

Supplementary data

Experimental

General information

All commercially available chemicals and reagents were used without further purification. Melting points were determined with an Electrothermal model 9100 apparatus and are uncorrected. FT-IR spectra were recorded on a Shimadzu 4300 spectrophotometer. The ¹H-NMR spectra were recorded in DMSO-*d*₆ on Bruker DRX-300 Avance spectrometers. Chemical shifts (δ) are reported in parts per million and are referenced to the NMR solvent. Mass spectra of the products were obtained with a HP (Agilent technologies) 5973 Mass Selective Detector.

General procedure for the synthesis of lawsone enaminoone derivatives 4a-k: In a 25-ml round-bottom flask, a mixture of 2-hydroxy-1,4-naphthoquinone (1.0 mmol), aromatic amine (1.0 mmol), triethyl orthoformate (1.0 mmol), and guanidine hydrochloride (10 mol %) were taken, and the mixture was stirred at 90°C in an oil bath for appropriate amount of time as indicated in Table 2. The progress of the reaction was monitored by thin-layer chromatography. After completion, the reaction mixture was cooled to room temperature. The resulting precipitate crystallized from acetonitrile to yield pure product **4**.

3-((Pyrimidin-2-ylamino)methylene)naphthalene-1,2,4(3H)-trione (4a): Yield: 85%; Yellow powder; M.P. = 271-273 °C; IR (KBr, cm⁻¹): ν = 3397, 3060, 1690, 1665, 1608, 1594, 1552, 1443, 1408, 1346, 1294, 1249; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 6.97 (m, 4H, Ar-H), 7.44-7.49 (m, 1H, Ar-H), 7.83-7.96 (m, 2H, Ar-H), 8.07-8.21 (m, 2H, Ar-H), 8.85-8.87 (m, 2H, Ar-H), 9.23 (d, 0.44H, *J* = 13.2 Hz, CH), 8.39 (d, 0.56H, *J* = 13.2 Hz, CH), 12.56 (d, 0.56H, *J* = 13.2 Hz, NH), 12.66 (d, 0.44H, *J* = 13.2 Hz, NH); MS *m/z* (%): 279 (M⁺) (68.5), 251 (5.6), 223 (31.7), 222 (100), 195 (18.8), 194 (42.2), 172 (4.6), 140 (6.7), 116 (5), 104 (7.8), 101 (12.5), 97 (6.5), 89 (11), 80 (24.9), 79 (20.6), 77 (10.8), 76 (26.6).

3-(((4,6-Dimethylpyrimidin-2-yl)amino)methylene)naphthalene-1,2,4(3H)-trione (4b): Yield: 82%; Brown powder; M.P. = 222-224 °C; IR (KBr, cm⁻¹): ν = 3203, 3066, 1698, 1667, 1606, 1577, 1531, 1438, 1375, 1293, 1208; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 2.46-2.47 (2 X s, 6H, 2 X CH₃), 7.20-7.21 (2 X s, 1H, pyrimidine-H5), 7.81-7.94 (m, 2H, Ar-H), 8.04-8.16 (m, 1H, Ar-H), 8.18 (d, 1H, *J* = 7.5 Hz, Ar-H), 9.19 (d, 0.45H, *J* = 13.2 Hz, CH), 9.37 (d, 0.55H, *J* = 13.5 Hz, CH), 12.45 (d, 0.55H, *J* = 13.5 Hz, NH), 12.59 (d, 0.45H, *J* = 13.2 Hz, NH); MS *m/z* (%): 307 (M⁺) (70.2), 279 (9.2), 251 (32.9), 236 (34.4), 223 (36.6), 222 (100), 221 (23.9), 174 (19.9), 123 (83.7), 108 (50.8), 105 (28.8), 96 (60.3), 95 (43.6), 89 (18.3), 82 (26.1), 77 (17.1), 76 (34.6).

3-(((3-Methylpyridin-2-yl)amino)methylene)naphthalene-1,2,4(3H)-trione (4c): Yield: 85%; Green powder; M.P. = 245-247 °C; IR (KBr, cm⁻¹): ν = 3378, 3056, 2926, 2866, 1697, 1668, 1614, 1569, 1466, 1443, 1359, 1319, 1239, 1167; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 2.33 (s, 3H, CH₃), 7.15-7.21 (m, 1H, Ar-H), 7.64-7.81 (m, 3H, Ar-H), 7.94 (t, 1H, *J* = 6.9 Hz, Ar-H), 8.05-8.27 (m, 2H, Ar-H), 9.21 (d, 0.42H, *J* = 12.6 Hz, CH), 9.38 (d, 0.58H, *J* = 12.9 Hz, CH), 13.08-13.12 (m, 1H, NH); MS *m/z* (%): 292 (M⁺) (60.7), 236 (25.7), 235 (100), 219 (16.3), 208 (17.7), 207 (40.1), 131 (7.5), 104 (11.7), 101 (11.8), 93 (30), 92 (29.6), 89 (11.1), 77 (11.8), 76 (21.7).

3-(((4-Methylpyridin-2-yl)amino)methylene)naphthalene-1,2,4(3H)-trione (4d): Yield: 88%; Green powder; M.P. = 224-225 °C; IR (KBr, cm⁻¹): ν = 3419, 3059, 2924, 2860, 1696, 1959, 1608, 1572, 1543, 1483, 1397, 1361, 1267, 1159; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 2.27 (s, 3H, CH₃), 7.10 (t, 1H, *J* = 3.9 Hz, Ar-H), 7.49 (s, 1H, Ar-H), 7.74-7.98 (m, 3H, Ar-H), 8.09 (d, 1H, *J* = 7.8 Hz, Ar-H), 8.26 (t, 1H, *J* = 4.5 Hz, Ar-H), 9.24 (d, 0.45H, *J* = 13.8 Hz, CH), 9.39 (d, 0.55H, *J* = 13.8 Hz, CH), 12.61-12.70 (m, 1H, NH); MS *m/z* (%): 292 (M⁺) (80.4), 264 (13.9), 236 (46.4), 235 (100), 225 (16.1), 219 (13.9), 208 (34.1), 207 (51.7), 108 (11.3), 104 (17.8), 101 (14.4), 93 (44.6), 92 (35.9), 89 (14.0), 80 (12.7), 77 (15.2), 76 (31.3).

3-(((6-Methylpyridin-2-yl)amino)methylene)naphthalene-1,2,4(3H)-trione (4e): Yield: 78%; Yellow powder; M.P. = 222-223 °C; IR (KBr, cm⁻¹): ν = 3493, 3067, 2963, 2923, 1697, 1659, 1611, 1553, 1455, 1426, 1370, 1294, 1267, 1196; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 2.49 (s, 3H, CH₃), 7.21 (t, 1H, *J* = 3.6 Hz, Ar-H), 7.52 (d, 1H, *J* = 4.5 Hz, Ar-H), 7.82-7.94 (m, 3H, Ar-H), 8.06 (s, 1H, Ar-H), 8.18 (t, 1H, *J* = 3.6 Hz, Ar-H), 9.33 (d, 0.46H, *J* = 8.4 Hz, CH), 9.48 (d, 0.54H, *J* = 8.1 Hz, CH), 12.76 (d, 0.54H, *J* = 8.1 Hz, NH), 12.81 (d, 0.46H, *J* = 7.8 Hz, NH); MS *m/z* (%): 292 (M⁺) (77.5), 264 (17.6), 236 (32.8), 235 (38.4), 222 (36.4), 221 (61.2), 208 (31.3), 207 (100), 206 (22.4), 108 (13.4), 104 (23.9), 101 (24.0), 93 (68.2), 92 (44.1), 89 (25.7), 77 (21.2), 76 (49.5).

3-(((5-Bromopyridin-2-yl)amino)methylene)naphthalene-1,2,4(3H)-trione (4f): Yield: 82%; Green powder; M.P. = 282-284 °C; IR (KBr, cm⁻¹): ν = 3161, 3061, 1694, 1662, 1599, 1544, 1465, 1435, 1356, 1313, 1260, 1166, 1095; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.72-7.96 (m, 3H, Ar-H), 8.08-8.10 (m, 1H, Ar-H), 8.19-8.21 (m, 2H, Ar-H), 8.65-8.67 (dd, 1H, *J* = 0.9, 4.2 Hz, Ar-H), 9.29 (d, 0.45H, *J* = 8.1 Hz, CH), 9.44 (d, 0.55H, *J* = 8.1 Hz, CH), 12.72 (d, 0.55H, *J* = 8.1 Hz, NH), 12.78 (d, 0.45H, *J* = 7.8 Hz, NH); MS *m/z* (%): 358 (M+2)⁺ (76.0), 356 (M⁺) (73.0), 330 (7.3), 328 (7.3), 302 (30.3), 301 (100), 300 (26.3), 299 (93.0), 285 (7.0), 283 (8.0), 273 (24.0), 271 (22.1), 220 (19.8), 192 (21.2), 172 (12.3), 157 (22.8), 101 (16), 89 (12.8), 77 (13.2), 76 (32.1).

3-((Phenylamino)methylene)naphthalene-1,2,4(3H)-trione (4g): Yield: 90%; Brown powder; M.P. = 227-229 °C; IR (KBr, cm⁻¹): ν = 3399, 3065, 1701, 1659, 1609, 1566, 1463, 1422, 1315, 1272, 1206; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.36 (t, 1H, *J* = 3.9 Hz, Ar-H), 7.51 (m, 2H, Ar-H), 7.69 (d, 2H, *J* = 4.5 Hz, Ar-H), 7.84-7.95 (m, 2H, Ar-H), 8.07 (t, 1H, *J* = 4.2 Hz, Ar-H), 8.19 (d, 1H, *J* = 4.5 Hz, Ar-H), 8.79 (d, 0.45H, *J* = 8.4 Hz, CH), 8.96 (d, 0.55H, *J* = 8.7 Hz, CH), 13.05-13.08 (m, 1H, NH); MS *m/z* (%): 277 (M⁺) (53.6), 249 (52.6), 248 (67.7), 220 (40.7), 204 (39.5), 193 (13.4), 172 (11.3), 165 (25.2), 144 (19.0), 129 (10.2), 117 (20.6), 105 (19.8), 104 (64.2), 101 (31.6), 90 (18.6), 89 (44.9), 77 (100), 76 (68.2).

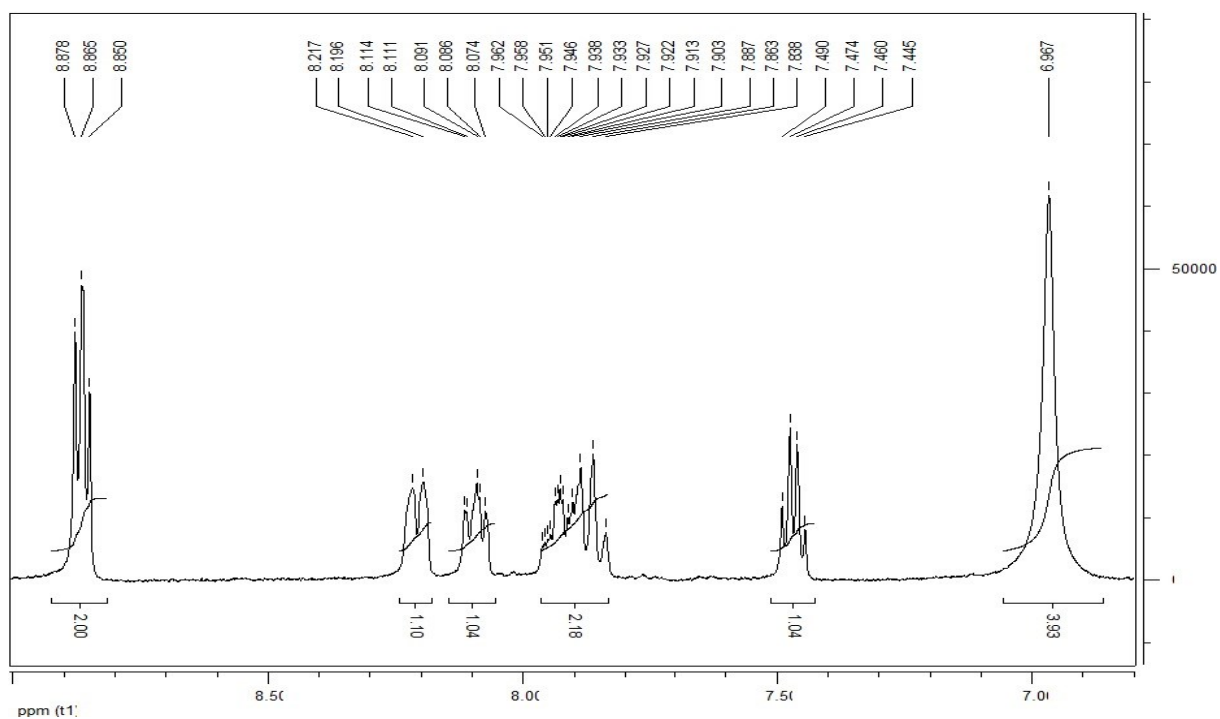
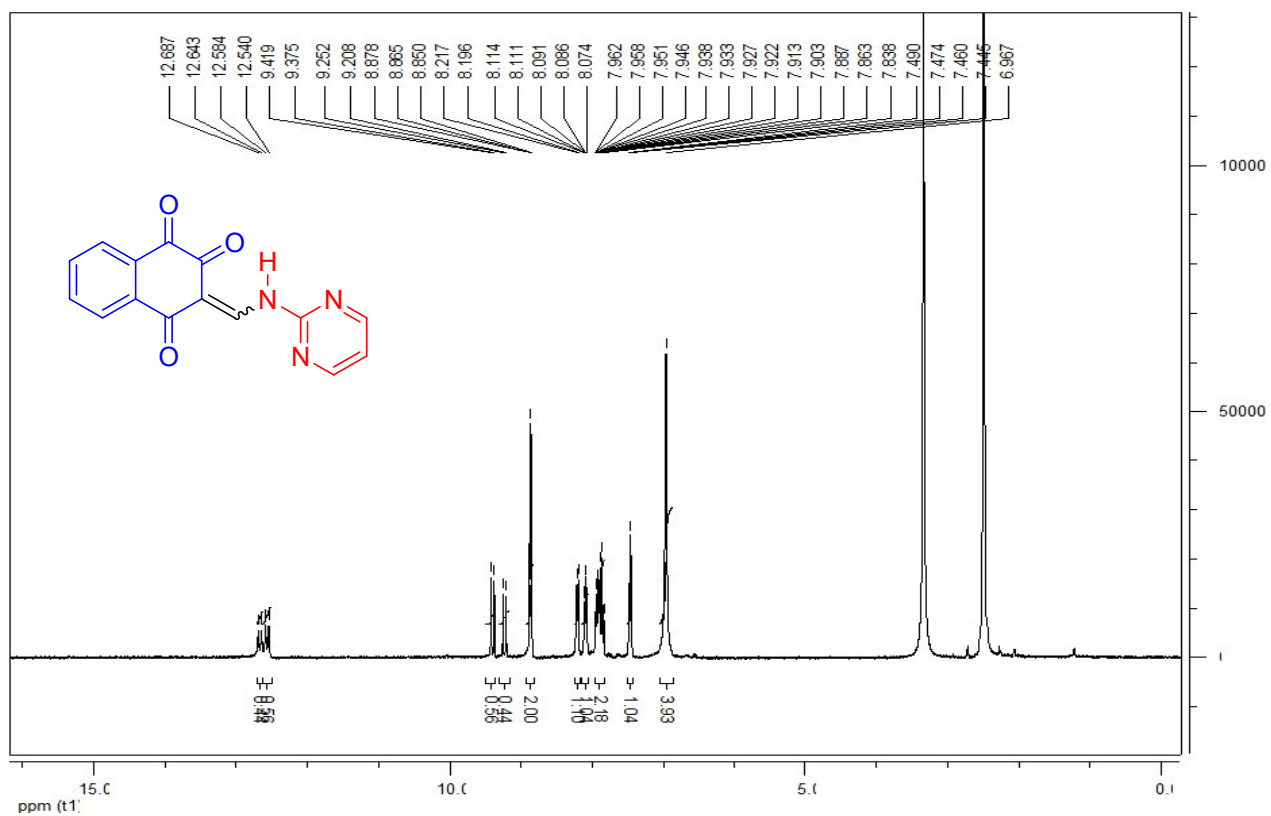
3-((*p*-Tolylamino)methylene)naphthalene-1,2,4(3H)-trione (4h): Yield: 87%; Orange powder; M.P. = 211-213 °C; IR (KBr, cm⁻¹): ν = 3341, 3066, 2950, 2916, 1700, 1660, 1611, 1566, 1458, 1430, 1318, 1276, 1213; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 2.33 (s,

3H, CH₃), 7.29 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.56 (d, 2H, *J* = 8.1 Hz, Ar-H), 7.82 (t, 1H, *J* = 7.2 Hz, Ar-H), 7.90 (t, 1H, *J* = 7.2 Hz, Ar-H), 8.04 (d, 1H, *J* = 7.8 Hz, Ar-H), 8.16 (d, 1H, *J* = 7.5 Hz, Ar-H), 8.74 (d, 0.44H, *J* = 13.5 Hz, CH), 8.90 (d, 0.56H, *J* = 13.8 Hz, CH), 13.04 (m, 1H, NH); MS *m/z* (%): 291 (M⁺) (65.9), 276 (8.1), 263 (35.0), 262 (37.9), 249 (23.2), 248 (100), 234 (21.5), 220 (18.5), 219 (14.0), 218 (22.4), 206 (11.0), 204 (10.8), 158 (14.9), 131 (18.9), 130 (15.2), 105 (18.8), 104 (45.9), 101 (22.8), 91 (29.2), 89 (17.7), 77 (25.7), 76 (25.5).

