

Supplementary Material

Efficient three-component synthesis of *N*-alkyl-3,6-diaryl- [1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amines under solvent-free condition

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Supplementary Material

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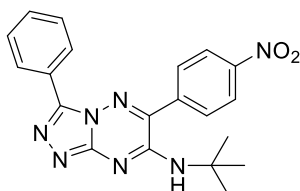
General information

All chemicals were purchased from Merck and Fluka companies. All yields refer to isolated products. IR spectra were recorded on a Shimadzu IR-460 spectrometer. ^1H and ^{13}C NMR spectra were recorded on a Bruker, Rheinstetten, Germany (at 500 and 400 MHz) NMR spectrometer using tetramethylsilane (TMS) as internal standard. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. Melting points were determined in a capillary tube and are not corrected. The progress of reaction was followed with TLC using silica gel SILG/UV 254 and 365 plates. All products are known compounds and their structures were deduced by ^1H and ^{13}C NMR spectroscopy.

General procedure for the preparation of products 4a–4h:

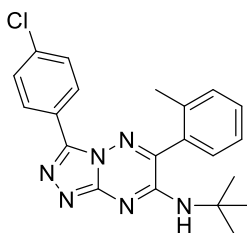
A mixture of appropriate 5-aryl-4*H*-1,2,4-triazole-3,4-diamine **1** (1.0 mmol), isocyanide **2** (1.0 mmol), and aldehyde **3** (1.0 mmol) was stirred in a sealed vessel at 150 °C under solvent-free condition for 4–9 h. After reaction completion (TLC), the reaction mixture was cooled to room temperature and the crude product was purified by column chromatography on silica gel using hexane–EtOAc (4:1) as eluent to afford products **4a–4h**.

Characterization data for compounds 4a–4h:

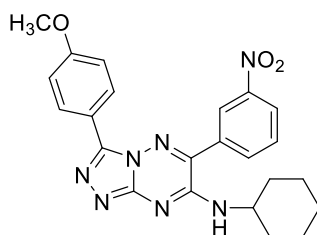


***N*-(*tert*-butyl)-3-(4-nitrophenyl)-6-phenyl-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4a):**

M.p = 218–220 °C; IR (KBr): 3379, 2936, 2875, 1628, 1500, 1548, 1423, 1366 cm⁻¹; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 0.99 (s, 9H), 4.65 (s, 1H), 7.19–7.22 (m, 3H), 7.51 (d, *J* = 9.0 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 2H), 8.51 (d, *J* = 8.0 Hz, 2H) ppm; ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 29.9, 59.9, 118.2, 121.5, 121.7, 124.3, 124.5, 127.5, 127.6, 128.4, 128.5, 132.0, 136.3, 149.3 ppm; MS (ESI): *m/z* [M + H]⁺ calcd for C₂₀H₁₉N₇O₂: 389.42; found: 389.39; Anal. Calcd for C₂₀H₁₉N₇O₂: C, 61.69; H, 4.92; N, 25.18. Found: C, 61.6; H, 4.9; N, 25.1.

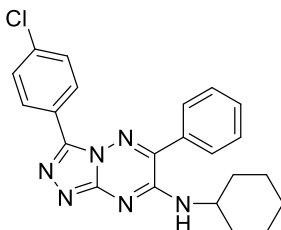
***N*-(*tert*-butyl)-3-(4-chlorophenyl)-6-(2-tolyl)-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4b):**

M.p = 224–226 °C; IR (KBr): 3370, 2930, 2852, 1601, 1570, 1565, 1489, 1382 cm⁻¹; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 0.99 (s, 9H), 2.32 (s, 3H), 4.56 (s, 1H), 6.85 (t, *J* = 7.0 Hz, 1H), 7.15 (t, *J* = 7.0 Hz, 1H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 7.0 Hz, 1H), 8.05 (d, *J* = 8.0 Hz, 2H), 8.38 (d, *J* = 7.0 Hz, 1H) ppm; ¹³C NMR (DMSO-*d*₆, 125 MHz): δ = 20.8, 30.0, 55.6, 116.3, 123.5, 123.8, 123.9, 124.0, 127.5, 127.6, 128.3, 128.4, 129.2, 132.4, 135.9, 137.9, 140.8 ppm; MS (ESI): *m/z* [M + H]⁺ calcd for C₂₁H₂₁ClN₆: 392.89; found: 392.85; Anal. Calcd for C₂₁H₂₁ClN₆: C, 64.20; H, 5.39; Cl, 9.02; N, 21.39. Found: C, 64.1; H, 5.3; Cl, 9.0; N, 21.2.

***N*-cyclohexyl-3-(4-methoxyphenyl)-6-(3-nitrophenyl)-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4c):**

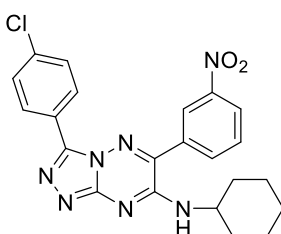
M.p = 188–190 °C; IR (KBr): 3277, 2944, 2856, 1654, 1527, 1530, 1428, 1338 cm⁻¹; ¹H NMR (DMSO-*d*₆, 500 MHz): δ = 1.08–1.70 (m, 10H), 2.81–2.84 (m, 1H), 4.00 (s, 3H), 4.79 (d, *J* = 6.0 Hz,

1H), 7.17 (d, $J = 7.5$ Hz, 1H), 7.28 (d, $J = 7.5$ Hz, 1H), 7.40 (t, $J = 7.5$ Hz, 1H), 7.51 (d, $J = 8.0$ Hz, 2H), 8.13 (t, $J = 7.5$ Hz, 1H), 8.33 (s, 1H) ppm; ^{13}C NMR (DMSO- d_6 , 125 MHz): $\delta = 24.3, 25.3, 33.4, 49.8, 56.2, 111.3, 111.5, 116.2, 123.2, 123.9, 124.9, 125.3, 127.7, 129.6, 130.0, 130.6, 134.2, 136.6, 143.1, 157.1$ ppm; MS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{23}\text{N}_7\text{O}_3$: 445.48; found: 445.42; Anal. Calcd for $\text{C}_{23}\text{H}_{23}\text{N}_7\text{O}_3$: C, 62.01; H, 5.20; N, 22.01; O, 10.77. Found: C, 61.9; H, 5.1; N, 21.9; O, 10.6.



