An amine template strategy to construct successive C–C bonds: Synthesis of benzo[*h*]quinolines by a deaminative ring contraction cascade

Timothy P. McFadden[†] Chideraa I. Nwachukwu[†] and Andrew G. Roberts[†*]

[†]Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City, Utah 84112, United States

Supporting Information

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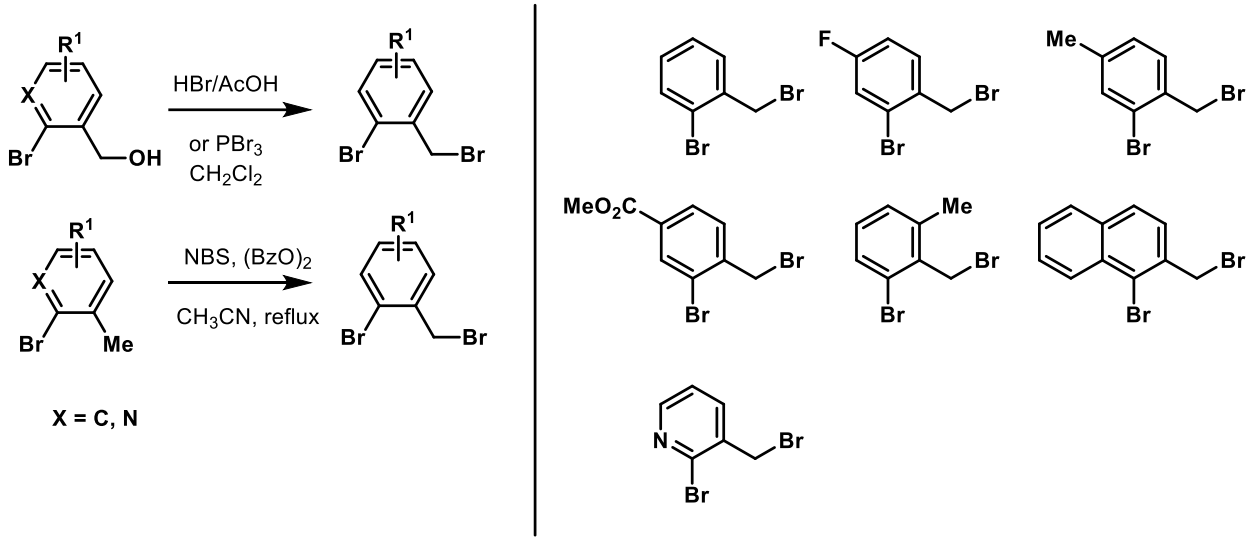
General information

Solvents and reagents were purchased from commercial distributors and used as received. All Ni-catalyzed reactions were performed under a positive pressure of N_2 in a round bottom flask equipped with a reflux condenser. ^1H and $^{13}C\{^1H\}$ NMR spectra were obtained on 400 or 500 MHz Varian Unity INOVA spectrometers. All ^1H NMR spectra are reported in parts per million (ppm) relative to residual $CHCl_3$ (7.26 ppm). Coupling constants, *J,* are reported in Hertz (Hz). All $^{13}C\{^1H\}$ NMR spectra are reported in ppm relative to residual $CHCl_3$ (77.2 ppm). High resolution mass spectra were recorded at the Mass Spectrometry Facility in the Department of Chemistry at the University of Utah on a Finnigan MAT® 95 double focusing high resolution mass spectrometer. Column chromatography was carried out using 230-400 mesh silica gel purchased from Silicycle and used as received. Benzylamines and benzyl bromide derivatives were prepared from the corresponding aldehyde or carboxylic acid and used without purification.

General procedure for the synthesis of benzyl halides

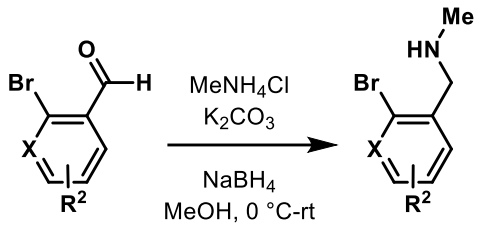
Benzyl halides were synthesized either from the benzyl alcohol or the phenyl methyl variant as shown. Reactions of the corresponding alcohol with hydrobromic acid and acetic acid or by phosphorus tribromide furnished the benzyl halide. The ester and the naphthyl substrates however, were synthesized by benzylic bromination using benzyol peroxide and N-bromosuccinimide. These benzyl bromides were used in the reaction without purification. Additionally, all benzyl bromides are also commercially available.



General procedure for the synthesis of the secondary amine

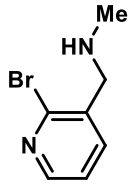
Methyl amine hydrochloride (3 equiv.), potassium carbonate (3 equiv.) was stirred in methanol (0.2 M) in a round bottom flask for 30 minutes. Aldehyde was then added to the flask and the mixture stirred for an additional 2 hrs. The mixture was then cooled to 0 ˚C and sodium borohydride (1 equiv.) was added slowly. The mixture was slowly warmed to room temperature and stirred for an additional 2 hr. The solvent was removed *in vacuo* and the crude mixture extracted with ethyl acetate (20 mL x 3). The organic extract was

the washed once with brine and then dried over anhydrous sodium sulfate. The solvent was again removed to afford the amine as a colorless oil.



X = C, N

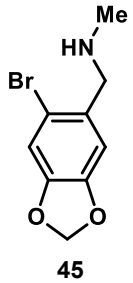
1-(2-bromopyridin-3-yl)-*N*-methylmethanamine



44

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.69 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.22 (dd, *J* = 7.5, 4.7 Hz, 1H), 3.77 (s, 2H), 2.43 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.4, 143.6, 138.0, 136.5, 122.9, 54.5, 36.0.

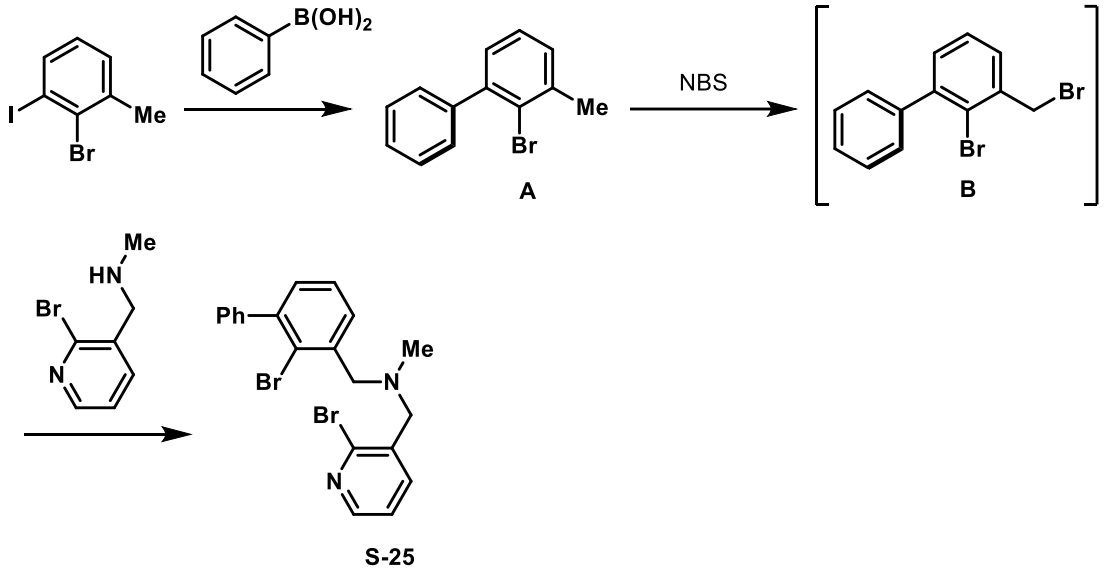
1-(2-bromopyridin-3-yl)-*N*-methylmethanamine



45

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.98 (s, 1H), 6.88 (s, 1H), 5.95 (s, 2H), 3.72 (s, 2H), 2.43 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 147.4 (d, *J* = 3.3 Hz), 132.2, 114.2, 112.8, 110.2, 101.7, 55.5, 35.6.

General route toward the synthesis of S-25

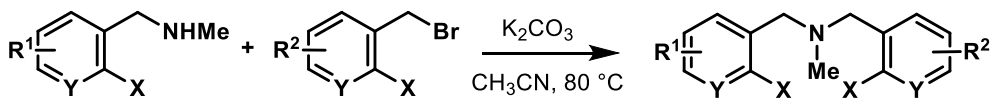


A was synthesized following the procedure from Luan and coworkers.[1] To an evacuated flask was added dioxane and water. The solution was degassed for 45 mins followed by the addition of aryl iodide, phenyl boronic acid, $Pd(PPh_3)_4$, K_2CO_3. The mixture was heated at 80 ˚C. After completion, the mixture was quenched by addition of water and the organic layer was extracted with ethyl acetate. The organic layer was washed with brine and dried over Na_2SO_4. After the removal of the solvent, the crude mixture was purified by flash column chromatography with hexanes. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.68 – 7.49 (m, 5H), 7.35 (s, 2H), 7.27 (d, *J* = 4.9 Hz, 1H), 2.63 (s, 1H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 143.5, 142.2, 139.0, 130.0, 129.6, 128.8, 128.0, 127.6, 126.9, 125.5, 24.4.

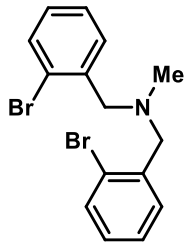
B was synthesized according to the procedure from Blakey.[2] To a round bottom was charged with **A** followed by NBS and MeCN. This was followed by addition of benzoyl peroxide. The mixture refluxed for 2hrs and then amine and potassium carbonate was added and reflux for further 2 hr. The mixture was cooled to room temperature and solvent was removed *in vacuo*. The crude mixture was the purified by flash column chromatography to afford **S-25**, see characterization on page S7.

General procedure for the synthesis of tertiary amines

Secondary amine (1 equiv.), benzyl halide (1.5 equiv.) and potassium carbonate (1 equiv.) were dissolved in acetonitrile (0.5 M) in a round bottom flask. The entire mixture was refluxed for 2 h with an oil bath set at 90 °C. After cooling to room temperature, the solid was filtered off and the solvent removed under reduced pressure. The crude mixture was purified by flash column chromatography on a silica gel packed column using a 10:1 mixture of hexanes and ethyl acetate to afford the corresponding tertiary amine.

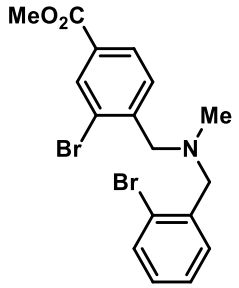


N-(2-bromobenzyl)-1-(2-bromophenyl)-*N*-methylmethanamine (**S-12**)



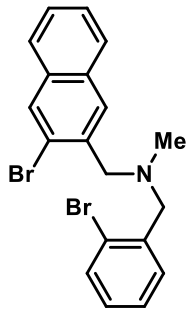
S-12 was isolated as a colorless oil. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.65 – 7.51 (m, 1H), 7.30 (t, *J* = 7.5 Hz, 1H), 7.11 (td, *J* = 7.6, 1.8 Hz, 1H), 3.73 (s, 1H), 2.28 (s, 1H). **^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):** δ 138.4, 132.8, 130.8, 128.4, 127.3, 124.6, 61.3, 42.3. Spectroscopic data match does previously reported.[3]

N-(2-bromobenzyl)-1-(2-bromophenyl)-*N*-methylmethanamine (**S-16**)



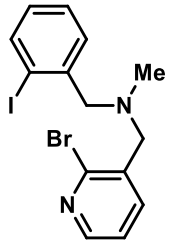
Reaction performed at 5.0 mmol scale. **S-16** was isolated as a yellow oil (0.78 g, 1.8 mmol, 36%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.12 (d, *J* = 2.9 Hz, 1H), 7.98 (dd, *J* = 7.9, 2.6 Hz, 1H), 7.53 – 7.46 (m, 1H), 7.45 – 7.29 (m, 4H), 3.88 (s, 3H), 3.38 (s, 2H), 3.34 (s, 2H), 2.41 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 165.9, 143.4, 133.8, 133.5, 132.9, 130.8, 130.77, 130.4, 128.6, 128.4, 127.4, 124.6, 124.2, 61.5, 61.1, 52.4, 42.4. **HRMS (ESI$^+$):** *Calcd.* for $C_{17}H_{18}Br_2NO_2$ $[M+H]^+$: 425.9704, found 425.9705

N-((2-bromobenzyl)-1-(3-bromonaphthalen-2-yl)-*N*-methylmethanamine (**S-17**)



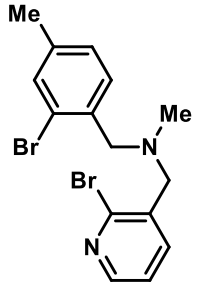
Reaction performed at 3.3 mmol scale. **S-17** was isolated as a yellow oil (0.52 g, 1.2 mmol, 36%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.31 (d, *J* = 8.6 Hz, 1H), 7.86 – 7.67 (m, 3H), 7.66 – 7.33 (m, 5H), 7.33 – 7.20 (m, 1H), 7.07 (td, *J* = 7.7, 2.0 Hz, 1H), 3.94 (s, 1H), 3.73 (s, 2H), 2.26 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 138.5, 136.9, 134.0, 132.9, 132.5, 131.0, 128.6, 128.2, 128.1, 127.6, 127.5, 127.39, 127.35, 126.4, 124.8, 124.3, 62.2, 61.6, 42.4. **HRMS (ESI$^+$):** *Calcd.* for $C_{19}H_{18}Br_2N$ $[M+H]^+$: 417.9806, found 417.9812.

1-(2-bromopyridin-3-yl)-*N*-(2-Iodobenzyl)-*N*-methylmethanamine (**S-18**)



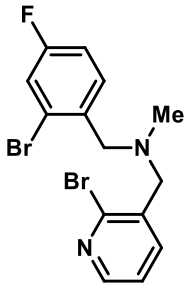
Reaction performed at 5.0 mmol scale. **S-18** was isolated as a yellow oil (1.05 g, 2.5 mmol, 50%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.18 (d, *J* = 2.2 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.27 – 7.12 (m, 2H), 7.05 (tt, *J* = 7.6, 1.8 Hz, 1H), 3.66 (s, 2H), 3.63 (s, 2H), 2.21 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.3, 143.7, 140.8, 139.6, 138.8, 136.0, 130.4, 129.0, 128.1, 123.0, 100.6, 66.2, 59.8, 42.2. **HRMS (ESI$^+$):** *Calcd.* for $C_{14}H_{15}BrIN_2$ $[M+H]^+$: 416.9463, found 416.9464.

N-(2-bromo-4-methylbenzyl)-1-(2-bromopyridin-3-yl)-*N*-methylmethanamine (**S-19**)



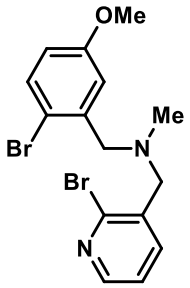
Reaction performed at 11.4 mmol scale. **S-19** was isolated as a yellow oil (3.1 g, 8.1 mmol, 70%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.24 (d, *J* = 4.7 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.41 – 7.30 (m, 2H), 7.29 – 7.18 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 1H), 3.68 (s, 2H), 3.66 (s, 2H), 2.31 (s, 3H), 2.26 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.3, 143.8, 138.8, 136.1, 134.8, 133.3, 133.1, 130.6, 128.1, 124.5, 122.9, 61.2, 59.9, 42.3, 20.7. **HRMS (ESI$^+$):** *Calcd.* for $C_{15}H_{17}Br_2N_2$ $[M+H]^+$: 382.9758, found 382.9764.

N-(2-bromo-4-fluorobenzyl)-1-(2-bromopyridin-3-yl)-*N*-methylmethanamine (**S-20**)



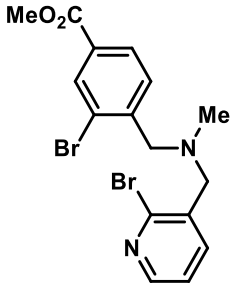
Reaction performed at 7.5 mmol scale. **S-20** was isolated as a colorless oil (2.8 g, 7.2 mmol, 94%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.22 (dd, *J* = 4.8, 2.1 Hz, 1H), 7.83 (dd, *J* = 7.6, 2.1 Hz, 1H), 7.45 (dd, *J* = 8.7, 6.2 Hz, 1H), 7.25 (ddd, *J* = 16.1, 7.9, 3.7 Hz, 2H), 6.99 (td, *J* = 8.2, 2.7 Hz, 1H), 3.66 (s, 2H), 3.65 (s, 2H), 2.23 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 161.4 (d, J_{CF} = 249.9 Hz), 148.4, 143.8, 138.7, 135.8, 133.8 (d, J_{CF} = 3.4 Hz), 131.6 (d, J_{CF} = 8.5 Hz), 124.4 (d, J_{CF} = 9.1 Hz), 122.9, 120.0 (d, J_{CF} = 24.3 Hz), 114.4 (d, J_{CF} = 20.6 Hz), 60.7, 60.0, 42.2. **HRMS (ESI$^+$):** *Calcd.* for $C_{14}H_{14}Br_2FN_2$ $[M+H]^+$: 386.9508, found 386.9512.

N-(2-bromo-5-methoxybenzyl)-1-(2-bromopyridin-3-yl)-*N*-methylmethanamine (**S-21**)



Reaction performed at 10.8 mmol scale. **S-21** was isolated as a colorless oil (2.1 g, 5.5 mmol, 49%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.17 (dd, *J* = 5.1, 1.9 Hz, 1H), 7.84 – 7.77 (m, 1H), 7.34 (dd, *J* = 8.7, 1.0 Hz, 1H), 7.18 (dd, *J* = 7.5, 4.6 Hz, 1H), 7.05 (d, *J* = 3.1 Hz, 1H), 6.61 (dd, *J* = 8.7, 3.1 Hz, 1H), 3.71 (s, 3H), 3.62 (s, 2H), 3.61 (s, 2H), 2.22 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 159.0, 148.4, 143.9, 139.0, 138.7,135.9, 133.3, 122.9, 116.2, 114.7, 114.2, 61.5, 60.2, 55.5, 42.5. **HRMS (ESI$^+$):** *Calcd.* for $C_{15}H_{17}Br_2N_2O$ $[M+H]^+$: 398.9708, found 398.9709.

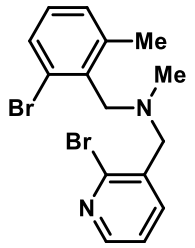
Methyl 3-bromo-((((-bromopyridin-3-yl)methyl)(methyl)amino)methyl)benzoate (**S-22**)



Reaction performed at 5.0 mmol scale. **S-22** was isolated as a colorless oil (0.86 g, 2.0 mmol, 40%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.22 – 8.16 (m, 1H), 8.13 (s, 1H), 7.87 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.82 – 7.76 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.18 (ddd, *J* = 7.6, 4.7, 1.0 Hz, 1H), 3.83 (d, *J* = 1.1 Hz, 3H), 3.68 (s,

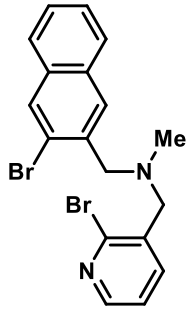
2H), 3.62 (s, 2H), 2.21 (s, 3H). **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 165.6, 148.5, 143.8, 143.1,138.6, 135.6, 133.9, 130.4, 130.3, 128.4, 124.2, 122.9, 61.3, 60.2, 52.4, 42.4. **HRMS (ESI^+):** *Calcd.* for $C_{16}H_{17}Br_2N_2O_2$ $[M+H]^+$: 426.9657, found 426.9656

N-(2-bromo-6-methylbenzyl)-1-(2-bromopyridin-3-yl)-*N*-methylmethanamine (**S-23**)



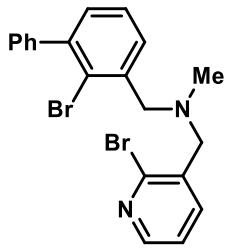
Reaction performed at 10.4 mmol scale. **S-23** was isolated as a yellow oil (2.9 g,7.6 mmol, 73%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.26 – 8.21 (m, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.34 (d, *J* = 7.5 Hz, 1H), 7.23 (ddd, *J* = 7.0, 4.7, 1.7 Hz, 1H), 7.21 – 7.10 (m, 2H), 3.73 (s, 2H), 3.69 (s, 2H), 2.42 (s, 3H), 2.27 (s, 3H). **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 148.3, 143.8, 138.7, 138.6, 138.2, 136.1, 129.6, 128.0, 127.2, 126.8, 122.9, 62.3, 60.1, 42.4, 23.9. **HRMS (ESI^+):** *Calcd.* for $C_{15}H_{17}Br_2N_2$ $[M+H]^+$: 382.9767, found 382.9765.

1-(3-bromonaphthalen-2-yl)-*N*-((2-bromopyridin-3-yl)methyl)-*N*-methylmethanamine (**S-24**)



Reaction performed at 8.0 mmol scale. **24** was isolated as a colorless oil (2.3 g, 5.5 mmol, 69%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.30 (d, *J* = 8.7 Hz, 1H), 8.24 – 8.18 (m, 1H), 7.85 (d, *J* = 7.5 Hz, 1H), 7.81 – 7.69 (m, 2H), 7.66 – 7.61 (m, 1H), 7.55 (ddd, *J* = 8.5, 7.0, 1.6 Hz, 1H), 7.50 – 7.42 (m, 1H), 7.20 (dq, *J* = 8.3, 3.6, 3.1 Hz, 1H), 3.94 (s, 2H), 3.70 (s, 2H), 2.27 (s, 3H). **$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$):** δ 148.5, 144.1, 138.9, 136.3, 136.1, 134.0, 132.6, 128.2, 127.9, 127.7, 127.52, 127.49, 126.5, 124.5, 123.0, 62.4, 60.3, 42.6. **HRMS (ESI^+):** *Calcd.* for $C_{18}H_{17}Br_2N_2$ $[M+H]^+$: 418.9758, found 418.9761.

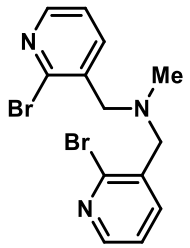
1-(2-bromo-[1,1'-biphenyl]-3-yl)-*N*-((2-bromopyridin-3-yl)methyl)-*N*-methylmethanamine (**S-25**)



Reaction performed at 8.0 mmol scale. **S-25** was isolated as a colorless oil (2.0 g, 4.5 mmol, 56%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.21 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.88 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.49 (dd, *J* =

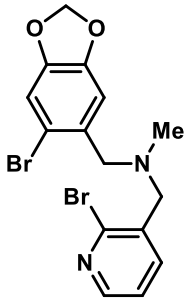
7.6, 1.8 Hz, 1H), 7.43 – 7.26 (m, 6H), 7.25 – 7.21 (m, 1H), 7.17 (dd, *J* = 7.5, 1.8 Hz, 1H), 3.77 (s, 2H), 3.70 (s, 2H), 2.30 (s, 3H). **13C{1H} NMR (125 MHz, CDCl3):** δ 148.3, 143.8, 146.6, 141.8, 138.8, 138.7, 136.0, 130.0, 129.5, 129.3, 127.9, 127.5, 126.9, 124.9, 122.9, 62.5, 60.2, 42.6. **HRMS (ESI+):** *Calcd.* for $C_{20}H_{19}Br_2N_2$ $[M+H]^+$: 444.9915, found 444.9922

1-(2-bromopyridin-3-yl)-*N*-((2-bromopyridin-3-yl)methyl)-*N*-methylmethanamine (**S-26**)



Reaction performed at 10.3 mmol scale. **50** was isolated as a white solid (1.25 g, 3.4 mmol, 33%). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.40 – 8.05 (m, 2H), 7.95 – 7.66 (m, 2H), 7.21 (dd, *J* = 5.2, 2.4 Hz, 2H), 3.66 (s, 4H), 2.23 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.7, 144.0, 138.8, 135.6, 123.0, 60.5, 42.5. **HRMS (ESI^+):** *Calcd.* for $C_{13}H_{14}Br_2N_3$ $[M+H]^+$: 369.9554, found 369.9555.

1-(6-bromobenzo[*d*][1,3]dioxol-5-yl)-*N*-((2-bromopyridin-3-yl)methyl)-*N*-methylmethanamine (**45**)



Reaction performed at 6.1 mmol scale. **45** was isolated as a colorless oil (1.2 g, 2.9 mmol, 48%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.26 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.87 (dd, *J* = 7.5, 2.1 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.04 (s, 1H), 7.00 (s, 1H), 5.98 (s, 2H), 3.67 (s, 2H), 3.64 (s, 2H), 2.27 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.4, 147.41, 147.38, 143.9, 138.7, 135.9, 131.2, 122.9, 114.7, 112.7, 110.3, 101.7, 61.2, 59.9, 42.2. **HRMS (ESI^+):** *Calcd.* for $C_{15}H_{15}Br_2N_2O_2$ $[M+H]^+$: 412.9500, found 412.9502.

Procedure for synthesis of biaryl-linked azepines

General procedure A

To a flame dried round bottom flask was charged with copper thiophene carboxylate (CuTC) (3 equiv.) and anhydrous NMP (0.12 M). The mixture was degassed with nitrogen and stirred at room temperature for 12 h. The mixture was then diluted with ethyl acetate (20 mL), followed by the addition of 2M NH_4OH until clear blue color appeared. The mixture was then extracted thrice with ethyl acetate (20 mL x 3), and then dried over anhydrous Na_2SO_4. The organic solvent was removed under reduced pressure and the crude mixture purified by flash column chromatography.[4]

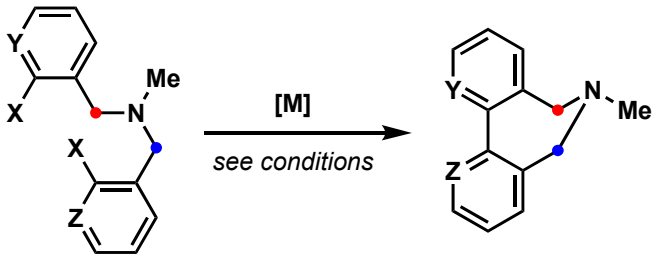
General procedure B

To a flame dried round bottom flask was charged with $NiBr_2(PPh_3)_2$ (1 equiv.), Et_4NI (1 equiv.) and zinc powder (10 equiv.). The zinc was activated with 2% hydrochloric acid prior to use. The flask was evacuated and back filled three times with nitrogen, followed by the addition of dry THF (0.025 M). The solution was again evacuated and back filled once with nitrogen, followed by the addition of the tertiary amine (1 equiv.) dissolved in dry THF. The resulting solution was stirred for 4h at 50 ˚C (oil bath) under nitrogen atmosphere. The mixture was cooled to room temperature, followed by addition of 2M NH_4OH (10 mL). The entire mixture was stirred for 15 minutes and solvent was removed *in vacuo*. The entire solution was then extracted with ethyl acetate (50 mL x 3). The combined organic layer was dried over Na_2SO_4, and filtered, and the solvent removed again under reduced pressure. The crude product was again dissolved with 1 mL of chloroform and triturated with ether. Excess triphenylphosphine oxide was filtered off and the filtrated again concentrate under reduced pressure. The crude product was purified by flash column chromatography with ethyl acetate and methanol to afford the azepines.[5]

General procedure C

To a flame dried round bottom flask was charged with Cu powder (6 equiv.) and anhydrous DMF (0.7 mL, 1.2 M). The mixture was refluxed for 15 minutes, followed by the addition of the corresponding tertiary amine (1 equiv.) The resulting solution was refluxed at 160 ˚C (oil bath) for 12 h. The mixture was the cooled to room temperature and diluted with 6N HCl (20 mL). Unreacted copper was removed by vacuum filtration. The solution was then made slightly alkaline with 2 N NaOH, and then very alkaline with 2M NH_4OH (20 mL). The mixture was then extracted thrice with ethyl acetate (10 mL x 3), and then dried over anhydrous Na_2SO_4. The organic solvent was removed under reduced pressure and the crude mixture purified by flash column chromatography with ethyl acetate and methanol to afford the azepine.[6]

a) *reductive cyclization of tertiary amine templates*



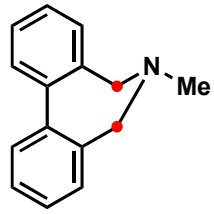
S-12, S16 – S26 *(step 1)* **12, 16 – 26**

condition A:
6 equiv CuTC, NMP
reflux, 2h

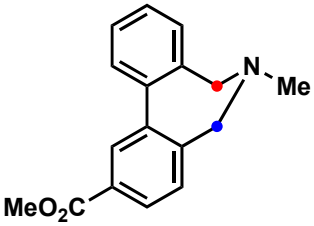
condition B:
1 equiv $NiBr_2(PPh_3)_2$
Et_4NI, Zn, THF
50 ºC, 2h

condition C:
6 equiv Cu, DMF
reflux, 2h

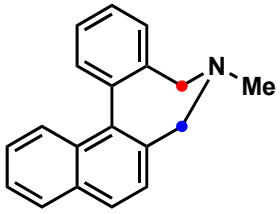
b) *accessible 1,1'-biaryl-linked azepines*



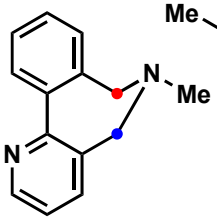
12
A: (**51%**)



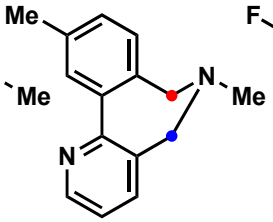
16
B: (**62%**)



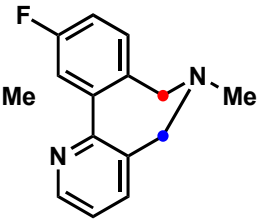
17
B: (**68%**)



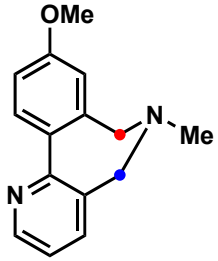
18
B: (**91%**)



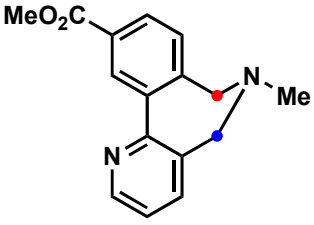
19
B: (**32%**)



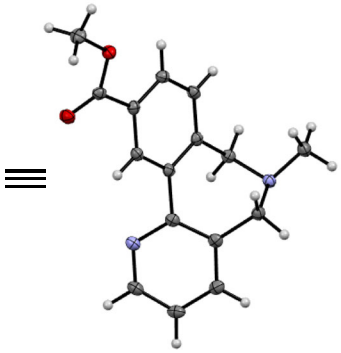
20
B: (**42%**)

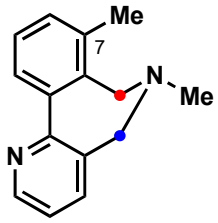


21
B: (**53%**)

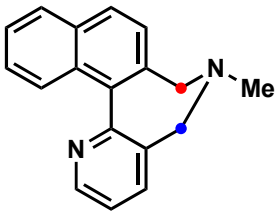


22
B: (**95%**)

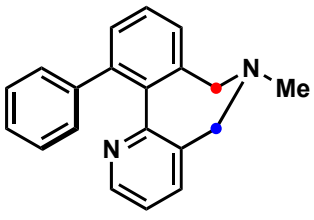




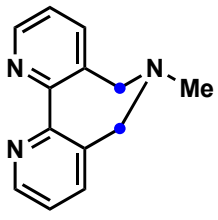
23
B: (**46%**)



24
B: (**54%**)

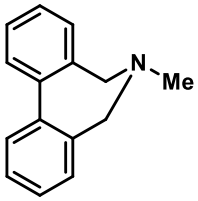


25
B: (**45%**)



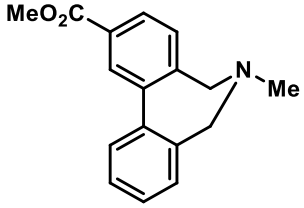
26
C: (**70%**)

6-methyl-6,7-dihydro-5*H*-dinemzobenzo[*c*-*e*]azepine (**12**)



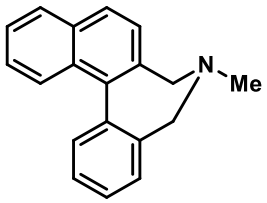
Using general procedure A with 23 mmol of tertiary amine, **S-12**, **12** was isolated as a yellow oil (2.47 g, 11.8 mmol, 51%) via flash column chromatography, with a mixture of 20:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.5 (5:1 EtOAc/MeOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.54 (d, *J* = 7.6 Hz, 1H), 7.50 – 7.45 (m, 1H), 7.42 – 7.38 (m,2H), 3.42 (s, 2H), 2.50 (s, 1H). **^{13}C NMR (124 MHz, $CDCl_3$):** δ 141.1, 134.3, 129.8, 128.2, 127.7, 57.2, 43.0. For prior characterization see: Enomoto, A., Shimbayashi, T., Fujita, K. *Heterocycles*, **98**, 1119.

Methyl 6-methyl-6,7-dihydro-5*H*-benzo[*c*]benzo[2,3-*e*]azepine-2-carboxylate (**16**)



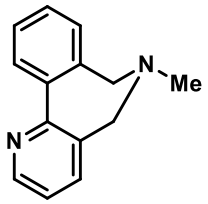
Using general procedure B with 1.6 mmol of tertiary amine, **S-16**, **16** was isolated as a yellow oil (0.27 g, 1.0 mmol, 62%) via flash column chromatography, with a mixture of 20:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.33 (5:1 EtOAc/MeOH). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.12 (t, *J* = 2.4 Hz, 1H), 7.98 (dt, *J* = 7.8, 2.5 Hz, 1H), 7.53 – 7.27 (m, 5H), 3.88 (s, 3H), 3.38 (s, 2H), 3.34 (s, 2H), 2.41 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 166.9, 141.3, 140.0, 138.6, 133.7, 130.3, 130.1, 130.0, 128.9, 128.6, 128.3, 128.0, 56.6, 56.4, 52.3, 42.6. **HRMS (ESI$^+$):** *Calcd.* for $C_{17}H_{18}NO_2$ $[M+H]^+$: 268.1338, found 268.1340.

6-methyl-6,7-dihydro-5*H*-benzo[*c*]naphtho[2,3-*e*]azepine (**17**)



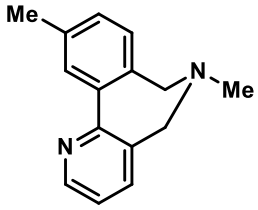
Using general procedure B with 0.67 mmol of tertiary amine, **S-17**, **17** was isolated as a yellow oil (0.12 g, 0.46 mmol, 68%) via flash column chromatography, with a mixture of 15:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.25 (5:1 EtOAc/MeOH). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.14 – 8.09 (m, 1H), 7.91 – 7.88 (m, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 7.62 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.51 – 7.39 (m, 8H), 3.65 (d, *J* = 12.6 Hz, 1H), 3.59 (d, *J* = 12.2 Hz, 1H), 3.28 (d, *J* = 12.6 Hz, 1H), 3.21 (d, *J* = 12.2 Hz, 1H), 2.44 (s, 4H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 138.4, 136.9, 135.1, 134.6 130.9, 130.8, 130.6, 130.2, 128.6, 128.2, 128.0, 128.0, 127.6, 126.5, 126.2, 125.9, 57.0, 56.5, 42.5. **HRMS (ESI$^+$):** *Calcd.* for $C_{19}H_{18}N$ $[M+H]^+$: 260.1339, found 260.1440.

6-methyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine (**18**)



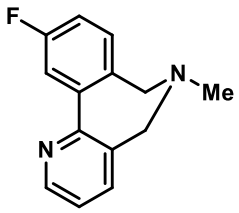
Using general procedure B with 2.4 mmol of tertiary amine, **S-18**, **18** was isolated as a brown oil (0.46 g, 2.1 mmol, 91%) via flash column chromatography, with a mixture of 3:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.25 (5:1 EtOAc/MeOH). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.66 (d, *J* = 4.8 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.41 (s, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.24 (dt, *J* = 9.0, 3.2 Hz, 1H), 3.40 (s, 2H), 3.32 (s, 2H), 2.44 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):** δ 158.6, 149.5, 140.2, 138.0, 130.1, 129.9, 129.5, 129.3, 128.8, 122.5, 56.6, 55.9, 42.5. **HRMS (ESI$^+$):** *Calcd.* for $C_{14}H_{15}N_2$ $[M+H]^+$: 211.1235, found 211.1234.

6,10-dimethyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine (**19**)



Using general procedure B with 6.0 mmol of tertiary amine **S-19**, **19** was isolated as a grey oil (0.72 g, 2.1 mmol, 35%) via flash column chromatography, with a mixture of 10:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.28 (5:1 EtOAc/MeOH): **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.72 – 8.67 (m, 1H), 7.71 – 7.64 (m, 2H), 7.30 – 7.21 (m, 3H), 3.41 (s, 4H), 3.35 (s, 2H), 2.47 (s, 3H), 2.45 (s, 3H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):** δ 158.9, 149.1, 140.0, 138.1, 137.6, 131.7, 130.5, 129.8, 129.8, 128.8, 122.3, 56.8, 56.5, 43.2, 21.3. **HRMS (ESI$^+$):** *Calcd.* for $C_{15}H_{17}N_2$ $[M+H]^+$: 225.1392, found 225.1396.

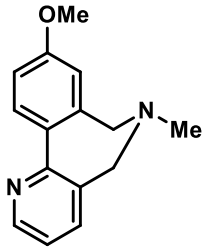
10-fluoro-6-methyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine (**20**)



Using general procedure B with 5.2 mmol of tertiary amine, **S-20**, **20** was isolated as a grey oil (0.50 g, 2.2 mmol, 42%) via flash column chromatography, with a mixture of 10:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.28 (5:1 EtOAc/MeOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.65 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.55 (td, *J* = 9.5, 3.2 Hz, 1H), 7.25 (qd, *J* = 10.2, 9.5, 5.0 Hz, 3H), 7.07 (tt, *J* = 10.0, 5.0 Hz, 2H), 3.35 (s, 2H), 3.31 (s, 2H), 2.42 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 162.7 (d, J_{CF} = 246.5 Hz), 157.6, 149.0 (d, J_{CF} = 2.8 Hz), 142.3 (d, J_{CF} = 8.0 Hz), 137.6, 131.2 (d, J_{CF} = 8.1 Hz), 130.4, 128.6 (d, J_{CF}

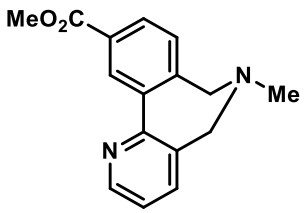
= 11.9 Hz), 122.6, 115.6 (d, J_{CF} = 21.5 Hz), 115.1 (d, J_{CF} = 22.4 Hz), 56.3, 56.2, 42.9. **HRMS (ESI$^+$):** *Calcd.* for $C_{14}H_{14}FN_2$ $[M+H]^+$: 229.1141, found 229.1145.

9-methoxy-6-methyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine (**21**)



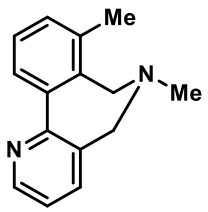
Using general procedure B with 4.7 mmol of tertiary amine, **S-21**, **21** was isolated as a dark-green oil (0.54 g, 2.5 mmol, 53%) via flash column chromatography, with a mixture of 20:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.33 (5:1 EtOAc/MeOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.66 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.65 (dd, *J* = 7.4, 1.7 Hz, 1H), 7.22 (dd, *J* = 7.4, 4.7 Hz, 1H), 7.03 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.89 (d, *J* = 2.6 Hz, 3H), 3.87 (s, 4H), 3.42 (s, 2H), 3.36 (s, 2H), 2.49 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 160.1, 158.5, 148.8, 137.3, 136.0, 132.8, 129.9, 129.5, 121.6, 115.1, 113.4, 57.2, 56.6, 55.3, 43.2. **HRMS (ESI$^+$):** *Calcd.* for $C_{15}H_{17}N_2O$ $[M+H]^+$: 241.1341, found 241.1343.

Methyl 6-methyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine-10-carboxylate (**22**)



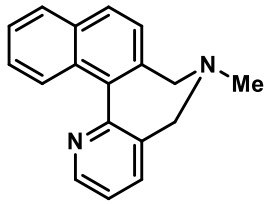
Using general procedure B with 1.9 mmol of tertiary amine, **S-22**, **22** was isolated as a white solid (0.48 g, 1.8 mmol, 95%) via flash column chromatography, with a mixture of 7:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.33 (5:1 EtOAc/MeOH). The solid was subsequently recrystallized from a hot solution of 7:1 EtOAc/MeoH to give colorless crystals suitable for x-ray structure determination (See S67). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.68 (d, *J* = 5.1 Hz, 1H), 8.50 (d, *J* = 7.3 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.25 (dt, *J* = 11.4, 5.7 Hz, 1H), 3.89 (s, 2H), 3.43 (s, 2H), 3.30 (s, 2H), 2.43 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 166.7, 157.7, 149.2, 140.4, 139.2, 137.5, 130.4, 130.3, 130.0, 129.9, 129.5, 122.6, 56.7, 56.3, 52.1, 43.1. **HRMS (ESI$^+$):** *Calcd.* for $C_{16}H_{17}N_2O_2$ $[M+H]^+$: 269.1290, found 269.1295.

6,8-dimethyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine (**23**)



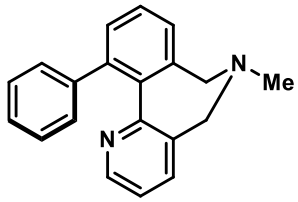
Using general procedure B with 1.3 mmol of tertiary amine, **S-23**, **23** was isolated as a brown oil (0.13 g, 0.6 mmol, 46%) via flash column chromatography, with a mixture of 10:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.28 (5:1 EtOAc/MeOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.61 (d, *J* = 4.8 Hz, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.26 – 7.14 (m, 3H), 7.08 (d, *J* = 6.9 Hz, 1H), 3.41 (d, *J* = 15.1 Hz, 2H), 3.06 (dd, *J* = 38.7, 12.5 Hz, 2H), 2.42 (s, 3H), 2.32 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 158.7, 148.0, 137.8, 137.0, 136.8, 134.1, 131.0, 130.9, 128.4, 127.2, 121.9, 57.0, 55.8, 42.8, 20.5. **HRMS (ESI^+):** *Calcd.* for $C_{15}H_{17}N_2$ $[M+H]^+$: 225.1392, found 225.1397.

6-methyl-6,7-dihydro-5*H*-naphtho[2,1-*c*]pyrido[2,3-*e*]azepine (**24**)



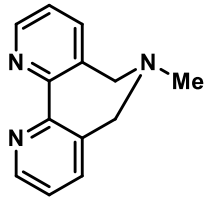
Using general procedure B with 2.4 mmol of tertiary amine, **S-24**, **24** was isolated as a brown oil (0.34 g, 1.3 mmol, 54%) via flash column chromatography, with a mixture of 7:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.22 (5:1 EtOAc/MeOH). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.81 – 8.76 (m, 1H), 8.41 (d, *J* = 8.1 Hz, 1H), 7.88 (t, *J* = 7.6 Hz, 2H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.48 (dd, *J* = 6.5, 2.9 Hz, 2H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.35 – 7.27 (m, 1H), 3.61 (d, *J* = 12.9 Hz, 1H), 3.54 (d, *J* = 12.1 Hz, 1H), 3.33 (d, *J* = 13.0 Hz, 1H), 3.08 (d, *J* = 12.1 Hz, 1H), 2.43 (s, 2H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 158.3, 148.6, 137.6, 135.3, 134.0, 132.1, 131.1, 129.5, 128.3, 127.8, 127.0, 126.4, 125.9, 122.3, 56.9, 55.9, 42.8. **HRMS (ESI^+):** *Calcd.* for $C_{18}H_{17}N_2$ $[M+H]^+$: 261.1392, found 261.1393.

6-methyl-11-phenyl-6,7-dihydro-5*H*-benzo[*c*]pyrido[2,3-*e*]azepine (**25**)



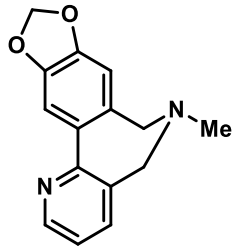
Using general procedure B with 1.1 mmol of tertiary amine, **S-25**, **25** was isolated as a yellow solid (0.14 g, 0.5 mmol, 45%) via flash column chromatography, with a mixture of 5:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.3 (2:1 EtOAc/MeOH). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.25 (d, *J* = 5.3 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.47 (dt, *J* = 15.1, 7.8 Hz, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 7.0 Hz, 3H), 7.10 – 7.03 (m, 3H), 3.60 (dd, *J* = 50.3, 12.5 Hz, 2H), 3.32 (dd, *J* = 51.5, 12.5 Hz, 2H), 2.46 (s, 3H). **^{13}C {1H} NMR (125 MHz, $CDCl_3$):** δ 158.3, 148.1, 141.6, 141.3, 137.4, 136.5, 134.4, 130.8, 130.7, 129.2, 128.6, 128.6, 127.8, 126.1, 121.7, 56.9, 55.9, 42.8. **HRMS (ESI^+):** *Calcd.* for $C_{20}H_{19}N_2$ $[M+H]^+$: 287.1548, found 287.1551.

6-methyl-6,7-dihydro-5*H*-dipyrido[3,2-*c*:2',3'-*e*]azepine (**26**)



Using general procedure C with 1.35 mmol of tertiary amine, S-**26**, **26** was isolated as a yellow oil (0.65 g, 0.95 mmol, 70%) via flash column chromatography, with a mixture of 15:1 ethyl acetate/ methanol as the eluent. $\mathbf{R_f}$ = 0.43 (5:1 EtOAc/MeOH). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.56 (d, *J* = 4.6 Hz, 1H), 7.43 (d, *J* = 7.8 Hz, 1H), 7.08 (td, *J* = 4.9, 2.3 Hz, 1H), 3.13 (s, 1H), 2.20 (s, 1H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 157.2, 150.0, 137.8, 130.8 123.5, 56.1, 43.2. **HRMS (ESI+):** *Calcd.* for $C_{13}H_{14}N_3$ [M+H]+: 212.1188, found 212.1186

6-methyl-6,7-dihydro-5*H*-[1,3]dioxolo[4',5':4,5]benzo[1,2-*c*]pyrido[2,3-*e*]azepine (**46**)

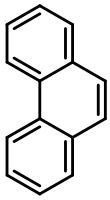


Using general procedure B with 2.9 mmol of tertiary amine, **45**, **46** was isolated as a white solid (0.34 g, 1.3 mmol, 45%) via flash column chromatography, with a mixture of 15:1 ethyl acetate/methanol as the eluent. $\mathbf{R_f}$ = 0.30 (5:1 EtOAc/MeOH). The solid was subsequently recrystallized from dichloromethane to give colorless crystals suitable for x-ray structure determination (See S78). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.62 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.61 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.33 (s, 1H), 7.19 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.77 (s, 1H), 5.98 (s, 2H), 3.30 (s, 2H), 3.28 (s, 2H), 2.42 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.4, 147.5, 147.4, 143.9, 138.7, 136.0, 131.2, 123.0, 114.7, 112.7, 110.3, 101.7, 61.2, 60.0, 42.3. **HRMS (ESI^+):** *Calcd.* for $C_{15}H_{15}N_2O_2$ $[M+H]^+$: 255.1134, found 255.1138.

