Supporting Information

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$ZrCl_4$-catalyzed one-pot multi-component synthesis of hexahydropyrano pyrimidinone derivatives

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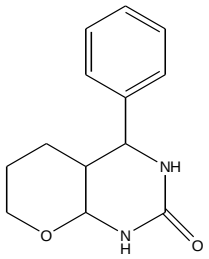
S1. Experimental section

S.1.1. General

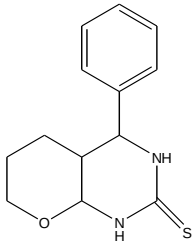
Commercially available reagent grade chemicals were used as received. TLC was carried out with E. Merck Kieselgel 60 F254. Spotswere visualized under UV light and/or visualized by iodine vapors/ spraying with a 20% aq. $KMnO_4$ or with a Dragondroff spray reagent. Column chromatography was performed on silica gel (230-400 mesh, E. Merck). IR spectra were recorded as thin films or in KBr solution with a Perkin–Elmer RX-1 (4000-450 cm^{-1}) spectrophotometer. The ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Bruker DRX-400 in DMSO-d_6. Chemical shift values are reported in parts per million relative to TMS as internal reference, unless otherwise stated; s (singlet), d (doublet), t(triplet), m (multiplet); J in Hertz. Mass spectra were recorded JeolSX-102 and ESI mass spectra with Quattro II (Micromass).

S.1.2. Experimental Procedure and Spectral Data of Compounds **4a-f**

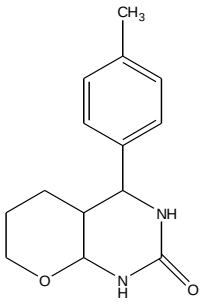
To a solution of benzaldehyde (1 mmol) in 5 ml ethanol, urea (1.2 mmol) was added and stirred at room temperature for 15 min. To this stirred solution, $ZrCl_4$ (10 mol%) was added followed by addition of 3,4-dihydro-2*H*-pyran (1.5 mmol) and was refluxed for specified time fitted with a reflux condenser and a calcium chloride guard tube. The progress of the reaction was monitored by TLC. After completion of the reaction the solvent was evaporated under reduced pressure and the product was purified by column chromatography over silica gel eluting with chloroform, methanol to afford the pure product. **4a**



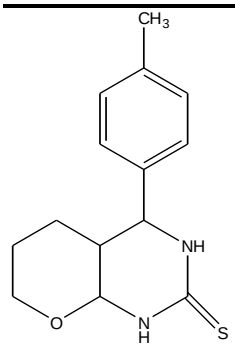
4a: White solid; mp. 215-217 ºC; IR (KBr): 3432, 2921, 1685, 1658, 1510 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ 7.37-7.28 (m, 6H), 6.58 (s, 1H), 4.55 (d, *J* = 10.8 Hz, 1H), 4.42 (s, 1H), 3.88 (d, *J* = 10.1 Hz, 1H), 3.44 (t, *J* = 10.6 Hz,1H), 1.81-1.70 (m, 2H), 1.56-1.51 (m, 1H), 1.26-1.19 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.2, 142.5, 129.3, 128.6, 128.4, 81.2, 66.7, 53.6, 38.7, 23.4, 20.8; MS (ESI) *m/z* 233 ($[M+H]^+$).



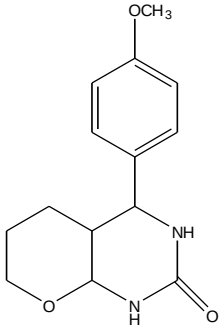
4b: White solid; mp. 236-238 ºC; IR (KBr): 3432, 3171, 2970, 1536, 1406 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 8.81 (d, *J* = 2.5 Hz, 1H), 8.38 (s,1H), 7.42-7.22 (m, 5H), 4.51 (d, *J* =4.1 Hz, 1H), 4.40 (t, *J* = 2.8Hz, 1H), 3.88 (d, *J* = 11.3 Hz, 1H), 3.47 (t, *J* = 10.3 Hz, 1H), 1.88-1.86 (m, 1H), 1.76-1.59 (m, 2H), 1.26 (d, *J* = 10.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 177.0, 140.7, 129.4, 128.8, 128.4, 78.7, 66.4, 54.9, 36.5` , 23.0, 21.0; MS (ESI): *m/z* 249 ($[M+H]^+$).



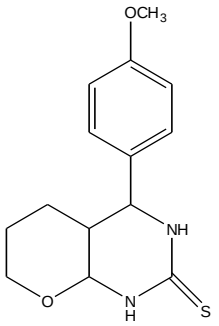
4c: White solid; mp. 254-256 ^{o}C; IR (KBr): 3284, 1690, 1502, 1477, 1183, 1130 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26-7.15 (m, 5H), 6.51 (s, 1H), 4.51 (d, J = 10.8 Hz, 1H), 4.42 (q, J = 1.9 Hz, 1H), 3.89 (d, J = 9.3 Hz, 1H), 3.44 (t, J = 9.9 Hz, 1H), 2.29 (s, 3H), 1.78-1.67 (m, 2H), 1.55-1.50 (m, 1H), 1.27-1.18 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.7, 139.4, 137.7, 129.8, 128.3, 81.2, 66.7, 53.3, 38.7, 23.8, 21.6, 21.3. MS (ESI) *m/z* 247 ([M+H]$^{+}$).



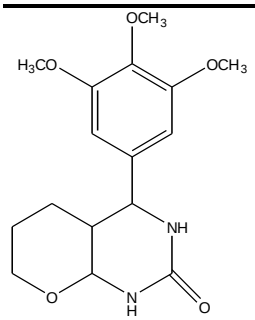
4d: White solid; mp. 267-269 ^{o}C; IR (KBr): 3196, 2953, 2859, 1572, 1536, 1513, 1203, 1036 cm^{-1}; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.79 (s, 1H), 8.31 (s, 1H), 7.17 (m, 4H), 4.46 (d, J = 10.4 Hz, 1H), 4.38 (s, 1H), 3.87 (d, J = 11.0 Hz, 1H), 3.47 (t, J = 11.0 Hz, 1H), 2.30 (s, 3H), 1.84-1.57 (m, 3H), 1.24 (d, J = 7.4 Hz, 1H); ^{13}C NMR (100 Mz, DMSO-d_6): δ177.0, 137.6, 137.4, 129.4, 127.8, 78.7, 66.0, 54.1, 39.0, 23.0, 21.2, 21.0; MS (ESI): *m/z* 263 ([M+H]$^{+}$).



