Oxalic/ Malonic Acids as Carbon Building Block for Benzazoles, Quinazoline and Quinazolinones Synthesis

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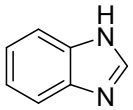
A. Methods and Materials

Reagents for synthesis were purchased from Sigma Aldrich and Loba-chemie, CDH, TCI, Silica gel (60-120) for column chromatography purchased from Sd Fine-chem Ltd. All solvents were used without further purification. Thin layer chromatography was performed using pre-coated silica gel plates 60 F254 (Merck) in UV light detector. ^{1}H and ^{13}C NMR spectra were recorded using a BrukerAvance 300 and 600 spectrometer operating at300 MHz (^{1}H) and 75 MHz (^{13}C)/ 600 MHz (^{1}H) and 150 MHz (^{13}C) respectively. Spectra were recorded at 25 °C in $CDCl_3$ [residual $CHCl_3$ (δ_H 7.26 ppm) or $CDCl_3$ (δ_C 77.00 ppm), DMSO-d_6 (δ_H 2.50 and 2.80 ppm) or (δ_C 39.5 ppm) and CD_3OD (δ_H 3.33 and 4.88 ppm) or CD_3OD (δ_C48.00 ppm) as international standard] with TMS as internal standard. Chemical shifts were recorded in δ (ppm) relative to the TMS and NMR solvent signal, coupling constants (*J*) are given in Hz and multiplicities of signals are reported as follows: s, singlet; d, doublet; dd, double doublet; t, triplet; m, multiplet. ESI-MS spectra were analysed using micromass Q-TOF ultima spectrometer.

General procedure for the formation of derivatives of 1*H*-Benzimidazole

1*H*-Benzoimidazole[1a] (2a)



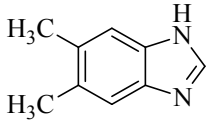
1,2-Phenylenediamine (100 mg, 0.9259 mmol), oxalic acid dihydtrate (583, 4.6295 mmol) and 1, 4-dioxane (2 mL) as a solvent were taken in a reaction tube and heated at 120 °C on magnetic stirrer for 6 hours. The progress of the reaction was monitored by TLC. On completion of the reaction, saturated solution of sodium bicarbonate (1 mL) was added in reaction mixture and organic part extracted with ethyl acetate (3x3 mL) and dried over anhydrous Na_2SO_4. After evaporation of the combined organic layer, organic part was washed with EtOA:Hexane (50:50) (6 mL) solution afforded 1*H*-benzimidazole (**2a**) as white solid (107 mg, 98%) and NMR data compared with literature.

^{1}H NMR (300 MHz; $CDCl_3$: DMSO-d_6) δ 6.62-6.65 (m, 2H), 7.03 (s, 2H), 7.51 (s, 1H)

^{13}C NMR (75 MHz; $CDCl_3$: DMSO-d_6) δ120.48, 139.89.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_7H_7N_2$ is 119.0609 obsd. = 119.0609.

5,6-Dimethyl-1*H*-benzoimidazole[1a] (2b) (Table 2, entry 1)



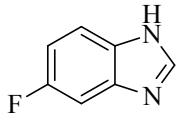
The above compound was prepared according to the general procedure described for **2a** starting from 4,5-dimethylbenzene-1,2-diamine (100 mg, 0.7352 mmol), oxalic acid dihydtrate (463 mg, 3.676 mmol) gave, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2b**) as yellow solid (99 mg, 92%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.36 (s, 6H), 7.36 (s, 2H), 8.01 (s, 1H).

^{13}C NMR (600 MHz; CD_3OD) δ 19.18, 114.95, 131.74, 136.18, 140.36.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_9H_{11}N_2$ is 147.0922 obsd. = 147.0925.

5-Fluoro-1*H*-benzoimidazole[1a] (2c) (Table 2, entry 2)

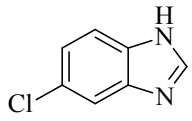


The above compound was prepared according to the general procedure described for **2a**starting from 4-fluororbenzene-1,2-diamine (100 mg, 0.7936 mmol), oxalic acid dihydtrate (600 mg, 4.7616 mmol) and heated at 120 ^{o}C for 2 hours, after purification by column chromatography with EtOAc:Hexane (40:60) solution to afford the product (**2c**) as yellow solid (100 mg, 93%) and NMR data compared with literature.

^{1}H NMR (300 MHz; $CDCl_3$) δ7.03-7.09 (t, *J* = 9.10 Hz, 1H), 7.33 (d, *J* = 7.44 Hz, 1H), 7.58 (m, 1H), 8.12 (s, 1H).

^{13}C NMR (75 MHz; $CDCl_3$) δ 101.27 (*J* = 26.25 Hz), 111.42 (*J* = 25.5 Hz), 116.27 (*J* = 11.25 Hz), 134.24, 137.53, 141.49, 158.25, 161.42.

5-Chloro-1*H*-benzoimidazole[1a] (2d) (Table 2, entry 3)



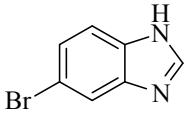
The above compound was prepared according to the general procedure described for **2a** starting from 4-chlorobenzene-1, 2-diamine (100 mg, 0.7017 mmol), oxalic acid dihydtrate (354 mg, 2.8068 mmol) gave, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2d**) as yellow solid (102 mg, 95%) and NMR data compared with literature.

^{1}H NMR (300 MHz; $CDCl_3$) δ 7.26 (s, 1H), 7.55-7.64 (m, 1H), 8.14 (s, 1H), 8.89 (s, 1H).

^{13}C NMR (75 MHz; $CDCl_3$) δ 115.33, 116.34, 123.61, 128.68, 136.35, 138.30, 141.67.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_7H_6ClN_2$ is 153.0220 obsd. = 153.0469.

5-Bromo-1*H*-benzoimidazole[1a] (2e) (Table 2, entry 4)



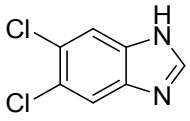
The above compound was prepared according to the general procedure for **2a** starting from 4-bromobenzene-1, 2-diamine (100 mg, 0.5347 mmol), oxalic acid dihydtrate (269 mg, 2.1388 mmol) gave, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2e**) as brown solid (89 mg,85%) and NMR data compared with literature.

^{1}H NMR (600 MHz; $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.82 (s, 1H), 8.07 (s, 1H).

^{13}C NMR (150 MHz; $CDCl_3$) δ 116.18, 126.35, 141.10.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_7H_6BrN_2$ is 196.9714 obsd. = 196.9443.

5,6-Dichloro-1*H*-benzoimidazole[1a] (2f) (Table 2, entry 5)



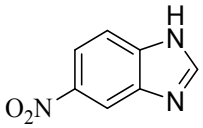
The above compound was prepared according to the general procedure described for **2a** starting from 4,5-dichlorobenzene-1,2-diamine (100 mg, 0.5649 mmol), oxalic acid dihydtrate (427 mg, 3.3894 mmol) gave, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2f**) as yellow solid (95 mg,90%) and NMR data compared with literature.

^{1}H NMR (300 MHz; DMSO-*d6*) δ 7.87 (s, 2H), 8.34 (s, 1H).

^{13}C NMR (75 MHz; DMSO-*d6*) δ 125.80, 126.60, 144.15, 163.86.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_7H_5Cl_2N_2$ is 186.9830 obsd. = 186.9820.

5-Nitro-1*H*-benzoimidazole[1a] (2g) (Table 2, entry 6)



The above compound was prepared according to the general procedure described for **2a** starting from 4-nitrobenzene-1 2-diamine (100 mg, 0.6535mmol), oxalic acid dihydtrate

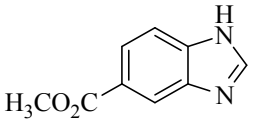
(329 mg, 2.614mmol) and heated at 120 ^{o}C for 8 hours, after washing the organic part with EtOAc:Hexane (60:40) solution to afford the product (**2g**) as yellow solid (90 mg,85%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 7.67 (d, J = 8.88 Hz, 1H), 8.13-8.14 (dd, J_1 = 8.88 Hz, J_2 = 2.1 Hz, 1H), 8.42 (s, 1H), 8.48 (s, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ 118.30, 144.08, 146.07.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_7H_6N_3O_2$is 164.0460 obsd. = 164.0458.

5-Methylester-1*H*-benzoimidazole[1a] (2h) (Table 2, entry 7)



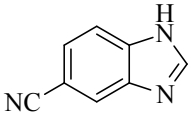
The above compound was prepared according to the general procedure described for **2a** starting from methyl 3,4-diaminobenzoate (100 mg, 0.6024mmol), oxalic acid dihydtrate (304 mg, 2.4096mmol) gave, after washing the organic part with EtOAc:Hexane (10:90) solution to afford the product (**2h**) as yellow solid (90 mg,85%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 3.92 (s, 3H), 7.64 (d, J = 8.52 Hz, 1H), 7.95 (d, J = 8.52 Hz, 1H), 8.32 (s, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ 51.60, 124.11, 124.87, 144.12, 167.98.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_9H_9N_2O_2$is 177.0664 obsd. 177.0659.

1*H*-Benzoimidazole-5-carbonitrile[1b] (2i) (Table 2, entry 8)



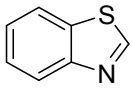
The above compound was prepared according to the general procedure described for **2a** starting from 5-cyanobenzene-1,2-diamine (100 mg, 0.7519 mmol), oxalic acid dihydtrate (379 mg, 3.0076 mmol) and heated at 120 ^{o}C for 8 hours, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2h**) as yellow solid (93 mg, 87%) and NMR data compared with literature.

^{1}H NMR (300 MHz; DMSO-*d6*) δ 7.58-7.60 (m, 1H), 7.75 (d, J = 8.28 Hz, 1H), 8.14 (s, 1H), 8.45 (s, 1H).

^{13}C NMR (75 MHz; DMSO-*d6*) δ 103.96, 120.06, 125.48, 145.31.

ESI-MS (m/z): [M+H]+calcd. for $C_8H_6N_3$ is 144.0562 obsd. 144.0562.

1*H*-Benzothiazole[1a] (2j) (Table 2, entry 9)

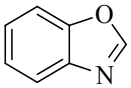


The above compound was prepared according to the general procedure described for **2a** starting from 2-amino benzothiazole (100 mg, 0.800 mmol), oxalic acid dihydtrate (403 mg, 3.2 mmol) gave, after washing the organic part with EtOAc/Hexane (10:90) solution to afford the product (**2j**) as white solid (86mg,80%) and NMR data compared with literature.

^{1}H NMR (600 MHz; $CDCl_3$) δ 7.43-7.45 (t, *J* = 6.0 Hz, 1H), 7.51-7.53 (t, *J* = 6.0 Hz, 1H), 7.95 (d, *J* = 12 Hz, 1H), 8.14 (d, *J* = 6.0 Hz, 1H), 8.99 (s, 1H).

^{13}C NMR (150 MHz; $CDCl_3$) δ 121.83, 123.59, 125.49, 126.12, 133.65, 153.20, 153.84.

1*H*-Benzoxazole[1a] (2k) (Table 2, entry 10)

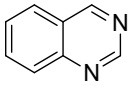


The above compound was prepared according to the general procedure described for **2a** starting from 2-aminophenol (100 mg, 0.9174 mmol), oxalic acid dihydtrate (462 mg, 3.6696 mmol) gave, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2j**) as yellow solid (85 mg, 78%) and NMR data compared with literature.

^{1}H NMR (600 MHz; DMSO-*d6*) δ 6.74-7.77 (m, 1H), 6.86-6.87 (m, 1H), 6.90-6.93 (m, 1H), 8.00 (d, *J* = 8.04 Hz, 1 H), 8.28 (s, 1H).

^{13}C NMR (150 MHz; DMSO-*d6*) δ 115.08, 118.95, 120.80, 124.16, 125.95, 146.71, 159.98.

Quinazoline[1c] (2l) (Table 2, entry 11)

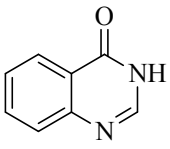


The above compound was prepared according to the general procedure described for **2a** starting from 2-aminobenzylamine (100 mg, 0.8197 mmol), oxalic acid dihydtrate (413 mg, 3.2788mmol) gave, after washing the organic part with EtOAc:Hexane (50:50) solution to afford the product (**2k**) as yellow solid (90 mg, 85%) and NMR data compared with literature.

^{1}H NMR (600 MHz; $CDCl_3$) δ 7.66-7.69 (m, 1H), 7.92-7.95 (m, 2H), 8.05-8.06 (t, *J* = 8.4 Hz, 1H), 9.33 (s, 1H), 9.41 (s, 1H).

^{13}C NMR (150 MHz; $CDCl_3$) δ 125.13, 127.22, 127.95, 128.44, 134.21, 150.05, 155.30, 160.24.

Quinazolin-4(3*H*)-one[2a] (4a) (Table 3, entry 1)

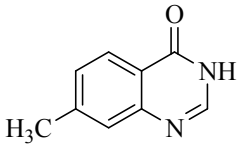


The above compound was prepared according to the general procedure described for **2a** starting from 2-aminobenzamide (100 mg, 0.7352 mmol), oxalic acid dihydtrate (371 mg, 2.9408 mmol) and heated at 120 ^{o}C for 14 hours, after washing the organic part with EtOAc:Hexane (10:90) solution to afford the product (**4a**) as white solid (91 mg, 85%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 7.54-7.57 (t, *J* = 7.56 Hz, 1H), 7.69 (d, *J* = 8.16 Hz, 1H), 7.82-7.83 (t, *J* = 8.34 Hz, 1H), 8.09 (s, 1H), 8.22 (d, *J* = 7.98 Hz, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ 122.77, 126.26, 126.83, 127.47, 134.95, 145.43, 148.71, 162.32.

7-Methylquinazolin-4(3*H*)-one[2a] (4b) (Table 3, entry 2)



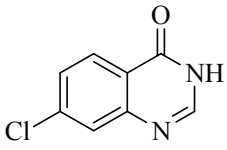
The above compound was prepared according to the general procedure described for **2a** starting from 2-amino-4-methylbenzamide (100 mg, 0.6667 mmol), oxalic acid dihydtrate (336 mg, 2.6668 mmol) and heated at 120 ^{o}C for 16 hours, after column chromatography with EtOAc:Hexane (30:70) solution to afford the product (**4b**) as white solid (95 mg, 89%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.54 (s, 3H), 7.40 (d, *J* = 16.0 Hz, 1H), 7.52 (s, 1H), 8.08 (s, 1H), 8.12 (d, *J* = 16.0 Hz, 1H).

^{13}C NMR (75 MHz; DMSO-d_6) δ 20.92, 120.21, 126.03, 126.42, 128.79, 145.11, 146.21, 148.64.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_9H_9N_2O$ is 161.0715 obsd. 161.0720.

7-Chloroquinazolin-4(3*H*)-one[2b] (4c) (Table 3, entry 3)



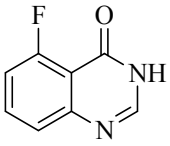
The above compound was prepared according to the general procedure described for **2a** starting from 2-amino-4-chlorobenzamide (100 mg, 0.5861 mmol), oxalic acid dihydtrate (295 mg, 2.3444 mmol) and heated at 120 ^{o}C for 14 hours, after column

chromatography with EtOAc:Hexane (30:70) solution to afford the product (**4c**) as white solid (88 mg, 83%) and NMR data compared with literature.

^{1}HNMR (600 MHz; CD_3OD) δ7.52-7.54 (m, 1H), 7.69 (d, *J* = 1.98 Hz, 1H), 8.10 (s, 1H), 8.17 (d, *J* = 8.58 Hz, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ 121.55, 126.42, 127.78, 128.07, 140.82, 146.76, 149.97, 161.56.

5-Fluoroquinazolin-4(3*H*)-one[2a] (4d) (Table 3, entry 4)



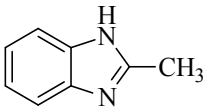
The above compound was prepared according to the general procedure described for **2a** starting from 2-amino-6-fluorobenzamide (100 mg, 0.6494 mmol), oxalic acid dihydtrate (327 mg, 2.5964 mmol) and heated at 120 °C for 20 hours, after column chromatography with EtOAc/Hexane (30:70) solution to afford the product(**4d**) as white solid (87 mg, 82%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ7.20-7.23 (m, 1H), 7.49 (d, J = 6.0 Hz, 1H), 7.76-7.80 (m, 1H), 8.06 (s, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ112.36 (d, *J* = 7.5 Hz), 113.63 (d, *J* = 21.00 Hz), 122.96, 135.44 (d, *J* = 10.5 Hz), 146.35, 150.91, 160.64, 162.38.

General procedure for the formation of derivatives of 2-methyl-1*H* benzimidazole

2-Methyl-1*H*-benzoimidazole[3a](5a) (Table 4, entry 1)



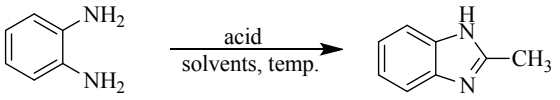
Mixture of 1,2-phenylenediamine (100 mg, 0.9259), malonic acid (578 mg, 5.5554 mmol) and 1, 4-dioxane (2 mL) as a solvent were taken in a reaction tube and heated at 120 °C on magnetic stirrer for 6 hours. The progress of the reaction was monitored by TLC. On completion of the reaction, saturated sodium bicarbonate solution (2 mL) was added in reaction mixture and organic part extracted with ethyl acetate (3x3 mL) and dried over anhydrous Na_2SO_4. After evaporation of the combined organic layer, organic part was washed with solution of EtOAc:Hexane (50:50) (6 mL) and afforded 2-methyl-1*H*benzimidazole (**5a**) as white solid (116 mg, 95%) NMR data compared with literature.

^{1}H NMR (600 MHz; $CDCl_3$) δ 2.67 (s, 3H), 7.23 (d, *J* = 6.0 Hz, 2H), 7.57 (d, *J*= 6.0 Hz, 2H).

^{13}C NMR (150 MHz; $CDCl_3$) δ 14.93, 114.50, 122.15, 138.75, 151.49.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_9N_2$ is 133.0766 obsd. 133.0755.

Table S1 Screening for the synthesis of 2-methyl-1*H*-benzimidazole

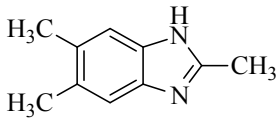


1a **5a**

Entry	Solvent	Temp. (°C)	Time (h)	Yield[b] (%)
1	1,4-dioxane	80	6	40
2	1,4-dioxane	100	6	60
3	1,4-dioxane	120	6	80
4	**1,4-dioxane**	**120**	**6**	**95**
5	1,4-dioxane	120	8	97
6	PEG-400	120	6	85
7	ACN	120	6	87

[a]Reaction conditions: 1,2-phenylenediamine (1 equiv.) malonic acid (6 equiv.), 1,4-dioxane (2 ml) and time 6 hours. [b]isolated yields.

2,5,6-Trimethyl-1*H*-benzoimidazole[3a] (5b) (Table 4, entry 2)



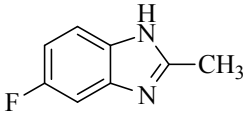
The above compound was prepared according to the general procedure described for **5a** starting from 4,5-dimethylbenzene-1,2-diamine (100 mg, 0.7352mmol), malonic acid (382 mg, 3.676mmol) gave, after column chromatography with EtOAc:Hexane (70:30) solution to afford the product (**5b**) as yellow solid (96 mg, 82%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.30 (s, 6H), 2.49 (s, 3H), 7.21 (s, 2H).

^{13}C NMR (150 MHz; CD_3OD) δ 13.21, 19.33, 114.31, 130.94, 137.14, 150.90.

ESI-MS (m/z): $[M+H]^+$calcd. For $C_{10}H_{13}N_2$ is 161.1079 obsd. 161.1072.

5-Fluoro-2-methyl-1*H*-benzoimidazole (5c) (Table 4, entry 3)



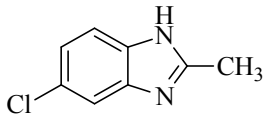
The above compound was prepared according to the general procedure described for **5a** starting from 4-fluorobenzene-1, 2-diamine (100 mg, 0.7936 mmol), malonic acid (495 mg, 4.7616 mmol) gave, after column chromatography EtOAc:Hexane (70:30) solution to afford the product (**5c**) as yellow solid (109 mg, 92%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.51 (s, 3H), 6.88-6.94 (t, *J* = 8.1 Hz 1H), 7.12-7.15 (t, *J* = 7.2 Hz, 1H), 7.35-7.40 (m, 1H)

^{13}C NMR (150 MHz; CD_3OD) δ 13.33, 100.12 (d, *J* = 45 Hz), 108.63, 109.78 (d, *J* = 51 Hz), 114.67 (d, *J* = 19.5 Hz), 135.09, 138.91 (d, *J* = 24 Hz), 153.37, 158.10, 161.23.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_8FN_2$is 151.0672 obsd. 151.0679.

5-Chloro-2-methyl-1*H*-benzoimidazole[3a] (5d) (Table 4, entry 4)



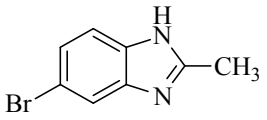
The above compound was prepared according to the general procedure described for **5a** starting from 4-chlorobenzene-1, 2-diamine (100 mg, 0.7017 mmol), malonic acid (438 mg, 4.2102 mmol) gave, after column chromatography with EtOAc/Hexane (70:30) solution to afford the product (**5d**) as yellow solid (110 mg, 94%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.54 (s, 3H), 7.15 (d, *J* = 9.0 Hz, 1H), 7.40 (d, *J* = 9.0 Hz, 1H), 7.45 (s, 1H).

^{13}C NMR (75 MHz; DMSO-d_6) δ 14.61, 114.53, 114.78, 121.20, 125.42, 152.95.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_8ClN_2$ is 167.0376 obsd. 167.0380.

5-Bromo-2-methyl-1*H*-benzoimidazole (5e) (Table 4, entry 5)



The above compound was prepared according to the general procedure described for **5a** starting from 4-bromobenzene-1, 2-diamine (100 mg, 0.5347 mmol), malonic acid (278 mg, 2.6735 mmol) gave, after column chromatography with EtOAc:Hexane (70:30)

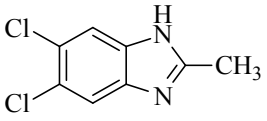
solution to afford the product (**5e**) as yellow solid(94 mg,83%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.55 (s, 3H), 7.26 (d, *J* = 1.8 Hz, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 7.61 (s, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ 13.32, 114.87, 115.39, 117.29, 125.13, 137.43, 140.21, 153.36.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_8BrN_2$ is 210.9871 obsd. 210.9870.

5,6-Dichloro-2-methyl-1*H*-benzoimidazole (5f) (Table 4, entry 6)



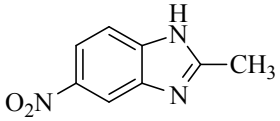
The above compound was prepared according to the general procedure described for **5a** starting from 4,5-dichlorobenzene-1, 2-diamine (100 mg, 0.5650 mmol), malonic acid (352 mg, 3.390 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) solution to afford the product (**5f**) as yellow solid (96 mg, 85%) and NMR data compared with literature.

^{1}H NMR (300 MHz; DMSO-*d6*) δ 2.49 (s, 3H), 7.70 (s, 2H).

^{13}C NMR (75 MHz; DMSO-*d6*) δ 14.61, 115.34, 115.68, 123.44, 138.36, 154.39.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_7Cl_2N_2$is 200.9986, obsd.200.9980.

2-Methyl-5-nitro-1*H*-benzoimidazole[3a] (5g) (Table 4, entry 7)



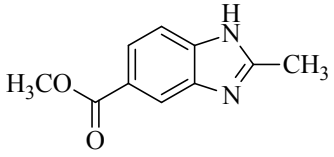
The above compound was prepared according to the general procedure described for **5a** starting from 4-nitrobenzene-1, 2-diamine (100 mg, 0.6535 mmol), malonic acid (408 mg, 3.9210 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) solution to afford the product (**5g**) as yellow solid (95 mg, 82%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.60 (s, 3H), 7.52 (d, *J* = 9.0 Hz, 1H), 8.06 (d, *J* = 9.0 Hz, 1H), 8.31 (s, 1H).

^{13}C NMR (150 MHz; CD_3OD) δ 13.91, 113.71, 117.47, 122.88-123.31, 143.21-143.73, 145.69, 156.68.

ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_8N_3O_2$is 178.0617, obsd. 178.0610.

Methyl 2-methyl-1*H*-benzoimidazole-5-carboxylate (5h) (Table 4, entry 8)



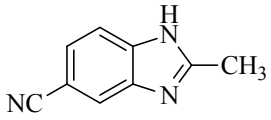
The above compound was prepared according to the general procedure described for **5a** starting from methyl-3,4-diaminobenzoate (100 mg, 0.6024 mmol), malonic acid (376 mg, 3.6144 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) solution to afford the product (**5h**) as yellow solid (105 mg, 92%)and NMR data compared with literature.

^{1}H NMR (300 MHz; DMSO-*d*$_6$) δ 2.53 (s, 3H), 3.85 (s, 3H), 7.52 (d, *J* = 8.37 Hz, 1H), 7.76 (s, 1H), 8.07 (s, 1H).

^{13}C NMR (75 MHz; DMSO-*d*$_6$) δ 14.64, 51.78, 122.26, 122.43, 142.56, 154.20, 154.69, 166.83

ESI-MS (m/z): $[M+H]^+$calcd. for $C_{10}H_{11}N_2O_2$is 191.0821, obsd. 191.0815.

2-Methyl-1*H*-benzoimidazole-5-carbonitrile (5i) (Table 4, entry 9)



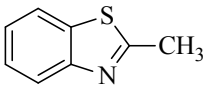
The above compound was prepared according to the general procedure described for **5a** starting from 4-nitrobenzene-1, 2-diamine (100 mg, 0.7518 mmol), malonic acid (469 mg, 4.5108 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) the product (**5i**) as white solid (106 mg, 90%) and NMR data compared with literature.

^{1}H NMR (300 MHz; DMSO-*d*$_6$) δ 2.53 (s, 3H), 7.46 (d, *J* = 8.22 Hz, 1H), 7.59 (d, *J* = 8.28 Hz, 1H), 7.97 (s, 1H).

^{13}C NMR (75 MHz; DMSO-*d*$_6$) δ 14.67, 102.82, 114.91, 119.62, 120.21, 124.67, 139.46, 141.56, 155.23.

ESI-MS (m/z): $[M+H]^+$calcd. for$C_9H_8N_3$ is 158.0718, obsd. 158.0711.

2-Methylbenzothiazole[3b] (5j) (Table 5, entry 10)



The above compound was prepared according to the general procedure described for **5a** starting from methyl-3,4-diaminobenzoate (100 mg, 0.8000 mmol), malonic

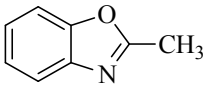
acid (333 mg, 3.2 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) the product (**5j**) as yellow solid (98 mg, 82%) and NMR data compared with literature.

^{1}H NMR (600 MHz; $CDCl_3$) δ 2.83 (s, 3H), 2.83 (s, 3H), 7.32-7.35 (m, 1H), 7.42-7.45 (m, 1H), 7.80 (dd, *J* = 7.98 Hz, 1H), 7.94 (d, *J* = 8.16 Hz, 1H).

^{13}C NMR (150 MHz; $CDCl_3$) δ 20.03, 121.32, 122.32, 124.62, 125.85, 135.59, 153.32, 166.88.

ESI-MS (m/z): $[M+H]^+$calcd. For C_8H_8NS is 150.0377, obsd.150.0360.

2-Methylbenzoxazole[3b] **(5k) (Table 4, entry 11)**



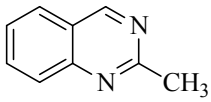
The above compound was prepared according to the general procedure described for **5a** starting from methyl-3,4-diaminobenzoate (100 mg, 0.9174 mmol), malonic acid (381 mg, 3.6696 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) the product (**5k**) as yellow solid (98 mg, 80%) and NMR data compared with literature.

^{1}H NMR (600 MHz; CD_3OD) δ 2.17 (s, 3H), 6.78-6.81 (m, 1H), 6.84-6.86 (m, 1H), 6.98-7.00 (m, 1H), 7.56-7.58 (m, 1H)

^{13}C NMR (75 MHz; DMSO-*d_6*) δ 23.61, 115.95, 118.98, 122.39, 124.66, 126.42, 147.90, 169.03.

