An Efficient Aldol-Type Direct Reaction of Isatin with $TMSCH_2CN$

V. U. Bhaskara Rao, Krishna Kumar, Ravi P. Singh*

Division of Organic Chemistry,
Indian Institute of Technology,
Hauz-Khas, New Delhi, India – 110016

Supporting Information

All the reactions were performed under dry nitrogen. Cesium fluoride was purchased from Sigma Aldrich and used directly. The Bruker AV-300 instrument (300 MHz and 75 MHz, respectively) was used to record ^1H and ^{13}C NMR spectra in deuterated solvents with residual protonated solvent signals as internal reference.^1H NMR's data is reported as follows: chemical shift (δ, ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), integration, coupling constant (Hz). ^{13}C NMR's data is recorded in terms of chemical shift (δ, ppm). Perkin Elmer FT-IR Spectrometer was used to record infrared spectra and are reported in frequency of absorption. MS-TOF mass spectrometer and ESI mass spectrometer were used to record low resolution and high resolution mass spectra. Column chromatographic separations were carried out on silica gel (100–200 mesh).

Materials: 2-trimethylsilylacetonitrile **2** was purchased from Sigma-aldrich and used without further purification. N-protected Isatins **1A-S** were prepared according to known literature procedures.[1]

General procedure for Cyanomethylation of isatin: To a solution of CsF (20 mol%) in dimethyl formamide (1 ml) was added ketone **1** (0.2 mmol) and trimethylsilyl acetonitrile (0.3 mmol) at 0 ^{o}C under N_2 atmosphere. The resulting mixture was warmed at room temperature and stirred for next 48 h. The progress of the reaction was monitored by TLC (thin layer chromatography). Once the reaction was completed, it was quenched by addition of methanol and 1M HCl (1.0 mL) solution. The resulting mixture was extracted with ethyl acetate (5 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide an oily residue that was purified by flash chromatography on silica gel (eluent: EtOAc/Petroleum ether = 1/3, v/v).

2-(3-hydroxy-2-oxoindolin-3-yl)acetonitrile (3a): white solid (8.6 mg, yield = 23%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.92 (d, *J* = 16.51 Hz, 1H), 3.02 (d, *J* = 16.51 Hz, 1H), 6.58 (s, 1H), 6.85 (d, *J* = 7.52 Hz, 1H), 7.01 (t, *J* = 7.52 Hz, 1H), 7.26 (t, *J* = 7.52 Hz, 1H), 7.44 (d, *J* = 7.34 Hz, 1H), 10.53 (s, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.12, 72.02, 110.07, 117.08, 122.00, 124.15, 129.78, 130.02, 141.59, 176.70; FTIR (KBr) cm^{-1}, 3425, 2361, 1655, 1001, 765. HRMS ESI: [M+Na]+, Calcd for $C_{10}H_8O_2N_2Na$ 211.0477 ; found 211.0496.

2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetonitrile (3b): white solid (13 mg, yield = 32%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3);^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.70 (d, *J* = 16.51 Hz, 1H), 3.05 (d, *J* = 16.51 Hz, 1H), 3.24 (s, 3H), 6.91 (d, *J* = 7.34 Hz, 1H), 7.17 (t, *J* = 7.15 Hz, 1H), 7.41 (t, *J* = 7.15 Hz, 1H), 7.66 (d, *J* = 6.79 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 26.57, 27.47, 72.58, 109.13, 115.27, 123.99, 124.28, 127.48, 131.02, 142.86, 175.32; FTIR (KBr) cm^{-1}, 3422, 2316, 1655, 1001, 824, 765. HRMS ESI: [M+Na]+, Calcd for $C_{11}H_{10}O_2N_2Na$ 225.0634; found 225.0639.

2-(1-benzyl-3-hydroxy-2-oxoindolin-3-yl)acetonitrile (3c): white solid (39 mg, yield = 71%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3);^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.71 (d, *J* = 16.20 Hz, 1H), 3.03 (d, *J* = 16.01 Hz, 1H), 4.74 (d, *J* = 14.13 Hz, 1H), 4.88 (d, *J* = 14.88, 1H), 6.71 (d, *J* = 6.03 Hz, 1H), 7.08 (bs, 1H), 7.24 (bs, 6H), 7.58 (d, *J* = 5.09 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 27.56, 44.24, 72.66, 110.20, 115.19, 123.98, 124.35, 127.24, 127.46, 128.01, 128.98, 130.96, 134.68, 142.12, 175.43; FTIR (KBr) cm^{-1}, 3419, 2216, 1652, 1011, 826, 769. HRMS ESI: [M+Na]+, Calcd for $C_{17}H_{14}O_2N_2Na$ 301.0946; found 301. 0947.

2-(3-hydroxy-1-(4-methoxybenzyl)-2-oxoindolin-3-yl)acetonitrile (3d): white solid (34 mg, yield = 55%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3);^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.67 (d, *J* = 16.58 Hz, 1H), 3.01 (d, *J* = 16.58 Hz, 1H), 3.68 (s, 3H), 4.66 (d, *J* = 15.45 Hz, 1H), 4.79 (d, *J* = 15.26 Hz, 1H), 6.67-6.78 (m, 3H), 7.03 (t, *J* = 7.54 Hz, 1H), 7.13-7.25 (m, 3H), 7.55 (d, *J* = 7.16 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 27.35, 43.64, 55.20, 72.69, 110.19, 114.29, 115.34, 123.87, 124.27, 126.65, 127.65, 128.62, 130.76, 141.98, 159.21, 175.61; FTIR (KBr) cm^{-1}, 3432, 2910, 2260, 1659, 1508, 1158, 741. HRMS ESI: [M+Na]+, Calcd for $C_{18}H_{16}O_3N_2Na$ 331.1053; found 331.1043.

2-(3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3e): white solid (67 mg, yield = 78%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.76 (d, *J* = 16.20 Hz, 1H), 2.95 (d, *J* = 16.2 Hz, 1H), 6.31 (d, *J* = 7.54 Hz, 1H), 6.91-6.99 (m, 2H), 7.15-7.20 (m, 9H), 7.37-7.44 (m, 7H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 28.14, 72.80, 75.12, 77.20, 115.37, 116.82, 123.45, 127.20, 127.44, 127.86, 129.22, 129.45, 141.26, 142.93, 177.26; FTIR (KBr) cm^{-1}, 3402, 2924, 2362, 1725, 1603, 1455, 1077, 738, 700. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{22}O_2N_2Na$ 453.1573; found 453.1540.

2-(3-hydroxy-5-methyl-2-oxo-1-tritylindolin-3-yl)acetonitrile (3f): white solid (64.8 mg, yield = 73%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.21 (s, 3H), 3.15 (s, 2H), 6.10 (d, *J* = 8.26 Hz, 1H), 6.68 (s, 1H), 6.80 (d, *J* = 7.93 Hz, 1H), 7.17-7.27 (m, 9H), 7.42-7.45 (m, 6H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 20.29, 26.69, 54.87, 71.89, 73.59, 115.30, 117.09, 124.15, 126.70, 127.64, 128.74, 129.66, 131.43, 139.75, 141.84, 176.70; FTIR (KBr) cm^{-1}, 3407, 2923, 2360, 1705, 1625, 1488, 1158, 741, 700. HRMS ESI: [M+Na]+, Calcd for $C_{30}H_{24}O_2N_2Na$ 467.1730; found 467.1710.

2-(3-hydroxy-5-methoxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3g): white solid (66.4 mg, yield = 72%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.19 (s, 2H), 3.67 (s, 3H), 6.13 (d, *J* = 8.85 Hz, 1H), 6.59 (d, J_1 = 2.83 Hz, J_2 = 9.04 Hz, 1H), 6.75 (s, 1H), 7.11 (d, *J* = 2.83 Hz, 1H), 7.18-7.23 (m, 2H), 7.25-7.30 (m, 6H), 7.44-7.47 (m, 6H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.64, 55.36, 72.04, 73.55, 79.15, 110.34, 113.03, 116.10, 126.69, 127.64, 128.72, 130.92, 135.09, 141.83, 154.96, 176.4; FTIR (KBr) cm^{-1}, 3439, 2928, 1722, 1598, 1487, 1194, 748, 704. HRMS ESI: [M+Na]+, Calcd for $C_{30}H_{24}O_3N_2Na$ 483.1679; found 483.1683.

2-(5-fluoro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3h): white solid (65.5 mg, yield = 73%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d6): δ 3.24 (s, 2H), 6.21 (dd, J_1 = 4.14, J_2 = 8.85 Hz), 6.87-6.94 (m, 2H), 7.18-7.23 (m, 2H), 7.25-7.35 (m, 7H), 7.43-7.45 (m, 6H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.41, 71.89, 73.77, 111.16 (d, *J* = 24.15 Hz), 114.79 (d, *J* = 23.05 Hz), 116.56 (d, *J* = 7.68 Hz), 116.95, 126.87, 127.78, 128.71, 131.54 (d, *J* = 8.23 Hz), 138.24 (d, *J* = 2.20 Hz), 141.58, 156.37 (d, *J* = 240 Hz), 176; FTIR (KBr) cm^{-1}, 3423, 2252, 1658, 1448, 1027, 824, 763. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2FNa$ 471.1479; found 471.1476.

2-(5-chloro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3i): white solid (65.9 mg, yield = 71%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.26 (s, 2H), 6.23 (d, J = 8.62 Hz, 1H), 6.91 (s, 1H), 7.10 (dd, J_1 = 2.02 Hz, J_2 =8.62 Hz, 1H), 7.19-7.31 (m, 8H), 7.42-7.44 (m, 6H), 7.51 (d, J = 1.83 Hz, 1H): ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.31, 71.74, 73.86, 79.17, 116.94, 123.76, 126.74, 126.90, 127.80, 128.33, 128.68, 131.72, 141.05, 141.46, 176.29; FTIR (KBr) cm^{-1}, 3430, 2252, 1651, 1598, 1025, 824, 764. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2ClK$ 503.0923; found 503.0966.

2-(5-bromo-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3j): white solid (71.2 mg, yield = 70%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.27 (s, 2H), 6.19 (d, J = 8.67 Hz, 1H), 6.91 (s, 1H), 7.19-7.23 (m, 2H), 7.26-7.31 (m, 7H), 7.42-7.45 (m, 6H), 7.63 (d, J = 1.88 Hz, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.29, 71.66, 73.82, 79.16, 114.52, 116.93, 117.38, 126.52, 126.87, 127.77, 128.66, 131.15, 132.03, 141.42, 176.16; FTIR (KBr) cm^{-1}, 3423, 2253, 1652, 1000, 824, 764. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2BrK$ 547.0418; found 547.0401.

2-(3-hydroxy-5-iodo-2-oxo-1-tritylindolin-3-yl)acetonitrile (3k): white solid (77 mg, yield = 69%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 2H), 6.06 (d, J = 8.44 Hz, 1H), 6.86 (s, 1H), 7.21-7.28 (m, 9H), 7.37-7.44 (m, 6H), 7.77 (s, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ 26.33, 71.53, 73.77, 86.14, 117.01, 117.80, 126.87, 127.78, 128.66, 132.07, 132.21, 136.93, 141.47, 142.00,176.05; FTIR (KBr) cm^{-1}, 3426, 2253, 2127, 1653, 1026, 825, 764. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2INa$ 579.0540; found 579.0562.

2-(3-hydroxy-2-oxo-5-(trifluoromethyl)-1-tritylindolin-3-yl)acetonitrile (3l): white solid (58 mg, yield = 58%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.32 (s, 2H), 6.44 (d, *J* = 8.62 Hz, 1H), 6.97 (s, 1H), 7.22-7.32 (m, 9H), 7.43-7.46 (m, 6H), 7.81 (s, 1H) ; ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.18, 71.44, 74.02, 115.68, 116.88, 120.52, 122.60, 123.03, 126.09, 126.94, 127.82, 128.62, 130.59, 141.28, 145.72, 176.64; FTIR (KBr) cm^{-1}, 3405, 2925, 2361, 1737, 1456, 1124, 703. HRMS ESI: [M+K]+, Calcd for $C_{30}H_{21}O_2N_2F_3K$ 537.1187; found 537.1174.

2-(3-hydroxy-2-oxo-5-(trifluoromethoxy)-1-tritylindolin-3-yl)acetonitrile (3m): white solid (64.8 mg, yield = 63%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.29 (s, 2H), 6.32 (d, *J* = 8.67 Hz, 1H), 6.96 (s, 1H), 7.08 (d, *J* = 8.85 Hz, 1H), 7.19-7.31 (m, 9H), 7.43-7.49 (m, 6H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.47, 71.82, 74.05, 116.67, 117.02, 117.18, 121.67, 127.11, 127.99, 128.79, 128.91, 131.65, 141.25, 141.55, 143.58, 176.71; FTIR (KBr) cm^{-1}, 3380, 2924, 2360, 1728, 1476, 1259, 773, 708. HRMS ESI: [M+K]+, Calcd for $C_{30}H_{21}O_3N_2F_3K$ 553.1136; found 553.1130.

2-(3-hydroxy-2-oxo-5-phenyl-1-tritylindolin-3-yl)acetonitrile (3n): white solid (66mg, yield = 65%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.28 (s, 2H), 6.31 (d, *J* = 8.44 Hz, 1H), 6.83 (s, 1H), 7.22-7.24 (m, 2H), 7.27-7.37 (m, 8H), 7.40-7.49 (m, 8H), 7.56-7.58 (m, 2H), 7.79 (s, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.55, 71.79, 73.70, 115.72, 117.13, 121.91, 126.08, 126.57, 126.76, 127.19, 127.69, 128.68, 128.93, 130.41, 134.29, 139.19, 141.58, 141.72, 176.70; FTIR (KBr) cm^{-1}, 3394, 2926, 2360, 1715, 1477, 1186, 1136, 741, 702. HRMS ESI: [M+Na]+, Calcd for $C_{35}H_{26}O_2N_2Na$ 529.1886; found 529.1879.

2-(4-chloro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3o): white solid (58 mg, yield = 62%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.23 (s, 2H), 6.11 (s, 1H), 6.87 (s, 1H), 7.10 (d, *J* = 8.10 Hz, 1H), 7.21-7.26 (m, 2H), 7.29-7.33 (m, 6H), 7.42-7.51 (m,7H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.35, 71.34, 73.89, 115.23, 116.91, 122.17, 125.08, 126.99, 127.81, 128.59, 128.66, 132.70, 141.24, 143.56, 176.53; FTIR (KBr) cm^{-1}, 3420, 2359, 2126, 1651, 1001, 824, 765. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2ClNa$ 487.1184; found 487.1205.

2-(4-bromo-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3p): white solid (75.3 mg, yield = 74%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.17 (d, *J* = 16.77 Hz, 1H), 3.51 (d, *J* = 16.58 Hz, 1H), 6.29 (d, *J* = 8.10 Hz, 1H), 6.94-7.00 (m, 2H), 7.17-7.21 (m, 2H), 7.24-7.31 (m, 7H), 7.42-7.44 (m, 6H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 23.82, 73.66, 74.07, 115.03, 116.22, 118.31, 126.53, 126.69, 126.90, 127.75, 128.78, 130.23, 141.37, 144.75, 175.73; FTIR (KBr) cm^{-1}, 3424, 2361, 2126, 1653, 1027, 824, 765. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2BrNa$ 531.0679; found 531.0654.

2-(6-chloro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3q): white solid (53.9 mg, yield = 58%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.76 (d, *J* = 16.32 Hz, 1H), 2.94 (d, *J* = 16.14 Hz, 1H), 6.27 (s, 1H), 6.95 (d, *J* = 7.15 Hz, 1H), 7.20-7.23 (m, 9H), 7.35 (m, 7H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 28.07, 72.41, 75.44, 115.12, 117.20, 123.55, 124.36, 125.86, 127.43, 128.01, 129.12, 135.37, 140.84, 144.12, 177.14; FTIR (KBr) cm^{-1}, 3404, 2926, 2360, 1735, 1610, 1085, 741, 703. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2ClNa$ 487.1184; found 487.1186.

2-(6-bromo-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3r): white solid (65.2 mg, yield = 64%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.74 (d, *J* = 16.36 Hz, 1H), 2.94 (d, *J* = 16.36 Hz, 1H), 6.40 (s, 1H), 7.11-7.25 (m, 11H), 7.31-7.37 (m, 6H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 27.90, 53.41, 72.48, 75.41, 115.14, 119.91, 123.28, 124.65, 126.43, 127.42, 127.99, 129.10, 140.80, 144.13, 177.07; FTIR (KBr) cm^{-1}, 3419, 2252, 1652, 1001, 824, 764. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2Br_1Na$ 531.0678; found 531.0670.

2-(7-fluoro-3-hydroxy-2-oxo-1-tritylindolin-3-yl)acetonitrile (3s): white solid (56.4 mg, yield = 63%). R_f = 0.4 (ethyl acetate/petroleum ether = 2/3); ^{1}H-NMR (300 MHz, DMSO-d_6) δ 3.25 (s, 2H), 6.90-6.97 (m, 2H), 7.10-7.21 (m, 3H), 7.23-7.28 (m, 6H), 7.38-7.43 (m, 7H); ^{13}C-NMR (75 MHz, DMSO-d_6) δ 26.55, 71.73, 74.10, 116.91, 118.74 (d, *J* = 23.60 Hz), 120.12 (d, *J* = 2.74 Hz), 124.73 (d, *J* = 7.14 Hz), 126.51, 127.49, 128.25 (d, *J* = 2.19 Hz), 128.94 (d, *J* = 7.68 Hz), 132.50 (d, *J* = 2.19 Hz), 143.23 (d, *J* = 2.20 Hz), 144.20 (d, *J* = 248 Hz), 176.20; FTIR (KBr) cm^{-1}, 3434, 2251, 2125, 1655, 1004, 824, 764. HRMS ESI: [M+Na]+, Calcd for $C_{29}H_{21}O_2N_2FNa$ 471.1479; found 471.1462.

2-(3-hydroxy-2-oxoindolin-3-yl)acetonitrile (3a): To a solution of compound **3d** (60 mg, 0.139 mmol) in DCM (2 ml), trifluoroacetic acid (39.17 mmol, 3 ml) was dropwise added at room temperature. The resulting reaction mixture was run at same temperature for next 12 h. The progress of the reaction was monitored by TLC. Once the reaction was completed, the reaction mixture was evaporated off under reduced pressure. The organic residue was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 80/20) to give the white solid as product (26.1 mg, yield = 93%); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.92 (d, *J* = 16.51 Hz, 1H), 3.02 (d, *J* = 16.51 Hz, 1H), 6.58 (s, 1H), 6.85 (d, *J* = 7.52 Hz, 1H),

7.01 (t, J = 7.52 Hz, 1H), 7.26 (t, J = 7.52 Hz, 1H), 7.44 (d, J = 7.34 Hz, 1H), 10.53 (s, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 26.12, 72.02, 110.07, 117.08, 122.00, 124.15, 129.78, 130.02, 141.59, 176.70; FTIR (KBr) cm^{-1}, 3425, 2361, 1655, 1001, 765. HRMS ESI: [M+Na]+, Calcd for $C_{10}H_8O_2N_2Na$ 211.0477 ; found 211.0496.

2-(6-bromo-3-hydroxy-2-oxoindolin-3-yl)acetonitrile (4): To a solution of compound **3p** (50 mg, 0.098 mmol) in DCM (1 ml), trifluoroacetic acid (27.61 mmol, 2.2 ml) was dropwise added at room temperature. The resulting solution was run at same temperature for next 12 h. The progress of the reaction was monitored by TLC. Once the reaction was completed, the reaction mixture was evaporated off under reduced pressure. The organic mixture was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 70/30) to give the white solid as product (24.1 mg, yield = 92%); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.95 (d, J = 16.58 Hz, 1H), 3.04 (d, J = 16.58 Hz, 1H), 6.68 (s, 1H), 7.02 (d, J = 1.32 Hz, 1H), 7.23 (dd, J_1 =1.51 Hz, J_2 = 7.91 Hz, 1H), 7.38 (d, J = 7.91 Hz, 1H), 10.68 (s, 1H); ^{13}C-NMR (75 MHz, DMSO-d_6): δ 25.74, 71.69, 112.83, 116.80, 122.57, 124.59, 125.93, 129.03, 143.24, 176.39; FTIR (KBr) cm^{-1}, 3409, 2252, 1651, 1002, 764. HRMS ESI: [M+Na]+, Calcd for $C_{10}H_7O_2N_2Br_1Na$ 288.9583; found 288.9560.

