One pot four component approach for the construction of dihydropyridines and dihydropyridinones using amines and activated alkynes

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Supplementary data

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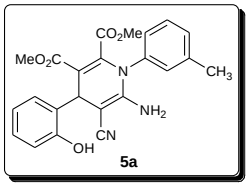
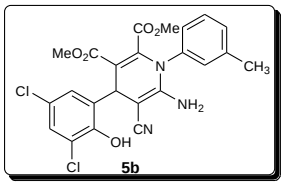
Typical procedure for the synthesis of dihydropyridines (5a-o)

To a mixture of 2-hydroxy aldehyde **1** (1 mmol), malononitrile **2a** (1 mmol), aromatic amine **3** (1 mmol) and L-Proline (10 mol %) was syringed out alkyne **4** (1 mmol). The reaction mixture was stirred vigorously at room temperature till the completion of the reaction as monitored by TLC. The product was isolated by flash chromatographic purification using 2:3 EtOAc/Hexane.

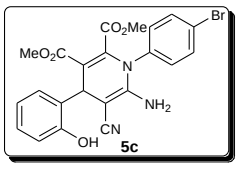
Spectral data for the synthesized compounds



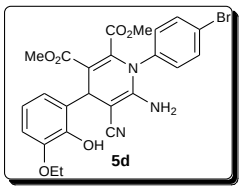
Dimethyl 6-amino-5-cyano-1,4-dihydro-4-(2-hydroxyphenyl)-1-*m*-tolylpyridine-2,3-dicarboxylate (5a). White solid. Yield: 84%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 190-192°C. IR (KBr): 3480, 3319, 2962, 2199, 1759, 1730, 1430, 1289, 1118, 729, 523 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6/ TMS): δ = 2.34 (s, 3H), 3.34 (s, 3H), 3.48 (s, 3H), 4.75 (s, 1H), 5.36 (s, 2H, -NH_2), 6.80 (t, *J* = 8.6 Hz, 2H), 7.04-7.12 (m, 4H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 9.61 (s, 1H, -OH) . ^{13}C NMR (100 MHz, DMSO-d_6/TMS): δ = 20.8, 33.6, 51.8, 52.3, 59.2, 103.4, 115.7, 119.1, 121.4, 127.2, 127.9, 128.5, 129.3, 130.5, 130.7, 131.1, 135.7, 139.2, 142.6, 151.3, 155.1, 163.4, 165.5 Elemental Analyses for $C_{23}H_{21}N_3O_5$, Calc: C, 65.86; H, 5.05; N, 10.02. Found: C, 65.88; H, 5.04; N, 10.01. MS (ESI): m/z 420.5 $[M+H]^+$.



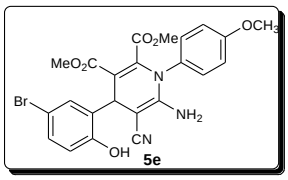
Dimethyl 6-amino-4-(3,5-dichloro-2-hydroxyphenyl)-5-cyano-1,4-dihydro-1-*m*-tolylpyridine-2,3-dicarboxylate (5b) White solid. Yield: 80%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 187-189°C. IR (KBr): 3452, 3323, 2955, 2186, 1744, 1726, 1454, 1440, 1247, 1122, 703, 626 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 2.34 (s, 3H), 3.30 (s, 3H), 3.74 (s, 3H), 4.88 (s, 1H), 5.56 (s, 2H, -NH_2), 7.08-7.12 (m, 3H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.37-7.42 (m, 2H), 9.50 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 20.8, 32.3, 51.0, 53.2, 58.0, 102.6, 107.5, 113.9, 120.8, 121.8, 123.0, 126.9, 127.1, 127.5, 129.3, 130.6, 135.2, 135.6, 139.2, 143.0, 151.6, 163.0, 165.0. Elemental Analyses for $C_{23}H_{19}Cl_2N_3O_5$ Calc: C, 56.57; H, 3.92; N, 8.61. Found: C, 56.60; H, 3.90; N, 8.60. MS (ESI): m/z 488.4 $[M+H]^+$.



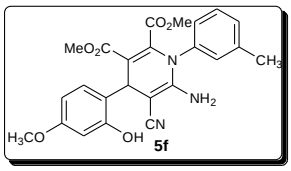
Dimethyl 6-amino-1-(4-bromophenyl)-5-cyano-1,4-dihydro-4-(2-hydroxyphenyl)pyridine-2,3-dicarboxylate (5c). White solid. Yield: 79%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 194-196°C. IR (KBr): 3461, 3350, 2950, 2181, 1744, 1707, 1648, 1569, 1412, 1353, 1228, 1118, 1012, 759, 722, 528 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 3.38 (s, 3H), 3.48 (s, 3H), 4.73 (s, 1H), 5.53 (s, 2H, -NH_2), 6.76-6.80 (m, 2H), 7.05-7.08 (m, 2H), 7.23 (d, *J* = 8.5 Hz, 2H), 7.69 (d, *J* = 8.5 Hz, 2H), 9.60 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 33.8, 51.8, 52.4, 59.2, 103.6, 115.7, 119.0, 121.2, 123.2, 127.9, 128.5, 130.9, 132.5, 132.6, 135.2, 142.2, 151.2, 155.1, 163.3, 165.4. Elemental Analyses for $C_{22}H_{18}BrN_3O_5$ Calc: C, 54.56; H, 3.75; N, 8.68. Found: C, 54.58; H, 3.74; N, 8.67. MS (ESI): m/z 484.7$[M+H]^+$.



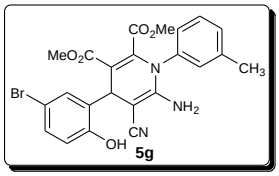
Dimethyl 6-amino-1-(4-bromophenyl)-5-cyano-4-(3-ethoxy-2-hydroxyphenyl)-1,4-dihydropyridine-2,3-dicarboxylate (5d). White solid. Yield: 77%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 180-182°C. IR (KBr): 3489, 3397, 2962, 2156, 1750, 1723, 1689, 1577, 1465, 1333, 1298, 1110, 1023, 789, 603 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 1.39 (t, *J* = 7 Hz, 3H), 3.36 (s, 3H), 3.47 (s, 3H), 4.04 (q, *J*= 7 Hz, 2H), 4.74 (s, 1H), 5.46 (s, 2H, -NH_2), 6.69-6.73 (m, 2H), 6.79-6.81 (m, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 8.48 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 14.7, 34.0, 51.7, 52.3, 58.9, 63.9, 103.4, 111.0, 118.5, 120.5, 121.2, 123.2, 131.0, 132.4, 132.7, 135.1, 142.0, 144.3, 146.6, 151.1, 163.2, 165.4. Elemental Analyses for $C_{24}H_{22}BrN_3O_6$ Calc: C, 54.56; H, 4.20; N, 7.95. Found: C, 54.58; H, 4.19; N, 7.94. MS (ESI): m/z 528.2$[M+H]^+$.



Dimethyl 6-amino-4-(5-bromo-2-hydroxyphenyl)-5-cyano-1,4-dihydro-1-(4-methoxyphenyl)pyridine-2,3-dicarboxylate (5e). White solid. Yield: 82%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 196-198°C. IR (KBr): 3487, 3369, 2982, 2156, 1754, 1710, 1621, 1522, 1423, 1300, 1298, 1150, 1069, 700, 689 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 3.37 (s, 3H), 3.50 (s, 3H), 3.79 (s, 3H), 4.71 (s, 1H), 5.45 (s, 2H, -NH_2), 6.79 (d, *J* = 7.5 Hz, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 7.18-7.23 (m, 4H), 9.98 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 33.8, 51.8, 52.3, 55.5, 58.2, 102.4, 109.9, 114.7, 117.9, 121.1, 127.8, 130.4, 130.8, 131.3, 133.6, 143.2, 151.8, 154.5, 159.9, 163.1, 165.2. Elemental Analyses for $C_{23}H_{20}BrN_3O_6$ Calc: C, 53.71; H, 3.92; N, 8.17. Found: C, 53.69; H, 3.93; N, 8.18. MS (ESI): m/z 514.6 $[M+H]^+$.

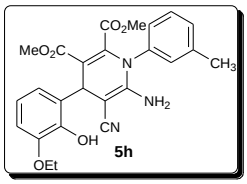


Dimethyl 6-amino-5-cyano-1,4-dihydro-4-(2-hydroxy-4-methoxyphenyl)-1-*m*-tolylpyridine-2,3-dicarboxylate (5f). White solid, Yield: 83%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 185-187°C. IR (KBr): 3452, 3321, 2920, 2177, 1752, 1736, 1655, 1566, 1499, 1326, 1256, 1122, 1000, 780, 600 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 2.34 (s, 3H), 3.33 (s, 3H), 3.48 (s, 3H), 3.68 (s, 3H), 4.66 (s, 1H), 5.29 (s, 2H, -NH_2), 6.37-6.40 (m, 2H), 6.99 (d, *J* = 8.5 Hz, 1H), 7.07-7.11 (m, 2H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.35 (t, *J* = 8 Hz, 1H), 9.61 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ 20.7, 33.0, 51.7, 52.1, 54.9, 59.6, 101.5, 103.5, 104.3, 121.3, 123.9, 127.1, 129.1, 129.2, 130.4, 130.6, 135.7, 139.1, 142.2, 151.0, 155.9, 159.0, 163.3, 165.5. Elemental Analyses for $C_{24}H_{23}N_3O_6$ Calc: C, 64.13; H, 5.16; N, 9.35. Found: C, 64.10; H, 5.18; N, 9.36. MS (ESI): m/z 450.2$[M+H]^+$.

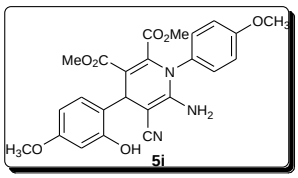


Dimethyl 6-amino-4-(5-bromo-2-hydroxyphenyl)-5-cyano-1,4-dihydro-1-*m*-tolylpyridine-2,3-dicarboxylate (5g). White solid. Yield: 78%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 195-197°C. IR (KBr): 3444, 3354, 2945, 2192, 1736, 1725, 1645, 1582, 1423, 1326, 1262, 1178, 1022, 783, 700, 623 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$/ TMS):

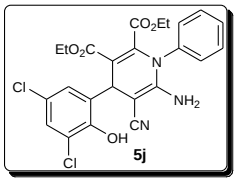
δ = 2.32 (s, 3H), 3.34 (s, 3H), 3.48 (s, 3H), 4.70 (s, 1H), 5.42 (s, 2H, -NH_2), 6.80 (d, *J* = 8.4 Hz, 1H), 7.04-7.06 (m, 2H), 7.19-7.23 (m, 2H), 7.29 (d, *J* = 7.6 Hz, 1H), 7.36 (t, *J* = 8 Hz, 1H), 10.16 (s, 1H, -OH) . ^{13}C NMR (100 MHz, DMSO-d_6/TMS): δ21.2, 34.1, 52.3, 52.8, 58.8, 103.4, 110.4, 118.3, 121.5, 127.3, 129.8, 130.7, 130.9, 131.1, 133.8, 135.8, 139.9, 143.3, 152.1, 154.9, 163.6, 165.6. Elemental Analyses for $C_{23}H_{20}BrN_3O_5$ Calc: C, 55.43; H, 4.05; N, 8.43. Found: C, 55.45; H, 4.04; N, 8.42. MS (ESI): m/z 498.2$[M+H]^+$.



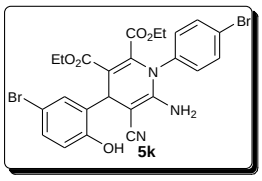
Dimethyl 6-amino-5-cyano-4-(3-ethoxy-2-hydroxyphenyl)-1,4-dihydro-1-*m*-tolylpyridine-2,3-dicarboxylate (5h). White solid. Yield: 81%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 199-201°C. IR (KBr): 3435, 3368, 2900, 2187, 1745, 1720, 1645, 1500, 1423, 1369, 1209, 1153, 1000, 789, 721, 598 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6/ TMS): δ = 1.38 (t, *J* = 7 Hz, 3H), 2.34 (s, 3H), 3.33 (s, 3H), 3.47 (s, 3H), 4.04 (q, *J*= 7 Hz, 2H), 4.80 (s, 1H), 5.33 (s, 2H, -NH_2), 6.72-6.76 (m, 2H), 6.81-6.83 (m, 1H), 7.13-7.16 (m, 2H), 7.30 (d, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 8.50 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ =14.7, 20.7, 33.3, 51.7, 52.2, 59.1, 63.9, 103.2, 111.0, 118.6, 120.2, 121.2, 127.2, 129.2, 130.4, 130.7, 131.4, 135.5, 139.1, 142.4, 144.0, 146.6, 151.2, 163.2, 165.4. Elemental Analyses for $C_{25}H_{25}N_3O_6$ Calc: C, 64.79; H, 5.44; N, 9.07. Found: C, 67.80; H, 5.42; N, 9.08. MS (ESI): m/z 464.7 $[M+H]^+$.



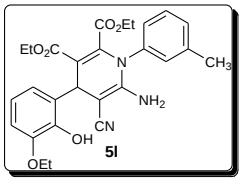
Dimethyl 6-amino-5-cyano-1,4-dihydro-4-(2-hydroxy-4-methoxyphenyl)-1-(4-methoxyphenyl)pyridine-2,3-dicarboxylate (5i). White solid. Yield: 85%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 203-205°C. IR (KBr): 3475, 3323, 2967, 2163, 1740, 1709, 1680, 1575, 1443, 1329, 1220, 1175, 1036, 726, 712, 589 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6/ TMS): δ = 3.35 (s, 3H), 3.48 (s, 3H), 3.68 (s, 3H), 3.79 (s, 3H), 4.65 (s, 1H), 5.29 (s, 2H, -NH_2), 6.36-6.39 (m, 2H), 6.97-7.02 (m, 3H), 7.20 (d, *J* = 9 Hz, 2H), 9.61 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 32.8, 51.7, 52.2, 54.9, 55.5, 59.3, 101.5, 103.2, 104.3, 108.7, 114.6, 121.4, 124.0, 128.0, 129.0, 131.5, 142.6, 151.3, 155.8, 159.0, 159.8, 163.4, 165.5. Elemental Analyses for $C_{24}H_{23}N_3O_7$ Calc: C, 61.93; H, 4.98; N, 9.03. Found: C, 61.95; H, 4.97; N, 9.02. MS (ESI): m/z 466.3 $[M+H]^+$.



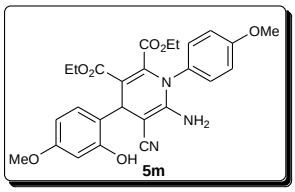
Diethyl 6-amino-4-(3,5-dichloro-2-hydroxyphenyl)-5-cyano-1,4-dihydro-1-phenylpyridine-2,3-dicarboxylate (5j). White solid. Yield: 84%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 210-212°C. IR (KBr): 3422, 3356, 2989, 2178, 1750, 1725, 1667, 1422, 1369, 1232, 1156, 1023, 777, 712, 533 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6/ TMS): δ = 0.82 (t, *J* = 7 Hz, 3H), 1.01 (t, *J* = 7 Hz, 3H), 3.72-3.79 (m, 2H), 3.91-3.94 (m, 2H), 4.87 (s, 1H), 5.50 (s, 2H, -NH_2), 7.11 (d, *J* = 3 Hz, 1H), 7.36-7.37 (m, 2H), 7.41 (d, *J* = 3 Hz, 1H), 7.50-7.51 (m, 3H), 9.79 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 13.1, 13.6, 34.8, 57.8, 60.4, 61.4, 102.4, 120.9, 121.7, 122.9, 127.4, 127.6, 129.5, 130.0, 130.7, 135.3, 135.7, 142.8, 149.9, 151.5, 162.3, 164.5. Elemental Analyses for $C_{24}H_{21}Cl_2N_3O_5$ Calc: C, 57.38; H, 4.21; N, 8.36. Found: C, 57.36; H, 4.22; N, 8.37. MS (ESI): m/z 502.6 $[M+H]^+$.



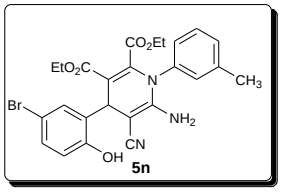
Diethyl 6-amino-4-(5-bromo-2-hydroxyphenyl)-1-(4-bromophenyl)-5-cyano-1,4-dihydropyridine-2,3-dicarboxylate (5k). White solid. Yield: 79%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 207-209°C. IR (KBr): 3452, 3350, 2981, 2150, 1770, 1704, 1669, 1584, 1421, 1335, 1282, 1181, 1025, 795, 719, 582 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 0.88 (t, *J* = 7 Hz, 3H), 1.03 (t, *J* = 7 Hz, 3H), 3.74-3.96 (m, 2H), 4.00-4.22 (m, 2H), 4.66 (s, 1H), 5.60 (s, 2H, -NH_2), 6.78 (d, *J* = 8.5 Hz, 1H), 7.19-7.24 (m, 4H), 7.71 (d, *J* = 8.5 Hz, 2H), 9.99 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 13.2, 13.7, 35.0, 59.8, 60.3, 61.4, 102.7, 109.8, 117.9, 121.1, 123.3, 130.4, 131.6, 132.5, 132.7, 133.2, 135.0, 142.3, 151.4, 155.0, 162.5, 164.6. Elemental Analyses for $C_{24}H_{21}Br_2N_3O_5$ Calc: C, 48.75; H, 3.58; N, 7.11. Found: C, 48.77; H, 3.57; N, 7.10. MS (ESI): m/z 589.7 $[M+H]^+$.



Diethyl 6-amino-5-cyano-4-(3-ethoxy-2-hydroxyphenyl)-1,4-dihydro-1-*m*-tolylpyridine-2,3-dicarboxylate (5l). White solid. Yield: 80%. R_f: 0.20 (2:3 EtOAc/Hexane). mp: 198-200°C. IR (KBr): 3400, 3310, 2982, 2118, 1777, 1713, 1645, 1567, 1408, 1362, 1229, 1110, 1011, 795, 710, 545 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 0.83 (t, *J* = 7 Hz, 3H), 1.01 (t, *J* = 7 Hz, 3H), 1.38 (t, *J* = 7 Hz, 3H), 2.34 (s, 3H), 3.72-3.83 (m, 2H), 3.90 (q, *J* = 7 Hz, 2H), 4.04 (q, *J* = 7 Hz, 2H), 4.80 (s, 1H), 5.30 (s, 2H, -NH_2), 6.74-6.76 (m, 2H), 6.81-6.83 (m, 1H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 1H), 7.37 (t, *J* = 8.5 Hz, 1H), 8.48 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 13.2, 13.7, 14.7, 20.7, 33.6, 58.9, 60.1, 61.1, 64.0, 103.3, 111.1, 113.5, 120.6, 121.3, 127.6, 129.2, 130.4, 131.1, 131.5, 135.5, 139.1, 142.2, 144.2, 146.5, 151.2, 162.7, 164.9. Elemental Analyses for $C_{27}H_{29}N_3O_6$ Calc: C, 65.97; H, 5.95; N, 8.55. Found: C, 65.99; H, 5.94; N, 8.54. MS (ESI): m/z 492.8 $[M+H]^+$.

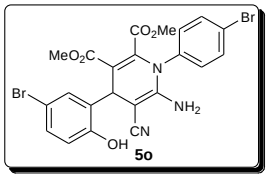


Diethyl 6-amino-5-cyano-1,4-dihydro-4-(2-hydroxy-4-methoxyphenyl)-1-(4-methoxyphenyl)pyridine-2,3-dicarboxylate (5m). white solid. Yield: 81%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 183-185°C. IR (KBr): 3444, 3326, 2987, 2120, 1725, 1702, 1654, 1523, 1469, 1355, 1230, 1110, 1026, 770, 759, 530 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 0.86 (t, *J* = 7 Hz, 3H), 1.03 (t, *J* = 7 Hz, 3H), 3.68 (s, 3H), 3.72-3.84 (m, 5H), 3.86-3.92 (m, 2H), 4.65 (s, 1H), 5.27 (s, 2H, -NH_2), 6.36-6.41 (m, 2H), 7.00 (t, *J* = 8.5 Hz, 3H), 7.22 (d, *J* = 8.5 Hz, 2H), 9.59 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 13.3, 13.8, 33.1, 54.9, 55.5, 59.1, 60.1, 61.1, 100.2, 101.4, 103.3, 104.2, 114.5, 121.5, 124.2, 128.0, 129.4, 131.8, 142.4, 151.4, 155.9, 159.0, 159.9, 162.9, 164.9. Elemental Analyses for $C_{26}H_{27}N_3O_7$ Calc: C, 63.28; H, 5.51; N, 8.51. Found: C, 63.29; H, 5.49; N, 8.52. MS (ESI): m/z 494.3 $[M+H]^+$.



Diethyl 6-amino-4-(5-bromo-2-hydroxyphenyl)-5-cyano-1,4-dihydro-1-m-tolylpyridine-2,3-dicarboxylate (5n). White solid. Yield: 84%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 206-208°C. IR (KBr):

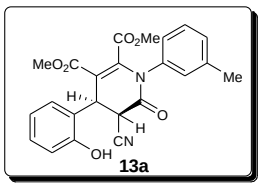
3420, 3318, 2999, 2164, 1755, 1729, 1697, 1568, 1473, 1333, 1215, 1148, 1098, 795, 726, 569 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 0.84 (t, *J* = 7 Hz, 3H), 1.04 (t, *J* = 7 Hz, 3H), 2.34 (s, 3H), 3.75-3.83 (m, 2H), 3.93 (q, *J* = 7 Hz, 2H), 4.70 (s, 1H), 5.44 (s, 2H, -NH_2), 6.79-6.81 (m, 1H), 7.09-7.11 (m, 2H), 7.22-7.23 (m, 2H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 9.98 (s, 1H, -OH) . ^{13}C NMR (125 MHz, $CDCl_3$/TMS): δ = 13.3, 13.7, 21.1, 32.7, 60.0, 61.7, 61.9, 104.0, 112.6, 119.2, 120.6, 127.1, 129.6, 130.7, 131.1, 131.2, 131.7, 133.2, 134.7, 140.3, 142.2, 151.2, 152.9, 162.7, 166.4. Elemental Analyses for $C_{25}H_{24}BrN_3O_5$ Calc: C, 57.04; H, 4.60; N, 7.98. Found: C, 57.03; H, 4.62; N, 7.97. MS (ESI): m/z 526.6 $[M+H]^+$.