3-(4-chlorophenyl)-N-cyclohexyl-6-phenyl-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4d):

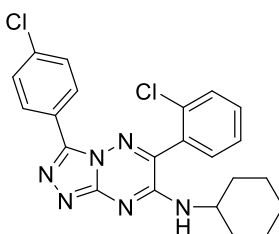
M.p = 212–214 °C; IR (KBr): 3294, 2973, 2844, 1600, 1528, 1483, 135 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz): $\delta = 0.91\text{--}1.59$ (m, 10H), 2.68–2.73 (m, 1H), 4.53 (s, 1H), 7.16 (m, 2H), 7.39–7.44 (m, 2H), 7.50–7.58 (m, 3H), 8.43 (d, $J = 8.0$ Hz, 2H) ppm; ^{13}C NMR (DMSO- d_6 , 125 MHz): $\delta = 24.0, 25.2, 32.9, 54.5, 118.6, 120.5, 120.7, 123.5, 126.5, 126.7, 127.4, 129.3, 132.3, 132.9, 133.8, 137.9$ ppm; MS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_6$: 404.90; found: 404.84; Anal. Calcd for $\text{C}_{22}\text{H}_{21}\text{ClN}_6$: C, 65.26; H, 5.23; Cl, 8.76; N, 20.76. Found: C, 65.2; H, 5.1; Cl, 8.7; N, 20.7.



3-(4-chlorophenyl)-N-cyclohexyl-6-(3-nitrophenyl)-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4e):

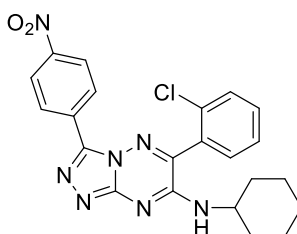
M.p = 185–187 °C; IR (KBr): 3270, 2900, 2810, 1628, 1544, 1525, 1489, 1366 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz): $\delta = 1.09\text{--}1.71$ (m, 10H), 2.80–2.82 (m, 1H), 4.78 (d, $J = 6.0$ Hz, 1H), 7.09 (d, $J = 7.5$ Hz, 1H), 7.18–7.31 (m, 3H), 7.34 (d, $J = 7.5$ Hz, 1H), 7.51 (d, $J = 8.0$ Hz, 2H), 8.13 (d, $J = 7.5$ Hz, 1H),

8.33 (s, 1H) ppm; ^{13}C NMR (DMSO- d_6 , 125 MHz): δ = 24.4, 25.3, 33.4, 52.8, 114.5, 117.2, 118.5, 120.8, 124.3, 124.6, 124.6, 127.7, 127.9, 128.1, 128.7, 157.3, 160.0 ppm; ; MS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{20}\text{ClN}_7\text{O}_2$: 449.90; found: 449.83; Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{ClN}_7\text{O}_2$: C, 58.73; H, 4.48; Cl, 7.88; N, 21.79. Found: C, 58.7; H, 4.4; Cl, 7.8; N, 21.7.



6-(2-chlorophenyl)-3-(4-chlorophenyl)-N-cyclohexyl-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4f):

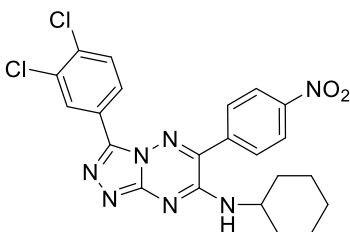
M.p = 190–192 °C; IR (KBr): 3230, 2917, 2860, 1625, 1587, 1555, 1364 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz): δ = 1.09–1.72 (m, 10H), 2.79 (m, 1H), 4.68 (d, J = 6.0 Hz, 1H), 6.84 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 7.14 (t, J = 7.5 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 7.5 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H) ppm; ^{13}C NMR (DMSO- d_6 , 125 MHz): δ = 24.4, 25.3, 33.4, 52.0, 111.0, 114.4, 116.4, 121.3, 123.1, 123.4, 124.6, 127.7, 130.1, 131.6, 135.3, 140.3, 157.1 ppm; MS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{20}\text{Cl}_2\text{N}_6$: 439.34; found: 439.31; Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{Cl}_2\text{N}_6$: C, 60.14; H, 4.59; Cl, 16.14; N, 19.13. Found: C, 60.0; H, 4.4; Cl, 16.0; N, 19.0.



-(2-chlorophenyl)-N-cyclohexyl-3-(4-nitrophenyl)-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4g):