2-(3-hydroxy-1-methyl-2-oxoindolin-3-yl)acetonitrile (3b): To a suspension of NaH (4.4 mg, 0.11 mmol) in dry DMF (1.0 mL), solution of compound **3a** (20 mg, 0.1 mmol) in dry DMF (0.5 mL0 was drop wise added at 0°C. The resulting mixture was stirred for 10 minutes at same temperature, then methyl iodide (0.114 mmol, 7 μL) was added to it. Subsequently, the reaction mixture was warmed to room temperature and stirred for next 12 h. The progress of the reaction was monitored by TLC. Once the reaction completed, it was quenched with water. The

biphasic mixture was transferred to the separating funnel with help of EtOAc (2.0 mL). The organic layer was separated and washed with water (2.0 mLx3). The combined aqueous layer was extracted with EtOAc (2.0 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 and evaporated under reduced pressure. The resulting residue was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 60/40) to give the white solid product (13.5 mg, yield = 67%). ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.70 (d, *J* = 16.51 Hz, 1H), 3.05 (d, *J* = 16.51 Hz, 1H), 3.24 (s, 3H), 6.91 (d, *J* = 7.34 Hz, 1H), 7.17 (t, *J* = 7.15 Hz, 1H), 7.41 (t, *J* = 7.15 Hz, 1H), 7.66 (d, *J* = 6.79 Hz, 1H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 26.57, 27.47, 72.58, 109.13, 115.27, 123.99, 124.28, 127.48, 131.02, 142.86, 175.32; FTIR (KBr) cm^{-1}, 3422, 2316, 1655, 1001, 824, 765. HRMS ESI: [M+Na]+, Calcd for $C_{11}H_{10}O_2N_2Na$ 225.0634; found 225.0639.

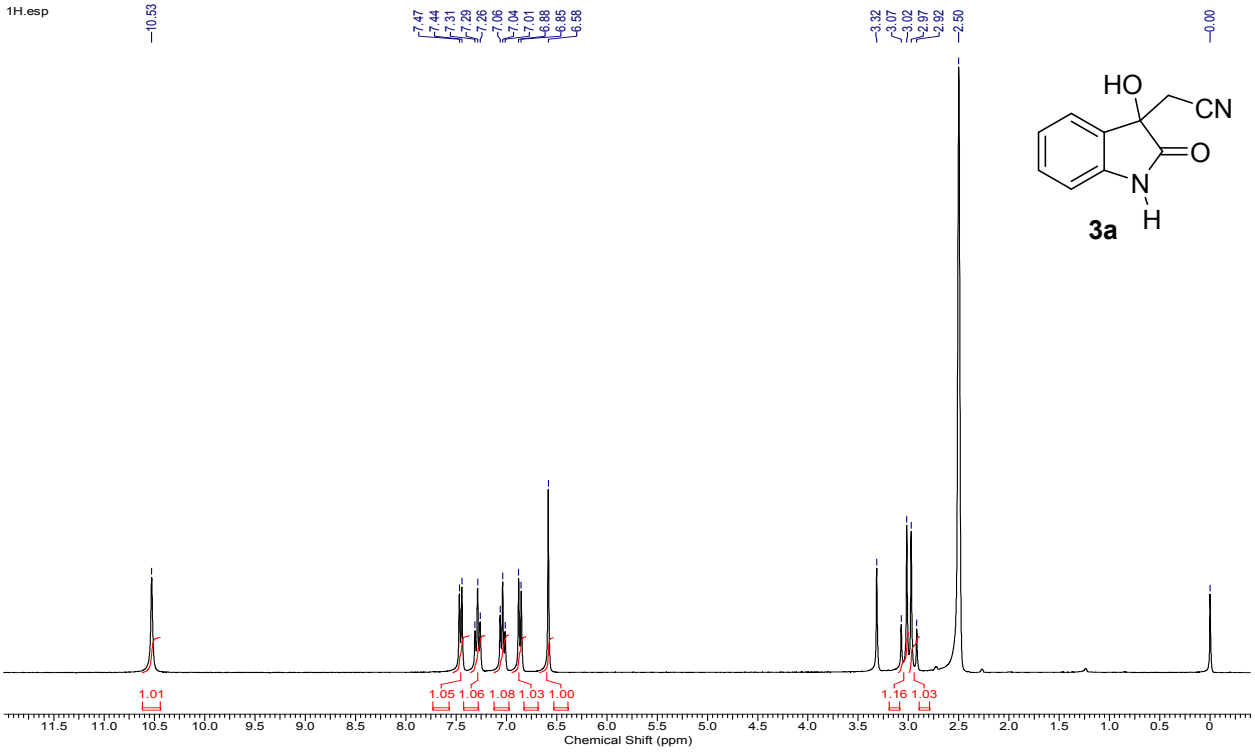
3-(cyanomethyl)-2-oxo-1-tritylindolin-3-yl acetate (5): To a solution of compound **3d** (20 mg, 0.046 mmol) in dry DCM (1 ml), acetyl chloride (0.28 mmol, 20 μL) was added drop wise at room temperature. The resulting solution was stirred for 5 minutes at same temperature, then K_2CO_3 (16 mg, 0.115 mmol) was added to it. The reaction was run at room temperature for 12 h. The progress of the reaction was monitored by TLC. Once the reaction completed, the reaction mixture was evaporated off under reduced pressure. The crude mixture was purified by flash chromatography (silica gel, ethyl acetate/petroleum ether = 5/95 to 30/20) to give the white solid product (12 mg, yield = 55%); ^{1}H-NMR (300 MHz, $CDCl_3$): δ 2.02 (s, 3H), 2.45 (d, *J* = 16.51 Hz, 1H), 2.99 (d, *J* = 16.51 Hz, 1H), 6.29 (d, *J* = 7.52 Hz, 1H), 6.90-6.93 (m, 2H), 7.14-7.19 (m, 9H), 7.38-7.41 (m, 7H); ^{13}C-NMR (75 MHz, $CDCl_3$): δ 20.47, 26.90, 75.19, 75.41, 114.82, 116.76, 122.42, 122.97, 124.86, 127.11, 127.63, 129.37, 129.57, 141.37, 143.17, 167.99, 172.06; FTIR

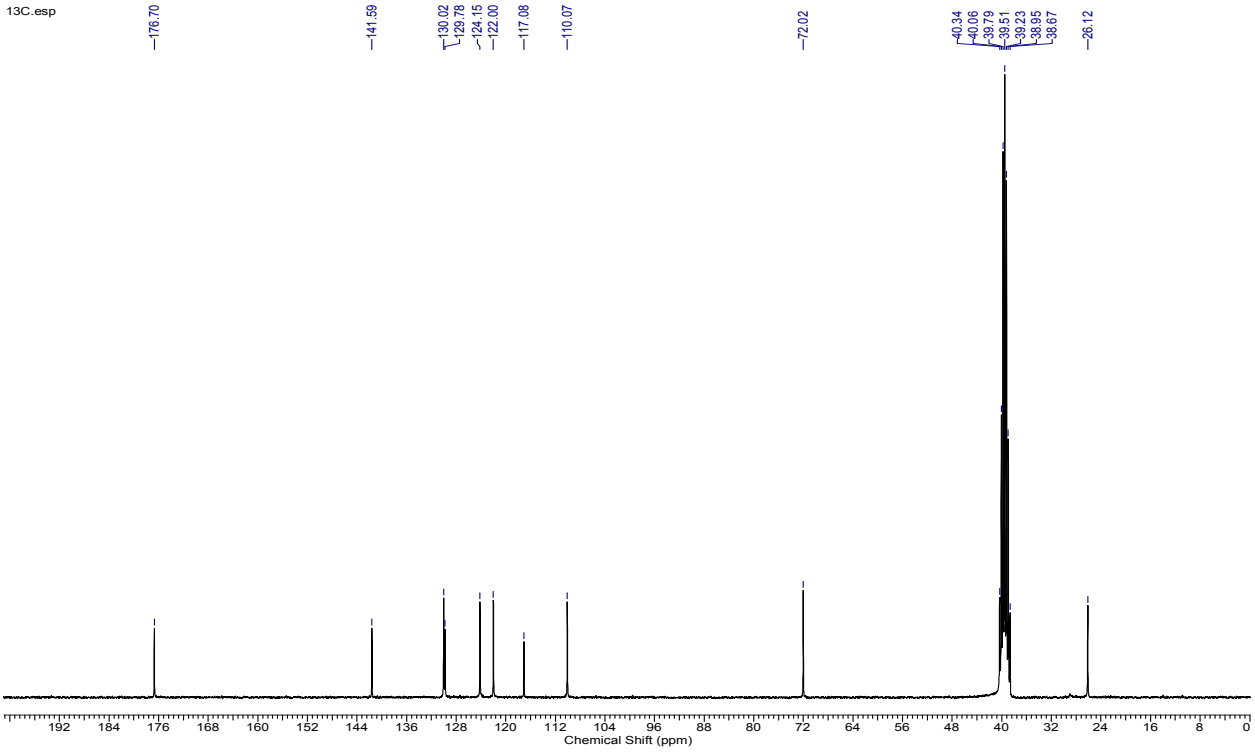
(KBr) cm^{-1}, 3437, 2926, 2362, 1744, 1103, 749, 704. HRMS ESI: [M+Na]+, Calcd for $C_{31}H_{24}O_3N_2Na$ 495.1679; found 495.1678.

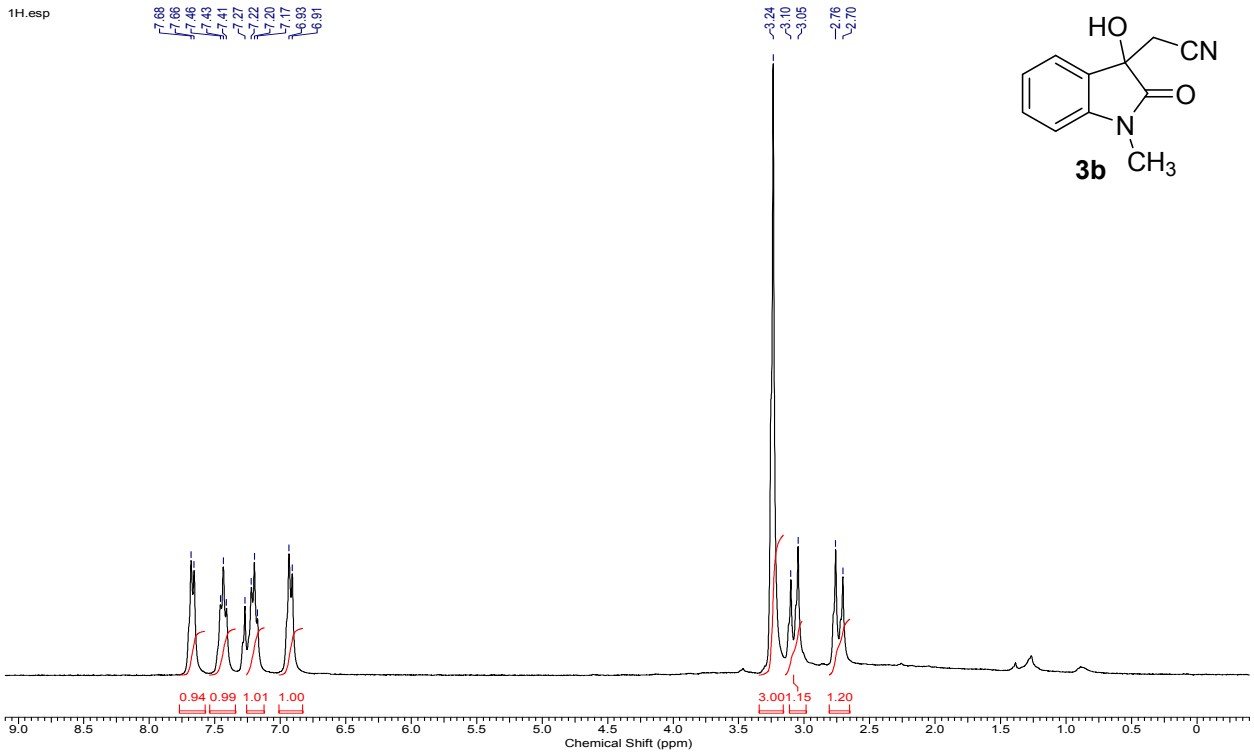
References

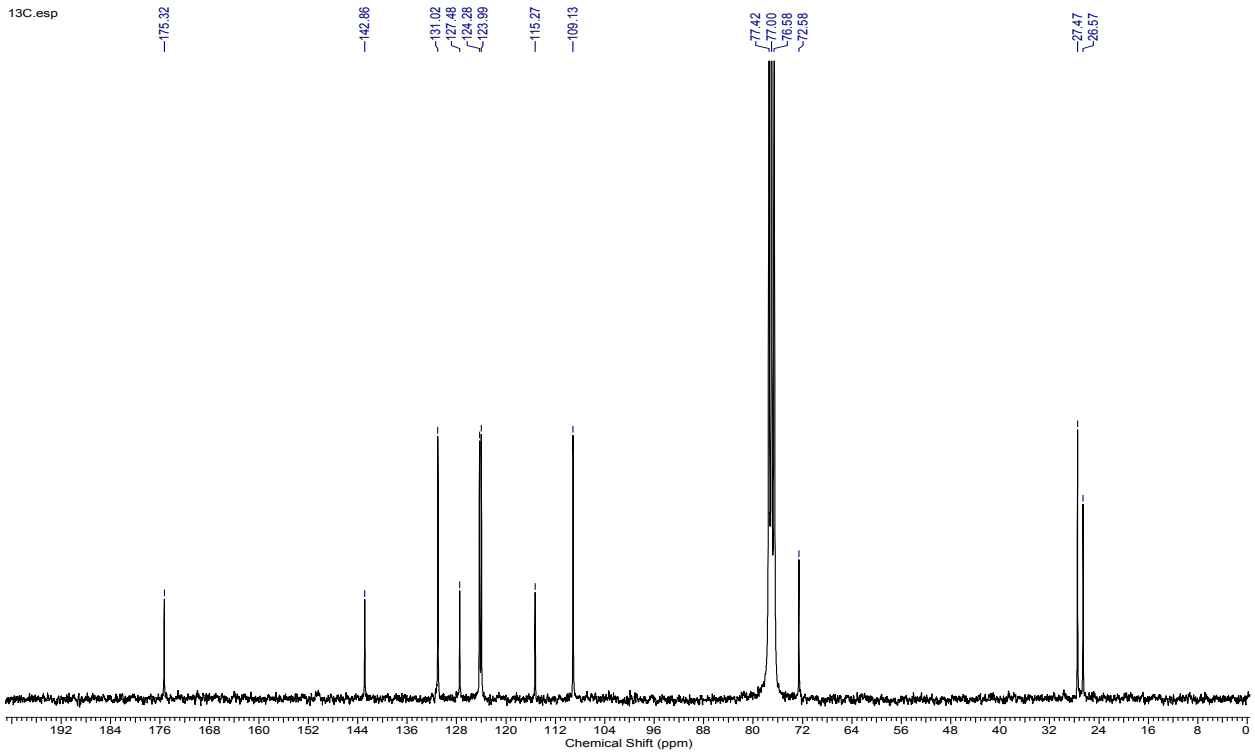
1. (a) H. H. Jung, A. W. Buesking and J. A. Ellman, *Org. Lett.*, 2011, **13**, 3912. (b) D. Chen and M. H. Xu, *Chem. Commun.* 2013, **49**, 1327.