ESI-MS (m/z): $[M+H]^+$calcd. forC_8H_8NO is 134.0606, obsd. 134.1182.

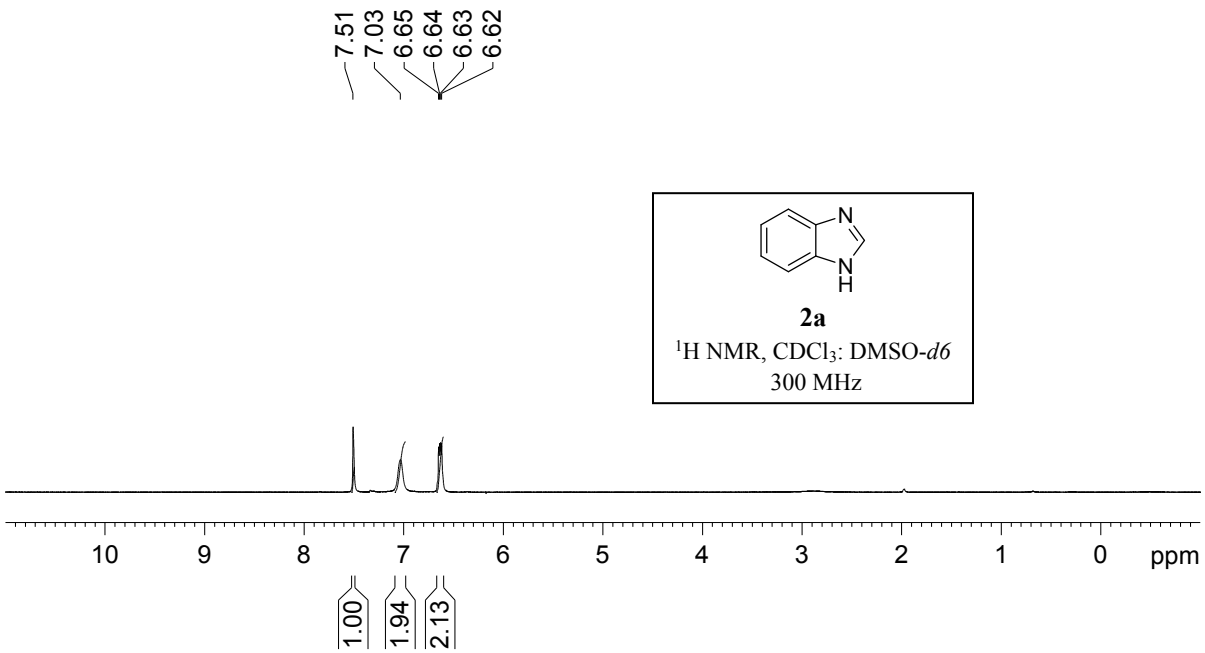
2-Methylquinazoline[3c] **(5l) (Table 4, entry 12)**

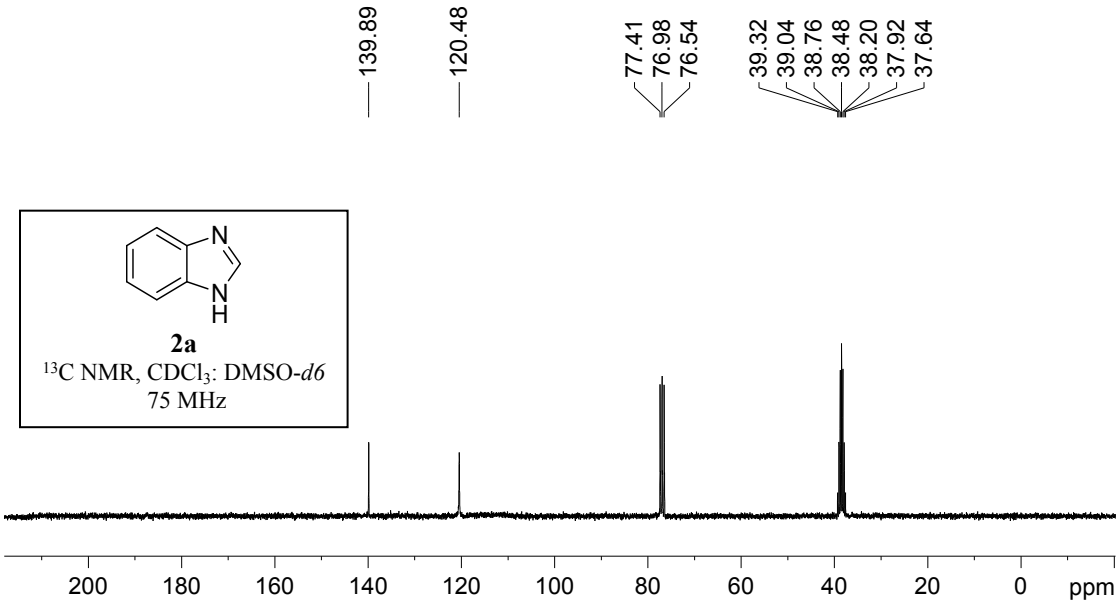


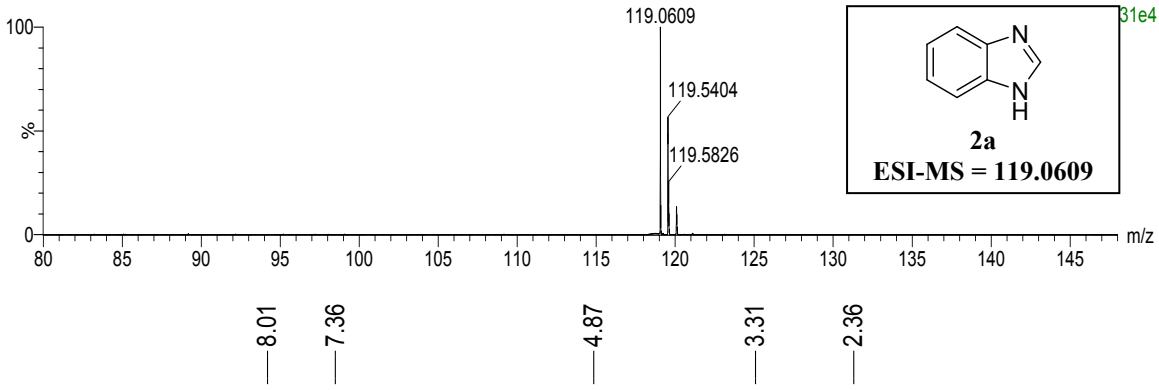
The above compound was prepared according to the general procedure described for **5a** starting from methyl-3,4-diaminobenzoate (100 mg, 0.8197 mmol), malonic acid (341 mg, 3.2788 mmol) gave, after column chromatography with EtOAc:Hexane (70:30) the product (**5l**) as yellow solid (88 mg, 75%) and NMR data compared with literature.

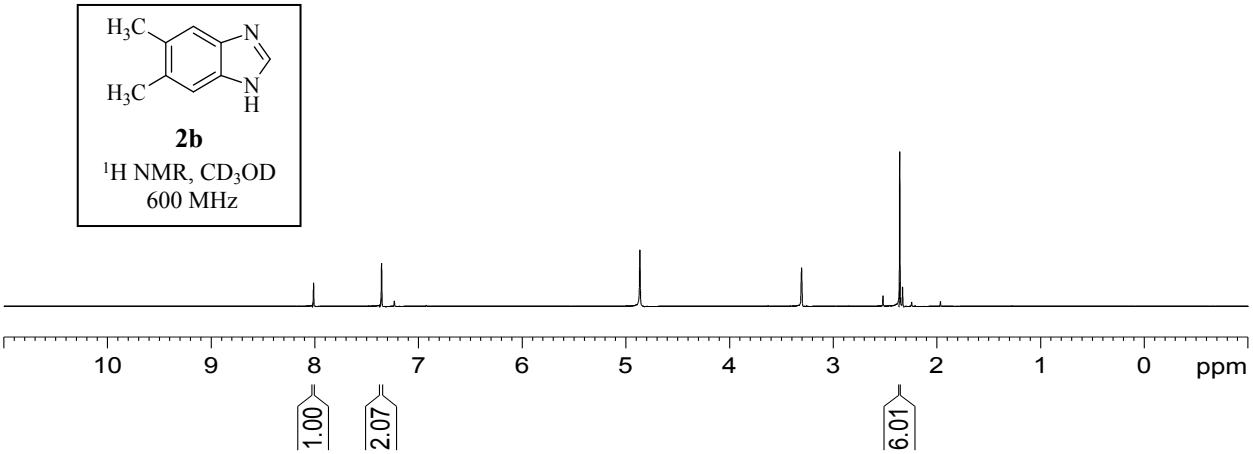
^{1}H NMR (600 MHz; $CDCl_3$) δ 2.69 (s, 3H), 7.16-7.18 (t, *J* = 7.5 Hz 1H), 7.57-7.69 (m, 3H), 8.38 (s, 1H).

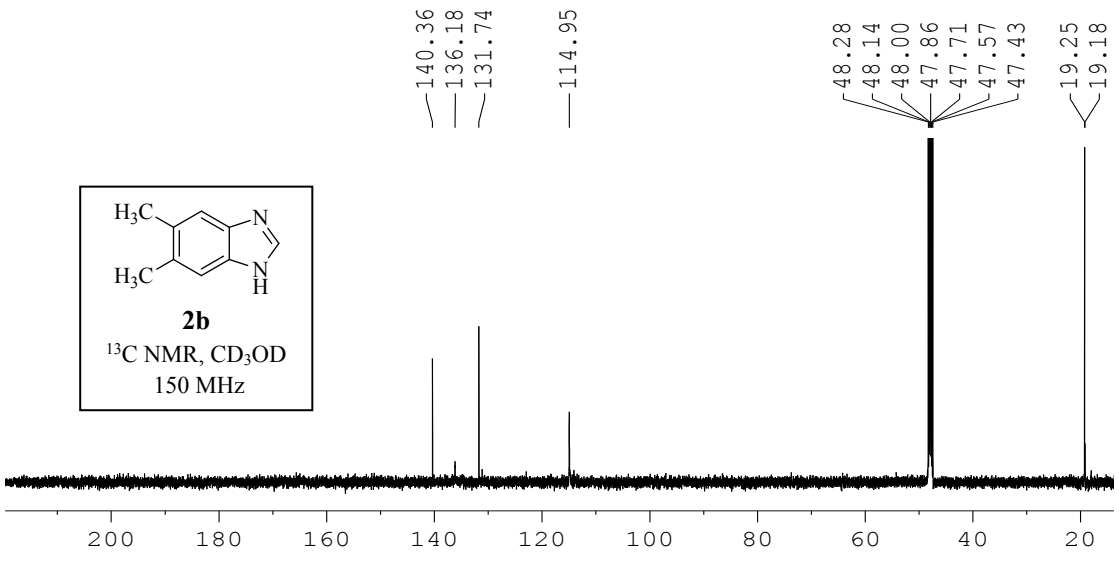
^{13}C NMR (150 MHz; $CDCl_3$) δ 24.71, 101.88, 116.37, 121.37, 124.13, 132.23, 134.19, 140.53, 168.56.

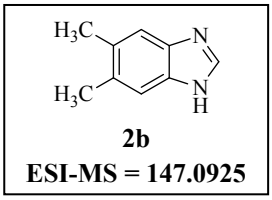

7.51
7.03
6.65
6.64
6.63
6.62
N
N
H
2a
1H NMR, CDCl3: DMSO-d6
300 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.94
2.13

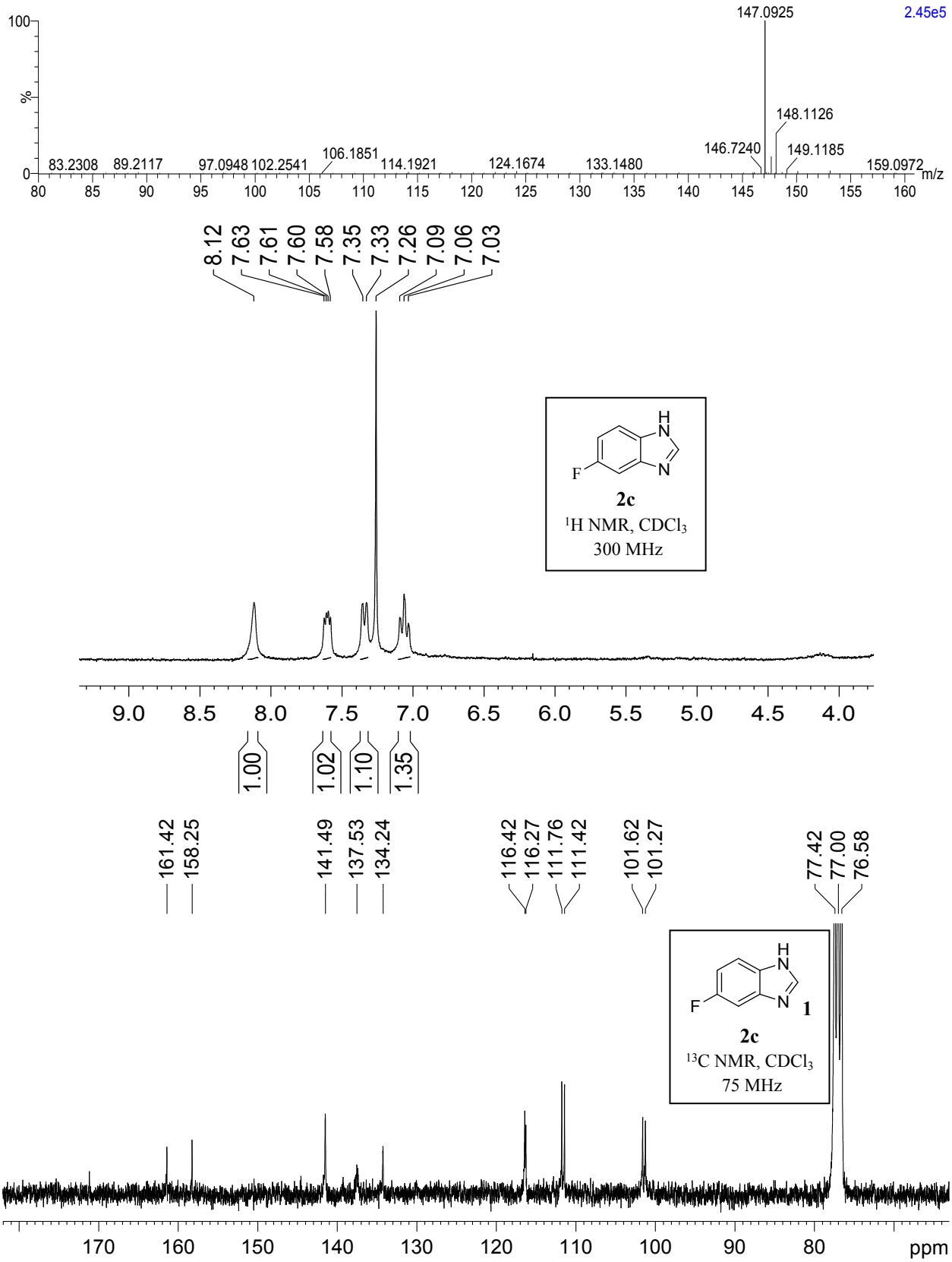

139.89
120.48
77.41
76.98
76.54
39.32
39.04
38.76
38.48
38.20
37.92
37.64
N
N
H
2a
13C NMR, CDCl3: DMSO-d6
75 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

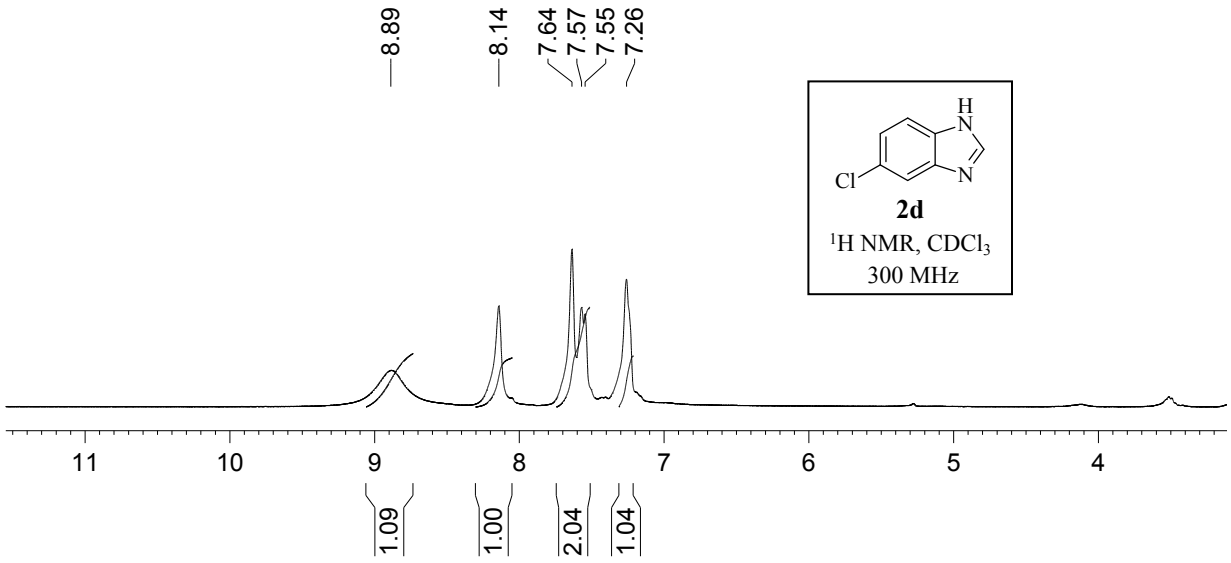

119.0609
119.5404
119.5826
31e4
100
%
0
80
85
90
95
100
105
110
115
120
125
130
135
140
145
m/z
2a
ESI-MS = 119.0609

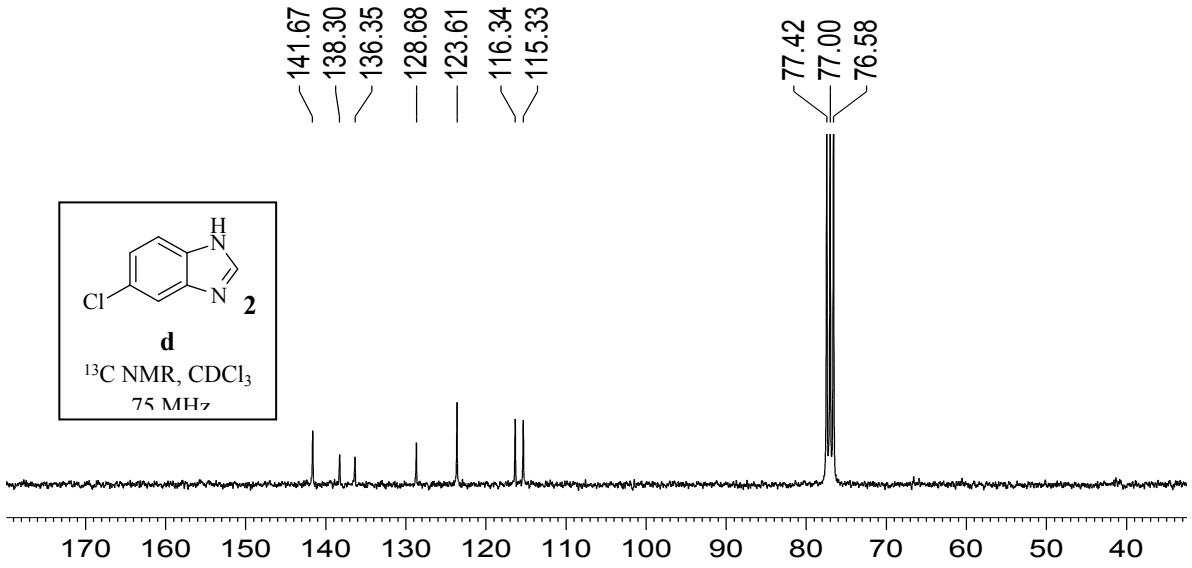

8.01
7.36
4.87
3.31
2.36
2b
1H NMR, CD3OD
600 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.07
6.01

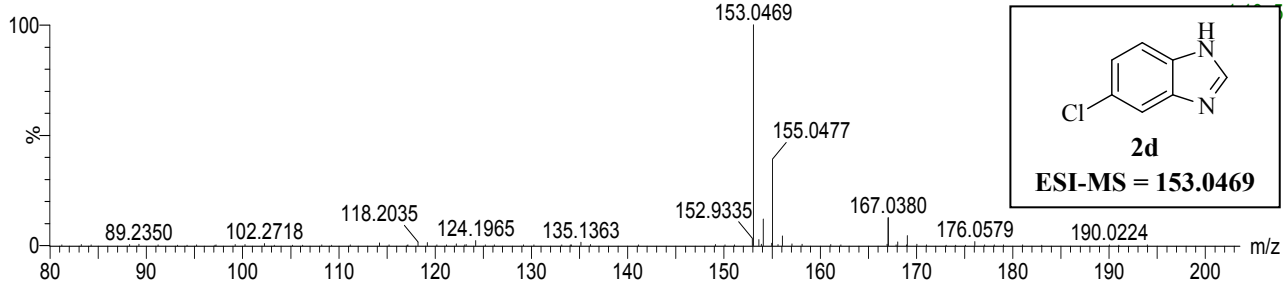

140.36
136.18
131.74
114.95
48.28
48.14
48.00
47.86
47.71
47.57
47.43
19.25
19.18
2b
13C NMR, CD3OD
150 MHz
200
180
160
140
120
100
80
60
40
20

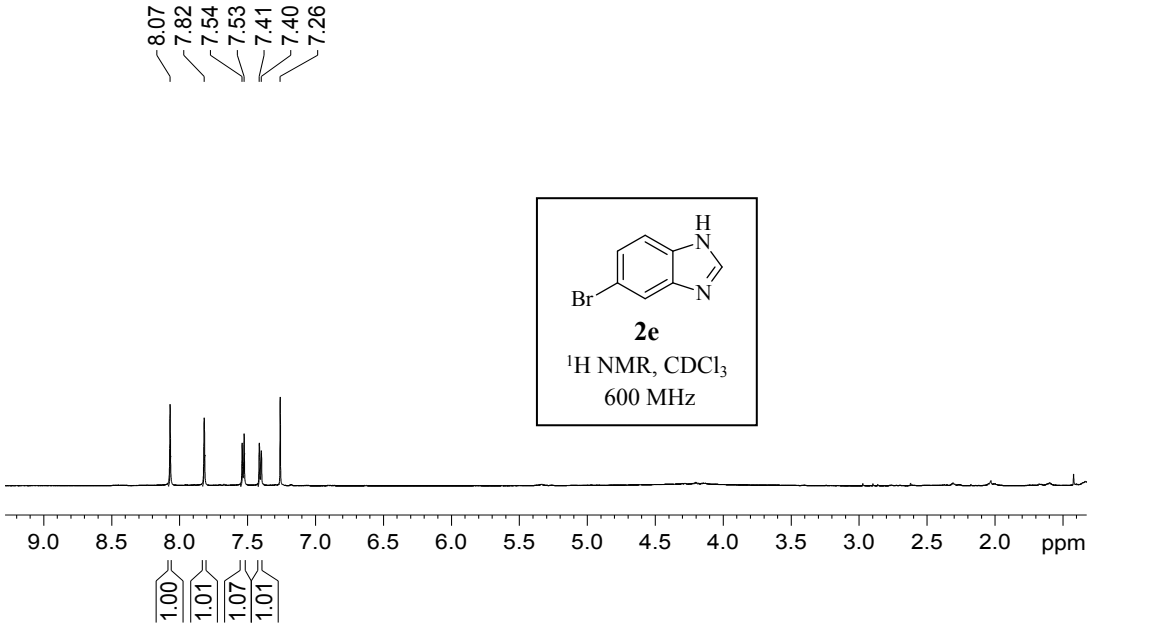

2b
ESI-MS = 147.0925

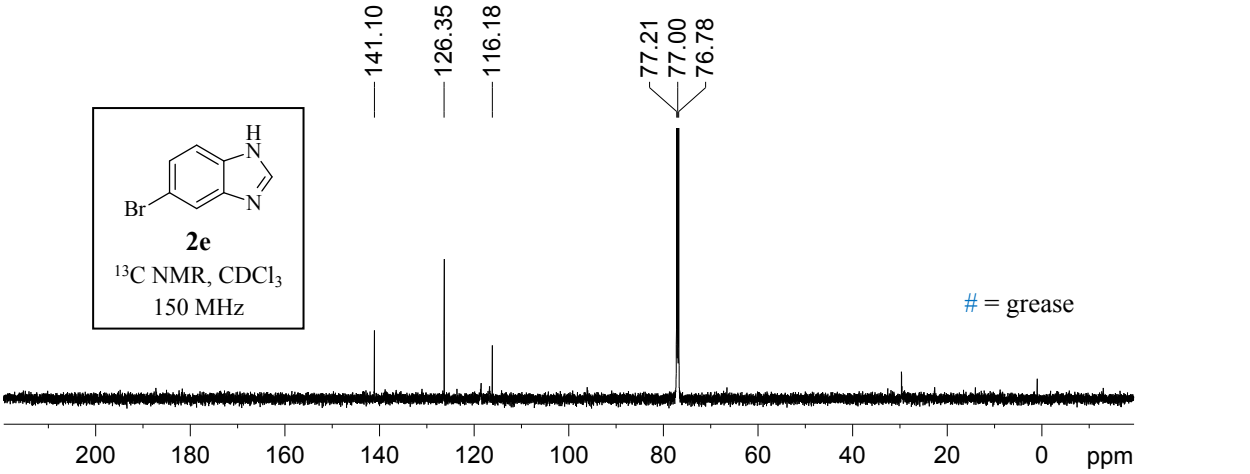

147.0925
2.45e5
148.1126
146.7240
149.1185
83.2308
89.2117
97.0948
102.2541
106.1851
114.1921
124.1674
133.1480
159.0972
m/z
8.12
7.63
7.61
7.60
7.58
7.35
7.33
7.26
7.09
7.06
7.03
2c
1H NMR, CDCl3
300 MHz
1.00
1.02
1.10
1.35
161.42
158.25
141.49
137.53
134.24
116.42
116.27
111.76
111.42
101.62
101.27
77.42
77.00
76.58
2c
13C NMR, CDCl3
75 MHz
ppm

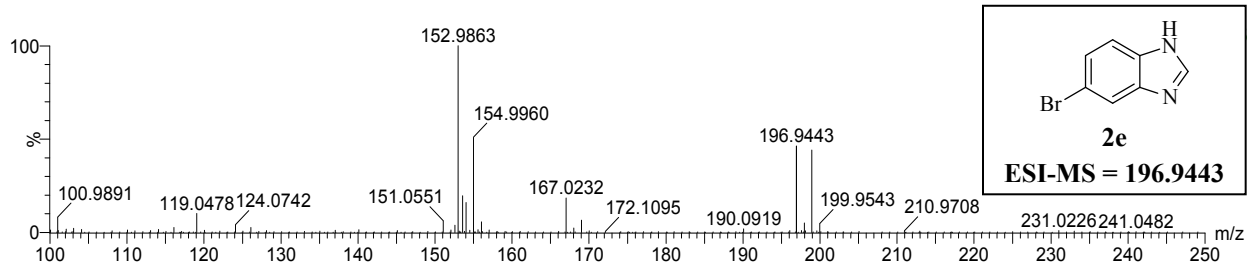

8.89
8.14
7.64
7.57
7.55
7.26
2d
1H NMR, CDCl3
300 MHz
11
10
9
8
7
6
5
4
1.09
1.00
2.04
1.04

