SUPPORTING INFORMATION TO

Three-component reaction of β-keto esters, aromatic aldehydes and urea/ thiourea promoted by caffeine: a green and naturally biodegradable catalyst for eco-safe Biginelli synthesis of 3, 4-dihydropyrimidin-2-(1*H*)-ones/tiones derivatives under solvent-free conditions

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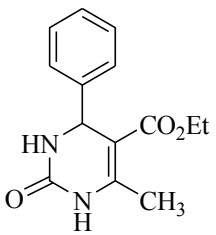
ANALYTICAL AND SPECTRAL DATA FOR THE SYNTHESISED COMPOUNDS

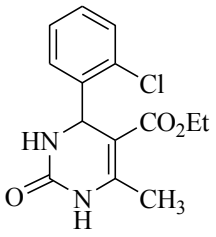
*5-Ethoxycarbonyl-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (**4a**) (Table II, entry 1).*



4a

Yield: 91%; M.p. 198-200 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): 1.10 (3H, t, *J*= 7.2 Hz, $\underline{CH_3}CH_2$), 2.26 (3H, s, CH_3), 3.99 (2H, q, *J*=7.2 Hz, CH_2O), 5.15 (1H, s, $H_{benzylic}$), 7.26 (3H, d, *J*= 7.2 Hz, H_{Ar}), 7.33 (2H, t, *J*=7.2 Hz, H_{Ar}), 7.76 and 9.21 (2H, 2s, 2NH).

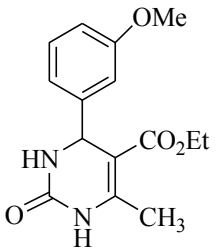
*5- Ethoxycarbonyl -6-methyl -4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1H) –one (**4b**) (Table II, entry 2).*



4b

Yield: 82%; M.p. 221-223 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.00 (3H , t, *J*= 9.2 Hz, $\underline{CH_3}CH_2$), 2.31 (3H, s, CH_3), 4.02 (2H, q, *J*=9.2 Hz, CH_2O), 5.63 (1H, s, $H_{benzylic}$), 7.25-7.34 (3H, m, H_{Ar}), 7.41 (1H, d, *J*=8.8 Hz, H_{Ar}), 7.73 and 9.29(2H, 2s, 2NH).

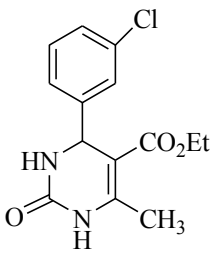
*5-Ethoxycarbonyl -6-methyl -4-(3-methoxyphenyl) -3,4-dihydropyrimidin-2(1H)–one (**4d**) (Table II, entry 4).*



4d

Yield: 84%; M.p.203-205°C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.13 (3H , t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.26(3H, s, CH_3), 3.74 (3H, s, OCH_3), 4.01 (2H, q, *J*=9.6 Hz, CH_2O), 5.13 (1H, s, $H_{benzylic}$), 6.78-6.86 (3H, m, H_{Ar}), 7.26(1H, t, *J*= 10.4Hz, H_{Ar}), 7.76 and 9.20 (2H, 2s, 2NH).

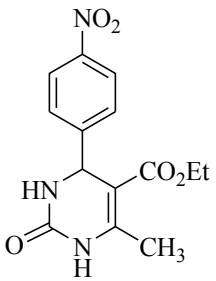
*5-Ethoxycarbonyl-6-methyl-4-(3-chlorophenyl)-3,4-dihydropyrimidin-2(1H)–one (**4f**) (Table II, entry 6).*



4f

Yield: 80%; M.p. 193-195 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.11 (3H , t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.26 (3H, s, CH_3), 4.01 (2H, q, *J*=9.6 Hz, CH_2O), 5.15 (1H, s, CHN), 7.19-7.26 (2H, m, ArH), 7.31-7.41 (2H, m, ArH), 7.83 and 9.30(2H, 2s, 2NH).

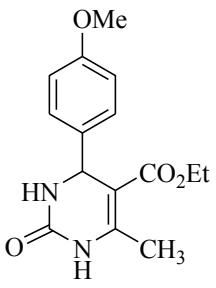
*5-Ethoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4g**) (Table II, entry 7)*



4g

Yield: 84%; M.p.209-210 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.10 (3H, t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.28(3H, s, CH_3), 3.99 (2H, q, *J*=9.6 Hz, CH_2O), 5.27 (1H, s, $H_{benzylic}$), 7.50-7.53 (2H, m, H_{Ar}), 7.23 (2H, d, *J*= 9.2Hz, H_{Ar}), 7.92and 9.38 (2H, 2s, 2NH).

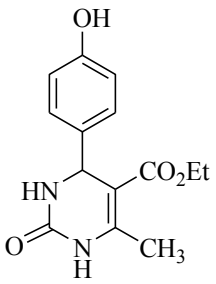
*5-Ethoxycarbonyl -6-methyl -4-(4-methoxyphenyl) -3,4-dihydropyrimidin-2(1H)–one (**4h**) (Table II, entry 8).*



4h

Yield: 87%; M.p.200-202°C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H , t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.24(3H, s, CH_3), 3.73 (3H, s, OCH_3), 3.99 (2H, q, *J*=9.6 Hz, CH_2O), 5.09 (1H, s, $H_{benzylic}$), 6.89 (2H, d, *J*= 8.4Hz, H_{Ar}), 7.15(2H, d, *J*= 8.8Hz, H_{Ar}), 7.70 and 9.18 (2H, 2s, 2NH).

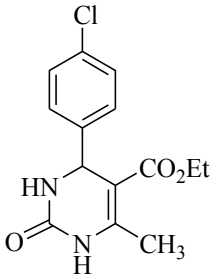
*5- Ethoxycarbonyl -6-methyl-4-(4-hydroxyphenyl)-3,4- dihydropyrimidin-2(1H)–one (**4i**) (Table II, entry 9).*



4i

Yield: 79%; M.p. 230-231 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H , t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.50 (3H, s, CH_3), 3.98 (2H, q, *J*=9.6 Hz, CH_2O), 5.04 (1H, s, $H_{benzylic}$), 6.68-7.04(4H, m, H_{Ar}), 7.64 and 9.13(2H, 2s, 2NH), 9.35 (1H, s, OH).

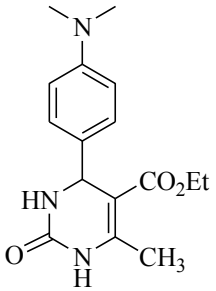
*5-Ethoxycarbonyl-6-methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)–one (**4j**) (Table II, entry 10).*



4j

Yield: 81%; M.p. 215-217 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.10 (3H , t, *J*= 9.2 Hz, $\underline{CH_3}CH_2$), 2.26 (3H, s, CH_3), 4.00 (2H, q, *J*=9.2 Hz, CH_2O), 5.14 (1H, s, CHN), 7.25 (2H, d, *J*= 11.2 Hz, ArH), 7.41 (2H, d, *J*= 11. 2 Hz, ArH), 7.79 and 9.27(2H, 2s, 2NH).

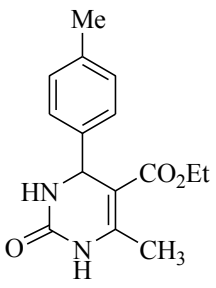
*5-Ethoxycarbonyl-6-methyl-4-(N,N-Dimethylphenyl)-3,4-dihydropyrimidin-2(1H)-one (**4k**) (Table II, entry 11).*



4k

Yield: 87%; M.p. 257-259 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.12 (3H, t, *J*= 9.2 Hz, $\underline{CH_3}CH_2$), 2.26 (3H, s, CH_3), 2.85 (6H, s, $2CH_3$), 3.99 (2H, q, *J*=9.2 Hz, CH_2O), 5.04 (1H, s, CHN), 6.66 (2H, d, *J*=11.6 Hz, ArH), 7.42 (2H, d, *J*=11.6Hz, ArH), 7.61 and 9.11 (2H, 2s, 2NH).

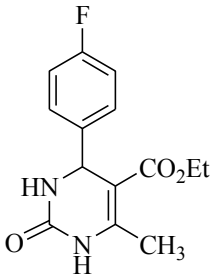
*5-Ethoxycarbonyl-6-methyl-4-(4-methylphenyl)-3,4-dihydropyrimidin-2(1H)-one (**4l**) (Table II, entry 12).*



4l

Yield: 88%; M.p. 204-206 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H, t, *J*= 7.2 Hz, $\underline{CH_3}CH_2$), 2.25 (3H, s, CH_3), 2.27 (3H, s, CH_3), 3.99 (2H, q, *J*=7.2 Hz, CH_2O), 5.11 (1H, s, CHN), 7.13 (4H, s, ArH), 7.70 and 9.17 (2H, 2s, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6): 14.0 ($\underline{CH_3}$-CH_2O), 17.6 (CH_3-CH=CH), 21.1 (CH_3), 53.7 (Ar-CHN), 59.1 (CH_3-$\underline{CH_2}O$), 99.2, 123.3 (CH_3-CH=CH), 126.8, 127.8, 128.2, 137.3, 144.7 and 148.0 (C_{Ar}), 151.9 (C=ONH), 165.3 (C=O ester).