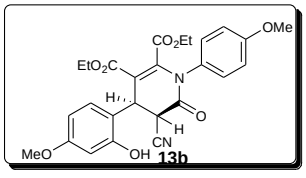
Dimethyl 6-amino-4-(5-bromo-2-hydroxyphenyl)-1-(4-bromophenyl)-5-cyano-1,4-dihydropyridine-2,3-dicarboxylate (5o). White solid. Yield: 82%. R_f: 0.25 (2:3 EtOAc/Hexane). mp: 214-216°C. IR (KBr): 3488, 3334, 2927, 2146, 1753, 1705, 1666, 1509, 1463, 1325, 1227, 1180, 1000, 780, 726, 690 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 3.38 (s, 3H), 3.49 (s, 3H), 4.67 (s, 1H), 5.65 (s, 2H, -NH_2), 6.78 (d, *J* = 8.5 Hz, 1H),7.16-7.31 (m, 4H), 7.71 (d, *J* = 8.5 Hz, 2H), 10.03 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ =34.3, 51.9, 52.5, 58.3, 102.9, 109.9, 118.0, 121.0, 123.3, 130.5, 131.0, 132.3, 132.6, 133.3, 135.1, 142.5, 151.4, 154.7, 163.1, 165.1. Elemental Analyses for $C_{22}H_{17}Br_2N_3O_5$ Calc: C, 46.92; H, 3.04; N, 7.46. Found: C, 46.90; H, 3.05; N, 7.47. MS (ESI): m/z 561.2 $[M+H]^+$.

Typical procedure for the synthesis of dihydropyridinones (13a-f)[22]

To a mixture of dihydropyridine **5** (1 mmol), 1N hydrochloric acid **(**1-2mL) was added and the reaction mixture was stirred under reflux at 75^0C for 30 minutes. The resultant solid was filtered off and recrystallized from methanol to afford the dihydropyridinones **13a-f**.

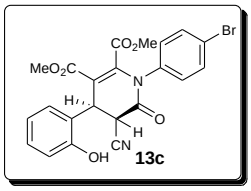


***(4S,5R)*-Dimethyl-5-cyano-1,4,5,6-tetrahydro-4-(2-hydroxyphenyl)-6-oxo-1-*m*-tolylpyridine-2,3-dicarboxylate (13a).** Yellow solid. Yield: 85%. R_f: 0.30 (2:3 EtOAc/Hexane). mp: 238-240°C. IR (KBr): 3330, 2986, 2187, 1740, 1723, 1699, 1563, 1428, 1364, 1296, 1122, 1065, 1036, 999, 710 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 2.34 (s, 3H), 3.34 (s, 3H), 3.56 (s, 3H), 4.71 (d, *J* = 9 Hz, 1H), 5.30 (d, *J* = 8.5 Hz, 1H), 6.81-6.87 (m, 2H), 6.99-7.10 (m, 2H), 7.14-7.20 (m, 2H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 10.20 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 20.7, 35.7, 52.2, 52.3, 115.3, 115.4, 119.2, 128.7, 129.4, 129.6, 129.9, 136.0 138.5, 142.9, 155.9, 162.3, 162.4, 164.6. Elemental Analyses for $C_{23}H_{20}N_2O_6$ Calc: C, 65.71; H, 4.79; N, 6.66. Found: C, 65.73; H, 4.78; N, 6.65. MS (ESI): m/z 421.2 $[M+H]^+$.

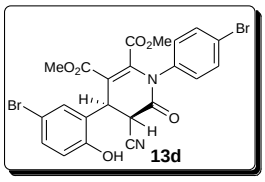


***(4S,5R)*-Diethyl 5-cyano-1,4,5,6-tetrahydro-4-(2-hydroxy-4-methoxyphenyl)-1-(4-methoxyphenyl)-6-oxopyridine-2,3-dicarboxylate (13b).** Yellow solid. Yield: 83%. R_f: 0.30 (2:3

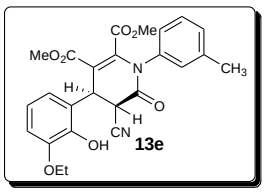
EtOAc/Hexane)., mp: 226-228°C. IR (KBr): 3392, 2950, 2181, 1739, 1707, 1620, 1514, 1436, 1325, 1233, 1104, 1063, 1035, 957, 708 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 0.85 (t, *J* = 7 Hz, 3H), 1.10 (t, *J* = 7 Hz, 3H), 3.69 (s, 3H), 3.77 (s, 3H), 3.79-3.90 (m, 2H), 3.97-4.01 (m, 2H), 4.61 (d, *J* = 9 Hz, 1H), 5.25 (d, *J* = 9.5 Hz, 1H), 6.40-6.44 (m, 2H), 6.99-7.01 (m, 2H), 7.08-7.28 (m, 3H), 10.23 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 13.2, 13.8, 36.3, 54.9, 55.5, 60.7, 61.4, 101.1, 104.5, 105.5, 113.9, 114.0, 115.5, 115.7, 128.5, 130.7, 142.8, 156.8, 159.5, 160.0, 161.8, 162.7, 164.1 Elemental Analyses for $C_{26}H_{26}N_2O_8$ Calc: C, 63.15; H, 5.30; N, 5.67. Found: C, 63.17; H, 5.29; N, 5.66; MS (ESI): m/z 495.7 $[M+H]^+$.



***(4S,5R)*-Dimethyl 1-(4-bromophenyl)-5-cyano-1,4,5,6-tetrahydro-4-(2-hydroxyphenyl)-6-oxopyridine-2,3-dicarboxylate (13c).** Yellow solid. Yield: 80%. R_f: 0.35 (2:3 EtOAc/Hexane). mp: 221-223°C. IR (KBr): 3398, 2956, 2119, 1740, 1726, 1632, 1523, 1467, 1364, 1264, 1102, 1066, 1034, 980, 710 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 3.38 (s, 3H), 3.57 (s, 3H), 4.70 (d, *J* = 9 Hz, 1H), 5.29 (d, *J* = 8.5 Hz, 1H), 6.80-6.86 (m, 2H), 7.14-7.20 (m, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 7.70 (d, *J* = 8.5 Hz, 2H), 10.22 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ =21.1, 37.4, 52.2, 52.6, 105.9, 115.2, 115.5, 119.2, 122.5, 123.0, 129.4, 130.8, 132.1, 135.5, 142.2, 155.9, 162.2, 162.4, 164.6. Elemental Analyses for $C_{22}H_{17}BrN_2O_6$ Calc: C, 54.45; H, 3.53; N, 5.77. Found: C, 54.43; H, 3.54; N, 5.78. MS (ESI): m/z 485.3 $[M+H]^+$.

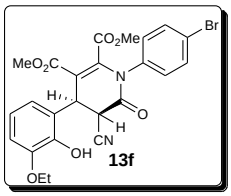


***(4S,5R)*-Dimethyl 4-(5-bromo-2-hydroxyphenyl)-1-(4-bromophenyl)-5-cyano-1,4,5,6-tetrahydro-6-oxopyridine-2,3-dicarboxylate (13d).** Yellow solid. Yield: 79%. R_f: 0.30 (2:3 EtOAc/Hexane). mp: 242-244°C. IR (KBr): 3375, 2963, 2177, 1734, 1710, 1648, 1523, 1419, 1329, 1230, 1110, 1000, 723 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 3.38 (s, 3H), 3.59 (s, 3H), 4.66 (d, *J* = 9 Hz, 1H), 5.30 (d, *J* = 8.5 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 7.18-7.20 (m, 2H), 7.32-7.36 (m, 2H), 7.72 (d, *J* = 9 Hz, 2H), 10.69 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 37.7, 52.4, 52.7, 104.9, 109.8, 115.2, 117.6, 122.7, 125.8, 130.7, 132.0, 132.2, 133.7, 135.4, 142.5, 155.5, 162.2, 162.4, 164.5. Elemental Analyses for $C_{22}H_{16}Br_2N_2O_6$ Calc: C, 46.84; H, 2.86; N, 4.97. Found: C, 46.86; H, 2.85; N, 4.96. MS (ESI): m/z 562.7 $[M+H]^+$.

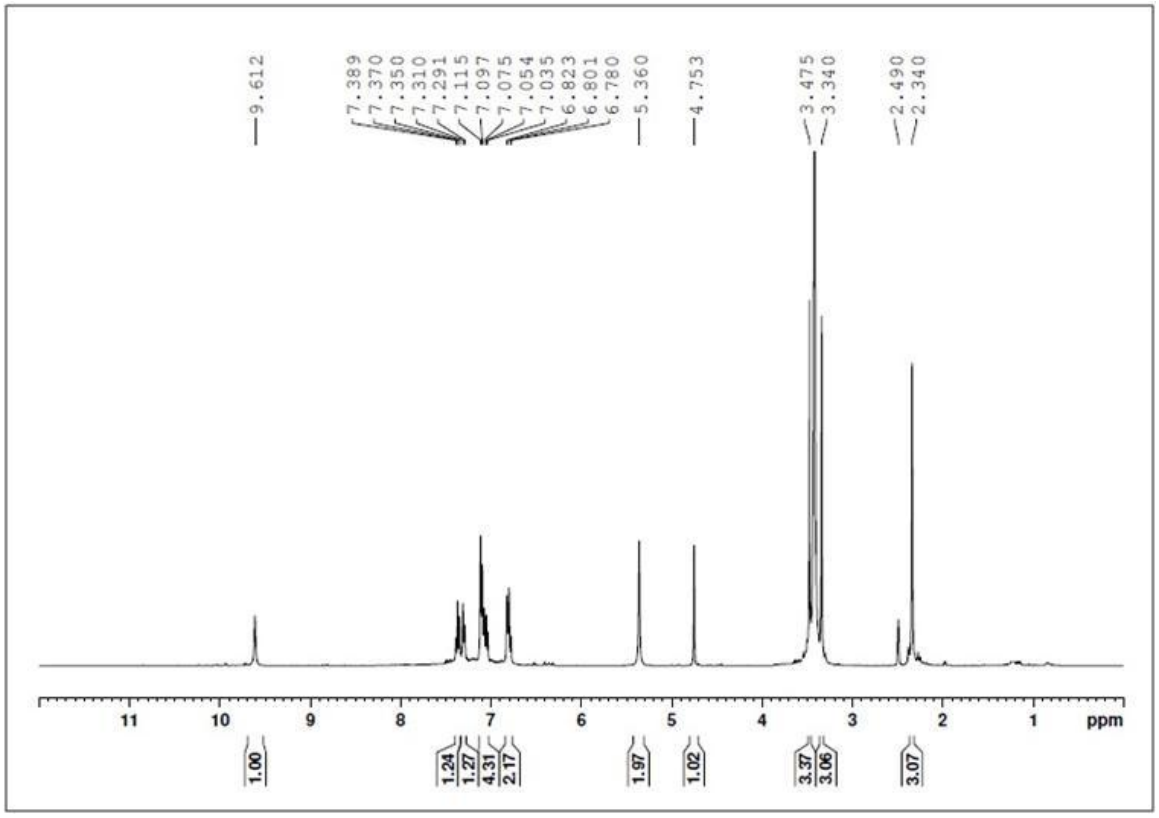


***(4S,5R)*-Dimethyl 5-cyano-4-(3-ethoxy-2-hydroxyphenyl)-1,4,5,6-tetrahydro-6-oxo-1-*m*-tolylpyridine-2,3-dicarboxylate (13e).** Yellow solid. Yield: 82%. R_f: 0.30 (2:3 EtOAc/Hexane). mp: 237-239°C. IR (KBr): 3359, 2945, 2180, 1778, 1745, 1636, 1523, 1438, 1331, 1213, 1156, 1019, 960, 700 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/ TMS): δ = 1.38 (t, *J* = 7 Hz, 3H), 2.35 (s, 3H), 3.34 (s, 3H), 3.55 (s, 3H), 4.05 (q, *J* = 7 Hz, 2H), 4.82 (d, *J* = 8.5 Hz, 1H), 5.33 (d, *J* = 8.5 Hz, 1H), 6.77-6.82 (m, 3H), 6.90-6.92 (m, 1H), 7.03-7.07 (m, 1H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.34-7.37 (m, 1H), 9.15 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 14.7, 20.8, 35.4, 52.2, 52.4, 64.0, 112.4, 115.3, 119.1,

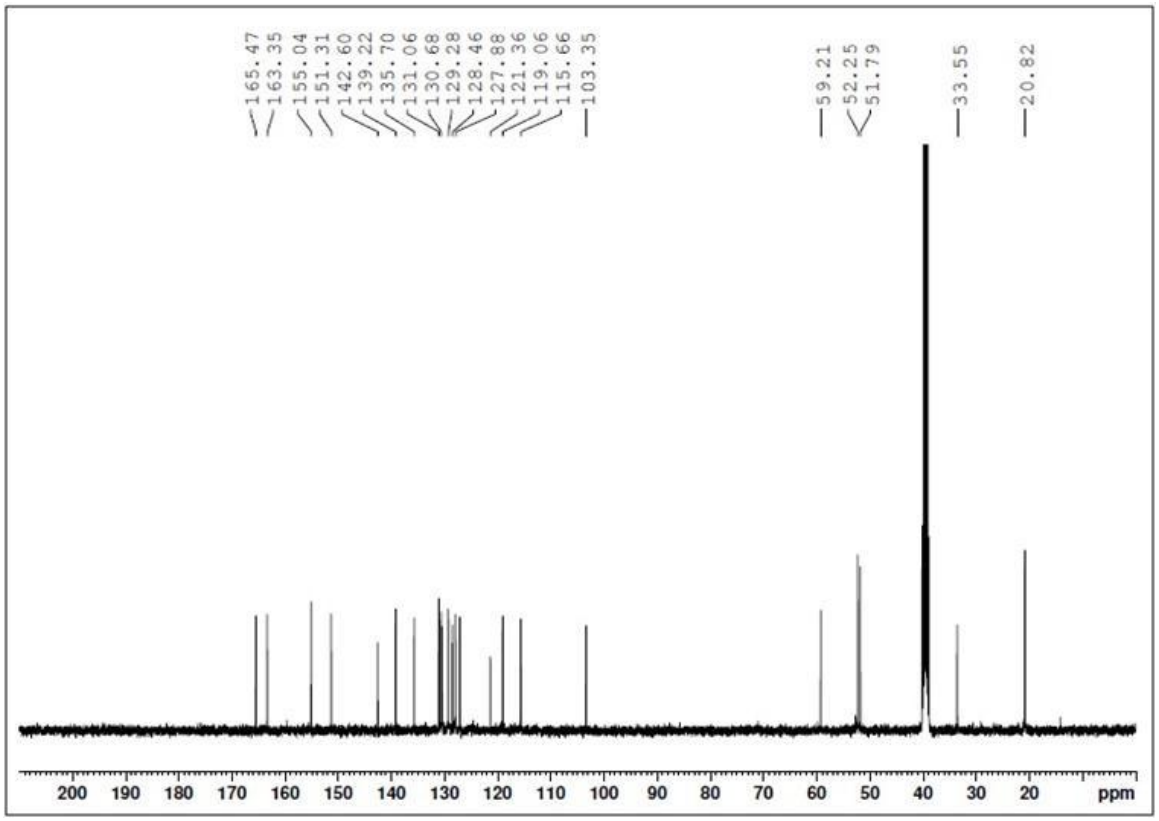
123.3, 128.7, 129.9, 136.0, 138.5, 143.0, 145.1, 146.7, 162.2, 162.3, 164.7. Elemental Analyses for $C_{25}H_{24}N_2O_7$ Calc: C, 64.65; H, 5.21; N, 6.03. Found: C, 64.67; H, 5.20; N, 6.02. MS (ESI): m/z 465.3 $[M+H]^+$.



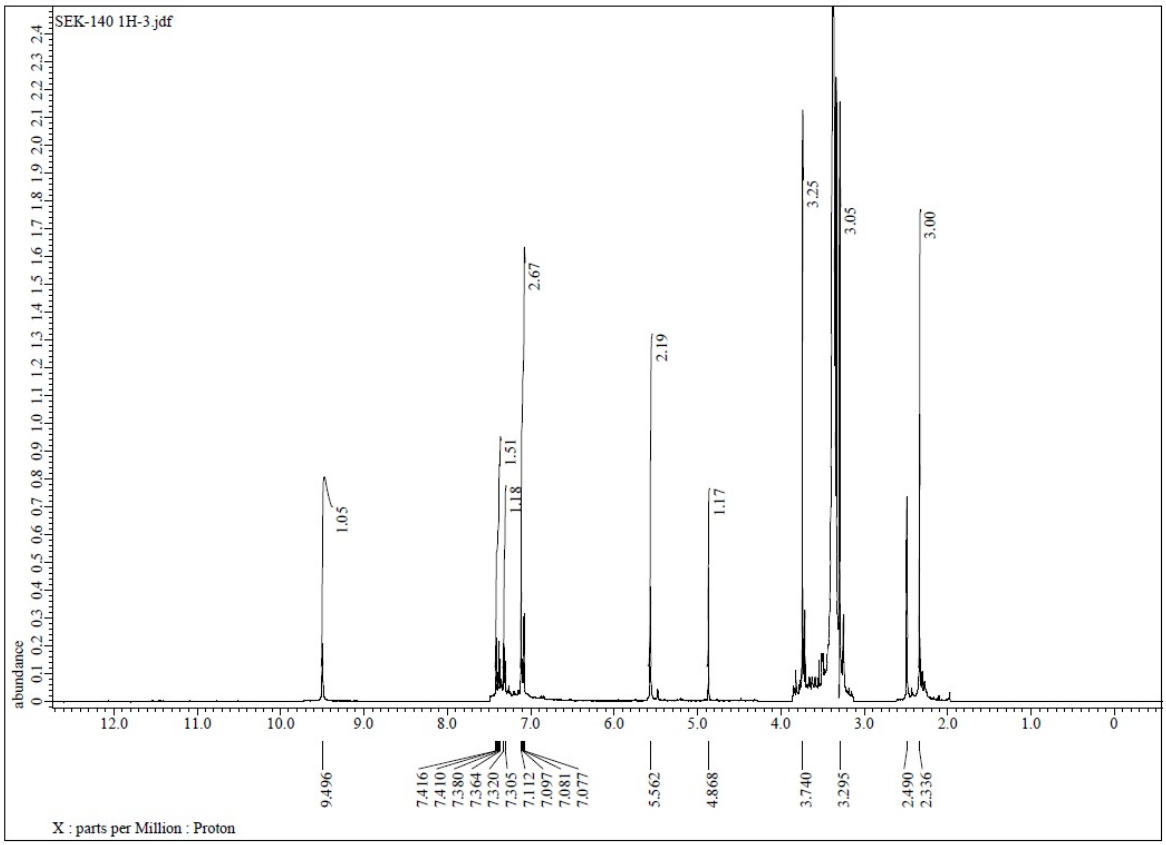
***(4S,5R)*-Dimethyl 1-(4-bromophenyl)-5-cyano-4-(3-ethoxy-2-hydroxyphenyl)-1,4,5,6-tetrahydro-6-oxopyridine-2,3-dicarboxylate (13f).** Yellow solid. Yield: 77%. R_f: 0.30 (2:3 EtOAc/Hexane). mp: 230-232°C. IR (KBr): 3398, 2963, 2196, 1703, 1710, 1623, 1553, 1469, 1300, 1296, 1167, 1100, 1019, 946, 723 cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6/TMS): δ = 1.38 (t, *J* = 7 Hz, 3H), 3.37 (s, 3H), 3.56 (s, 3H), 4.05 (q, *J* = 7 Hz, 2H), 4.75 (d, *J* = 8.5 Hz, 1H), 5.29 (d, *J* = 8.5 Hz, 1H), 6.73-6.80 (m, 2H), 6.90-6.92 (m, 1H), 7.21-7.47 (m, 2H), 7.68 (d, *J* = 8 Hz, 2H), 9.16 (s, 1H, -OH) . ^{13}C NMR (125 MHz, DMSO-d_6/TMS): δ = 14.7, 36.8, 52.2, 52.6, 63.9, 105.8, 112.3, 115.1, 118.9, 121.9, 122.6, 123.2, 131.7, 132.0, 135.4, 142.3, 145.1, 146.6, 162.2, 162.3, 164.6. Elemental Analyses for $C_{24}H_{21}BrN_2O_7$ Calc: C, 54.46; H, 4.00; N, 5.29. Found: C, 54.48; H, 3.99; N, 5.28. MS (ESI): m/z 529.2 $[M+H]^+$.



