

Supporting Information

Advanced and green Guareschi-Thorpe synthesis of pyridines at bufferic pH-controlled aqueous medium with ammonium carbonate

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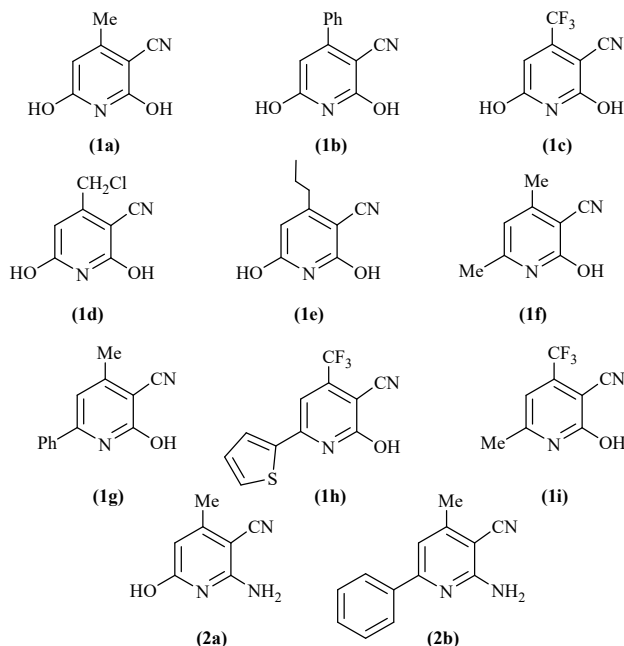
Preparation of cyanopyridines with ethyl cyanoacetate and β -ketoesters or 1,3-diketones:

A mixture of β -ketoester or 1,3-diketone (1 mmol), ethyl cyanoacetate (1 mmol, 0.11 mL) and $(\text{NH}_4)_2\text{CO}_3$ (2 mmol, 0.192 g) in H_2O and EtOH (1:1, v/v) was stirred vigorously at 80 °C for 5-8 h in a round-bottom flask. The progress of the reaction was monitored *via* TLC (EtOAc: Hexane) (30:70) analysis. After the reaction finishing, the precipitated product by adding ice cold water (20 mL) to the reaction mixture was filtered, washed, and dried..

Preparation of cyanopyridines with cyanoacetamide and β -ketoesters or 1,3-diketones:

A solution containing cyanoacetamide (1 mmol), ethyl cyanoacetate (1 mmol, 0.11 mL) and $(\text{NH}_4)_2\text{CO}_3$ (1 mmol, 0.096 g) in 2 mL of H_2O and EtOH (1:1) was stirred at 80 °C for 1-6 h. After completion of the reaction, the resulting solid was collected like the previous method.

Scope of cyanopyridines:



Analytical and spectra data for selected products:

2,6-Dihydroxy-4-methylpyridine-3-carbonitrile (**1a**)

white solid, m.p.: 323-328, FT-IR (KBr): $\bar{\nu}_{\max}$ 3150-2900 (OH stretching), 2223 (C≡N), 1598 (C=N) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 2.22 (s, 3H, CH₃), 5.59 (s, 1H, CH ring), 12.00 (br s, 2H, OH) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ_{C} 21.5, 90.1, 93.5, 117.9, 161.2, 161.8, 162.7 ppm.

4-(Trifluoromethyl)-2,6-dihydroxypyridine-3-carbonitrile (**1c**)

white solid, m.p.: 225-230 °C, FT-IR (KBr): $\bar{\nu}_{\max}$ 3391-2934 (OH stretching), 2226 (C≡N), 1618 (C=N ring) cm^{-1} .

2,6-Dihydroxy-4-propylpyridine-3-carbonitrile (**1e**)

white solid, m.p.: 295-300 °C, FT-IR (KBr): $\bar{\nu}_{\max}$ 3200-2800 (OH stretching), 2223 (C≡N), 1599 (C=N ring) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 0.92 (t, $J=7$ Hz, 3H, CH₃), 1.57 (m, $J=7.5$ Hz, 2H, CH₂CH₃), 2.49 (t, $J=7.5$ Hz, 2H, CH₂CH₂), 4.90 (br s, 2H, OH) 5.58 (s, 1H, CH ring) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ_{C} 14.2, 14.6, 21.8, 32.2, 46.5, 59.9, 61.2, 80.0, 109.9, 111.4, 111.5, 115.0, 145.2, 149.5, 165.9, 168.9 ppm.

2-Hydroxy-4,6-dimethylpyridine-3-carbonitrile (**1f**)

white solid, m.p.: 367-370 °C, FT-IR (KBr): $\bar{\nu}_{\max}$ 3100-2800 (OH stretching), 2218 (C≡N), 1618 (C=N ring) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 2.21 (s, 3H, CH₃), 2.33 (s, 3H, CH₃), 6.13 (s, 1H, CH ring), 12.24 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ_{C} 19.7, 21.5, 99.9, 108.3, 116.6, 152.1, 161.3, 161.4 ppm.

2-Hydroxy-4-methyl-6-phenylpyridine-3-carbonitrile (**1g**)

white solid, m.p.: 290-296, FT-IR (KBr): $\bar{\nu}_{\max}$ 3100-3000 (OH stretching), 2222 (C≡N), 1608 (C=N ring) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 2 (s, 3H, ₃), 5.70 (s, 1H), 7.83 (d, $J=7$ Hz, 2H), 7.41-7.45 (m, $J=7$ Hz, 3H), 10.03 (s, 1H, OH) ppm.

4-(Trifluoromethyl)-2-hydroxy-6-(thiophen-2-yl) pyridine-3-carbonitrile (**1h**)

yellow solid, m.p.: 285 °C, FT-IR (KBr): $\bar{\nu}_{\max}$ 3102 (NH stretching), 2231 (C≡N), 1642 (C=O) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 7.27 (t, $J=4$ Hz, 1H, CH ring), 7.67 (s, 1H, CH ring), 7.91 (d, $J=5$ Hz, 1H, CH ring), 8.19 (s, 1H, CH ring), 13-14 (br s, 1H, OH) ppm.

4-(Trifluoromethyl)-2-hydroxy-6-methylpyridine-3-carbonitrile (**1i**)

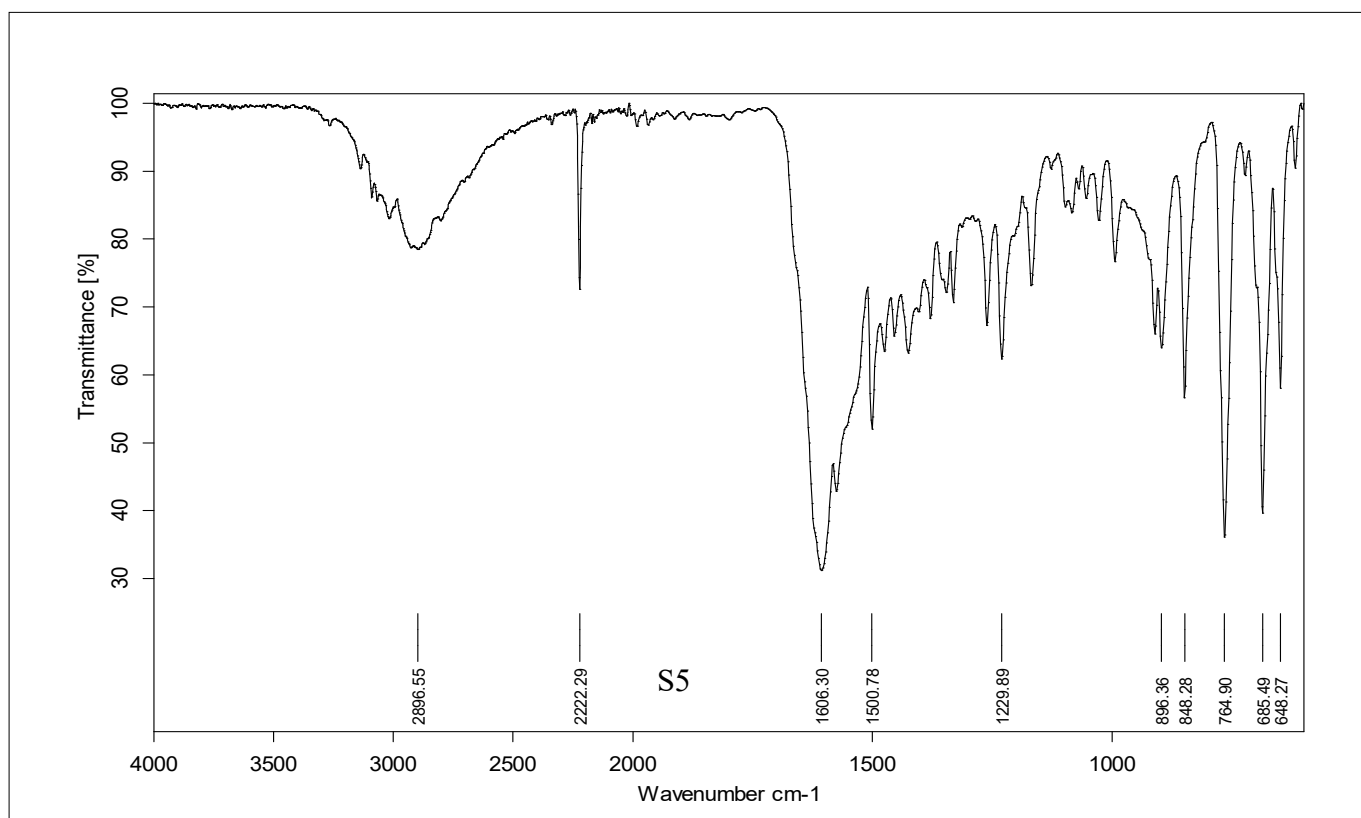
white solid. M.p.: 232-236 °C, FT-IR (KBr): $\bar{\nu}_{\max}$ 3102 (NH stretching), 2231 (C≡N), 1641 (C=O) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 2.38 (s, 3H, CH₃), 6.61 (s, 1H, CH ring), 13.35 (s, 1H, OH) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ_{C} 19.5, 96.1, 101.5, 113.4, 121.9 (q, $J=273.75$ Hz, CF₃), 145.8 (q, $J=32.5$ Hz, C-CF₃), 156.9, 160.4 ppm.