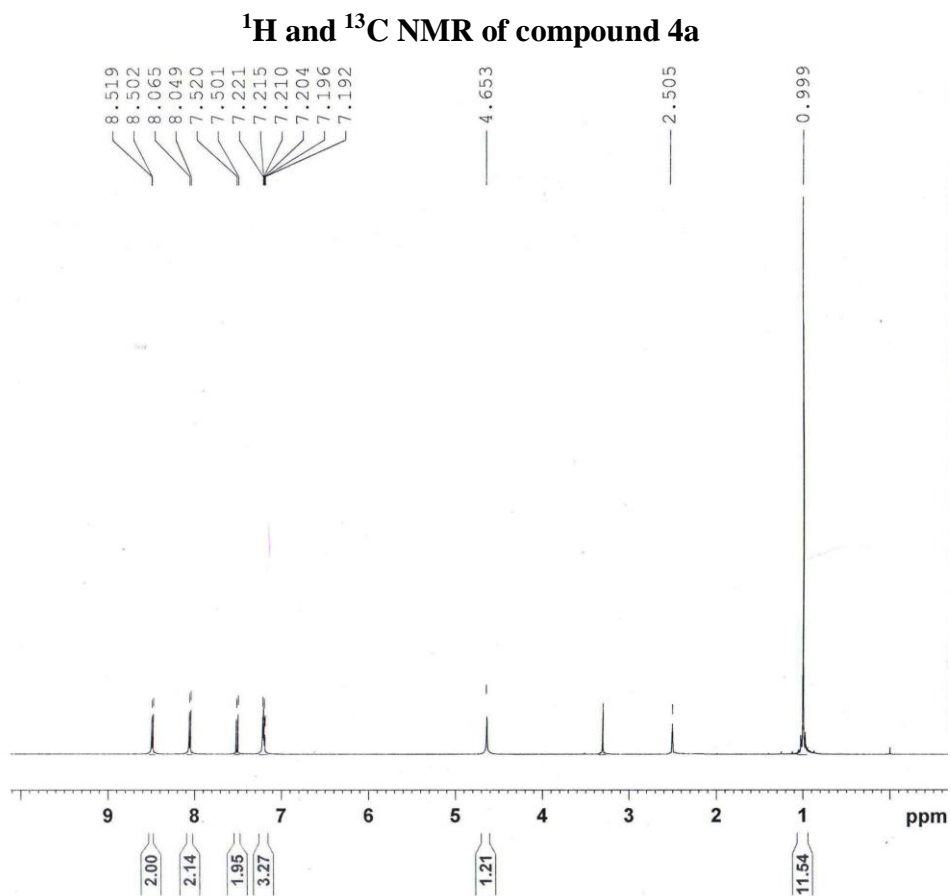
M.p = 202–204 °C; IR (KBr): 3285, 2900, 2827, 1615, 1577, 1515, 1479, 1365 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz): δ = 1.12–1.79 (m, 10H), 2.85–2.90 (m, 1H), 4.98 (s, 1H), 7.23 (t, J = 7.5 Hz, 1H), 7.52 (d, J = 7.5 Hz, 1H), 7.73 (t, J = 7.5 Hz, 1H), 8.11 (d, J = 8.0 Hz, 2H), 8.36 (d, J = 7.5 Hz, 1H),

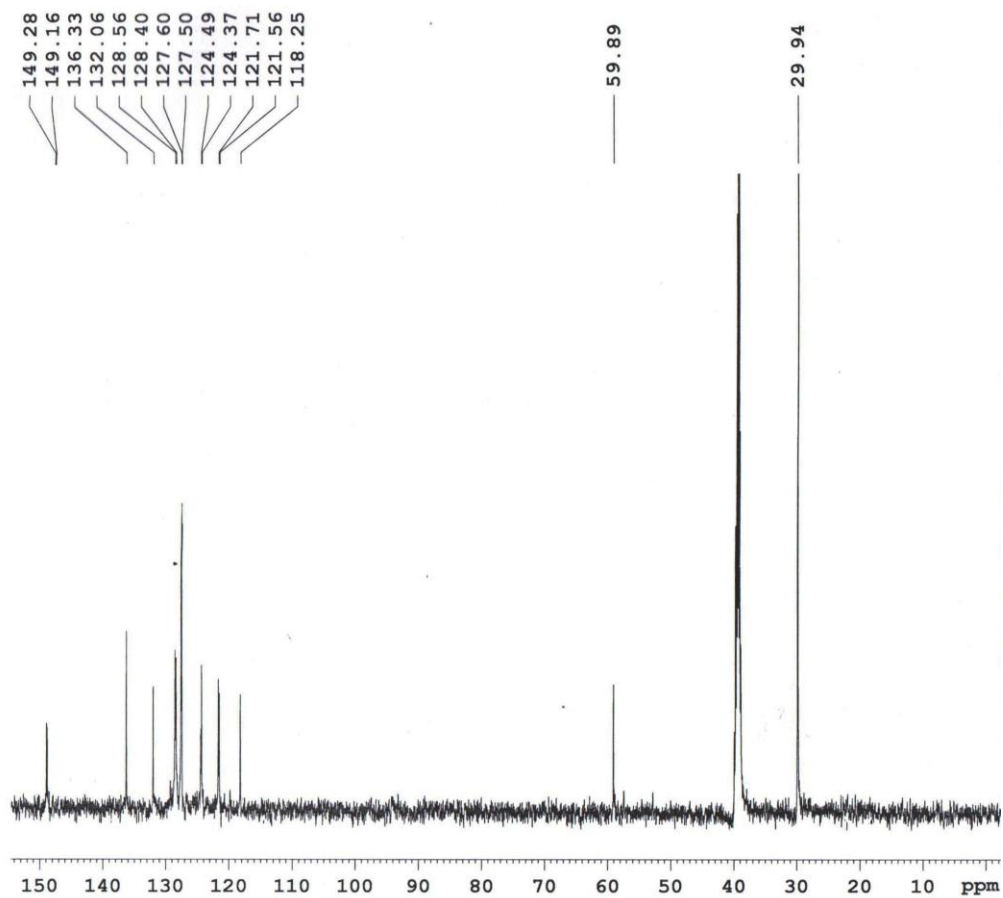
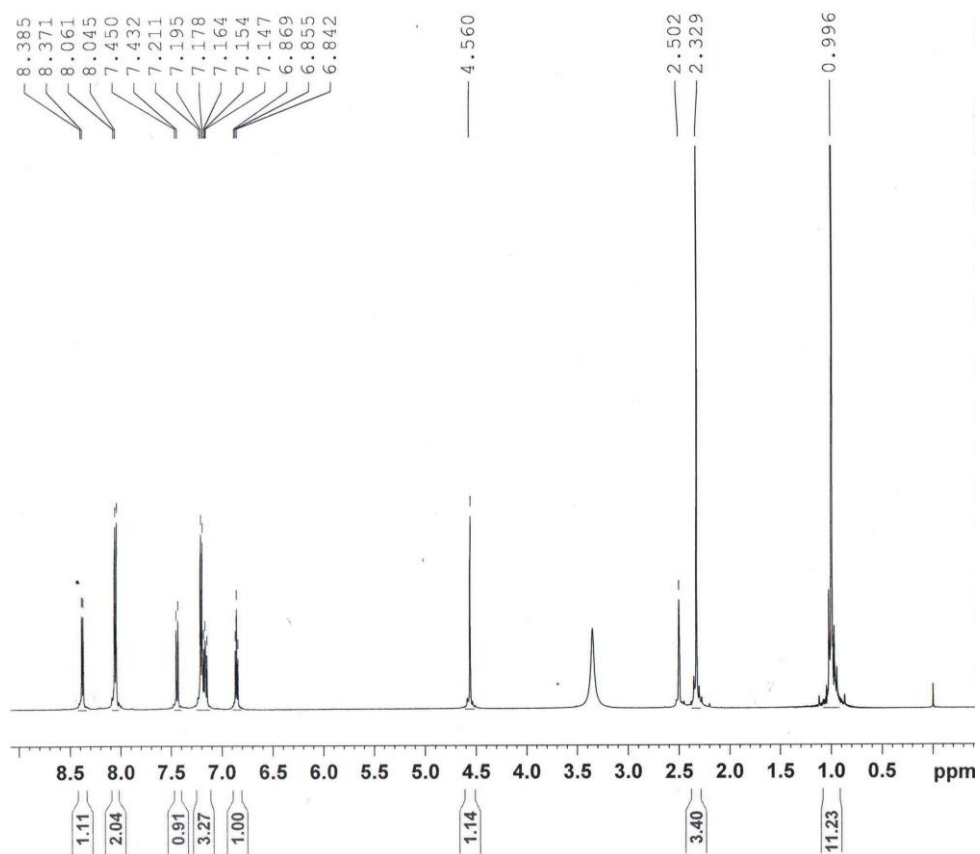
8.66 (d, $J = 8.0$ Hz, 2H) ppm; ^{13}C NMR (DMSO- d_6 , 125 MHz): $\delta = 24.4, 25.3, 33.5, 56.7, 116.8, 117.0, 121.1, 121.1, 123.5, 123.6, 124.4, 124.6, 129.7, 132.0, 132.2, 136.3, 140.7, 148.1$ ppm; MS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{20}\text{ClN}_7\text{O}_2$: 449.90; found: 449.82; Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{ClN}_7\text{O}_2$: C, 58.73; H, 4.48; Cl, 7.88; N, 21.79. Found: C, 58.7; H, 4.4; Cl, 7.7; N, 21.7.