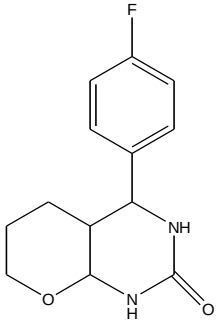
4e: White solid; mp. 222-224 ^{o}C; IR (KBr): 3266, 1684, 1612, 1506, 1169, 1083 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.27 (s, 1H), 7.25 (d, J = 8.0 Hz, 2H), 6.92 (d, J = 8.0 Hz, 2H), 6.50 (s,1H), 4.51 (d, J = 10.9 Hz, 1H), 4.42 (s, 1H), 3.88 (d, J = 8.1 Hz, 1H), 3.44 (t, J = 11.2 Hz, 1H), 1.78-1.67 (m, 2H), 1.55-1.50 (m, 1H), 1.27-1.17 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.7, 155.7, 134.2, 129.5, 129.3, 114.7, 81.3, 66.7, 56.0, 52.9, 38.8, 23.8, 21.3; MS (ESI): *m/z* 263 ([M+H]$^{+}$).



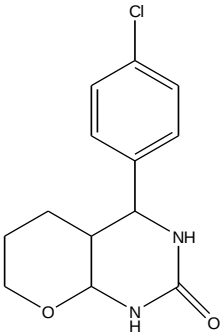
4f: White solid; mp. 247-248 ^{o}C; IR (KBr): 3179, 2976, 2945, 1612, 1561, 1463, 1249, 1050 cm^{-1}; ^{1}H NMR (400 Mz, DMSO-d_6): δ 8.79 (d, J = 2.2 Hz, 1H), 8.18 (s, 1H), 7.23 (d, J = 8.3 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 4.47 (d, J = 10.6 Hz, 1H), 4.40 (s, 1H), 3.88 (d, J = 11.0 Hz, 1H), 3.75 (s, 1H), 3.46 (t, J = 11.0 Hz, 1H), 1.85-1.57 (m, 3H), 1.26-1.21 (m, 2H); ^{13}C NMR (100 Mz, DMSO-d_6): δ 176.9, 159.8, 132.8, 129.6, 114.7, 78.8, 66.6, 56.0, 54.2, 37.0, 23.5, 21.0; MS (ESI): *m/z* 279 ([M+H]$^{+}$).



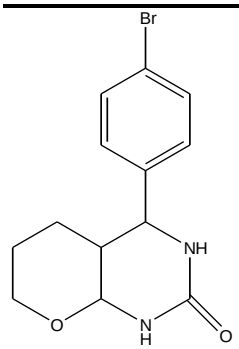
4g: White solid; mp. 238-240 ^{o}C; IR (KBr): 3371, 3215, 1683, 1597, 1460, 1127, 1033 cm^{-1}; ^{1}H NMR (400 Mz, DMSO-d_6): δ 7.30 (brs, 1H, NH), 6.69 (s, 2H), 6.53 (s, 1H, NH), 4.98 (d, J = 10.64 Hz, 1H), 4.50-4.47 (m, 1H), 4.00-3.95 (m, 1H), 3.82 (s, 6H, OCH_3), 3.69 (s, 3H, OCH_3), 3.55- 3.47 (m, 1H), 1.93-1.21 (m, 5H); ^{13}C NMR (100 Mz, DMSO-d_6): δ 154.8, 152.8, 136.9, 128.1, 125.5, 104.7, 80.2, 65.8, 60.0, 55.9, 52.9, 37.5, 23.0, 20.3; MS (ESI): *m/z* 323 ([M+H]$^{+}$).



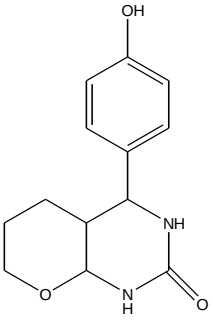
4h: White solid; mp. 218-220 ^{0}C; IR (KBr): 3301, 3245, 1692, 1508, 1220, 1183, 1027 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ 8.84 (S. 1H), 8.42 (S, 1H), 7.37-7.29 (m, 2H), 7.09-7.00 (m, 2H), 4.53 (d, J = 10.76 Hz, 1H), 4.40 (s, 2H), 3.87 (d, J = 10.76 Hz, 2H), 3.47 (t, J = 11.58 Hz, 1H), 1.93-1.28 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.7, 137.5, 129.5, 129.4, 115.2, 114.9, 80.2, 65.8, 51.9, 37.7, 22.8, 20.2; MS (LCMS): *m/z* 251([M+H]$^{+}$).



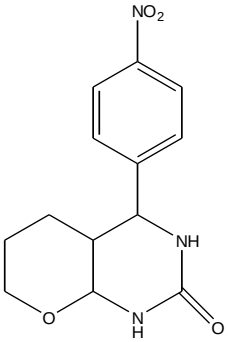
4i: White solid; mp. 274-275 ^{o}C; IR (KBr): 3306, 3242, 2954, 1742, 1697, 1489, 1210, 1182 cm^{-}1; ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.43-7.32 (m, 5H), 6.67 (s, 1H), 4.57 (d, *J* = 10.8Hz, 1H), 4.43 (d, *J* = 1.7Hz, 1H), 3.89 (d, *J* = 9.6Hz, 1H), 3.44 (t, *J* =11.4Hz, 1H), 1.80-1.72 (m, 2H), 1.58-1.55 (m, 1H), 1.24-1.19 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.6, 141.5, 133.0, 130.4, 129.3, 81.2, 66.7, 53.0, 38.6, 23.8, 21.2; MS (ESI): *m/z* 267 ([M+H]$^{+}$).



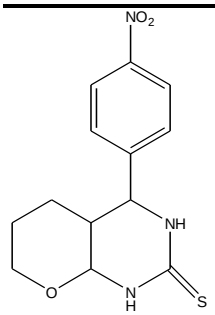
4j: White solid; m.p. 254-255 ^{0}C; IR (KBr): 3303, 3208, 1700, 1489, 1297, 1179, 1028 cm^{-1};^{1}H NMR (400 MHz, DMSO-d_6): δ 7.52 (d, J = 7.93 Hz, 2H, ArH), 7.30 (d, J = 7.93 Hz, 2H), 7.20 (s, 1H, NH), 6.52 (s, 1H, NH), 4.53 (d, *J* = 10.76 Hz, 1H), 4.43 (m, 1H), 3.90 (d, *J*= 11.14 Hz, 1H), 3.47 (t, *J*= 11.14 Hz, 1H), 1.84-1.19 (m, 5H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 154.5, 140.8, 131.1, 129.6, 120.5, 81.2, 65.6, 52.0, 37.5, 22.7, 20.2; MS (LCMS): *m/z* 311 ([M+H]$^{+}$).



