Electronic Supplementary Material (ESI) for Green Chemistry.

Electronic Supplementary Material

Guanidine Hydrochloride (GuHCl) Catalysed Microwave-Mediated Solvent- and Metal-Free Synthesis of Pyrimido[1,2-a]benzimidazole from Aryl Aldehyde and Aryl Methyl Ketone

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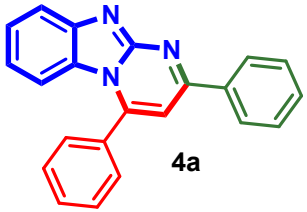
Experimental Section

General information

All chemicals and solvents were purchased from commercial suppliers and used without further purification. All reactions were carried out in oven-dried glassware with magnetic stirring. Commercially available chemicals were used without further purification. The starting materials acetophenone **1**, benzaldehyde **2**, 2-benzimidazole **3** and GuHCl were purchased from commercial source. Monitoring of the reaction was performed by thin-layer chromatography using TLC silica gel 60 F254 plates. Flash column chromatography was performed using silica gel 243-400 mess typically using a n-hexane/ethyl acetate eluent system. NMR spectra were calibrated to the solvent residual signals of DMSO. ^{1}H NMR spectra were recorded at 400 MHz Jeol, 500 & 600 MHz Bruker instruments. Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, qui: quintuplet, m: multiplet), coupling constant (*J* in Hz) and integration. ^{13}C NMR spectra were recorded at 101, 126 and 151 MHz using broadband proton decoupling and chemicals shifts are reported in ppm using residual solvent peaks as reference. High resolution mass spectra (HRMS) were recorded on a Orbitrap (Exploris 240) mass spectrometer with an orthogonal Z-spray–electrospray interface. Reported yields are based upon isolation following purification by silica gel column chromatography; isolated material was judged to be homogeneous based upon TLC and NMR. Pyrimido[1,2-a]benzimidazole 4a[1],4b[1b], 4c[1], 4d[1d], 4g[1d] and 4p[1].

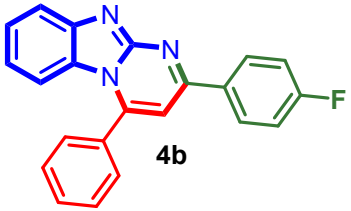
General procedure of pyrimido[1,2-a]benzimidazole synthesis: Aryl methyl ketone **1** (2.0 mmol), benzaldehyde **2** (2.0 mmol), 2-aminobenzimidazole **3** (2.0 mmol) were taken in vial and entire mixture was irradiated in microwave at 720W for 2X5 min. Then, the reaction mass was purified by column chromatography (ethyl acetate/n-hexane) to afford the pure product.

General procedure for chromatography-free Synthesis of 2,4-diaryl pyrimido [1,2-a]benzimidazoles: Aryl methyl ketone **1** (2.0 mmol), aryl aldehyde **2** (2.0 mmol), and 2-aminobenzimidazole **3** (2.0 mmol) were irradiated under microwave at 720W for 2X5 min. Then, the reaction mixture was dissolved in 2.0 mL of DMSO, followed by precipitation of the product through the addition of water (2.0 mL). The solid was filtered and washed with water (10 mL) to remove DMSO and guanidine hydrochloride. After air-drying for a few hours, the solid was further washed with a 20% ethyl acetate-hexane (10 mL) to eliminate low-polarity impurities. Finally, the product was purified by precipitation or crystallization from ethyl acetate/hexane.



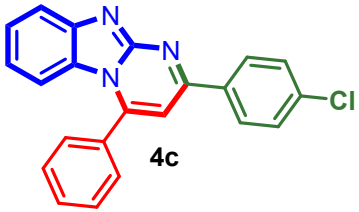
4a

2,4-diphenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4a**): Yellow amorphous solid (494 mg, 77%); R_f = 0.82 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.36 – 8.26 (m, 2H), 7.97 (d, *J* = 8.2 Hz, 1H), 7.76 – 7.61 (m, 5H), 7.59-7.51 (m, 3H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.27 (s, 1H), 7.03 (t, *J* = 7.8 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 1H); δ_C (151 MHz, $CDCl_3$) 161.3, 152.3, 149.5, 145.7, 136.9, 132.8, 131.4, 131.2, 129.6, 129.1, 128.5, 128.0, 127.6, 126.1, 121.3, 120.4, 114.7, 105.5.



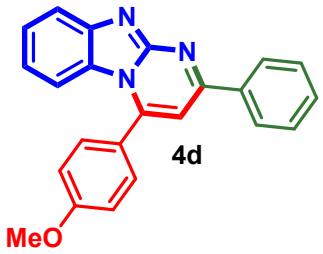
4b

2-(4-fluorophenyl)-4-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4b**): Yellow crystalline solid (576 mg, 85%); R_f = 0.72 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.38 – 8.30 (m, 2H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.80 – 7.62 (m, 5H), 7.46 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.26 – 7.15 (m, 3H), 7.04 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.71 – 6.64 (m, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 165.0 (d, *J* 250 Hz), 160.0, 152.1, 149.6, 145.6, 133.0 (d, J 3 Hz), 132.6, 131.3, 130.0 (d, *J*9 Hz), 129.6, 128.5, 127.5, 126.1, 121.4, 120.3, 116.1 (d, J 22 Hz), 114.6, 105.1; **ESI-MS**: *m*/*z* =$[M+H]^+$calcd. for $C_{22}H_{15}FN_3$: 340.1245; found 340.1241.

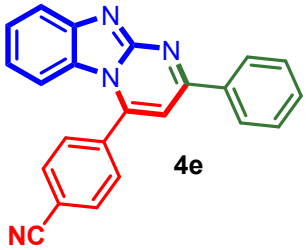


4c

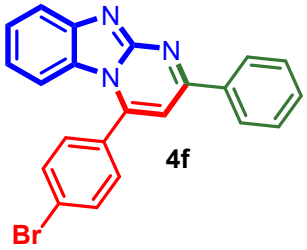
2-(4-chlorophenyl)-4-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4c**): Yellow amorphous solid (576 mg, 81%); R_f = 0.61 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.29 – 8.21 (m, 2H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.78 – 7.59 (m, 5H), 7.53 – 7.43 (m, 3H), 7.23 (s, 1H), 7.04 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 159.9, 152.1, 149.7, 145.6, 137.8, 135.2, 132.6, 131.3, 129.6, 129.3, 129.2, 128.5, 127.5, 126.2, 121.5, 120.4, 114.7, 105.1; **ESI-MS**: *m*/*z* =$[M+H]^+$calcd. for $C_{22}H_{15}ClN_3$: 356.0949; found 356.0945.



4-(4-methoxyphenyl)-2-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4d**): Yellow amorphous solid (499 mg, 71%); R_f = 0.42 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.37 – 8.21 (m, 2H), 7.96 (ddd, *J* = 8.2, 0.8 Hz, 1H), 7.62 – 7.56 (m, 2H), 7.53 (ddd, *J* = 4.6, 2.6, 1.4 Hz, 3H), 7.46 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.23 (s, 1H), 7.20 – 7.13 (m, 2H), 7.06 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.84 (dt, *J* = 8.5, 1.0 Hz, 1H), 3.98 (s, 3H); δ_C (101 MHz, CHLOROFORM-*D*) 161.8, 161.2, 152.5, 149.6, 145.7, 136.9, 131.4, 130.0, 129.1, 128.0, 127.7, 126.0, 124.9, 121.1, 120.3, 114.8, 114.8, 105.6, 55.7, 29.8.

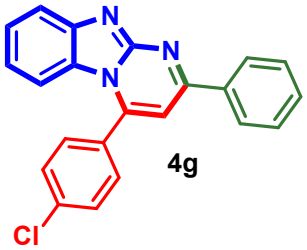


4-(2-phenylbenzo[4,5]imidazo[1,2-a]pyrimidin-4-yl)benzonitrile (**4e):** Yellow amorphous solid (581 mg, 84%); R_f = 0.80 (petroleum ether/EtOAc 1:1) ; δ_H (400 MHz, Chloroform-*d*) δ 8.33 – 8.28 (m, 2H), 8.02 – 7.99 (m, 3H), 7.86 – 7.81 (m, 2H), 7.60-7.53 (m, 4H), 7.53 – 7.47 (m, 1H), 7.13-7.05 (m, 1H), 6.67 – 6.59 (m, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 161.1, 151.9, 147.0, 145.6, 136.8, 136.3, 133.3, 131.7, 129.6, 129.2, 127.9, 127.1, 126.4, 121.9, 120.8, 117.9, 115.3, 114.0, 105.6; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{23}H_{15}N_4$: 347.1291; found 347.1298.



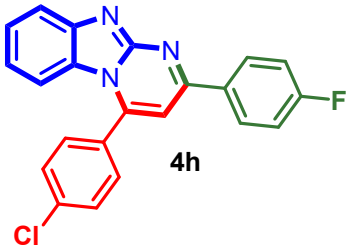
4-(4-bromophenyl)-2-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4f**): Yellow amorphous solid (672 mg, 83%); R_f = 0.53 (petroleum ether/EtOAc 1:1); δ_H ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.33 – 8.24 (m, 2H), 7.98 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.87 – 7.79 (m, 2H),

7.58 – 7.51 (m, 5H), 7.48 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.24 (s, 1H), 7.09 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.77 (dt, *J* = 8.5, 1.0 Hz, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 161.2, 152.1, 148.2, 145.6, 136.6, 132.9, 131.6, 131.5, 130.2, 129.1, 127.9, 127.4, 126.2, 125.8, 121.6, 120.5, 114.5, 105.5; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{22}H_{15}BrN_3$: 400.0444; found 400.0440..



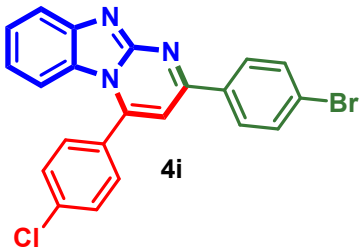
4g

4-(4-chlorophenyl)-2-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4g**): Yellow amorphous solid (626 mg, 88%); R_f = 0.79 (petroleum ether/EtOAc 5/5); δ_H (400 MHz, Chloroform-*d*) δ 8.37 – 8.23 (m, 2H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.65 – 7.59 (m, 2H), 7.56 – 7.51 (m, 3H), 7.48 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.26 (s, 3H), 7.09 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.76 (d, *J* = 8.5 Hz, 1H); δ_C (151 MHz, $CDCl_3$) 161.2, 152.2, 148.2, 145.7, 137.6, 136.7, 131.6, 131.1, 130.0, 130.0, 129.1, 128.0, 127.4, 126.2, 121.6, 120.6, 114.4, 105.6; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{22}H_{15}ClN_3$: 356.0949; found 356.0946.



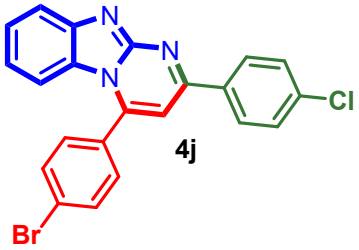
4h

4-(4-chlorophenyl)-2-(4-fluorophenyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4h**): Yellow amorphous solid (628 mg, 84%); R_f = 0.76 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.34 – 8.25 (m, 2H), 7.96 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.63 – 7.58 (m, 2H), 7.47 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.24 – 7.16 (m, 3H), 7.08 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.74 (dt, *J* = 8.5, 0.9 Hz, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 165.1 (d, *J* 251 Hz), 160.0, 152.0, 148.4, 145.6, 137.6, 132.8 (d, *J* 3 Hz), 130.9, 130.1, 130.1 (d, *J* 9 Hz), 129.9, 127.4, 126.3, 121.6, 120.6, 116.2 (d, *J* 21 Hz), 114.4, 105.2; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{22}H_{14}ClFN_3$: 374.0855; found 374.0851.



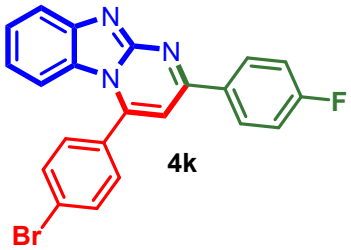
4i

2-(4-bromophenyl)-4-(4-chlorophenyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4i**): Yellow crystalline solid (757 mg, 84%); R_f = 0.78 (petroleum ether/EtOAc 1:1); δ_H (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.75 – 7.57 (m, 6H), 7.51 – 7.42 (m, 1H), 7.17 (s, 1H), 7.12 – 7.03 (m, 1H), 6.74 (d, *J* = 8.4 Hz, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 159.9, 151.9, 148.5, 145.6, 137.7, 135.4, 132.3, 130.8, 130.0, 129.9, 129.3, 127.3, 126.4, 126.4, 121.7, 120.6, 114.5, 105.1; **ESI-MS**: *m*/*z* =$[M+H]^+$calcd. for $C_{22}H_{14}BrClN_3$: 434.0054; found 434.0051.



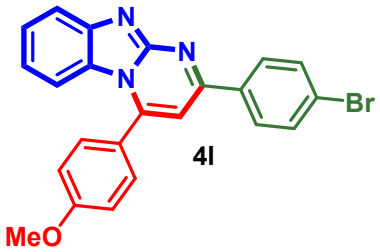
4j

4-(4-bromophenyl)-2-(4-chlorophenyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4j**): Yellow crystalline solid (696 mg, 84%); R_f = 0.80 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.29 – 8.19 (m, 2H), 8.02 – 7.93 (m, 1H), 7.87 – 7.78 (m, 2H), 7.57 – 7.52 (m, 2H), 7.52 – 7.45 (m, 3H), 7.18 (s, 1H), 7.14 – 7.05 (m, 1H), 6.80 – 6.71 (m, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 159.8, 151.9, 148.5, 145.7, 137.9, 135.0, 132.9, 131.3, 130.1, 129.4, 129.2, 127.4, 126.4, 125.9, 121.7, 120.6, 114.5, 105.1; **ESI-MS**: *m*/*z* =$[M+H]^+$calcd. for $C_{22}H_{14}BrClN_3$: 434.0054; found 434.0049.

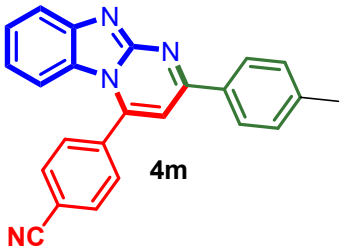


4k

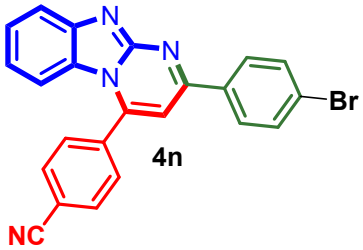
4-(4-bromophenyl)-2-(4-fluorophenyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4k**): Yellow crystalline solid (652 mg, 78%); R_f = 0.81 (petroleum ether/EtOAc 1:1); δ_H (400 MHz, Chloroform-*d*) δ 8.37 – 8.28 (m, 2H), 8.03 – 7.94 (m, 1H), 7.89 – 7.77 (m, 2H), 7.57 – 7.52 (m, 2H), 7.49 (ddd, *J* = 8.3, 7.2, 1.1 Hz, 1H), 7.25 – 7.20 (m, 2H), 7.19 (s, 1H), 7.10 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 6.77 (dt, *J* = 8.5, 1.0 Hz, 1H); δ_C (126 MHz, CHLOROFORM-*D*) 165.1 (d, *J* 250 Hz) 160.0, 152.0, 148.4, 145.6, 132.9, 131.4, 130.1, 130.1, 130.1, 127.4, 126.3, 125.9, 121.6, 120.6, 116.3 (d, 90 Hz), 114.4, 105.2; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{22}H_{14}BrFN_3$: 418.0350; found 418.0346.



2-(4-bromophenyl)-4-(4-methoxyphenyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4l**): Yellow crystalline solid (611 mg, 71%); R_f = 0.68 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) δ 8.15 (d, *J* = 8.5 Hz, 2H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J* = 8.6 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.22 – 7.13 (m, 3H), 7.08 (t, *J* = 7.8 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 3.98 (s, 3H); δ_C (151 MHz, $CDCl_3$) 161.9, 160.1, 152.2, 150.0, 145.5, 135.7, 132.4, 130.0, 129.4, 127.6, 126.3, 124.7, 121.4, 120.7, 120.3, 114.9, 114.9, 105.3, 55.7; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{23}H_{17}BrN_3O$: 430.0550, found 430.0545.

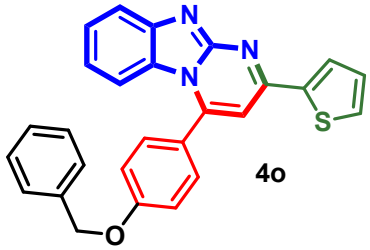


4-(2-(p-tolyl)benzo[4,5]imidazo[1,2-a]pyrimidin-4-yl)benzonitrile (**4m**): Orange amorphous solid (641 mg, 89%); R_f = 0.79 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) δ 8.16 (d, *J* = 7.4 Hz, 2H), 8.05-7.85 (m, 3H), 7.85-7.75 (m, 2H), 7.46 (t, *J* = 7.1 Hz, 1H), 7.32 (d, *J* = 7.7 Hz, 2H), 7.20 (s, 1H), 7.06 (t, *J* = 7.7 Hz, 1H), 6.66 – 6.56 (m, 1H), 2.43 (s, 3H); δ_C (151 MHz, $CDCl_3$) 161.1, 152.0, 146.9, 145.6, 142.4, 136.9, 133.6, 133.3, 129.9, 129.6, 127.9, 127.2, 126.3, 121.7, 120.7, 117.9, 115.3, 114.0, 105.5, 21.7; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{24}H_{17}N_4$: 361.1448; found .; found 361.1454.



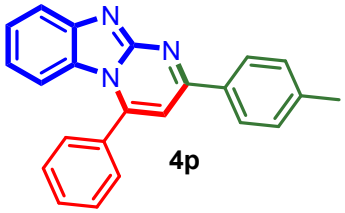
4n

4-(2-(4-bromophenyl)benzo[4,5]imidazo[1,2-a]pyrimidin-4-yl)benzonitrile (**4n**): Orange amorphous solid (706 mg, 83%); R_f = 0.52 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 8.6 Hz, 2H), 8.00 (d, *J* = 8.2 Hz, 2H), 7.95 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 1H), 7.17 (s, 1H), 7.07 (t, *J* = 7.8 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H); δ_C (101 MHz, DMSO-D_6) (151 MHz, $CDCl_3$) 159.8, 151.6, 147.3, 145.7, 136.7, 135.2, 133.4, 132.4, 129.6, 129.3, 127.1, 126.7, 126.6, 122.1, 120.9, 117.8, 115.5, 114.0, 105.1; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{23}H_{13}BrN_4$: 425.0396; found .; found 425.0391.



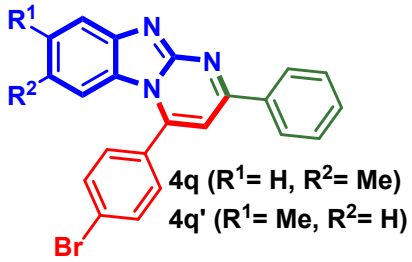
4o

4-(4-(benzyloxy)phenyl)-2-(thiophen-2-yl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4o**): Yellow amorphous solid (703 mg, 81%); R_f = 0.51 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) δ 7.92 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 3.5 Hz, 1H), 7.60-7.54 (m, 3H), 7.54-7.48 (m, 2H), 7.47 – 7.38 (m, 4H), 7.23 (d, *J* = 8.6 Hz, 2H), 7.19 – 7.14 (m, 1H), 7.06 (s, 1H), 7.03 (t, *J* = 7.7 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 5.23 (s, 2H); δ_C (151 MHz, $CDCl_3$) 161.0, 156.3, 152.1, 149.3, 145.6, 143.1, 136.3, 131.7, 130.1, 128.9, 128.8, 128.5, 127.9, 127.7, 125.9, 124.9, 121.2, 120.2, 115.8, 114.6, 104.9, 70.5; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{27}H_{20}N_3OS$: 434.1322;found .; 434.1329.



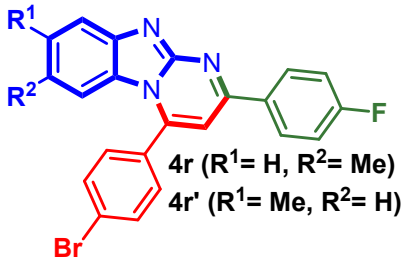
4p

4-phenyl-2-(p-tolyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4p**): Yellow amorphous solid (462 mg, 69%); R_f = 0.90 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 8.1 Hz, 2H), 7.94 (d, *J* = 8.2 Hz, 1H), 7.81 – 7.55 (m, 5H), 7.44 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.23 (s, 1H), 7.01 (t, *J* = 7.7 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 2.43 (s, 3H); δ_C (151 MHz, $CDCl_3$) 161.3, 152.4, 149.3, 145.6, 142.0, 134.0, 132.8, 131.1, 129.8, 129.5, 128.5, 127.9, 127.6, 126.0, 121.2, 120.2, 114.6, 105.3, 21.6.



4q (R^1= H, R^2= Me)
4q' (R^1= Me, R^2= H)

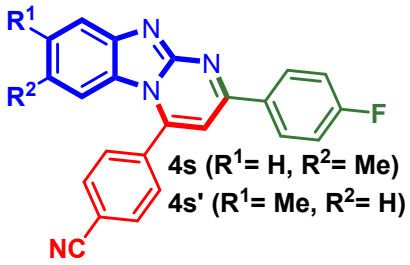
Compound **4q** and **4q'**: Yellow amorphous solid (653 mg, 79%); R_f = 0.83 (petroleum ether/EtOAc 1:1); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.27-8.23 (m, 2H), 7.90 –7.74 (m, 3H), 7.58 – 7.48 (m, 5H), 7.33 – 7.27 (m) and 6.97 – 6.84 (m) (1H), 7.18 (d, *J* = 7.7 Hz, 1H), 6.63 (m) and 6.54 (s) (1H), 2.50 (s) and 2.33 (s) (3H); δ_C (151 MHz, $CDCl_3$) 160.6, 160.4, 152.1, 151.8, 147.8, 147.8, 145.9, 143.6, 136.6, 136.3, 132.7, 132.6, 131.5, 131.5, 131.4, 131.3, 130.1, 130.0, 128.9, 127.8, 127.7, 127.3, 125.6, 125.5, 123.1, 120.0, 114.0, 113.8, 105.3, 105.1, 22.1, 21.9; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{23}H_{17}BrN_3$: 414.0600; found 414.0609.



4r (R^1= H, R^2= Me)
4r' (R^1= Me, R^2= H)

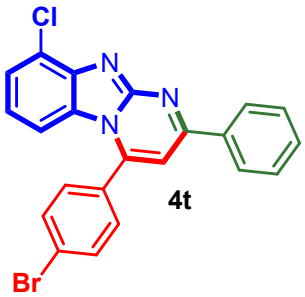
Compound **4r** and **4r'**: Yellow amorphous solid (672 mg, 78%); R_f = 0.80 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) 8.27- 8.25 (2 H, m), 7.88 – 7.77 (3 H, m), 7.55 (2 H, dd, *J* 8.0, 6.0), 7.29 (d, *J* 8.3) and 6.89 (d, *J* 8.5) (1H), 7.19 (2 H, t, *J* 8.3), 7.12 (1 H, d, *J* 8.1), 6.65- 6.50 (1H, m), 2.49 (s) and 2.32 (1 H) (3H); δ_C (151 MHz, $CDCl_3$) 164.3 (d, *J* 250 Hz), 159.2 (d, *J* 27 Hz), 151.8 (d, *J* 52 Hz), 148.0, 147.9 (d, *J* 9 Hz), 143.6, 136.4, 132.7, 132.6, 131.5, 131.4, 131.4, 130.0, 130.0, 129.9, 129.8, 127.9, 127.3,

125.6, 125.6, 125.2, 123.2, 119.9, 116.1, 115.9, 114.0, 113.8, 104.9, 104.7, 22.1, 21.8; **ESI-MS**: *m/z* =[M+H]$^+$calcd. for $C_{23}H_{16}BrFN_3$: 432.0506; found 432.0508.



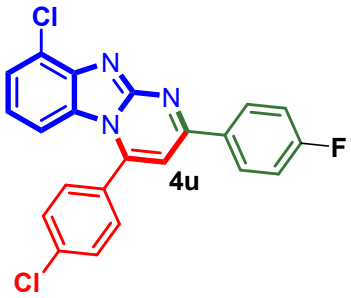
4s (R^1= H, R^2= Me)
4s' (R^1= Me, R^2= H)

Compound **4s** and **4s'**: Yellow amorphous solid (529 mg, 71%); R_f = 0.75 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) 8.38-8.8.10 (2 H, m), 7.99 – 7.52 (5 H, m), 7.30 (d, *J* 8.0) and 6.90 (d, *J* 8.2) (1H), 7.24 – 7.08 (3 H, m), 6.69 – 6.40 (1 H, m), 2.50 (s) and 2.33 (s) (3H); δ_C (151 MHz, $CDCl_3$) 165.0 (d, *J* 252 Hz), 159.5(d, *J* 27 Hz), 152.1, 148.1 (d, *J* 10 Hz), 146.0, 143.7, 137.6, 136.6, 132.9, 131.7, 131.0, 130.0, 130.0, 129.9, 129.8, 128.1, 125.4, 123.4, 120.1, 116.3, 116.1, 114.1, 114.0, 105.2, 105.0, 22.2, 22.0; **ESI-MS**: *m/z* =[M+H]$^+$calcd. for $C_{24}H_{16}FN_4$: 379.1354; found 379.1348.

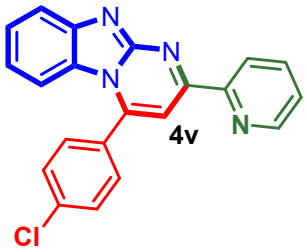


4t

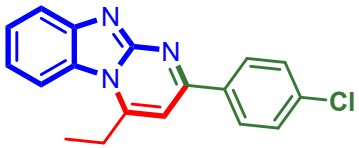
4-(4-bromophenyl)-9-chloro-2-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4t**): Yellow amorphous solid (710 mg, 82%); R_f = 0.85 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) 8.28 (2 H, dd, *J* 7.8, 1.5), 7.84 (2 H, d, *J* 8.3), 7.57 (2 H, d, *J* 8.3), 7.55 – 7.49 (3 H, m), 7.46 (1 H, d, *J* 7.6), 7.26 (1 H, s), 6.97 (1 H, t, *J* 8.1), 6.64 (1 H, d, *J* 8.3); δ_C (151 MHz, $CDCl_3$) 161.7, 152.1, 148.4, 142.9, 136.2, 133.0, 131.8, 131.1, 130.2, 129.1, 128.2, 128.0, 126.0, 125.9, 125.1, 121.7, 113.0, 106.1; **ESI-MS**: *m/z* =[M+H]$^+$calcd. for $C_{22}H_{14}BrClN_3$: 434.0054; found 434.0064.



9-chloro-4-(4-chlorophenyl)-2-(4-fluorophenyl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4u**): Yellow amorphous solid (529 mg, 76%); R_f = 0.75 (petroleum ether/EtOAc 1:1); δ_H (600 MHz, Chloroform-*d*) 8.32 (2 H, dd, *J* 8.7, 5.4), 7.71-7.65 (2 H, m), 7.63-7.57 (2 H, m), 7.50 (1 H, d, *J* 7.7), 7.24 – 7.18 (3 H, m), 7.00 (1 H, t, *J* 8.1), 6.65 (1 H, d, *J* 8.4); δ_C (151 MHz, $CDCl_3$) 165.7 (d, *J* 210 Hz), 160.5, 148.4, 142.8, 137.8, 132.4, 130.4, 130.1, 130.1, 129.9 (d, *J* 5 Hz), 128.1, 125.9, 125.1, 121.7, 116.3, 116.1, 112.8, 105.7; **ESI-MS**: *m*/*z* =$[M+H]^+$calcd. for $C_{22}H_{13}Cl_2FN_3$: 408.0465; found 408.0468.

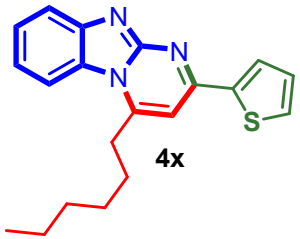


4-(4-chlorophenyl)-2-(pyridin-2-yl)benzo[4,5]imidazo[1,2-a]pyrimidine (**4v**): Yellow crystalline solid (434 mg, 61%); R_f = 0.25 (MeOH/DCM 1:4) δ_H (600 MHz, DMSO-d_6) 9.55 (1 H, d, *J* 2.0), 8.77 (2 H, dd, *J* 13.6, 6.4), 7.88 (1 H, d, *J* 8.2), 7.85 – 7.81 (3 H, m), 7.79 (1 H, t, *J* 7.5), 7.74 (2 H, t, *J* 7.3), 7.64 (1 H, dd, *J* 7.9, 4.9), 7.48 (1 H, t, *J* 7.7), 7.09 (1 H, t, *J* 7.8), 6.57 (1 H, d, *J* 8.3). * Due to its highly insoluble nature, we were unable to record the ^{13}C NMR spectrum; **ESI-MS**: *m*/*z* =$[M+H]^+$calcd. for $C_{21}H_{14}ClN_4$: 357.0902; found 357.0895.



4w

2-(4-chlorophenyl)-4-ethylbenzo[4,5]imidazo[1,2-a]pyrimidine (**4w**): Yellow amorphous solid (375 mg, 61%); R_f = 0.80 (petroleum ether/EtOAc 1:1); ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.43 (s, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.44 – 7.33 (m, 2H), 7.14 (s, 1H), 3.45 (q, *J* = 7.4 Hz, 2H), 1.62 (t, *J* = 7.4 Hz, 3H); δ $_C$ (151 MHz, $CDCl_3$) 159.4, 153.7, 151.8, 145.5, 138.8, 133.9, 130.8, 130.4, 127.5, 126.3, 126.0, 123.2, 121.9, 120.5, 114.9, 101.7, 29.7, 10.8; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{18}H_{15}ClN_3$: 308.0949; found 308.0941.



4x

*4-hexyl-2-(thiophen-2-yl)benzo[4,5]imidazo[1,2-a]*pyrimidine (**4x**): Yellow amorphous solid (430 mg, 64%); R_f = 0.85 (petroleum ether/EtOAc 1:1); 1H NMR (600 MHz, Chloroform-d) δ 7.98 (d, J = 8.2 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 7.85 (dd, *J* = 3.7, 0.9 Hz, 1H), 7.58 (dd, *J* = 5.0, 0.9 Hz, 1H), 7.54 (t, *J* = 7.7 Hz, 1H), 7.40 – 7.34 (m, 1H), 7.18 (dd, *J* = 4.9, 3.8 Hz, 1H), 7.03 (s, 1H), 3.57 – 3.02 (m, 2H), 1.96 (t, J = 7.7 Hz, 2H), 1.67 – 1.60 (m, 2H), 1.48 – 1.36 (m, 4H), 0.94 (t, *J* = 7.1 Hz, 3H); δ $_C$ (151 MHz, $CDCl_3$) 156.1, 151.9, 145.6, 143.1, 131.4, 128.5, 128.3, 127.8, 125.7, 121.6, 120.4, 114.5, 102.3, 77.2, 77.0, 76.8, 33.3, 31.5, 29.0, 26.2, 22.5, 14.0; **ESI-MS**: *m/z* =$[M+H]^+$calcd. for $C_{20}H_{22}N_3S$: 336.1529; found 336.1525.

References:

1. a) A. Kumar, M. Kumar, S. Maurya, and R. S. Khanna. *J. Org. Chem*. 2014, **79**, 6905-6912. (b) V. V. Shinde and Y. T. Jeong, *New J. Chem*. 2015, **39**, 4977-4986. (c) M. Rawat and D. S. Rawat, Tet. Lett. 2018, **59**, 2341-2346. (d) J. Wu, H. Luo, T.

Wang, H. Sun, Q. Zhang, and Y. Chai. *Tetrahedron*, 2019, **75**, 1052-1063. (e) M. V. Reddy, G. C. S. Reddy, N. T. K. Lien, D. W. Kim and Y. T. Jeong, *Tetrahedron*, 2017, **73**, 1317-1323.

Green matrix Calculation

1. For Our Work

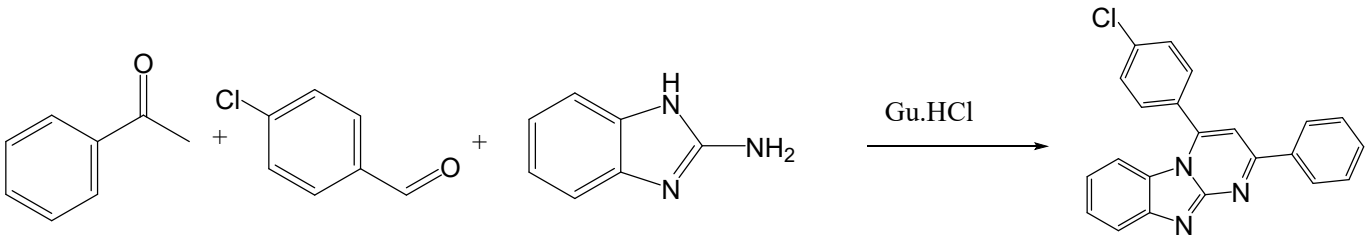
Calculation of EcoScale score for the catalysed synthetic process to synthesize2,4-diphenylbenzo[4,5]imidazo[1,2-a]pyrimidine.