Initial procedure for ring contraction

To a 25 mL oven dried round bottom flask equipped with a magnetic stir bar was added amine, **12** (0.5 g, 2.4 mmol, 1 equiv.), manganese (39.4 mg, 7.2 mmol, 3 equiv.), trimethylphosphate (1.18 mL, 1.34 g, 9.6 mmol, 4 equiv.) and DMF (48 mL, 0.05 M) under a positive flow of nitrogen. The flash was equipped with a reflux condenser and the entire mixture was stirred under nitrogen at 140 ˚C (oil bath) for 48 h. The mixture was then cooled to room temperature and quenched with 5 mL of 2 M NH_4OH. The mixture was extracted three times with ethyl acetate (20 mL × 3). The combined organic extract was washed with brine (10 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude material was then purified by flash column chromatography on a silica gel. Three different fractions containing both **14** and **15**, as these two compounds could not be separated. Combined mass of 236 mg was recovered. The combined product contained **15** and **14** in a 1:1.1 ratio as determined by ^{1}H NMR analysis. The corresponding peaks for **14** and **15** are identical to that reported in the literature[7,8]. The combined product was recrystallized from ether to afford pure **15** in 7% yield.

Phenanthrene (**15**)

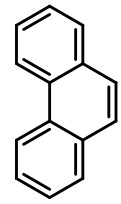


^{1}H NMR (400 MHz, $CDCl_3$): δ 8.72 (d, *J* = 8.0 Hz, 1H), 8.03 – 7.89 (m, 1H), 7.79 – 7.73 (m, 1H), 7.71 – 7.66 (m, 1H), 7.63 (td, *J* = 7.9, 2.4 Hz, 1H).

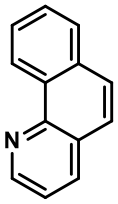
General procedure for ring contraction

Synthesis of benzoquinolines and phenanthrenes

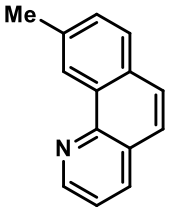
To a 25 mL oven dried round bottom flask equipped with a magnetic stir bar was added amine (0.50 mmol, 1 equiv.), manganese (110 mg, 2 mmol, 4 equiv.), trimethylphosphate (1.18 mL, 1.4 g, 10 mmol, 20 equiv.) and DMA (5 mL, 0.1 M) under a positive flow of nitrogen. The flash was equipped with a reflux condenser and the entire mixture was stirred under nitrogen at 140 ˚C (oil bath) for 48 h. The mixture was then cooled to room temperature and quenched with 5 mL of 2 M NH_4OH. The mixture was extracted three times with ethyl acetate (10 mL × 3). The combined organic extract was washed with brine (10 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude material was then purified by flash column chromatography on a silica gel to afford the desired product.



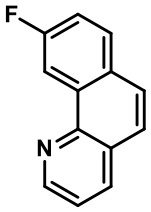
15 (40%)



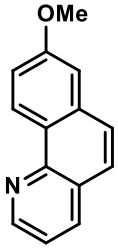
27 (40%)



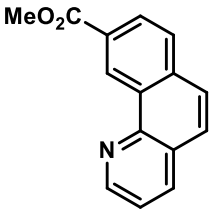
29 (12%)



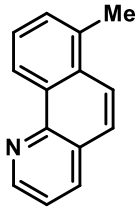
30 (22%)



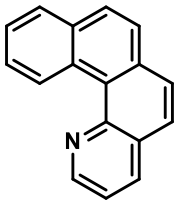
31 (16%)



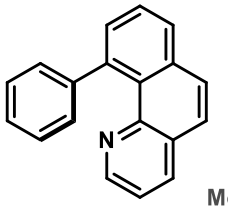
32 (17%)



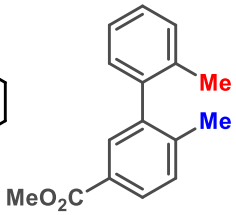
33 (<5%)



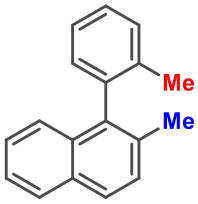
34 (7%)



35 (20%)

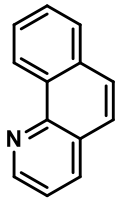


39 (73%)



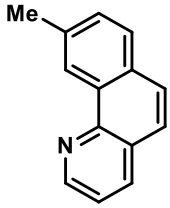
41 (47%)

Benzo[*h*]quinoline (**27**)



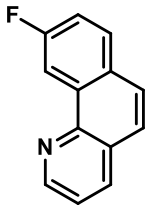
27 was isolated as a light yellow solid (36 mg, 0.2 mmol, 40%) via flash column chromatography, with a mixture of 50:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.38 (20:1 hexanes/EtOAc). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.33 (dd, *J* = 8.3, 1.5 Hz, 1H), 9.04 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.20 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 8.6 Hz, 1H), 7.81 – 7.75 (m, 3H), 7.59 – 7.52 (m, 1H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 149.0, 146.7, 136.0, 133.7, 131.6, 128.3, 128.0, 127.9, 127.2, 126.5, 125.5, 124.5, 121.9. Spectroscopic data for **27** match those previously reported in literature.[9]

9-methylbenzo[*h*]quinoline (**29**)



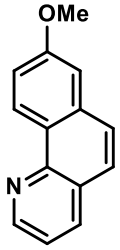
29 was isolated as a light yellow oil (11.4 mg, 0.06 mmol, 12%) via flash column chromatography, with a mixture of 50:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.38 (20:1 hexanes/EtOAc). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.08 – 9.03 (m, 1H), 8.96 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.13 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.76 (dd, *J* = 12.5, 8.5 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 1H), 7.54 – 7.44 (m, 2H), 2.62 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.7, 146.0, 137.1, 136.0, 132.8, 131.6, 130.0, 127.9, 127.8, 126.7, 124.5, 123.9, 121.8, 22.1. Spectroscopic data for **29** match those previously reported in literature.[10]

9-fluorobenzo[*h*]quinoline (**30**)



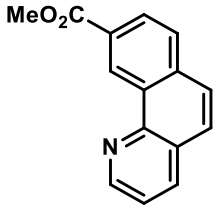
30 was isolated as a white solid (21.6 mg, 0.11 mmol, 22%) via flash column chromatography, with a mixture of 40:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.45 (20:1 hexanes/EtOAc).**^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.96 (dd, *J* = 4.3, 1.8 Hz, 1H), 8.88 (dd, *J* = 10.6, 2.7 Hz, 1H), 8.15 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.86 (dd, *J* = 8.8, 5.5 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.52 (dd, *J* = 8.1, 4.4 Hz, 1H), 7.41 (td, *J* = 8.5, 2.7 Hz, 1H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.0, 135.7, 132.5, 130.9, 129.93 (d, *J* = 8.8 Hz), 128.8, 127.1, 126.7, 124.5, 122.3, 117.35 (d, *J* = 24.4 Hz), 109.32 (d, *J* = 22.9 Hz). **^{19}F NMR (471 MHz, $CDCl_3$):** -111.6 (m). **HRMS (ESI^+):** *Calcd.* for $C_{13}H_9FN$ $[M+H]^+$: 198.0719, found 198.0719.

8-methoxybenzo[*h*]quinoline (**31**)



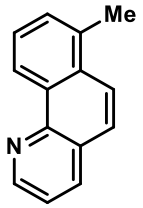
31 was isolated as a light yellow oil (16.8 mg, 0.08 mmol, 12%) via flash column chromatography, with a mixture of 50:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.38 (20:1 hexanes/EtOAc). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.16 (d, *J* = 9.0 Hz, 1H), 8.92 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.10 (dd, *J* = 9.1, 2.6 Hz 1H), 7.70 (d, *J* = 8.8 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.42 (dd, *J* = 8.0, 4.4 Hz, 1H), 7.33 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.26 – 7.20 (m, 1H), 3.94 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 159.7, 148.9, 135.8, 135.2, 129.5, 127.3, 126.1, 126.0, 125.9, 125.3, 120.9, 117.5, 107.9, 55.5. Spectroscopic data for **31** match those previously reported in literature.[9]

Methyl benzo[*h*]quinoline-9-carboxylate (3**2**)



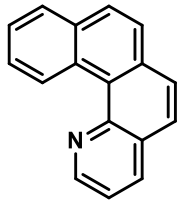
32 was isolated as a white oil (20 mg, 0.086 mmol, 17%) via flash column chromatography, with a mixture of 25:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.16 (20:1 hexanes/EtOAc). **^{1}H NMR (400 MHz, $CDCl_3$):** δ 9.96 (dt, *J* = 1.6, 0.7 Hz, 1H), 9.03 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.29 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.17 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.93 (d, *J* = 8.3 Hz, 1H), 7.85 – 7.73 (m, 2H), 7.54 (dd, *J* = 8.0, 4.4 Hz, 1H), 3.99 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 167.3, 149.4, 136.2, 136.1, 128.5, 128.5, 128.3, 128.1, 127.8, 127.3, 126.8, 126.6, 122.3, 52.3. **HRMS (ESI^+):** *Calcd.* for $C_{15}H_{12}NO_2$ $[M+H]^+$: 238.0868, found 238.0869.

7-methylbenzo[*h*]quinoline (**33**)



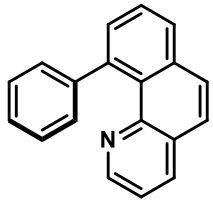
33 was isolated as a white solid (4 mg, 0.021 mmol, 4.1%) via flash column chromatography, with a mixture of 50:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.68 (20:1 hexanes/EtOAc). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 9.06 (dd, *J* = 4.3, 1.9 Hz, 1H), 8.19 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.82 (dd, *J* = 8.9, 5.7 Hz, 2H), 7.74 – 7.63 (m, 1H), 7.62 – 7.57 (m, 2H), 7.51 (dd, *J* = 8.0, 4.3 Hz, 1H), 3.38 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 149.1, 147.3, 138.9, 135.5, 135.3, 131.3, 130.1, 128.9, 127.6, 127.4, 126.9, 125.6, 120.9, 27.4. **HRMS (ESI^+):** *Calcd.* for $C_{14}H_{12}N$ $[M+H]^+$: 194.0970, found 194.0967.

Naphtho[2,1-*h*]quinoline (**34**)



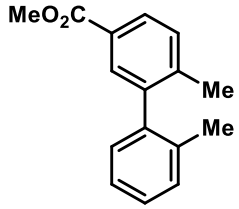
34 was isolated as a white solid (8.2 mg, 0.036 mmol, 7%) via flash column chromatography, with a mixture of 50:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.52 (20:1 hexanes/EtOAc). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 11.23 (d, *J* = 8.8 Hz, 1H), 9.25 (dd, *J* = 4.2, 1.9 Hz, 1H), 8.34 (dd, *J* = 8.0, 1.9 Hz, 1H), 8.05 (t, *J* = 8.2 Hz, 2H), 8.00 (d, *J* = 8.5 Hz, 1H), 7.92 (dd, *J* = 10.2, 8.5 Hz, 2H), 7.87 (dd, *J* = 6.9, 1.7 Hz, 1H), 7.71 (td, *J* = 7.4, 6.7, 1.3 Hz, 1H), 7.60 (dd, *J* = 8.1, 4.2 Hz, 1H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 148.6, 148.5, 136.6, 134.1, 133.8, 131.8, 130.8, 130.0, 128.8, 128.6, 128.0, 127.5, 127.1, 126.7, 126.6, 126.4, 120.7. **HRMS (ESI$^+$):** *Calcd.* for $C_{17}H_{12}N$ $[M+H]^+$: 230.0970, found 230.0973.

10-phenylbenzo[*h*]quinoline (**35**)



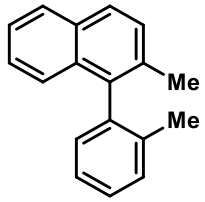
35 was isolated as a colorless oil (25 mg, 0.1 mmol, 20%) via flash column chromatography, with a mixture of 50:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.52 (20:1 hexanes/EtOAc). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.25 (d, *J* = 5.3 Hz, 1H), 7.64 (d, *J* = 7.6 Hz, 1H), 7.47 (dt, *J* = 15.1, 7.8 Hz, 2H), 7.31 (d, *J* = 7.3 Hz, 1H), 7.19 (d, *J* = 7.0 Hz, 3H), 7.10 – 7.03 (m, 3H), 3.66 (d, *J* = 12.0 Hz, 1H), 3.55 (d, *J* = 13.0 Hz, 1H), 3.37 (d, *J* = 11.7 Hz, 1H), 3.27 (d, *J* = 13.1 Hz, 1H), 2.46 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 147.0, 147.0, 146.6, 141.9, 135.3, 135.1, 131.6, 129.2, 128.9, 128.4, 128.1, 127.5, 127.4, 127.2, 126.1, 125.8, 121.2. **HRMS (ESI$^+$):** *Calcd.* for $C_{19}H_{14}N$ $[M+H]^+$: 256.1126, found 256.1127.

Methyl 2',6-dimethyl-[1,1'-biphenyl]-3-carboxylate (**39**)



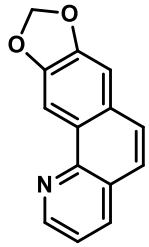
39 was isolated as a colorless oil (44 mg, 0.18 mmol, 73%) via flash column chromatography, with a mixture of 60:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.55 (20:1 hexanes/EtOAc). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.97 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.84 (d, *J* = 1.9 Hz, 1H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.11 (dd, *J* = 7.1, 1.1 Hz, 1H), 3.92 (s, 3H), 2.14 (s, 3H), 2.07 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 167.3, 141.9, 141.8, 140.6, 135.8, 130.6, 130.1, 130.1, 129.3, 128.5, 127.8, 127.7, 125.8, 52.1, 20.2, 19.9. **HRMS (ESI$^+$):** *Calcd.* for $C_{16}H_{17}NaO_2$ $[M+H+Na]^+$: 263.1048, found 263.1056.

2-methyl-1-o(tolyl)naphthalene (**40**)



40 was isolated as a colorless oil (54 mg, 0.24 mmol, 47%) via flash column chromatography, with hexanes as the eluent (mixture of atropisomers). $\mathbf{R_f}$ = 0.53 (50:1 hexanes/EtOAc).**^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.34 (d, *J* = 8.4 Hz, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 8.7 Hz, 1H), 7.90 – 7.84 (m, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.67 (ddd, *J* = 8.5, 6.9, 1.4 Hz, 1H), 7.61 (ddd, *J* = 8.1, 6.8, 1.2 Hz, 1H), 7.52 (s, 1H), 7.48 – 7.40 (m, 2H), 7.41 – 7.36 (m, 2H), 7.37 – 7.30 (m, 2H), 7.26 (d, *J* = 8.5 Hz, 1H), 7.18 – 7.11 (m, 1H), 2.19 (s, 3H), 1.94 (s, 3H). **^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$):** δ 139.2, 138.0, 137.5, 136.8, 134.7, 133.1, 132.5, 132.0, 131.2, 130.1, 130.0, 129.0, 128.6, 128.4, 128.4, 128.3, 128.0, 127.8, 127.4, 127.1, 126.8, 126.0, 125.9, 125.7, 124.8, 41.3, 29.8, 20.4, 19.6.

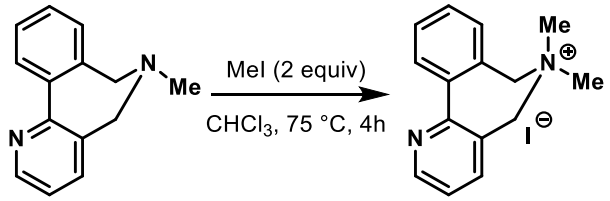
[1,3]dioxolo[4',5':4,5]benzo[1,2-*h*]quinoline (**42**)



42 was isolated as a colorless oil (11.6 mg, 0.05 mmol, 10%) via flash column chromatography, with a mixture of 60:1 hexanes/EtOAc as the eluent. $\mathbf{R_f}$ = 0.55 (20:1 hexanes/EtOAc). **^{1}H NMR (500 MHz, CDCl$_3$):** δ 8.95 (dd, *J* = 4.4, 1.9 Hz, 1H), 8.66 (s, 1H), 8.16 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.70 (d, *J* = 8.7 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 1H), 7.47 (dd, *J* = 7.9, 4.5 Hz, 1H), 7.27 (s, 1H), 7.27 (s, 1H), 6.15 (s, 2H). **^{13}C{^{1}H} NMR (125 MHz, CDCl$_3$):** δ 149.1, 148.7, 148.5, 136.0, 130.5, 127.3, 125.8, 123.9, 121.2, 105.2, 102.5, 101.6. **HRMS (ESI$^+$):** *Calcd.* for $C_{14}H_{10}NO_2$ $[M+H]^+$: 224.0712, found 224.0712.

Mechanistic studies

Methylation of azepine (**18**)

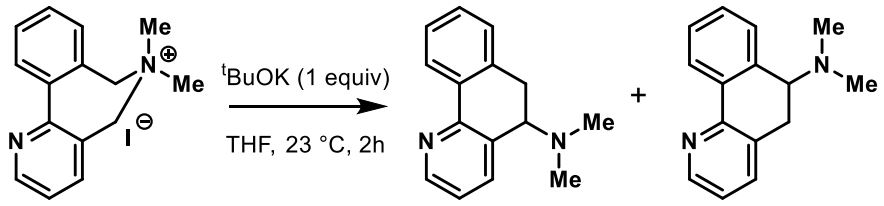


18 **36**

To a 25 mL round flask was added amine **18** (200 mg, 0.95 mmol), chloroform (5 mL, 0.2 M). Methyl iodide (0.12 mL, 274 mg, 1.9 mmol) was added dropwise. The flask was then equipped with a reflux condenser and the entire mixture refluxed overnight. The mixture was cooled and then 5 mL ether was added to the mixture. The resulting solid was filtered off and dried under vacuum to afford **36** as a yellow solid (187 mg, 0.53 mmol, 56%). **^{1}H NMR (400 MHz, CDCl$_3$):** δ 8.87 (d, *J* = 4.8 Hz, 1H), 8.23 (d, *J* = 7.6

Hz, 2H), 8.01 (d, *J* = 7.7 Hz, 2H), 7.69 (d, *J* = 8.2 Hz, 3H), 7.59 (t, *J* = 7.5 Hz, 2H), 7.46 (dd, *J* = 7.7, 5.0 Hz, 2H), 4.45 (s, 3H), 4.27 (s, 3H), 3.69 (s, 9H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 158.2, 152.4, 140.2, 140.1, 131.9, 131.9, 130.9, 129.9, 127.3, 123.8, 123.7, 65.7, 64.1, 54.0, 51.6. **HRMS (ESI$^+$):** *Calcd.* for $C_{15}H_{17}N_2$ [M-I]: 225.1392, found 225.1395.

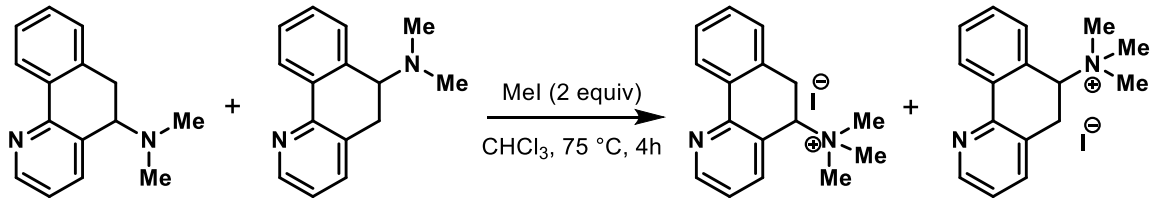
Procedure for [1,2]-Stevens rearrangement towards the synthesis of (Int-**37ab**)



36 **37ab** major minor

To a 25 mL round flask under nitrogen was added **26** (150 mg, 0.42 mmol), tetrahydrofuran (6 mL, 0.07 M), potassium tert-butoxide (47 mg, 0.42 mmol). The mixture was stirred at room temperature for 2 h. The solvent was then removed under reduced pressure and the residue dissolved in ethyl acetate (10 mL). The organic layer was washed with water (5 mL x 2) and dried over anhydrous Na_2SO_4. The solvent was again removed under reduced pressure and the crude product was purified by flash column chromatography with a 5:1 mixture of hexanes and ethyl acetate. **37ab** was obtained as a yellow oil (48 mg, 0.21 mmol, 51%) in a 9:1 ratio of regioisomers as determined by ^{1}H NMR spectroscopy. **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.52 – 8.43 (m, 1H), 8.34 (d, *J* = 7.6 Hz, 1H), 7.46 (d, *J* = 7.9 Hz, 1H), 7.40 – 7.31 (m, 3H), 7.08 (dd, *J* = 7.5, 4.8 Hz, 1H), 3.64 (t, *J* = 5.5 Hz, 1H), 3.07 (d, *J* = 5.7 Hz, 1H), 3.00 (d, *J* = 5.5 Hz, 1H), 2.17 (s, 6H). **^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$):** δ 152.0, 147.7, 136.9, 135.7, 134.7, 130.3, 128.9, 128.1, 125.1, 122.5, 61.56, 42.2, 29.4. **HRMS (ESI$^+$):** *Calcd.* for $C_{15}H_{17}N_2$ $[M+H]^+$: 225.1392, found 225.1395.

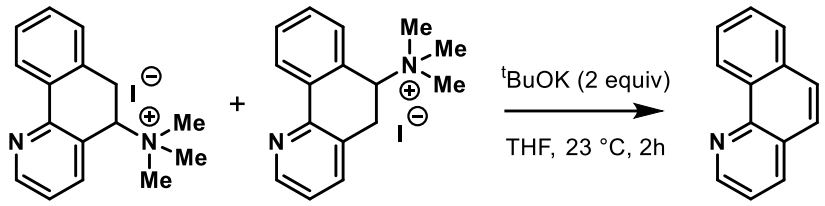
Methylation of [1,2]-Stevens rearrangement product



37a major **37b** minor **38a** major **38b** minor

To a 25 mL round bottom flask was added amine (24.2 mg, 0.1mmol), ethyl acetate (5 mL, 0.02 M). Methyl iodide (12.5 µL, 28.2 mg, 0.2 mmol) was added dropwise. The mixture stirred at room temperature for 2 h. The resulting solid was filtered off and dried under vacuum to afford **38a** and **38b** as a white solid solid (24.5 mg, 0.061 mmol, 61%). **^{1}H NMR (500 MHz, $CDCl_3$):** δ 8.64 (d, *J* = 5.0 Hz, 1H), 8.55 (s, 1H), 8.10 (d, *J* = 7.3 Hz, 1H), 7.97 (d, *J* = 7.4 Hz, 1H), 7.70 (d, *J* = 7.3 Hz, 1H), 7.55 (d, *J* = 7.1 Hz, 1H), 7.31 (dd, *J* = 9.5, 4.7 Hz, 1H), 5.73 (d, *J* = 5.8 Hz, 1H), 4.19 (d, *J* = 18.8 Hz, 1H), 3.55 (dq, *J* = 18.7, 5.8 Hz, 1H), 3.31 (s, 8H). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$):** δ 150.6, 149.4, 136.5, 136.3, 133.6, 132.3, 129.9, 127.0, 126.4, 125.8, 124.3, 69.4, 52.5, 29.0. **HRMS (ESI$^+$):** *Calcd.* for $C_{16}H_{19}N_2$ [M-I]: 239.1548, found 239.1550.

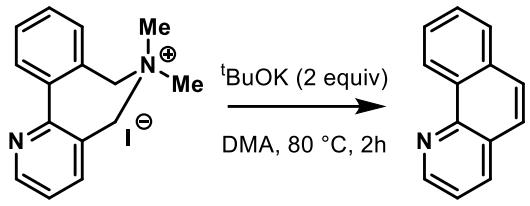
Hofmann elimination



38a **38a** **27**

To a 25 mL round bottom flask was added ammonium salt (14 mg, 0.038 mmol), ethyl acetate (1 mL, 0.04 M). The entire mixture was stirred at 120 ˚C (oil bath) for 2 h. The mixture was then cooled to room temperature and quenched with 1 mL of 2 M NH_4OH. The mixture was extracted three times with ethyl acetate (5 mL × 3). The combined organic extract was washed with brine (5 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude material was then purified by flash column chromatography with a mixture of 50:1 hexanes/EtOAc to afford **27** (5.2 mg, 0.29 mmol, 76%).

Procedure for [1,2]-Stevens rearrangement/Hofmann sequence



36 **27**

To a 25 mL round bottom flask was added ammonium salt (23 mg, 0.065 mmol), DMA (1 mL, 0.07 M), potassium tert-butoxide (15.7 mg, 0.13 mmol). The entire mixture was stirred at 80 ˚C (oil bath) for 2 h. The mixture was then cooled to room temperature and quenched with 1 mL of 2 M NH_4OH. The mixture was extracted three times with ethyl acetate (5 mL × 3). The combined organic extract was washed with brine (5 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude material was then purified by flash column chromatography with a mixture of 50:1 hexanes/EtOAc to afford **27** (10.9 mg, 0.061 mmol, 93%).

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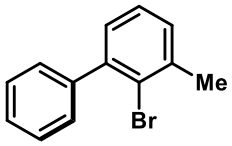
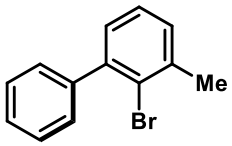
^{1}H and $^{13}C\{^{1}H\}$ NMR Spectra

400 MHz, $CDCl_3$



A



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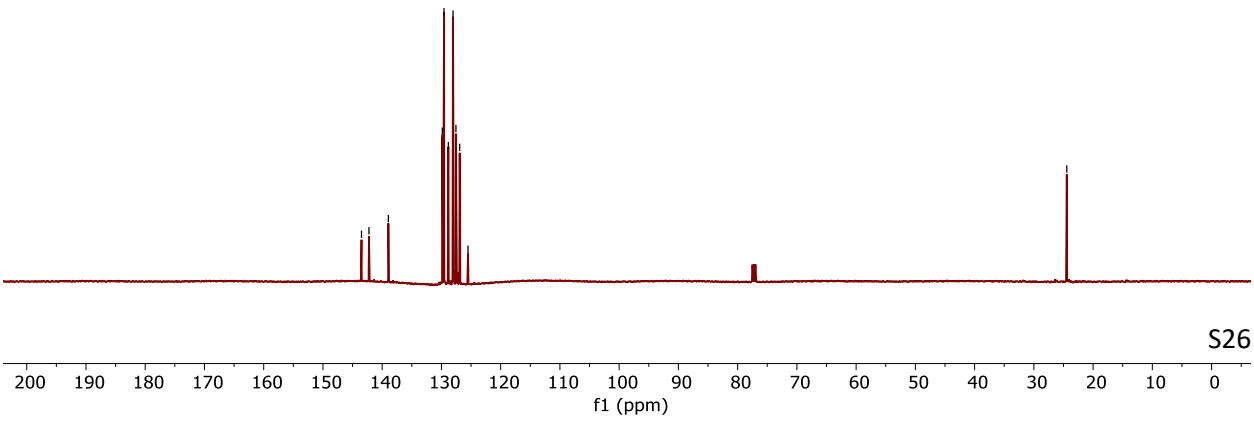

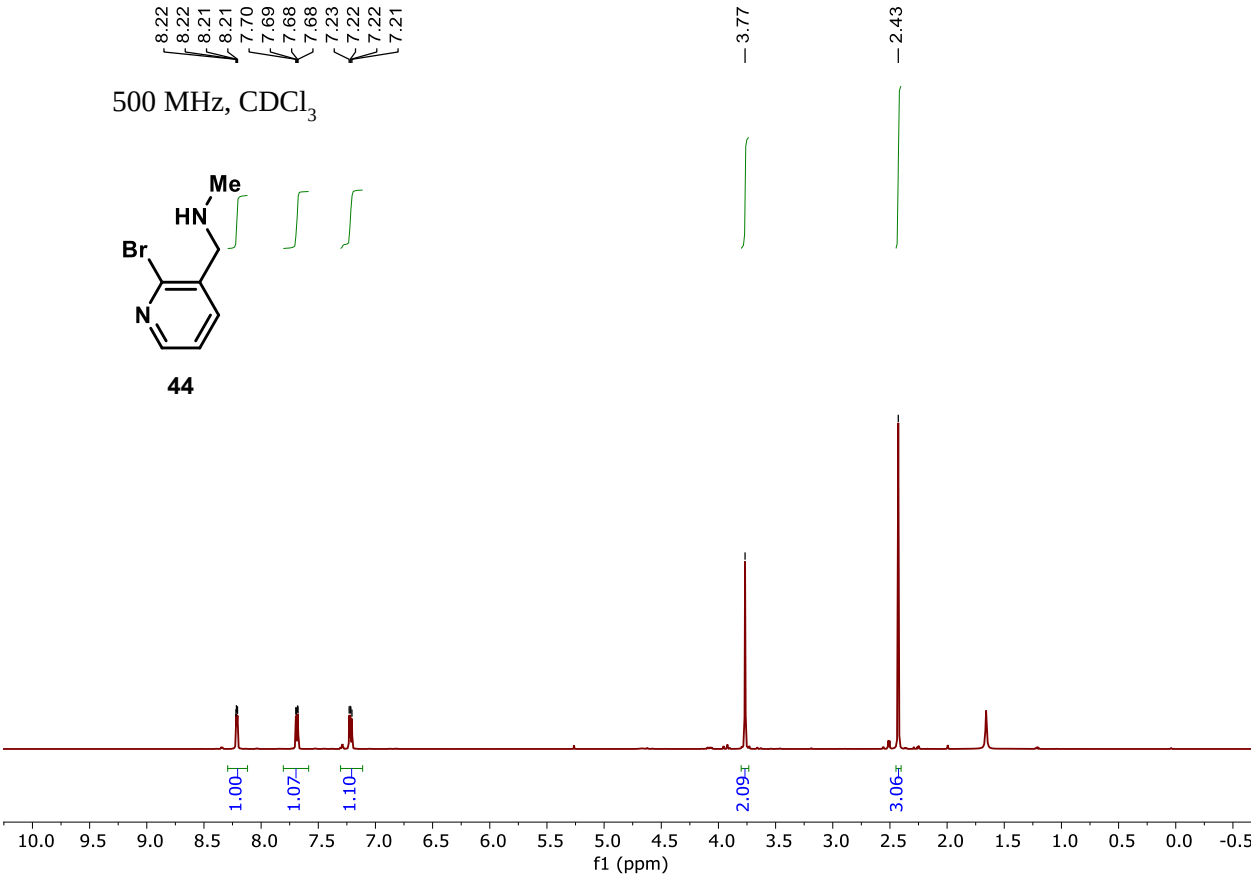
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7.70
7.69
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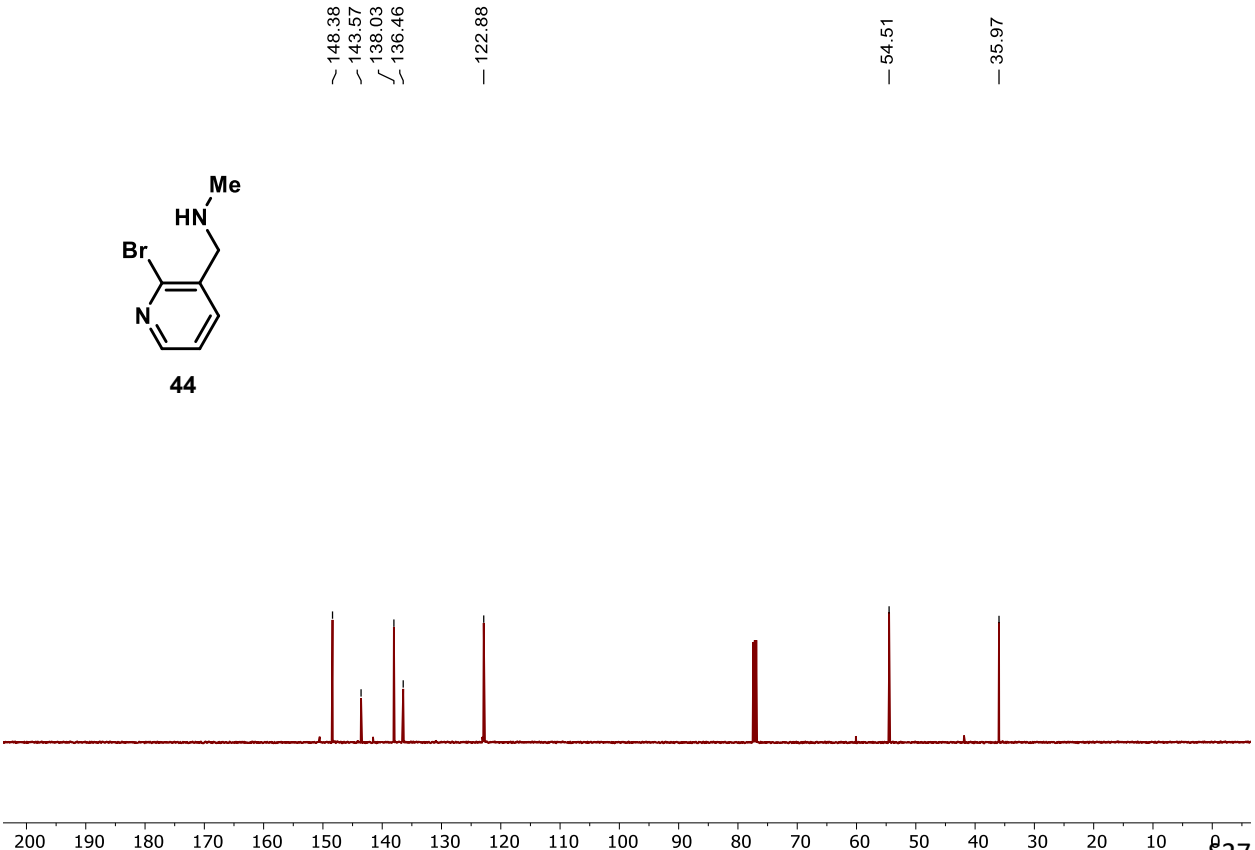
7.68
7.23
7.22
7.22
7.21
3.77
2.43
500 MHz, CDCl3
Me
HN
Br
N
44
1.00
1.07
1.10
2.09
3.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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143.57
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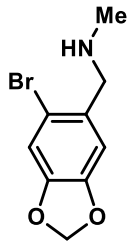
54.51
35.97
Me
HN
Br
N
44
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

500 MHz, $CDCl_3$



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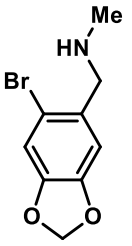

