Hz, 2H), 2.85 (t, J = 7.6 Hz, 2H), 2.64 (s, 3H), 2.06 (m, 2H), 1.42 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 157.5, 145.9, 138.3, 137.2, 123.1, 61.9, 44.2, 32.1, 30.0, 22.6, 14.5. IR (NaCl, thin film) ν 2960, 1716, 1573, 1445, 1369, 1312, 1184, 1138, 1028 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 242.1, found 242.1.



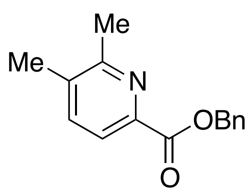
Ethyl 6-methyl-5-phenylpicolinate (3fa). Yellow viscous liquid. R_f = 0.23 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J = 7.6 Hz, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.43 (m, 3H), 7.32 (m, 2H), 4.49 (q, J = 7.2 Hz, 2H), 2.60 (s, 3H), 1.45 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 156.7, 146.6, 140.5, 139.2, 138.0, 128.9, 128.7, 128.1, 122.7, 62.0, 23.9, 14.5. IR (NaCl, thin film) ν 2982, 1716, 1561, 1446, 1369, 1309, 1200, 1142, 1027, 861, 763, 703 cm^{-1}. HRMS (ESI) *m*/*z* [M+H] calcd 242.1181, found 242.1179.



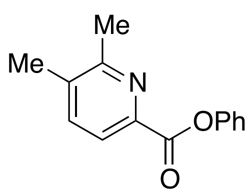
Ethyl 6-butyl-5-propylpicolinate (3ga). Pale yellow viscous liquid. R_f = 0.47 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 2.81 (t, *J* = 8.0 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 1.66-1.52 (m, 4H), 1.36 (m, 2H), 1.34 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 161.2, 145.6, 139.4, 137.3, 122.7, 61.7, 35.0, 34.4, 32.0, 23.7, 23.0, 14.5, 14.1. IR (NaCl, thin film) ν 2960, 1717, 1572, 1456, 1369, 1312, 1178, 1138, 1024 cm^{-1}. HRMS (ESI) *m*/*z* [M+H] calcd 250.1807, found 250.1809.



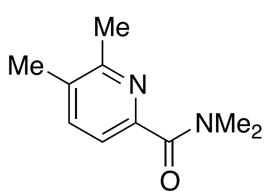
Ethyl 6-ethylpicolinate (3ha). Colorless viscous liquid. R_f = 0.07 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.34 (dd, *J* = 7.6, 0.8 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 2.93 (q, *J* = 7.6 Hz, 2H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.32 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 164.3, 148.0, 137.3, 125.4, 122.6, 61.9, 31.6, 14.5, 14.2. IR (NaCl, thin film) ν 2976, 1718, 1591, 1463, 1368, 1235, 1139, 761 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 180.1, found 180.1.



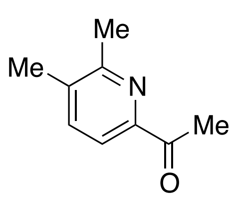
Benzyl 5,6-dimethylpicolinate (3cb). Yellow viscous liquid. R_f = 0.21 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.48 (m, 2H), 7.38-7.30 (m, 3H), 5.43 (s, 2H), 2.59 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 158.1, 145.1, 137.7, 136.1, 128.6, 128.5, 128.3, 123.2, 67.3, 23.0, 19.6. IR (NaCl, thin film) ν 2954, 1716, 1587, 1456, 1398, 1308, 1255, 1185, 1131, 1002, 782, 698 cm^{-1}. HRMS (ESI) *m*/*z* [M+H] calcd 242.1181, found 242.1173.



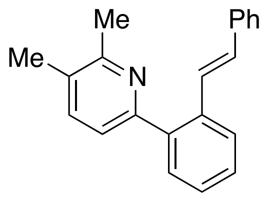
Phenyl 5,6-dimethylpicolinate (3cc). Off-white solid. R_f = 0.24 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.42 (m, 2H), 7.26 (m, 3H), 2.64 (s, 3H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 158.3, 151.3, 144.7, 137.9, 136.7, 129.5, 126.1, 123.9, 122.0, 23.1, 19.7. IR (NaCl, thin film) ν 2923, 1732, 1591, 1493, 1309, 1196, 1109, 746 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 228.1, found 228.1.



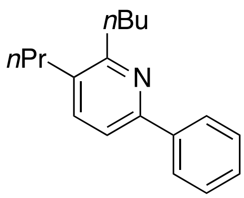
***N*,*N*,5,6-Tetramethylpicolinamide (3cd).** Pale yellow viscous liquid. R_f = 0.21 (EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 3.11 (s, 3H), 3.07 (s, 3H), 2.52 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 156.0, 151.3, 138.1, 132.7, 121.1, 39.2, 35.9, 22.5, 19.3. IR (NaCl, thin film) ν 2926, 1637, 1575, 1441, 1397, 1274, 1175, 1104, 843 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 179.1, found 179.1.



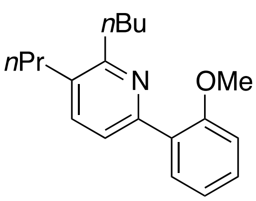
1-(5,6-Dimethylpyridin-2-yl)ethanone (3ce). Pale yellow viscous liquid. R_f = 0.26 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6, 1H), 7.51 (d, *J* = 8.0, 1H), 2.70 (s, 3H), 2.55 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 156.8, 151.2, 137.7, 136.0, 119.5, 25.9, 22.9, 19.6. IR (NaCl, thin film) ν 2926, 1696, 1573, 1459, 1355, 1301, 1177, 1122, 956, 839 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 150.1, found 150.2.



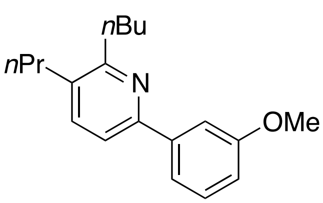
(E)-2,3-Dimethyl-6-(2-styrylphenyl)pyridine (2-styrenyl-3cf). Pale yellow viscous liquid. R_f = 0.66 (20:1 DCM/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.55 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.46 (d, *J* = 7.6 Hz, 1H), 7.41-7.19 (m, 9H), 7.04 (d, *J* = 16.4 Hz, 1H), 2.60 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.9, 155.6, 137.9, 137.3, 135.9, 130.4, 129.7, 128.7, 128.4, 128.1, 127.8, 127.5, 126.7, 126.3, 122.7, 22.9, 19.1. IR (NaCl, thin film) ν 2922, 1737, 1589, 1462, 1236, 1129, 961, 836, 761, 692 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 286.2, found 286.2.



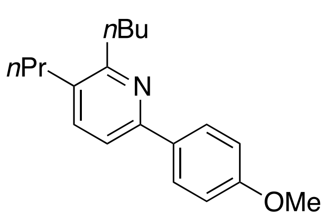
2-Butyl-6-phenyl-3-propylpyridine (3gf). Pale yellow viscous liquid. R_f = 0.11 (1:1 hexanes/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (m, 2H), 7.50-7.35 (m, 5H), 2.87 (t, *J* = 8.0 Hz, 2H), 2.64 (t, *J* = 8.0 Hz, 2H), 1.82 (m, 2H), 1.66 (m, 2H), 1.48 (m, 2H), 1.02 (t, *J* = 7.2 Hz, 3H), 1.00 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 154.2, 137.4, 133.8, 128.7, 128.4, 126.8, 117.7, 34.8, 34.2, 31.7, 23.9, 23.0, 14.3, 14.2. IR (NaCl, thin film) ν 2959, 2871, 1585, 1564, 1457, 1379, 833, 758, 693 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 254.2, found 254.2.



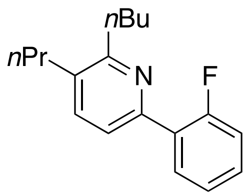
2-Butyl-6-(2-methoxyphenyl)-3-propylpyridine (3gg). Colorless viscous liquid. R_f = 0.20 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.33 (ddd, *J* = 6.8, 6.8, 1.6 Hz, 1H), 7.07 (ddd, *J* = 7.6, 7.6, 0.8 Hz, 1H), 6.98 (dd, *J* = 8.0, 0.8 Hz, 1H), 3.85 (s, 3H), 2.86 (t, *J* = 8.0 Hz, 2H), 2.63 (t, *J* = 8.0, 2H), 1.77 (m, 2H), 1.66 (m, 2H), 1.47 (m, 2H), 1.03 (t, *J* = 7.6 Hz, 3H), 0.98 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 157.1, 152.7, 136.4, 133.2, 131.4, 129.4, 122.3, 121.2, 111.5, 55.7, 34.9, 34.2, 32.1, 24.0, 23.1, 14.3. IR (NaCl, thin film) ν 2958, 1585, 1493, 1461, 1240, 1027, 752 cm^{-1}. HRMS (ESI) *m*/*z* [M+H] calcd 284.2014, found 284.2013.



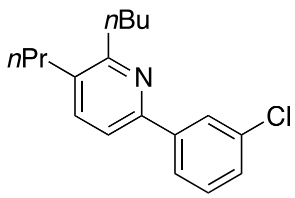
2-Butyl-6-(3-methoxyphenyl)-3-propylpyridine (3gh). Colorless viscous liquid. R_f = 0.45 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, *J* = 2.8, 1.6 Hz, 1H), 7.56 (ddd, 7.6, 1.6, 1.2 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.36 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.92 (ddd, *J* = 8.0, 2.8, 0.8 Hz, 1H), 3.89 (s, 3H), 2.86 (t, *J* = 8.0 Hz, 2H), 2.63 (t, *J* = 8.0 Hz, 2H), 1.80 (m, 2H), 1.65 (m, 2H), 1.47 (m, 2H), 1.01 (t, *J* = 5.4, 3H), 0.99 (t, *J* = 5.4, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 153.9, 141.6, 137.4, 134.0, 130.0, 119.3, 117.8, 114.2, 112.3, 55.4, 34.8, 34.2, 31.6, 23.9, 23.0, 14.3, 14.2. IR (NaCl, thin film) ν 2958, 2871, 1566, 1463, 1222, 1048, 826, 782 cm^{-1}. HRMS (ESI) *m*/*z* [M+H] calcd 284.2014, found 284.2015.



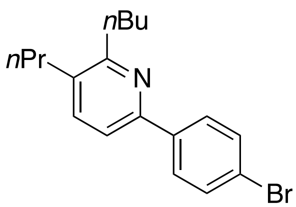
2-Butyl-6-(4-methoxyphenyl)-3-propylpyridine (3gi). Colorless viscous liquid. R_f = 0.43 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (m, 2H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 6.98 (m, 2H), 3.86 (s, 3H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H), 1.80 (m, 2H), 1.64 (m, 2H), 1.47 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H), 0.99 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.1, 160.0 153.9, 137.4, 133.0, 128.1, 117.0, 114.1, 55.5, 34.8, 34.1, 31.7, 24.0, 23.0, 14.3, 14.2. IR (NaCl, thin film) ν 2958, 1609, 1585, 1513, 1456, 1249, 1181, 1032, 825 cm^{-1}. LRMS (ESI + APCI) *m*/*z* [M+H] calcd 284.2, found 284.2.



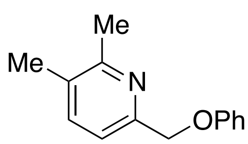
2-Butyl-6-(2-fluorophenyl)-3-propylpyridine (3gj). Colorless viscous liquid. R_f = 0.16 (1:1 hexanes/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (ddd, *J* = 8.0, 8.0, 2.0 Hz, 1H), 7.55 (dd, *J* = 8.0, 2.4 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.33 (m, 1H), 7.25 (ddd, *J* = 7.6, 7.6, 1.2 Hz), 7.13 (ddd, *J* = 11.6, 8.0, 1.2 Hz, 1H), 2.87 (t, *J* = 8.0 Hz, 2H), 2.64 (t, *J* = 7.6 Hz, 2H), 1.79 (m, 2H), 1.66 (m, 2H), 1.47 (m, 2H), 1.02 (t, *J* = 7.2, 3H), 0.99 (t, *J* = 7.2, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (d, *J* = 247.7 Hz), 160.4, 151.1 (d, *J* = 2.2), 137.0, 134.2, 131.2 (d, *J* = 3.1), 129.8 (d, *J* = 8.4), 124.5 (d, *J* = 3.4), 121.8 (d, *J* = 9.2), 116.3, 116.0, 34.8, 34.2, 31.8, 23.9, 23.0, 14.2. IR (NaCl, thin film) ν 2959, 2872, 1585, 1491, 1455, 1387, 1212, 1109, 816, 757 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 272.2, found 272.2.



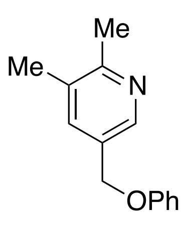
2-Butyl-6-(3-chlorophenyl)-3-propylpyridine (3gk). Colorless viscous liquid. R_f = 0.38 (1:1 hexanes/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (ddd, *J* = 2.0, 1.6, 0.4 Hz, 1H), 7.88 (ddd, *J* = 7.2, 1.6, 1.6 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.37 (ddd, *J* = 8.0, 7.2, 0.4 Hz, 1H), 7.33 (ddd, *J* = 8.0, 2.0, 1.6 Hz, 1H), 2.86 (t, *J* = 8.0 Hz, 2H), 2.63 (t, *J* = 8.0 Hz, 2H), 1.80 (m, 2H), 1.65 (m, 2H), 1.48 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H), 1.00 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 152.6, 141.9, 137.5, 134.8, 134.5, 129.9, 128.4, 127.0, 124.9, 117.7, 34.8, 34.2, 31.6, 23.9, 23.0, 14.2. IR (NaCl, thin film) ν 2959, 2871, 1561, 1454, 1379, 1078, 784 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 288.2, found 288.2.



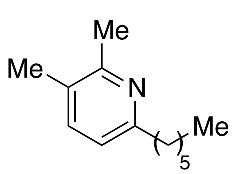
6-(4-Bromophenyl)-2-butyl-3-propylpyridine (3gl). Colorless viscous liquid. R_f = 0.63 (10:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (m, 2H), 7.56 (m, 2H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.44 (d, *J* = 7.6 Hz, 1H), 2.85 (t, *J* = 7.6 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.78 (m, 2H), 1.64 (m, 2H), 1.46 (m, 2H), 1.01 (t, *J* = 7.6 Hz, 3H), 0.98 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 152.9, 138.9, 137.5, 134.3, 131.8, 128.4, 122.8, 117.4, 34.8, 34.2, 31.6, 23.9, 23.0, 14.3, 14.2. IR (NaCl, thin film) ν 2958, 2930, 2871, 1586, 1454, 1377, 1072, 1009, 818 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 332.1, found 332.1.



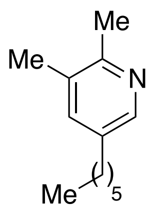
2,3-Dimethyl-6-(phenoxymethyl)pyridine (3cm). Pale yellow viscous liquid. R_f = 0.38 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.6 Hz, 1H), 7.28 (m, 3H), 6.96 (m, 3H), 5.17 (s, 2H), 2.53 (s, 3H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 156.6, 153.8, 138.3, 130.6, 129.6, 121.1, 119.0, 115.0, 70.4, 22.4, 19.1. IR (NaCl, thin film) ν 2923, 1599, 1496, 1403, 1242, 1060, 753, 691 cm^{-1}. HRMS (ESI) *m/z* [M+H] calcd 214.1232, found 214.1232.



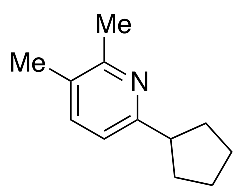
2,3-Dimethyl-5-(phenoxymethyl)pyridine (5cm). Pale yellow viscous liquid. R_f = 0.09 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 1.5, 1H), 7.51 (d, *J* = 0.9, 1H), 7.30 (m, 2H), 6.98 (m, 3H), 5.01 (s, 2H), 2.51 (s, 3H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6, 157.3, 145.9, 136.8, 131.6, 130.0, 129.7, 121.3, 114.9, 67.6, 22.5, 19.3. IR (NaCl, thin film) ν 2923, 1598, 1496, 1240, 1031, 754, 691 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 214.1, found 214.1.



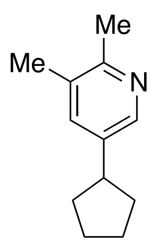
6-Hexyl-2,3-dimethylpyridine (3cn). Pale yellow viscous liquid. R_f = 0.52 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 8.0 Hz), 2.70 (t, *J* = 7.6 Hz, 2H), 2.47 (s, 3H), 2.23 (s, 3H), 1.67 (m, 2H), 1.37-1.25 (m, 6H), 0.87 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 156.1, 137.4, 128.1, 119.8, 38.1, 31.7, 30.2, 29.1, 22.6, 22.5, 18.7, 14.1. IR (NaCl, thin film) ν 2926, 2857, 1578, 1467, 1397, 824 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 192.2, found 192.2.



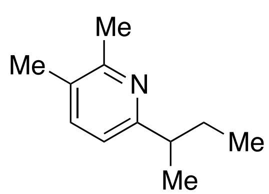
5-Hexyl-2,3-dimethylpyridine (5cn). Pale yellow viscous liquid. R_f = 0.26 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 2.0 Hz, 1H), 7.20 (d, J = 1.6 Hz, 1H), 2.52 (t, J = 7.6 Hz, 2H), 2.45 (s, 3H), 2.24 (s, 3H), 1.57 (m, 2H), 1.28 (m, 6H), 0.87 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 146.5, 137.3, 135.5, 130.9, 32.6, 31.8, 31.4, 29.0, 22.7, 22.2, 19.2, 14.2. IR (NaCl, thin film) ν 2928, 2857, 1474, 1412, 1139, 1020, 899, 727 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 192.2, found 192.2.



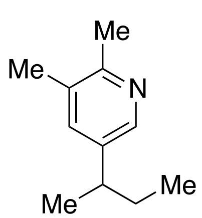
6-Cyclopentyl-2,3-dimethylpyridine (3co). Pale yellow viscous liquid. R_f = 0.60 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 8.0, 1H), 6.93 (d, J = 8.0 Hz, 1H), 3.11 (m, 1H), 2.47 (s, 3H), 2.23 (s, 3H), 2.07 (m, 2H), 1.81-1.66 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6, 156.1, 137.5, 128.3, 118.3, 48.0, 33.9, 25.8, 22.8, 18.9. IR (NaCl, thin film) ν 2952, 2868, 1578, 1465, 1400, 1127, 825 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 176.1, found 176.2.



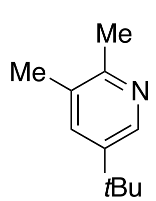
5-Cyclopentyl-2,3-dimethylpyridine (5co). Pale yellow viscous liquid. R_f = 0.19 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, J = 2.0 Hz, 1H), 7.25 (d, J = 2.0 Hz, 1H), 2.93 (m, 1H), 2.45 (s, 3H), 2.25 (s, 3H), 2.05 (m, 2H), 1.82-1.50 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 145.6, 139.1, 135.8, 130.9, 43.0, 34.6, 25.6, 22.2, 19.4. IR (NaCl, thin film) ν 2953, 2869, 1475, 1242, 1020, 892, 732 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 176.1, found 176.1.



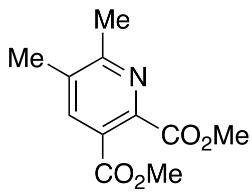
6-(sec-Butyl)-2,3-dimethylpyridine (3cq). Pale yellow viscous liquid. R_f = 0.65 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 7.6 Hz, 1H), 6.87 (d, J = 7.6 Hz, 1H), 2.75 (m, 2H), 2.47 (s, 3H), 2.23 (s, 3H), 1.72 (m, 1H), 1.57 (m, 1H), 1.24 (d, J = 7.2 Hz, 3H), 0.85 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5, 156.1, 137.6, 128.4, 118.2, 43.4, 30.2, 22.7, 20.7, 18.9, 12.3. IR (NaCl, thin film) ν 2962, 2927, 1741, 1578, 1467, 1377, 1107, 827 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 164.1, found 164.2.



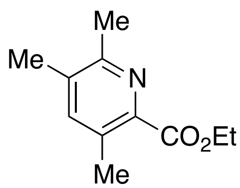
5-(*sec*-Butyl)-2,3-dimethylpyridine (5cq). Pale yellow viscous liquid. R_f = 0.23 (5:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (bs, 1H), 7.22 (bs, 1H), 2.56 (m, 1H), 2.47 (s, 3H), 2.26 (s, 3H), 1.58 (m, 2H), 1.22 (d, J = 7.2 Hz, 3H), 0.82 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 145.3, 140.1, 135.7, 131.0, 38.6, 30.9, 21.9, 21.6, 19.2, 12.1. IR (NaCl, thin film) ν 2963, 2926, 2875, 1740, 1459, 1376, 1240, 1111, 1019, 898, 733 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 164.1, found 164.2.



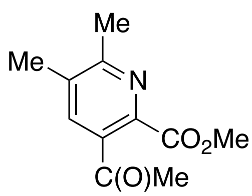
5-(*tert*-Butyl)-2,3-dimethylpyridine (5cr). Yellow viscous liquid. R_f = 0.10 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 2.4 Hz, 1H), 7.39 (d, J = 2.4 Hz, 1H), 2.46 (s, 3H), 2.26 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 143.7, 143.6, 134.6, 130.6, 33.2, 31.2, 22.0, 19.5. IR (NaCl, thin film) ν 2962, 1481, 1397, 1167, 733 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 164.1439, found 164.2.



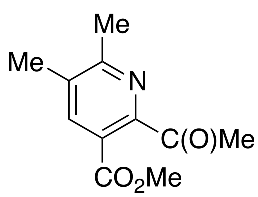
Dimethyl 5,6-dimethylpyridine-2,3-dicarboxylate (7ca). White solid. R_f = 0.19 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 3.96 (s, 3H), 3.89 (s, 3H), 2.57 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 166.1, 160.9, 148.2, 138.2, 133.7, 123.7, 53.1, 52.8, 22.9, 19.1. IR (NaCl, thin film) ν 2955, 1732, 1597, 1428, 1309, 1151, 1046, 797 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 224.1, found 224.1.



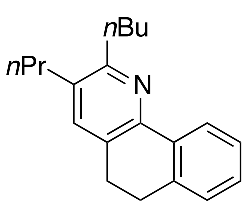
Ethyl 3,5,6-trimethylpicolinate (7cb). Pale yellow viscous liquid. R_f = 0.23 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (s, 1H), 4.42 (q, J = 7.2 Hz, 2H), 2.50 (s, 3H), 2.47 (s, 3H), 2.27 (s, 3H), 1.41 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 154.7, 144.7, 140.8, 134.6, 132.4, 61.5, 22.4, 19.5, 19.1, 14.4. IR (NaCl, thin film) ν 2981, 1719, 1462, 1310, 1237, 1155, 1062, 713 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 194.1, found 194.1.



Methyl 3-acetyl-5,6-dimethylpicolinate (7cc). White solid. R_f = 0.11 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 1H), 3.97 (s, 3H), 2.59 (s, 3H), 2.53 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5, 166.8, 159.7, 144.1, 136.2, 135.1, 134.8, 53.2, 29.7, 22.9, 19.4. IR (NaCl, thin film) ν 2954, 1744, 1692, 1591, 1552, 1429, 1365, 1301, 1261, 1161, 1137, 1019 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 208.1, found 208.1.



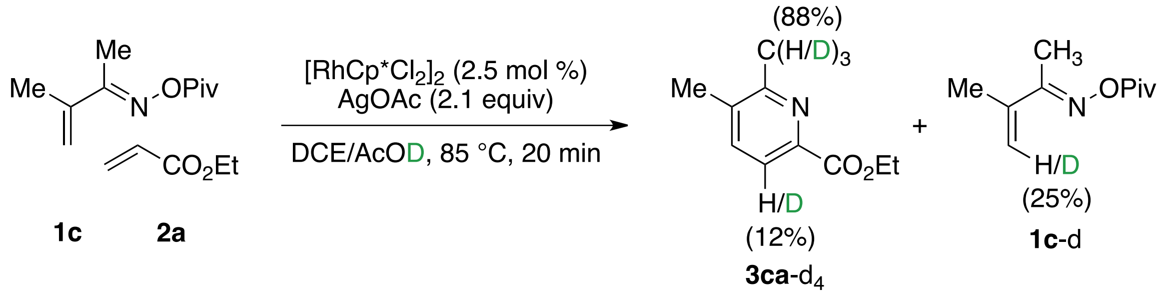
Methyl 2-acetyl-5,6-dimethylnicotinate (8cc). White solid. R_f = 0.34 (3:1 hexanes/EtOAc). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 3.89 (s, 3H), 2.65 (s, 3H), 2.56 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.0, 167.9, 159.4, 152.6, 137.6, 134.0, 124.4, 52.9, 27.5, 22.8, 19.2. IR (NaCl, thin film) ν 2955, 1733, 1595, 1432, 1356, 1301, 1272, 1161, 1131, 1022 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 208.1, found 208.1.

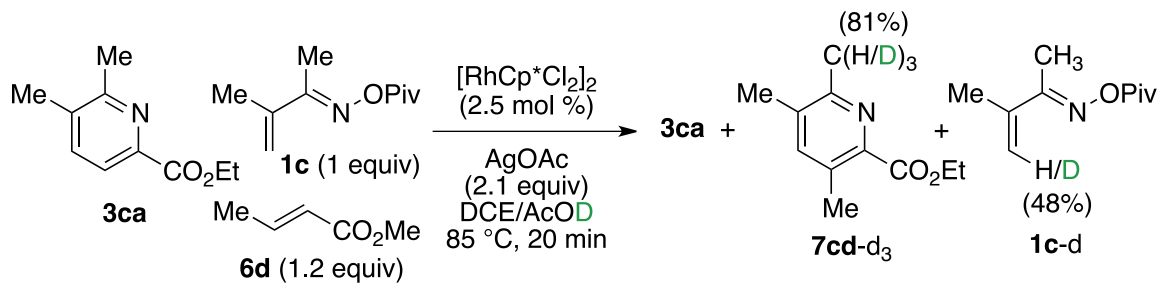


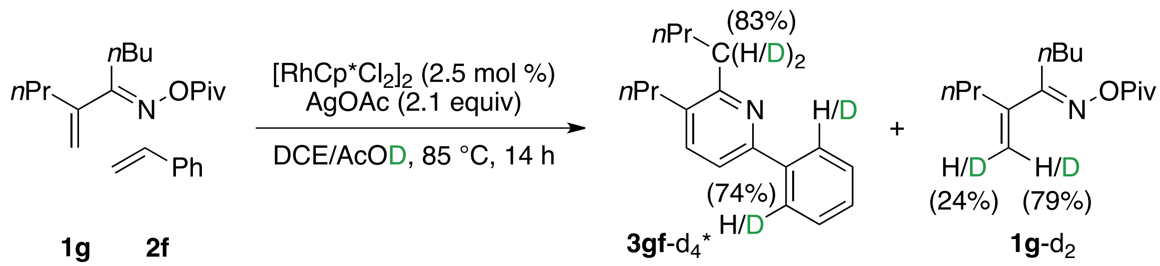
2-Butyl-3-propyl-5,6-dihydrobenzo[h]quinoline (10). Colorless viscous liquid. R_f = 0.14 (3:1 hexanes/DCM). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 7.6 Hz, 1H), 7.36-7.19 (m, 4H), 2.94-2.81 (m, 6H), 2.60 (t, J = 7.6 Hz, 2H), 1.80 (m, 2H), 1.64 (m, 2H), 1.47 (m, 2H), 1.01 (t, J = 5.7, 3H), 0.99 (t, J = 5.4, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 149.3, 137.9, 136.3, 135.2, 134.0, 128.8, 128.4, 127.7, 127.1, 124.8, 34.4, 34.2, 31.7, 28.5, 27.8, 24.0, 23.0, 14.3. IR (NaCl, thin film) ν 2957, 2931, 2870, 1553, 1461, 1438, 1377, 915, 740 cm^{-1}. LRMS (ESI + APCI) *m/z* [M+H] calcd 280.2, found 280.2.

Mechanistic Experiments

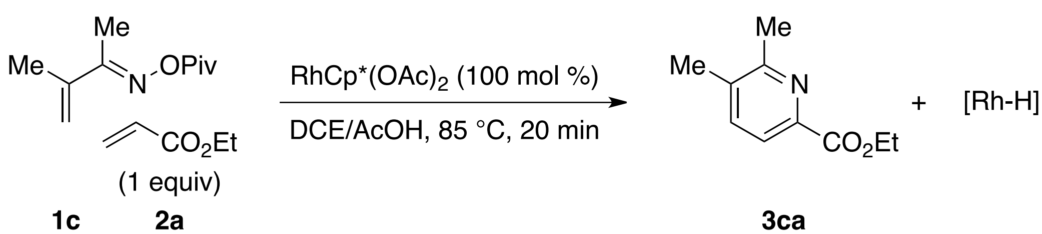
Isotope experiments were conducted with AcOD (purchased from Sigma-Aldrich Co. and used as received) according to the reaction procedure described above for the length of time indicated. Deuterium incorporation was determined by integration of the ^{1}H NMR spectra collected with first relaxation delay (d1) = 15 seconds of the crude reaction mixtures.

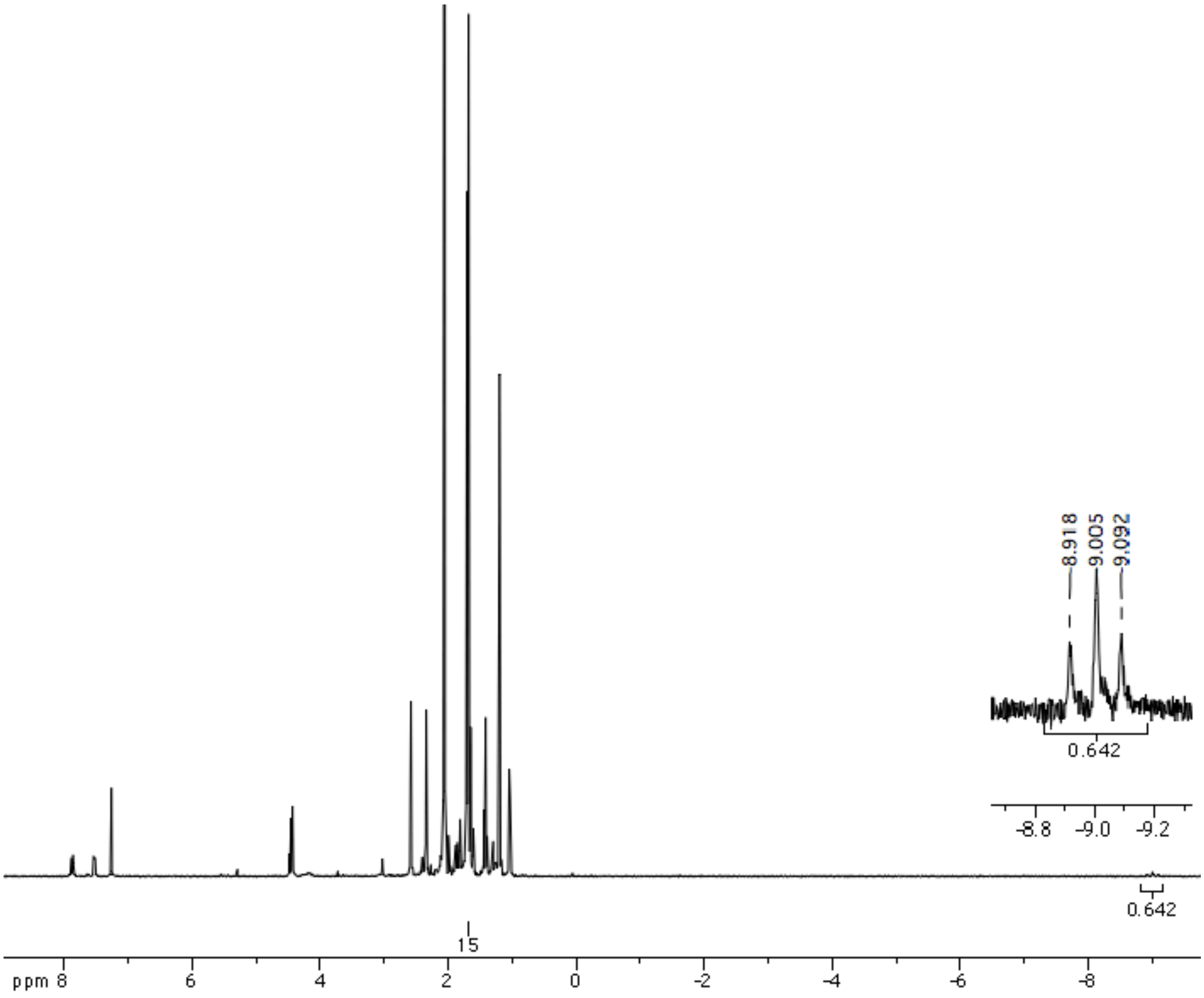




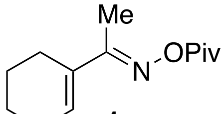


A stoichiometric experiment was performed according to the following procedure. A 0.5 dram vial was charged with RhCp*$(OAc)_2$ (9.6 mg, 100 mol %)[6] and a solution of **1c** (0.027 mmol) and **2a** (2.7 mg, 1 equiv) in 0.09 mL 2:1 DCE/AcOH was added. The vial was flushed with argon, sealed and heated at 85 °C in an aluminum heating block for 20 minutes. The solvent was removed and the reaction mixture was analyzed by ^{1}H NMR (300 MHz, $CDCl_3$). The key upfield signal at -9.005 ppm consistent with a Rh-H is highlighted in the spectrum provided below.





[1] Fujita, K.; Takahashi, Y.; Owaki, M.; Yamamoto, K.; Yamaguchi, R. *Org. Lett.* **2004**, *6*, 2785.
[2] Ezequias, S. F. P.; Rodrigues, J. A. R.; Moran, P. J. S. *Tetrahedron-Asymmetr.* **2001**, *12*, 847.
[3] Tan, Y.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 3676.
[4] Ohashi, M.; Takeda, I.; Ikawa, M.; Ogoshi, S. *J. Am. Chem. Soc.* **2011**, *133*, 18018.
[5] Martin, R. M.; Bergman, R. G.; Ellman, J. A. *J. Org. Chem.* **2012**, *77*, 2501.
[6] $RhCp^*(OAc)_2$ was prepared as previously reported with the following modifications: dichloromethane was used as the solvent at a concentration of 0.05 M for a reaction time of 48 hours. See: Boyer, P. M.; Roy, C. P.; Bielski, J. M.; Merola, J. S. *Inorg. Chim. Acta* **1996**, *245*, 7.