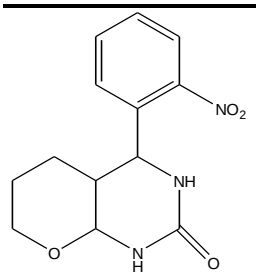
4k: White solid; mp: 222-224 ^{0}C; IR (KBr, cm^{-1}) 3325, 3250, 2927, 2363, 1682, 1609; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ = 1.14-1.27 (m, 2H), 1.52-1.67 (m, 1H), 1.73-1.81 (m, 2 H), 42 (t, 1H), 3.90 (d, *J* = 8.02 Hz, 1H), 4.38 - 4.40 (s, 1H), 4.45 (d, *J* = 10.7 Hz, 1H), 5.78 (s, 1H), 6.40 (bs, 1H), 6.96 (d, *J* = 8.02 Hz, 2H), 7.21 (d, 2H), 7.43 (s, 1H) 9.29 (s 1H); MS (ESI): *m/z* 339 ([M+H]$^{+}$).



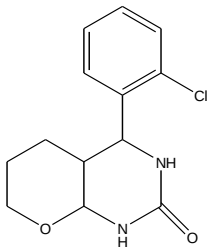
4l: White solid; mp: 256-261 ^{0}C; IR (KBr, cm^{-1}): 3309, 3244, 3071, 2941, 2360, 1680, 1617, 1526, 1440; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ = 1.20-1.25 (m, 2H), 1.58-1.79 (m, 2H), 1.87 (d, *J* =10.2 Hz, 1H), 3.46-3.50 (m, 1H), 3.88 (d, *J* =11.6 Hz, 1H,), 4.50 (s, 1H), 4.52 (d, *J* =10.5 Hz, 1H), 6.67 (bs, 1H), 7.02 (bs, 1H), 7.38 (d, 2H), 8.18 (d, 2H); ^{13}C NMR (100 MHz, DMSO-*d*$_6$): δ 21.2, 23.5, 38.3, 53.2, 66.7, 80.8, 124.2, 129.3, 147.9, 149.4, 155.9; (ESI): *m/z* 278 ([M+H]$^+$).



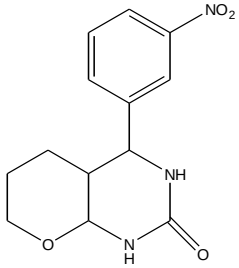
4m: White solid; Mp 265-267 ^{0}C; IR (KBr): 3352, 3183, 3056, 2946, 2846, 2362, 1605, 1533, 1517 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d$_6$): δ = 1.11-1.22 (m, 2H), 1.69-1.93 (m, 3H), 3.43-3.58 (m,1H), 3.89 (d, *J*=17.2 Hz,1H), 4.41-4.38 (s,1H), 4.70 (d, *J*=15.6 Hz, 1H), 7.62 (d, *J*=13.0 Hz, 2H), 8.24 (d, *J*=13.0 Hz, 2H), 8.59 (br s, 1H, NH), 8.91 (br s, 1H, NH); ^{13}C NMR (50 MHz, DMSO-d$_6$): δ = 21.2, 23.3, 36.8, 54.2, 66.4, 79.0, 124.4, 129.9, 148.0, 148.9, 177.5; (ESI): *m/z* 294 ([M+H]$^+$).



4n: White solid; Mp 235-237 ^{0}C; IR (KBr): 3422, 3021, 2359, 1669, 1593 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d$_6$): δ =1.24-1.27 (m, 2H), 1.44-1.68 (m, 2H), 2.07 (d, *J*=6.72 Hz, 1H), 3.38-3.46 (m, 1H), 3.83 (d, *J*=11.4 Hz, 1H), 4.45-4.48 (m, 1H), 4.94 (d, *J*=10.1 Hz, 1H), 6.74 (br s, 1H, NH), 7.30 (br s, 1H, NH), 7.53-7.58 (m, 1H), 7.68-7.78 (m, 1H), 7.86 (d, *J*=7.95 Hz, 1H); ^{13}C NMR (50 MHz, DMSO-d$_6$): δ = 20.8, 22.9, 36.9, 47.6, 65.0, 79.8, 123.7, 128.9, 129.6, 133.2, 135.0, 149.9, 154.4; (ESI): *m/z* 278 ([M+H]$^+$).



4o: White solid; Mp: 242-244 ^{0}C; IR (KBr): 3311, 3208, 3095, 2369, 1700, 1574 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ =1.12-1.42 (m, 2H, CH2), 1.52-1.79 (m, 2H, CH2), 1.92 (d, *J*=13.4 Hz, 1H), 3.42-3.47 (m, 1H), 3.83 (d, *J*=16.7 Hz, 1H), 4.43 (br s, 1H), 4.94 (d, *J*=15.5 Hz, 1H), 6.63 (br s, 1H, NH), 7.29-7.49 (m, 5H, ArH and NH); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 22.1, 23.7, 38.1, 50.5, 66.1, 80.9,128.6, 130.0, 130.2, 133.7, 139.9, 155.4; (ESI): *m/z* 267 ([M+H]$^+$).



4p: White solid; Mp: 252-254 ^{0}C; IR (KBr): 3020, 2401, 2361, 2105, 1666, 1596 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.16-1.28 (m, 2H), 1.44-1.66 (m, 2H), 1.77 (d, *J*=10.6 Hz, 1H), 3.30-3.42 (m, 1H), 3.82 (d, *J*=9.86 Hz, 1H), 4.38-4.49 (m, 1H), 4.61 (d, J=10.8 Hz, 1H), 6.22 (br s,1H, NH), 6.90 (br s, 1H, NH), 6.38-7.62 (m, 2H), 7.93-8.02 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δ = 20.40, 22.71, 38.70, 52.51, 65.83, 80.0, 121.74, 122.52, 129.34, 133.56, 154.72; (ESI): *m/z* 278 ([M+H]$^+$).

