Rhodium(III)-Catalyzed Heterocycle Synthesis Using Internal Oxidant: Improved Reactivity and Mechanistic Studies

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†Prof. Keith Fagnou passed away unexpectedly on November 11, 2009.

Supporting Information

General Methods

All rhodium-catalyzed isoquinolone formations were carried out without any particular precautions to extrude moisture or oxygen. ^{1}H and ^{13}C spectra were recorded in $CDCl_3$, DMSO-d_6 or Acetone-d_6 solutions on a Bruker AVANCE 400 MHz or a Bruker AVANCE 300 MHz spectrometer. High-resolution mass spectra were obtained by EI on a Kratos Concept IIH. Low resolution mass spectra were obtained using an Agilent 5975C Series GC/MSD system. Infrared analysis was performed on an ABB Bomem Arid-Zone and the spectra were obtained as neat films on a sodium chloride window. $[Cp^*RhCl_2]_2$ was prepared from $RhCl_3.xH_2O$ (bought from Pressure Chemicals) following a literature procedure[1] and stored in a dessicator. $[Cp^*RhCl_2]_2$ could alternatively be bought from Strem Chemicals. All other reagents were used as is from commercial sources. Unless otherwise noted below, all other compounds have been reported in the literature or are commercially available.

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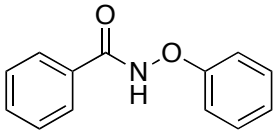
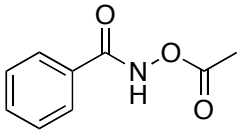
PREPARATION OF THE SUBSTRATES BEARING DIFFERENT INTERNAL OXIDANTS

N-phenoxybenzamide (1c)



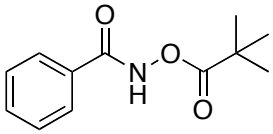
To a solution of 2 parts EtOAc in one part H_2O containing Na_2CO_3 (2 equiv.) was added *O*-phenylhydroxyamine hydrochloride (1 equiv.) (prepared following a literature procedure[2]). The mixture was cooled to 0°C and benzoyl chloride (1 equiv.) was added dropwise to the mixture. It was then allowed to stir at 0°C for 2 hours. The reaction was then quenched with sat. $NaHCO_3$ and more EtOAc was added. The organic layer was washed twice with sat. $NaHCO_3$. It was then dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 20% EtOAc in pet. ether as eluent. The product obtained is a white solid (207 mg, 94%).
^{1}H-NMR (400 MHz; DMSO-d_6, 293K): δ 12.48 (s, 1H), 7.90-7.87 (m, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.55-7.51 (m, 2H), 7.38-7.32 (m, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.04 (tt, *J* = 7.3, 0.9 Hz, 1H).
^{13}C NMR (100 MHz, DMSO-d_6, 293K): δ 164.9, 159.6, 132.1, 131.4, 129.5, 128.7, 127.3, 122.4, 113.0
IR (ν_{max}/cm^{-1}): 3186, 1660, 1591, 1489, 1200
HRMS calculated for $C_{13}H_{11}N_1O_2$ (M^+): 213.0790; Found 213.0797
R_f: 0.62 with 50% EtOAc in pet. ether
Melting Point: 131-133 °C

N-acetoxybenzamide (1d)



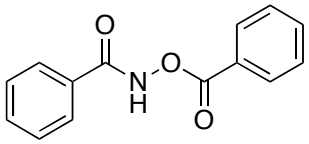
Benzohydroxamic acid (411 mg, 3 mmol, 1 equiv.), CH_2Cl_2 (9 mL) and NaOH 2M were charged in a round bottom flask. Ac_2O (312 µL, 3.3 mmol, 1.1 equiv.) was added via syringe. After stirring at room temperature for 3 h, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic fractions were washed with brine, dried with $MgSO_4$, filtered and evaporated under reduced pressure to afford the desired product as a white solid (514 mg, 96%).
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): δ 9.45 (br s, 1H), 7.84-7.81 (m, 2H), 7.61-7.56 (m, 1H), 7.50-7.45 (m, 2H), 2.31 (s, 3H).
Spectral data matched the one previously reported.[3]

***N*-(pivaloyloxy)benzamide (1e)**



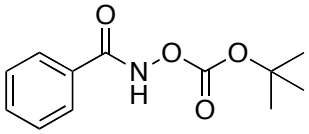
Pivalic anhydride (18.3 mmol, 3.70 mL, 1 equiv.) was added to a suspension of benzohydroxamic acid (21.9 mmol, 3.0 g, 1.2 equiv.) in dichloromethane (100 mL). The resulting mixture was allowed to stir at room temperature for 16 hours. It was then transferred to a separatory funnel and washed with sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash chromatography using 15% ethyl acetate in pet. ether as eluent. The product obtained is a white solid (3.28 g, 81%).
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): 9.58 (br s, 1H), 7.81-7.79 (m, 2H), 7.56-7.52 (m, 1H), 7.45-7.41 (m, 2H), 1.35 (s, 9H).
Spectral data was consistent with that previously reported.[3]

***N*-(benzoyloxy)benzamide (1f)**



Benzohydroxamic acid (1.00 g, 7.29 mmol, 1 equiv.) and sodium *tert*-Butoxide (701 mg, 7.29 mmol, 1 equiv.) were stirred together at room temperature in diethyl ether (30 mL) for 30 min. Benzoyl chloride (850 µL, 7.29 mmol, 1 equiv.) was then added dropwise and the reaction mixture was allowed to stir at room temperature for 16 h. It was then diluted with EtOAc and washed with water and sat. $NaHCO_3$. The organic fraction containing the product in the solid form was diluted with acetone to dissolve it almost completely. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure to afford the desired product as a white solid (1.24 g, 70%) in an analytically pure form.
^{1}H NMR (400 MHz, DMSO-d_6, 293K): δ 12.64 (s, 1H), 8.10-8.08 (m, 2H), 7.89-7.86 (m, 2H), 7.78 (tt, *J* = 7.5, 1.5 Hz, 1H), 7.66-7.61 (m, 3H), 7.57-7.53 (m, 2H).
^{13}C NMR (100 MHz, DMSO-d_6, 293K): δ 164.8, 164.4, 134.4, 132.4, 131.0, 129.5, 129.2, 128.7, 127.4, 126.9
IR (ν_{max}/cm^{-1}): 3193, 1767, 1653, 1239
HRMS calculated for $C_{14}H_{11}N_1O_3$ (M^+): 241.0739; Found 241.0700
R_f: 0.63 with 50% EtOAc in pet. ether
Melting Point: 154-157°C

***N*-(*tert*-butoxycarbonyloxy)benzamide (1g)**



Boc_2O (5.5 mmol, 1,26 mL, 1.1 equiv.) was added to a suspension of benzohydroxamic acid (5 mmol, 686 mg, 1 equiv.) in CH_2Cl_2 (20 mL). As seen by TLC, the conversion was low after

2h stirring at room temperature. NaOtBu (0.25 mmol, 24 mg, 0.05 equiv.) was added and the reaction mixture was allowed to stir for 16 hours at room temperature. More CH_2Cl_2 was added and the reaction mixture was washed twice with sat. $NaHCO_3$ after which the organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 10-30% EtOAc in pet. ether as eluent.

^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.27 (s, 1H), 7.82-7.80 (m, 2H), 7.57-7.53 (m, 1H), 7.46-7.42 (m, 2H), 1.55 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 166.8, 152.8, 132.7, 130.7, 128.8, 127.5, 86.0, 27.6

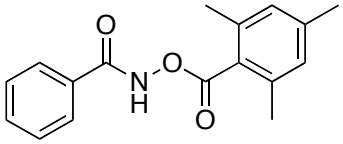
IR (ν_{max}/cm^{-1}): 3216, 1988, 1787, 1667, 1246, 1150

HRMS calculated for $C_7H_7NO_2$ ((M-CO_2*t*-Bu)$^+$): 137.0477; Found 137.0470

R_f: 0.56 with 50% EtOAc in pet. ether

Melting Point: 112-115 °C with gas evolution

***N*-(2,4,6-trimethylbenzoyloxy)benzamide (1h)**



Benzoyl chloride (0.92 mmol, 107 µL, 1 equiv.) was added dropwise at 0 °C to a biphasic solution of *O*-mesytoylhydroxylamine hydrochloride (prepared according to a literature procedure,[4] 0.92 mmol, 200 mg, 1 equiv.) and Na_2CO_3 (1.84 mmol, 195 mg, 2 equiv.) in a 2:1 EtOAc:H_2O mixture (4.5 mL). The resulting mixture was allowed to reach room temperature and it was stirred for 16 hours. More EtOAc was added and the organic phase was washed with sat. $NaHCO_3$ after which it was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 15% EtOAc in pet. ether as eluent. The product obtained is a white solid (208 mg, 80%).

^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.65 (d, *J* = 0.2, 1H), 7.89 (dd, *J* = 8.3, 1.3, 2H), 7.61-7.56 (m, 1H), 7.48 (t, *J* = 7.6, 2H), 6.91 (d, *J* = 0.5, 2H), 2.43 (s, 6H), 2.31 (s, 3H)

^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 168.5, 166.6, 141.0, 136.9, 132.8, 130.8, 128.9, 128.7, 127.6, 126.5, 21.3, 20.1

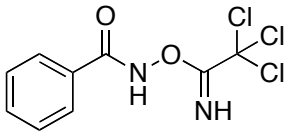
IR (ν_{max}/cm^{-1}): 3196, 1772, 1653, 1506, 1237

HRMS found only the 2,4,6-trimethylbenzoic acid mass, $C_{10}H_{12}O_2$ (M^+) calculated: 164.0837; Found 164.0850

R_f: 0.63 with 50% EtOAc in pet. ether

Melting Point: 151-152 °C

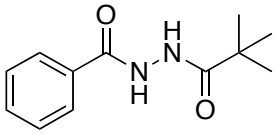
***N*-(2,2,2-trichloro-1-iminoethoxy)benzamide (1i)**



Triethylamine (3.3 mmol, 460 µL, 1.1 equiv.) was added to a suspension of benzohydroxamic acid (3 mmol, 411 mg, 1 equiv) in CH_2Cl_2 (10 mL) under Ar atmosphere. Trichloroacetonitrile (3.3 mmol, 330 µL, 1.1 equiv.) was then added and the reaction was stirred for 2 hours at room temperature. More CH_2Cl_2 was added and the reaction mixture was washed with sat.

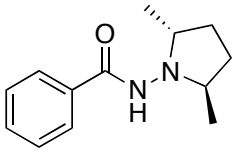
$NaHCO_3$. The aqueous phase was then extracted twice with CH_2Cl_2. The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 10% EtOAc in pet. ether as eluent. The product obtained is a beige solid (45 mg, 5%).
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.82 (br s, 1H), 8.64 (br s, 1H), 7.54-7.51 (m, 2H), 7.40-7.35 (m, 2H), 7.19 (tt, *J* = 7.4, 1.3 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ
IR (v_{max}/cm^{-1}): 3314, 1707, 1537, 1499, 1449, 1231
HRMS calculated for $C_9H_7N_2O_2Cl_3$ (M^+): 279.9573; Found 279.9616
R_f: 0.25 with 10% EtOAc in pet. ether
Melting Point: 157-161°C

***N'*-pivaloylbenzohydrazide (1j)**



Pivalic anhydride (8.1 mmol, 1,6 mL, 1.1 equiv.) was added to a mixture of benzhydrazide (1.0 g, 7.3 mmol, 1 equiv.) in CH_2Cl_2 (50 mL). The reaction was allowed to stir at room temperature for 16 hours. The mixture was then washed 3 times with sat. NH_4Cl and 3 times with $NaHCO_3$ after which the organic fraction was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 50% EtOAc in pet. ether as eluent. The product obtained is a white solid (1.31 g, 81%).
^{1}H-NMR (400 MHz; DMSO-d_6, 293K, TMS): δ 10.20 (s, 1H), 9.54 (s, 1H), 7.89-7.87 (m, 2H), 7.59-7.54 (m, 1H), 7.51-7.47 (m, 2H), 1.19 (s, 9H).
^{13}C NMR (100 MHz, DMSO-d_6, 293K, TMS): δ 176.9, 165.6, 132.8, 131.7, 128.4, 127.4, 37.6, 27.3
IR (v_{max}/cm^{-1}): 3263, 1651, 1526, 1486
HRMS calculated for $C_{12}H_{16}N_2O_2$ (M^+): 220.1212; Found 220.1197
R_f: 0.53 with 80% EtOAc in pet. ether
Melting Point: 187-189 °C

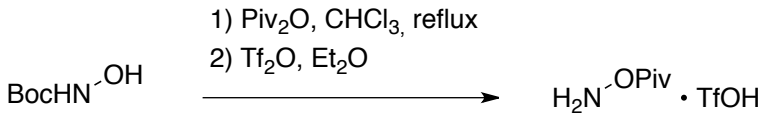
***N*-((2*R*,5*R*)-2,5-dimethylpyrrolidin-1-yl)benzamide (1k)**



1k was prepared according to a literature procedure[5] and obtained as a generous gift from Christian Clavette.

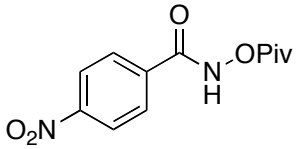
ISOQUINOLONE SCOPE SUBSTRATES

_O_-pivaloylhydroxyamine triflic acid S1



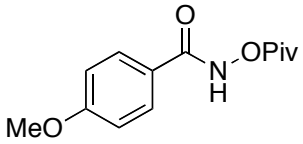
Pivalic anhydride (3.66 mL, 18.02 mmol, 1.2 equiv.) was added to a solution of *tert*-Butyl hydroxycarbamate (2.00 g, 15.02 mmol, 1 equiv.) in chloroform (40 mL). The reaction mixture was refluxed for 16 hours. The mixture was then quenched with sat. $NaHCO_3$ and diluted with CH_2Cl_2. The organic phase was washed 3 times with sat. $NaHCO_3$ after which it was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The white solid obtained (3,53g, 16.23 mmol) was dissolved in diethylether (40 mL) and triflic acid (1.44 mL, 16.23 mmol, 1 equiv.) was added dropwise at 0°C. The reaction was allowed to reach rt and it was diluted with pet. ether (40 mL) to precipitate the product. The mixture was filtrated to obtain the desired product as a white solid (2.85 g, 71% over 2 steps).
^{1}H NMR (400 MHz; DMSO-d_6, 293K): δ 1.18 (s, 9H)
^{13}C NMR (100 MHz, DMSO-d_6, 293K): δ 174.9, 120.8 (q, *J* = 322.2 Hz, 1C), 38.0, 26.6.
^{19}F NMR (377 MHz, DMSO-d_6, 293K): δ -77.8
HRMS calculated for $C_{13}H_{17}NO_3$ (M^+): 235.1208; Not found. Found only PivOH: calculated for $C_5O_2H_{10}$ (M+): 102.0681; Found 102.0640

4-nitro-*N*-(pivaloyloxy)benzamide (1l)



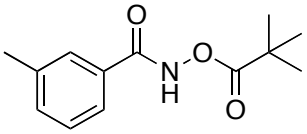
To a solution of 2 parts EtOAc in one part H_2O containing Na_2CO_3 (212 mg, 2.0 mmol, 2 equiv.) was added *O*-pivaloylhydroxyamine triflic acid **S1** (267 mg, 1 mmol, 1 equiv.). The mixture was cooled to 0°C and 4-nitrobenzoyl chloride (186 mg, 1 mmol, 1 equiv.) was added to the mixture. It was then allowed to stir at 0°C for 2 hours. The reaction was then quenched with sat. $NaHCO_3$ and more EtOAc was added. The organic layer was washed twice with sat. $NaHCO_3$. It was then dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 25% EtOAc in pet. ether as eluent. The product obtained is a white solid (86 mg, 32%).
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.50 (br s, 1H), 8.31 (d, *J* = 9.0 Hz, 2H), 7.99 (d, *J* = 8.9 Hz, 2H), 1.37 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 176.8, 164.5, 150.2, 136.4, 128.8, 124.0, 38.51, 27.0
IR (ν_{max}/cm^{-1}): 3320, 2971, 1752, 1700, 1534, 1087
GC-MSD mass: calculated for $C_8H_6N_2O_5$ (M^+-(*t*-Bu)): 210.0; Found = 210.1
R_f: 0.33 with 20% EtOAc in pet. ether
Melting Point: 110-112 °C

4-methoxy-*N*-(pivaloyloxy)benzamide (1m)



To a solution of 2 parts EtOAc in one part H_2O containing Na_2CO_3 (424 mg, 4.0 mmol, 2 equiv.) was added *O*-pivaloylhydroxyamine triflic acid **S1** (534 mg, 2 mmol, 1 equiv.). The mixture was cooled to 0°C and 4-methoxybenzoyl chloride (270 µL, 1 mmol, 1 equiv.) was added to the mixture. It was then allowed to stir at 0°C for 2 hours. The reaction was then quenched with sat. $NaHCO_3$ and more EtOAc was added. The organic layer was washed twice with sat. $NaHCO_3$. It was then dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 25% EtOAc in pet. ether as eluent. The product obtained is a white solid (403 mg, 80%).
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.36 (br s, 1H), 7.79 (d, *J* = 8.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 2H), 3.85 (s, 3H), 1.36 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 177.3, 166.7, 163.1, 129.4, 123.0, 114.0, 55.4, 38.5, 27.0
IR (ν_{max}/cm^{-1}): 3243, 2978, 1774, 1653, 1606, 1496, 1261, 1072, 1029
GC-MSD mass: calculated for $C_9H_9NO_3$ (M^+-(*t*-Bu)): 251.2; Found = 251.1
R_f: 0.27 with 20% EtOAc in pet. ether
Melting Point: 138-140 °C

3-methyl-*N*-(pivaloyloxy)benzamide (1n)



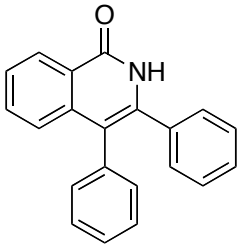
Oxalyl chloride (102 µL, 1.2 mmol, 1.2 equiv.) was added to a solution of 3-toluic acid in dichloromethane. 2 drops of DMF were added and the reaction was stirred at room temperature for 3 h. Then, volatiles were removed under reduced pressure to afford the crude 3-toluic acid chloride.
To a solution of 2 parts EtOAc in one part H_2O containing Na_2CO_3 (424 mg, 4.0 mmol, 2 equiv.) was added *O*-pivaloylhydroxyamine triflic acid **S1** (534 mg, 2 mmol, 1 equiv.). The mixture was cooled to 0°C and 3-toluic acid chloride was added to the mixture. It was then allowed to stir at 0°C for 2 hours. The reaction was then quenched with sat. $NaHCO_3$ and more EtOAc was added. The organic layer was washed twice with sat. $NaHCO_3$. It was then dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 25% EtOAc in pet. ether as eluent. The product obtained is a white solid (403 mg, 80%).
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.64 (s, 1H), 7.61-7.57 (m, 2H), 7.34-7.27 (m, 2H), 2.36 (s, 3H), 1.34 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 177.0, 166.9, 138.6, 133.4, 130.8, 128.6, 128.1, 124.5, 38.4, 27.0, 21.3
IR (ν_{max}/cm^{-1}): 3213, 2982, 1781, 1657, 1479, 1078
HRMS calculated for $C_{13}H_{17}NO_3$ (M^+): 235.1208; Found 235.1140
R_f: 0.46 with 20% EtOAc in pet. ether
Melting Point: 80-82 °C

SYNTHESIS OF DISUBSTITUTED ISOQUINOLONES

General Procedure A

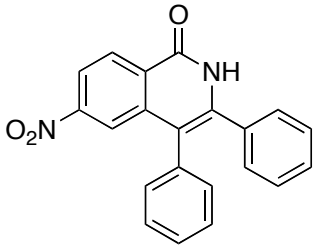
Without any particular precautions to extrude oxygen or moisture, the pivaloyl-protected hydroxamic acid (**1**)(1 equiv.), the alkyne (if solid) (1.1 equiv.), $[Cp^*RhCl_2]_2$ (0.5 mol%) and CsOAc (2 equiv.) were weighted in a 13x100 mm test tube equipped with a stir bar. MeOH (0.2 M) was then added (followed immediately by the alkyne if it is a liquid). The reaction was stirred at room temperature for 16 hours. Afterwards, it was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel (see below for specific eluents).

3,4-diphenylisoquinolin-1(2*H*)-one (3a)



3a was an off-white solid obtained in 96% yield (80.6 mg) from **1e** (4.52 mmol, 1.00 g, 1 equiv.) following general procedure A. The product was isolated by column chromatography using 40% EtOAc in pet. ether.
^{1}H NMR (400 MHz, DMSO-d_6, 293K, TMS): δ 11.56 (1H, s), 8.33 (1H, dd, *J* = 8.0, 1.1 Hz), 7.64 (1H, ddd, *J* = 8.3, 7.0, 1.4 Hz), 7.54-7.50 (1H, m), 7.30-7.22 (8H, m), 7.17-7.15 (3H, m)
^{13}C NMR (100 MHz, DMSO-d_6, 293K, TMS): δ 161.7, 138.6, 138.1, 135.8, 134.6, 132.5, 131.7, 129.8, 128.2, 128.2, 127.7, 127.1, 126.8, 126.3, 125.0, 124.9, 115.4
IR (ν_{max}/cm^{-1}): 2928, 1647, 694, 557
HRMS calculated for $C_{21}H_{15}NO$ (M^+): 297.1154; Found 297.1167
R_f: 0.45 with EtOAc 50% in pet. ether
Melting Point: 242-246 °C

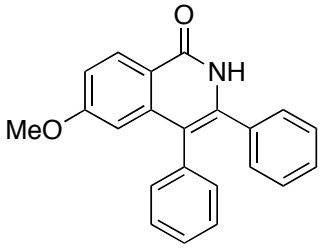
6-nitro-3,4-diphenylisoquinolin-1(2H)-one (3b)



The desired compound was a yellow solid obtained in 90% yield (62.0 mg) from **1l** (0.20 mmol, 45 mg, 1 equiv.) following general procedure A. The product was isolated by column chromatography using 50% Et_2O in pet. ether.
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): δ 10.15 (1H, s), 8.58-8.56 (1H, m), 8.23-8.20 (2H, m), 7.38-7.26 (8H, m), 7.19-7.17 (2H, m)
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 161.7, 150.6, 139.7, 139.5, 134.3, 134.1, 131.6, 129.6, 129.2, 129.2, 128.9, 128.6, 128.5, 128.1, 121.2, 120.1, 117.1

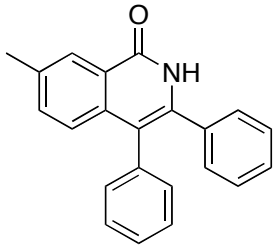
IR (neat, v_{max}/cm^{-1}): 3173, 3032, 2924, 2857, 1657, 1620, 1533, 1345, 902, 835, 795, 744, 701
HRMS calculated for $C_{21}H_{14}N_2O_3$ (M^+): 342.1004; Found 342.1021
Melting Point: 251-252 °C
R_f: 0.17 with 50% Et_2O in pet. ether

6-nethoxy-3,4-diphenylisoquinolin-1(2H)-one (3c)



The desired compound was a pale orange solid obtained in 89% yield (87.4 mg) from **1m** (0.30 mmol, 75 mg, 1 equiv.) following general procedure A. The product was isolated by column chromatography using 2% isopropanol in toluene.
^{1}H NMR (300 MHz, DMSO-d_6, 303K, TMS): δ 11.36 (1H, s), 8.25 (1H, d, *J* = 8.8 Hz), 7.30-7.13 (11H, m), 6.51 (1H, d, *J* = 2.0 Hz), 3.67 (3H, s)
^{13}C NMR (75 MHz, DMSO-d_6, 303K, TMS): δ 162.3, 161.4, 140.1, 139.2, 135.9, 134.6, 131.7, 129.8, 129.1, 128.2, 128.2, 127.7, 127.1, 118.9, 115.1, 114.5, 107.2, 55.2
IR (nujol mull, v_{max}/cm^{-1}): 3129, 1647, 1613, 1278, 868, 781
HRMS calculated for $C_{22}H_{17}NO_2$ (M^+): 327.1259; Found 327.1251
Melting Point: decomposes above 225°C
R_f: 0.20 with 75% CH_2Cl_2, 23% pet. ether and 2% MeOH

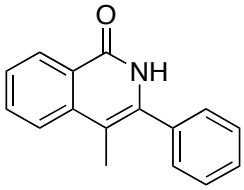
7-methyl-3,4-diphenylisoquinolin-1(2*H*)-one (3d)



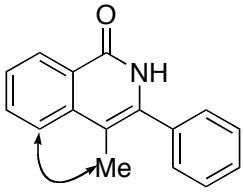
The desired compound was a pale orange solid obtained in 92% yield (86.4 mg) from **1n** (0.30 mmol, 71 mg, 1 equiv.) following general procedure A. The product was isolated by column chromatography using 2% isopropanol in dichloromethane.
^{1}H NMR (300 MHz, DMSO-d_6, 303K, TMS): δ 11.46 (s, 1H), 8.12 (dd, *J* = 1.2, 0.6 Hz, 1H), 7.47 (ddd, *J* = 8.4, 2.0, 0.5 Hz, 1H), 7.32-7.21 (m, 8H), 7.14-7.12 (m, 2H), 7.06 (d, *J* = 8.3 Hz, 1H), 2.45 (s, 3H)
^{13}C NMR (75 MHz, DMSO-d_6, 303K, TMS): δ 161.6, 137.5, 136.0, 135.8, 134.6, 133.8, 131.7, 129.8, 128.2, 128.1, 127.7, 127.0, 126.4, 125.0, 115.4, 20.9 (2 signals missing due to overlap)
IR (v_{max}/cm^{-1}): 2925, 1646, 1616, 1492, 1345
HRMS calculated for $C_{22}H_{17}NO$ (M^+): 311.1310; Found 311.1308
Melting Point: decomposes above 270°C

R_f: 0.38 with 3% isopropanol in dichloromethane

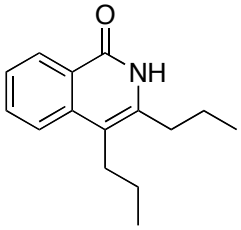
4-methyl-3-phenylisoquinolin-1(2*H*)-one (3e)



The desired compound was an off-white solid obtained in 92% yield (65.1mg) from **1e** (0.30 mmol, 66 mg, 1 eq.) following general procedure A. The purification was performed by flash column chromatography using 3% isopropanol in toluene.
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): δ 9.61 (1H, br s), 8.42 (1H, d, *J* = 7.96 Hz), 7.76-7.72 (2H, m), 7.75-7.43 (6H, m), 2.26 (3H, s)
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 162.6, 138.8, 136.8, 135.3, 132.7, 129.3, 129.0, 128.7, 127.7, 126.3, 125.4, 123.6, 109.1, 13.9
IR (v_{max}/cm^{-1}): 1653, 761, 701
HRMS calculated for $C_{16}H_{13}NO$ (M^+): 235.0997; Found 235.1019
R_f: 0.29 with EtOAc 50% in pet. ether
Melting Point: decomposes at 200-204 °C
NOESY (400 MHz, $CDCl_3$, 293K, TMS); COSY (400 MHz, $CDCl_3$, 293K, TMS)

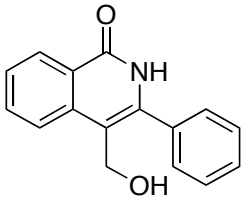


3,4-dipropylisoquinolin-1(2*H*)-one (3f)



The desired compound was an off-white solid obtained in 70% yield (47.9 mg) from **1e** (0.30 mmol, 66 mg, 1 eq.) following general procedure A. The purification was performed by flash column chromatography using 5 to 10% acetone in dichloromethane.
^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): δ 11.38 (s, 1H), 8.46 (d, *J* = 7.9 Hz, 1H), 7.67 (dd, *J* = 4.5, 1.1 Hz, 2H), 7.46-7.42 (m, 1H), 2.72-2.67 (m, 4H), 1.76 (sextet, *J* = 7.6 Hz, 2H), 1.66-1.54 (m, 2H) , 1.08-1.03 (m, 6H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 163.8, 138.5, 138.3, 132.3, 127.7, 125.3, 125.1, 123.0, 113.0, 33.0, 28.6, 23.6, 22.8, 14.4, 14.0
IR (v_{max}/cm^{-1}): 2955, 2874, 1660, 1633
HRMS calculated for $C_{15}H_{19}NO$ (M^+): 229.1467; Found 229.1452
R_f: 0.54 with 40% ethyl acetate in pet. ether
Melting Point: decomposes at 176-180 °C

4-(hydroxymethyl)-3-phenylisoquinolin-1(2*H*)-one (4g)



The desired compound was an off-white solid obtained in 99% yield (74.8 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure A. The purification was performed by flash column chromatography using 5% isopropanol in toluene.

^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): δ 8.78 (1H, br s), 8.44 (1H, dd, *J* = 8.1, 1.2 Hz), 8.01 (1H, d, *J* = 8.2 Hz), 7.77 (1H, ddd, *J* = 8.3, 7.1, 1.4 Hz), 7.56-7.51 (6H, m), 4.74 (2H, s)

^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 162. 4, 139.8, 137.6, 134.2, 133.3, 129.9, 129.0, 128.8, 127.9, 126.9, 125.6, 124.0, 112.5, 58.6

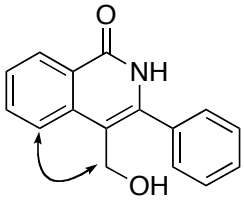
IR (v_{max}/cm^{-1}): 1650, 1345, 758, 691

HRMS calculated for $C_{16}H_{13}NO$ (M+): 251.0946; Found 251.0967

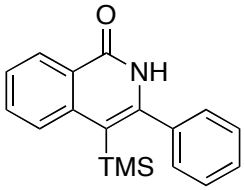
R_f: 0.15 with isopropanol 5% in toluene

Melting Point: Turns black over 280 °C

NOESY (400 MHz, $CDCl_3$, 293K, TMS); COSY (400 MHz, $CDCl_3$, 293K, TMS)



3-phenyl-4-(trimethylsilyl)isoquinolin-1(2*H*)-one (3h)



The desired compound was an off-white solid obtained in 55% yield (74.8 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure A. The purification was performed by flash column chromatography using 5% acetone in pet. ether.

^{1}H NMR (400 MHz, $CDCl_3$, 293K, TMS): δ 7.80 (dt, *J* = 7.5, 0.9 Hz, 1H), 7.60 (s, 1H), 7.44-7.34 (m, 4H), 7.19-7.15 (m, 1H), 7.12-7.10 (m, 2H), 6.12 (d, *J* = 8.0 Hz, 1H), 0.25 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 168.3, 140.7, 139.7, 136.6, 131.9, 130.2, 129.0, 128.9, 128.3, 126.7, 125.1, 124.6, 123.0, 0.4

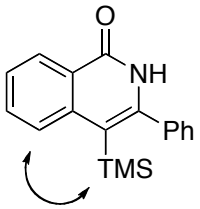
IR (v_{max}/cm^{-1}): 3223, 1701, 1613, 849

HRMS calculated for $C_{18}H_{19}NOSi$ (M+): 293.1236; Found 293.1241

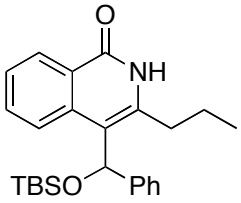
R_f: 0.76 with 50% EtOAc in pet. ether.

Melting Point: 202-208 °C

NOESY (300 MHz, $CDCl_3$, 293K, TMS)



4-((*tert*-butyldimethylsilyloxy)(phenyl)methyl)-3-propylisoquinolin-1(2*H*)-one (3j)



The desired compound was an off-white solid obtained in 83% yield (102.8 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure A. The corresponding alkyne was prepared according to a literature procedure.[6] The purification was performed by flash column chromatography using 10% ethyl acetate in pet. ether.

^{1}H NMR (300 MHz, $CDCl_3$, 293K, TMS): δ 11.84 (s, 1H), 8.41 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.87-7.84 (m, 1H), 7.45-7.18 (m, 7H), 6.31 (s, 1H), 2.94-2.73 (m, 2H), 1.78-1.74 (m, 2H), 1.07 (t, *J* = 7.2 Hz, 3H), 0.91 (s, 9H), 0.19 (s, 3H), -0.22 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 164.5, 144.5, 140.1, 137.1, 131.6, 128.2, 127.0, 126.6, 125.6, 125.5, 125.5, 114.7, 70.4, 33.3, 25.8, 23.1, 18.3, 14.3, 4.5, 4.9

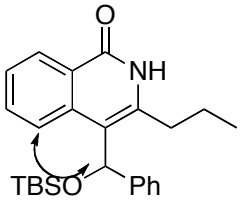
IR (v_{max}/cm^{-1}):

HRMS calculated for $C_{25}H_{33}NO_2Si$ (M+): 407.2281; Found: 407.2283

R_f: 0.82 with 40% EtOAc in pet. ether.

Melting Point: 154-160 °C

NOESY (300 MHz, $CDCl_3$, 293K, TMS)

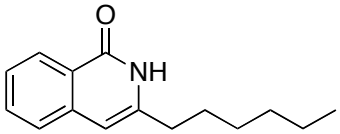


SYNTHESIS OF MONOSUBSTITUTED ISOQUINOLONES

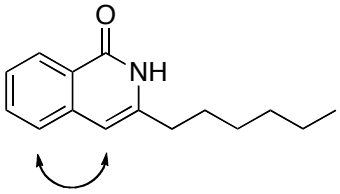
General Procedure B

Without any particular precautions to extrude oxygen or moisture, the pivaloyl-protected hydroxamic acid (**1**)(1 equiv.), the alkyne (if solid) (1.1 equiv.), $[Cp^*RhCl_2]_2$ (2.5 mol%) and CsOAc (2 equiv.) were weighted in a 13x100 mm test tube equipped with a stir bar. MeOH (0.2 M) was then added (followed immediately by the alkyne if it is a liquid). The reaction was stirred at room temperature for 16 hours. Afterwards, it was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel (see below for specific eluents).

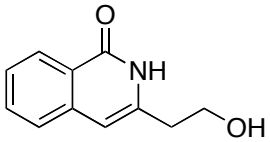
3-hexylisoquinolin-1(2*H*)-one (4a)



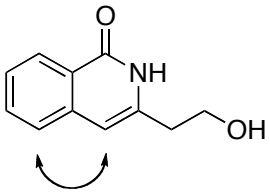
The desired compound was an off-white solid obtained in 92% yield (63.2 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure A. The purification was performed by flash column chromatography using 2% isopropanol in dichloromethane.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 11.51 (d, *J* = 0.4 Hz, 1H), 8.39 (dt, *J* = 8.1, 0.6 Hz, 1H), 7.61 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.42 (ddd, *J* = 8.1, 7.0, 1.1 Hz, 1H), 6.32 (s, 1H), 2.65 (t, *J* = 7.7 Hz, 2H), 1.76 (dt, *J* = 15.3, 7.6 Hz, 2H), 1.44-1.29 (m, 6H), 0.90-0.87 (m, 3H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 164.8, 142.3, 138.7, 132.5, 127.2, 125.6, 124.4, 103.8, 33.4, 31.5, 28.8, 28.3, 22.6, 14.1 (one signal missing due to overlap)
IR (v_{max}/cm^{-1}): 2928, 2854, 1662, 1635
HRMS calculated for $C_{15}H_{19}NO$ (M^+): 229.1467; Found 229.1458
R_f: 0.66 with 40% EtOAc in pet. ether
Melting Point: 114-117 °C
NOESY (300 MHz, $CDCl_3$, 293K, TMS)



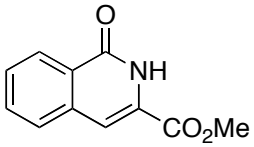
3-(2-hydroxyethyl)isoquinolin-1(2*H*)-one (4b)



The desired compound was an off-white solid obtained in 92% yield (63.2 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure B The reaction was run at 60 °C instead of room temperature. The purification was performed by flash column chromatography using 2% isopropanol in dichloromethane.
^{1}H-NMR (400 MHz; DMSO-d_6, 293K, TMS): δ 11.17 (s, 1H), 8.13 (dd, *J* = 7.5, 0.5 Hz, 1H), 7.63 (ddd, *J* = 8.0, 7.0, 1.2 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.41-7.37 (m, 1H), 6.36 (s, 1H), 4.77 (t, *J* = 5.3 Hz, 1H), 3.70 (q, *J* = 5.9 Hz, 2H), 2.64 (t, *J* = 6.5 Hz, 2H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 163.0, 140.8, 138.7, 132.8, 127.0, 126.2, 125.9, 124.9, 103.7, 60.0, 36.5
IR (v_{max}/cm^{-1}): 3387, 2941, 1666, 1643, 1553, 1049
HRMS calculated for $C_{11}H_{11}NO_2$ (M^+): 189.0790; Found 189.0790
R_f: 0.32 with 20% isopropanol in toluene
Melting Point: 172-175 °C
NOESY (300 MHz, $CDCl_3$, 293K, TMS)



Methyl 1-oxo-1,2-dihydroisoquinoline-3-carboxylate (4c)



The desired compound was an off-white solid obtained in 49% yield (29.7 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure B. The reaction was run at 60 °C instead of room temperature. The purification was performed by flash column chromatography using 45% ethyl acetate in pet. ether.