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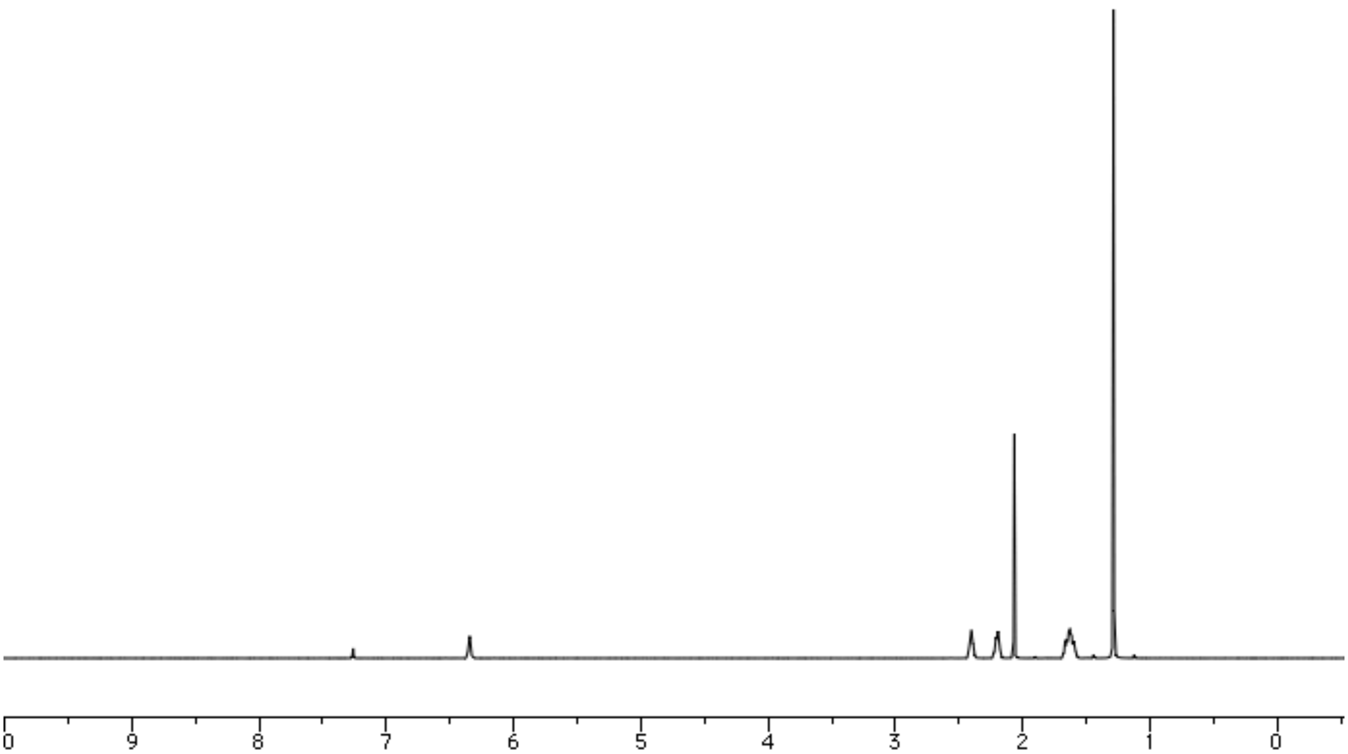

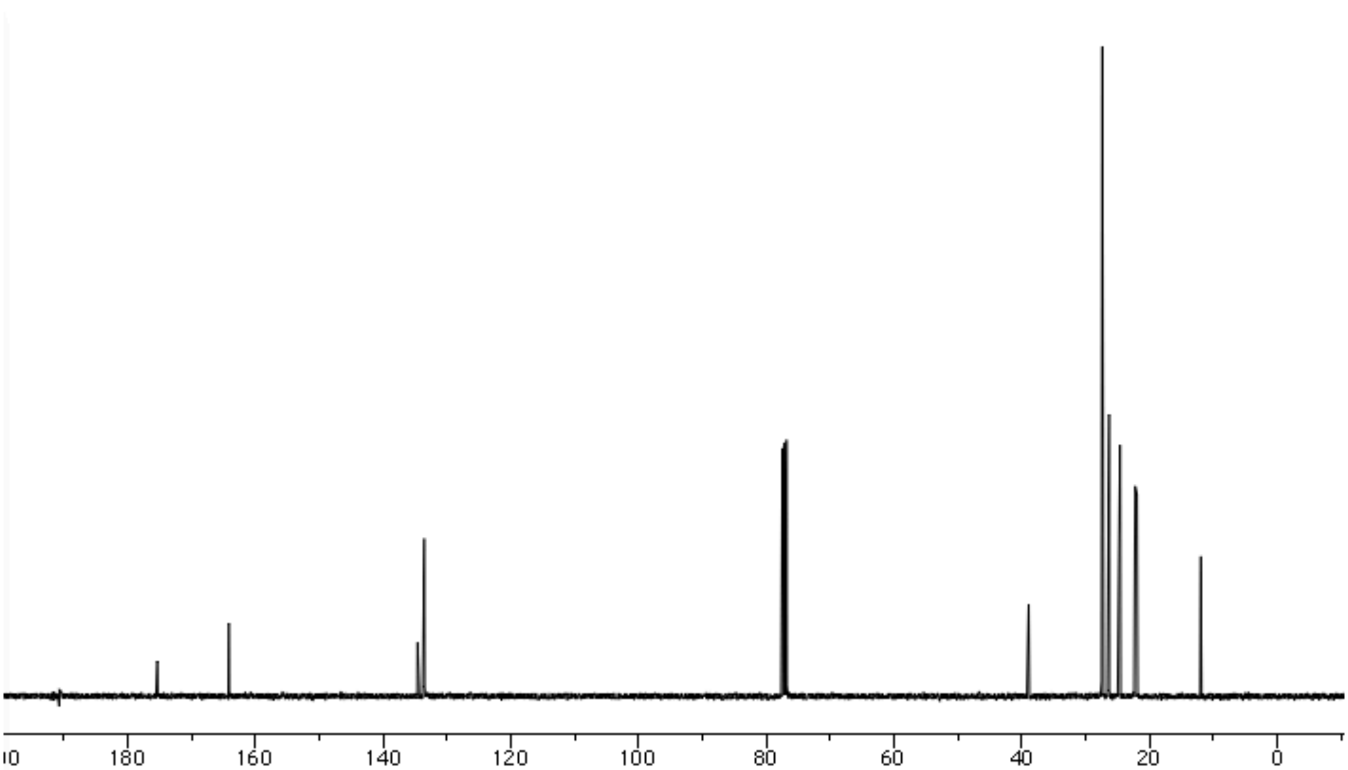

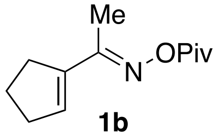

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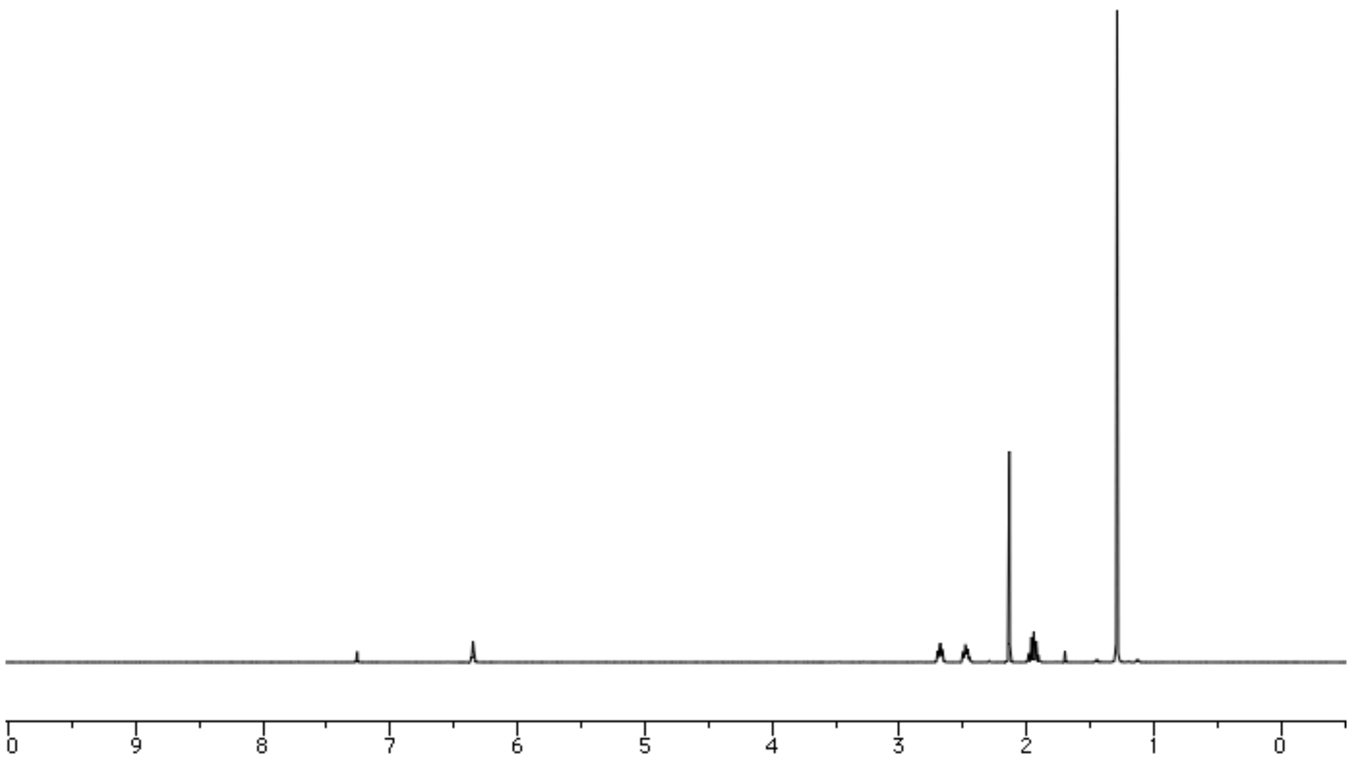

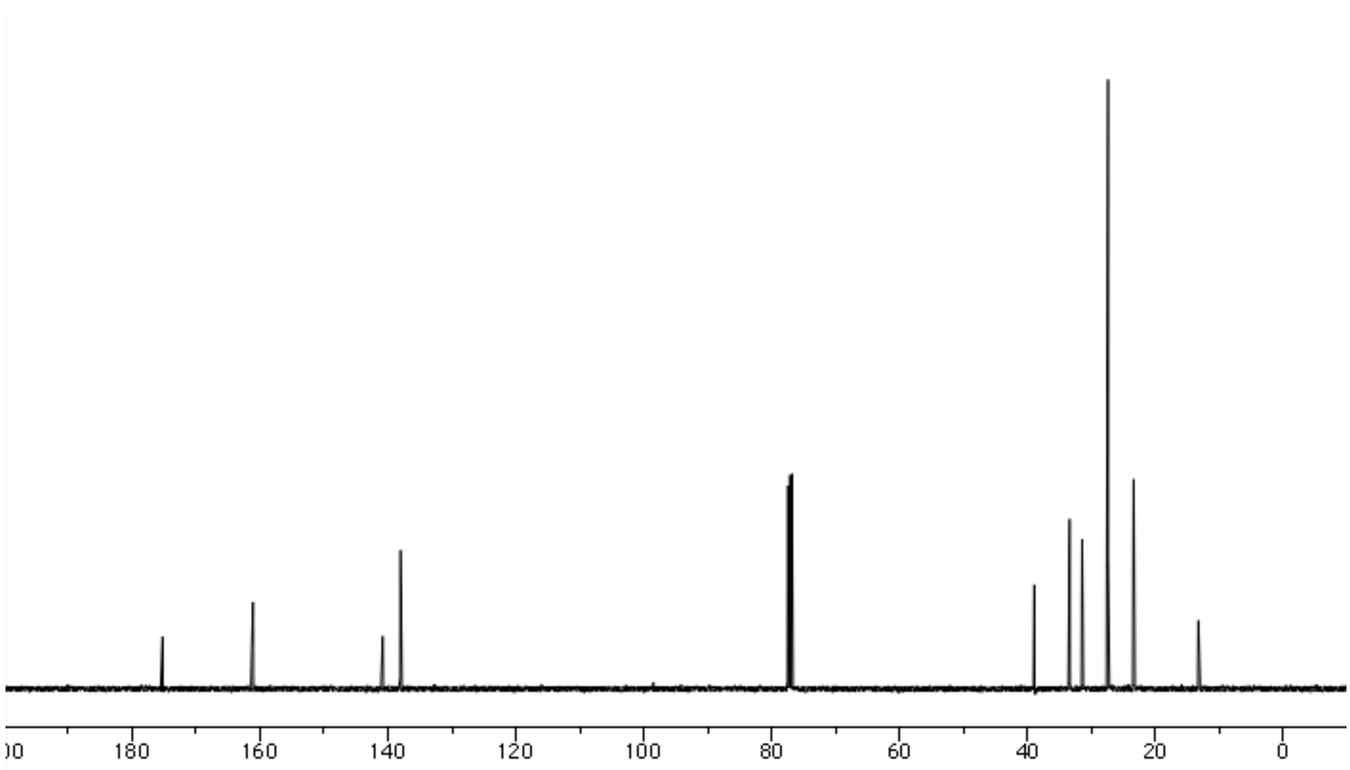

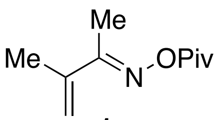

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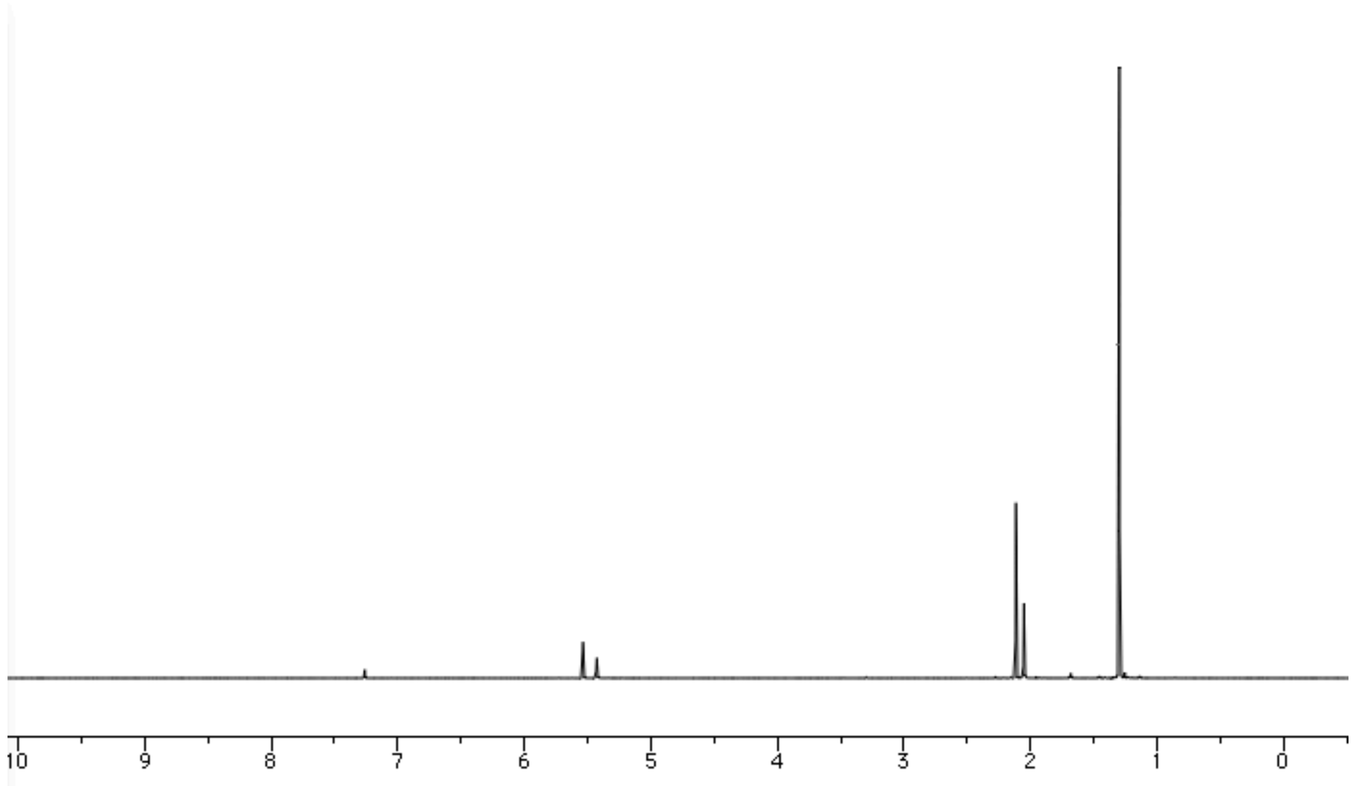

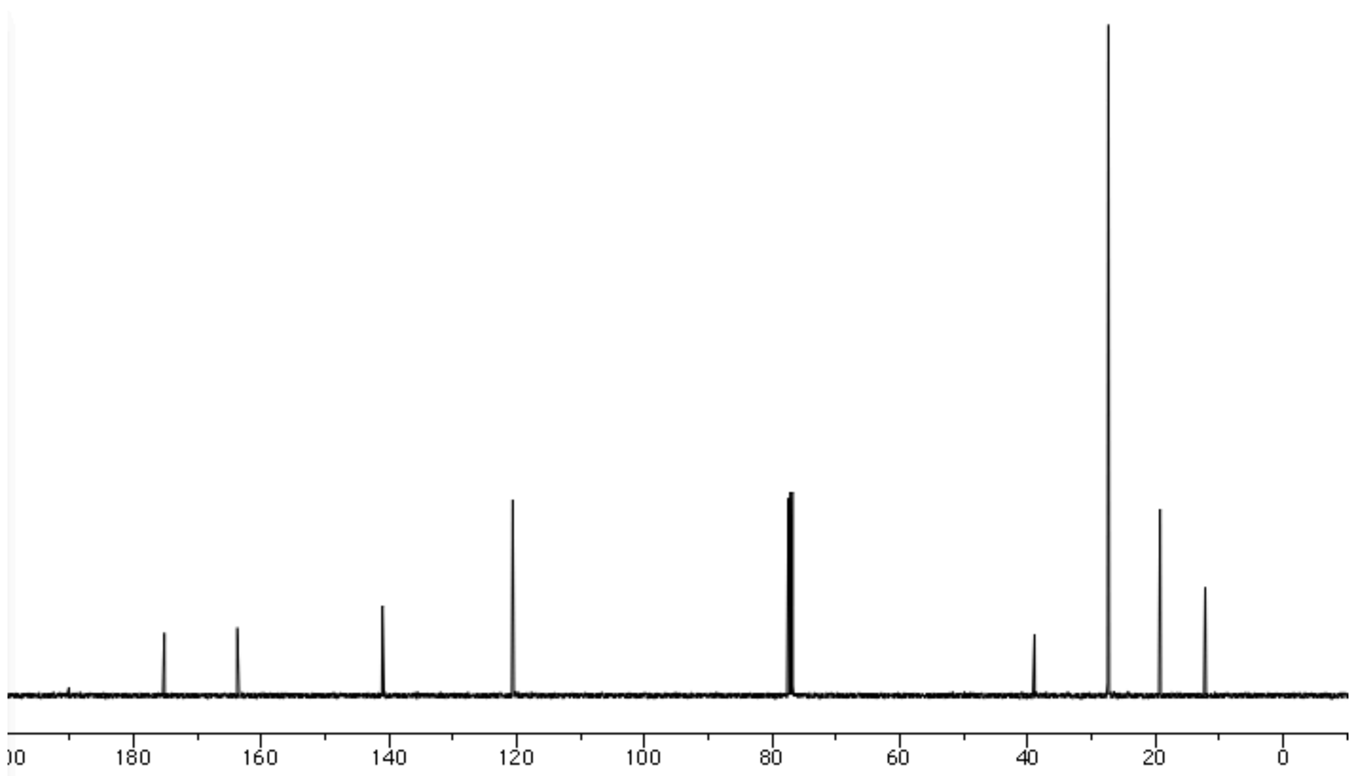

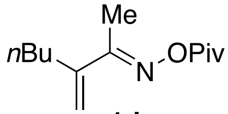

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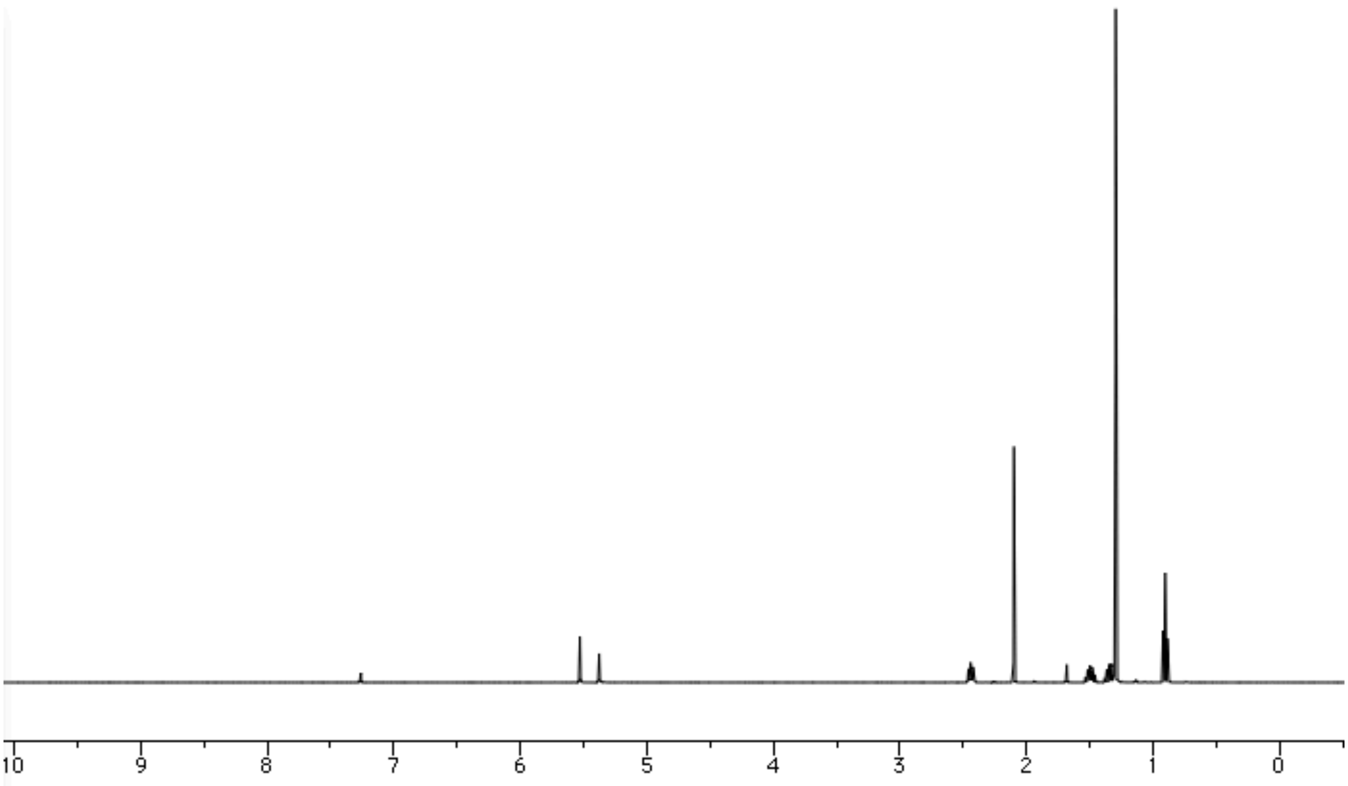

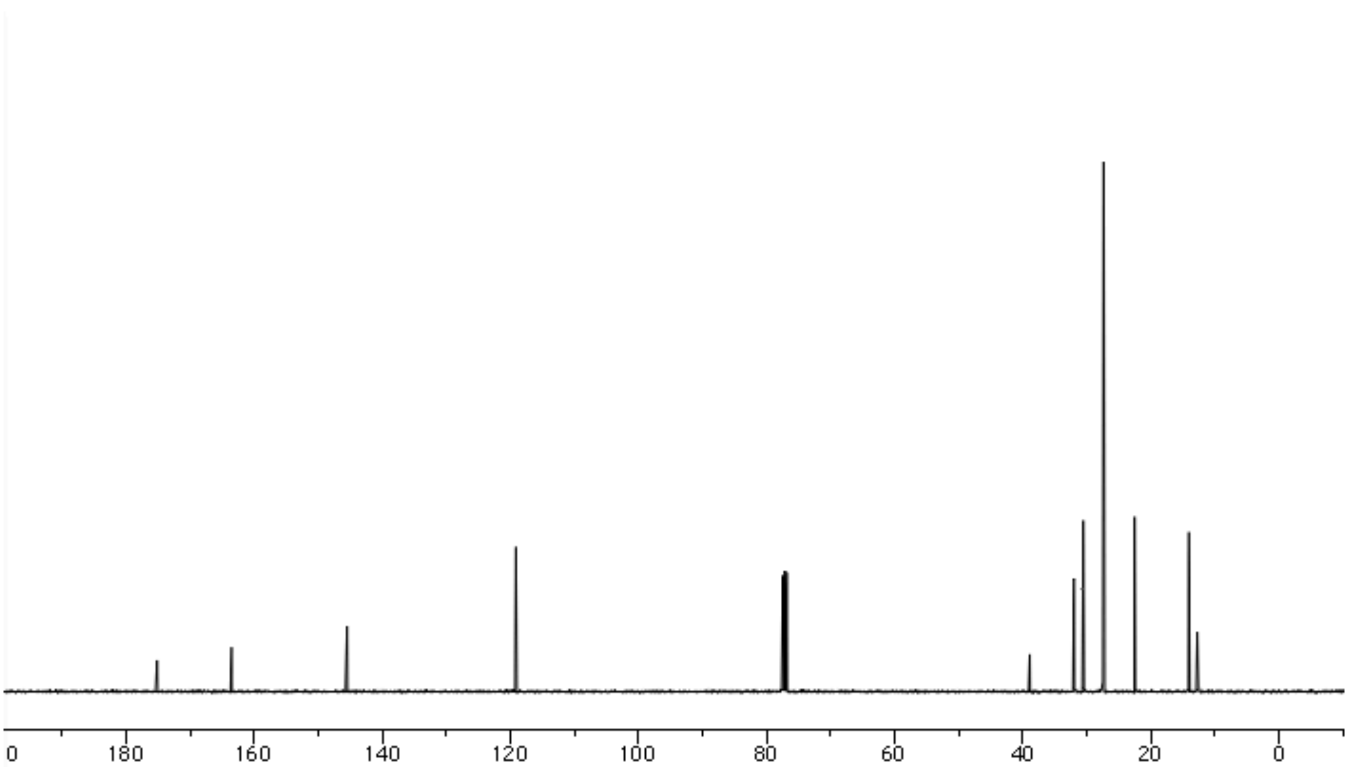

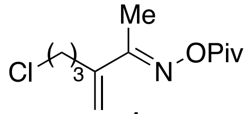

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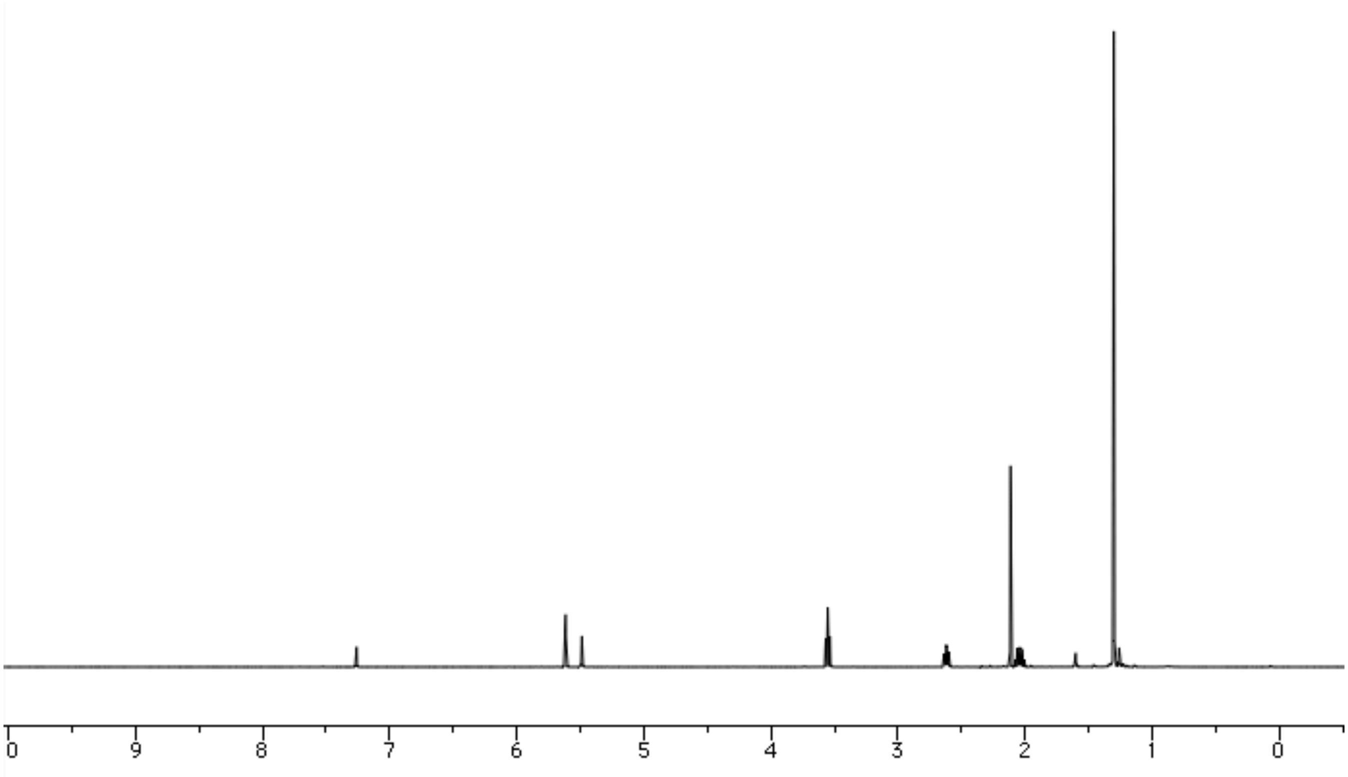

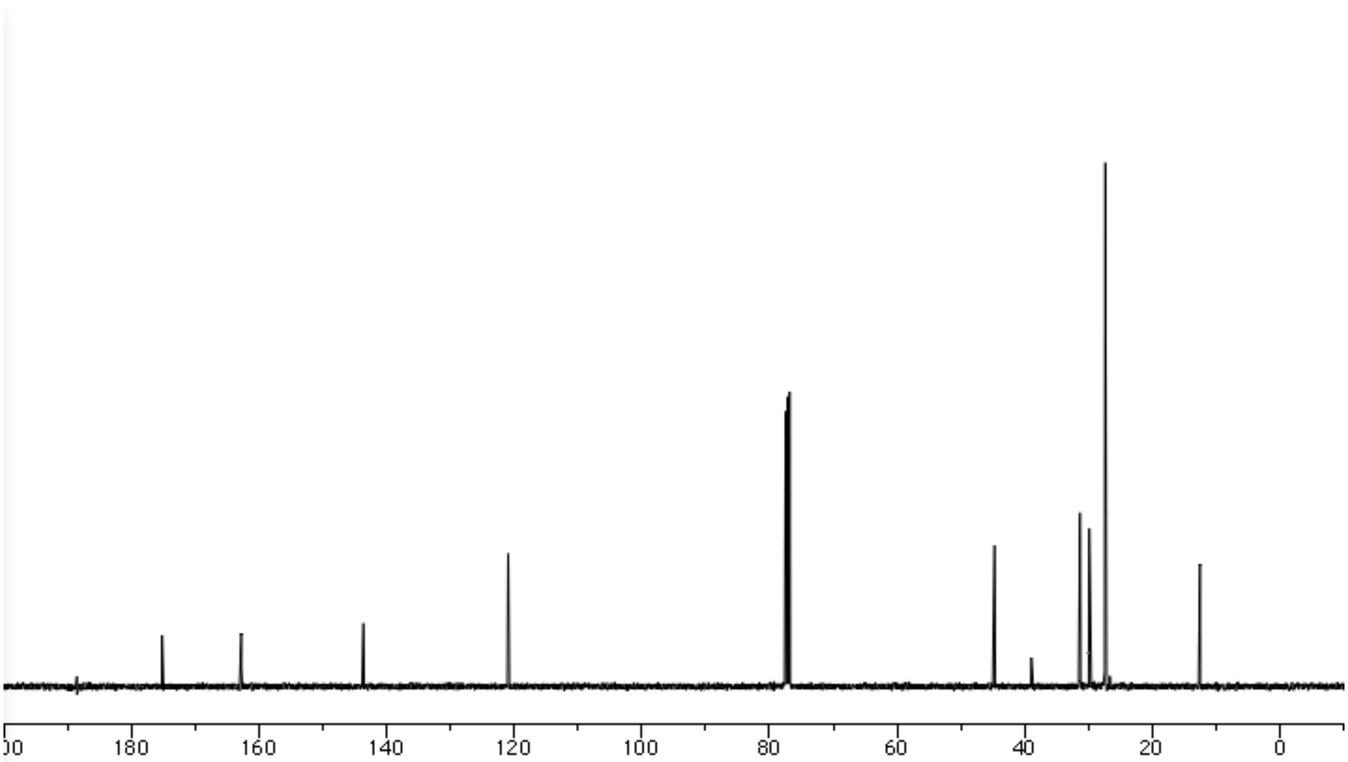

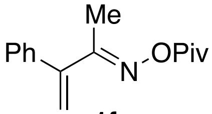

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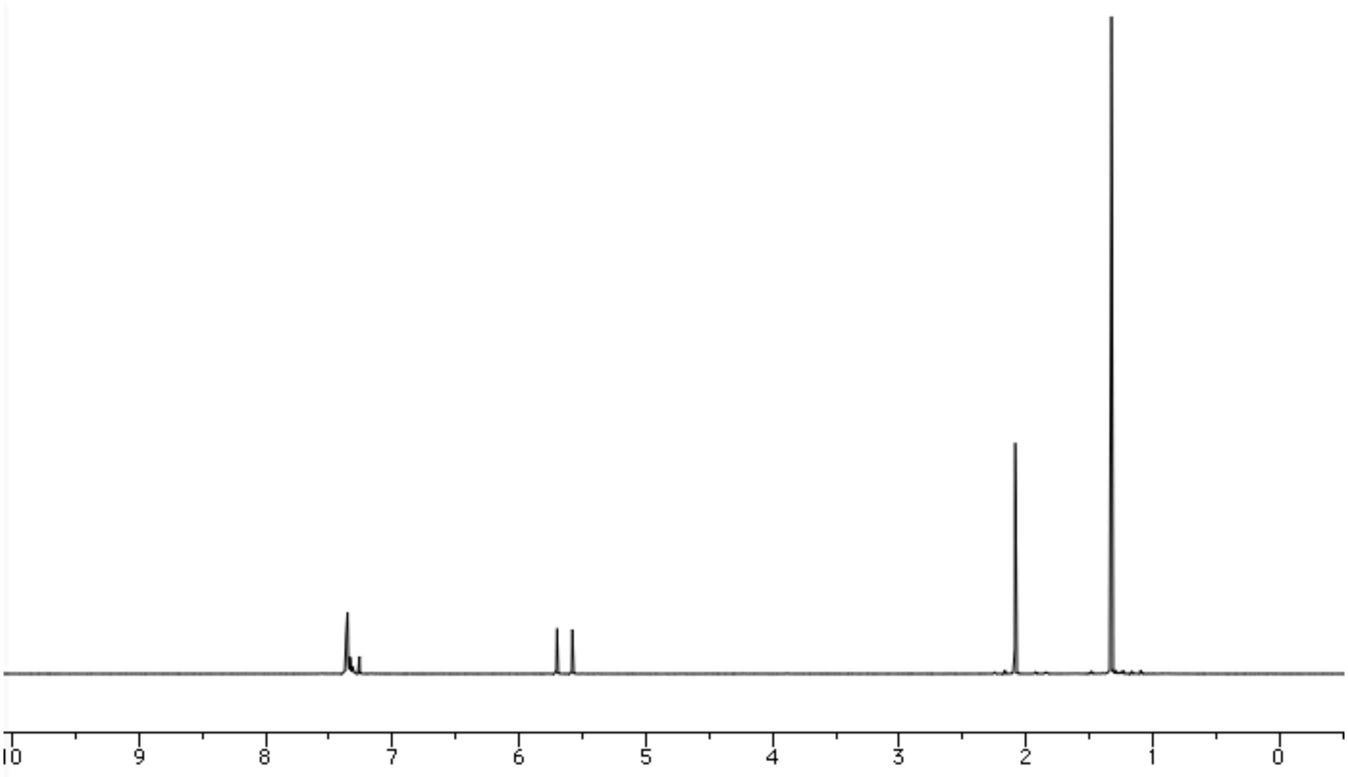