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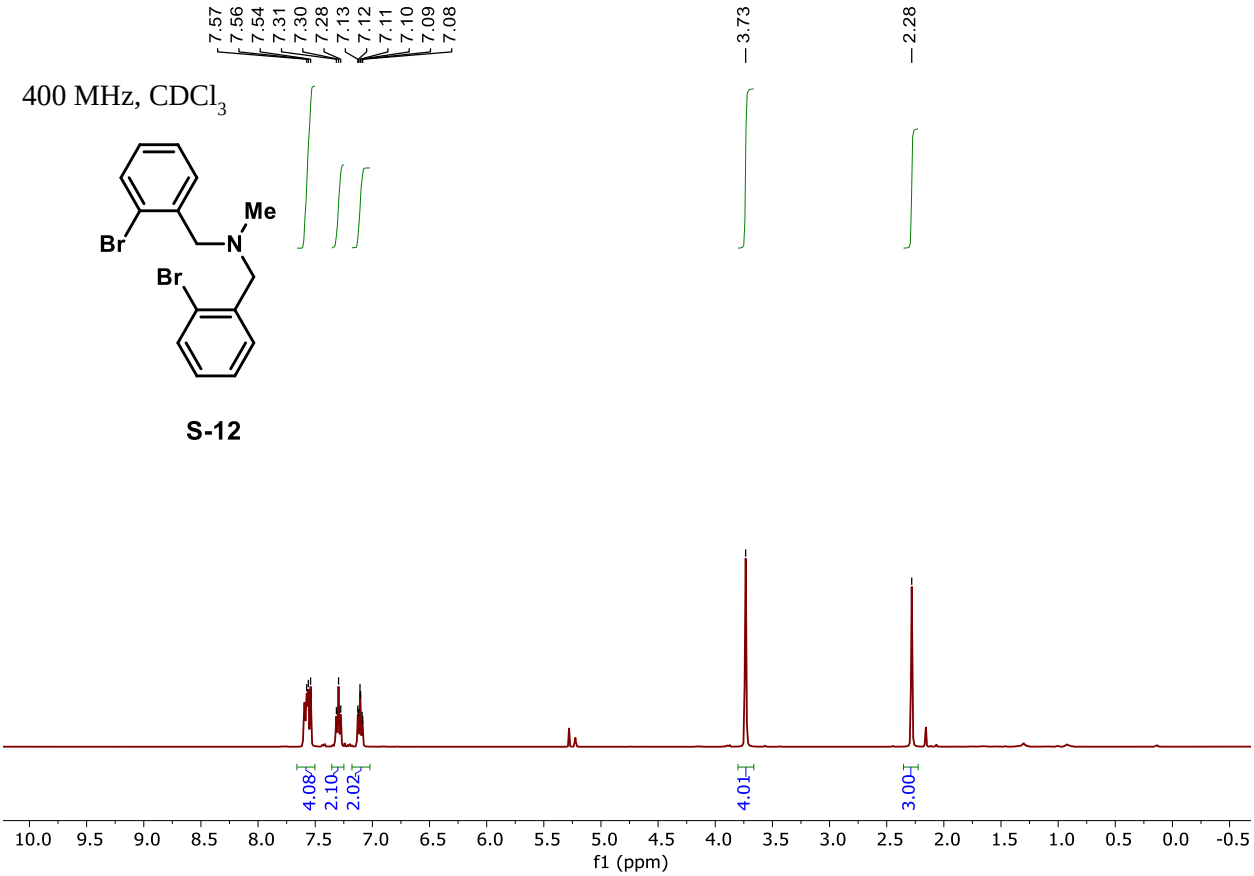
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7.10
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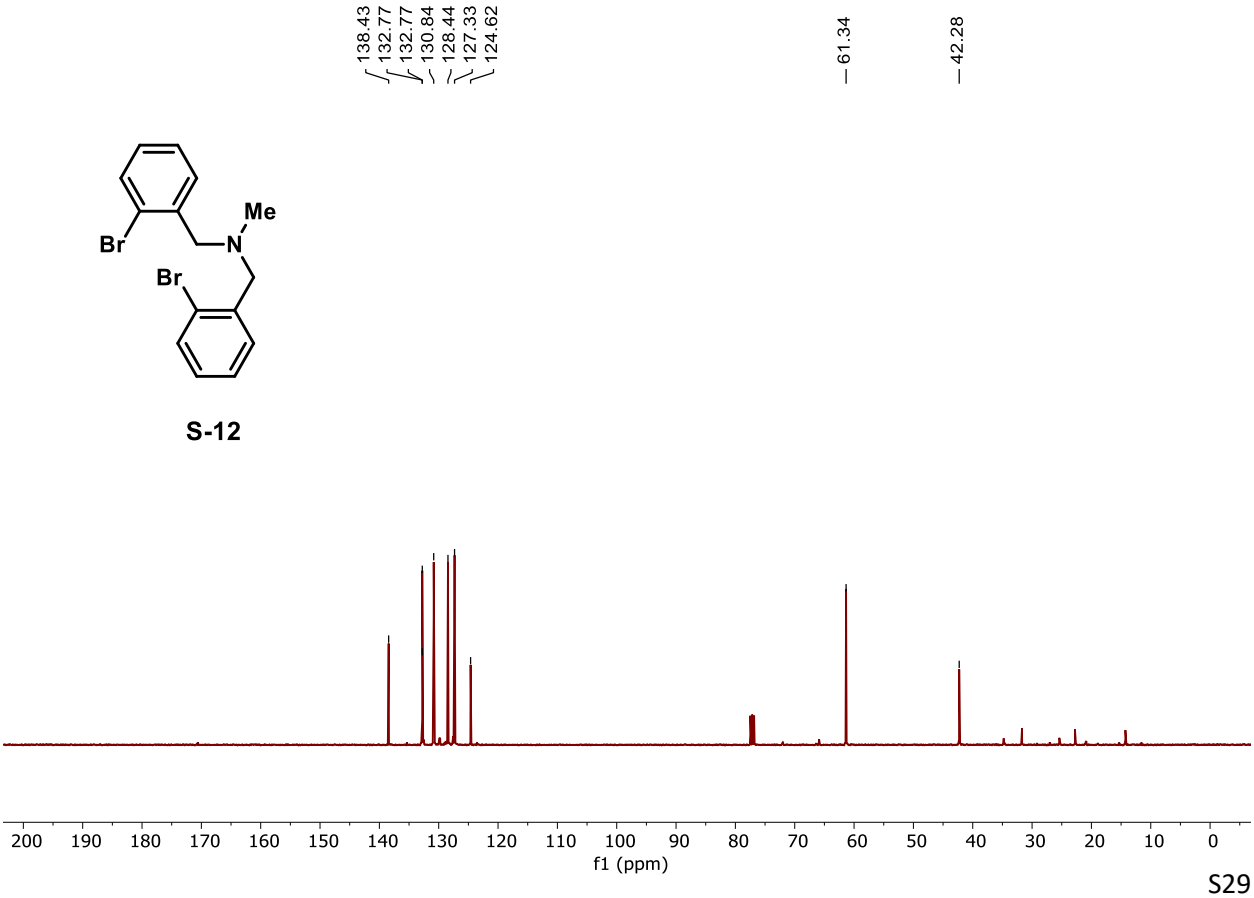
7.08
3.73
2.28
400 MHz, CDCl3
Me
N
Br
Br
S-12
4.08
2.10
2.02
4.01
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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Br
Br
S-12
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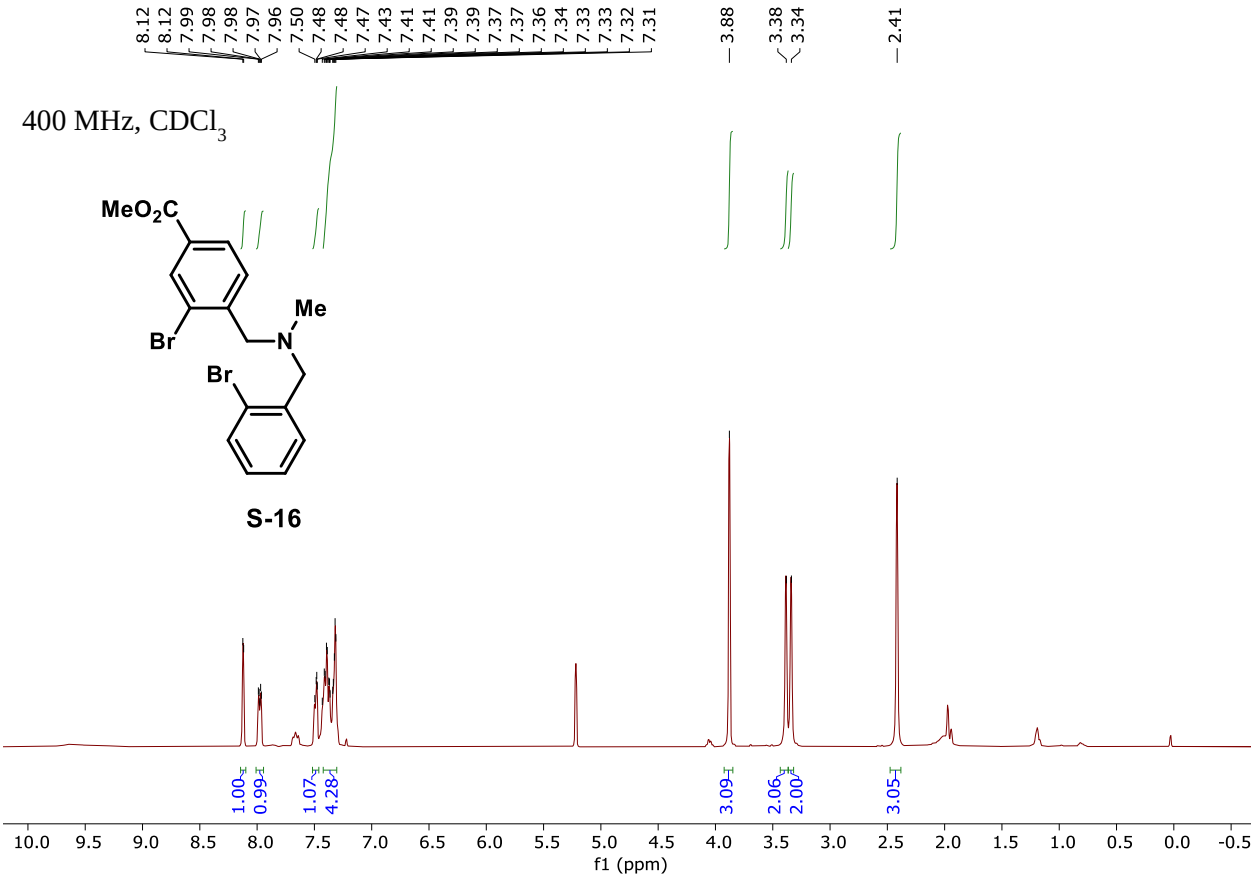
f1 (ppm)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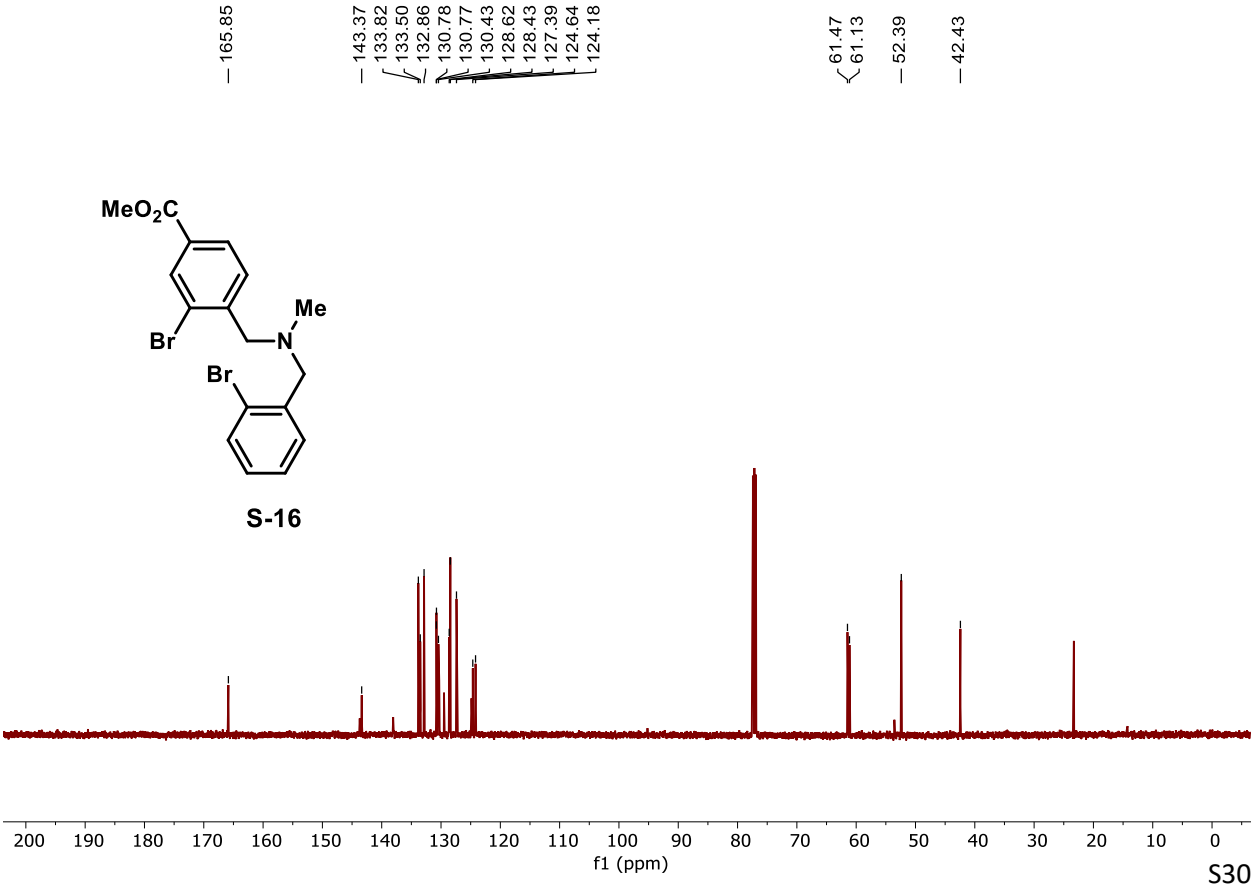
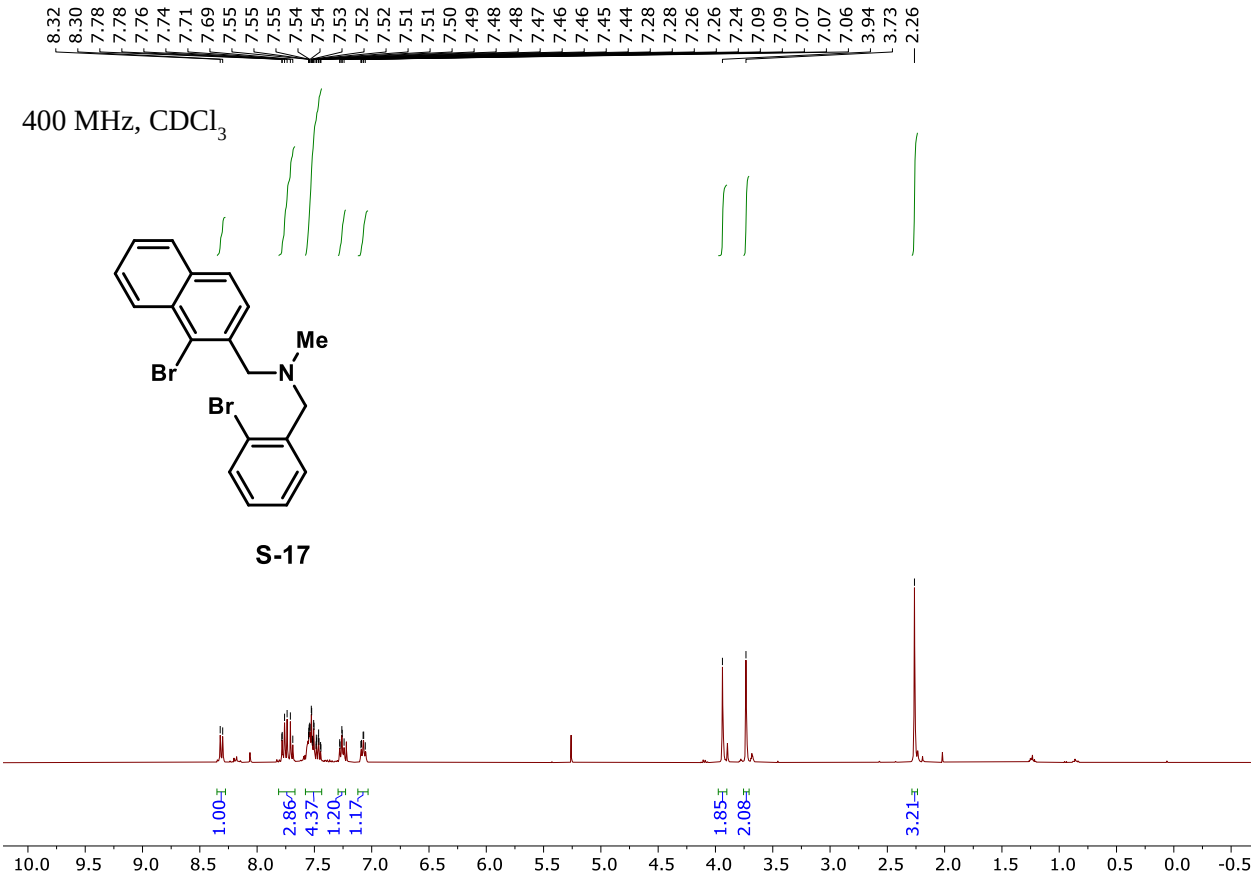
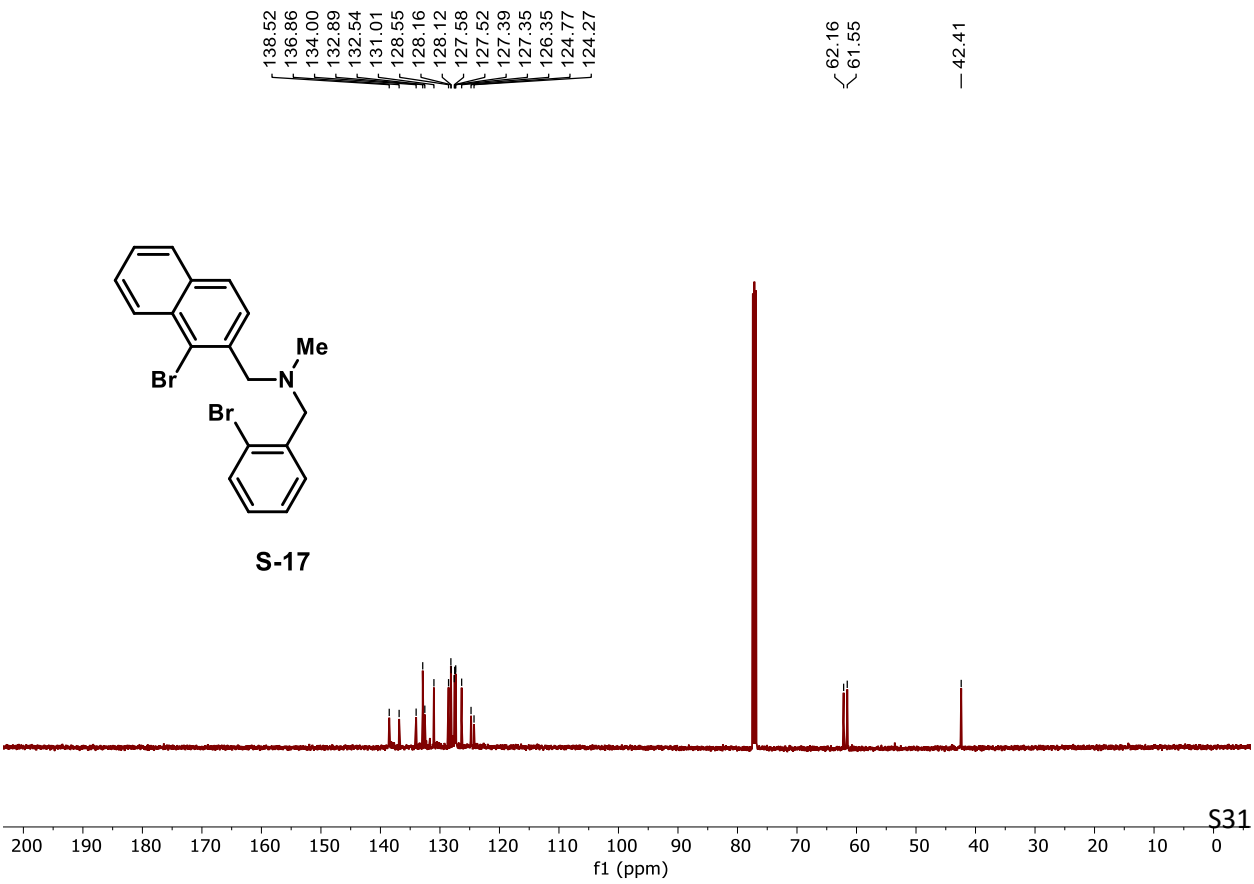
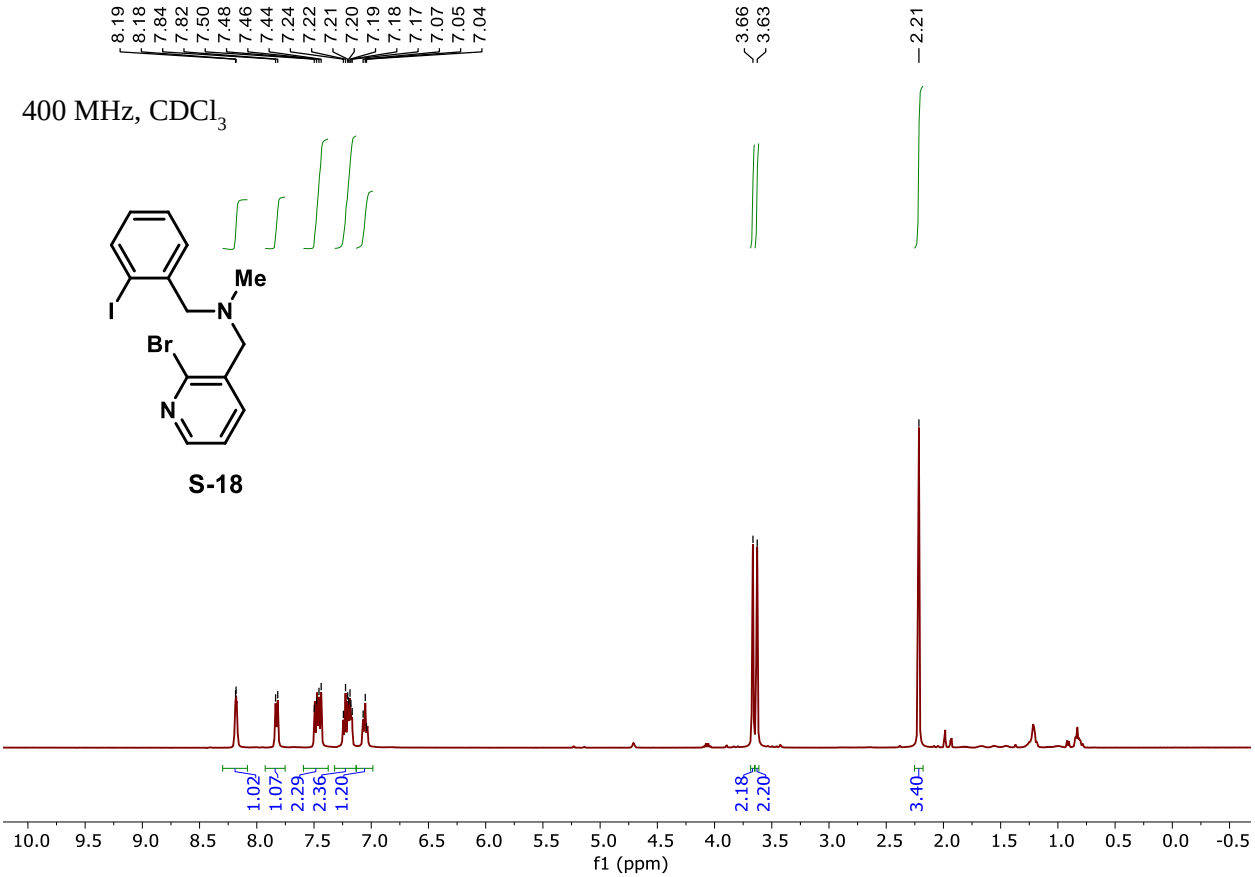
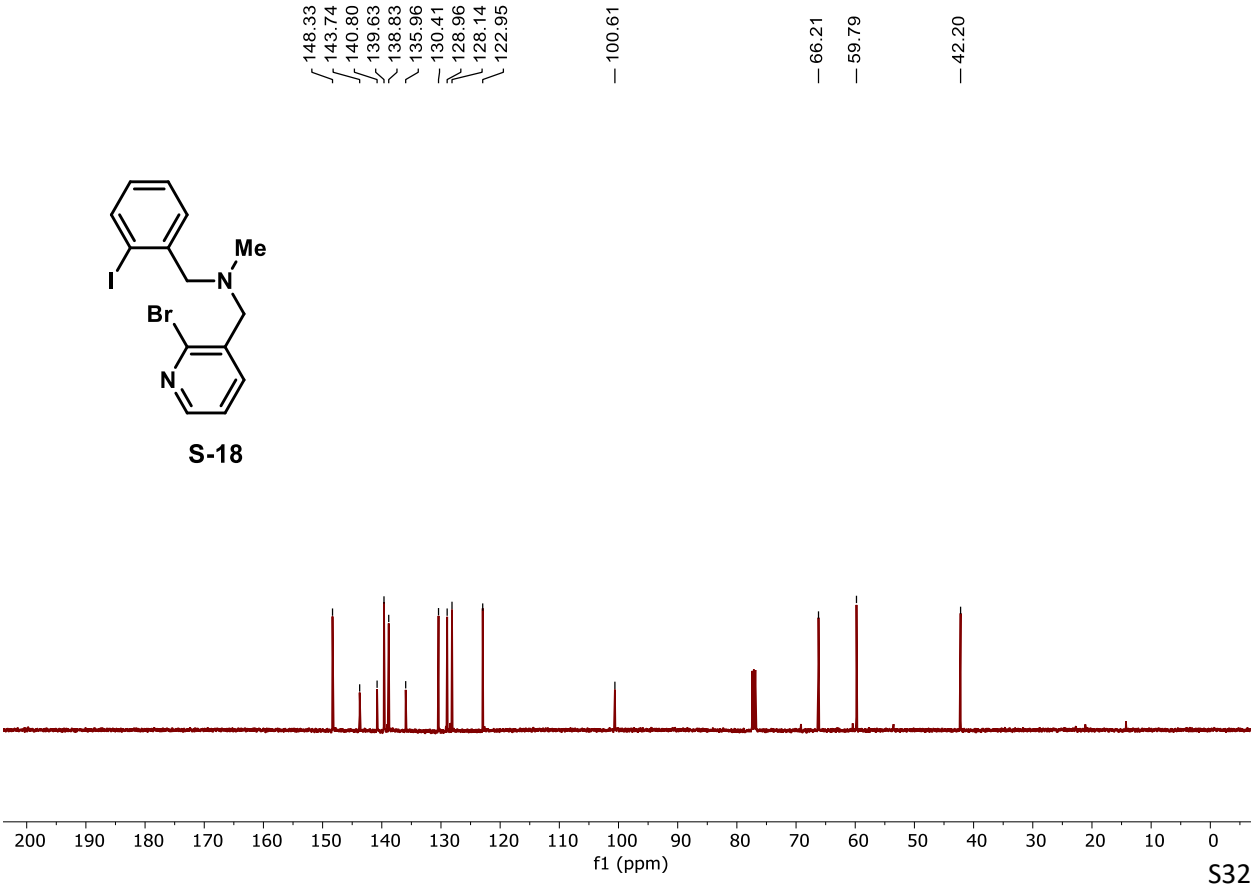
7.31
3.88
3.38
3.34
2.41
400 MHz, CDCl3
MeO2C
Br
N
Me
Br
S-16
1.00
0.99
1.07
4.28
3.09
2.06
2.00
3.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

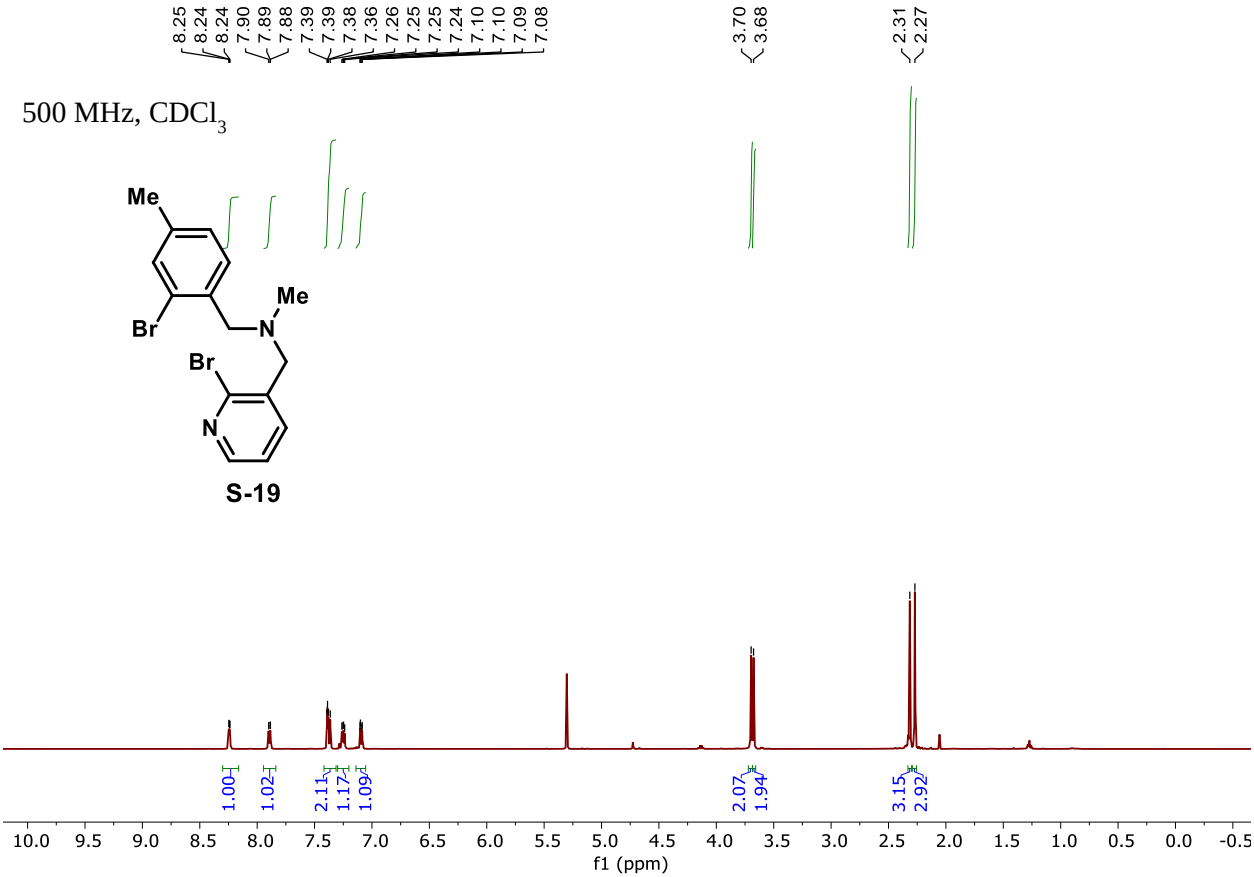

165.85
143.37
133.82
133.50
132.86
130.78
130.77
130.43
128.62
128.43
127.39
124.64
124.18
61.47
61.13
52.39
42.43
MeO2C
Br
N
Me
Br
S-16
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

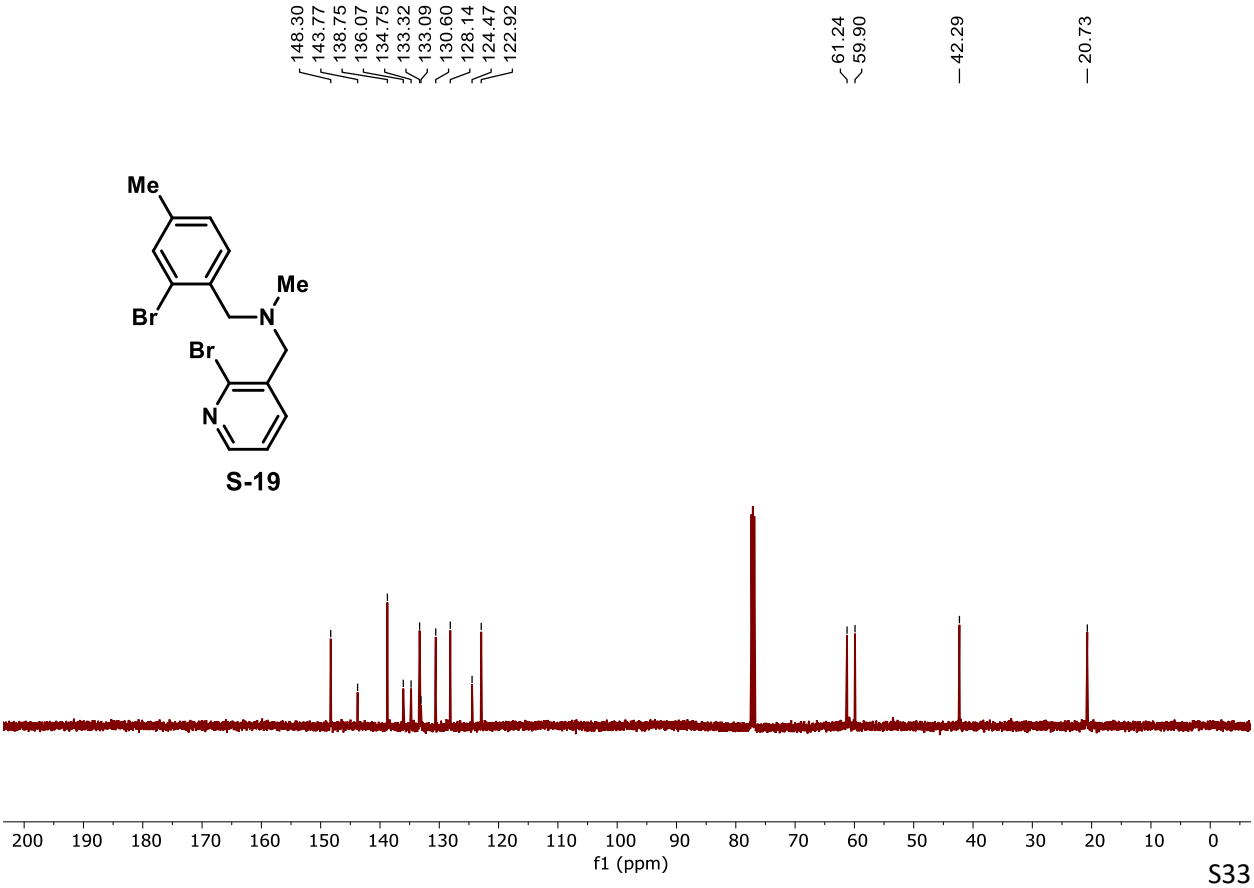

8.32 8.30 7.78 7.78 7.76 7.74 7.71 7.69 7.55 7.55 7.55 7.54 7.54 7.53 7.52 7.52 7.51 7.51 7.50 7.49 7.48 7.48 7.47 7.46 7.46 7.45 7.44 7.28 7.28 7.26 7.26 7.24 7.09 7.09 7.07 7.07 7.06 3.94 3.73 2.26
400 MHz, CDCl3
Me
N
Br
Br
S-17
1.00 2.86 4.37 1.20 1.17 1.85 2.08 3.21
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5

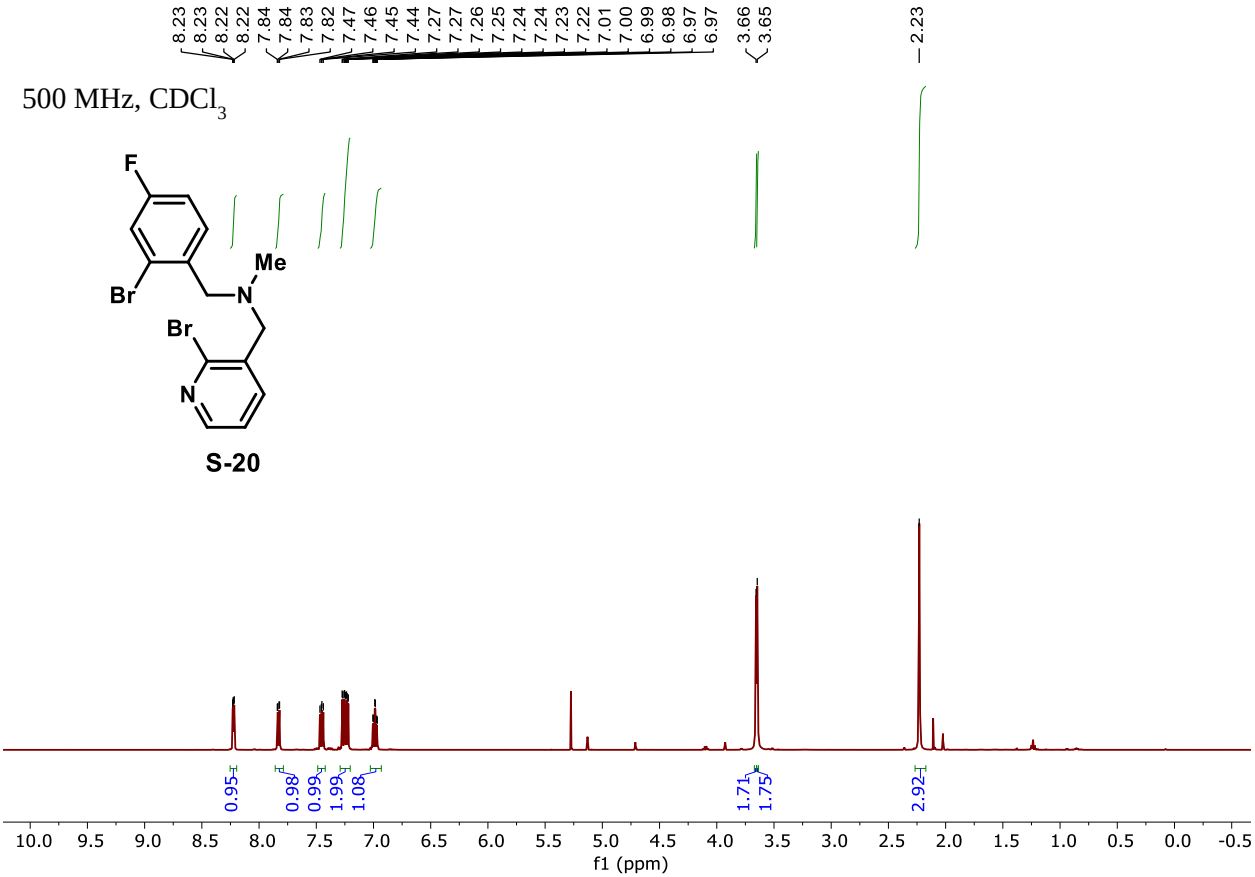

138.52 136.86 134.00 132.89 132.54 131.01 128.55 128.16 128.12 127.58 127.52 127.39 127.35 126.35 124.77 124.27
62.16 61.55
42.41
Me
N
Br
Br
S-17
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

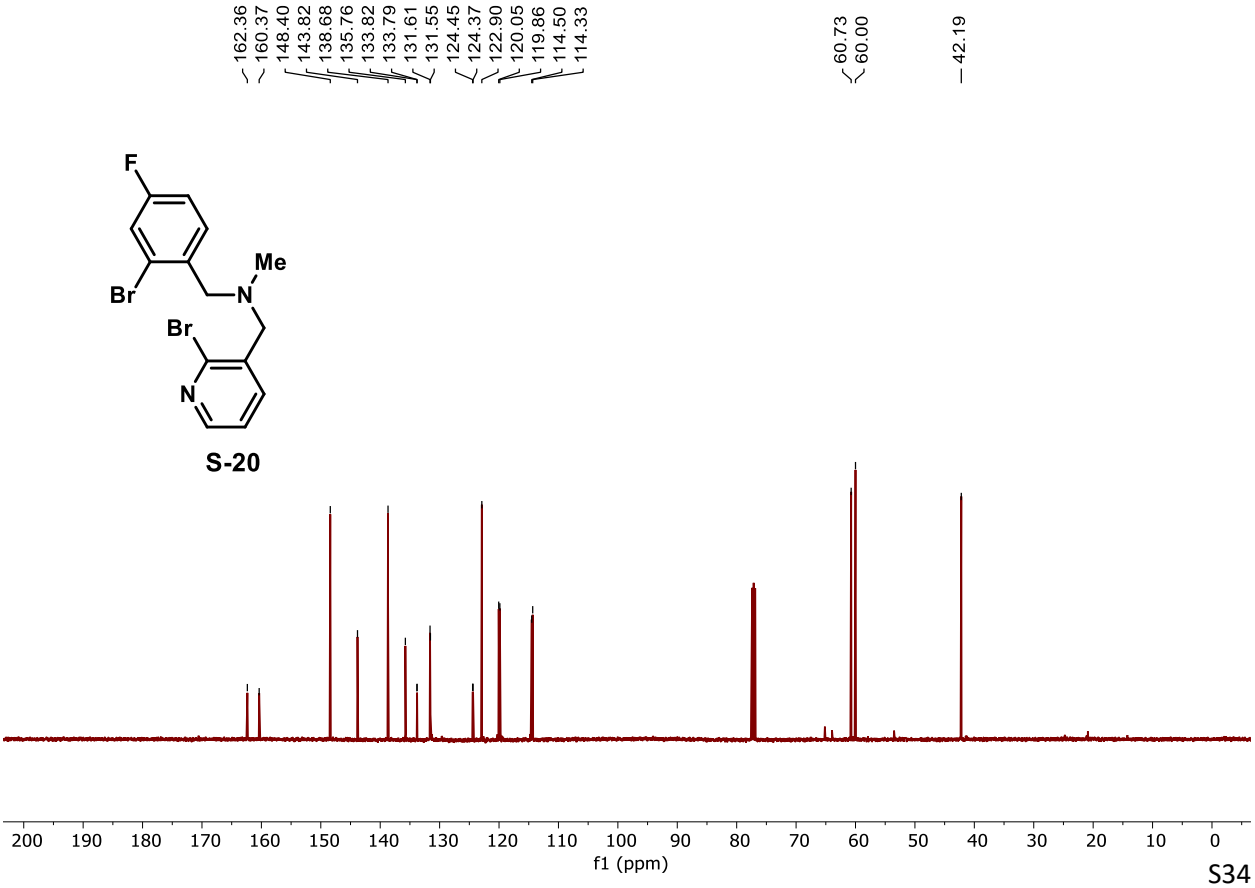

8.19
8.18
7.84
7.82
7.50
7.48
7.46
7.44
7.24
7.22
7.21
7.20
7.19
7.18
7.17
7.07
7.05
7.04
3.66
3.63
2.21
400 MHz, CDCl3
Me
N
I
Br
N
S-18
1.02
1.07
2.29
2.36
1.20
2.18
2.20
3.40
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

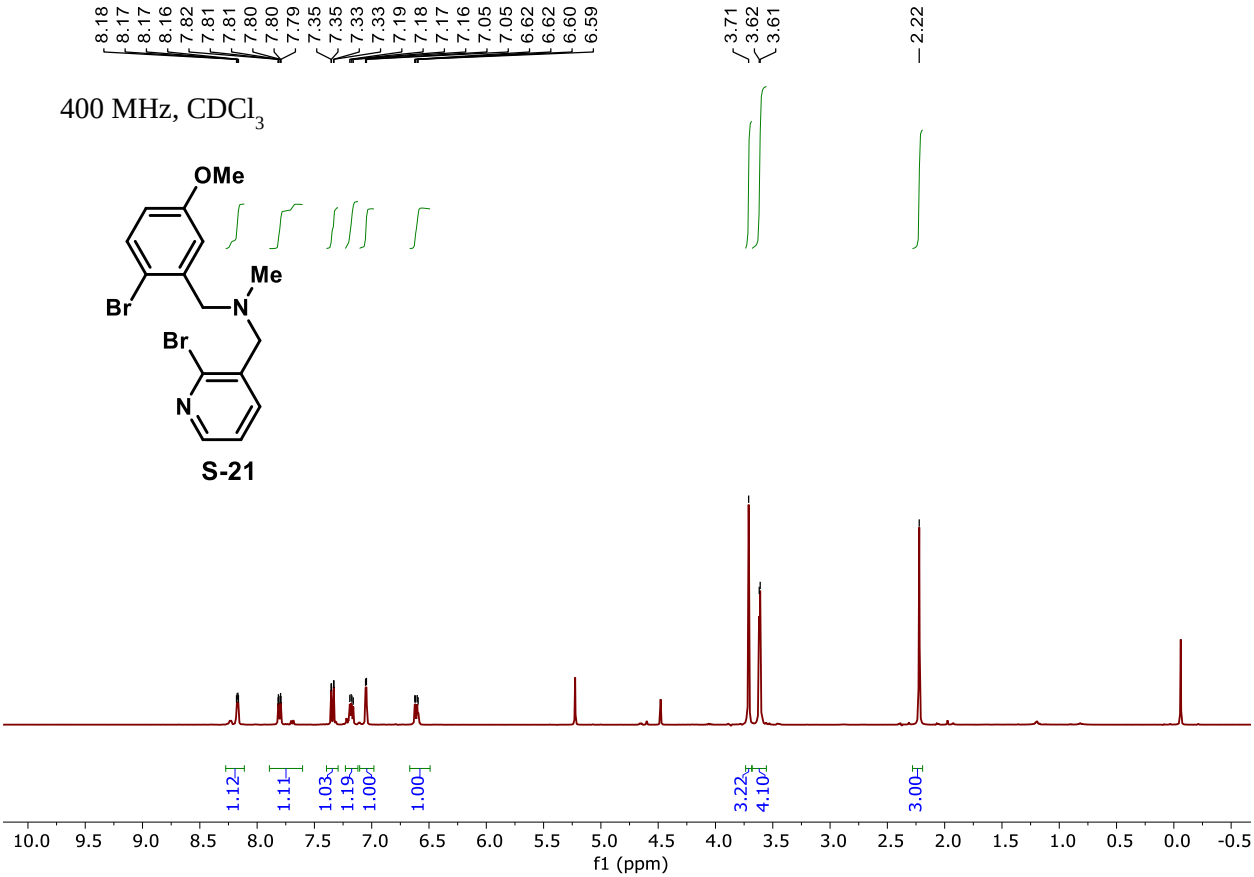

148.33
143.74
140.80
139.63
138.83
135.96
130.41
128.96
128.14
122.95
100.61
66.21
59.79
42.20
Me
N
I
Br
N
S-18
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

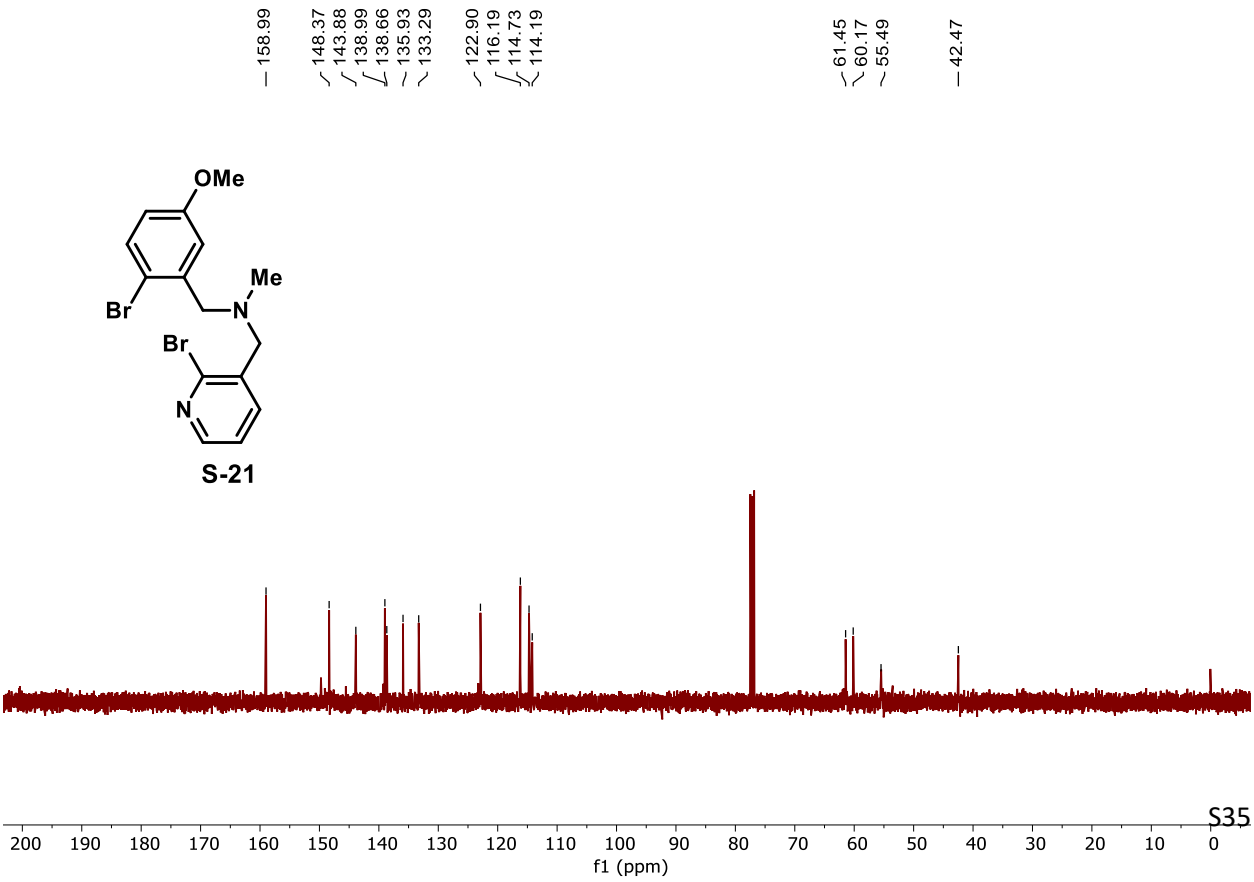

8.25
8.24
8.24
7.90
7.89
7.88
7.39
7.39
7.38
7.36
7.26
7.25
7.25
7.24
7.10
7.10
7.09
7.08
3.70
3.68
2.31
2.27
500 MHz, CDCl3
Me
Br
N
Me
Br
N
S-19
1.00
1.02
2.11
1.17
1.09
2.07
1.94
3.15
2.92
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

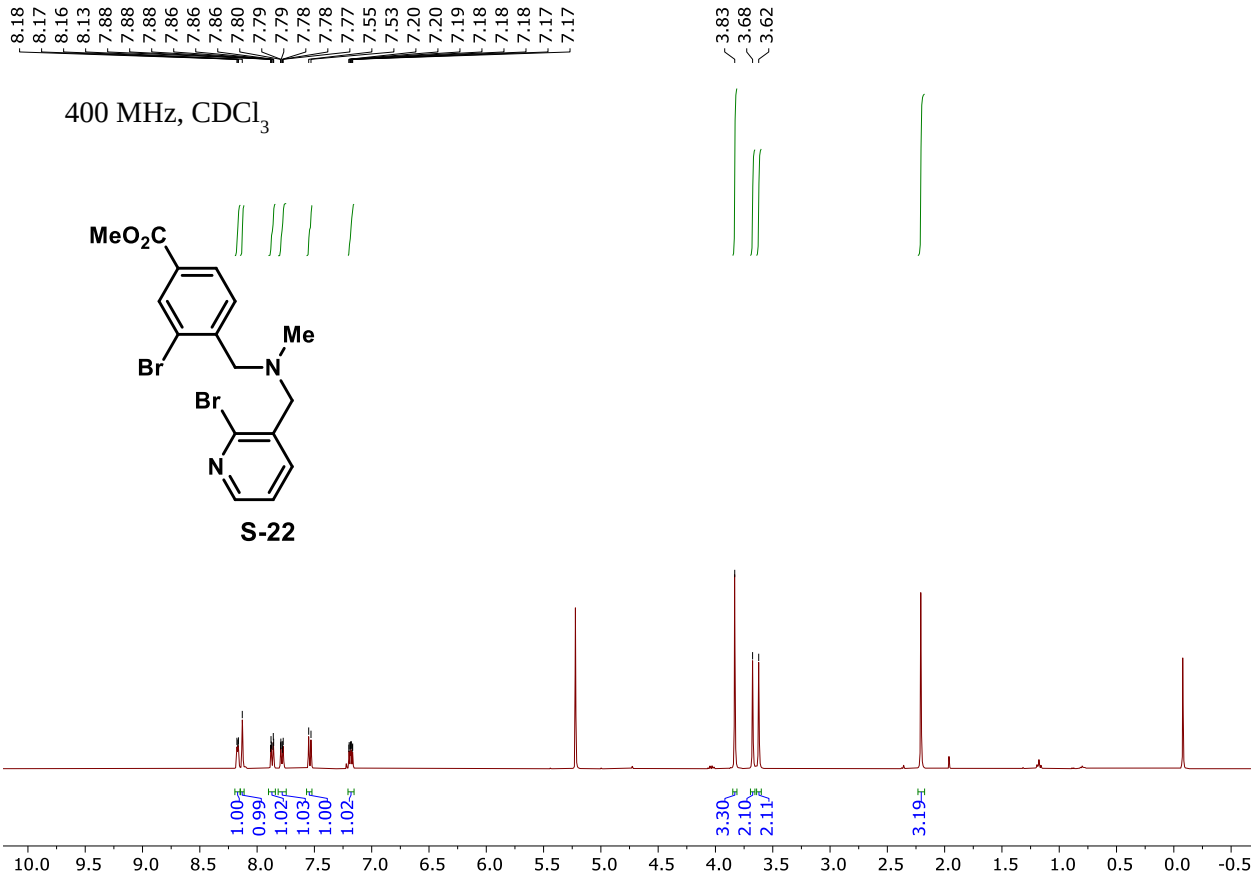

148.30
143.77
138.75
136.07
134.75
133.32
133.09
130.60
128.14
124.47
122.92
61.24
59.90
42.29
20.73
Me
Br
N
Me
Br
N
S-19
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

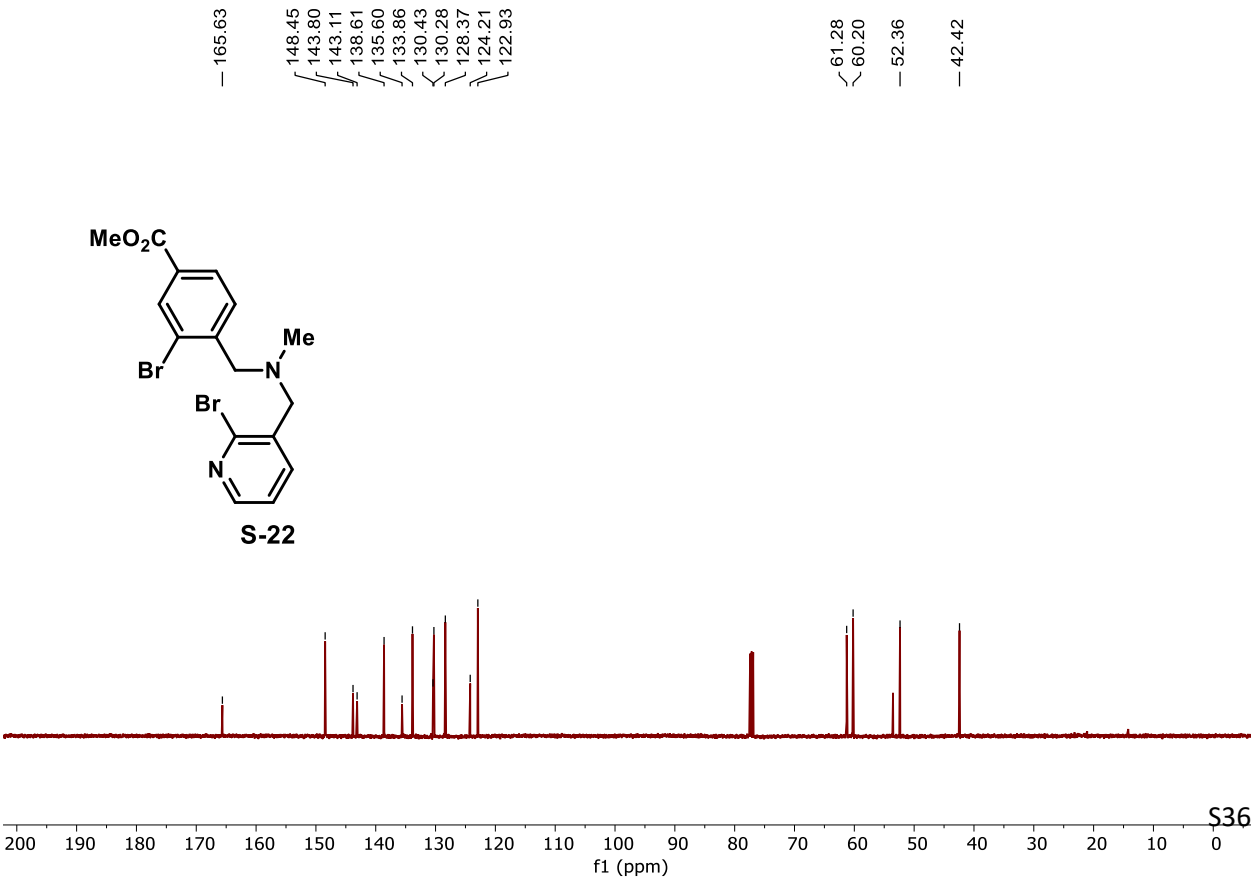

8.23
8.23
8.22
8.22
7.84
7.84
7.83
7.82
7.47
7.46
7.45
7.44
7.27
7.27
7.26
7.25
7.24
7.24
7.23
7.22
7.01
7.00
6.99
6.98
6.97
6.97
3.66
3.65
2.23
500 MHz, CDCl3
F
Br
Me
N
Br
N
S-20
0.95
0.98
0.99
1.99
1.08
1.71
1.75
2.92
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

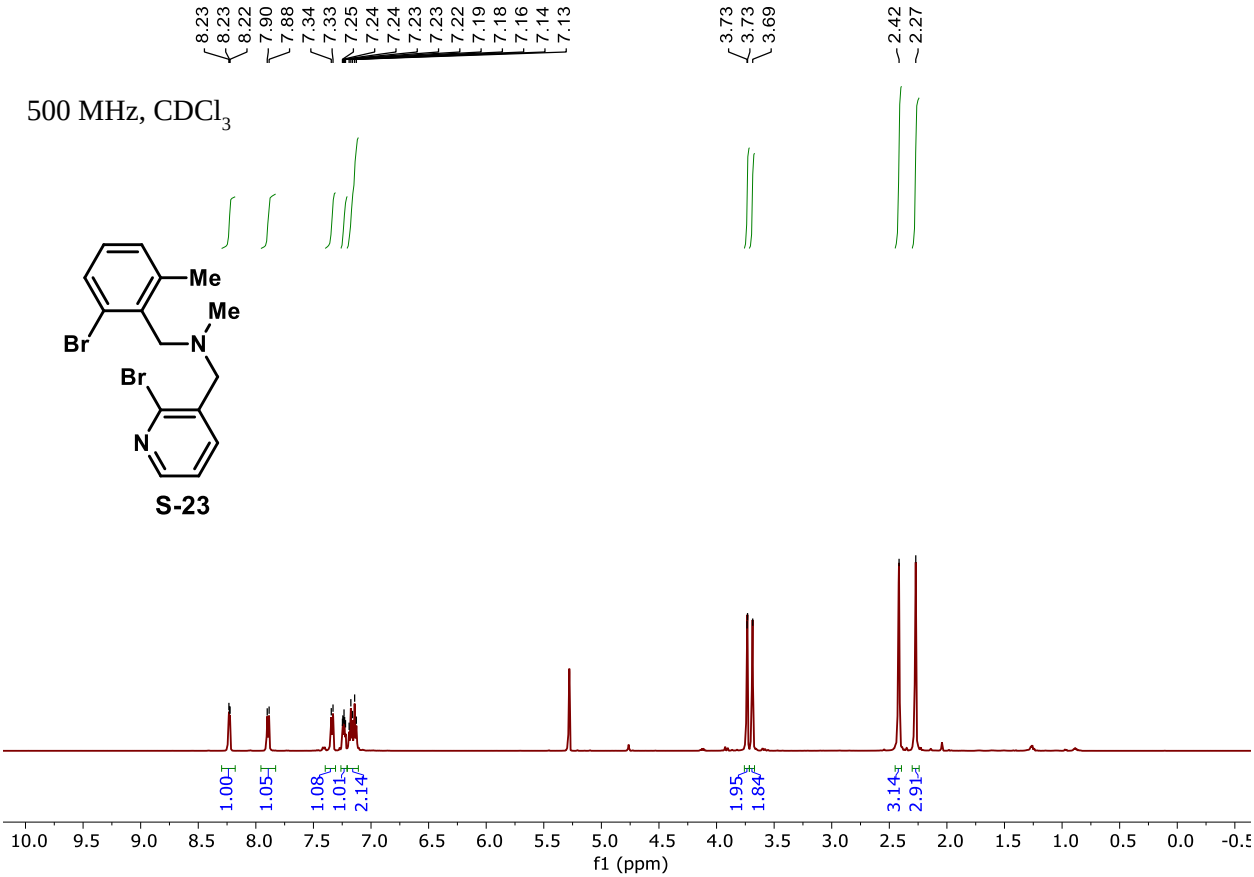

162.36
160.37
148.40
143.82
138.68
135.76
133.82
133.79
131.61
131.55
124.45
124.37
122.90
120.05
119.86
114.50
114.33
60.73
60.00
42.19
F
Br
Me
N
Br
N
S-20
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