^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 9.26 (s, 1H), 8.46 (dt, *J* = 8.0, 0.6 Hz, 1H), 7.76-7.61 (m, 3H), 7.39 (s, 1H), 4.00 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 162.2, 161.8, 136.0, 133.1, 129.5, 128.3, 128.2, 128.0, 127.7, 111.4, 53.2

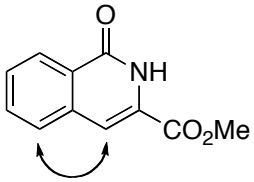
IR (ν_{max}/cm^{-1}): 2928, 1731, 1663, 1301

HRMS calculated for $C_{11}H_9NO_3$ (M^+): 203.0582; Found 203.0574

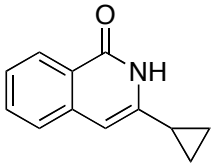
R_f: 0.33 with 50% ethyl acetate in pet. ether

Melting Point: 148-153 °C

NOESY (300 MHz, $CDCl_3$, 293K, TMS)



3-cyclopropylisoquinolin-1(2*H*)-one (4d)



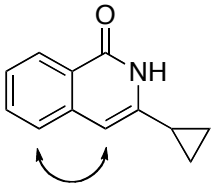
The desired compound was an off-white solid obtained in 95% yield (52.6 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure B. The purification was performed by flash column chromatography using 15% isopropanol in toluene. (contains 3% of the other regioisomer)

^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 11.11 (s, 1H), 8.37 (dt, *J* = 8.1, 0.7 Hz, 1H), 7.60 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H), 7.45-7.37 (m, 2H), 6.21 (s, 1H), 1.99-1.92 (m, 1H), 1.07-1.02 (m, 2H), 0.95-0.91 (m, 2H).

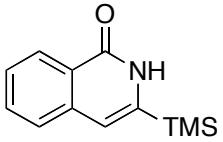
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 164.4, 143.5, 138.7, 132.5, 127.3, 125.6, 124.4, 101.4, 13.5, 7.4 (1 signal missing due to overlap)

IR (ν_{max}/cm^{-1}): 2998, 1643, 1553, 1479

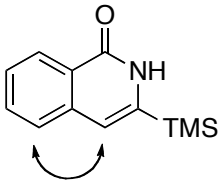
HRMS calculated for $C_{12}H_{11}NO$ (M^+): 185.0841; Found 185.0862
R_f: 0.49 with 50% EtOAc in pet. ether
Melting Point: 151-164 °C
NOESY (300 MHz, $CDCl_3$, 293K, TMS)



3-(trimethylsilyl)isoquinolin-1(2*H*)-one (4e)



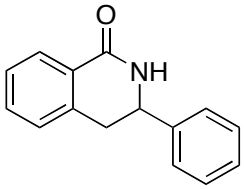
The desired compound was an off-white solid obtained in 75% yield (49.2 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure B. The purification was performed by flash column chromatography using 7% ethyl acetate in dichloromethane.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 10.63 (s, 1H), 8.40 (dt, *J* = 8.0, 0.6 Hz, 1H), 7.65 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H), 7.54-7.47 (m, 2H), 6.65 (s, 1H), 0.41 (s, 9H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 164.2, 143.4, 137.5, 132.4, 127.2, 126.8, 126.2, 126.0, 113.4, 2.2
IR (ν_{max}/cm^{-1}): 3127, 3028, 2955, 2901, 1653, 1617, 1254
HRMS calculated for $C_{12}H_{15}NOSi$ (M^+): 217.0923; Found 217.0901
R_f: 0.76 with 50% EtOAc in pet. ether
Melting Point: 154-158 °C
NOESY (300 MHz, $CDCl_3$, 293K, TMS);



SYNTHESIS OF 3,4-DIHYDROISOQUINOLONES

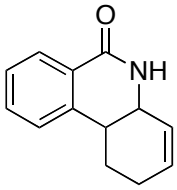
General procedure C
Without any particular precautions to extrude oxygen or moisture, the pivaloyl-protected hydroxamic acid (**1**)(1 equiv.), $[Cp^*RhCl_2]_2$ (0.5 mol%) and CsOAc (2 equiv.) were weighted in a 13x100 mm test tube equipped with a stir bar. MeOH (0.2 M) was then added followed immediately by the alkene (1.1 equiv.). The reaction was stirred at room temperature for 16 hours. Afterwards, it was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel (see below for specific eluents). Then, the resulting compound was dissolved in MeCN and washed with pet. ether to remove residual pivalic acid that seems to stick to these molecules.

3-phenylisoquinolin-1(2*H*)-one (6a)



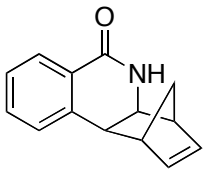
The desired compound was an off-white solid obtained in 90% yield (60.3 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 30% ethyl acetate in pet. ether.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.12 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.46 (td, *J* = 7.5, 1.5 Hz, 1H), 7.41-7.34 (m, 6H), 7.18 (d, *J* = 7.5 Hz, 1H), 6.13 (s, 1H), 4.86 (ddd, *J* = 10.9, 4.9, 1.1 Hz, 1H), 3.23-3.09 (m, 2H).
Spectral data matched the one previously reported.[7]

1,2,4a,5-tetrahydrophenanthridin-6(10b*H*)-one (6b)



The desired compound was an off-white solid obtained in 77% yield (46.2 mg) from **1e** (0.30 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 3% isopropanol in toluene.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.08 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.49 (td, *J* = 7.5, 1.5 Hz, 1H), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H), 7.27-7.24 (m, 1H), 6.06-6.01 (m, 2H), 5.80 (ddt, *J* = 9.8, 4.8, 2.4 Hz, 1H), 4.29-4.27 (m, 1H), 2.97-2.92 (m, 1H), 2.25-2.19 (m, 2H), 2.04-1.93 (m, 1H), 1.73-1.67 (m, 1H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 165.0, 142.8, 132.5, 132.3, 128.0, 127.5, 127.2, 127.1, 124.4, 48.0, 37.8, 25.2, 25.0.
IR (ν_{max}/cm^{-1}): 3206, 2931, 1668, 1466, 1398
HRMS calculated for $C_{13}H_{13}NO$ (M^+): 199.0997; Found 199.0984
R_f: 0.36 with 50% EtOAc in pet. ether
Melting Point: 141-148 °C

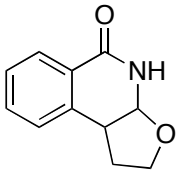
6c



The desired compound was a white solid obtained in 91% yield (288.2 mg) from **1e** (1.50 mmol, 332 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 50% ethyl acetate in pet. ether.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.14 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.51-7.47 (m, 1H), 7.33-7.29 (m, 2H), 6.75 (s, 1H), 6.39 (dt, *J* = 4.3, 2.3 Hz, 1H), 6.14 (td, *J* = 3.5, 2.1 Hz, 1H),

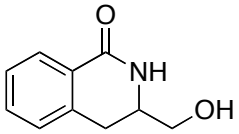
3.73 (d, *J* = 8.8 Hz, 1H), 3.09 (d, *J* = 8.8 Hz, 1H), 2.92 (t, *J* = 1.8 Hz, 2H), 1.64 (d, *J* = 9.4 Hz, 1H), 1.47 (dt, *J* = 9.4, 1.6 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 164.2, 140.0, 139.3, 134.8, 132.4, 128.4, 127.7, 126.4, 126.1, 54.2, 52.9, 52.2, 42.7, 39.3.
IR (v_{max}/cm^{-1}): 2941, 1673, 1459, 1335
HRMS calculated for C_9H_7NO (M^+-cyclopentadiene): 145.0528; Found 145.0539
R_f: 0.38 with 50% EtOAc in pet. ether
Melting Point: melts with gas formation at 190 °C

1,2,3a,4-tetrahydrofuro[2,3-*c*]isoquinolin-5(9b*H*)-one (6d)



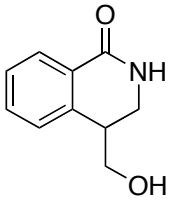
The desired compound was an off-white solid obtained in 77% yield (43.8 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 8% isopropanol in toluene.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.16 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.57 (td, *J* = 7.4, 1.5 Hz, 1H), 7.52-7.46 (m, 2H), 7.38 (s, 1H), 4.83 (d, *J* = 4.4 Hz, 1H), 4.35 (t, *J* = 4.5 Hz, 1H), 4.09-3.99 (m, 2H), 2.43 (dtd, *J* = 13.2, 8.9, 5.6 Hz, 1H), 2.24 (dddd, *J* = 13.1, 7.0, 3.9, 2.2 Hz, 1H).
^{13}C NMR (100 MHz, $CDCl_3$, 293K, TMS): δ 164.8, 135.3, 132.6, 129.3, 129.0, 127.9, 127.4, 75.2, 66.7, 54.2, 34.9
IR (v_{max}/cm^{-1}): 3213, 2885, 1669, 1606, 1583, 1409, 1334, 1045, 760
HRMS calculated for $C_{11}H_{11}NO_2$ (M^+): 189.0790; Found 189.0785
R_f: 0.10 with 50% EtOAc in pet. ether
Melting Point: 132-138 °C

3-(hydroxymethyl)-3,4-dihydroisoquinolin-1(2*H*)-one (6e-regio 1)



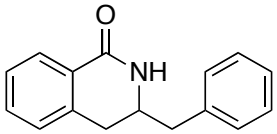
The desired compound was an off-white solid obtained in 37% yield (19.9 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 15% isopropanol in toluene.
^{1}H-NMR (400 MHz; DMSO-d_6, 293K, TMS): δ 7.83 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.75 (s, 1H), 7.46 (td, *J* = 7.5, 1.4 Hz, 1H), 7.34-7.28 (m, 2H), 4.92 (s, 1H), 3.59-3.41 (m, 2H), 2.99 (dd, *J* = 16.0, 5.1 Hz, 1H), 2.86 (dd, *J* = 15.9, 8.1 Hz, 1H).
Spectral data is consistent with that previously reported.[8]

4-(hydroxymethyl)-3,4-dihydroisoquinolin-1(2*H*)-one (6e-regio 2)



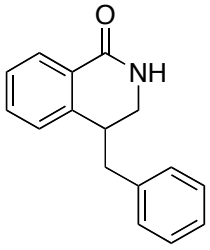
The desired compound was an off-white solid obtained in 48% yield (25.5 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 15% isopropanol in toluene.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.04 (d, *J* = 7.4 Hz, 1H), 7.46 (td, *J* = 7.5, 1.1 Hz, 1H), 7.35 (td, *J* = 7.6, 1.0 Hz, 1H), 7.28-7.23 (m, 1H), 6.50 (s, 1H), 3.78-3.67 (m, 4H), 3.05-3.01 (m, 1H), 2.57 (s, 1H).
^{13}C NMR (100 MHz, DMSO-d_6, 293K, TMS): δ 164.5, 140.5, 132.2, 129.5, 128.3, 127.5, 127.4, 62.3. (2 signals missing due to overlap with DMSO signal)
IR (v_{max}/cm^{-1}): 3307, 2931, 2874, 1657, 1479
HRMS calculated for $C_{10}H_{11}NO_2$ (M^+): 177.0790; Found 177.0781
R_f: 0.12 with 50% EtOAc in pet. ether
Melting Point: 120-127°C

3-benzyl-3,4-dihydroisoquinolin-1(2*H*)-one (6f-regio 1)



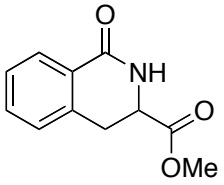
The desired compound was an off-white solid obtained in 57% yield (40.6 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 2.5% isopropanol in toluene.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.09 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.41 (td, *J* = 7.4, 1.6 Hz, 1H), 7.36 (td, *J* = 7.5, 1.4 Hz, 1H), 7.29 (ddd, *J* = 7.9, 6.4, 1.4 Hz, 2H), 7.23-7.20 (m, 1H), 7.14-7.11 (m, 2H), 7.08 (dd, *J* = 7.2, 0.9 Hz, 1H), 6.30 (s, 1H), 3.58 (ddd, *J* = 12.5, 4.3, 0.9 Hz, 1H), 3.28 (ddd, *J* = 12.5, 4.7, 2.9 Hz, 1H), 3.11-3.06 (m, 1H), 3.00-2.87 (m, 2H).
^{13}C NMR (100 MHz, DMSO-d_6, 293K, TMS): δ 166.1, 142.4, 139.1, 132.2, 129.1, 128.6, 128.3, 128.1, 127.3, 127.1, 126.6, 43.0, 40.0, 39.8
IR (v_{max}/cm^{-1}): 3210, 3069, 3025, 2925, 1669, 1476, 1335.
HRMS calculated for $C_{16}H_{15}NO$ (M^+): 237.1154; Found 237.1166
R_f: 0.27 with 50% EtOAc in pet. ether
Melting Point: 120-122°C

4-benzyl-3,4-dihydroisoquinolin-1(2*H*)-one (6f-regio 2)



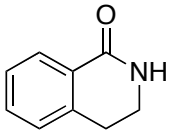
The desired compound was an off-white solid obtained in 28% yield (19.9 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.) following general procedure C. The purification was performed by flash column chromatography using 2.5% isopropanol in toluene.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.06 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.45 (td, *J* = 7.5, 1.4 Hz, 1H), 7.37-7.32 (m, 3H), 7.29-7.25 (m, 1H), 7.20 (dt, *J* = 7.0, 2.4 Hz, 3H), 6.06 (s, 1H), 3.99-3.91 (m, 1H), 3.03-2.80 (m, 4H).
^{13}C NMR (100 MHz, DMSO-d_6, 293K, TMS): δ 166.1, 137.7, 136.6, 132.4, 129.2, 129.0, 128.6, 128.0, 127.5, 127.2, 52.5, 41.8, 34.2. (1 signal missing due to overlap)
IR (ν_{max}/cm^{-1}): 3203, 2928, 1669, 1606, 1466, 1345
HRMS calculated for $C_{16}H_{15}NO$ (M^+): 237.1154; Found 237.1152
R_f: 0.39 with 50% EtOAc in pet. ether
Melting Point: 142-147°C

methyl 1-oxo-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (6g)



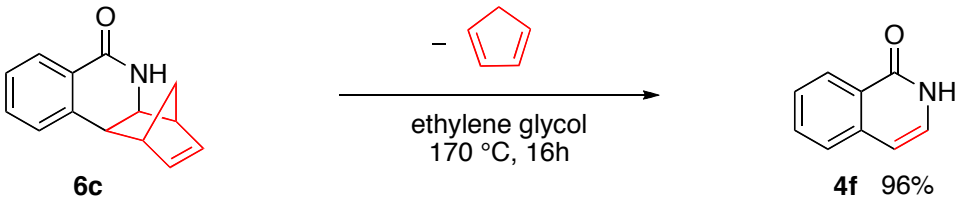
The desired compound was obtained as a 4.5:1 mixture of regioisomers that were inseparable by flash chromatography in 95% yield (19.9 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.) following general procedure C, but with the use of 2.5 mol% $[Cp^*RhCl_2]_2$. The purification was performed by flash column chromatography using 5% isopropanol in toluene.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.10-8.07 (m, 1H), 7.51-7.46 (m, 1H), 7.41-7.37 (m, 1H), 7.25 (d, *J* = 7.9 Hz, 1H), 6.39 (s, 1H), 4.42 (ddd, *J* = 10.2, 5.1, 1.9 Hz, 1H), 3.81 (s, 3H), 3.36-3.31 (m, 1H), 3.22 (dd, *J* = 15.6, 10.2 Hz, 1H).
Spectral data of the major regioisomer match the data previously reported.[9]

3,4-dihydroisoquinolin-1(2*H*)-one (6h)



Without any particular precautions to extrude oxygen or moisture, the pivaloyl-protected hydroxamic acid (**1**)(1 equiv.), $[Cp^*RhCl_2]_2$ (0.5 mol%) and CsOAc (2 equiv.) were weighted in a 13x100 mm test tube equipped with a stir bar. MeOH (0.2 M) was then added and ethylene was bubbled through the reaction mixture for about 3 min. The needle was pulled out of the solvent and the vial was sealed under an ethylene atmosphere (balloon). The reaction was stirred at room temperature for 16 hours. Afterwards, it was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel. The desired compound was obtained in 98% yield (43.1 mg) from **1e** (0.3 mmol, 66 mg, 1 equiv.). The purification was performed by flash column chromatography using 4% isopropanol in dichloromethane.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 8.08-8.06 (m, 1H), 7.45 (td, *J* = 7.5, 1.5, 1H), 7.38-7.34 (m, 1H), 7.23-7.21 (m, 1H), 6.38 (s, 1H), 3.58 (td, *J* = 6.6, 2.9, 2H), 3.01 (t, *J* = 6.6, 2H)
Spectral data match the one previously reported.[10]

Retro Diels-Alder Reaction

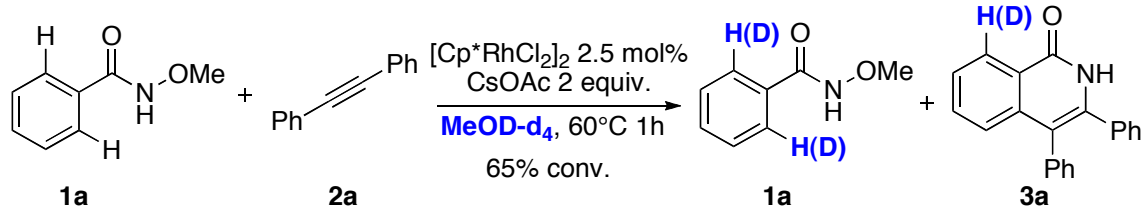


6c **4f** 96%

6c (0.30 mmol, 63.4 mg) was dissolved in ethylene glycol (0.3M) and heated for 16h at 170 °C. The resulting mixture was then cooled down to room temperature and diluted with dichloromethane and brine. The aqueous phase was extracted with dichloromethane and the combined organic fractions were washed with more brine. The organic fraction was dried over $MgSO_4$, filtered and evaporated under reduced pressure to afford **4f** as a white solid. The compound was analyticaly pure without any further purification necessary.
^{1}H-NMR (400 MHz; $CDCl_3$, 293K, TMS): δ 10.69 (br s, 1H), 8.43 (dt, *J* = 8.1, 0.7 Hz, 1H), 7.68 (ddd, *J* = 8.0, 7.0, 1.3 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.52 (ddd, *J* = 8.1, 7.1, 1.1 Hz, 1H), 7.15 (dd, *J* = 7.2, 0.3 Hz, 1H), 6.56 (d, *J* = 7.1 Hz, 1H).
Spectral data is consistent with that previously reported.[11]

MECHANISTIC EXPERIMENTS

Irreversibility of alkyne insertion



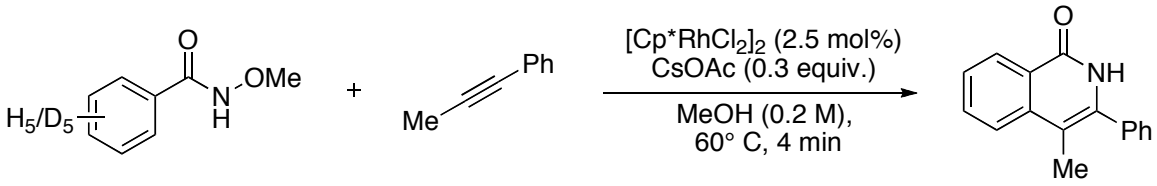
1a **2a** **1a** **3a**

- No deuterium incorporation on **3a**
- No deuterium incorporation on recovered starting material

Without any particular precautions to extrude oxygen or moisture, **1a** (60 mg, 0.40 mmol, 1 equiv.), **2a** (78.4 mg, 0.44 mmol, 1.1 equiv.) $[Cp^*RhCl_2]_2$ (6.2 mg, 0.025 mmol, 2.5 mol%) and CsOAc (153 mg, 0.80 mmol, 2 equiv.) were weighed in a 13x100 mm test tube equipped with a stir bar. MeOH (1 mL) was added and the mixture was stirred at 60°C for 5 h after which the reaction mixture was diluted with CH_2Cl_2 and transferred to a round bottom flask. Silica was added to the flask and volatiles were evaporated under reduced pressure. The purification was performed by flash column chromatography on silica gel using 40% EtOAc in pet. ether. Both **1a** and **3a** were isolated and no deuterium incorporation was found.

KIE experiments

With 1a/1a D-5 as substrate

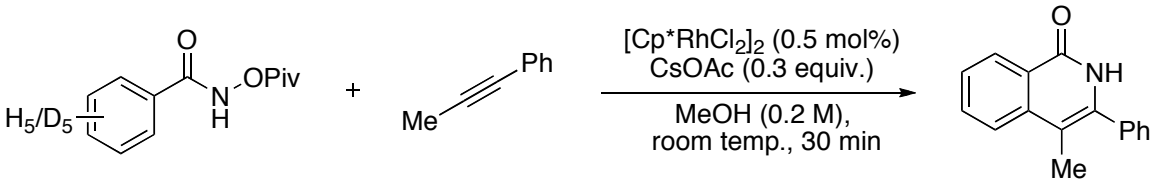


1a	**2c**	**8.9 (± 0.4) x 10^{-5} M/s**	**$k_{H/D}$ = 1.0 ± 0.1**
1a-d_5		**8.8 (± 0.8) x 10^{-5} M/s**	

Without any particular precautions to extrude oxygen or moisture, **1a** (78 mg, 0.50 mmol, 1 equiv.), **2c** (69 µL, 0.55 mmol, 1.1 equiv.), CsOAc (29 mg, 0.15 mmol, 0.3 equiv.) and the internal standard trimethoxybenzene (28 mg, 0.167 mmol, 0.33 equiv.), were weighed in a 10 mL round bottom flask equipped with a stir bar. MeOH (2.5 mL, 0.2M) was added and the mixture was stirred at 60 °C for 5 min. $[Cp^*RhCl_2]_2$ (6.2 mg, 0.025 mmol, 2.5 mol%) was then added in one portion and timing was started. An aliquot of 0.5 mL was taken every minute for 4 minutes and immediately quenched in a mixture of TFA (30 µL) and chloroform (1 mL). Volatiles were removed under a flow or air and ^{1}H NMR was taken. The yield was found by integrating the methyl peak of the isoquinolone.

	[3e]			
time (sec)	H-5 run 1	H-5 run 2	D-5 run 1	D-5 run 2
60	0,0162	0,0156	0,0168	0,0144
120	0,0236	0,022	0,0244	0,0206
180	0,0292	0,0274	0,0294	0,025
240	0,033	0,0308	0,0342	0,029

With 1e/1e D-5 as substrate



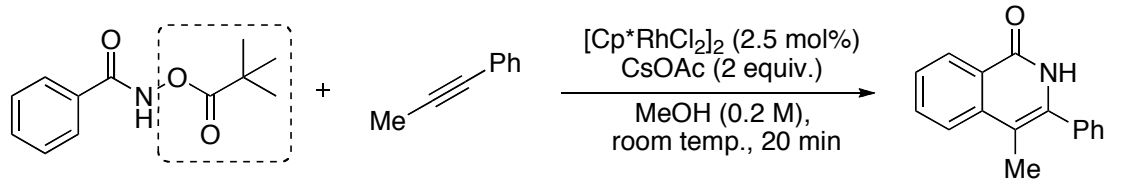
1e	**2c**	**4.8 (± 0.2) x 10^{-5} M/s**	**$k_{H/D}$ = 14.6 ± 0.1**
1e-d_5		**0.33 (± 0.01) x 10^{-5} M/s**	

Without any particular precautions to extrude oxygen or moisture, **1e** (155 mg, 0.70 mmol, 1 equiv.), **2c** (96.4 µL, 0.77 mmol, 1.1 equiv.), CsOAc (153 mg, 0.80 mmol, 2 equiv.) and trimethoxybenzene (39 mg, 0.233 mmol, 0.33 equiv.), the internal standard, were weighed in a 10 mL round bottom flask equipped with a stir bar. MeOH (3.5 mL, 0.2M) was added and the mixture was stirred at rt for 2 min. $[Cp^*RhCl_2]_2$ (2.2 mg, 0.005 mmol, 0.5 mol%) was then added in one portion and timing was started. An aliquot of 0.5 mL was taken every 5 minutes

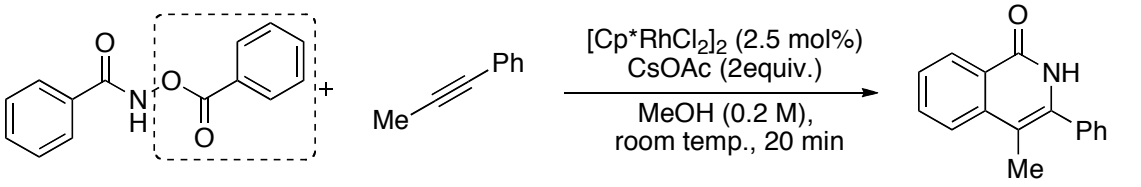
for 30 minutes and immediately quenched in a mixture of TFA (30 µL) and dichloromethane (1 mL). Volatiles were removed under a flow or air and ^{1}H NMR was taken. The yield was found by integrating the methyl peak of the isoquinolone.

time (sec)	[3e] H-5 run 1	H-5 run 2	D-5 run 1	D-5 run 2
300	0,008	0,01	0,00086	0,00092
600	0,02	0,022	0,00172	0,0018
900	0,032	0,034	0,00268	0,00284
1200	0,046	0,048	0,00368	0,00364
1500	0,06	0,066	0,00432	0,00486
1800	0,078	0,084	0,00568	0,00604

Rate with different internal oxidants



1e **2c** **k = 4.2 x 10^{-5} M/s**



1f **2c** **k = 2.5 x 10^{-5} M/s**

$k_{OPiv/OBz}$ = 1.68

Rate with substrate **1e** was calculated in the KIE experiment, see above.

Rate with substrate 1f

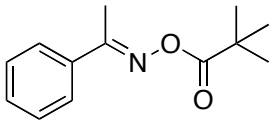
Without any particular precautions to extrude oxygen or moisture, **1f** (169 mg, 0.70 mmol, 1 equiv.), **2c** (96.4 µL, 0.77 mmol, 1.1 equiv.), CsOAc (153 mg, 0.80 mmol, 2 equiv.) and trimethoxybenzene (39 mg, 0.233 mmol, 0.33 equiv.), the internal standard, were weighed in a 10 mL round bottom flask equipped with a stir bar. MeOH (3.5 mL, 0.2M) was added and the mixture was stirred at rt for 2 min. $[Cp^*RhCl_2]_2$ (2.2 mg, 0.005 mmol, 0.5 mol%) was then added in one portion and timing was started. An aliquot of 0.5 mL was taken every 5 minutes for 20 minutes and immediately quenched in a mixture of TFA (30 µL) and dichloromethane (1 mL). Volatiles were removed under a flow or air and ^{1}H NMR was taken. The yield was found by integrating the methyl peak of the isoquinolone.

time (sec)	[3e]
300	0,007
600	0,0146
900	0,022
1200	0,0296

ISOQUINOLINE SYNTHESIS RELATED EXPERIMENTS

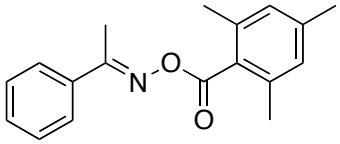
Preparation of the starting materials

(*E*)-acetophenone *O*-pivaloyl oxime (7a)



Pivalic anhydride (2.23 mL, 11 mmol, 1.1 equiv.) was added to a solution of acetophenone oxime (1.35 g, 10 mmol, 1 equiv.) in dichloromethane (30 mL). The reaction mixture was allowed to stir for 16 h at room temperature after which it was diluted with more dichloromethane and washed with sat. $NaHCO_3$. The organic layer was dried over $MgSO_4$, filtered and evaporated under reduced pressure to afford **7a** in an analytically pure form (2.09 g, 95%).
^{1}H-NMR (300 MHz; $CDCl_3$, 293K, TMS): δ 7.76-7.73 (m, 2H), 7.42-7.38 (m, 3H), 2.37 (s, 3H), 1.33 (s, 9H)
^{13}C NMR (100 MHz, DMSO-d_6, 293K, TMS): δ 175.0, 163.1, 134.9, 130.5, 128.5, 127.0, 38.8, 27.3, 14.3
IR (ν_{max}/cm^{-1}): 2974, 1760, 1309, 1114
HRMS calculated for $C_{13}H_{17}NO_2$ (M^+): 219.1259; Found 219.1248
Melting Point: 60-62°C

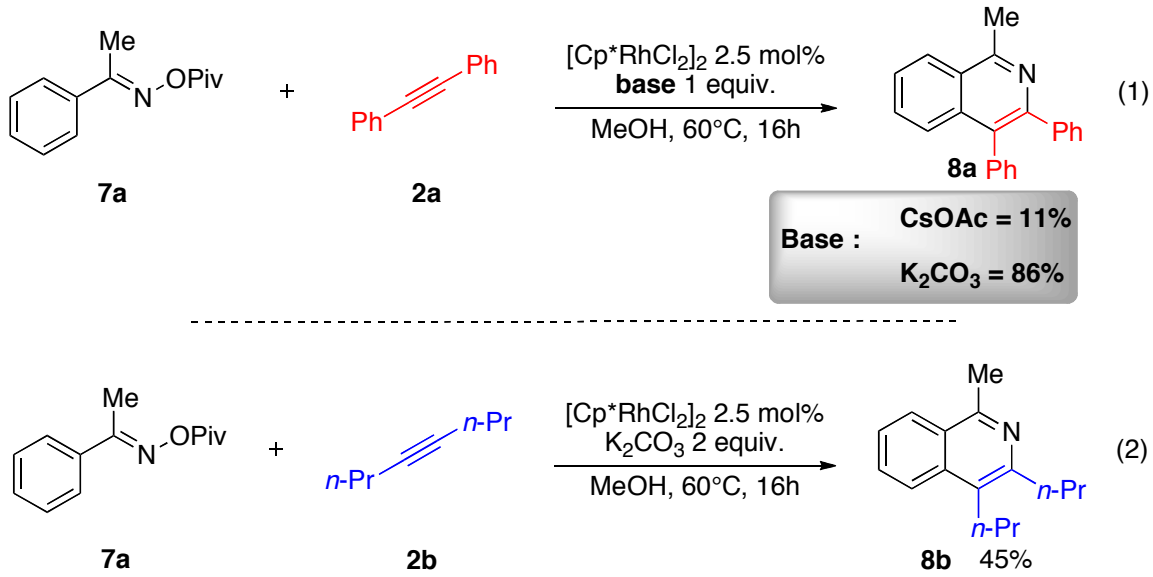
(*E*)-acetophenone *O*-2,4,6-trimethylbenzoyl oxime (7b)



Acetophenone oxime (2.00 g, 14.8 mmol, 1 equiv.) and NaO*t*Bu (1.42 g, 14.8 mmol, 1 equiv.) were stirred together at room temperature for 30 min. Then, the mixture was cooled down to 0 °C and mesitoyl chloride (2.47 mL, 14.8 mmol, 1 equiv.) was added dropwise. It was then brought back to room temperature and stirred until completion as judge by TLC. The reaction was then quenched with sat. $NaHCO_3$ and the organic phase was washed three times with sat. $NaHCO_3$ after which it was dried over $MgSO_4$, filtered and evaporated under reduced pressure. The purification was made by flash column chromatography using 7% ethyl acetate in pet. ether to afford a white solid (2.94 g, 71%).
^{1}H-NMR (300 MHz; $CDCl_3$, 293K, TMS): δ 7.82-7.79 (m, 2H), 7.46-7.40 (m, 3H), 6.91 (d, *J* = 0.6 Hz, 2H), 2.40 (s, 3H), 2.39 (s, 6H).

^{13}C NMR (100 MHz, DMSO-d$_6$, 293K, TMS): δ 167.35, 163.3, 139.8, 135.7, 134.8, 130.6, 129.4, 128.6, 128.4, 127.1, 21.2, 19.9, 14.6
IR (ν_{max}/cm^{-1}): 2922, 1756, 1612, 1240, 1163, 1048
GC-MSD mass: calculated for $C_8H_6N_2O_5$ (M^+-(*t*-Bu)): 210.0; Found = 210.1
Melting Point: 82-85°C

Base effect in isoquinoline synthesis

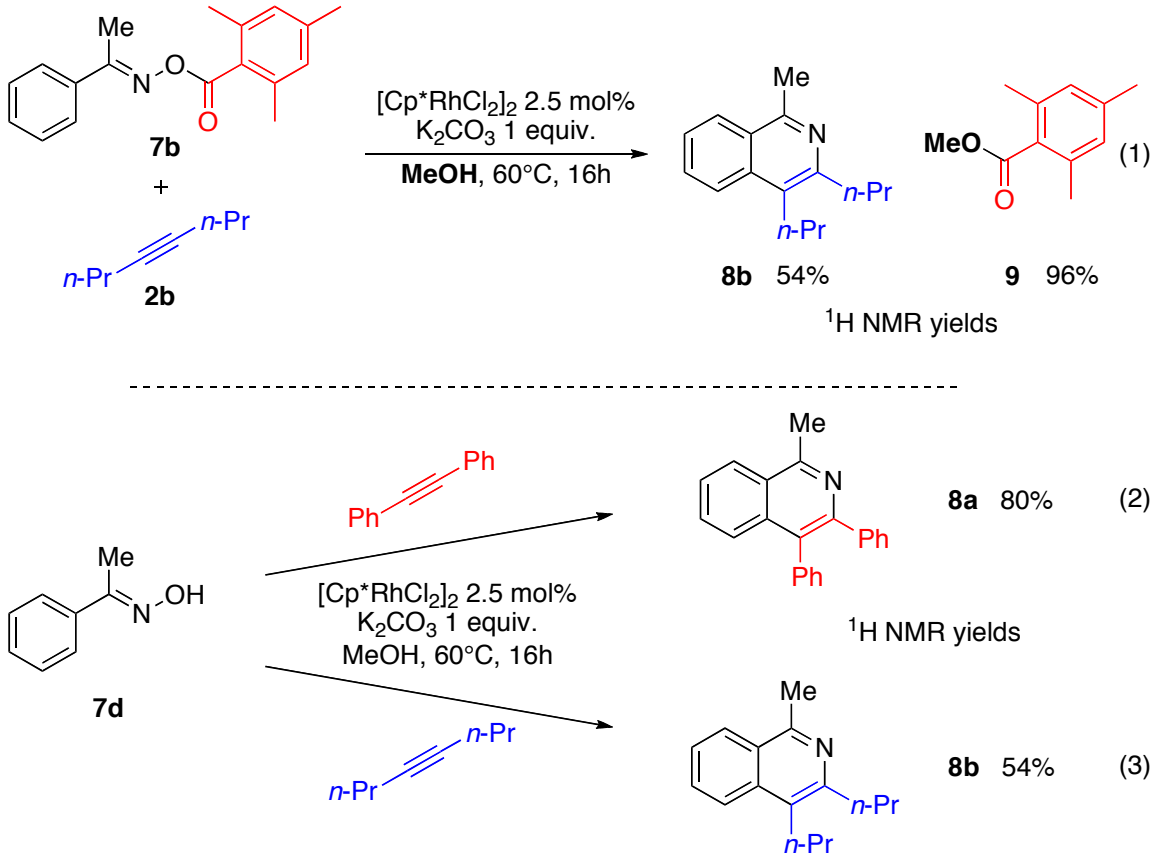


Scheme 11, eq 1
7a (44 mg, 0.20 mmol, 1 equiv.), **2a** (39 mg, 0.22 mmol, 1.1 equiv.) [Cp*RhCl$_2$]$_2$ and the base (0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

Scheme 12, eq 2

7a (44 mg, 0.20 mmol, 1 equiv.), **2b** (32 µL, 0.22 mmol, 1.1 equiv.) [Cp*RhCl$_2$]$_2$ and K_2CO_3 (28 mg, 0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

Observation of a methy ester side product



Scheme 12, eq 1

7b (56 mg, 0.20 mmol, 1 equiv.), **2b** (32 µL, 0.22 mmol, 1.1 equiv.) $[Cp^*RhCl_2]_2$ and K_2CO_3 (28 mg, 0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

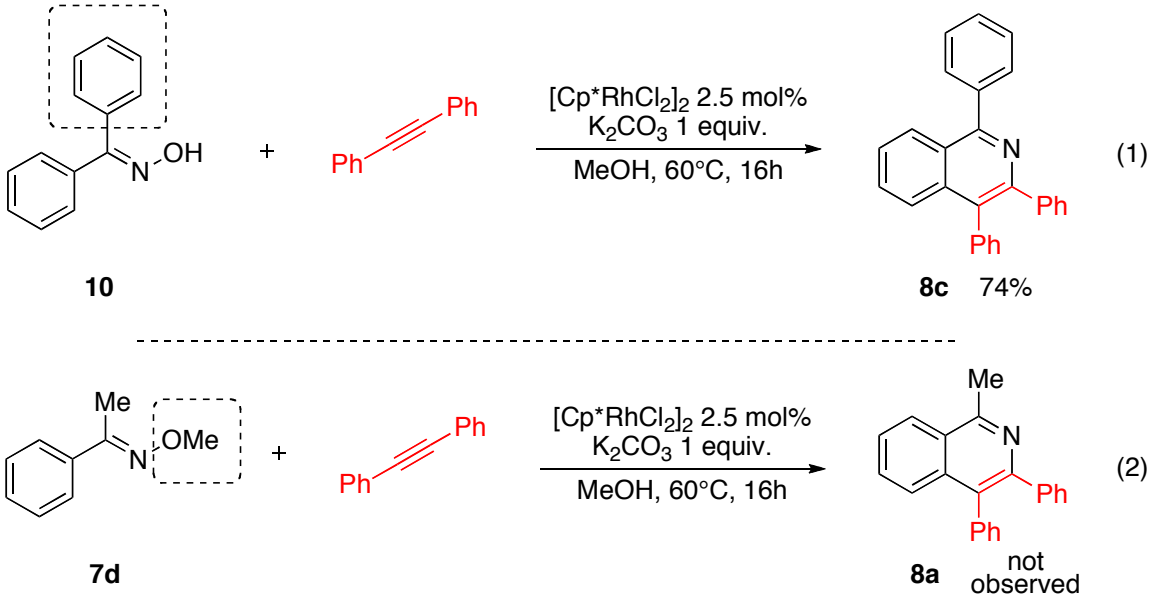
Scheme 12, eq 2

7d (27 mg, 0.20 mmol, 1 equiv.), **2a** (39 mg, 0.22 mmol, 1.1 equiv.) $[Cp^*RhCl_2]_2$ and K_2CO_3 (28 mg, 0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

Scheme 12, eq 3 :

7d (27 mg, 0.20 mmol, 1 equiv.), **2b** (32 µL, 0.22 mmol, 1.1 equiv.) $[Cp^*RhCl_2]_2$ and K_2CO_3 (28 mg, 0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

Control experiments



Scheme 13 eq 1

10 (39 mg, 0.20 mmol, 1 equiv.), **2a** (39 mg, 0.22 mmol, 1.1 equiv.) $[Cp^*RhCl_2]_2$ and K_2CO_3 (28 mg, 0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

Scheme 13, eq 2

7d (30 mg, 0.20 mmol, 1 equiv.), **2a** (39 mg, 0.22 mmol, 1.1 equiv.) $[Cp^*RhCl_2]_2$ and K_2CO_3 (28 mg, 0.2 mmol, 1 equiv.) were weighed in a 13 x 100 mm test tube. MeOH (1 mL) was added and the reaction mixture was stirred in an oil bath at 60 °C for 16h. The reaction was cooled down and diluted with dichloromethane. Next, trimethoxybenzene (11.2 mg, 0.066 mmol, 0.33 equiv.) was added as internal standard. Volatiles of an aliquot were then evaporated and the resulting mixture was analyzed by ^{1}H NMR.