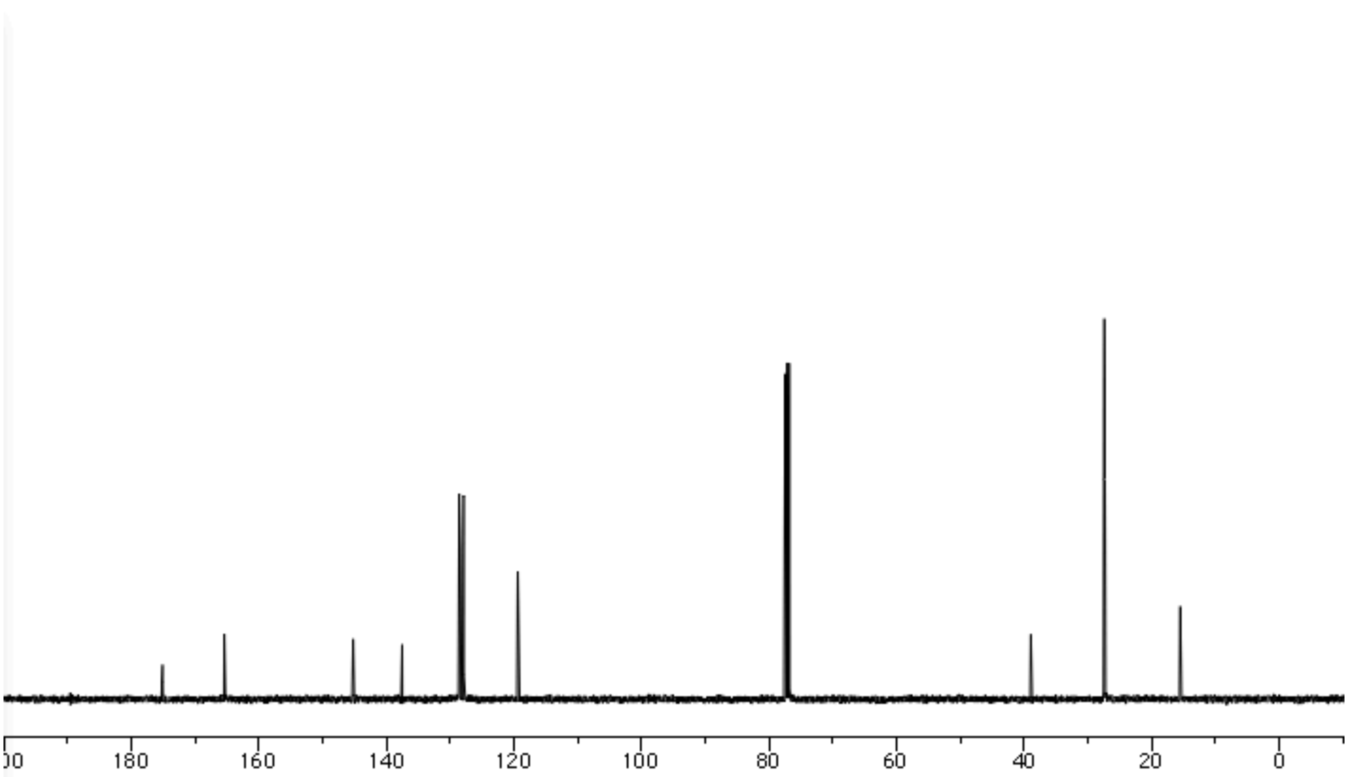

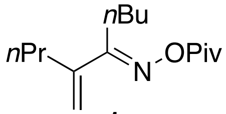

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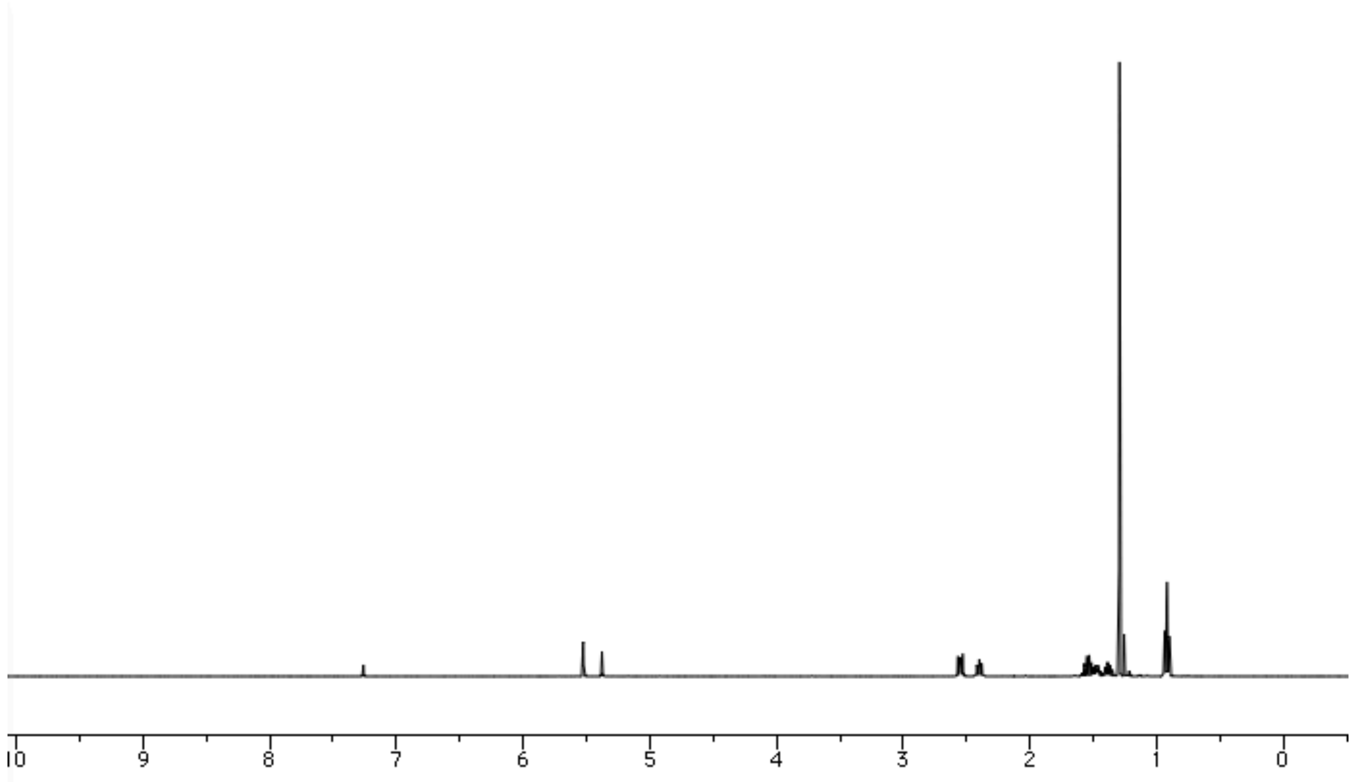
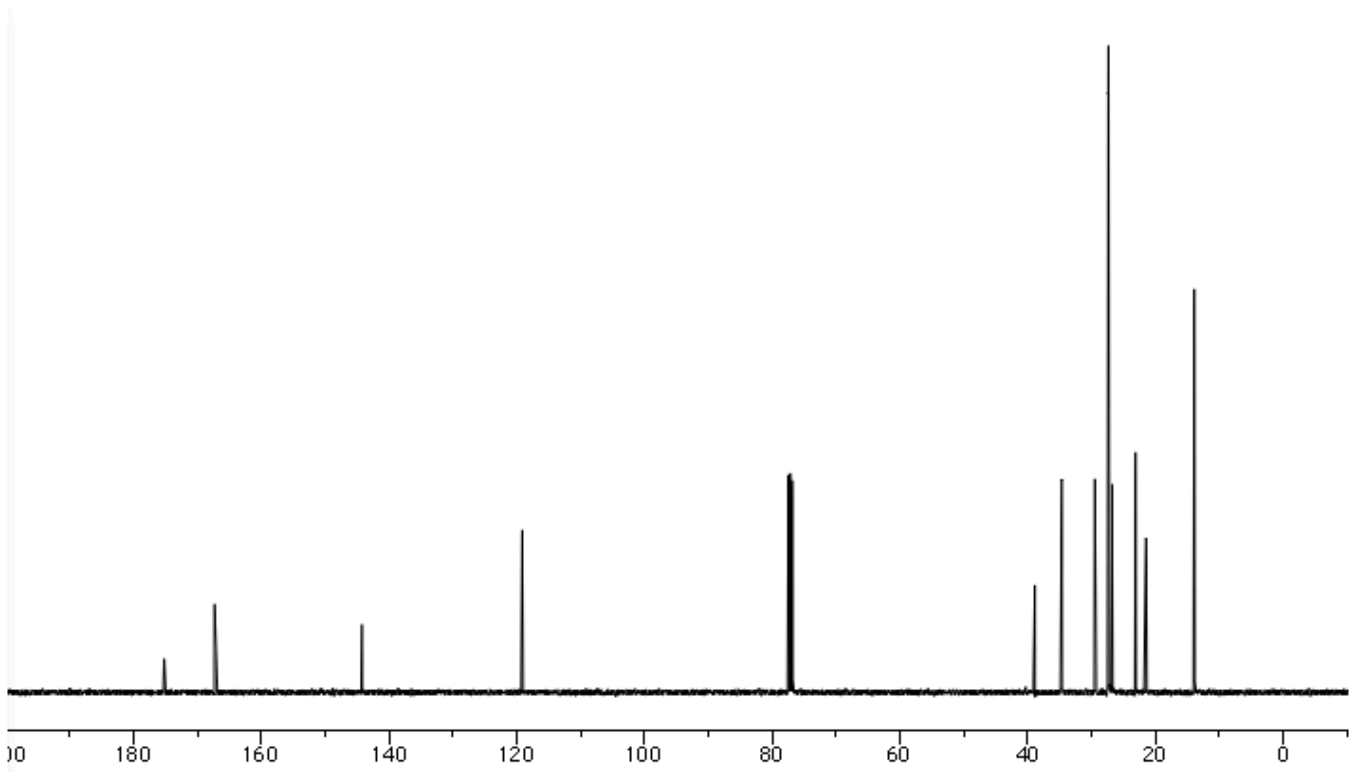
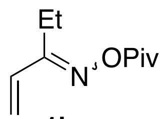
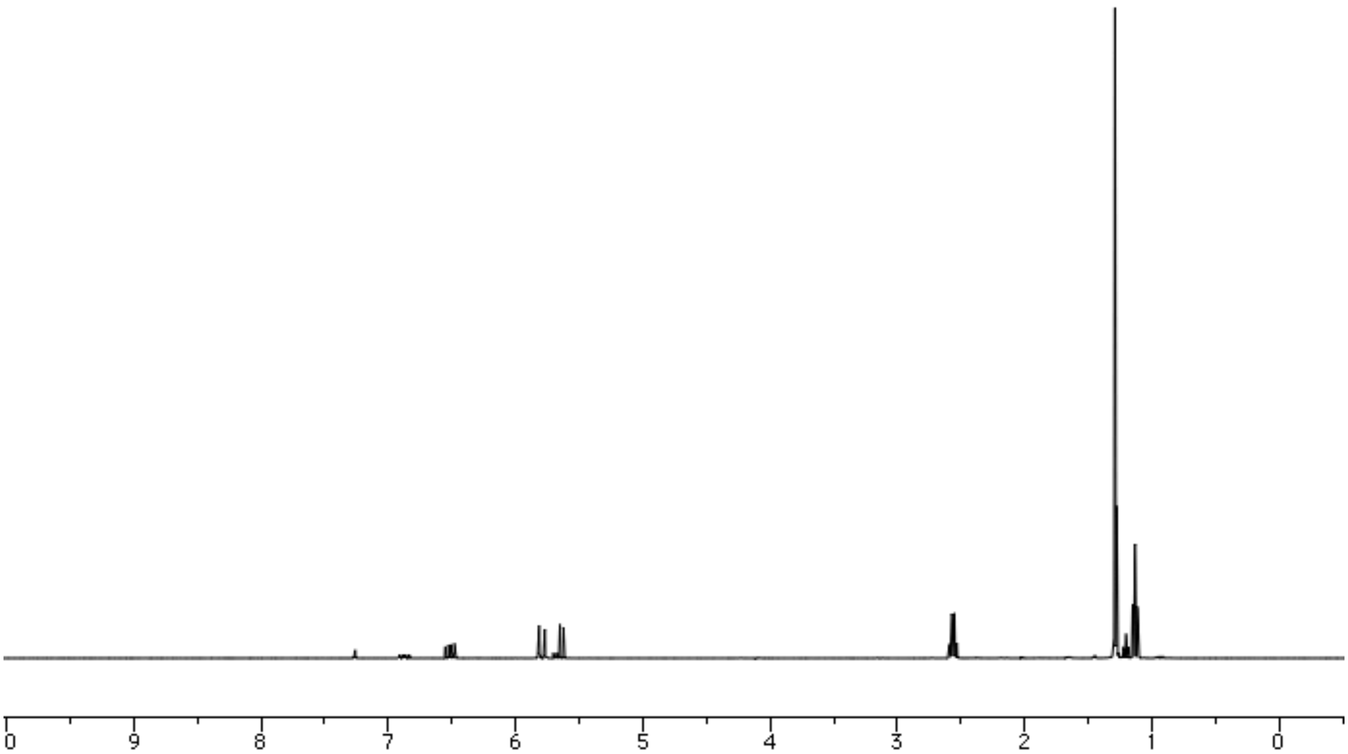
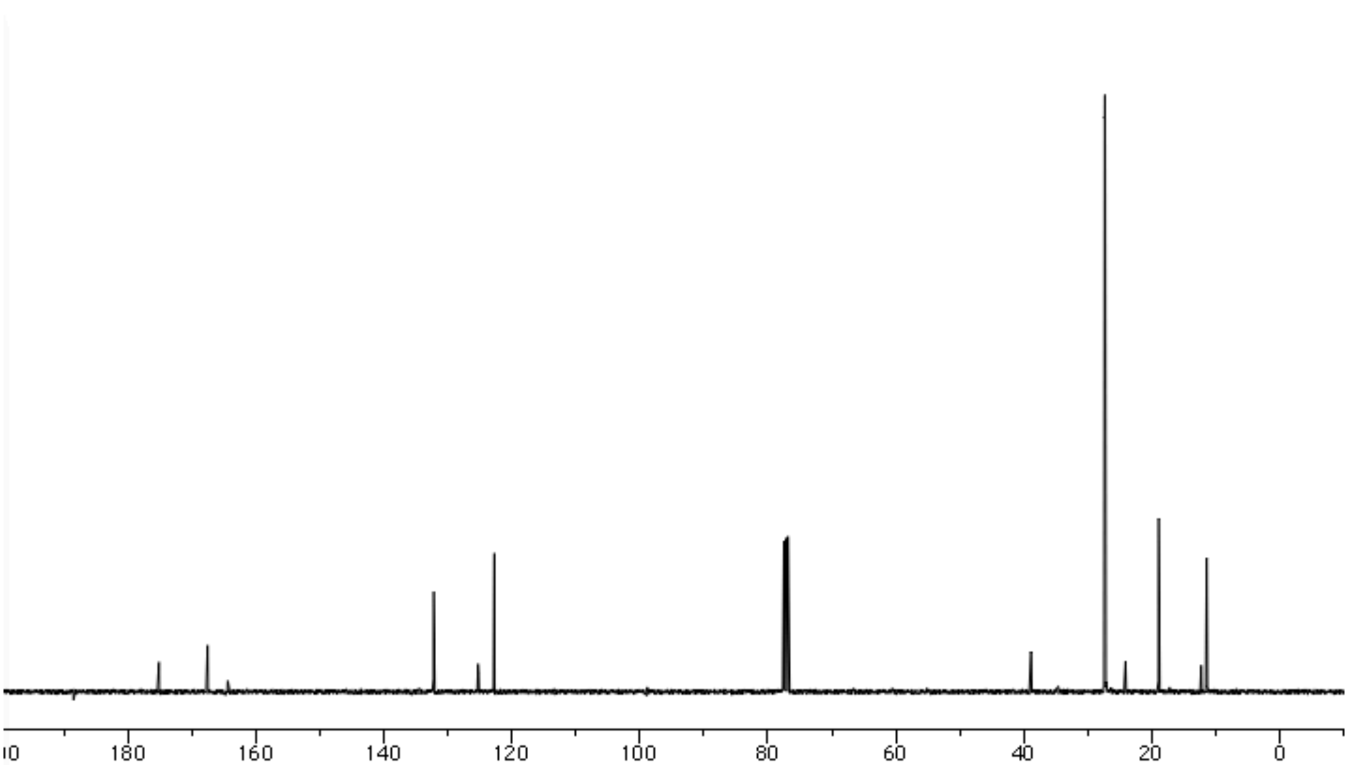


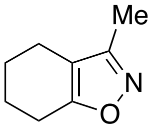




1h







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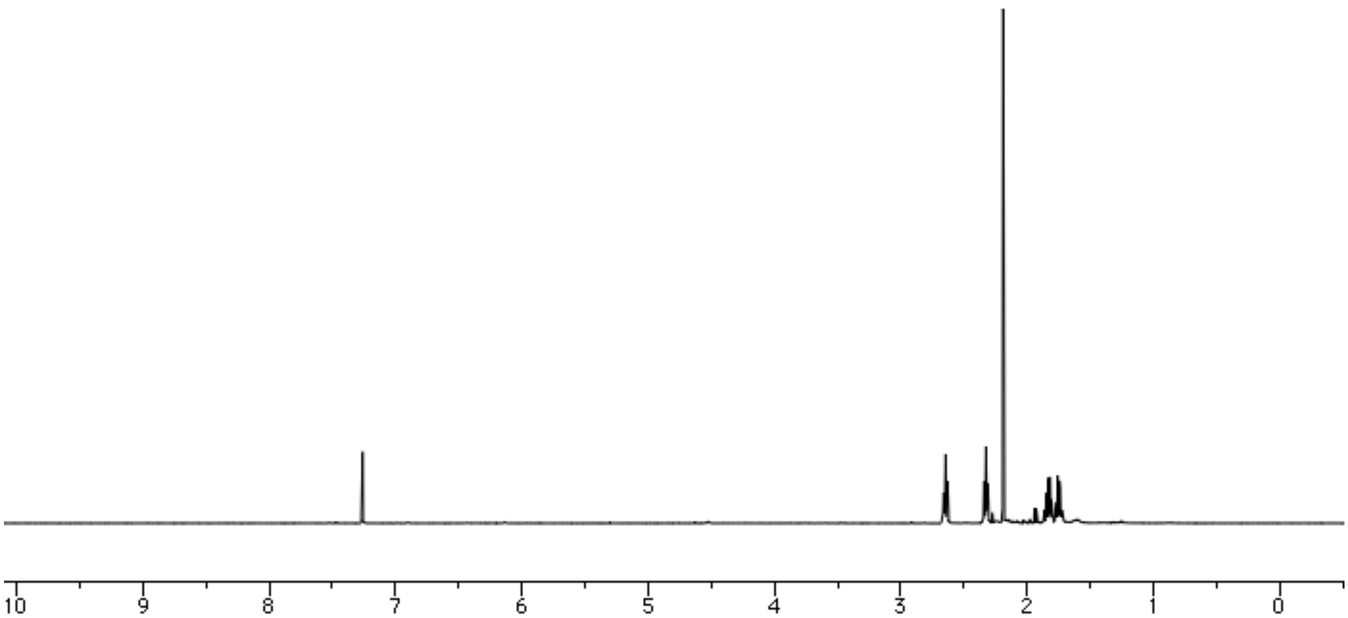

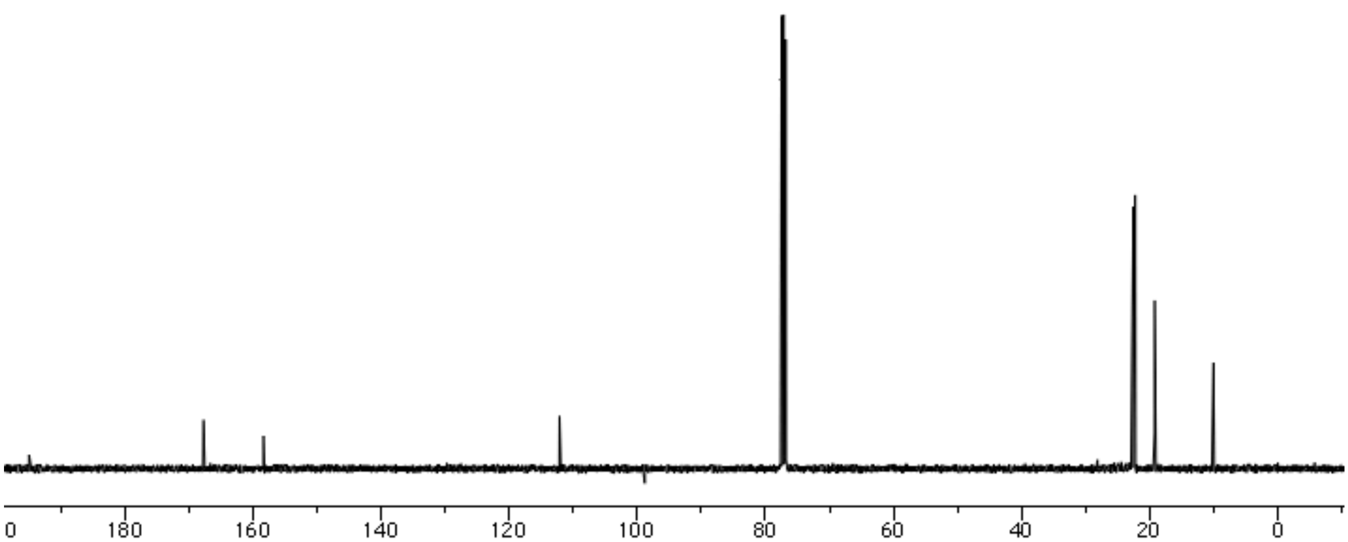

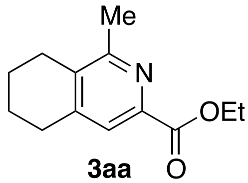

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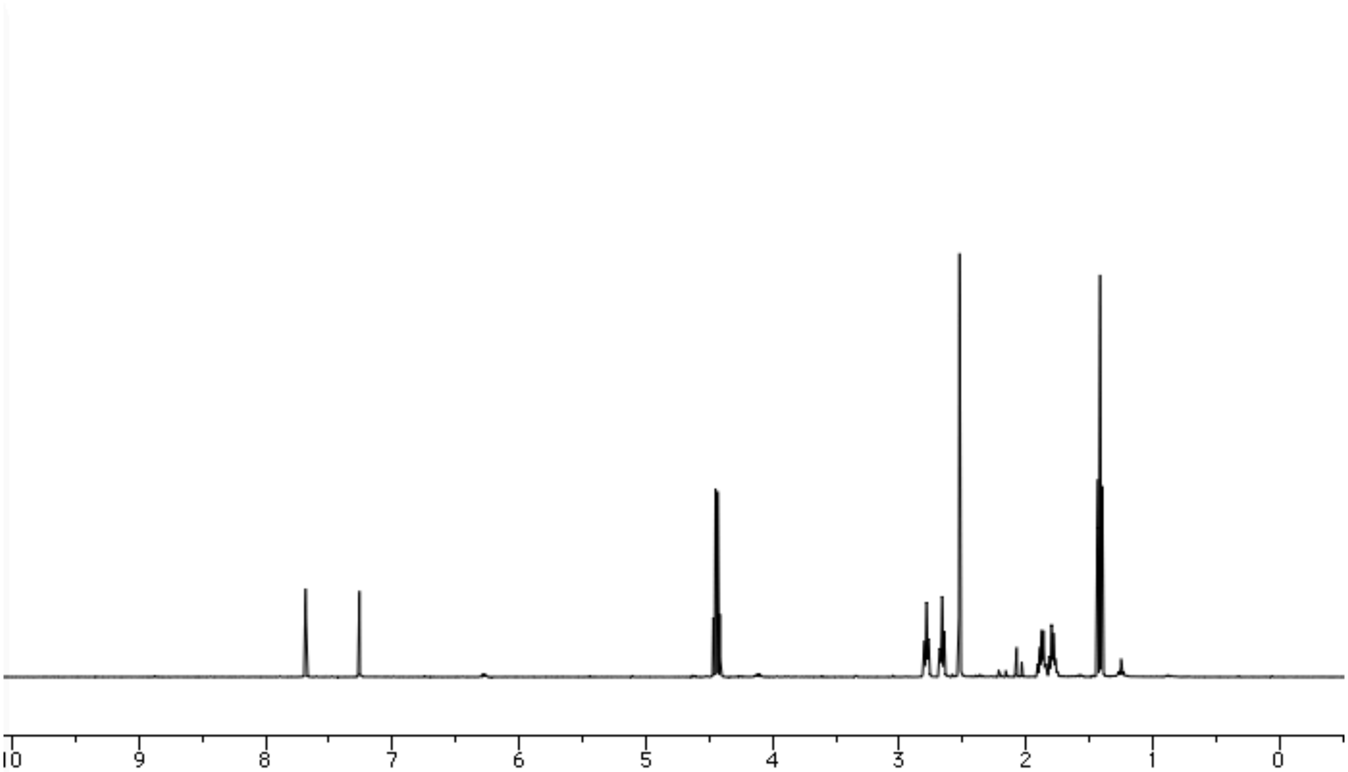

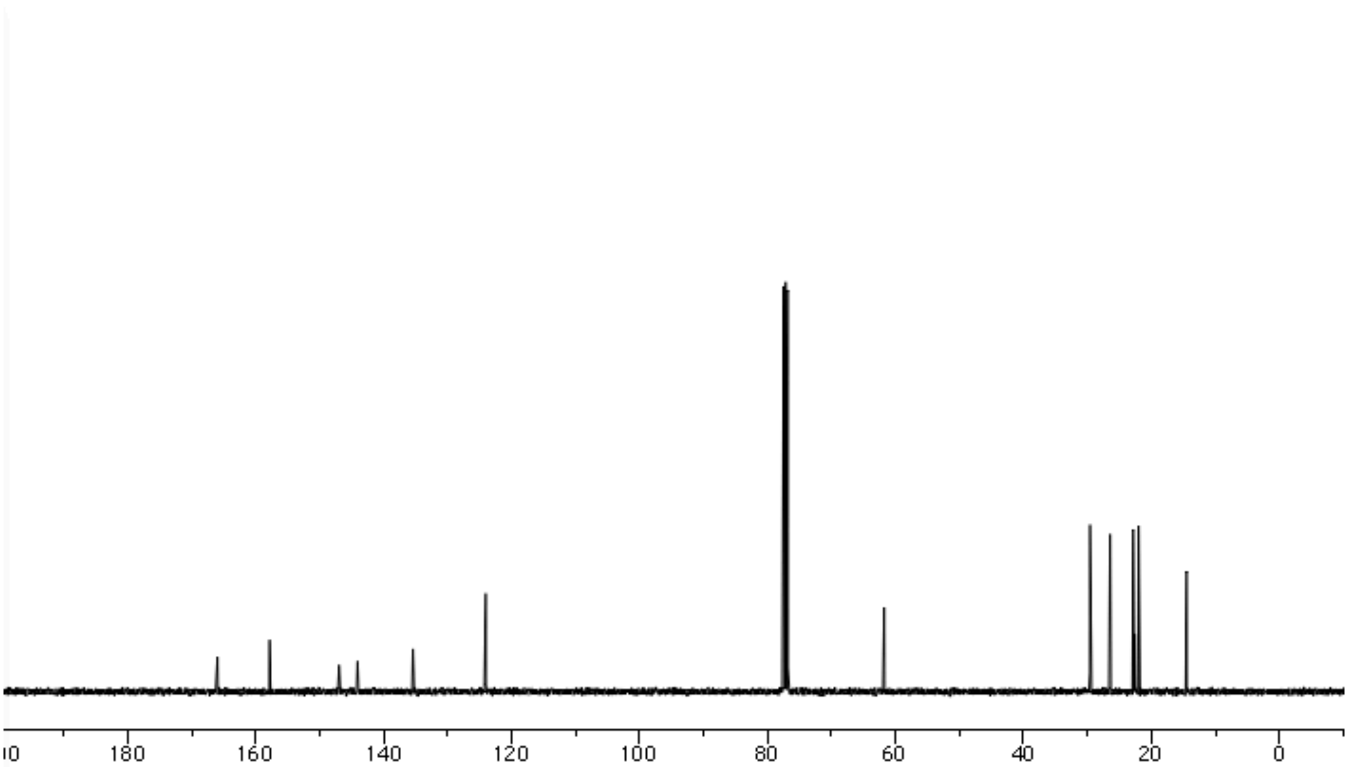

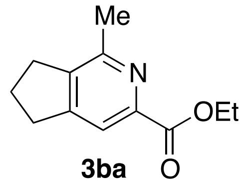

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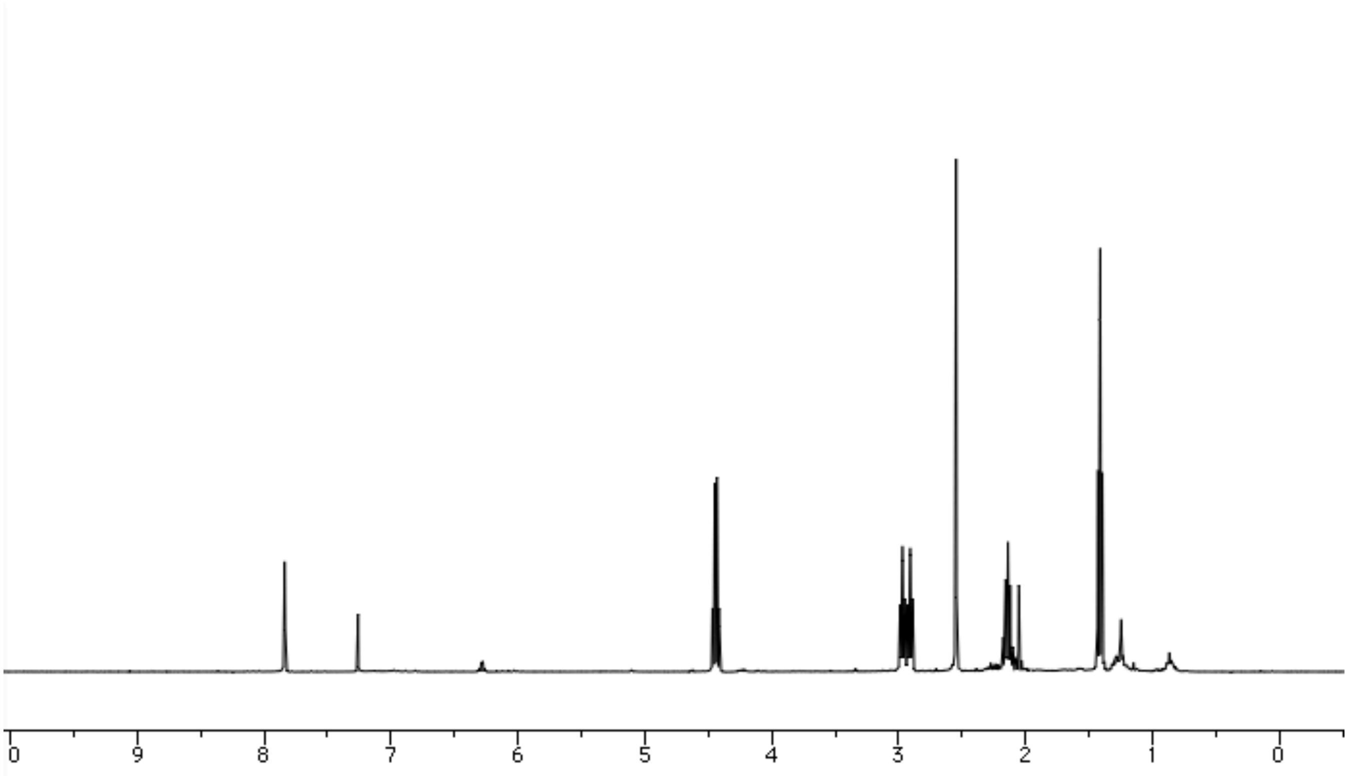

