Supporting Information

Metal-Free Cyclic Iminium Induced One-pot Double Annulation Cascade: Access to Dihydroisoquinolinium (DHIQ) Salts

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Experimental section

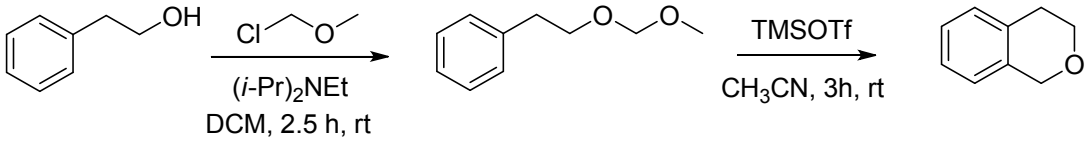
General information

In this section the preparations of all the compounds that have been made in the course of synthesis of pyridoimidazo-DHIQ salts have been discussed. For the experiments, all starting material and reagents are purchased from standard commercial sources or were prepared in laboratory. All the glass wares were cleaned with soap water followed by acetone and dried in hot air oven at 100 ˚C for 2h. Solvents were distilled prior to use.

IR spectra were recorded on the Bruker Tensor 37 (FTIR) spectrophotometer. ^{1}H NMR spectra were recorded on Bruker Avance 400 (400 MHz) spectrometer at 295K in $CDCl_3$; chemical shifts value (δ ppm) and coupling constants (Hz) are reported in standard fashion with reference to either tetramethylsilane (TMS) (δ-H = 0.00 ppm) or $CHCl_3$ (δ-H = 7.26 ppm). ^{13}C NMR spectra were recorded on Bruker Avance 400 (100 MHz) spectrometer at 298K in $CDCl_3$; chemical shifts (δ ppm) are reported relative to $CHCl_3$ [(δ-C = 77.00 ppm) central line of triplet]. In ^{13}C NMR the nature of carbons (C, CH, CH_2, and CH_3) was determined by recording the DEPT-135 spectra. In ^{1}H NMR, the following abbreviations were used throughout the thesis; s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, m = multiplet and br. s = broad singlet. The assignment of the signals was confirmed by ^{1}H, ^{13}C and DEPT spectra. Reactions were monitored by TLC on silica gel (254 mesh) using a combination of DCM and MeOH as eluents.

Preparation of starting material

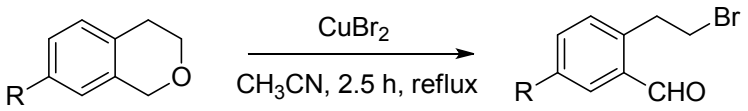
a) General Procedure for preparation of isochromans.[1]



A mixture of the substituted phenylethyl alcohol (4.97 mmol), chloromethyl methyl ether (7.046 mmol) and *N,N*-diisopropylethylamine (9.95 mmol) in dry dichloromethane (15 ml) was stirred under nitrogen atmosphere for 2.5 h at rt. The reaction mixture was then washed with water, dried (Na_2SO_4) and the solvent was removed in vaccuo. The crude MOM acetal was dissolved in dried acetonitrile and added to cooled (0 ^{o}C) solution of trimethylsilyl trifluoromethanesulfonate (TMSOTf) (4.97 mmol). The reaction was carried out under nitrogen atmosphere for 3h. Then the mixture was quenched by the addition of l M $NaHCO_3$. The organic

phase was washed with brine, dried with anhydrous sodium sulphate and evaporated under reduced pressure. Purification by column chromatography afforded corresponding substituted isochromans.

b) General procedure for the preparation of benzaldehydes 1a-1c[1]:



R= H, **1a**, 68%
R= Me, **1b**, 60%
R= Br, **1c**, 74%

To a solution of the substituted isochroman (7.46 mmol) derivatives in acetonitrile (15 ml), $CuBr_2$ (8.95 mmol) was added under nitrogen atmosphere. The solution was refluxed for about 2h and then cooled to room temperature. To the reaction mixture was added water, extracted with ethyl acetate. The combined organic extracts were washed with brine, dried with anhydrous Na_2SO_4, filtered and concentrated and then purified by silica gel column chromatography to afford the product (**1a-1c)** in 68-74% yield.

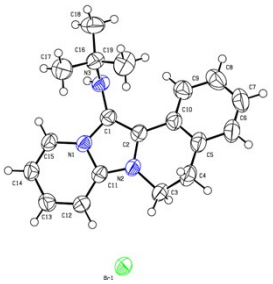
General experimental procedure for the synthesis of pyridoimidazo-DHIQ salts (4aaa-4akc): 2-(2-Bromoethyl)benzaldehyde (**1**, 0.23 mmol) and 2-aminoazine (**2,** 0.23 mmol) were taken in a 5 mL round bottom flask. Then isocyanide **3** (0.23 mmol) was added in succession to the reaction mixture and the reaction was stirred at 80 ^oC for 10-20 min. After completion of the reaction (monitored by TLC in 5% MeOH/DCM), the crude reaction mixture was purified by filtration through a short pad of silica gel (100-200 mesh) column using DCM and MeOH as eluents to yield the desired products (**4aaa-4akc)** in 61-93% yields.

Experimental procedure for the scale-up synthesis of pyridoimidazodihydroisoquinolinium salt (4aaa): 2-(2-Bromoethyl)benzaldehyde (**1a,** 2 g**,** 9.3 mmol) and 2-aminopyridine (**2a**, 0.87 g, 9.3 mmol) were taken in a 25 mL round bottom flask. Then cyclohexylisocyanide (**3a**, 1.01 g, 9.3 mmol) was added in succession to the reaction mixture and the reaction was stirred at 80 ^oC for 15 min. After completion of the reaction (monitored by TLC in 5% MeOH/DCM, 0.4 Rf), the crude reaction mixture was washed with 5% ethylacetate in hexane to yield the desired product **4aaa** (3.2 g, 86%).

Studies to probe reaction mechanism:

To probe the reaction mechanism, we have performed the reaction of 2-(2-bromoethyl)benzaldehyde with 2-aminopyridine under standard conditions, which afforded the compound (iminium ion "2-(pyridin-2-yl)-3,4-dihydroisoquinolin-2-ium bromide" intermediate) was purified by column chromatography (15% ethylacetate:hexane). the HRMS of the compound conformed the formation of cyclic iminium (azadiene), however ^{1}H NMR spectrum was not informative due to complex peaks. Moreover, to further conform/support the formation of cyclic iminium, we have quoted our previous report and other reports where in cyclic iminium was formed by the reaction of 2-(2-bromoethyl)benzaldehyde with aniline. (7b, 10 references in manuscript).

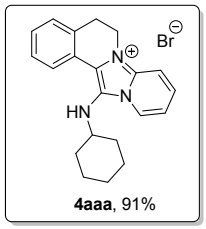
Single crystal X-ray structure data of compound 4aab (CCDC 1478558): Thermal ellipsoids are drawn at 50% probability level.



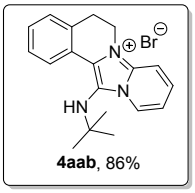
Identification code	exp_4568
Empirical formula	$C_{9.5}H_{11}N_{1.5}Br_{0.5}$
Formula weight	372.31
Temperature/K	300
Crystal system	Triclinic
Space group	P-1
a/Å	9.8675(5)
b/Å	10.2949(5)
c/Å	11.0351(6)
α/°	117.594(5)
β/°	105.751(5)
γ/°	97.854(4)
Volume/Å^3	909.81(11)
Z	2
ρ_{calc}g/cm^3	1.3589
μ/mm^{-1}	3.087
F(000)	383.5

Crystal size/mm^3	0.6 × 0.4 × 0.2
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	9.74 to 141.4
Index ranges	-8 ≤ h ≤ 12, -12 ≤ k ≤ 12, -13 ≤ l ≤ 10
Reflections collected	7192
Independent reflections	3402 [R_{int} = 0.0439, R_{sigma} = 0.0396]
Data/restraints/parameters	3402/0/214
Goodness-of-fit on F^2	1.050
Final R indexes [I>=2σ (I)]	R_1 = 0.0354, wR_2 = 0.0904
Final R indexes [all data]	R_1 = 0.0396, wR_2 = 0.0939
Largest diff. peak/hole / e Å^{-3}	0.61/-0.65

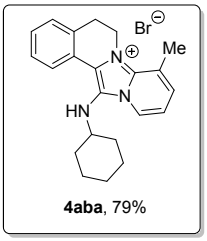
Spectral data for the compounds (4aaa-4akc):



13-(Cyclohexylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aaa): White solid (83 mg, 91%); mp 235−238 ˚C; IR (MIR-ATR, 4000−600 cm^{-1}): ν_{max} = 3411, 3174, 3017, 2927, 2853, 1646, 1615, 1527, 1450, 1417, 1266, 1224, 1156, 1082, 891, 728; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.4 (d, J = 6.8 Hz, 1H), 8.35−8.28 (m, 2H), 7.79−7.75 (m, 1H), 7.37−7.25 (m, 4H), 5.84 (d, J = 6.8 Hz, 1H), 4.65 (t, J = 6.6 Hz, 2H), 3.28 (t, J = 6.6 Hz, 2H), 3.02−2.95 (m, 1H), 1.87 (d, J = 10.3 Hz, 2H), 1.71−1.52 (m, 5H), 1.19−1.10 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 134.9, 132.8, 132.4, 130.1, 128.7, 127.9, 127.2, 126.9, 125.8, 123.3, 122.5, 116.3, 111.0, 58.0, 42.2, 33.9, 28.0, 25.3, 25.1; HR-MS (ESI$^+$) *m/z* calculated for $[C_{21}H_{24}N_3]^+$ = 318.1965; found: 318.1968.



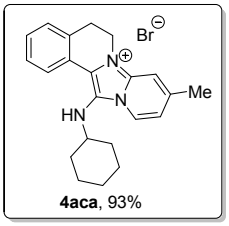
13-(Tert-butylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aab): Pale yellow solid (73 mg, 86%); mp 195−196 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3192, 3040, 2967, 1647, 1528, 1472, 1365, 1265, 1202, 1157, 1029, 899, 729, 699, 618; ^1H NMR (400 MHz, $CDCl_3$) δ ppm = 9.4 (d, J = 6.8 Hz, 1H), 8.62–8.60 (m, 1H), 8.22 (d, J = 9.3 Hz, 1H), 7.73 (t, J = 7.8 Hz, 1H), 7.39–7.31 (m, 3H), 7.26–7.24 (m, 1H), 5.61 (s, 1H), 4.58 (br. s, 2H), 3.28 (t, J = 5.9 Hz, 2H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 135.4, 133.1, 132.7, 130.5, 128.5, 127.8, 127.7, 127.0, 125.5, 123.7, 116.1, 110.5, 57.9, 42.4, 30.5, 28.1; HR-MS (ESI^+) *m/z* calculated for $[C_{19}H_{22}N_3]^+$ = 292.1808; found: 292.1812.



13-(Cyclohexylamino)-8-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aba):

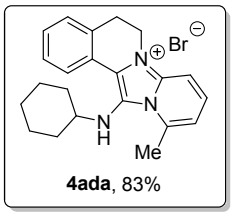
Brown semisolid (75 mg, 79%); IR (MIR-ATR, 4000−600 cm^{-1}): ν_{max} = 3744, 3669, 3395, 3182,3007, 2925, 2850, 2350, 2155, 1983, 1726, 1633, 1570, 1511, 1489, 1451, 1421, 1368, 1302, 1260, 1210, 1090, 1040, 949, 889, 802, 763, 731, 668, 605, 558; ^1H NMR (400 MHz, $CDCl_3$) δ ppm = 9.35 (d, J = 6.8 Hz, 1H), 8.40−8.38 (m, 1H), 7.5 (d, J = 6.8 Hz, 1H), 7.42−7.35 (m, 3H), 7.25−7.23 (m, 1H), 5.86 (br. s, 1H), 4.84 (t, J = 6.6 Hz, 2H), 3.33 (t, J = 6.6 Hz, 2H),

3.01 (t, J = 10.8 Hz, 1H), 2.92 (s, 3H), 1.87 (d, J = 10.3 Hz, 2H), 1.73−1.62 (m, 4H), 1.56 (dd, J_a = 15.2 and J_b = 11.2 Hz, 2H), 1.26−1.16 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 134.6, 134.5, 132.1, 129.9, 128.2, 127.9, 127.4, 126.0, 125.5, 123.6, 123.0, 121.7, 116.2, 57.6, 44.2, 33.8, 28.7, 25.3, 25.1, 20.1; HR-MS (ESI$^+$) *m/z* calculated for $[C_{22}H_{26}N_3]^+$ = 332.2121; found: 332.2131.



13-(Cyclohexylamino)-9-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aca):

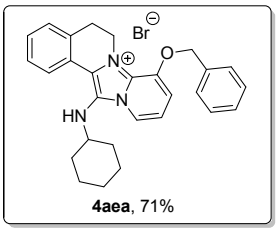
White solid (88 mg, 93%); mp 248–250 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3424, 3175, 3007, 2926, 2853, 2453, 1967, 1651, 1532, 1457, 1312, 1263, 1233, 1152, 1083, 889, 604, 540; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.22–9.18 (m, 1H), 8.27–8.25 (m, 1H), 8.06–8.03 (m, 1H), 7.31–7.30 (m, 3H), 7.06 (d, J = 6.8 Hz, 1H), 5.65–5.61 (m, 1H), 4.55 (t, J = 6.4 Hz, 2H), 3.26–3.23 (m, 2H), 2.97–2.94 (m, 1H), 2.5 (s, 3H), 2.11 (br. s, 1H), 1.84 (d, J = 7.8 Hz, 3H), 1.69 (br. s, 2H), 1.58–1.53 (m, 2H), 1.23–1.14 (m, 3H), ; ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 145.8, 135.3, 132.3, 129.9, 128.7, 127.9, 126.7, 126.1, 125.7, 123.5, 122.0, 118.8, 109.3, 57.9, 41.9, 33.9, 28.0, 25.3, 25.1,21.8; HR-MS (ESI$^+$) *m/z* calculated for $[C_{22}H_{26}N_3]^+$ = 332.2121; found: 332.2127.



4ada, 83%

13-(Cyclohexylamino)-11-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4ada):

White solid (79 mg, 83%); mp 295–297 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3744, 3733, 3395, 3196, 3085, 3007, 2923, 2851, 2373, 2350, 2320, 2129, 1992, 1947, 1731, 1632, 1512, 1464, 1453, 1420, 1303, 1260, 1171, 1091, 1040, 889, 803, 763, 744, 668, 605, 576, 559; ^{1}H NMR (DMSO D_6, 400 MHz) δ ppm = 8.71 (d, J = 6.8 Hz, 1H), 8.34 (d, J = 6.8 Hz, 1H), 7.71 (d, J = 6.8 Hz, 1H), 7.45–7.41 (m, 4H), 5.56 (d, 1H), 4.87 (t, J = 6.4 Hz, 2H), 3.31–3.27 (m, 2H), 2.95 (s, 1H), 2.9 (s, 3H), 1.85 (d, J = 11.7 Hz, 2H), 1.7 (br. s, 2H), 1.56 (br. s, 1H), 1.37 (d, J = 10.3 Hz, 2H), 1.15 (br. s, 3H), ^{13}C NMR (100 MHz, $CDCl_3$+DMSO D_6) δ ppm = 134.8, 134.0, 129.6, 128.2, 127.3, 125.9, 125.2, 123.3, 122.8, 122.5, 116.2,56.5, 33.3, 27.8, 25.0,24.5,19.0; HR-MS (ESI^+) m/z calculated for $[C_{22}H_{26}N_3]^+$ = 332.2121; found: 332.2120.

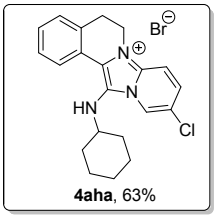


4aea, 71%

8-(Benzyloxy)-13-(cyclohexylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aea):

Brown solid (82 mg, 71%); mp 157–158 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3744, 3733, 3395, 3196, 3085, 3007, 2923, 2851, 2373, 2350, 2320, 2129, 1992, 1947, 1731, 1632, 1512,

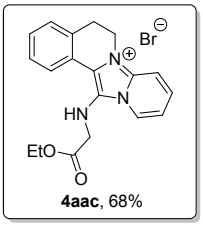
1464, 1453, 1420, 1303, 1260, 1171, 1091, 1040, 889, 803, 763, 744, 668, 605, 576, 559; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.06 (d, J = 6.4 Hz, 1H), 8.4 (d, J = 6.8 Hz, 1H), 7.5-7.49 (m, 2H), 7.44-7.41 (m, 4H), 7.39-7.35 (m, 2H), 7.33-7.31 (m, 2H), 6.02 (d, J = 6.4 Hz, 1H), 5.4 (s, 2H), 4.75 (t, J = 6.4 Hz, 2H), 3.2 (t, J = 6.4 Hz, 2H), 3.01-2.98 (m, 1H), 1.87 (d, J = 12.2 Hz, 2H), 1.7-1.5 (m, 5H), 1.4-1.09 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 144.5, 134.2, 132.1, 129.9, 129.0, 128.2, 128.1, 128.0, 127.9, 126.1, 123.5, 123.0, 119.8, 116.6,112.4, 72.6, 57.7, 44.1, 33.8, 28.4, 25.3, 25.1; HR-MS (ESI$^+$) *m/z* calculated for $[C_{28}H_{30}N_3O]^+$ = 424.2383; found: 424.2398.



4aha, 63%

10-Chloro-13-(cyclohexylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aha):

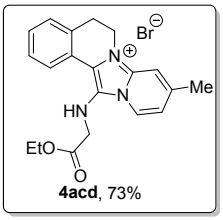
Pale yellow solid (62 mg, 63%); mp 158−160 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3745, 3396, 3174, 2923, 2852, 1955, 1731, 1646, 1612, 1522, 1467, 1451, 1305, 1264, 1226, 1050, 888, 808, 767, 731; ^{1}H NMR (DMSO D_6, 400 MHz) δ ppm = 9.13 (s, 1H), 8.35–8.27 (m, 2H), 8.09 (dd, J_a = 9.3 and J_b = 1.5 Hz, 1H), 7.52–7.46 (m, 3H), 5.68 (d, J = 6.8 Hz, 1H), 4.6 (t, J = 6.6 Hz, 2H), 3.3 (t, J = 6.4 Hz, 2H), 2.98–2.95 (m, 1H), 1.87 (d, J = 11.7, 2H), 1.67 (br. s, 2 H), 1.53 (br. s, 1 H), 1.37 (d, J = 9.8 Hz, 2H), 1.23–1.13 (m, 3H); ^{13}C NMR (DMSO D_6, 100 MHz) δ ppm = 134.0, 133.4, 132.9, 129.9, 128.8, 127.5, 126.5, 125.2, 123.6, 123.2, 122.9, 112.2, 79.2, 56.8, 41.3, 33.1, 26.9, 25.1, 24.6; HR-MS (ESI$^+$) *m/z* calculated for $[C_{21}H_{23}ClN_3]^+$ = 352.1575; found: 352.1590.



4aac, 68%

13-((2-Ethoxy-2-oxoethyl)amino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aac):

Brown semisolid (64 mg, 68%); IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3774, 3654, 3179, 3037, 2981, 2032, 1975, 1739, 1649, 1622, 1527, 1449, 1408, 1265, 1197, 1155, 1110, 1022, 862, 727, 697, 600; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.5 (d, 1H), 8.20–8.18 (m, 1H), 8.1 (d, J = 8.8 Hz, 1H), 7.28–7.74 (m, 1H), 7.41–7.38 (m, 2H), 7.37–7.33 (m, 1H), 7.26–7.24 (m, 1H), 6.84 (t, J = 6.24 Hz, 1H), 4.58 (t, J = 6.6 Hz, 2H), 4.02–3.96 (m, 4H), 3.28 (t, J = 6.4 Hz, 2H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 171.5, 134.8, 132.9, 132.3, 130.2, 128.8, 128.4, 127.7, 125.5, 123.0, 121.0, 115.8, 109.9, 61.1, 47.5, 42.1, 28.0, 14.0; HR-MS (ESI^+) *m/z* calculated for $[C_{19}H_{20}N_3O_2]^+$ = 322.1550; found: 322.1554.