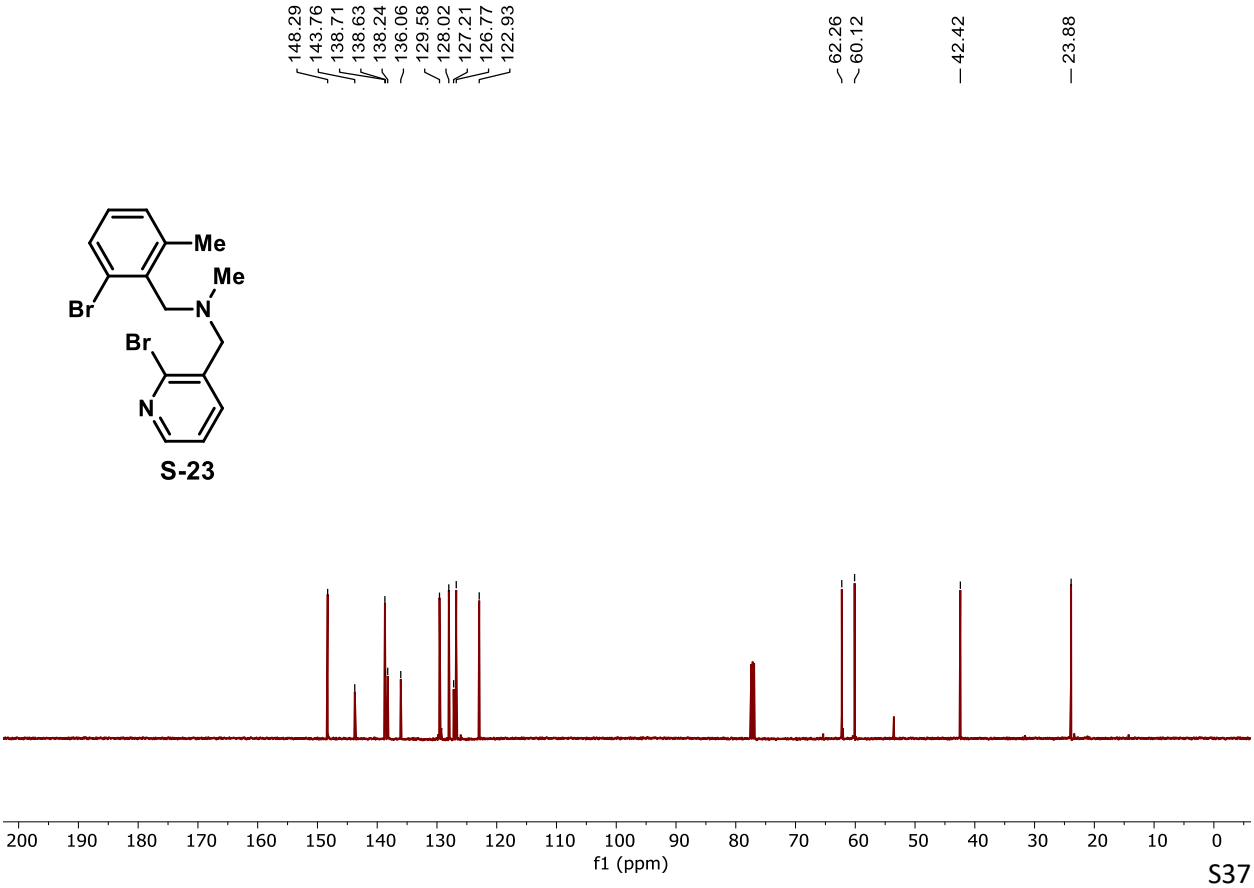

8.18
8.17
8.17
8.16
7.82
7.81
7.81
7.80
7.80
7.79
7.35
7.35
7.33
7.33
7.19
7.18
7.17
7.16
7.05
7.05
6.62
6.62
6.60
6.59
3.71
3.62
3.61
2.22
400 MHz, CDCl3
OMe
Me
Br
N
Br
N
S-21
1.12
1.11
1.03
1.19
1.00
1.00
3.22
4.10
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

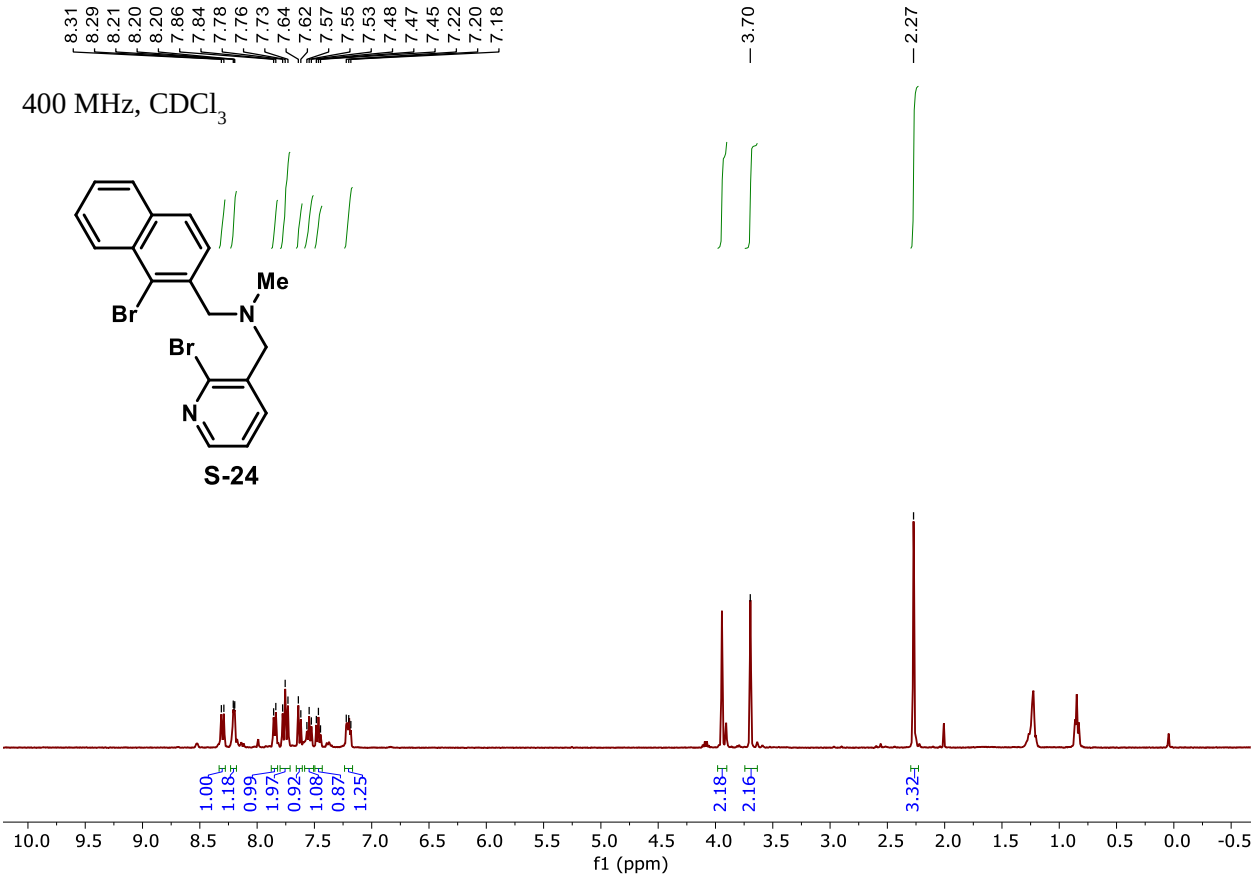

158.99
148.37
143.88
138.99
138.66
135.93
133.29
122.90
116.19
114.73
114.19
61.45
60.17
55.49
42.47
OMe
Me
Br
N
Br
N
S-21
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

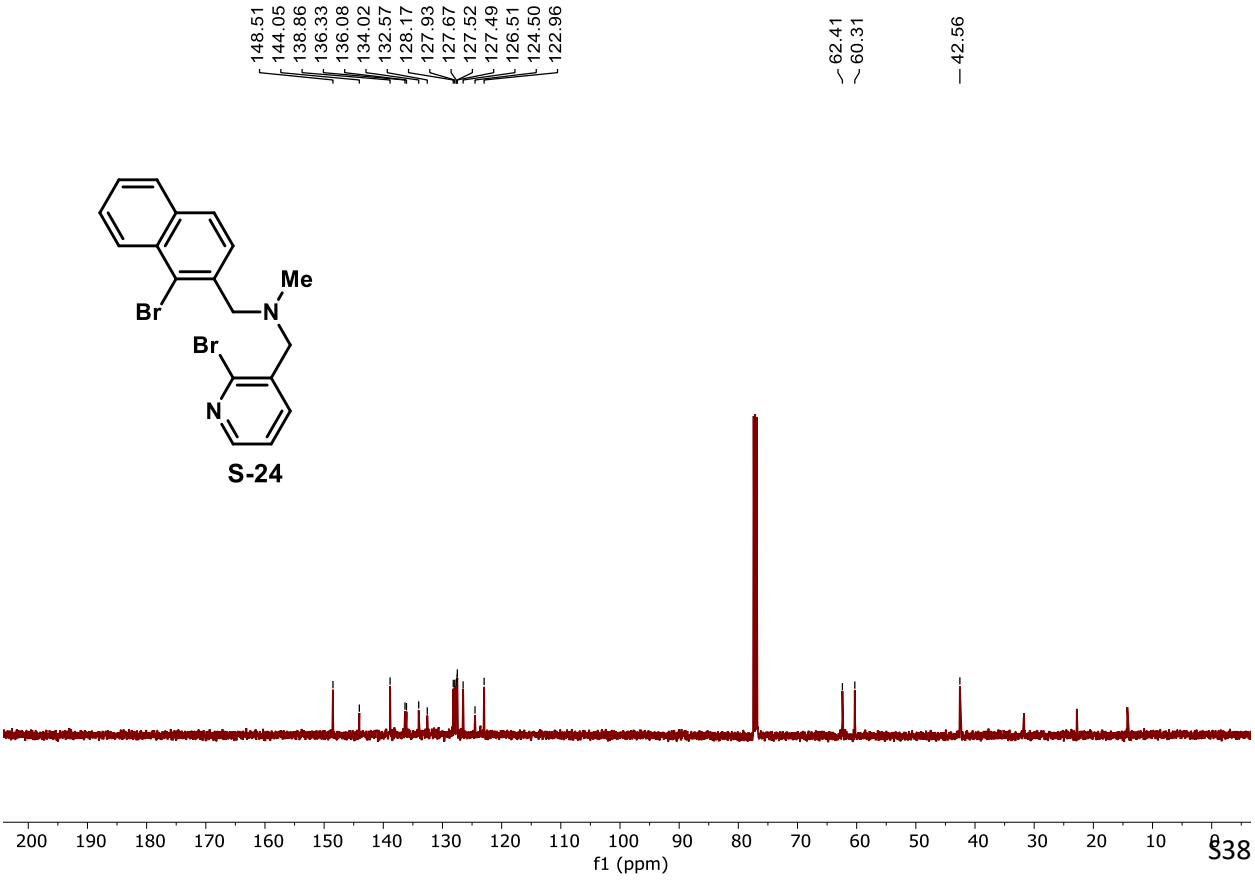

8.18
8.17
8.16
8.13
7.88
7.88
7.88
7.86
7.86
7.86
7.80
7.79
7.79
7.78
7.78
7.77
7.55
7.53
7.20
7.20
7.19
7.18
7.18
7.18
7.17
7.17
3.83
3.68
3.62
400 MHz, CDCl3
MeO2C
Br
N
Me
Br
N
S-22
1.00
0.99
1.02
1.03
1.00
1.02
3.30
2.10
2.11
3.19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


165.63
148.45
143.80
143.11
138.61
135.60
133.86
130.43
130.28
128.37
124.21
122.93
61.28
60.20
52.36
42.42
MeO2C
Br
N
Me
Br
N
S-22
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

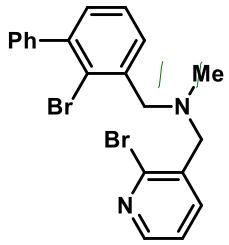

8.23
8.23
8.22
7.90
7.88
7.34
7.33
7.25
7.24
7.24
7.23
7.23
7.22
7.19
7.18
7.16
7.14
7.13
3.73
3.73
3.69
2.42
2.27
500 MHz, CDCl3
Me
Me
Br
N
Br
N
S-23
1.00
1.05
1.08
1.01
2.14
1.95
1.84
3.14
2.91
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


148.29
143.76
138.71
138.63
138.24
136.06
129.58
128.02
127.21
126.77
122.93
62.26
60.12
42.42
23.88
Me
Me
Br
N
Br
N
S-23
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.31
8.29
8.21
8.20
8.20
7.86
7.84
7.78
7.76
7.73
7.64
7.62
7.57
7.55
7.53
7.48
7.47
7.45
7.22
7.20
7.18
3.70
2.27
400 MHz, CDCl3
Me
Br
N
Br
N
S-24
1.00
1.18
0.99
1.97
0.92
1.08
0.87
1.25
2.18
2.16
3.32
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

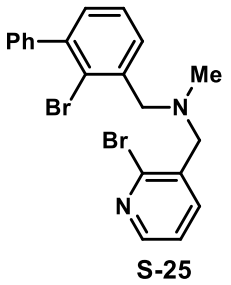

148.51
144.05
138.86
136.33
136.08
134.02
132.57
128.17
127.93
127.67
127.52
127.49
126.51
124.50
122.96
62.41
60.31
42.56
Me
Br
N
Br
N
S-24
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

400 MHz, $CDCl_3$

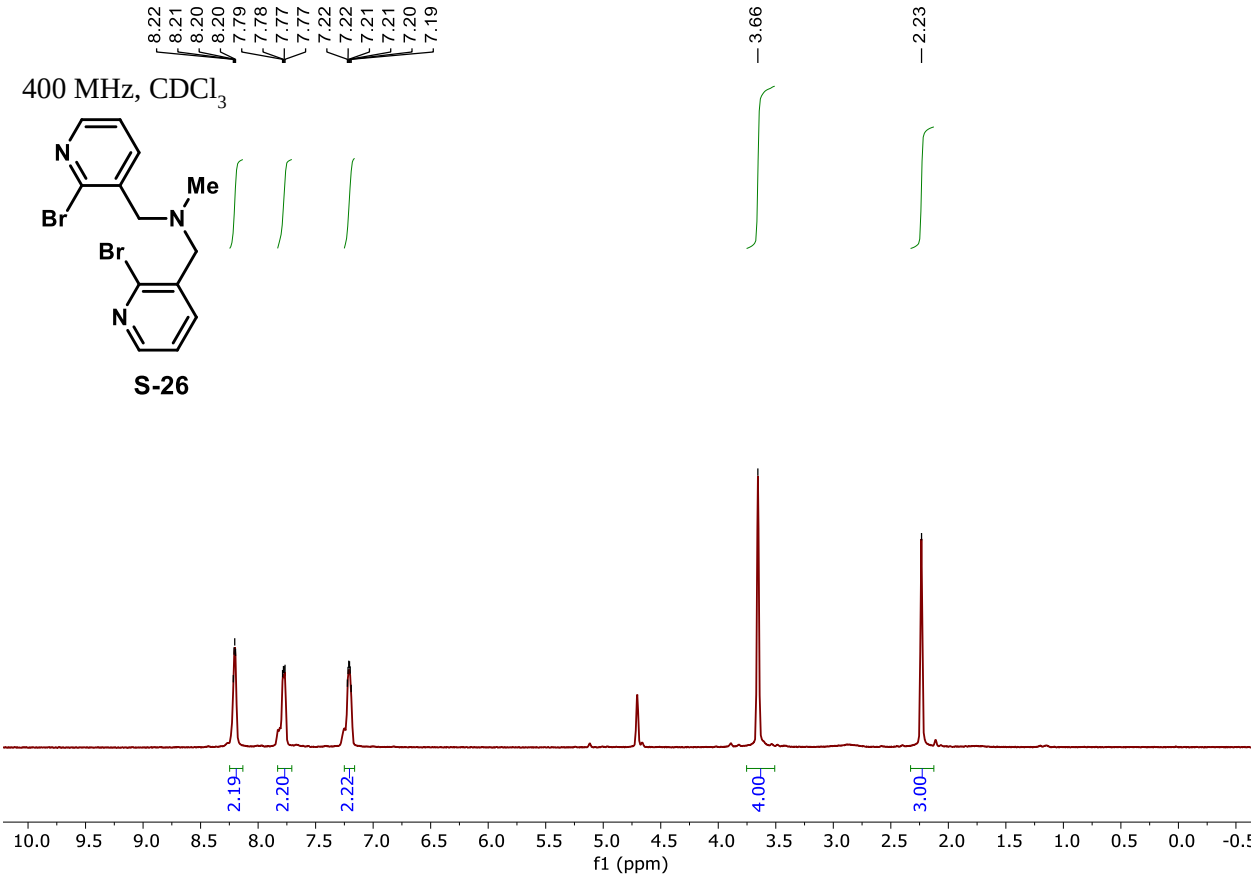


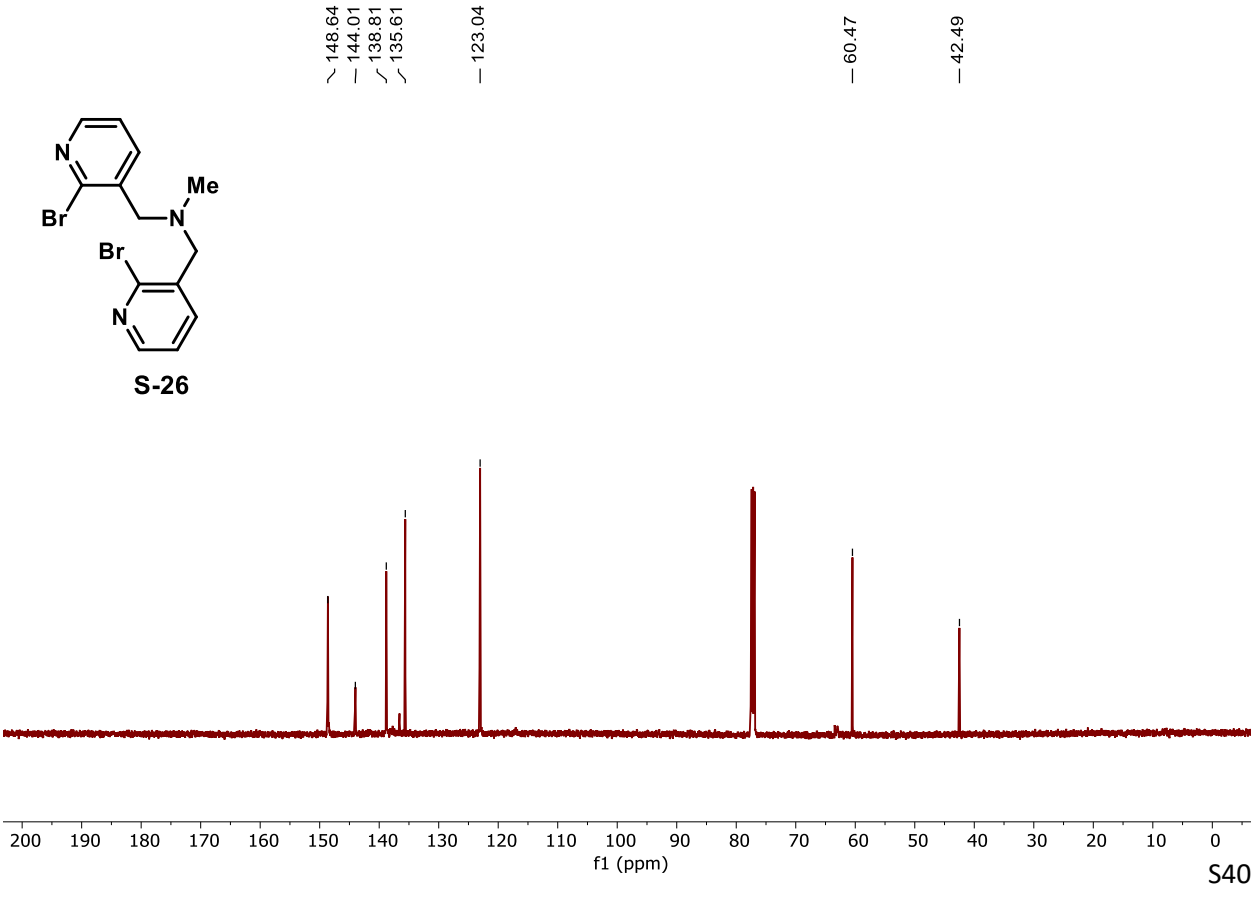
S-25

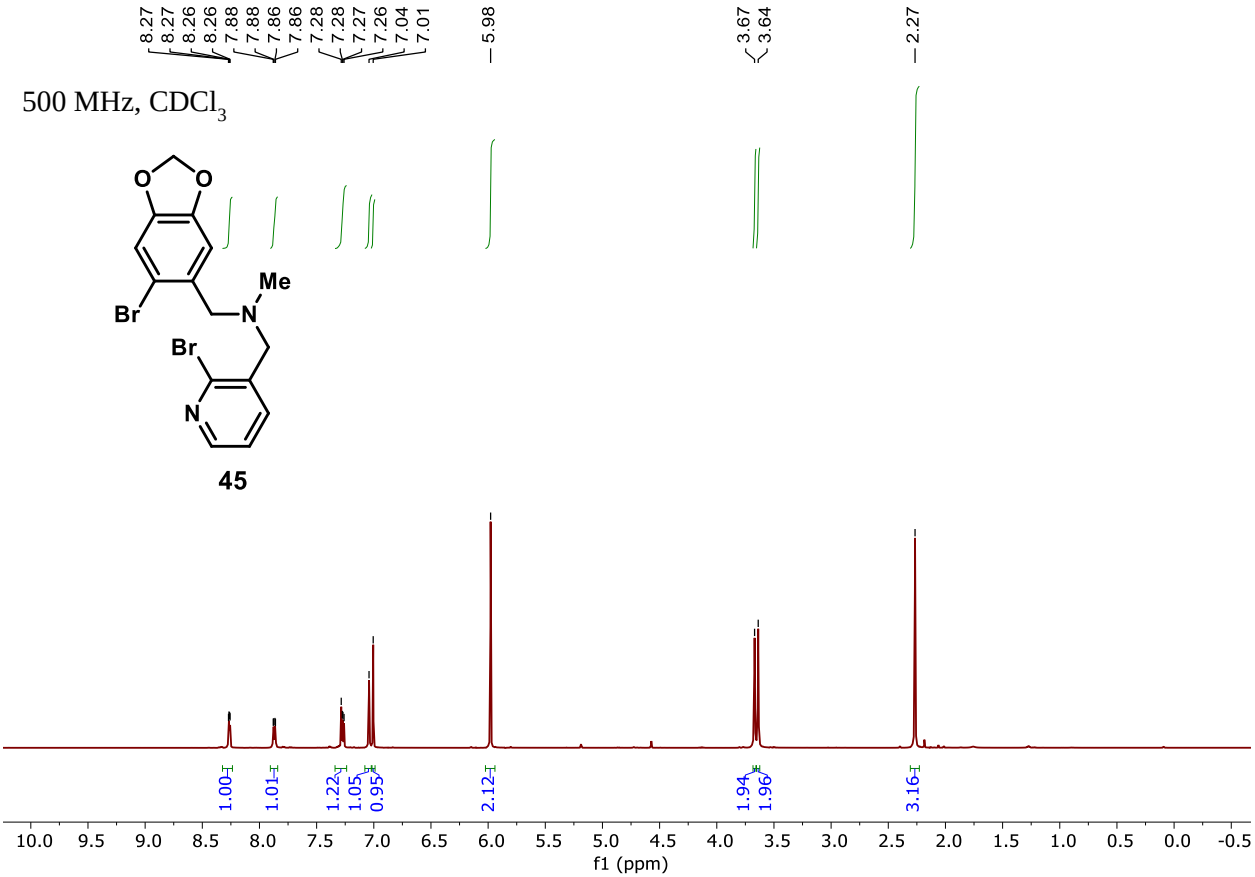
500 MHz, $CDCl_3$

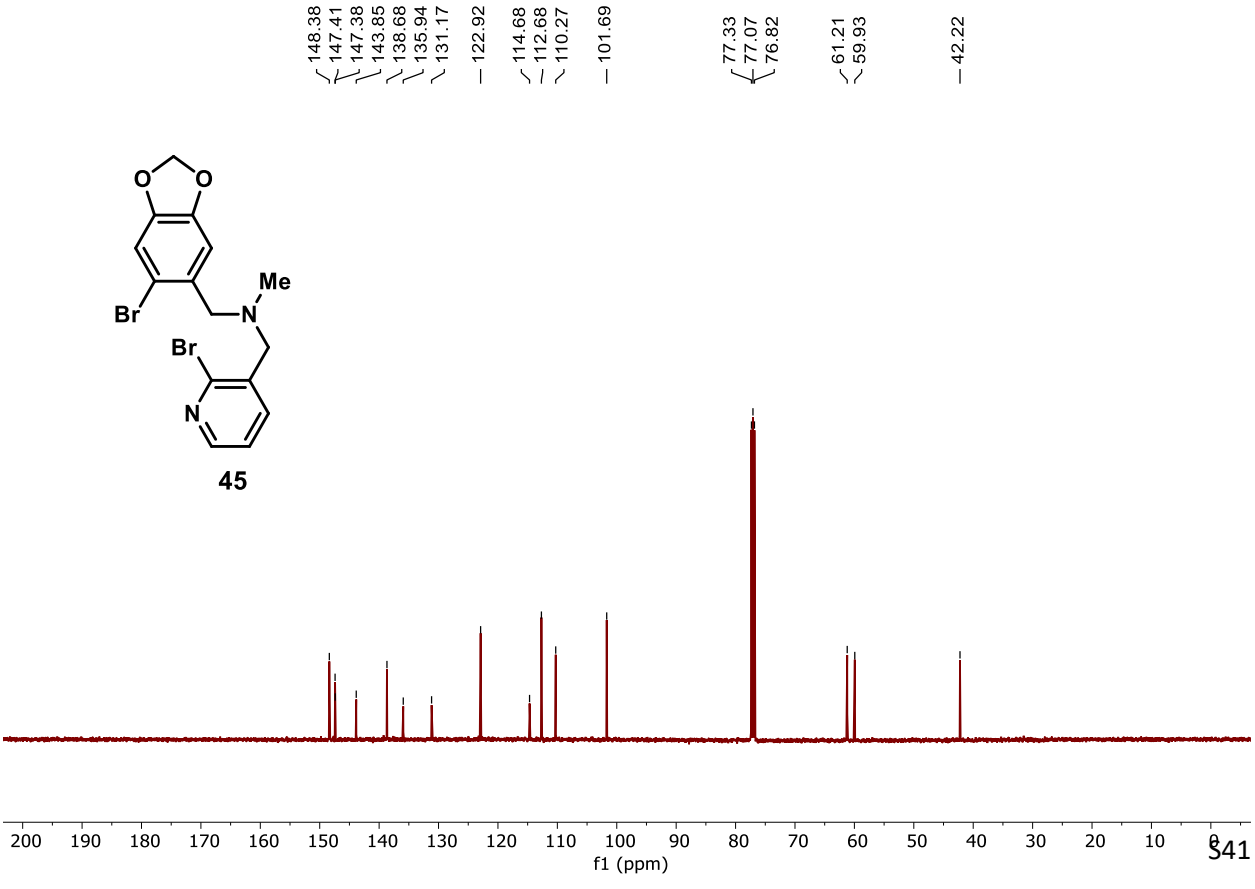


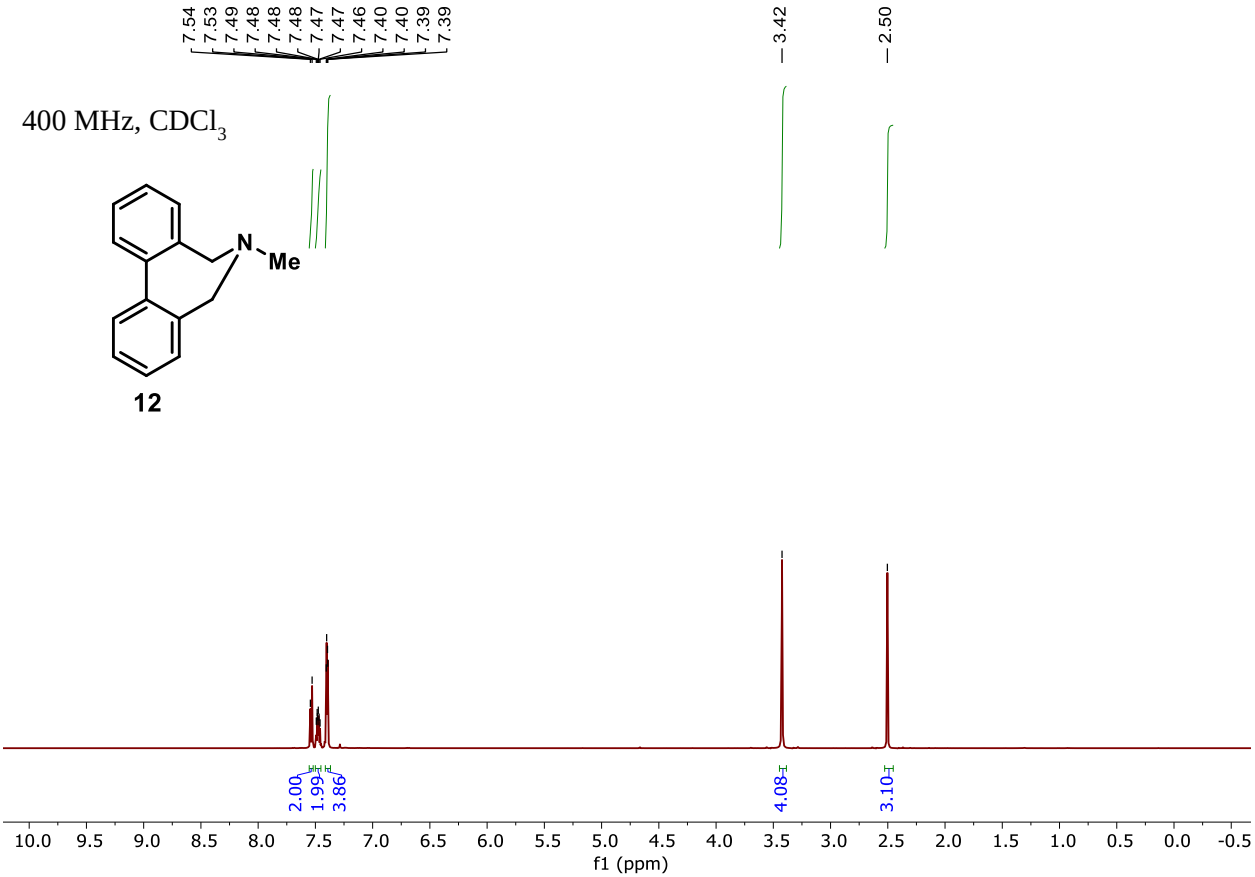
S-25

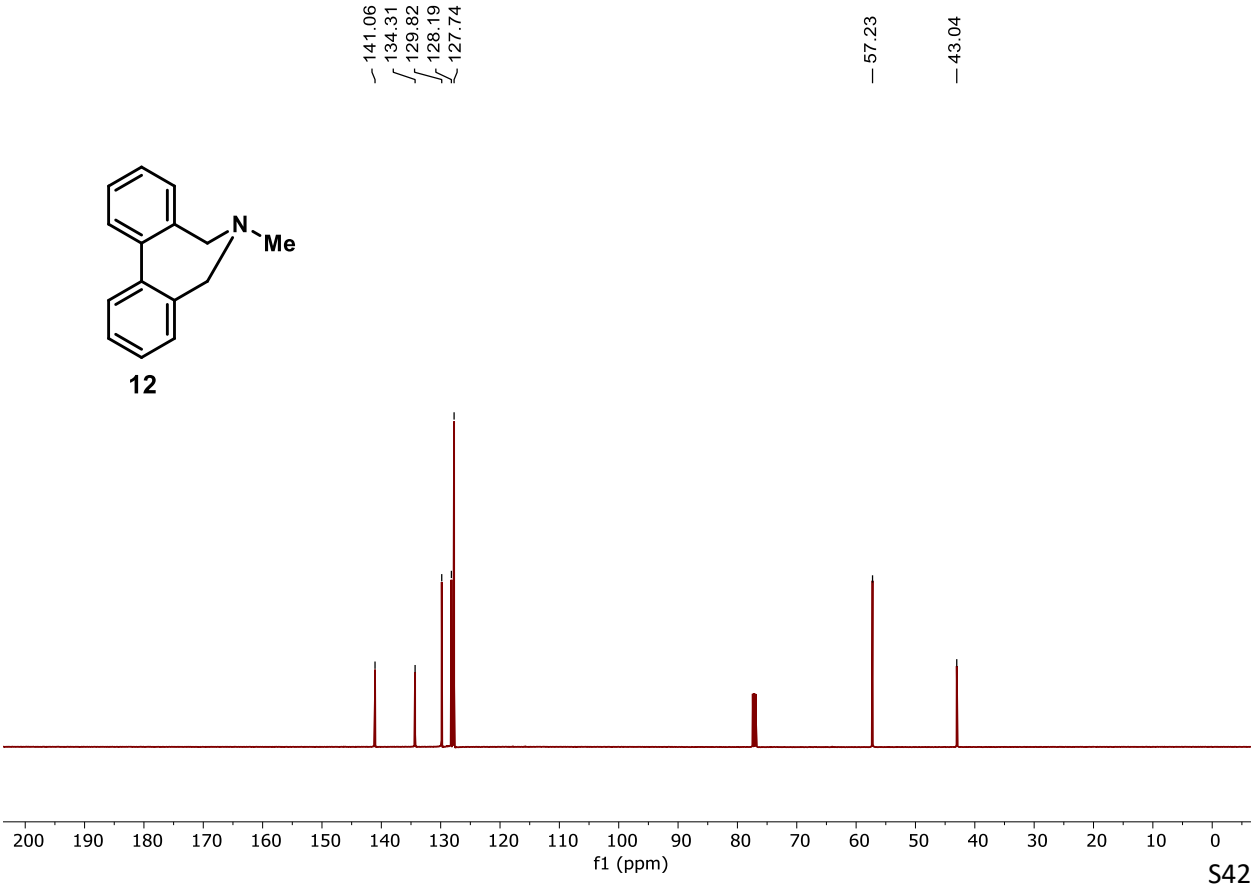

8.22
8.21
8.20
8.20
7.79
7.78
7.77
7.77
7.22
7.22
7.21
7.21
7.20
7.19
3.66
2.23
400 MHz, CDCl3
N
Br
Me
N
Br
N
S-26
2.19
2.20
2.22
4.00
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

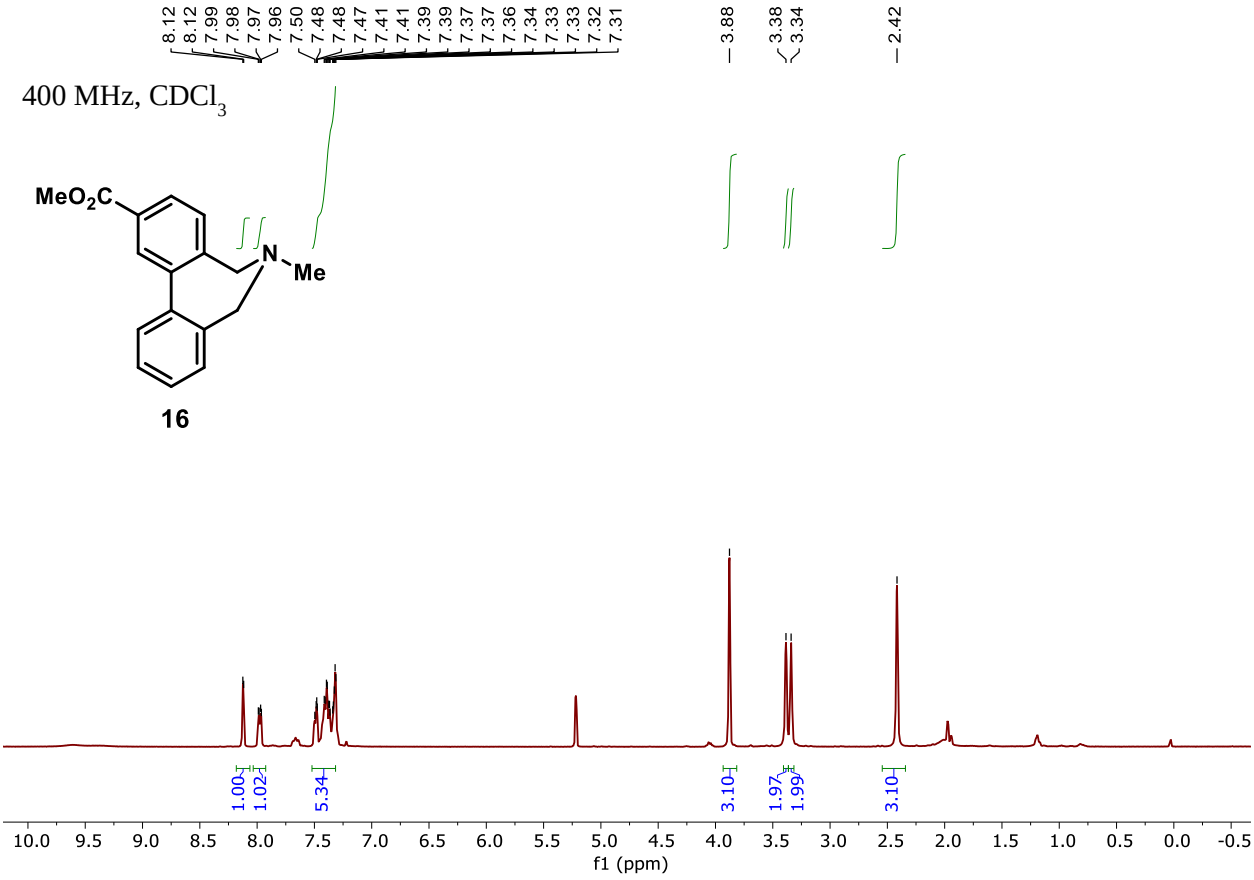

148.64
144.01
138.81
135.61
123.04
60.47
42.49
N
Br
Me
N
Br
N
S-26
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

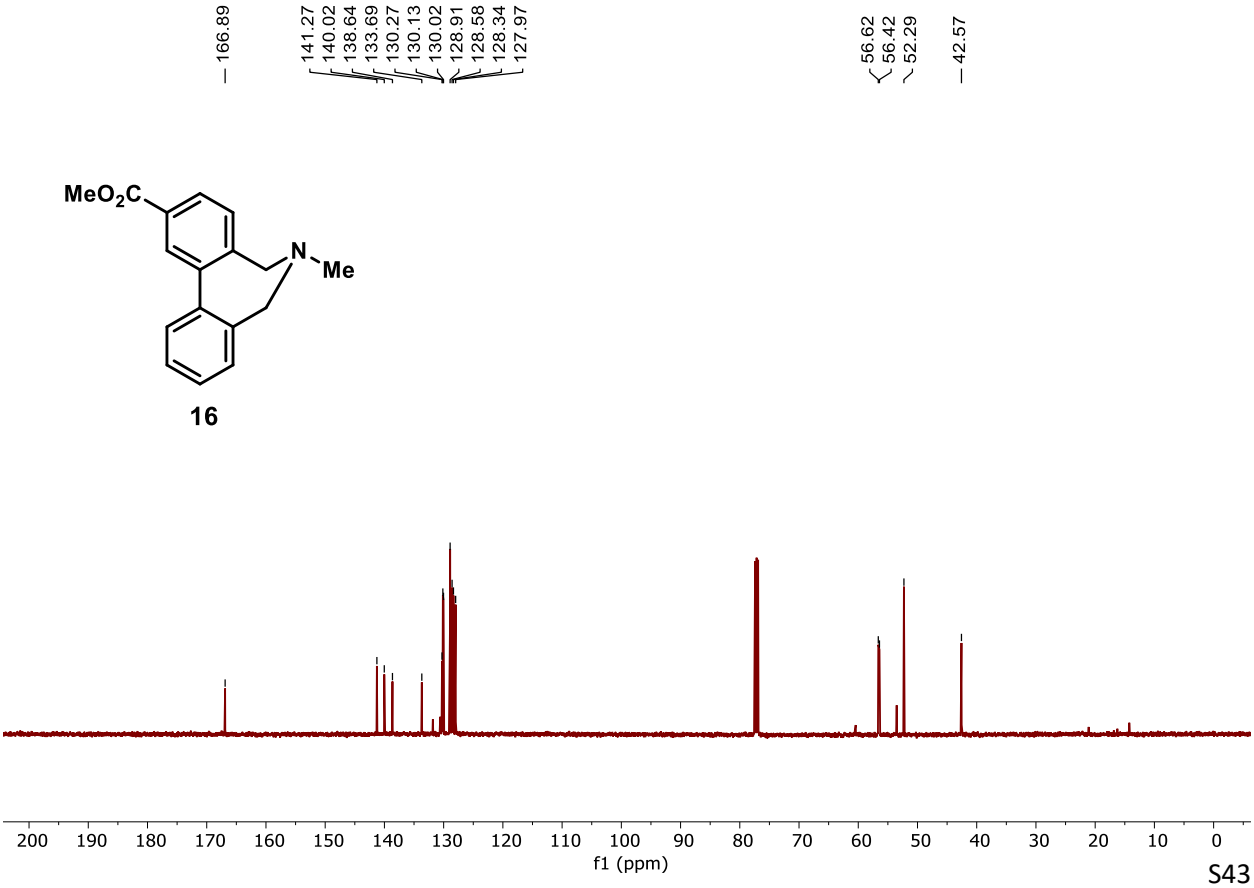

8.27
8.27
8.26
8.26
7.88
7.88
7.86
7.86
7.28
7.28
7.27
7.26
7.04
7.01
5.98
3.67
3.64
2.27
500 MHz, CDCl3
O
O
Br
Me
N
Br
N
45
1.00
1.01
1.22
1.05
0.95
2.12
1.94
1.96
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

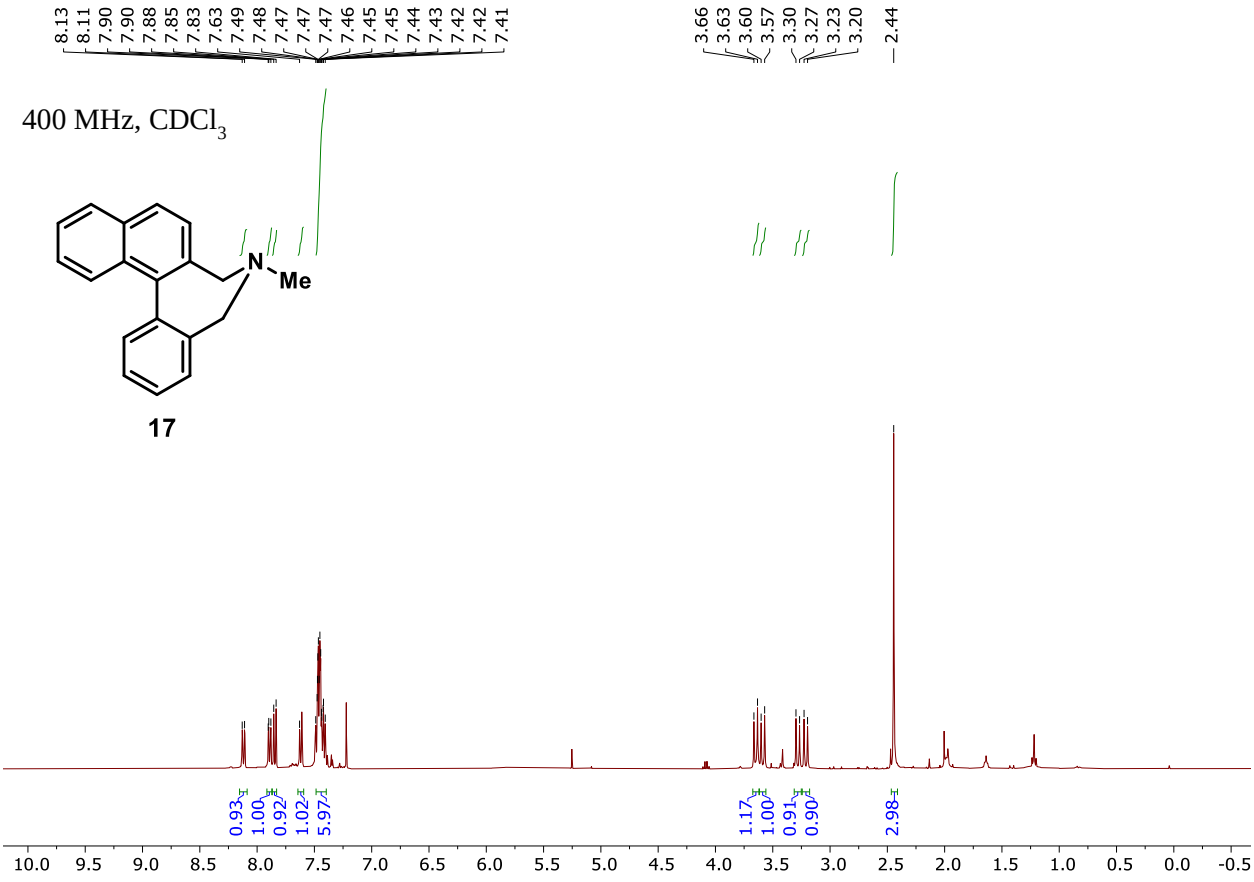

148.38
147.41
147.38
143.85
138.68
135.94
131.17
122.92
114.68
112.68
110.27
101.69
77.33
77.07
76.82
61.21
59.93
42.22
O
O
Br
Me
N
Br
N
45
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