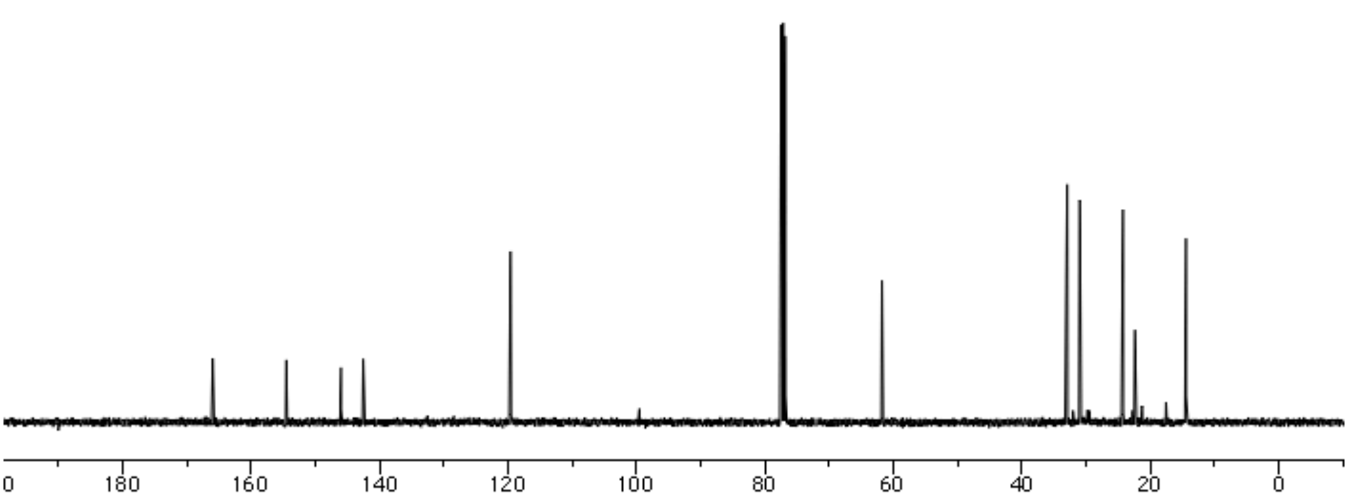

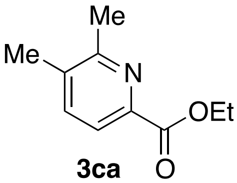

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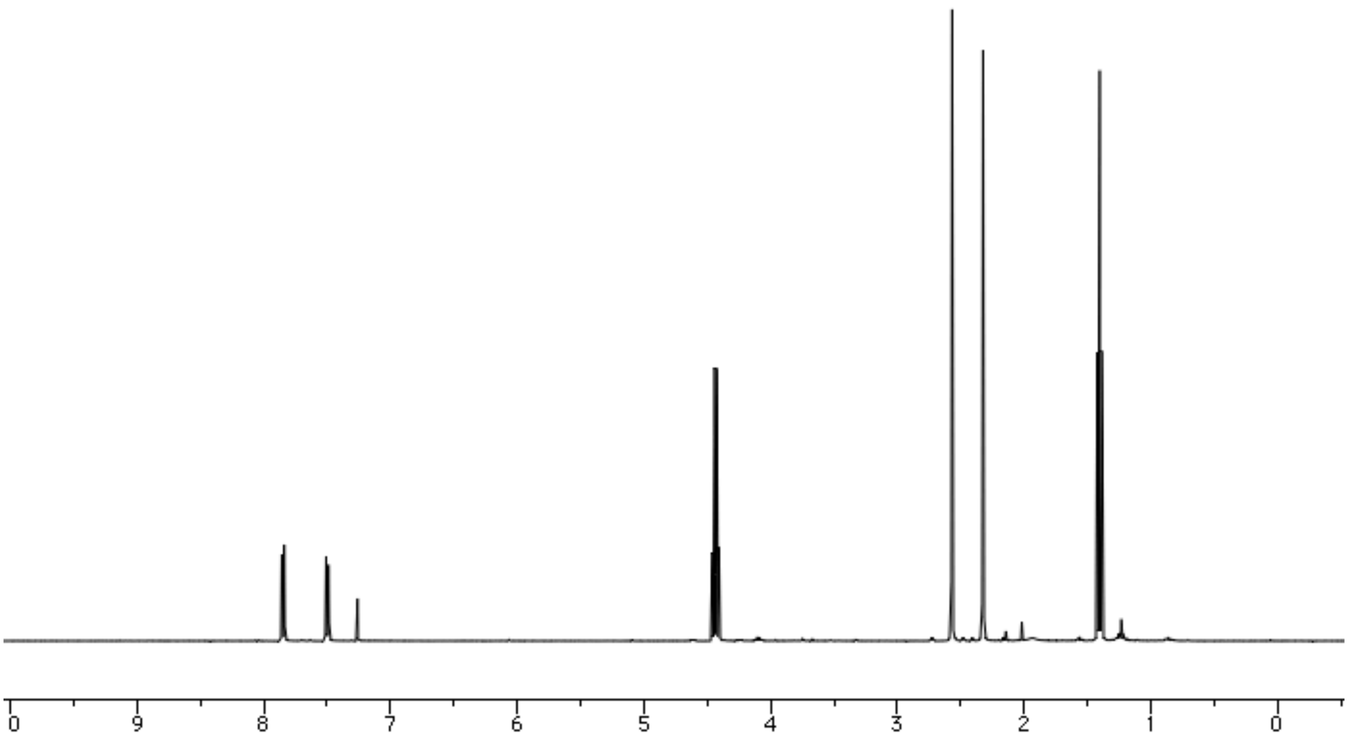

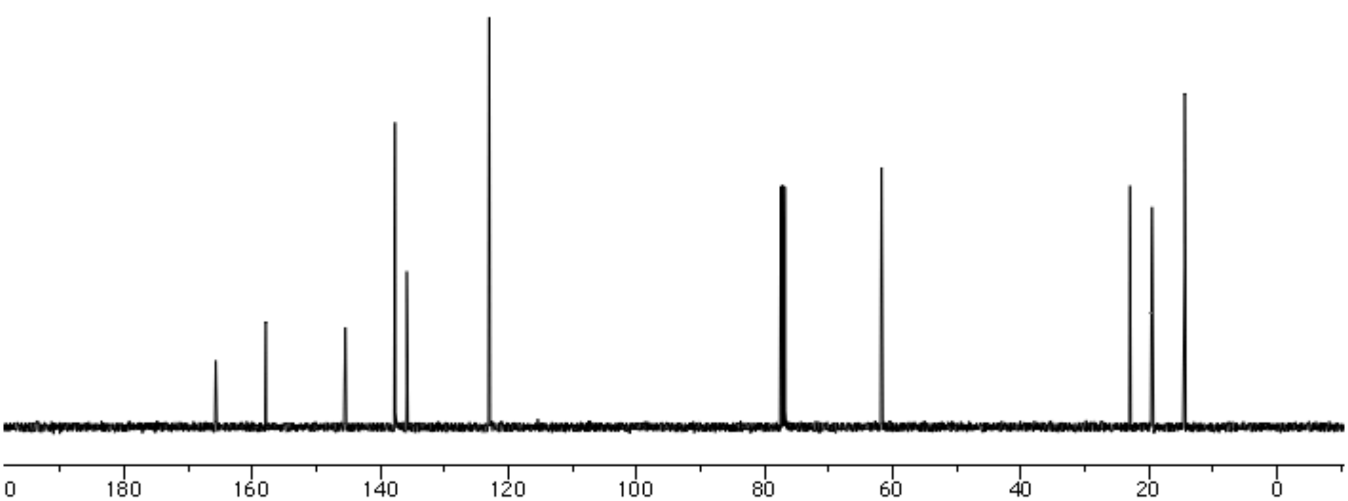

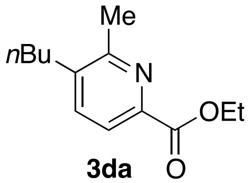

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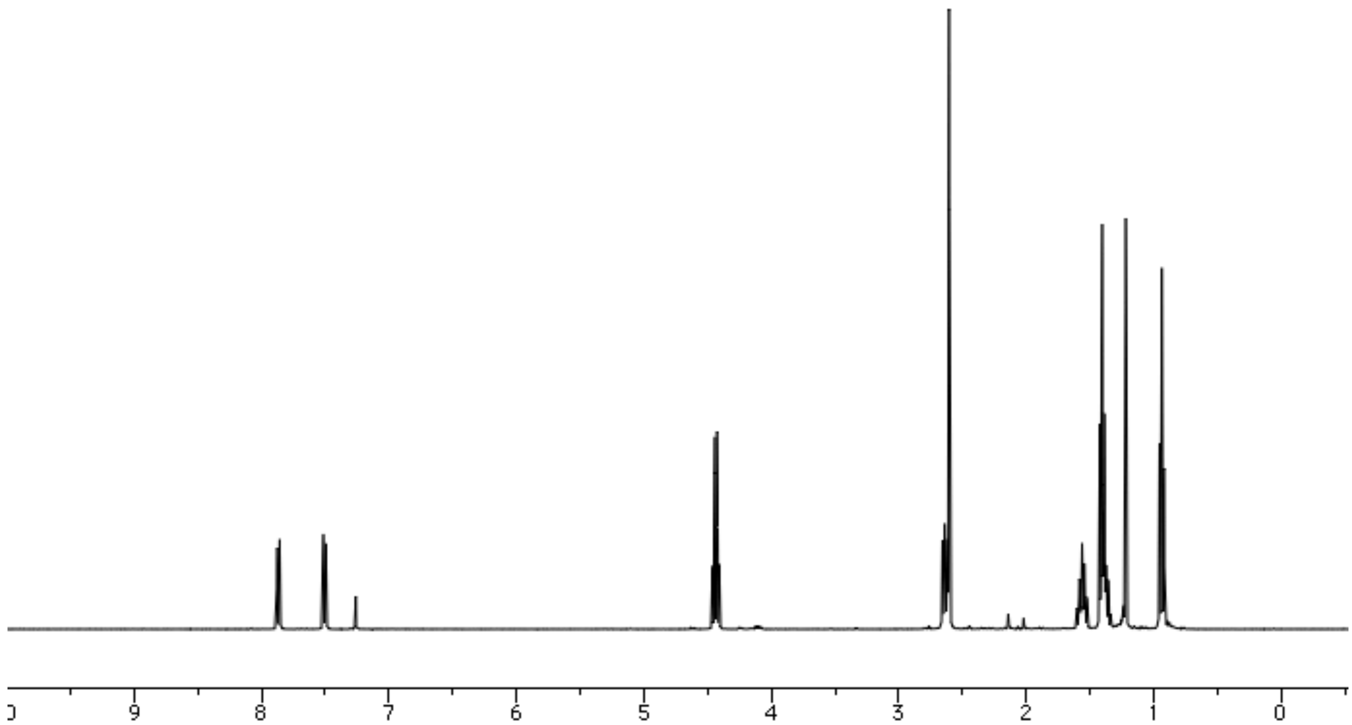

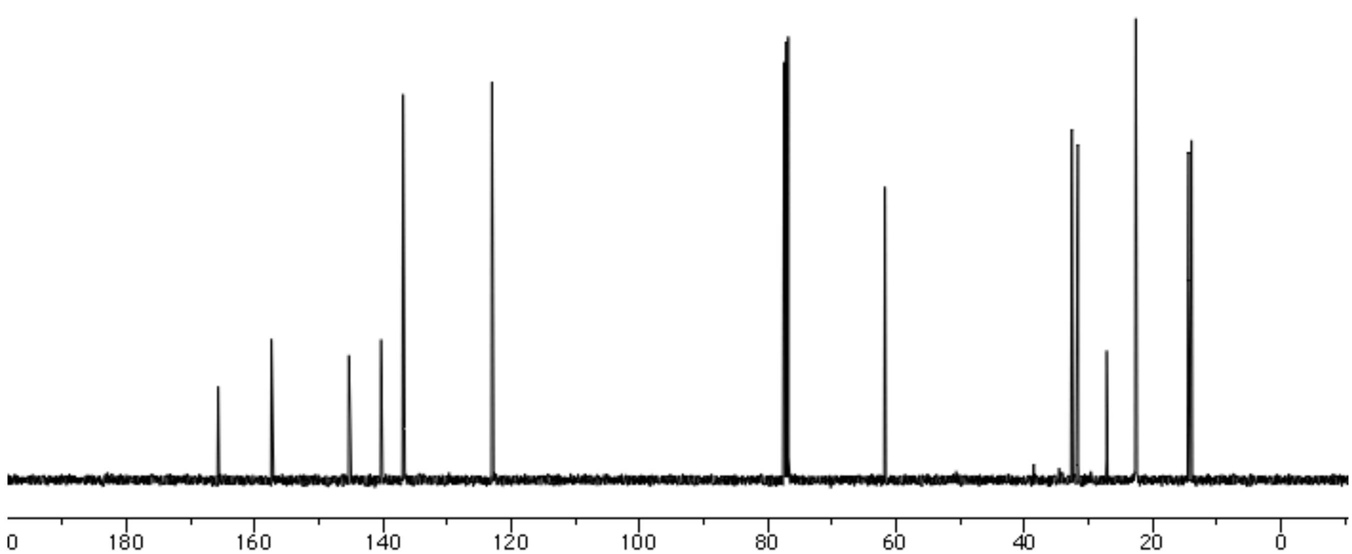

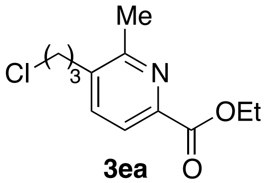

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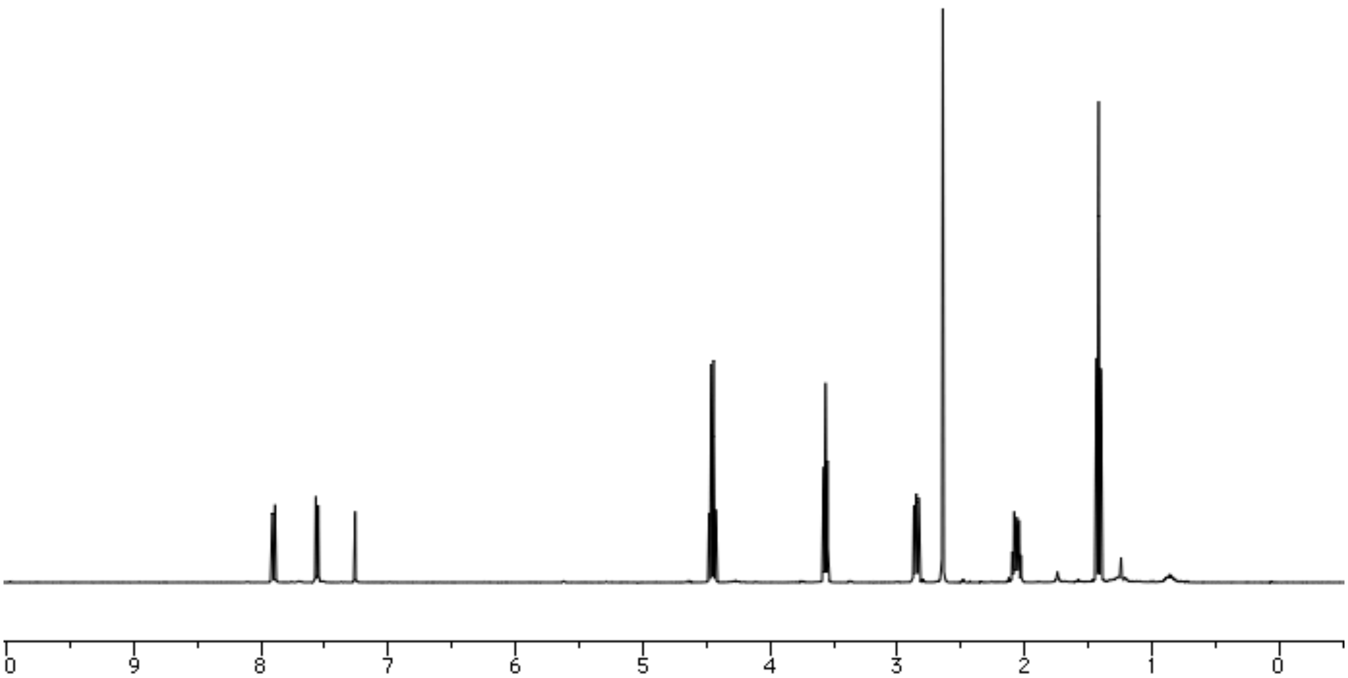

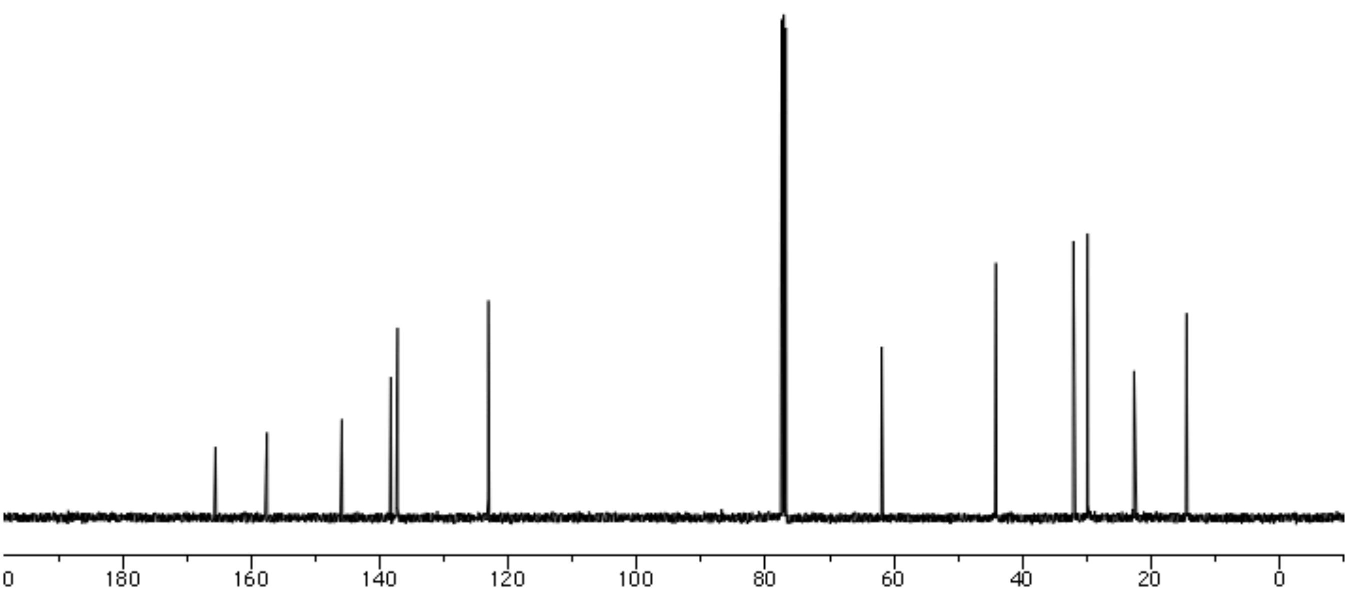

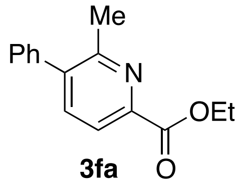

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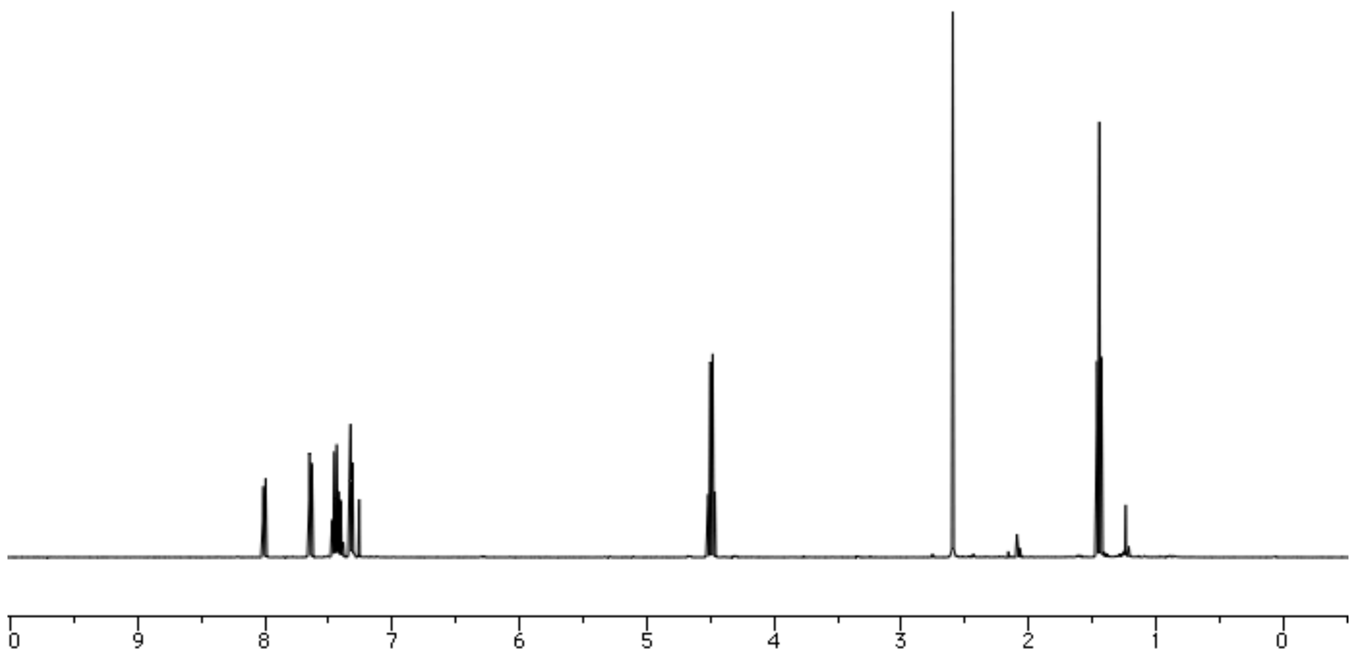

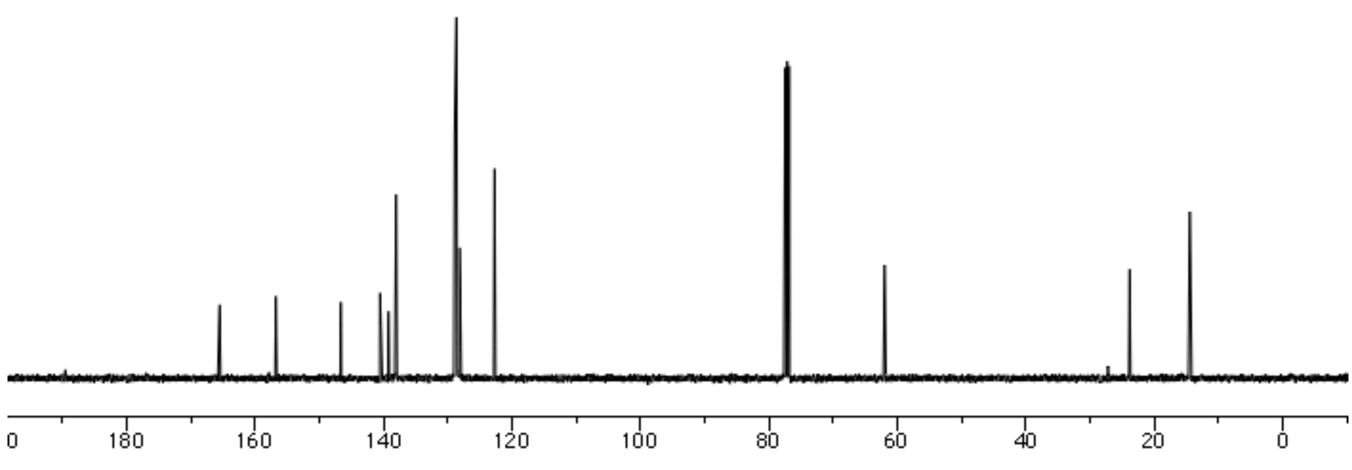

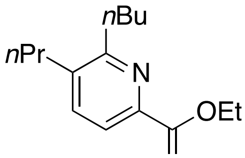

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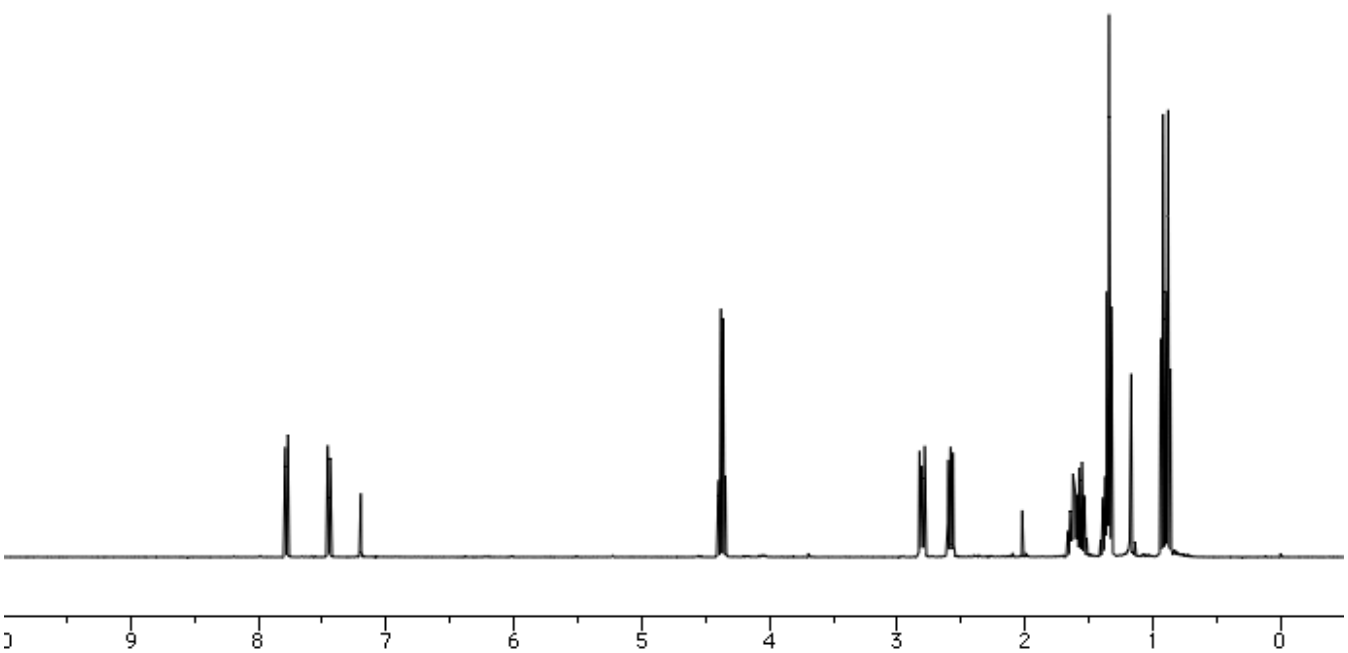

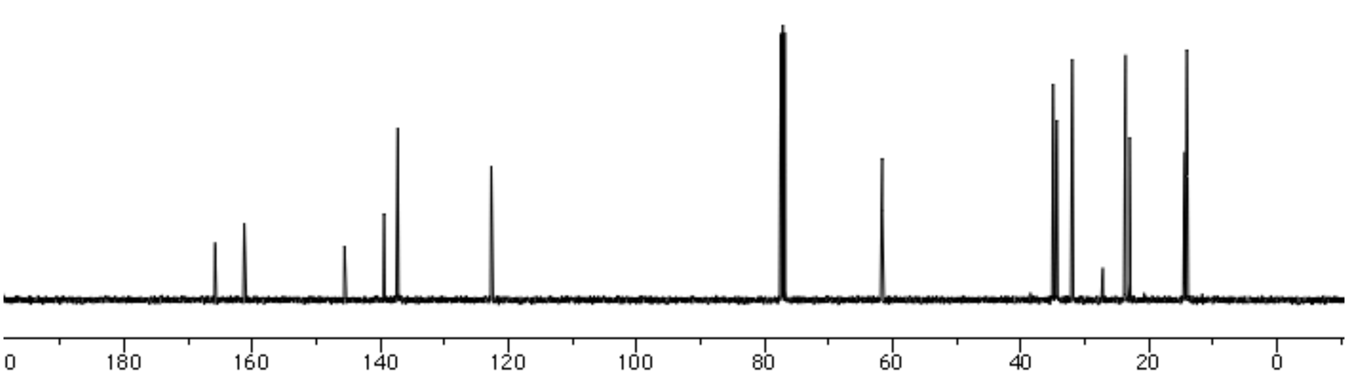

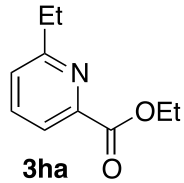

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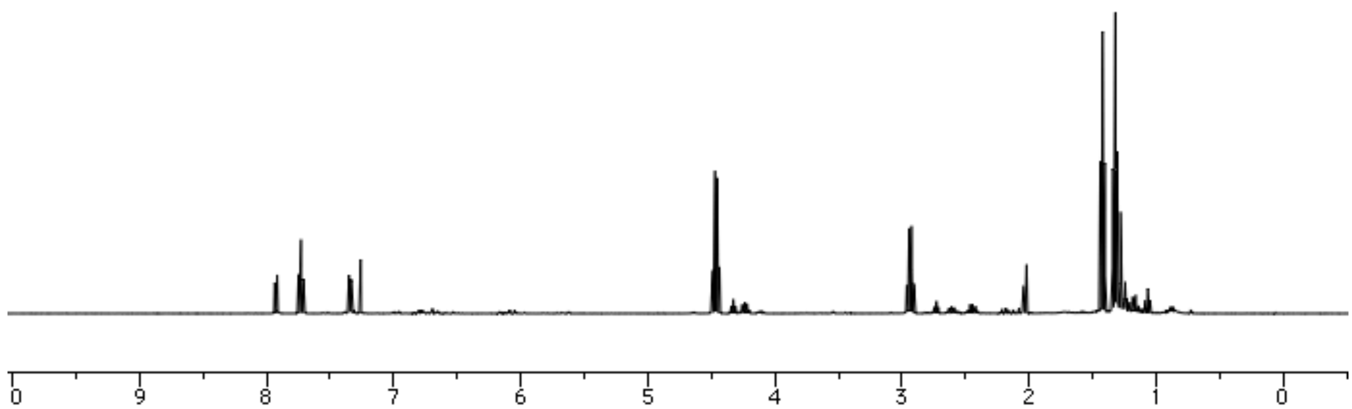

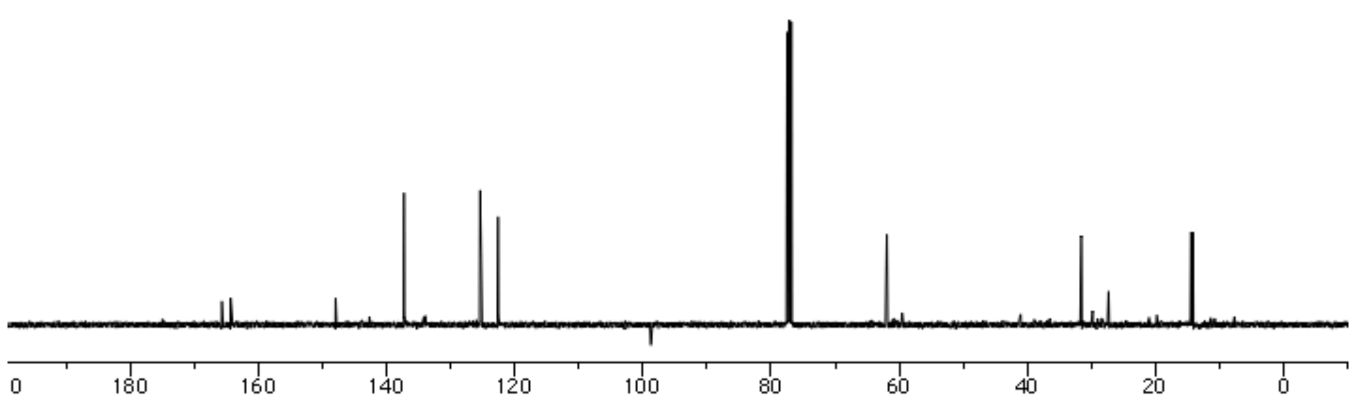

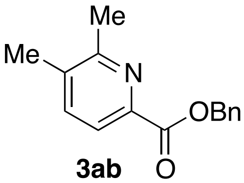

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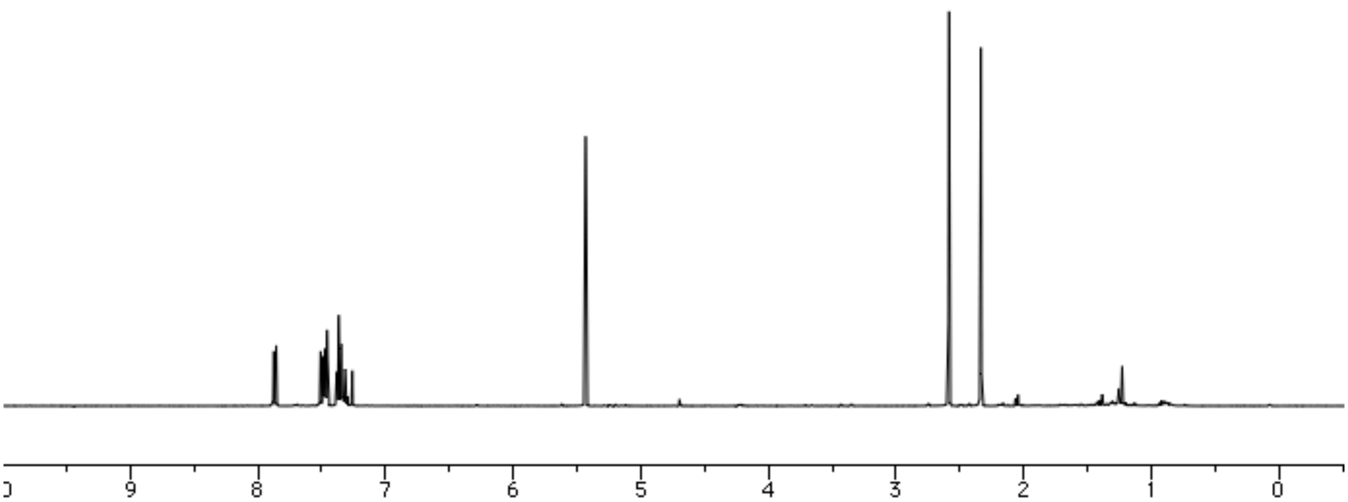