EcoScale evaluation

Price calculated for 10 mmol reaction scale, prices obtained from Avra Synthesis Private Limited/and or Sigma-Aldrich (20.06.2024)

	Parameters	Penalty points
1	Yield: (100- % of yield) / 2 = (100-88)/2 = 6	6
2.	Price of reaction components (to obtain 10 mmol of end product, **4**)	
A.	acetophenone (**1**) =11.3 mmol = 1.348 g = 0.012 USD	
B	4-chlorobenzaldehyde (**2**) 11.3 mmol = 1.573g = 0.094 USD	
C	2-Amino-benzimidazole 11.3 mmole (**3**) = 1.4896 gm = 5.68 USD	
D	Guanidine hydrochloride = 1.1 mmol = 0.124 g = 0.0061USD	
	Total cost of synthesis of **4** = 7.6881 USD Thus expensive, since $ 10 < (total cost of synthesis of 10 mmol of **5**) <$50	0
3.	Safety:	0
4.	Technical setup	

	Instruments for controlled addition of chemicals	2
5.	Temperature/ Time	
	Heating<1	2
6.	Workup and purification	
	Classical chromatography	10
	Total penalty points:	**20**
B.	Eco Scale calculation:	
	EcoScale score = (100-20) = **80**(> 75; it is an excellent)	



Acetophenone MW 120.4 **1** (2 mmol)

4-Chloro benzaldehyde MW 140.5 **2** (2 mmol)

2-aminobenzimidazole MW 133.2 **2** (2 mmol)

MW 355.8 **4 (**1.75 mmol)

Yield of product = 88 %

Atom Economy (%) = $\frac{\text{Mol. Wt of Product}}{\text{Mol .wt of all reactants}} = \frac{355}{120.4+140.5+133.2} \times 100 = 90.07$

Atom efficiency (%) = (% yield of product × % atom economy) × 100 = (88 % × 90.07 %)/100 =79.26 %

Carbon Efficiency (%) = $\frac{\text{No. of moles of product x no. of carbons in product x 100}}{\text{(Moles of 2 × no. of carbon in 1) + (Moles of 2 × no. of carbon in 2) + (Moles of 2 × no. of carbon in 3)}}$

$= \frac{1.75 \text{ x } 22 \text{ x } 100}{(2 \text{ x } 8) + (2 \text{ x } 7) + (2 \text{ x } 7)} = 87.5\ \%$

Reaction Mass Efficiency (%) = $\frac{\text{Mass of isolated product}}{\text{Mass of all reactant}} \times 100 = \frac{0.626 \text{ x } 100}{0.240+0.280+0.266} = 79.64\ \%$

Effective Mass Yield (%) EMY = $\frac{\text{Mass of isolated product}}{\text{Mass of raw materials + reagents}} \times 100 = \frac{0.626 \text{ x } 100}{0.240+0.280+0.266} = 79.64\%$

Mass Intensity (MI) = $\frac{\text{Mass of input materials excluding water}}{\text{Mass of raw material + reagents}} = \frac{0.626}{0.240+0.280+0.266} = 0.794 \text{ gm}$

$$\textbf{Mass Productivity (MP)} = \frac{\text{Mass of product x 100}}{\text{Mass of all input material excluding water}} = \frac{0.626 \times 100}{0.240+0.280+0.266} = 79.64\%$$

$$\textbf{Process Mass Efficacy} = \frac{\text{Mass of product x 100}}{\text{Mass of all input material including water}} = \frac{0.626 \times 100}{0.240+0.280+0.266} = 79.64\%$$

$$\textbf{Process Mass Intensity} = \frac{\text{Mass of all input material}}{\text{Mass of product}} = \frac{0.240+0.280+0.266}{0.626} = 1.25 \text{ gm}$$

$$\textbf{Reaction Mass Intensity} = \frac{\text{mass of all raw materials + mass of all reagents}}{\text{Mass of product}} = \frac{0.240+0.280+0.266}{0.626} = 1.25 \text{ gm}$$

$$\textbf{Optimum Efficiency} = \frac{\text{Reaction Mass Efficiency x 100}}{\text{Atom Economy}} = \frac{81.4 \times 100}{90.07} = 90.37\%$$

$$\textbf{Simple E factor} = \frac{\text{(Mass of all raw materials + mass of all raw reagents) - mass of product}}{\text{Mass of raw material + reagents}}$$

$$= \frac{(0.240+0.280+0.266)-0.626}{0.240+0.280+0.266} = 0.20 \text{ gm}$$

$$\textbf{Complete E Factor} = \frac{\text{Mass of all input material incl. water – mass of product}}{\text{Mass of product}}$$

$$= \frac{(0.240+0.280+0.266)-0.626}{0.626} = 0.25 \text{ gm}$$

	Compoundname	Mol. wt	Eq.wt	mMole	Amount
Reactant1:	acetophenone	120.4	1	2	0.240 g
Reactant2	4-chlorobenzaldehyde	140.5	1	2	0.280 g
Reactant 3	2-Aminobenzimidazole	133.15	1	2	0.266 g
Catalyst	Guanidine hydrochloride	95.53	0.1	0.1	0.0955 g
Product:	synthesize 4-(4-chlorophenyl)-2-phenylbenzo[4,5]imidazo[1,2-a]pyrimidine	355.08	1	1.78	0.632 g

$$\textbf{E-factor} = \frac{\text{Total waste (g)}}{\text{Total product}} = \frac{(0.240+0.280+0.266)-0626}{0.626} = 0.25 \text{ g waste/ g product}$$

Eco Scale = 100 - Sum of individual penalties = (100-20) = **80** (> 50; it is an acceptable synthesis)

2. Calculation of Green Matrix for ref. *J. Org. Chem* 2014, *79*, 6905-691

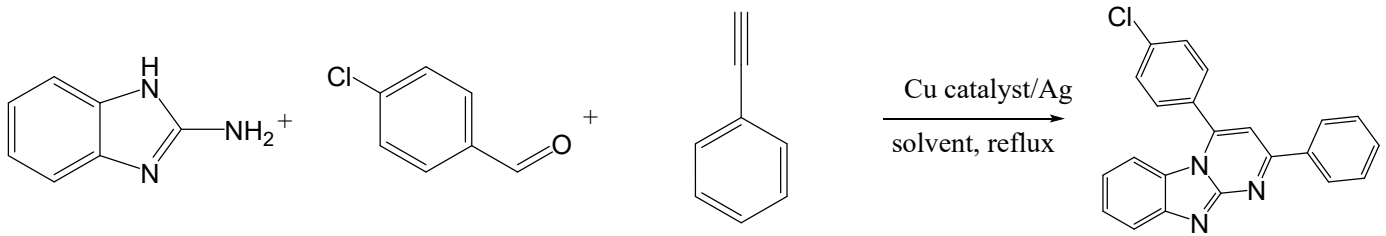
Calculation of EcoScale score for the Regioselective Synthesis of Fused Imidazo[1,2-a]pyrimidines via Intramolecular C−N Bond Formation/6-Endo-Dig Cycloisomerization.

EcoScale evaluation

Price calculated for 10 mmol reaction scale, prices obtained from Avra Synthesis Private Limited/and or Sigma-Aldrich (20.06.2024)

	Parameters	Penalty points
1	Yield: (100- % of yield) / 2 = (100-72)/2 = 14	14
2.	Price of reaction components (to obtain 10 mmol of end product, **4**)	
A.	2-Amino-benzimidazole (**1**) 13.88 mmol = 1.846 g = 7.08 USD	
B	4-chlorobenzaldehyde (**2**) 13.88 mmol = 1.94 g = 0.11 USD	
C	phenylacetylene (**3**) =27.76 mmol = 2.831 g = 3.07 USD	
D	CuI (20 mol%) = 0.380 g = 0.0844 USD	
E	Silver carbonate 20 mmol% = 0.540 g = 3.84 USD	

	Total cost of synthesis of **4** = 14.18 USD Thus expensive, since $ 10 > (total cost of synthesis of 10 mmol of **4**) <$50	3
3.	Safety: (F+)	10
4.	Technical setup	
	Common setup	0
5.	Temperature/ Time	
	Heating, < 1 h	2
6.	Workup and purification	
	Classical chromatography	10
	Total penalty points:	**39**
B.	Eco Scale calculation:	
	EcoScale score = (100-26) = **61** (>50; it is an acceptable)	



2-aminobenzimidazole | **4-Chloro benzaldehyde** | **phenylacetylene**

MW 133.2 | MW 140.5 | MW 102 | MW 355.8

1 (1 mmol) | **2** (1 mmol) | **3** (2 mmol) | **4 (**0.72 mmol)

Yield of product = 72 %

	Compoundname	Mol. wt	Eq.wt	mMole	Amount
Reactant1:	2-Amino-benzimidazole	134.2	1	1	0.133 g
Reactant2	4- chlorobenzaldehyde	140	1	1	0.140 g
Reactant 3	Phenylacetylene	102	2	2	0.204 g
Catalyst	CuI	-	-	-	0.038 g
	Silver carbonate	-	-	-	0.054
Product:	synthesize 2,4-diphenylbenzo[4,5]imidazo[1,2-a]pyrimidine	364.4	1	1	0.355 g

$$\textbf{Atom Economy (\%)} = \frac{\text{Mol. Wt of Product}}{\text{Mol .wt of all reactants}}^{2} = \frac{355}{133.15+140.5+2\ \text{X}\ 102} \times 100 = 74.32\ \%$$

Atom efficiency (%) = (% yield of product × % atom economy) / 100 = (72% × 74.32 %)/100 =53.51 %

$$\textbf{Carbon Efficiency (\%)} = \frac{\text{No. of moles of product x no. of carbons in product x 100}}{\text{(Moles of 1 × no. of carbon in 1) + (Moles of 1 × no. of carbon in 2) + (Moles of 2 × no. of carbon in 3)}}$$

$$= \frac{0.72 \text{ x } 22 \text{ x } 100}{(1 \text{ x } 7) + (1 \text{ x } 7) + (2 \text{ x } 8)} = 79.2\%$$

$$\textbf{E-factor} = \frac{\text{Total waste (g)}}{\text{Total product}} = \frac{(0.133+0.140+0.204)-0.255}{0.255} = 0.87 \text{ g waste/ g product}$$

3. Calculation of Green Matrix for ref. New. J. Chem. 2015, 39,4977-4986)

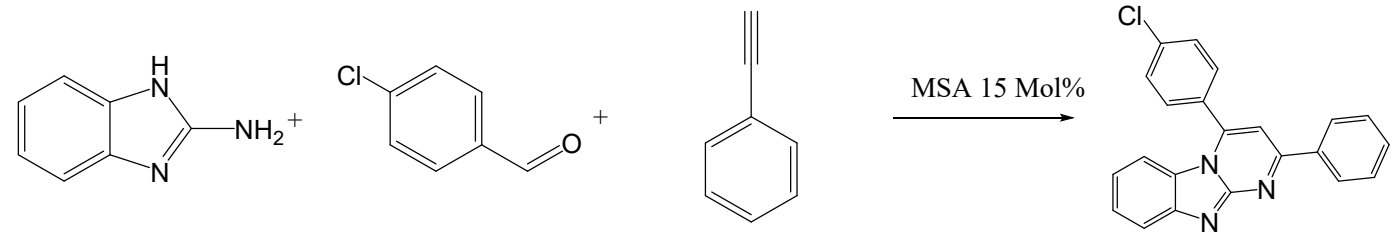
Calculation of EcoScale score for the Molybdate sulfuric acid (MSA): an efficient solid acid catalyst for the synthesis of diversely functionalized fused imidazo[1,2-a] pyrimidines under solvent-free conditions

EcoScale evaluation

Price calculated for 10 mmol reaction scale, prices obtained from Avra Synthesis Private Limited /and or Sigma-Aldrich (20.06.2024)

	Parameters	Penalty points
1	Yield: (100- % of yield) / 2 = (100-85)/2 = 7.5	7.5
2.	Price of reaction components (to obtain 10 mmol of end product, **4**)	
A.	2-Amino-benzimidazole (**1**) 11.7 mmol = 1.55 g = 5.7 USD	
B	para-chloro benzaldehyde (**2**) 11.7 mmol = 1.63 g = 0.11 USD	
C	phenylacetylene (**3**) =17.55 mmol = 1.790 g = 1.95 USD	
D	MSA (15 mol%) 1.755 mmol= Anh. Sodium molybdate 1.755 mmol = 4.68 USD Chlorosulfonic acid 3.51 mmol= 0.12 USD	
	Total cost of synthesis of **4** = 12.56 USD Thus expensive, since $ 10 < (total cost of synthesis of 10 mmol of **4a**) <$50	3
3.	Safety: (F+)	10
4.	Technical setup	
	Common setup	0
5.	Temperature/ Time	
	Heating, > 1 h	3

6.	Workup and purification	
	Classical chromatography	10
	Total penalty points:	**33.5**
B.	Eco Scale calculation:	
	EcoScale score = (100-33.5) = **66.5**(> 75; it is an excellent)	



2-aminobenzimidazole **4-Chloro benzaldehyde** **phenylacetylene**

MW 133.2 MW 140.5 MW 102 MW 355.8

1 (1 mmol) **2** (1 mmol) **3** (1.5 mmol) **4 (**1.27 mmol)

Yield of product = 85 %

	Compoundname	Mol. wt	Eq.wt	mMole	Amount
Reactant1:	2-Amino-benzimidazole	133.1	1	1	0.133 g
Reactant2	Para-chloro benzaldehyde	140	1	1	0.140 g

Reactant 3	Phenylacetylene	102	1.5	1.5	0.153 g
Catalyst	MSA	95.53	0.1	-	0g
Product:	synthesize 2,4-diphenylbenzo[4,5]imidazo[1,2-a]pyrimidine	355	1	1	0.355 g

$$\textbf{Atom Economy (\%)} = \frac{\text{Mol. Wt of Product}}{\text{Mol .wt of all reactants}} = \frac{355}{133.15+140.5+1.5 \text{ X } 102} \times 100 = 83.33$$

Atom efficiency (%) = (% yield of product × % atom economy) / 100 = (85% × 83.33 %)/100 =70.83 %

$$\textbf{Carbon Efficiency (\%)} = \frac{\text{No. of moles of product x no. of carbons in product x 100}}{\text{(Moles of 1 × no. of carbon in 1) + (Moles of 1 × no. of carbon in 2) + (Moles of 1.5 × no. of carbon in 3)}}$$

$$= \frac{0.85 \text{ x } 22 \text{ x } 100}{(1 \text{ x } 7) + (1 \text{ x } 7) + (1.5 \text{ x } 8)} = 71.92\%$$

4. **Calculation** $\textbf{E-factor} = \frac{\text{Total waste (g)}}{\text{Total product}} = \frac{(0.133+0.140+0.153)-0.301}{0.301} = 0.4152$ g waste/ g product

~~rix for ref. Tet. Lett 2~~ ~~, 59, 2341-2346~~

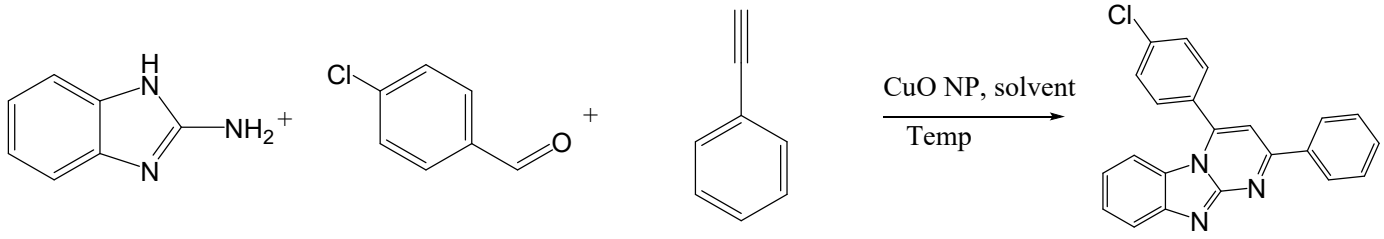
Calculation of EcoScale score f ıanoparticle cat :sis of imidazo[1,2-a] pyrimidine derivatives, their optical properties and selective fluorescent sensor towards zinc ion

EcoScale evaluation

Price calculated for 10 mmol reaction scale, prices obtained from Avra Synthesis Private Limited /and or Sigma-Aldrich (20.06.2024)

	Parameters	Penalty points
1	Yield: (100- % of yield) / 2 = (100-90)/2 = 5	5
2.	Price of reaction components (to obtain 10 mmol of end product, **4**)	
A.	2-Amino-benzimidazole (**1**) 11.1 mmol = 1.476 g = 5.68 USD	
B	para-chloro benzaldehyde (**2**) 11.1 mmol = 1.5 g = 0.1 USD	
C	phenylacetylene (**3**) =11.1 mmol = 1.132 g = 1.23 USD	
D	CuO NPs 0.2g = 0.0104 USD	
	Total cost of synthesis of **4** = **6.9304** USD Thus expensive, since $ 10 < (total cost of synthesis of 0.5 mmol of **4b**) <$50	0
3.	Safety: (F+)	10
4.	Technical setup	
	Common setup	0
5.	Temperature/ Time	
	Heating<1	2
6.	Workup and purification	
	Classical chromatography	10

	Total penalty points: **27**
B.	Eco Scale calculation:
	EcoScale score = (100-27) = 73(> 75; it is an excellent)



2-aminobenzimidazole **4-Chloro benzaldehyde** **phenylacetylene**

MW 133.2 MW 140.5 MW 102 MW 355.8

1 (0.5 mmol) **2** (0.5 mmol) **3** (0.5 mmol) **4 (**0.45 mmol)

Yield of product = 90 %

$$\textbf{Atom Economy (\%)} = \frac{\text{Mol. Wt of Product}}{\text{Mol .wt of all reactants}} = \frac{355}{133.15+140.5+102.14} \times 100 = 94.16$$

Atom efficiency (%) = (% yield of product × % atom economy) / 100 = (90 % × 94.46 %)/100 =85.01 %

$$\textbf{Carbon Efficiency (\%)} = \frac{\text{No. of moles of product x no. of carbons in product x 100}}{\text{(Moles of 0.5 × no. of carbon in 1) + (Moles of 0.5 × no. of carbon in 2) + (Moles of 0.5 × no. of carbon in 3)}}$$

$$= \frac{0.45 \text{ x } 22 \text{ x } 100}{(0.5 \text{ x } 7) + (0.5 \text{ x } 7) + (0.5 \text{ x } 8)} = 90\ \%$$

	Compoundname	Mol. wt	Eq.wt	mMole	Amount
Reactant1:	2-Amino-benzimidazole	133.1	1	0.5	0.066 g
Reactant2	Para-chloro benzaldehyde	140.5	1	0.5	0.070 g
Reactant 3	Phenylacetylene	102	1	0.5	0.051g
Catalyst	CuO NPs	95.53	0.1	-	0.01 g
Product:	synthesize 2,4-diphenylbenzo[4,5]imidazo[1,2-a]pyrimidine	355	1	0.45	0.1775g

$$\textbf{E-factor} = \frac{\text{Total waste (g)}}{\text{Total product}} = \frac{(0.066+0.070+0.051)-0.16}{0.16} = 0.168 \text{ g waste/ g product}$$

5. Calculation of Green Matrix for ref. Tetrahedron 2019, 75, 1052-1063)

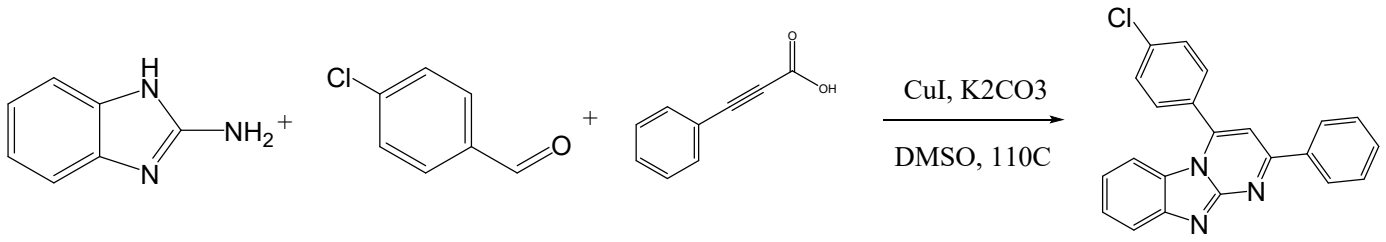
Calculation of EcoScale score for the Diverse synthesis of pyrimido[1,2-a]benzimidazoles and imidazo[2,1- b]benzothiazoles via CuI-catalyzed decarboxylic multicomponent reactions of heterocyclic azoles, aldehydes and alkynecarboxylic acids

Table 1. EcoScale evaluation

Price calculated for 10 mmol reaction scale, prices obtained from Avra Synthesis Private Limited /and or Sigma-Aldrich (20.06.2024)

	Parameters	Penalty points
1	Yield: (100- % of yield) / 2 = (100-62)/2 = 19	19
2.	Price of reaction components (to obtain 10 mmol of end product, **4**)	
A.	2-Amino-benzimidazole (**1**) 16.12 mmol = 2.143 g = 8.22 USD	
B	4- chlorobenzaldehyde (**2**) 17.73 mmol = 2.482 g = 0.15 USD	
C	phenylpropiolic acid (**3**) =19.34 mmol = 2.823 g = 17.47 USD	
D	CuI (1 mmol) = 0.198 g = 0.044 USD	
E	K2CO3 12 mmol = 1.65 g = 0.031 USD	
	Total cost of synthesis of **4** = 25.915 USD Thus expensive, since $ 10 < (total cost of synthesis of 10 mmol of **4a**) <$50	3
3.	Safety: DMSO	0
4.	Technical setup	
	Common setup	0

5.	Temperature/ Time	
	Heating, > 1 h	3
6.	Workup and purification	
	Classical chromatography	10
	Total penalty points:	**35**
B.	Eco Scale calculation:	
	EcoScale score = (100-35) = **65** (>50; it is an acceptable)	



2-aminobenzimidazole | **Chloro Benzaldehyde** | **phenylpropiolic acid**

MW 133.2 | MW 140.5 | MW 146.1 | MW 355.8

1 (1 mmol) | **2** (1.1 mmol) | **3** (1.2 mmol) | **4 (**0.65 mmol)

Yield of product = 62 %

	Compoundname	Mol. wt	Eq.wt	mMole	Amount
Reactant1:	2-Amino-benzimidazole	133.1	1	1	0.133 g
Reactant2	4- chlorobenzaldehyde	140	1	1.1	0.154 g
Reactant 3	phenylpropiolic acid	146	1	1.2	0.175g
Catalyst	CuI	95.53	0.1	1	0.019 g
	K2CO3			1.2	0.166 g
Product:	synthesize 2,4-diphenylbenzo[4,5]imidazo[1,2-a]pyrimidine	355	1	1	0.355 g

$$\textbf{Atom Economy (\%)} = \frac{\text{Mol. Wt of Product}}{\text{Mol .wt of all reactants}} = \frac{355}{133.15+1.1 \times 140.5+1.2 \times 146} \times 100 = 79.09\ \%$$

Atom efficiency (%) = (% yield of product × % atom economy) / 100 = (62% × 79.09 %)/100 =49.03 %

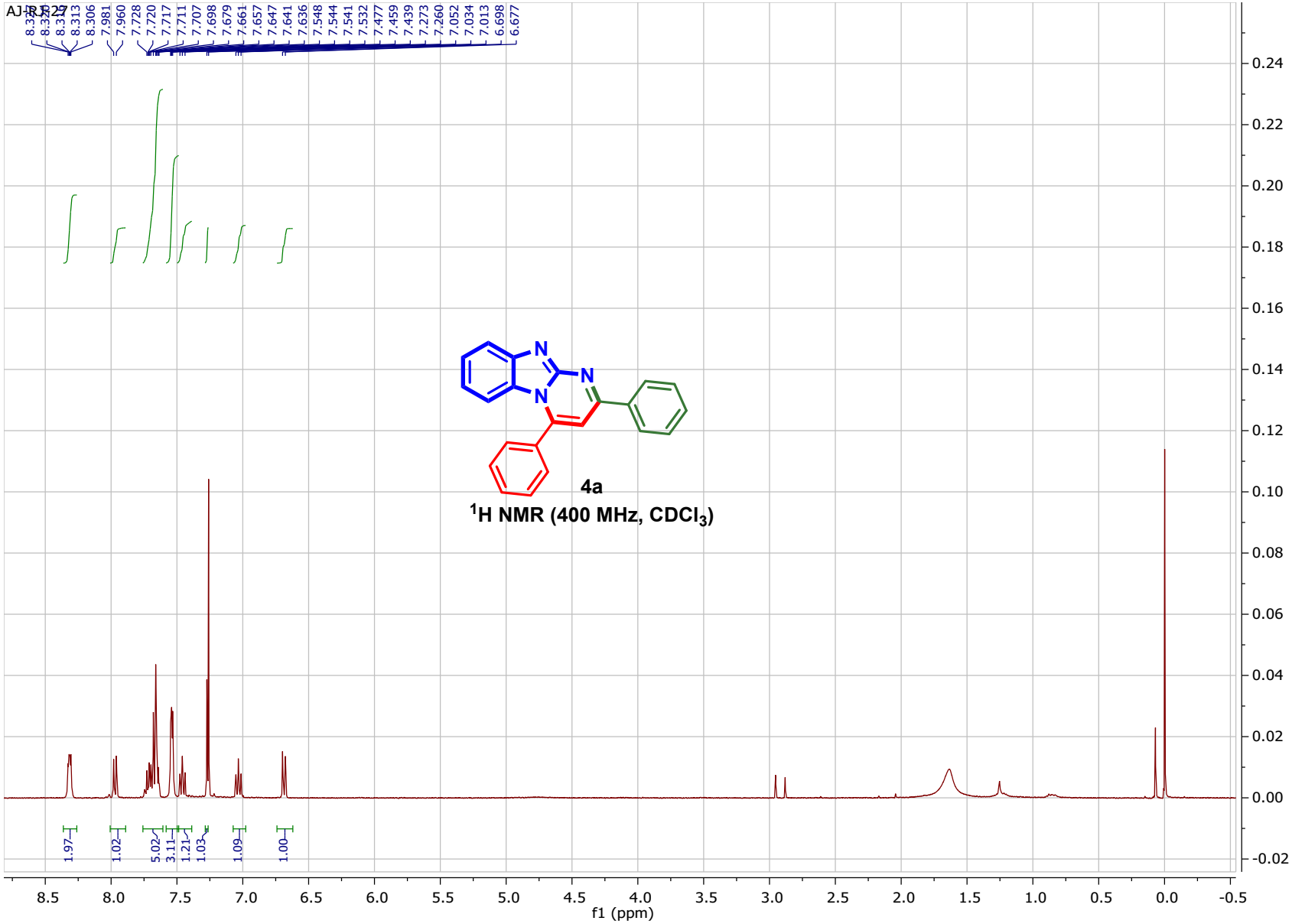
$$\textbf{Carbon Efficiency (\%)} = \frac{\text{No. of moles of product x no. of carbons in product x 100}}{\text{(Moles of 1 × no. of carbon in 1) + (Moles of 1.1 × no. of carbon in 2) + (Moles of 1.2 × no. of carbon in 3)}}$$

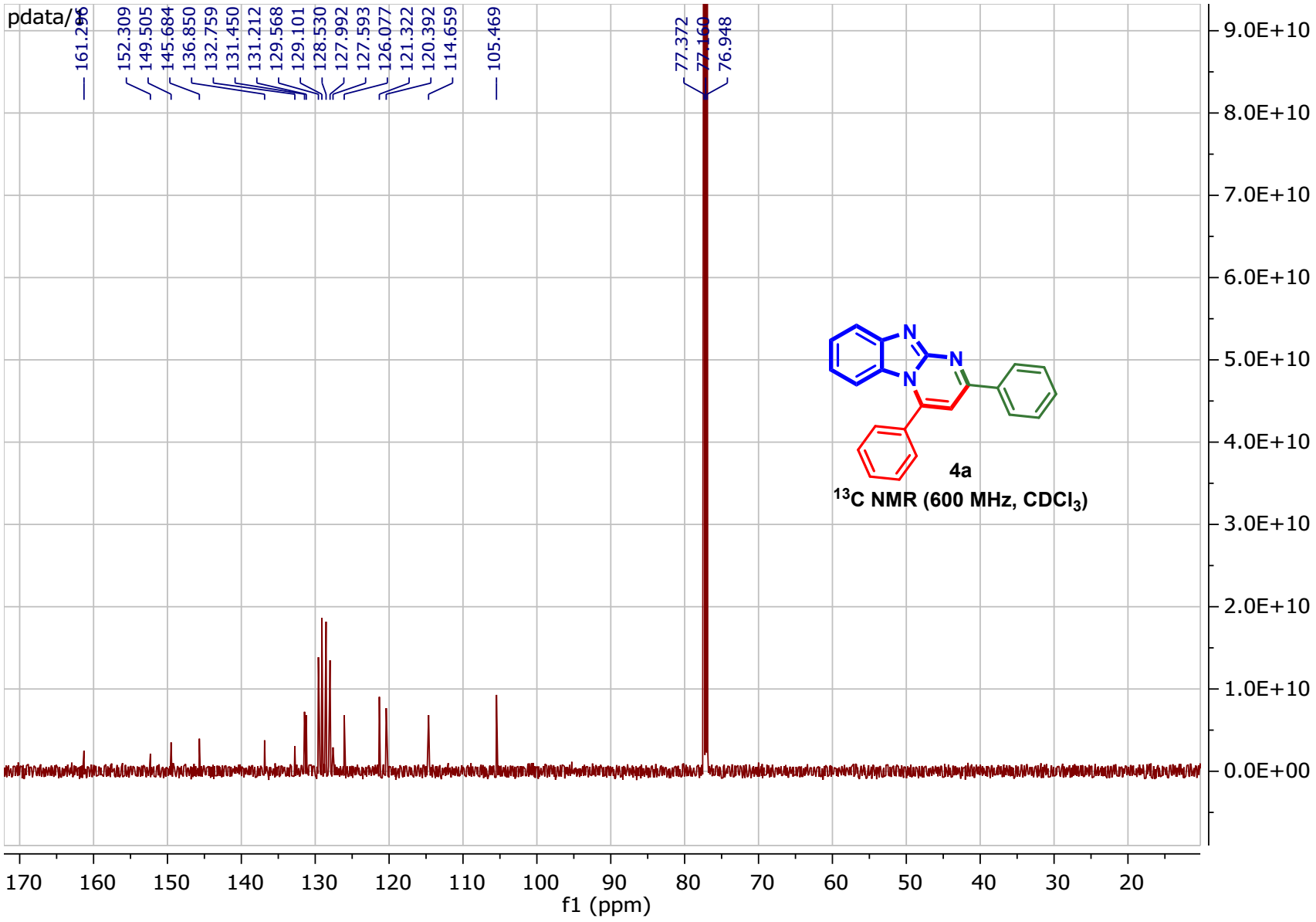
$$= \frac{0.62 \times 22 \times 100}{(1 \times 7) + (1.1 \times 7) + (1.2 \times 9)} = 53.49\%$$

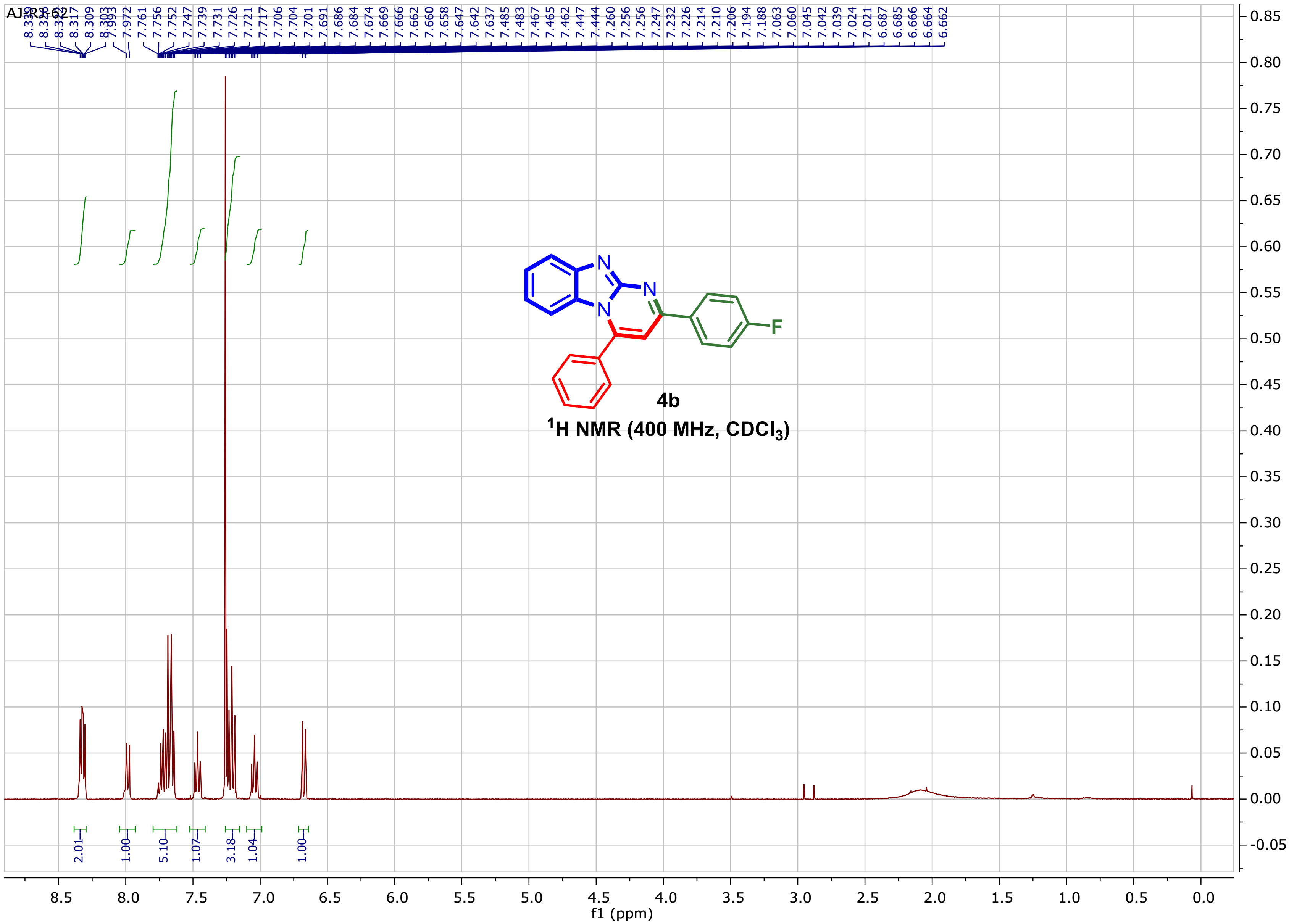
$$\textbf{E-factor} = \frac{\text{Total waste (g)}}{\text{Total product}} = \frac{(0.133+0.154+0.175)-0.230}{0.230} = 1.008 \text{ g waste/ g product}$$