2-Amino-4-methyl-6-hydroxypyridine-3-carbonitrile (**2a**)

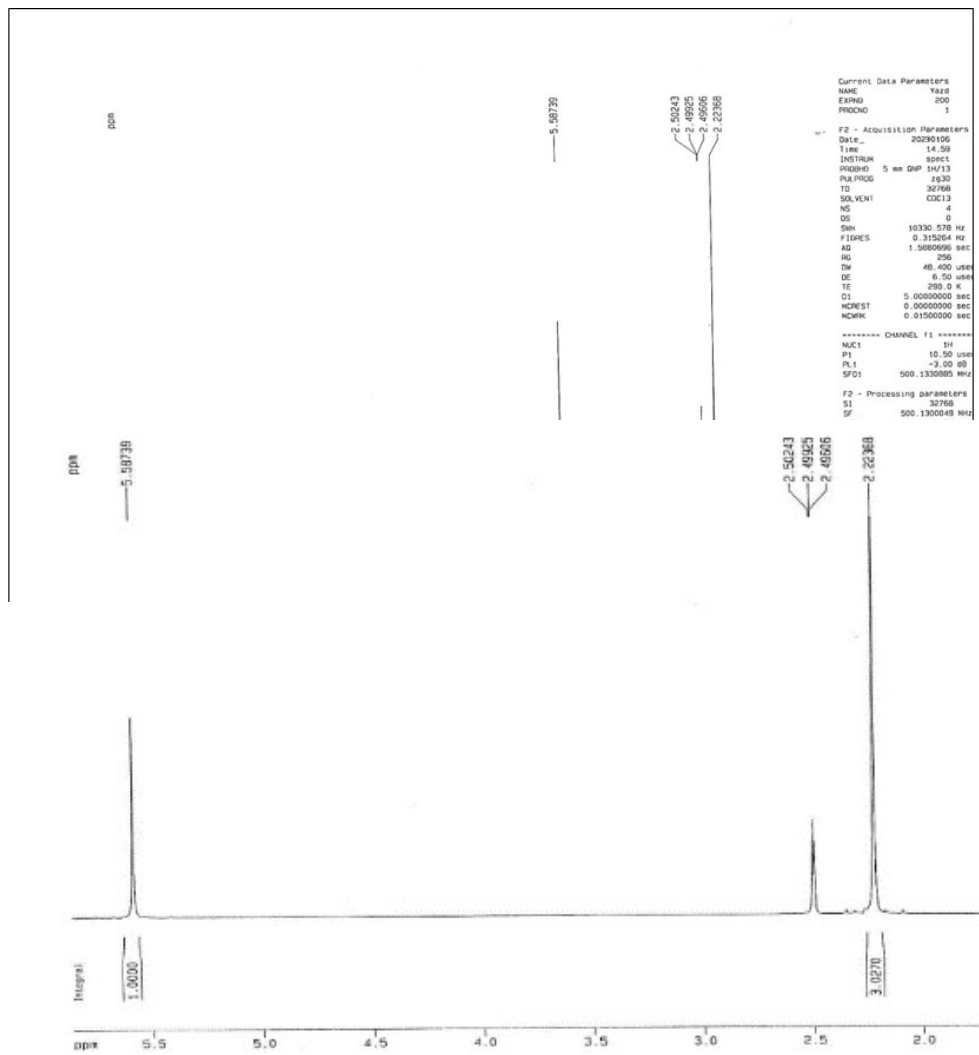
pale yellow solid, m.p.: 132-134 °C FT-IR (KBr): $\bar{\nu}_{\max}$ 3381, 3230, 3326 (NH stretching), 2215 (C≡N), 1723 (C=O), 1646 (C=N ring) cm^{-1} .

2-Amino-4-methyl-6-phenylpyridine-3-carbonitrile (**2b**)

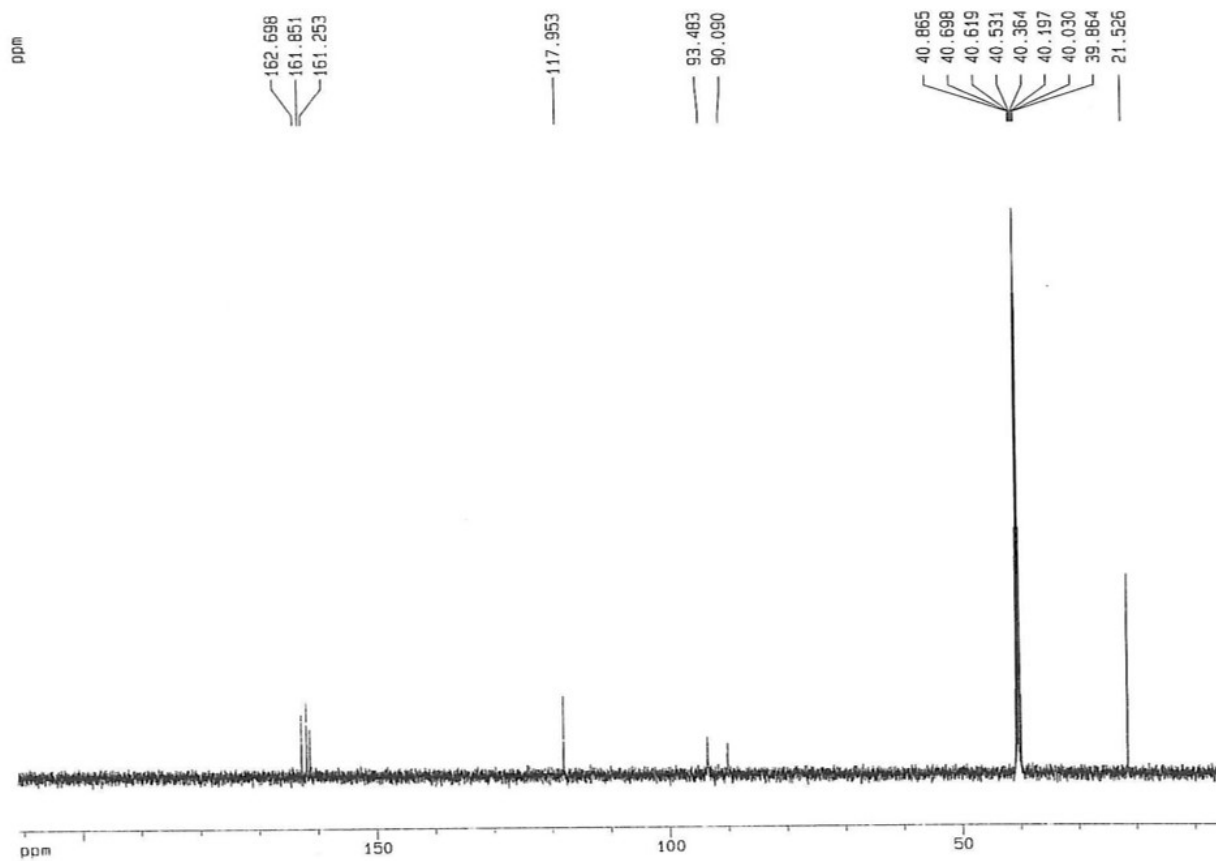
pale pink solid, m.p.: 185-189 °C FT-IR (KBr): $\bar{\nu}_{\max}$ 3469, 3344, 3239 (NH stretching), 2211 (C≡N), 1640 (C=N ring) cm^{-1} . ^1H NMR (500 MHz, DMSO- d_6): δ_{H} 2.45 (s, 3H, CH₃), 6.68 (s, 2H, NH), 6.75 (s, 1H, CH ring), 7.51-7.54 (m, 5H) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ_{C} 21.4, 115.9, 116.6, 119.5, 128.8, 129.1, 129.7, 148.7, 150.1, 153.9 ppm.

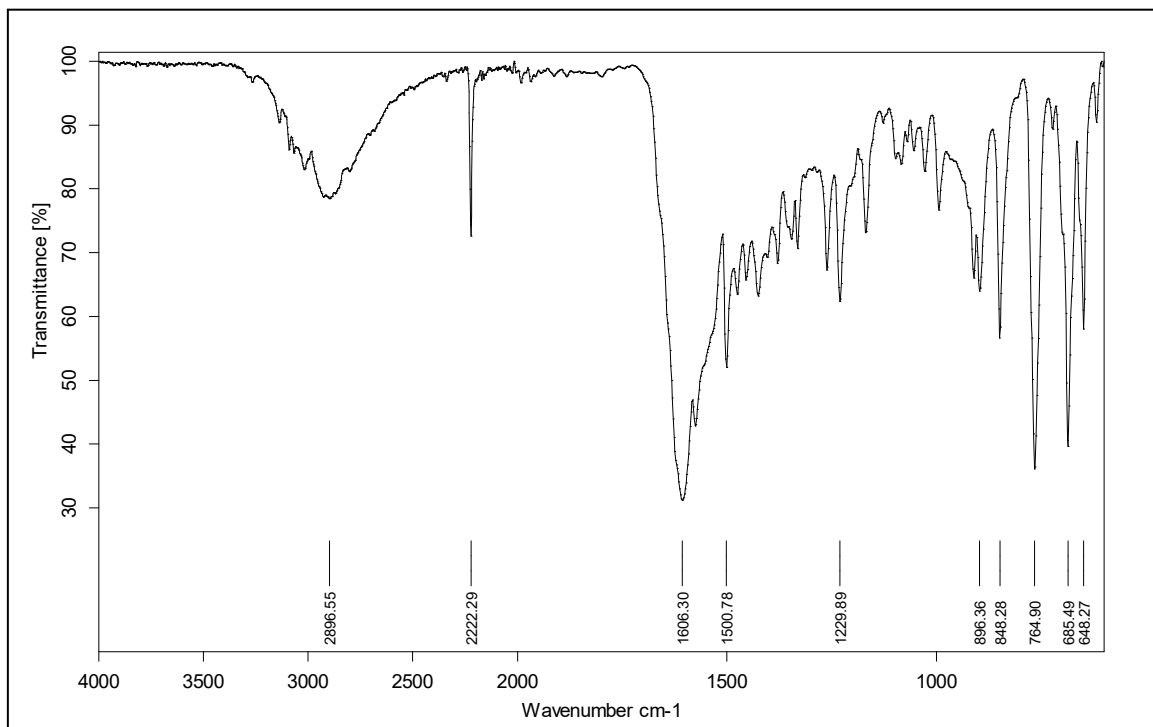


FT-IR (KBr) spectrum of (1a)