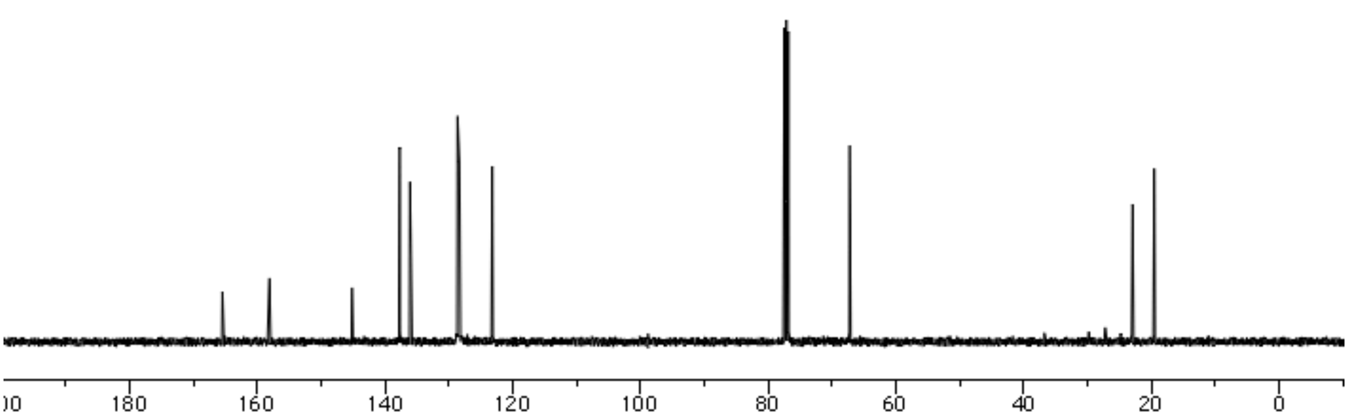

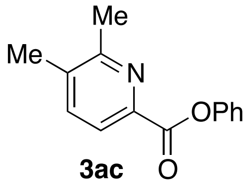

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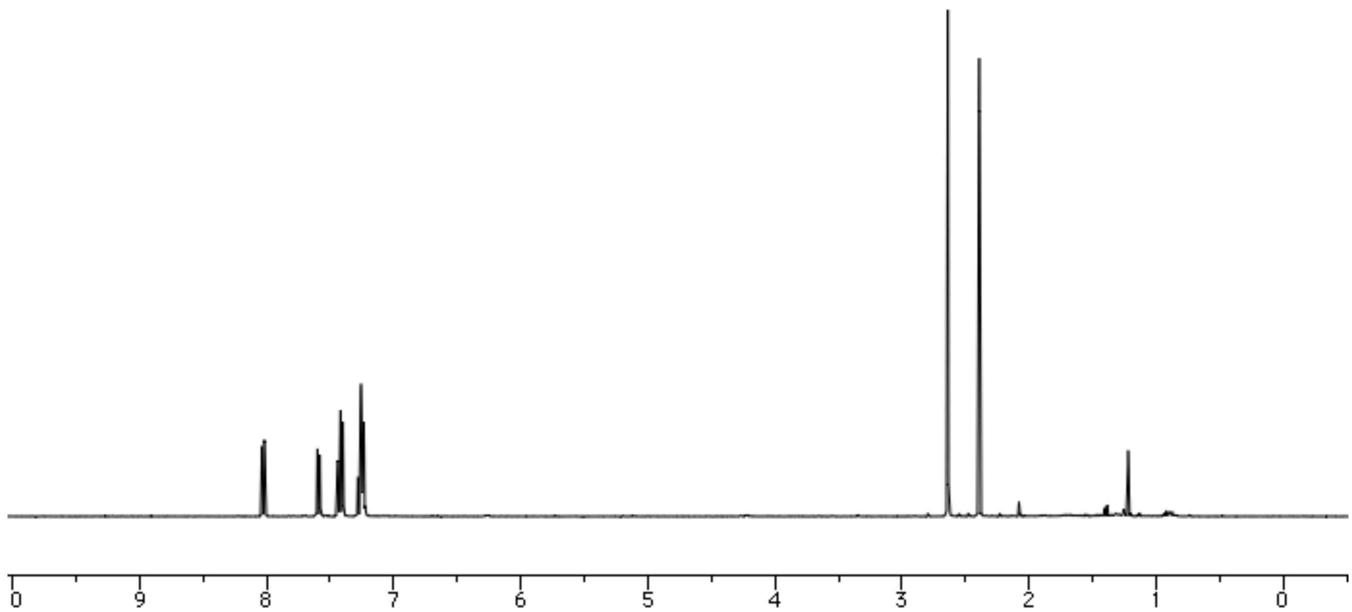

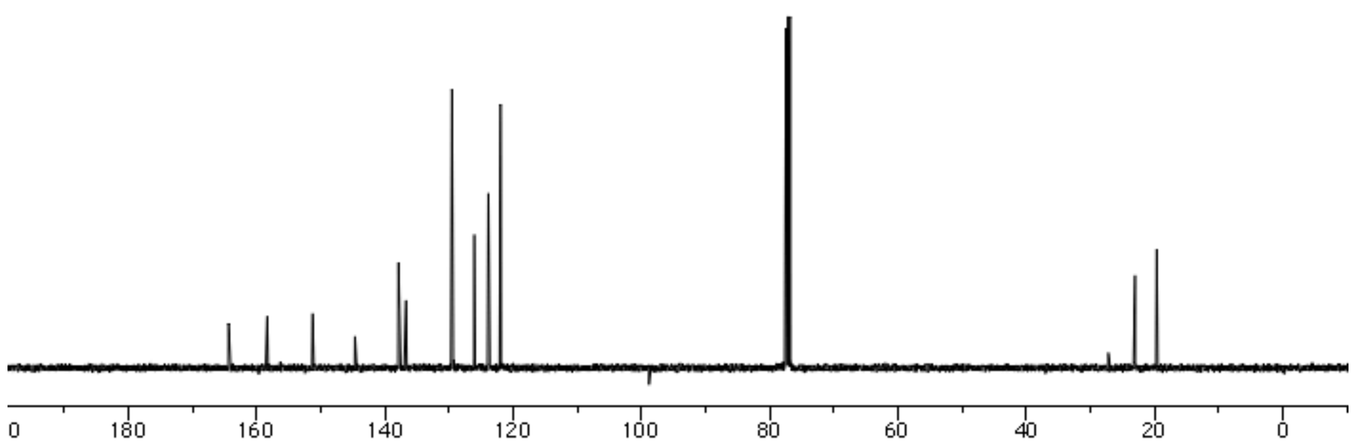

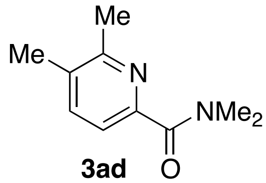

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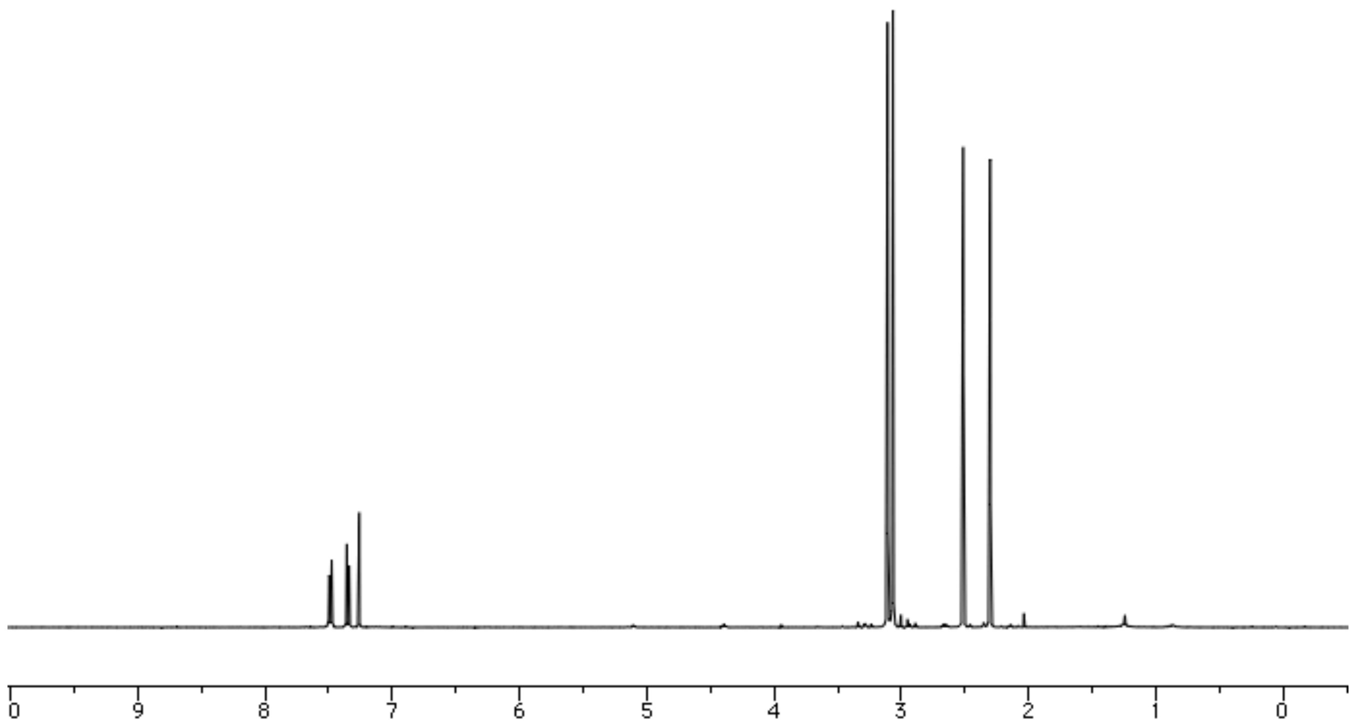

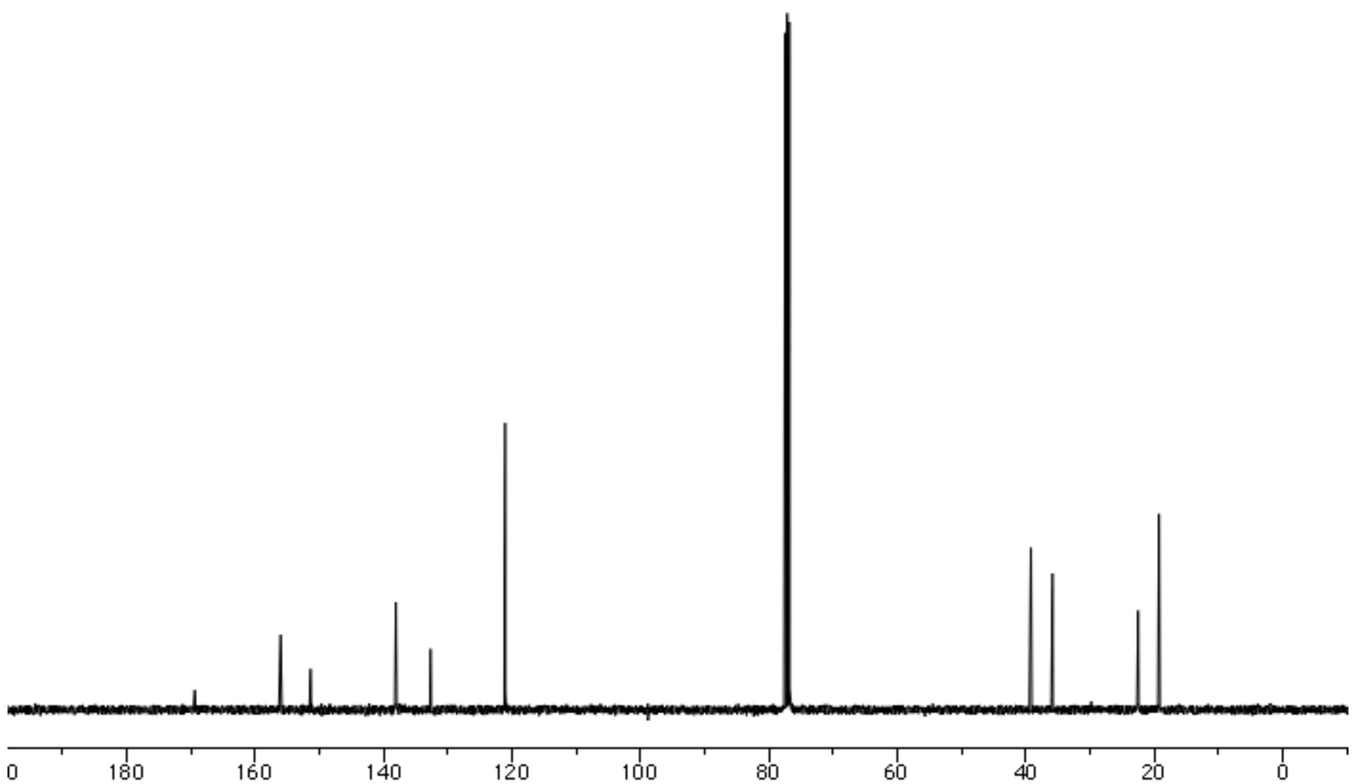

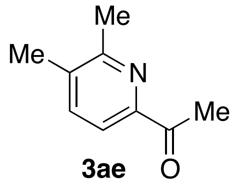

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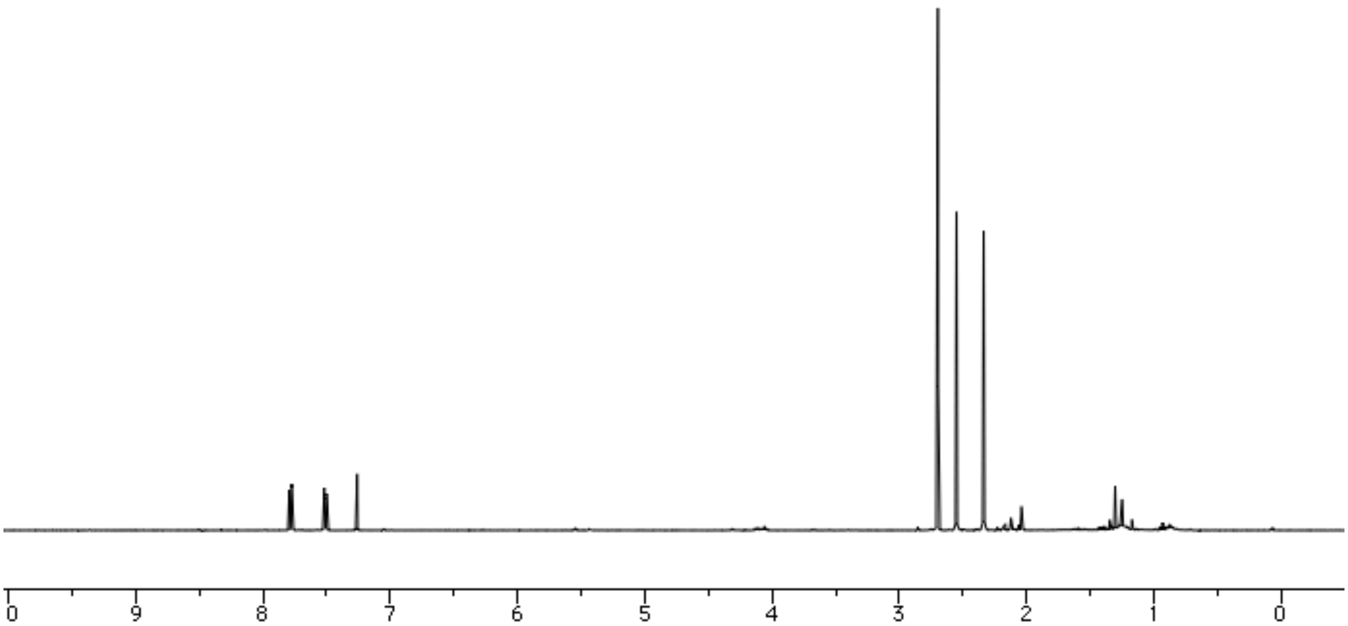

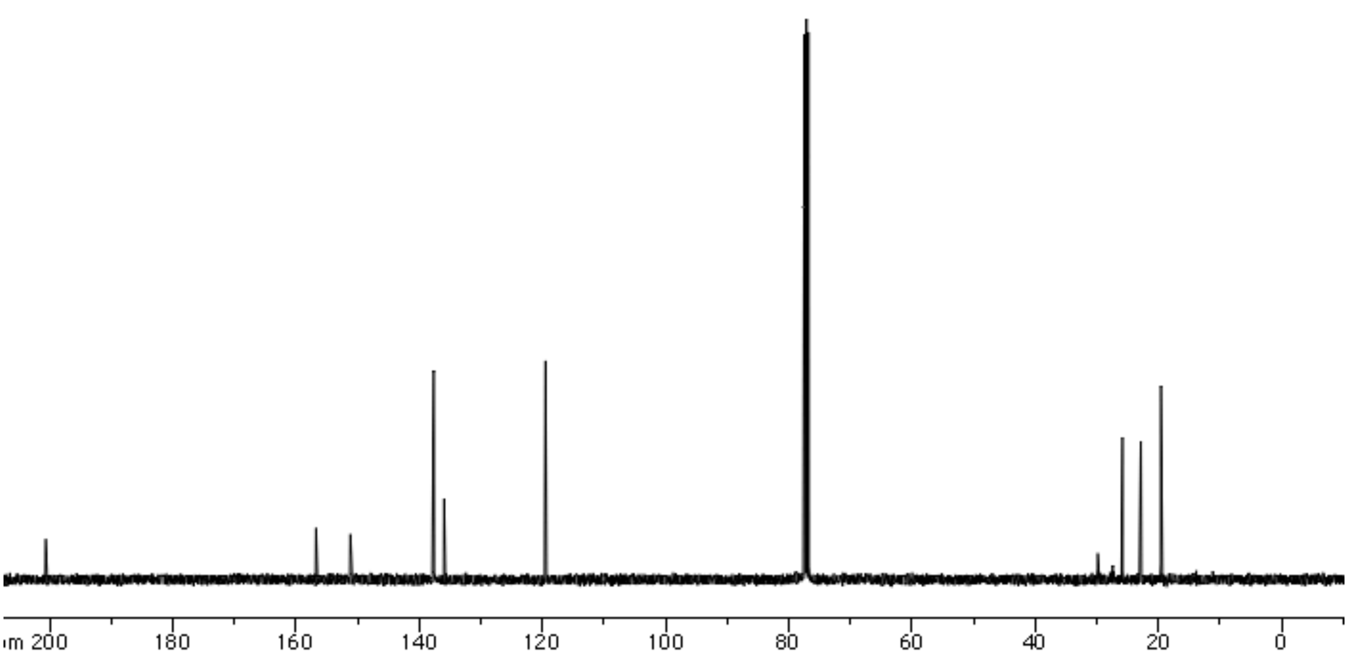

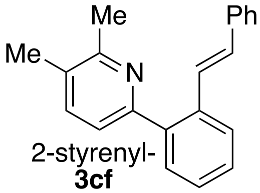

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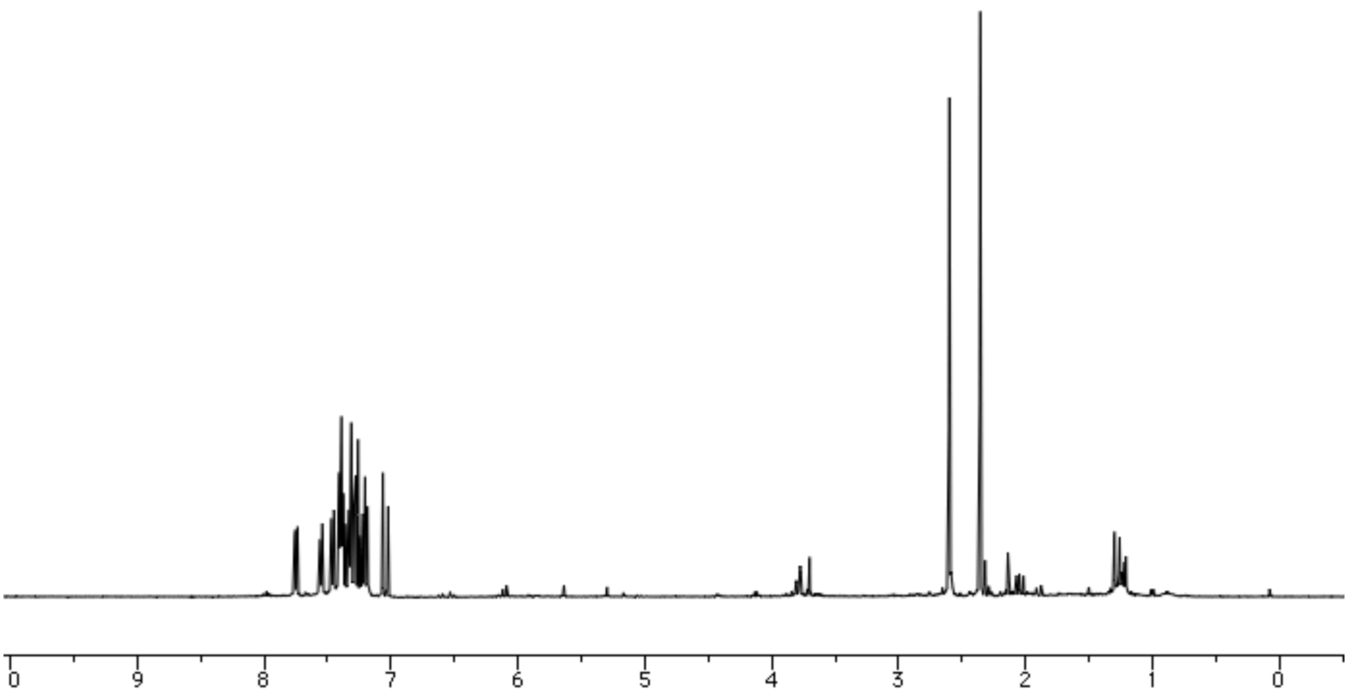

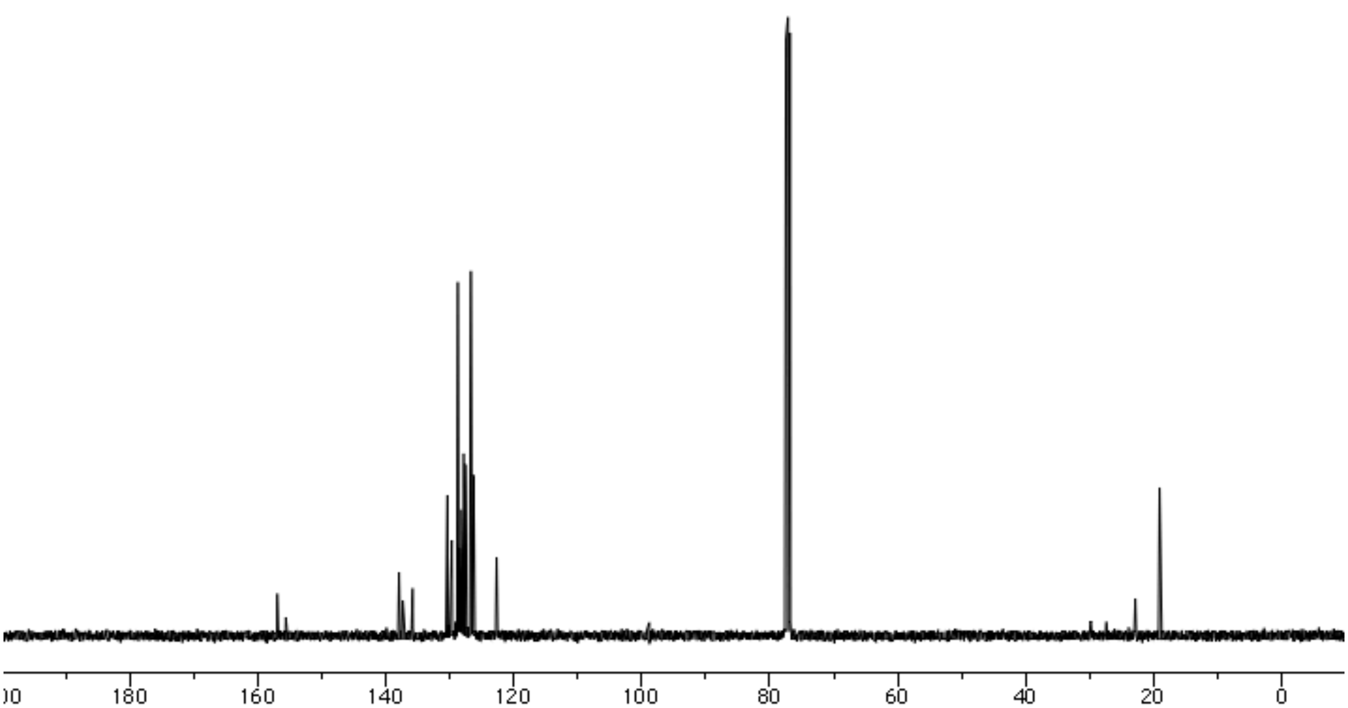

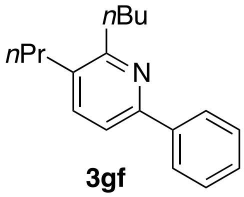

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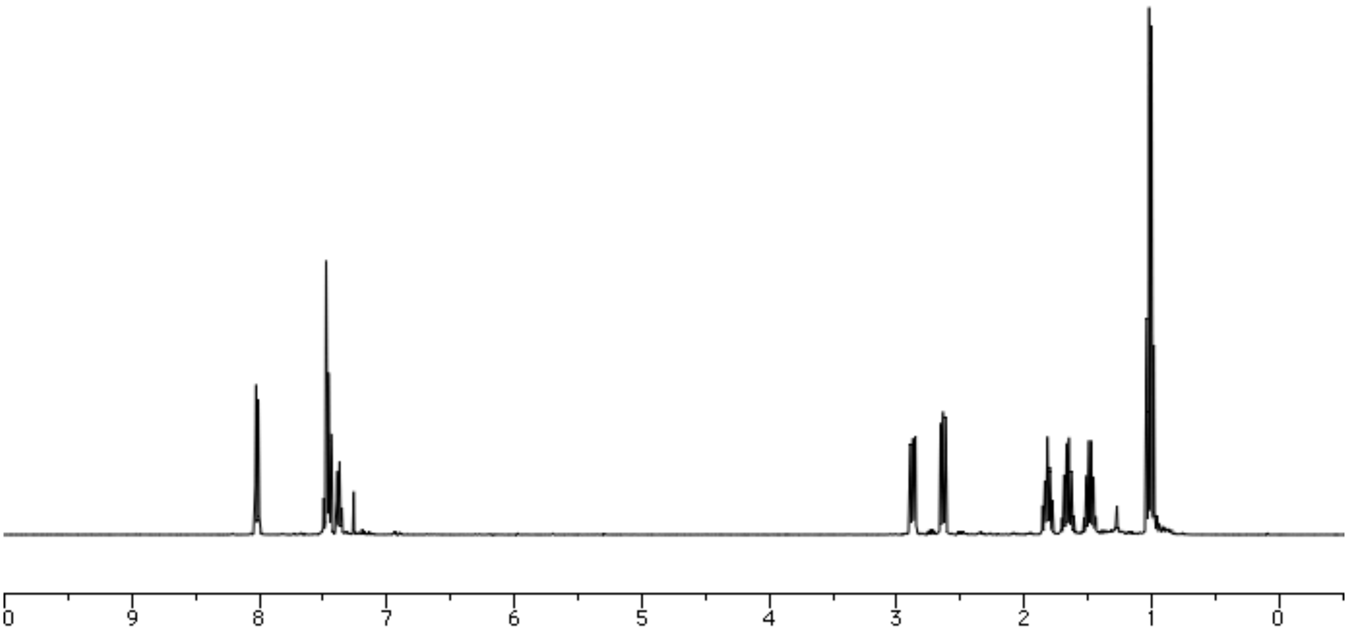

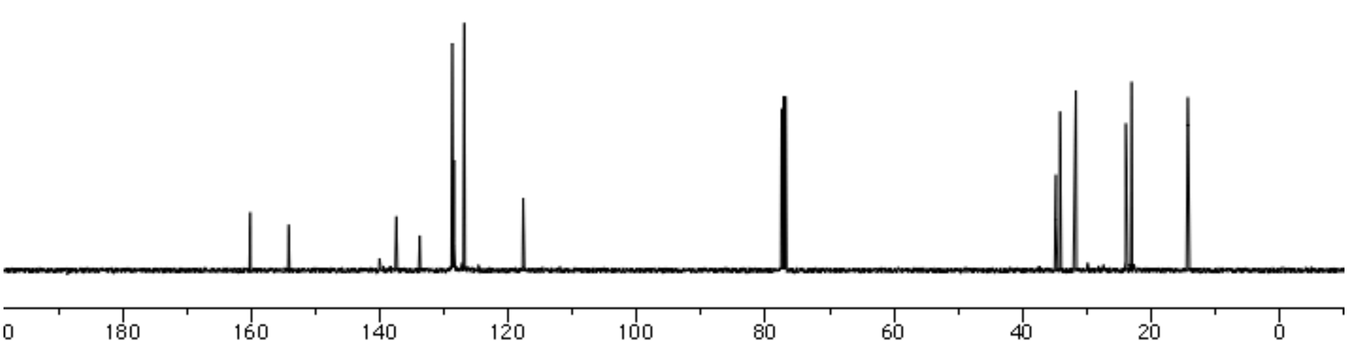

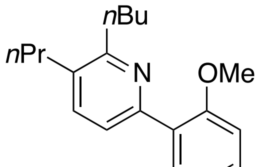

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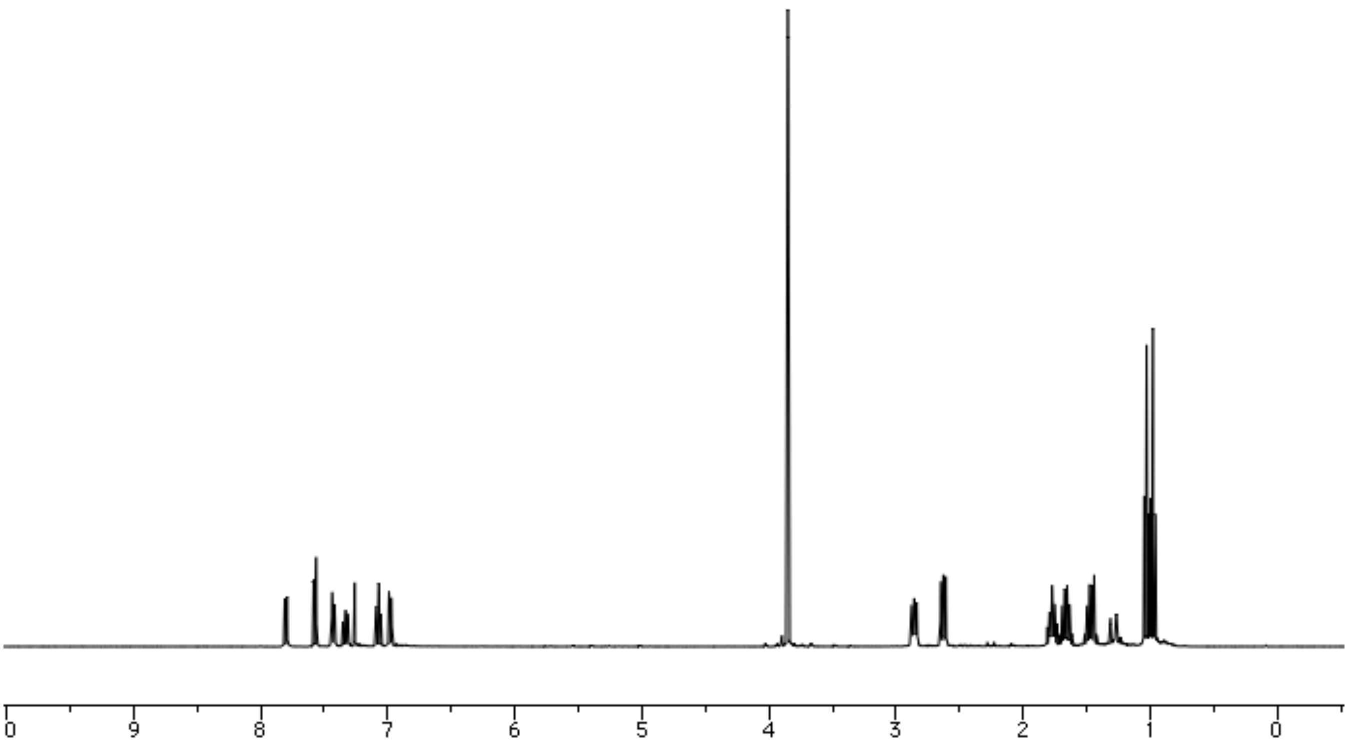

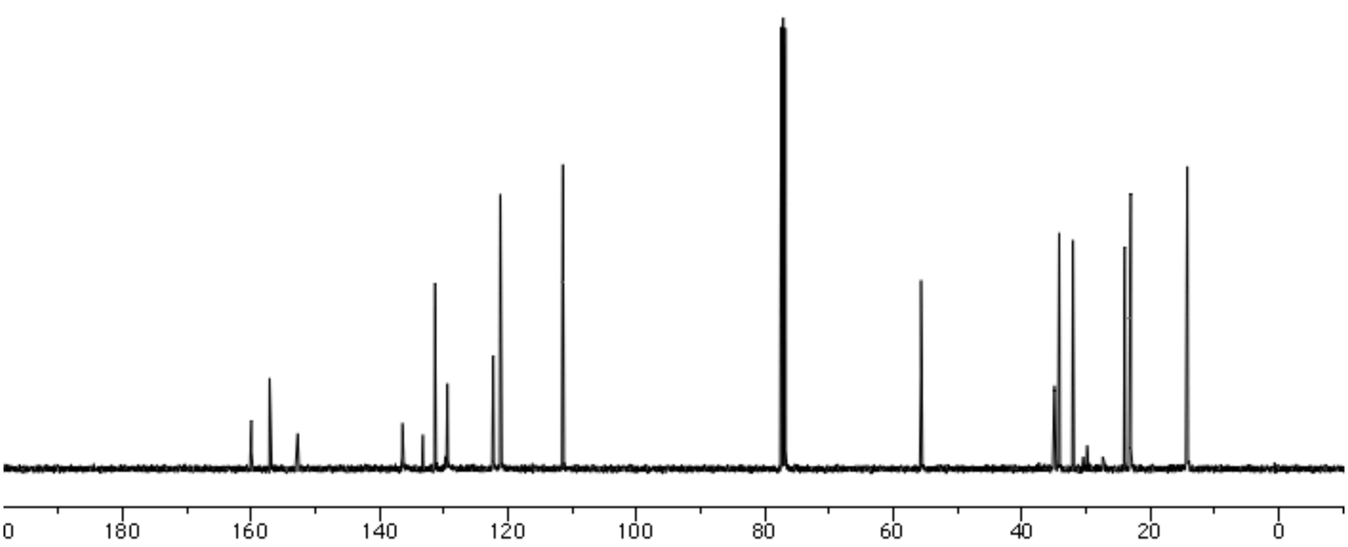

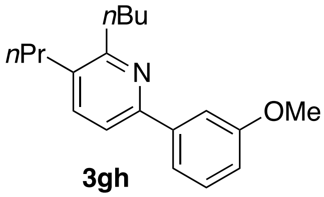

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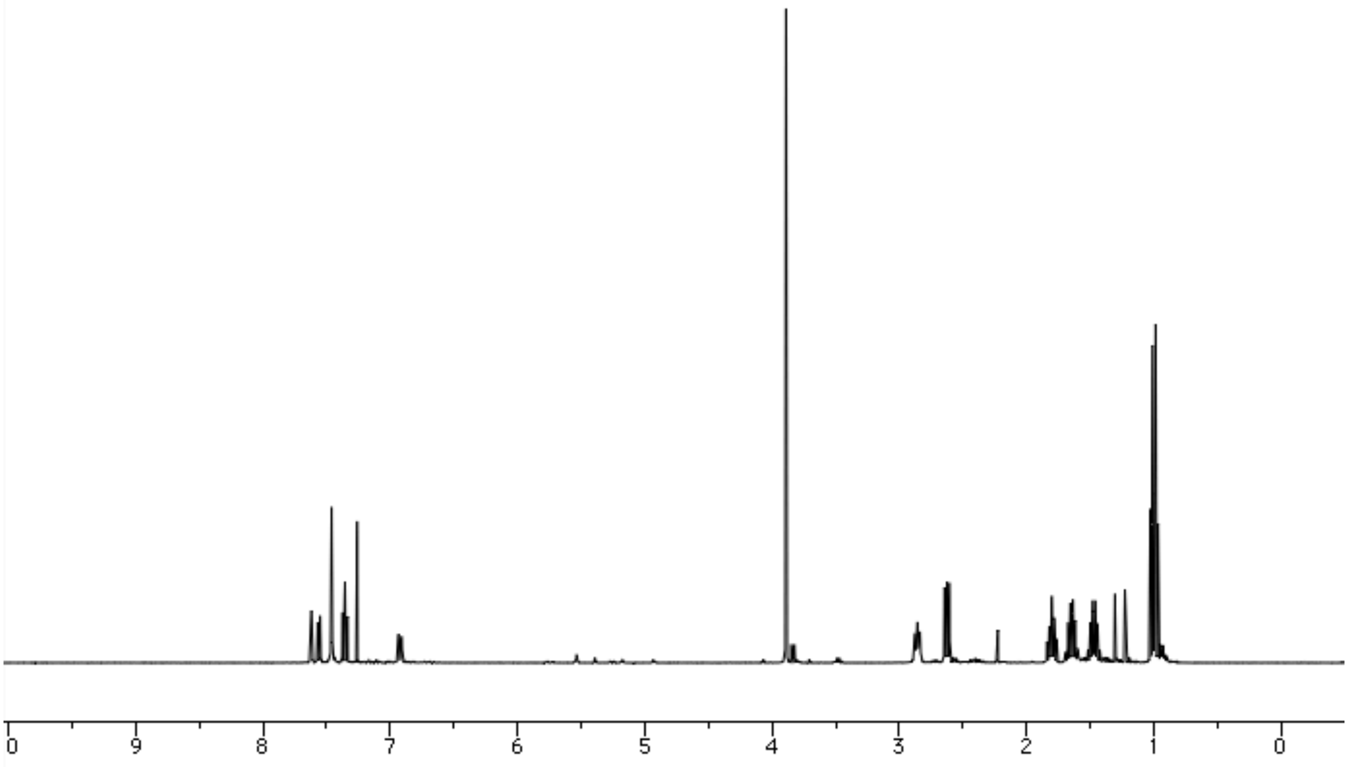