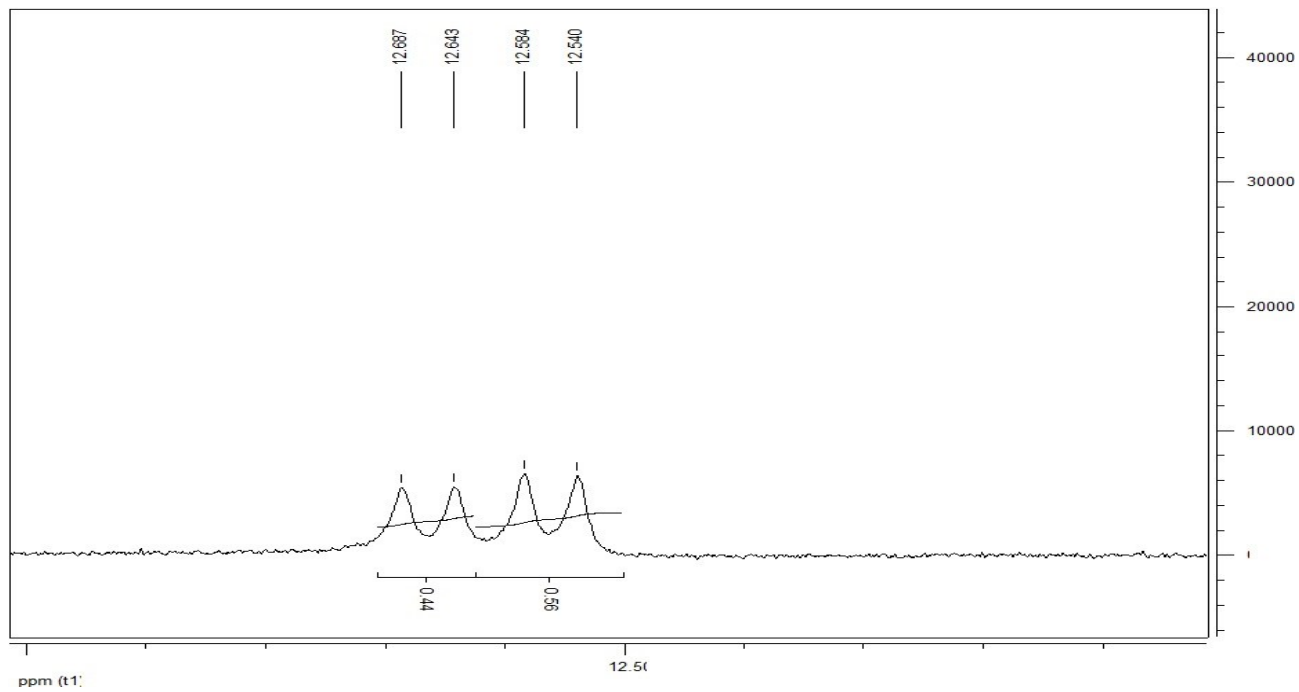
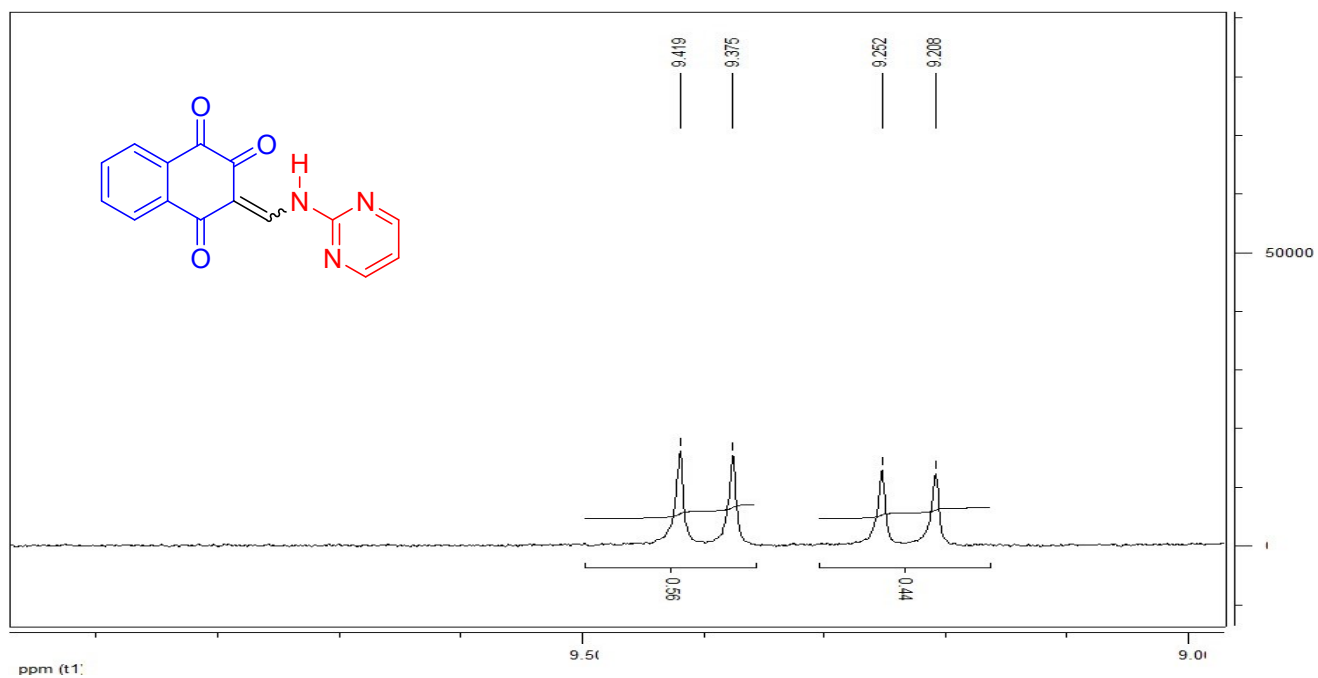
3-(((3-Chlorophenyl)amino)methylene)naphthalene-1,2,4(3H)-trione (4i): Yield: 83%; Yellow powder; M.P. = 228-230 °C; IR (KBr, cm⁻¹): ν = 3172, 3076, 1701, 1659, 1614, 1589, 1558, 1445, 1412, 1312, 1271, 1230, 1166; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.38 (d, 1H, *J* = 7.5 Hz, Ar-H), 7.47-7.67 (m, 2H, Ar-H), 7.80-7.94 (m, 3H, Ar-H), 8.05 (d, 1H, *J* = 7.5 Hz, Ar-H), 8.18 (d, 1H, *J* = 7.5 Hz, Ar-H), 8.77 (d, 0.45H, *J* = 14.1 Hz, CH), 8.93 (d, 0.55H, *J* = 14.1 Hz, CH), 12.89-12.96 (m, 1H, NH); MS *m/z* (%): 313 (M+2)⁺ (35.7), 311(M⁺) (83.3), 285 (20.1), 284 (23.0), 283 (51.8), 282 (37.1), 254 (24.1), 249 (29.4), 248 (100), 238 (21.4), 220 (19.9), 204 (11.5), 178 (12.6), 165 (18.9), 151 (20.3), 132 (16.2), 111 (22.3), 105 (28), 104 (86.8), 101 (26.6), 89 (21.1), 77 (20.7), 76 (37.4).

3-(((4-Chlorophenyl)amino)methylene)naphthalene-1,2,4(3H)-trione (4j): Yield: 85%; Brown powder; M.P. = 280-281 °C; IR (KBr, cm⁻¹): ν = 3430, 3054, 1698, 1661, 1608, 1562, 1460, 1432, 1407, 1332, 1281, 1229, 1094; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.55 (d, 2H, *J* = 8.7 Hz, Ar-H), 7.73 (d, 2H, *J* = 8.7 Hz, Ar-H), 7.83 (t, 1H, *J* = 7.2 Hz, Ar-H), 7.91 (t, 1H, *J* = 7.2 Hz, Ar-H), 8.06 (d, 1H, *J* = 7.5 Hz, Ar-H), 8.17 (d, 1H, *J* = 7.2 Hz, Ar-H), 8.74 (d, 0.42H, *J* = 13.2 Hz, CH), 8.90 (d, 0.58H, *J* = 14.1 Hz, CH), 12.94-12.99 (m, 1H, NH); MS *m/z* (%): 313 (M+2)⁺ (19.0), 311(M⁺) (47.1), 284 (9.4), 283 (16.9), 282 (19.6), 254 (12.0), 249 (22.0), 248 (100), 238 (11.4), 220 (11.5), 165 (11.9), 157 (9.4), 151 (9.5), 129 (9.5), 111 (19.8), 105 (23.5), 104 (67.7), 101 (24.7), 89 (18.9), 77 (20.9), 76 (36.2).

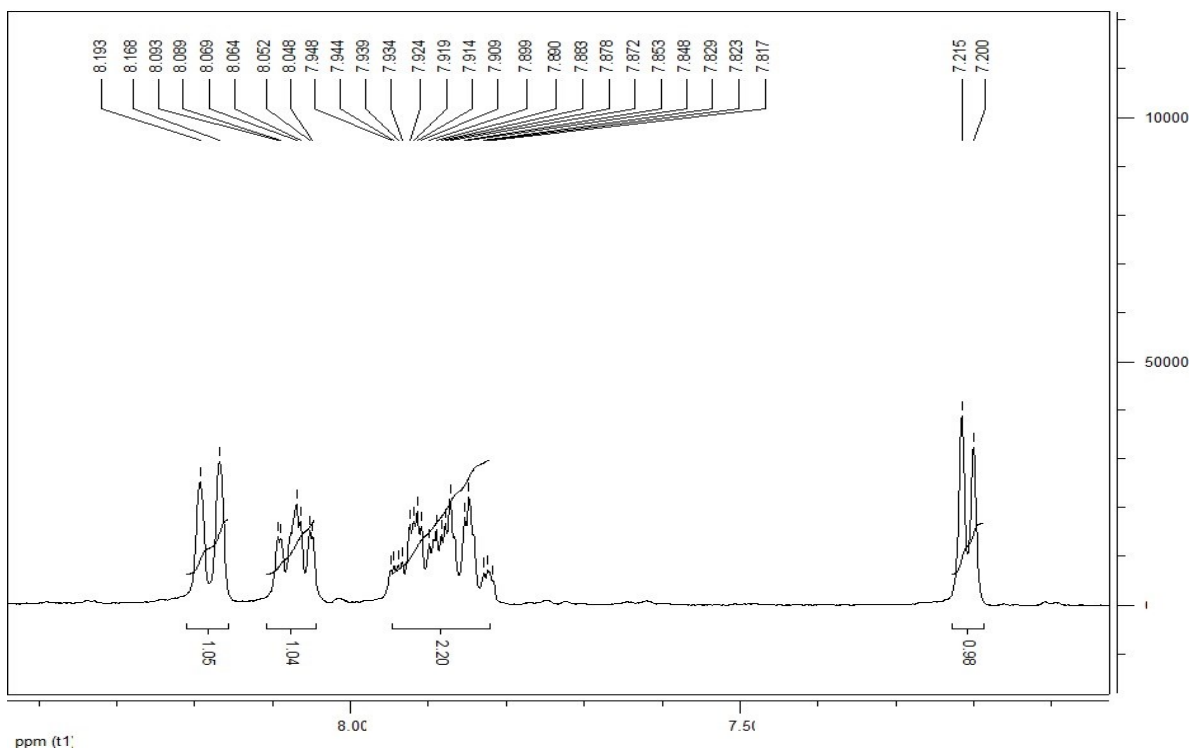
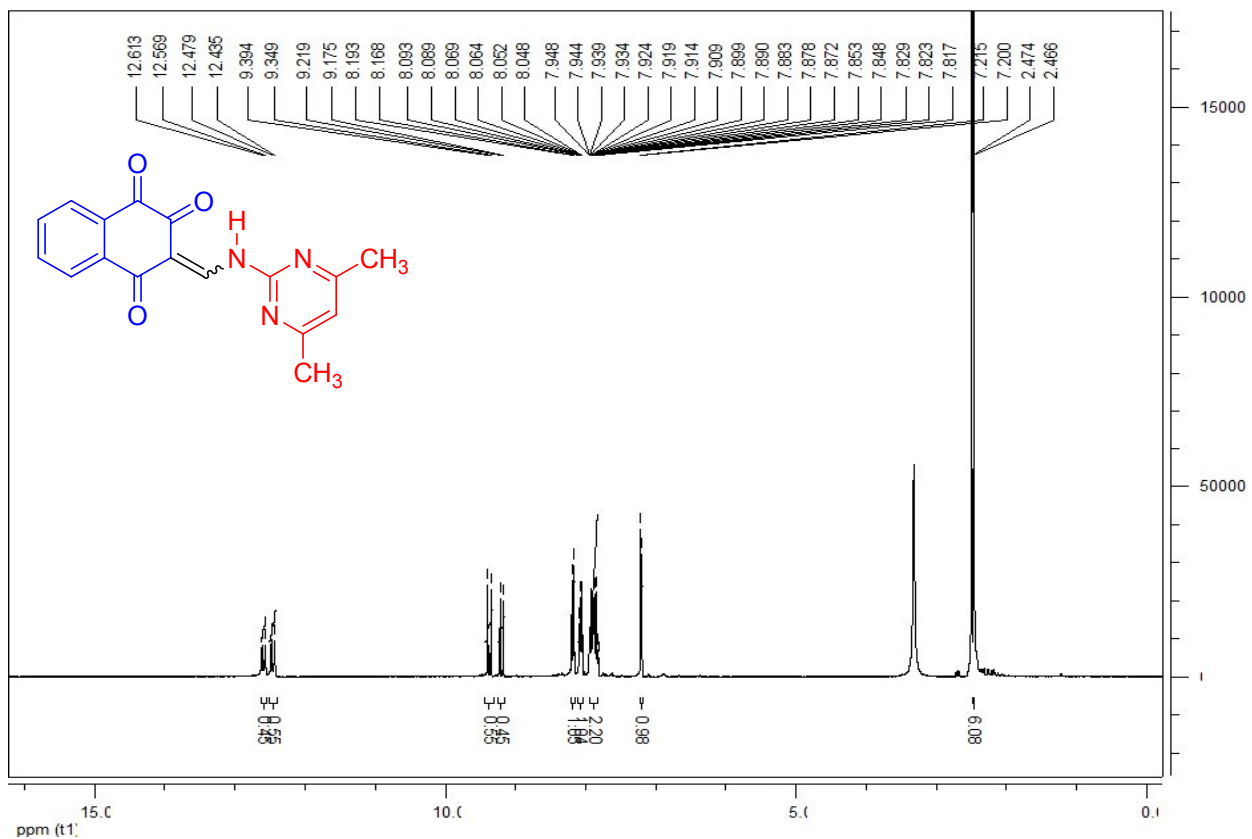
3-(((4-Nitrophenyl)amino)methylene)naphthalene-1,2,4(3H)-trione (4k): Yield: 81%; Brown powder; M.P. = 288-290 °C; IR (KBr, cm⁻¹): ν = 3444, 3059, 1698, 1666, 1608, 1579, 1513, 1436, 1345, 1303, 1272, 1229, 1109; ¹H-NMR (300 MHz, DMSO-*d*₆): δ = 7.82-7.92 (m, 2H, Ar-H), 7.95 (d, 2H, *J* = 8.1 Hz, Ar-H), 8.05-8.09 (m, 1H, Ar-H), 8.18-8.21 (m, 1H, Ar-H), 8.29 (d, 1H, *J* = 3.3 Hz, Ar-H), 8.33 (d, 1H, *J* = 3.3 Hz, Ar-H), 8.83 (d, 0.45H, *J* = 13.8 Hz, CH), 8.98 (d, 0.55H, *J* = 13.8 Hz, CH), 12.91 (d, 0.55H, *J* = 14.1 Hz, NH), 12.98 (d, 0.45H, *J* = 14.1 Hz, NH); MS *m/z* (%): 322 (M⁺) (28.2), 294 (14.9), 277 (11.9), 248 (31.8), 247 (21.9), 219 (18.1), 191 (14.6), 190 (12.1), 165 (22.7), 146 (13.7), 129 (22.3), 116 (17.1), 105 (28.6), 104 (100), 102 (23.5), 101 (48.4), 89 (36.4), 77 (37.7), 76 (98.1).