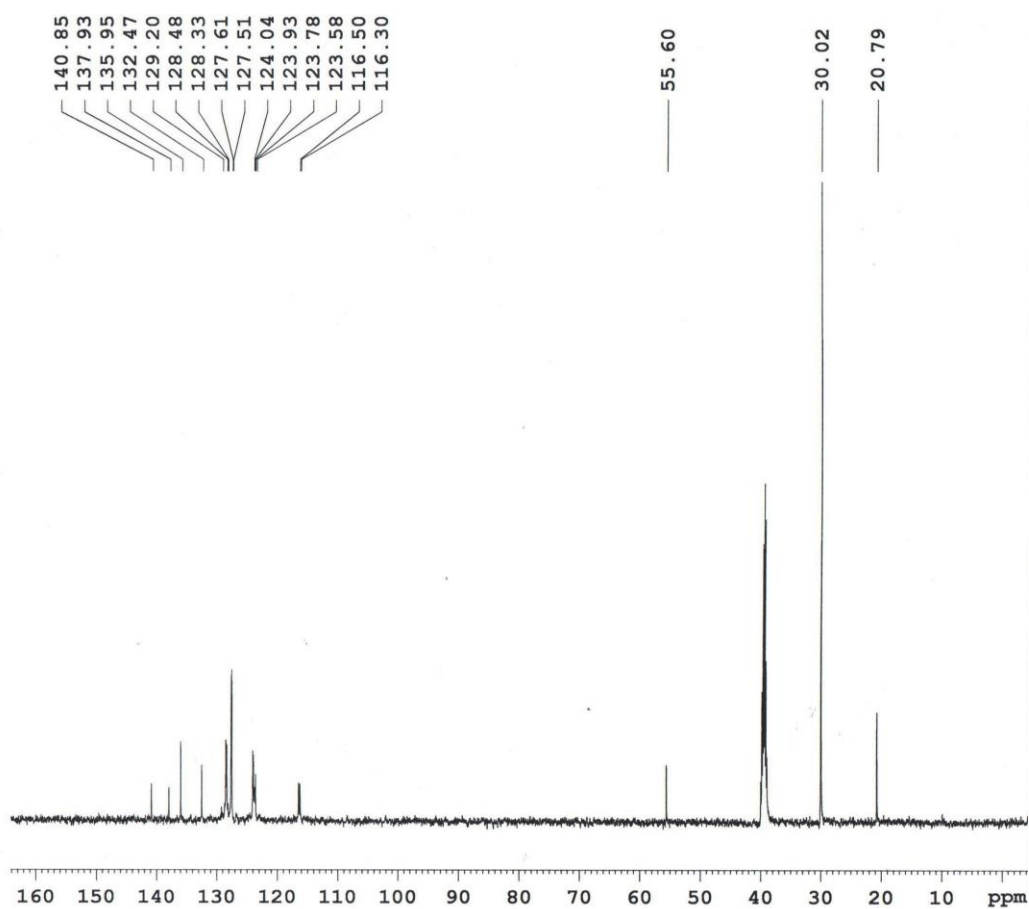
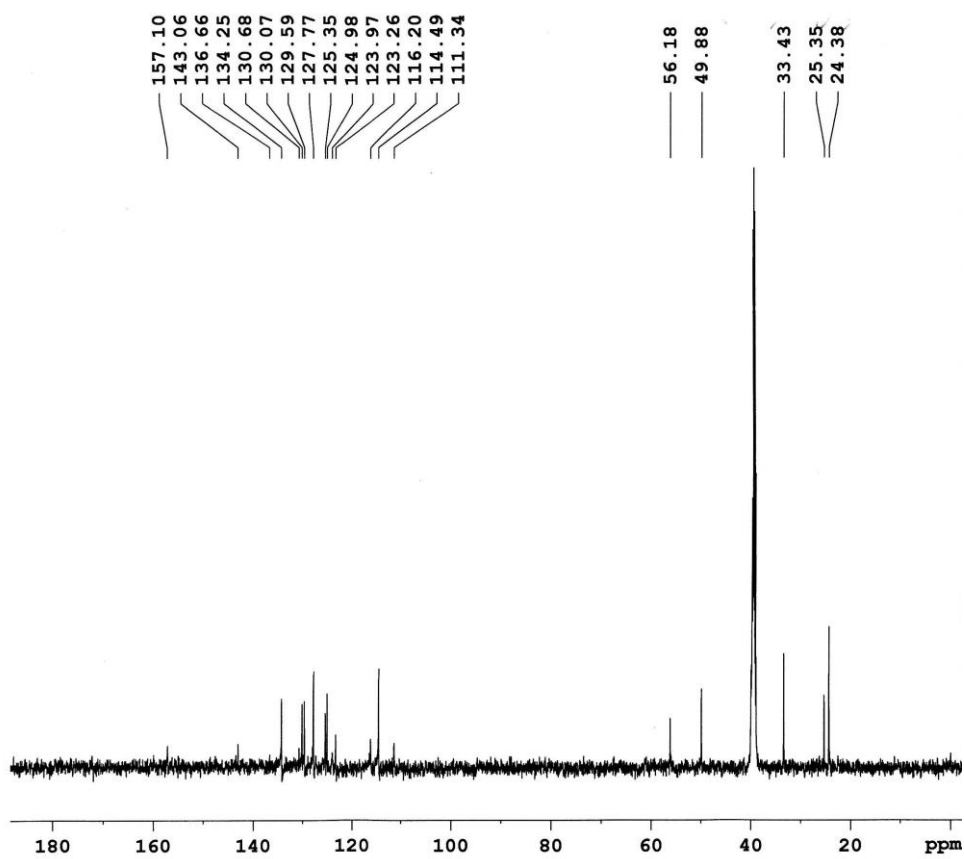