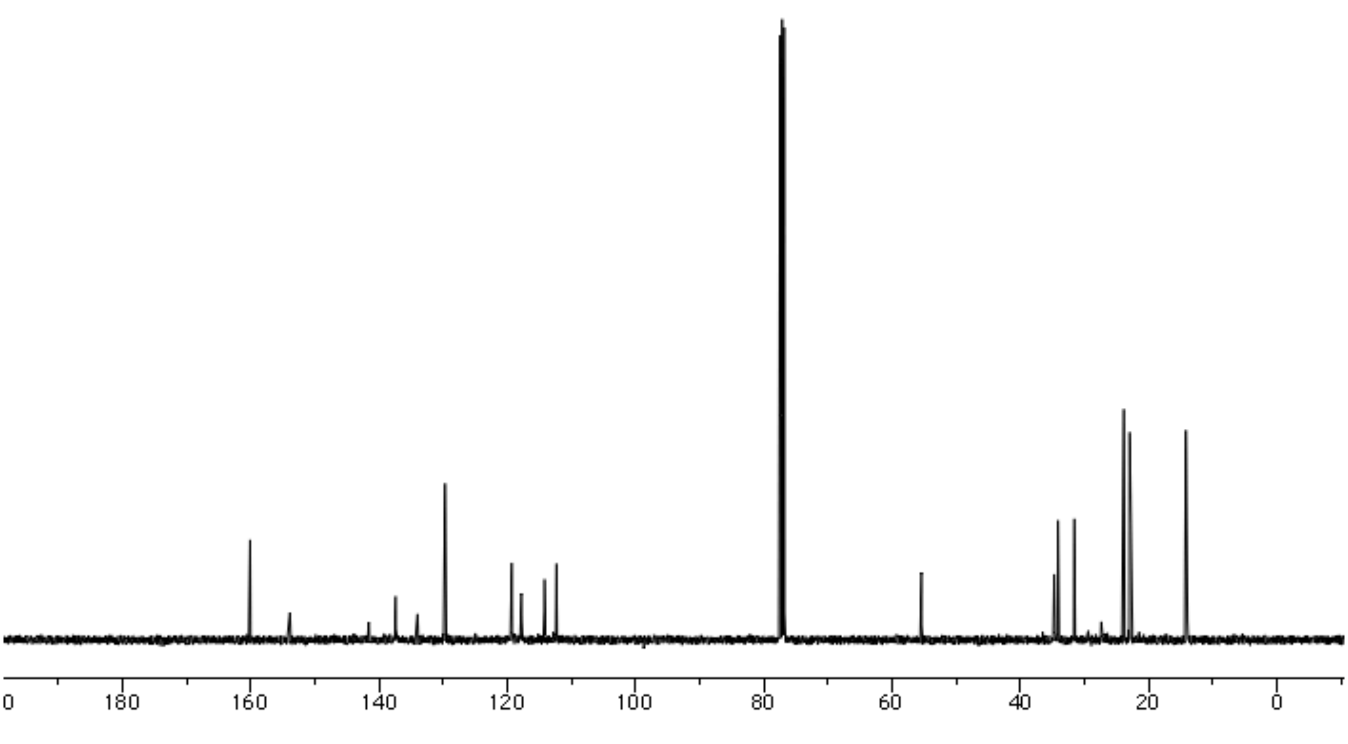

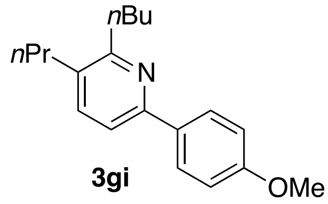

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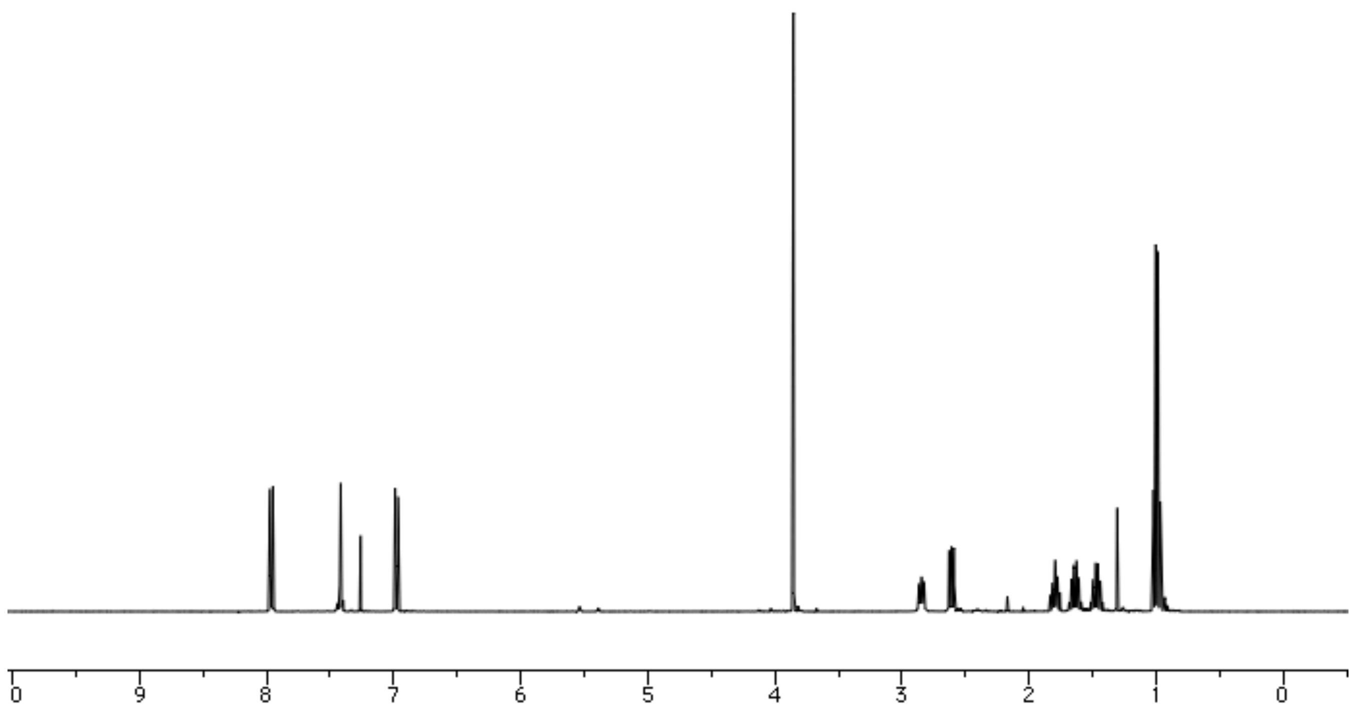

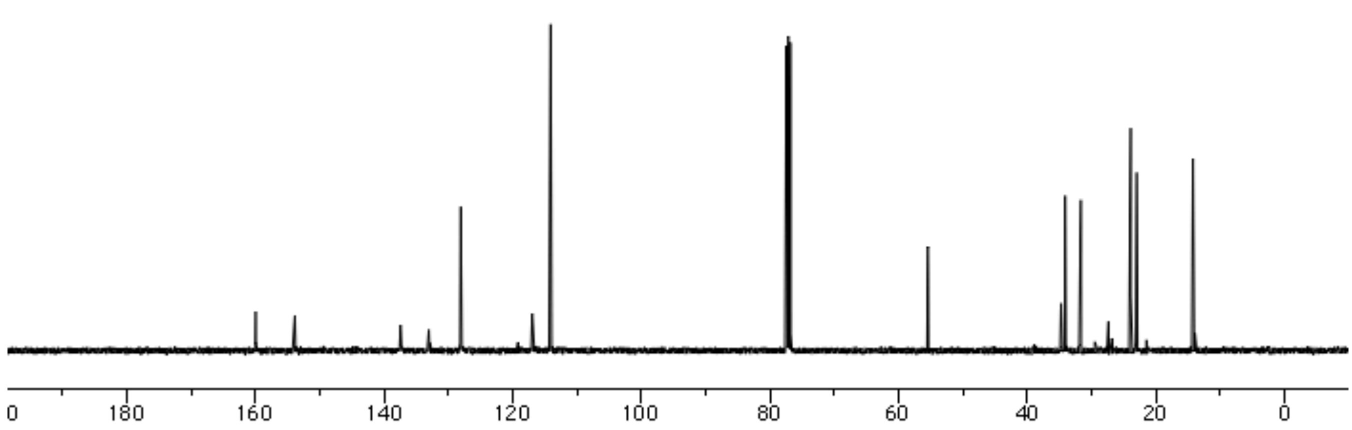

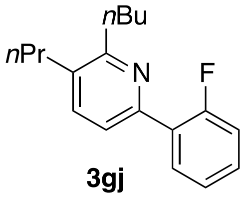

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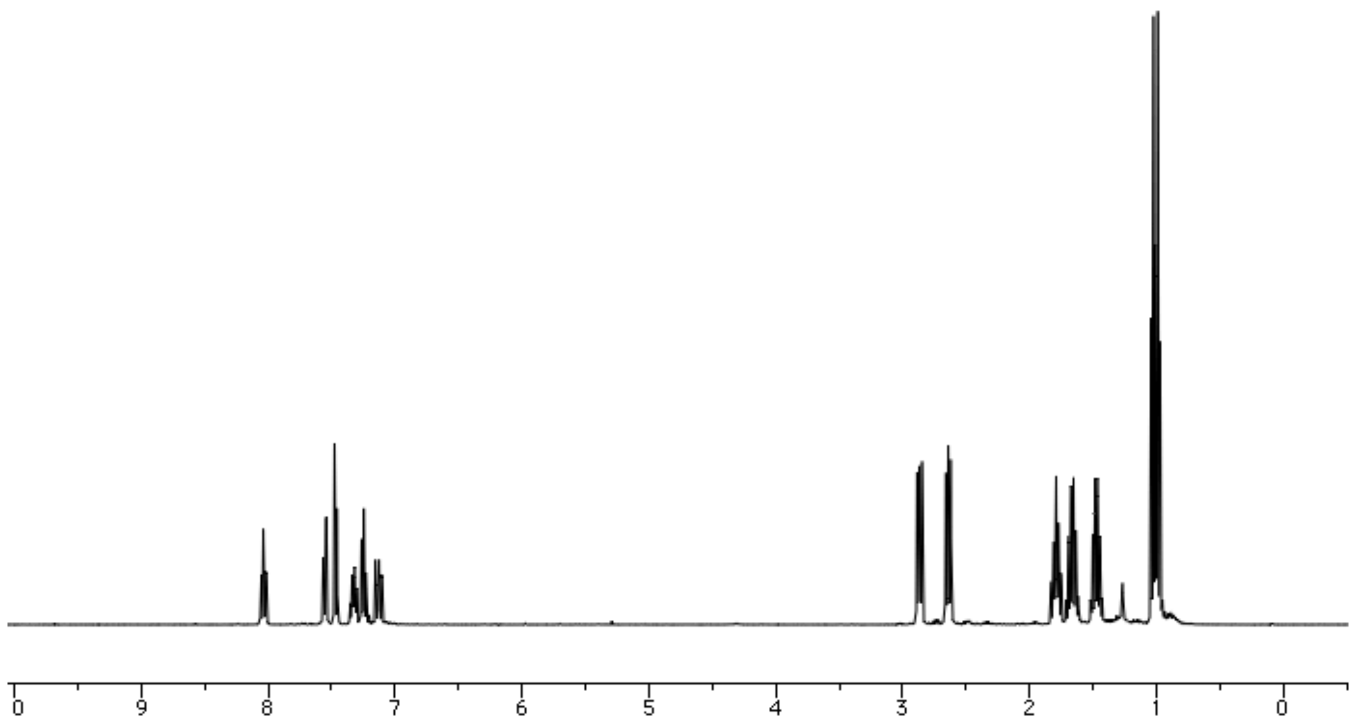

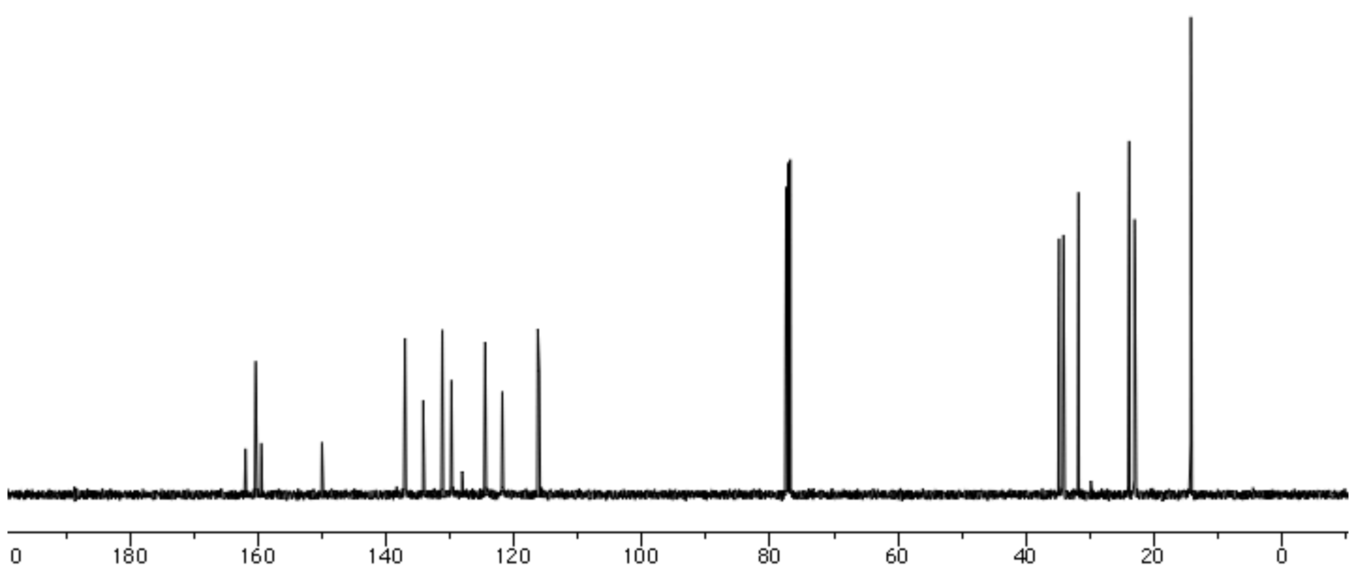

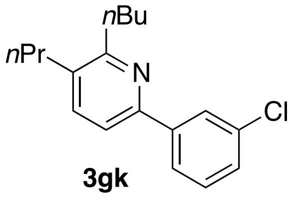

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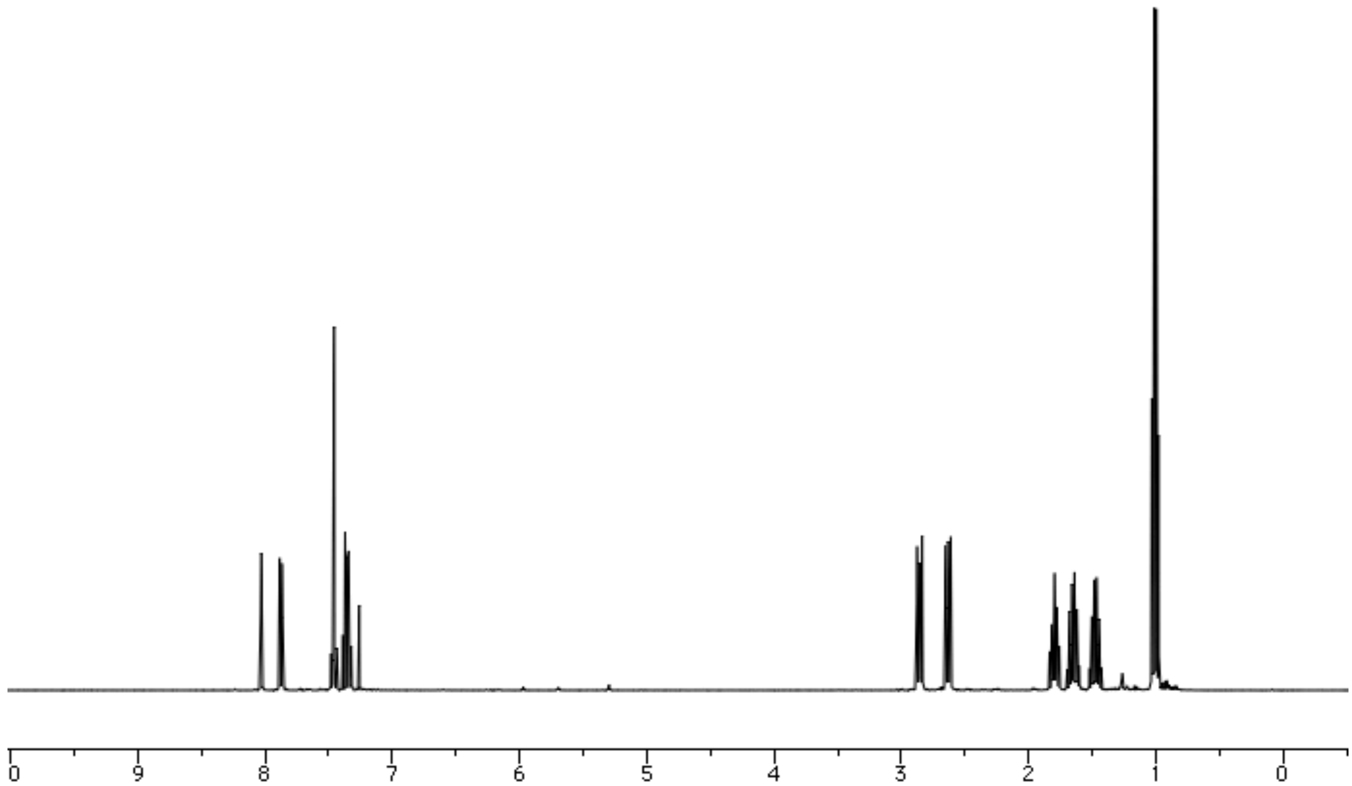

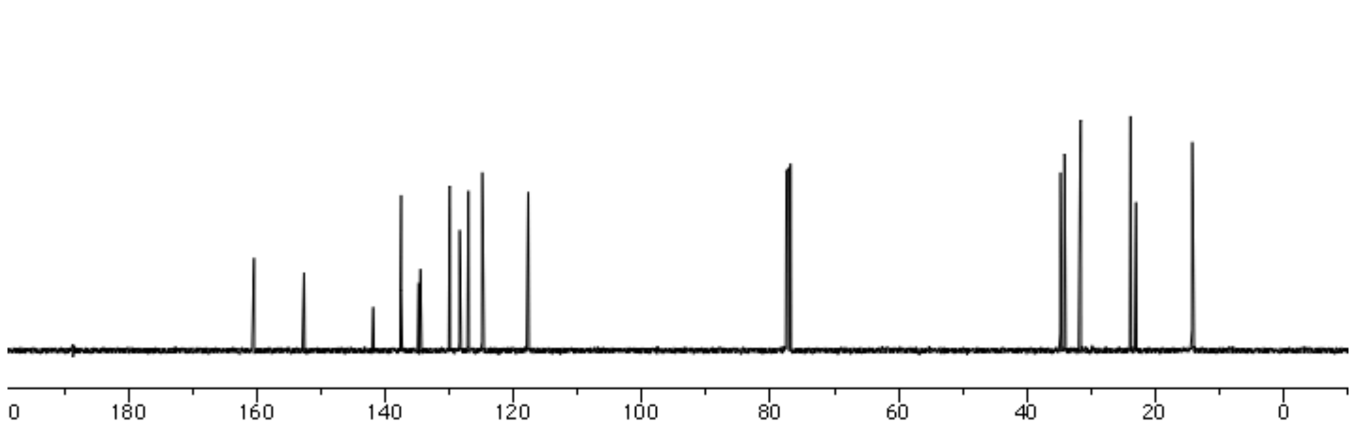

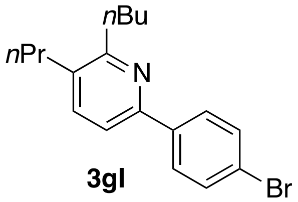
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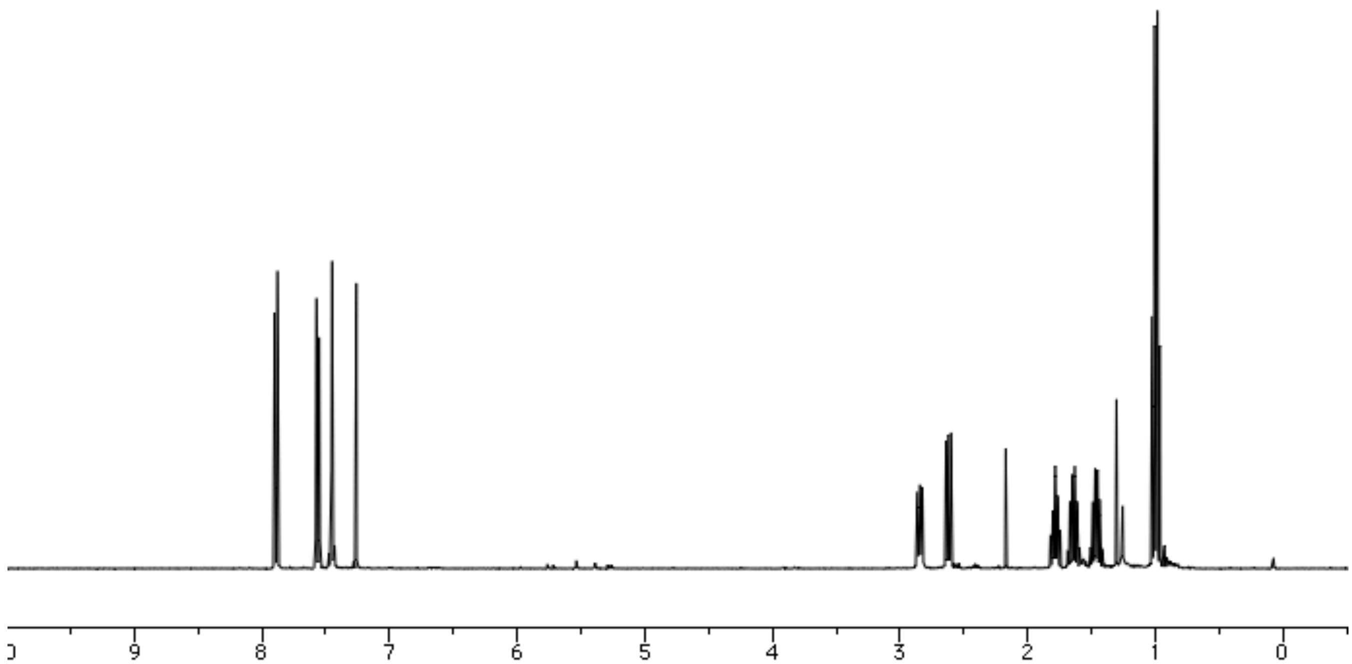
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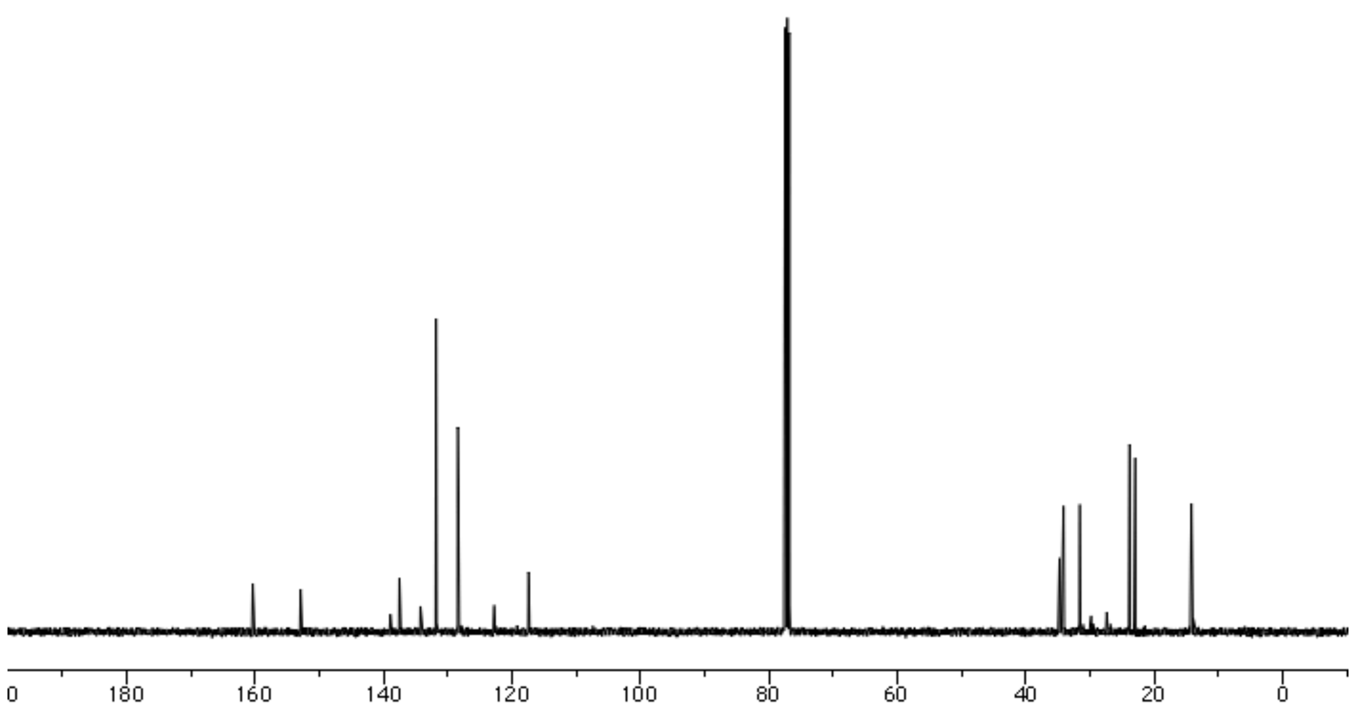
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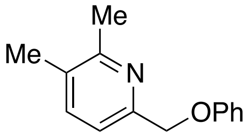

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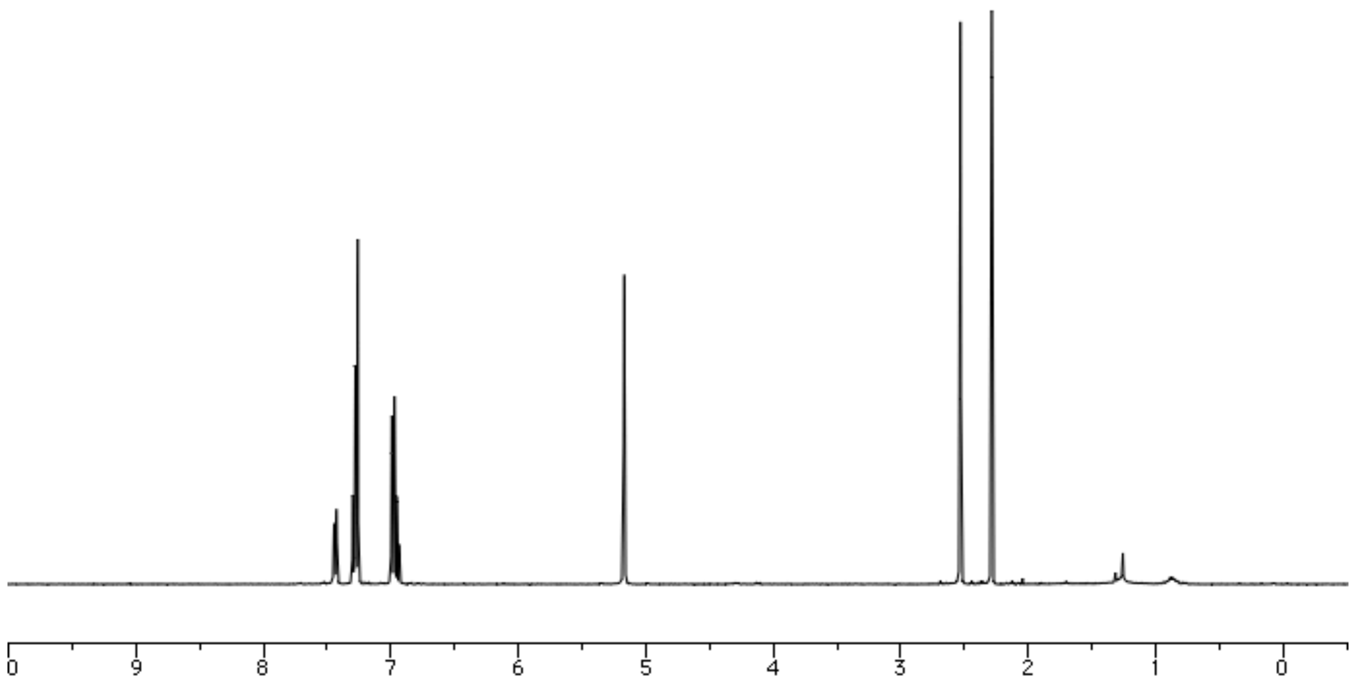

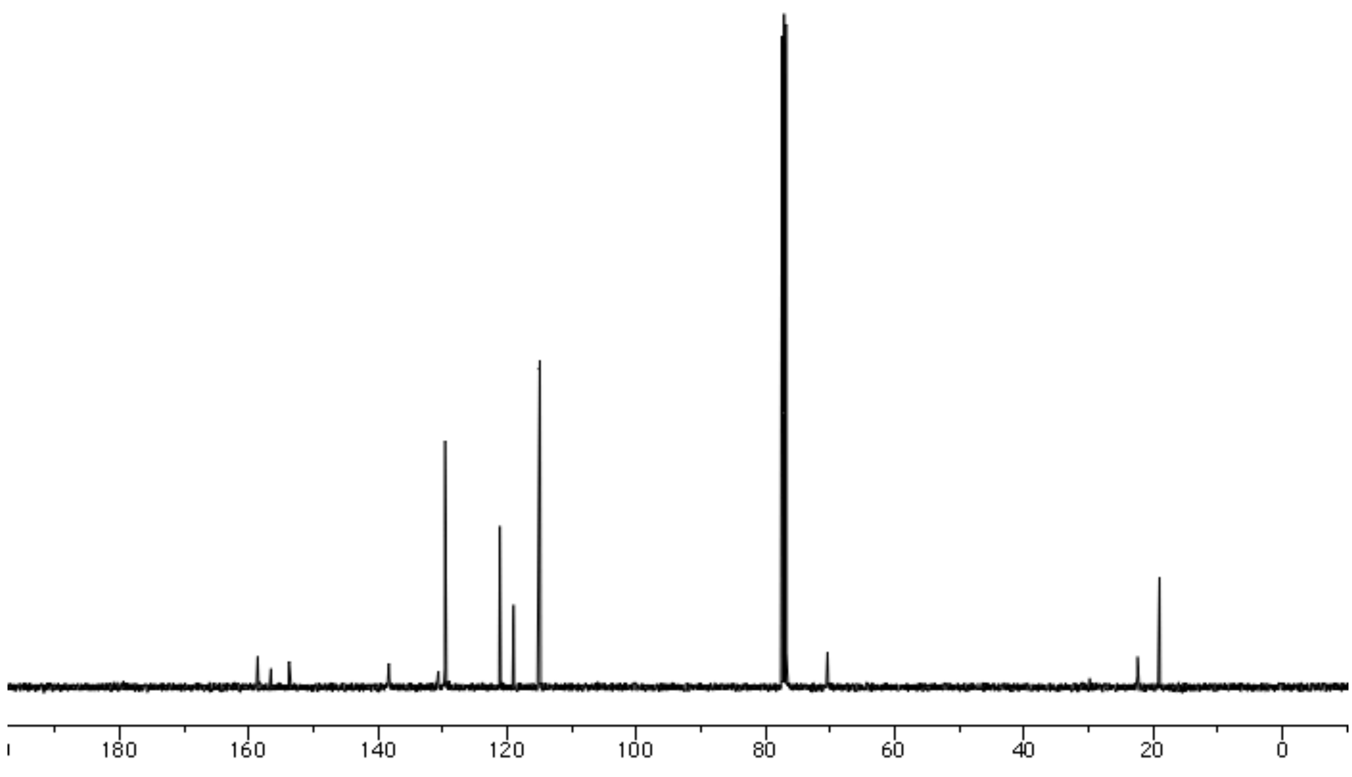

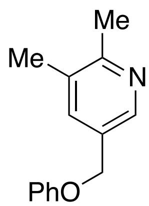

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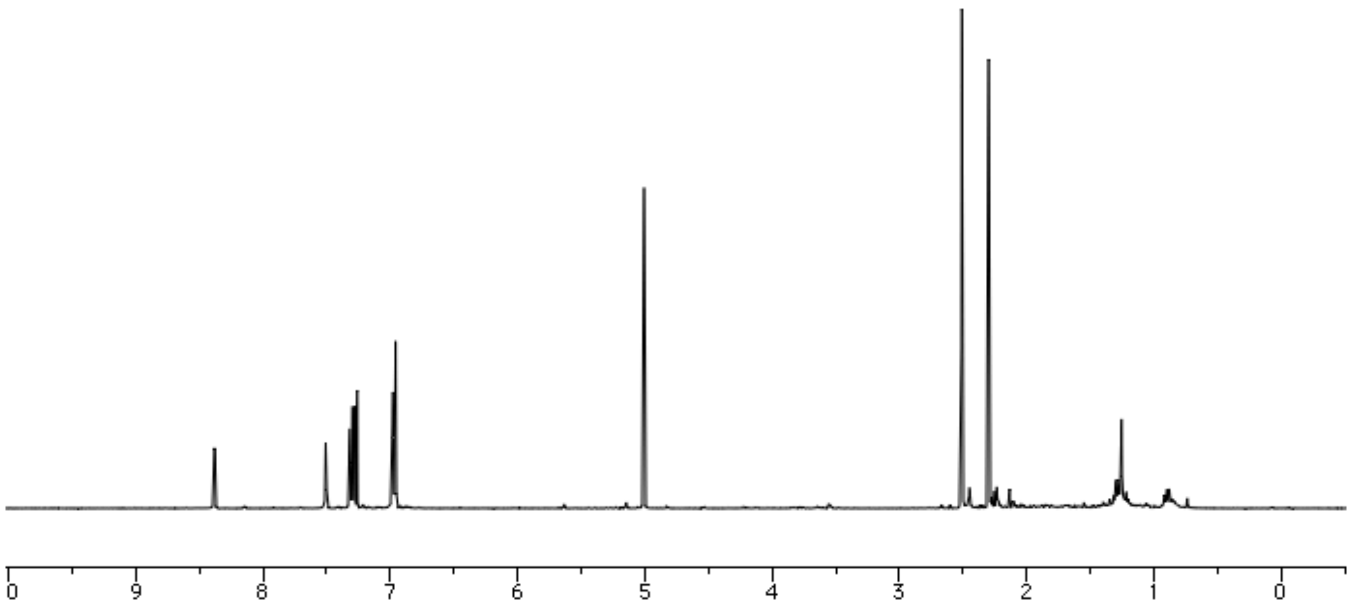

