Supporting Information

Synthesis of novel bisazlactones and their applications in the synthesis of a new family of pseudo-peptide enamides with anti-cancer properties

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Experimental section

General. All chemicals and solvents were obtained from commercial sources and used as received. The ^{1}H and ^{13}C NMR spectra of products were recorded on a Bruker AMX 300 MHz spectrometers referenced to internal Me_4Si at 0.00 ppm. Reaction monitoring was carried out by thin-layer chromatography using TLC silica gel 60 F254 plates. High-resolution mass spectrum (HRMS) (ESI-TOF) was recorded using Waters LCT Premier XE mass spectrometer in the positive-ion mode an on a THERMO SCIENTIFIC Exactive instrument equipped with an APCI source in the positive-ion mode. IR spectra were recorded on a Perkin-Elmer Spectrum RXI FT-IR Spectrometer. Elemental analysis performed by a Perkin–Elmer 2004 (II) CHNS/O analyzer.

Procedure for synthesizing of 2,2'-(terephthaloylbis(azanediyl))diacetic acid (3)[1]:

A solution of terephethaloyl chloride 1 (5 gr, 24.62 mmol) in dioxane (30 mL) was added dropwise (approx. over 2 hour) to a stirred ice-cooled vessel containing glycine (4.99 g, 66.6 mmol) and MgO (3.5 g, 87.5 mmol) in 20 mL of water. After the addition of the acid chloride was completed, stirring was continued at ice-bath temperature for 30 minutes and finally at room temperature for further 30 minutes. Concentrated hydrochloric acid was then added dropwise to the reaction vessel until a pH of 1-2 was obtained. The insoluble 2,2'-(terephthaloylbis(azanediyl))diacetic acid **3** was collected by filtration and suspended in 100 mL of boiling water. The mixture was filtered, washed with water, and dried in a vacuum oven at 65 ℃ to give the pure product in 79 % yield.

General procedure for synthesis of bisazlactones 4a-l:

A mixture of diacid 3 (1 mmol), an aldehyde (3 mmol), acetic anhydride (5 mmol), and anhydrous NaOAc (1.5 mmol) was refluxed for 1h. The reaction color turned in to yellow during reflux. The reaction mixture was cooled and kept in the fridge for overnight. The yellow solid was filtered and washed well with distilled water to eliminate acetic anhydride and sodium acetate. Recrystallization in large volume of ethyl acetate afforded the pure products.

General procedure for the synthesis of pseudo-peptide enamides 6a-r

Bisazlactone (0.25 mmol) and a primary amine (1 mmol) were refluxed in ethanol (3 mL) for 2 h. The reaction mixture was cooled to room temperature and the solid was collected by filtration to afford the crude product. Purification was carried out by recrystallization in ethanol.

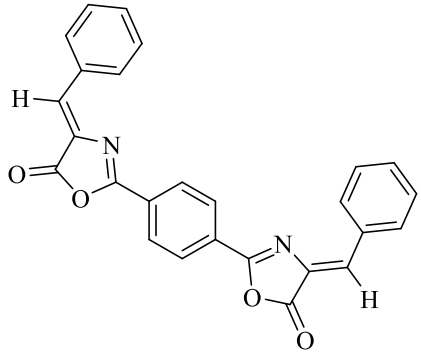
General procedure for the synthesis of pseudo-peptide enamides 6s-6ab

Bisazlactone (0.25 mmol) and a secondary amine or primary aromatic amine (1 mmol) were refluxed in toluene (3 mL) for 2 h. The reaction mixture was cooled to room temperature and the solid was collected by filtration to afford the crude product. Purification was carried out by recrystallization in ethanol.

Cell toxicity test

The MTT assay was used to assess the cytotoxicity of the synthesized compounds on Human Dermal Fibroblasts (HDF) cell line, representing healthy cells, and hepatocellular carcinoma (HEPG2) cell line, representing cancer cell line. HEPG2 and HDF cell lines (1×10^5/well) were cultured overnight in medium (Gibco, Germany) supplemented with 10% fetal bovine serum (FBS), 1% penicillin-streptomycin, and 0.1% amphotericin B at 37°C in a 5% CO2 environment in 96-well culture plates. We evaluated all generated compounds on the cells after a 24-hour incubation period. Subsequently, 10 µl of the MTT solution at a concentration of 5 mg/ml in PBS was added to each well, achieving a final concentration of 0.05 percent. The supernatant was obtained after 3–4 hours, and the formazan crystals were dissolved by adding 50 µl of dimethyl sulfoxide to each well. Next, we gently stirred the microplates in darkness for 4 hours before measuring them using a Stat FAX303 plate reader at a wavelength of 590 nm.[2]

1. Kleinspehn, G. G., A Novel Route to Certain 2-Pyrrolecarboxylic Esters and Nitriles, *J. Am. Chem. Soc.* **1955**, *77*, 1546-1548.
2. Tondro, G.; Mohammadi, A.; Rajabzadeh, G.; Moradi, H. R.; Negah, S. S. Niosomal Curcumin Inhibited Gliomagenesis-Related Markers in U87 Cell Line. Research square, 2023, https://doi.org/10.21203/rs.3.rs-2817911/v1



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-benzylidene)oxazol-5(4H)-one) (**4a):** Yellow powder (yield 81%); mp 217-220 ℃; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.35 (s, 4H), 8.26-8.23 (m, 4H),7.54-7.51 (m, 6H), 7.36 (s, 2H) ppm; IR (KBr) ν 1791, 1771, 1651, 1319, 1293, 1171, 980, 862, 853 cm^{-1}; EI-MS m/z (%) 420.2 (M^{+}], 276.1 (100), 132.0, 104.1, 76.1; Anal. calcd for $C_{26}H_{16}N_2O_4$: C, 74.28; H, 3.84; N, 6.66. Found: C, 73.86; H, 3.63; N, 6.84.

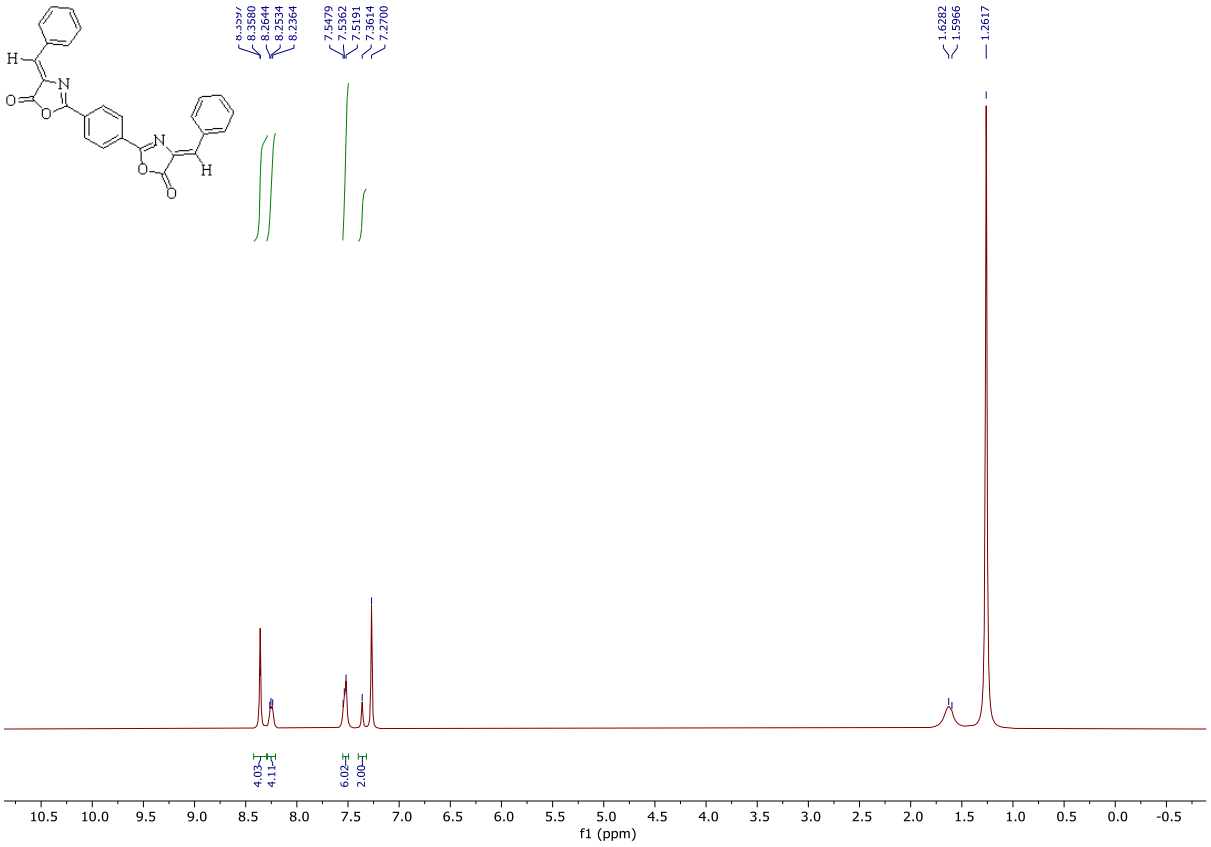


Figure 1. ^{1}H NMR spectra for **4a**

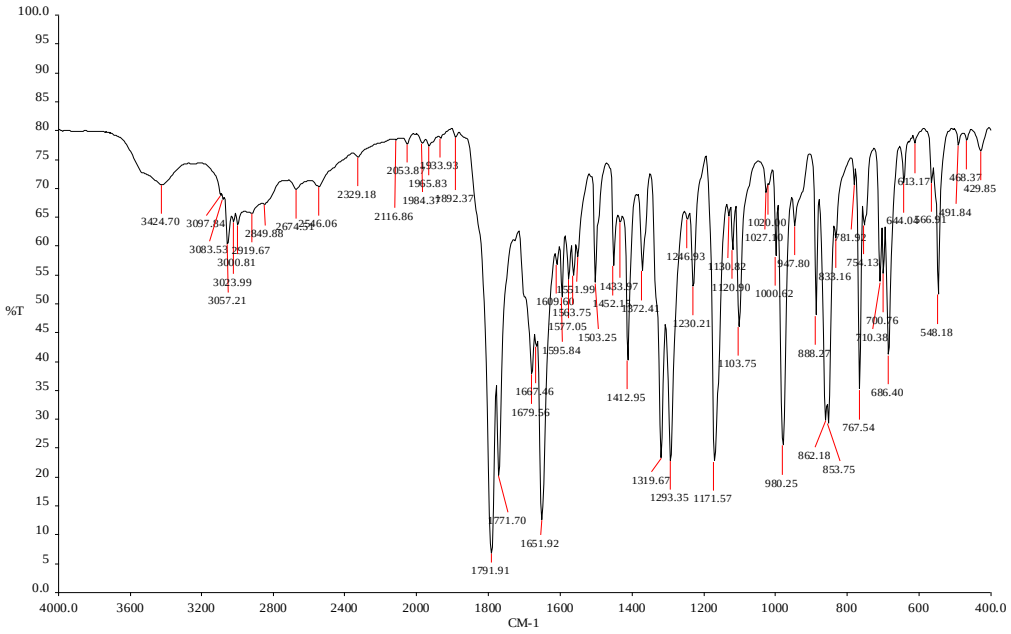


Figure 2. IR spectra for **4a**

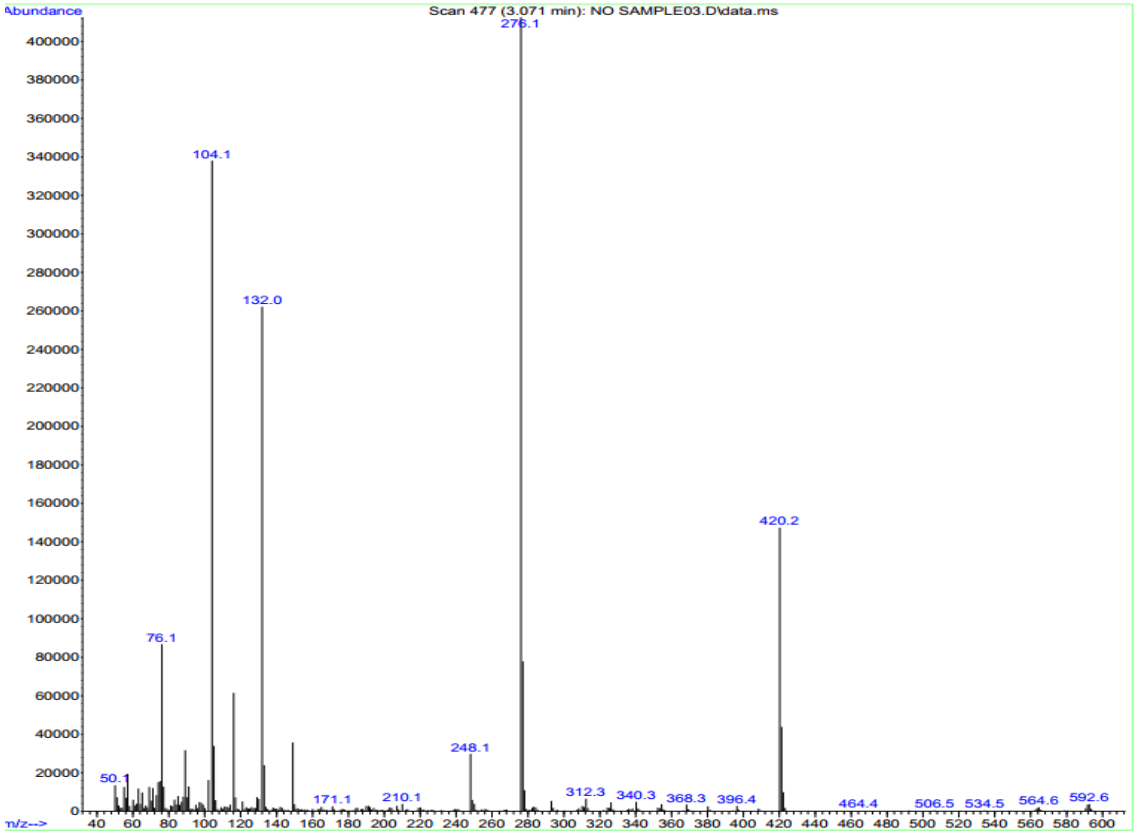
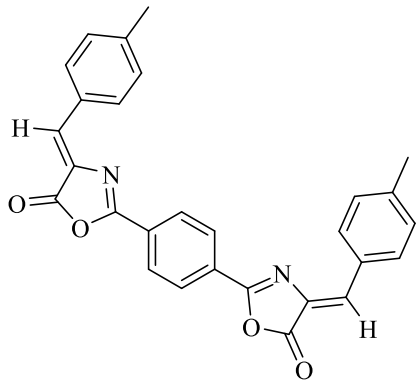


Figure 3. Mass spectra for **4a**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-4-methylbenzylidene)oxazol-5(4H)-one) (**4b):** Yellow powder (yield 80%); mp 303-305 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.22-8.20 (s, 4H), 8.15-8.12 (m, 4H), 7.38 (m, 4H), 7.35 (s, 2H), 2.38 (s, 6H) ppm; IR (KBr) ν 1795, 1772, 1653, 1604, 1318, 1294, 1166, 982, 890, 697 cm^{-1}; EI-MS m/z (%): 448.2 [M^{+}], 307.1, 149.1 (100), 121.1, 65.1; Anal. calcd for $C_{28}H_{20}N_2O_4$: C, 74.99; H, 4.50; N, 6.25. Found: C, 74.72; H, 4.30; N, 5.84.

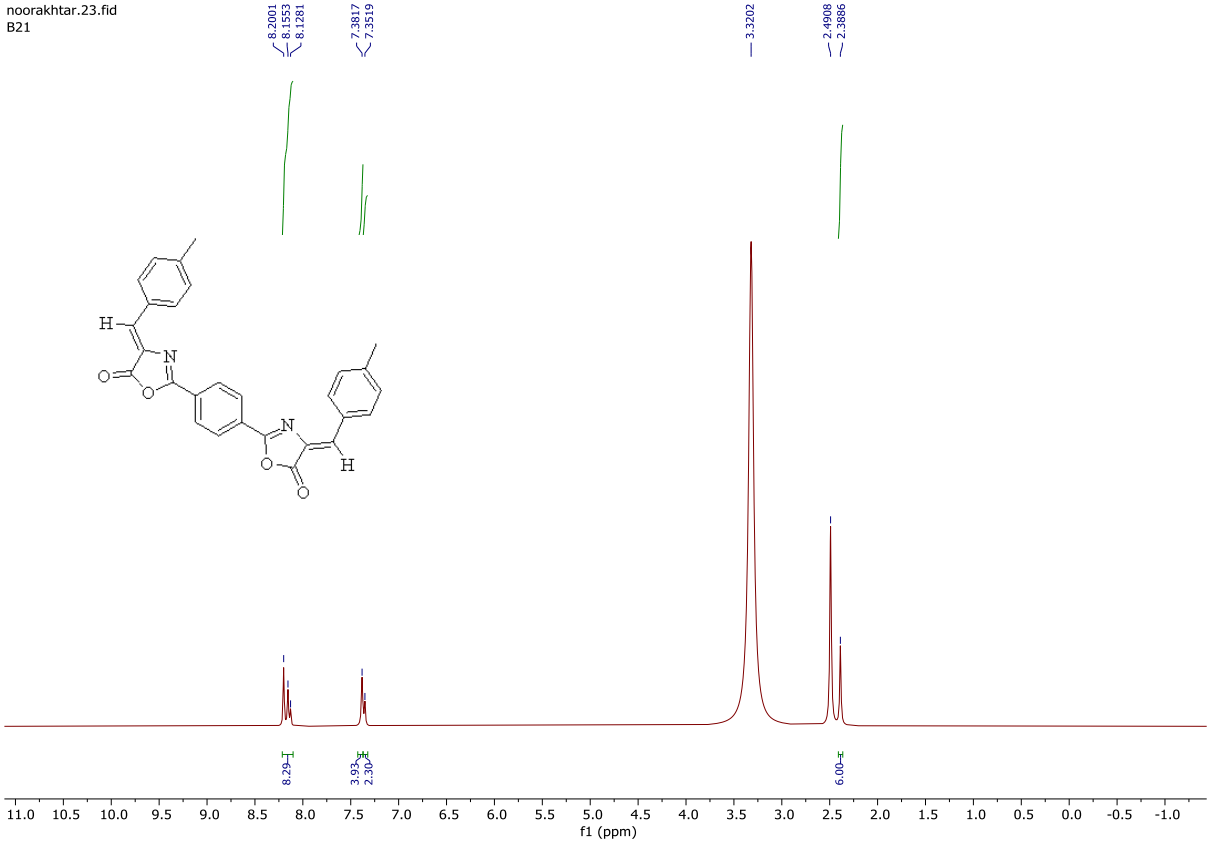


Figure 4. ^{1}H NMR spectra for **4b**

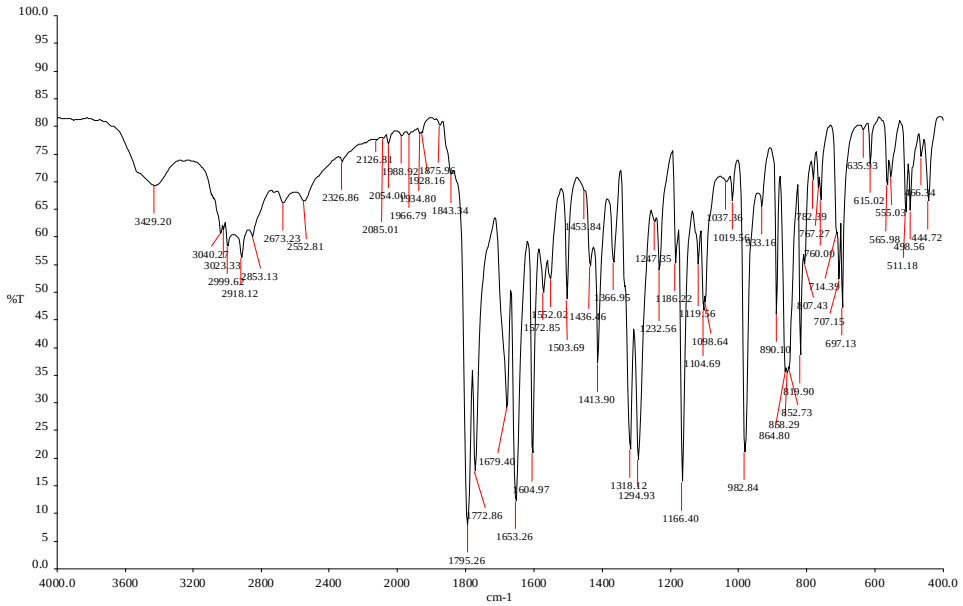


Figure 5. IR spectra for **4b**

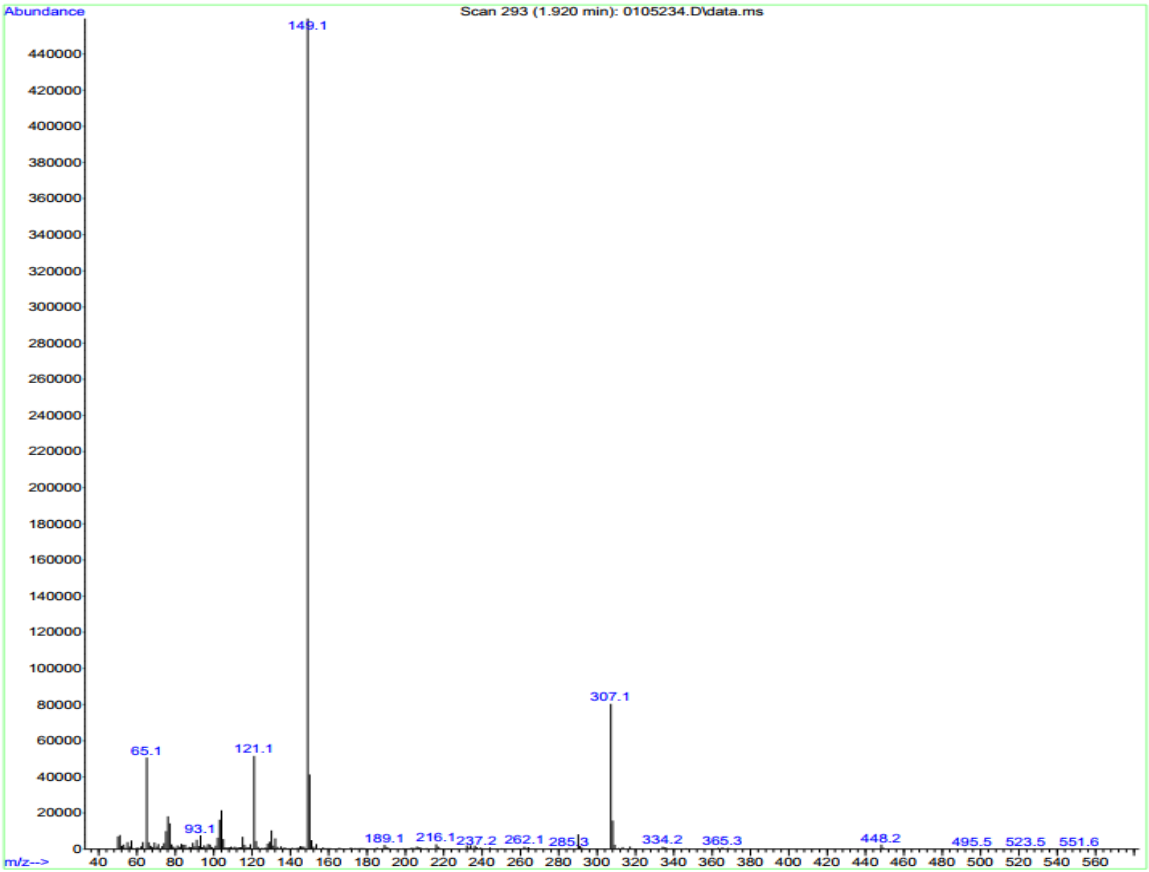
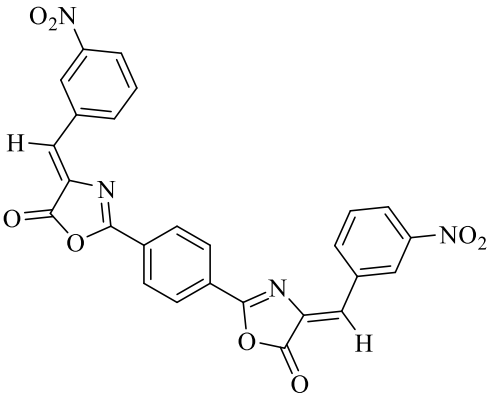


Figure 6. Mass spectra for **4b**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-3-nitrobenzylidene)oxazol-5(4H)-one) **(4c):** light yellow powder (yield 58%); mp 307-309 °C; ^{1}H NMR (300 MHz, DMSO-d_6)) δ 9.18 (s, 2H), 8.75 (d, J = 7.6 Hz, 2H), 8.31 (d, J = 8.2 Hz, 2H), 8.18-8.14 (m, 4H), 7.84 (t, J = 7.9 Hz, 2H), 7.60 (s, 2H) ppm; IR (KBr) ν 1810, 1660, 1536, 1408, 1347, 1129, 983, 858, 821, 624 cm^{-1}; Anal. calcd for $C_{26}H_{14}N_4O_8$: C, 61.18; H, 2.76; N, 10.98. Found: C, 60.82; H, 2.61; N, 10.52.

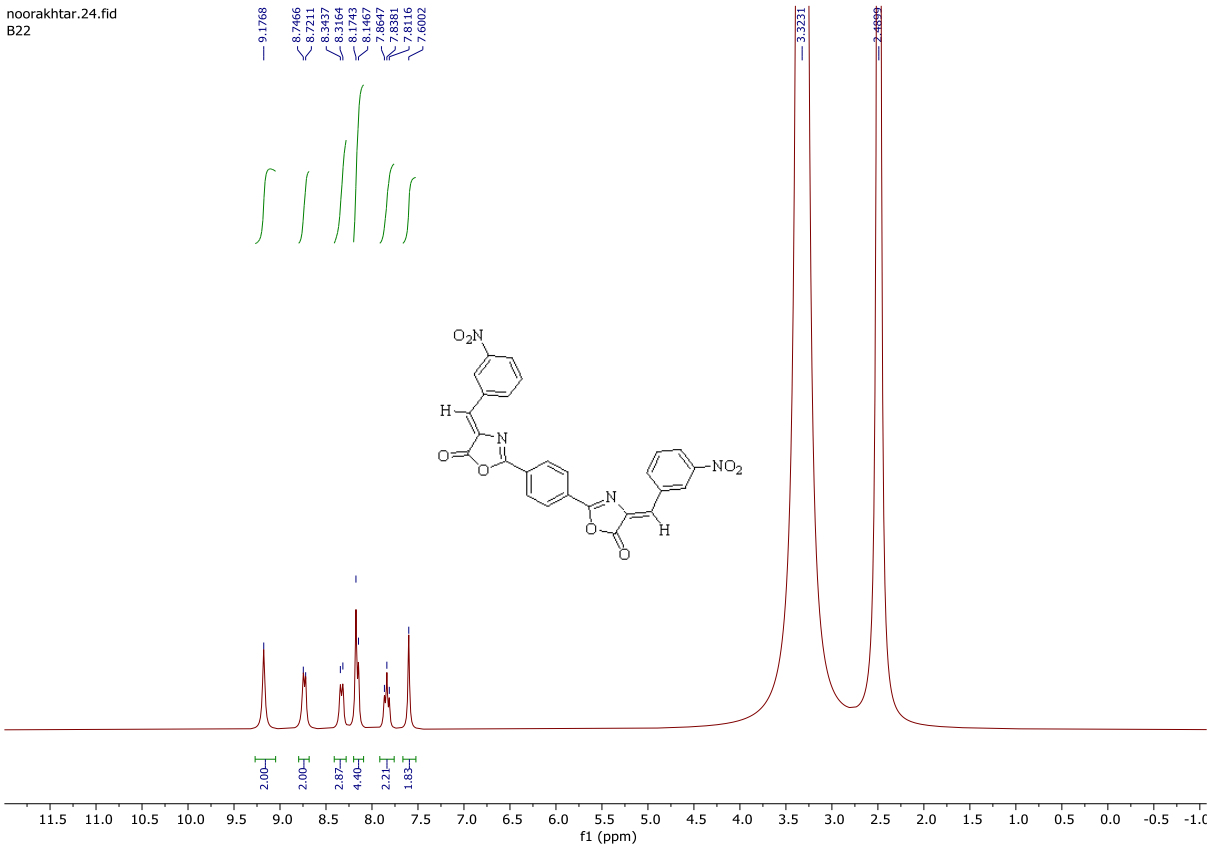


Figure 7. ^{1}H NMR spectra for **4c**

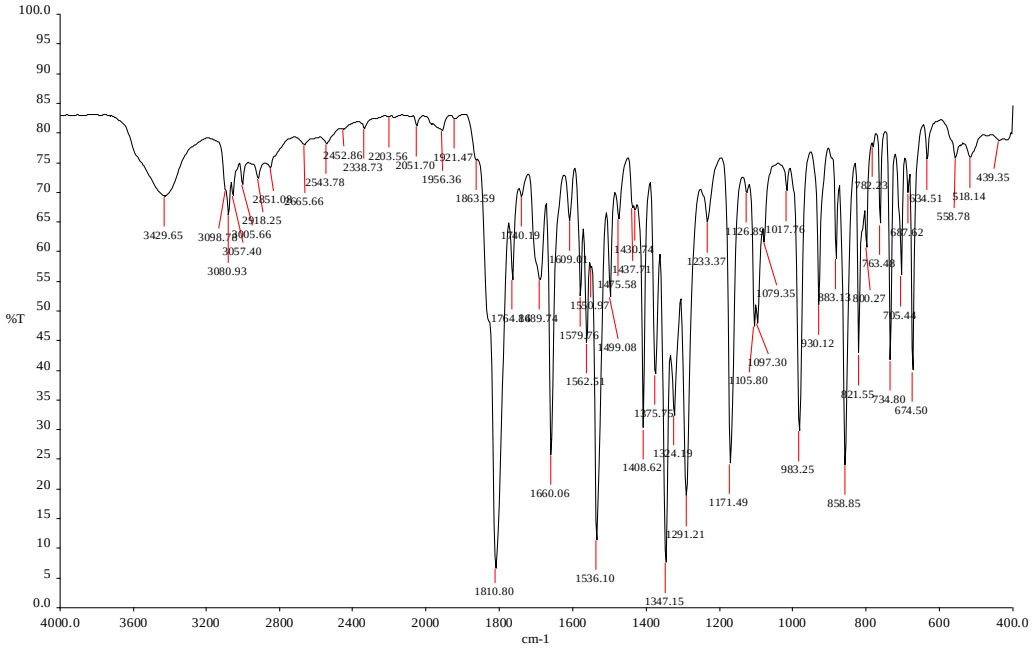
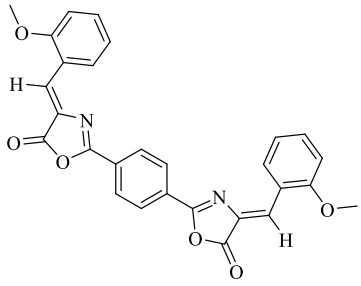


Figure 8. IR spectra for **4c**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-2-methoxybenzylidene)oxazol-5(4H)-one) **(4d):** Yellow powder (yield 83%); mp 303-305 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.75 (d, J = 7.6 Hz, 2H), 8.22-8.12 (m, 4H), 7.63 (s, 2H), 7.53 (t, J = 7.8 Hz, 2H), 7.17-7.12 (m, 4H), 3.92 (s, 6H) ppm; IR (KBr) ν 1790, 1772, 1649, 1484, 1293, 1249, 977, 857, 762, 707 cm^{-1}; HRMS (ESI^{+}) calcd for $C_{28}H_{21}N_2O_6$ 481.1400 $[M+H]^{+}$; found: 481.1418; Anal. calcd for $C_{28}H_{20}N_2O_6$: C, 69.99; H, 4.20; N, 5.83. Found: C, 69.87; H, 3.80; N, 5.46.

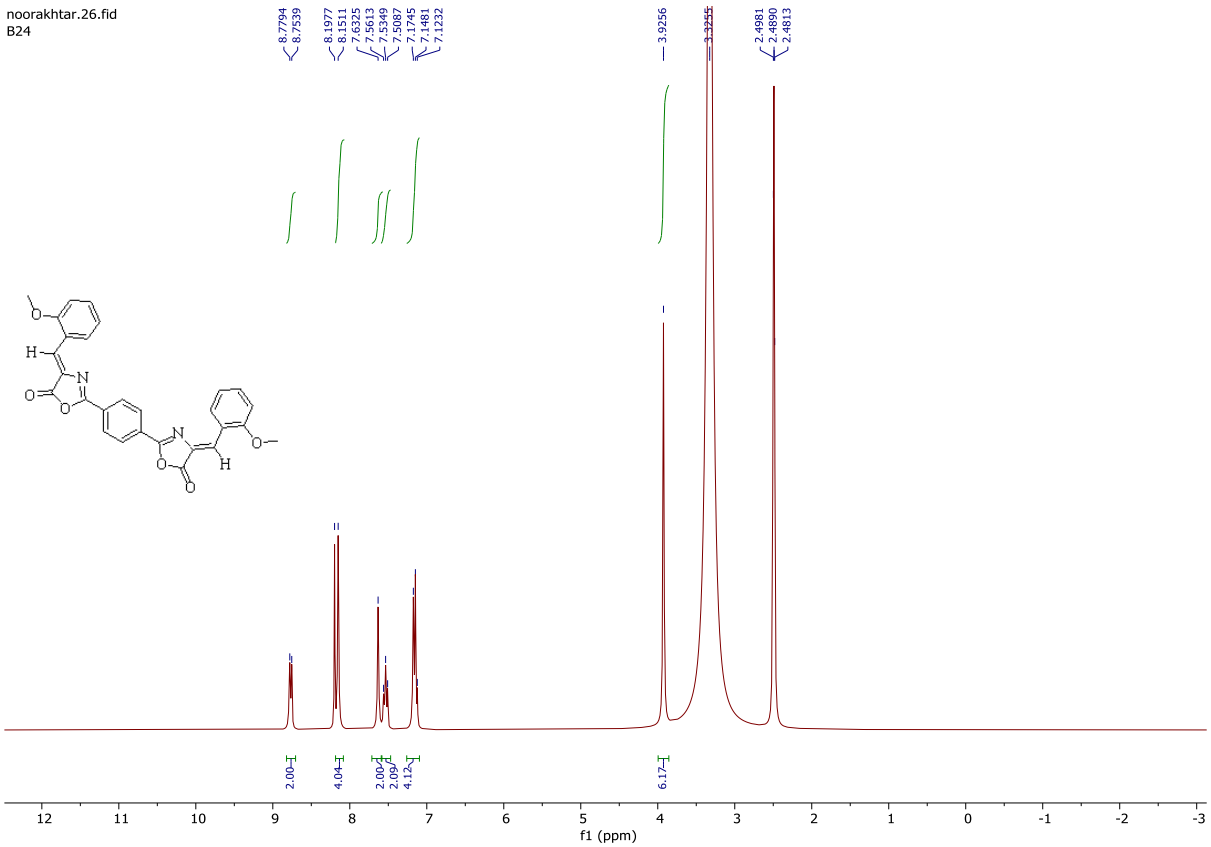


Figure 9. ^{1}H NMR spectra for **4d**

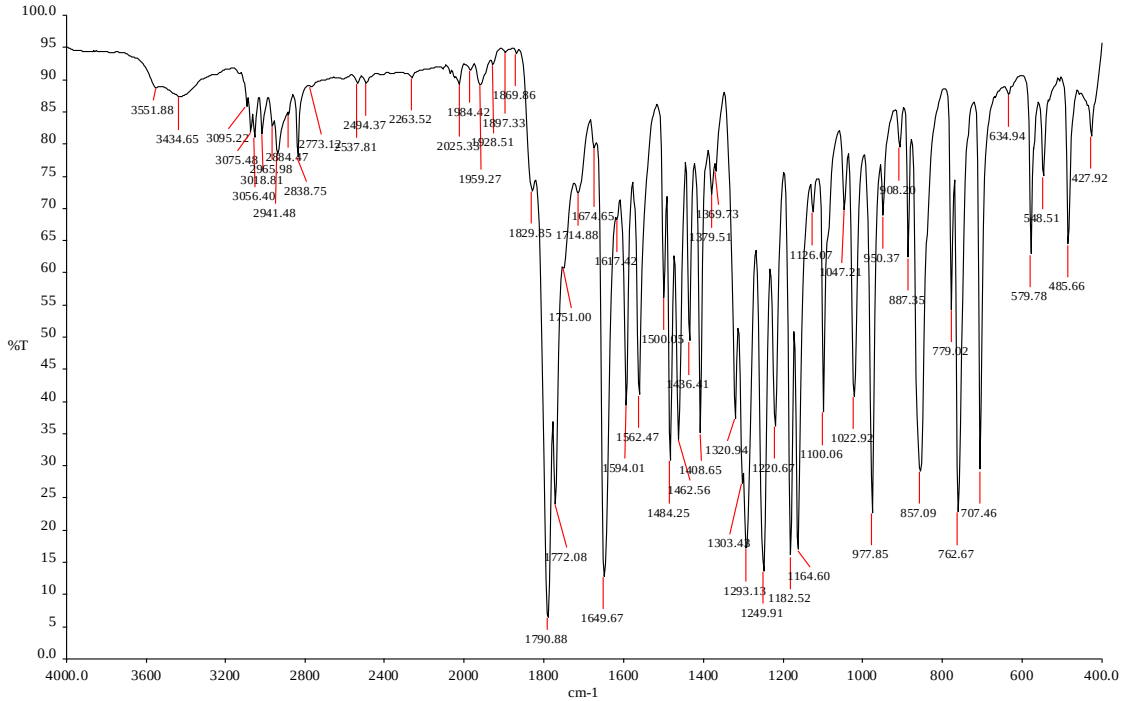


Figure 10. IR spectra for **4d**

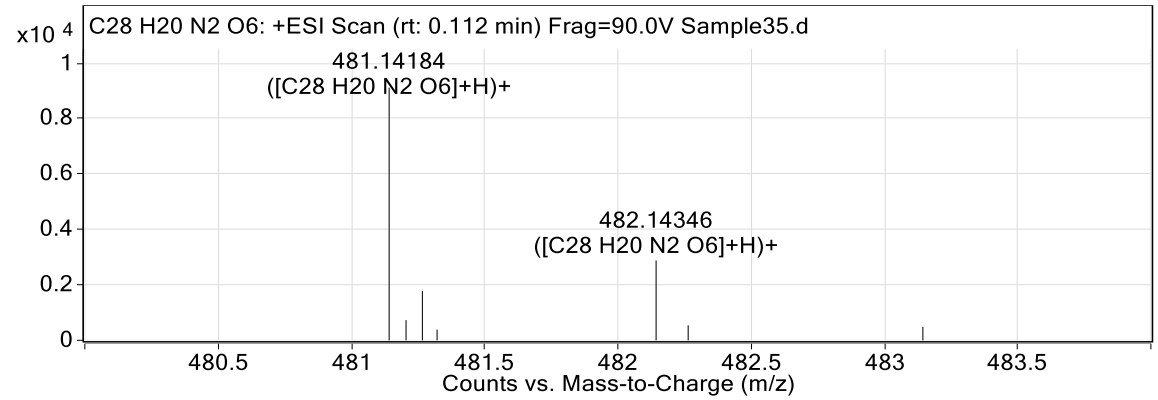
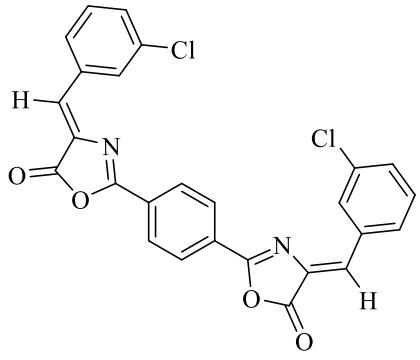


Figure 11. HRMS spectra for **4d**

s



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-3-chlorobenzylidene)oxazol-5(4H)-one) **(4e):** yellow powder (yield 61%); mp 264-266 ℃; We couldn't get suitable ^{1}H NMR spectra for this compound due to the low solubility in NMR solvents; IR (KBr) *v* 1802, 1649, 1573, 1501, 1410, 979, 847, 778, 704, 675 cm^{-1}; EI-MS m/z (%): 488.1 [M^{+}], 310.1 (100), 282.1, 132.1, 104.1, 76.1; Anal. calcd for $C_{26}H_{14}Cl_2N_2O_4$: C, 63.82; H, 2.88; N, 5.73. Found: C, 63.48; H, 2.53; N, 5.98.

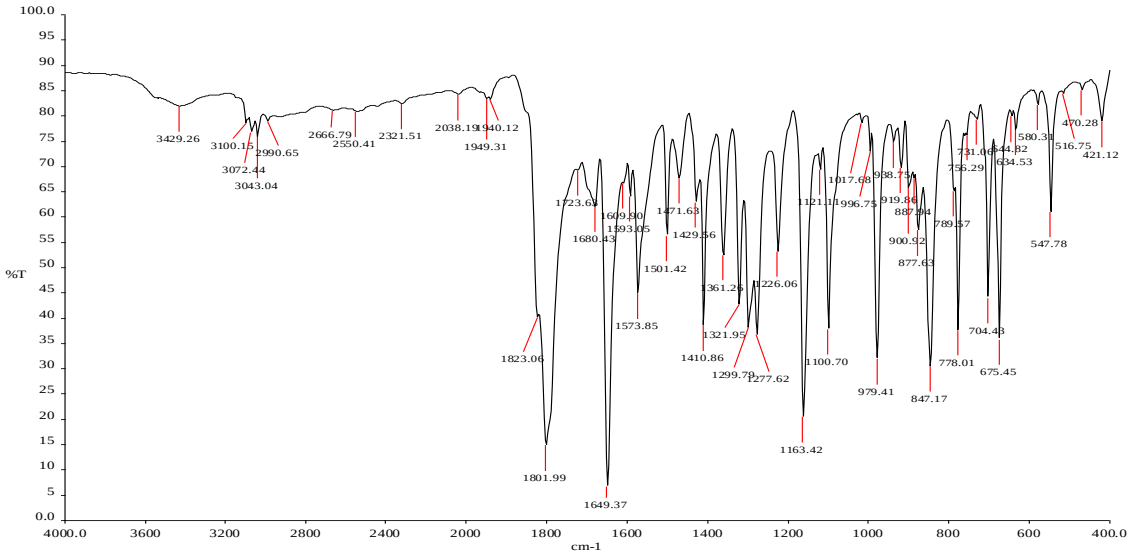


Figure 12. IR spectra for **4e**

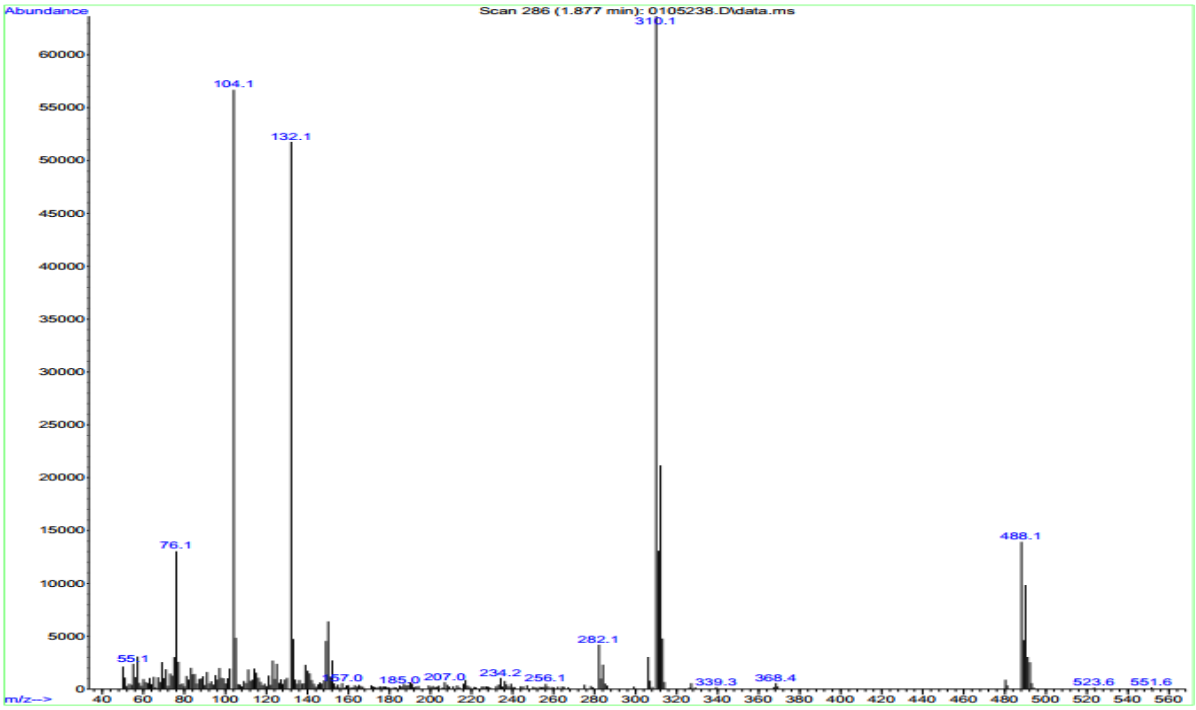


Figure 13. Mass spectra for **4e**

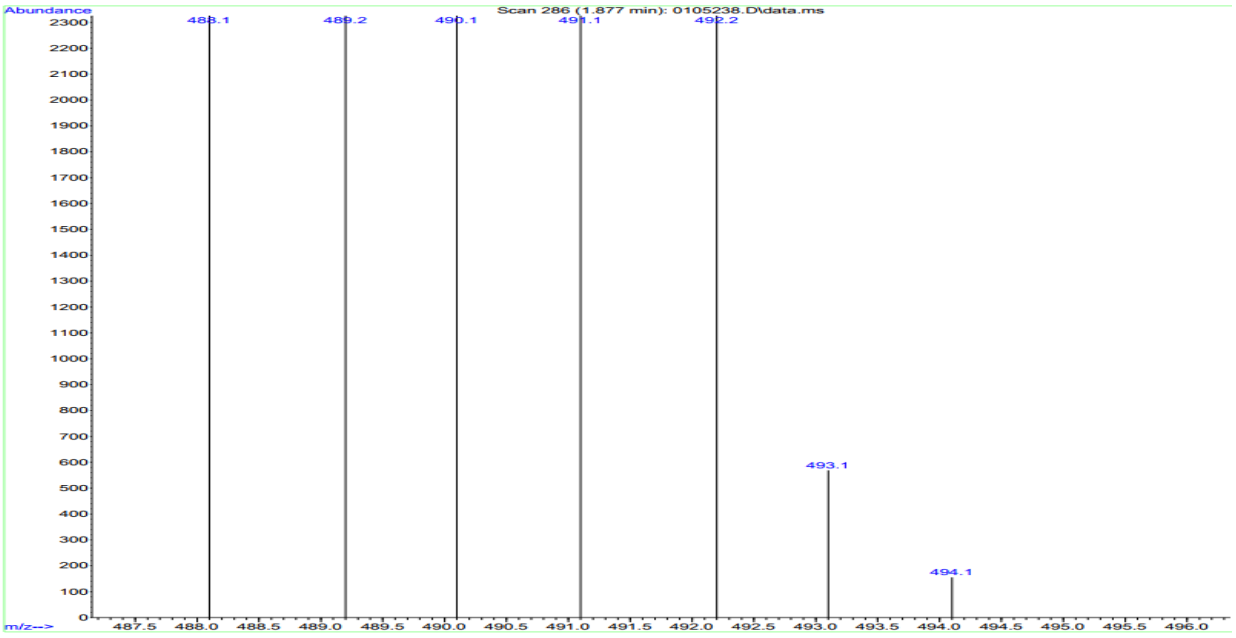
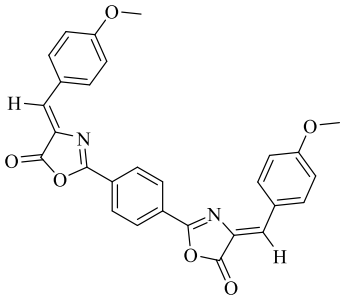


Figure 14. Expanded mass spectra for **4e**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-4-methoxybenzylidene)oxazol-5(4H)-one) **(4f):** Orange powder (yield 85%); mp 306-308 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.34-8.31 (m, 8H), 7.41 (s, 2H), 7.14-7.10 (d, J = 8.6 Hz, 4H), 3.87 (s, 6H) ppm; IR (KBr) v 1787, 1767, 1650, 1598, 1509, 1315, 1291, 1304, 1259, 978, 886,857, 830, 706, 527 cm^{-1}; EI-MS m/z (%): 480.2 [M^{+}], 368.4, 306.1, 234.1, 149.1 (100), 104.1, 83.1, 57.1; Anal. calcd for $C_{28}H_{20}N_2O_6$: C, 69.99; H, 4.20; N, 5.83. Found: C, 69.75; H, 3.86; N, 5.40.