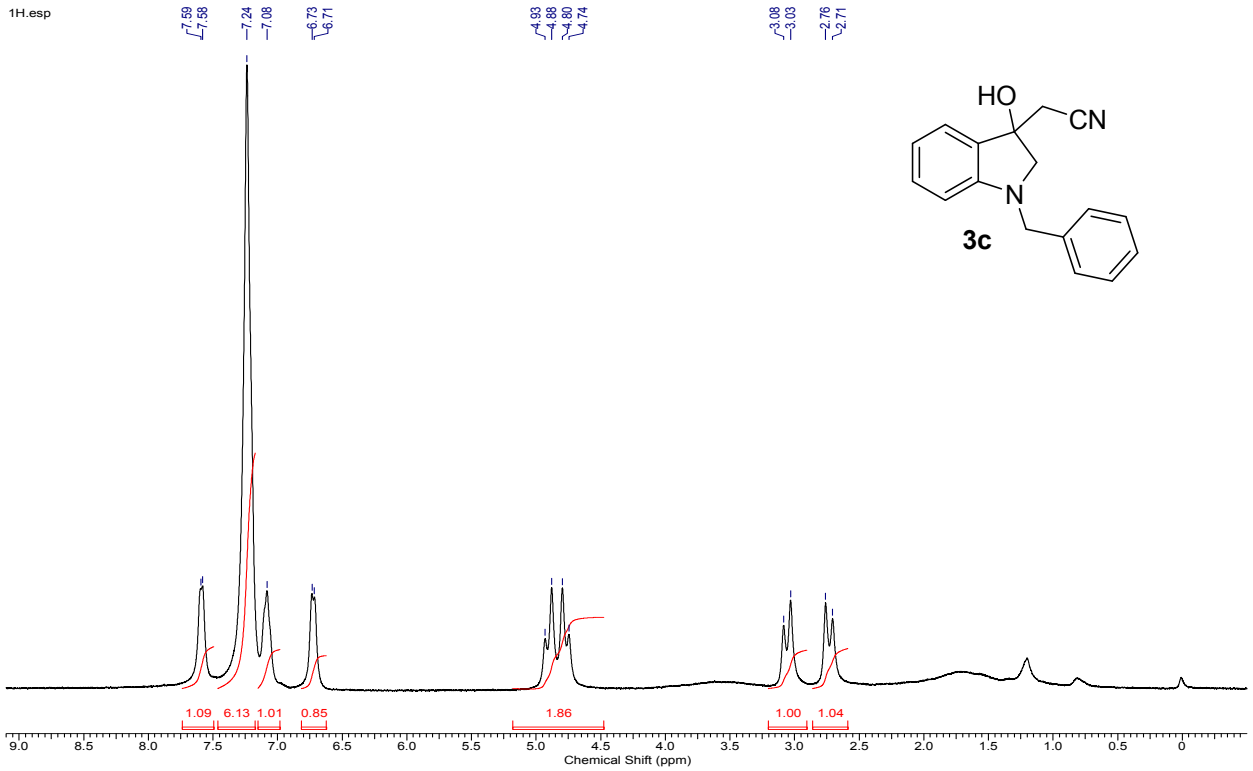
^{1}H and ^{13}C NMR Spectra

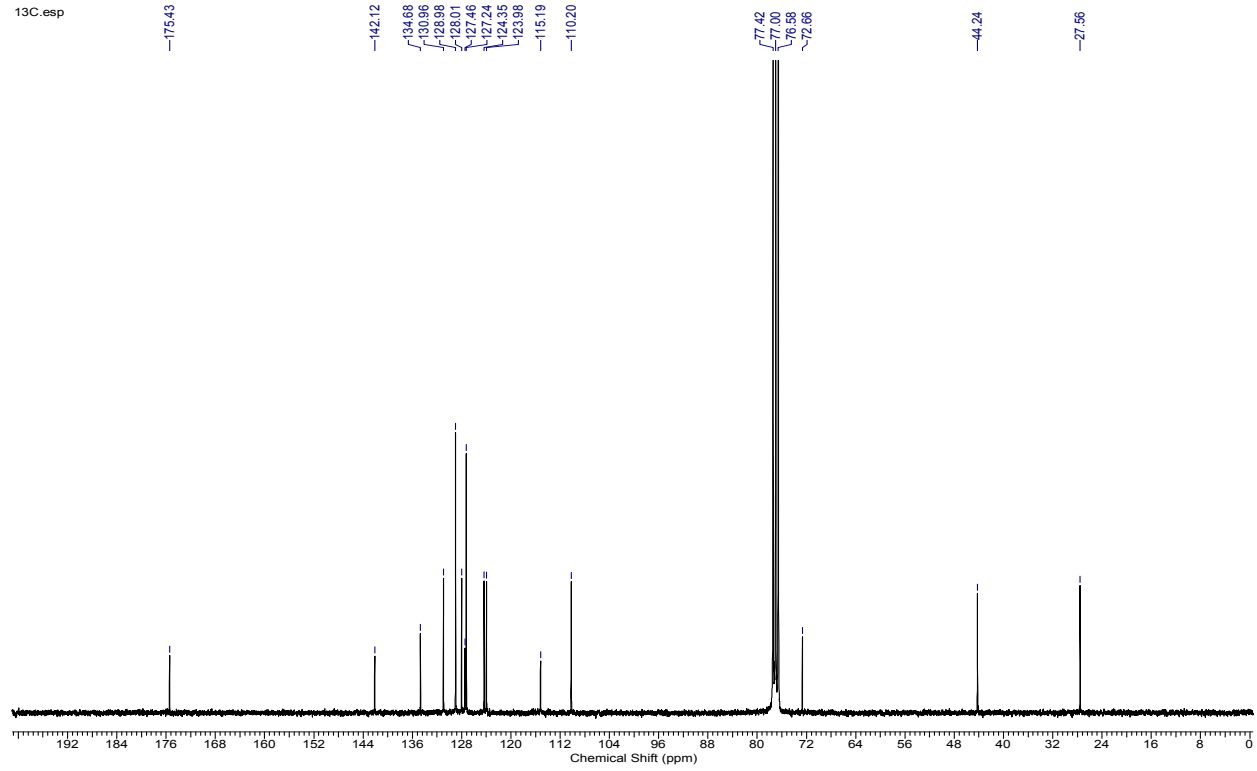


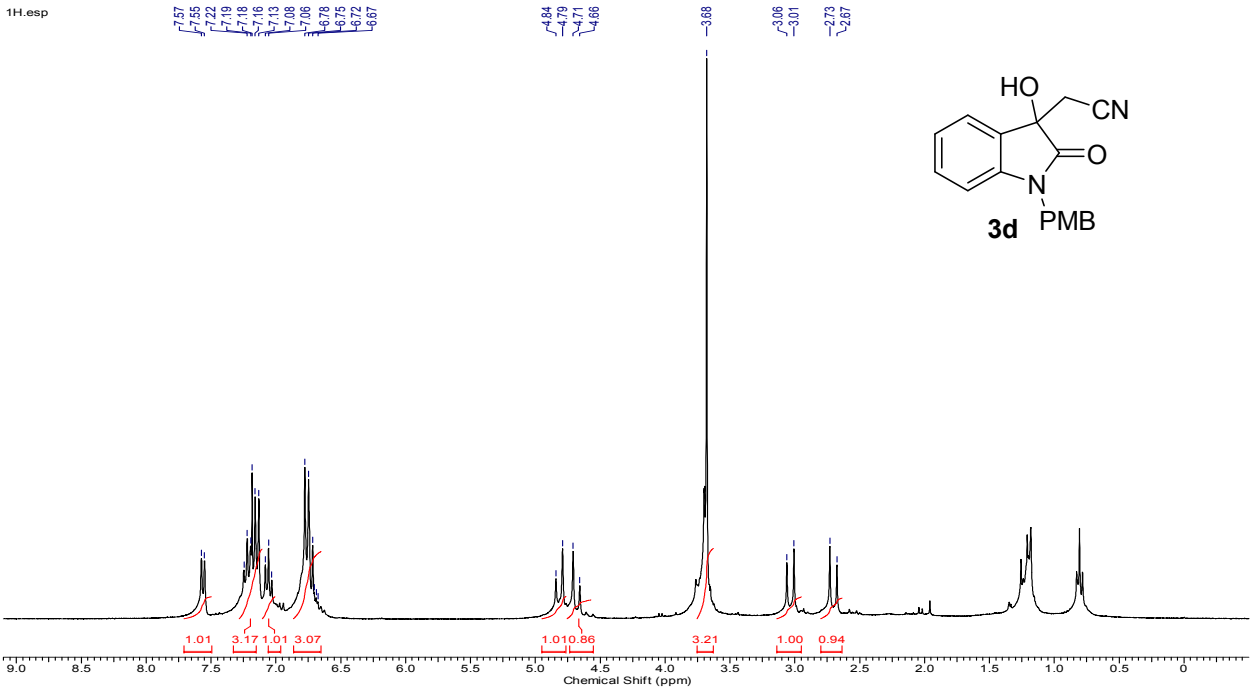


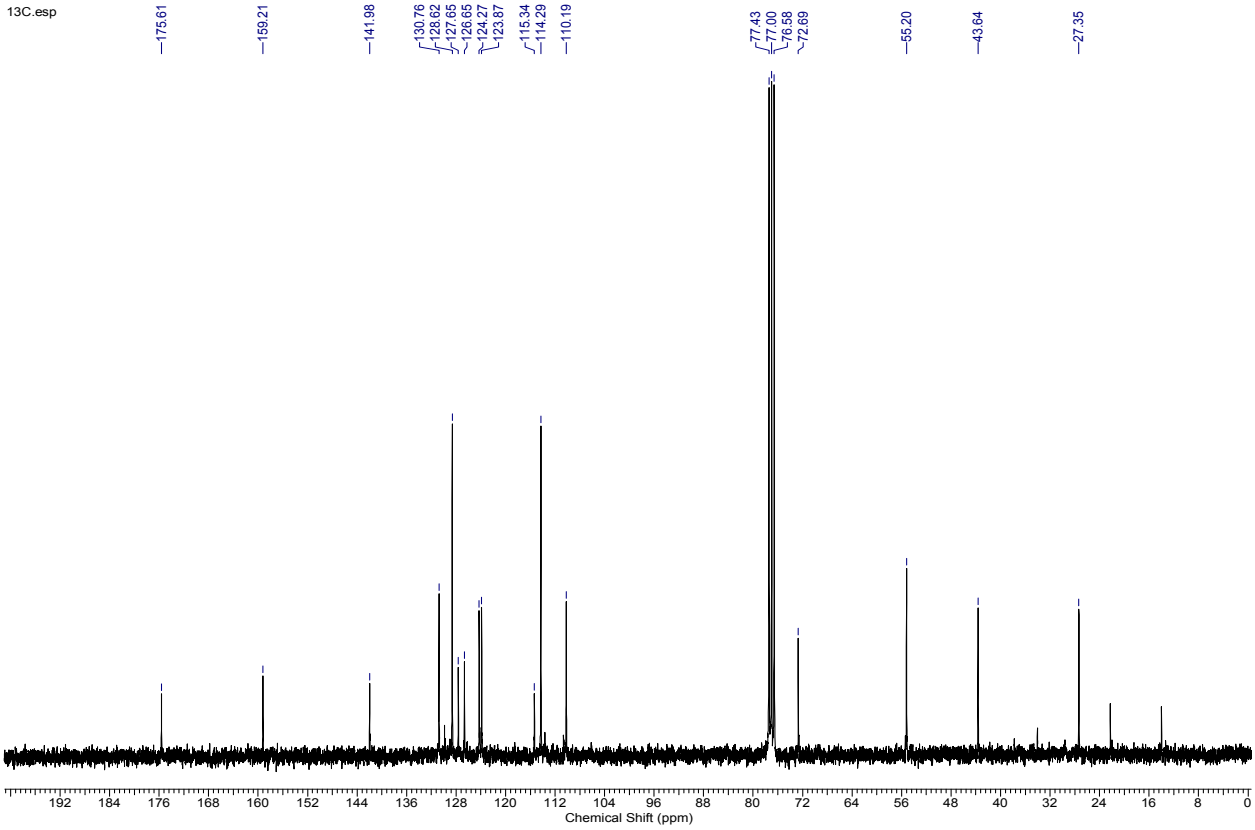

1H.esp
7.68
7.66
7.46
7.43
7.41
7.27
7.22
7.20
7.17
6.93
6.91
3.24
3.10
3.05
2.76
2.70
HO
CN
O
N
CH3
3b
0.94 0.99 1.01 1.00
3.00 1.15 1.20
Chemical Shift (ppm)

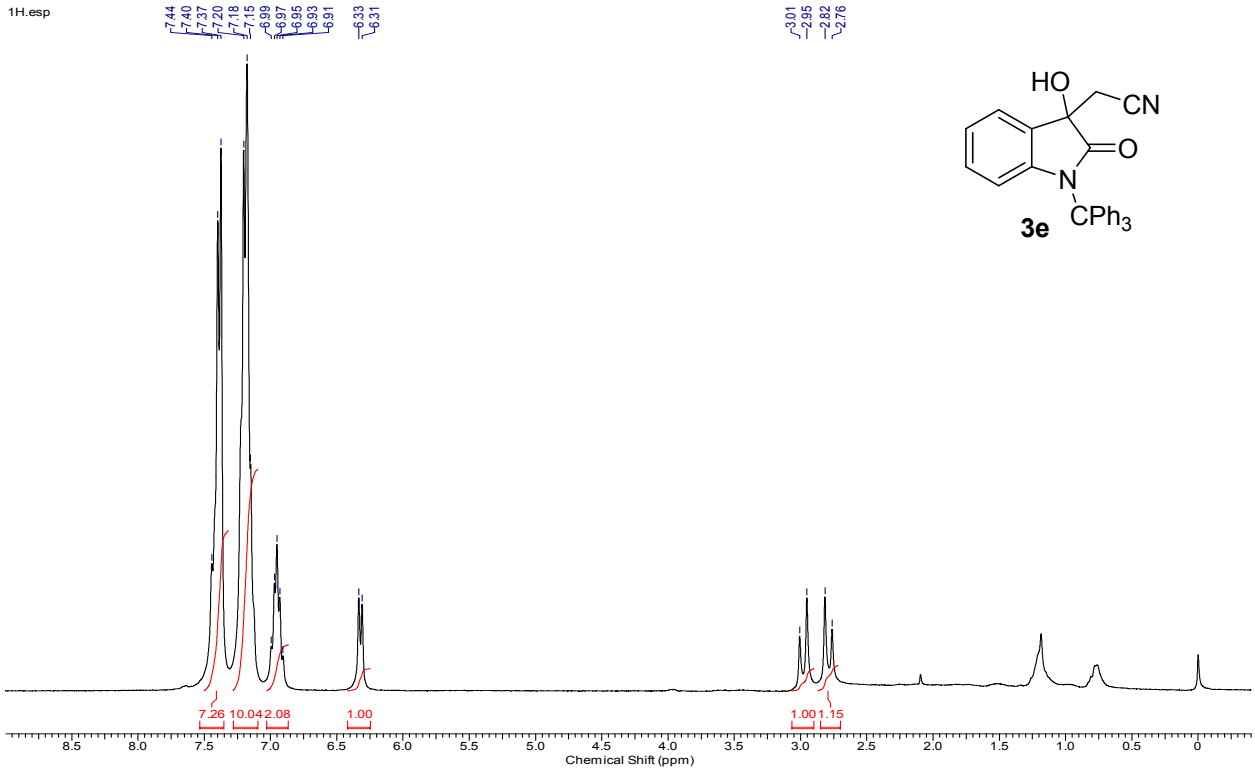

13C.esp
175.32
142.86
131.02
127.48
124.28
123.99
115.27
109.13
77.42
77.00
76.58
72.58
27.47
26.57
Chemical Shift (ppm)

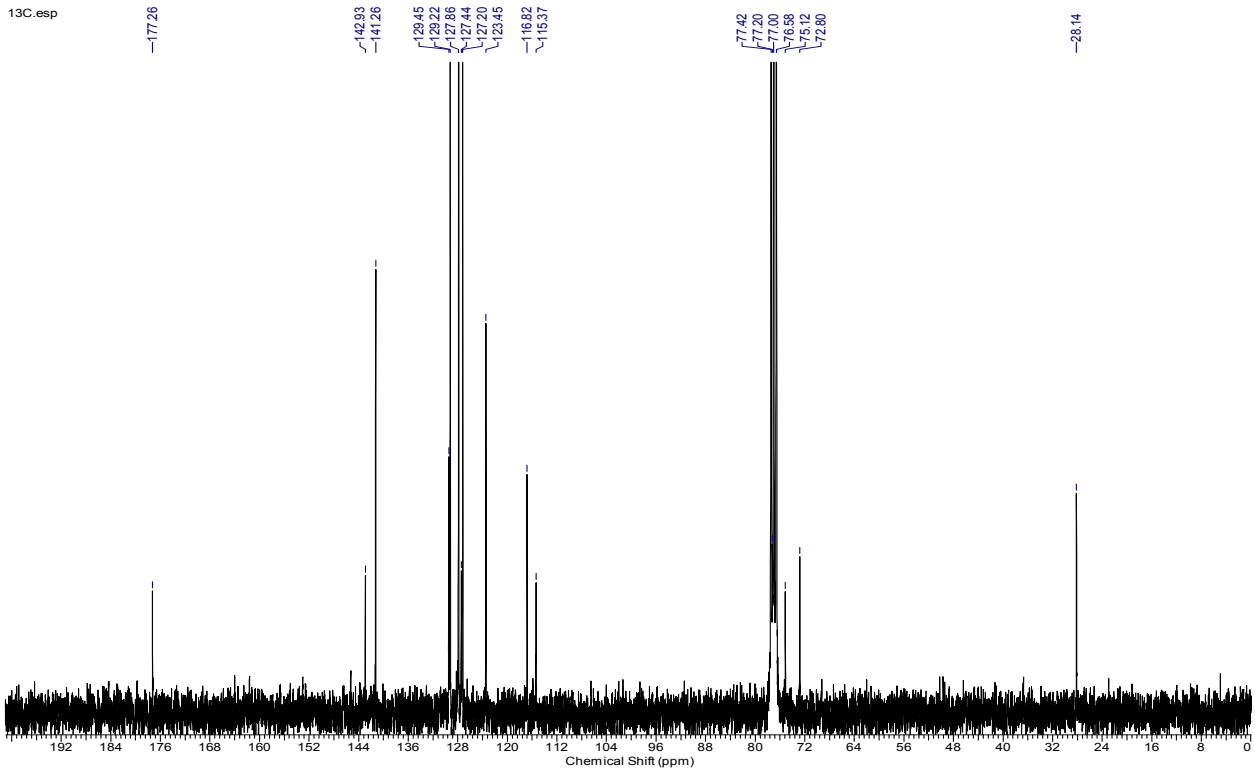

1H.esp
7.59
7.58
7.24
7.08
6.73
6.71
4.93
4.88
4.80
4.74
3.08
3.03
2.76
2.71
HO
CN
N
3c
1.09
6.13
1.01
0.85
1.86
1.00
1.04
Chemical Shift (ppm)

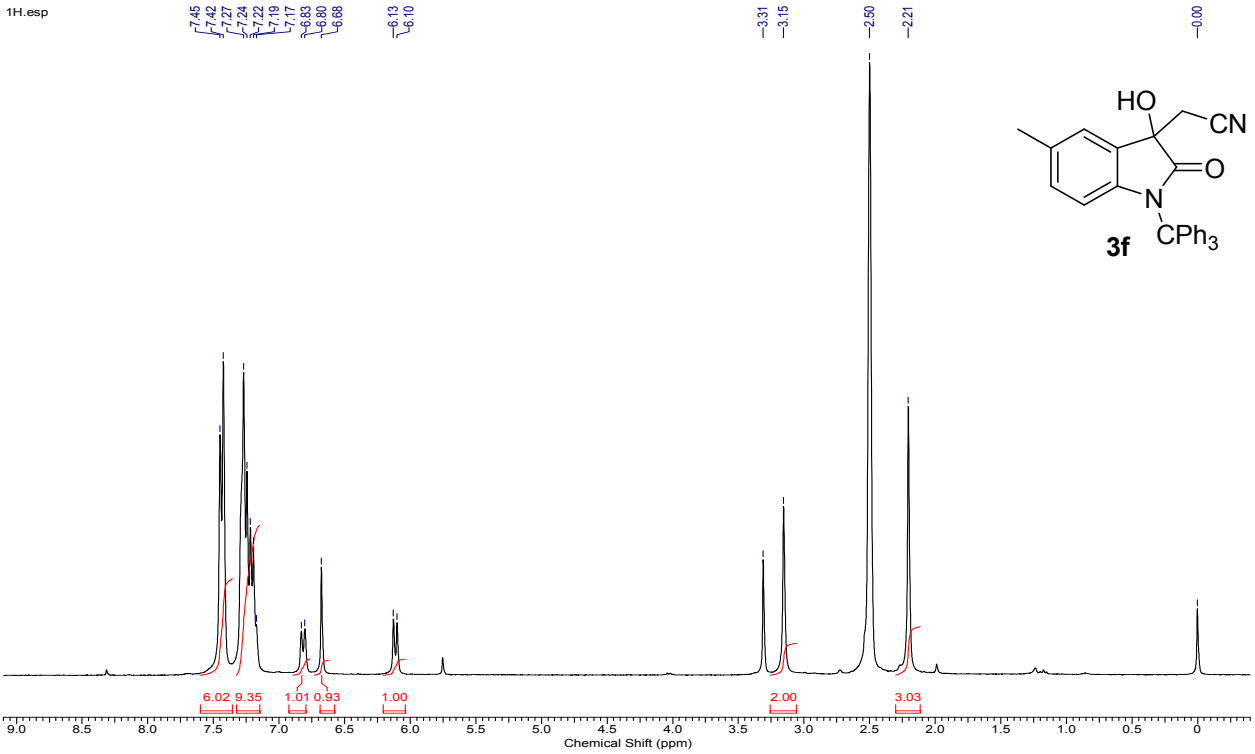

13C.esp
175.43
142.12
134.68
130.96
128.98
128.01
127.46
127.24
124.35
123.98
115.19
110.20
77.42
77.00
76.58
72.66
44.24
27.56
Chemical Shift (ppm)

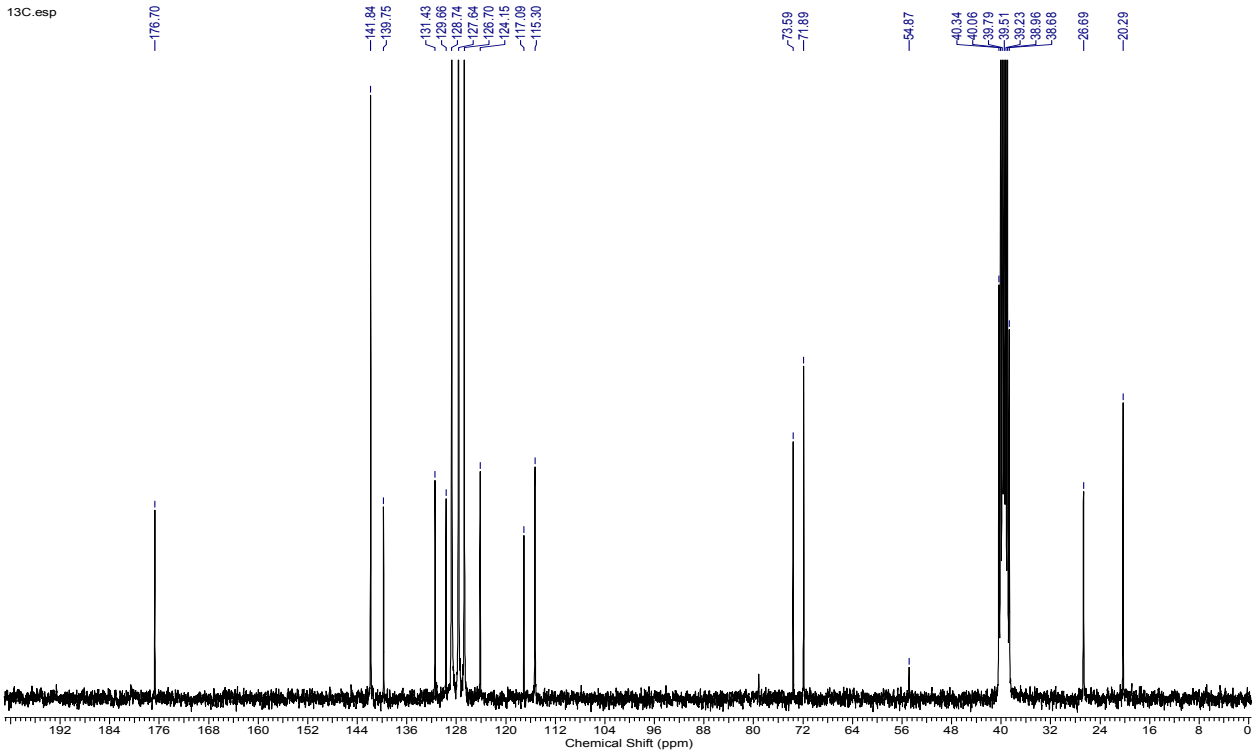

1H.esp
7.57
7.55
7.22
7.19
7.18
7.16
7.13
7.08
7.06
6.78
6.75
6.72
6.67
4.84
4.79
4.71
4.66
3.68
3.06
3.01
2.73
2.67
HO
CN
O
N
PMB
3d
1.01
3.17
1.01
3.07
1.01
0.86
3.21
1.00
0.94
Chemical Shift (ppm)

