Supporting information

Functionalised dihydroazo pyrimidine derivatives from Morita-Baylis-Hillman Acetates: Synthesis and studies against Acetylcholinesterase inhibitors.

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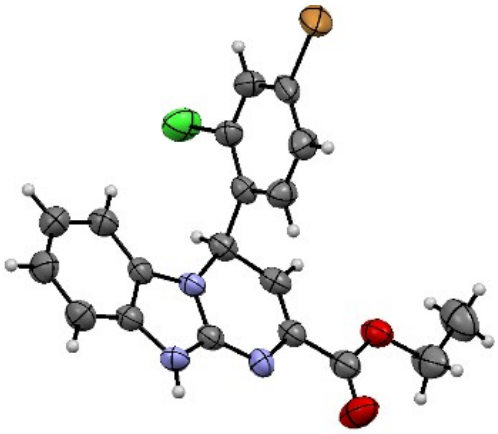
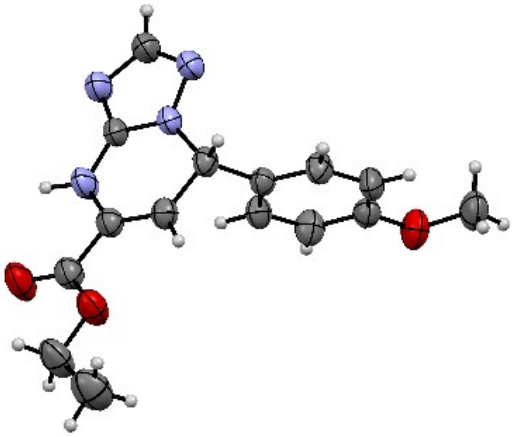
X-ray Crystallographic data



Compound 3e

CCDC Number: 1446736



Compound 4b

CCDC Number: 1456725

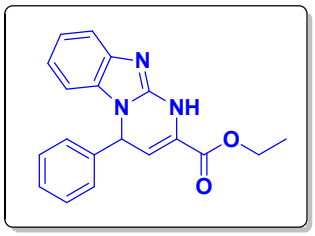
General information

Morita-Baylis-Hillman Acetates of nitroalkenes **1** were synthesized according to literature.[11] All experiments were performed under nitrogen atmosphere. All solvents and reagents are procured from commercially available sources like Aldrich, Alfa-aser, spectrochem. Commercially available pre packed silica gel (230-400 mesh) plugs, hexane and ethyl acetate solvents were used for column chromatographic purification. Isolated yields correspond to products of greater $>$ 90% purity as determined by LC-MS and NMR. All NMR (^{1}H, ^{13}C) chemical shifts are reported in parts per million (ppm), all coupling constants are reported in Hertz (Hz) and tetramethylsilane used as internal standard for ^{1}H NMR. Liquid chromatography- mass spectrometry (LC-MS) was used for reaction monitoring and identification for product mass.

Experimental procedure for synthesis of compound (3a-3l):

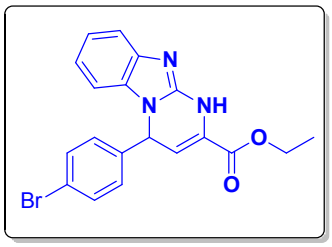
To a solution of 2-aminobenzimidazole (0.15 mmol) in acetonitrile (1.0 mL) was mixed with MBH Acetate of nitro alkene (0.18 mmol) followed by the addition of cesium carbonate (0.3 mmol) and the reaction mixture was stirred for 12h at RT. After completion of reaction (monitored by LCMS), the reaction mixture was quenched with water (5 mL). The reaction mixture was extracted with ethyl acetate (3x 10 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated. To this crude product was added methanol (4 mL) and stirred for 30 min at RT. A white precipitate was obtained which was filtered gave the product (60% - 82%). The mother liquid contains a small amount of product by LCMS.

Ethyl 4-phenyl-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3a):



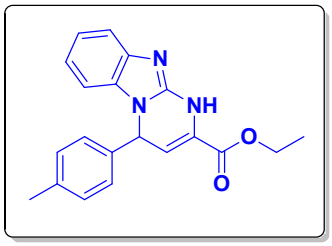
White solid; yield 46 mg, 82%; MP: 145-147 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 7.55 (dd, *J* = 7.9, 3.0 Hz, 1H), 7.39 - 7.28 (m, 5H), 7.17-7.13(m, 1H), 6.97-6.93(m, 1H), 6.79-6.77 (m, 1H), 6.19 (d, *J* = 4.0 Hz, 1H), 5.99 (d, *J* = 4.0 Hz, 1H), 4.38-4.30 (dq, J= 7.2 Hz, 4.8Hz, 2.0Hz, 2H), 1.35 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ 162.39, 144.42, 143.65, 137.79, 133.55, 129.53, 129.07, 128.19, 126.39, 122.96, 122.39, 122.19, 118.64, 109.97, 62.75, 59.28, 14.10. **LCMS:** *m/z* calculated for $C_{19}H_{17}N_3O_2$: 319.13; Observed mass: 320.2 (M+1); Anal. Calculated for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.44; H, 5.35; N, 13.18.

Ethyl-4-(4-bromophenyl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3b):



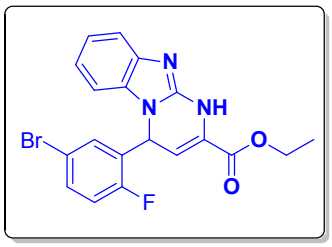
Pale brown solid; yield 57 mg, 80%; MP: 151-153 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 7.57 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 1.8 Hz, 1H), 7.50 (d, *J* = 1.9 Hz, 1H), 7.21 – 7.14 (m, 3H), 6.99-6.95 (m, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.17 (d, *J* = 4.0 Hz, 1H). 5.92 (d, *J* = 4.0 Hz, 1H), 4.35 (qq, *J* = 7.3, 3.7 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ 161.71, 146.59, 142.04, 138.62, 132.44, 132.04, 131.51, 128.11, 126.17, 122.70, 122.52, 120.67, 117.21, 109.41, 105.84, 62.36, 57.40, 14.07. **LCMS:** *m/z* calculated for $C_{19}H_{16}BrN_3O_2$: 397.04; Observed mass: 398.2, 400.2 (M+1, M+3); Anal. Calculated for $C_{19}H_{16}BrN_3O_2$: C, 57.30; H, 4.05; N, 10.55;. Found: C, 57.31; H, 4.07; N, 10.54.

Ethyl-4-(p-tolyl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3c):



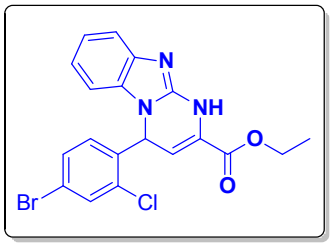
White solid; yield 46 mg, 77%; MP: 143-145 ^{o}C; **^{1}H NMR** (400 MHz, DMSO-*d6*) δ (ppm) 7.93 (d, *J* = 6.56 Hz, 2H), 7.84–7.81 (m, 2H), 7.61-7.56 (m, 2H), 7.34-7.29 (m, 2H), 6.57 (d, *J* = 4.0 Hz, 1H), 6.16 (d, *J* = 4.0 Hz, 1H), 4.17 (q, *J* = 6.8 Hz, 2H), 2.11 (s, 3H), 1.23 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** δ (ppm) 161.94, 148.24, 144.41, 143.67, 133.13, 127.23, 126.11, 124.90, 123.99, 123.49, 122.88, 119.06, 63.05, 58.43, 23.08, 14.08. **LCMS:** *m/z* calculated for $C_{20}H_{19}N_3O_2$: 333.15; Observed mass: 334.2 (M+1). Anal. Calculated for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60; Found: C, 72.07; H, 5.75; N, 12.64

Ethyl-4-(5-bromo-2-fluorophenyl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3d):



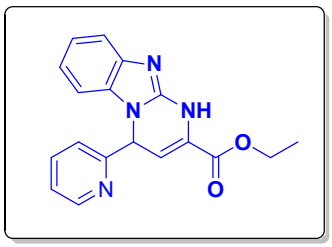
Yellow solid; yield 46 mg, 68%; MP: 150-152 ^{o}C; **^{1}H NMR** (300 MHz, DMSO-*d6*): δ 10.15 (bs, 1H), 7.79 (s, 1H), 7.54 (dd, J – 8.2, 2.2 Hz, 1H), 7.37 (d, J = 7.7 Hz, 1H), 7.08-7.03 (m, 2H), 6.90 (t, J = 7.6 Hz, 1H), 6.73-6.70 (m, 2H), 5.83 (d, *J* = 3.9 Hz, 1H), 4.25 (q, *J* = 7.0 Hz, 2H), 1.28 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO) δ 166.89, 161.63, 153.30, 150.78, 142.39, 131.47, 131.41, 130.59, 127.97, 125.85, 125.56, 123.80, 123.76, 121.28, 121.24, 118.20, 106.17, 62.18, 59.24, 14.31. **LCMS:** *m/z* calculated for $C_{19}H_{15}BrFN_3O_2$: 415.03; Observed mass: 416.2, 418.2 (M+1, M+3); Anal. Calculated for $C_{19}H_{15}BrFN_3O_2$: C, 54.82; H, 3.63; N, 10.10; Found: C, 54.83; H, 3.65; N, 10.12.

Ethyl-4-(4-bromo-2-chlorophenyl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3e):



White solid; yield 54 mg, 70%; MP: 153-155 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 7.65 (d, *J* = 1.6 Hz, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.31 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.20 (t, 7.2 Hz, 1H), 7.02 (t, *J* = 8.0 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 4.0 Hz, 1H), 6.01 (d, *J* = 4.0 Hz, 1H), 4.36 (qq, *J* = 7.2 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ 161.47, 135.37, 132.69, 131.32, 129.56, 126.72, 122.93, 122.81, 121.13, 117.19, 109.15, 103.84, 62.52, 50.80, 14.07. **LCMS:** *m/z* calculated for $C_{19}H_{15}BrClN_3O_2$: 431.00; Observed mass: 431.2, 433.2 (M+1, M+3); Anal. Calculated for $C_{19}H_{15}BrClN_3O_2$: C, 52.74; H, 3.49; N, 9.71; Found: C, 52.76; H, 3.50; N, 9.73.

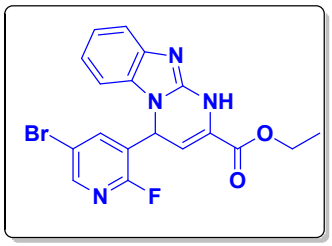
Ethyl-4-(pyridin-2-yl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3f):



White solid; yield 40 mg, 70%; MP: 155-156 °C; **^{1}H NMR** (300 MHz, DMSO-*d6*): δ 7.73-7.61 (m, 4H), 7.48 (d, *J* = 7.8 Hz, 1H), 7.10-7.06 (m, 2H), 6.85-6.81 (m, 1H), 6.46 (d, *J* = 3.9 Hz, 1H), 5.86 (d, *J* = 3.9 Hz, 1H), 4.25 (qq, *J* = 7.2, 3.6 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 166.88, 161.51, 153.29, 150.95, 150.65, 140.81, 139.03, 136.16, 131.40, 128.88, 125.86, 124.63, 121.25, 121.30 118.20, 103.72, 62.26, 59.34, 14.33. **LCMS:** *m/z* calculated for $C_{18}H_{16}N_4O_2$: 320.13; Observed mass:

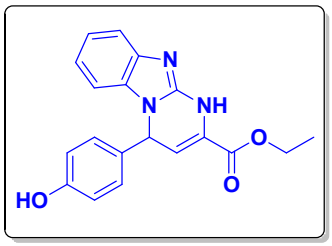
321.2 (M+1). Anal. Calculated for $C_{18}H_{16}N_4O_2$: C, 67.49; H, 5.03; N, 17.49; Found: C, 67.51; H, 5.03; N, 17.48.

Ethyl-4-(5-bromo-2-fluoropyridin-3-yl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3g):



Brown solid; yield 50 mg, 67%; MP: 162-164 ^oC; **^{1}H NMR** (300 MHz, Chloroform-*d*): 8.35 (s, 1H), 7.81 (s, 1H), 7.62-7.55 (m, 2H), 7.35-7.25 (m, 2H), 6.67 (d, J= 3.9 Hz, 1H), 6.02 (d, J= 3.9 Hz, 1H), 4.36 (q, J= 7.2 Hz, 2H), 1.36 (t, J= 7.2 Hz, 3H).). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ 162.32, 143.99, 143.68, 140.10, 133.40, 127.46, 127.22, 126.80, 126.16, 123.40, 123.10, 122.48, 118.79, 109.70, 62.82, 53.92, 14.11. **LCMS**: *m/z* calculated for $C_{18}H_{14}BrFN_4O_2$: 416.03; Observed mass: 417.2, 419.2 (M+1, M+3); Anal. Calculated for $C_{18}H_{14}BrFN_4O_2$: C, 51.82; H, 3.38; N, 13.43; Found: C, 51.83; H, 3.40; N, 13.46.

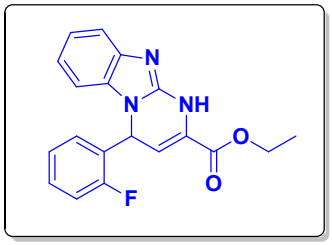
Ethyl-4-(3-hydroxyphenyl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3h):



Colour less gummy nature; yield 44 mg, 73%; MP: 134-137 ^oC; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 7.88 – 7.86 (m, 1H), 7.78 (dd, J = 8.8, 2.4 Hz, 2H), 7.69-7.66 (m, 2H), 7.18 (dd, J = 8.8, 2.4 Hz, 1H), 7.15 (d, J = 2.4 Hz, 1H), 6.73 (d, J = 4.0 Hz, 1H), 6.39 (d, J = 4.0 Hz, 1H), 5.88 (bs, 1H), 4.18 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.48, 151.75, 150.36, 139.70, 133.37, 131.35, 131.05, 129.22, 127.78, 126.54, 126.03, 122.34, 120.94, 119.11, 104.86, 62.52, 59.58, 14.12. **LCMS**:

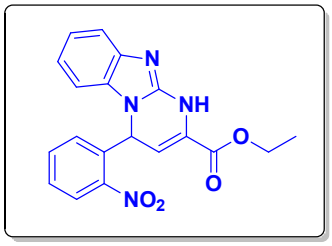
m/z calculated for $C_{19}H_{17}N_3O_3$: 335.13; Observed mass: 336.2 (M+1); Anal. Calculated for $C_{19}H_{17}N_3O_3$: C, 68.05; H, 5.11; N, 12.53; Found: C, 68.07; H, 5.13; N, 12.55.

Ethyl-4-(2-fluorophenyl)-4,10-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3i):



Pale yellow solid; yield 36 mg, 60%; MP: 141-143 ^oC; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 8.74 (dd, *J* = 7.2, 2.4 Hz, 1H), 8.27 (s, 1H), 7.90 (m, 1H), 7.82 - 7.79 (m, 2H), 7.56 – 7.49 (m, 1H), 7.48 – 7.43 (m, 2H), 7.38 (d, *J* = 4.0 Hz, 1H), 6.55 (d, *J* = 4.0 Hz, 1H), 4.54 (q, *J* = 7.2 Hz, 2H), 1.48 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 162.47, 160.06, 144.40, 143.60, 133.54, 129.81, 128.50, 127.76, 122.92, 122.33, 121.74, 118.58, 114.83, 110.04, 62.72, 58.73, 14.11. **LCMS:** *m/z* calculated for $C_{19}H_{16}FN_3O_2$: 337.12; Observed mass: 338.2 (M+1); Anal. Calculated for $C_{19}H_{16}FN_3O_2$: C, 67.65; H, 4.78; N, 12.46; Found: C, 67.65; H, 4.76; N, 12.45.

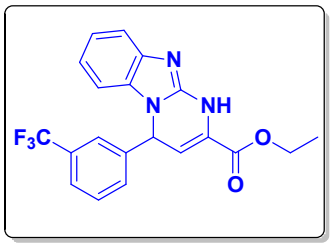
Ethyl-4-(2-nitrophenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3j):



white solid; yield 33 mg, 51%; MP: 150-153 ^oC; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 8.13 (dd, *J* = 7.2 Hz, 2.0 Hz, 1H), 7.57-7.48 (m, 3H), 7.18 (dt, *J* = 7.2 Hz, 1H), 7.03 (dd, *J* = 7.2 Hz, 2.0 Hz, 1H), 6.99-6.97 (m, 1H), 6.95 (d, *J* = 4.0 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.27 (d, *J* = 4.0 Hz, 1H), 4.38 (dq, *J* = 7.2Hz, 2H), 1.37 (t, *J* = 7.2 Hz,

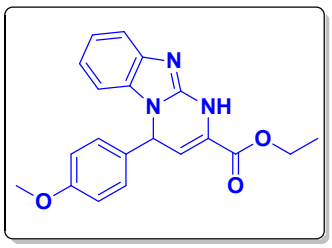
3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.78, 156.28, 148.83, 140.06, 134.69, 129.78, 129.16, 127.69, 127.24, 124.47, 121.53, 119.41, 114.12, 111.95, 61.94, 58.09, 14.24. **LCMS:** *m/z* calculated for $C_{19}H_{16}N_4O_4$: 364.12; Observed mass: 365.2 (M+1); Anal. Calculated for $C_{19}H_{16}N_4O_4$: C, 62.63; H, 4.43; N, 15.38; Found: C, 62.65; H, 4.44; N, 15.40.

Ethyl-4-(3-(trifluoromethyl)phenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3k):



white powder; yield 50 mg, 72%; MP: 140-142 °C; **^{1}H NMR** (300 MHz, Chloroform-*d*): δ 7.61-7.50 (m, 4H), 7.32 (m, 2H), 7.14 (m, 2H), 6.29 (d, *J* = 3.9 Hz, 1H), 5.90 (d, *J* = 3.9 Hz, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 166.04, 161.61, 151.97, 150.24, 148.71, 138.70, 132.69, 132.22, 131.51, 128.85, 128.47, 127.53, 125.99, 123.03, 122.31, 120.90, 119.22, 105.49, 62.37, 60.03, 14.13. **LCMS:** *m/z* calculated for $C_{20}H_{16}F_3N_3O_2$: 387.12; Observed mass: 388.2 (M+1); Anal. Calculated for $C_{20}H_{16}F_3N_3O_2$: C, 62.01; H, 4.16; N, 10.85; Found: C, 62.03; H, 4.17; N, 10.87.

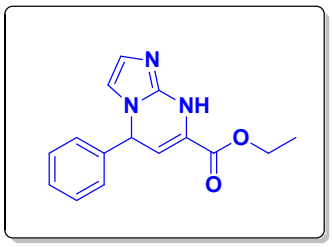
Ethyl-4-(4-methoxyphenyl)-1,4-dihydrobenzo[4,5]imidazo[1,2-a]pyrimidine-2-carboxylate (3l):



White solid; yield 47 mg, 75%; MP: 146-147 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 9.68 (bs, 1H), 7.61-7.56 (m, 2H), 7.35-7.31 (m, 1H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.16-7.12 (m, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.17 (d, *J* = 4.0 Hz, 1H), 5.93 (d, *J* = 4.0 Hz, 1H), 4.41-4.29 (m, 2H), 3.80 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 161.82, 160.01, 150.06, 148.62, 132.03, 131.57, 128.54, 127.18, 125.97, 122.29,

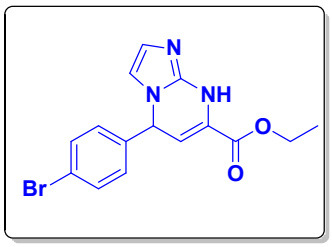
120.88, 119.27, 114.40, 106.45, 62.19, 60.05, 55.33, 14.14. **LCMS:** *m/z* calculated for $C_{20}H_{19}N_3O_3$: 349.14; Observed mass: 350.2 (M+1); Anal. Calculated for $C_{20}H_{19}N_3O_3$: C, 68.75; H, 5.48; N, 12.03; Found: C, 68.77; H, 5.49; N, 12.05.

Ethyl-5-phenyl-5,8-dihydroimidazo[1,2-a]pyrimidine-7-carboxylate (3m):



Colourless solid; yield 30 mg, 62%; MP: 162-164 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 7.43-7.25 (m, 5H), 7.15 (dd, *J* = 3.9 Hz, 8.4 Hz, 1H), 6.53 (d, *J* = 3.6 Hz, 1H), 6.21 (dd, *J* = 3.9 Hz, 8.4 Hz, 1H), 5.92 (dd, *J* = 3.9 Hz, 8.4 Hz, 1H), 4.36 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 161.78, 148.83, 140.06, 134.69, 129.78, 129.16, 127.69, 127.24, 124.47, 121.53, 119.41, 111.95, 61.94, 58.09, 14.24. **LCMS:** *m/z* calculated for $C_{15}H_{15}N_3O_2$: 269.12; Observed mass: 270.2 (M+1); Anal. Calculated for $C_{15}H_{15}N_3O_2$: C, 66.90; H, 5.61; N, 15.60; Found: C, 66.92; H, 5.60; N, 15.62.

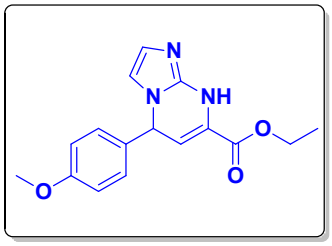
Ethyl-5-(4-bromophenyl)-5,8-dihydroimidazo[1,2-a]pyrimidine-7-carboxylate (3n):



Pale brown solid; yield 41 mg, 66%; MP: 169-172 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 10.25 (bs, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.38 (d, *J* = 1.6 Hz, 2H), 7.16-7.11 (m, 1H), 6.54 (d, *J* = 3.6 Hz, 1H), 6.16 (d, *J* = 4.0 Hz, 1H), 5.85 (d, *J* = 4.0 Hz, 1H), 4.36 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz,

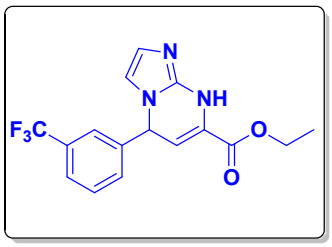
DMSO) δ 161.67, 150.63, 149.25, 140.47, 132.20, 129.49, 127.73, 121.94, 114.08, 106.46, 62.15, 59.11, 14.34. **LCMS**: *m/z* calculated for $C_{15}H_{14}BrN_3O_2$: 347.03; Observed mass: 348.2, 350.2 (M+1, M+3); Anal. Calculated for $C_{15}H_{14}BrN_3O_2$: C, 51.74; H, 4.05; N, 12.07; Found: C, 51.76; H, 4.07; N, 12.08.

Ethyl-5-(4-methoxyphenyl)-5,8-dihydroimidazo[1,2-a]pyrimidine-7-carboxylate (3o):



White solid; yield 31 mg, 59%; MP: 162-164 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 9.59 (bs, 1H), 7.27-7.24 (m, 2H), 7.12 (d, *J* = 3.2 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.53 (d, *J* = 3.6 Hz, 1H), 6.15 (d, *J* = 3.6 Hz, 1H), 5.29 (d, *J* = 3.6 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.80 (s, 3H), 1.35 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR:** (75 MHz, Chloroform-*d*) δ 161.58, 150.20, 148.70, 138.71, 132.33, 128.84, 128.57, 127.57, 123.01, 105.39, 62.12, 61.58, 54.35, 14.16. **LCMS**: *m/z* calculated for $C_{16}H_{17}N_3O_3$: 299.13; Observed mass: 300.2 (M+1); Anal. Calculated for $C_{16}H_{17}N_3O_3$: C, 64.20; H, 5.72; N, 14.04; Found: C, 64.22; H, 5.74; N, 14.06.

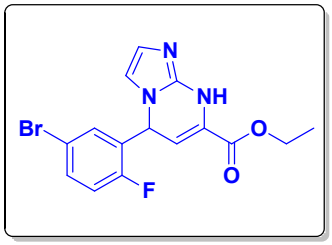
Ethyl-5-(3-(trifluoromethyl)-phenyl)-5,8-dihydroimidazo[1,2-a]pyrimidine-7-carboxylate (3p):



yield 40 mg, 66%; MP: 155-157 °C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ 7.72-7.61 (m, 2H), 7.57-7.46 (m, 2H), 7.04 (d, *J* = 4.0 Hz, 1H), 6,51 (d, *J* = 4.0 Hz, 1H), 6.27 (d, *J* = 3.8 Hz, 1H), 5.90 (d, *J* = 4.0 Hz, 1H), 4.38 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 161.62, 150.80, 149.35, 142.41,

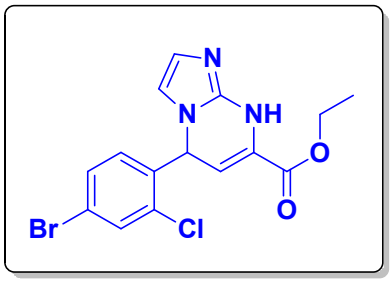
131.49, 130.63, 129.69, 127.91, 125.62, 123.79, 113.91, 106.18, 62.19, 59.20, 14.33. **LCMS:** *m/z* calculated for $C_{16}H_{14}F_3N_3O_2$: 337.10; Observed mass: 338.2 (M+1); Anal. Calculated for $C_{16}H_{14}F_3N_3O_2$: C, 56.97; H, 4.18; N, 12.46; Found: C, 56.96; H, 4.19; N, 12.48.