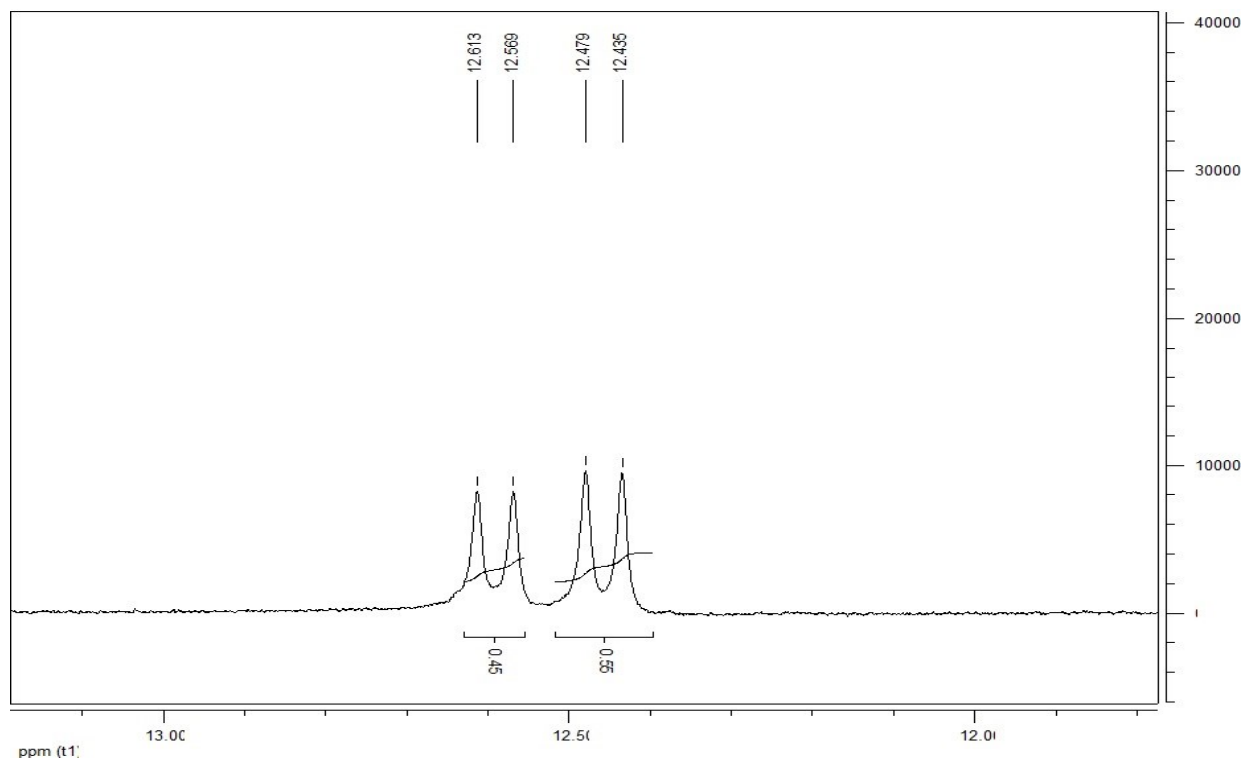
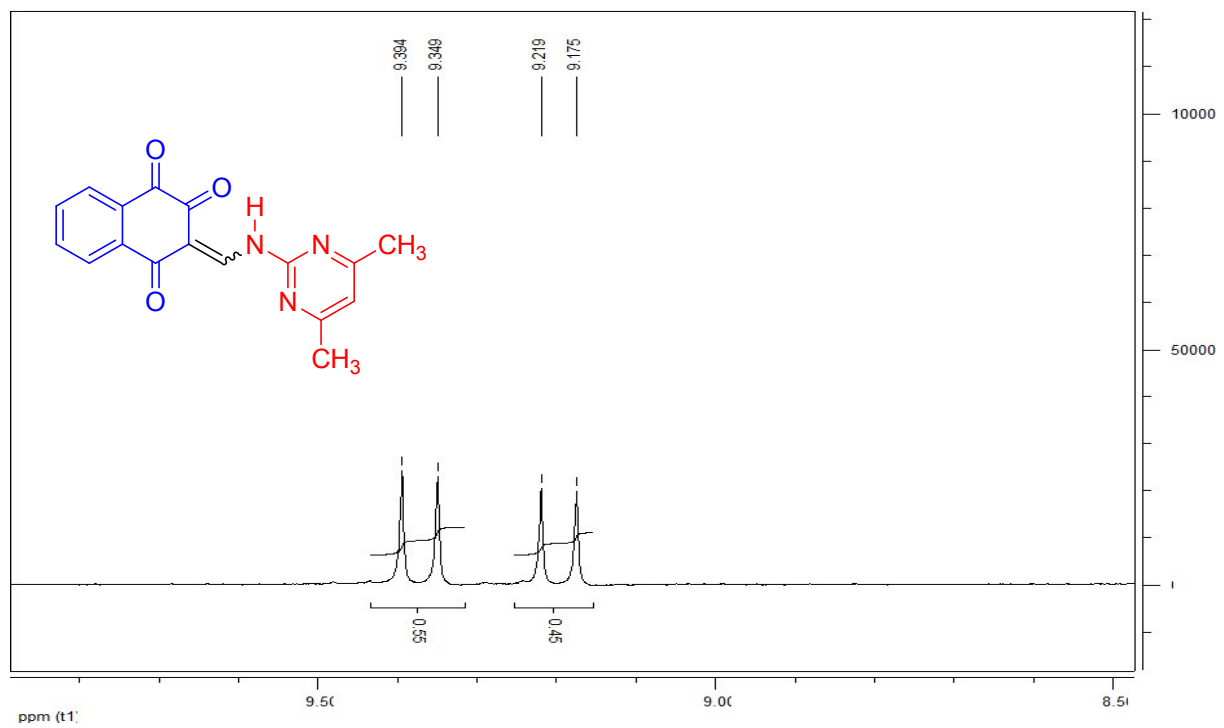
¹H-NMR 4a (DMSO-d₆)



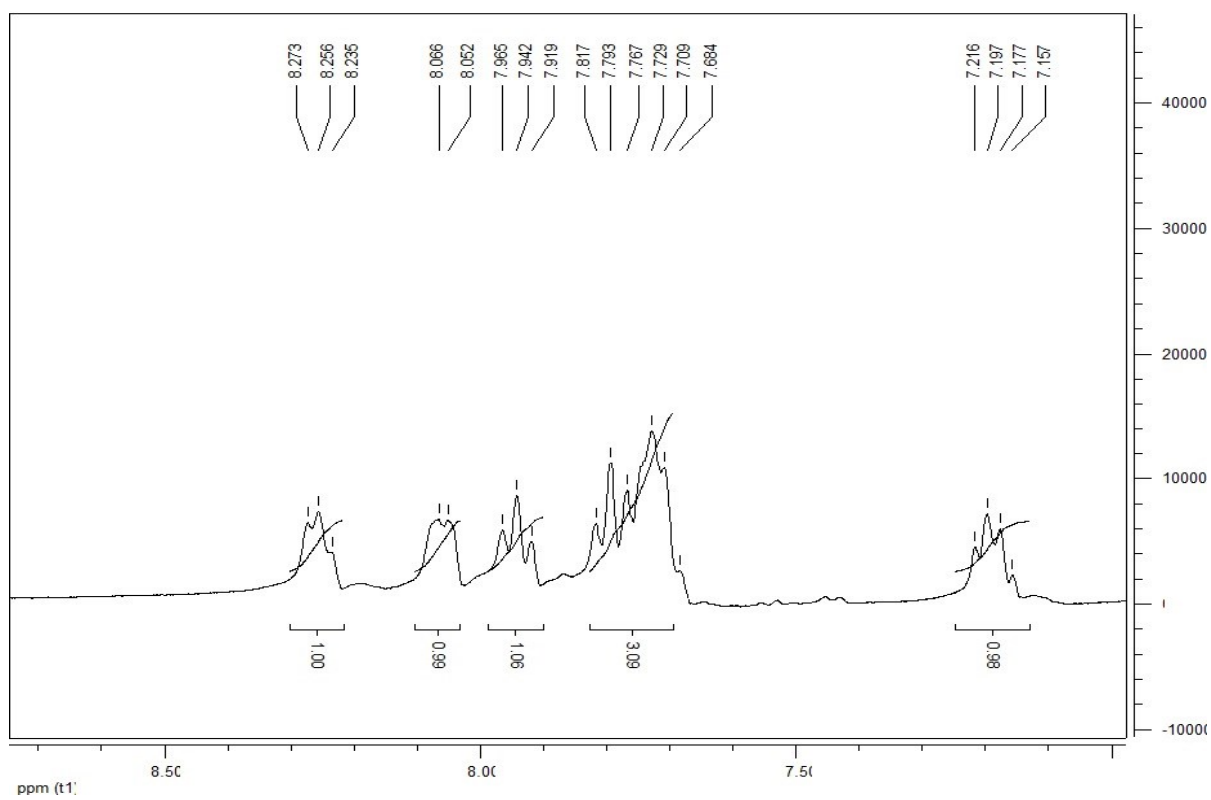
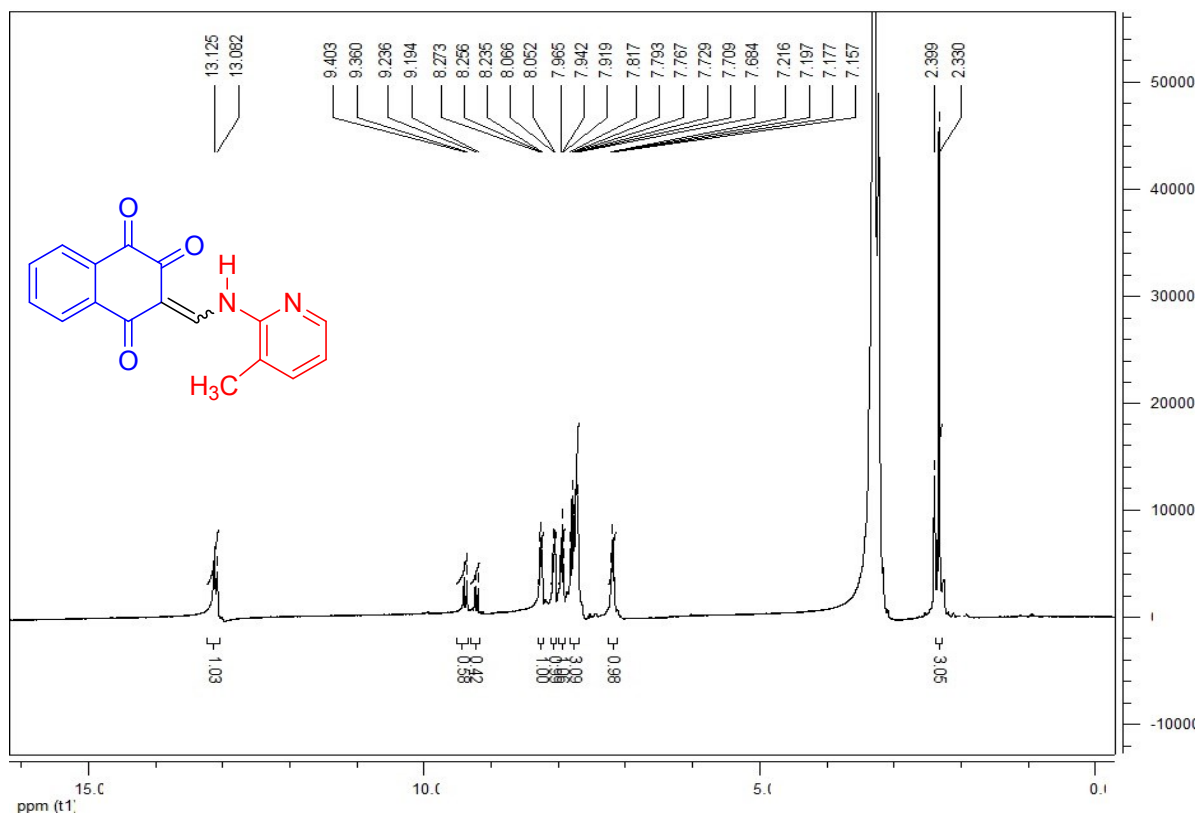
$^1\text{H-NMR}$ **4a** (DMSO-d_6)



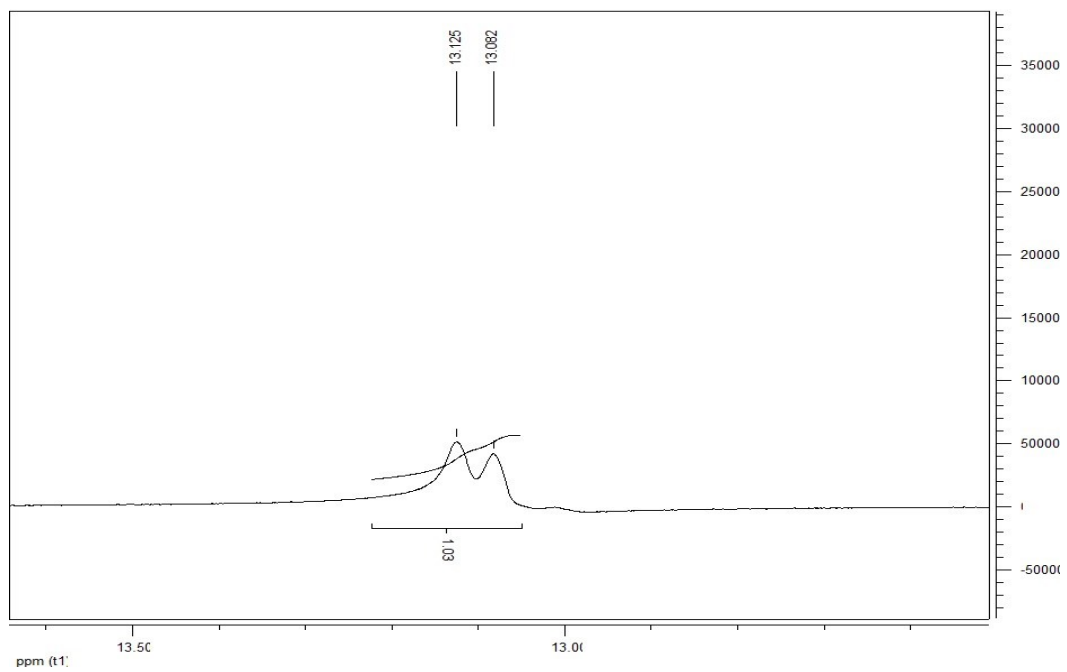
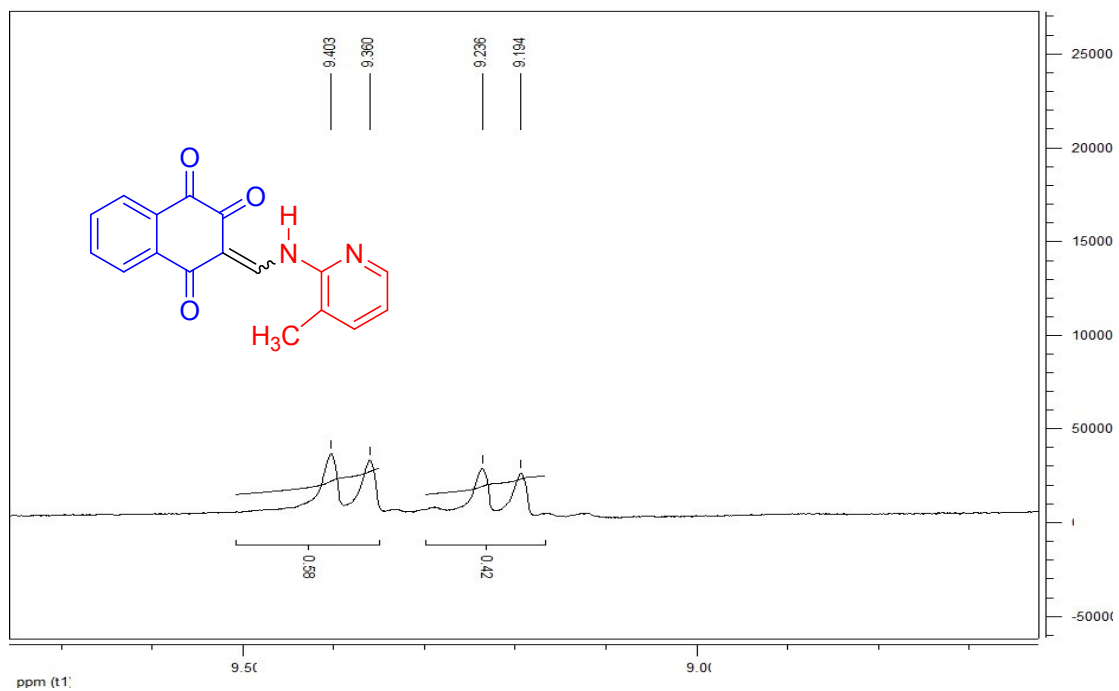
¹H-NMR **4b** (DMSO-d₆)