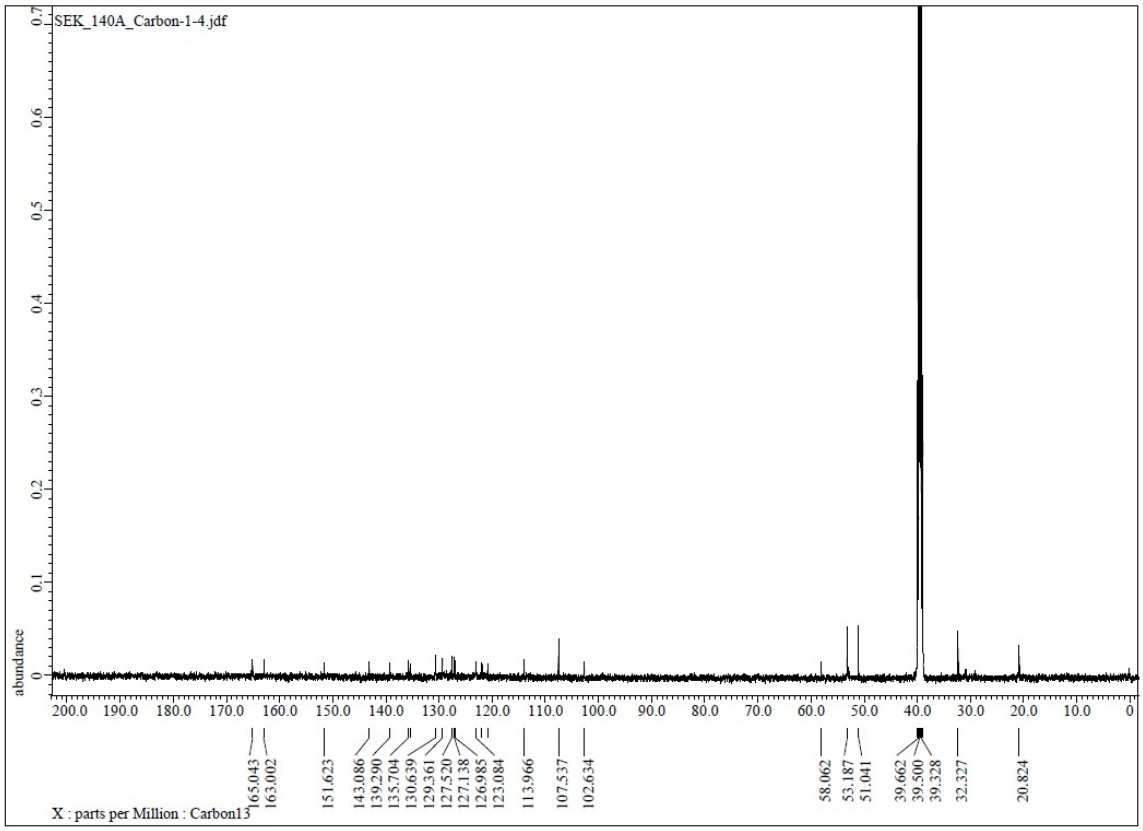
^{1}H NMR spectrum of compound **5a**



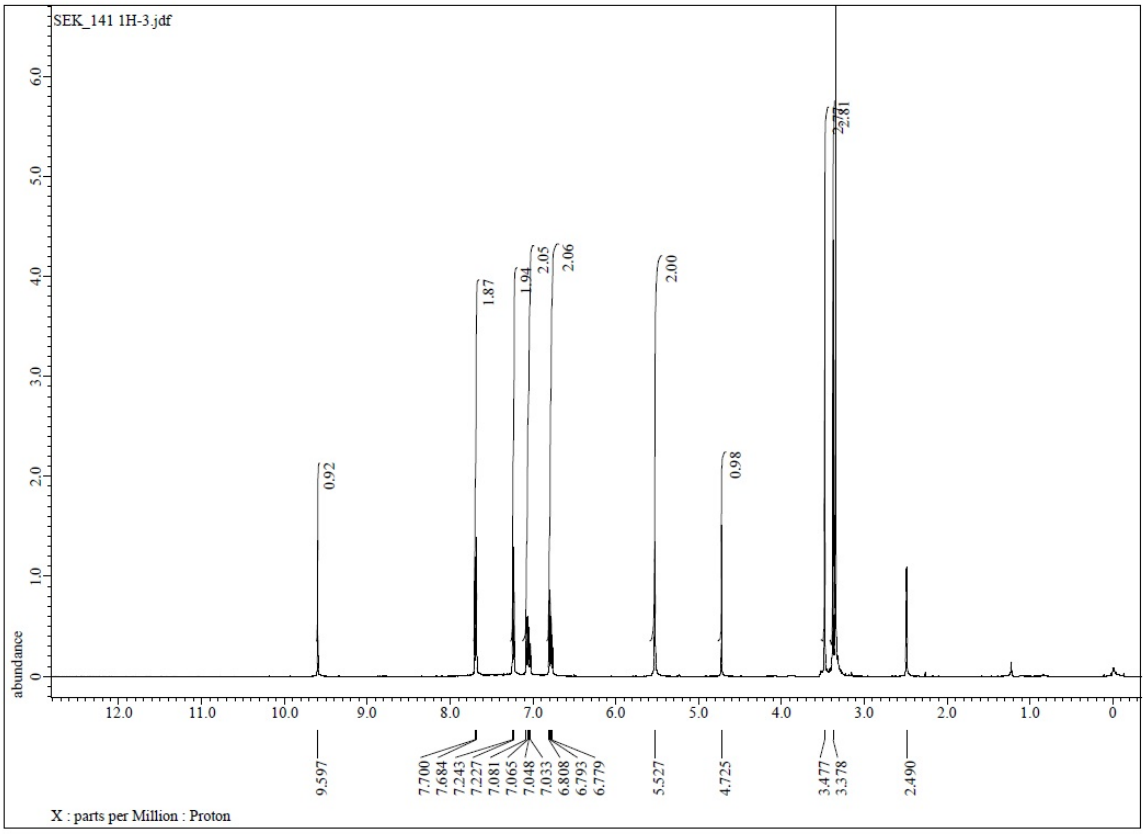
^{13}C NMR spectrum of compound **5a**



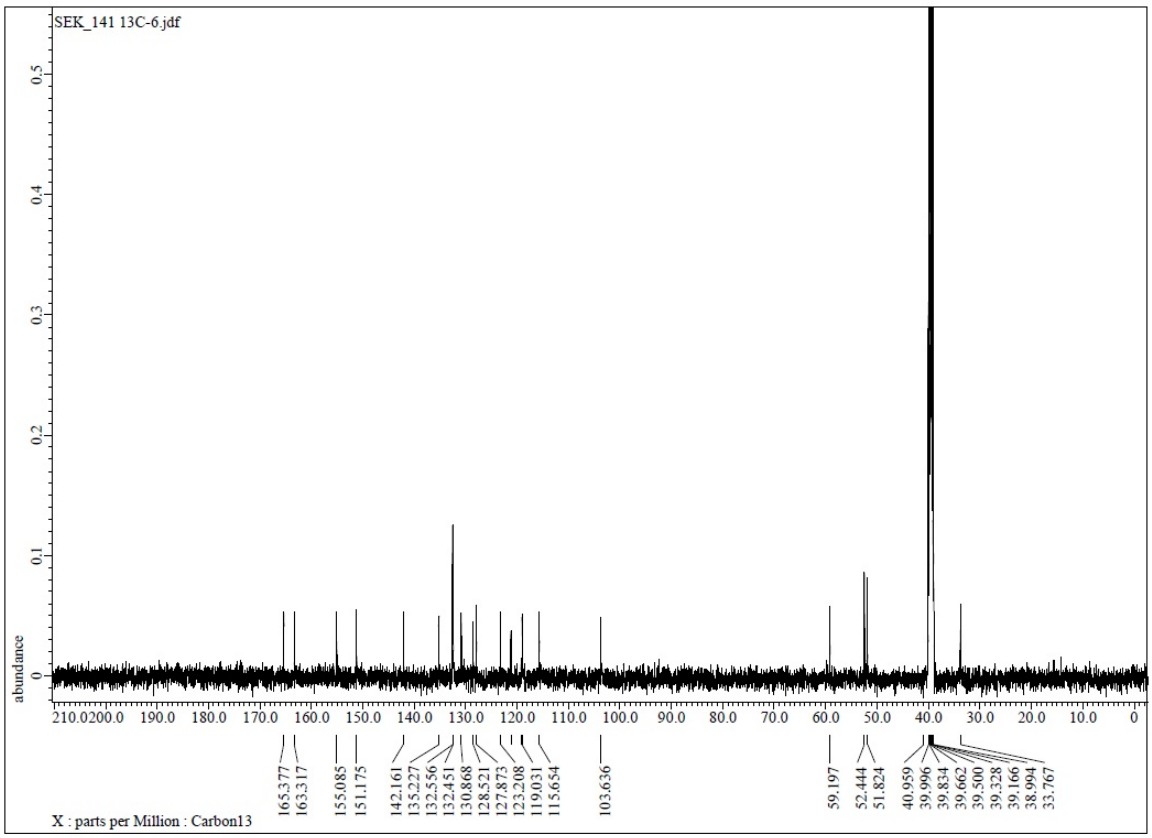
^{1}H NMR spectrum of compound **5b**



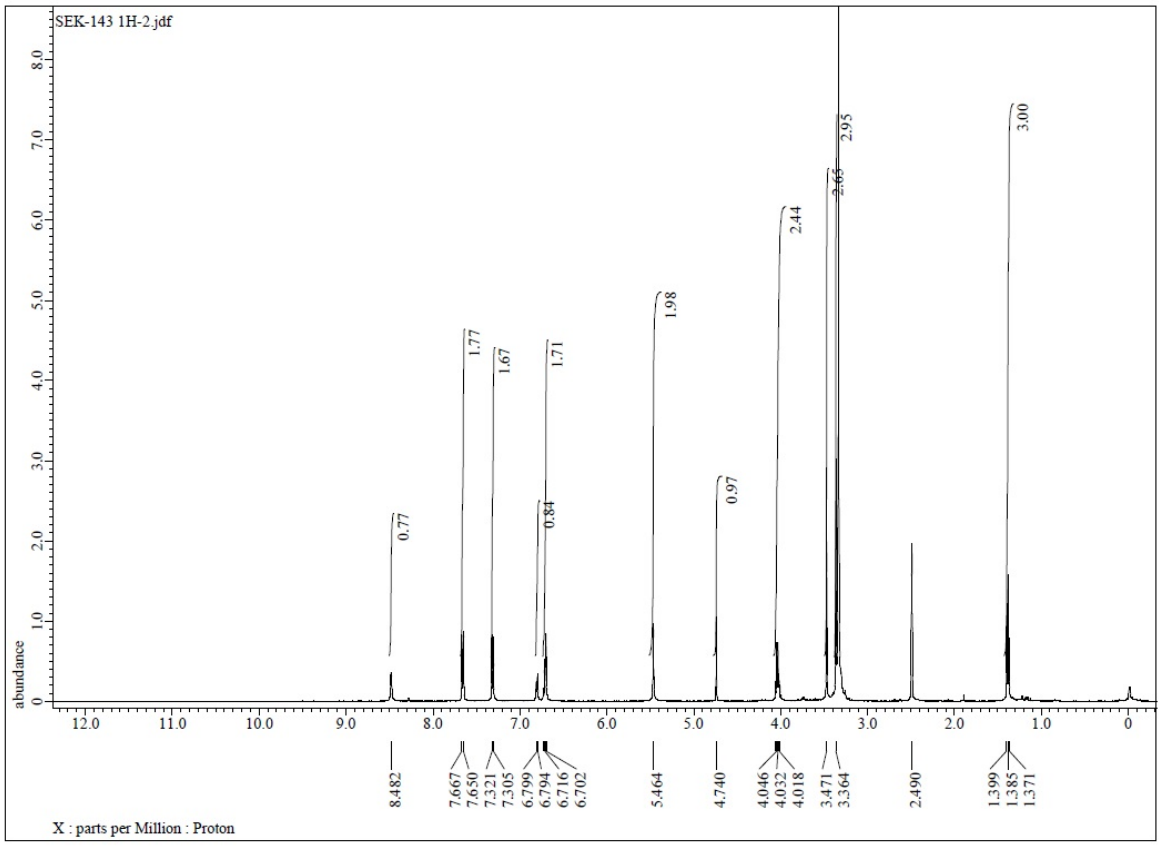
^{13}C NMR spectrum of compound **5b**



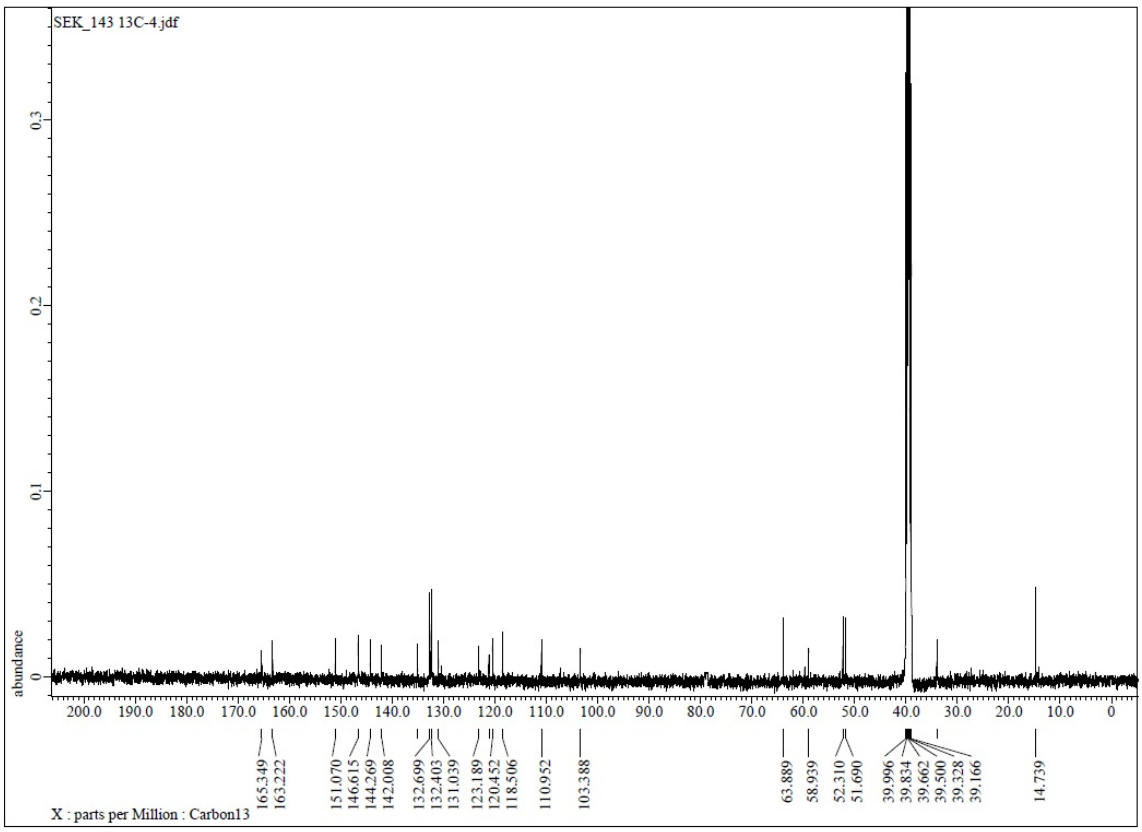
^{1}H NMR spectrum of compound **5c**



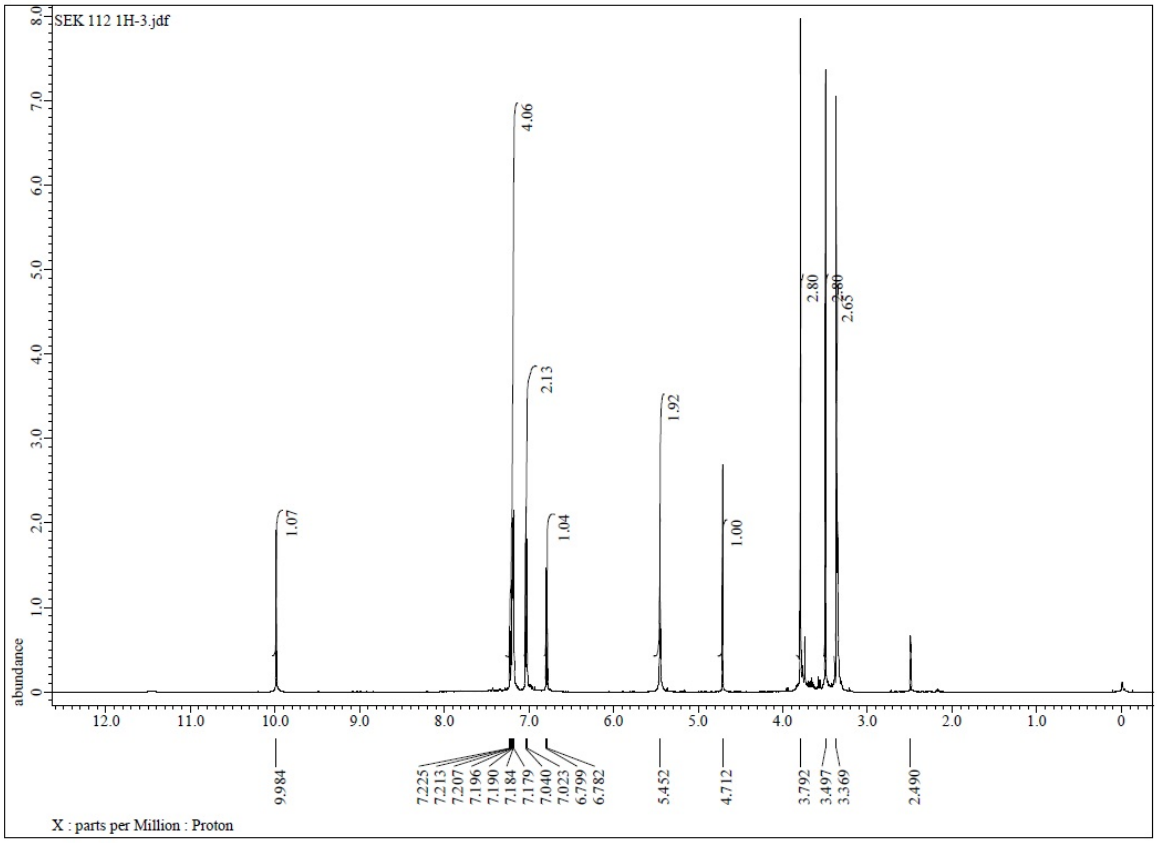
^{13}C NMR spectrum of compound **5c**



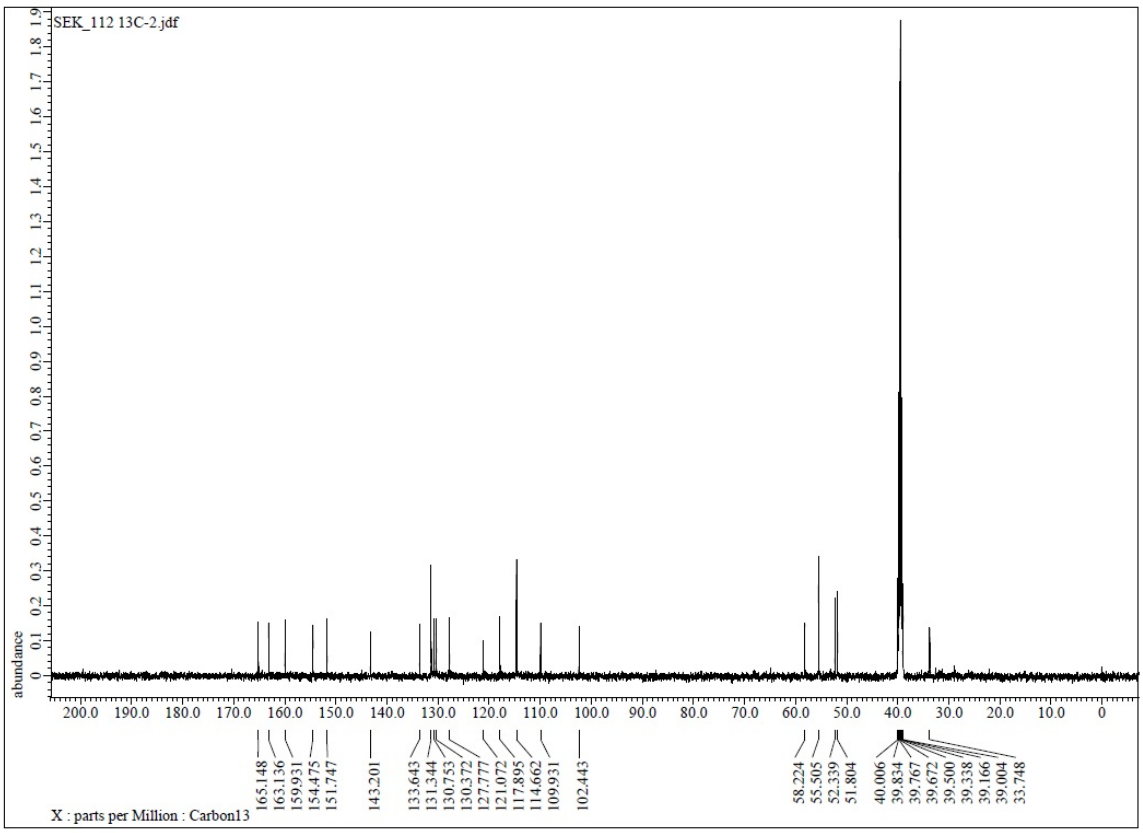
^{1}H NMR spectrum of compound **5d**



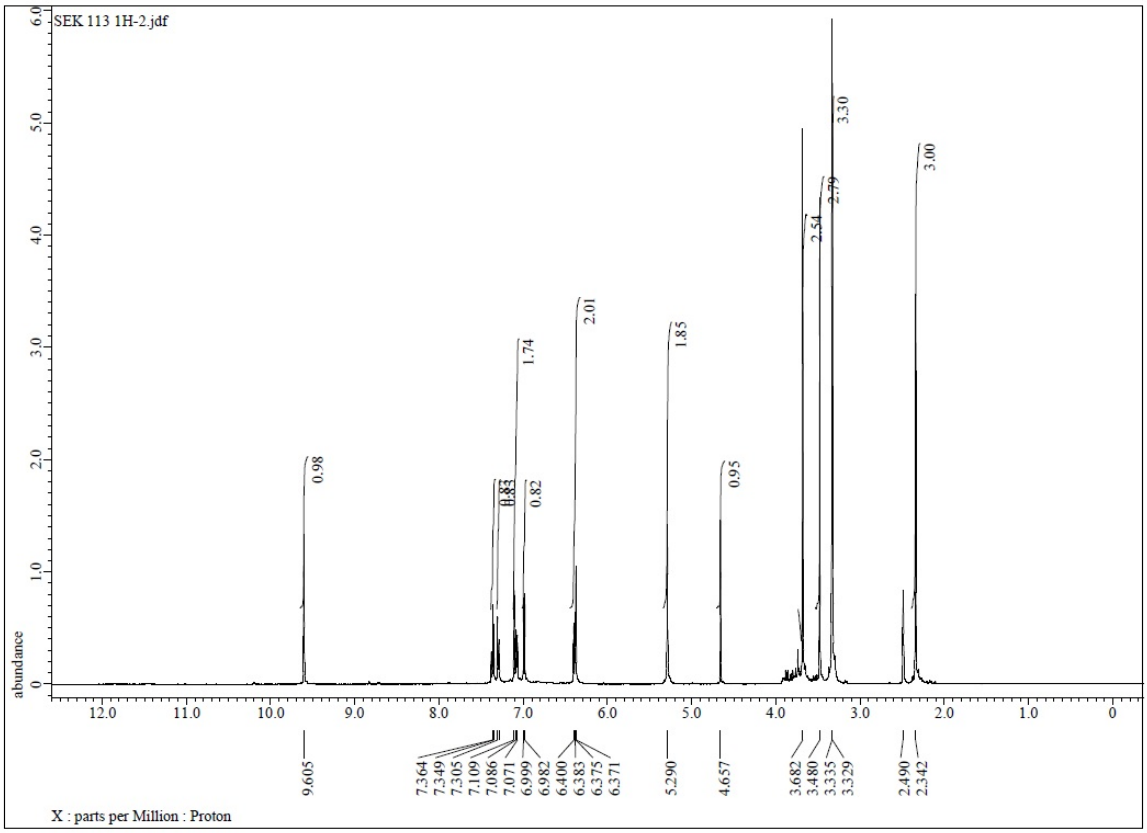
^{13}C NMR spectrum of compound **5d**