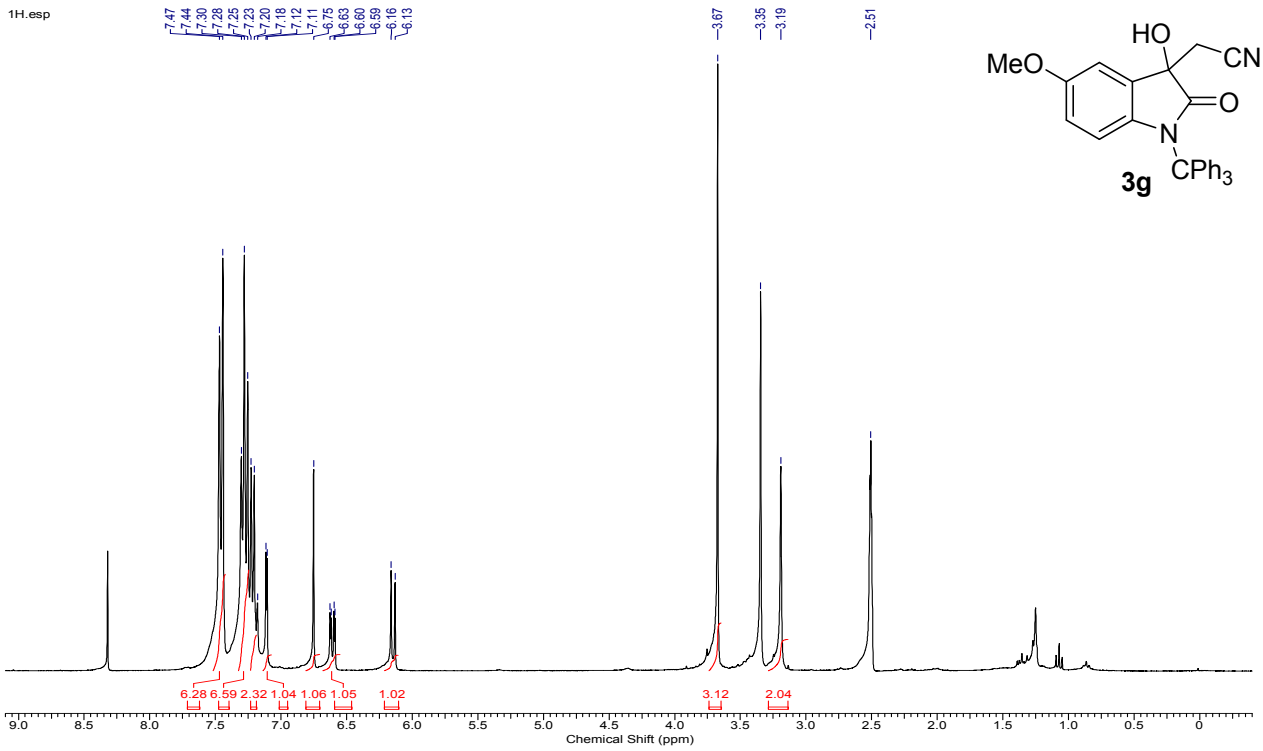

13C.esp
175.61
159.21
141.98
130.76
128.62
127.65
126.65
124.27
123.87
115.34
114.29
110.19
77.43
77.00
76.58
72.69
55.20
43.64
27.35
Chemical Shift (ppm)

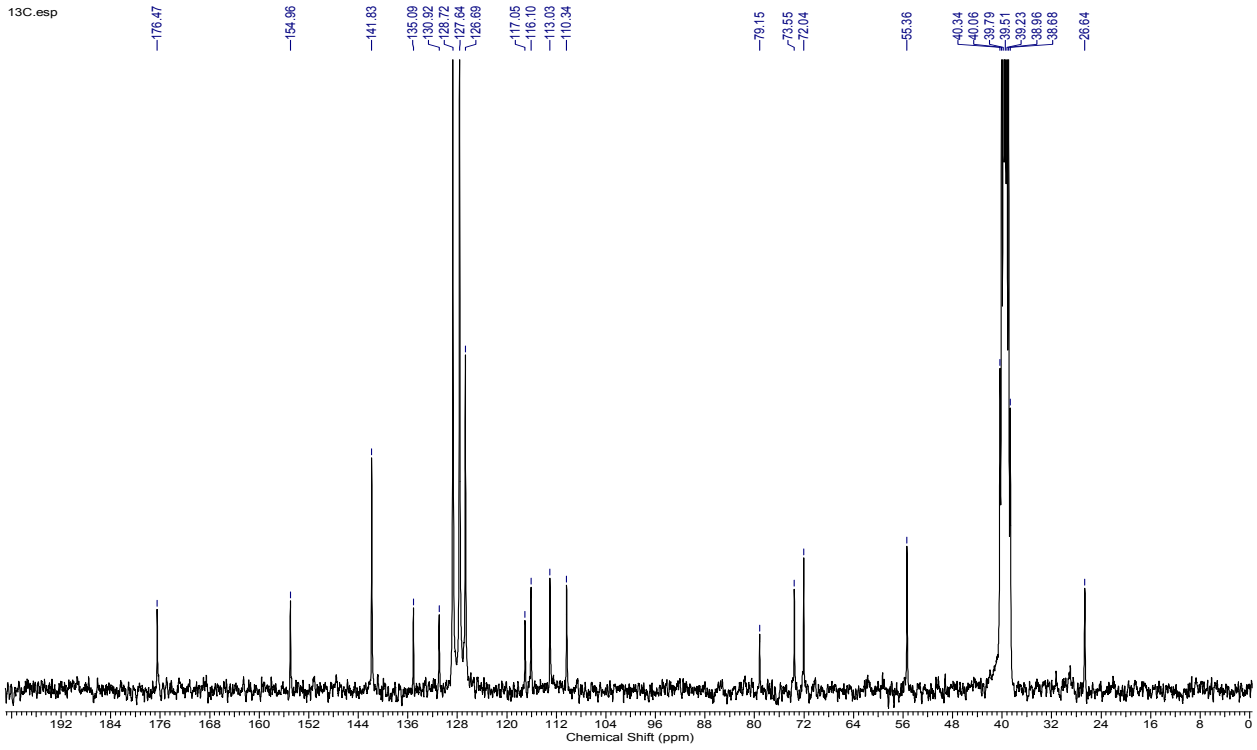

1H.esp
7.44
7.40
7.37
7.20
7.18
7.15
6.99
6.97
6.95
6.93
6.91
6.33
6.31
3.01
2.95
2.82
2.76
HO
CN
O
N
CPh3
3e
7.26
10.04
2.08
1.00
1.00
1.15
Chemical Shift (ppm)

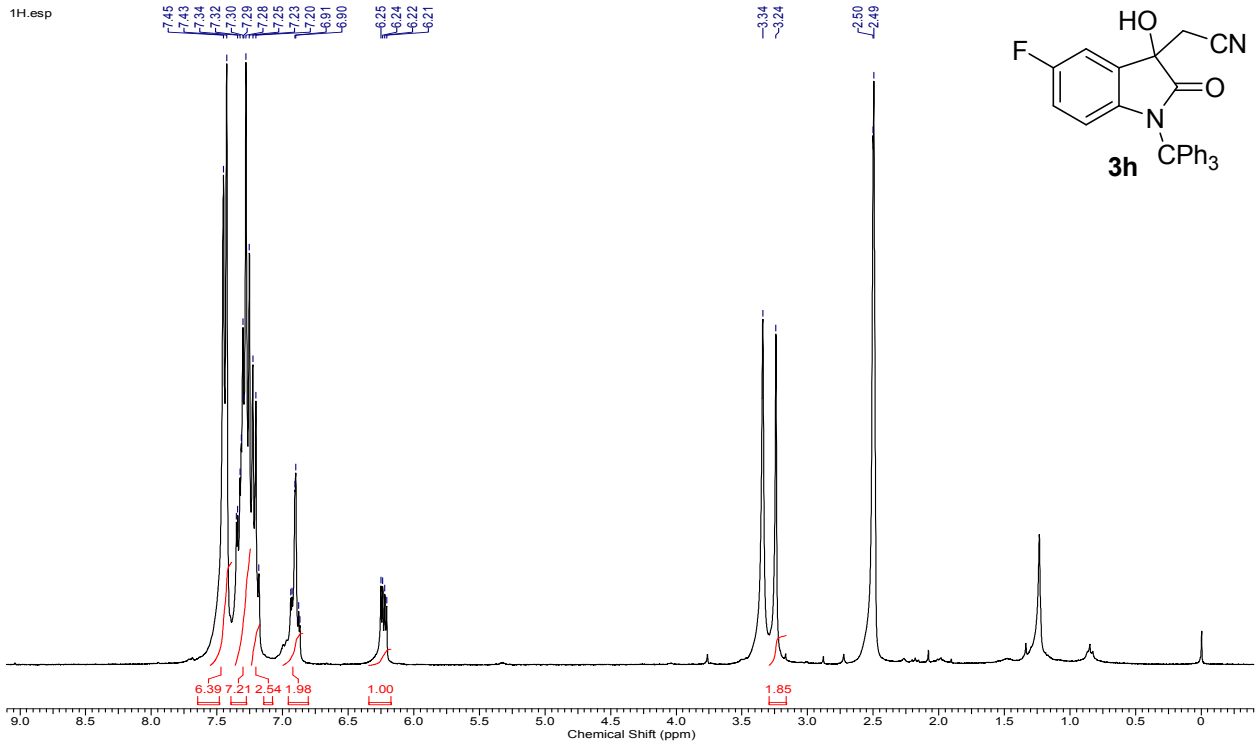

13C.esp
177.26
142.93
141.26
129.45
129.22
127.86
127.44
127.20
123.45
116.82
115.37
77.42
77.20
77.00
76.58
75.12
72.80
28.14
Chemical Shift (ppm)

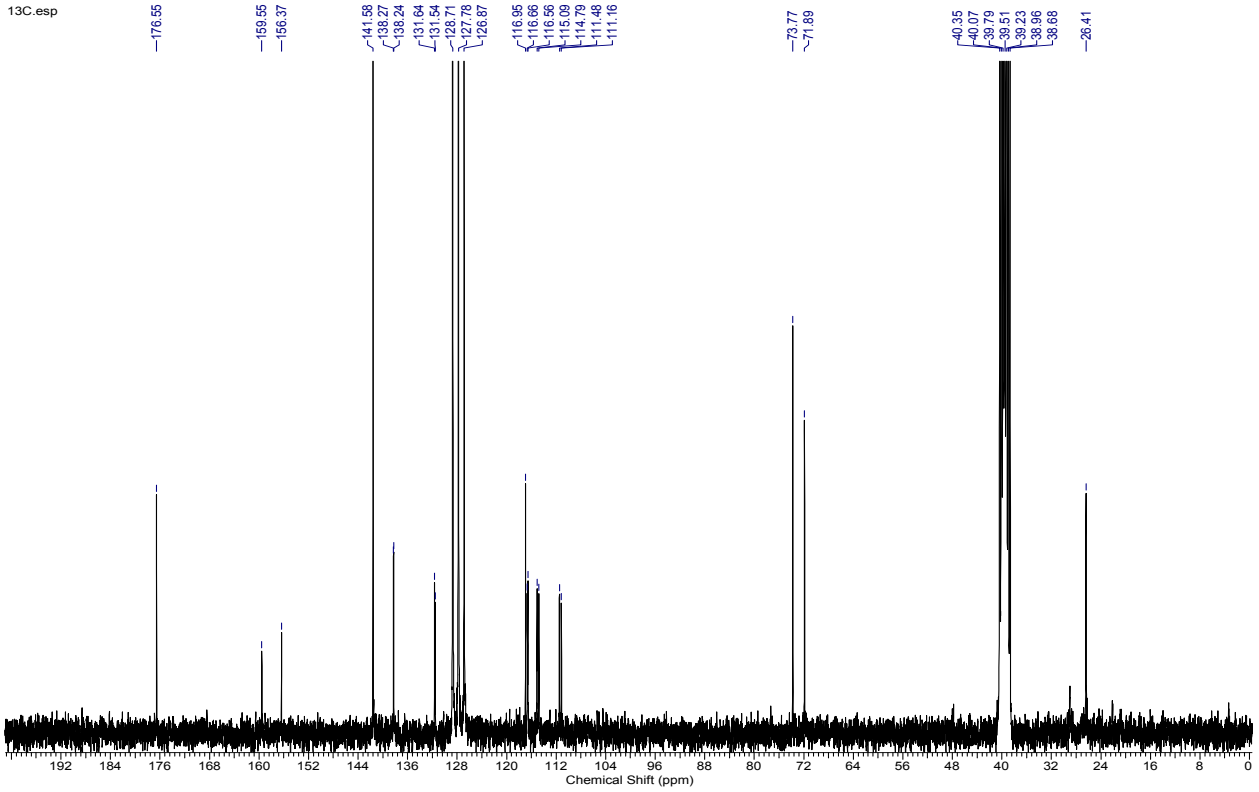

1H.esp
7.45
7.42
7.27
7.24
7.22
7.19
7.17
6.83
6.80
6.68
6.13
6.10
3.31
3.15
2.50
2.21
0.00
HO
CN
O
N
CPh3
3f
6.02
9.35
1.01
0.93
1.00
2.00
3.03
Chemical Shift (ppm)

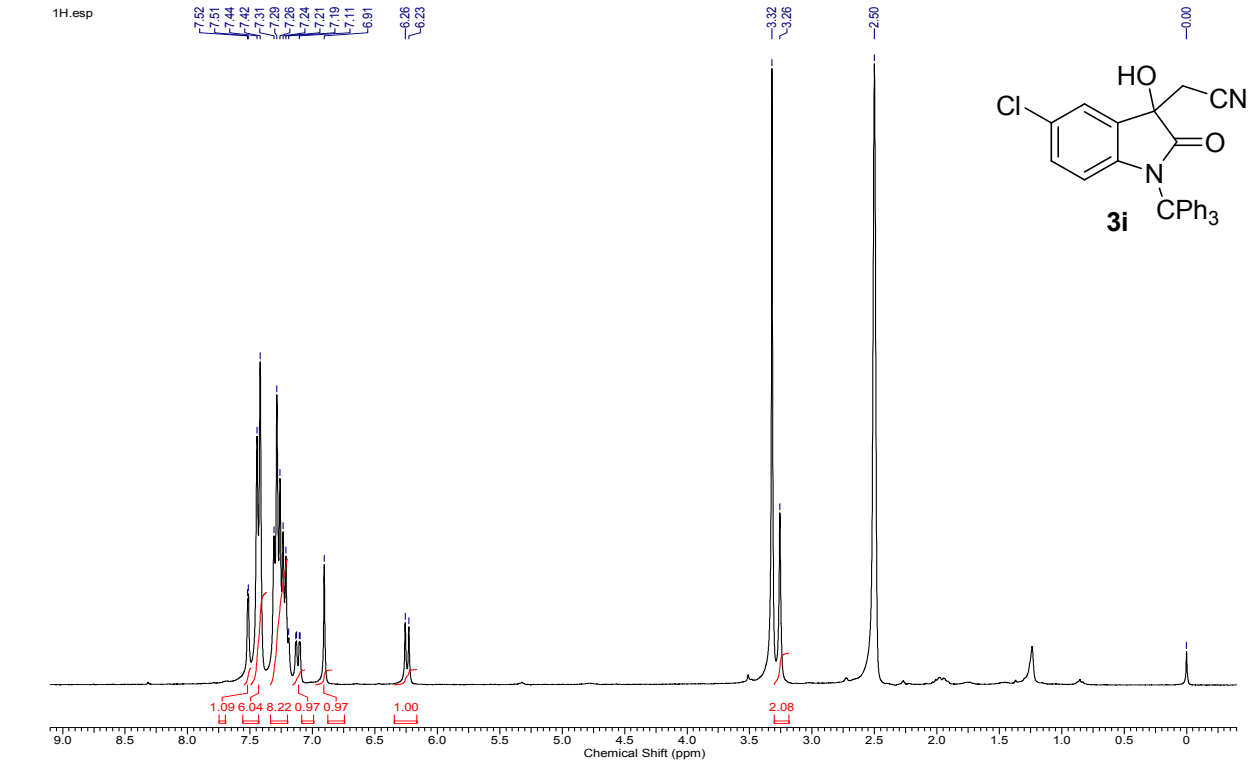

13C.esp
176.70
141.84
139.75
131.43
129.66
128.74
127.64
126.70
124.15
117.09
115.30
73.59
71.89
54.87
40.34
40.06
39.79
39.51
39.23
38.96
38.68
26.69
20.29
Chemical Shift (ppm)

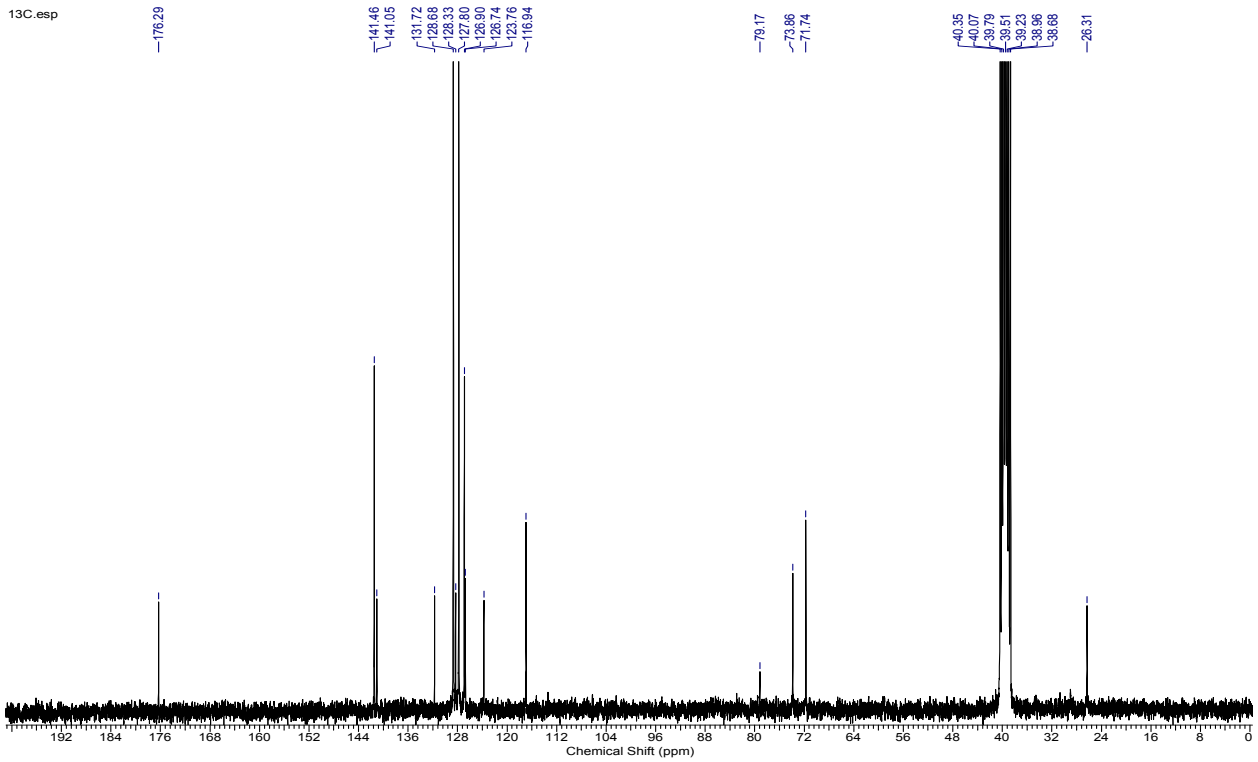

1H.esp
7.47
7.44
7.30
7.28
7.25
7.23
7.20
7.18
7.12
7.11
6.75
6.63
6.60
6.59
6.16
6.13
3.67
3.35
3.19
2.51
6.28 6.59 2.32 1.04 1.06 1.05 1.02
3.12 2.04
Chemical Shift (ppm)
HO
CN
MeO
O
N
CPh3
3g