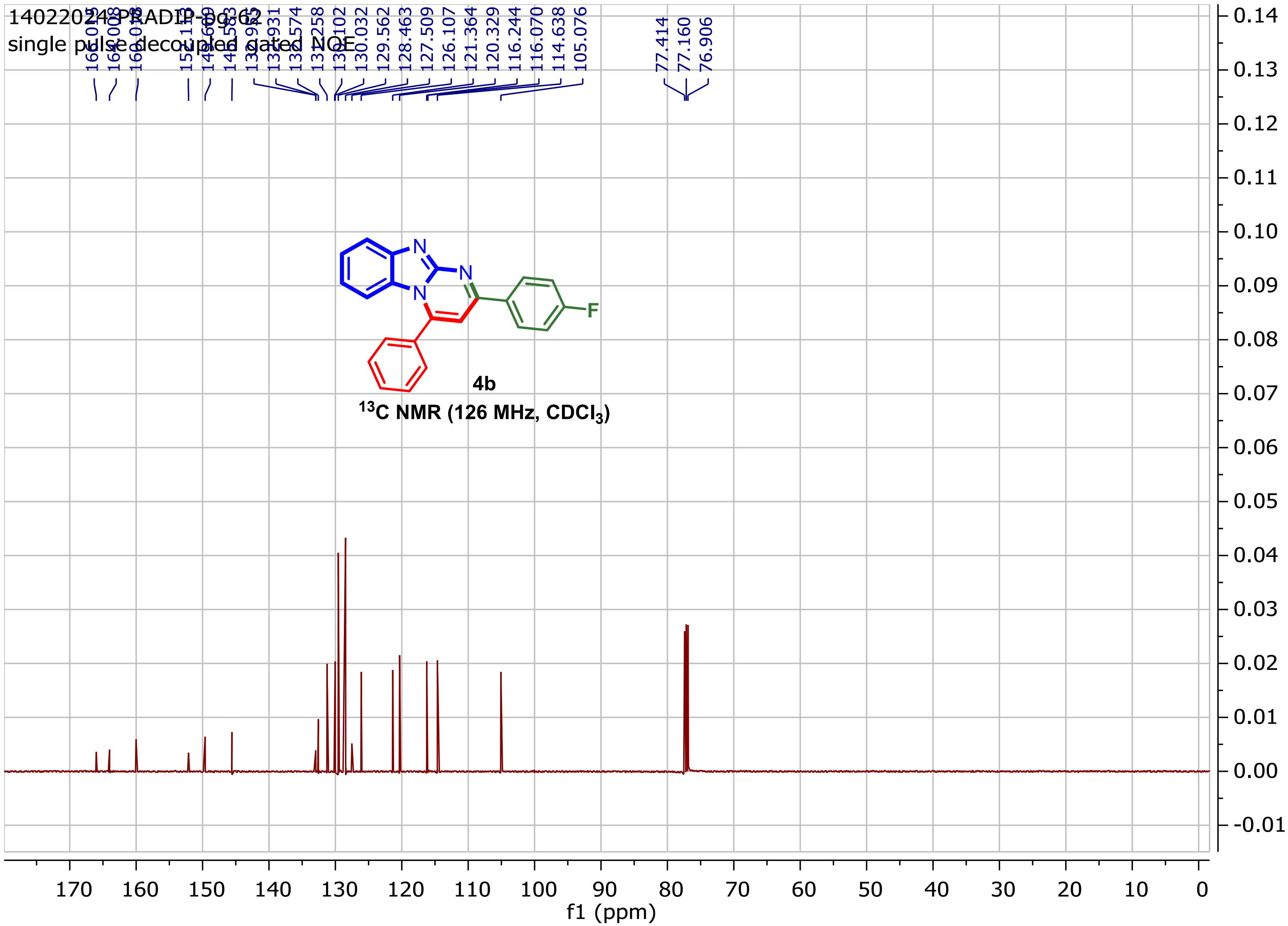
Summary of Green Matrix

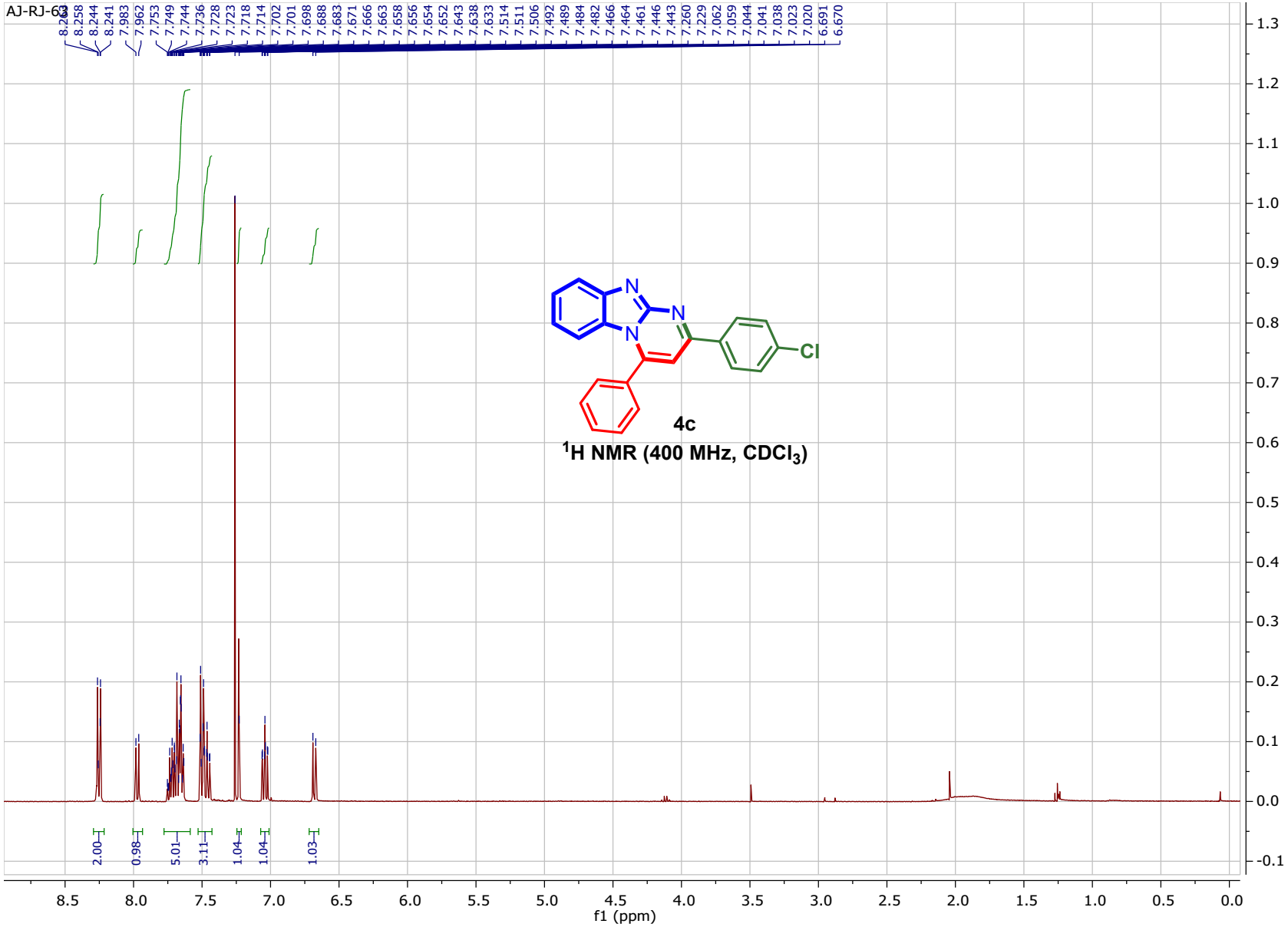
Ref.	Ecoscale	Atom Economy (%)	Atom efficiency (%)	Carbon efficiency (%)	E factor
Our work	**80**	**90.07**	**79.26**	**87.5**	**0.25**
***J.Org. Chem.* 2014, 79, 6905-6912**	61	74.32	53.51	79.2	0.87
***New. J. Chem.* 2015, 39, 4977-4986**	66.5	83.33	70.83	71.92	0.4152
***Tet. Lett.* 2018, 59, 2341-2346**	73	94.16	85.01	90	0.168
***Tetrahedron* 2019, 75, 1052-1063**	65	79.09	49.03	53.49	1.008


AJ-R327
8.331
8.325
8.317
8.313
8.306
7.981
7.960
7.728
7.720
7.717
7.711
7.707
7.698
7.679
7.661
7.657
7.647
7.641
7.636
7.548
7.544
7.541
7.532
7.477
7.459
7.439
7.273
7.260
7.052
7.034
7.013
6.698
6.677
N
N
N
4a
1H NMR (400 MHz, CDCl3)
1.97
1.02
5.02
3.11
1.21
1.03
1.09
1.00
f1 (ppm)


pdata/1
161.296
152.309
149.505
145.684
136.850
132.759
131.450
131.212
129.568
129.101
128.530
127.992
127.593
126.077
121.322
120.392
114.659
105.469
77.372
77.160
76.948
9.0E+10
8.0E+10
7.0E+10
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)
4a
13C NMR (600 MHz, CDCl3)

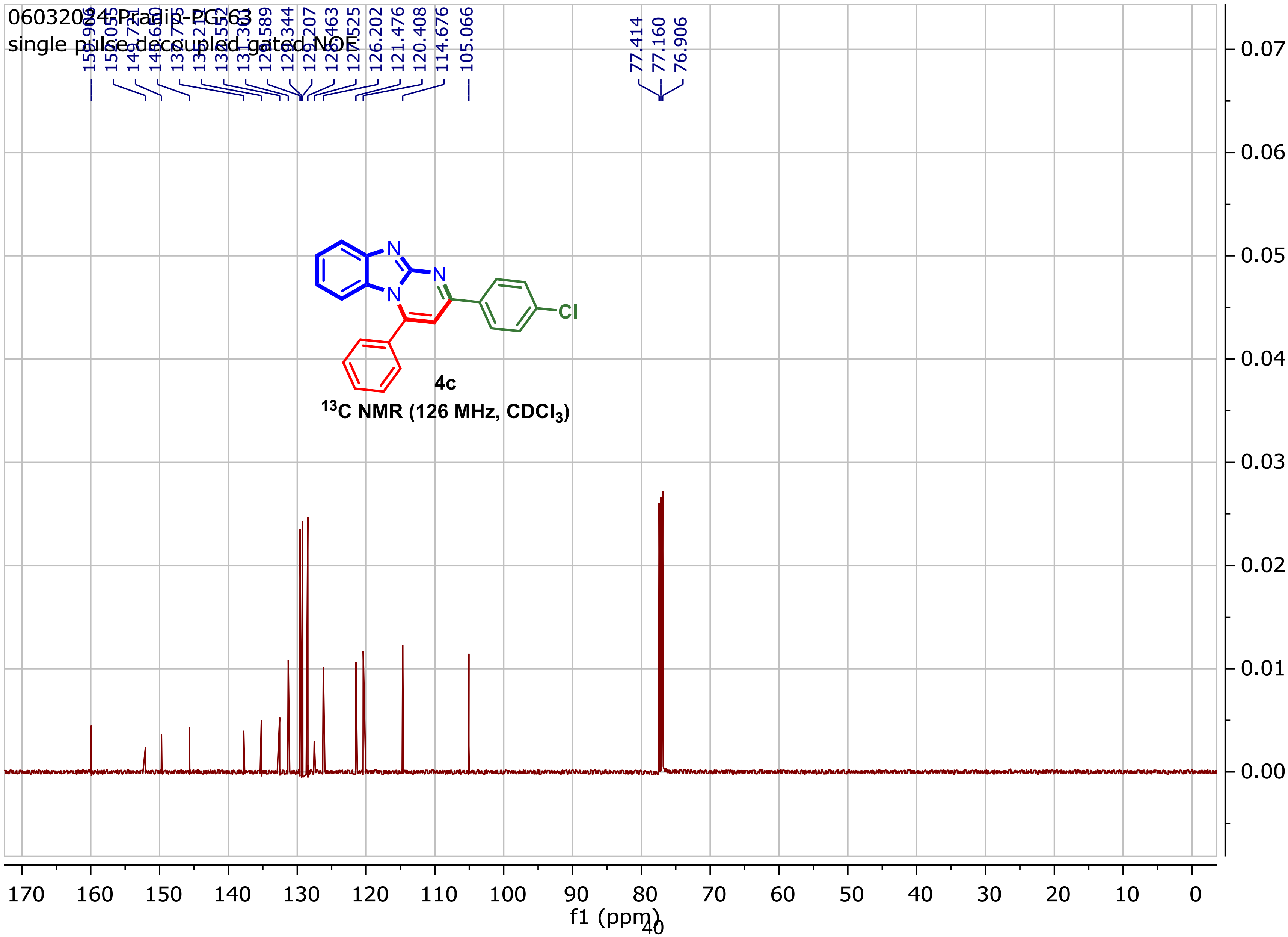

AJR3-62
8.317
8.309
8.303
7.993
7.972
7.761
7.756
7.752
7.747
7.739
7.731
7.726
7.721
7.717
7.706
7.704
7.701
7.691
7.686
7.684
7.674
7.669
7.666
7.662
7.660
7.658
7.647
7.642
7.637
7.485
7.483
7.467
7.465
7.462
7.447
7.444
7.260
7.256
7.256
7.247
7.232
7.226
7.214
7.210
7.206
7.194
7.188
7.063
7.060
7.045
7.042
7.039
7.024
7.021
6.687
6.685
6.666
6.664
6.662
N
N
N
F
4b
1H NMR (400 MHz, CDCl3)
2.01
1.00
5.10
1.07
3.18
1.04
1.00
f1 (ppm)

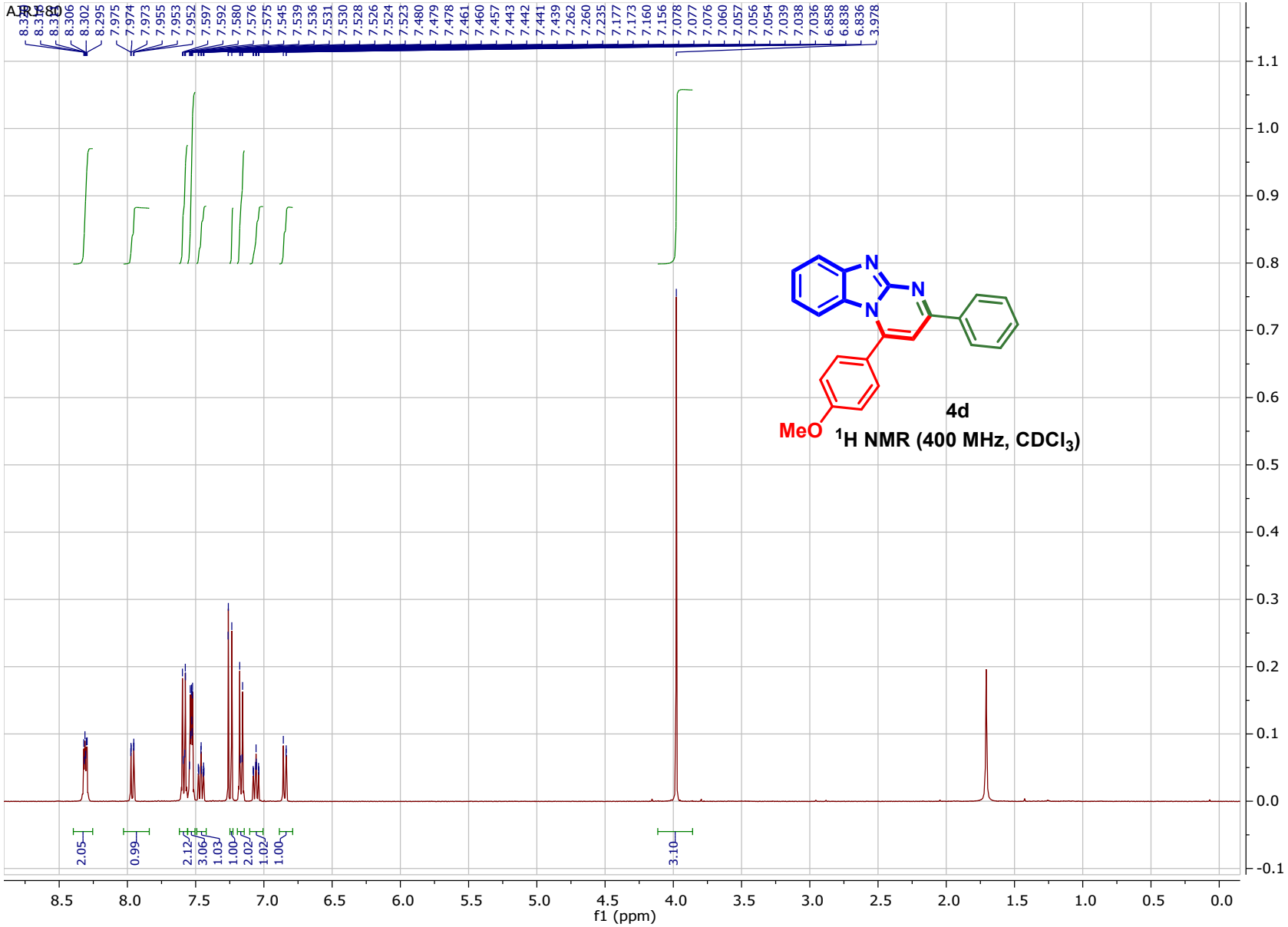

single pulse decoupled gated NOE
131.931
131.574
131.258
130.102
130.032
129.562
128.463
127.509
126.107
121.364
120.329
116.244
116.070
114.638
105.076
77.414
77.160
76.906
N
N
N
F
4b
^{13}C NMR (126 MHz, CDCl$_3$)
f1 (ppm)



4c

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


06032024-Pradip-PG-63
single pulse decoupled gated NOE
126.202
121.476
120.408
114.676
105.066
77.414
77.160
76.906
N
N
N
Cl
4c
13C NMR (126 MHz, CDCl3)
f1 (ppm)


AJR180
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8.310
8.306
8.302
8.295
7.975
7.974
7.973
7.955
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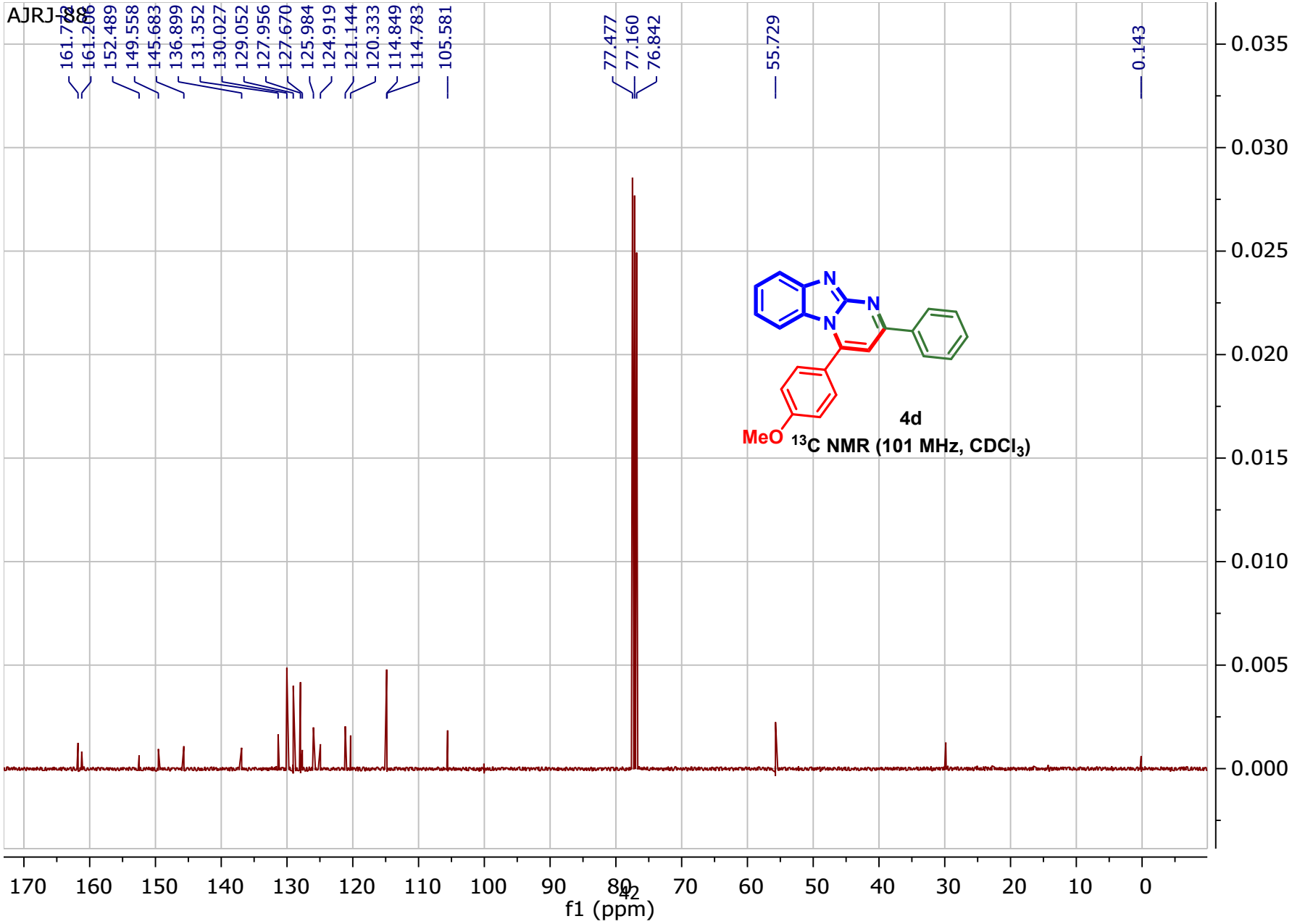
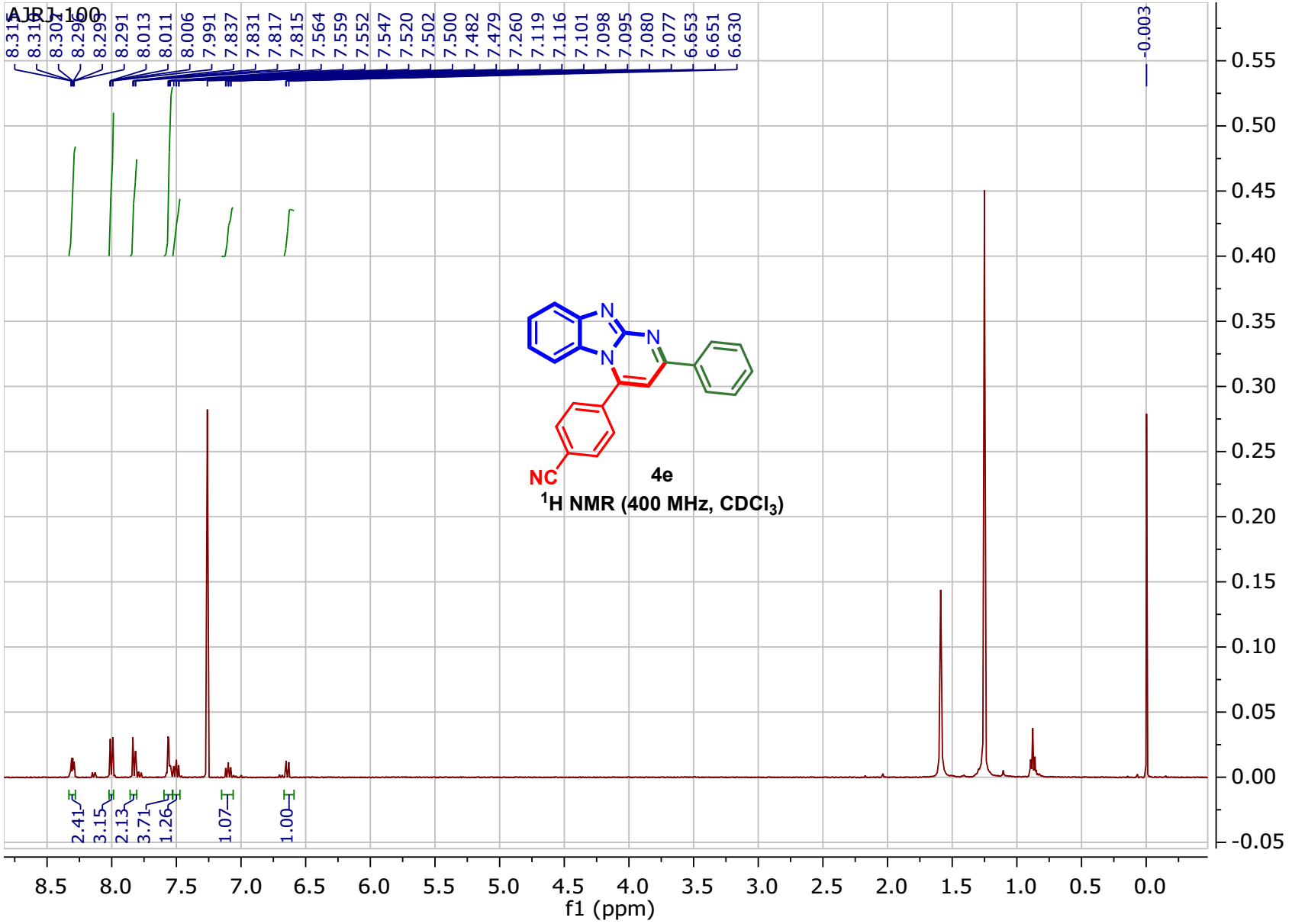
7.952
7.597
7.592
7.580
7.576
7.575
7.545
7.539
7.536
7.531
7.530
7.528
7.526
7.524
7.523
7.480
7.479
7.478
7.461
7.460
7.457
7.443
7.442
7.441
7.439
7.262
7.260
7.235
7.177
7.173
7.160
7.156
7.078
7.077
7.076
7.060
7.057
7.056
7.054
7.039
7.038
7.036
6.858
6.838
6.836
3.978
N
N
N
MeO
4d
^{1}H NMR (400 MHz, CDCl$_3$)
2.05
0.99
2.12
3.06
1.03
1.00
2.02
1.02
1.00
3.10
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
-0.1
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


AJRJ-88
161.771
161.266
152.489
149.558
145.683
136.899
131.352
130.027
129.052
127.956
127.670
125.984
124.919
121.144
120.333
114.849
114.783
105.581
77.477
77.160
76.842
55.729
0.143
N
N
N
MeO
4d
13C NMR (101 MHz, CDCl3)
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