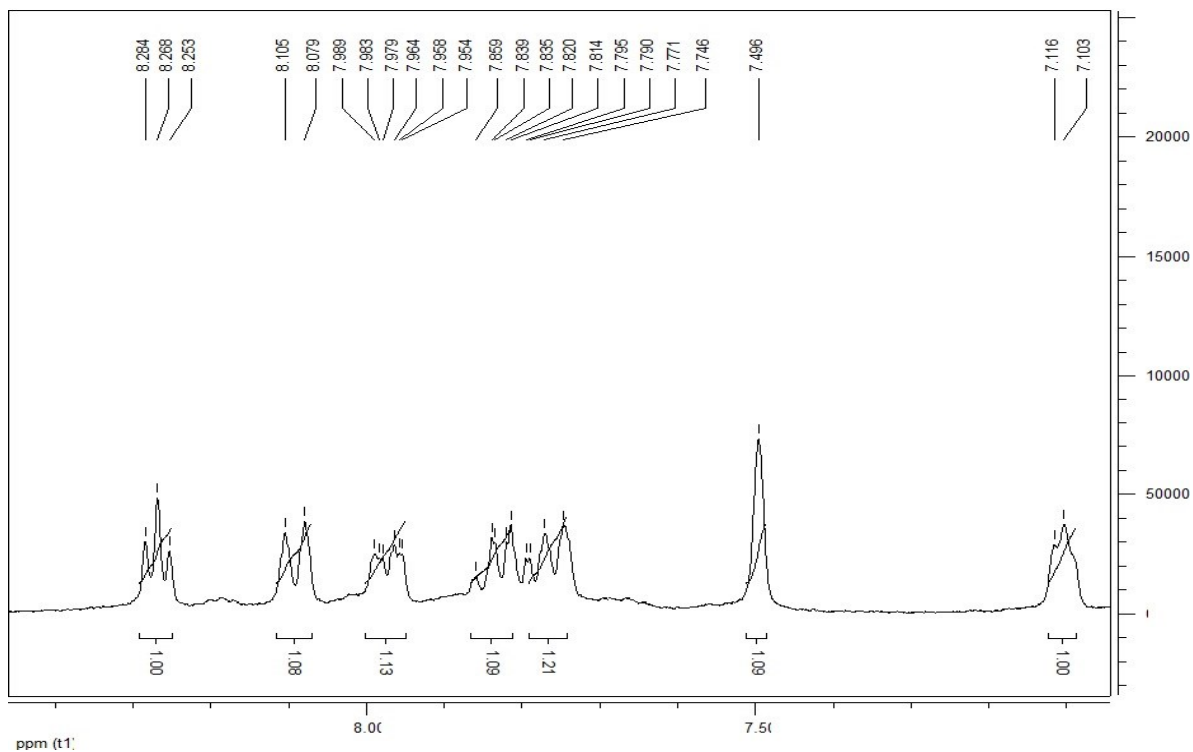
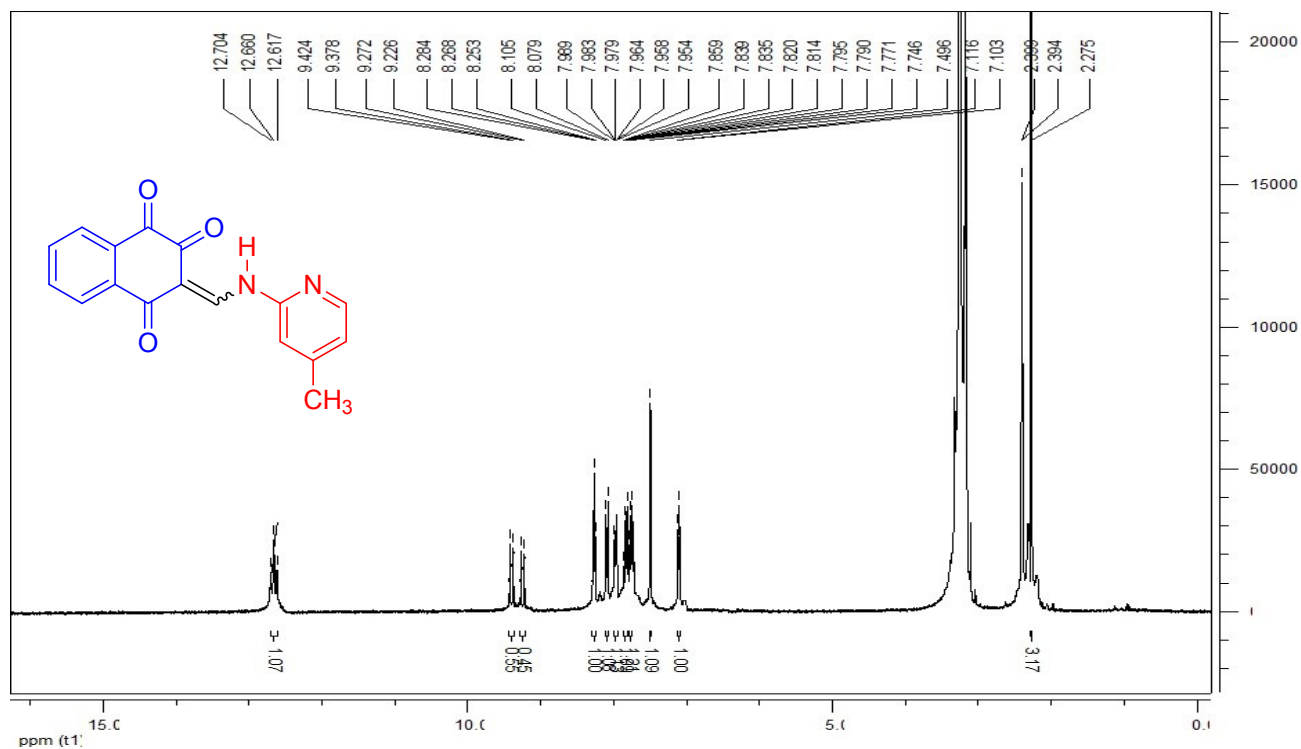
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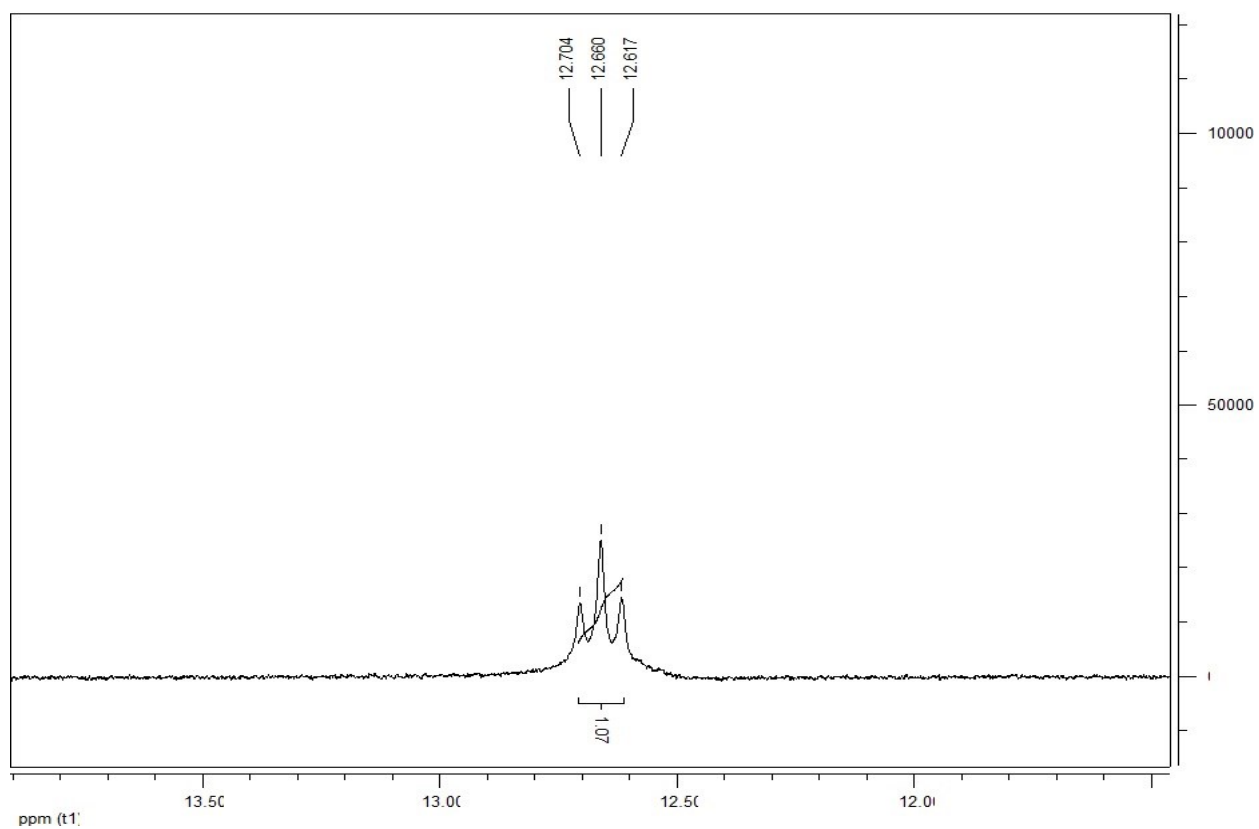
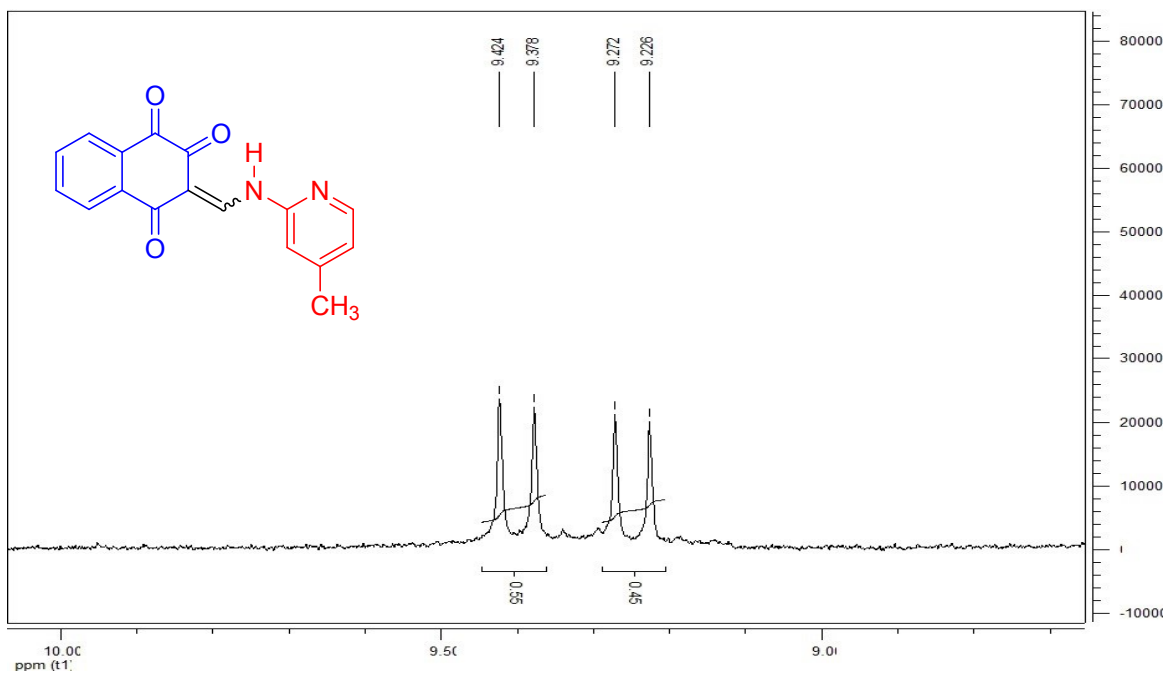
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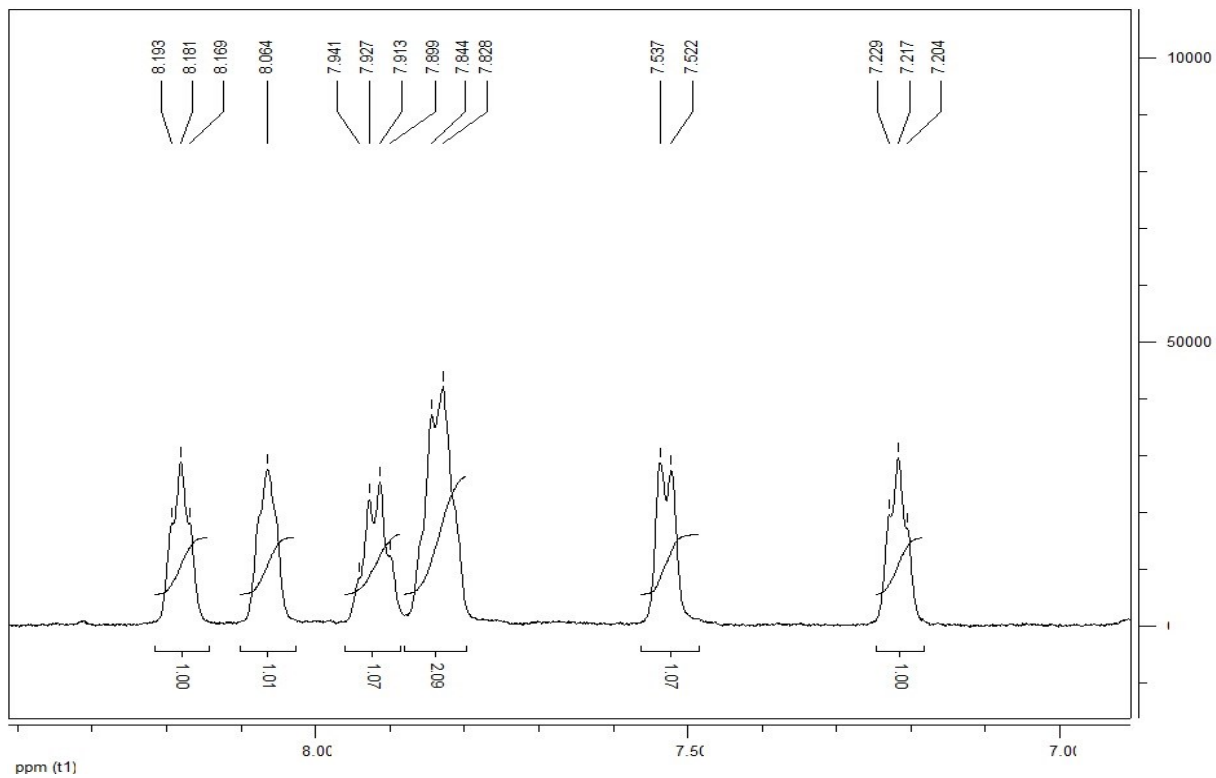
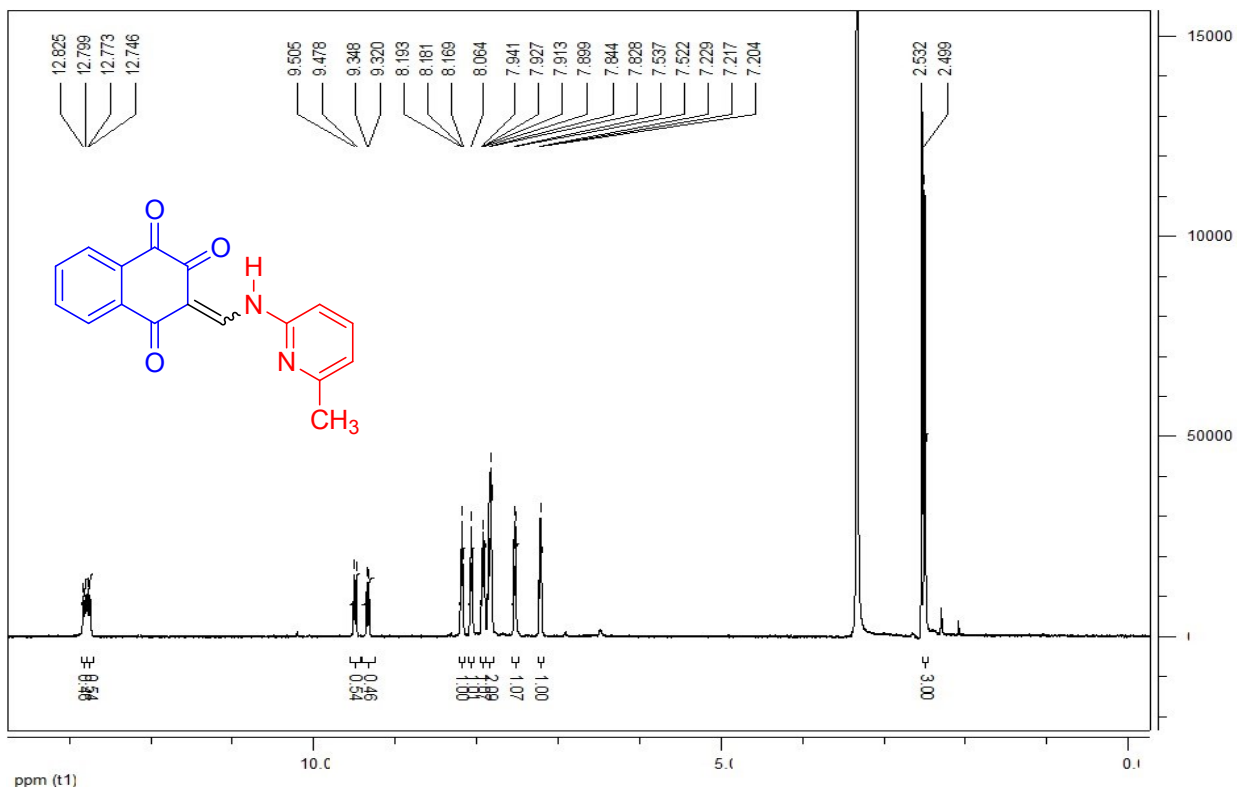
$^1\text{H-NMR}$ **4c** (DMSO-d_6)