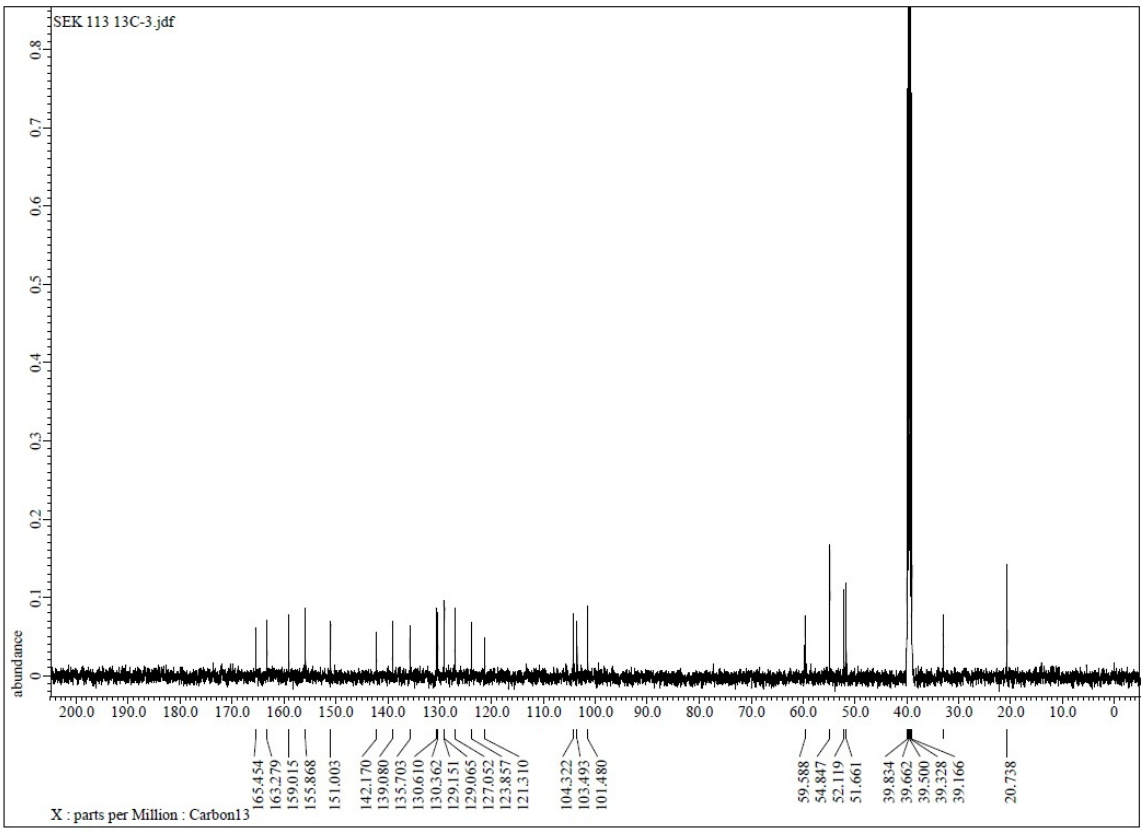
^{1}H NMR spectrum of compound **5e**



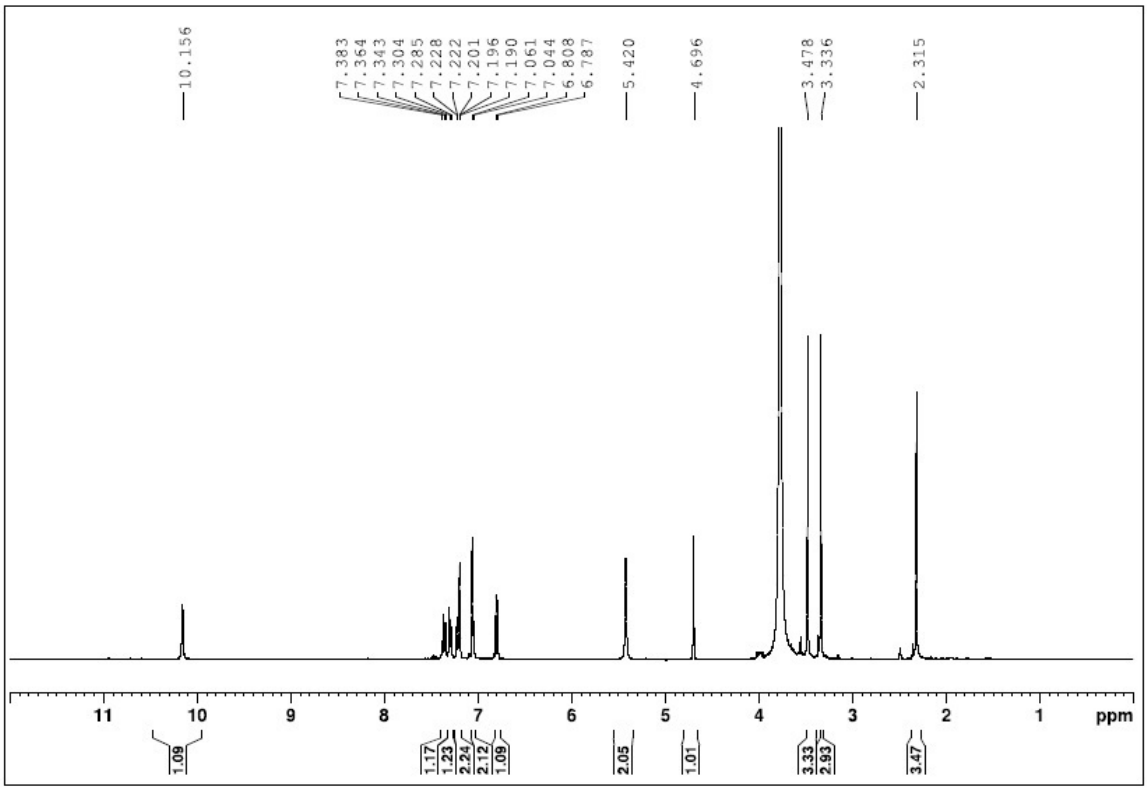
^{13}C NMR spectrum of compound **5e**



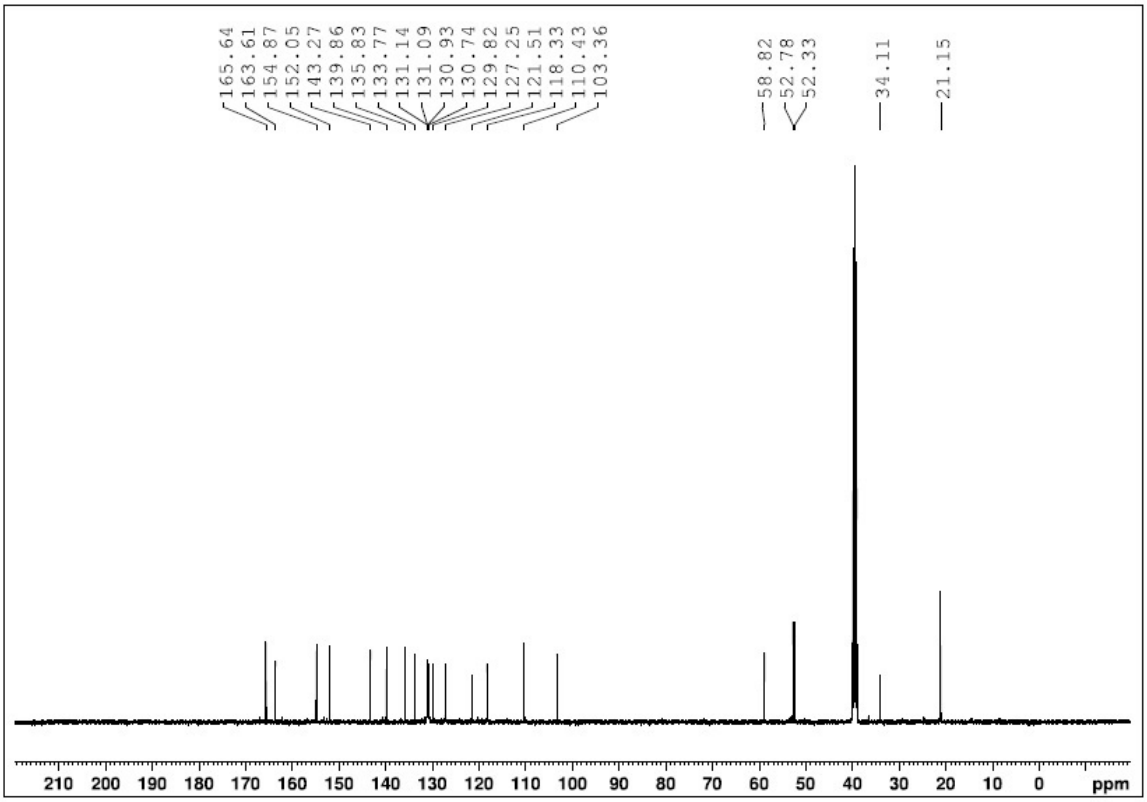
^{1}H NMR spectrum of compound **5f**



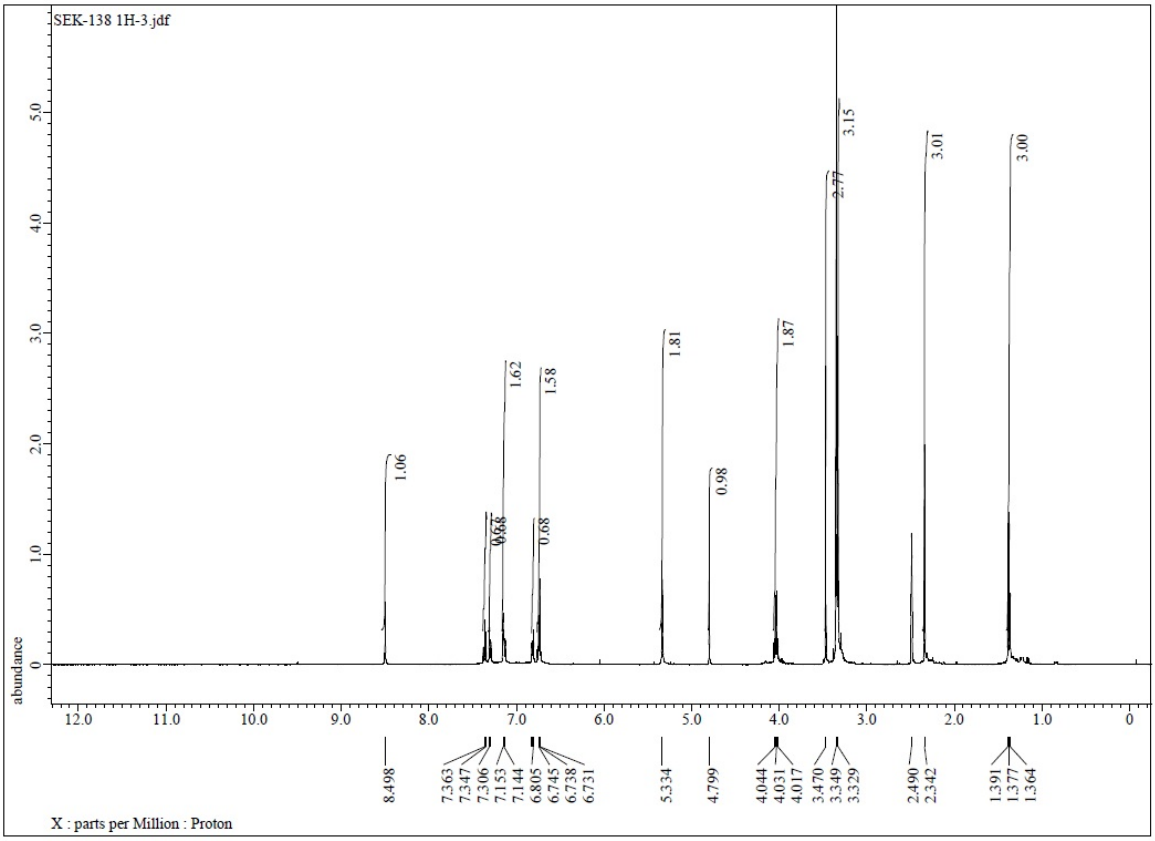
^{13}C NMR spectrum of compound **5f**



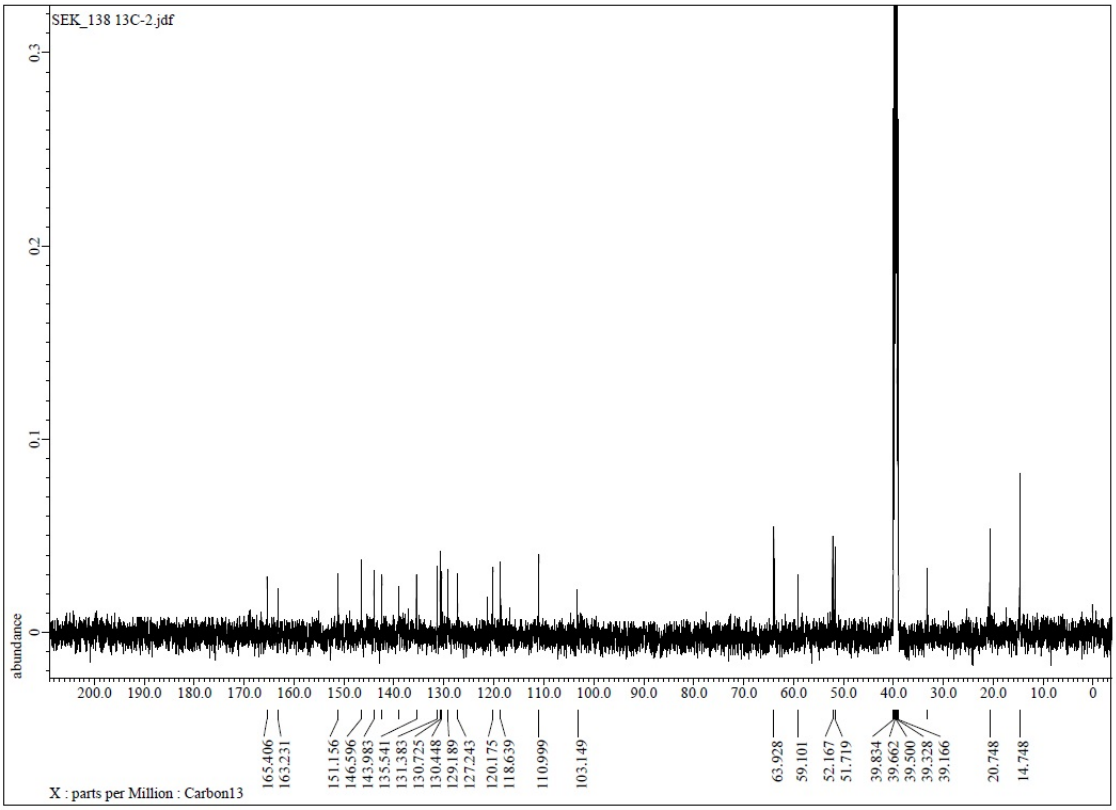
^{1}H NMR spectrum of compound **5g**



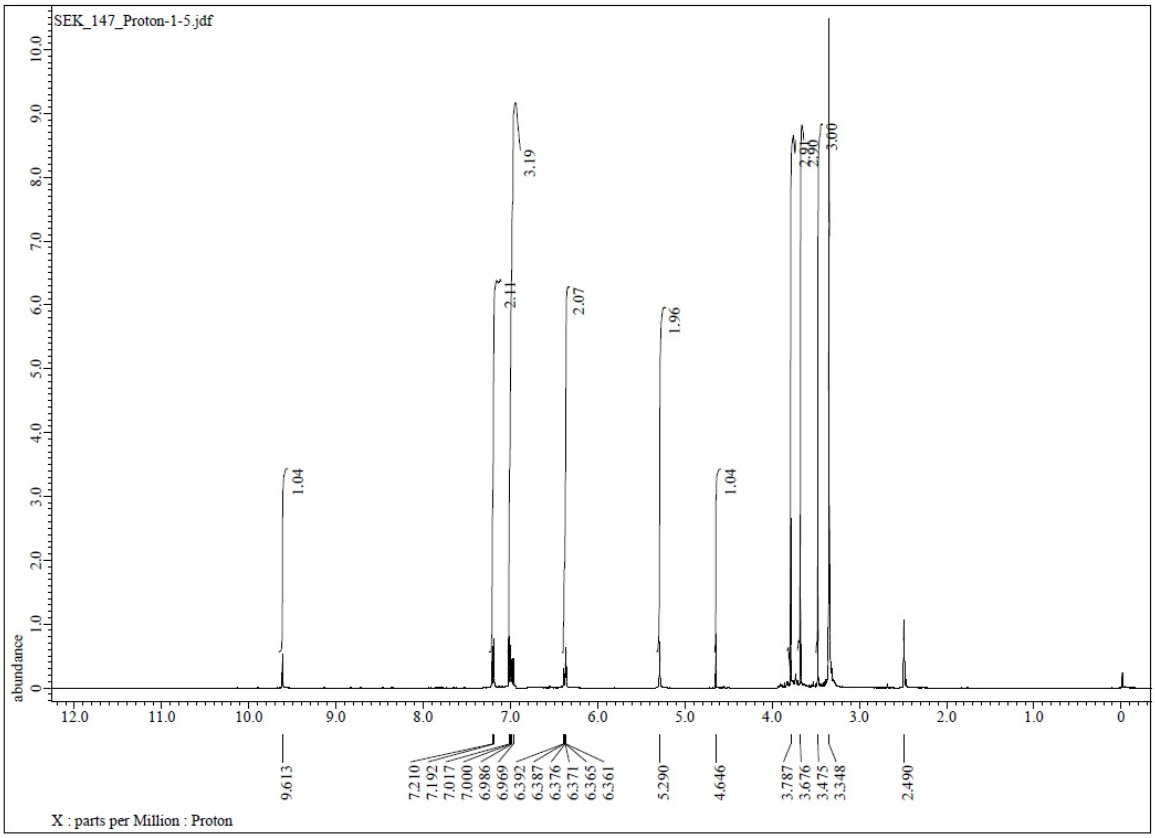
^{13}C NMR spectrum of compound **5g**



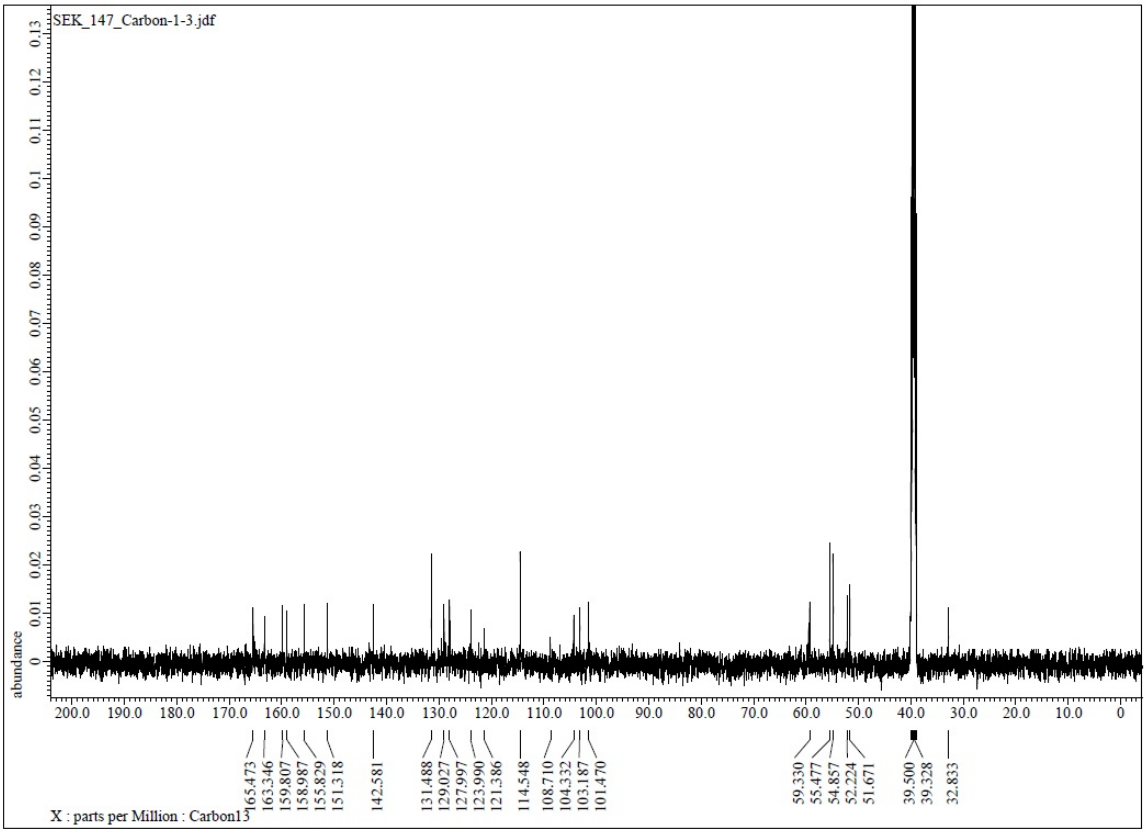
^{1}H NMR spectrum of compound **5h**



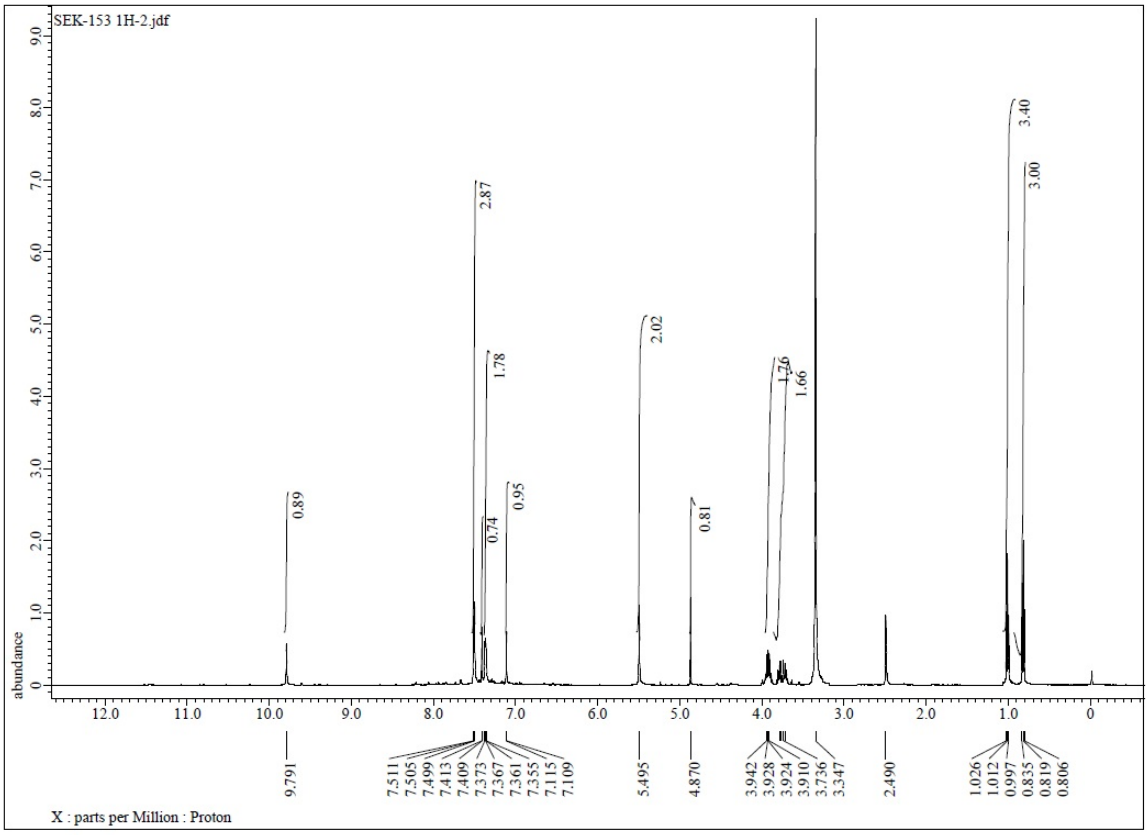
^{13}C NMR spectrum of compound **5h**



