Supporting Information

Micellar Catalysis of Suzuki-Miyaura Cross-Couplings with Heteroaromatics in Water

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Contents

Abbreviations

dtbpf: 1,1'-bis(di-*tert*-butylphosphino)-ferrocene; A-^{ta}Phos: 4-(di-tert-butylphosphino)-N,N-dimethylaniline; X-Phos: dicyclohexyl(2',4',6'-triisopropylbiphenyl-2-yl)phosphine; EI: electron ionization; ESI: electrosprayionization; PTS: poly(oxyethanyl) α-tocopheryl sebacate; TPGS: α-tocopheryl polyethylene glycol 1000 succinate.

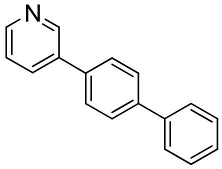
General Information

PTS was obtained from Zymes, LLC, TPGS from Eastman, and Pd(dtbpf)Cl_2 (**3,**CAS# 95408-45-0) and Pd(A-^{ta}Phos)$_2$$Cl_2$ (**2,** CAS# 887919-35-9) from Johnson Matthey. These and all commercially available chemicals were used as supplied, except for Et_3N, which was distilled from CaH_2 prior to use. Water (HPLC grade) was purchased from ACROS and degassed with argon prior to use. For TLC analyses precoated Kieselgel 60 F_{254} plates (Merck, 0.25 mm thick) were used; for column chromatography Silia *Flash*® P60 (SiliCycle, 40-63 μm) was used.

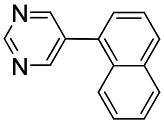
Reactions were monitored using a Hewlett-Packard HP6890 gas chromatograph. ^1H and ^{13}C NMR spectra were obtained using a Varian UNITY INOVA 400 MHz NMR spectrometer. High-resolution mass analyses were obtained using a VG70 double-focusing magnetic sector instrument (VG Analytical) for EI and a PE Sciex QStar Pulsar quadrupole/TOF instrument (API) for ESI. Melting points were measured on a Fisher-Johns Melting Point Apparatus and are uncorrected.

Preparation of 2% w/w PTS/water Solution. A 60 mL serum bottle equipped with a large Teflon-coated stirbar was charged with PTS (1.0 g), degassed on a high vacuum manifold, backflushed with argon, and then fitted with a Teflon-lined septum (crimp top). While under a positive flow of argon, degassed water (49.0 mL) was added via syringe, and the mixture was then stirred for several hours until a homogenous (clear, slightly hazy, colorless) solution was formed. The solution was stored under argon on the bench-top for several weeks without noticeable decomposition. Solutions of other concentrations of PTS and other surfactants (Triton X-100, TPGS) were prepared in an analogous fashion.

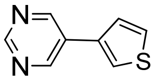
General Procedure for Suzuki-Miyaura Cross-Couplings of Aryl/Heteroaryl Bromides. Pd(dtbpf)Cl_2 (**3,** 6.5 mg, 0.01 mmol), aryl/heteroaryl boronic acid (1.00 mmol) and aryl bromide (0.50 mmol) were added under argon to a 5.0 mL microwave vial equipped with a large stir bar. Under a positive flow of argon, aqueous PTS (2% w/w, 1 mL) and Et_3N (0.21 mL, 1.5 mmol) were each added via syringe while vigorously stirring. The vial was then immediately fitted with an unpierced Teflon-lined septum (crimp top), and stirred for 4-20 h at rt or in an oil bath at 40 ^oC. Reaction progress was monitored by TLC and/or GC. Upon completion the reaction mixture was diluted with brine and extracted with EtOAc. The organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The resulting crude product was purified by column chromatography on silica gel.



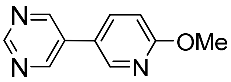
3-(Biphenyl-4-yl)pyridine (Table 1, entry 1). Using the general procedure for aryl/heteroaryl bromides with 3-bromopyridine (48 μL, 0.50 mmol) and biphenyl-4-ylboronic acid (149 mg, 0.75 mmol) the reaction mixture was stirred at rt for 20 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% EtOAc, 84% petroleum ether, 1% Et_3N) to yield the product as a white solid (95 mg, 82%), ^{1}H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.[1]



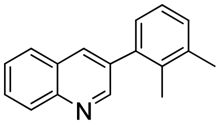
5-(Naphthalene-1-yl)pyrimidine (Table 1, entry 2A). Using the general procedure for aryl/heteroaryl bromides with 5-bromopyrimidine (79.5 mg, 0.50 mmol) and naphthalen-1-ylboronic acid (172 mg, 1.00 mmol) the reaction mixture was stirred at rt for 6 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (5% EtOAc, 94% petroleum ether, 1% Et_3N) to yield the product as a white solid (99 mg, 96%) mp 82-83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.44 (dd, *J* = 7.2, 1.2Hz, 1H), 7.53-7.62 (m, 3H), 7.77 (d, *J* = 8.4Hz, 1H), 7.96-7.99 (m, 2H), 8.92 (s, 2H), 9.32 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 124.7, 125.6, 126.6, 127.3, 127.9, 128.9, 129.6, 131.3, 132.6, 134.0, 134.5, 157.5, 157.8, HREI-MS *m/z* calculated for $C_{14}H_{10}N_2$ $(M)^+$ 206.0844 found 206.0846.



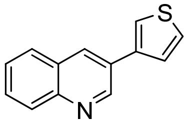
5-(Thiophen-3-yl)pyrimidine (Table 1, entry 2B). Using the general procedure for aryl/heteroaryl bromides with 5-bromopyrimidine (79.5 mg, 0.50 mmol) and thiophen-3-ylboronic acid (128 mg, 1.00 mmol) the reaction mixture was stirred at rt for 6 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (20% EtOAc, 79% petroleum ether, 1% Et_3N) to yield the product as an off-white solid (81 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.[2]



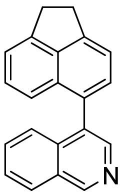
5-(6-Methoxypyridin-3-yl)pyrimidine (Table 1, entry 2C). Using the general procedure for aryl/heteroaryl bromides with 5-bromopyrimidine (79.5 mg, 0.50 mmol) and 6-methoxypyridin-3-ylboronic acid (153 mg, 1.00 mmol) the reaction mixture was stirred at rt for 16 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% EtOAc, 84% petroleum ether, 1% Et_3N) to yield the product as a white solid (89 mg, 95%), mp 163-164 °C, ^1H NMR (400 MHz, $CDCl_3$) 4.01 (s, 3H), 6.92 (dd, *J* = 8.4, 0.8Hz, 1H), 7.80 (dd, *J* = 8.8, 2.8Hz, 1H), 8.41 (dd, 2.8, 0.8Hz, 1H), 8.93 (s, 2H), 9.23 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 53.6, 111.6, 123.1, 131.4, 136.8, 145.0, 154.2, 157.4, 164.5, HREI-MS *m/z* calculated for $C_{10}H_9N_3O$ $(M)^+$ 187.0746 found 187.0737.



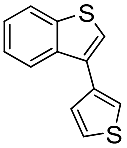
3-(2,3-Dimethylphenyl)quinoline (Table 1, entry 3A) Using the general procedure for aryl/heteroaryl bromides with 3-bromoquinoline (68 μL, 0.50 mmol) and 2,3-dimethylphenylboronic acid (150 mg, 1.00 mmol) the reaction mixture was stirred at rt for 10 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (5% EtOAc, 94% petroleum ether, 1% Et_3N) to yield the product as a clear liquid (100 mg, 86%). ^1H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.[3]



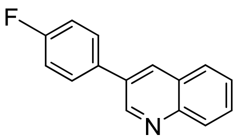
3-(Thiophen-3-yl)quinoline (Table 1, entry 3B). Using the general procedure for aryl/heteroaryl bromides with 3-bromoquinoline (68 μL, 0.50 mmol) and thiophen-3-ylboronic acid (128 mg, 1.00 mmol) the reaction mixture was stirred at rt for 7 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (10% EtOAc, 89% petroleum ether, 1% Et_3N) to yield the product as an off-white solid (102 mg, 97%). ^1H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.



4-(1,2-Dihydroacenaphthylen-5-yl)isoquinoline (Table 1, entry 4). Using the general procedure for aryl/heteroaryl bromides with 4-bromoisoquinoline (104 mg, 0.50 mmol) and 1,2-dihydroacenaphthylen-5-ylboronic acid (148 mg, 0.75 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 4 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (6% EtOAc, 93% petroleum ether, 1% Et_3N) to yield the product as an off-white solid (140 mg, 99%), mp 104-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 3.52 (s, 4H), 7.16-7.12 (m, 1H), 7.36-7.33 (m, 2H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 6.8 Hz, 1H), 7.56-7.55 (m, 2 H), 7.65-7.59 (m, 1H), 8.09 (dt, *J* = 8, 1.5 Hz, 1 H), 8.59 (s, 1H), 9.35; (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 30.1, 30.4, 118.9, 119.5, 120.8, 125.3, 127.0, 127.6, 128.1, 128.2, 129.7, 129.9, 130.2, 130.9, 131.4, 135.3, 139.2, 143.7, 146.1, 146.5, 152.0 HREI-MS *m/z* calculated for $C_{21}H_{15}N$ $(M)^+$ 281.1204, found 281.1198.

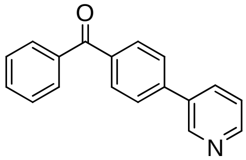


3-(Thiophen-3-yl)benzo[*b*]thiophene (Table 1, entry 5). Using the general procedure for aryl/heteroaryl bromides with 3-bromobenzo[*b*]thiophene (65 μL, 0.50 mmol) and thiophen-3-ylboronic acid (128 mg, 1.00 mmol) the reaction mixture was stirred at rt for 16 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (100% petroleum ether) to yield the product as a slightly yellow oil (105 mg, 97%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.51-7.35 (m, 6H), 7.93-7.90 (m, 1H), 8.01-7.98 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 121.9, 122.81, 122.85, 123.1, 124.3, 124.4, 125.8, 127.9, 132.6, 136.2, 137.7, 140.4, HREI-MS *m/z* calculated for $C_{12}H_8S_2$ (M^+) 216.0067, found 216.0063.

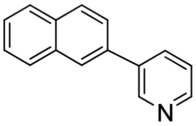


3-(4-Fluorophenyl)quinoline (**8,** Table 1, entry 6). Using the general procedure for aryl/heteroaryl bromides with 1-bromo-4-fluorobenzene (55 μL, 0.50 mmol) and quinolin-3-ylboronic acid (172 mg, 1.00

mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 9 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (2.5% EtOAc, 96.5% petroleum ether, 1% Et_3N) to yield the product as a white solid (106 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.[4]

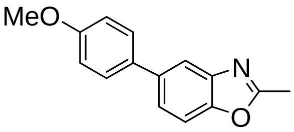


Phenyl(4-(pyridin-3-yl)phenyl)methanone (**11,** Table 1, entry 7). Using the general procedure for aryl/heteroaryl bromides with (4-bromophenyl)(phenyl)methanone (130.5 mg, 0.50 mmol) and quinolin-3-ylboronic acid (123 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 6 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (25% EtOAc, 74% petroleum ether, 1% Et_3N) to yield the product as an off-white solid (118 mg, 91%), mp 77-79 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.43 (dd, *J* = 8, 3.2 Hz, 1H), 7.54-7.51 (m, 2H), 7.65-7.61 (m, 1H), 7.73-7.71 (m, 2H) 7.86-7.84 (m, 2H), 7.97-7.93 (m, 3H), 8.67 (d, *J* = 3.6 Hz, 1H), 8.93 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 123.9, 127.2, 128.5, 130.2, 131.0, 132.8, 134.7, 135.6, 147.1, 137.6, 141.9, 148.5, 149.4, HREI-MS *m/z* calculated for $C_{18}H_{13}NO$ (M^+) 259.0997, found 259.1001.



3-(Naphthalene-2-yl)pyridine (**13,** Table 1, entry 8). Using the general procedure for aryl/heteroaryl bromides with 2-bromonaphthalene (103.5 mg, 0.50 mmol) and quinolin-3-ylboronic acid (123 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 12 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (10% EtOAc, 89% petroleum ether, 1% Et_3N) to yield the product as an off-white solid (92 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.[5]

General Procedure for Suzuki-Miyaura Cross-Couplings of Aryl/Heteroaryl Chlorides. Pd(A-^{ta}Phos)$_2$Cl$_2$ (**2**, 7 mg, 0.01 mmol), aryl/heteroaryl boronic acid (1.00 mmol) and aryl chloride (0.50 mmol) were added under argon to a 5.0 mL microwave vial equipped with a large stir bar. Under a positive flow of argon, aqueous PTS (2% w/w, 1 mL) and Et_3N (0.21 mL, 1.5 mmol) were each added via syringe while vigorously stirring. The vial was then immediately fiited with an unpierced Teflon-lined septum (crimp top), and stirred for 19-24 h at rt or in an oil bath at 40 °C. Reaction progress was monitored by TLC and/or GC. Upon completion the reaction mixture was diluted with brine and extracted with EtOAc. The organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The resulting crude product was purified by column chromatography on silica gel.

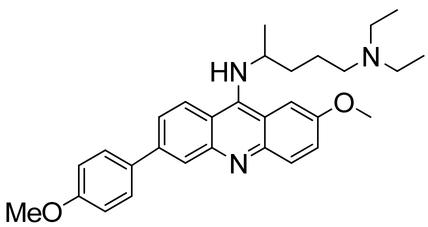


5-(4-Methoxyphenyl)-2-methylbenzo[*d*]oxazole (**14,** Table 2, entry A, 2% PTS). Using the general procedure for aryl/heteroaryl chlorides 5-chloro-2-methylbenzo[*d*]oxazole (84 mg, 0.50 mmol) and 4-methoxyphenylboronic acid (152 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% EtOAc/85% petroleum ether) to yield the product as a slightly yellow solid (113 mg, 95%), mp 68-69 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.67 (s, 3H), 3.87 (s, 3H), 7.01 (d, 8.4 Hz), 7.47-7.56 (m, 4H), 7.80 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 14.4, 55.1, 109.9, 114.1, 117.2, 123.4, 128.2, 133.4, 137.4, 131.9, 150.0, 158.9, 164.2, HREI-MS *m/z* calculated for $C_{15}H_{13}NO_2$ (M^+) 239.0946, found 239.0939.