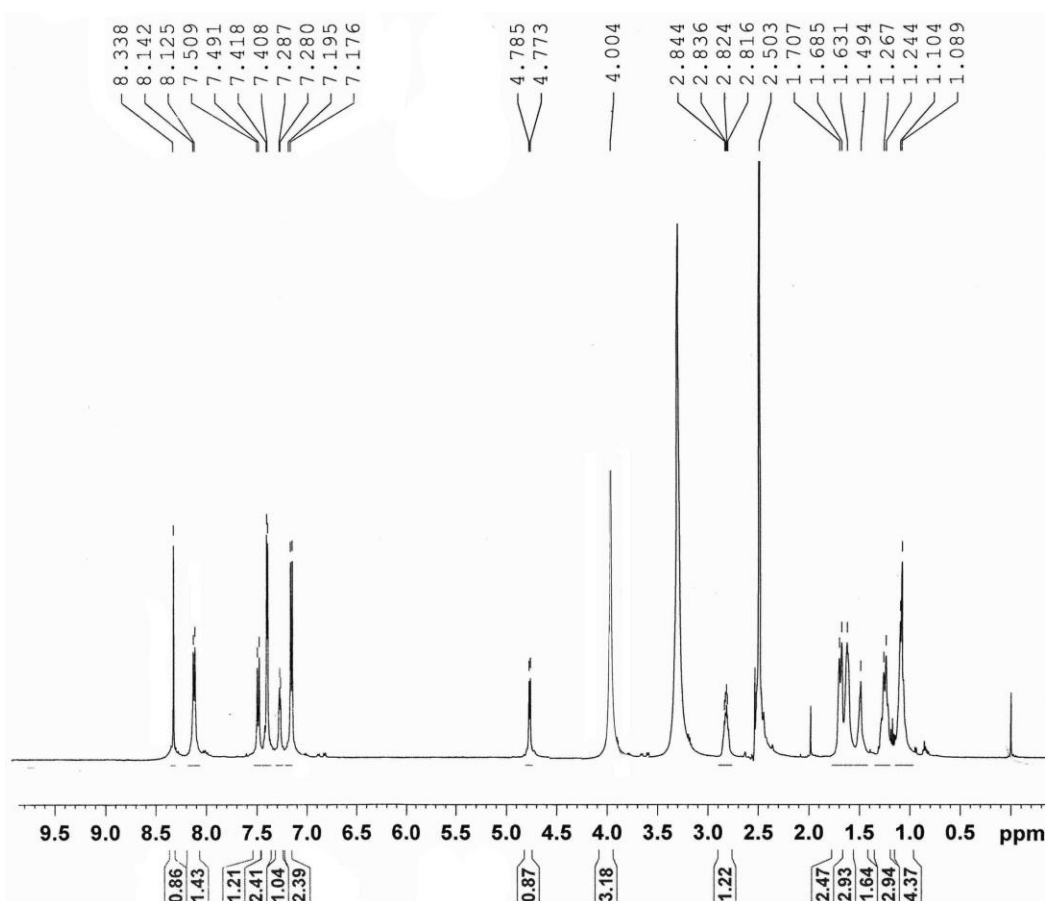
***N*-cyclohexyl-3-(3,4-dichlorophenyl)-6-(3-nitrophenyl)-[1,2,4]triazolo[4,3-*b*][1,2,4]triazin-7-amine (4h):**

M.p = 217–219 °C; IR (KBr): 3280, 2925, 2847, 1615, 1577, 1535, 1479, 1360 cm^{-1} ; ^1H NMR (DMSO- d_6 , 500 MHz): $\delta = 1.11\text{--}1.78$ (m, 10H), 2.84–2.88 (m, 1H), 5.05 (s, 1H), 7.26 (d, $J = 9.5$ Hz, 1H), 7.58 (d, $J = 9.5$ Hz, 1H), 7.74 (t, $J = 8.0$ Hz, 1H), 8.14 (d, $J = 8.0$ Hz, 1H), 8.57 (s, 1H), 8.63 (d, $J = 8.0$ Hz, 1H) 9.09 (d, $J = 8.0$ Hz, 1H) ppm; ^{13}C NMR (DMSO- d_6 , 125 MHz): $\delta = 24.5, 25.2, 33.5, 56.9, 119.0, 120.3, 120.6, 121.2, 121.3, 125.1, 127.8, 129.8, 132.0, 132.1, 132.7, 135.9, 139.0, 148.1$ ppm; MS (ESI): m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{22}\text{H}_{19}\text{Cl}_2\text{N}_7\text{O}_2$: 484.34; found: 484.26; Anal. Calcd for $\text{C}_{22}\text{H}_{19}\text{Cl}_2\text{N}_7\text{O}_2$: C, 54.56; H, 3.95; Cl, 14.64; N, 20.24. Found: C, 54.5; H, 3.8; Cl, 14.5; N, 20.2.