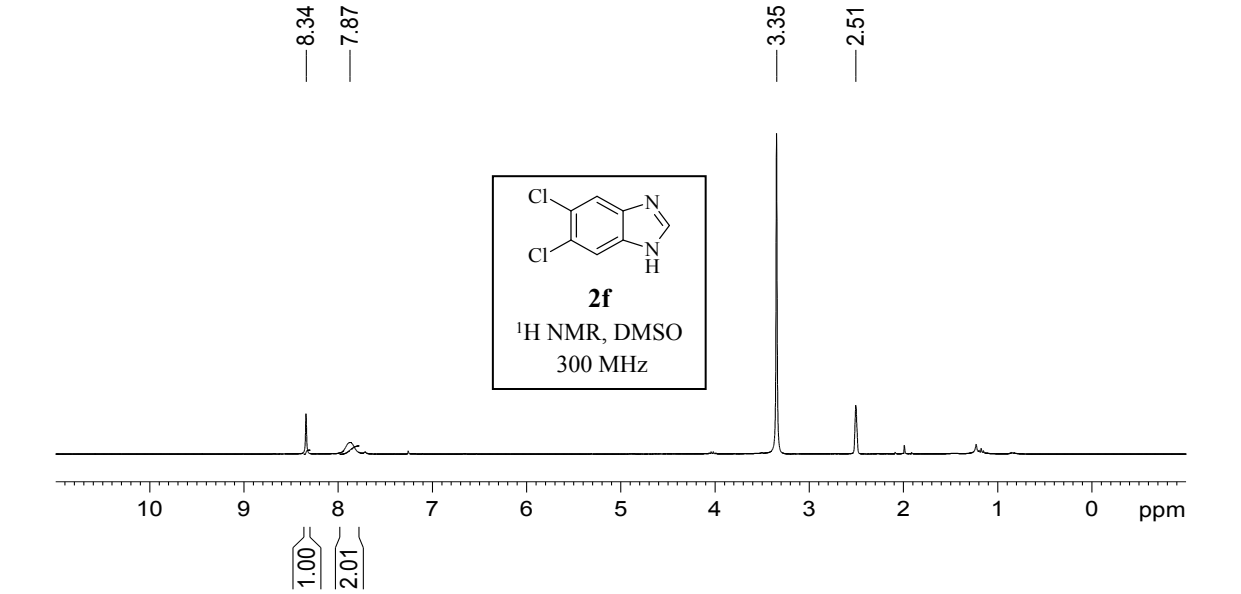

141.67
138.30
136.35
128.68
123.61
116.34
115.33
77.42
77.00
76.58
2
d
13C NMR, CDCl3
75 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
40

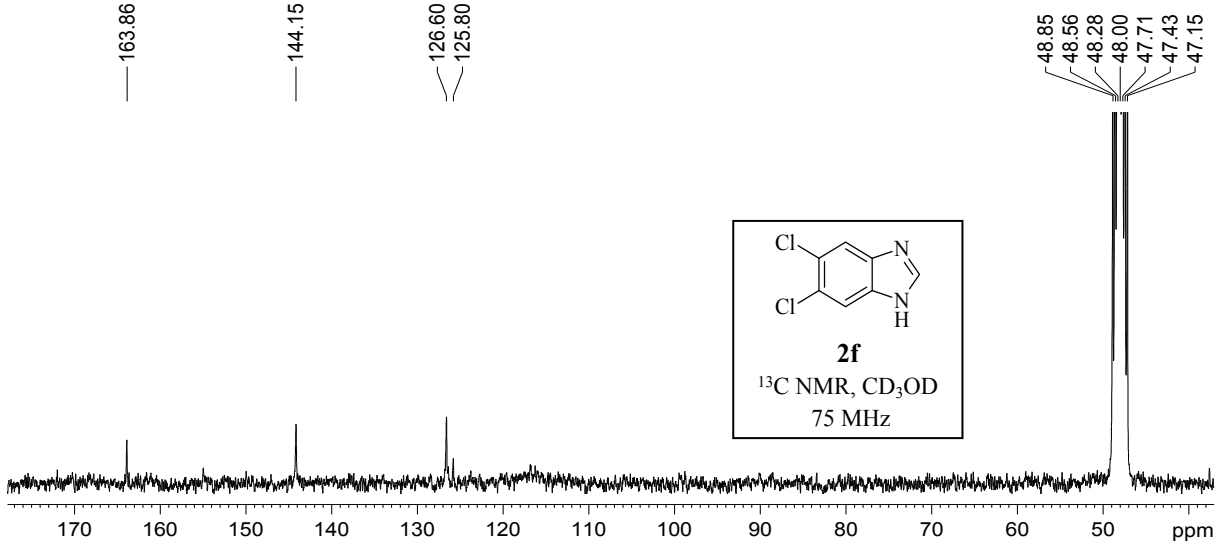

153.0469
155.0477
152.9335
167.0380
118.2035
124.1965
135.1363
89.2350
102.2718
176.0579
190.0224
%
m/z
2d
ESI-MS = 153.0469

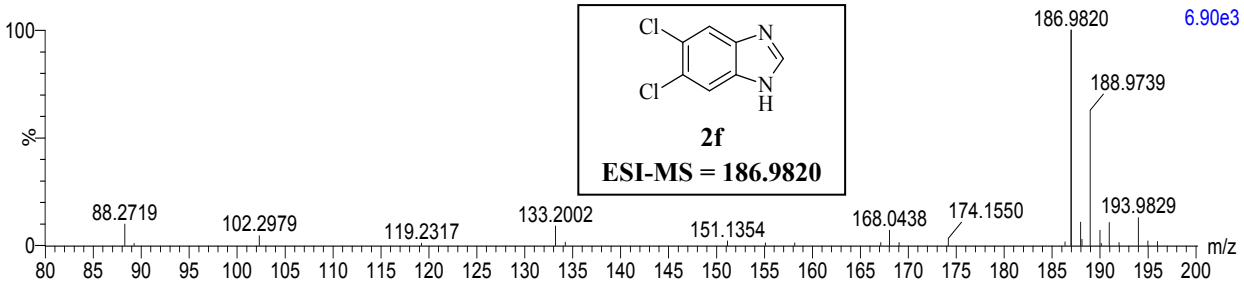

8.07
7.82
7.54
7.53
7.41
7.40
7.26
2e
1H NMR, CDCl3
600 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm
1.00
1.01
1.07
1.01

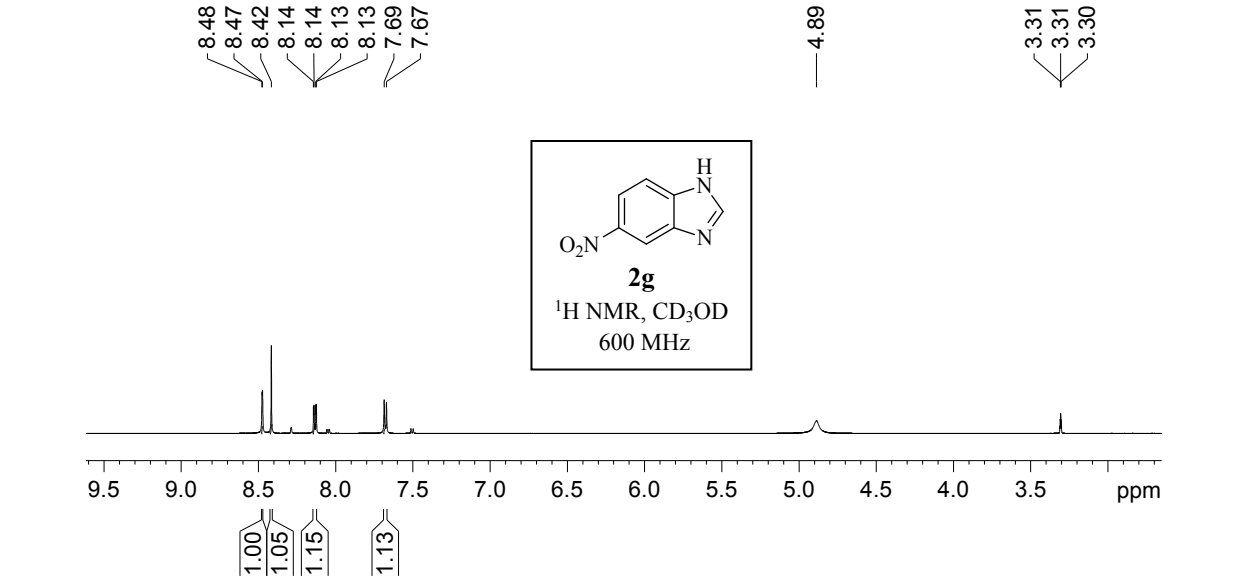

141.10
126.35
116.18
77.21
77.00
76.78
2e
13C NMR, CDCl3
150 MHz
= grease
200 180 160 140 120 100 80 60 40 20 0 ppm

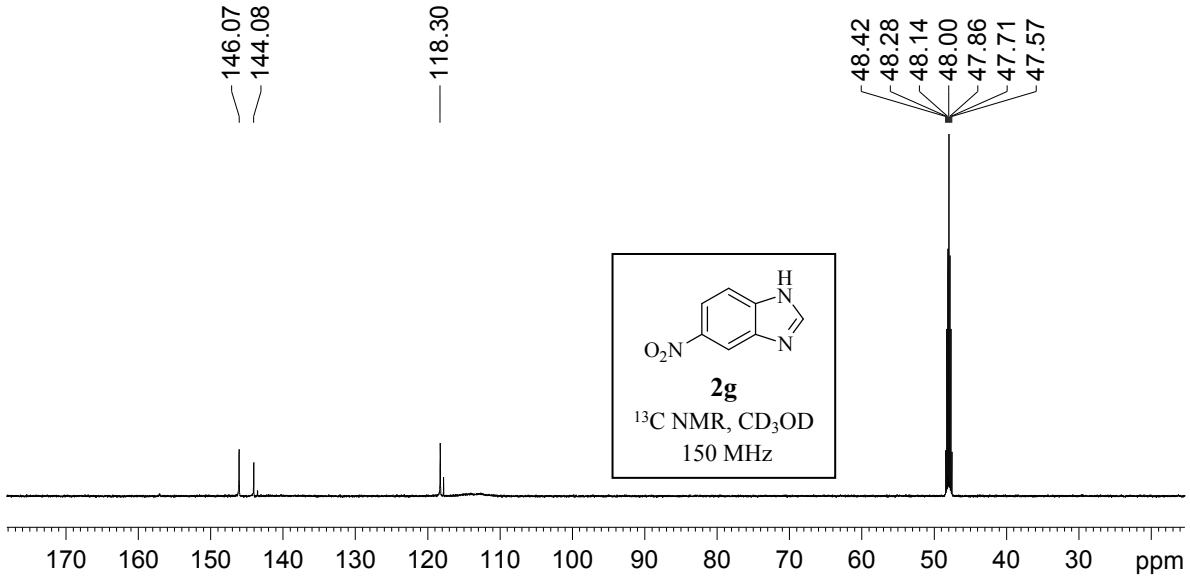

152.9863
154.9960
196.9443
100.9891
119.0478
124.0742
151.0551
167.0232
172.1095
190.0919
199.9543
210.9708
231.0226
241.0482
%
m/z
2e
ESI-MS = 196.9443

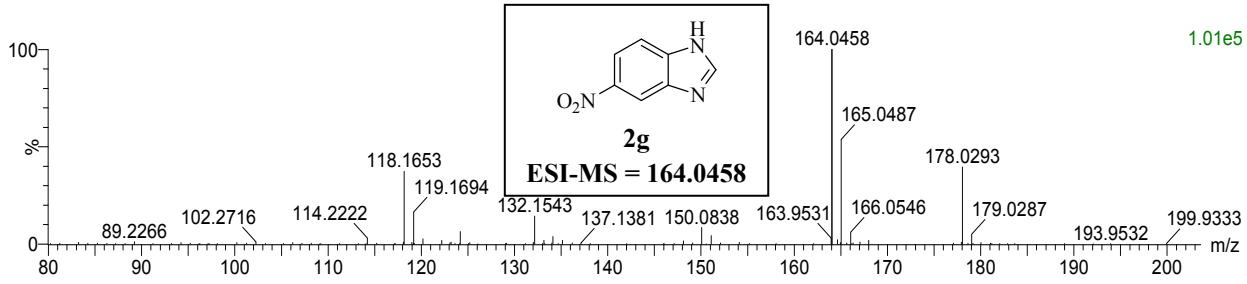

8.34
7.87
3.35
2.51
Cl
Cl
N
N
H
2f
1H NMR, DMSO
300 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
2.01

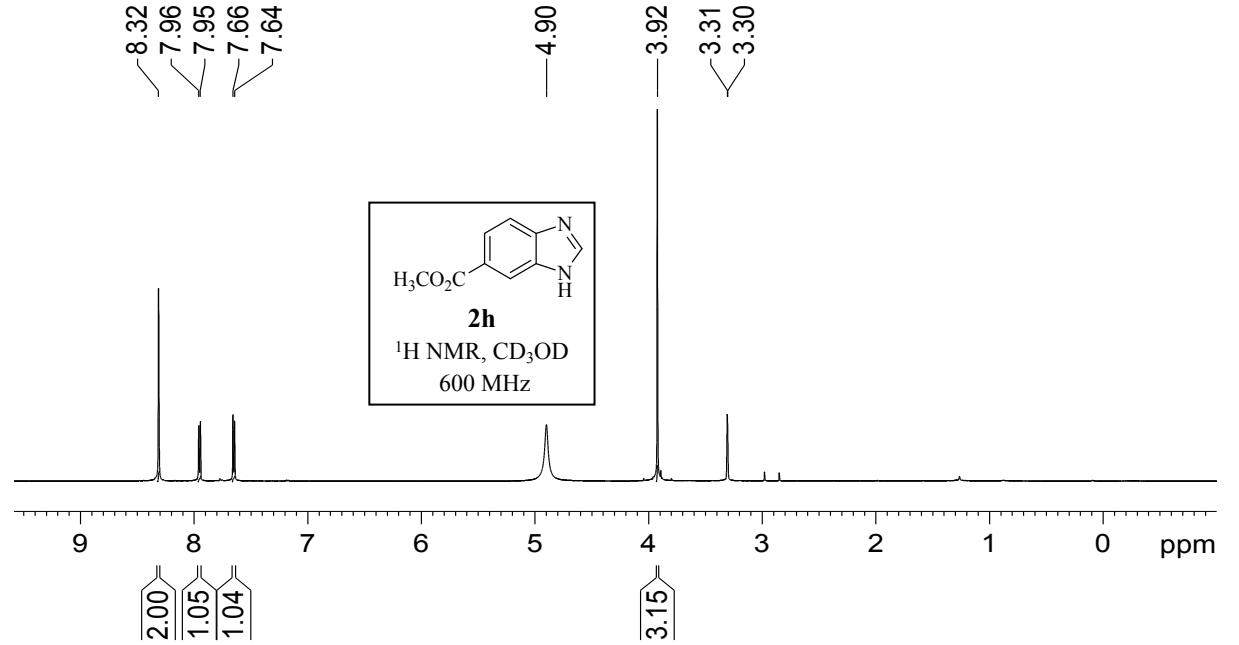

163.86
144.15
126.60
125.80
48.85
48.56
48.28
48.00
47.71
47.43
47.15
Cl
Cl
N
N
H
2f
13C NMR, CD3OD
75 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
ppm

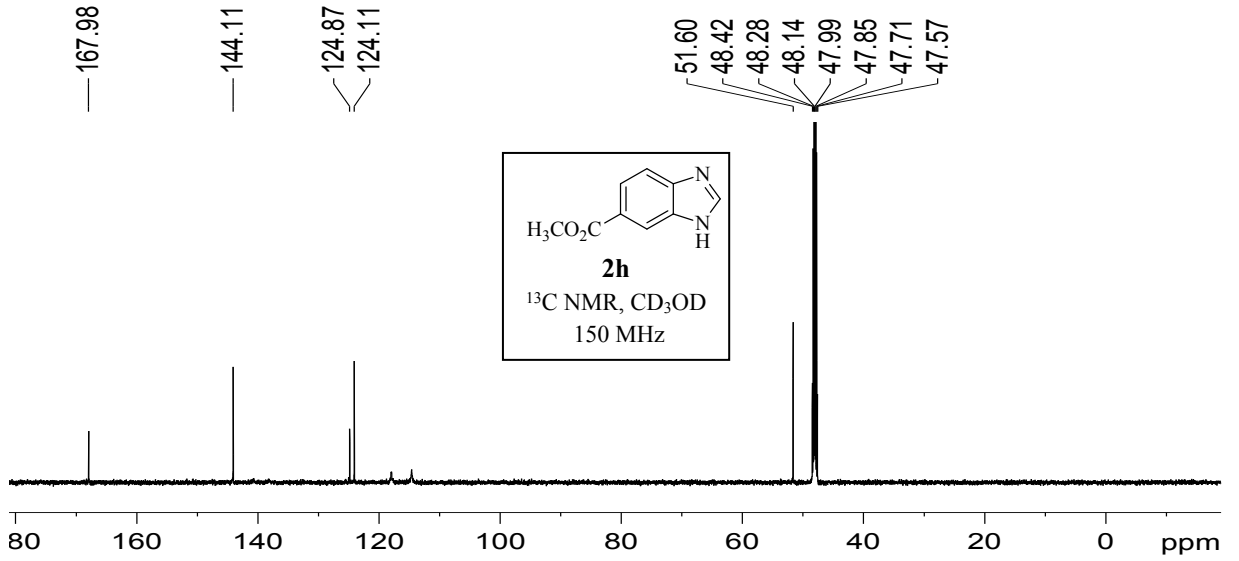

Cl
Cl
N
N
H
2f
ESI-MS = 186.9820
100
%
0
186.9820
6.90e3
188.9739
193.9829
88.2719
102.2979
119.2317
133.2002
151.1354
168.0438
174.1550
80
85
90
95
100
105
110
115
120
125
130
135
140
145
150
155
160
165
170
175
180
185
190
195
200
m/z

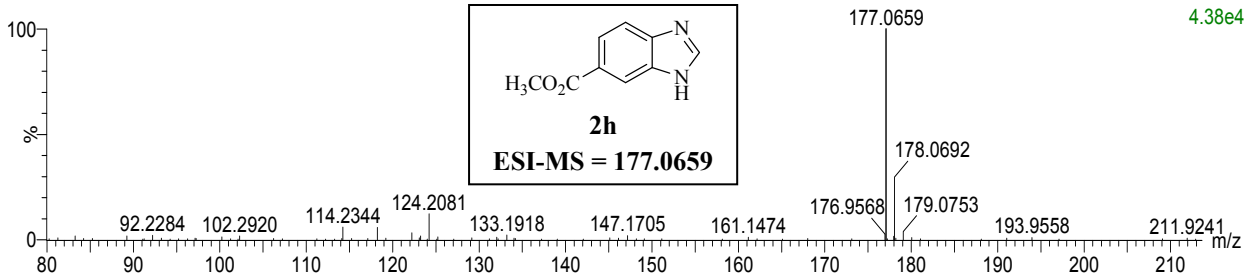

8.48
8.47
8.42
8.14
8.14
8.13
8.13
7.69
7.67
4.89
3.31
3.31
3.30
2g
1H NMR, CD3OD
600 MHz
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
1.00
1.05
1.15
1.13

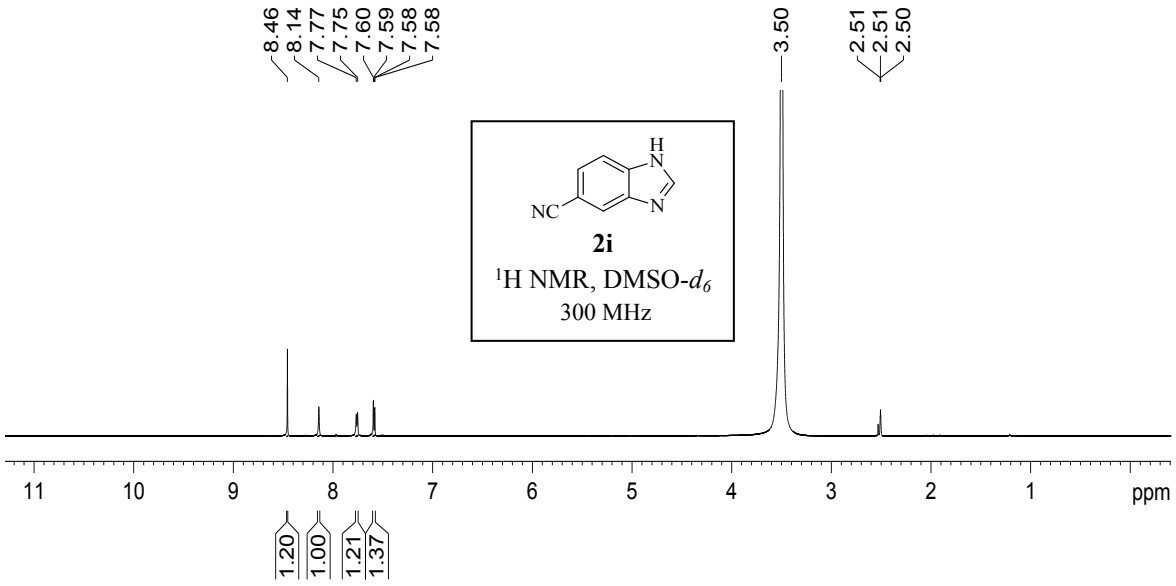

146.07
144.08
118.30
48.42
48.28
48.14
48.00
47.86
47.71
47.57
2g
13C NMR, CD3OD
150 MHz
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
ppm

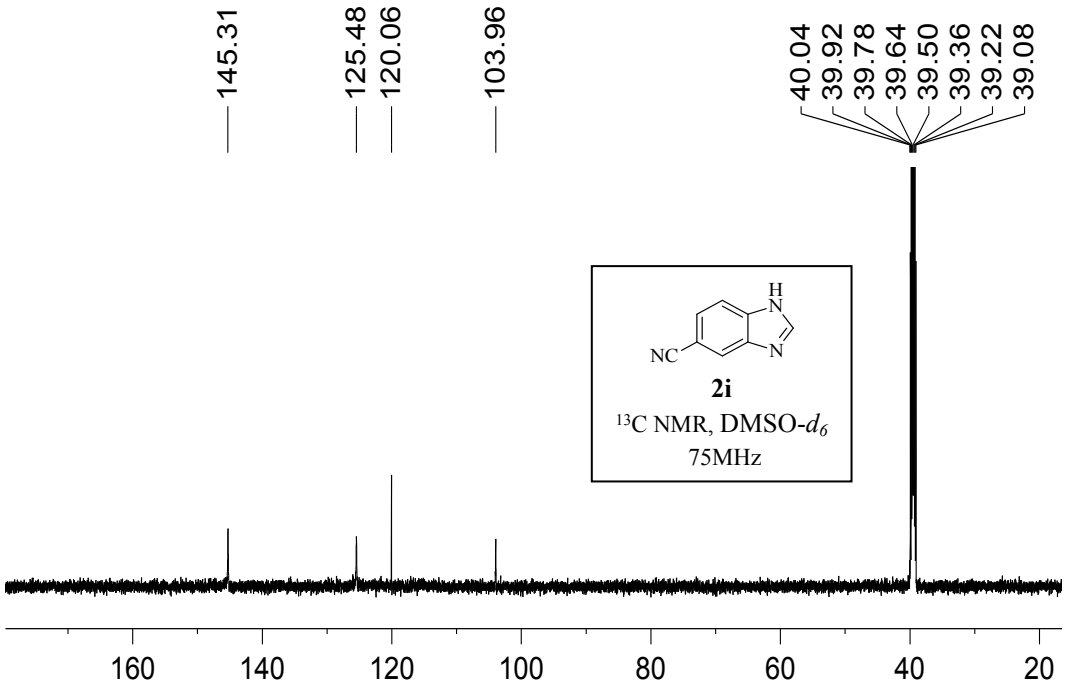

2g
ESI-MS = 164.0458
1.01e5
100
%
0
164.0458
165.0487
178.0293
118.1653
119.1694
89.2266
102.2716
114.2222
132.1543
137.1381
150.0838
163.9531
166.0546
179.0287
193.9532
199.9333
m/z
80
90
100
110
120
130
140
150
160
170
180
190
200

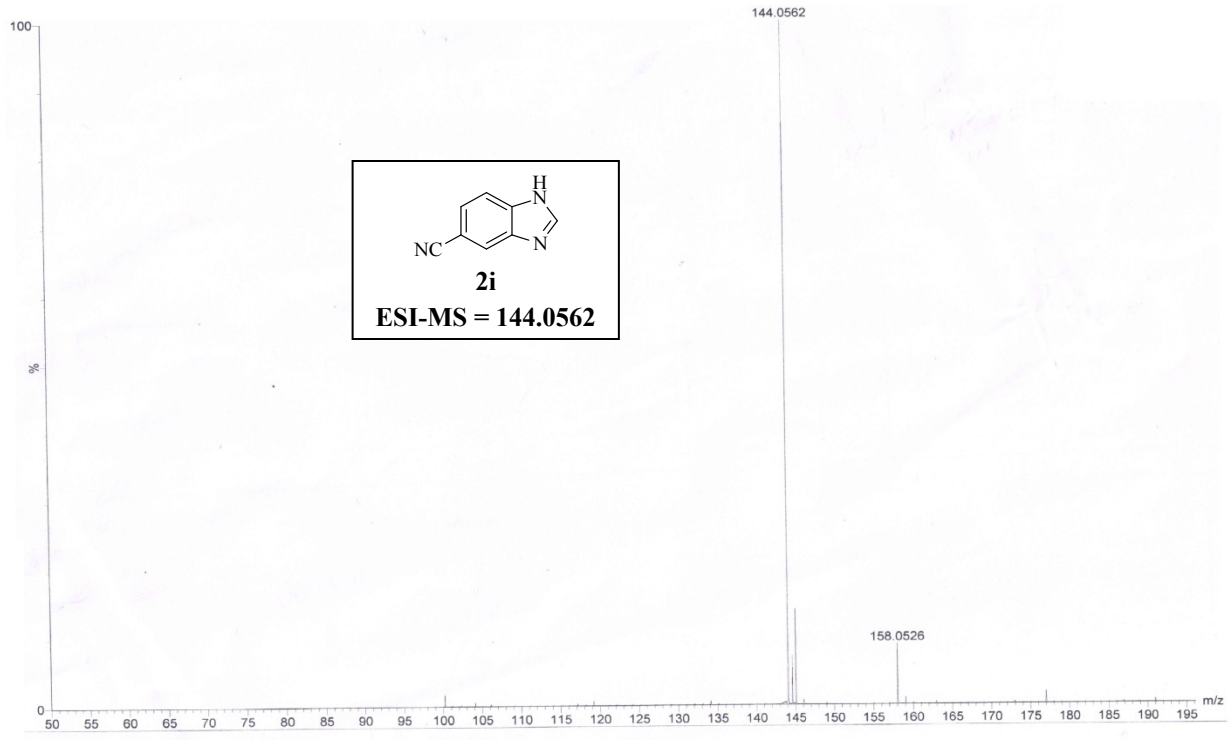

8.32
7.96
7.95
7.66
7.64
4.90
3.92
3.31
3.30
2h
1H NMR, CD3OD
600 MHz
2.00
1.05
1.04
3.15
ppm


167.98
144.11
124.87
124.11
51.60
48.42
48.28
48.14
47.99
47.85
47.71
47.57
2h
13C NMR, CD3OD
150 MHz
ppm


2h
ESI-MS = 177.0659
177.0659
4.38e4
178.0692
179.0753
176.9568
92.2284
102.2920
114.2344
124.2081
133.1918
147.1705
161.1474
193.9558
211.9241
%
m/z