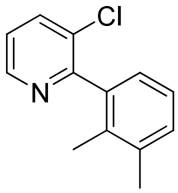
5-(4-Methoxyphenyl)-2-methylbenzo[*d*]oxazole (**14,** Table 2, entry A, 1% PTS). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 1% w/w aqueous PTS as solvent 5-chloro-2-methylbenzo[*d*]oxazole (84 mg, 0.50 mmol) and 4-methoxyphenylboronic acid (152 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% EtOAc/ 85% petroleum ether) to yield the product as a slightly yellow solid (91 mg, 76%), ^{1}H NMR (400 MHz, $CDCl_3$) matches data reported above.

5-(4-Methoxyphenyl)-2-methylbenzo[*d*]oxazole (**14,** Table 2, entry A, 2% TPGS). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 2% w/w aqueous TPGS as solvent 5-chloro-2-methylbenzo[*d*]oxazole (84 mg, 0.50 mmol) and 4-methoxyphenylboronic acid (152 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% EtOAc/ 85% petroleum ether) to yield the product as a slightly yellow solid (97 mg, 80%), ^{1}H NMR (400 MHz, $CDCl_3$) matches data reported above.

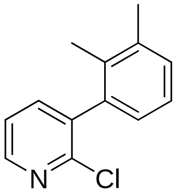
5-(4-Methoxyphenyl)-2-methylbenzo[*d*]oxazole (**14,** Table 2, entry A, 2% Triton X-100). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 2% w/w aqueous Triton X-100 as solvent 5-chloro-2-methylbenzo[*d*]oxazole (84 mg, 0.50 mmol) and 4-methoxyphenylboronic acid (152 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% EtOAc/ 85% petroleum ether) to yield the product as a slightly yellow solid (91 mg, 76%), ^{1}H NMR (400 MHz, $CDCl_3$) matches data reported above.



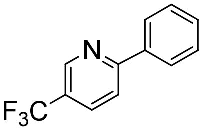
***N*^{1},*N*^{1}-diethyl-*N*^{4}-(2-methoxy-6-(4-methoxyphenyl)acridin-9-yl)pentane-1,4-diamine** (**15,** Table 2 entry B). Pd(A-^{ta}Phos)$_2$Cl$_2$ (**2**, 3 mg, 0.004 mmol), 4-methoxyphenylboronic acid (1.00 mmol) and *N*^{4}-(6-chloro-2-methoxyacridin-9-yl)-*N*^{1},*N*^{1}-diethylpentane-1,4-diamine (quinacrine, LKT Laboratories, Inc.) dihydrochloride dihydrate (102 mg, 0.2 mmol) were added under argon to a 5.0 mL microwave vial equipped with a large stir bar. Under a positive flow of argon, aqueous PTS (2% w/w, 1 mL) and Et_3N (0.14 mL, 1.0 mmol) were each added via syringe while vigorously stirring. The vial was then immediately fiited with an unpierced Teflon-lined septum (crimp top), and stirred for 24 h in an oil bath set at 40 °C. Upon completion the reaction mixture was diluted with brine and extracted with EtOAc. The organic extracts were washed with saturated aqueous $NaHCO_3$, dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The resulting crude product was purified by column chromatography on silica gel (60% EtOAc, 38% petroleum ether, 2% Et_3N) to yield a bright yellow, very viscous oily residue (82 mg, 87%); 0.97 (t, *J* = 7.2Hz, 6H), 1.31 (d, *J* = 6.3Hz, 3H), 1.16-1.75 (m, 4H), 2.39-2.42 (m, 2H), 2.48 (q, *J* = 7.2 Hz, 4H), 3.90 (s, 3H), 3.99 (s, 3H), 4.06-4.10 (m, 1H), 4.40-4.44 (m, 1H), 7.04-7.07 (m, *J* = 8.8, 2.1Hz, 2H), 7.28 (d *J* = 2.8Hz, 1H), 7.43 (dd, *J* = 8, 2.8Hz, 1H), 7.69-7.79 (m, 3H), 8.06 (d, *J* = 9.2Hz, 1H), 8.12 (d, *J* = 9.2 Hz, 1H) 8.30 (d, *J* = 2 Hz, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 11.4, 22.2, 23.9, 36.9, 46.7, 52.7, 55.2, 55.4, 55.7, 99.4, 114.3, 117.9, 119.1, 122.6, 123.7, 124.1, 126.0, 128.2, 131.4, 132.4, 140.6, 146.7, 148.3, 148.8, 155.7, 159.5, HRESI-MS *m/z* calculated for $C_{15}H_{13}NO_2$ $(M+H)^+$ 239.0946, found 239.0939.



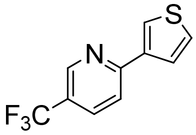
3-Chloro-2-(2,3-dimethylphenyl)pyridine (Table 2, entry C). Using the general procedure for aryl/heteroaryl chlorides 2,3-dichloropyridine (74 mg, 0.50 mmol) and 2,3-dimethylphenylboronic acid (79 mg, 0.52 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 20 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (10% EtOAc/90% petroleum ether) to yield a clear, colorless liquid (67 mg, 62%) ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.06 (s, 3H), 2.36 (s, 3H), 7.11-7.13 (m, 1H), 7.20-7.29 (m, 3H), 7.82 (dd, *J* = 8, 1.6Hz, 1H), 8.60-8.61 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 16.2, 20.3, 123.1, 125.3, 126.5, 130.1, 134.3, 137.00, 137.03, 138.4, 147.2, 158.6, HREI-MS *m/z* calculated for $C_{13}H_{12}ClN$ (M^+), 217.0658 found 217.0666.



2-chloro-3-(2,3-dimethylphenyl)pyridine (Table 2, entry C). Also isolated following chromatography of the previous reaction mixture as a clear, colorless liquid (20 mg, 18%); ^{1}H NMR (400 MHz, $CDCl_3$) 2.04 (s, 3H), 2.36 (s, 3H), 7.00 (d, *J* = 7.2Hz, 1H) 7.19-7.34 (m, 3H), 7.58-7.61 (m, 1H), 8.42-8.44 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) 16.8, 20.7, 122.5, 125.6, 127.3, 130.3, 134.9, 137.4, 137.6, 137.8, 140.0, 148.7, 150.9. HREI-MS *m/z* calculated for $C_{13}H_{12}ClN$ (M^+), 217.0658 found 217.0662.

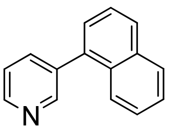


2-Phenyl-5-(trifluoromethyl)pyridine (**16,** Table 2, entry D). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 1% w/w aqueous PTS as solvent 2-chloro-5-(trifluoromethyl)pyridine (90.5 mg, 0.50 mmol) and phenylboronic acid (122 mg, 1.00 mmol) the reaction mixture was stirred at rt for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (15% Dichloromethane/ 84% petroleum ether, 1% Et_3N) to yield the product as a white solid (105 mg, 94%). ^{1}H NMR (400 MHz, CDCl$_3$) matched spectral data previously reported.[6]



2-(Thiophen-3-yl)-5-(trifluoromethyl)pyridine (**17**, Table 2, entry E, from boronic acid). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 1% w/w aqueous PTS as solvent 2-chloro-5-(trifluoromethyl)pyridine (90.5 mg, 0.50 mmol) and thiophen-3-ylboronic acid (128 mg, 1.00 mmol) the reaction mixture was stirred at rt for 19 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (4% dichloromethane/95% petroleum ether, 1% Et$_3$N) to yield the product as a white solid (113 mg, 99%), mp 86-87; ^{1}H NMR (400 MHz, CDCl$_3$) δ (ppm) 7.45 (dd, *J* = 5.2, 3.0Hz, 1H) 7.705 (dd, *J* = 7.7, 1.2Hz, 1H), 7.73 (d, 8.0 Hz), 7.93-7.96 (m, 1H), 8.035 (dd, *J* = 3.0, 1.2Hz, 1H),8.875-8.880 (m, 1H), ^{13}C NMR (100 MHz, CDCl$_3$) δ (ppm) 119.5, 123.7 (q, *J* = 271Hz), 124.2 (q, *J* = 33Hz), 125.4, 126.1, 126.8, 133.8 (q, *J* = 4 Hz), 140.8, 146.5 (q, *J* = 4 Hz), 156.4, HREI-MS *m/z* calculated for $C_{15}H_{13}NO_2$ (M$^+$) 229.0173, found 229.0163.

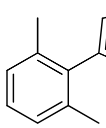
2-(Thiophen-3-yl)-5-(trifluoromethyl)pyridine (**17**, Table 2, entry E from trifuloroborate). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 1% w/w aqueous PTS as solvent 2-chloro-5-(trifluoromethyl)pyridine (90.5 mg, 0.50 mmol) and Potassium (3-thienyl)trifluoroborate, prepared from thiophen-3-ylboronic acid by the literature method,[7] (190 mg, 1.00 mmol) the reaction mixture was stirred at rt for 19 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (4% dichloromethane/95% petroleum ether, 1% Et$_3$N) to yield the product as a white solid (89 mg, 78%), ^{1}H NMR (400 MHz, CDCl$_3$) matches data reported above.



3-(Naphthalen-1-yl)pyridine (**18,** Table 2, entry F, 2% PTS). Using the general procedure for aryl/heteroaryl chlorides 3-chloro-pyridine (48 μL, 0.50 mmol) and naphthalen-1-ylboronic acid (172 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (5% EtOAc/94% petroleum ether, 1% Et$_3$N) to yield the product as a clear slightly yellow liquid (99 mg, 97%); ^{1}H NMR (400 MHz, CDCl$_3$). ^{1}H NMR (400 MHz, CDCl$_3$) matched spectral data previously reported.[8]

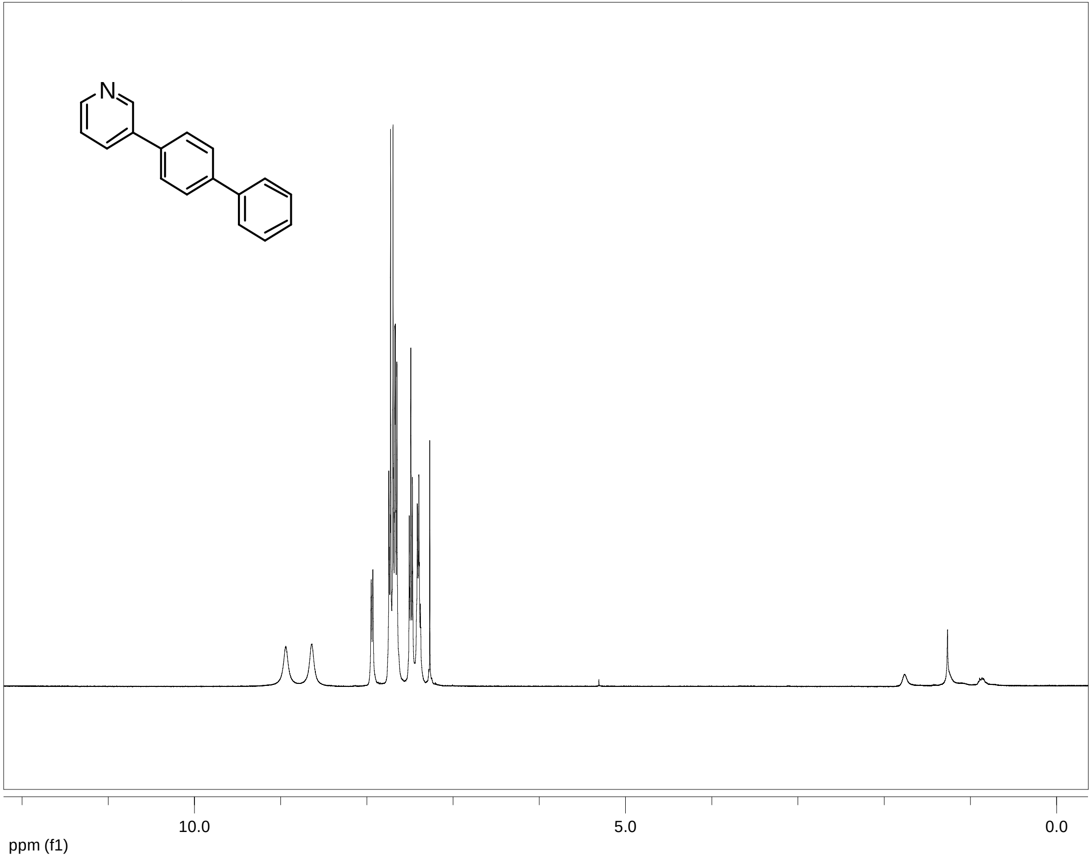
3-(Naphthalen-1-yl)pyridine (**18**, Table 2, entry F, 2% TPGS). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 2% w/w aqueous TPGS as solvent 3-chloro-pyridine (48 μL, 0.50 mmol) and naphthalen-1-ylboronic acid (172 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (5% EtOAc/94% petroleum ether, 1% Et_3N) to yield the product as a clear faintly yellow liquid (85 mg, 83%); ^1H NMR (400 MHz, $CDCl_3$) matches data reported above.

3-(Naphthalen-1-yl)pyridine (**18**,Table 2, entry F, 2% Triton X-100). Using the general procedure for aryl/heteroaryl chlorides with 1 mL of 2% w/w aqueous Triton X-100 as solvent 3-chloro-pyridine (48 μL, 0.50 mmol) and naphthalen-1-ylboronic acid (172 mg, 1.00 mmol) the reaction mixture was stirred in an oil bath set at 40 °C for 24 h. Following the standard workup, the crude product was purified by column chromatography on silica gel (5% EtOAc/94% petroleum ether, 1% Et_3N) to yield the product as a clear faintly yellow liquid (90 mg, 88%); ^1H NMR (400 MHz, $CDCl_3$) matches data reported above.