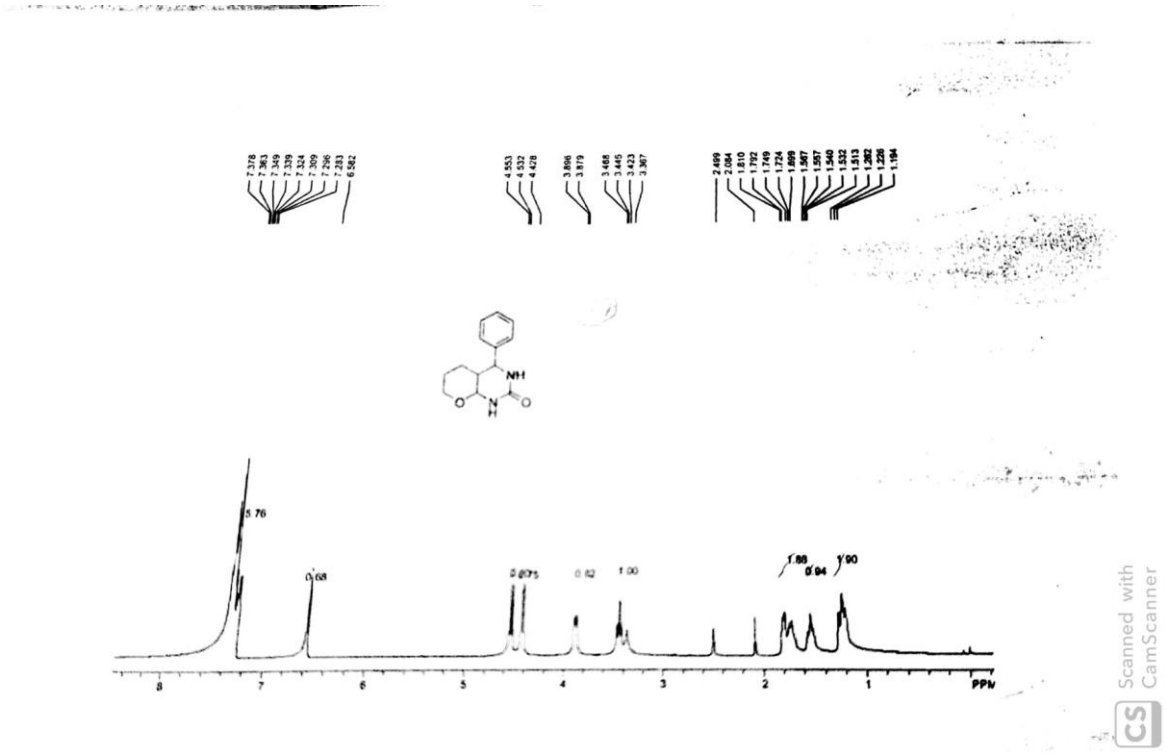


Figure S1: ^{1}H-NMR Spectrum of compound **4a**

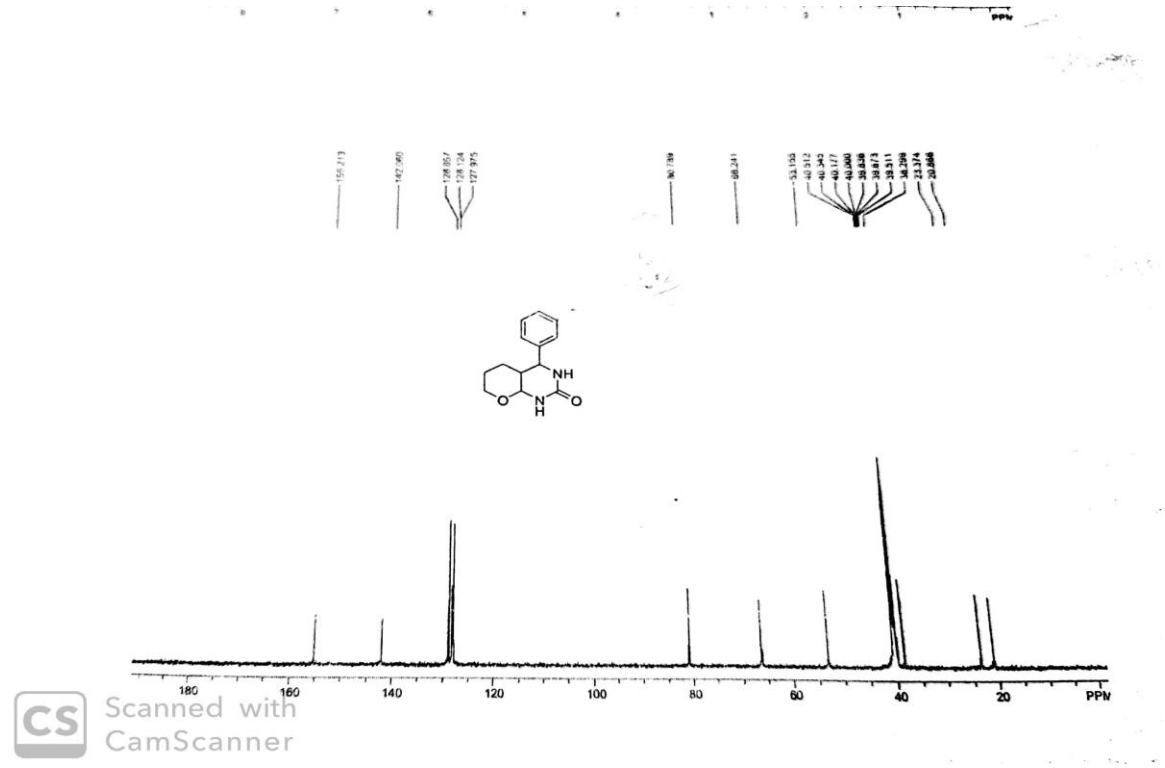


Figure S2: ^{13}C-NMR Spectrum of compound **4a**

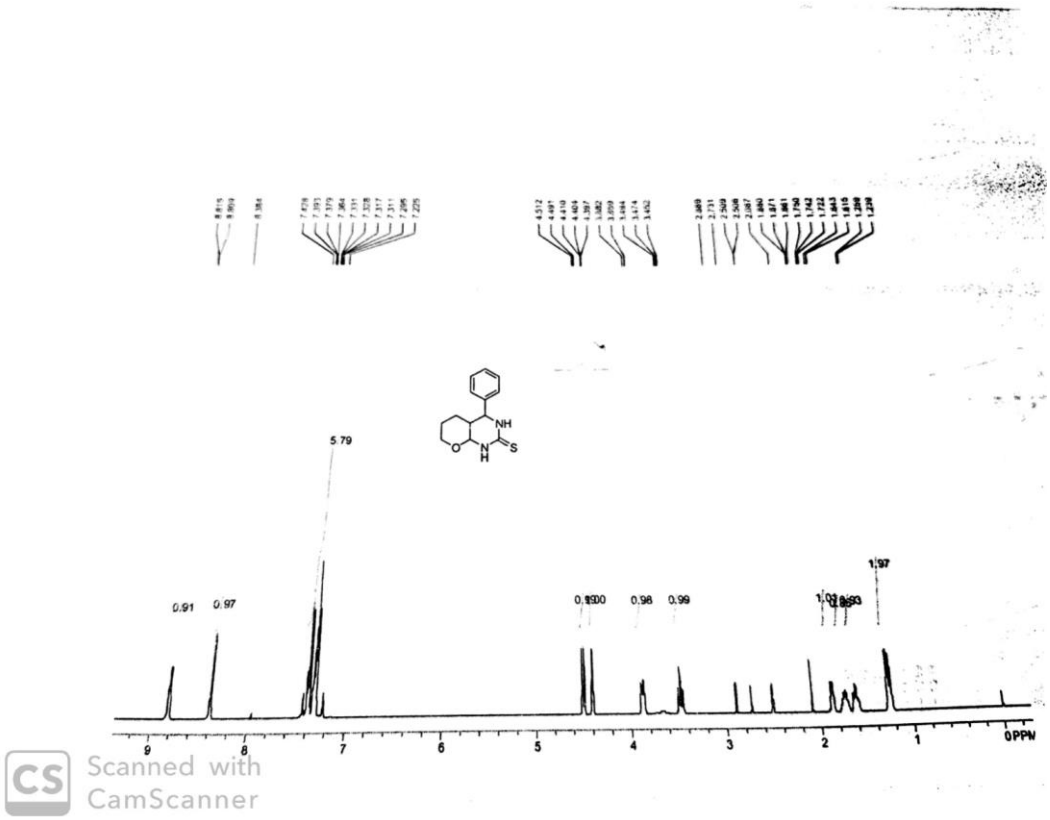