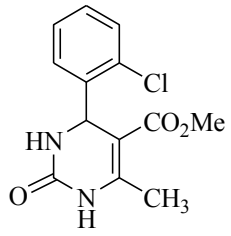
*5-Ethoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3,4-dihydropyrimidin-2(1H)–one (**4m**) (Table II, entry 13).*



4m

Yield: 93%; M.p. 172-174 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.11 (3H , t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.25(3H, s, CH_3), 3.99 (2H, q, *J*=9.6 Hz, CH_2O), 5.14 (1H, s, CHN), 7.13-7.20 (2H, m, ArH), 7.24-7.29 (2H, m, ArH), 7.78 and 9.25 (2H, 2s, 2NH).

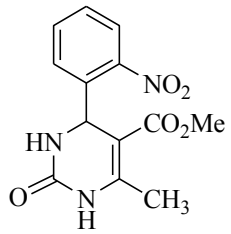
*5-Methoxycarbonyl-6-methyl-4-(2-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4n**) (Table II, entry 14).*



4n

Yield: 84%; M.p. 251-253 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 2.31 (3H, s, CH_3), 3.46 (3H, s, OCH_3), 5.62 (1H, s, $H_{benzylic}$), 7.28-7.34 (3H, m, H_{Ar}), 7.42 (1H, d, *J*=7.2 Hz, H_{Ar}), 7.72 and 9.36(2H, 2s, 2NH).

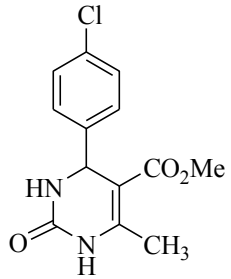
*5-Methoxycarbonyl-6-methyl-4-(2-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4o**) (Table II, entry 15).*



4o

Yield: 92%; M.p. 275-277 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 2.29 (3H, s, CH_3), 3.56 (3H, s, OCH_3), 5.29 (1H, s, $H_{benzylic}$), 7.51-7.53 (2H, m, H_{Ar}), 8.21-8.24 (2H, m, H_{Ar}), 7.93 and 9.40 (2H, 2s, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6): 17.7 (CH_3-CH=CH), 50.7 (Ar-CHN), 53.6 (CO_2-$\underline{CH_3}$), 98.9, 123.2 (CH_3-CH=CH), 126.7, 127.9, 128.3, 137.4, 144.5 and 148.4 (C_{Ar}), 151.9 (C=ONH), 165.8 (C=O ester).

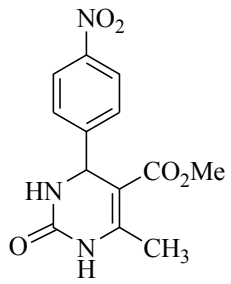
*5-Methoxycarbonyl-6-methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4p**) (Table II, entry 16).*



4p

Yield: 84%; M.p. 206-208 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 2.26 (3H, s, CH_3), 3.55 (3H, s, OCH_3), 5.15 (1H, s, $H_{benzylic}$), 7.25 (1H, d, *J*=11.2 Hz, H_{Ar}), 7.41 (1H, d, *J*=11.2 Hz, H_{Ar}), 7.80 and 9.28 (2H, 2s, 2NH).

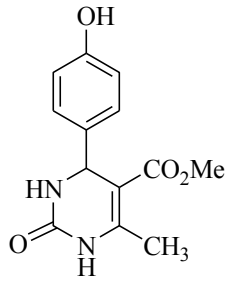
*5-Methoxycarbonyl-6-methyl-4-(4-nitrophenyl)-3,4-dihydropyrimidin-2(1H)-one (**4q**) (Table II, entry 17).*



4q

Yield: 89%; M.p. 215-217 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 2.28(3H, s, CH_3), 3.55 (3H, s, OCH_3), 5.28 (1H, s, $H_{benzylic}$), 7.52 (2H, d, *J*= 8.8Hz, H_{Ar}), 8.23 (2H, d, *J*= 8.8Hz, H_{Ar}), 7.93 and 9.40 (2H, 2s, 2NH).

*5-Methoxycarbonyl-6-methyl-4-(4-hydroxyphenyl)-3,4-dihydropyrimidin-2(1H)–one (**4r**) (Table II, entry 18).*

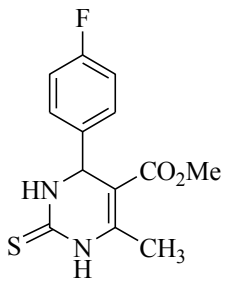


4r

Yield: 83%; M.p. 244-246 °C;^{1}H NMR (300 MHz, DMSO-d_6): 2.31 (3H, s, CH_3), 3.46 (3H, s, OCH_3), 5.04 (1H, s, CHN), 6.70 (2H, d, *J*=11.6 Hz, ArH), 7.02 (2H, d, *J*=11.6 Hz, ArH), 7.67 and 9.16(2H, 2s, 2NH), 9.36 (1H,s, OH).

*5-Methoxycarbonyl-6-methyl-4-(4-fluorophenyl)-3,4-dihydropyrimidin-2(1H)-thione (**4s**) (Table II, entry*

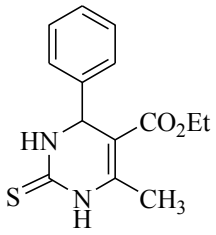
19).



4s

Yield: 92%; M.p. 210-212 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 2.31 (3H, s, CH_3), 3.57 (3H, s, OCH_3), 5.19 (1H, s, $H_{benzylic}$), 7.17-7.44 (4H, m, H_{Ar}), 9.70 and 10.41 (2H, 2s, 2NH).

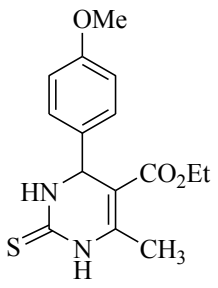
*5-Ethoxycarbonyl-6-methyl-4-phenyl- 3,4-dihydropyrimidin-2(1H)-thione (**4u**) (Table II, entry 21).*



4u

Yield: 88%; M.p. 208-209 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.11 (3H , t, *J*= 7.2 Hz, $\underline{CH_3}CH_2$), 2.31 (3H, s, CH_3), 4.02 (2H, q, *J*=7.2 Hz, CH_2O), 5.19 (1H, s, $H_{benzylic}$), 7.23 (2H, d, *J*=7.2 Hz, H_{Ar}), 7.28 (1H, t, *J*=7.2 Hz, H_{Ar}), 7.36(2H, t, *J*=7.2 Hz, H_{Ar}), 9.68 and 10.36 (2H, 2s, 2NH).

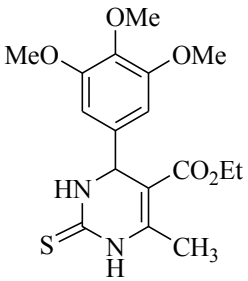
*5-Ethoxycarbonyl-6-methyl-4-(4–methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-thione (**4v**) (Table II, entry 22).*



4v

Yield: 85%; M.p. 151-153 °C; ^{1}H NMR (300 MHz, DMSO-d_6): 1.13 (3H , t, *J*= 9.6 Hz, $\underline{CH_3}CH_2$), 2.29 (3H, s, CH_3), 3.74 (3H, s, OCH_3), 4.03 (2H, q, *J*=9.6 Hz, CH_2O), 5.15 (1H, s, CHN), 6.77 (2H, m, ArH), 6.87 (1H, m, ArH), 7.28 (1H, t, *J*=9.6 Hz, ArH), 9.66 and 10.37 (2H, 2s, 2NH).

5-Ethoxycarbonyl-6-methyl-4-(3,4,5–trimethoxyphenyl)-3,4-dihydropyrimidin-2(1H)-thione ***(4w)*** *(Table II, entry 23).*



4w

Yield: 83%; M.p. 195-197 °C; ^{1}H NMR (400 MHz, DMSO-d_6): 1.16 (3H , t, *J*= 7.2 Hz, $\underline{CH_3}CH_2$), 2.30 (3H, s, CH_3), 3.65 (3H, s, OCH_3), 3.74 (6H, s, $2OCH_3$), 4.07 (2H, q, *J*=7.2 Hz, CH_2O), 5.16 (1H, s, CHN), 6.52 (2H, s, ArH), 9.65 and 10.37 (2H, 2s, 2NH); ^{13}C NMR (100 MHz, DMSO-d_6): 14.6 ($\underline{CH_3}$-CH_2O), 17.6 (CH_3-CH=CH), 54.1 (Ar-CHN), 56.2, 60.1 and 60.4 ($3OCH_3$), 60.4 (CH_3-$\underline{CH_2}O$), 101 and 103.8 (CH_3-CH=CH), 137.4, 139.5, 139.5, 145.4, 145.6 and 153.3 (Ar), 165.6 (C=O ester), 174.9 (C=SNH); MS (EI) m/z (%): 366 (M , 118), 306 (10), 293 (77), 277 (17), 261 (12), 246 (17), 232 (12), 219 (9), 199 (100), 186 (5), 171 (47), 153 (49), 138 (4), 126 (19), 112 (18), 94 (12), 81 (11), 66 (18), 42 (32).