3-(2,6-dimethylphenyl)thiophene (**20**, Scheme 2). $Pd(OAc)_2$ (3.3 mg, 0.015 mmol), X-Phos (4) (14 mg, 0.03 mmol), and thiophen-3-ylboronic acid (1.5 mmol) were added under argon to a 5.0 mL microwave vial equipped with a large stir bar. Under a positive flow of argon, aqueous PTS (2% w/w, 1.5 mL) and Et_3N (0.33 mL, 2.25 mmol) and 2-chloro-1,3-dimethylbenzene (100 μL, 0.75 mmol) were each added via syringe while vigorously stirring. The vial was then immediately fitted with an unpierced Teflon-lined septum (crimp top), and stirred for 10 h in an oil bath at 38 °C. Upon completion the reaction mixture was diluted with brine and extracted with ethyl A\acetate. The organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated by rotary evaporation. The resulting crude product was purified by column chromatography on silica gel using hexanes to yield the product as a clear, colorless oil that eventually became a clear, colorless solid after several hours on a high vacuum manifold (120 mg, 90%). ^1H NMR (400 MHz, $CDCl_3$) matched spectral data previously reported.[9]

Table 1; Entry 1



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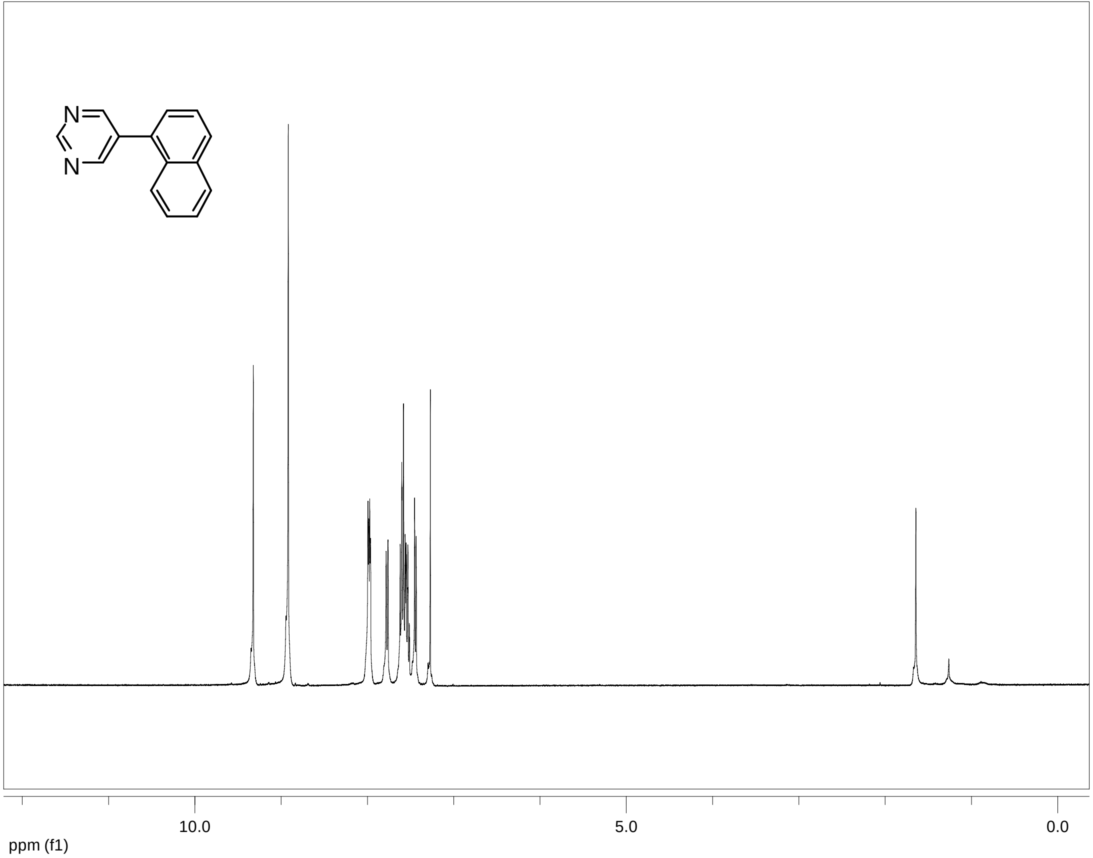

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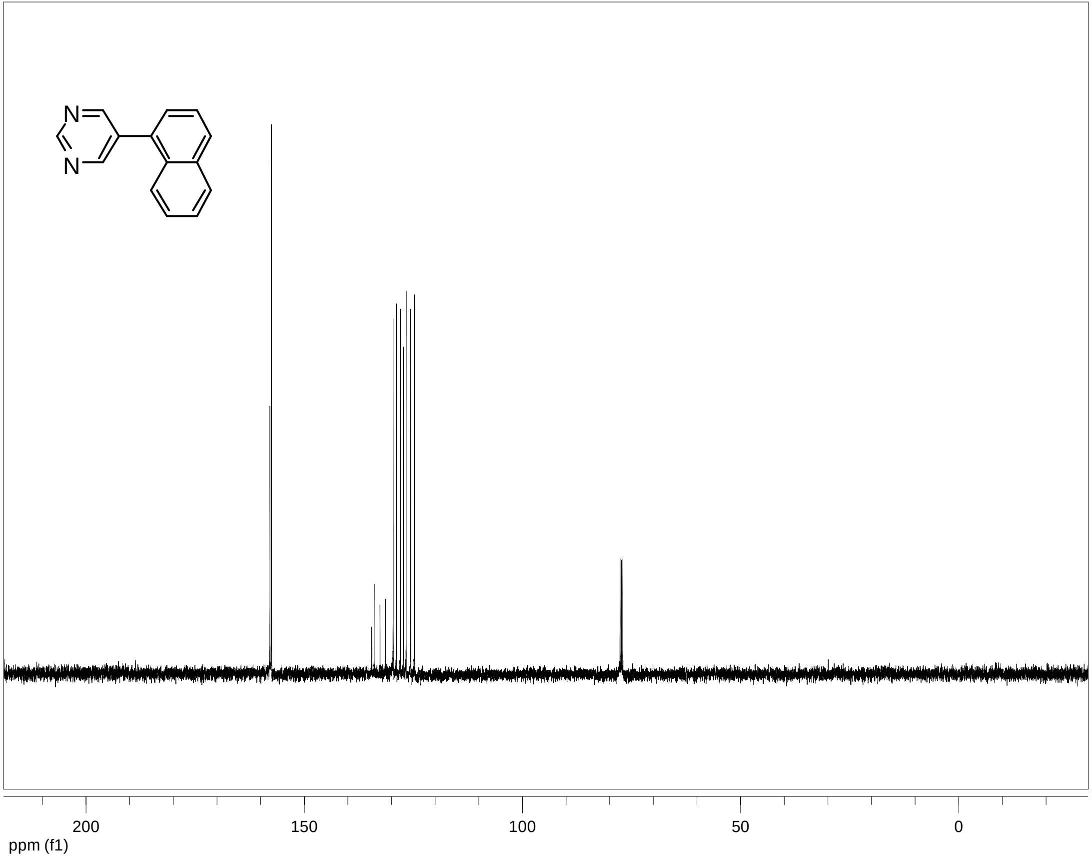

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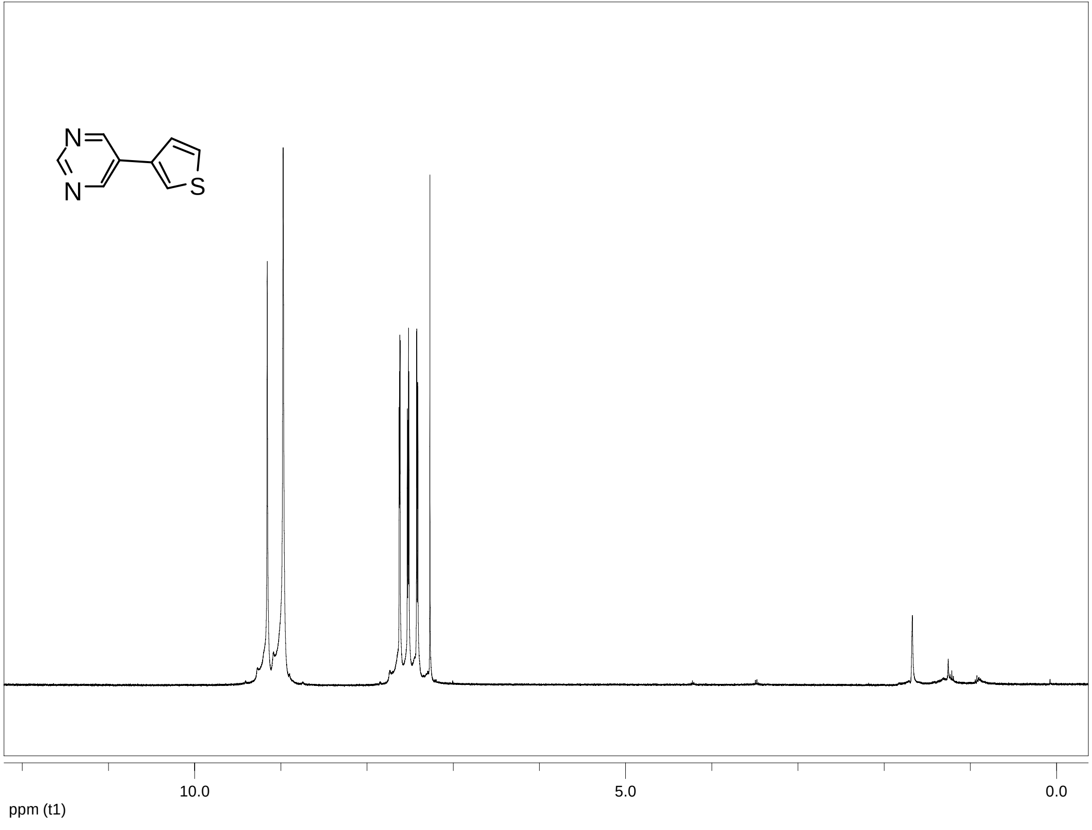

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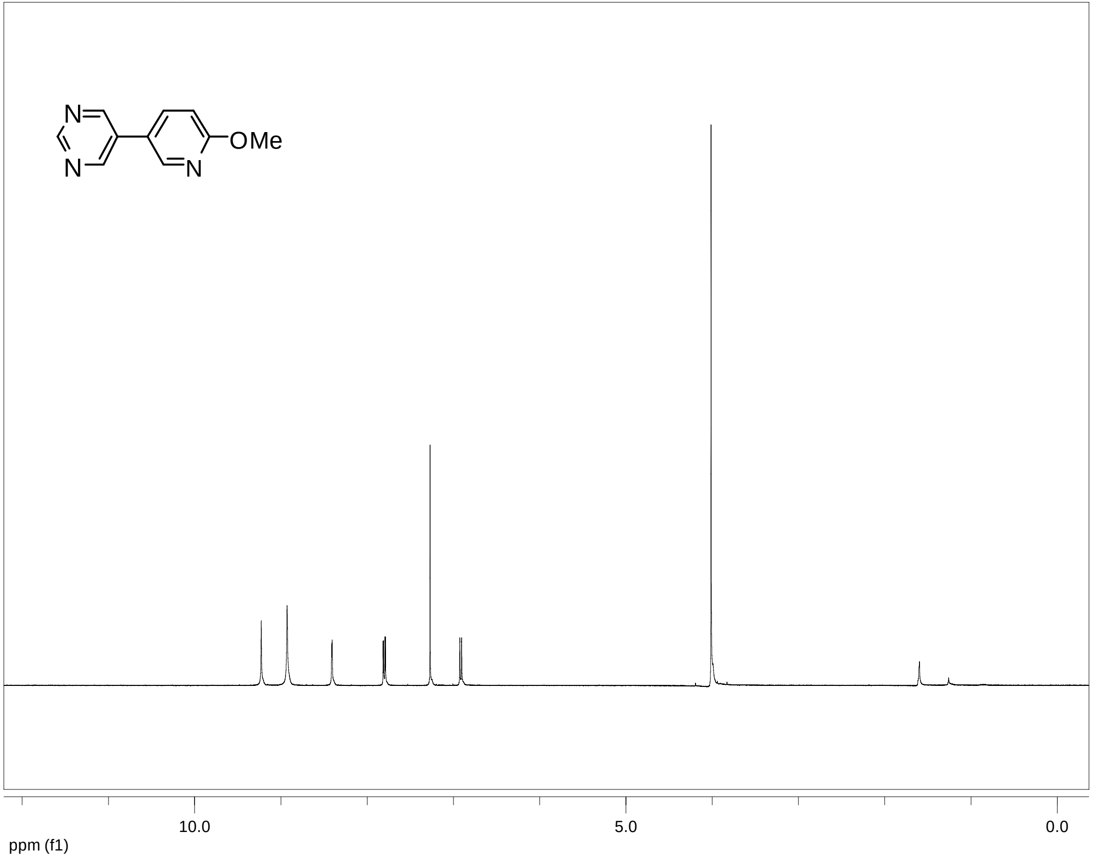

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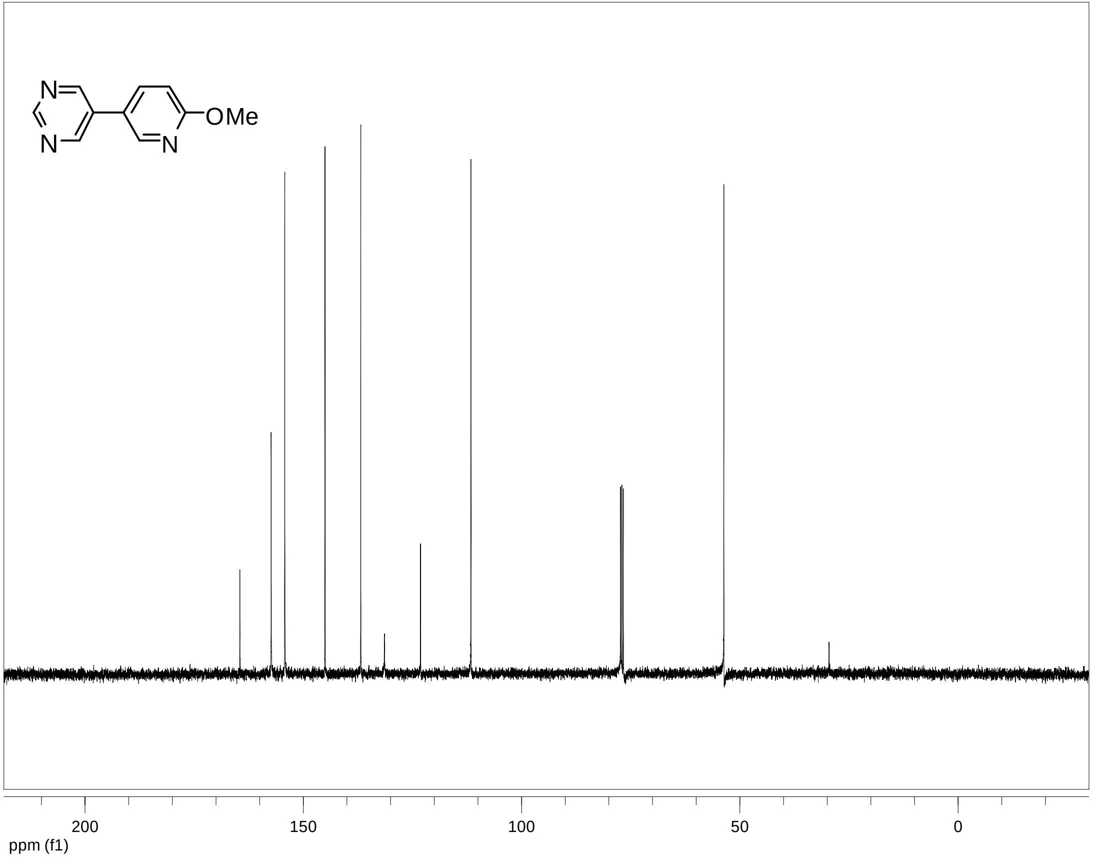