Figure S3: ^{1}H-NMR Spectrum of compound **4b**

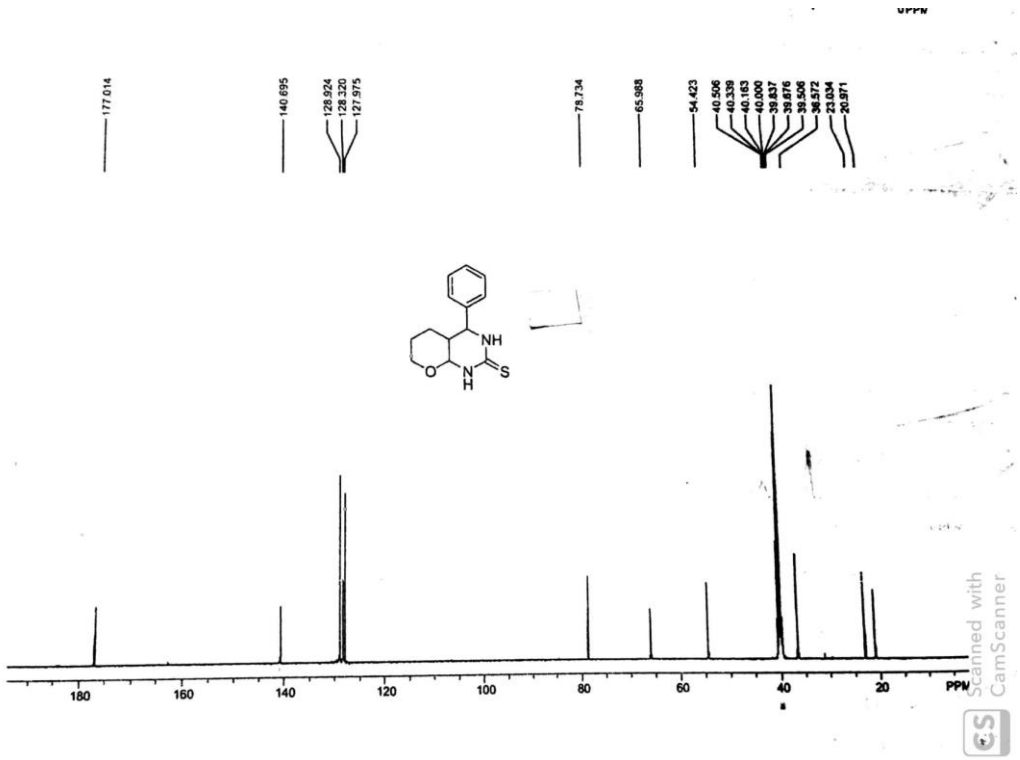


Figure S4: ^{13}C-NMR Spectrum of compound **4b**

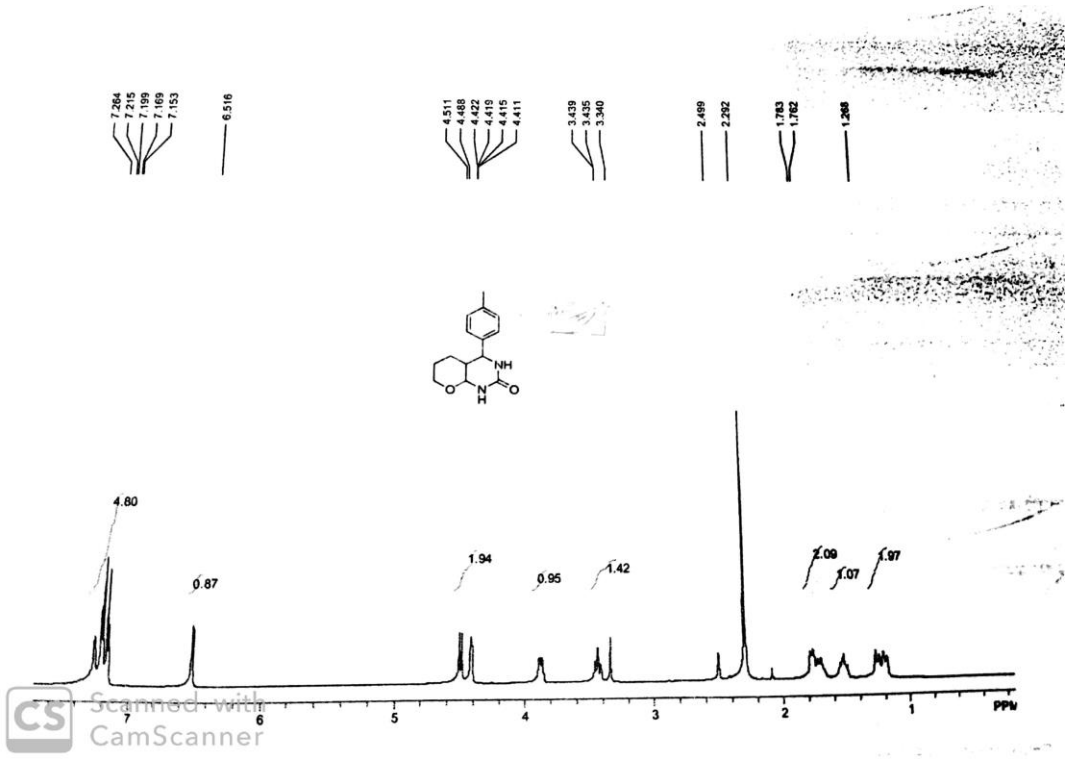


Figure S5: ^{1}H-NMR Spectrum of compound **4c**