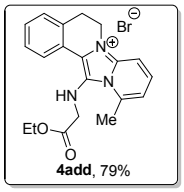


4acd, 73%

13-((2-Ethoxy-2-oxoethyl)amino)-9-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4acd):

Brown semisolid (70 mg, 73%); IR (MIR-ATR, 4000–600 cm^{-1}) ν_{max} = 3412, 3189, 2981, 2066, 2015, 1738, 1654, 1629, 1532, 1462, 1406, 1372, 1262, 1199, 1107, 1025, 859, 769, 729, 697, 608; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.4 (d, J = 6.8 Hz, 1H), 8.17-8.15 (m, 1H), 7.9 (s,

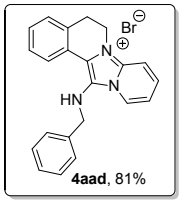
1H), 7.40-7.34 (m, 3H), 7.07 (dd, J = 7.3 Hz, 1H), 6.78 (t, J = 6.4 Hz, 1H), 4.52 (t, J = 6.6 Hz, 2H), 4.01-3.96 (m, 4H), 3.26 (t, J = 6.4 Hz, 2H), 2.53 (s, 3H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 171.6, 145.9, 135.1, 132.2, 129.9, 128.8, 128.4, 128.1, 128.3, 127.6, 127.2, 125.4, 123.2, 120.4, 118.2, 108.5, 61.1, 47.5, 41.9, 28.0, 21.9, 14.0; HR-MS (ESI+) m/z calculated for $[C_{20}H_{22}N_3O_2]^+$ = 336.1707; found: 336.1712.



4add, 79%

13-((2-Ethoxy-2-oxoethyl)amino)-11-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide(4add):

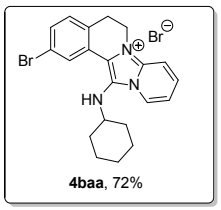
Brown semisolid; (77 mg, 79%); IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3745, 3180, 3035, 2957, 2318, 1986, 1738, 1649, 1530, 1472, 1456, 1302, 1265, 1113, 1022, 948, 864, 768, 727, 697, 663, 602, 574; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 8.29 (dd, J = 5.1, 3.7 Hz, 1H), 8.02 (d, J = 9.3 Hz, 1H), 7.7 (dd, J_a = 9.3 and J_b = 7.3 Hz, 1H), 7.39-7.31 (m, 3H), 6.99 (d, J = 6.8 Hz, 1H), 6.29 (t, J = 4.4 Hz, 1H), 4.53 (t, J = 6.4 Hz, 2H), 4.03-3.96 (m, 4H), 3.38 (s, 3H), 3.27 (t, J = 6.6 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 171.3, 142.4, 136.8, 133.3, 132.9, 130.4, 128.8, 128.6, 128.4, 126.3, 124.1, 122.7, 118.6, 108.2, 60.9, 47.9, 41.9, 28.1, 21.6, 14.0; HR-MS (ESI+) *m/z* calculated for $[C_{20}H_{22}N_3O_2]^+$ = 336.1707; found: 336.1713.



4aad, 81%

13-(Benzylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide(4aad):

White solid; (75 mg, 81%); mp = 232-235 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3745, 3397, 3195, 2978, 2943, 2690, 1691, 1649, 1527, 1469, 1453, 1392, 1314, 1227, 1159, 1068, 1026, 755, 734, 702, 632; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.03 (d, J = 6.8 Hz, 1H), 8.25-8.24 (m, 1H), 8.17 (d, J = 9.3 Hz, 1H), 7.66 (ddd, J_a = 9, J_b = 7.1 and J_c = 1 Hz, 1H), 7.38-7.36 (m, 3H), 7.18 (dd, J_a = 6.6 and J_b = 2.7 Hz, 2H), 7.08-7.05 (m, 4H), 6.74 (t, J = 5.9 Hz, 1H), 4.58 (t, J = 6.6 Hz, 2H), 4.32 (d, J = 5.4 Hz, 2H), 3.21 (t, J = 6.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 138.6, 134.7, 132.7, 132.3, 130.2, 128.6, 128.4, 128.1, 127.6, 127.5, 126.6, 126.1, 123.0, 122.3, 116.0, 110.5, 51.0, 42.1, 28.1; HR-MS (ESI+) *m/z* calculated for $[C_{22}H_{20}N_3]^+$ = 326.1652; found: 326.1663.

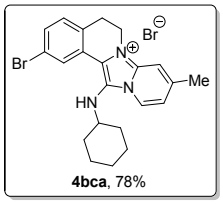


4baa, 72%

2-Bromo-13-(cyclohexylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4baa):

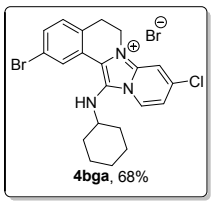
Pale yellow solid; (79 mg, 72%); mp 275-278 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3779, 3426, 3192, 3025, 2927, 2853, 1929, 1648, 1622, 1526, 1467, 1449, 1342, 1318, 1292, 1258, 1229, 1085, 874, 833, 759, 597; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.48-9.46 (m, 1H), 8.38-8.37 (m, 1H), 8.24-8.21 (m, 1H), 7.73-7.69 (m, 1H), 7.46-7.43 (m, 1H), 7.24-7.21 (m, 2H), 6.03 (d, J = 7.3 Hz, 1H), 4.64 (t, J = 6.6 Hz, 2H), 3.26 (t, J = 6.4 Hz, 2H), 2.96-2.93 (m, 1H), 1.87 (d, J = 12.2 Hz, 2H), 1.7-1.5 (m, 5H), 1.4-1.09 (m, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ = 135.1,

133.2, 132.8, 131.1, 130.3, 128.3, 128.0, 127.2, 125.1, 121.6, 120.7, 116.5, 111.0, 58.5, 42.2, 34.1, 27.5, 25.24, 25.2; HR-MS (ESI+) *m/z* calculated for $[C_{21}H_{23}BrN_3]^+$ = 396.1070; found: 396.1067.



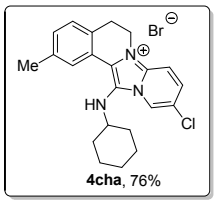
2-Bromo-13-(cyclohexylamino)-9-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1 a]isoquinolin-7-ium bromide(4bca):

White solid; (89 mg, 78%); mp = 180–183 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3779, 3638, 3407, 3317, 3197, 3041, 2927, 2853, 1975, 1652, 1622, 1559, 1531, 1446, 1372, 1313, 1259, 1185, 1084, 1040, 890, 808, 730, 603, 563; ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 9.3 (d, *J* = 7.3 Hz, 1H), 8.32 (d, *J* = 2 Hz, 1H), 8.05 (s, 1H), 7.36 (dd, *J* = 8.3 Hz, 1H), 7.18 (d, *J* = 8.3 Hz, 1H), 7.06 (d, *J* = 6.4 Hz, 1H), 5.94 (d, *J* = 6.8 Hz, 1H), 4.55 (t, *J* = 6.4 Hz, 2H), 3.2 (t, *J* = 6.4 Hz, 2H), 2.91-2.84 (m, 1H), 2.5 (s, 3H), 1.83-1.80 (m, 2H), 1.67 (d, *J* = 10.3 Hz, 2H), 1.60-1.49 (m, 3H), 1.14-1.11 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.2, 135.4, 132.4, 130.9, 130.3, 128.1, 127.6, 126.5, 125.2, 121.5, 120.0, 118.9, 109.5, 58.5, 41.8, 34.0, 27.5, 25.2, 25.1, 21.9; HR-MS (ESI+) *m/z* calculated for $[C_{22}H_{25}BrN_3]^+$ = 410.1226; found: 410.1228.



2-Bromo-9-chloro-13-(cyclohexylamino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide(4bga):

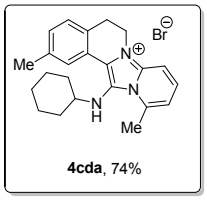
Pale yellow solid; (81 mg, 68%); mp = 155- 157 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3691, 3570, 3406, 3181, 3006, 2927, 2853, 1977, 1707, 1647, 1616, 1597, 1560, 1522, 1464, 1424, 1369, 1343, 1308, 1257, 1097, 1078, 945, 890, 840, 816, 731, 665; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.47 (d, J = 7.3 Hz, 1H), 8.53 (d, J = 9.3 Hz, 1H), 8.32 (d, J = 2Hz, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.48 (dd, J = 7.8 Hz, 1H), 7.24 (d, J = 8.3 Hz, 1H), 5.96 (d, J = 7.3 Hz, 1H), 4.76 (t, J = 6.4 Hz, 2H), 3.27 (t, J = 6.1 Hz, 2H), 2.96-2.94 (m, 1H), 1.86 (m, J = 9.3 Hz, 2H), 1.76 (d, J = 12.7 Hz, 2H), 1.60-1.64 (m, 4H), 1.22-1.18 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 133.9, 133.5, 132.4, 133.2, 131.2, 130.3, 128.4, 127.9, 125.2, 124.7, 124.4, 121.7, 112.4, 58.4, 42.8, 34.1, 27.4, 25.2, 25.1; HR-MS (ESI+) *m/z* calculated for $[C_{21}H_{22}BrClN_3]^+$ = 430.0680; found: 430.0689.



10-Chloro-13-(cyclohexylamino)-2-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4cha):

White solid; (67 mg, 76%); IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3413, 3180, 2926, 2853, 2028, 1647, 1613, 1524, 1490, 1450, 1344, 1307, 1266, 1228, 1148, 1093, 1049, 947, 890, 817, 730, 699, 602, 558; ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.41 (d, J = 1 Hz, 1H), 8.54 (d, J = 9.8 Hz, 1H), 8.1 (s, 1H), 7.61 (dd, J_a = 9.5 and J_b = 1.7 Hz, 1H), 7.22-7.18 (m, 2H), 5.9 (d, J = 6.8 Hz, 1H), 4.69 (t, J = 6.6 Hz, 2H), 3.23 (t, J = 6.6 Hz, 2H), 3.0-2.97 (m, 1H), 2.4 (s, 3H), 1.88-1.80

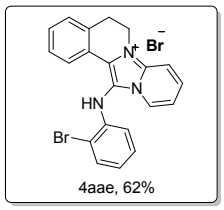
(m, 3H), 1.72-1.58 (m, 4H), 1.28-1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 137.9, 133.3, 133.1, 131.3, 129.4, 128.5, 127.2, 126.3, 124.9, 124.2, 123.6, 122.7, 112.2, 57.9, 43.1, 34.1, 27.4, 25.2, 25.1, 21.2; HR-MS (ESI+) *m/z* calculated for $[C_{22}H_{25}ClN_3]^+$ = 366.1732; found: 366.1738.



4cda, 74%

13-(Cyclohexylamino)-2,11-dimethyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4cda):

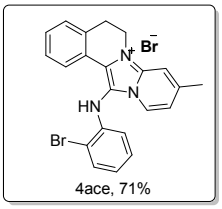
Pale yellow solid; (73 mg, 74 %); mp 217-219 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3395, 3195, 3027, 2925, 2852, 1729, 1646, 1532, 1491, 1449, 1420, 1386, 1264, 1210, 1140, 1110, 868, 820, 781, 727, 696, 592; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.25 (s, 1H), 8.11(d, *J* = 8.8 Hz, 1H), 7.63 (dd, *J* = 8.8 Hz, 1H), 7.18-7.13 (m, 2H), 6.93 (d, *J* = 7.3 Hz, 1H), 5.12 (d, *J* = 2.4 Hz, 1H), 4.51 (t, *J* = 6.4 Hz, 2H), 3.26 (s, 3H), 3.18 (t, *J* = 6.4 Hz, 2H), 2.97-2.91 (m, 1H), 2.02 (br. s, 1H), 1.8 (d, *J* = 12.2 Hz, 2H), 1.64-1.52 (m, 3H), 1.3-1.18 (m, 4H), 1.09-1.05 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 141.0, 137.7, 136.9, 133.1, 131.2, 130.0, 128.2, 127.5, 127.2, 126.2, 123.1, 118.8, 108.9, 58.1, 42.2, 33.3, 29.6, 27.8, 25.6, 24.8, 21.2, 21.2; HR-MS (ESI+) *m/z* calculated for $[C_{23}H_{28}N_3]^+$ = 346.2278; found: 346.2277.



4aae, 62%

13-((2-bromophenyl)amino)-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide* (4aae)*:

White solid; (79 mg, 62%); mp 173-175 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): v_{max} = 3417, 1650, 1591, 1525, 1497, 1417, 1321, 1299, 1186, 1121, 1028, 1011, 751, 682, 567; ^1H NMR (400 MHz, $CDCl_3$) δ ppm = 8.52 (d, *J* = 9.3 Hz, 1H), 8.36 (d, *J* = 6.4 Hz, 1H), 7.95 (t, *J* = 7.8 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H), 7.61 (dd, *J* = 1.5, 8.3 Hz, 1H), 7.46 - 7.33 (m, 4H), 7.32 - 7.28 (m, 1H), 7.12 - 7.06 (m, 1H), 6.83 (dt, *J* = 1.2, 7.7 Hz, 1H), 6.47 (dd, *J* = 1.2, 8.1 Hz, 1H), 4.87 (t, *J* = 6.6 Hz, 2H), 3.41 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ppm = 140.2, 136.7, 134.2, 133.7, 133.5, 131.2, 129.0, 128.9, 128.6, 128.2, 126.3, 125.2, 122.4, 122.1, 119.0, 117.5, 114.2, 112.3, 110.5, 42.6, 28.1; HR-MS (ESI+) *m/z* calculated for $[C_{21}H_{17}BrN_3]^+$ = 390.0600; found: 390.0599.

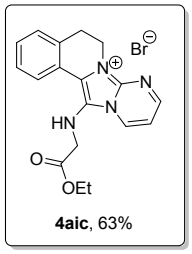


4ace, 71%

***13-((2-bromophenyl)amino)-9-methyl-5,6-dihydropyrido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide)* (4ace):**

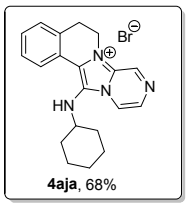
White solid; (93 mg, 71%); mp 185-187 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): v_{max} = 3421, 3132, 2923, 1732, 1654, 1587, 1528, 1495, 1420, 1315, 1237, 1024, 752, 661, 490; ^1H NMR (DMSO D_6, 400 MHz) δ ppm = 8.41 (d, *J* = 6.8 Hz, 1H), 8.26 (s, 1H), 8.20 (s, 1H), 7.73 - 7.64 (m, 2H), 7.54 - 7.50 (m, 1H), 7.49 - 7.43 (m, 1H), 7.42 - 7.34 (m, 2 H), 7.12 - 7.05 (m, 1H), 6.86 - 6.78 (m, 1H), 6.55 (dd, *J* = 1.5, 8.3 Hz, 1H), 4.61 (t, *J* = 6.6 Hz, 2 H), 3.36 (t, *J* = 6.4 Hz, 2H), 2.61 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ ppm = 146.1, 141.1, 136.8, 133.9, 133.3, 130.5, 129.0,

128.9, 127.7, 125.8, 125.0, 124.6, 122.5, 121.7, 119.5, 118.4, 114.3, 109.9, 109.4, 40.8, 27.0, 21.3; HR-MS (ESI+) *m/z* calculated for $[C_{22}H_{19}BrN_3]^+$ = 404.0757; found: 404.0752.



4aic, 63%

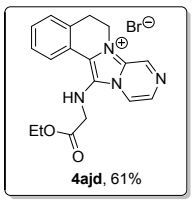
13-((2-Ethoxy-2-oxoethyl)amino)-5,6-dihydropyrimido[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aic): white solid; (58 mg, 63 %); mp 186-188 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3185, 3102, 2181, 2123, 1969, 1738, 1641, 1609, 1536, 1471, 1436, 1376, 1333, 1274, 1207, 1154, 1111, 1030, 760, 736, 637, 568; ^1H NMR ($CDCl_3$, 400 MHz): δ ppm = 10.22 (dd, J_a = 7.1 and J_b = 1.7 Hz, 1H), 8.81 (s, 1H), 8.21-8.19 (m, 1H), 7.51 (dd, J_a = 6.8 and J_b = 4.4 Hz, 1H), 7.46-7.38 (m, 3H), 7.19 (t, J = 6.6 Hz, 1H), 4.60-4.57 (m, 2H), 4.0-3.96 (m, 4H), 3.28 (t, J = 6.6 Hz, 2H), 1.12 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 171.8, 155.7, 138.0, 137.9, 132.6, 130.7, 128.9, 128.6, 126.5, 125.9, 122.8, 121.3, 122.8, 61.2, 47.3, 40.6, 27.8, 14.0; HR-MS (ESI+) *m/z* calculated for $[C_{18}H_{19}N_4O_2]^+$ = 323.1503; found: 323.1509.



4aja, 68%

13-(Cyclohexylamino)-5,6-dihydropyrazino[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aja):

Green solid; (63 mg, 68%); mp 183-185 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3422, 3182, 3040, 2930, 2855, 1584, 1529, 1294, 1264, 1083, 1027, 892, 768, 728, 698, 593, 570; ^1H NMR (400 MHz, $CDCl_3$) δ = 9.97 (s, 1H), 9.43 (d, J = 3.9 Hz, 1H), 8.31-8.28 (m, 2H), 7.42-7.35 (m, 3H), 6.11 (d, J = 7.8 Hz, 1H), 4.93 (t, J = 6.4 Hz, 2H), 3.36 (t, J = 6.4 Hz, 2H), 3.02-2.98 (m, 1H), 1.85 (d, J = 10.8 Hz, 2H), 1.71-1.51 (m, 5H), 1.19-1.09 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 137.0, 133.9, 133.0, 131.1, 128.9, 128.5, 128.1, 126.3, 124.2, 122.7, 118.5, 58.1, 43.3, 34.0, 27.7, 25.1; 27.4, 25.2, 25.1, 21.2; HR-MS (ESI+) *m/z* calculated for $[C_{20}H_{23}N_4]^+$ = 319.1917; found: 319.1933.

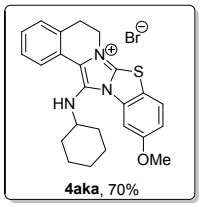


4ajd, 61%

13-((2-Ethoxy-2-oxoethyl)amino)-5,6-dihydropyrazino[2',1':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4ajd):

White solid; (64 mg, 61%); mp 212-214 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3744, 3733, 3611, 3395, 3162, 2977, 2378, 2322, 2211, 2154, 2130, 1992, 1735, 1679, 1640, 1587, 1530, 1471, 1394, 1298, 1201, 1114, 1025, 931, 856, 770, 652, 605, 575; ^1H NMR (400 MHz, $CDCl_3$) δ ppm = 9.7 (d, J = 1.5 Hz, 1H), 8.97 (dd, J = 4.6 Hz, 1H), 8.56 (d, J = 4.4 Hz, 1H), 8.24-8.22 (m, 1H), 7.56-7.53 (m, 3H), 6.51-6.47 (m, 1H), 4.74 (t, J = 6.6 Hz, 2H), 4.05-3.98 (m, 4H), 3.31 (t, J = 6.8 Hz, 2H), 1.1 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 171.1, 137.5,

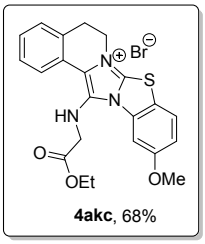
133.9, 133, 130.6, 128.9, 127.9, 127.5, 122.8, 122.6, 118.0, 60.7, 47.6, 41.7, 26.7, 13.8; HR-MS (ESI+) *m/z* calculated for $[C_{18}H_{19}N_4O_2]^+$ = 323.1503; found: 323.1512.



4aka, 70%

14-(Cyclohexylamino)-11-methoxy-5,6-dihydrobenzo[4',5']thiazolo[2',3':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4aka):

White solid; (79 mg, 70%); mp 292 - 293 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3745, 3730, 3670, 3611, 3395, 3181, 2926, 2852, 2370, 2322, 2168, 2128, 1992, 1840, 1786, 1678, 1641, 1535, 1484, 1451, 1301, 1246, 1164, 1028, 870, 818, 706, 667, 590, 574; ^{1}H NMR (DMSO D_6, 400 MHz): δ ppm = 8.28-8.22 (m, 2H), 8.01 (d, *J* = 2.4, 1H), 7.48-7.37 (m, 4H), 5.67 (d, *J* = 5.9 Hz, 1H), 4.45 (t, *J* = 6.4 Hz, 2H), 3.89 (s, 3H), 3.25 (t, *J* = 6.6 Hz, 2H), 2.97-2.94 (m, 1H), 1.94 (d, *J* = 11.7 Hz, 2H), 1.66 (br. s, 2H), 1.53 (m, 1H), 1.33-1.28 (m, 2H), 1.11 (br. s, 3H); ^{13}C NMR (100 MHz, DMSO D_6) δ ppm = 157.9, 141.6, 132.1, 130.4, 129.0, 128.8, 127.4, 125.7, 125.1, 124.3, 124.0, 116.5, 115.4, 109.6, 57.2, 56.0, 43.6, 32.8, 27.2, 25.2, 24.5; HR-MS (ESI+) *m/z* calculated for $[C_{24}H_{26}BrN_3OS]^+$ = 404.1791; found: 404.1787.