Ethyl-5-(5-bromo-2-fluorophenyl)-5,8-dihydroimidazo[1,2-a]pyrimidine-7-carboxylate (3q):



Pale brown solid; yield 30 mg, 45%; MP: 170-172 °C; **^{1}H NMR** (300 MHz, Chloroform-*d*): δ 10.02 (bs, 1H), 7.52 (dd, *J* = 7.0 Hz, 1.8 Hz, 1H), 7.27-7.16 (m, 2H), 7.10 (d, *J* = 3.6 Hz, 1H), 6.53 (d, *J* = 3.6 Hz, 1H), 6.16 (d, *J* = 3.9 Hz, 1H), 5.87 (d, *J* = 3.9 Hz, 1H), 4.35 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.35 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 161.59, 150.80, 149.25, 141.91, 131.86, 131.60, 131.45, 129.36, 128.01, 127.67, 113.64, 105.78, 62.20, 58.61, 14.34. **LCMS:** *m/z* calculated for $C_{15}H_{13}BrFN_3O_2$: 365.02; Observed mass: 366.2, 368.2 (M+1, M+3); Anal. Calculated for $C_{15}H_{13}BrFN_3O_2$: C, 49.20; H, 3.58; N, 11.48; Found: C, 49.22; H, 3.59; N, 11.50.

Ethyl 5-(4-bromo-2-chlorophenyl)-5,8-dihydroimidazo[1,2-a]pyrimidine-7-carboxylate (3r):



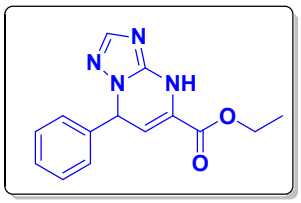
White solid; Yield 34 mg, 54%; MP: 171-173 °C; ^{1}H NMR (500 MHz, DMSO) δ 10.22 (s, 1H), 7.69 (s, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 2.0

Hz, 1H), 7.18 – 7.16 (m, 1H), 6.81 (s, 1H), 6.35 (d, *J* = 3.9 Hz, 1H), 5.83 (d, *J* = 3.9 Hz, 1H), 4.25 – 4.20 (m, 2H), 1.31 – 1.24 (m, 3H); ^{13}C NMR (126 MHz, DMSO) δ 161.59, 150.80, 149.25, 141.91, 131.86, 131.60, 131.45, 129.36, 128.01, 127.67, 113.64, 105.78, 62.20, 58.61, 14.34; **LCMS:** *m/z* calculated for $C_{15}H_{13}BrClN_3O_2$: 381.00; Observed mass: 382.2, 384.2 (M+1, M+3); Anal. Calculated for $C_{15}H_{13}BrClN_3O_2$: C, 47.08; H, 3.42; N, 10.98; Found: C, 47.09; H, 3.44; N, 11.00.

Experimental procedure for synthesis of compound (4a-4h):

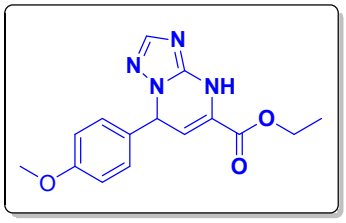
To a solution of 3-amino 1, 2, 4-triazole (0.30 mmol) in DMF (2.0 mL) was mixed with MBH Acetate of nitro alkene (0.36 mmol) and cesium carbonate (0.6 mmol) and the reaction mixture was heated to 60^{o}C for 4h. After completion of reaction (monitored by LCMS), the reaction mixture was quenched with water (30 mL). The reaction mixture was extracted with ethyl acetate (3x 30 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated over vacuum to give the crude product. To this crude product was added methanol (4 mL) and stirred for 30 min at RT. A white precipitate was obtained which was filtered gave the product (55% - 70%). The mother liquid contains a small amount of product along with small amount of other region isomer by LCMS.

Ethyl-7-phenyl-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate-(4a):



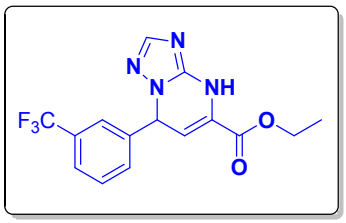
White solid; yield 60 mg, 60%; MP: 182-184 ^{o}C; **^{1}H NMR** (400 MHz, Chloroform-*d*): δ (ppm) 10.23 (bs, 1H), 7.78 (s, 1H), 7.42-7.28 (m, 5H), 6.22 (d, *J* = 4.0 Hz, 1H), 5.94 (d, *J* = 4.0 Hz, 1.6 Hz, 1H), 4.38 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ (ppm) 161.82, 150.06, 148.99, 139.91, 129.02, 128.79, 127.42, 127.12, 106.10, 62.13, 60.63, 14.17; **LCMS:** *m/z* calculated for $C_{14}H_{14}N_4O_2$: 270.11; Observed mass: 271.2 (M+1); Anal. Calculated for $C_{14}H_{14}N_4O_2$: C, 62.21; H, 5.22; N, 20.73; Found: C, 62.22; H, 5.24; N, 20.75.

Ethyl-7-(4-methoxyphenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4b):



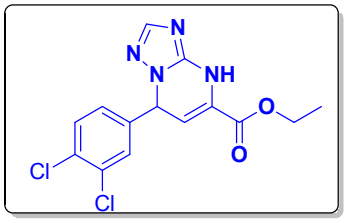
White solid; yield 70 mg, 65%; MP: 180-182 ^{o}C; **^{1}H NMR** (300 MHz, Chloroform-*d*): δ 9.86 (bs, 1H), 7.74 (s, 1H), 7.24 (dd, *J* = 9.0 Hz, 2.7 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 6.16 (d, *J* = 3.9 Hz, 1H), 5.93 (d, *J* = 3.9 Hz, 1H), 4.36 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 3.81 (s, 3H), 1.36 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ 161.82, 159.98, 149.93, 148.64, 132.05, 128.54, 127.24, 114.38, 106.35, 62.15, 60.05, 55.33, 14.16. LCMS: *m/z* calculated for $C_{15}H_{16}N_4O_3$: 300.12; Observed mass: 301.2 (M+1); Anal. Calculated for $C_{15}H_{16}N_4O_3$: C, 59.99; H, 5.37; N, 18.66; Found: C, 59.98; H, 5.39; N, 18.68.

Ethyl-7-(3-(trifluoromethyl)phenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4c):



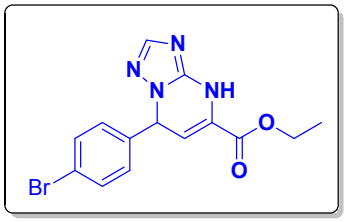
White solid; yield 70 mg, 58%; MP: 174-176 ^{o}C; **^{1}H NMR** (300 MHz, Chloroform-*d*): δ 10.45 (bs, 1H), 7.80 (s, 1H), 7.64-7.48 (m, 4H), 6.30 (d, *J* = 3.9 Hz, 1H), 5.91 (d, *J* = 3.9 Hz, 1H), 4.40 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 161.53, 150.37, 148.82, 140.73, 131.62, 130.63, 129.63, 127.79, 125.76, 123.89, 105.05, 62.41, 60.25, 14.13. **LCMS:** *m/z* calculated for $C_{15}H_{13}F_3N_4O_2$: 338.12; Observed mass: 339.2 (M+1); Anal. Calculated for $C_{15}H_{13}F_3N_4O_2$: C, 53.26; H, 3.87; N, 16.56; Found: C, 53.28; H, 3.89; N, 16.58.

Ethyl-7-(3,4-dichlorophenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4d):



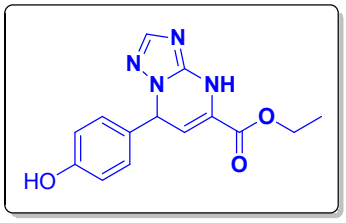
White solid; yield 75 mg, 62%; MP: 185-187 ^{o}C; ^{1}H NMR (300 MHz, Chloroform-*d*): δ 9.80 (bs, 1H), 7.77 (s, 1H), 7.46 (dd, *J* = 8.2 Hz, 1H), 7.28-7.26 (m, 1H), 7.18 (d, *J* = 8.4 Hz, 1H), 6.18 (d, *J* = 3.9 Hz, 1H), 5.87 (d, *J* = 3.9 Hz, 1H), 4.38 (dq, *J* = 7.2 Hz, 3.6 Hz, 2H), 1.37 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 161.51, 150.68, 140.81, 139.08, 136.15, 128.84, 124.65, 103.72, 62.27, 59.33, 14.34. LCMS: *m/z* calculated for $C_{14}H_{12}Cl_2N_4O_2$: 338.03; Observed mass: 339.2 (M+1); Anal. Calculated for $C_{14}H_{12}Cl_2N_4O_2$: C, 49.58; H, 3.57; N, 16.52; Found: C, 49.60; H, 3.58; N, 16.54.

Ethyl-7-(4-bromophenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4e):



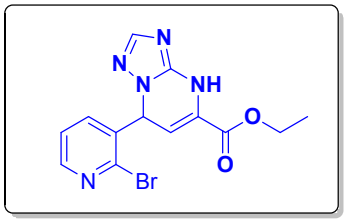
White solid; yield 83 mg, 67%; MP: 191-193 ^{o}C; **^{1}H NMR** (300 MHz, Chloroform-*d*): δ 9.65 (bs, 1H), 7.75 (s, 1H), 7.53 (d, *J* = 8.4 Hz, 2H), 7.19 (dd, *J* = 8.4 Hz, 1.8 Hz, 2H), 6.18 (d, *J* = 3.9 Hz, 1H), 5.90 (d, *J* = 3.9 Hz, 1H), 4.36 (dq, *J* = 7.2 Hz, 3.0 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (300 MHz, Chloroform-*d*): 161.58, 150.12, 148.70, 138.71, 132.20, 128.84, 128.57, 127.57, 123.01, 105.39, 62.33, 60.02, 14.14: LCMS: *m/z* calculated for $C_{14}H_{13}BrN_4O_2$: 348.02; Observed mass: 349.2, 351.2 (M+1, M+3); Anal. Calculated for $C_{14}H_{13}BrN_4O_2$: C, 48.16; H, 3.75; N, 16.05; Found: C, 48.18; H, 3.76; N, 16.07.

Ethyl-7-(4-hydroxyphenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4f):



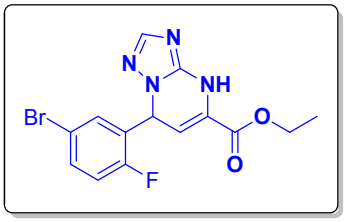
White solid; yield 53 mg, 52%; MP: 173-175 °C; **^{1}H NMR** (400 MHz, DMSO) δ 10.02 (s, 1H), 7.62 (s, 1H), 7.17 – 7.11 (m, 2H), 6.95 – 6.88 (m, 2H), 6.22 (d, *J* = 4.0 Hz, 1H), 5.79 (d, *J* = 4.0 Hz, 1H), 4.30 – 4.19 (m, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, Chloroform-*d*) δ 161.98, 159.93, 149.82, 148.54 132.05, 128.64, 126.35, 114.15, 107.24, 62.38, 60.17, 14.04. **LCMS:** *m/z* calculated for $C_{14}H_{14}N_4O_3$: 286.11; Observed mass: 287.2 (M+1); Anal. Calculated for $C_{14}H_{14}N_4O_3$: C, 58.73; H, 4.93; N, 19.57; Found: C, 58.75; H, 4.95; N, 19.59.

Ethyl-7-(2-bromopyridin-3-yl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4g):



Brown solid; yield 77 mg, 62%; MP: 197-200 °C; ^{1}H NMR (400 MHz, Chloroform-*d*): δ 9.88 (bs, 1H), 8.36 (s, 1H), 7.83 (m, 1H), 7.28-7.16 (m, 2H), 6.67 (d, *J* = 4.0 Hz, 1H), 6.01 (d, *J* = 4.0 Hz, 1H), 4.37 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO) δ 160.50 (m), 150.81, 150.21, 149.16, 141.20, 136.84, 135.49, 128.86, 124.66, 103.72, 62.27, 59.33, 14.34; LCMS: *m/z* calculated for $C_{13}H_{12}BrN_5O_2$: 349.02; Observed mass: 350.2, 352.2 (M+1, M+3); Anal. Calculated for $C_{13}H_{12}BrN_5O_2$: C, 44.59; H, 3.45; N, 20.00; Found: C, 44.58; H, 3.46; N, 20.02.

Ethyl-7-(5-bromo-2-fluorophenyl)-4,7-dihydro-[1,2,4]triazolo[1,5-a]pyrimidine-5-carboxylate (4h):



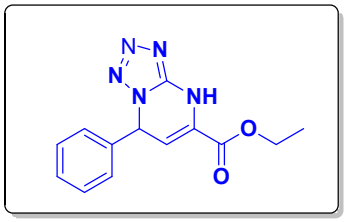
Plae brown solid; yield 35 mg, 53%; MP: 192-194 °C; ^{1}H NMR (300 MHz, DMSO-*d6*): δ 10.18 (bs, 1H), 7.70-7.60 (m, 3H), 7.48 (d, *J* = 7.2 Hz, 1H), 6.45

(d, *J* = 3.9 Hz, 1H), 5.86 (d, *J* = 3.9 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (75MHz, DMSO-*d6*) δ 164.40, 152.93, 145.45, 140.82, 128.59, 128.41, 126.42, 125.18, 123.64, 65.93, 60.17, 13.14. LCMS: *m/z* calculated for $C_{14}H_{12}BrFN_4O_2$: 366.01; Observed mass: 367.1, 369.1 (M+1, M+3); Anal. Calculated for $C_{14}H_{12}BrFN_4O_2$: C, 45.80; H, 3.29; N, 15.26; Found: C, 45.82; H, 3.30; N, 15.28.

Experimental procedure for synthesis of compound (5a & 5b):

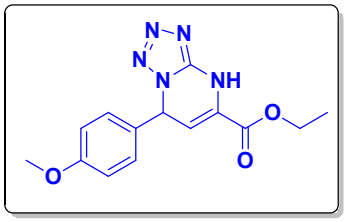
To a solution of 5-amino tetrazole (0.075 mmol) in DMF (1.0 mL) was mixed with MBH Acetate of nitro alkene (0.09 mmol) and cesium carbonate (0.15 mmol) and the reaction mixture was heated to 60^{o}C for 4h. After completion of reaction (monitored by LCMS), the reaction mixture was quenched with water (10 mL). The reaction mixture was extracted with ethyl acetate (3x 10 mL). The combined organic layers were dried over anhydrous sodium sulphate, filtered and concentrated over vacuum to give the crude product. To this crude product was added methanol (2 mL) and stirred for 30 min at RT. A white precipitate was obtained which was filtered gave the product (70% - 75%). The mother liquid contains a small amount of product along with small amount of other region isomer by LCMS.

Ethyl-7-phenyl-4,7-dihydrotetrazolo[1,5-a]pyrimidine-5-carboxylate (5a):



yield 18 mg, 75%; MP: 201-204 ^{o}C; **^{1}H NMR** (300 MHz, Chloroform-*d*): δ 7.62-7.55 (m, 3H), 7.35-7.25 (m, 2H), 6.67 (d, *J* = 3.9 Hz, 1H), 6.02 (d, *J* = 3.9 Hz, 1H), 4.36 (q, *J* = 7.2 Hz, 2H), 1.36 (t, *J* = 7.2 Hz, 3H). **LCMS:** *m/z* calculated for $C_{13}H_{13}N_5O_2$: 271.11; Observed mass: 272.2 (M+1).

Ethyl-7-(4-methoxyphenyl)-4,7-dihydrotetrazolo[1,5-a]pyrimidine-5-carboxylate (5b):



yield 19 mg, 72%; MP: 200-202 ^{o}C; **^{1}H NMR** (300 MHz, DMSO-*d6*): δ 10.01 (s, 1H), 7.14 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.21 (d, *J* = 3.9 Hz, 1H), 5.78 (dd, *J* = 3.9 Hz, 1.5 Hz, 1H), 4.25 (dq, *J* = 7.2 Hz, 2H), 3.72 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H). **LCMS:** *m/z* calculated for $C_{14}H_{15}N_5O_3$: 301.12; Observed mass: 302.2 (M+1).

Figure 1: Imidazopyrimidine containing drugs

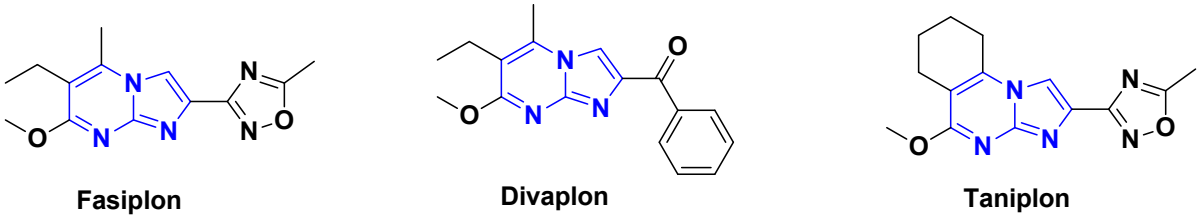
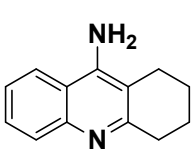
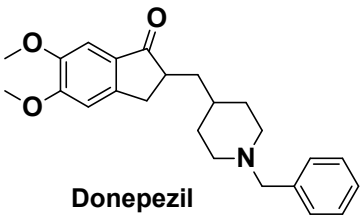


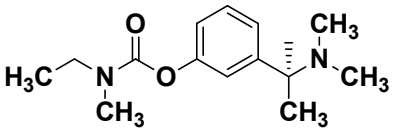
Figure 2: AChE inhibitors clinically used for the treatment of AD



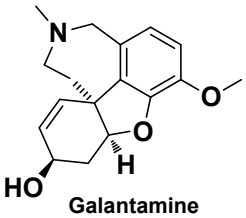
Tacrine



Donepezil

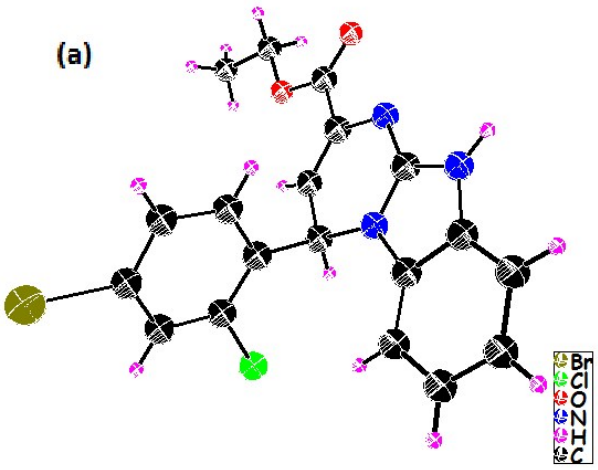


Rivastigmine



Galantamine

Figure 3: ORTEP diagram of (a) compound **3e** and (b) compound **4b**



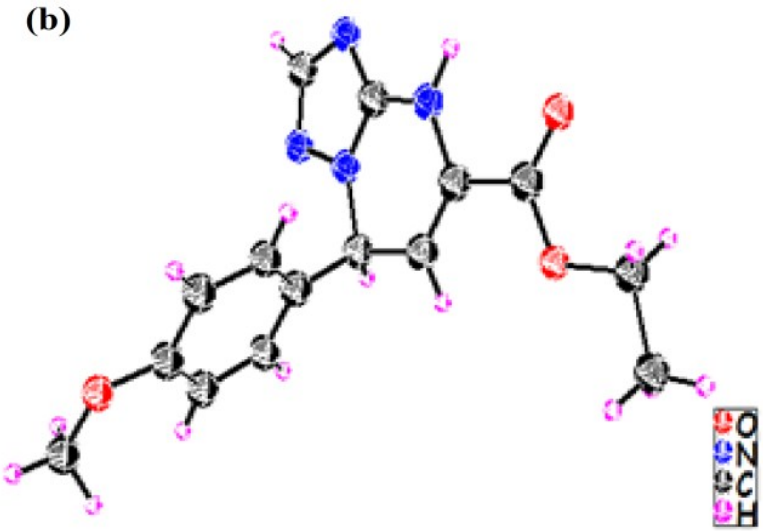
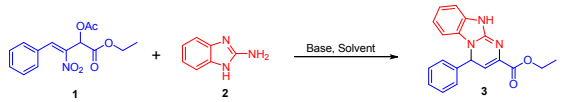


Table 1. Screening of reaction conditions [a]



S.No	Base	Solvent	Temp	Yield[b] (%)
1	--	THF	RT	0
2	--	THF	70°C	0
3	Et_3N	THF	RT	20
4	DIPEA	THF	RT	22
5	Pyridine	THF	RT	40
6	2,6-Lutidine	THF	RT	40
7	DABCO	THF	RT	44
8	DBU	THF	RT	49
9	K_2CO_3	THF	RT	60
10	Cs_2CO_3	THF	RT	80
11	Cs_2CO_3	CH_2Cl_2	RT	45
12	Cs_2CO_3	$CHCl_3$	RT	48
13	Cs_2CO_3	MeOH	RT	60
14	Cs_2CO_3	EtOH	RT	68
15	Cs_2CO_3	CH_3CN	RT	82
16	Cs_2CO_3	1,4-dioxane	RT	81

Biology

Enzyme Inhibition studies

The *in vitro* inhibitory effect of newly synthesized ligands was assessed by Ellman's method[22] using AMPLITE™ AChE assay kit(AAT Bioquest, Inc., Sunnyvale, CA).The assay system consists of AChE from electric eel (EC 3.1.1.7), 5,5-dithiobis-(2-nitrobenzoic acid) (DTNB, known as Ellman's reagent) and acetylcholine. The assay procedure is as follows, an aliquots (total volume 100µL) was prepared by mixing 5.7 nMAChE (prepared in 0.1 % of BSA containing distilled water) with acetylcholine (500 µM) and DTNB in a reaction buffer of pH 7.4. As a result of enzyme substrate interaction, the yellow colour formation was monitored and measured at 405 nm using a spectrophotometer at a time interval 2 minutes each for 20 minutes. Later the optical density was plotted against time. The same experiment (in triplicate) was repeated by incubating (15 minutes) the enzyme with different ligands. The relative activities of all ligands were expressed and compared with that of native enzyme activity. Finally the half maximal inhibitory concentration (IC_{50}) was determined for each ligands.