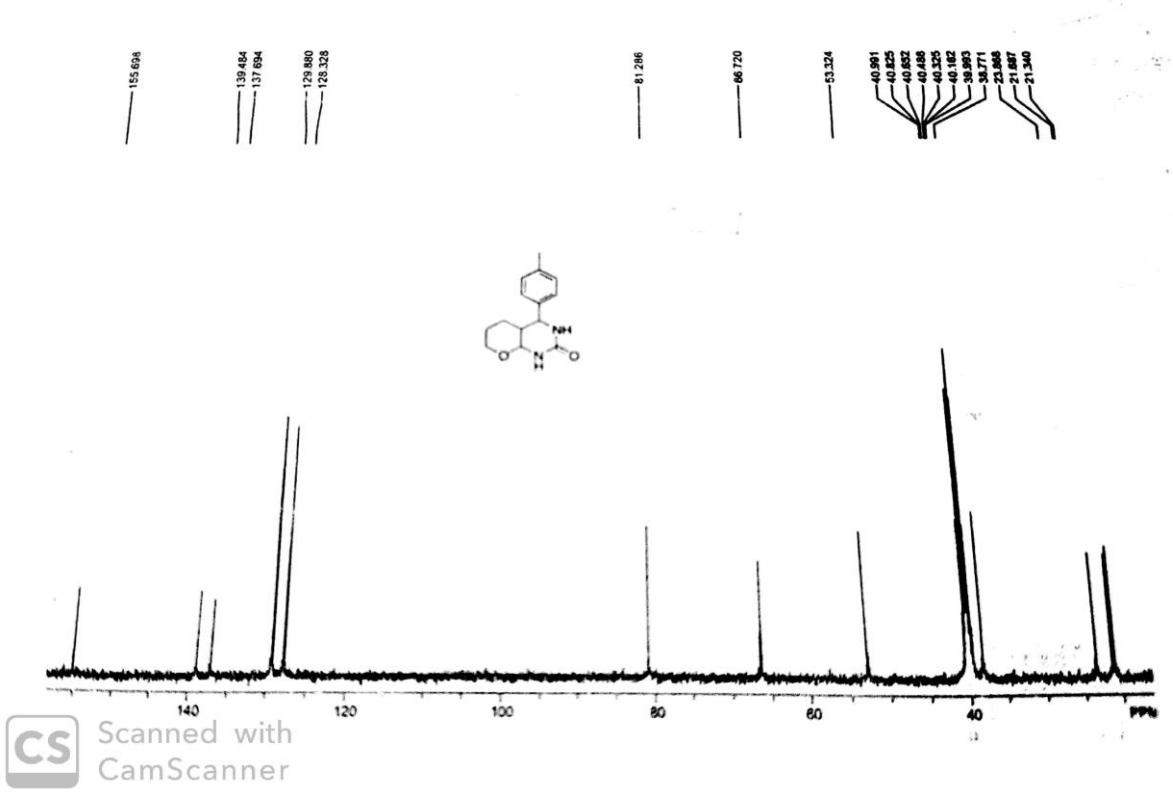


Figure S6: ^{13}C-NMR Spectrum of compound **4c**

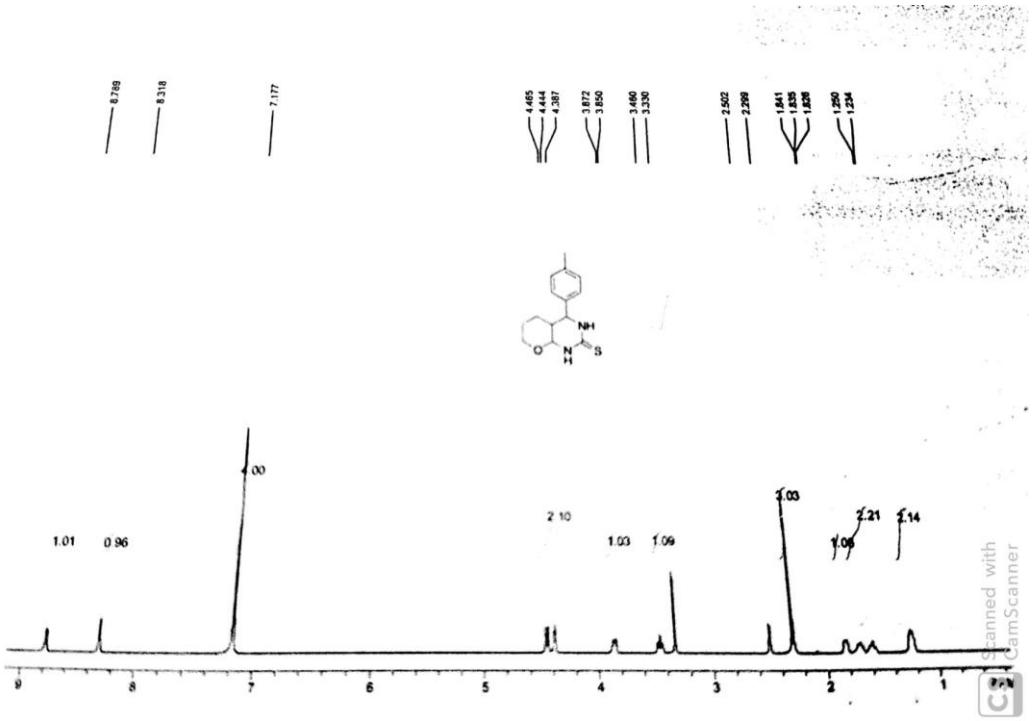


Figure S7: ^{1}H-NMR Spectrum of compound **4d**

