SUPPORTING INFORMATION

Syn-1,2-Diaminobenzocyclobutenes from [2+2] cycloaddition of 2-imidazolones with arynes

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1. General information

General Techniques

General: All chemicals were obtained from commercial sources and used as supplied without prior purification. All dry solvents including tetrahydrofuran, dichloromethane and dimethylformamide were obtained from an MB SPS-800 solvent purification system. Acetonitrile was obtained from Sigma Aldrich with sure seal and further dried with molecular sieves. Reactions requiring anhydrous conditions were carried out in oven-dried apparatus under nitrogen. Note: All 2-imidazolone derivatives were prepared according to the literature.[1]

Chromatography: Flash column chromatography was carried out using 40-63 μm silica gel (VWR chemicals, BDH). Thin layer chromatography (TLC) was performed on aluminium backed plates pre-coated with silica gel 60 F_{254} and visualized using a UV lamp (λ_{max} 254/365 nm).

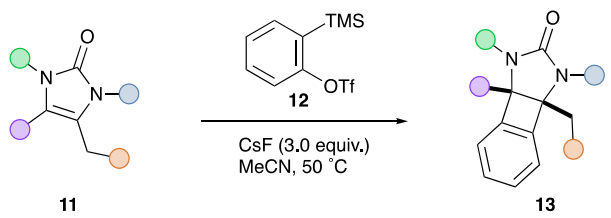
Nuclear Magnetic Resonance Spectroscopy: ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance UltraShield AV400 or AV(III)400 spectrometer (400 MHz, 101 MHz, 376 MHz, and 162 MHz). ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ and referenced to the residual solvent peak at 7.26 ppm (^{1}H) or solvent peak at 77.2 ppm (^{13}C). Chemical shifts are quoted in parts per million (ppm) to 2 dp for ^{1}H NMR spectra and 1 dp for the ^{13}C NMR spectra. Coupling constants (*J*) were measured in Hertz (Hz) to 1 dp. Spectral data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint. = quintet, sept. = septet, dd = doublet of doublets, ddd = doublet of doublets of doublets, td = triplet of doublets, m = multiplet, br. = broad), coupling constant (*J*) and integration.

Infrared (IR) spectroscopy: IR spectra were recorded on a PerkinElmer Spectrum 65 FT-IR spectrometer and are reported in wavenumbers (cm^{-1}) to the nearest integer.

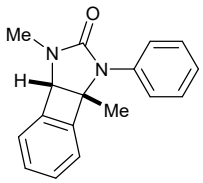
High resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2-Si High-Definition Mass Spectrometry system equipped with an Acquity UPLC BEH C18 column (2.1 x 50 mm; 130 Å) using a solvent gradient (0-100% CH_3CN in Water + 0.1% formic acid) in positive electrospray ionisation (ESI+) mode. Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) tests were performed on an Ultraflex-TOF/TOF instrument (Bruker Daltonics).

[1] V. A. Peshkov, O. P. Pereshivkov, S. Sharma, T. Meganathan, V. S. Parmar, D. S. Ermalot'ev and E. V. Van der Eycken, *J. Org. Chem*., 2011, **76**, 2867

2. General procedure, synthesis and characterisation of benzocyclobutenes



2-Imidazolone (1.0 equiv.) was added to a solution of *o*-(trimethylsilyl)aryl triflate (1.0 equiv.) and CsF (3.0 equiv.) in acetonitrile (0.15 M). The resulting mixture was heated at 50 °C for 14 h. The reaction mixture was then allowed to cool to room temperature and filtered to remove insoluble solids. The solvent was removed *in vacuo* and the crude mixture was purified by silica gel flash column chromatography to afford the target compound.



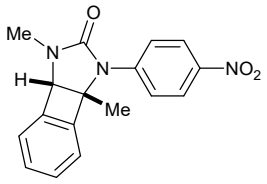
(3a*R,7b*S**)-1,3a-Dimethyl-3-phenyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13aa).** 1,4-Dimethyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (200 mg, 1.06 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13aa** (111 mg, 0.420 mmol, 40%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2924, 1693, 1500, 1454, 1377, 1346, 1263, 1195, 744, 719, 694, 634, 509.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 8.5, 1.1 Hz, 2H), 7.41 – 7.28 (m, 6H), 7.23 – 7.13 (m, 1H), 4.78 (s, 1H), 3.05 (s, 3H), 1.73 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 149.8, 143.3, 137.8, 129.4, 129.3, 128.9, 124.8, 124.6, 123.2, 122.4, 66.8, 66.0, 29.0, 20.8.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{17}H_{16}N_2O$ 287.1160, found 287.1177.



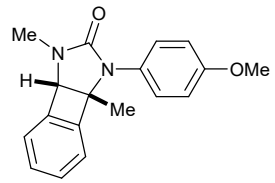
(3a*R,7b*S**)-1,3a-Dimethyl-3-(4-nitrophenyl)-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ba).** 1,4-Dimethyl-3-(4-nitrophenyl)-1,3-dihydro-2*H*-imidazol-2-one (42 mg, 0.180 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ba** (31 mg, 0.100 mmol, 56%) as pale yellow solid.

IR (neat) ν_{max}/cm^{-1} 2970, 2364, 1734, 1365, 1217, 528.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 9.3 Hz, 2H), 7.78 (d, *J* = 9.3 Hz, 2H), 7.41 (m, 3H), 7.35 – 7.31 (m, 1H), 4.80 (s, 1H), 3.08 (s, 3H), 1.87 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 148.1, 144.3, 143.0, 142.7, 130.1, 125.1, 124.8, 123.5, 122.9, 120.6, 66.3, 65.9, 29.2, 20.9.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{15}N_3O_3$ 310.1192, found 310.1190.



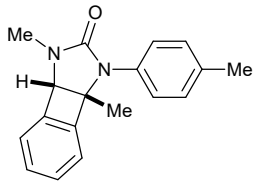
(3a*R,7b*S**)-3-(4-Methoxyphenyl)-1,3a-Dimethyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ca).** 3-(4-Methoxyphenyl)-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (500 mg, 2.29 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ca** (300 mg, 1.019 mmol, 45%) as a pale yellow solid.

IR (neat) ν_{max}/cm^{-1} 2971, 1689, 1510, 1425, 1386, 1294, 1242, 1180, 1161, 1114, 1033, 823, 744, 707, 642, 548.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 2H), 7.30 – 7.27 (m, 1H), 7.25 (d, *J* = 2.3 Hz, 1H), 7.24 – 7.21 (m, 2H), 6.96 – 6.88 (m, 2H), 4.78 (s, 1H), 3.82 (s, 3H), 3.04 (s, 3H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 157.7, 150.1, 143.4, 130.5, 129.4, 129.3, 127.9, 123.2, 122.1, 114.4, 67.1, 66.1, 55.6, 29.1, 20.8.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{18}N_2O_2$ 317.1266, found 317.1266.



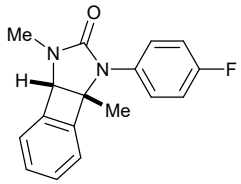
(3a*R,7b*S**)-1,3a-Dimethyl-3-(*p*-tolyl)-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13da).** 1,4-Dimethyl-3-(*p*-tolyl)-1,3-dihydro-2*H*-imidazol-2-one (153 mg, 0.757 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13da** (55 mg, 0.254 mmol, 34%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2926, 1691, 1514, 1425, 1386, 1346, 1261, 1199, 1112, 1047, 995, 815, 746, 707, 642, 555, 511.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.32 (m, 2H), 7.29 (m, 4H), 7.20 (m, 2H), 4.77 (s, 1H), 3.04 (s, 3H), 2.35 (s, 3H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 150.0, 143.4, 135.1, 135.0, 129.6, 129.5, 129.3, 125.3, 123.2, 122.3, 66.9, 66.0, 29.1, 21.1, 20.8.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{18}N_2O$ 301.1317, found 301.1312.



(3a*R,7b*S**)-3-(4-Fluorophenyl)-1,3a-dimethyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ea).** 3-(4-Fluorophenyl)-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (245 mg, 3.55 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ea** (382 mg, 1.35 mmol, 39%) as a pale-yellow oil.

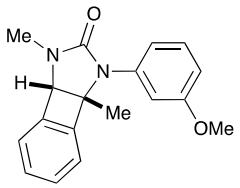
IR (neat) ν_{max}/cm^{-1} 2926, 1693, 1506, 1425, 1388, 1215, 1201, 1153, 1114, 831, 746, 707, 516.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 5H), 7.27 – 7.25 (m, 1H), 7.11 – 7.04 (m, 2H), 4.79 (s, 1H), 3.04 (s, 3H), 1.69 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9 ($^1J_{C\text{-}F}$ = 273 Hz), 161.6, 157.6, 149.7, 143.3, 133.6, 129.5, 127.2, 123.3, 122.2, 115.8 ($^2J_{C\text{-}F}$ = 23 Hz), 67.0, 66.1, 29.8, 20.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ –117.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{17}H_{15}FN_2O$ 283.1247, found 283.1250.



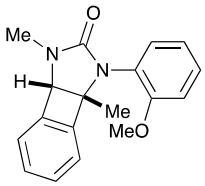
(3a*R,7b*S**)-3-(3-Methoxyphenyl)-1,3a-dimethyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13fa).** 3-(3-Methoxyphenyl)-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (65.3 mg, 0.299 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13fa** (19.6 mg, 0.066 mmol, 22%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2931, 1696, 1637, 1597, 1450, 1427, 1381, 1226, 1118, 1049, 748.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 5H), 7.09 (t, *J* = 2.1 Hz, 1H), 7.05 – 7.02 (m, 1H), 6.73 (dd, *J* = 8.3, 2.1 Hz, 1H), 4.77 (s, 1H), 3.82 (s, 3H), 3.05 (s, 3H), 1.75 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 157.4, 149.9, 143.4, 139.1, 129.6, 129.51, 129.49 123.3, 122.6, 116.6, 110.7, 110.2, 66.9, 66.1, 55.5, 29.1, 20.9.

LCMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{18}N_2O_2$ 295.1447, found 295.1.



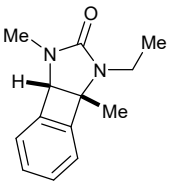
(3a*R,7b*S**)-3-(2-Methoxyphenyl)-1,3a-dimethyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ga).** 3-(2-Methoxyphenyl)-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (176 mg, 0.807 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ga** (135 mg, 0.458 mmol, 57%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2924, 1697, 1504, 1458, 1427, 1388, 1357, 1242, 1211, 1111, 1026, 748, 632.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 4H), 7.18 – 7.14 (m, 2H), 6.98 – 6.94 (m, 2H), 4.82 (s, 1H), 3.74 (s, 3H), 3.03 (s, 3H), 1.56 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 157.2, 151.2, 143.2, 131.0, 129.2, 129.0, 128.9, 126.2, 123.0, 121.9, 120.8, 112.3, 67.6, 66.7, 55.7, 29.2, 20.1.

LCMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{18}N_2O_2$ 295.1447, found 295.1.



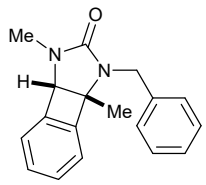
(3a*R,7b*S**)-3-ethyl-1,3a-Dimethyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ha).** 3-Ethyl-1,4-dimethyl-1,3-dihydro-2H-imidazol-2-one (452 mg, 3.23 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ha** (188 mg, 0.871 mmol, 27%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2926, 1685, 1427, 1396, 1377, 1354, 1259, 1220, 1120, 1028, 806, 750, 717, 553.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.27 (m, 2H), 7.23 – 7.16 (m, 2H), 4.61 (s, 1H), 3.54 – 3.41 (m, 1H), 3.39 – 3.25 (m, 1H), 2.94 (s, 3H), 1.71 (s, 3H), 1.21 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 150.3, 143.1, 129.1, 128.9, 122.9, 121.4, 66.0, 65.9, 35.4, 28.8, 20.3, 15.5.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{13}H_{16}N_2O$ 239.1160, found 239.1149.



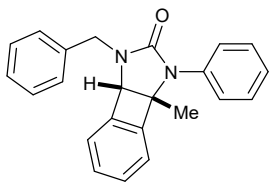
(3a*R,7b*S**)-3-Benzyl-1,3a-dimethyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ia).** 3-Benzyl-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (500 mg, 2.47 mmol.) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ia** (268 mg, 0.963 mmol, 39%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2922, 1681, 1433, 1392, 1354, 1255, 1188, 1116, 1047, 979, 744, 698, 549, 443.

1H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.23 (m, 4H), 7.22 – 7.16 (m, 3H), 7.09 (td, *J* = 7.4, 1.4 Hz, 1H), 6.34 (d, *J* = 7.4, 1H), 4.70 (d, *J* = 15.1 Hz, 1H), 4.61 (s, 1H), 4.39 (d, *J* = 15.1 Hz, 1H), 3.00 (s, 3H), 1.59 (s, 3H).

13C NMR (101 MHz, $CDCl_3$) δ 159.4, 150.0, 143.0, 139.1, 129.0, 128.9, 128.6, 128.5, 127.3, 122.8, 121.8, 66.2, 66.1, 44.9, 29.1, 20.5.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{18}N_2O$ 301.1317, found 301.1320.



(3a*R,7b*S**)-1-Benzyl-3a-methyl-3-phenyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ja).** 1-Benzyl-4-methyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (39 mg, 0.145 mmol.) was subjected to

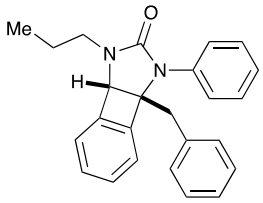
the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ja** (19 mg, 0.056 mmol, 39%) as a yellow powder.

IR (neat) ν_{max}/cm^{-1} 2970, 2922, 1739, 1439, 1365, 1217, 1091, 896, 698.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.44 (m, 4H), 7.40 – 7.31 (m, 10H), 6.00 (q, *J* = 1.3 Hz, 1H), 4.83 (s, 2H), 1.93 (d, *J* = 1.3 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3, 153.1, 137.2, 135.2, 129.5, 129.3, 129.0, 128.9, 128.2, 127.9, 127.8, 127.5, 119.9, 119.3, 107.2, 63.8, 63.1, 47.1, 11.3.

HRMS (ESI) m/z: [M + H]+ calcd for $C_{23}H_{20}N_2O$ 341.1654, found 341.1653

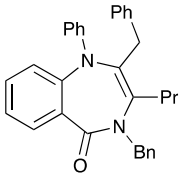


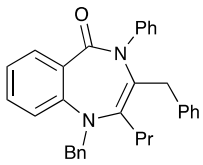
(3a*R,7b*S**)-3a-benzyl-3-phenyl-1-propyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ka)**. 4-Benzyl-3-phenyl-1-propyl-1,3-dihydro-2*H*-imidazol-2-one (62 mg, 0.212 mmol) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (9:1 n-hexane: ethyl acetate) to afford the target compound **13ka** (25 mg, 0.068 mmol, 32%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.53 (m, 2H), 7.46-7.32 (m, 5H), 7.21 – 7.15 (m, 5H), 6.97 (dd, *J* = 6.6, 2.8 Hz, 2H), 4.87 (s, 1H), 3.57 (d, *J* = 14.0 Hz, 1H), 3.41 – 3.19 (m, 3H), 1.64 – 1.59 (m, 2H), 0.83 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.7, 149.1, 143.9, 138.2, 136.2, 129.8, 129.4, 129.0, 128.4, 126.9, 124.5, 124.0, 123.4, 122.9, 121.2, 70.5, 61.4, 44.4, 38. 8, 21.5, 11.3.

HRMS (ES+) m/z: [M + Na]+ calcd for $C_{25}H_{24}N_2O$ 391.1786, found 391.1787.





2,4-Dibenzyl-1-phenyl-3-propyl-1,4-dihydro-5*H*-benzo[*e*][1,4]diazepin-5-one (14la) & 1,3-dibenzyl-4-phenyl-2-propyl-1,4-dihydro-5*H*-benzo[*e*][1,4]diazepin-5-one (14la'). 1,4-Dibenzyl-3-phenyl-5-propyl-1,3-dihydro-2*H*-imidazol-2-one (48 mg, 0.127 mmol) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (9:1 n-hexane: ethyl acetate) to afford **14la** (11 mg, 0.023 mmol, 18%) and **14la'** (8 mg, 0.017 mmol, 13%) as white oils.

Data for 2,4-Dibenzyl-1-phenyl-3-propyl-1,4-dihydro-5*H*-benzo[*e*][1,4]diazepin-5-one (14la):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 1H), 7.62-7.41 (m, 9H), 7.38 – 7.31 (m, 3H), 7.23– 7.15 (m, 1H), 6.98– 6.90 (m, 1H), 6.83 (t, *J* = 7.6 Hz, 2H), 6.26 (dd, *J* = 7.9, 1.5 Hz, 2H), 4.82 (s, 2H), 4.04 (d, *J* = 14.8 Hz, 1H), 3.69 (d, *J* = 14.8 Hz, 1H), 2.07 (m, 2H), 1.22 – 1.08 (m, 2H), 0.60 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.0, 145.2, 140.2, 135.3, 132.7, 132.3, 130.2, 129.2, 129.0, 128.8, 127.7, 127.5, 127.1, 126.5, 125.1, 124.3, 123.1, 122.3, 55.5, 38.8, 30.8, 21.1, 14.9.

HRMS (ES+) m/z: [M + Na]+ calcd. for $C_{32}H_{30}N_2O$ 481.2256, found 481.2254.

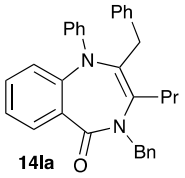
Data for 1,3-dibenzyl-4-phenyl-2-propyl-1,4-dihydro-5*H*-benzo[*e*][1,4]diazepin-5-one (14la'):

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.3, 1.3 Hz, 1H), 7.58 – 7.53 (m, 2H), 7.43 – 7.28 (m, 6H), 7.22 (t, *J* = 7.9 Hz, 1H), 7.15 (d, *J* = 7.6 Hz, 1H), 6.99 (ddt, *J* = 8.6, 7.3, 1.2 Hz, 1H), 6.88 – 6.78 (m, 3H), 6.55 – 6.48 (m, 2H), 6.17 (dd, *J* = 7.0, 1.9 Hz, 2H), 4.60 (d, *J* = 14.9 Hz, 1H), 4.53 (d, *J* = 14.9 Hz, 1H), 3.04 (d, *J* = 14.8 Hz, 1H), 2.96 (d, *J* = 14.8 Hz, 2H), 2.48 – 2.27 (m, 2H), 0.50 (d, *J* = 3.3 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 150.3, 145.9, 137.9, 135.7, 132.8, 131.9, 129.6, 129.1, 128.8, 128.7, 127.9, 127.9, 125.9, 124.0, 123.6, 122.7, 119.1, 75.1, 44.4, 34.9, 15.9, 13.7.

