Supporting Information for

Tuning the Biginelli Reaction Mechanism by Ionic Liquid Effect: The Combine Role of Supported Heteropolyacid Derivatives and the Acidic Strength

Elon F. Freitas,[a] Roberto Y. Souza,[b] Saulo T. A. Passos,[b] José A. Dias,[a]

Sílvia C. L. Dias.[a]* Brenno A. D. Neto,[b]*

[a] Laboratory of Catalysis, Chemistry Institute, (IQ-UnB), University of Brasília, Campus Universitário Darcy Ribeiro – Asa Norte, 70910-900, Brasília-DF, Brazil. E-mail: scdias@unb.br

[b] Laboratory of Medicinal and Technological Chemistry, University of Brasília, Chemistry Institute (IQ-UnB), Campus Universitário Darcy Ribeiro, 70904-970, Brasília, DF, Brazil. E-mail: brenno.ipi@gmail.com

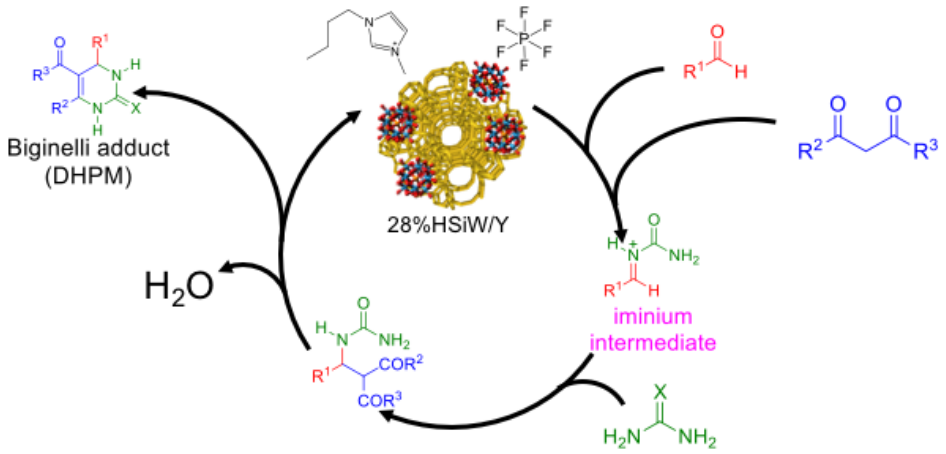

Table S1. Total acidity of HPA catalysts based on the amount of their protons.

Catalyst	**$n_{(H+)}$ HPA[a] (mmol g^{-1})**	**$n_{(H+)}$ HPA (mmol g^{-1}) in 30 mg catalyst[b]**	**$n_{(H+)}$ HPA (mmol g^{-1}) in 50 mg catalyst[c]**
HPW	1.04	0.031	0.052
HSiW	1.40	0.042	0.070
32% HPW/Y	0.33	0.009	0.017
46% HPW/Y	0.48	0.014	0.024
14% HSiW/Y	0.19	0.006	0.009
28% HSiW/Y	0.39	0.012	0.019
44% HSiW/Y	0.62	0.019	0.031

[a] Actual number of protons (mmol g^{-1}) on the catalyst based on HPA content. [b] Actual number of protons (mmol g^{-1}) on the 50 mg of catalyst based on HPA content. [c] Wt.% catalyst based on urea used in the reaction (60 mg).

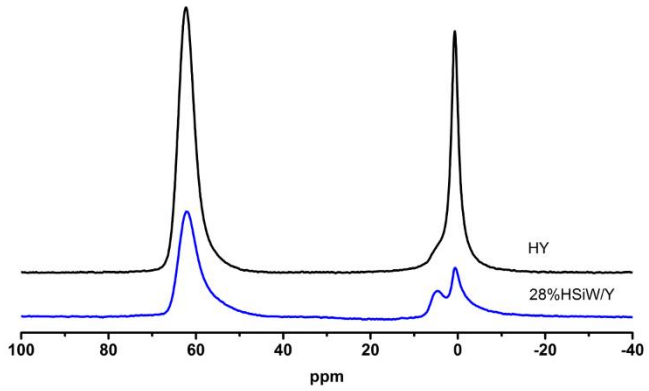

Figure S1. ^{27}Al MAS NMR spectra of calcined zeolite Y and calcined supported 28% HSiW/Y.

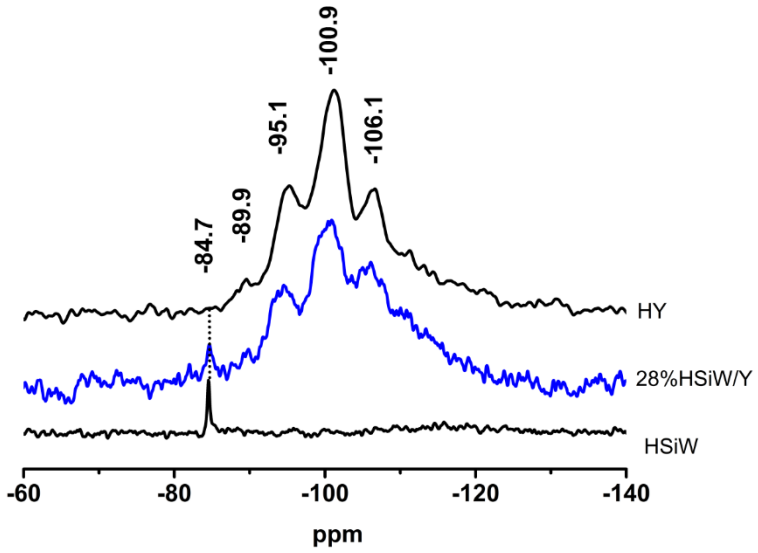

Figure S2. ^{29}Si MAS NMR spectra of HY, HSiW and 28% HSiW/Y.

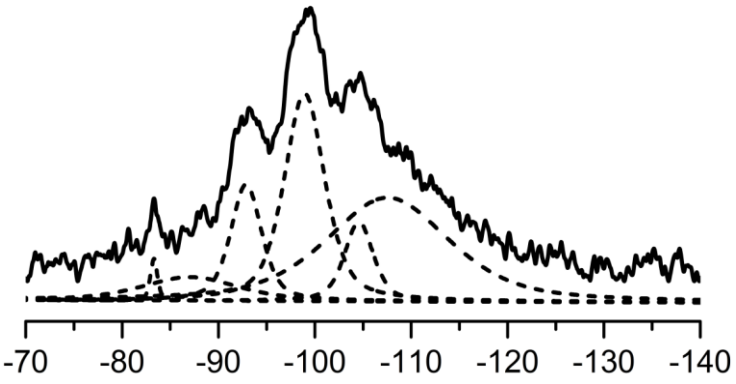

Figure S3. ^{29}Si MAS NMR spectrum and deconvolution of sample 28% HSiW/Y.

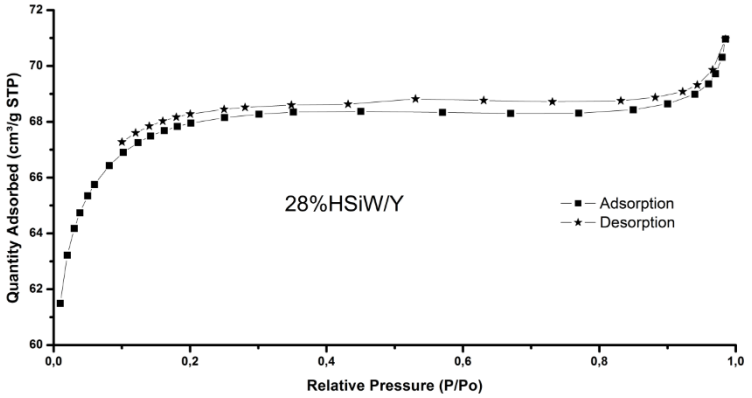

Figure S4. N_2 adsorption and desorption isotherm of 28% HSiW/Y.

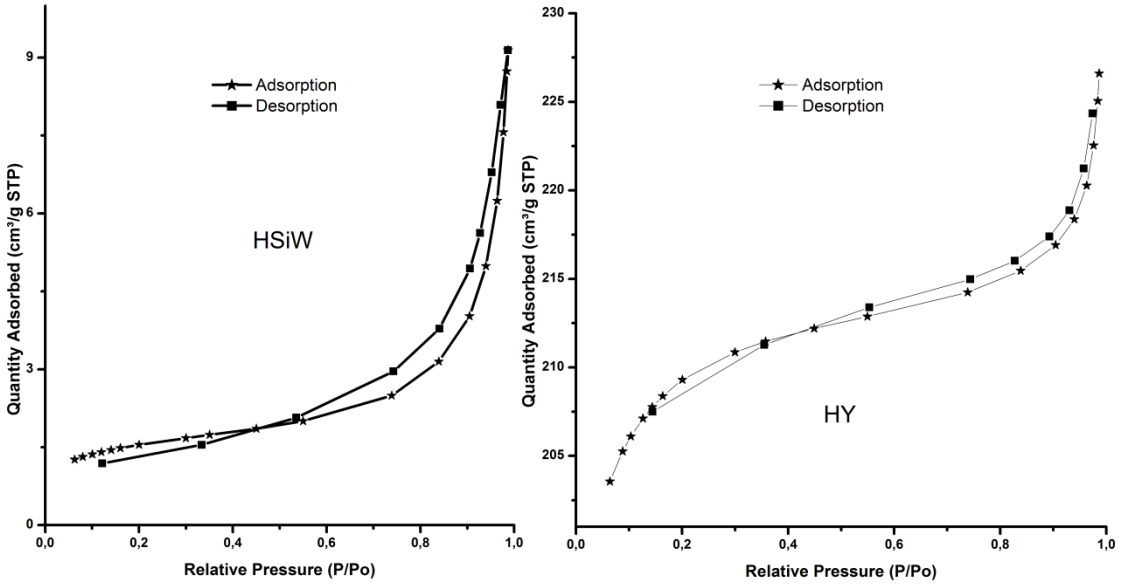

Figure S5. N_2 adsorption and desorption isotherms of HSiW and HY.

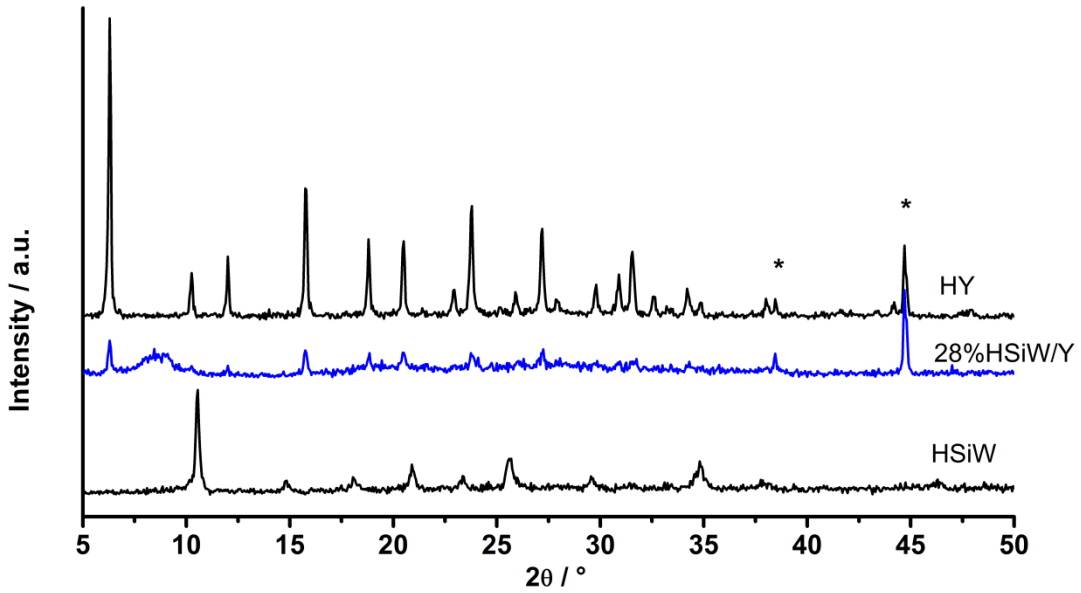

Figure S6. The XRD patterns of calcined zeolite Y, 28% HSiW/Y and HSiW. The (*) denotes peaks related to the aluminum sample holder.