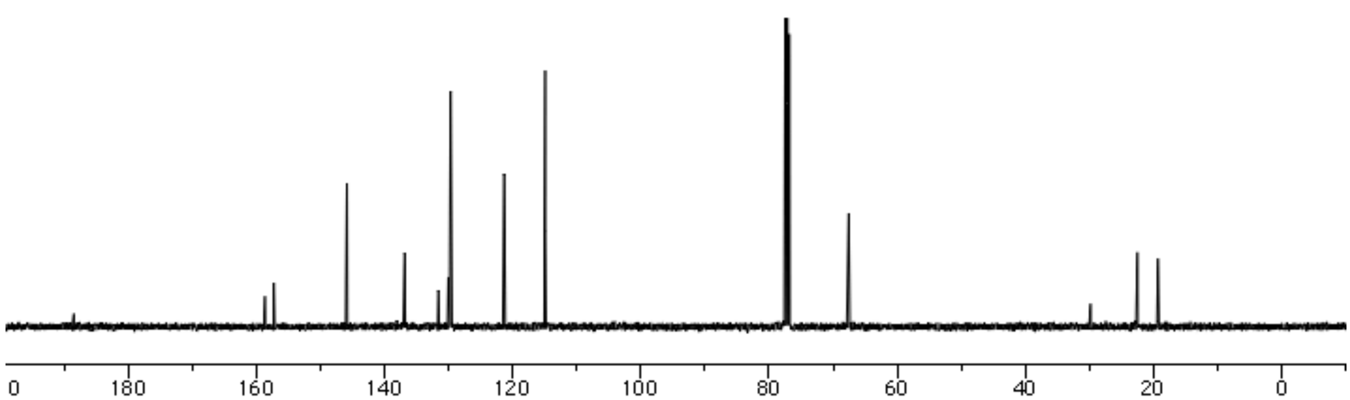

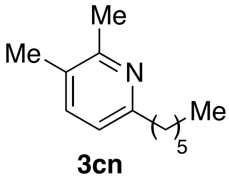

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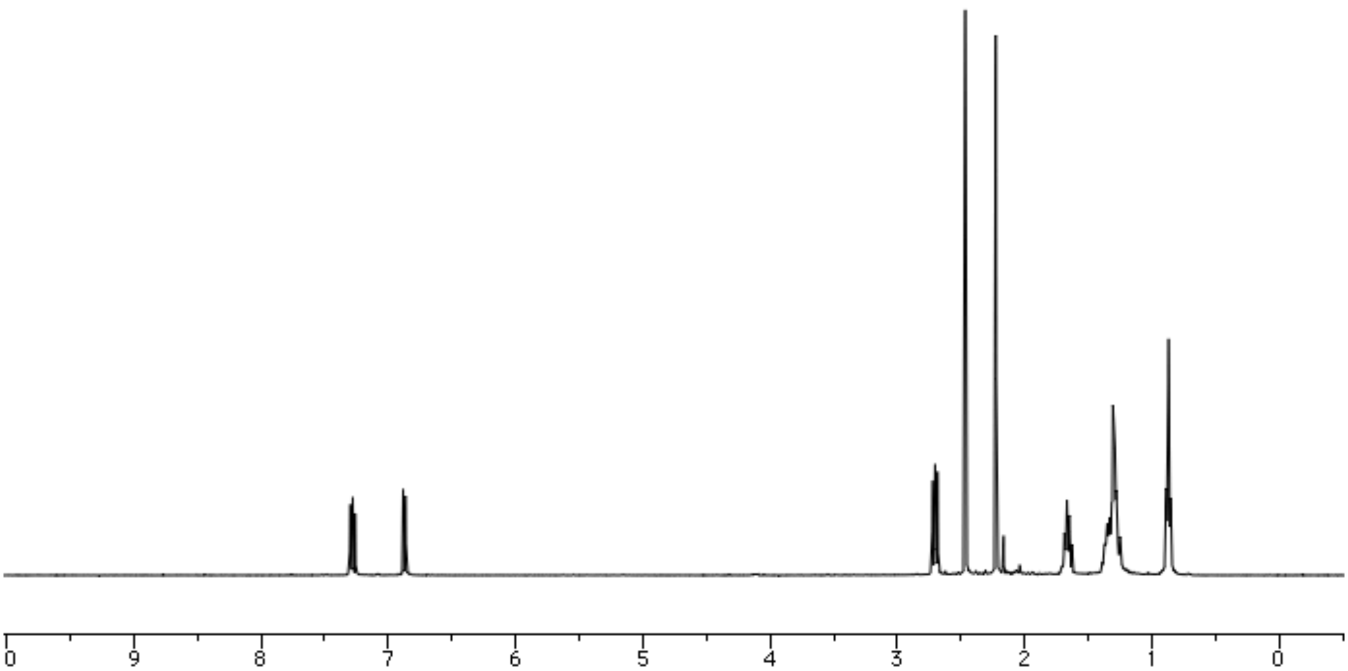

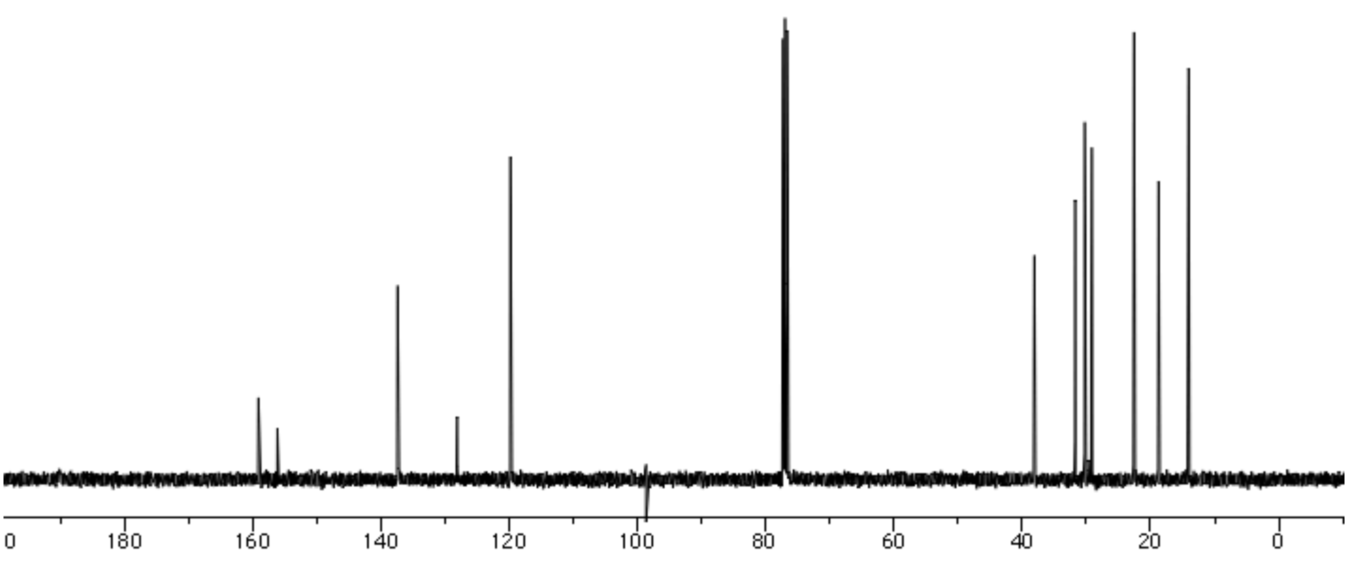

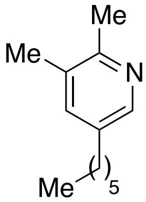

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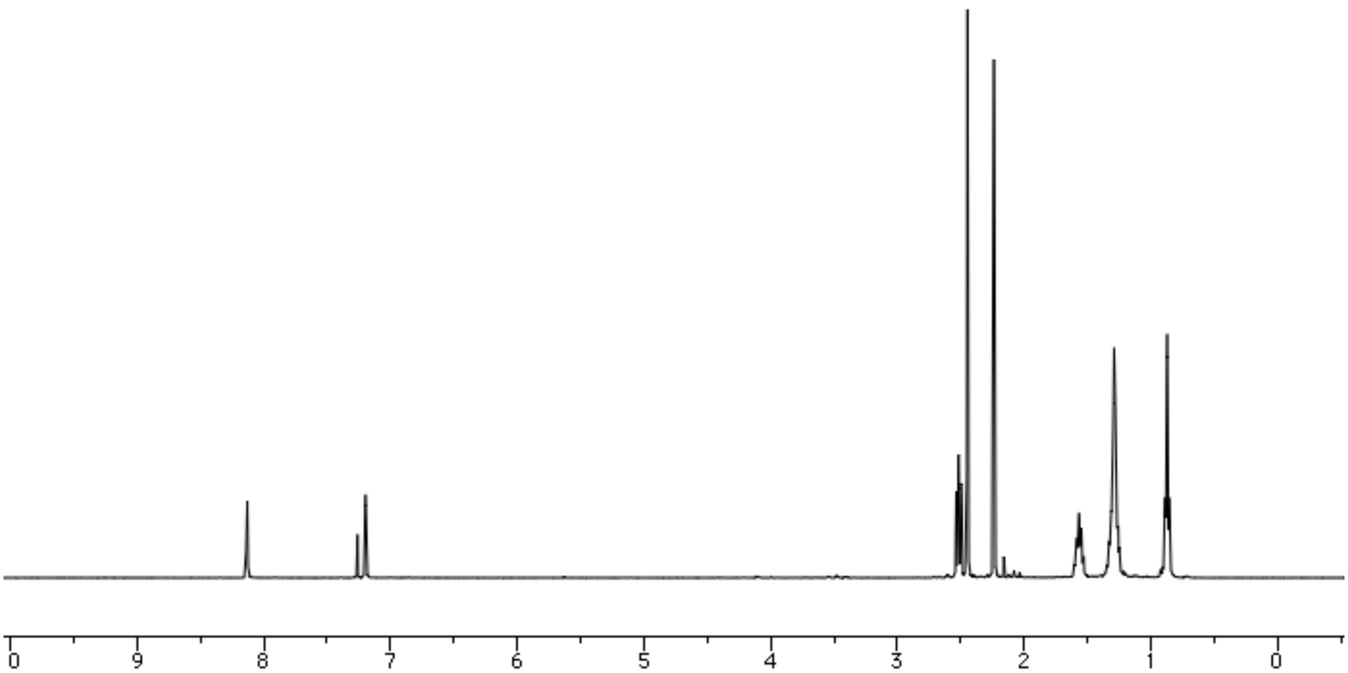

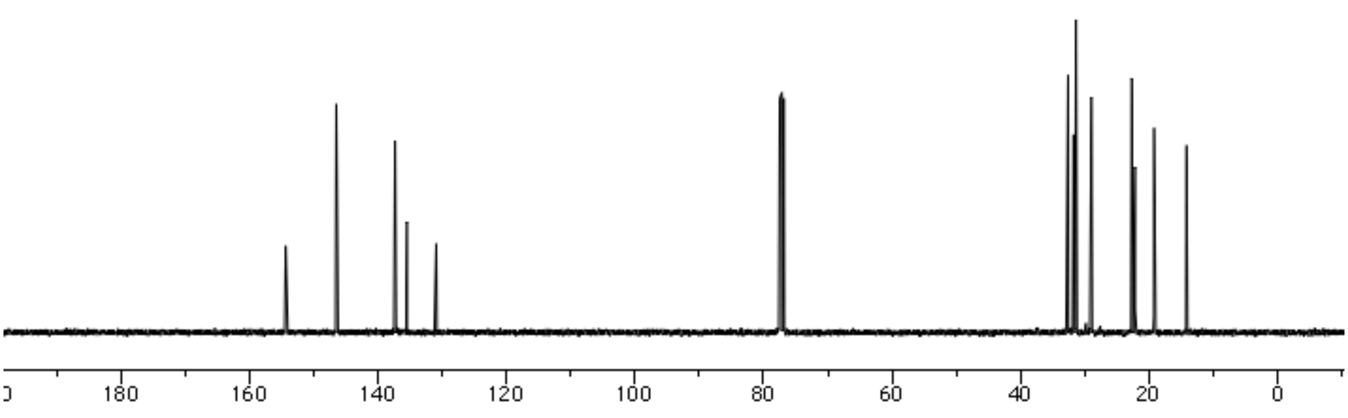

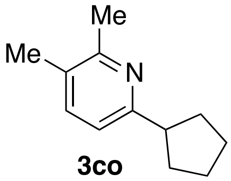

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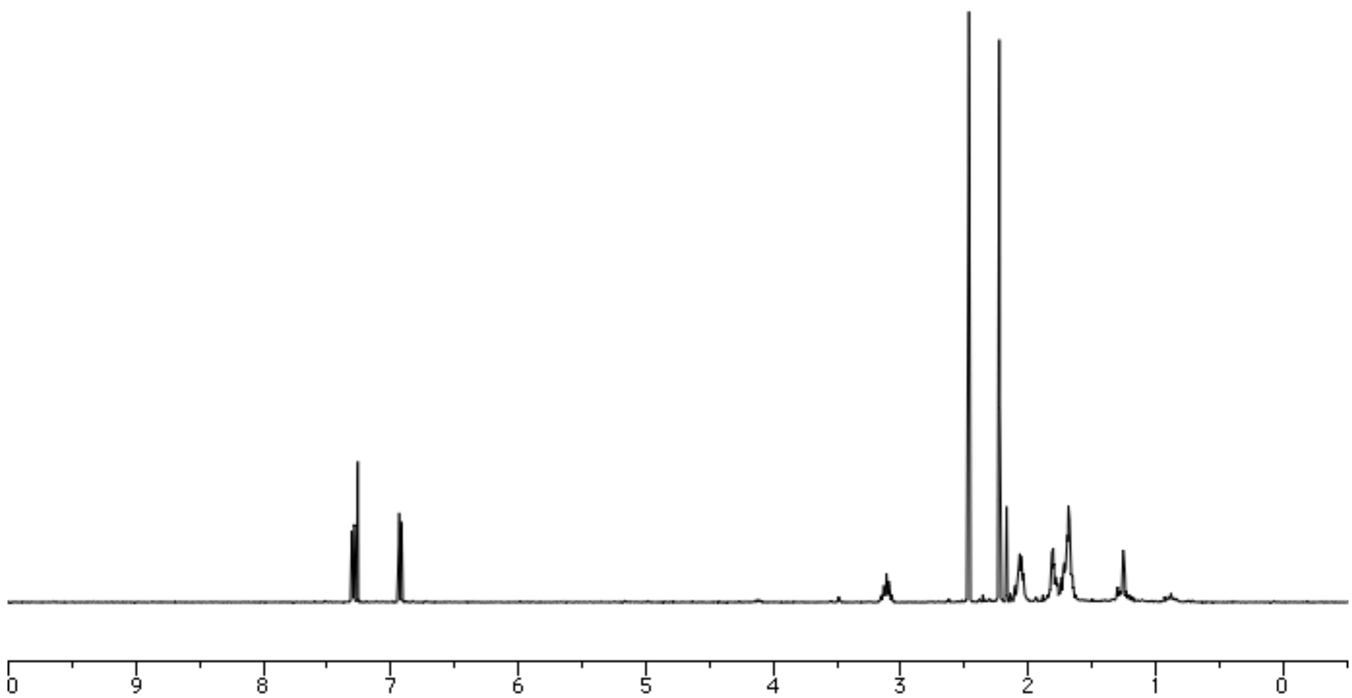

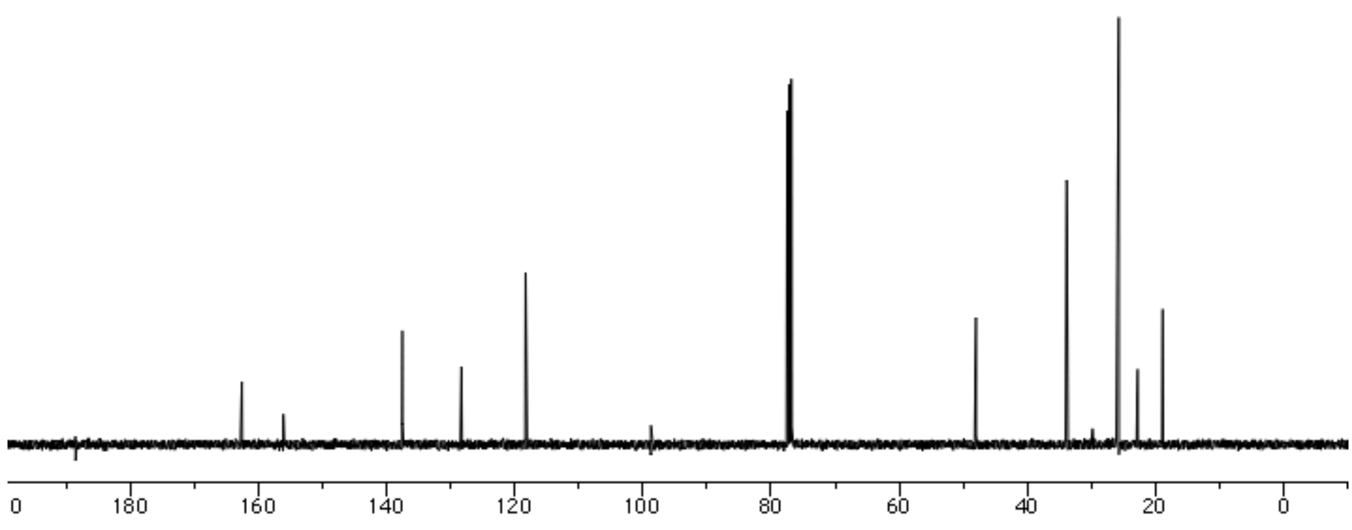

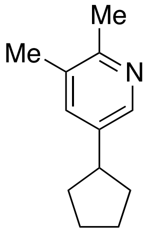

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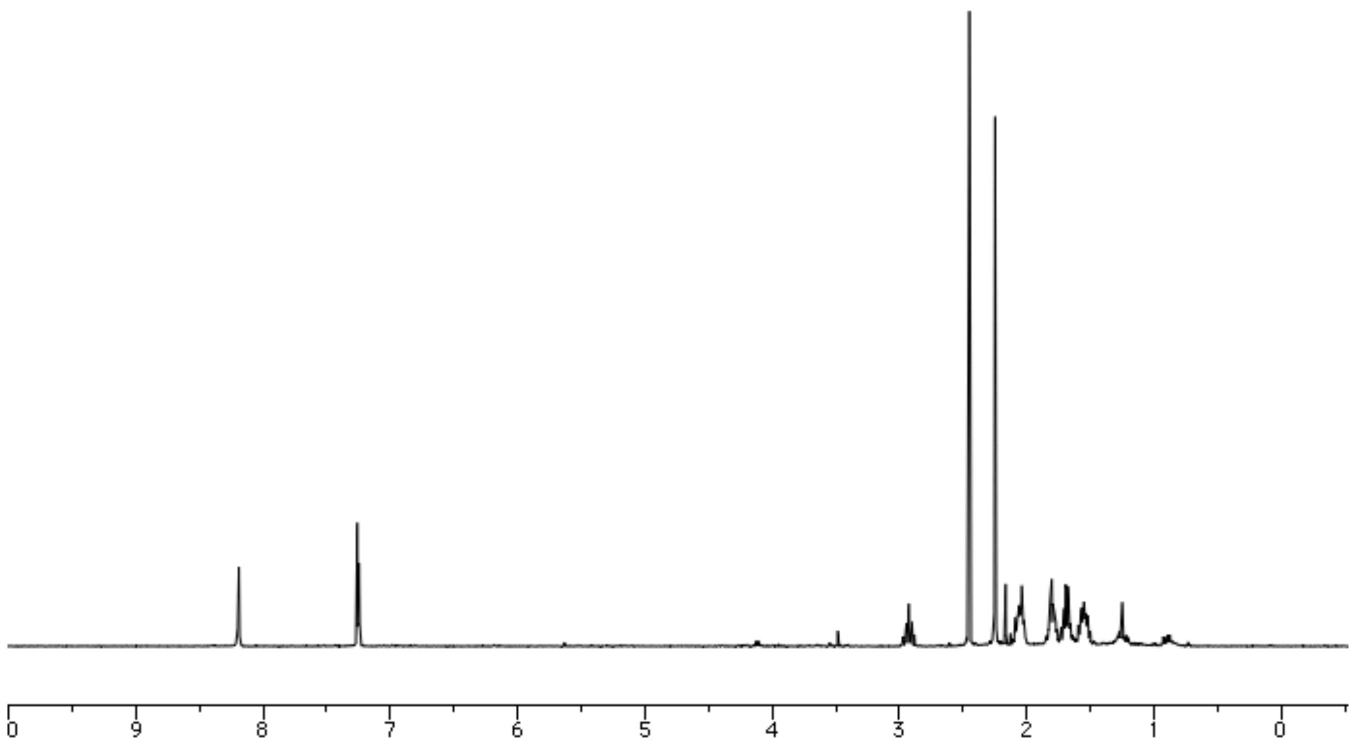

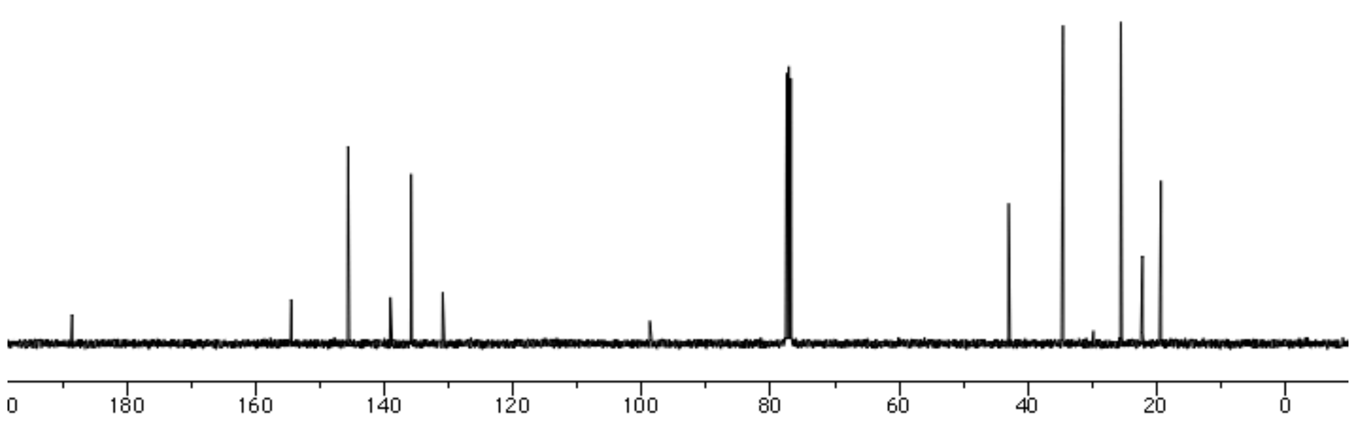

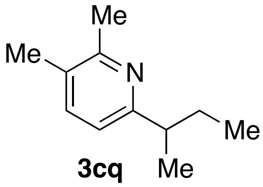

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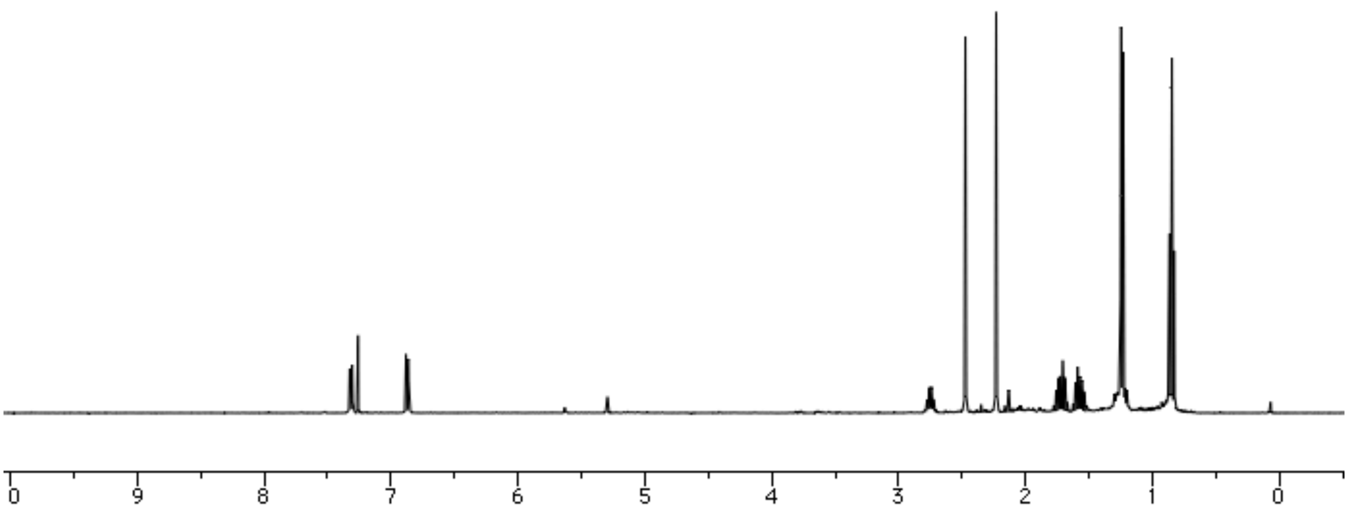

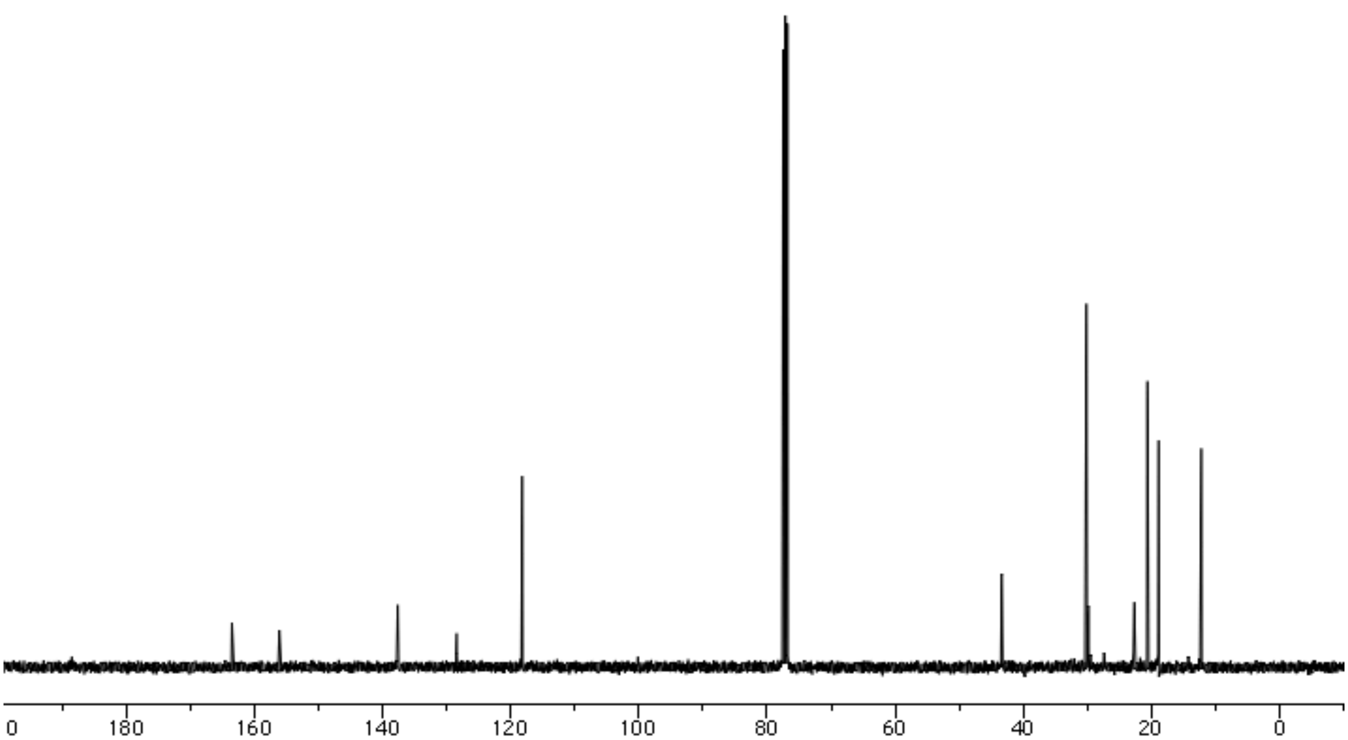

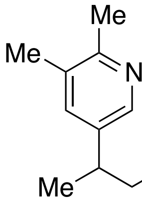

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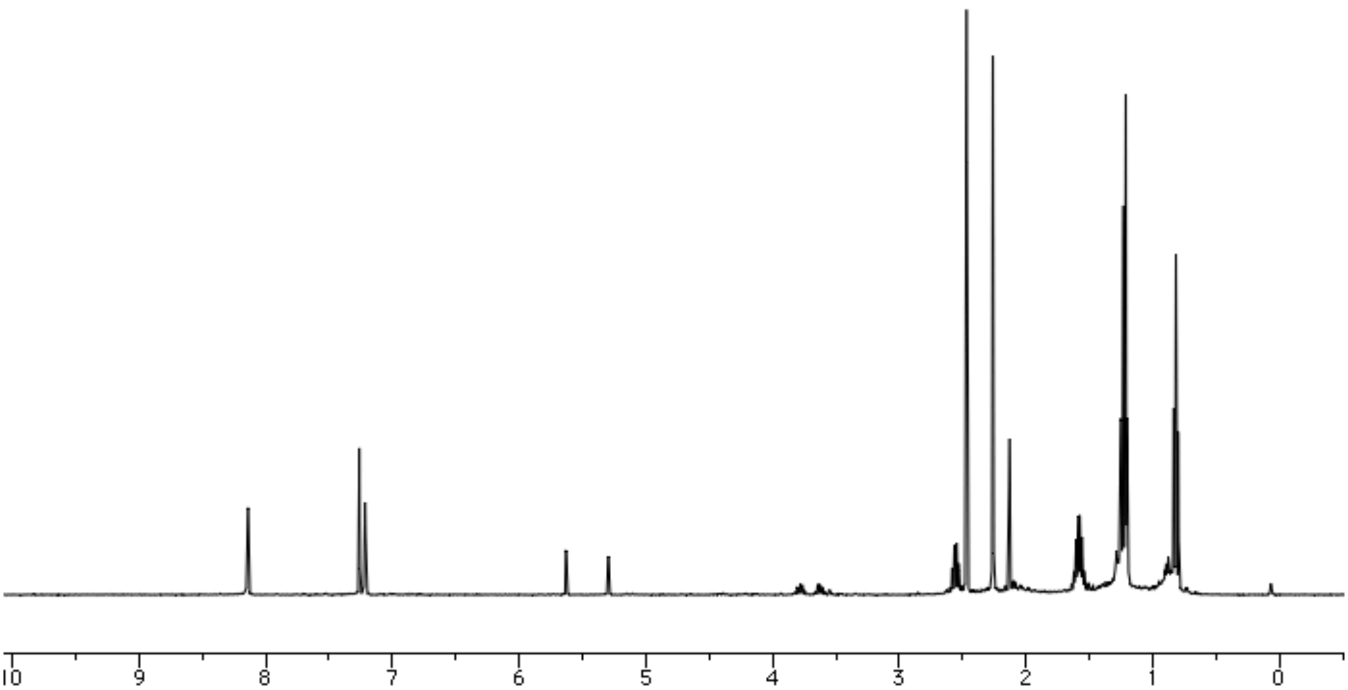

