Piperidinium borate as efficient and recyclable catalyst for one-pot, three-component, environmentally friendly synthesis of pyran-annulated heterocycles and 2-amino-3-cyano-4*H*-pyrans

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1. Experimental:

1.1 General methods and materials

All solvents and reagents were obtained from Avra Synthesis, Spectrochem, and SD Fine Chemicals and were utilized without purification. All reactions were carried out in an oven-dried glassware fuming hood, magnetically agitated, and heated in an oil bath. Melting points were recorded on the Analab ThermoCal instrument in open glass capillaries and were uncorrected. The reactions were monitored by TLC on Merck silica gel G F254 plates. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra are recorded on MR500 NMR spectrometer, Agilent Technologies DMSO-d_6 with tetramethylsilane (TMS) as the internal standard.

1.2 General procedure for the synthesis of pyrano[3,2-*c*]pyrazoles, 1*H*-pyrano[2,3-*d*] pyrimidine-2,4(3*H*,5*H*)-dione and 2-amino-3-cyano-4*H*-pyrans

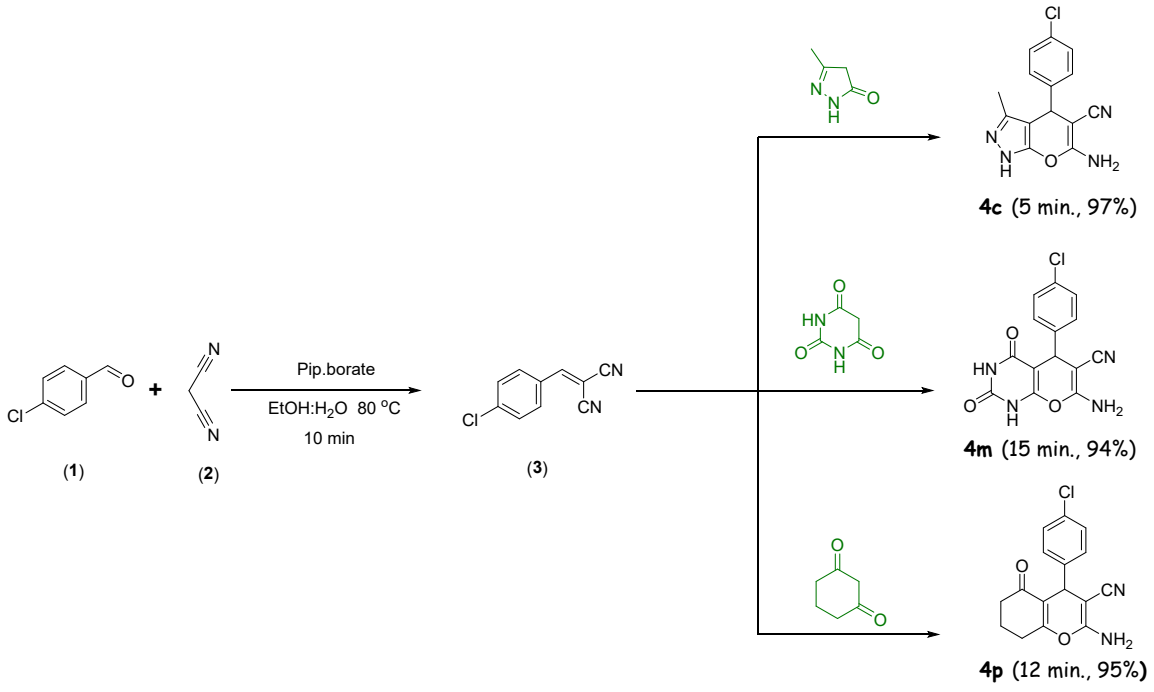
Aromatic aldehyde (1 equiv.), malononitrile (1 equiv.), 5-methyl-2,4-dihydro-3*H*-pyrazol-3-one/ barbituric acid/ mono or 1,3-dicarbonyl compound (1 equiv.), and piperidinium borate (20 mol%) were weighed and transferred into a round-bottomed flask and stirred at 80 °C in a preheated oil bath till the completion of the reaction, as monitored by TLC. After completion of the reaction, cool to room temperature. The solid product was separated by filtration, washed with cold water, and recrystallized from hot ethanol. The structure of pure compounds was confirmed by melting point and ^{1}H and $^{13}C\{^{1}H\}$ NMR spectroscopy.

2. Mechanistic understanding of operative reaction pathways:

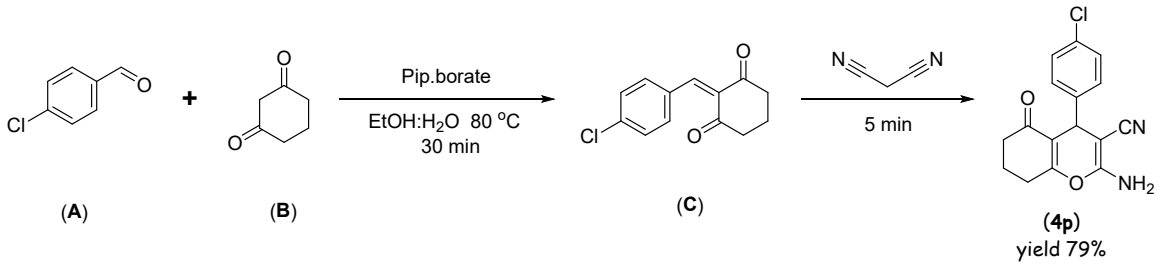
The possible pathways (I and II) were taken into consideration, and appropriate experiments were designed to validate their operational feasibility.

The validation was carried out by sequentially adding the reactants under optimized reaction conditions and monitoring the reaction progress using TLC. Two parallel sets (Pathway I and Pathway II) of reactions were planned for each of the reaction pathways. In pathway I, reactants 1 and 2 were treated in the presence of piperidinium borate, and the progress of the reaction was monitored by TLC for 10 min at 5 min. intervals. The formation of Knoevenagel product **3** was confirmed by TLC and ^{1}H NMR. Afterwards, the addition of 1,3-cyclohexadione to the Knoevenagel product results in the desired product 4p, obtained in 5 minutes (Scheme S1).

In pathway 2, the reaction involving two reactants, **A** and **B**, was conducted in the presence of piperidinium borate, and the progress of the reaction was monitored by TLC for 30 minutes at 5-minute intervals. The formation of Knoevenagel product **C** was confirmed by TLC. Afterwards, the addition of malononitrile to the Knoevenagel product results in the desired product D, obtained in 10 minutes (Scheme S2). The synthesized product was confirmed by melting point and ^{1}H NMR.

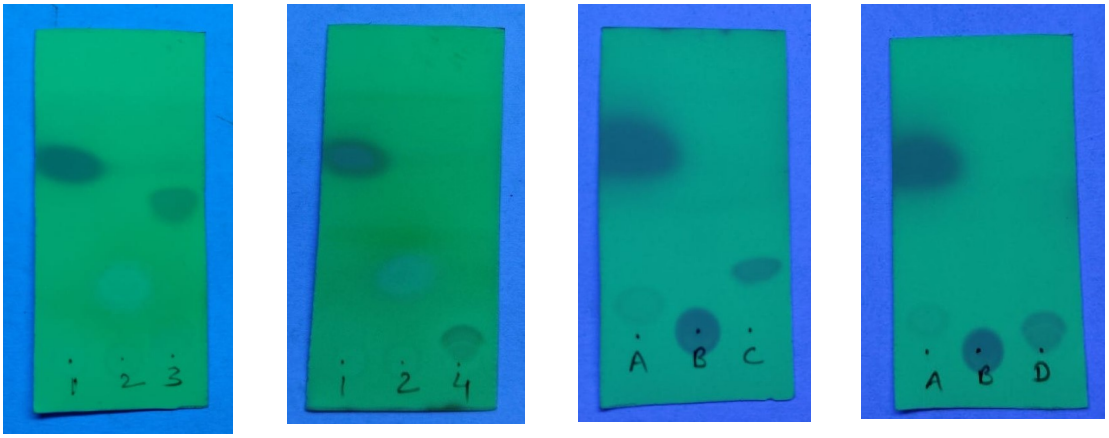


Scheme 1: Synthesis of 4p via Pathway I



Scheme 2: Synthesis of 4p via Pathway II

Based on the outcomes of the sequential addition of reactants under reaction pathways I and II, as well as the respective overall yield of product and the time required for the reaction, the involvement of pathway II can be eliminated due to its lower yield and longer reaction time.



(a) **(b)** **(c)** **(d)**

Figure 1: Representative experimental design by TLC to understand the operative mechanistic pathway. On TLC **a** and **b**: 4-chlorobenzaldehyde (1); malononitrile (2); Knoevenagel product (3); product 4p (4), whereas on TLC **c** and **d:** 4-chlorobenzaldehyde (A); 1,3-cyclohexandione (B); Knoevenagel product (C); product 4p (D).

3. Green chemistry metrics calculation

The following green chemistry metrics were calculated for the reaction.

a. **Environmental factor or E-factor:** The ideal value of the E-factor is considered zero

E-factor = [mass of waste] ÷ mass of product

Where,

mass of waste = total mass of raw materials minus the total mass of product

For example, E factor calculation for compound 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile, 4a

E-factor = [(250 mg + 156 mg + 231mg) - 580mg] ÷ 580mg

= 0.098

b. **Atom economy (AE):** The ideal value of the AE factor is 100%

AE = MW of product ÷ Σ(MW of stoichiometric reactants) × 100

Example, Atom economy calculation for compound 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile, 4a

Atom economy = 252.28 ÷ (106.12 + 66.06 + 98.1) × 100

= 93.34%

c. **Reaction mass efficiency (RME):** The RME value ranges from 0 to 100%. A larger number is considered better, and it measures the “cleanness” of a reaction.

RME = mass of product ÷ Σ(mass of stoichiometric reactants) × 100

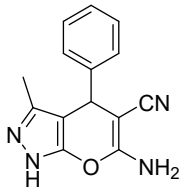
Example, RME calculation for compound 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile, 4a

= 0.580 gm ÷ (0.25gm + 0.156gm + 0.231gm) × 100

= 91.01%

4. Characterization data of synthesized compounds:

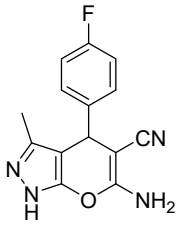
1. 6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4a)



4a (10 min., 97%)

White solid; (0.58 g, 97% yield); M.P.- 240-242 °C (lit.[1] 239-241 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.15 (s, 1H), 7.43 – 7.39 (m, 1H), 7.39 – 7.18 (m, 3H), 7.17 (dt, *J* = 7.7, 1.3 Hz, 1H), 6.95 (s, 2H), 4.63 (s, 1H), 1.79 (s, 3H).

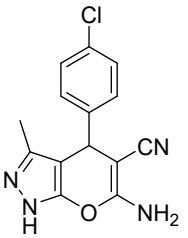
2. 6-amino-4-(4-fluorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4b)



4b (10 min., 96%)

White solid; (0.52 g, 96% yield); M.P.- 218-220 °C (lit.[2] 216-218 °C); ^{1}H NMR (600 MHz, DMSO-D_6) δ 12.07 (s, 1H), 7.18 – 7.15 (m, 2H), 7.11 (d, *J* = 10.0 Hz, 2H), 6.84 (s, 2H), 4.59 (s, 1H), 1.75 (s, 3H).

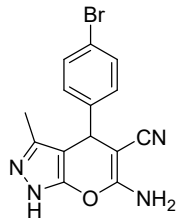
3. 6-amino-4-(4-chlorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4c)



4c (5 min., 97%)

Pale Yellow solid; (0.49 g, 97% yield); M.P.- 227-230 °C (lit.[1] 226-228 °C);^{1}H NMR (600 MHz, DMSO-d_6) δ 7.38 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.2 Hz, 2H), 6.92 (s, 2H), 4.63 (s, 1H), 1.79 (s, 3H).

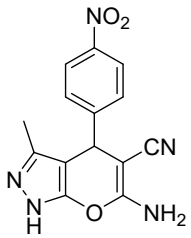
4. **6-amino-4-(4-bromophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4d)**



4d (5 min., 97%)

Yellow solid; (0.43 g, 97% yield); M.P.- 178-181 °C (lit.[1] 178-180 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.49 (d, *J* = 8.3 Hz, 2H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.92 (s, 2H), 4.60 (s, 1H), 1.77 (s, 3H).

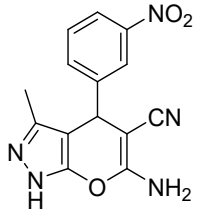
5. **6-amino-3-methyl-4-(4-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4e)**



4e (10 min., 94%)

Yellow solid; (0.46 g, 94% yield); M.P.- 249-250 °C (lit.[1] 247-248 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.20 (s, 1H), 8.21 (d, *J* = 8.6 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.04 (s, 2H), 4.83 (s, 1H), 1.80 (s, 3H).

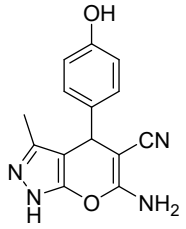
6. **6-amino-3-methyl-4-(3-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4f)**



4f (10 min., 94%)

White solid; (0.46 g, 94% yield); M.P.- 230-232 °C (lit.[1] 225-238 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.20 (s, 1H), 8.11 (d, *J* = 7.7 Hz, 1H), 8.00 (s, 1H), 7.67 – 7.61 (m, 2H), 7.04 (s, 2H), 4.86 (s, 1H), 1.78 (s, 3H).

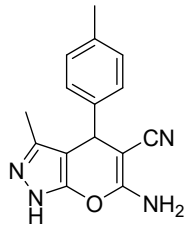
7. **6-amino-4-(4-hydroxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4g)**



4g (8 min., 95%)

Yellow solid; (0.52 g, 95% yield); M.P.- 220-224 °C (lit.[3] 223-224 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.00 (s, 1H), 9.23 (s, 1H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.73 (s, 2H), 6.65 (d, *J* = 8.5 Hz, 2H), 4.43 (s, 1H), 1.74 (s, 3H).

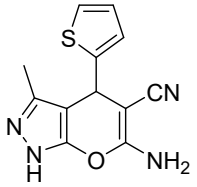
8. **6-amino-3-methyl-4-(p-tolyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4h)**



4h (8min., 94%)

White solid; (0.49 g, 94% yield); M.P.- 208-210 °C (lit.[2] 207-208 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.82 (s, 2H), 4.52 (s, 1H), 2.25 (s, 3H), 1.76 (s, 3H).

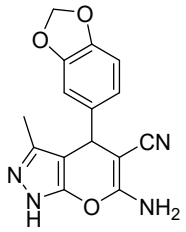
9. **6-amino-3-methyl-4-(thiophen-2-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4i)**



4i (10 min., 92%)

Bown solid; (0.53 g, 92% yield); M.P.- 214-216 °C (lit.[4] 211-212 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.33 (d, *J* = 5.1 Hz, 1H), 6.97 (d, *J* = 3.9 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 3H), 4.95 (s, 1H), 1.88 (s, 3H).

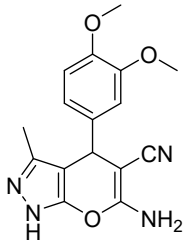
10. **6-amino-4-(benzo[*d*][1,3]dioxol-5-yl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4j)**



4j (10 min., 90%)

White solid; (0.44 g, 90% yield); M.P.- 192-194 °C (lit.[5] 190 °C); ^{1}H NMR (600 MHz, DMSO-d_6) δ 12.05 (s, 1H), 6.83 – 6.77 (m, 3H), 6.65 – 6.59 (m, 2H), 5.95 (d, *J* = 5.5 Hz, 2H), 4.49 (s, 1H), 1.78 (s, 3H).

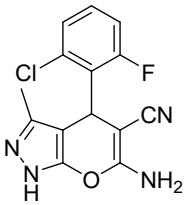
11. 6-amino-4-(3,4-dimethoxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4k)



4k (10 min., 92%)

White solid; (0.61 g, 92% yield); M.P.- 190-192 °C (lit.[7] 195-196 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.06 (s, 1H), 6.87 (d, *J* = 8.3 Hz, 1H), 6.81 (s, 2H), 6.73 (d, *J* = 2.1 Hz, 1H), 6.66 (dd, *J* = 8.2, 2.1 Hz, 1H), 4.53 (s, 1H), 3.71 (s, 3H), 3.68 (s, 3H), 1.80 (s, 3H).

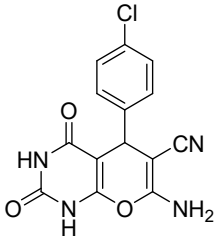
12. 6-amino-4-(2-chloro-6-fluorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (4l)



4l (10 min., 93%)

White solid; (0.44 g, 93% yield); M.P.- 250-252 °C (lit.[9] 252-253 °C), ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.09 (s, 1H), 7.32 (t, *J* = 7.3 Hz, 2H), 7.11 (s, 1H), 6.98 (s, 2H), 5.22 (s, 1H), 1.82 (s, 3H).

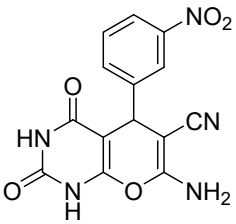
13. 7-amino-5-(4-chlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carbonitrile (4m)



4m (15 min., 94%)

White solid; (0.52 g, 94% yield); M.P.- 236-238 °C (lit.[10] 235-237 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.07 (s, 1H), 11.07 (s, 1H), 7.32 (d, *J* = 8.6 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.15 (s, 2H), 4.22 (s, 1H).

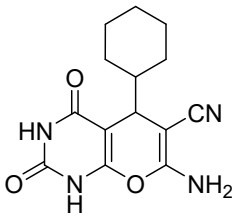
14. 7-amino-5-(3-nitrophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carbonitrile (4n)



4n (20 min., 90%)

White solid; (0.48 g, 90% yield); M.P.- 258-260 °C (lit.[10] 256-258 °C);^{1}H NMR (500 MHz, DMSO-d_6) δ 12.13 (s, 1H), 11.07 (s, 1H), 8.09 – 8.03 (m, 2H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.24 (s, 2H), 4.46 (s, 1H).