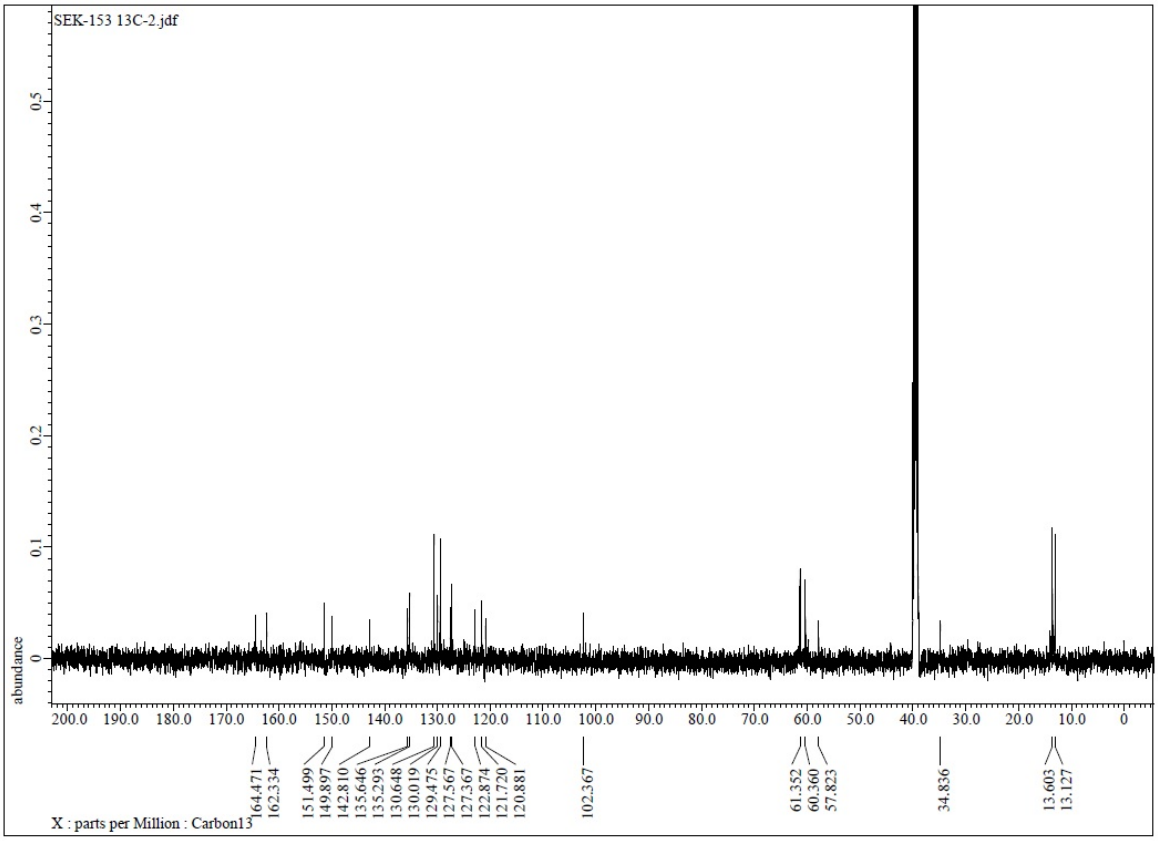
^{1}H NMR spectrum of compound **5i**



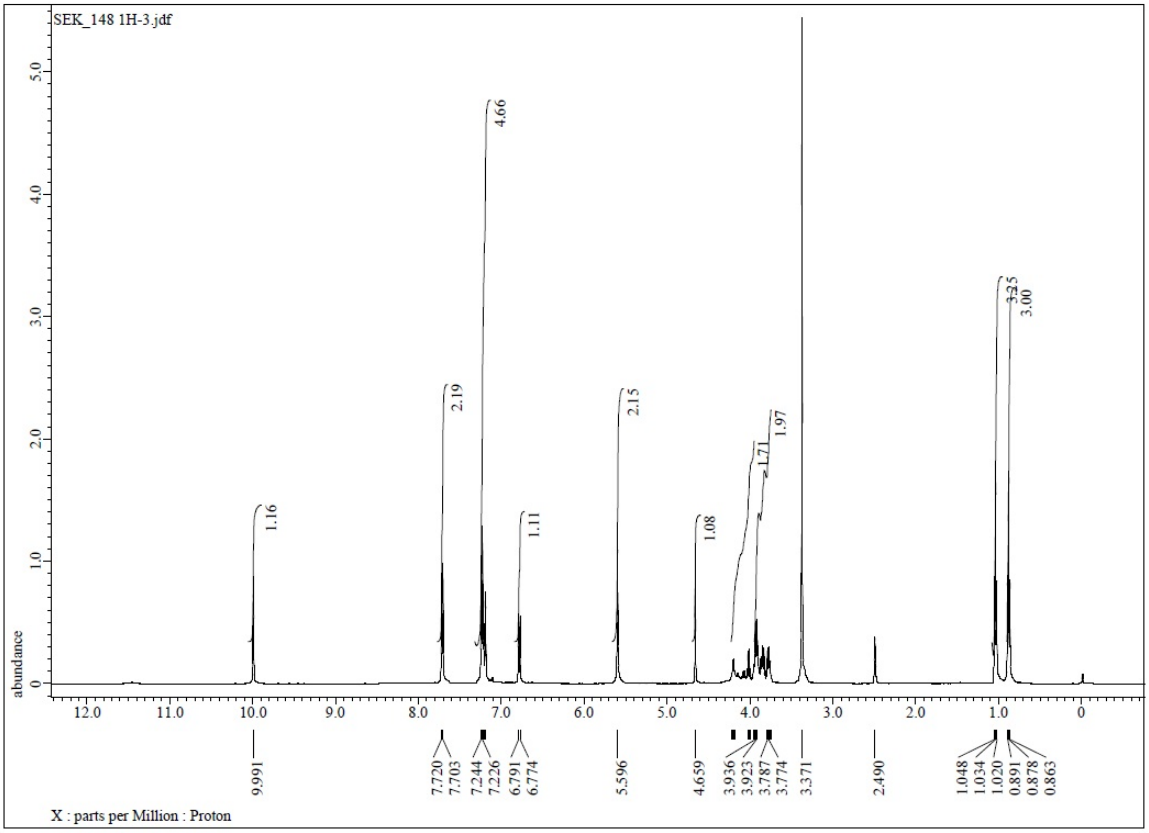
^{13}C NMR spectrum of compound **5i**



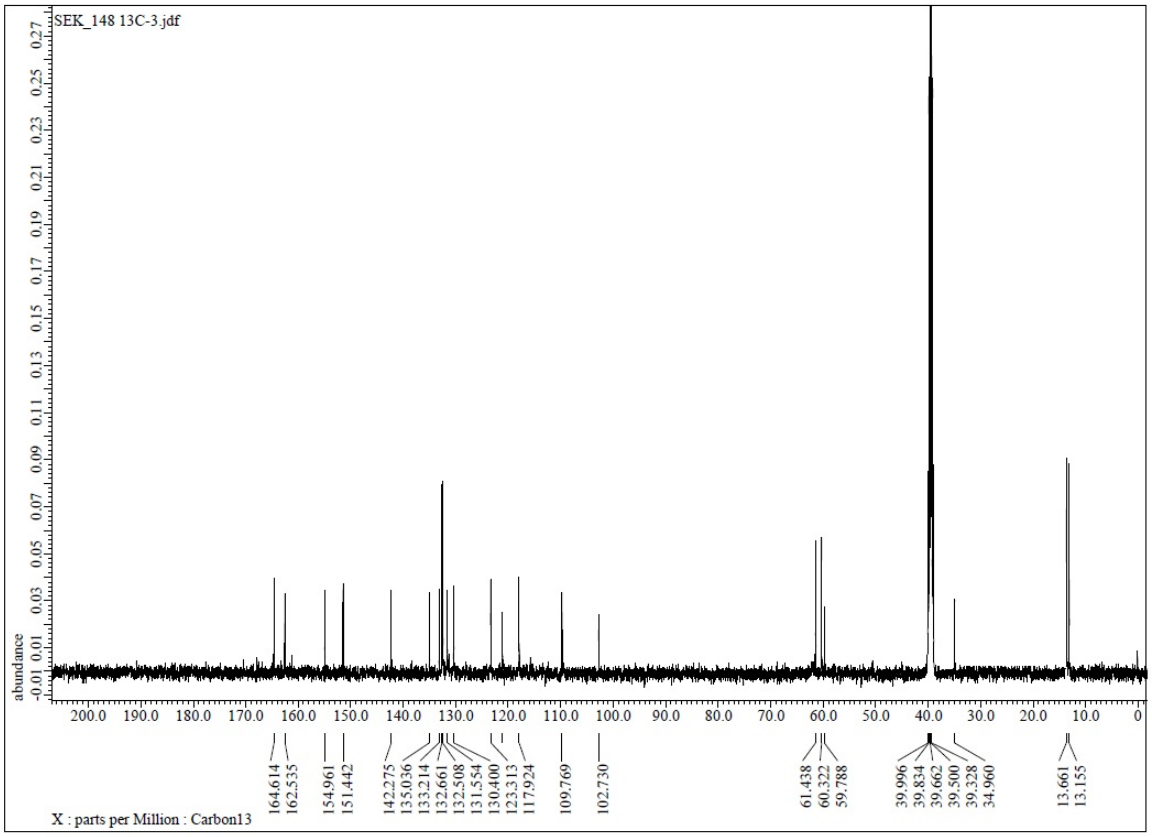
^{1}H NMR spectrum of compound **5j**



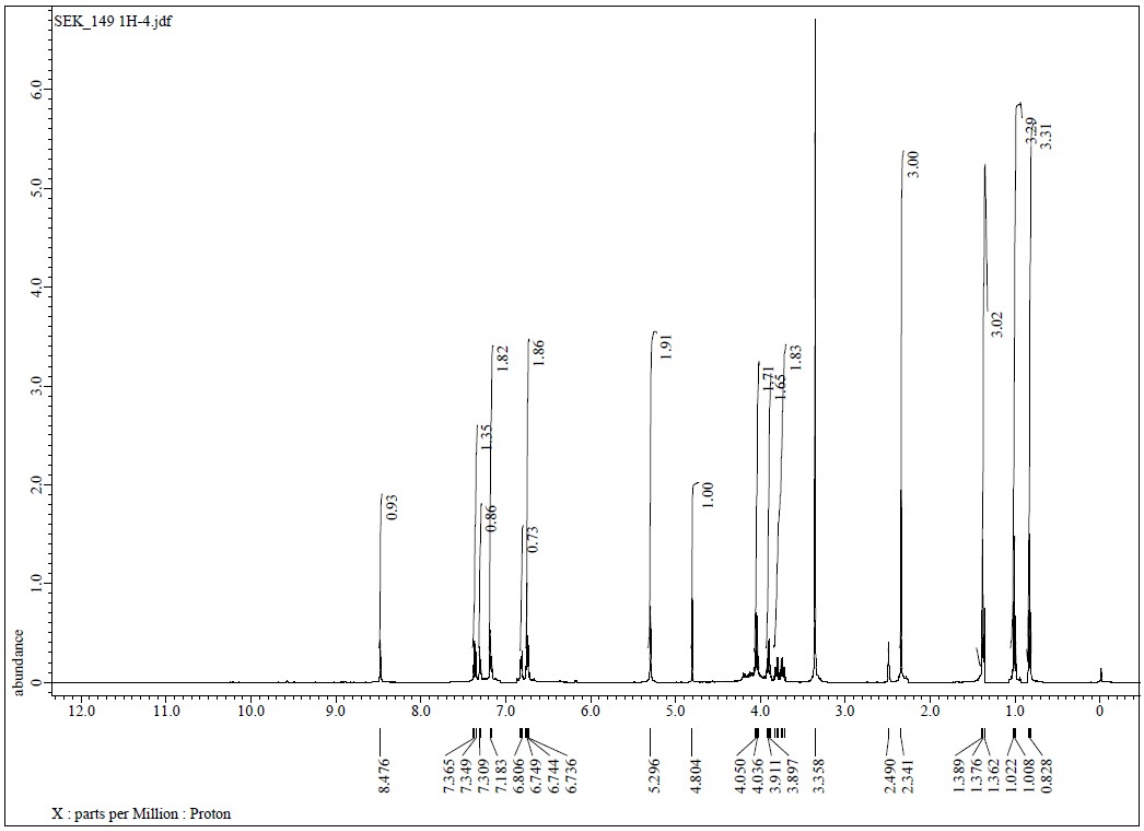
^{13}C NMR spectrum of compound **5j**



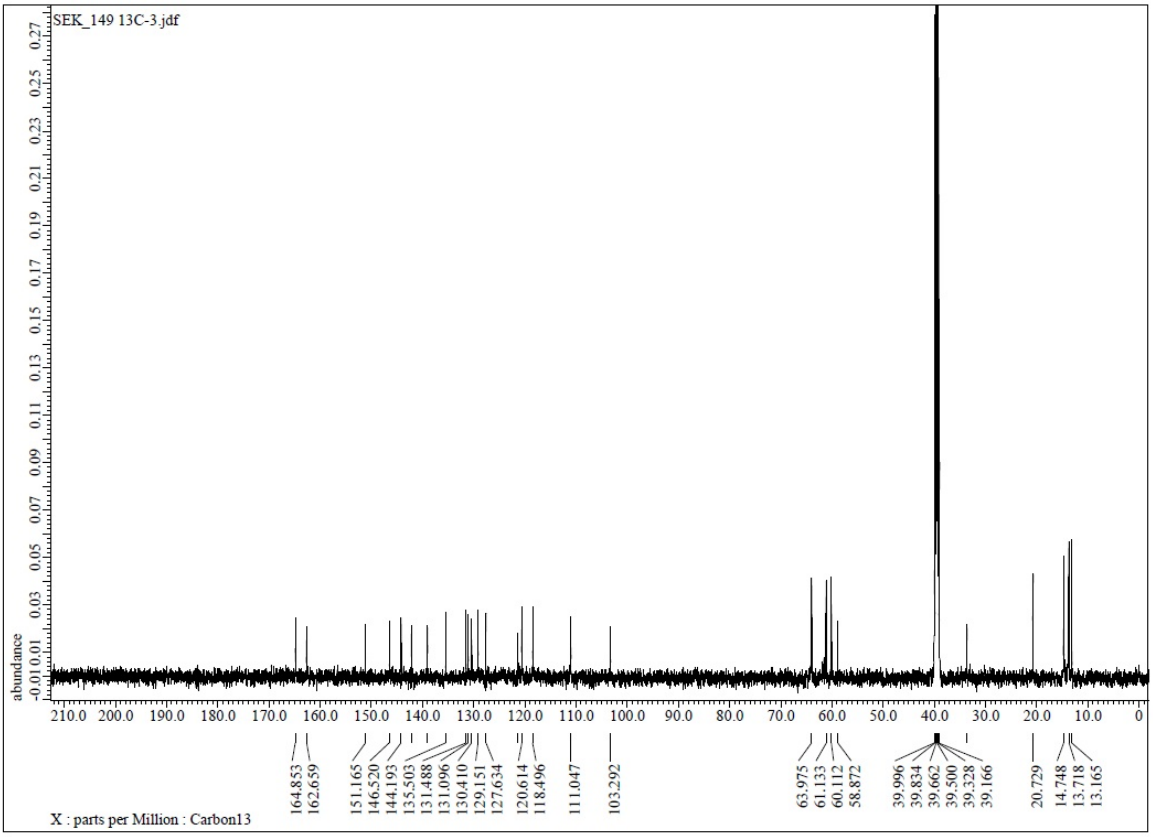
^{1}H NMR spectrum of compound **5k**



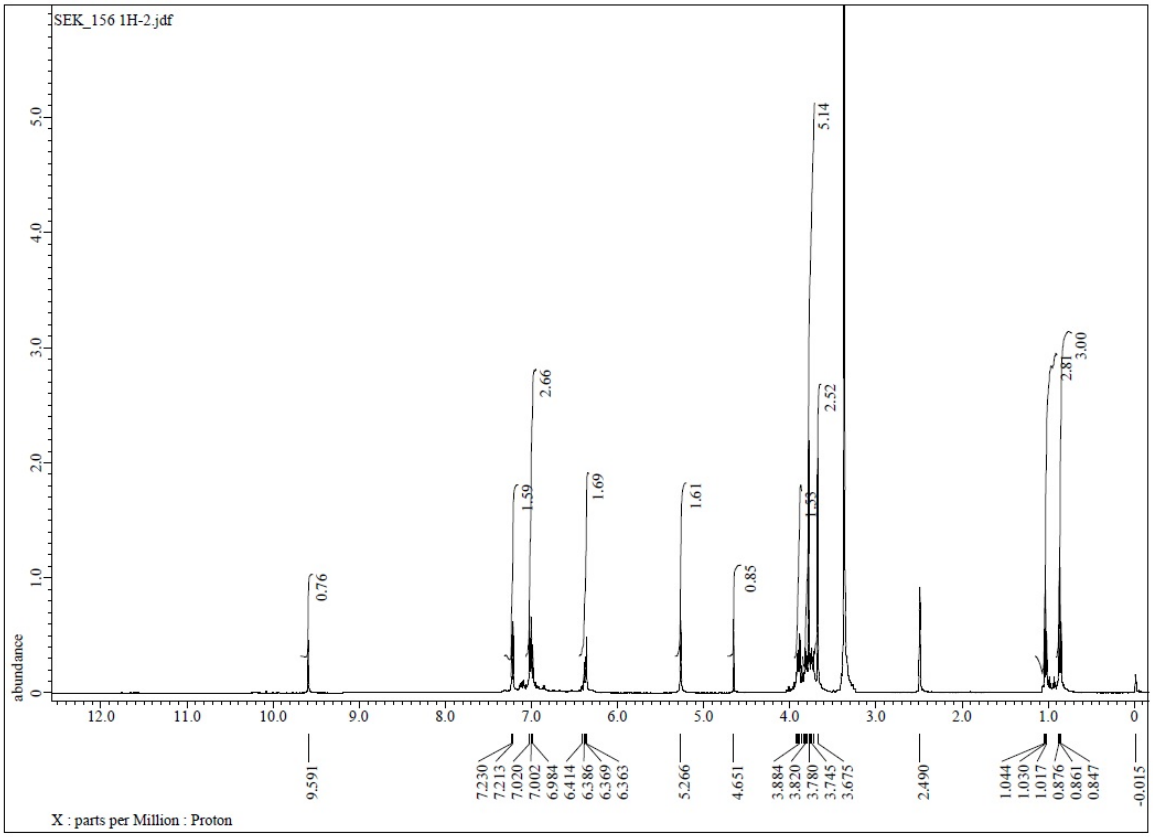
^{13}C NMR spectrum of compound **5k**



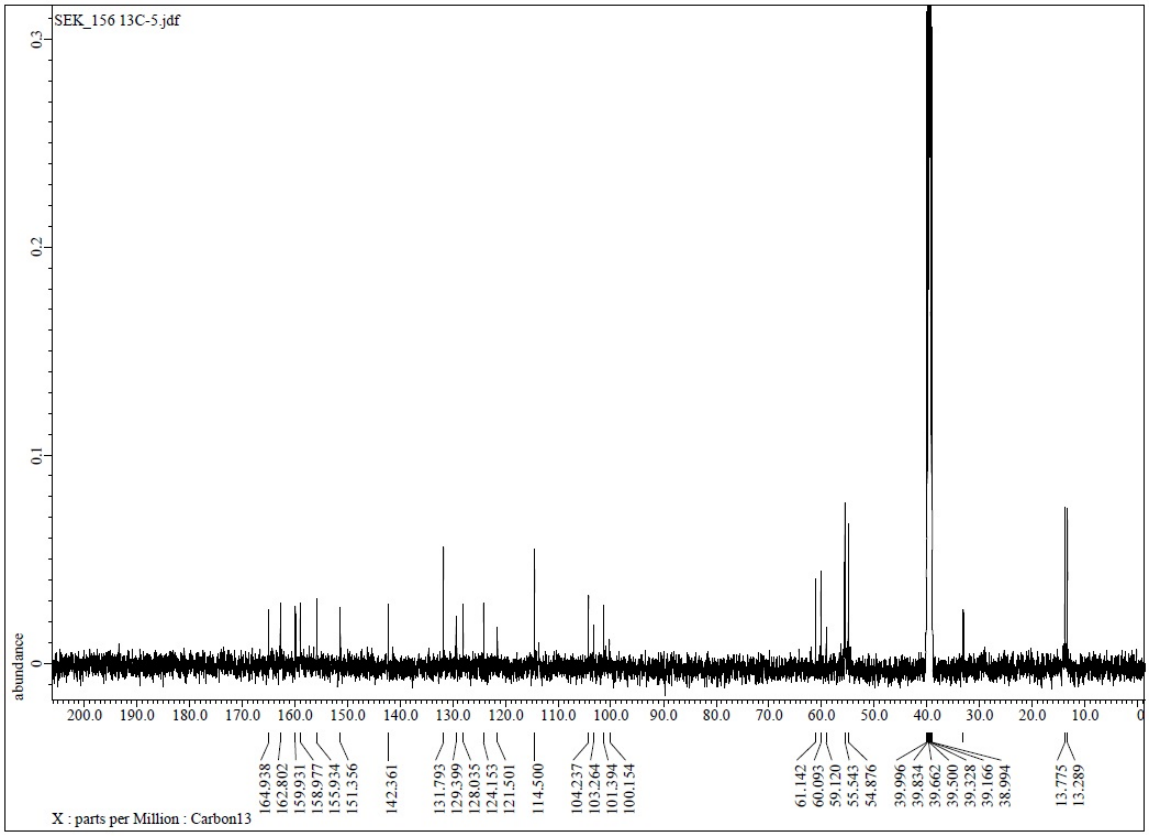
^{1}H NMR spectrum of compound **5l**



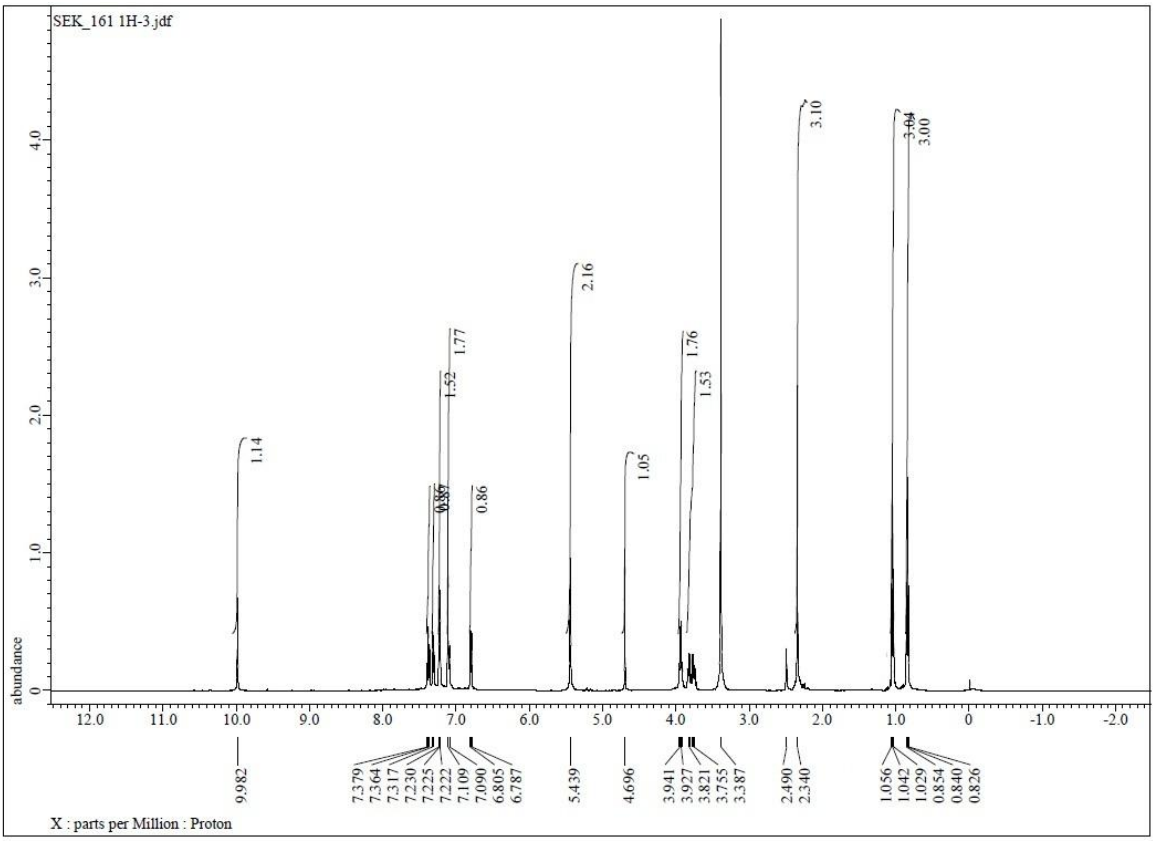
^{13}C NMR spectrum of compound **5l**