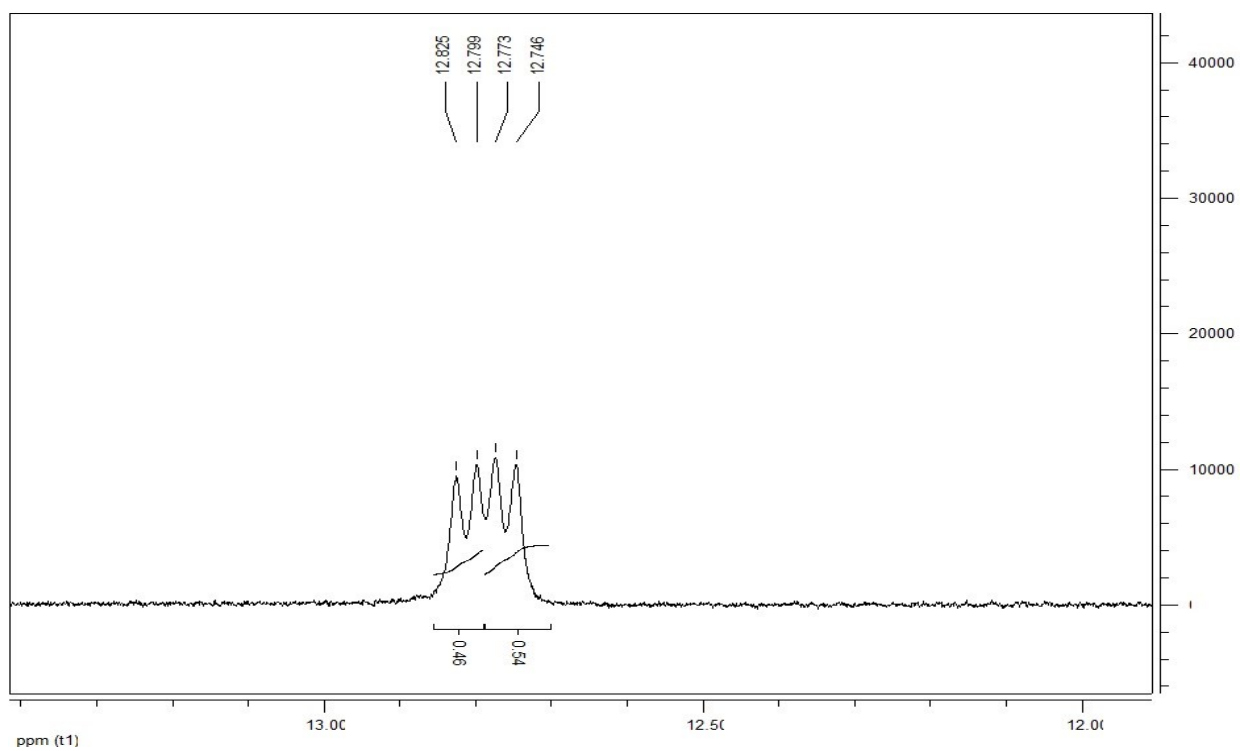
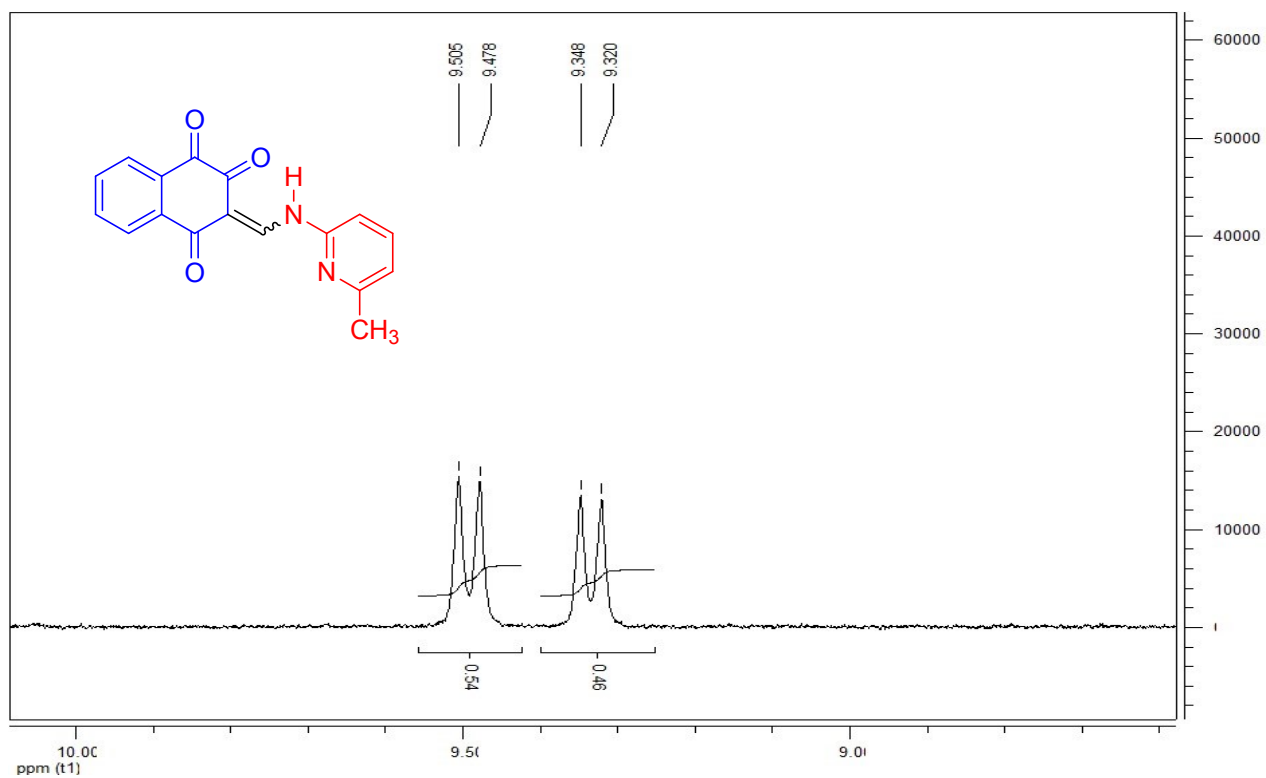
¹H-NMR 4d (DMSO-d₆)



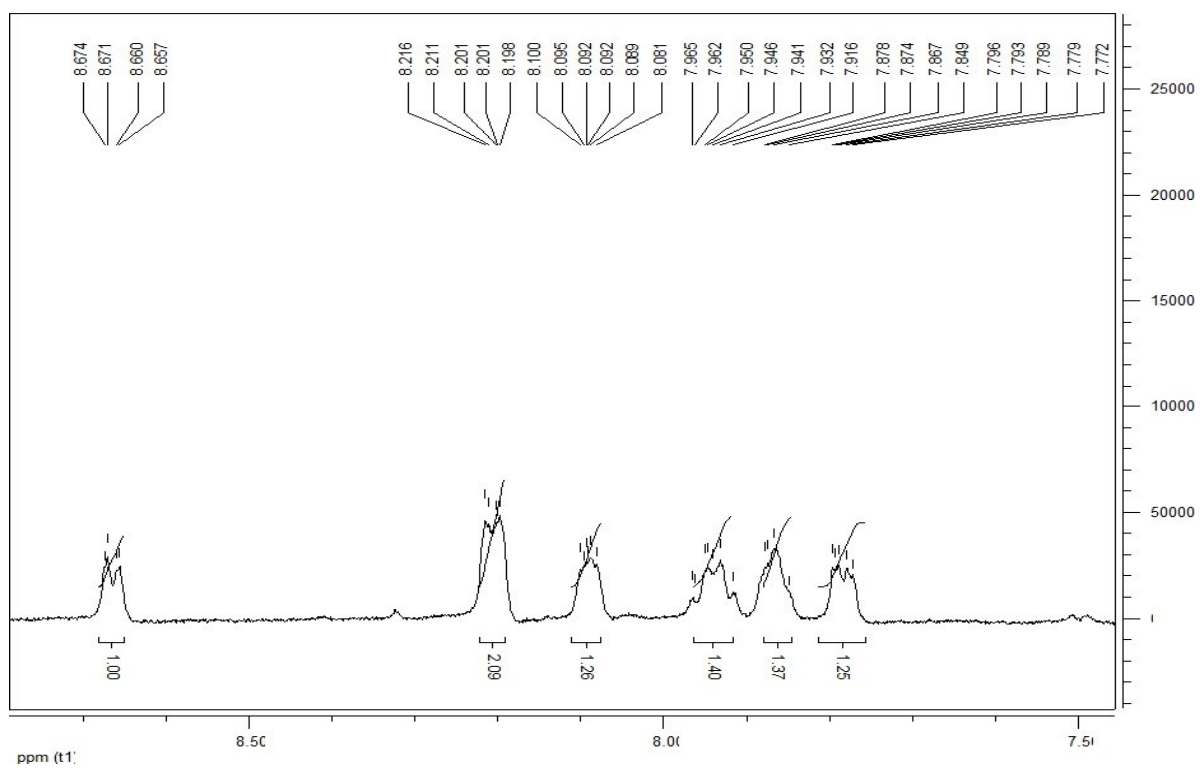
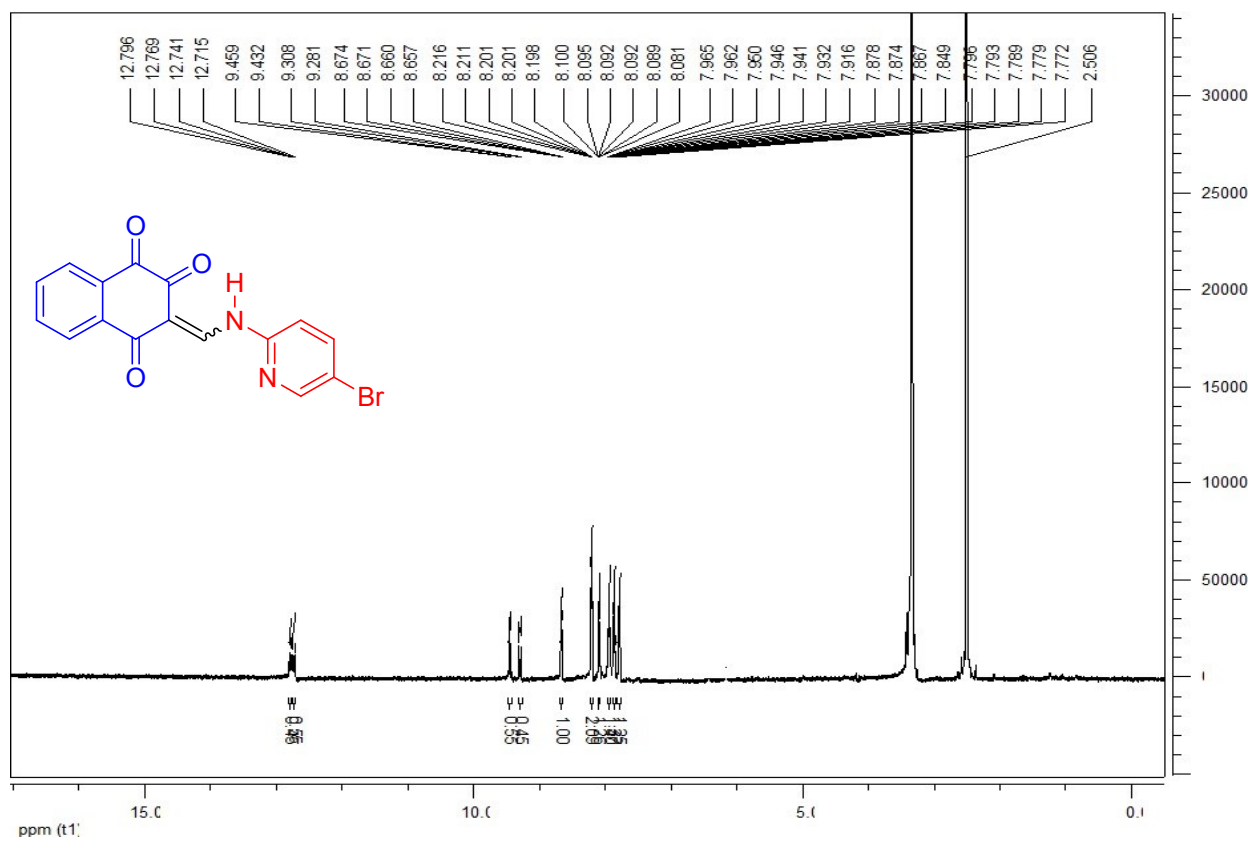
¹H-NMR 4d (DMSO-d₆)



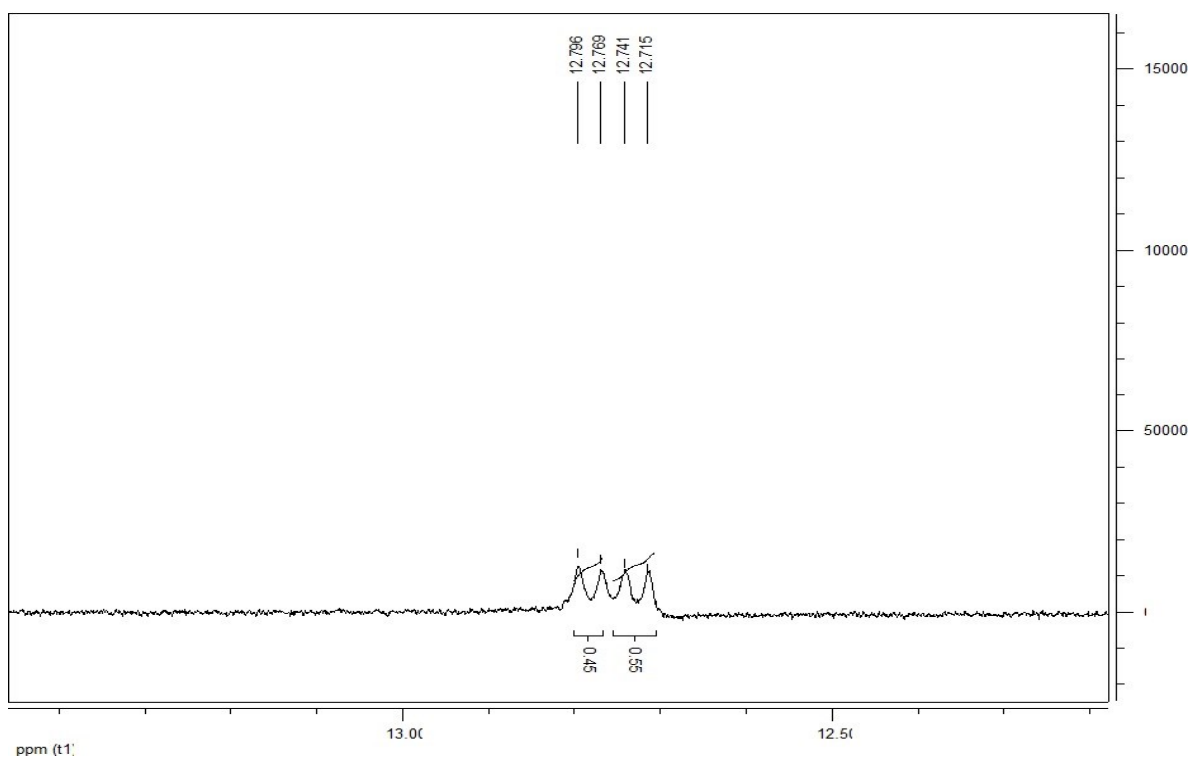
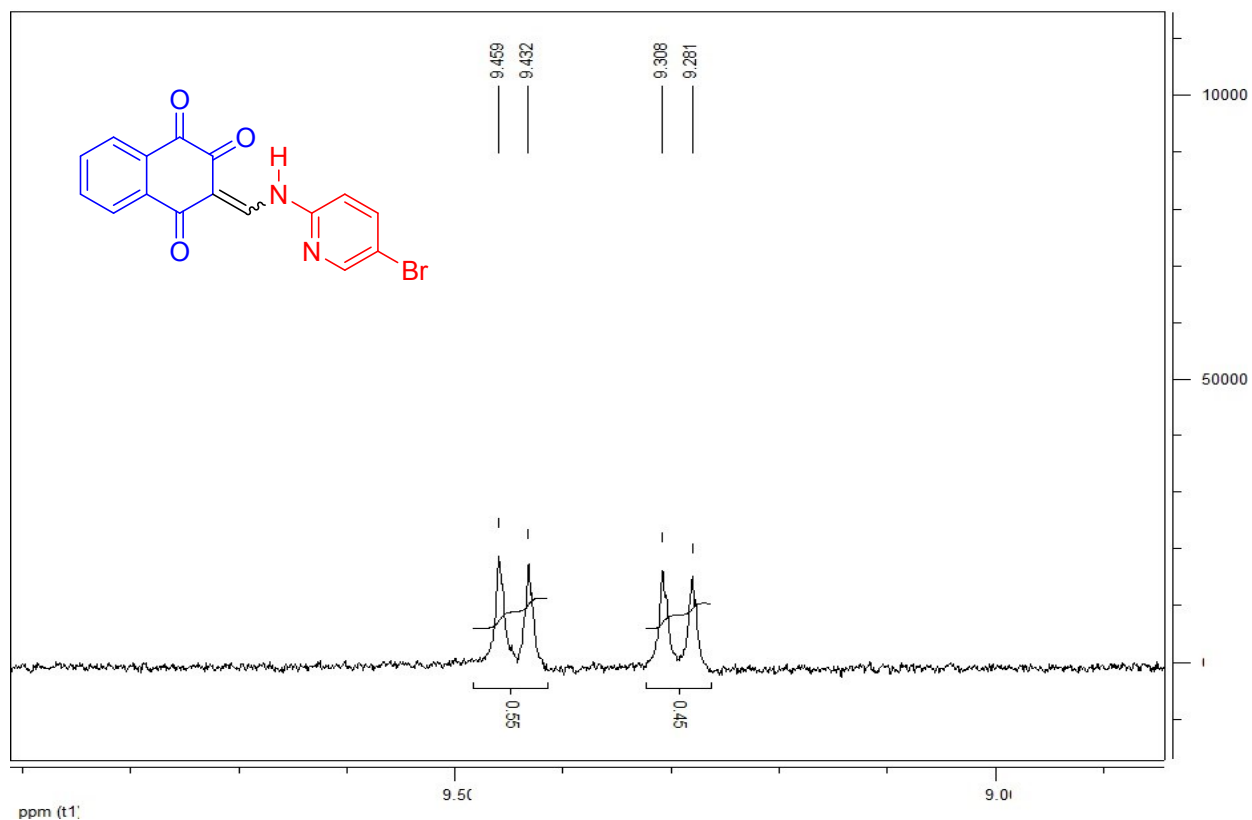
¹H-NMR 4e (DMSO-d₆)