AJRJ-100
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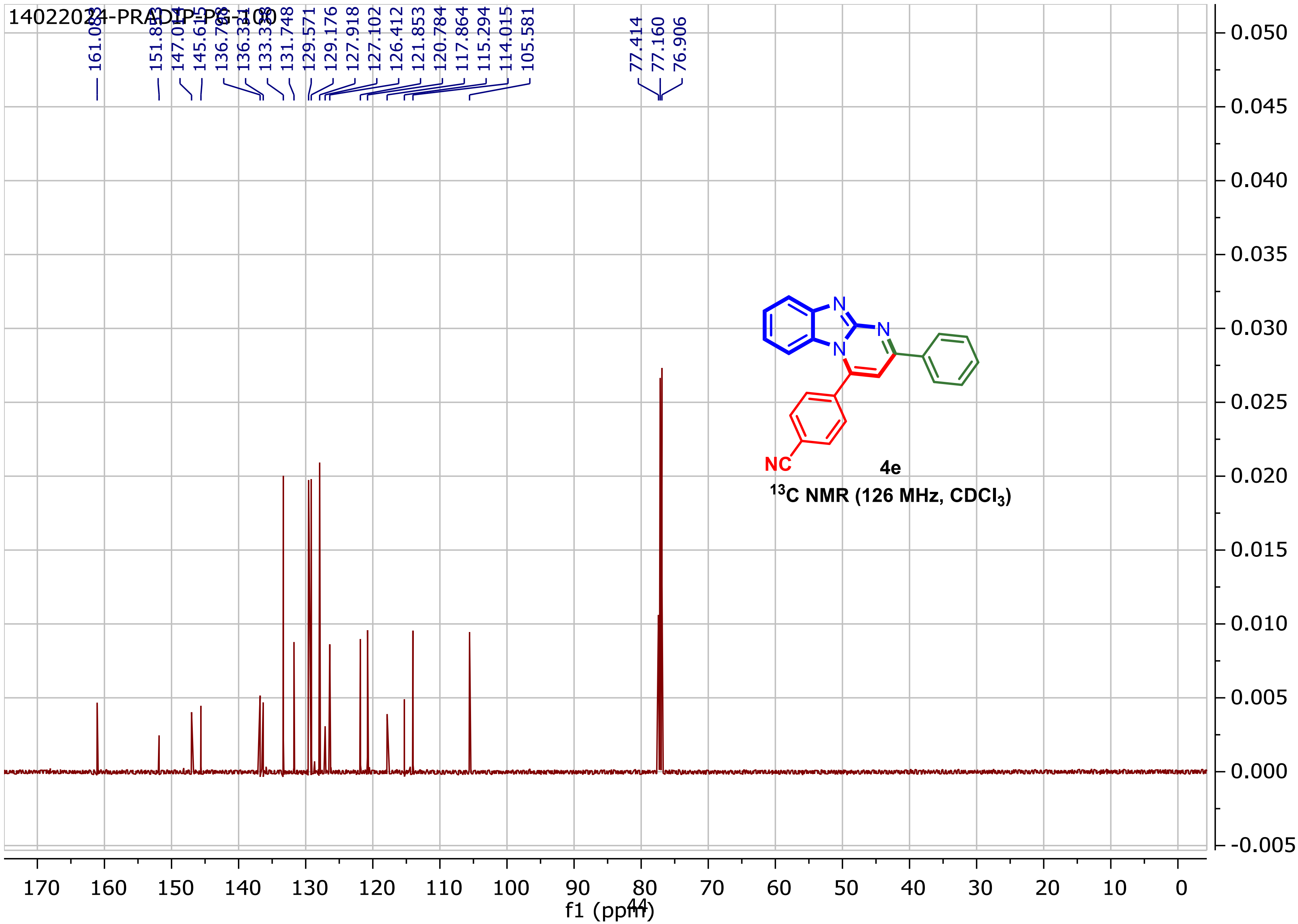
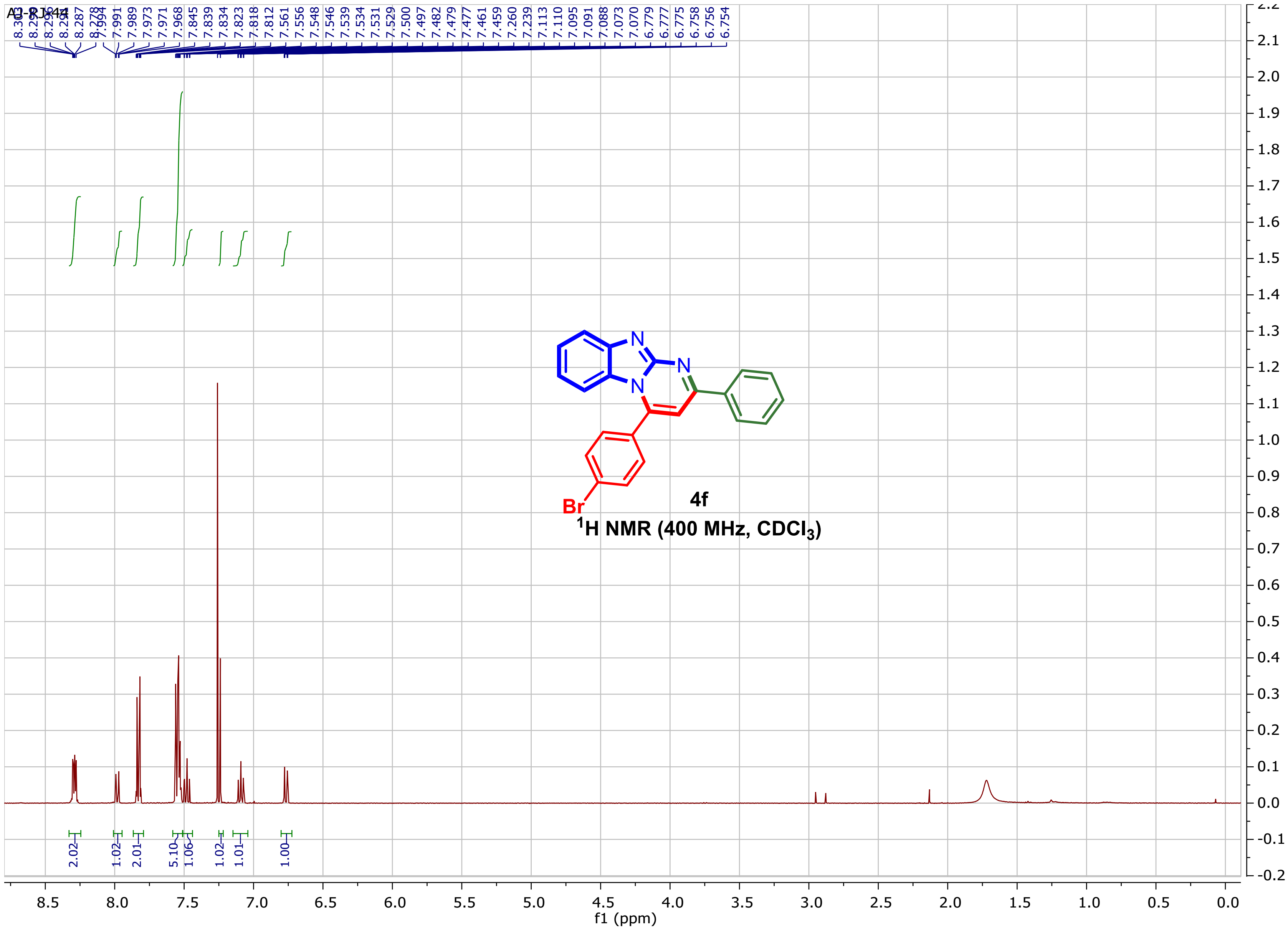
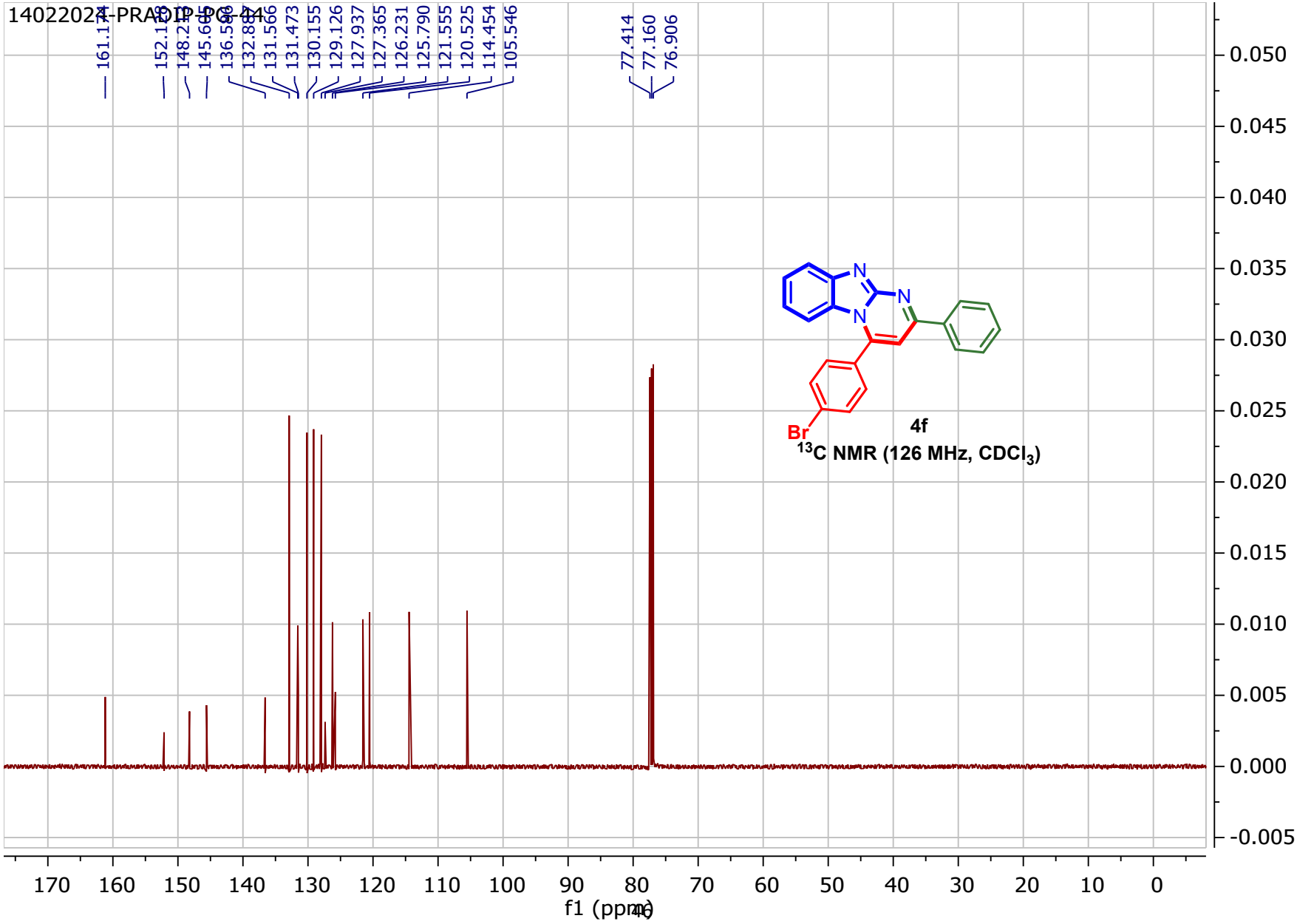
8.310
8.303
8.299
8.299
8.291
8.013
8.011
8.006
7.991
7.837
7.831
7.817
7.815
7.564
7.559
7.552
7.547
7.520
7.502
7.500
7.482
7.479
7.260
7.119
7.116
7.101
7.098
7.095
7.080
7.077
6.653
6.651
6.630
-0.003
N
N
N
NC
4e
1H NMR (400 MHz, CDCl3)
2.41
3.15
2.13
3.71
1.26
1.07
1.00
f1 (ppm)


14022024-PRADIP-PG-100
161.083
151.853
147.014
145.615
136.798
136.331
133.338
131.748
129.571
129.176
127.918
127.102
126.412
121.853
120.784
117.864
115.294
114.015
105.581
77.414
77.160
76.906
N
N
N
NC
4e
^{13}C NMR (126 MHz, $CDCl_3$)
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



8.287
8.278
7.994
7.991
7.989
7.973
7.971
7.968
7.845
7.839
7.834
7.823
7.818
7.812
7.561
7.556
7.548
7.546
7.539
7.534
7.531
7.529
7.500
7.497
7.482
7.479
7.477
7.461
7.459
7.260
7.239
7.113
7.110
7.095
7.091
7.088
7.073
7.070
6.779
6.777
6.775
6.758
6.756
6.754
N
N
N
Br
4f
1H NMR (400 MHz, CDCl3)
2.02
1.02
2.01
5.10
1.06
1.02
1.01
1.00
f1 (ppm)


14022024-PRADIP-PG-44
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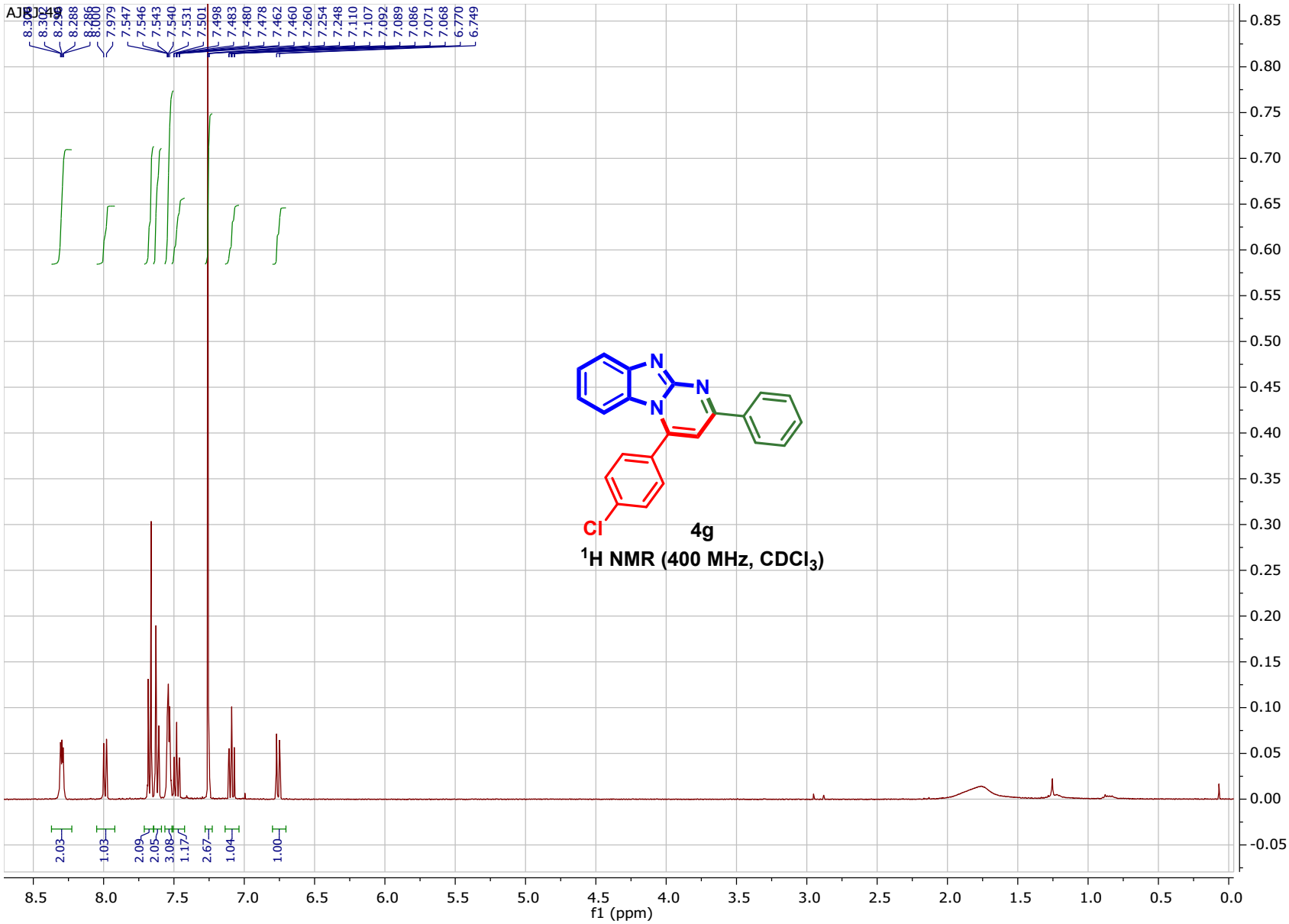
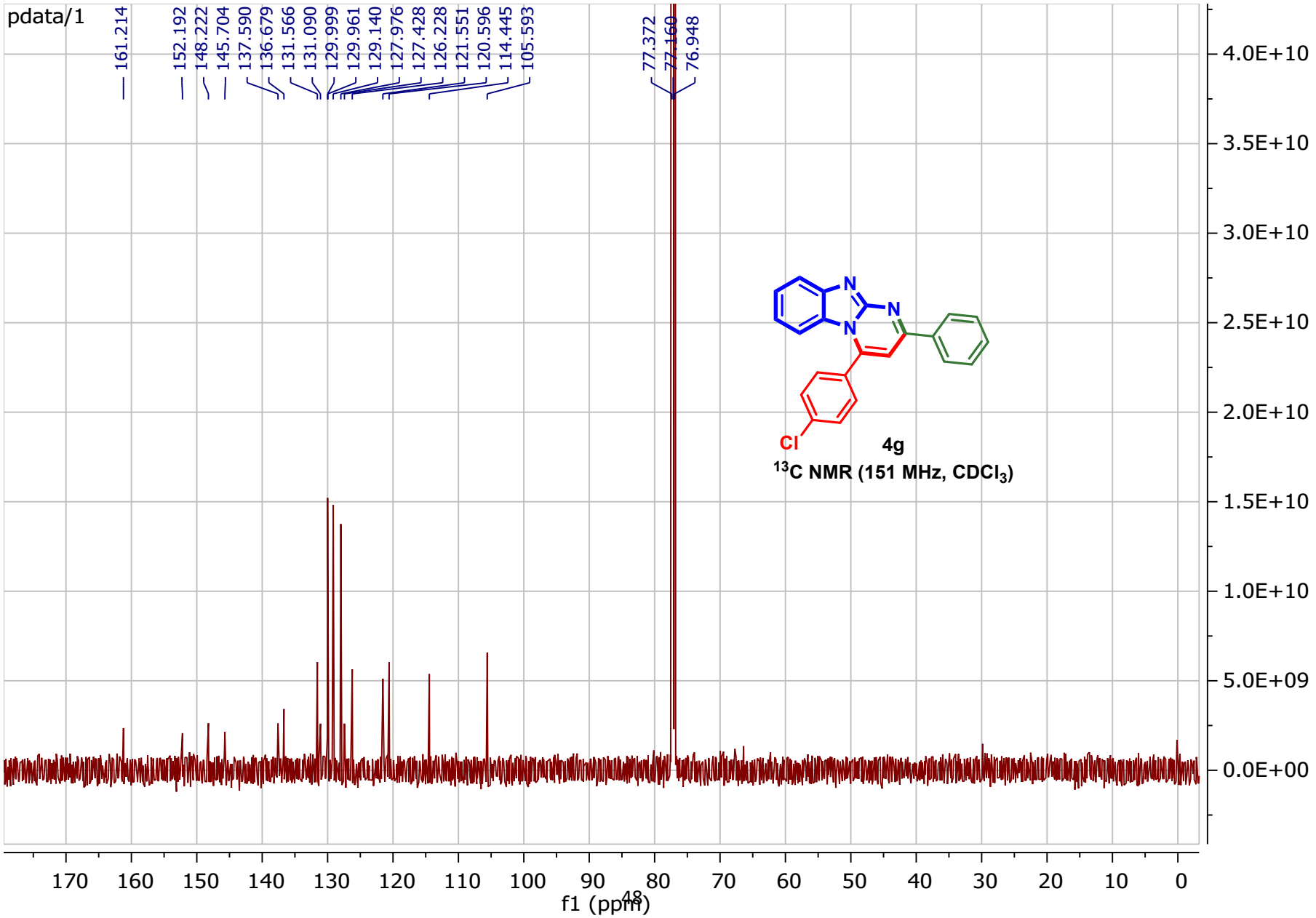
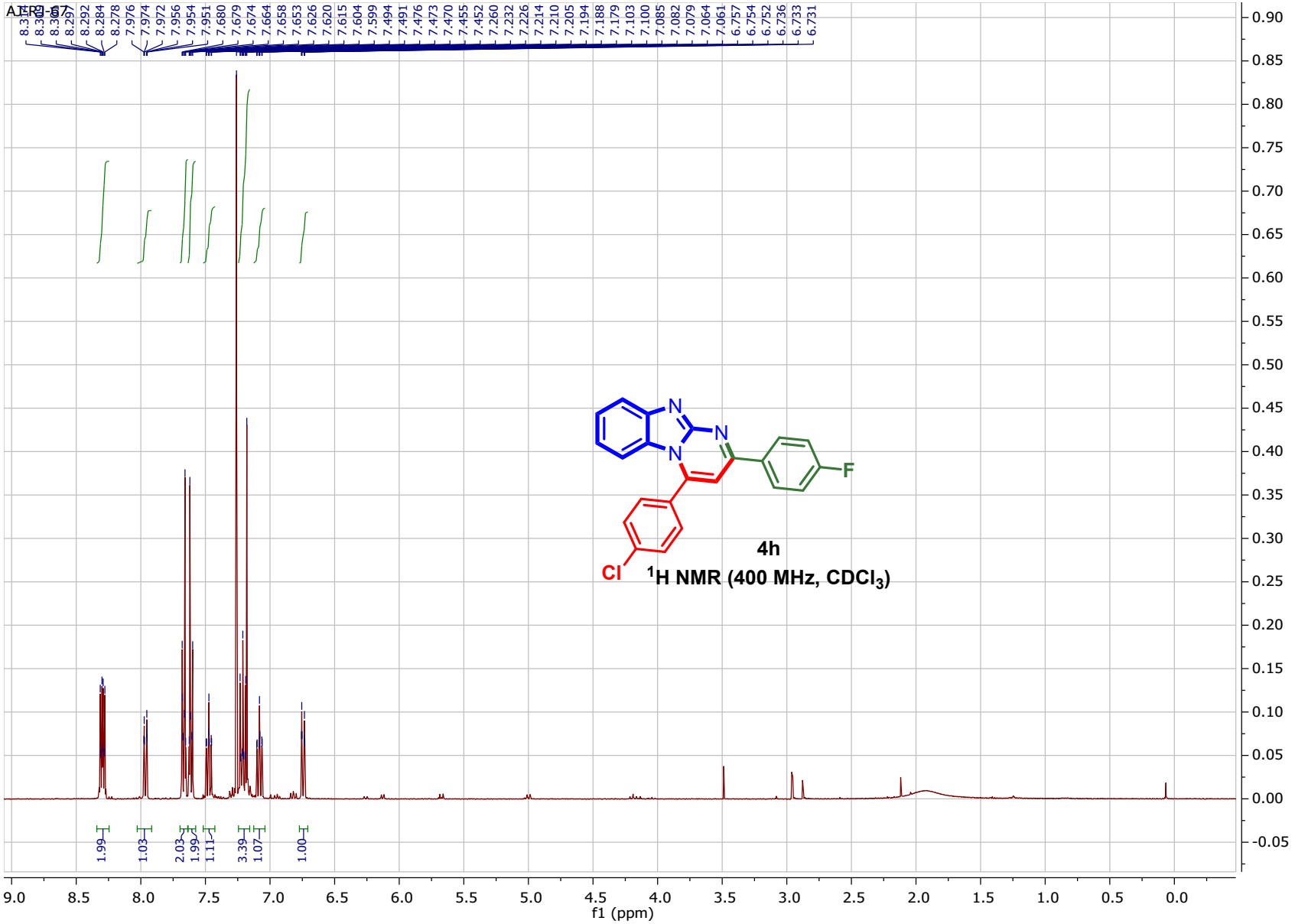
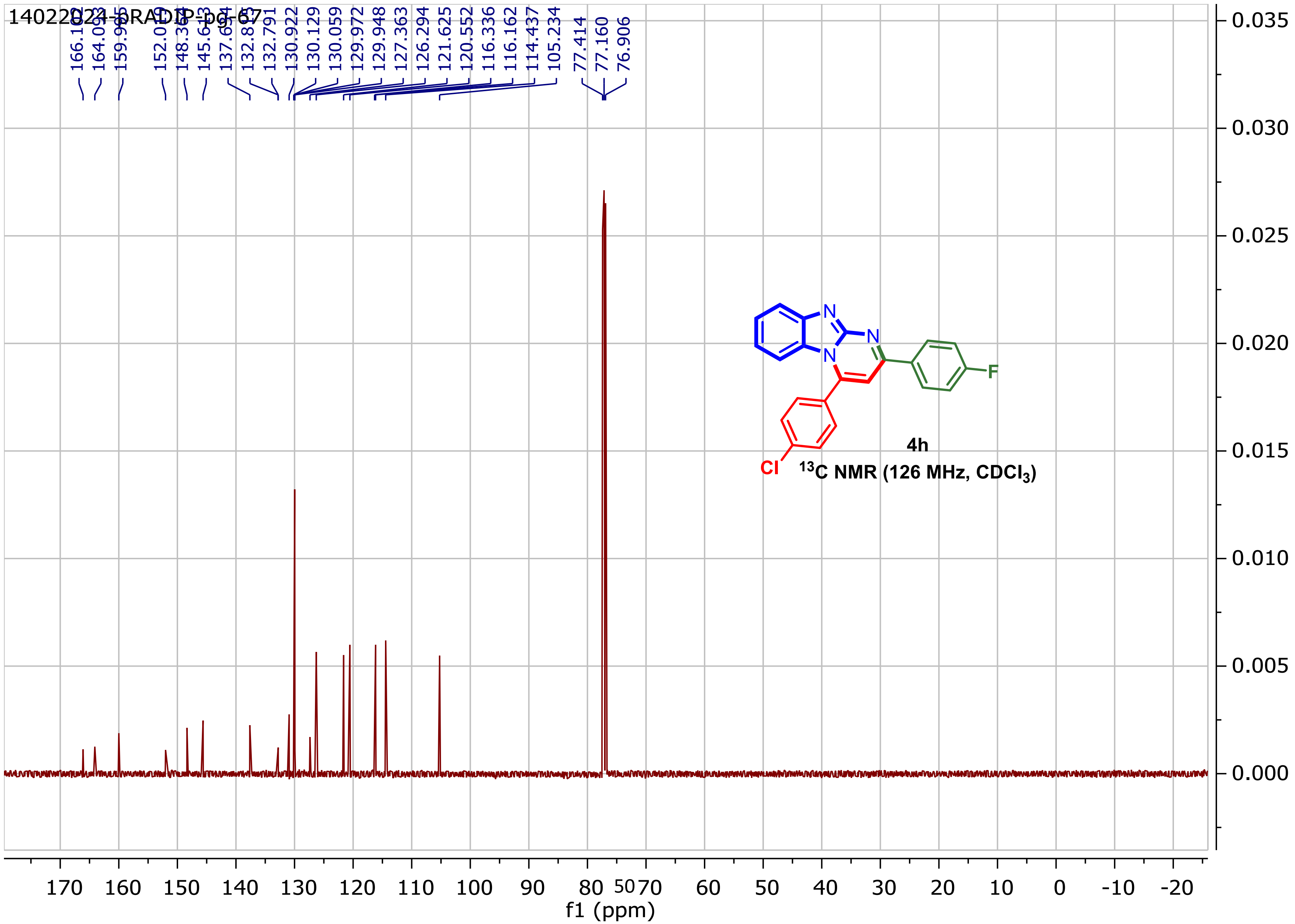
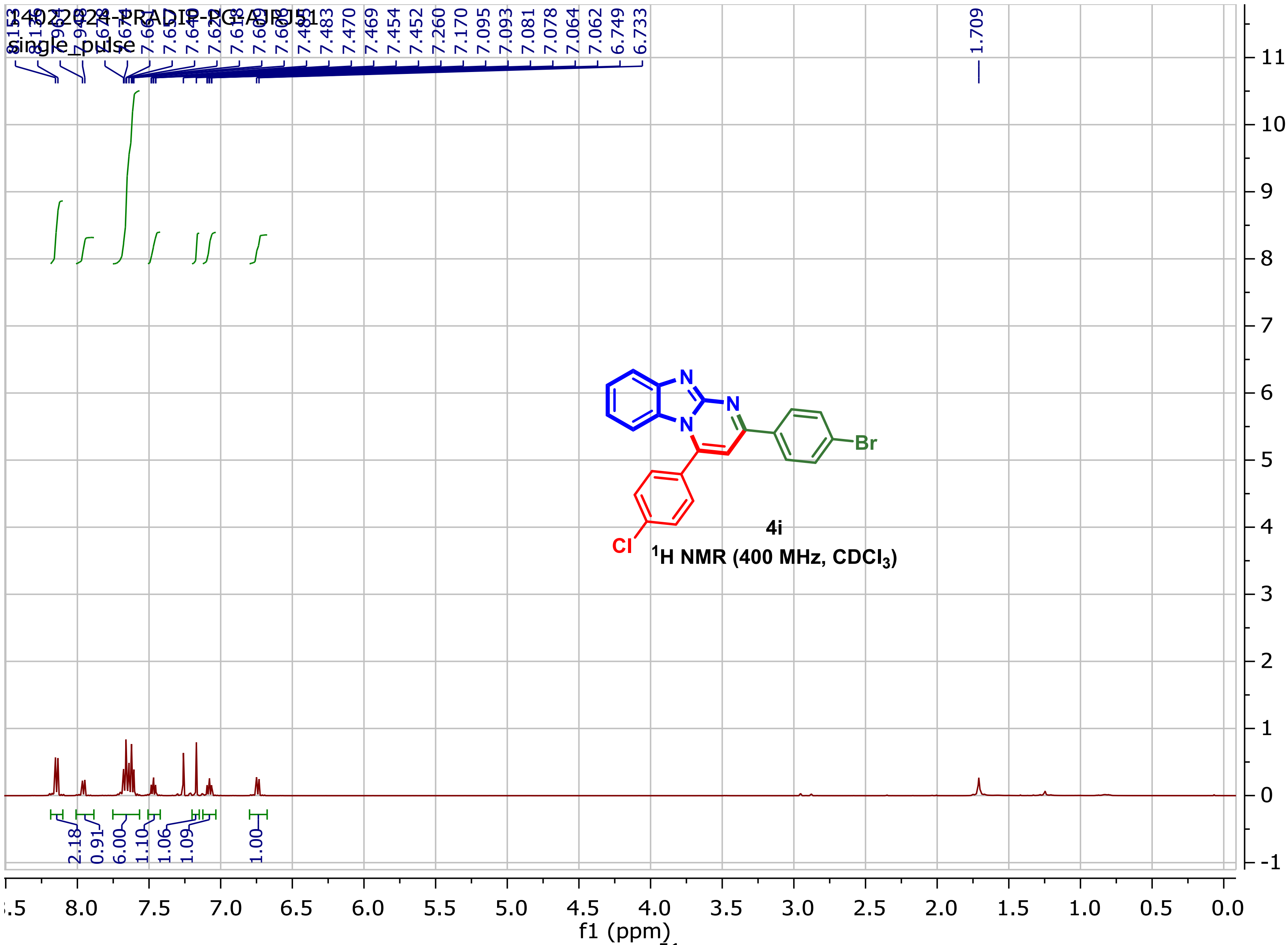
152.114
148.214
145.666
136.596
132.884
131.566
131.473
130.155
129.126
127.937
127.365
126.231
125.790
121.555
120.525
114.454
105.546
77.414
77.160
76.906
N
N
N
Br
4f
13C NMR (126 MHz, CDCl3)
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

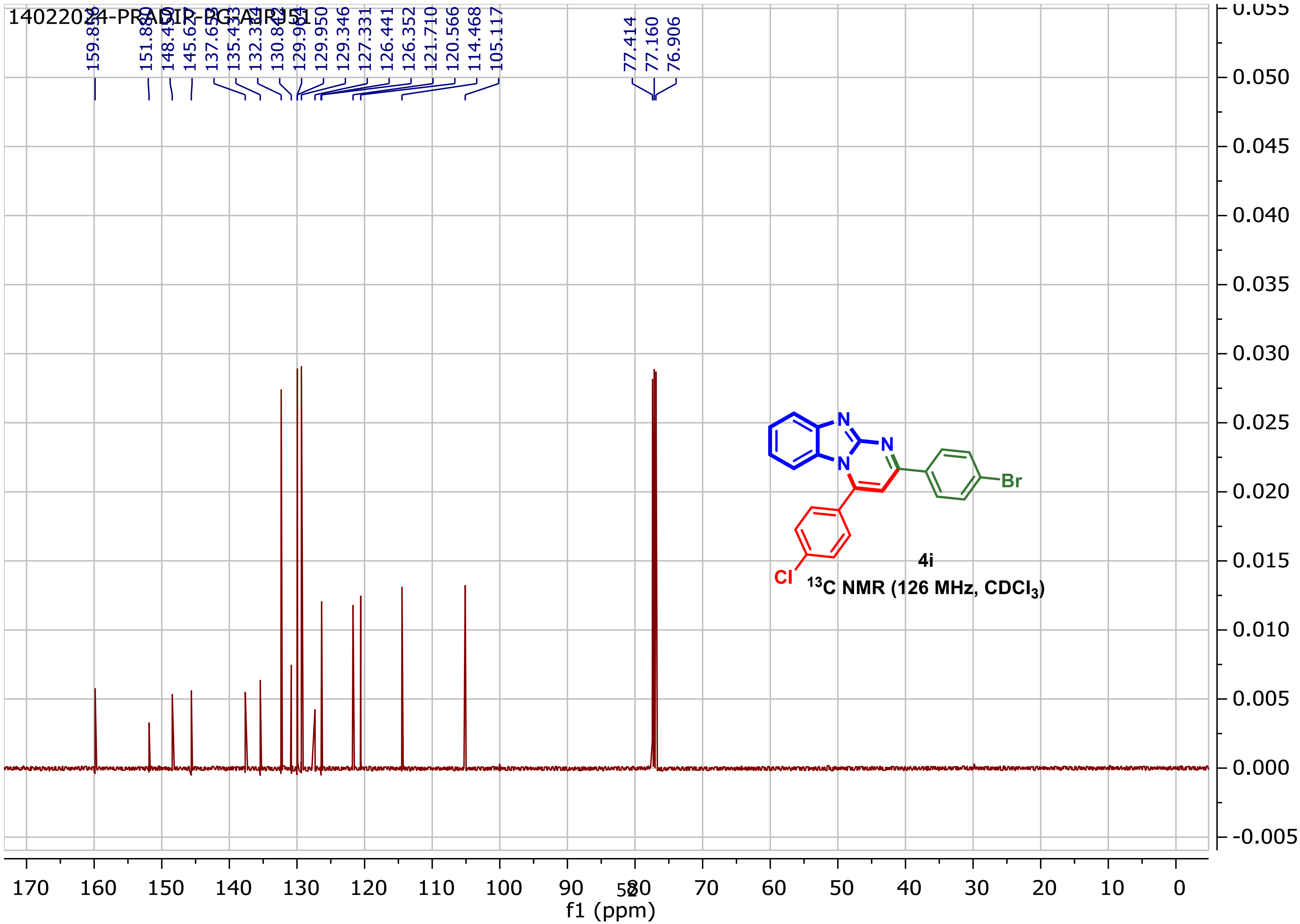

AJR-2-49
8.302
8.299
8.288
8.286
8.000
7.979
7.547
7.546
7.543
7.540
7.531
7.501
7.498
7.483
7.480
7.478
7.462
7.460
7.260
7.254
7.248
7.110
7.107
7.092
7.089
7.086
7.071
7.068
6.770
6.749
N
N
N
Cl
4g
^{1}H NMR (400 MHz, CDCl$_3$)
2.03
1.03
2.09
2.05
3.08
1.17
2.67
1.04
1.00
f1 (ppm)

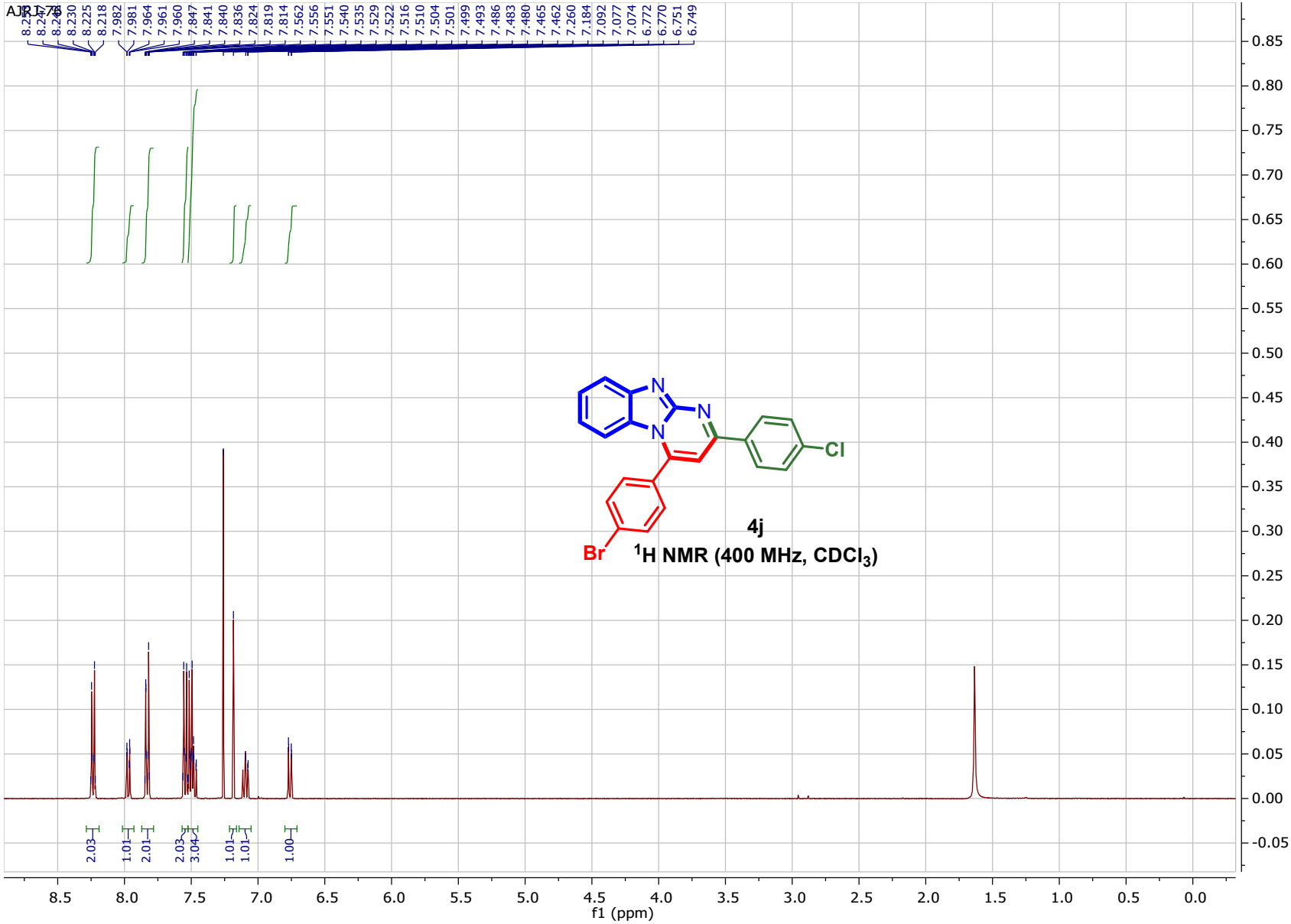

pdata/1
161.214
152.192
148.222
145.704
137.590
136.679
131.566
131.090
129.999
129.961
129.140
127.976
127.428
126.228
121.551
120.596
114.445
105.593
77.372
77.160
76.948
4.0E+10
3.5E+10
3.0E+10
2.5E+10
2.0E+10
1.5E+10
1.0E+10
5.0E+09
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
N
N
N
Cl
4g
13C NMR (151 MHz, CDCl3)