Table 2: The *in vitro* AChE inhibitory profile of compounds 3a-3j

S. No	Compound	% of Inhibition at 208 nM	hAChE IC50 (nM)+ SD
1	3a	53	70.78 ± 10.01

2	3b	70	52.64 ± 1.07
3	3c	62	91.8 ± 3.6
4	3d	76	46.86 ± 1.16
5	3e	74	42.52 ± 5.17
6	3g	69	71.48 ± 5.04
7	3h	61	67.32 ± 4.94
8	3i	67	52.58 ± 15.65
9	3j	65	68.4 ± 7.94
10	Tacrine		551.58 ±19.17
11	Galanthamine		360 ±10[1]

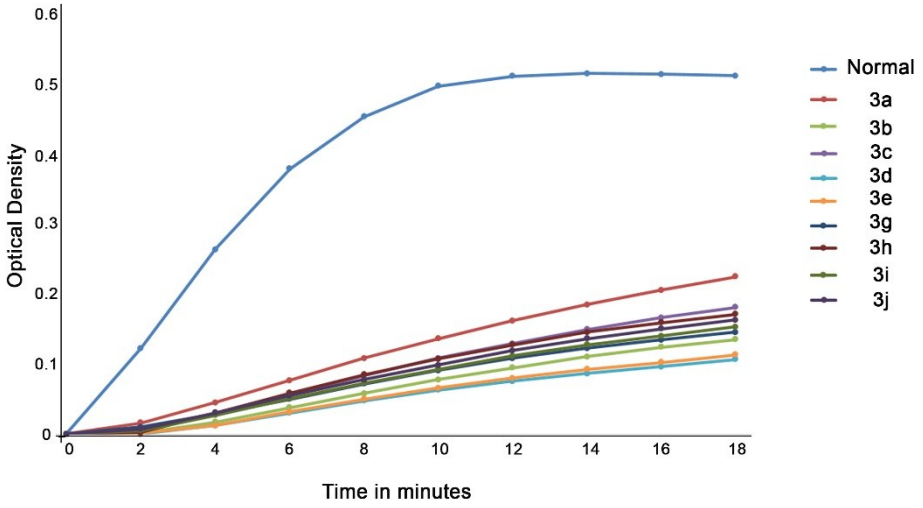
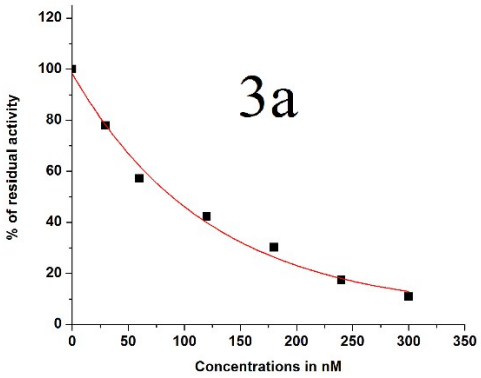
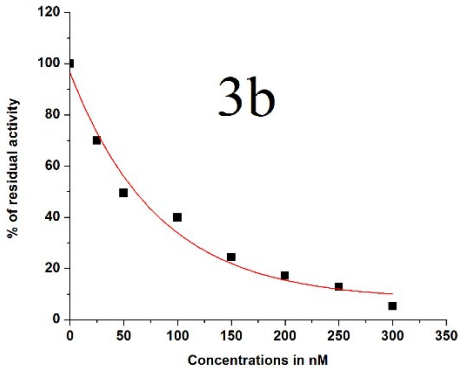
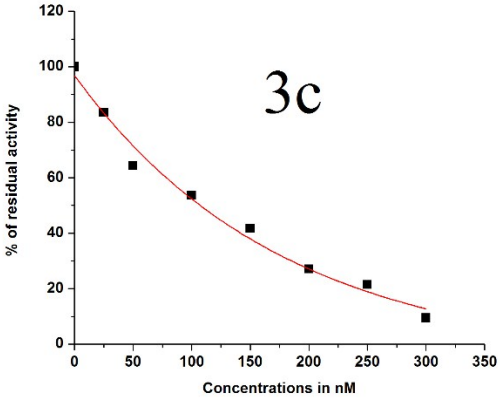


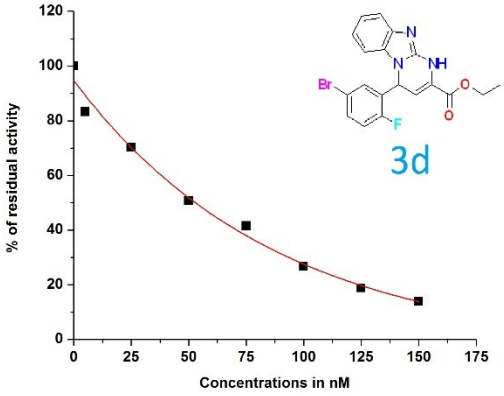
Figure 4: Velocity time graph obtained for native enzyme and in presence of compounds (208 nM)

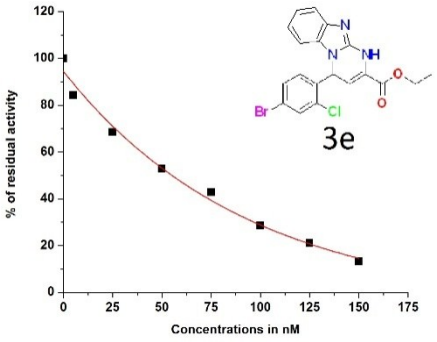
IC50 graphs for compounds 3a-3j

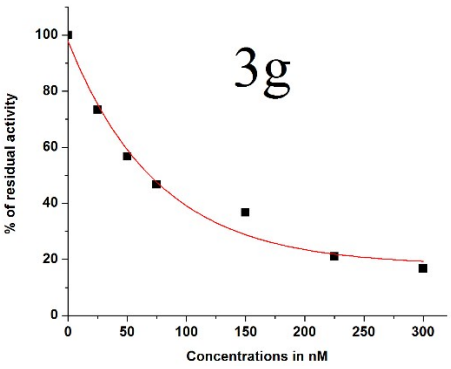

3a
% of residual activity
Concentrations in nM

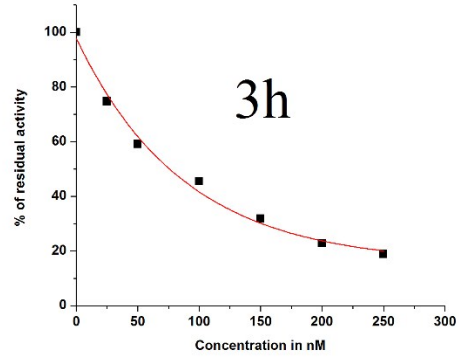

3b
% of residual activity
Concentrations in nM

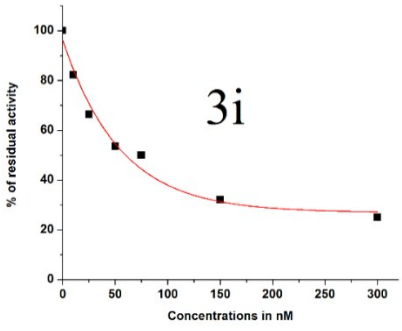

3c
% of residual activity
Concentrations in nM


3d
% of residual activity
Concentrations in nM


3e
% of residual activity
Concentrations in nM


3g
% of residual activity
Concentrations in nM


3h
% of residual activity
Concentration in nM


3i
% of residual activity
Concentrations in nM

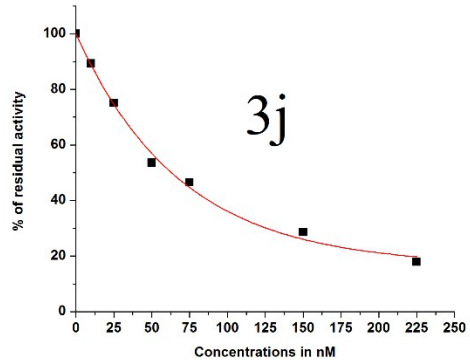
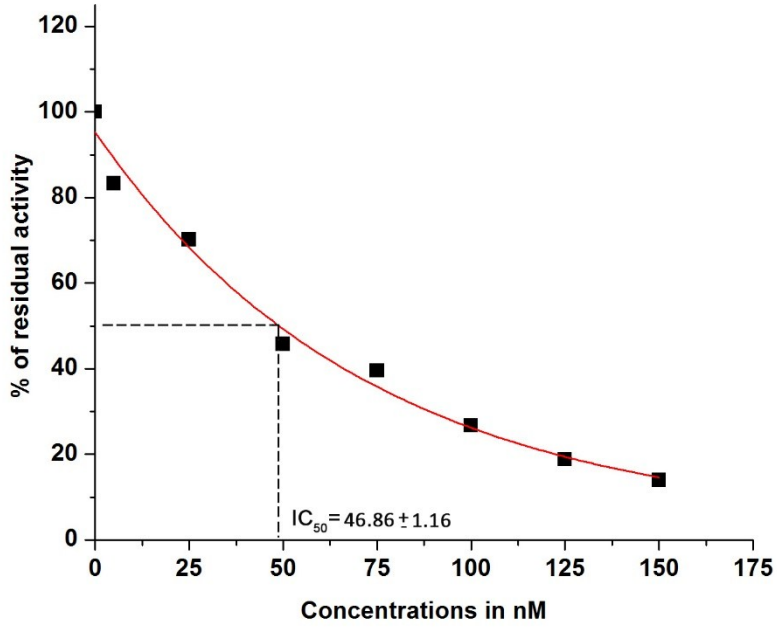
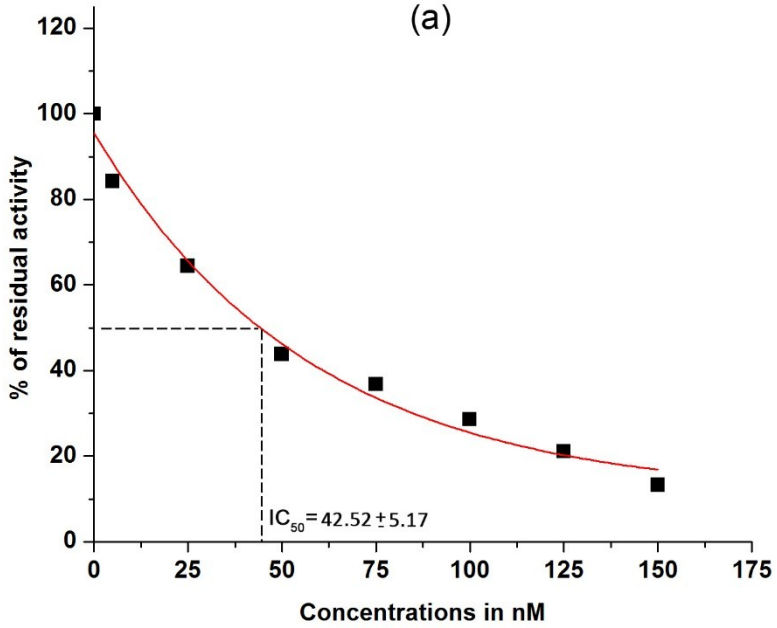


Figure 5: Relative residual activity of AChE plotted against the different concentrations of the most potent compounds **3d (a)** and **3e (b).**



(a)



(b)

Table 3: ADME profile of the compounds predicted by QikProp program

Compound	MW (≤ 450 Da)	HBD (≤ 3)	HBA (≤ 7)	LogP (≤ 5)	CNS (≥0)	Rotor (≤ 7)	N and O (≤7)

3a	319	1	3	4.35	0	2	5
3b	398	1	3	4.92	0	2	5
3c	333	1	3	4.66	0	2	5
3d	416	1	3	5.01	0	2	5
3e	433	1	3	5.32	0	2	5
3g	417	1	4	4.41	0	2	6
3h	335	2	4	3.58	-2	3	6
3i	337	1	3	4.53	0	2	5
3j	348	1	5	3.51	-2	3	7

Compound	BBB (-1.2 -1.2)	SASA (320-735 Å^2)	Volume (≤1250 Å^3)	PSA (60 –70 Å^2)	Caco (≥ 500 nm/s)	MDCK (≥ 500 nm/s)	% HOA
3a	-0.51	605	1052	64	1171	587	100
3b	-0.35	634	1105	64	1171	1554	100
3c	-0.54	637	1112	64	1171	587	100
3d	-0.27	641	1118	64	1170	2391	100
3e	-0.22	649	1141	63	1174	3126	100
3g	-0.51	634	1106	76	675	1362	100
3h	-1.12	618	1077	86	355	161	94
3i	-0.43	612	1065	64	1169	899	100
3j	-1.16	620	1090	96	319	144	92

Table 4: The binding energetics of the compounds at the active site of hAChE

Name	Glide score	Binding energy	Interacting residues
3a	-8.24	-74.38	F338,H447,Y337 and W86
3b	-8.62	-75.55	F338,H447, Y337, Y124 and W86
3c	-8.09	-72.60	F338,H447,Y124,Y337 and W86
3d	-9.15	-87.03	F338,H447, Y341,Y124,Y337 andW86
3e	-9.79	-92.26	F338,H447,Y341,Y337, Y124 and W86
3g	-8.70	-85.55	F338,Y124,Y337 and W86
3h	-9.11	-75.07	F338,Y124,Y133, G121 and W86
3i	-8.90	-76.65	F338,H447,Y124,Y337 and W86
3j	-9.04	-74.13	F338,H447,Y124,Y337 andW86
Galanthamine	-9.69	-81.51	F338,S203,E202 and Y337

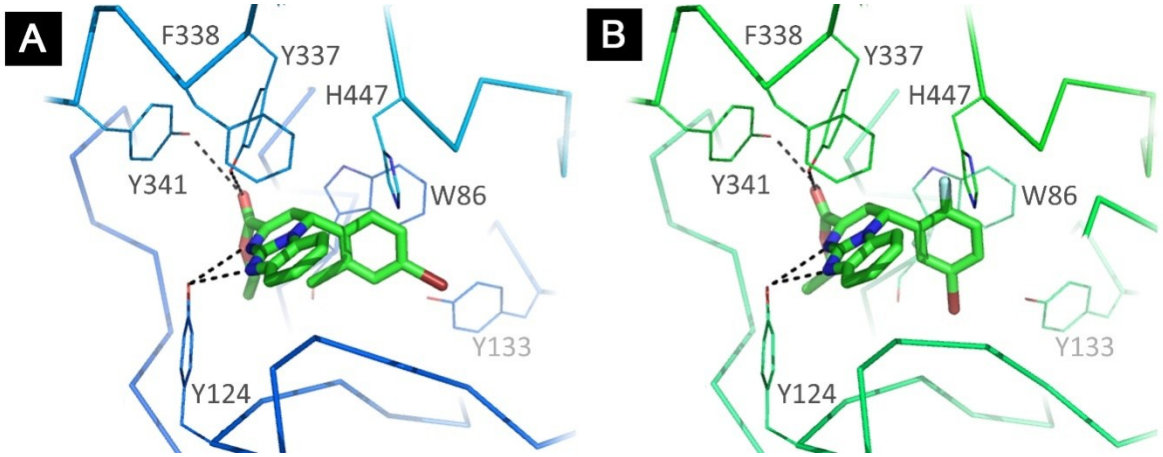


Figure 6: Binding pattern of compounds 3e (A) and 3d (B) at the active site of hAChE. The protein residues are shown in lines and the compounds are shown in stick. The hydrogen bonds are indicated by dotted lines

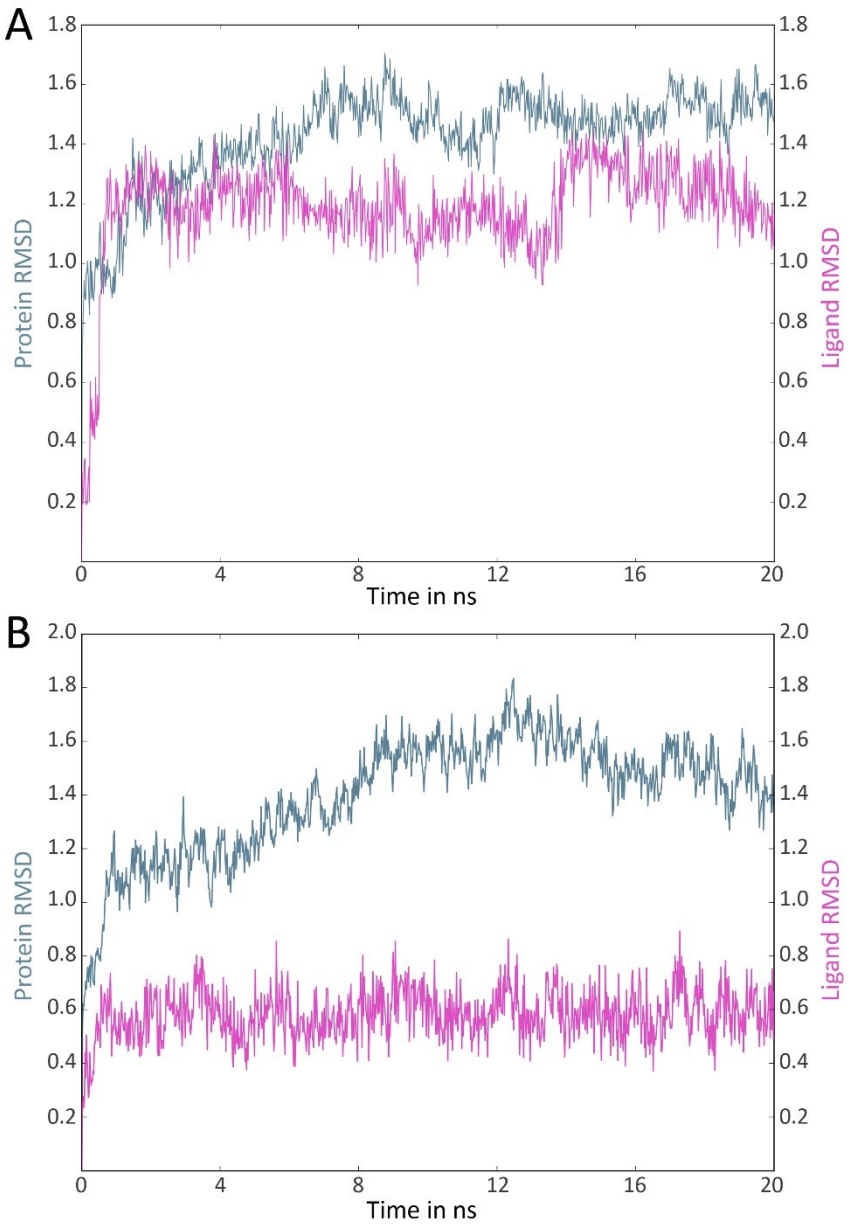
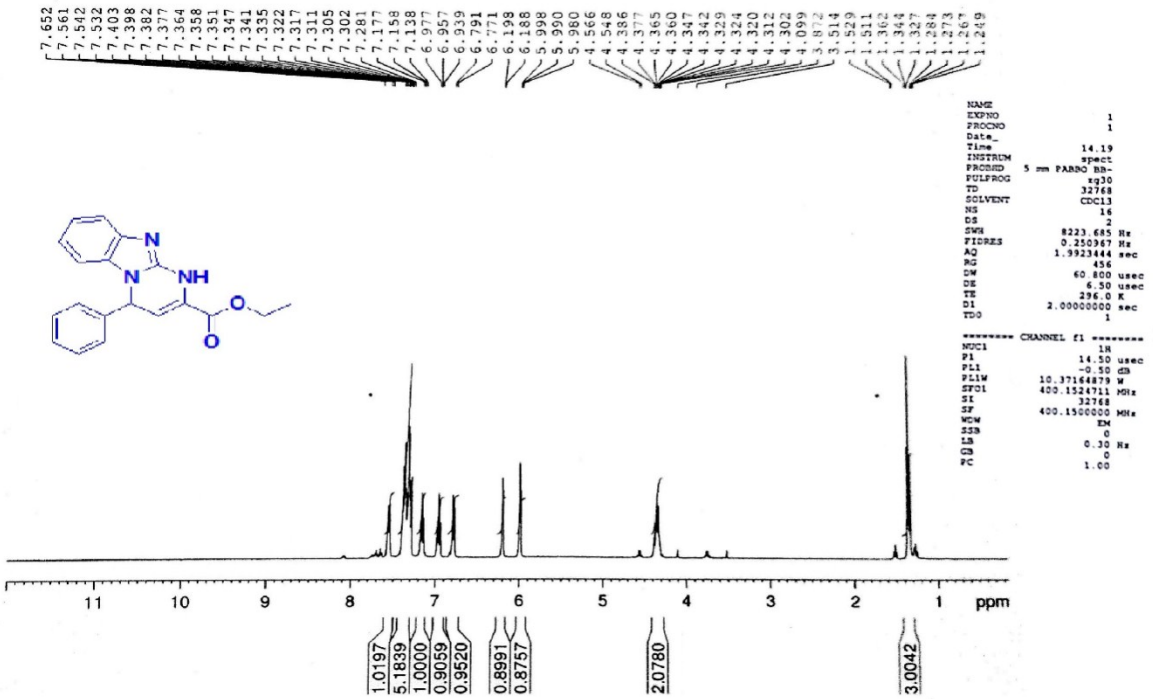
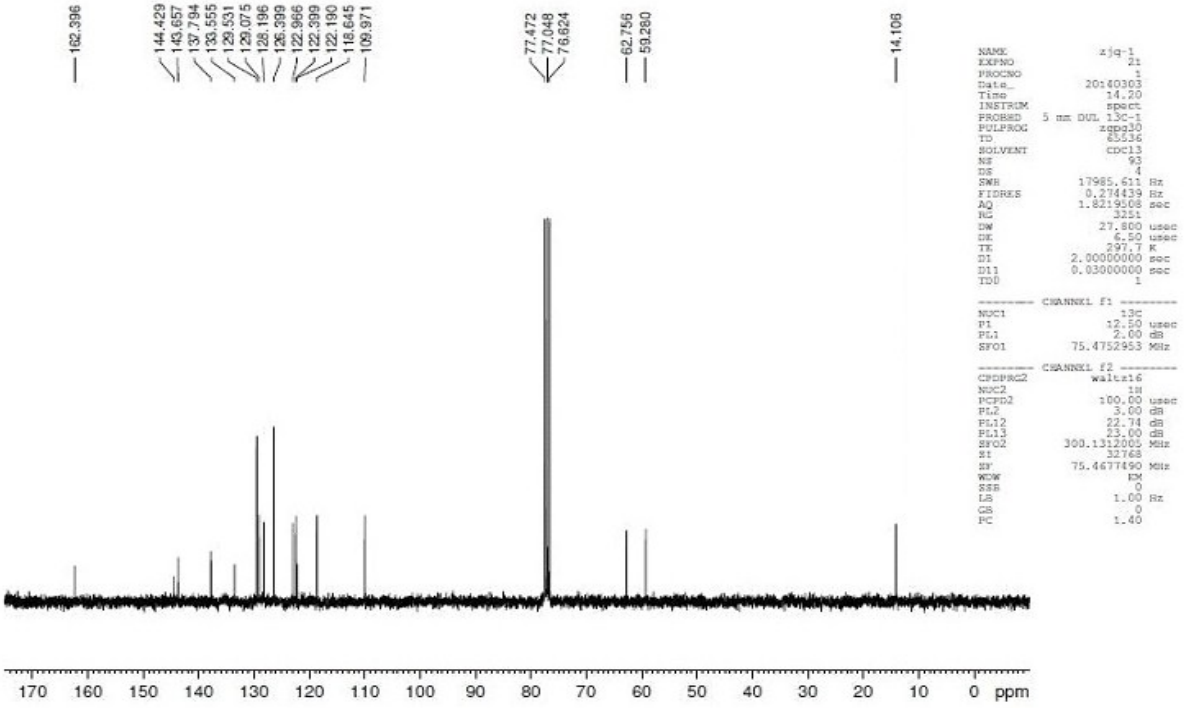


Figure 7: The RMSD graph of Cα (blue in colour), ligand displacement (pink in colour) of 3d (A) 3e (B) respectively

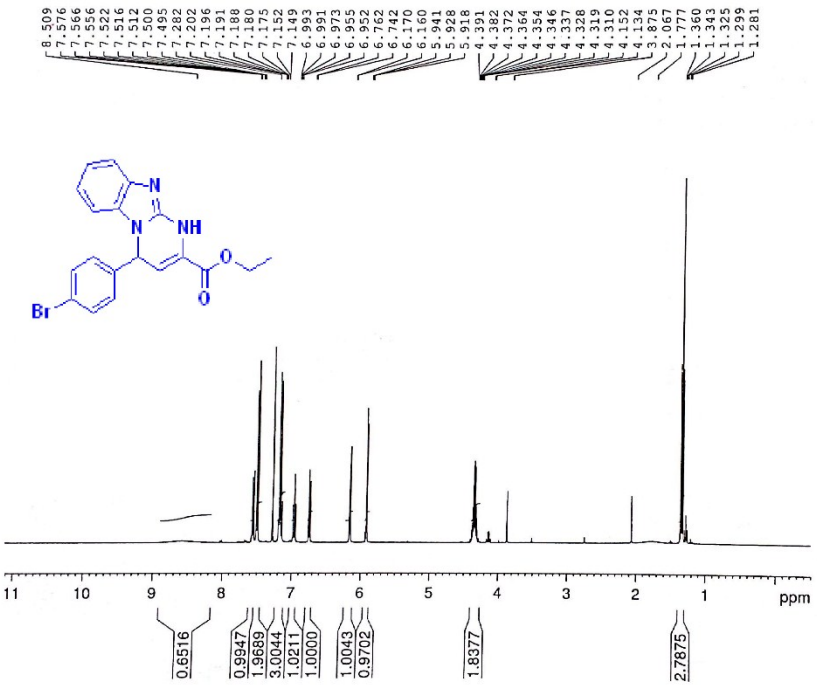
^{1}H NMR for compound 3a



^{13}C for compound 3a



[1]H NMR for compound 3b

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DE                 6.50 usec
TE                296.3 K
D1             1.00000000 sec
TD0                    1

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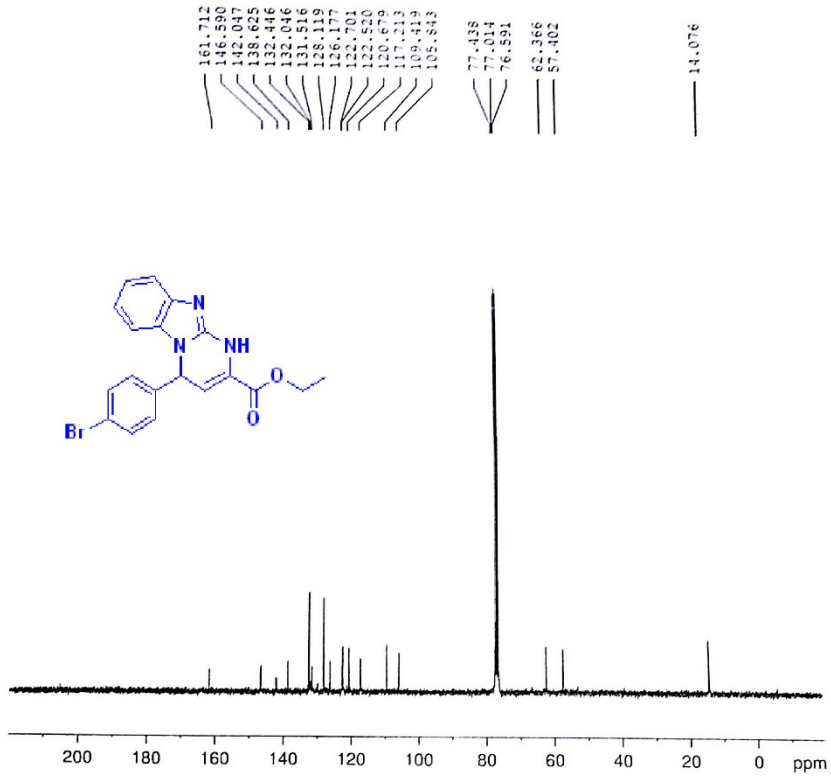
[13]C NMR for compound 3b