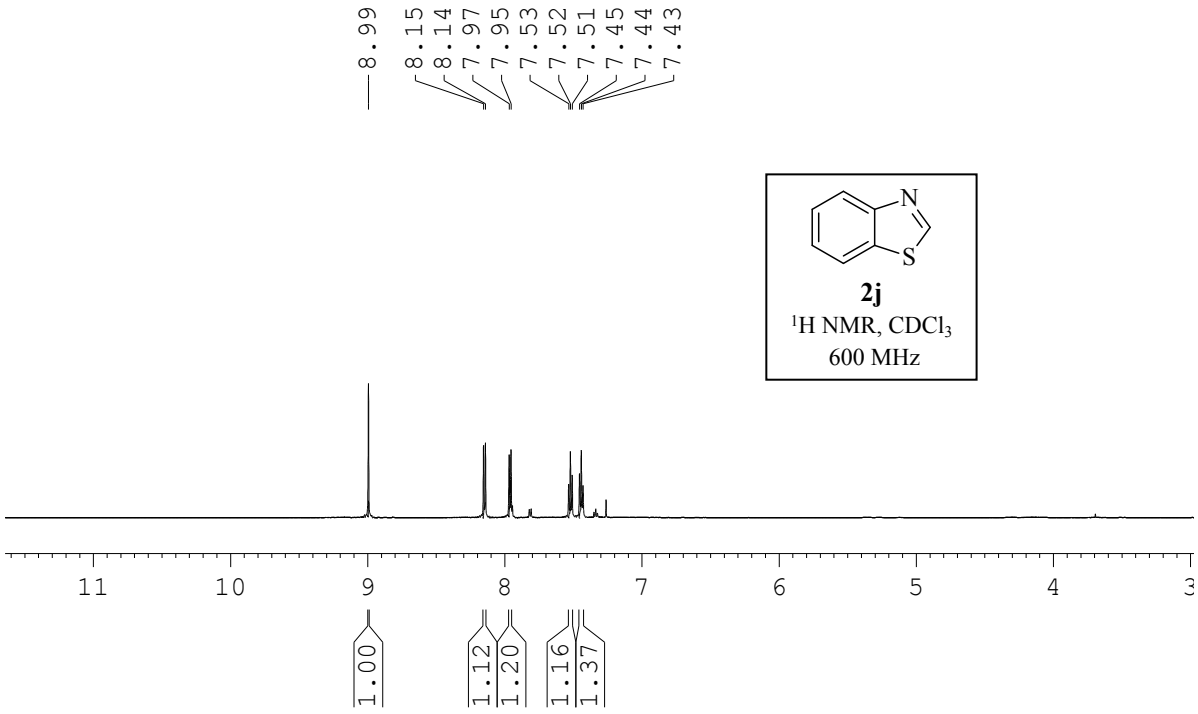

8.46
8.14
7.77
7.75
7.60
7.59
7.58
7.58
3.50
2.51
2.51
2.50
NC
H
N
N
2i
1H NMR, DMSO-d6
300 MHz
11
10
9
8
7
6
5
4
3
2
1
ppm
1.20
1.00
1.21
1.37


145.31
125.48
120.06
103.96
40.04
39.92
39.78
39.64
39.50
39.36
39.22
39.08
NC
H
N
N
2i
13C NMR, DMSO-d6
75MHz
160
140
120
100
80
60
40
20



2i

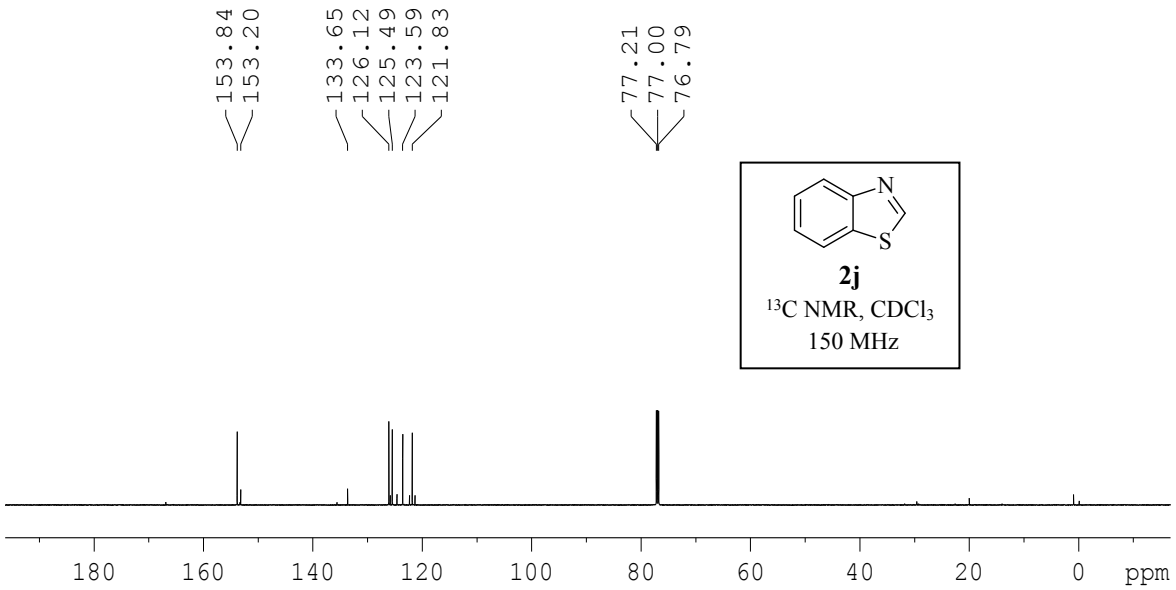
ESI-MS = 144.0562

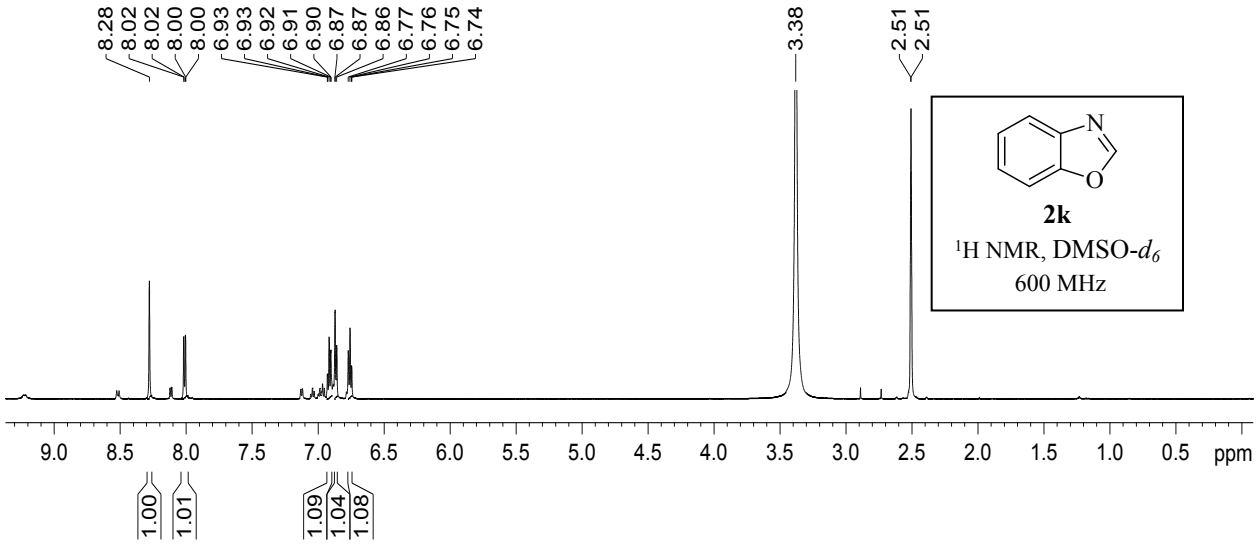


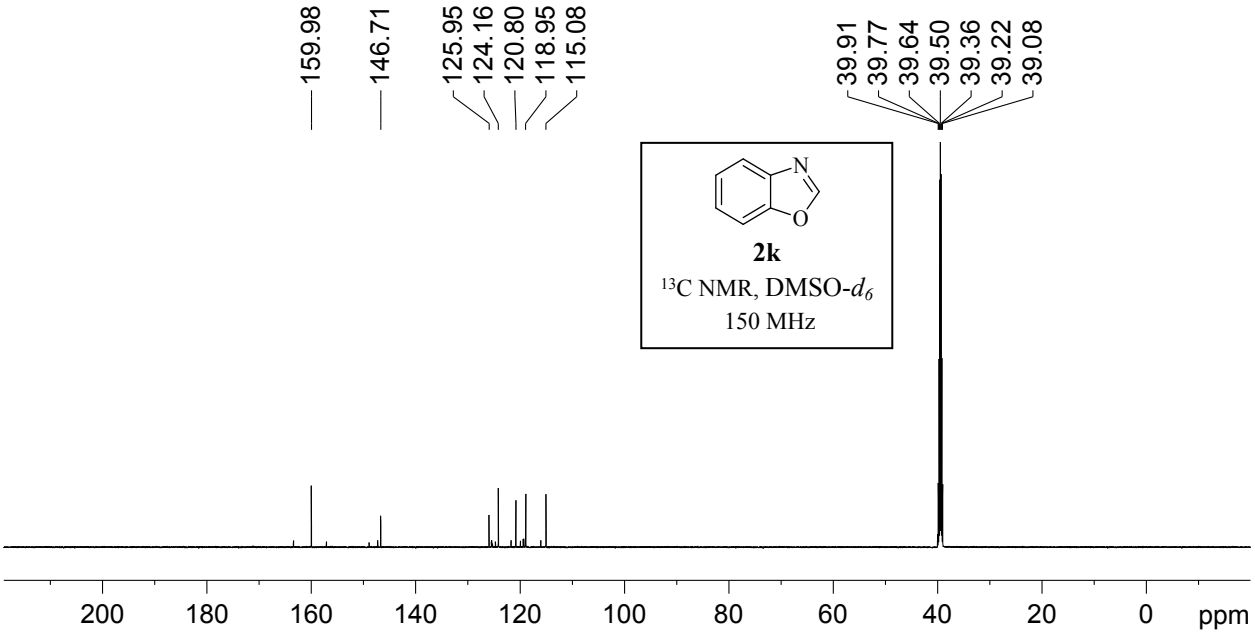
2j

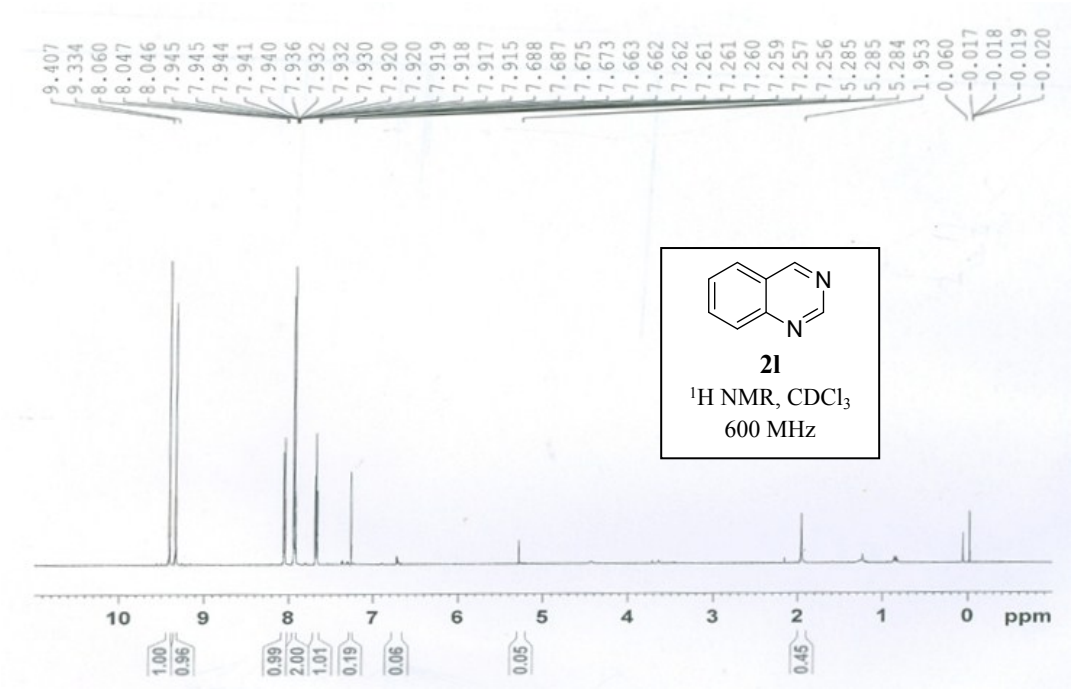
^{1}H NMR, $CDCl_3$

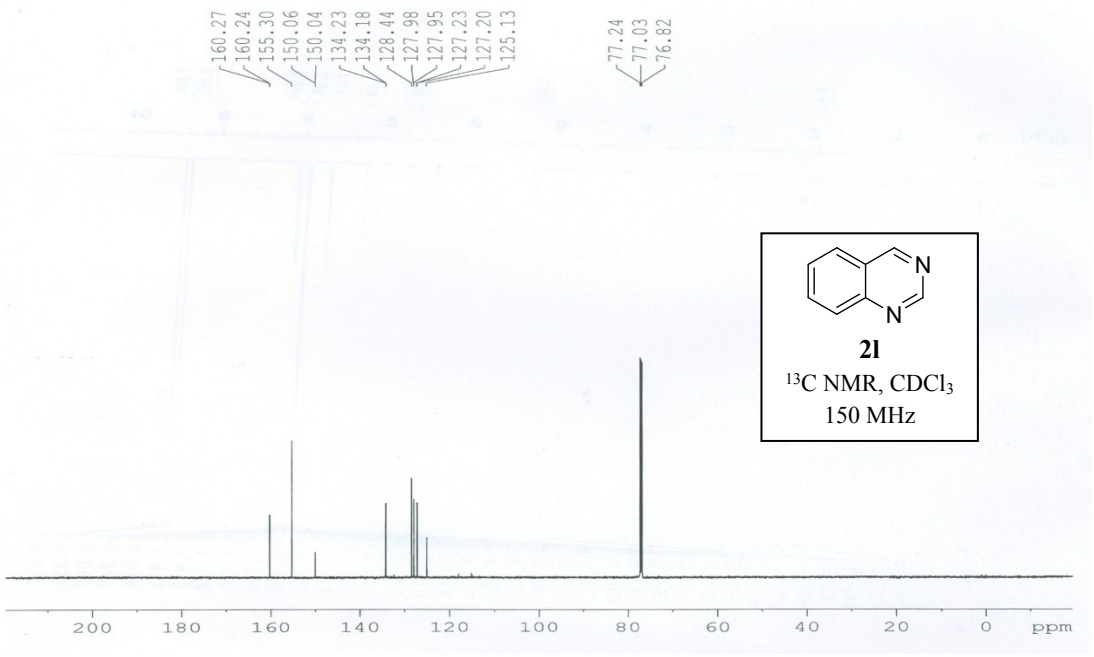
600 MHz


153.84
153.20
133.65
126.12
125.49
123.59
121.83
77.21
77.00
76.79
N
S
2j
13C NMR, CDCl3
150 MHz
180
160
140
120
100
80
60
40
20
0
ppm


8.28
8.02
8.02
8.00
8.00
6.93
6.93
6.92
6.91
6.90
6.87
6.87
6.86
6.77
6.76
6.75
6.74
3.38
2.51
2.51
N
O
2k
1H NMR, DMSO-d6
600 MHz
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.01
1.09
1.04
1.08


159.98
146.71
125.95
124.16
120.80
118.95
115.08
39.91
39.77
39.64
39.50
39.36
39.22
39.08
N
O
2k
13C NMR, DMSO-d6
150 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

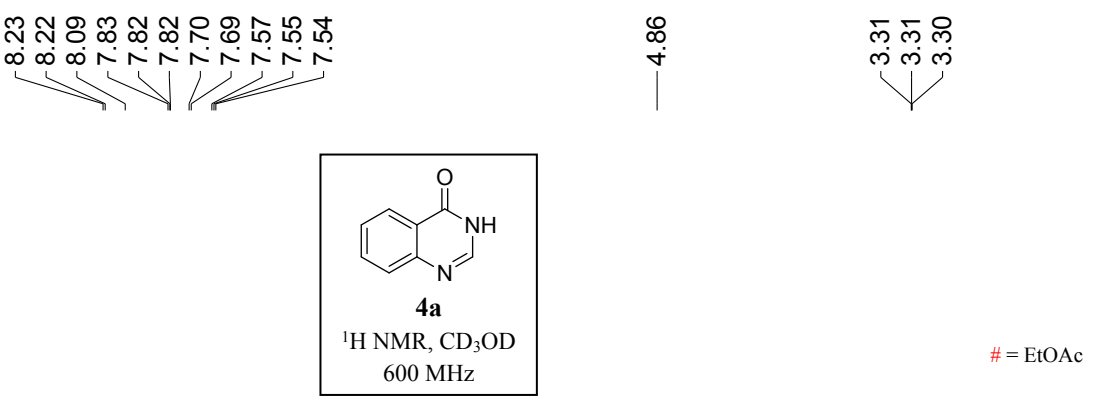

9.407
9.334
8.060
8.047
8.046
7.945
7.945
7.944
7.941
7.940
7.936
7.932
7.932
7.930
7.920
7.920
7.919
7.918
7.917
7.915
7.688
7.687
7.675
7.673
7.663
7.662
7.262
7.261
7.261
7.260
7.259
7.257
7.256
5.285
5.285
5.284
1.953
0.060
-0.017
-0.018
-0.019
-0.020
N
N
2l
1H NMR, CDCl3
600 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.96
0.99
2.00
1.01
0.19
0.06
0.05
0.45



2l

^{13}C NMR, $CDCl_3$

150 MHz

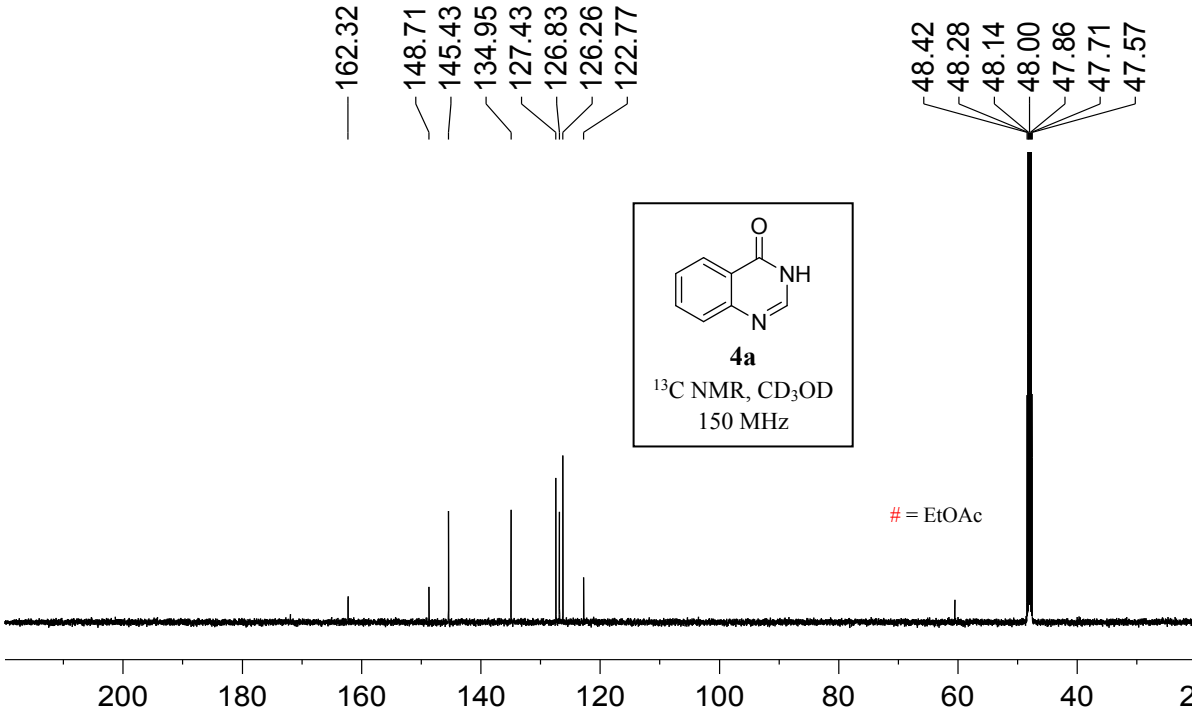


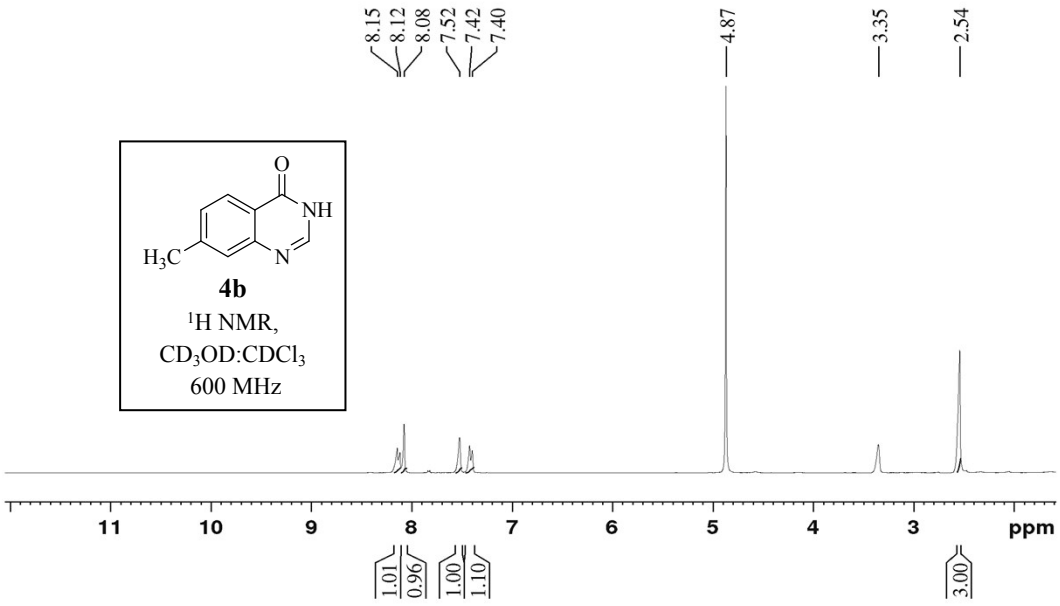
4a

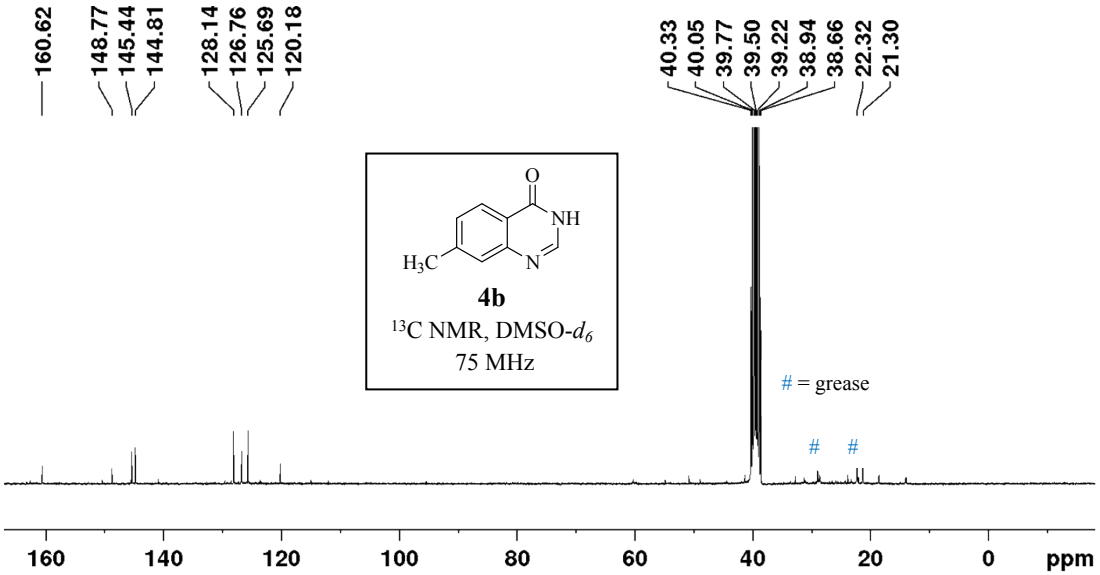
^{1}H NMR, CD_3OD

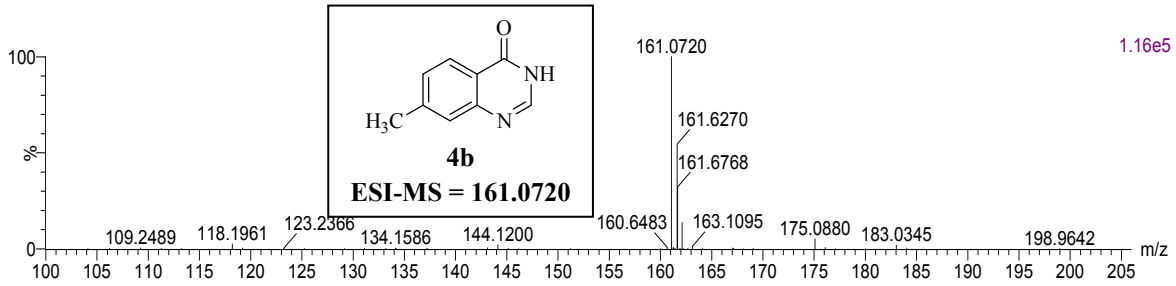
600 MHz

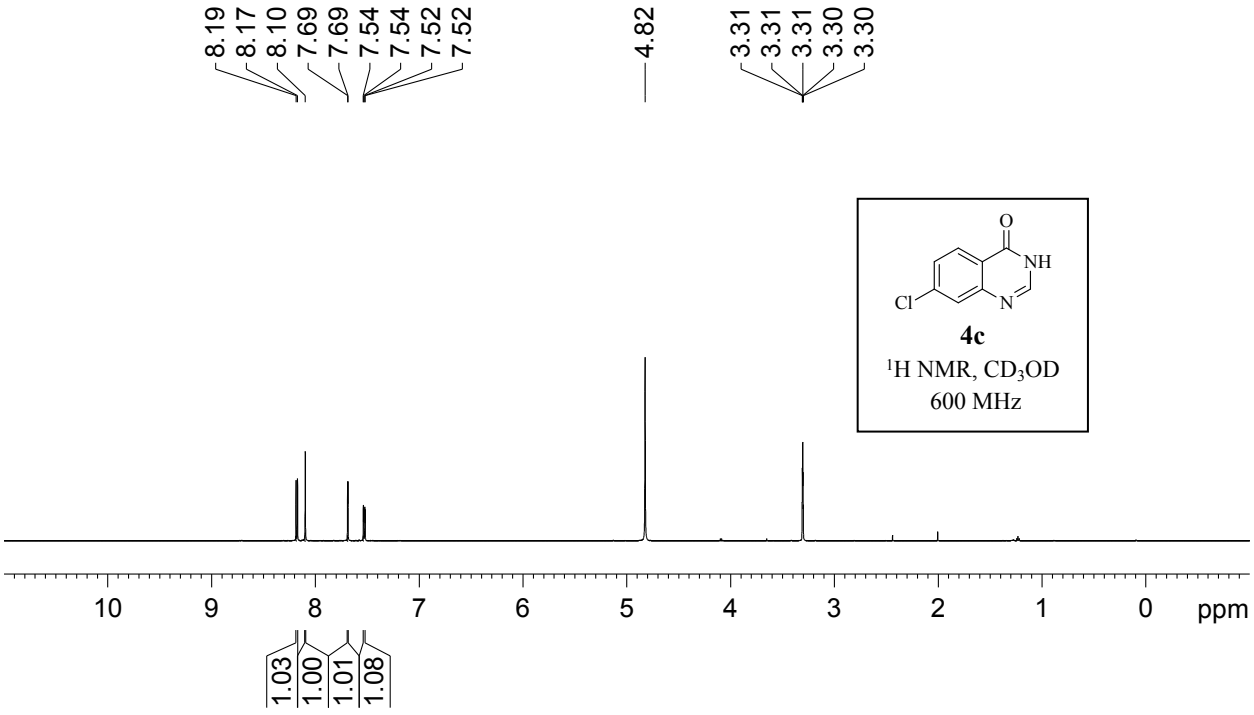
= EtOAc

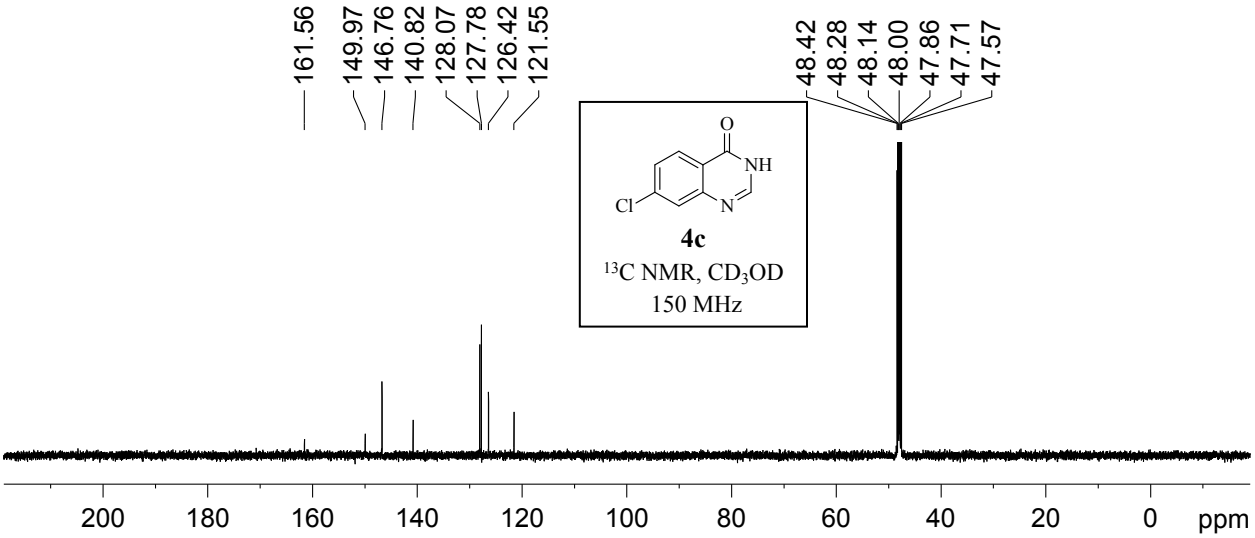

162.32
148.71
145.43
134.95
127.43
126.83
126.26
122.77
48.42
48.28
48.14
48.00
47.86
47.71
47.57
O
NH
N
4a
13C NMR, CD3OD
150 MHz
= EtOAc
200
180
160
140
120
100
80
60
40