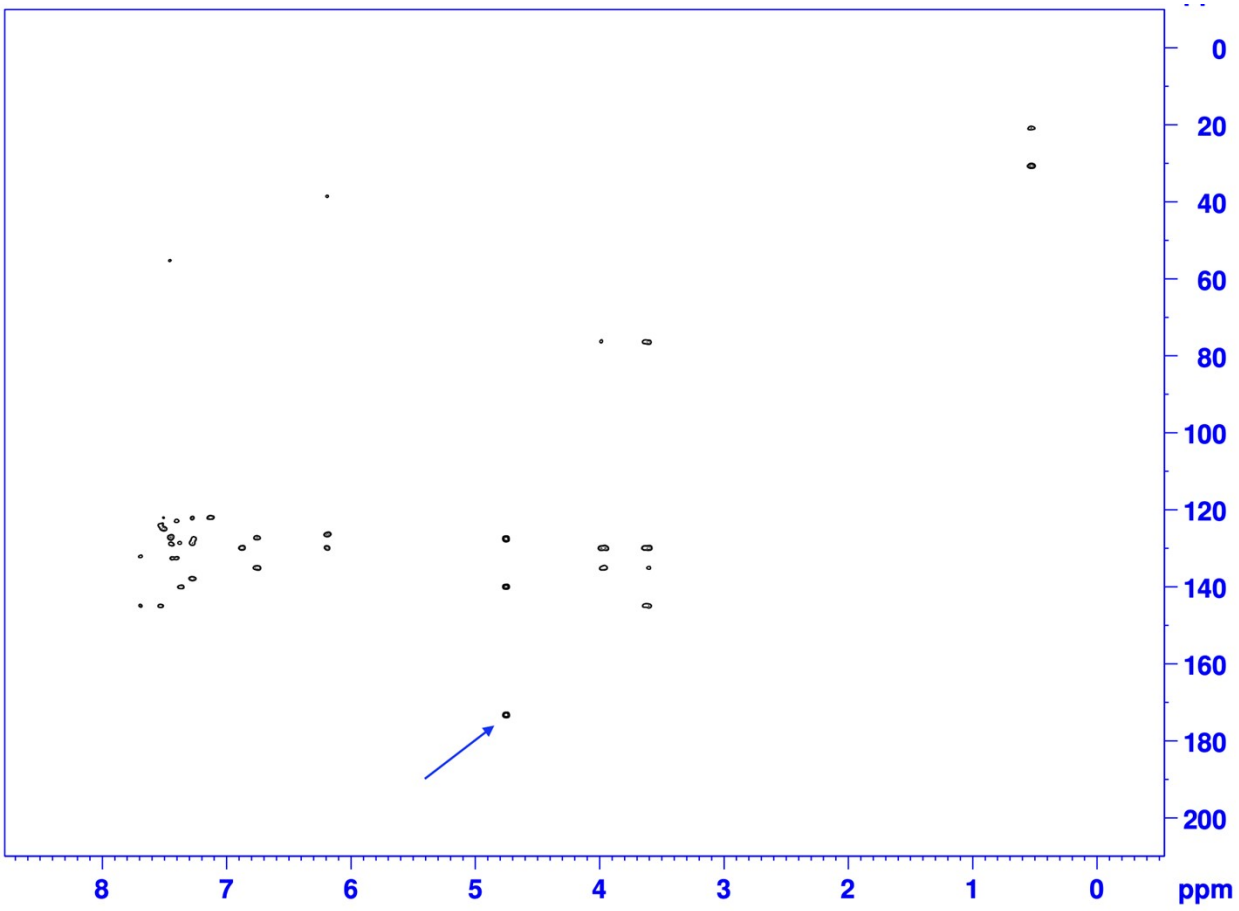
HRMS (ES+) m/z: [M + Na]+ calcd. for $C_{32}H_{30}N_2O$ 481.2256, found 481.2249.

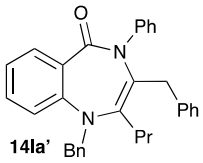
Regioisomer assignment for benzodiazepines 14la and 14la':



14la

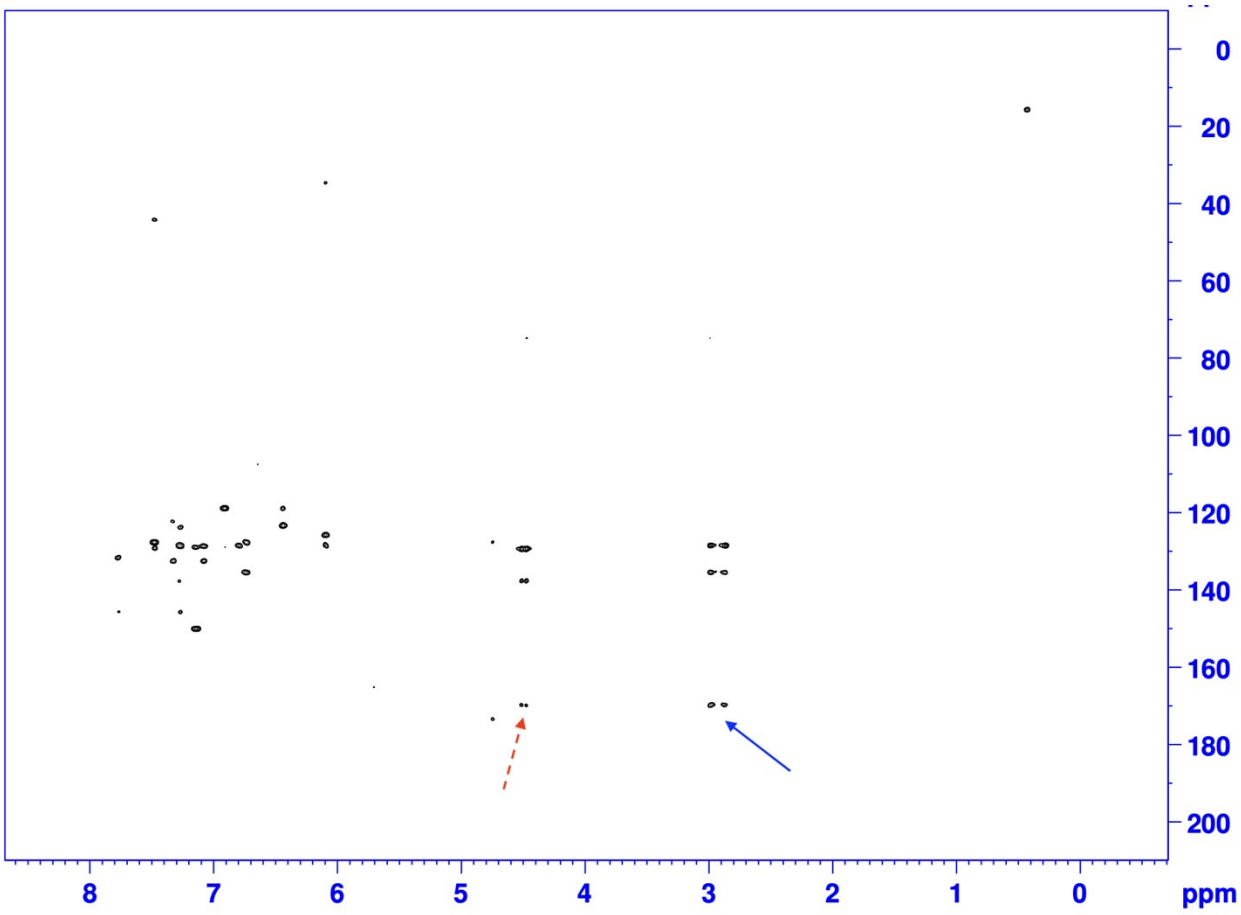
Strong correlation in HMBC spectrum between amide C=O and N-CH_2Ph (blue arrow), suggesting N-Bn group is part of the amide. No correlation between amide C=O and the exocyclic CH_2Ph site.

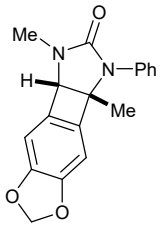




14la'

Strong correlation in HMBC spectrum between amide C=O and the exocyclic CH_2Ph (blue arrow), suggesting proximity of the two sites. Weak correlation between amide C=O and N-CH_2Ph (red dashed arrow).





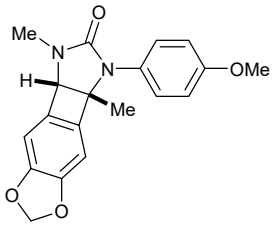
(4b*R,7a*S**)-4b,7-Dimethyl-5-phenyl-4b,5,7,7a-tetrahydro-6*H*-[1,3]dioxolo[4'',5'':4',5']benzo[1',2':3,4]cyclobuta[1,2-*d*]imidazol-6-one (13ab).** 1,4-Dimethyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (400 mg, 2.12 mmol) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ab** (267 mg, 0.866 mmol, 41%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2900, 1678, 1462, 1417, 1384, 1375, 1344, 1303, 1238, 1118, 1035, 754, 742, 690,

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 2H), 7.37 (d, *J* = 1.4 Hz, 2H), 7.20 – 7.15 (m, 1H), 6.80 (d, *J* = 0.6 Hz, 1H), 6.78 (d, *J* = 0.6 Hz, 1H), 5.95 (d, *J* = 1.4 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 4.62 (s, 1H), 3.02 (s, 3H), 1.67 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.5, 148.7, 148.6, 142.7, 137.8, 136.0, 129.0, 125.0, 124.9, 104.7, 104.1, 100.7, 65.3, 64.6, 28.9, 21.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{16}N_2O_3$ 309.1239, found 309.1218.



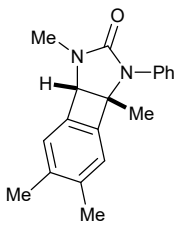
(4b*R,7a*S**)-5-(4-Methoxyphenyl)-4b,7-dimethyl-4b,5,7,7a-tetrahydro-6*H*-[1,3]dioxolo[4'',5'':4',5']benzo[1',2':3,4]cyclobuta[1,2-*d*]imidazol-6-one (13cb).** 3-(4-Methoxyphenyl)-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (140 mg, 0.646 mmol) was subjected to general the procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13cb** (80 mg, 0.237 mmol, 38%) as a pale yellow solid.

IR (neat) ν_{max}/cm^{-1} 2926, 1687, 1510, 1460, 1388, 1305, 1244, 1116, 1031, 939, 827, 746, 563.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 9.0 Hz, 2H), 6.77 (d, *J* = 0.6 Hz, 1H), 6.69 (d, *J* = 0.6 Hz, 1H), 5.94 (d, *J* = 1.4 Hz, 1H), 5.93 (d, *J* = 1.4 Hz, 1H), 4.62 (s, 1H), 3.82 (s, 3H), 3.00 (s, 3H), 1.60 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.1, 157.8, 148.6, 148.5, 142.9, 136.0, 130.4, 128.1, 114.4, 104.7, 103.8, 100.7, 65.5, 64.6, 55.6, 29.0, 21.0.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{18}N_2O_4$ 361.1164, found 361.1164.



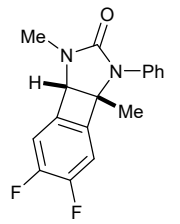
(3a*R,7b*S**)-1,3a,5,6-Tetramethyl-3-phenyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ac).** 1,4-Dimethyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (50 mg, 0.265 mmol) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ac** (14 mg, 0.049 mmol, 19%) as a colourless solid.

IR (neat) ν_{max}/cm^{-1} 2920, 2364, 1695, 1597, 1500, 1421, 1386, 1344, 1269, 1188, 1118, 1051, 995, 869, 750, 692, 632, 511, 410.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.38 (m, 2H), 7.16 (m, 1H) 7.13 (s, 1H), 7.09 (s, 1H) 4.72 (s, 1H), 3.02 (s, 3H), 2.30 (s, 3H), 2.29 (s, 3H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 147.5, 141.0, 138.3, 138.2, 138.0, 128.9, 124.5, 124.2, 124.0, 123.3, 66.5, 65.8, 29.0, 21.0, 20.7. 20.6.

HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{19}H_{20}N_2O$ 315.1473, found 315.1477.



(3a*R,7b*S**)-5,6-Difluoro-1,3a-dimethyl-3-phenyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13ad).** 1,4-Dimethyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (24 mg, 0.128 mmol) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ad** (32 mg, 0.106 mmol, 83%) as a colourless thick oil.

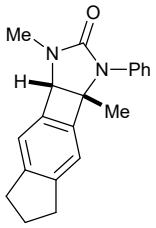
IR (neat) ν_{max}/cm^{-1} 2933, 1695, 1476, 1349, 730.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.32 (m, 4H), 7.25 – 7.11 (m, 3H), 4.74 (s, 1H), 3.03 (s, 3H), 1.70 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 152.4 (d, $^1J_{C\text{-}F}$ = 248 Hz, 2 x ArC), 145.4, 138.8, 137.3, 129.1, 125.5, 125.1, 113.2 (d, $^2J_{C\text{-}F}$ = 18.1 Hz), 112.5 (d, $^2J_{C\text{-}F}$ = 18.4 Hz), 66.3, 65.4, 29.0, 20.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ –134.0, –134.4.

HRMS (ESI) m/z: [M + H]+ calcd for $C_{17}H_{14}F_2N_2O$ 301.1152, found 301.1149



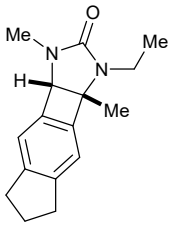
(3a*R,8b*S**)-1,3a-Dimethyl-3-phenyl-3,3a,5,6,7,8b-hexahydroindeno[5',6':3,4]cyclobuta[1,2-d]imidazol-2(1*H*)-one (13ae)**. 1,4-Dimethyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (60 mg, 0.324 mmol), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13ae** (46 mg, 0.151 mmol, 47%) as a pale yellow oil.

IR (neat) ν_{max}/cm^{-1} 2927, 1695, 1598, 1498, 1423, 1386, 1342, 1118, 750, 694, 507.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.5 Hz, 2H), 7.22 (s, 1H), 7.16 (t, *J* = 3.5 Hz, 2H), 4.69 (s, 1H), 3.03 (s, 3H), 2.92 (t, *J* = 7.2 Hz, 4H), 2.11 – 2.01 (m, 2H), 1.71 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 147.6, 145.5, 145.4, 141.0, 138.0, 128.9, 124.5, 124.3, 119.4, 118.7, 65.6, 65.0, 33.3, 33.3, 29.0, 25.4, 21.0.

HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{20}H_{20}N_2O$ 305.1654, found 305.1652.



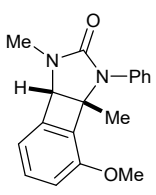
(3a*R,8b*S**)-3-Ethyl-1,3a-dimethyl-3,3a,5,6,7,8b-hexahydroindeno[5',6':3,4]cyclobuta[1,2-*d*]imidazol-2(1*H*)-one (13fe).** 3-Ethyl-1,4-dimethyl-1,3-dihydro-2*H*-imidazol-2-one (190 mg, 1.35 mmol) was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13fe** (164 mg, 0.64 mmol, 47%) as a pale yellow thick oil.

IR (neat) ν_{max}/cm^{-1} 2970, 1681, 1394, 1354, 1217, 750, 543.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (s, 2H), 4.51 (s, 1H), 3.45 (dq, *J* = 14.6, 7.4 Hz, 1H), 3.30 (dq, *J* = 14.6, 7.4 Hz, 1H), 2.91 (s, 3H), 2.87 (t, *J* = 7.4 Hz, 4H), 2.03 (m, 2H), 1.67 (s, 3H), 1.20 (apparent t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 148.2, 145.0, 144.9, 140.9, 119.2, 117.7, 65.1, 64.8, 35.5, 33.3, 33.2, 28.8, 25.3, 20.7, 15.7.

HRMS (ESI) m/z: [M + H]+ calcd for $C_{16}H_{20}N_2O$ 257.1654, found 257.1658



(3a*R,7b*S**)-7-Methoxy-1,3a-dimethyl-3-phenyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one (13af).** 1,4-Dimethyl-3-phenyl-1,3-dihydro-2*H*-imidazol-2-one (85 mg, 0.452 mmol.), was subjected to the general procedure. The crude mixture was purified by silica gel flash column chromatography (5:1 *n*-hexane: ethyl

acetate) to afford the target compound **13af** (50 mg, 0.170 mmol, 38%) as a colourless thick oil and a single regioisomer.

IR (neat) ν_{max}/cm^{-1} 2950, 1700, 1500, 1475, 13,80, 1350, 1260, 1275, 1068, 750, 690, 510.

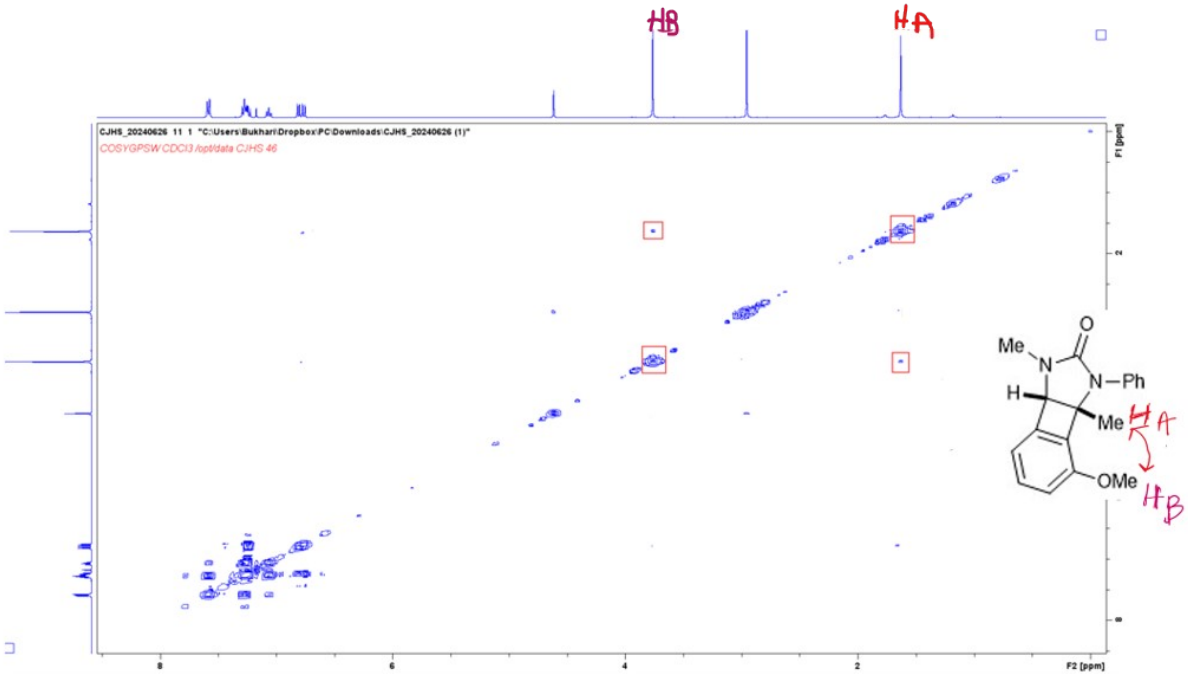
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.64 (m, 2H), 7.39 – 7.30 (m, 3H), 7.18 – 7.12 (m, 1H), 6.92 – 6.83 (m, 2H), 4.70 (s, 1H), 3.86 (s, 3H), 3.04 (s, 3H), 1.71 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 153.5, 144.7, 137.8, 136.3, 131.2, 128.6, 125.3, 124.6, 115.3, 111.7, 66.3, 65.6, 55.4, 29.0, 20.5.