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D11            0.03000000 sec
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PL12               16.85 dB
PL13               17.00 dB
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PL13W          0.26963872 W
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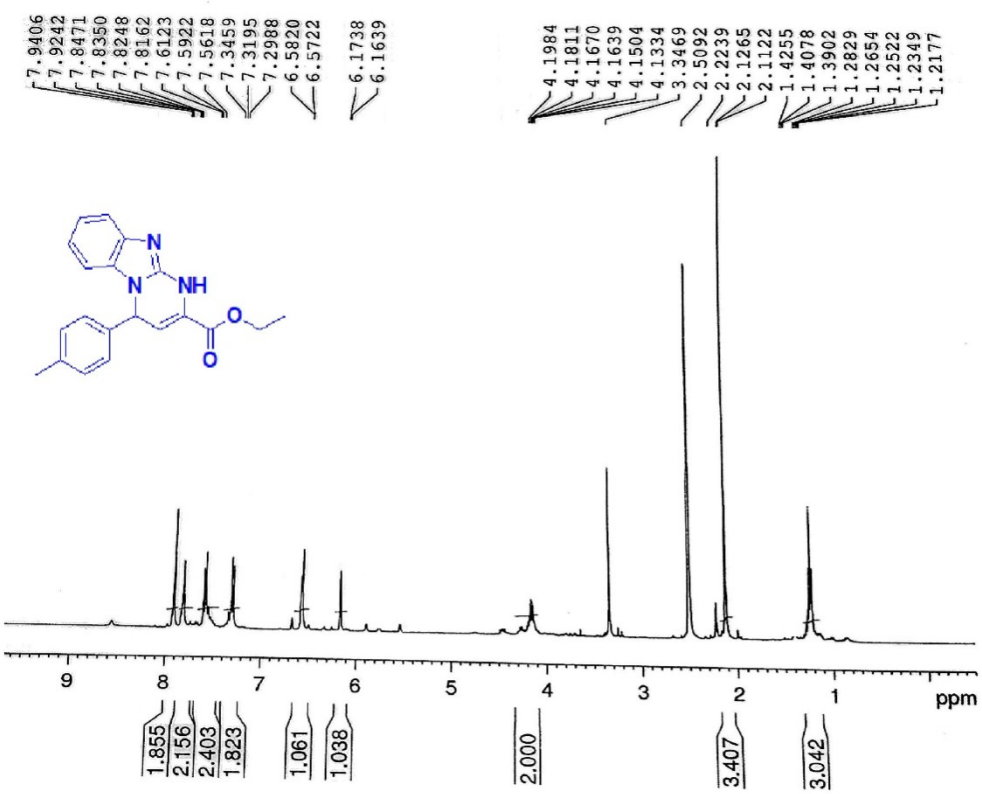
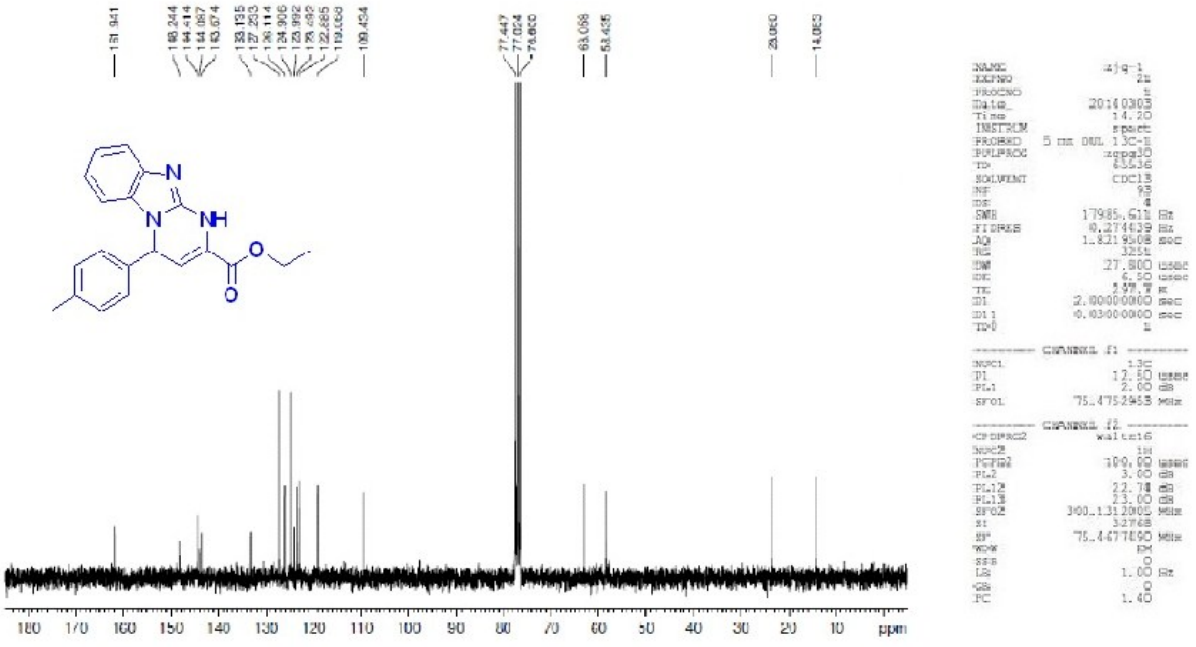
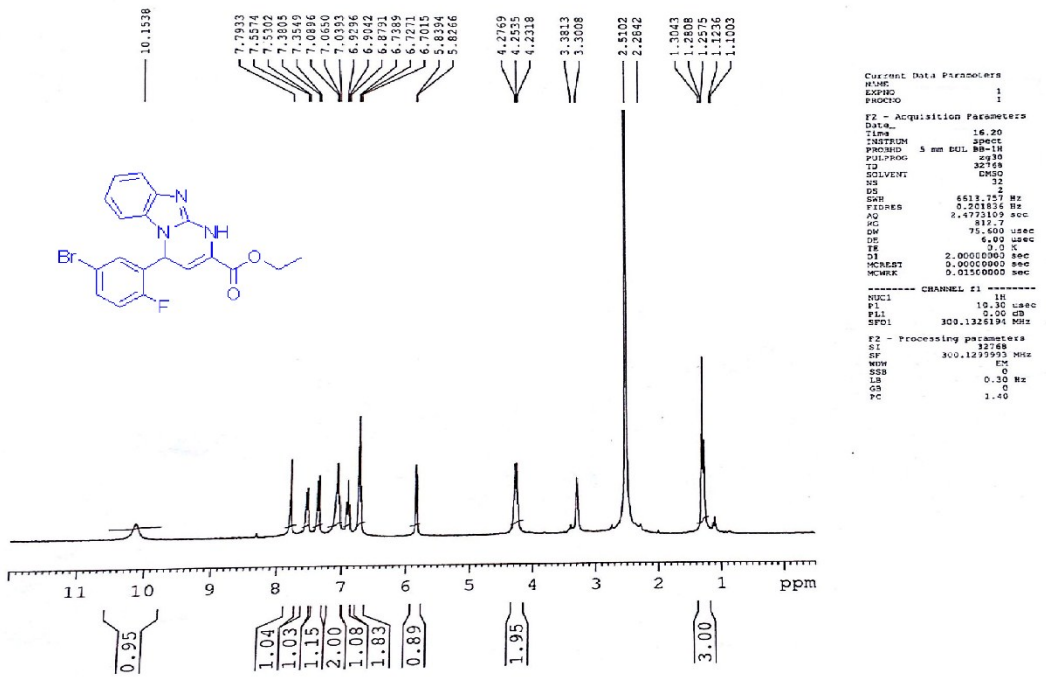
^{1}H NMR for compound 3c (DMSO-d6, 400 MHz)



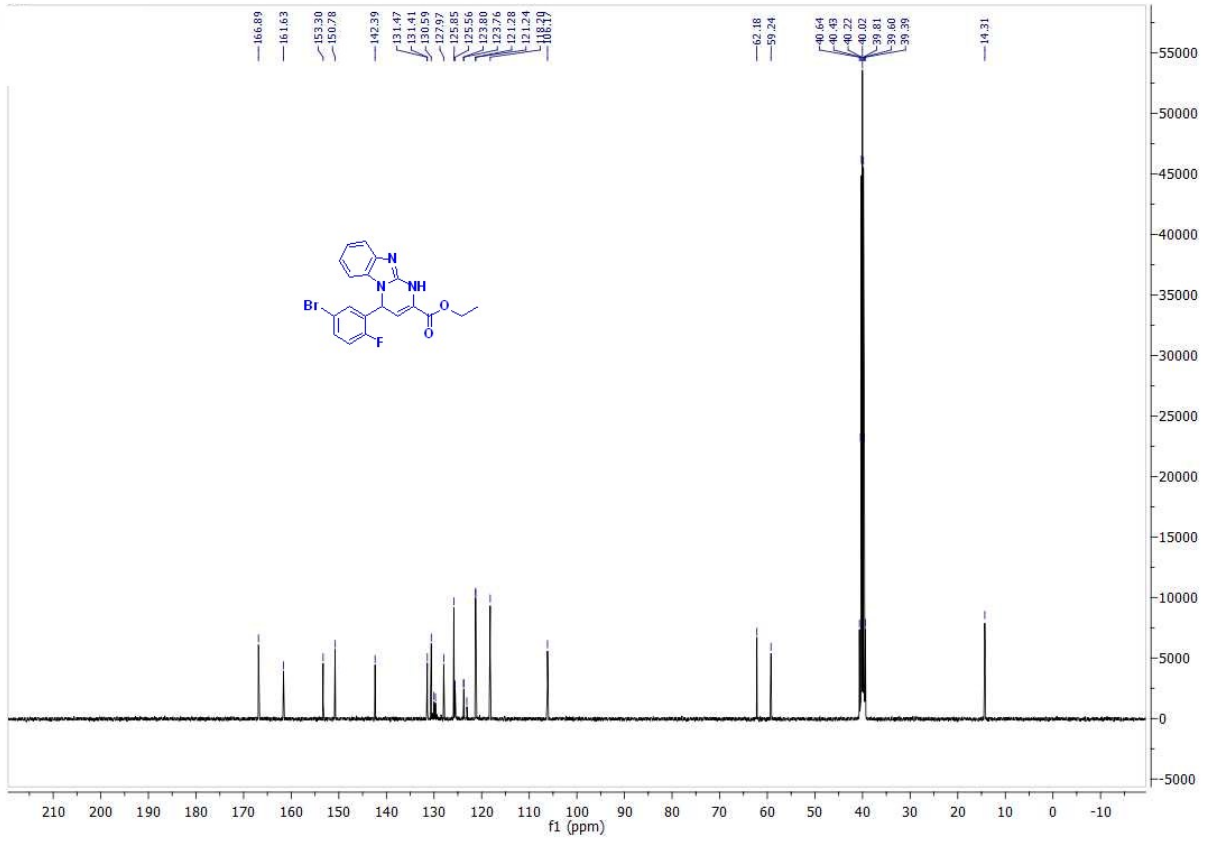
^{13}C NMR for compound 3c



^{1}H NMR for compound 3d (DMSO-d6, 300 MHz)



^{13}C NMR for compound 3d



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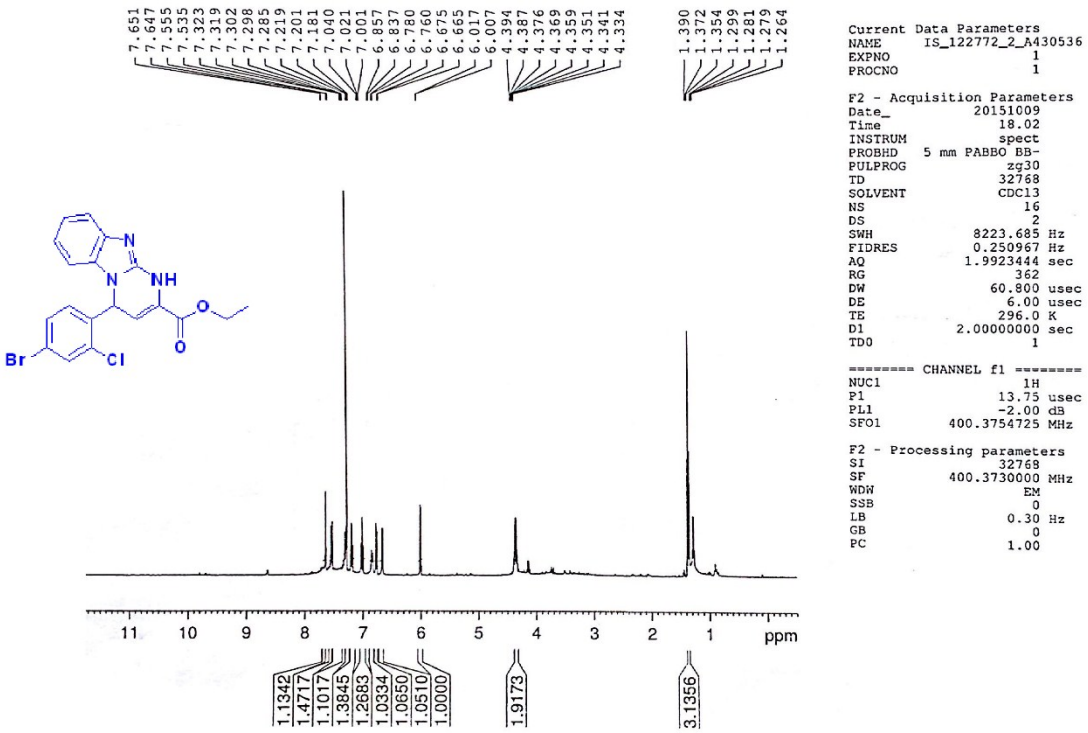

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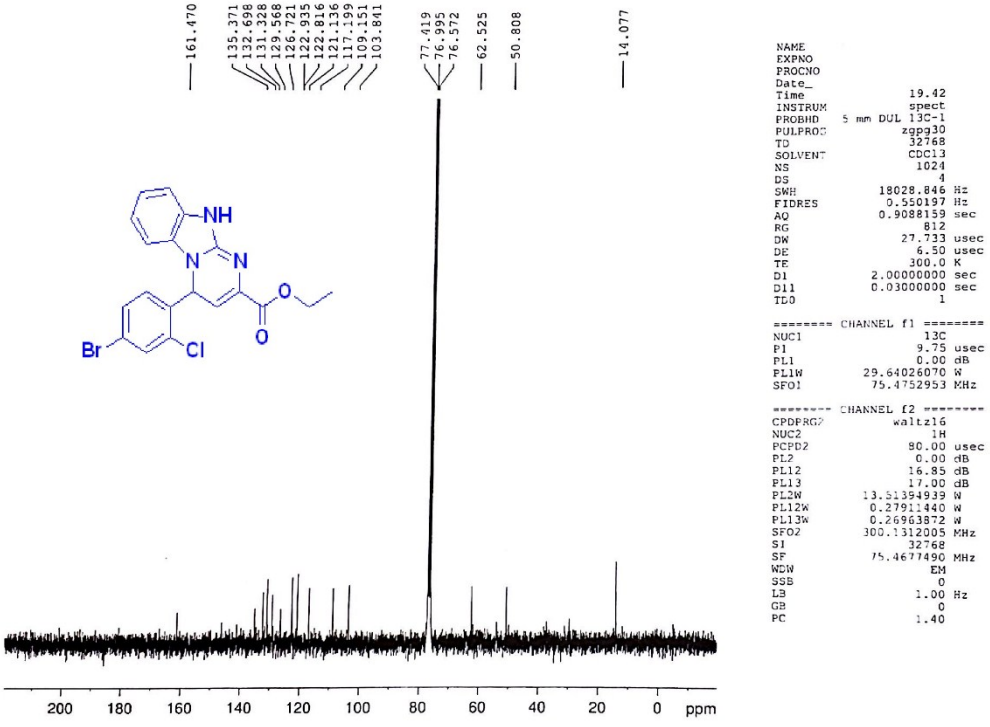
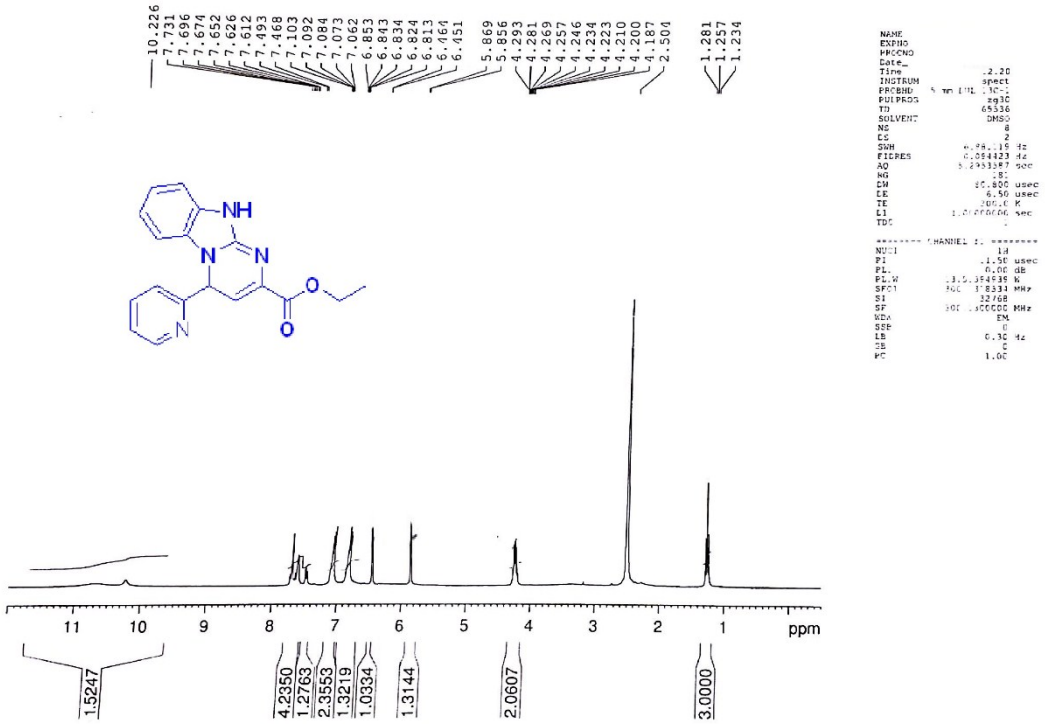


^{1}H NMR compound 3f



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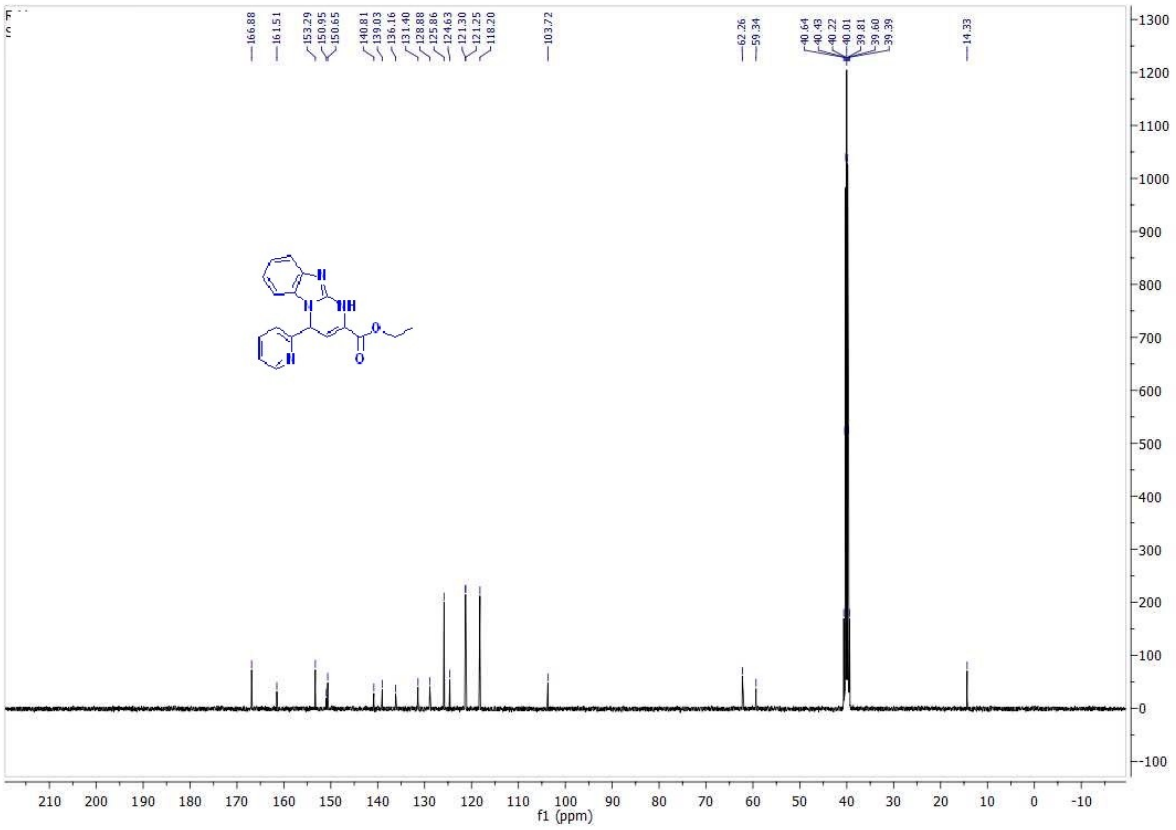
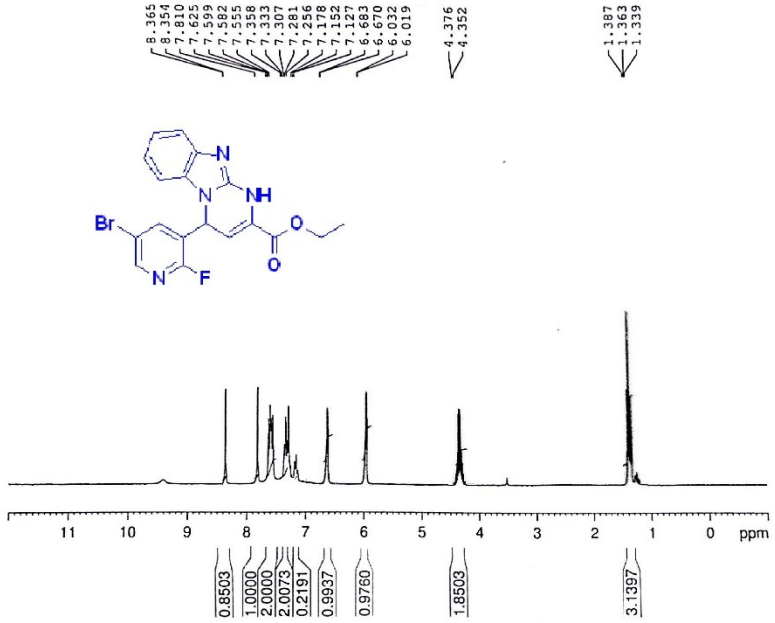