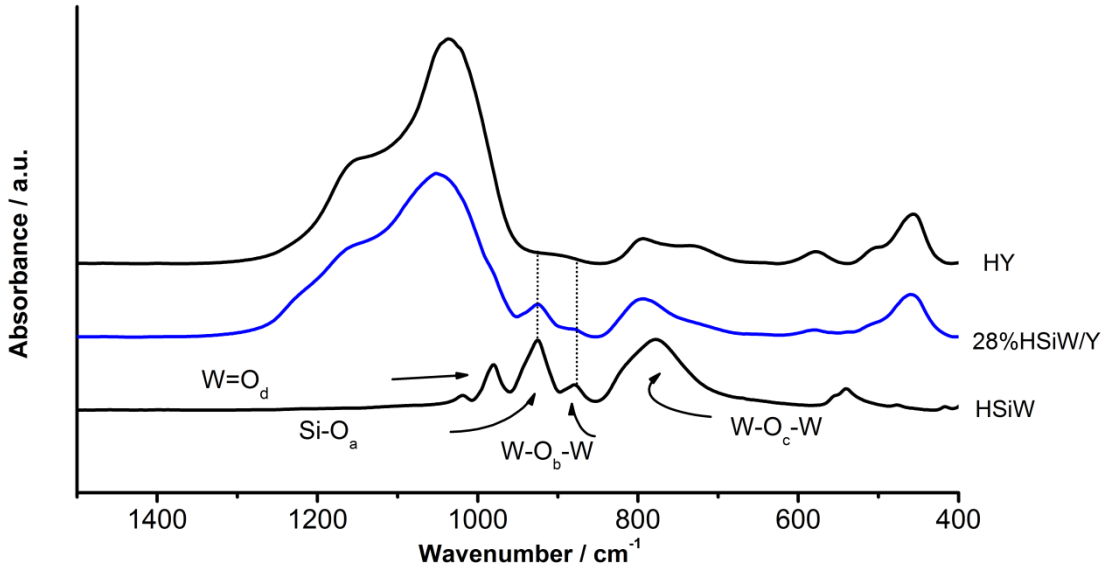

Figure S7. The FT-IR spectra of calcined zeolite Y, 28% HSiW/Y and HSiW.

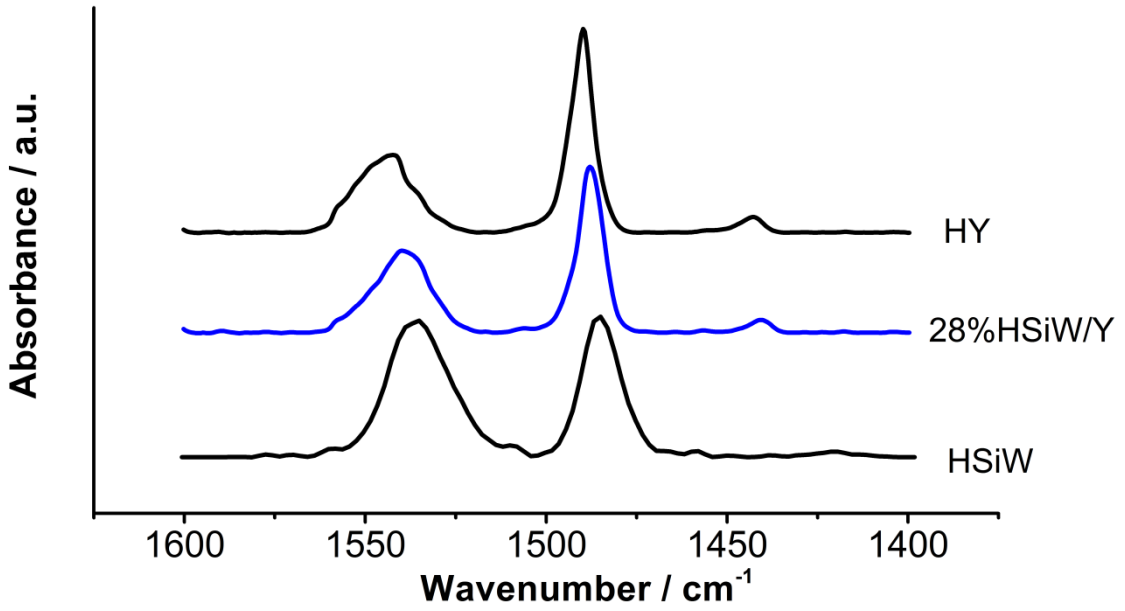

Figure S8. The FT-IR spectra after pyridine gas adsorption on calcined zeolite Y, 28% HSiW/Y and HSiW.

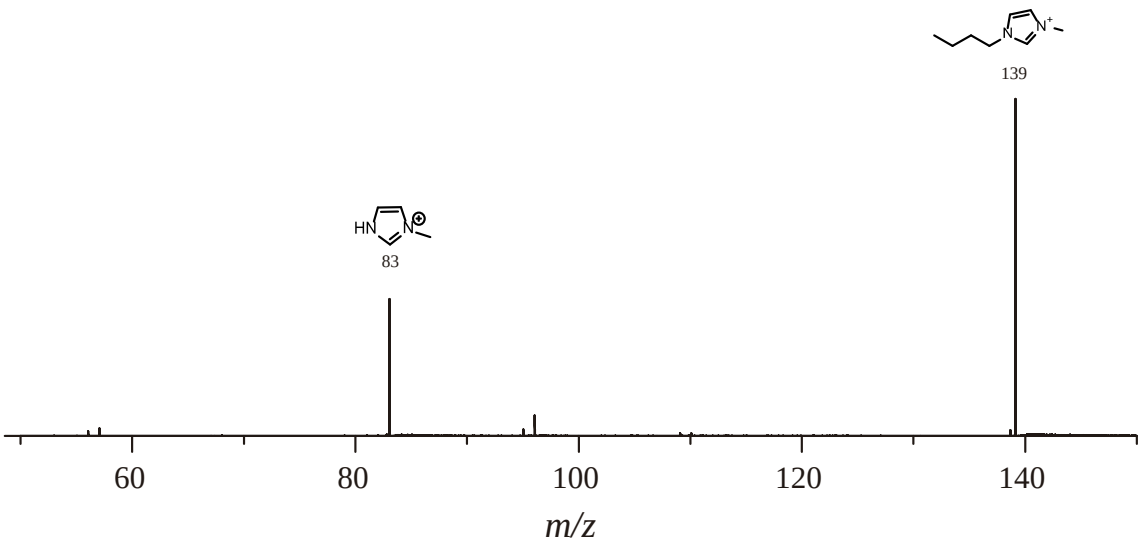

Figure S9. ESI(+)-MS/MS of the cation of *m/z* 139.

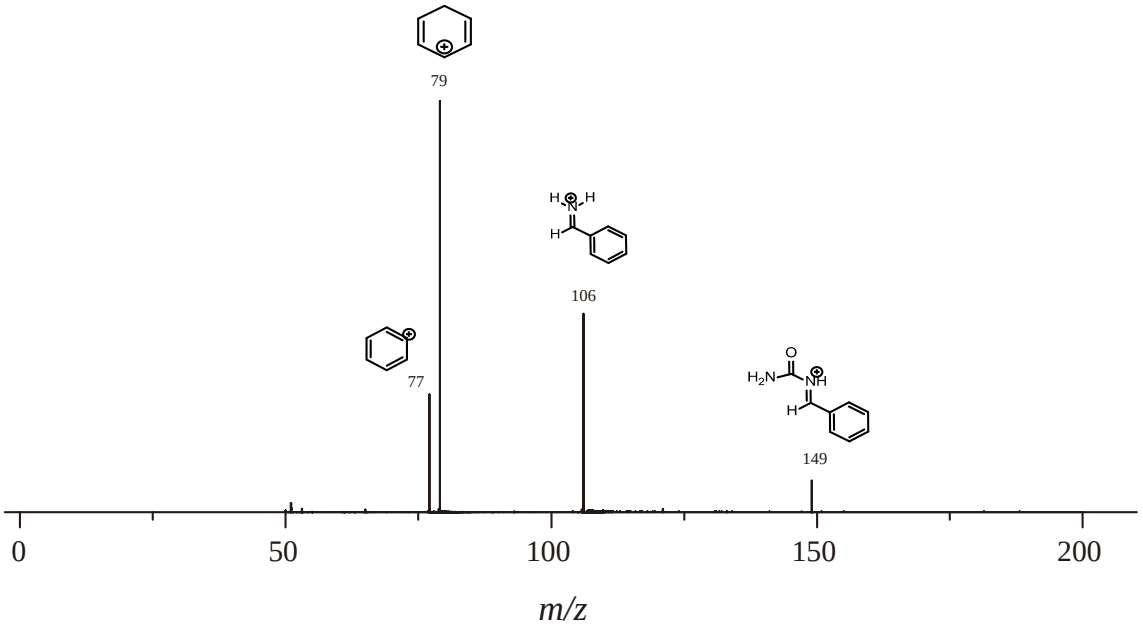

Figure S10. ESI(+)-MS/MS of the iminium intermediate of *m/z* 149.