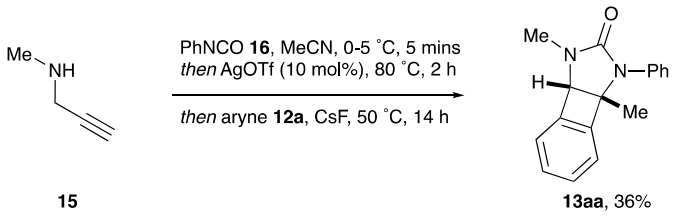
HRMS (ESI) m/z: $[M + Na]^+$ calcd for $C_{18}H_{18}N_2O_2$ 317.1266, found 317.1271.

Regioisomer assignment for 13af:

Observe long-range COSY correlation between the OMe and Me groups, supporting assignment that they are on the same side of the structure.



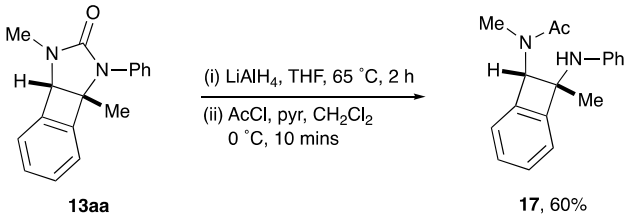
3. Procedure for the one-pot, three-stage preparation of benzocyclobutenes direct from propargylic amines:



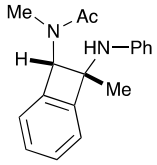
15 **13aa**, 36%

To a solution of methylpropargylamine (50 mg, 0.723 mmol) in MeCN (0.4 M) at 0-5 ^{o}C was added phenyl isocyanate (86 mg, 0.723 mmol). After 5 min of stirring, silver triflate (19 mg, 0.072 mmol, 10 mol%) was added, and the reaction mixture was sealed and stirred for 2 h at 80 ^{o}C. CsF (329 mg, 2.169 mmol) and 2-trimethylsilylphenyl triflate (215 mg, 0.723 mmol) were then added and the reaction mixture was left to stir for 14 hours at 50 ^{0}C. The reaction mixture was allowed to cool to room temperature, filtered and MeCN was removed *in vacuo*. The crude product was purified by silica gel column chromatography (5:1 *n*-hexane: ethyl acetate) to afford the target compound **13aa** (100 mg, 0.378 mmol, 36%) as a pale yellow thick oil.

4. Procedure for the ring opening of cyclic ureas:



13aa **17**, 60%



***N*-Methyl-*N*-((7*S**,8*R**)-8-methyl-8-(phenylamino)bicyclo[4.2.0]octa-1(6),2,4-trien-7-yl)acetamide (17).** $LiAlH_4$ (95 mg, 2.5mmol mmol) was added in two portions to a stirred solution of (3a*R*,7b*S*)-1,3a-Dimethyl-3-phenyl-1,3,3a,7b-tetrahydro-2*H*-benzo[3,4]cyclobuta[1,2-*d*]imidazol-2-one **(13aa)** (133 mg, 0.503 mmol) in THF (5.0 mL) at 0 °C. The resulting mixture was heated at reflux for 2 h. After cooling to room temperature, water (0.076 mL), 10% aqueous NaOH solution (0.076 mL) and water (0.228 mL) were added sequentially to the reaction mixture. The precipitated aluminum salts were removed by filtration through Celite and the solvent removed *in vacuo*. The crude mixture was redissolved in dichloromethane (5.0 mL) and cooled to 0 ˚C. Pyridine (0.041 mL, 0.503 mmol) and acetyl chloride (0.036 mL, 0.503 mmol) were added and the resulting mixture was stirred at 0 ˚C for 20 mins. The reaction mixture was poured into saturated aqueous $NaHCO_3$ (5.0 mL) and extracted with dichloromethane (2 x 5.0 mL). The combined organic phases were dried over

$MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by silica gel flash column chromatography (1:1 *n*-hexane: ethyl acetate) to afford the target compound **17** (85 mg, 0.303 mmol, 60%) as a colourless oil.

IR (neat) ν_{max}/cm^{-1} 3347, 2926, 1632, 1602, 1498, 1397, 1319, 1259, 1021, 752, 697.

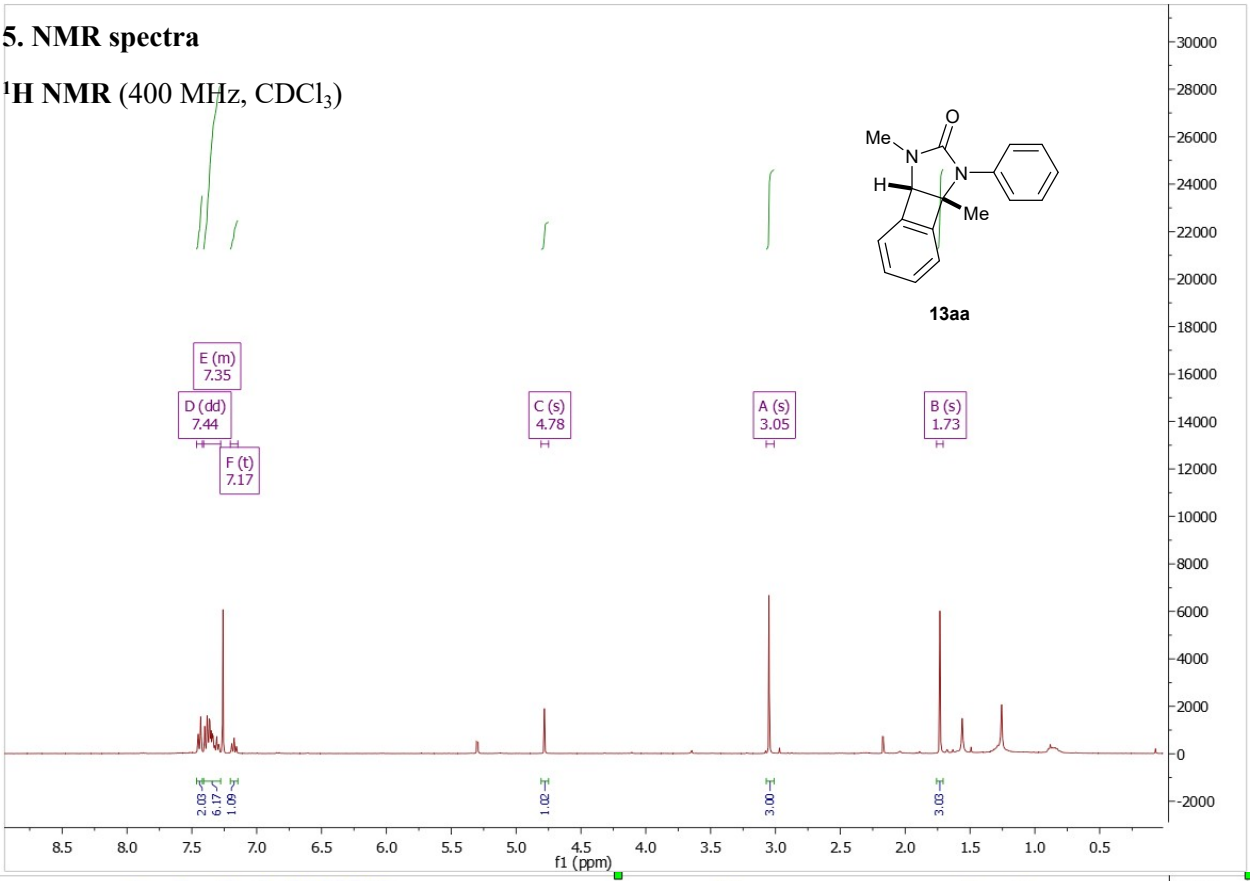
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.35 (m, 3H), 7.21 (d, *J* = 6.6 Hz, 1H), 7.08 (t, *J* = 6.2 Hz, 2H), 6.69 – 6.60 (m, 3H), 5.78 (s, 1H), 3.99 (br s, 1H), 2.71 (s, 3H), 1.95 (s, 3H), 1.82 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 149.9, 146.1, 140.7, 129.5, 129.3, 128.9, 125.1, 121.9, 117.9, 115.3, 68.8, 67.0, 34.2, 25.1, 22.3.

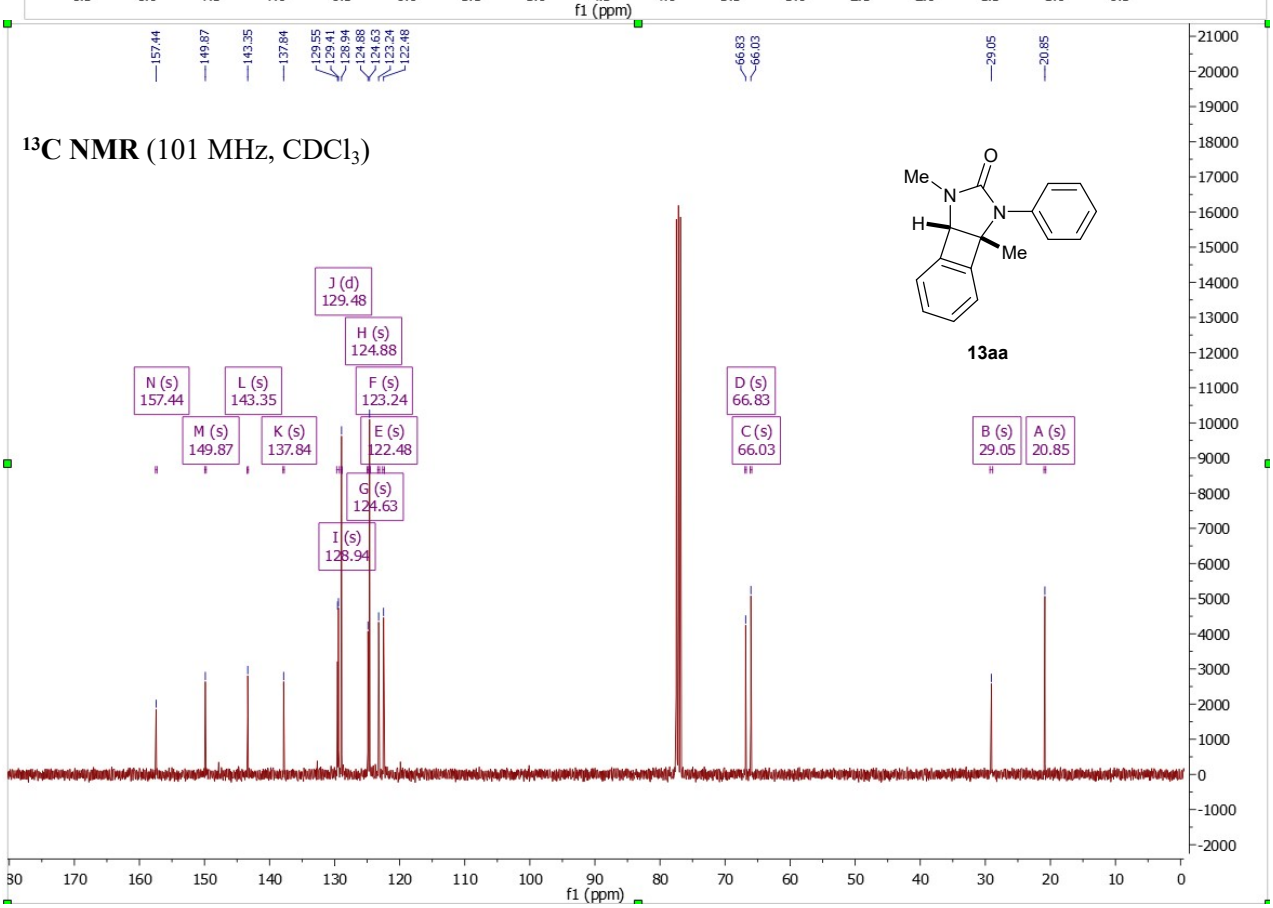
HRMS (ES+) m/z: $[M + H]^+$ for $C_{18}H_{20}N_2O$ 281.1654, found 281.1651.

5. NMR spectra

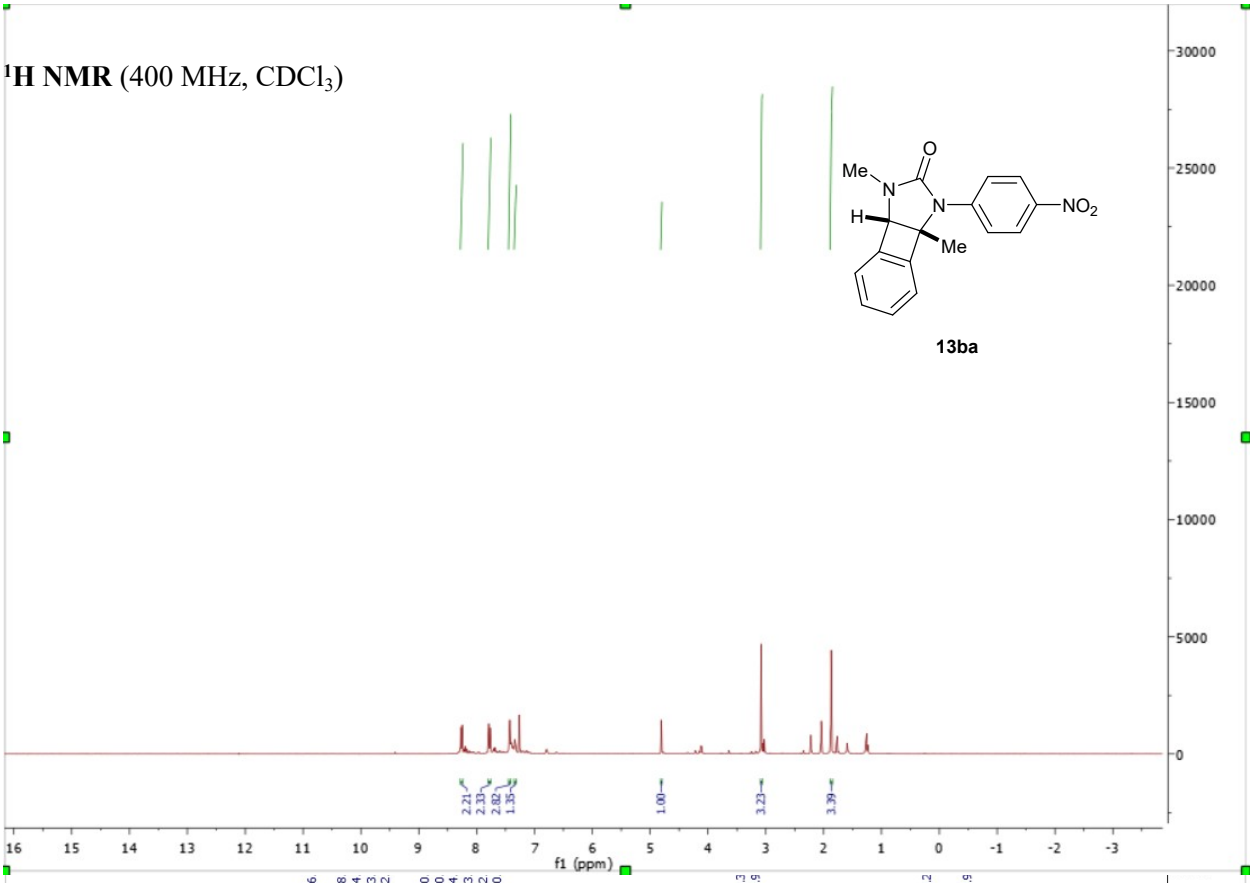
^{1}H NMR (400 MHz, $CDCl_3$)



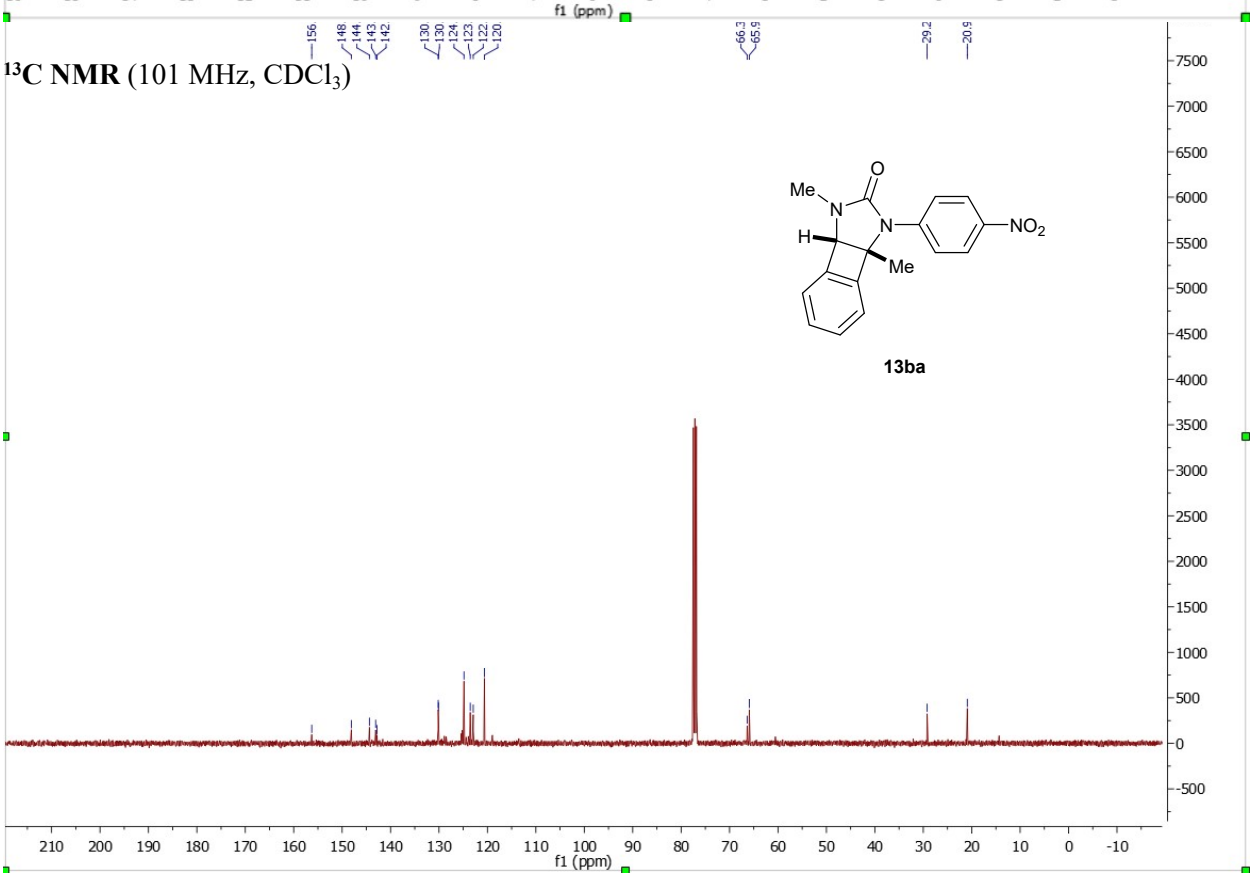
^{13}C NMR (101 MHz, $CDCl_3$)