^{1}H NMR for compound 3g

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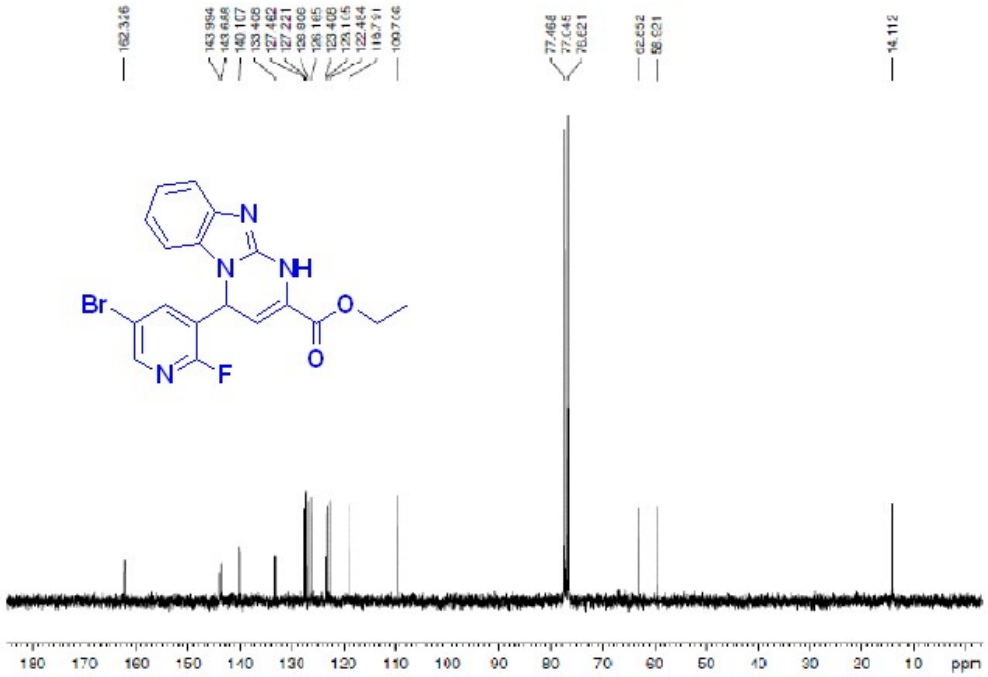
DE                   6.50 usec
TE                  300.0 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                  11.50 usec
PL1                  0.00 dB
PLIW           13.51394939 W
SFO1          300.1318534 MHz
SI                   32768
SF            300.1300000 MHz
WDW                    EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  1.00
```

^{13}C NMR for compound 3g

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SOLVENT              CDCl3
PROBHD     5 mm DUL 13C-1
SWH               17985.611 Hz
FIDRES            0.274439 Hz
AQ                1.8219508 sec
RG                    1290.2
DW                  27.800 usec
DE                   6.50 usec
TE                  297.4 K
D1                2.00000000 sec
D11               0.0500000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.50 usec
PL1                  2.00 dB
SFO1          75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2               100.00 usec
PL2                  3.00 dB
PL12                22.74 dB
PL13                23.00 dB
SFO2          300.1312005 MHz
SI                   32768
SF            75.4677490 MHz
WDW                    EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  1.40
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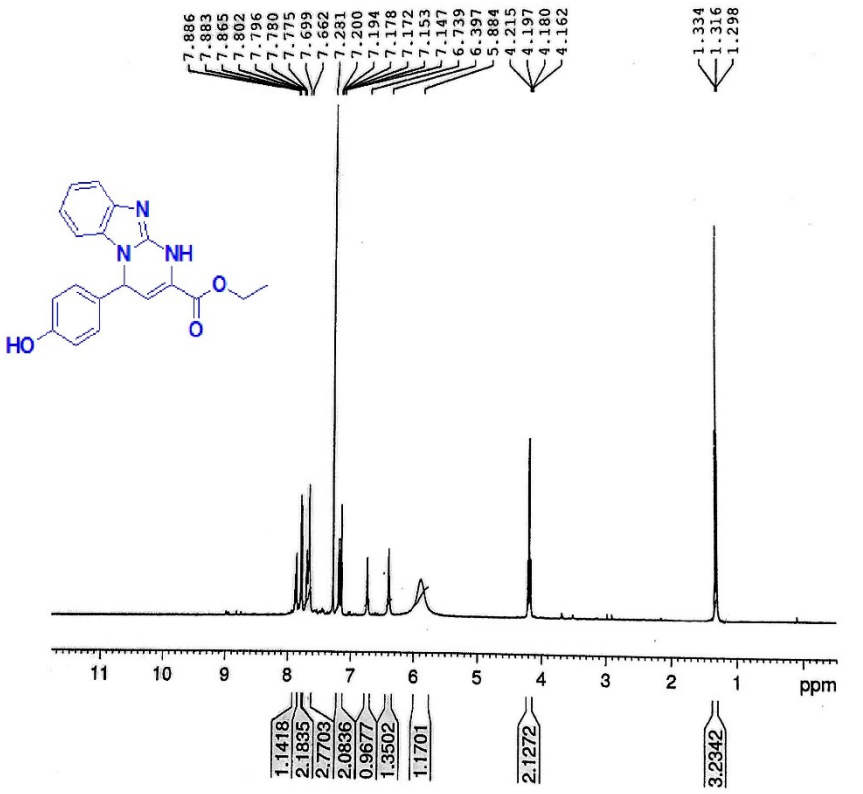
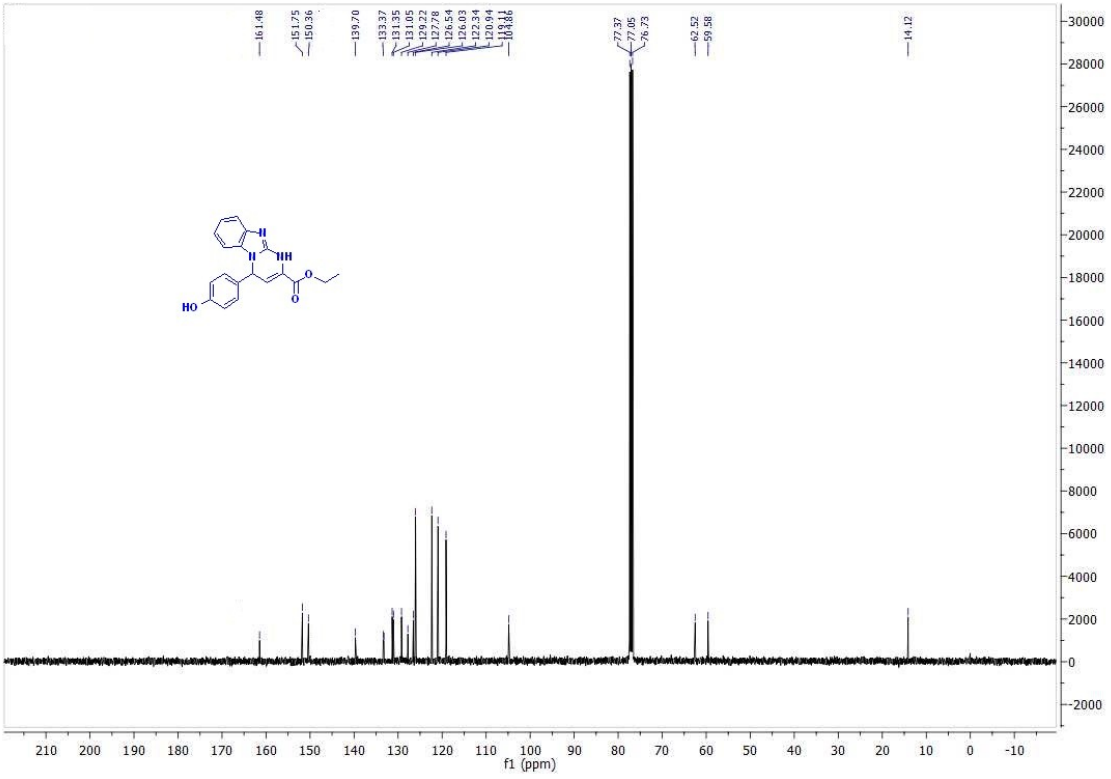
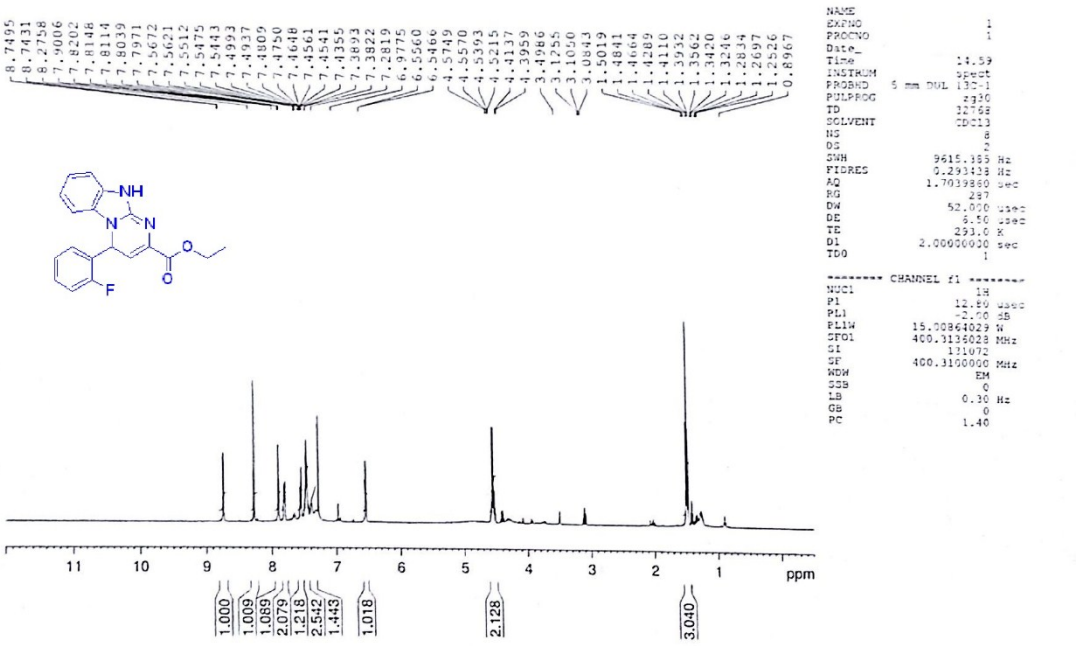
^{1}H NMR for compound 3h (CDCl3, 400 MHz)



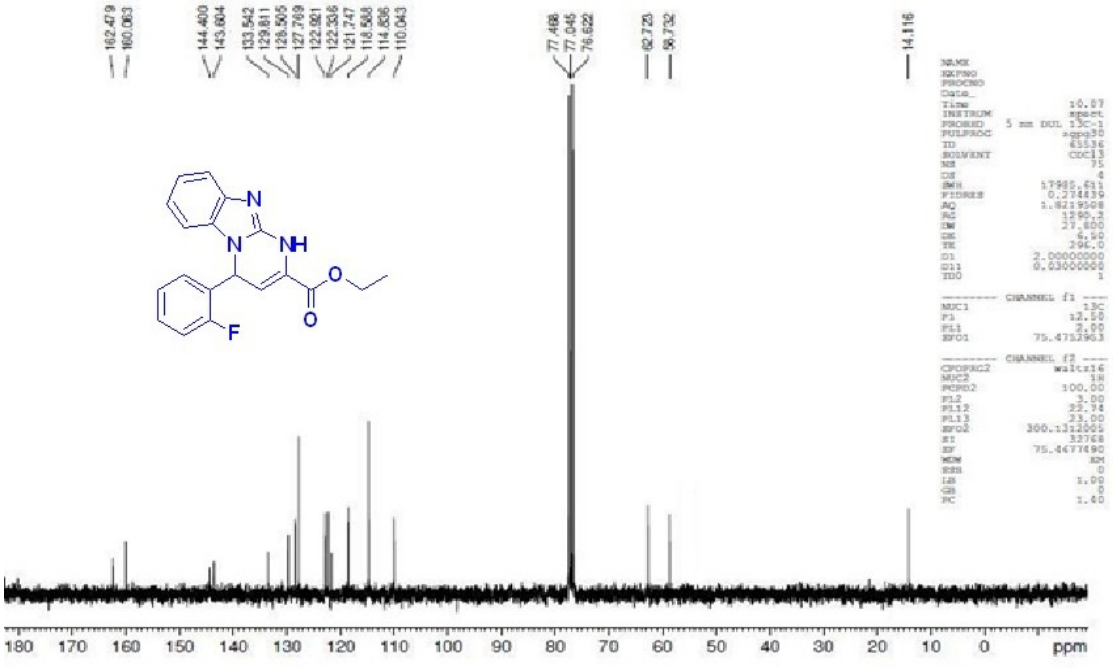
^{13}C NMR for compound 3h



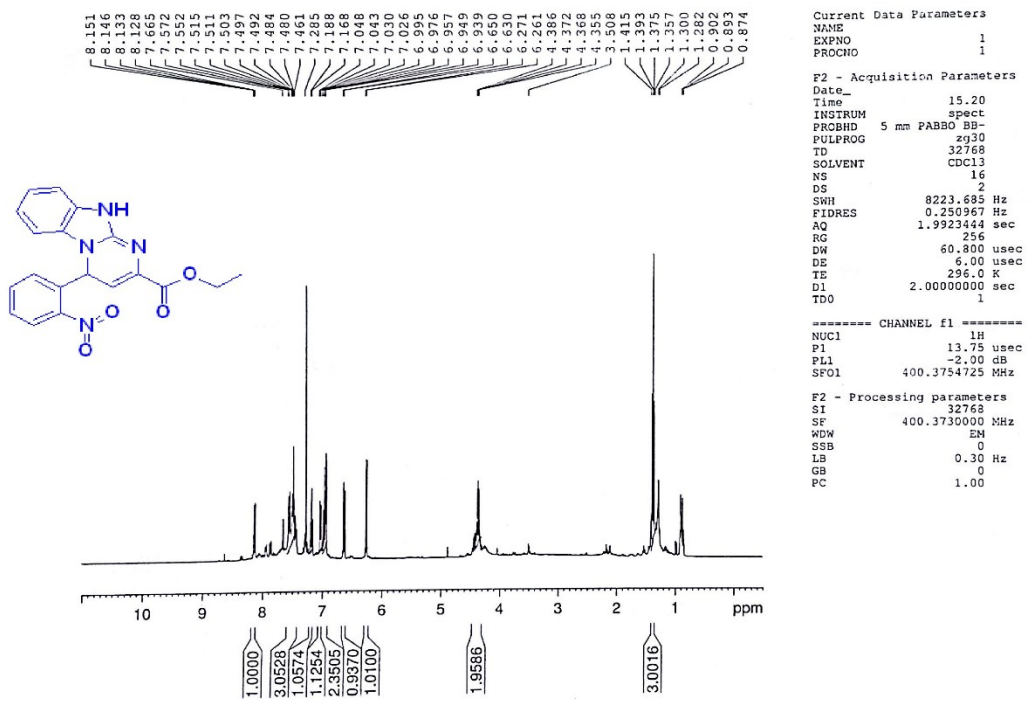
^{1}H NMR for compound 3i



^{13}C NMR for compound 3i



^{1}H NMR for compound 3j