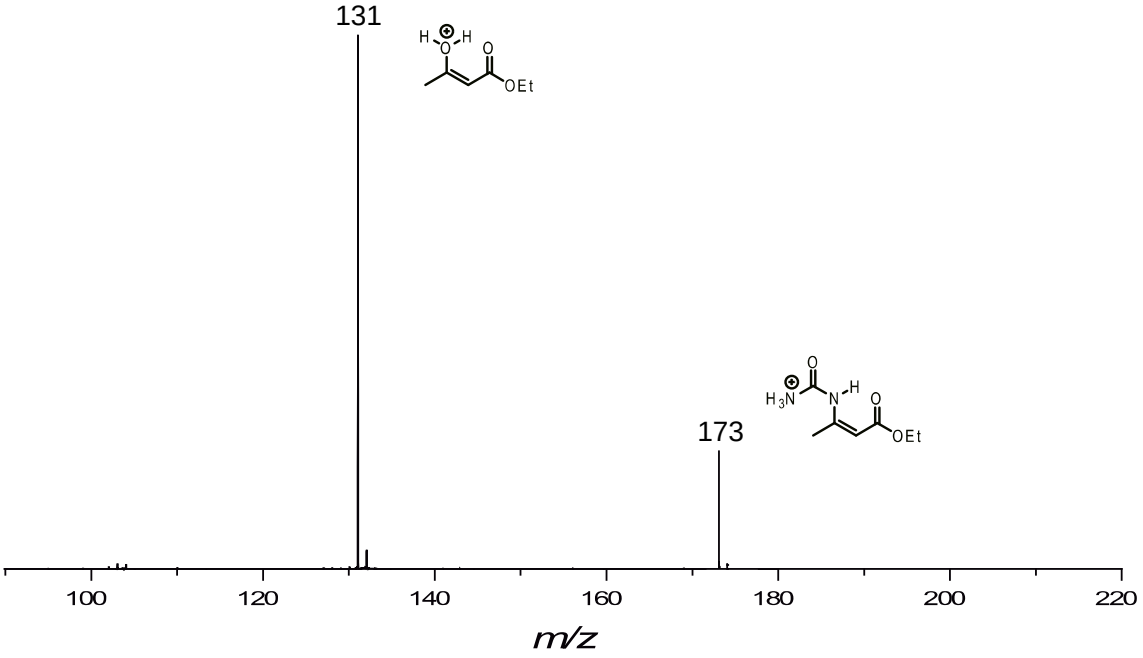

Figure S11. ESI(+)-MS/MS of the iminium intermediate of *m/z* 173.

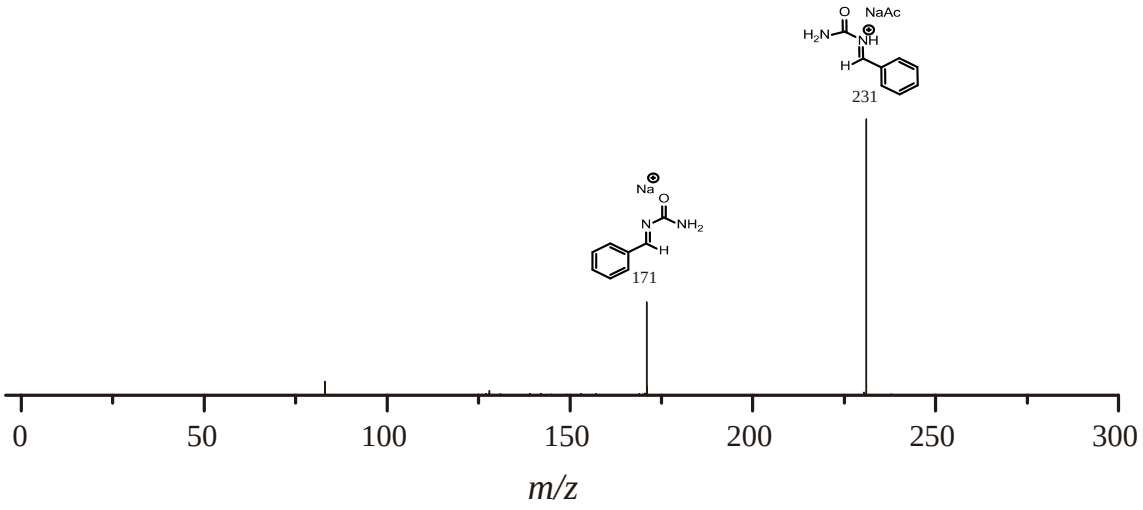

Figure S12. ESI(+)-MS/MS of the iminium intermediate (as AcONa adduct) of *m/z* 231.

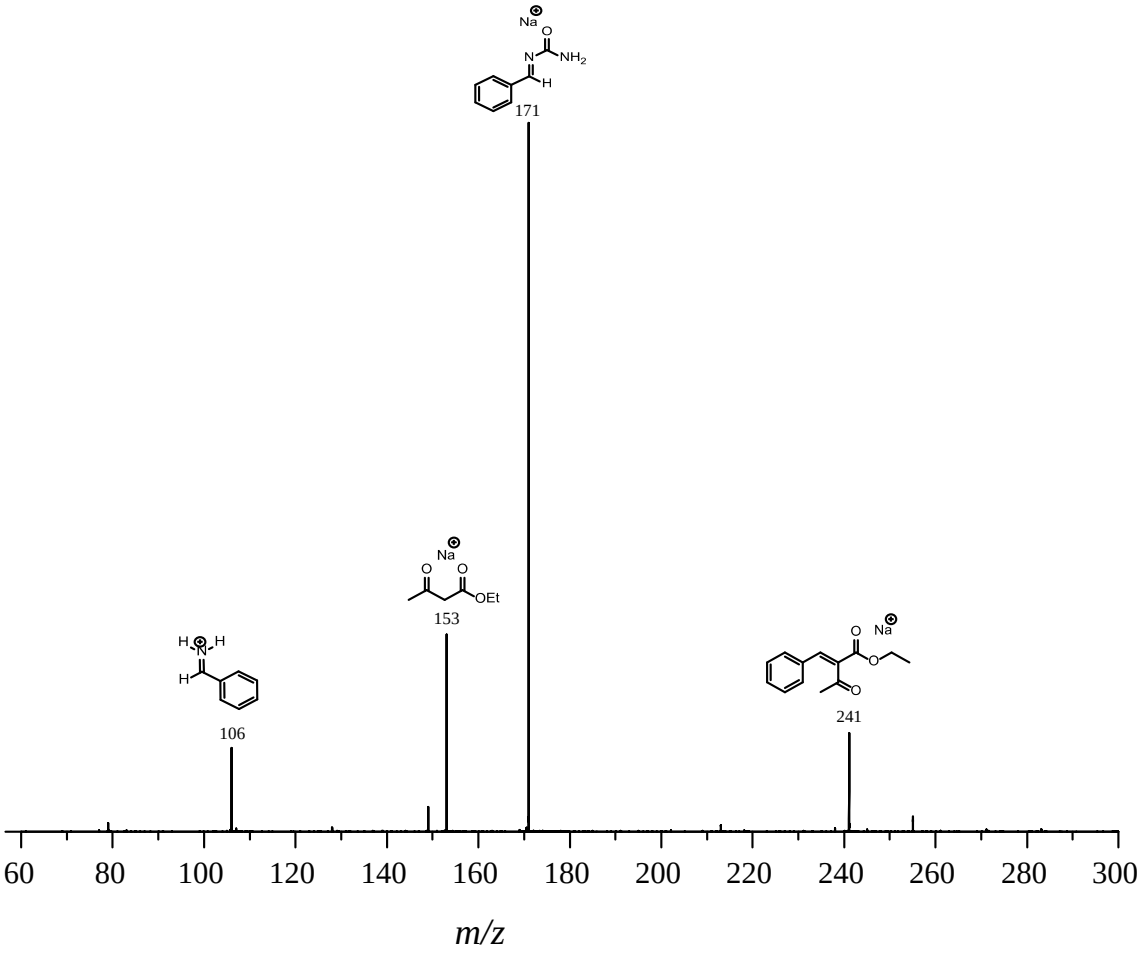

Figure S13. ESI(+)-MS/MS of the sodiated Knoevenagel intermediate of *m/z* 241.

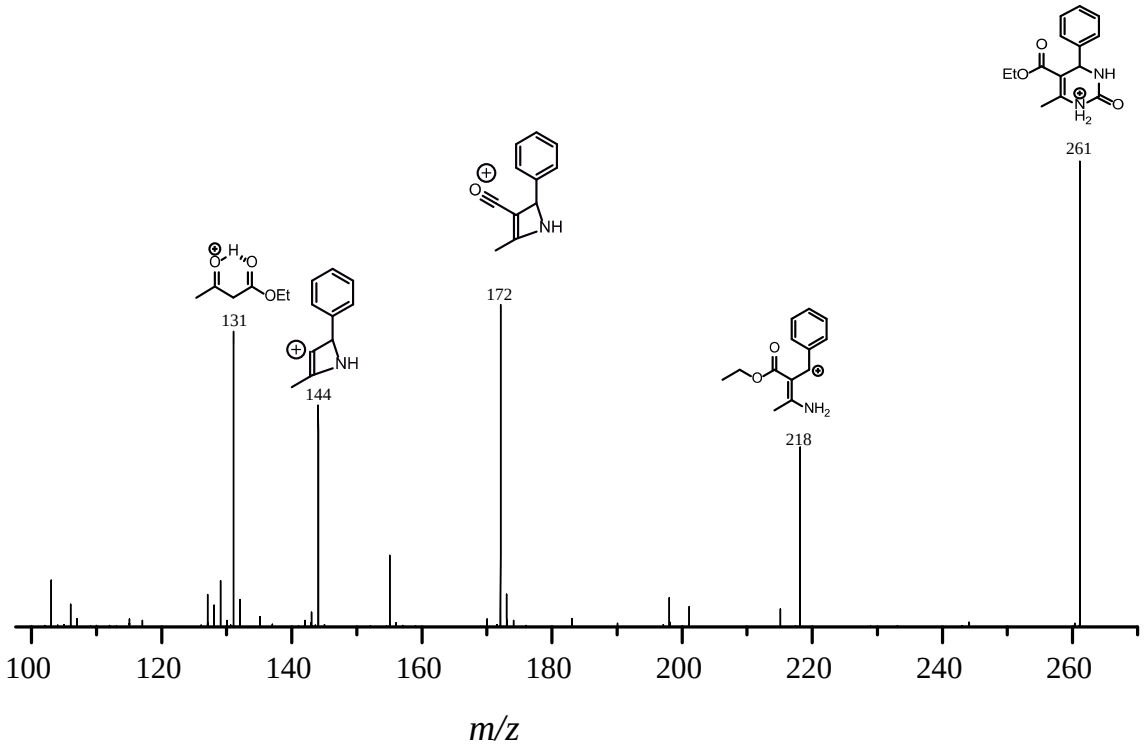

Figure S14. ESI(+)-MS/MS of the protonated Biginelli adduct of *m/z* 261.

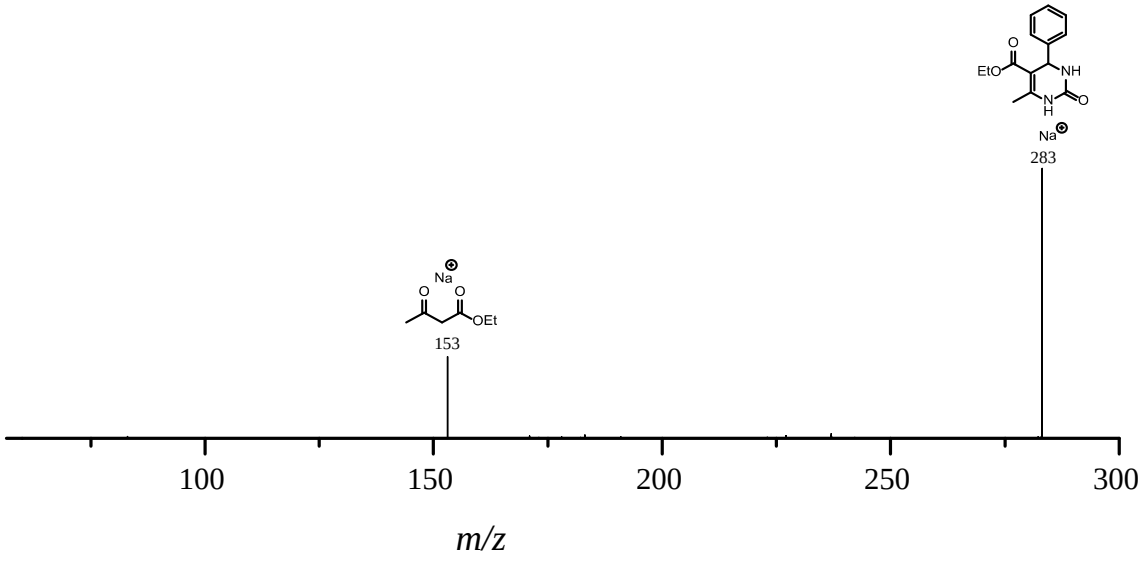

Figure S15. ESI(+)-MS/MS of the sodiated Biginelli adduct of *m/z* 283.