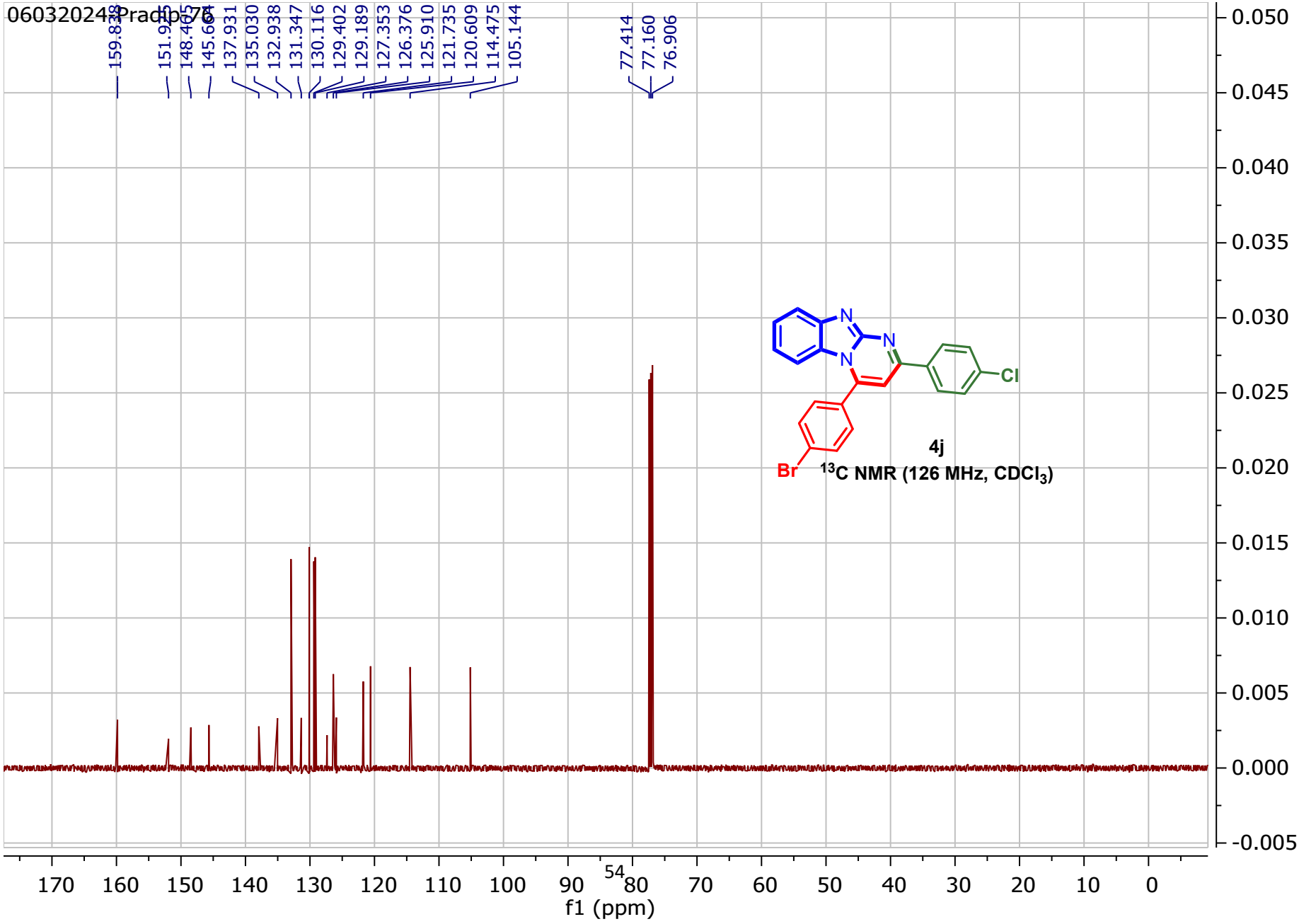

ATR2-67
8.316
8.306
8.297
8.292
8.284
8.278
7.976
7.974
7.972
7.956
7.954
7.951
7.680
7.679
7.674
7.664
7.658
7.653
7.626
7.620
7.615
7.604
7.599
7.494
7.491
7.476
7.473
7.470
7.455
7.452
7.260
7.232
7.226
7.214
7.210
7.205
7.194
7.188
7.179
7.103
7.100
7.085
7.082
7.079
7.064
7.061
6.757
6.754
6.752
6.736
6.733
6.731
1.99
1.03
2.03
1.99
1.11
3.39
1.07
1.00
f1 (ppm)
4h
1H NMR (400 MHz, CDCl3)

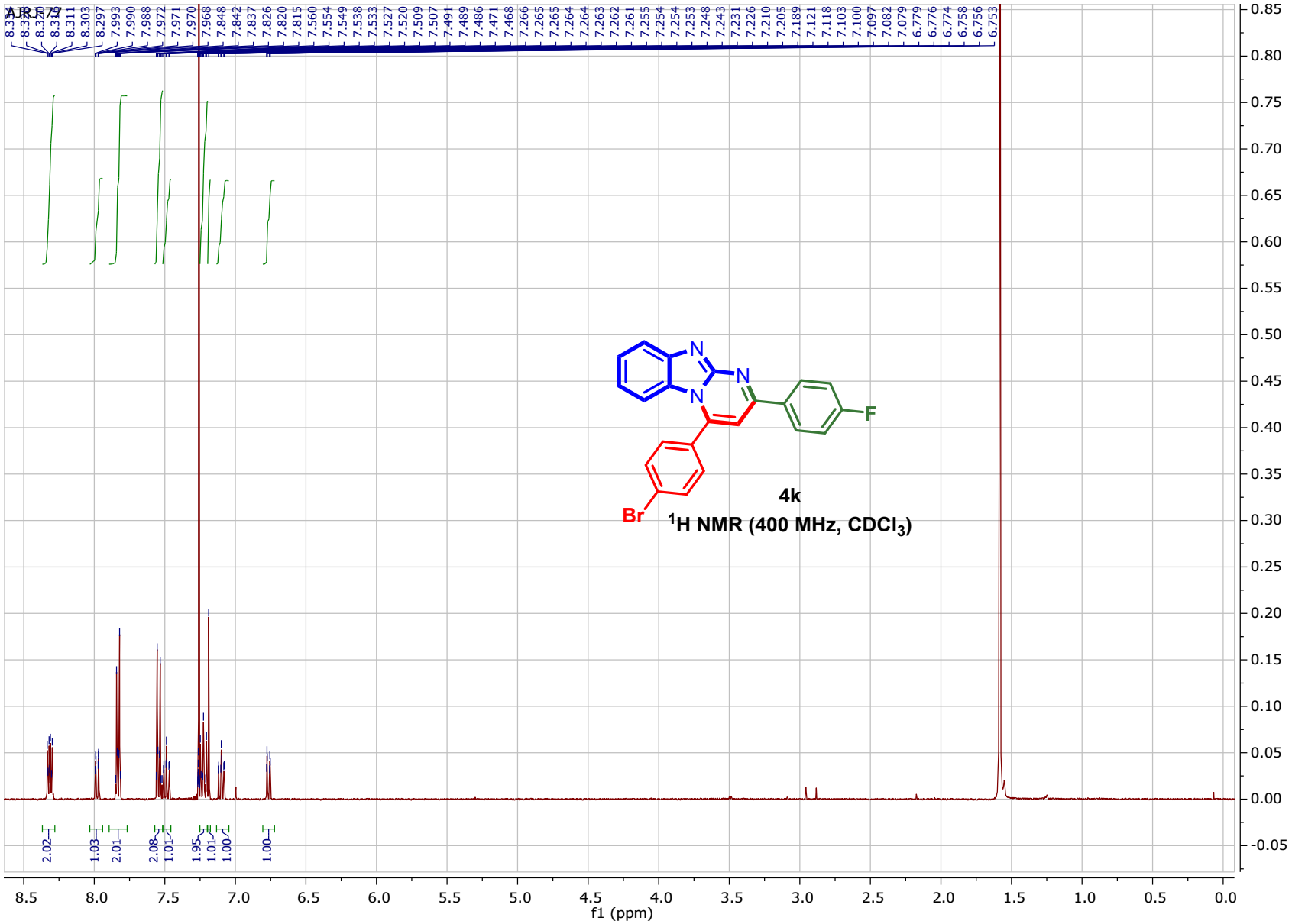

14022024-bRADIP-pg-67
166.1
164.0
159.9
152.0
148.3
145.6
137.6
132.85
132.791
130.922
130.129
130.059
129.972
129.948
127.363
126.294
121.625
120.552
116.336
116.162
114.437
105.234
77.414
77.160
76.906
N
N
N
F
Cl
4h
13C NMR (126 MHz, CDCl3)
f1 (ppm)

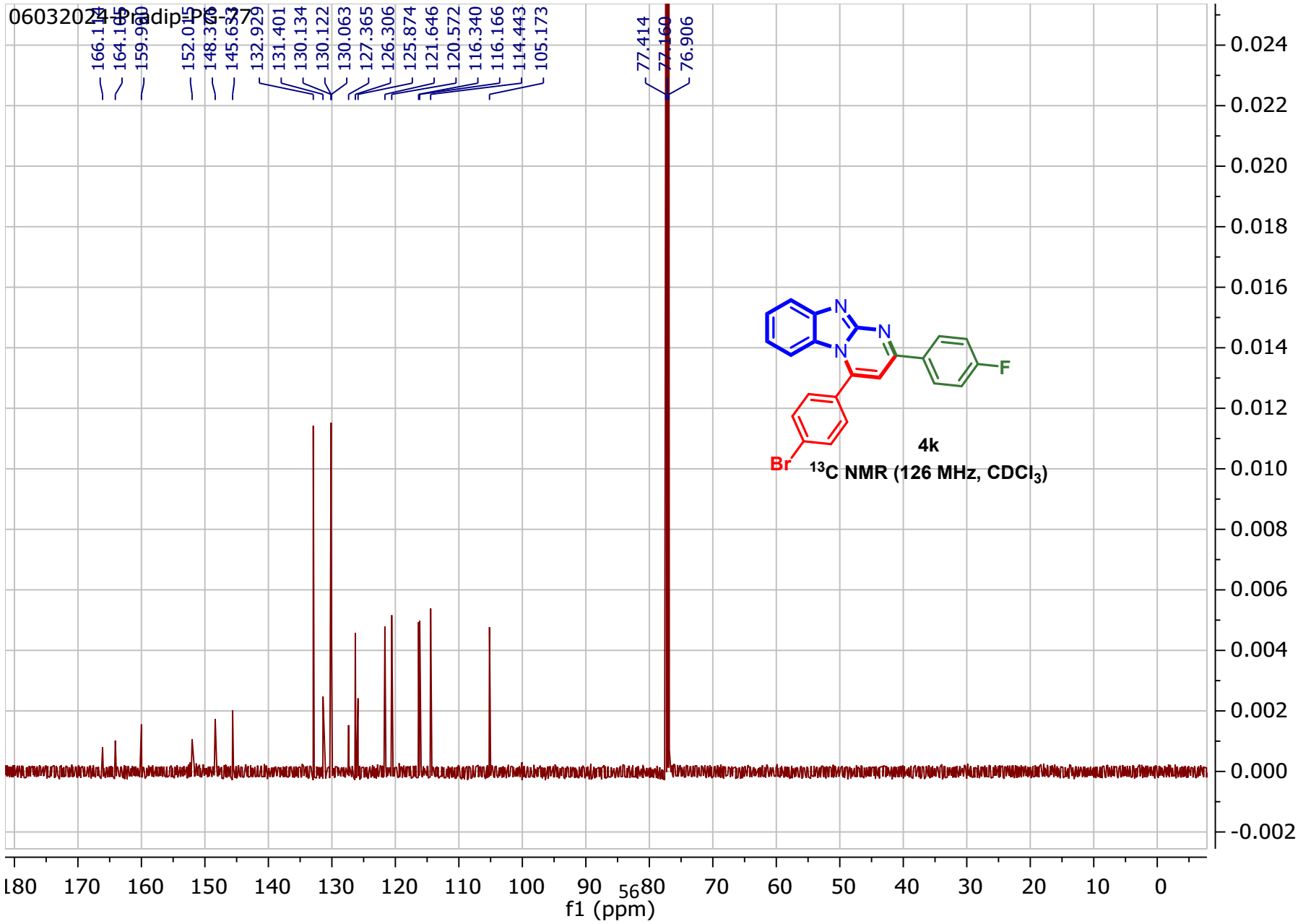

single_pulse
7.483
7.470
7.469
7.454
7.452
7.260
7.170
7.095
7.093
7.081
7.078
7.064
7.062
6.749
6.733
1.709
2.18
0.91
6.00
1.10
1.06
1.09
1.00
f1 (ppm)
N
N
N
Br
Cl
4i
^{1}H NMR (400 MHz, $CDCl_3$)

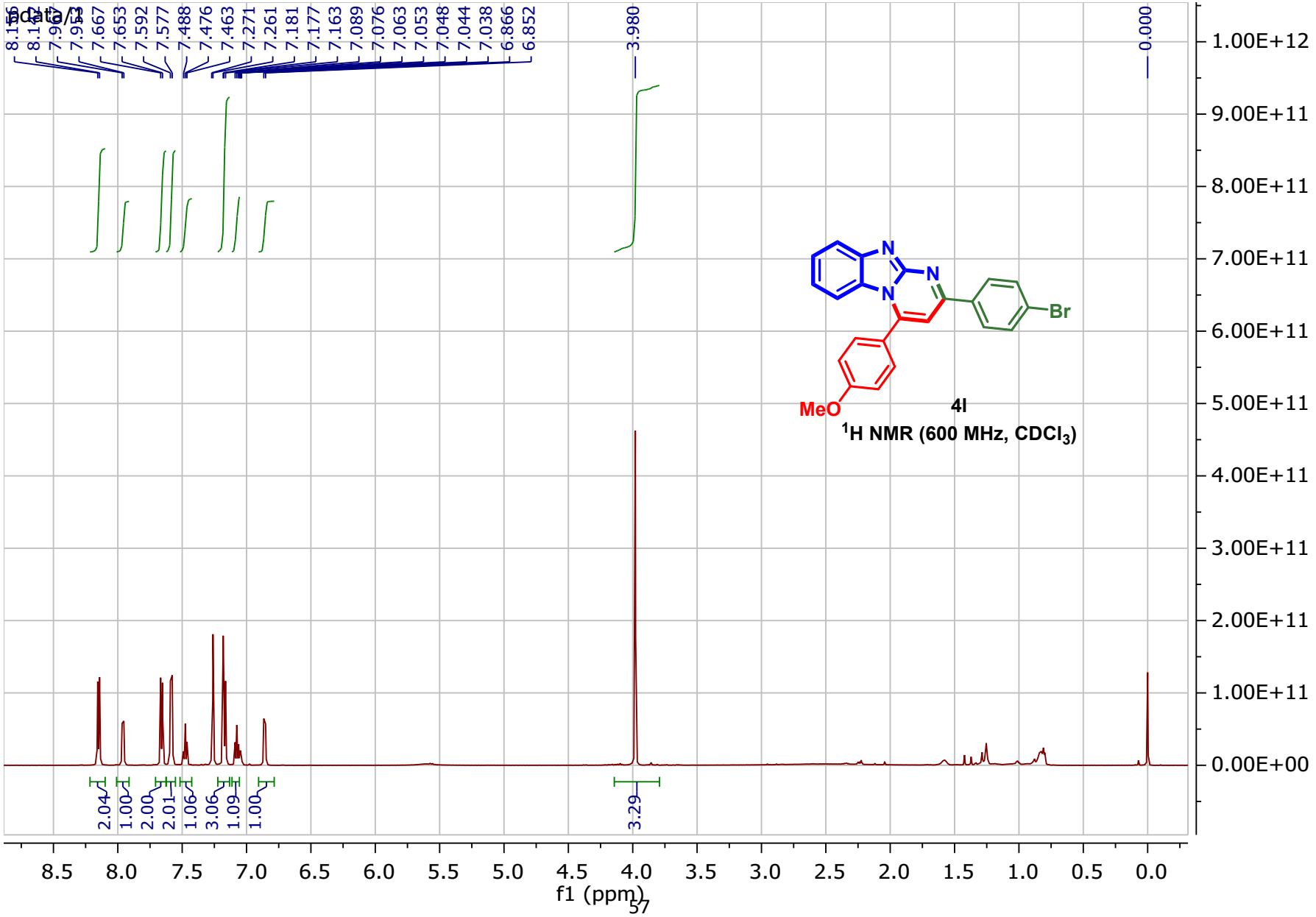

14022024-PRADIP-PG-AJRJ51
129.950
129.346
127.331
126.441
126.352
121.710
120.566
114.468
105.117
77.414
77.160
76.906
N
N
N
Br
Cl
4i
^{13}C NMR (126 MHz, CDCl$_3$)
f1 (ppm)

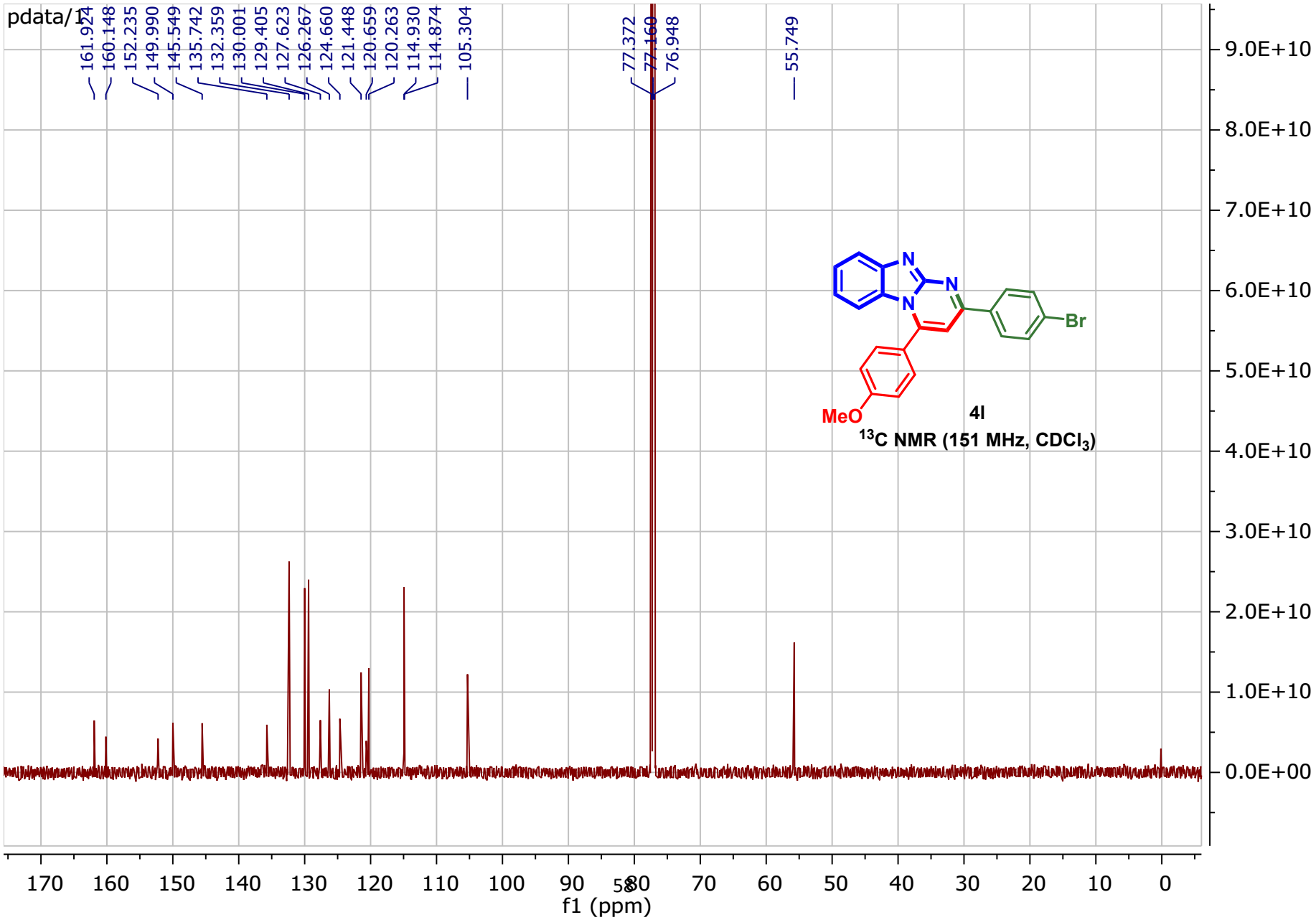

AJR1-78
8.247
8.230
8.225
8.218
7.982
7.981
7.964
7.961
7.960
7.847
7.841
7.840
7.836
7.824
7.819
7.814
7.562
7.556
7.551
7.540
7.535
7.529
7.522
7.516
7.510
7.504
7.501
7.499
7.493
7.486
7.483
7.480
7.465
7.462
7.260
7.184
7.092
7.077
7.074
6.772
6.770
6.751
6.749
N
N
N
Cl
Br
4j
^{1}H NMR (400 MHz, CDCl$_3$)
2.03
1.01
2.01
2.03
3.04
1.01
1.01
1.00
f1 (ppm)

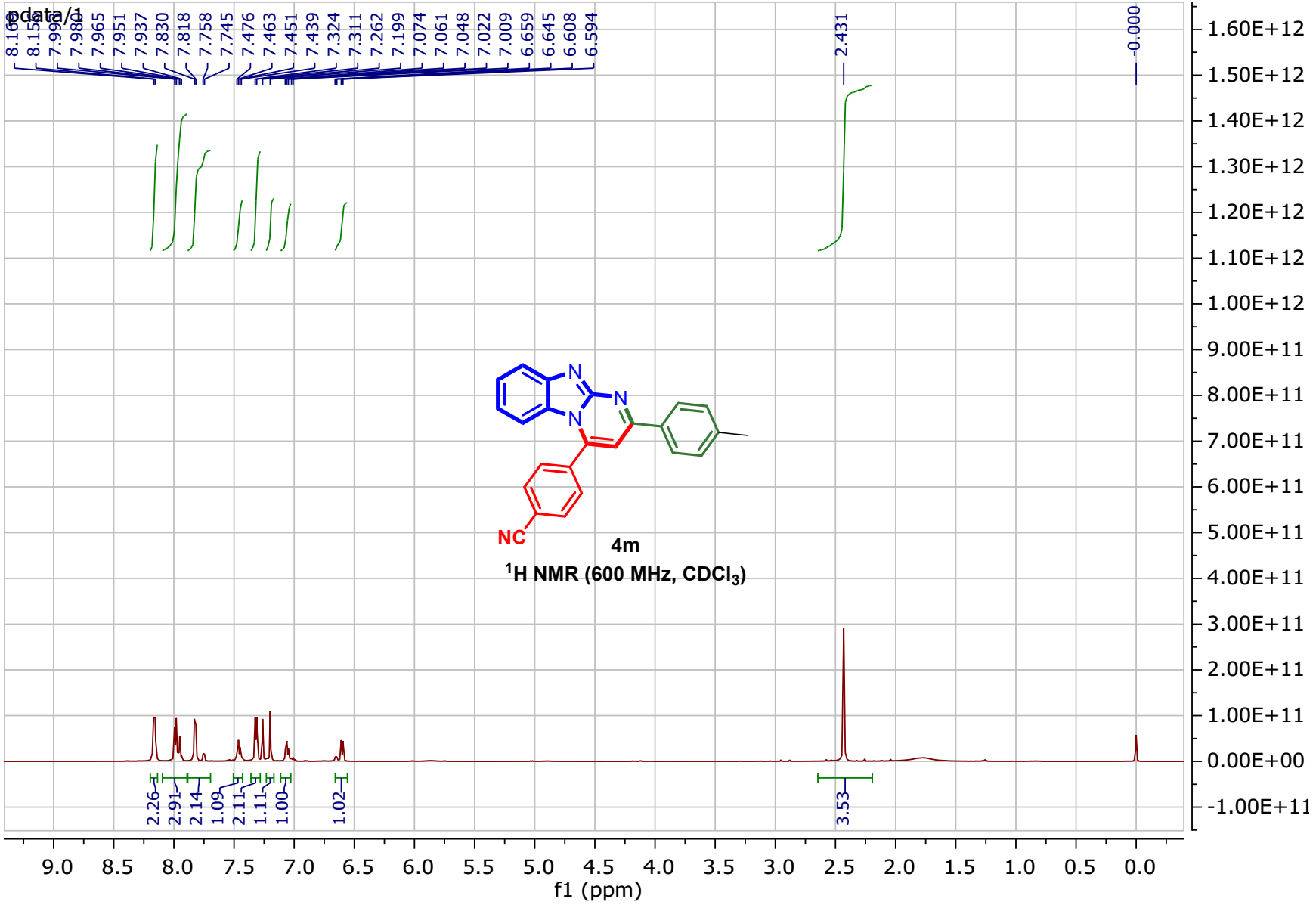

060320243Pradip76
159.838
151.925
148.465
145.664
137.931
135.030
132.938
131.347
130.116
129.402
129.189
127.353
126.376
125.910
121.735
120.609
114.475
105.144
77.414
77.160
76.906
N
N
N
Cl
Br
4j
^{13}C NMR (126 MHz, CDCl$_3$)
0.050
0.045
0.040
0.035
0.030
0.025
0.020
0.015
0.010
0.005
0.000
-0.005
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

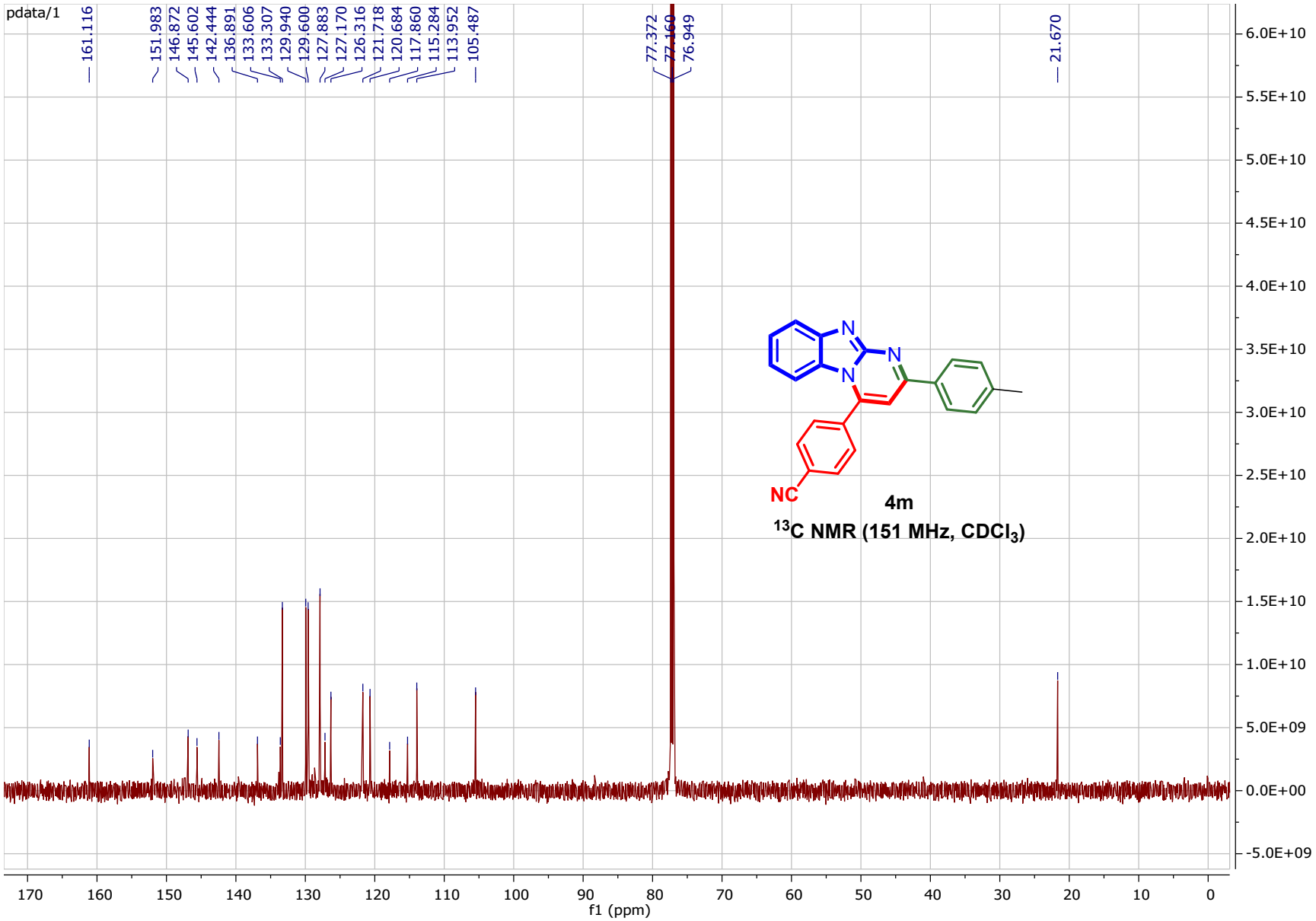

AJR72
8.334 8.327 8.320 8.314 8.311 8.303 8.297 7.993 7.990 7.988 7.972 7.971 7.970 7.968 7.848 7.842 7.837 7.826 7.820 7.815 7.560 7.554 7.549 7.538 7.533 7.527 7.520 7.509 7.507 7.491 7.489 7.486 7.471 7.468 7.266 7.265 7.265 7.264 7.264 7.263 7.262 7.261 7.255 7.254 7.254 7.253 7.248 7.243 7.231 7.226 7.210 7.205 7.189 7.121 7.118 7.103 7.100 7.097 7.082 7.079 6.779 6.776 6.774 6.758 6.756 6.753
N
N
N
F
Br
4k
^{1}H NMR (400 MHz, CDCl$_3$)
2.02 1.03 2.01 2.08 1.01 1.95 1.01 1.00 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
0.85 0.80 0.75 0.70 0.65 0.60 0.55 0.50 0.45 0.40 0.35 0.30 0.25 0.20 0.15 0.10 0.05 0.00 -0.05