DFT CALCULATIONS

All density functional calculations were performed at the B3LYP[12]/TZVP[13] level (DZVP[14] for Rh) using the Gaussian 03 package.[15] Spin-restricted treatment was used for all closed-shell species. Tight SCF convergence criteria were used for all calculations. The converged wave functions were tested to confirm that they corresponded to ground-state surfaces. The second-order derivative of the energy with respect to nuclear positions was evaluated to determine the nature of the stationary points. Gibbs free energy of species was evaluated at 298 K and 1 atm using the harmonic oscillator approximation and unscaled

vibrational frequencies. Intrinsic reaction coordinate (IRC)[16] calculations were used to confirm the reaction pathways through the corresponding transition states (TSs) for all reaction steps.

Solvent effects were evaluated at the single-point calculations of the solvation energies using the gas-phase geometries. Solvation energies in methanol were calculated using the PCM model[171819] with the united atom topological model (UAHF). Gibbs free energies in the solution were estimated by addition of the solvation energies ΔG_{solv} to gas-phase Gibbs free energies.

Table S1. Electronic and Gibbs free energies (a.u.) at 298K in the gas-phase, and solvation energies in methanol (kcal mol^{-1}).

	E (a.u.)	G (a.u.)	ΔG_{solv}
$[Rh(Cp)(OAc)_2]$	-5338.421910	-5338.280229	-15.2
$[Rh(Cp)(OAc)]^+$	-5109.585916	-5109.487983	-60.6
$[Rh(Cp)(OAc)(MeOH)]^+$	-5225.398238	-5225.252295	-53.7
$[Rh(Cp)(OAc)(C_2H_2)]^+$	-5186.981631	-5186.857753	-52.8
MeOH	-115.770989	-115.742706	-6.2
AcOH	-229.178653	-229.144517	-1.5
AcO^-	-228.611690	-228.591421	-36.4
C_2H_2	-77.362338	-77.354297	-1.1
Reactant	-628.994060	-628.866895	-8.4
C_9H_7NO (final product)	-477.334616	-477.226869	-10.4

Table S2. Relative Gibbs free energies (kcal mol^{-1}) at 298K in the gas-phase and in methanol (Schemes 8-9).

	$\Delta G_{gas\text{-}phase}$	$\Delta G_{methanol}$
$[Rh(Cp)(OAc)_2]$	0.0	0.0
$[Rh(Cp)(OAc)]^+$	126.0	8.8
$[Rh(Cp)(OAc)(MeOH)]^+$	112.5	8.4
$[Rh(Cp)(OAc)(C_2H_2)]^+$	116.3	8.0
II	4.9	7.9
TS from II to III	19.0	20.5
TS from II to III, cationic form	127.5	34.7
III	-0.2	4.9
IV	2.5	-4.3
V	4.3	-1.3
TS from V to VI	18.9	11.4
VI	-8.6	-13.8
TS from VI to VII	6.1	-0.2
VII	-19.8	-24.0
TS from VII to VIII	-19.1	-23.2
VIII	-86.1	-91.0

Optimized atomic coordinates (Å)

Reactant

C	3.977538	-0.632747	0.238949
C	3.049957	-1.448444	-0.401096
C	1.746283	-1.005264	-0.593572
C	1.363892	0.262573	-0.144637
C	2.304182	1.083365	0.483291
C	3.602955	0.634663	0.678345
H	4.992384	-0.980583	0.388301
H	3.343011	-2.427550	-0.759150
H	1.039477	-1.633828	-1.119976
H	1.999323	2.069264	0.808763
H	4.325275	1.273642	1.171053
C	-0.021048	0.808990	-0.314514
O	-0.278390	1.991448	-0.336795
N	-0.981945	-0.188684	-0.492307
H	-0.941153	-1.011705	0.105961
O	-2.306743	0.297500	-0.518592
C	-3.156533	-0.431713	0.256545
O	-2.791209	-1.378052	0.908615
C	-4.558313	0.088451	0.142061
H	-5.139082	-0.603748	-0.471123
H	-5.004839	0.112181	1.135134
H	-4.583525	1.076706	-0.310884

Entry I (Scheme 8)

Rh	-0.277402	-0.361067	-0.045496
C	-2.172551	0.103729	0.966593
H	-2.212404	0.778047	1.804947
C	-2.304595	0.479418	-0.404492
H	-2.408661	1.492389	-0.753579
C	-2.139419	-0.682766	-1.197865
H	-2.141237	-0.720414	-2.275524
C	-1.953722	-1.807640	-0.315433
H	-1.798323	-2.831045	-0.616278
C	-1.987522	-1.319024	1.009574
H	-1.825422	-1.904240	1.901291
C	2.046447	-1.344058	0.065922
O	1.427663	-1.289378	-1.038425
O	1.421653	-1.008688	1.121128
C	3.485634	-1.755646	0.126781
H	4.103506	-0.863478	0.001342
H	3.714483	-2.200003	1.094174
H	3.716124	-2.449306	-0.680380
O	0.884207	1.333119	-0.291085
C	0.444456	2.521621	0.011293

O	-0.680702	2.798050	0.413094
C	1.510687	3.594328	-0.171009
H	2.255611	3.493112	0.621144
H	2.024555	3.467577	-1.123845
H	1.055828	4.580773	-0.111848

Entry II (Scheme 8)

Rh	-0.674953	-0.823255	-0.357941
N	-0.212940	0.979776	0.616181
C	-0.059762	-2.476680	-1.783849
H	0.142812	-3.479823	-1.442938
C	-1.307167	-1.978382	-2.194594
H	-2.232593	-2.531127	-2.229620
C	-1.152721	-0.574167	-2.489832
H	-1.922808	0.106942	-2.810693
C	0.214803	-0.239687	-2.299098
H	0.626987	0.749881	-2.405639
C	0.891635	-1.393242	-1.817833
H	1.933139	-1.453236	-1.547781
O	-2.439966	-0.886155	0.883093
O	-0.587432	-1.752380	1.629355
C	-1.796689	-1.428908	1.834275
C	-2.441155	-1.643431	3.169356
H	-3.515069	-1.782850	3.055594
H	-1.993199	-2.497738	3.674458
H	-2.272466	-0.753442	3.780293
O	-1.325050	1.852264	0.794723
C	0.957069	1.694498	0.565888
C	2.213922	0.865311	0.549822
C	2.359031	-0.307051	1.295271
C	3.300294	1.348929	-0.184176
C	3.570770	-0.992362	1.288961
H	1.529865	-0.676866	1.882790
C	4.502787	0.652639	-0.203229
H	3.191374	2.281634	-0.722991
C	4.641235	-0.521079	0.534372
H	3.679457	-1.892790	1.881785
H	5.336779	1.032329	-0.781270
H	5.582908	-1.057009	0.531264
O	1.020919	2.918161	0.580828
C	-1.744921	2.546349	-0.298024
O	-1.363951	2.354463	-1.424555
C	-2.761966	3.572208	0.121978
H	-3.412172	3.183436	0.904582
H	-2.227558	4.435554	0.524160
H	-3.343137	3.882647	-0.743194

Transition state from II to III (CMD IS, one imaginary frequency at 944*i* cm^{-1})

Rh	0.029663	-0.825669	-0.427882
N	-0.870766	0.801000	0.474712
C	0.509085	-0.525465	-2.589535
H	1.075188	0.322504	-2.938621
C	1.047371	-1.807802	-2.212761
H	2.089539	-2.081991	-2.209359
C	-0.028617	-2.626211	-1.823933
H	0.047402	-3.631775	-1.441000
C	-1.247858	-1.878602	-1.974095
H	-2.242052	-2.239204	-1.766888
C	-0.905859	-0.596009	-2.479415
H	-1.590362	0.222035	-2.640453
O	-0.414554	-1.924348	1.335139
O	1.240523	-0.963338	2.488607
C	0.258535	-1.746363	2.393639
C	-0.163144	-2.517179	3.622503
H	0.716295	-2.875103	4.156246
H	-0.701483	-1.835570	4.284652
H	-0.817414	-3.344123	3.357078
O	-2.231078	0.844278	0.828729
C	-0.200819	1.969578	0.647220
C	1.254775	1.742825	0.352249
C	1.732342	0.418626	0.295878
C	2.099593	2.819906	0.118919
C	3.079512	0.208102	-0.041801
H	1.397220	-0.335434	1.295067
C	3.432070	2.587741	-0.207852
H	1.698070	3.823493	0.187725
C	3.923006	1.283921	-0.289702
H	3.478965	-0.799685	-0.053898
H	4.093735	3.424392	-0.398340
H	4.965472	1.112256	-0.530479
O	-0.674867	3.042942	0.993810
C	-3.078907	1.378180	-0.103504
C	-4.435756	1.577257	0.514192
H	-4.669525	0.782779	1.221532
H	-4.423547	2.522124	1.061951
H	-5.187103	1.631375	-0.270190
O	-2.772754	1.640339	-1.235698

Transition state from II to III (CMD TS, cationic form, one imaginary frequency at 801*i* cm^{-1})

Rh	-0.125815	-0.874977	-0.186049
N	-0.628657	1.228988	-0.175792
C	0.719500	-1.819436	-2.032551

H	1.624025	-1.473120	-2.505502
C	0.636144	-2.798610	-0.977475
H	1.462024	-3.333010	-0.536834
C	-0.737240	-2.980333	-0.664561
H	-1.124616	-3.622497	0.111260
C	-1.504699	-2.094542	-1.469375
H	-2.575726	-1.982022	-1.462475
C	-0.593055	-1.391702	-2.327661
H	-0.875011	-0.628699	-3.035114
O	-0.963531	-0.981290	1.740935
O	0.819148	-0.074656	2.733052
C	-0.323510	-0.589821	2.775515
C	-0.992983	-0.784211	4.111904
H	-0.461158	-1.568238	4.654838
H	-0.910220	0.131650	4.696216
H	-2.034296	-1.070539	3.991761
O	-1.868406	1.857346	0.077712
C	0.355330	2.076585	-0.155373
C	1.699662	1.506033	-0.178799
C	1.820602	0.180624	0.303947
C	2.795258	2.216050	-0.657252
C	3.087795	-0.414359	0.257449
H	1.235328	-0.047244	1.410730
C	4.040546	1.594086	-0.688907
H	2.679143	3.235222	-1.002402
C	4.185503	0.284275	-0.236978
H	3.229182	-1.408354	0.663986
H	4.900818	2.135842	-1.060439
H	5.161731	-0.184239	-0.249994
C	-2.918900	1.461836	-0.757069
C	-4.202495	2.037648	-0.245473
H	-4.597811	1.374152	0.527775
H	-4.057634	3.020008	0.201138
H	-4.917880	2.089961	-1.062503
O	-2.755449	0.755234	-1.704662
O	0.222901	3.389320	-0.100113
H	-0.717676	3.629807	-0.059112

Entry III (Scheme 8)

Rh	0.005950	-0.926006	-0.222065
N	-0.735043	0.893838	0.583442
C	-1.129240	-1.254925	-2.079729
H	-1.511018	-0.420972	-2.643811
C	0.135096	-1.898689	-2.246363
H	0.913104	-1.590875	-2.925598
C	0.223139	-2.929963	-1.288811

H	1.063601	-3.587145	-1.131714
C	-1.058372	-3.022183	-0.614139
H	-1.302768	-3.726094	0.166004
C	-1.884148	-2.021582	-1.110007
H	-2.889032	-1.799641	-0.790662
O	1.026275	-1.403812	1.677348
O	0.500397	0.418845	2.874299
C	1.087717	-0.733457	2.714996
C	1.873248	-1.210238	3.901917
H	2.723562	-0.542680	4.055593
H	1.254619	-1.163589	4.798668
H	2.229175	-2.223385	3.736839
O	-2.081786	1.053131	1.031516
C	-0.223095	2.061347	-0.001046
C	1.137082	1.761824	-0.526680
C	1.489754	0.419013	-0.667186
C	2.033948	2.780077	-0.847569
C	2.771259	0.095149	-1.101167
H	0.003203	0.678738	2.006413
C	3.308470	2.452500	-1.291071
H	1.717328	3.810636	-0.739342
C	3.675964	1.113052	-1.408612
H	3.080614	-0.938515	-1.201361
H	4.015772	3.233525	-1.541328
H	4.673974	0.855318	-1.745126
O	-0.775986	3.142019	-0.014134
C	-3.040436	1.244968	0.074523
C	-4.333687	1.636256	0.737143
H	-4.448193	1.156172	1.707841
H	-4.318320	2.717053	0.894093
H	-5.165259	1.387957	0.081357
O	-2.864278	1.115817	-1.106058

Entry IV (Scheme 8)

Rh	0.201943	-0.772777	-0.052913
N	0.452393	1.192161	0.127546
C	0.618803	-2.345912	1.397913
H	0.304711	-2.255246	2.425518
C	-0.136060	-2.943375	0.338812
H	-1.136611	-3.332854	0.420445
C	0.637220	-2.850549	-0.832394
H	0.341350	-3.168200	-1.819512
C	1.936971	-2.307231	-0.477792
H	2.732443	-2.090293	-1.172617
C	1.934853	-2.025500	0.881817
H	2.734267	-1.572686	1.445825

O	1.647386	1.849358	0.493830
C	-0.642734	2.055302	0.233069
C	-1.895170	1.261263	0.060604
C	-1.759357	-0.123021	-0.074750
C	-3.138709	1.880160	0.025871
C	-2.907518	-0.887795	-0.257099
C	-4.282062	1.105443	-0.150625
H	-3.193940	2.956970	0.134094
C	-4.162947	-0.272516	-0.294550
H	-2.853071	-1.962526	-0.380716
H	-5.258255	1.573623	-0.178168
H	-5.049891	-0.879463	-0.437541
O	-0.578146	3.253571	0.410477
C	2.705724	1.669200	-0.349588
C	3.841337	2.554377	0.091784
H	3.642093	3.574367	-0.243807
H	3.923795	2.575524	1.177854
H	4.767072	2.204516	-0.358646
O	2.716976	0.920451	-1.289669

Entry V (Scheme 8)

Rh	0.002444	-0.892819	0.274657
N	-0.705644	1.042961	0.079458
C	0.559685	-2.478049	-1.282602
H	1.551754	-2.483765	-1.702917
C	0.137276	-3.169262	-0.124348
H	0.737073	-3.838505	0.472030
C	-1.269561	-2.907639	0.061699
H	-1.881471	-3.309547	0.853944
C	-1.682772	-2.023356	-0.937155
H	-2.664908	-1.599593	-1.066284
C	-0.538638	-1.702953	-1.751664
H	-0.545798	-1.047370	-2.606871
O	-1.989224	1.401701	0.560458
C	0.153643	2.103147	0.009231
C	1.537428	1.572363	-0.172111
C	1.731628	0.199070	-0.046980
C	2.613459	2.422523	-0.418942
C	3.015526	-0.326872	-0.146155
C	3.893532	1.896722	-0.538347
H	2.422796	3.486155	-0.499909
C	4.092380	0.524863	-0.400845
H	3.198829	-1.388691	-0.028787
H	4.735371	2.550219	-0.731497
H	5.090463	0.110335	-0.487048
O	-0.148035	3.285667	0.071024

C	-0.328002	-0.440200	2.450823
H	-1.248266	0.011438	2.747360
C	0.813745	-0.880947	2.379193
H	1.809579	-1.182462	2.613764
C	-2.978685	1.419986	-0.384635
O	-2.859129	1.019024	-1.509622
C	-4.224164	2.018904	0.214427
H	-5.078391	1.781405	-0.414894
H	-4.385974	1.662781	1.231541
H	-4.099295	3.102826	0.259367

Transition state from V to VI (TS2, one imaginary frequency at 380*i* cm^{-1})

Rh	-0.060777	-0.916792	0.293012
N	-0.704531	1.054919	0.152706
C	0.231177	-2.319227	-1.556600
H	1.037879	-2.169014	-2.255815
C	0.293343	-3.102465	-0.357746
H	1.133863	-3.692474	-0.027810
C	-0.980937	-3.043476	0.273679
H	-1.255739	-3.544706	1.188310
C	-1.797930	-2.164100	-0.473983
H	-2.822770	-1.905281	-0.265207
C	-1.039790	-1.725642	-1.621060
H	-1.394190	-1.026108	-2.360790
O	-1.999513	1.445102	0.574189
C	0.175800	2.089313	0.126394
C	1.554391	1.537045	-0.069806
C	1.801398	0.198081	0.251395
C	2.565759	2.324660	-0.613694
C	3.056328	-0.356964	-0.018633
C	3.812592	1.772066	-0.876034
H	2.344043	3.361295	-0.836689
C	4.050992	0.426323	-0.591152
H	3.265958	-1.387694	0.242882
H	4.597632	2.381470	-1.306383
H	5.020576	-0.009382	-0.802025
O	-0.081275	3.283778	0.201371
C	0.008632	-0.504892	2.329724
H	-0.754611	-0.560577	3.081248
C	1.235795	-0.328202	2.080685
H	2.214098	-0.301728	2.519419
C	-2.948781	1.454643	-0.404617
O	-2.788607	1.049158	-1.524601
C	-4.218805	2.052049	0.143884
H	-5.050499	1.793928	-0.507287
H	-4.407246	1.713869	1.162332

H	-4.106937	3.138017	0.171059

Entry VI (Scheme 8)

Rh	-0.002187	0.766219	0.202848
N	0.886895	-1.072996	-0.171271
C	-0.079053	2.515785	-1.469093
H	-0.591157	2.432968	-2.414907
C	-0.691702	2.928618	-0.216594
H	-1.716487	3.242457	-0.093264
C	0.293844	2.920145	0.783175
H	0.164444	3.213131	1.812261
C	1.481848	2.358998	0.202584
H	2.435082	2.241236	0.692276
C	1.244945	2.195910	-1.221122
H	1.957208	1.777148	-1.912789
O	2.138545	-1.518307	0.332228
C	-0.056015	-2.042423	-0.117685
C	-1.424503	-1.382697	-0.275044
C	-2.087779	-0.808581	0.840927
C	-2.110310	-1.518121	-1.494858
C	-3.429396	-0.411814	0.691102
C	-3.423128	-1.106688	-1.618358
H	-1.600304	-1.983304	-2.329318
C	-4.088339	-0.561109	-0.514704
H	-3.946697	0.007199	1.546097
H	-3.942667	-1.224526	-2.561286
H	-5.124491	-0.257582	-0.604489
O	0.074220	-3.248688	-0.009251
C	-0.266308	0.076917	2.098182
H	0.388003	0.296810	2.933907
C	-1.379780	-0.638336	2.144678
H	-1.807474	-1.071889	3.046279
C	3.226522	-1.071884	-0.343431
O	3.203279	-0.293123	-1.261295
C	4.464718	-1.708841	0.236231
H	5.340924	-1.155192	-0.092492
H	4.417781	-1.744501	1.324013
H	4.534261	-2.737182	-0.124942

Transition state from VI to VII (TS3, one imaginary frequency at 375*i* cm^{-1})

Rh	-0.597136	-0.987519	0.217956
N	-0.163660	1.089044	0.474637
C	-1.166101	-2.401143	-1.599750
H	-0.438552	-2.739928	-2.319783
C	-1.444217	-3.028068	-0.321441
H	-0.999330	-3.946413	0.030526

C	-2.489916	-2.316921	0.316894
H	-2.954828	-2.566486	1.256613
C	-2.726138	-1.155267	-0.459541
H	-3.448334	-0.382363	-0.251343
C	-1.930650	-1.246917	-1.676694
H	-1.916582	-0.504283	-2.457536
O	-1.212206	1.965596	0.843380
C	0.968079	1.764478	0.078572
C	2.133498	0.855058	-0.093799
C	2.293042	-0.329897	0.664089
C	3.127542	1.245192	-0.992332
C	3.465514	-1.082749	0.469116
C	4.261592	0.473509	-1.188830
H	2.983380	2.173252	-1.530192
C	4.426815	-0.697387	-0.449215
H	3.614415	-1.981309	1.056696
H	5.016197	0.783971	-1.900323
H	5.315112	-1.303536	-0.580813
O	1.021145	2.973172	-0.101848
C	0.083120	-0.418120	1.958551
H	-0.442034	-0.358130	2.905669
C	1.392669	-0.720804	1.758098
H	1.872007	-1.287326	2.555400
C	-1.965108	2.448313	-0.196883
O	-1.899039	2.051546	-1.326760
C	-2.869744	3.536677	0.313951
H	-3.703982	3.664946	-0.371868
H	-3.225743	3.320446	1.320471
H	-2.294145	4.463946	0.353102

Entry VII (Scheme 8)

Rh	1.266292	-0.557734	-0.179009
N	-0.023380	1.140038	-0.157296
C	0.927157	-2.284618	1.499732
H	0.443891	-2.101009	2.446104
C	0.250139	-2.491565	0.230541
H	-0.817349	-2.598358	0.109758
C	1.229920	-2.769931	-0.769084
H	1.044654	-3.049319	-1.793074
C	2.477465	-2.470633	-0.186903
H	3.436063	-2.528544	-0.679670
C	2.284254	-2.245840	1.242750
H	3.069358	-2.038253	1.952865
O	0.747598	2.408719	-0.018038
C	-1.086454	1.142941	0.861832
C	-2.325401	0.531455	0.418830

C	-2.546668	0.189728	-0.947406
C	-3.350335	0.353525	1.368265
C	-3.817308	-0.326810	-1.298593
C	-4.570906	-0.161227	0.995394
H	-3.150983	0.634169	2.394282
C	-4.800480	-0.499951	-0.352771
H	-4.004542	-0.588618	-2.333497
H	-5.351776	-0.303933	1.731281
H	-5.762881	-0.901486	-0.647390
O	-0.841915	1.622052	1.947390
C	-0.284808	0.833550	-1.518881
C	-1.523514	0.398386	-1.905471
H	0.474962	1.158419	-2.211216
H	-1.696042	0.180148	-2.950104
C	2.073968	2.253318	-0.110145
C	2.800758	3.541346	0.123489
H	2.385495	4.336947	-0.495049
H	2.675973	3.833007	1.168412
H	3.855599	3.399636	-0.096570
O	2.613240	1.184591	-0.347993

Transition state from VII to VIII (TS4, one imaginary frequency at 106*i* cm^{-1})

Rh	1.294092	-0.530468	-0.213901
N	-0.060623	1.079266	-0.140764
C	1.045803	-2.271254	1.461429
H	0.566257	-2.108560	2.413460
C	0.365019	-2.505603	0.200856
H	-0.698154	-2.657356	0.090771
C	1.345588	-2.737827	-0.811128
H	1.160924	-3.022451	-1.833802
C	2.586535	-2.392545	-0.240615
H	3.540916	-2.408953	-0.744407
C	2.398808	-2.176099	1.189456
H	3.181817	-1.937015	1.891895
O	0.686570	2.415220	0.060917
C	-1.099567	1.008698	0.899131
C	-2.359340	0.446649	0.442320
C	-2.618807	0.217416	-0.938357
C	-3.358968	0.195532	1.401253
C	-3.898621	-0.263514	-1.298800
C	-4.592071	-0.283306	1.019245
H	-3.131364	0.390185	2.441181
C	-4.858791	-0.510614	-0.344227
H	-4.113805	-0.439004	-2.346404
H	-5.354129	-0.482982	1.761641
H	-5.830461	-0.884109	-0.645020

O	-0.826029	1.391104	2.015450
C	-0.368649	0.895380	-1.508969
C	-1.612548	0.495741	-1.901101
H	0.400603	1.213912	-2.193776
H	-1.808057	0.355667	-2.955137
C	2.004086	2.301067	-0.073249
C	2.715674	3.588914	0.216849
H	2.234828	4.422813	-0.293544
H	2.666325	3.781318	1.290810
H	3.754309	3.499061	-0.091324
O	2.571372	1.261412	-0.383865

Entry VIII (Scheme 8)

Rh	-1.308134	-0.365376	0.123539
N	0.674687	0.247879	0.081940
C	-1.492363	-2.346467	-0.810071
H	-0.818282	-2.630512	-1.600543
C	-1.258715	-2.539522	0.567836
H	-0.382536	-2.995341	0.994735
C	-2.349853	-1.933794	1.277989
H	-2.441571	-1.870978	2.351372
C	-3.275666	-1.403689	0.332540
H	-4.168422	-0.841474	0.544514
C	-2.743342	-1.634949	-0.957276
H	-3.178692	-1.292845	-1.881983
O	-3.944817	1.346466	-0.608296
C	1.681385	-0.706092	-0.129632
C	3.080894	-0.237392	-0.090337
C	3.378997	1.126313	0.117843
C	4.119013	-1.160890	-0.271294
C	4.727870	1.530556	0.139996
C	5.437346	-0.745825	-0.243931
H	3.859633	-2.198713	-0.432481
C	5.739221	0.607521	-0.038008
H	4.962747	2.576737	0.298111
H	6.236518	-1.463280	-0.382903
H	6.773199	0.931150	-0.018869
O	1.408469	-1.888415	-0.344587
C	1.011621	1.566221	0.268682
C	2.285739	2.030146	0.293948
H	0.168141	2.228181	0.396605
H	2.467875	3.084901	0.452643
C	-3.018017	2.055775	-0.243791
C	-3.154546	3.565581	-0.138471
H	-4.172394	3.865945	-0.376190
H	-2.892692	3.895972	0.868047

H	-2.458617	4.044998	-0.829508
O	-1.817299	1.633330	0.081315

Final product

C	1.713809	1.315538	-0.000013
C	0.363221	0.919365	-0.000022
C	0.068067	-0.465043	-0.000018
C	1.103585	-1.407269	0.000004
C	2.421994	-0.994450	0.000024
C	2.723938	0.373976	0.000018
H	1.953220	2.372482	-0.000022
H	0.840126	-2.456887	-0.000002
H	3.221118	-1.724952	0.000041
H	3.758296	0.696367	0.000039
C	-1.326859	-0.938431	-0.000004
O	-1.678860	-2.108845	-0.000047
N	-2.274078	0.083090	0.000064
H	-3.233682	-0.232114	0.000090
C	-0.716539	1.870287	-0.000036
C	-1.990086	1.428474	0.000020
H	-0.510041	2.931106	-0.000073
H	-2.846402	2.088444	0.000012