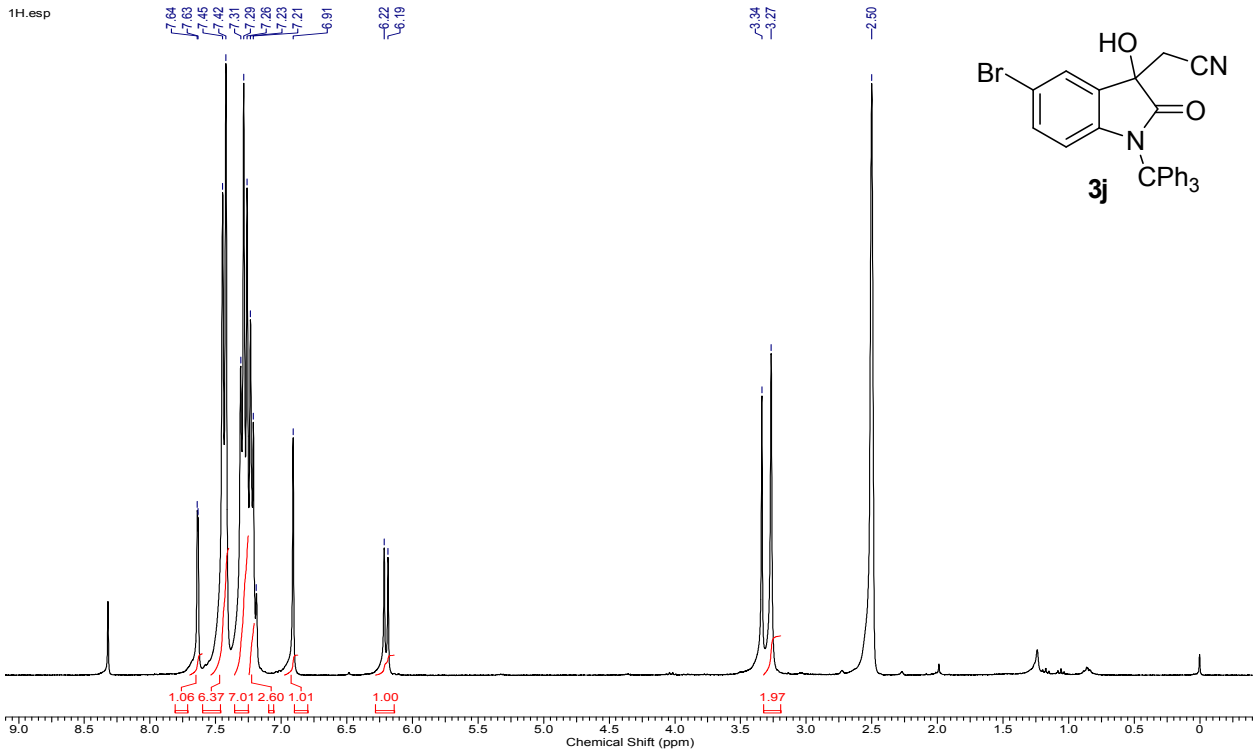

13C.esp
176.47
154.96
141.83
135.09
130.92
128.72
127.64
126.69
117.05
116.10
113.03
110.34
79.15
73.55
72.04
55.36
40.34
40.06
39.79
39.51
39.23
38.96
38.68
26.64
Chemical Shift (ppm)

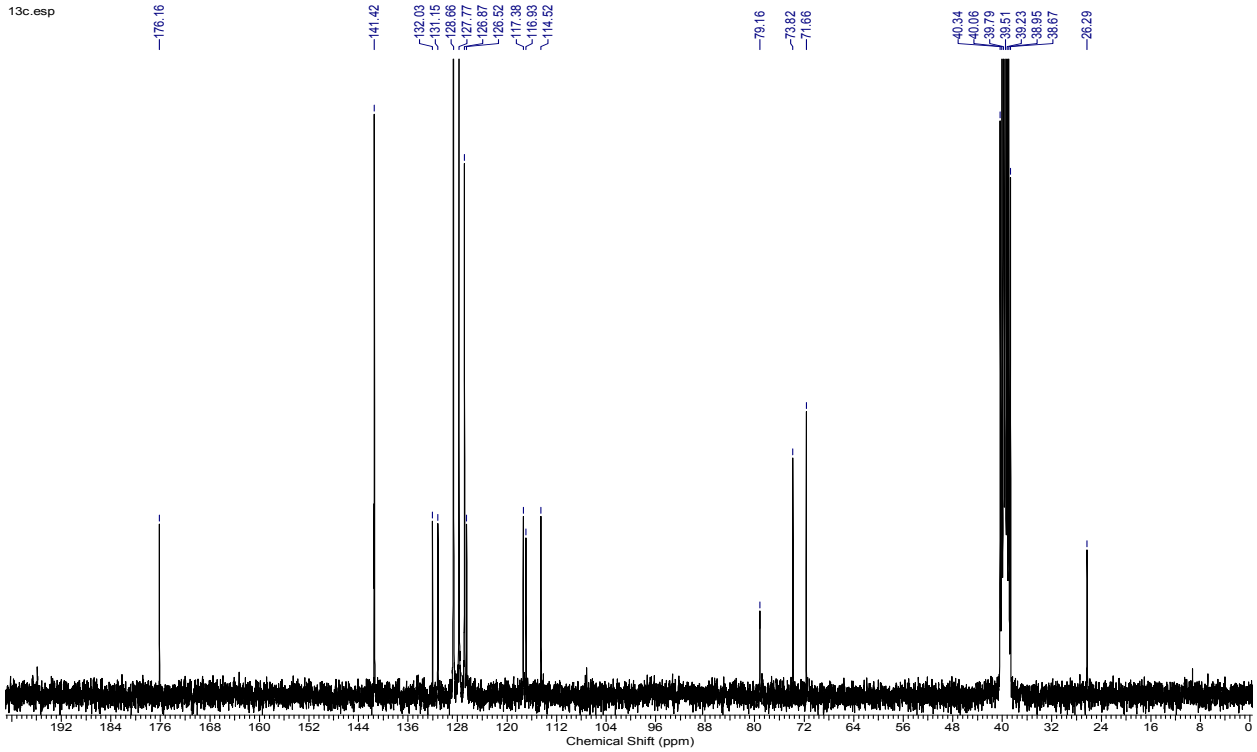

1H.esp
7.45
7.43
7.34
7.32
7.30
7.29
7.28
7.25
7.23
7.20
6.91
6.90
6.25
6.24
6.22
6.21
3.34
3.24
2.50
2.49
HO
CN
F
O
N
CPh3
3h
6.39
7.21
2.54
1.98
1.00
1.85
Chemical Shift (ppm)

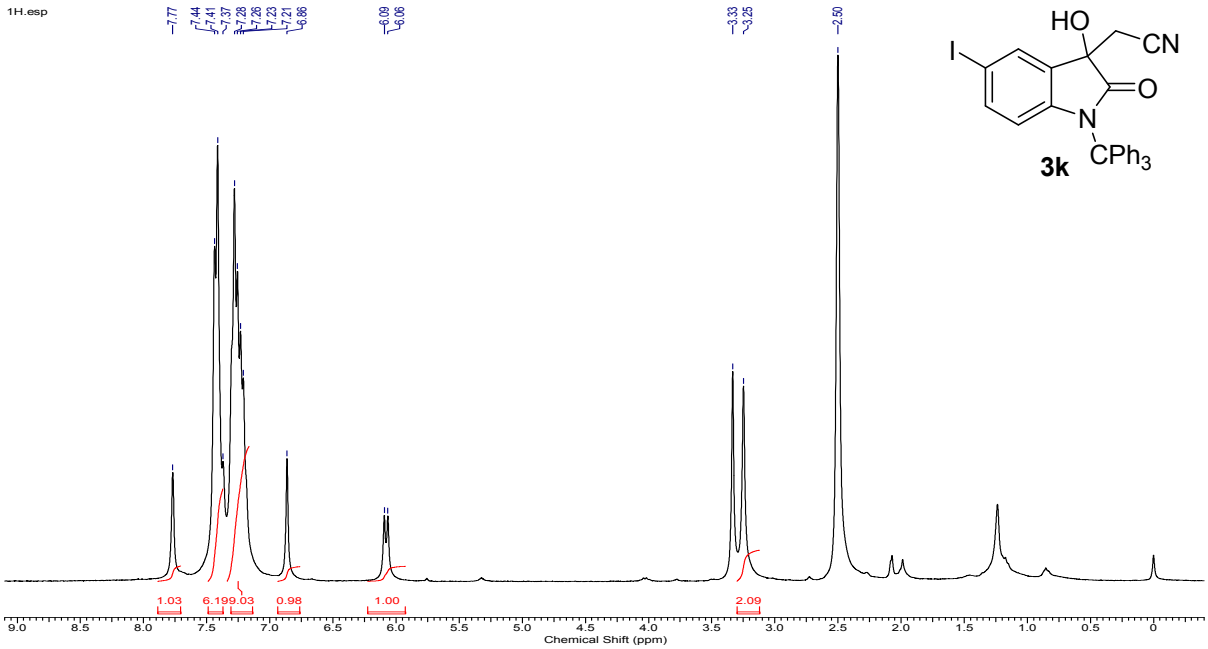

13C.esp
176.55
159.55
156.37
141.58
138.27
138.24
131.64
131.54
128.71
127.78
126.87
116.95
116.66
116.56
115.09
114.79
111.48
111.16
73.77
71.89
40.35
40.07
39.79
39.51
39.23
38.96
38.68
26.41
Chemical Shift (ppm)

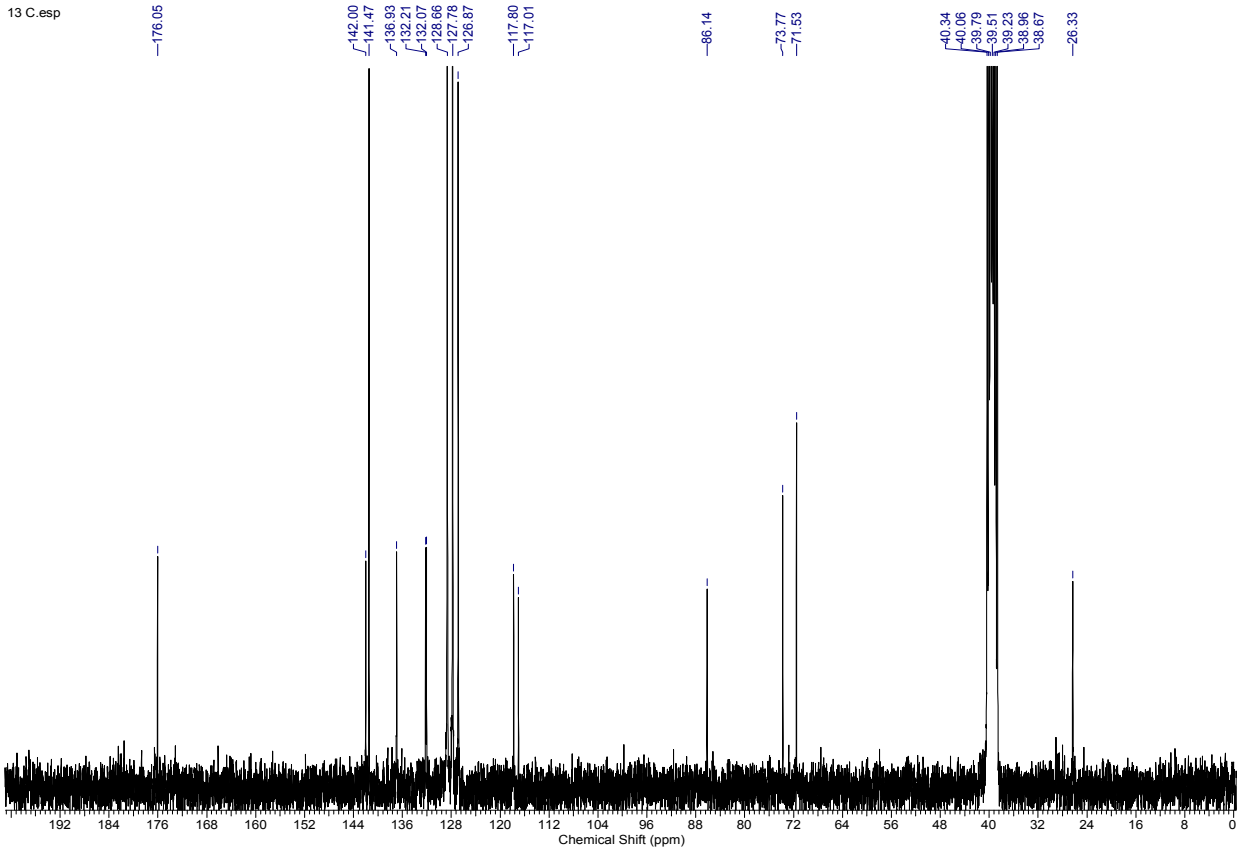

1H.esp
7.52
7.51
7.44
7.42
7.31
7.29
7.26
7.24
7.21
7.19
7.11
6.91
6.26
6.23
3.32
3.26
2.50
0.00
1.09 6.04 8.22 0.97 0.97
1.00
2.08
Chemical Shift (ppm)
HO
CN
Cl
O
N
CPh3
3i

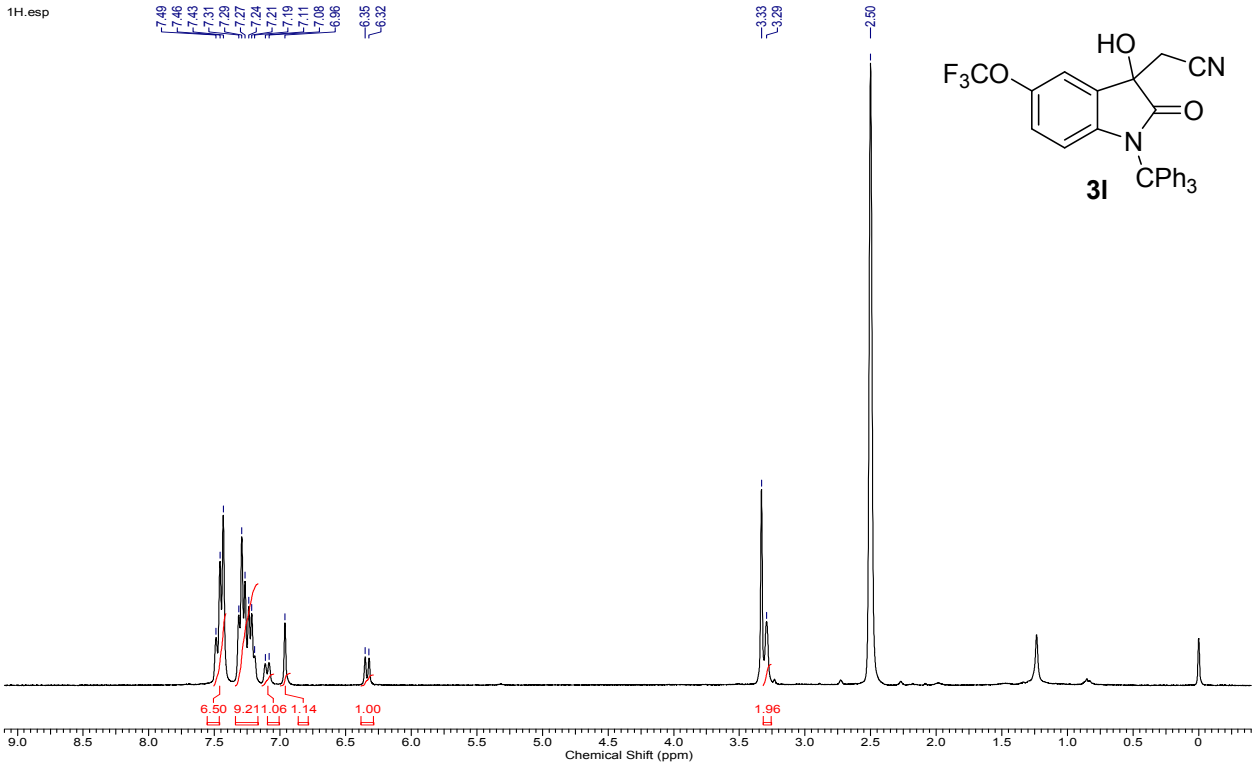

13C.esp
176.29
141.46
141.05
131.72
128.68
128.33
127.80
126.90
126.74
123.76
116.94
79.17
73.86
71.74
40.35
40.07
39.79
39.51
39.23
38.96
38.68
26.31
Chemical Shift (ppm)

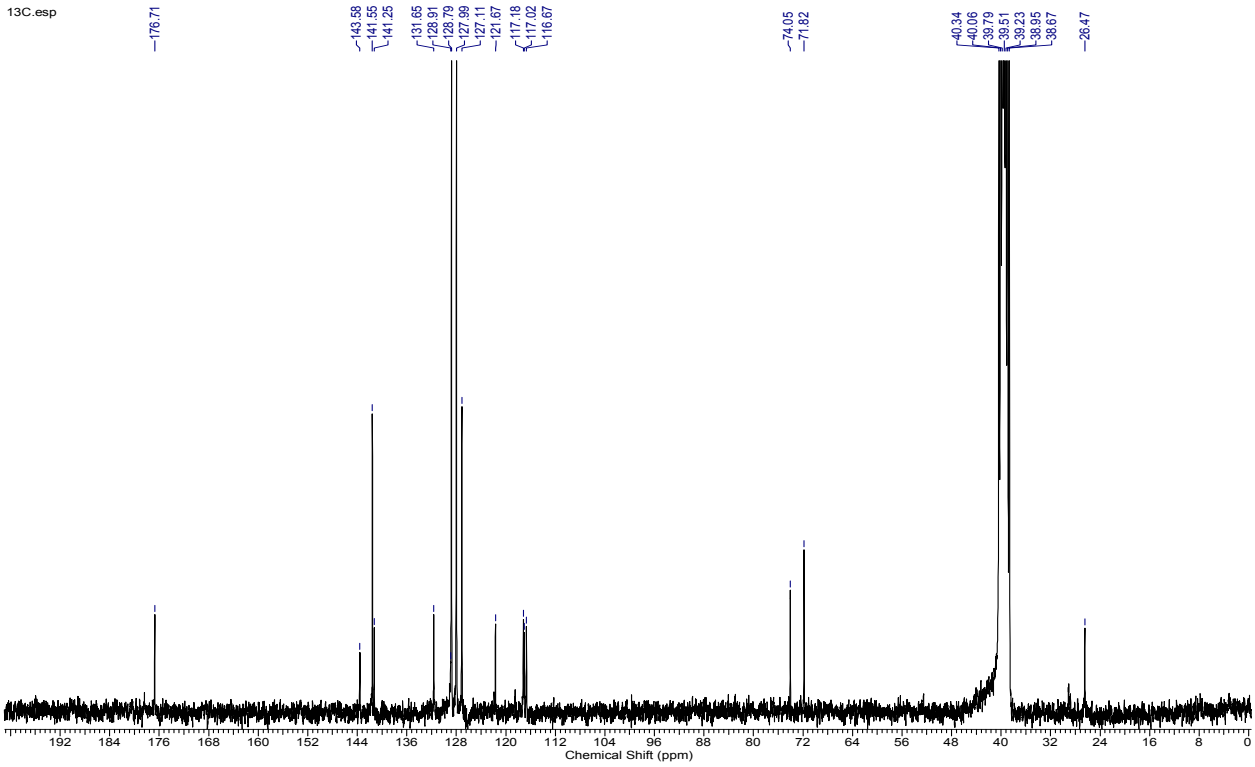

1H.esp
7.64
7.63
7.45
7.42
7.31
7.29
7.26
7.23
7.21
6.91
6.22
6.19
3.34
3.27
2.50
HO
CN
Br
O
N
CPh3
3j
1.06 6.37 7.01 2.60 1.01
1.00
1.97
Chemical Shift (ppm)