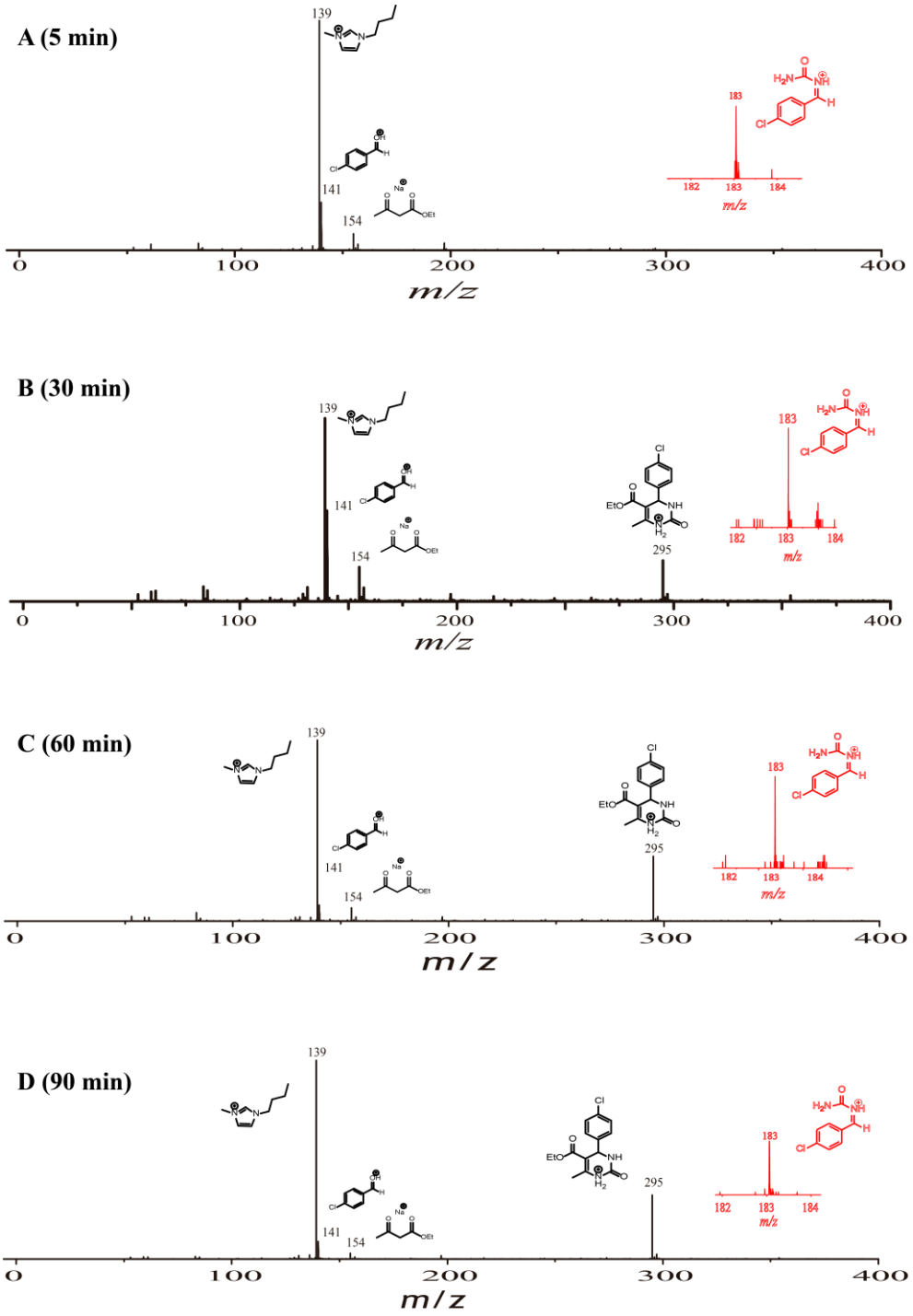

Figure S16. ESI-MS(+) monitoring of the Biginelli reaction in the presence of the ionic liquid BMI.PF_6 after 5, 30, 60 and 90 min of reaction. Reactions conditions: Catalyst (0.5 mol%), BMI.PF_6 (5.0 μM), 4-chloro benzaldehyde (5.0 μM), ethyl acetoacetate (5.0 μM), urea (5.0 μM). Analyses performed dissolving the reaction mixture in methanol affording the described concentrations. The inset (red) is the iminium ion intermediate of *m/z* 183.

Ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylatev(A). Pale yellow solid, mp 204-205 °C. ^{1}H NMR (600 MHz, DMSO-d_6) δ ppm 9.19 (1 H, s) 7.74 (1 H, br. s.) 7.36 - 7.30 (2 H, m) 7.29 - 7.22 (4 H, m) 5.15 (1 H, d, *J*=3.30 Hz) 3.99 (2 H, q, *J*=7.21 Hz) 2.26 (3 H, s) 1.10 (4 H, t, *J*=7.15 Hz). ^{13}C NMR (150 MHz, DMSO-d_6) δ ppm 165.3, 152.1, 148.3, 144.8, 128.4, 127.2, 126.2, 99.2, 59.1, 53.9, 17.7, 14.0. Yield: 99% (257 mg).

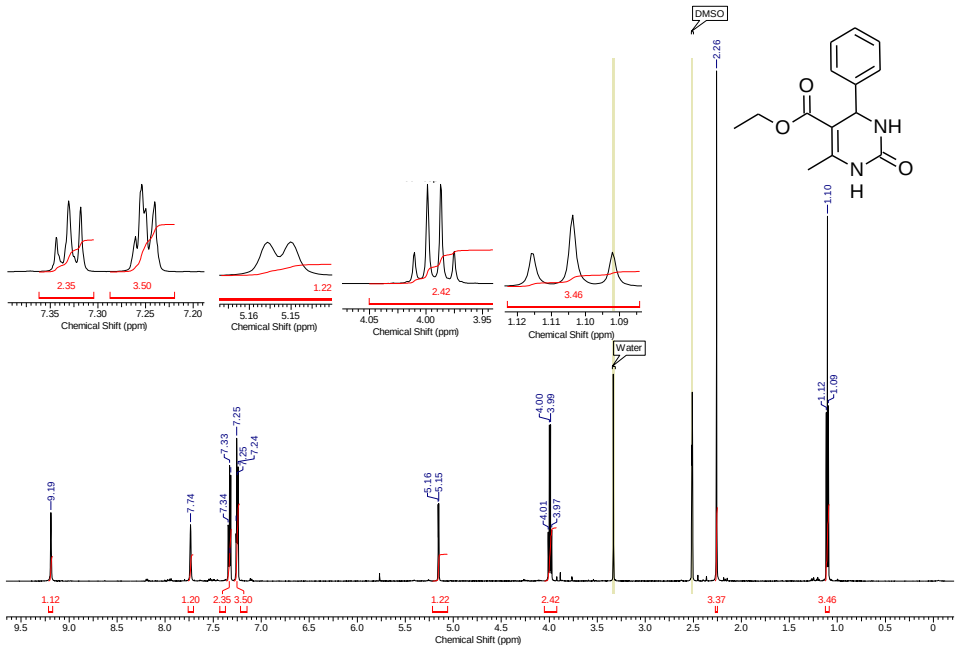

Figure S17. ^{1}H NMR (600 MHz, DMSO-d$_6$) of DHPM **a**.

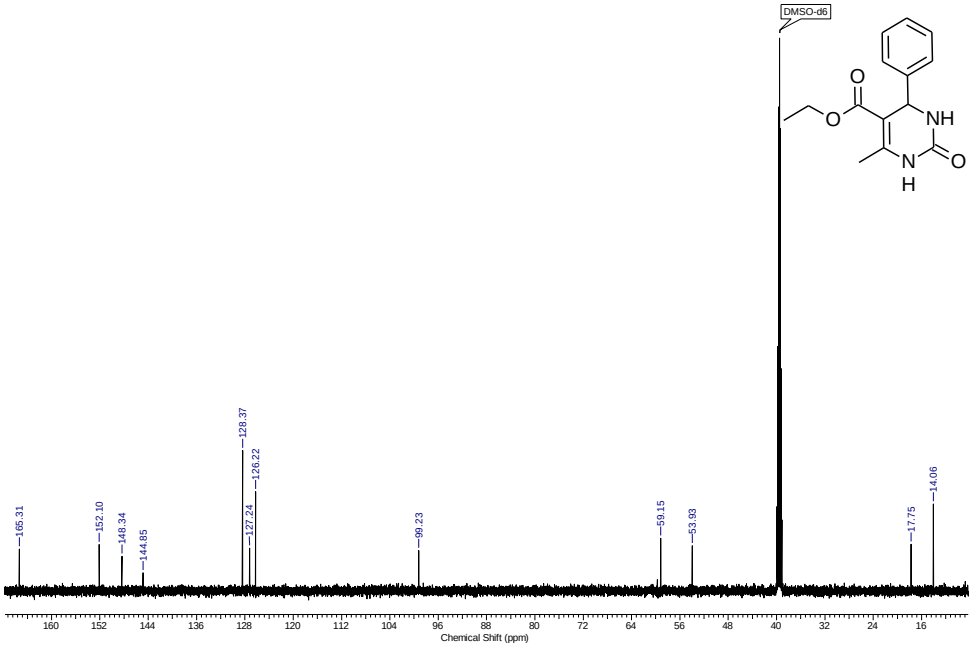

Figure S18. ^{13}C NMR (150 MHz, DMSO-d_6) of DHPM **a**.

Ethyl 4-(3-hydroxyphenyl)-6-mEthyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5 carboxylate. White solid, mp 188-189 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.30 (1 H, s) 9.68 - 9.55 (1 H, m) 9.44 (1 H, s) 7.12 (1 H, t, *J*=7.77 Hz) 6.73 - 6.56 (3 H, m) 5.08 (1 H, d, *J*=3.81 Hz) 4.02 (2 H, q, *J*=7.03 Hz) 2.28 (3 H, s) 1.12 (3 H, t, *J*=7.03 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 174.2, 165.2, 157.5, 144.8, 129.5, 117.0, 114.6, 113.2, 100.8, 59.6, 54.0, 17.2, 14.0. Yield: 89% (260 mg).