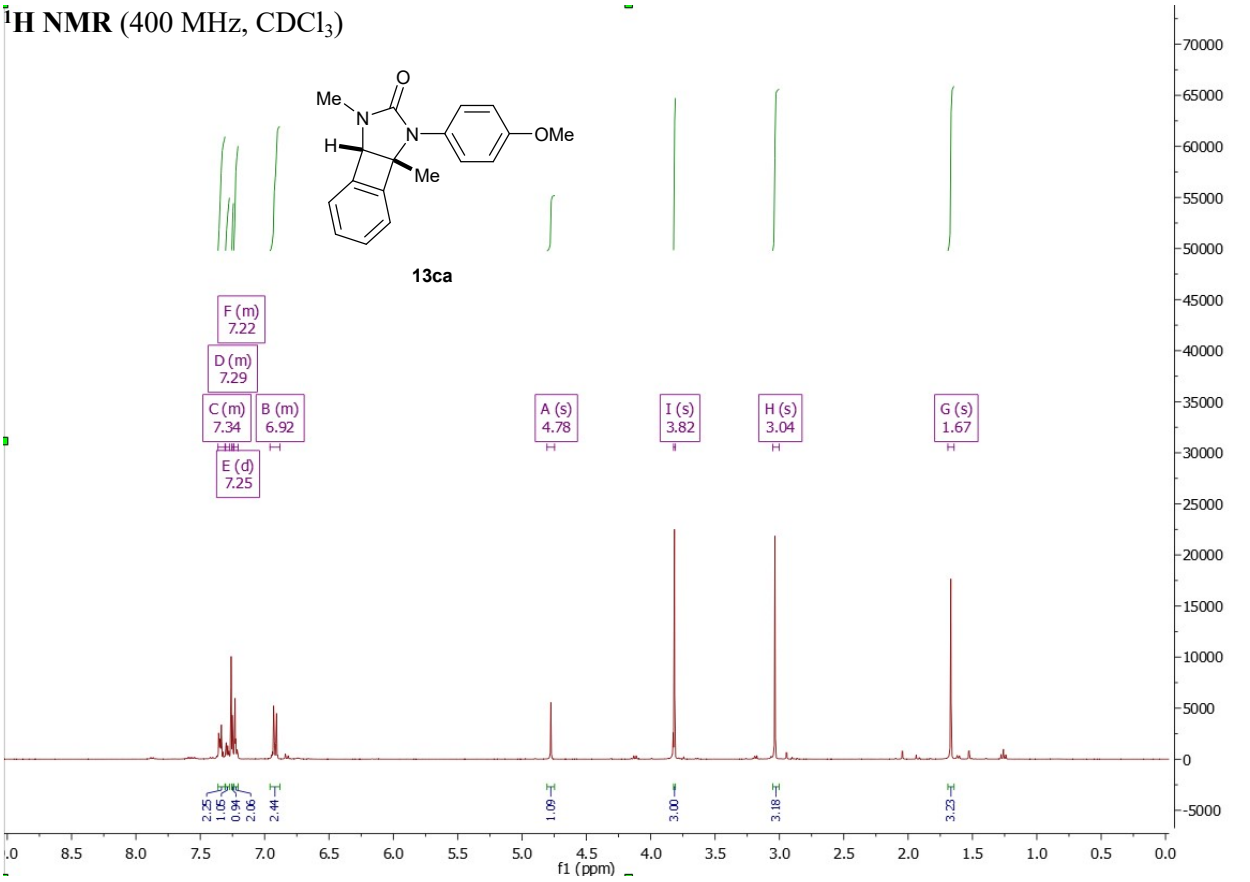
^{1}H NMR (400 MHz, $CDCl_3$)



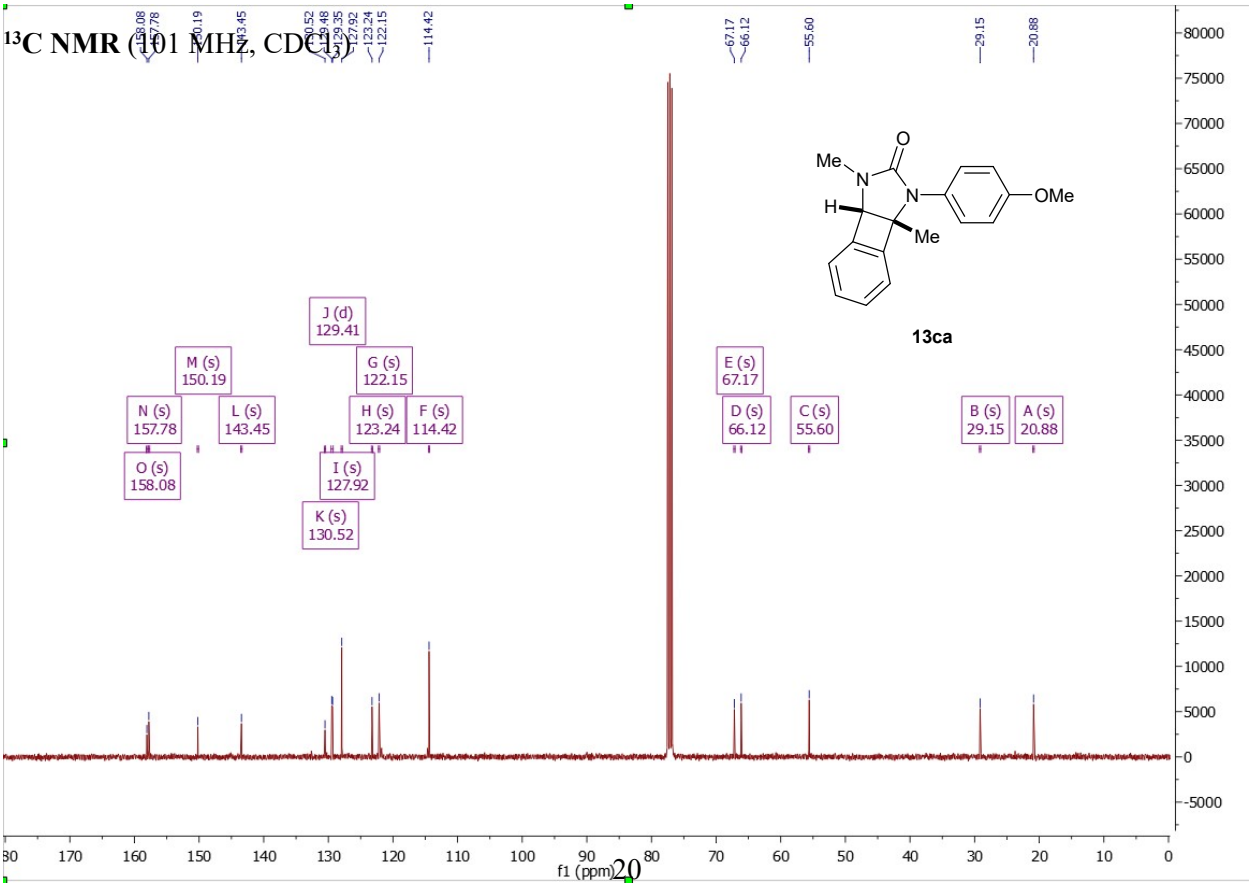
^{13}C NMR (101 MHz, $CDCl_3$)



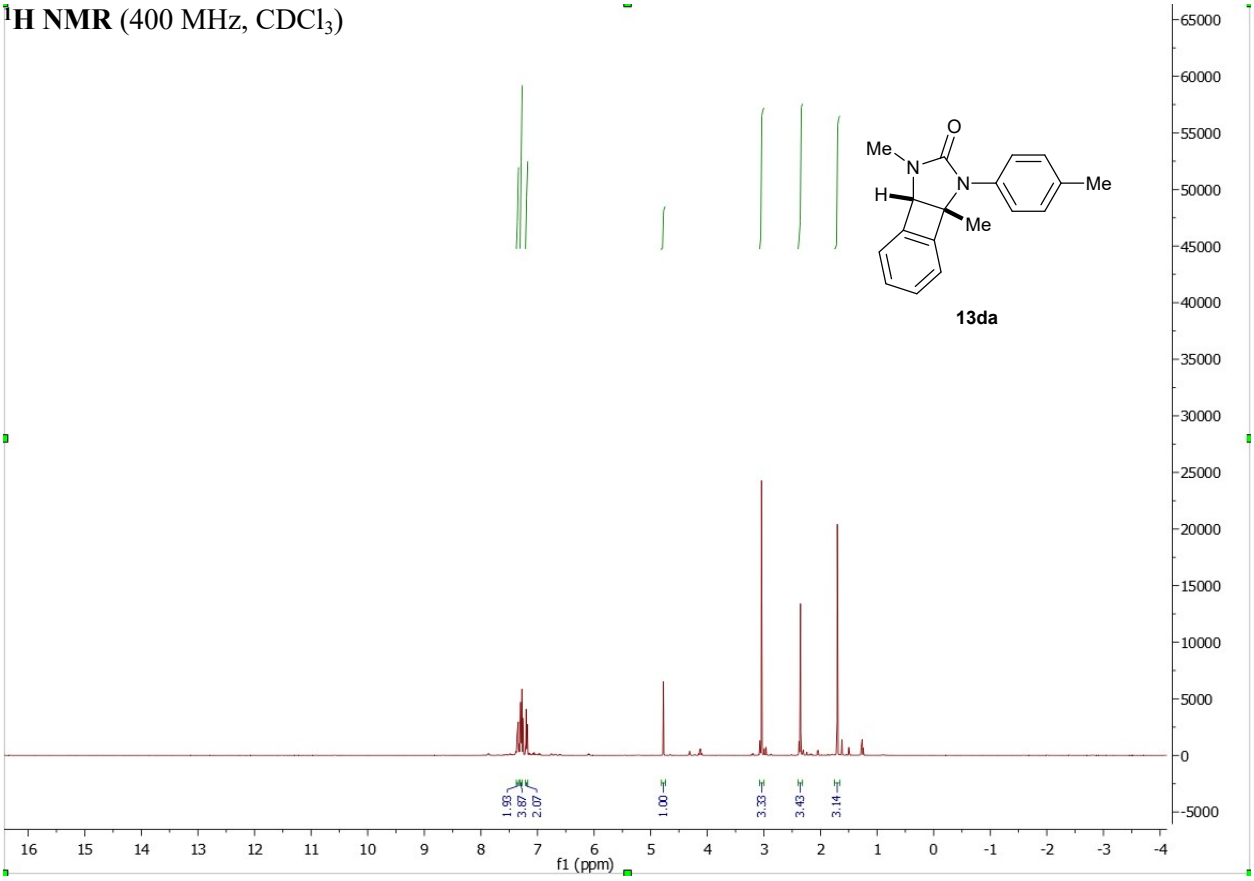
^{1}H NMR (400 MHz, $CDCl_3$)



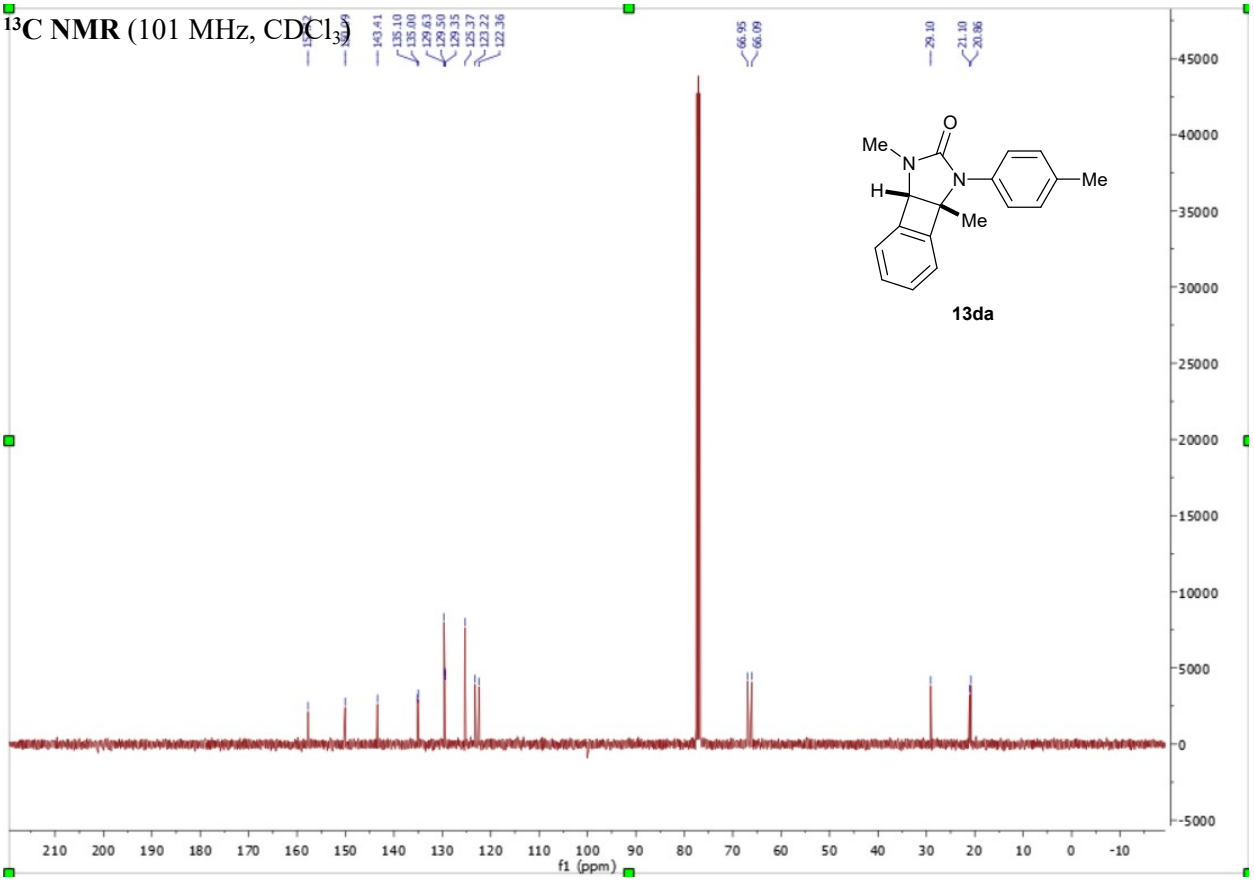
^{13}C NMR (101 MHz, $CDCl_3$)



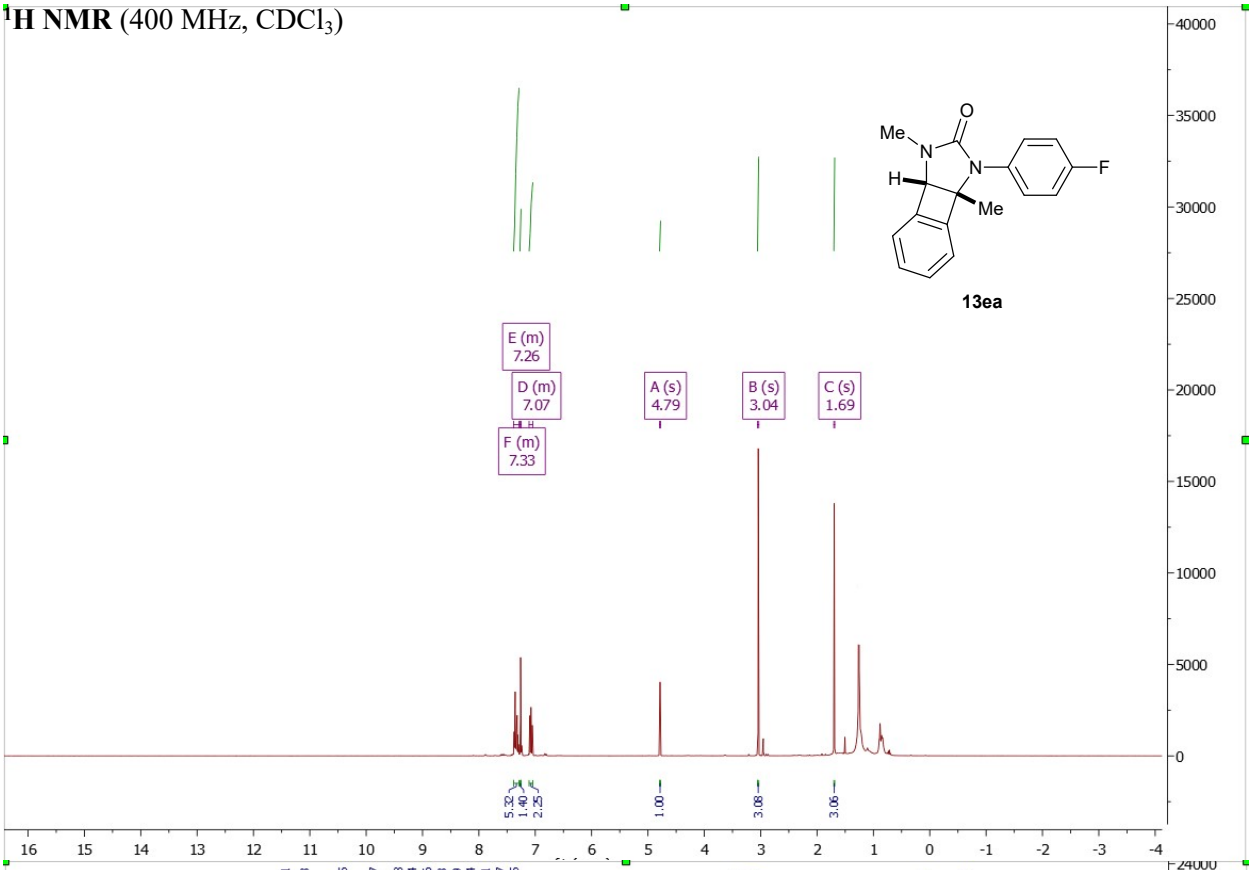
^{1}H NMR (400 MHz, $CDCl_3$)