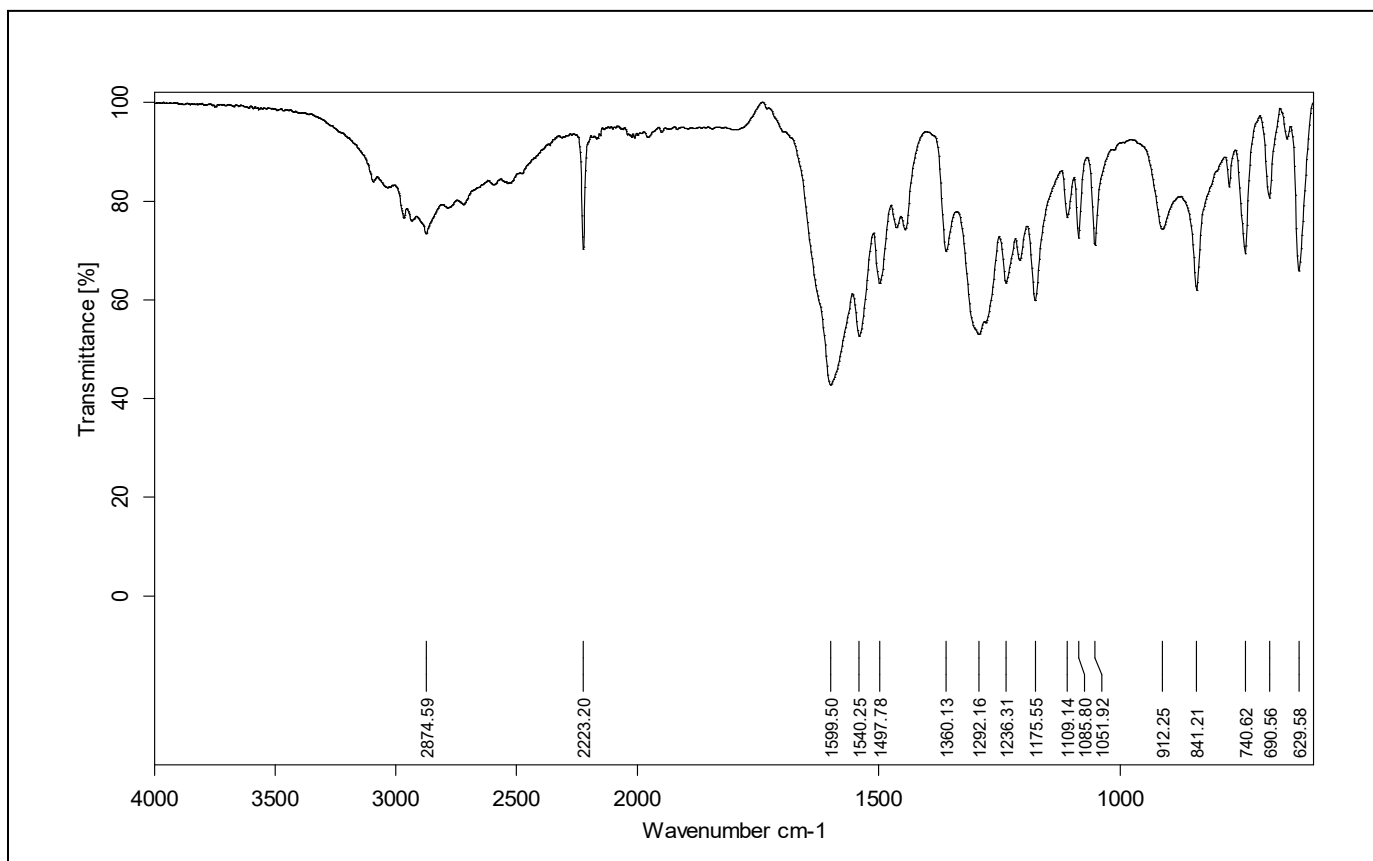


Expand of ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1a**)

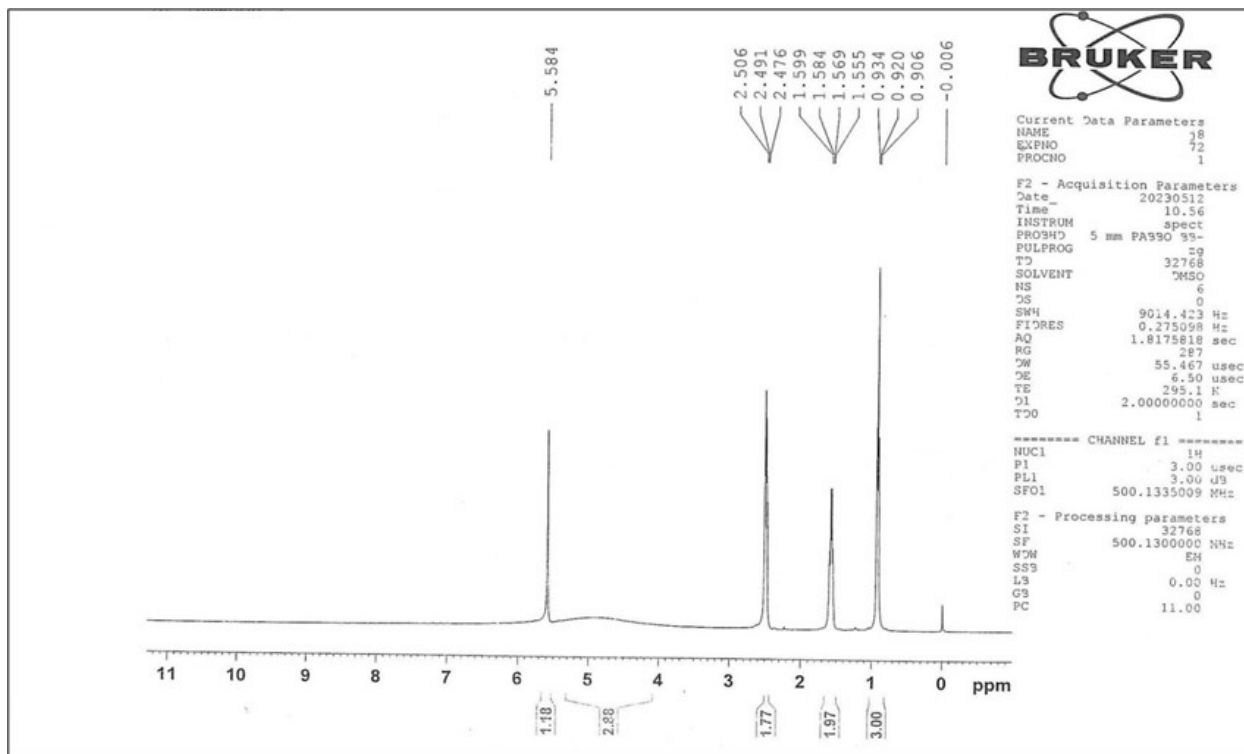




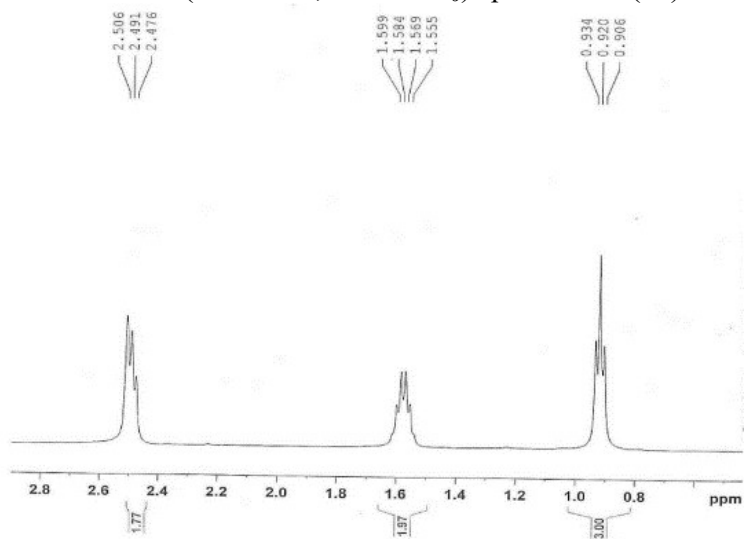
FT-IR (KBr) spectrum of (**1c**)