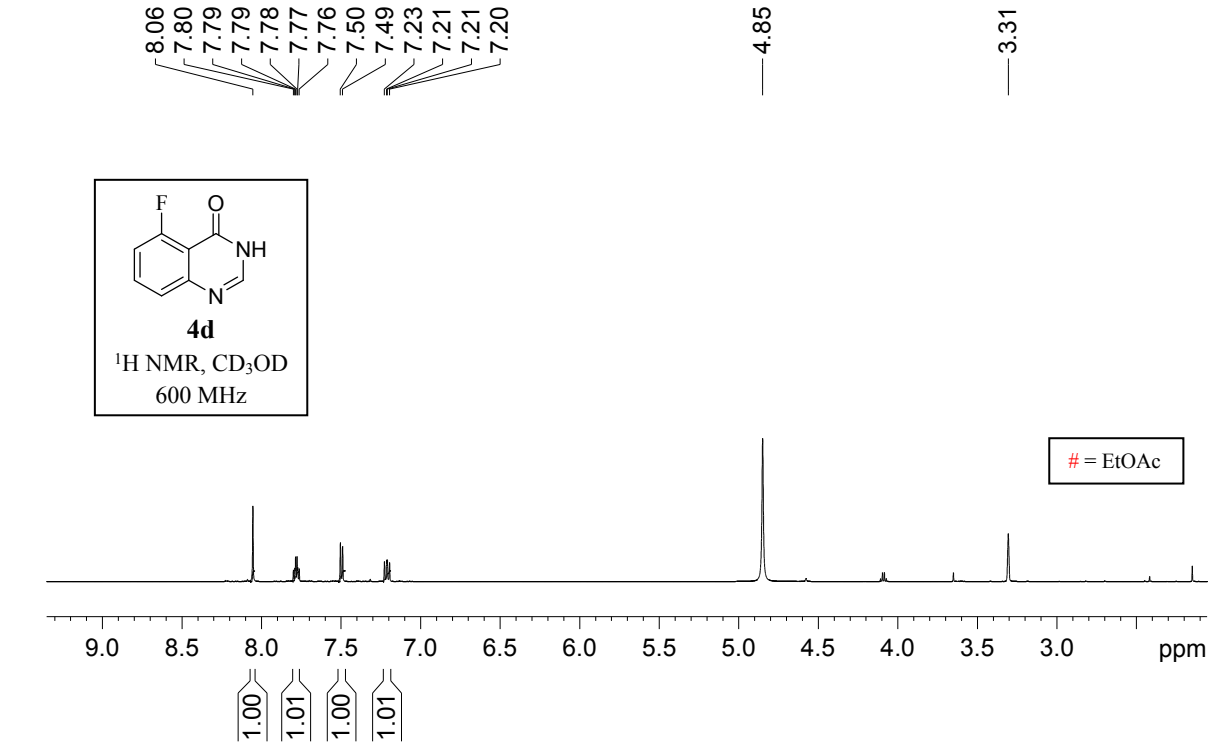

8.15
8.12
8.08
7.52
7.42
7.40
4.87
3.35
2.54
O
NH
H3C
N
4b
1H NMR,
CD3OD:CDCl3
600 MHz
11
10
9
8
7
6
5
4
3
ppm
1.01
0.96
1.00
1.10
3.00

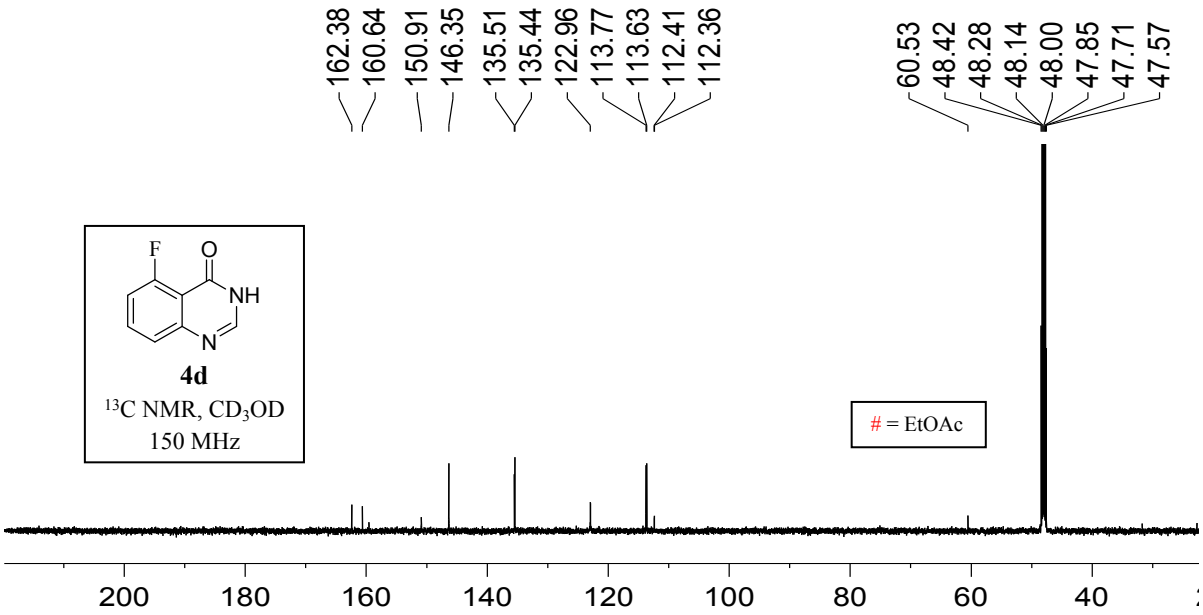

160.62
148.77
145.44
144.81
128.14
126.76
125.69
120.18
40.33
40.05
39.77
39.50
39.22
38.94
38.66
22.32
21.30
4b
13C NMR, DMSO-d6
75 MHz
= grease
160
140
120
100
80
60
40
20
0
ppm

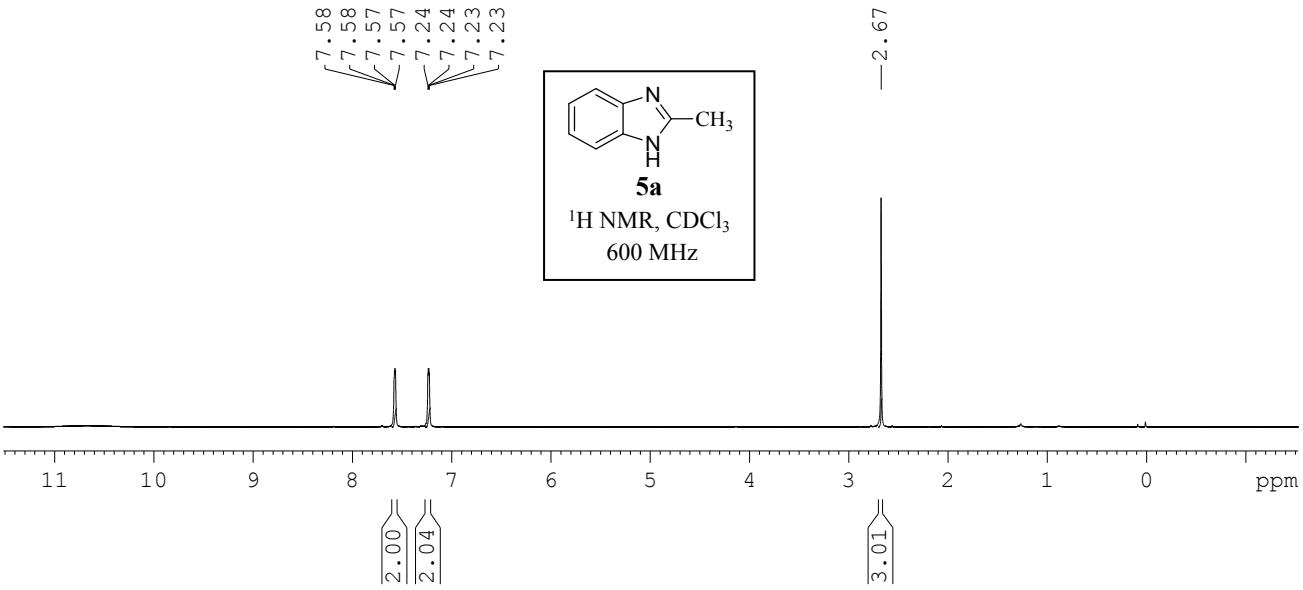

4b
ESI-MS = 161.0720
161.0720
161.6270
161.6768
160.6483
163.1095
109.2489
118.1961
123.2366
134.1586
144.1200
175.0880
183.0345
198.9642
1.16e5
m/z

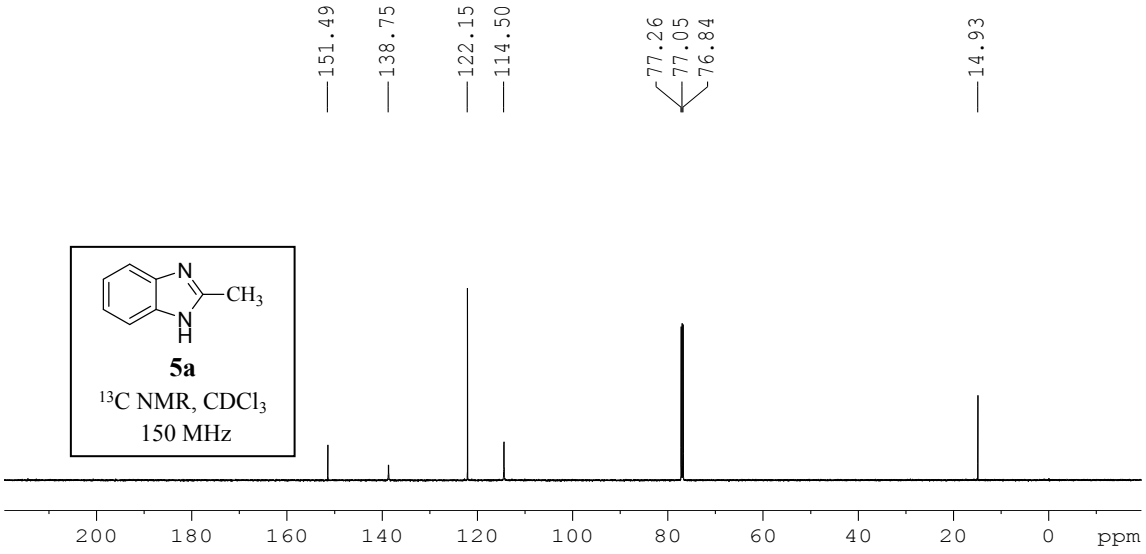

8.19
8.17
8.10
7.69
7.69
7.54
7.54
7.52
7.52
4.82
3.31
3.31
3.31
3.30
3.30
4c
1H NMR, CD3OD
600 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.03
1.00
1.01
1.08

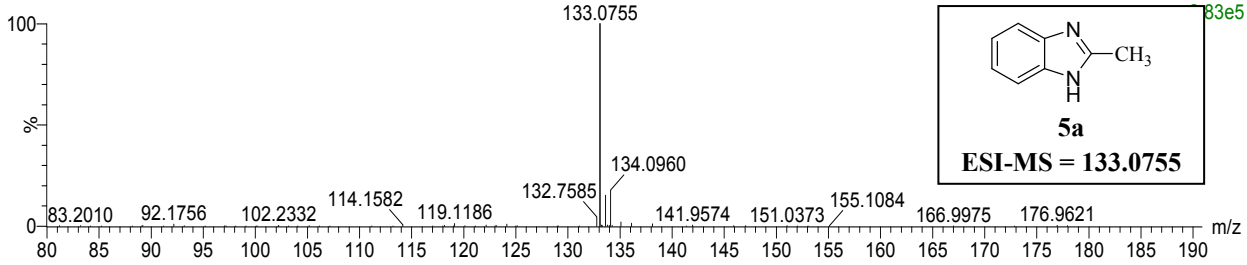

161.56
149.97
146.76
140.82
128.07
127.78
126.42
121.55
48.42
48.28
48.14
48.00
47.86
47.71
47.57
O
NH
Cl
N
4c
13C NMR, CD3OD
150 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

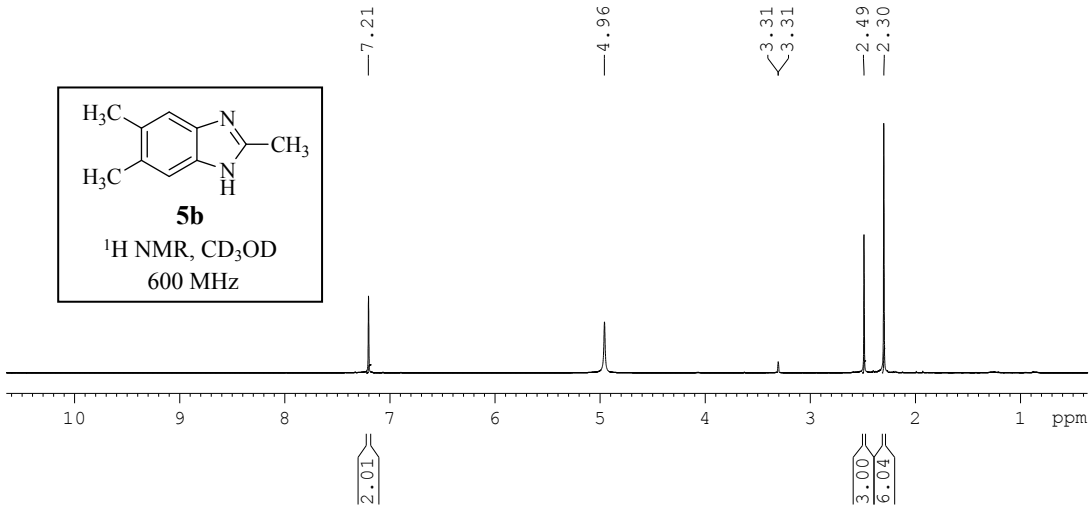

8.06
7.80
7.79
7.79
7.78
7.77
7.76
7.50
7.49
7.23
7.21
7.21
7.20
4.85
3.31
F
O
NH
N
4d
1H NMR, CD3OD
600 MHz
= EtOAc
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
1.00
1.01
1.00
1.01

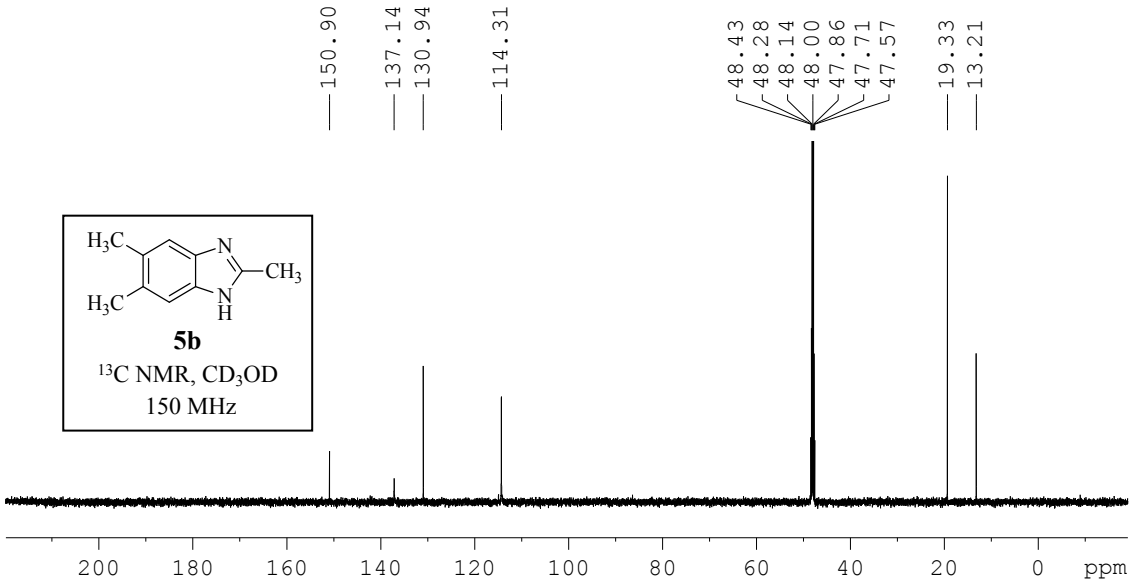

162.38
160.64
150.91
146.35
135.51
135.44
122.96
113.77
113.63
112.41
112.36
60.53
48.42
48.28
48.14
48.00
47.85
47.71
47.57
F
O
NH
N
4d
13C NMR, CD3OD
150 MHz
= EtOAc
200
180
160
140
120
100
80
60
40

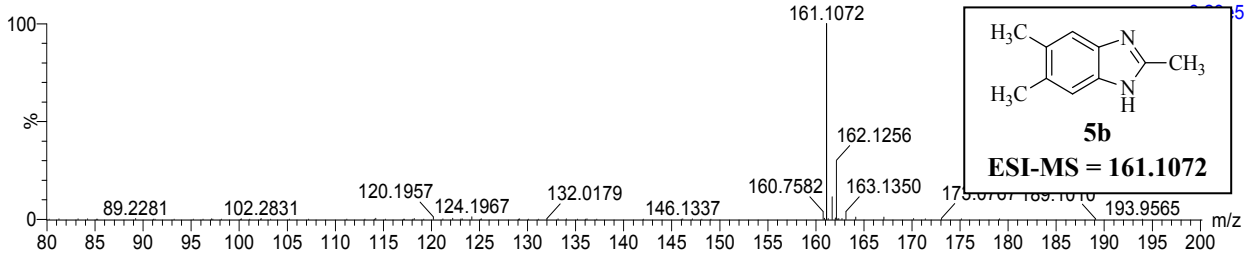

7.58
7.58
7.57
7.57
7.24
7.24
7.23
7.23
2.67
N
CH3
N
H
5a
1H NMR, CDCl3
600 MHz
11
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
2.04
3.01

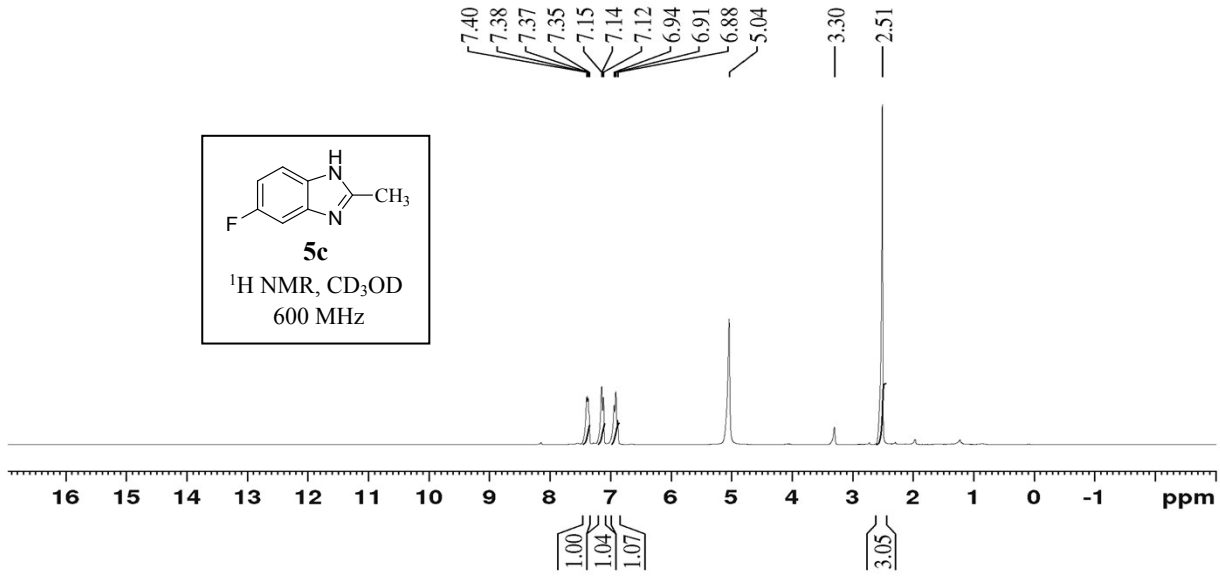

151.49
138.75
122.15
114.50
77.26
77.05
76.84
14.93
5a
13C NMR, CDCl3
150 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

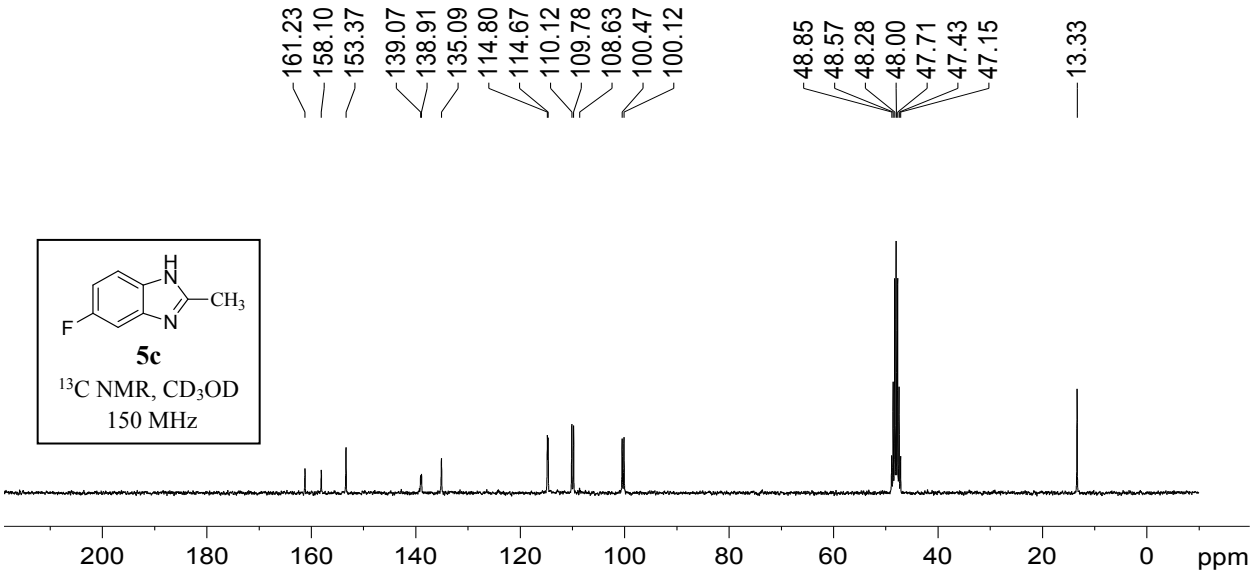

133.0755
134.0960
132.7585
114.1582
119.1186
83.2010
92.1756
102.2332
141.9574
151.0373
155.1084
166.9975
176.9621
%
m/z
5a
ESI-MS = 133.0755

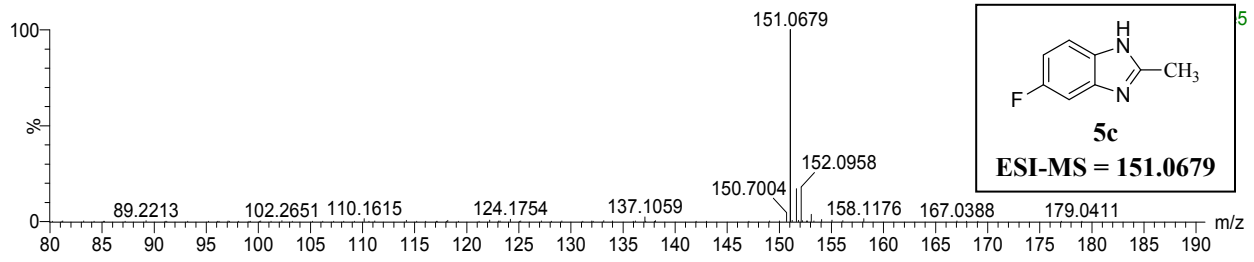

7.21
4.96
3.31
3.31
2.49
2.30
5b
1H NMR, CD3OD
600 MHz
ppm
2.01
3.00
6.04

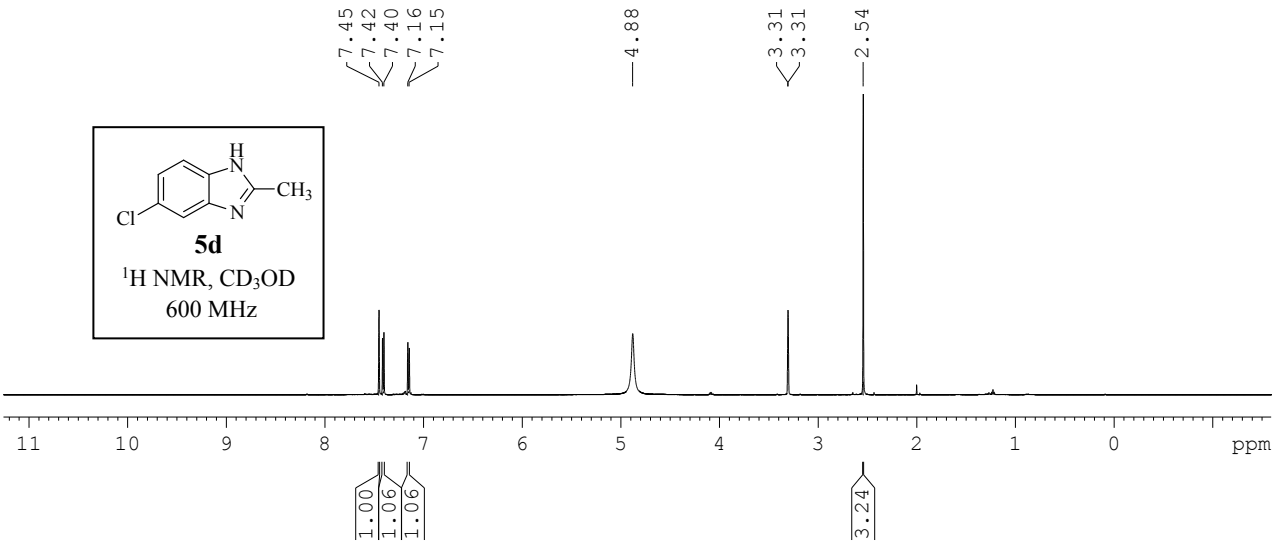

150.90
137.14
130.94
114.31
48.43
48.28
48.14
48.00
47.86
47.71
47.57
19.33
13.21
5b
13C NMR, CD3OD
150 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