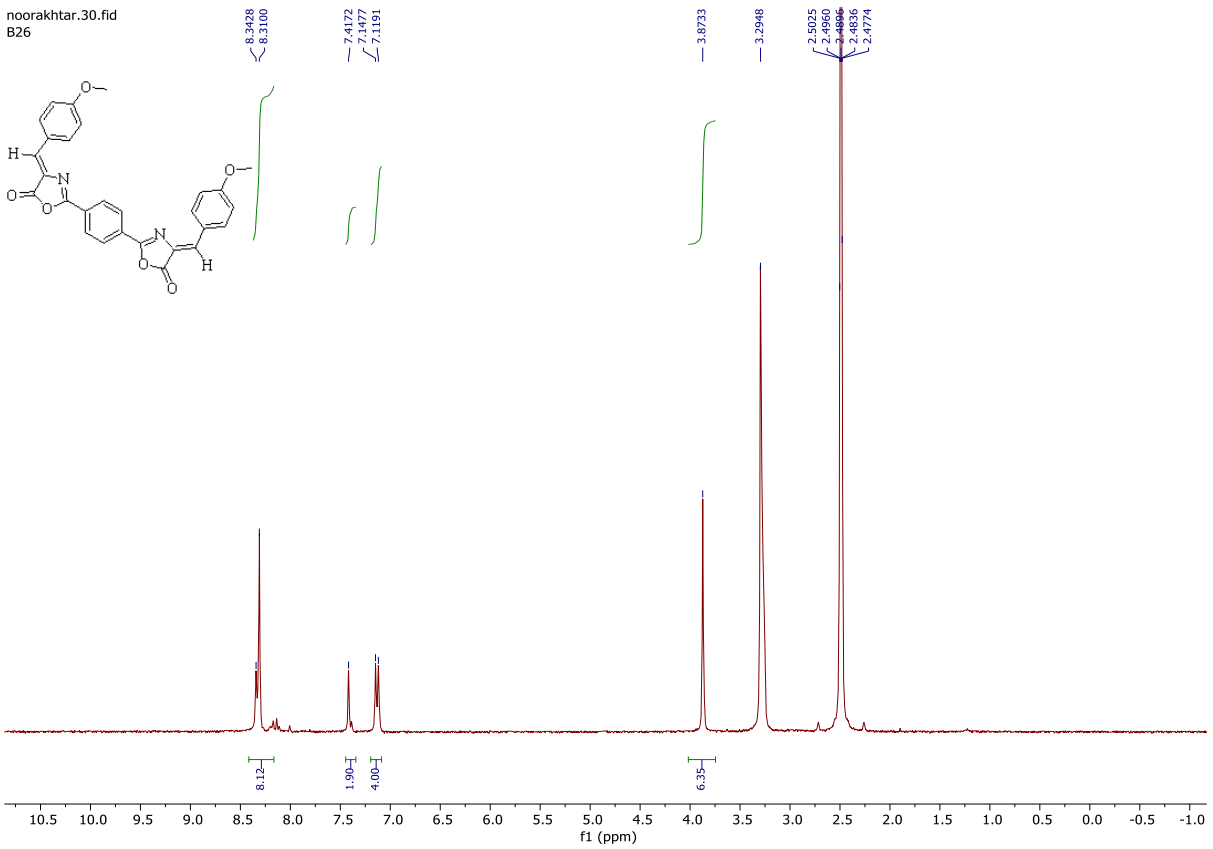


Figure 15. ^{13}H NMR spectra for **4f**

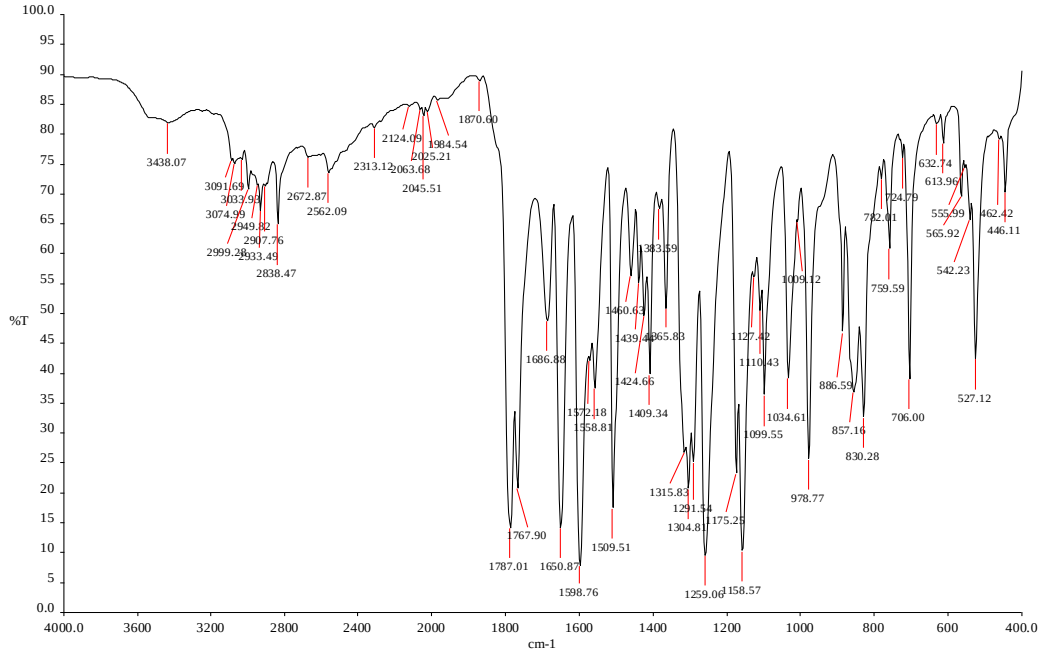


Figure 16. IR spectra for **4f**

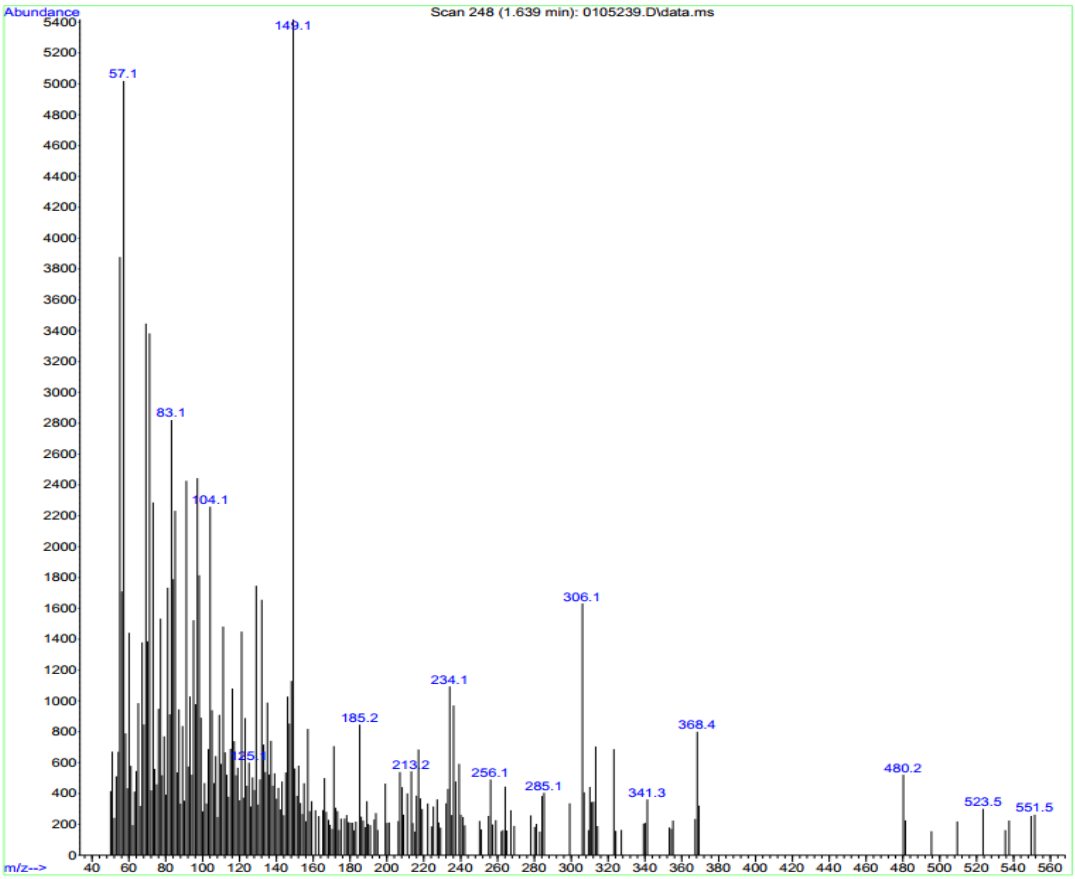
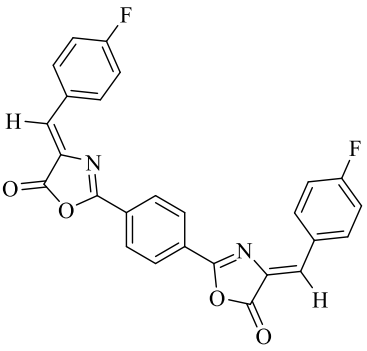


Figure 17. Mass spectra for **4f**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-4-fluorobenzylidene)oxazol-5(4H)-one) **(4g)**: Yellow powder (yield 70%); mp 280-282 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.43-8.40 (m, 4H), 8.16-8.13 (m, 4H), 7.45-7.37 (m, 6H) ppm; IR (KBr) ν 1793, 1766, 1659, 1599, 1504, 1291, 1239, 1157, 977, 855, 829, 698, 511, 504, 463, 411 cm^{-1}; HRMS (ESI) calcd for $C_{26}H_{14}F_2N_2O_4$: 456.09 $[M+H]^+$; 457.1000; found 457.0999; Anal. calcd for $C_{26}H_{14}F_2N_2O_4$: C, 68.42; H, 3.09; N, 6.14. Found: C, 68.20; H, 2.74; N, 5.80.

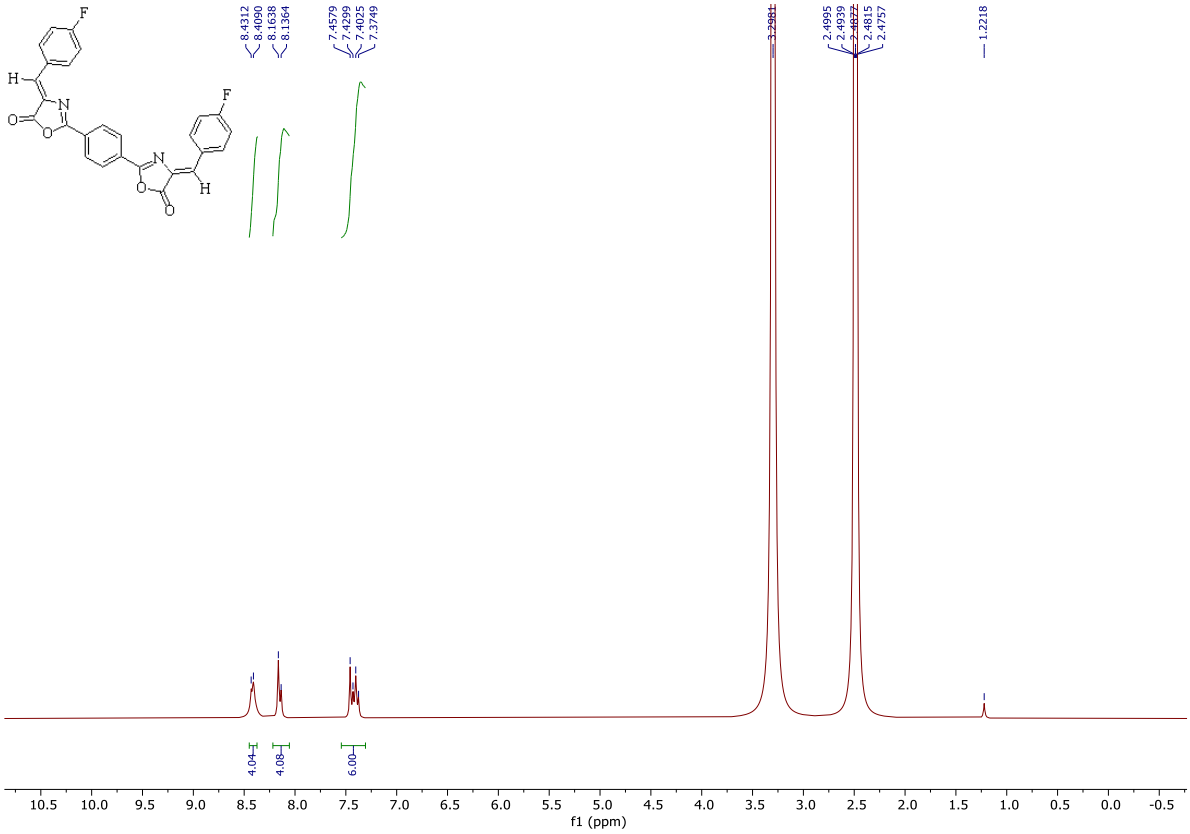


Figure 18. ^{1}H NMR spectra for **4g**

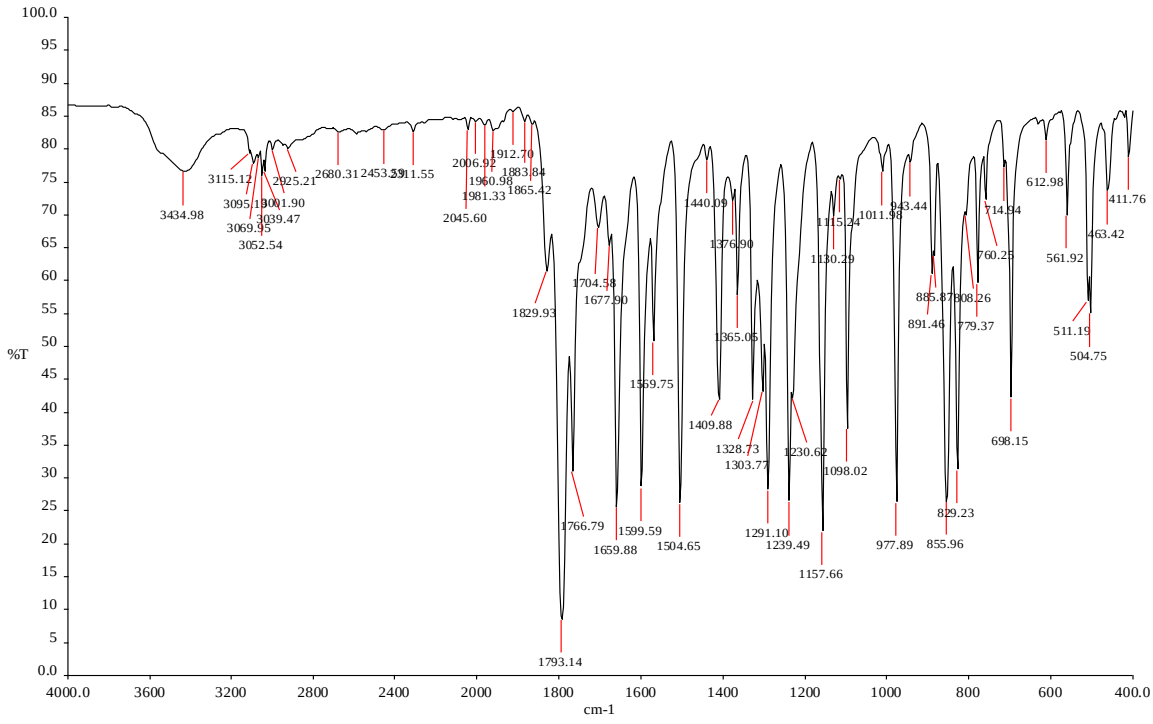


Figure 19. IR spectra for **4g**

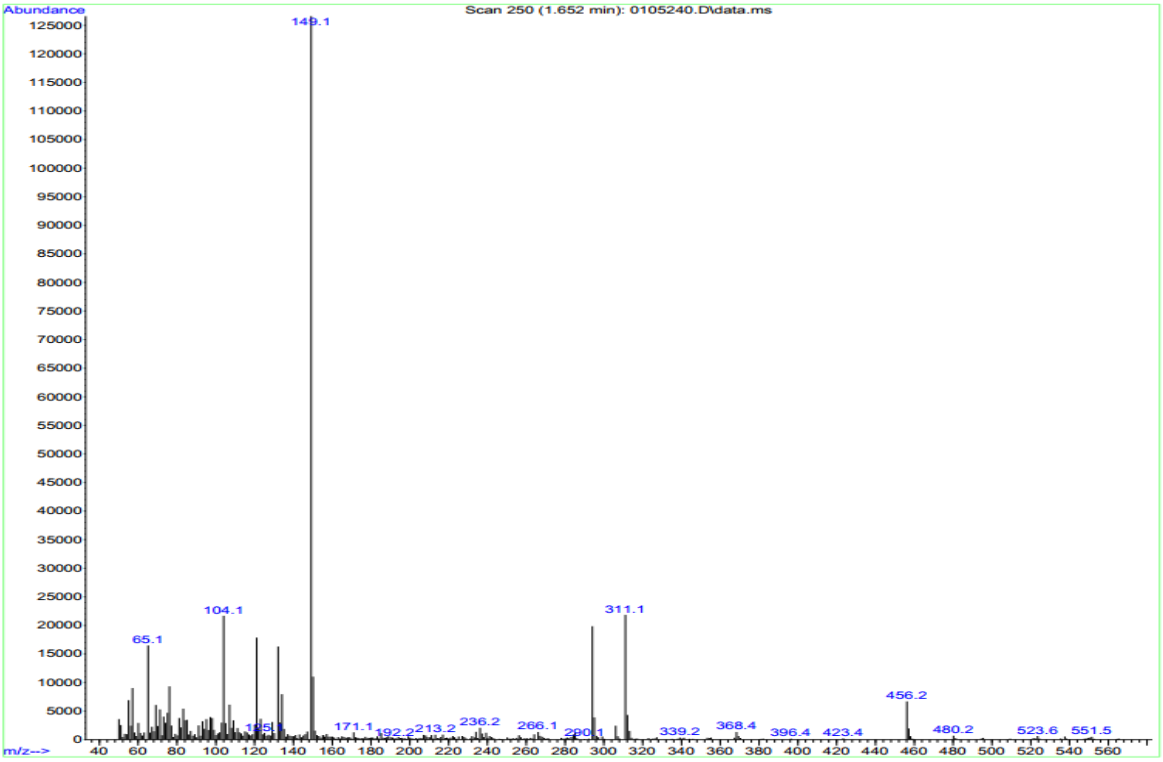


Figure 20. mass spectra for **4g**

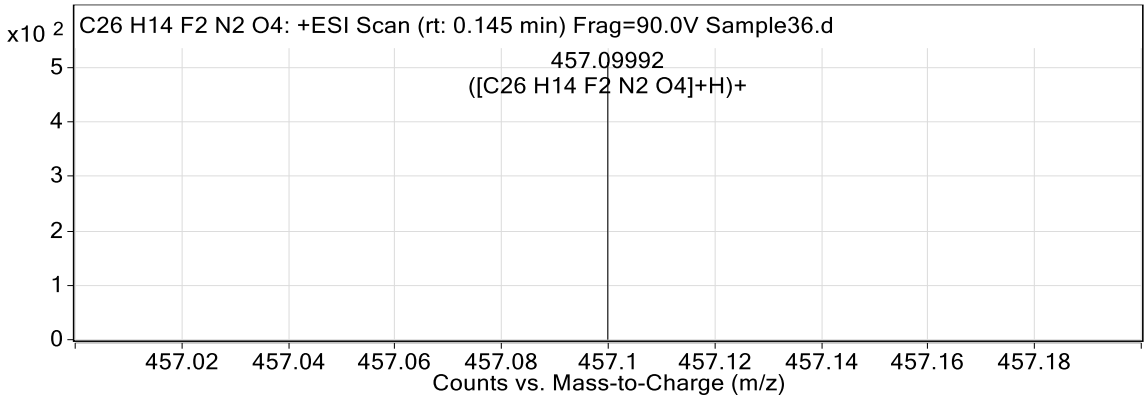
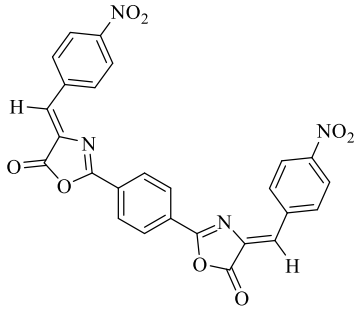


Figure 21. HRMS spectra for **4g**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-4-nitrobenzylidene)oxazol-5(4H)-one) (**4h):** Yellow powder (yield 61%); mp 250-252 °C; We couldn't get suitable ^{1}H NMR spectra for this compound due to the low solubility in NMR solvents; IR (KBr) *ν* 1801, 1651, 1519, 1341, 1323, 1302, 1161, 974, 857, 844, 684 cm^{-1}; EI-MS m/z (%) 510.1 [M^{+}], 346.2, 317.2 (100), 216.1, 149.1, 104.1, 77.1; Anal. calcd for $C_{26}H_{14}N_4O_8$: C, 61.18; H, 2.76; N, 10.98. Found: C, 61.26; H, 2.49; N, 10.66.

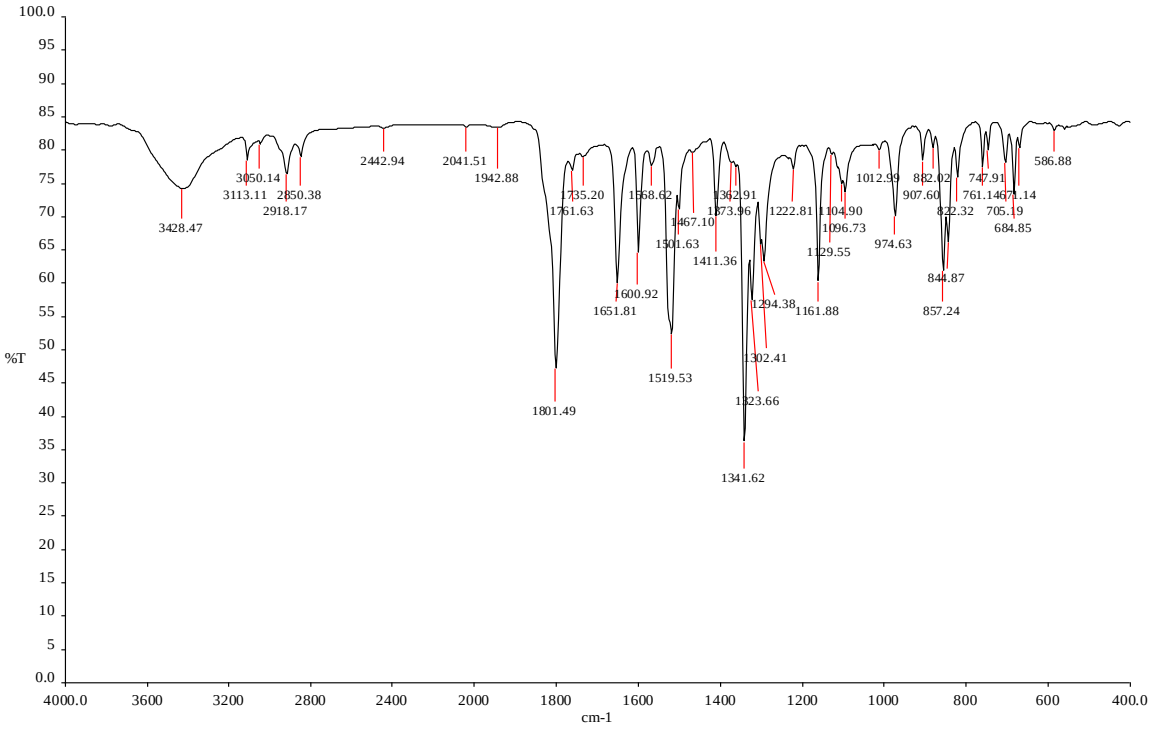


Figure 22. IR spectra for **4h**

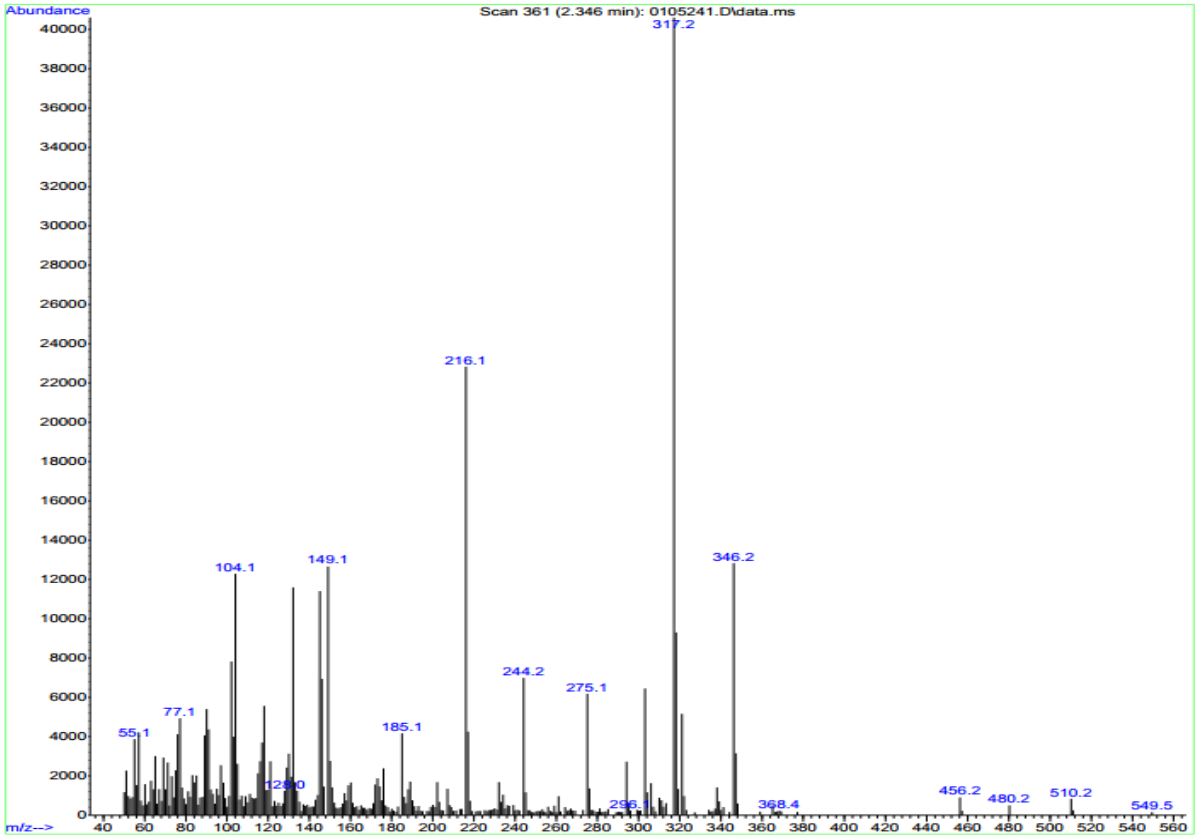
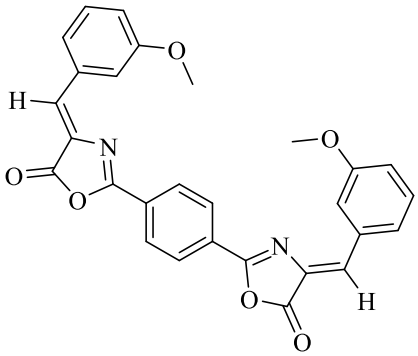


Figure 23. mass spectra for **4h**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-3-methoxybenzylidene)oxazol-5(4H)-one) **(4i):** Yellow powder (yield 83%); mp 260-263 °C; We couldn't get suitable ^{1}H NMR spectra for this compound due to the low solubility in NMR solvents; IR (KBr) *v* 1793, 1763, 1650, 1579, 1289, 1277, 1266, 982, 852, 464, 685; EI-MS m/z (%): 480.2 [M^{+}], 306.1 (100), 278.1, 132.1, 104.1, 76.1; Anal. calcd for $C_{28}H_{20}N_2O_6$: C, 69.99; H, 4.20; N, 5.83. Found: C, 69.83; H, 4.63; N, 5.99.

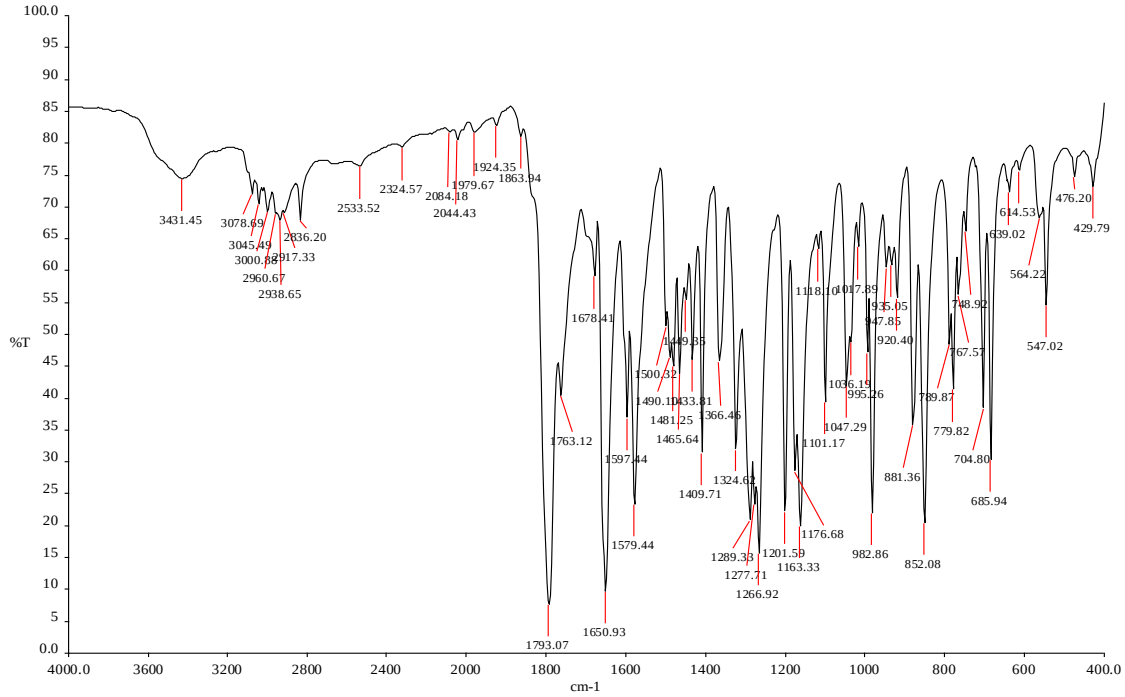


Figure 24. IR spectra for **4i**

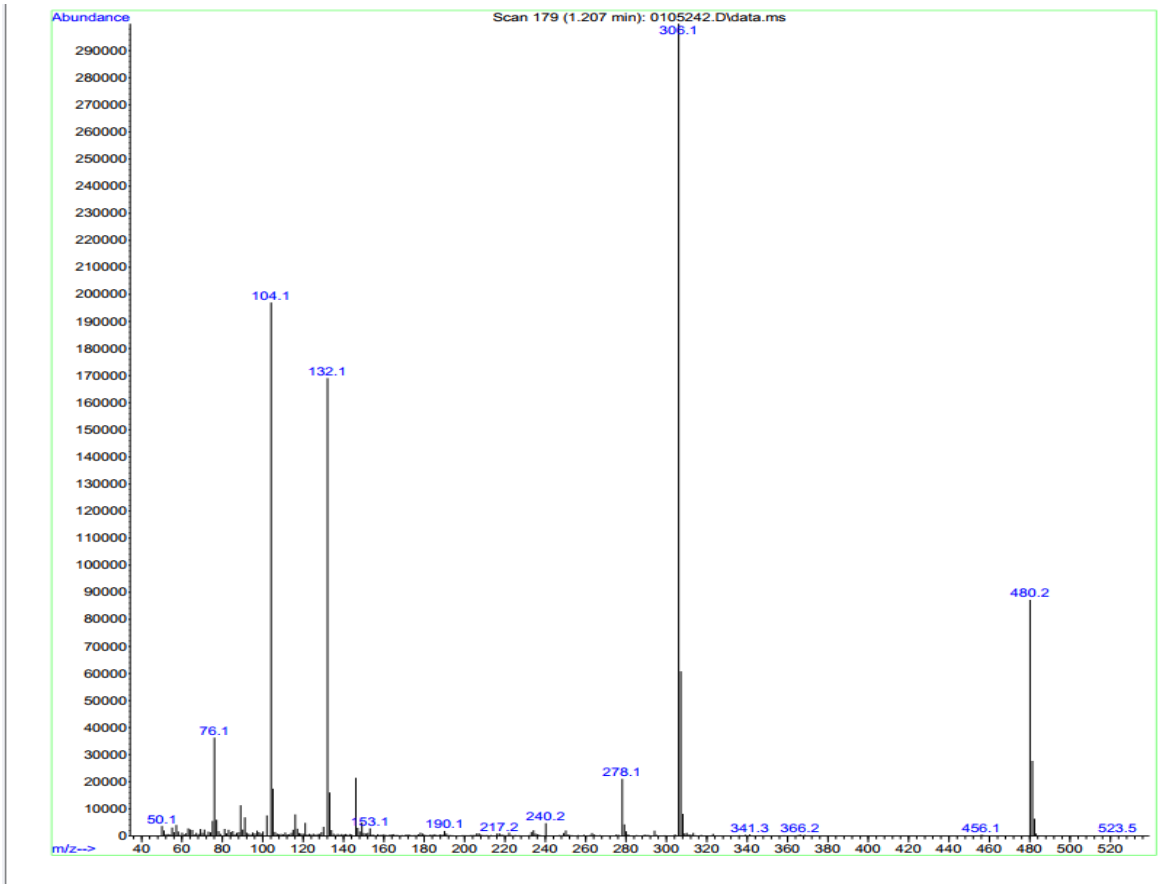
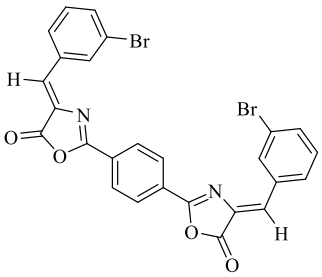


Figure 25. Mass spectra for **4i**



(Z)-2,2'-(1,4-phenylene)bis(4-((Z)-3-bromobenzylidene)oxazol-5(4H)-one) **(4j):** Yellow powder (yield 75%); mp 325-327 °C; We couldn't get suitable ^{1}H NMR spectra for this compound due to the low solubility in NMR solvents; IR (KBr) *v* 1800, 1648, 1569, 1410, 1298, 1163, 982, 979, 855, 547 cm^{-1}; EI-MS m/z (%) 578.1 [M^{+}], 356.0, 313.4, 132.1, 104.1 (100), 76.1; HRMS m/z [M+H]$^{+}$ calcd for $C_{26}H_{14}Br_2N_2O_4$ 576.9399; found 576.9398.

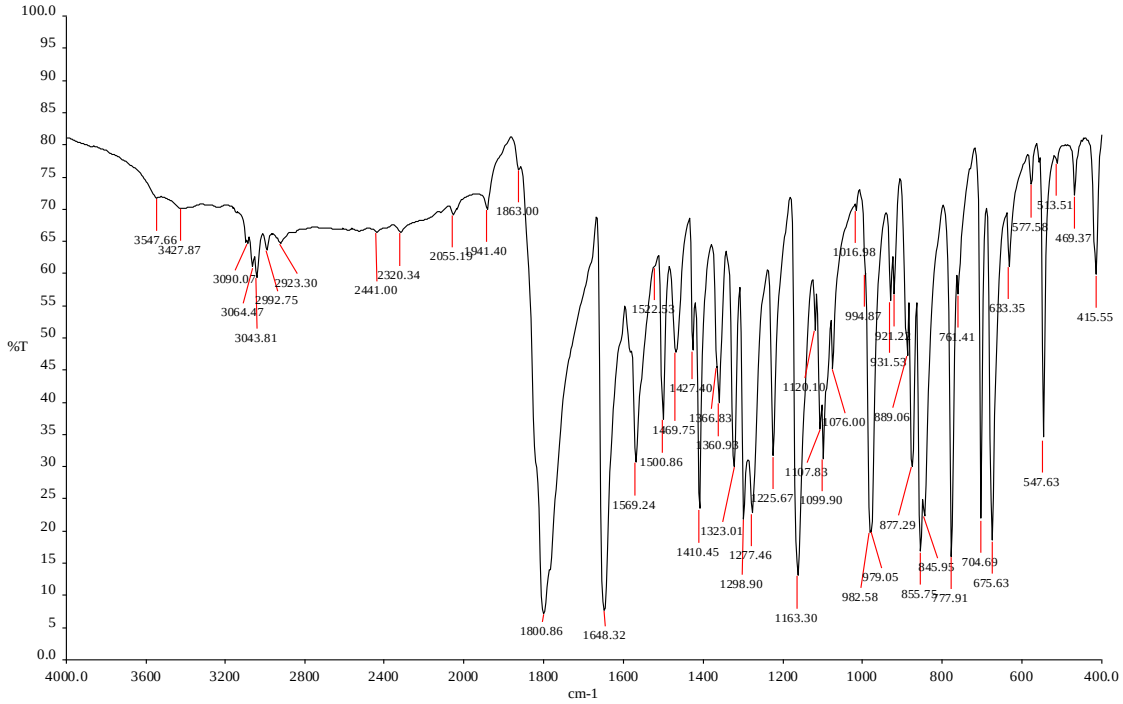


Figure 26. IR spectra for **4j**

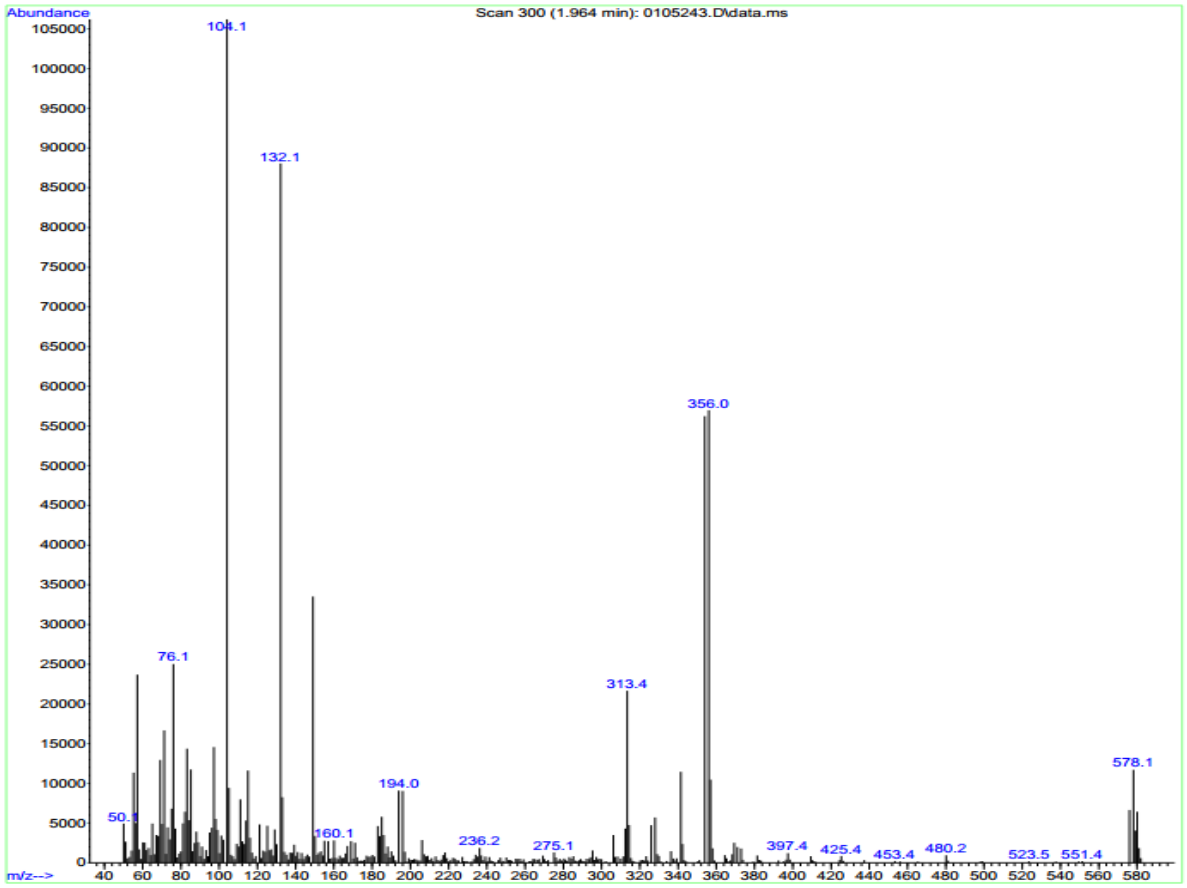


Figure 27. mass spectra for **4j**

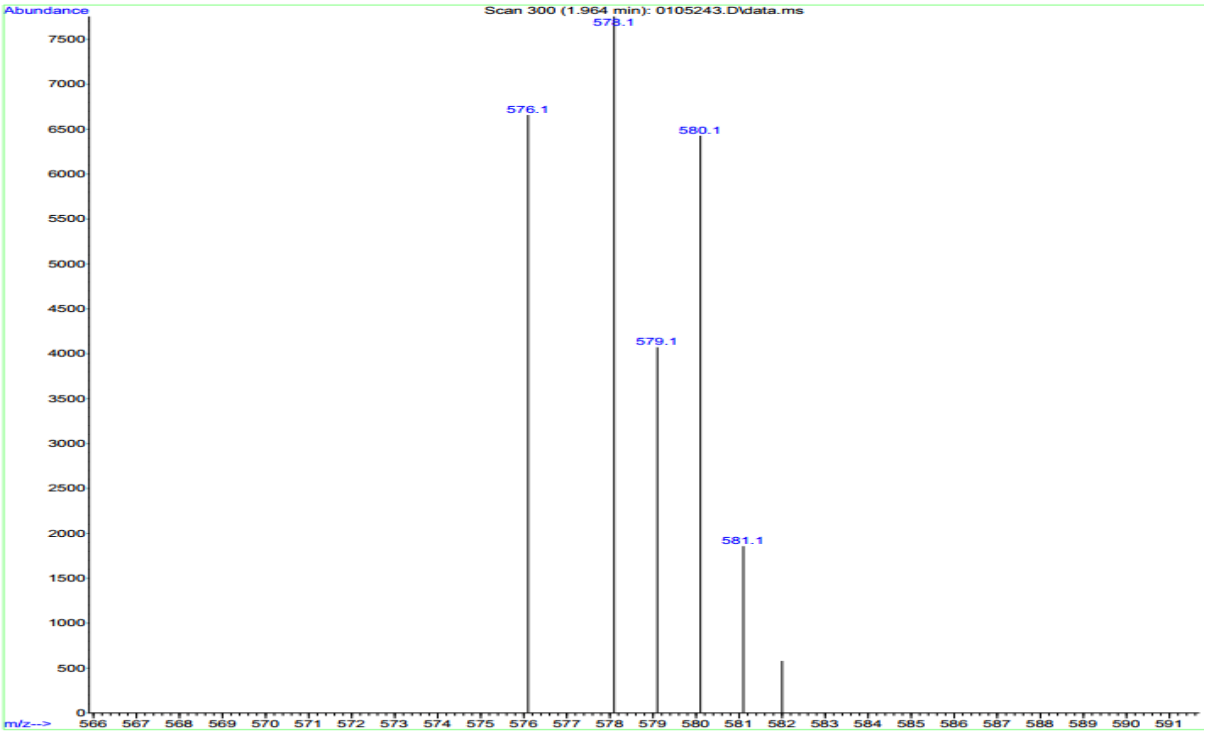


Figure 28. mass spectra for **4j**

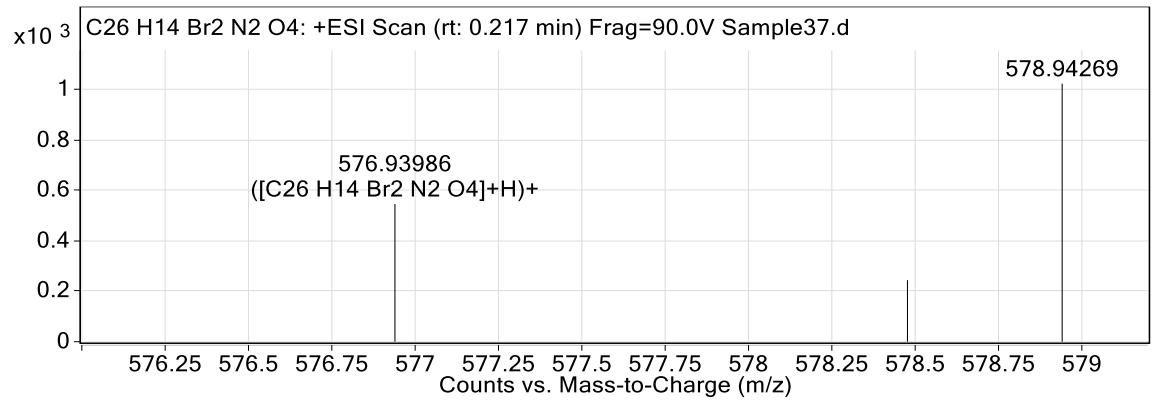
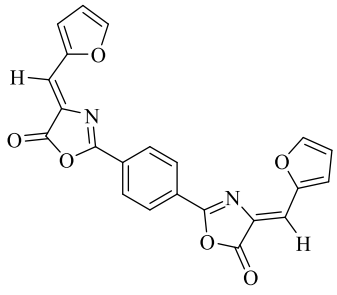


Figure 29. HRMS spectra for **4j**



(4Z,4'Z)-2,2'-(1,4-phenylene)bis(4-(furan-2-ylmethylene)oxazol-5(4H)-one) **(4k):** Orange powder (yield 60%); mp 250-253 ℃; We couldn't get suitable ^{1}H NMR spectra for this compound due to the low solubility in NMR solvents; IR (KBr) *v* 1787, 1653, 1465, 1290, 1232, 856, 738, 595 cm^{-1}; HRMS (ESI) m/z $[M+H]^{+}$ calcd for $C_{22}H_{12}N_2O_6$ 401.0774; found 401.0788.

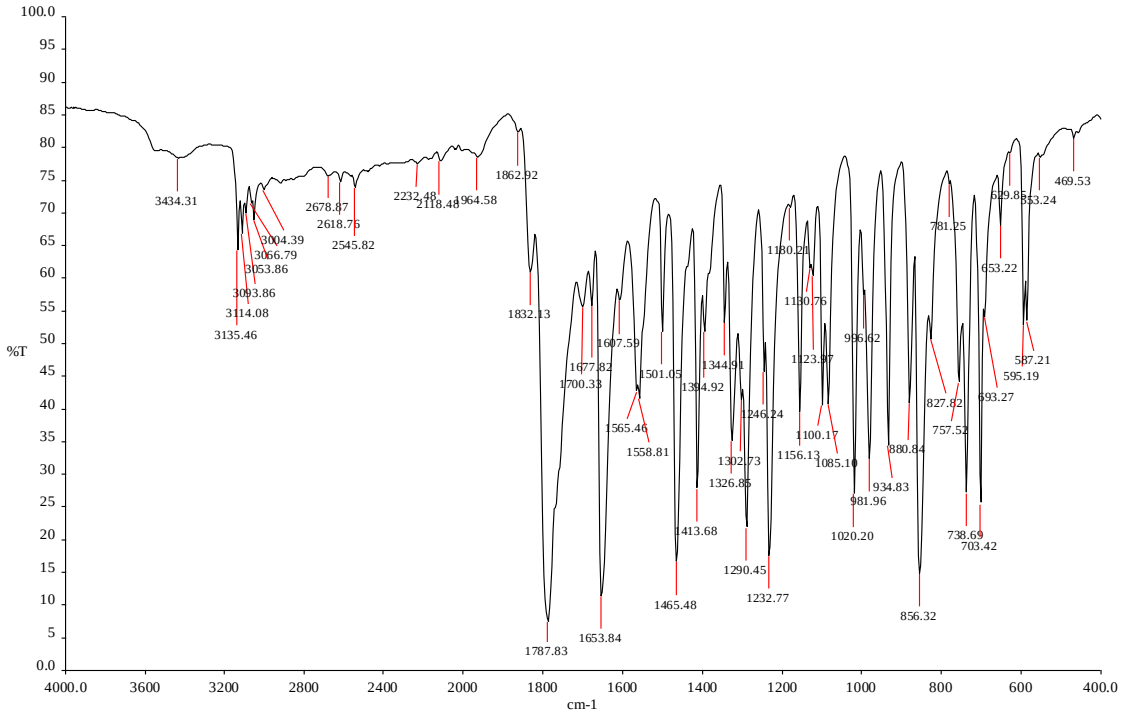


Figure 30. IR spectra for **4k**

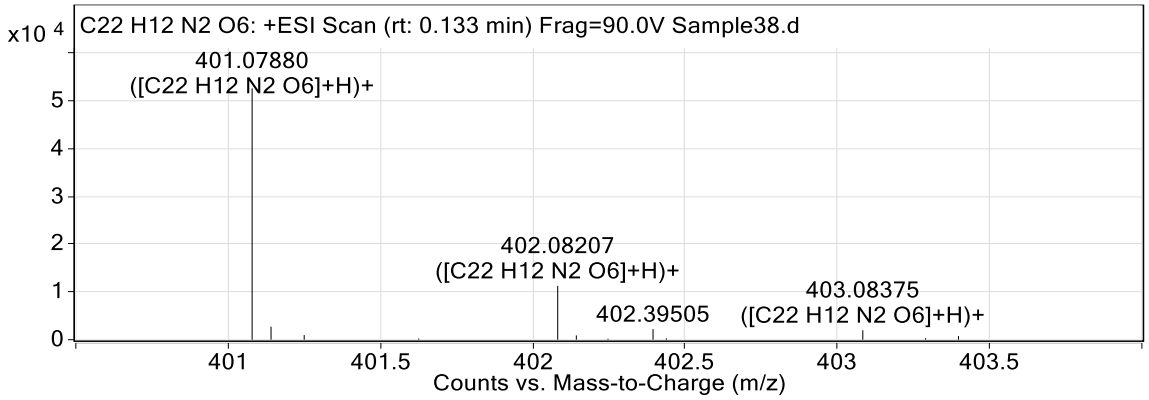
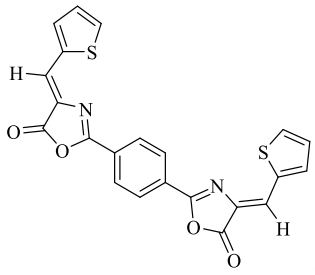


Figure 31. HRMS spectra for **4k**



(4Z,4'Z)-2,2'-(1,4-phenylene)bis(4-(thiophen-2-ylmethylene)oxazol-5(4H)-one) **(4l):** Orange powder (yield 83%); mp 315-317 °C; We couldn't get suitable ^{1}H

NMR spectra for this compound due to the low solubility in NMR solvents; IR (KBr) ν 1788, 1770, 1645, 1411, 1322, 1293, 983, 864, 855, 724, 562 cm^{-1}; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{22}H_{12}N_2O_4S_2$ 433.0317; found 433.03233.