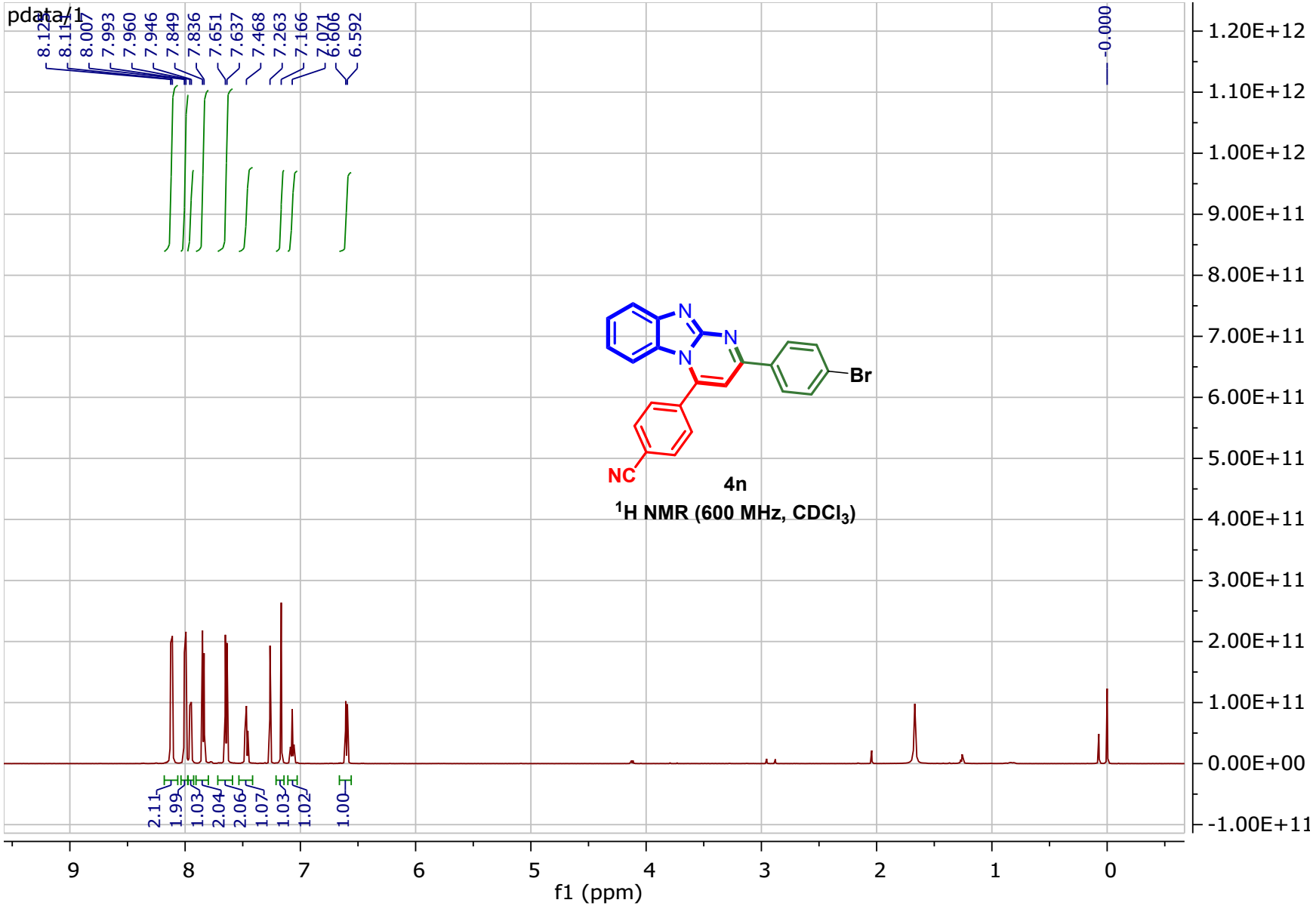

06032024 Pradip PS-27
166.114
164.185
159.980
152.015
148.316
145.633
132.929
131.401
130.134
130.122
130.063
127.365
126.306
125.874
121.646
120.572
116.340
116.166
114.443
105.173
77.414
77.160
76.906
N
N
N
F
Br
4k
^{13}C NMR (126 MHz, CDCl$_3$)
0.024
0.022
0.020
0.018
0.016
0.014
0.012
0.010
0.008
0.006
0.004
0.002
0.000
-0.002
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

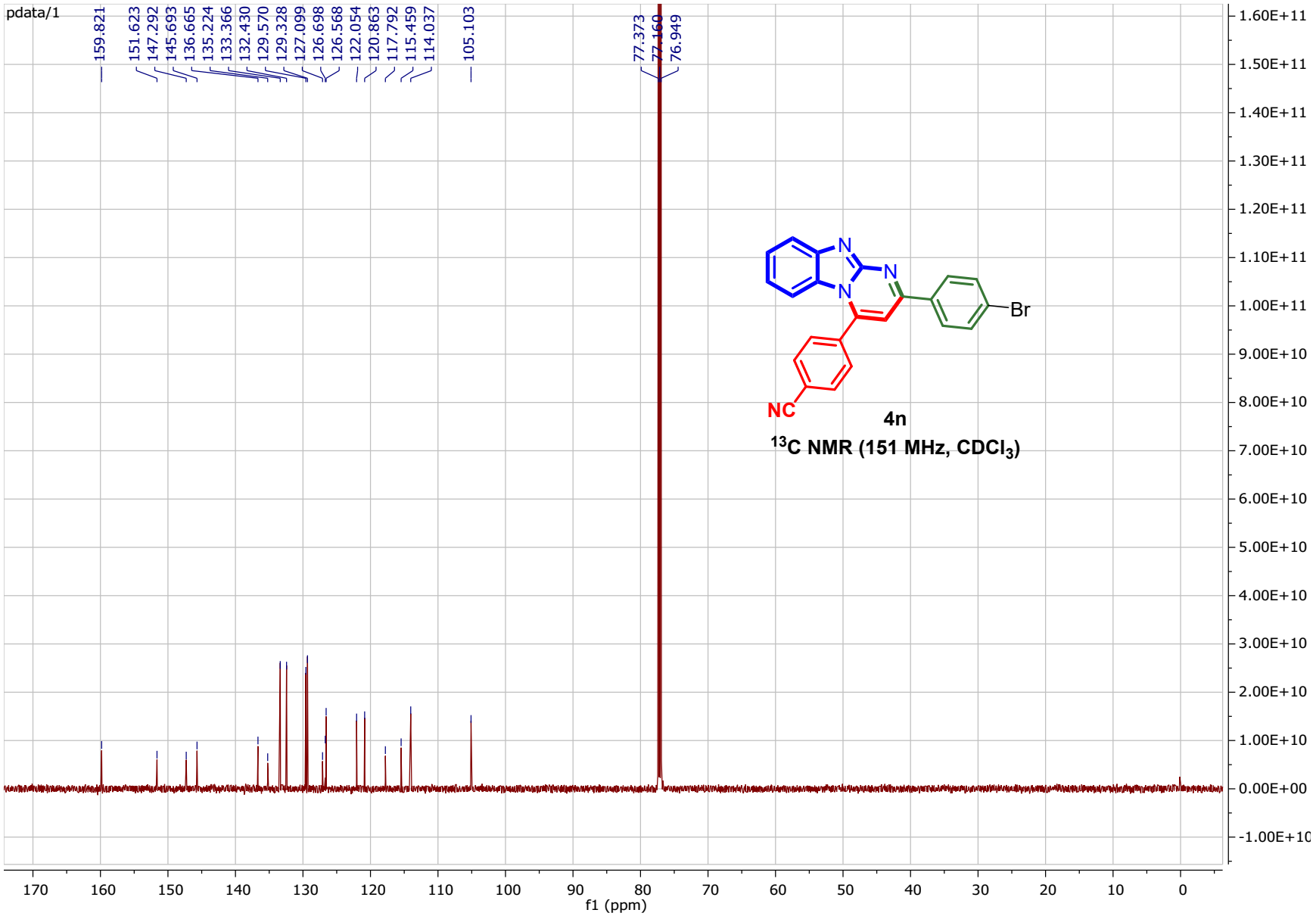

pdata/1
8.156
8.142
7.954
7.953
7.667
7.653
7.592
7.577
7.488
7.476
7.463
7.271
7.261
7.181
7.177
7.163
7.089
7.076
7.063
7.053
7.048
7.044
7.038
6.866
6.852
3.980
0.000
2.04
1.00
2.00
2.01
1.06
3.06
1.09
1.00
3.29
N
N
N
Br
MeO
4l
^{1}H NMR (600 MHz, CDCl$_3$)
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

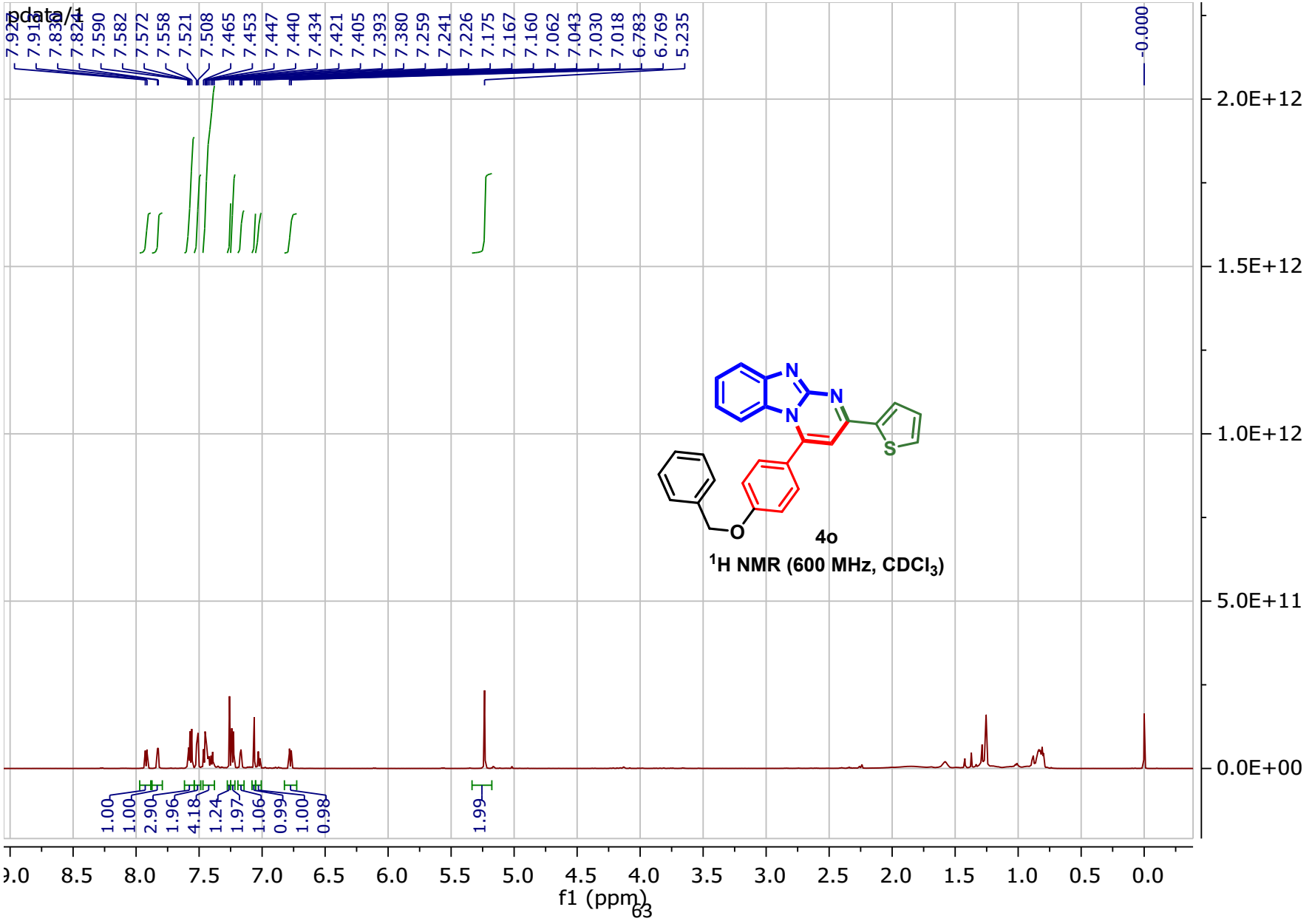

pdata/1
161.924
160.148
152.235
149.990
145.549
135.742
132.359
130.001
129.405
127.623
126.267
124.660
121.448
120.659
120.263
114.930
114.874
105.304
77.372
77.160
76.948
55.749
N
N
N
Br
MeO
4l
13C NMR (151 MHz, CDCl3)
9.0E+10
8.0E+10
7.0E+10
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

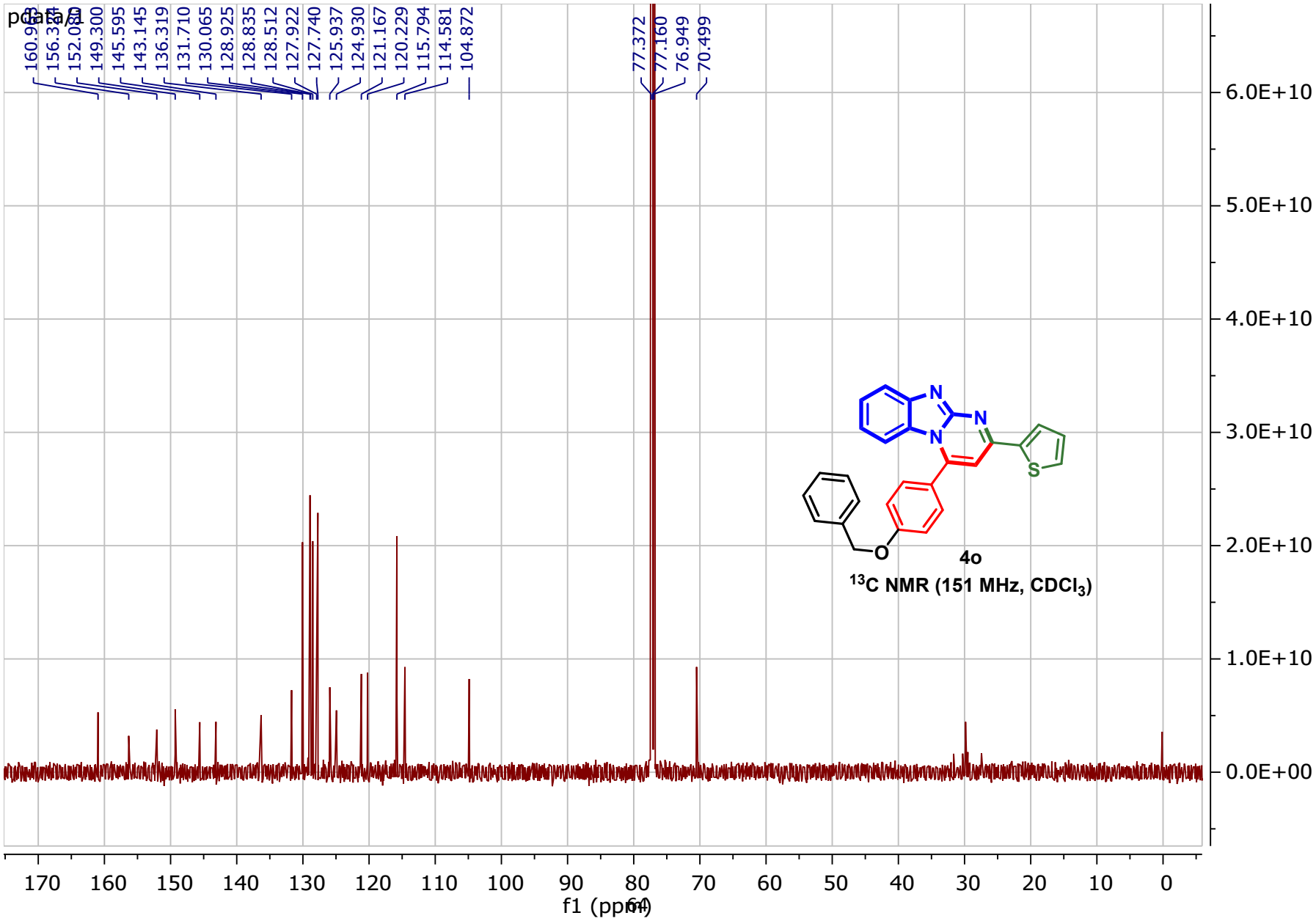

pdata/1
8.166
8.156
7.990
7.980
7.965
7.951
7.937
7.830
7.818
7.758
7.745
7.476
7.463
7.451
7.439
7.324
7.311
7.262
7.199
7.074
7.061
7.048
7.022
7.009
6.659
6.645
6.608
6.594
2.431
-0.000
N
N
N
NC
4m
1H NMR (600 MHz, CDCl3)
2.26
2.91
2.14
1.09
2.11
1.11
1.00
1.02
3.53
1.60E+12
1.50E+12
1.40E+12
1.30E+12
1.20E+12
1.10E+12
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

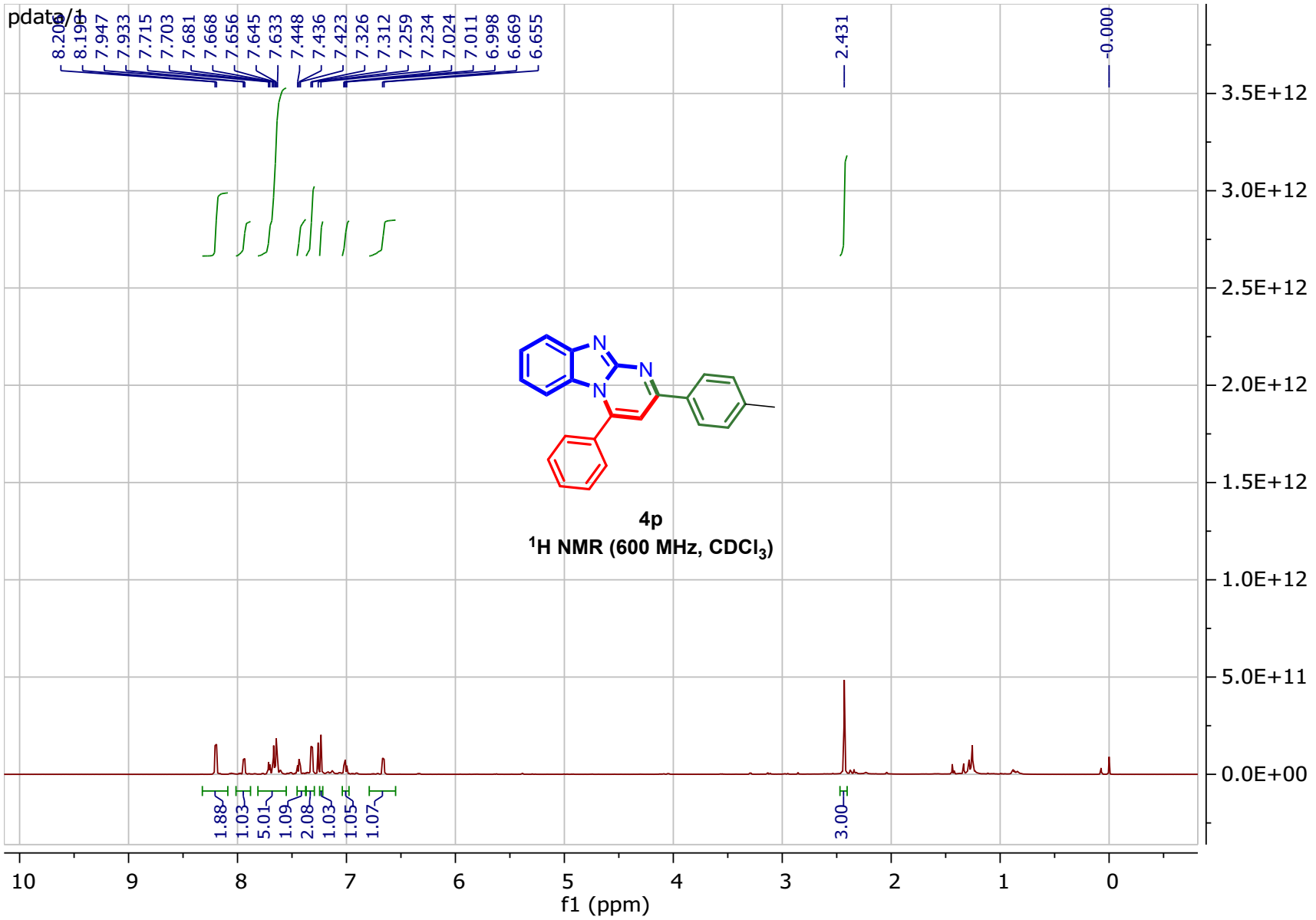

pdata/1
161.116
151.983
146.872
145.602
142.444
136.891
133.606
133.307
129.940
129.600
127.883
127.170
126.316
121.718
120.684
117.860
115.284
113.952
105.487
77.372
77.160
76.949
21.670
6.0E+10
5.5E+10
5.0E+10
4.5E+10
4.0E+10
3.5E+10
3.0E+10
2.5E+10
2.0E+10
1.5E+10
1.0E+10
5.0E+09
0.0E+00
-5.0E+09
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
N
N
N
NC
4m
13C NMR (151 MHz, CDCl3)


pdata/1
8.127
8.111
8.007
7.993
7.960
7.946
7.849
7.836
7.651
7.637
7.468
7.263
7.166
7.071
7.066
6.592
-0.000
N
N
N
Br
NC
4n
^{1}H NMR (600 MHz, CDCl$_3$)
2.11
1.99
1.03
2.04
2.06
1.07
1.03
1.02
1.00
1.20E+12
1.10E+12
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


pdata/1
159.821
151.623
147.292
145.693
136.665
135.224
133.366
132.430
129.570
129.328
127.099
126.698
126.568
122.054
120.863
117.792
115.459
114.037
105.103
77.373
77.160
76.949
N
N
N
Br
NC
4n
13C NMR (151 MHz, CDCl3)
1.60E+11
1.50E+11
1.40E+11
1.30E+11
1.20E+11
1.10E+11
1.00E+11
9.00E+10
8.00E+10
7.00E+10
6.00E+10
5.00E+10
4.00E+10
3.00E+10
2.00E+10
1.00E+10
0.00E+00
-1.00E+10
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

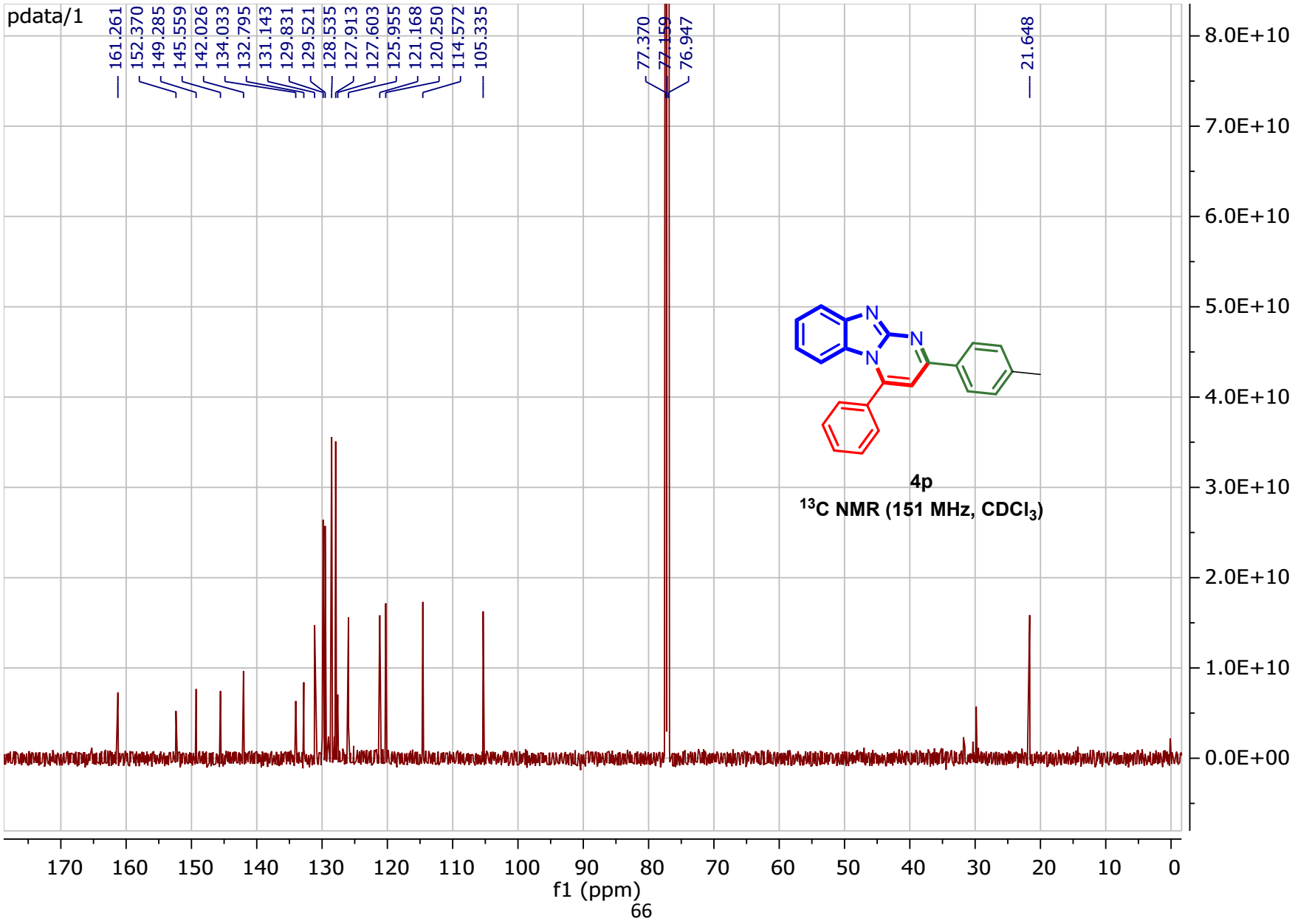

pdata/1
7.925
7.914
7.835
7.824
7.590
7.582
7.572
7.558
7.521
7.508
7.465
7.453
7.447
7.440
7.434
7.421
7.405
7.393
7.380
7.259
7.241
7.226
7.175
7.167
7.160
7.062
7.043
7.030
7.018
6.783
6.769
5.235
-0.000
2.0E+12
1.5E+12
1.0E+12
5.0E+11
0.0E+00
1.00
1.00
2.90
1.96
4.18
1.24
1.97
1.06
0.99
1.00
0.98
1.99
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
N
N
N
S
O
4o
^{1}H NMR (600 MHz, CDCl$_3$)

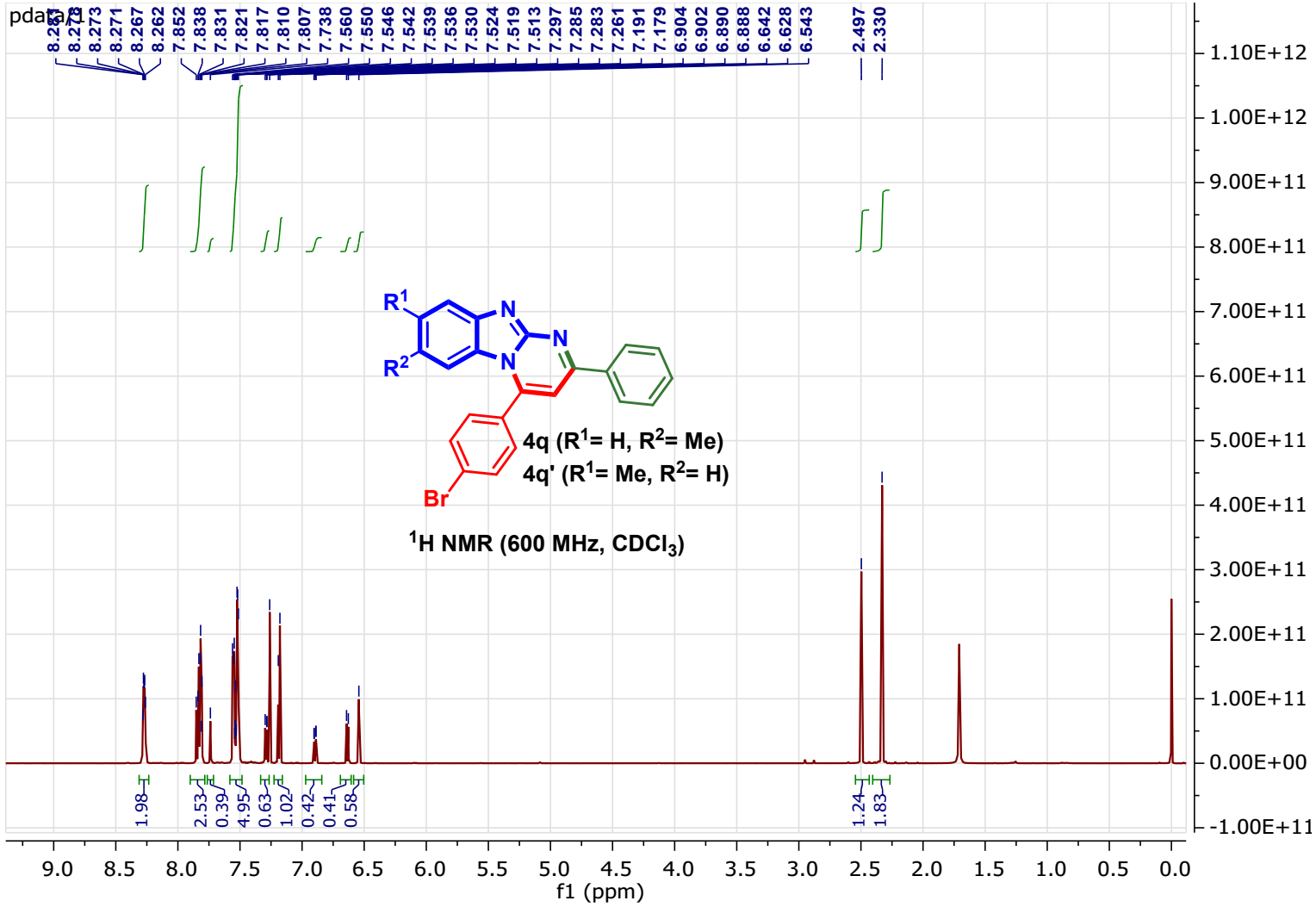

pdata/1
160.963
156.334
152.082
149.300
145.595
143.145
136.319
131.710
130.065
128.925
128.835
128.512
127.922
127.740
125.937
124.930
121.167
120.229
115.794
114.581
104.872
77.372
77.160
76.949
70.499
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
N
N
N
S
O
4o
^{13}C NMR (151 MHz, $CDCl_3$)