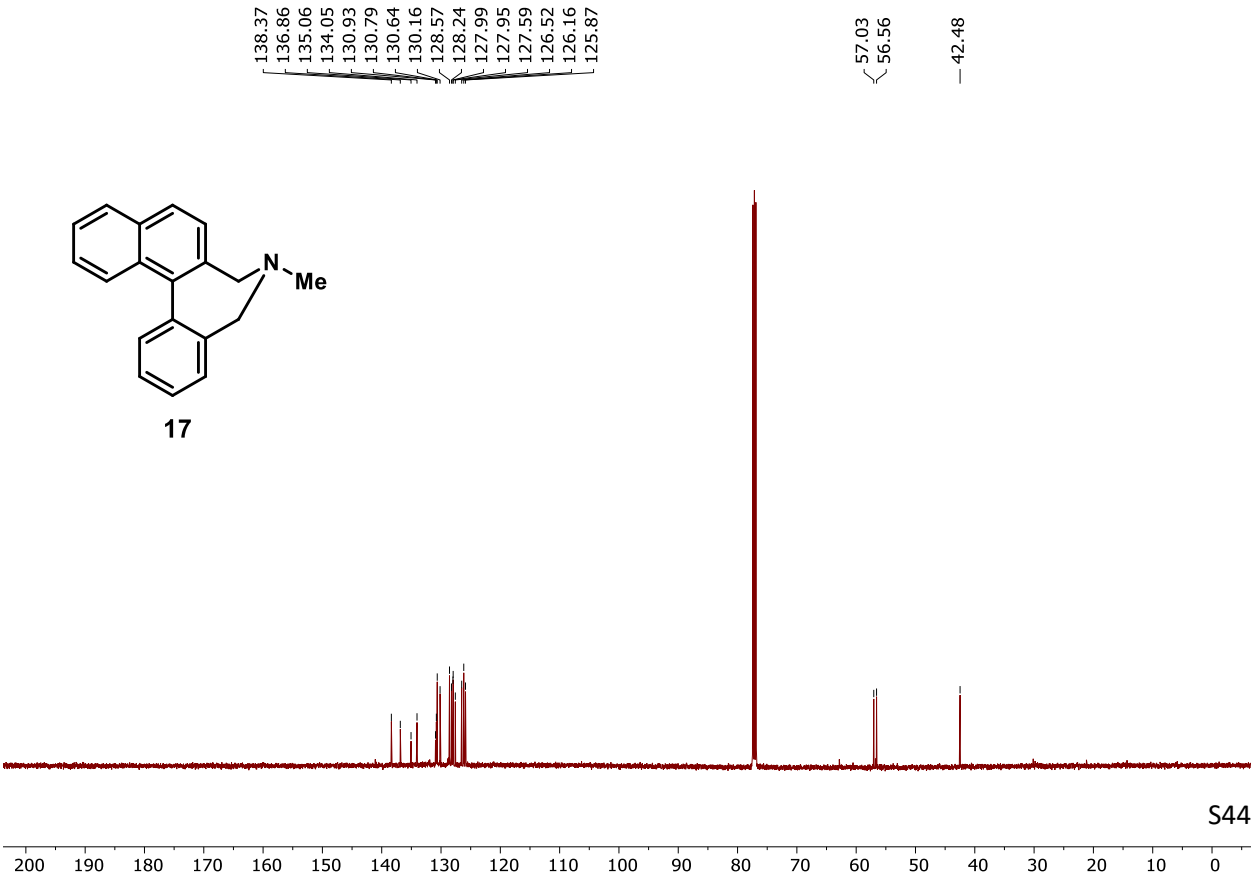

7.54
7.53
7.49
7.48
7.48
7.48
7.47
7.47
7.46
7.40
7.40
7.39
7.39
3.42
2.50
400 MHz, CDCl3
N
Me
12
2.00
1.99
3.86
4.08
3.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

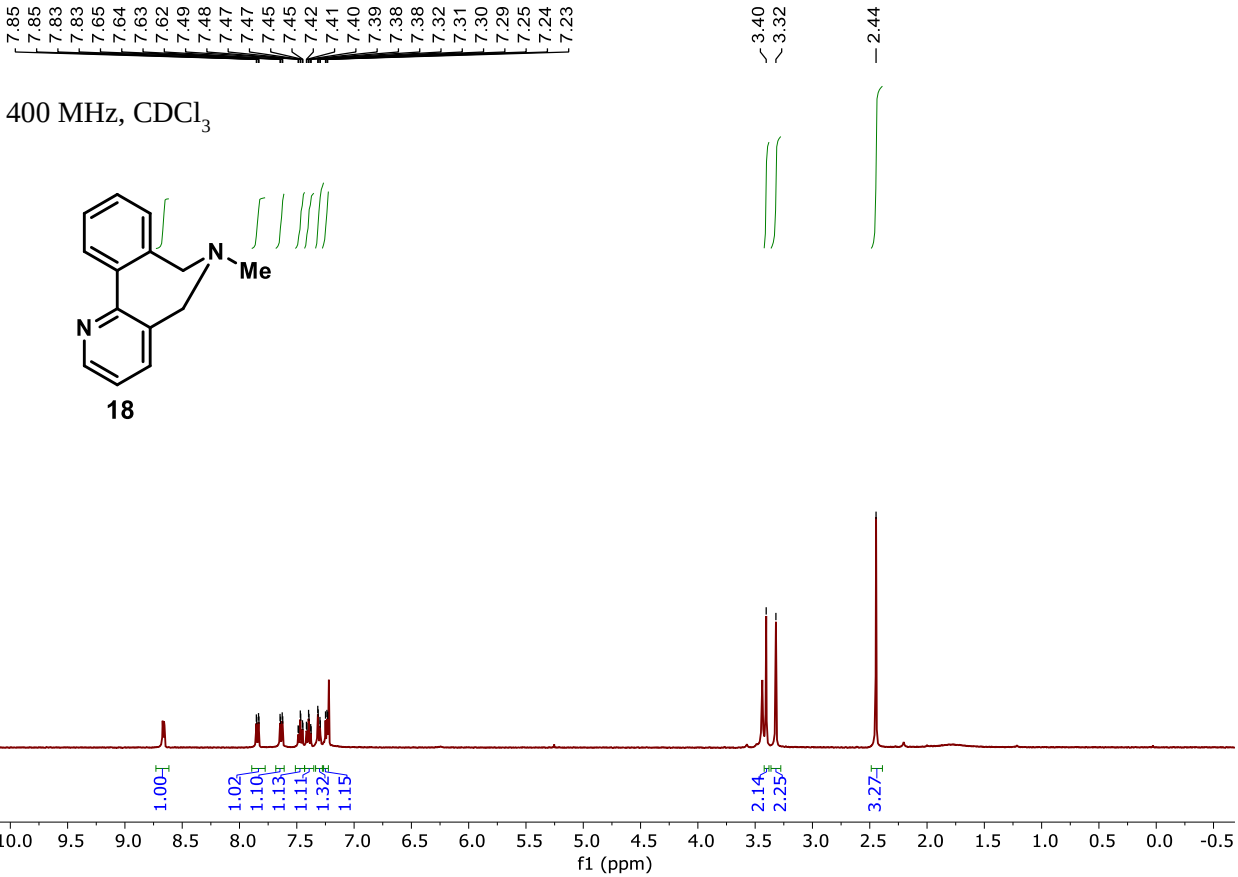

141.06
134.31
129.82
128.19
127.74
57.23
43.04
N
Me
12
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

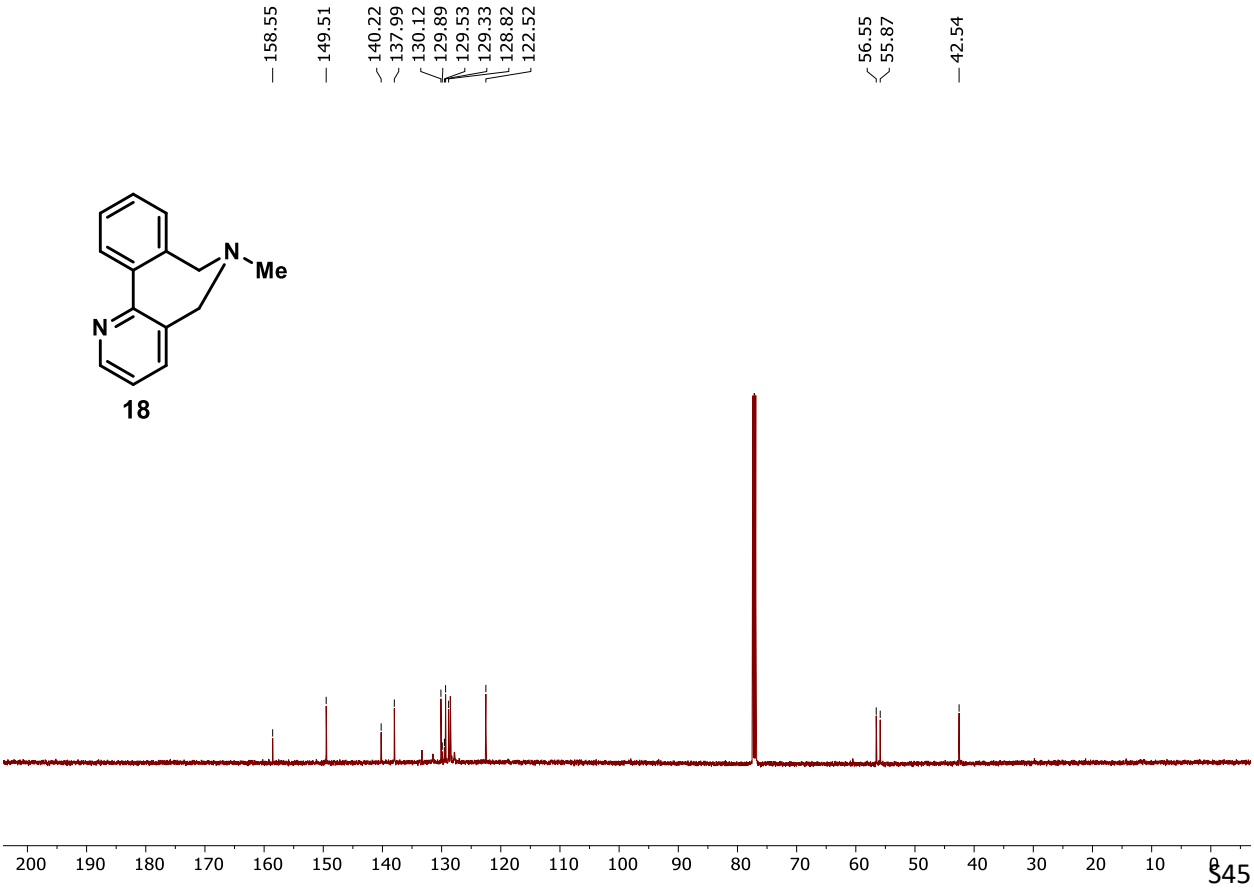

8.12
8.12
7.99
7.98
7.97
7.96
7.50
7.48
7.48
7.47
7.41
7.41
7.39
7.39
7.37
7.37
7.36
7.34
7.33
7.33
7.32
7.31
3.88
3.38
3.34
2.42
400 MHz, CDCl3
MeO2C
N
Me
16
1.00
1.02
5.34
3.10
1.97
1.99
3.10
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


166.89
141.27
140.02
138.64
133.69
130.27
130.13
130.02
128.91
128.58
128.34
127.97
56.62
56.42
52.29
42.57
MeO2C
N
Me
16
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

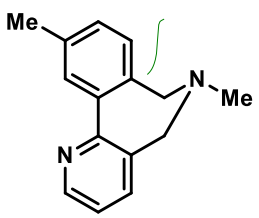

8.13
8.11
7.90
7.90
7.88
7.85
7.83
7.63
7.49
7.48
7.47
7.47
7.47
7.46
7.45
7.45
7.44
7.43
7.42
7.42
7.41
3.66
3.63
3.60
3.57
3.30
3.27
3.23
3.20
2.44
400 MHz, CDCl3
N
Me
17
0.93
1.00
0.92
1.02
5.97
1.17
1.00
0.91
0.90
2.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5


138.37
136.86
135.06
134.05
130.93
130.79
130.64
130.16
128.57
128.24
127.99
127.95
127.59
126.52
126.16
125.87
57.03
56.56
42.48
N
Me
17
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

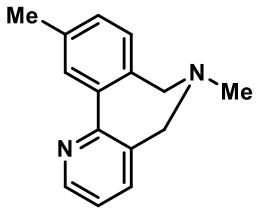

7.85
7.85
7.83
7.83
7.65
7.64
7.63
7.62
7.49
7.48
7.47
7.47
7.45
7.45
7.42
7.41
7.40
7.39
7.38
7.38
7.32
7.31
7.30
7.29
7.25
7.24
7.23
3.40
3.32
2.44
400 MHz, CDCl3
N
Me
N
18
1.00
1.02
1.10
1.13
1.11
1.32
1.15
2.14
2.25
3.27
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


158.55
149.51
140.22
137.99
130.12
129.89
129.53
129.33
128.82
122.52
56.55
55.87
42.54
N
Me
N
18
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

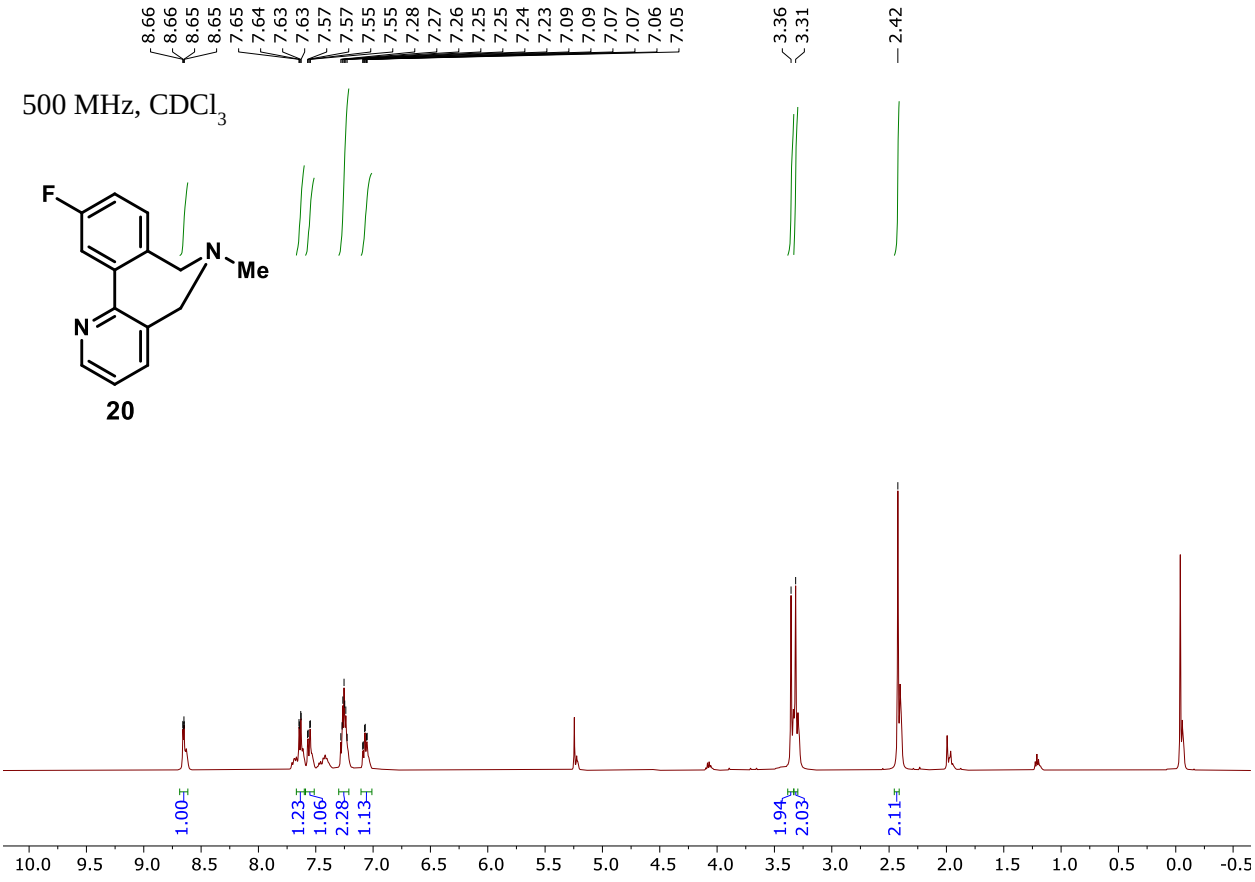
500 MHz, $CDCl_3$

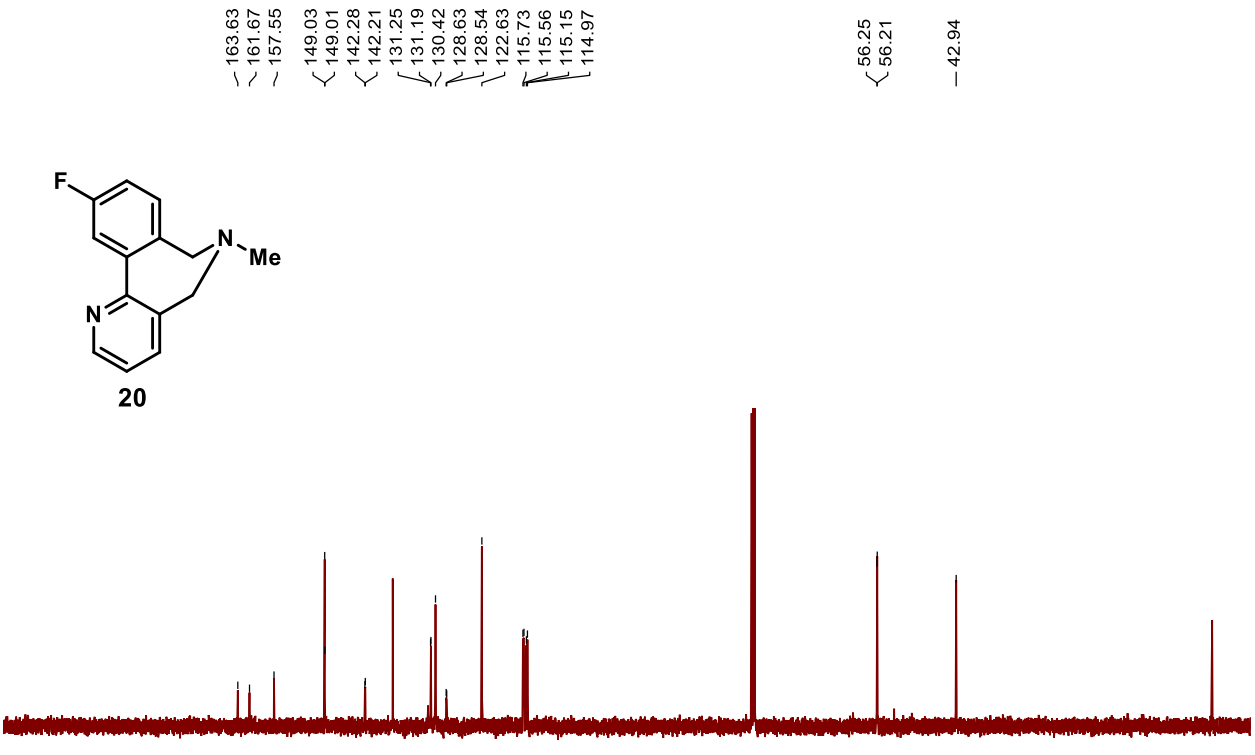


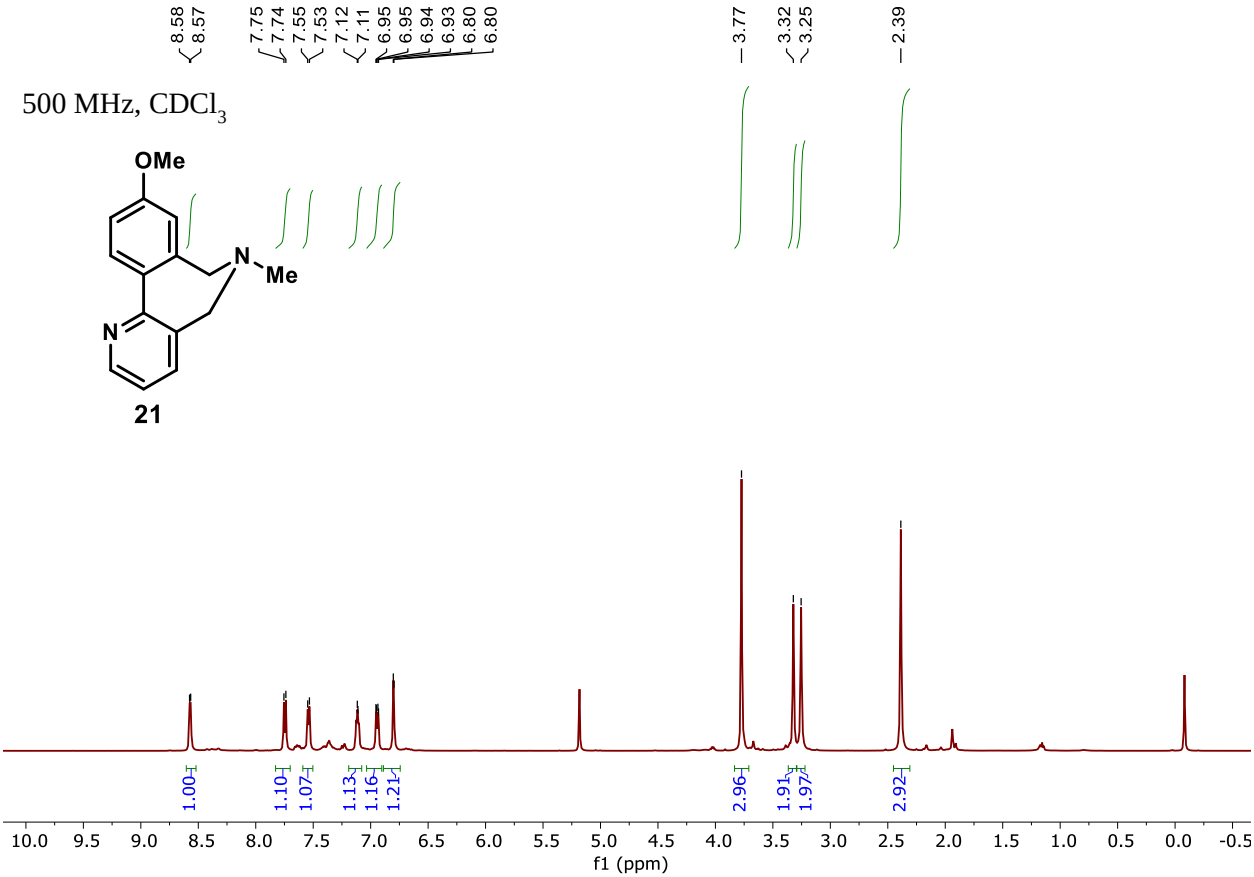
19

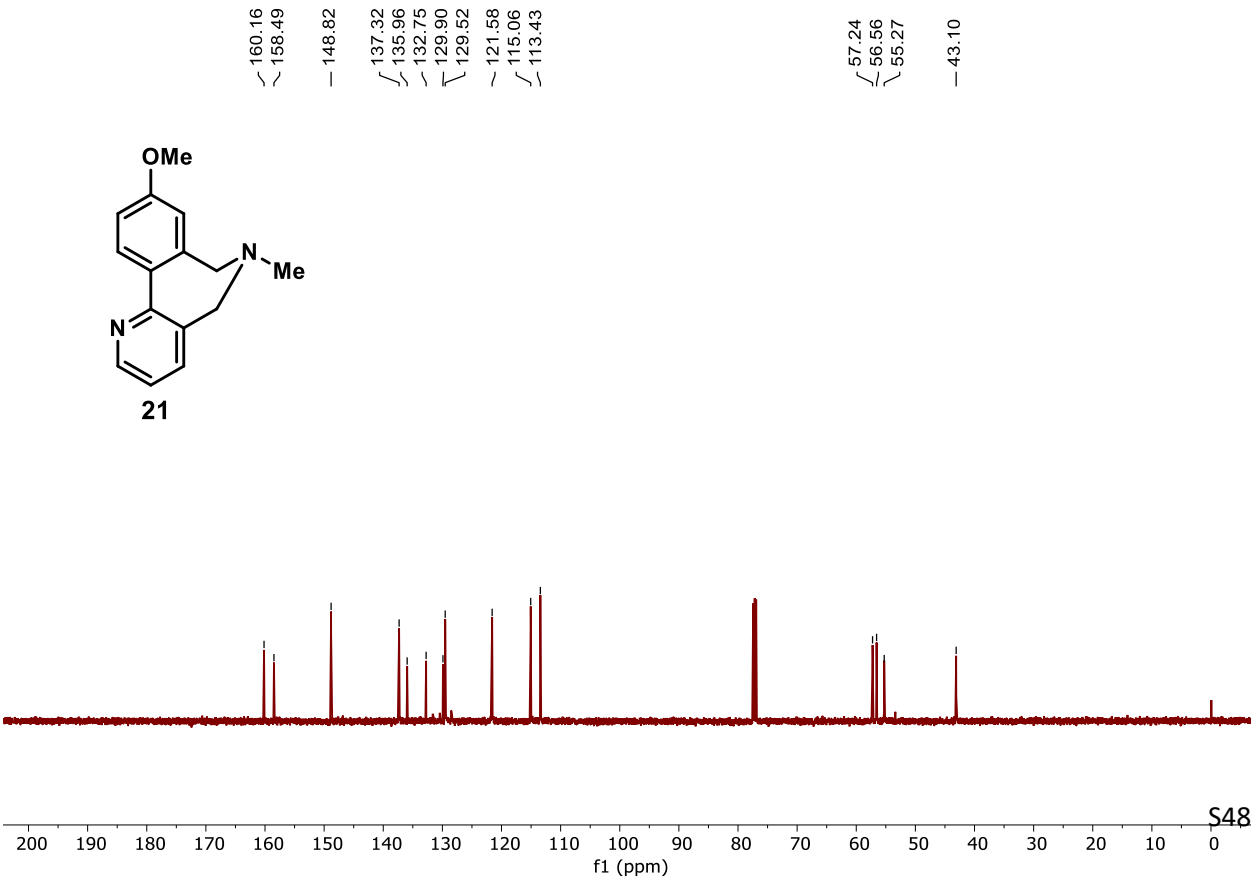


19

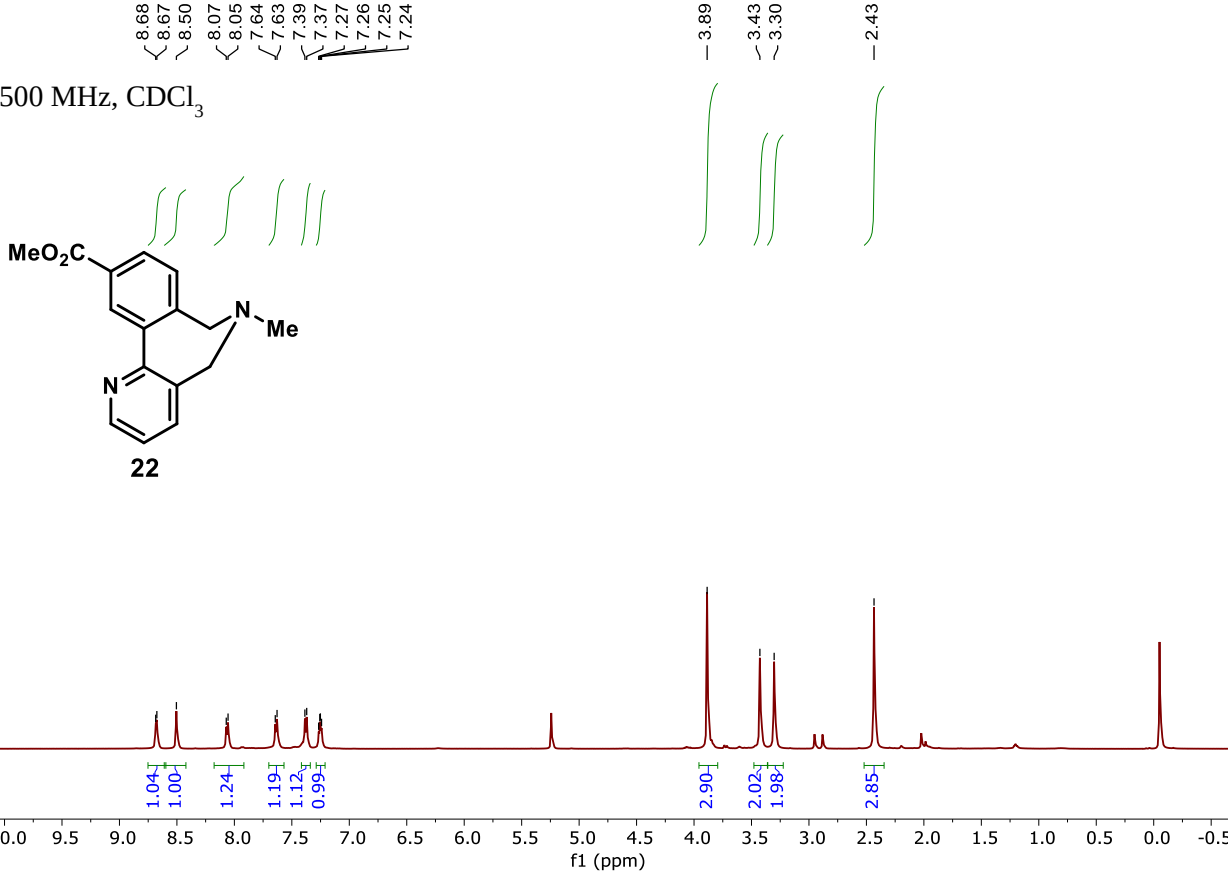

8.66
8.66
8.65
8.65
7.65
7.64
7.63
7.63
7.57
7.57
7.55
7.55
7.28
7.27
7.26
7.25
7.25
7.24
7.23
7.09
7.09
7.07
7.07
7.06
7.05
3.36
3.31
2.42
500 MHz, CDCl3
F
N
Me
N
20
1.00
1.23
1.06
2.28
1.13
1.94
2.03
2.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

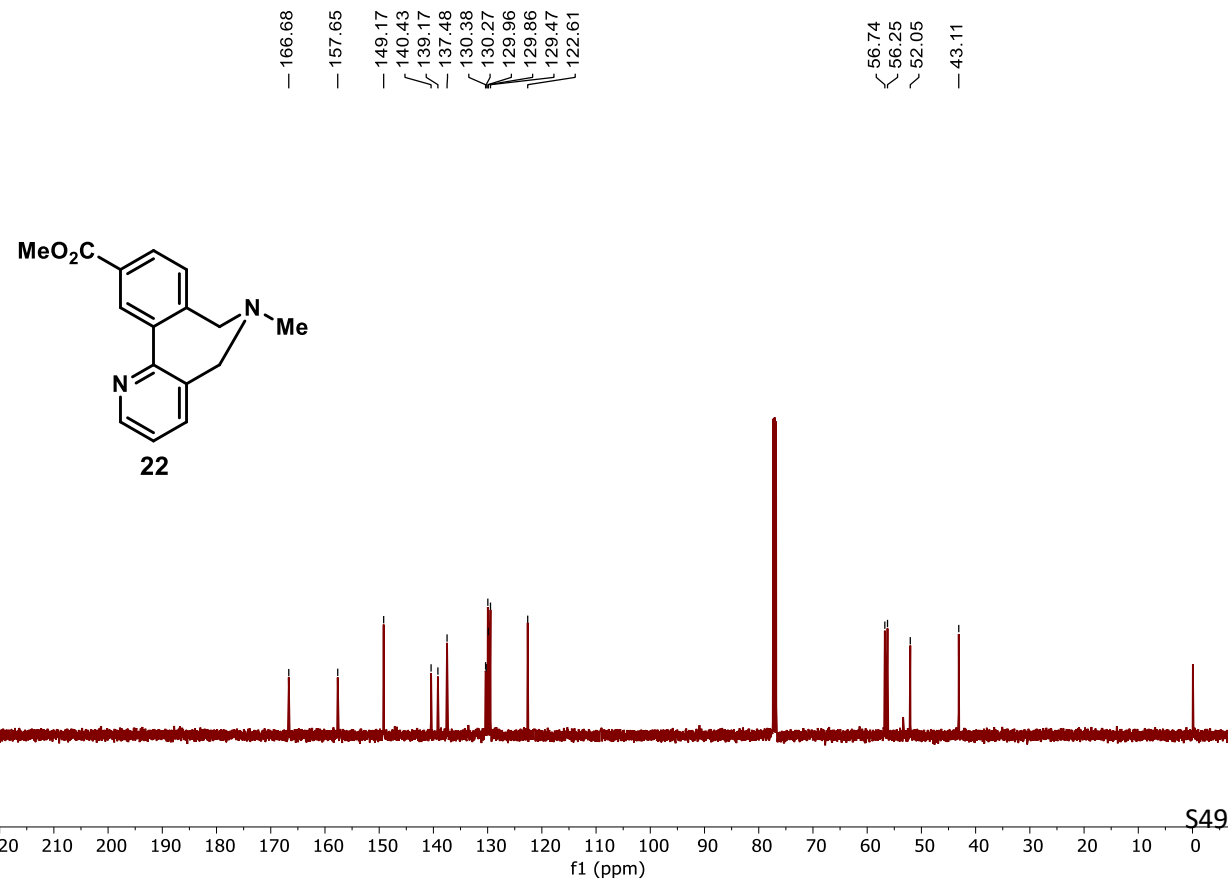

163.63
161.67
157.55
149.03
149.01
142.28
142.21
131.25
131.19
130.42
128.63
128.54
122.63
115.73
115.56
115.15
114.97
56.25
56.21
42.94
F
N
Me
N
20
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

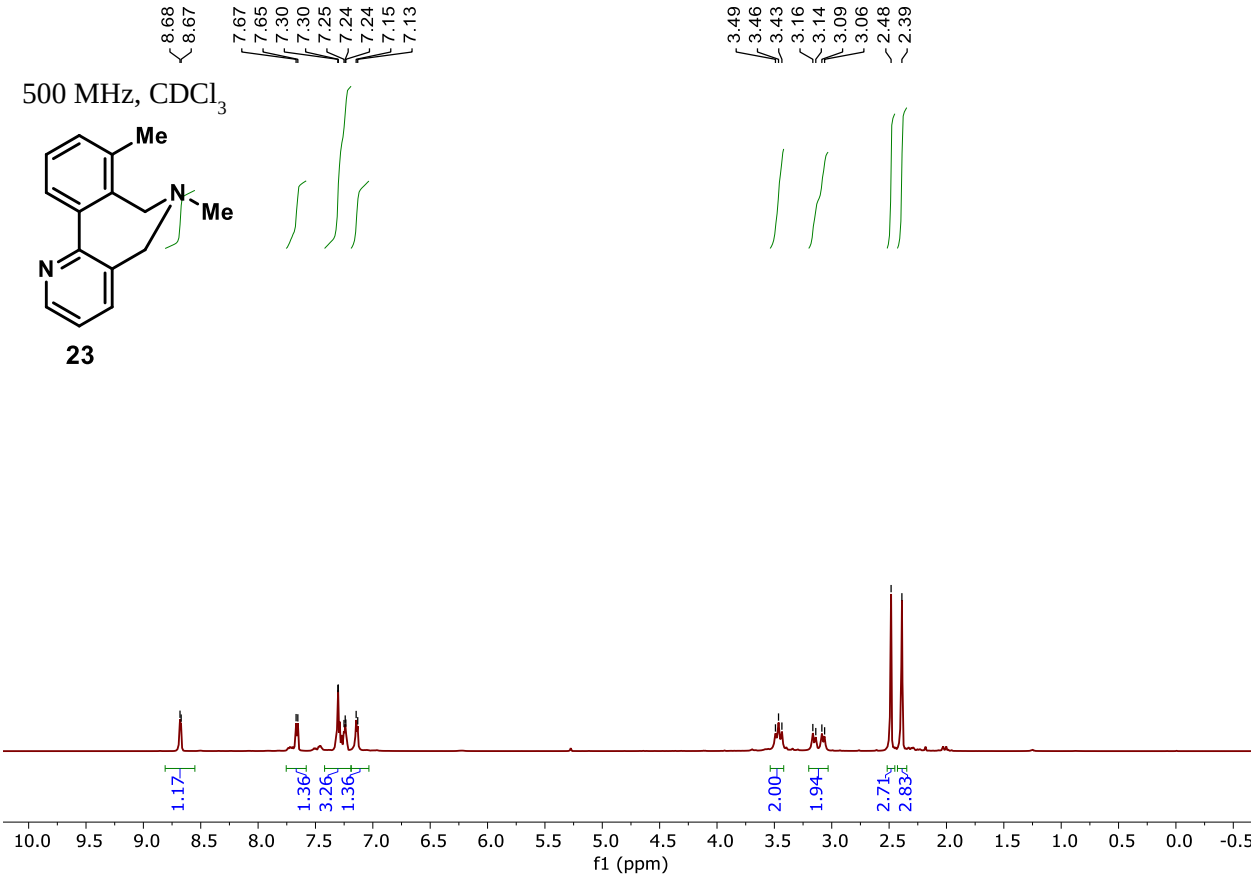

8.58
8.57
7.75
7.74
7.55
7.53
7.12
7.11
6.95
6.95
6.94
6.93
6.80
6.80
3.77
3.32
3.25
2.39
500 MHz, CDCl3
OMe
N
Me
N
21
1.00
1.10
1.07
1.13
1.16
1.21
2.96
1.91
1.97
2.92
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

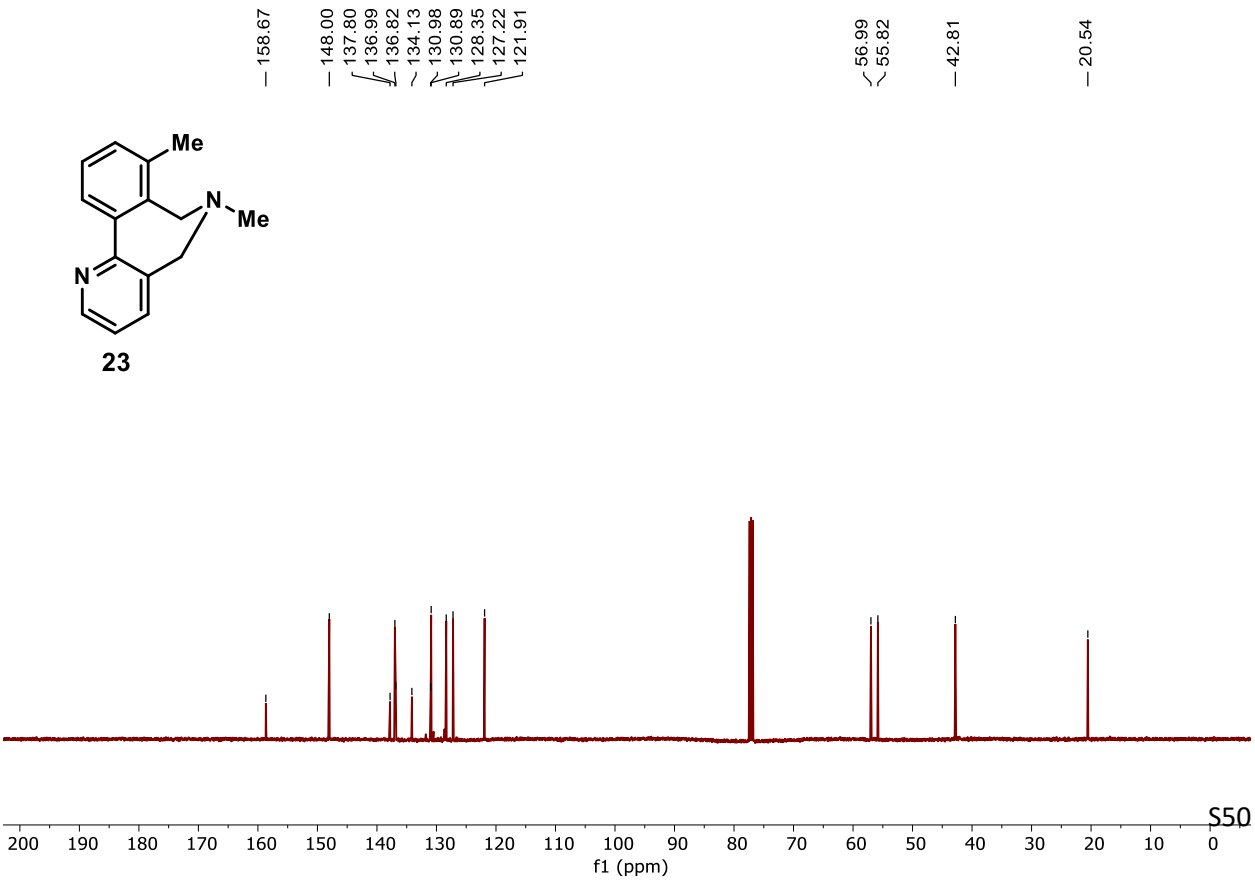

160.16
158.49
148.82
137.32
135.96
132.75
129.90
129.52
121.58
115.06
113.43
57.24
56.56
55.27
43.10
OMe
N
Me
N
21
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

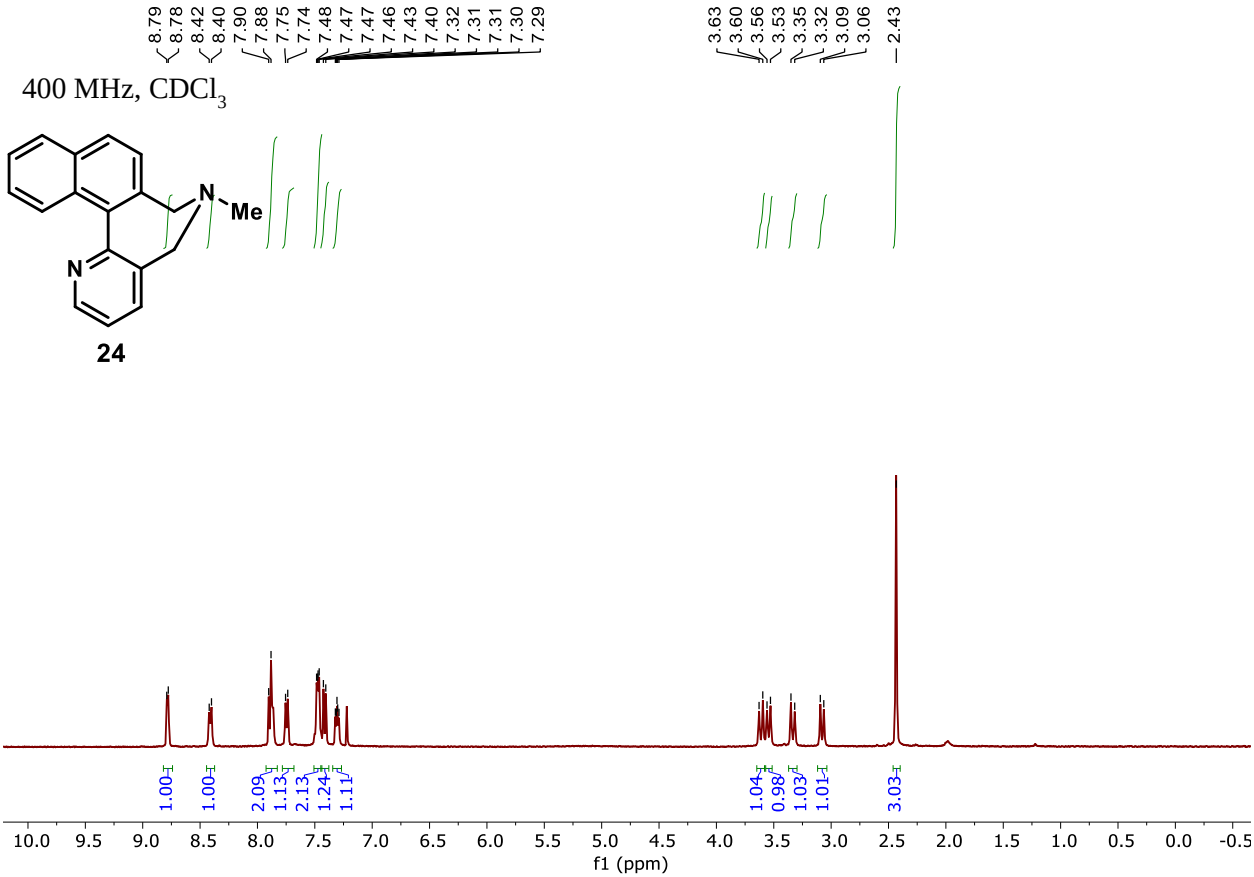
500 MHz, $CDCl_3$

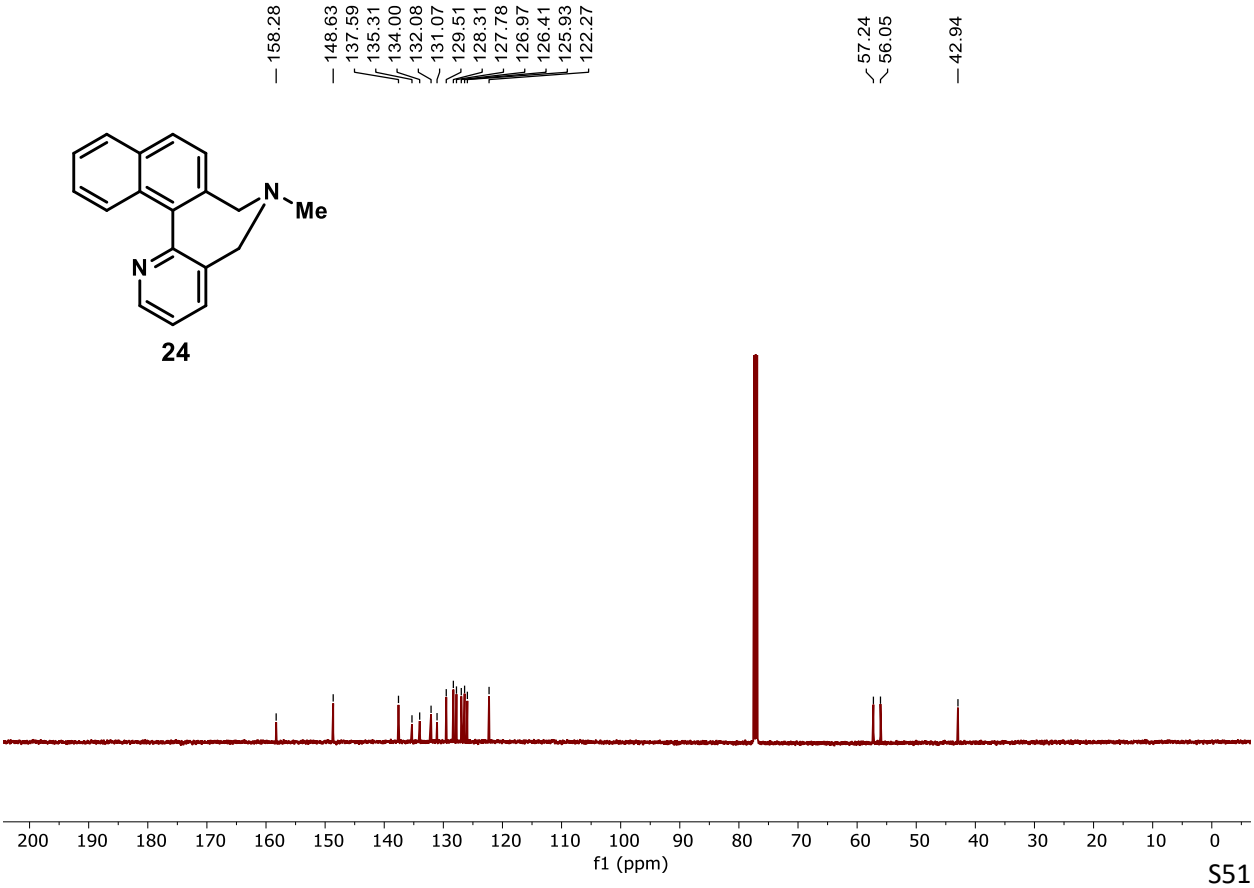


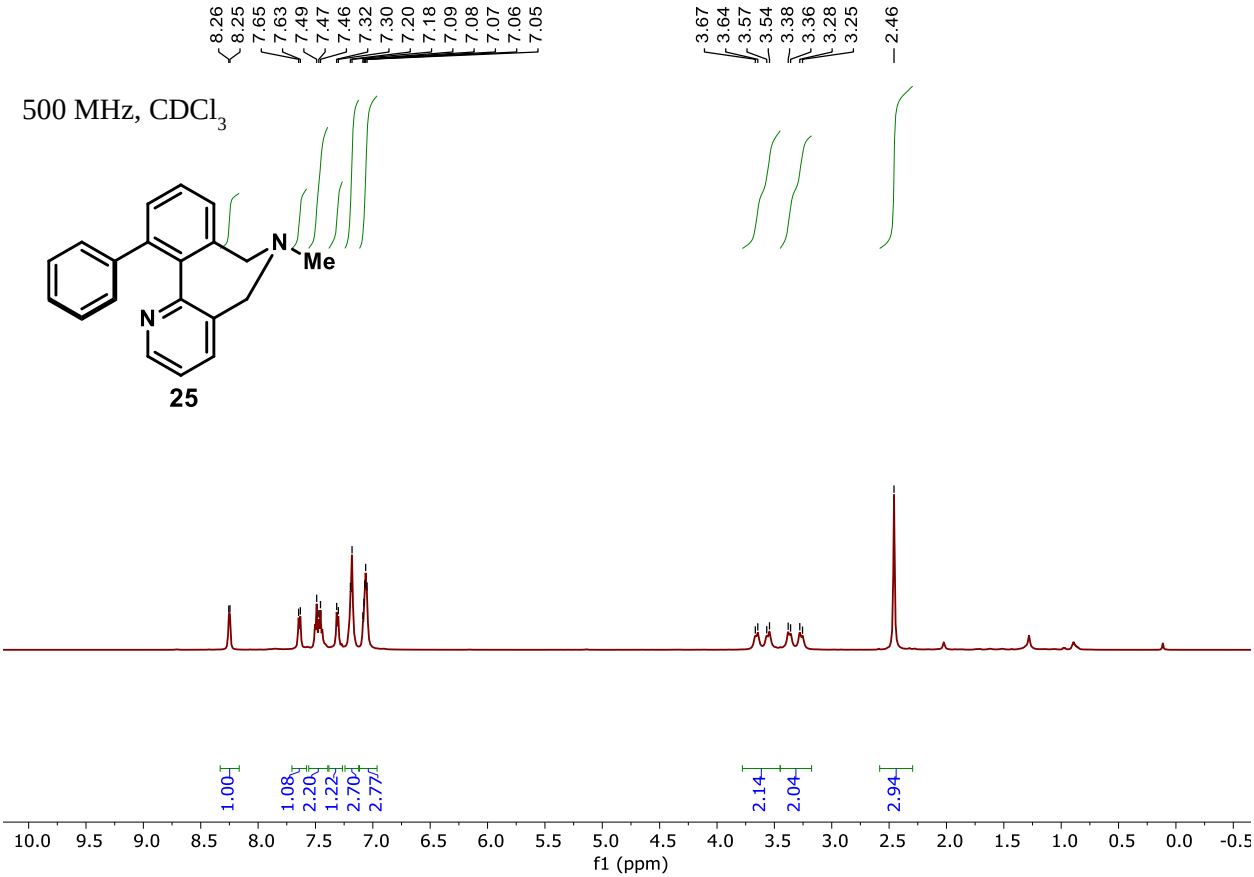


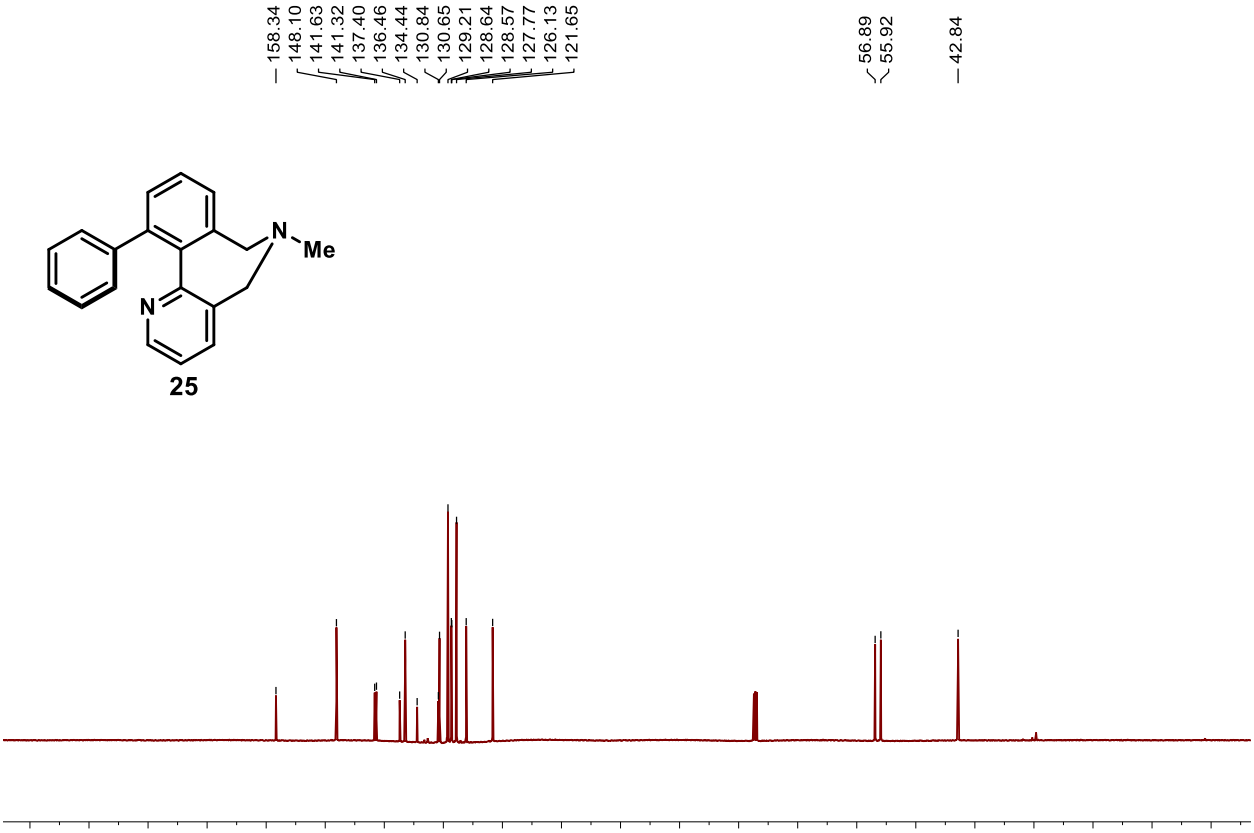

8.68
8.67
7.67
7.65
7.30
7.30
7.25
7.24
7.24
7.15
7.13
3.49
3.46
3.43
3.16
3.14
3.09
3.06
2.48
2.39
500 MHz, CDCl3
Me
N
Me
N
23
1.17
1.36
3.26
1.36
2.00
1.94
2.71
2.83
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