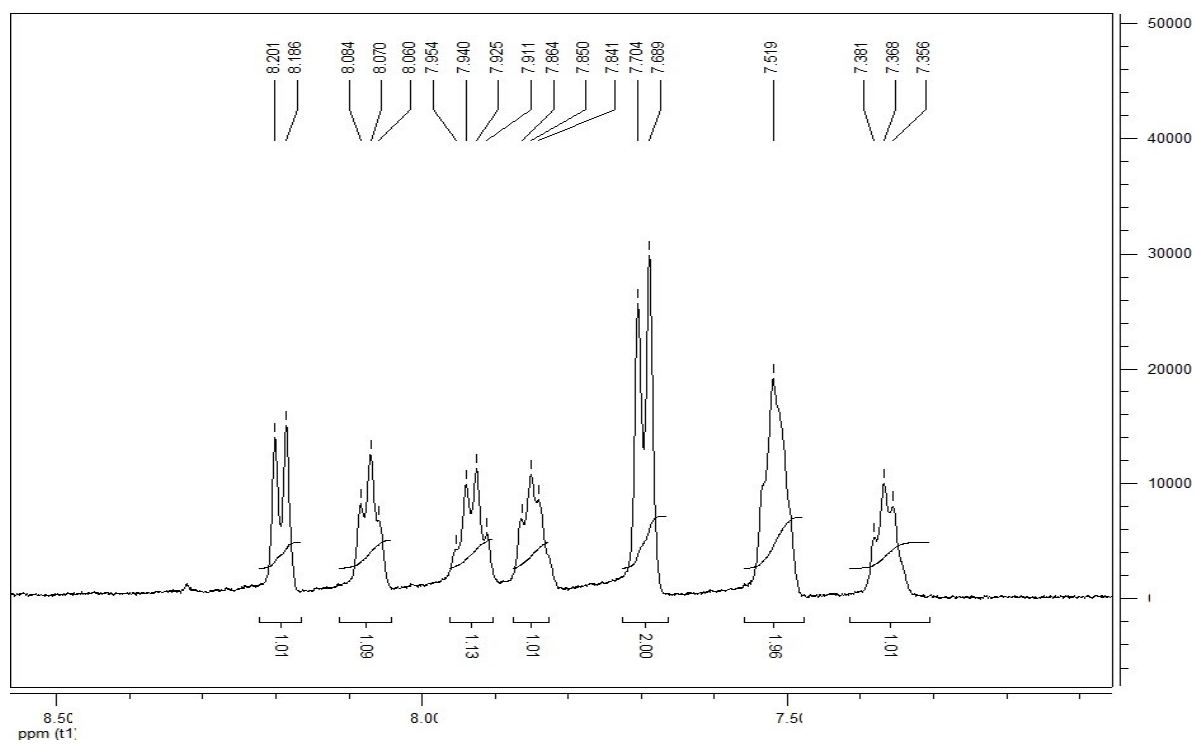
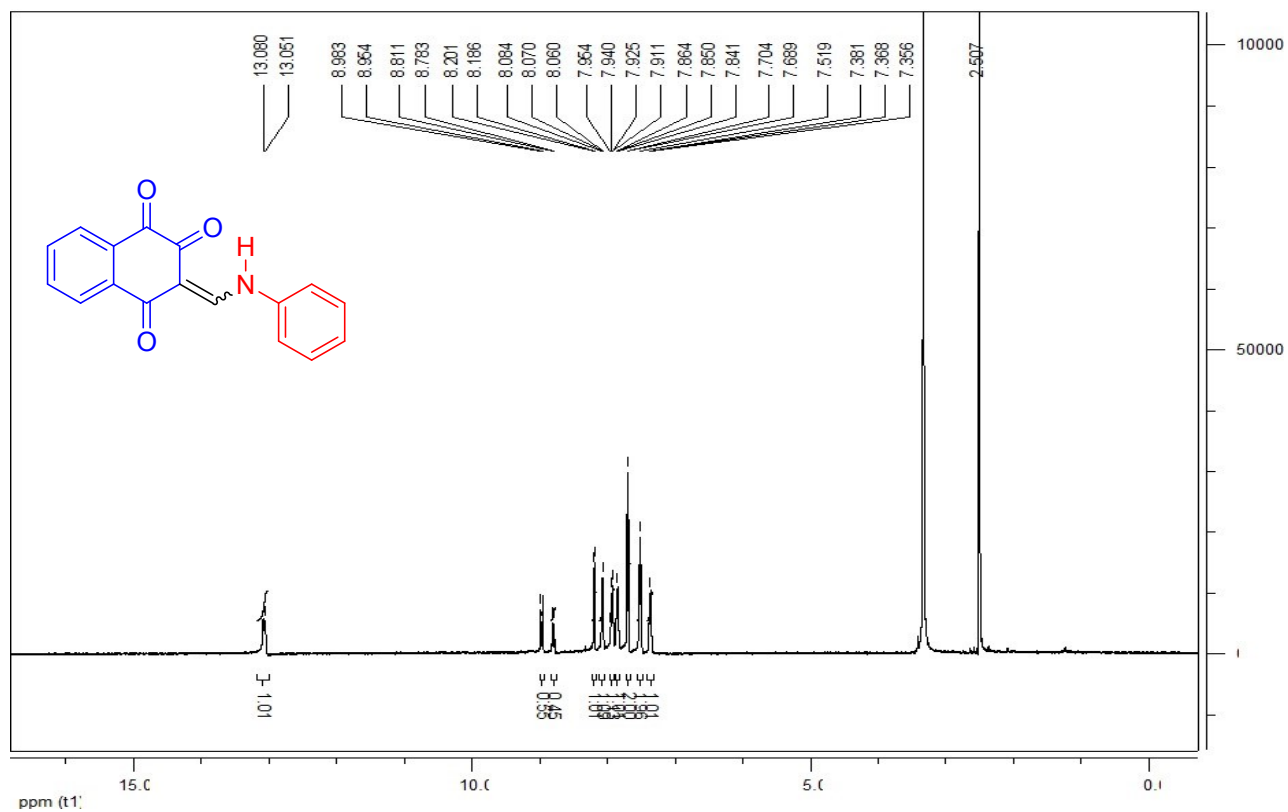
¹H-NMR 4e (DMSO-d₆)



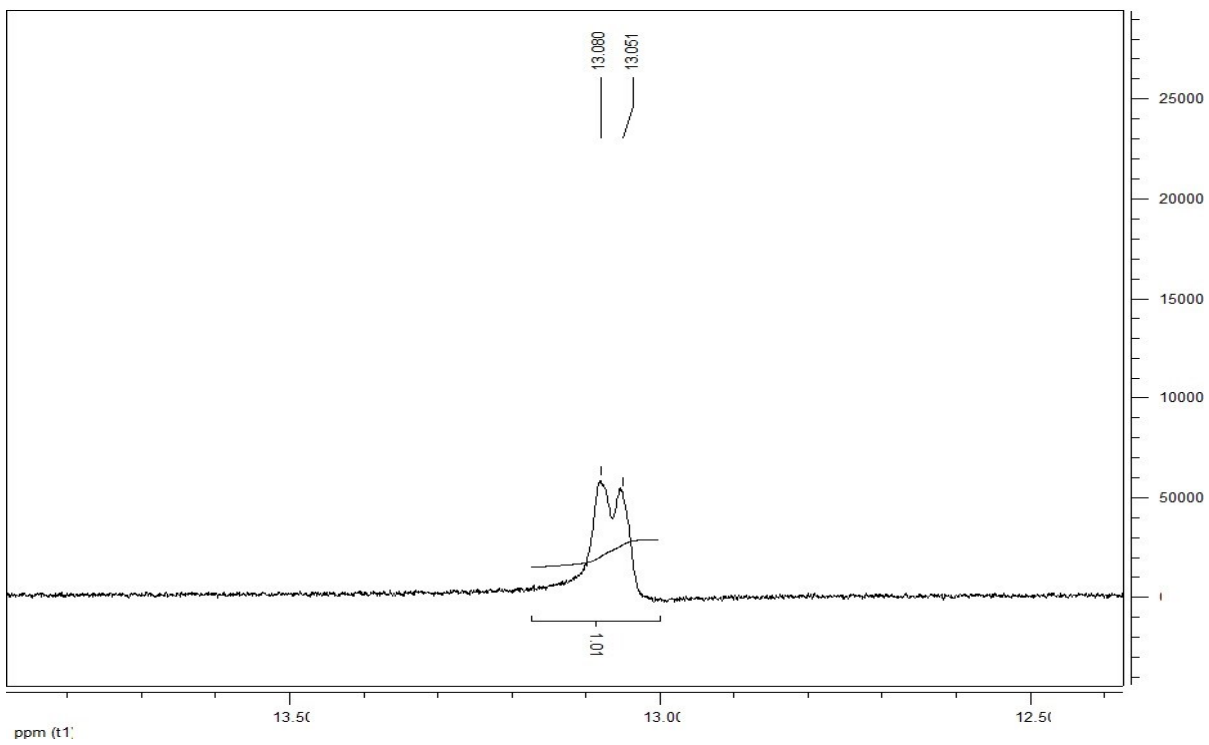
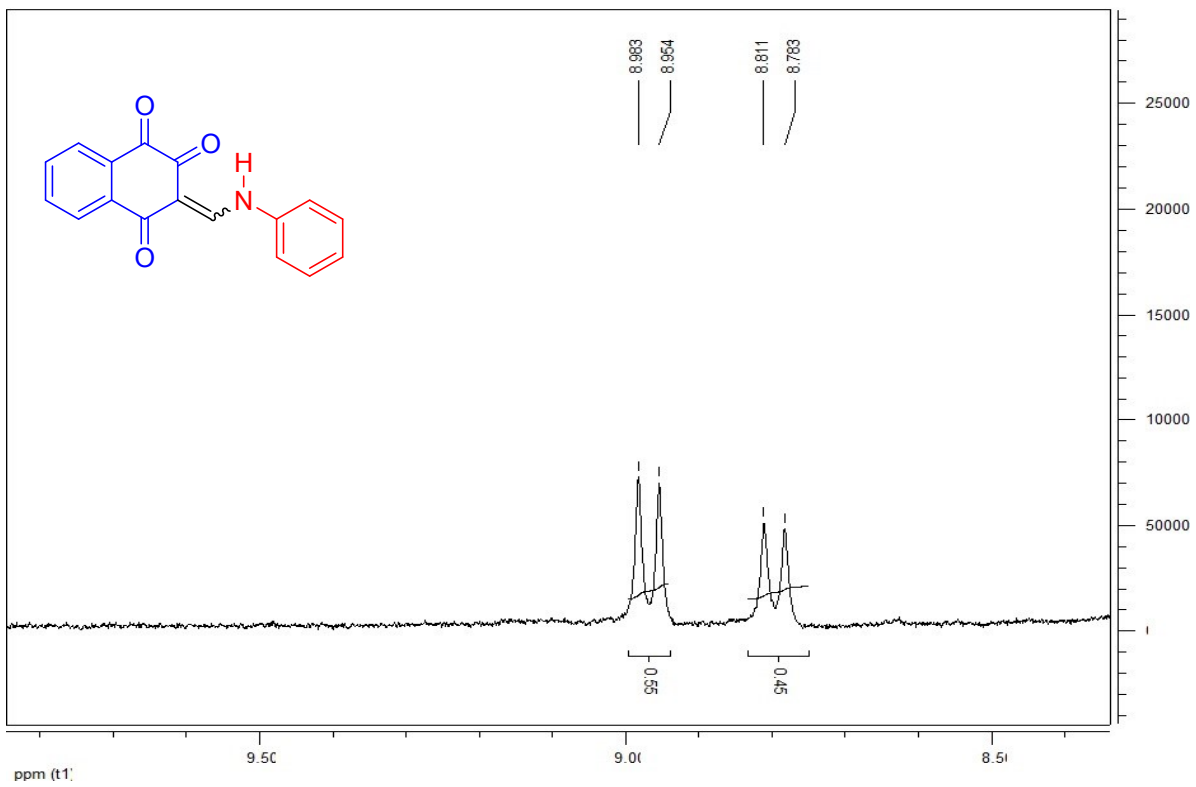
$^1\text{H-NMR}$ 4f (DMSO- d_6)



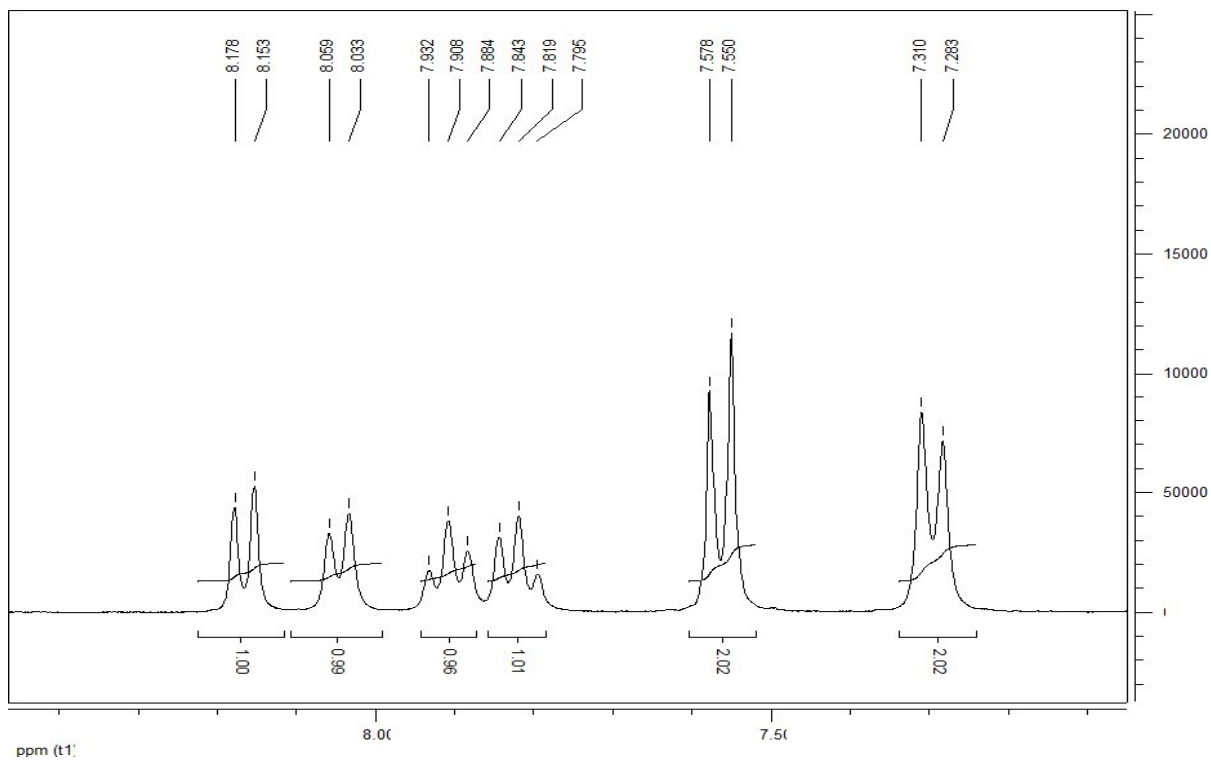
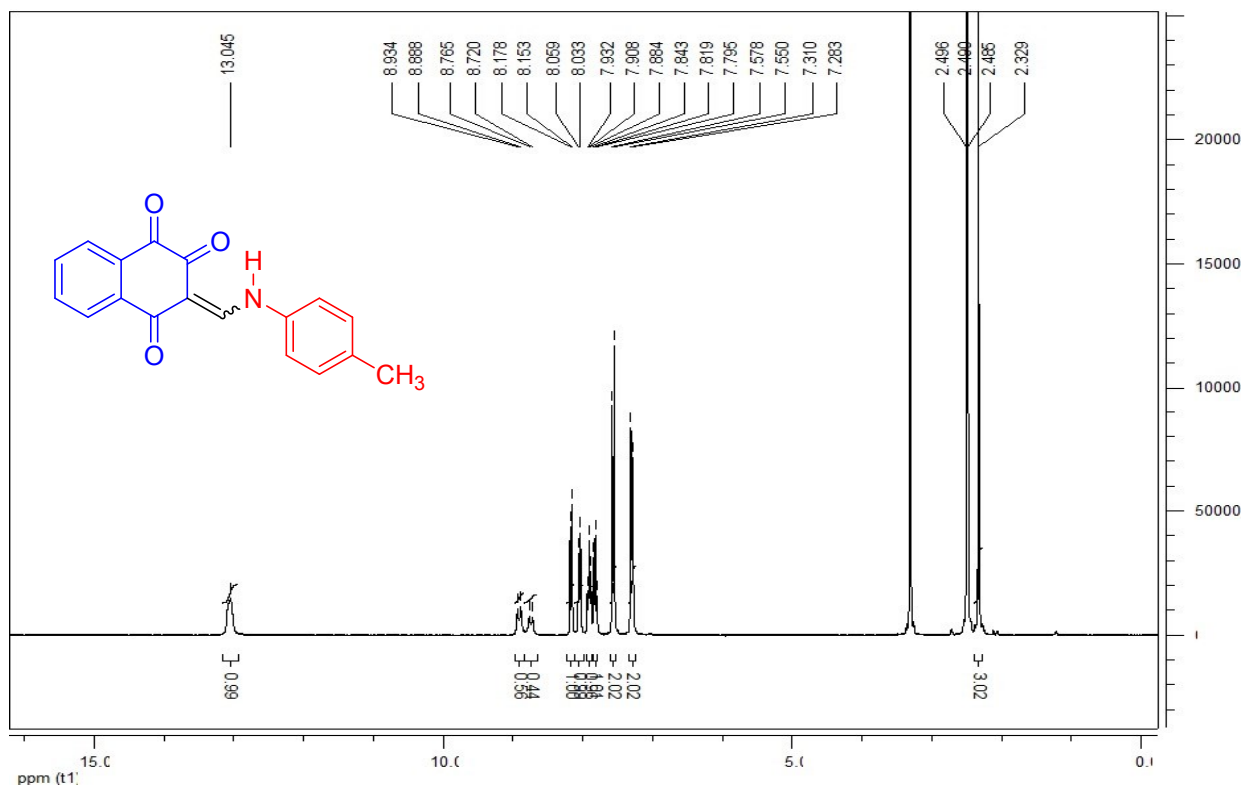
$^1\text{H-NMR}$ **4f** (DMSO- d_6)