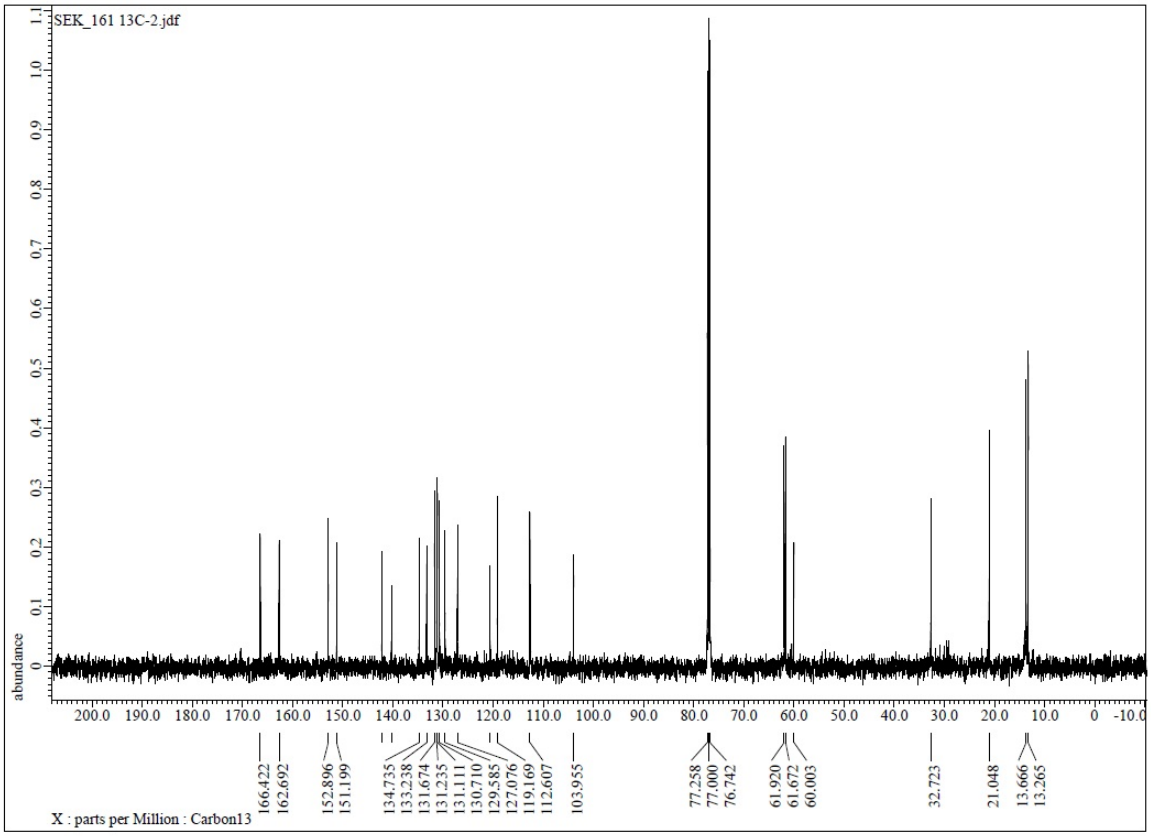
^{1}H NMR spectrum of compound **5m**



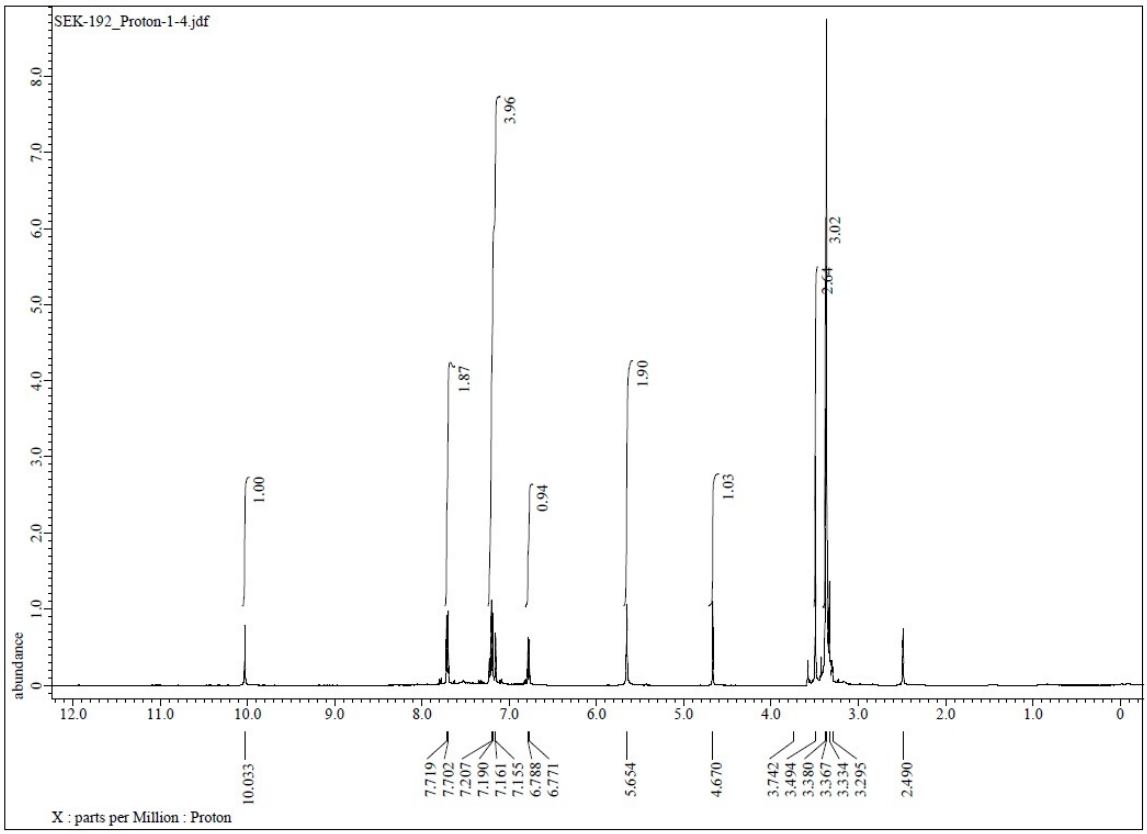
^{13}C NMR spectrum of compound **5m**



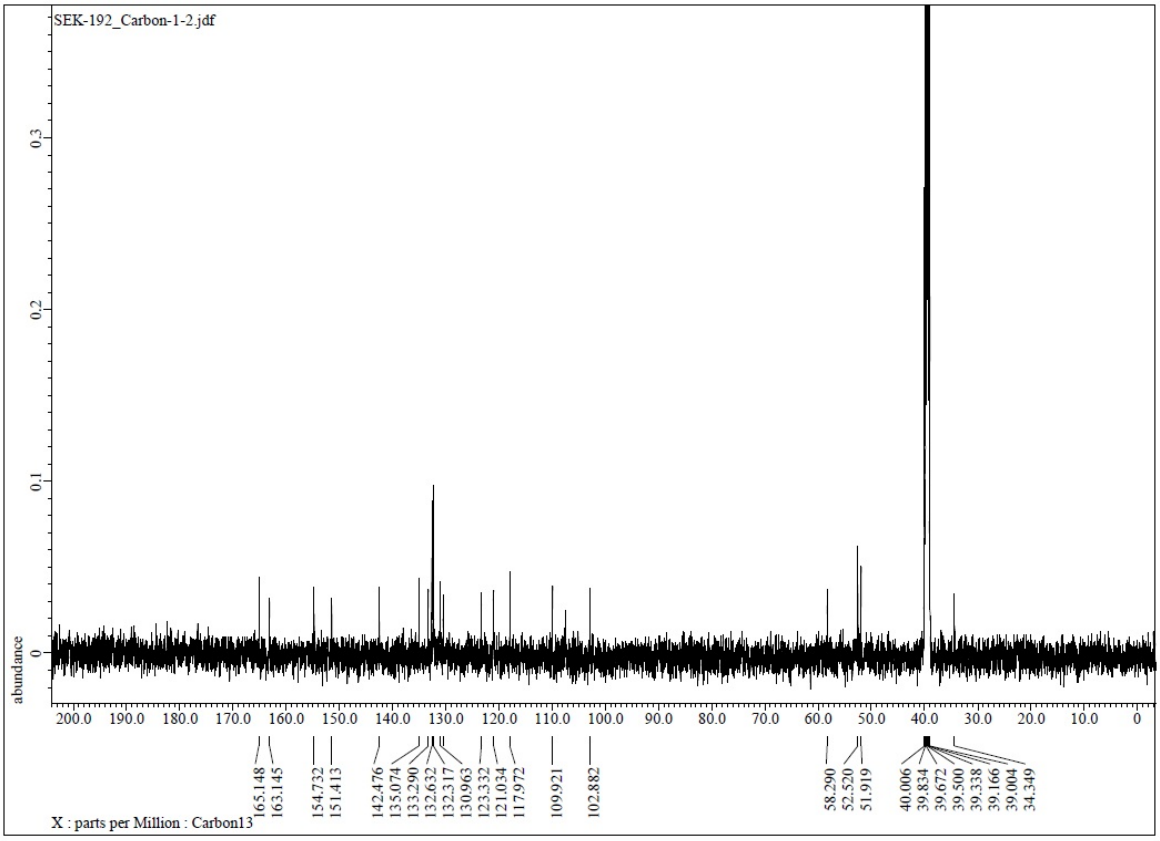
^{1}H NMR spectrum of compound **5n**



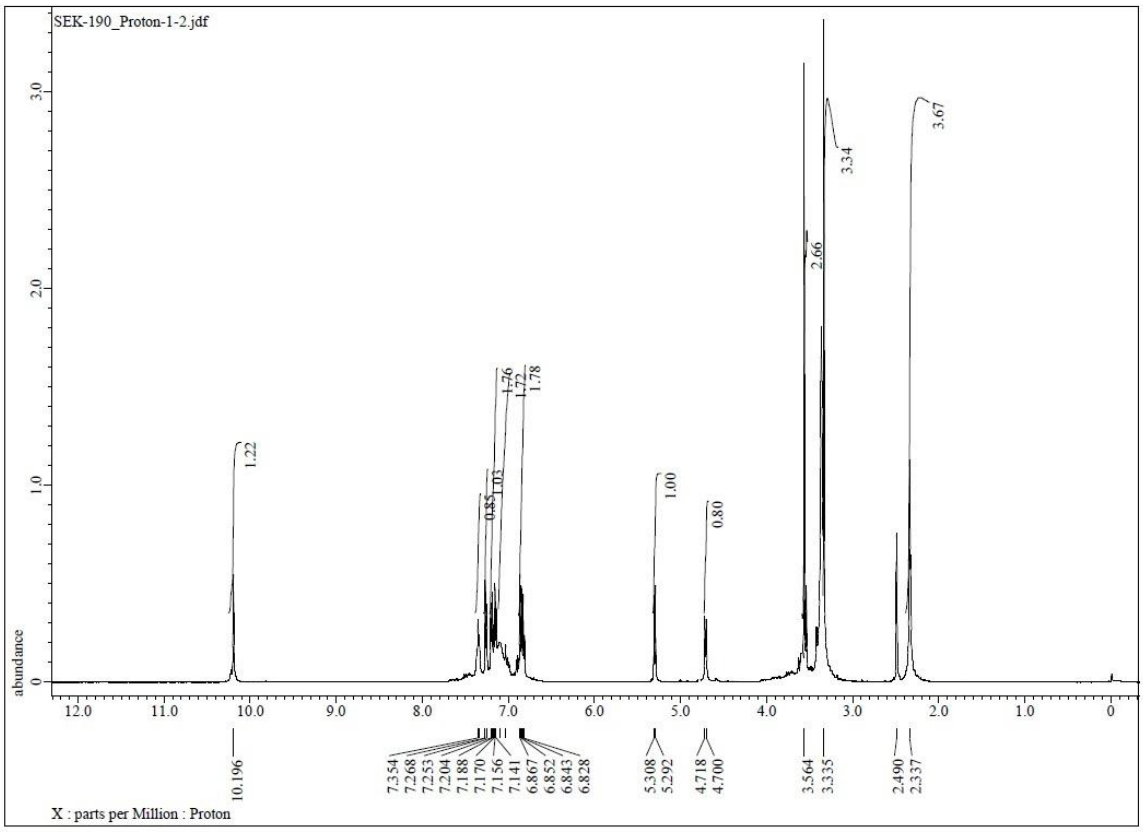
^{13}C NMR spectrum of compound **5n**



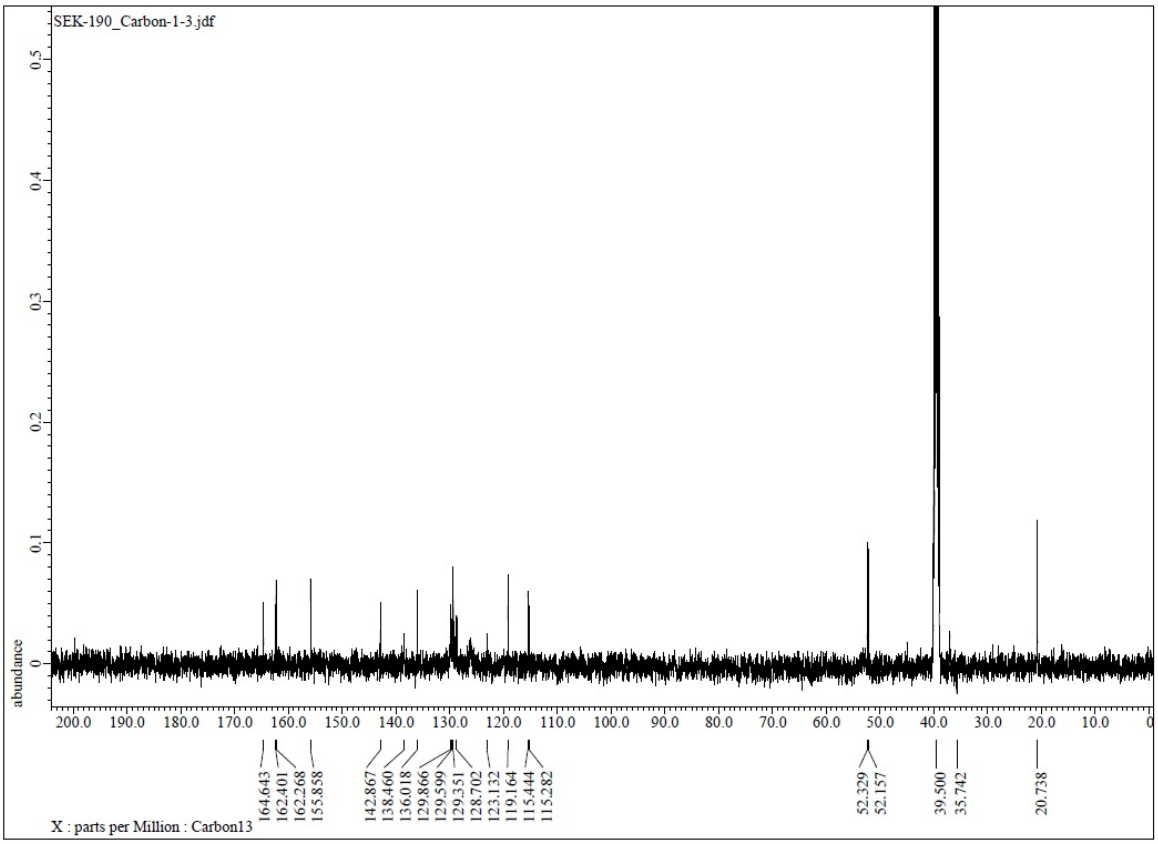
^{1}H NMR spectrum of compound **5o**



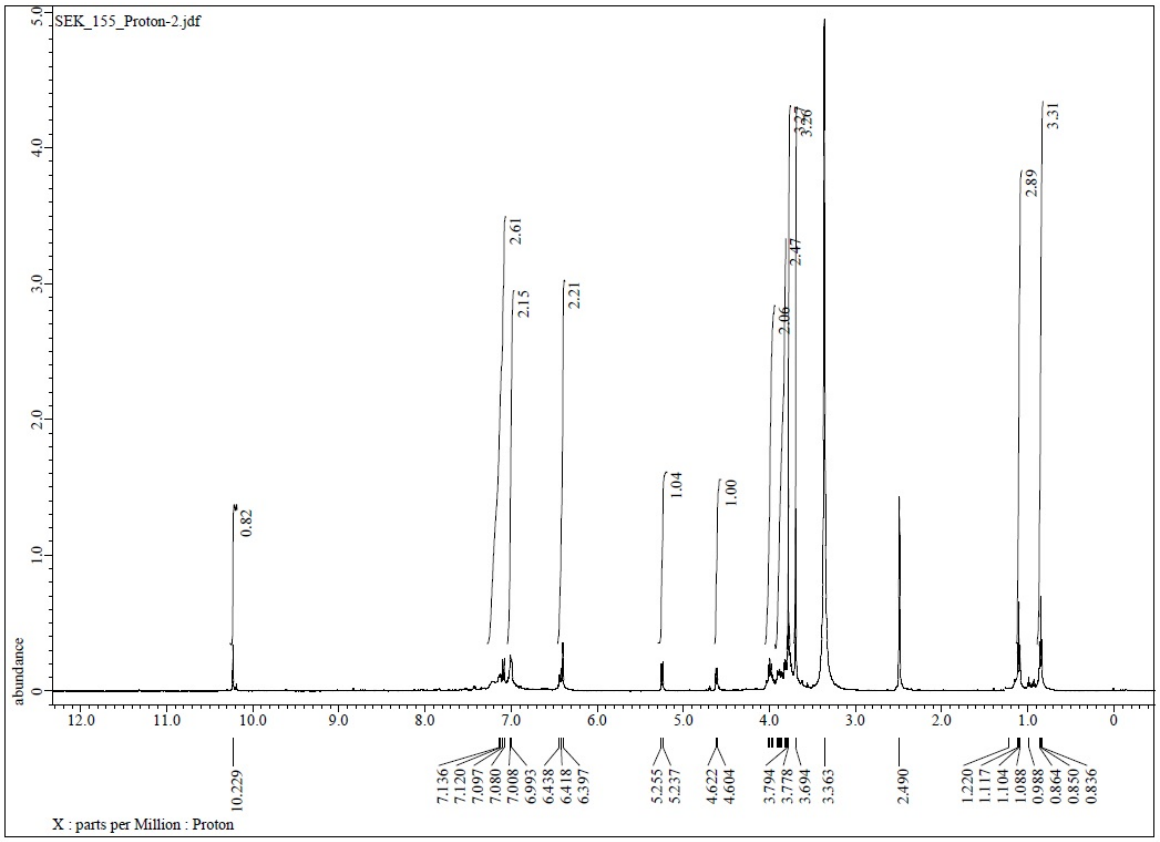
^{13}C NMR spectrum of compound **5o**



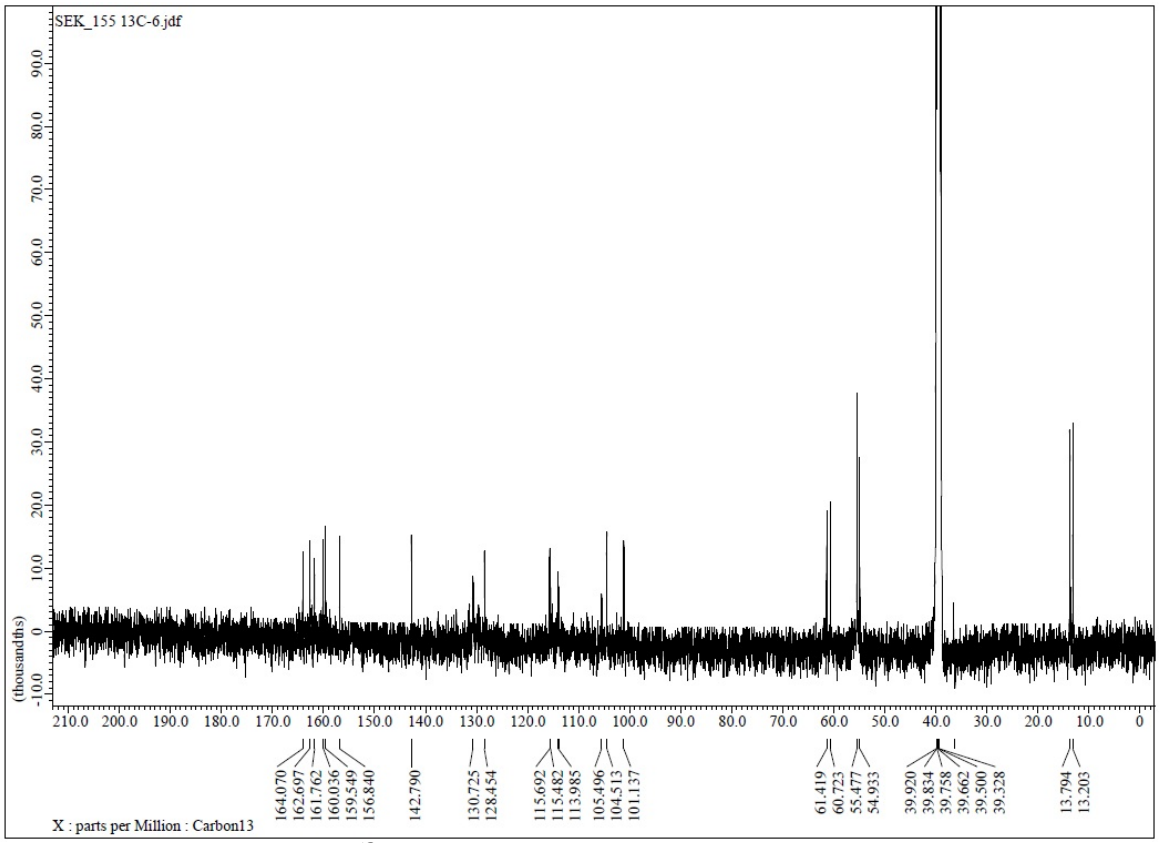
^{1}H NMR spectrum of compound **13a**



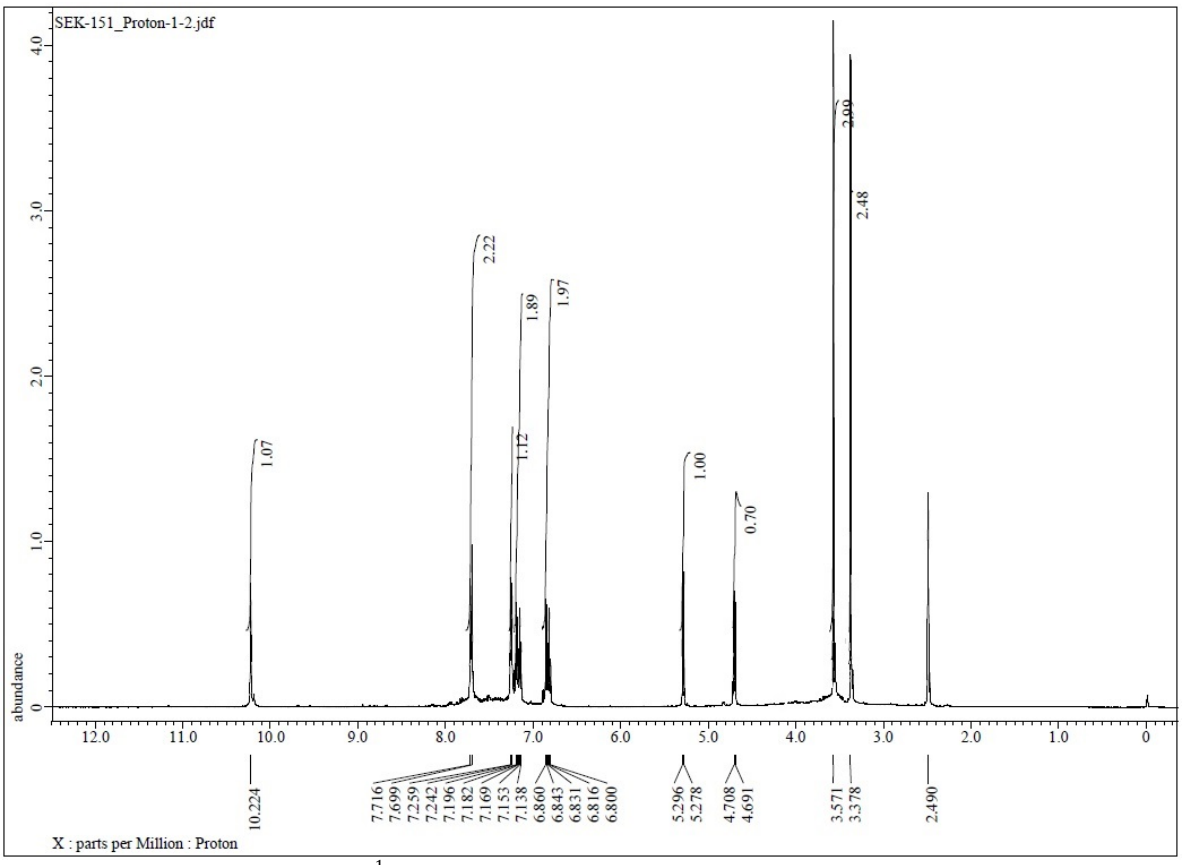
^{13}C NMR spectrum of compound **13a**