SPECTRAL DATA

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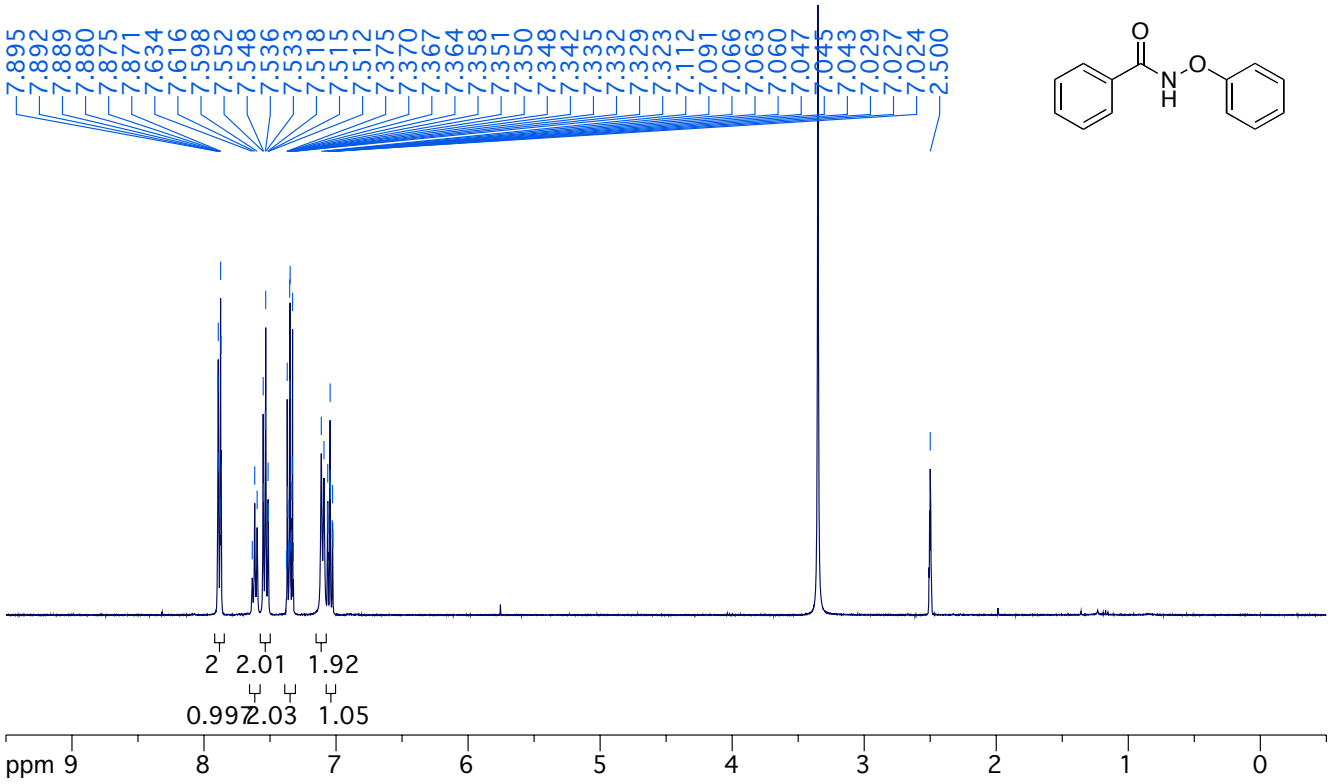
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7.533
7.518
7.515
7.512
7.375
7.370
7.367
7.364
7.358
7.351
7.350
7.348
7.342
7.335
7.332
7.329
7.323
7.112
7.091
7.066
7.063
7.060
7.047
7.045
7.043
7.029
7.027
7.024
2.500
O
N
H
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1.05
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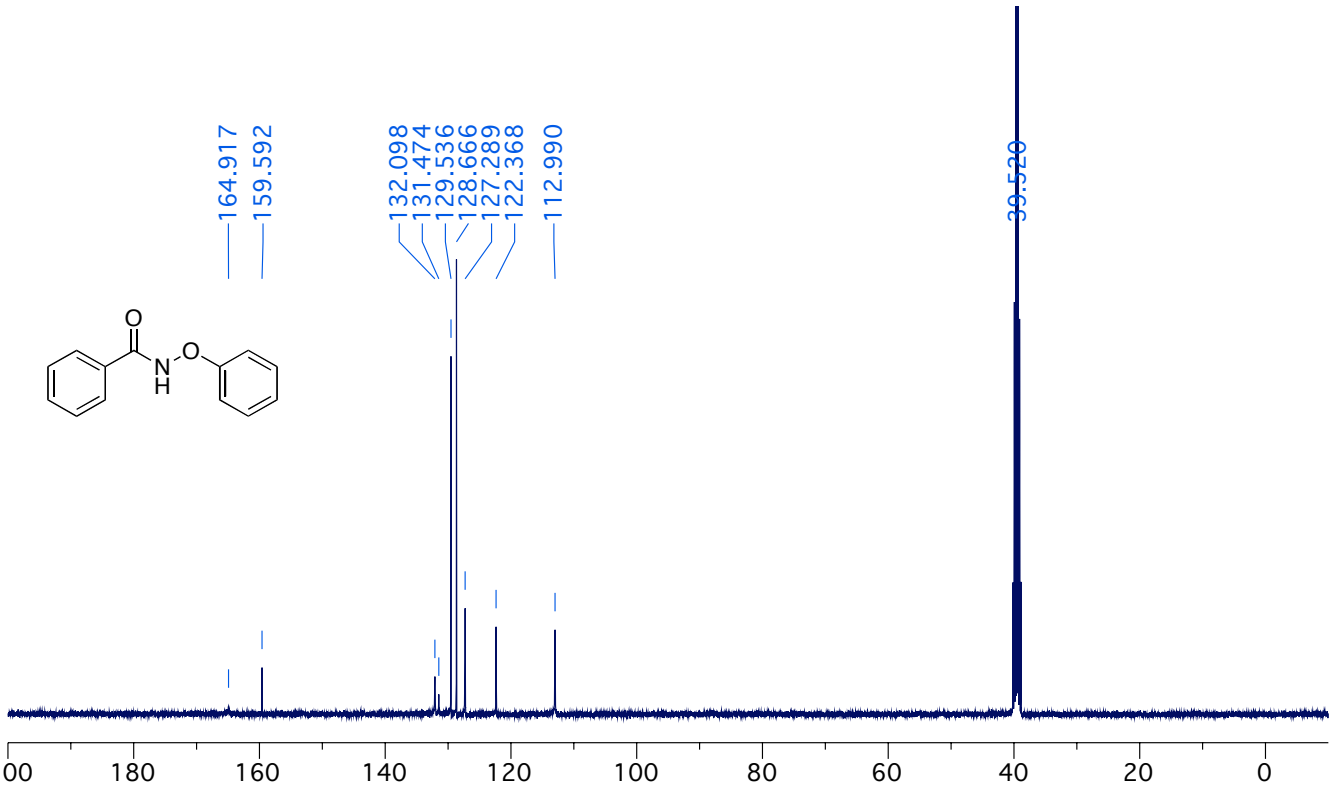
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H
O
00
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140
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60
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20
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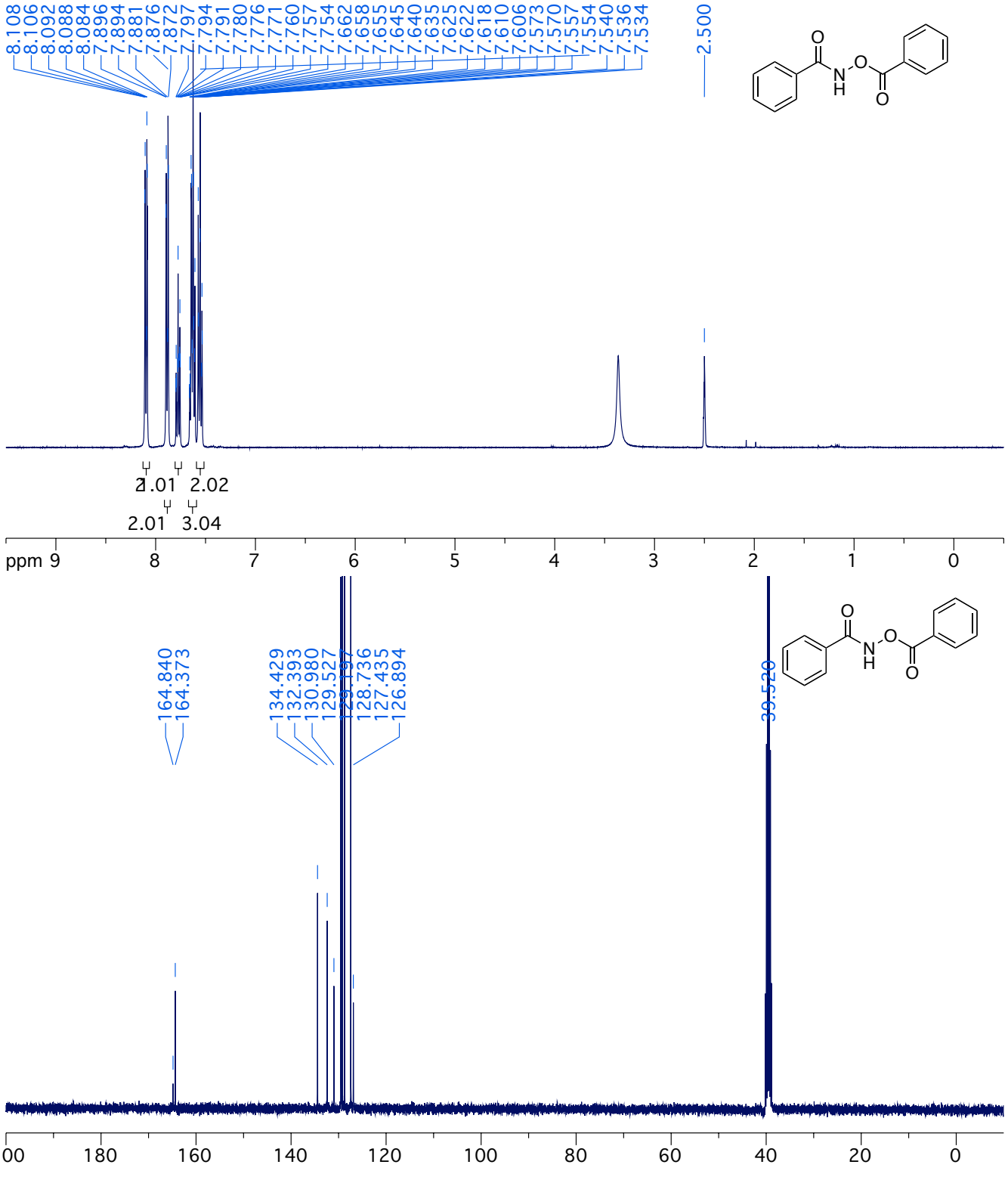
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7.771
7.760
7.757
7.754
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7.658
7.655
7.645
7.640
7.635
7.625
7.622
7.618
7.610
7.606
7.573
7.570
7.557
7.554
7.540
7.536
7.534
2.500
2.01
2.02
2.01
3.04
ppm 9
8
7
6
5
4
3
2
1
0
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164.373
134.429
132.393
130.980
129.527
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127.435
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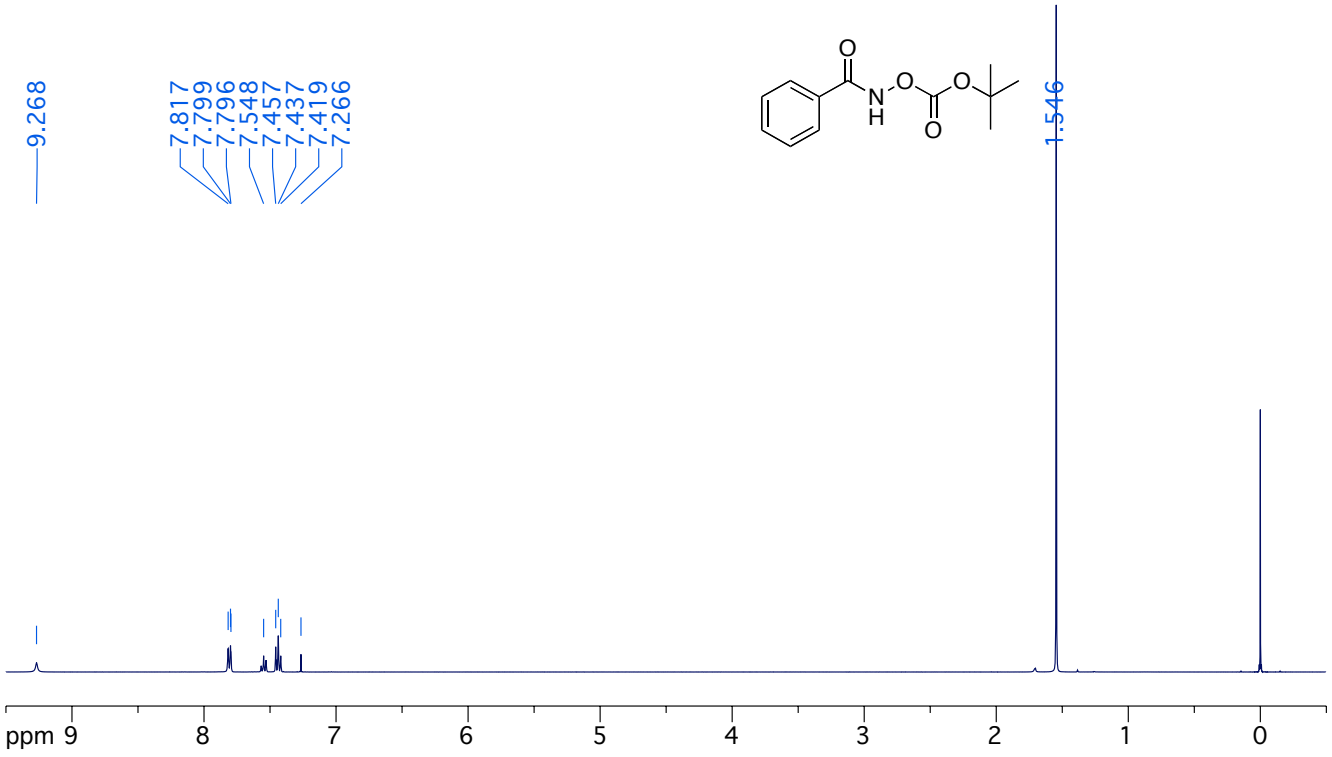
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1
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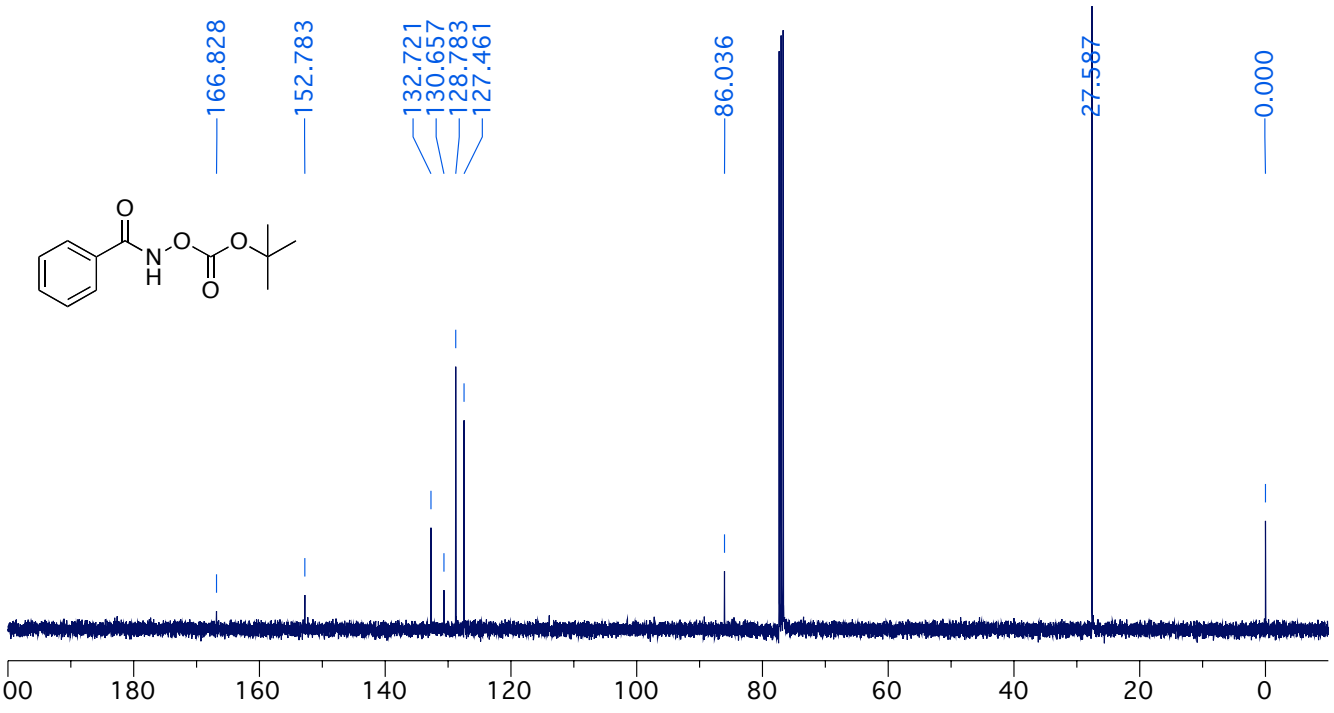
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140
120
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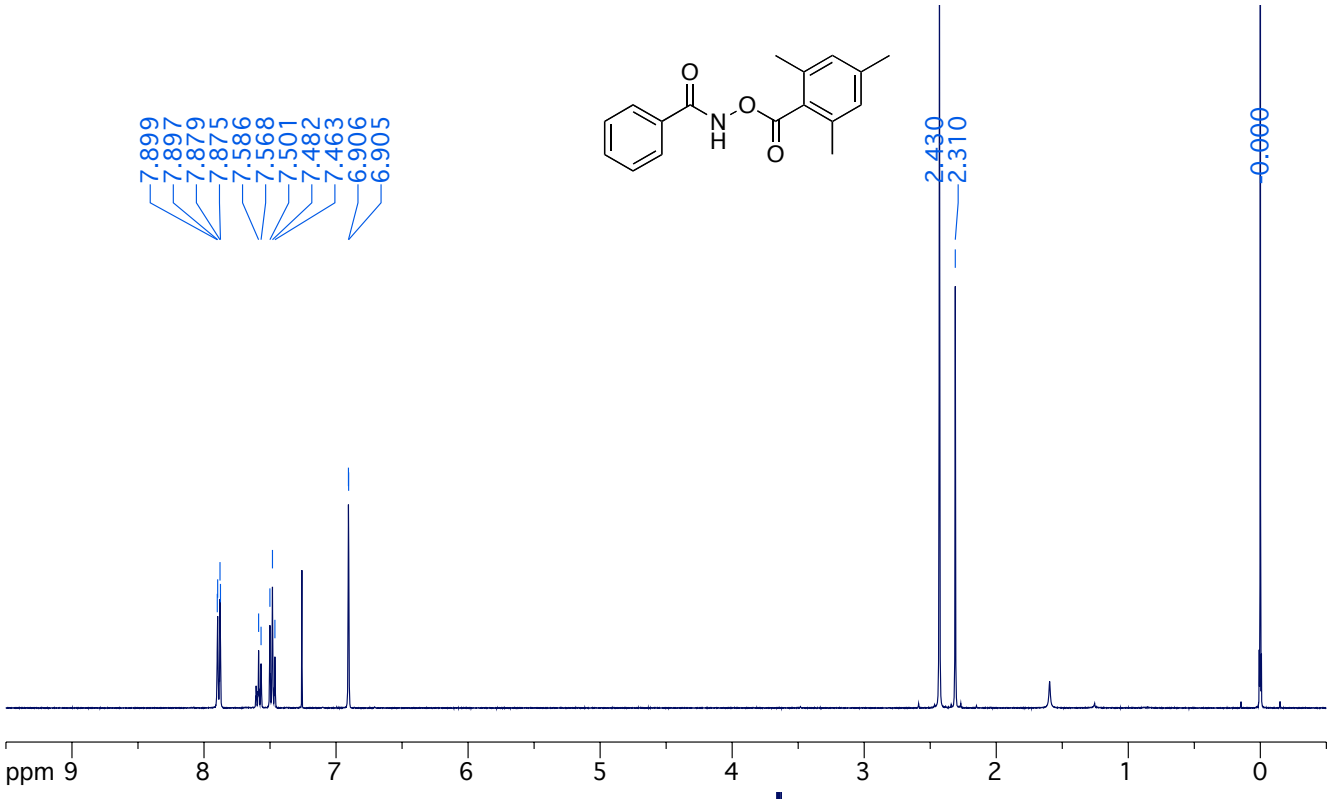
80
60
40
20
0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7.482
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2.310
0.000
ppm 9
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7
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4
3
2
1
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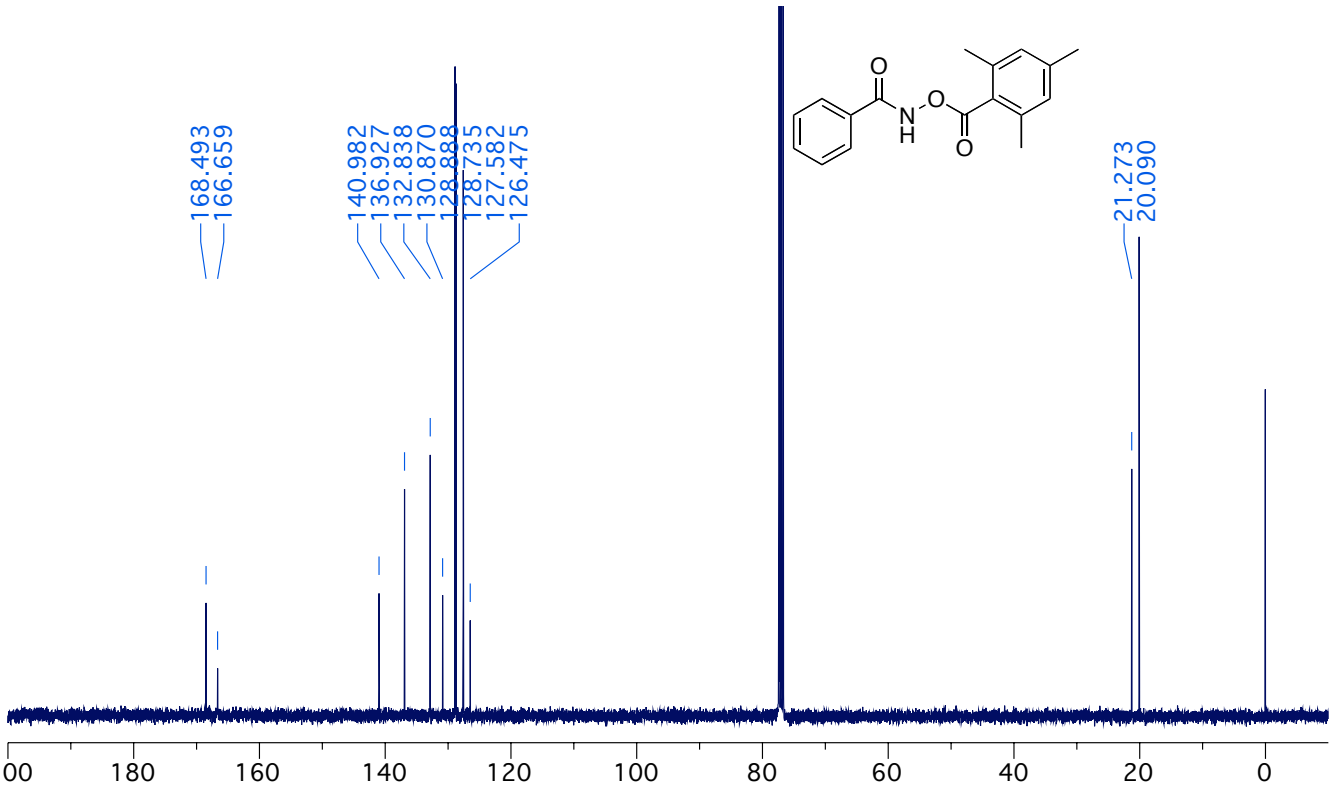
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20.090
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140
120
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80
60
40
20
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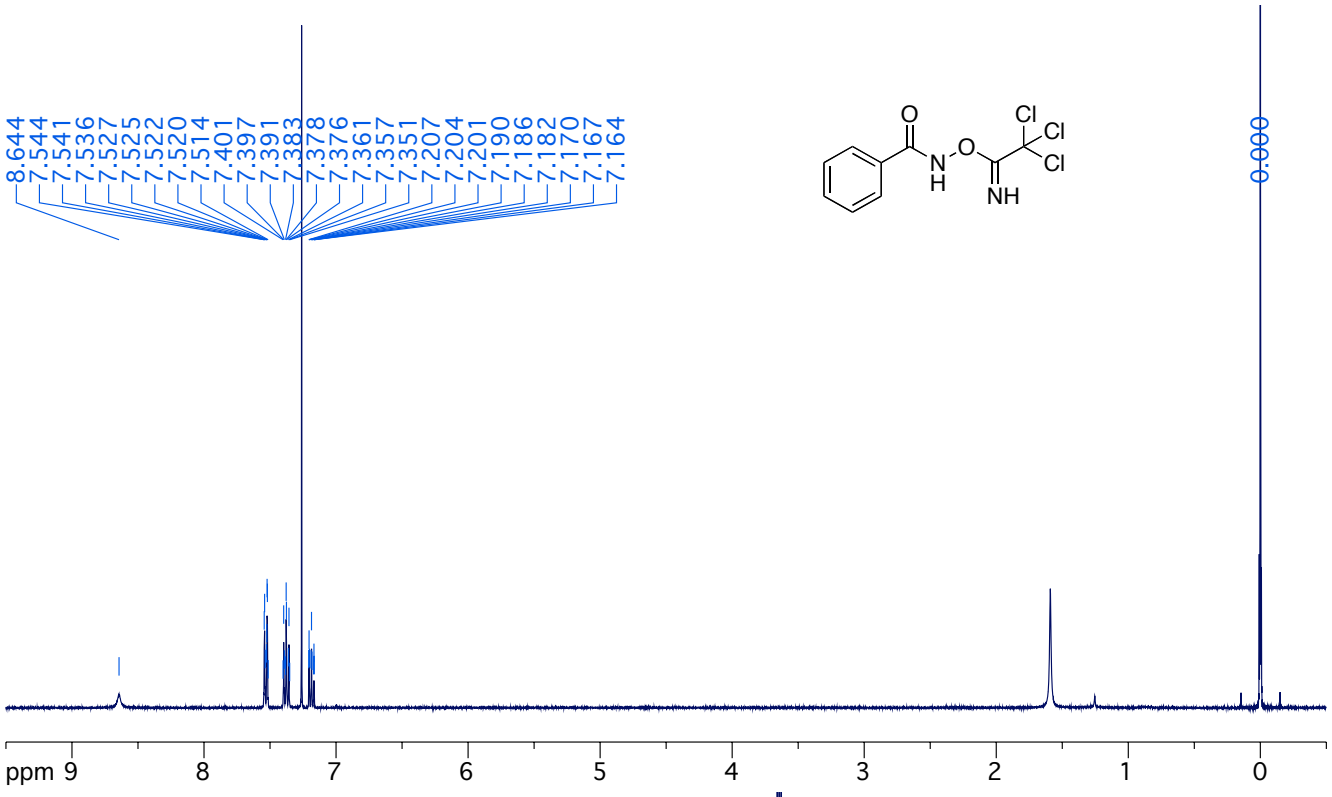
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7.536
7.527
7.525
7.522
7.520
7.514
7.401
7.397
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7.383
7.378
7.376
7.361
7.357
7.351
7.207
7.204
7.201
7.190
7.186
7.182
7.170
7.167
7.164
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Cl
Cl
Cl
NH
0.000
ppm 9
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7
6
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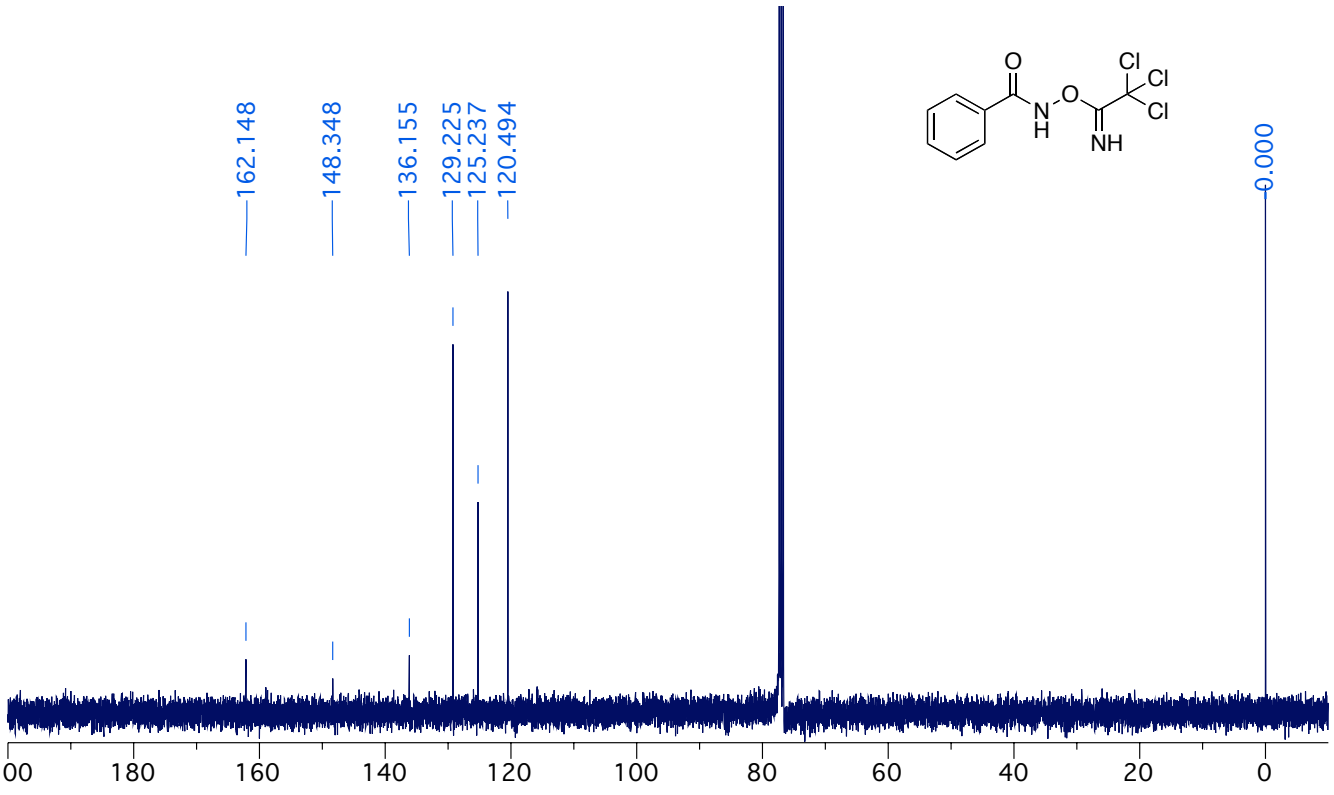
3
2
1
0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Cl
Cl
Cl
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00
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140
120
100
80
60
40
20
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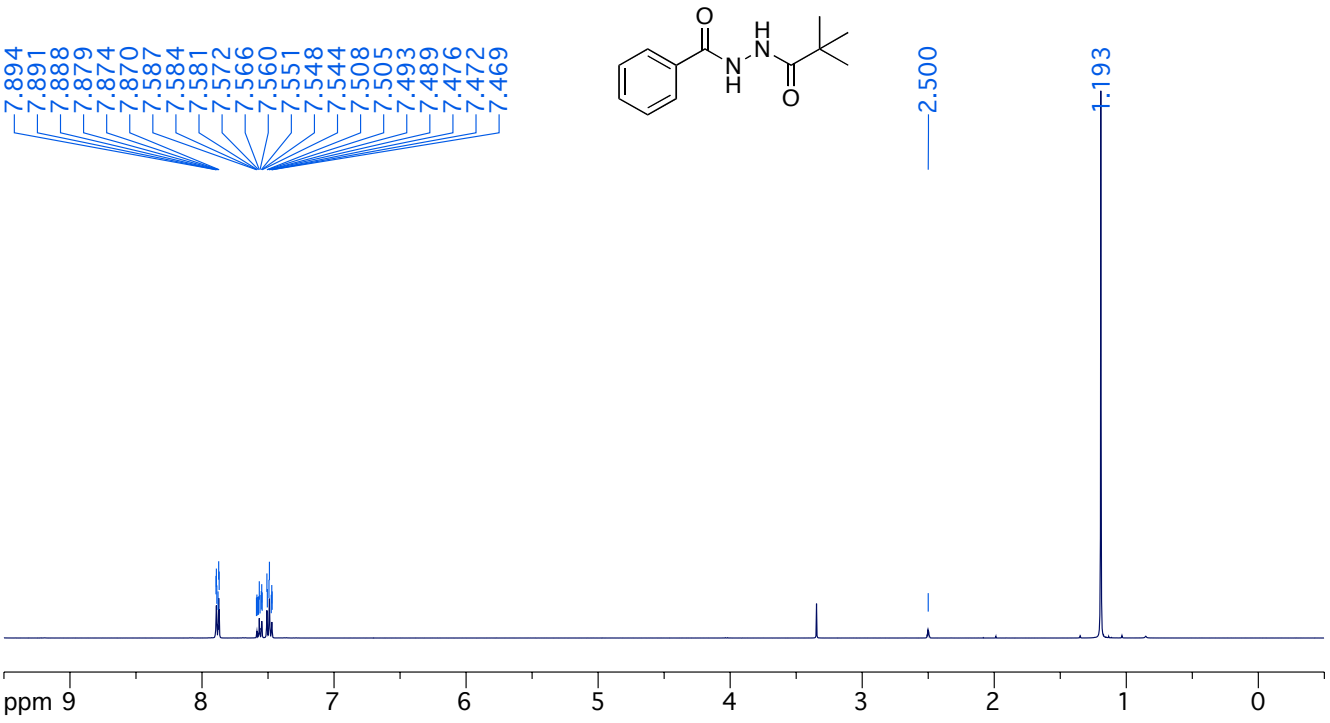
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7.587
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7.572
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7.560
7.551
7.548
7.544
7.508
7.505
7.493
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3
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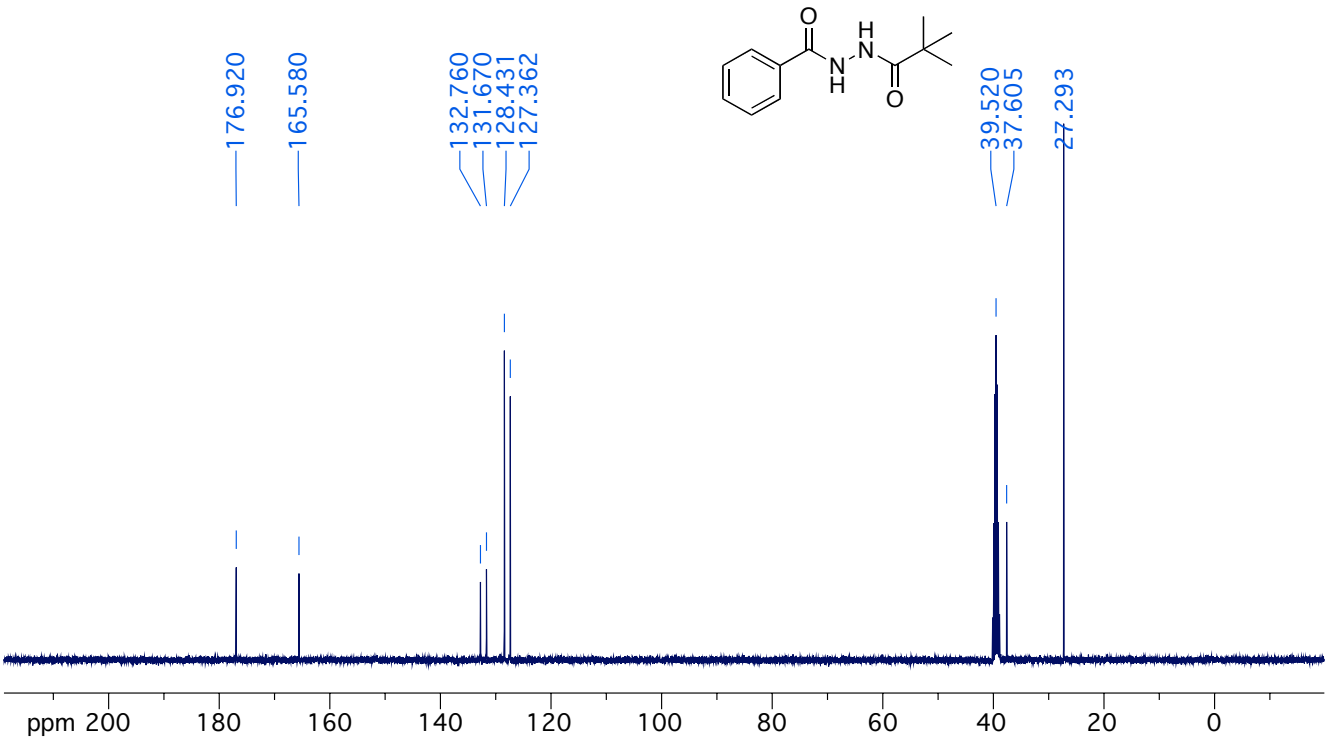
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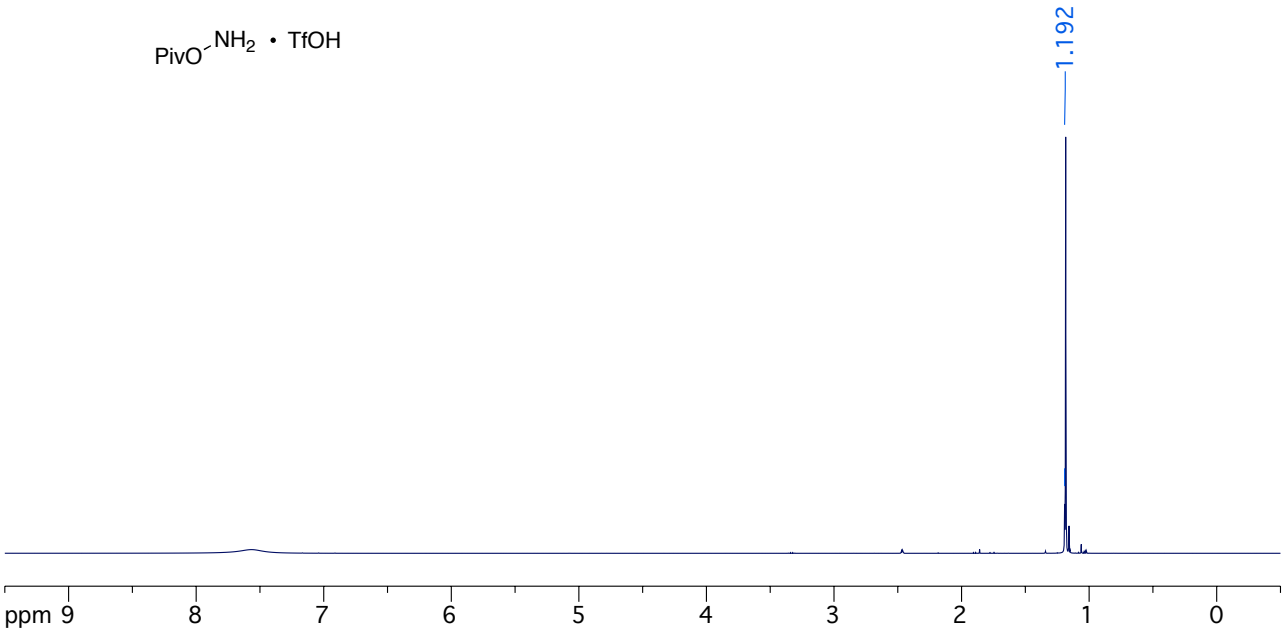
140
120
100
80
60
40
20
0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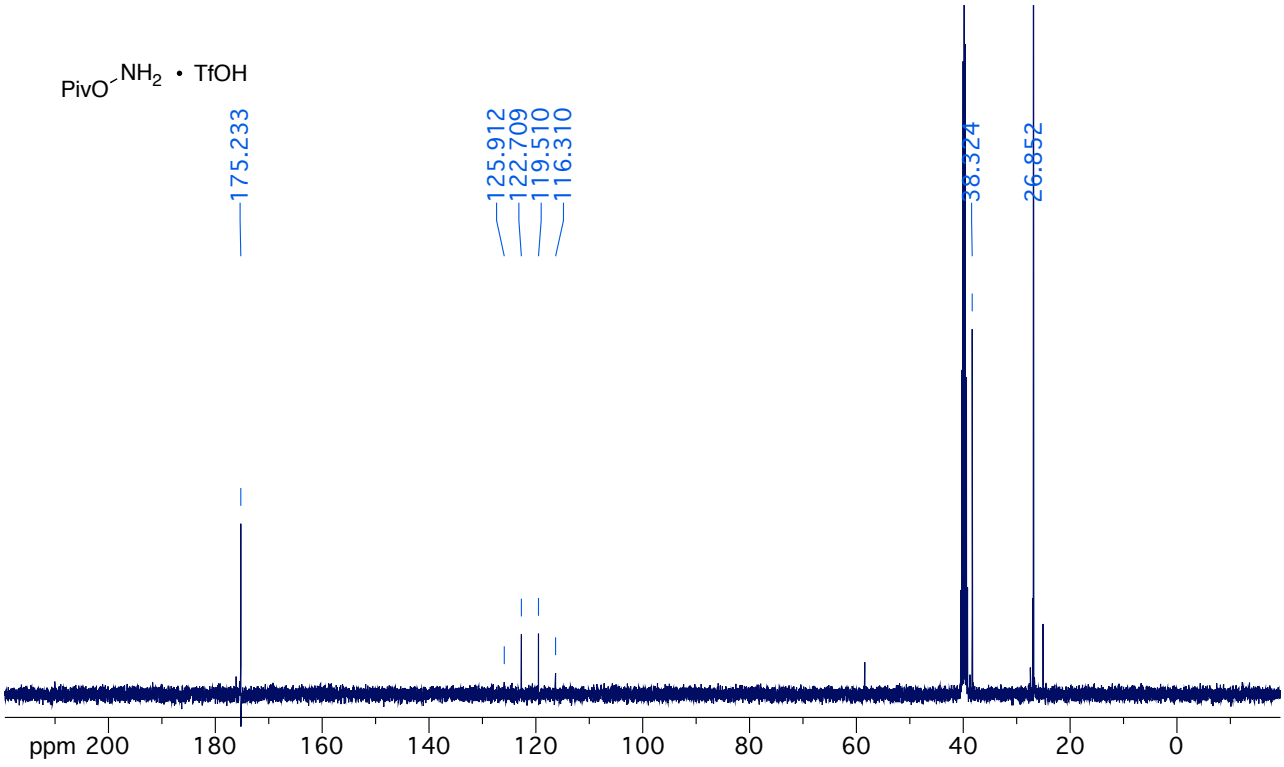
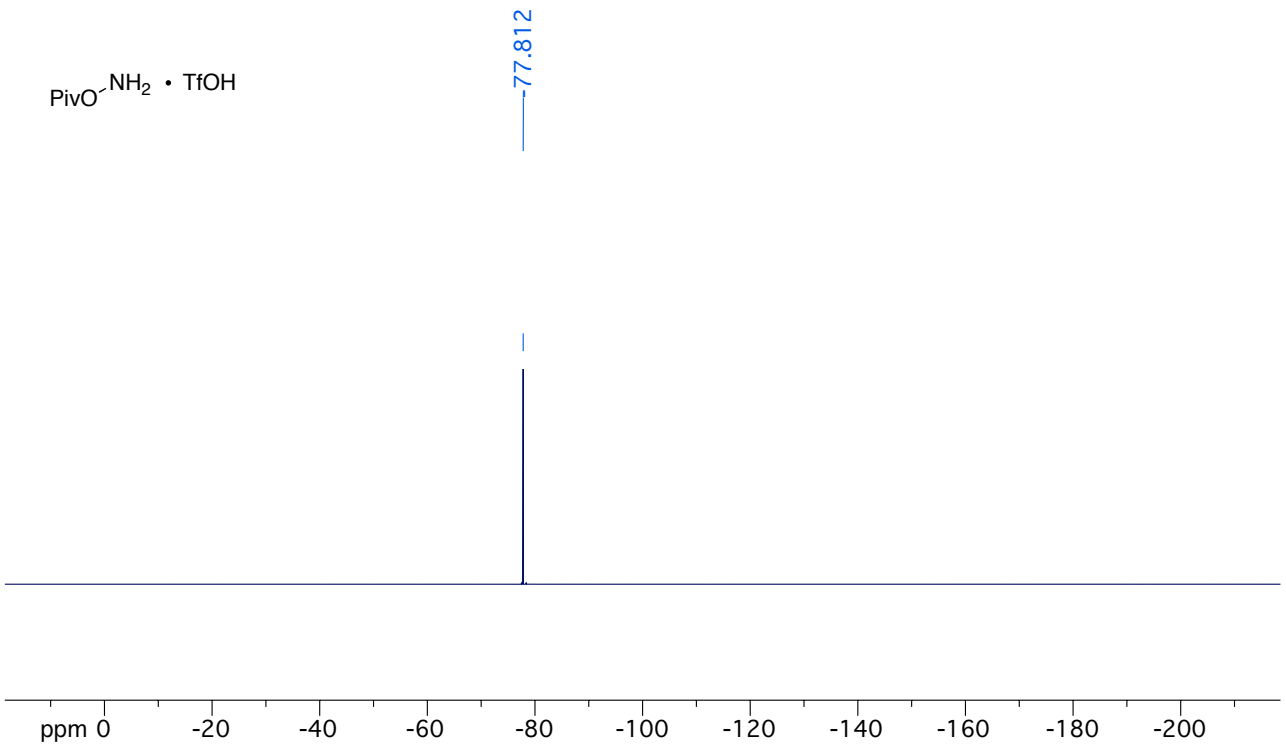
7
6
5
4
3
2
1
0