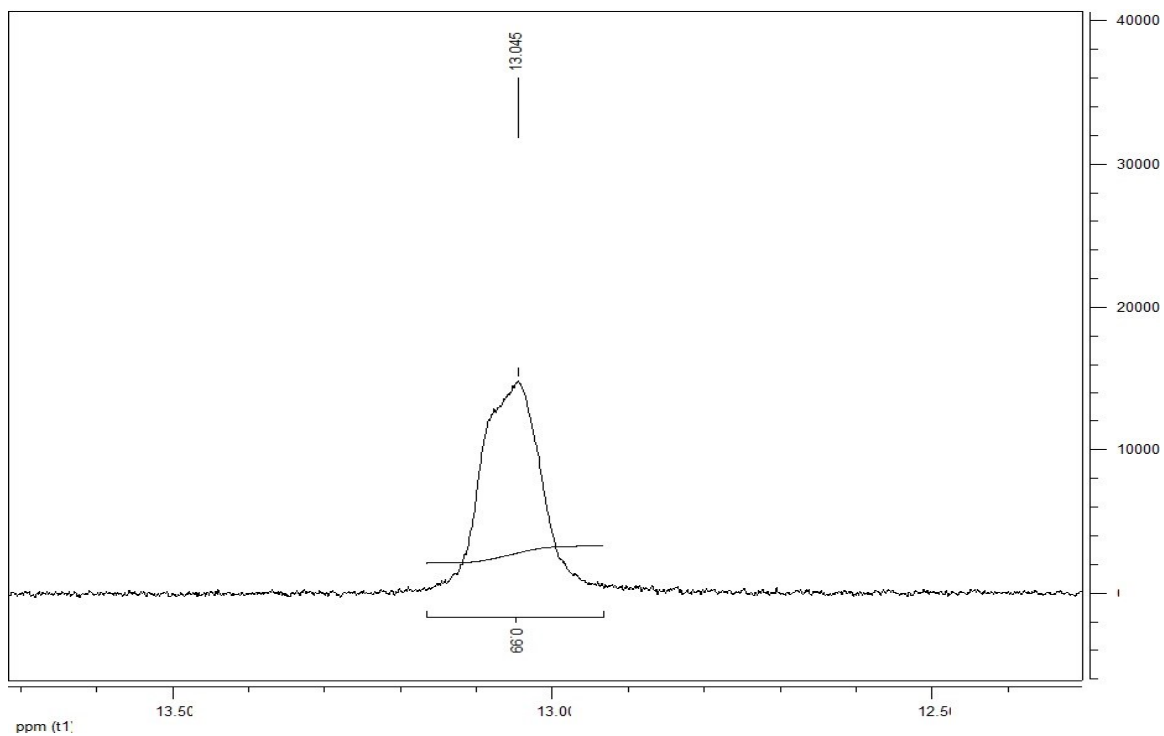
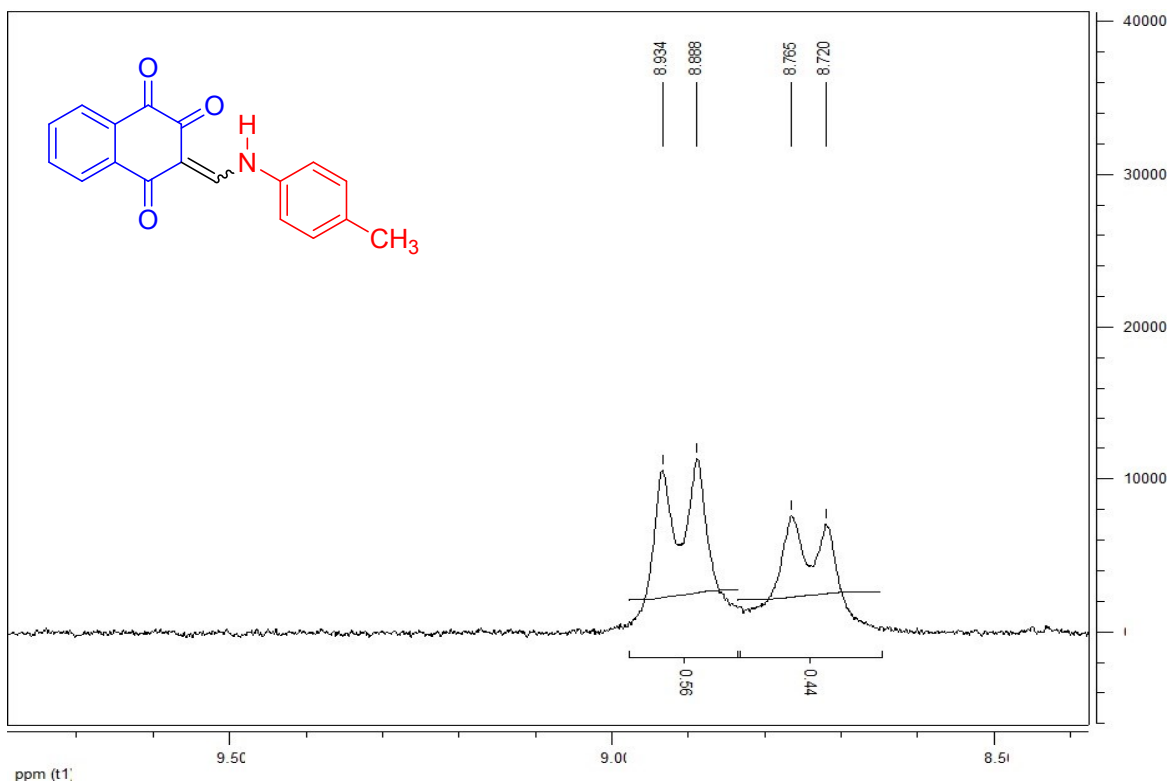
¹H-NMR 4g (DMSO-d₆)



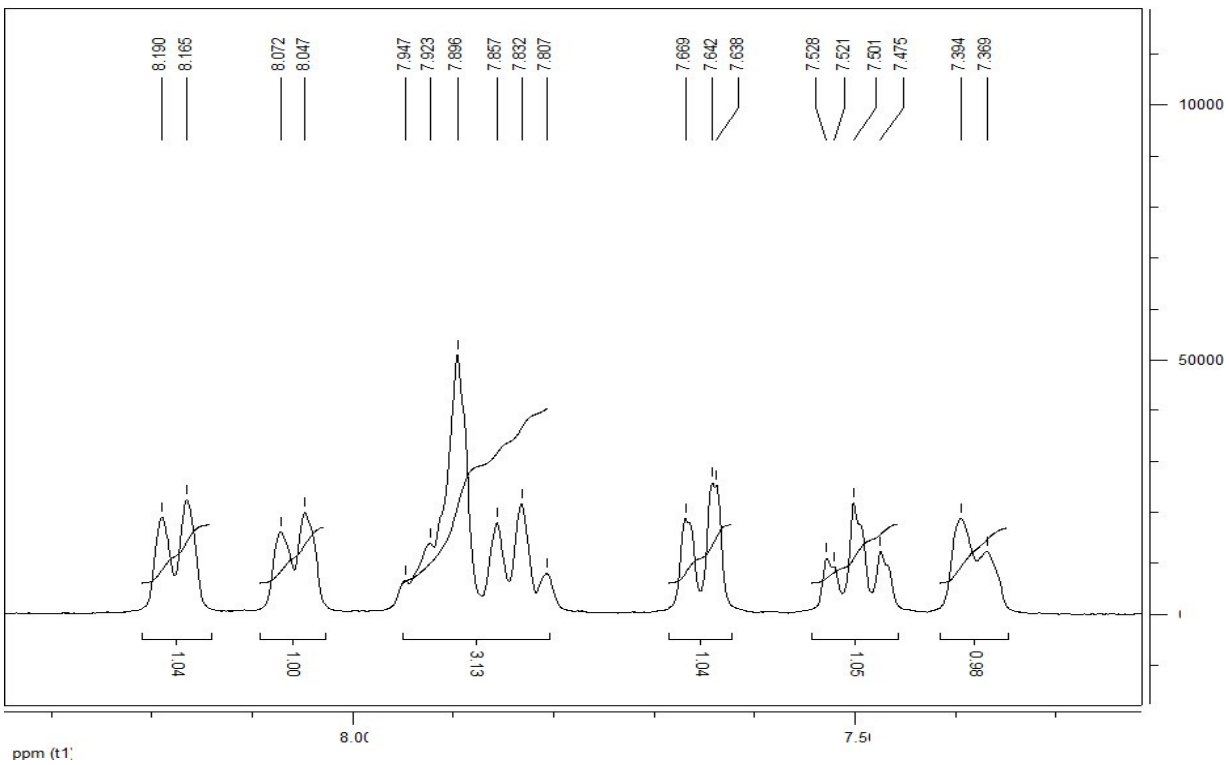
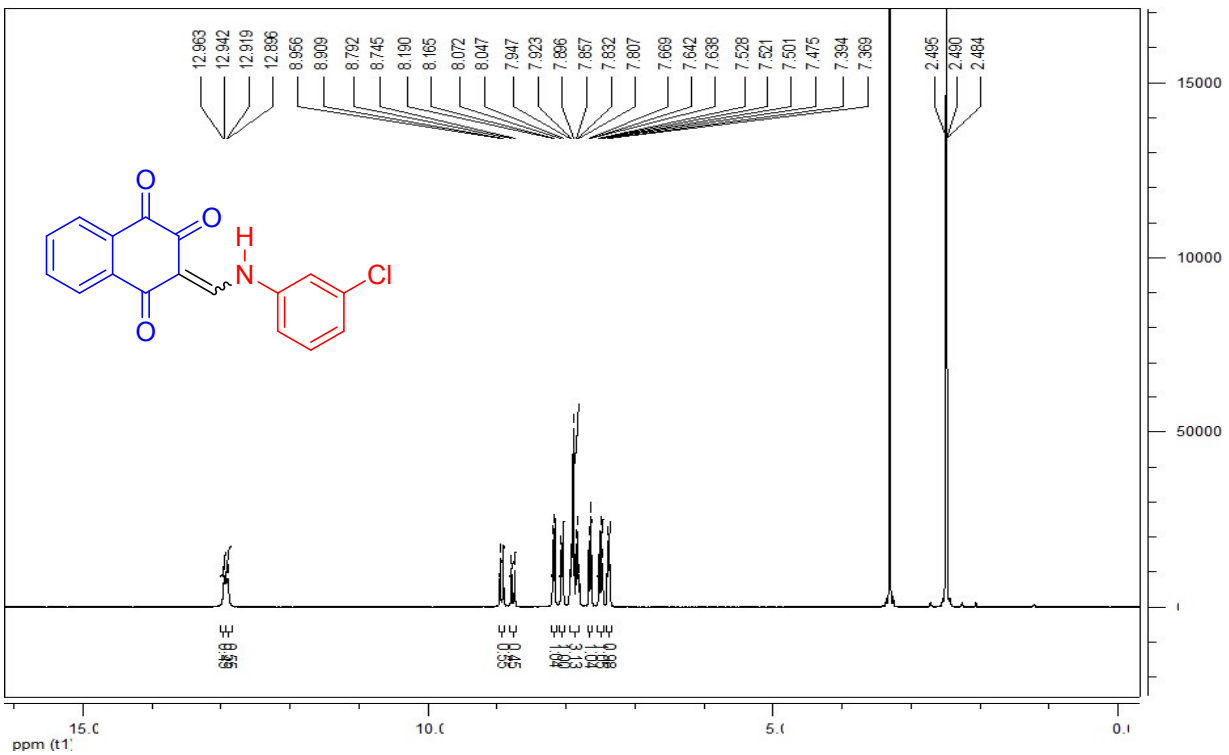
¹H-NMR 4g (DMSO-d₆)



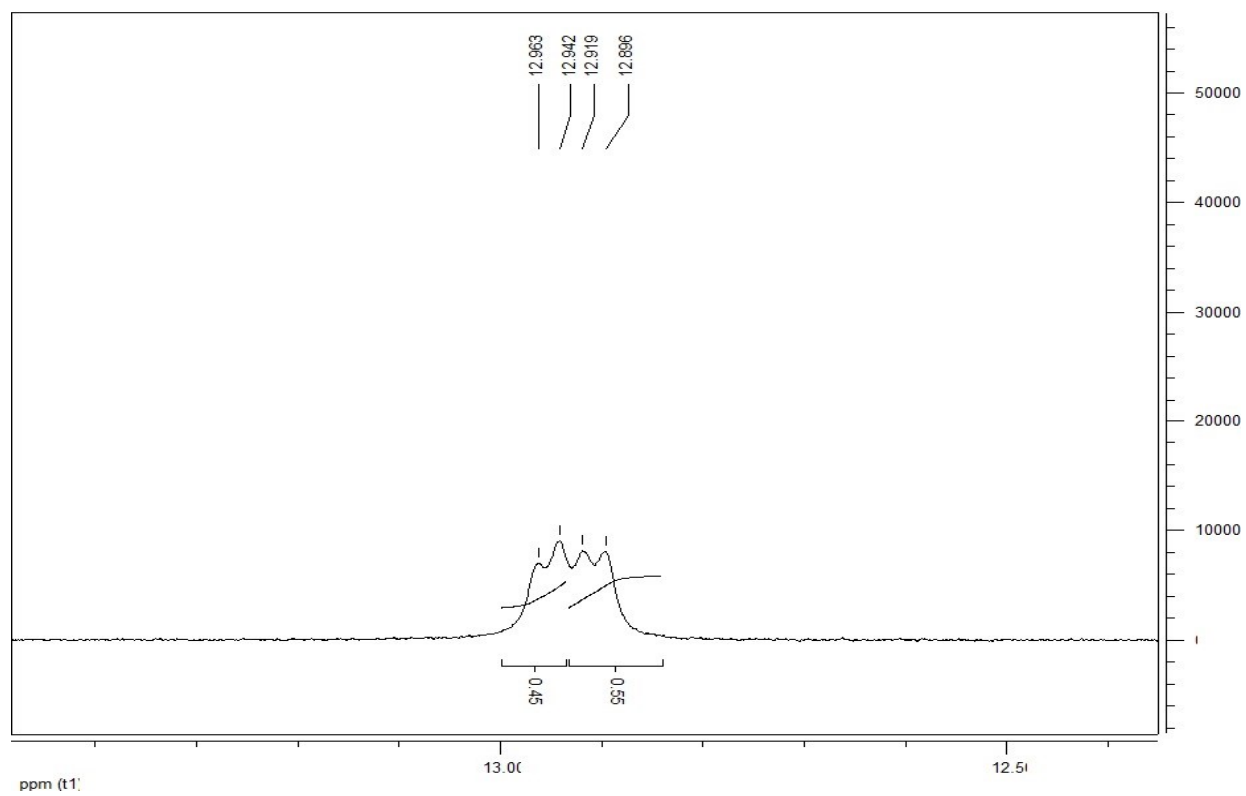
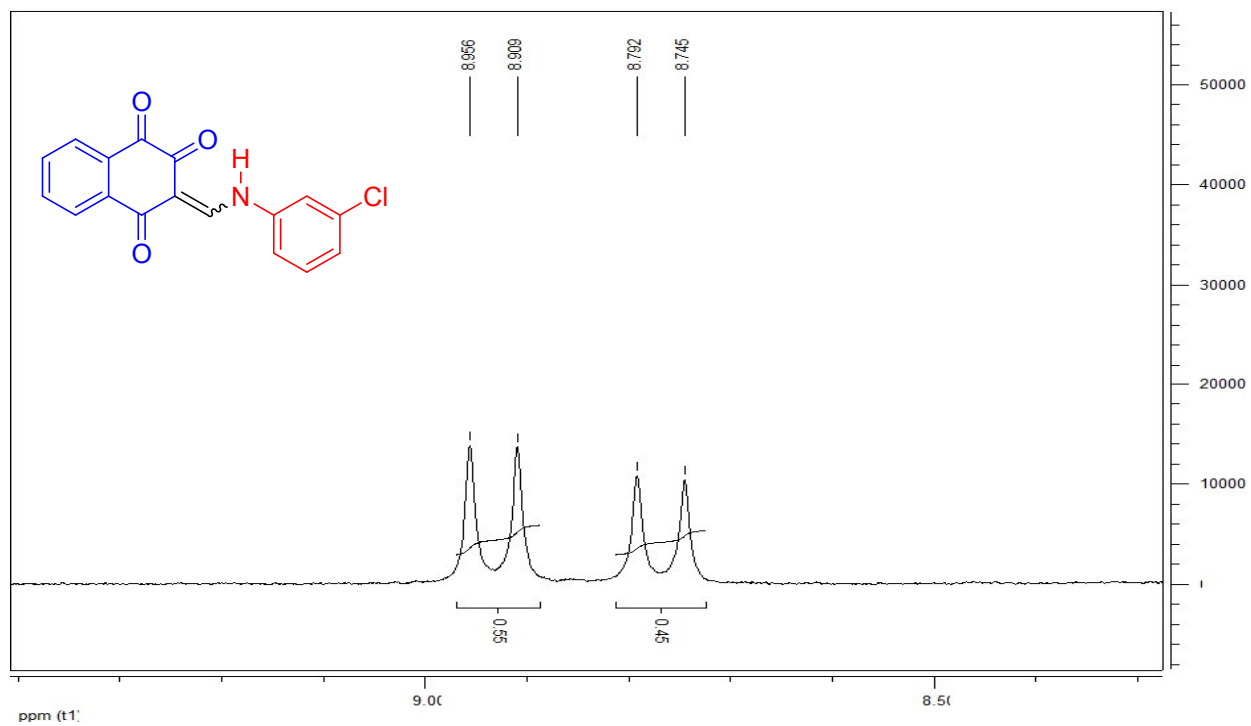
¹H-NMR **4h** (DMSO-d₆)