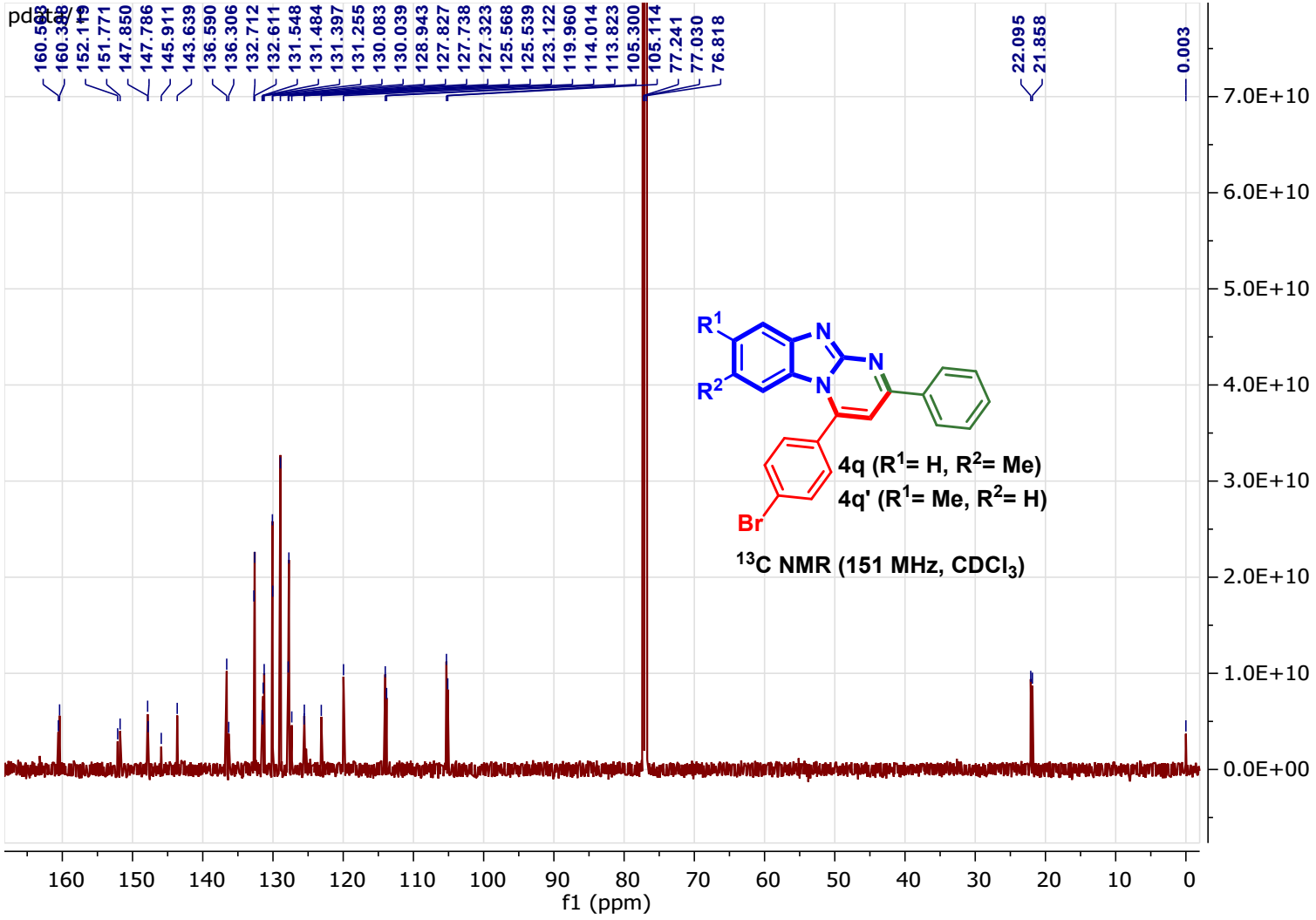


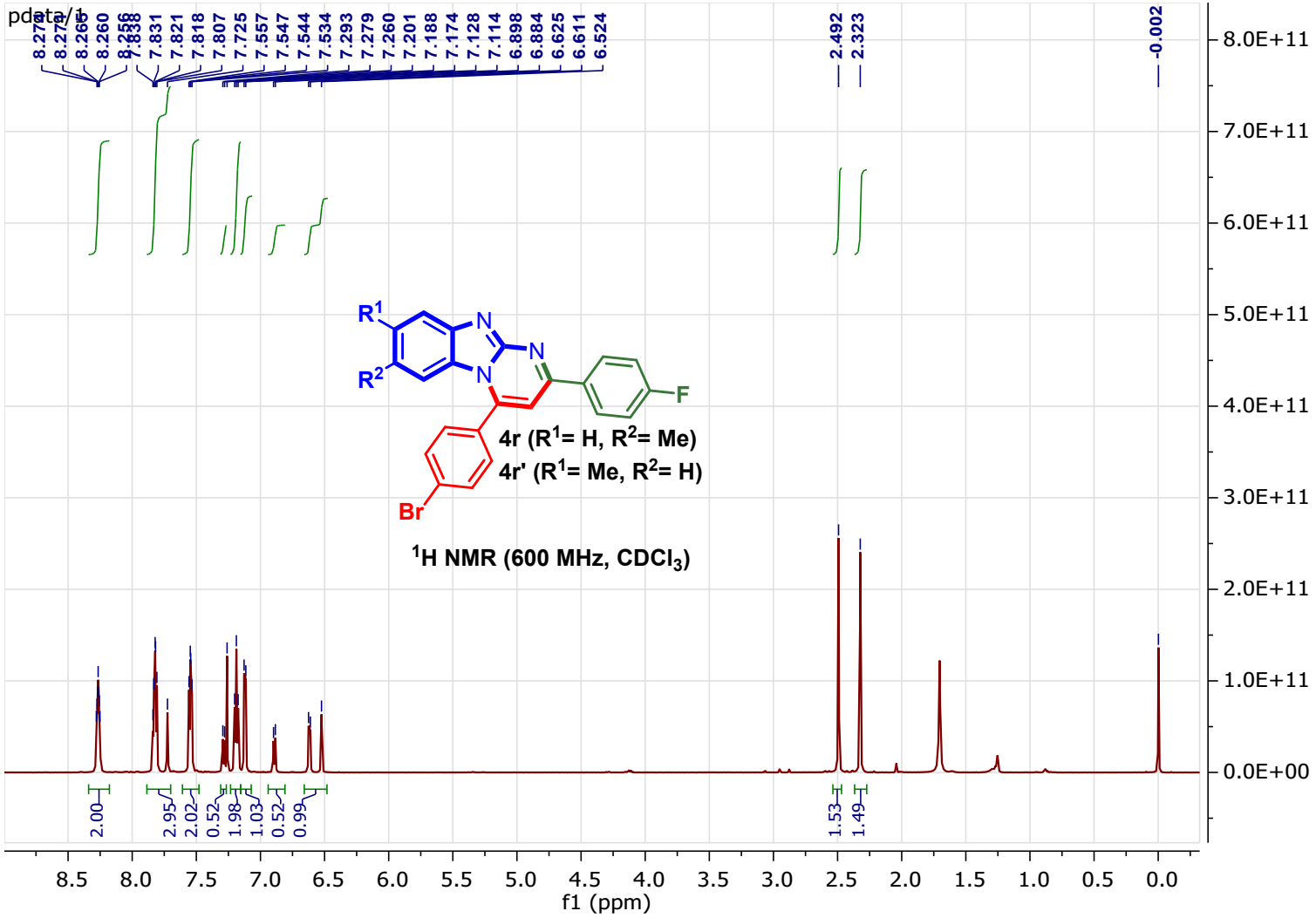
4p

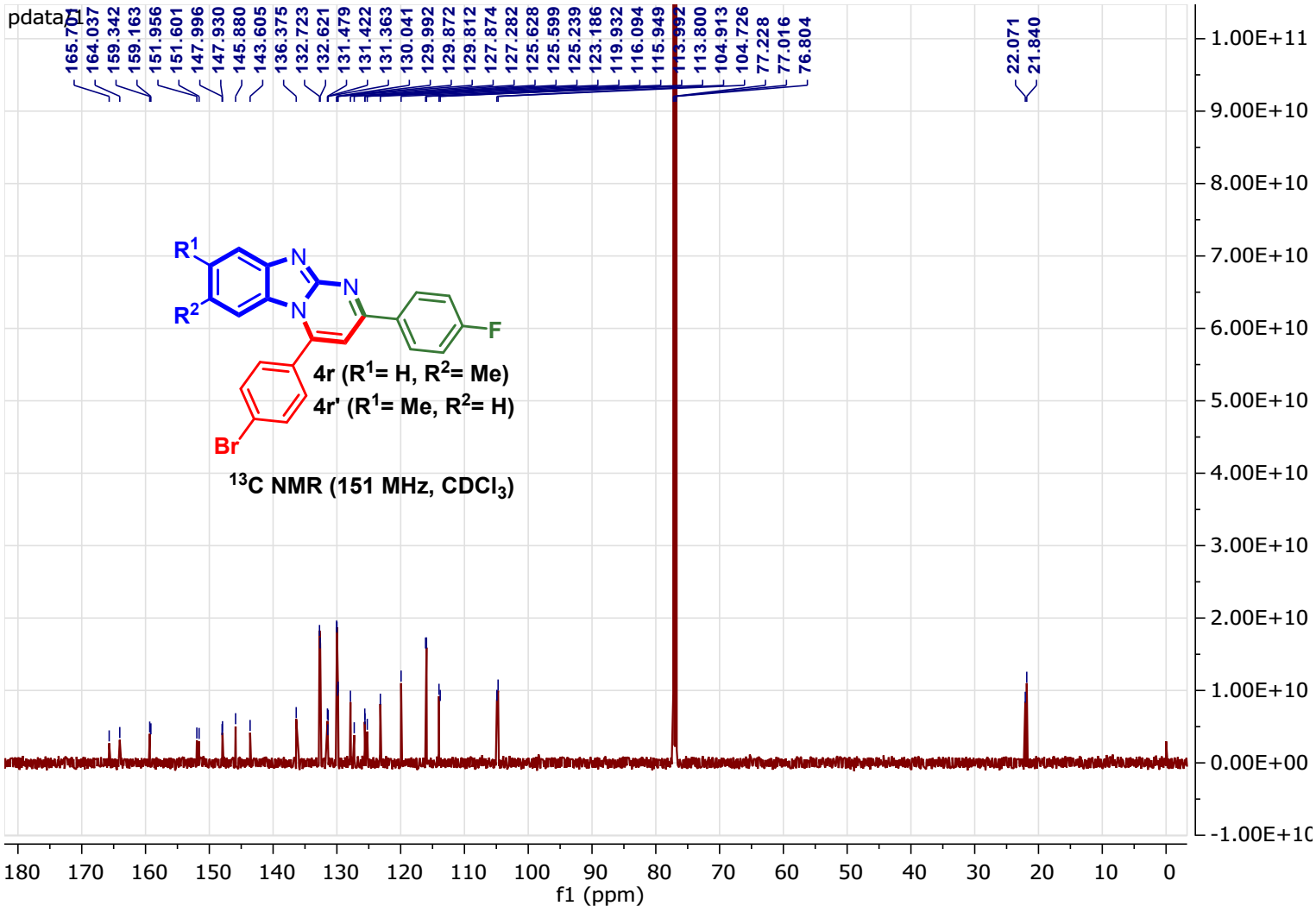
^{1}H NMR (600 MHz, $CDCl_3$)

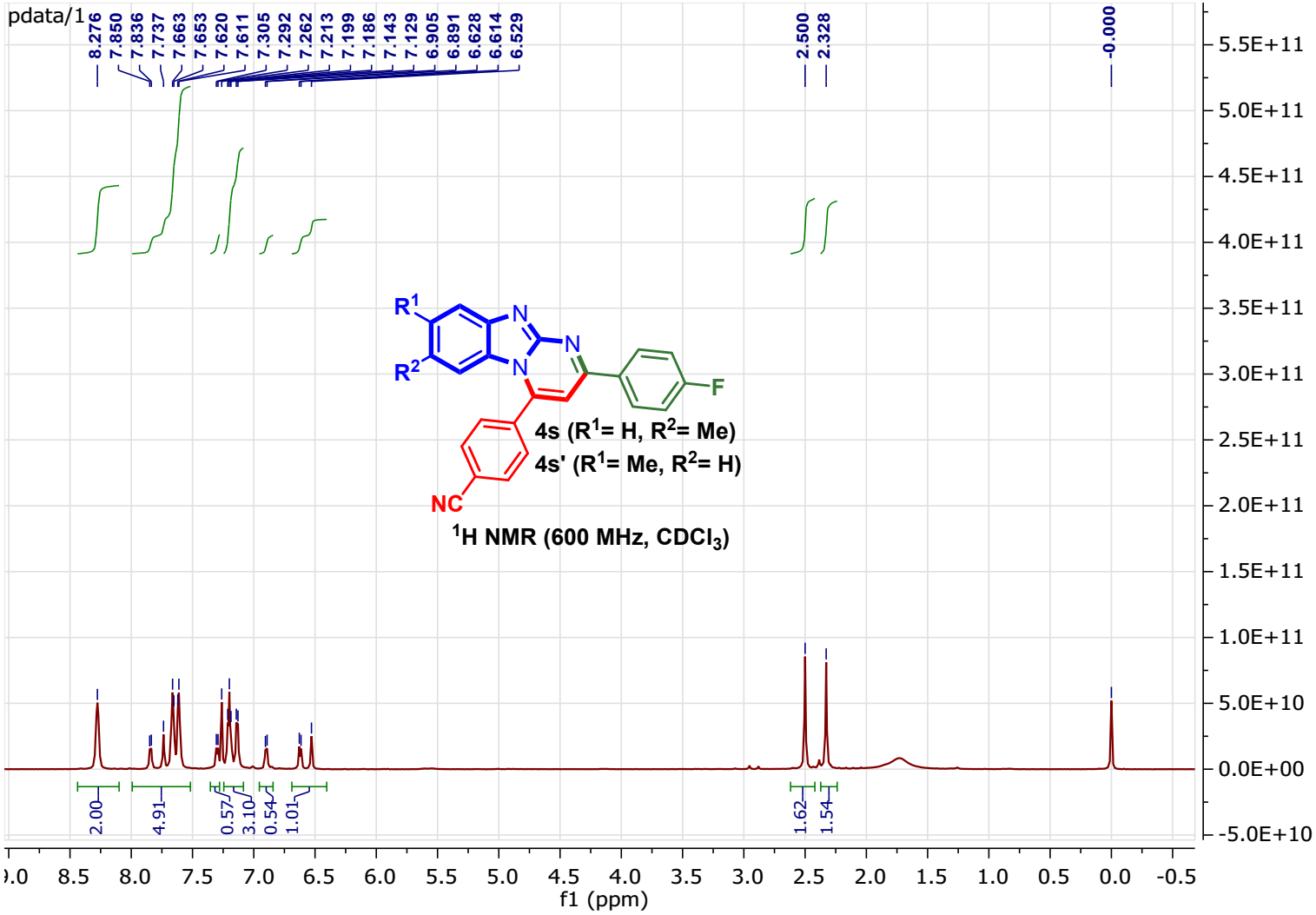

pdata/1
161.261
152.370
149.285
145.559
142.026
134.033
132.795
131.143
129.831
129.521
128.535
127.913
127.603
125.955
121.168
120.250
114.572
105.335
77.370
77.159
76.947
21.648
8.0E+10
7.0E+10
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
4p
13C NMR (151 MHz, CDCl3)

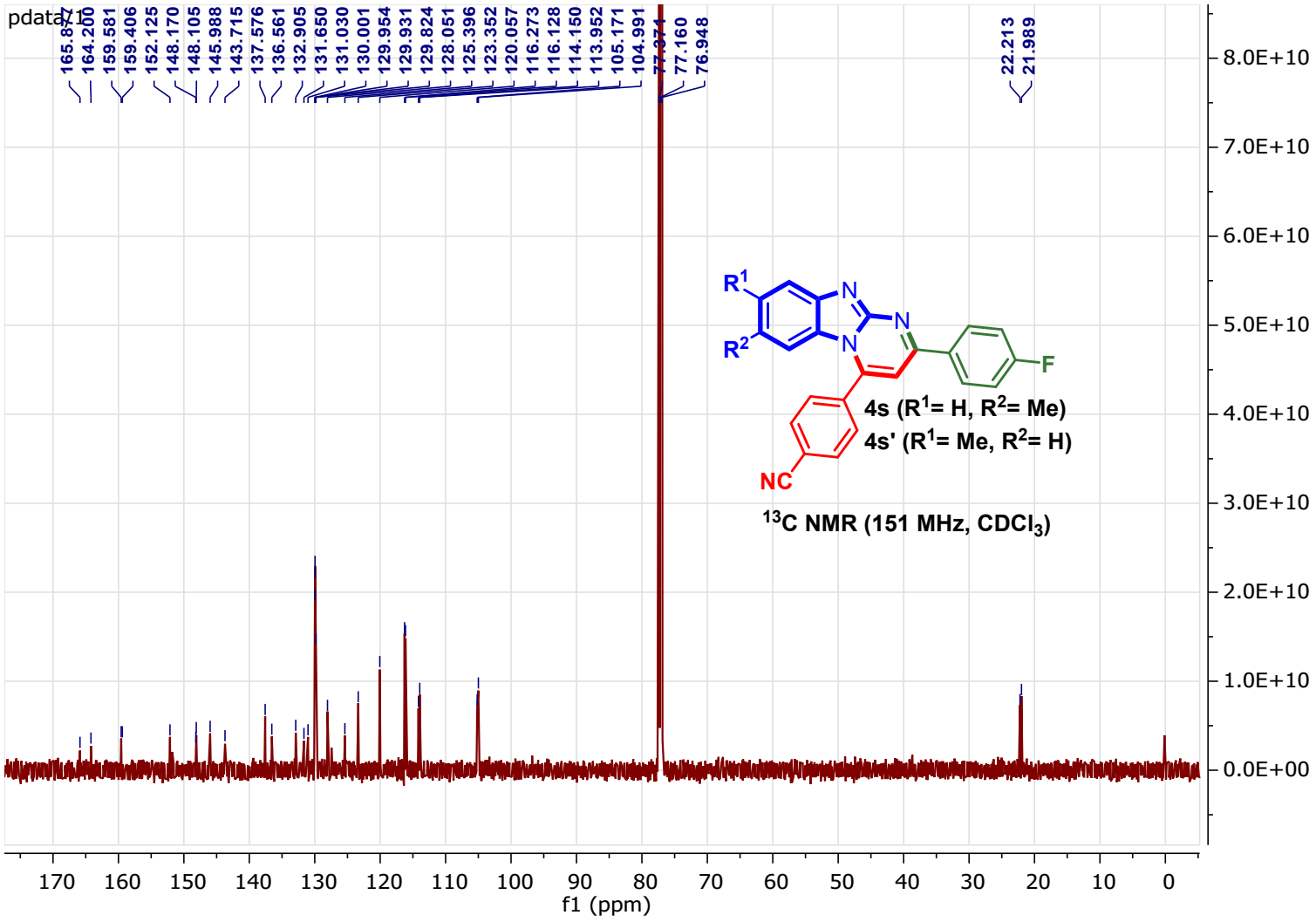

pdata/1
8.267
8.262
7.852
7.838
7.831
7.821
7.817
7.810
7.807
7.738
7.560
7.550
7.546
7.542
7.539
7.536
7.530
7.524
7.519
7.513
7.297
7.285
7.283
7.261
7.191
7.179
6.904
6.902
6.890
6.888
6.642
6.628
6.543
2.497
2.330
R1
R2
N
N
N
Br
4q (R1= H, R2= Me)
4q' (R1= Me, R2= H)
1H NMR (600 MHz, CDCl3)
1.98
2.53
0.39
4.95
0.63
1.02
0.42
0.41
0.58
1.24
1.83
1.10E+12
1.00E+12
9.00E+11
8.00E+11
7.00E+11
6.00E+11
5.00E+11
4.00E+11
3.00E+11
2.00E+11
1.00E+11
0.00E+00
-1.00E+11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

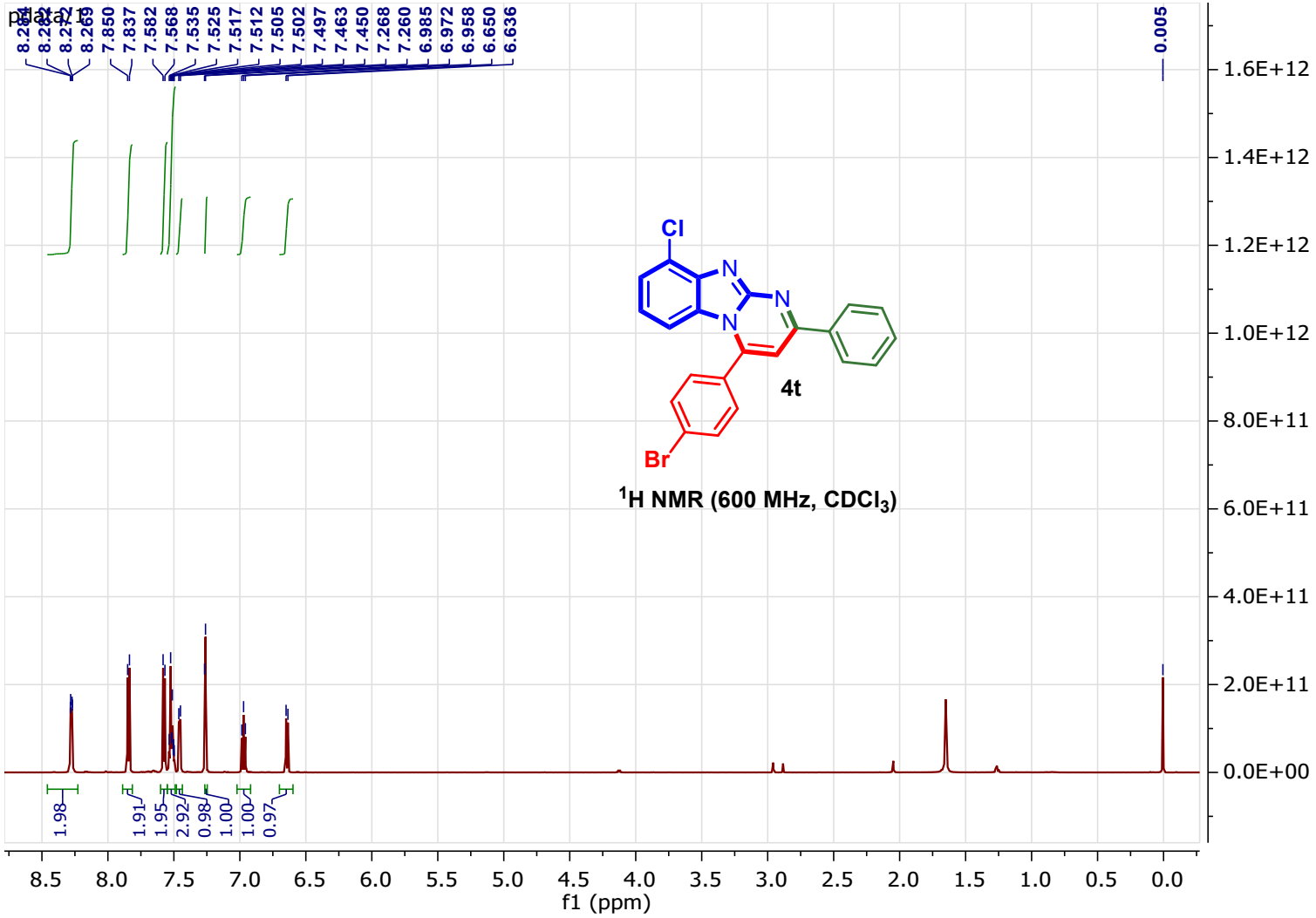

pda3
160.543
160.348
152.113
151.771
147.850
147.786
145.911
143.639
136.590
136.306
132.712
132.611
131.548
131.484
131.397
131.255
130.083
130.039
128.943
127.827
127.738
127.323
125.568
125.539
123.122
119.960
114.014
113.823
105.300
105.114
77.241
77.030
76.818
22.095
21.858
0.003
7.0E+10
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
R1
R2
N
N
N
Br
4q (R1= H, R2= Me)
4q' (R1= Me, R2= H)
13C NMR (151 MHz, CDCl3)

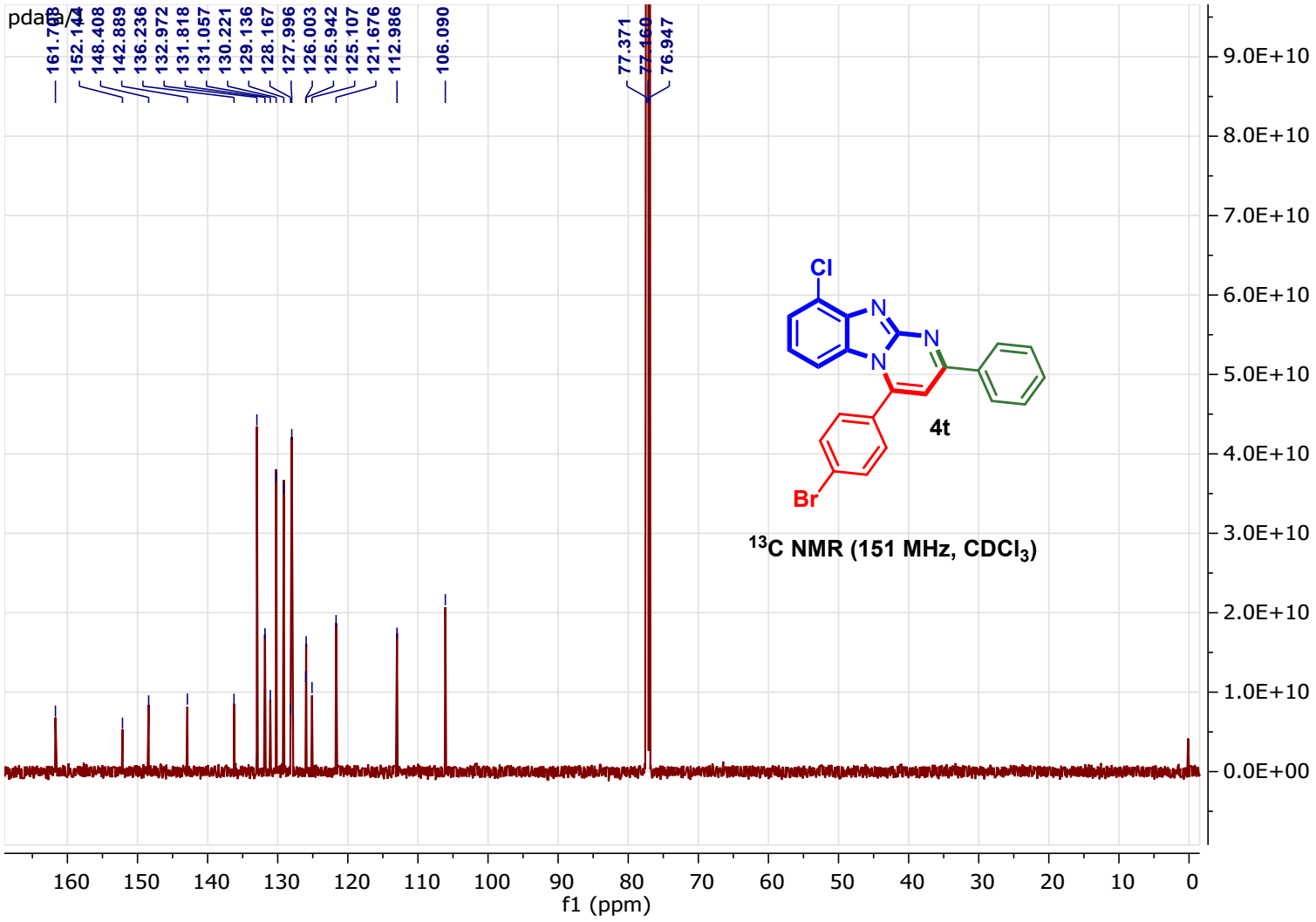

pdata/1
8.277
8.272
8.265
8.260
8.256
7.838
7.831
7.821
7.818
7.807
7.725
7.557
7.547
7.544
7.534
7.293
7.279
7.260
7.201
7.188
7.174
7.128
7.114
6.898
6.884
6.625
6.611
6.524
2.492
2.323
-0.002
R1
R2
N
N
N
F
Br
4r (R1= H, R2= Me)
4r' (R1= Me, R2= H)
1H NMR (600 MHz, CDCl3)
2.00
2.95
2.02
0.52
1.98
1.03
0.52
0.99
1.53
1.49
8.0E+11
7.0E+11
6.0E+11
5.0E+11
4.0E+11
3.0E+11
2.0E+11
1.0E+11
0.0E+00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

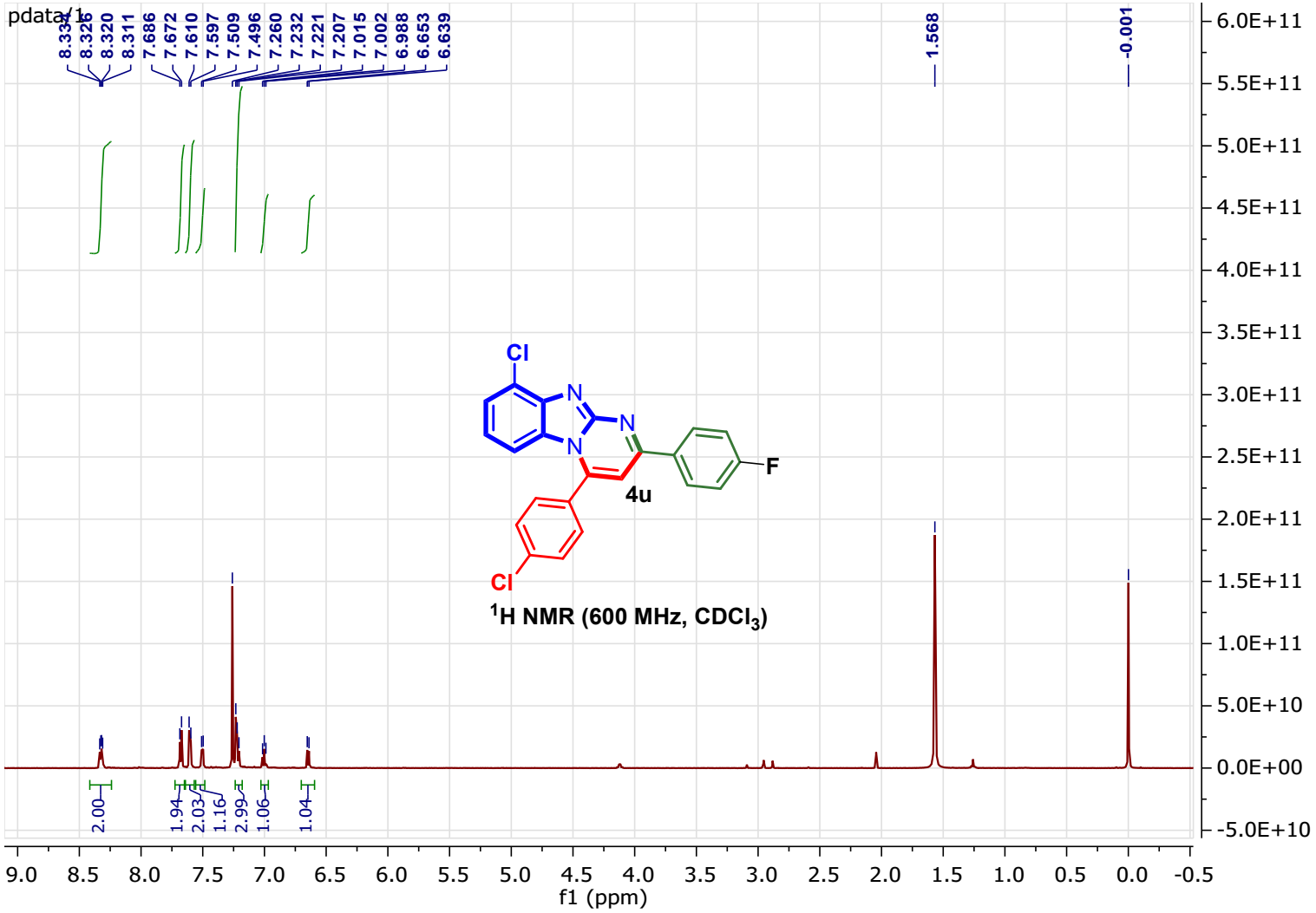

pdata/1
165.701
164.037
159.342
159.163
151.956
151.601
147.996
147.930
145.880
143.605
136.375
132.723
132.621
131.479
131.422
131.363
130.041
129.992
129.872
129.812
127.874
127.282
125.628
125.599
125.239
123.186
119.932
116.094
115.949
113.992
113.800
104.913
104.726
77.228
77.016
76.804
22.071
21.840
R1
R2
N
N
N
F
Br
4r (R1= H, R2= Me)
4r' (R1= Me, R2= H)
13C NMR (151 MHz, CDCl3)
1.00E+11
9.00E+10
8.00E+10
7.00E+10
6.00E+10
5.00E+10
4.00E+10
3.00E+10
2.00E+10
1.00E+10
0.00E+00
-1.00E+10
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

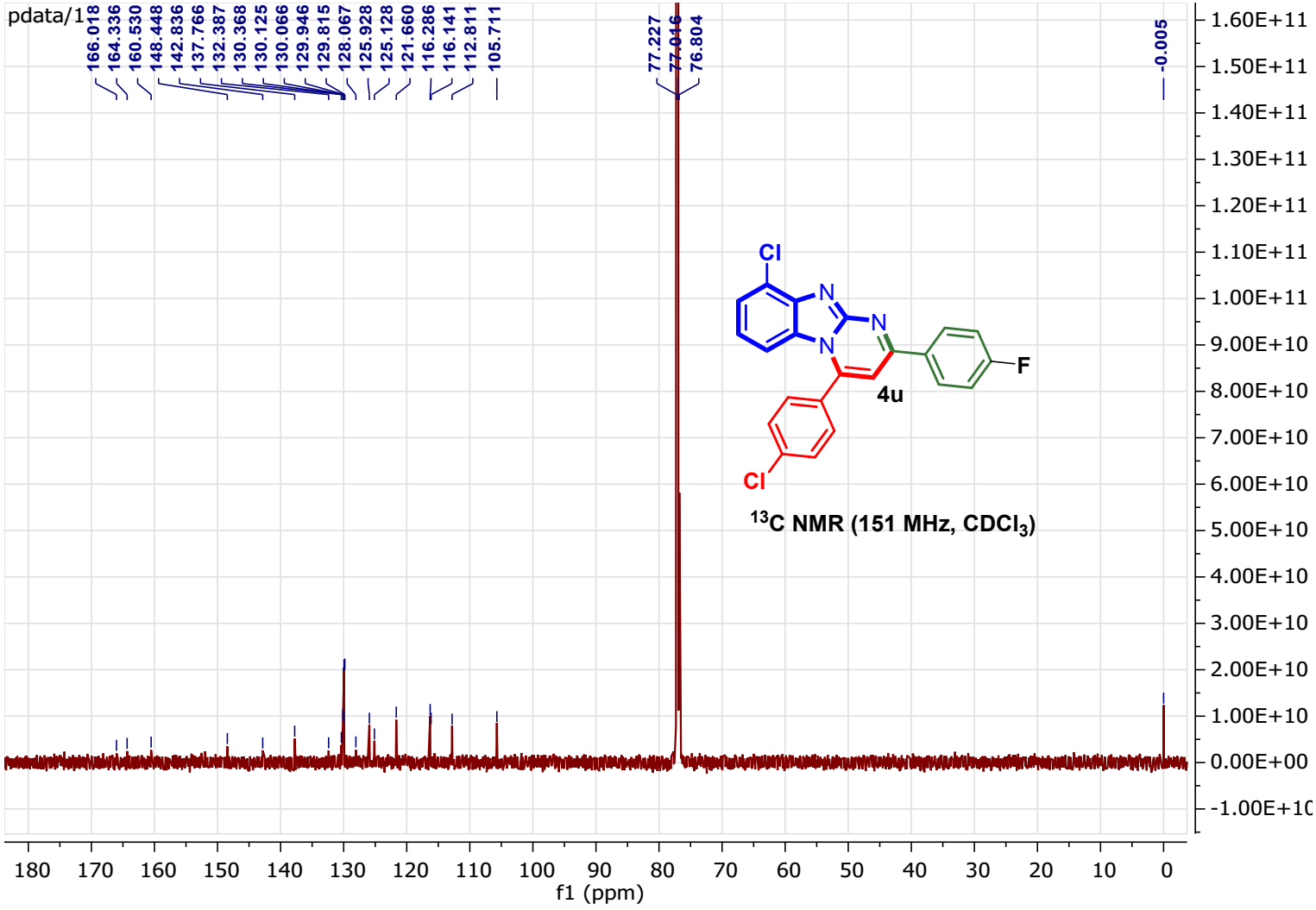

pdata/1
8.276
7.850
7.836
7.737
7.663
7.653
7.620
7.611
7.305
7.292
7.262
7.213
7.199
7.186
7.143
7.129
6.905
6.891
6.628
6.614
6.529
2.500
2.328
-0.000
R1
R2
N
N
N
F
NC
4s (R1= H, R2= Me)
4s' (R1= Me, R2= H)
1H NMR (600 MHz, CDCl3)
2.00
4.91
0.57
3.10
0.54
1.01
1.62
1.54
5.5E+11
5.0E+11
4.5E+11
4.0E+11
3.5E+11
3.0E+11
2.5E+11
2.0E+11
1.5E+11
1.0E+11
5.0E+10
0.0E+00
-5.0E+10
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