4akc, 68%

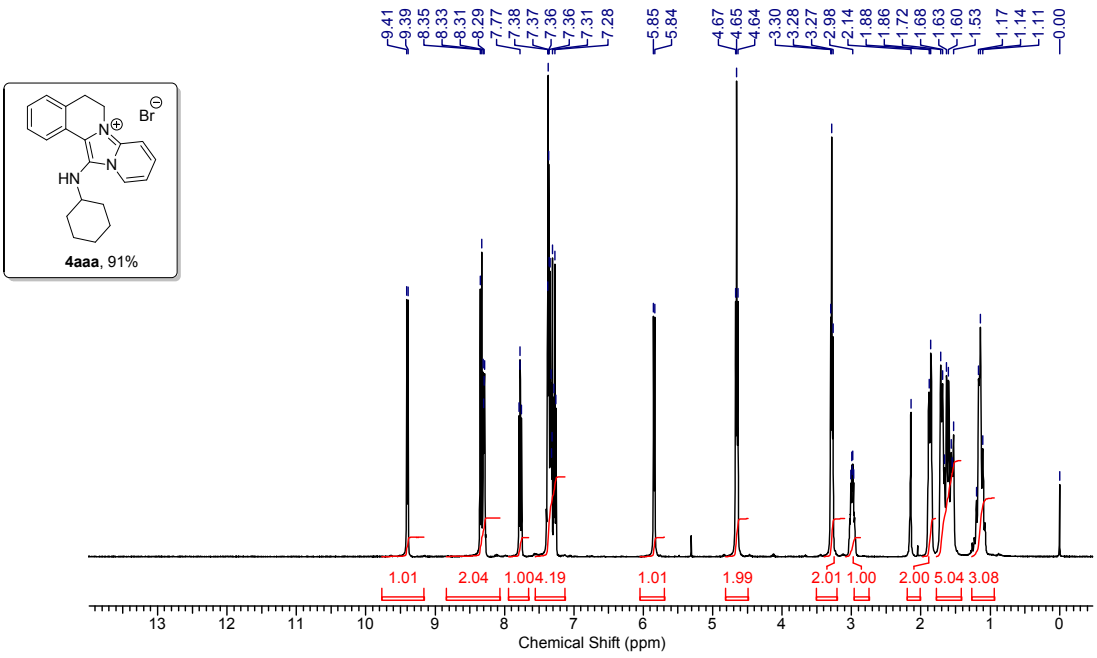
14-((2-Ethoxy-2-oxoethyl)amino)-11-methoxy-5,6 dihydrobenzo[4',5']thiazolo[2',3':2,3]imidazo[5,1-a]isoquinolin-7-ium bromide (4akc):

White solid; (63 mg, 68%); mp 242-244 ˚C; IR (MIR-ATR, 4000–600 cm^{-1}): υ_{max} = 3190, 2976, 2935, 1740, 1604, 1539, 1479, 1464, 1377, 1300, 1273, 1236, 1200, 1111, 1092, 1045, 1019, 813, 769, 726, 691, 596; ^{1}H NMR (DMSO D_6, 400 MHz): δ ppm = 8.47 (d, J = 8.8 Hz, 1H), 8.11 (d, J = 7.3 Hz, 1H), 7.98 (d, J = 2 Hz, 1H), 7.49-7.40 (m, 3H), 7.33 (dd, J = 9, 2.2 Hz, 1H), 6.16 (s, 1H), 4.45 (t, J = 6.4 Hz, 2H), 4.04-3.97 (m, 4H), 3.89 (s, 3H), 3.23 (t, J = 6.1 Hz, 2H), 1.06 (t, J = 7.1 Hz, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ ppm = 171.1, 130.7, 130.0, 129.6, 128.7, 125.1, 115.6, 61.0, 56.0, 14.0; HR-MS (ESI+) *m/z* calculated for $[C_{22}H_{22}BrN_3O_3S]^+$ = 408.1376; found: 408.1381.

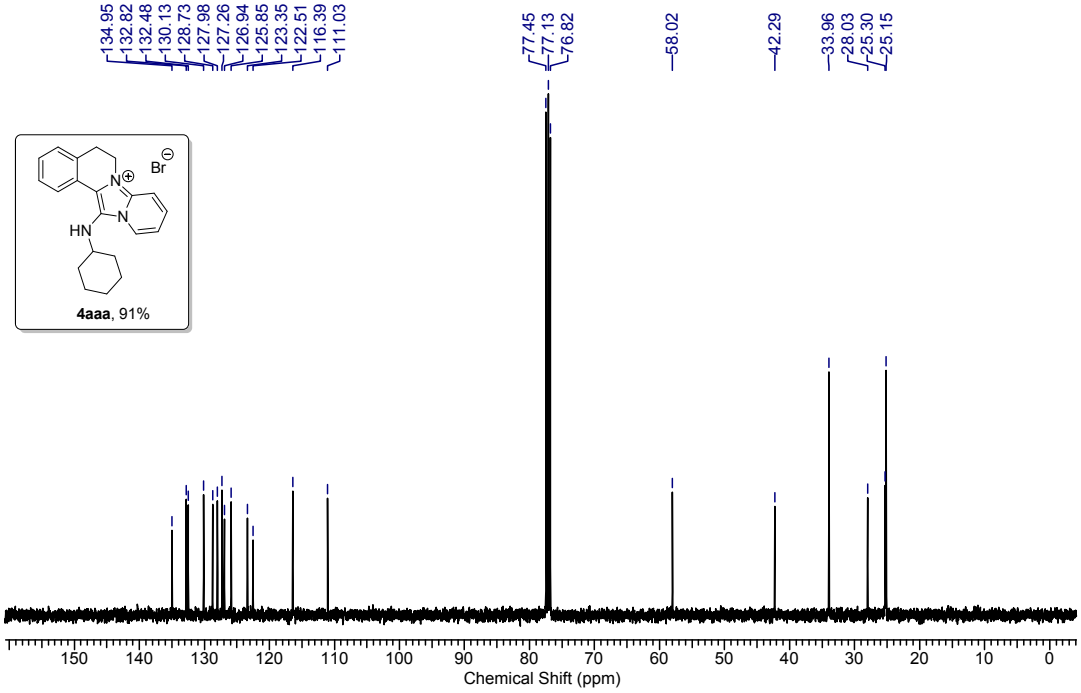
References:

1. (a) A. H. Shinde, N. Archith, S. Malipatel and D. S. Sharada, *Tetrahedron Lett.,* 2014, **55**, 6821.
   (b) A. H. Shinde, S. Vidyacharan and D. S. Sharada, *Org. Biomol. Chem.,* 2016, **14**, 3207.

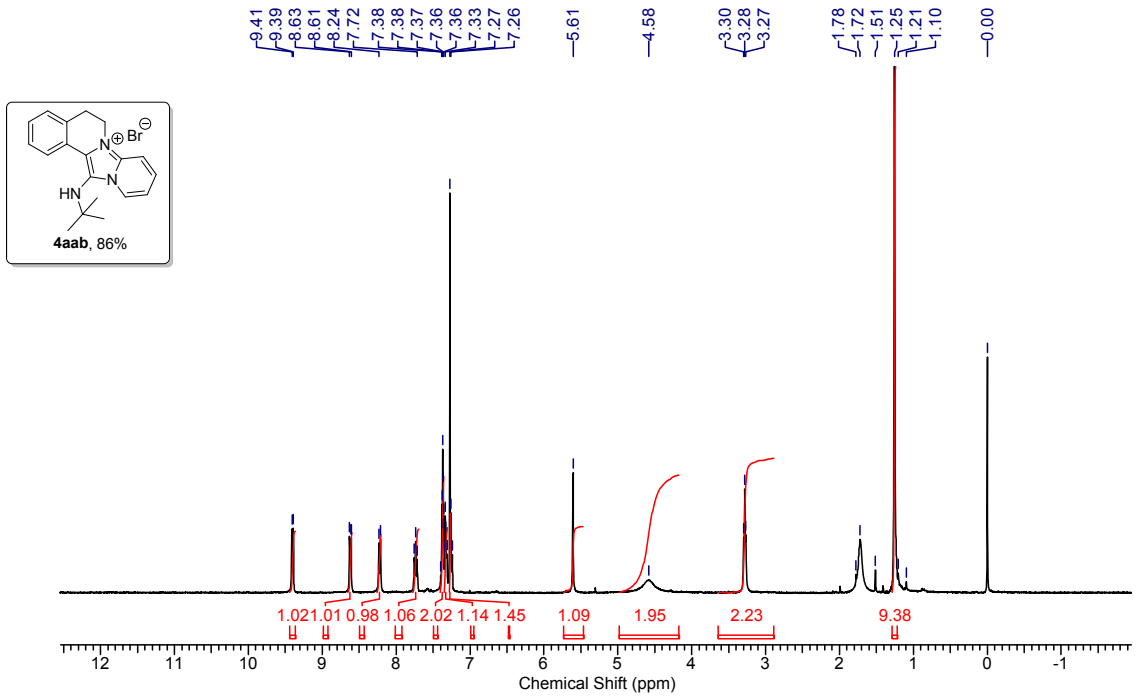
Copies of ^{1}H and ^{13}C NMR spectra of compounds 4aaa-4akc



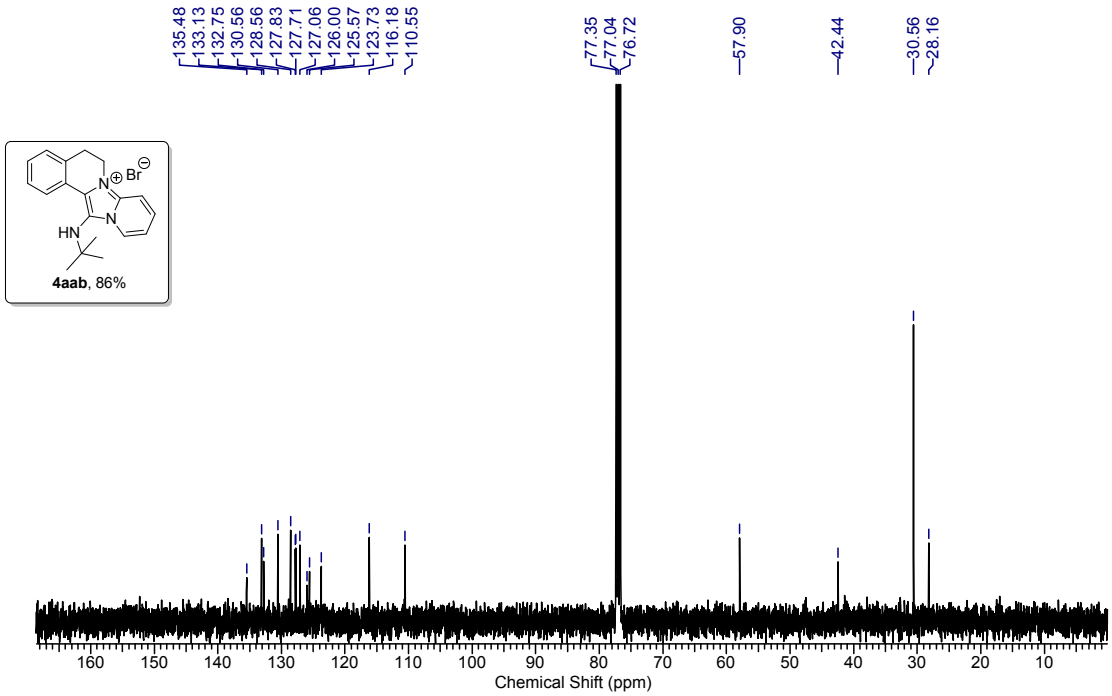
^{1}H NMR (400 MHz) spectrum of compound **4aaa** in $CDCl_3$



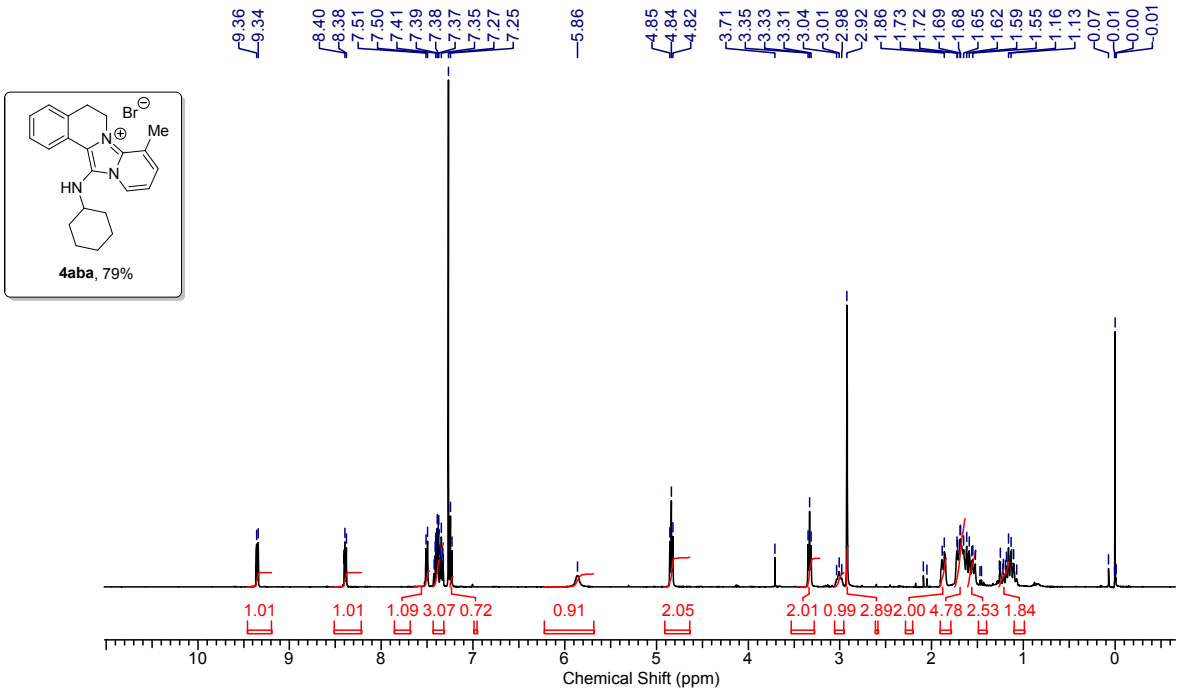
^{13}C NMR (100 MHz) spectrum of compound **4aaa** in $CDCl_3$



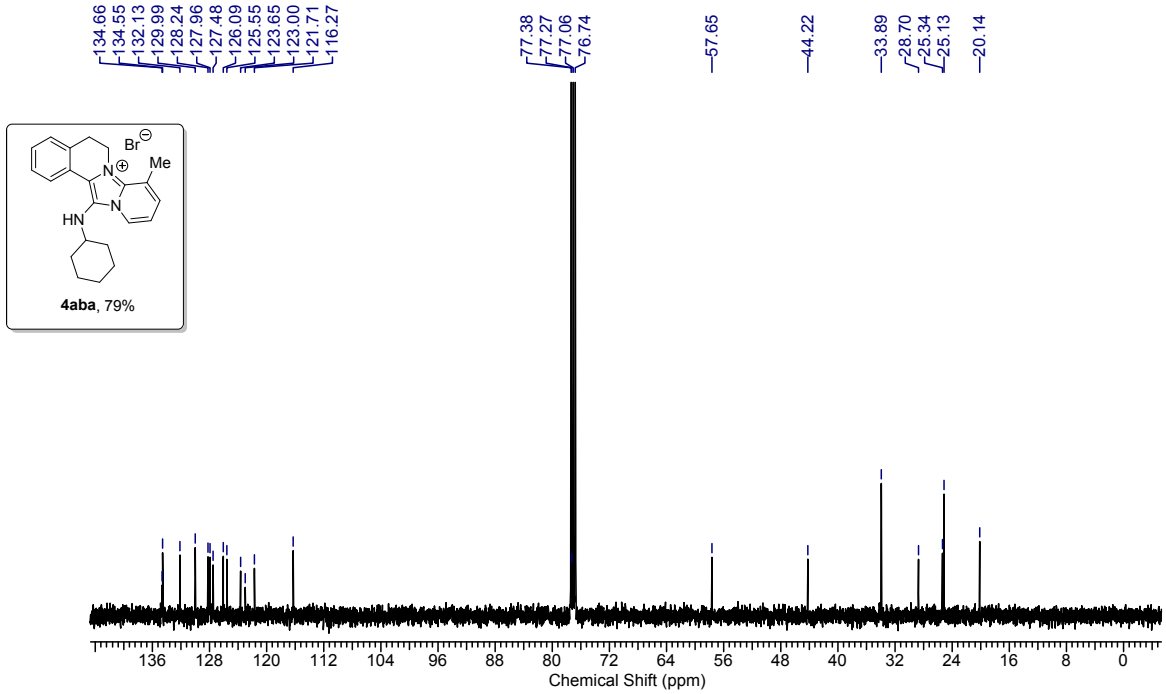
^{1}H NMR (400 MHz) spectrum of compound **4aab** in $CDCl_3$



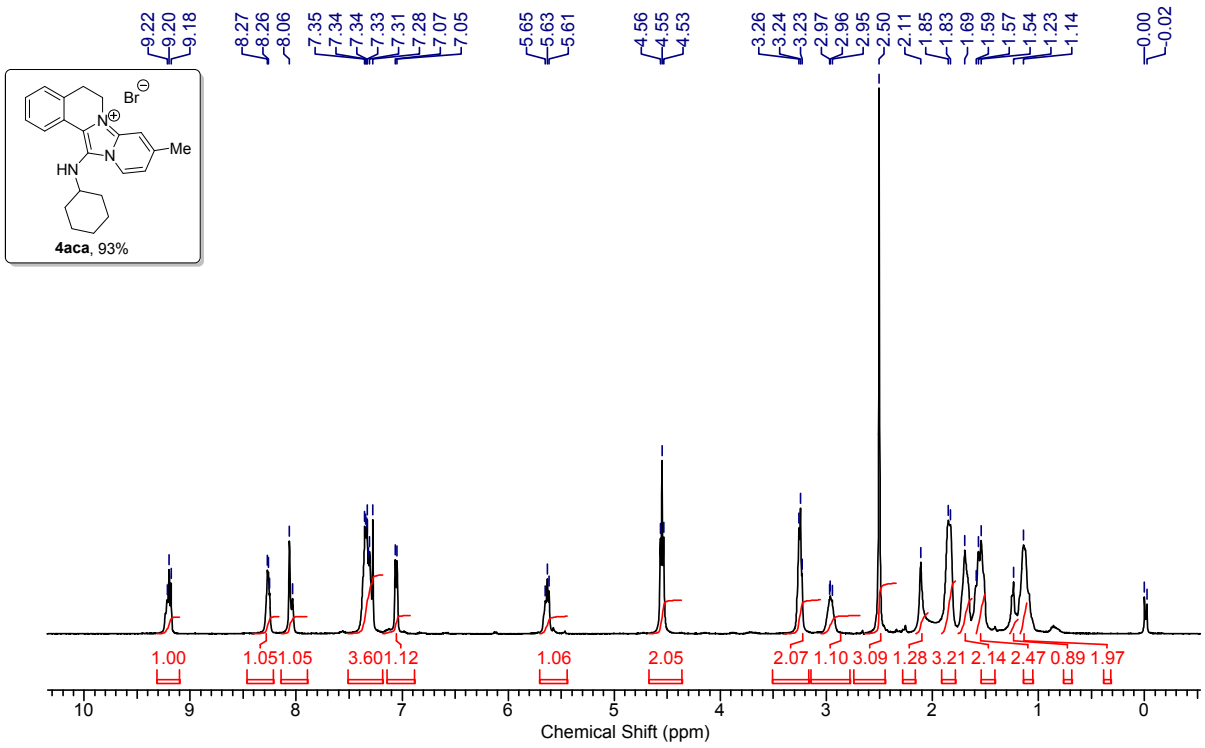
^{13}C NMR (100 MHz) spectrum of compound **4aab** in $CDCl_3$