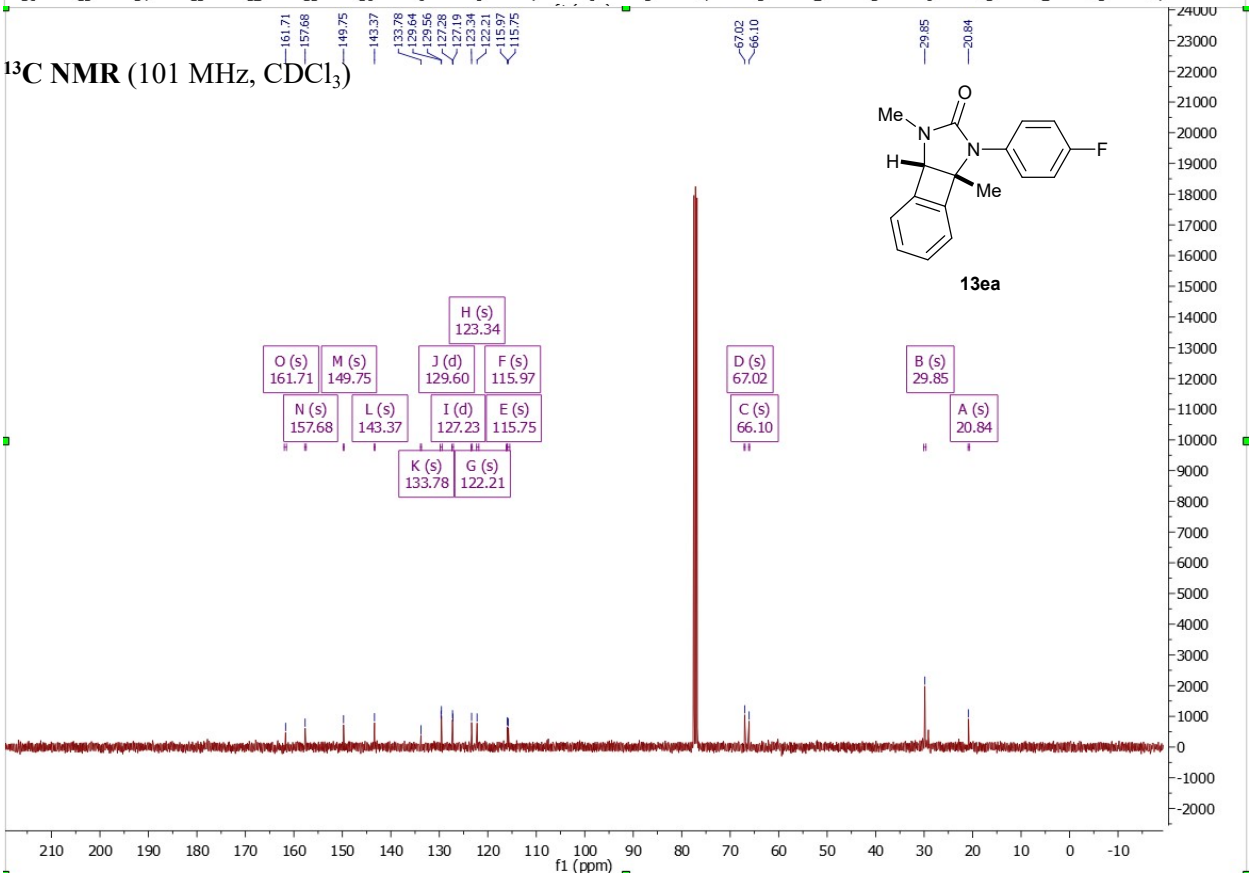
^{13}C NMR (101 MHz, $CDCl_3$)



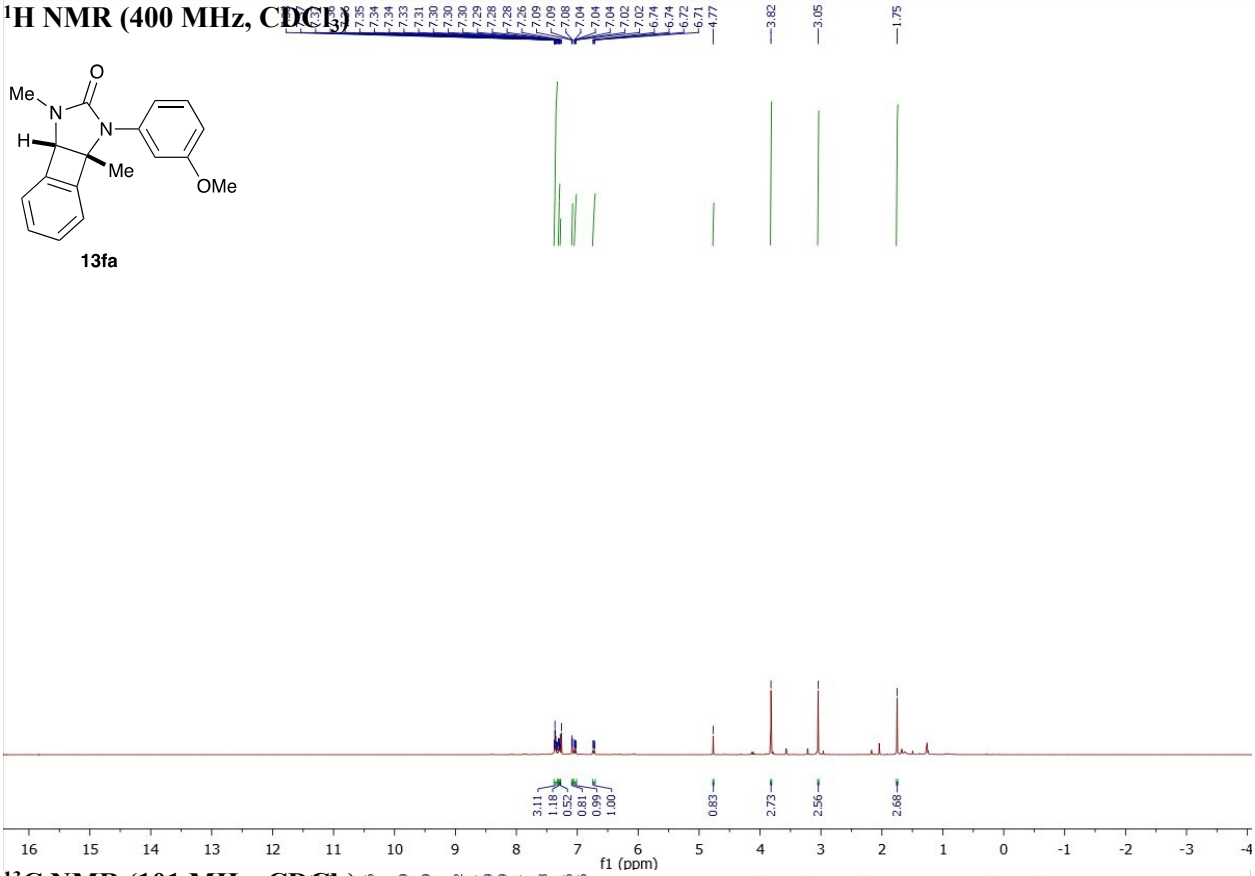
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

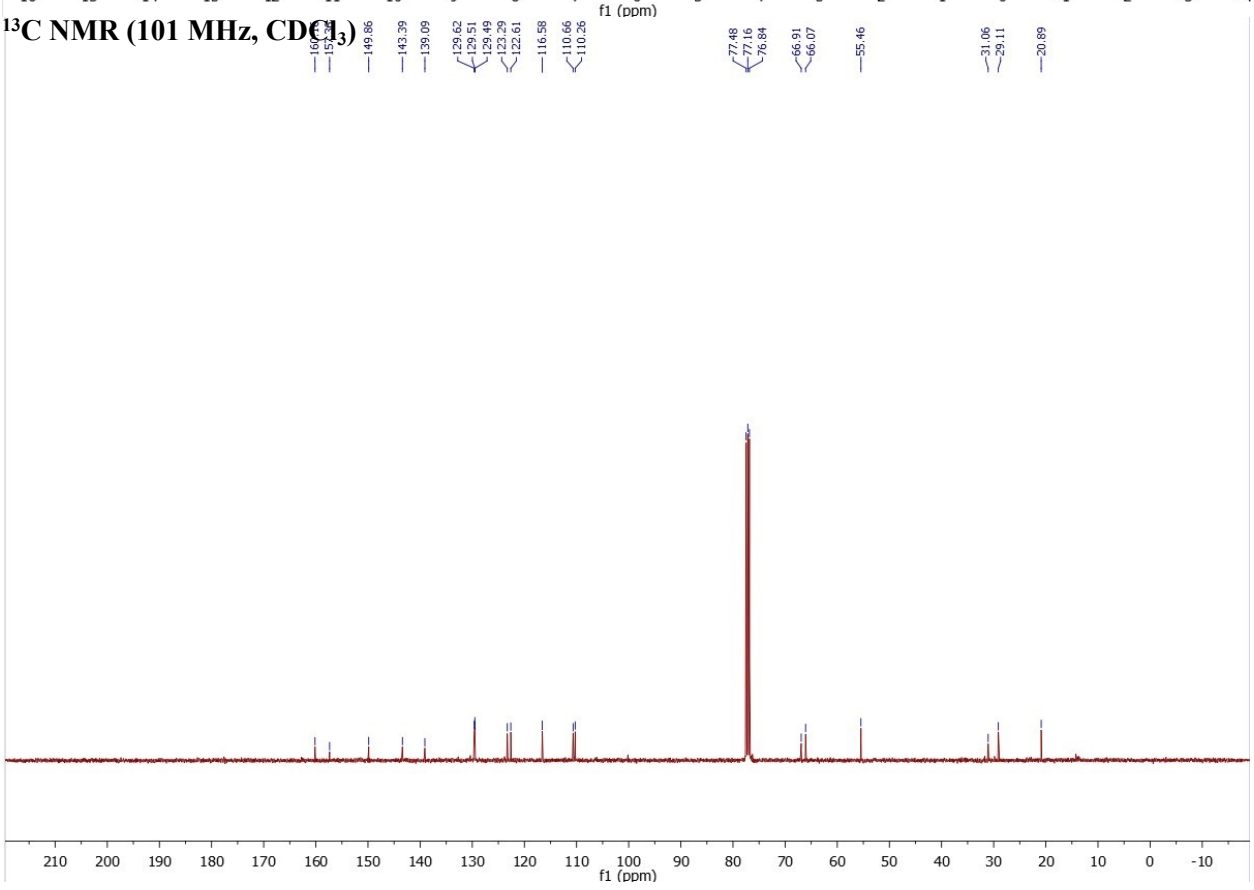


^{1}H NMR (400 MHz, $CDCl_3$)

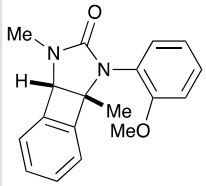


13fa

^{13}C NMR (101 MHz, $CDCl_3$)

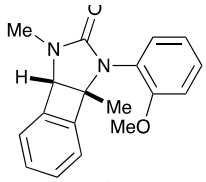


^{1}H NMR (400 MHz, $CDCl_3$)



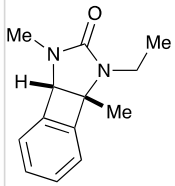
13ga

^{13}C NMR (101 MHz, $CDCl_3$)



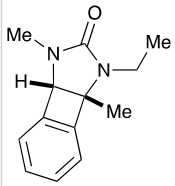
13ga

^{1}H NMR (400 MHz, $CDCl_3$)



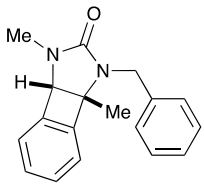
13ha

^{13}C NMR (101 MHz, $CDCl_3$)



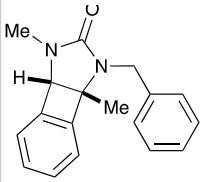
13ha

^{1}H NMR (400 MHz, $CDCl_3$)



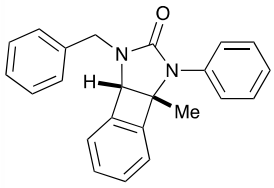
13ia

^{13}C NMR (101 MHz, $CDCl_3$)



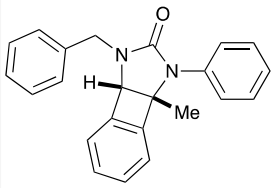
13ia

^{1}H NMR (400 MHz, $CDCl_3$)



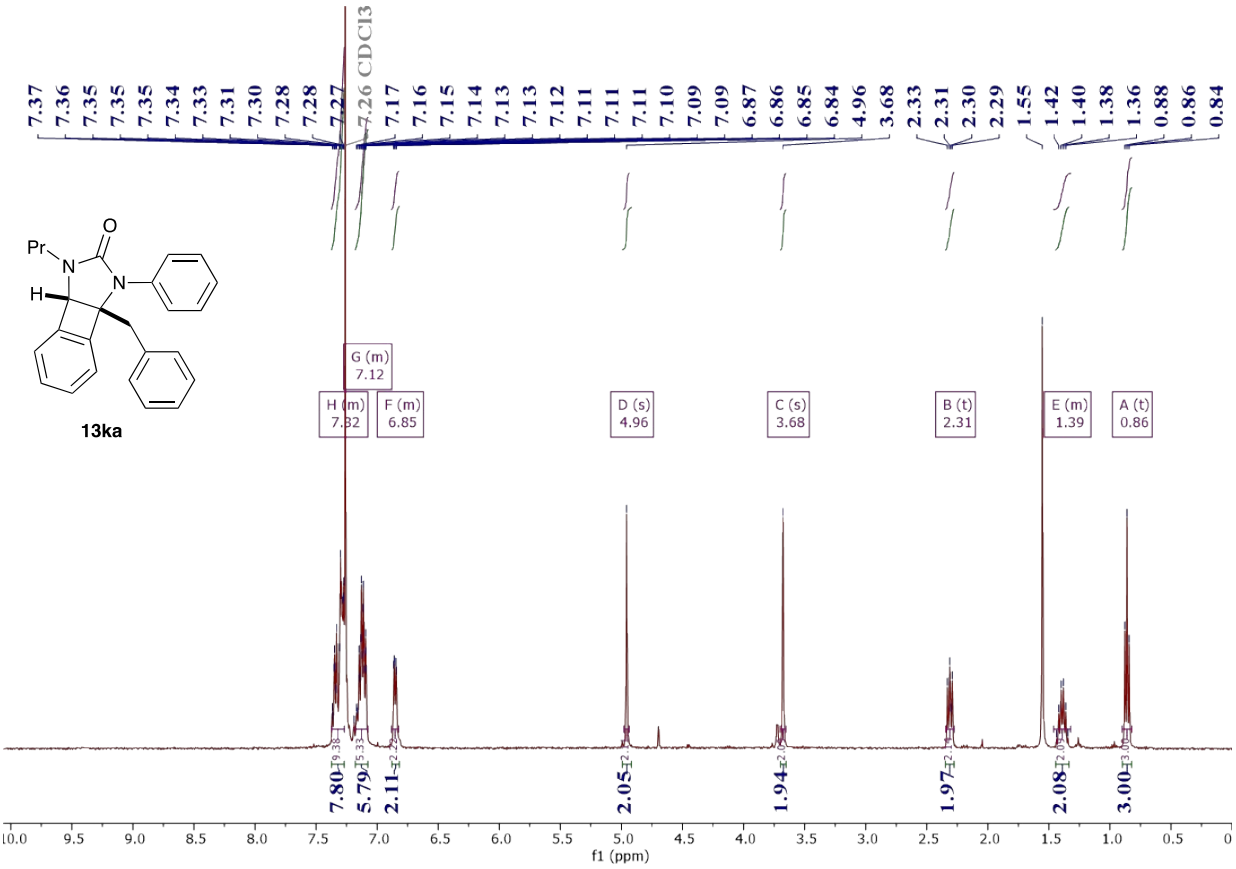
13ja

^{13}C NMR (101 MHz, $CDCl_3$)

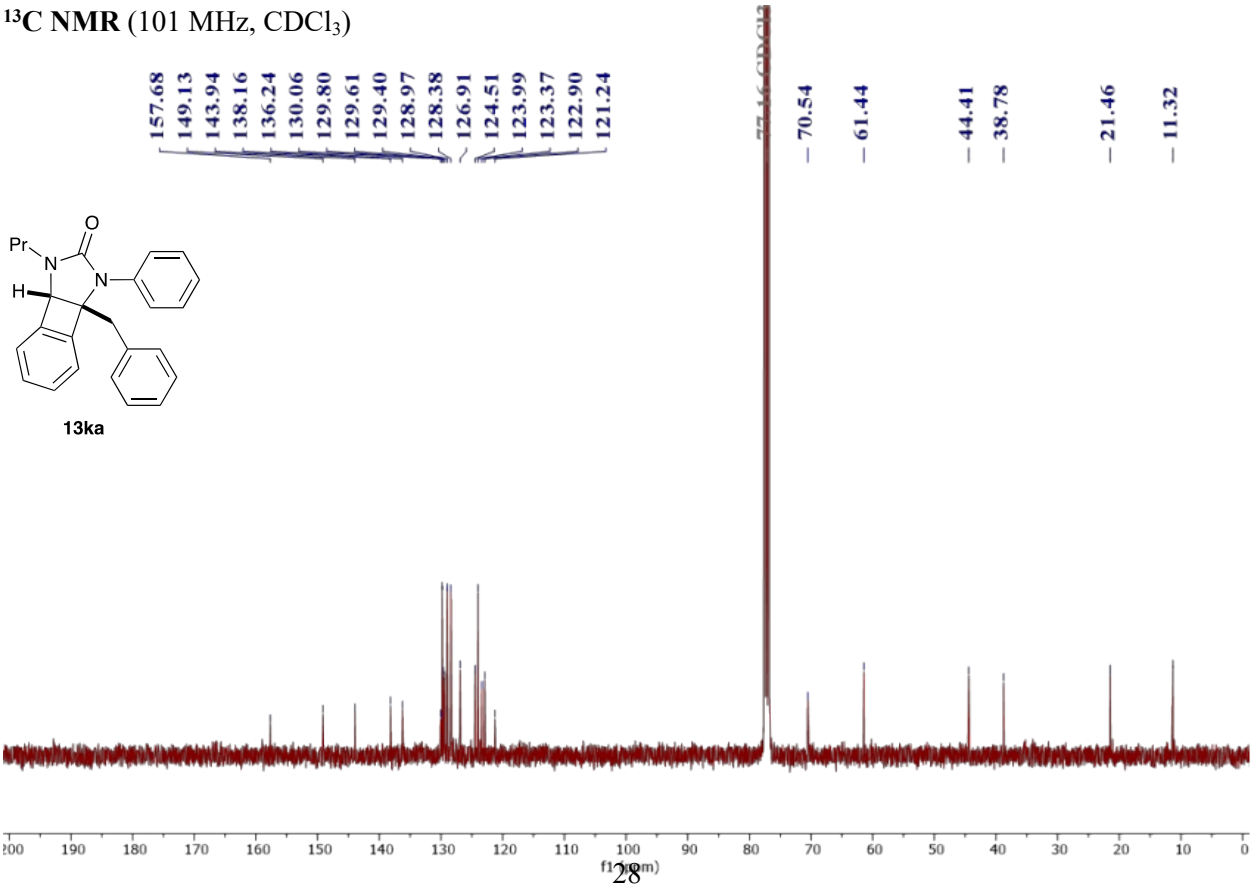


13ja

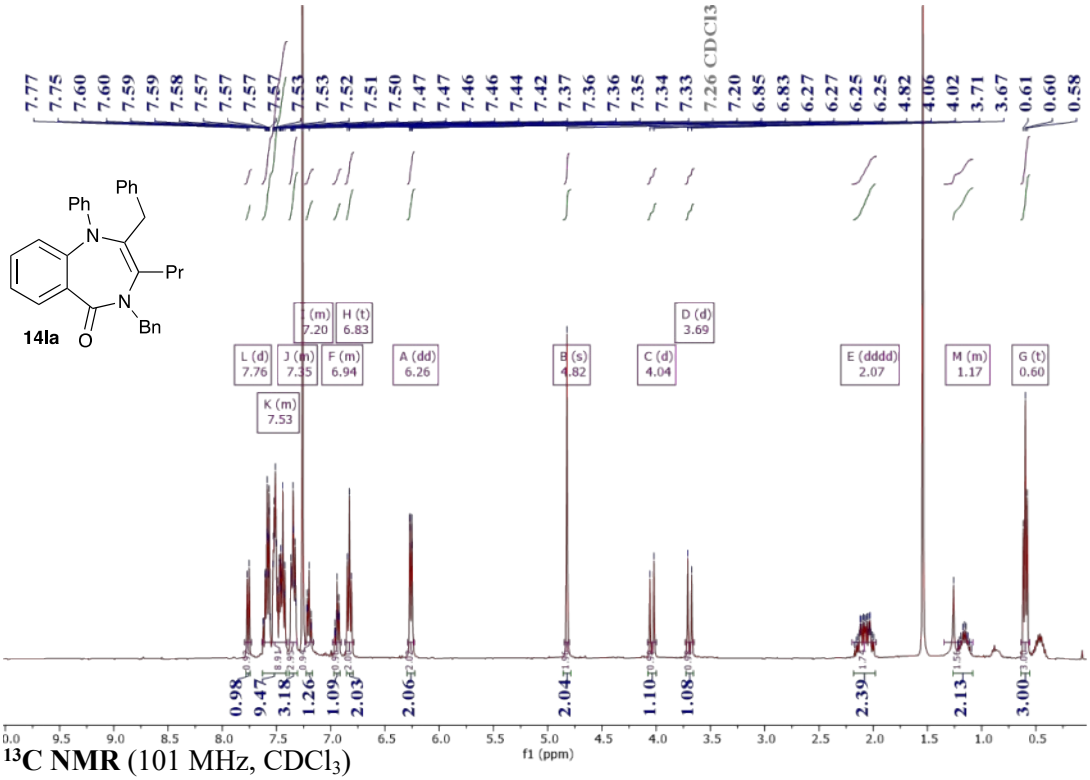
^{1}H NMR (400 MHz, $CDCl_3$)