PivO NH2 • TfOH
175.233
125.912
122.709
119.510
116.310
38.324
26.852
ppm 200
180
160
140
120
100
80
60
40
20
0


PivO
NH2 • TfOH
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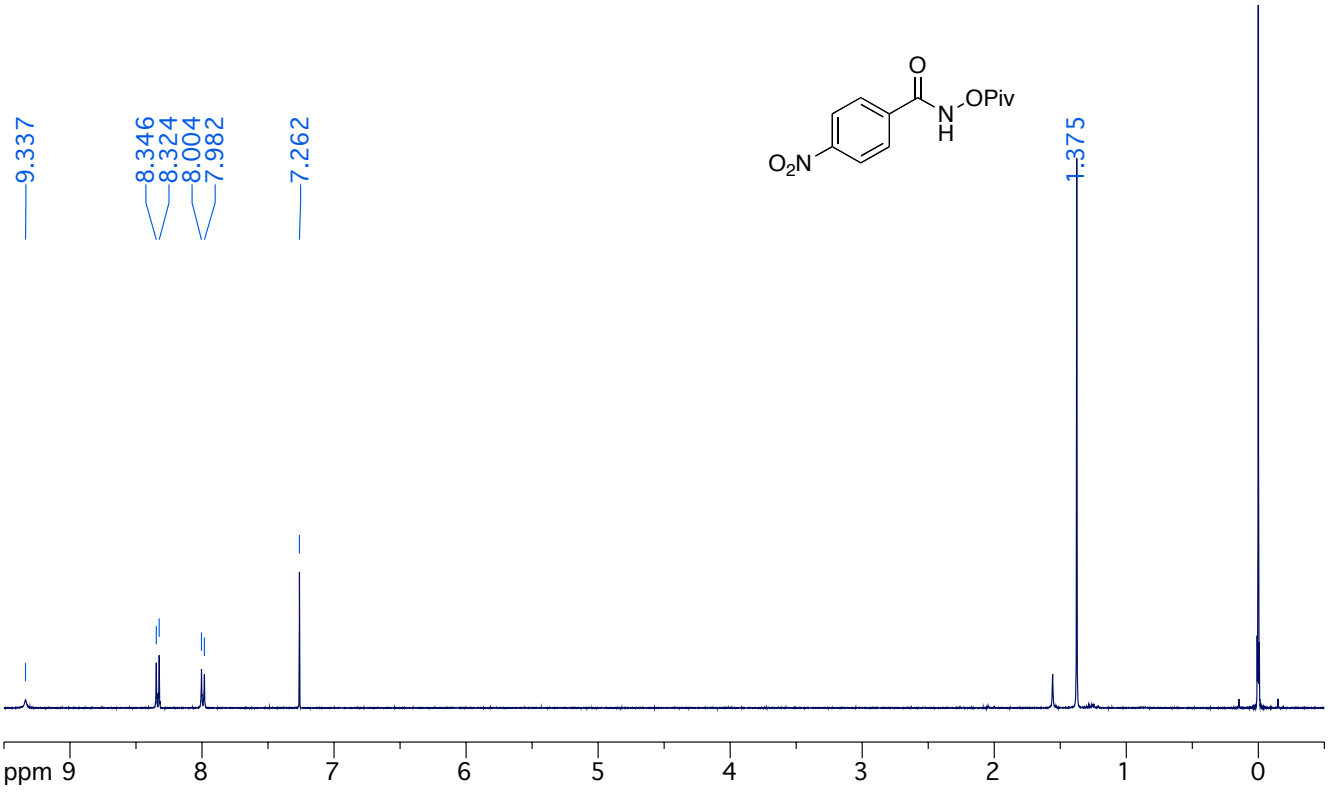
-40
-60
-80
-100
-120
-140
-160
-180
-200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8.004
7.982
7.262
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O
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H
OPiv
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ppm 9
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7
6
5
4
3
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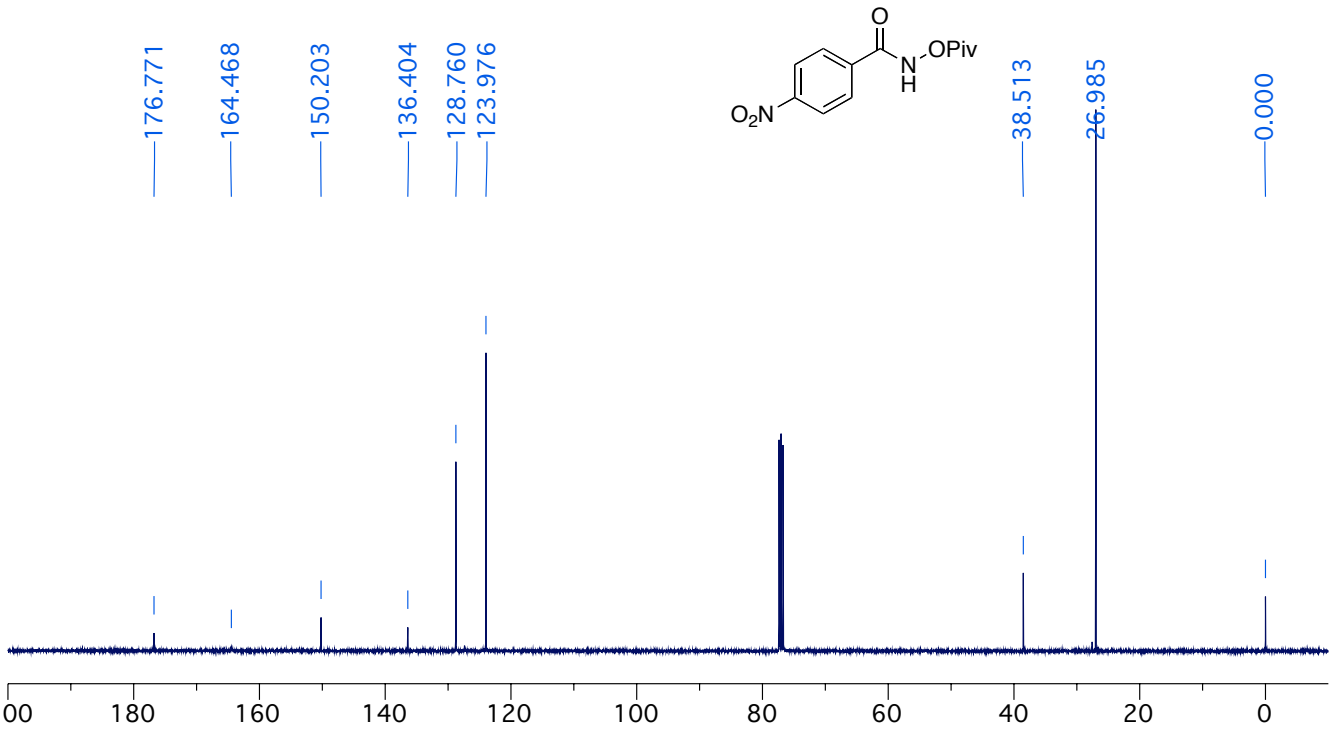
1
0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150.203
136.404
128.760
123.976
38.513
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O2N
00
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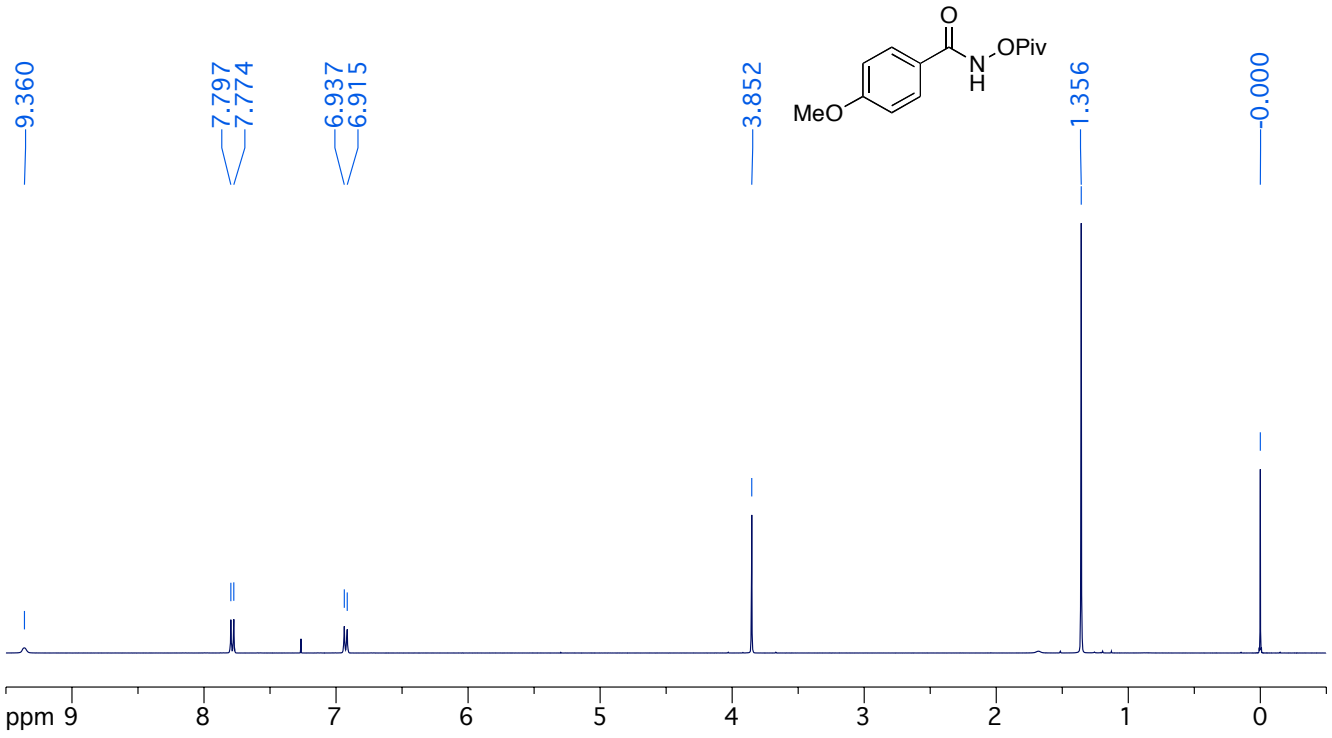
140
120
100
80
60
40
20
0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6.937
6.915
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N
H
OPiv
MeO
ppm 9
8
7
6
5
4
3
2
1
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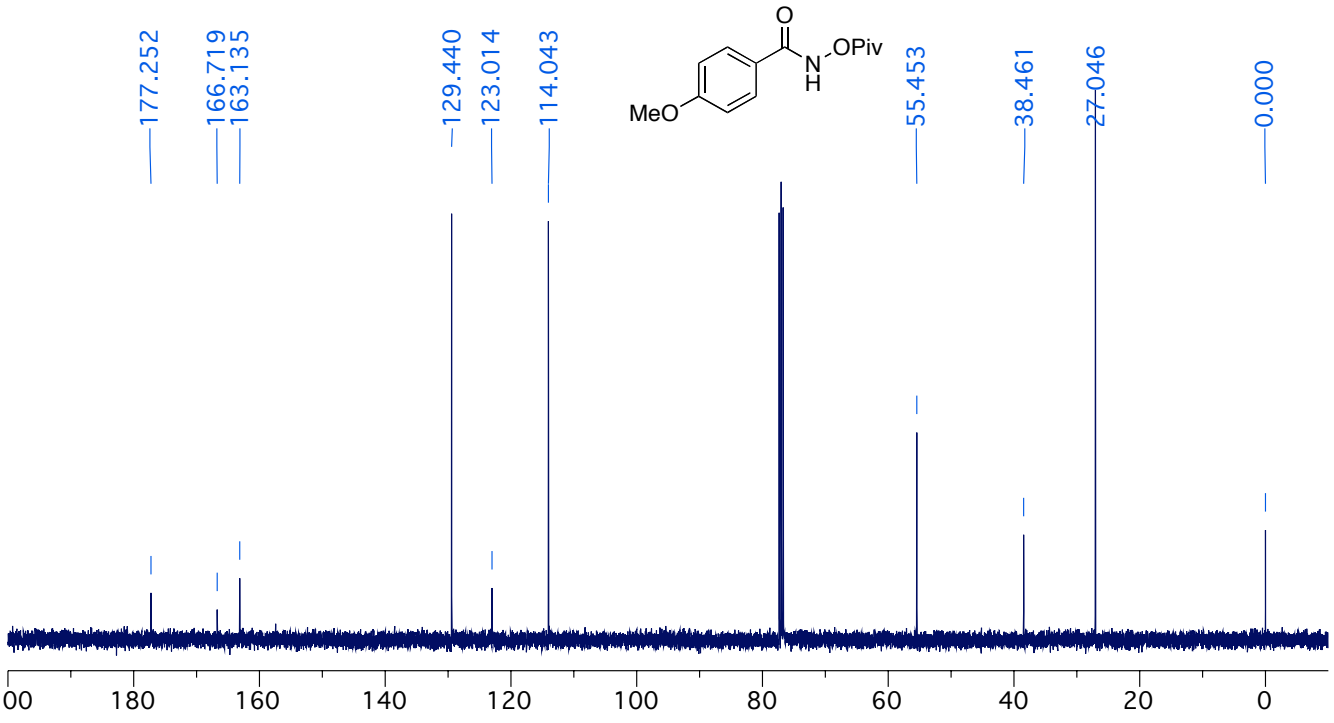
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55.453
38.461
27.046
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H
OPiv
MeO
00
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140
120
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40
20
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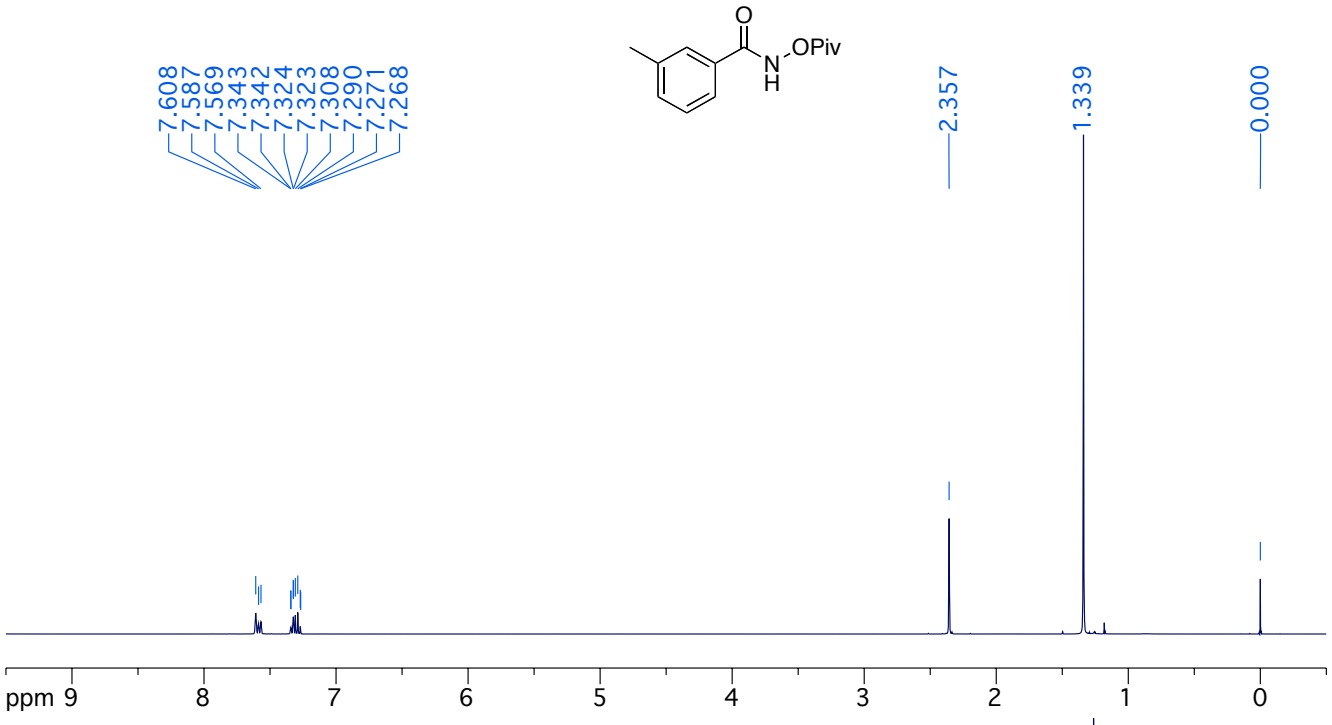
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7.308
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7.271
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OPiv
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7
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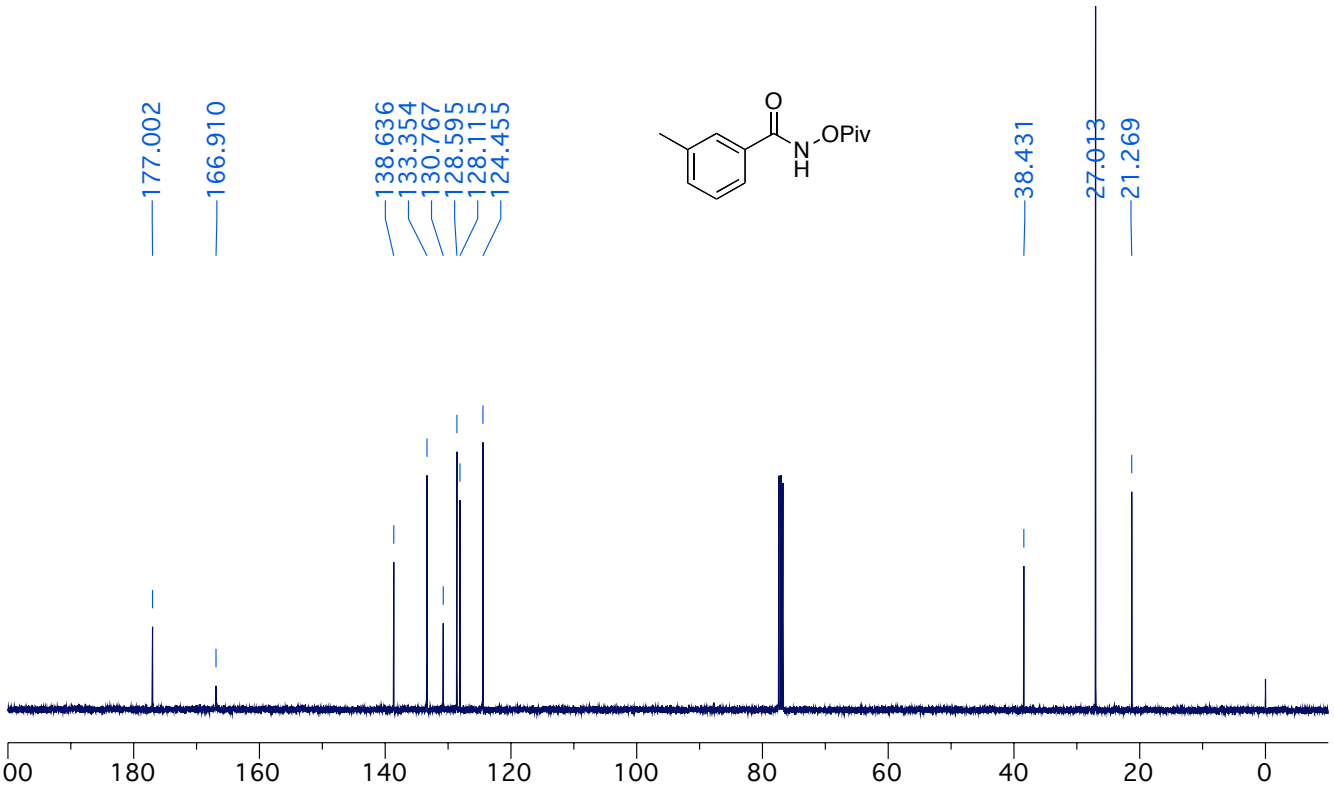
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133.354
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128.115
124.455
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27.013
21.269
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140
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20
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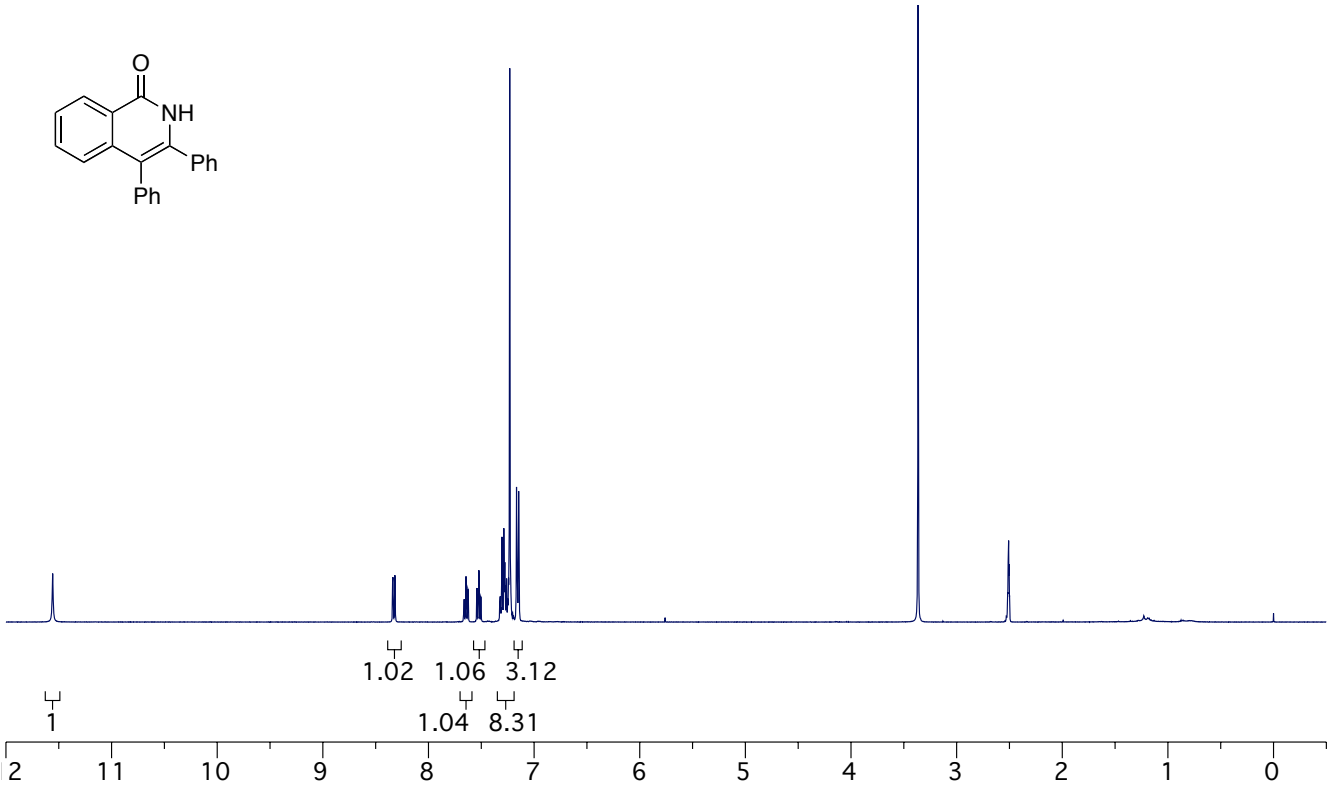
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Ph
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1.04
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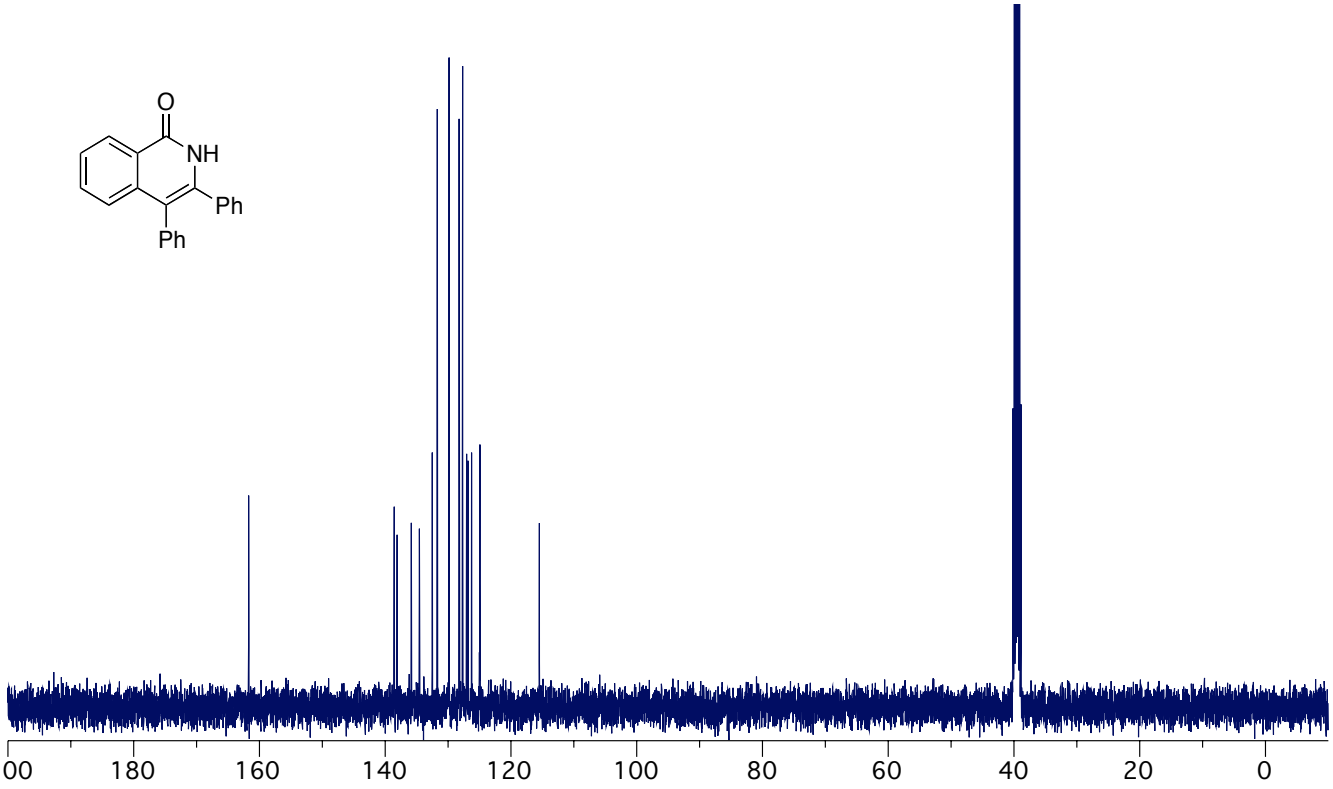
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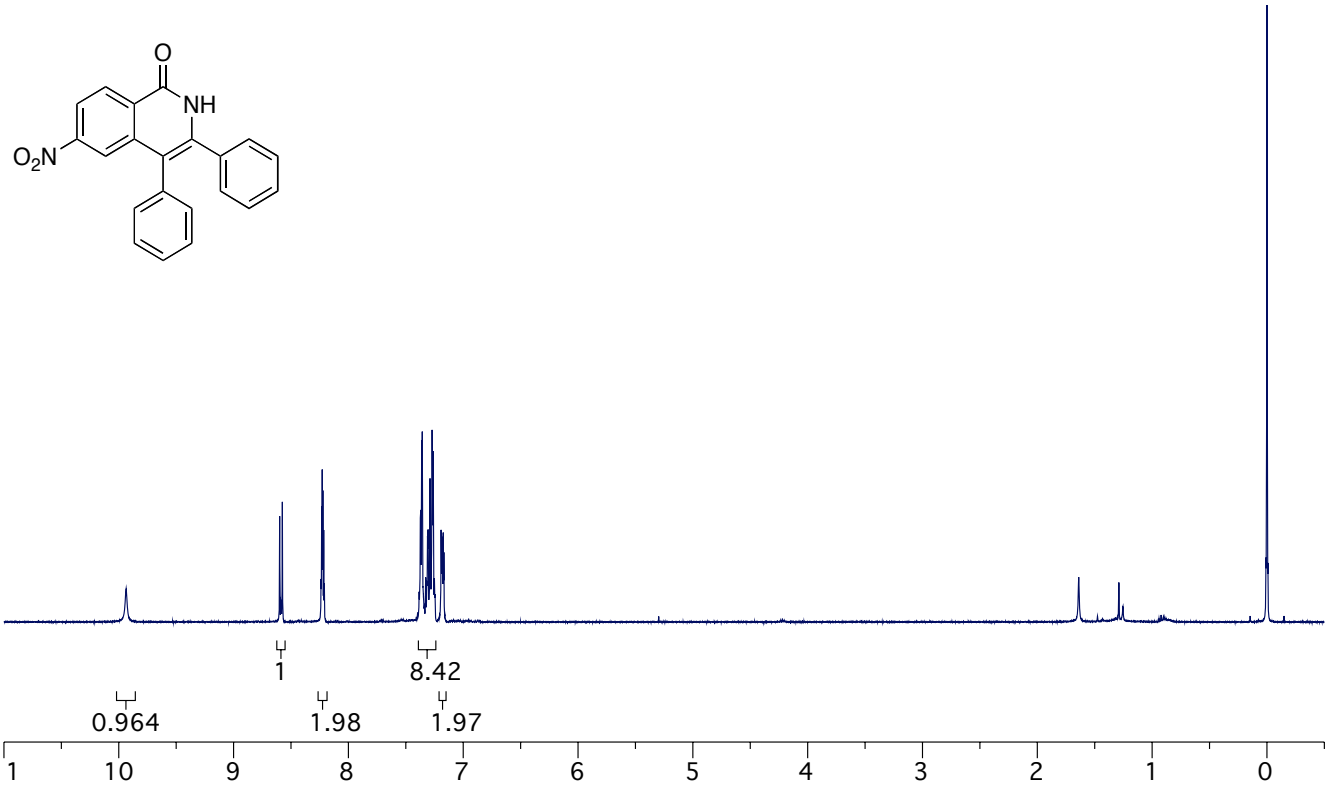
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O2N
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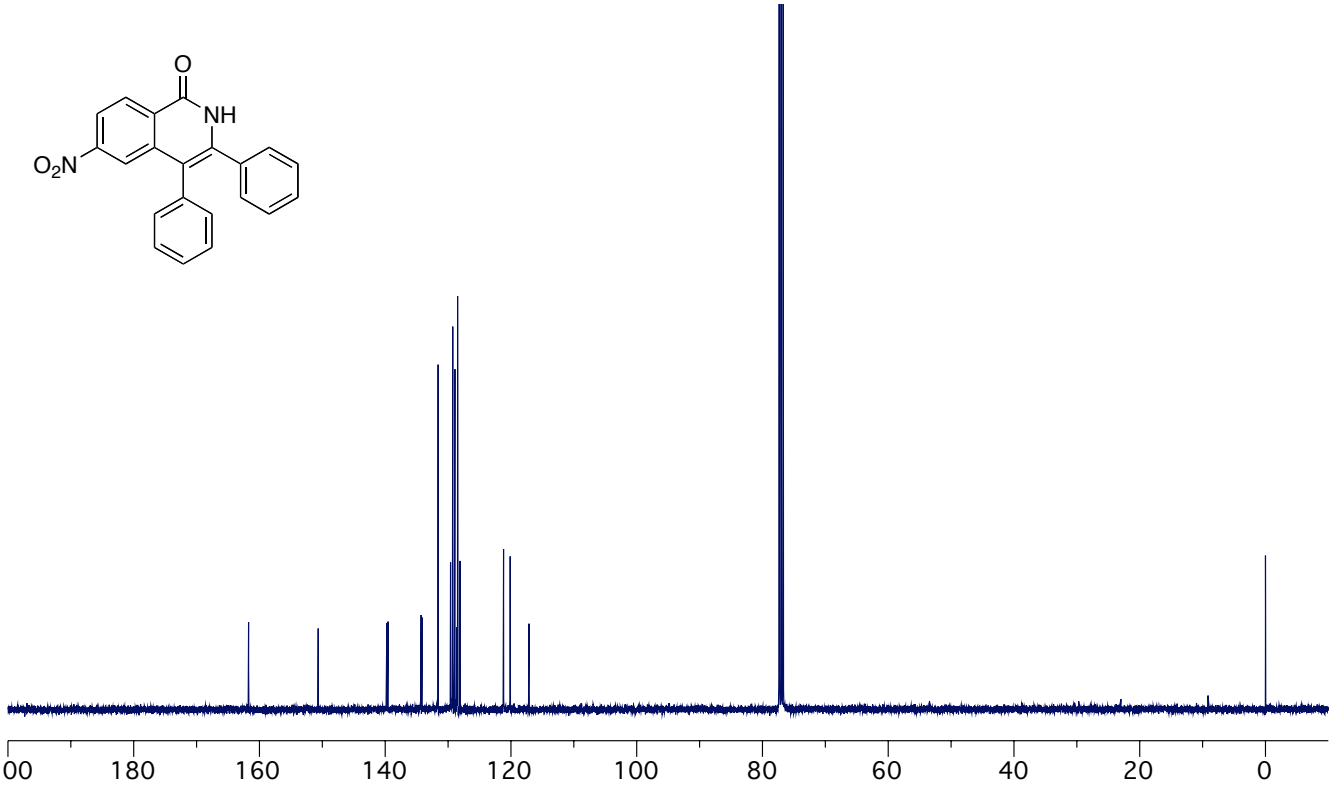
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O2N
00
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140
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60
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20
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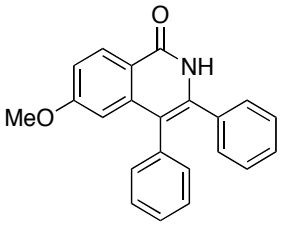
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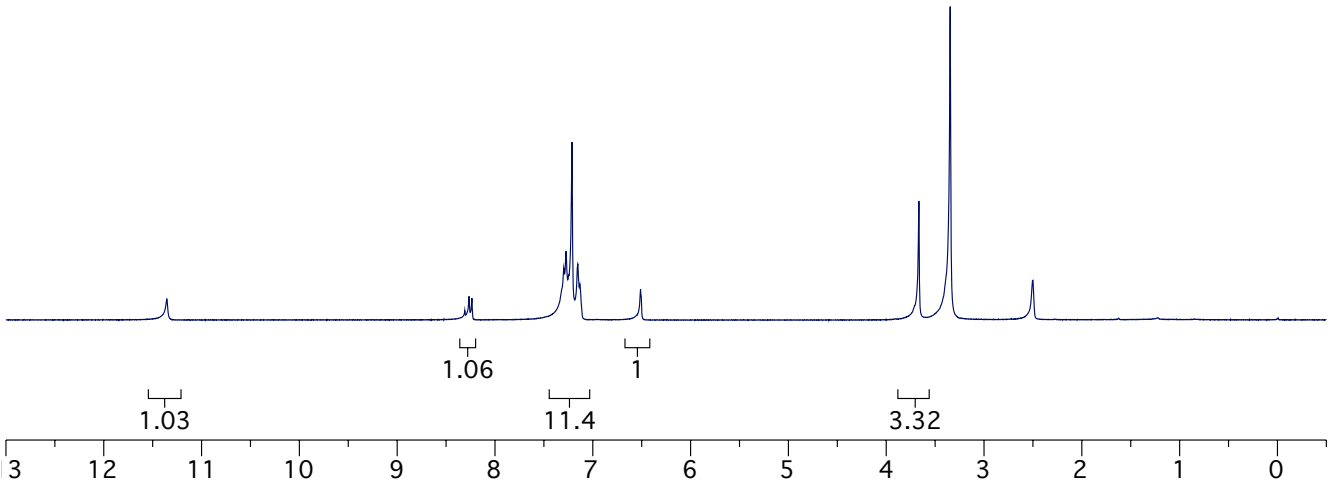
MeO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11
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1
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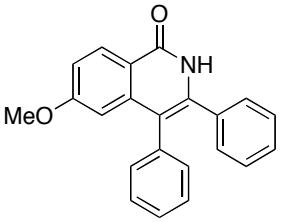
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MeO