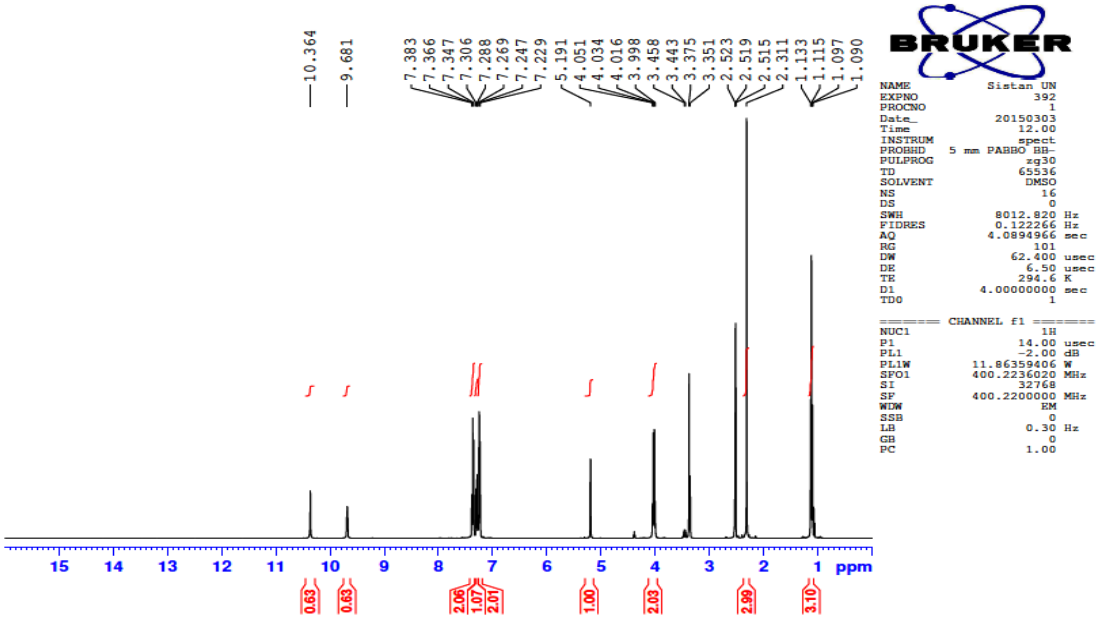


Fig. S-1.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4a**

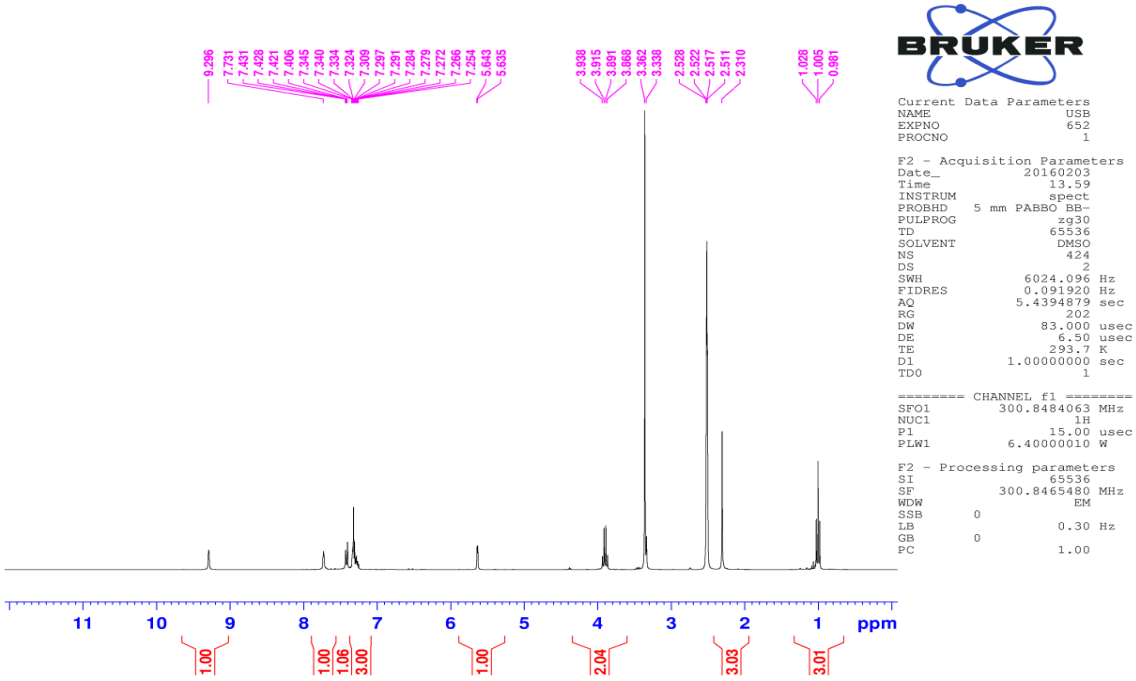


Fig. S-2.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4b**

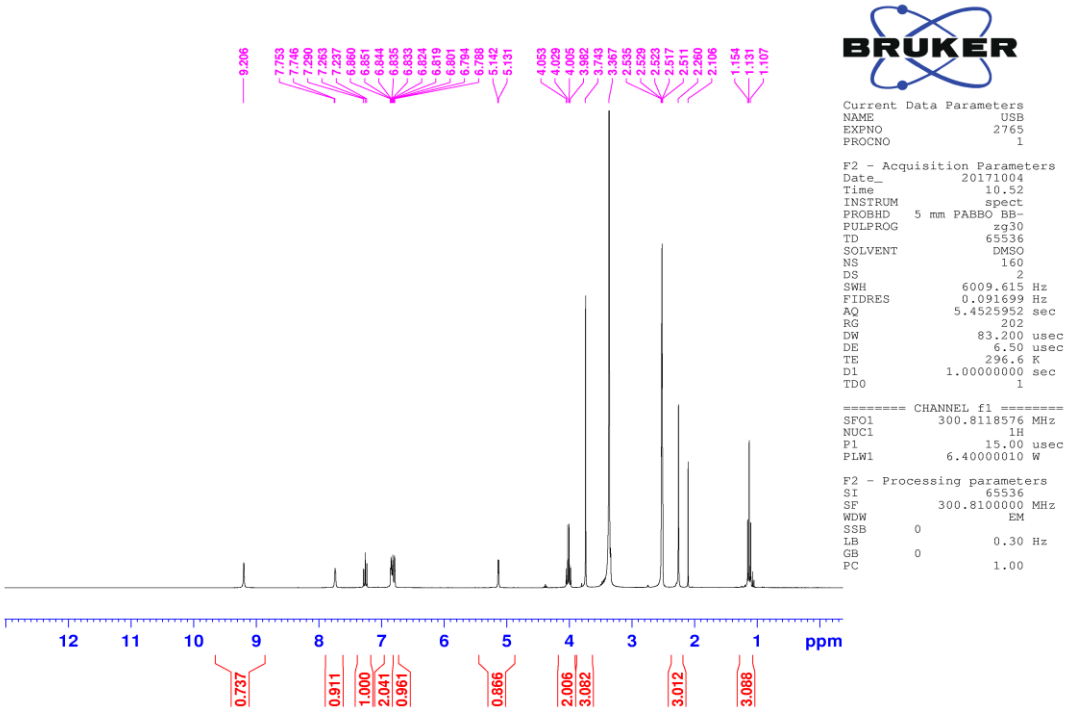


Fig. S-3.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4d**

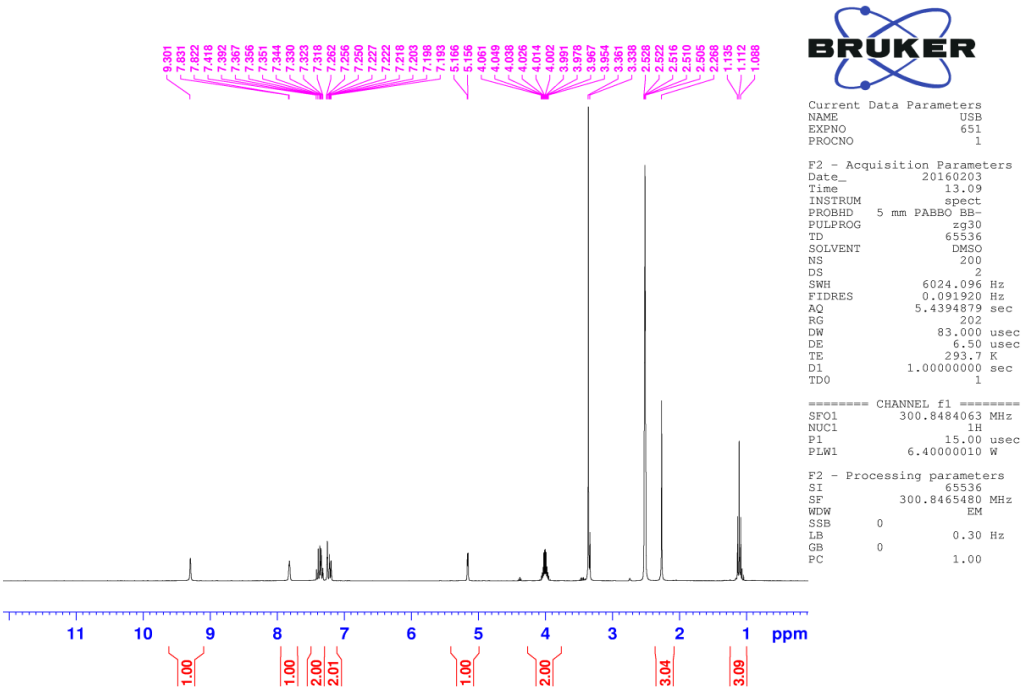


Fig. S-4.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4f**