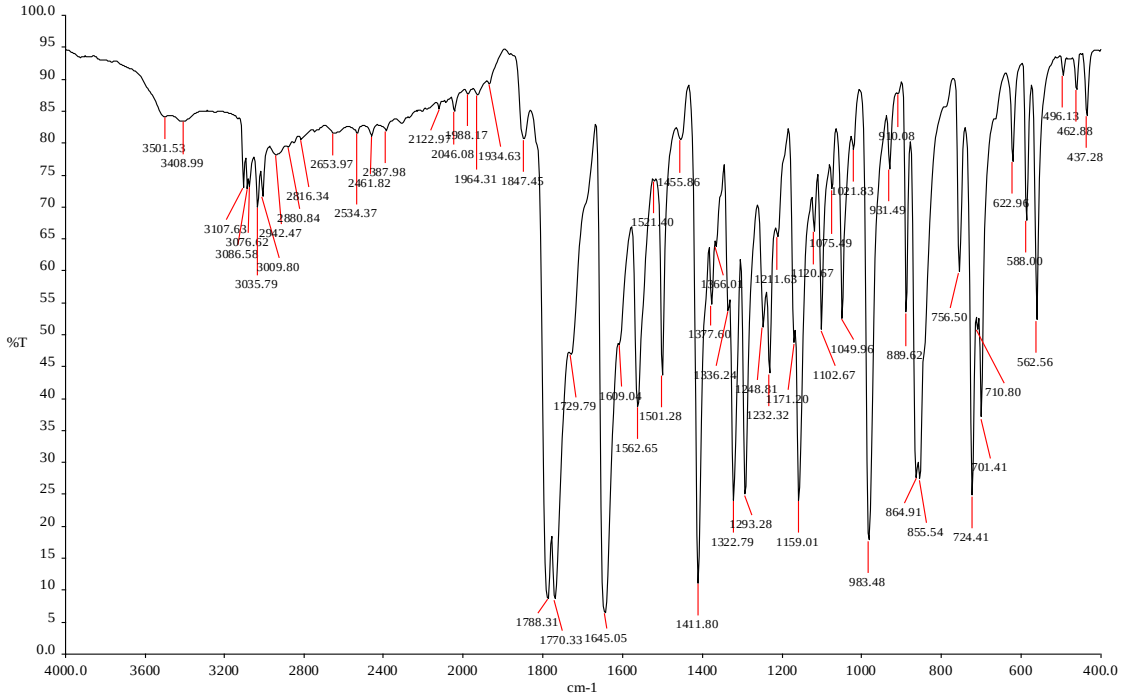


Figure 32. IR spectra for **4l**

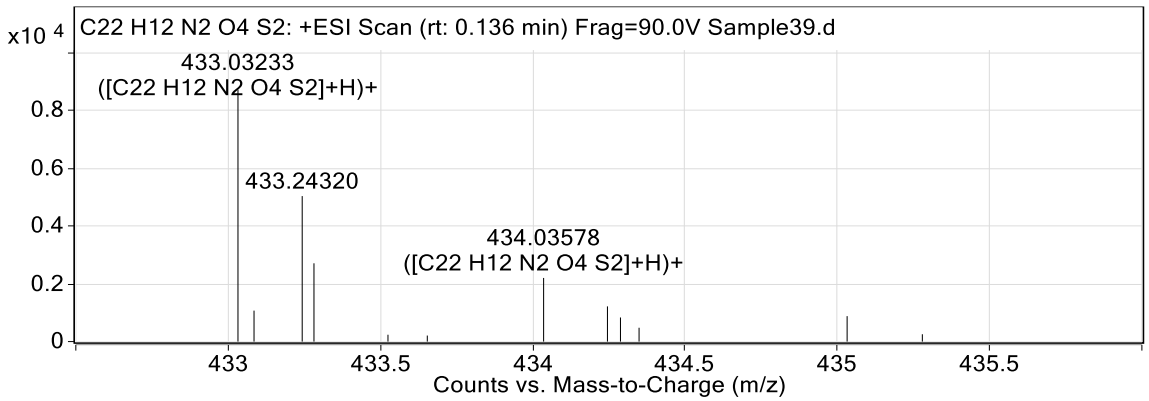
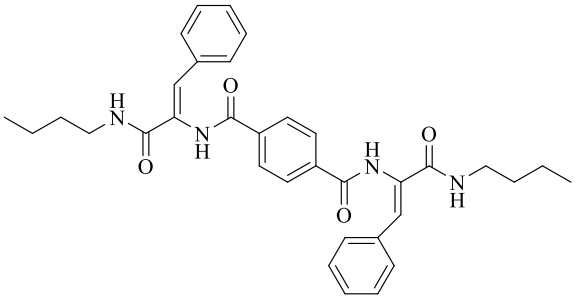


Figure 33. HRMS spectra for **4l**



N1-((E)-3-(butylamino)-3-oxo-1-phenylprop-1-en-2-yl)-N4-((E)-3-oxo-1-phenyl-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6a):** white powder (125 mg, yield 88%); mp 245-247 °C; IR (KBr) *v* 3326, 3188, 2957, 2931, 1643, 1622, 1531, 1479, 1279, 687 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.98 (s, 2H), 8.15-8.09 (m, 6H), 7.55-7.53 (m, 4H), 7.35-7.27 (m, 6H), 7.21 (s, 2H), 3.17-3.12 (m, 4H), 1.50-1.40 (m, 4H), 1.36-1.23 (m, 4H), 0.88 (t, J = 7.3 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 164.6, 136.2, 134.2, 130.2, 129.2, 128.8, 128.5, 128.4, 127.7, 38.8, 31.2, 19.5, 13.7 ppm; Anal. calcd for $C_{34}H_{38}N_4O_4$: C, 72.06; H, 6.76; N, 9.89; Found: C, 71.78; H, 6.64; N, 9.55.

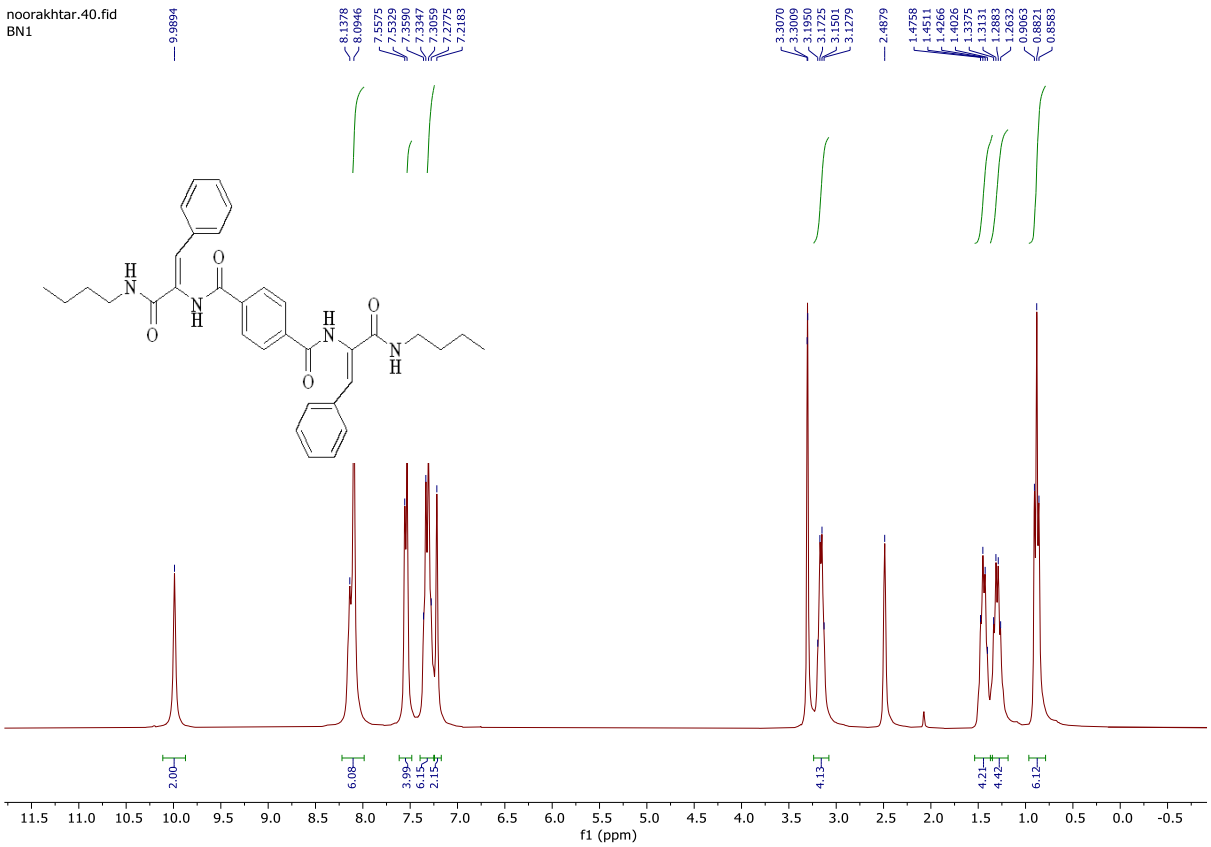


Figure 34. ^{1}H NMR spectra for **6a**

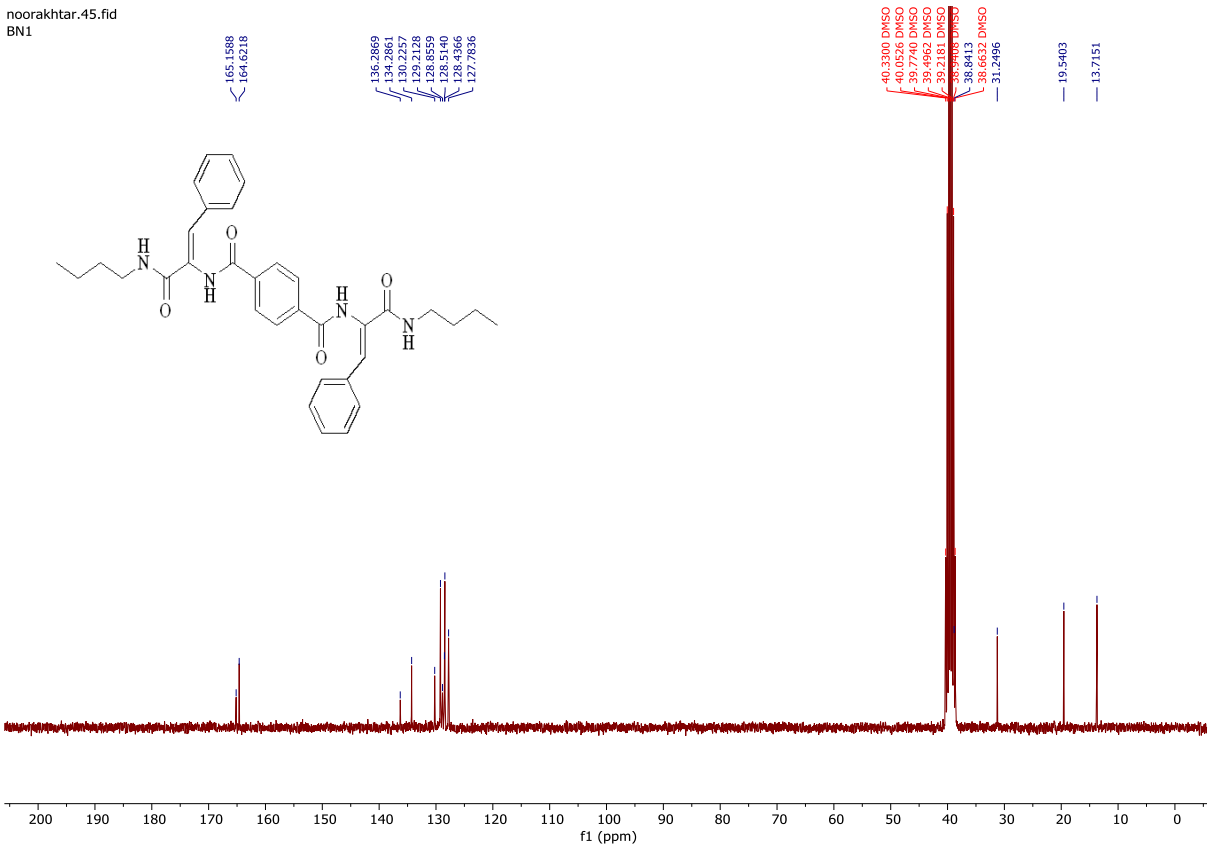


Figure 35. ^{13}C NMR spectra for **6a**

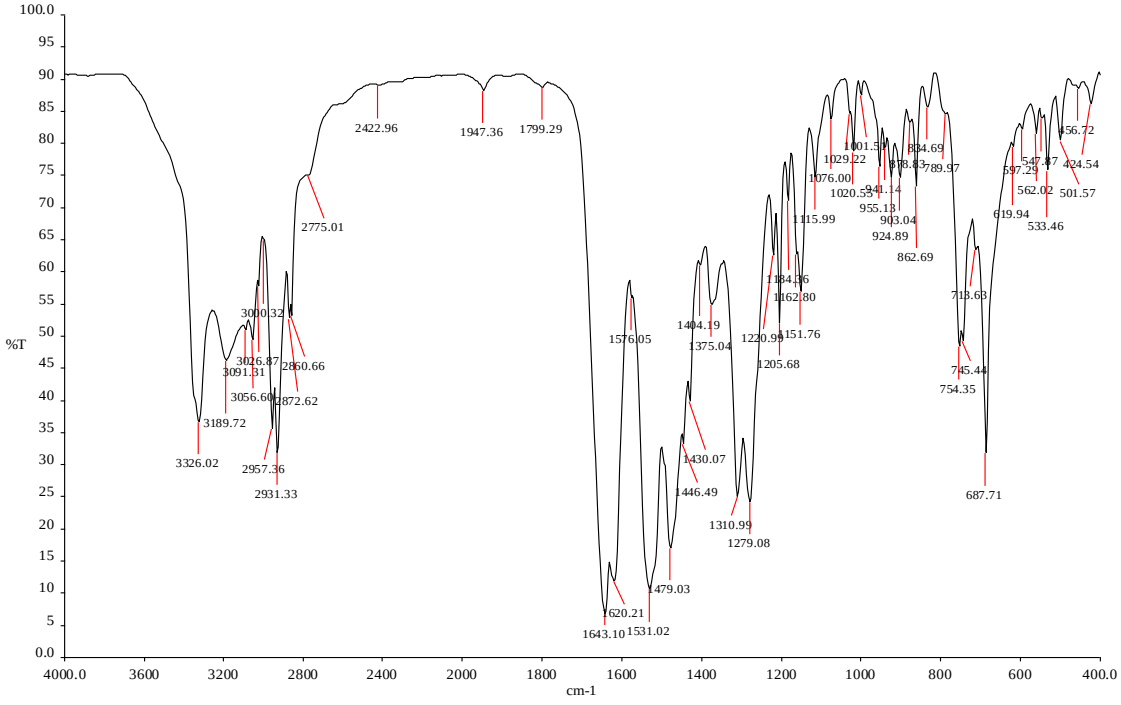
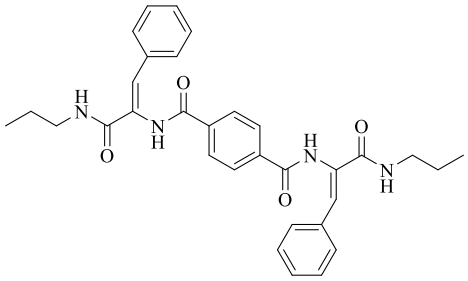


Figure 36. IR spectra for **6a**



N1,N4-bis((E)-3-oxo-1-phenyl-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6b):** white powder (100 mg, yield 74%); mp 264-266 °C; IR (KBr) *v* 3312, 3174, 2872, 1639, 1619, 1540, 1478, 1283, 934, 753, 694 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.0 (s, 2H), 8.18-8.10 (m, 6H), 7.56-7.54 (m, 4H), 7.36-7.28 (m, 6H), 7.23 (s, 2H), 3.16-3.10 (m, 4H), 1.54-1.42 (m, 4H), 0.86 (t, J = 7.3 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 164.6, 136.2, 134.2, 130.2, 129.2, 128.8, 128.5, 128.4, 127.7, 40.9, 22.3, 11.3 ppm; Anal. calcd for $C_{32}H_{34}N_4O_4$: C, 71.35; H, 6.36; N, 10.40. Found: C, 71.22; H, 6.19; N, 9.92

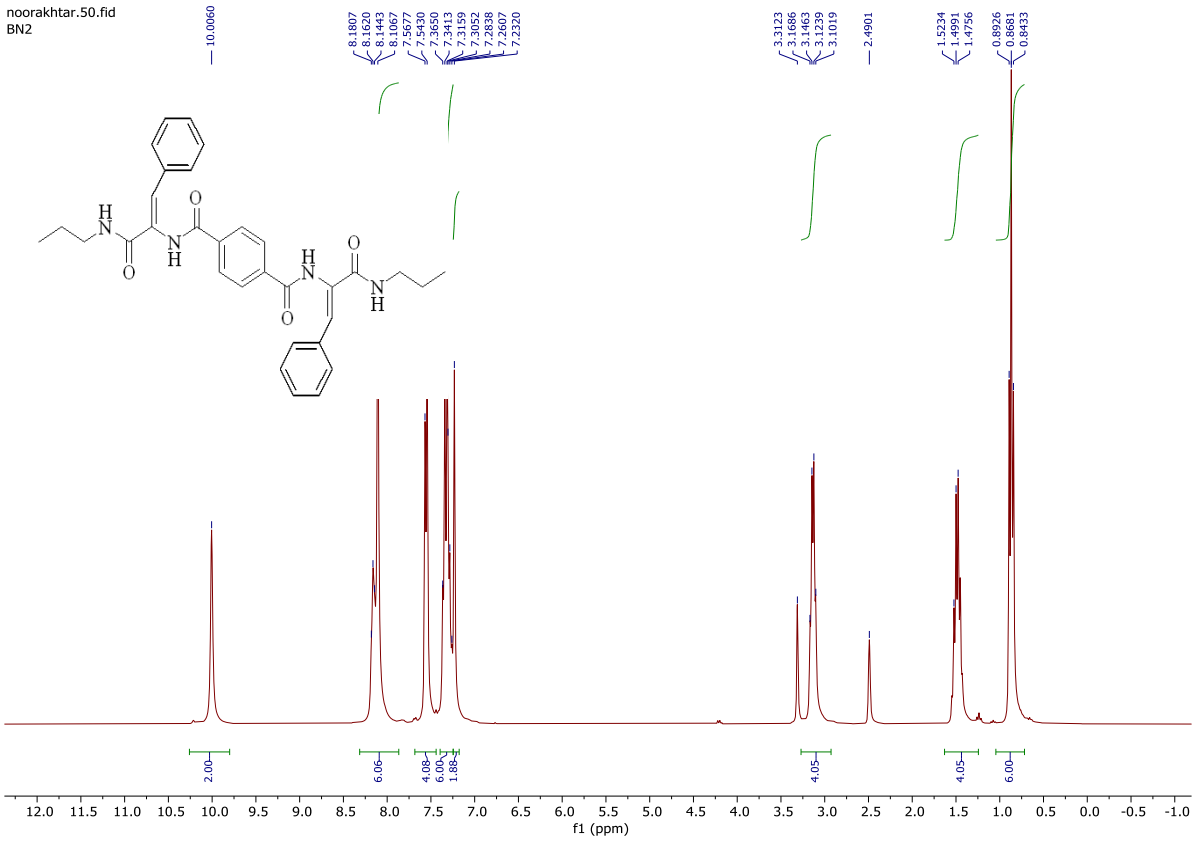


Figure 37. ^{1}H NMR spectra for **6b**

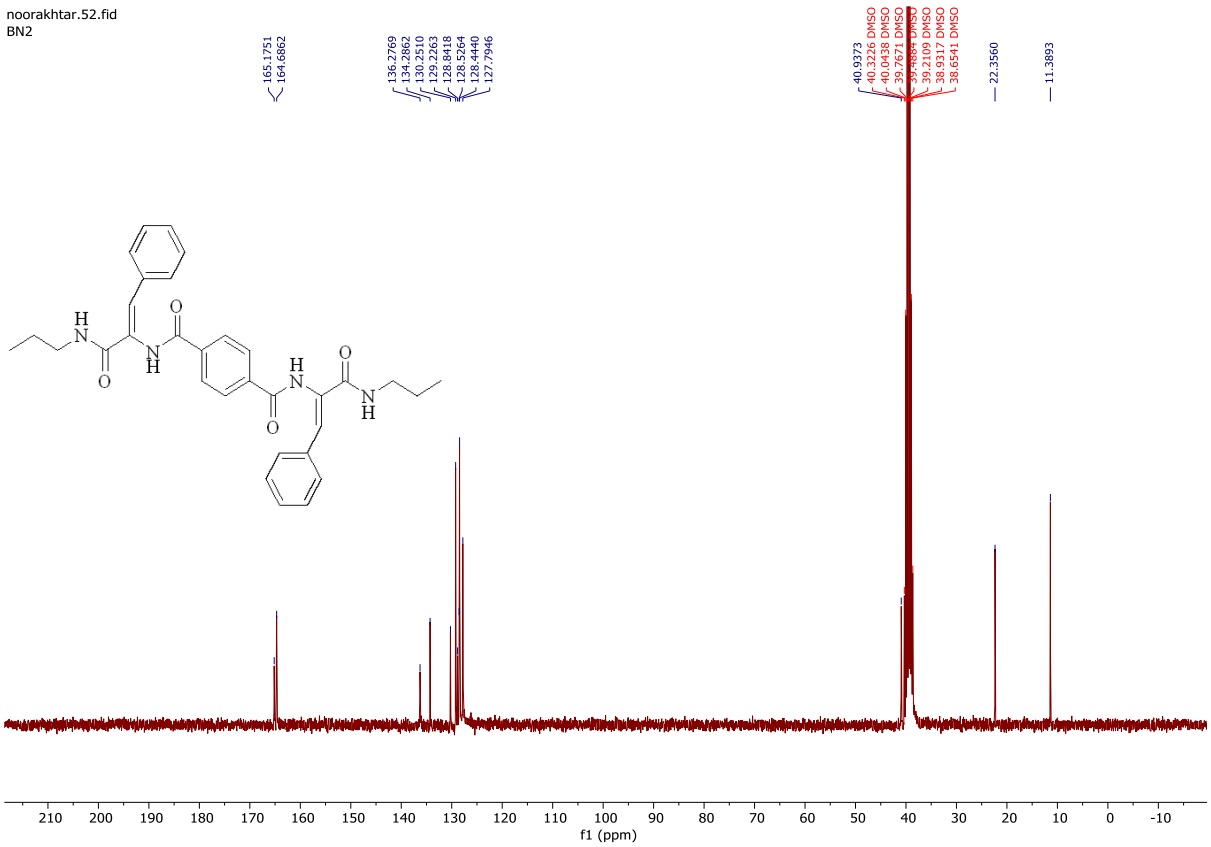


Figure 38. ^{13}C NMR spectra for **6b**

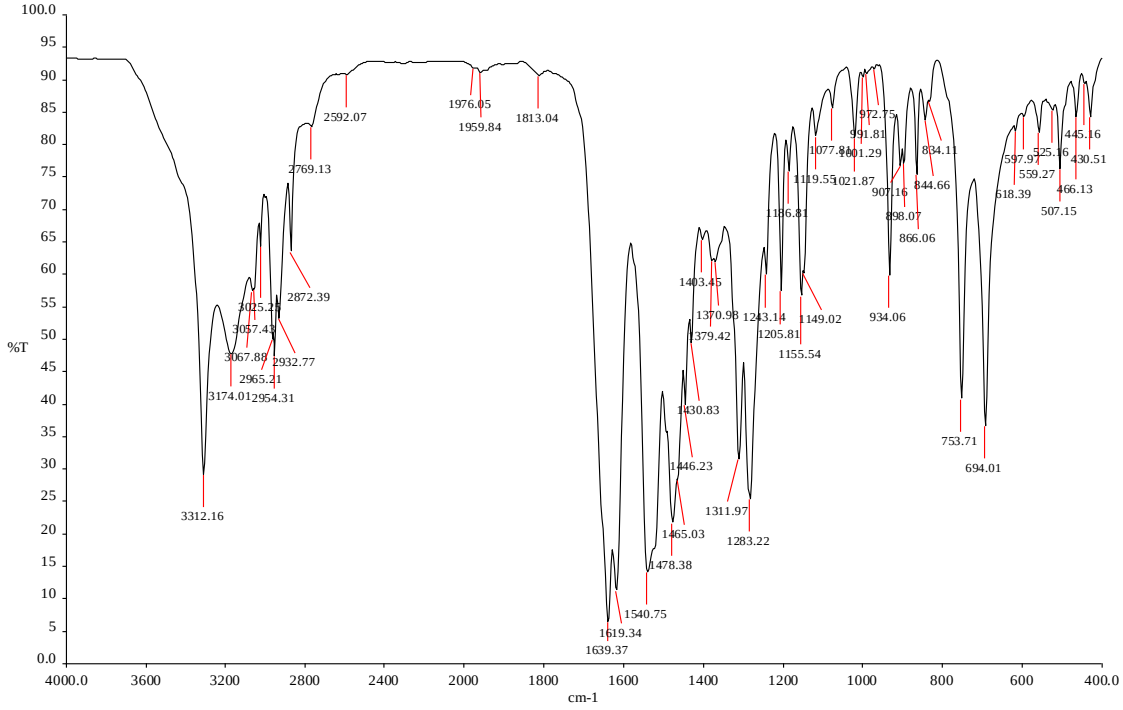
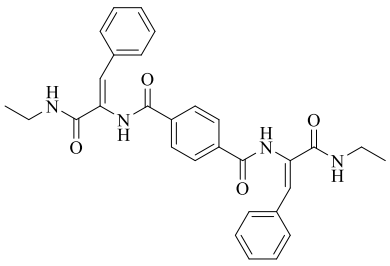


Figure 39. IR spectra for **6b**



N1,N4-bis((E)-3-(ethylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6c):** white powder (101 mg, yield 79%); mp 262-264 °C; IR (KBr) *v* 3310, 2973, 2935, 1657, 1622, 1525, 1311, 1277, 688 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.98 (s, 2H), 8.19 (s, 2H), 8.16-8.09 (m, 4H), 7.55-7.53 (m, 4H), 7.36-7.28 (m, 6H), 7.23 (s, 2H), 3.22-3.15 (m, 4H), 1.07 (t, *J* = 7.17 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 164.5, 136.2, 134.2, 130.1, 129.2, 128.9, 128.5, 128.4, 127.7, 34.0, 14.7 ppm; Anal. calcd for $C_{30}H_{30}N_4O_4$: C, 70.57; H, 5.92; N, 10.97. Found: C, 70.26; H, 5.73; N, 10.63.

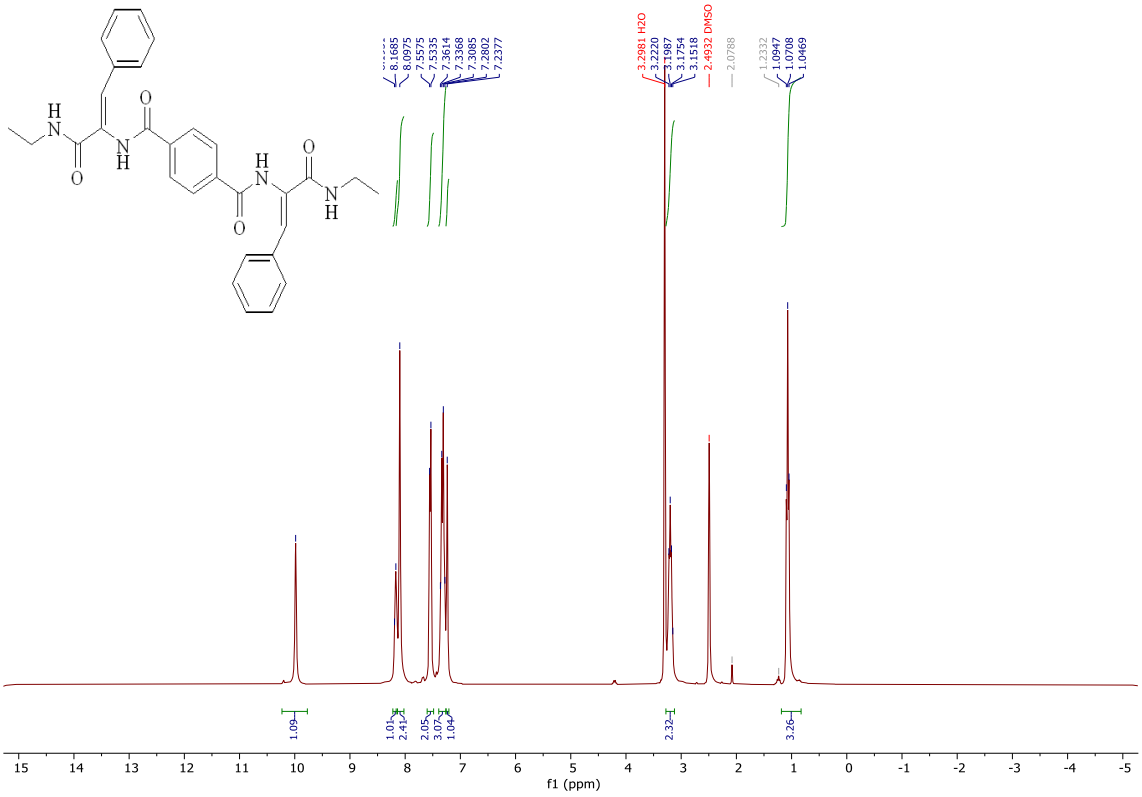


Figure 40. ^{1}H NMR spectra for **6c**

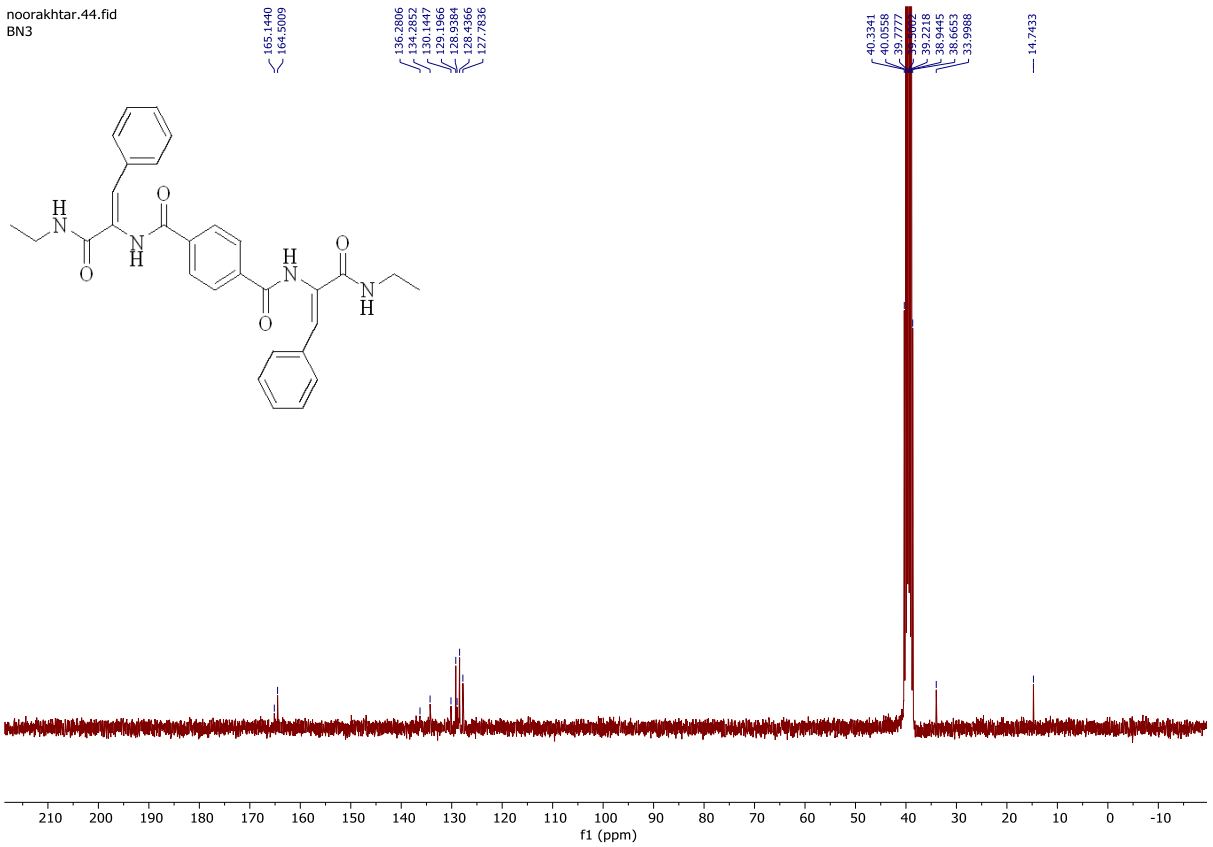


Figure 41. ^{13}C NMR spectra for **6c**

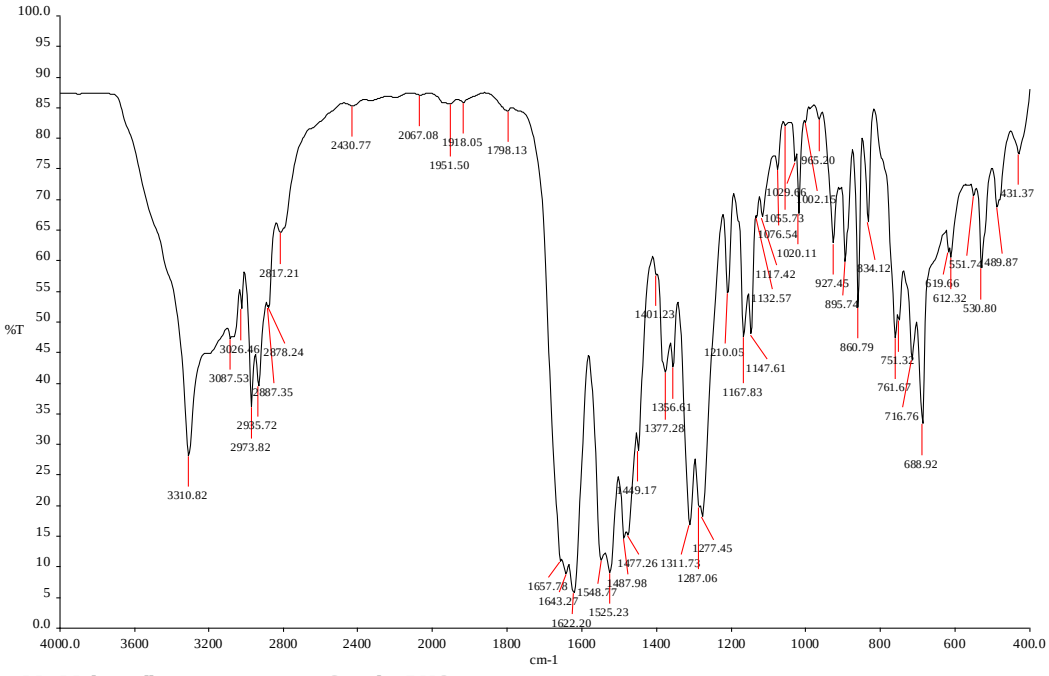
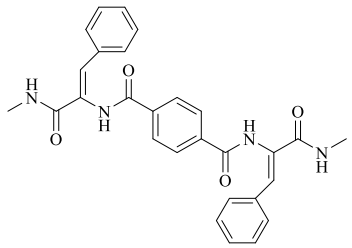


Figure 42. IR spectra for **6c**



N1,N4-bis((E)-3-(methylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6d):** white powder (105mg, yield 87%); mp 242-244 °C; IR (KBr) *v* 3452, 3200, 1661, 1646, 1528, 1477, 1410, 1322, 893, 763, 749 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.01 (s, 2H), 8.12-8.09 (m, 6H), 7.55-7.52 (m, 4H), 7.36-7.26 (m, 8H), 2.69 (d, *J*= 4.4 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1 (2C), 136.2, 134.2, 129.9, 129.3, 129.2, 128.5, 128.4, 127.7, 26.2 ppm; Anal. calcd for $C_{28}H_{26}N_4O_4$: C, 69.70; H, 5.43; N, 11.61. Found: C, 70.0; H, 5.34; N, 11.25.

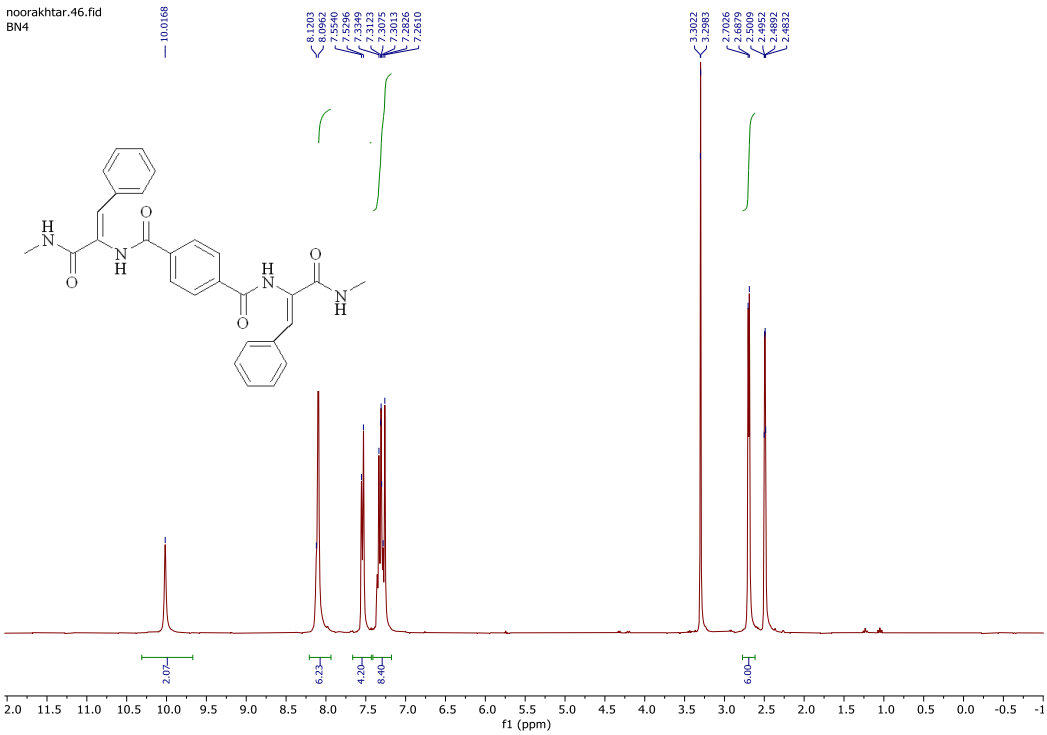


Figure 43. ^{1}H NMR spectra for **6d**

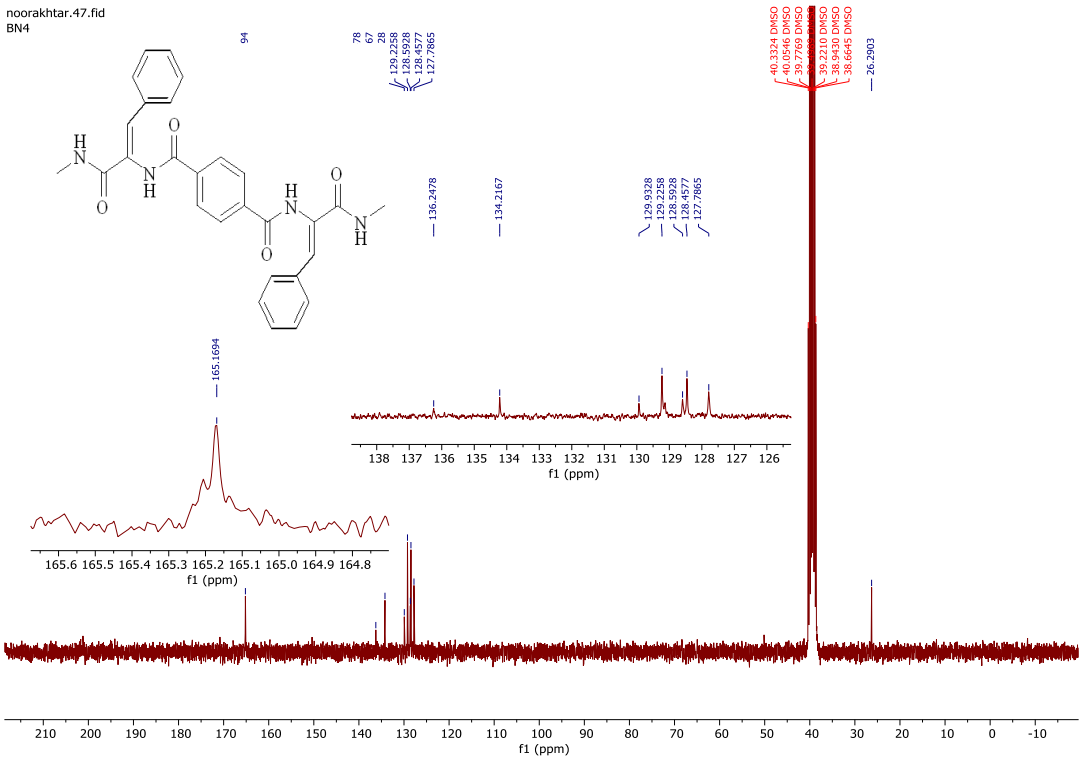


Figure 44. ^{13}C NMR spectra for **6d**

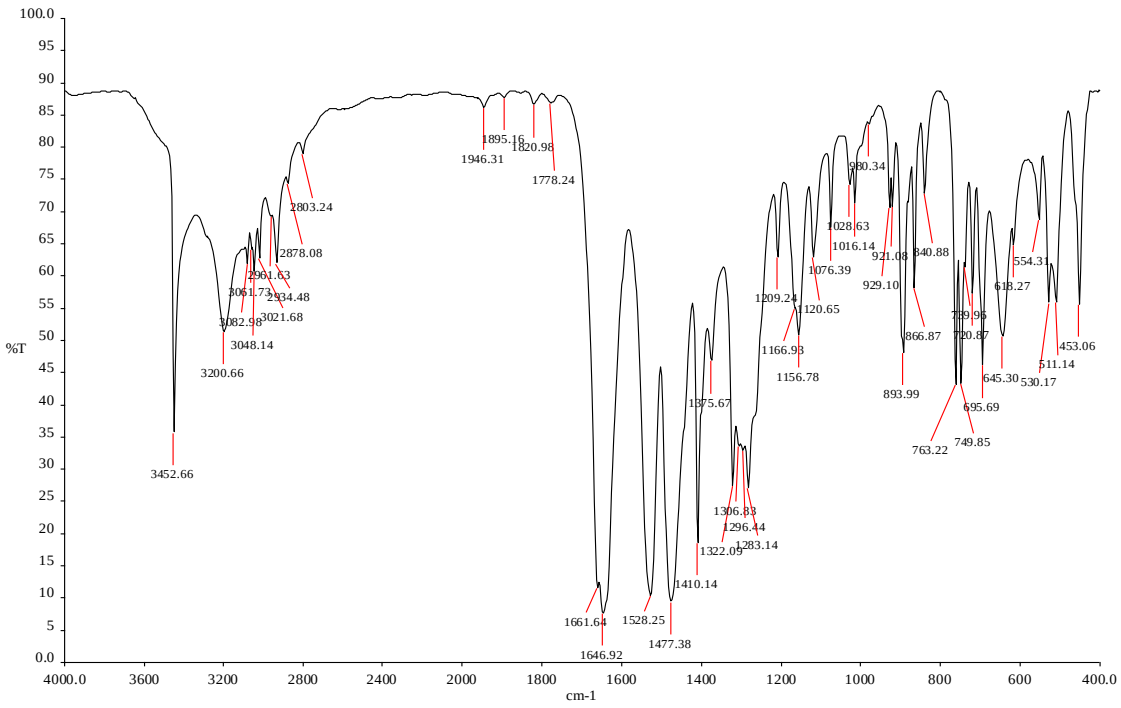
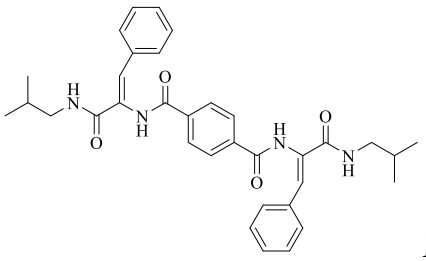


Figure 45. IR spectra for **6d**



N1,N4-bis((E)-3-(isobutylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6e):** white powder (104 mg, yield 73%); mp 262-264 °C; IR (KBr) *v* 3314, 3177, 2962, 2925, 1636, 1539, 1466, 1280, 1154, 949, 753, 688 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.01 (s, 2H), 8.17-8.10 (m, 6H), 7.56-7.54 (m, 4H), 7.36-7.21 (m, 8H), 2.98 (t, J = 6.4 Hz, 4H), 1.84-1.72 (m, 2H), 0.85 (d, J = 6.6 Hz, 12H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.2, 164.7, 136.2, 134.2, 130.3, 129.2, 128.7, 128.4, 128.4, 127.7, 46.6, 28.0, 20.1 ppm; Anal. calcd for $C_{34}H_{38}N_4O_4$: C, 72.06; H, 6.76; N, 9.89. Found: C, 71.64; H, 6.57; N, 9.72.

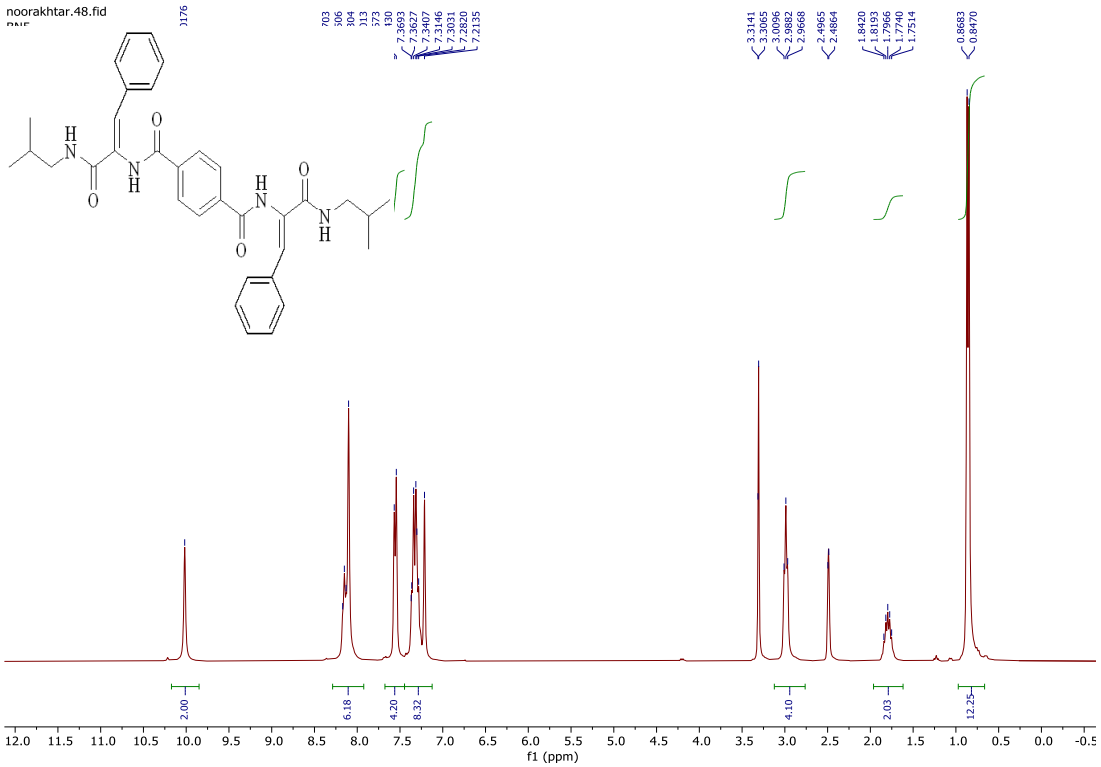


Figure 46. ^{1}H NMR spectra for **6e**

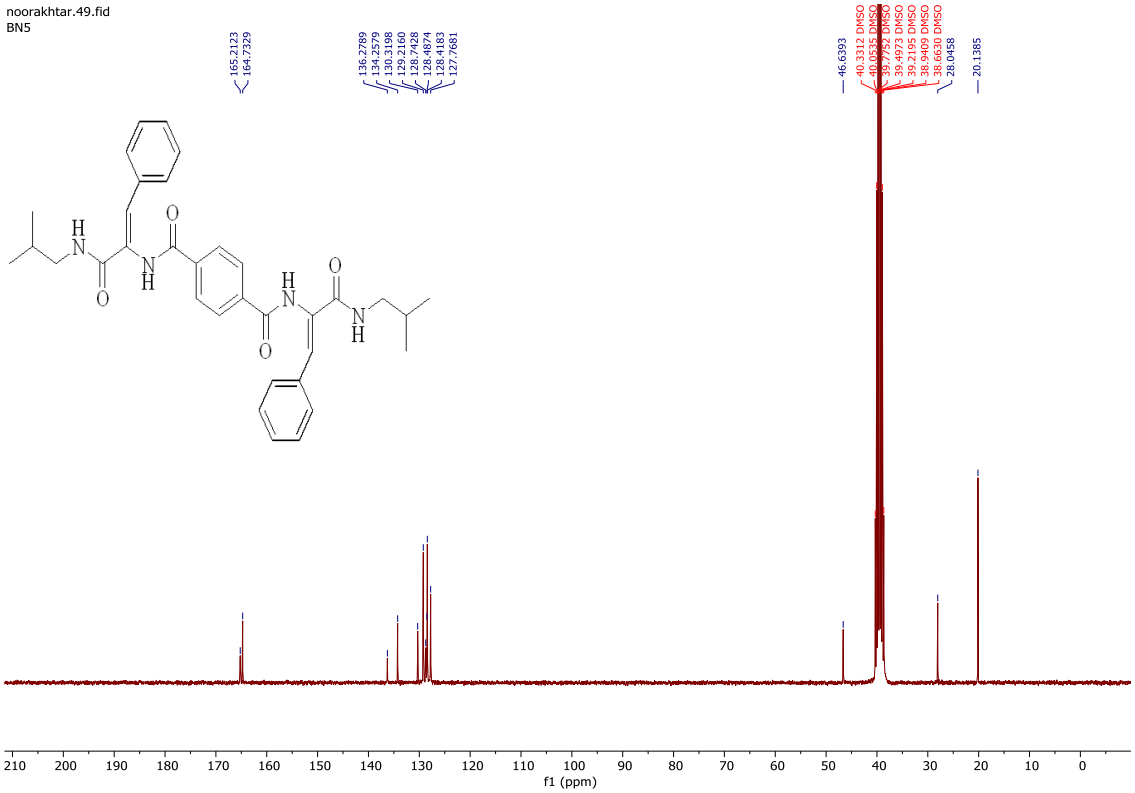


Figure 47. ^{13}C NMR spectra for **6e**

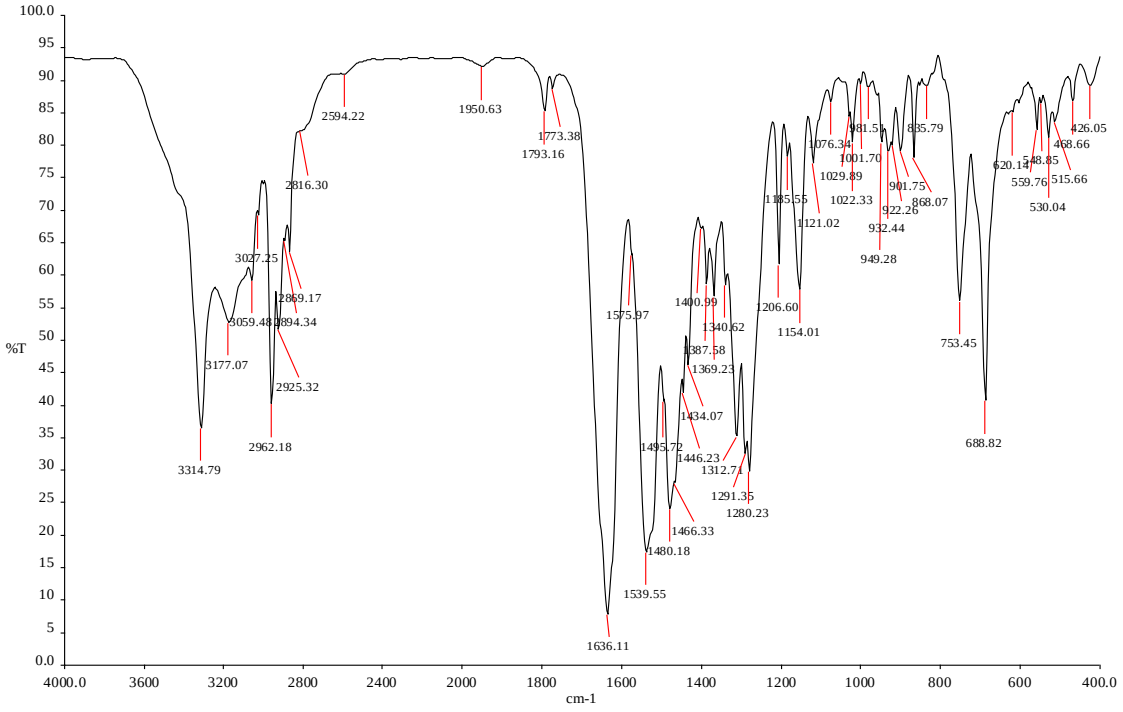
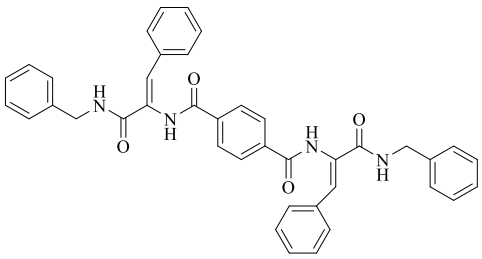


Figure 48. IR spectra for **6e**



N1,N4-bis((E)-3-(benzylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6f):** white powder (122 mg, yield 77%); mp 256-258 °C; IR (KBr) *v* 3321, 3167, 2926, 1637, 1539, 1493, 1279, 1029, 757, 688 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.12 (s, 2H), 8.76 (t, J = 6.1 Hz, 2H), 8.14 (s, 4H), 7.59-7.56 (m, 4H), 7.34-7.19 (m, 18H), 4.42 (d, J = 6.1 Hz, 4H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.3, 164.8, 139.7, 136.3, 134.1, 129.9, 129.6, 129.3, 128.6, 128.4, 128.1, 127.8, 127.0, 126.5, 42.5 ppm; Anal. calcd for $C_{40}H_{34}N_4O_4$: C, 75.69; H, 5.40; N, 8.83. Found: C, 75.36; H, 5.18; N, 8.68.