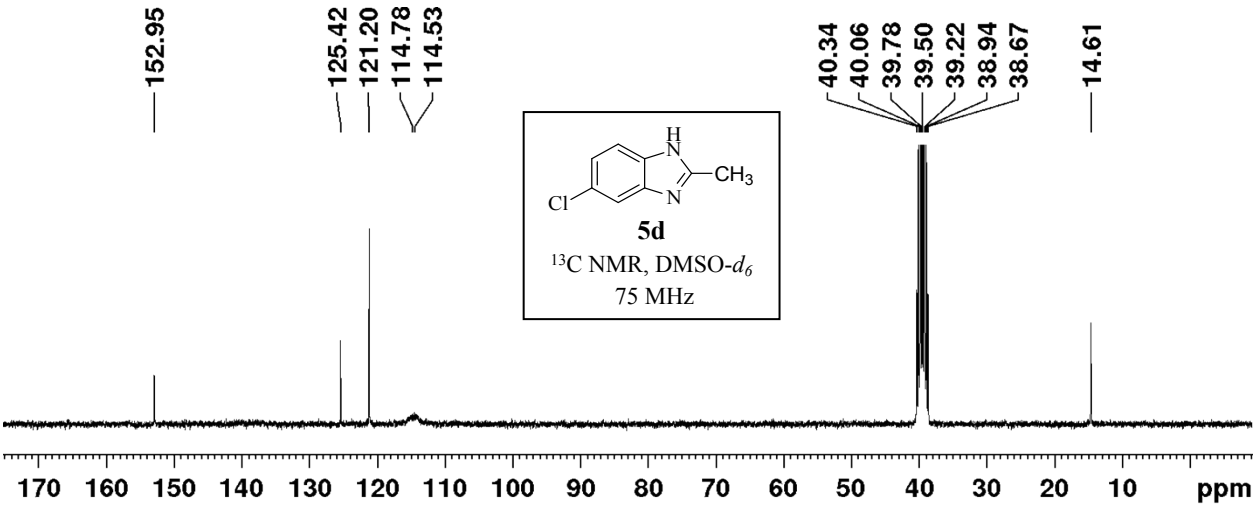

161.1072
162.1256
160.7582
163.1350
120.1957
124.1967
132.0179
146.1337
89.2281
102.2831
193.9565
100
%
0
m/z
5b
ESI-MS = 161.1072

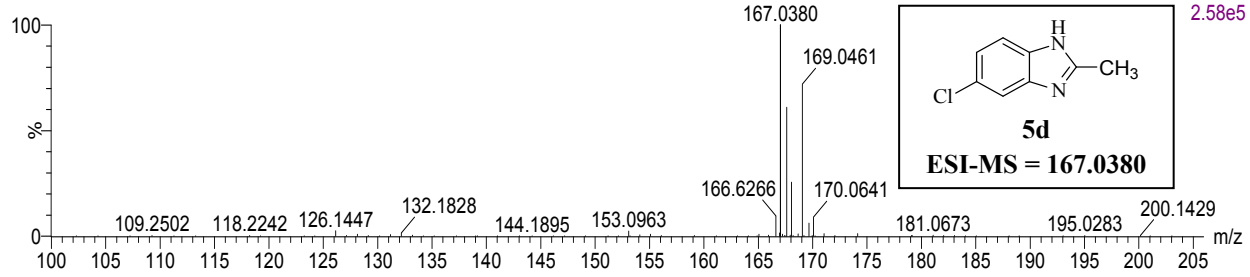

7.40
7.38
7.37
7.35
7.15
7.14
7.12
6.94
6.91
6.88
5.04
3.30
2.51
5c
1H NMR, CD3OD
600 MHz
ppm
1.00
1.04
1.07
3.05

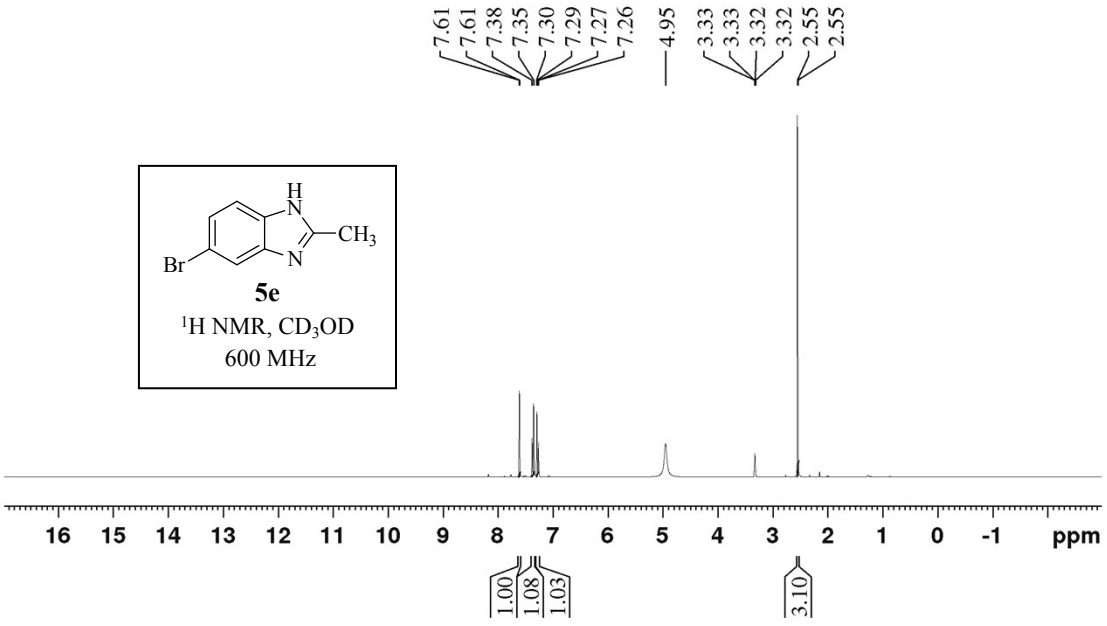

161.23
158.10
153.37
139.07
138.91
135.09
114.80
114.67
110.12
109.78
108.63
100.47
100.12
48.85
48.57
48.28
48.00
47.71
47.43
47.15
13.33
5c
13C NMR, CD3OD
150 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

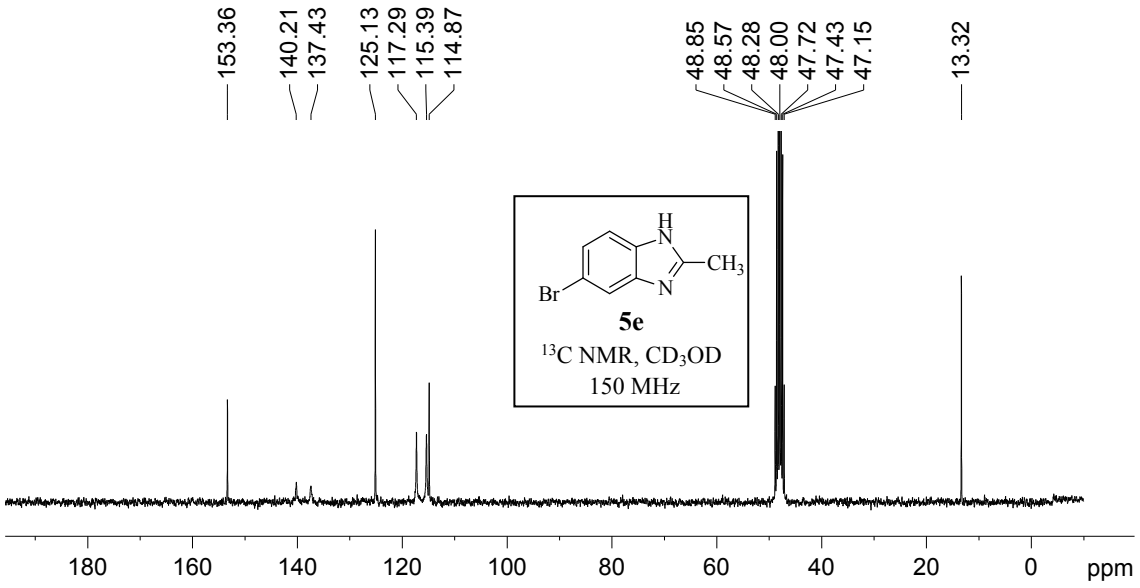

151.0679
152.0958
150.7004
89.2213
102.2651
110.1615
124.1754
137.1059
158.1176
167.0388
179.0411
100
%
0
m/z
5c
ESI-MS = 151.0679

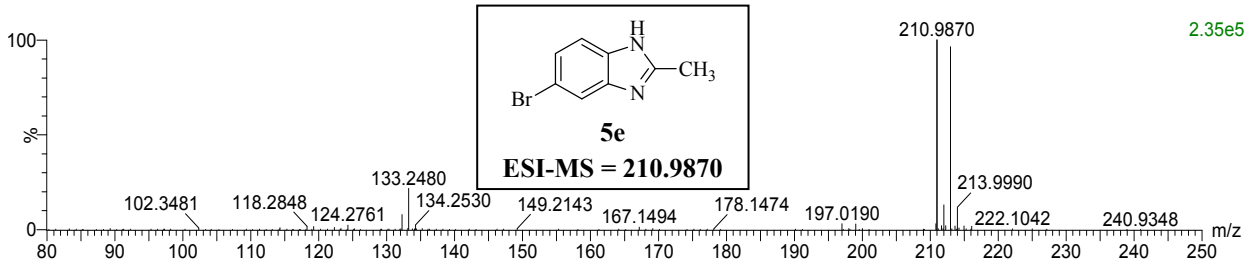

7.45
7.42
7.40
7.16
7.15
4.88
3.31
3.31
2.54
5d
1H NMR, CD3OD
600 MHz
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.06
1.06
3.24

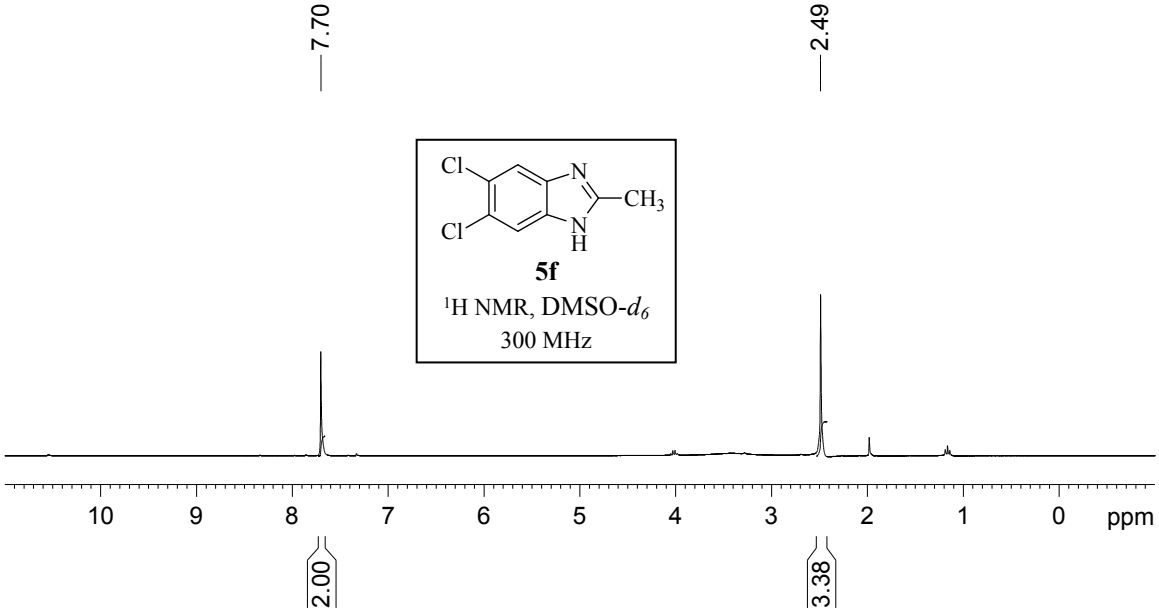

152.95
125.42
121.20
114.78
114.53
40.34
40.06
39.78
39.50
39.22
38.94
38.67
14.61
5d
13C NMR, DMSO-d6
75 MHz
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

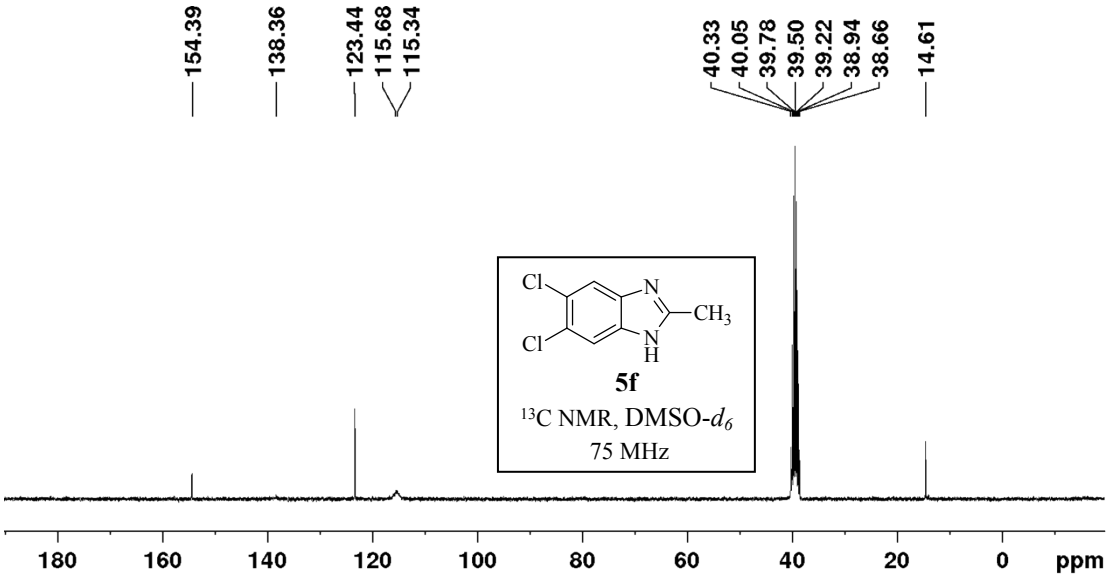

167.0380
169.0461
166.6266
170.0641
109.2502
118.2242
126.1447
132.1828
144.1895
153.0963
181.0673
195.0283
200.1429
2.58e5
5d
ESI-MS = 167.0380
m/z

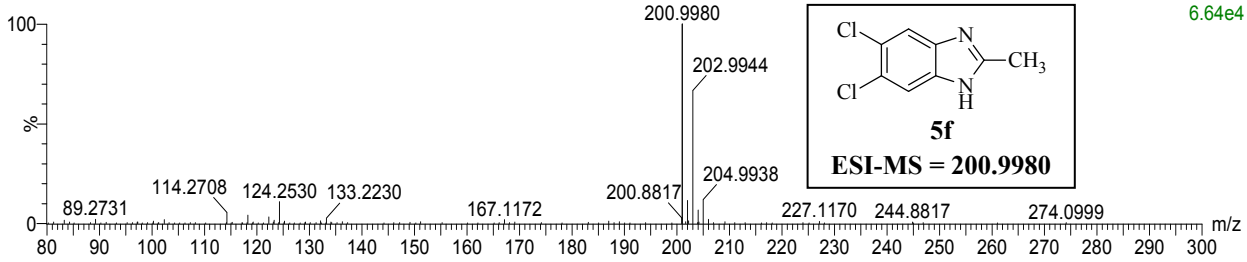

7.61
7.61
7.38
7.35
7.30
7.29
7.27
7.26
4.95
3.33
3.33
3.32
3.32
2.55
2.55
5e
1H NMR, CD3OD
600 MHz
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 ppm
1.00
1.08
1.03
3.10

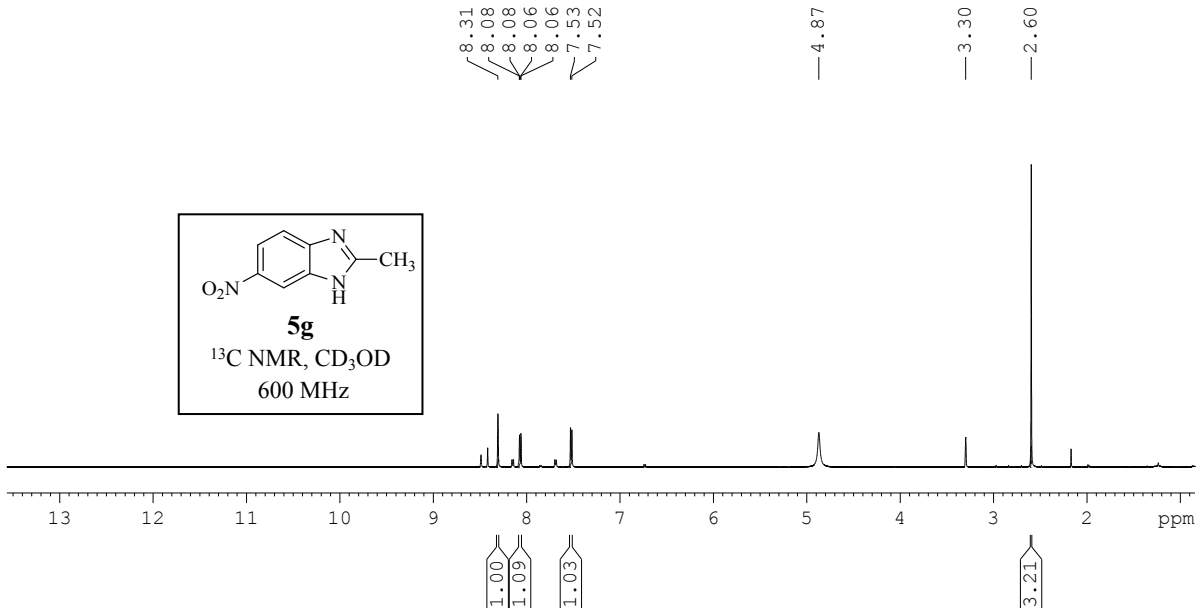

153.36
140.21
137.43
125.13
117.29
115.39
114.87
48.85
48.57
48.28
48.00
47.72
47.43
47.15
13.32
5e
13C NMR, CD3OD
150 MHz
180
160
140
120
100
80
60
40
20
0
ppm

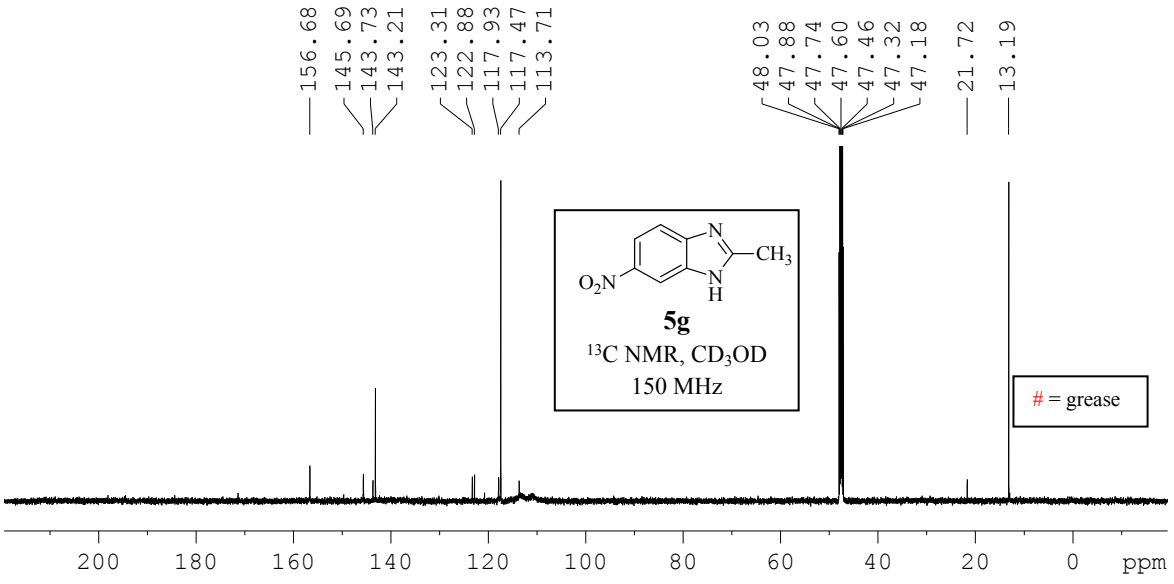

5e
ESI-MS = 210.9870
100
%
0
210.9870
2.35e5
213.9990
222.1042
240.9348
133.2480
134.2530
102.3481
118.2848
124.2761
149.2143
167.1494
178.1474
197.0190
m/z

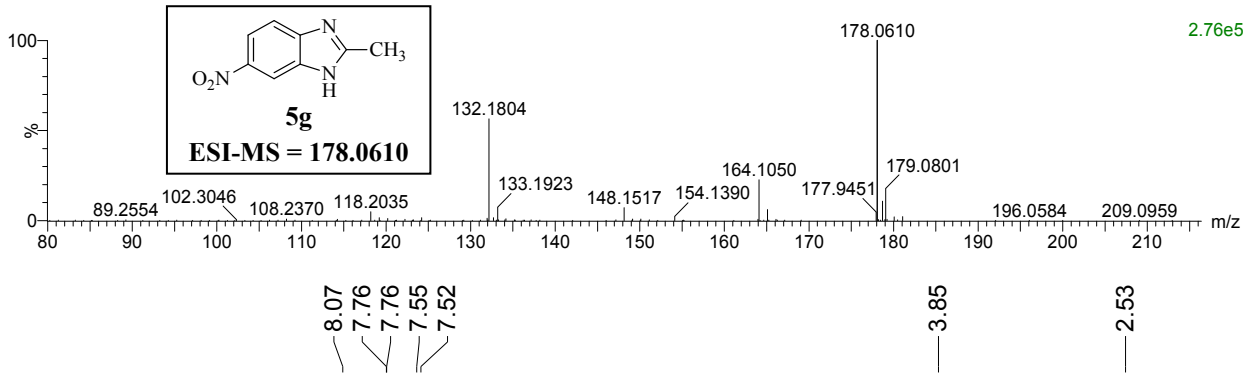

7.70
2.49
5f
1H NMR, DMSO-d6
300 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
2.00
3.38

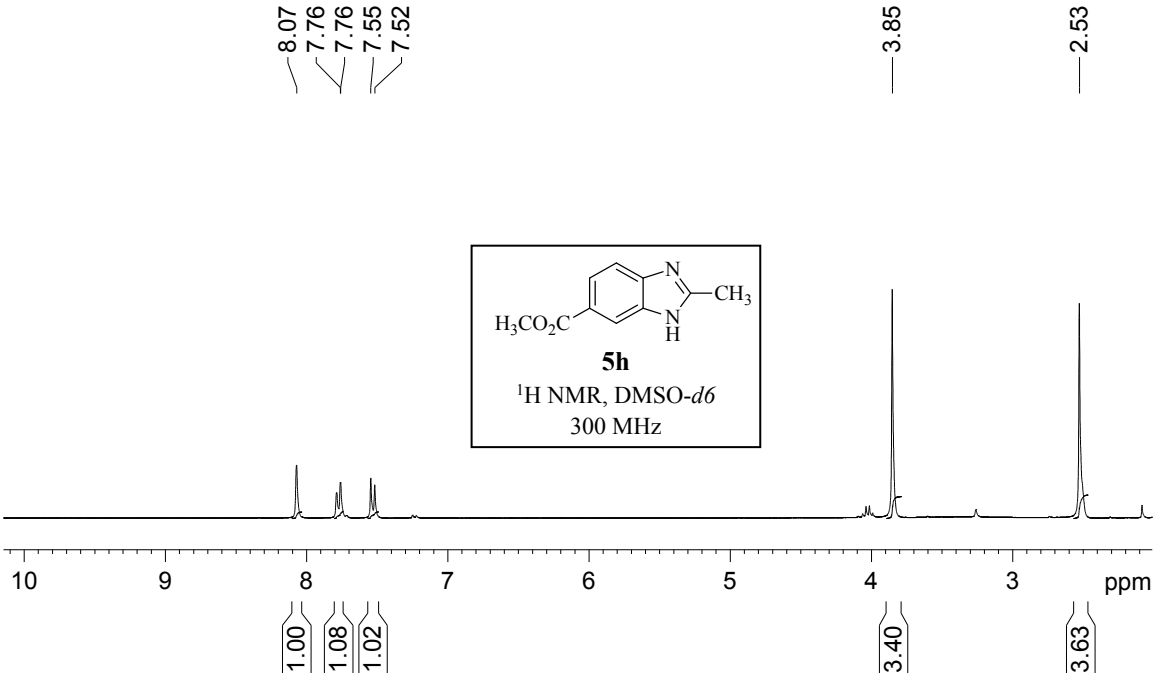

154.39
138.36
123.44
115.68
115.34
40.33
40.05
39.78
39.50
39.22
38.94
38.66
14.61
Cl
Cl
N
CH3
N
H
5f
13C NMR, DMSO-d6
75 MHz
180
160
140
120
100
80
60
40
20
0
ppm

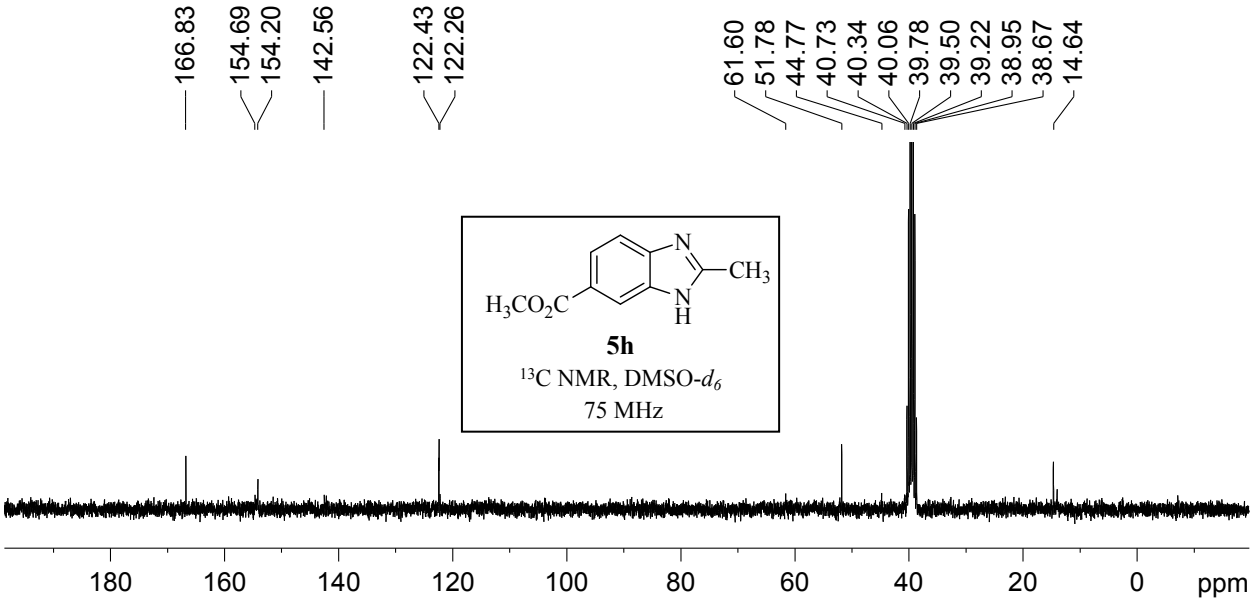

100
%
0
200.9980
202.9944
204.9938
200.8817
114.2708
124.2530
133.2230
89.2731
167.1172
227.1170
244.8817
274.0999
6.64e4
m/z
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
240
250
260
270
280
290
300
Cl
Cl
N
CH3
N
H
5f
ESI-MS = 200.9980