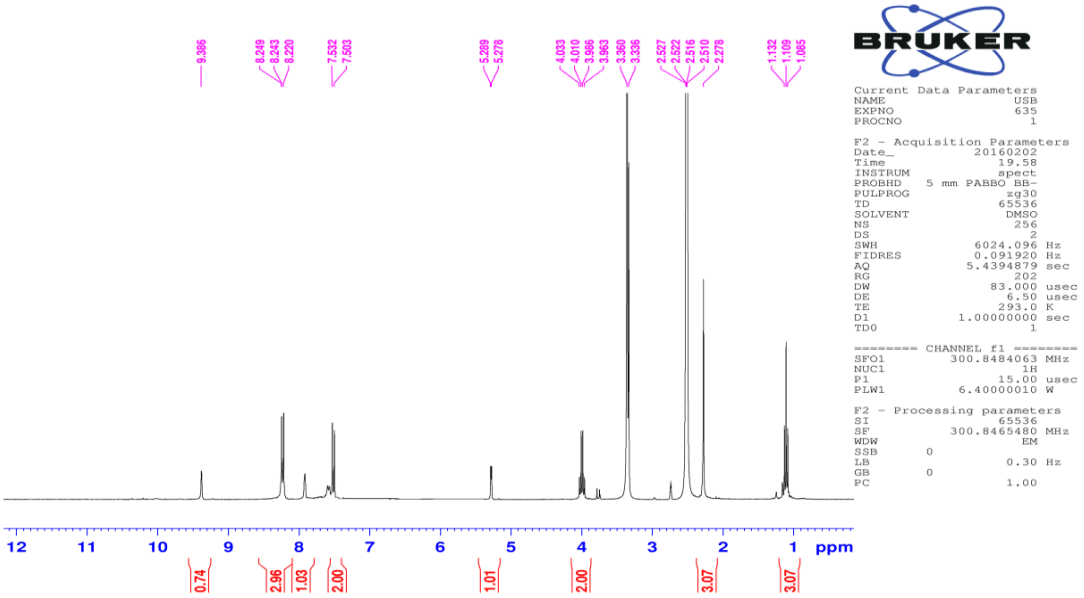


Fig. S-5.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4g**

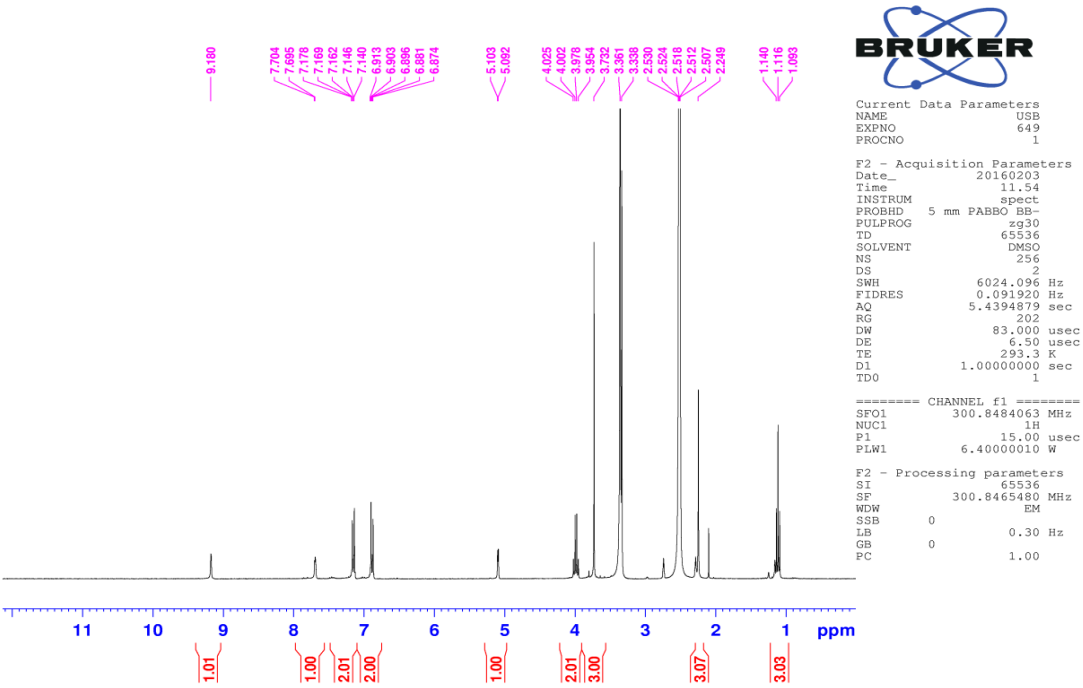


Fig. S-6.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4h**

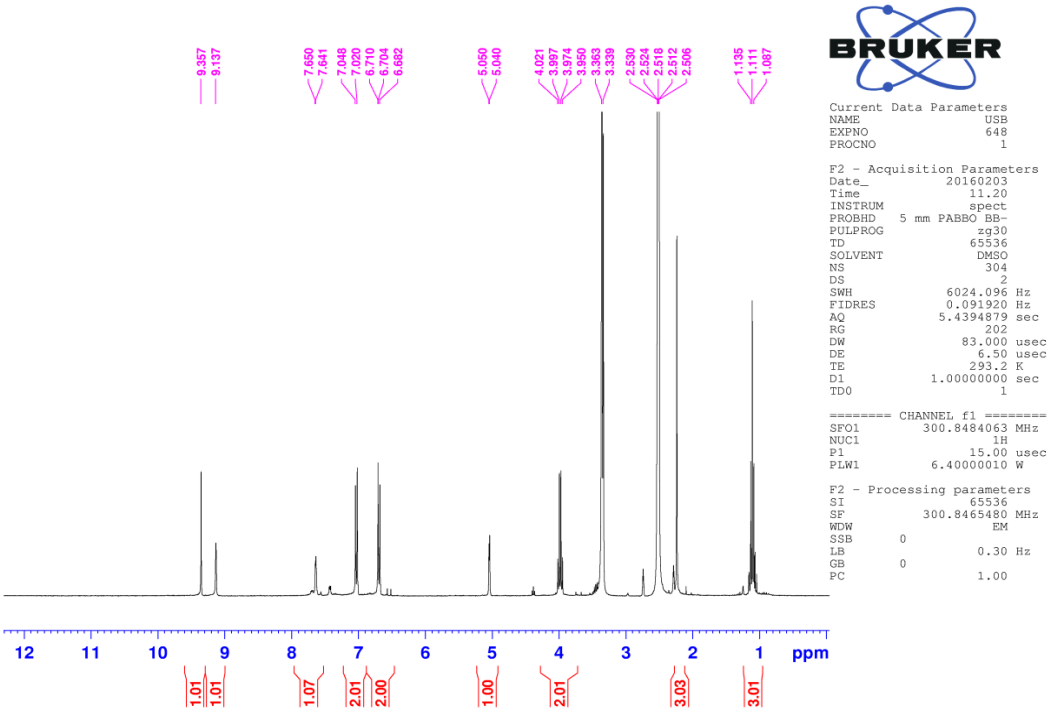


Fig. S-7.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4i**

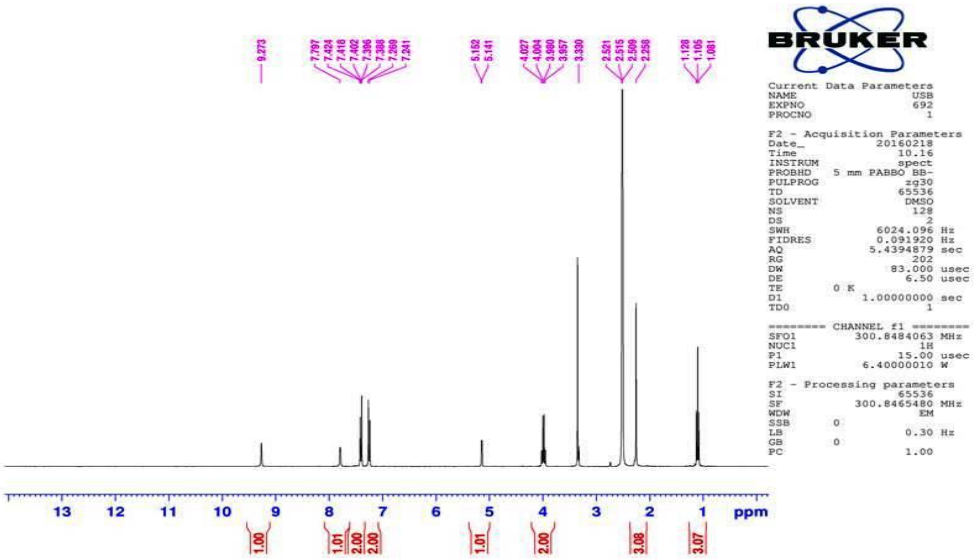


Fig. S-8.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4j**