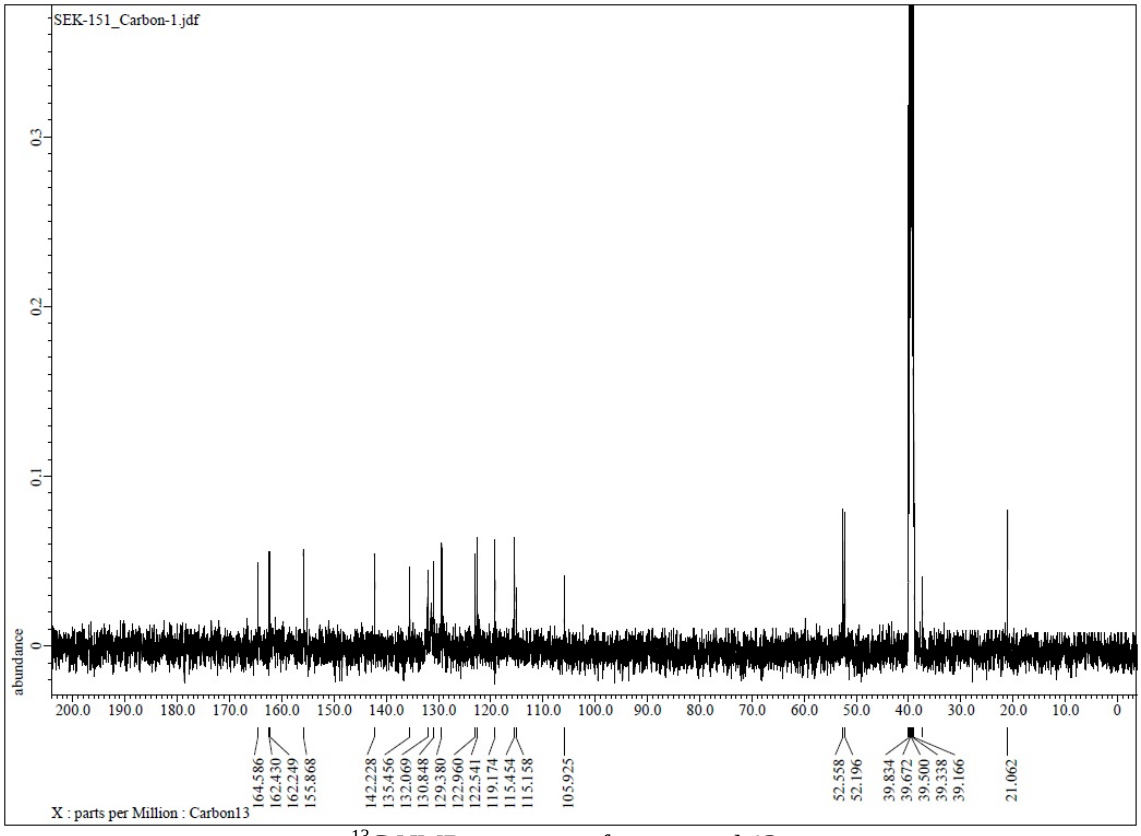
^{1}H NMR spectrum of compound **13b**



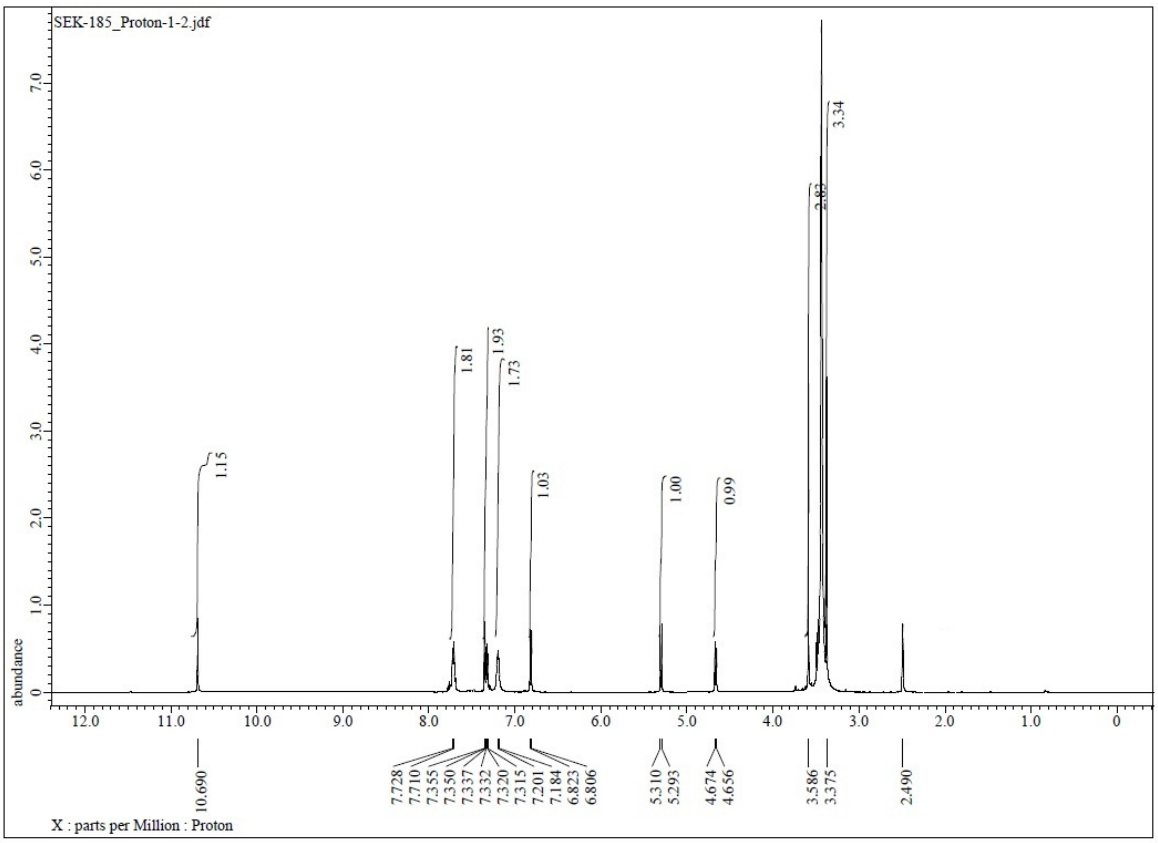
^{13}C NMR spectrum of compound **13b**



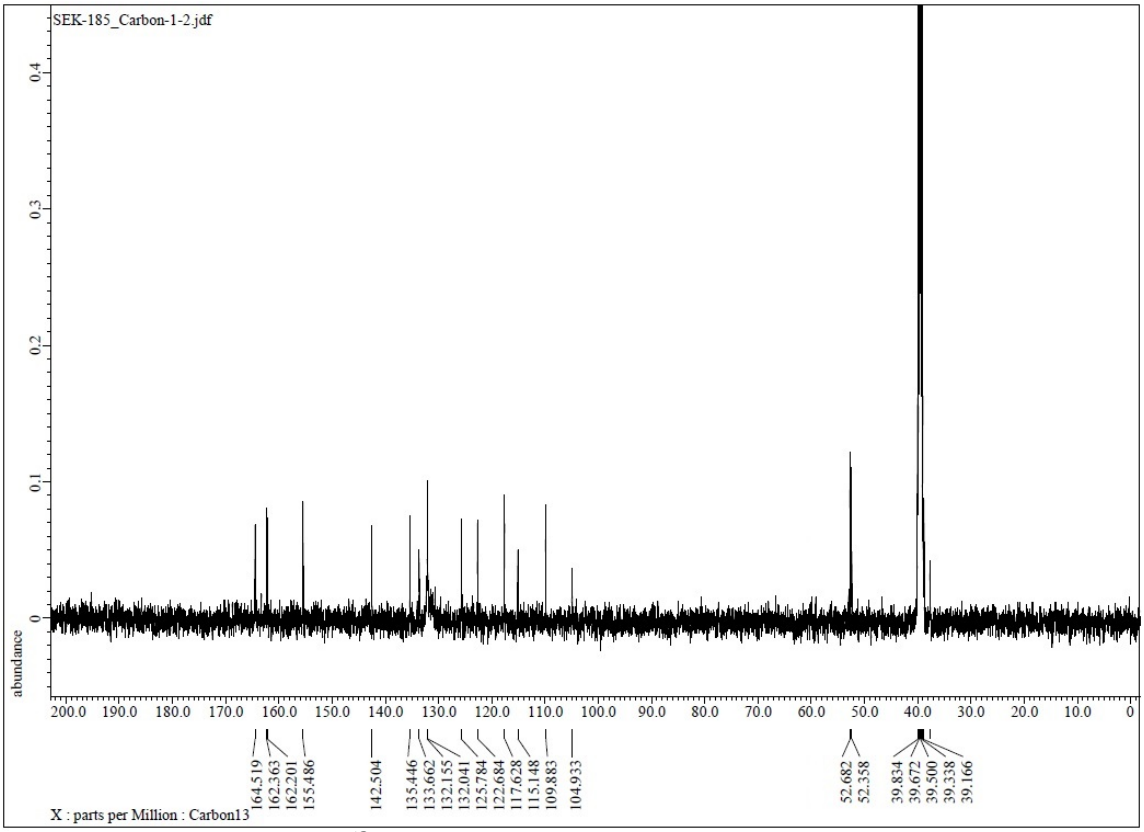
^{1}H NMR spectrum of compound **13c**



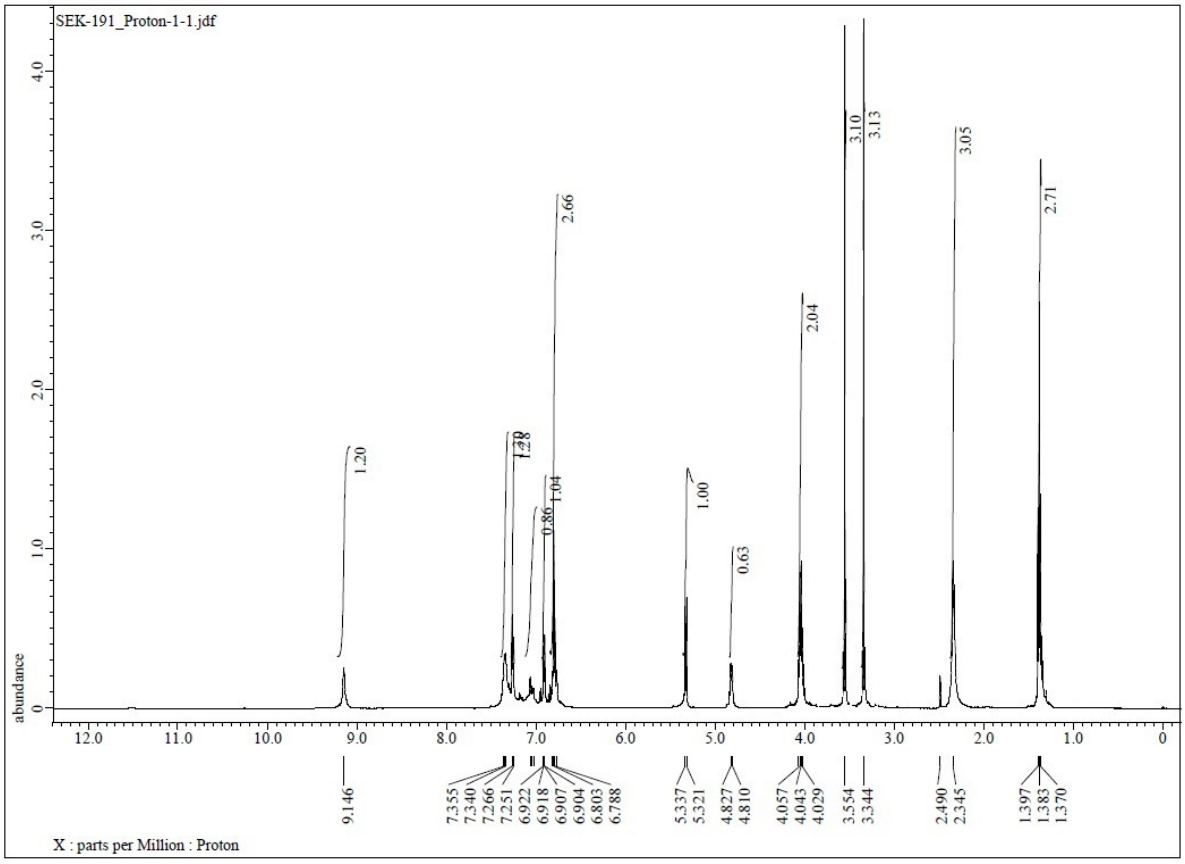
^{13}C NMR spectrum of compound **13c**



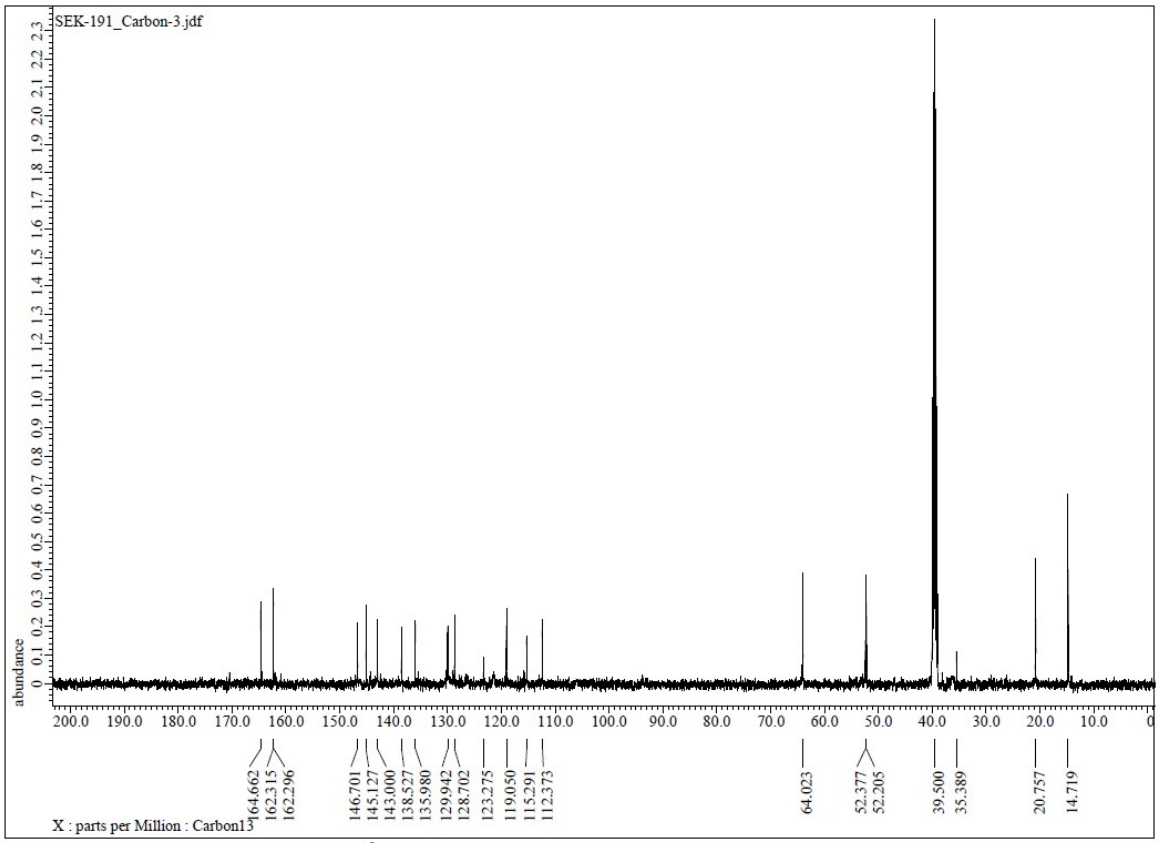
^{1}H NMR spectrum of compound **13d**



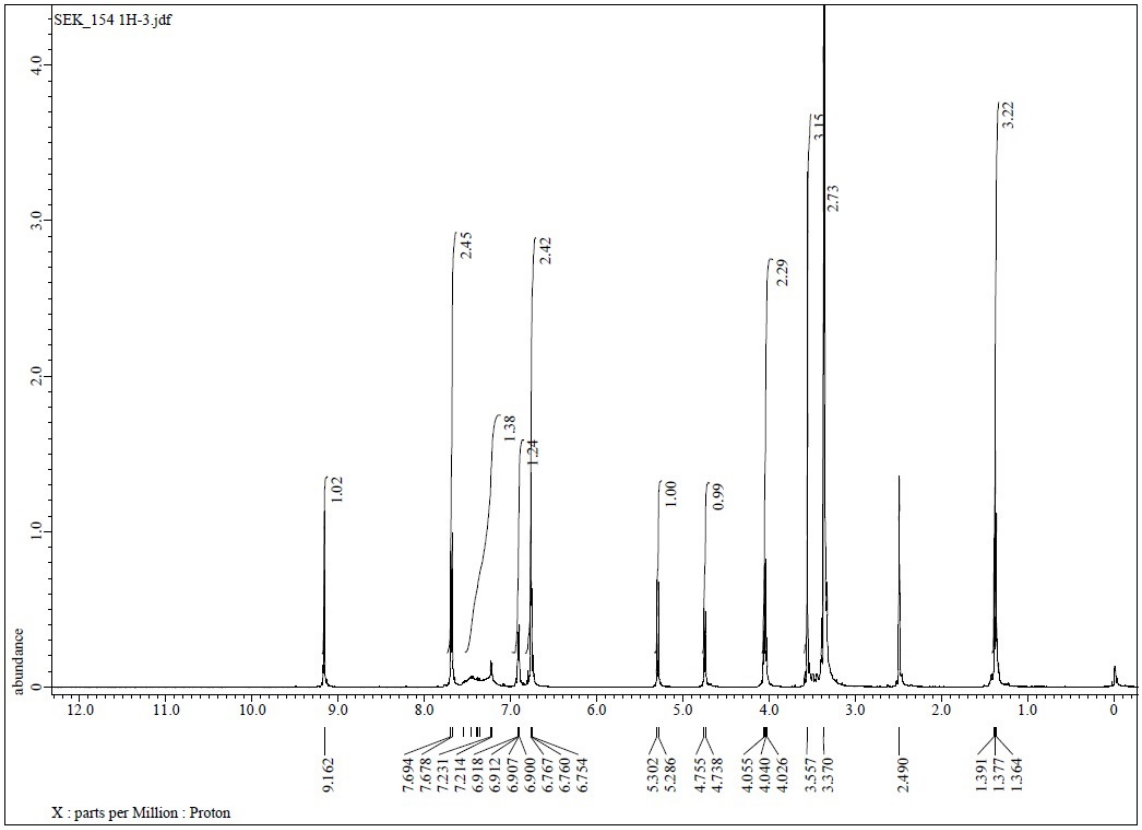
^{13}C NMR spectrum of compound **13d**



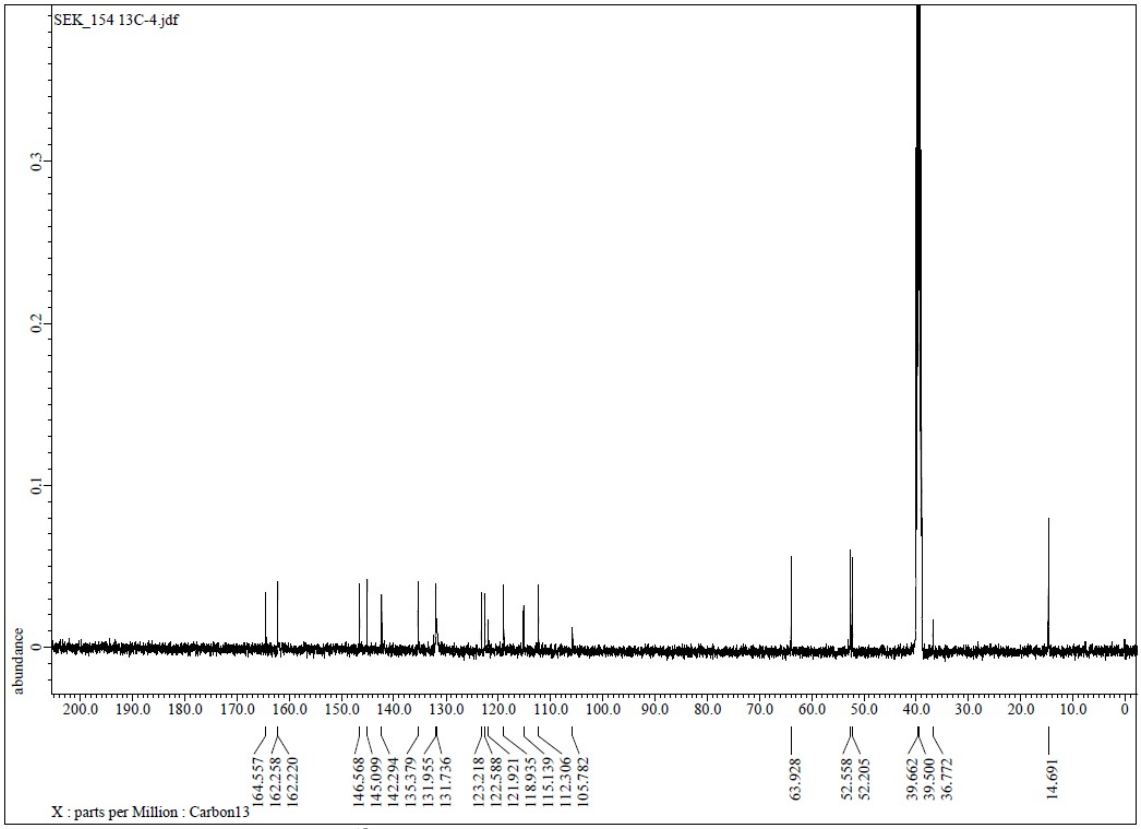
^{1}H NMR spectrum of compound **13e**



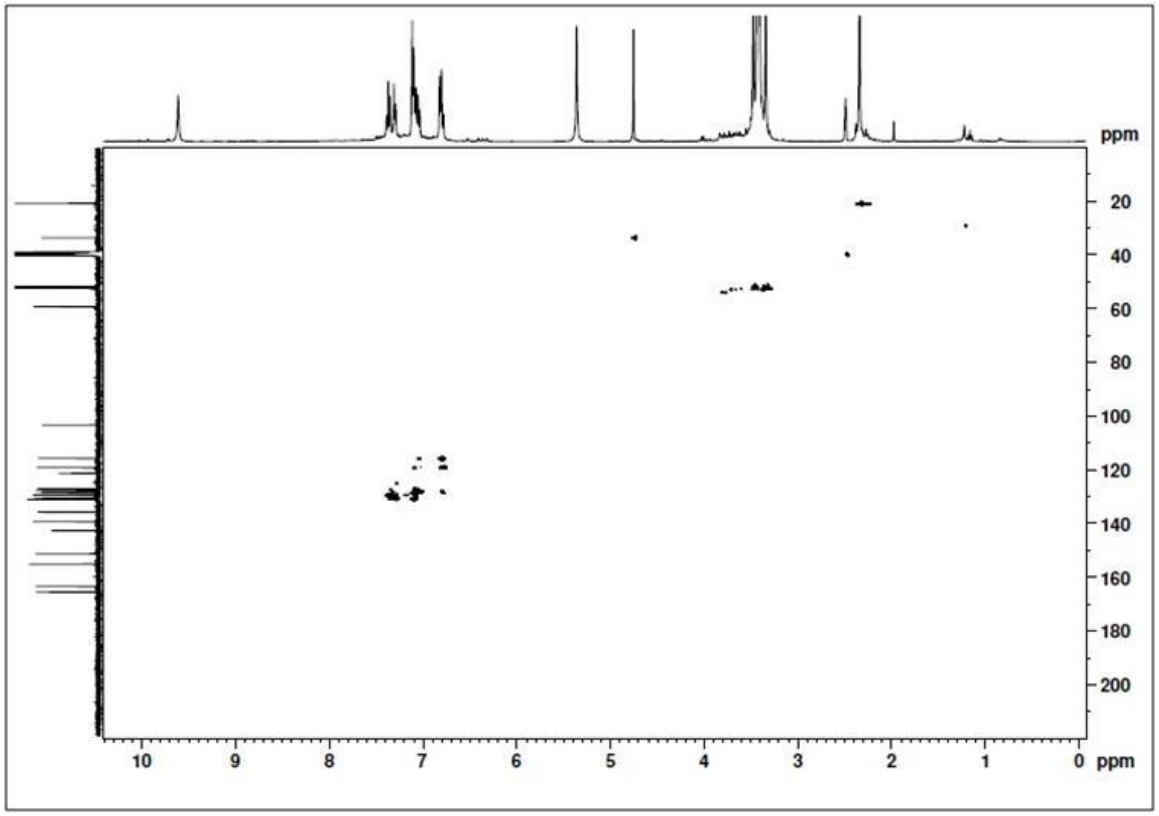
^{13}C NMR spectrum of compound **13e**