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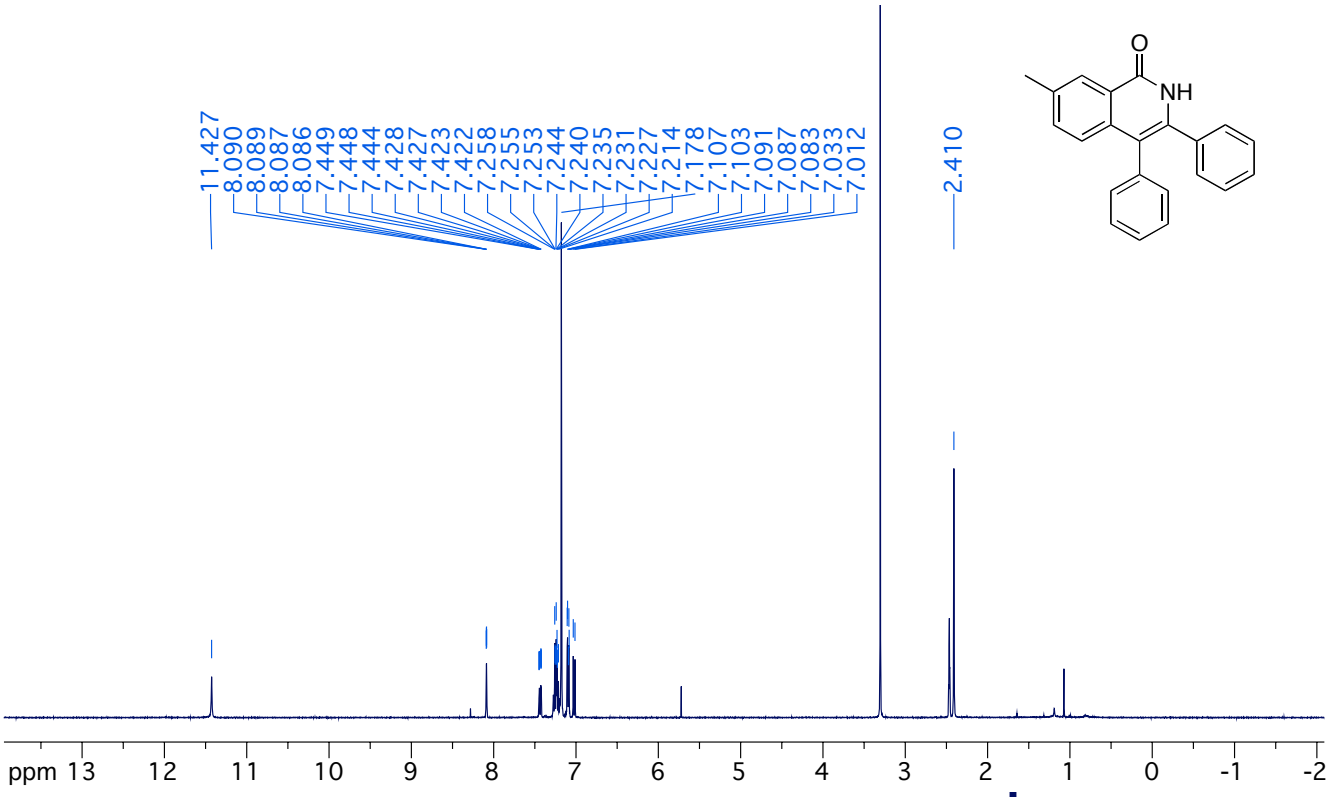
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8.086
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7.427
7.423
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7.258
7.255
7.253
7.244
7.240
7.235
7.231
7.227
7.214
7.178
7.107
7.103
7.091
7.087
7.083
7.033
7.012
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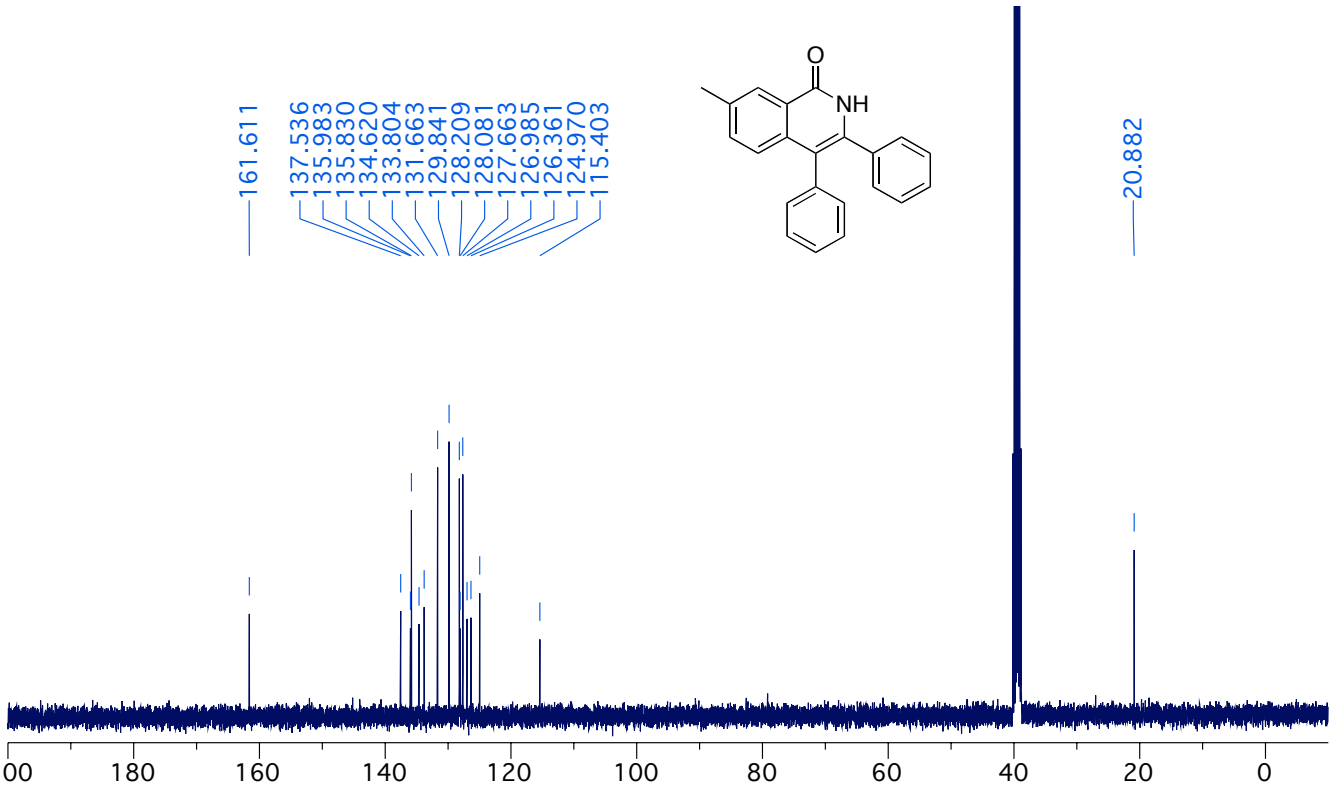
-2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126.985
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20
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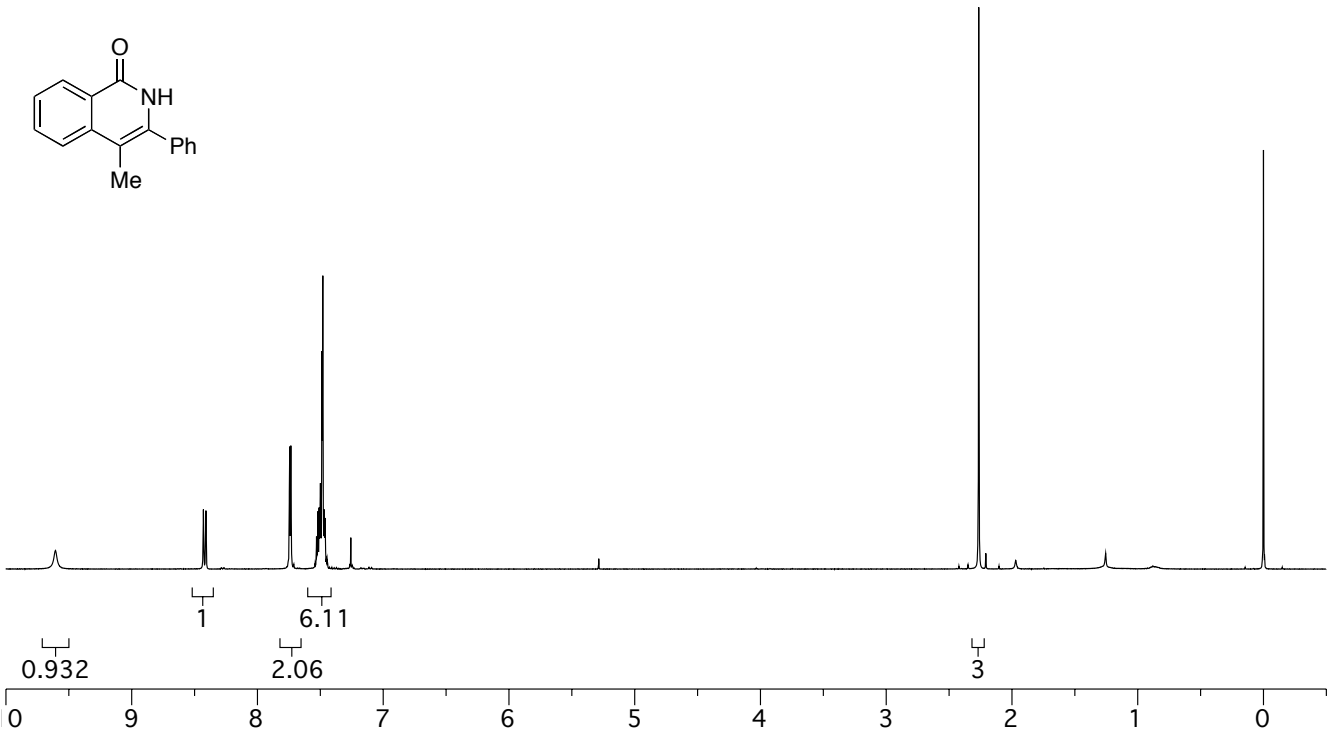
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1
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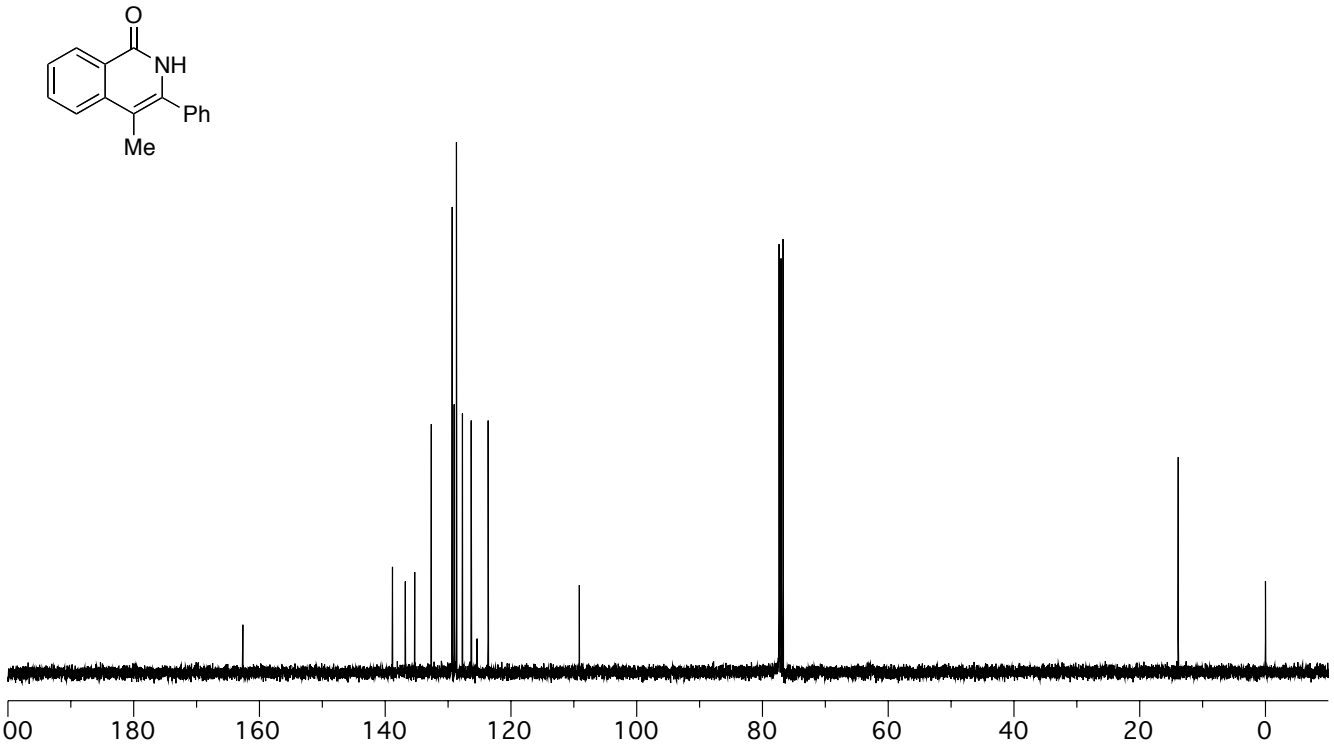
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Ph
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00
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100
80
60
40
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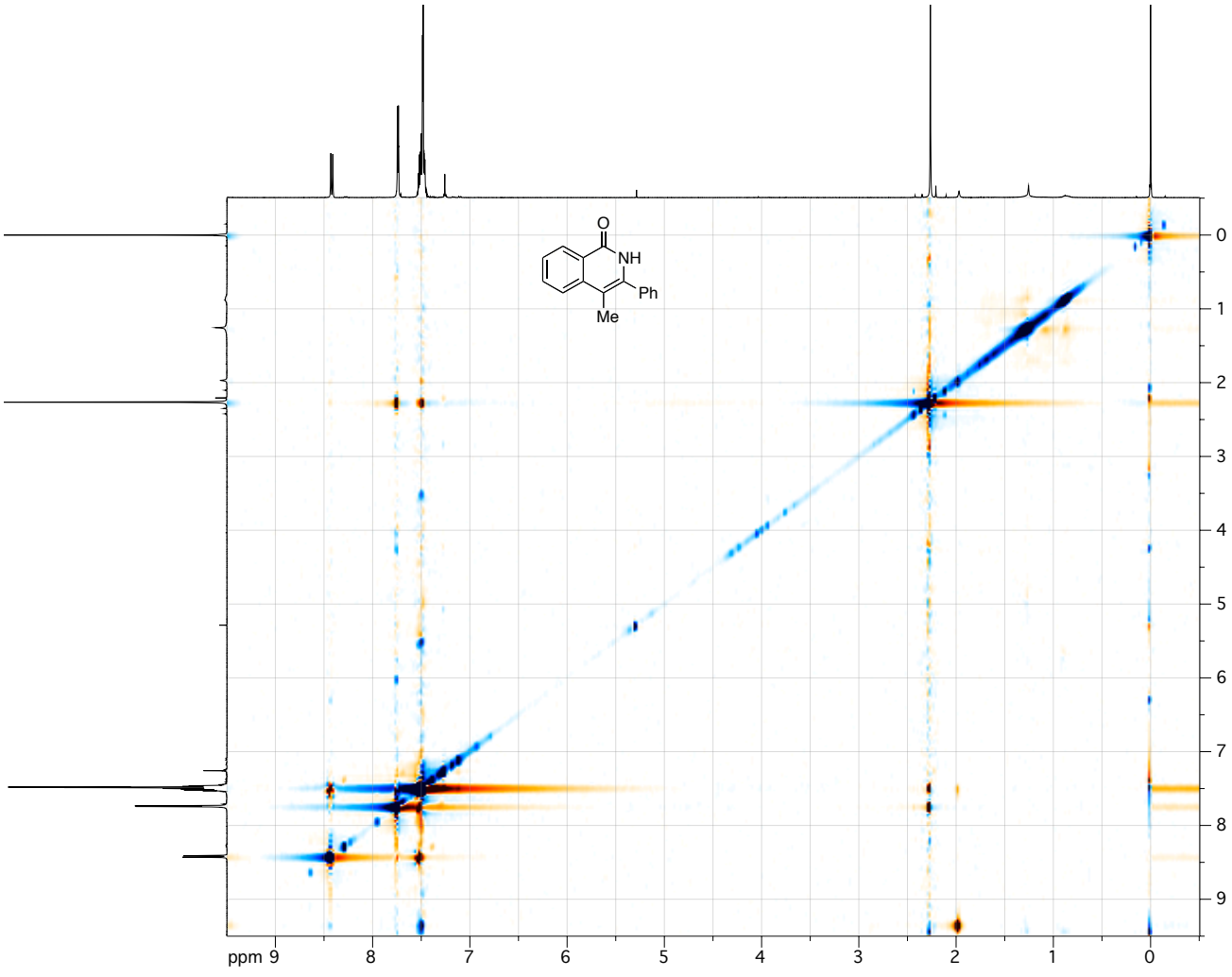
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Ph
Me
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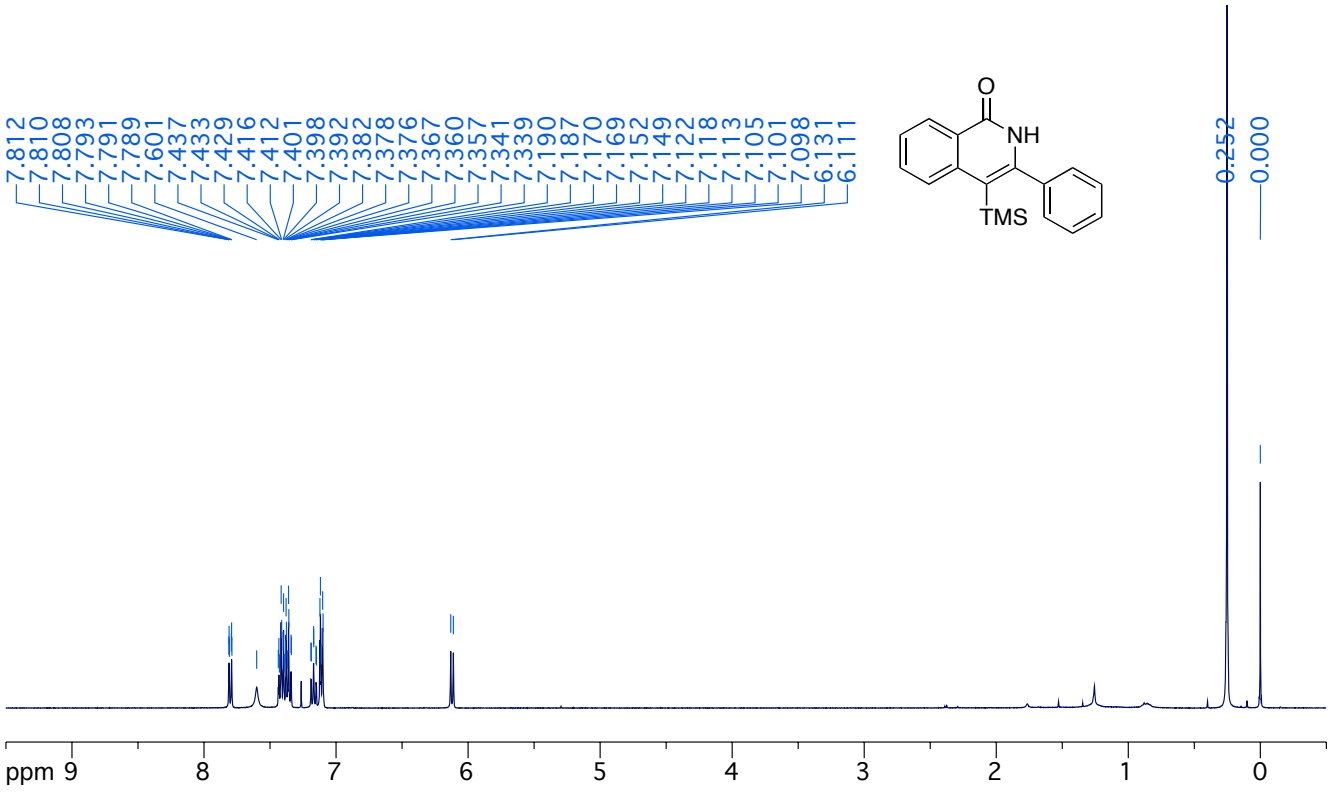
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7.401
7.398
7.392
7.382
7.378
7.376
7.367
7.360
7.357
7.341
7.339
7.190
7.187
7.170
7.169
7.152
7.149
7.122
7.118
7.113
7.105
7.101
7.098
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NH
TMS
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0.000
ppm 9
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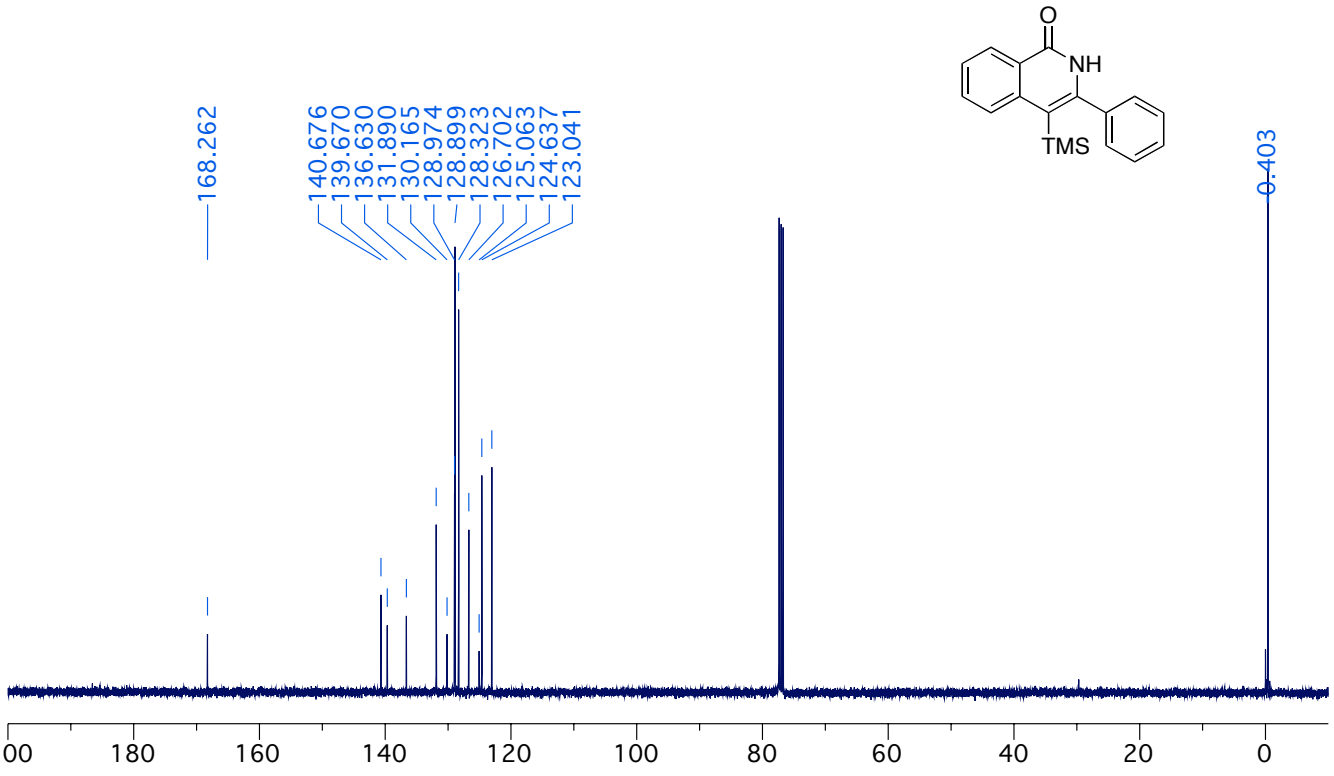
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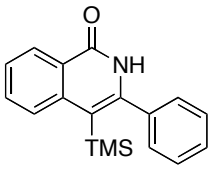
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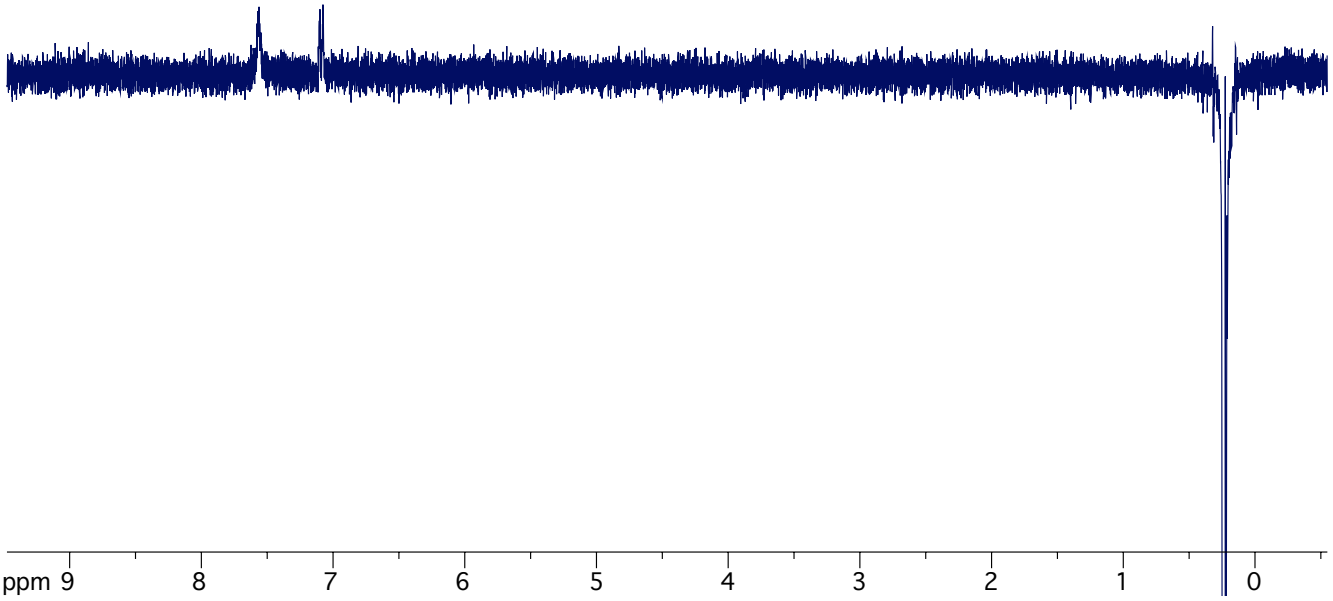
NH
TMS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8
7
6
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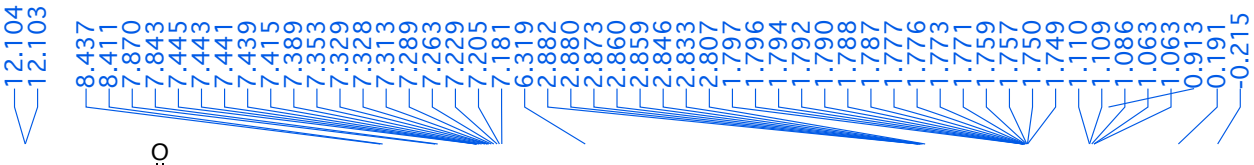
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7.353
7.329
7.328
7.313
7.289
7.263
7.229
7.205
7.181
6.319
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2.880
2.873
2.860
2.859
2.846
2.833
2.807
1.797
1.796
1.794
1.792
1.790
1.788
1.787
1.777
1.776
1.773
1.771
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1.109
1.086
1.063
1.063
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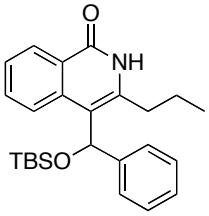
0.191
0.215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NH
TBSO