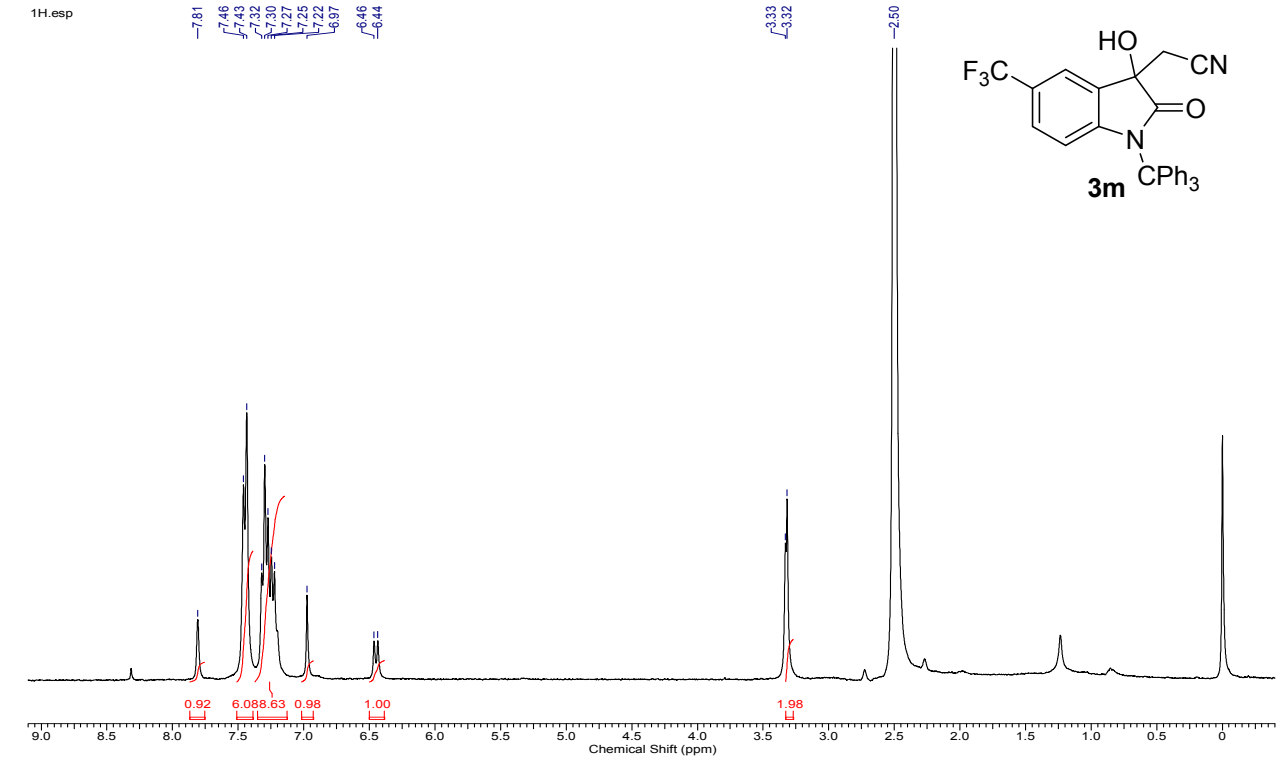

13c.esp
176.16
141.42
132.03
131.15
128.86
127.77
126.87
126.52
117.38
116.83
114.52
79.16
73.82
71.66
40.34
40.06
39.79
39.51
39.23
38.95
38.67
26.29
Chemical Shift (ppm)

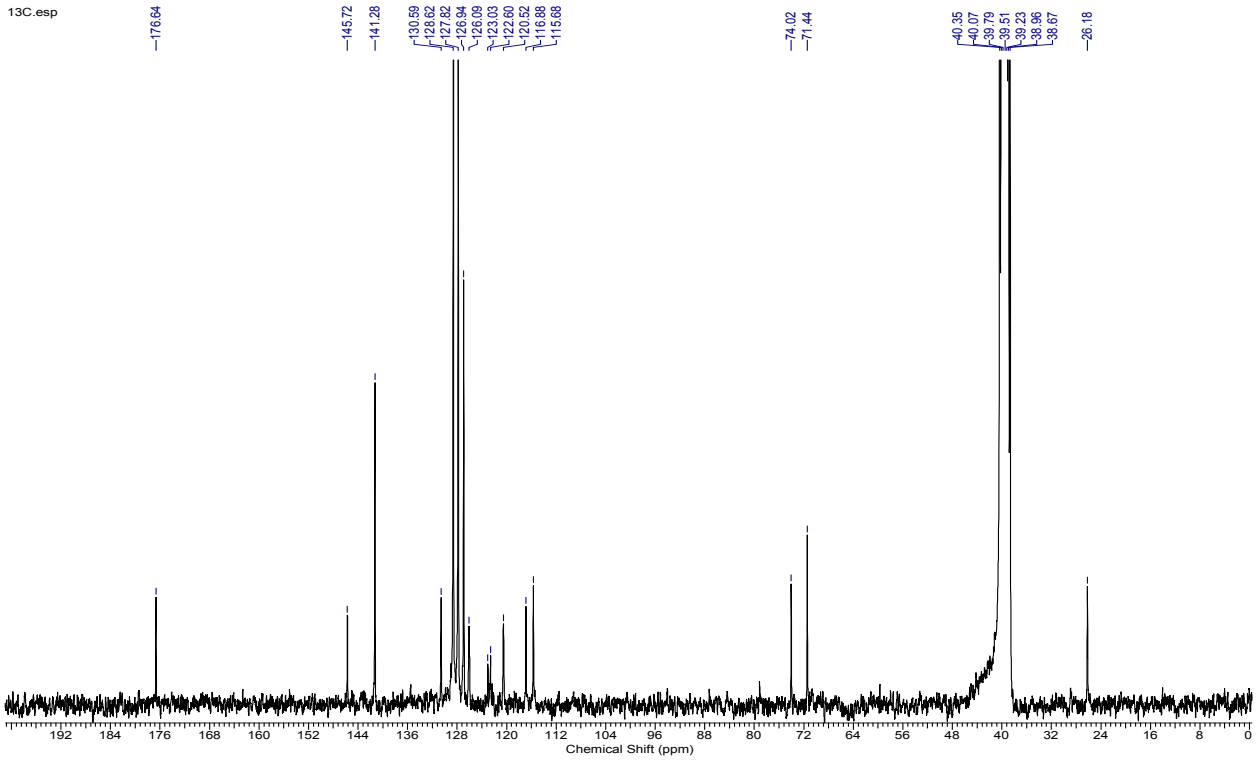

1H.esp
7.77
7.44
7.41
7.37
7.28
7.26
7.23
7.21
6.86
6.09
6.06
3.33
3.25
2.50
HO
CN
I
O
N
CPh3
3k
1.03
6.19
9.03
0.98
1.00
2.09
Chemical Shift (ppm)

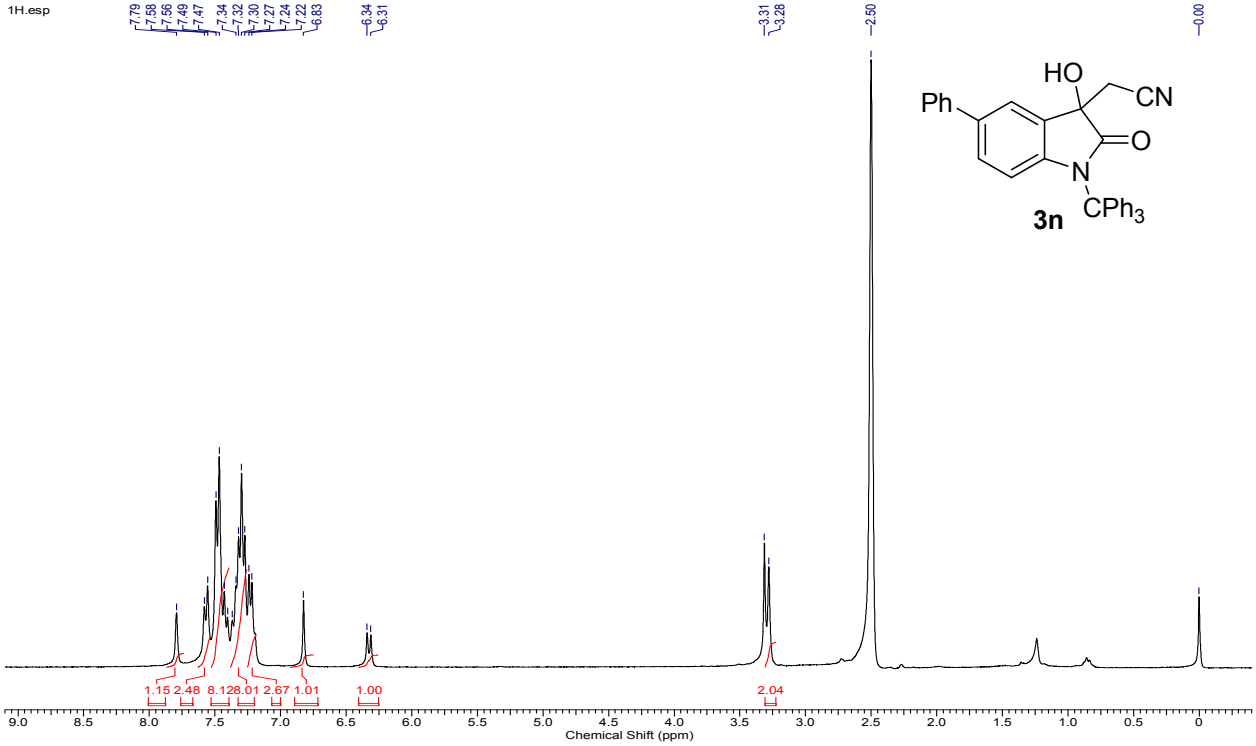

13 C.esp
176.05
142.00
141.47
136.93
132.21
132.07
128.66
127.78
126.87
117.80
117.01
86.14
73.77
71.53
40.34
40.06
39.79
39.51
39.23
38.96
38.67
26.33
Chemical Shift (ppm)

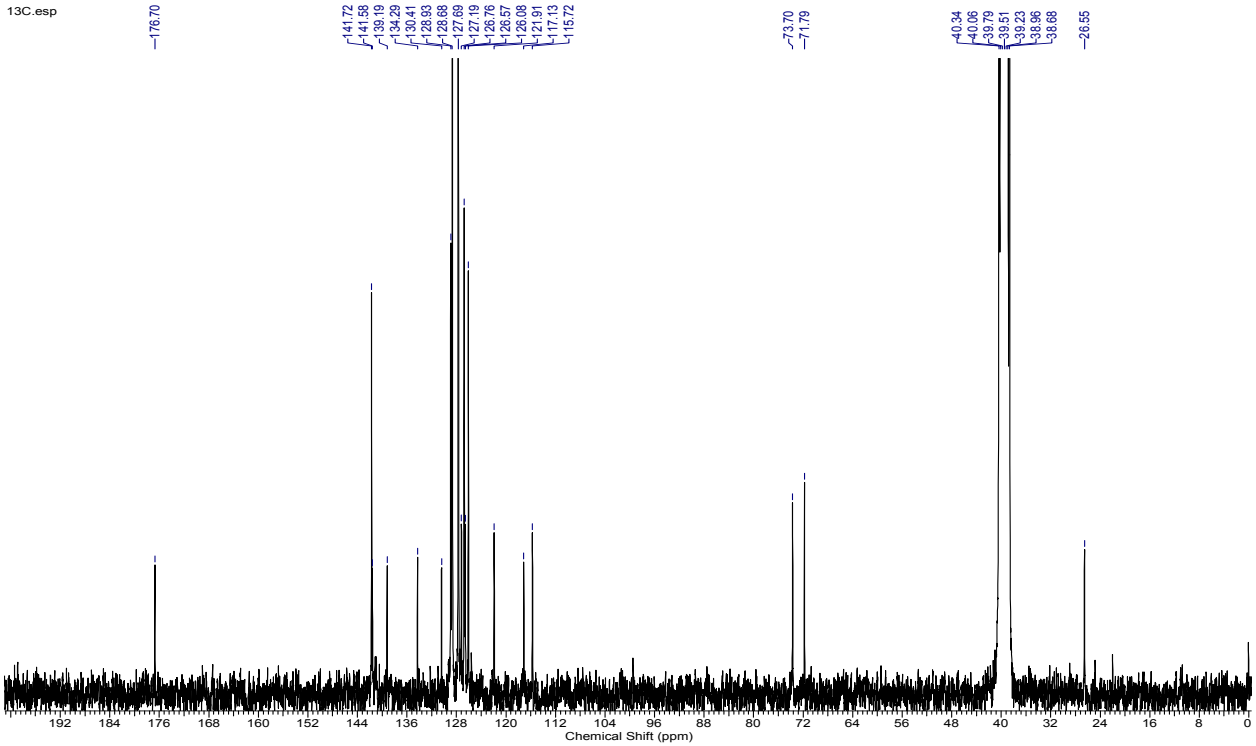

1H.esp
7.49
7.46
7.43
7.31
7.29
7.27
7.24
7.21
7.19
7.11
7.08
6.96
6.35
6.32
3.33
3.29
2.50
6.50
9.21
1.06
1.14
1.00
1.96
Chemical Shift (ppm)
HO
CN
F3CO
O
N
CPh3
3l

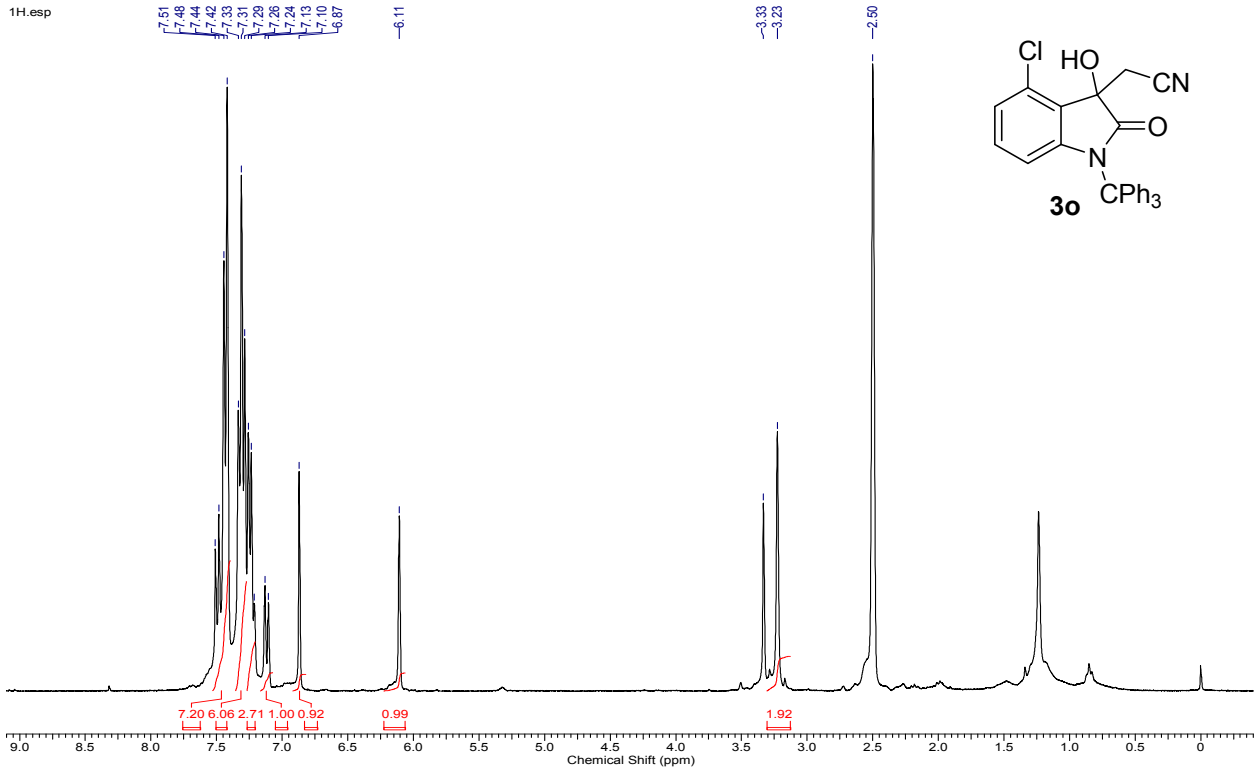

13C.esp
176.71
143.58
141.55
141.25
131.65
128.91
128.79
127.99
127.11
121.67
117.18
117.02
116.67
74.05
71.82
40.34
40.06
39.79
39.51
39.23
38.95
38.67
26.47
Chemical Shift (ppm)

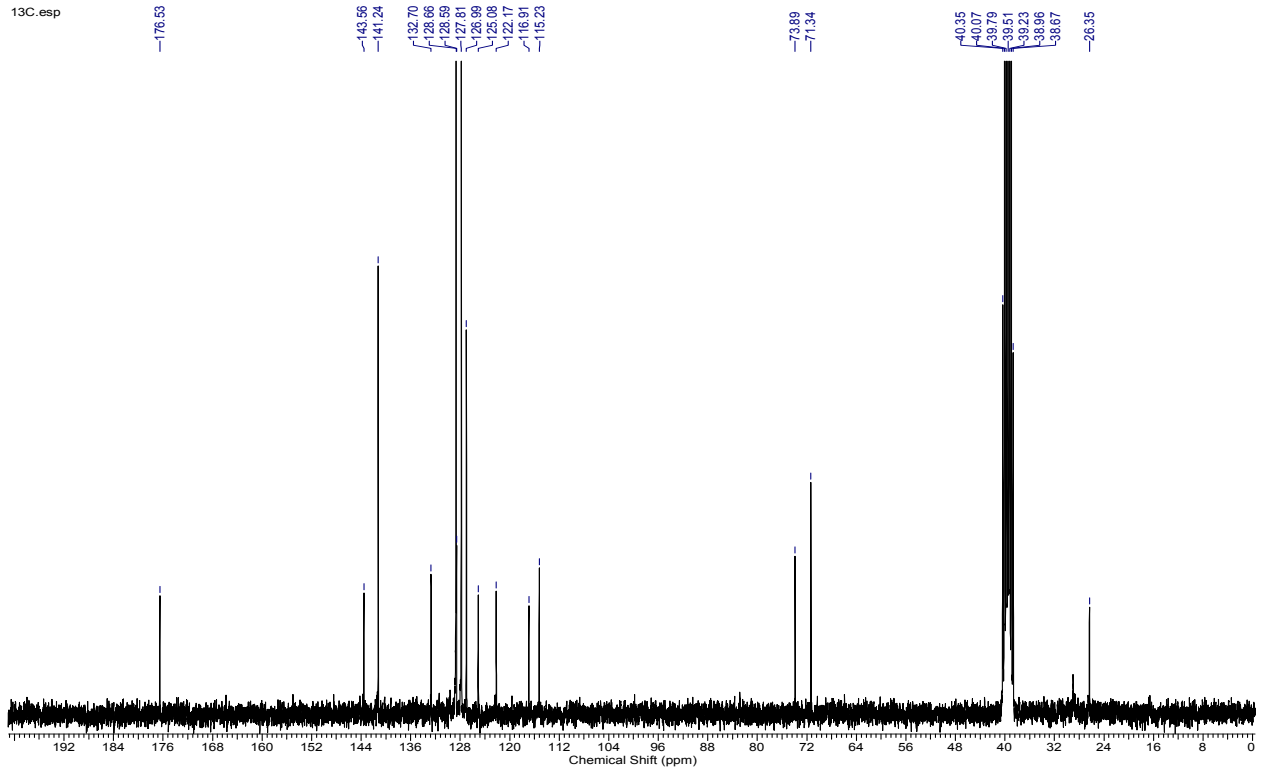

1H.esp
7.81
7.46
7.43
7.32
7.30
7.27
7.25
7.22
6.97
6.46
6.44
3.33
3.32
2.50
HO
CN
F3C
O
N
CPh3
3m
0.92
6.08
8.63
0.98
1.00
1.98
Chemical Shift (ppm)