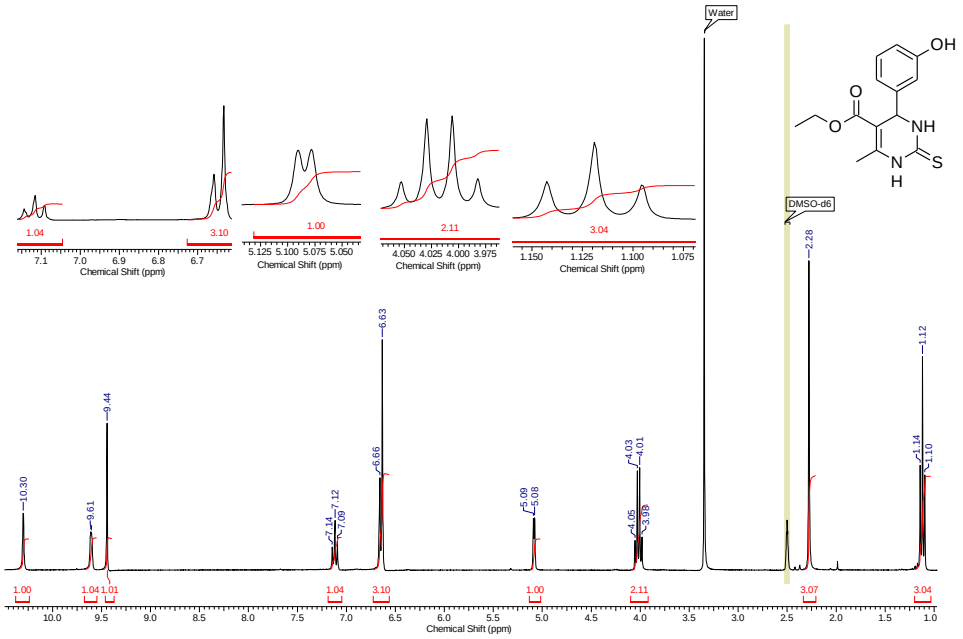

Figure S19. ^{1}H NMR (300 MHz, DMSO-d_6) of DHPM **b**.

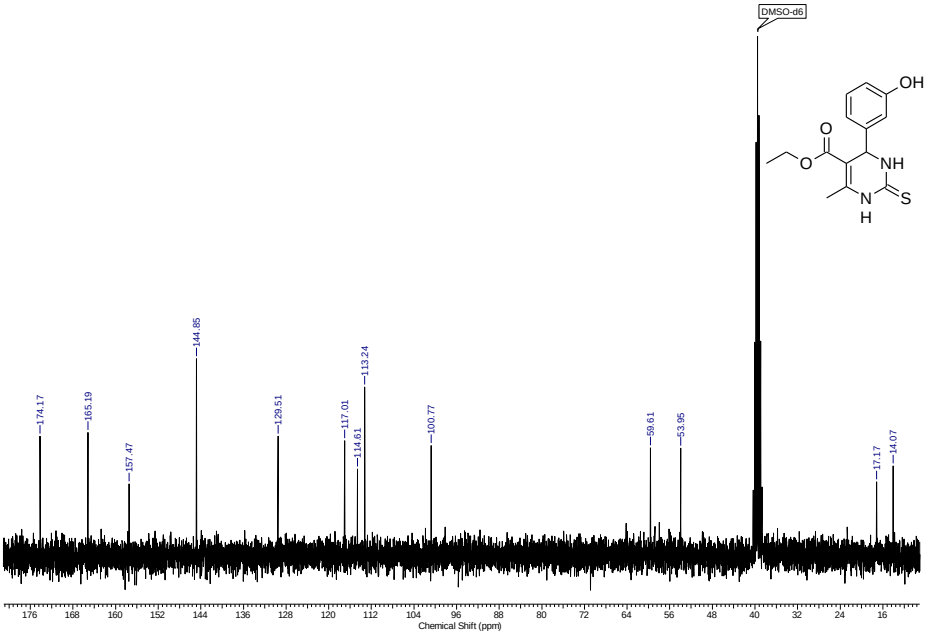

Figure S20. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **b**.

Ethyl 4-(benzo[d][1,3]dioxol-5-yl)-6-mEthyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. Pale yellow solid, mp 174-175 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.37 (1 H, s) 9.72 (1 H, br. s.) 6.99 - 6.82 (1 H, m) 6.77 - 6.60 (2 H, m) 6.00 (2 H, s) 5.12 (1 H, d, *J*=3.52 Hz) 4.01 (2 H, q, *J*=7.03 Hz) 2.30 (3 H, s) 1.11 (3 H, t, *J*=7.03 Hz)^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 165.0, 147.4, 146.8, 144.8, 137.3, 119.7,108.2, 106.8, 101.1, 100.9, 59.7, 53.8, 17.2, 14.0. Yield: 83% (265 mg).

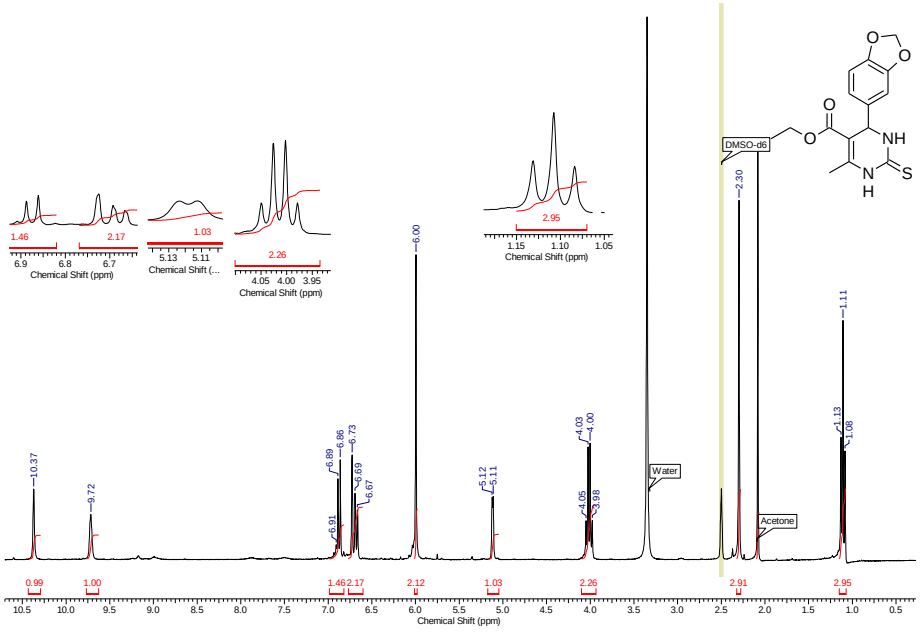

Figure S21. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **c**.

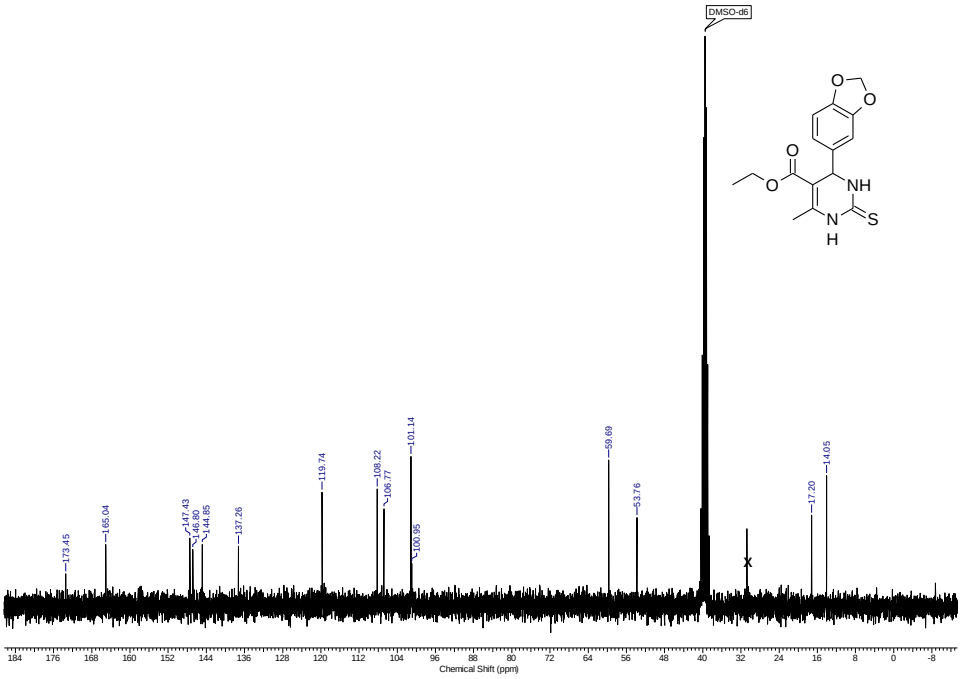

Figure S22. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **c**.

Ethyl 4-(4-hydroxy-3-methoxyphenyl)-6-mEthyl-2-thioxo-1,2,3,4 tetrahydropyrimidine-5-carboxylate. White solid, mp 208-209 °C, ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.26 (1 H, s) 9.56 (1 H, br. s.) 9.02 (1 H, s) 6.84 - 6.65 (2 H, m) 6.59 (1 H, d, *J*=7.91 Hz) 5.08 (1 H, br. s.) 4.02 (2 H, q, *J*=7.03 Hz) 3.72 (3 H, s) 2.28 (3 H, s) 1.12 (3 H, t, *J*=7.03 Hz)^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 174.0, 165.3, 147.4, 146.2, 144.6, 134.6, 118.5, 115.4, 110.9, 101.0, 59.6, 55.6, 53.7, 17.1, 14.1. Yield: 90% (275.4 mg).

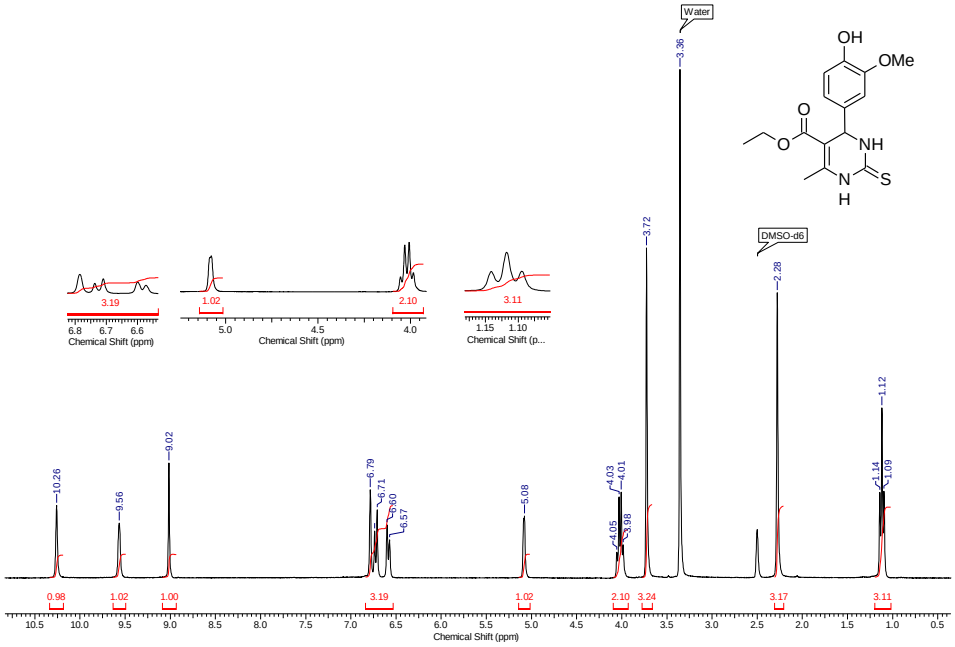

Figure S23. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **d**.