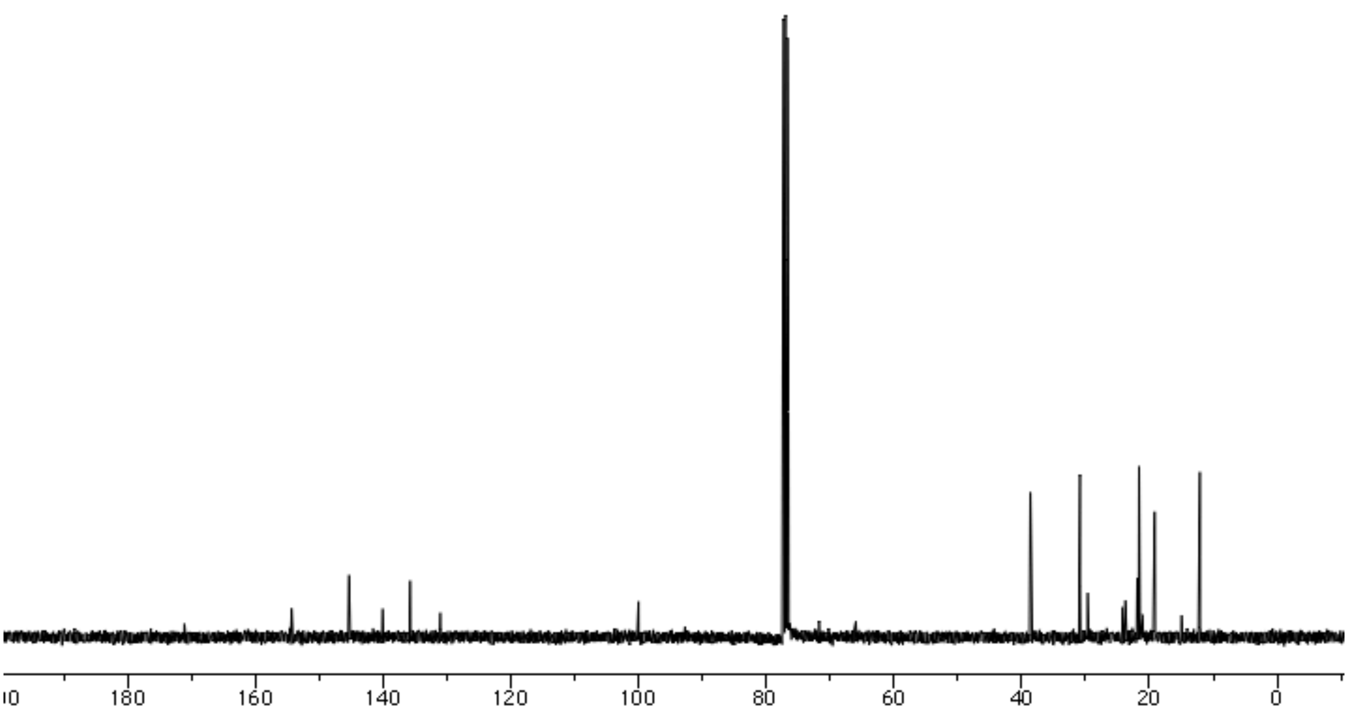

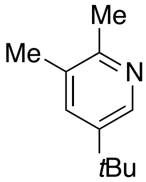

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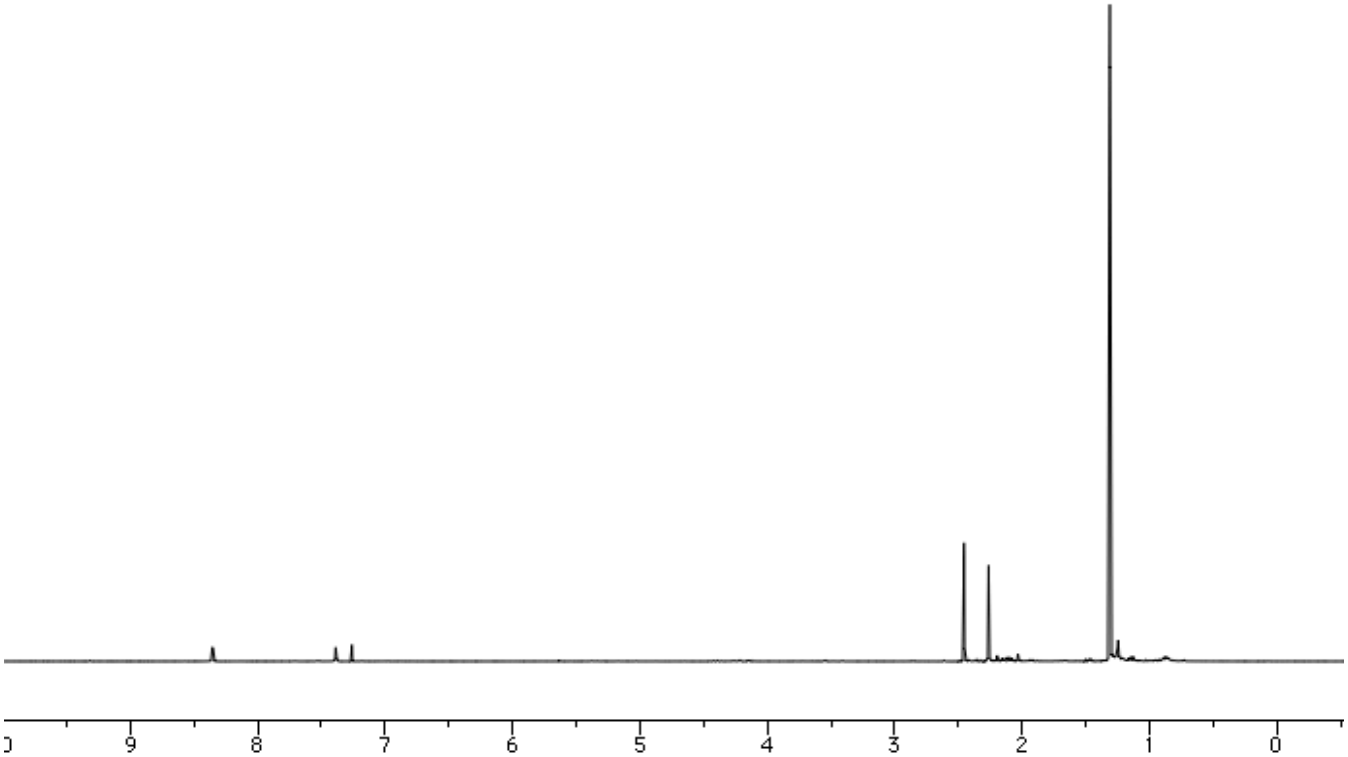

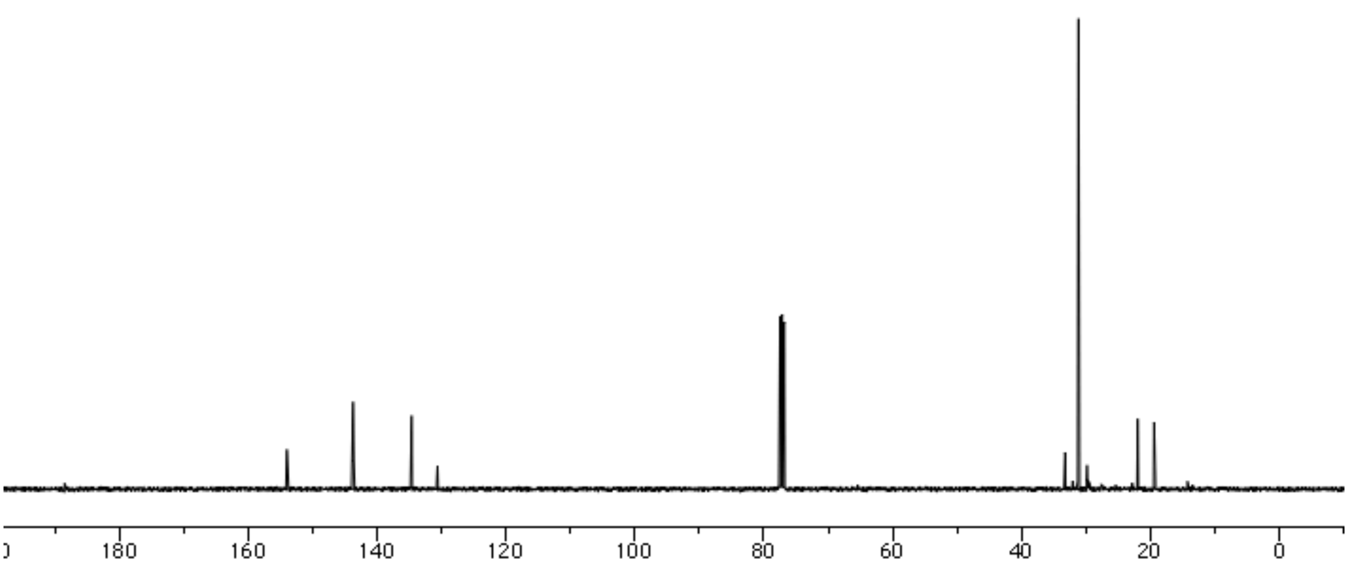

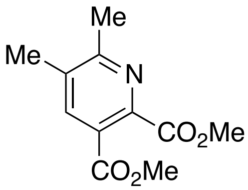

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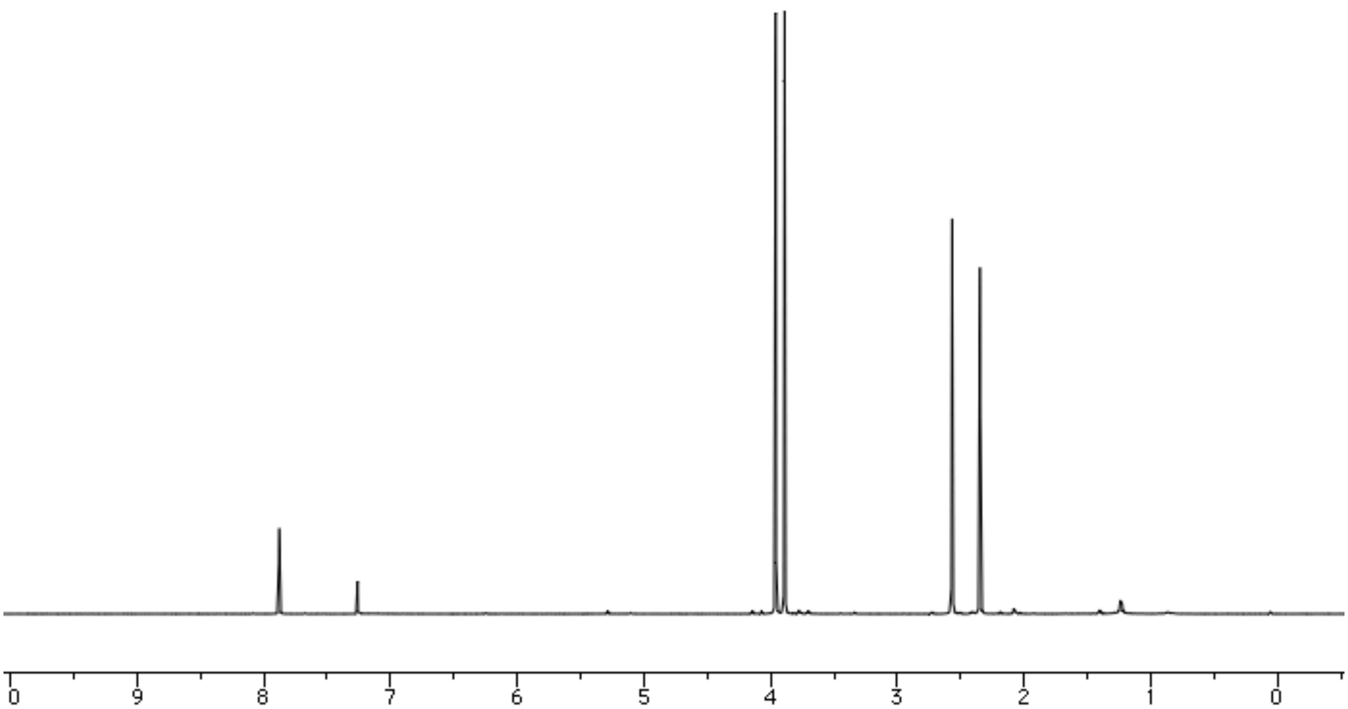

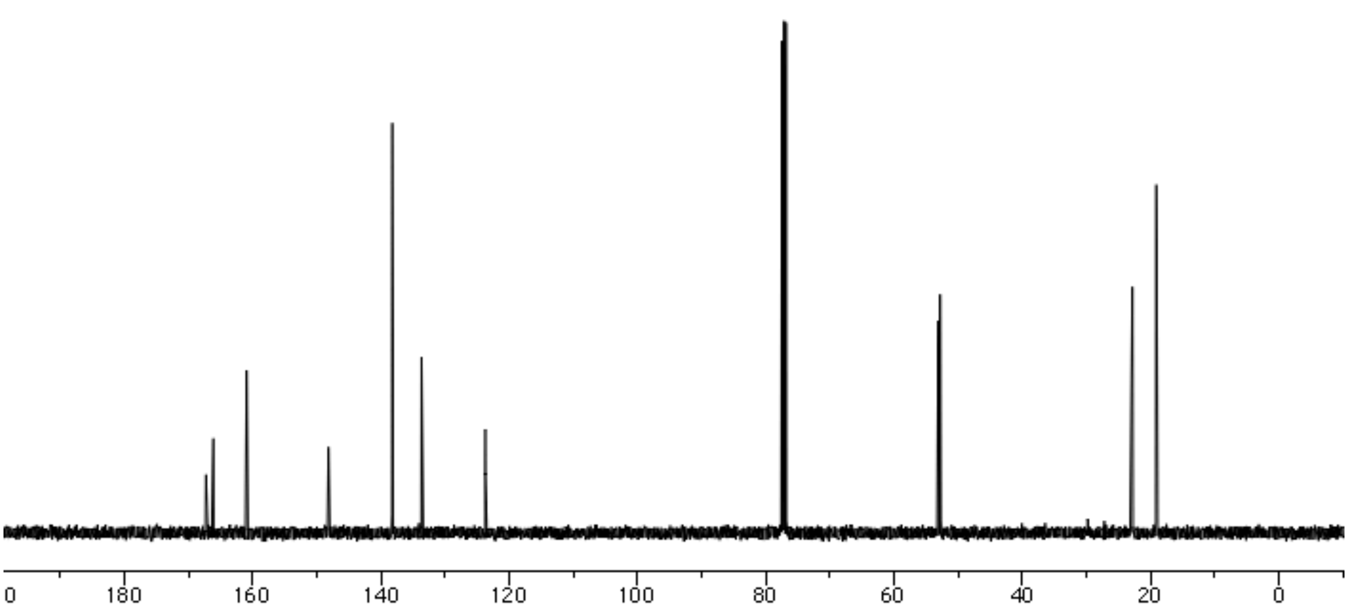

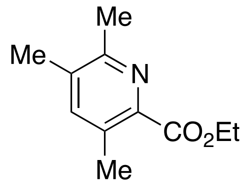

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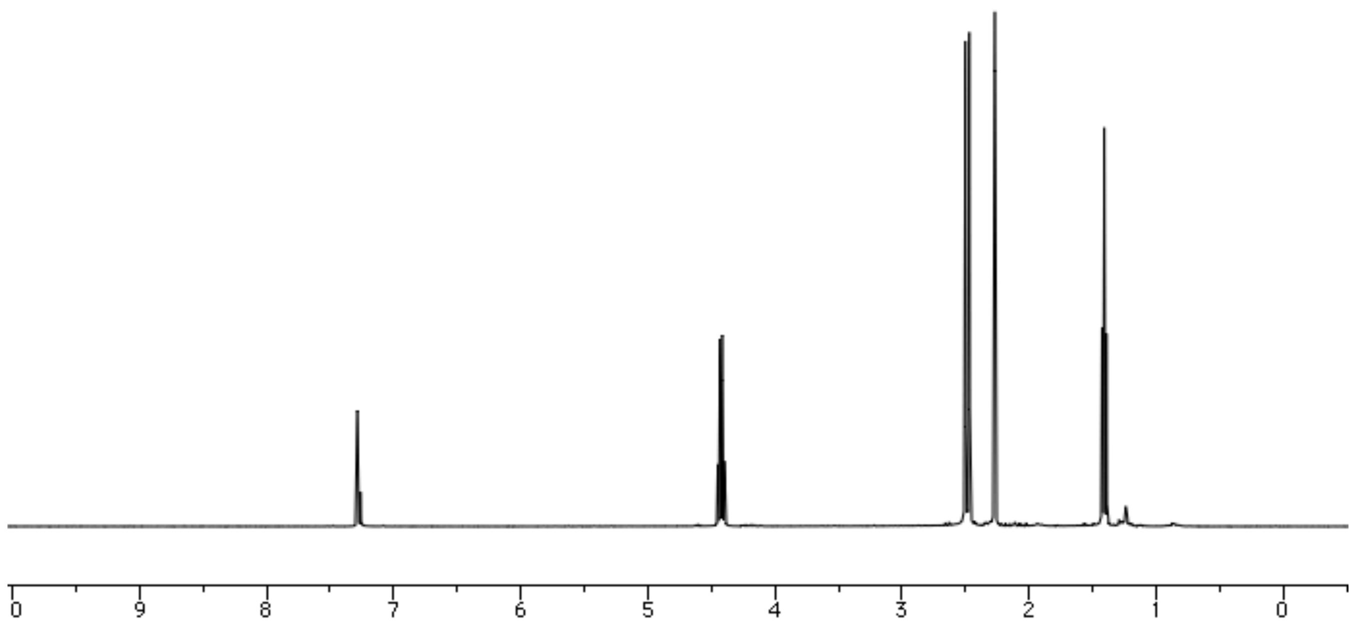

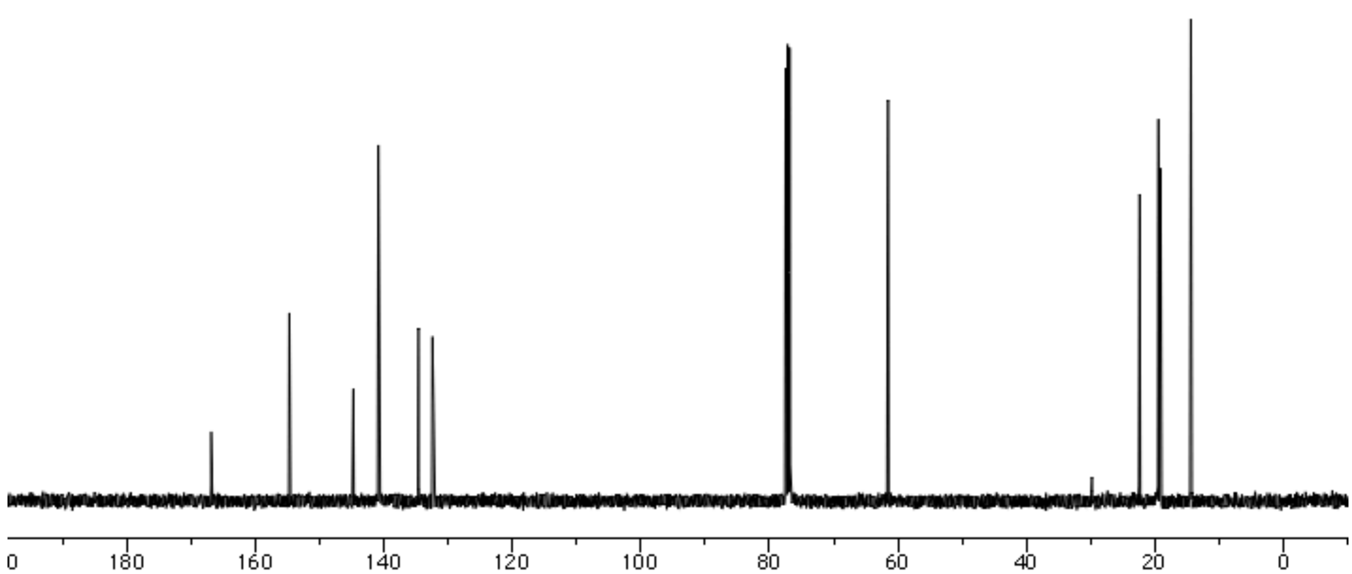

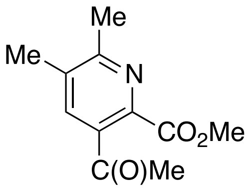
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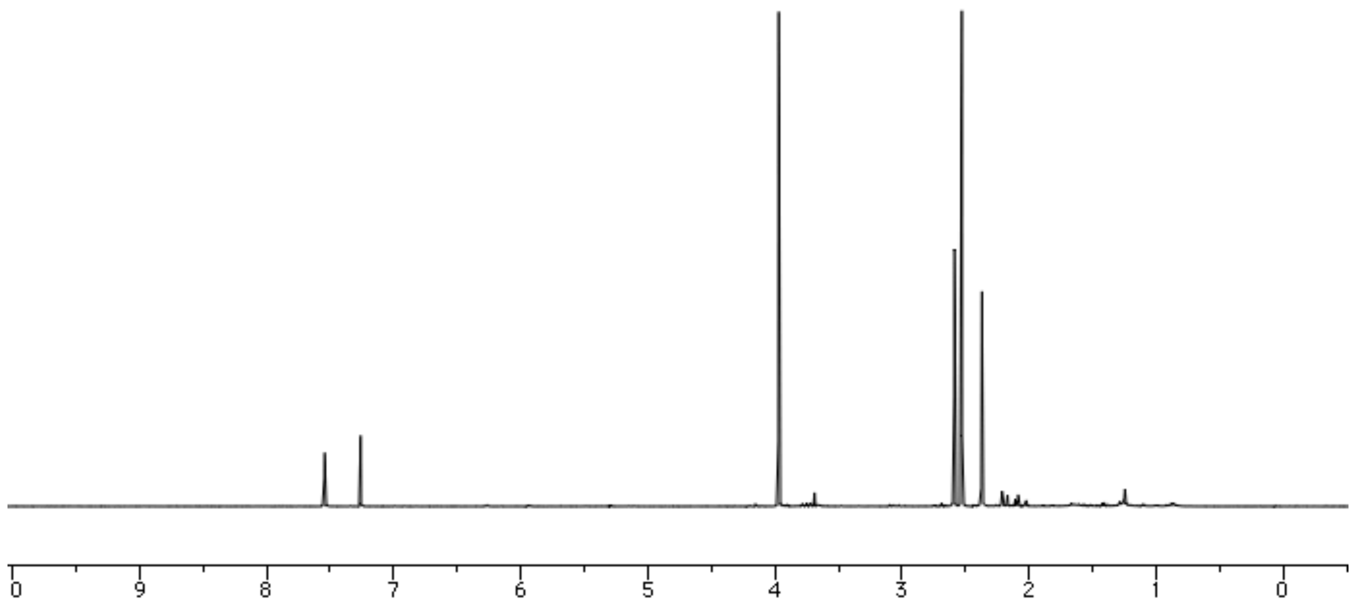
Me
N
CO2Me
C(O)Me

7cc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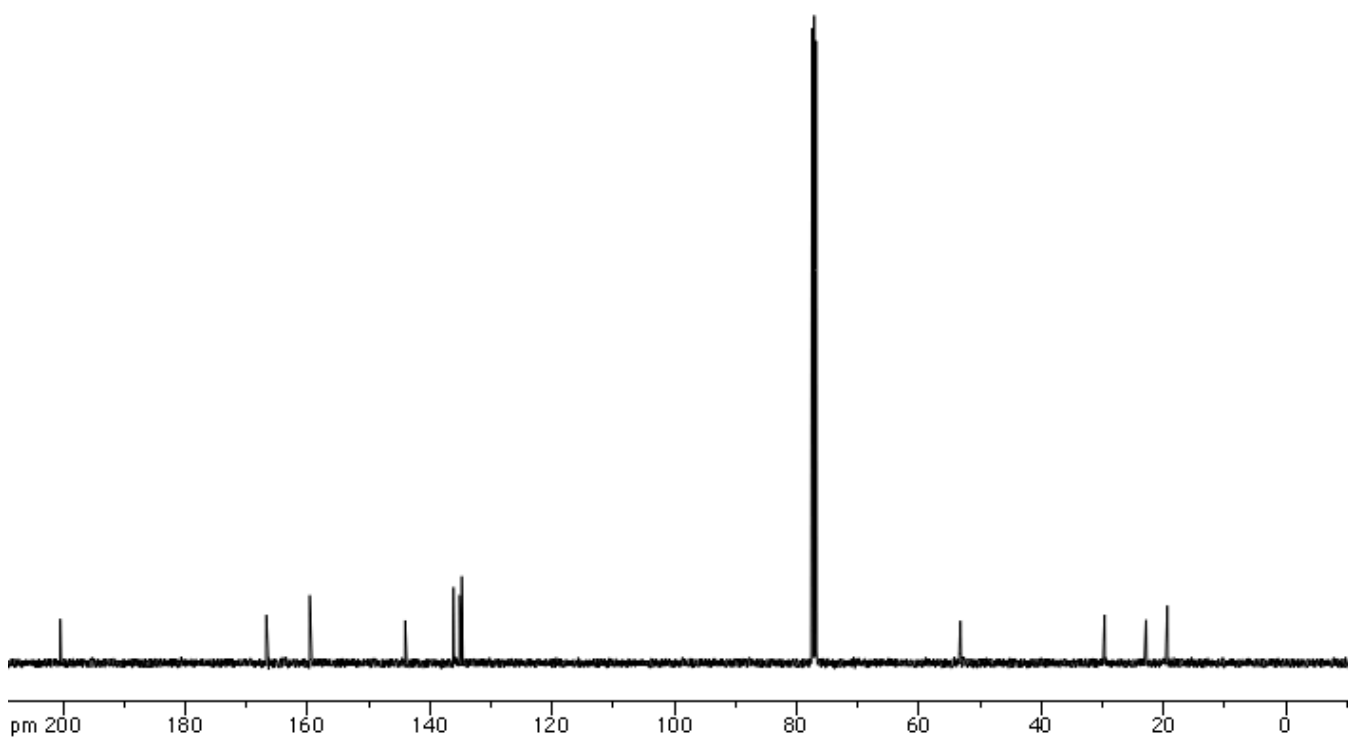
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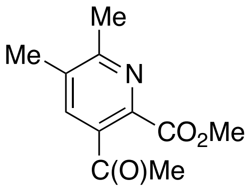

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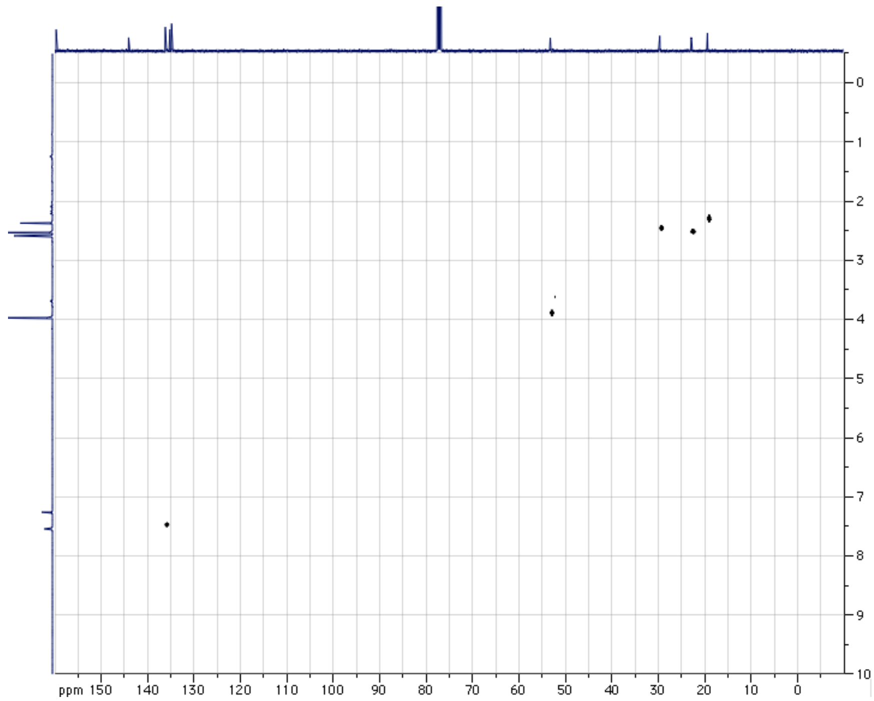

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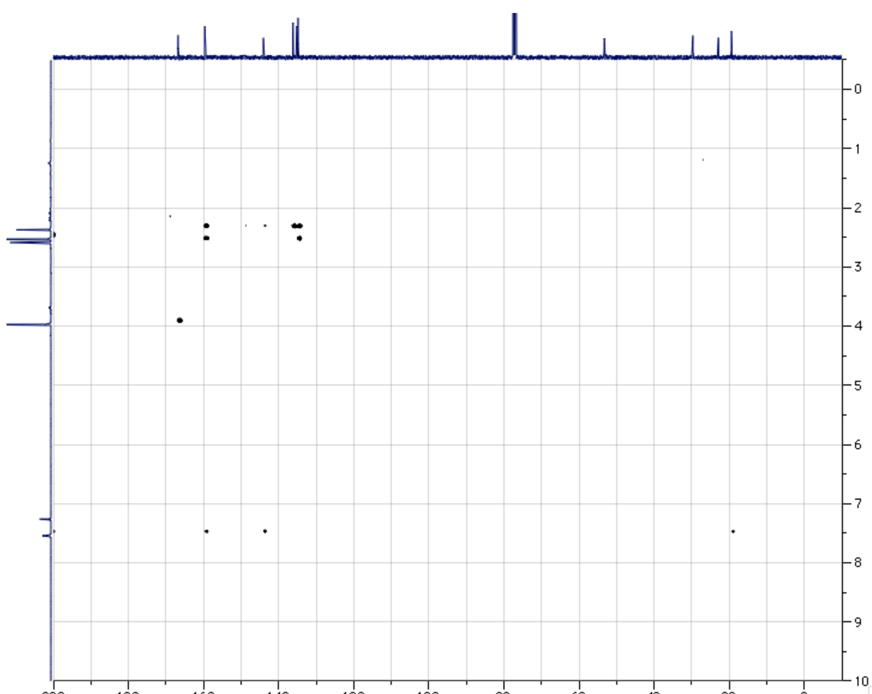

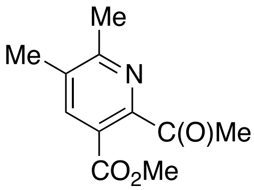
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Me
N
C(O)Me
CO2Me

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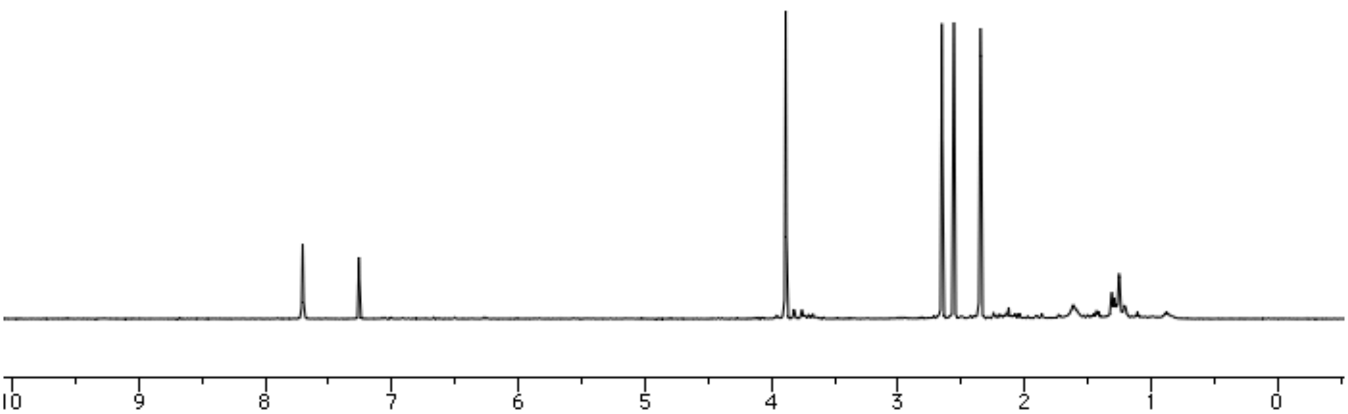
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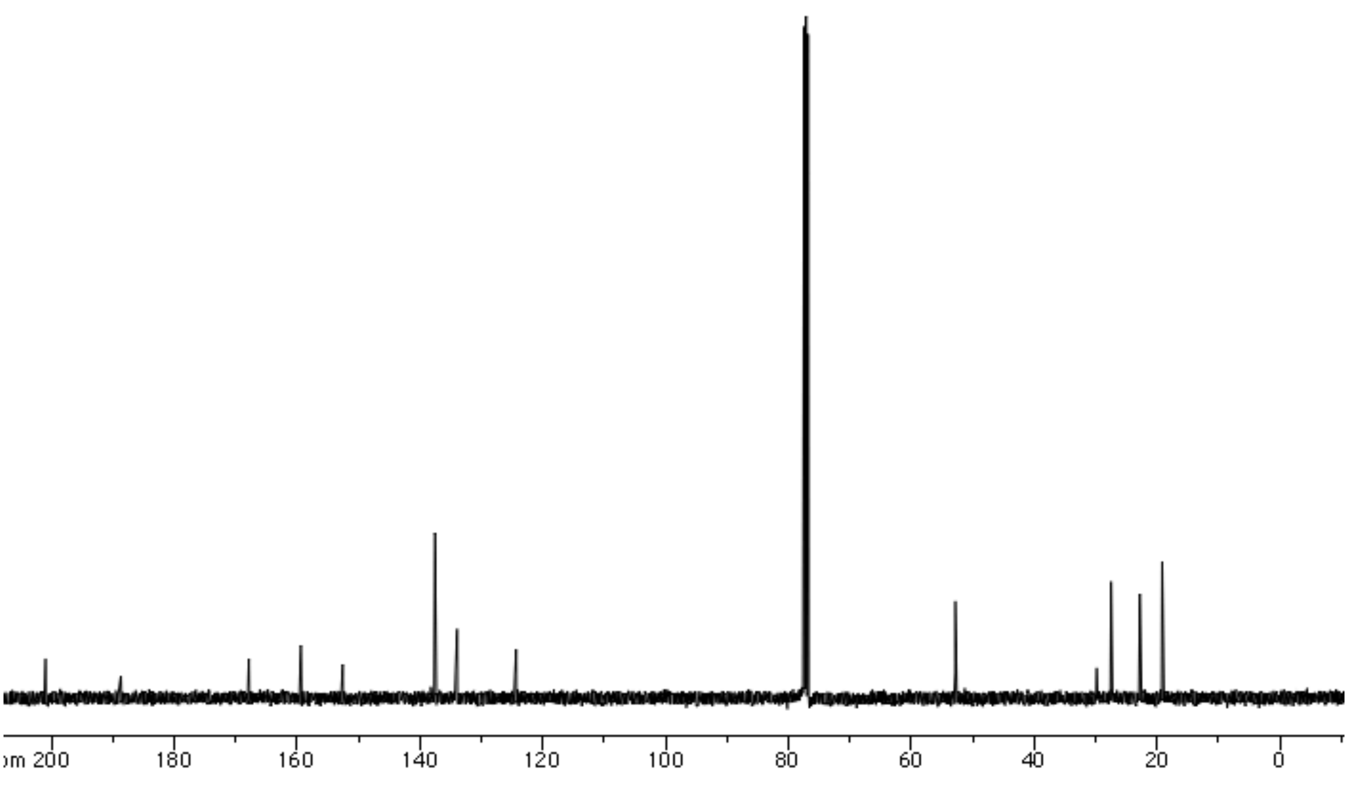
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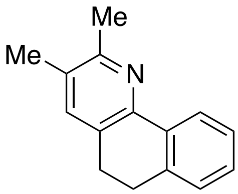

10