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Current Data Parameters
NAME
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_
Time                15.20
INSTRUM             spect
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PULPROG             zg30
TD                 32768
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.250967 Hz
AQ              1.9923444 sec
RG                   256
DW                60.800 usec
DE                 6.00 usec
TE                296.0 K
D1             2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                13.75 usec
PL1               -2.00 dB
SFO1         400.3754725 MHz

F2 - Processing parameters
SI                 32768
SF          400.3730000 MHz
WDW                   EM
SSB                    0
LB                0.30 Hz
GB                     0
PC                1.00
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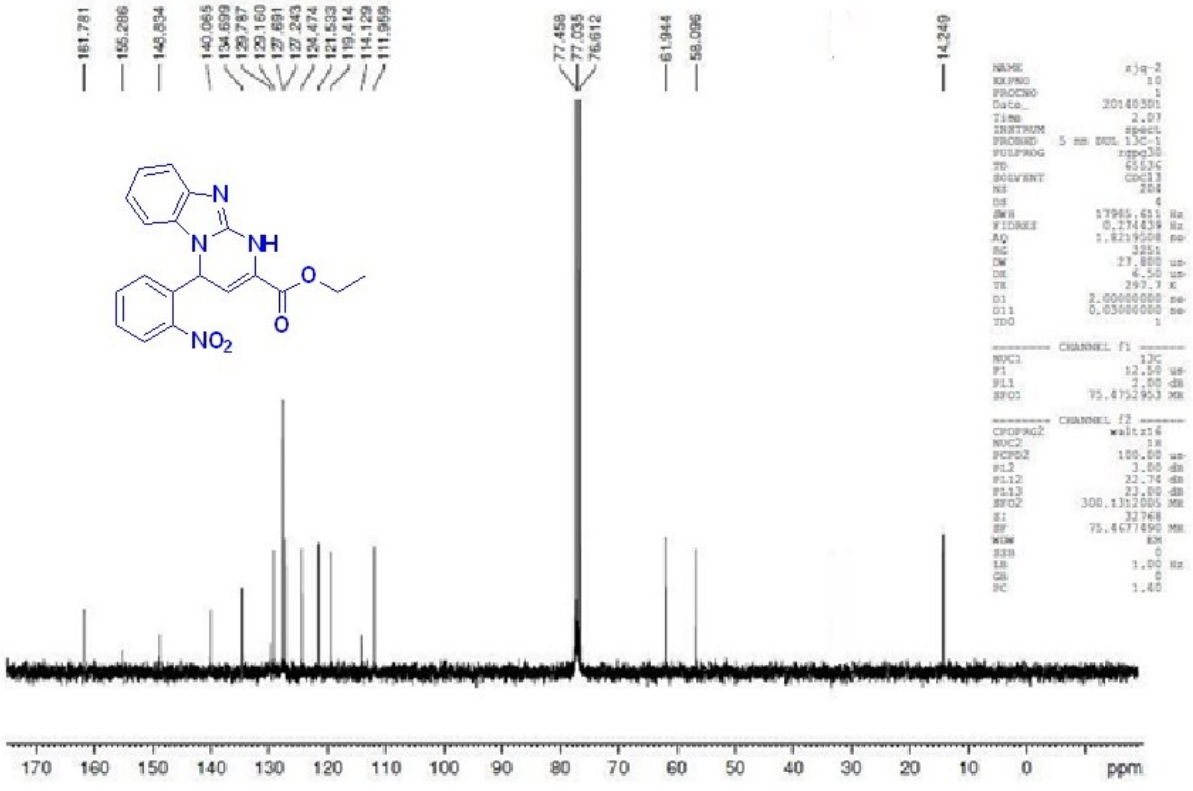
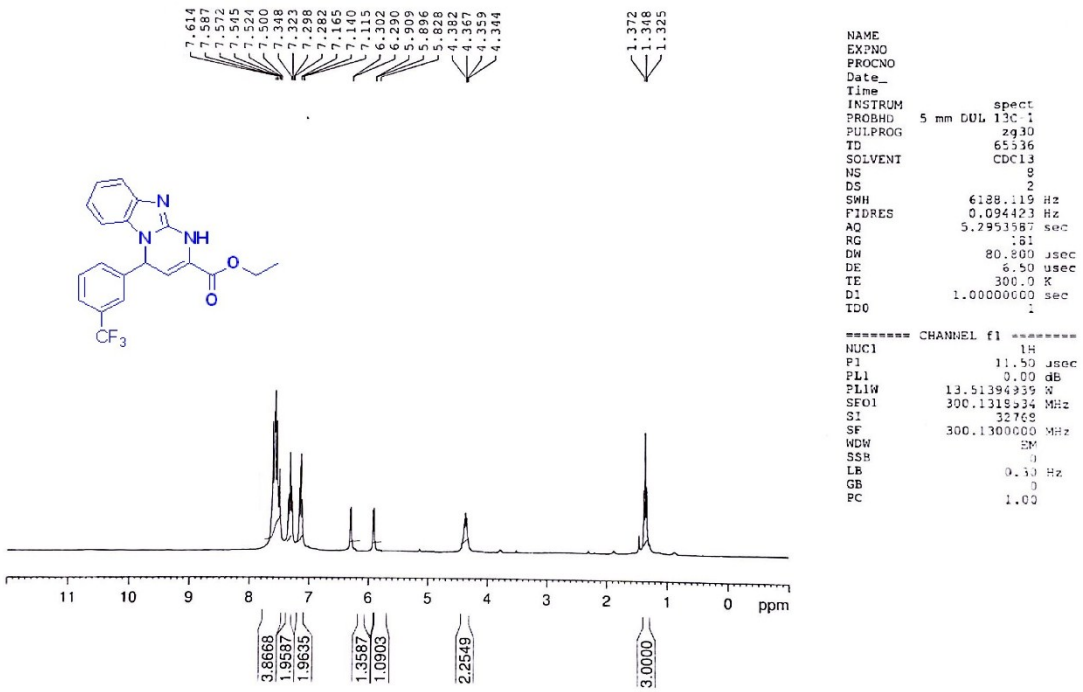
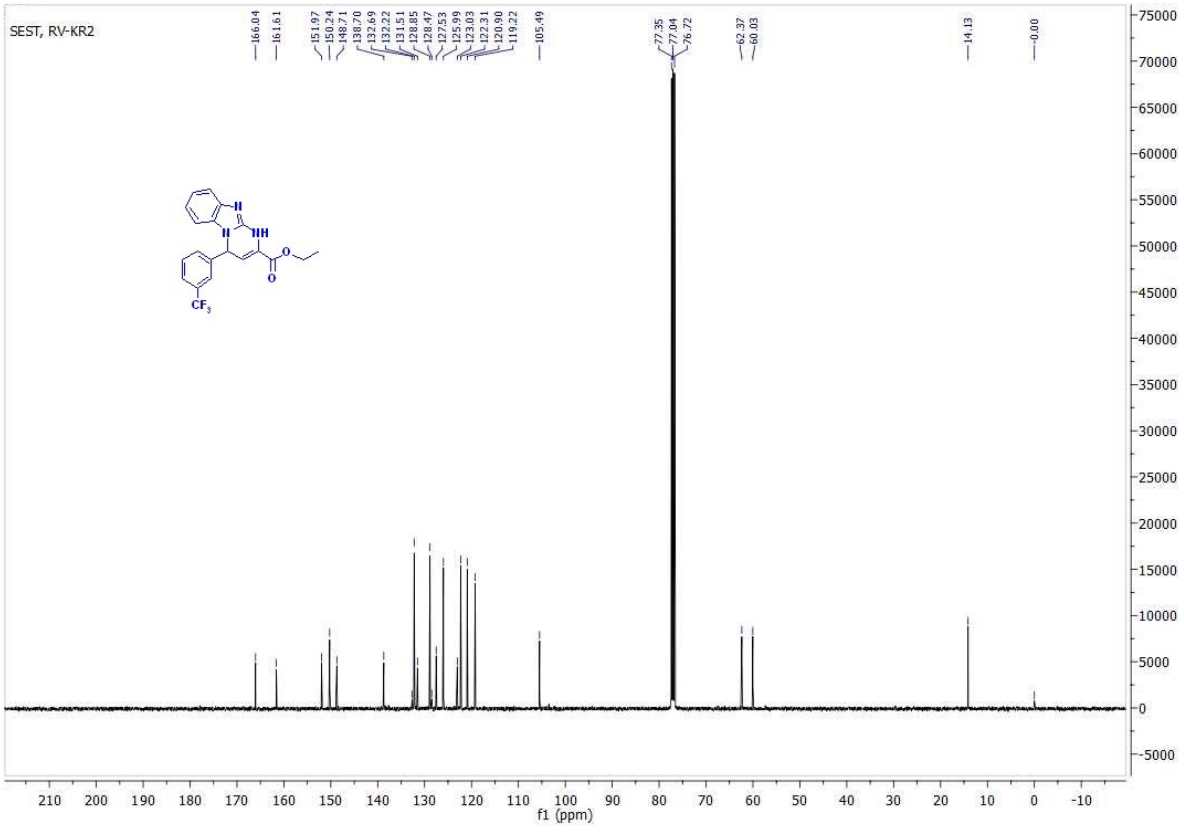
^{13}C NMR for compound 3j



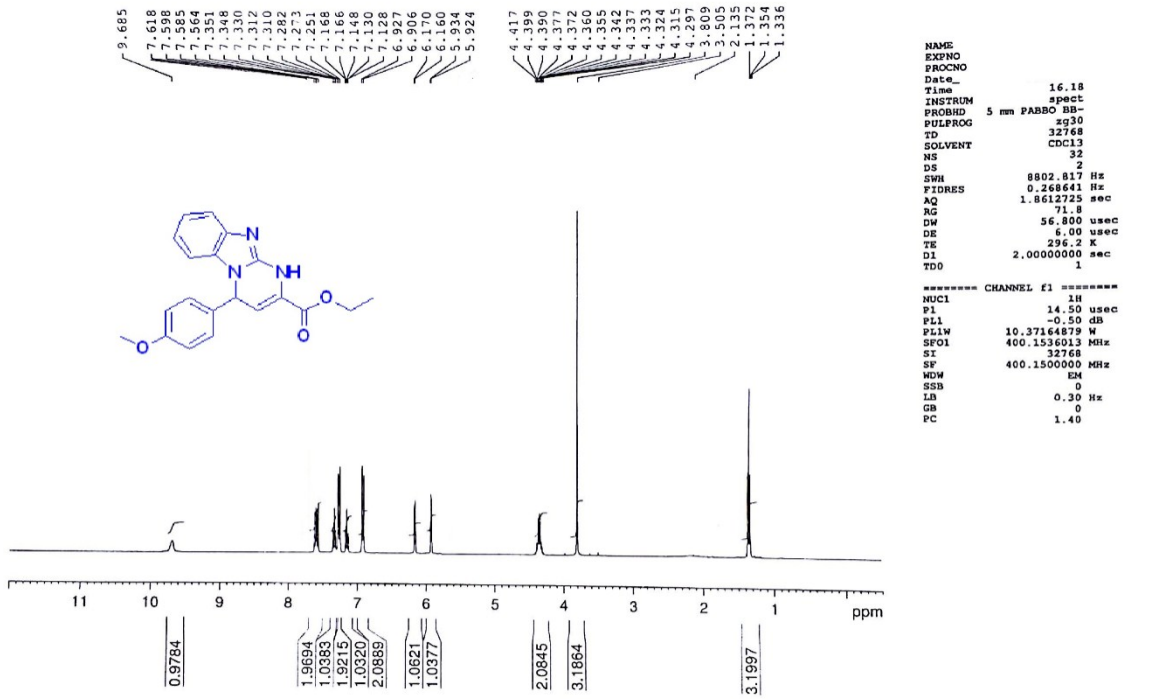
^{1}H NMR for compound 3k



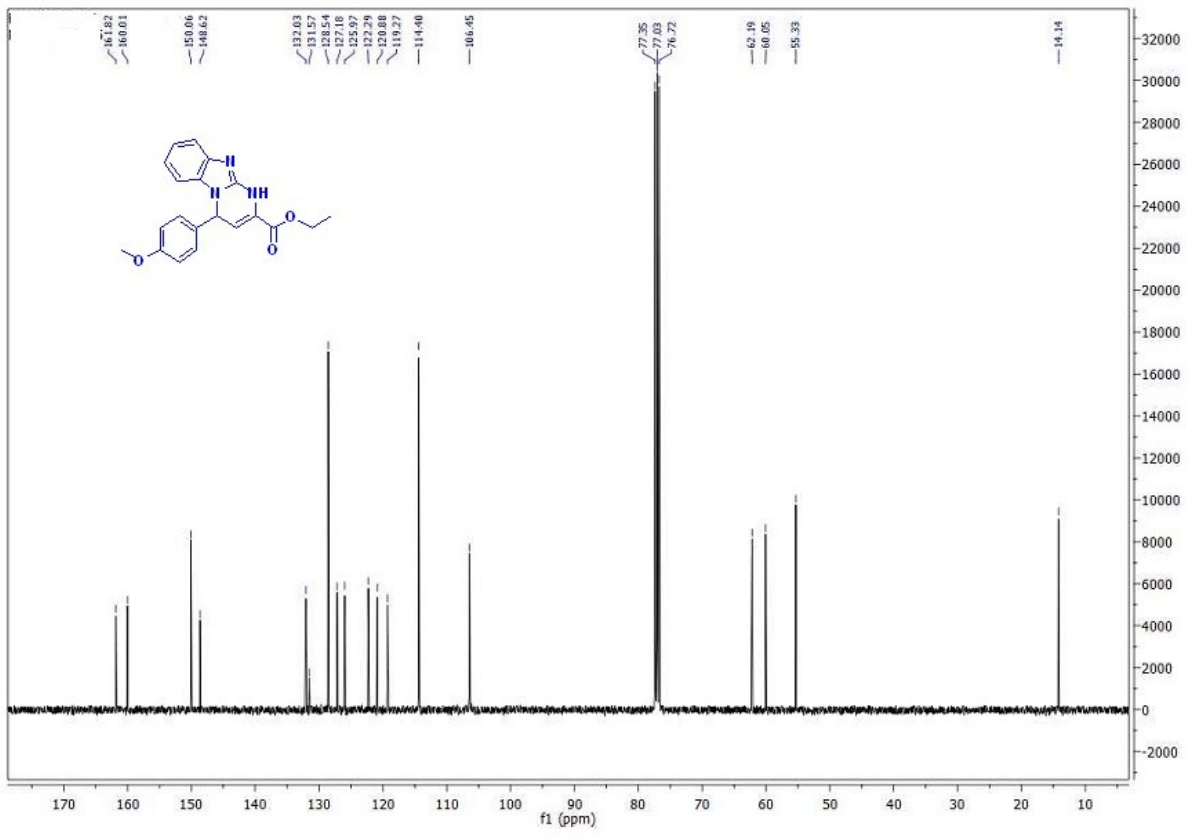
^{13}C NMR for compound 3k



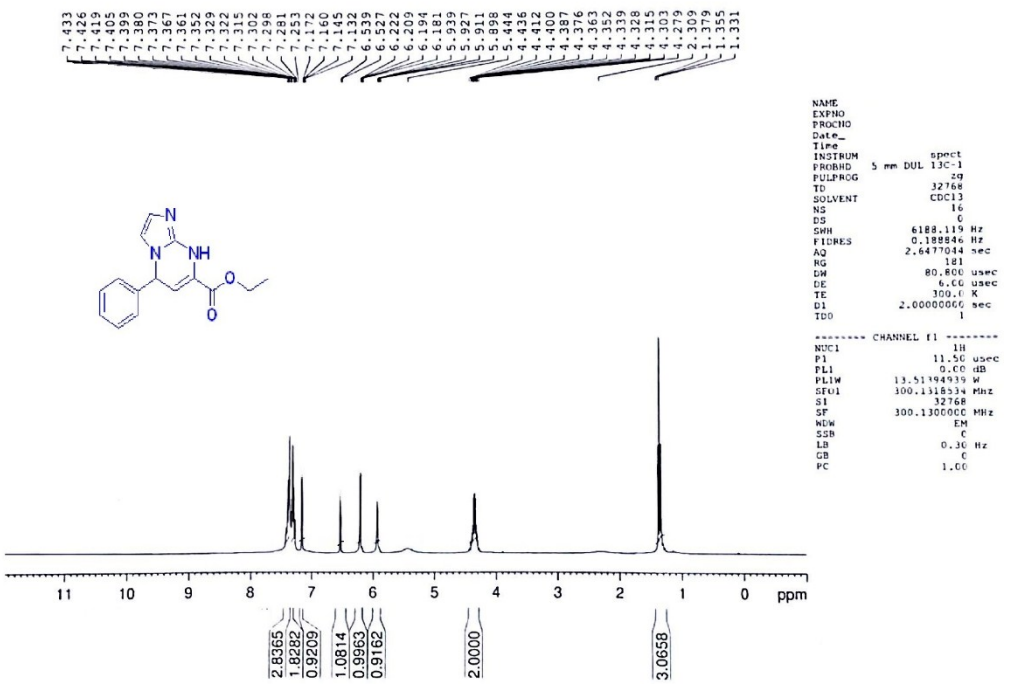
^{1}H NMR for compound 3l



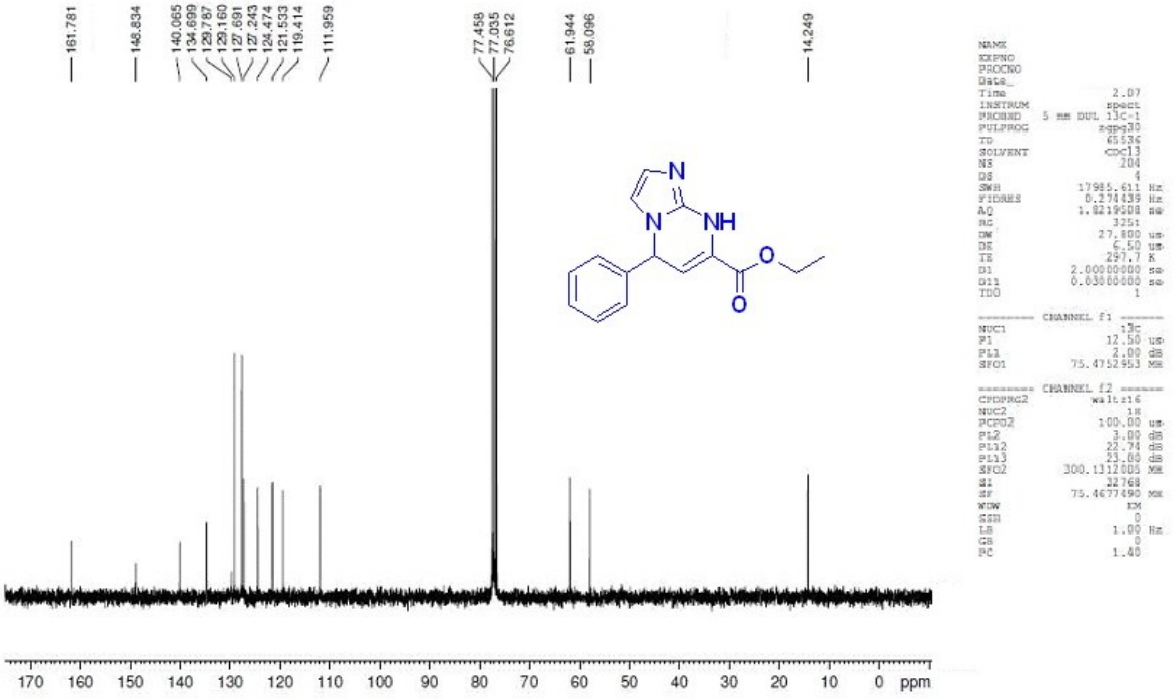
^{13}C NMR for compound 3l



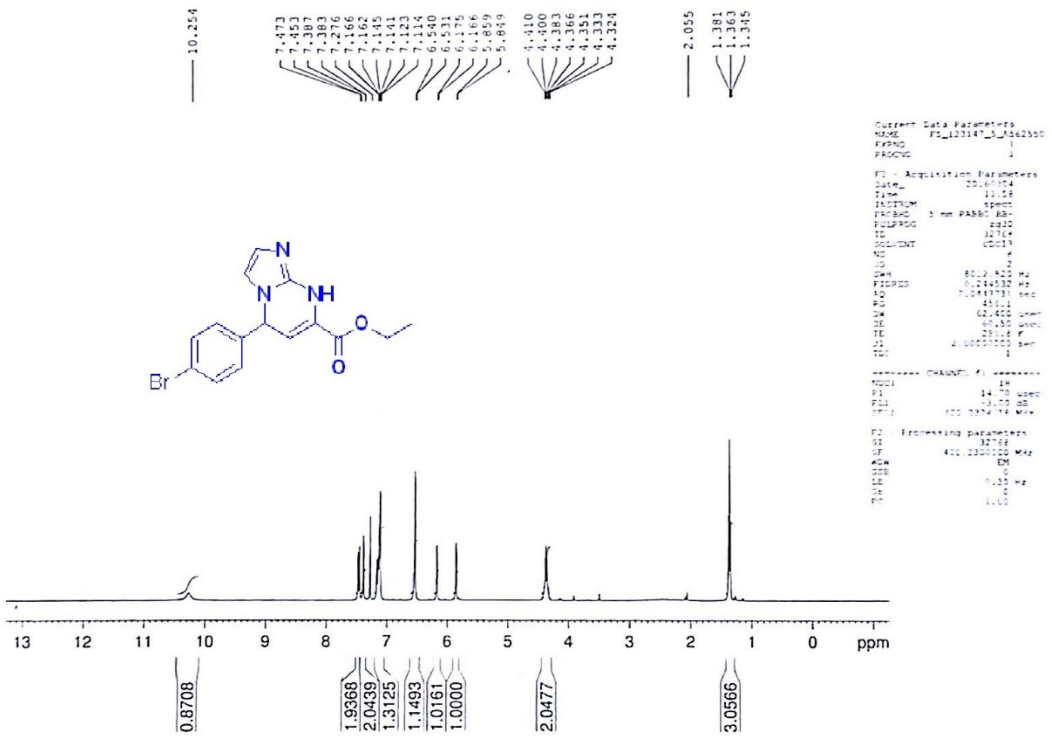
^{1}H NMR for compound 3m



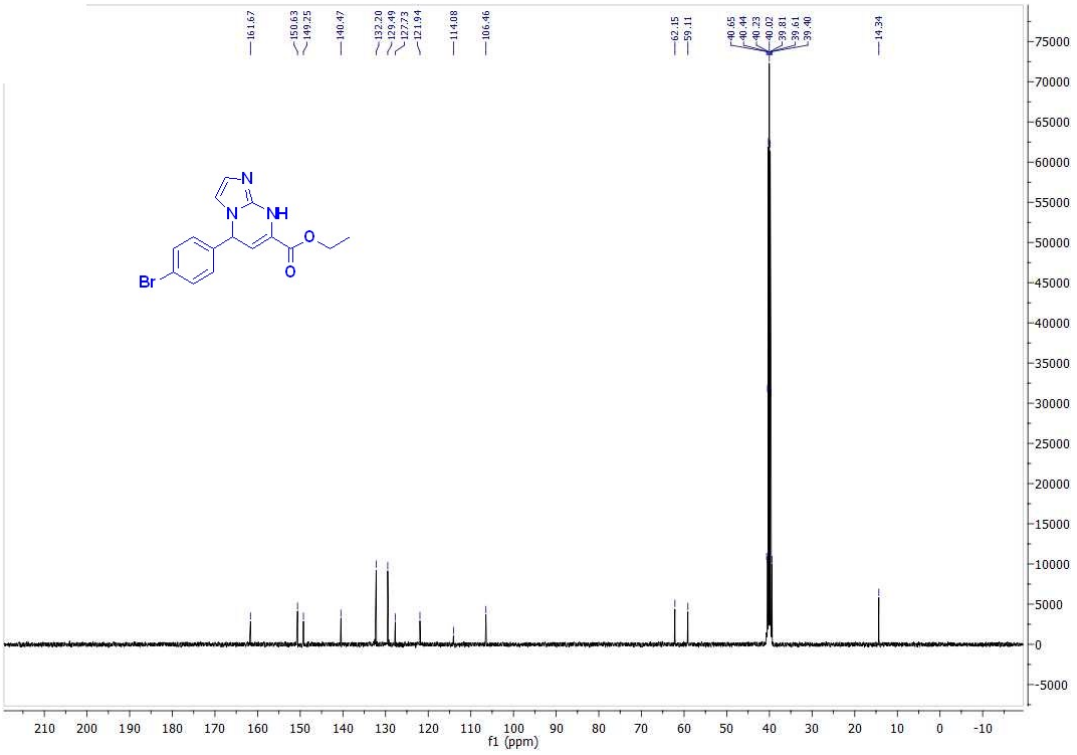
^{13}C NMR for compound 3m



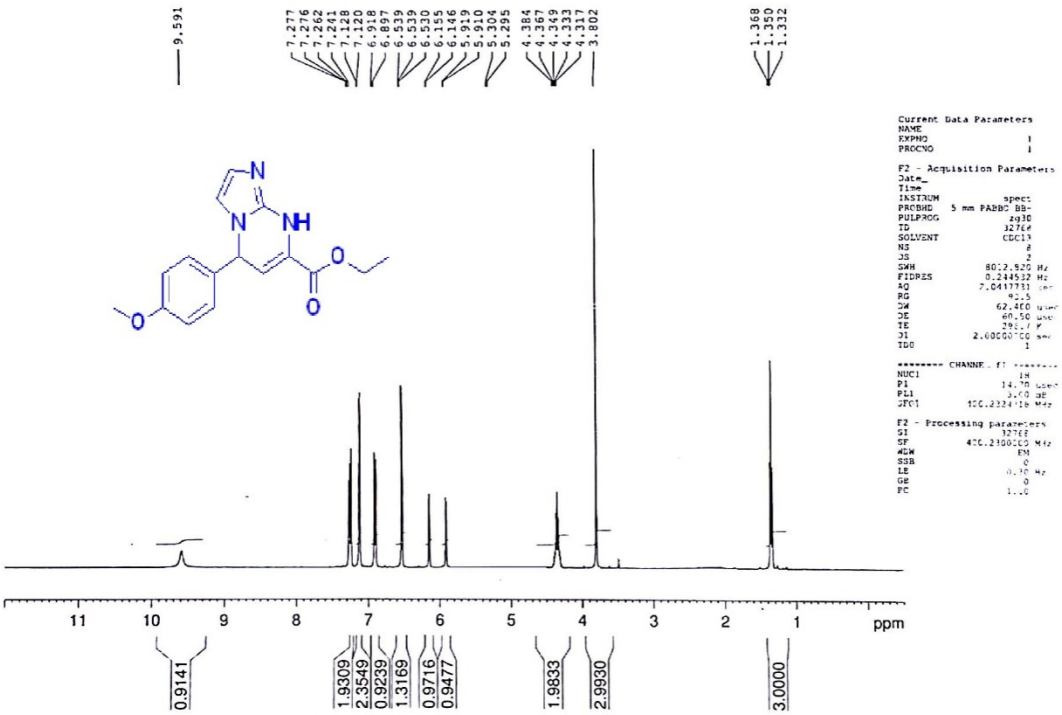
^{1}H NMR for compound 3n



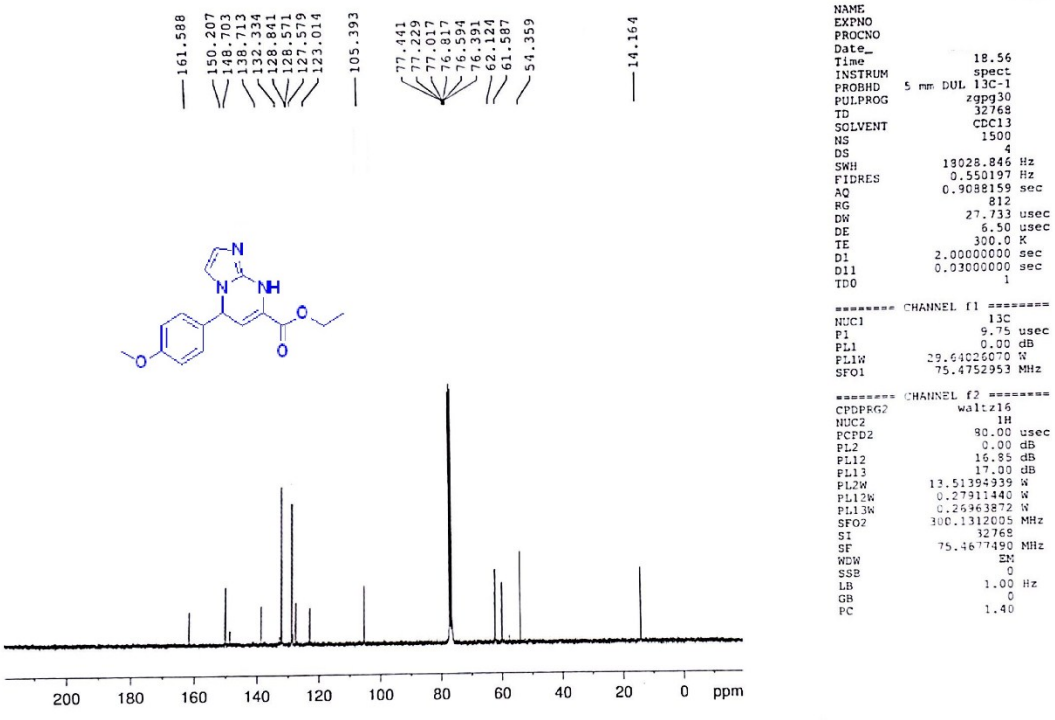
^{13}C NMR for compound 3n



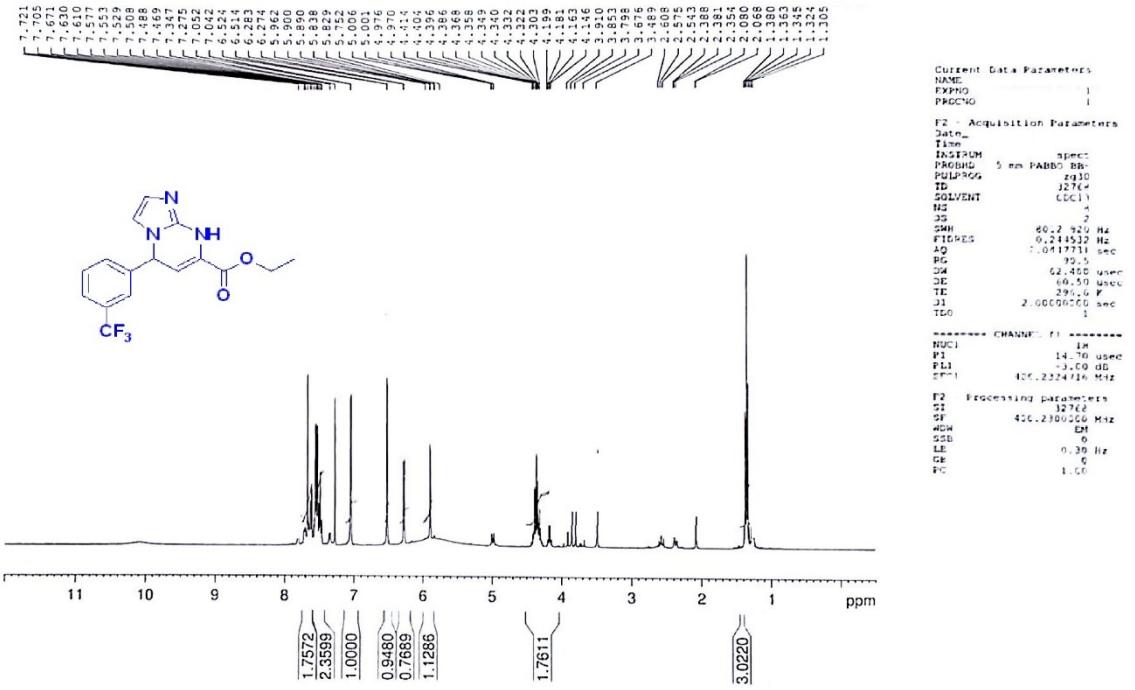
^{1}H NMR for compound 3o



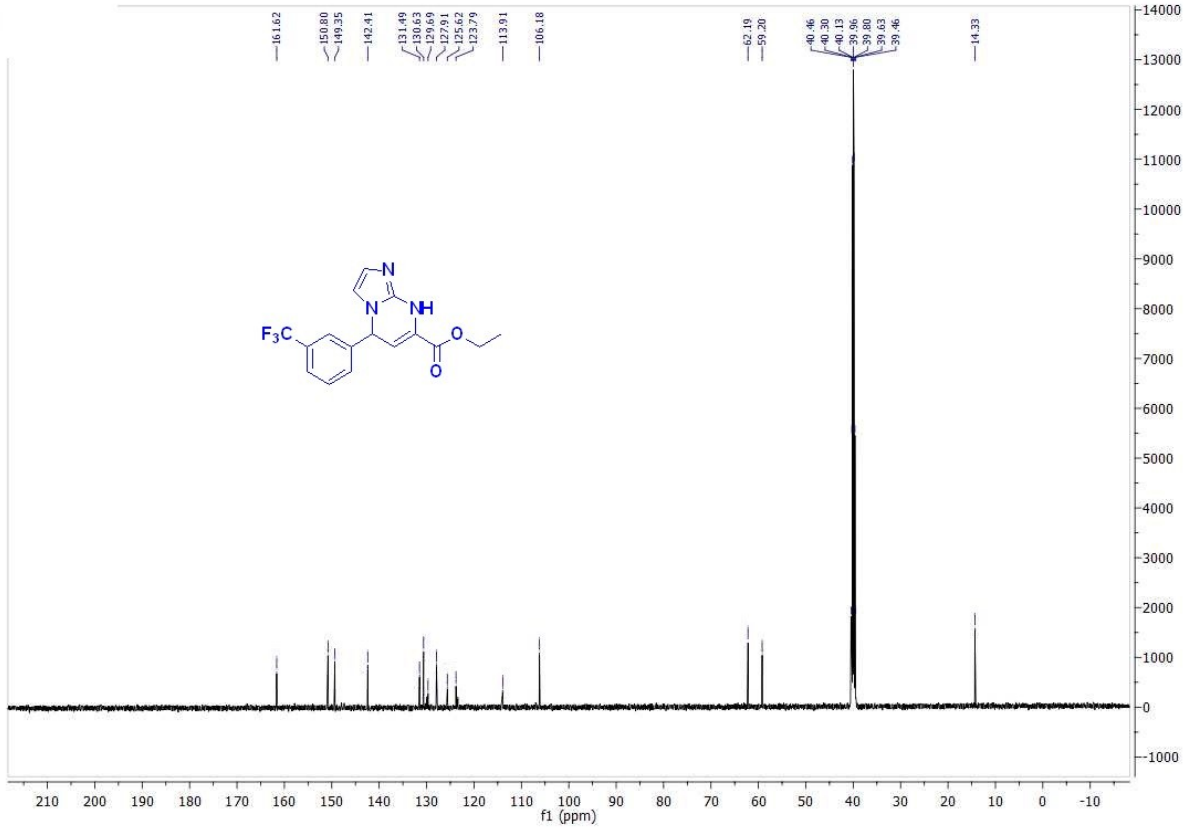
^{13}C NMR for compound 3o



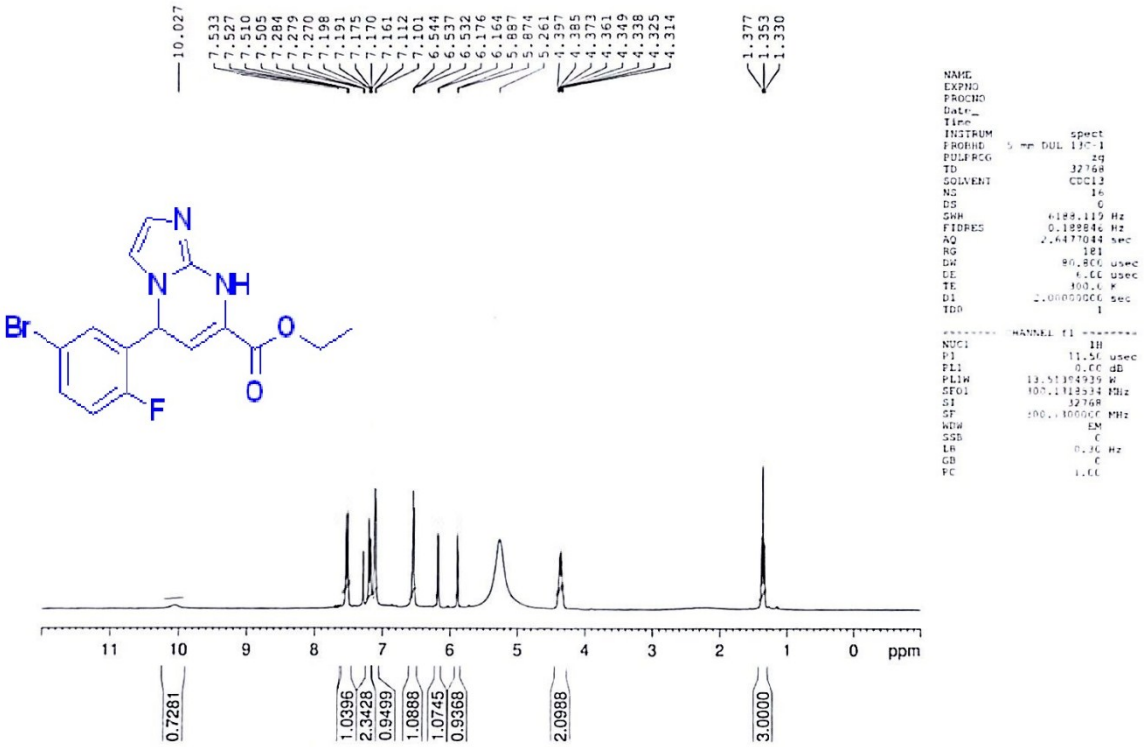