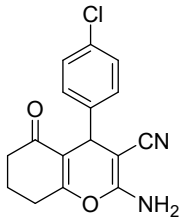
15. 7-amino-5-cyclohexyl-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carbonitrile (4o)



4o (20 min., 92%)

White solid; (0.59 g, 92% yield); M.P.- 258-260 °C; FTIR vmax: 3394.1, 3328.33, 2911.99, 2206.17, 1616.91, 1515.78, 1392.35, 1087.66, 825.384 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.90 (s, 1H), 11.06 (s, 1H), 7.01 (s, 2H), 3.05 (d, *J* = 2.9 Hz, 1H), 1.67 (dd, *J* = 22.1, 12.5 Hz, 2H), 1.60 – 1.45 (m, 3H), 1.36 (d, *J* = 12.9 Hz, 1H), 1.29 – 0.98 (m, 4H), 0.84 (q, *J* = 12.4 Hz, 1H). ^{13}C {^{1}H} NMR (126 MHz, DMSO-d_6) δ 163.24, 160.63, 153.52, 149.93, 121.10, 88.80, 54.09, 43.73, 35.60, 30.63, 27.36, 26.65, 26.48, 26.15. Anal. Calcd: C, 58.32; H, 5.59; N, 19.43; Found: C, 57.78; H, 5.28; N,19.07.

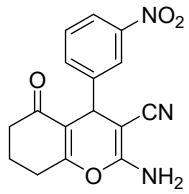
16. 2-amino-4-(4-chlorophenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4p)



4p (12 min., 95%)

Yellow solid; (0.5 g, 95% yield); M.P: 268-270 °C (lit.[11] 267-269 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.32 (d, *J* = 8.6 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.05 (s, 2H), 4.18 (s, 1H), 2.58 (q, *J* = 5.5 Hz, 2H), 2.32 – 2.19 (m, 2H), 1.96 – 1.82 (m, 2H).

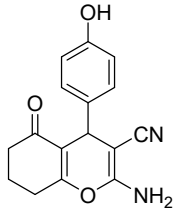
17. 2-amino-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4q)



4q (15 min., 93%)

Yellow solid; (0.47 g, 93% yield); M.P: 248-250 °C (lit.[11] 247-249 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.05 (d, *J* = 9.2 Hz, 1H), 7.97 (s, 1H), 7.66 (d, *J* = 7.8 Hz, 1H), 7.59 (t, *J* = 7.9 Hz, 1H), 7.16 (s, 2H), 4.39 (s, 1H), 2.66 – 2.58 (m, 2H), 2.32 – 2.21 (m, 2H), 1.97 – 1.84 (m, 2H).

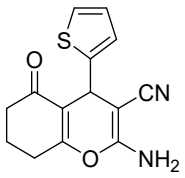
18. 2-amino-4-(4-hydroxyphenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4r)



4r (10 min., 96%)

Yellow solid; (0.55 g, 96% yield); M.P: 258-260 °C (lit.[11] 257-259 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.23 (s, 1H), 6.93 – 6.89 (m, 4H), 6.63 (d, *J* = 8.6 Hz, 2H), 4.05 (s, 1H), 2.56 (q, *J* = 5.1 Hz, 2H), 2.30 – 2.19 (m, 2H), 1.96 – 1.81 (m, 2H).

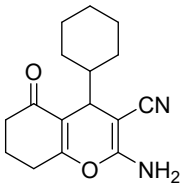
19. 2-amino-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4s)



4s (15 min., 89%)

White solid; (0.54 g, 89% yield); M.P: 236-240 °C (lit.[12] 238-240 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.29 (d, *J* = 5.0 Hz, 1H), 7.11 (s, 2H), 6.90 – 6.87 (m, 1H), 6.83 (d, *J* = 3.7 Hz, 1H), 4.51 (s, 1H), 2.56 (t, *J* = 6.2 Hz, 2H), 2.31 (q, *J* = 6.3 Hz, 2H), 1.98 – 1.92 (m, 1H), 1.87 – 1.80 (m, 1H).

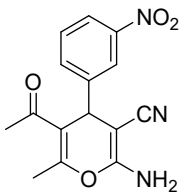
20. 2-amino-4-cyclohexyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4t)



4t (20 min., 90%)

White solid; (0.54 g, 90% yield); M.P: 208-212 °C (lit.[13] 208-210 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.89 (s, 2H), 3.01 (d, *J* = 3.2 Hz, 1H), 2.52 – 2.47 (m, 3H), 2.35 – 2.25 (m, 2H), 1.96 – 1.81 (m, 2H), 1.70 – 1.62 (m, 2H), 1.56 (d, *J* = 11.7 Hz, 1H), 1.48 (d, *J* = 12.5 Hz, 1H), 1.38 (d, *J* = 12.7 Hz, 1H), 1.27 – 0.97 (m, 5H), 0.79 (qd, *J* = 12.3, 3.7 Hz, 1H).

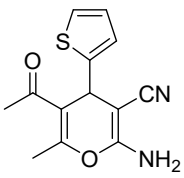
21. 5-acetyl-2-amino-6-methyl-4-(3-nitrophenyl)-4*H*-pyran-3-carbonitrile (4u)



4u (15 min., 91%)

Pale yellow solid; (0.45 g, 91% yield); M.P: 168-170 °C (lit.[14] 166 °C); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 – 8.07 (m, 1H), 8.00 – 7.97 (m, 1H), 7.66 – 7.61 (m, 2H), 7.02 (s, 2H), 4.68 (s, 1H), 2.27 (s, 3H), 2.10 (s, 3H).

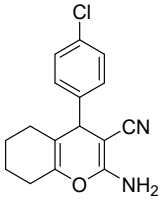
22. 5-acetyl-2-amino-6-methyl-4-(thiophen-2-yl)-4*H*-pyran-3-carbonitrile (4v)



4v (20 min., 87%)

Brown solid; (0.5 g, 87% yield); FTIRvmax: 3336.2, 3232.1, 2931.2, 2206.1, 1639.2, 1484.9, 1384.6, 1265.05, 1091.5, 1006.6, 956.5, 833.1 cm^{-1}; M.P: 170-172 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.36 (d, *J* = 5.1 Hz, 1H), 6.94 (s, 2H), 6.93 – 6.91 (m, 1H), 6.87 (d, *J* = 3.6 Hz, 1H), 4.80 (s, 1H), 2.20 (s, 3H), 2.16 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6) δ 198.40, 159.15, 155.51, 149.87, 127.47, 125.62, 124.60, 120.15, 115.98, 58.16, 34.35, 30.16, 19.01. Anal. Calcd: C, 59.98; H, 4.65; N, 10.76; S, 12.32; Found: C, 59.72; H, 4.4.32; N, 10.61; S, 11.76.

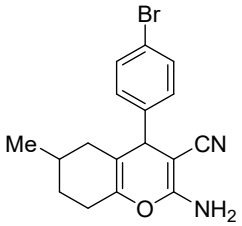
23. 2-amino-4-(4-chlorophenyl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4w)



4w (15 min., 90%)

White solid; (0.45 g, 90% yield); M.P: 276-280 ^{o}C (lit.[15] 274-277 °C);^{1}H NMR (500 MHz, DMSO-d_6) δ 7.63 – 7.42 (m, 4H), 7.37 (s, 2H), 5.71 (s, 1H), 3.62 (d, *J* = 12.6 Hz, 1H), 2.78 (t, *J* = 11.5 Hz, 1H), 2.16 (d, *J* = 19.8 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.64 (s, 1H), 1.43 (d, *J* = 10.9 Hz, 2H), 0.89 – 0.79 (m, 1H).

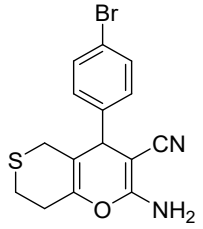
24. 2-amino-4-(4-bromophenyl)-6-methyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile (4x)



4x (15 min., 87%)

White solid; (0.40 g, 87% yield); M.P.: 224-226 °C; FTIRvmax: 3316.9, 2954.4, 2329.2, 1716.3, 1600.6, 1373.07, 1187.94, 937.23, 647.96 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.71 (d, J = 8.3 Hz, 1H), 7.64 (d, J = 8.3 Hz, 1H), 7.55 (d, J = 8.9 Hz, 1H), 7.38 (d, J = 3.5 Hz, 1H), 7.37 (s, 2H), 5.69 (s, 1H), 2.85 (t, J = 13.2 Hz, 1H), 2.24 (dd, J = 13.4, 5.0 Hz, 1H), 1.70 – 1.59 (m, 2H), 1.33 (dd, J = 12.8, 4.9 Hz, 1H), 0.79 (d, J = 5.6 Hz, 3H), 0.63 (q, J = 11.6 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6) δ 143.81, 134.88, 134.41, 132.14, 129.74, 128.77, 122.97, 120.85, 116.61, 112.70, 81.87, 50.16, 43.08, 35.70, 34.62, 34.05, 28.02, 22.24. Anal. Calcd: C, 59.14; H, 4.96; N, 8.11; Found: C, 59.04; H, 4.37; N, 8.03.

25. 2-amino-4-(4-bromophenyl)-7,8-dihydro-4*H*,5*H*-thiopyrano[4,3-*b*]pyran-3-carbonitrile (4y)

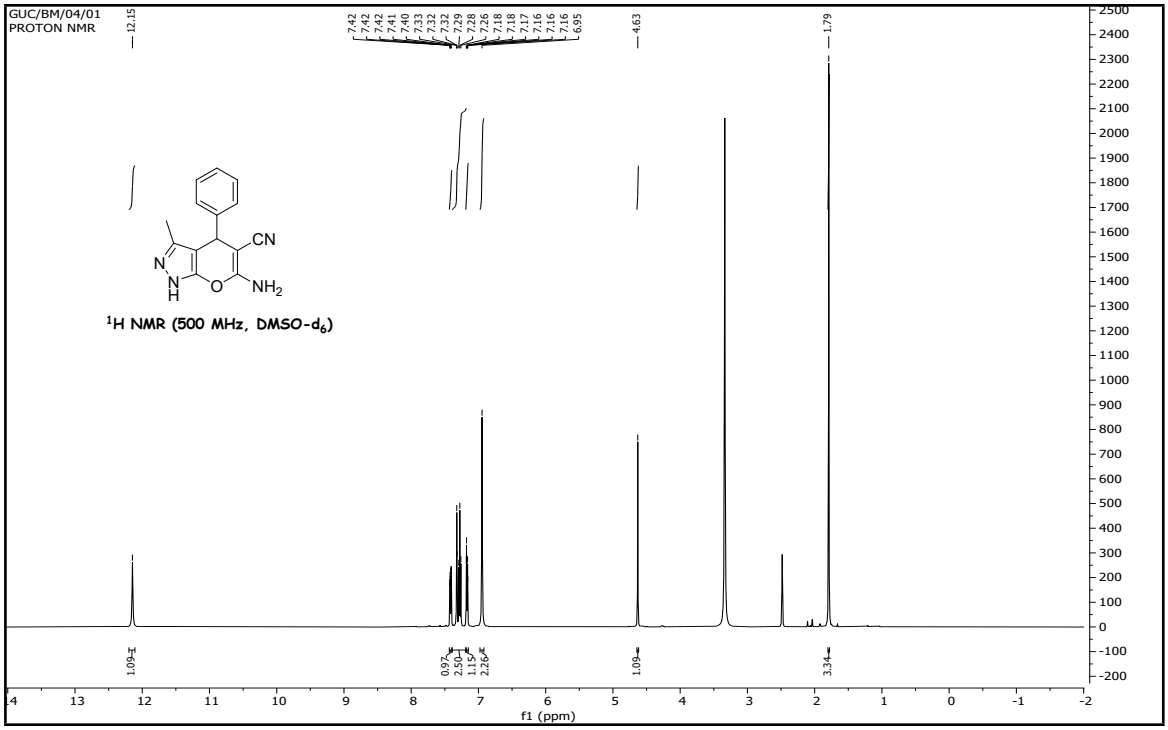


4y (20 min., 85%)

Pale-yellow solid; (0.39 g, 85% yield); FTIRvmax: 3340.1, 2969.8, 2206.1, 1635.3, 1392.3, 1056.8, 1010.5, 7983, 721.2 cm^{-1}; M.P.: 255-257 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.70 (d, *J* = 7.3 Hz, 1H), 7.60 (d, *J* = 14.9 Hz, 1H), 7.54 (s, 3H), 7.40 (d, *J* = 19.8 Hz, 1H), 5.96 – 5.92 (m, 1H), 3.74 (d, *J* = 12.5 Hz, 1H), 3.42 (dt, *J* = 18.3, 2.8 Hz, 2H), 3.15 (dd, *J* = 18.2, 5.6 Hz, 1H), 2.32 – 2.18 (m, 2H). $^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6) δ 144.39, 133.71, 132.39, 129.89, 123.29, 118.20, 116.44, 112.59, 112.39, 81.95, 49.18, 43.07, 35.33, 28.10, 25.44. Anal. Calcd: C, 51.59; H, 3.75; N, 8.02; S, 9.18; Found: C, 51.07; H, 3.69; N, 7.91; S, 8.90.

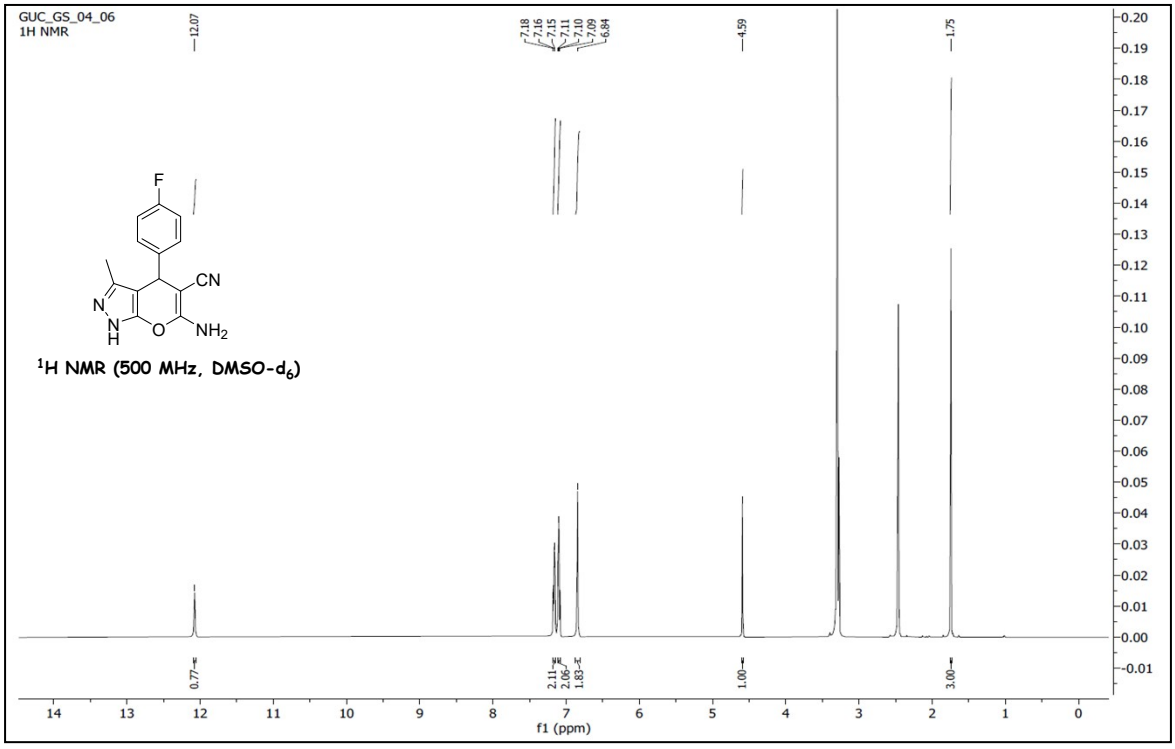
5. Copies of Spectra of synthesized compounds:

1. **6-amino-3-methyl-4-phenyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile[1]**



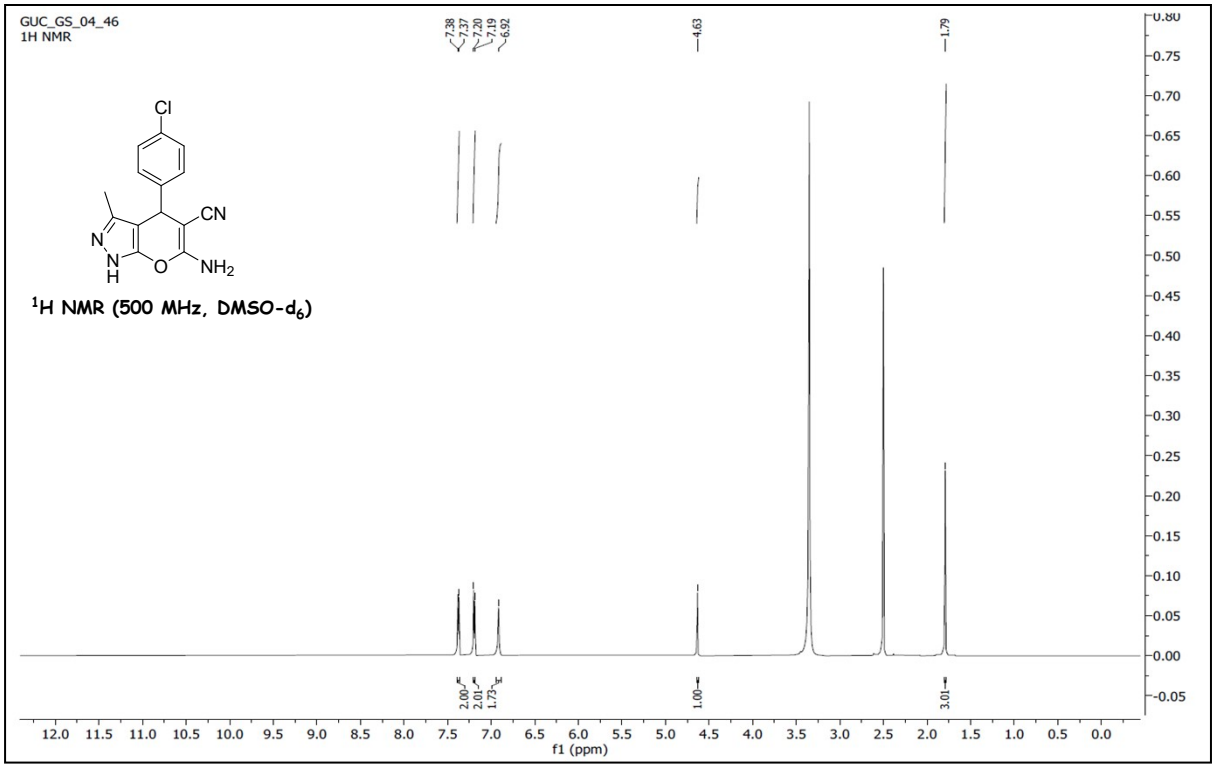
^{1}H NMR (500 MHz, DMSO-d_6)