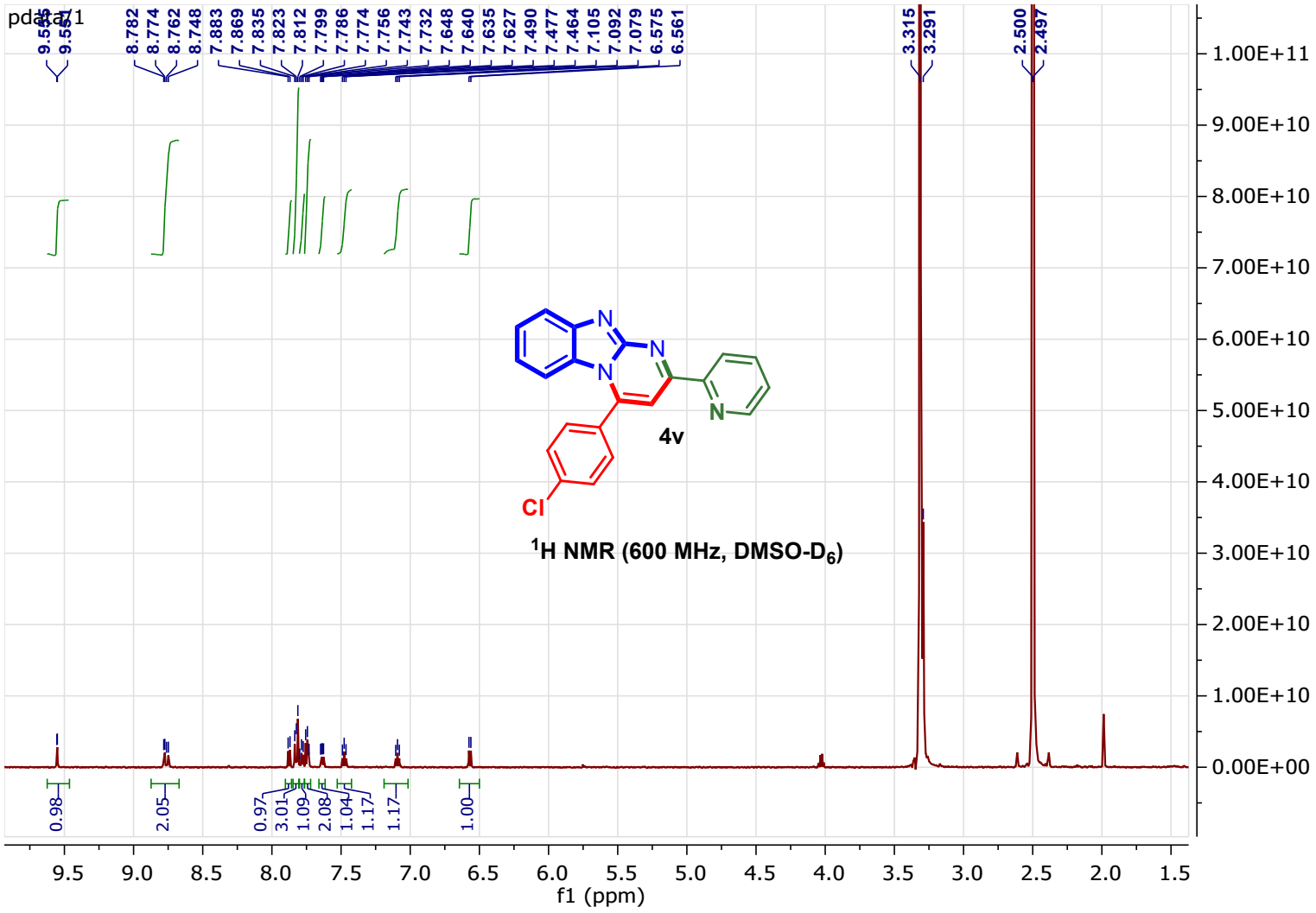

pdata/1
165.877
164.200
159.581
159.406
152.125
148.170
148.105
145.988
143.715
137.576
136.561
132.905
131.650
131.030
130.001
129.954
129.931
129.824
128.051
125.396
123.352
120.057
116.273
116.128
114.150
113.952
105.171
104.991
77.374
77.160
76.948
22.213
21.989
8.0E+10
7.0E+10
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
R1
R2
N
N
N
F
NC
4s (R1= H, R2= Me)
4s' (R1= Me, R2= H)
13C NMR (151 MHz, CDCl3)

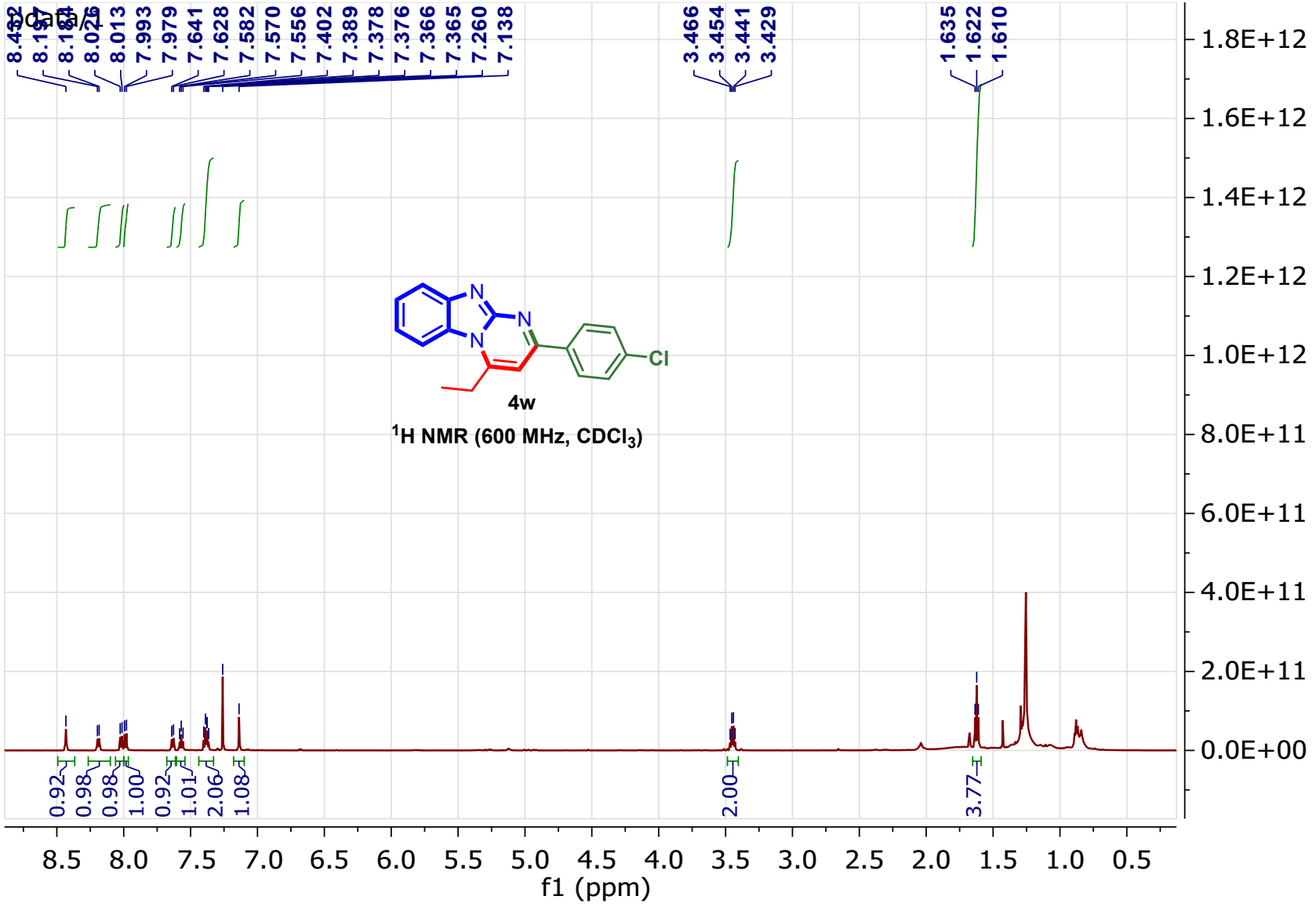

pdata 1
8.269
7.850
7.837
7.582
7.568
7.535
7.525
7.517
7.512
7.505
7.502
7.497
7.463
7.450
7.268
7.260
6.985
6.972
6.958
6.650
6.636
0.005
Cl
N
N
N
Br
4t
1H NMR (600 MHz, CDCl3)
1.98
1.91
1.95
2.92
0.98
1.00
1.00
0.97
1.6E+12
1.4E+12
1.2E+12
1.0E+12
8.0E+11
6.0E+11
4.0E+11
2.0E+11
0.0E+00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

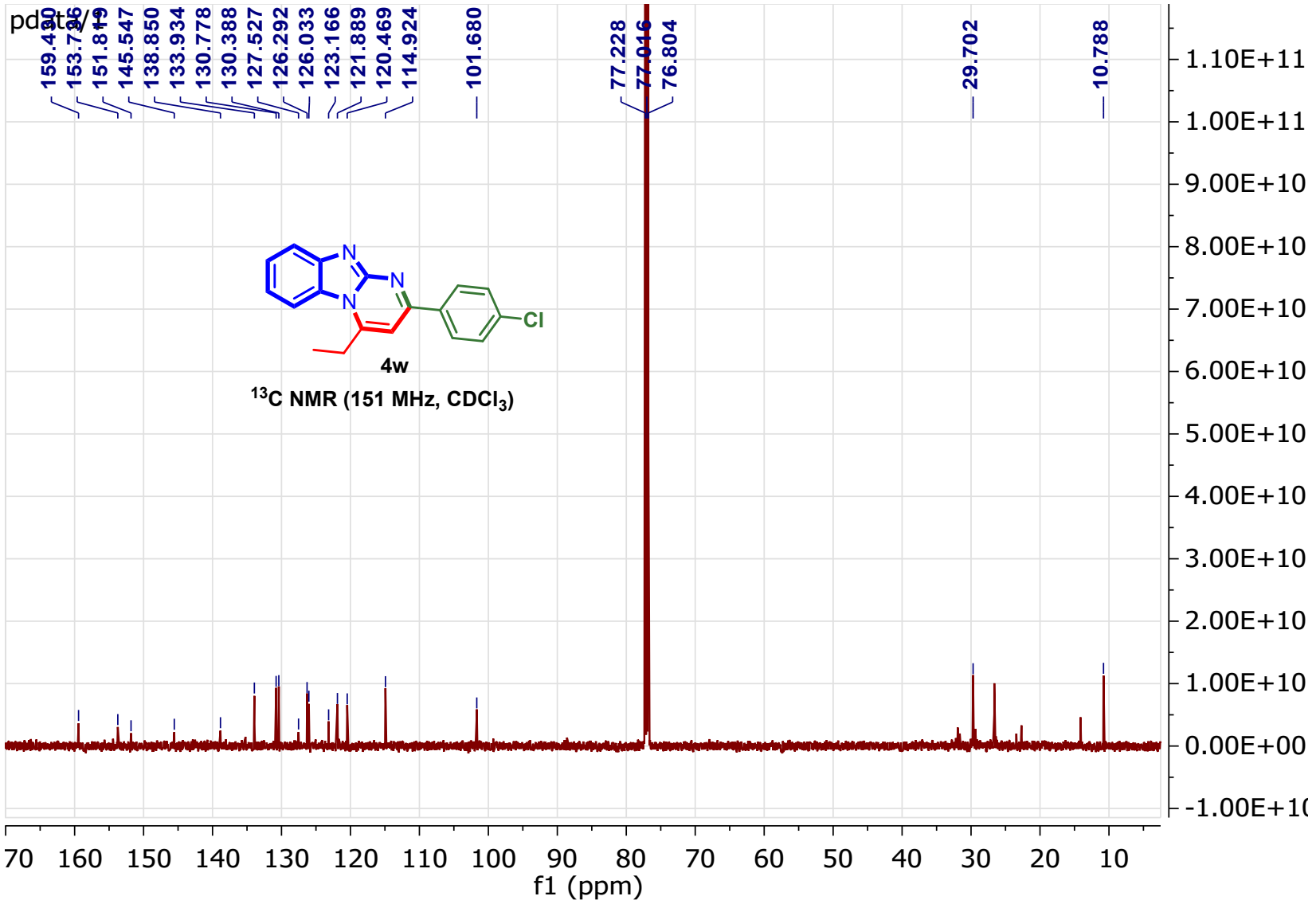

161.768
152.144
148.408
142.889
136.236
132.972
131.818
131.057
130.221
129.136
128.167
127.996
126.003
125.942
125.107
121.676
112.986
106.090
77.371
77.160
76.947
Cl
N
N
N
4t
Br
^{13}C NMR (151 MHz, CDCl$_3$)
9.0E+10
8.0E+10
7.0E+10
6.0E+10
5.0E+10
4.0E+10
3.0E+10
2.0E+10
1.0E+10
0.0E+00
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

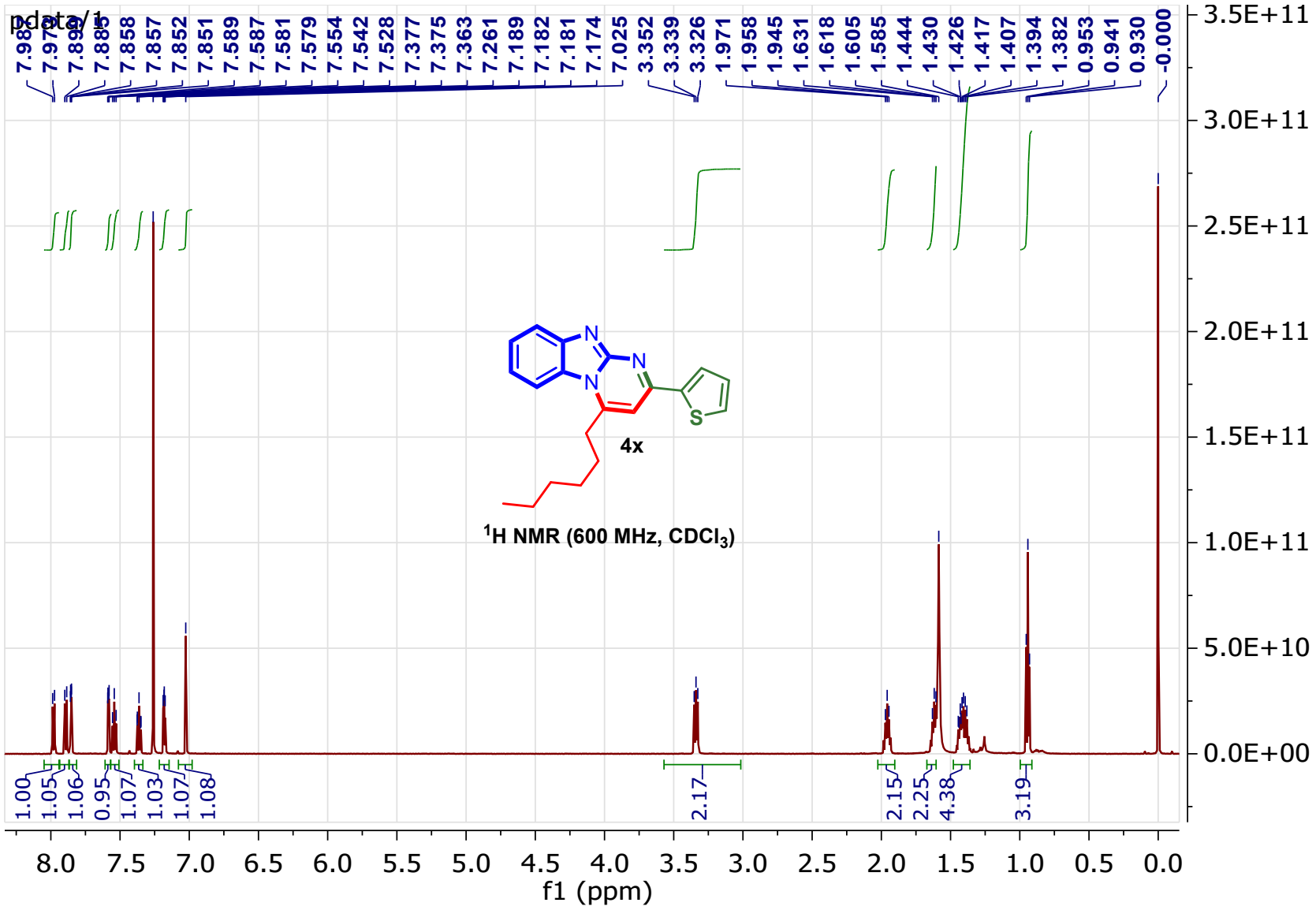

pdata/1
8.334
8.326
8.320
8.311
7.686
7.672
7.610
7.597
7.509
7.496
7.260
7.232
7.221
7.207
7.015
7.002
6.988
6.653
6.639
1.568
-0.001
Cl
N
N
N
F
4u
Cl
1H NMR (600 MHz, CDCl3)
2.00
1.94
2.03
1.16
2.99
1.06
1.04
6.0E+11
5.5E+11
5.0E+11
4.5E+11
4.0E+11
3.5E+11
3.0E+11
2.5E+11
2.0E+11
1.5E+11
1.0E+11
5.0E+10
0.0E+00
-5.0E+10
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


pdata/1
166.018
164.336
160.530
148.448
142.836
137.766
132.387
130.368
130.125
130.066
129.946
129.815
128.067
125.928
125.128
121.660
116.286
116.141
112.811
105.711
77.227
77.016
76.804
-0.005
Cl
N
N
N
F
4u
Cl
^{13}C NMR (151 MHz, CDCl$_3$)
1.60E+11
1.50E+11
1.40E+11
1.30E+11
1.20E+11
1.10E+11
1.00E+11
9.00E+10
8.00E+10
7.00E+10
6.00E+10
5.00E+10
4.00E+10
3.00E+10
2.00E+10
1.00E+10
0.00E+00
-1.00E+10
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


pdata/1
9.561
9.551
8.782
8.774
8.762
8.748
7.883
7.869
7.835
7.823
7.812
7.799
7.786
7.774
7.756
7.743
7.732
7.648
7.640
7.635
7.627
7.490
7.477
7.464
7.105
7.092
7.079
6.575
6.561
3.315
3.291
2.500
2.497
4v
Cl
N
N
N
N
^{1}H NMR (600 MHz, DMSO-D$_6$)
0.98
2.05
0.97
3.01
1.09
2.08
1.04
1.17
1.17
1.00
1.00E+11
9.00E+10
8.00E+10
7.00E+10
6.00E+10
5.00E+10
4.00E+10
3.00E+10
2.00E+10
1.00E+10
0.00E+00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)


acata
8.432
8.197
8.184
8.027
8.013
7.993
7.979
7.641
7.628
7.582
7.570
7.556
7.402
7.389
7.378
7.376
7.366
7.365
7.260
7.138
3.466
3.454
3.441
3.429
1.635
1.622
1.610
N
N
N
Cl
4w
1H NMR (600 MHz, CDCl3)
0.92
0.98
0.98
1.00
0.92
1.01
2.06
1.08
2.00
3.77
1.8E+12
1.6E+12
1.4E+12
1.2E+12
1.0E+12
8.0E+11
6.0E+11
4.0E+11
2.0E+11
0.0E+00
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
f1 (ppm)


pdata/1
159.430
153.736
151.819
145.547
138.850
133.934
130.778
130.388
127.527
126.292
126.033
123.166
121.889
120.469
114.924
101.680
77.228
77.016
76.804
29.702
10.788
N
N
N
Cl
4w
13C NMR (151 MHz, CDCl3)
1.10E+11
1.00E+11
9.00E+10
8.00E+10
7.00E+10
6.00E+10
5.00E+10
4.00E+10
3.00E+10
2.00E+10
1.00E+10
0.00E+00
-1.00E+10
70 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


pdata/1
7.987
7.976
7.899
7.885
7.858
7.857
7.852
7.851
7.589
7.587
7.581
7.579
7.554
7.542
7.528
7.377
7.375
7.363
7.261
7.189
7.182
7.181
7.174
7.025
3.352
3.339
3.326
1.971
1.958
1.945
1.631
1.618
1.605
1.585
1.444
1.430
1.426
1.417
1.407
1.394
1.382
0.953
0.941
0.930
-0.000
N
N
N
S
4x
^{1}H NMR (600 MHz, CDCl$_3$)
1.00
1.05
1.06
0.95
1.07
1.03
1.07
1.08
2.17
2.15
2.25
4.38
3.19
3.5E+11
3.0E+11
2.5E+11
2.0E+11
1.5E+11
1.0E+11
5.0E+10
0.0E+00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

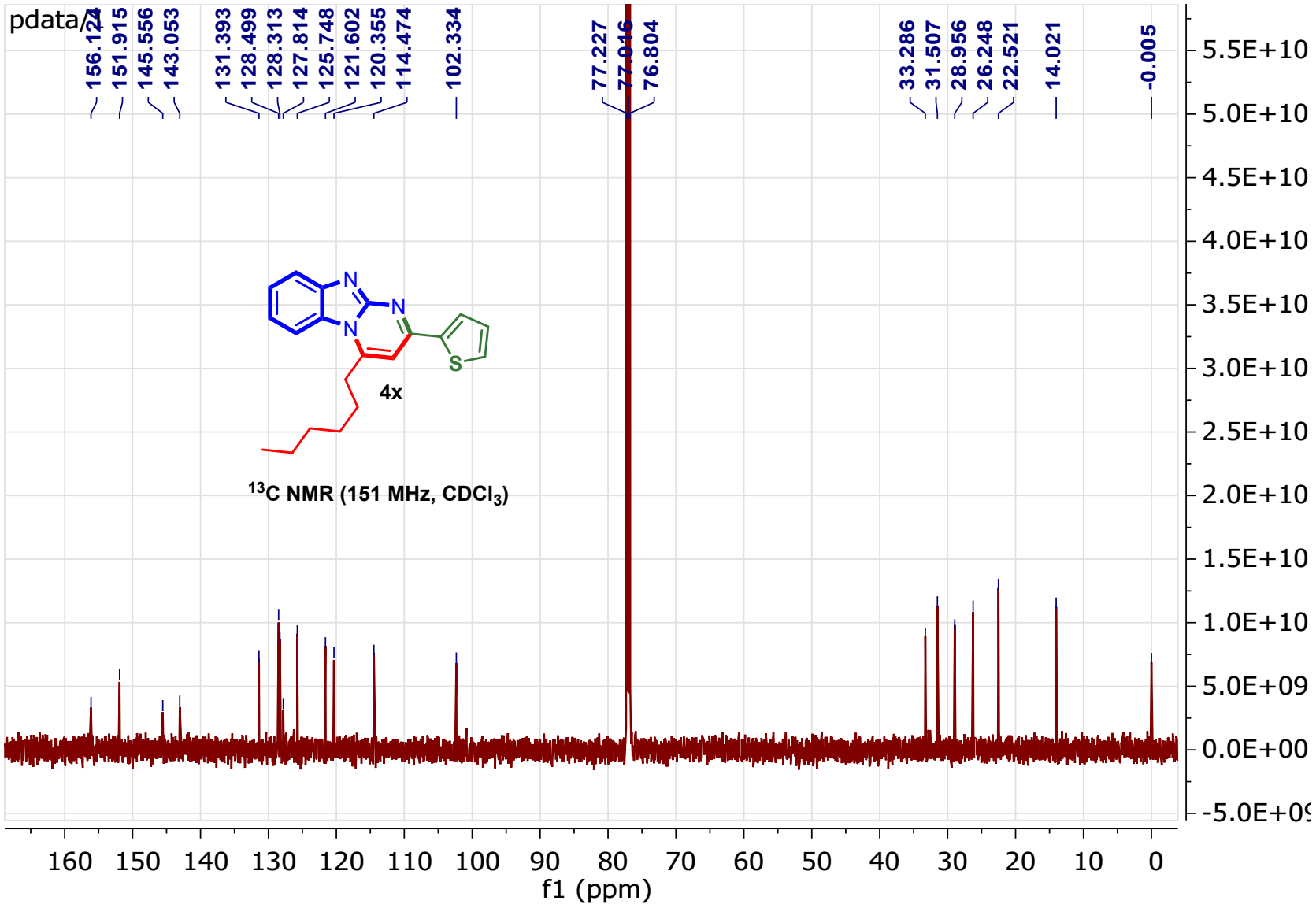
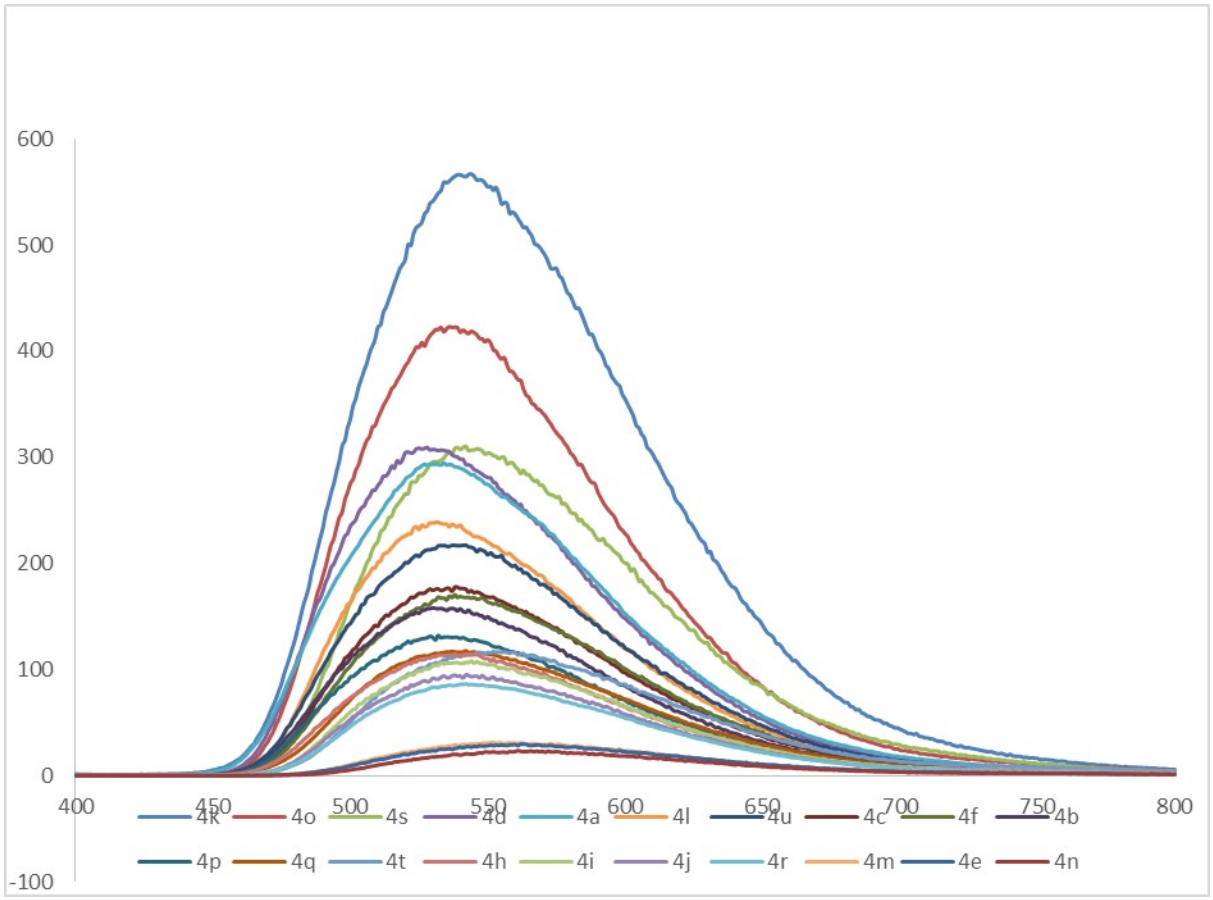
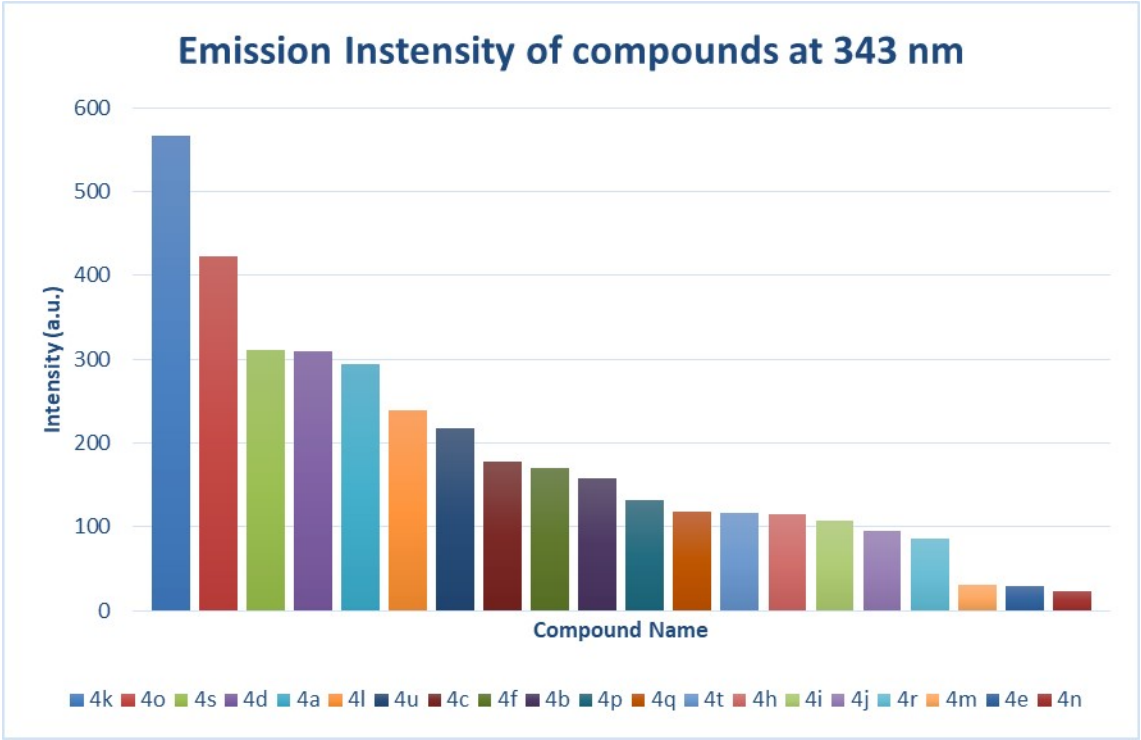

pdata/1
156.124
151.915
145.556
143.053
131.393
128.499
128.313
127.814
125.748
121.602
120.355
114.474
102.334
77.227
77.016
76.804
33.286
31.507
28.956
26.248
22.521
14.021
-0.005
N
N
N
S
4x
^{13}C NMR (151 MHz, CDCl$_3$)
5.5E+10
5.0E+10
4.5E+10
4.0E+10
3.5E+10
3.0E+10
2.5E+10
2.0E+10
1.5E+10
1.0E+10
5.0E+09
0.0E+00
-5.0E+09
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

Figure 1: a) Fluroscence emission Overlay spectra of 2,4-diaryl pyrimido[1,2-a]benzimidazoles at excitation wavelength of 343 nm; b) Comparison of fluorescene intensity of 2,4-diaryl pyrimido[1,2-a]benzimidazoles at excitation wavelength of 343 nm



(a)



(b

Instrumentation Parameter

Scan Software Version: 1.2(147)	
Instrument	Cary Eclipse
Instrument Serial Number	MY2144CG01
Data mode	Fluorescence
Scan mode	Emission
X Mode	Wavelength (nm)

Start (nm)	400.00
Stop (nm)	800.00
Ex. Wavelength (nm)	343.00
Ex. Slit (nm)	10
Em. Slit (nm)	20
Scan rate (nm/min)	600.00
Data interval (nm)	1.0000
Averaging Time (s)	0.1000
Excitation filter	Auto
Emission filter	Open
PMT voltage (V)	Medium

Details of Fluorescence Study:

- The emission spectra compounds **4a-v** was recorded at room temperature using chloroform as solvent.
- Concentration 500 µg/ml was used to record the fluorescence spectrum.
- Fluorescence spectrum was recorded in the 10 mm fluorescence cuvette.
- At first, UV-vis absorbance spectrum of the sample was recorded to get the excitation wavelength.
- Excitation wavelength of 343 nm, with an excitation slit width of 10 nm and an emission slit width of 20 nm was employed.
- Emission spectrum by scanning over 400-800 nm wavelength range was recorded to capture the fluorescence emission.
- Baseline spectrum to correct for any background fluorescence or scattering from the solvent was recorded.
- Integrated fluorescence intensity (that is, the area of the fluorescence spectrum) from the fully corrected fluorescence spectrum was calculated.

Precautions taken for high temperature reaction in DMSO:

- Kept away from open flames and sources of ignition.
- DMF is incompatible with a variety of chemicals like strong acid/base, oxidant, and halogenated compounds. Hence, we kept the reaction away from above reagents.
- Avoided contact with skin, eyes or clothing.
- The reaction was monitored in fume-hood.
- The reaction wasn't kept the experiment overnight.
- Used precise temperature control equipment to avoid overheating, which can lead to decomposition of DMSO and fire or explosion.

Additionally, we analyzed the reaction mixture using DSC for calorimetric insights, confirming the safety of using DMSO under basic and thermal conditions.

Differential Scanning Calorimetry (DSC)

DSC measurements were taken out using a Discovery DSC 2500 from TA Instruments with Trios software. DSC 2500 consists of a finer air-cooling system, auto sampler, and discover liquid nitrogen pump. All data were collected in pierced flat-bottomed aluminum pans of 40 µL. Heating rate was 10 °C min^{-1} in the range from 25 to 130 °C. Sample amount: **1a** (0.01 mmol, 1.20 mg), **2a** (0.01 mmol, 1.06 mg), **3a** (0.01 mmol, 1.33 mg), NaOH (0.01 mmol, 0.04 mg) and DMSO 25 µl.