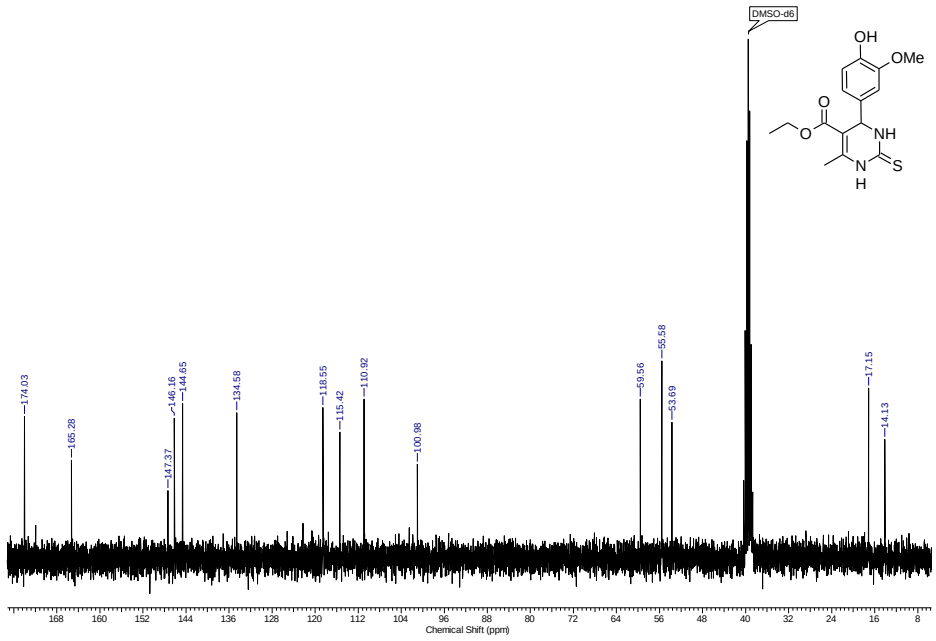

Figure S24. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **d**.

Ethyl 6-mEthyl-4-phenyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. Pale yellow solid, mp 198-200 °C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.34 (1 H, br. s.) 9.66 (1 H, br. s.) 7.38 - 7.20 (6 H, m) 5.17 (1 H, br. s.) 4.01 (2 H, q, *J*=7.04 Hz) 2.29 (3 H, br. s.) 1.10 (3 H, t, *J*=6.45 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 174.2, 165.1, 145.0, 143.5, 128.6, 127.7, 126.4, 100.7, 59.6, 54.0, 17.2, 14.0. Yield: 96% (265 mg).

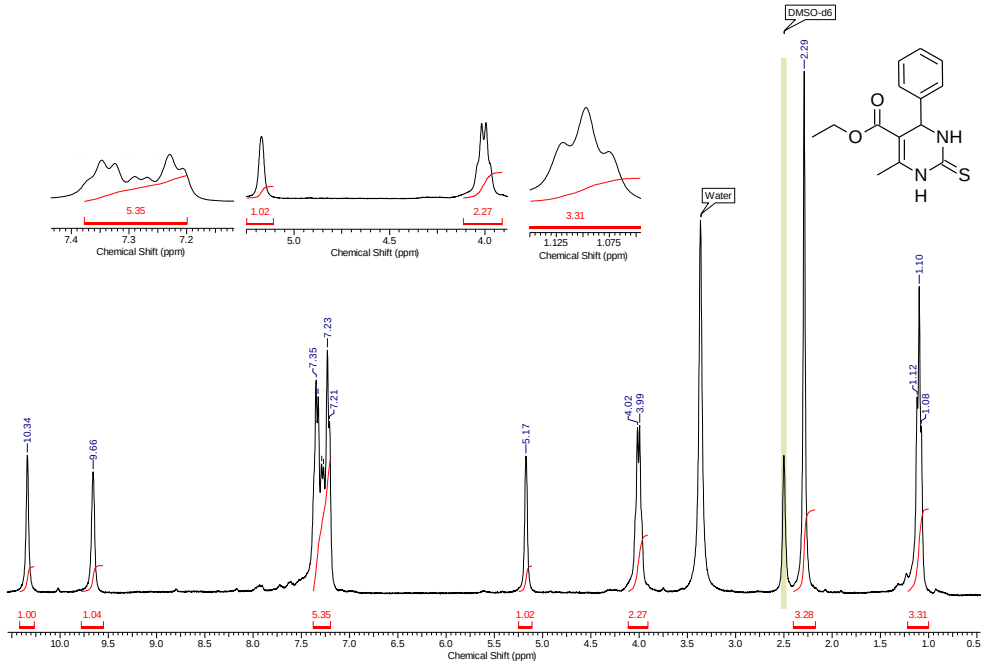

Figure S25. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **e**.

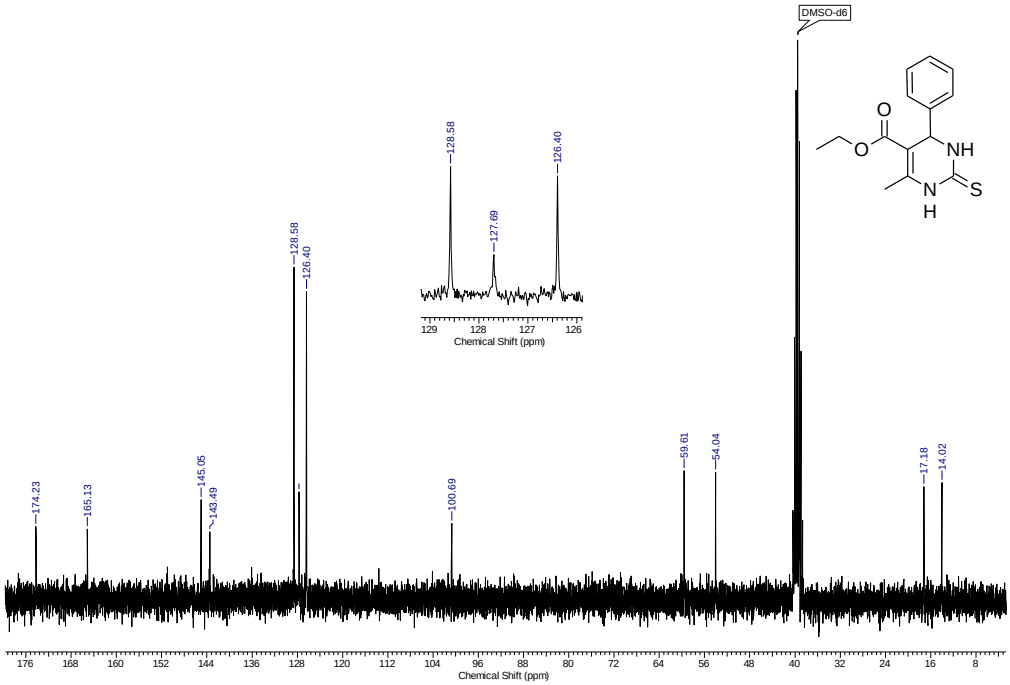

Figure S26. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **e**.

Ethyl 4-(2-hydroxyphenyl)-6-mEthyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. White solid, mp 190-191°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.32 (1 H, d, *J*=3.52 Hz) 9.10 (1 H, s) 7.22 - 7.13 (2 H, m) 6.97 - 6.89 (1 H, m) 6.79 (1 H, d, *J*=7.91 Hz) 4.52 (1 H, dd, *J*=4.84, 2.49 Hz) 3.97 (2 H, q, *J*=7.13 Hz) 1.83 (3 H, s) 1.00 (3 H, t, *J*=7.03 Hz)**.** ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 176.3, 167.1, 150.78, 129.2, 129.1, 122.4, 121.1, 116.4, 81.3, 60.6, 47.2, 43.1, 24.1, 13.7. Yield: 88% (257 mg).

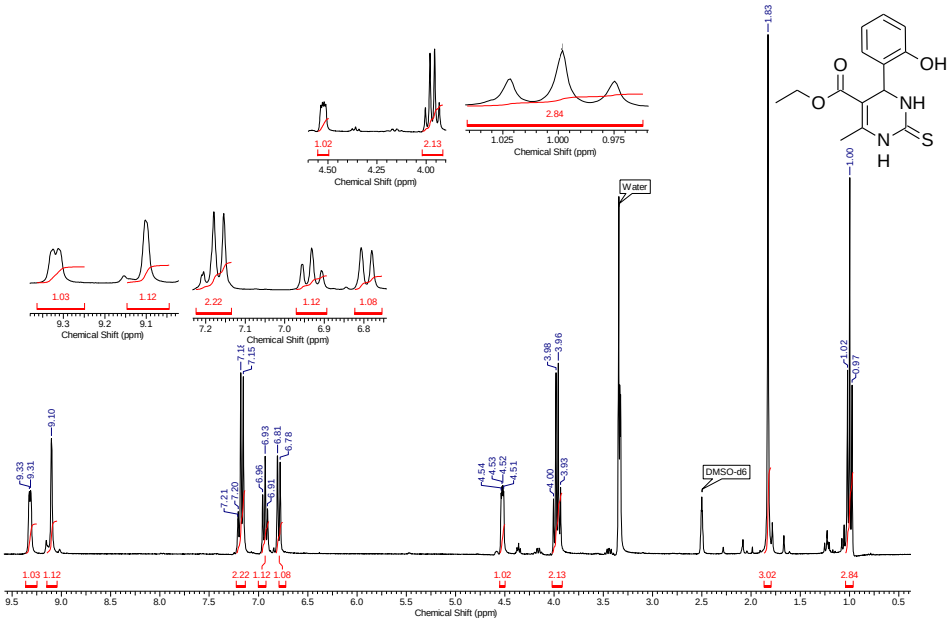

Figure S27. ^{1}H NMR (300 MHz, DMSO-d_6) of DHPM **f**.