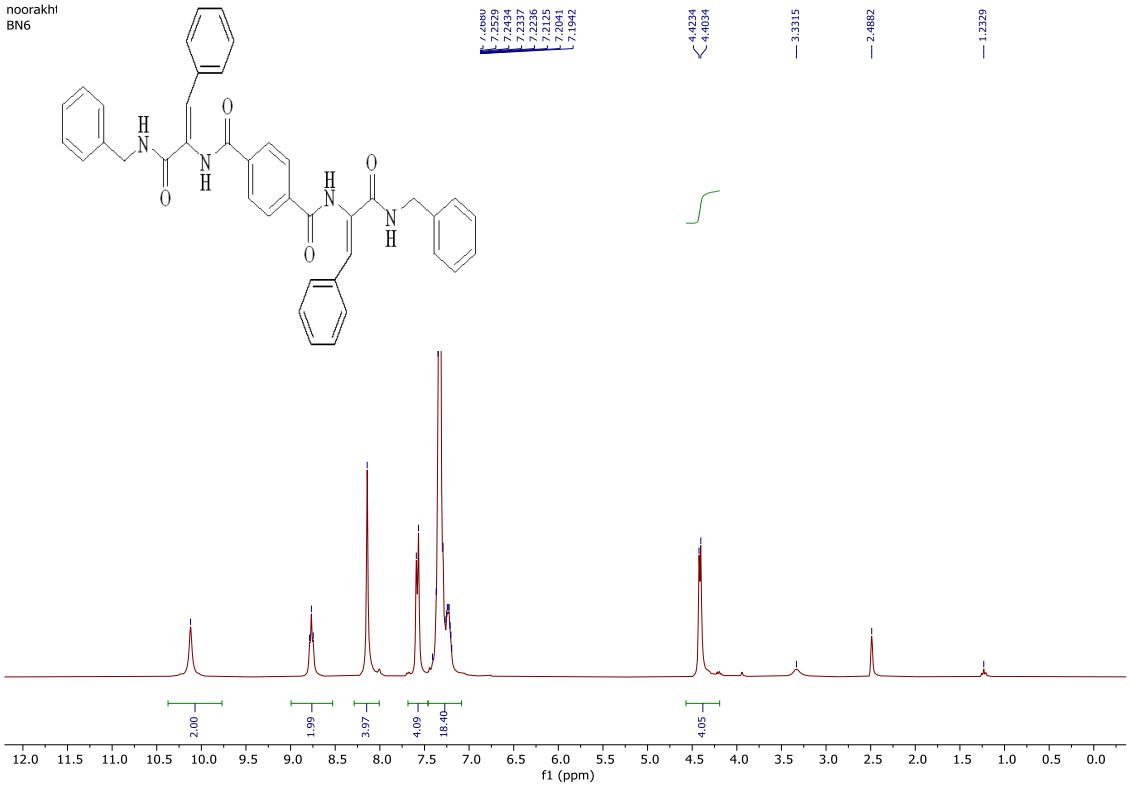


Figure 49. ^{1}H NMR spectra for **6f**

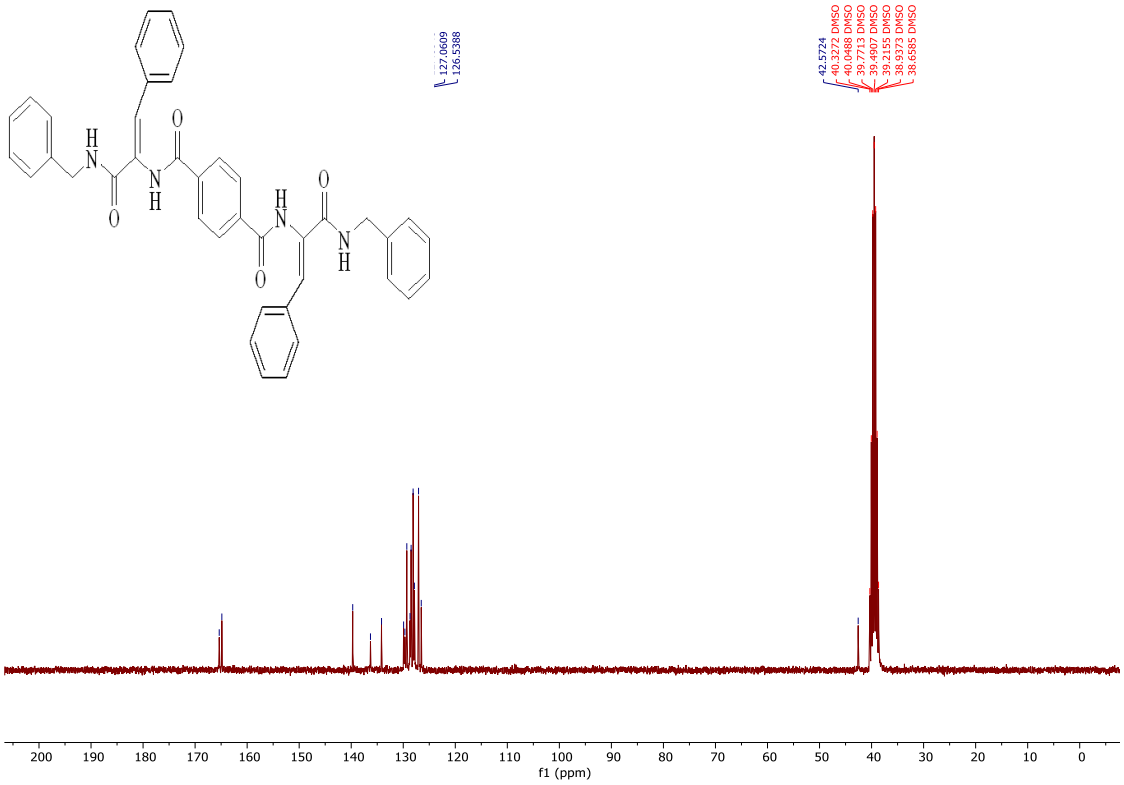


Figure 50. ^{13}C NMR spectra for **6f**

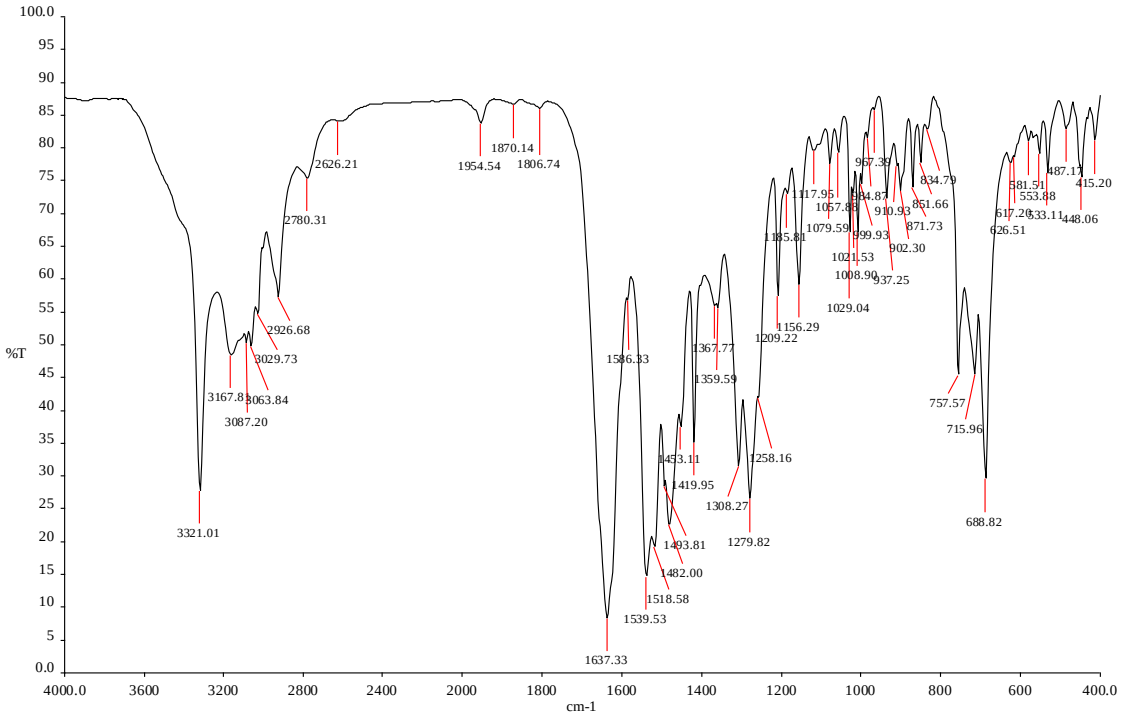
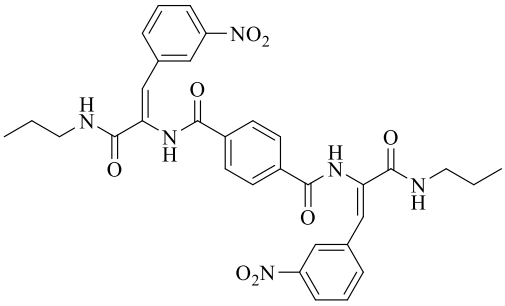


Figure 51. IR spectra for **6f**



N1,N4-bis((E)-1-(3-nitrophenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6g):** white powder (130 mg, yield 83%); mp 248-250 °C; IR (KBr) *v* 3312, 2964, 1641, 1624, 1536, 1283, 825, 723, 678 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.14 (brs, 2H), 8.45 (s, 2H), 8.32 (t, *J*= 5.7 Hz, 2H), 8.14-8.07 (m, 6H), 7.96-7.93 (m, 2H) 7.64 (t, *J* = 7.8 Hz, 2H), 7.28 (s, 2H), 3.16 (t, *J* = 6.5 Hz, 4H), 1.55-1.42 (m, 4H), 0.87 (t, *J* =7.3 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.2, 164.3, 147.7, 136.3, 136.2, 135.7, 132.6, 130.0, 127.8, 126.0, 123.1, 122.8, 41.0, 22.3, 11.4 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{32}H_{32}N_6O_8$ 629.2360; found 629.2369.

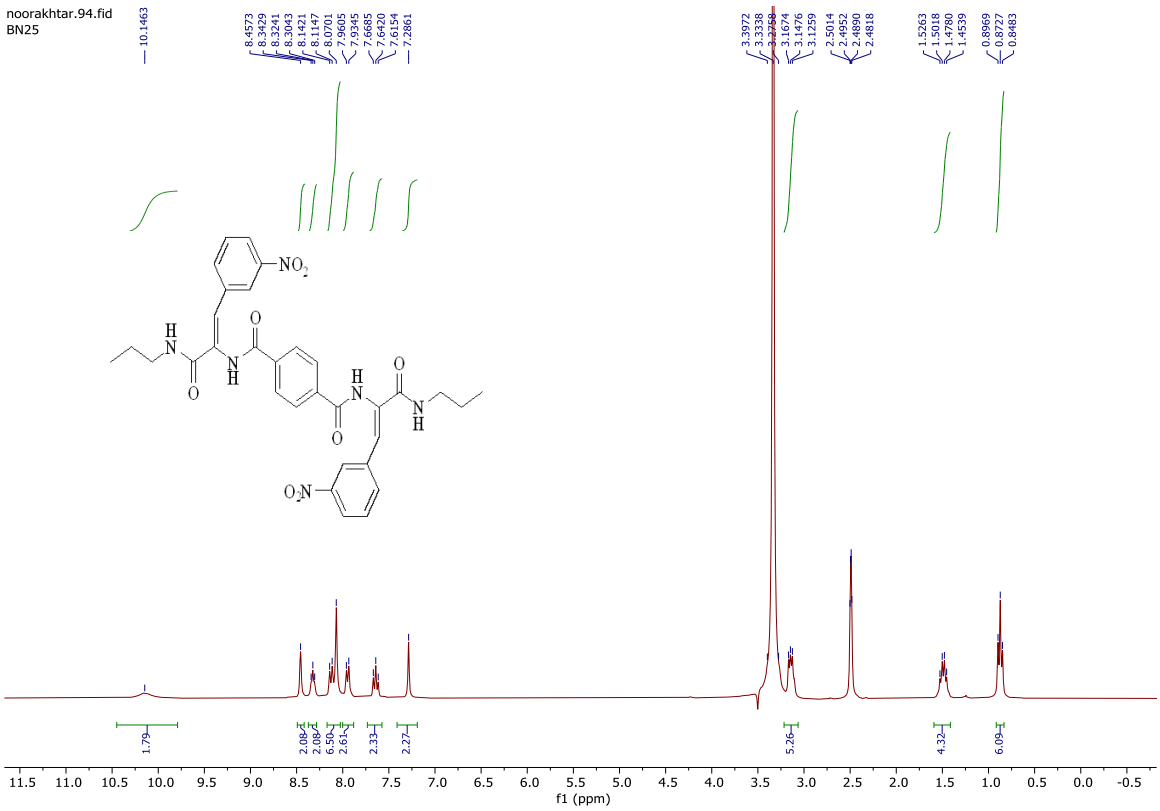


Figure 52. ^{1}H NMR spectra for **6g**

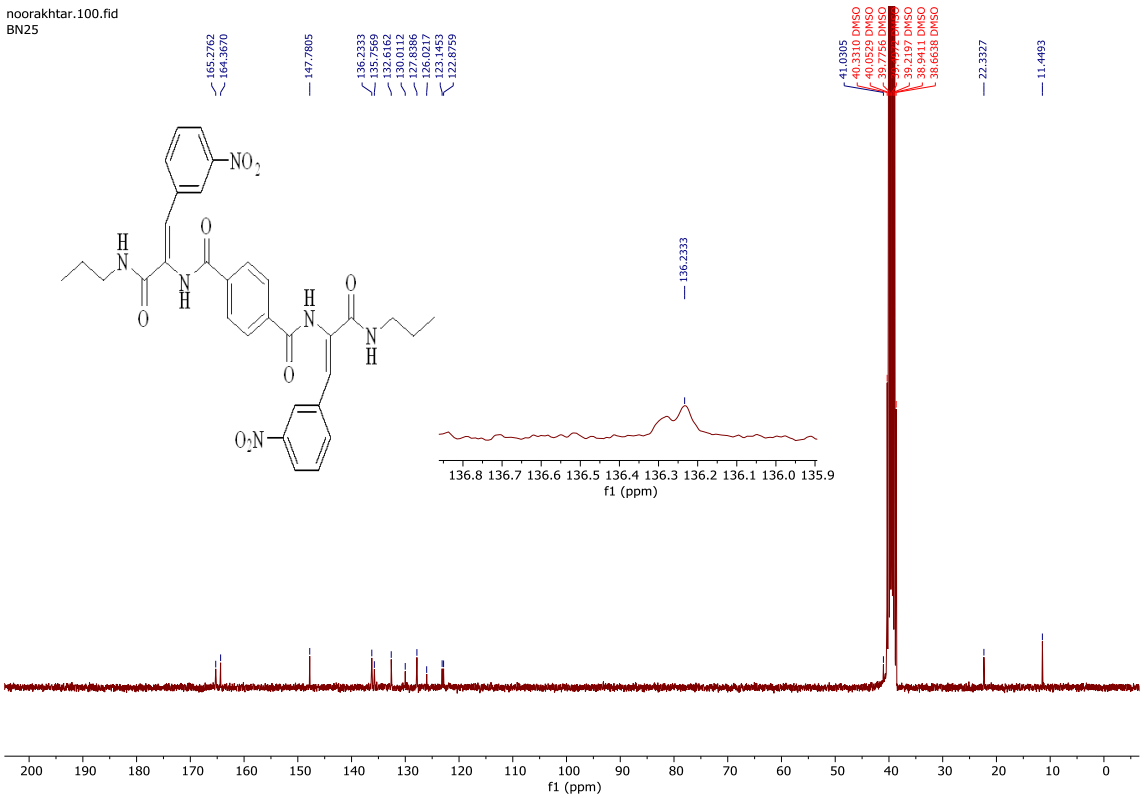


Figure 53. ^{13}C NMR spectra for **6g**

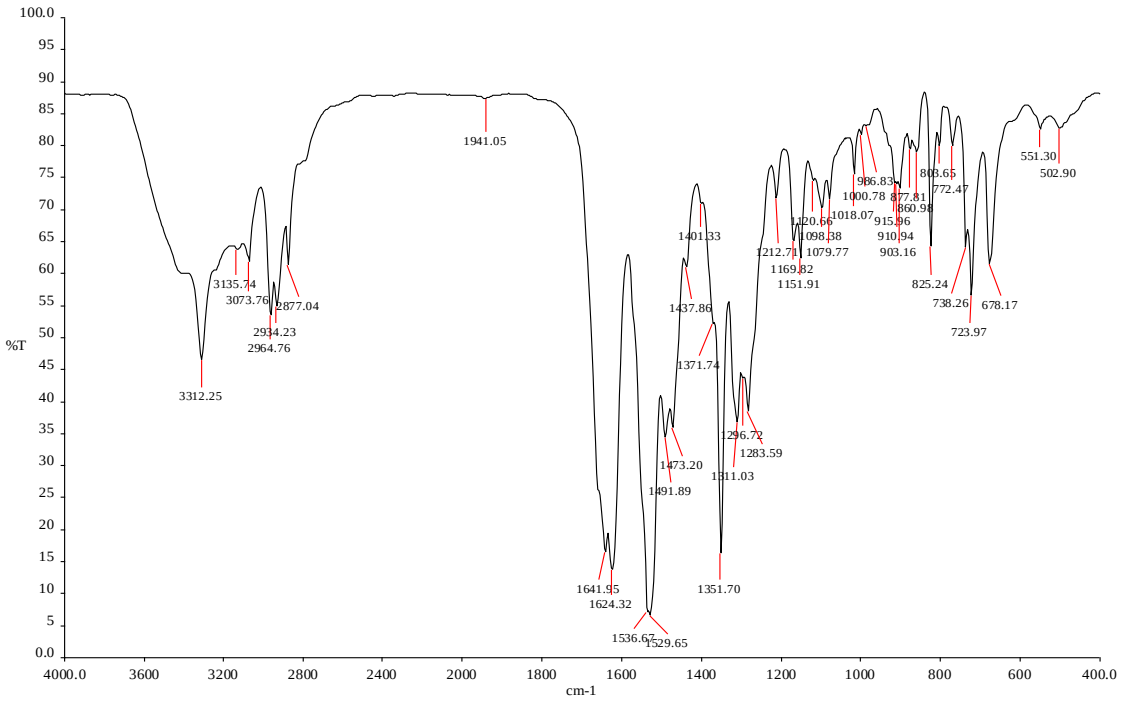


Figure 54. IR spectra for **6g**

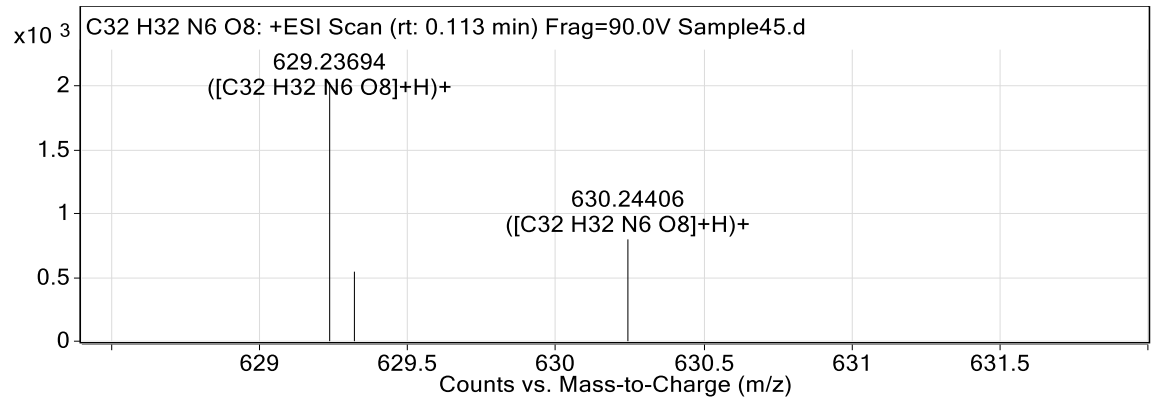
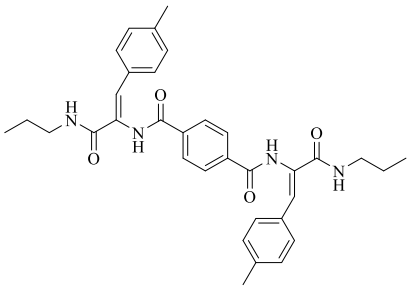


Figure 55. HRMS spectra for **6g**



N1,N4-bis((E)-3-oxo-3-(propylamino)-1-(p-tolyl)prop-1-en-2-yl)terephthalamide **(6h):** white powder (120 mg, yield 85%); mp 263-265 °C; IR (KBr) *v* 3332, 3204, 2963, 1640, 1612, 1524, 1468, 1278, 1186, 813 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.97 (s, 2H), 8.16-8.09 (m, 6H), 7.45 (d, J = 7.1 Hz, 4H), 7.19-7.13 (m, 6H) 3.14-3.08 (m, 4H), 2.26 (s, 6H), 1.50-1.43 (m, 4H), 0.85 (t, J = 7.2 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-*d*6) δ 165.1, 164.8, 138.2, 136.1, 135.9, 131.4, 129.4, 129.2, 129.1, 127.8, 40.9, 22.4, 20.8, 11.4 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{34}H_{38}N_4O_4$ 567.2971; found 567.2979.

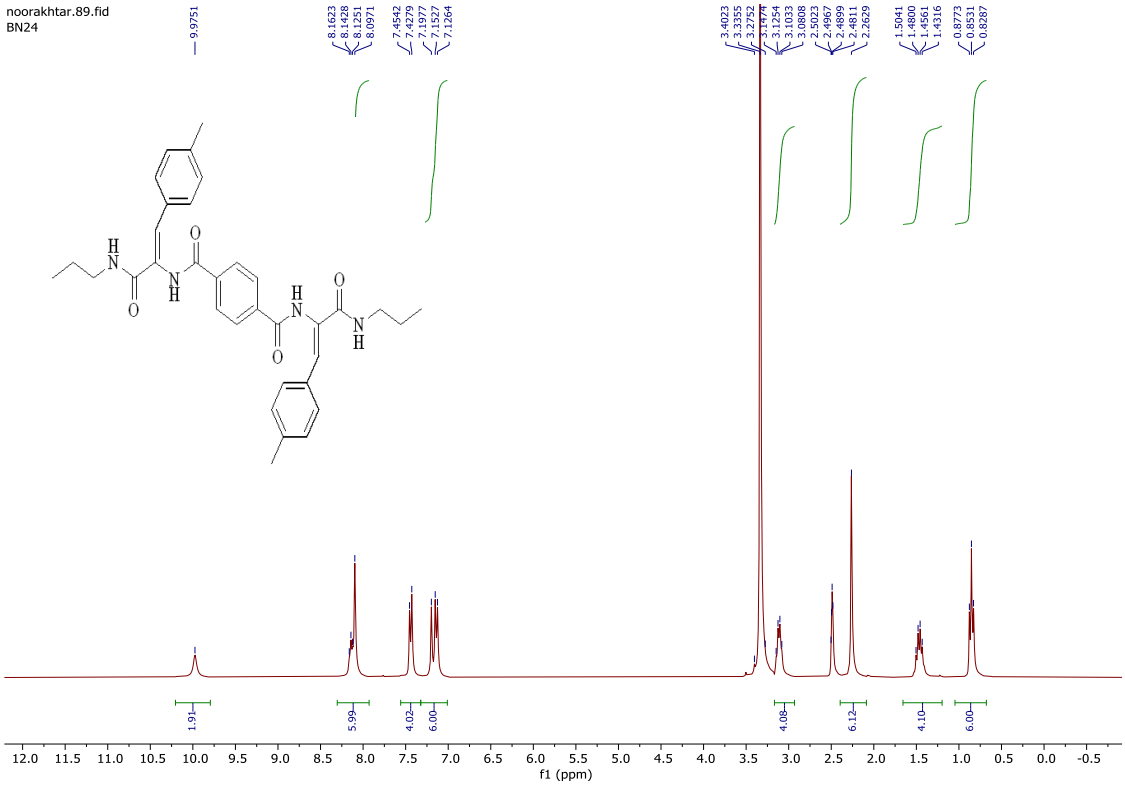


Figure 56. ^{1}H NMR spectra for **6h**

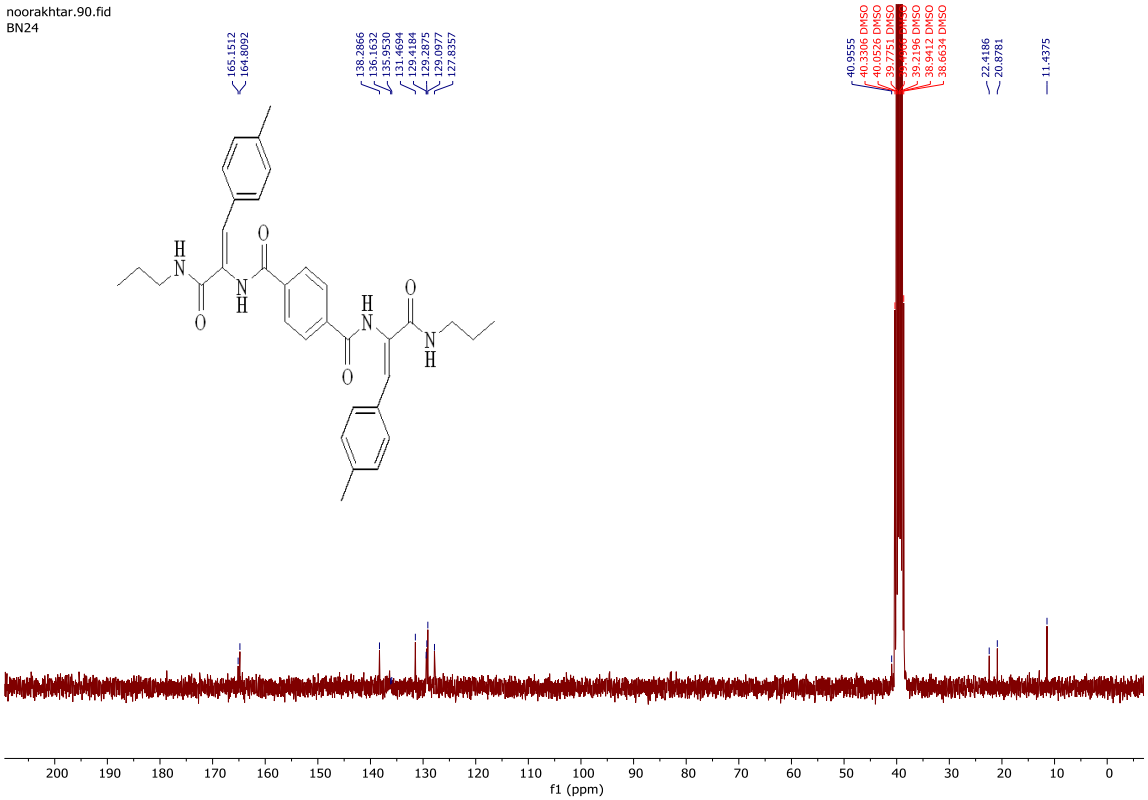


Figure 57. ^{13}C NMR spectra for **6h**

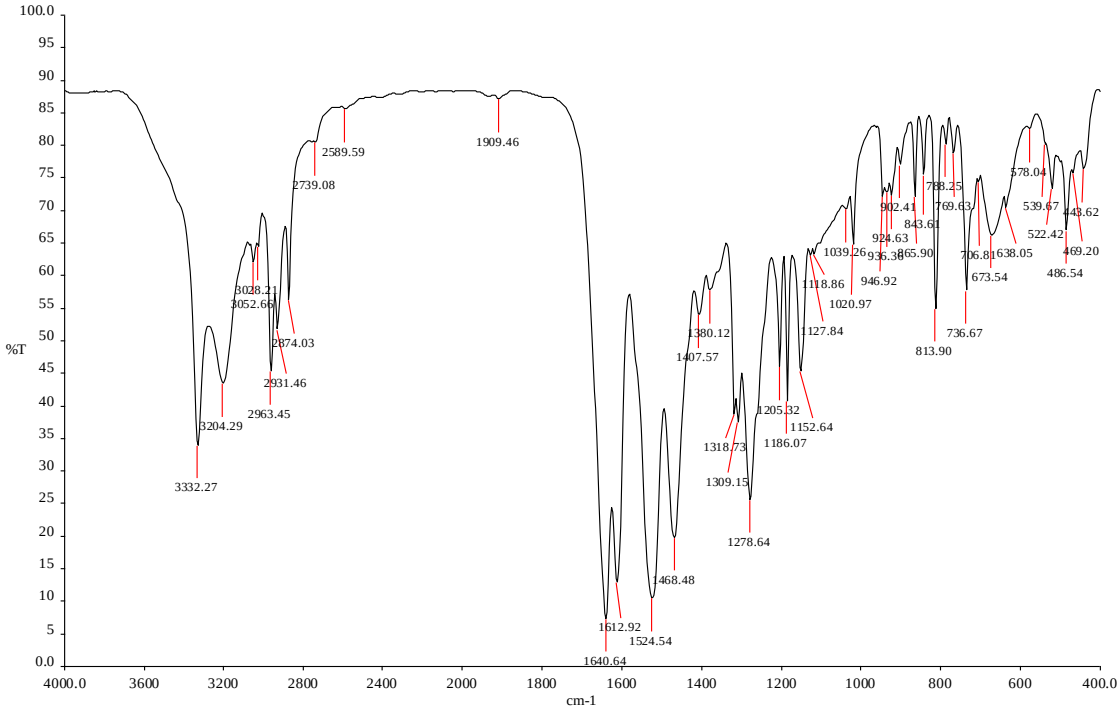


Figure 58. IR spectra for **6h**

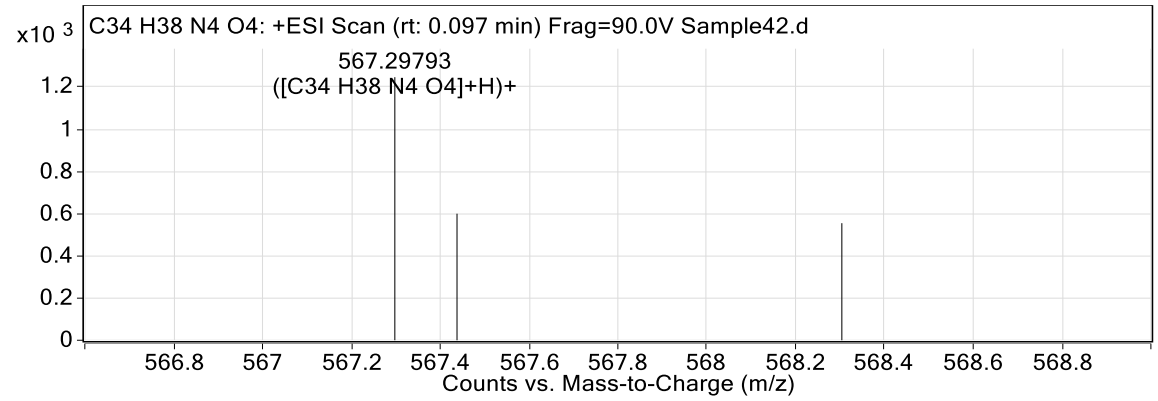
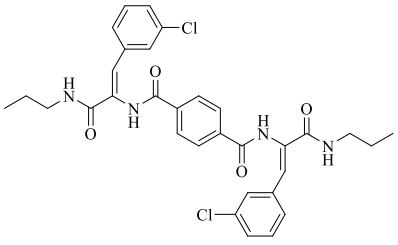


Figure 59. HRMS spectra for **6h**



N1,N4-bis((E)-1-(3-chlorophenyl)-3-oxo-3-(propylamino)prop-1-en-2yl)terephthalamide **(6i):** white powder (125 mg, yield 82%); mp 264-266 °C; IR (KBr) *v* 3324, 3234, 2961, 1657, 1618, 1524, 1469, 1281, 1150, 886 cm^{-1}; ^{1}H

NMR (300 MHz, DMSO-d_6) δ 10.05 (s, 2H), 8.24 (t, J = 5.9 Hz, 2H), 8.07 (s, 4H), 7.62 (m, 2H), 7.49-7.43 (m, 2H),7.39-7.32 (m, 4H), 7.18 (s, 2H) 3.15-3.08 (m, 4H), 1.53-1.45 (m, 4H), 0.89 (t, J = 7.3 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.2, 164.4, 136.5, 136.2, 133.1, 131.5, 130.2, 128.5, 128.1, 127.9, 127.8, 127.1, 40.9, 22.3, 11.4 ppm; Anal. calcd for $C_{32}H_{32}Cl_2N_4O_4$: C, 63.26; H, 5.31; N, 9.22. Found: C, 63.15; H, 4.94; N, 8.96.

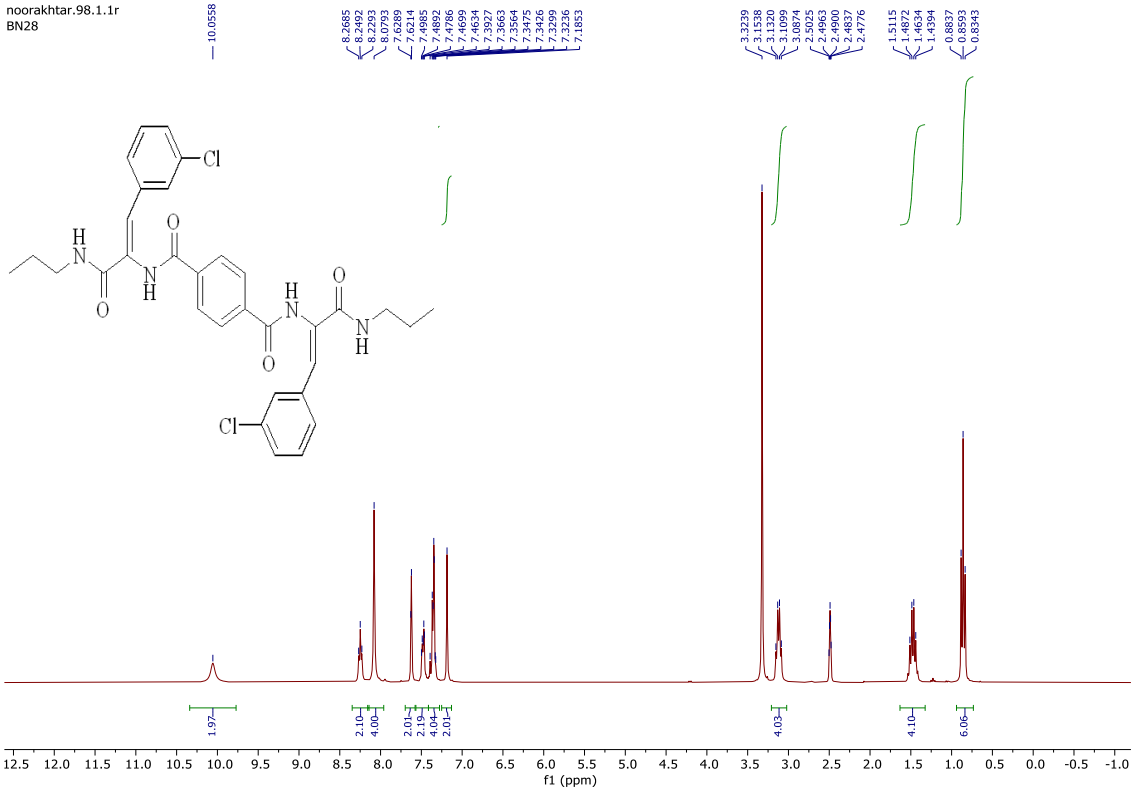


Figure 60. ^{1}H NMR spectra for **6i**

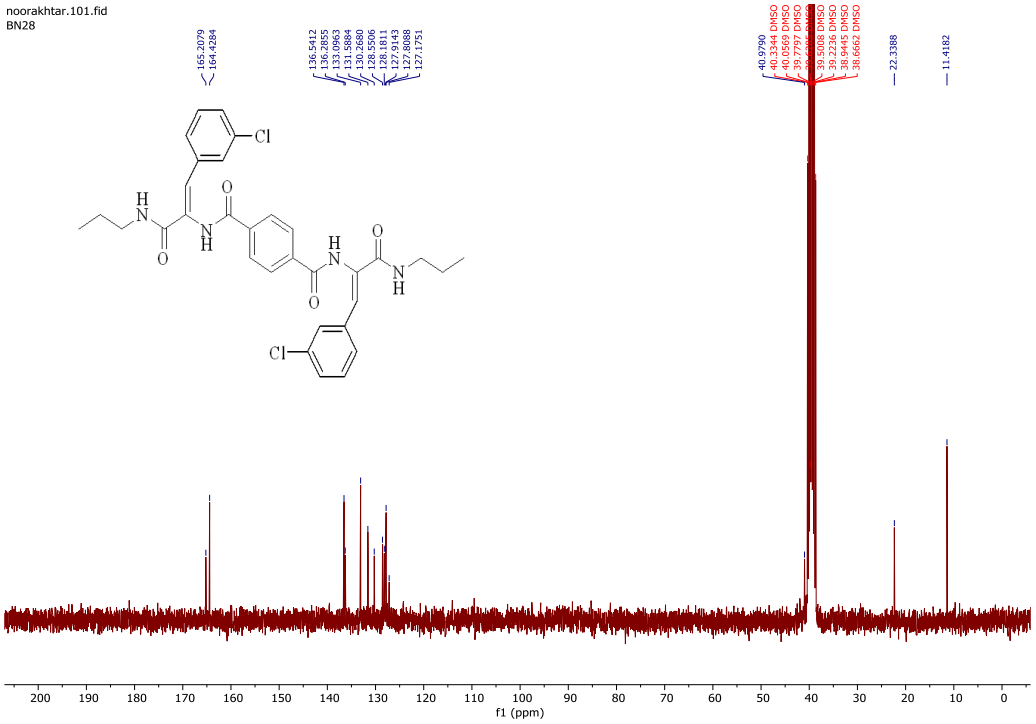


Figure 61. ^{13}C NMR spectra for **6i**

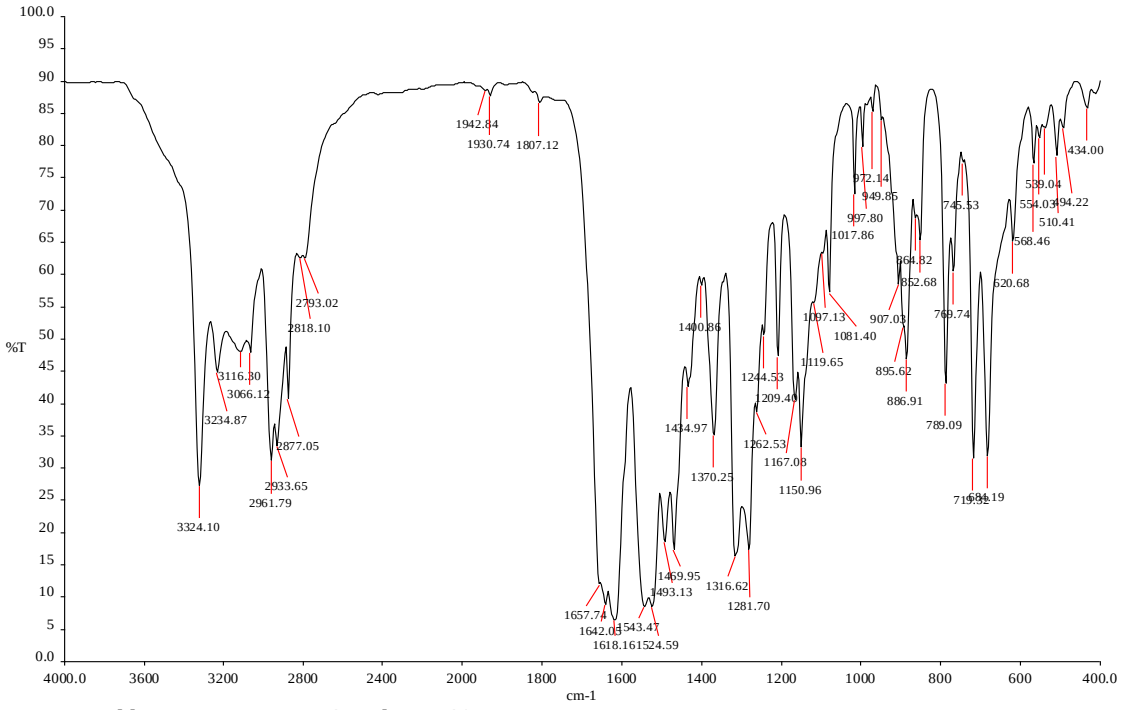
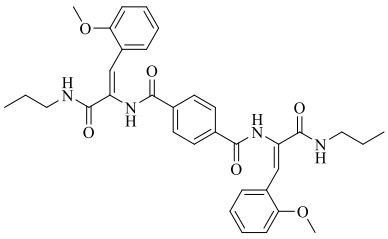


Figure 62. IR spectra for **6i**



N1,N4-bis((E)-1-(2-methoxyphenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6j):** white powder (134 mg, yield 90%); mp 263-265 °C; IR (KBr) *v* 3320, 3192, 2954, 1639, 1614, 1577, 1491, 1250, 1027, 944, 753 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.85 (s, 2H), 8.09 (t, J = 5.8 Hz, 2H), 8.01 (s, 4H), 7.46-7.43 (m, 2H), 7.38 (s, 2H),7.29-7.23 (m, 2H), 7.04-7.01(m, 2H), 6.84-6.79 (m, 2H), 3.81 (s, 6H), 3.13-3.07 (m, 4H), 1.52-1.40 (m, 4H), 0.84 (t, J = 7.4 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.2, 164.7, 157.1, 136.2, 130.1, 130.0, 128.4, 127.7, 123.7, 122.8, 120.1, 111.2, 55.5, 40.9, 22.3, 11.4 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{34}H_{38}N_6O_6$ 599.2870; found 599.2896.

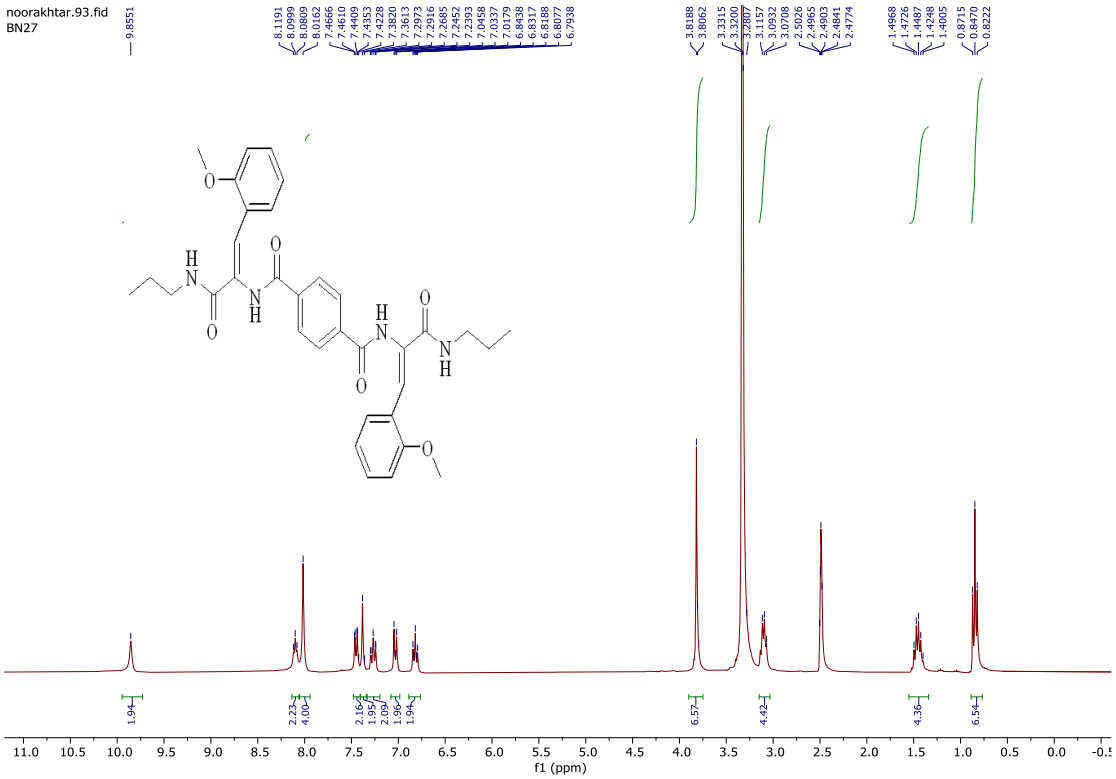


Figure 63. ^{1}H NMR spectra for **6j**

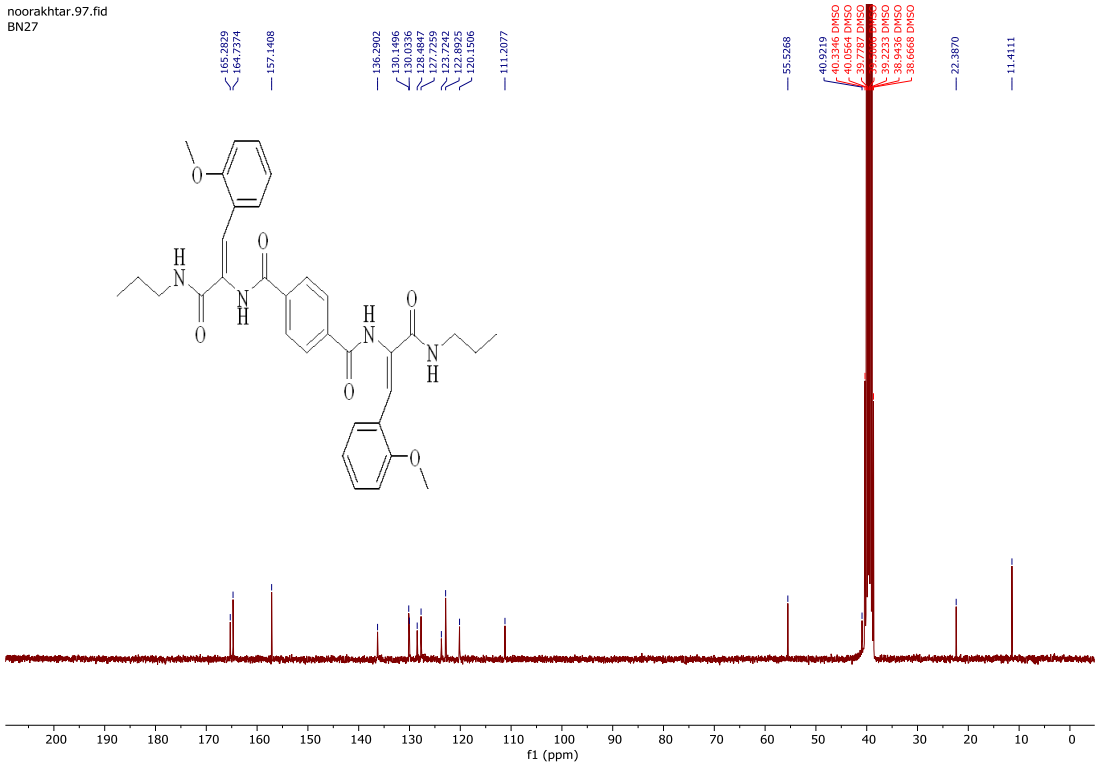


Figure 64. ^{13}C NMR spectra for **6j**

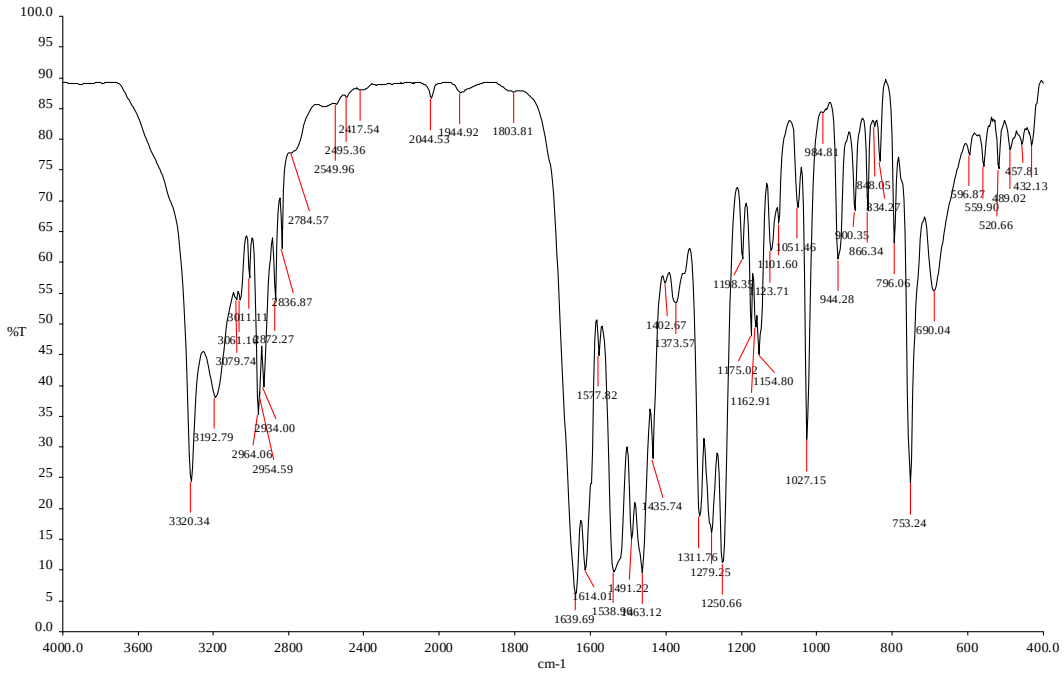


Figure 65. IR spectra for **6j**

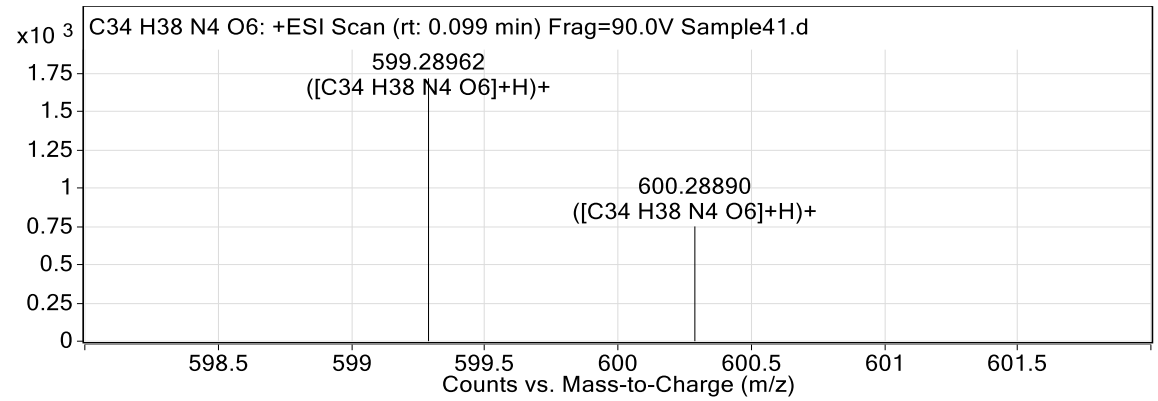
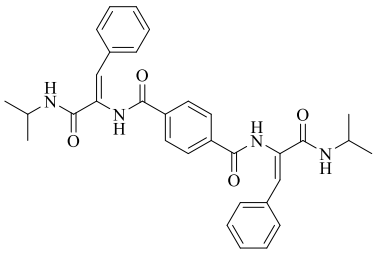


Figure 66. HRMS spectra for **6j**



N1,N4-bis((E)-3-(isopropylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6k):** white powder (97 mg, yield 72%); mp 257-259 °C; IR (KBr) *v* 3317, 3250, 2972, 1633, 1524, 1476, 731273, 1172, 928, 691, 563 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.95 (s, 2H), 8.09 (s, 4H), 7.94-7.91 (d, J = 9.4 Hz, 2H), 7.56-7.53 (m, 4H), 7.43-7.25 (m, 6H), 7.13 (s, 2H), 4.03-3.94 (m, 2H), 1.13 (d, J = 6.9 Hz, 12H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.0, 164.0, 136.3, 134.3, 130.4, 129.8, 129.1, 128.4, 128.2, 127.7, 40.9, 22.2 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{32}H_{34}N_4O_4$ 539.2658; found 539.2685.