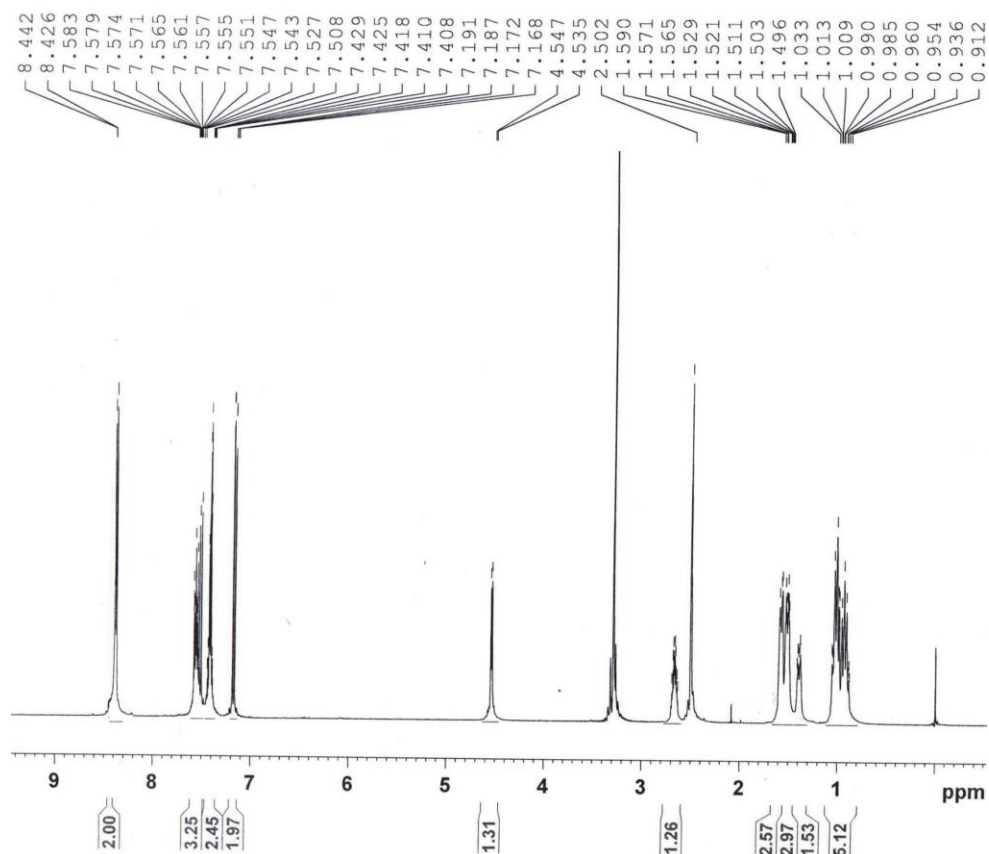


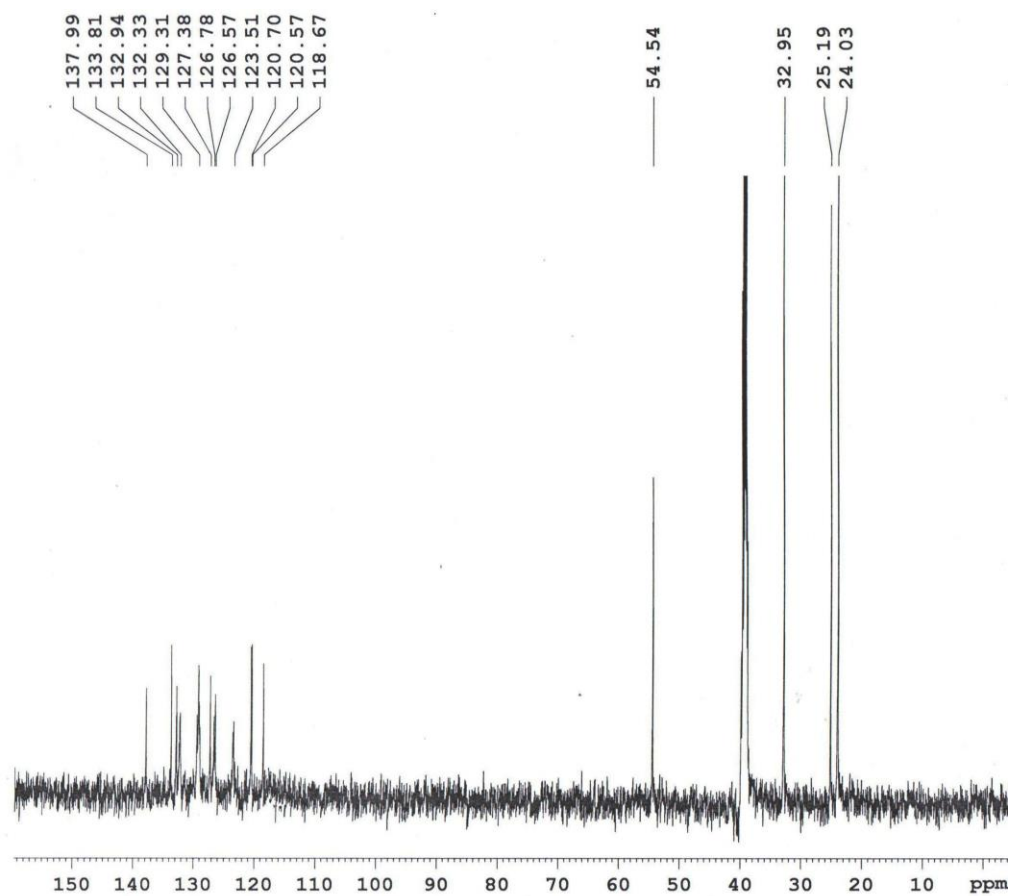
 ^1H and ^{13}C NMR of compound 4b

 ^1H and ^{13}C NMR of compound 4c