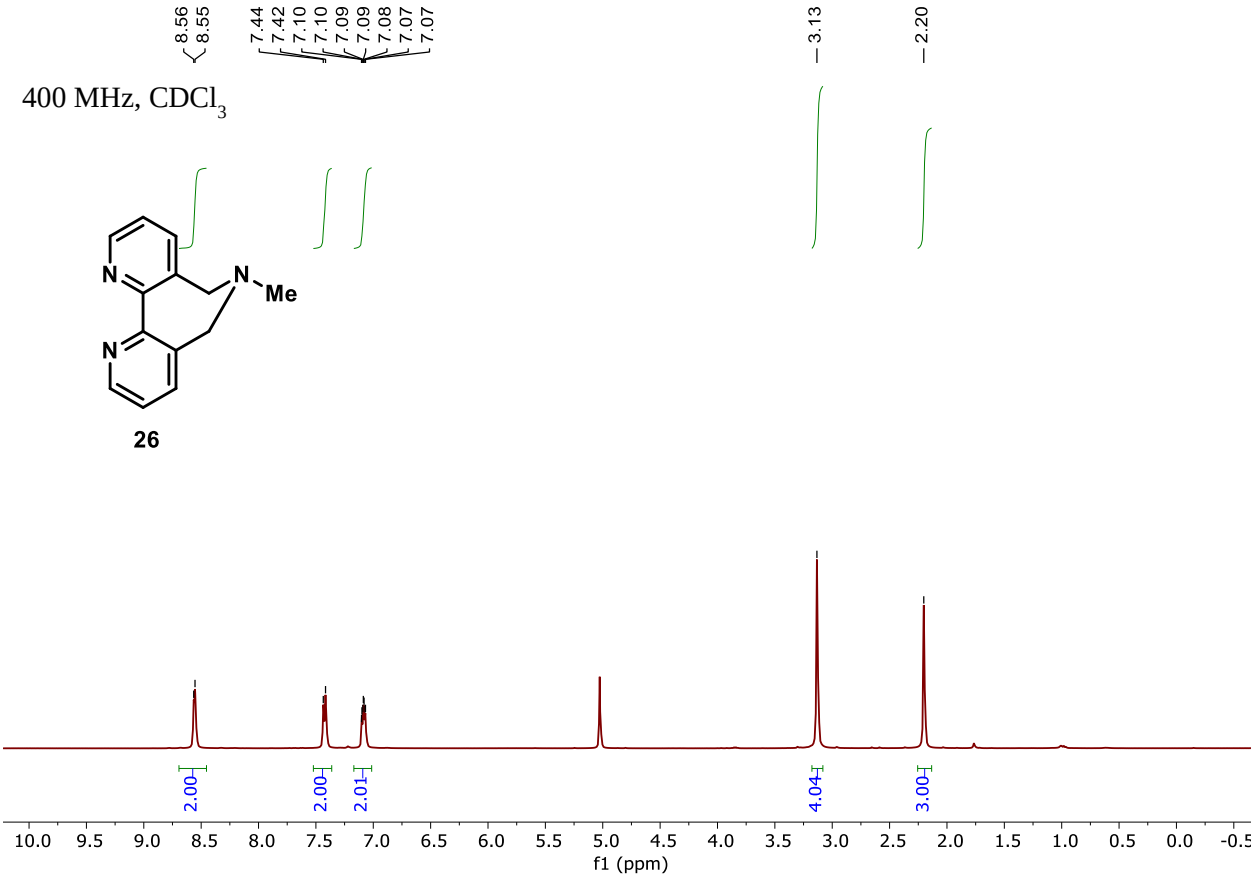

158.67
148.00
137.80
136.99
136.82
134.13
130.98
130.89
128.35
127.22
121.91
56.99
55.82
42.81
20.54
Me
N
Me
N
23
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

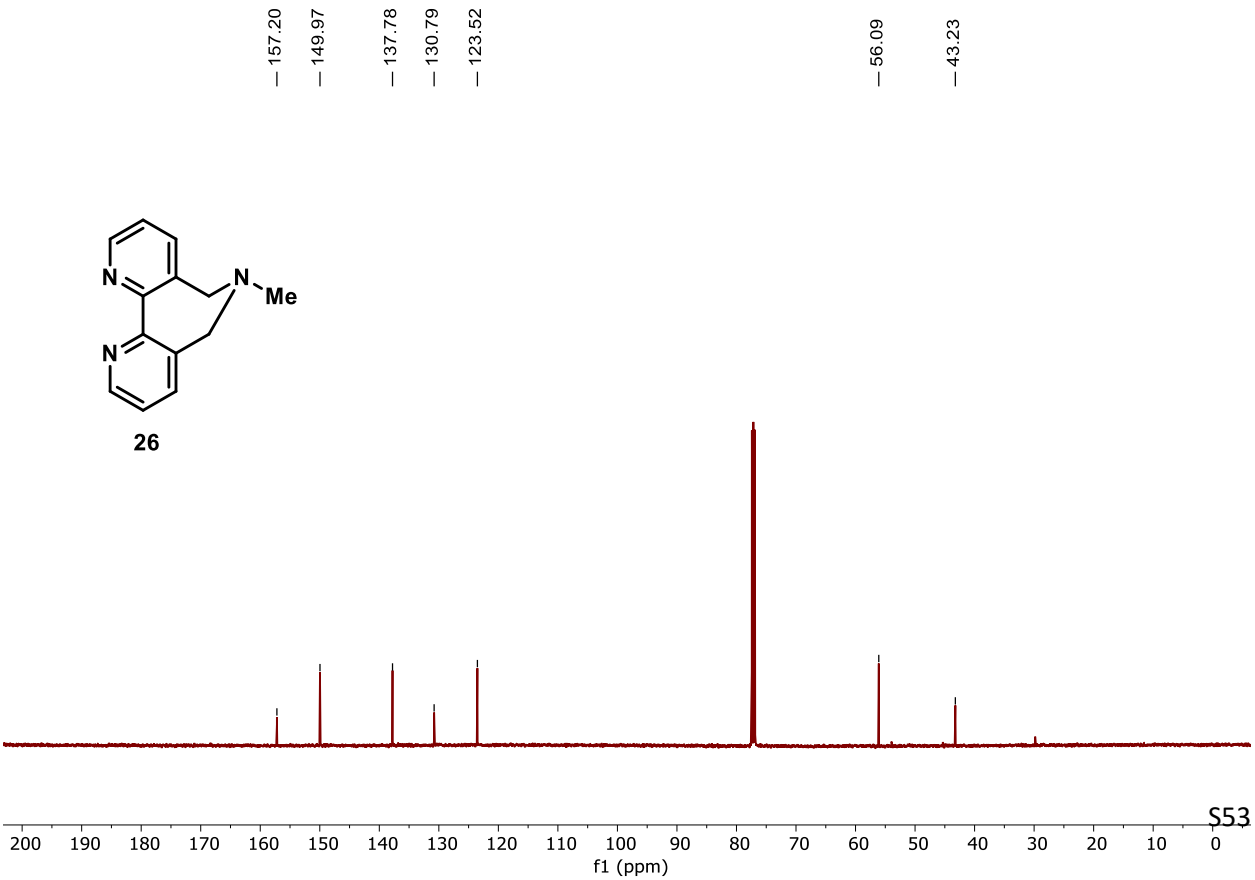

8.79
8.78
8.42
8.40
7.90
7.88
7.75
7.74
7.48
7.47
7.47
7.46
7.43
7.40
7.32
7.31
7.31
7.30
7.29
3.63
3.60
3.56
3.53
3.35
3.32
3.09
3.06
2.43
400 MHz, CDCl3
N
Me
N
24
1.00
1.00
2.09
1.13
2.13
1.24
1.11
1.04
0.98
1.03
1.01
3.03
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

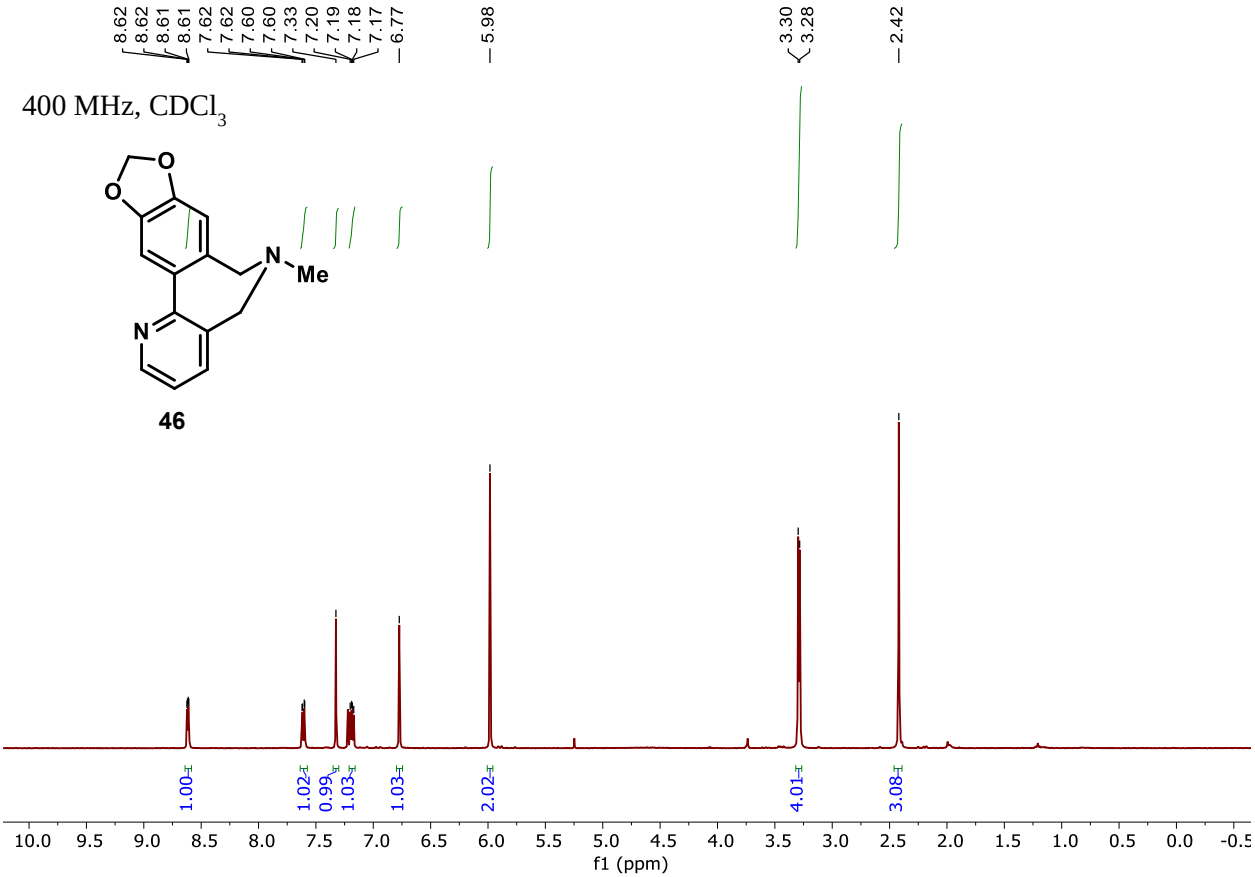

158.28
148.63
137.59
135.31
134.00
132.08
131.07
129.51
128.31
127.78
126.97
126.41
125.93
122.27
57.24
56.05
42.94
N
Me
N
24
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

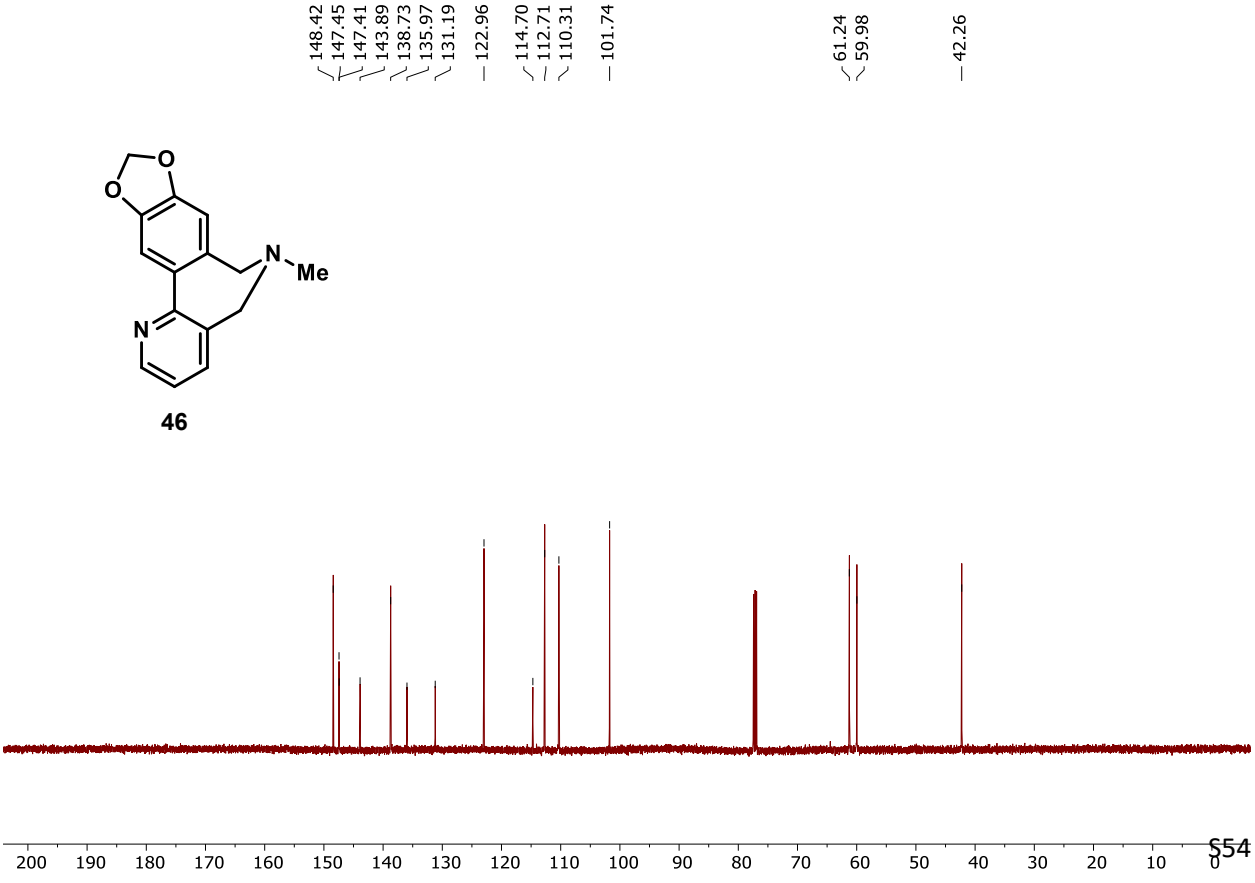

8.26
8.25
7.65
7.63
7.49
7.47
7.46
7.32
7.30
7.20
7.18
7.09
7.08
7.07
7.06
7.05
3.67
3.64
3.57
3.54
3.38
3.36
3.28
3.25
2.46
500 MHz, CDCl3
N
Me
N
25
1.00
1.08
2.20
1.22
2.70
2.77
2.14
2.04
2.94
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


158.34
148.10
141.63
141.32
137.40
136.46
134.44
130.84
130.65
129.21
128.64
128.57
127.77
126.13
121.65
56.89
55.92
42.84
N
Me
N
25
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

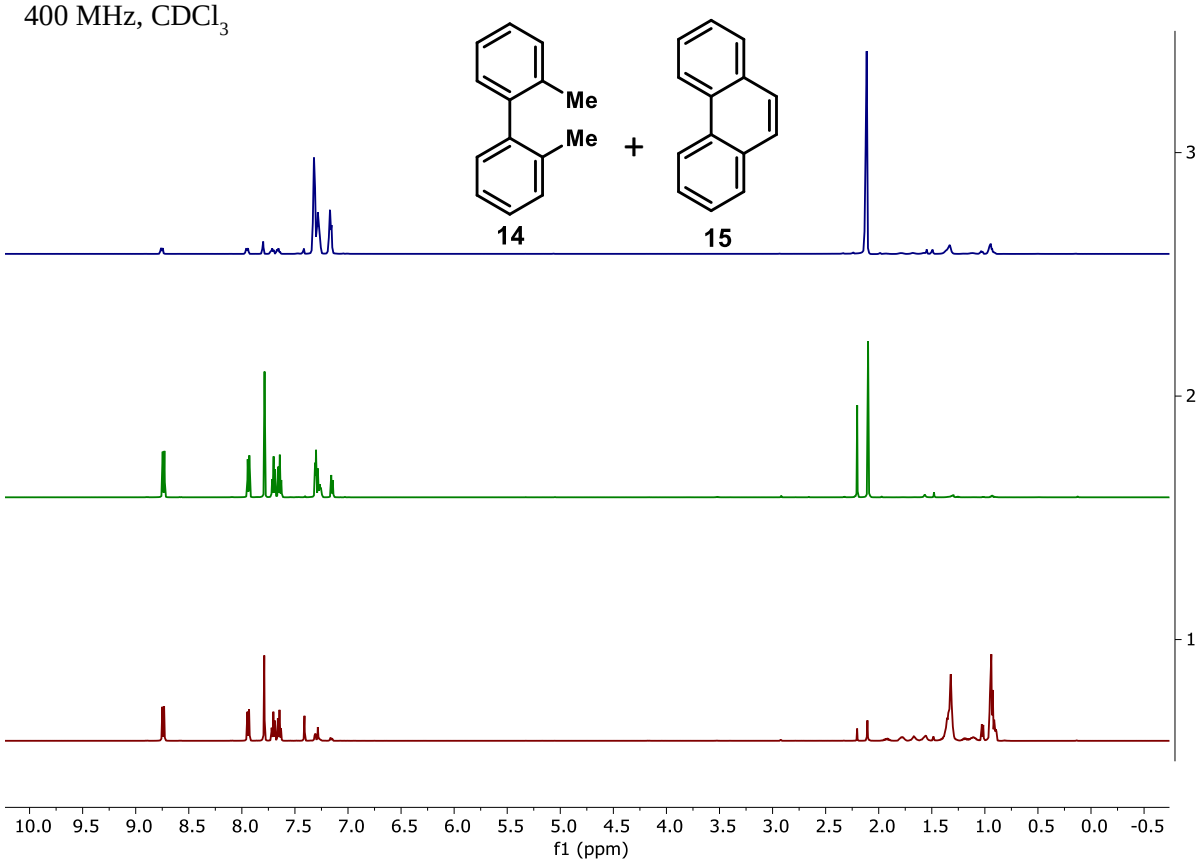

8.56
8.55
7.44
7.42
7.10
7.10
7.09
7.09
7.08
7.07
7.07
3.13
2.20
400 MHz, CDCl3
N
N
N
Me
26
2.00
2.00
2.01
4.04
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


157.20
149.97
137.78
130.79
123.52
56.09
43.23
N
N
N
Me
26
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

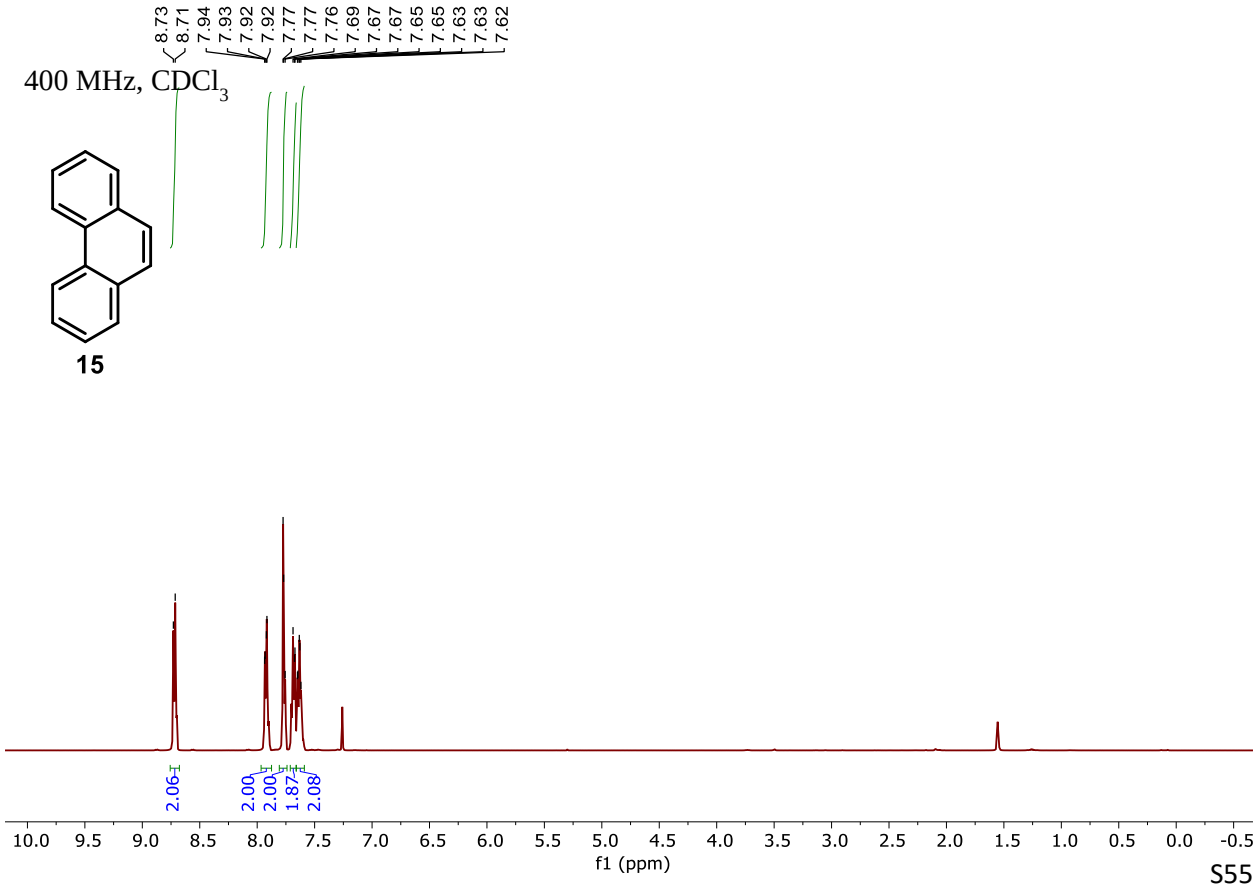

8.62
8.62
8.61
8.61
7.62
7.62
7.60
7.60
7.33
7.20
7.19
7.18
7.17
6.77
5.98
3.30
3.28
2.42
400 MHz, CDCl3
O
O
N
Me
N
46
1.00
1.02
0.99
1.03
1.03
2.02
4.01
3.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

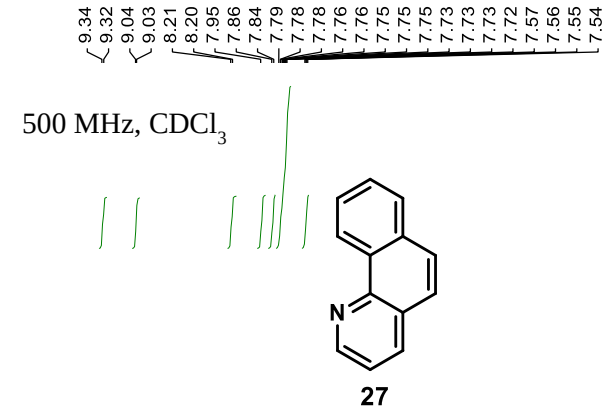

148.42
147.45
147.41
143.89
138.73
135.97
131.19
122.96
114.70
112.71
110.31
101.74
61.24
59.98
42.26
O
O
N
Me
N
46
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

400 MHz, $CDCl_3$

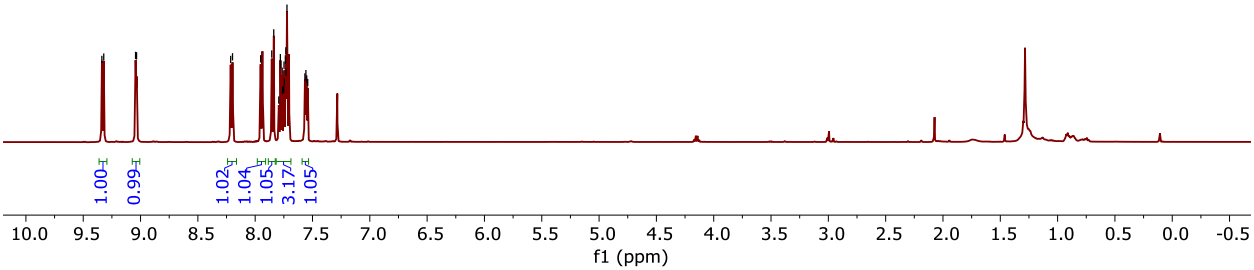


400 MHz, $CDCl_3$

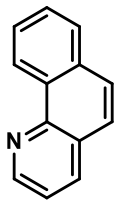



9.34
9.32
9.04
9.03
8.21
8.20
7.95
7.86
7.84
7.79
7.78
7.78
7.76
7.76
7.75
7.75
7.75
7.73
7.73
7.73
7.72
7.57
7.56
7.55
7.54
500 MHz, CDCl3
N

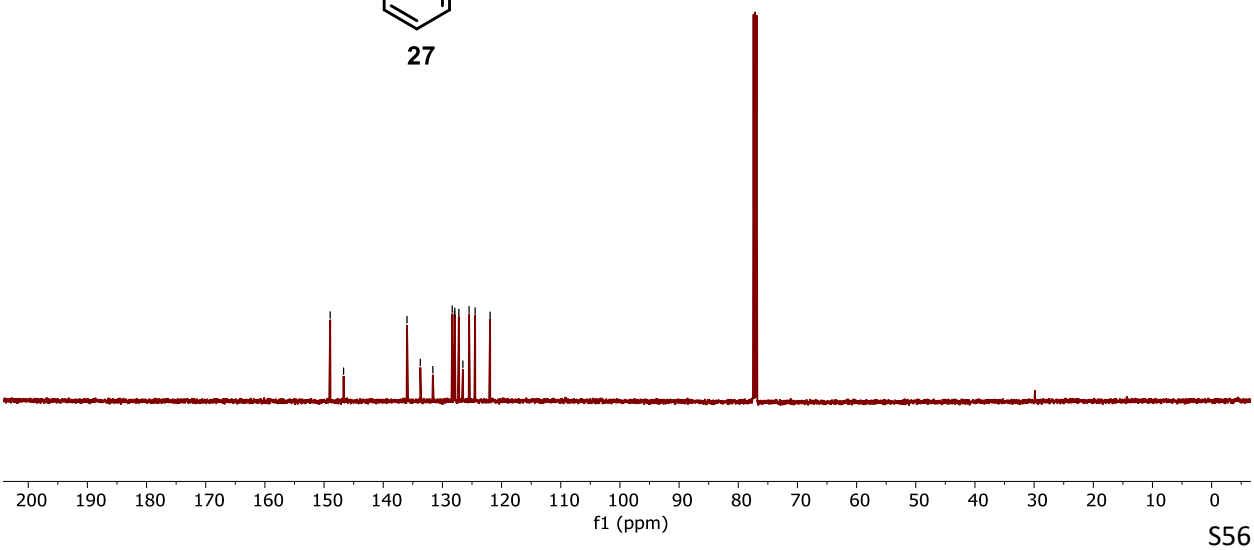
27


1.00
0.99
1.02
1.04
1.05
3.17
1.05
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

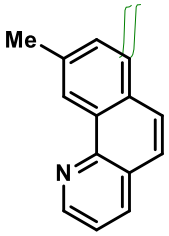

148.97
146.70
135.98
133.73
131.62
128.34
127.96
127.91
127.22
126.54
125.49
124.47
121.94