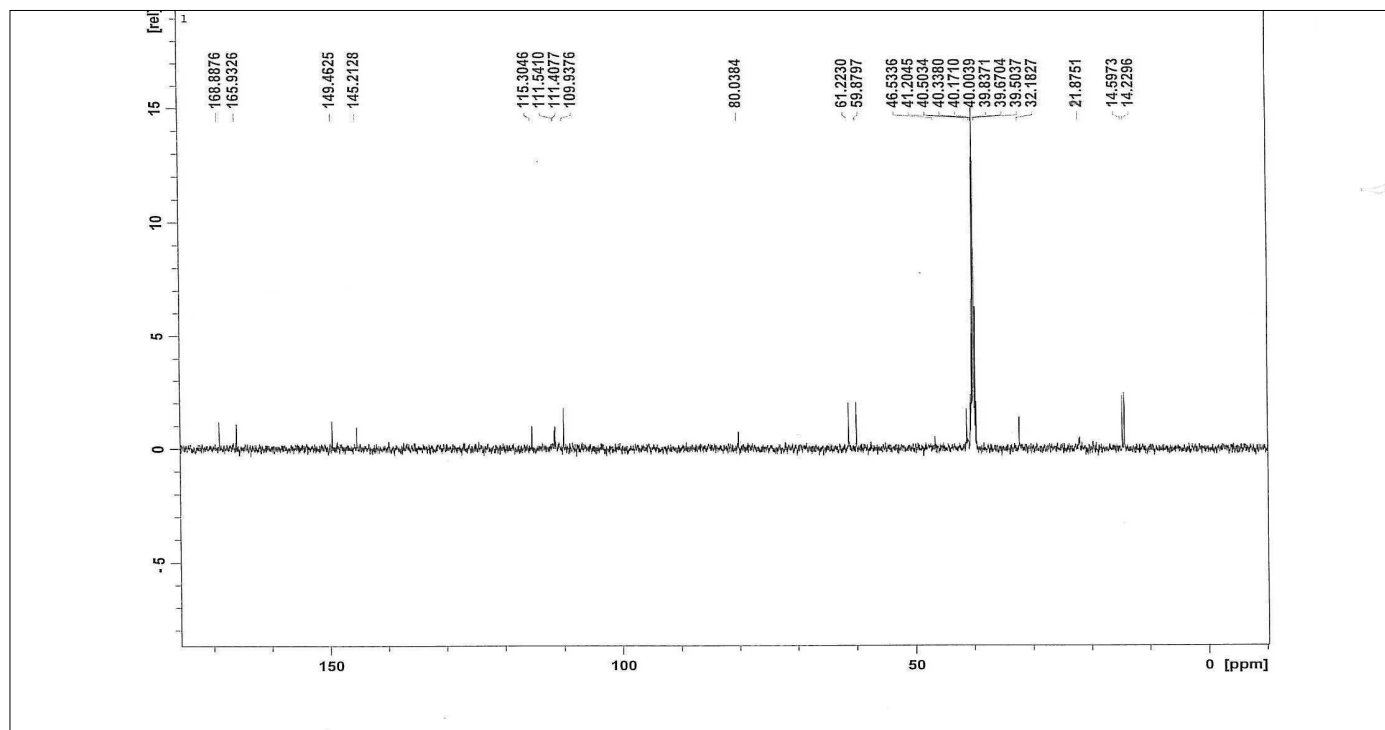
FT-IR (KBr) spectrum of **1e**



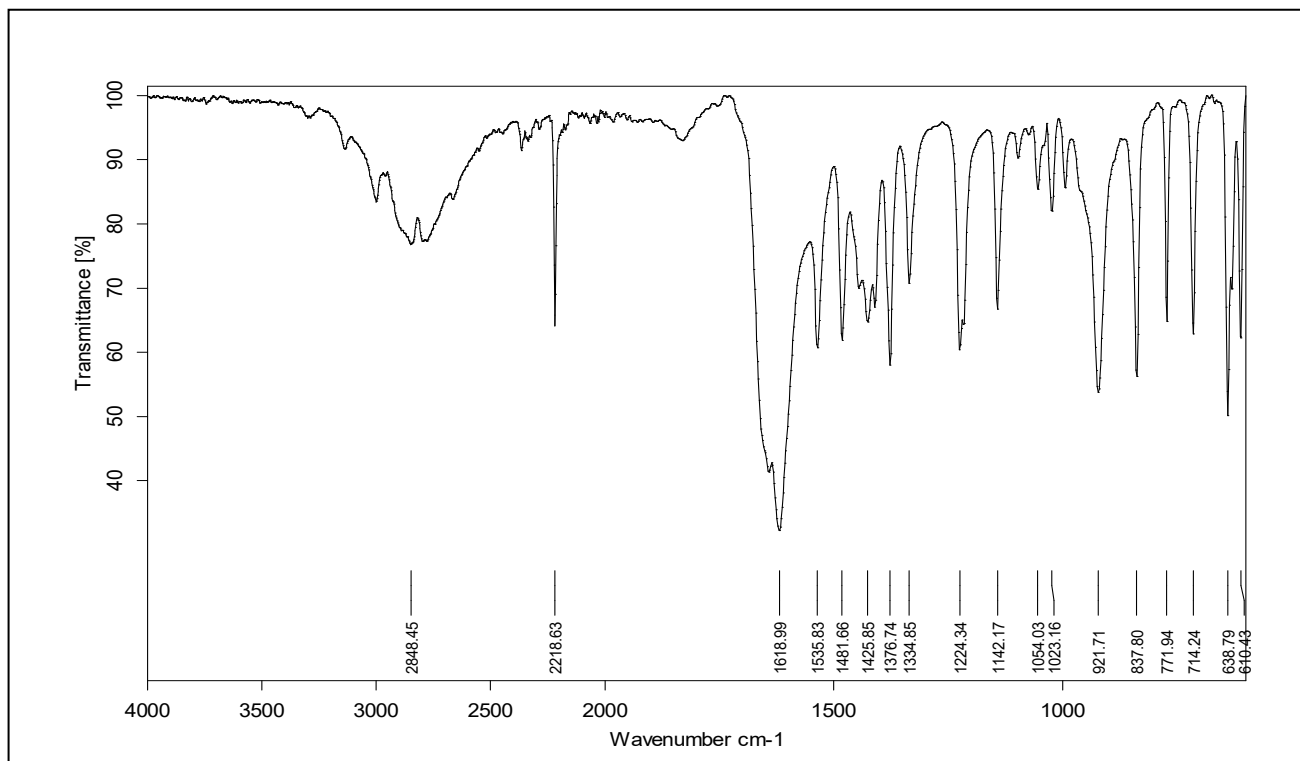
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1e**)



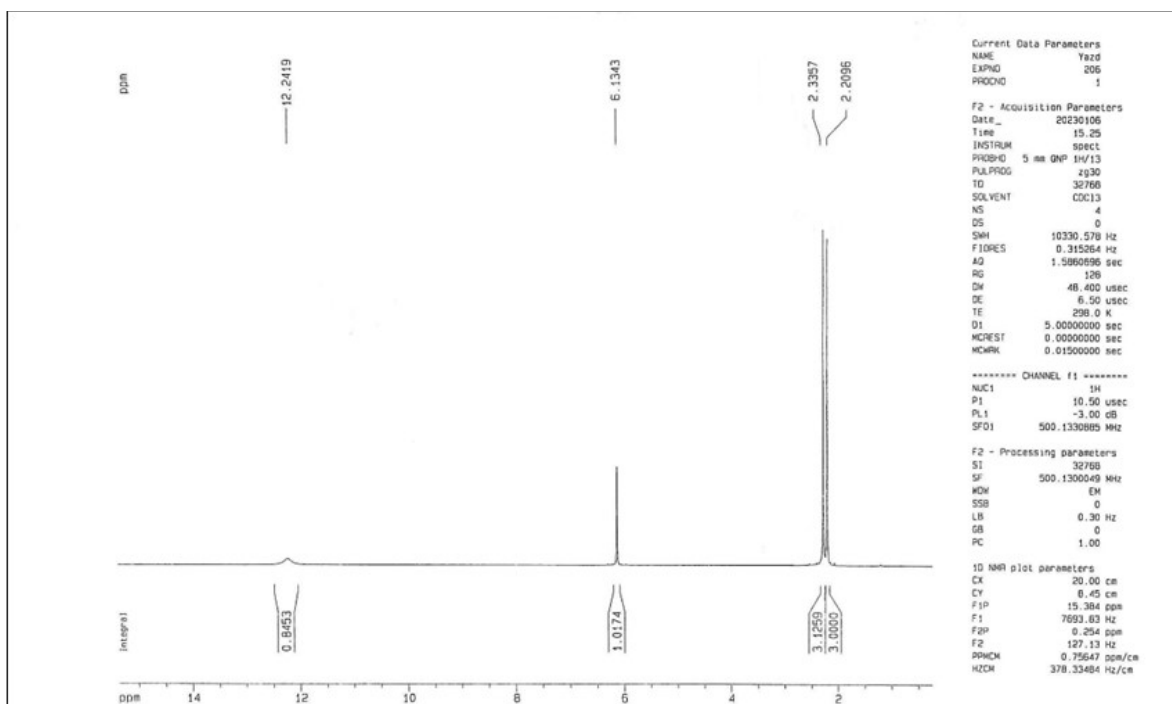
Expand of ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1e**)



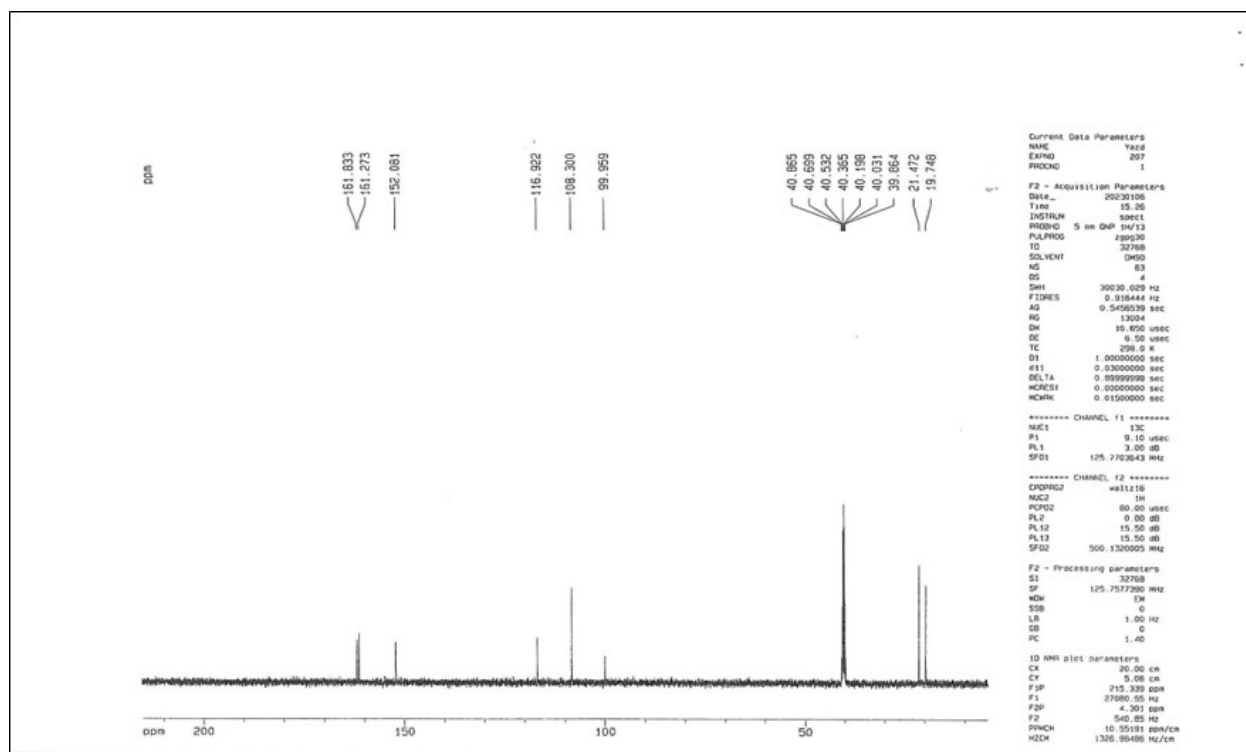
¹³C NMR (125 MHz, DMSO-*d*₆) spectrum of **(1e)**