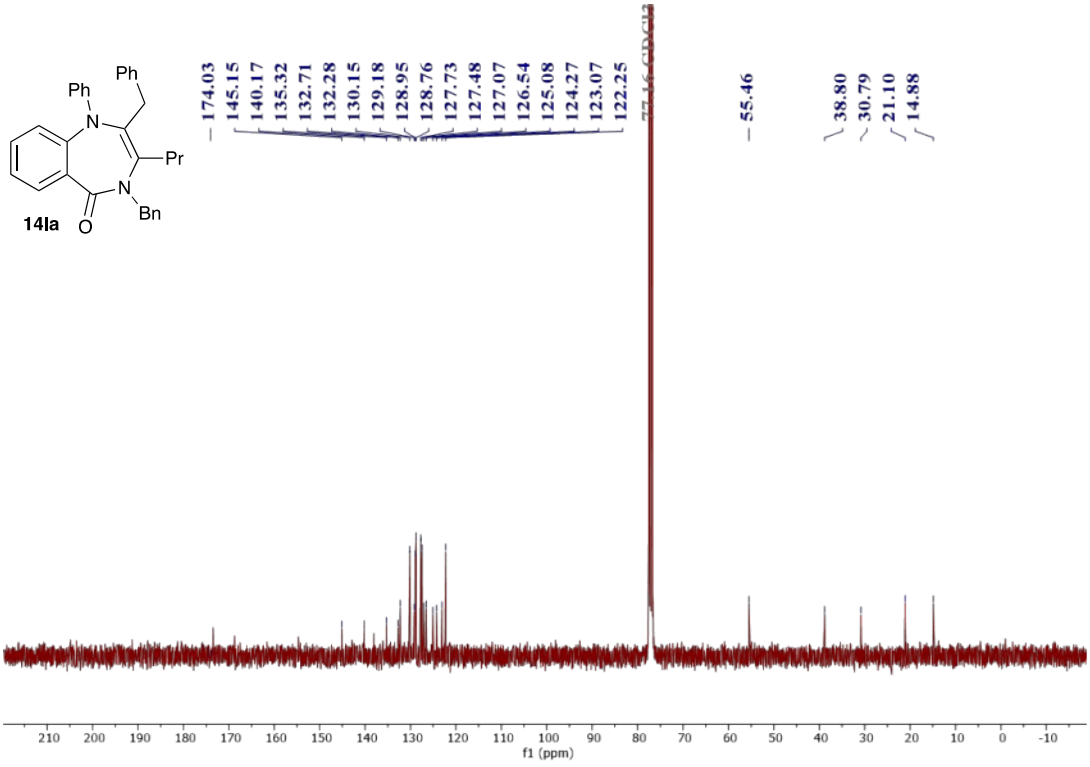
^{13}C NMR (101 MHz, $CDCl_3$)



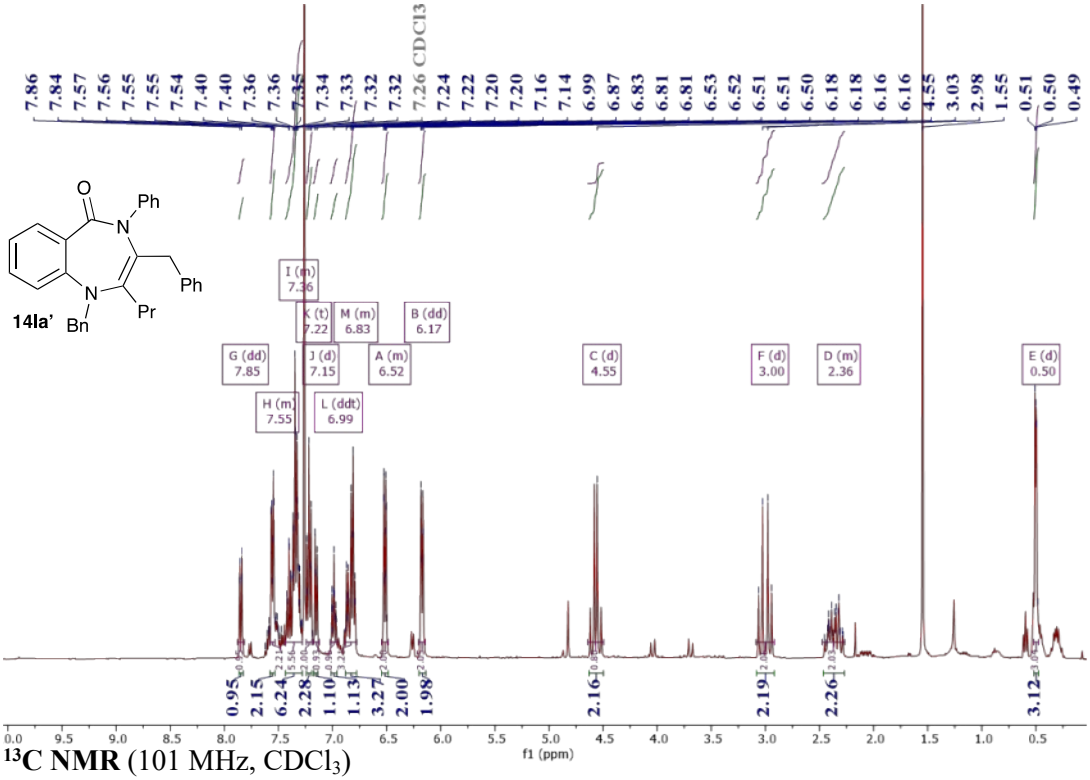
^{1}H NMR (400 MHz, $CDCl_3$)



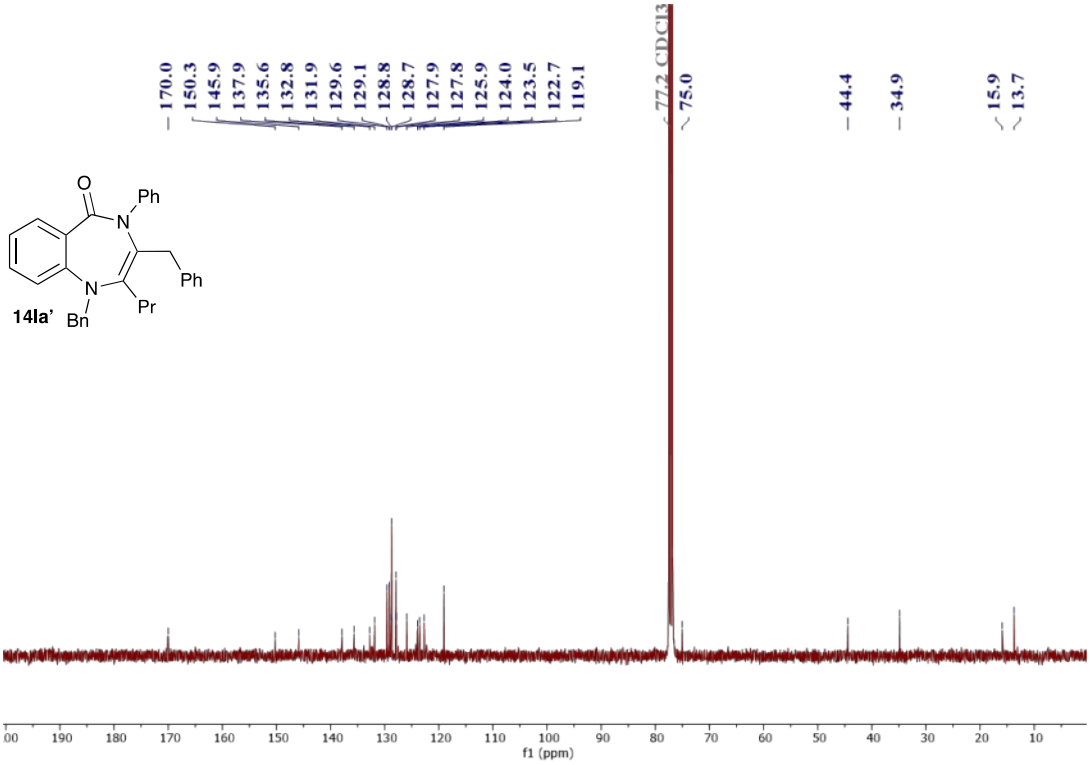
^{13}C NMR (101 MHz, $CDCl_3$)



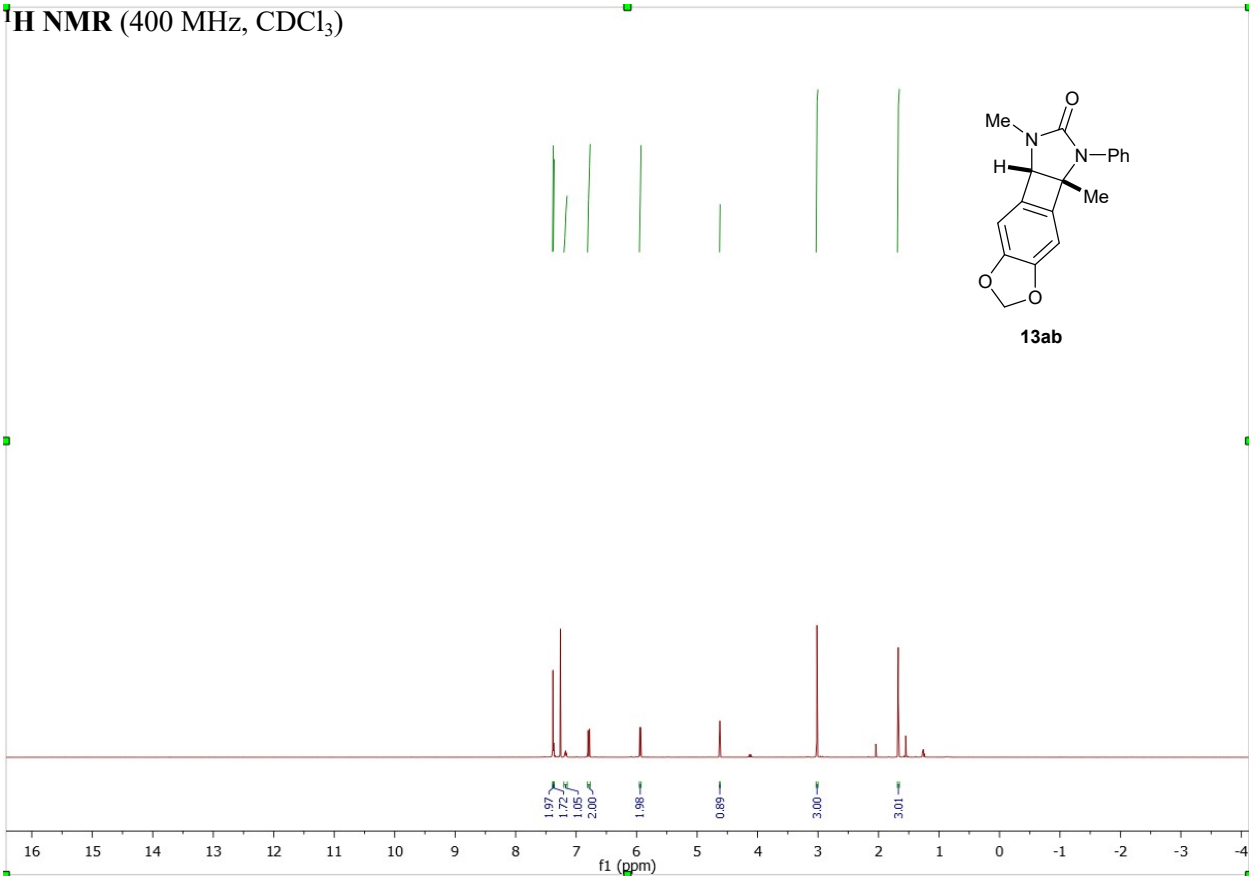
^{1}H NMR (400 MHz, $CDCl_3$)



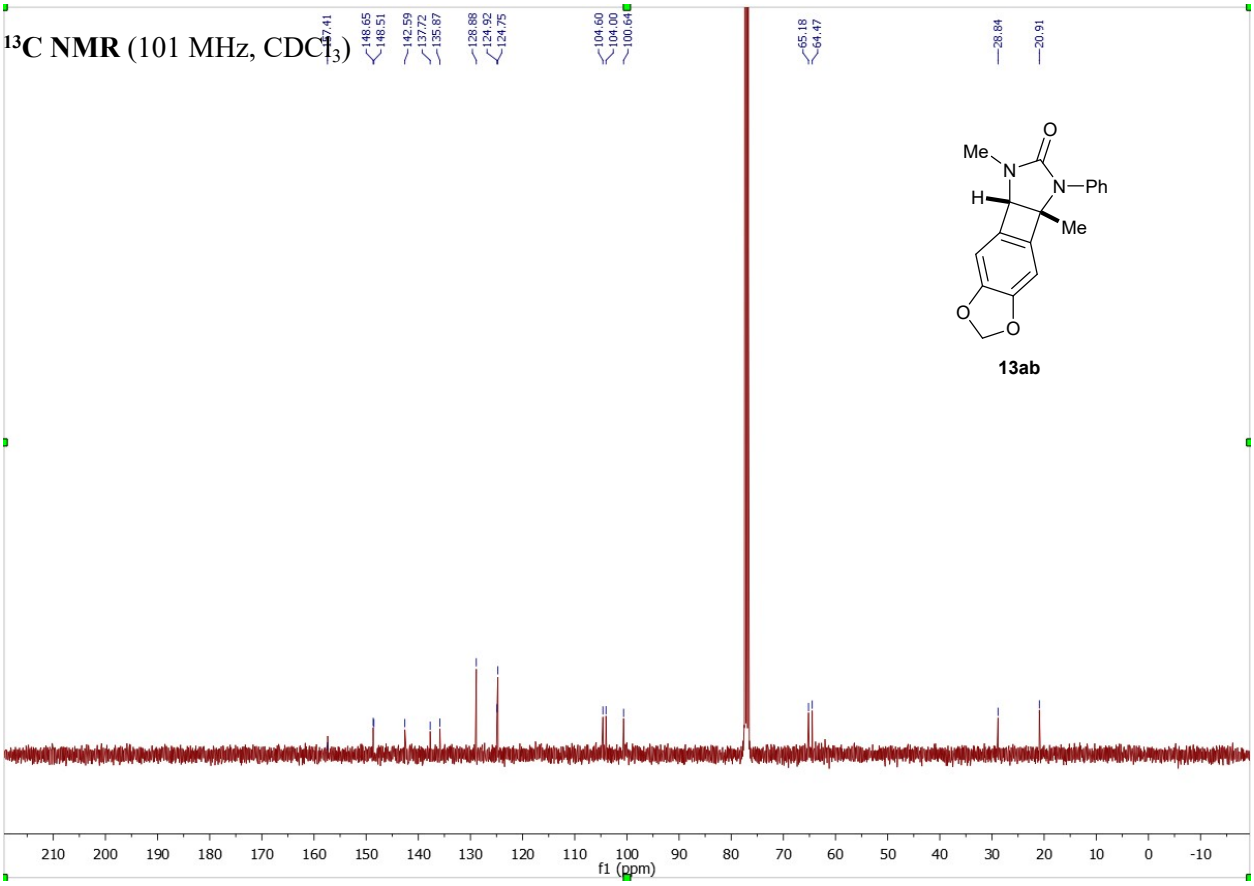
^{13}C NMR (101 MHz, $CDCl_3$)