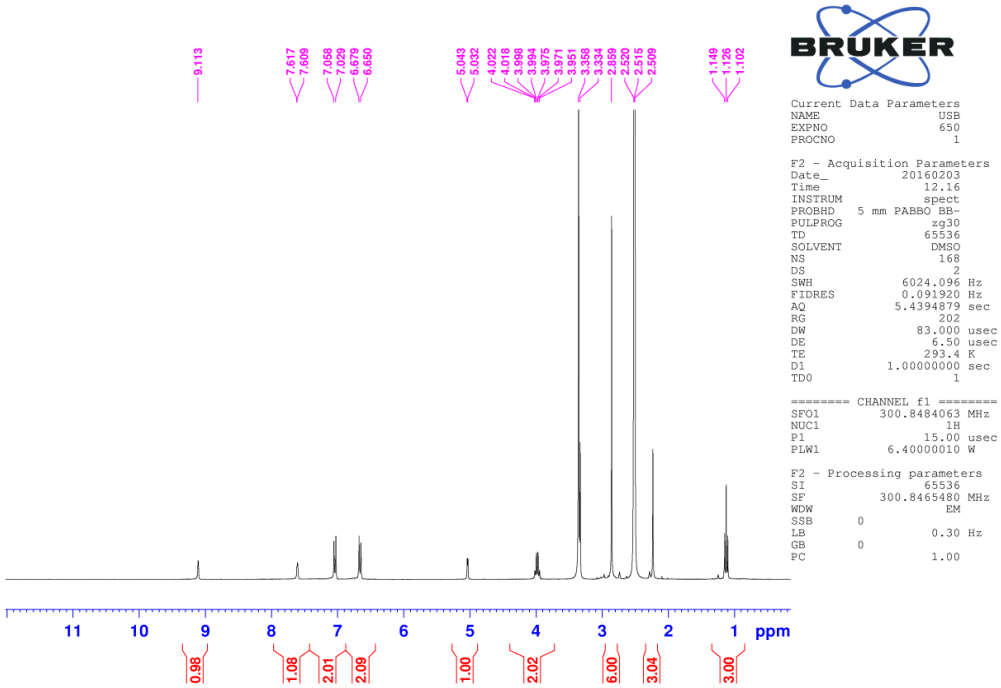


Fig. S-9.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4k**

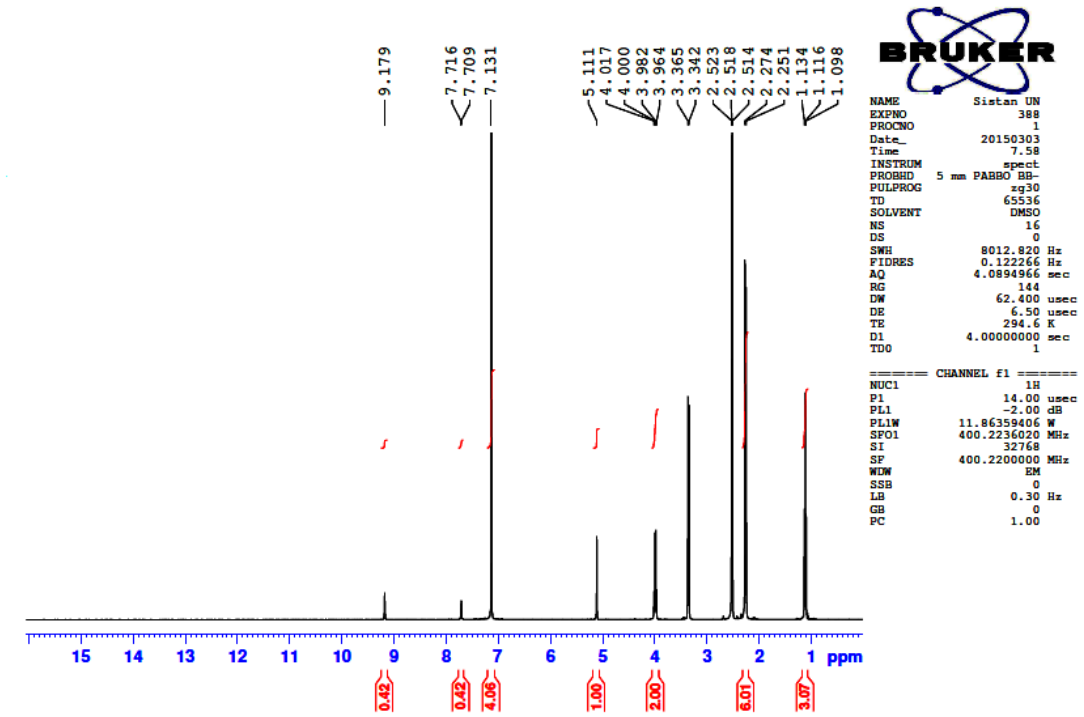


Fig. S-10.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4l**

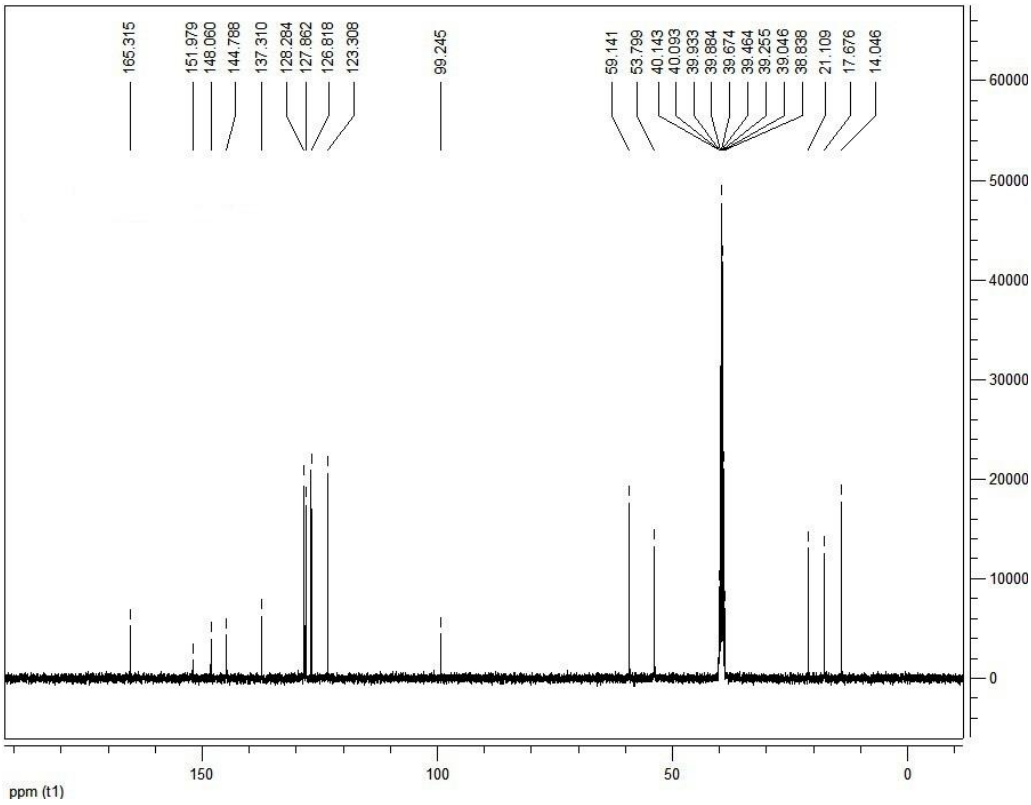


Fig. S-11. ^{13}C NMR Spectrum of compound (100 MHz, DMSO-d_6) of **4l**

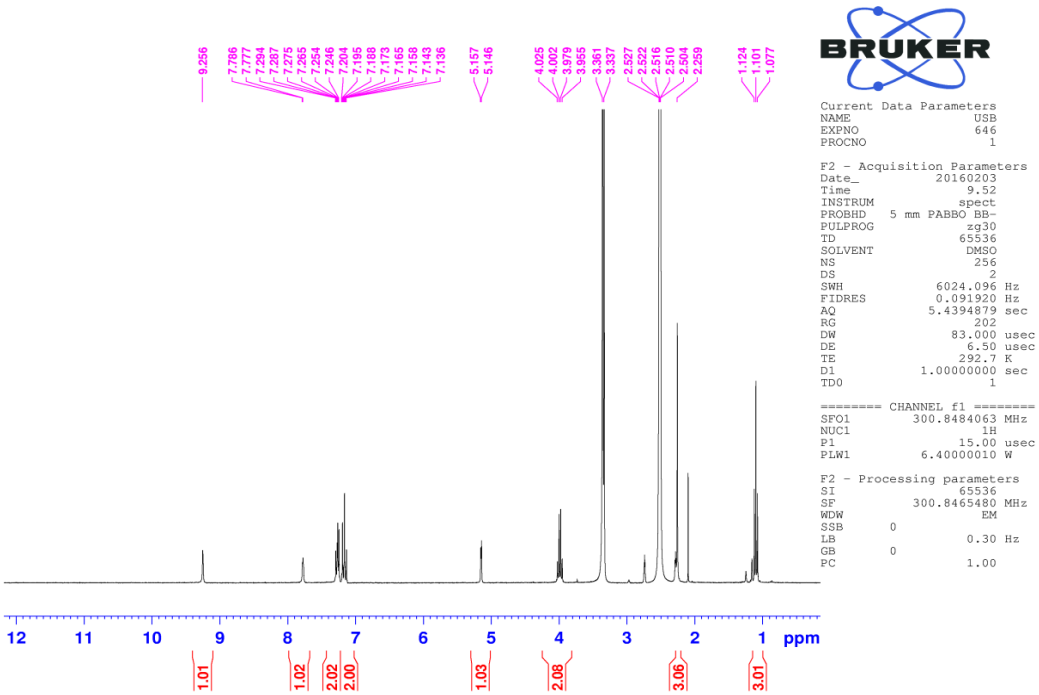


Fig. S-12. ^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4m**