2. **6-amino-4-(4-fluorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile[2]**

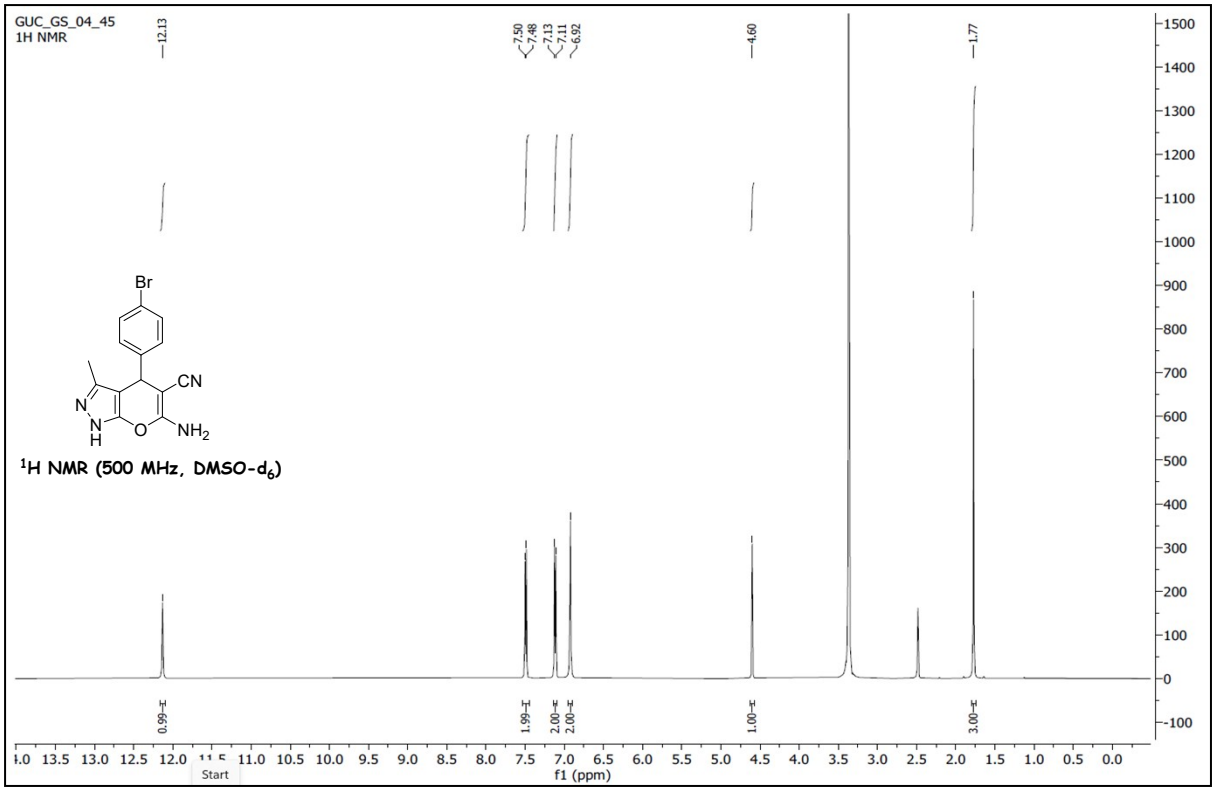


^{1}H NMR (500 MHz, DMSO-d_6)

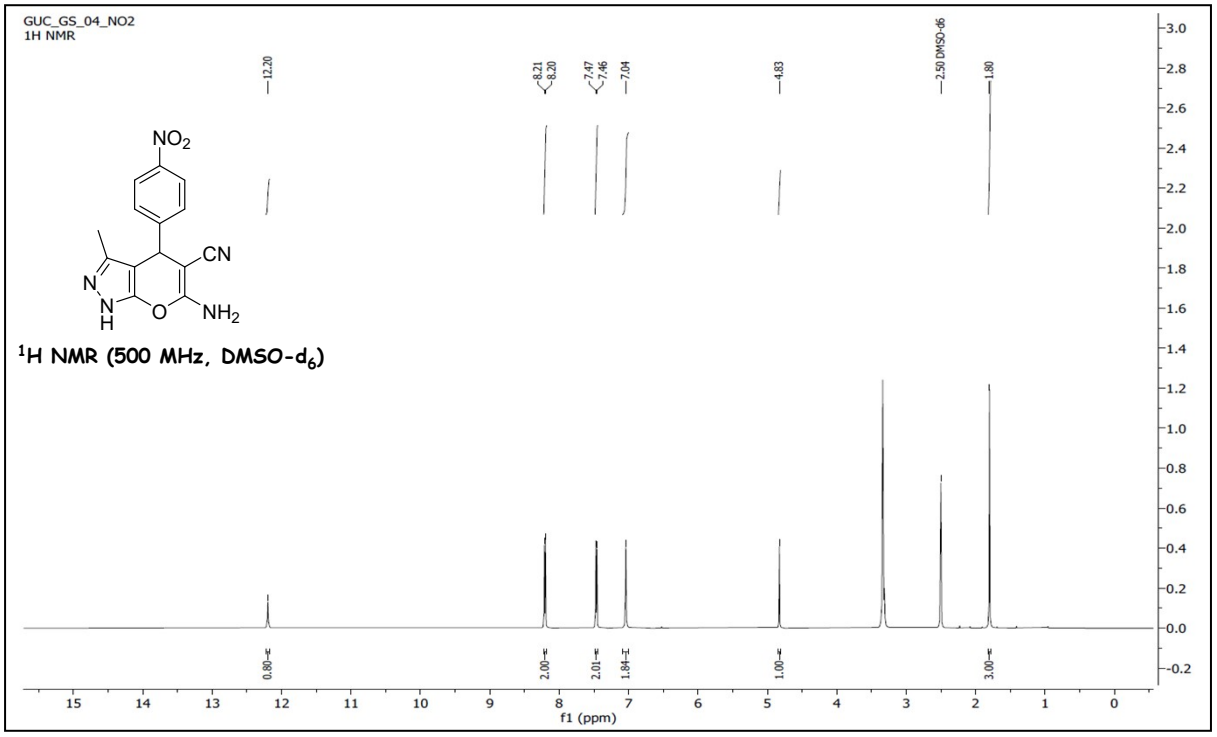
3. **6-amino-4-(4-chlorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile**[1]



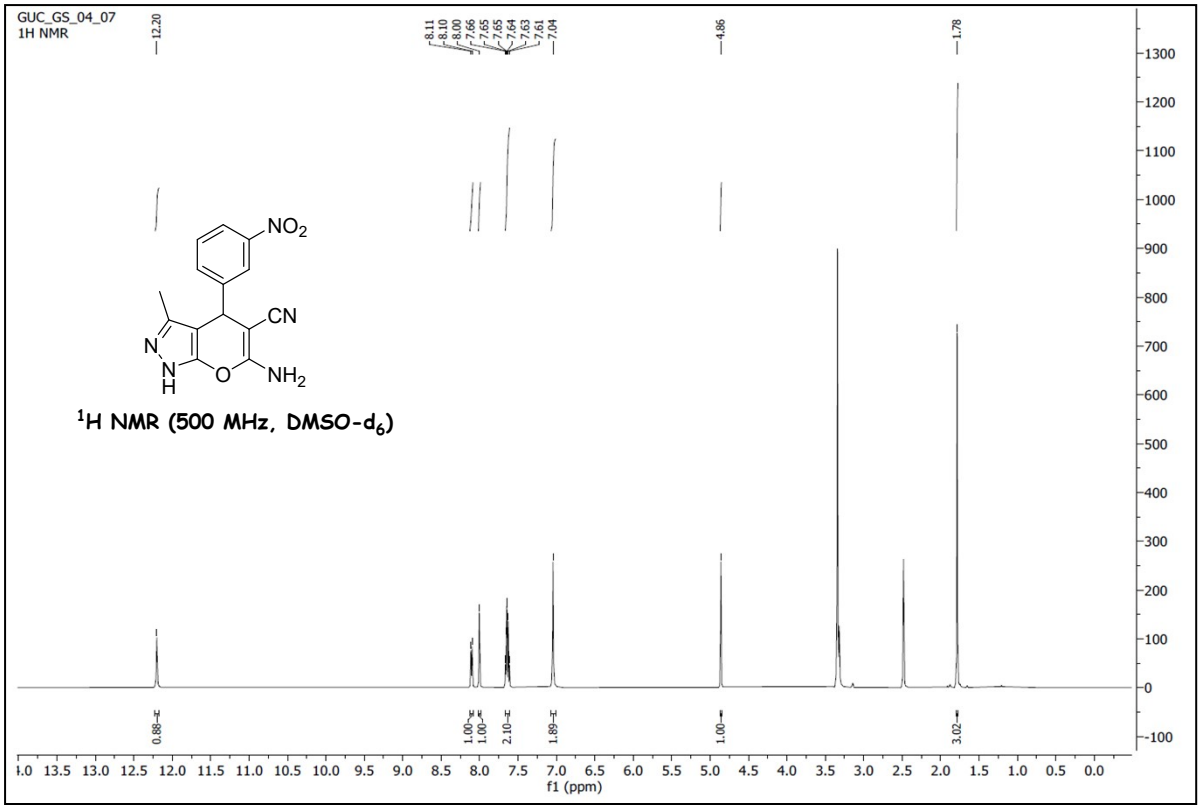
4. **6-amino-4-(4-bromophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile**[3]



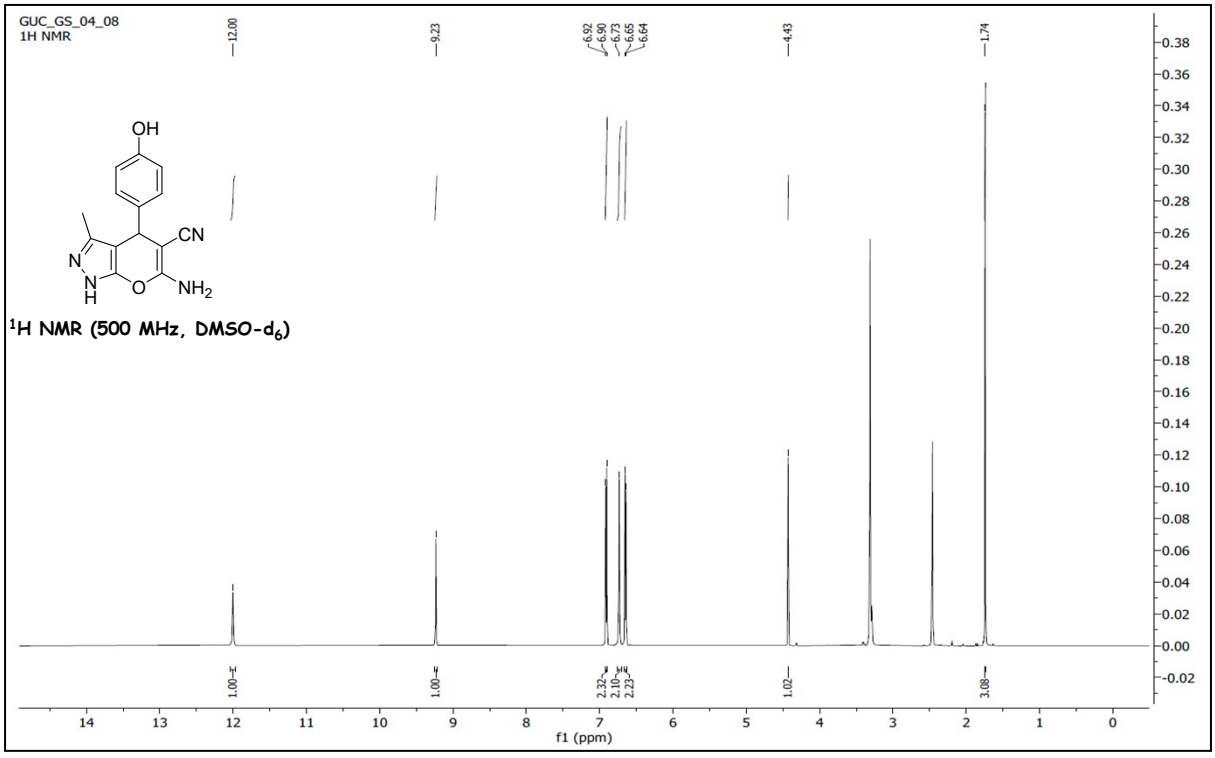
5. **6-amino-3-methyl-4-(4-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile**[1]



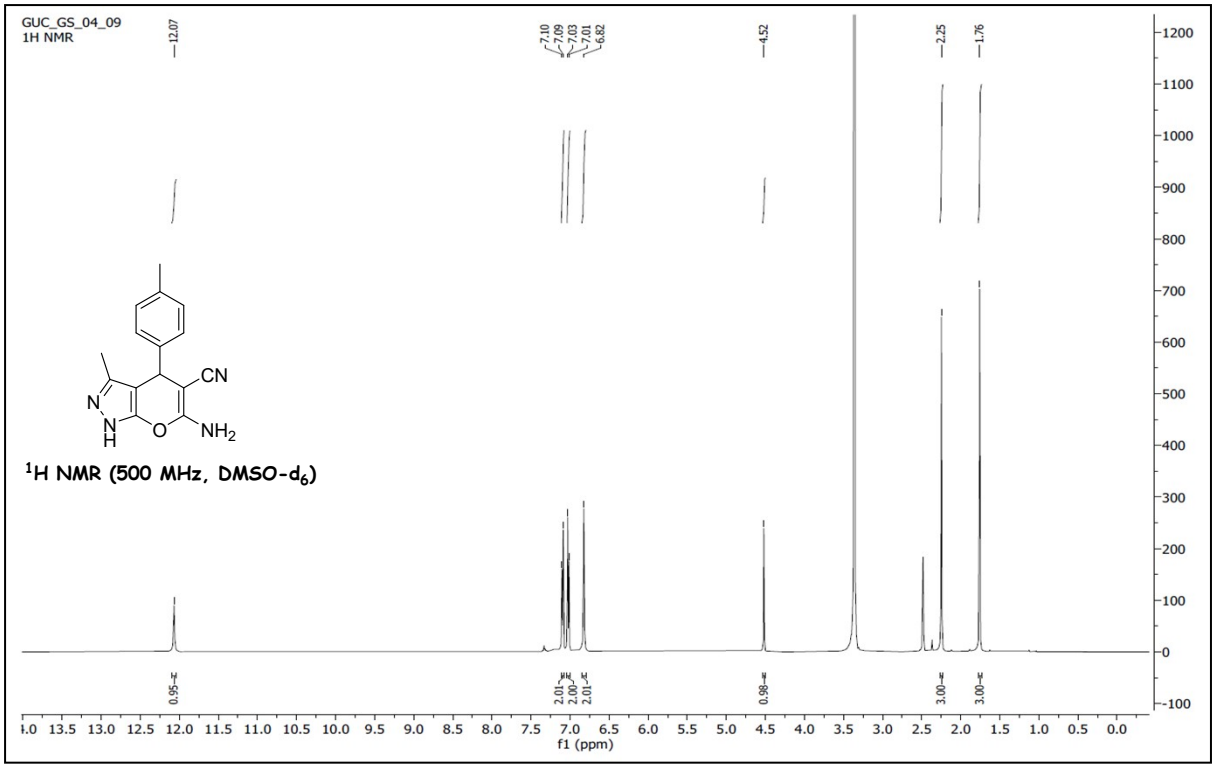
6. **6-amino-3-methyl-4-(3-nitrophenyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile**[1]