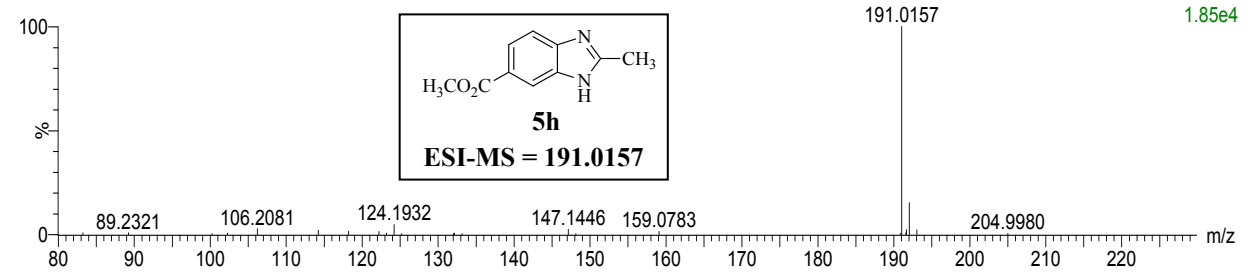

8.31
8.08
8.08
8.06
8.06
7.53
7.52
4.87
3.30
2.60
O2N
N
CH3
N
H
5g
13C NMR, CD3OD
600 MHz
13
12
11
10
9
8
7
6
5
4
3
2
ppm
1.00
1.09
1.03
3.21

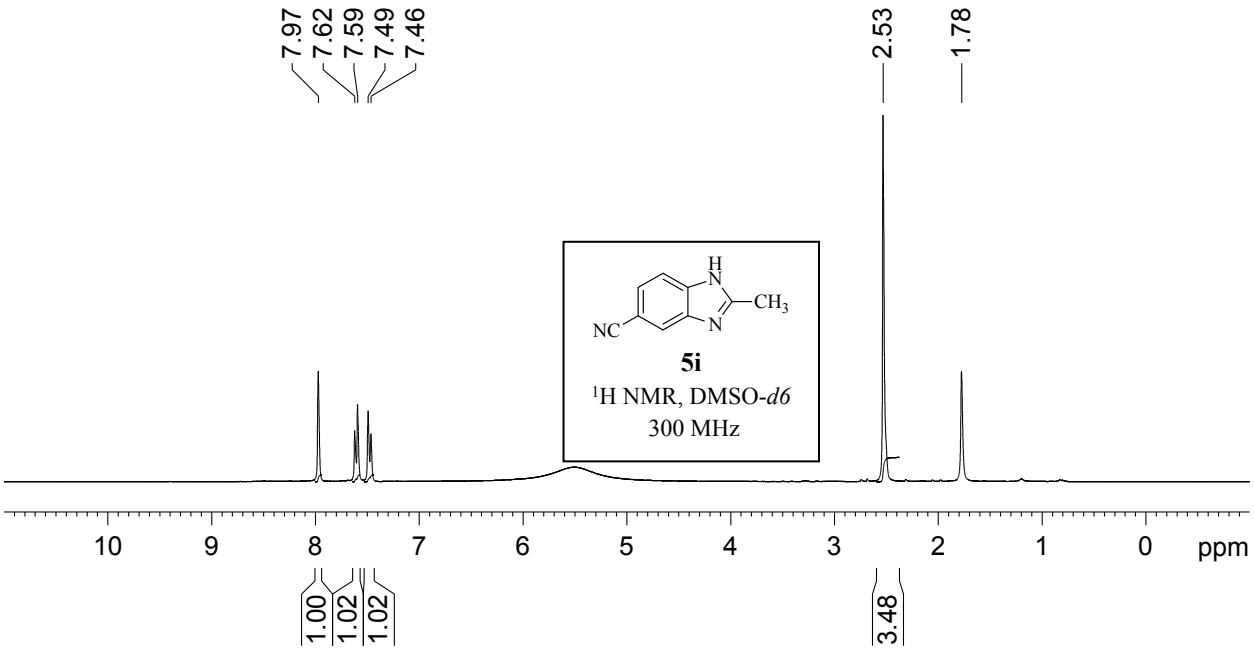

156.68
145.69
143.73
143.21
123.31
122.88
117.93
117.47
113.71
48.03
47.88
47.74
47.60
47.46
47.32
47.18
21.72
13.19
5g
13C NMR, CD3OD
150 MHz
= grease
200
180
160
140
120
100
80
60
40
20
0
ppm

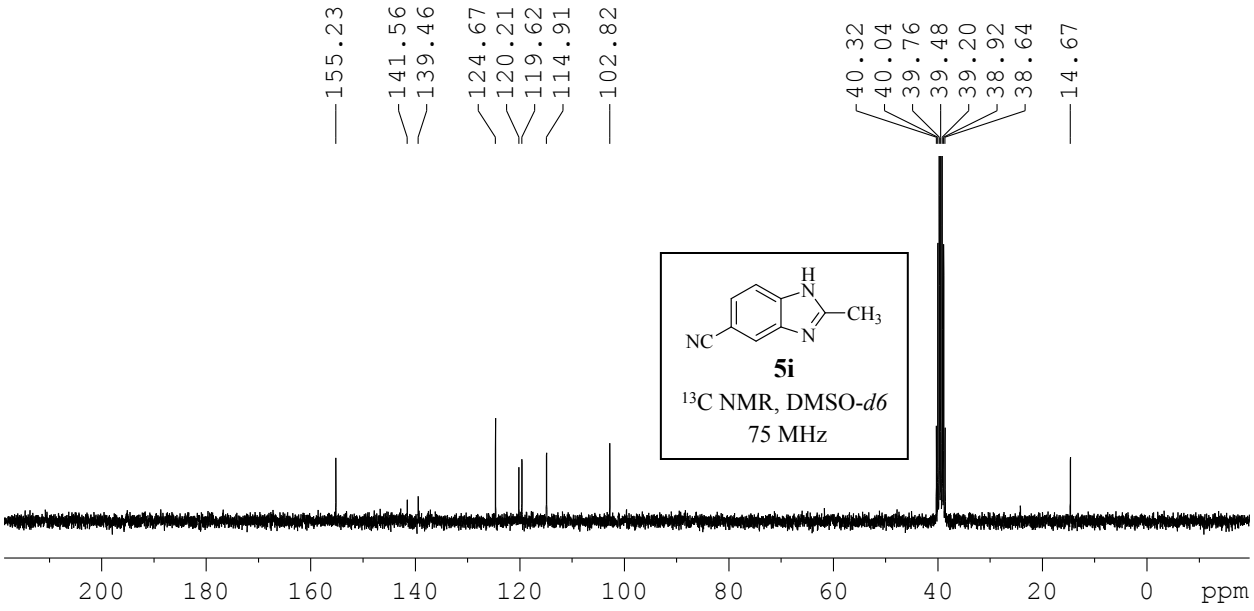

5g
ESI-MS = 178.0610
178.0610
2.76e5
132.1804
133.1923
164.1050
179.0801
177.9451
154.1390
148.1517
102.3046
89.2554
108.2370
118.2035
196.0584
209.0959
m/z

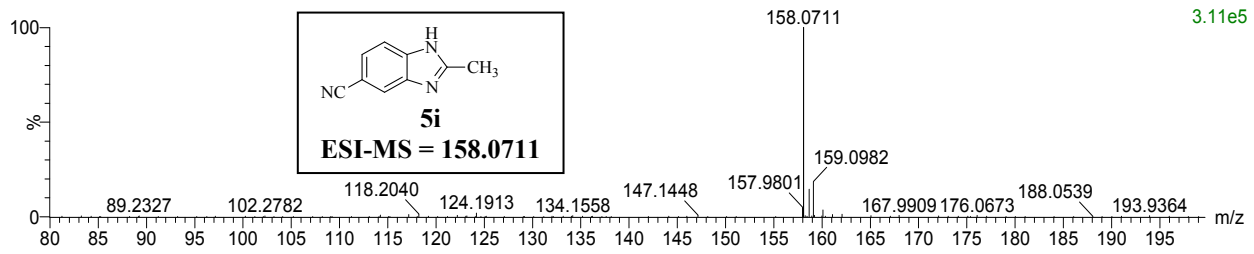

8.07
7.76
7.76
7.55
7.52
3.85
2.53
5h
1H NMR, DMSO-d6
300 MHz
10
9
8
7
6
5
4
3
ppm
1.00
1.08
1.02
3.40
3.63

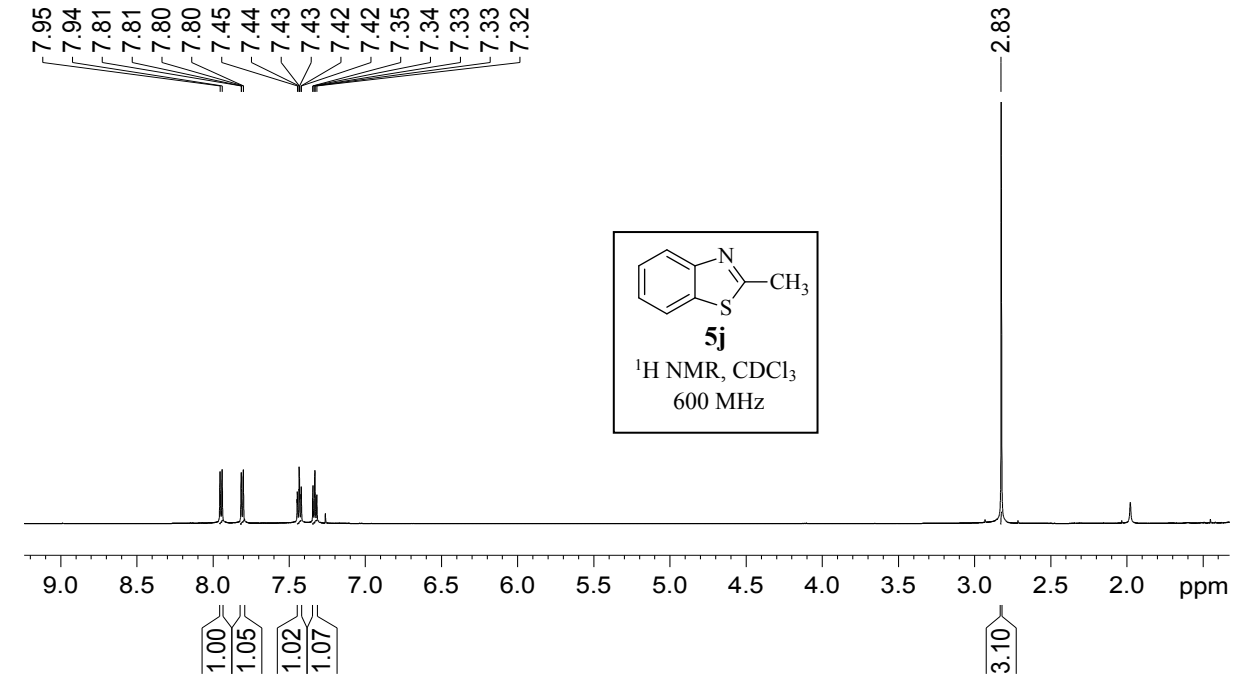

166.83
154.69
154.20
142.56
122.43
122.26
61.60
51.78
44.77
40.73
40.34
40.06
39.78
39.50
39.22
38.95
38.67
14.64
5h
13C NMR, DMSO-d6
75 MHz
180
160
140
120
100
80
60
40
20
0
ppm

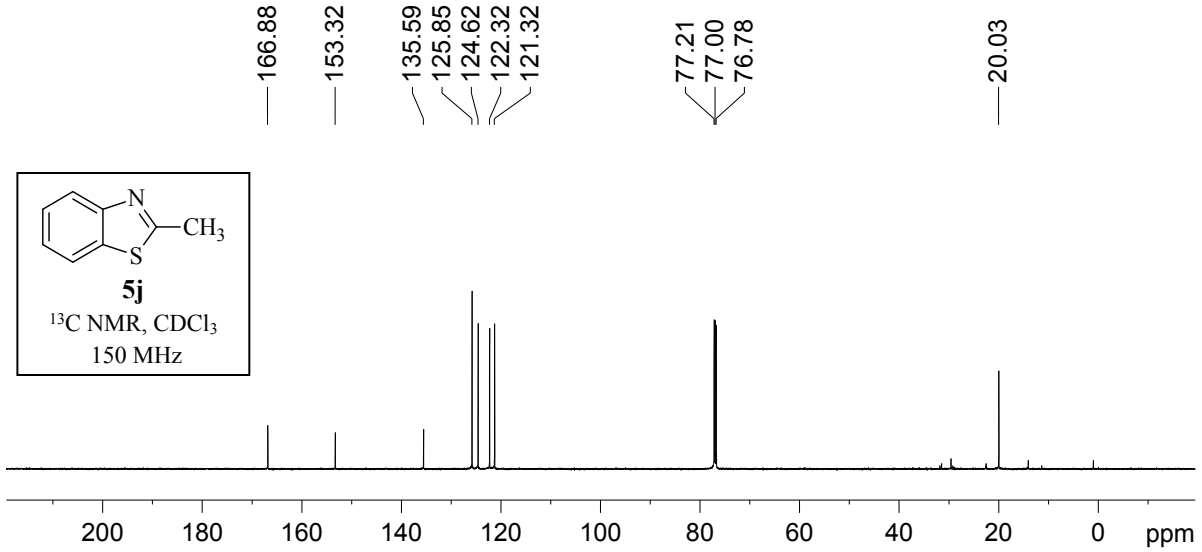

100
%
0
191.0157
1.85e4
5h
ESI-MS = 191.0157
89.2321
106.2081
124.1932
147.1446
159.0783
204.9980
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
m/z

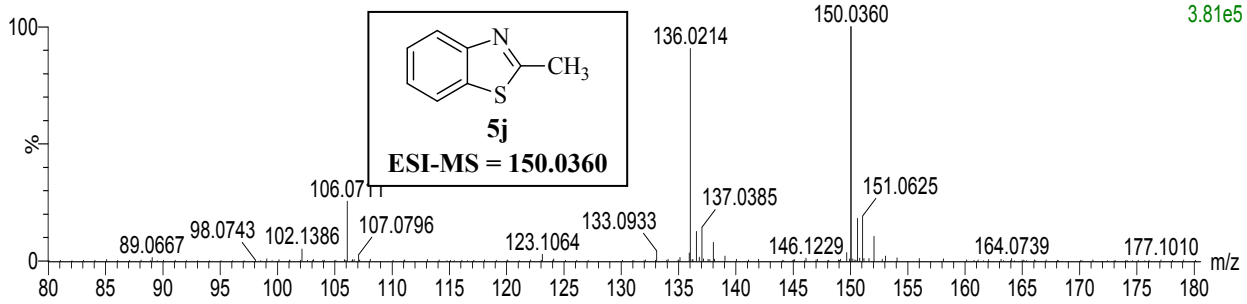

7.97
7.62
7.59
7.49
7.46
2.53
1.78
5i
1H NMR, DMSO-d6
300 MHz
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.02
1.02
3.48

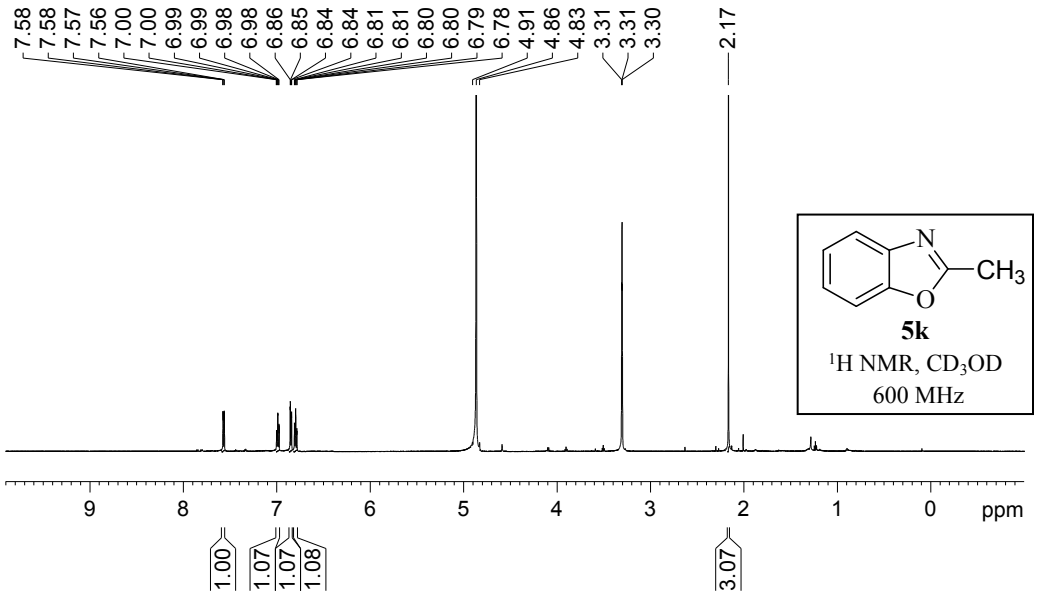

155.23
141.56
139.46
124.67
120.21
119.62
114.91
102.82
40.32
40.04
39.76
39.48
39.20
38.92
38.64
14.67
5i
13C NMR, DMSO-d6
75 MHz
200 180 160 140 120 100 80 60 40 20 0 ppm

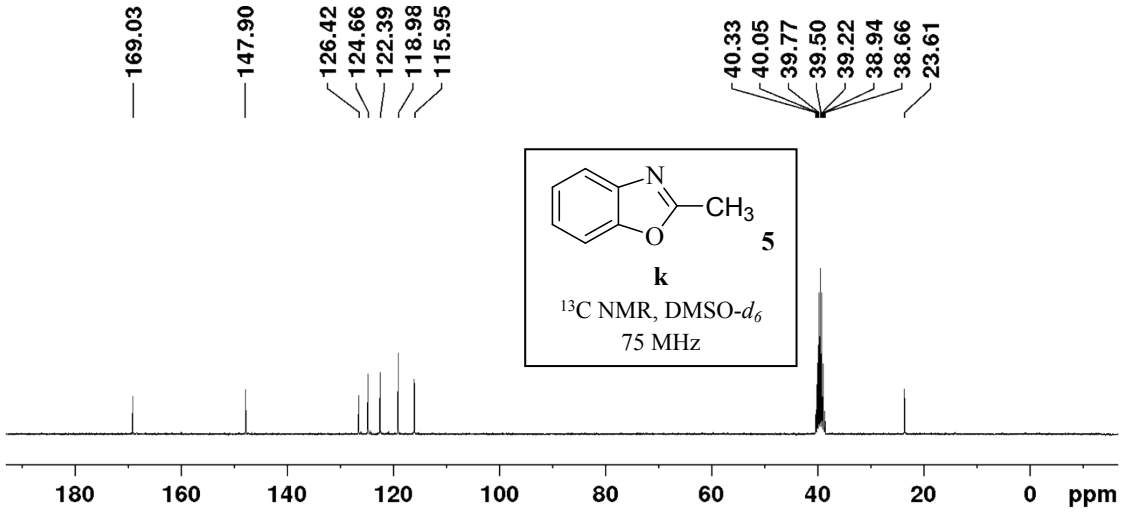

5i
ESI-MS = 158.0711
158.0711
3.11e5
159.0982
157.9801
89.2327
102.2782
118.2040
124.1913
134.1558
147.1448
167.9909
176.0673
188.0539
193.9364
m/z

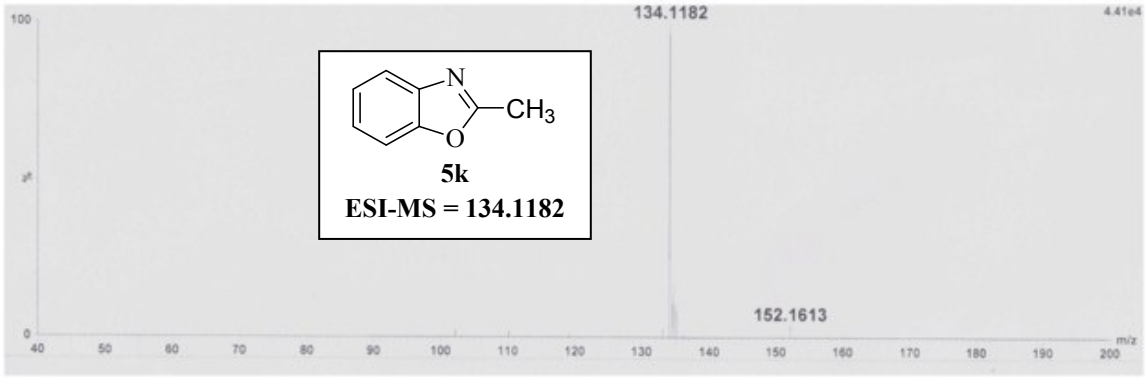

7.95
7.94
7.81
7.81
7.80
7.80
7.45
7.44
7.43
7.43
7.42
7.42
7.35
7.34
7.33
7.33
7.32
2.83
5j
1H NMR, CDCl3
600 MHz
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 ppm
1.00
1.05
1.02
1.07
3.10

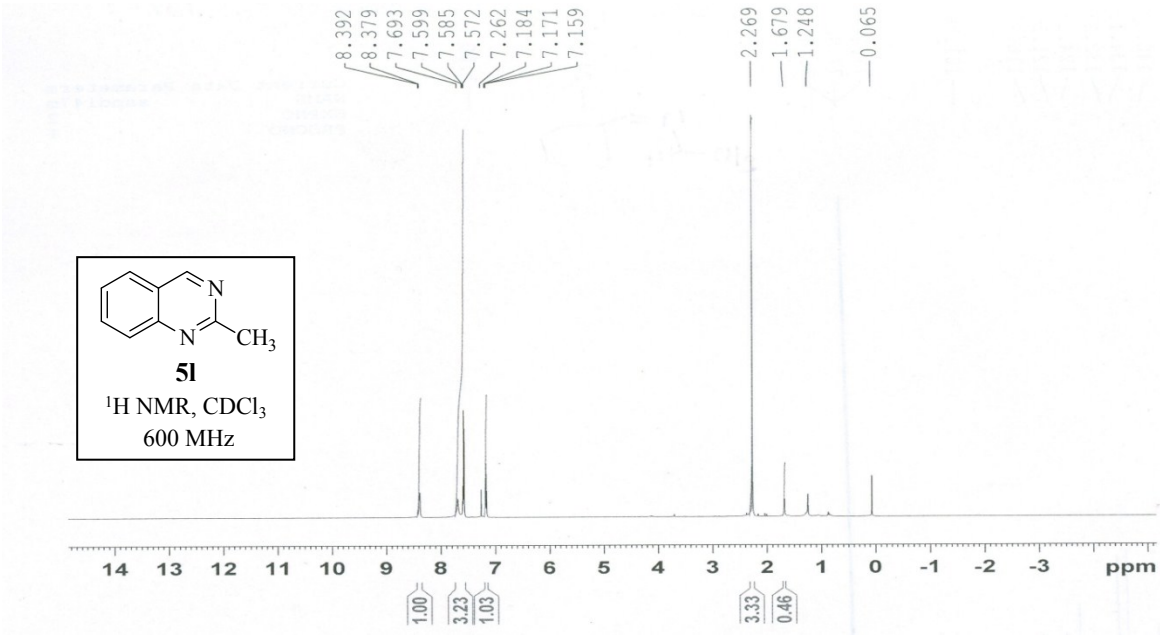

166.88
153.32
135.59
125.85
124.62
122.32
121.32
77.21
77.00
76.78
20.03
N
CH3
S
5j
13C NMR, CDCl3
150 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm

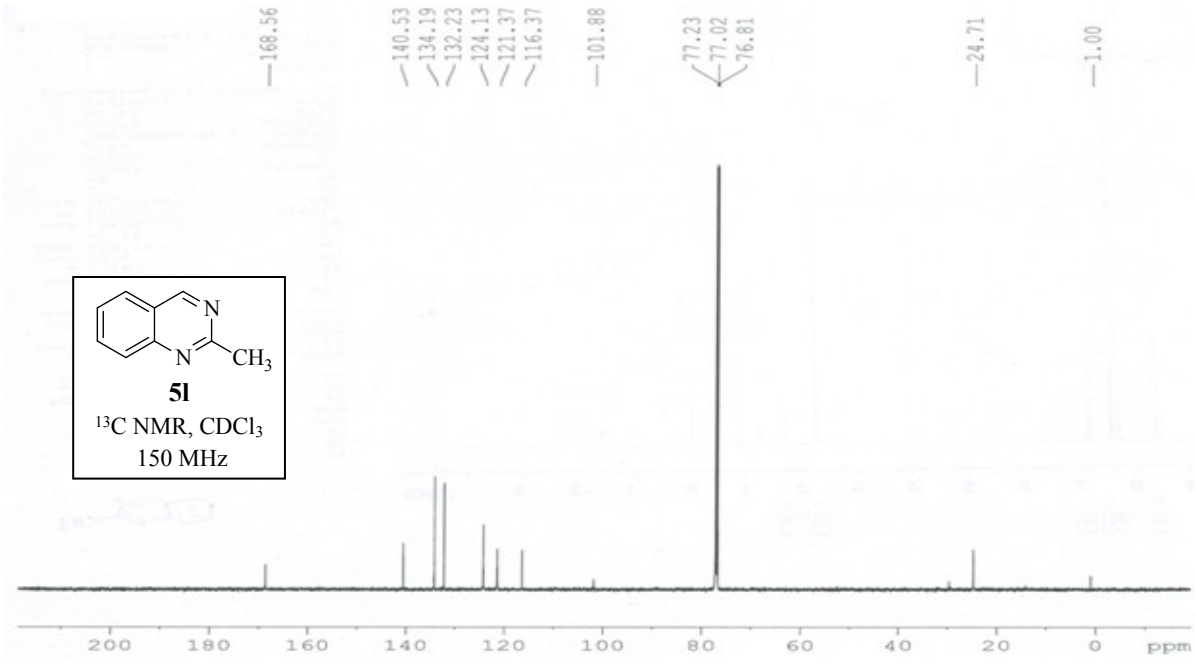

100
%
0
N
CH3
S
5j
ESI-MS = 150.0360
150.0360
3.81e5
136.0214
106.0711
137.0385
151.0625
89.0667
98.0743
102.1386
107.0796
123.1064
133.0933
146.1229
164.0739
177.1010
m/z
80
85
90
95
100
105
110
115
120
125
130
135
140
145
150
155
160
165
170
175
180


7.58
7.58
7.57
7.56
7.00
7.00
6.99
6.99
6.98
6.98
6.86
6.85
6.84
6.84
6.81
6.81
6.80
6.80
6.79
6.78
4.91
4.86
4.83
3.31
3.31
3.30
2.17
N
CH3
O
5k
1H NMR, CD3OD
600 MHz
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.07
1.07
1.08
3.07


169.03
147.90
126.42
124.66
122.39
118.98
115.95
40.33
40.05
39.77
39.50
39.22
38.94
38.66
23.61
N
CH3
O
5
k
13C NMR, DMSO-d6
75 MHz
180
160
140
120
100
80
60
40
20
0
ppm


134.1182
152.1613
N
CH3
O
5k
ESI-MS = 134.1182


8.392
8.379
7.693
7.599
7.585
7.572
7.262
7.184
7.171
7.159
2.269
1.679
1.248
0.065
N
N
CH3
5l
1H NMR, CDCl3
600 MHz
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
ppm
1.00
3.23
1.03
3.33
0.46



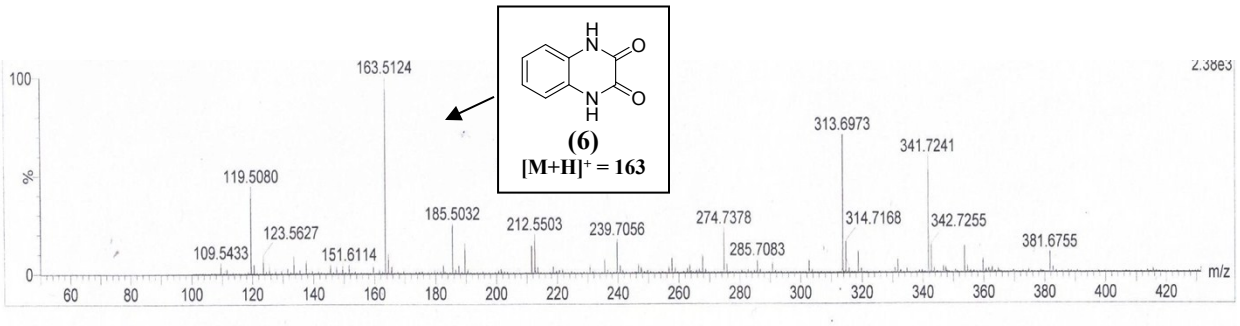
Scheme 2: The compound **2a** at gram scale, was prepared according to the general procedure described for **2a** (small scale) starting from 1,2-Phenylenediamine (1.0 gm, 9.259 mmol), oxalic acid dihydtrate (5.8 gm, 46.295 mmol) and 1, 4-dioxane (10 mL) as a solvent were taken in a round bottom. After completion of the reaction and washing the organic part with EtOA:Hexane (50:50) solution afforded 1*H*-benzimidazole (**2a**) as white solid (874 mg, 80%).