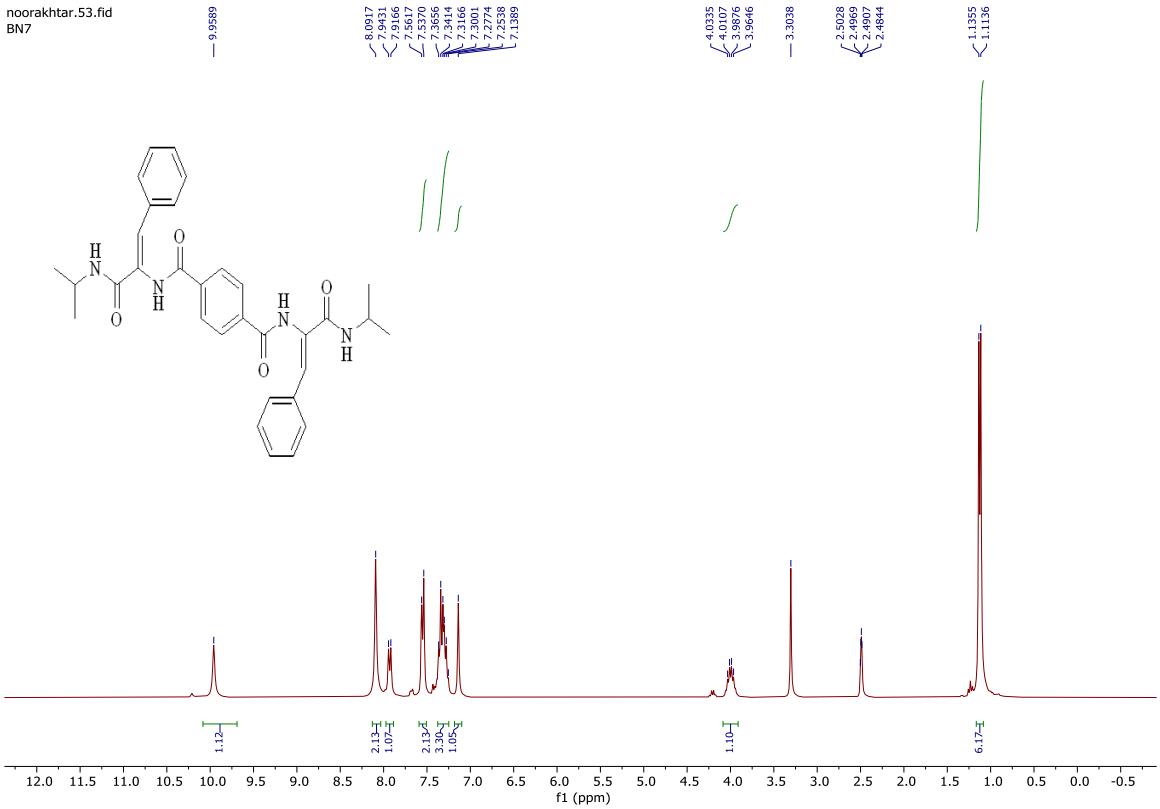


Figure 67. ^{1}H NMR spectra for **6k**

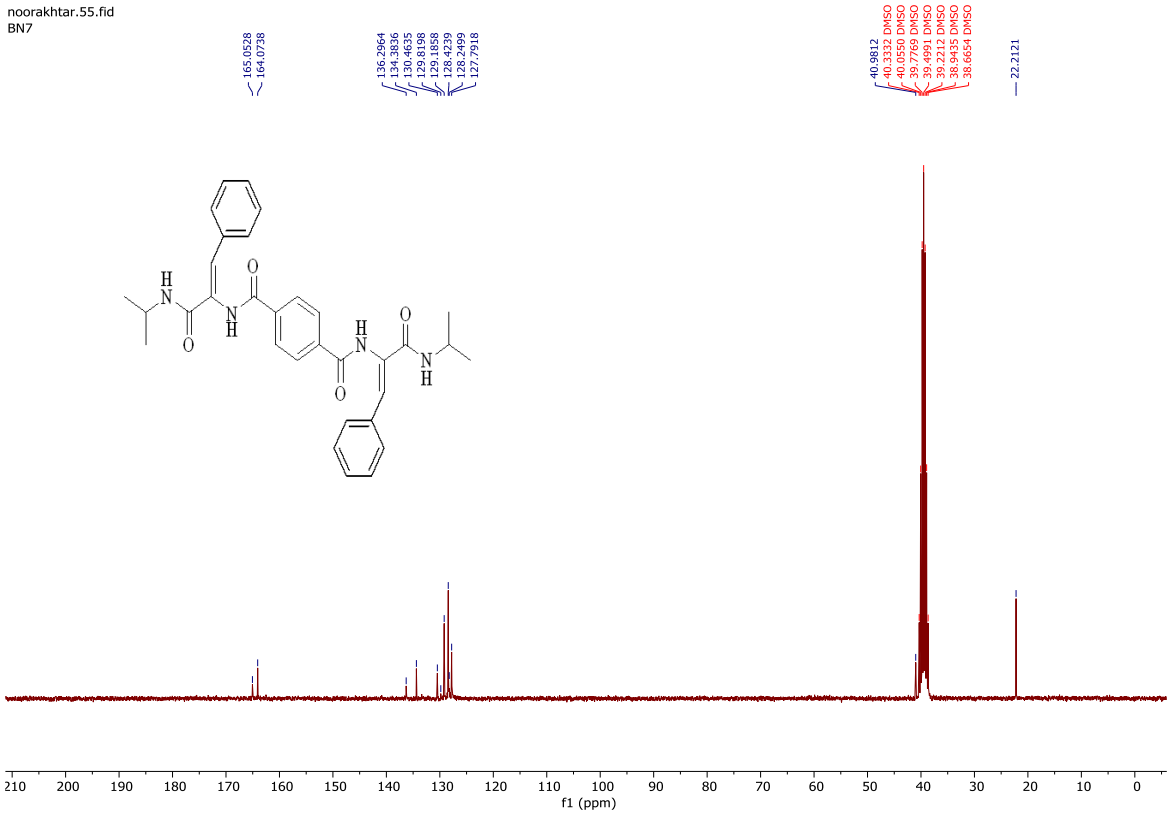


Figure 68. ^{13}C NMR spectra for **6k**

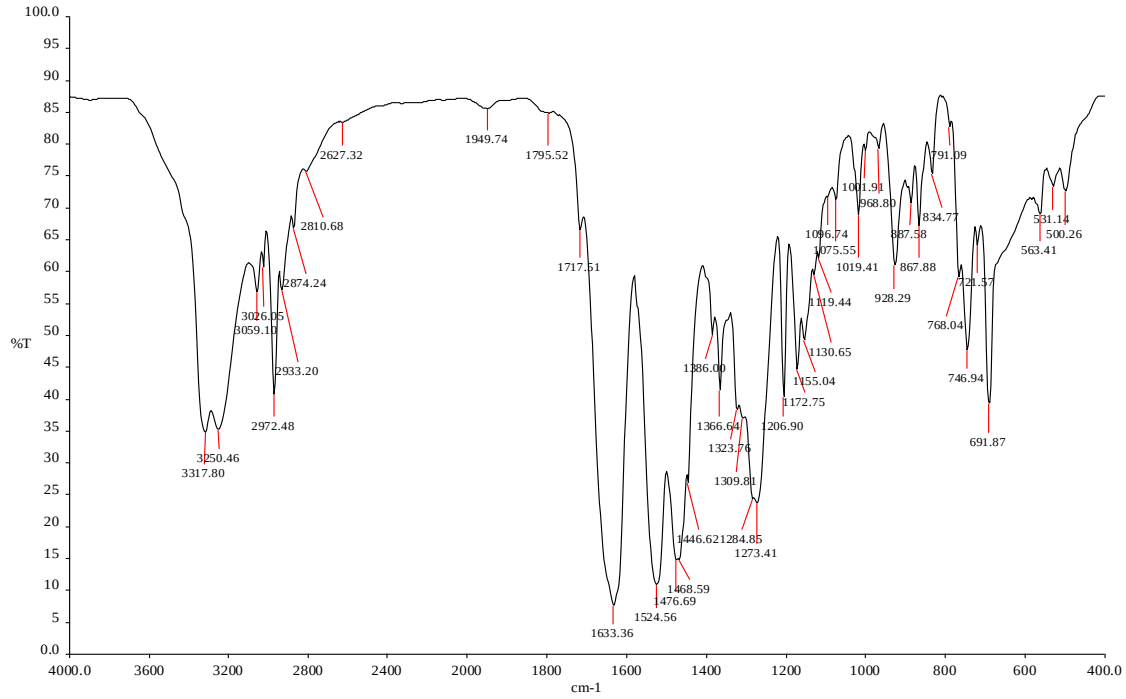


Figure 69. IR spectra for **6k**

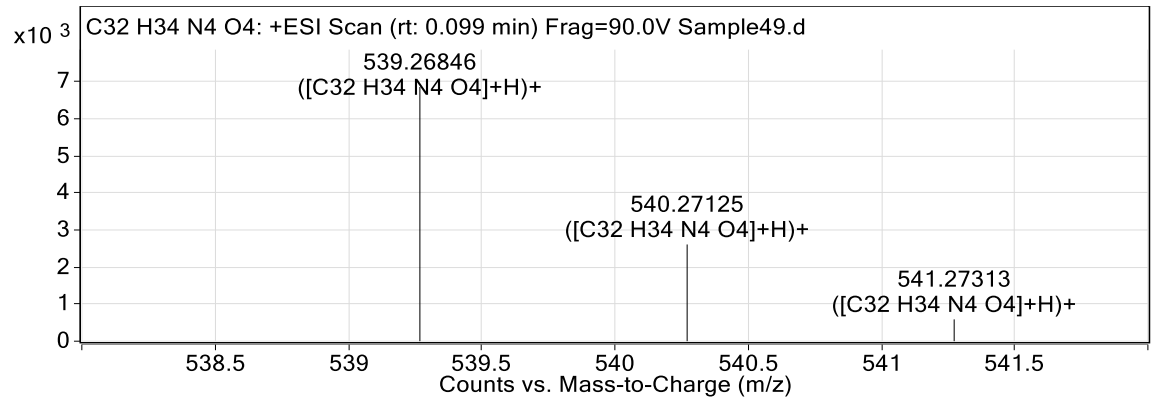
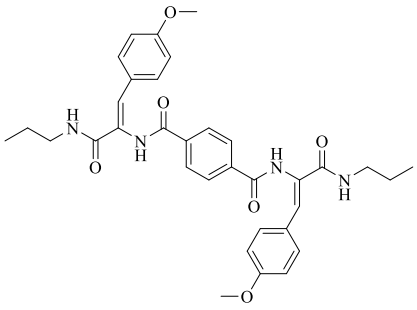


Figure 70. HRMS spectra for **6k**



N1,N4-bis((E)-1-(4-methoxyphenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6l):** white powder (130 mg, yield 87%); mp 262-265 °C; IR (KBr) *v* 3322, 3199, 2954, 1640, 1539, 1478, 1255, 1029, 933, 826 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.95 (s, 2H), 8.12-8.06 (m, 6H), 7.53 (d, J = 8.37 Hz, 4H), 7.21 (s, 2H), 6.91 (d, J = 8.34 Hz, 4H), 3.73 (s, 6H), 3.14-3.08 (m, 4H), 1.50-1.40 (m, 4H), 0.85 (t, J = 7.38 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 164.8, 159.5, 142.8, 136.3, 130.9, 129.1, 129.0, 128.0, 127.8, 126.6, 113.9, 55.1, 40.9, 22.4, 11.4 ppm; Anal. calcd for $C_{34}H_{38}N_4O_6$: C, 68.21; H, 6.40; N, 9.36. Found: C, 68.52; H, 6.20; N, 8.98.

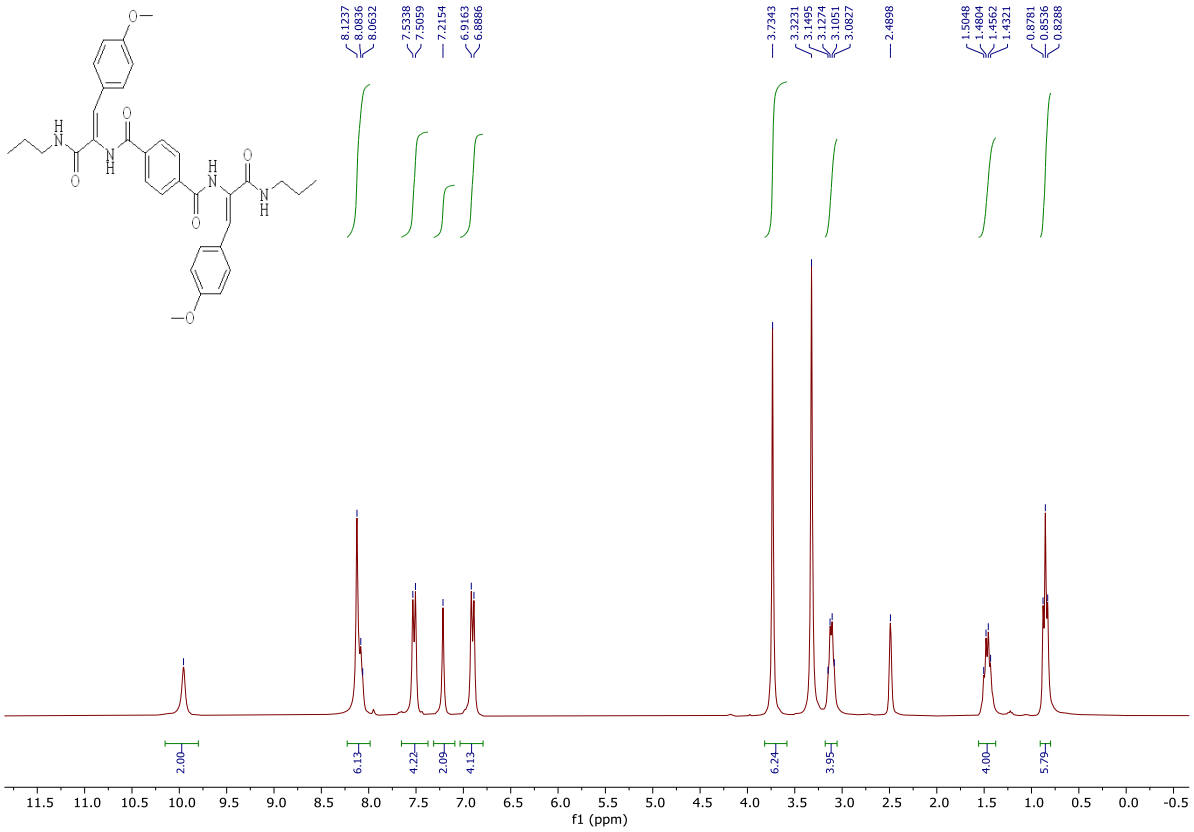


Figure 71. ^{1}H NMR spectra for **6l**

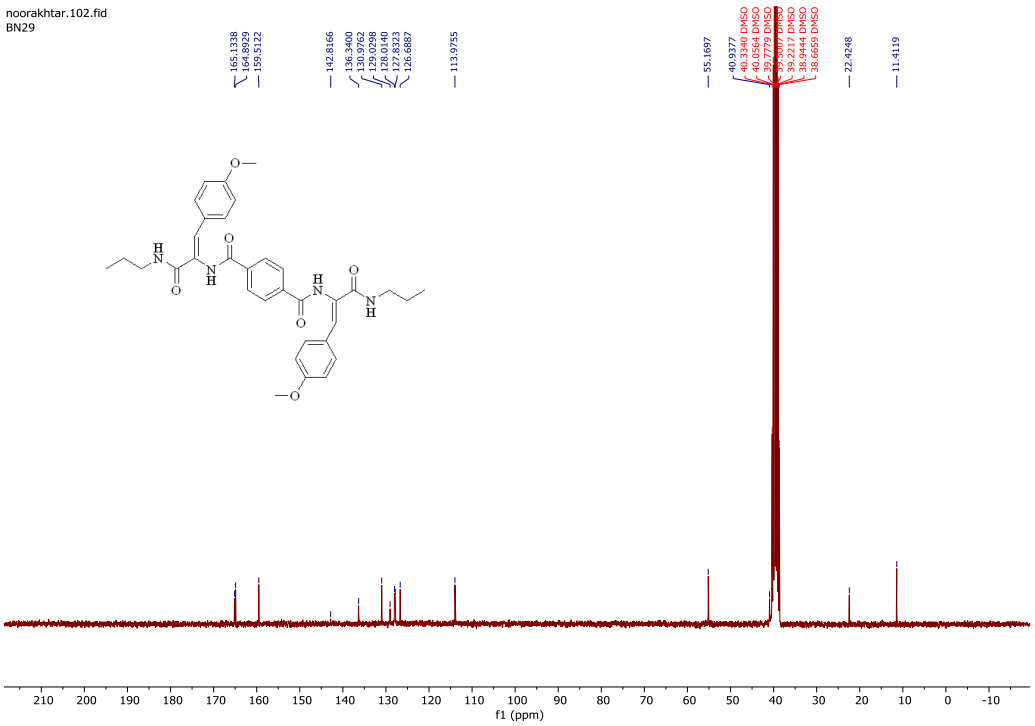


Figure 72. ^{13}C NMR spectra for **6l**

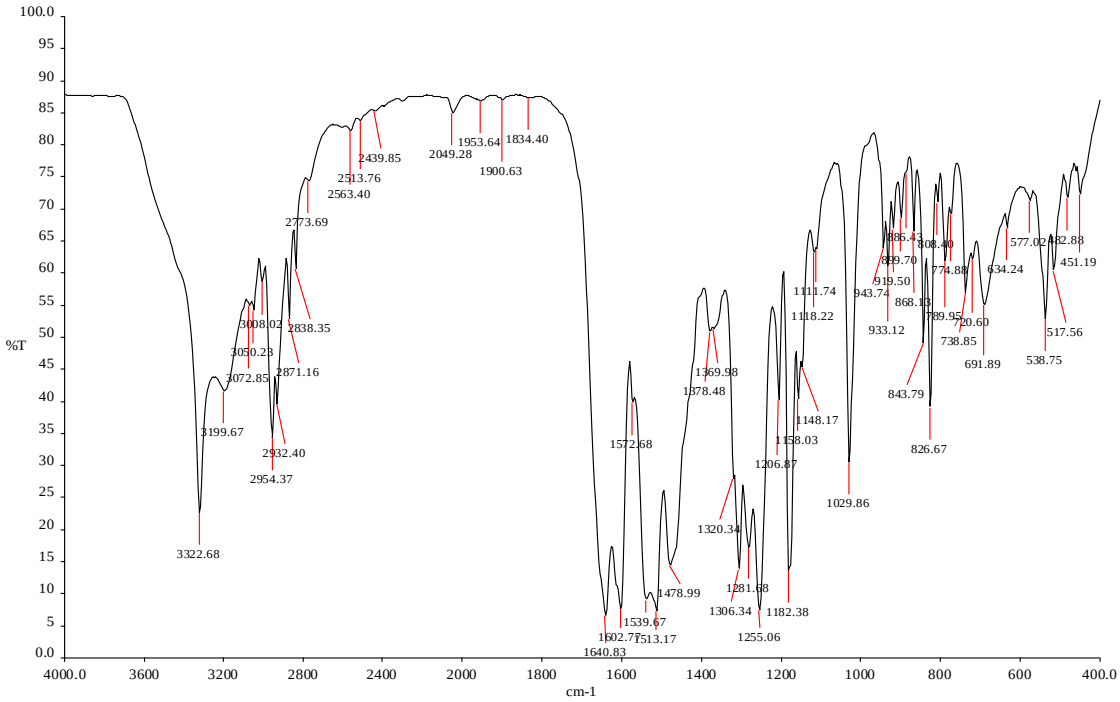
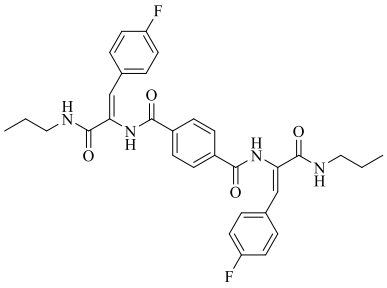


Figure 73. IR spectra for **6l**



N1,N4-bis((E)-1-(4-fluorophenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6m):** white powder (110 mg, yield 76%); mp 266-268 °C; IR (KBr) ν 3317, 3184, 2955, 1641, 1510, 1478, 1230, 1161, 831cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.99 (s, 2H), 8.16 (s, 2H), 8.07-8.02 (m, 4H), 7.59-7.56 (m, 4H), 7.18-7.17 (m, 4H), 7.15 (s, 2H), 3.12-3.05 (m, 4H), 1.47-1.39 (m, 4H), 0.84 (t, J = 4.53 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 164.6, 163.4 (d, $^{1}J_{C\text{-}F}$ = 245 Hz), 136.2, 131.4, 131.3, 130.8, 130.0, 127.8, 127.6, 115.5, 115.3, 40.9, 22.3, 11.4 ppm; Anal. calcd for $C_{32}H_{32}F_2N_4O_4$: C, 66.89; H, 5.61; N, 9.75. Found: C, 66.87; H, 5.34; N, 9.44.

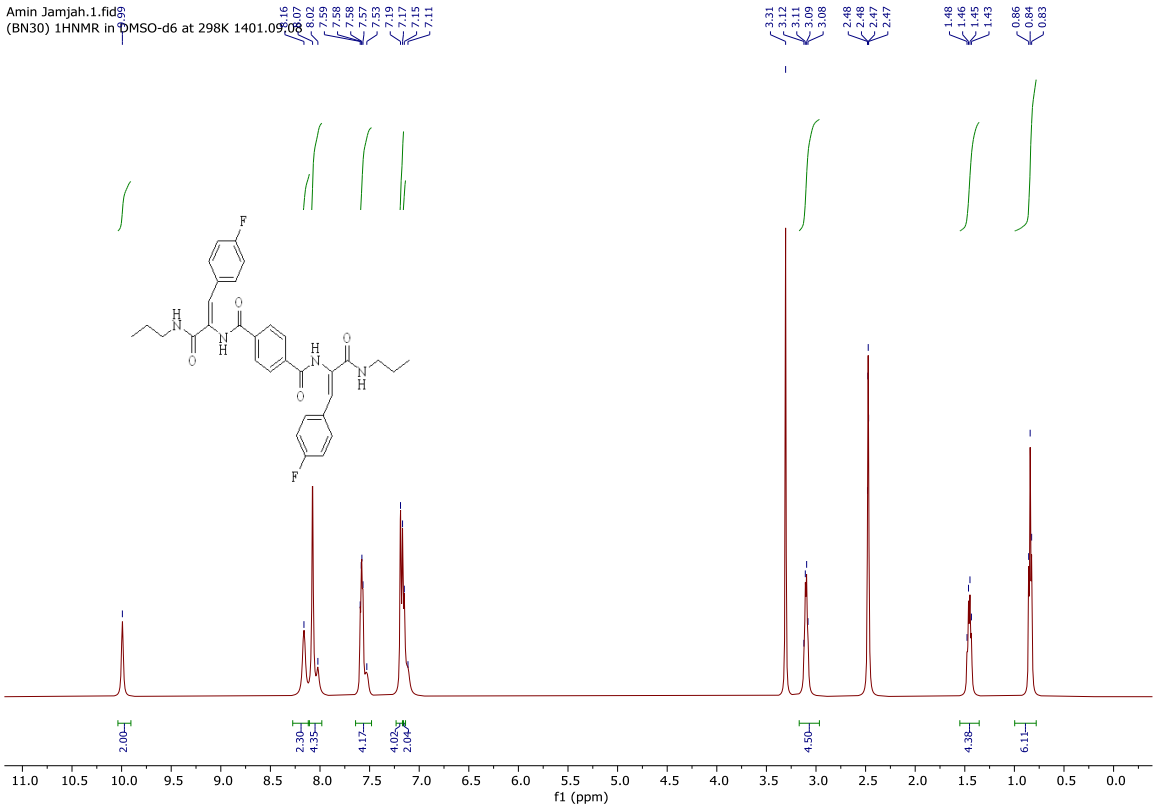


Figure 74. ^{1}H NMR spectra for **6m**

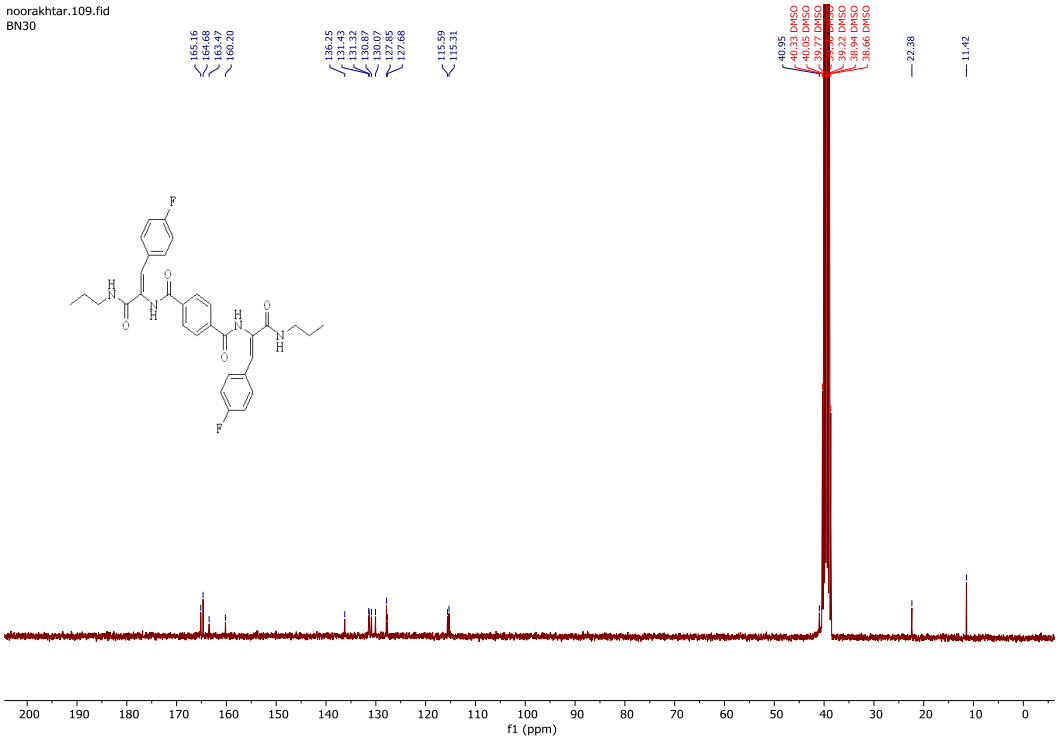


Figure 75. ^{13}C NMR spectra for **6m**

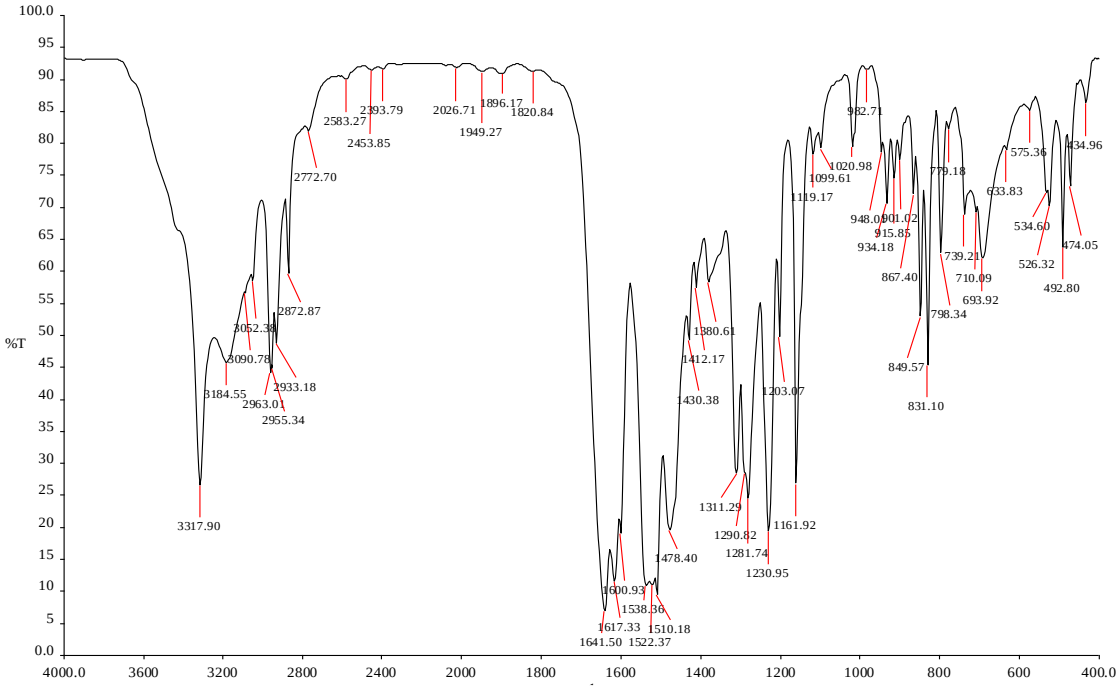
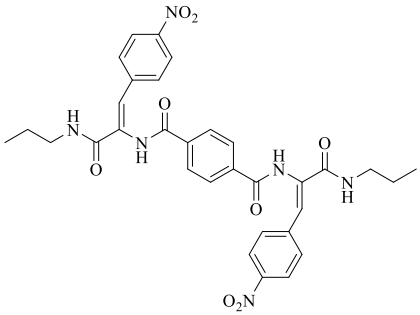


Figure 76. IR spectra for **6m**



N1,N4-bis((E)-1-(4-nitrophenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6n):** white powder (129 mg, yield 82 %); mp 259-260 °C; IR (KBr) *v* 3313, 3113, 1641, 1622, 1518, 1345, 1283, 1149, 857, 748, 687 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.17 (brs, 2H), 8.36-8.32 (t, J = 5.4 Hz, 2H), 8.20-8.14 (m, 4H), 8.06-8.05 (m, 4H), 7.79-7.74 (m, 4H), 7.18-7.17 (m, 2H), 3.16-3.10 (m, 4H), 1.55-1.45 (m, 4H), 0.89-0.83 (t, J = 7.3 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.0, 164.4, 146.4, 141.5, 133.6, 131.7, 130.0, 127.9, 125.3, 123.5, 41.0, 22.2, 11.4 ppm.

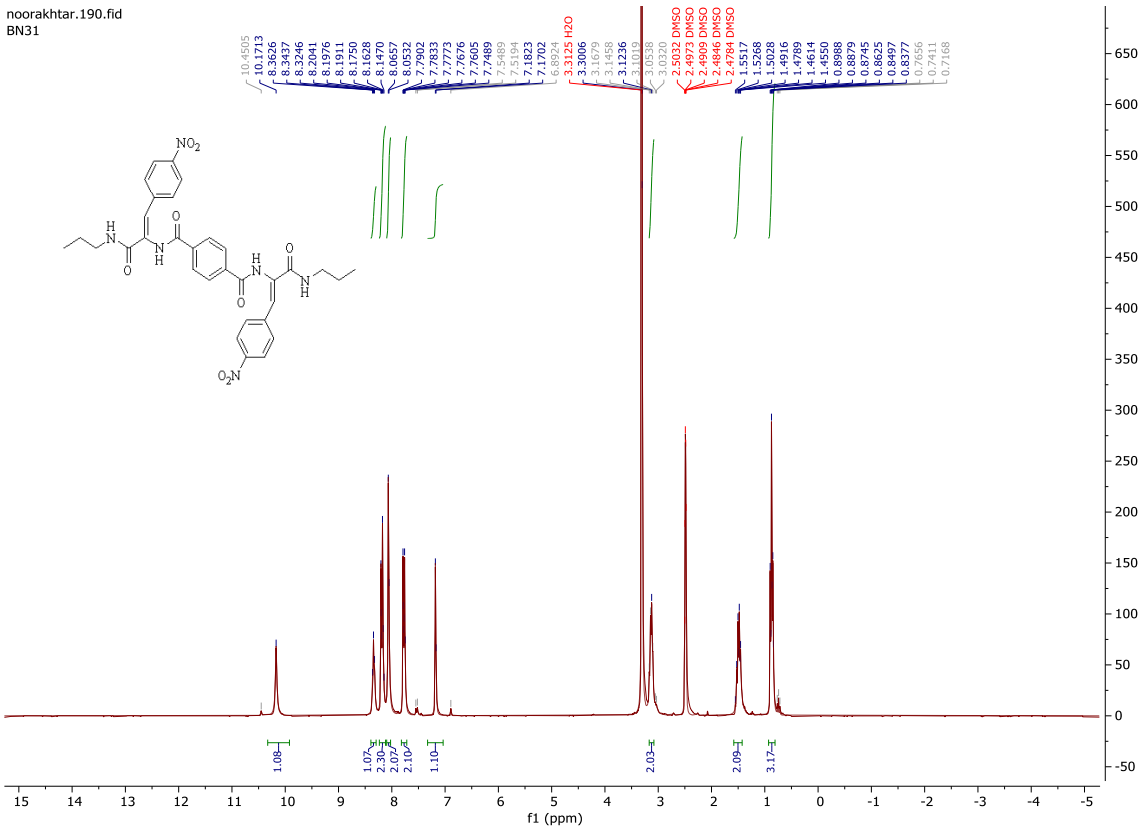


Figure 77. ^{1}H NMR spectra for **6n**

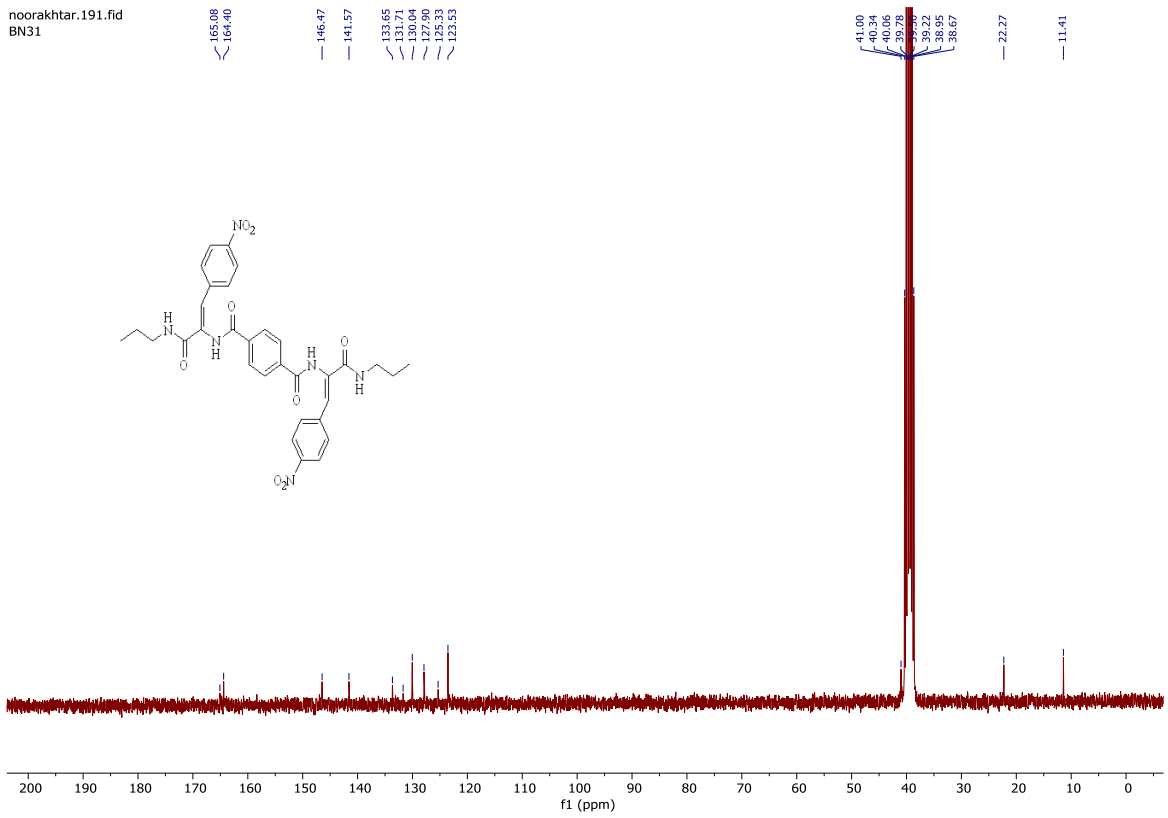


Figure 78. ^{13}C NMR spectra for **6n**

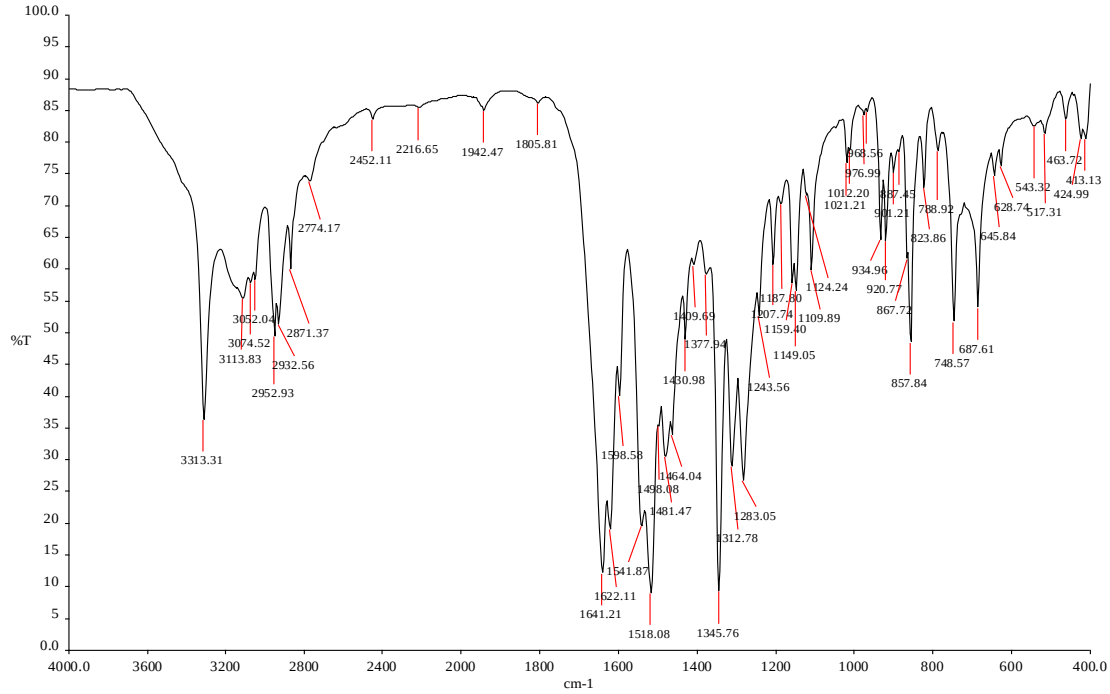
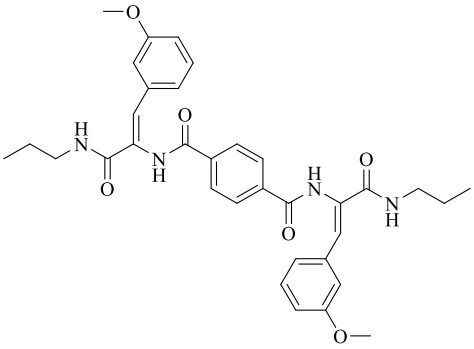


Figure 79. IR spectra for **6n**



N1,N4-bis((E)-1-(3-methoxyphenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6o):** white powder (119 mg, yield 80%); mp 237-239 ℃; IR (KBr) *v* 3307, 3188, 2954, 1639, 1615, 1540, 1493, 1255, 1038, 789, 687 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.0 (s, 2H), 8.17 (s, 2H), 8.09 (s, 4H), 7.24-7.21 (t, J = 4.7 Hz, 2H), 7.19-7.13 (m, 4H), 7.09 (d, J = 4.5 Hz, 2H), 6.86-6.84 (m, 2H), 3.60 (s, 6H), 3.12-3.08 (m, 4H), 1.49-1.42 (m, 4H), 0.84 (t, J = 4.4 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.1, 164.6, 159.0, 136.2, 135.5, 130.4, 129.4, 128.8, 127.7, 121.9, 114.5, 114.1, 54.8, 40.9, 22.3, 11.4 ppm; Anal. calcd for $C_{34}H_{38}N_4O_6$: C, 68.21; H, 6.40; N, 9.36; Found: C, 68.03; H, 6.29; N, 9.25.

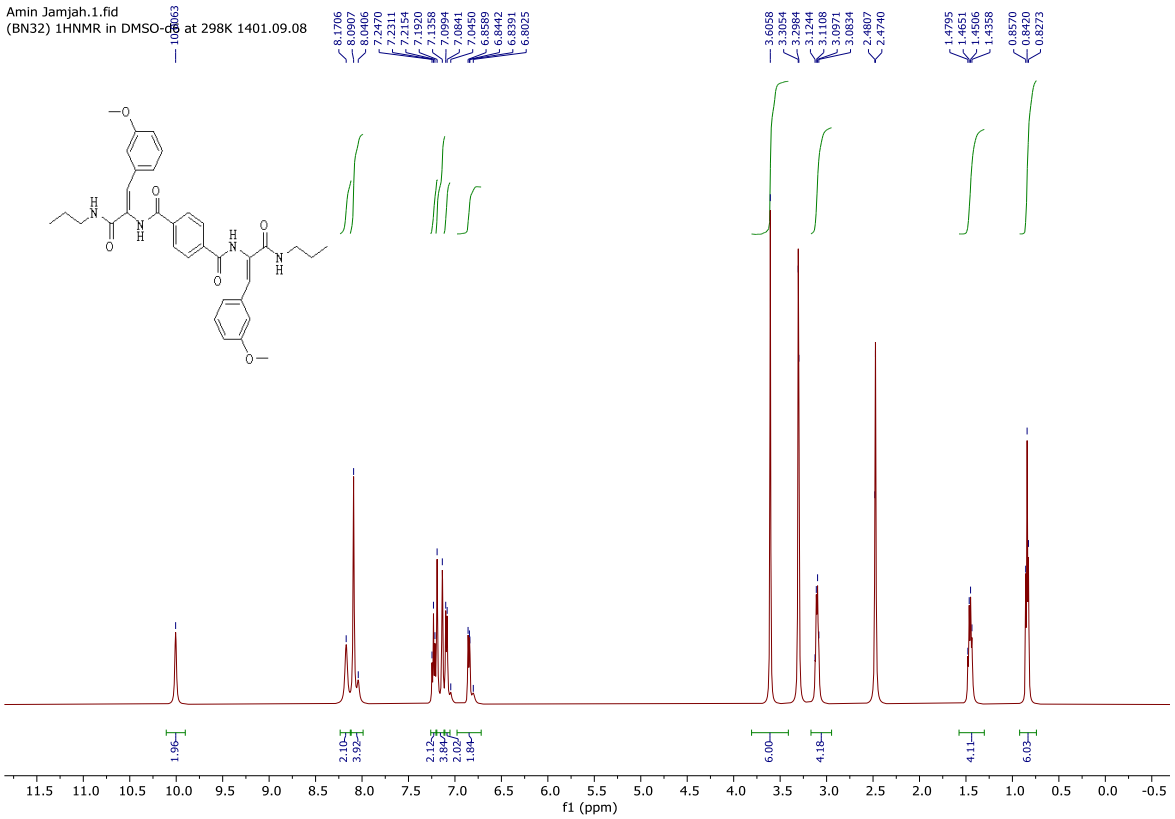


Figure 80. ^{1}H NMR spectra for **6o**

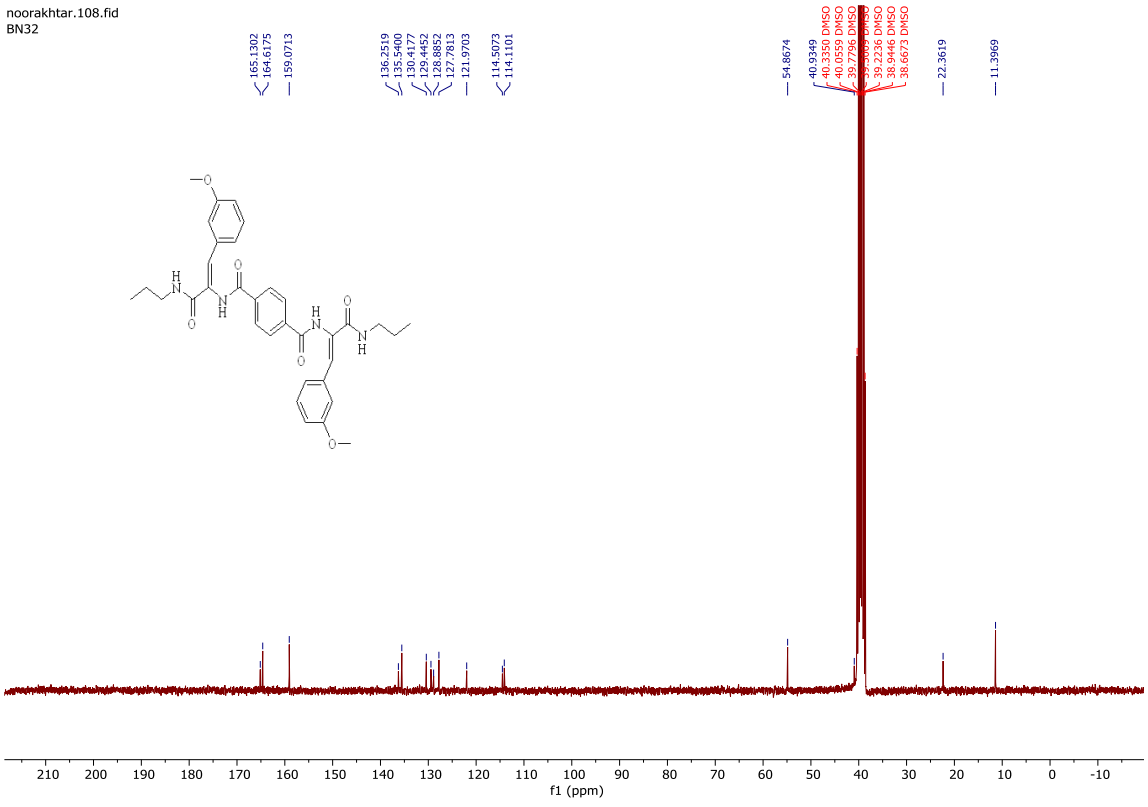


Figure 81. ^{13}C NMR spectra for **6o**

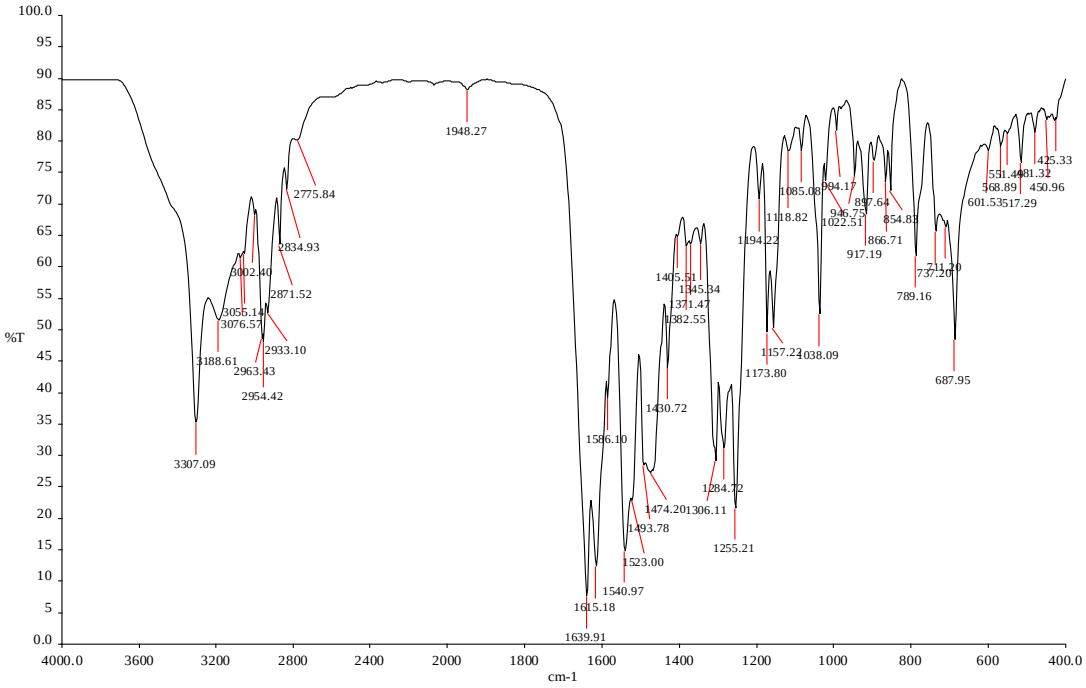
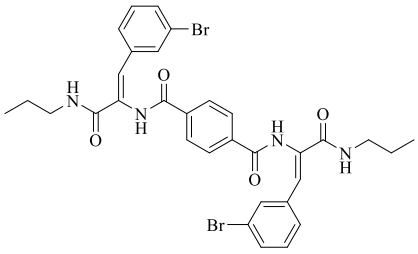


Figure 82. IR spectra for **6o**



N1,N4-bis((E)-1-(3-bromophenyl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6p):** white powder (149 mg, yield 86%); mp 260-263 ℃; IR (KBr) *v* 3323, 3240, 2963, 1641, 1622, 1544, 1524, 1493, 1315, 1281, 1151, 877, 719 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 10.05 (s, 2H), 8.22 (s, 2H), 8.07 (s, 4H), 7.77 (s, 2H), 7.52-7.46 (m, 4H), 7.31-7.28 (m, 2H), 7.17 (s, 2H) 3.12 (m, 4H), 1.49-1.47 (m, 4H), 0.84 (t, J = 5.3 Hz, 6H) ppm; 13C NMR (75 MHz, DMSO-d_6) δ 165.0, 164.0, 149.8, 144.4, 137.9, 136.4, 127.8, 127.3, 122.7, 117.4, 113.7, 112.1, 40.9, 22.3, 11.3 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{32}H_{32}Br_2N_4O_4$ 697.0848; found 697.0882.