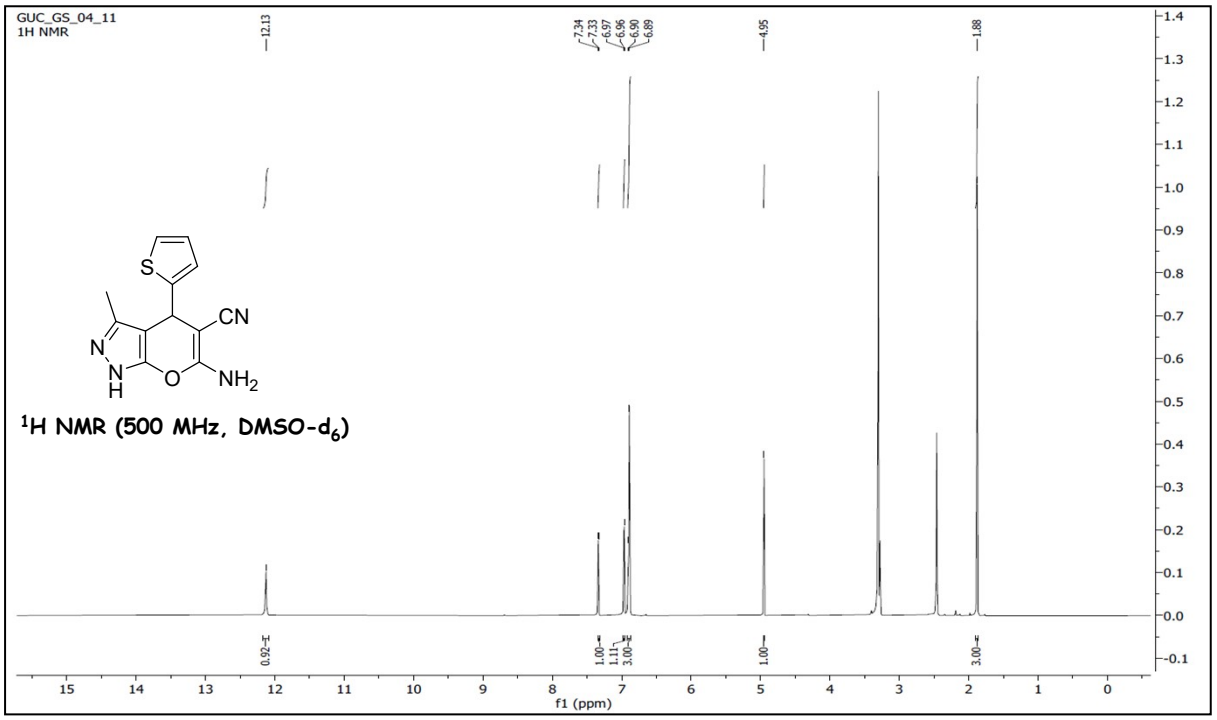
7. **6-amino-4-(4-hydroxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile[3]**



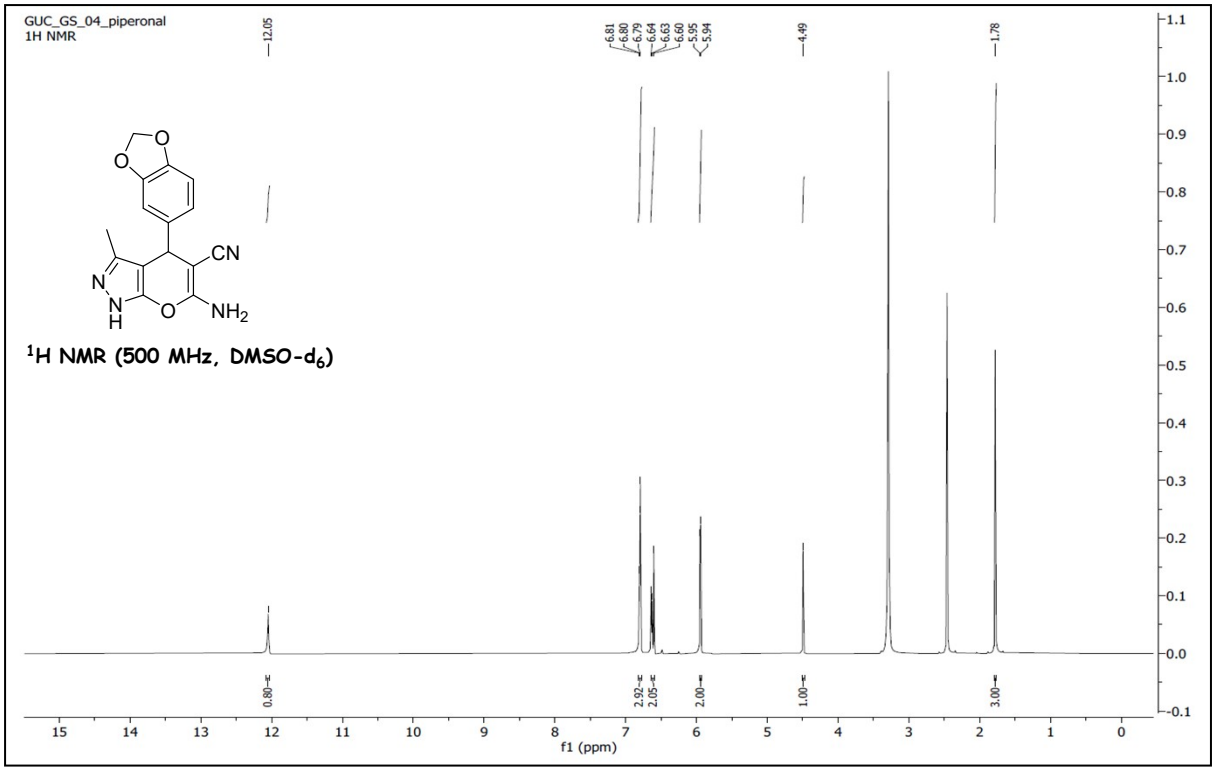
8. **6-amino-3-methyl-4-(p-tolyl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile[2]**



9. **6-amino-3-methyl-4-(thiophen-2-yl)-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile**[4]

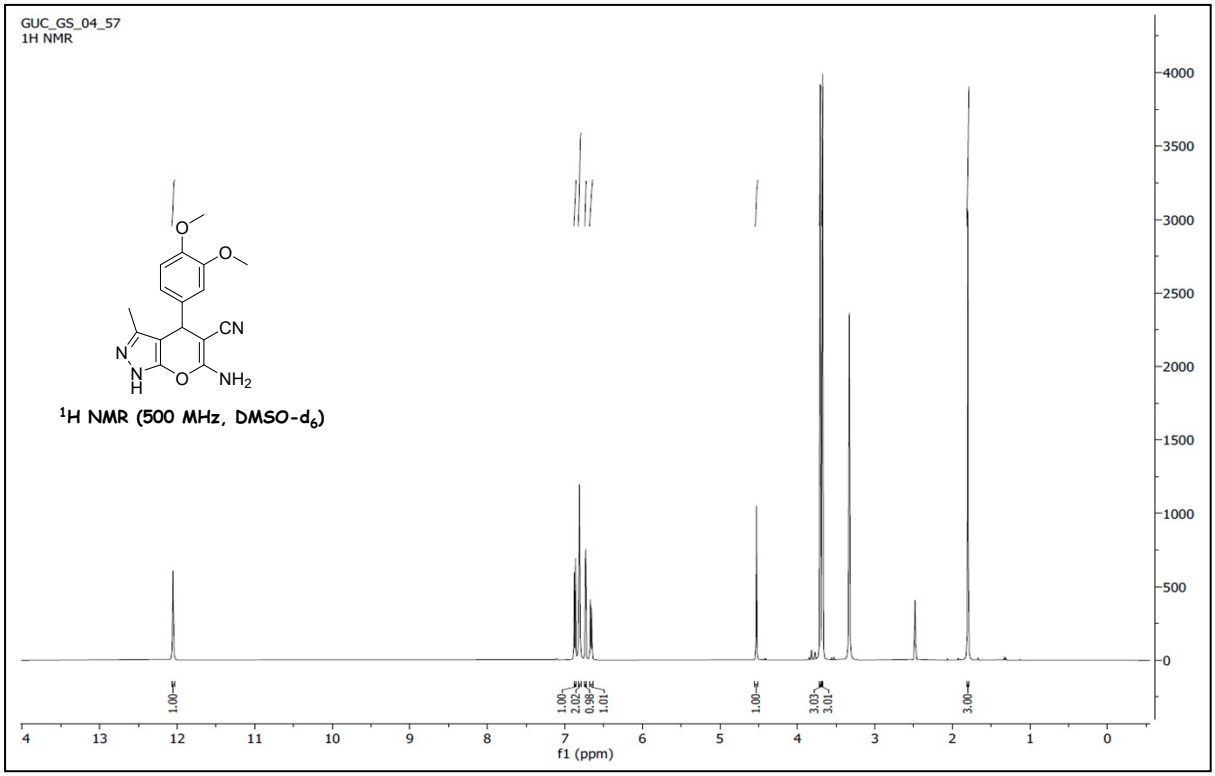


10. **6-amino-4-(benzo[*d*][1,3]dioxol-5-yl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile**[6]



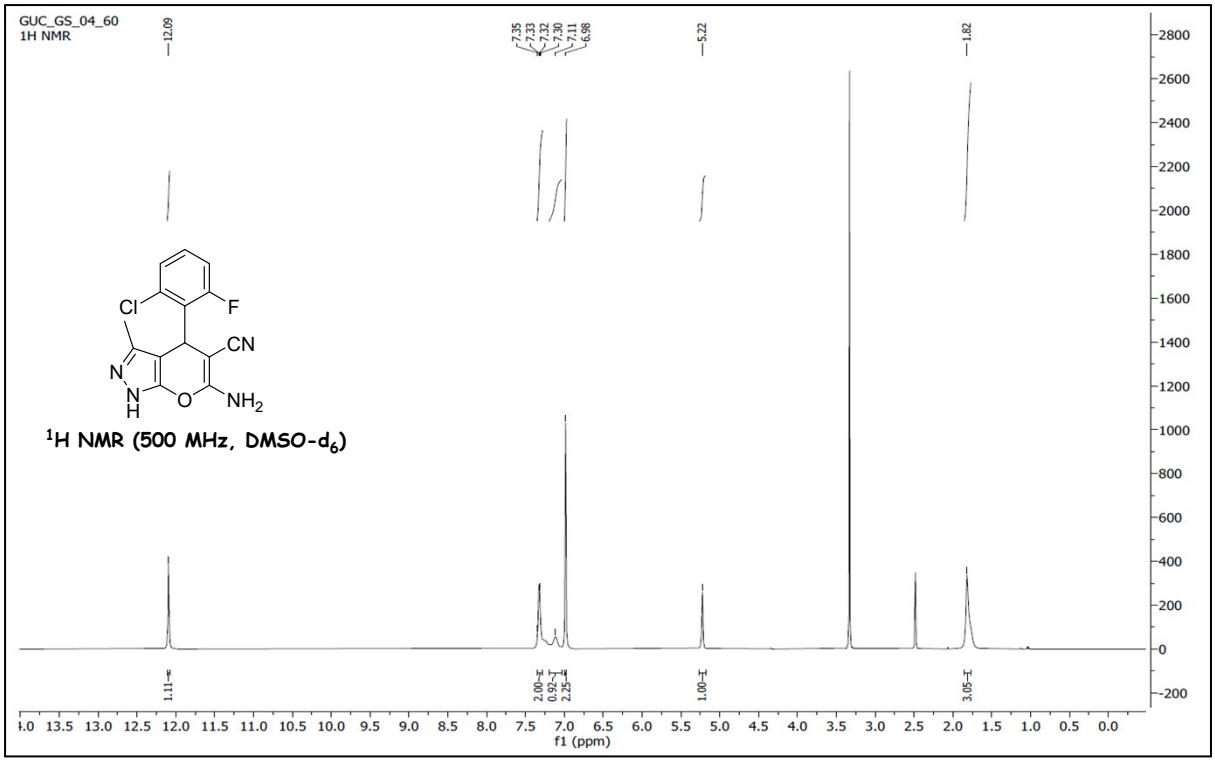
^{1}H NMR (500 MHz, DMSO-d_6)

11. **6-amino-4-(3,4-dimethoxyphenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile[8]**

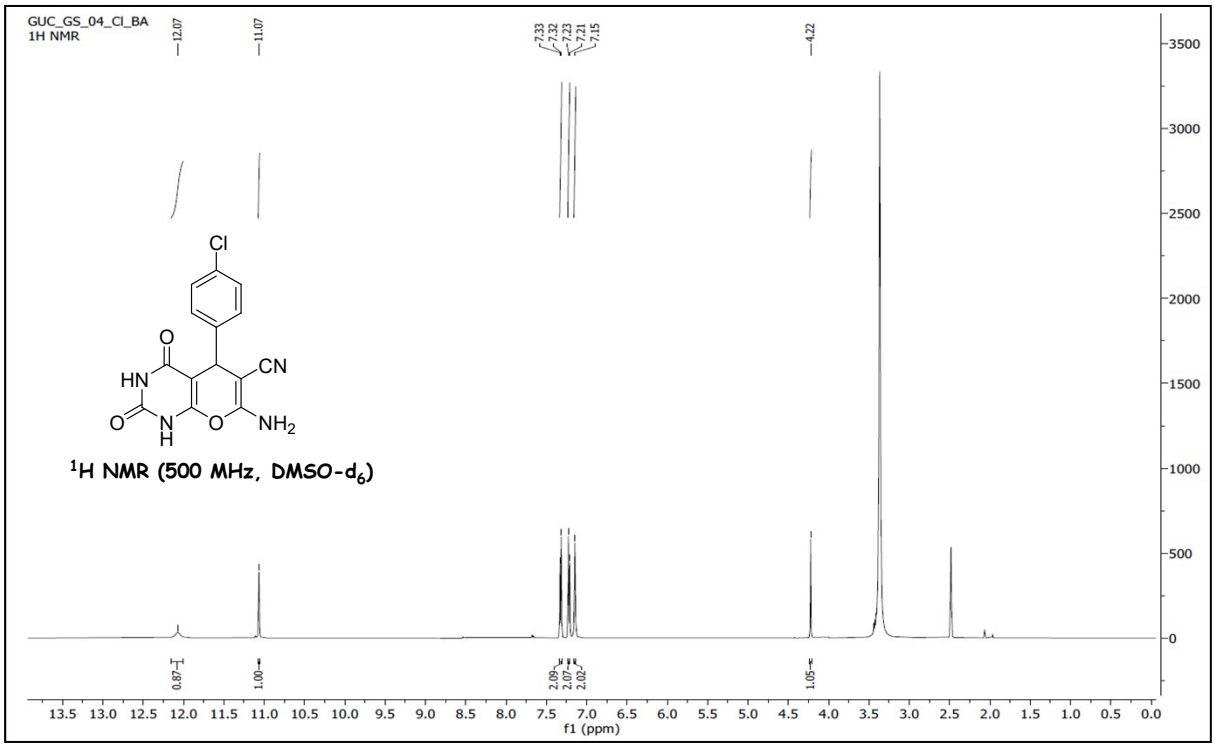


^{1}H NMR (500 MHz, DMSO-d_6)

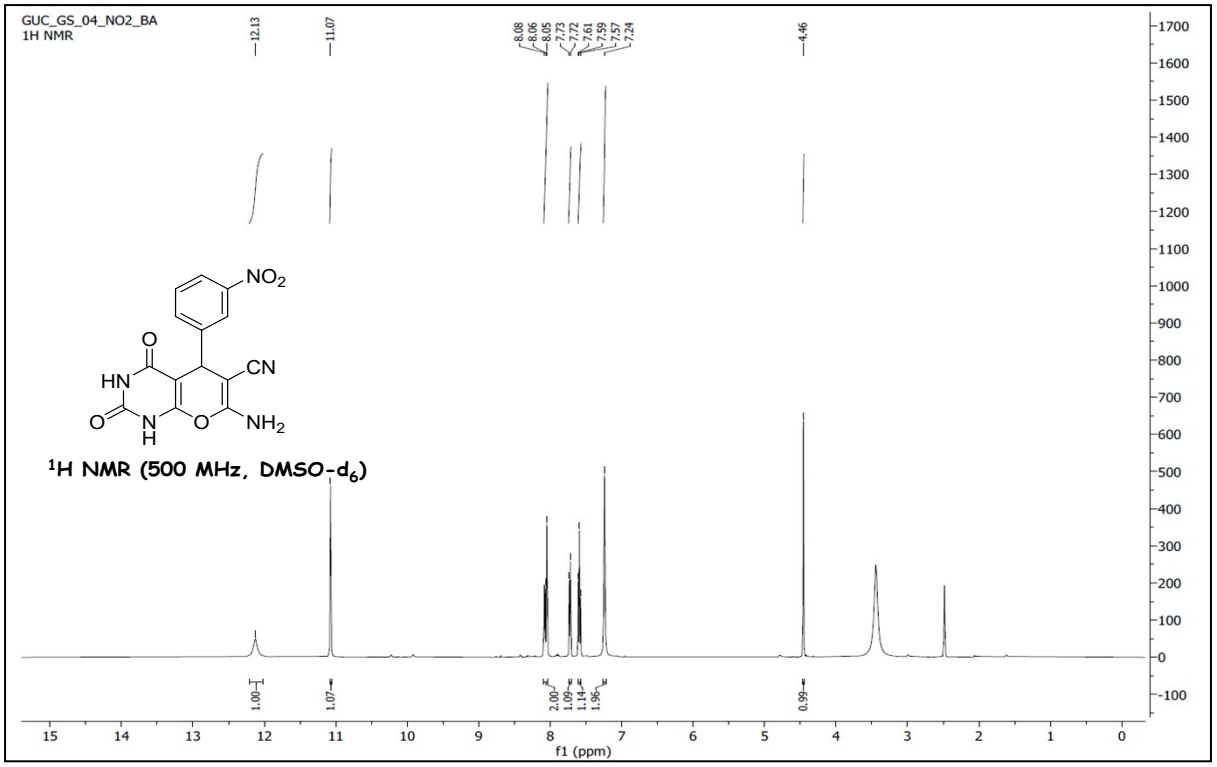
12. **6-amino-4-(2-chloro-6-fluorophenyl)-3-methyl-1,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile[9]**