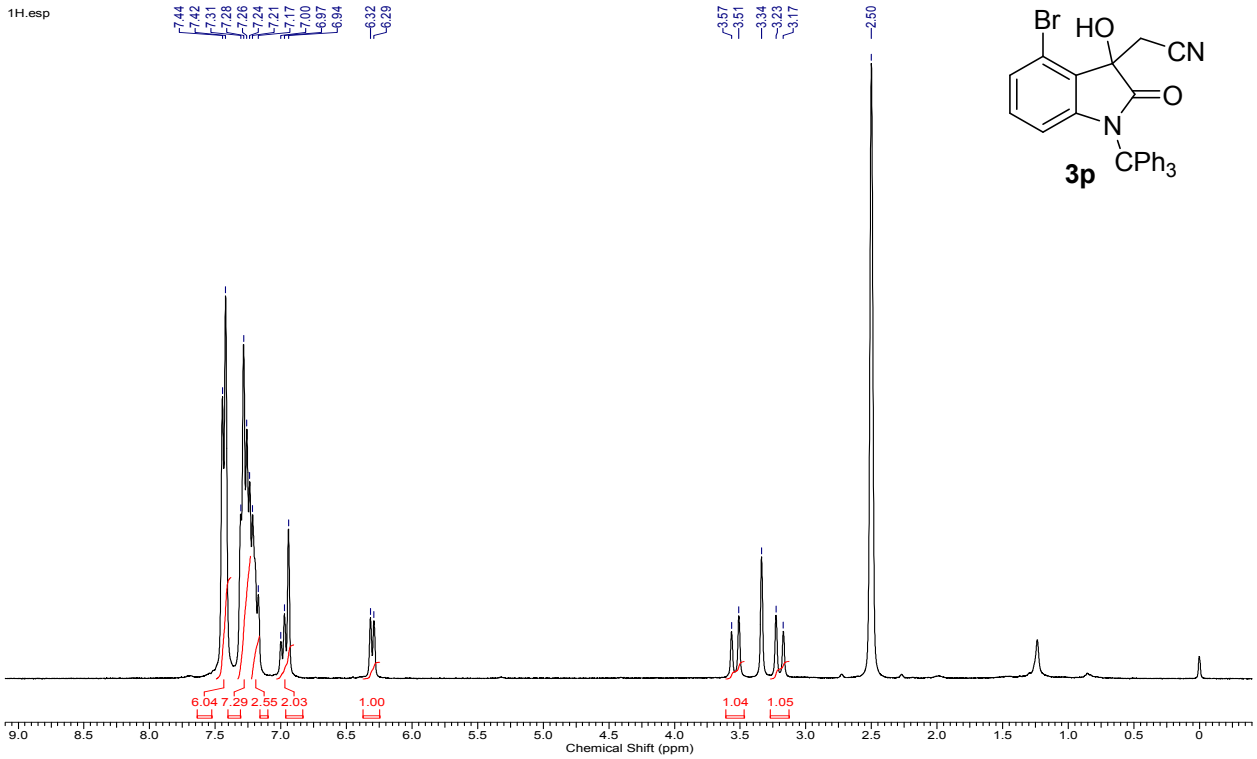

13C.esp
176.64
145.72
141.28
130.59
128.62
127.82
126.94
126.09
123.03
122.60
120.52
116.88
115.68
74.02
71.44
40.35
40.07
39.79
39.51
39.23
38.96
38.67
26.18
Chemical Shift (ppm)

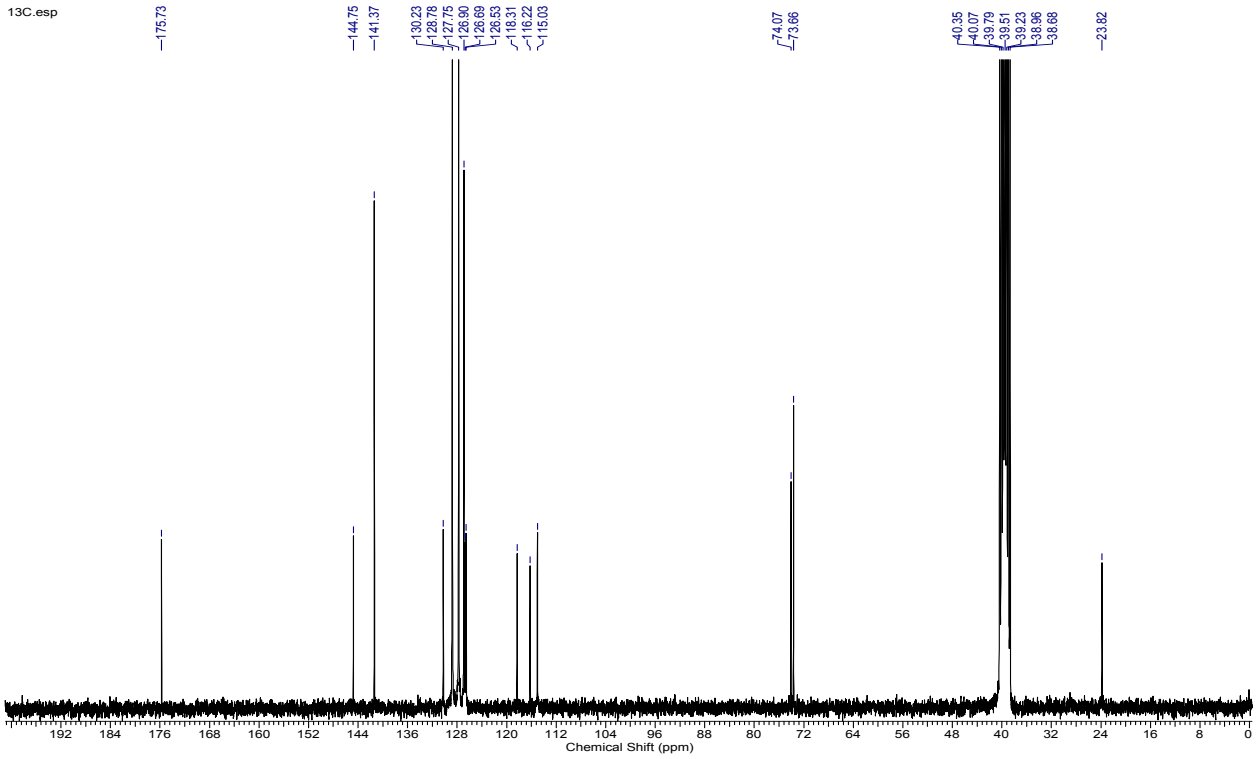

1H.esp
7.79
7.58
7.56
7.49
7.47
7.34
7.32
7.30
7.27
7.24
7.22
6.83
6.34
6.31
3.31
3.28
2.50
0.00
HO
CN
Ph
O
N
CPh3
3n
1.15 2.48 8.12 8.01 2.67 1.01
1.00
2.04
Chemical Shift (ppm)

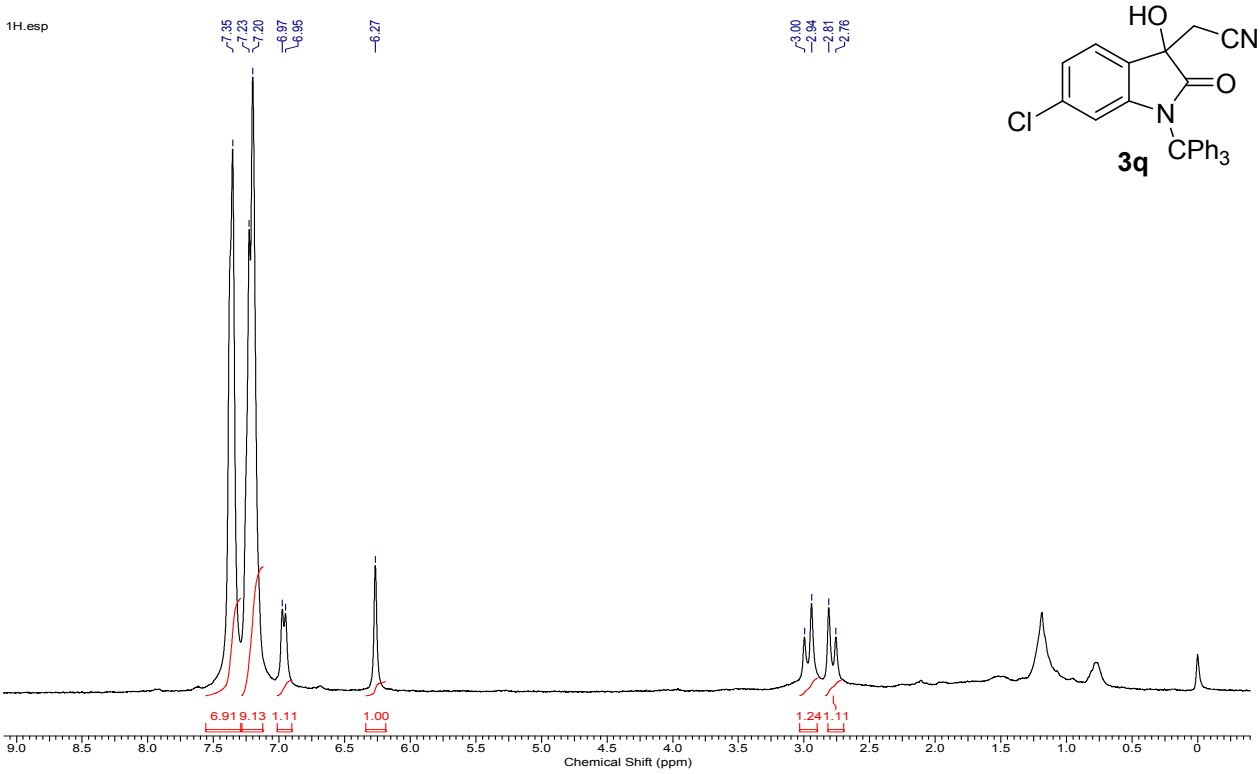

13C.esp
176.70
141.72
141.58
139.19
134.29
130.41
128.93
128.68
127.69
127.19
126.76
126.57
126.08
121.91
117.13
115.72
73.70
71.79
40.34
40.06
39.79
39.51
39.23
38.96
38.68
26.55
Chemical Shift (ppm)


1H.esp
7.51
7.48
7.44
7.42
7.33
7.31
7.29
7.26
7.24
7.13
7.10
6.87
6.11
3.33
3.23
2.50
Cl
HO
CN
O
N
CPh3
3o
7.20 6.06 2.71 1.00 0.92
0.99
1.92
Chemical Shift (ppm)


13C.esp
176.53
143.56
141.24
132.70
128.66
128.59
127.81
126.99
125.08
122.17
116.91
115.23
73.89
71.34
40.35
40.07
39.79
39.51
39.23
38.96
38.67
26.35
Chemical Shift (ppm)

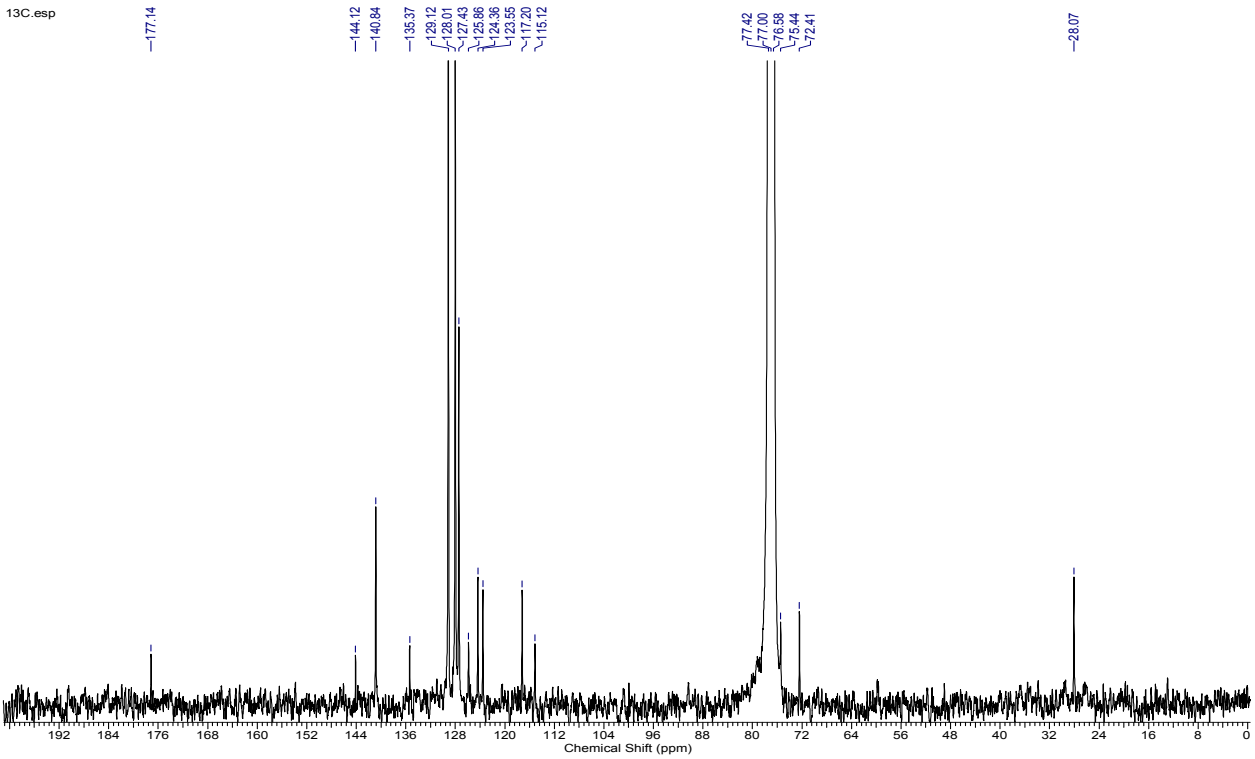

1H.esp
7.44
7.42
7.31
7.28
7.26
7.24
7.21
7.17
7.00
6.97
6.94
6.32
6.29
3.57
3.51
3.34
3.23
3.17
2.50
Br
HO
CN
O
N
CPh3
3p
6.04 7.29 2.55 2.03
1.00
1.04
1.05
Chemical Shift (ppm)

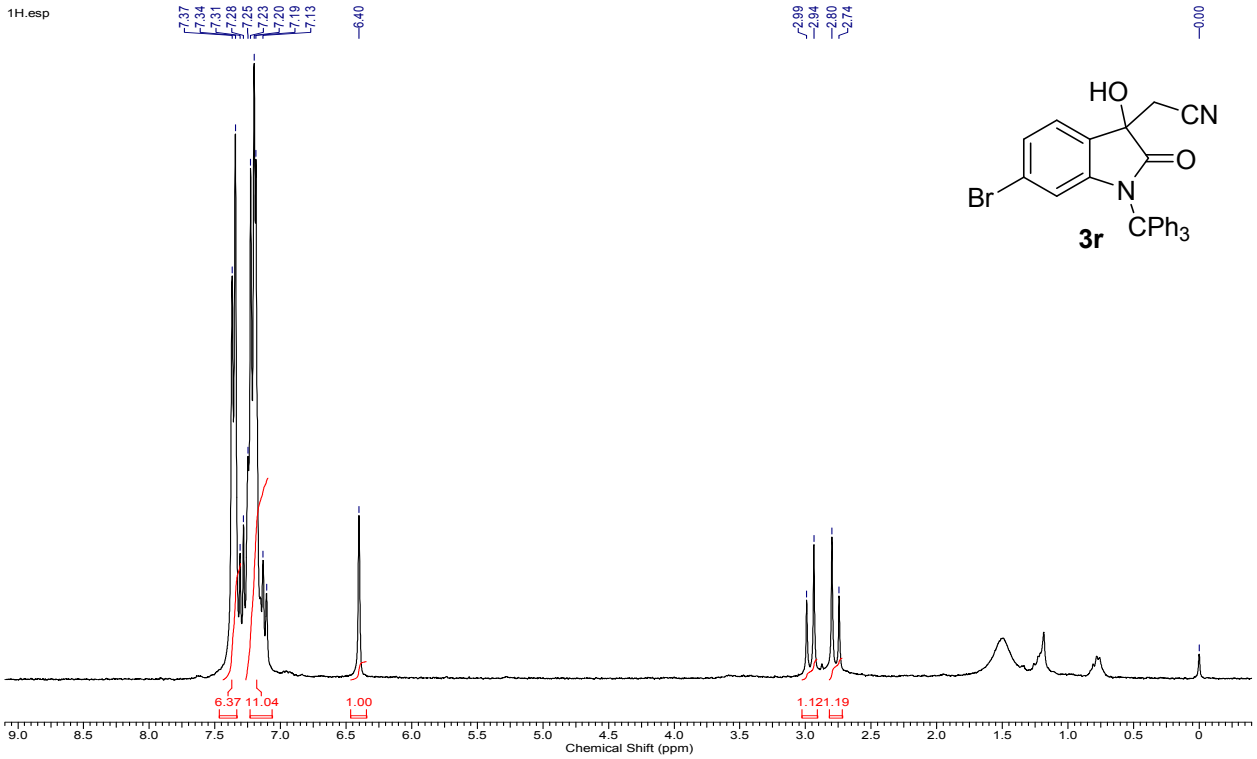

13C.esp
175.73
144.75
141.37
130.23
128.78
127.75
126.90
126.69
126.53
118.31
116.22
115.03
74.07
73.66
40.35
40.07
39.79
39.51
39.23
38.96
38.68
23.82
Chemical Shift (ppm)

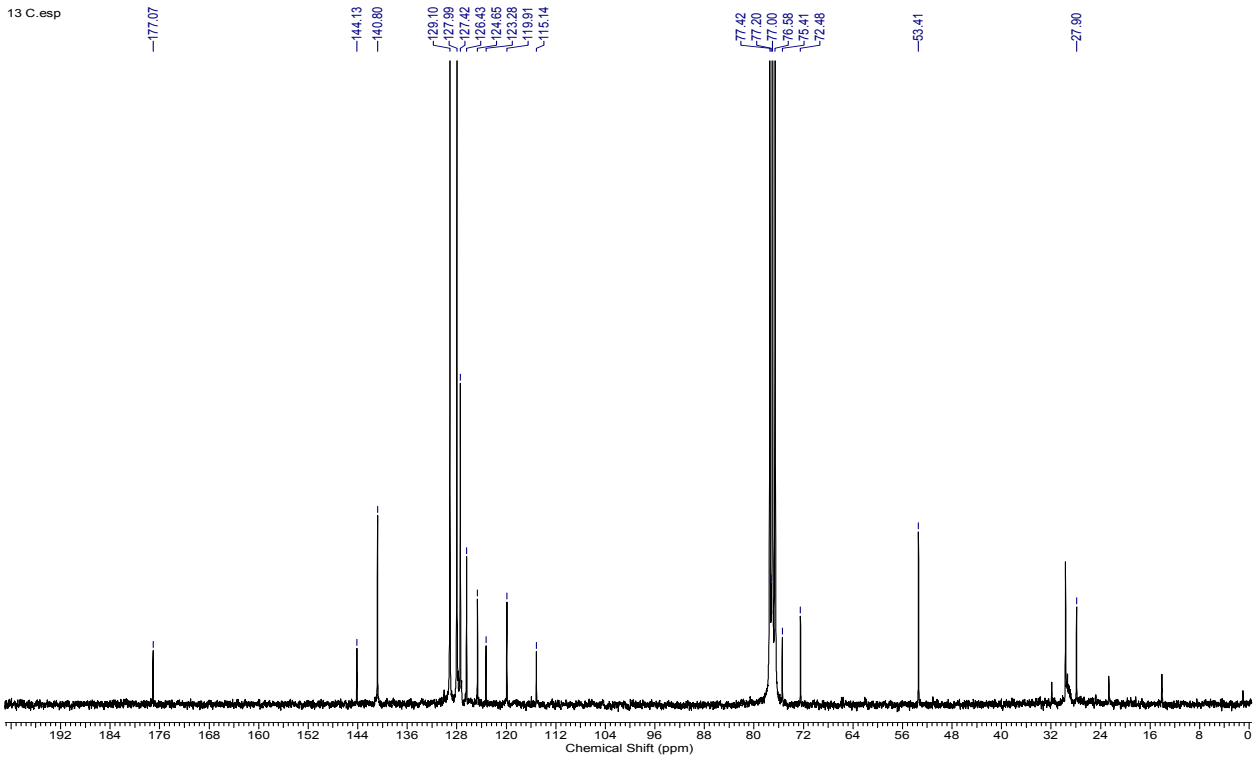

1H.esp
7.35
7.23
7.20
6.97
6.95
6.27
3.00
2.94
2.81
2.76
6.91 9.13 1.11 1.00 1.24 1.11
Chemical Shift (ppm)