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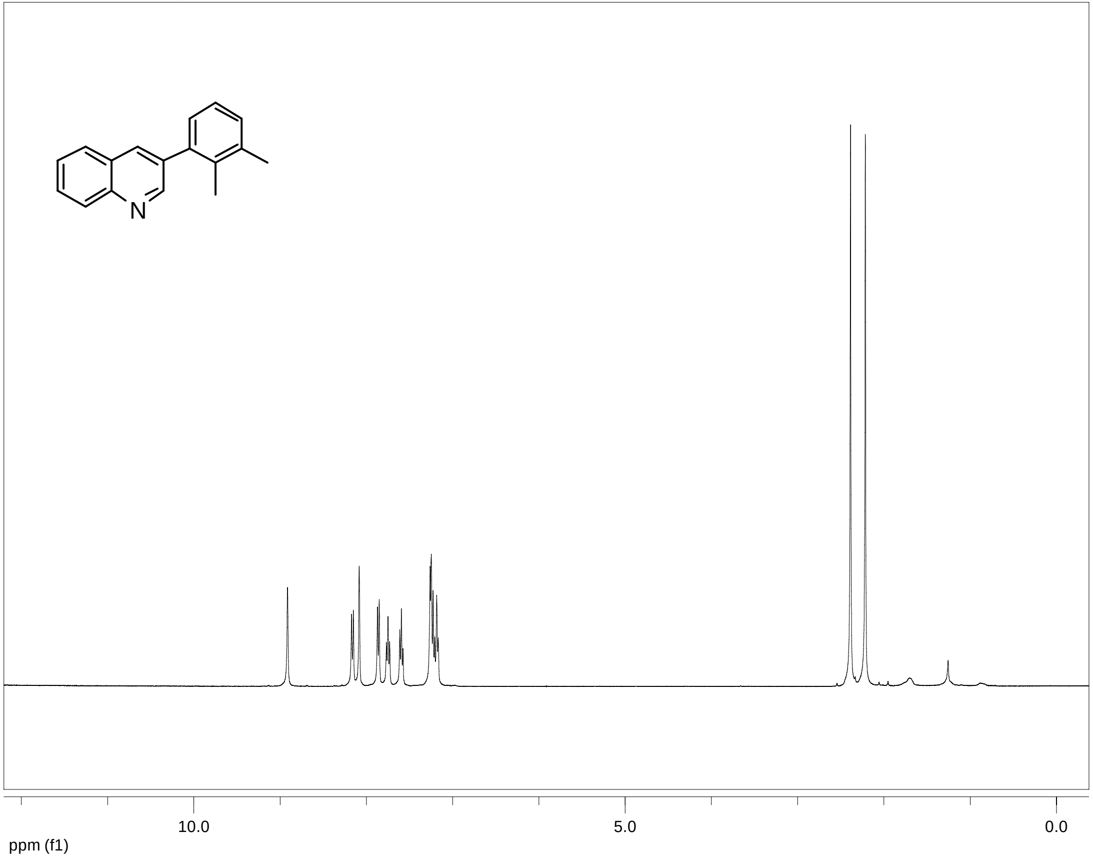

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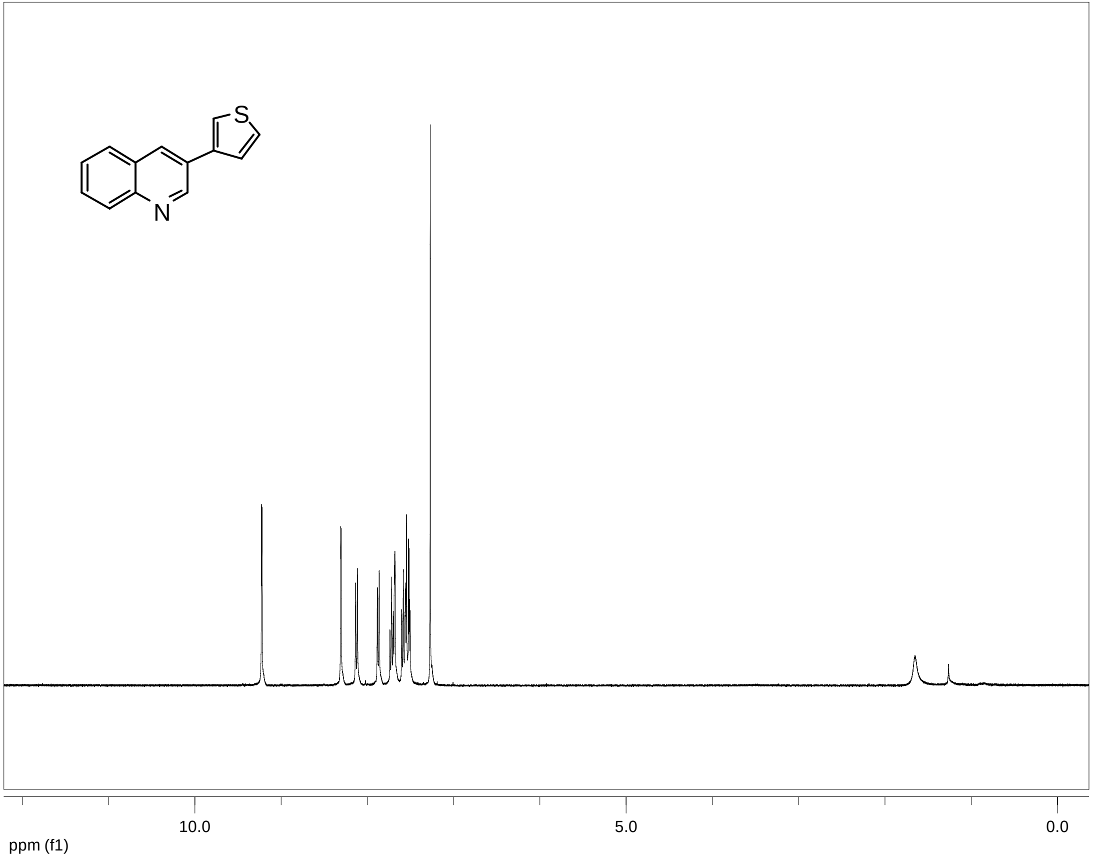

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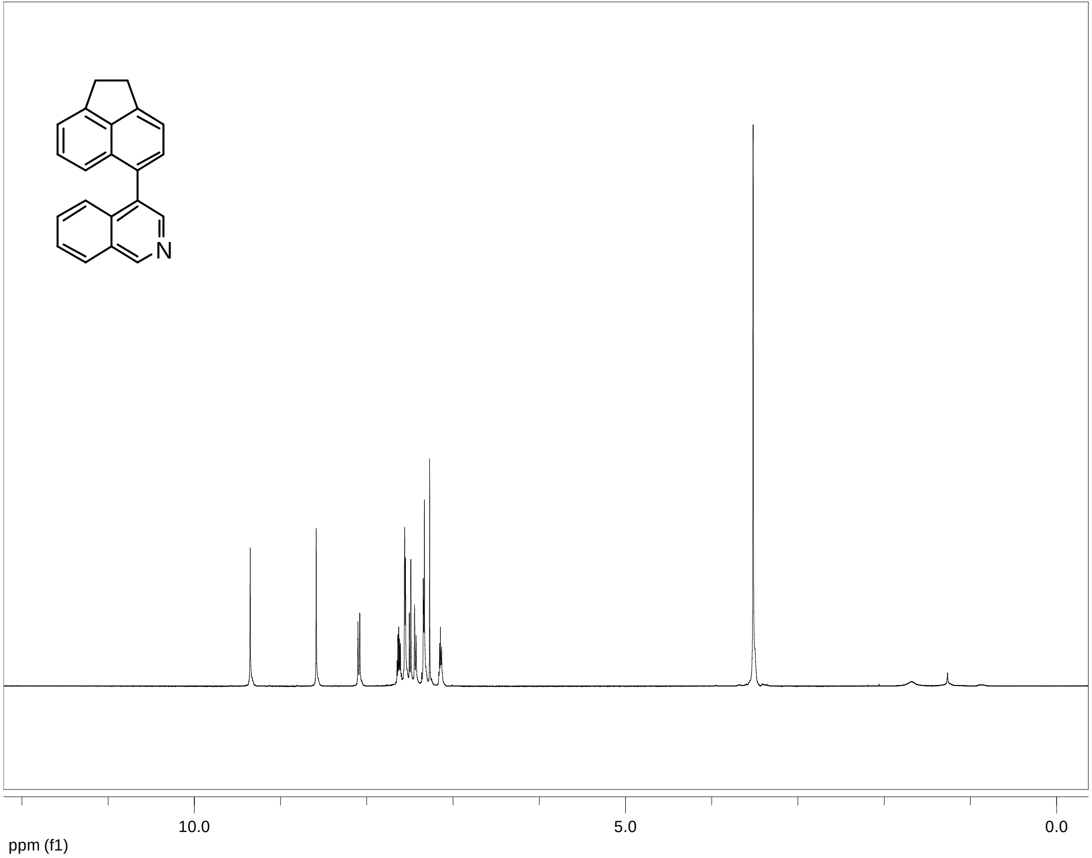

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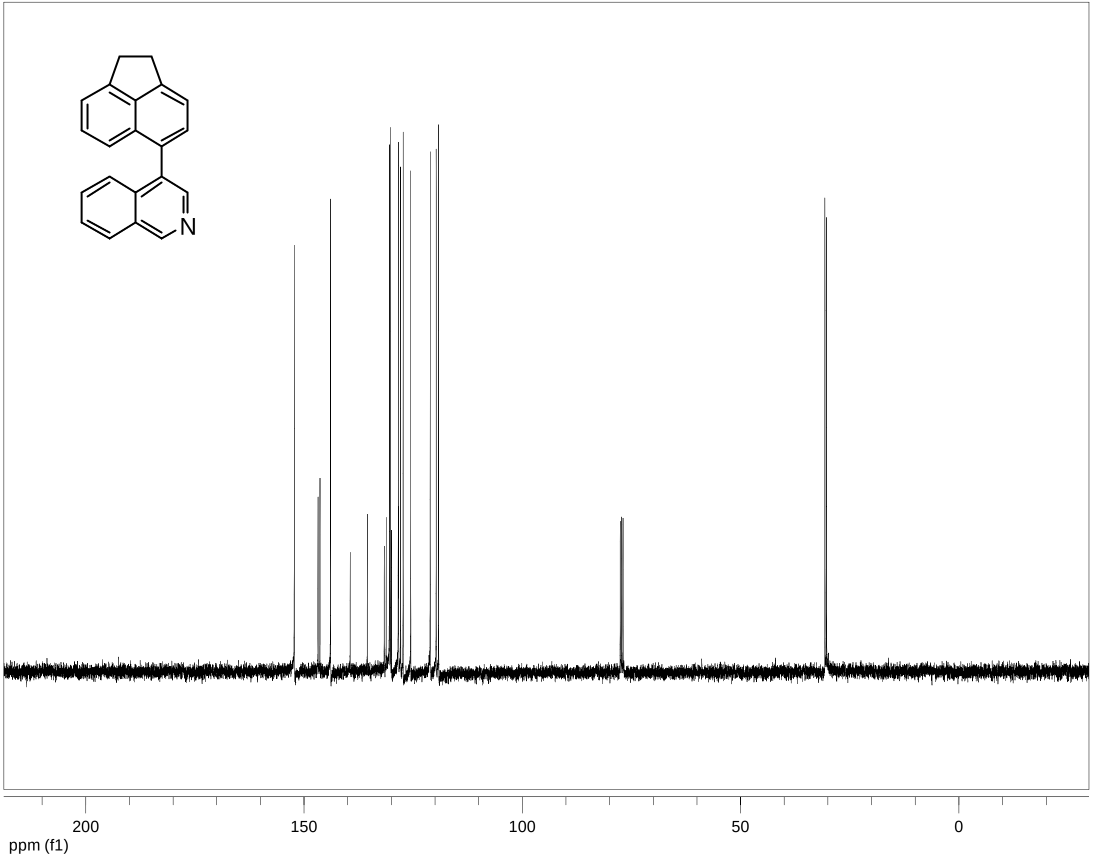