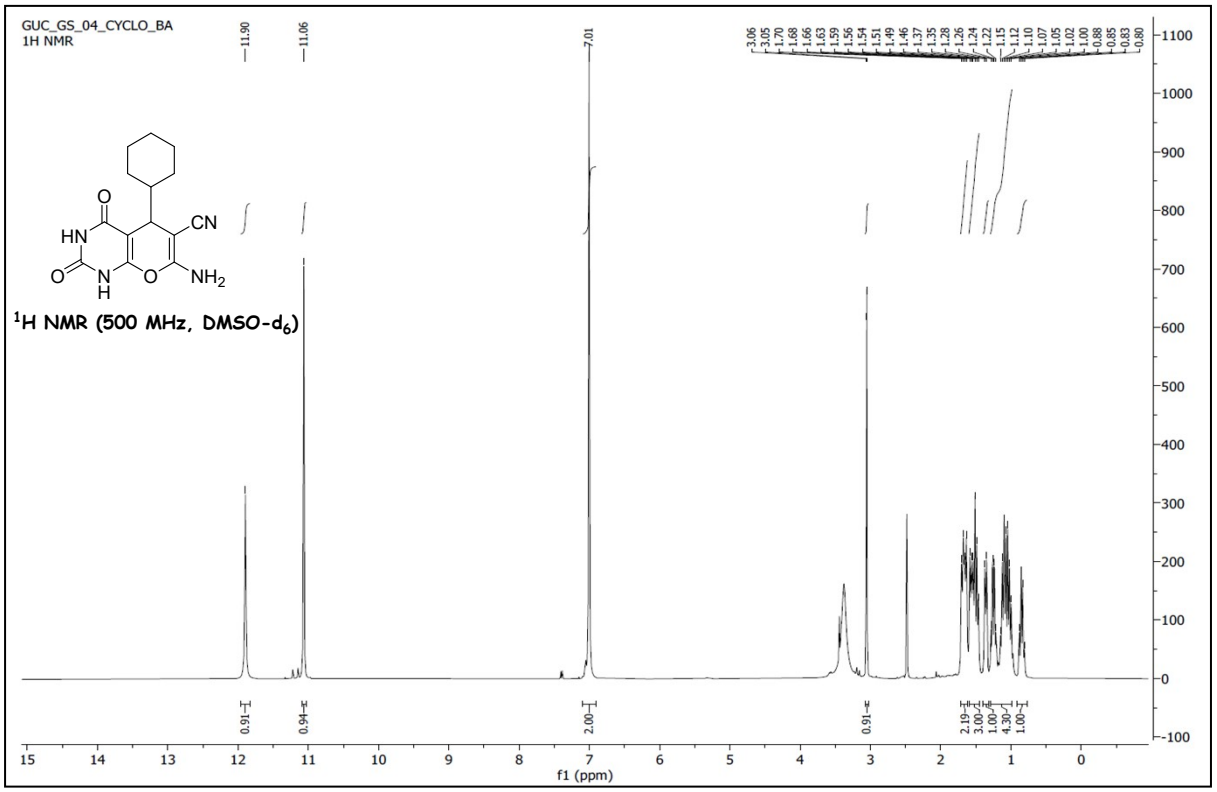
13. **7-amino-5-(4-chlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*] pyrimidine-6-carbonitrile[10]**

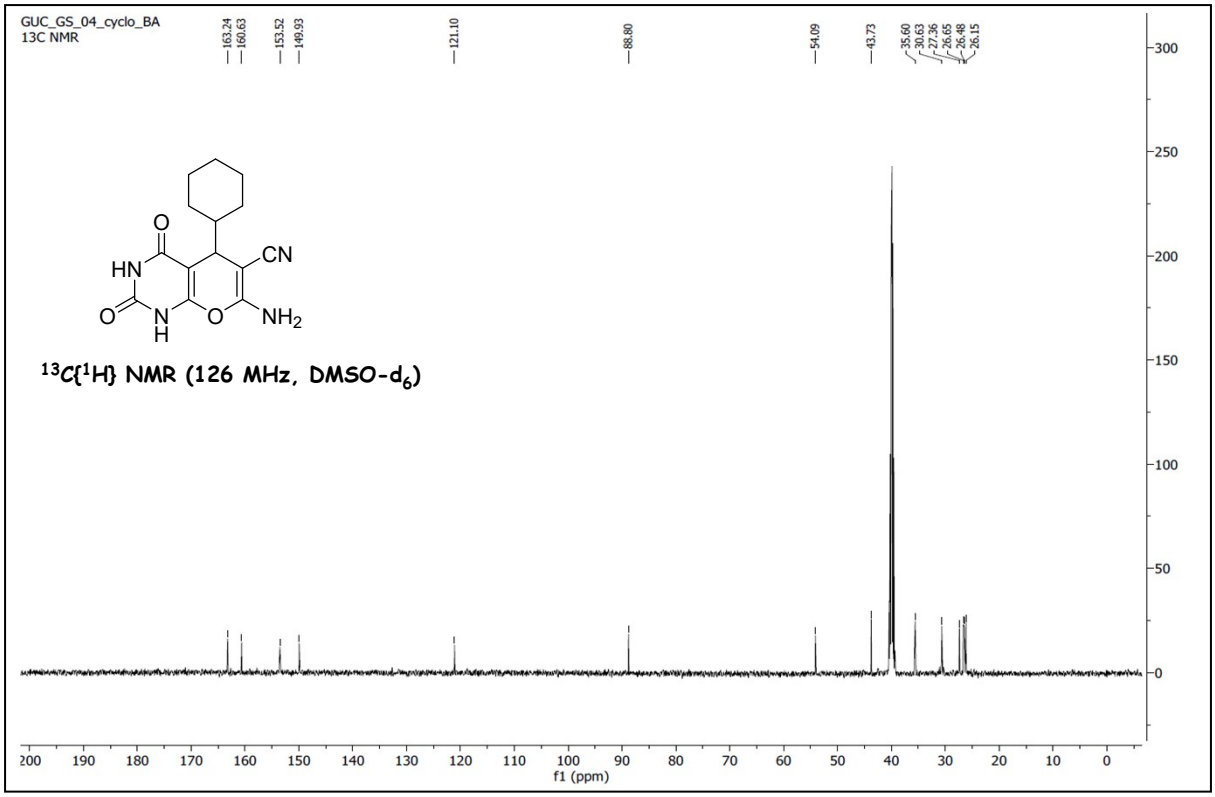


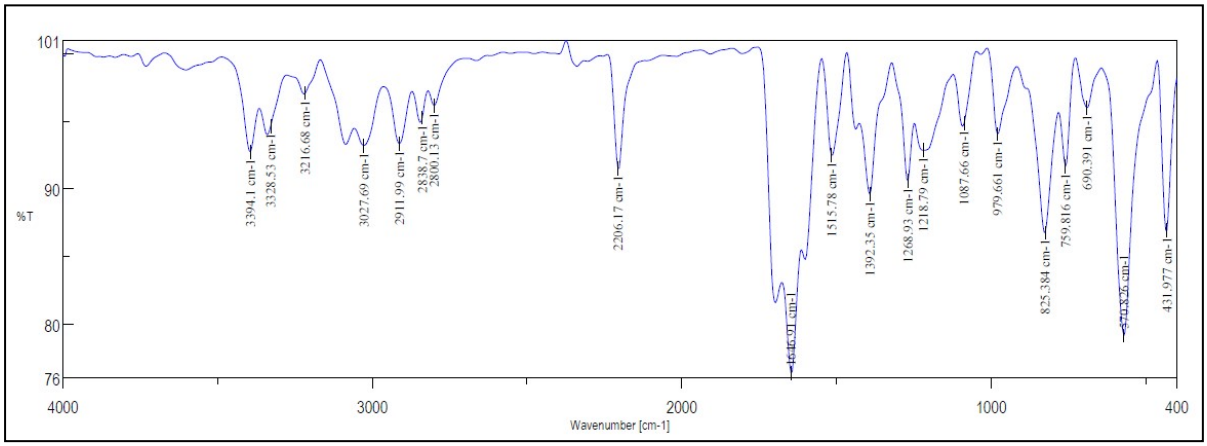
14. **7-amino-5-(3-nitrophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carbonitrile[10]**



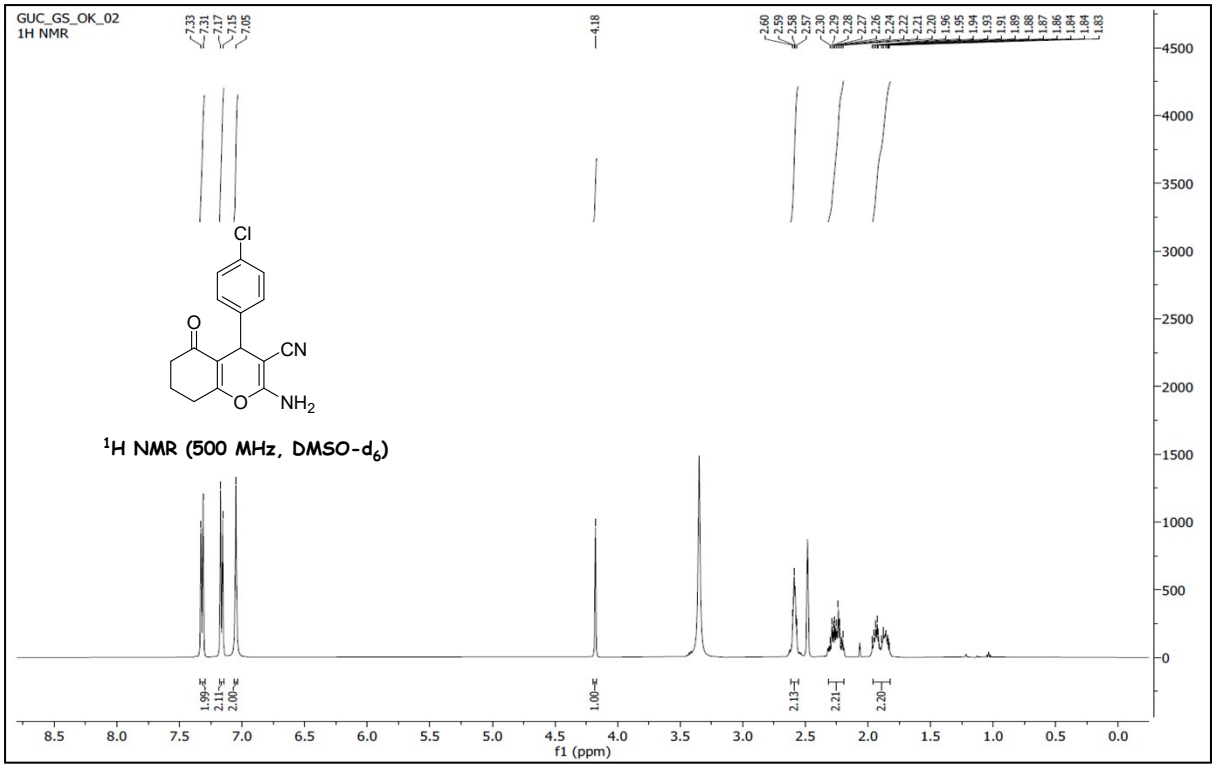
15. **7-amino-5-cyclohexyl-2,4-dioxo-1,3,4,5-tetrahydro-2*H*-pyrano[2,3-*d*]pyrimidine-6-carbonitrile**



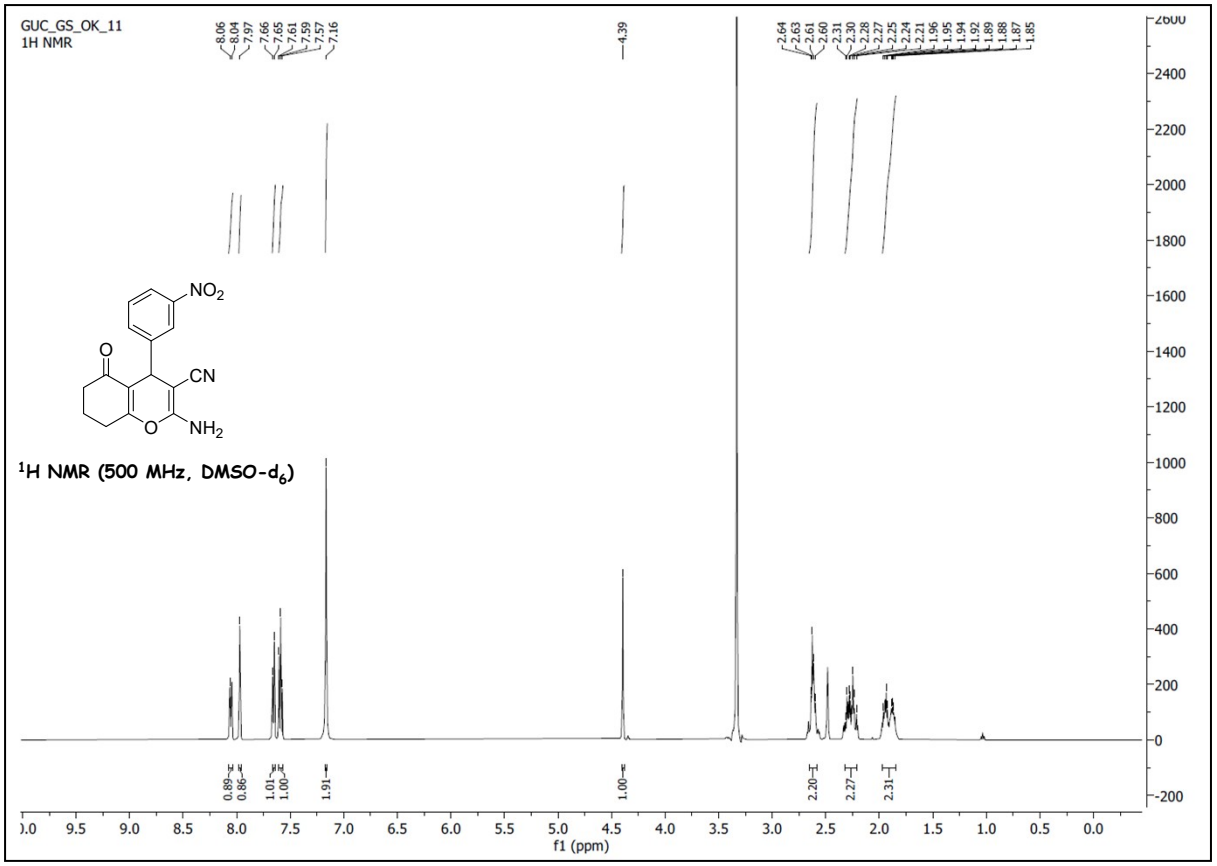




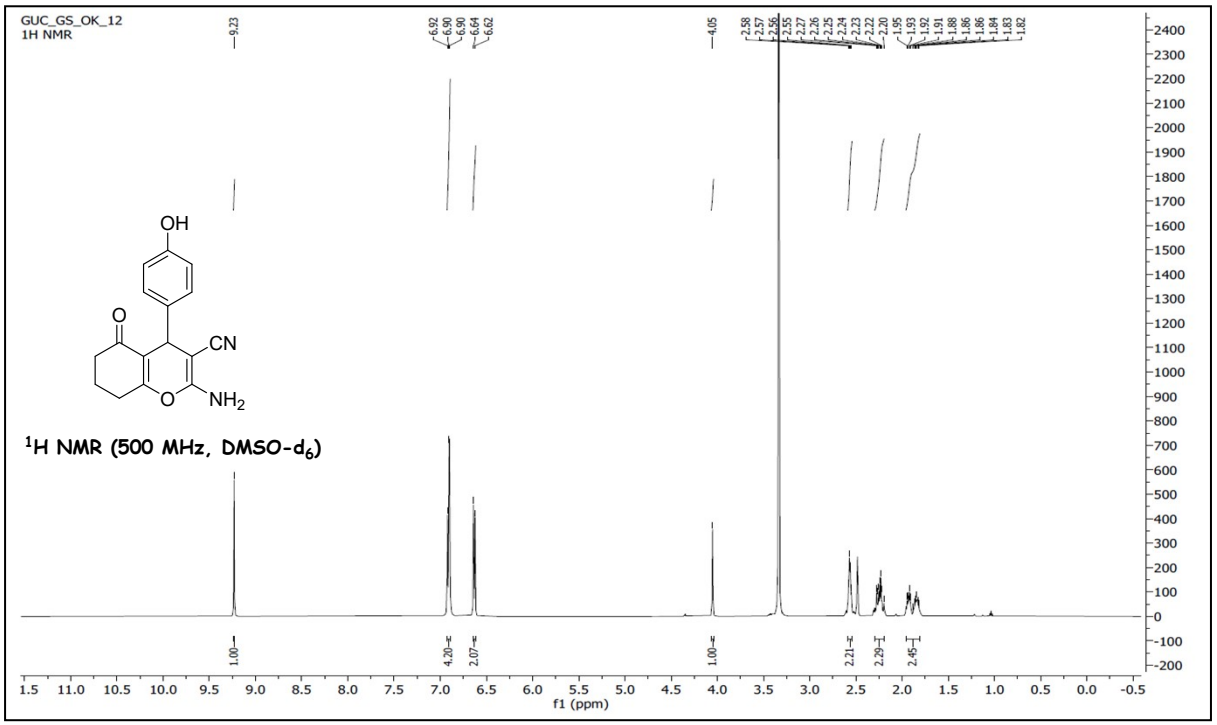
16. **2-amino-4-(4-chlorophenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile**[11]