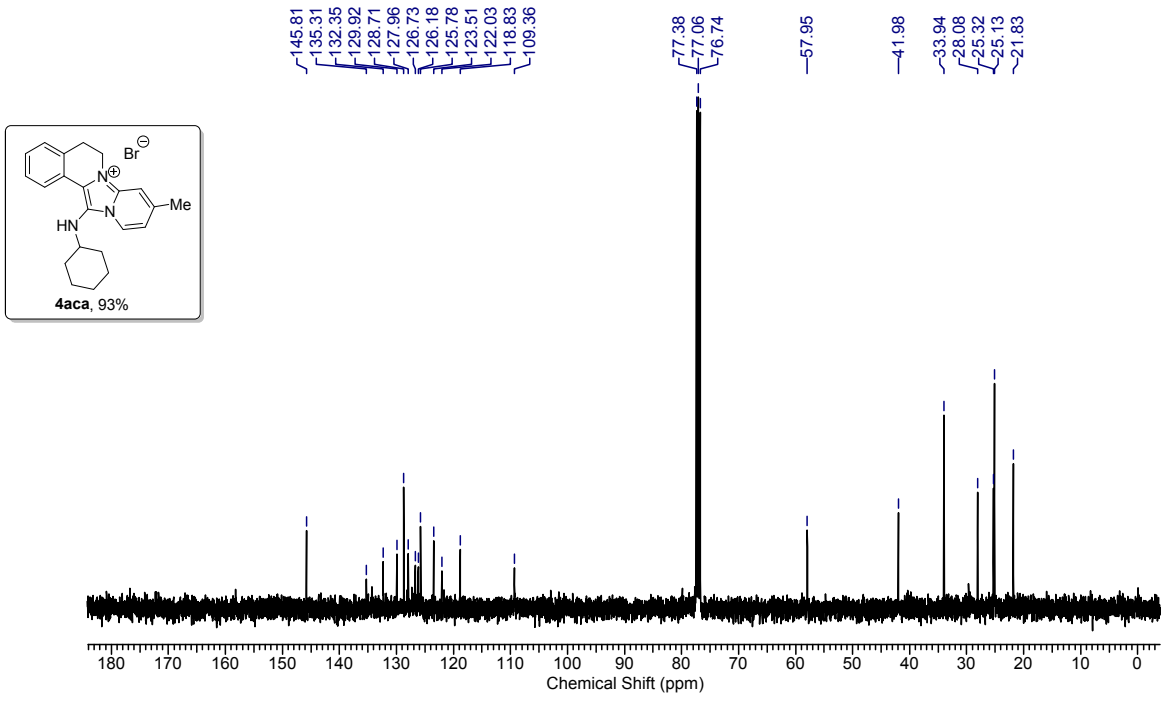
^{1}H NMR (400 MHz) spectrum of compound **4aba** in $CDCl_3$



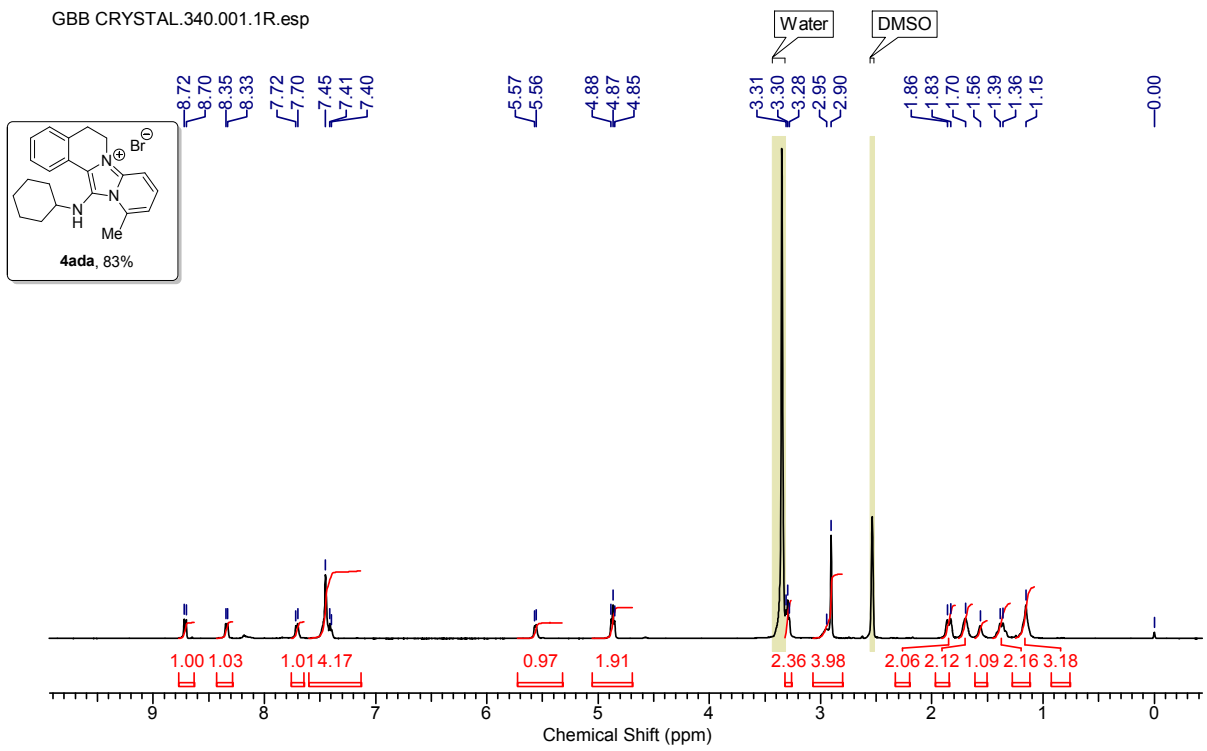
^{13}C NMR (100 MHz) spectrum of compound **4aba** in $CDCl_3$



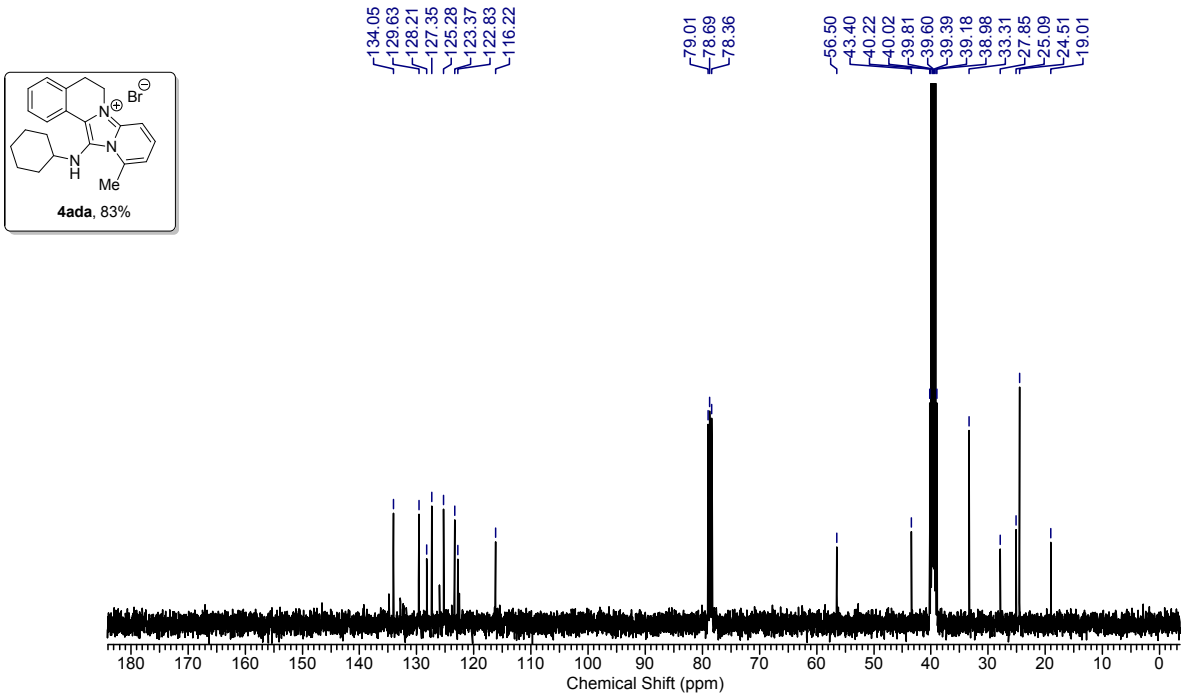
^{1}H NMR (400 MHz) spectrum of compound **4aca** in $CDCl_3$



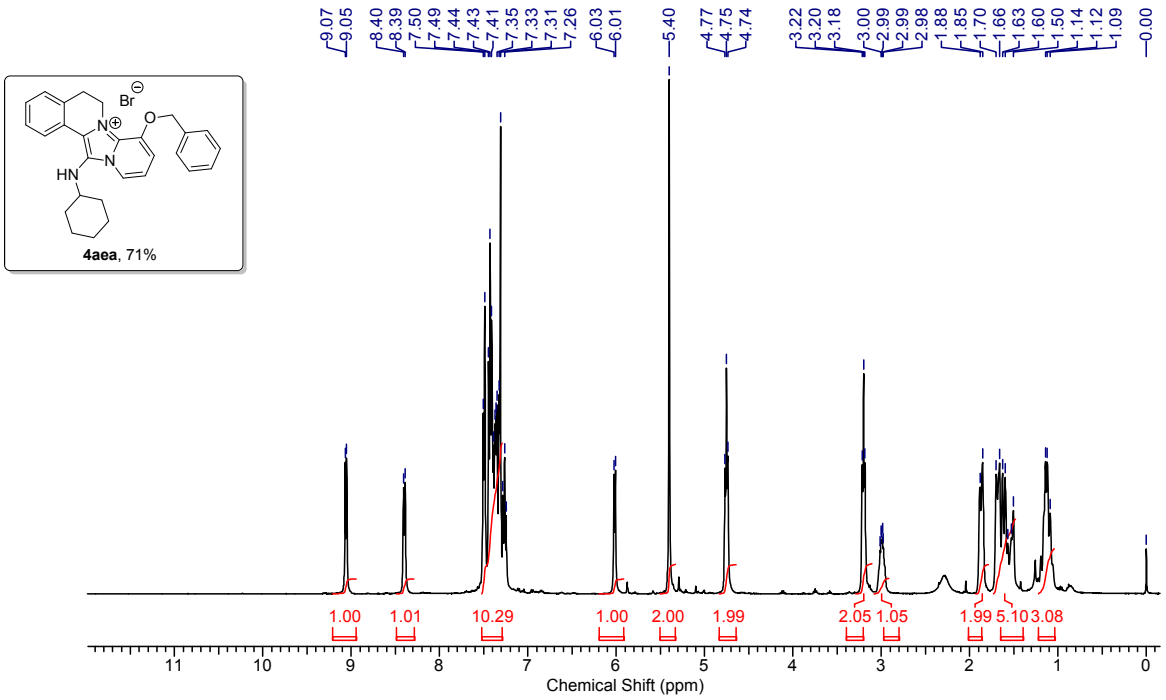
^{13}C NMR (100 MHz) spectrum of compound **4aca** in $CDCl_3$



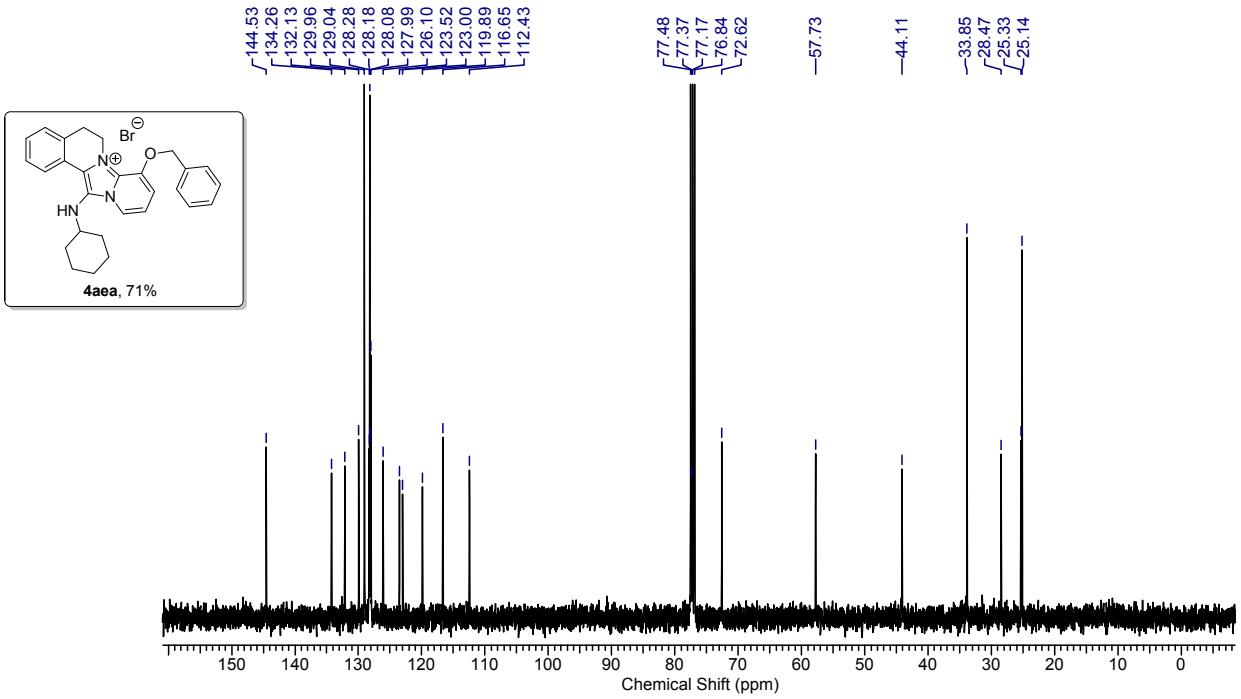
^{1}H NMR (400 MHz) spectrum of compound **4ada** in DMSO D_6



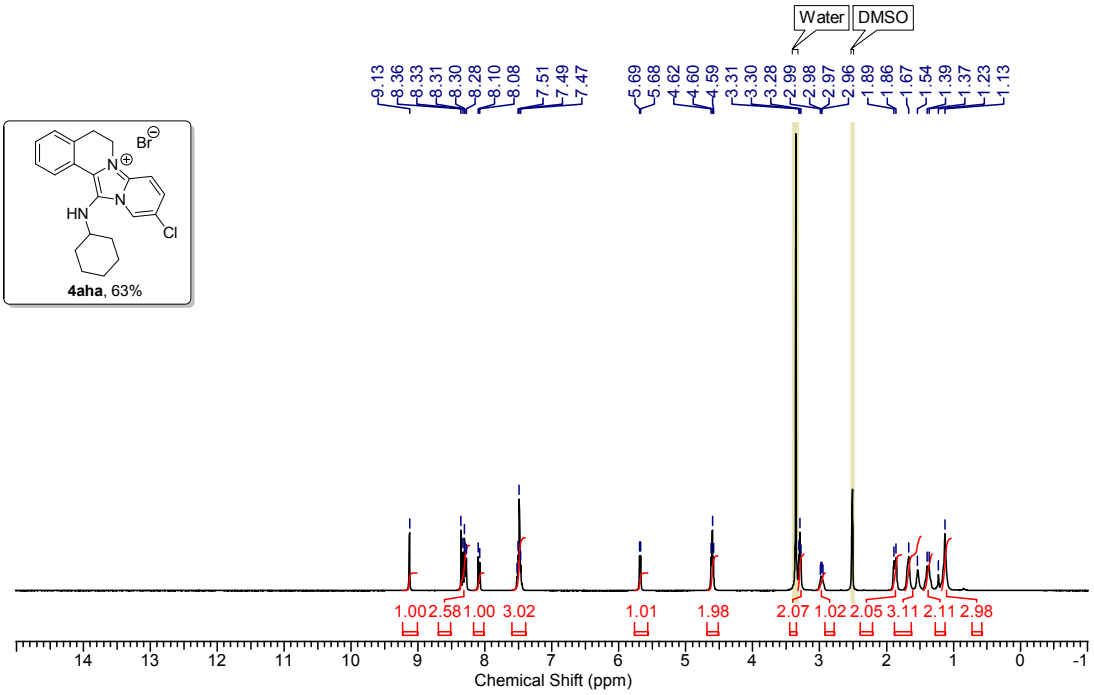
^{13}C NMR (100 MHz) spectrum of compound **4ada** in $CDCl_3$+DMSO D_6



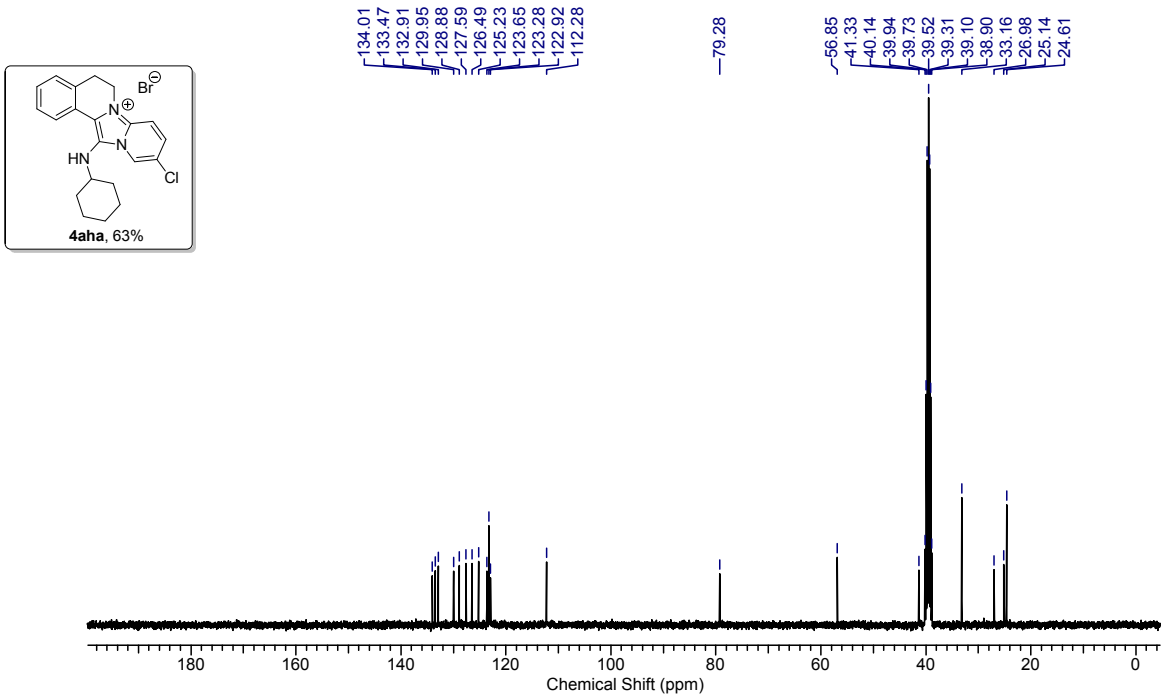
^{1}H NMR (400 MHz) spectrum of compound **4aea** in $CDCl_3$



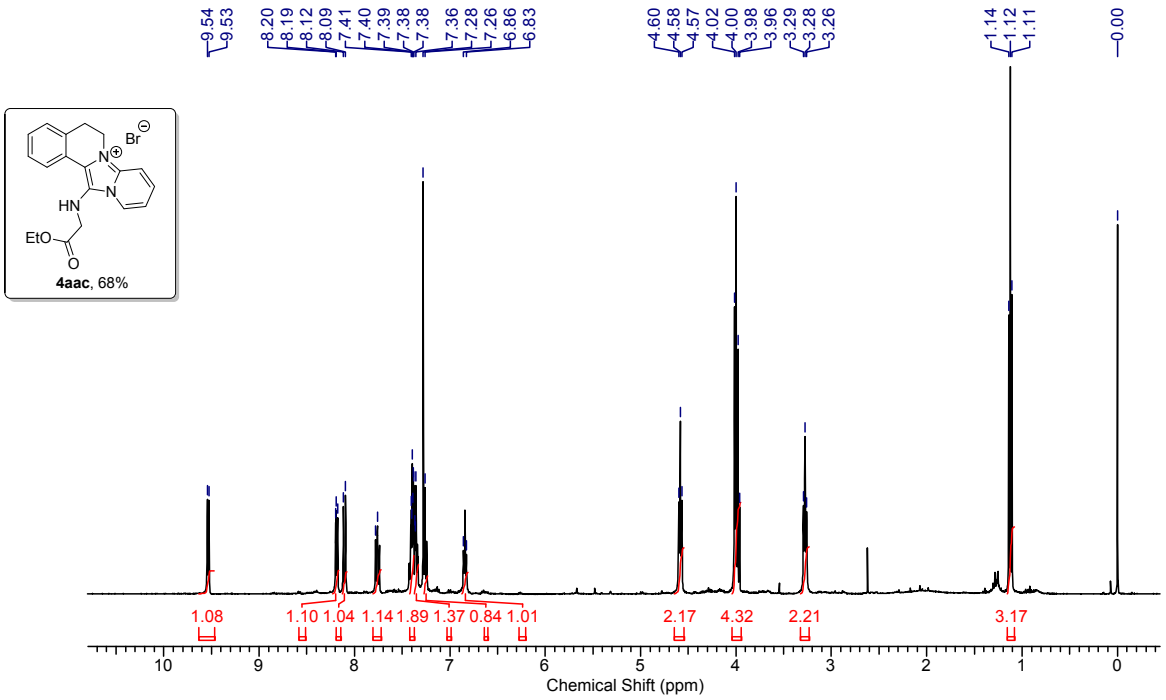
^{13}C NMR (100 MHz) spectrum of compound **4aea** in $CDCl_3$