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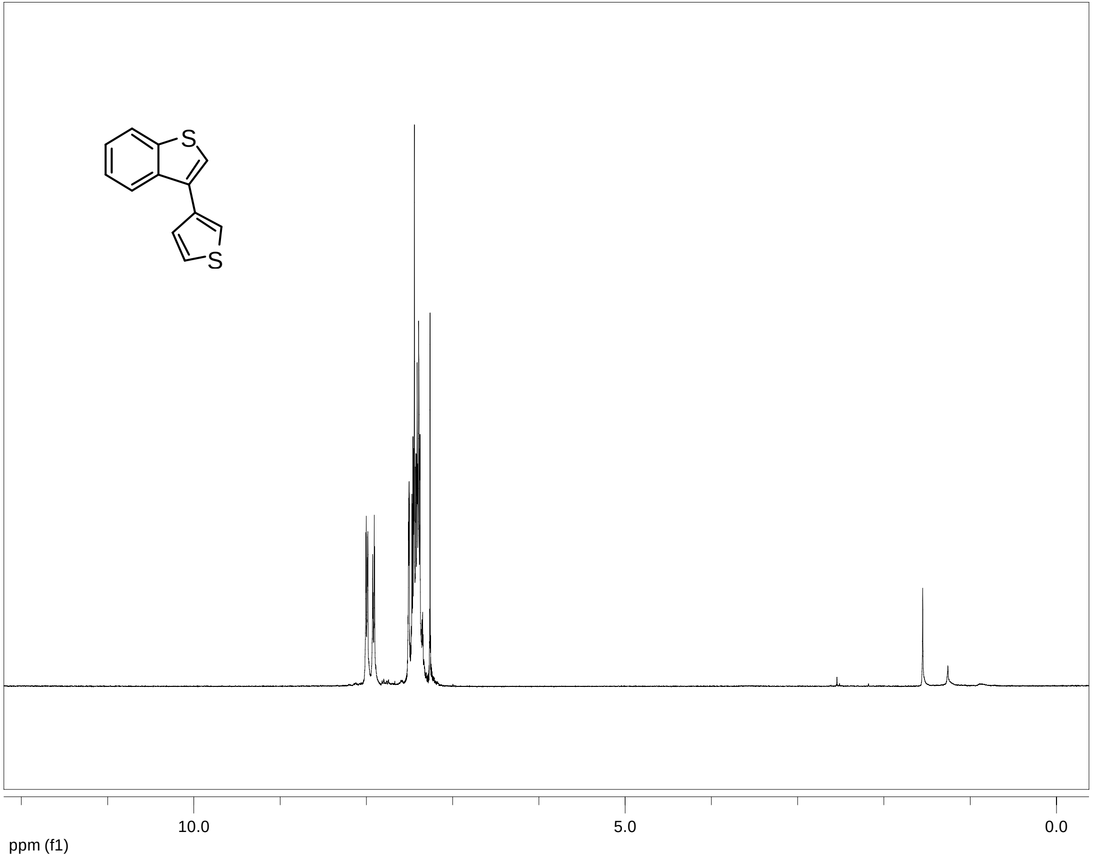

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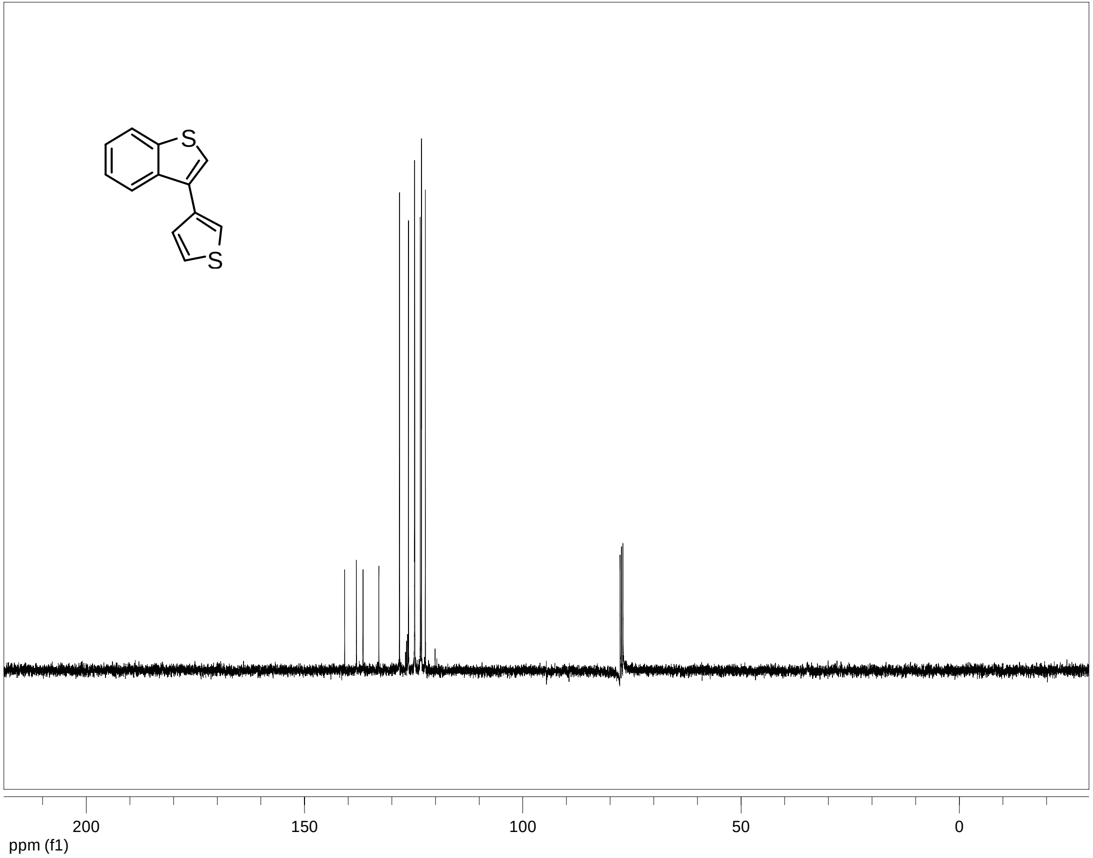

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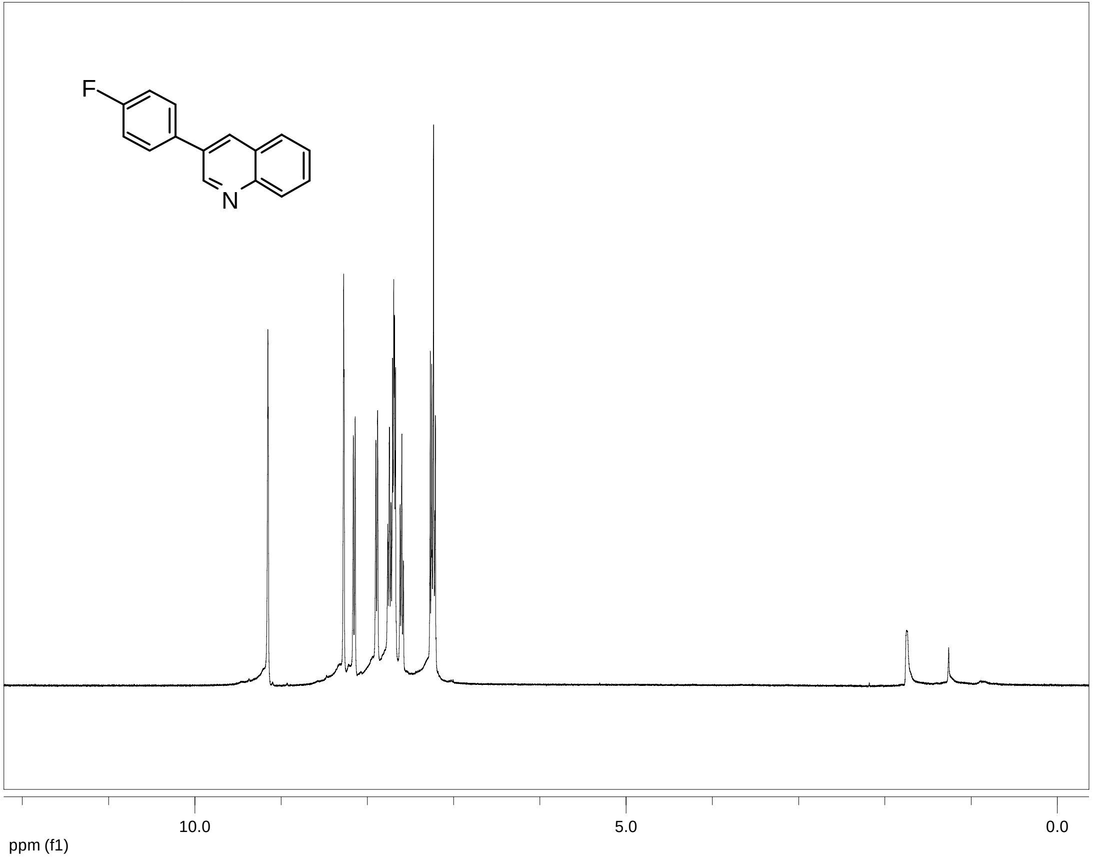

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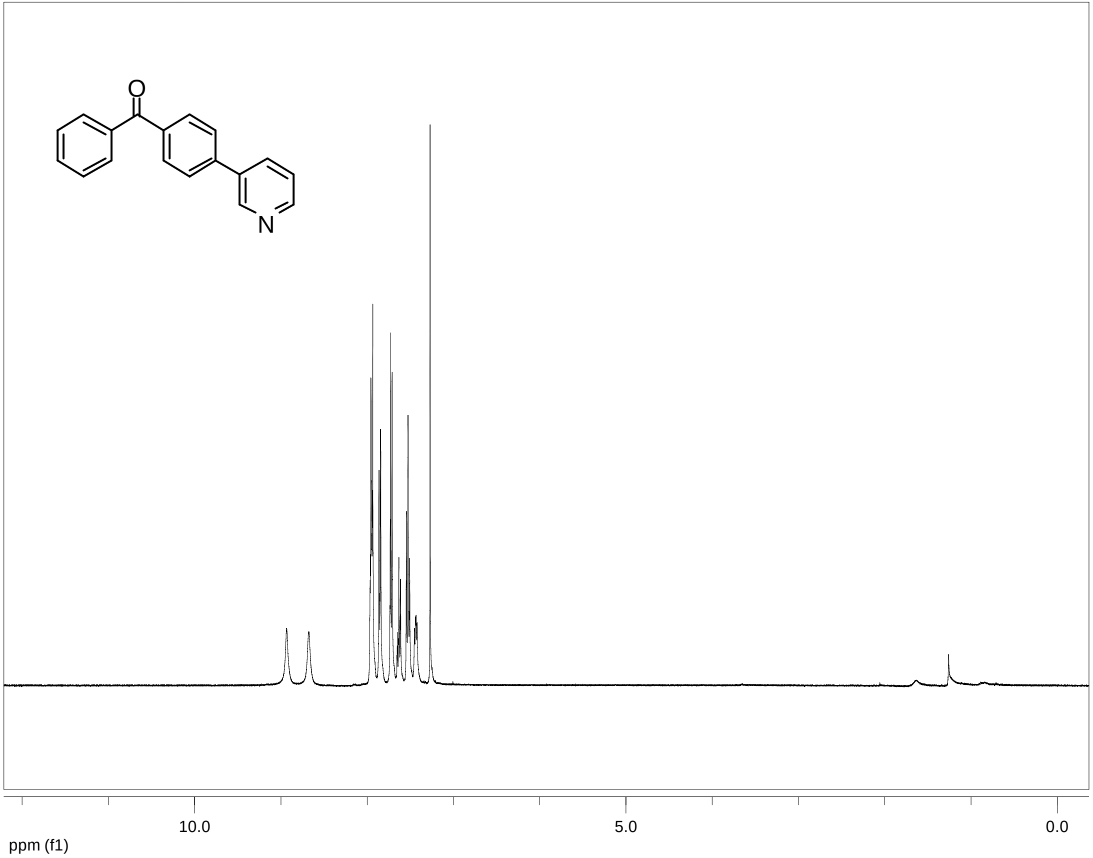

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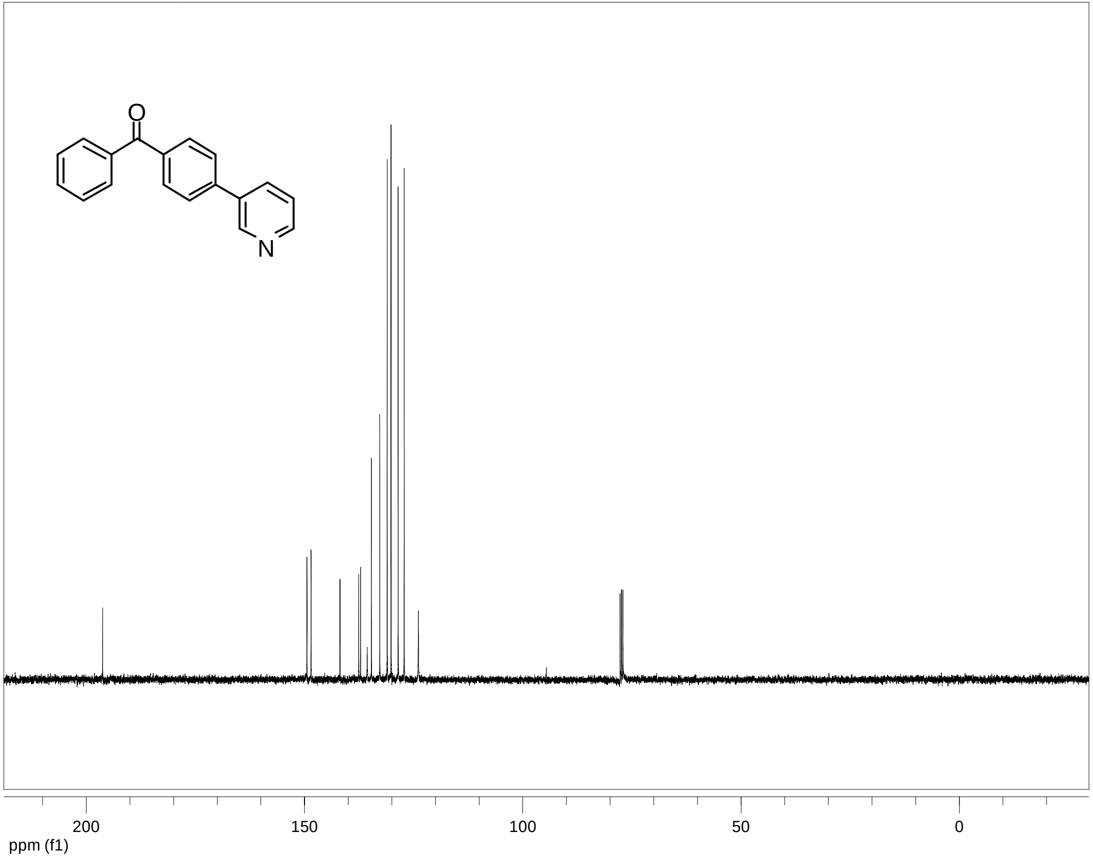