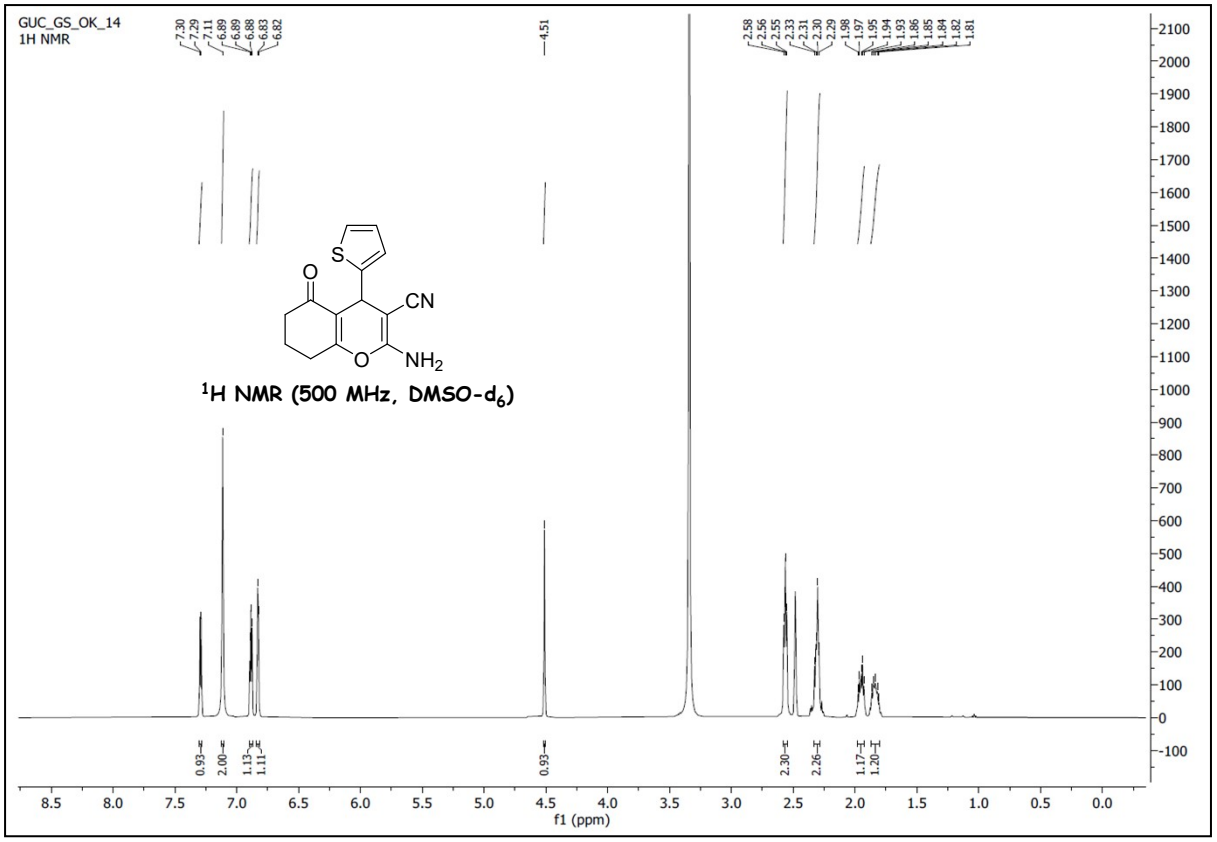
17. **2-amino-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile**[11]



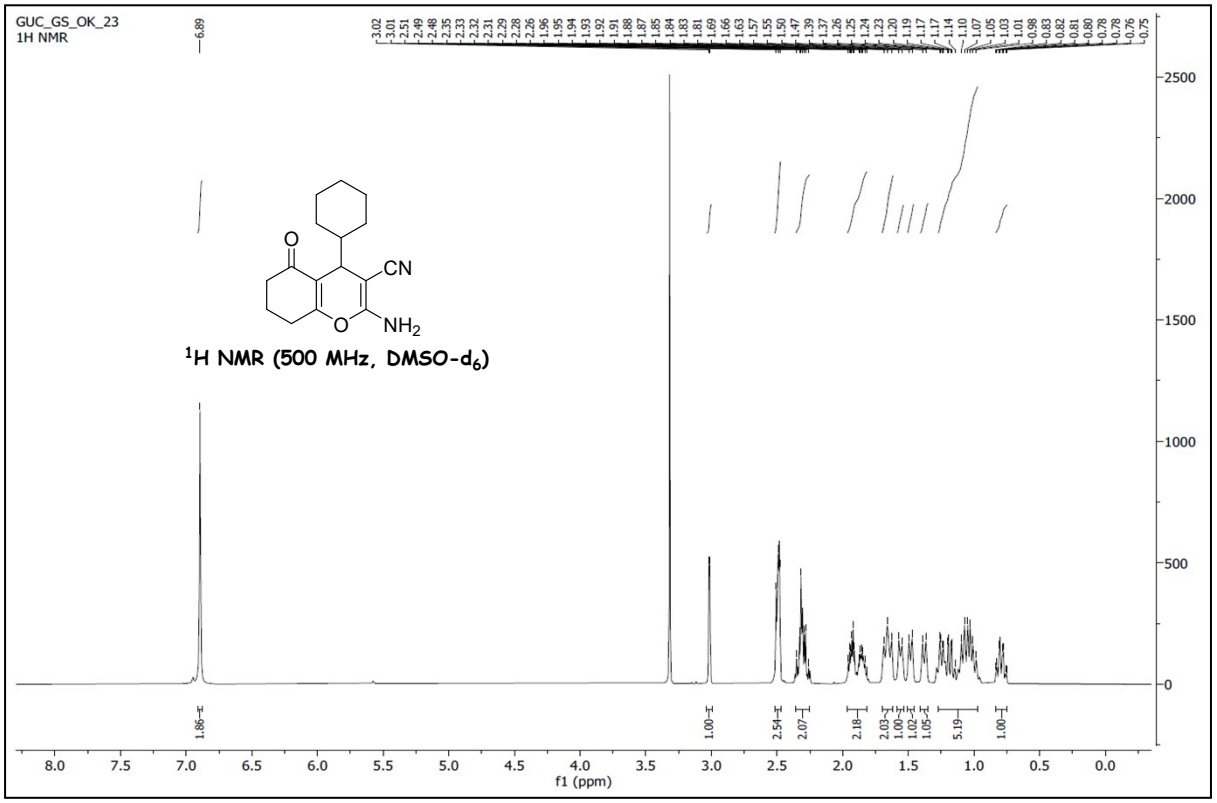
18. **2-amino-4-(4-hydroxyphenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile**[11]



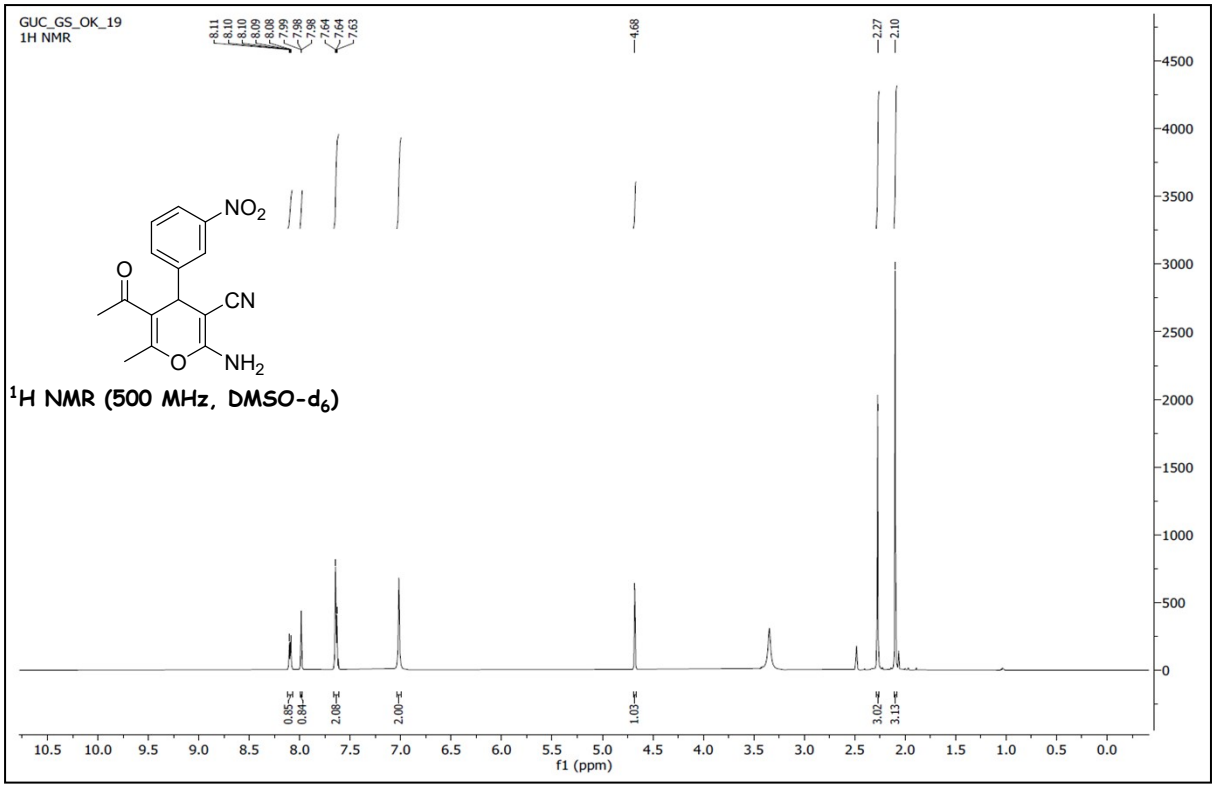
19. **2-amino-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile**[12]



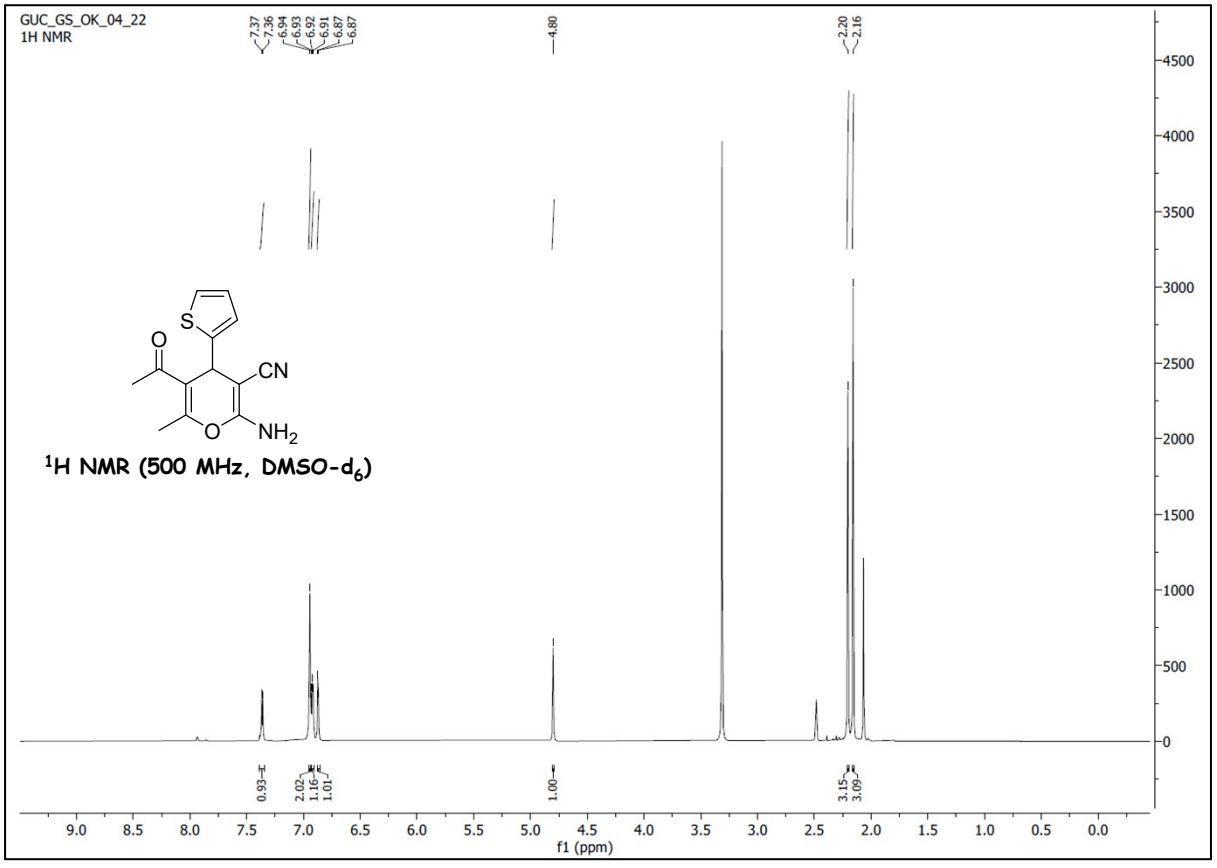
20. **2-amino-4-cyclohexyl-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile**

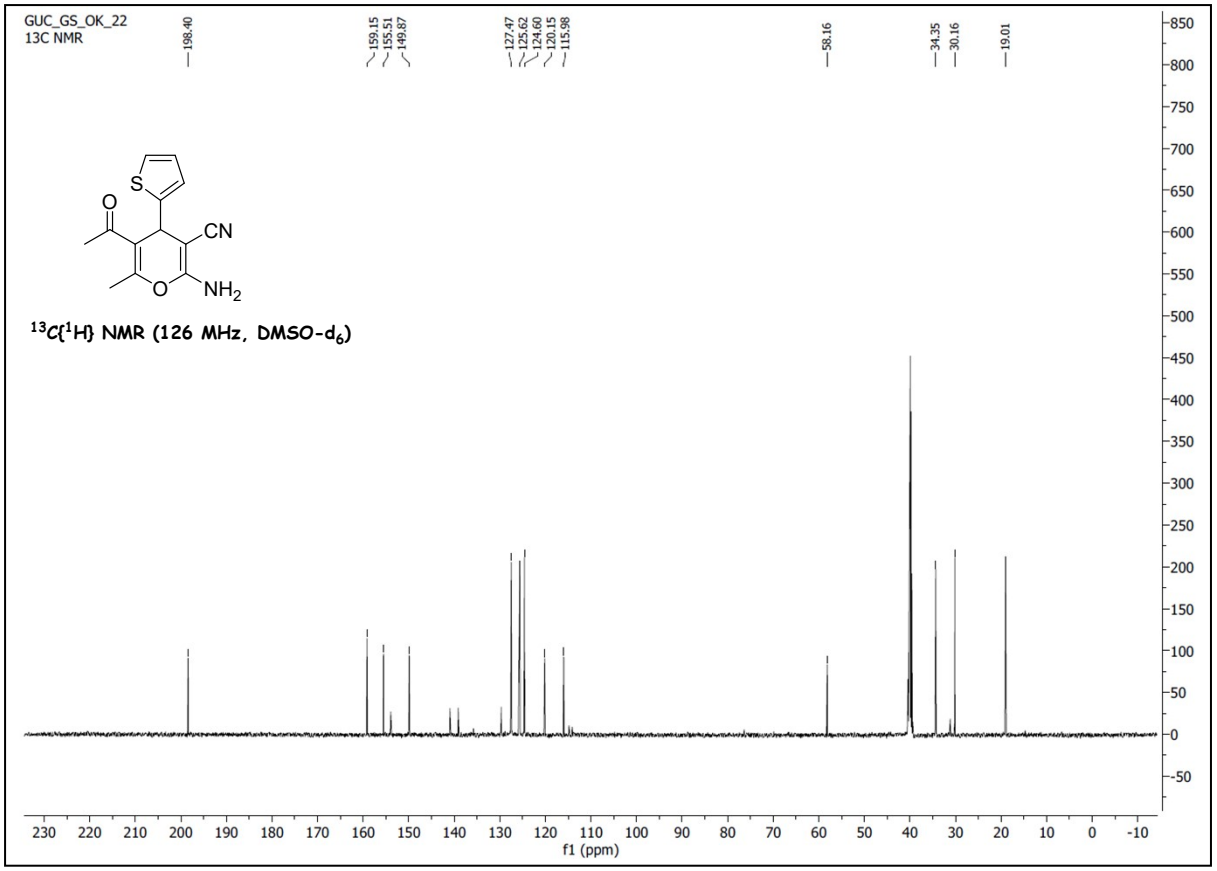


21. **5-acetyl-2-amino-6-methyl-4-(3-nitrophenyl)-4*H*-pyran-3-carbonitrile**[14]