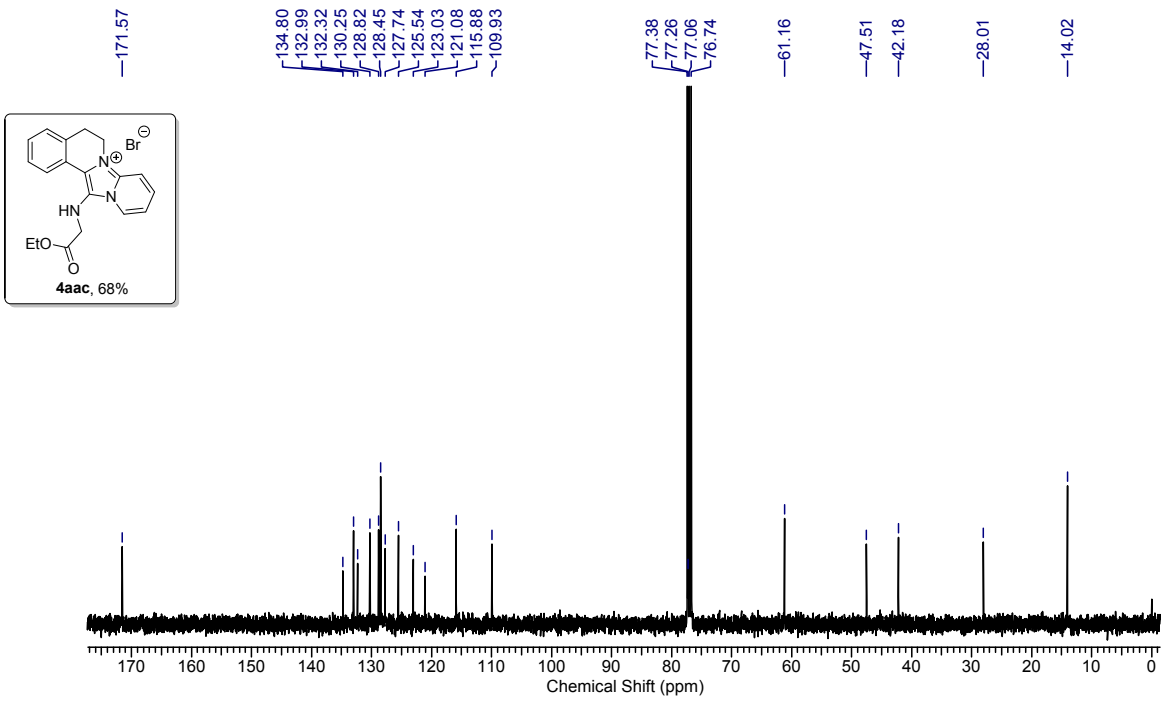
^{1}H NMR (400 MHz) spectrum of compound **4aha** in DMSO-d_6



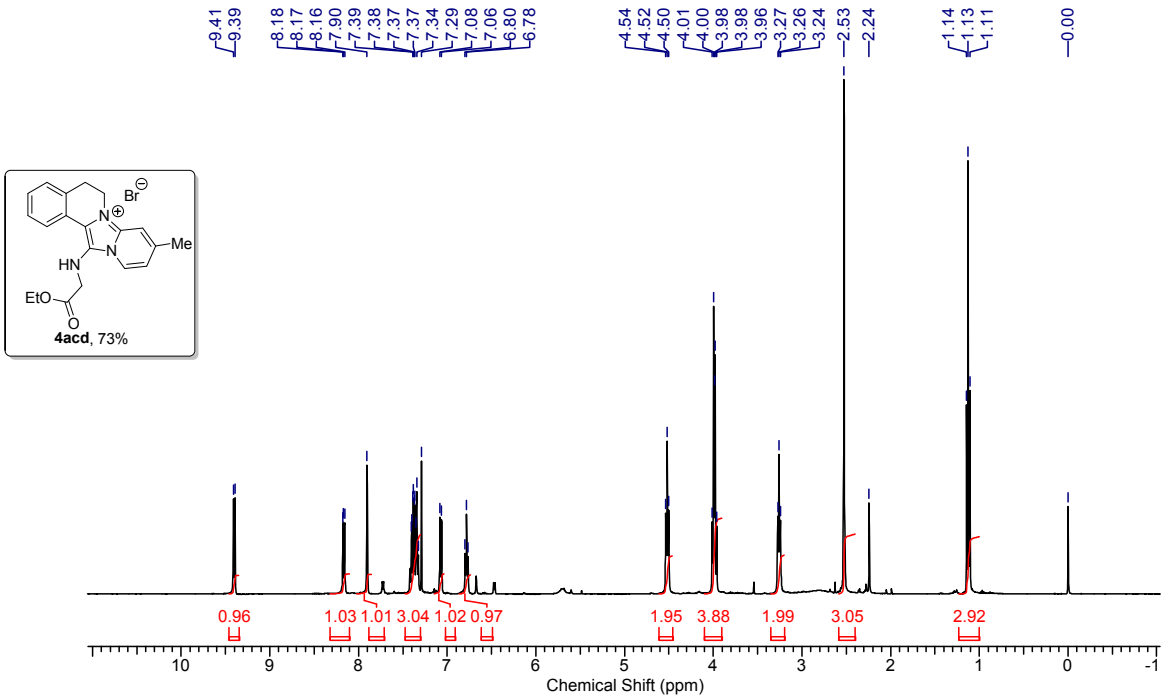
^{13}C NMR (100 MHz) spectrum of compound **4aha** in DMSO-d_6



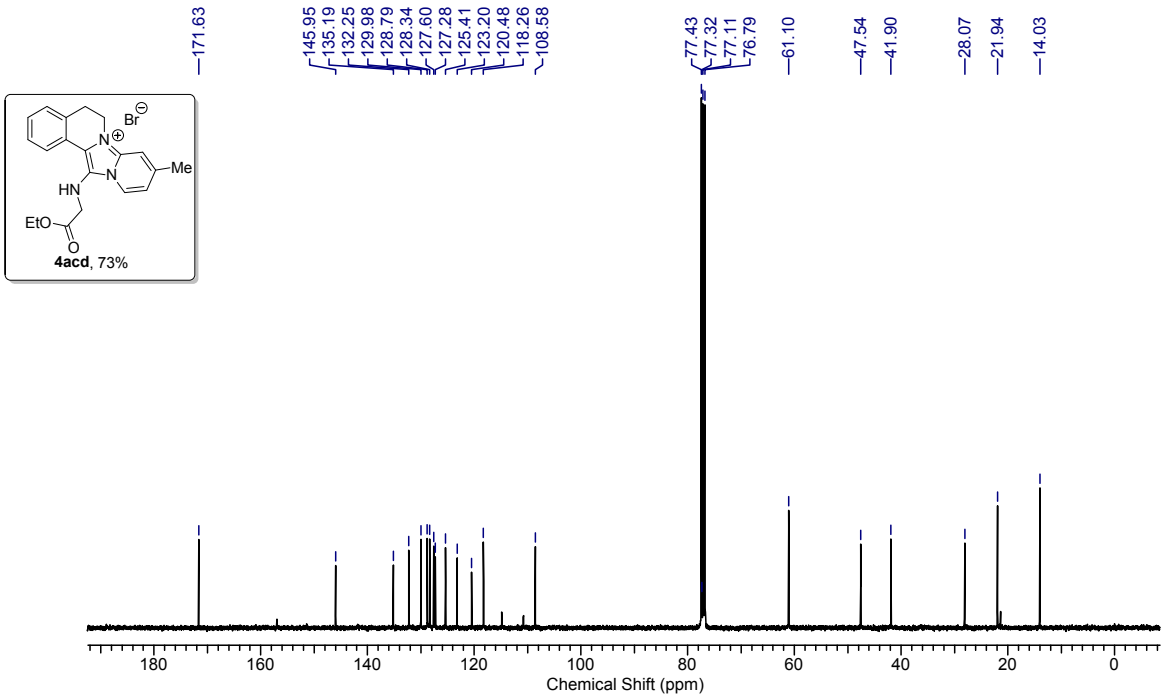
^{1}H NMR (400 MHz) spectrum of compound **4aac** in $CDCl_3$



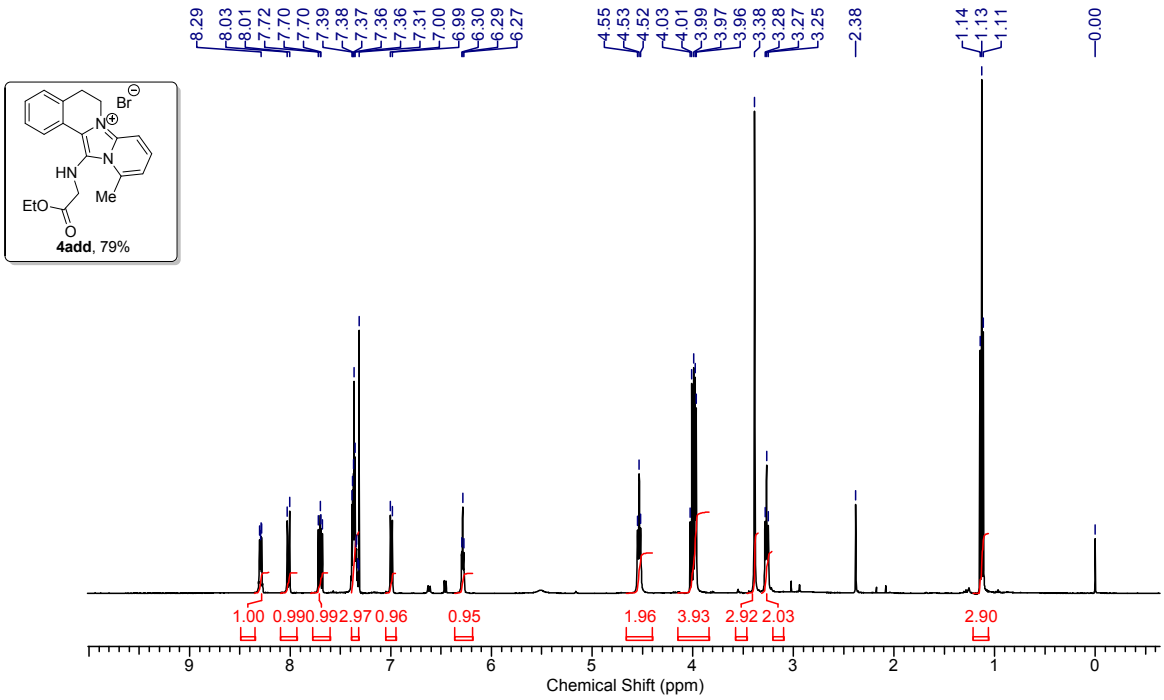
^{13}C NMR (100 MHz) spectrum of compound **4aac** in $CDCl_3$



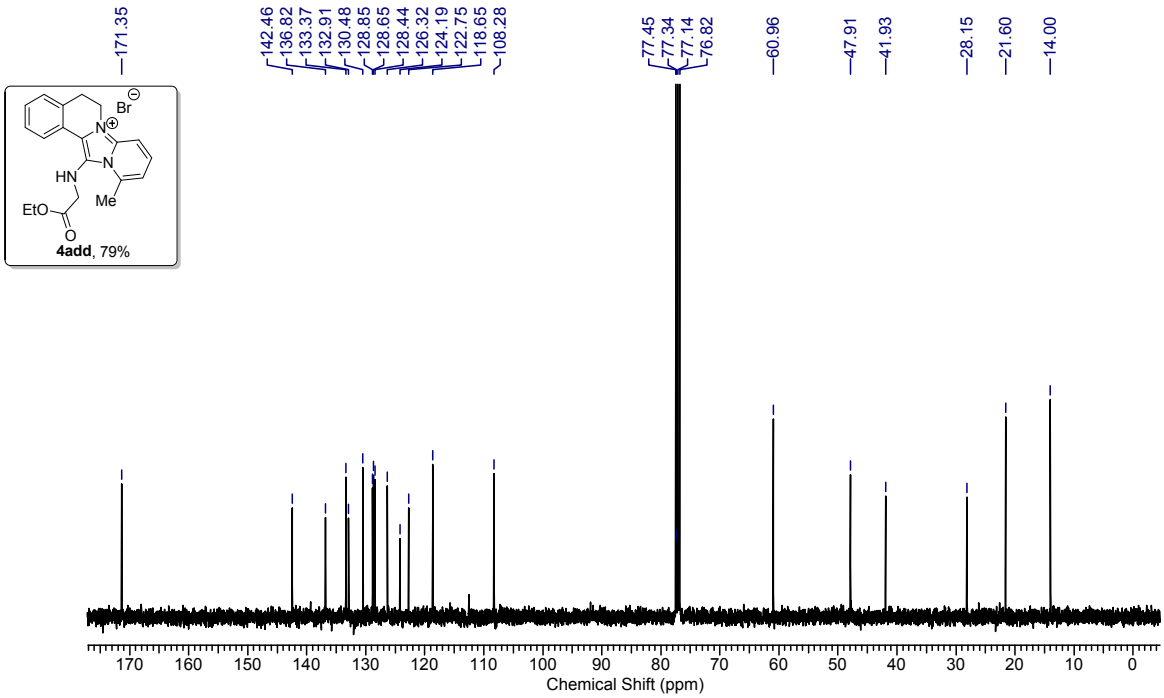
^{1}H NMR (400 MHz) spectrum of compound **4acd** in $CDCl_3$



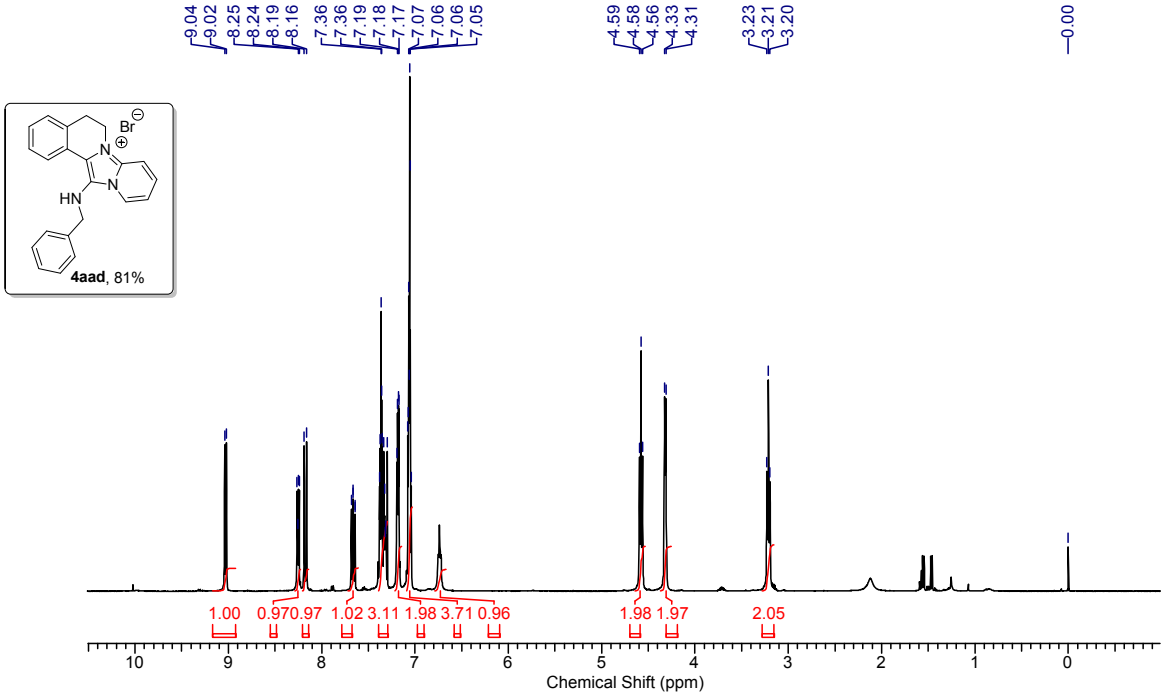
^{13}C NMR (100 MHz) spectrum of compound **4acd** in $CDCl_3$



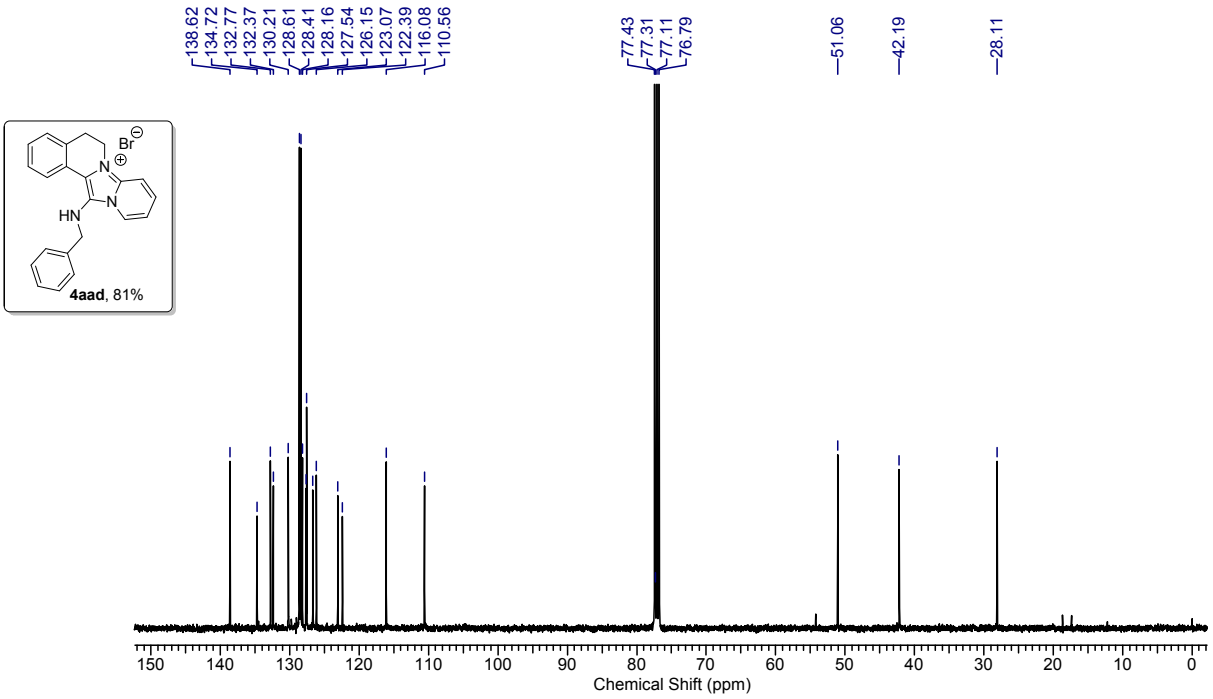
^{1}H NMR (400 MHz) spectrum of compound **4add** in $CDCl_3$



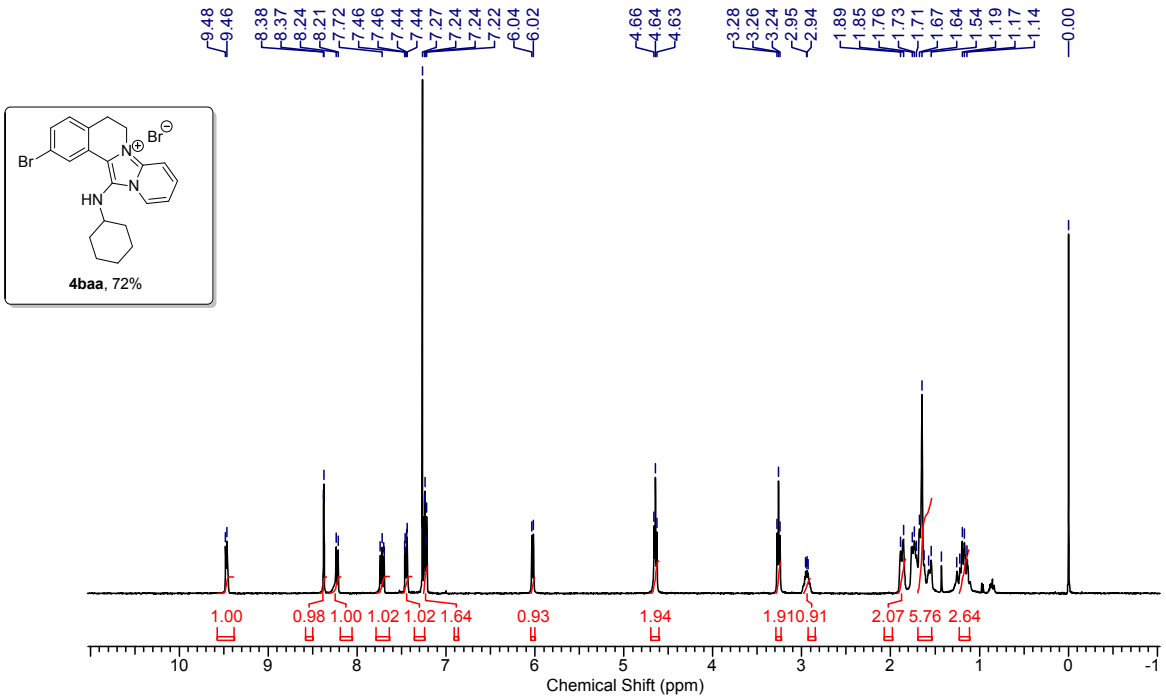
^{13}C NMR (100 MHz) spectrum of compound **4add** in $CDCl_3$