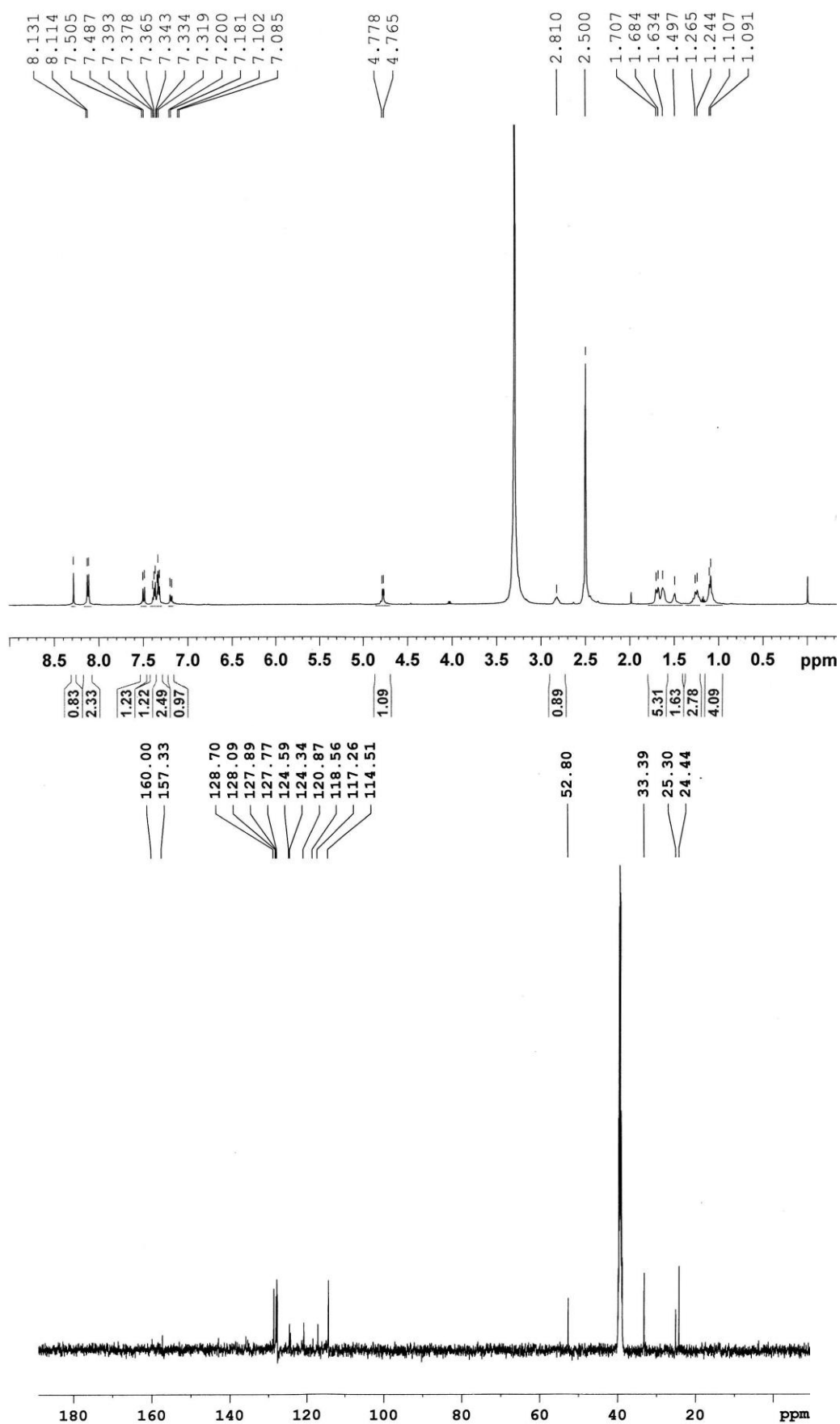


¹H and ¹³C NMR of compound 4d

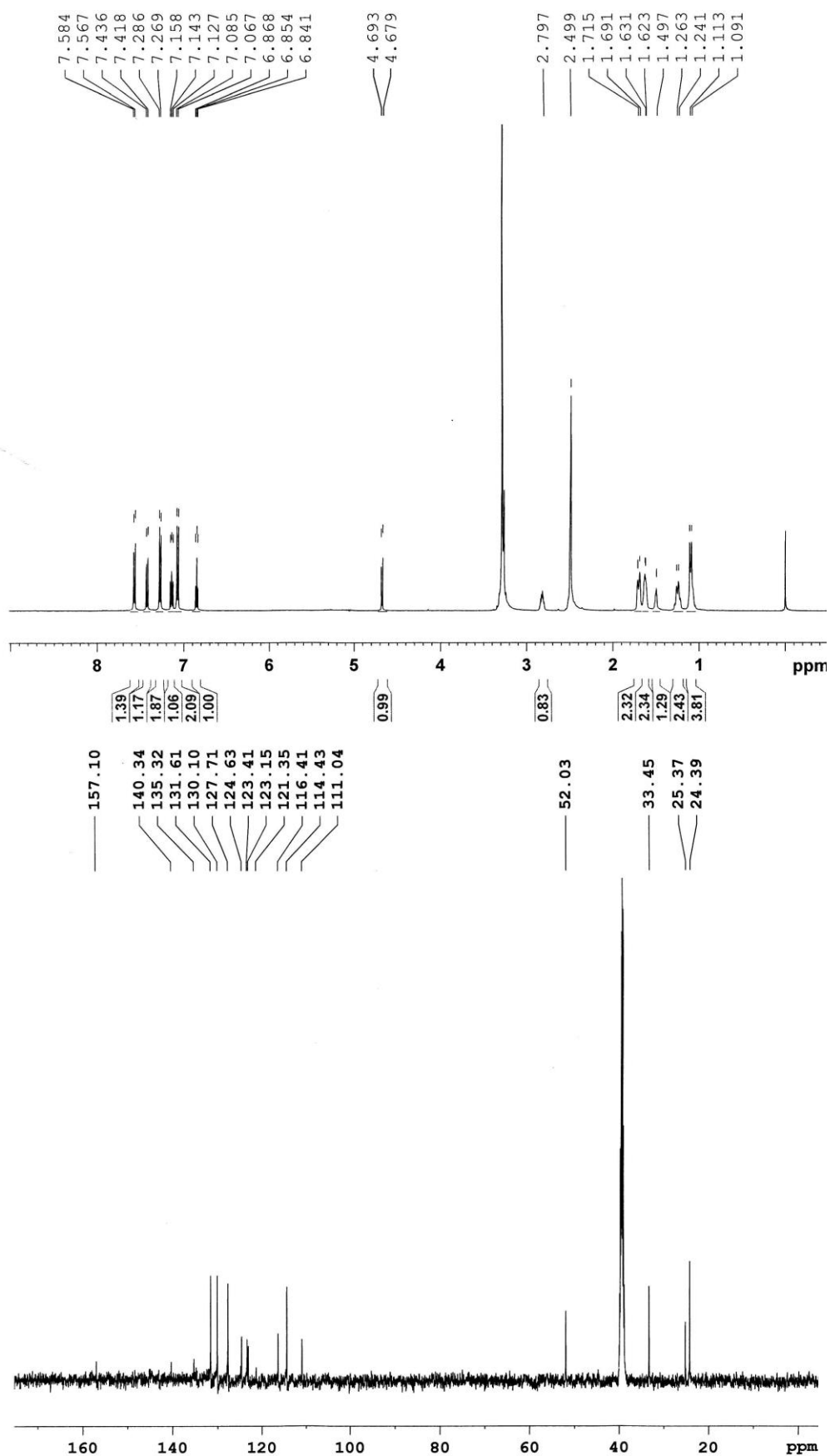


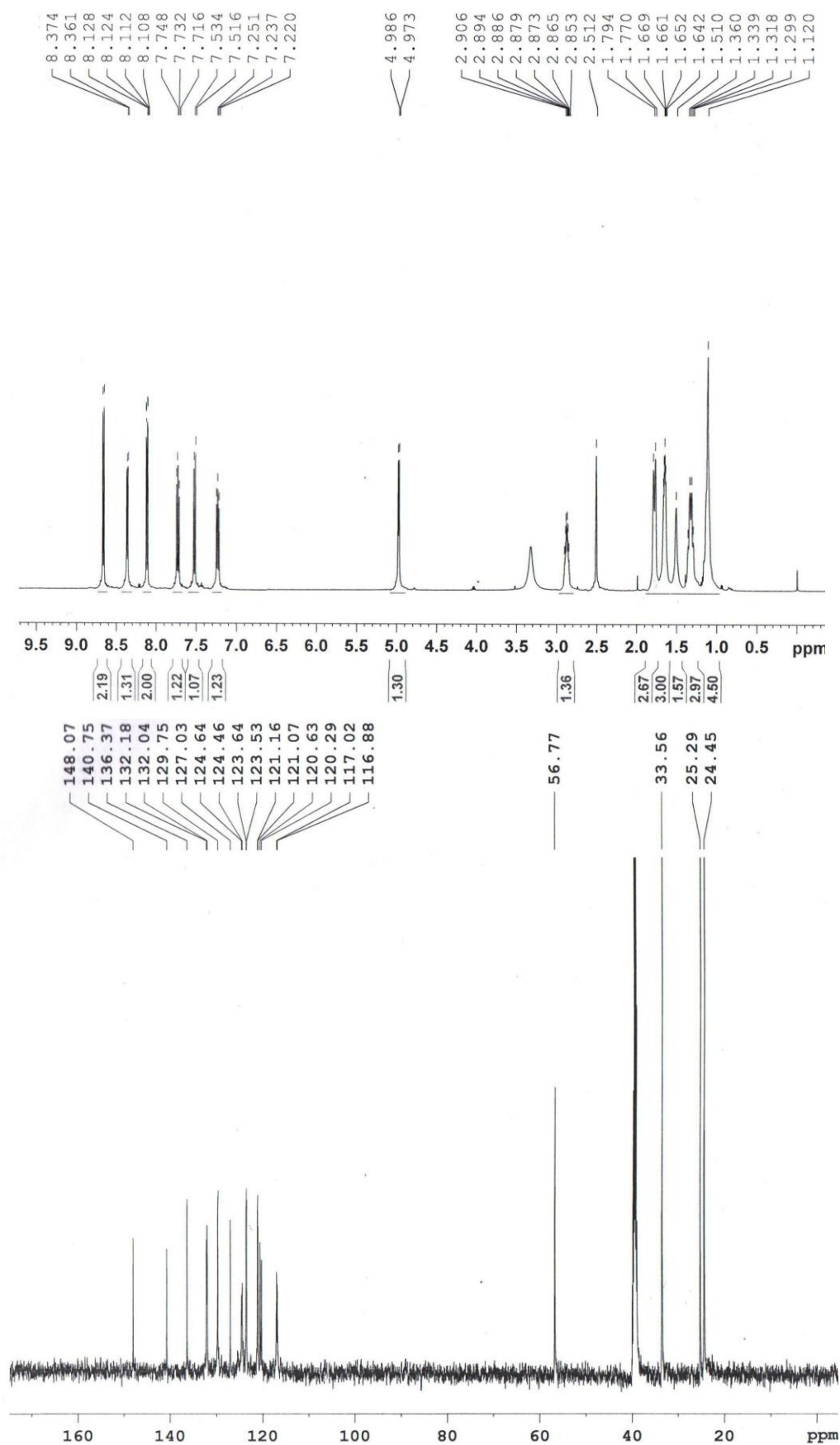


^1H and ^{13}C NMR of compound 4e



¹H and ¹³C NMR of compound 4f

 ^1H and ^{13}C NMR of compound 4g

 ^1H and ^{13}C NMR of compound 4h