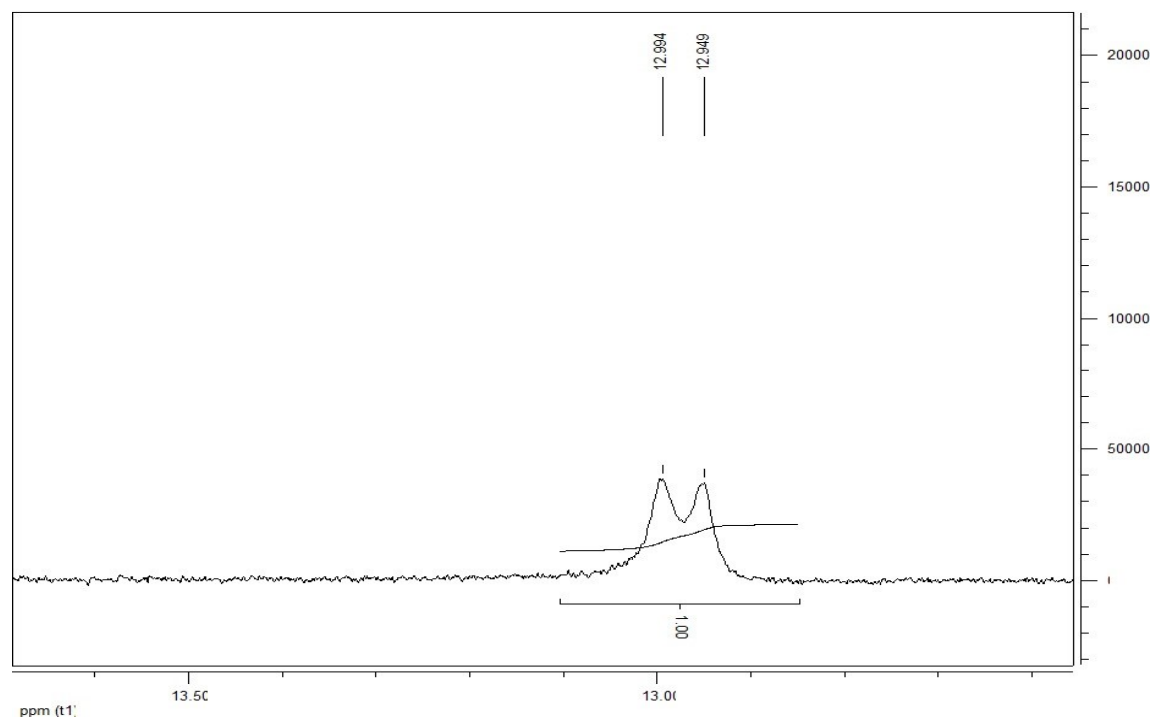
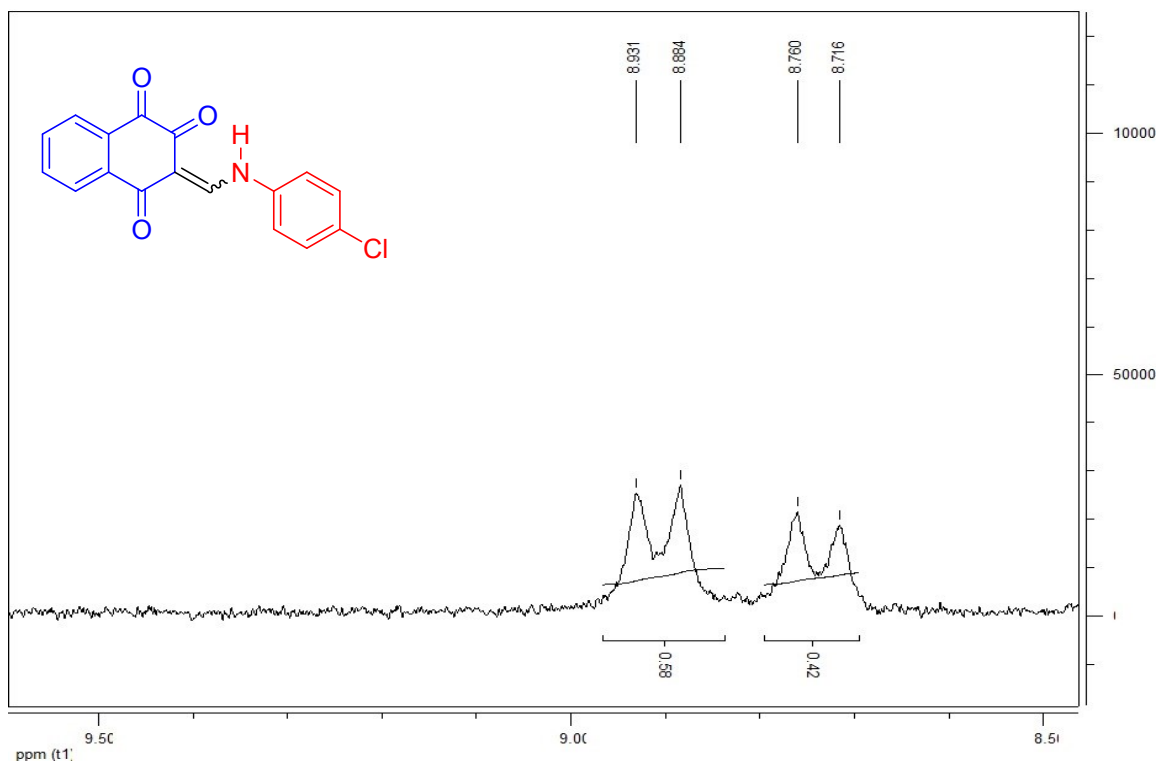
$^1\text{H-NMR}$ **4h** (DMSO-d_6)



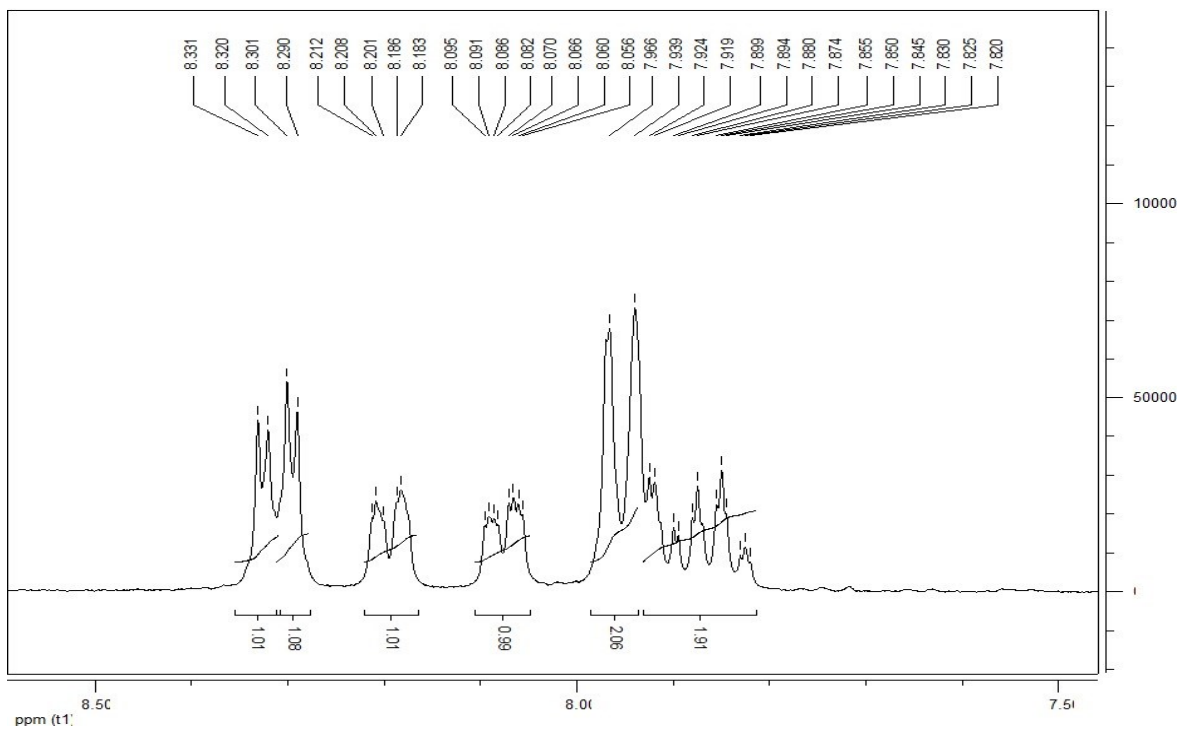
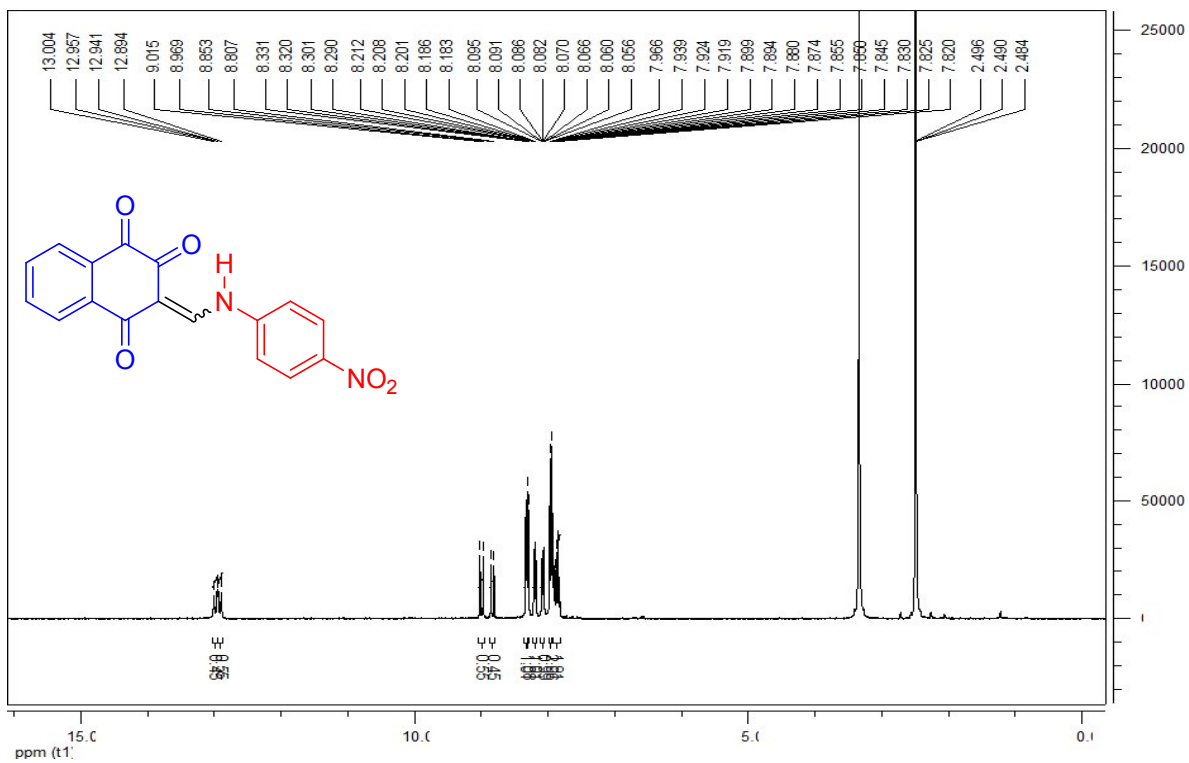
¹H-NMR 4i (DMSO-d₆)



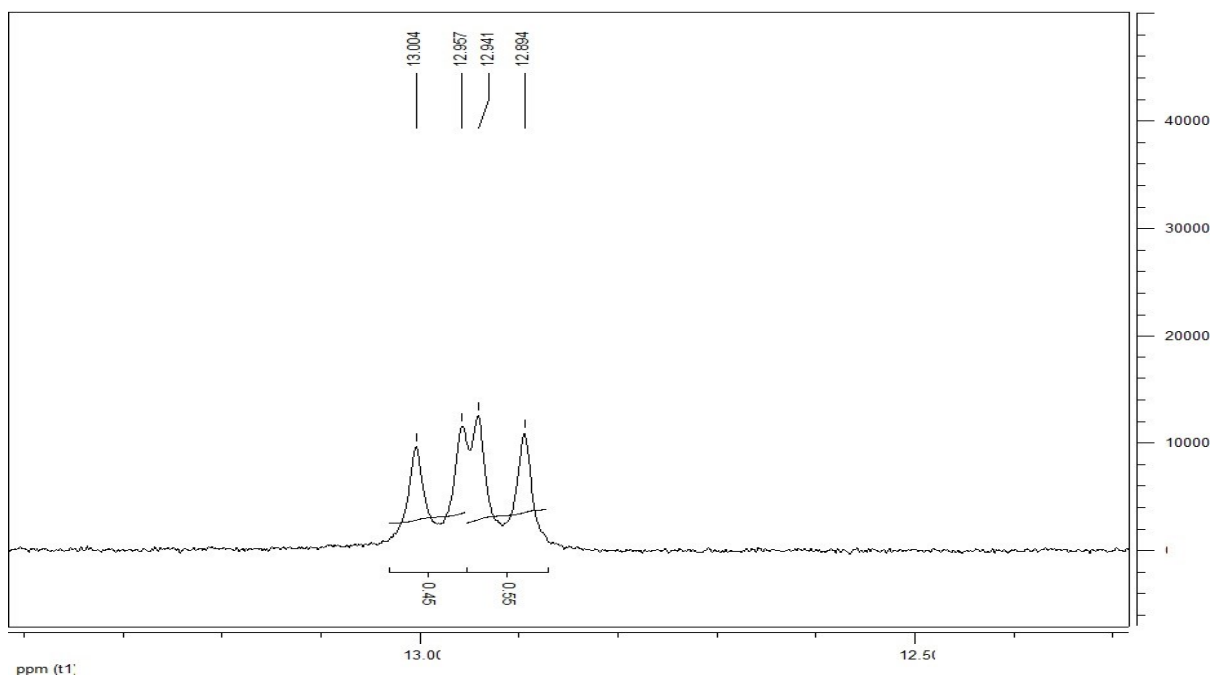
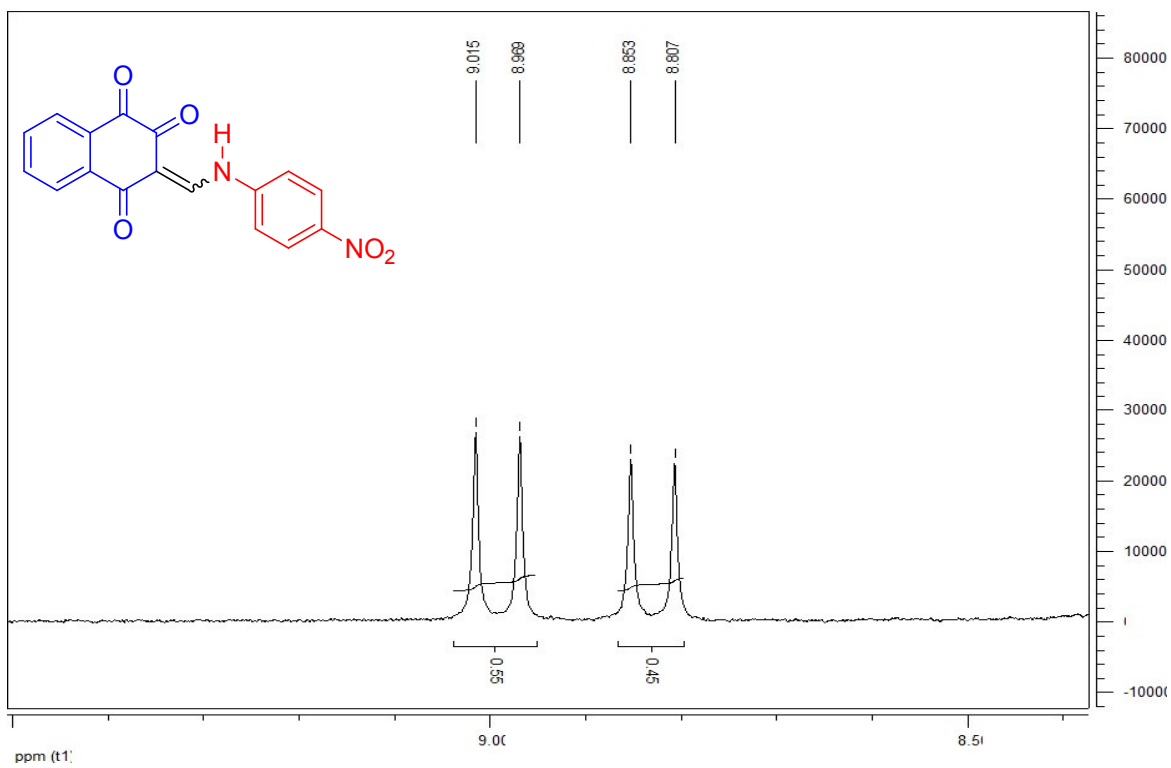
$^1\text{H-NMR}$ **4i** (DMSO- d_6)



$^1\text{H-NMR}$ **4j** (DMSO- d_6)



¹H-NMR 4k (DMSO-d₆)



$^1\text{H-NMR}$ **4k** (DMSO-d_6)