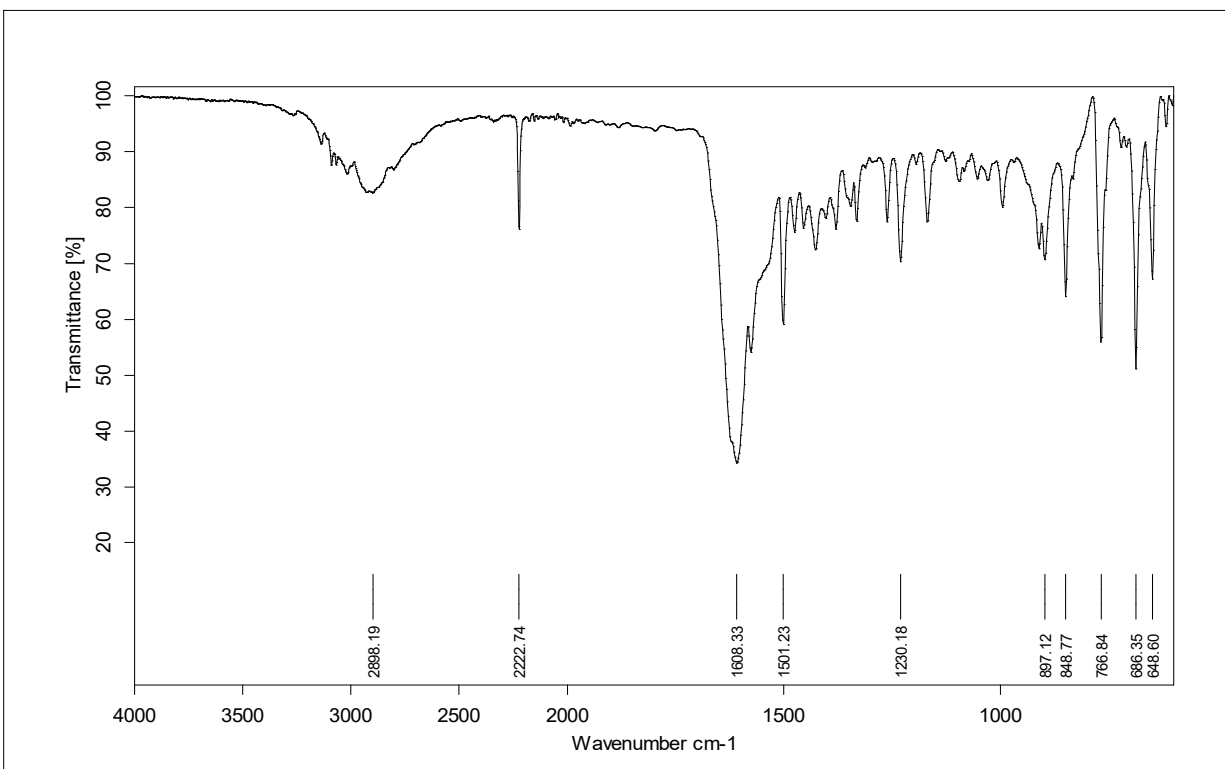
FT-IR (KBr) spectrum of (**1f**)



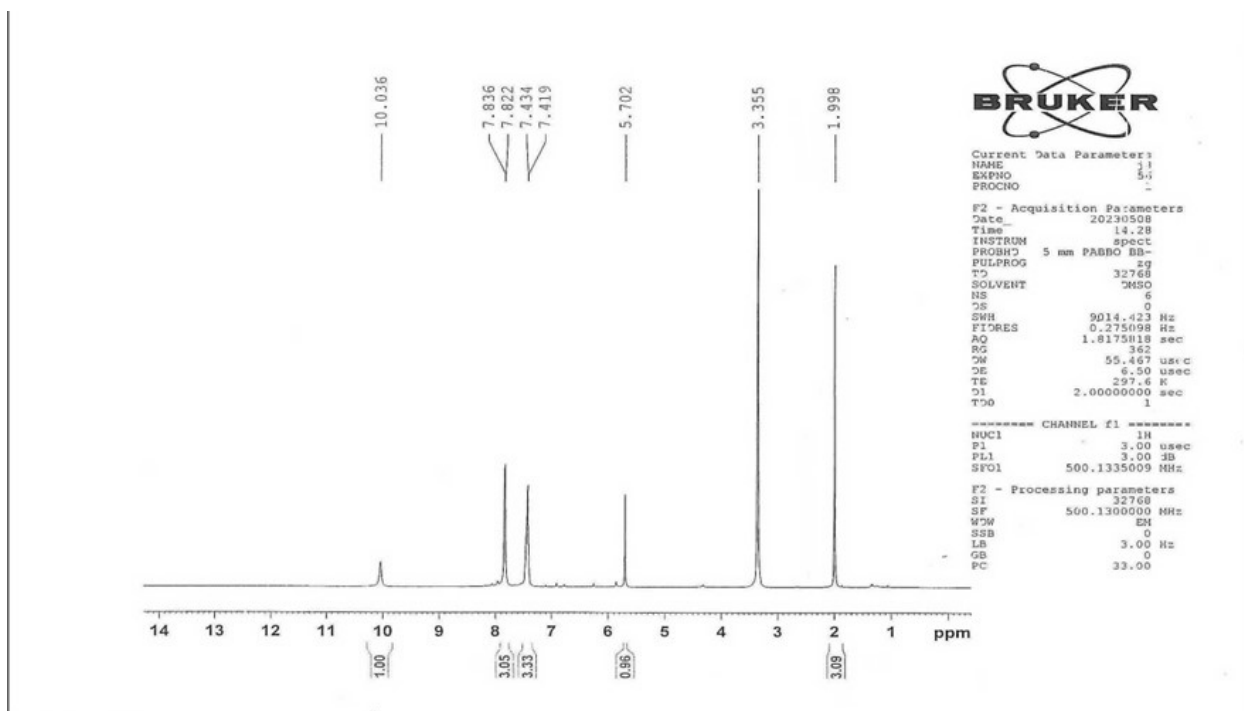
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1f**)



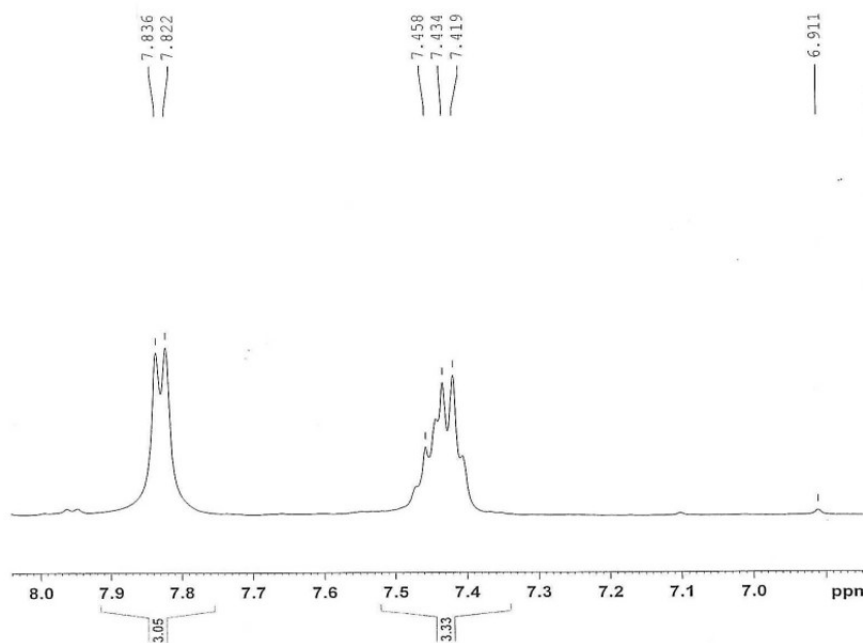
^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (**1f**)