Further synthesis of compound **5a** at gram scale was prepared according to the general procedure described for **5a** (small scale) starting from 1,2-Phenylenediamine (1.0 gm, 9.259 mmol), malonic acid (5.78 gm, 55.554 mmol) and 1, 4-dioxane (10 mL) as a solvent were taken in a round bottom flask. After completion of reaction and washing the organic part with EtOA:Hexane (50:50) solution afforded 2-methyl-1*H*-benzimidazole (**5a**) as white solid (953 mg, 78%).

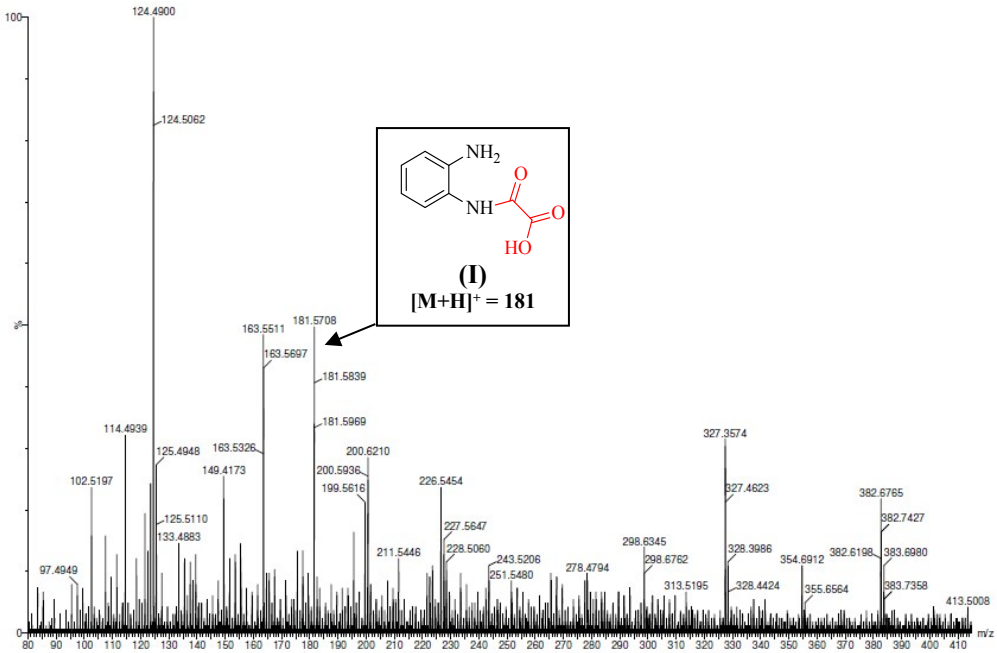
Scheme 3: The compound **6** was synthesised by reported method 1,2-Phenylenediamine (100 mg, 0.9259 mmol), oxalic acid dihydtrate (175 mg, 1.3888 mmol) and hydrochloric acid (0.5

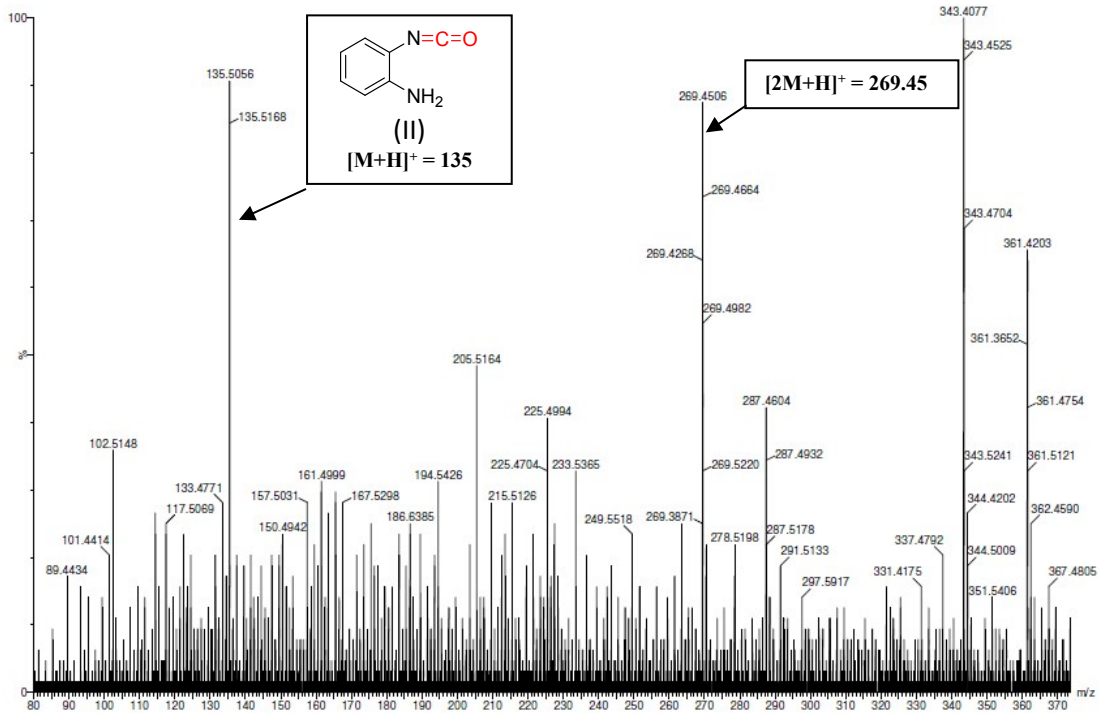
mL) were taken in round bottom flask and refluxed at 100 °C for 8 hrs. After completion of reaction, the brown precipitate was washed with distilled water to afford the product (90%, 135 mg) and confirmed by ESI-MS.

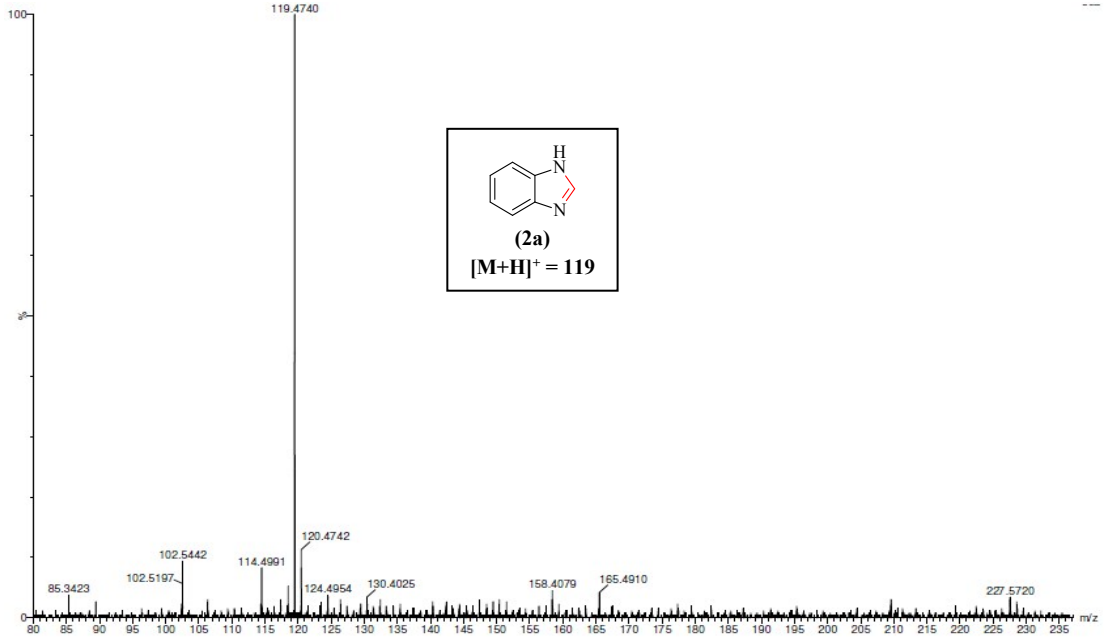
ESI-MS (m/z): $[M+H]^+$calcd. for $C_8H_7N_2O_2$ is 163.0508 obsd. = 163.5124.

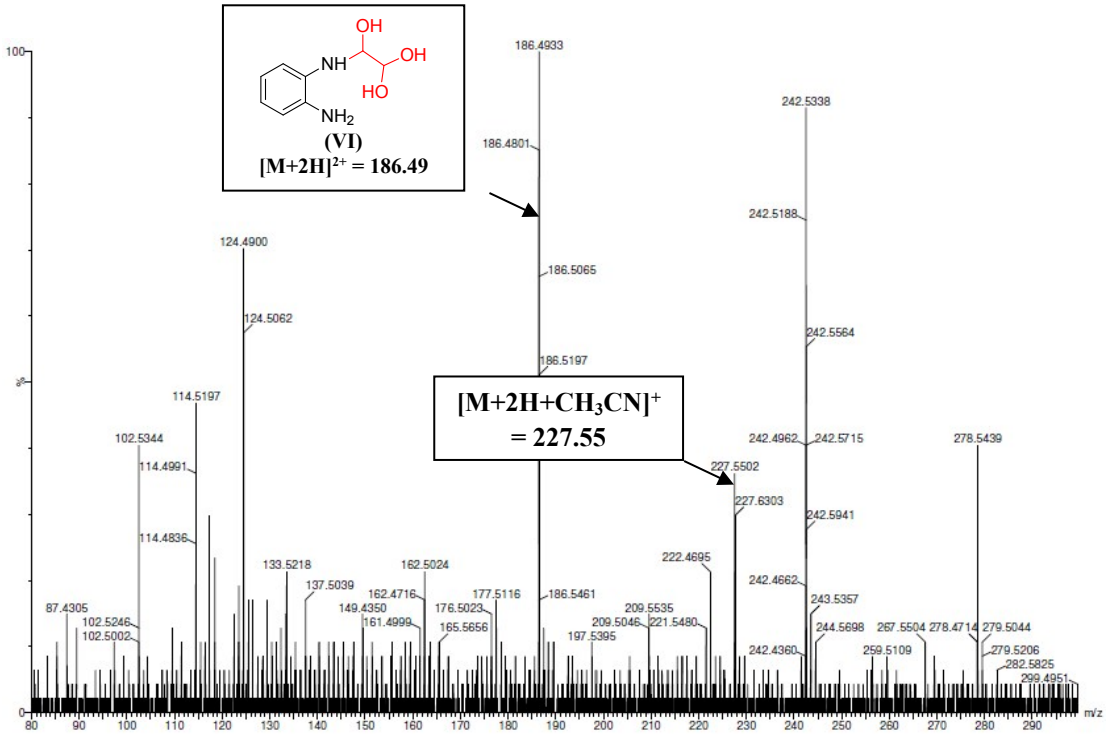


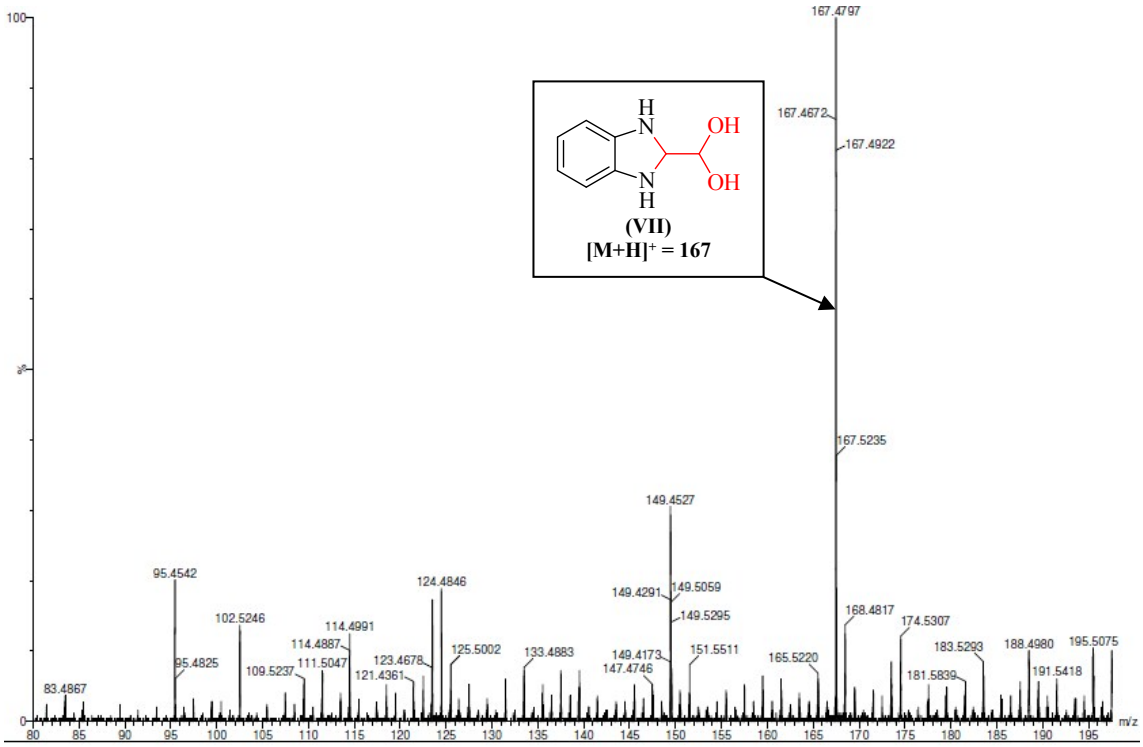
Scheme 4:

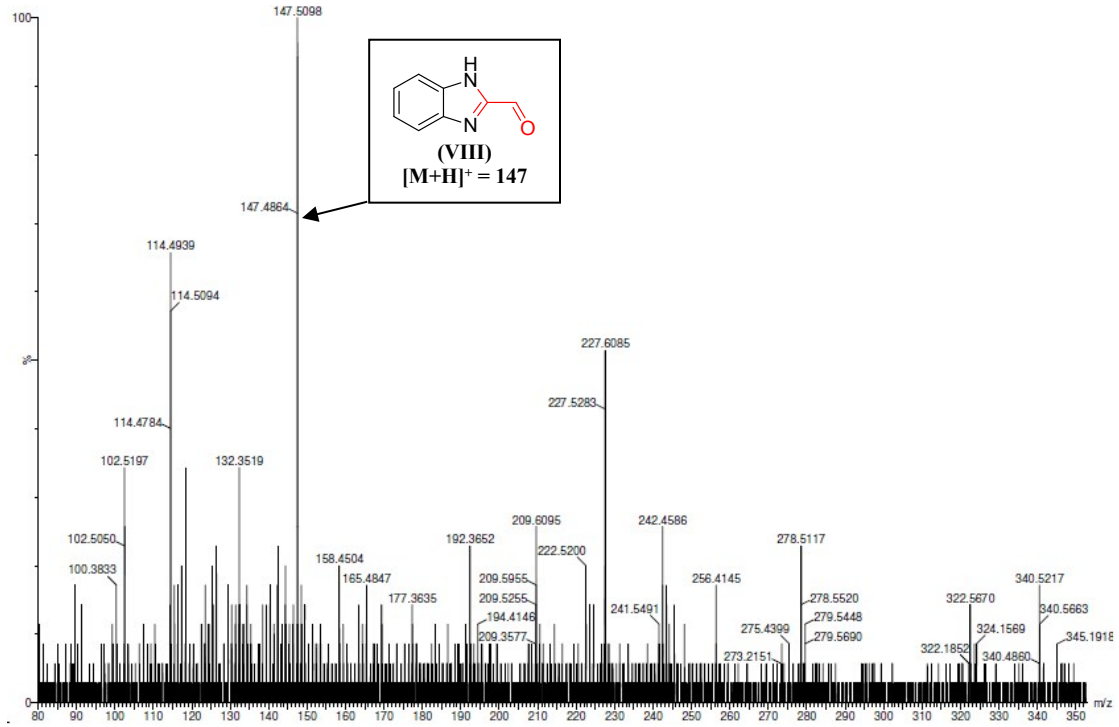


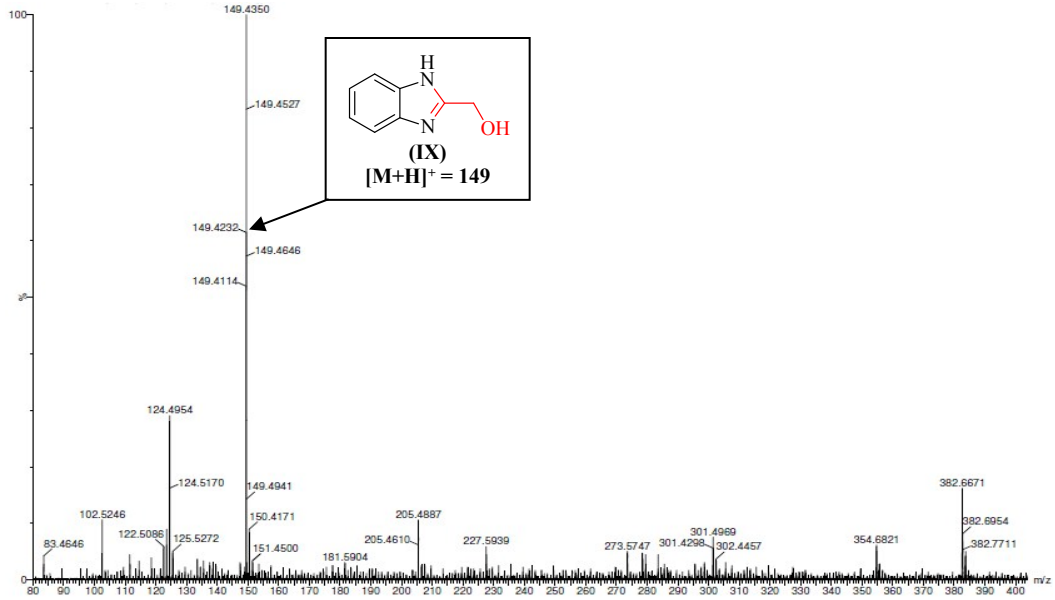

N=C=O
NH2
(II)
[M+H]+ = 135
[2M+H]+ = 269.45
135.5056
135.5168
269.4506
343.4077
343.4525
269.4664
343.4704
361.4203
269.4268
269.4982
361.3652
205.5164
287.4604
361.4754
225.4994
102.5148
225.4704
233.5365
287.4932
269.5220
343.5241
361.5121
161.4999
194.5426
133.4771
157.5031
167.5298
215.5126
344.4202
362.4590
117.5069
186.6385
249.5518
269.3871
287.5178
101.4414
150.4942
278.5198
337.4792
291.5133
344.5009
89.4434
331.4175
367.4805
297.5917
351.5406
m/z
(III)
[M+H]+ = 135
135.4887
149.5236
149.5118
135.5056
149.5414
251.4560
135.4662
149.4823
251.5020
149.5532
114.4939
121.4680
124.4846
178.4979
181.5773
107.4503
182.4182
203.5332
227.5574
102.5393
182.4378
151.5511
95.4495
137.5266
203.5608
253.5521
223.5446
163.5264
95.4401
177.5244
240.5664
205.5718
261.5073
222.4911
267.4872
83.4735
m/z

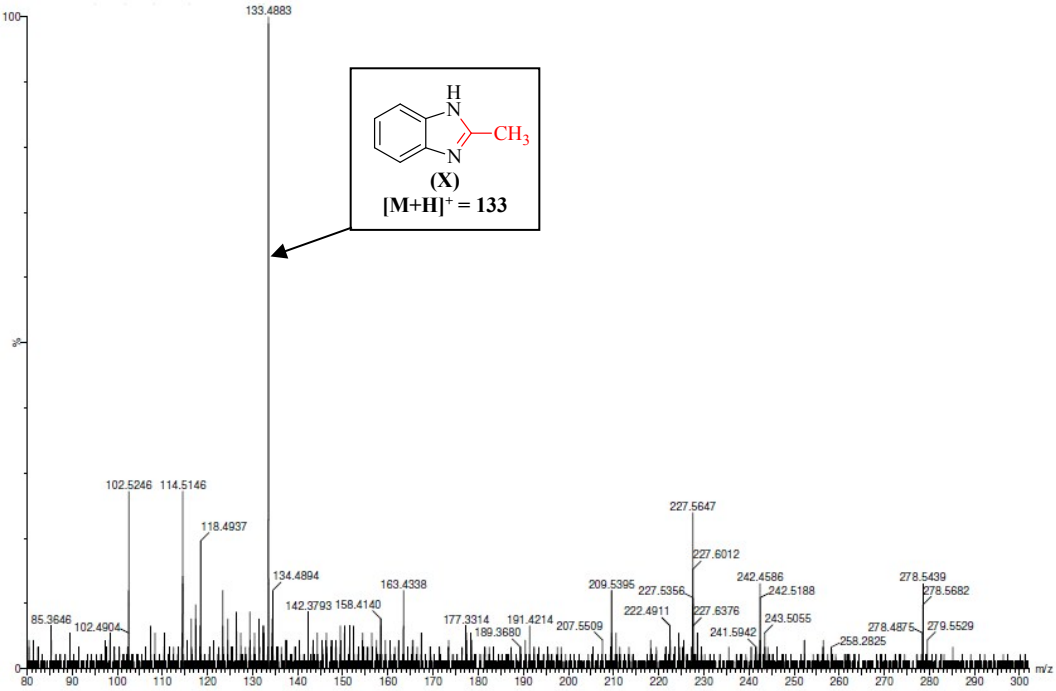

119.4740
(2a)
[M+H]+ = 119
120.4742
102.5442
114.4991
102.5197
85.3423
124.4954
130.4025
158.4079
165.4910
227.5720
m/z


(VI)
[M+2H]2+ = 186.49
[M+2H+CH3CN]+
= 227.55
186.4933
186.4801
186.5065
186.5197
242.5338
242.5188
242.5564
242.4962
242.5715
227.5502
227.6303
242.5941
242.4662
243.5357
242.4360
278.5439
124.4900
124.5062
114.5197
102.5344
114.4991
114.4836
133.5218
162.5024
137.5039
162.4716
149.4350
161.4999
177.5116
176.5023
165.5656
186.5461
222.4695
209.5535
209.5046
221.5480
197.5395
87.4305
102.5246
102.5002
244.5698
267.5504
278.4714
279.5044
259.5109
279.5206
282.5825
299.4951
m/z


(VII)
[M+H]+ = 167
167.4797
167.4672
167.4922
167.5235
149.4527
95.4542
124.4846
149.4291
149.5059
149.5295
102.5246
114.4991
114.4887
168.4817
174.5307
123.4678
125.5002
133.4883
149.4173
151.5511
165.5220
183.5293
188.4980
195.5075
111.5047
147.4746
181.5839
191.5418
109.5237
121.4361
83.4867
95.4825
%
m/z


(VIII)
[M+H]+ = 147
147.5098
147.4864
114.4939
114.5094
227.6085
227.5283
114.4784
102.5197
132.3519
209.6095
242.4586
102.5050
192.3652
278.5117
222.5200
158.4504
100.3833
165.4847
256.4145
340.5217
209.5955
177.3635
209.5255
278.5520
322.5670
340.5663
241.5491
194.4146
279.5448
324.1569
275.4399
209.3577
279.5690
345.1918
322.1852
340.4860
273.2151
%
m/z


149.4350
149.4527
149.4232
149.4646
149.4114
124.4954
124.5170
149.4941
102.5246
150.4171
122.5086
125.5272
205.4887
83.4646
205.4610
227.5939
151.4500
181.5904
273.5747
301.4969
301.4298
302.4457
354.6821
382.6671
382.6954
382.7711
H
N
N
OH
(IX)
[M+H]+ = 149
m/z


133.4883
102.5246
114.5146
118.4937
134.4894
163.4338
142.3793
158.4140
85.3646
102.4904
177.3314
191.4214
189.3680
207.5509
209.5395
227.5356
222.4911
227.5647
227.6012
227.6376
242.4586
242.5188
241.5942
243.5055
258.2825
278.4875
278.5439
278.5682
279.5529
H
N
N
CH3
(X)
[M+H]+ = 133
m/z

We have performed several LC-MS analyses at different interval of time to identify the intermediate and steps involve in the reaction. The LC-MS chromatogram of the reaction mixture in which retention time at 7.20 and 1.44 represent the mass 167 (**VII**) and 119 (**2a**). It was observed that the peak corresponds to retention time 7.20 getting reduced with time and the peak corresponds to retention time 1.44 was formed accordingly. The corresponding mass spectra revealed that the compound **VII** could be a possible intermediate which finally leads to the formation of product **2a** (Figure 1 and 2).

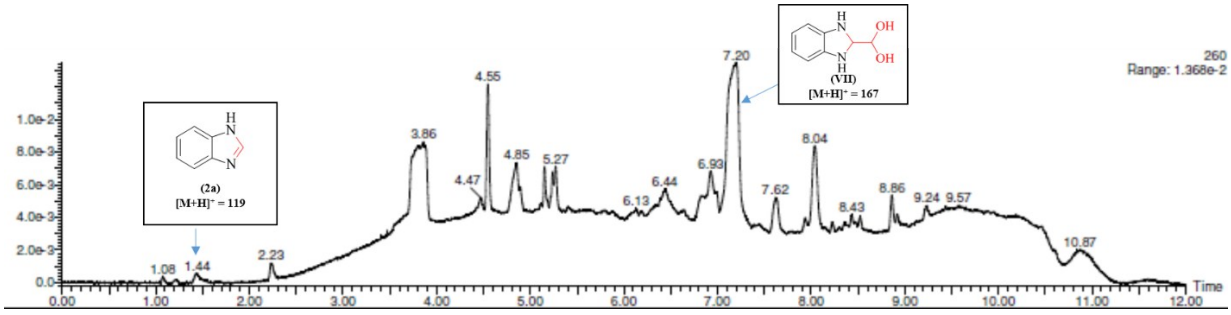


Figure 1.

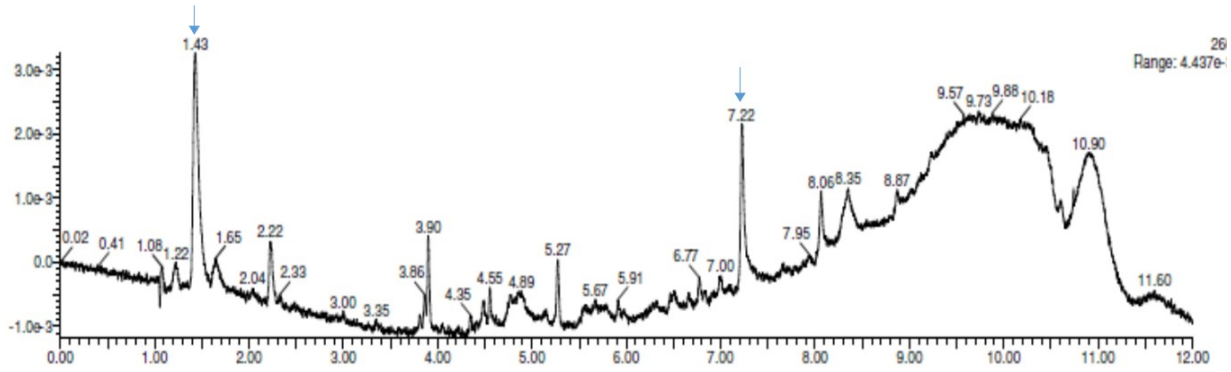


Figure 2.

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2. (a) T. Yoshimura, D. Yuanjun, Y. Kimura, H. Yamada, A. Toshimitsu and T. Kondo, *Heterocycles*, 2015, **90**, 857-865. (b) F. Li, L. Lu, and P. Liu, *Org. Lett.,* 2016, **18**, 2580−2583.
3. (a) S. Majumdar, A. Chakraborty, S. Bhattacharjee, S. Debnath and D. K. Maiti, *Tetrahedron Letters*, 2016, **57**, 4595–4598. (b) F. Feng, J. Ye, Z. Cheng, X. Xu, Q. Zhang, L. Ma, C. Lu, X. Li, *RSC Advances*, 2016, **6**, 72750-72755. (c) M. Saha, P. Mukherjee and A. R. Das, *Tetrahedron Letters*, 2017, **58**, 2044-2049.