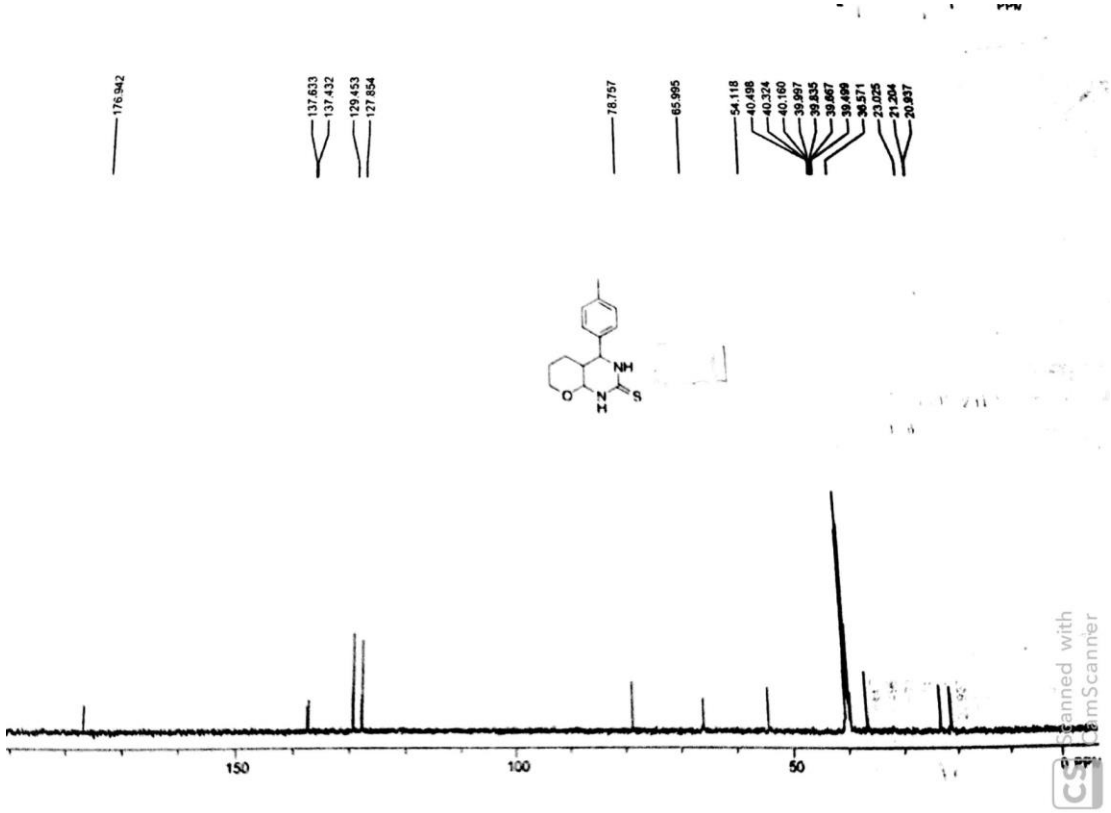


Figure S8: ^{13}C-NMR Spectrum of compound **4d**

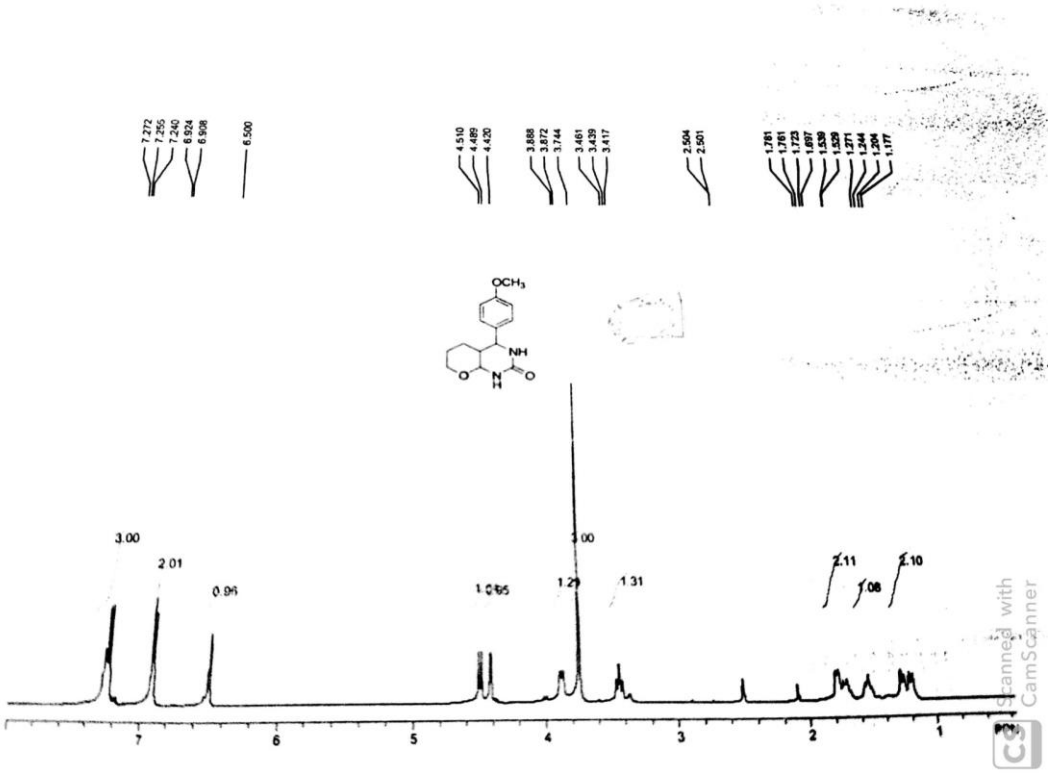


Figure S9: ^{1}H-NMR Spectrum of compound **4e**

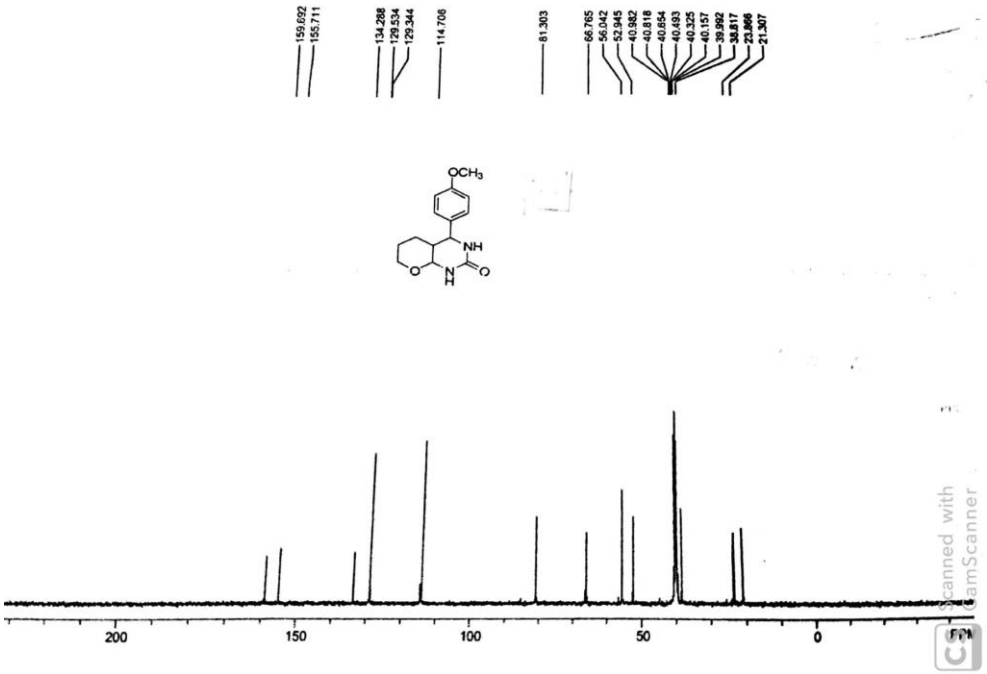