N

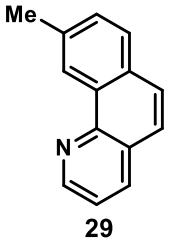
27


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

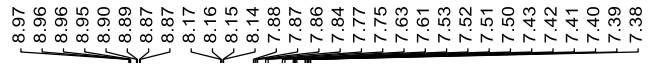
400 MHz, $CDCl_3$



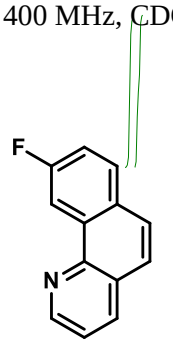
29



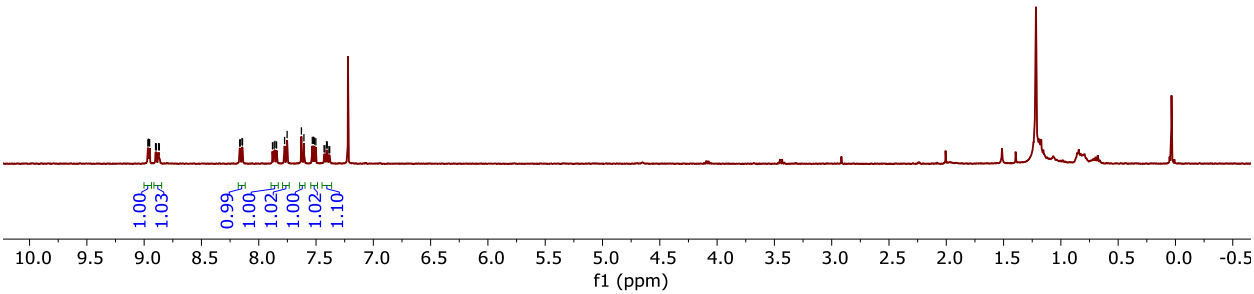
29

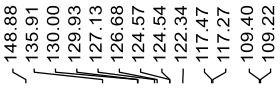


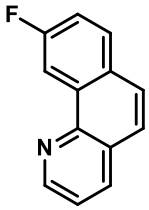
400 MHz, $CDCl_3$



30

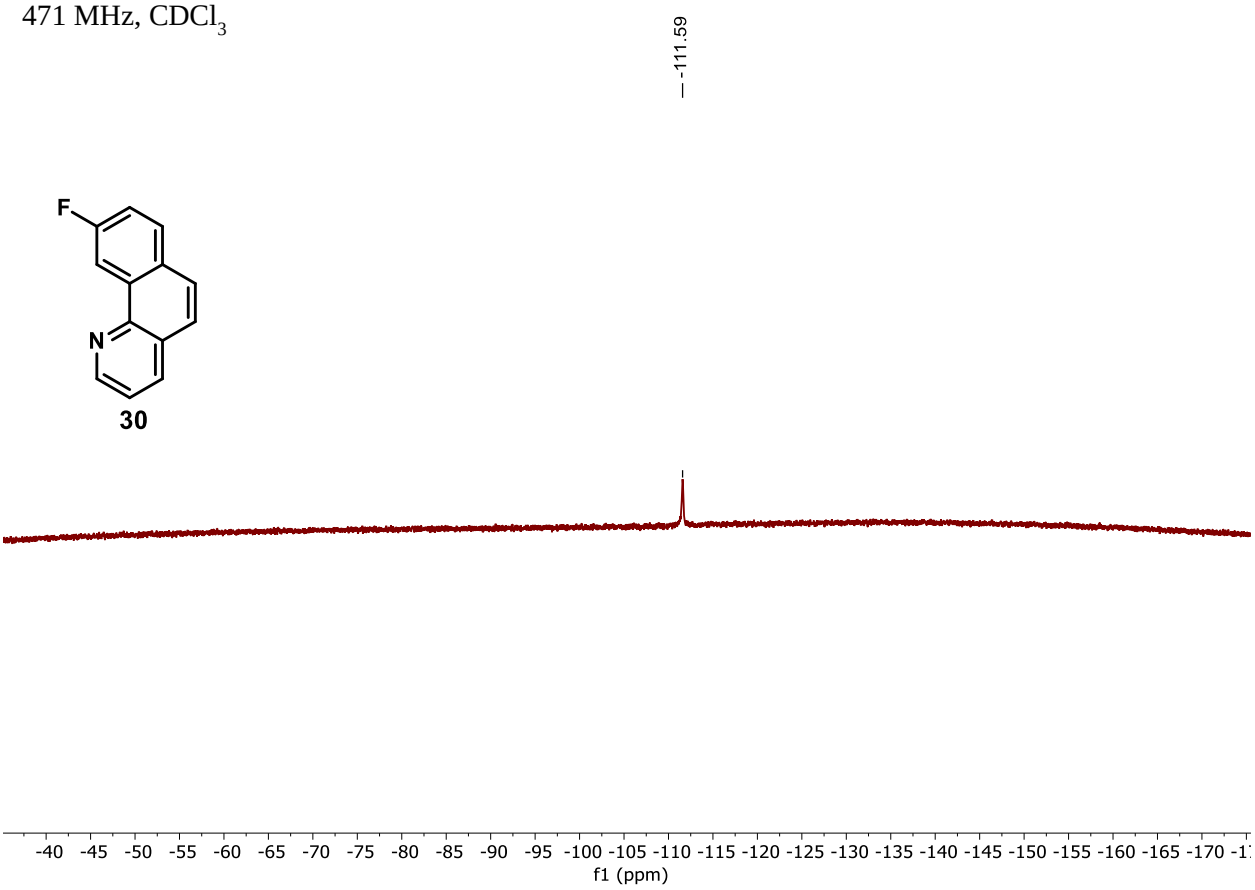


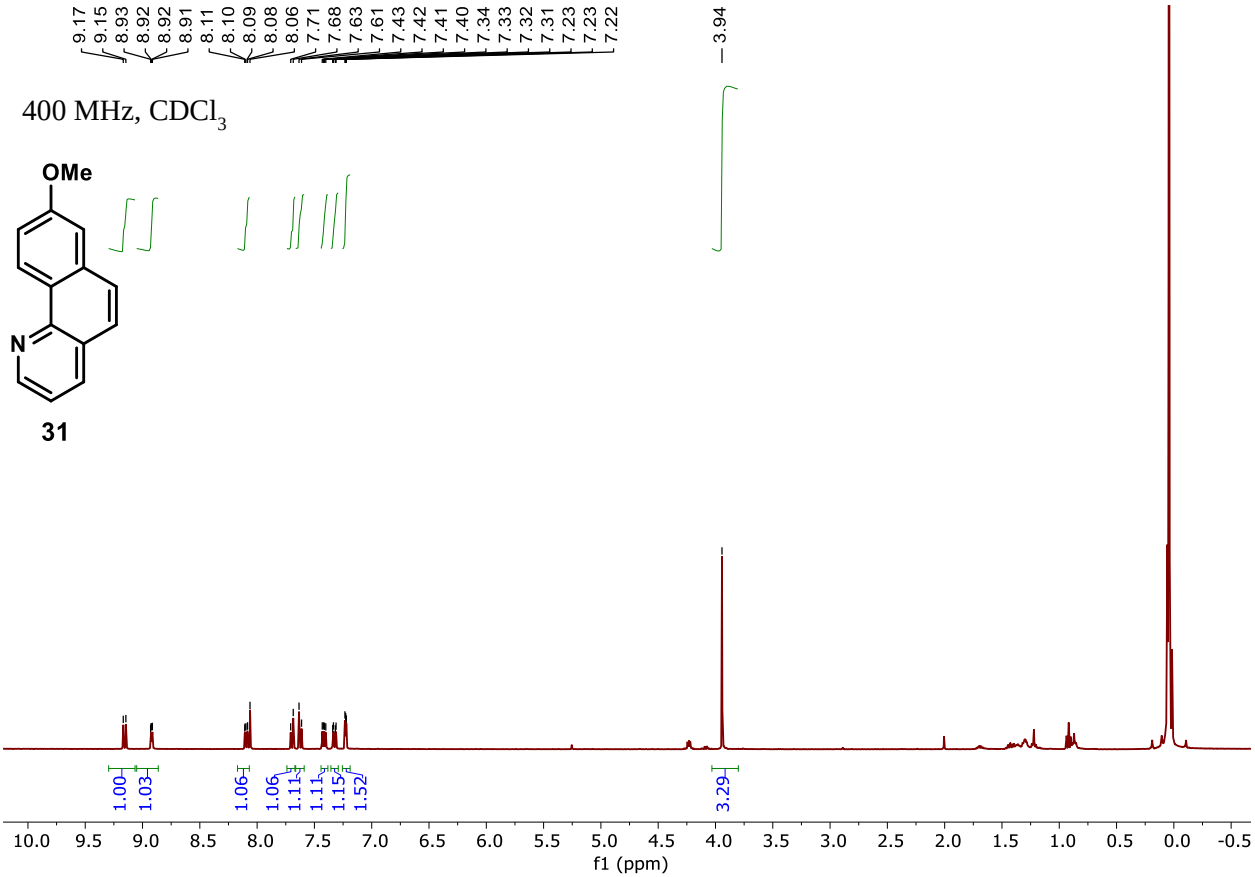


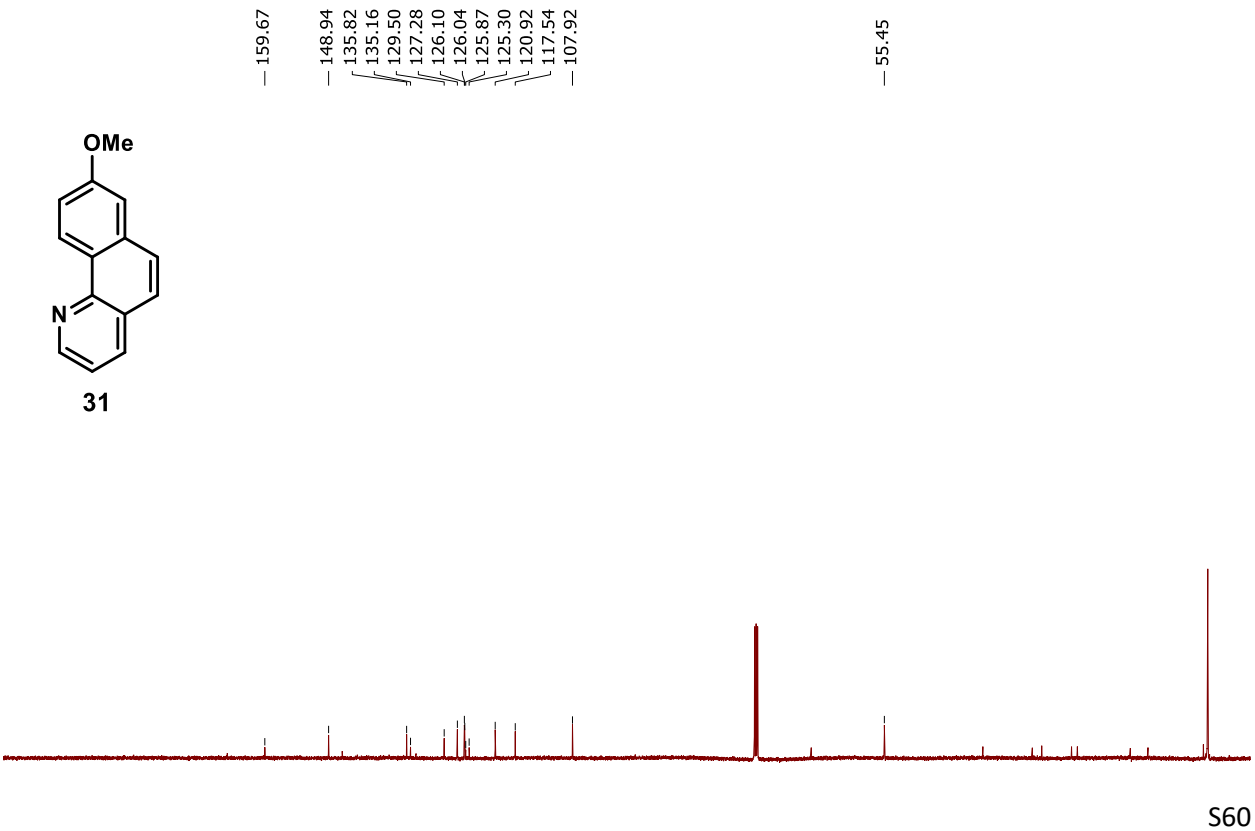


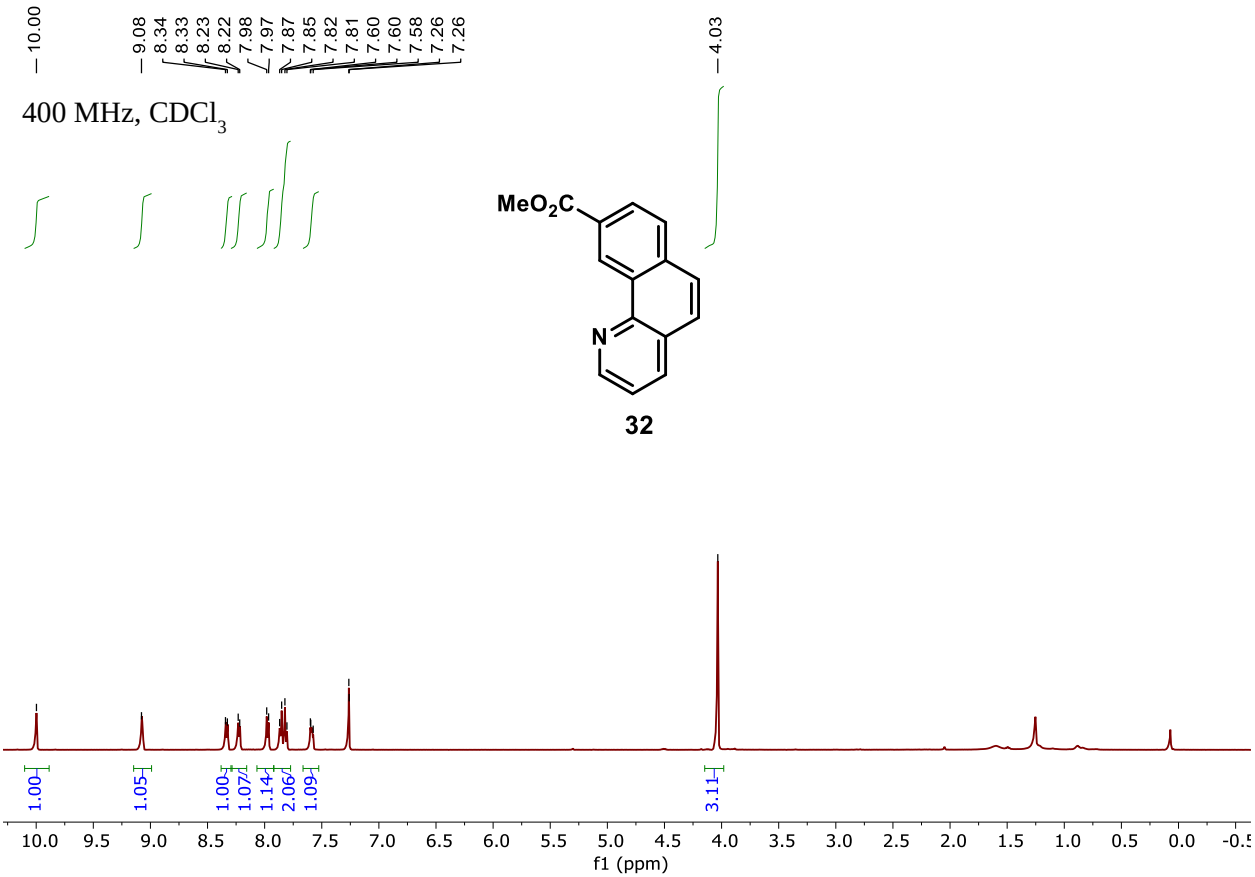
30

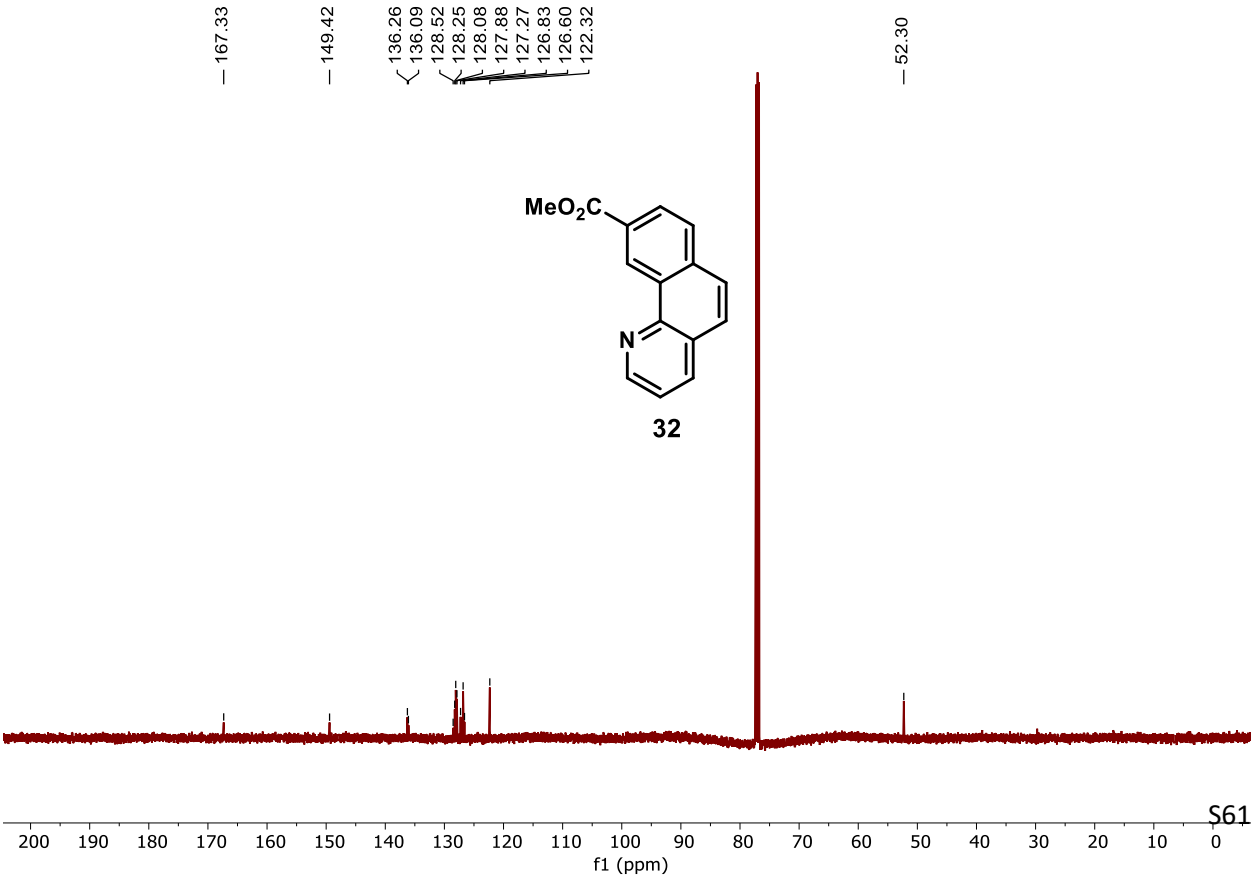
471 MHz, $CDCl_3$

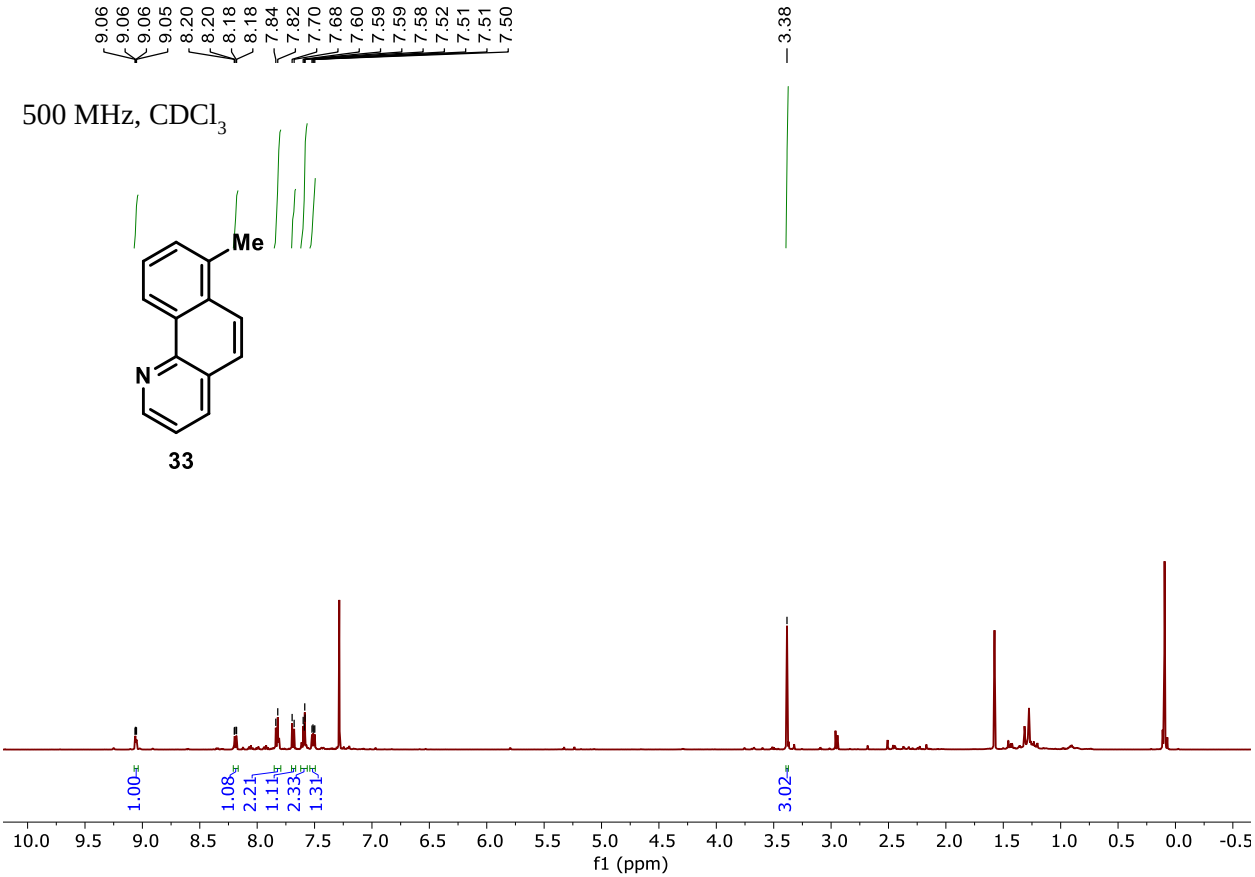


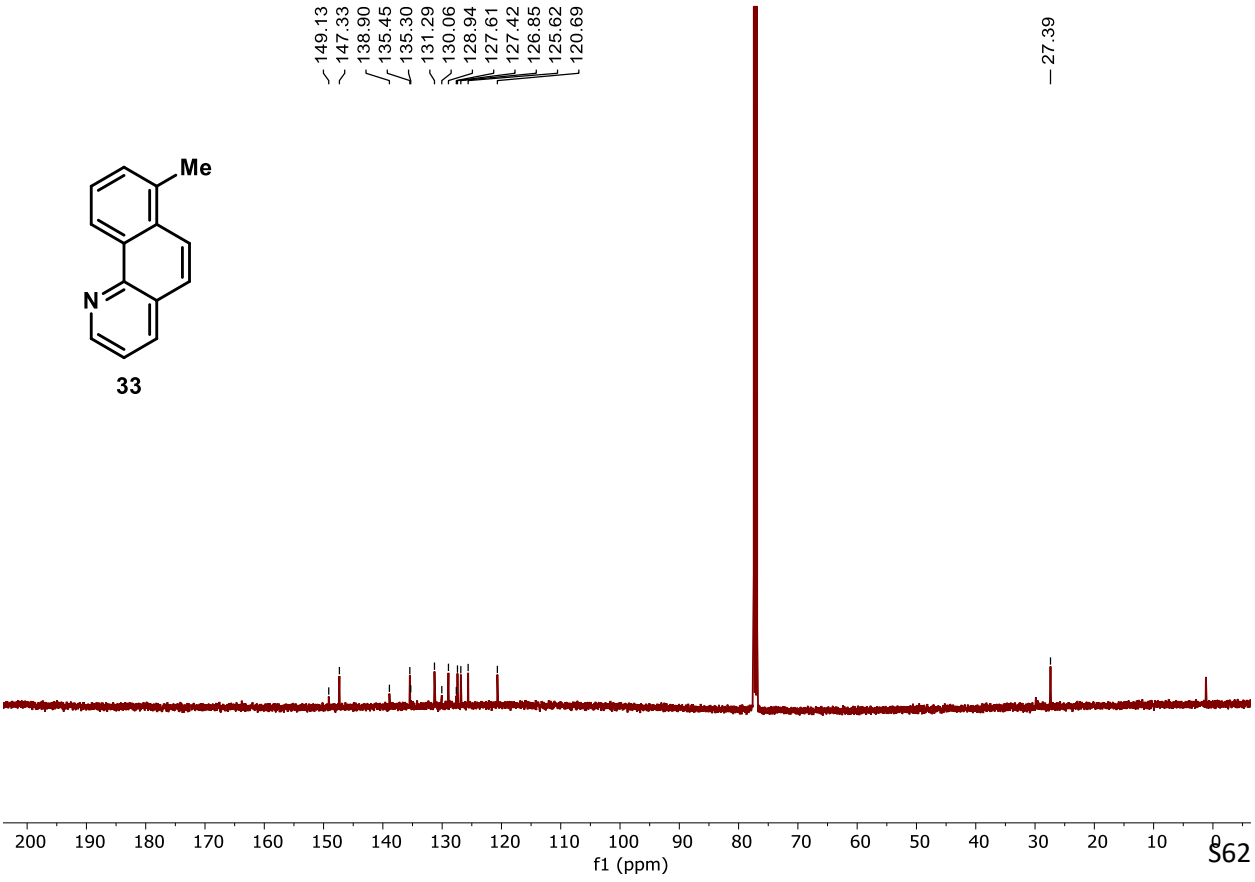

9.17
9.15
8.93
8.92
8.92
8.91
8.11
8.10
8.09
8.08
8.06
7.71
7.68
7.63
7.61
7.43
7.42
7.41
7.40
7.34
7.33
7.32
7.31
7.23
7.23
7.22
3.94
400 MHz, CDCl3
OMe
N
31
1.00
1.03
1.06
1.06
1.11
1.11
1.15
1.52
3.29
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

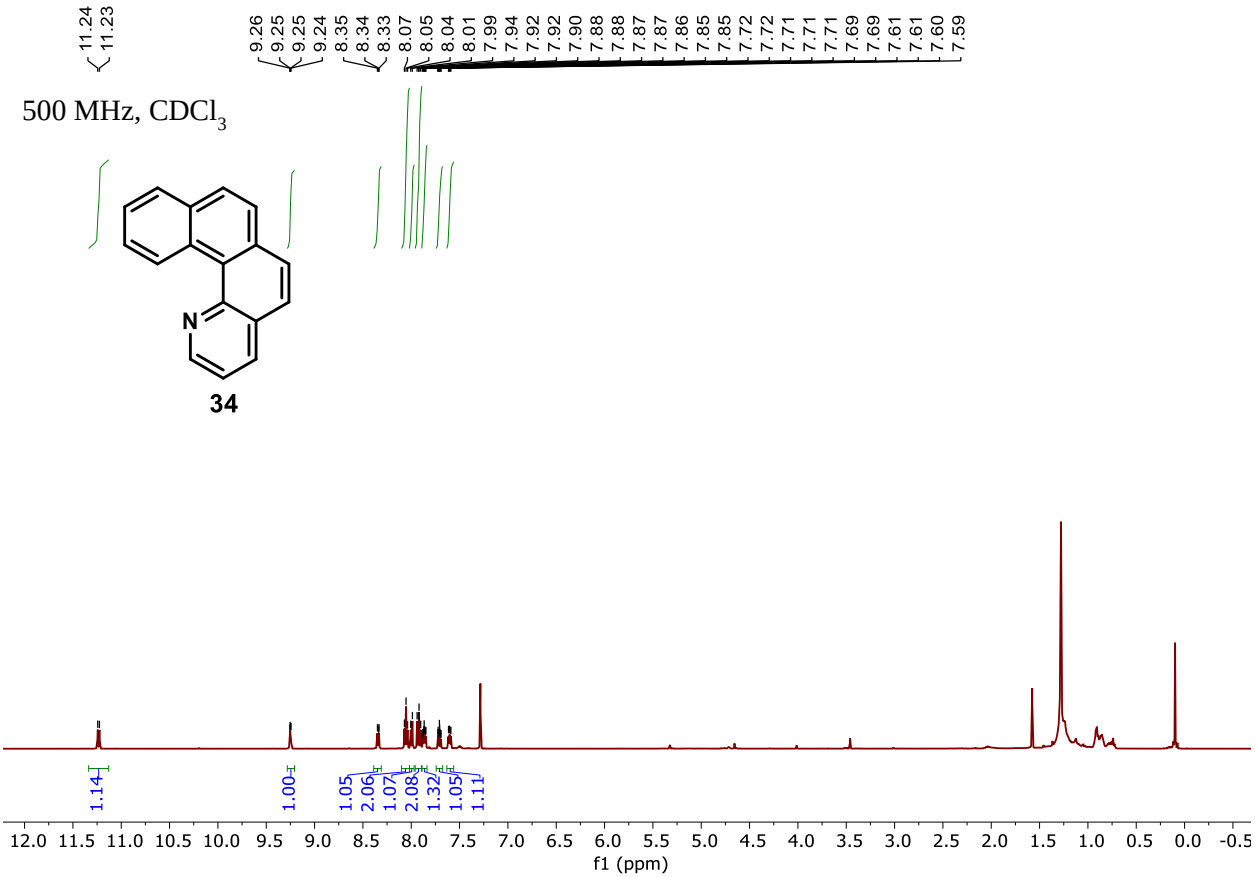

159.67
148.94
135.82
135.16
129.50
127.28
126.10
126.04
125.87
125.30
120.92
117.54
107.92
55.45
OMe
N
31
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

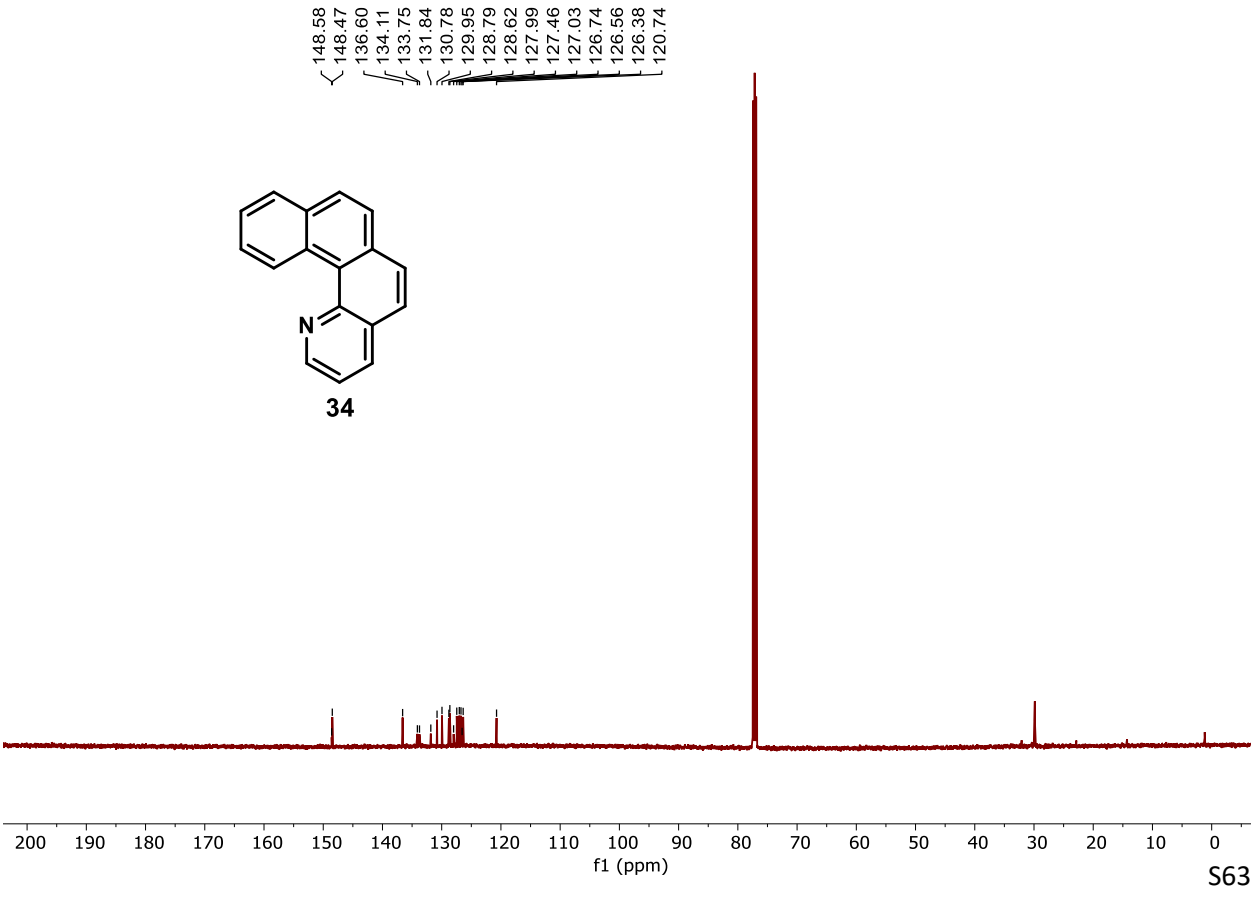

10.00
9.08
8.34
8.33
8.23
8.22
7.98
7.97
7.87
7.85
7.82
7.81
7.60
7.60
7.58
7.26
7.26
4.03
400 MHz, CDCl3
MeO2C
N
32
1.00
1.05
1.00
1.07
1.14
2.06
1.09
3.11
f1 (ppm)

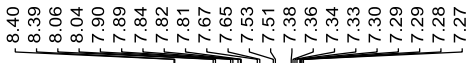

167.33
149.42
136.26
136.09
128.52
128.25
128.08
127.88
127.27
126.83
126.60
122.32
52.30
MeO2C
N
32
f1 (ppm)


9.06
9.06
9.06
9.05
8.20
8.20
8.18
8.18
7.84
7.82
7.70
7.68
7.60
7.59
7.59
7.58
7.52
7.51
7.51
7.50
3.38
500 MHz, CDCl3
Me
N
33
1.00
1.08
2.21
1.11
2.33
1.31
3.02
f1 (ppm)

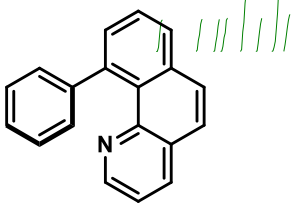

149.13
147.33
138.90
135.45
135.30
131.29
130.06
128.94
127.61
127.42
126.85
125.62
120.69
27.39
Me
N
33
f1 (ppm)


11.24
11.23
9.26
9.25
9.25
9.24
8.35
8.34
8.33
8.07
8.05
8.04
8.01
7.99
7.94
7.92
7.92
7.90
7.88
7.88
7.87
7.87
7.86
7.85
7.85
7.72
7.71
7.71
7.71
7.69
7.69
7.61
7.61
7.60
7.59
500 MHz, CDCl3
N
34
1.14
1.00
1.05
2.06
1.07
2.08
1.32
1.05
1.11
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

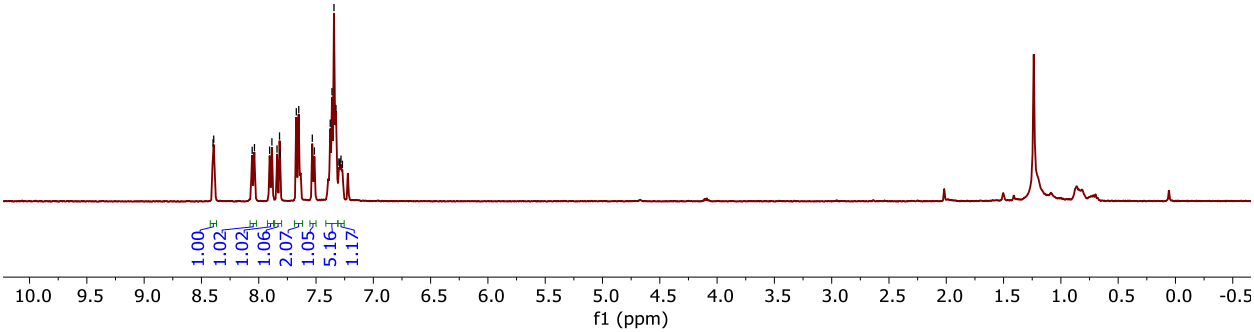

148.58
148.47
136.60
134.11
133.75
131.84
130.78
129.95
128.79
128.62
127.99
127.46
127.03
126.74
126.56
126.38
120.74
N
34
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

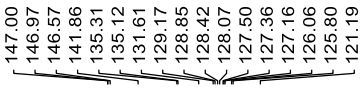


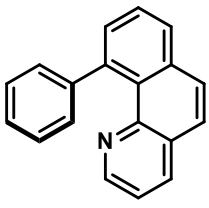
500 MHz, $CDCl_3$



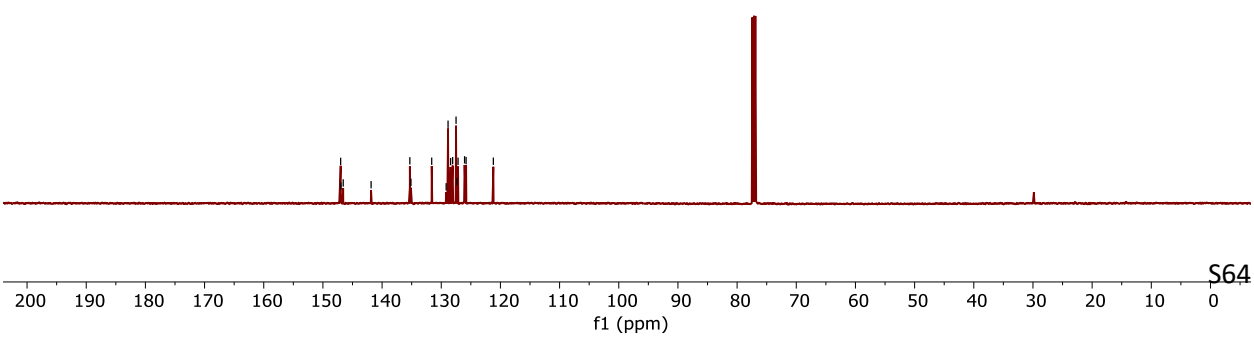
35



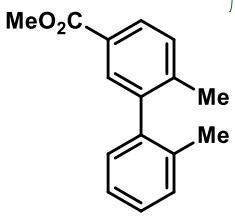




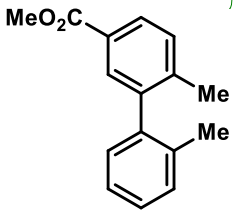
35



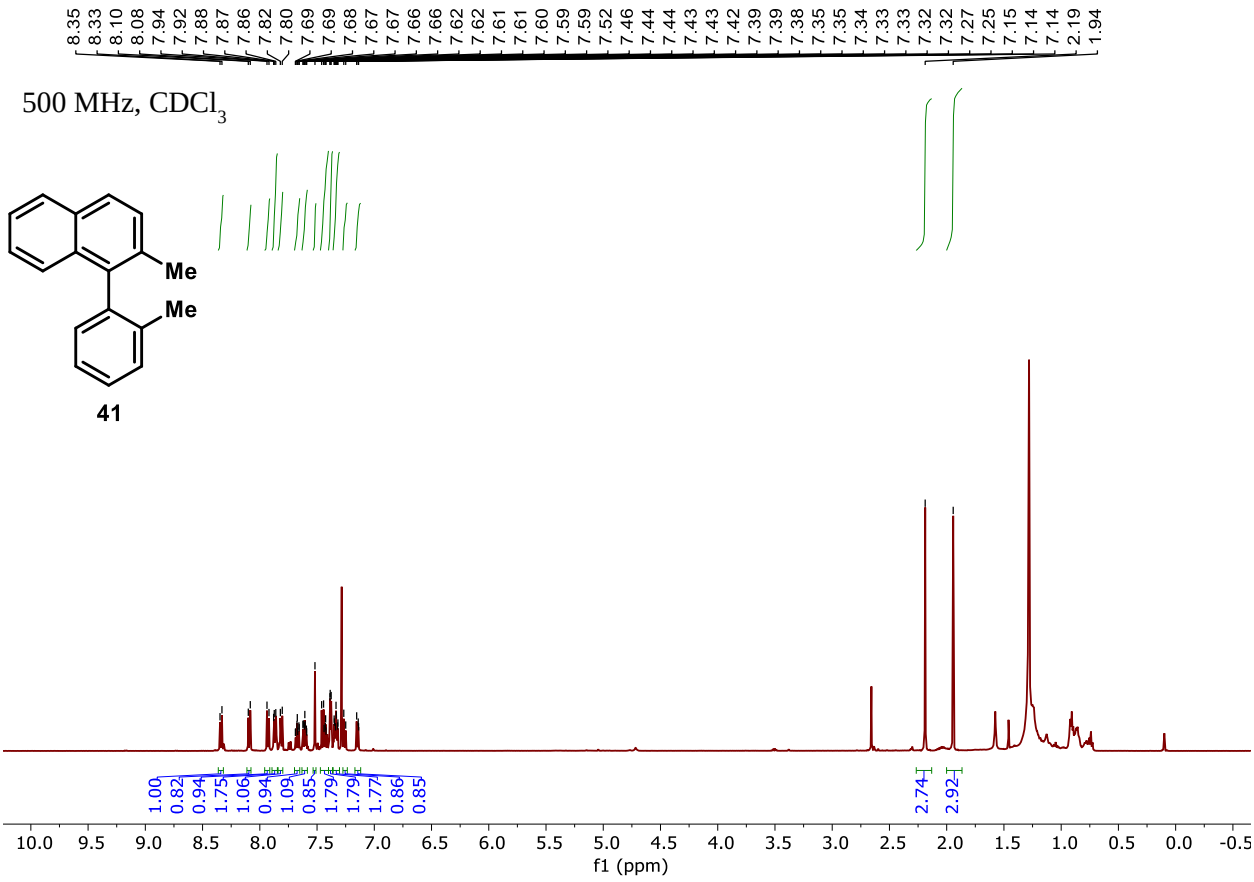
500 MHz, $CDCl_3$

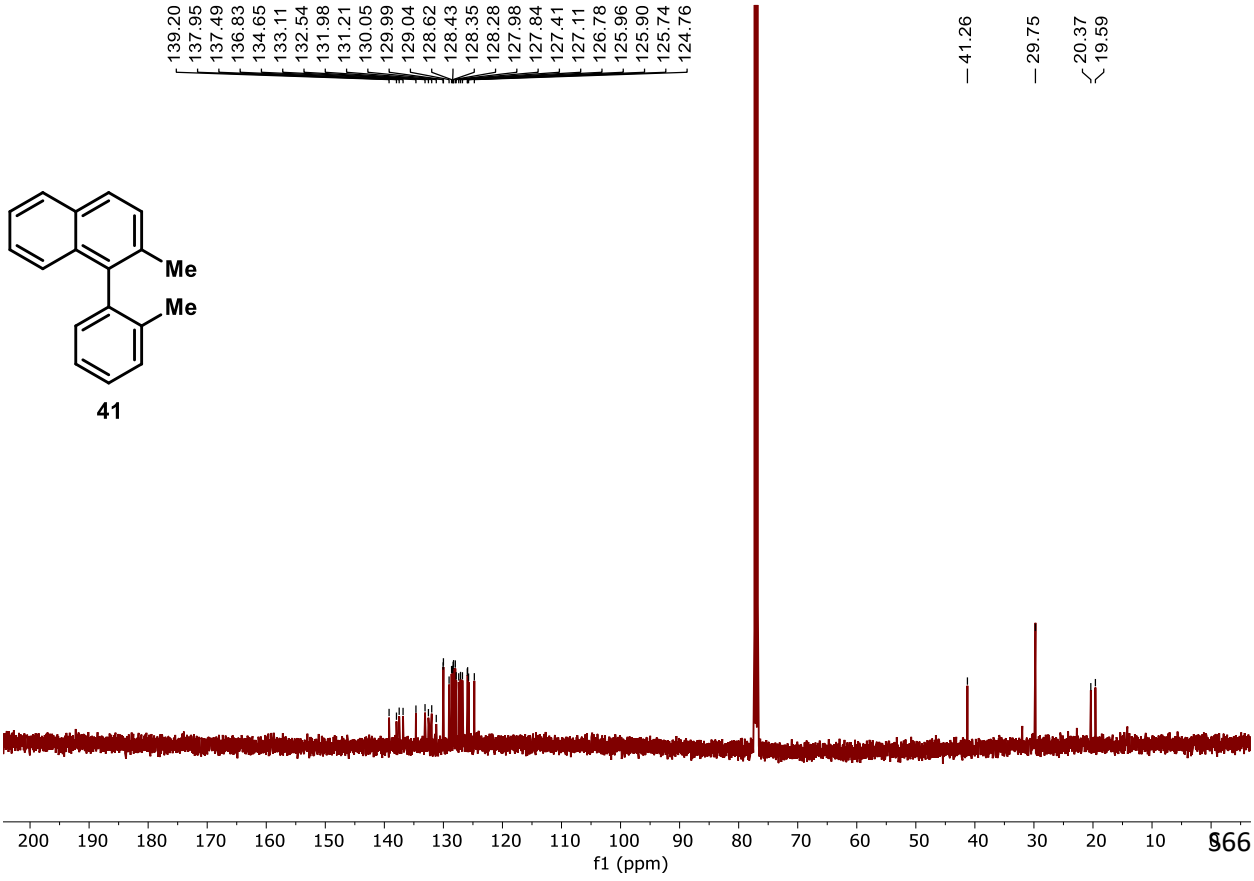


39



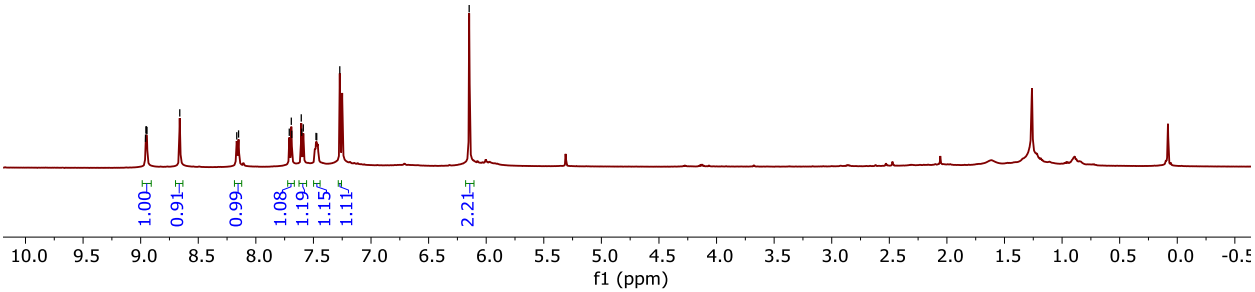
39

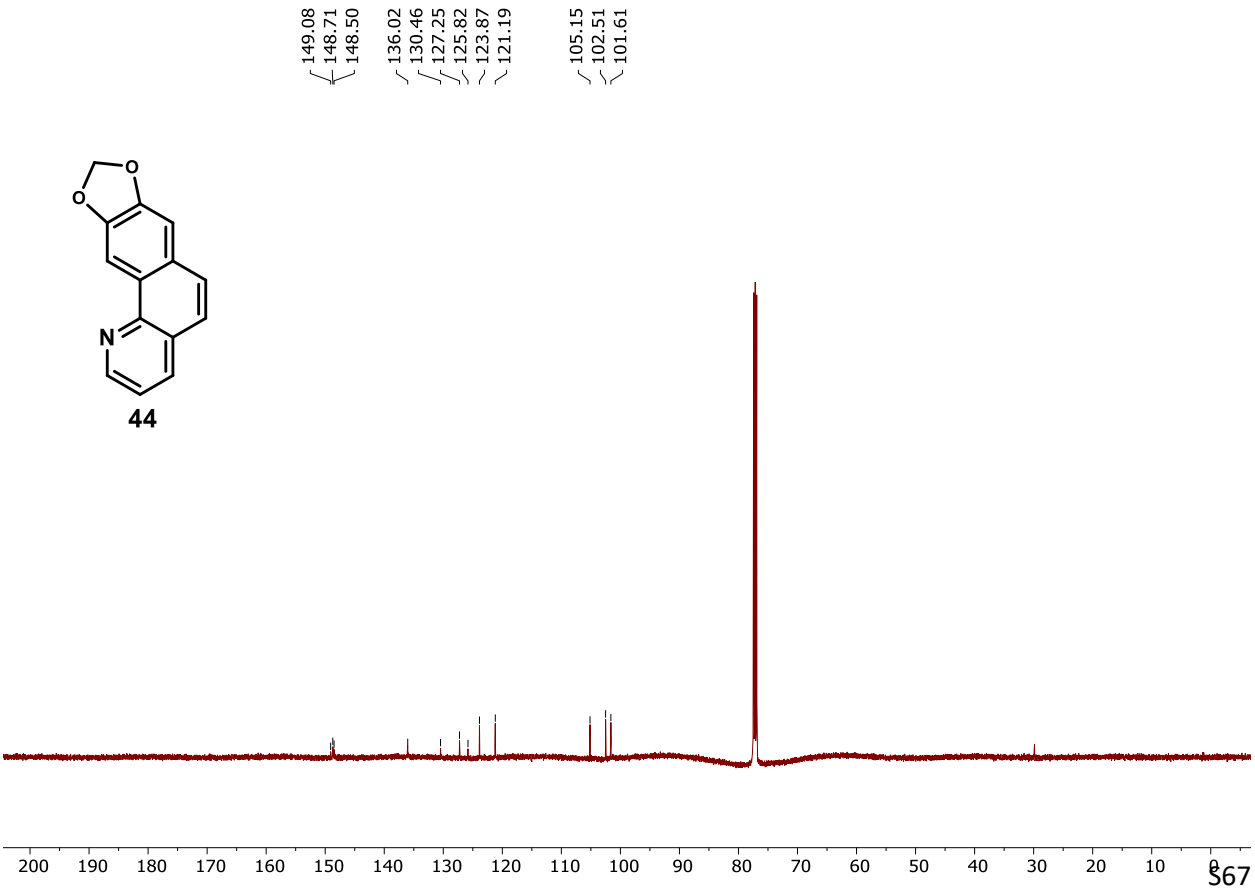

8.35 8.33 8.10 8.08 7.94 7.92 7.88 7.87 7.86 7.82 7.80 7.69 7.69 7.68 7.67 7.67 7.66 7.66 7.62 7.62 7.61 7.61 7.60 7.59 7.59 7.52 7.46 7.44 7.44 7.43 7.43 7.42 7.39 7.39 7.38 7.35 7.35 7.34 7.33 7.33 7.32 7.32 7.27 7.25 7.15 7.14 7.14 2.19 1.94
500 MHz, CDCl3
Me
Me
41
1.00 0.82 0.94 1.75 1.06 0.94 1.09 0.85 1.79 1.79 1.77 0.86 0.85
2.74 2.92
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


139.20 137.95 137.49 136.83 134.65 133.11 132.54 131.98 131.21 130.05 129.99 129.04 128.62 128.43 128.35 128.28 127.98 127.84 127.41 127.11 126.78 125.96 125.90 125.74 124.76
41.26
29.75
20.37 19.59
Me
Me
41
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


8.96
8.95
8.95
8.95
8.66
8.17
8.15
7.71
7.69
7.69
7.61
7.60
7.59
7.48
7.47
7.27
6.15
500 MHz, CDCl3
O
O
N

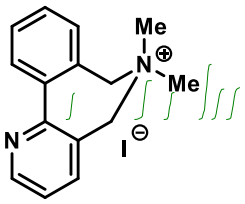
44


1.00
0.91
0.99
1.08
1.19
1.15
1.11
2.21
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

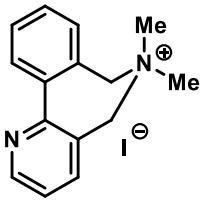

149.08
148.71
148.50
136.02
130.46
127.25
125.82
123.87
121.19
105.15
102.51
101.61
O
O
N
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

44

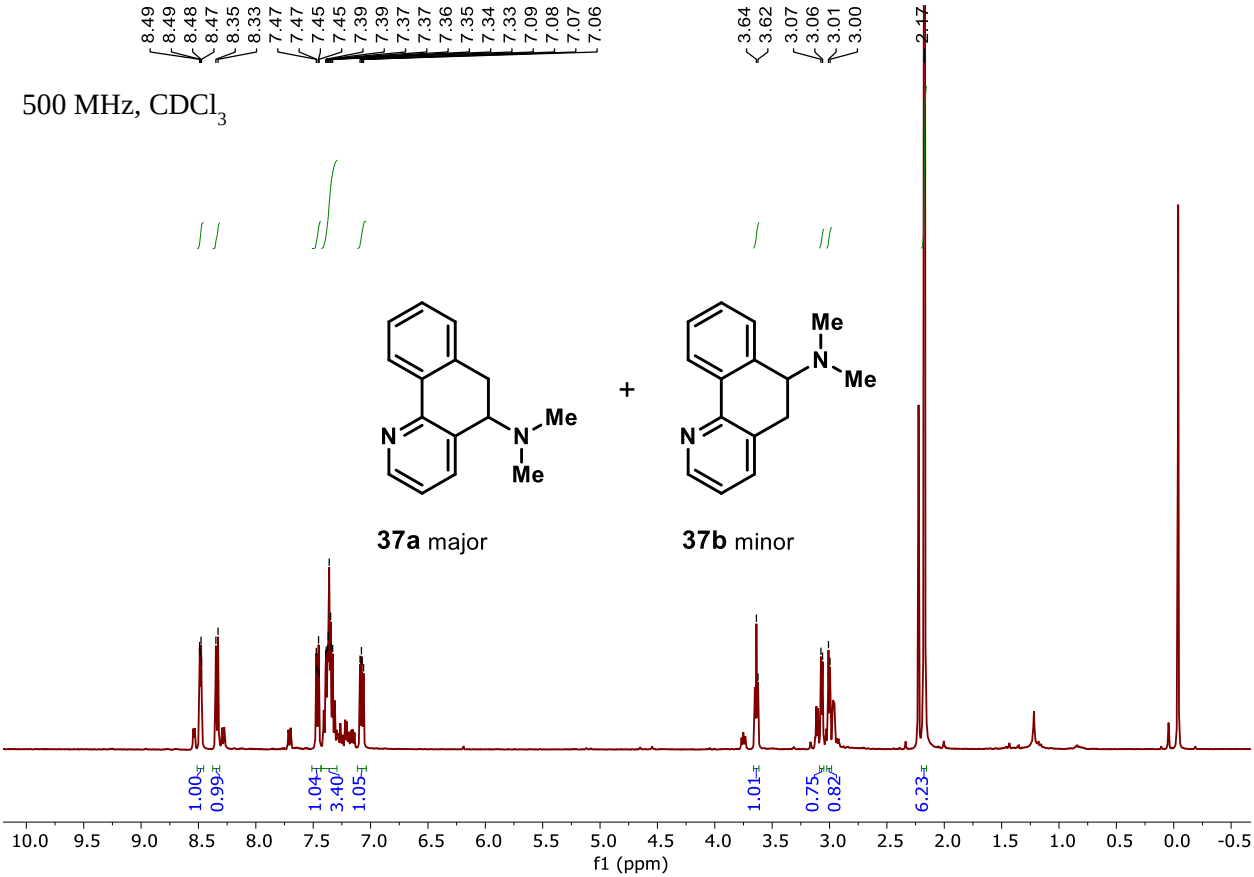
500 MHz, $CDCl_3$

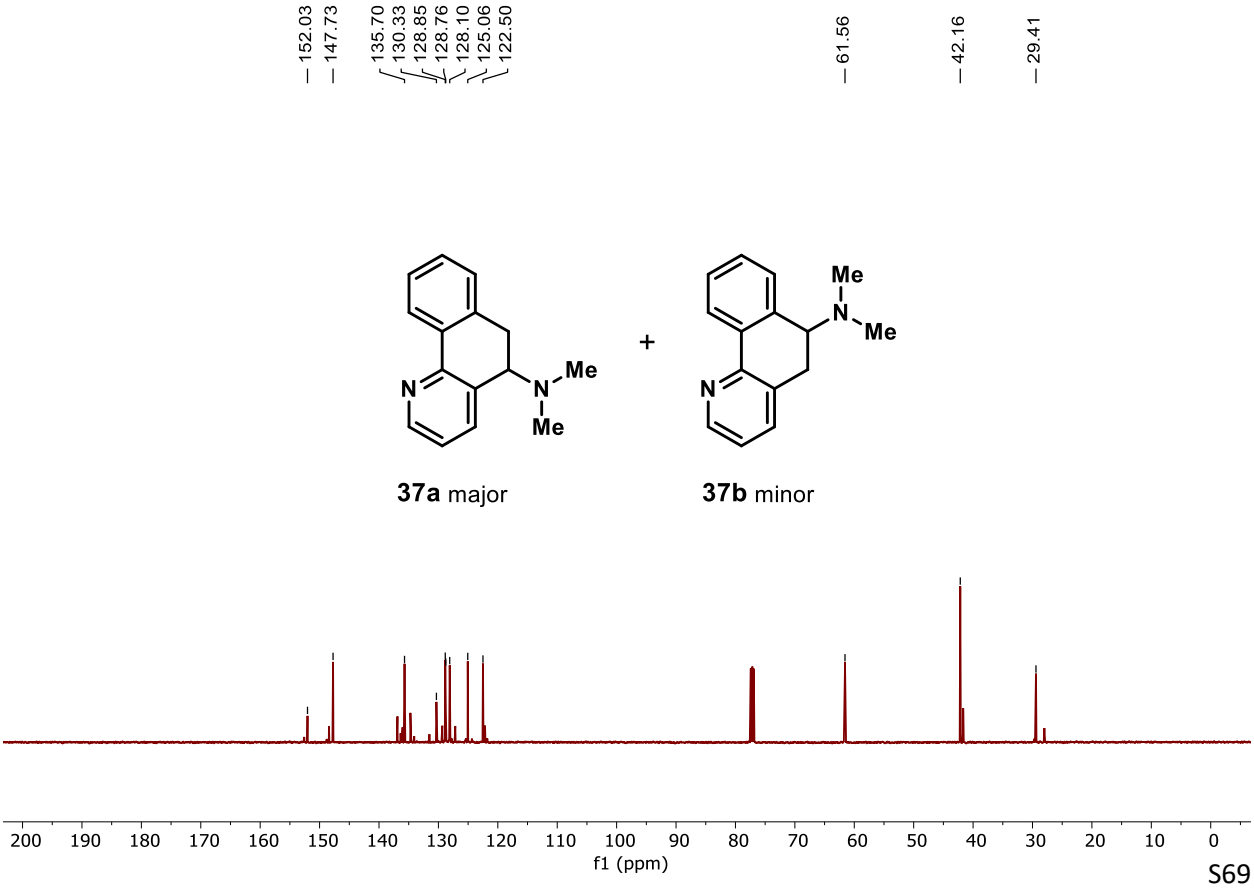


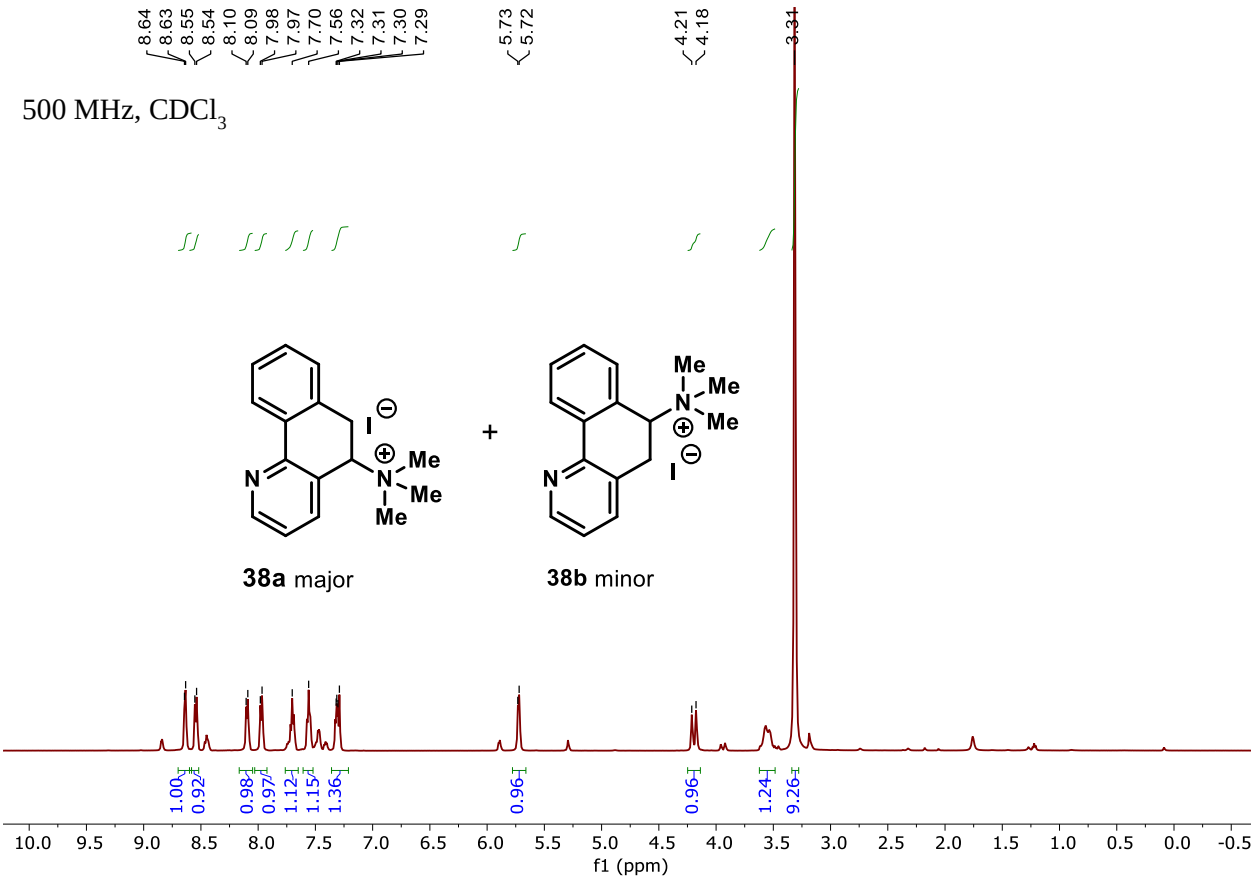
36

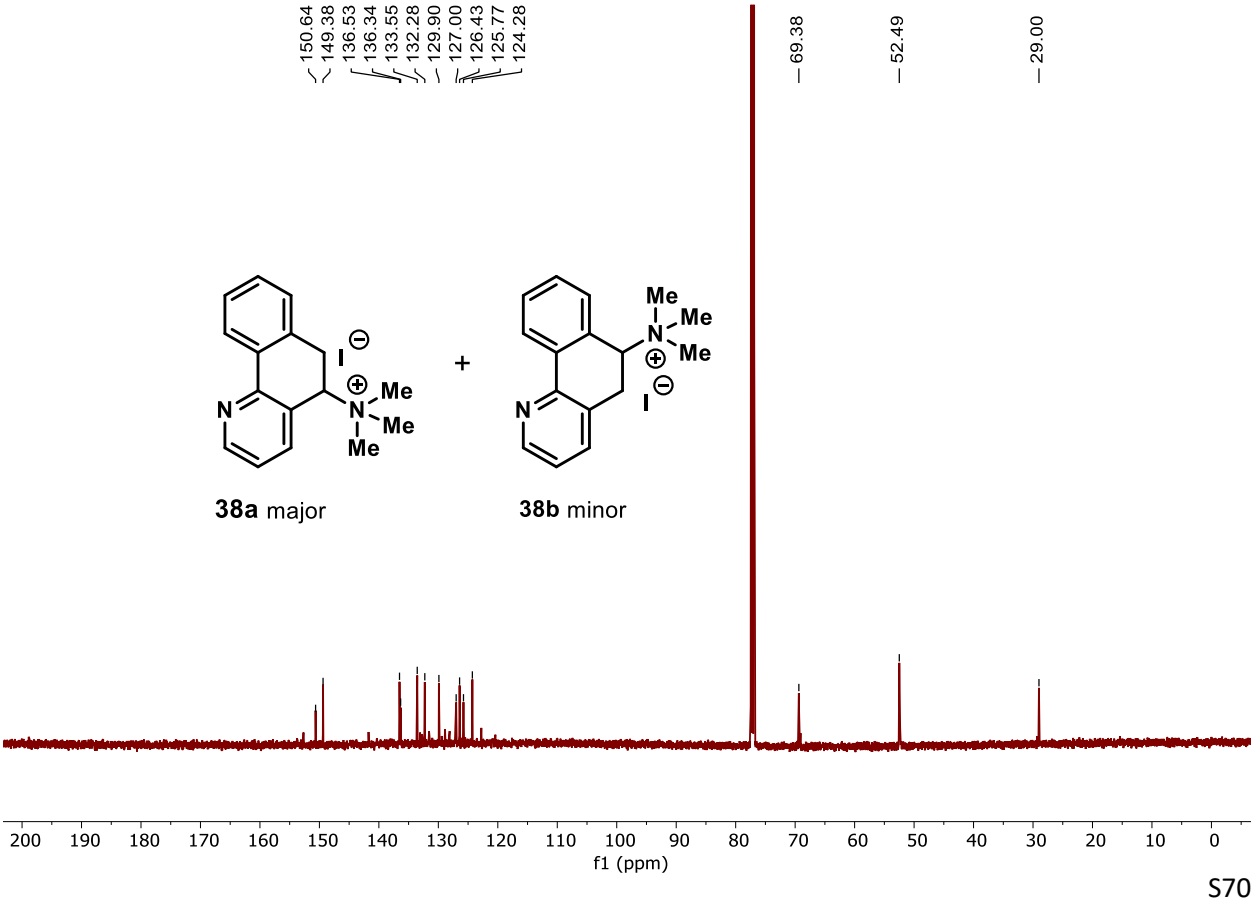


36


8.49
8.49
8.48
8.47
8.35
8.33
7.47
7.47
7.45
7.45
7.39
7.39
7.37
7.37
7.36
7.35
7.34
7.33
7.09
7.08
7.07
7.06
3.64
3.62
3.07
3.06
3.01
3.00
2.17
500 MHz, CDCl3
Me
N
Me
+
Me
N
Me
37a major
37b minor
1.00
0.99
1.04
3.40
1.05
1.01
0.75
0.82
6.23
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