^{1}H NMR for compound 3p



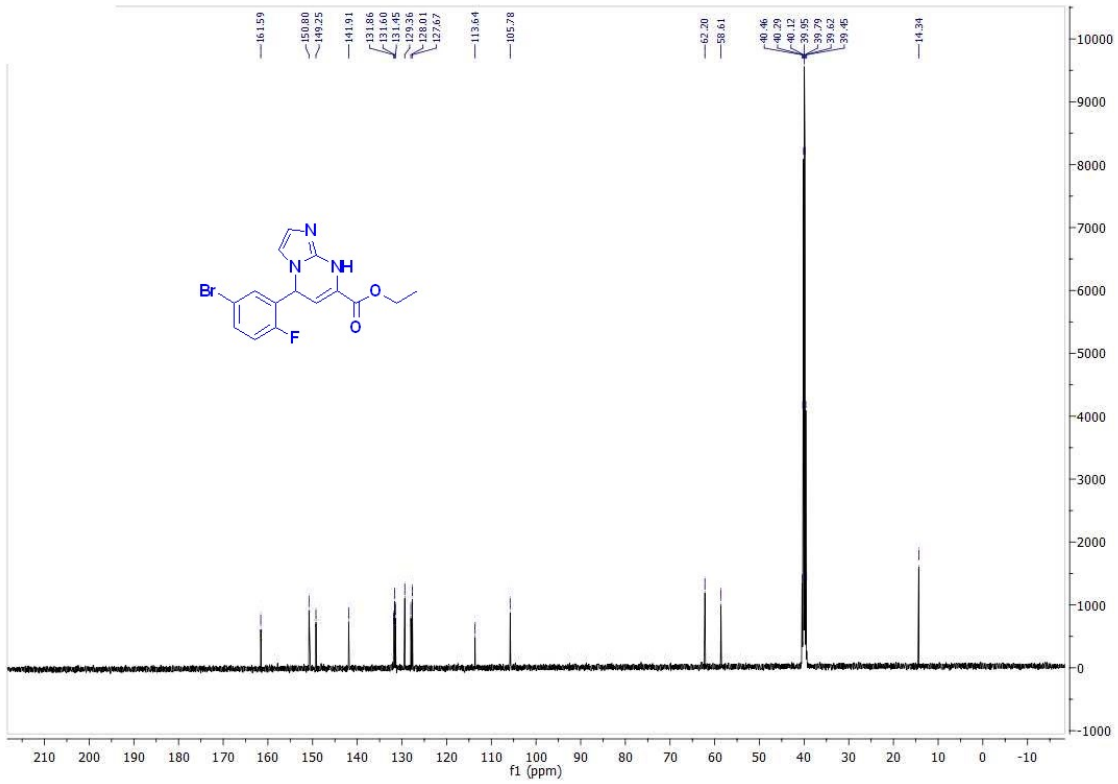
^{13}C NMR for compound 3p



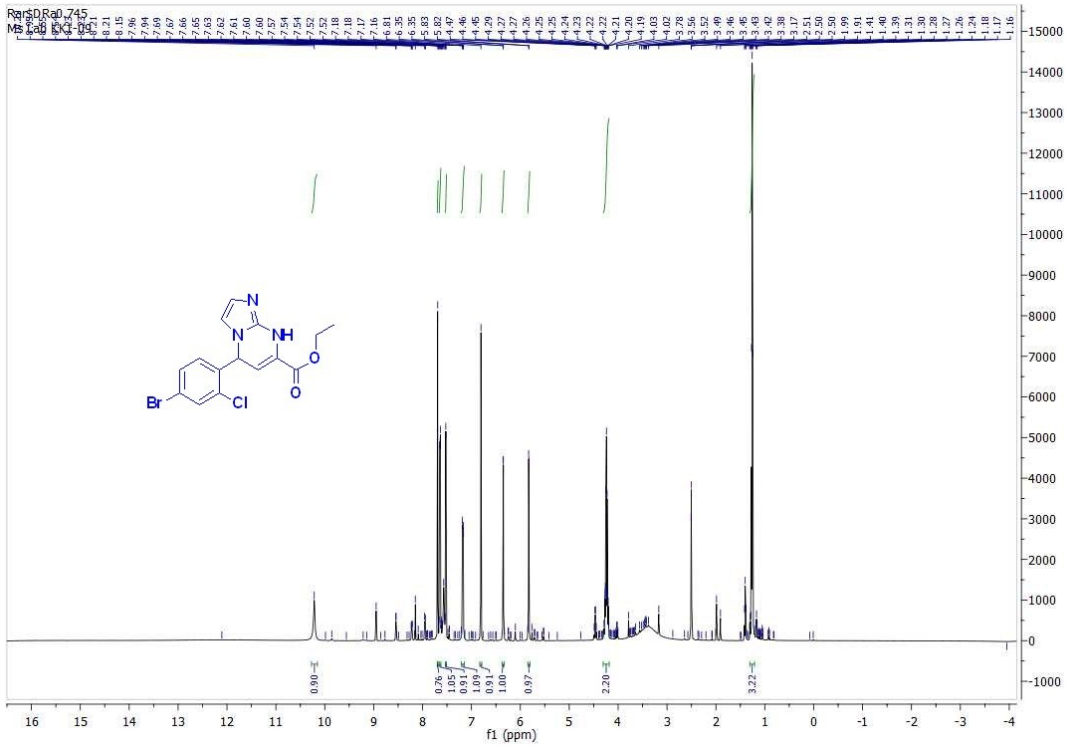
^{1}H NMR for compound 3q



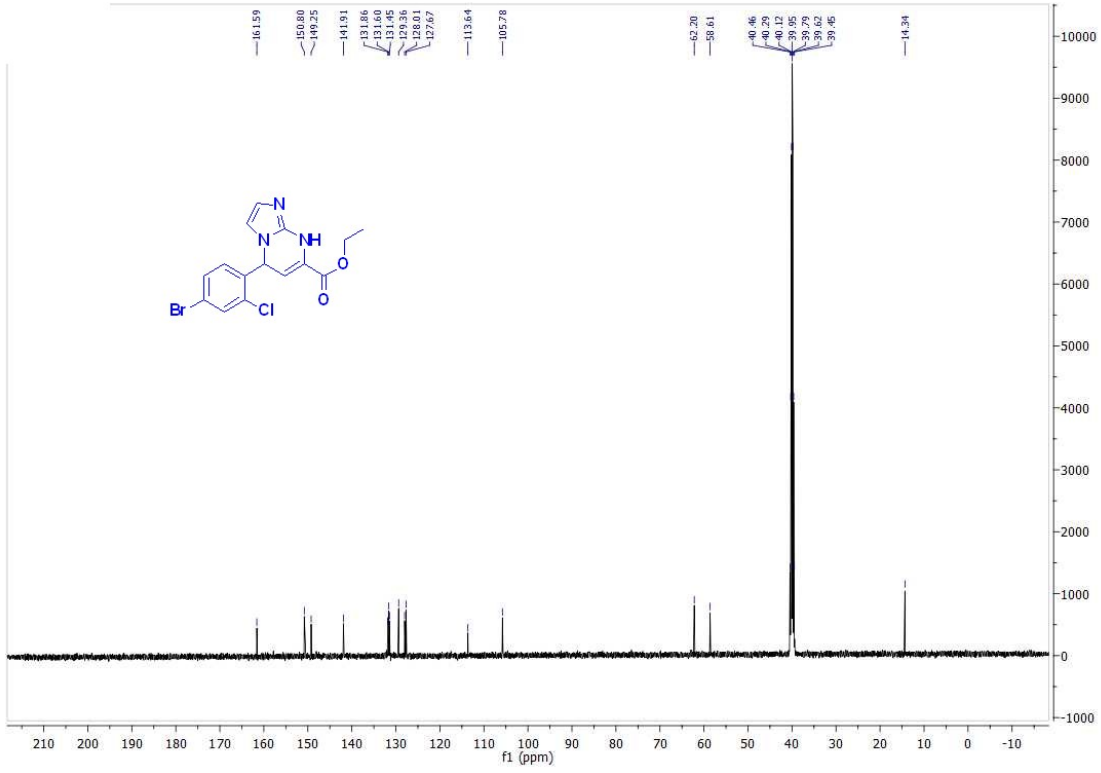
^{13}C NMR for compound 3q



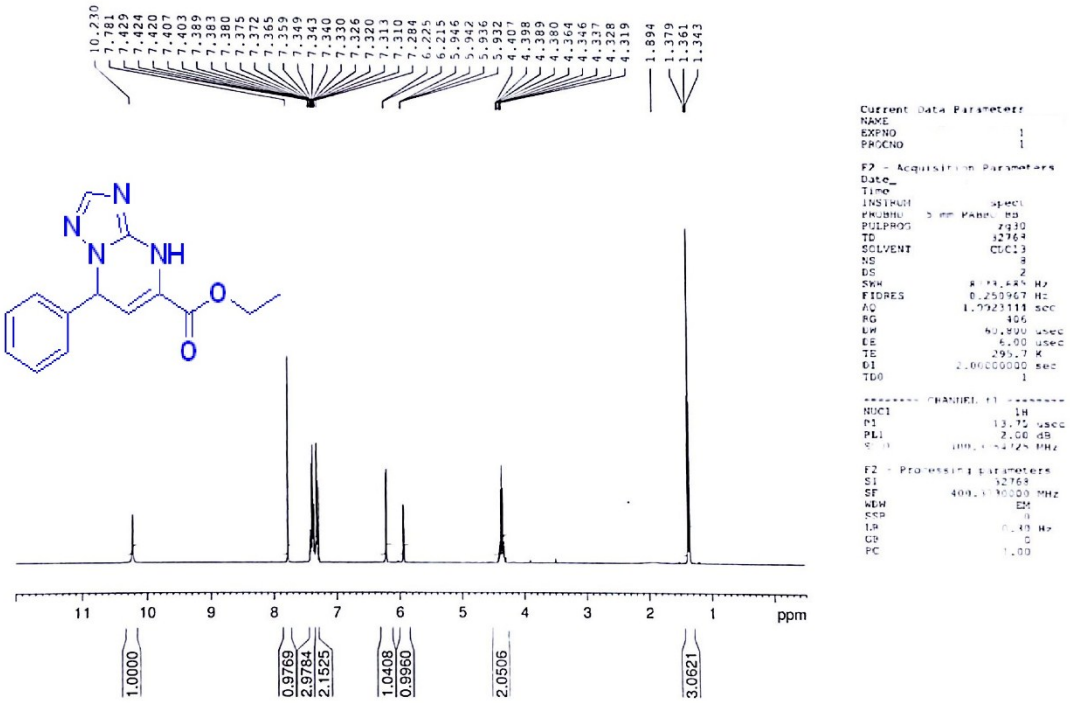
^{1}H NMR for compound 3r



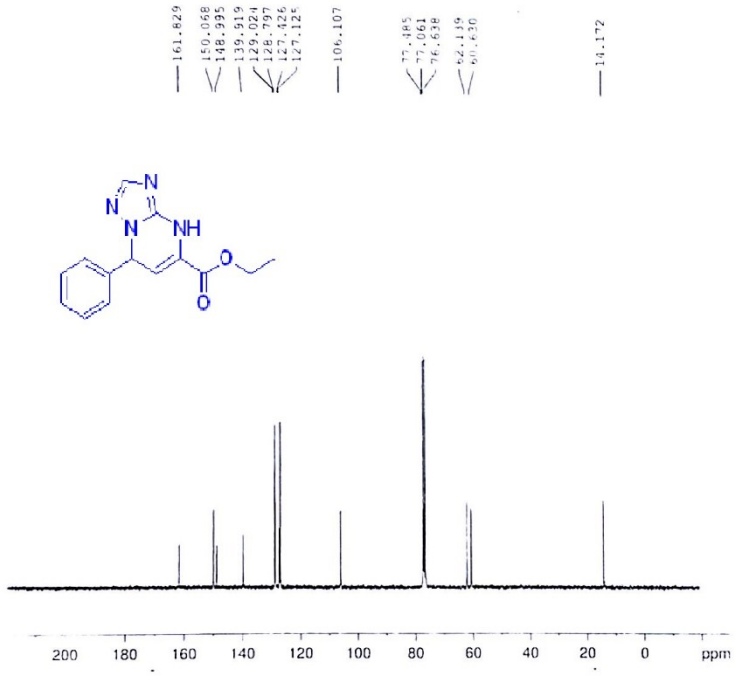
^{13}C NMR for compound 3r



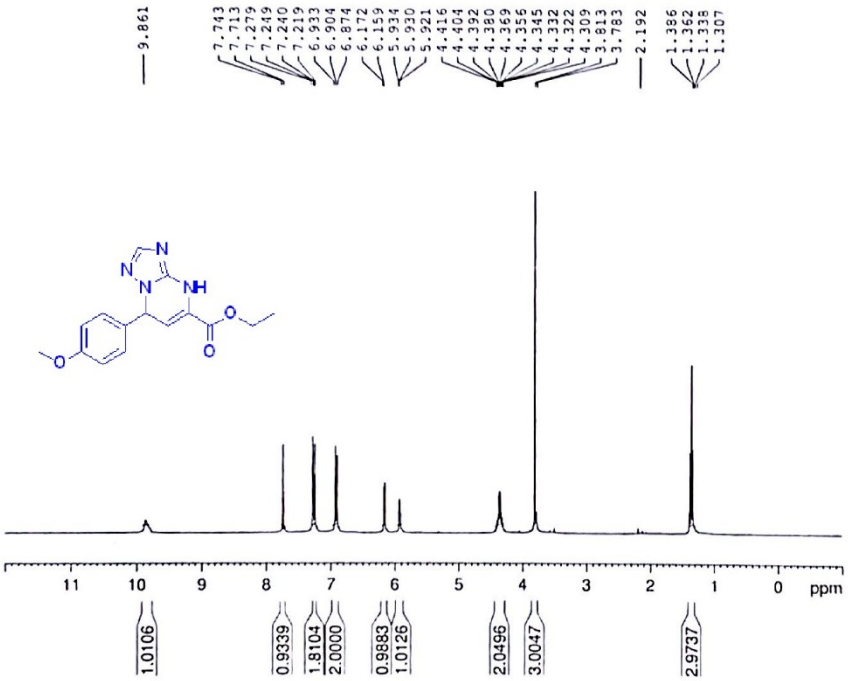
^{1}H NMR for compound 4a



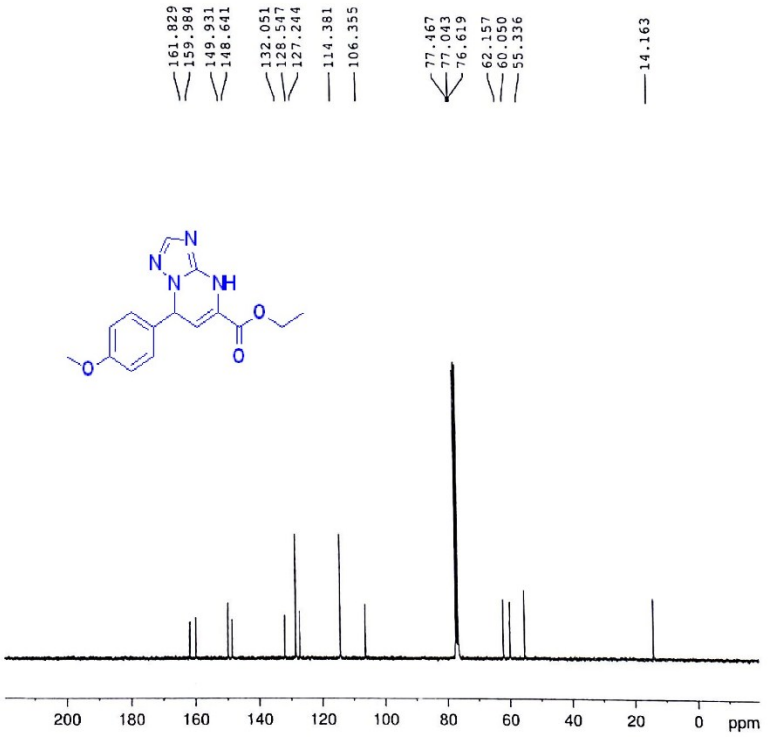
^{13}C NMR for compound 4a



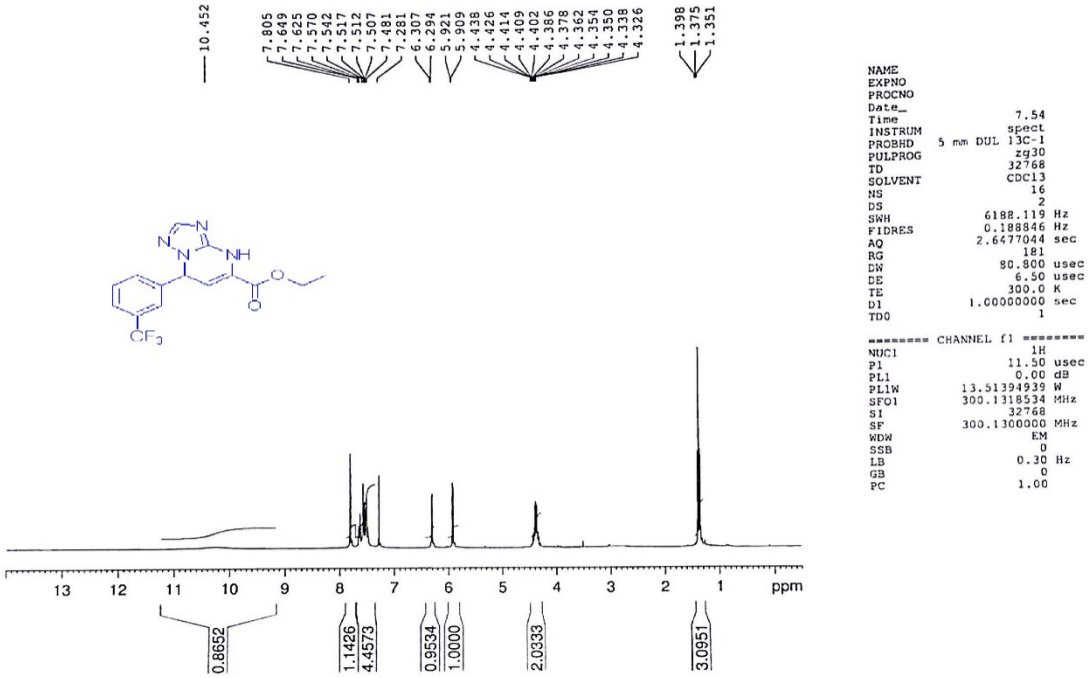
^{1}H NMR for compound 4b



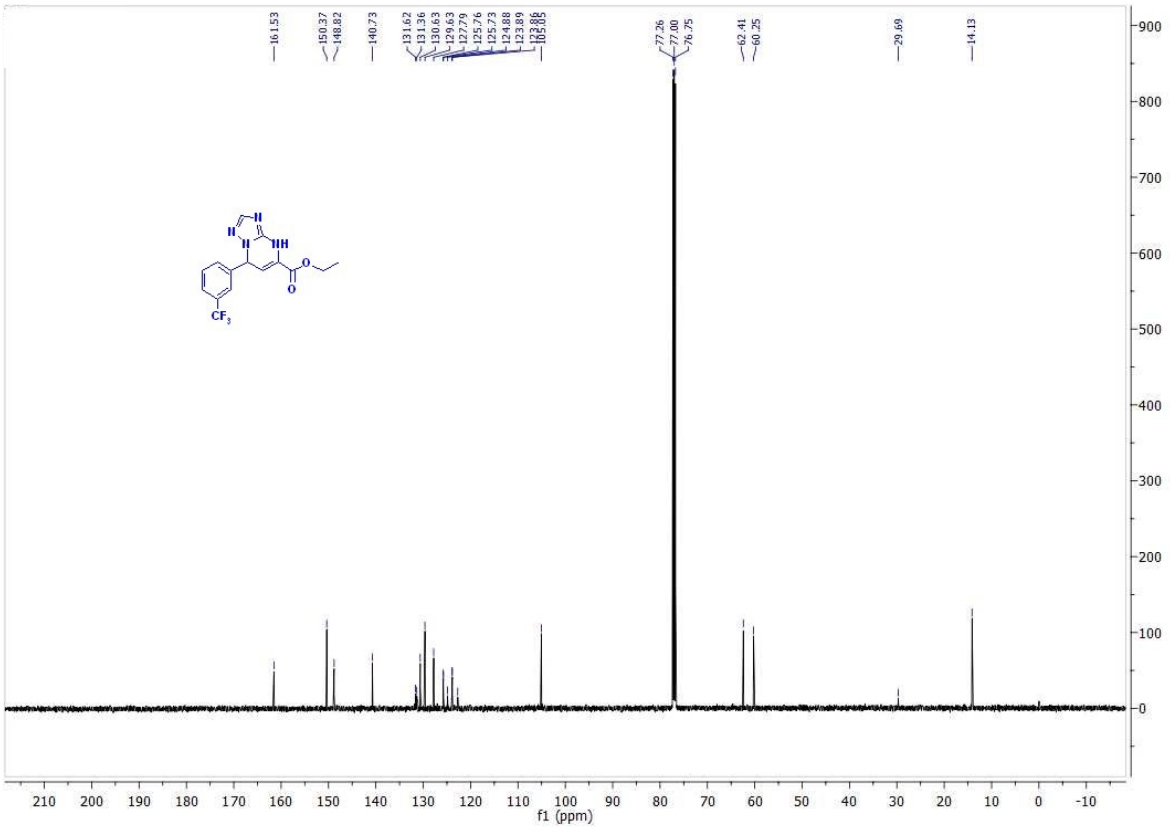
^{13}C for compound 4b



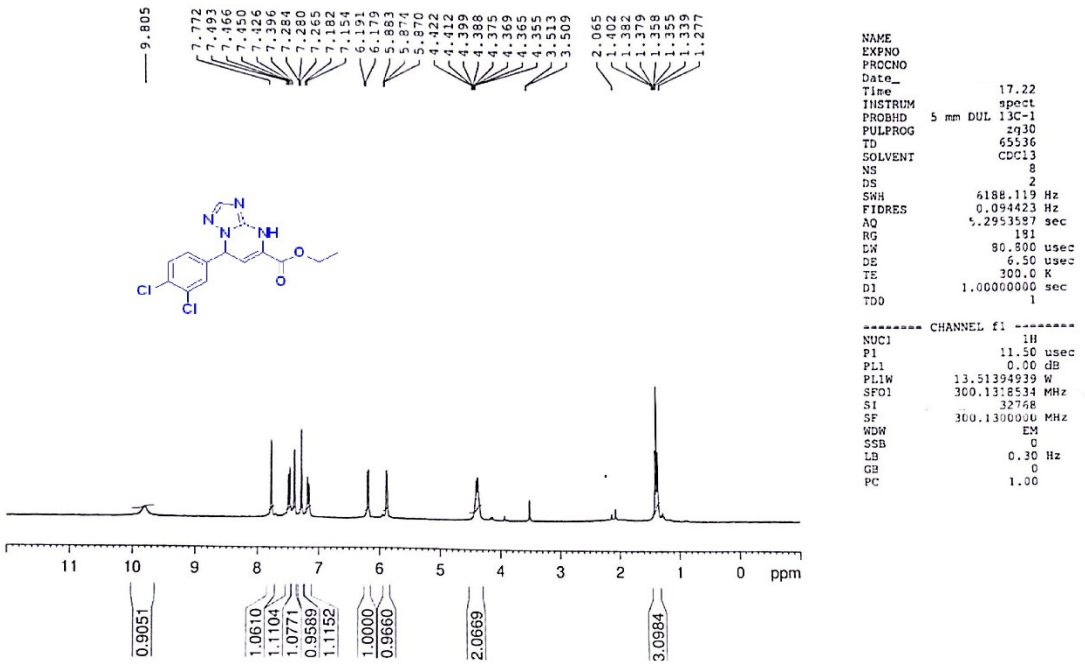
[1]H NMR compound 4c



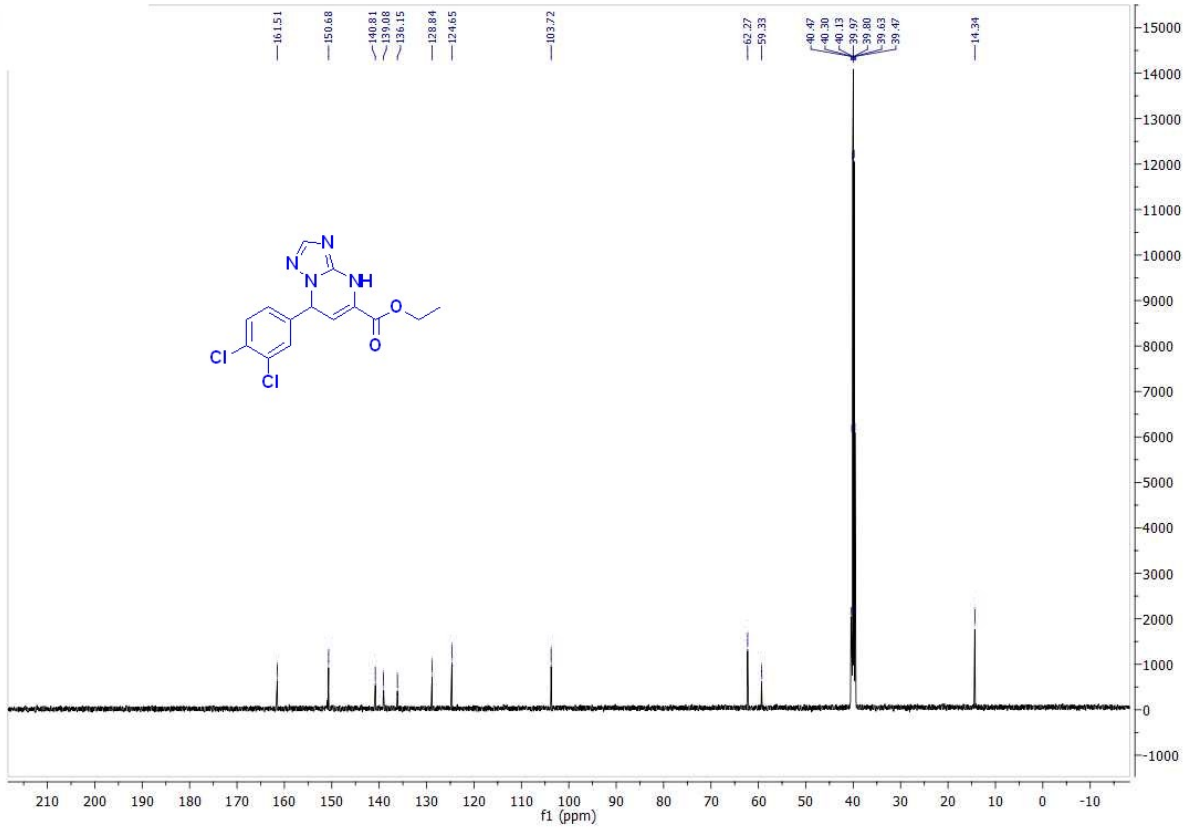
[13]C NMR for compound 4c



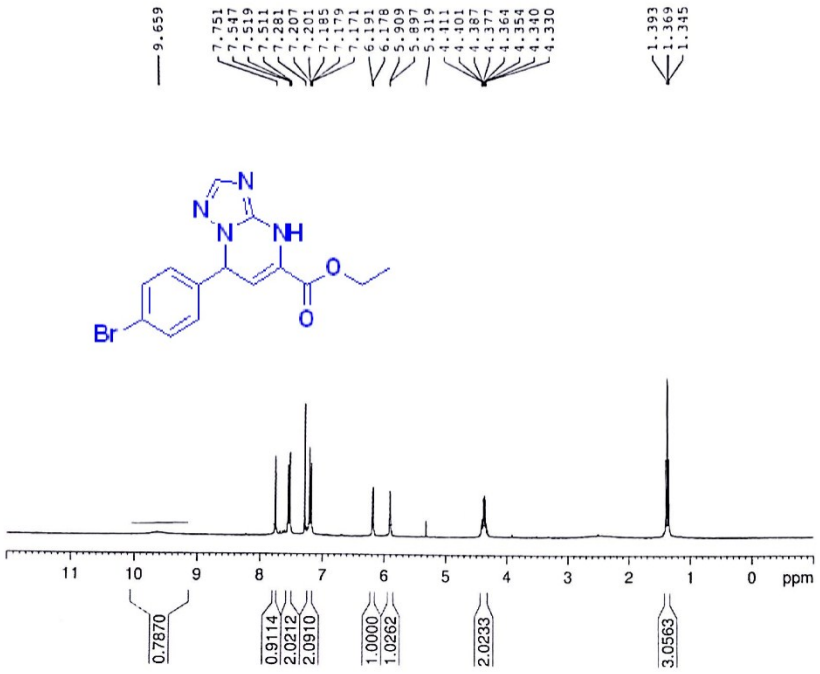
^{1}H NMR for compound 4d



^{13}C NMR for compound 4d



[1]H NMR for compound 4e

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NAME
EXPNO
PROCNO
Date_
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INSTRUM               spect
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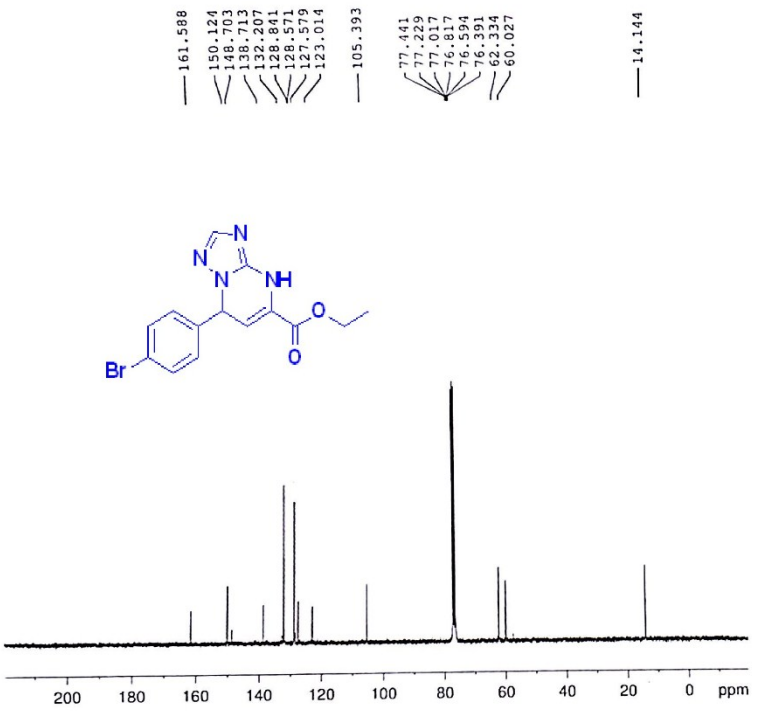
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH                6188.119 Hz
FIDRES                0.094423 Hz
AQ                 5.2953587 sec
RG                     181
DW                  80.800 usec
DE                   6.50 usec
TE                  300.0 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   11.50 usec
PL1                   0.00 dB
PL1W            13.51394939 W
SFO1           300.1318534 MHz
SI                   32768
SF              300.1300000 MHz
WDW                     EM
SSB                      0
LB                    0.30 Hz
GB                       0
PC                    1.00
```