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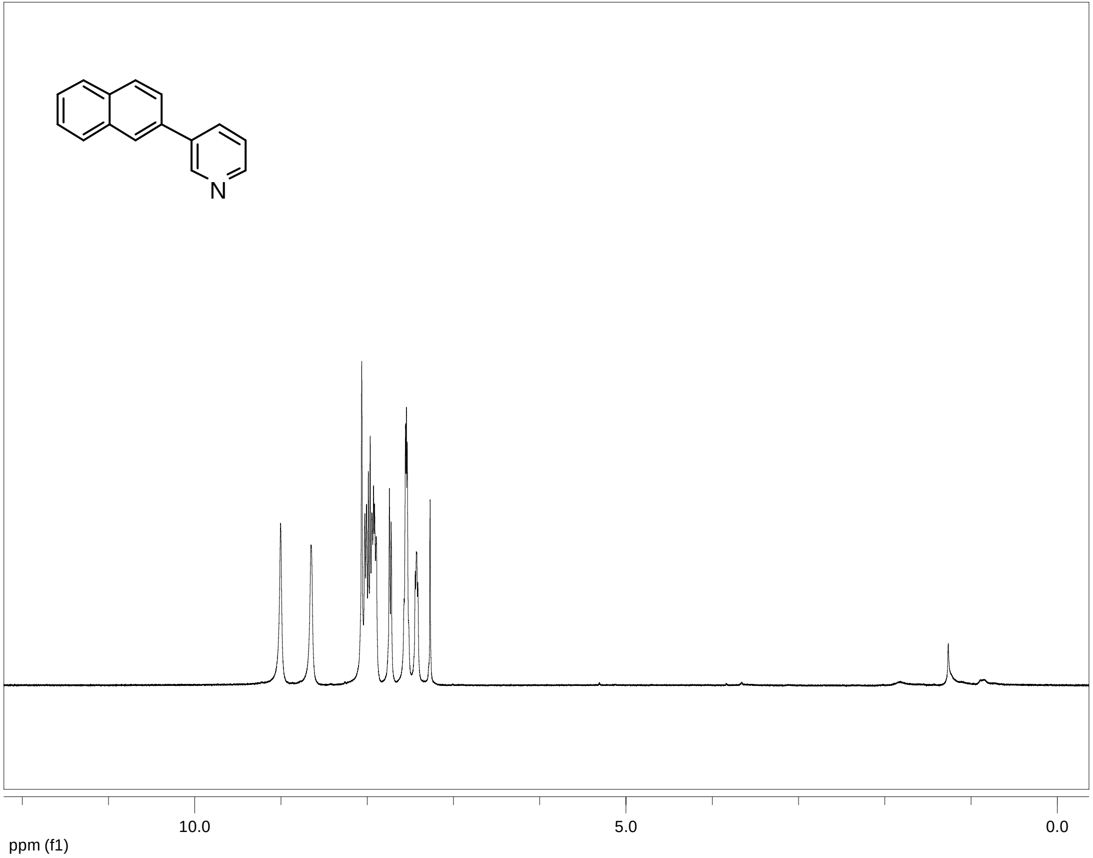

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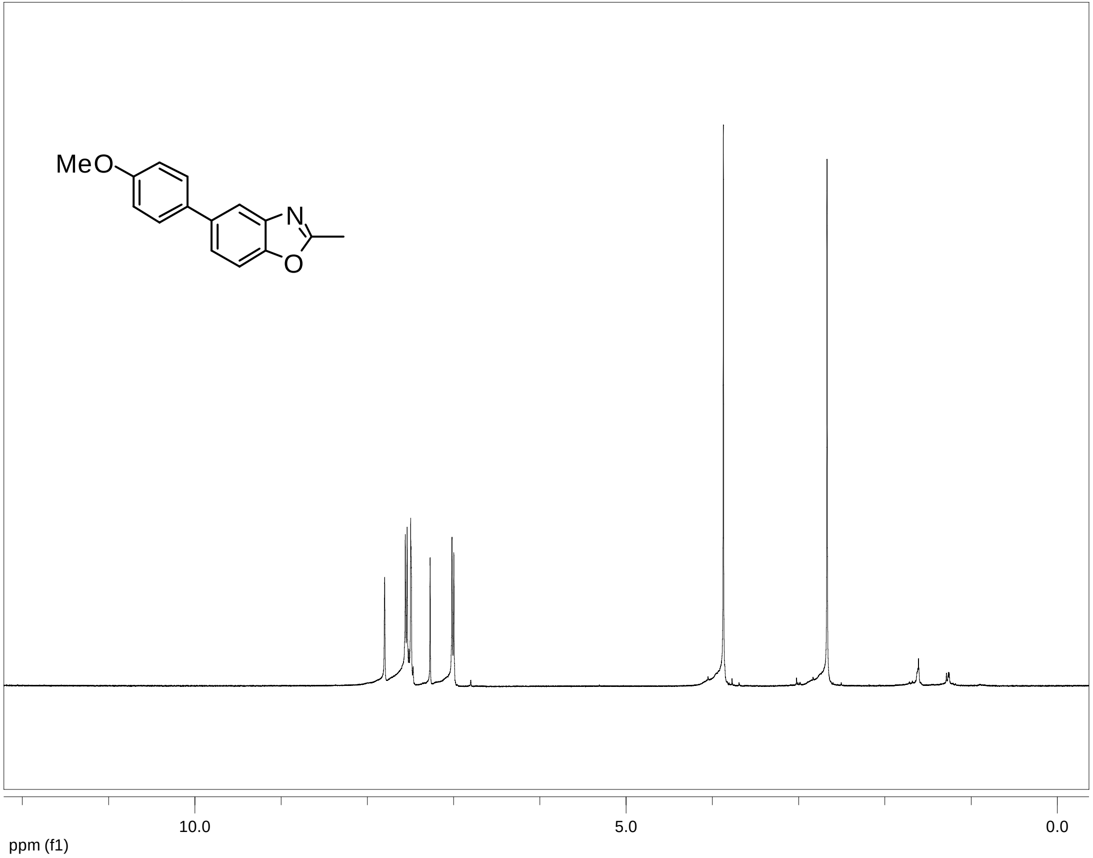

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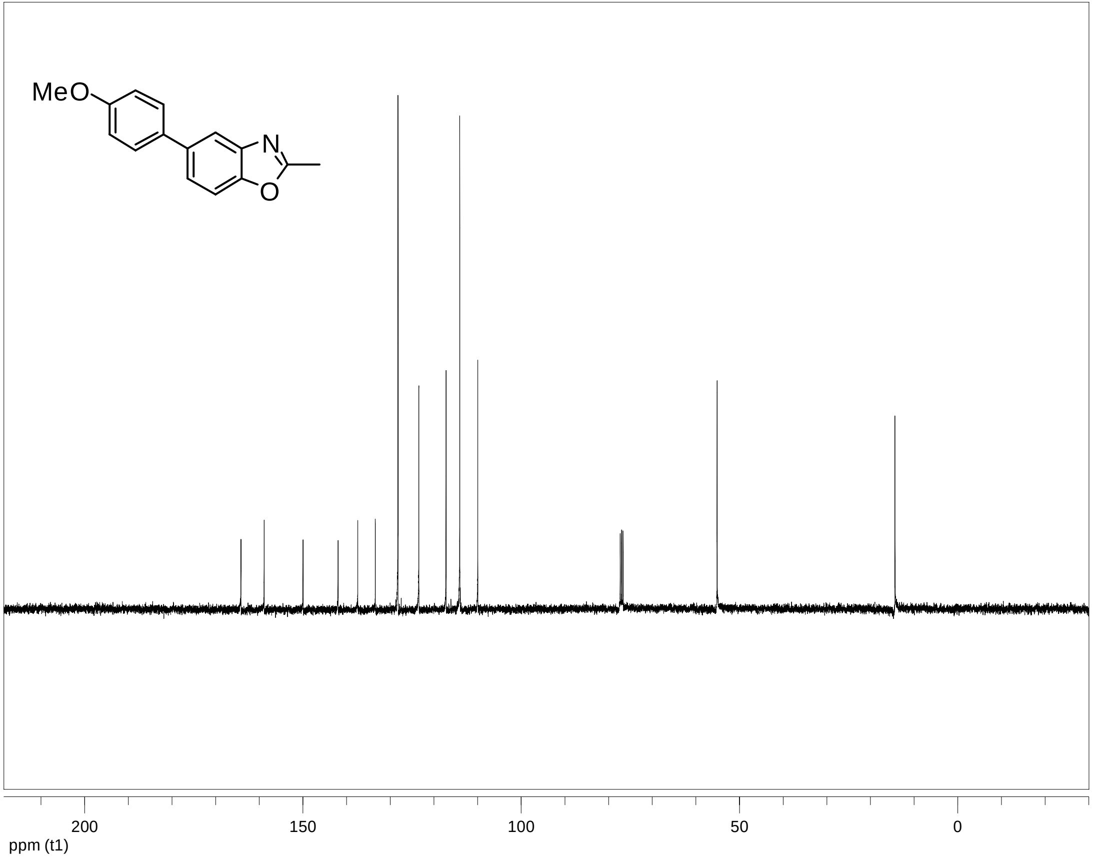

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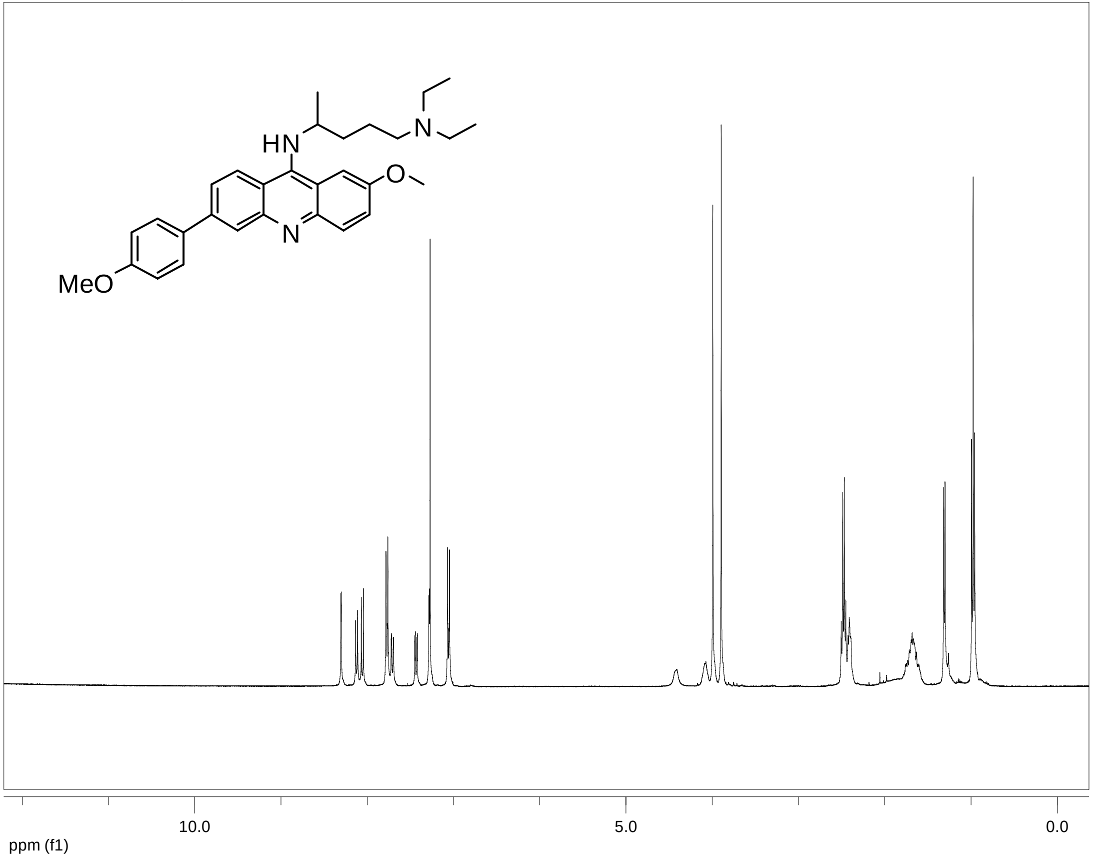

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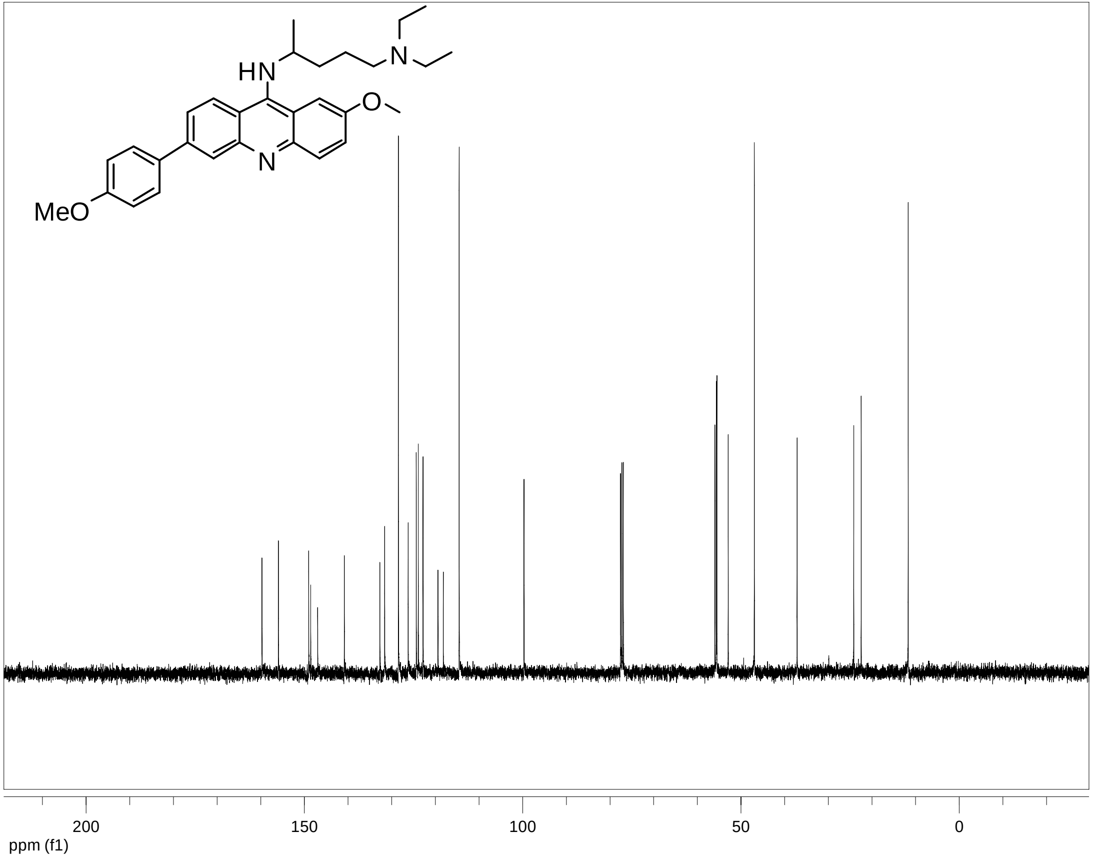