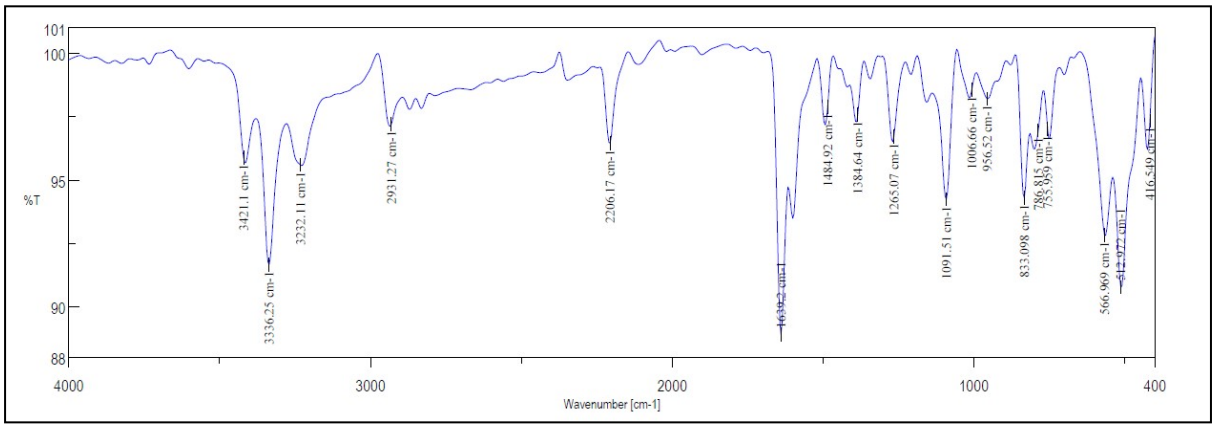


22. **5-acetyl-2-amino-6-methyl-4-(thiophen-2-yl)-4*H*-pyran-3-carbonitrile**

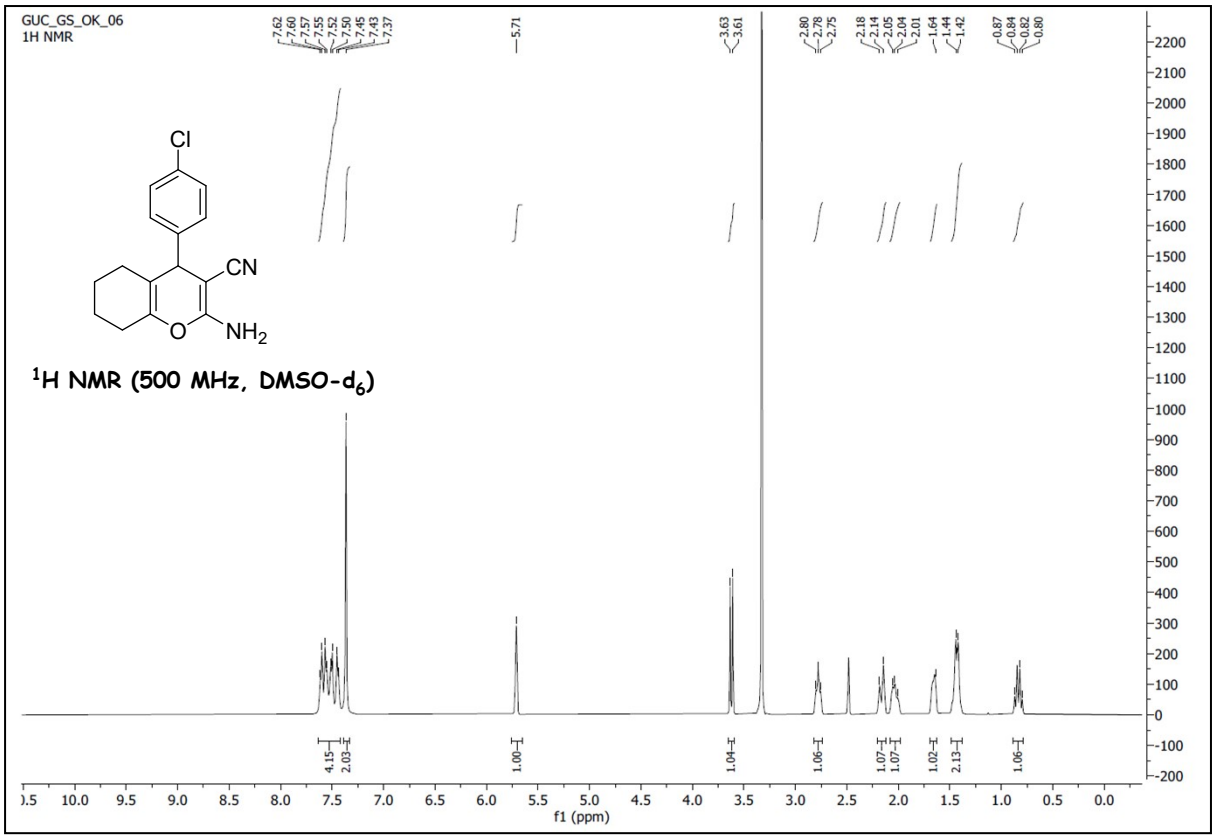




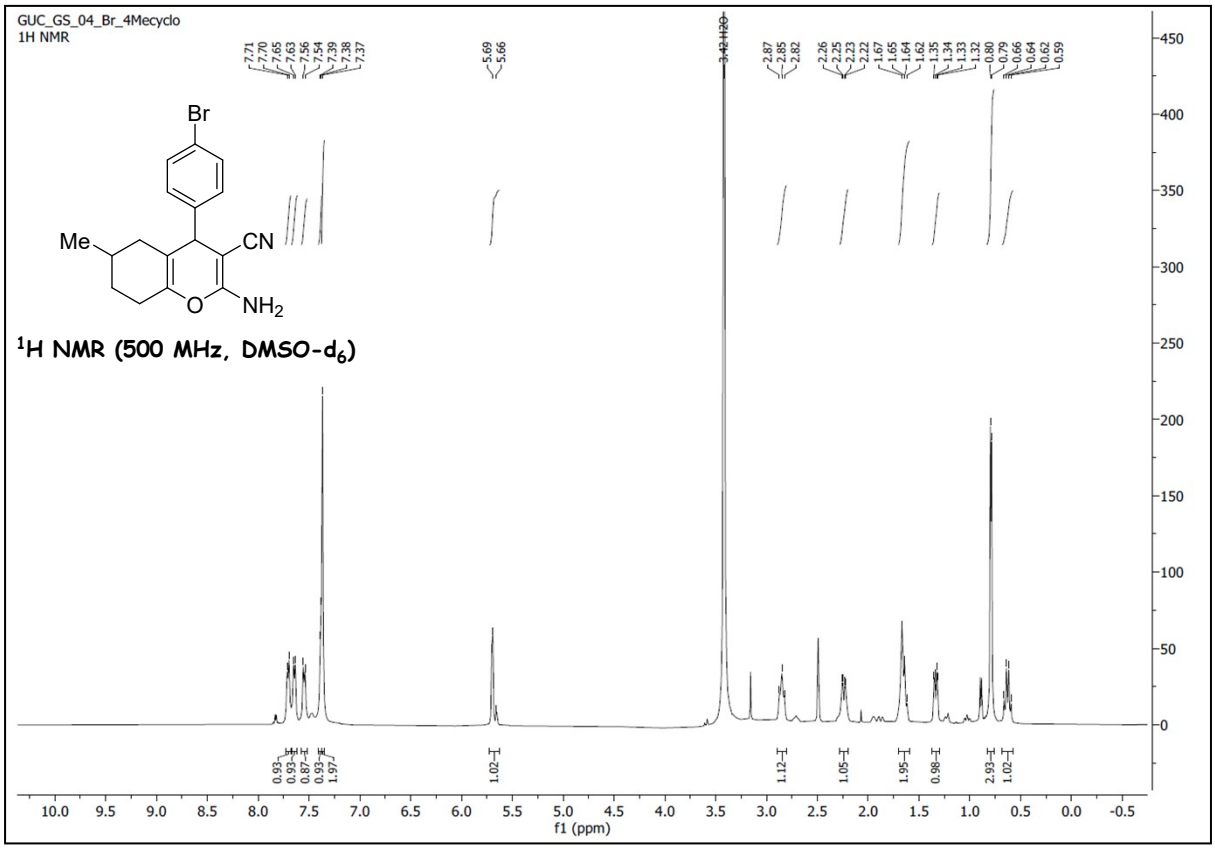
$^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6)

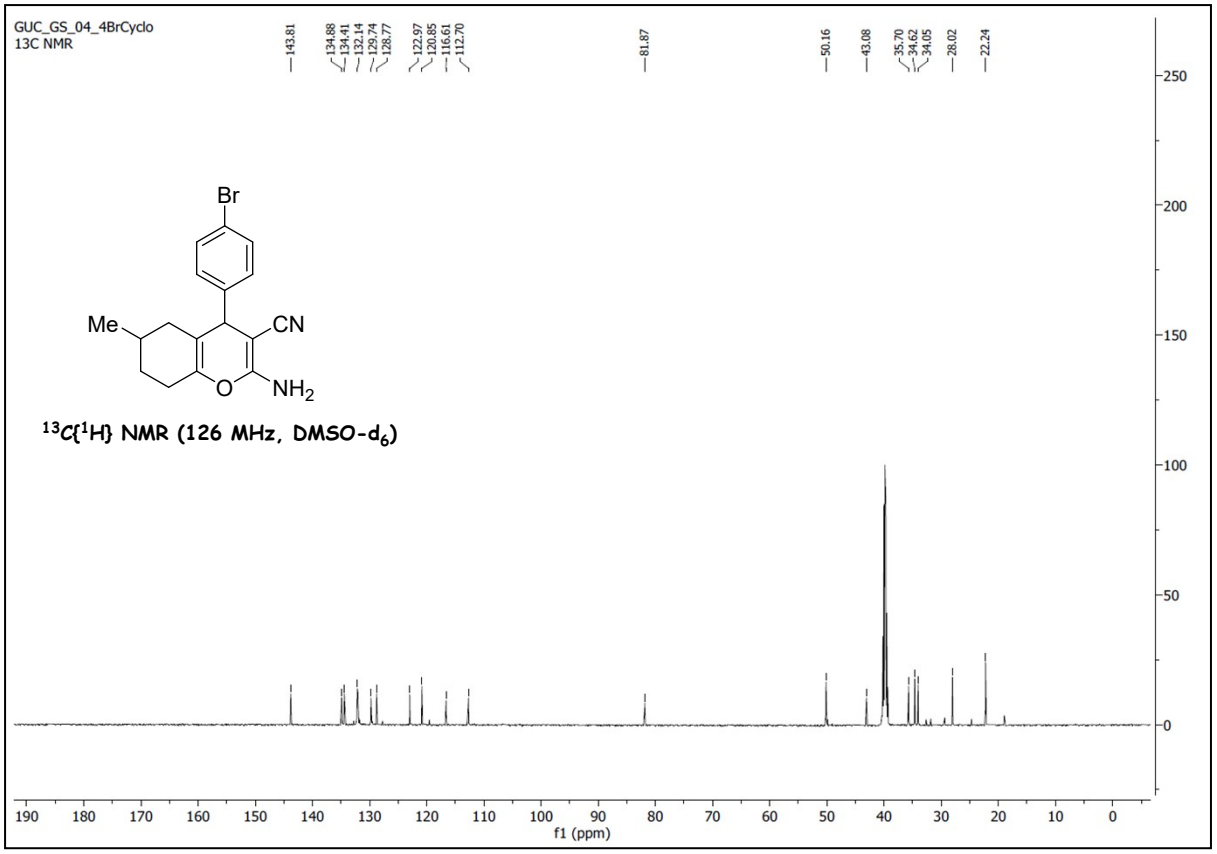


23. **2-amino-4-(4-chlorophenyl)-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile[15]**

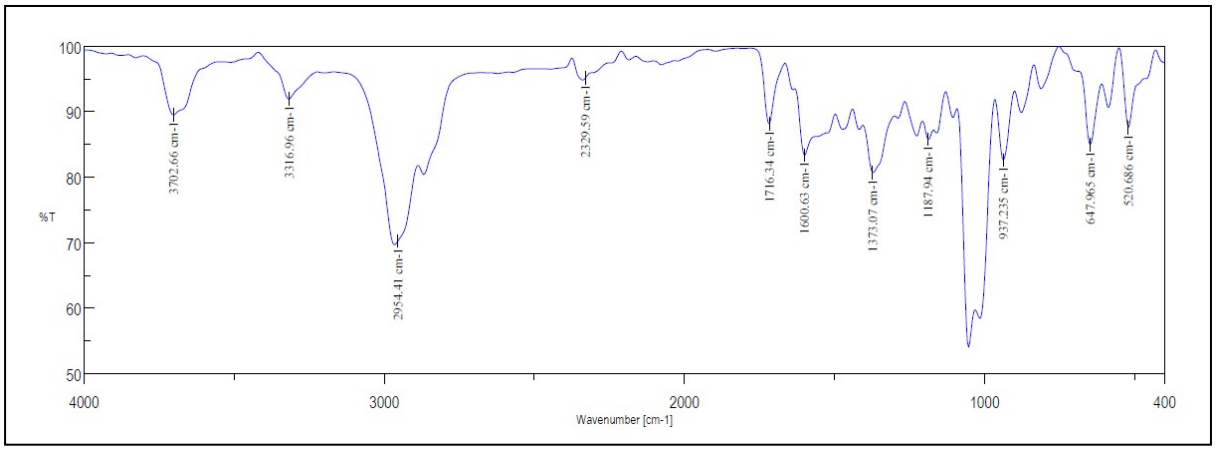


24. **2-amino-4-(4-bromophenyl)-6-methyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile**

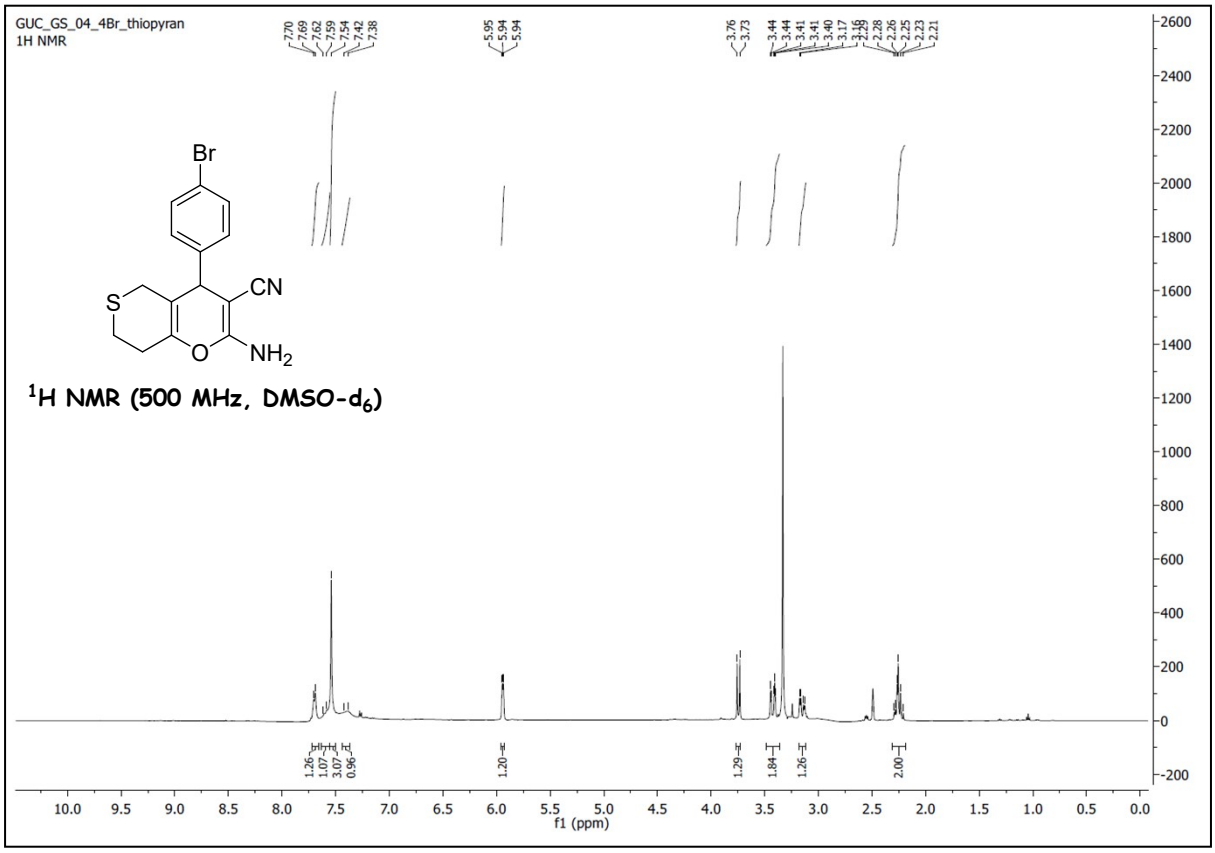




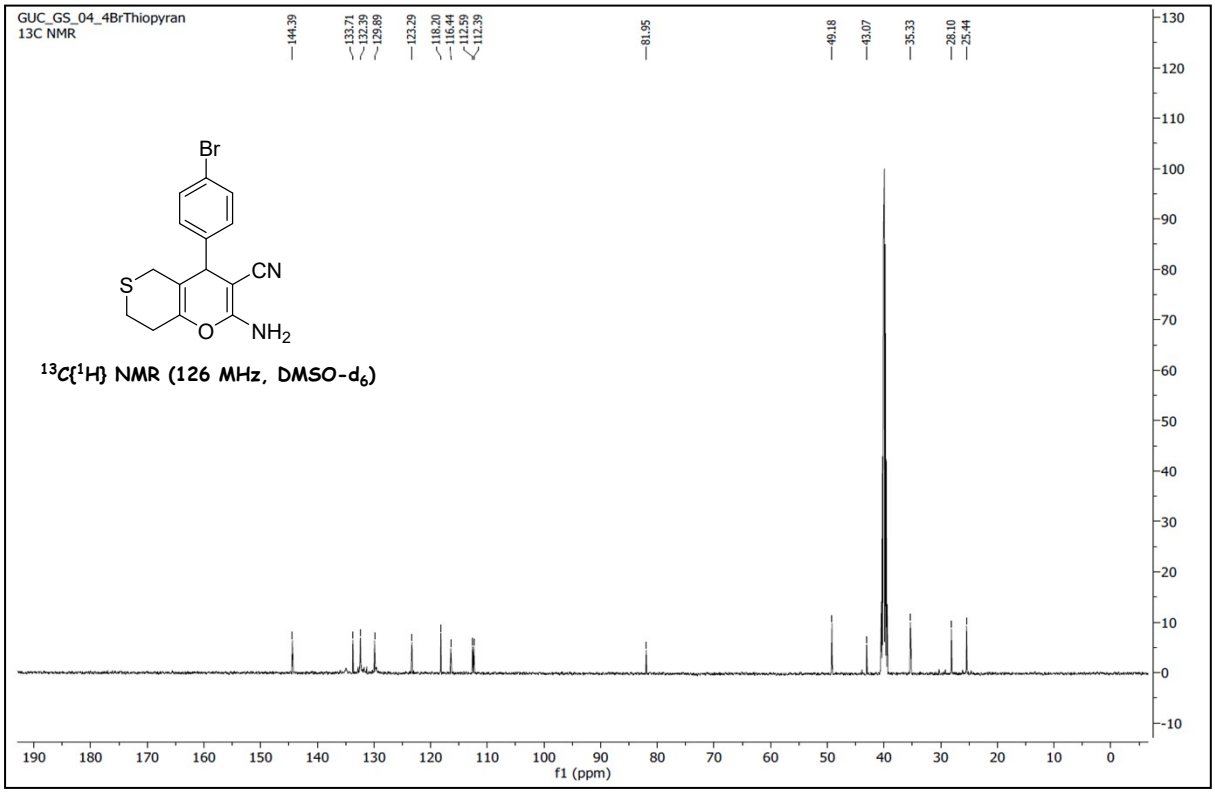
$^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6)