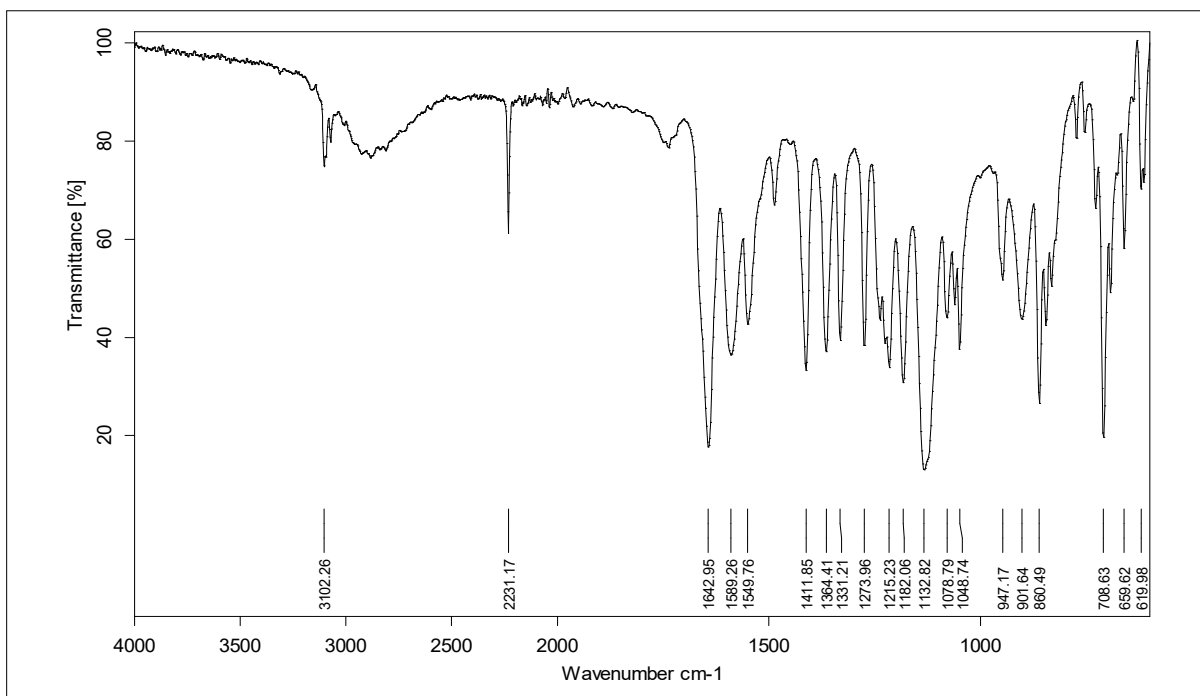
FT-IR (KBr) spectrum of **(1g)**



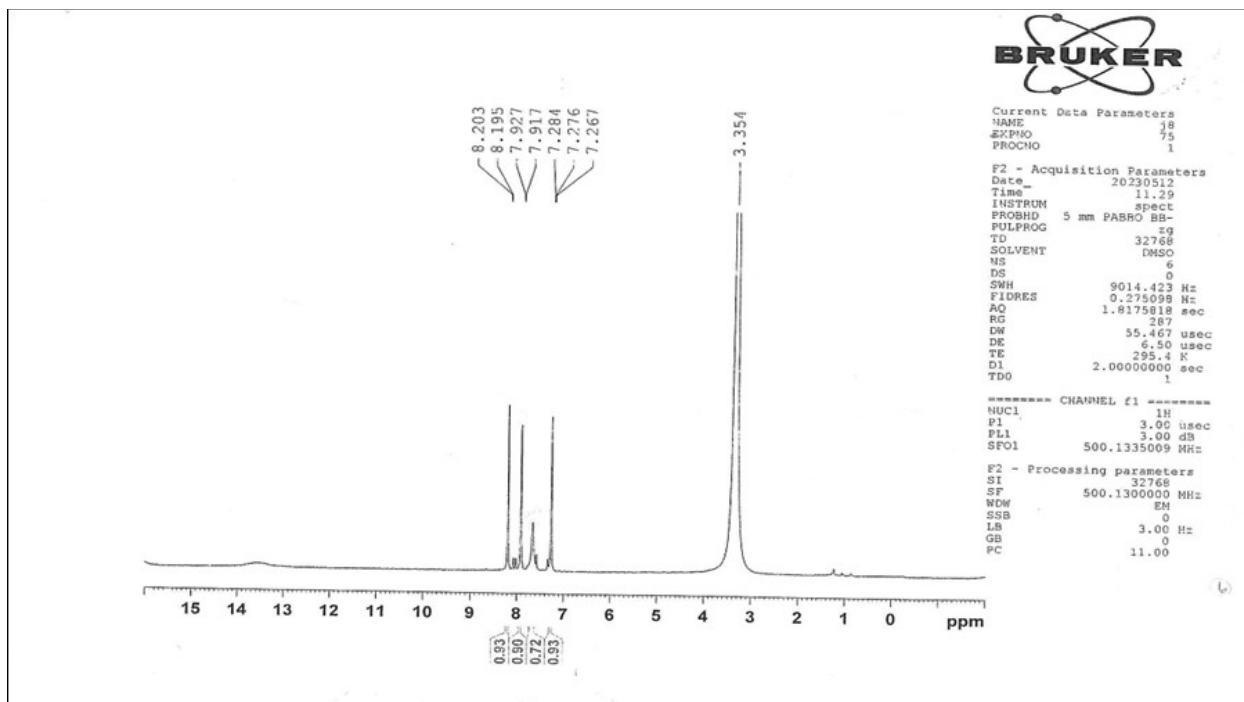
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1g**)



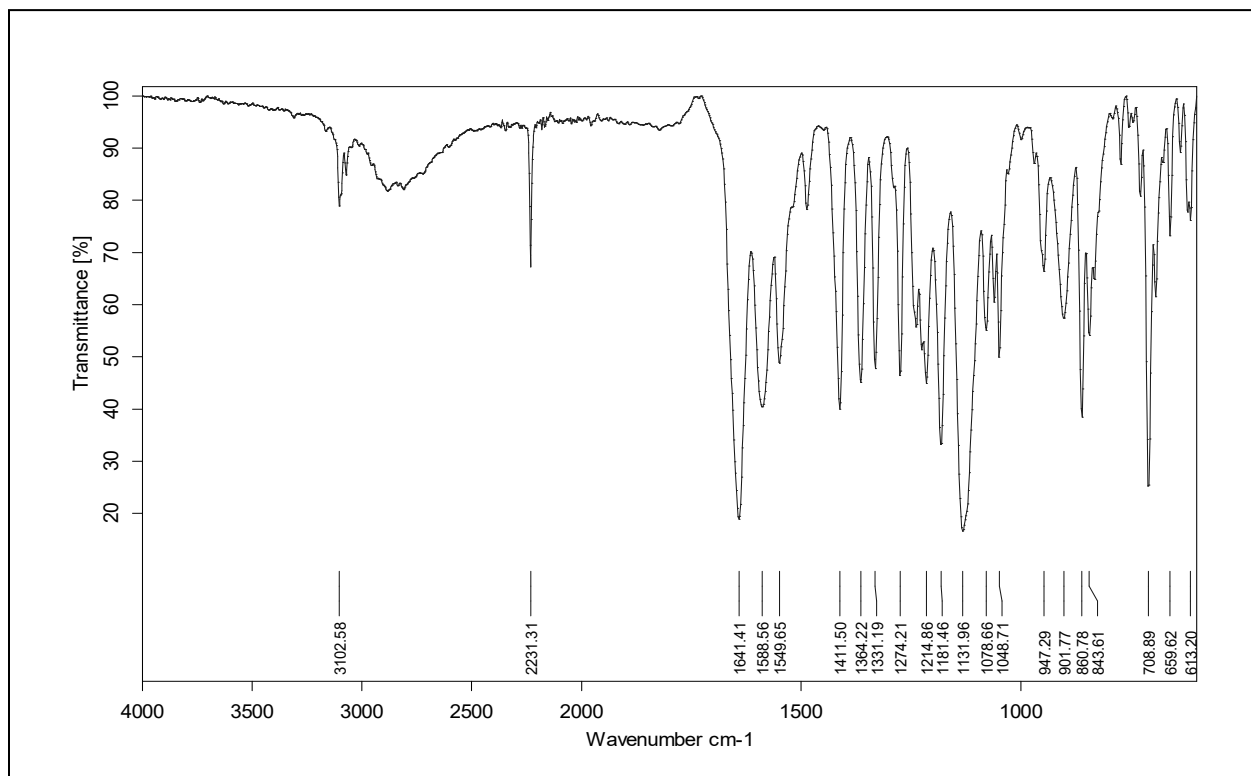
Expand of ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1g**)



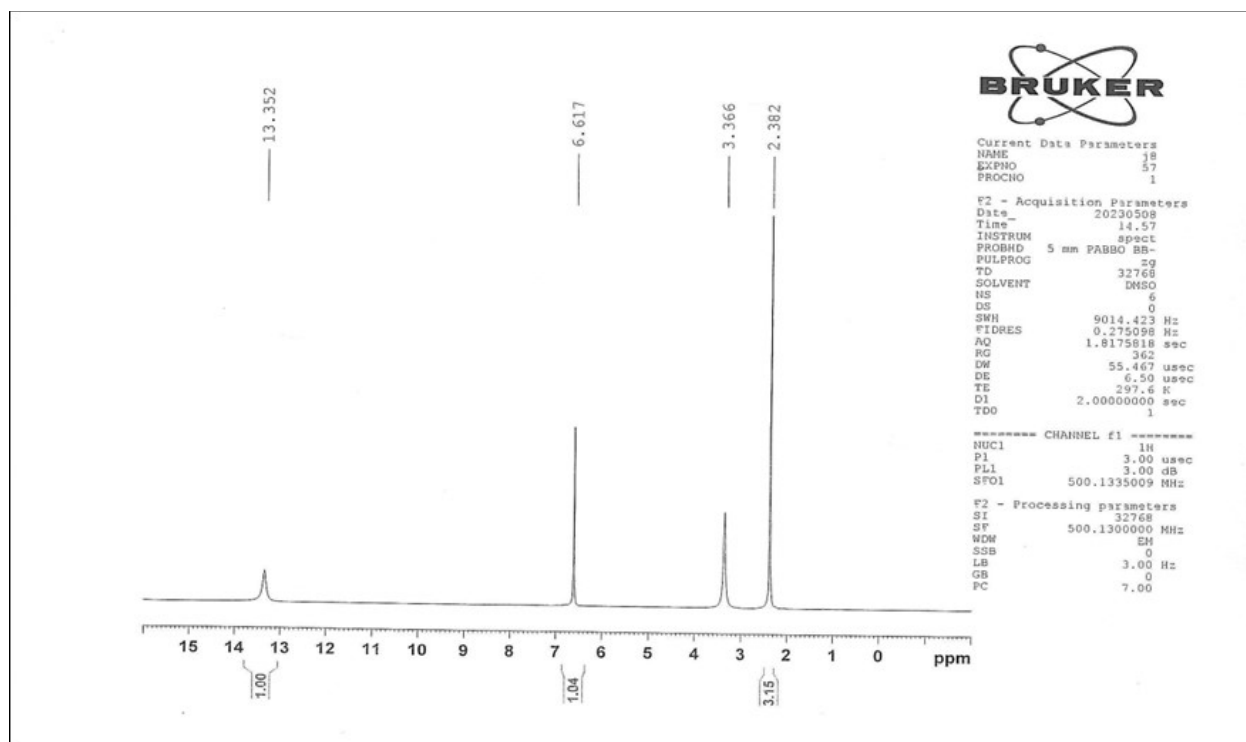
FT-IR (KBr) spectrum of (**1h**)



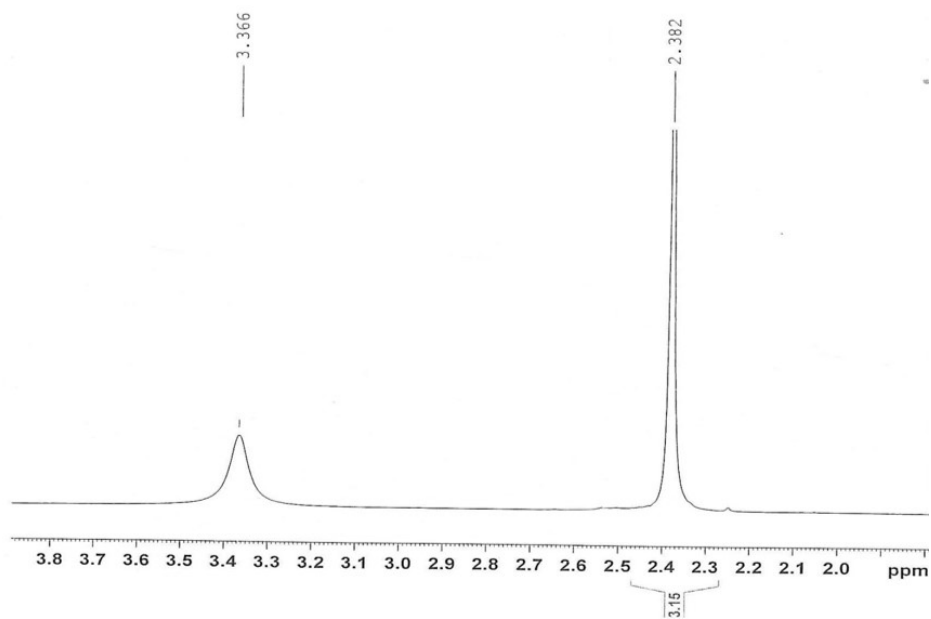
¹H NMR (500 MHz, DMSO-*d*₆) spectrum of (**1h**)