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12
11
10
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7
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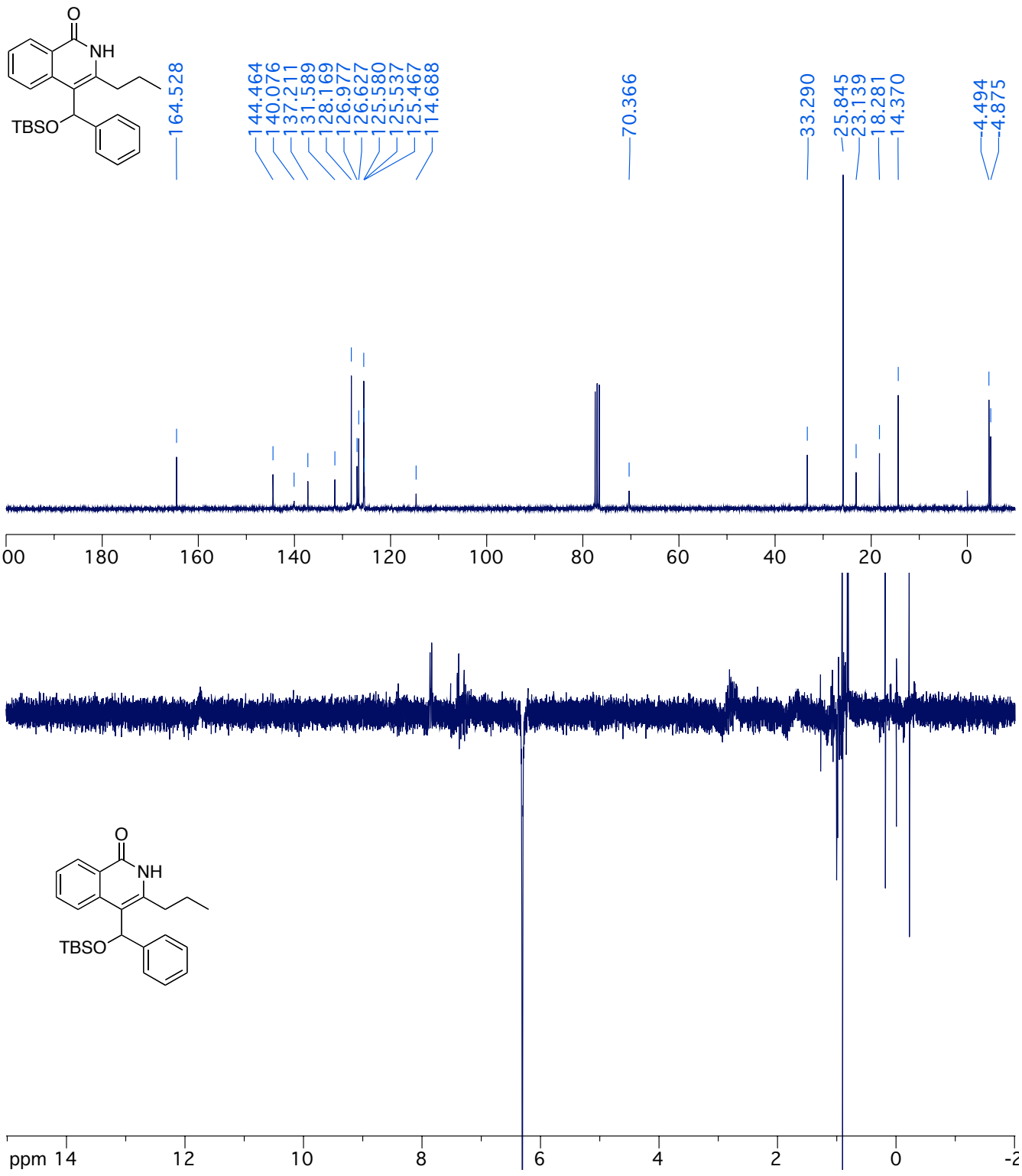
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NH
TBSO
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126.627
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125.537
125.467
114.688
70.366
33.290
25.845
23.139
18.281
14.370
-4.494
-4.875
00
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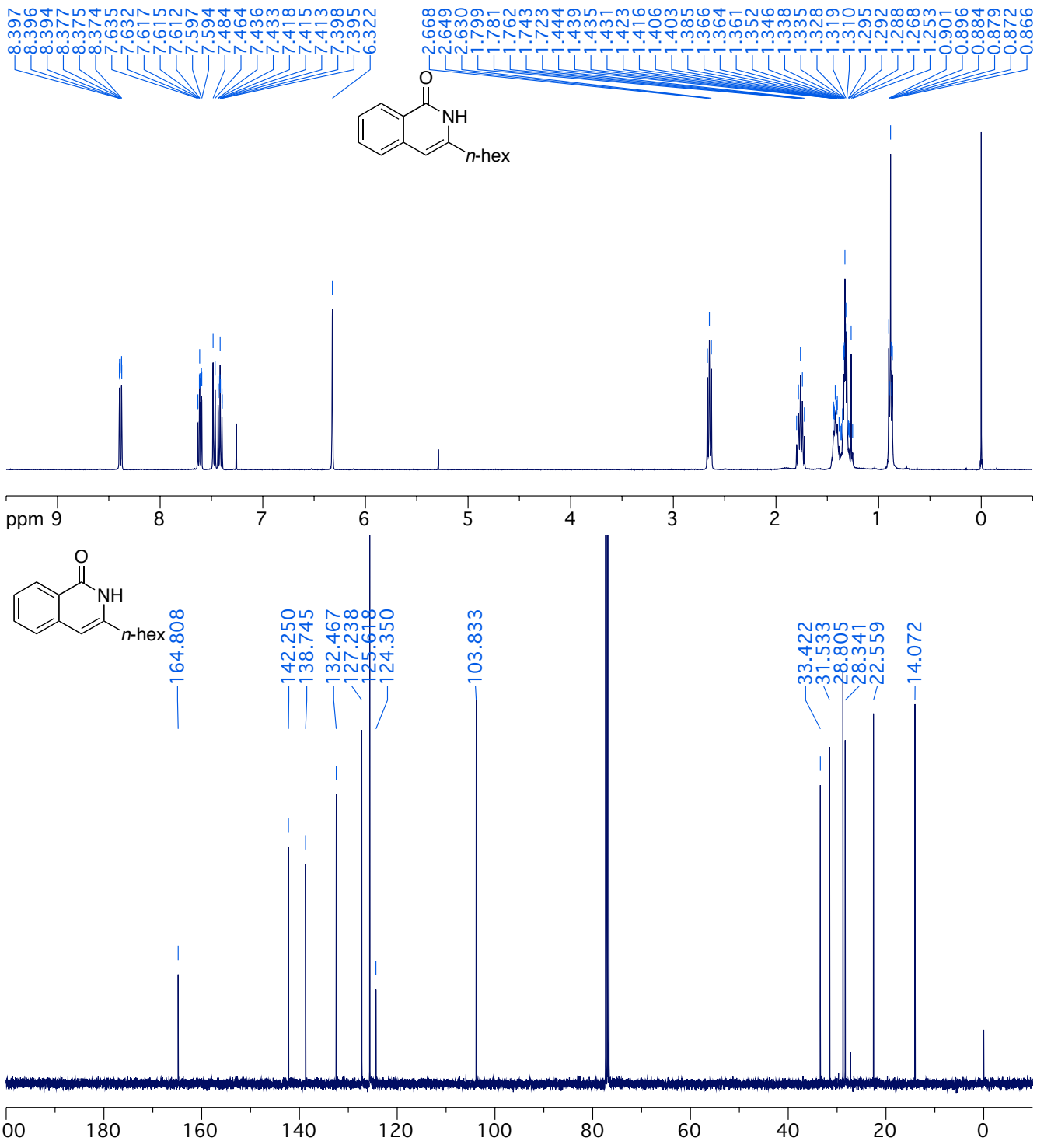
100
80
60
40
20
0
ppm 14
12
10
8
6
4
2
0
-2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8.394
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8.374
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7.632
7.617
7.615
7.612
7.597
7.594
7.484
7.464
7.436
7.433
7.418
7.415
7.413
7.398
7.395
6.322
2.668
2.649
2.630
1.799
1.781
1.762
1.743
1.723
1.444
1.439
1.435
1.431
1.423
1.416
1.406
1.403
1.385
1.366
1.364
1.361
1.352
1.346
1.338
1.335
1.328
1.319
1.310
1.295
1.292
1.288
1.268
1.253
0.901
0.896
0.884
0.879
0.872
0.866
O
NH
n-hex
ppm 9
8
7
6
5
4
3
2
1
0
O
NH
n-hex
164.808
142.250
138.745
132.467
127.238
125.618
124.350
103.833
33.422
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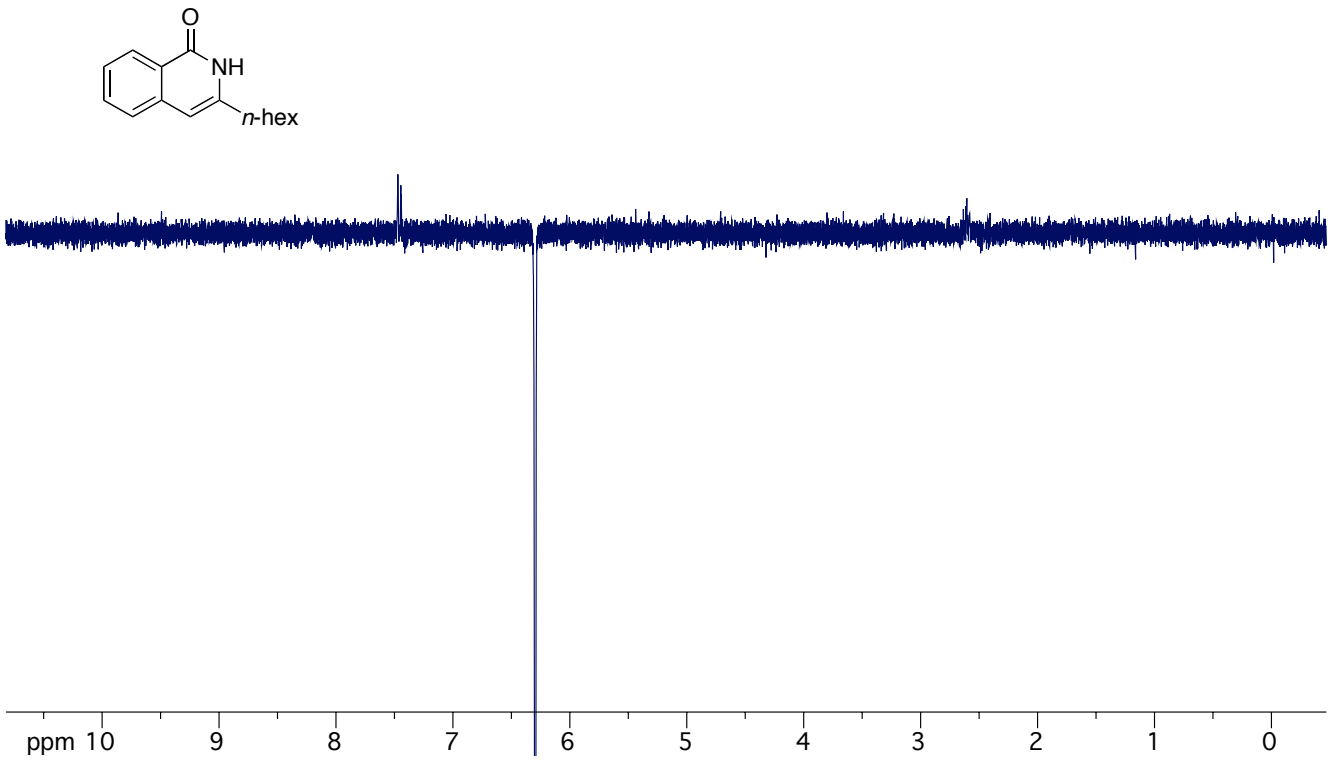
28.805
28.341
22.559
14.072
00
180
160
140
120
100
80
60
40
20
0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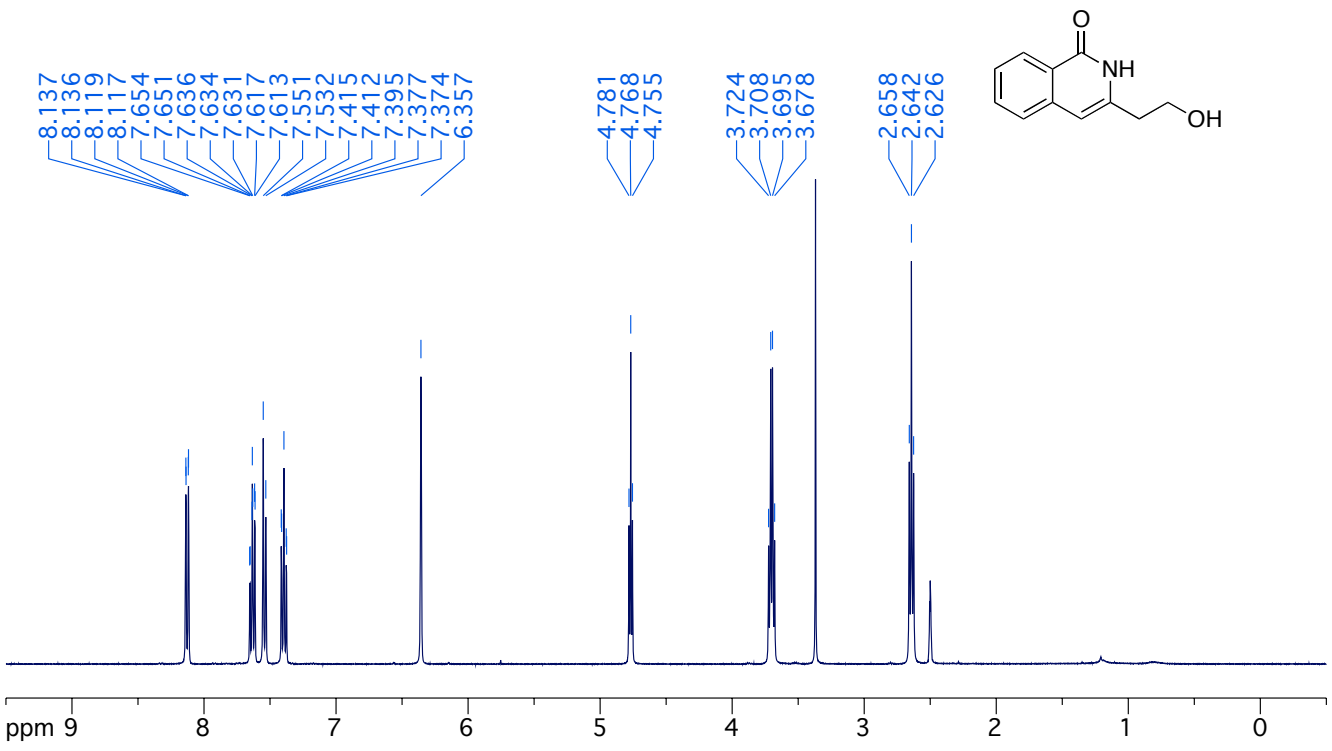
NH
n-hex
ppm 10 9 8 7 6 5 4 3 2 1 0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7.636
7.634
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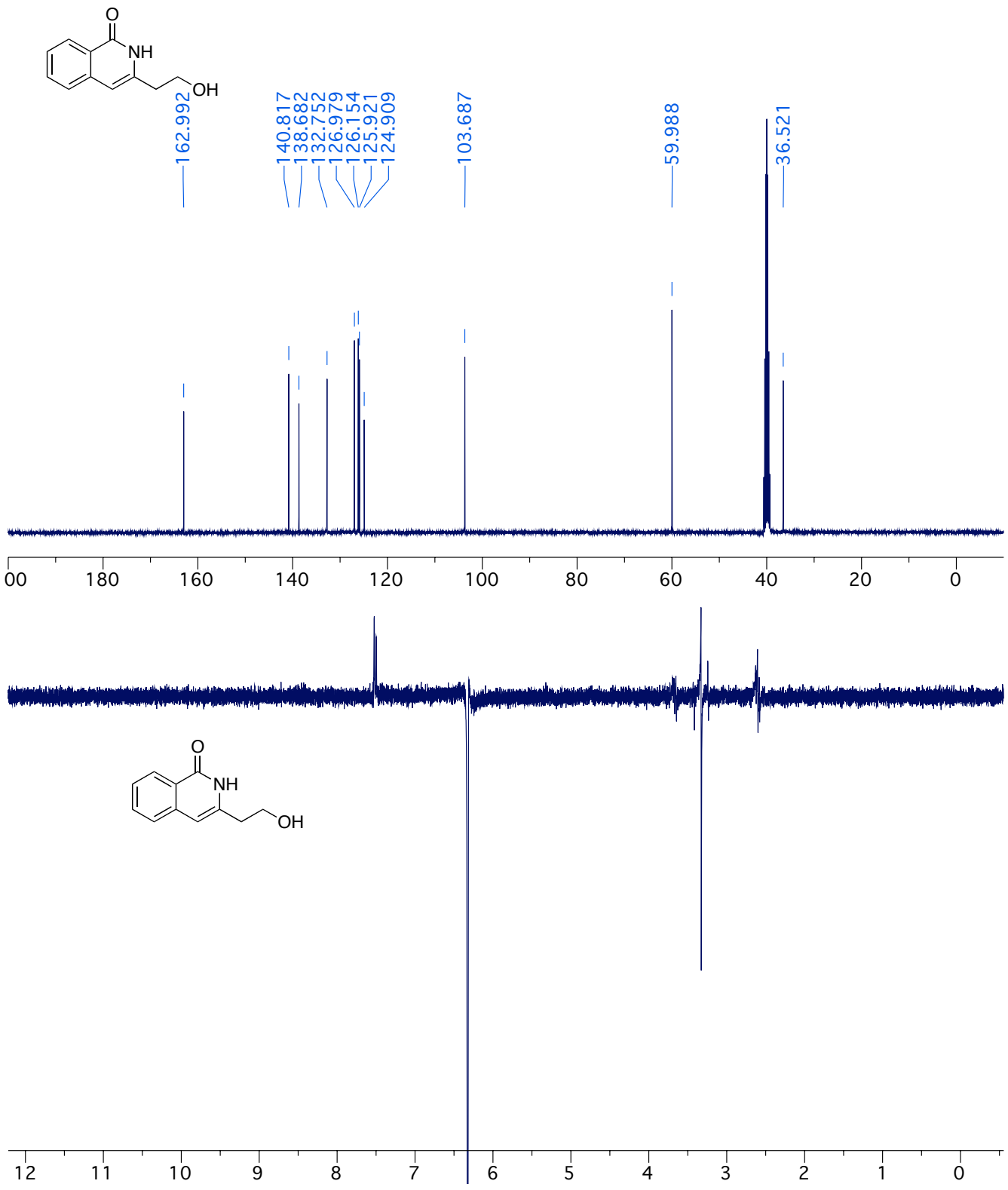
7.617
7.613
7.551
7.532
7.415
7.412
7.395
7.377
7.374
6.357
4.781
4.768
4.755
3.724
3.708
3.695
3.678
2.658
2.642
2.626
O
NH
OH
ppm 9 8 7 6 5 4 3 2 1 0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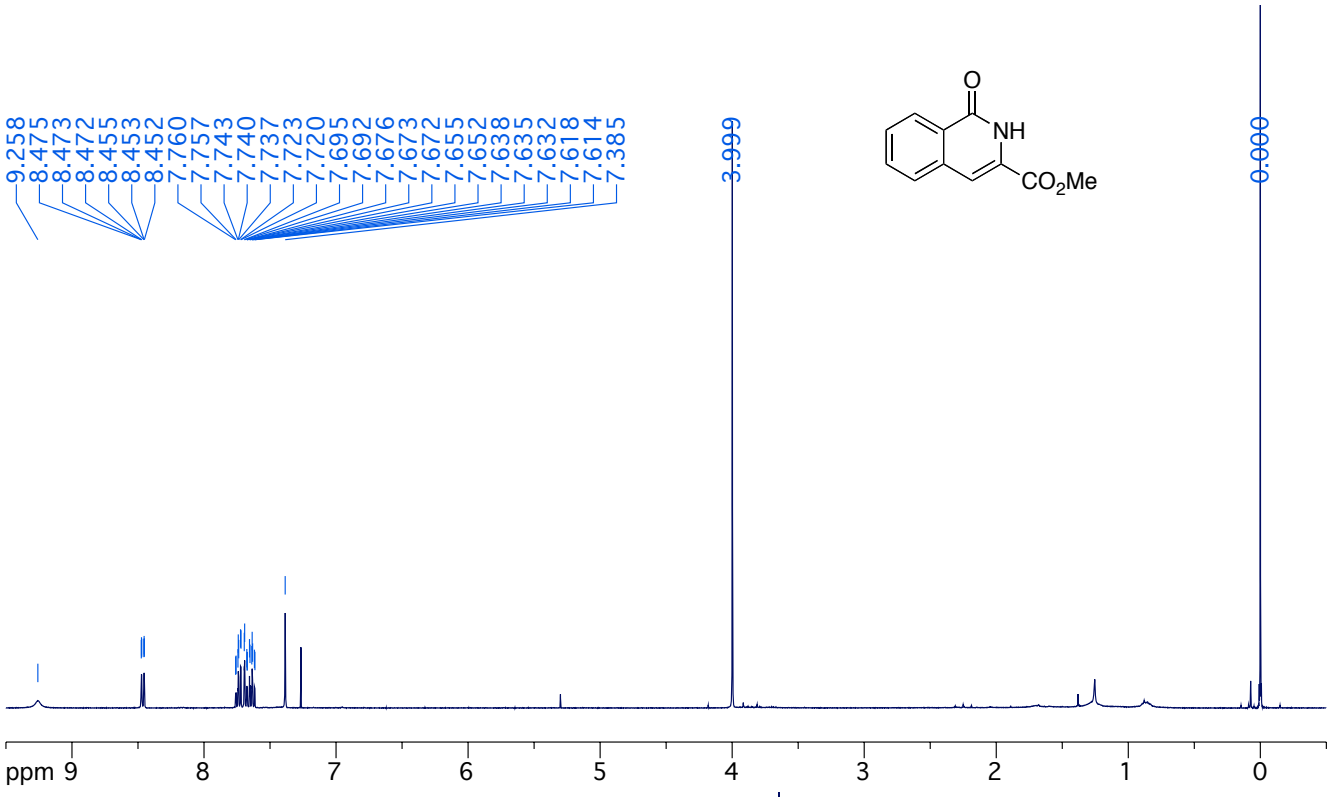
124.909
103.687
59.988
36.521
00
180
160
140
120
100
80
60
40
20
0
O
NH
OH
12
11
10
9
8
7
6
5
4
3
2
1
0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8.452
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7.740
7.737
7.723
7.720
7.695
7.692
7.676
7.673
7.672
7.655
7.652
7.638
7.635
7.632
7.618
7.614
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0.000
O
NH
CO2Me
ppm 9
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7
6
5
4
3
2
1
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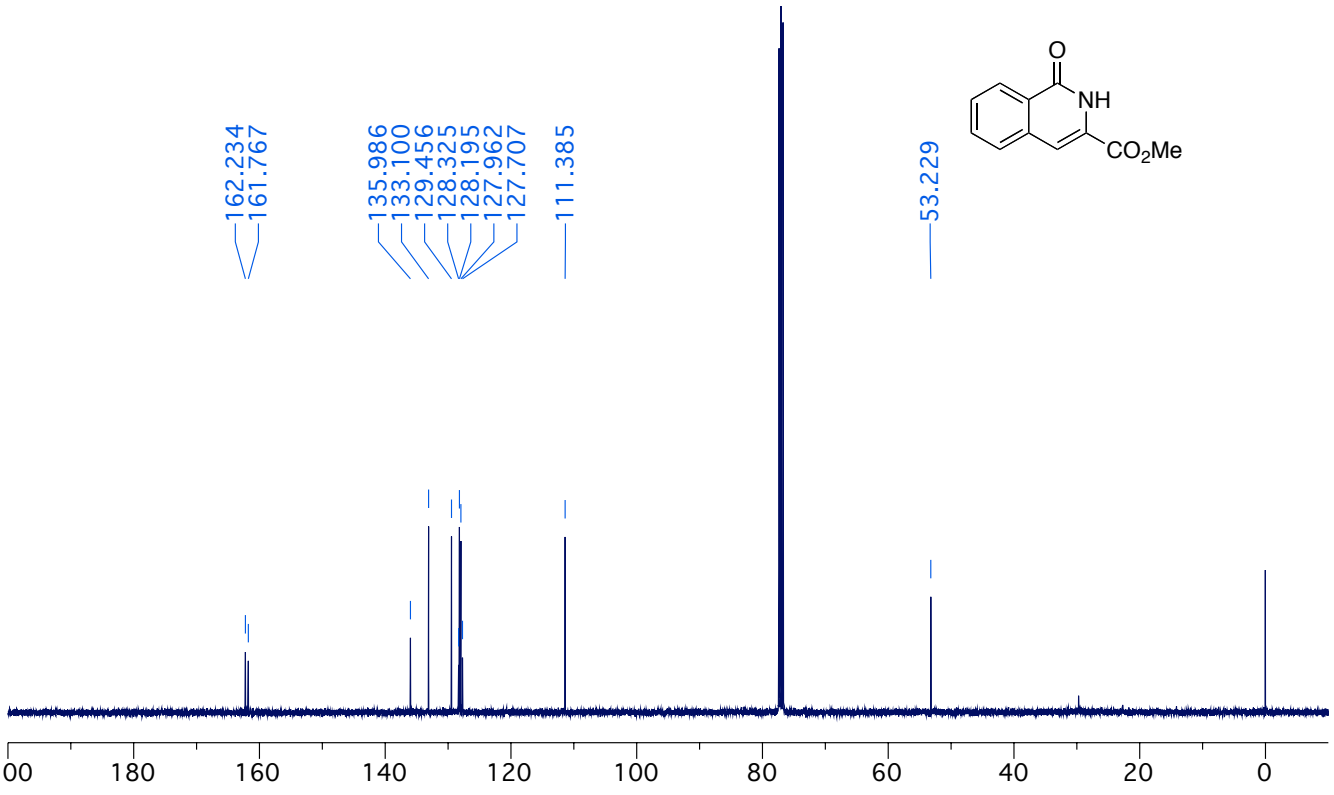
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128.325
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127.962
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53.229
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NH
CO2Me
00
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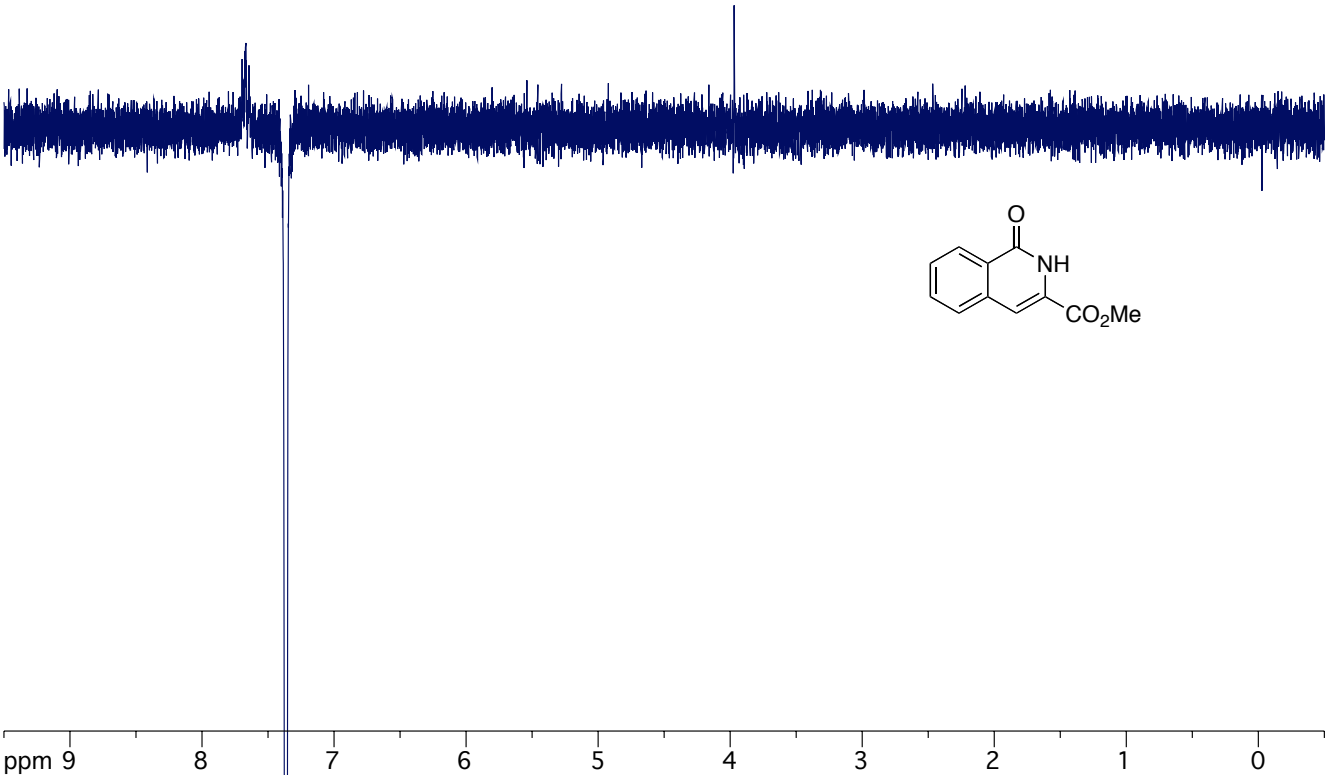
160
140
120
100
80
60
40
20
0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NH
CO2Me
ppm 9
8
7
6
5
4
3
2
1
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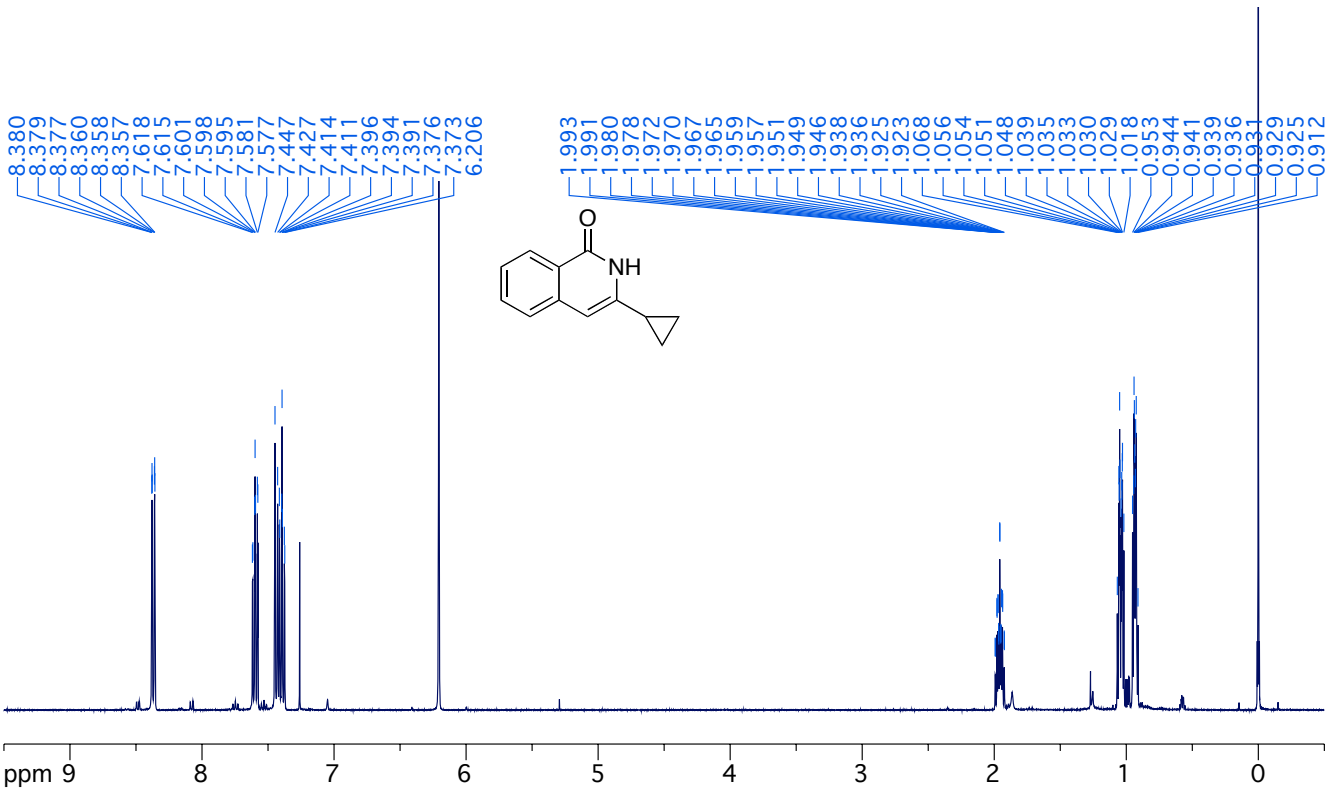
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8.357
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7.615
7.601
7.598
7.595
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7.577
7.447
7.427
7.414
7.411
7.396
7.394
7.391
7.376
7.373
6.206
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1.991
1.980
1.978
1.972
1.970
1.967
1.965
1.959
1.957
1.951
1.949
1.946
1.938
1.936
1.925
1.923
1.068
1.056
1.054
1.051
1.048
1.039
1.035
1.033
1.030
1.029
1.018
0.953
0.944
0.941
0.939
0.936
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1
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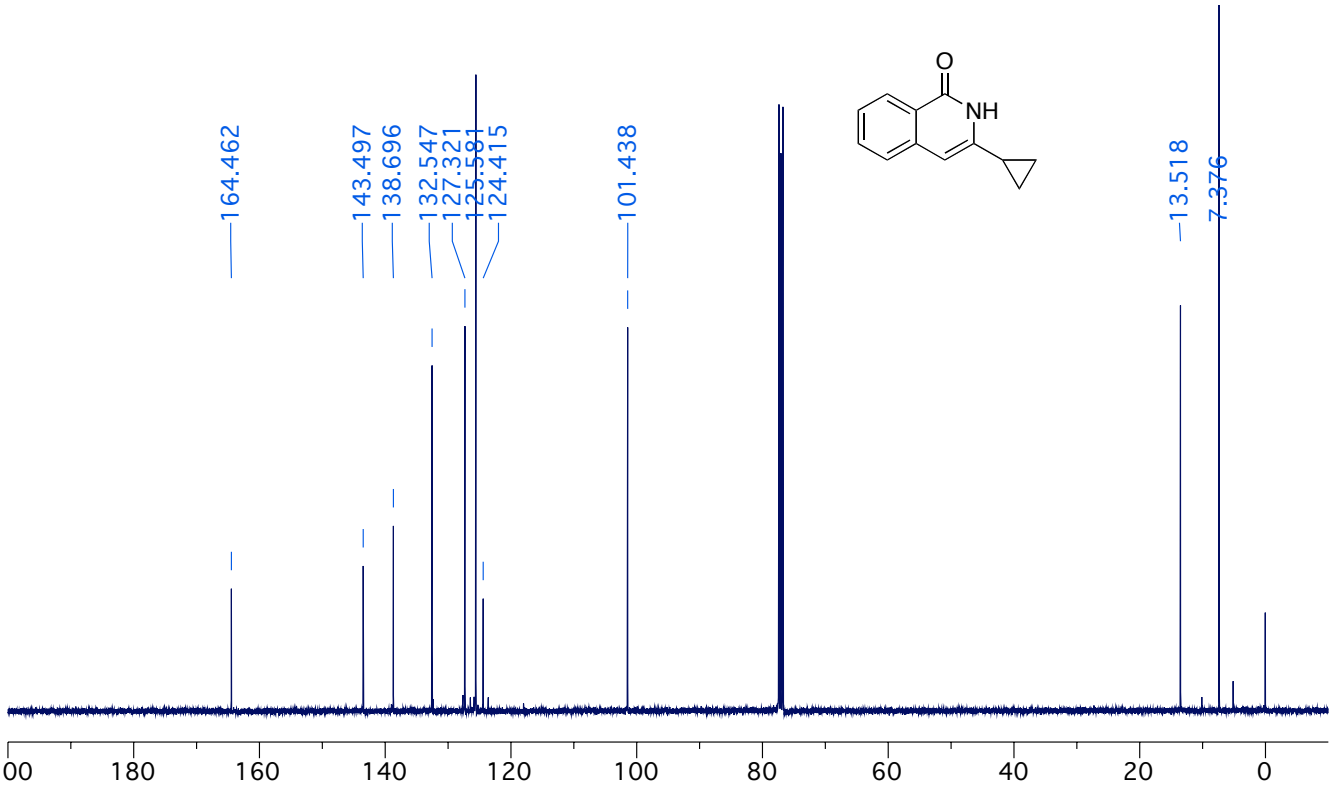
O
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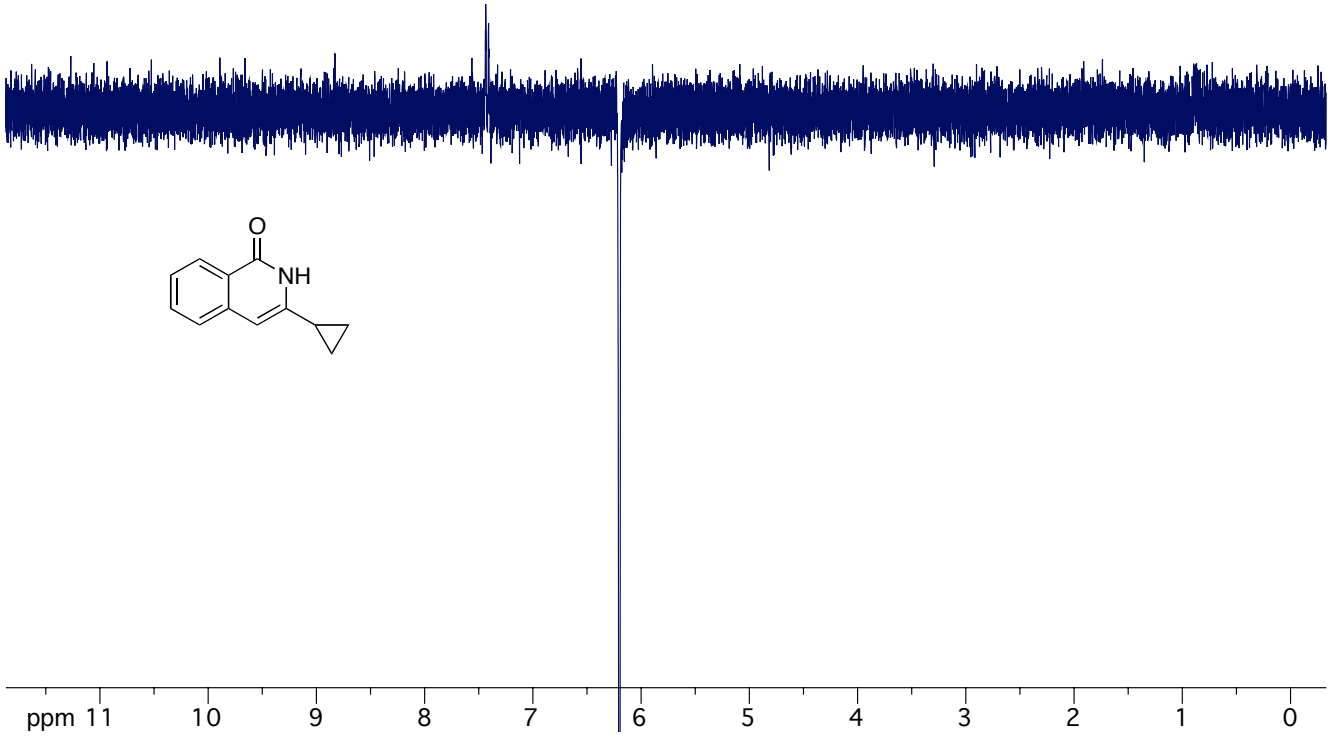
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ppm 11
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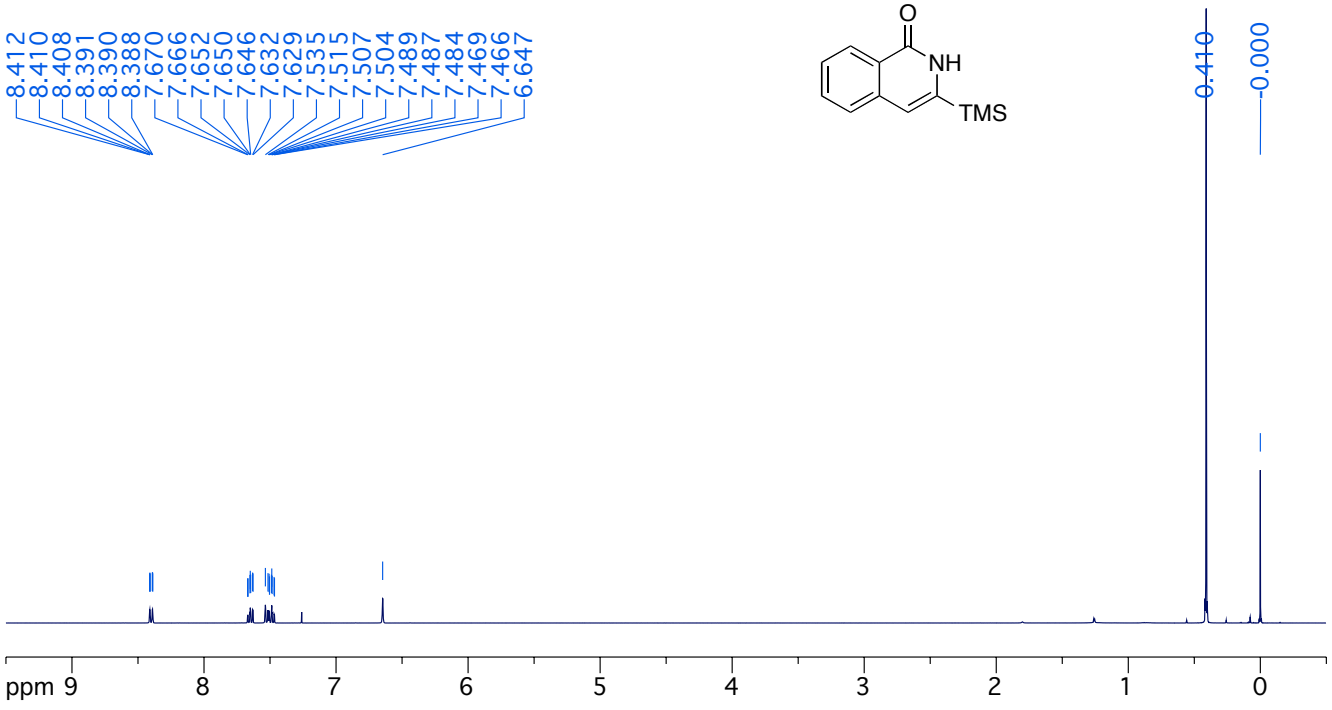
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7.646
7.632
7.629
7.535
7.515
7.507
7.504
7.489
7.487
7.484
7.469
7.466
6.647