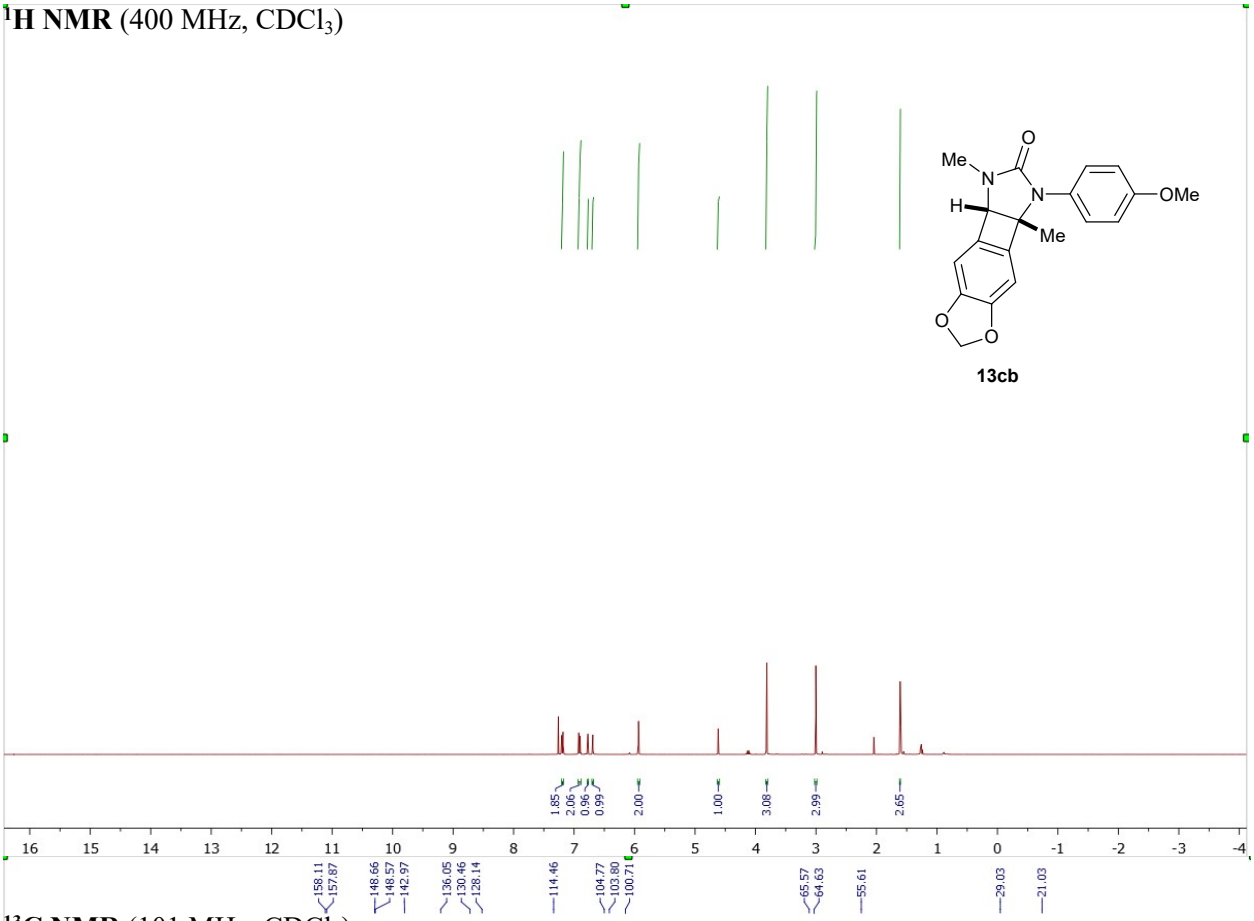
^{1}H NMR (400 MHz, $CDCl_3$)



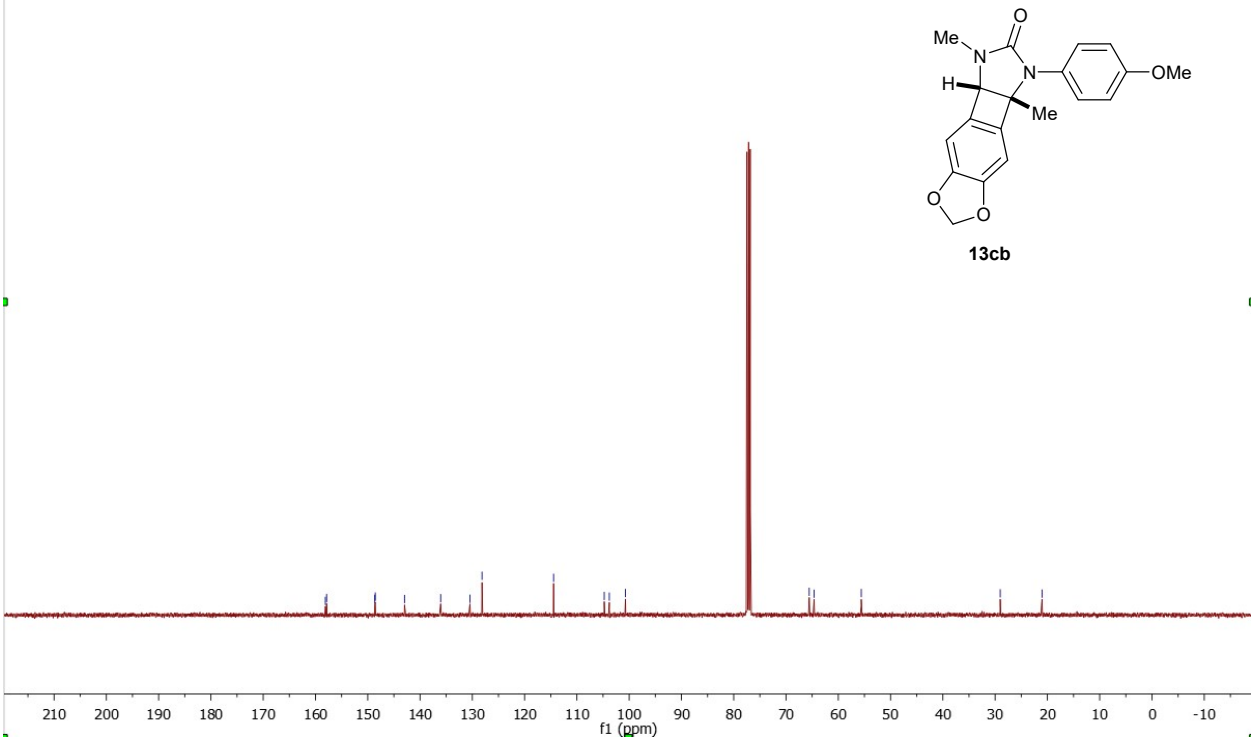
^{13}C NMR (101 MHz, $CDCl_3$)



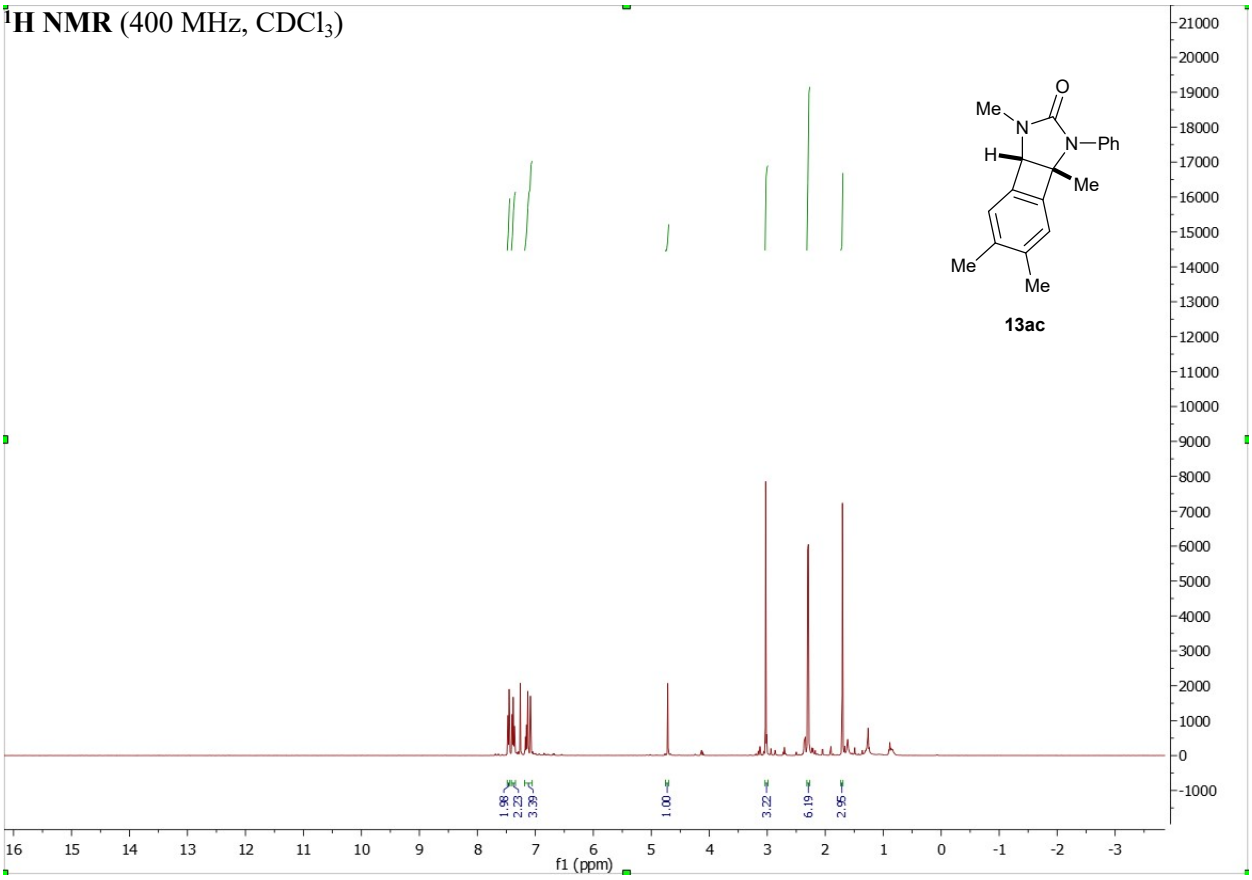
^{1}H NMR (400 MHz, $CDCl_3$)



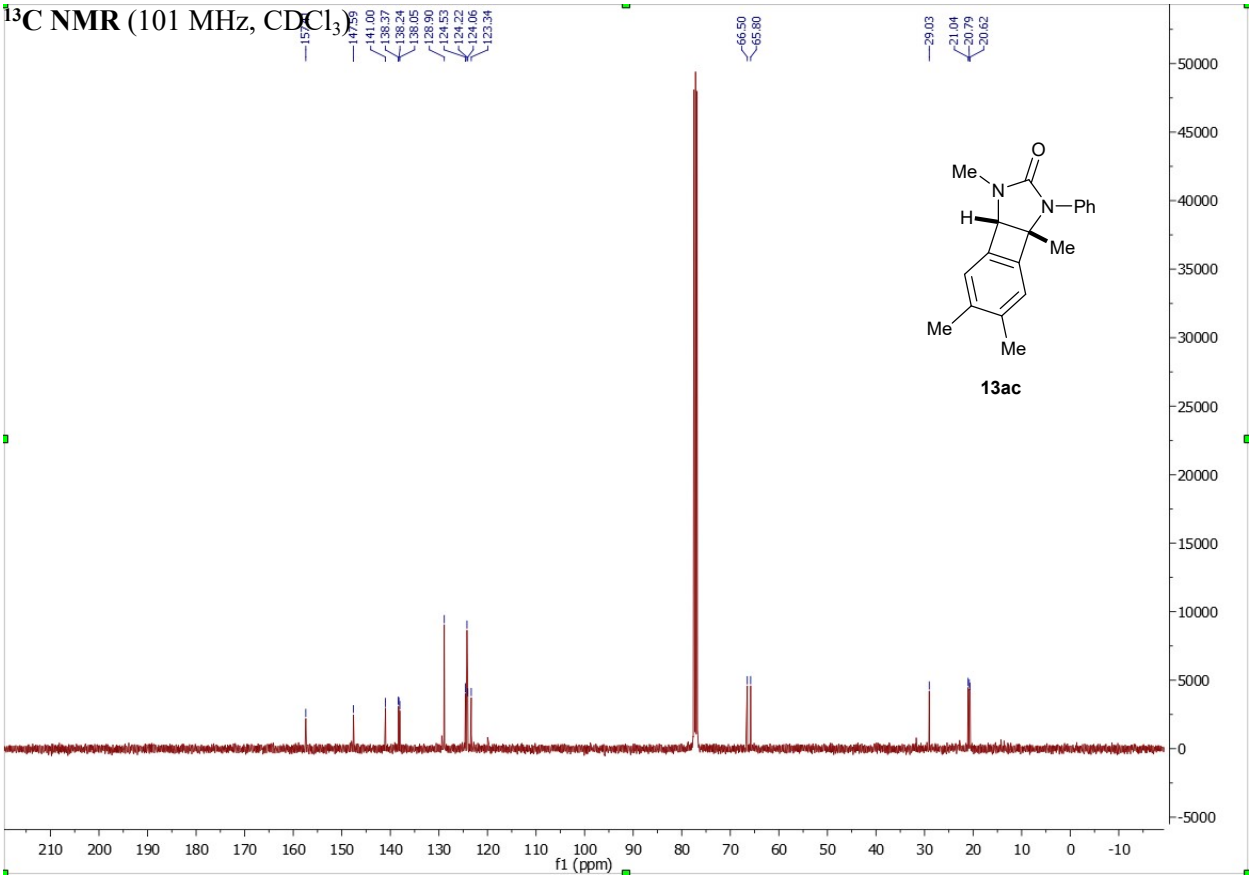
^{13}C NMR (101 MHz, $CDCl_3$)



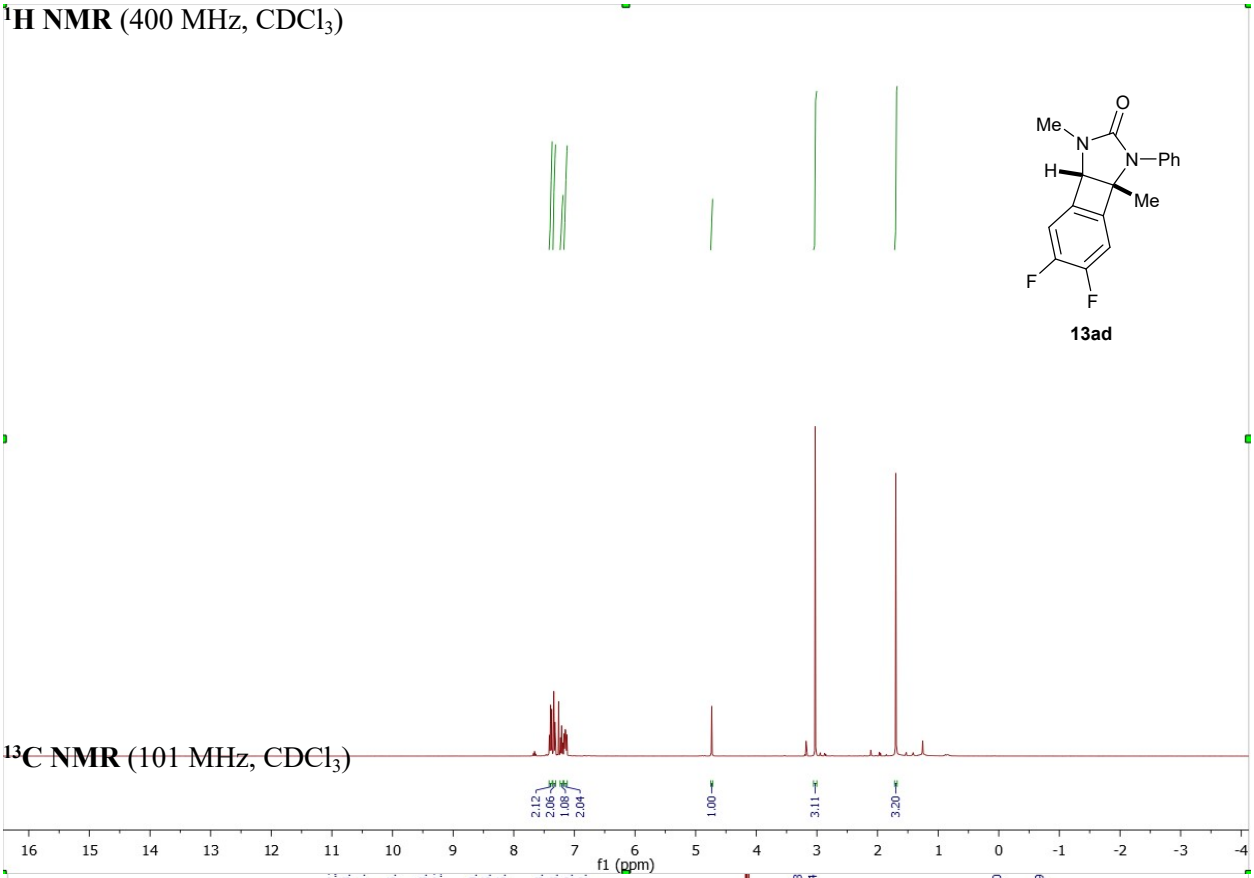
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

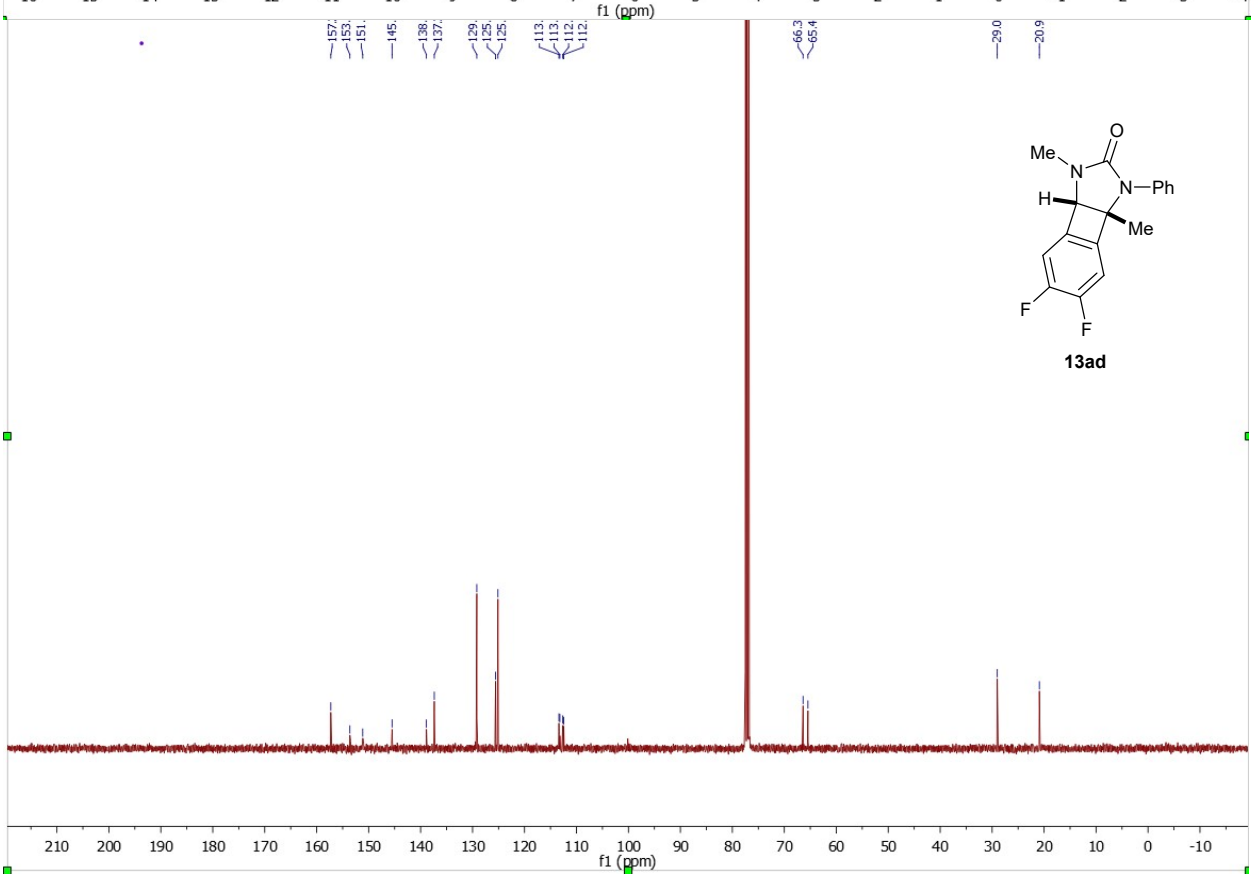


^{1}H NMR (400 MHz, $CDCl_3$)