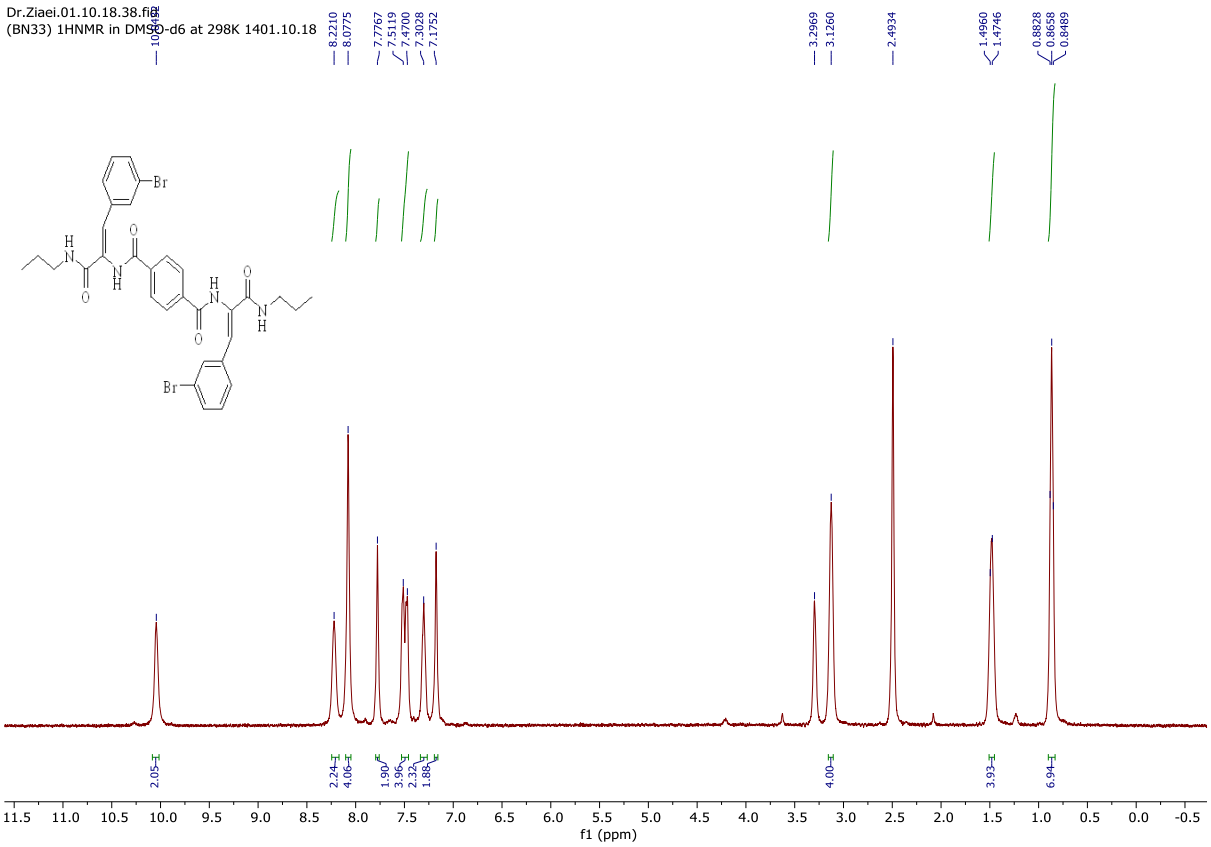


Figure 83. ^{1}H NMR spectra for **6p**

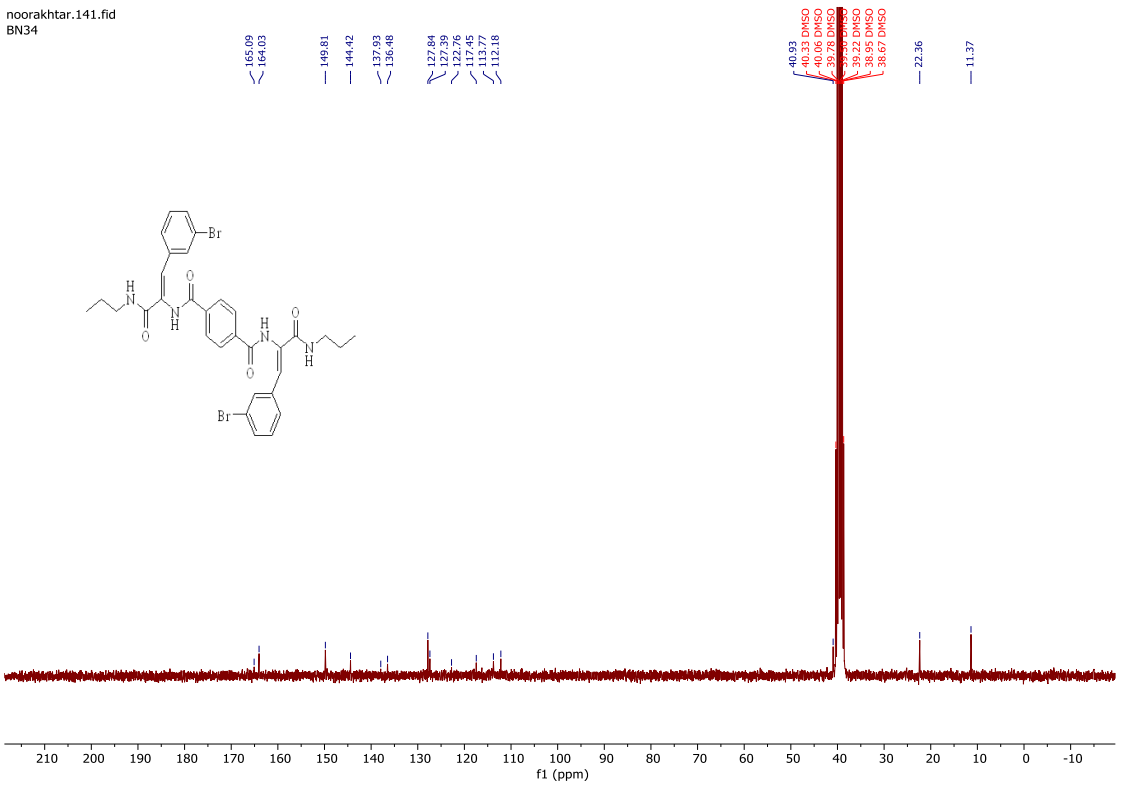


Figure 84. ^{13}C NMR spectra for **6p**

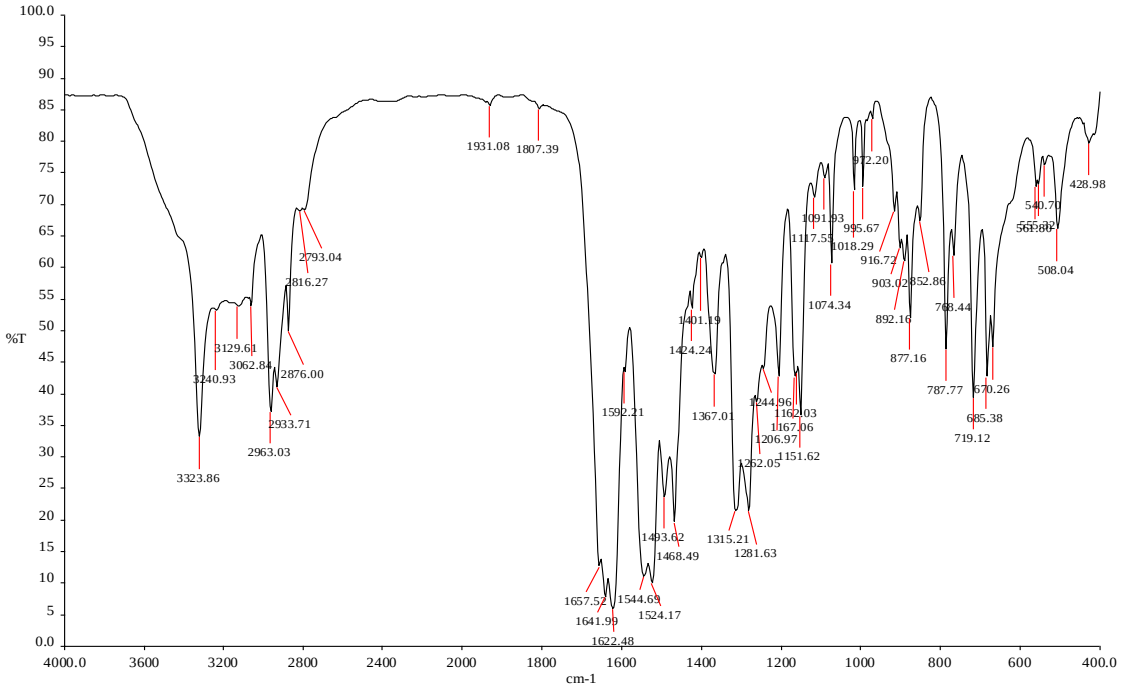


Figure 85. IR spectra for **6p**

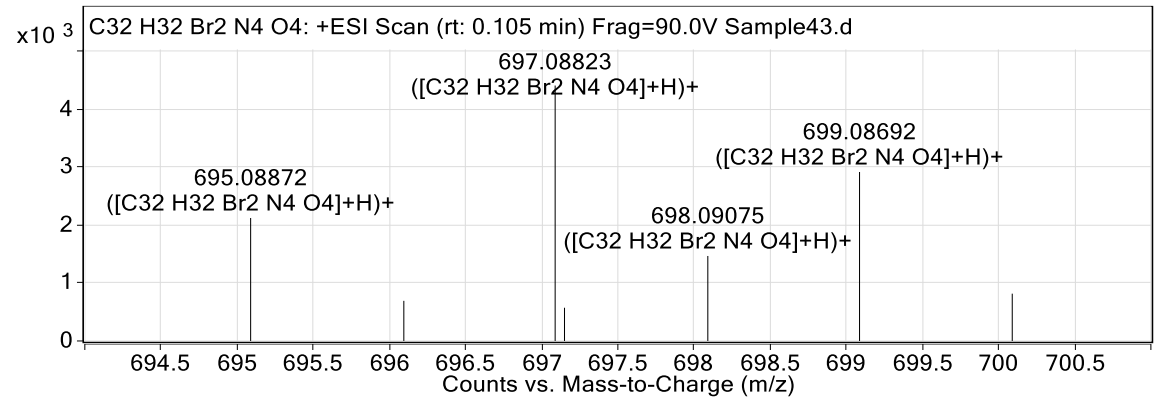
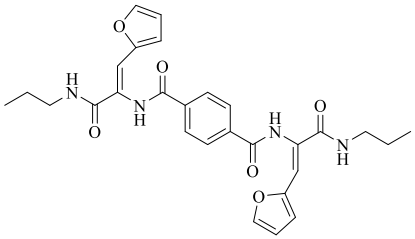


Figure 86. HRMS spectra for **6p**



N1,N4-bis((E)-1-(furan-2-yl)-3-oxo-3-(propylamino)prop-1-en-2-yl)terephthalamide **(6q):** white powder (110 mg, yield 85%); mp 265-267 °C; IR (KBr) *v* 3430, 3309, 2963, 1673, 1682, 1650, 1631, 1523, 1281, 1152, 752, 718 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 9.89 (s, 2H), 8.16-8.12 (m, 6H), 7.71 (d, J = 1.8 Hz, 2H), 7.15 (s, 2H), 6.68-6.64 (m, 2H), 6.56-6.55 (m, 2H), 3.15-3.07 (m, 4H), 1.52-1.40 (m, 4H), 0.84 (t, J = 7.3 Hz,

6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.0, 164.0, 149.8, 144.4, 136.4, 127.8, 127.3, 117.4, 113.7, 112.1, 40.9, 22.3, 11.3 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{28}H_{30}N_4O_6$ 519.2244; found 519.2255.

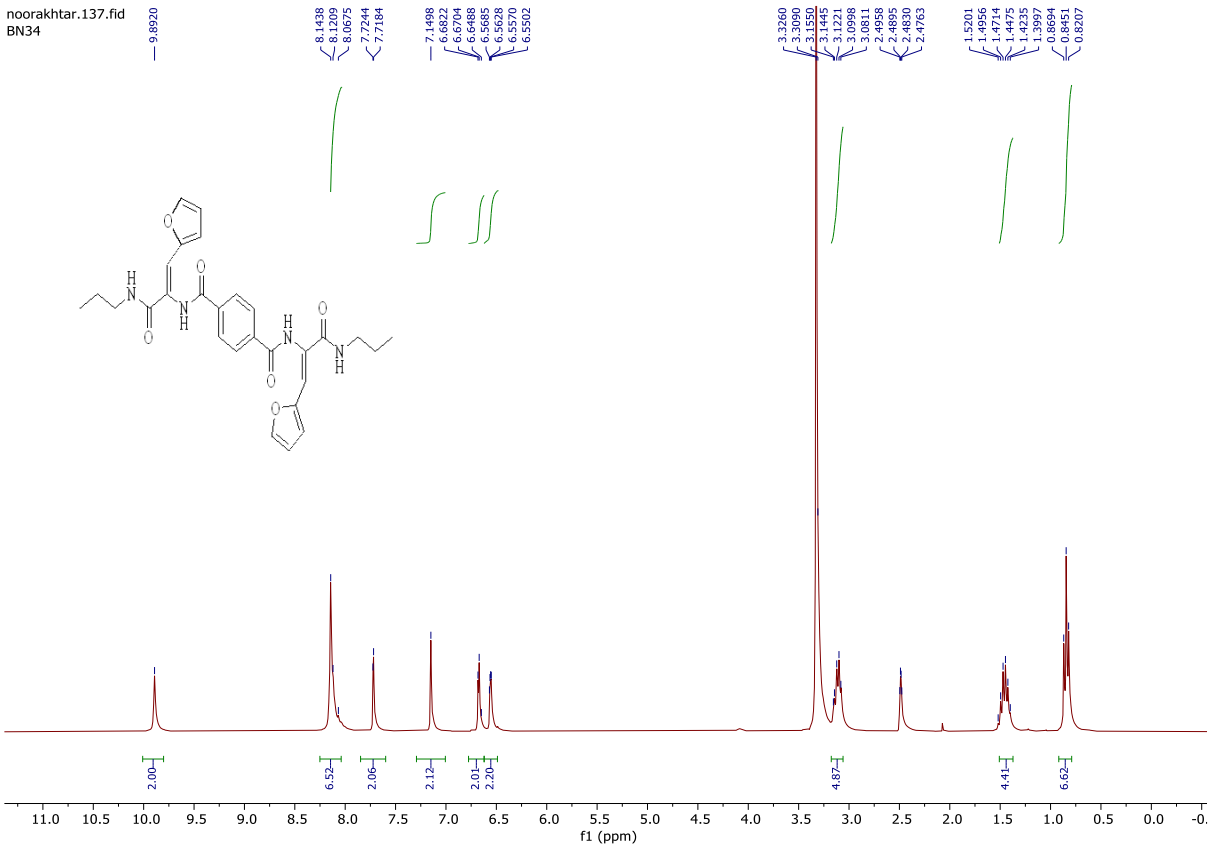


Figure 87. ^{1}H NMR spectra for **6q**

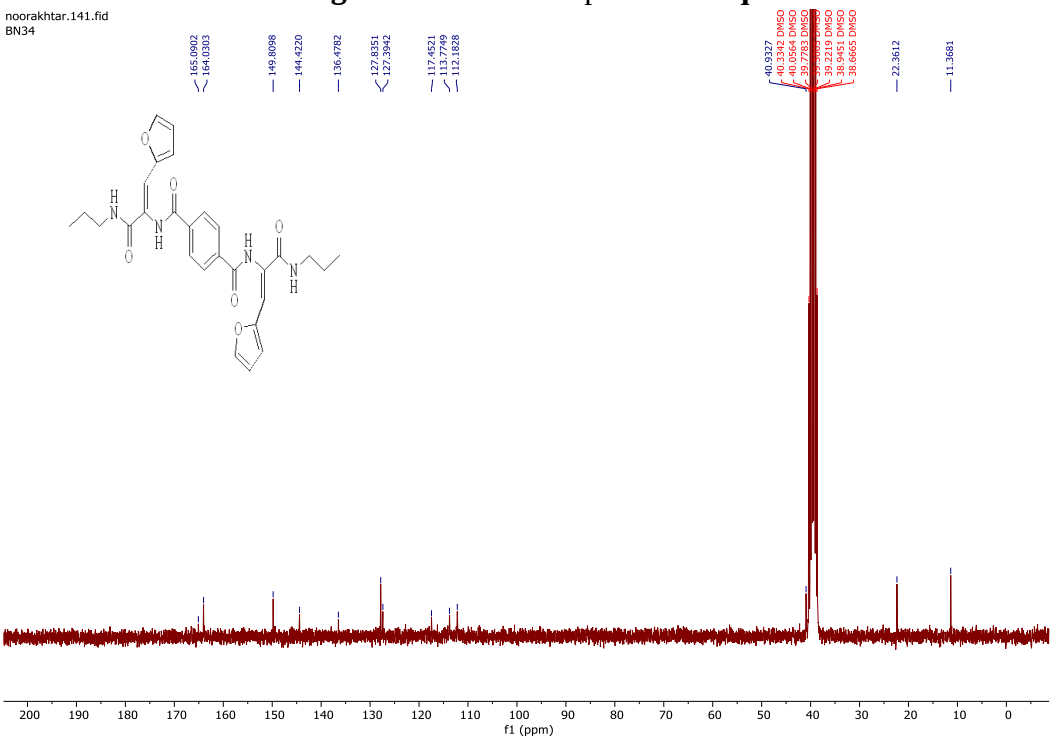


Figure 88. ^{13}C NMR spectra for **6q**

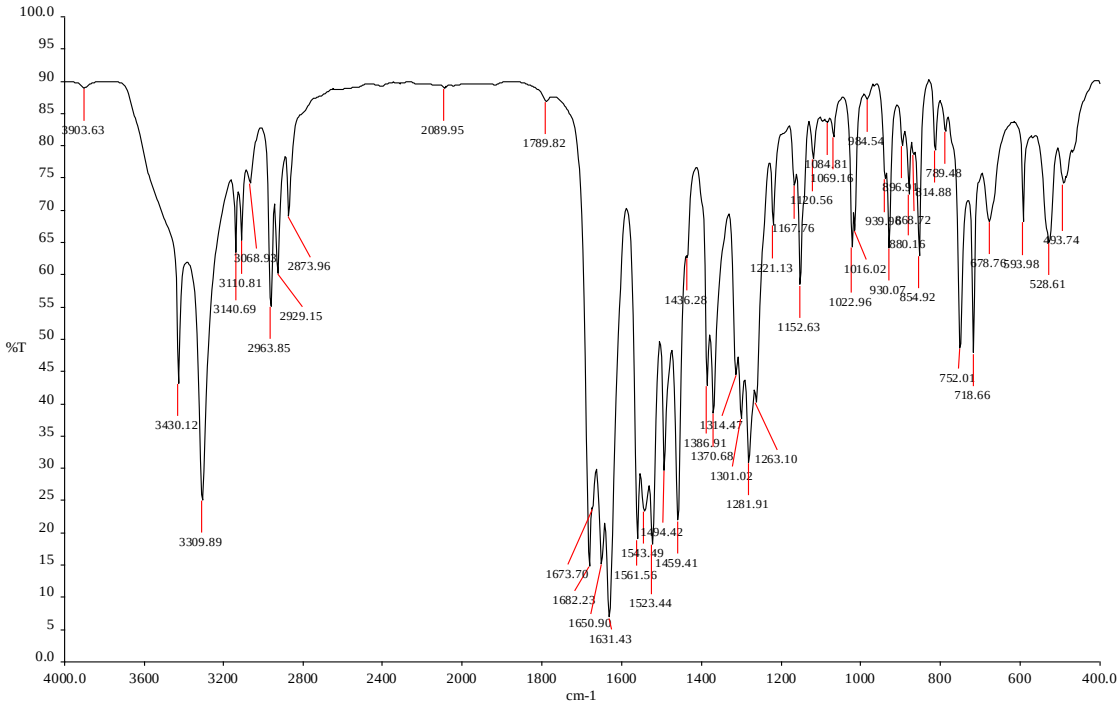


Figure 89. IR spectra for **6q**

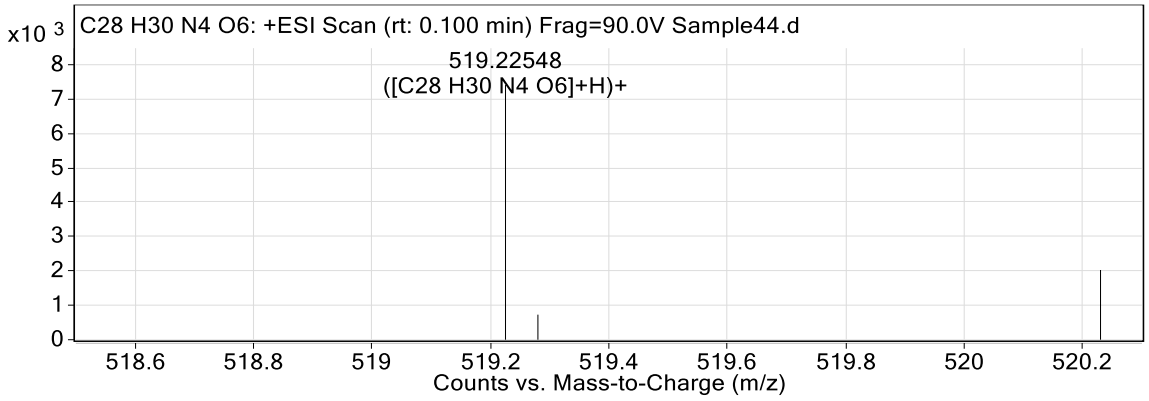
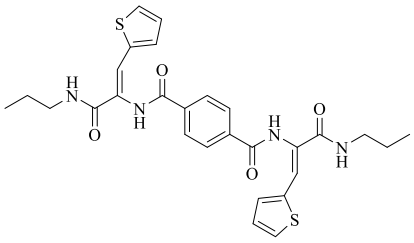


Figure 90. HRMS spectra for **6q**



N1,N4-bis((E)-3-oxo-3-(propylamino)-1-(thiophen-2-yl)prop-1-en-2-yl)terephthalamide **(6r):** white powder (120 mg, yield 87%); mp 264-266 °C; IR (KBr) *v* 3307, 3160, 2952, 1649, 1637, 1552, 1528, 1290, 1149, 861, 708 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.06 (s, 2H), 8.24 (t, J = 5.8 Hz, 2H), 8.07 (s, 2H), 7.77 (m, 2H), 7.52-7.45 (m, 4H), 7.31-7.26 (m, 2H), 7.16 (s, 2H), 3.14-3.08 (m, 4H), 1.53-1.40 (m, 4H), 0.85 (t, J = 7.3 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.2, 164.4, 136.8, 131.5, 131.4,

131.0, 130.5, 128.2, 127.7, 121.6, 40.9, 22.3, 11.4 ppm; Anal. calcd for $C_{28}H_{30}N_4O_4S_2$: C, 61.07; H, 5.49; N, 10.17. Found: C, 61.02; H, 5.11; N, 10.03.

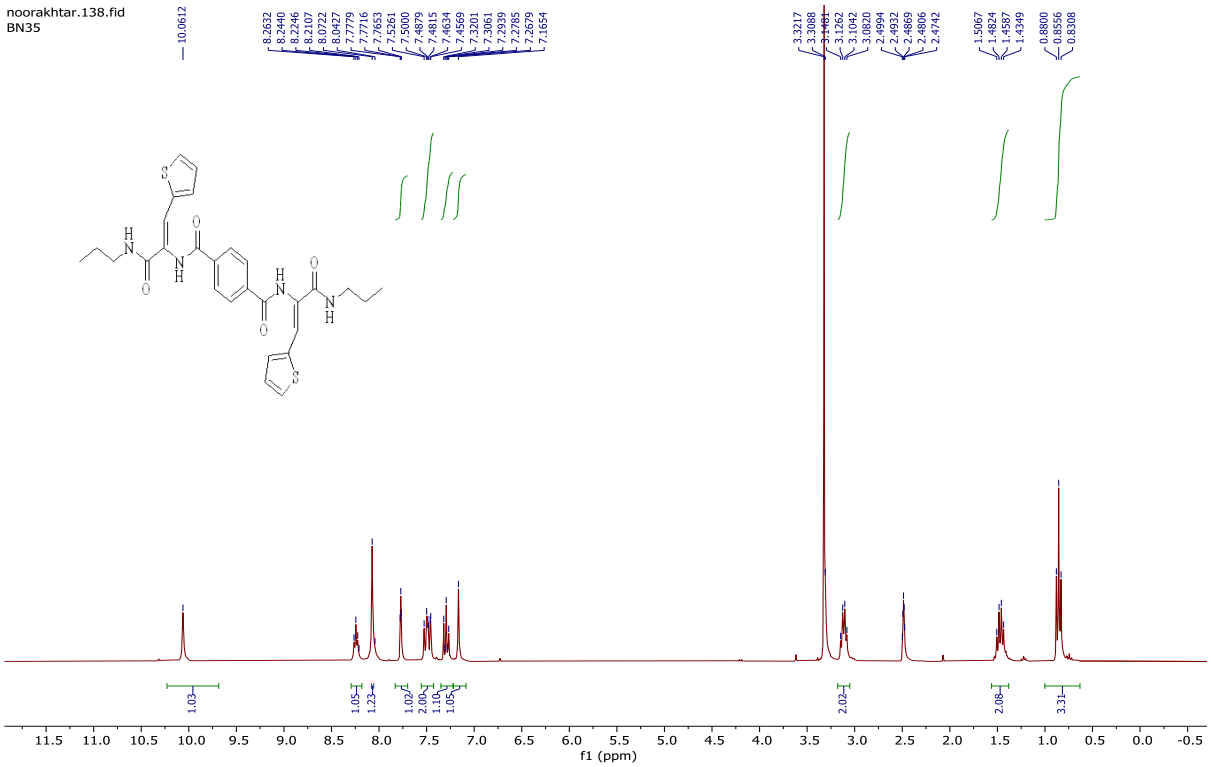


Figure 91. ^{1}H NMR spectra for **6r**

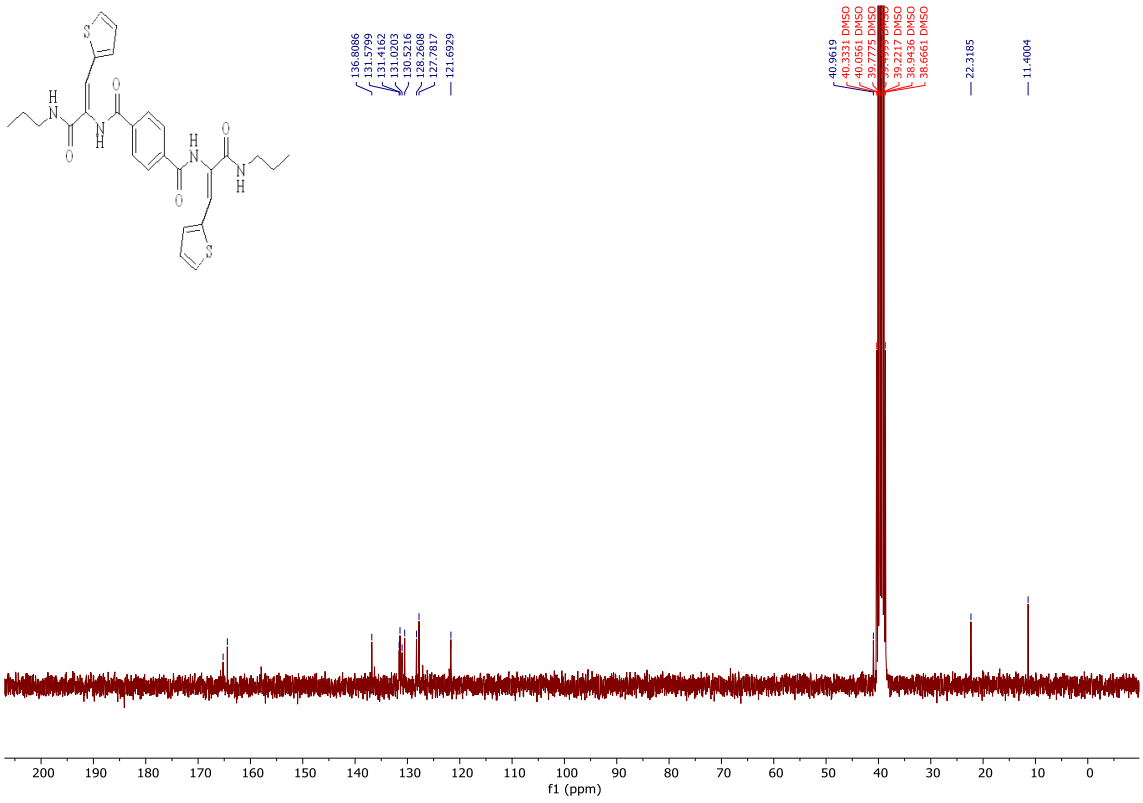


Figure 92. ^{13}C NMR spectra for **6r**

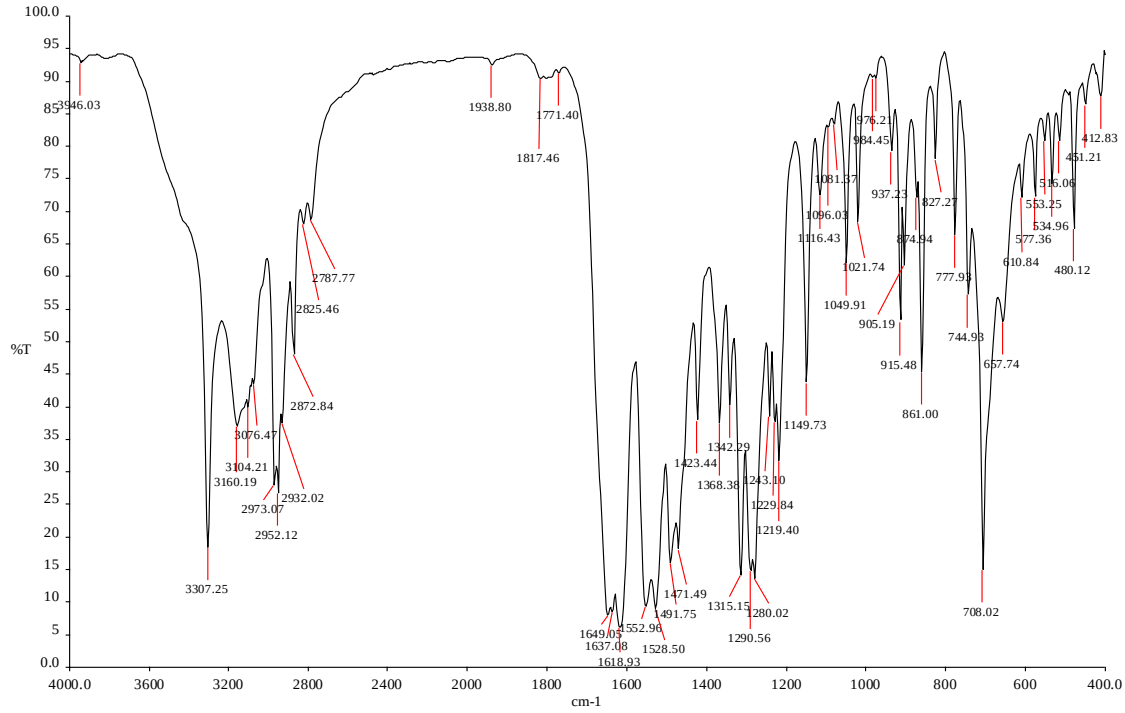
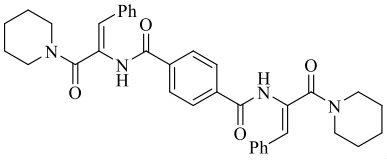


Figure 93. IR spectra for **6r**



N1,N4-bis((E)-3-oxo-1-phenyl-3-(piperidin-1-yl)prop-1-en-2-yl)terephthalamide **(6s):** white powder (124 mg, yield 84%); IR (KBr) *v* 3335, 3239, 2854, 1661, 1615, 1473, 1277, 1137, 866, 698 cm^{-1}; mp 259-261 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.49 (s, 2H), 8.04 (s, 4H), 7.36-7.23 (m, 10H), 6.63 (s, 2H), 3.62 (brs, 2H), 3.20 (brs, 6H), 1.46-1.37 (brs, 10H), 0.56 (brs, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.7, 163.6, 144.0, 136.0, 134.4, 131.7, 128.3, 127.8, 127.2, 115.8, 47.0, 41.4, 24.3, 24.1, 21.4 ppm; Anal. calcd for $C_{36}H_{38}N_4O_4$: C, 73.20; H, 6.48; N, 9.48. Found: C, 73.19; H, 6.57; N, 9.40.

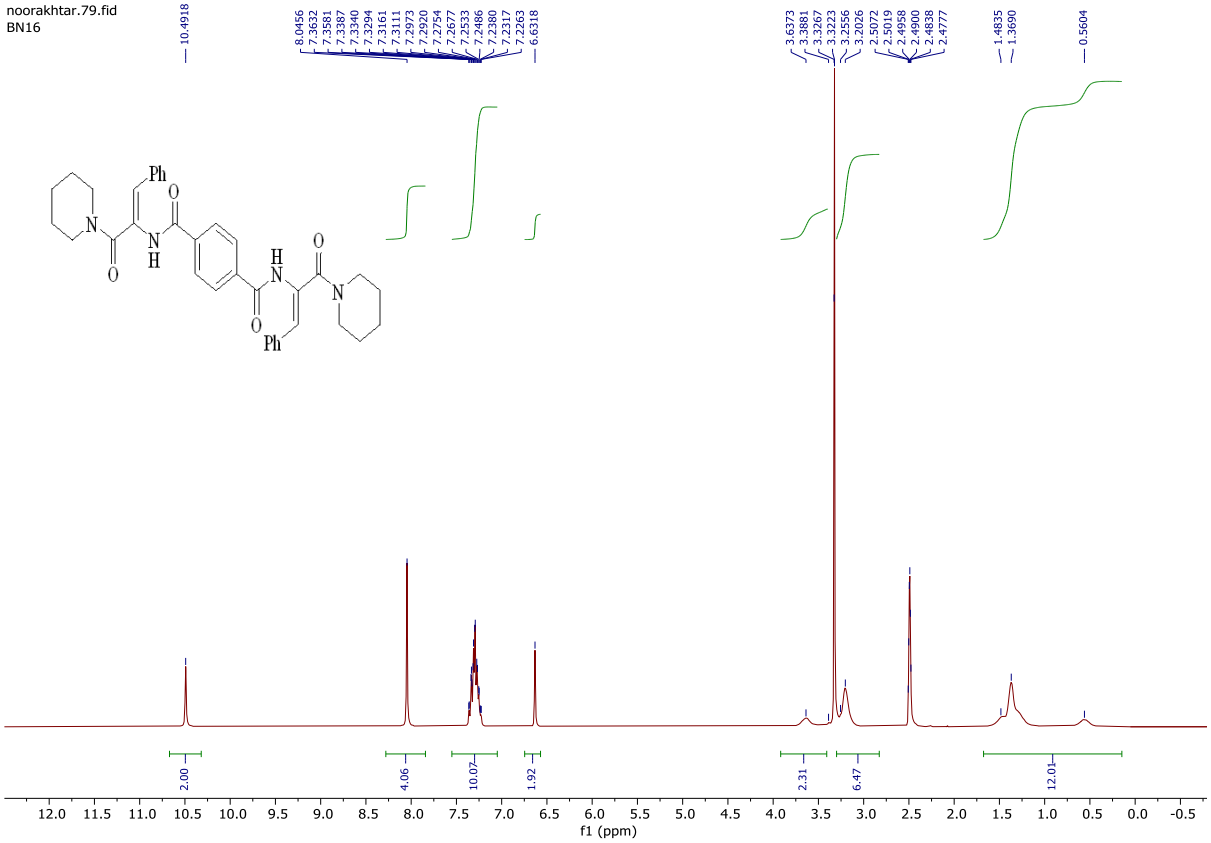


Figure 94. ^{1}H NMR spectra for **6s**

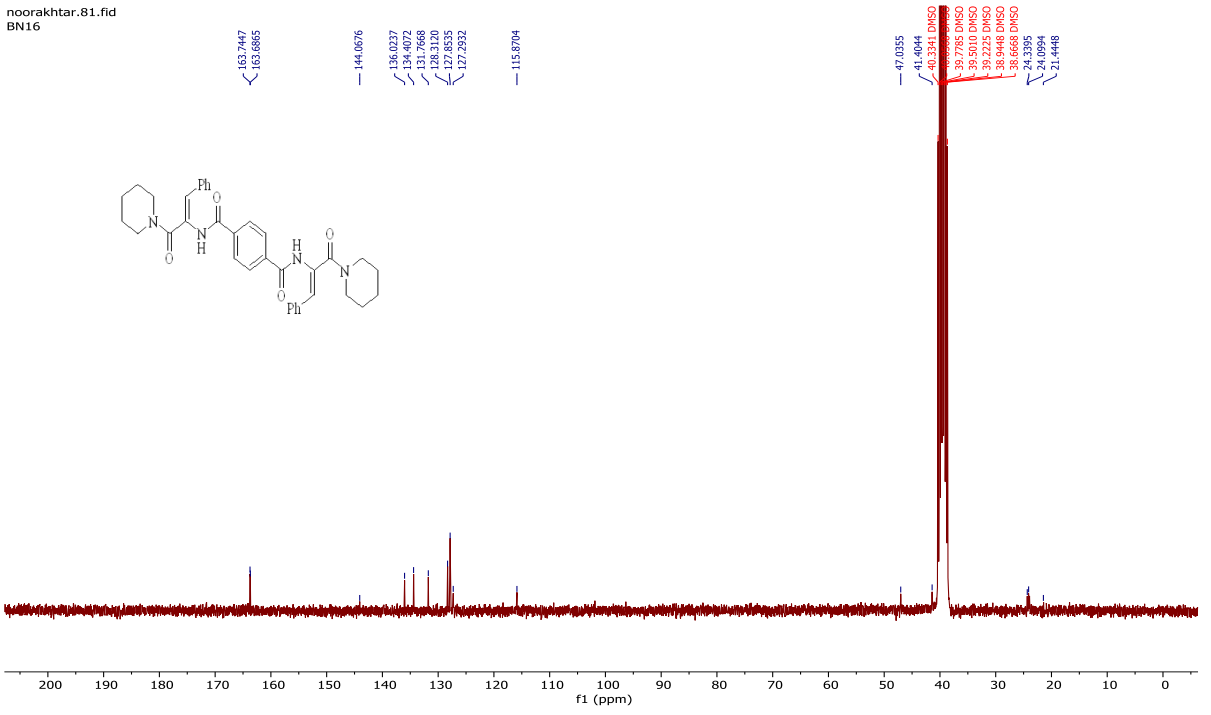


Figure 95. ^{13}C NMR spectra for **6s**

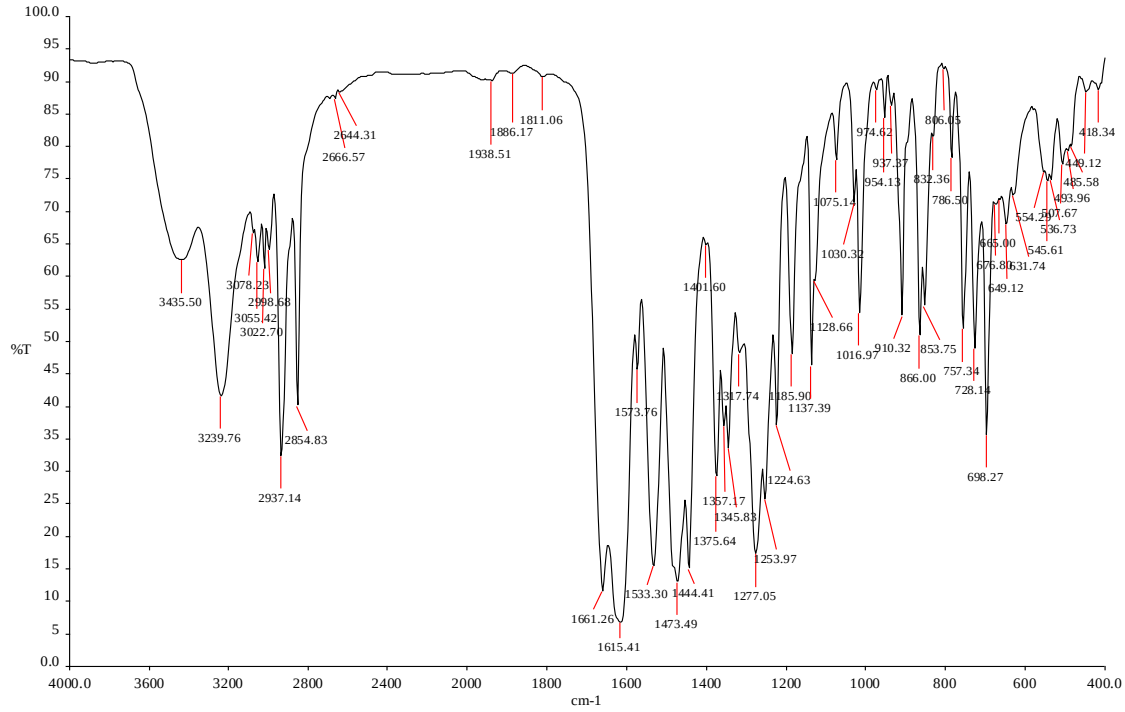
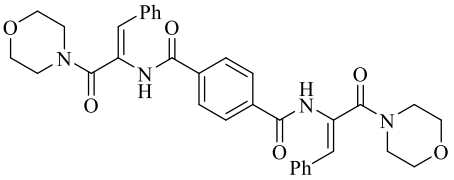


Figure 96. IR spectra for **6s**



N1,N4-bis((E)-3-morpholino-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6t):** white powder (134 mg, yield 90%); mp 273-275 °C; IR (KBr) ν 3435, 3226, 2981, 1659, 1614, 1535, 1475, 1274, 1108, 1032, 701 m^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.57 (s, 2H), 8.06 (s, 4H), 7.39-7.27 (m, 10H), 6.66 (s, 2H), 3.49-3.39 (brs, 8H), 3.24 (brs, 4H), 2.55 (m, 4H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 164.2, 163.8, 149.2, 135.8, 134.1, 130.9, 128.4, 127.8, 127.5, 116.8, 79.1, 64.9, 46.5, 40.3 ppm; Anal. calcd for $C_{34}H_{34}N_4O_6$: C, 68.67; H, 5.76; N, 9.42. Found: C, 68.20; H, 5.61; N, 9.52.