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TMS
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0.000
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7
6
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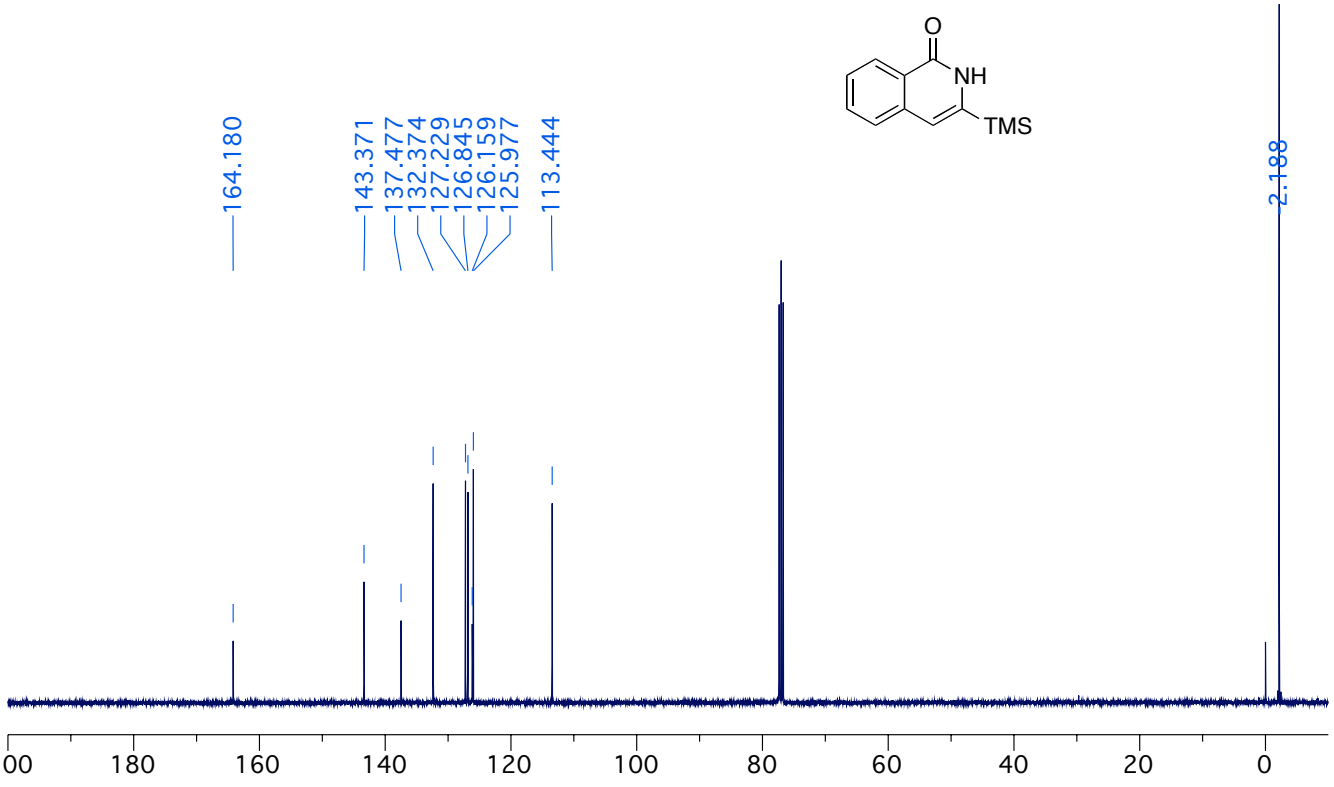
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20
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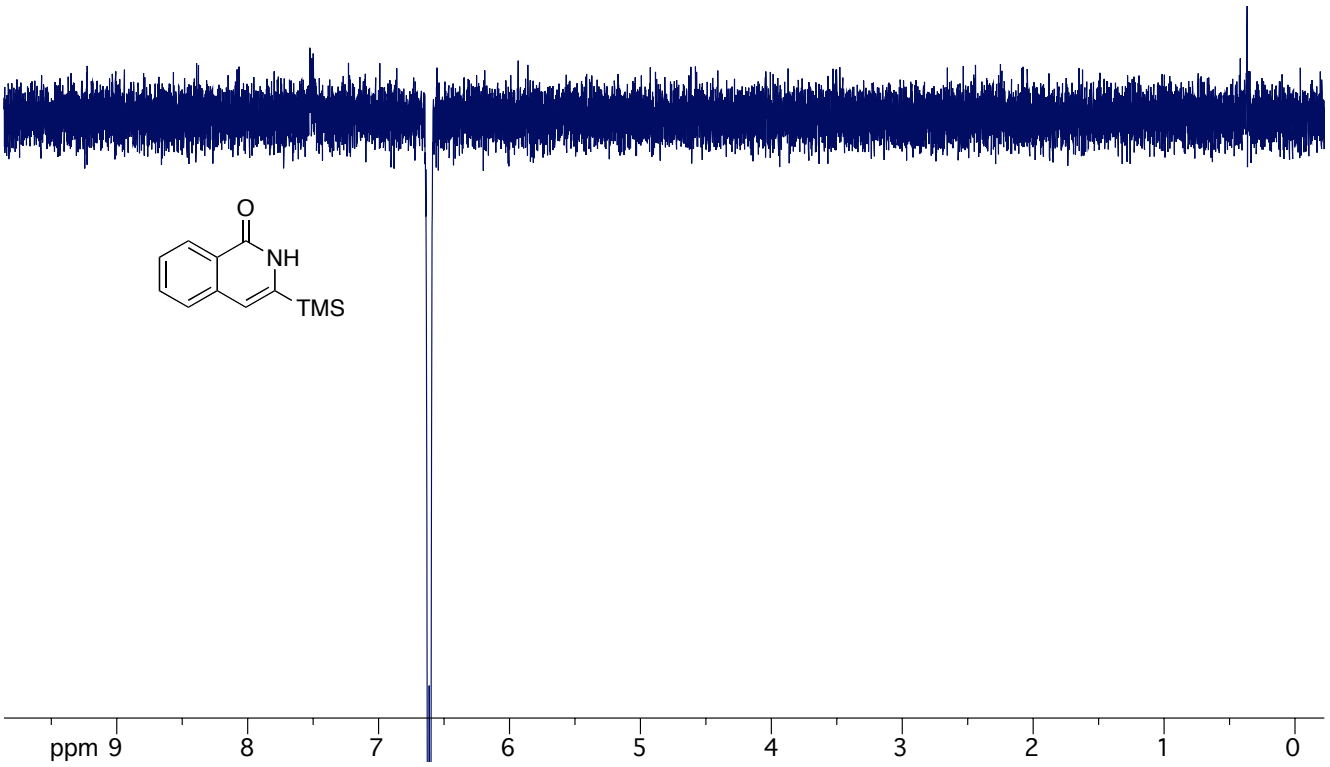
O
NH
TMS
ppm 9
8
7
6
5
4
3
2
1
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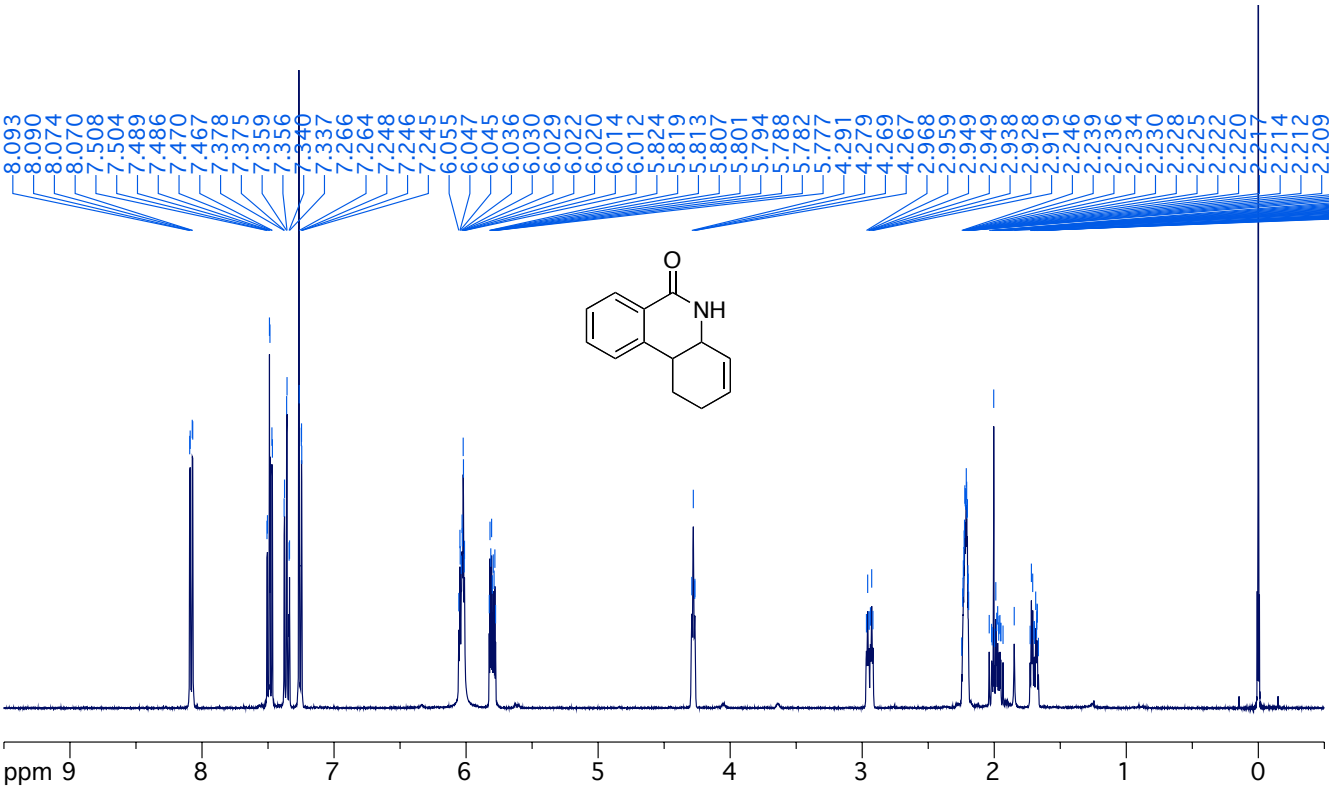
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7.375
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7.356
7.340
7.337
7.266
7.264
7.248
7.246
7.245
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6.047
6.045
6.036
6.030
6.029
6.022
6.020
6.014
6.012
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5.819
5.813
5.807
5.801
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5.782
5.777
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4.279
4.269
4.267
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2.949
2.938
2.928
2.919
2.246
2.239
2.236
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2.222
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2.209
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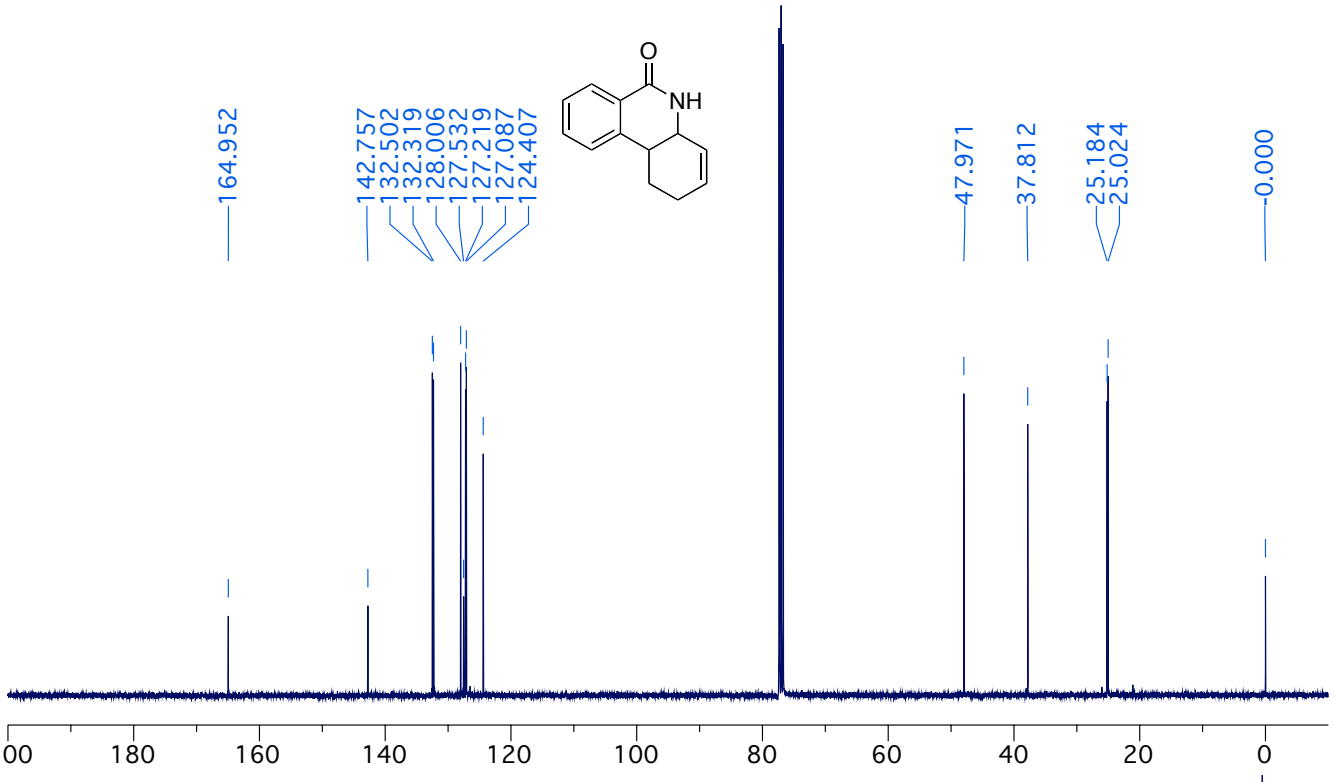
O
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124.407
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140
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20
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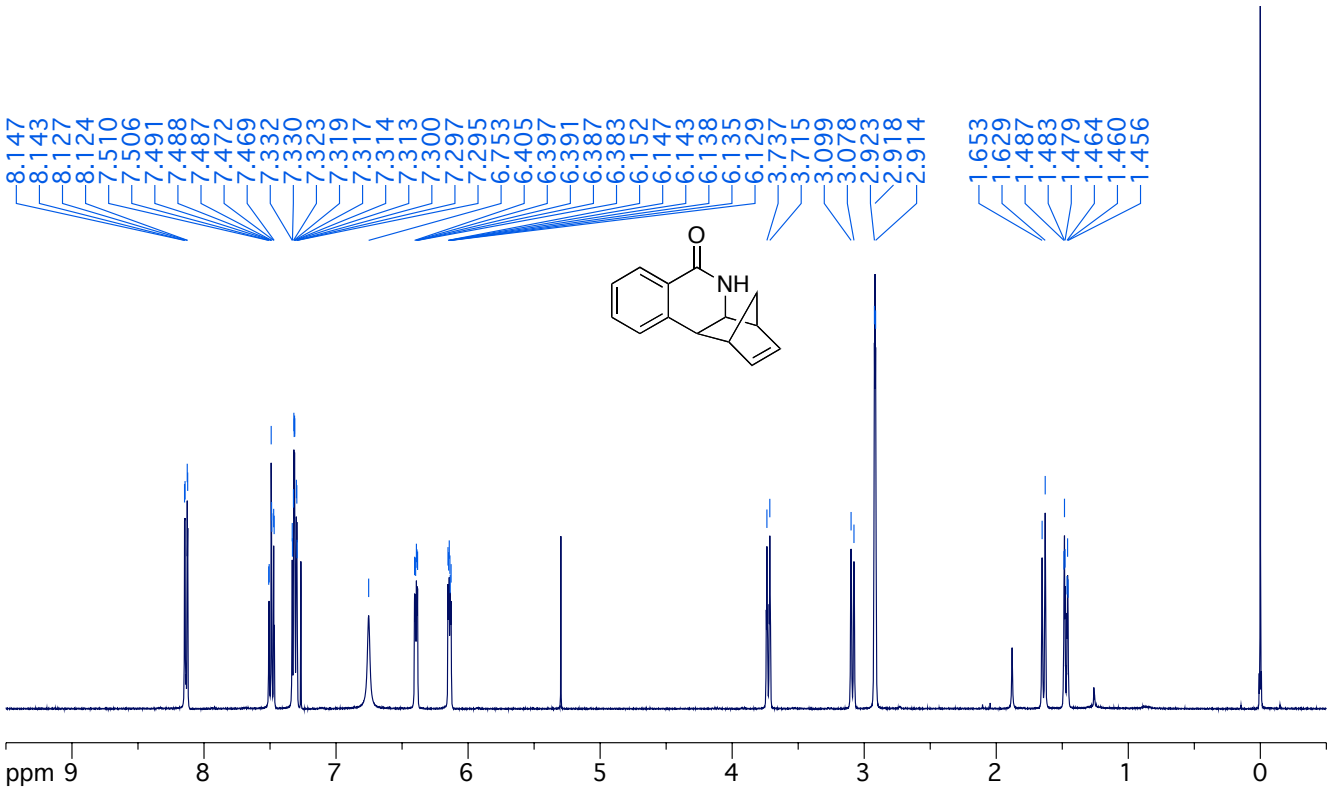
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7.469
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7.323
7.319
7.317
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7.313
7.300
7.297
7.295
6.753
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6.387
6.383
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6.147
6.143
6.138
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6.129
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3.715
3.099
3.078
2.923
2.918
2.914
1.653
1.629
1.487
1.483
1.479
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1.460
1.456
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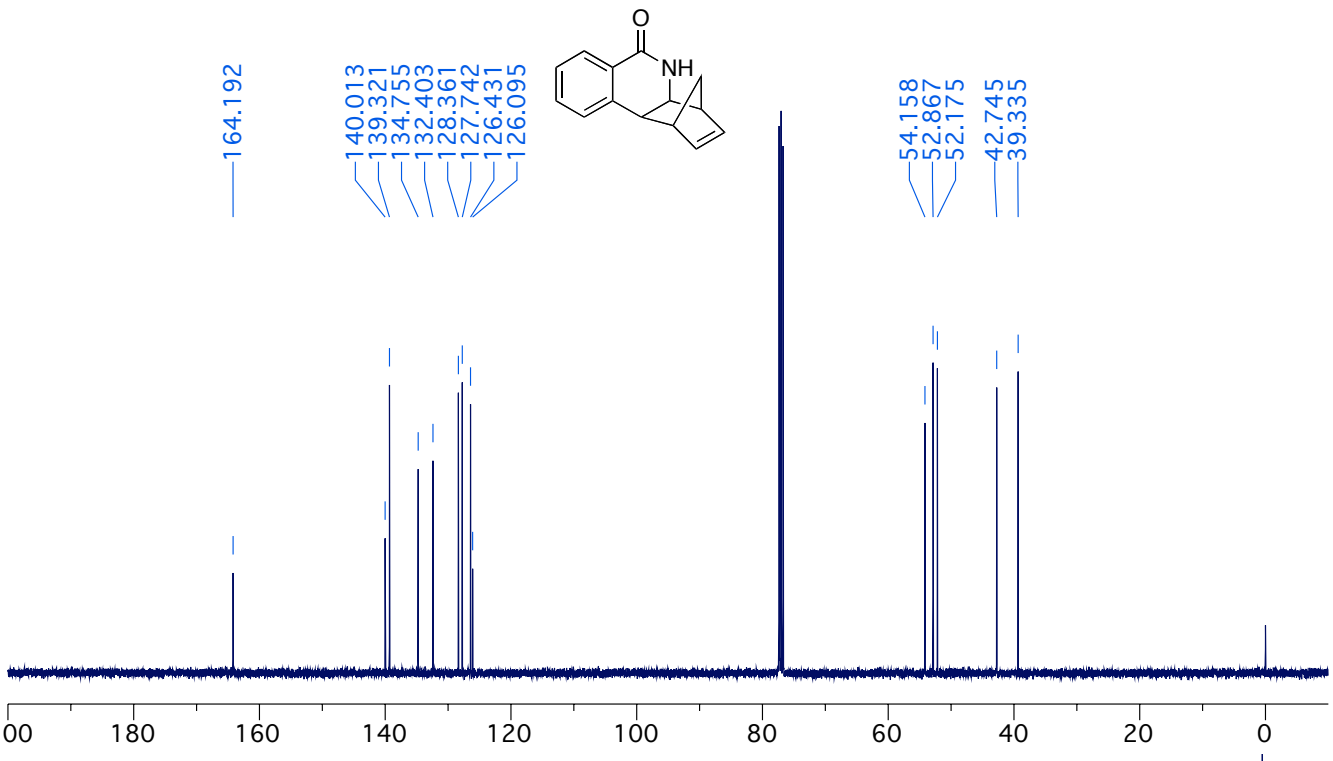
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126.095
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52.175
42.745
39.335
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160
140
120
100
80
60
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20
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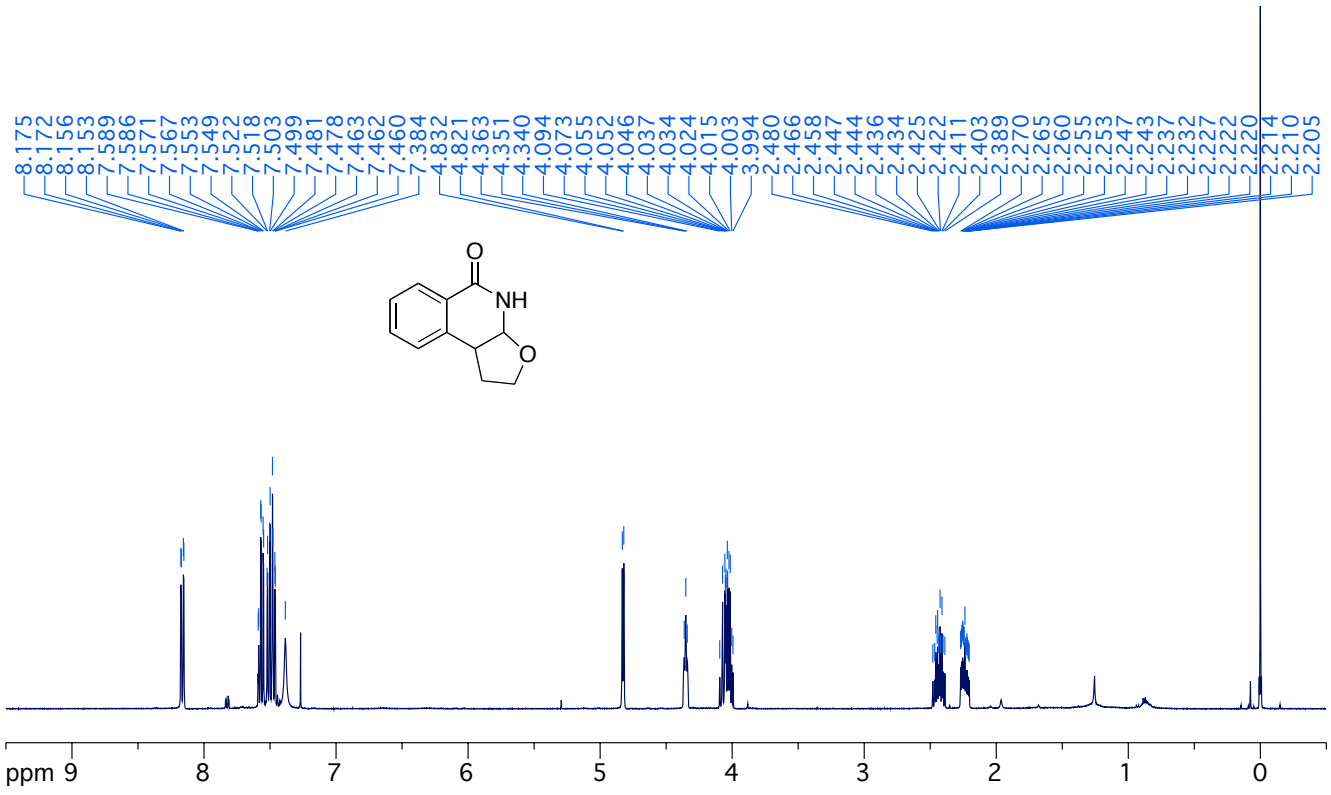
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7.549
7.522
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7.503
7.499
7.481
7.478
7.463
7.462
7.460
7.384
4.832
4.821
4.363
4.351
4.340
4.094
4.073
4.055
4.052
4.046
4.037
4.034
4.024
4.015
4.003
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2.434
2.425
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2.237
2.232
2.227
2.222
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2.205
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NH
O
ppm 9
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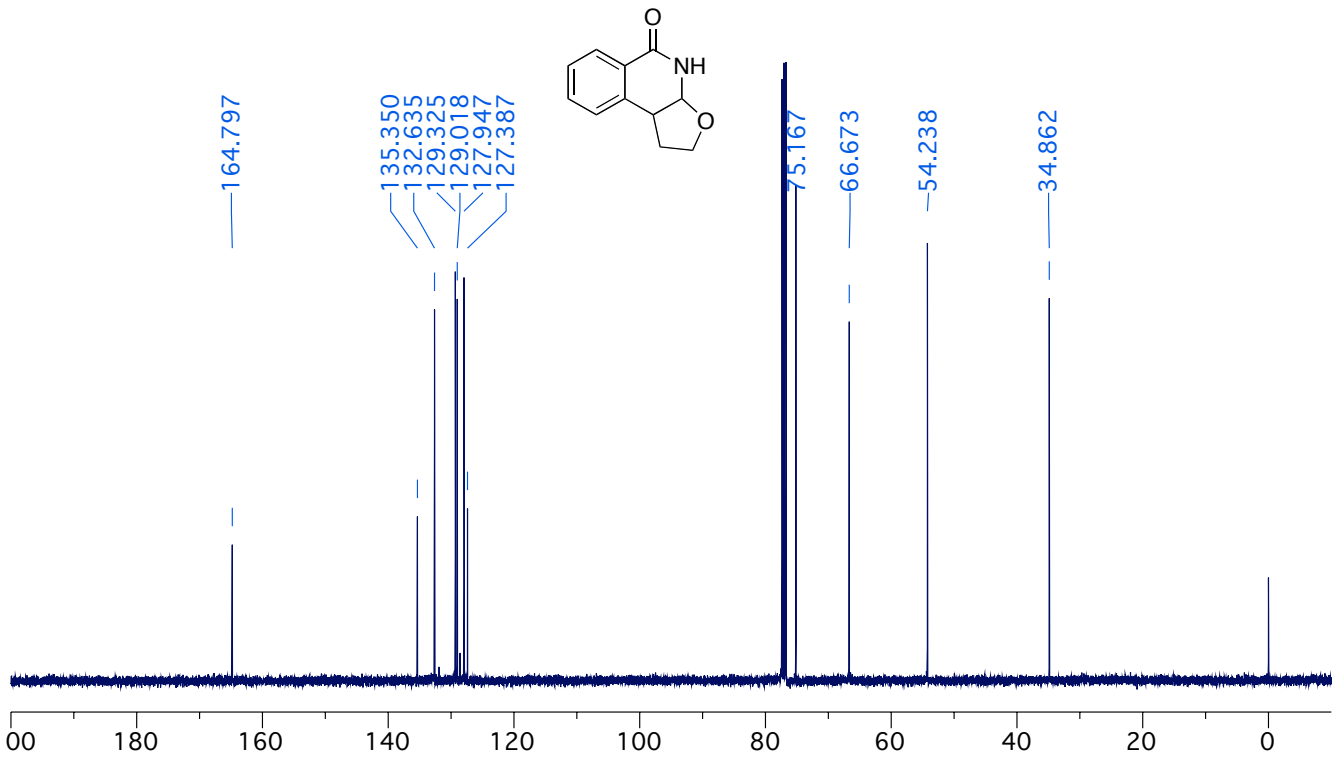
O
NH
O
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54.238
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00
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140
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60
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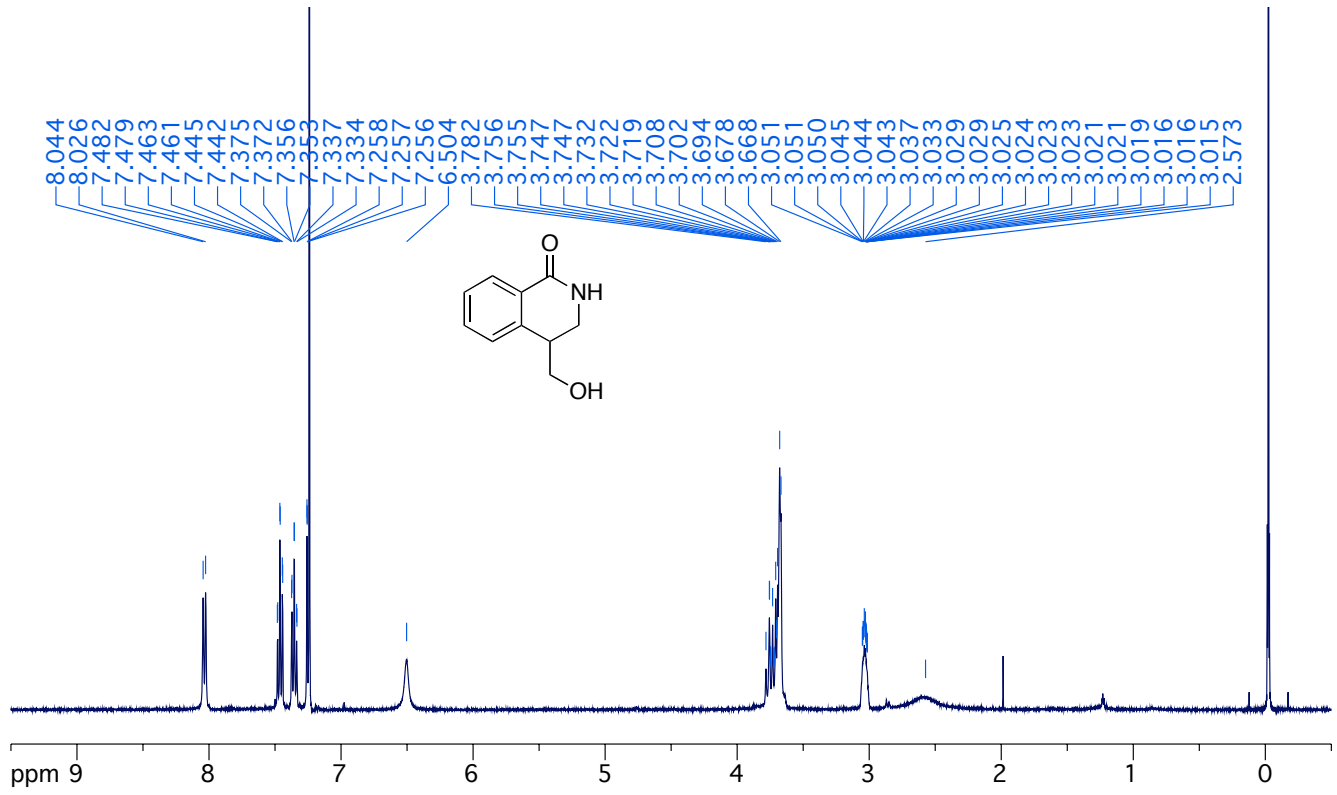
20
0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3.015
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O
NH
OH
ppm 9
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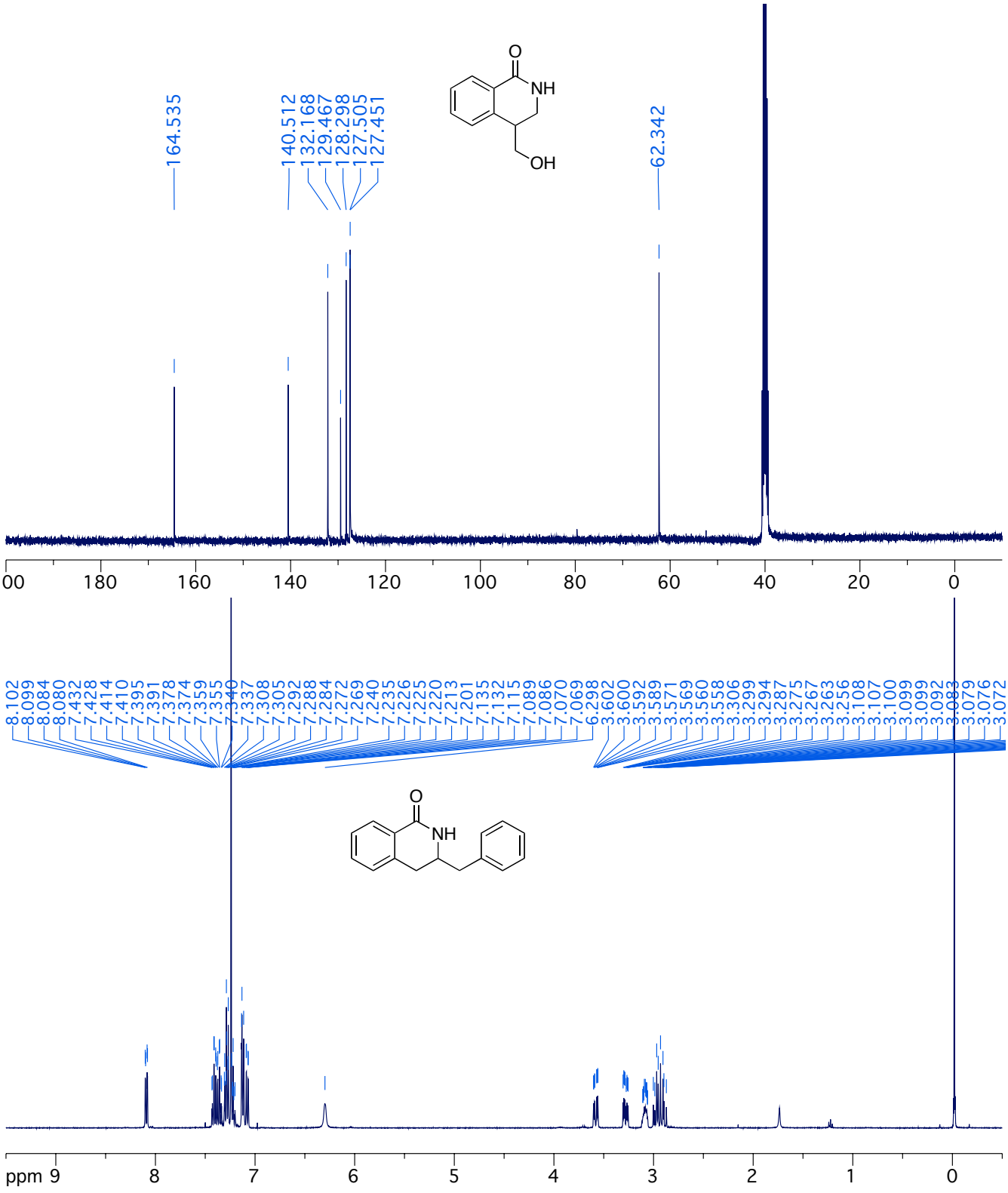
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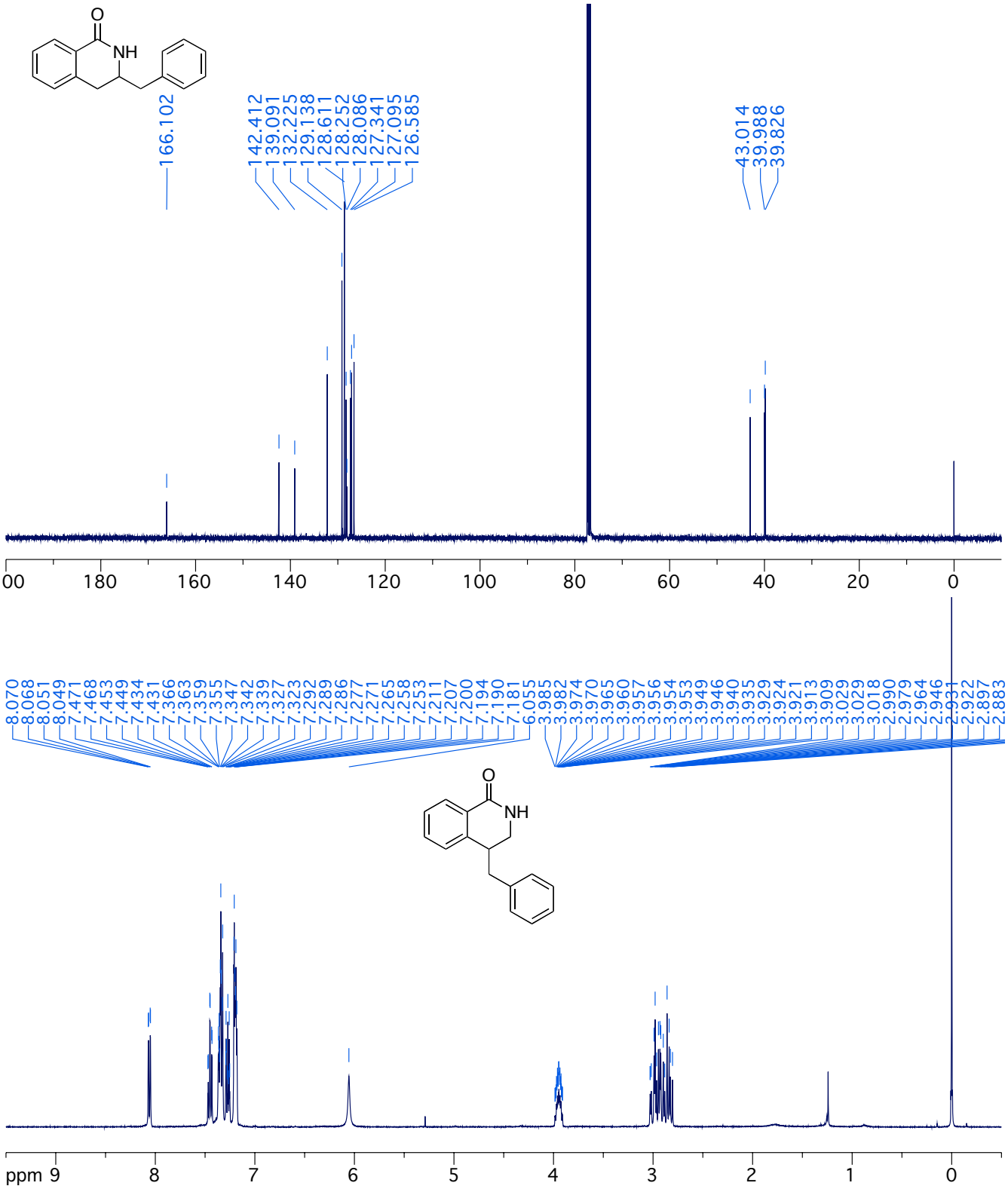
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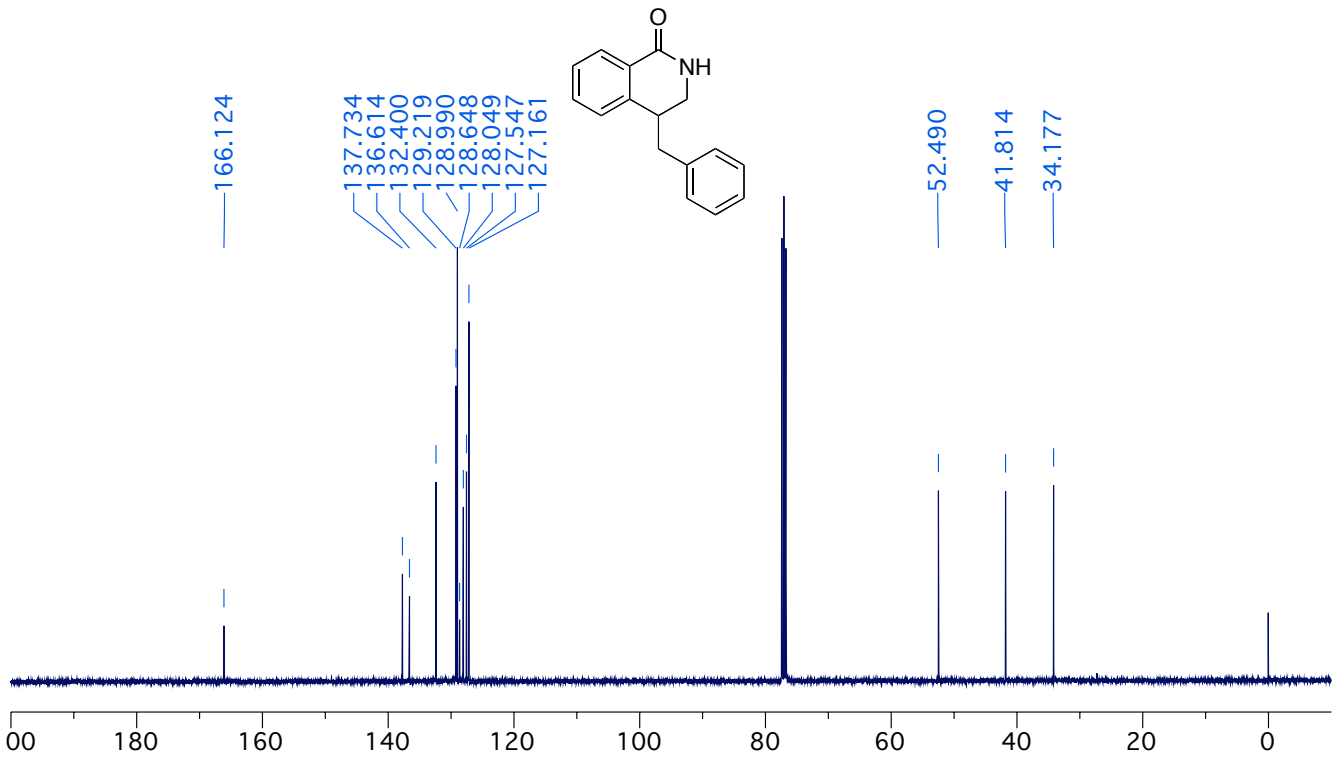
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