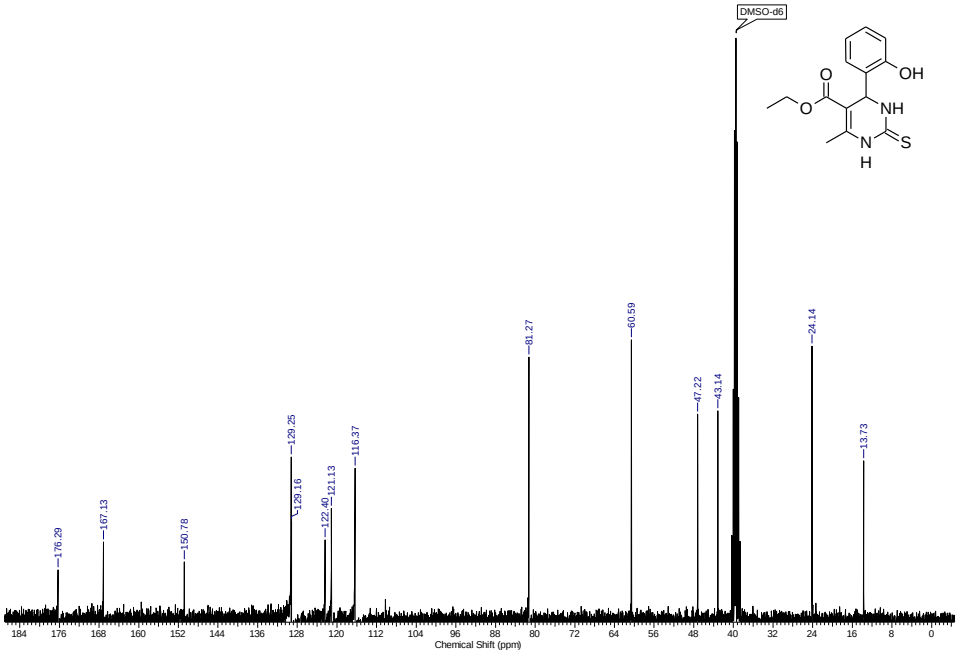

Figure S28. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **f**.

Ethyl 4-(3-hydroxyphenyl)-6-mEthyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. White solid, mp 169-170°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.37 (1 H, s) 9.15 (1 H, s) 7.68 (1 H, br. s.) 7.09 (1 H, t, *J*=8.06 Hz) 6.70 - 6.58 (3 H, m) 5.05 (1 H, d, *J*=3.22 Hz) 3.99 (2 H, q, *J*=7.03 Hz) 2.23 (3 H, s) 1.08 - 1.15 (3 H, m). ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 165.4, 157.3. 152.2, 148.1, 146.3, 129.3, 116.9, 114.2, 113.1, 104.8, 99.4, 59.2, 53.8, 17.8, 14.1. Yield: 91% (236 mg).

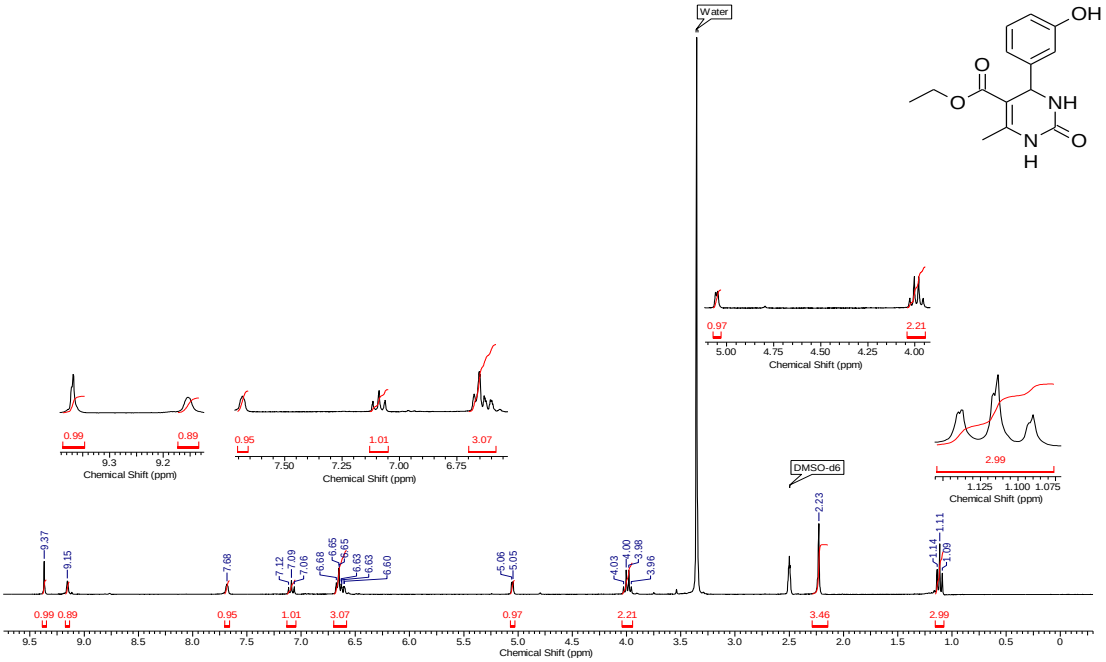

Figure S29. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **g**.

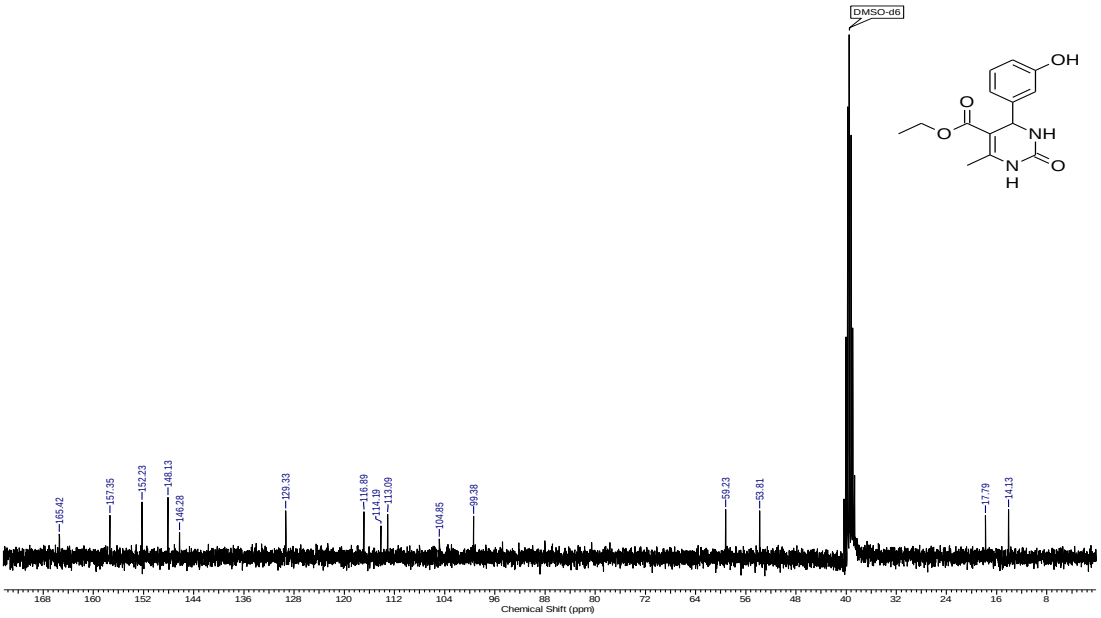

Figure S30. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **g**.

Ethyl 4-(4-chlorophenyl)-6-mEthyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. Pale yellow solid, mp 211-213°C.^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 9.25 (1 H, br. s.) 7.78 (1 H, br. s.) 7.39- 7.24 (4 H,) 5.13 (1 H, br. s.) 3.98 (2 H, q, *J*=6.94 Hz) 2.24 (3 H, s) 1.09 (3 H, t, *J*=6.89 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 165.2, 151.9, 148.7, 143.8, 131.8, 128.4 128.2, 98.8, 59.2, 53.4, 17.8, 14.1. Yield: 70% (205.6 mg).

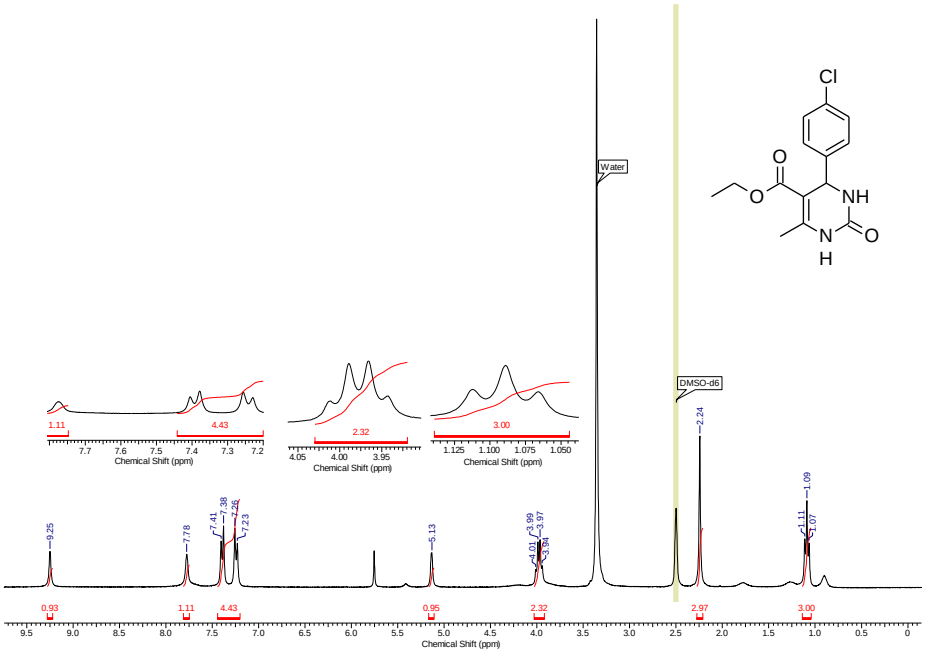

Figure S31. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **h**.

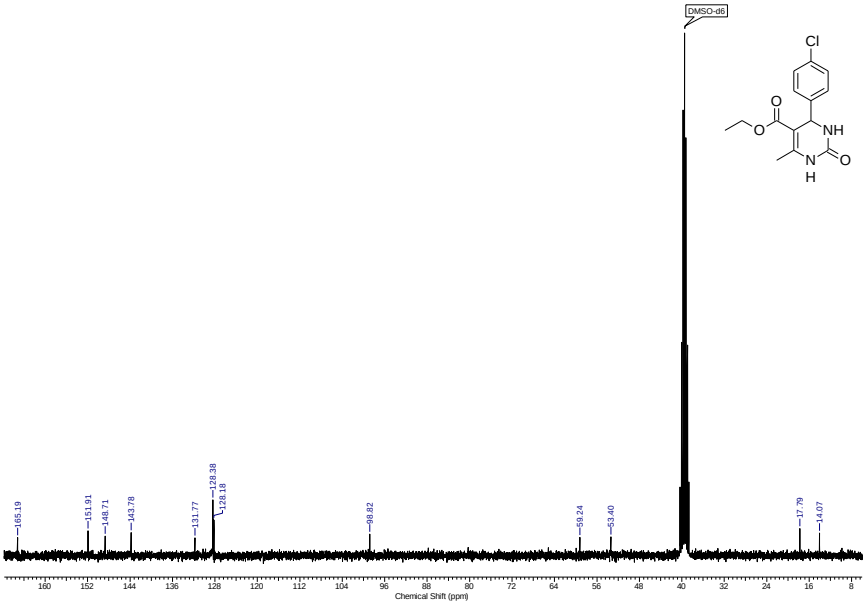

Figure S32. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **h**.