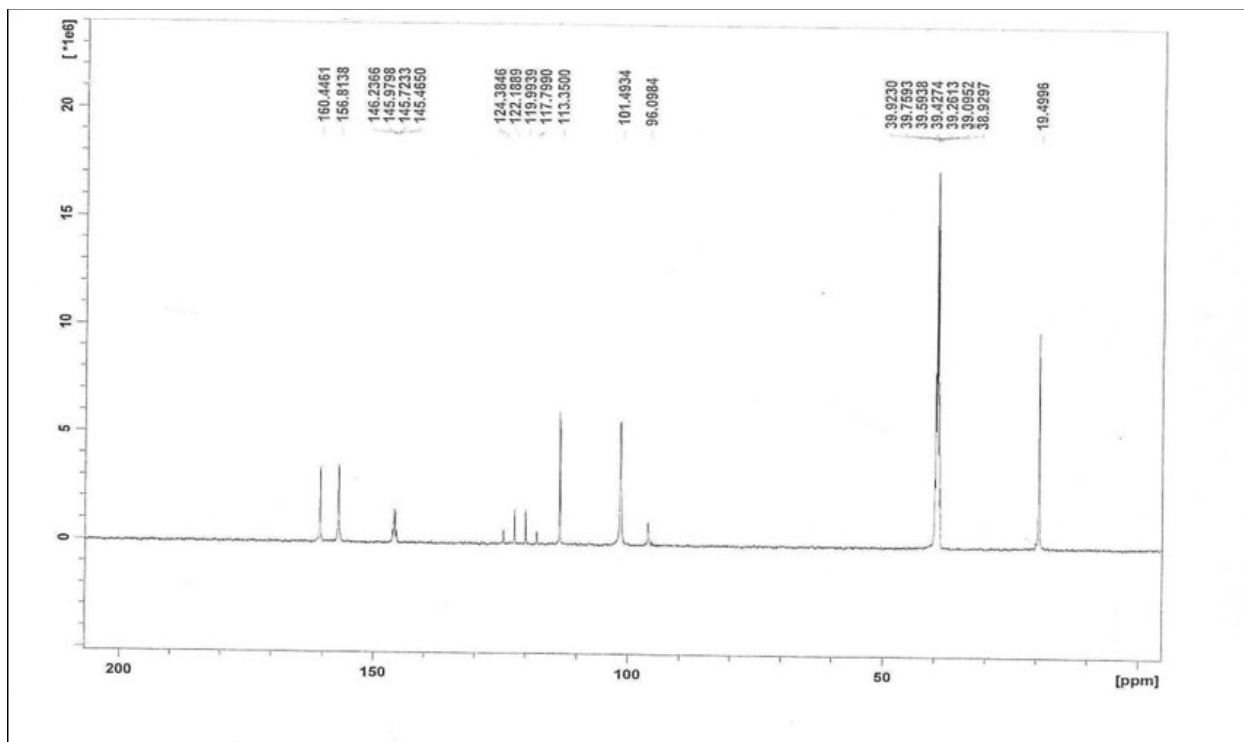
FT-IR (KBr) spectrum of (1i)



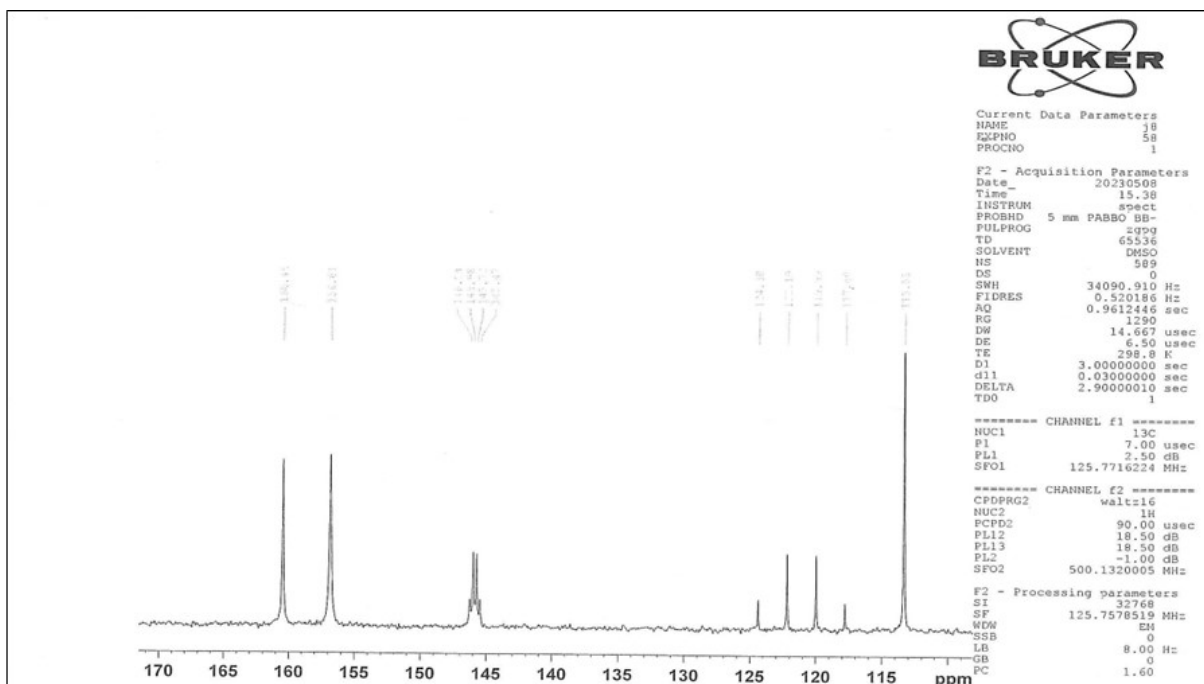
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1i**)



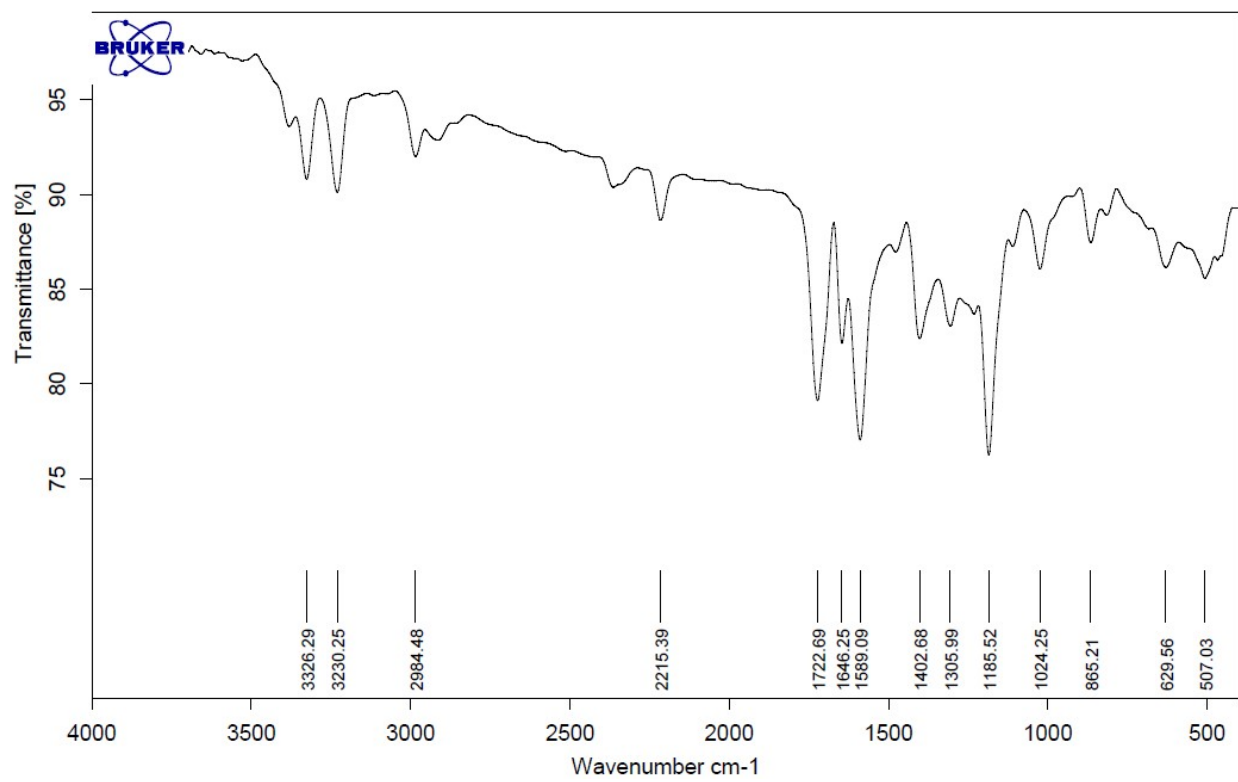
Expand of ^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectrum of (**1i**)



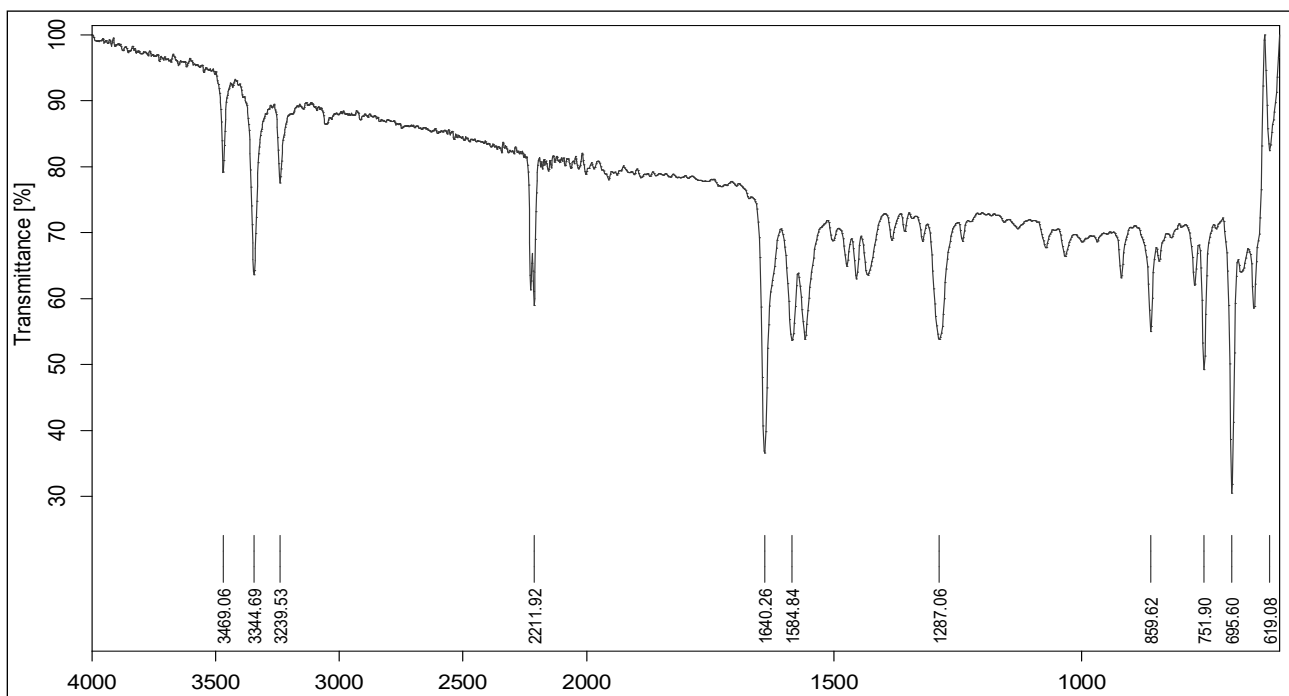
^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (**Ii**)