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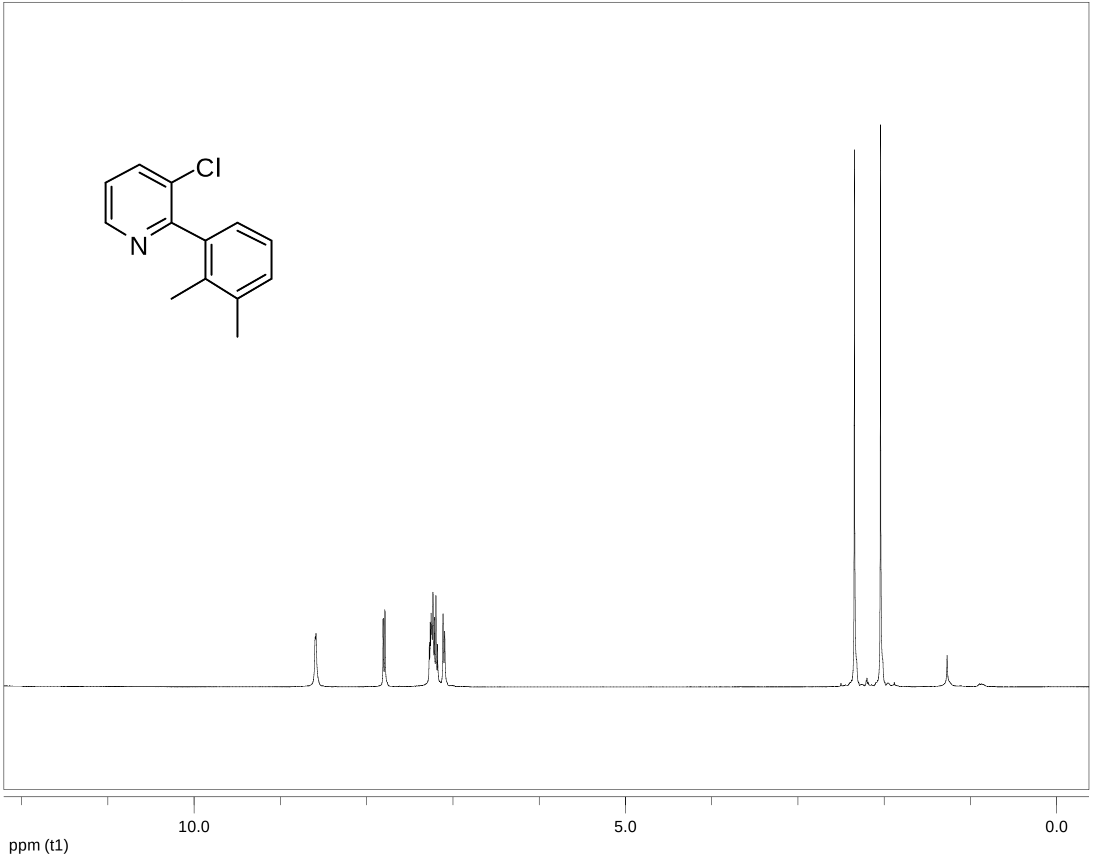

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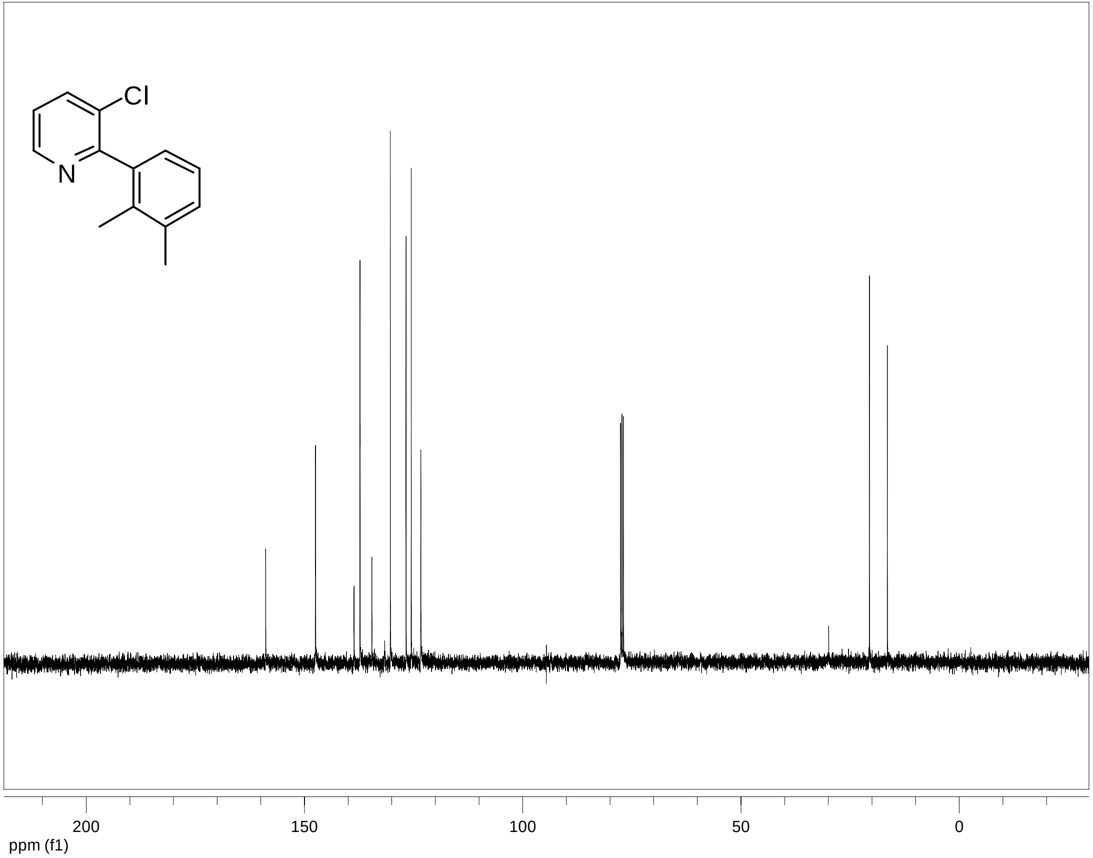

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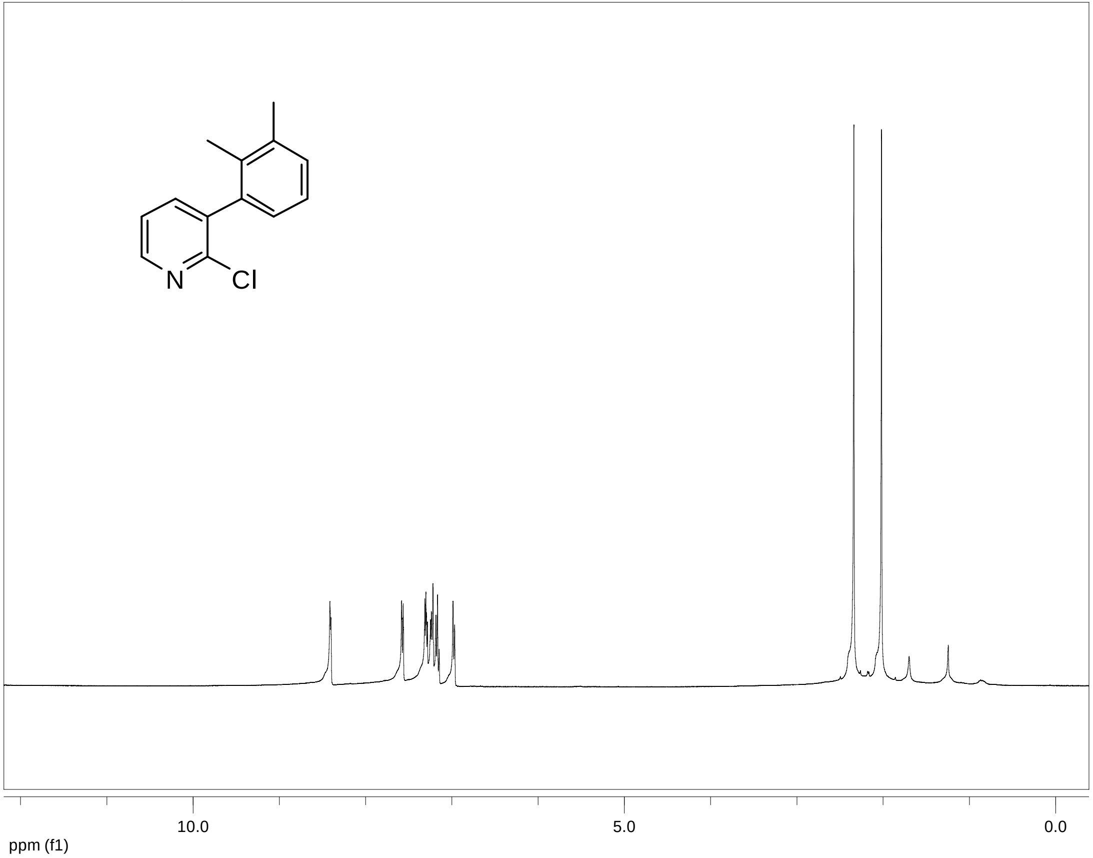

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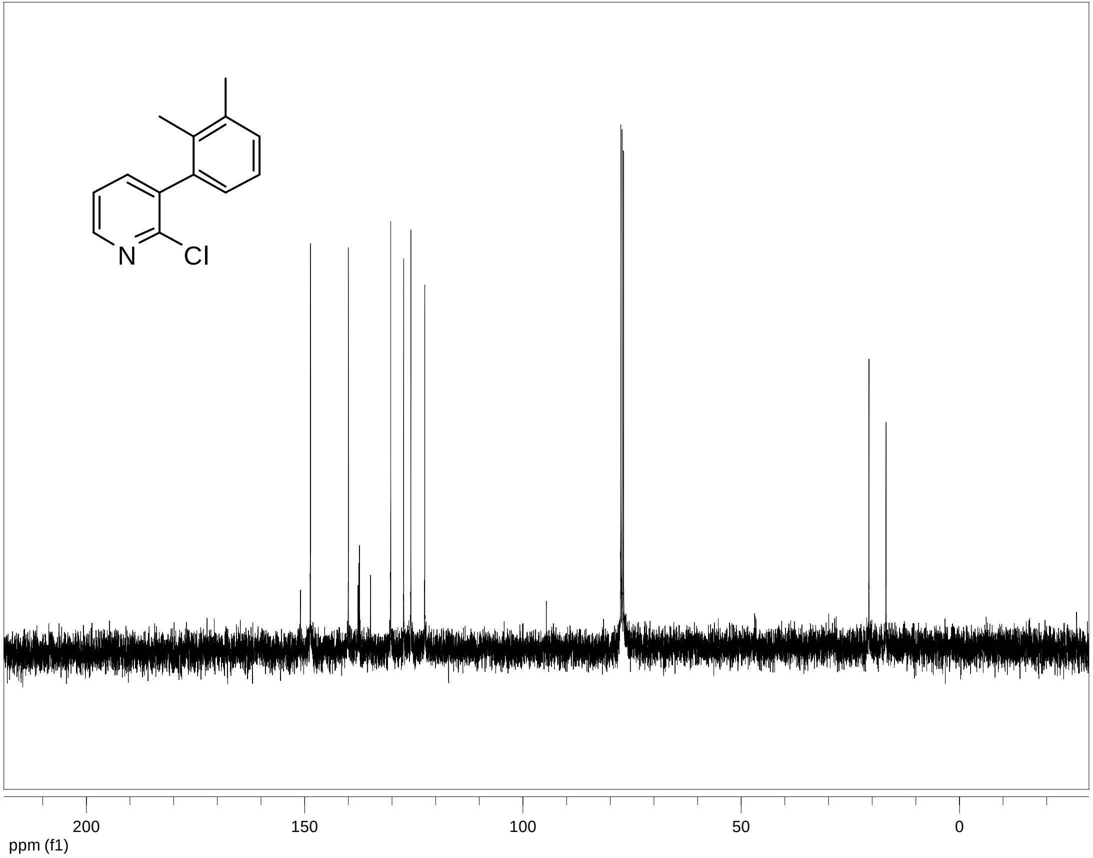