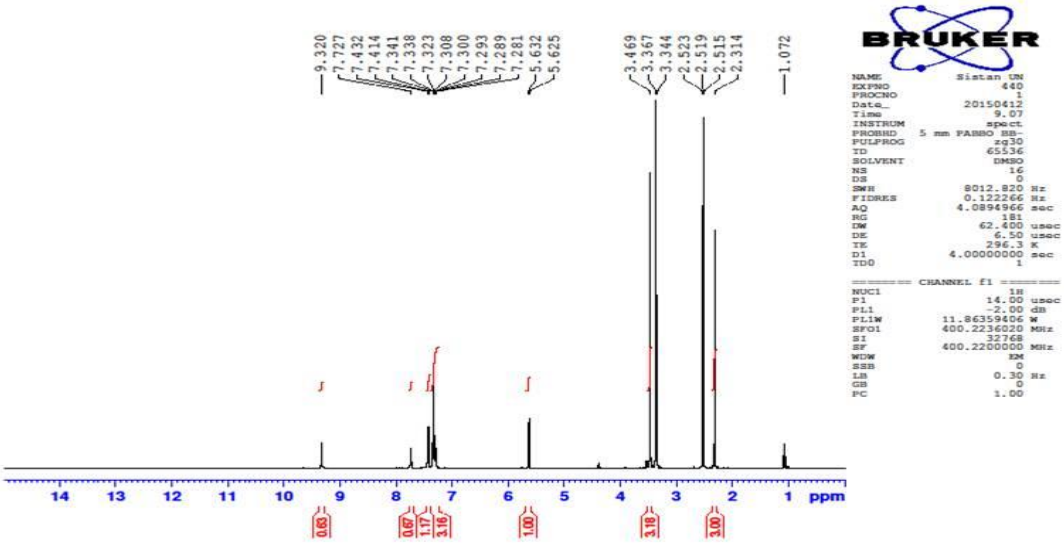


Fig. S-13.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4n**

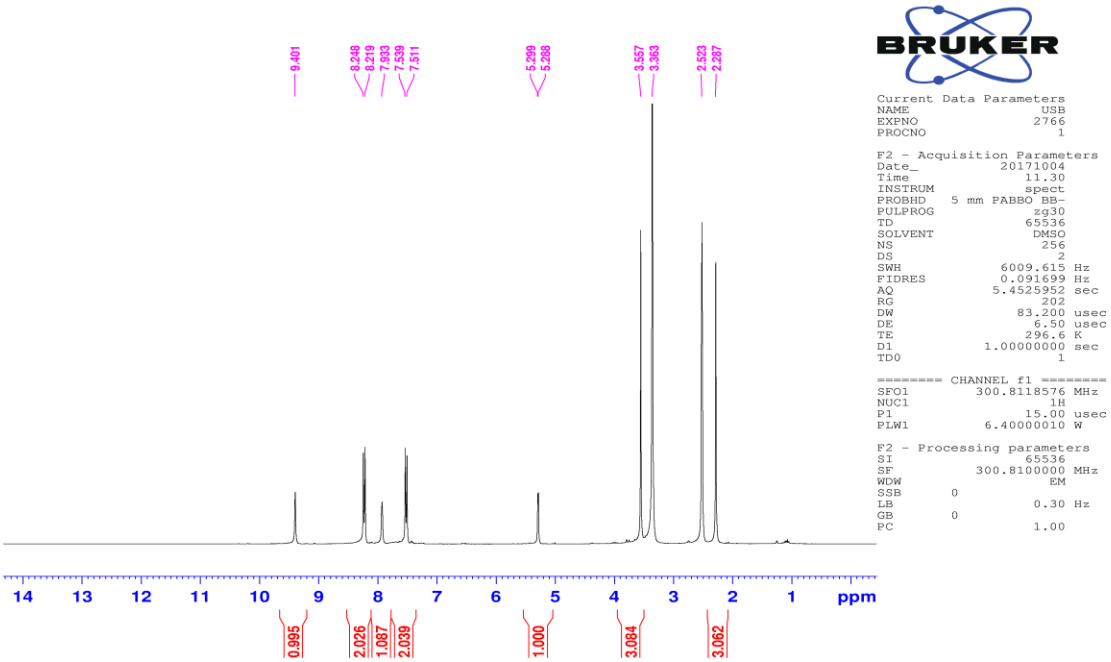


Fig. S-14.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4o**

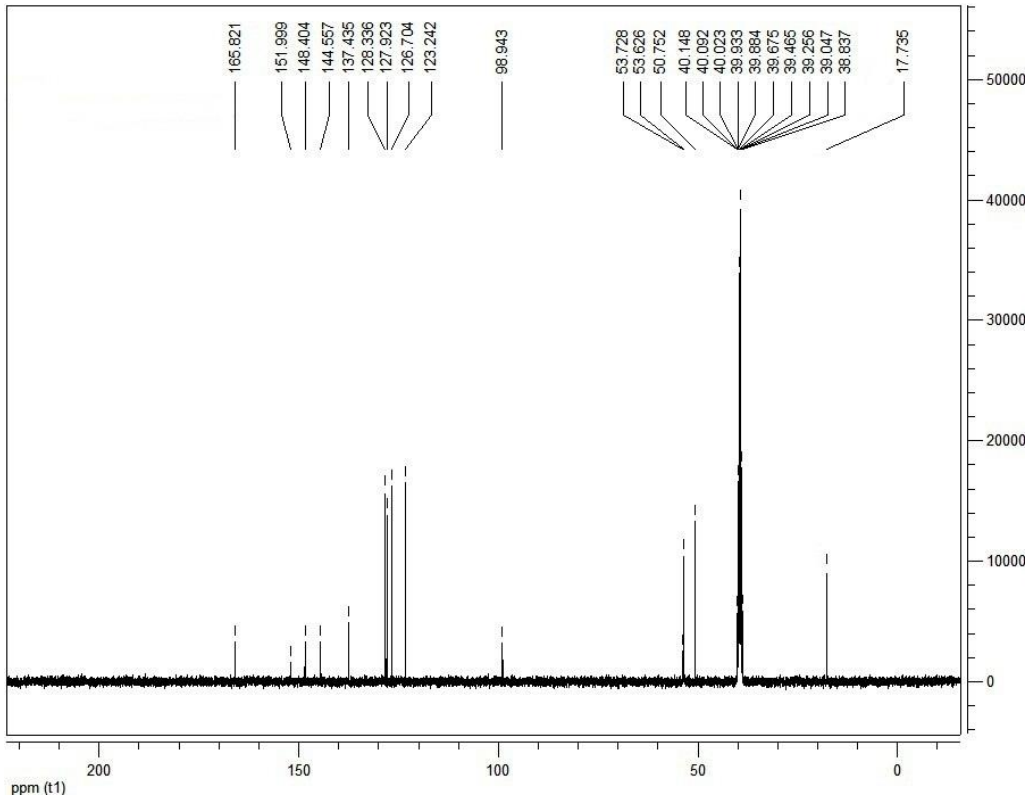


Fig. S-15.^{13}C NMR Spectrum of compound (100 MHz, DMSO-d_6) of **4o**

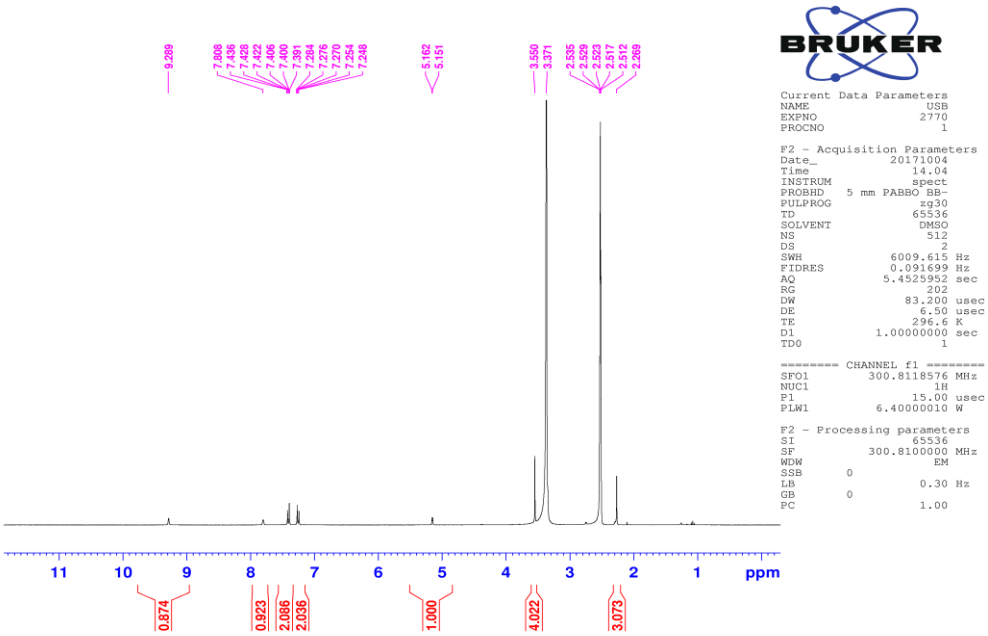


Fig. S-16.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4p**