Figure S10: ^{13}C-NMR Spectrum of compound **4e**

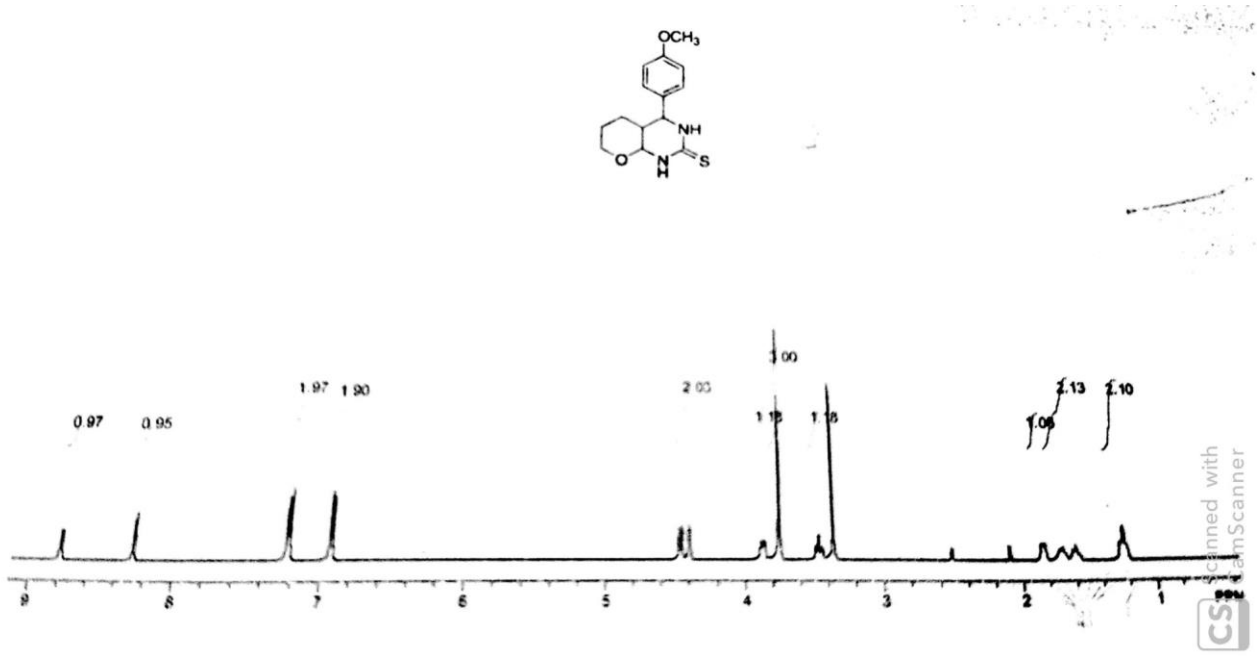


Figure S11: ^{1}H-NMR Spectrum of compound **4f**

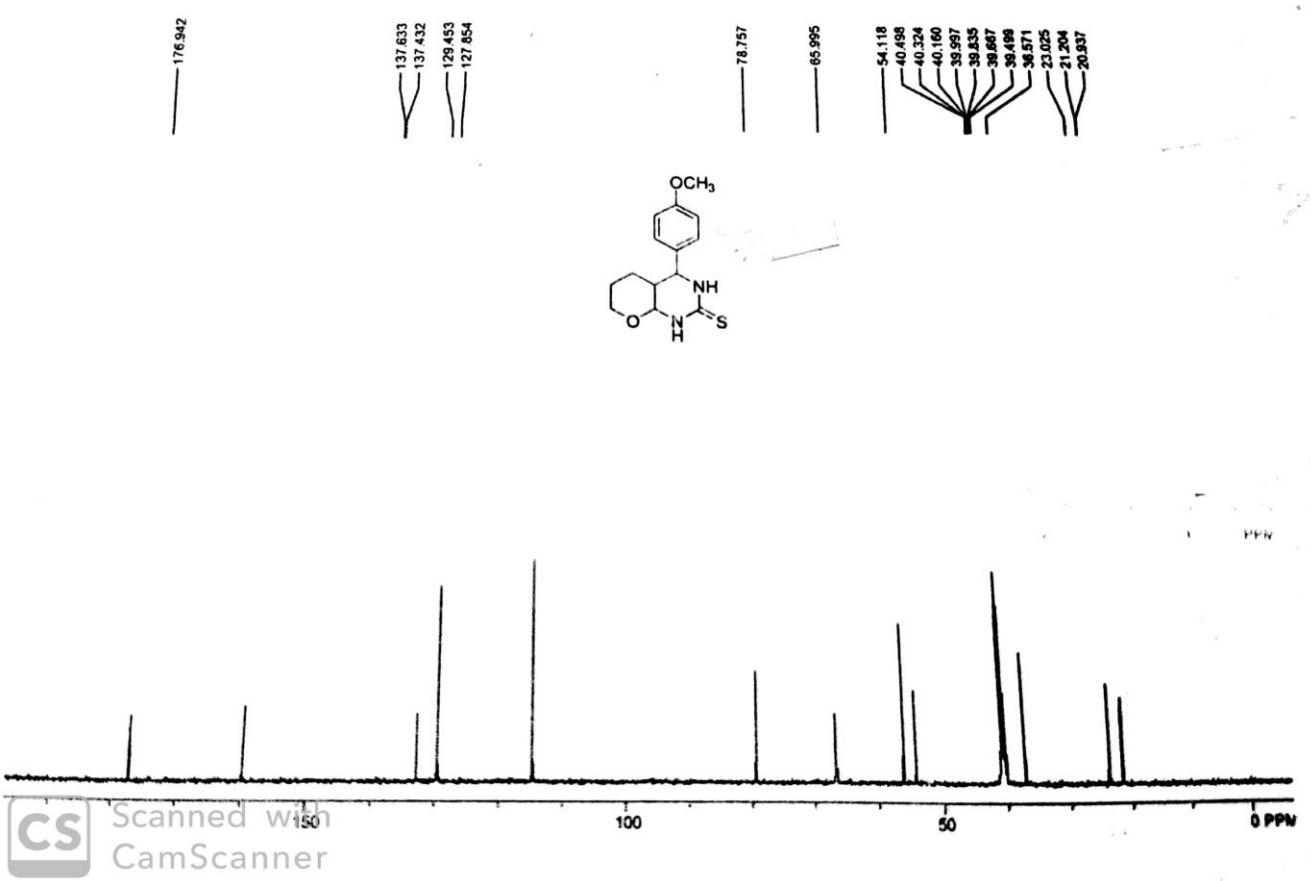


Figure S12: ^{13}C-NMR Spectrum of compound **4f**