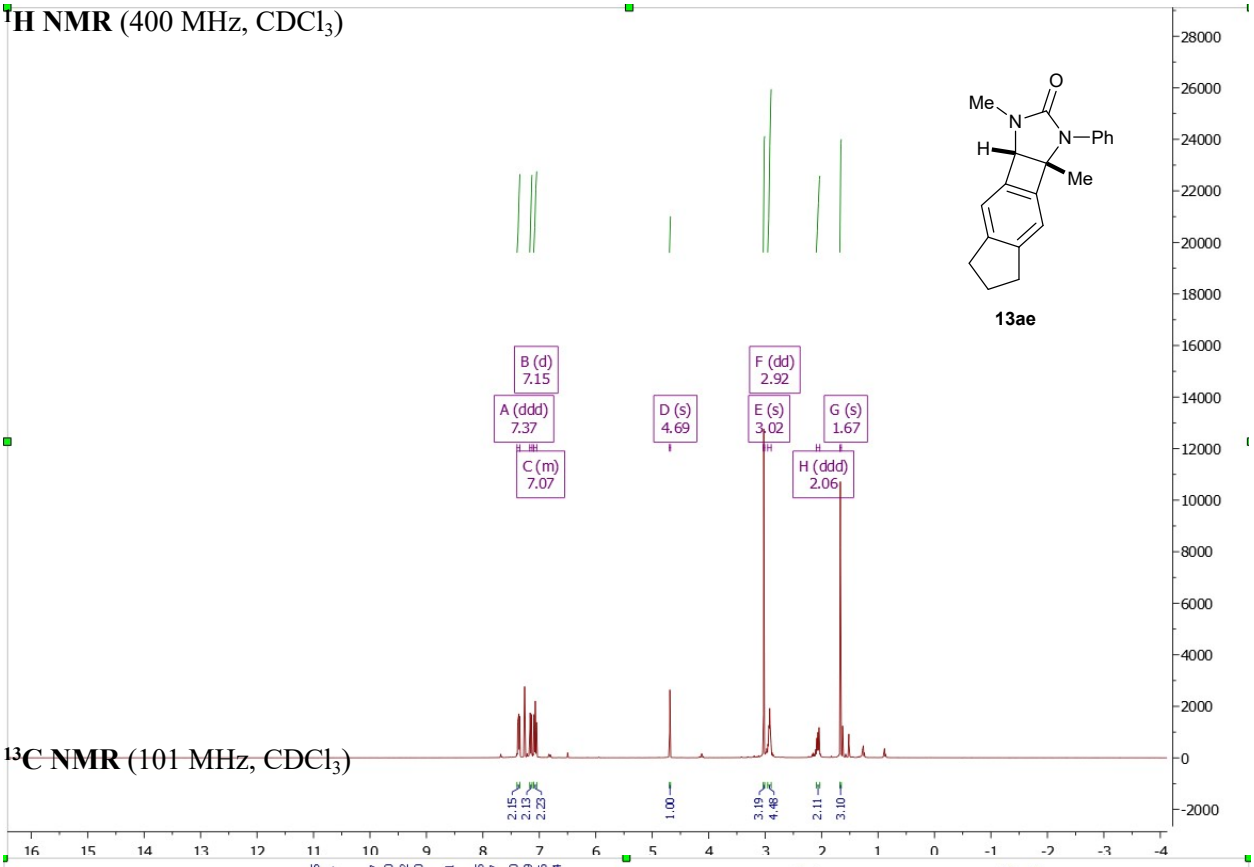
13ad

^{13}C NMR (101 MHz, $CDCl_3$)

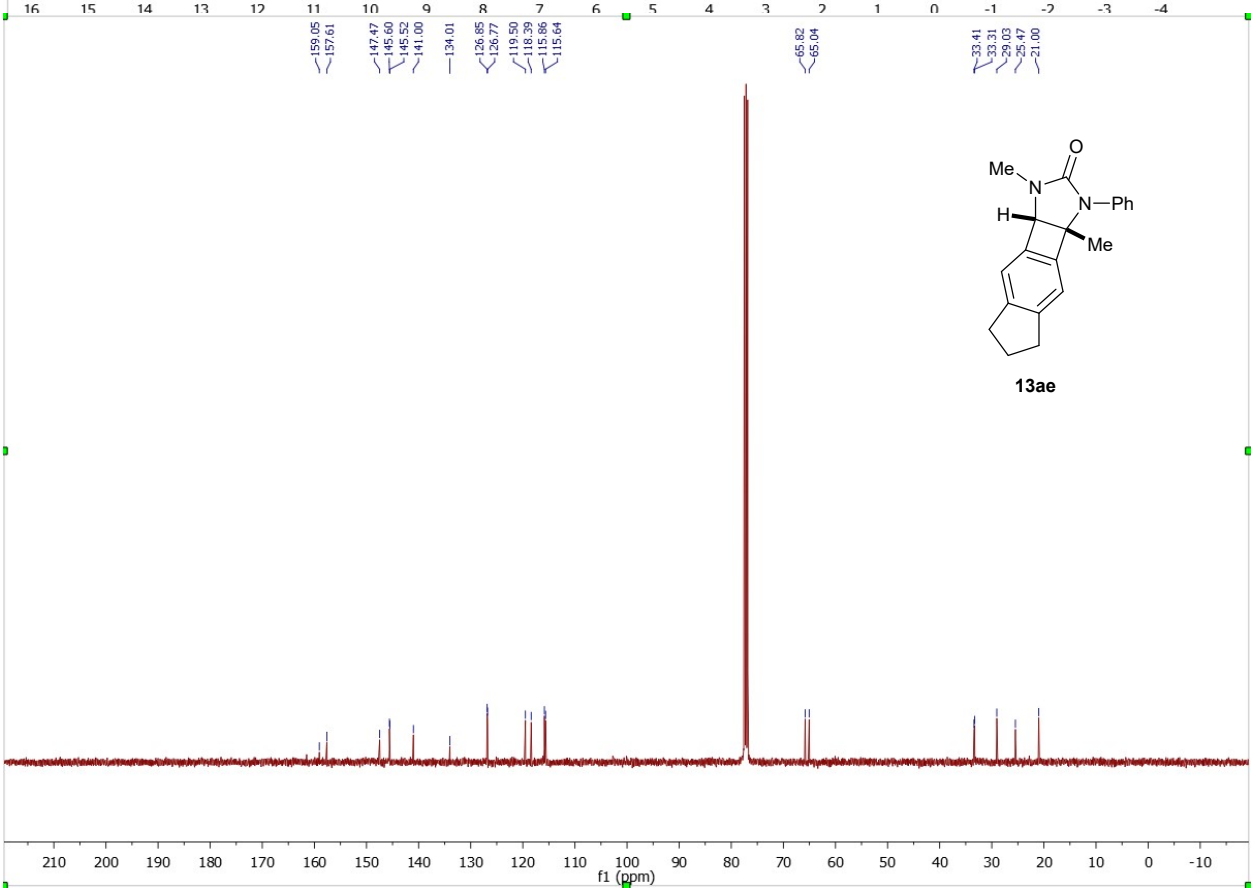


13ad

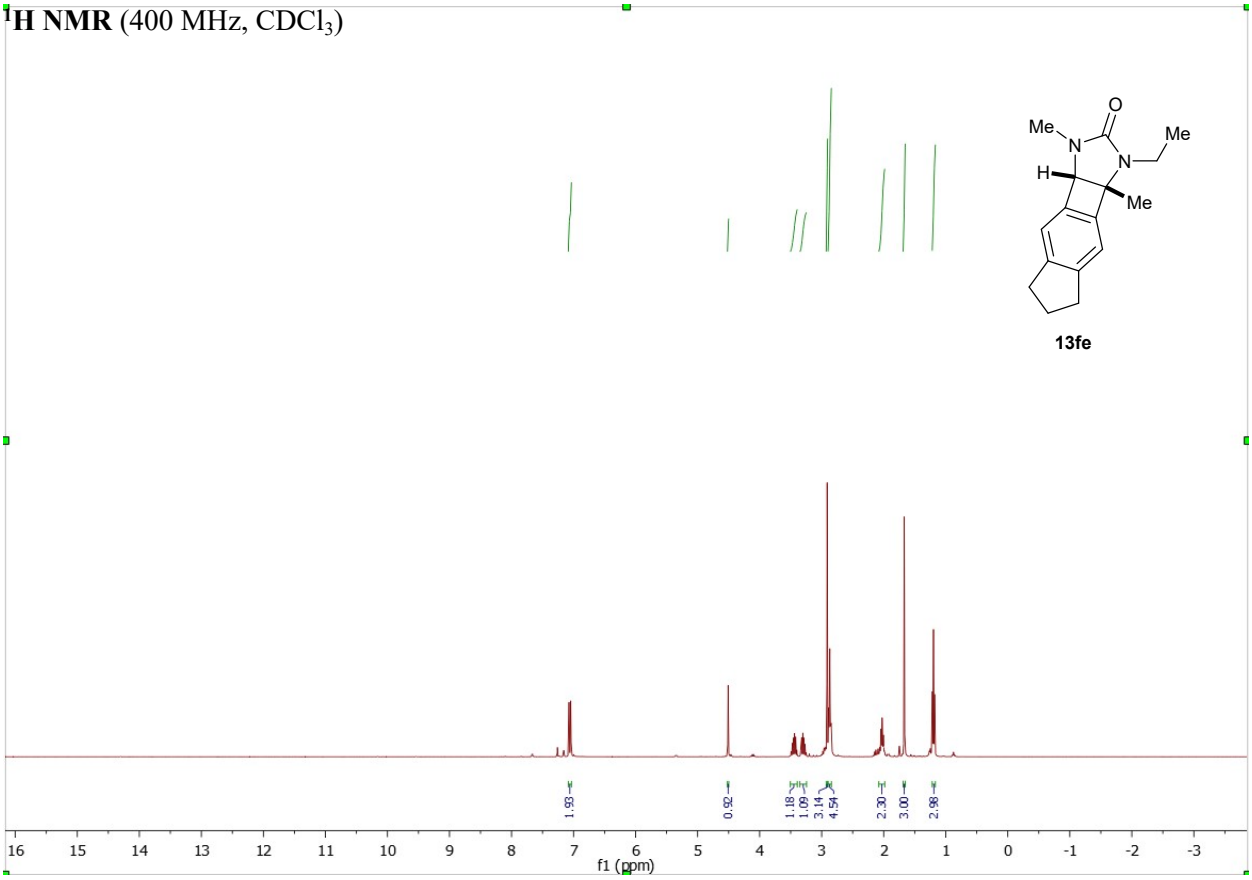
^{1}H NMR (400 MHz, $CDCl_3$)



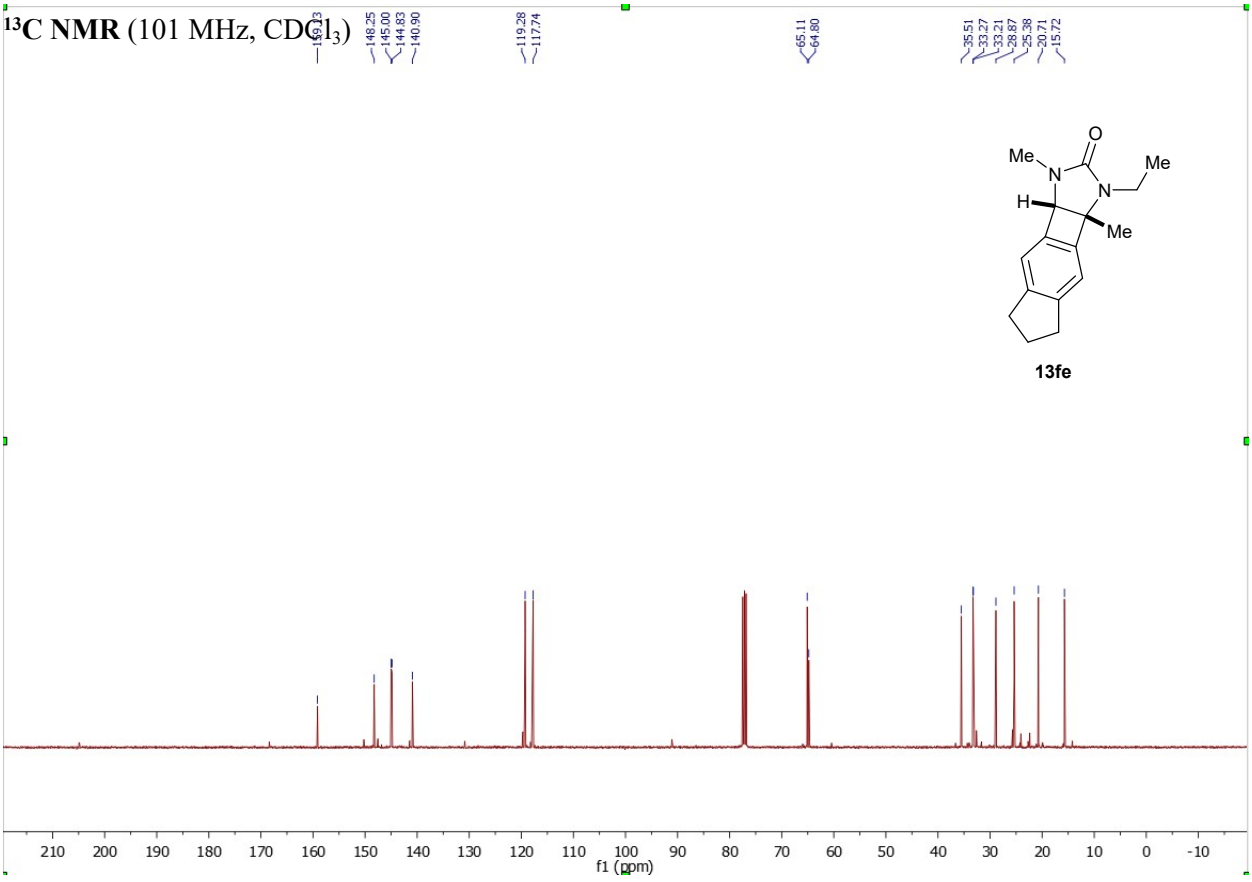
^{13}C NMR (101 MHz, $CDCl_3$)



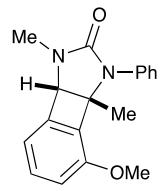
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

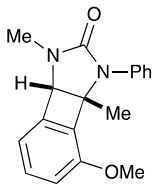


^{1}H NMR (400 MHz, $CDCl_3$)



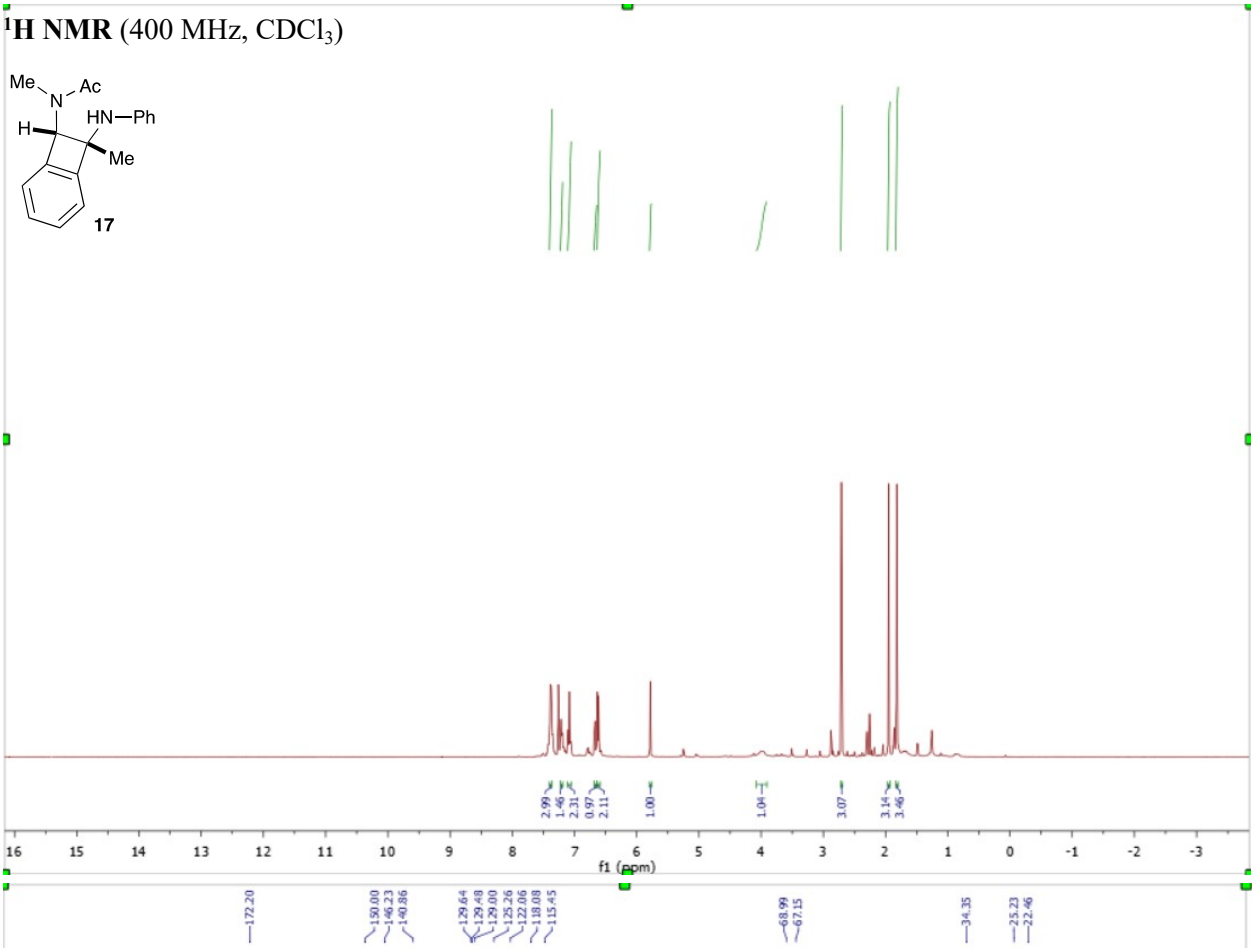
13af

^{13}C NMR (101 MHz, $CDCl_3$)



13af

^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)