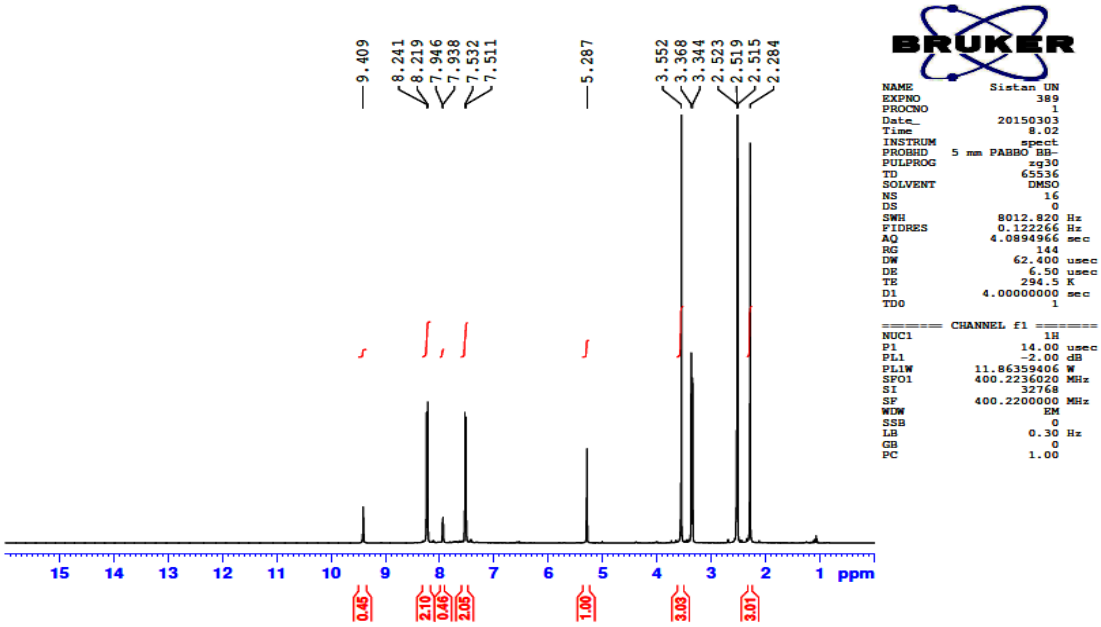


Fig. S-17.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4q**

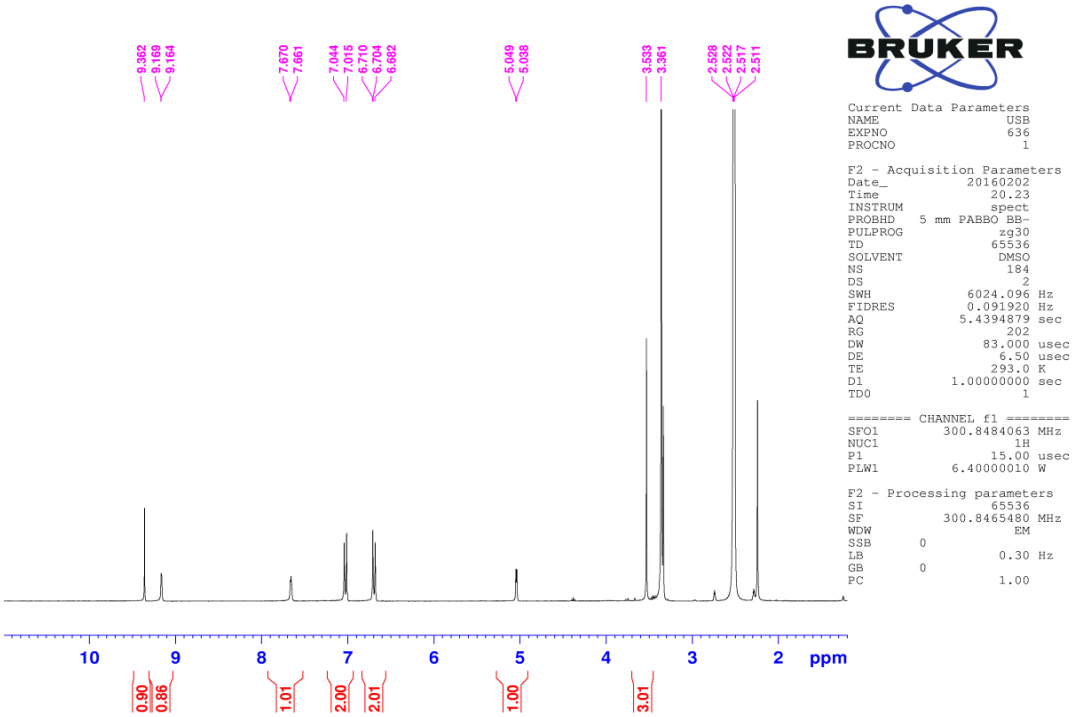


Fig. S-18.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4r**

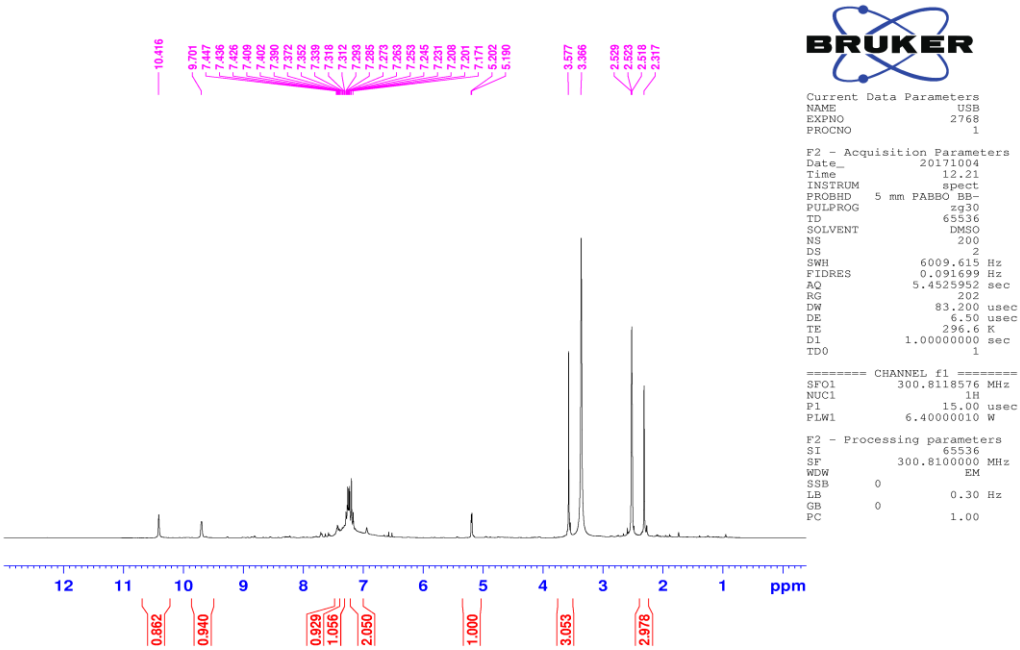


Fig. S-19.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4s**

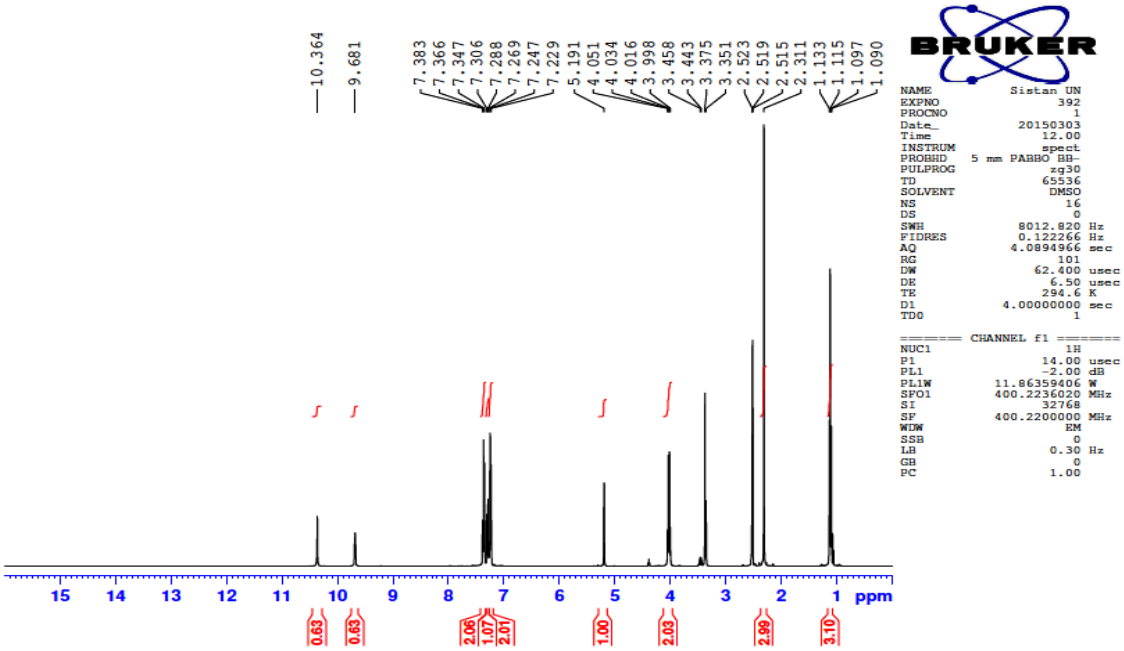


Fig. S-20.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4u**