Table 2; Entry D

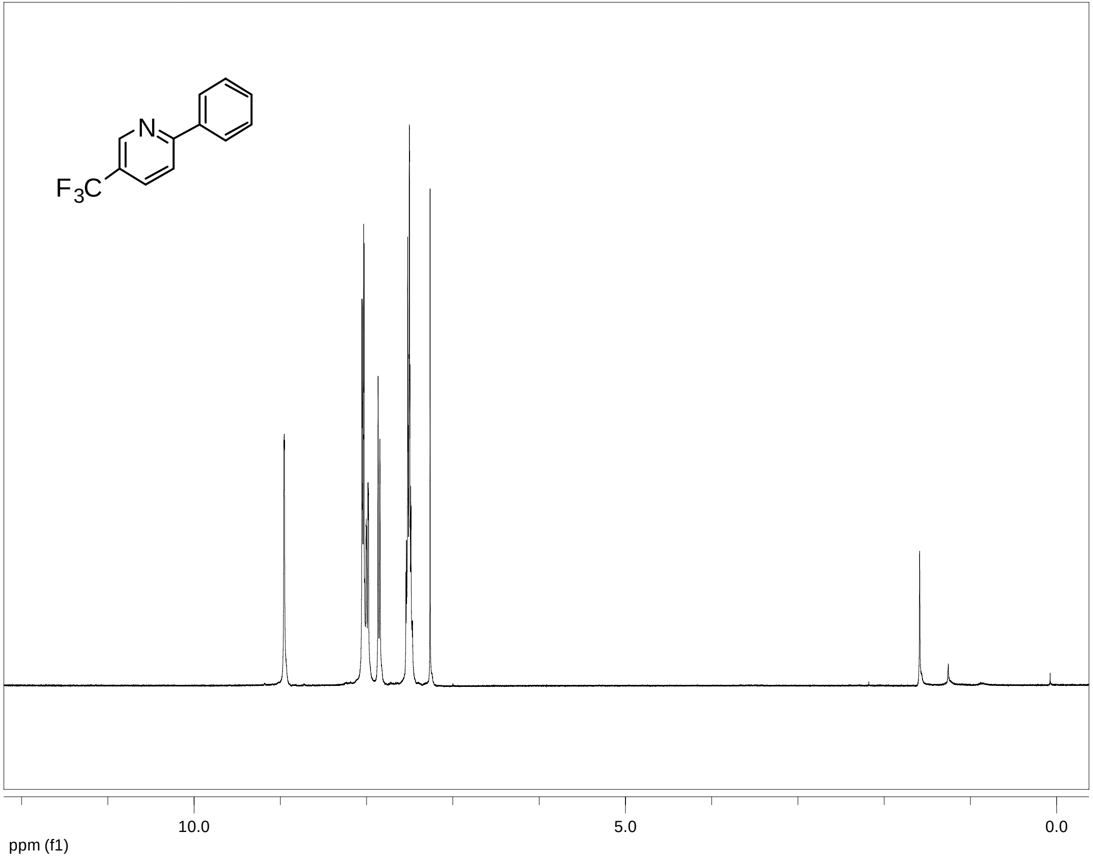
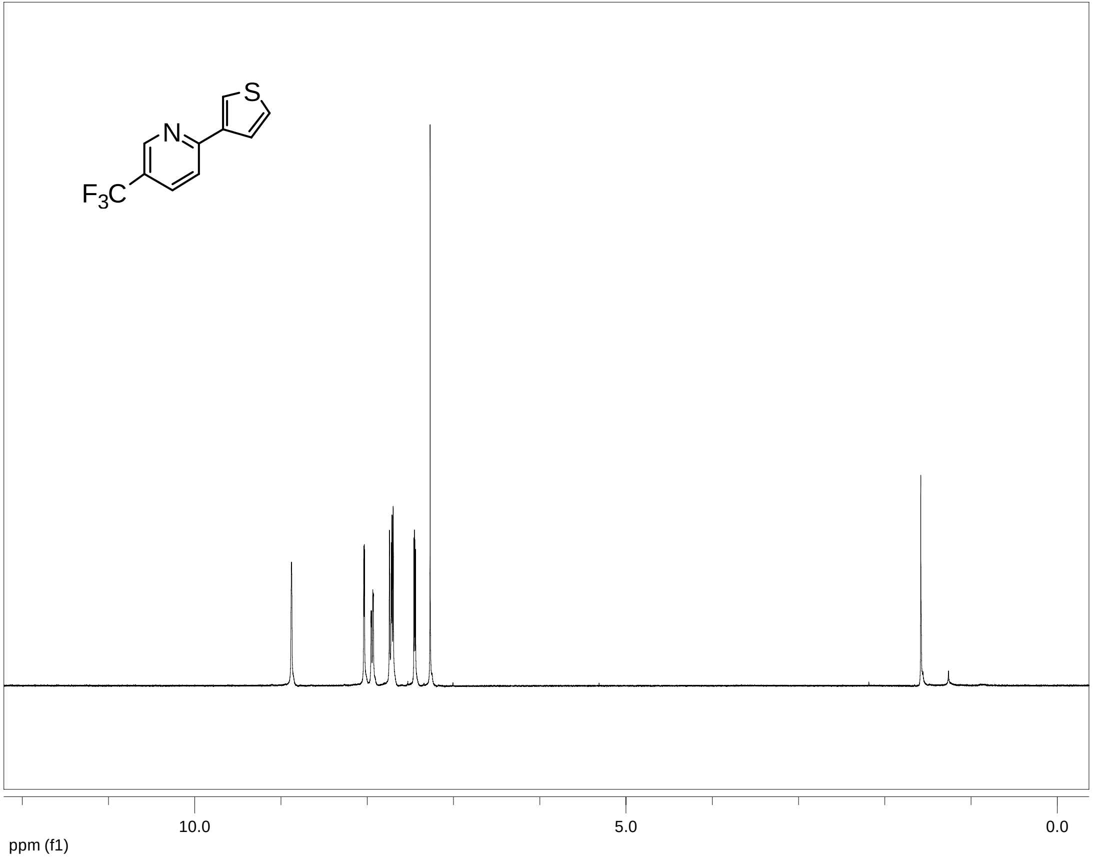


Table 2; Entry E



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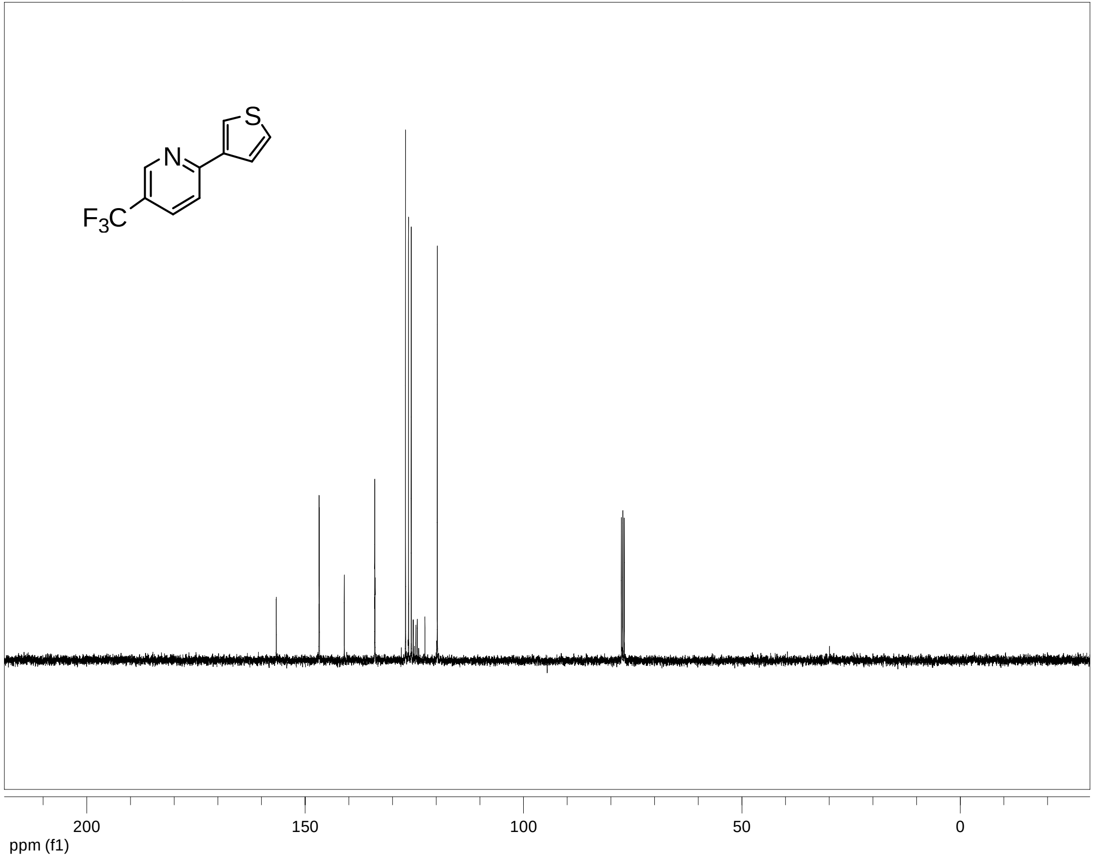

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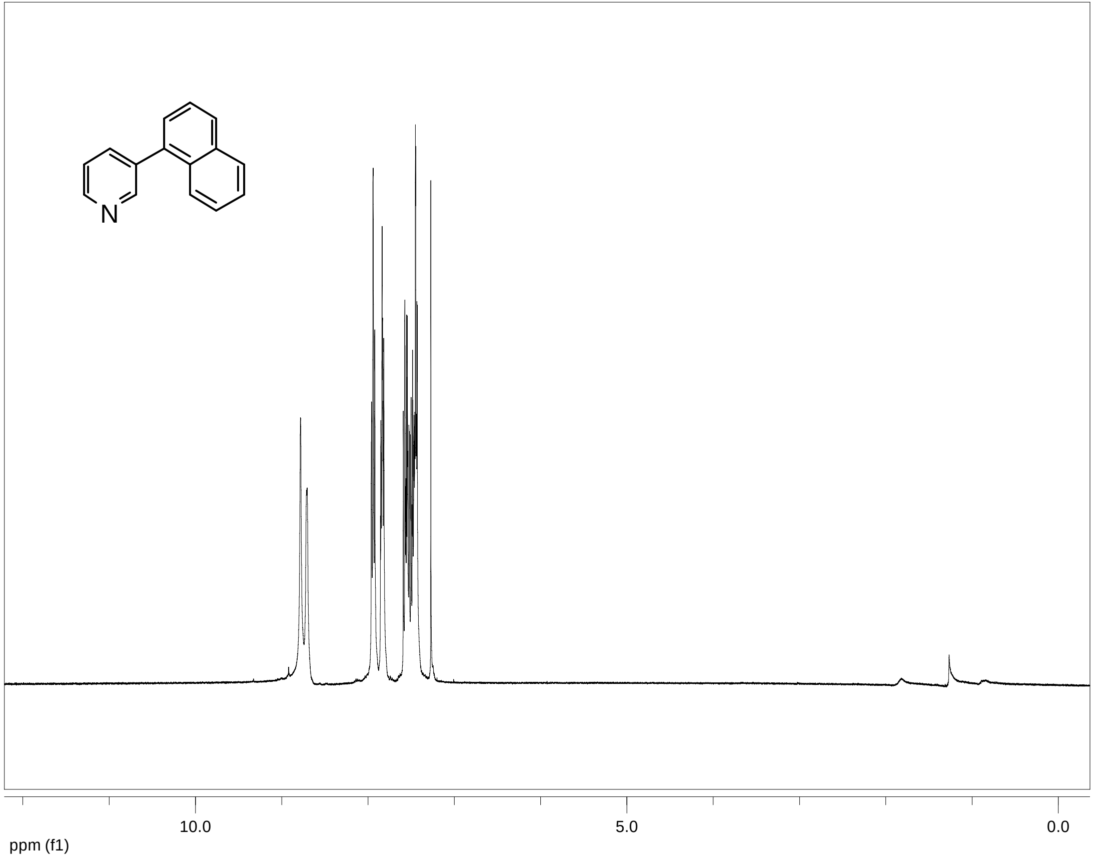
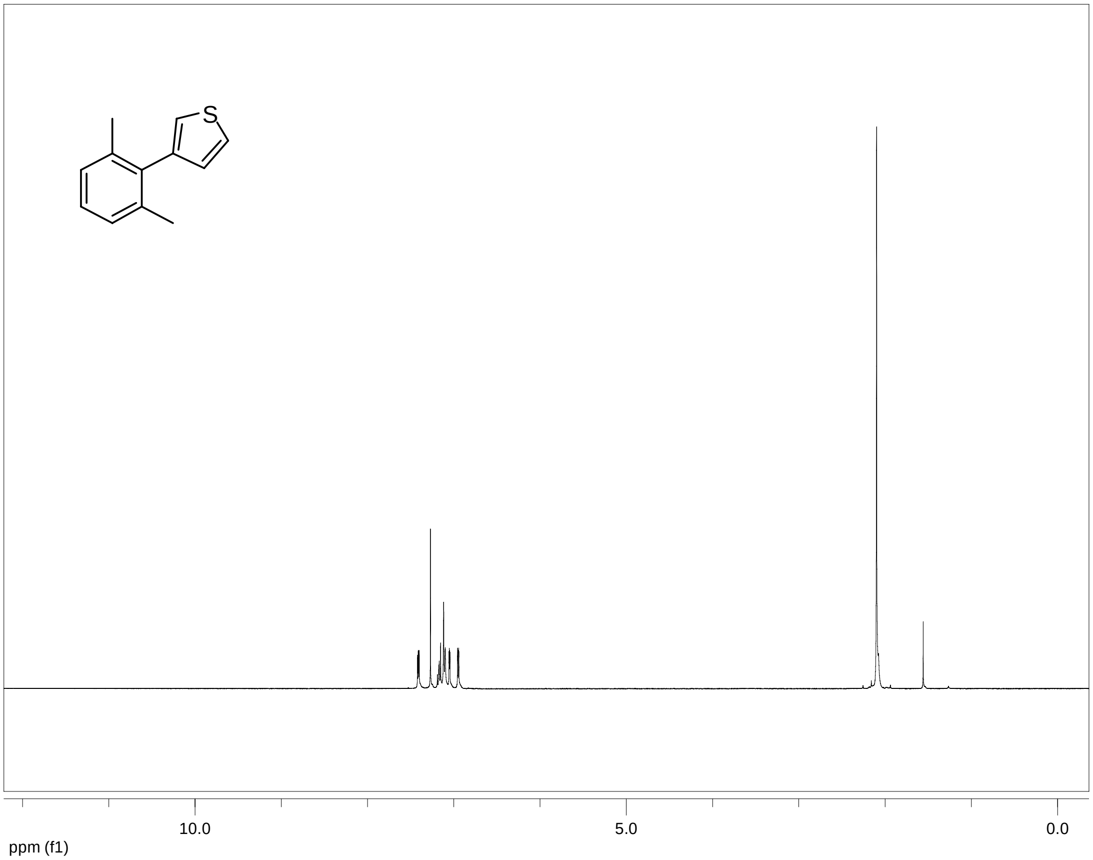


Scheme 2



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