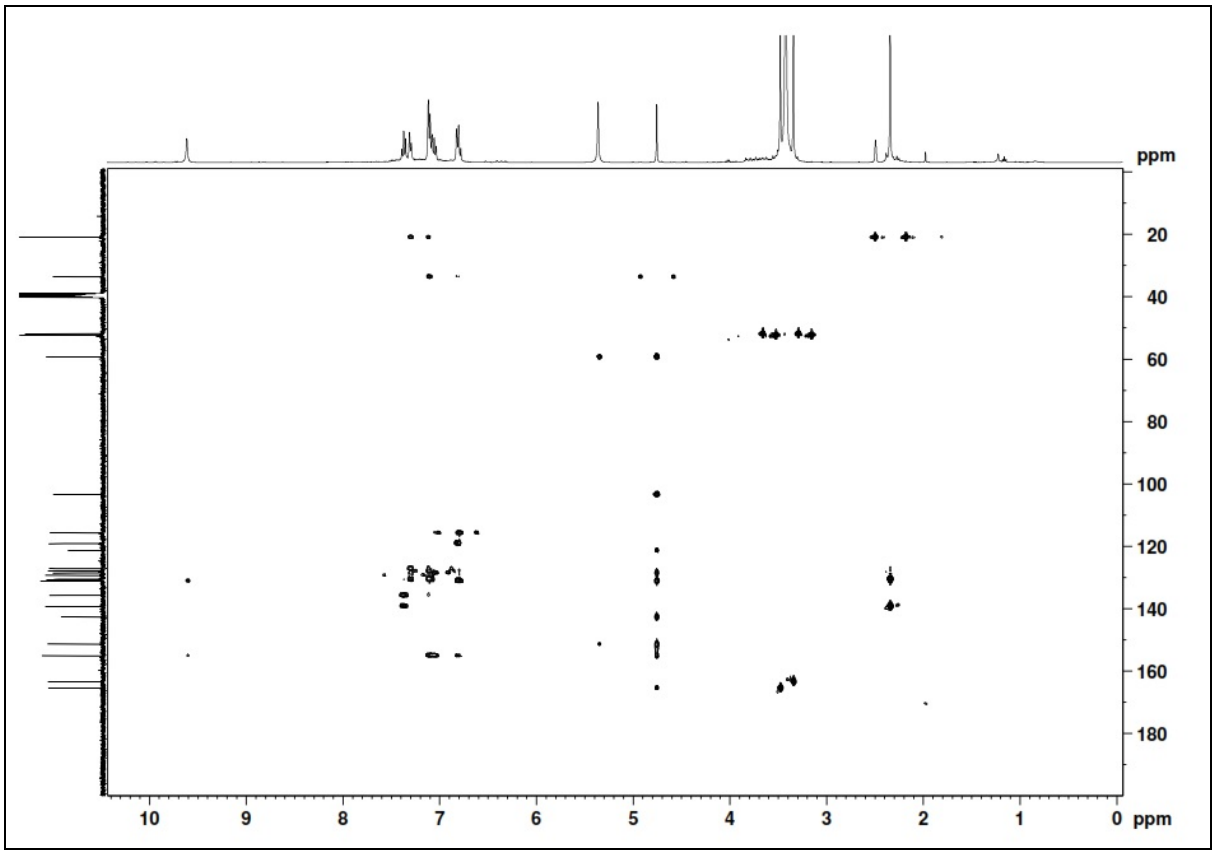
^{1}H NMR spectrum of compound **13f**



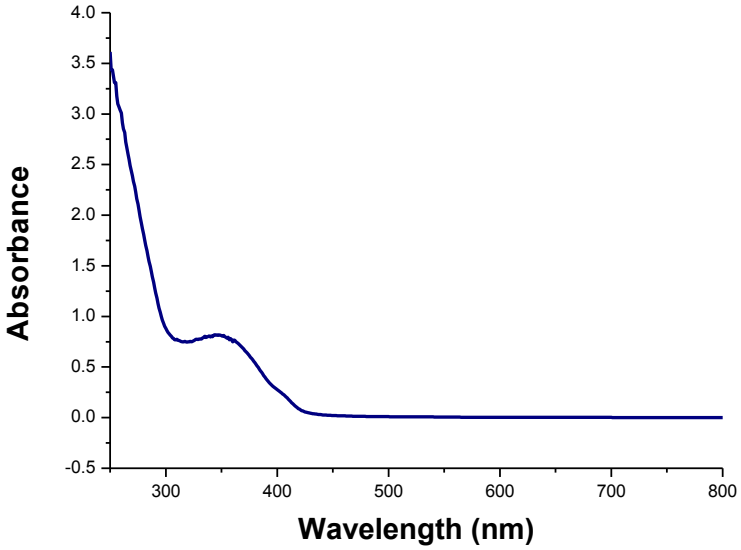
^{13}C NMR spectrum of compound **13f**



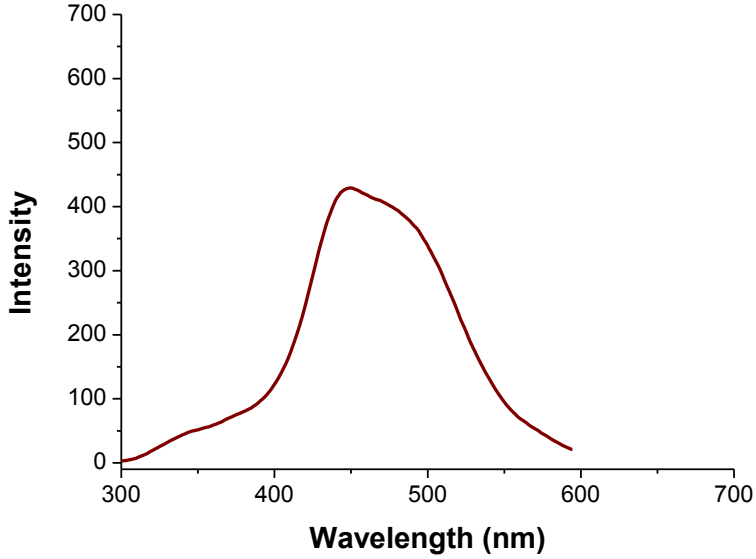
HSQC spectrum of **5a**



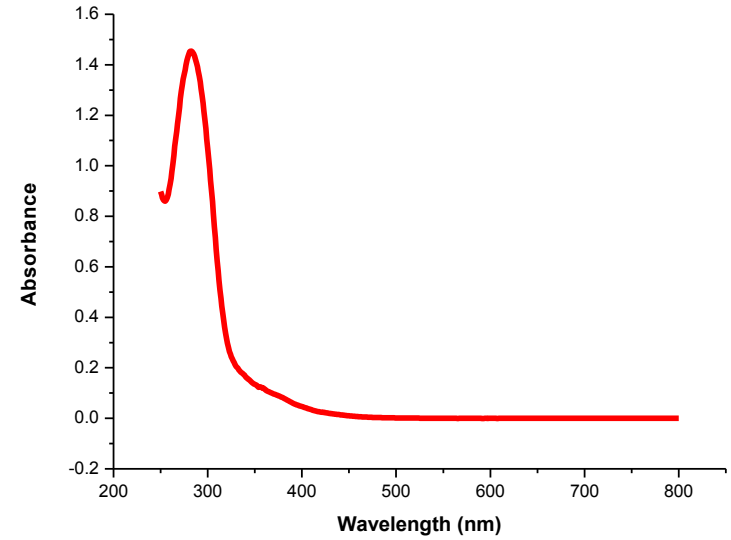
HMBC spectrum of **5a**



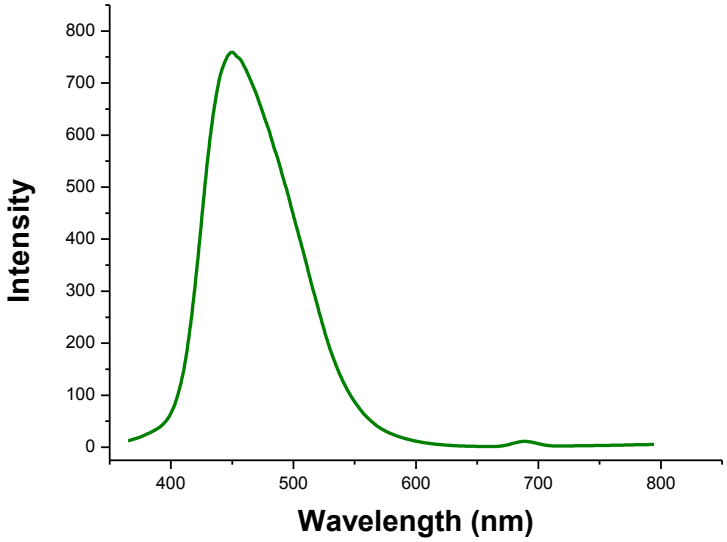
UV absorption spectrum of compound **5a**



Emission spectrum of Compound **5a**

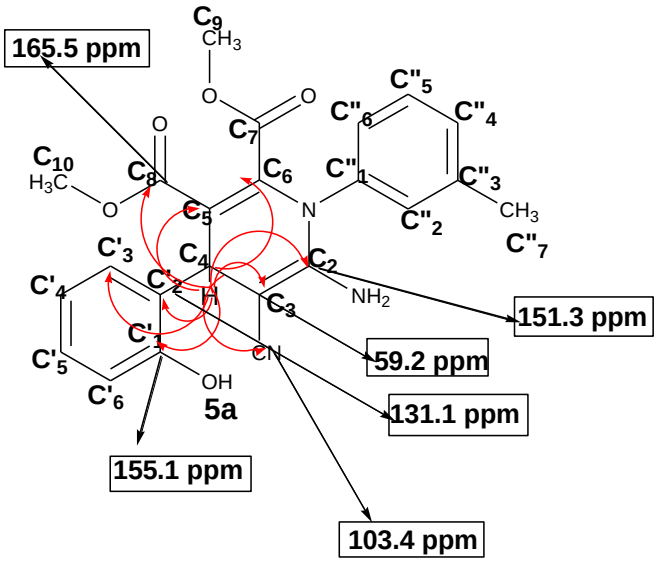


UV absorption spectrum of Compound **13a**



Emission Spectrum of Compound **13a**

Correlation shown for H4 proton appearing at δ 4.75



Correlation shown for proton appearing at δ 9.61