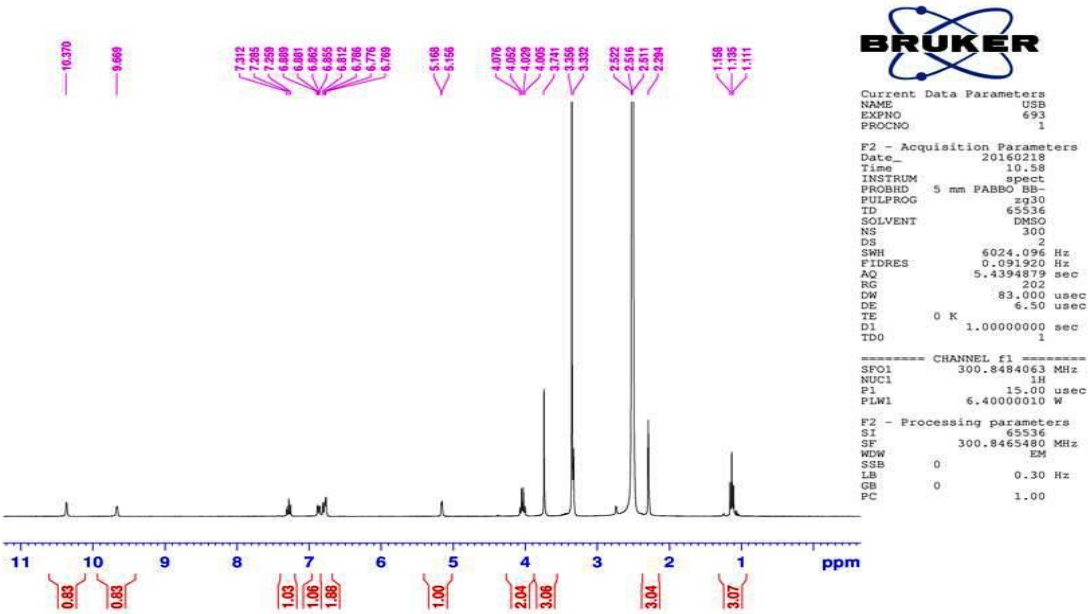


Fig. S-21.^{1}H NMR Spectrum of compound (300 MHz, DMSO-d_6) of **4v**

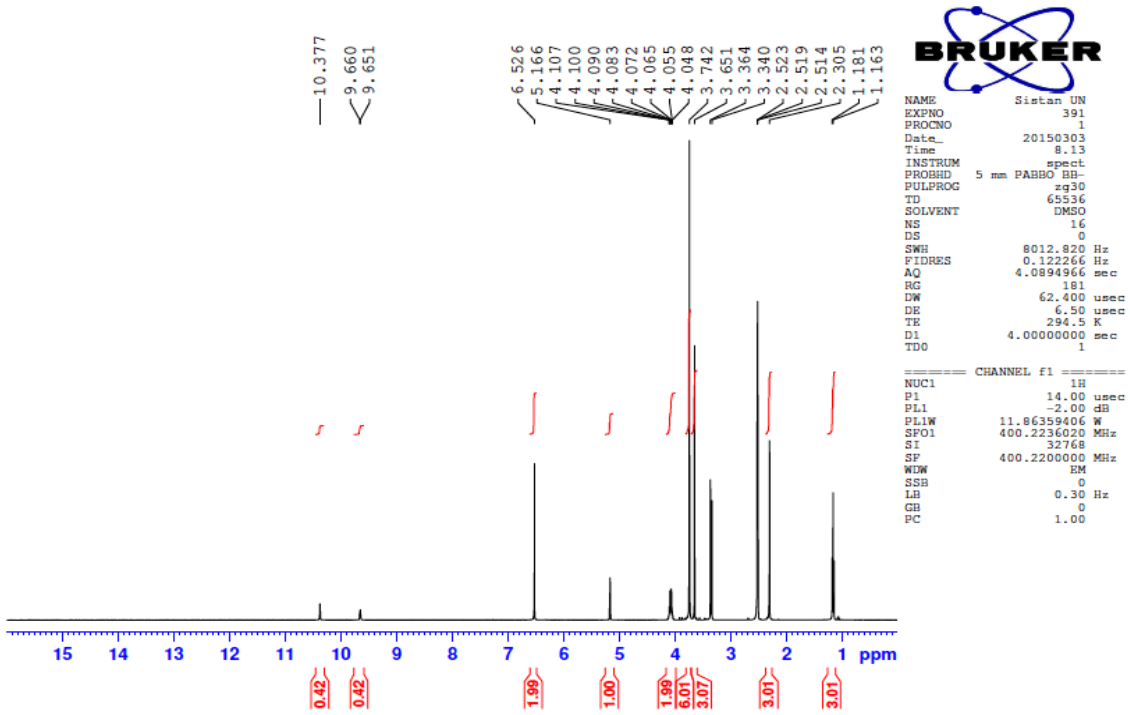


Fig.S-22.^{1}H NMR Spectrum of compound (400 MHz, DMSO-d_6) of **4w**

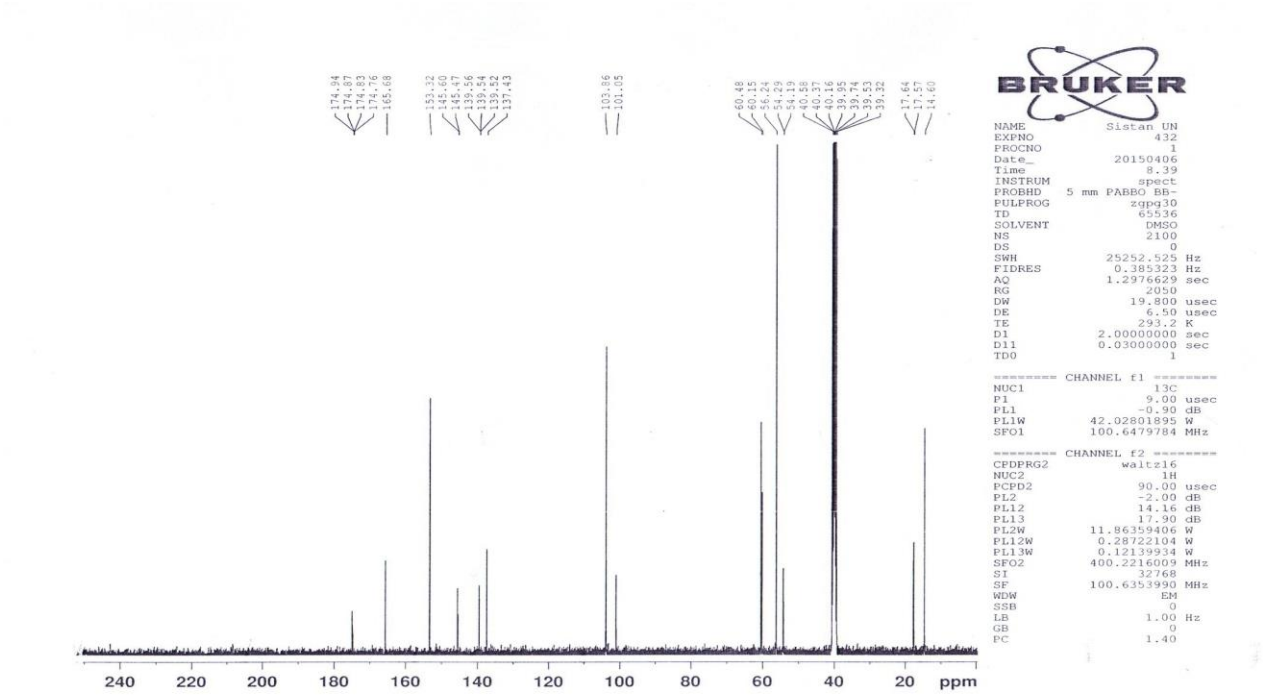


Fig. S-23. ^{13}C NMR Spectrum of compound (100 MHz, DMSO-d_6) of **4w**

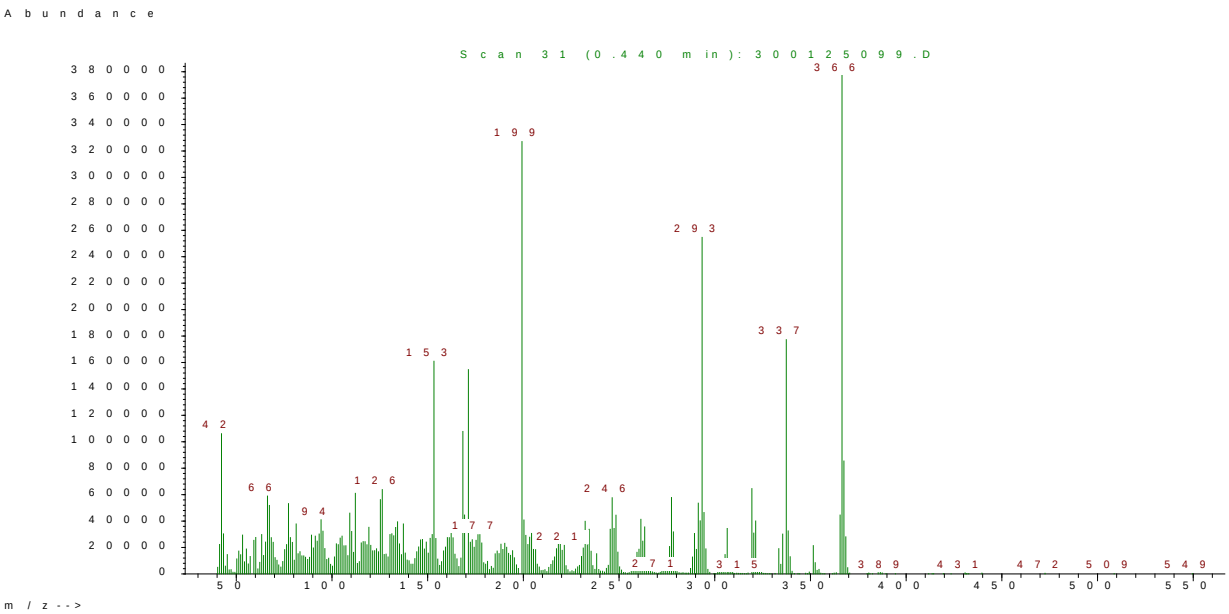


Fig. S-24. Mass Spectrum of compound **4w**