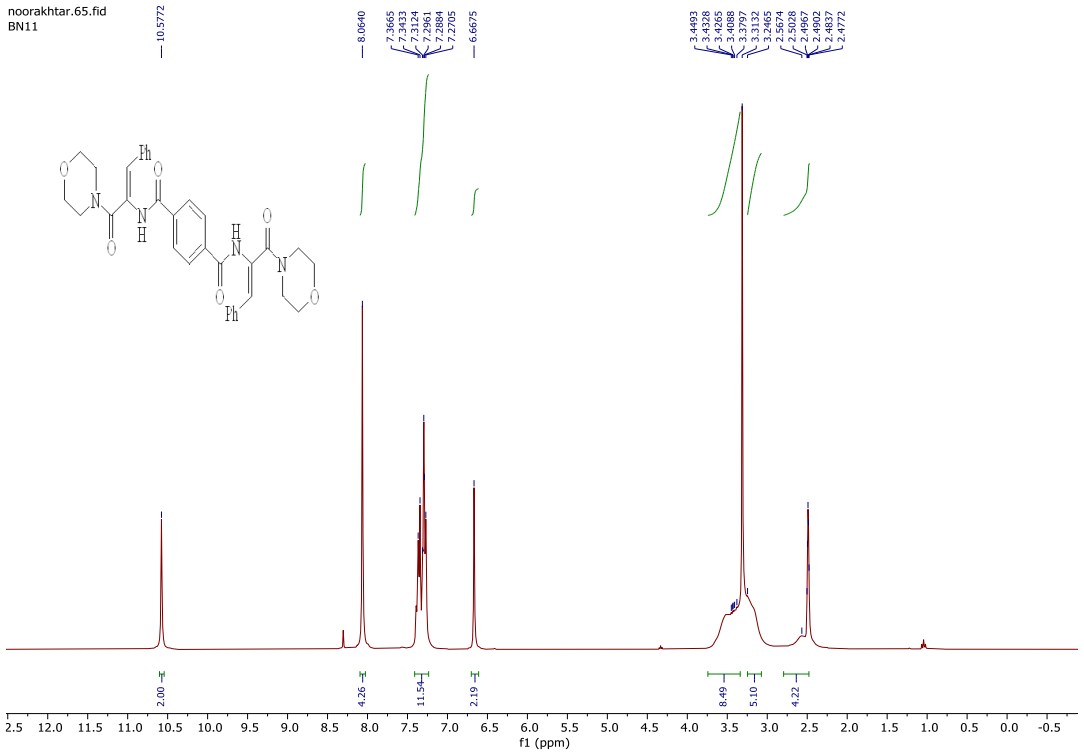


Figure 97. ^{1}H NMR spectra for **6t**

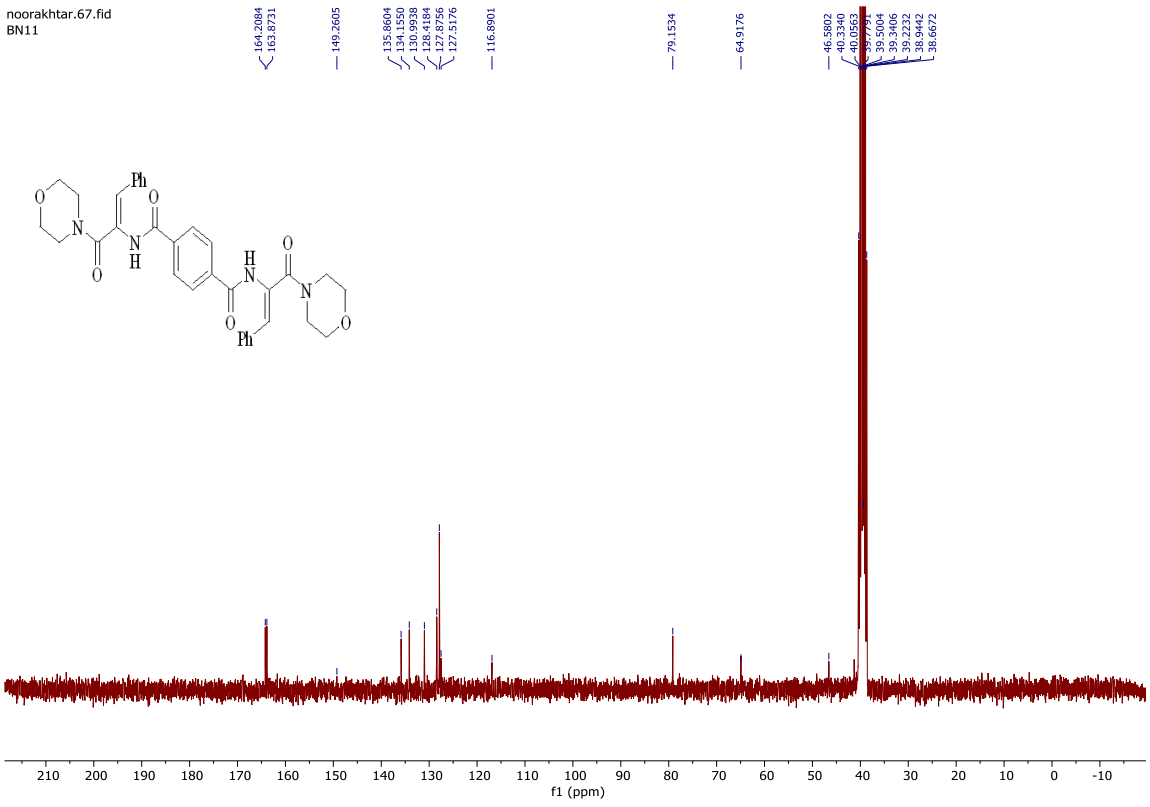


Figure 98. ^{13}C NMR spectra for **6t**

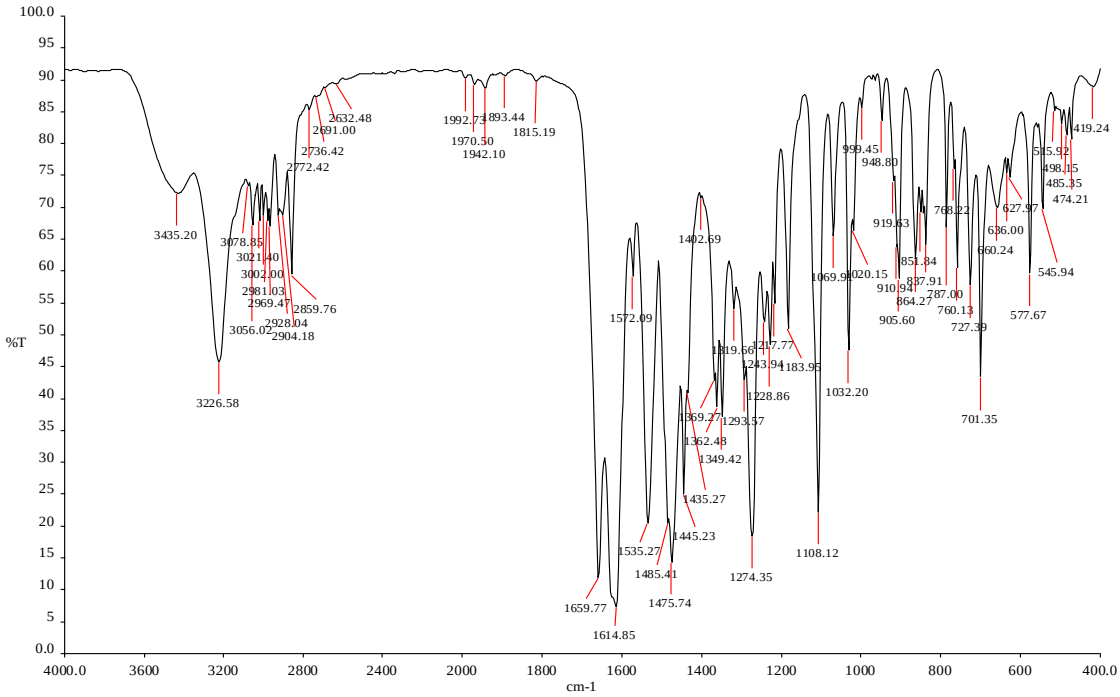
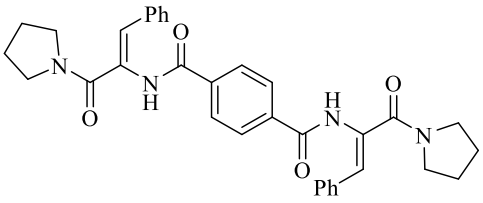


Figure 99. IR spectra for **6t**



N1,N4-bis((E)-3-oxo-1-phenyl-3-(pyrrolidin-1-yl)prop-1-en-2-yl)terephthalamide **(6u):** white powder (123 mg, yield 87%); mp 275-277 °C; IR (KBr) *v* 3427, 3226, 2970, 1656, 1613, 1534, 1466, 1276, 909, 699 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.48 (s, 2H), 8.05 (s, 4H), 7.35-7.22 (m, 10H), 6.60 (s, 2H), 3.33-3.28 (m, 4H), 3.12-3.07 (m, 4H), 2.48 (brs, 2H), 1.64-1.54 (m, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 163.9, 163.6, 144.9, 135.9, 134.4, 132.8, 128.3, 127.8, 127.4, 116.6, 46.6, 44.9, 25.0, 23.8 ppm; Anal. calcd for $C_{34}H_{34}N_4O_4$: C, 72.58; H, 6.09; N, 9.96. Found: C, 71.94; H, 6.09; N, 9.99.

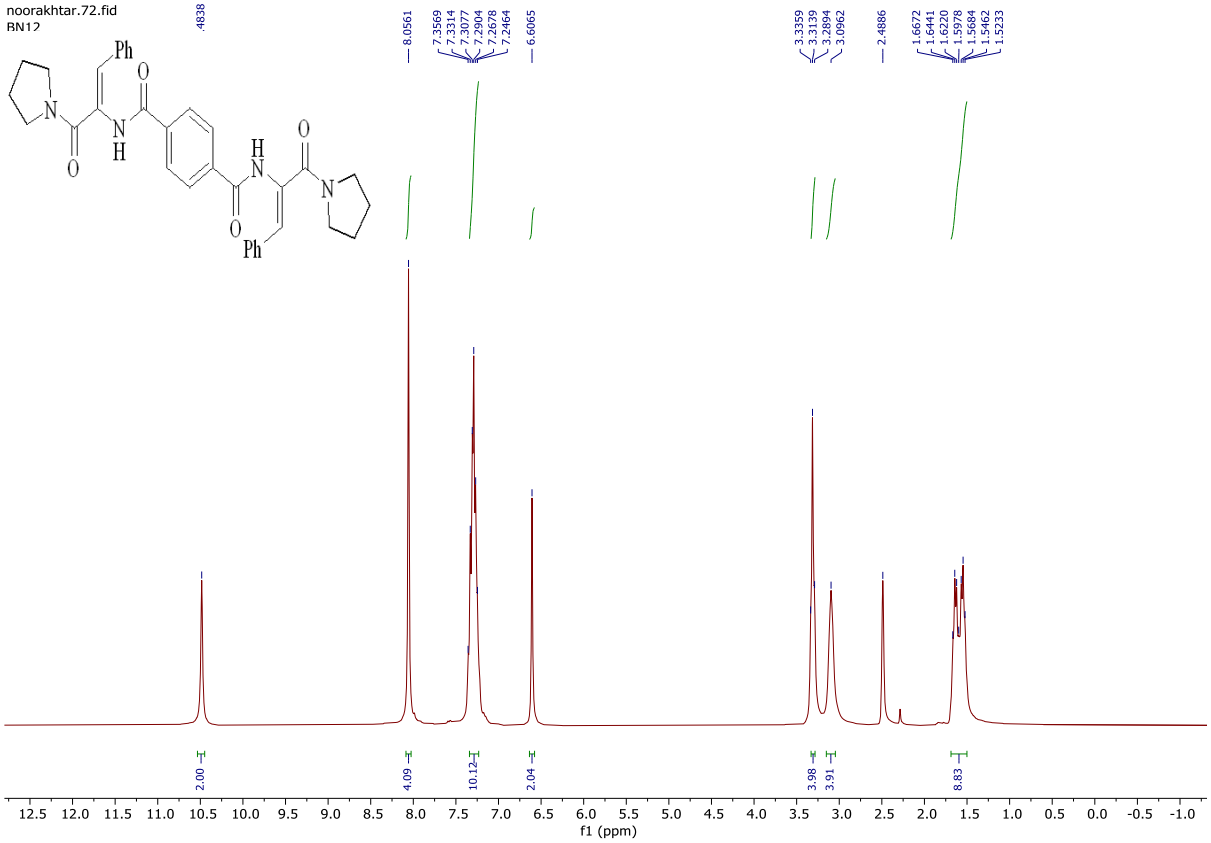


Figure 100. ^{1}H NMR spectra for **6u**

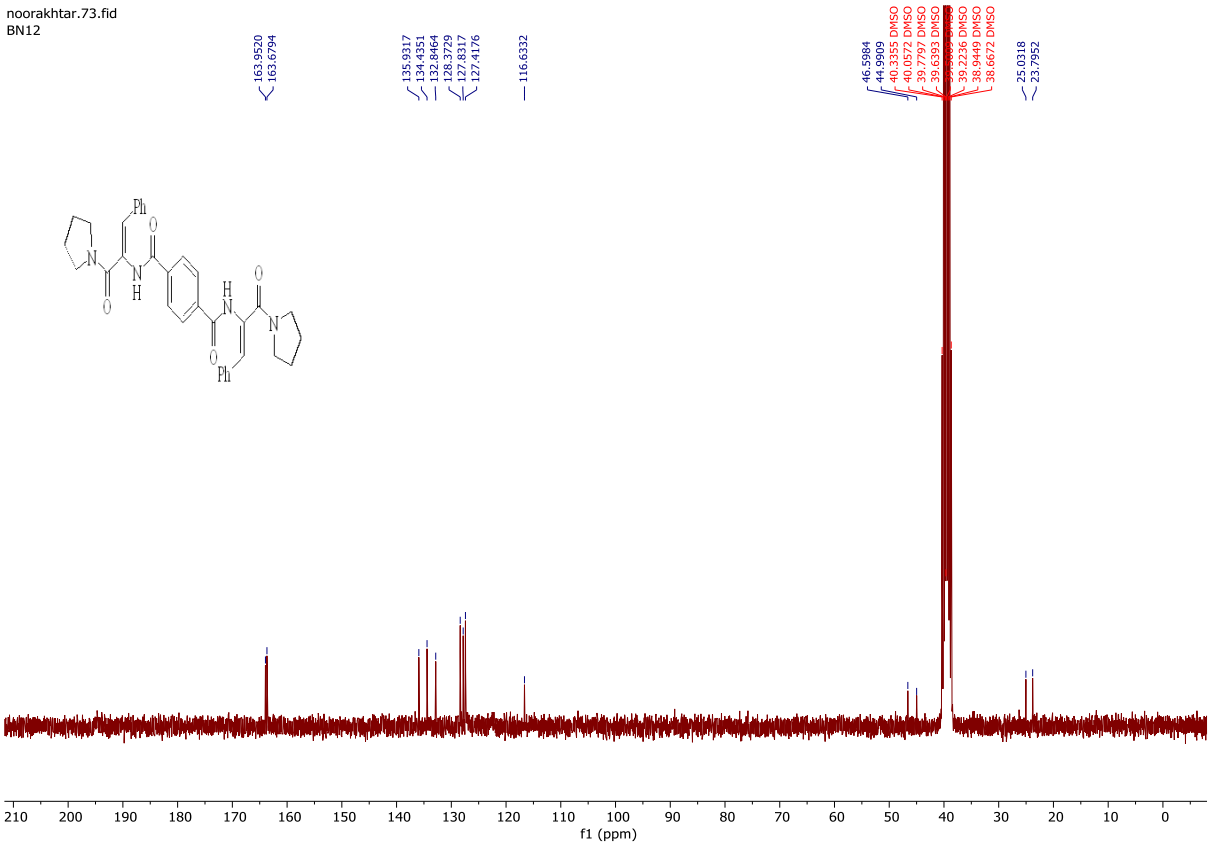


Figure 101. ^{13}C NMR spectra for **6u**

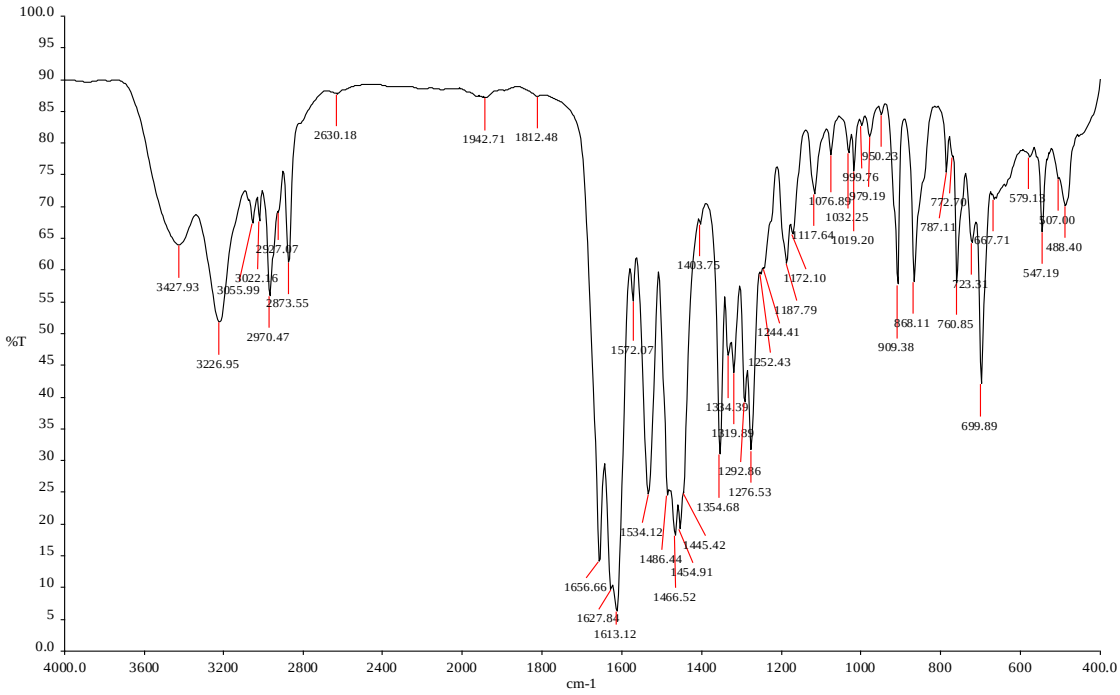
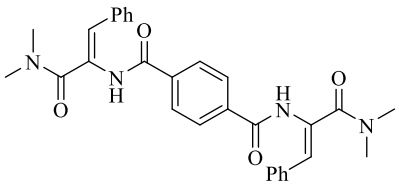


Figure 102. IR spectra for **6u**



N1,N4-bis((E)-3-(dimethylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6v):** white powder (100 mg, yield 78%); mp 262-264 °C; IR (KBr) *v* 3424, 3239, 2938, 1661, 1618, 1535, 1486, 1277, 1140, 909, 700 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.49 (s, 2H), 8.05 (bs, 4H), 7.36-7.22 (m, 10H), 6.63 (s, 2H), 2.81 (s, 6H), 2.71 (s, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) δ 165.6, 163.7, 135.9, 134.4, 131.7, 128.4, 127.8, 127.4, 127.3, 116.1, 37.1, 33.9 ppm; Anal. calcd for $C_{30}H_{30}N_4O_4$: C, 70.57; H, 5.92; N, 10.97. Found: C, 70.23; H, 5.90; N, 11.07.

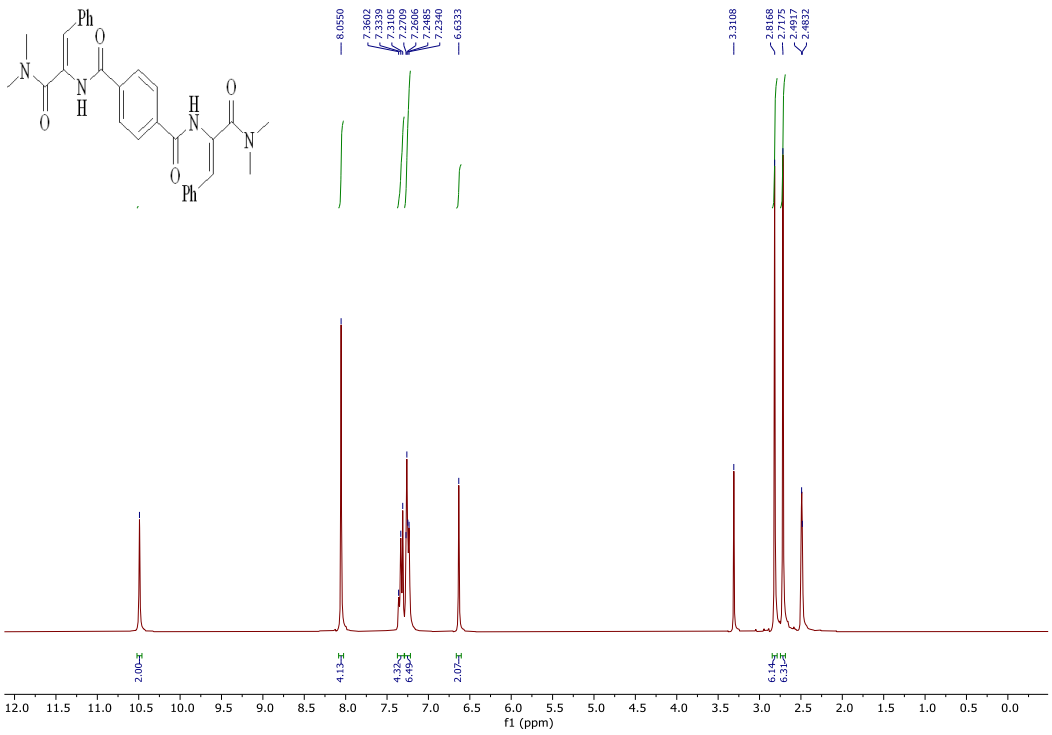


Figure 103. ^{1}H NMR spectra for **6v**

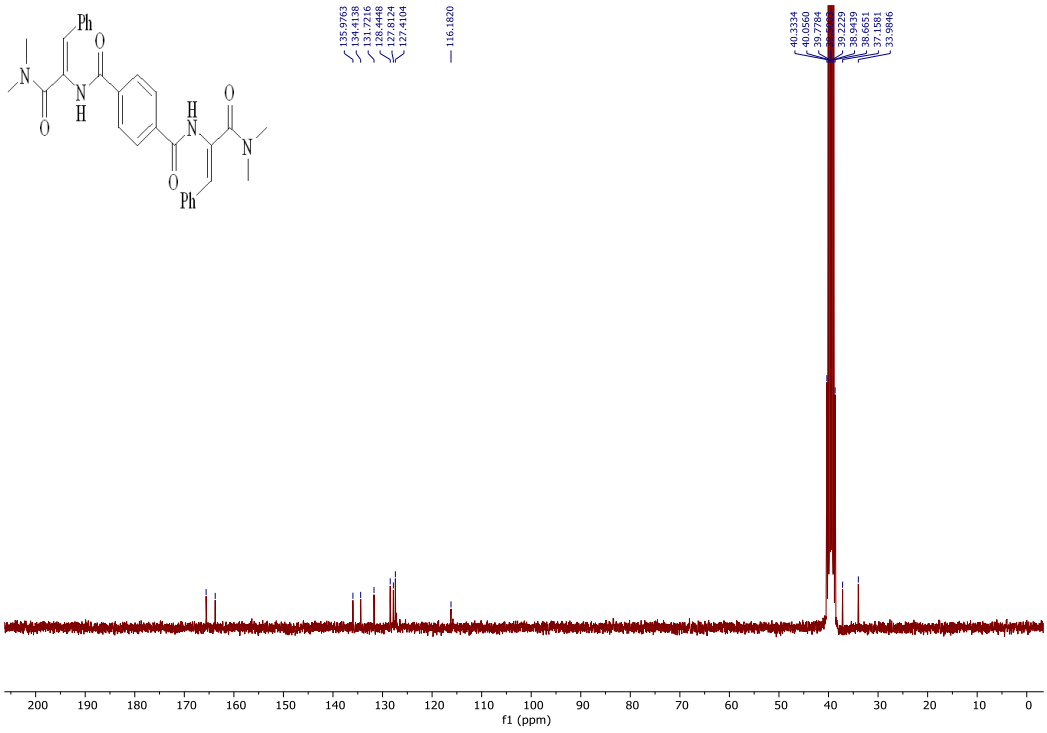


Figure 104. ^{13}C NMR spectra for **6v**

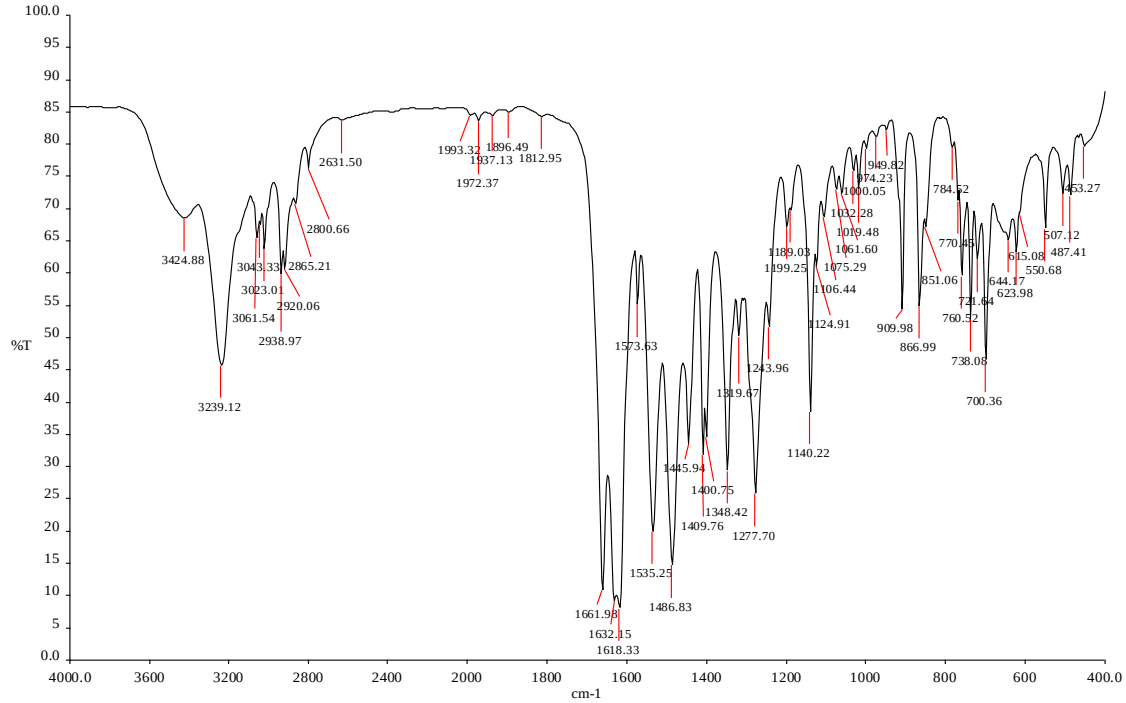
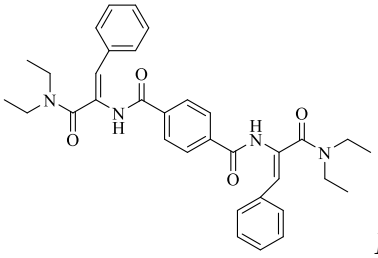


Figure 105. IR spectra for **6v**



N1,N4-bis((E)-3-(diethylamino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6w):** white powder (112 mg, yield 79%); mp 269-271 °C; IR (KBr) *v* 3258, 2978, 1667, 1611, 1537, 1480, 1274, 1143, 910, 691 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.42 (s, 2H), 8.03 (s, 4H), 7.33-7.20 (m, 10H), 6.65 (s, 2H), 3.37 (m, 4H), 3.24-3.17 (m, 4H), 1.05 (t, J = 6.9 Hz, 6H), 0.68 (t, J = 6.9 Hz, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) 164.7, 163.5, 151.0, 136.1, 134.5, 132.2, 128.2, 127.8, 127.1, 115.1, 40.0, 37.8, 12.4, 11.5 ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{34}H_{38}N_4O_4$ 567.2971; found 567.2999.

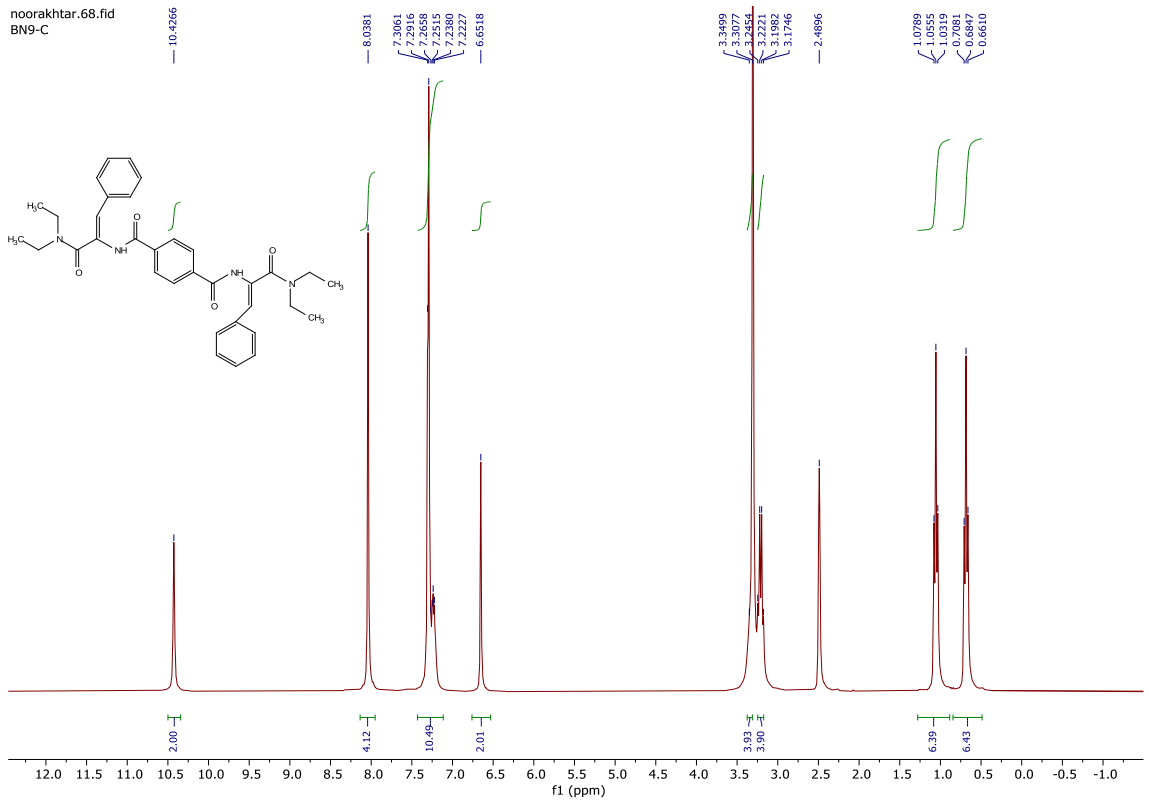


Figure 106. ^{1}H NMR spectra for **6w**

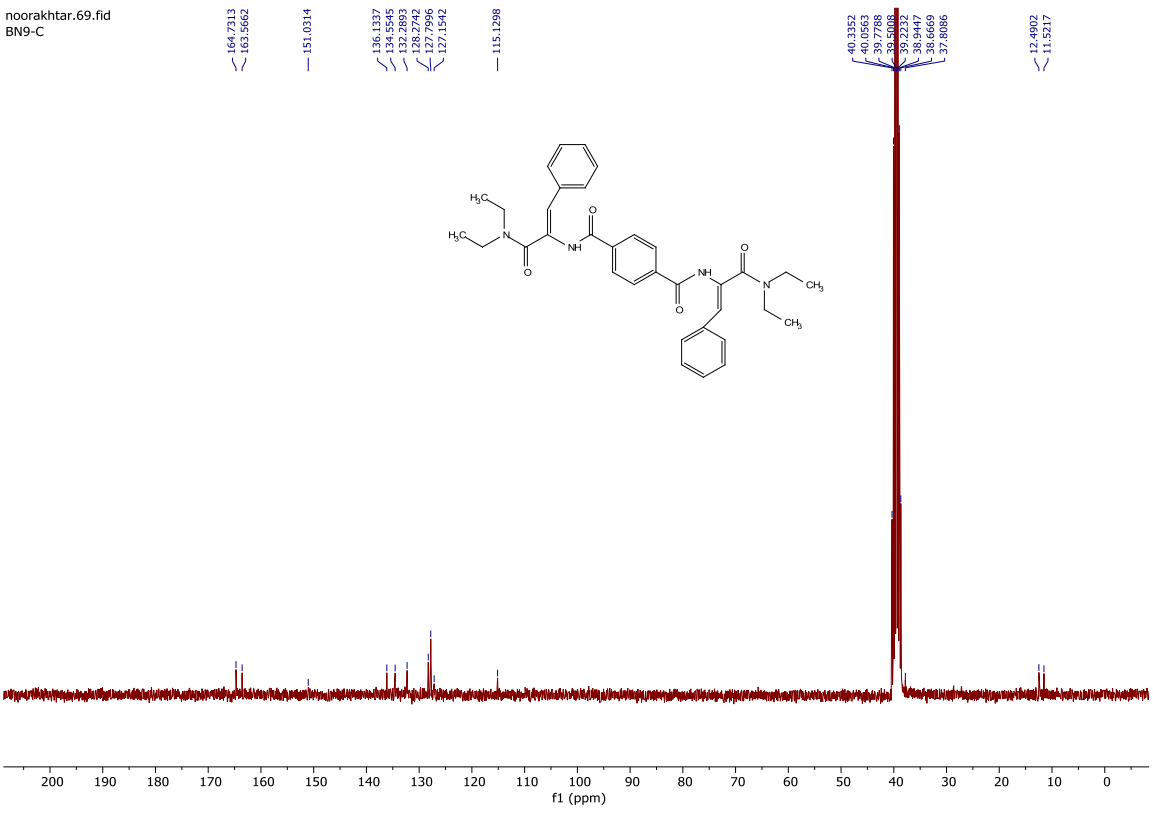


Figure 107. ^{13}C NMR spectra for **6w**

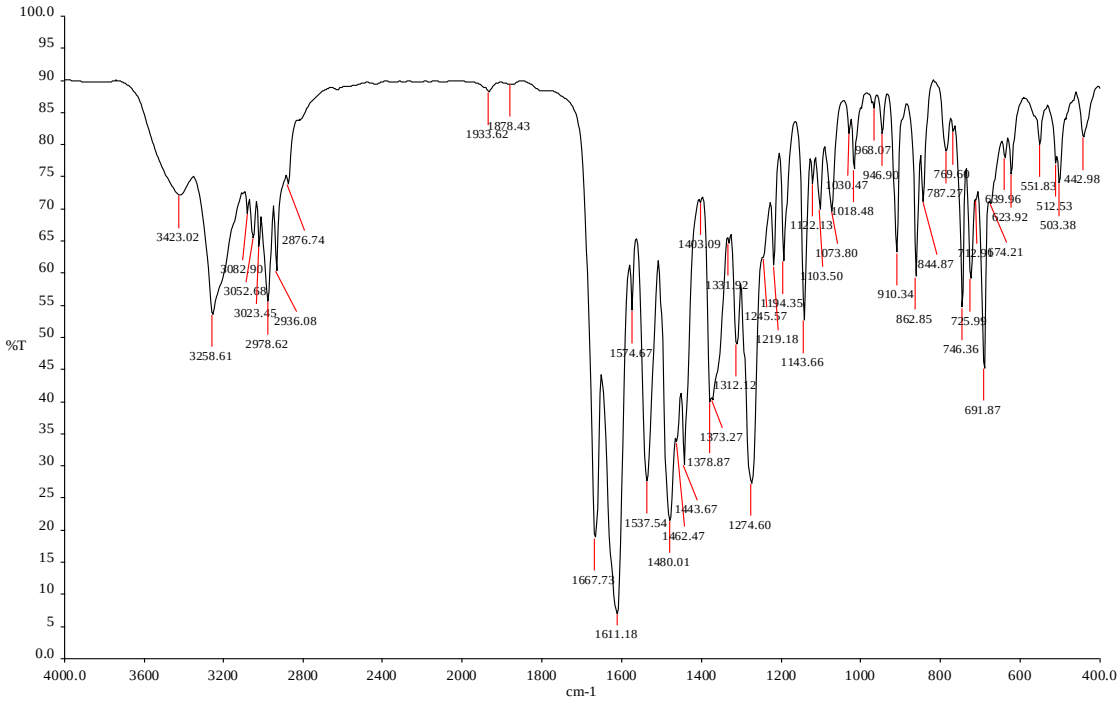


Figure 108. IR spectra for **6w**

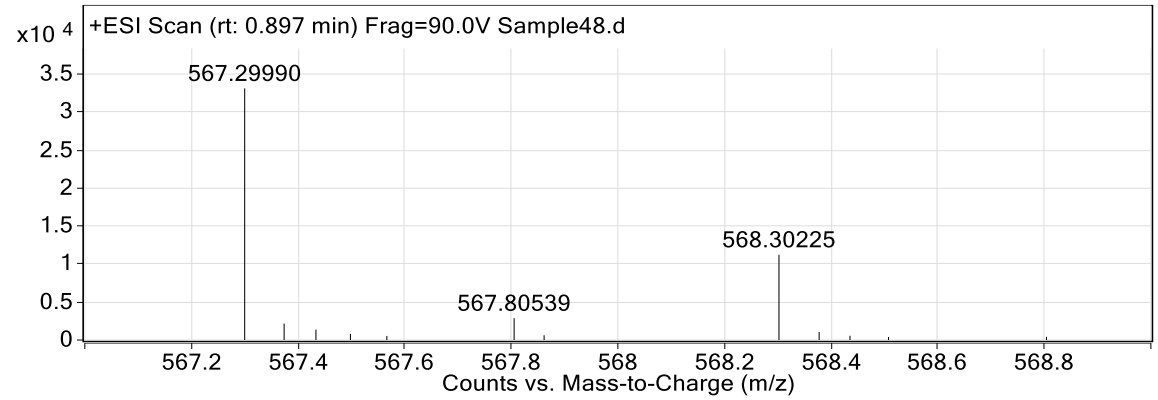
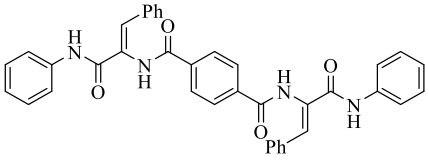


Figure 109. HRMS spectra for **6w**



N1,N4-bis((E)-3-oxo-1-phenyl-3-(phenylamino)prop-1-en-2-yl)terephthalamide **(6x):** white powder (126 mg, yield 83%); mp 265-267 °C; IR (KBr) *v* 3272, 1639, 1598, 1319, 1253, 748, 690 m^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.27 (s, 2H), 10.20 (s, 2H), 8.14 (s, 4H), 7.74 (d, J = 8.1 Hz, 4H), 7.62 (d, J = 7.7 Hz, 4H), 7.42-7.30 (m, 10H), 7.18 (s, 2H), 7.07 (t, J = 7.5 Hz, 2H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) 165.3, 164.1,

155.5, 139.2, 136.1, 134.2, 130.8, 129.5, 128.7, 128.5, 128.5, 127.9, 123.4, 120.1 ppm; Anal. calcd for $C_{38}H_{30}N_4O_4$: C, 75.23; H, 4.98; N, 9.24. Found: C, 75.38; H, 4.94; N, 9.20.

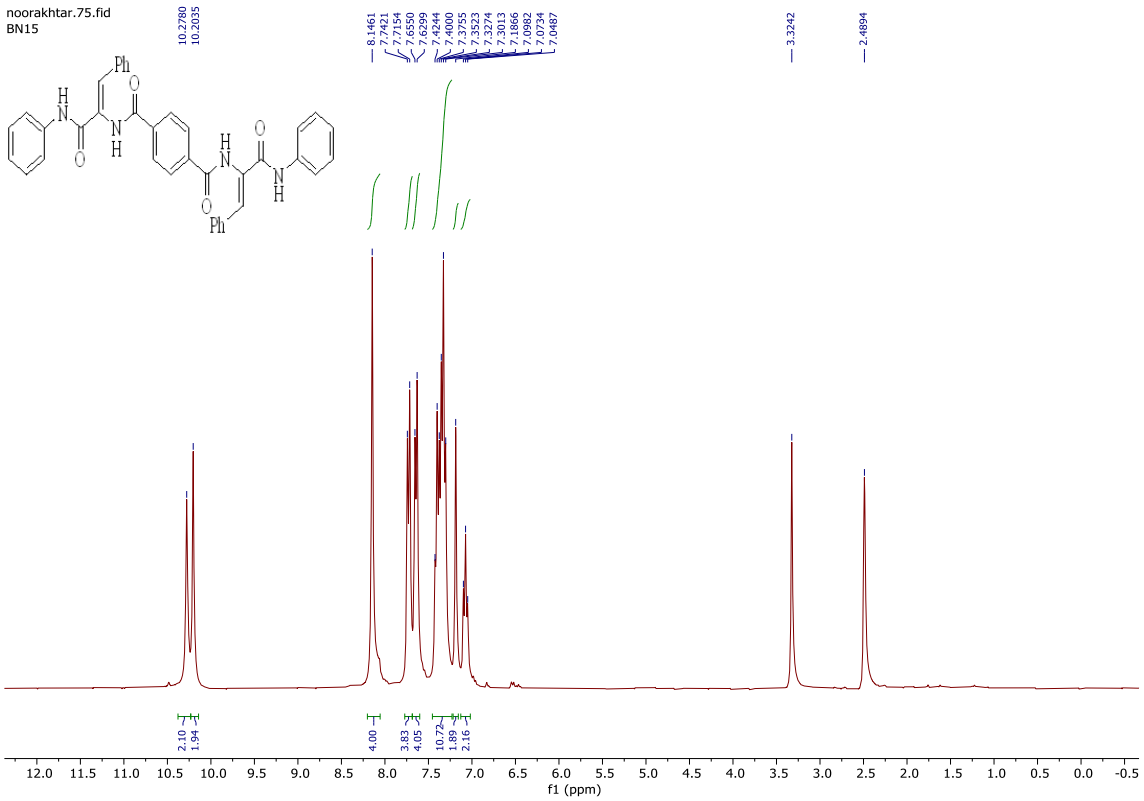


Figure 110. ^{1}H NMR spectra for **6x**

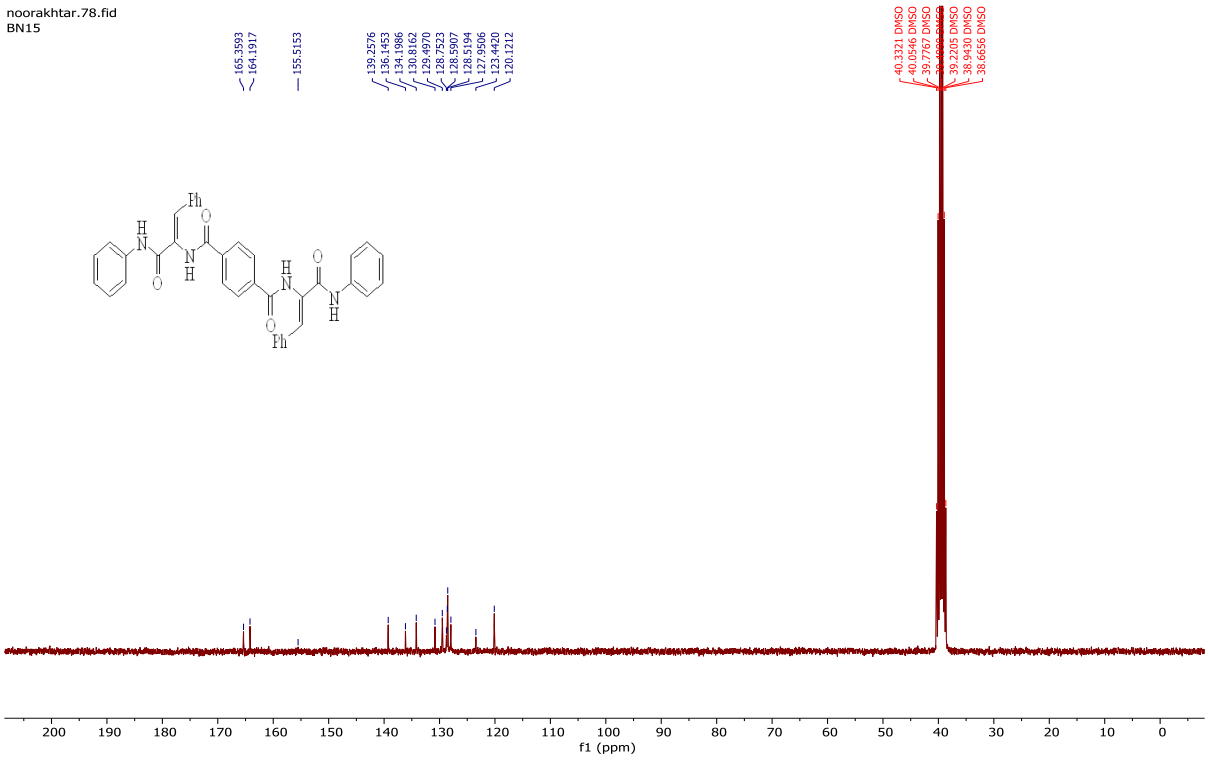


Figure 111. ^{13}C NMR spectra for **6x**

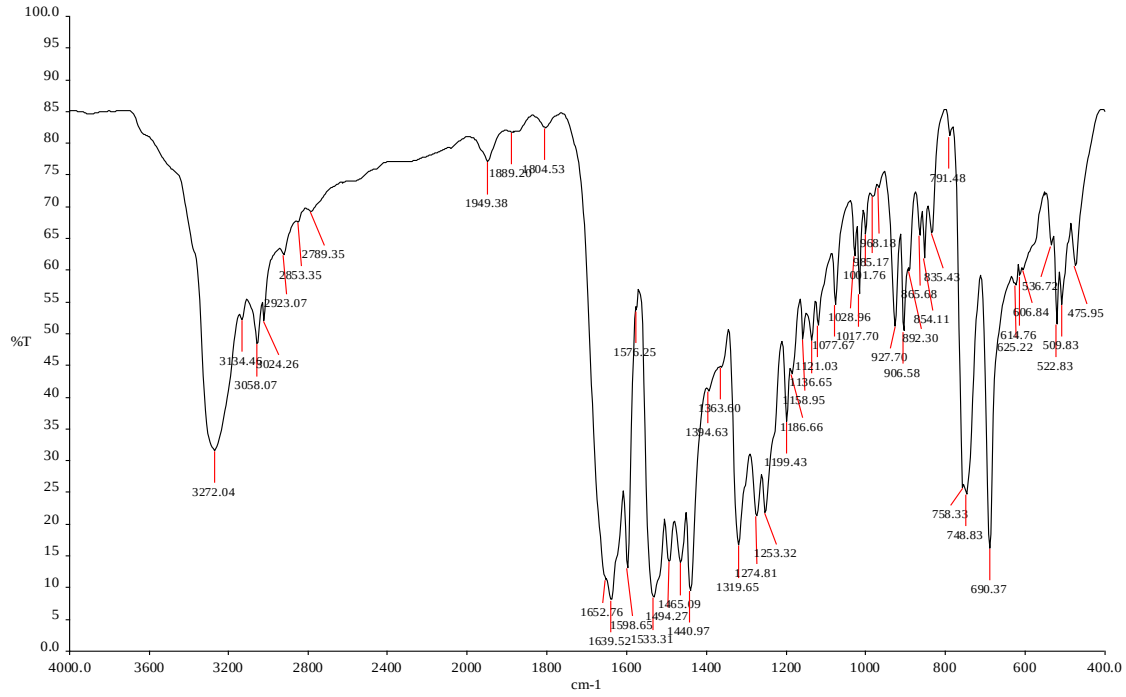
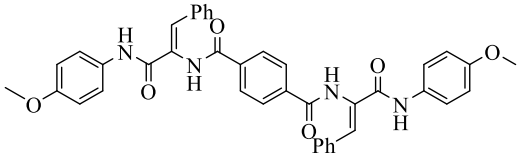


Figure 112. IR spectra for **6x**



N1,N4-bis((E)-3-((4-methoxyphenyl)amino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6y):** white powder (120 mg, yield 72%); mp 215-217 °C; IR (KBr) *v* 3419, 3219, 1651, 1529, 1249, 1027, 755 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.48 (s, 2H), 9.01 (s, 2H), 8.16 (s, 4H), 8.14 (d, J = 7.9 Hz, 2H), 7.64 (d, J = 7.9, 4H), 7.50 (s, 2H), 7.41-7.34 (m, 6H), 7.08-6.95 (m, 6H), 3.68 (s, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) 166.0, 162.5, 148.8, 136.2, 133.7, 129.6, 129.3, 128.7, 128.0, 127.0, 124.4, 120.6, 120.1, 111.0, 55.8 ppm; Anal. calcd for $C_{40}H_{34}N_4O_6$: C, 72.06; H, 5.14; N, 8.40. Found: C, 72.23; H, 4.99; N, 8.58.

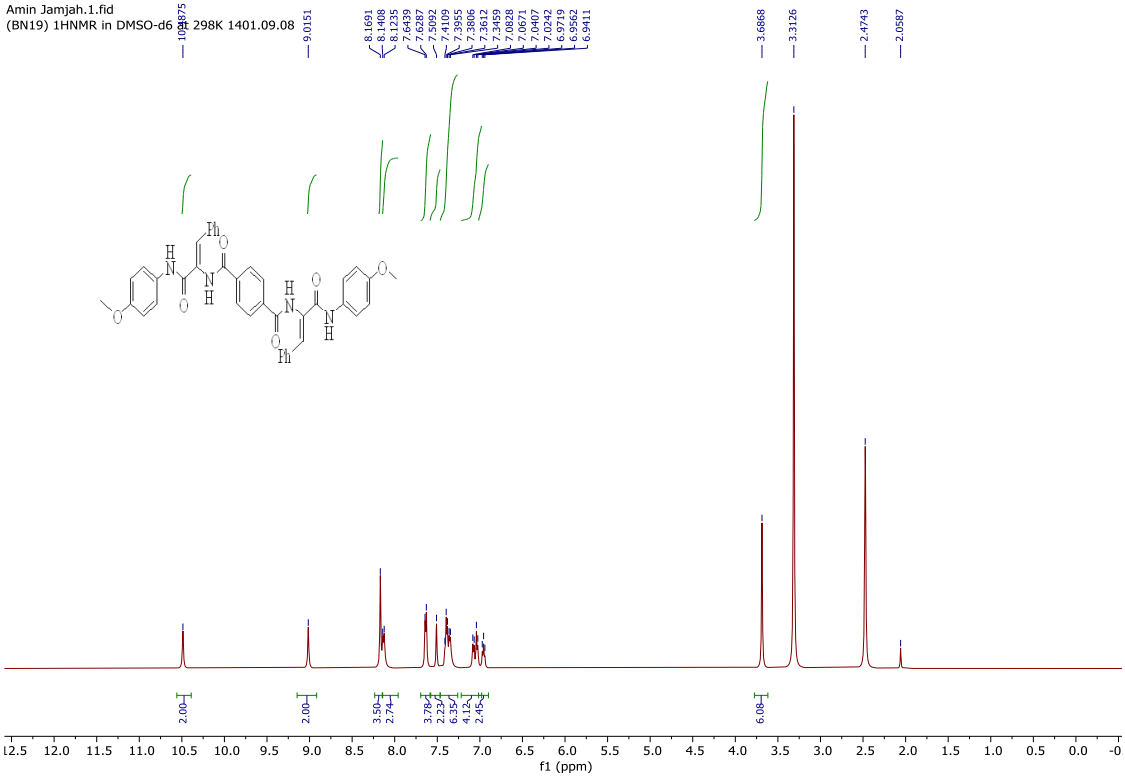


Figure 113. ^{1}H NMR spectra for **6y**

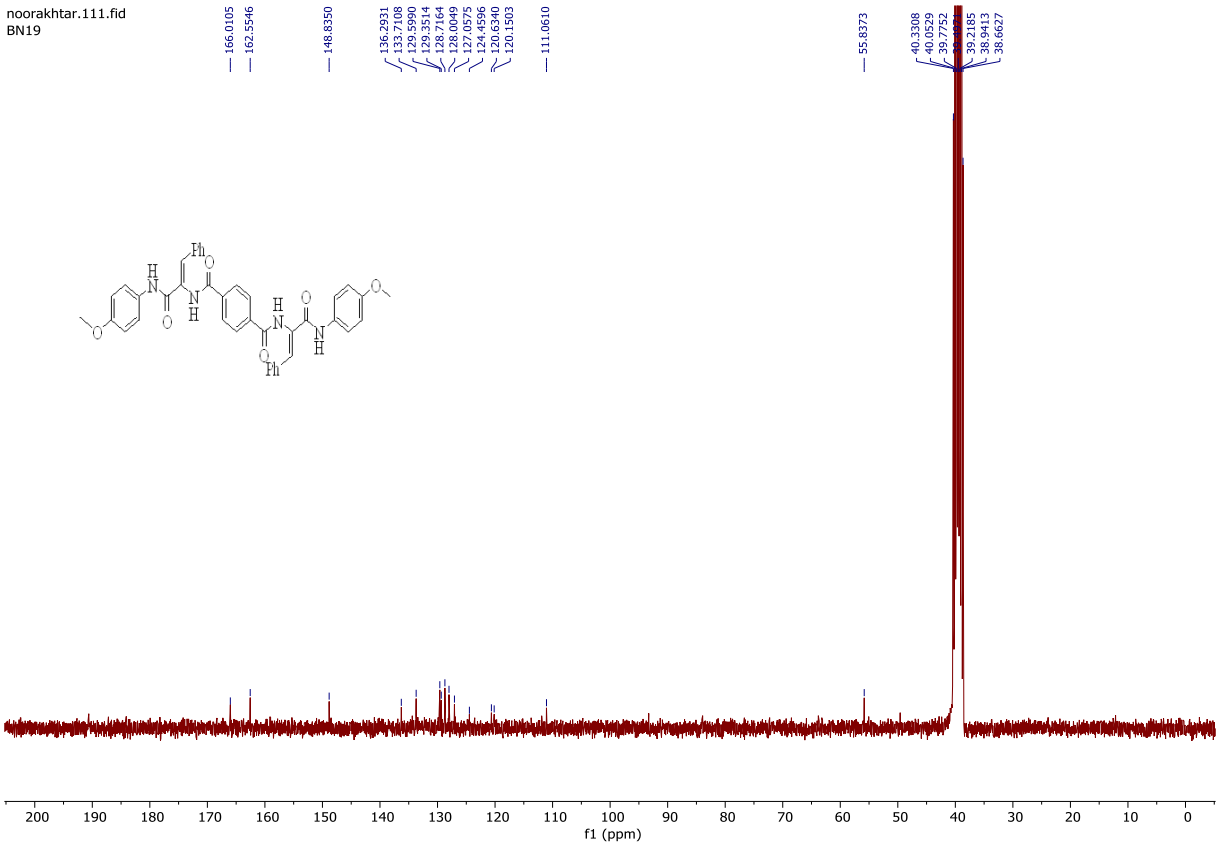


Figure 114. ^{13}C NMR spectra for **6y**

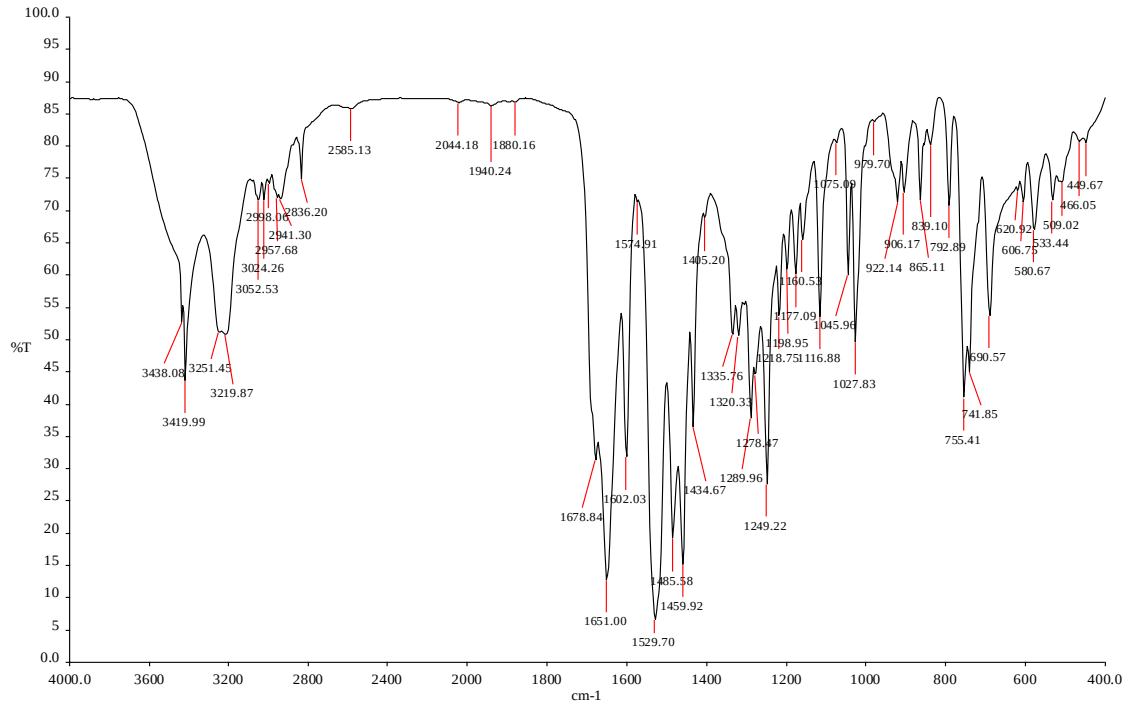
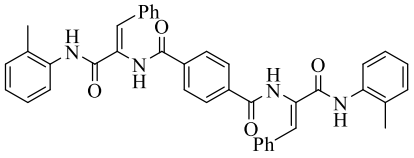


Figure 115. IR spectra for **6y**



N1,N4-bis((E)-3-oxo-1-phenyl-3-(o-tolylamino)prop-1-en-2-yl)terephthalamide **(6z)**: white powder (113 mg, yield 71%); IR (KBr) ν 3205, 1658, 1515, 1462, 1287, 911, 688 m^{-1}; mp 230-233 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.28 (s, 2H), 9.62 (s, 2H), 8.16 (s, 4H), 7.64 (d, J = 7.9 Hz, 4H), 7.40-7.31 (m, 10H), 7.24-7.09 (m, 6H), 2.21 and 2.07 (s, 6H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) 165.6, 163.8, 136.4, 136.2, 134.1, 133.4, 130.3, 130.2, 129.5, 129.4, 128.8, 128.6, 127.9, 126.1, 125.8, 125.7, 17.8 ppm; Anal. calcd for $C_{40}H_{34}N_4O_4$: C, 75.69; H, 5.40; N, 8.83. Found: C, 75.52; H, 5.23; N, 8.83.