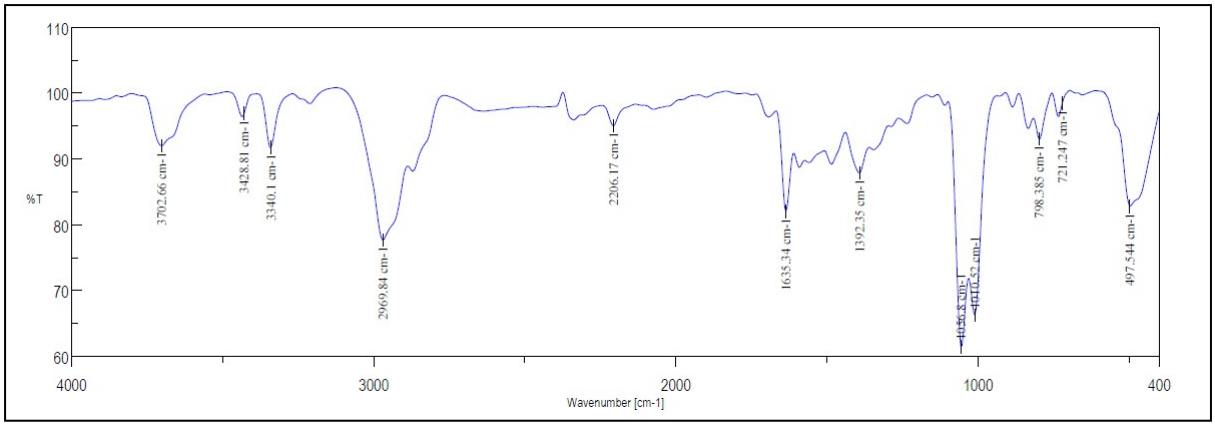
25. **2-amino-4-(4-bromophenyl)-7,8-dihydro-4*H*,5*H*-thiopyrano[4,3-*b*]pyran-3-carbonitrile**



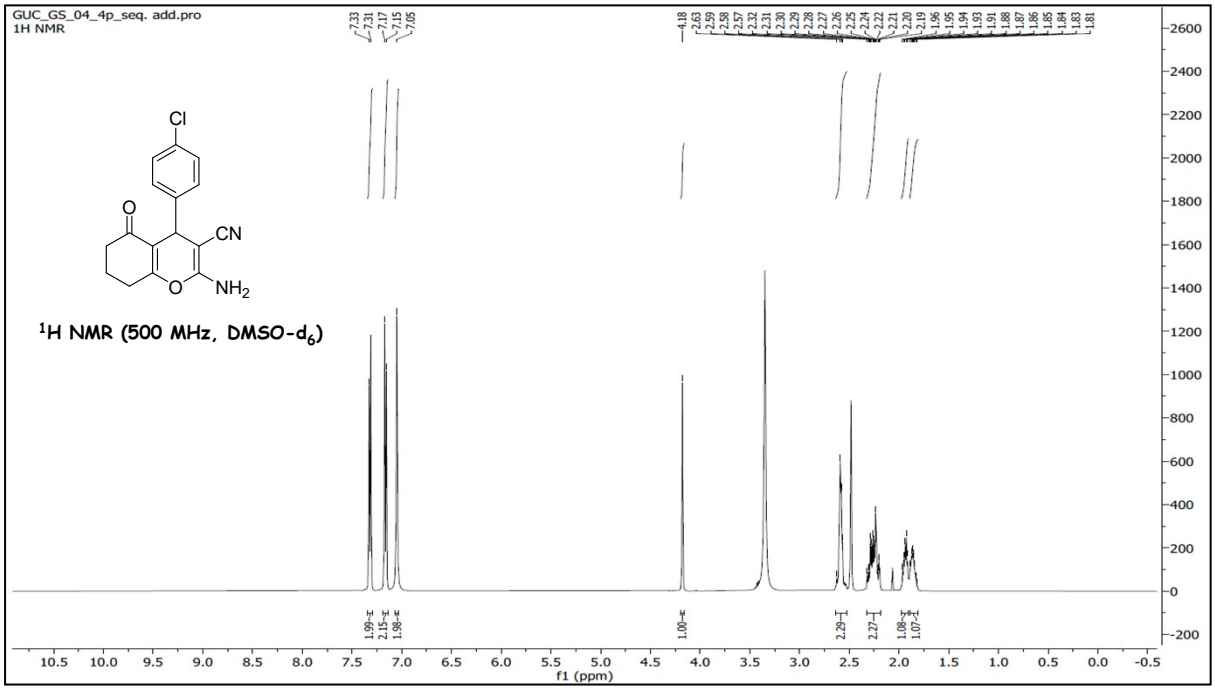
^{1}H NMR (500 MHz, DMSO-d_6)



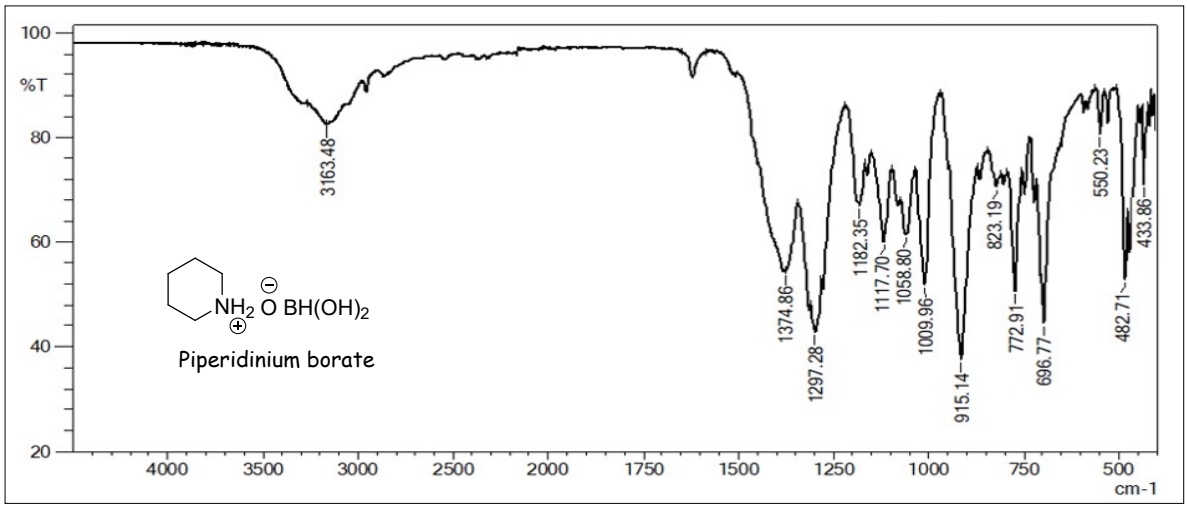
$^{13}C\{^{1}H\}$ NMR (126 MHz, DMSO-d_6)



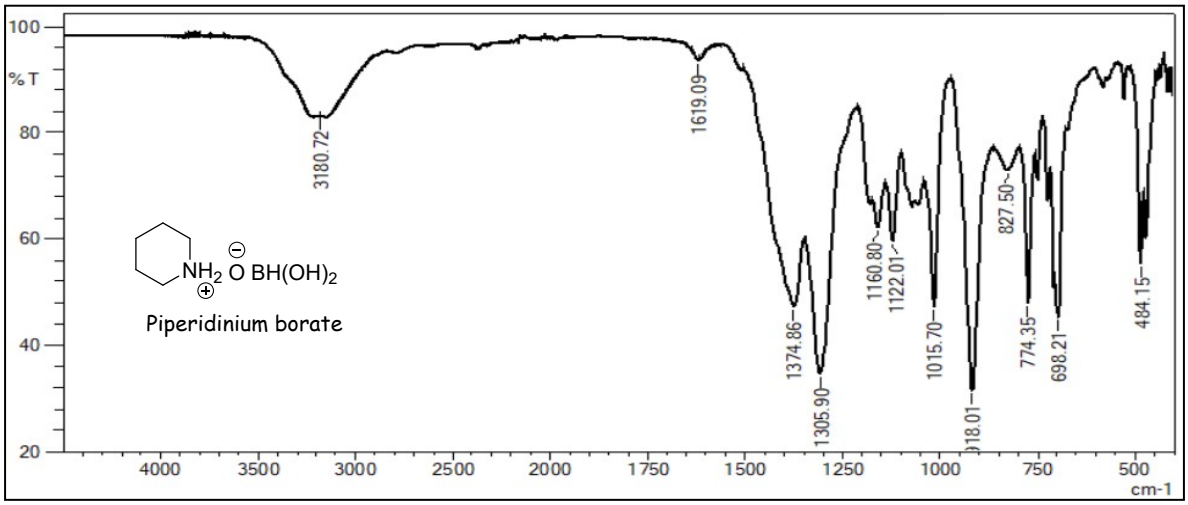
26. **NMR spectra of 2-amino-4-(4-chlorophenyl)-5-oxo-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile 4p via Pathway II:**



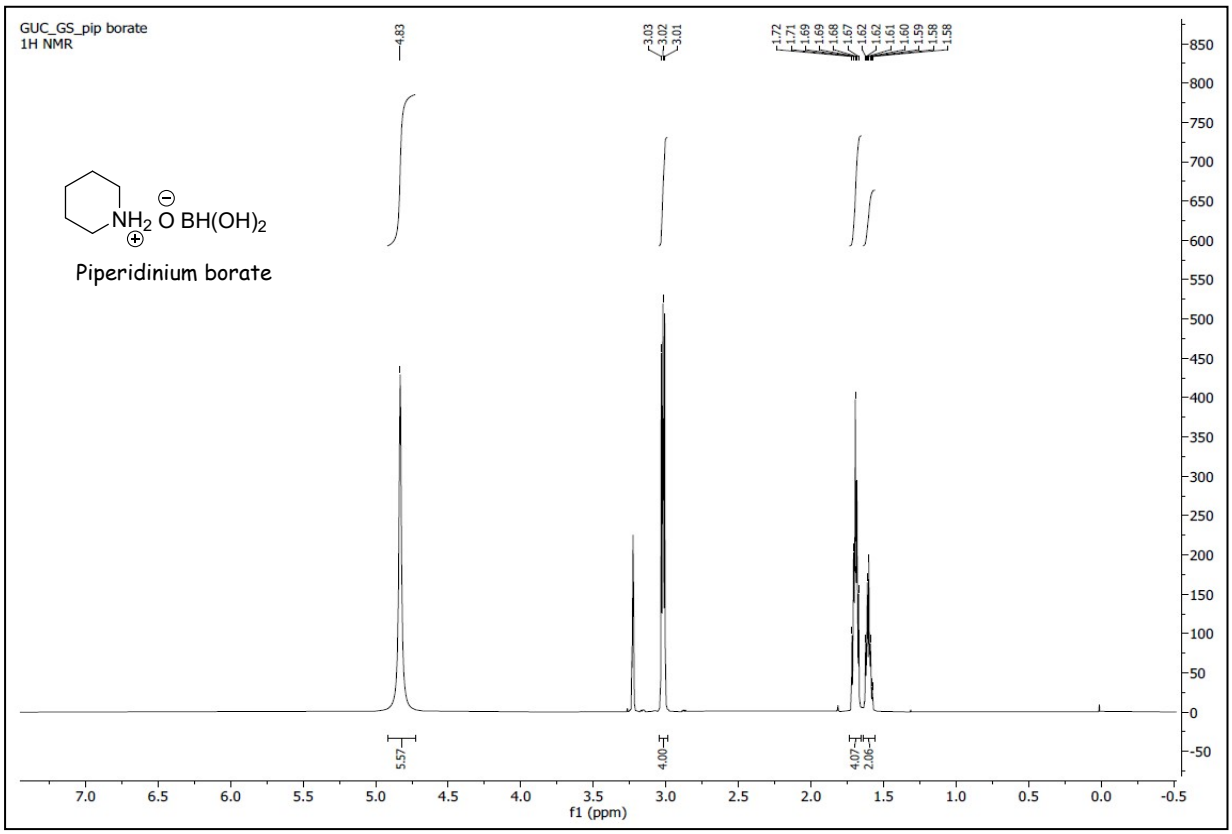
5. **FTIR spectrum of piperidinium borate**



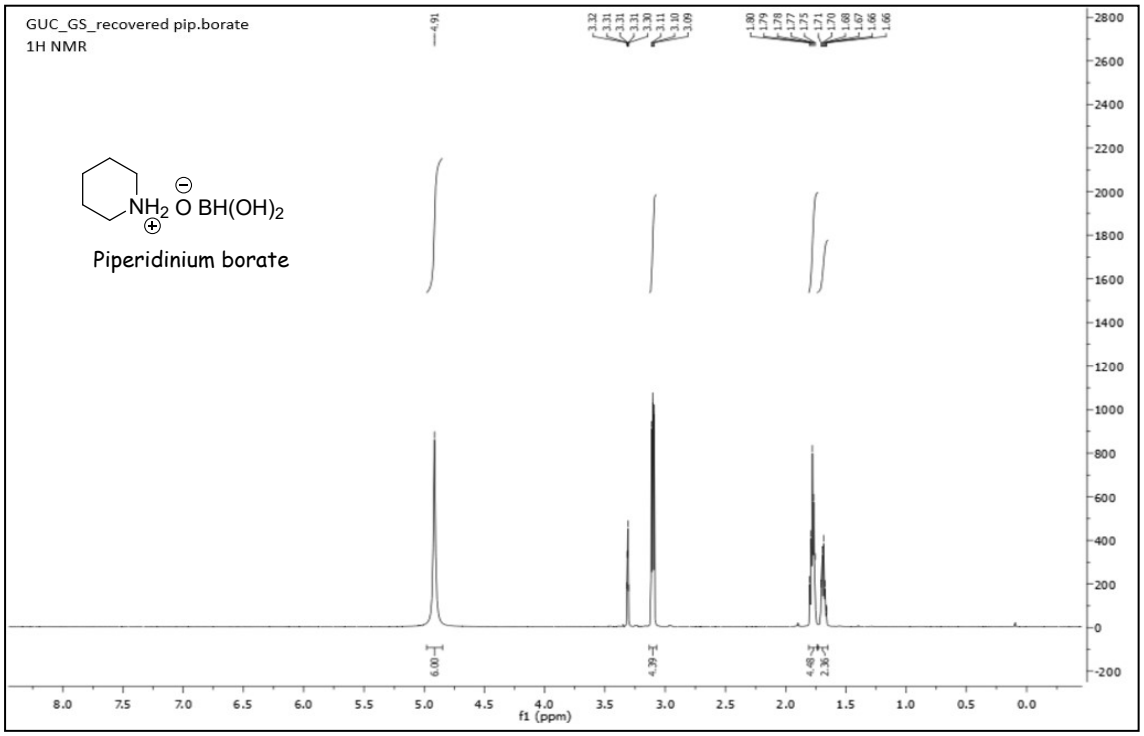
6. **FTIR spectrum of recovered piperidinium borate**



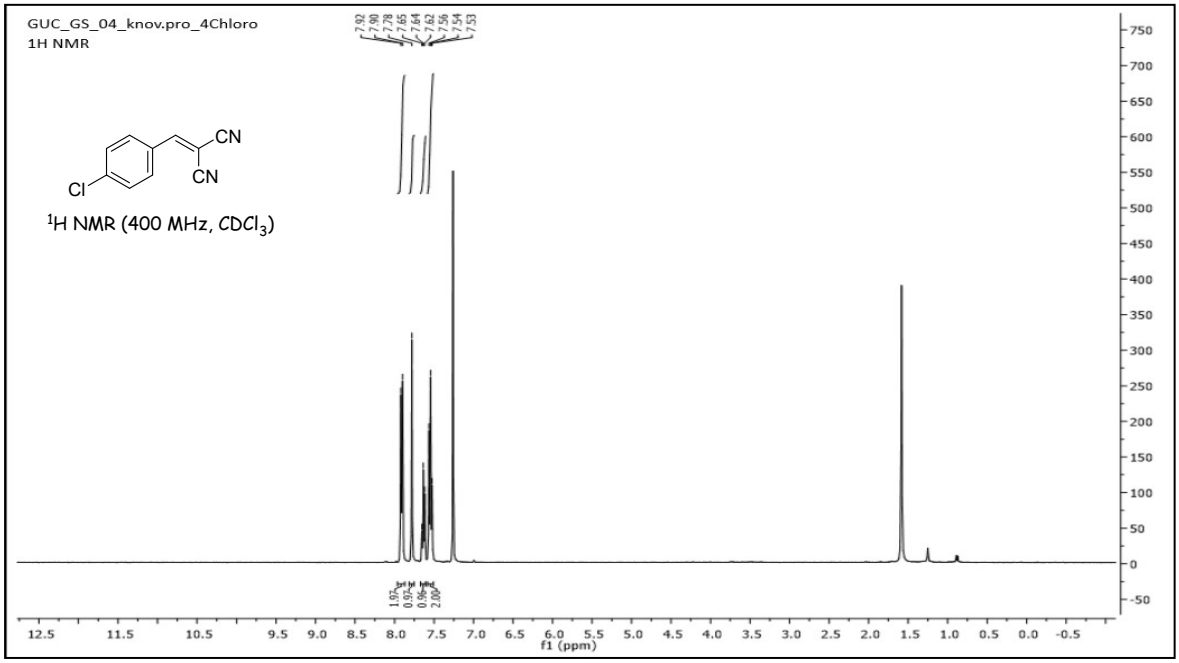
7. **^{1}H NMR spectrum of piperidinium borate**



8. **^{1}H NMR spectrum of recovered piperidinium borate**



9. **^{1}H NMR Spectra of Knoevenagel product (3) formed as an intermediate during reaction:**



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