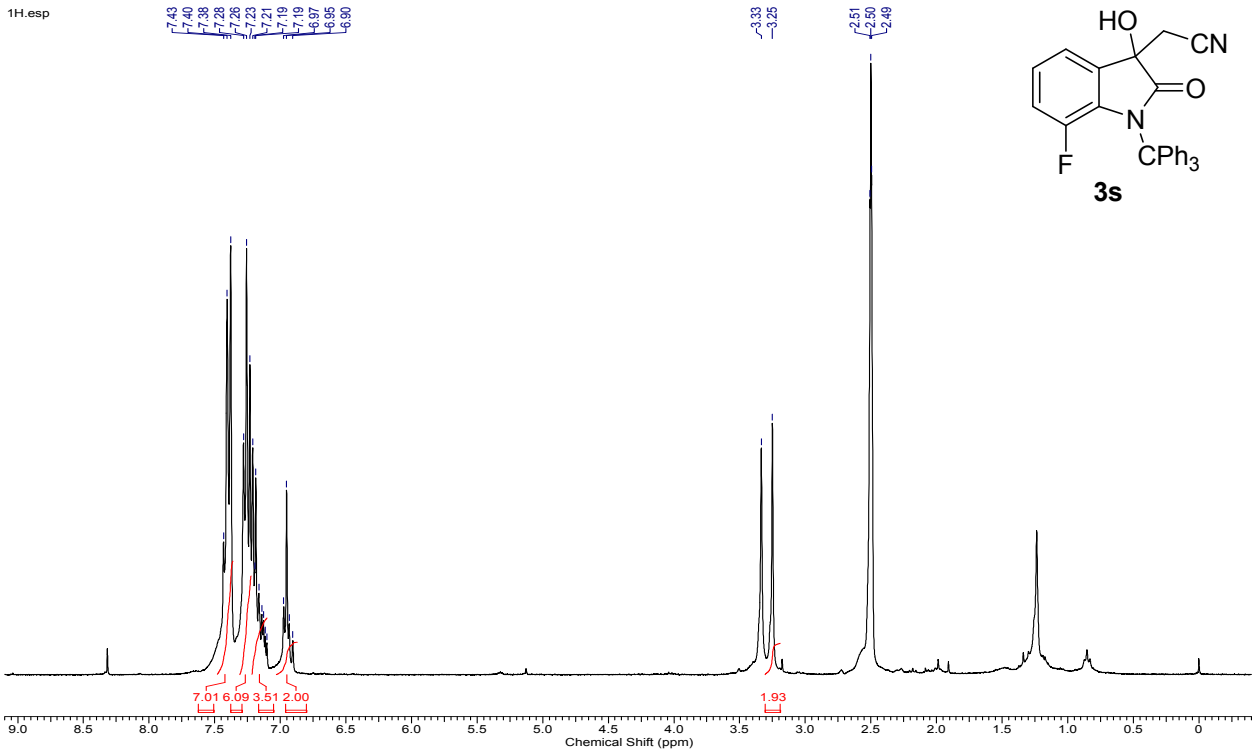
HO
CN
O
N
Cl
CPh3

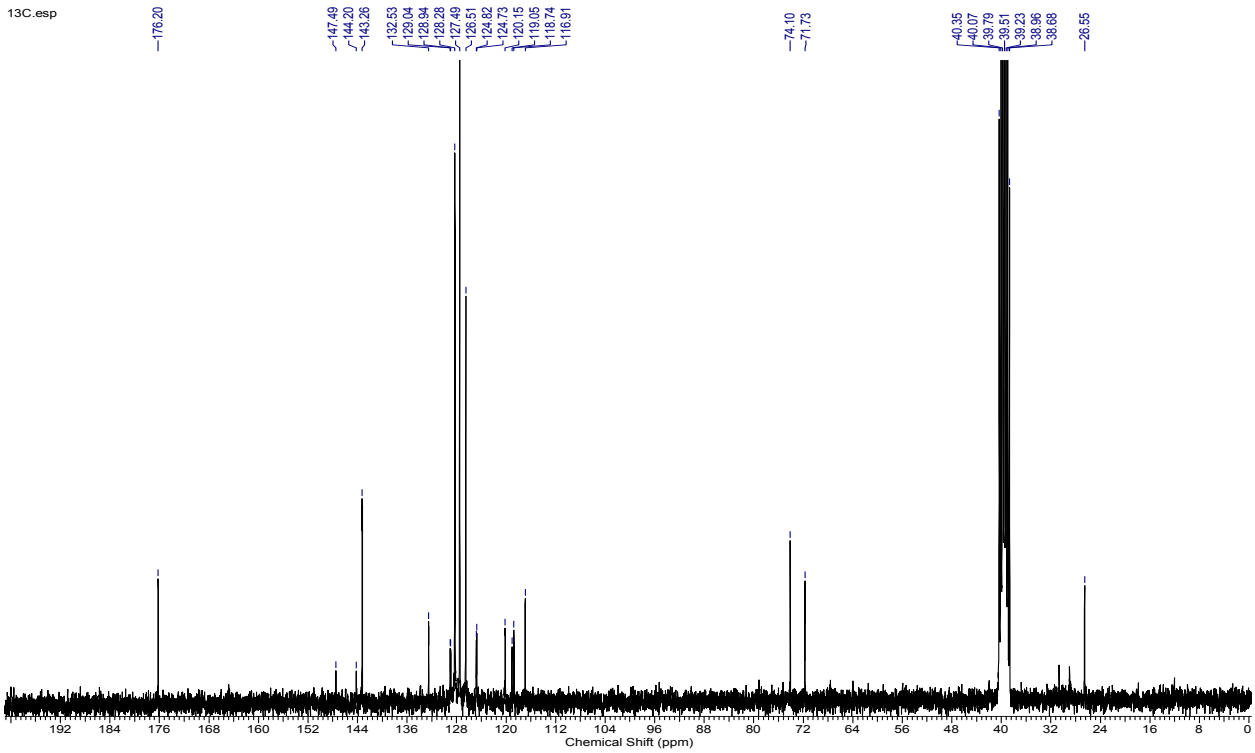
3q

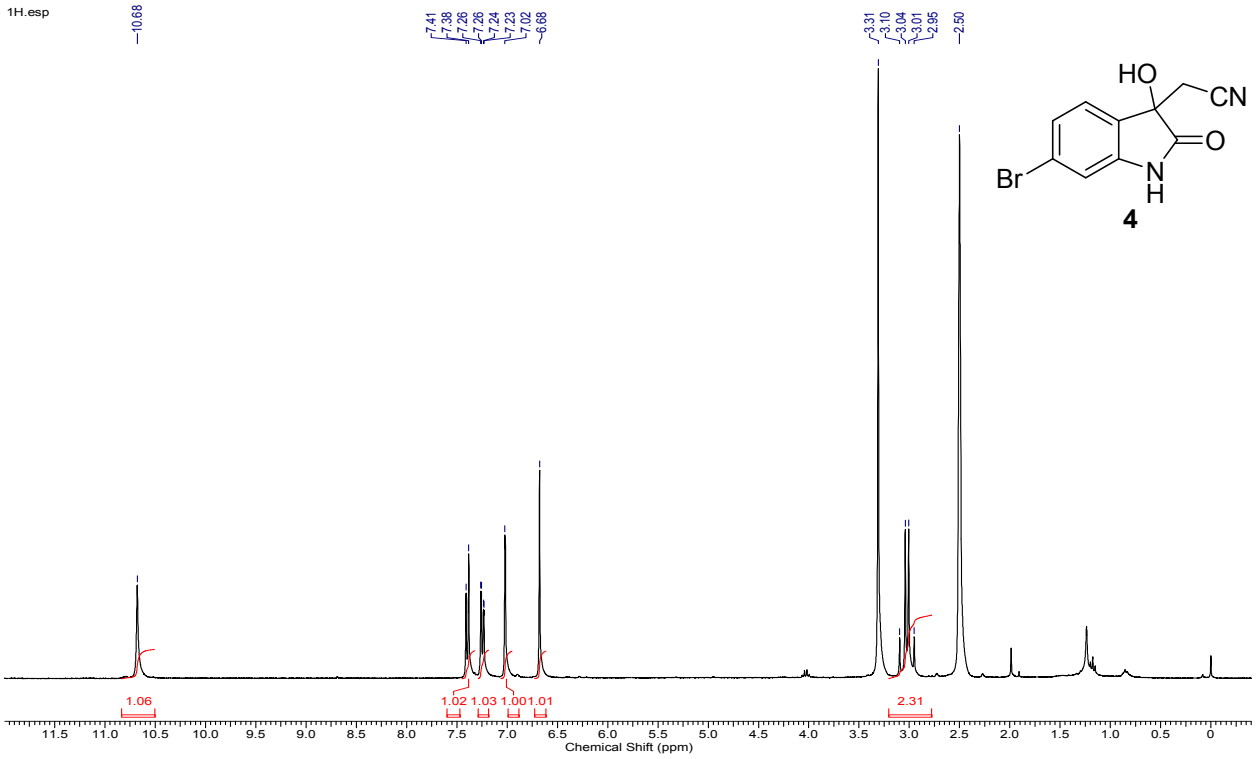

13C.esp
177.14
144.12
140.84
135.37
129.12
128.01
127.43
125.86
124.36
123.55
117.20
115.12
77.42
77.00
76.58
75.44
72.41
28.07
Chemical Shift (ppm)

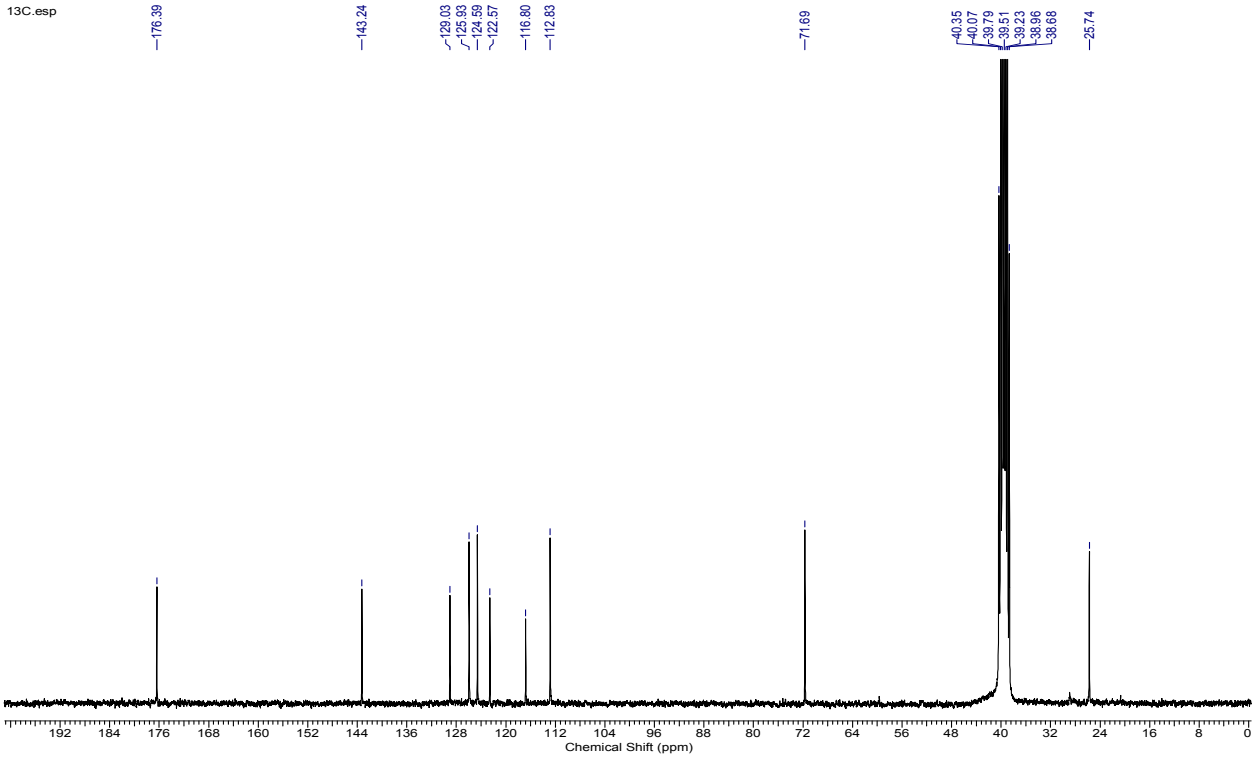

1H.esp
7.37
7.34
7.31
7.28
7.25
7.23
7.20
7.19
7.13
6.40
2.99
2.94
2.80
2.74
0.00
HO
CN
O
Br
N
CPh3
3r
6.37
11.04
1.00
1.12
1.19
Chemical Shift (ppm)

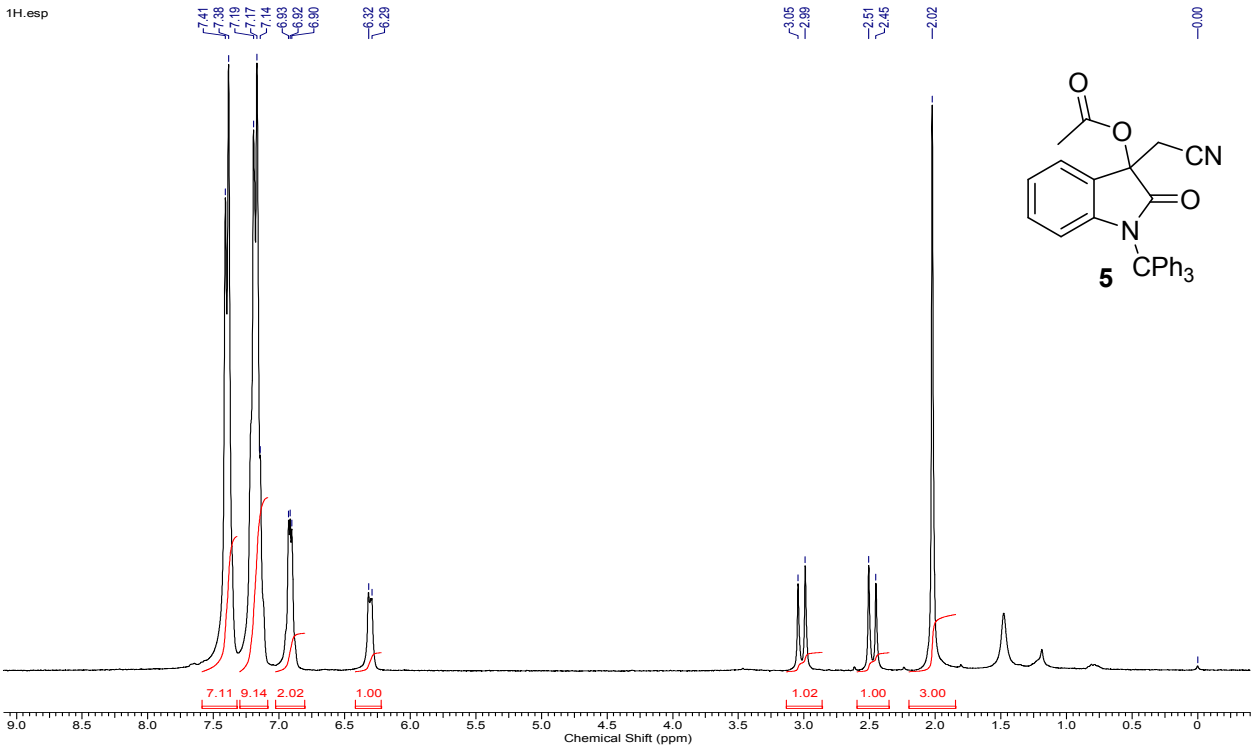

13 C.esp
177.07
144.13
140.80
129.10
127.99
127.42
126.43
124.65
123.28
119.91
115.14
77.42
77.20
77.00
76.58
75.41
72.48
53.41
27.90
Chemical Shift (ppm)

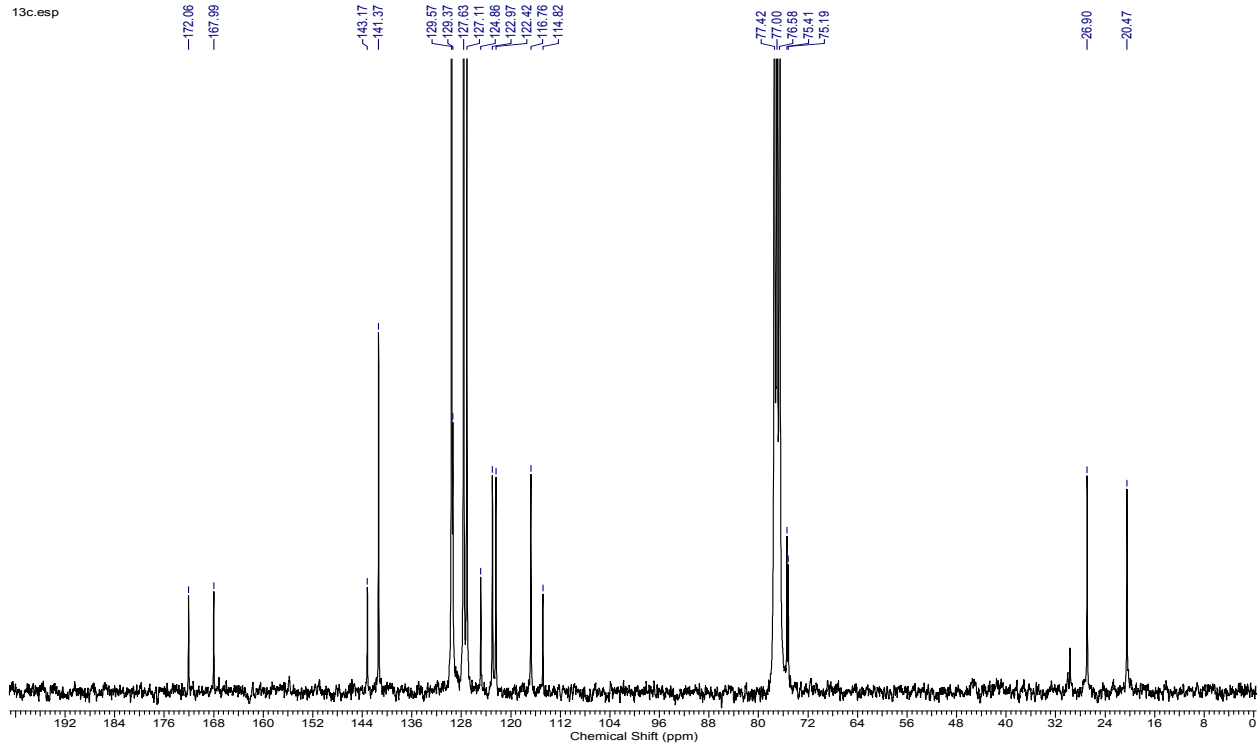

1H.esp
7.43
7.40
7.38
7.28
7.26
7.23
7.21
7.19
7.19
6.97
6.95
6.90
3.33
3.25
2.51
2.50
2.49
HO
CN
O
N
CPh3
F
3s
7.01 6.09 3.51 2.00
1.93
Chemical Shift (ppm)


13C.esp
176.20
147.49
144.20
143.26
132.53
129.04
128.94
128.28
127.49
126.51
124.82
124.73
120.15
119.05
118.74
116.91
74.10
71.73
40.35
40.07
39.79
39.51
39.23
38.96
38.68
26.55
Chemical Shift (ppm)


1H.esp
10.68
7.41
7.38
7.26
7.26
7.24
7.23
7.02
6.88
3.31
3.10
3.04
3.01
2.95
2.50
HO
CN
O
Br
N
H
4
1.06
1.02
1.03
1.00
1.01
2.31
Chemical Shift (ppm)


13C.esp
176.39
143.24
129.03
125.93
124.59
122.57
116.80
112.83
71.69
40.35
40.07
39.79
39.51
39.23
38.96
38.68
25.74
Chemical Shift (ppm)


1H.esp
7.41
7.38
7.19
7.17
7.14
6.93
6.92
6.90
6.32
6.29
3.05
2.99
2.51
2.45
2.02
0.00
7.11
9.14
2.02
1.00
1.02
1.00
3.00
Chemical Shift (ppm)
O
O
CN
O
N
CPh3
5


13c.esp
172.06
167.99
143.17
141.37
129.57
129.37
127.63
127.11
124.86
122.97
122.42
116.76
114.82
77.42
77.00
76.58
75.41
75.19
26.90
20.47
Chemical Shift (ppm)