Ethyl 4-(4-bromophenyl)-6-mEthyl-2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. Yellow solid, mp 190-191°C. ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 10.39 (1 H, s) 9.70 - 9.65 (1 H, m) 7.58 - 7.52 (2 H, m) 7.20 - 7.14 (2 H, m) 5.16 (1 H, d, *J*=3.81 Hz) 4.00 (2 H, q, *J*=6.94 Hz) 2.29 (3 H, s) 1.06 - 1.13 (3 H, m)**.** ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 174.2, 165.0, 145.4, 142.8, 131.5, 128.7, 120.9 100.2, 59.7, 53.6, 17.2, 14.0. Yield: 84% (297 mg).

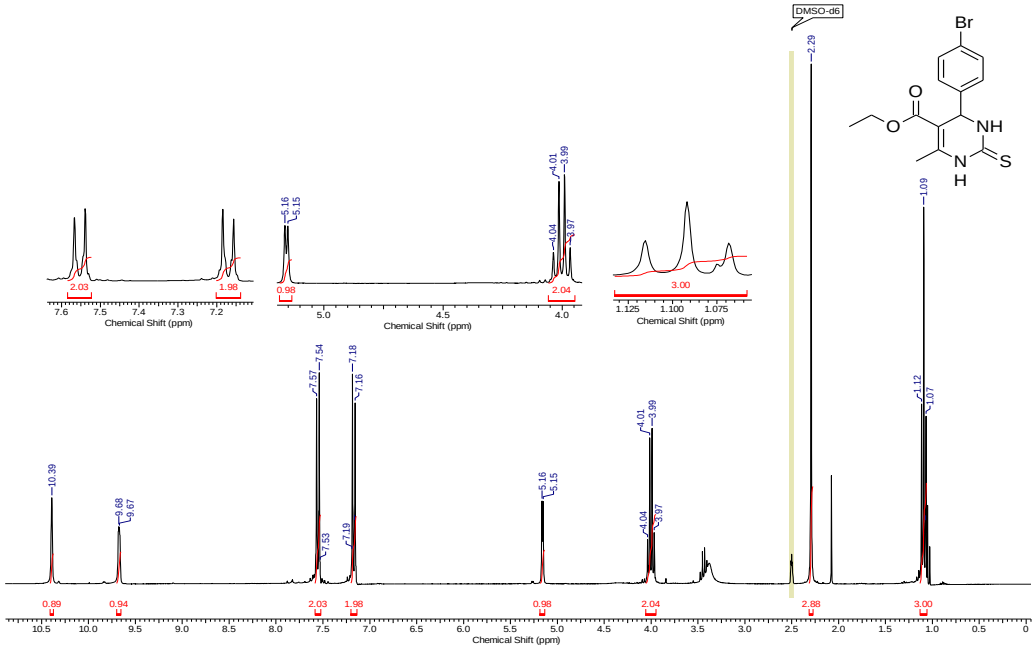

Figure S33. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **i**.

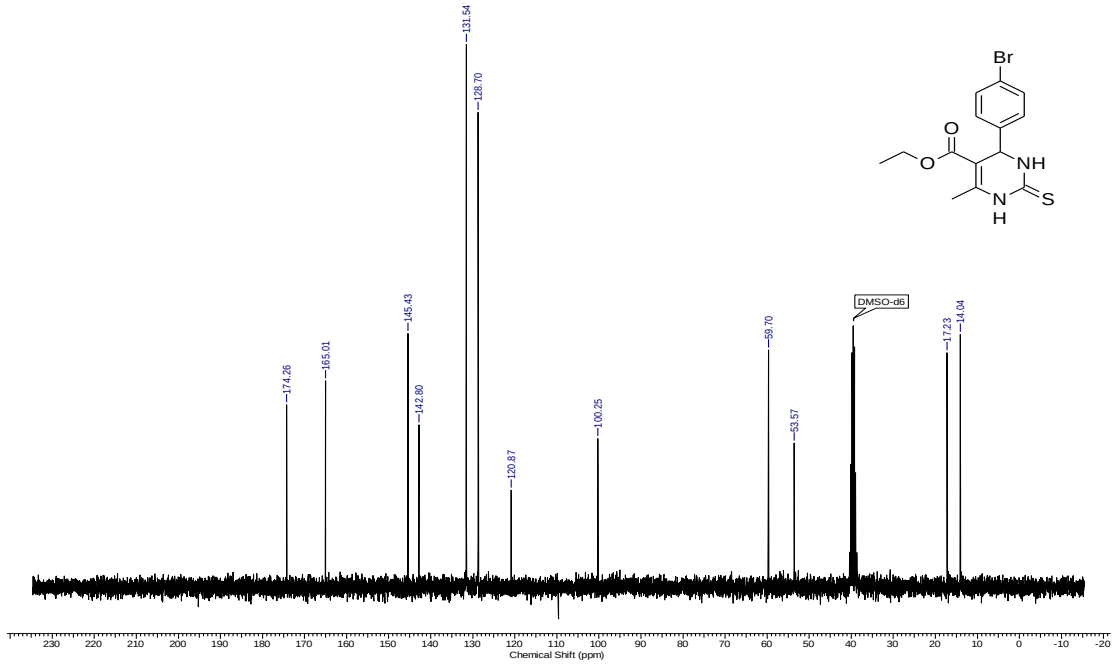

Figure S34. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **i**.

Ethyl 4-(4-bromophenyl)-6-mEthyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate. Pale yellow solid, mp 194-196°C. ^{1}H NMR (600 MHz, DMSO-d_6) δ ppm 9.23 (1 H, s) 7.76 (1 H, br. s.) 7.52 (2 H, d, *J*=8.44 Hz) 7.18 (2 H, d, *J*=8.44 Hz) 5.12 (1 H, d, *J*=3.30 Hz) 3.98 (2 H, q, *J*=6.97 Hz) 2.24 (3 H, s) 1.09 (3 H, t, *J*=6.97 Hz). ^{13}C NMR (75 MHz, DMSO-d_6) δ ppm 165.2, 152.0, 148.8, 144.2, 131.4, 128.6, 120.3, 98.8, 59.3, 53.5, 17.8, 14.1. Yield: 70% (249 mg).

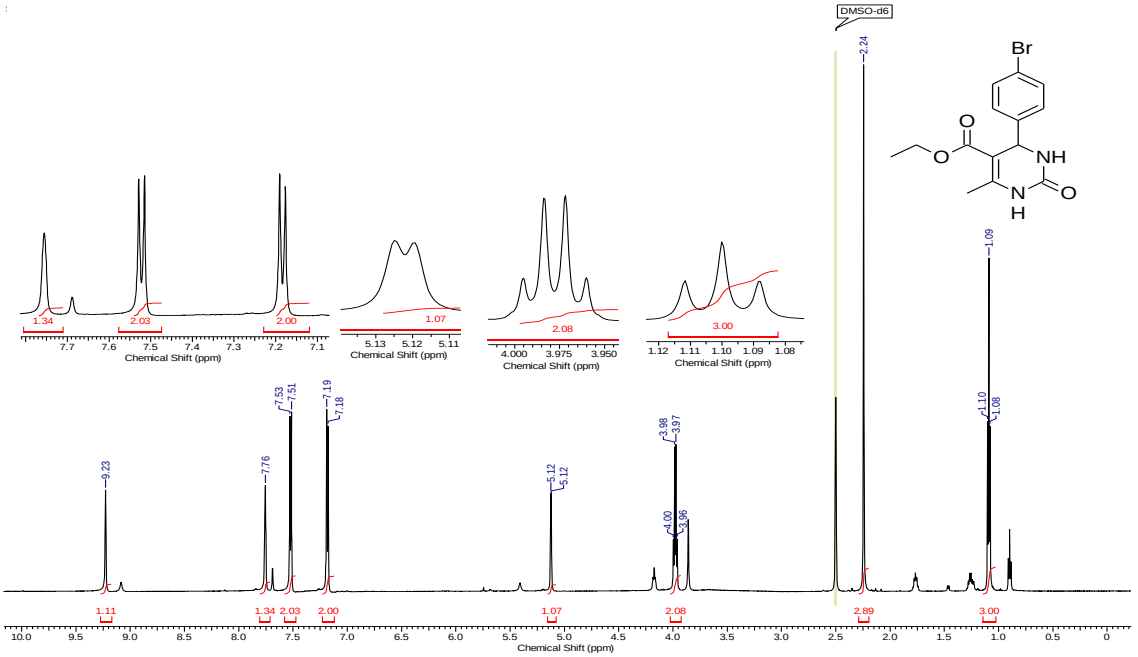

Figure S35. ^{1}H NMR (300 MHz, DMSO-d$_6$) of DHPM **j**.

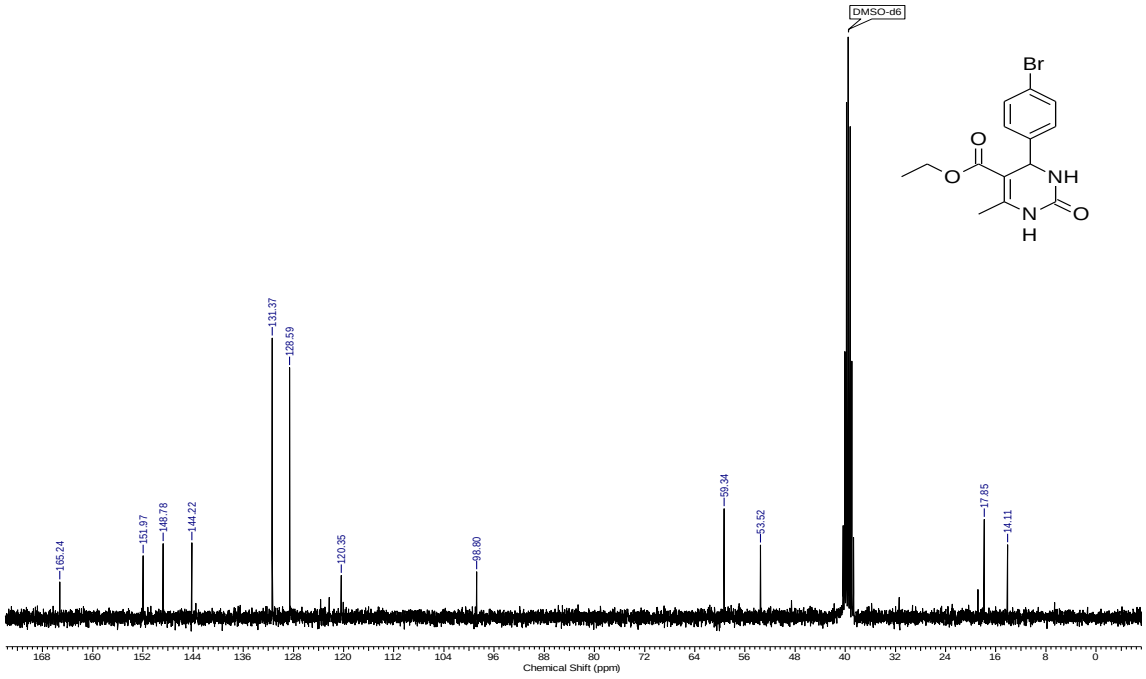

Figure S36. ^{13}C NMR (75 MHz, DMSO-d_6) of DHPM **j**.