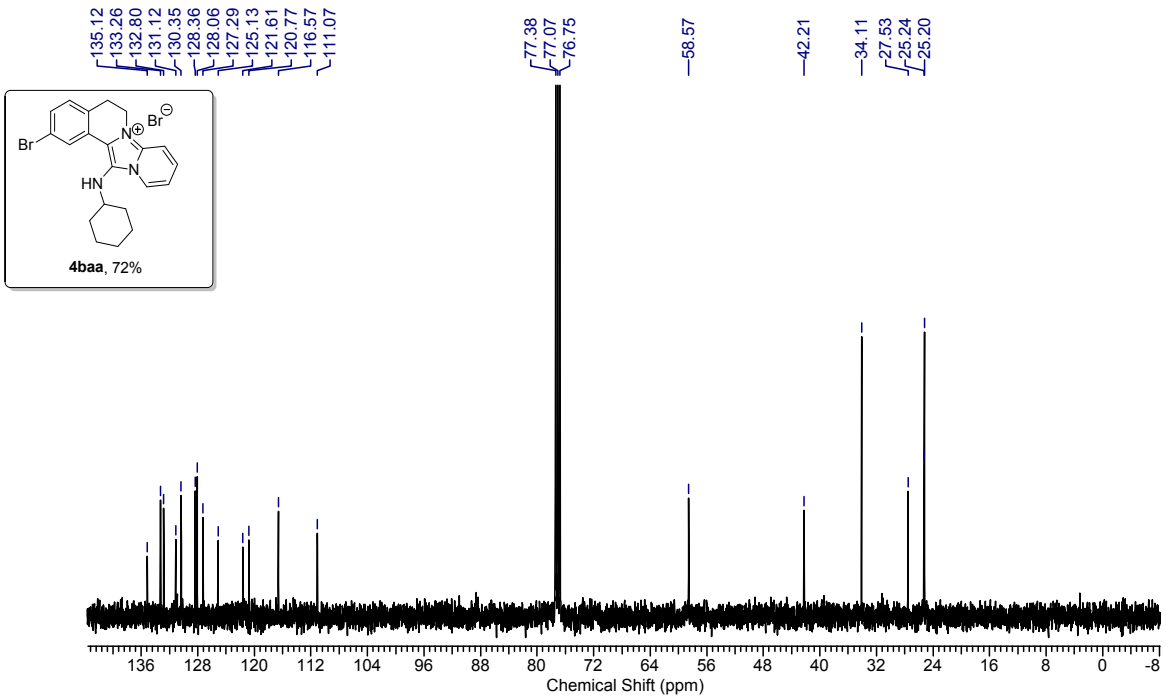
^{1}H NMR (400 MHz) spectrum of compound **4aad** in $CDCl_3$



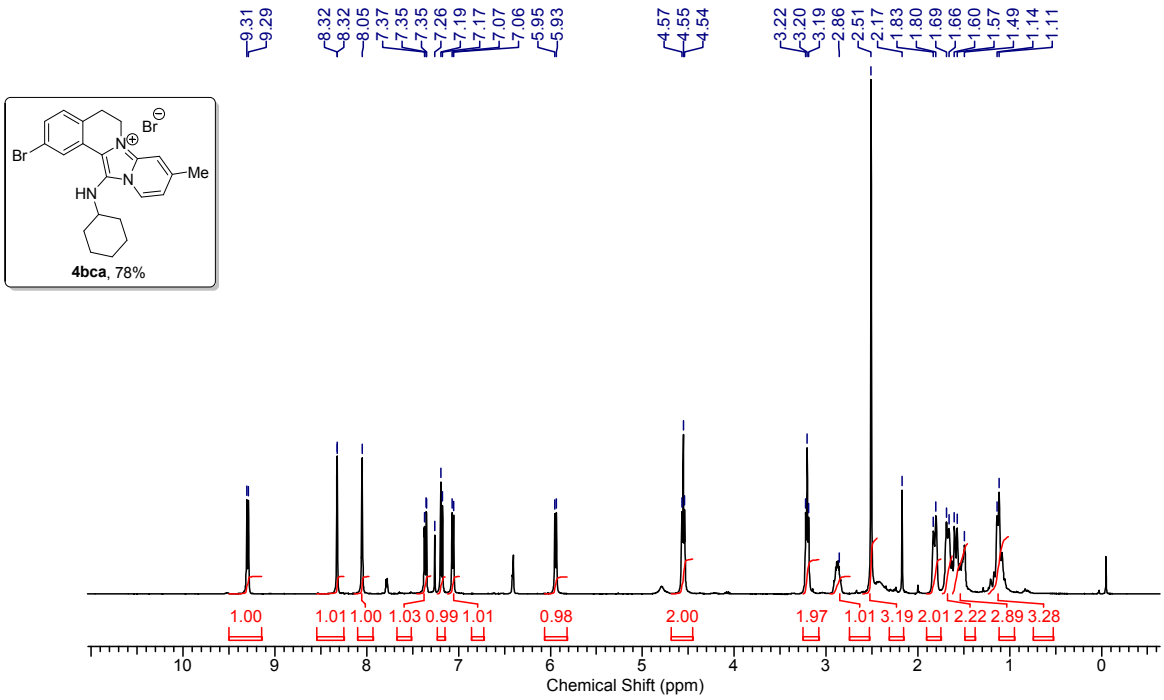
^{13}C NMR (100 MHz) spectrum of compound **4aad** in $CDCl_3$



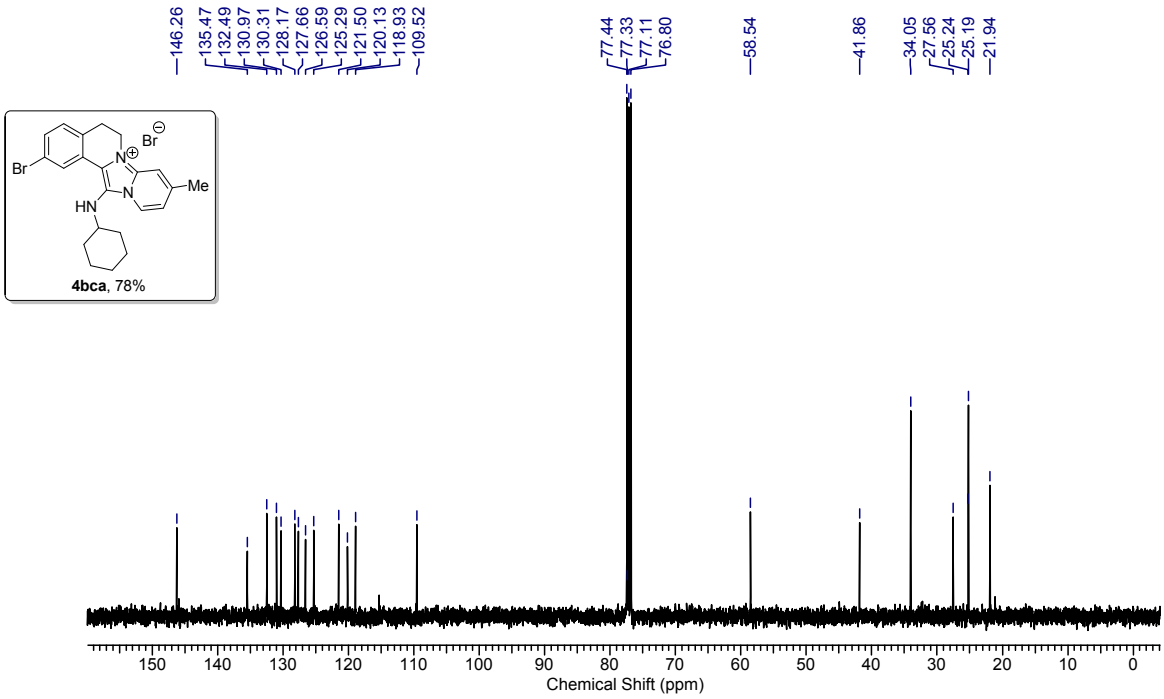
^{1}H NMR (400 MHz) spectrum of compound **4baa** in $CDCl_3$



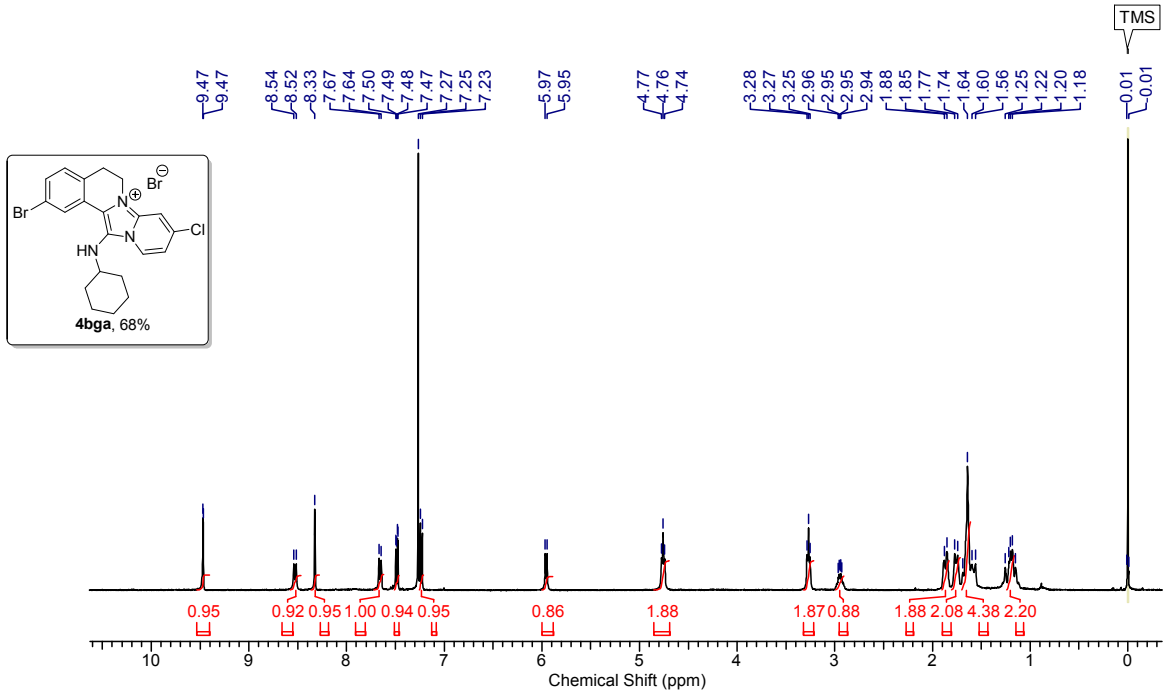
^{13}C NMR (100 MHz) spectrum of compound **4baa** in $CDCl_3$



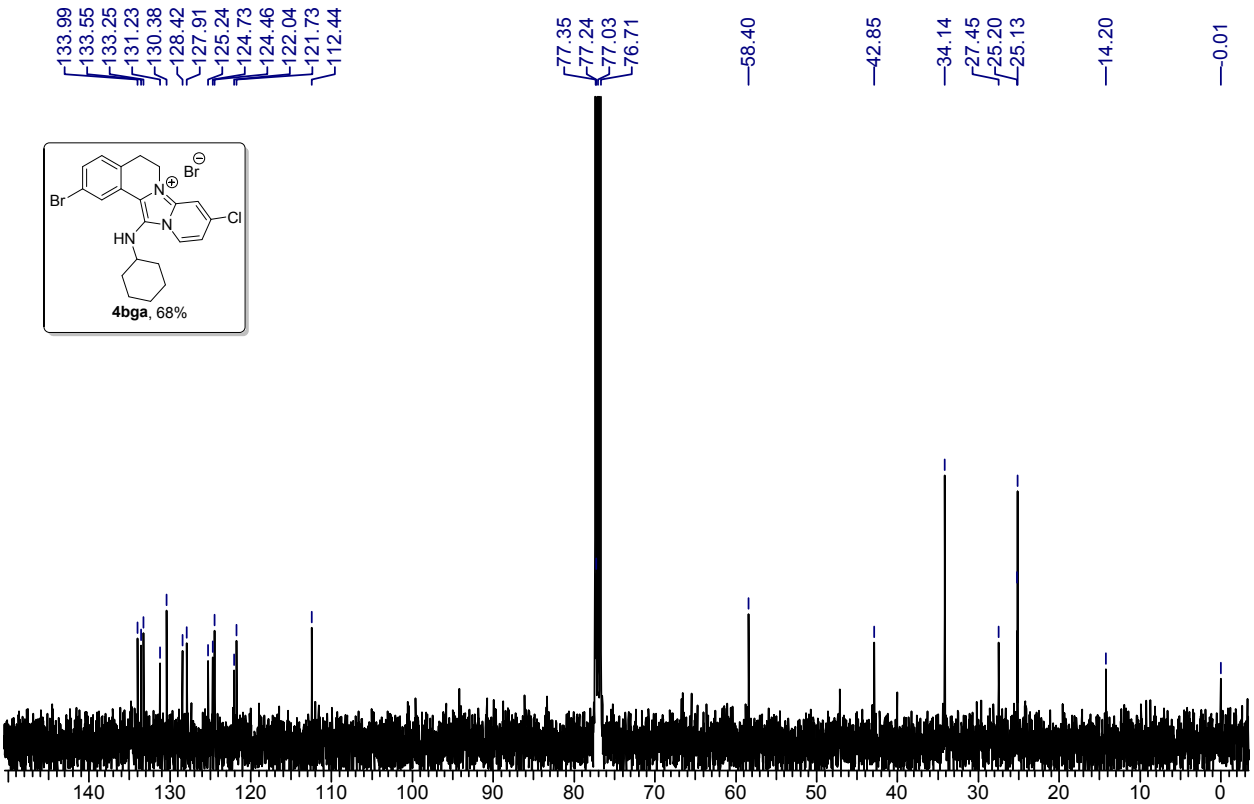
^{1}H NMR (400 MHz) spectrum of compound **4bca** in $CDCl_3$



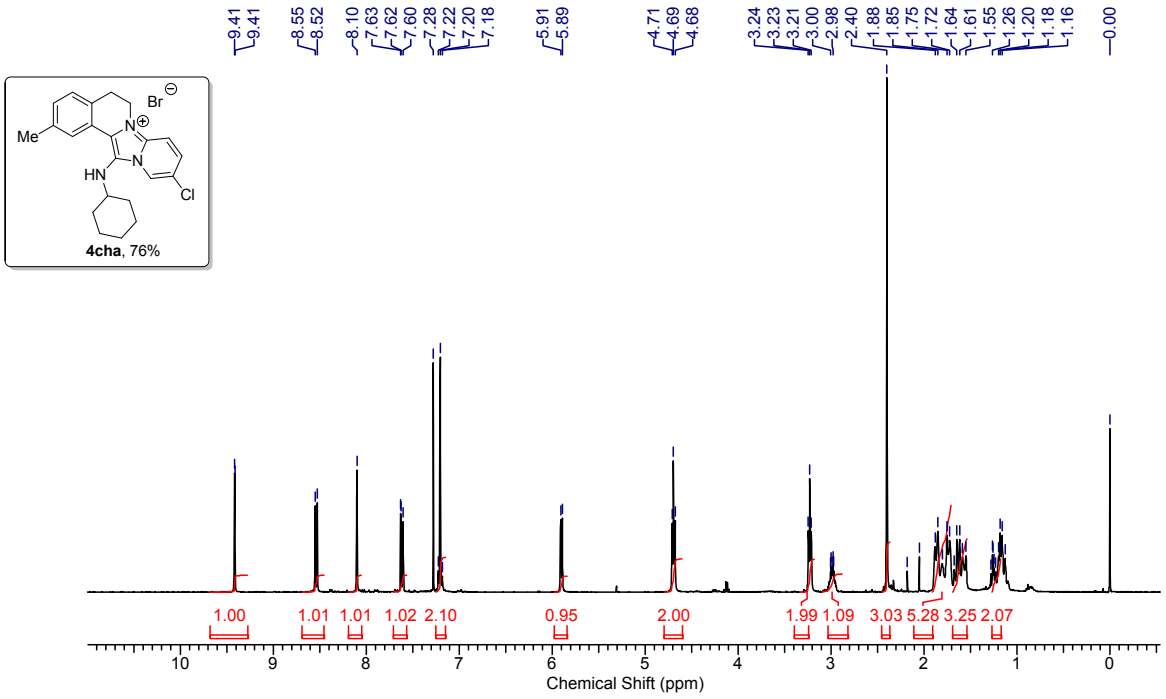
^{13}C NMR (100 MHz) spectrum of compound **4bca** in $CDCl_3$



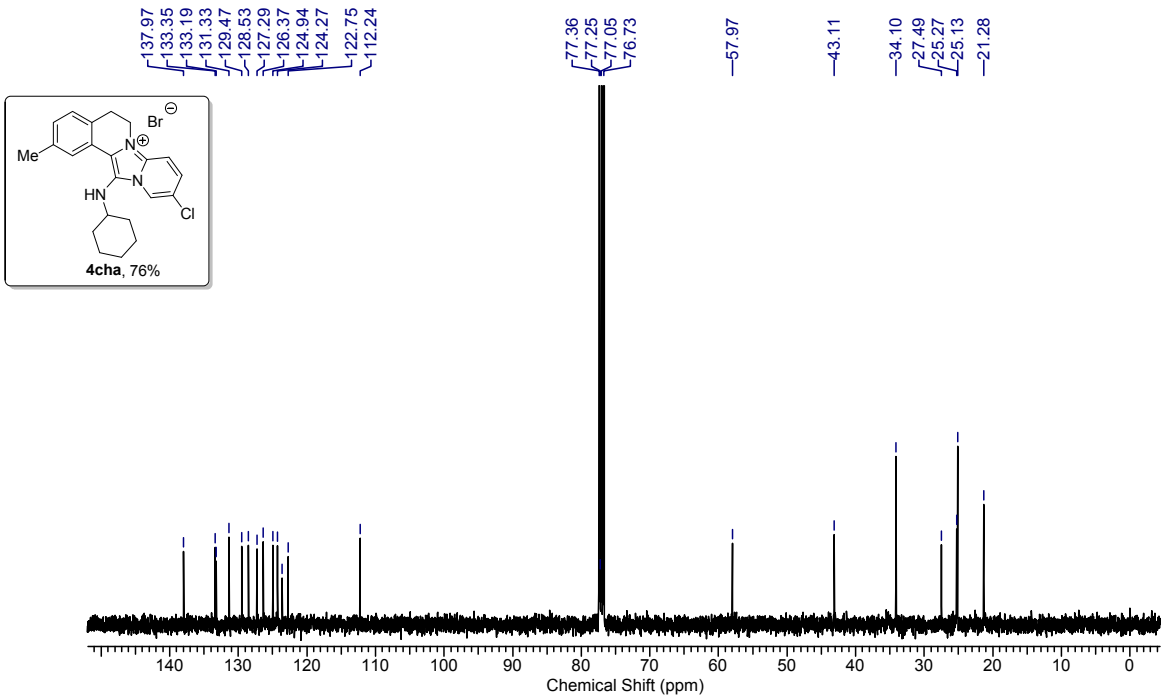
^{1}H NMR (400 MHz) spectrum of compound **4bga** in $CDCl_3$