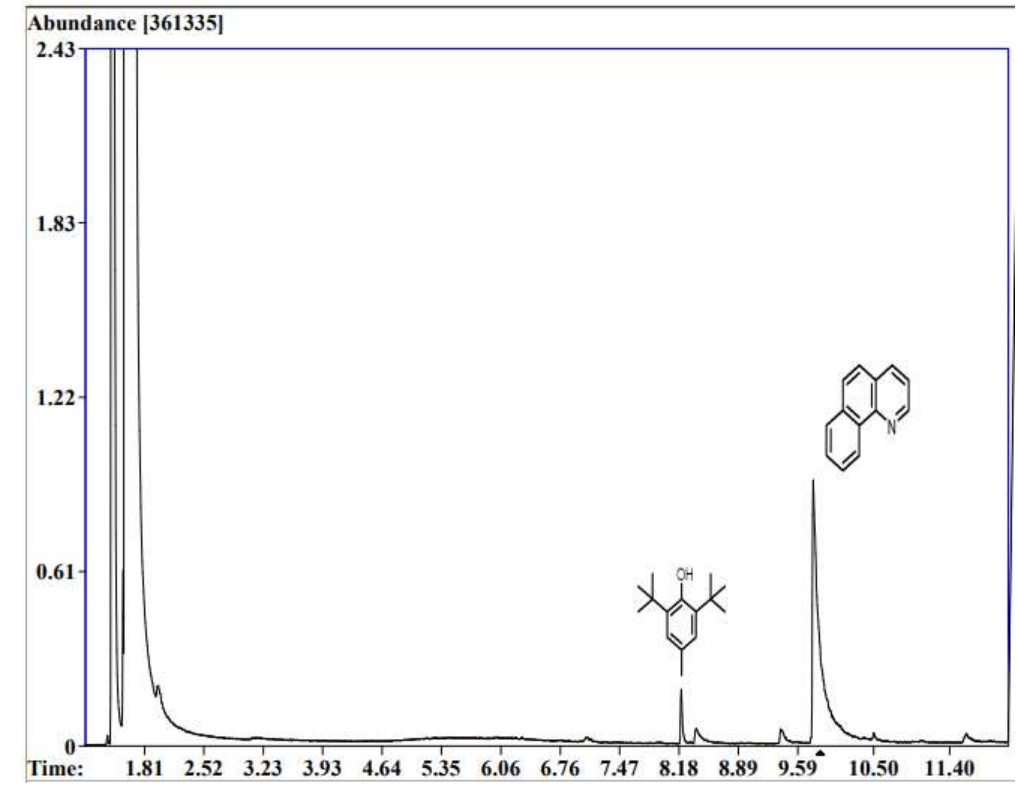

152.03
147.73
135.70
130.33
128.85
128.76
128.10
125.06
122.50
61.56
42.16
29.41
Me
N
Me
+
Me
N
Me
37a major
37b minor
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

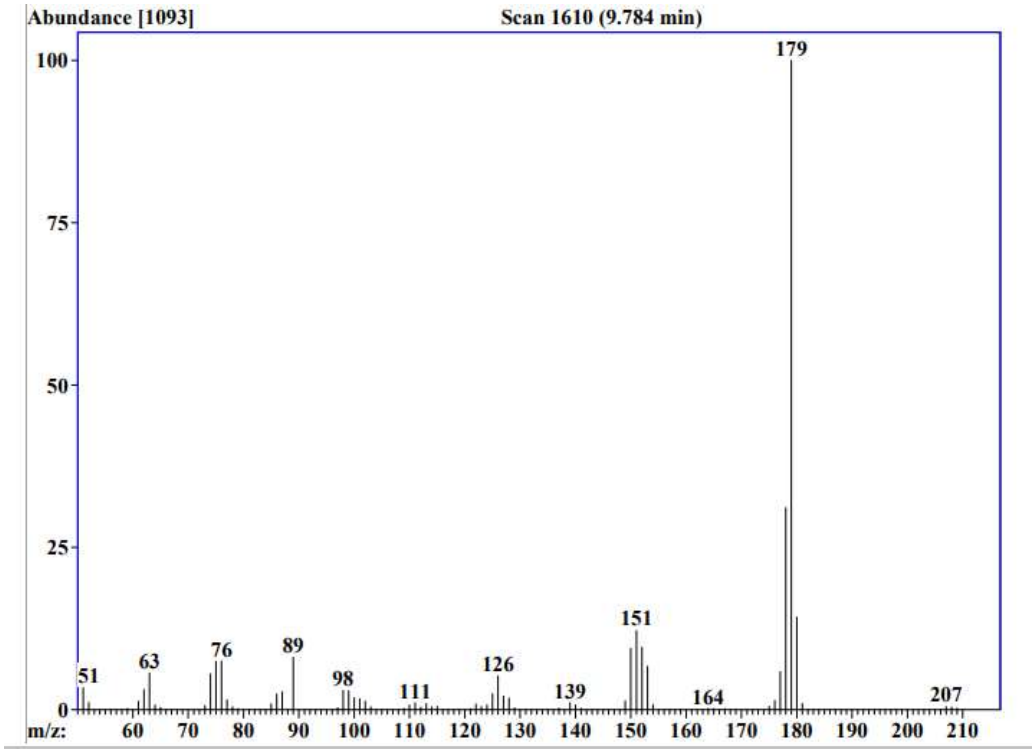

8.64
8.63
8.55
8.54
8.10
8.09
7.98
7.97
7.70
7.56
7.32
7.31
7.30
7.29
5.73
5.72
4.21
4.18
3.31
500 MHz, CDCl3
38a major
38b minor
1.00
0.92
0.98
0.97
1.12
1.15
1.36
0.96
0.96
1.24
9.26
f1 (ppm)


150.64
149.38
136.53
136.34
133.55
132.28
129.90
127.00
126.43
125.77
124.28
69.38
52.49
29.00
38a major
38b minor
f1 (ppm)

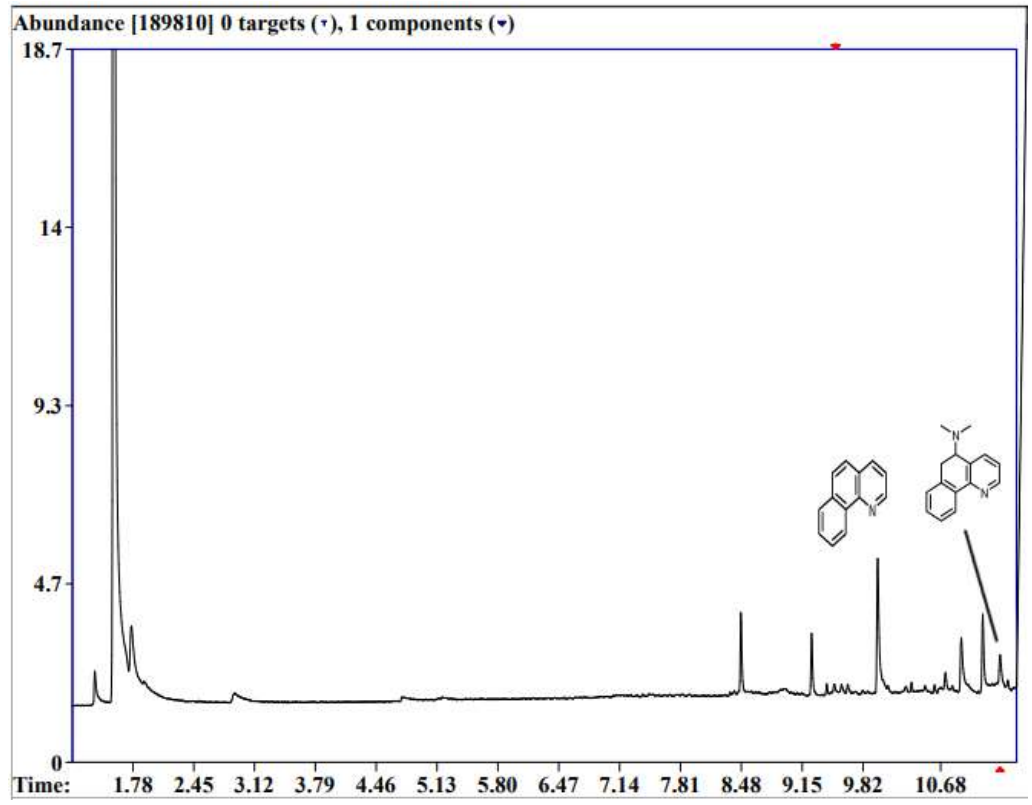
GC/MS trace

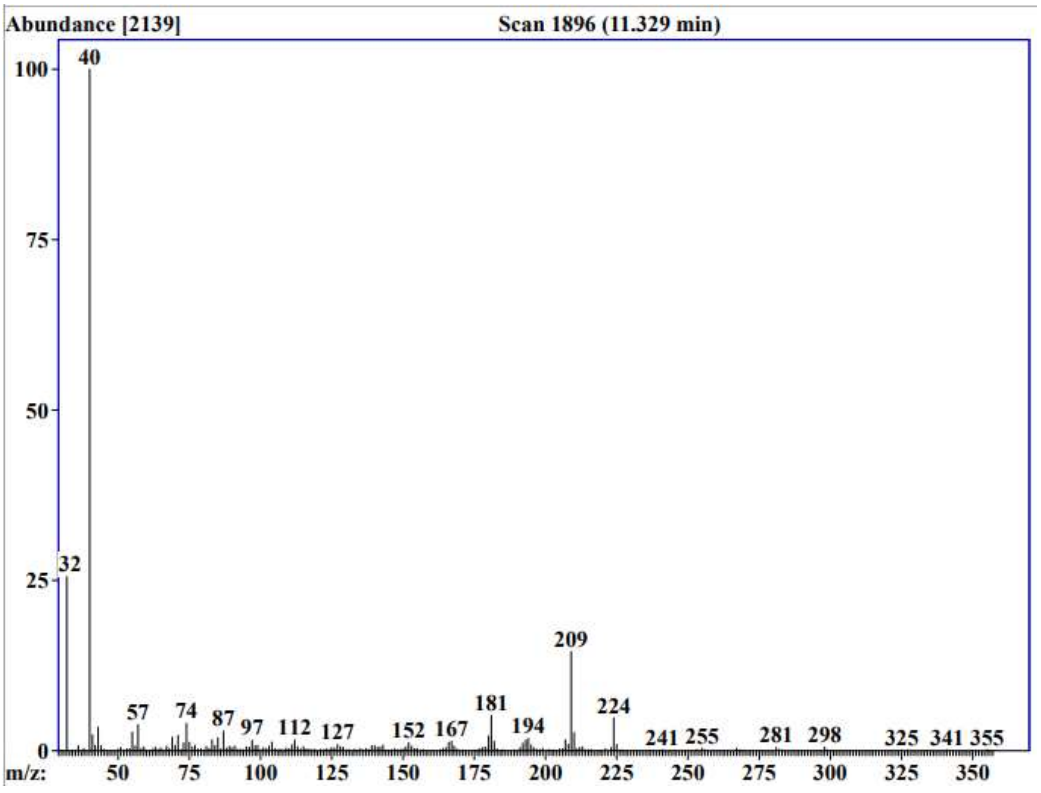
GC/MS chromatogram of the crude reaction mixture showing only **27** and BHT from solvent



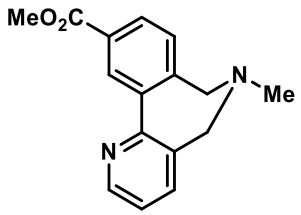


GC/MS chromatogram of partial conversion of **18**, showing the presence of the Stevens rearrangement product, **37ab**





Crystal Structure Report for 20122 (CCDC 2087414)



22

A clear colourless block-like specimen of $C_{16}H_{16}N_2O_2$, approximate dimensions 0.070 mm x 0.130 mm x 0.130 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 1.54178 Å).

Table 1: Data collection details for 20122.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Phi	37.014	91.23	91.60	0.00	-44.50	0.50	720	3.50	1.54184	50	1.2	100
Omega	37.014	-20.04	-122.73	180.00	44.50	0.50	205	1.00	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	-120.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Phi	37.014	106.23	13.21	-124.00	24.00	0.50	368	5.00	1.54184	50	1.2	100
Omega	37.014	-35.04	-131.86	90.00	44.50	0.50	193	2.50	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	80.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	40.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	-80.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	160.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	91.23	91.60	270.00	-44.50	0.50	165	3.50	1.54184	50	1.2	100
Omega	37.014	-20.04	-122.73	90.00	44.50	0.50	205	2.50	1.54184	50	1.2	100
Phi	37.014	106.23	110.18	-212.00	-24.00	0.50	384	5.00	1.54184	50	1.2	100
Phi	37.014	20.04	1.34	0.00	44.50	0.50	720	2.50	1.54184	50	1.2	100
Phi	37.014	0.00	0.00	0.00	54.74	0.50	360	0.75	1.54184	50	1.2	100
Omega	37.014	91.23	91.60	0.00	-44.50	0.50	165	3.50	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	0.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	-160.00	65.50	0.50	220	5.00	1.54184	50	1.2	100

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	37.014	106.23	1.34	-40.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	106.23	1.34	120.00	65.50	0.50	220	5.00	1.54184	50	1.2	100
Omega	37.014	-35.04	-131.86	180.00	44.50	0.50	193	1.10	1.54184	50	1.2	100
Omega	37.014	-50.04	-54.96	0.00	-65.50	0.50	190	1.40	1.54184	50	1.2	100
Omega	37.014	76.23	76.92	0.00	-44.50	0.50	204	2.50	1.54184	50	1.2	100
Omega	37.014	91.23	91.60	180.00	-44.50	0.50	165	3.50	1.54184	50	1.2	100
Omega	37.014	-50.04	-54.96	102.00	-65.50	0.50	190	1.40	1.54184	50	1.2	100
Omega	37.014	91.23	91.60	90.00	-44.50	0.50	165	3.50	1.54184	50	1.2	100
Omega	37.014	-50.04	-54.96	-54.00	-65.50	0.50	190	1.40	1.54184	50	1.2	100
Omega	37.014	76.23	76.92	180.00	-44.50	0.50	204	2.50	1.54184	50	1.2	100

A total of 6966 frames were collected. The total exposure time was 6.61 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 19803 reflections to a maximum θ angle of 72.11° (0.81 Å resolution), of which 2626 were independent (average redundancy 7.541, completeness = 99.7%, R_{int} = 3.04%, R_{sig} = 1.77%) and 2485 (94.63%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.9992(5) Å, b = 11.2900(5) Å, c = 12.2822(6) Å, β = 105.733(2)°, volume = 1334.60(11) $Å^3$, are based upon the refinement of the XYZ-centroids of 9878 reflections above 20 σ(I) with 7.477° < 2θ < 144.2°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.932. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9120 and 0.9510.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/n 1, with Z = 4 for the formula unit, $C_{16}H_{16}N_2O_2$. The final anisotropic full-matrix least-squares refinement on F^2 with 183 variables converged at R1 = 3.25%, for the observed data and wR2 = 8.30% for all data. The goodness-of-fit was 1.043. The largest peak in the final difference electron density synthesis was 0.218 $e^-/Å^3$ and the largest hole was -0.261 $e^-/Å^3$ with an RMS deviation of 0.043 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.335 g/cm^3 and F(000), 568 e^-.

Table 2. Sample and crystal data for 20122.

Identification code	20122	
Chemical formula	$C_{16}H_{16}N_2O_2$	
Formula weight	268.31 g/mol	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal size	0.070 x 0.130 x 0.130 mm	
Crystal habit	clear colourless block	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 9.9992(5) Å	α = 90°
	b = 11.2900(5) Å	β = 105.733(2)°
	c = 12.2822(6) Å	γ = 90°
Volume	1334.60(11) $Å^3$	
Z	4	
Density (calculated)	1.335 g/cm^3	
Absorption coefficient	0.720 mm^{-1}	
F(000)	568	

Table 3. Data collection and structure refinement for 20122.

Theta range for data collection	5.08 to 72.11°
Index ranges	-12<=h<=12, -13<=k<=13, -15<=l<=15
Reflections collected	19803
Independent reflections	2626 [R(int) = 0.0304]
Coverage of independent reflections	99.7%

Absorption correction	Multi-Scan
Max. and min. transmission	0.9510 and 0.9120
Structure solution technique	direct methods
Structure solution program	SHELXT 2014/5 (Sheldrick, 2014)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2018/3 (Sheldrick, 2018)
Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	2626 / 0 / 183
Goodness-of-fit on F^2	1.043
Final R indices	2485 data; $I>2\sigma(I)$ R1 = 0.0325, wR2 = 0.0817
	all data R1 = 0.0340, wR2 = 0.0830
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0392P)^2+0.5494P]$ where $P=(F_o^2+2F_c^2)/3$
Largest diff. peak and hole	0.218 and -0.261 eÅ^{-3}
R.M.S. deviation from mean	0.043 eÅ^{-3}

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for 20122.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O1	0.52528(8)	0.97147(6)	0.18219(6)	0.01892(18)
O2	0.69604(8)	0.04081(7)	0.32771(6)	0.02278(19)
N1	0.29056(9)	0.58037(8)	0.15183(7)	0.0168(2)
N2	0.69291(9)	0.48438(8)	0.40380(7)	0.0178(2)
C1	0.15426(11)	0.53611(10)	0.08877(9)	0.0207(2)
C2	0.40168(11)	0.53224(9)	0.10620(9)	0.0161(2)
C3	0.44523(10)	0.40636(9)	0.14139(8)	0.0150(2)
C4	0.52734(10)	0.38458(9)	0.25228(8)	0.0155(2)
C5	0.57708(10)	0.27069(9)	0.28281(8)	0.0160(2)
C6	0.54335(10)	0.17760(9)	0.20601(9)	0.0160(2)
C7	0.59909(11)	0.05810(10)	0.24568(9)	0.0166(2)
C8	0.56935(12)	0.85223(10)	0.21646(10)	0.0227(2)
C9	0.41118(11)	0.31203(10)	0.06546(8)	0.0164(2)
C10	0.45801(10)	0.19804(9)	0.09687(9)	0.0165(2)
C11	0.31267(11)	0.55162(10)	0.27248(9)	0.0180(2)
C12	0.46073(11)	0.56625(9)	0.34278(8)	0.0166(2)
C13	0.56217(11)	0.48266(9)	0.33597(8)	0.0157(2)
C14	0.72672(11)	0.57293(10)	0.47865(9)	0.0195(2)
C15	0.63528(12)	0.66087(10)	0.49112(9)	0.0207(2)
C16	0.49970(12)	0.65601(9)	0.42268(9)	0.0193(2)

Table 5. Bond lengths (Å) for 20122.

O1-C7	1.3406(13)	O1-C8	1.4433(13)

O2-C7	1.2097(13)	N1-C1	1.4610(13)
N1-C11	1.4740(13)	N1-C2	1.4769(13)
N2-C14	1.3381(14)	N2-C13	1.3464(14)
C1-H10	0.98	C1-H11	0.98
C1-H1	0.98	C2-C3	1.5147(14)
C2-H9	0.99	C2-H8	0.99
C3-C9	1.3956(15)	C3-C4	1.4082(14)
C4-C5	1.3930(15)	C4-C13	1.4866(14)
C5-C6	1.3913(14)	C5-H5	0.95
C6-C10	1.3993(14)	C6-C7	1.4903(14)
C8-H3	0.98	C8-H4	0.98
C8-H2	0.98	C9-C10	1.3879(15)
C9-H6	0.95	C10-H7	0.95
C11-C12	1.5071(14)	C11-H15	0.99
C11-H16	0.99	C12-C16	1.3908(15)
C12-C13	1.4044(15)	C14-C15	1.3860(16)
C14-H14	0.95	C15-C16	1.3890(15)
C15-H12	0.95	C16-H13	0.95

Table 6. Bond angles (°) for 20122.

C7-O1-C8	115.75(8)	C1-N1-C11	108.77(8)
C1-N1-C2	111.26(8)	C11-N1-C2	112.17(8)
C14-N2-C13	117.25(9)	N1-C1-H10	109.5
N1-C1-H11	109.5	H10-C1-H11	109.5

N1-C1-H1	109.5	H10-C1-H1	109.5
H11-C1-H1	109.5	N1-C2-C3	115.13(8)
N1-C2-H9	108.5	C3-C2-H9	108.5
N1-C2-H8	108.5	C3-C2-H8	108.5
H9-C2-H8	107.5	C9-C3-C4	119.06(9)
C9-C3-C2	121.75(9)	C4-C3-C2	119.14(9)
C5-C4-C3	119.57(9)	C5-C4-C13	120.12(9)
C3-C4-C13	120.30(9)	C6-C5-C4	120.77(9)
C6-C5-H5	119.6	C4-C5-H5	119.6
C5-C6-C10	119.84(10)	C5-C6-C7	117.51(9)
C10-C6-C7	122.64(9)	O2-C7-O1	123.86(10)
O2-C7-C6	124.23(10)	O1-C7-C6	111.85(9)
O1-C8-H3	109.5	O1-C8-H4	109.5
H3-C8-H4	109.5	O1-C8-H2	109.5
H3-C8-H2	109.5	H4-C8-H2	109.5
C10-C9-C3	121.27(9)	C10-C9-H6	119.4
C3-C9-H6	119.4	C9-C10-C6	119.43(9)
C9-C10-H7	120.3	C6-C10-H7	120.3
N1-C11-C12	114.09(9)	N1-C11-H15	108.7
C12-C11-H15	108.7	N1-C11-H16	108.7
C12-C11-H16	108.7	H15-C11-H16	107.6
C16-C12-C13	117.57(10)	C16-C12-C11	121.86(10)
C13-C12-C11	120.36(9)	N2-C13-C12	123.32(10)
N2-C13-C4	116.40(9)	C12-C13-C4	120.27(9)
N2-C14-C15	124.04(10)	N2-C14-H14	118.0

C15-C14-H14	118.0	C14-C15-C16	118.01(10)
C14-C15-H12	121.0	C16-C15-H12	121.0
C15-C16-C12	119.77(10)	C15-C16-H13	120.1
C12-C16-H13	120.1		

Table 7. Torsion angles (°) for 20122.

C1-N1-C2-C3	-78.45(11)	C11-N1-C2-C3	43.64(12)
N1-C2-C3-C9	108.05(11)	N1-C2-C3-C4	-74.74(12)
C9-C3-C4-C5	2.33(15)	C2-C3-C4-C5	-174.96(9)
C9-C3-C4-C13	-178.37(9)	C2-C3-C4-C13	4.35(14)
C3-C4-C5-C6	-1.83(15)	C13-C4-C5-C6	178.87(9)
C4-C5-C6-C10	-0.28(15)	C4-C5-C6-C7	-179.18(9)
C8-O1-C7-O2	-0.79(15)	C8-O1-C7-C6	-178.26(9)
C5-C6-C7-O2	-18.65(15)	C10-C6-C7-O2	162.48(10)
C5-C6-C7-O1	158.82(9)	C10-C6-C7-O1	-20.05(14)
C4-C3-C9-C10	-0.76(15)	C2-C3-C9-C10	176.45(9)
C3-C9-C10-C6	-1.33(15)	C5-C6-C10-C9	1.85(15)
C7-C6-C10-C9	-179.31(9)	C1-N1-C11-C12	166.39(9)
C2-N1-C11-C12	42.88(12)	N1-C11-C12-C16	110.41(11)
N1-C11-C12-C13	-74.96(12)	C14-N2-C13-C12	-1.97(15)
C14-N2-C13-C4	179.12(9)	C16-C12-C13-N2	1.22(15)
C11-C12-C13-N2	-173.63(9)	C16-C12-C13-C4	-179.91(9)
C11-C12-C13-C4	5.24(15)	C5-C4-C13-N2	40.13(14)
C3-C4-C13-N2	-139.17(10)	C5-C4-C13-C12	-138.82(10)

C3-C4-C13-C12	41.88(14)	C13-N2-C14-C15	0.93(16)
N2-C14-C15-C16	0.82(17)	C14-C15-C16-C12	-1.58(16)
C13-C12-C16-C15	0.63(15)	C11-C12-C16-C15	175.39(10)

Table 8. Anisotropic atomic displacement parameters (Å^2) for 20122.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U^{13}	U_{12}
O1	0.0197(4)	0.0139(4)	0.0214(4)	0.0002(3)	0.0025(3)	0.0001(3)
O2	0.0260(4)	0.0210(4)	0.0173(4)	0.0002(3)	-0.0009(3)	0.0036(3)
N1	0.0161(4)	0.0191(4)	0.0145(4)	0.0009(3)	0.0032(3)	0.0016(3)
N2	0.0176(4)	0.0193(4)	0.0153(4)	-0.0002(3)	0.0025(3)	-0.0012(3)
C1	0.0170(5)	0.0241(5)	0.0197(5)	0.0009(4)	0.0026(4)	0.0008(4)
C2	0.0174(5)	0.0166(5)	0.0147(5)	0.0015(4)	0.0050(4)	-0.0002(4)
C3	0.0130(5)	0.0177(5)	0.0154(5)	0.0013(4)	0.0056(4)	-0.0004(4)
C4	0.0134(5)	0.0182(5)	0.0154(5)	-0.0005(4)	0.0048(4)	-0.0014(4)
C5	0.0143(5)	0.0192(5)	0.0143(5)	0.0008(4)	0.0033(4)	-0.0007(4)
C6	0.0145(5)	0.0172(5)	0.0169(5)	0.0010(4)	0.0055(4)	-0.0003(4)
C7	0.0177(5)	0.0186(5)	0.0146(5)	-0.0010(4)	0.0064(4)	-0.0007(4)
C8	0.0271(6)	0.0148(5)	0.0248(6)	0.0021(4)	0.0046(5)	0.0015(4)
C9	0.0154(5)	0.0204(5)	0.0132(5)	0.0011(4)	0.0034(4)	-0.0012(4)
C10	0.0164(5)	0.0181(5)	0.0154(5)	-0.0019(4)	0.0049(4)	-0.0026(4)
C11	0.0172(5)	0.0212(5)	0.0161(5)	0.0009(4)	0.0054(4)	0.0019(4)
C12	0.0193(5)	0.0176(5)	0.0132(5)	0.0028(4)	0.0052(4)	0.0002(4)

	U_{11}	U_{22}	U_{33}	U_{23}	U^{13}	U_{12}
C13	0.0176(5)	0.0163(5)	0.0134(5)	0.0020(4)	0.0045(4)	-0.0013(4)
C14	0.0205(5)	0.0208(5)	0.0153(5)	0.0003(4)	0.0014(4)	-0.0037(4)
C15	0.0289(6)	0.0170(5)	0.0147(5)	-0.0011(4)	0.0037(4)	-0.0030(4)
C16	0.0255(6)	0.0166(5)	0.0165(5)	0.0017(4)	0.0067(4)	0.0028(4)

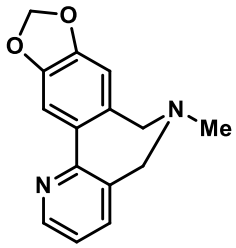
Table 9. Hydrogen atomic coordinates and isotropic atomic displacement parameters ($Å^2$) for 20122.

	x/a	y/b	z/c	U(eq)
H10	0.1500	0.4504	0.1000	0.031
H11	0.1394	0.5530	0.0081	0.031
H1	0.0820	0.5753	0.1160	0.031
H9	0.4842	0.5841	0.1308	0.019
H8	0.3699	0.5355	0.0226	0.019
H5	0.6347	0.2564	0.3569	0.019
H3	0.6580	-0.1638	0.1997	0.034
H4	0.4991	-0.2040	0.1751	0.034
H2	0.5808	-0.1565	0.2979	0.034
H6	0.3549	0.3261	-0.0092	0.02
H7	0.4323	0.1344	0.0447	0.02
H15	0.2837	0.4687	0.2789	0.022
H16	0.2522	0.6032	0.3039	0.022
H14	0.8191	0.5757	0.5262	0.023
H12	0.6645	0.7226	0.5449	0.025

	x/a	y/b	z/c	U(eq)
H13	0.4338	0.7138	0.4304	0.023

Crystal Structure Report for 20210324AR (CCDC: 2087413)

A clear colourless irregular-like specimen of $C_{15}H_{14}N_2O_2$, approximate dimensions 0.300 mm x 0.350 mm x 0.450 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured (λ = 0.71073 Å).



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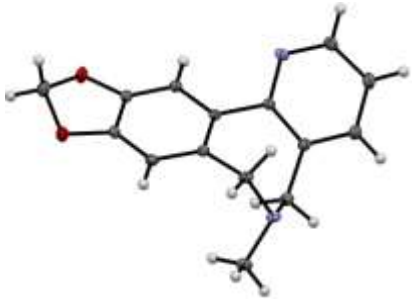

Table 1: Data collection details for 20210324AR.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	39.940	-39.06	-141.62	120.00	54.74	1.00	102	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-37.82	-40.00	-55.50	1.00	93	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-37.82	-160.00	-55.50	1.00	93	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-141.62	160.00	54.74	1.00	102	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-141.62	-120.00	54.74	1.00	102	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-141.62	0.00	54.74	1.00	102	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-141.62	-80.00	54.74	1.00	102	5.00	0.71073	50	35.0	100

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	39.940	-39.06	-141.62	40.00	54.74	1.00	102	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-37.82	80.00	-55.50	1.00	93	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-37.82	-80.00	-55.50	1.00	93	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-37.82	120.00	-55.50	1.00	93	5.00	0.71073	50	35.0	100
Omega	39.940	-39.06	-37.82	0.00	-55.50	1.00	93	5.00	0.71073	50	35.0	100

A total of 1170 frames were collected. The total exposure time was 1.62 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 18138 reflections to a maximum θ angle of 35.63° (0.61 Å resolution), of which 5526 were independent (average redundancy 3.282, completeness = 99.7%, R_{int} = 3.59%, R_{sig} = 4.04%) and 4242 (76.76%) were greater than $2\sigma(F^2)$. The final cell constants of a = 7.6358(9) Å, b = 9.0784(11) Å, c = 9.7663(13) Å, α = 109.932(3)°, β = 107.117(3)°, γ = 92.339(3)°, volume = 600.71(13) $Å^3$, are based upon the refinement of the XYZ-centroids of 4733 reflections above 20 σ(I) with 4.830° < 2θ < 73.58°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.941. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9580 and 0.9720.

The final anisotropic full-matrix least-squares refinement on F^2 with 172 variables converged at R1 = 4.45%, for the observed data and wR2 = 12.44% for all data. The goodness-of-fit was 1.022. The largest peak in the final difference electron density synthesis was 0.616 $e^-/Å^3$ and the largest hole was -0.263 $e^-/Å^3$ with an RMS deviation of 0.062 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.406 g/cm^3 andF(000), 268 e^-.

Table 2. Sample and crystal data for 20210324AR.

Identification code	20210324AR	
Chemical formula	$C_{15}H_{14}N_2O_2$	
Formula weight	254.28 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal size	0.300 x 0.350 x 0.450 mm	
Crystal habit	clear colourless irregular	
Crystal system	triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.6358(9) Å	α = 109.932(3)°
	b = 9.0784(11) Å	β = 107.117(3)°
	c = 9.7663(13) Å	γ = 92.339(3)°
Volume	600.71(13) $Å^3$	
Z	2	
Density (calculated)	1.406 g/cm^3	
Absorption coefficient	0.095 mm^{-1}	
F(000)	268	

Table 3. Data collection and structure refinement for 20210324AR.

Theta range for data collection	2.68 to 35.63°	
Index ranges	-12<=h<=12, -14<=k<=14, -16<=l<=16	
Reflections collected	18138	
Independent reflections	5526 [R(int) = 0.0359]	
Coverage of independent reflections	99.7%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.9720 and 0.9580	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2017/1 (Sheldrick, 2017)	
Function minimized	$\Sigma\ w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	5526 / 0 / 172	
Goodness-of-fit on F^2	1.022	
Δ/σ_{max}	0.001	
Final R indices	4242 data; $I>2\sigma(I)$	R1 = 0.0445, wR2 = 0.1130
	all data	R1 = 0.0625, wR2 = 0.1244
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0659P)^2+0.0913P]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.616 and -0.263 eÅ^{-3}	
R.M.S. deviation from mean	0.062 eÅ^{-3}	

Table 4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for 20210324AR.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O1	0.95290(9)	0.12826(8)	0.33346(7)	0.01585(13)
O2	0.13498(9)	0.09074(8)	0.17628(7)	0.01650(13)
N3	0.41644(11)	0.19534(10)	0.87765(9)	0.01477(14)
N4	0.82584(10)	0.38650(9)	0.70667(8)	0.01218(13)
C5	0.95237(12)	0.04627(12)	0.17891(10)	0.01683(17)
C6	0.13769(11)	0.15685(10)	0.42218(9)	0.01141(14)
C7	0.24730(12)	0.13575(10)	0.32767(9)	0.01156(14)
C8	0.43785(12)	0.15900(10)	0.38565(9)	0.01212(14)
C9	0.51949(11)	0.20639(10)	0.54659(9)	0.01057(14)
C10	0.40841(11)	0.22832(10)	0.64191(9)	0.01074(14)
C11	0.21274(11)	0.20234(10)	0.57929(9)	0.01201(14)
C12	0.49780(11)	0.27108(10)	0.80995(9)	0.01136(14)

	x/a	y/b	z/c	U(eq)
C13	0.49737(13)	0.22930(12)	0.02886(10)	0.01674(16)
C14	0.65903(13)	0.33728(12)	0.11844(10)	0.01700(17)
C15	0.74012(12)	0.41772(11)	0.04840(10)	0.01532(16)
C16	0.65914(11)	0.38589(10)	0.89140(9)	0.01209(14)
C17	0.73099(12)	0.47801(10)	0.81157(10)	0.01371(15)
C18	0.72757(11)	0.22280(10)	0.61712(10)	0.01225(14)
C19	0.84486(13)	0.46973(11)	0.60621(11)	0.01617(16)

Table 5. Bond lengths (Å) for 20210324AR.

O1-C6	1.3807(10)	O1-C5	1.4362(11)
O2-C7	1.3790(10)	O2-C5	1.4457(11)
N3-C13	1.3397(11)	N3-C12	1.3464(11)
N4-C19	1.4612(11)	N4-C17	1.4730(11)
N4-C18	1.4741(11)	C5-H5A	0.99
C5-H5B	0.99	C6-C11	1.3728(11)
C6-C7	1.3915(11)	C7-C8	1.3750(12)
C8-C9	1.4087(11)	C8-H8	0.95
C9-C10	1.4063(11)	C9-C18	1.5125(12)
C10-C11	1.4131(12)	C10-C12	1.4813(11)
C11-H11	0.95	C12-C16	1.4106(12)
C13-C14	1.3895(13)	C13-H13	0.95
C14-C15	1.3919(13)	C14-H14	0.95
C15-C16	1.3936(12)	C15-H15	0.95
C16-C17	1.5057(12)	C17-H17A	0.99
C17-H17B	0.99	C18-H18A	0.99
C18-H18B	0.99	C19-H19A	0.98
C19-H19B	0.98	C19-H19C	0.98

Table 6. Bond angles (°) for 20210324AR.

C6-O1-C5	104.08(6)	C7-O2-C5	104.09(6)
C13-N3-C12	117.47(8)	C19-N4-C17	109.09(7)
C19-N4-C18	111.60(7)	C17-N4-C18	111.59(6)
O1-C5-O2	106.67(7)	O1-C5-H5A	110.4
O2-C5-H5A	110.4	O1-C5-H5B	110.4
O2-C5-H5B	110.4	H5A-C5-H5B	108.6
C11-C6-O1	128.28(7)	C11-C6-C7	122.19(8)
O1-C6-C7	109.52(7)	C8-C7-O2	128.42(7)
C8-C7-C6	122.15(7)	O2-C7-C6	109.43(7)

C7-C8-C9	117.14(7)	C7-C8-H8	121.4
C9-C8-H8	121.4	C10-C9-C8	120.59(7)
C10-C9-C18	119.33(7)	C8-C9-C18	119.94(7)
C9-C10-C11	121.15(7)	C9-C10-C12	119.38(7)
C11-C10-C12	119.39(7)	C6-C11-C10	116.78(7)
C6-C11-H11	121.6	C10-C11-H11	121.6
N3-C12-C16	123.12(7)	N3-C12-C10	116.42(7)
C16-C12-C10	120.46(7)	N3-C13-C14	123.80(8)
N3-C13-H13	118.1	C14-C13-H13	118.1
C13-C14-C15	118.41(8)	C13-C14-H14	120.8
C15-C14-H14	120.8	C14-C15-C16	119.32(8)
C14-C15-H15	120.3	C16-C15-H15	120.3
C15-C16-C12	117.84(8)	C15-C16-C17	121.88(7)
C12-C16-C17	120.14(7)	N4-C17-C16	113.89(7)
N4-C17-H17A	108.8	C16-C17-H17A	108.8
N4-C17-H17B	108.8	C16-C17-H17B	108.8
H17A-C17-H17B	107.7	N4-C18-C9	115.53(7)
N4-C18-H18A	108.4	C9-C18-H18A	108.4
N4-C18-H18B	108.4	C9-C18-H18B	108.4
H18A-C18-H18B	107.5	N4-C19-H19A	109.5
N4-C19-H19B	109.5	H19A-C19-H19B	109.5
N4-C19-H19C	109.5	H19A-C19-H19C	109.5
H19B-C19-H19C	109.5		

Table 7. Torsion angles (°) for 20210324AR.

C6-O1-C5-O2	-24.36(9)	C7-O2-C5-O1	23.83(9)
C5-O1-C6-C11	-165.45(9)	C5-O1-C6-C7	15.77(10)
C5-O2-C7-C8	165.94(9)	C5-O2-C7-C6	-14.20(9)
C11-C6-C7-C8	0.05(13)	O1-C6-C7-C8	178.92(8)
C11-C6-C7-O2	-179.82(8)	O1-C6-C7-O2	-0.96(10)
O2-C7-C8-C9	179.55(8)	C6-C7-C8-C9	-0.30(13)
C7-C8-C9-C10	0.01(12)	C7-C8-C9-C18	175.67(8)
C8-C9-C10-C11	0.52(12)	C18-C9-C10-C11	-175.16(7)
C8-C9-C10-C12	177.24(7)	C18-C9-C10-C12	1.56(12)
O1-C6-C11-C10	-178.17(8)	C7-C6-C11-C10	0.47(13)
C9-C10-C11-C6	-0.75(12)	C12-C10-C11-C6	-177.46(8)
C13-N3-C12-C16	-1.77(13)	C13-N3-C12-C10	178.43(8)
C9-C10-C12-N3	-137.08(8)	C11-C10-C12-N3	39.70(11)
C9-C10-C12-C16	43.11(12)	C11-C10-C12-C16	-140.11(9)
C12-N3-C13-C14	-0.02(14)	N3-C13-C14-C15	1.42(15)

C13-C14-C15-C16	-1.04(14)	C14-C15-C16-C12	-0.59(13)
C14-C15-C16-C17	175.00(8)	N3-C12-C16-C15	2.09(13)
C10-C12-C16-C15	-178.12(8)	N3-C12-C16-C17	-173.59(8)
C10-C12-C16-C17	6.21(12)	C19-N4-C17-C16	164.92(7)
C18-N4-C17-C16	41.14(10)	C15-C16-C17-N4	108.92(9)
C12-C16-C17-N4	-75.59(10)	C19-N4-C18-C9	-76.55(9)
C17-N4-C18-C9	45.80(10)	C10-C9-C18-N4	-74.41(10)
C8-C9-C18-N4	109.87(9)		

Table 8. Anisotropic atomic displacement parameters (Å^2) for 20210324AR.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	0.0109(3)	0.0231(3)	0.0097(3)	0.0030(2)	0.0017(2)	0.0008(2)
O2	0.0145(3)	0.0233(3)	0.0088(3)	0.0040(2)	0.0026(2)	-0.0015(2)
N3	0.0144(3)	0.0194(4)	0.0121(3)	0.0074(3)	0.0051(2)	0.0001(3)
N4	0.0113(3)	0.0122(3)	0.0146(3)	0.0054(2)	0.0061(2)	0.0002(2)
C5	0.0134(4)	0.0224(4)	0.0103(3)	0.0021(3)	0.0026(3)	-0.0001(3)
C6	0.0103(3)	0.0127(3)	0.0104(3)	0.0036(3)	0.0031(2)	0.0006(3)
C7	0.0133(3)	0.0120(3)	0.0088(3)	0.0034(3)	0.0036(3)	0.0001(3)
C8	0.0134(3)	0.0125(3)	0.0117(3)	0.0041(3)	0.0063(3)	0.0007(3)
C9	0.0104(3)	0.0105(3)	0.0113(3)	0.0039(3)	0.0047(3)	0.0005(2)
C10	0.0107(3)	0.0120(3)	0.0100(3)	0.0045(3)	0.0038(2)	0.0005(2)
C11	0.0102(3)	0.0154(4)	0.0106(3)	0.0045(3)	0.0043(2)	0.0007(3)
C12	0.0102(3)	0.0140(3)	0.0101(3)	0.0047(3)	0.0036(2)	0.0009(3)
C13	0.0167(4)	0.0225(4)	0.0131(3)	0.0089(3)	0.0054(3)	0.0018(3)
C14	0.0153(4)	0.0239(4)	0.0108(3)	0.0064(3)	0.0029(3)	0.0034(3)
C15	0.0116(3)	0.0196(4)	0.0118(3)	0.0038(3)	0.0023(3)	0.0006(3)
C16	0.0104(3)	0.0139(3)	0.0116(3)	0.0041(3)	0.0040(3)	0.0009(3)
C17	0.0138(3)	0.0127(3)	0.0150(3)	0.0041(3)	0.0066(3)	0.0003(3)
C18	0.0106(3)	0.0115(3)	0.0154(3)	0.0050(3)	0.0054(3)	0.0015(3)
C19	0.0173(4)	0.0162(4)	0.0190(4)	0.0092(3)	0.0087(3)	0.0010(3)

Table 9. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for 20210324AR.

	x/a	y/b	z/c	U(eq)
H5A	-0.1434	0.0774	0.1051	0.02
H5B	-0.0744	-0.0699	0.1504	0.02

	x/a	y/b	z/c	U(eq)
H8	0.5113	0.1438	0.3200	0.015
H11	0.1368	0.2157	0.6429	0.014
H13	0.4410	0.1765	1.0777	0.02
H14	0.7129	0.3558	1.2249	0.02
H15	0.8496	0.4935	1.1070	0.018
H17A	0.6257	0.5152	0.7520	0.016
H17B	0.8185	0.5729	0.8906	0.016
H18A	0.7537	0.1614	0.6855	0.015
H18B	0.7793	0.1742	0.5333	0.015
H19A	0.9079	0.4094	0.5361	0.024
H19B	0.7216	0.4803	0.5461	0.024
H19C	0.9178	0.5753	0.6691	0.024