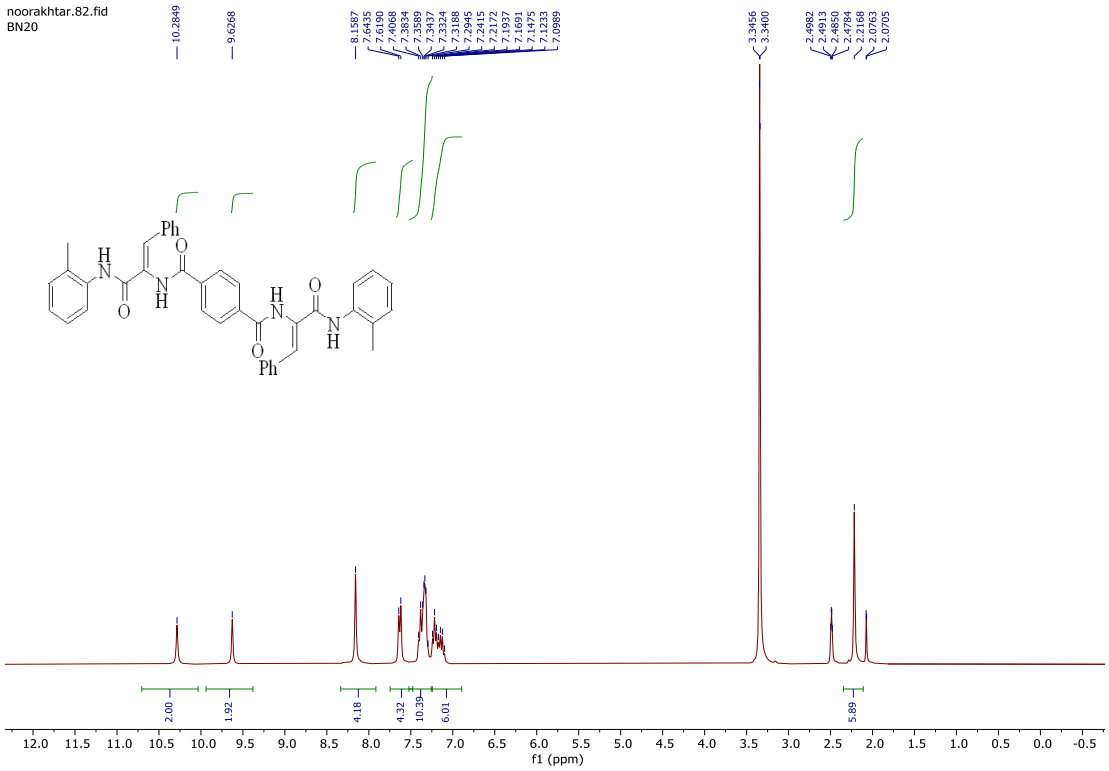


Figure 116. ^{1}H NMR spectra for **6z**

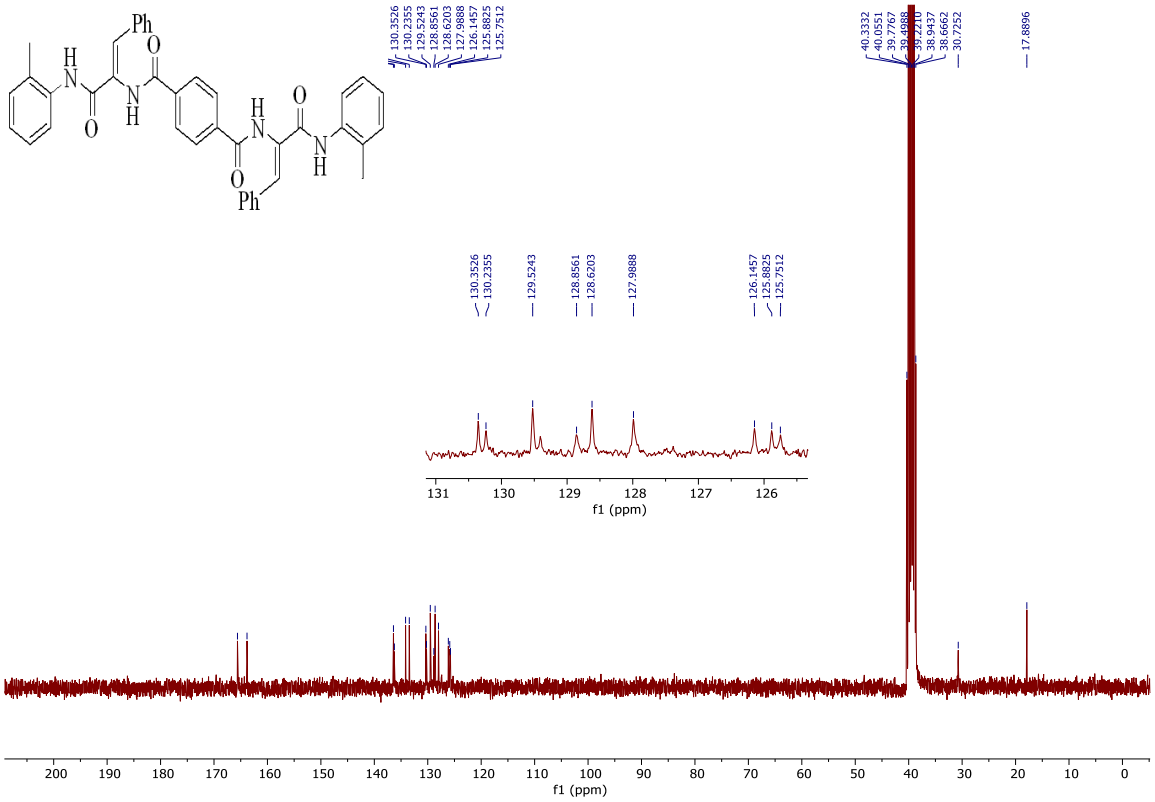


Figure 117. ^{13}C NMR spectra for **6z**

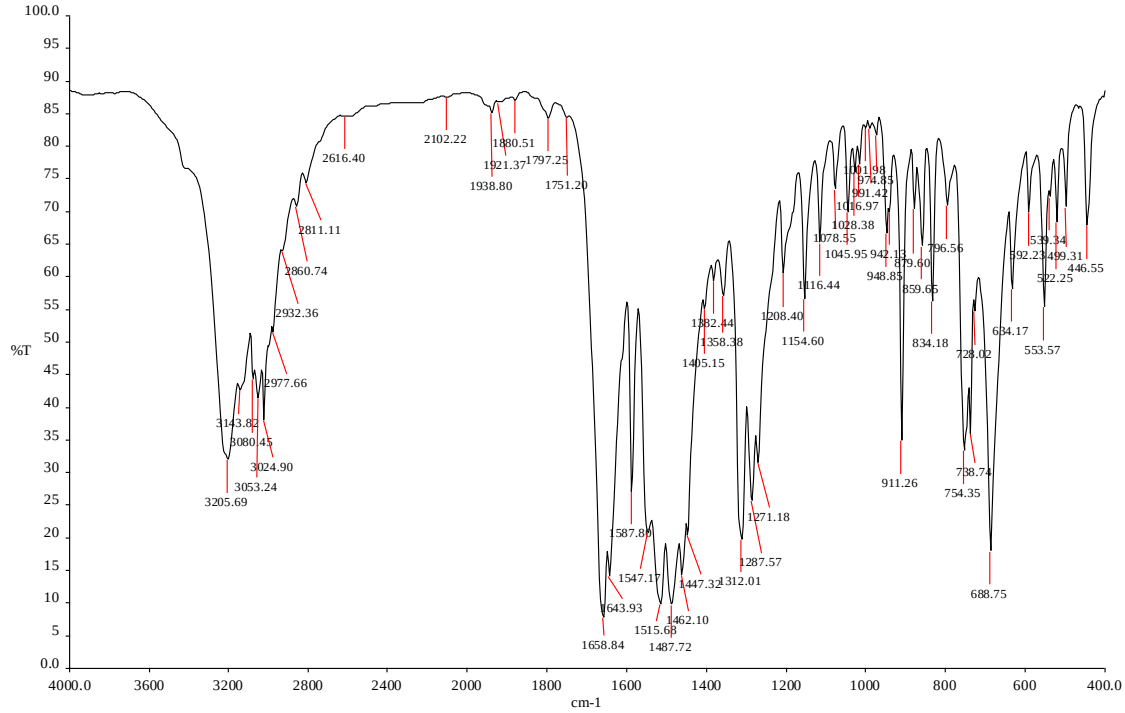
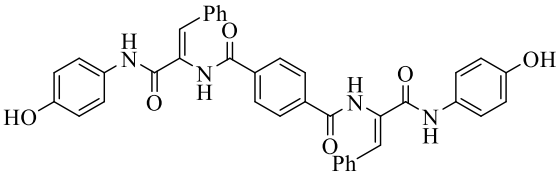


Figure 118. IR spectra for **6z**



N1,N4-bis((E)-3-((4-hydroxyphenyl)amino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6aa):** white powder (120 mg, yield 75%); mp 228-230 °C; IR (KBr) ν 3259, 1674, 1646, 1513, 1237, 825, 691 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.20 (s, 2H), 9.93 (s, 2H), 9.23 (s, 2H) 8.13 (s, 4H), 7.62-7.18 (m, 16H), 6.70-6.68 (m, 4H) ppm; ^{13}C NMR We couldn't get suitable ^{13}C NMR spectra for this compound; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{38}H_{30}N_4O_6$ 639.2244; found 639.2258.

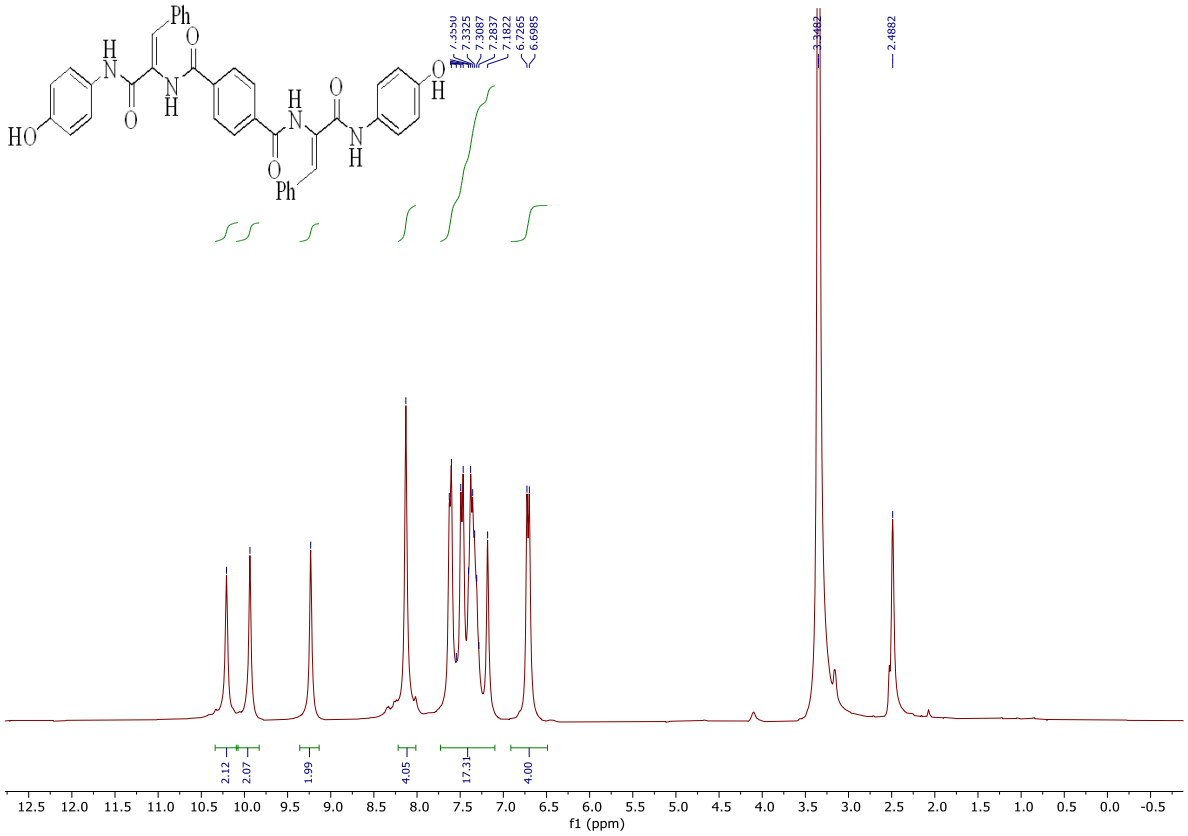


Figure 119. ^{1}H NMR spectra for **6aa**

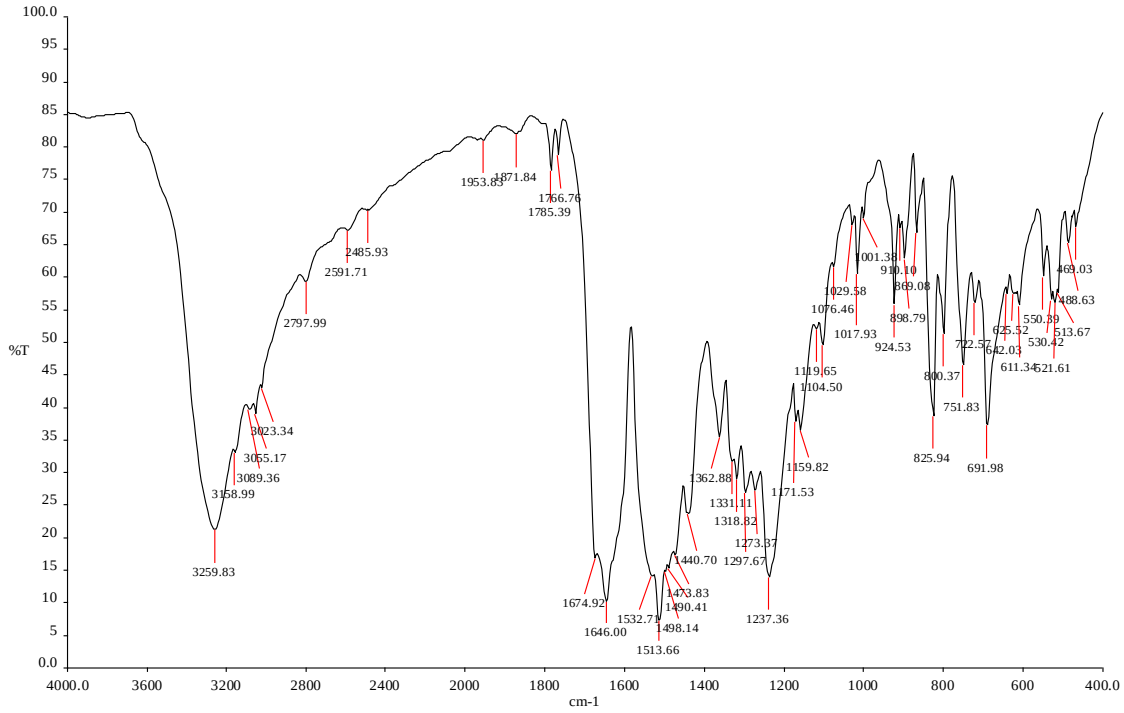


Figure 120. IR spectra for **6aa**

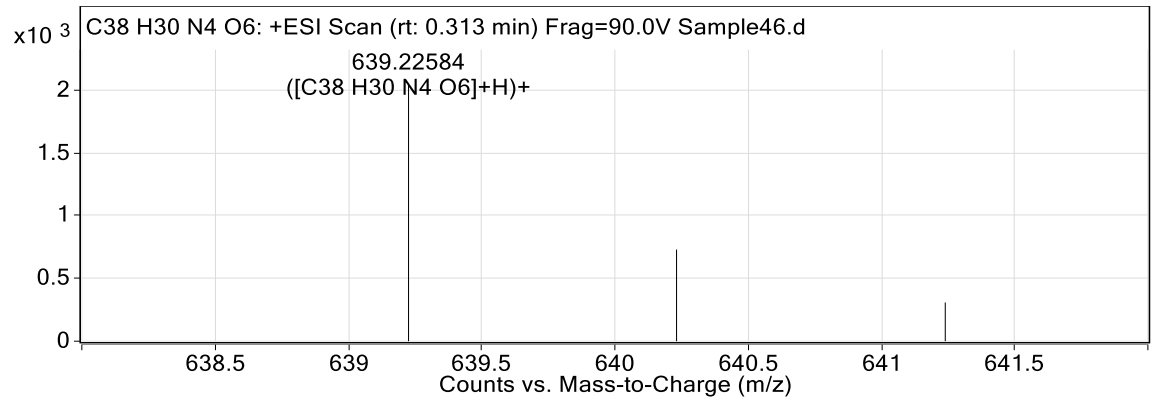
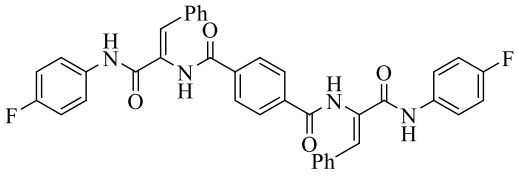


Figure 121. HRMS spectra for **6aa**



N1,N4-bis((E)-3-((4-fluorophenyl)amino)-3-oxo-1-phenylprop-1-en-2-yl)terephthalamide **(6ab):** white powder (140 mg, yield 87%); mp 228-230 °C; IR (KBr) *v* 3280, 1653, 1509, 1408, 1226, 832, 692 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.26-10.24 (brs, 4H), 8.12 (s, 4H), 7.73-7.39 (m, 8H), 7.36-7.11 (m, 12H) ppm; ^{13}C NMR (75 MHz, DMSO-d_6) 165.3, 164.1, 159.7 (d, $^{1}J_{C\text{-}F}$ = 238 Hz), 136.1, 135.6, 134.1, 130.7, 129.5, 128.7, 128.6, 127.9, 121.9, 121.8, 115.2 (d, $^{3}J_{C\text{-}F}$ = 21.7 Hz) ppm; HRMS (ESI) m/z $[M+H]^+$ calcd for $C_{38}H_{28}F_2N_4O_4$ 643.2157; found 643.2187.

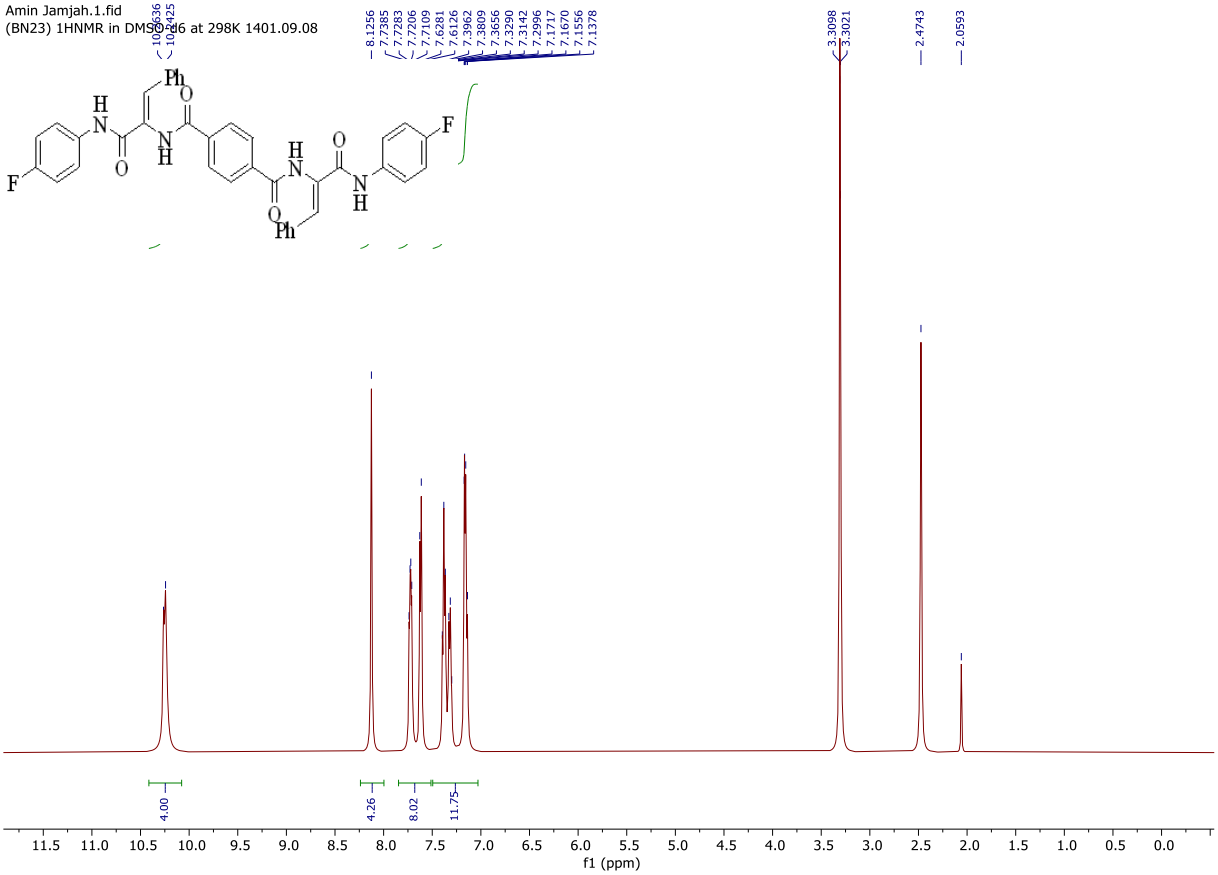


Figure 122. ^{1}H NMR spectra **6ab**

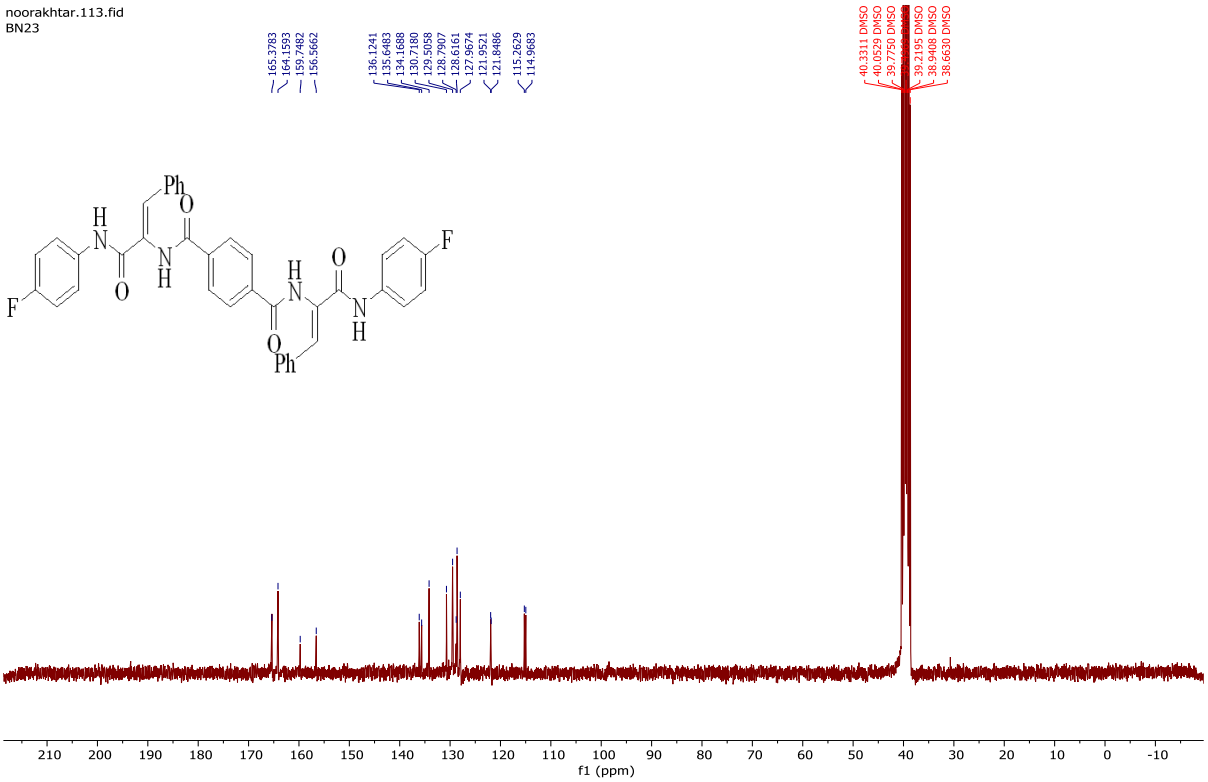


Figure 123. ^{13}C NMR spectra **6ab**

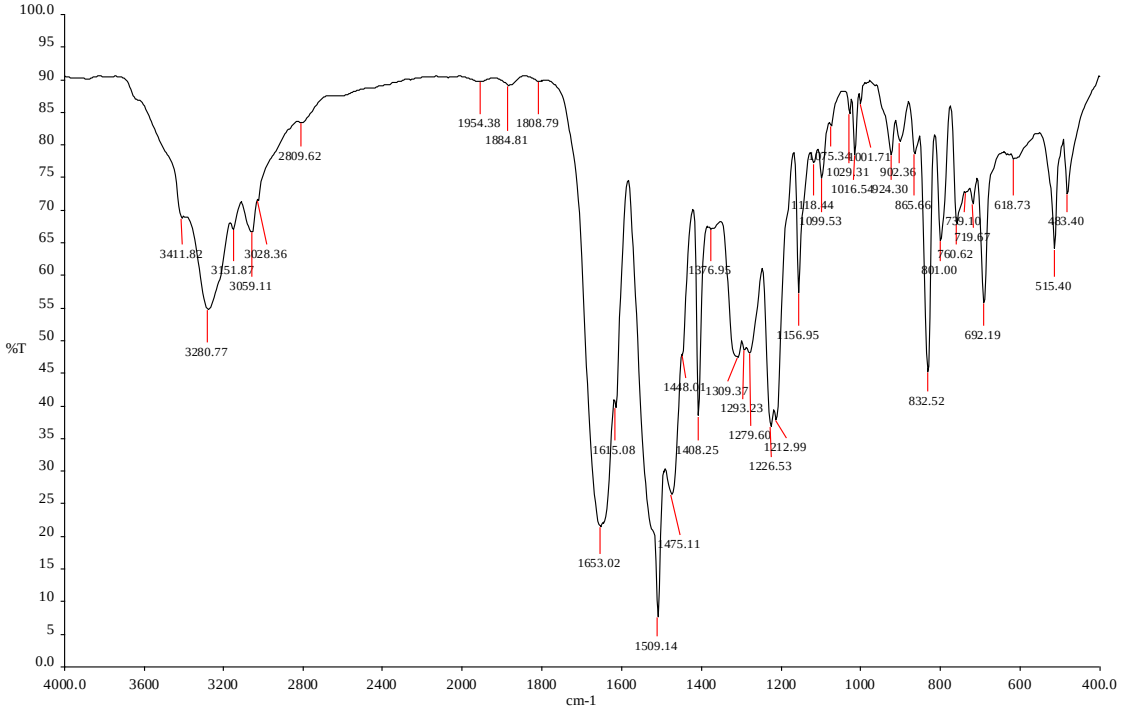


Figure 124. IR spectra for **6ab**

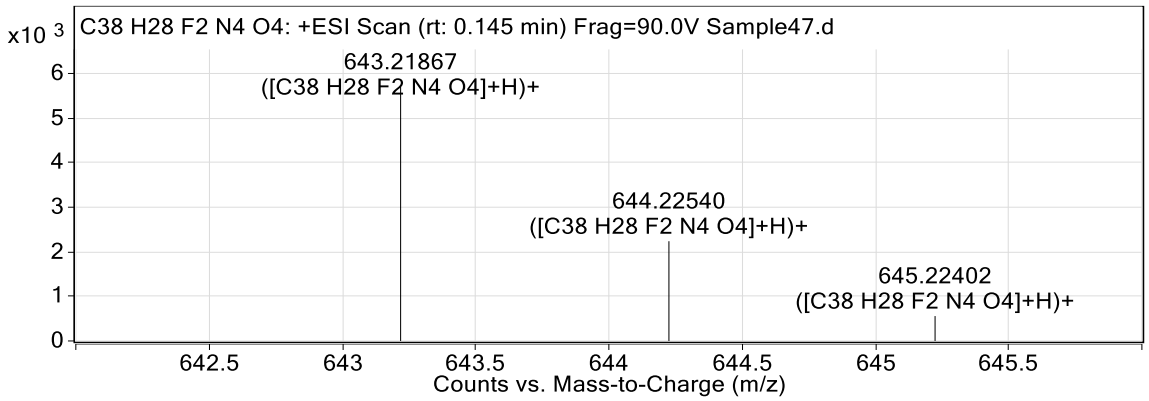
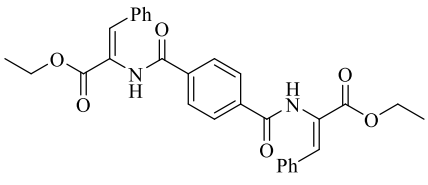


Figure 125. HRMS spectra for **6ab**



Diethyl 2,2'-(terephthaloylbis(azanediyl))(2E,2'E)-bis(3-phenylacrylate) **(6ac):** white powder (106 mg, yield 83%); mp 226-228 °C; IR (KBr) ν 3250, 1719, 1651, 1525, 1489, 1263, 1204, 1086, 770 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.23 (s, 2H), 8.09 (s, 4H), 7.69-7.66 -7.40 (m, 10H), 7.38 (s, 2H), 4.23-4.16 (q, J = 7.2 Hz, 4H), 1.22 (t, J = 7.3 Hz, 6H) ^{13}C NMR (75 MHz, DMSO-d_6) 165.5, 164.7, 136.1, 133.3, 133.1,

129.8, 129.5, 128.6, 127.8, 126.6, 60.9, 14.1 ppm; Anal. calcd for $C_{30}H_{28}N_2O_6$: C, 70.30; H, 5.51; N, 5.47; Found: C, 70.55; H, 5.30; N, 5.51.

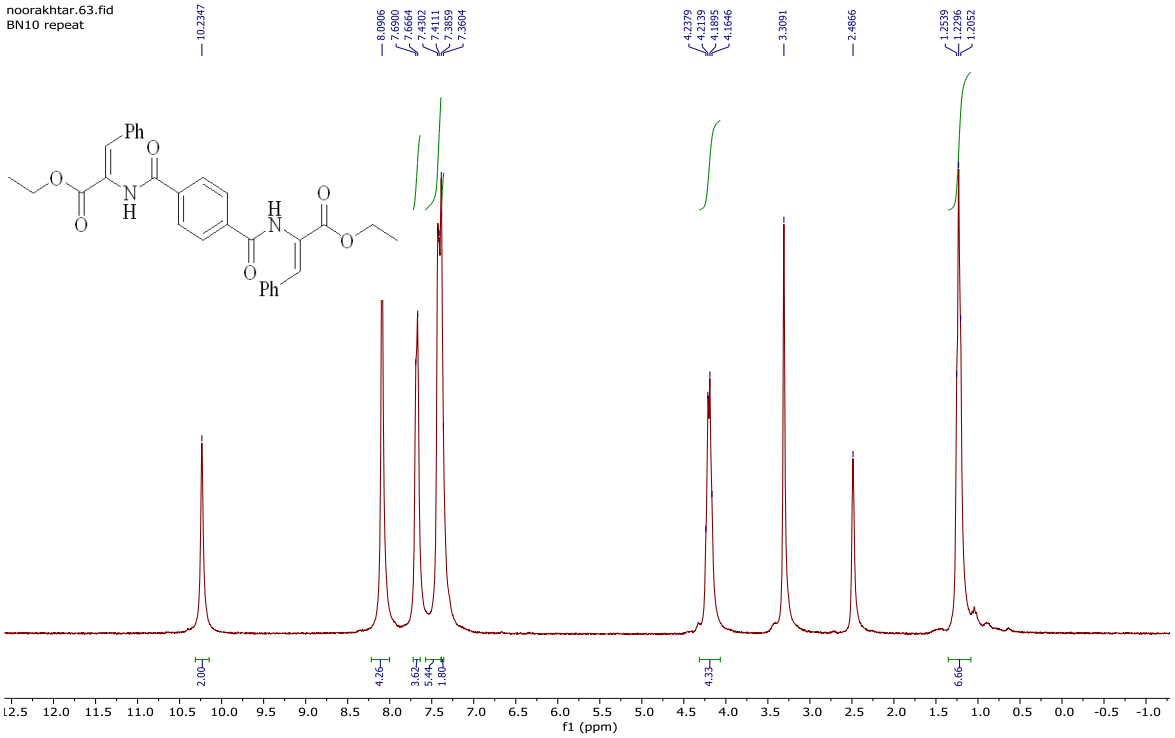


Figure 126. ^{1}H NMR spectra for **6ac**

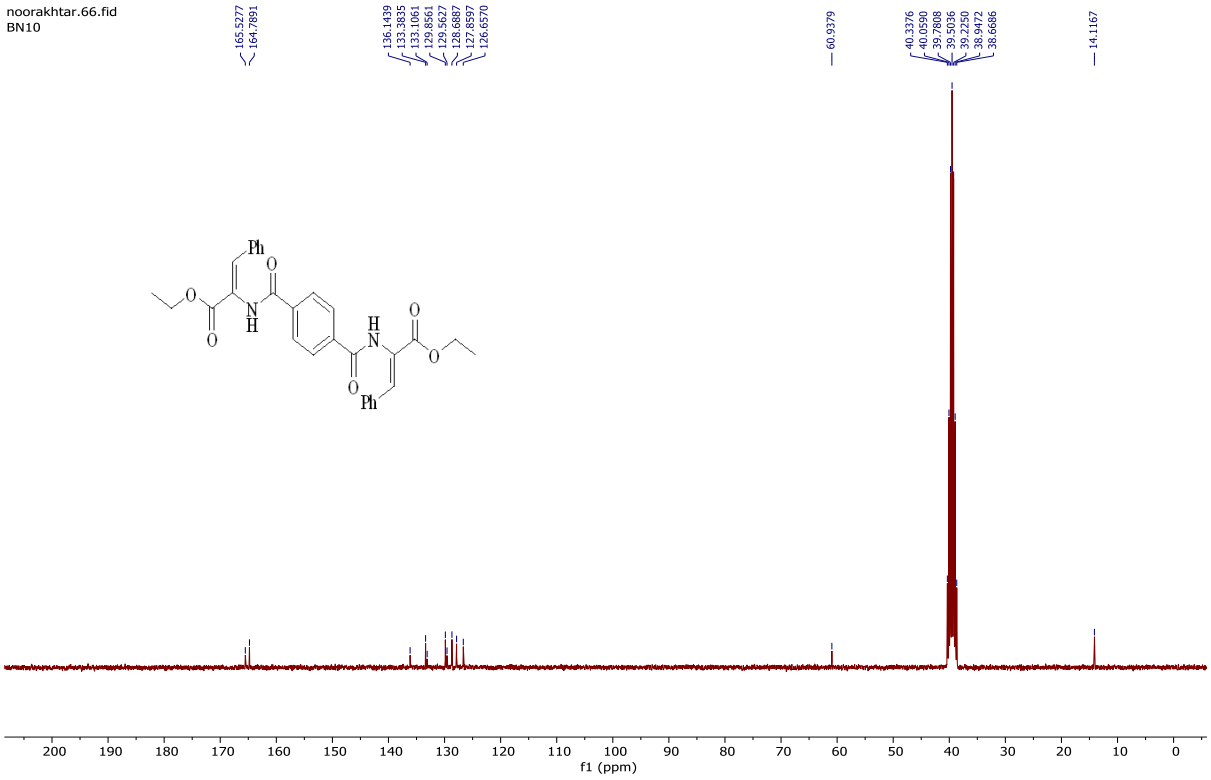


Figure 127. ^{13}C NMR spectra for **6ac**

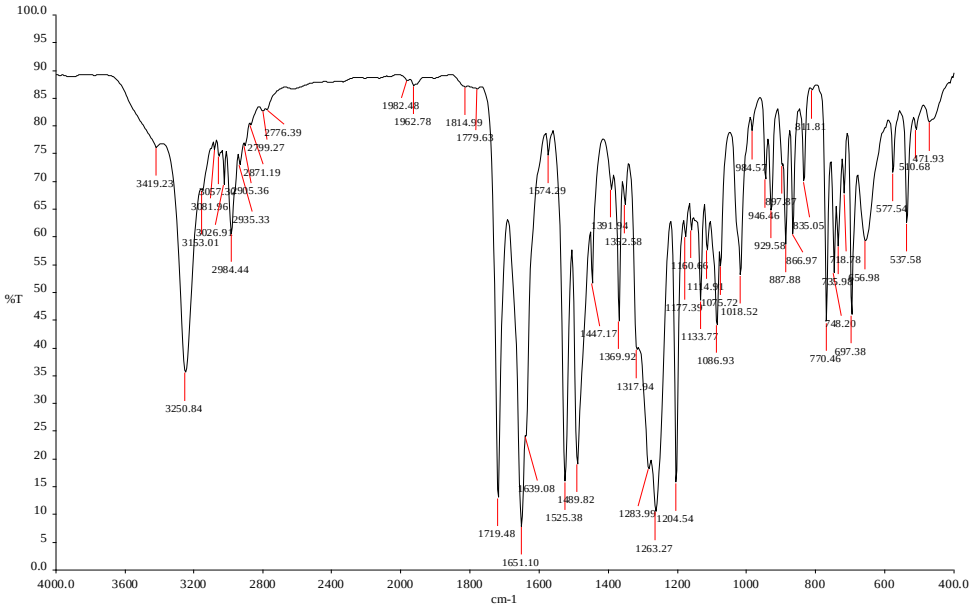
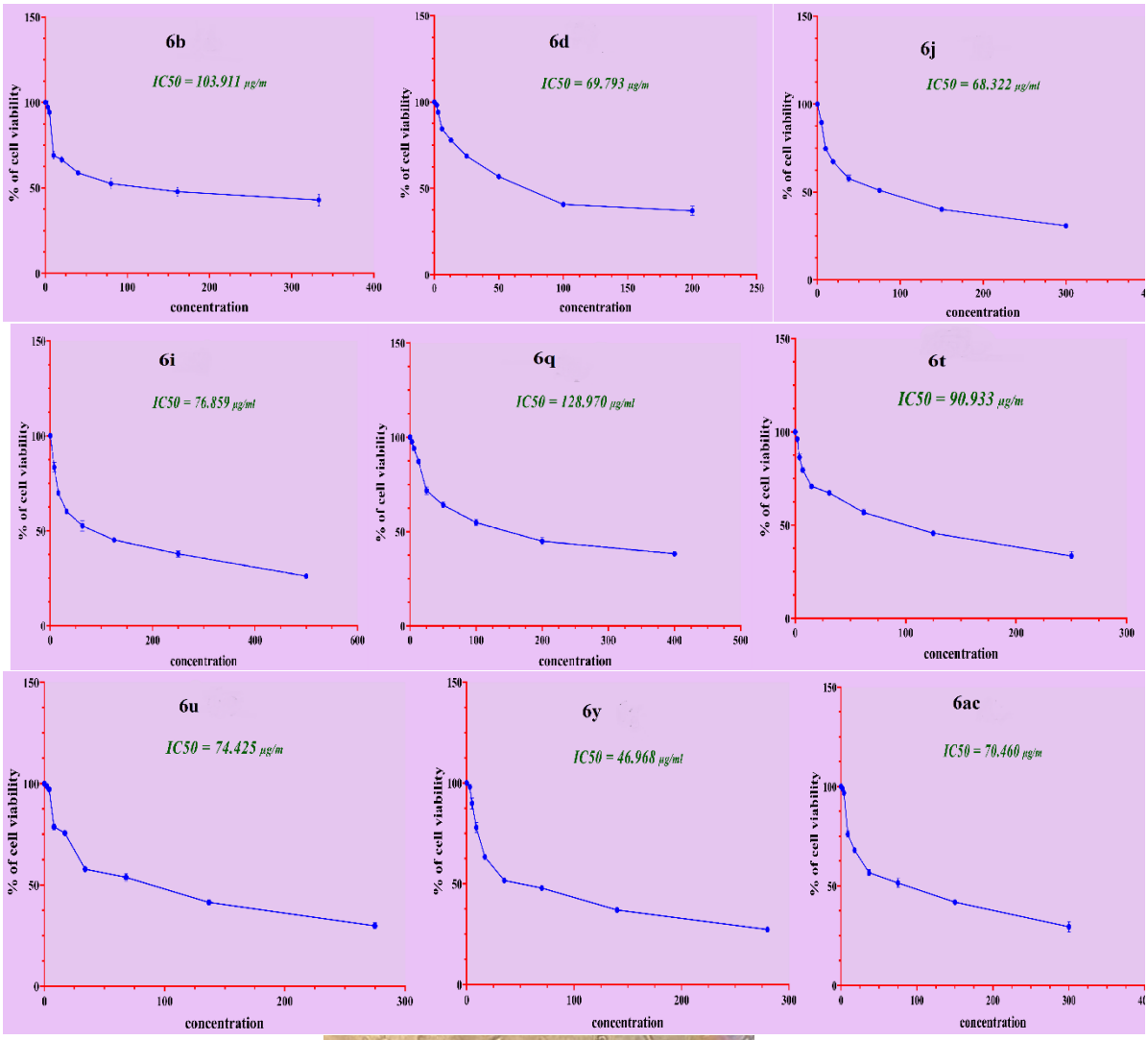


Figure 128. IR spectra for **6ac**

MTT Test

A



B

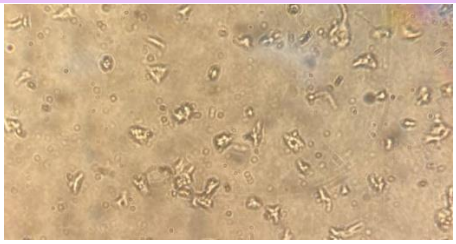


Fig. 129 (**A**) the IC50 values in hepatocellular carcinoma (HEPG2) cell line for 24 hours. The IC50 values of **6y** approximately 46.968 µg/ml displaying superior anti-cancer action compared to the others. (**B**) HEPG2 cell line shrinkage and cytopathic effects, suggesting that the chemicals are cytotoxic.

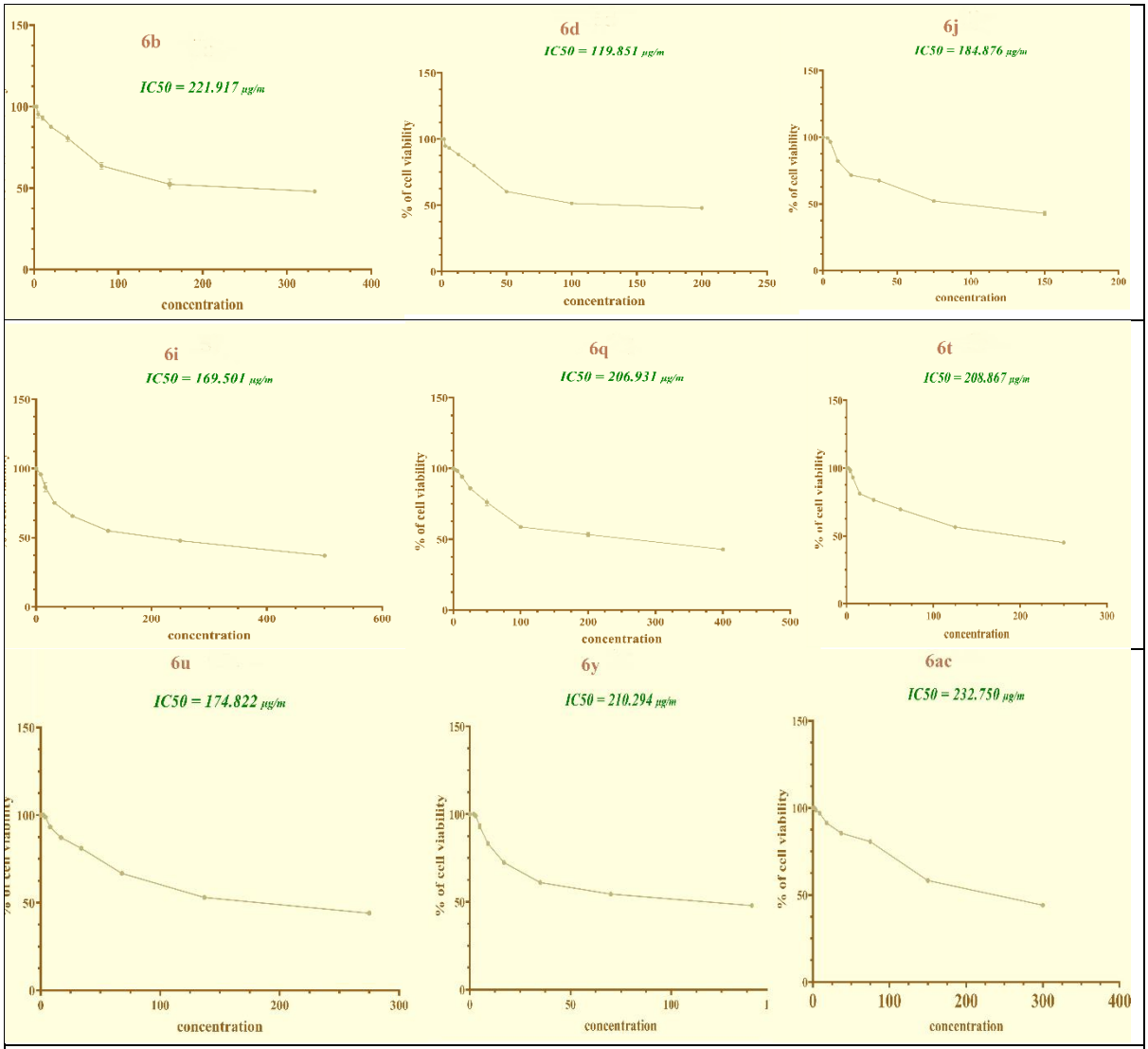


Fig. 130. The IC50 values in Human Dermal Fibroblasts (HDF), as a normal cell line, for 24 hours. Demonstrating selective toxicity and negligible effects on normal mammalian cells.