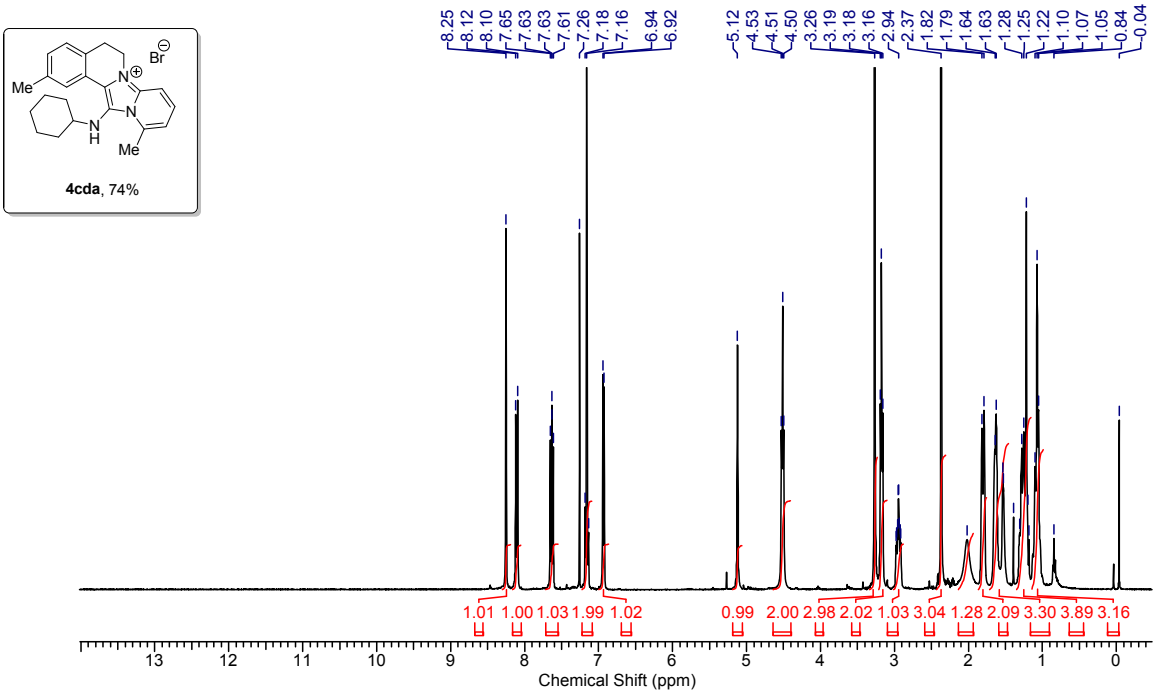
^{13}C NMR (100 MHz) spectrum of compound **4bga** in $CDCl_3$



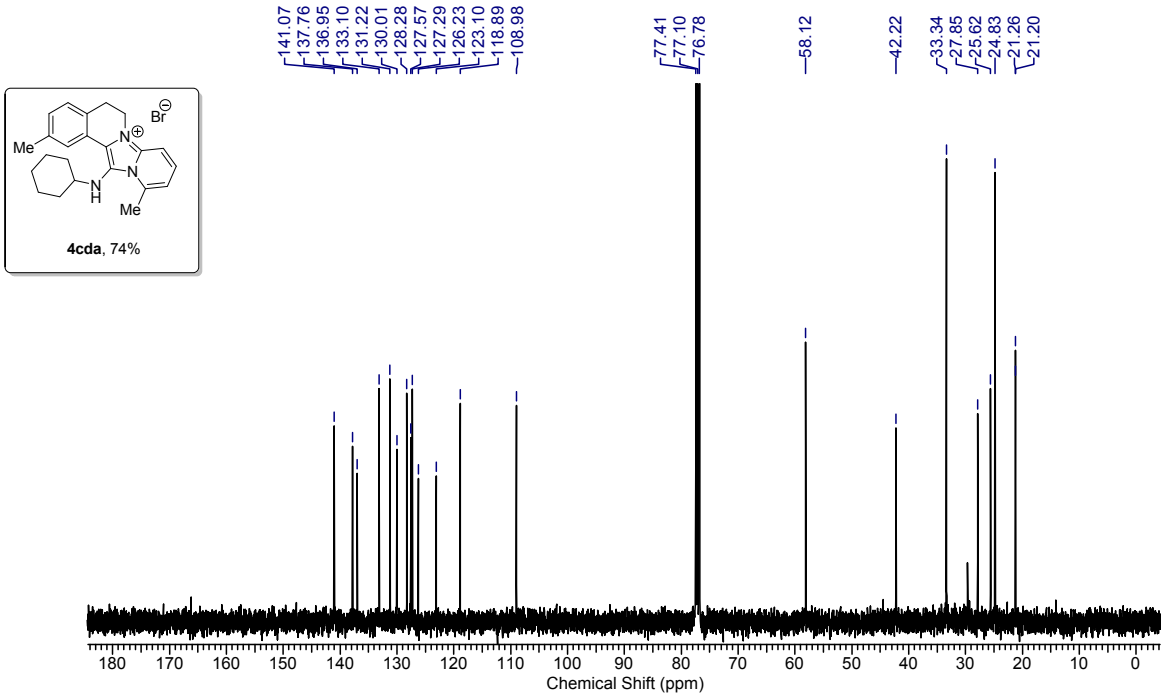
^{1}H NMR (400 MHz) spectrum of compound **4cha** in $CDCl_3$



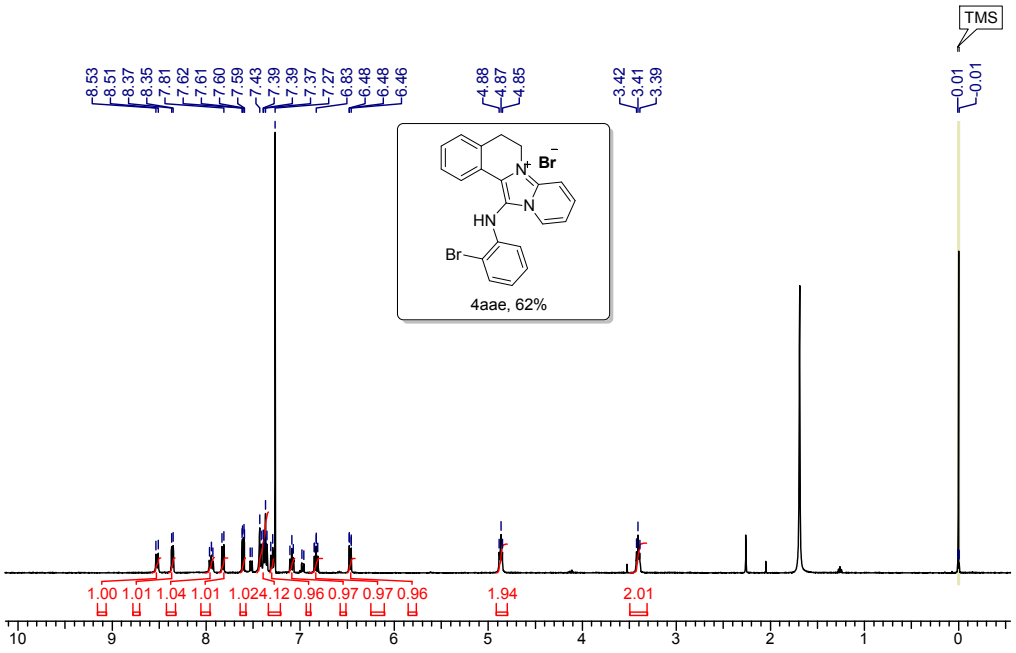
^{13}C NMR (100 MHz) spectrum of compound **4cha** in $CDCl_3$



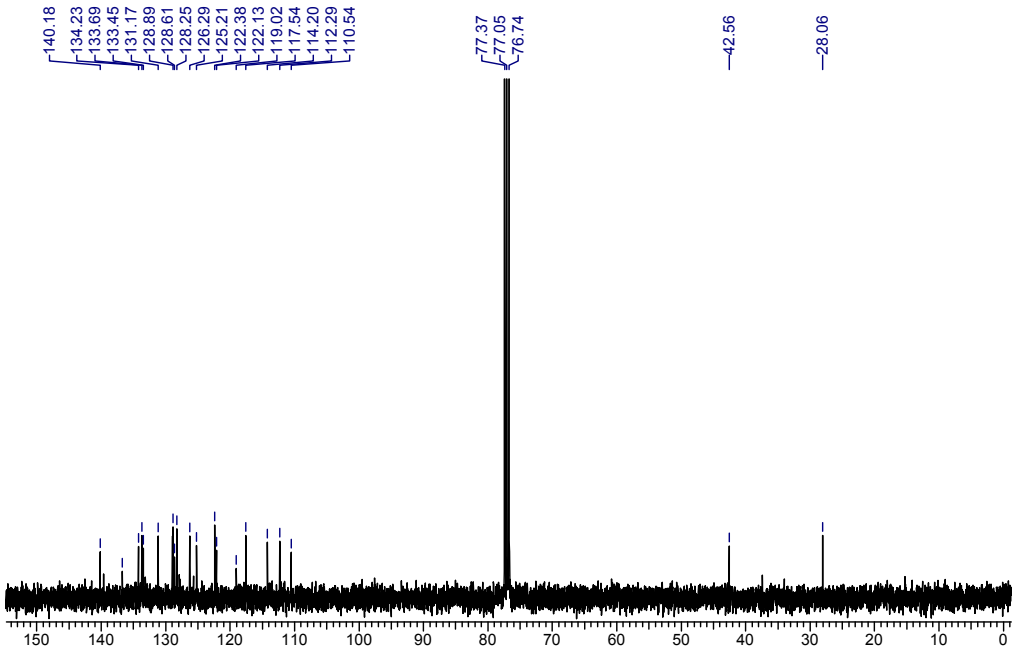
^{1}H NMR (400 MHz) spectrum of compound **4cda** in $CDCl_3$



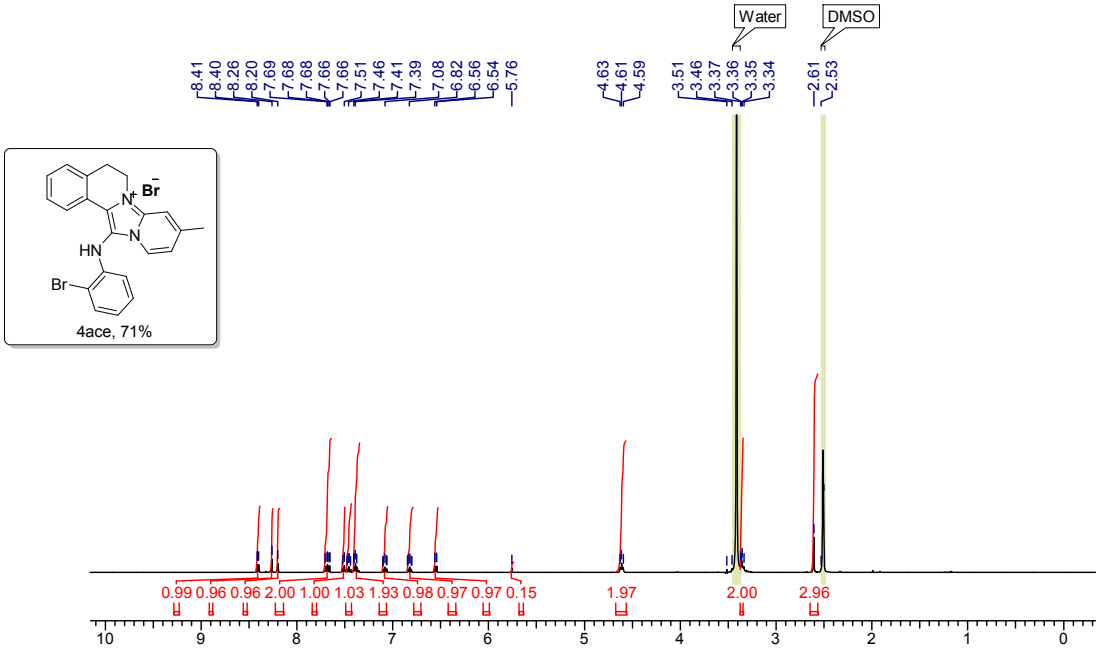
^{13}C NMR (100 MHz) spectrum of compound **4cda** in $CDCl_3$



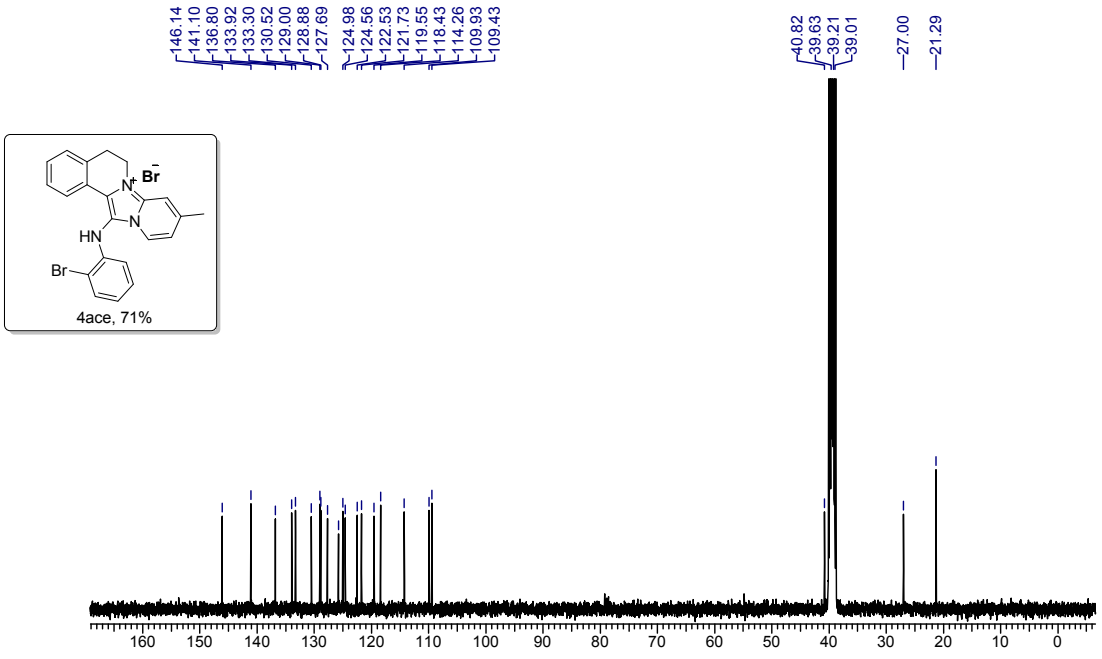
^{1}H NMR (400 MHz) spectrum of compound **4aae** in $CDCl_3$



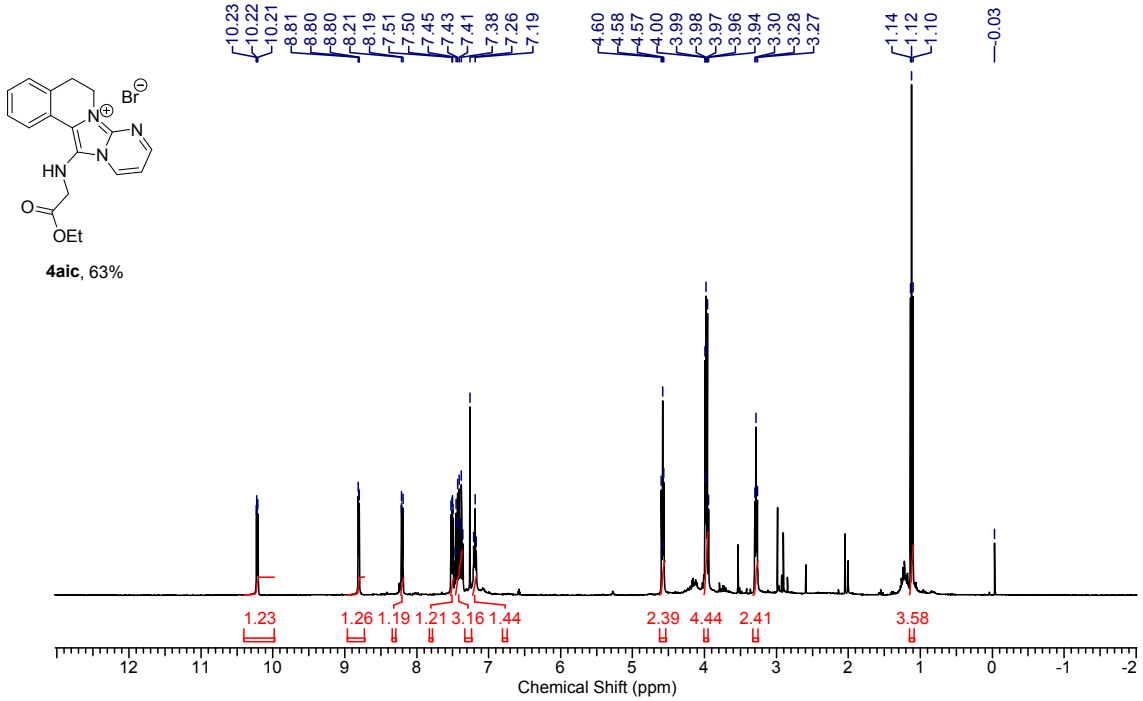
^{13} C NMR (100 MHz) spectrum of compound **4aae** in $CDCl_3$



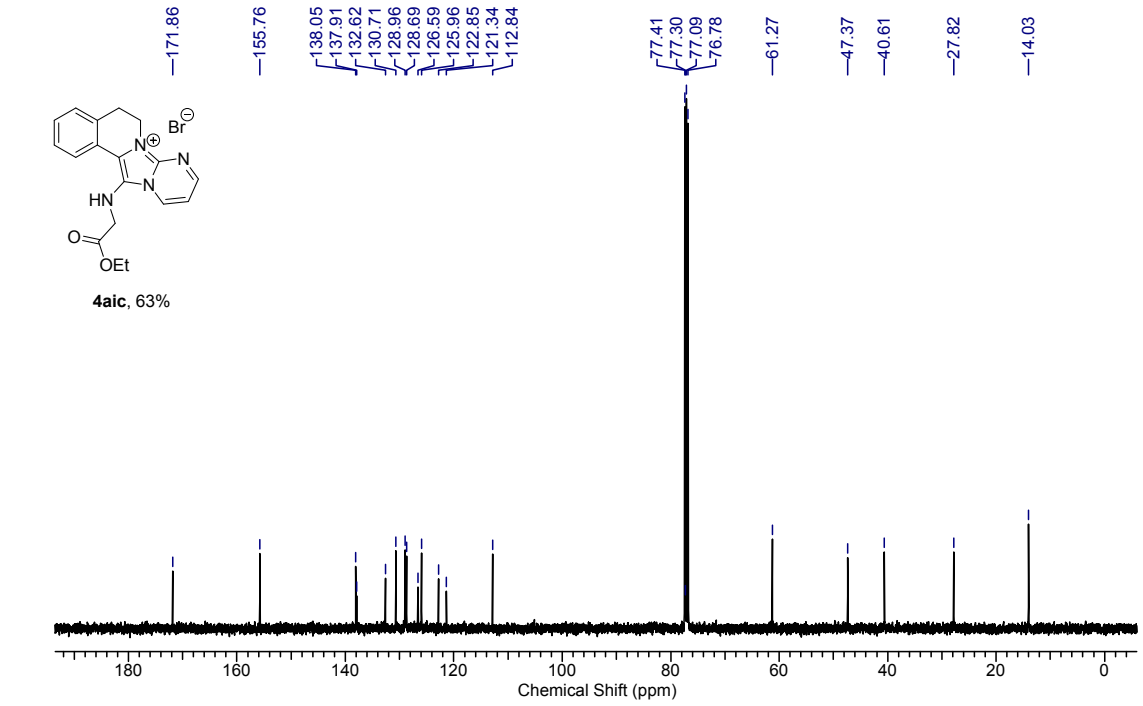
^{1}H NMR (400 MHz) spectrum of compound **4ace** in DMSO-d_6



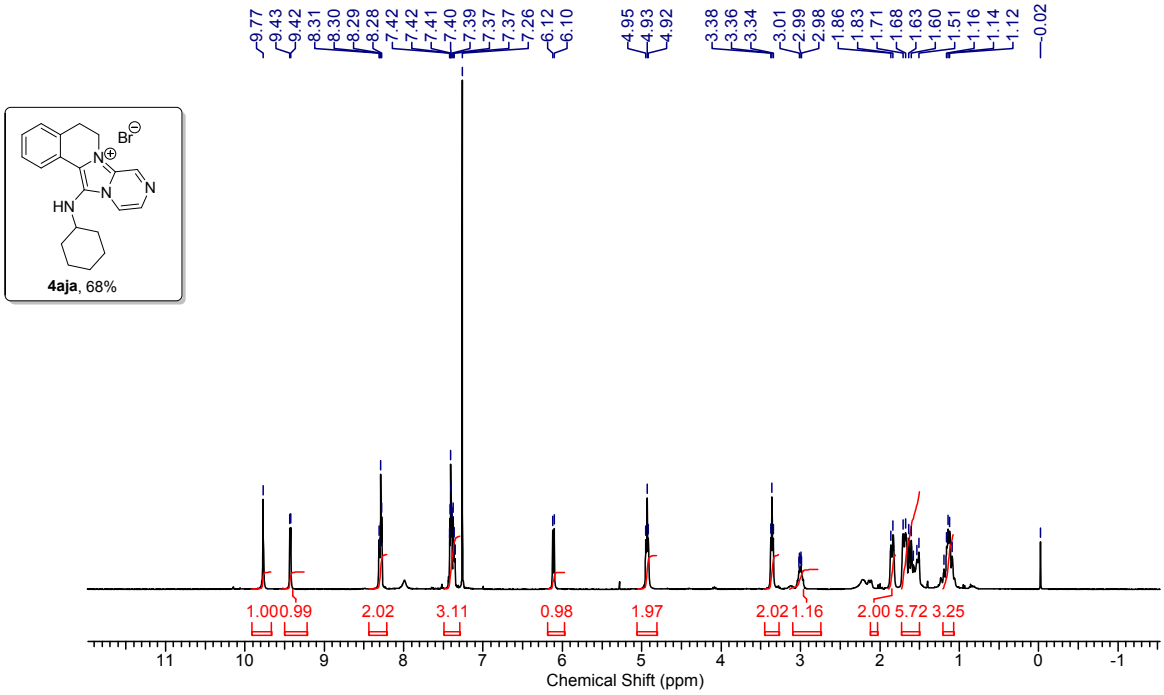
^{13}C NMR (100 MHz) spectrum of compound **4ace** in DMSO-d_6