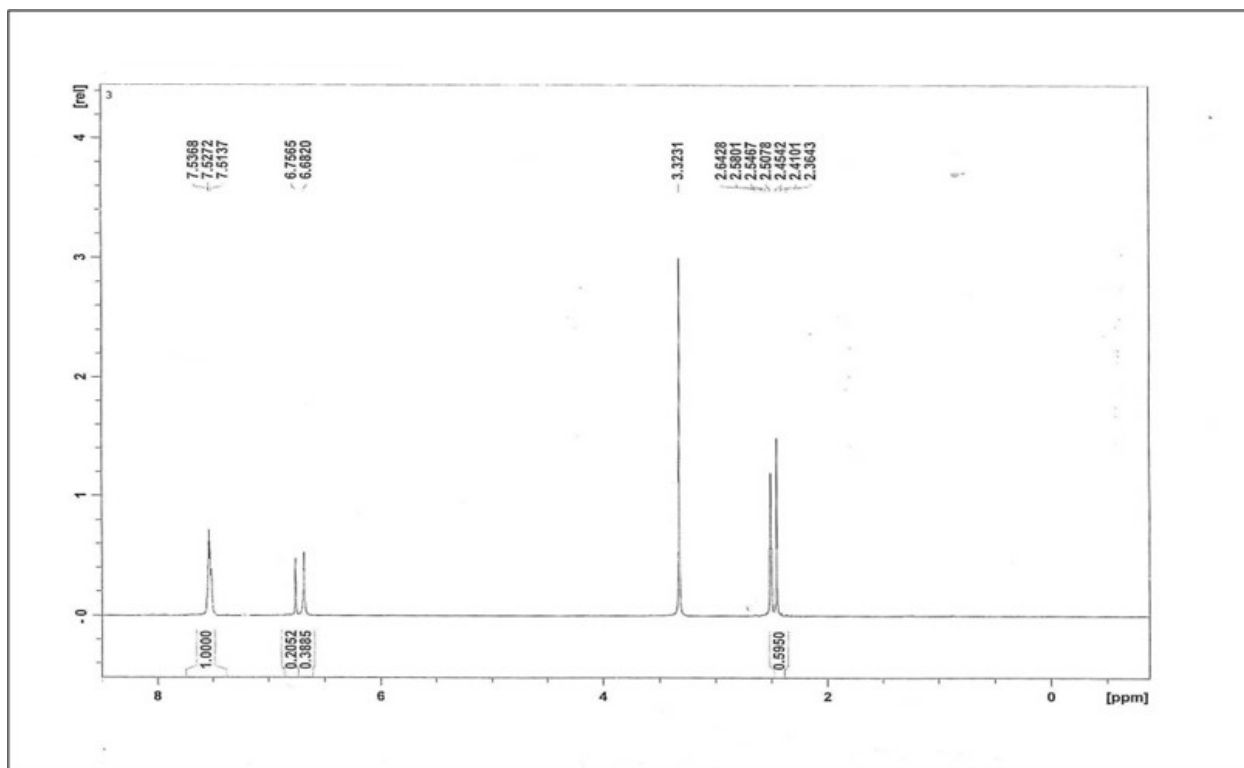
Expand of ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectrum of (**Ii**)



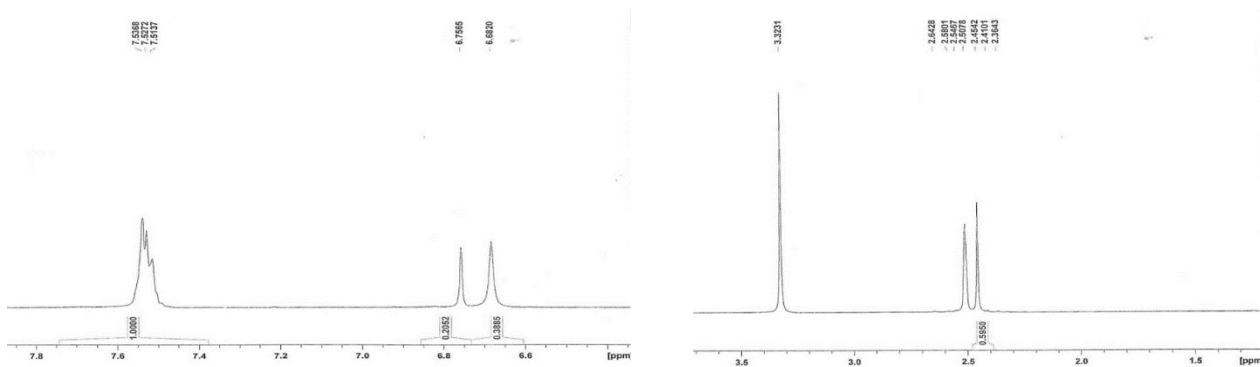
FT-IR (KBr) spectrum of (2a)



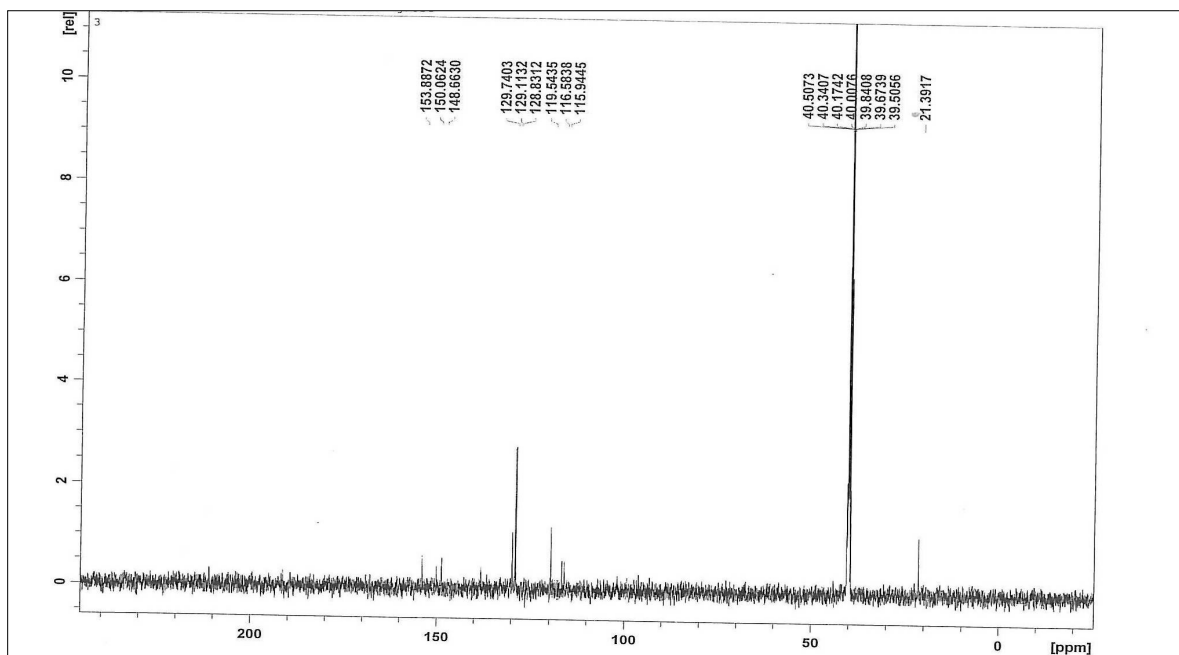
FT-IR (KBr) spectrum of **(2b)**



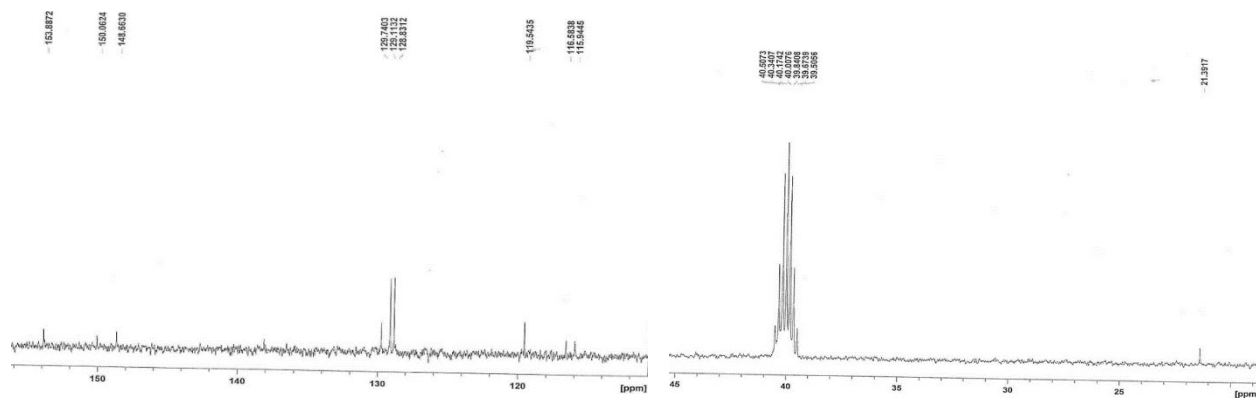
^1H NMR (500 MHz, $\text{DMSO}-d_6$) spectrum of (**2b**)



Expand of ^1H NMR (500 MHz, $\text{DMSO}-d_6$) spectrum of (**2b**)



¹³C NMR (125 MHz, DMSO-*d*₆) spectrum of **(2b)**



Expand of ¹³C NMR (125 MHz, DMSO-*d*₆) spectrum of **(2b)**