[13]C NMR for compound 4e

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EXPNO
PROCNO
Date_
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INSTRUM               spect
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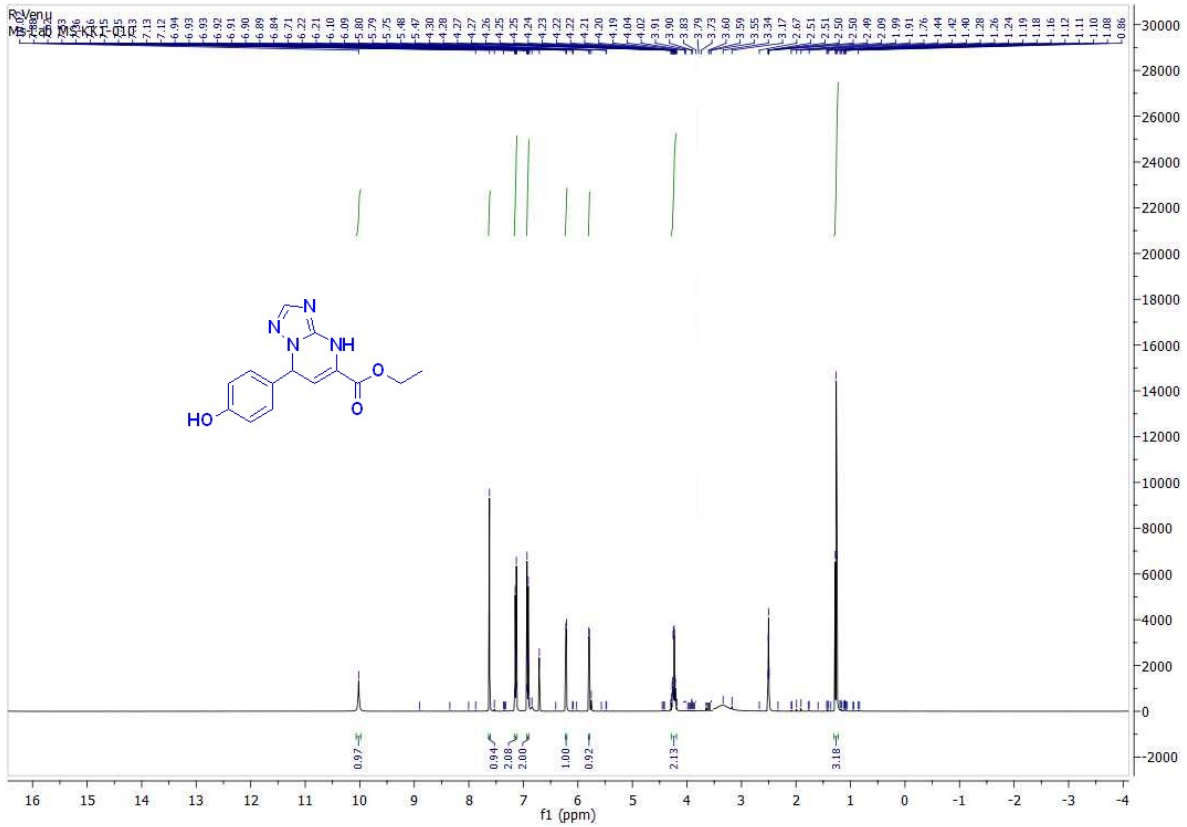
PULPROG             zgpg30
TD                   32768
SOLVENT              CDCl3
NS                    1500
DS                       4
SWH               19028.846 Hz
FIDRES                0.550197 Hz
AQ                 0.9088159 sec
RG                     812
DW                  27.733 usec
DE                   6.50 usec
TE                  300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

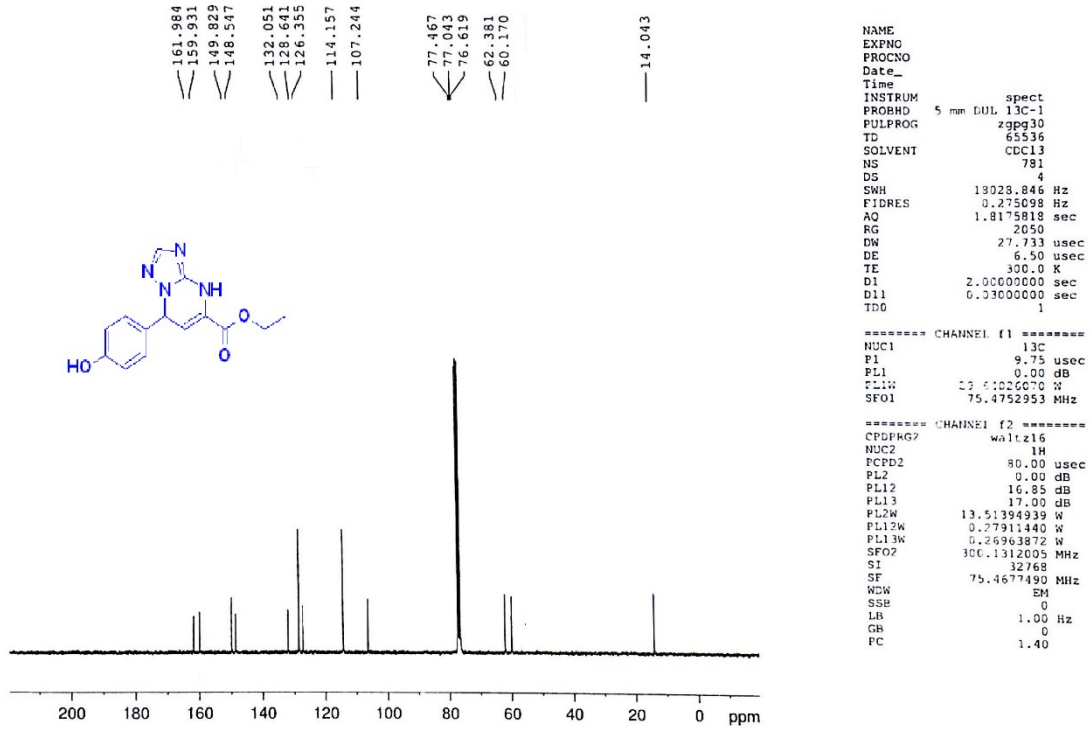
======== CHANNEL f1 ========
NUC1                   13C
P1                    9.75 usec
PL1                   0.00 dB
PL1W            29.64026070 W
SFO1            75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 16.85 dB
PL13                 17.00 dB
PL2W            13.51394939 W
PL12W           0.27911440 W
PL13W           0.26963872 W
SFO2           300.1312005 MHz
SI                   32768
SF              75.4677490 MHz
WDW                     EM
SSB                      0
LB                    1.00 Hz
GB                       0
PC                    1.40
```

^{1}H NMR for compound 4f



^{13}C NMR for compound 4f

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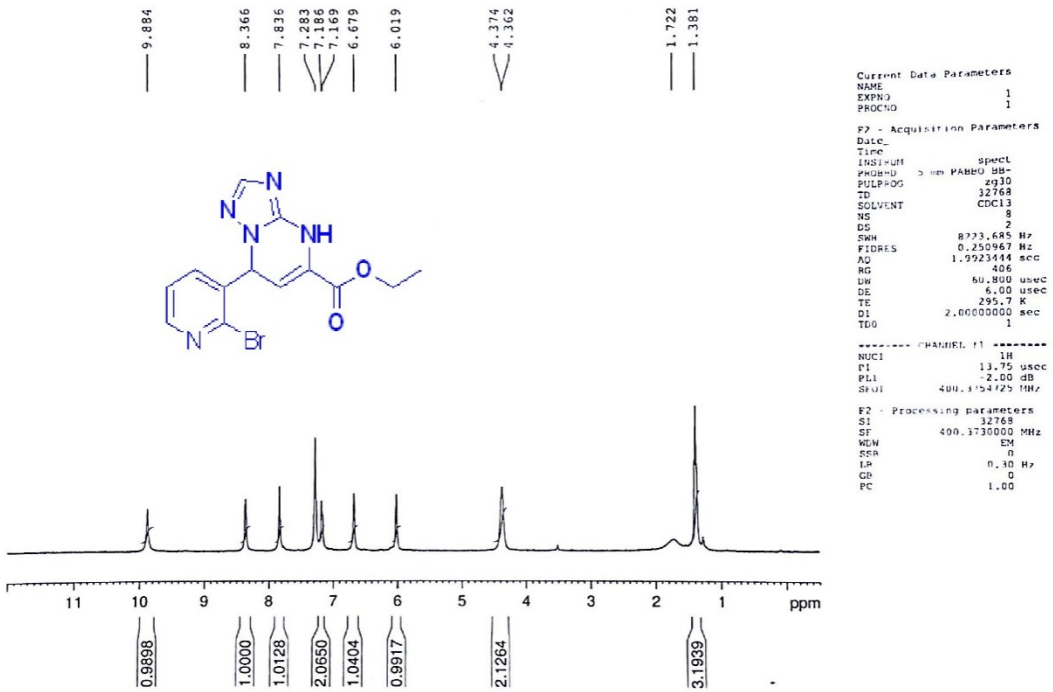
NAME
EXPNO
PROCNO
Date_
Time
INSTRUM                spect
PROBHD     5 mm DUL 13C-1
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      781
DS                        4
SWH               18028.846 Hz
FIDRES            0.275098 Hz
AQ                1.8175818 sec
RG                     2050
DW                  27.733 usec
DE                   6.50 usec
TE                   300.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

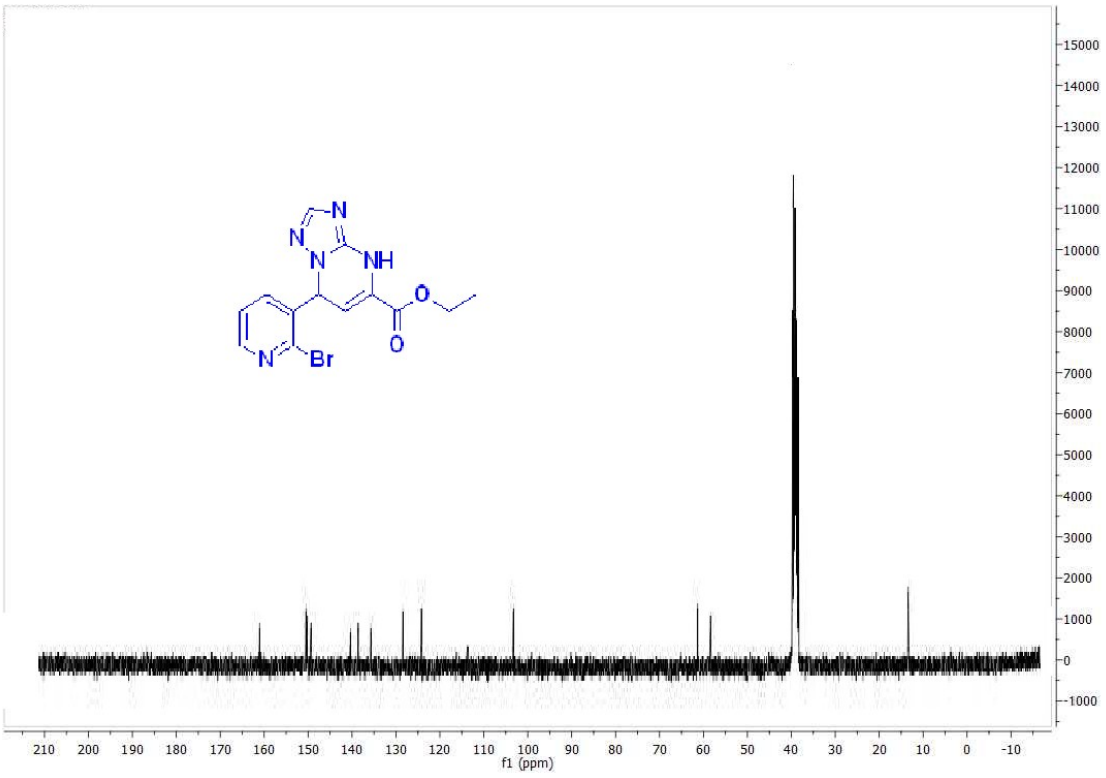
======== CHANNEL f1 ========
NUC1                    13C
P1                    9.75 usec
PL1                   0.00 dB
PLW1            33.51026070 W
SFO1            75.4752953 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   0.00 dB
PL12                 16.85 dB
PL13                 17.00 dB
PL2W            13.51394939 W
PL12W           0.27911440 W
PL13W           0.26963872 W
SFO2            300.1312005 MHz
SI                    32768
SF              75.4677490 MHz
WDW                      EM
SSB                       0
LB                     1.00 Hz
GB                        0
PC                     1.40
```

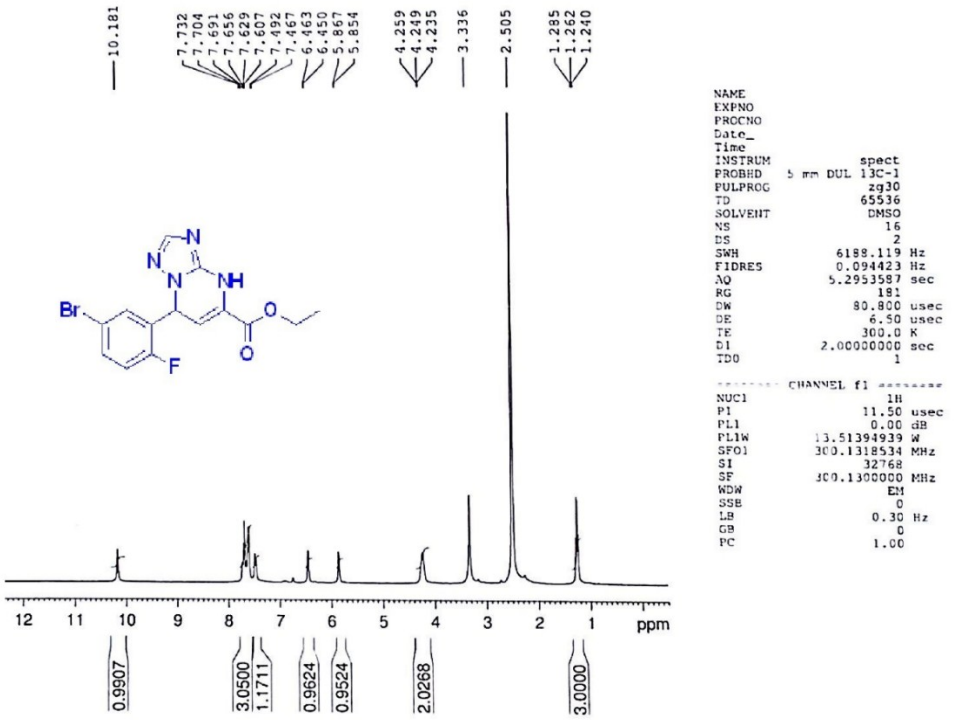
^{1}H NMR for compound 4g



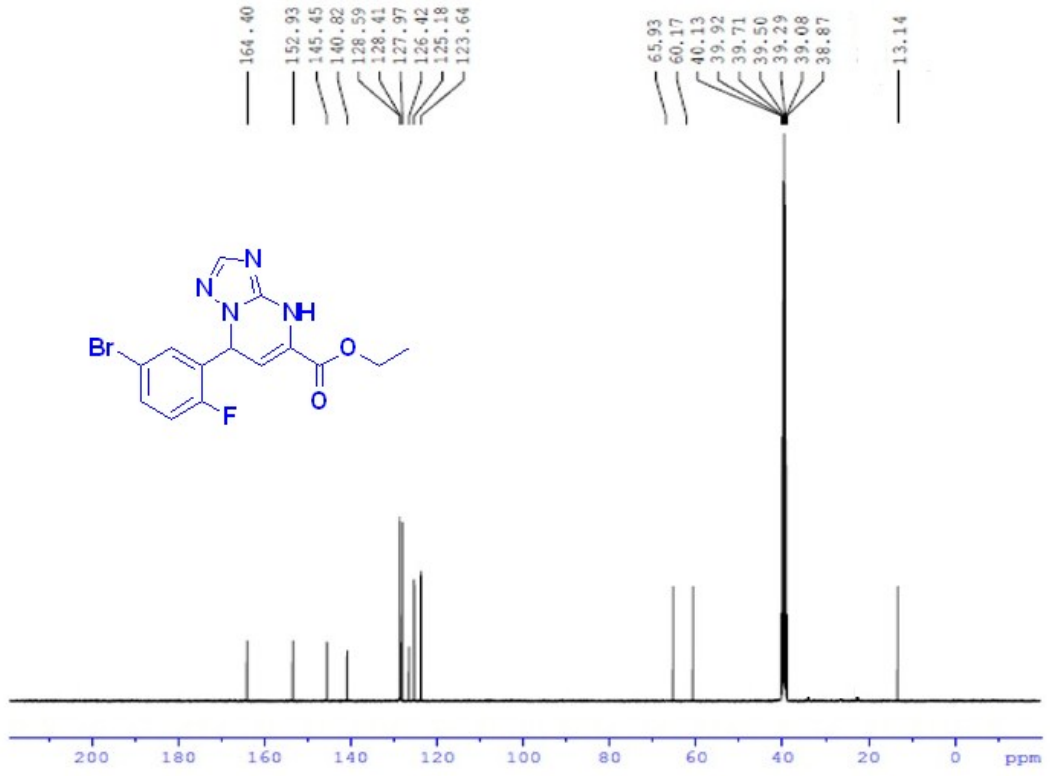
^{13}C NMR for compound 4g



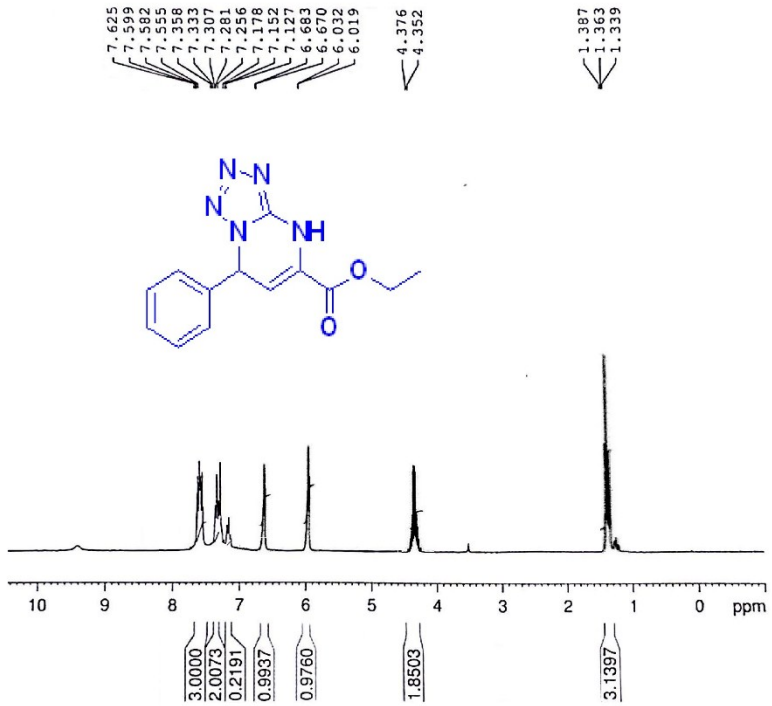
^{1}H ^{1}NMR for compound 4h



^{13}C NMR for compound 4h (DMSO-*d6*)



[1]H NMR for compound 5a

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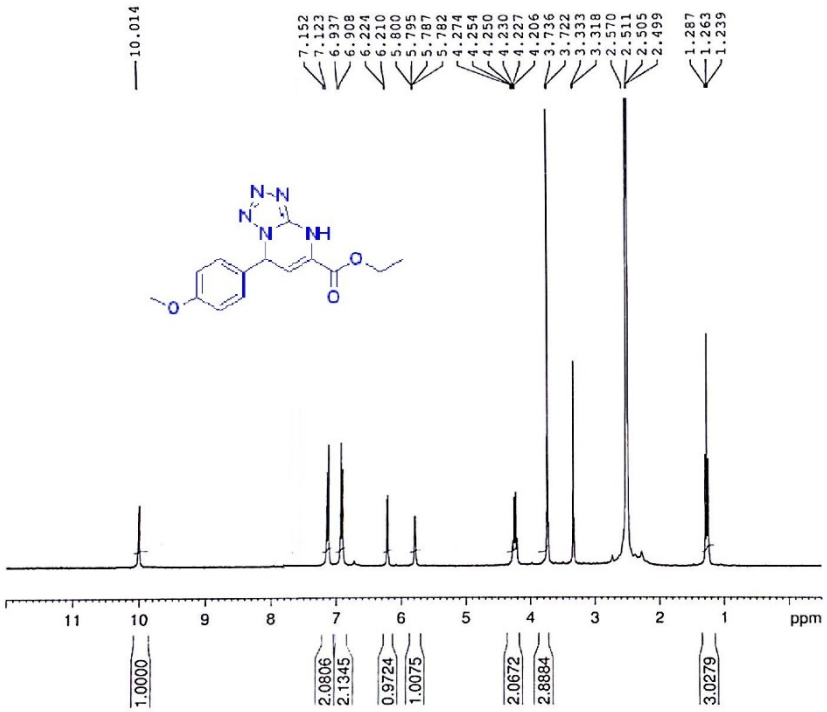
NAME
EXPNO
PROCNO
Date_
Time                  12.42
INSTRUM               spect
PROBHD     5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH               6188.119 Hz
FIDRES            0.094423 Hz
AQ                5.2953587 sec
RG                     181
DW                80.800 usec
DE                 6.50 usec
TE                 300.0 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                 11.50 usec
PL1                 0.00 dB
PL1W          13.51394939 W
SFO1          300.1318534 MHz
SI                   32768
SF            300.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```

[1]H NMR for compound 5b




```
NAME
EXPNO
PROCNO
Date_
Time
INSTRUM               spect
PROBHD     5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT               DMSO
NS                       8
DS                       2
SWH               6188.119 Hz
FIDRES            0.094423 Hz
AQ                5.2953587 sec
RG                     181
DW                80.800 usec
DE                 6.50 usec
TE                 300.0 K
D1              2.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                 11.50 usec
PL1                 0.00 dB
PL1W          13.51394939 W
SFO1          300.1318534 MHz
SI                   32768
SF            300.1300000 MHz
WDW                    EM
SSB                     0
LB                 0.30 Hz
GB                      0
PC                 1.00
```