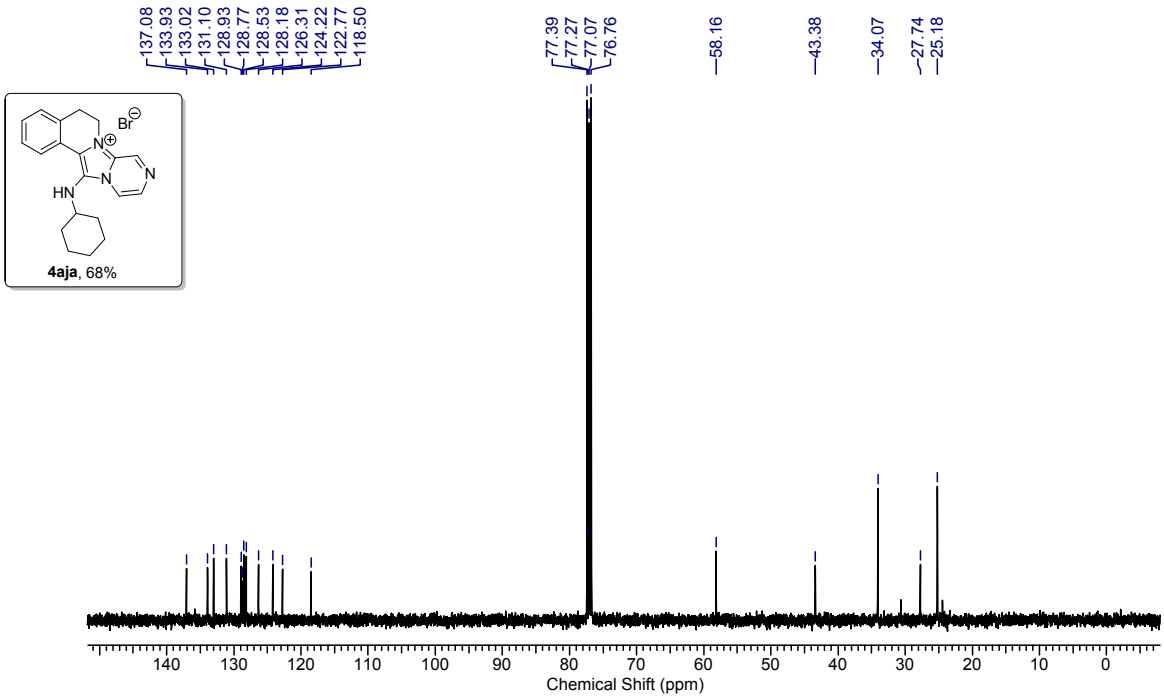
^{1}H NMR (400 MHz) spectrum of compound **4aic** in $CDCl_3$



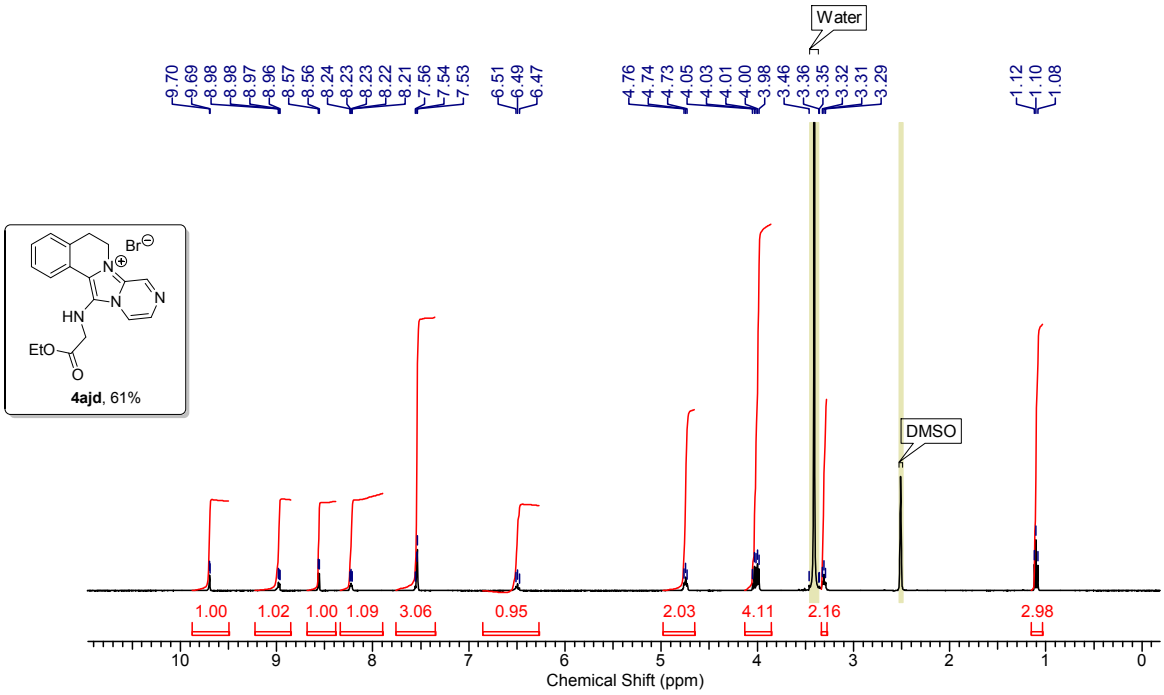
^{13}C NMR (100 MHz) spectrum of compound **4aic** in $CDCl_3$



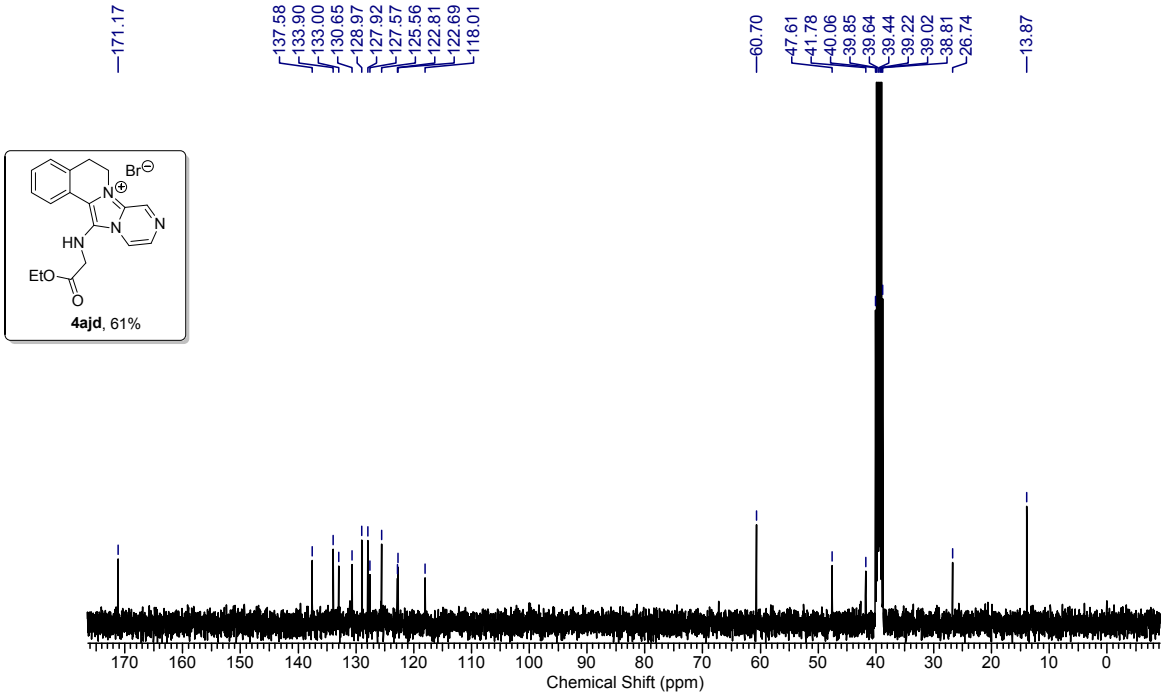
^{1}H NMR (400 MHz) spectrum of compound **4aja** in $CDCl_3$



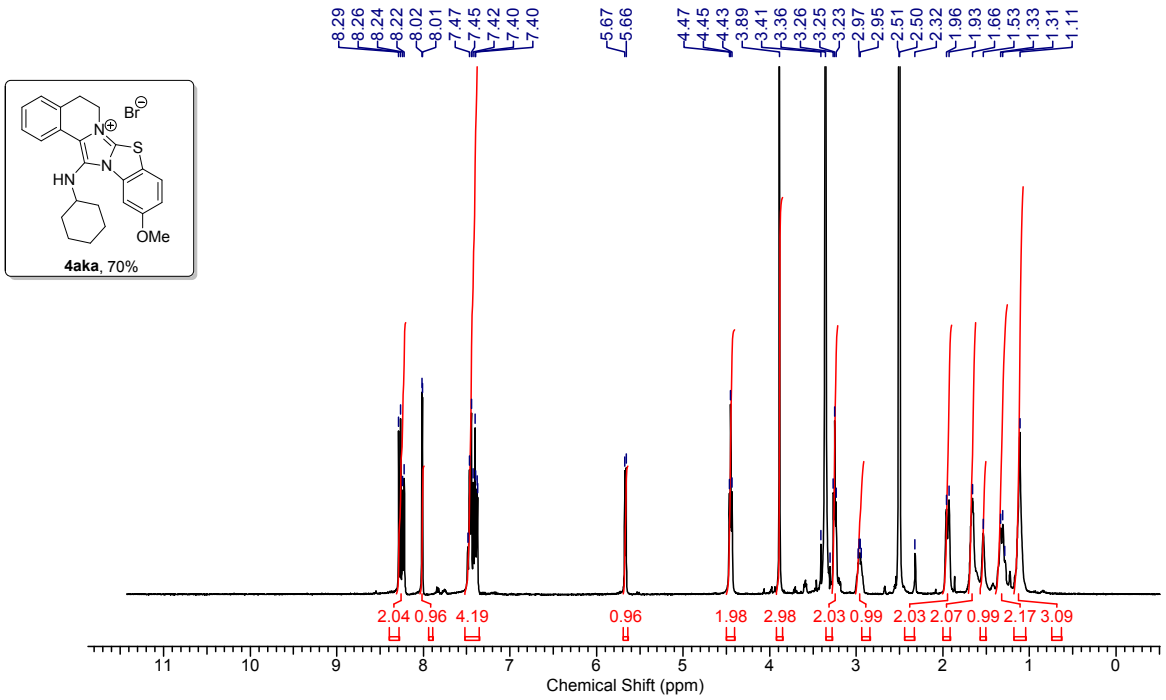
^{13}C NMR (100 MHz) spectrum of compound **4aja** in $CDCl_3$



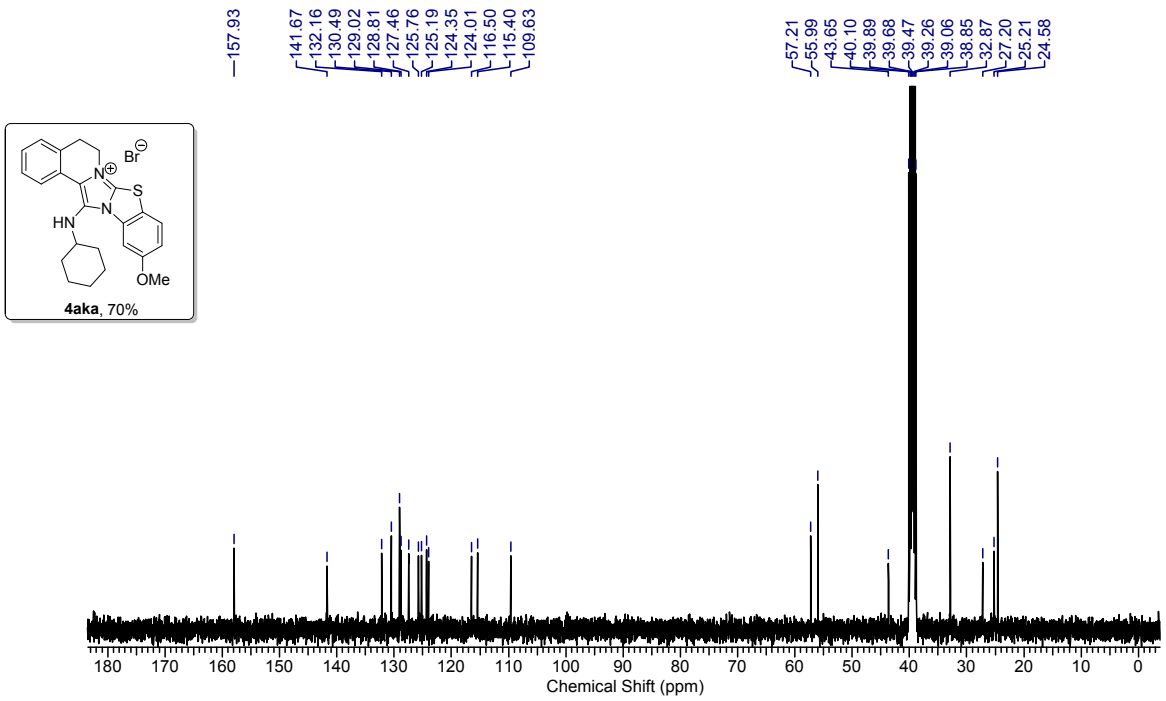
^{1}H NMR (400 MHz) spectrum of compound **4ajd** in DMSO-d_6



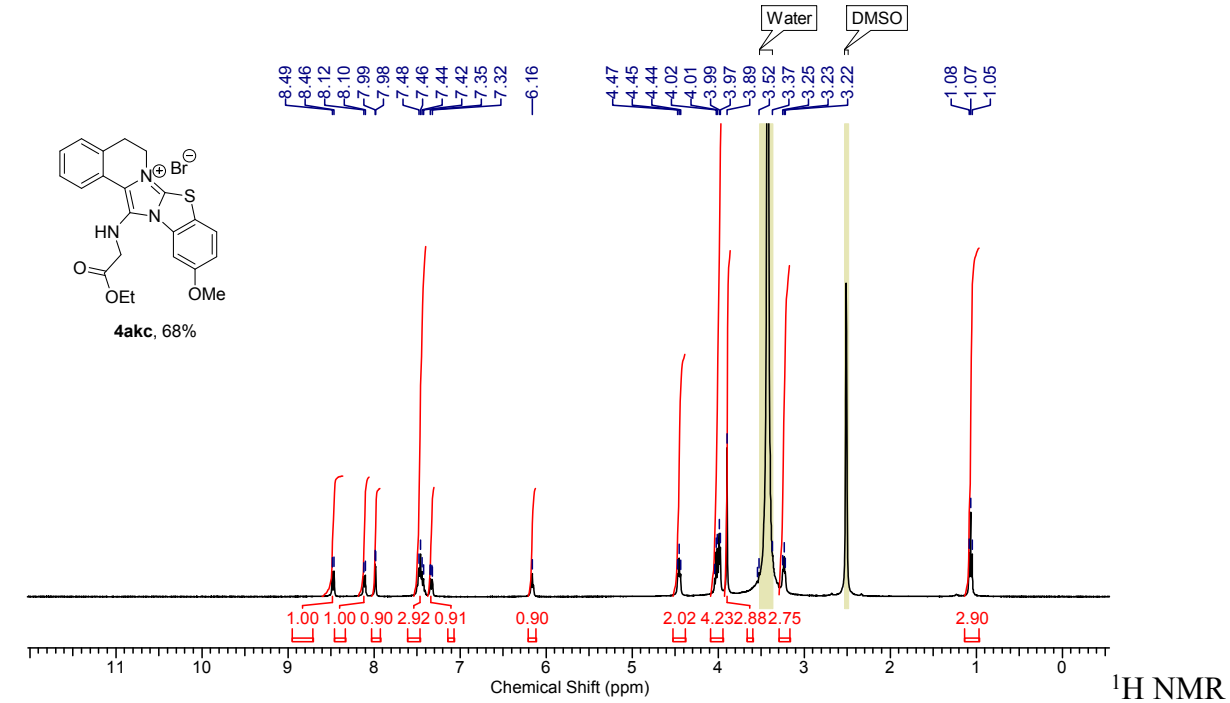
^{13}C NMR (100 MHz) spectrum of compound **4ajd** in DMSO-d_6



^{1}H NMR (400 MHz) spectrum of compound **4aka** in $CDCl_3$

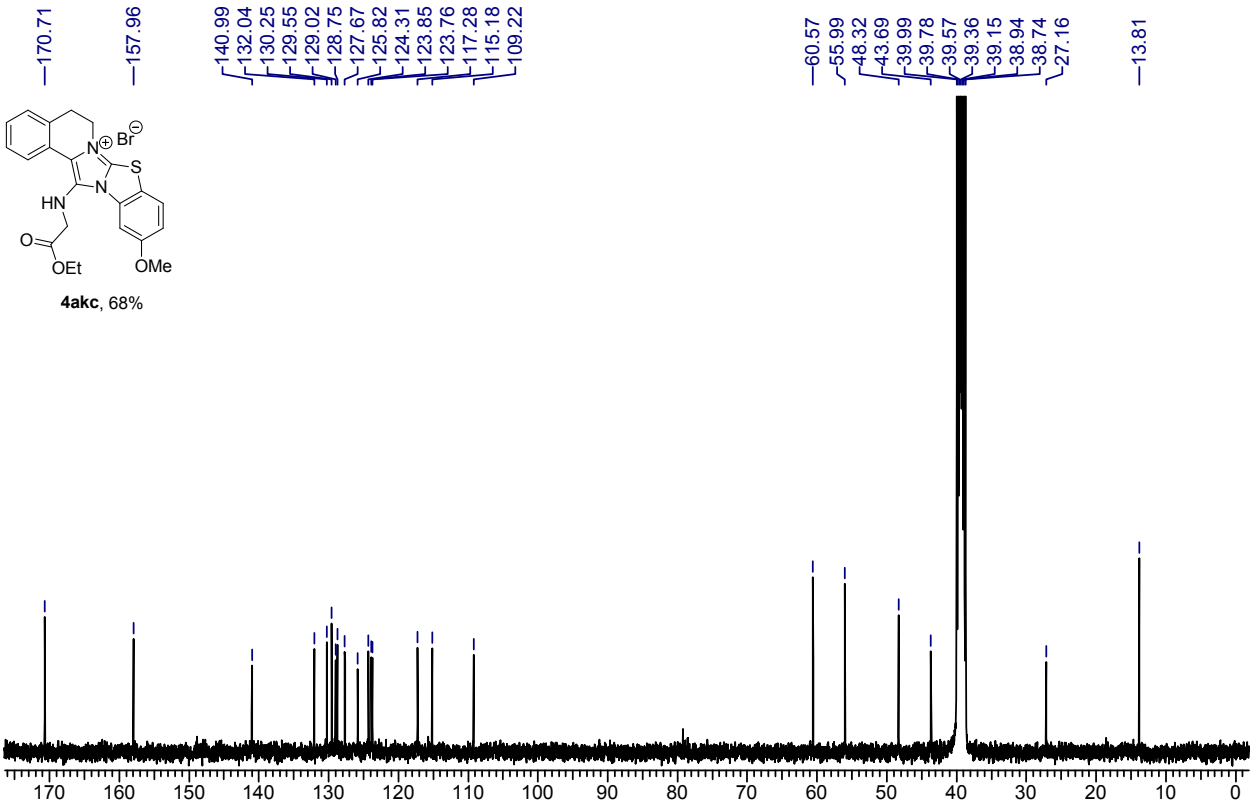


^{13}C NMR (100 MHz) spectrum of compound **4aka** in $CDCl_3$



4akc, 68%

^{1}H NMR (400 MHz) spectrum of compound **4akc** in DMSO-d_6



4akc, 68%

^{13}C NMR (100 MHz) spectrum of compound **4akc** in DMSO-d_6