$ZnBr_2$-mediated synthesis of indoles in a ball mill by intramolecular hydroamination of 2-alkynylanilines

Electronic Supporting information

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General information

General information: All chemicals were purchased from Sigma–Aldrich or Alfa Aesar and were used as received. Reactions were accomplished in a "Fritsch Pulverisette 7 classic line" planetary ball mill by using milling beakers (45 ml) made from hardened steel. 6 milling balls (d = 15 mm) were applied that consisted of hardened steel, respectively. ESI HRMS spectrometry was performed with an ESI-(Q)-TOFMS MICROTOF II (Bruker Daltonics GmbH) mass spectrometer. ATR-FTIR measurements were performed on a Perkin-Elmer Spectrum 100, NMR measurements on a Bruker Advance AC200 or AC400 with deuterated solvents as internal standard. Melting points were measured on a Stuart Scientific SMP10 and are uncorrected.

Representative preparation of the *o*-alkynyl anilines

A solution of 2-iodoaniline (45.7 mmol, 10 g), phenylacetylene (**1a**; 46 mmol, 4.7 g), $Pd(PPh_3)_4$ (5 mol-%) and CuI (10 mol-%) in Et_3N (150 mL) was stirred for 3 h under an argon atmosphere. The resulting mixture was extracted with EtOAc, dried over $MgSO_4$ and concentrated under vacuum. The resulting compound was purified by column chromatography and recrystallization.

2-(Phenylethynyl)aniline (**2a**):[1] yellowish needles, 85%; Mp.: 87-88 °C (*n*-hexane); Lit.: 89-91 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.44 - 7.67 (m, 2 H), 7.19 - 7.44 (m, 4 H), 7.03 - 7.19 (m, 1 H), 6.63 - 6.93 (m, 2 H), 5.00 ppm (br. s., 2 H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 145.6, 131.9, 131.2, 129.3, 128.0, 127.9, 122.8, 118.8, 115.0, 108.8, 94.7, 85.2 ppm; IR: 3459, 3367, 3065, 2206, 1606, 1494, 1308, 1251, 690 cm^{-1}.

2-(4-Tolylethynyl)aniline (**2b**):[2] yellow powder, 82%; Mp.: 104-105 °C (*n*-hexane); Lit.: 105 °C; ^{1}H NMR (acetone-D_6, 400 MHz): δ = 7.44 (d, *J* = 8.1 Hz, 2 H), 7.13 - 7.34 (m, 3 H), 7.08 (t, *J* = 7.5 Hz, 1 H), 6.78 (d, *J* = 8.4 Hz, 1 H), 6.59 (t, *J* = 7.3 Hz, 1 H), 5.10 (br. s., 2 H), 2.34 ppm (s, 3 H); ^{13}C NMR (acetone-D_6, 101 MHz): δ = 150.2, 139.0, 132.6, 132.0, 130.4, 130.0, 121.4, 117.3, 114.8, 107.7, 95.0, 86.5, 21.4 ppm; IR: 3474, 3373, 3026, 2919, 2205, 1609, 1488, 1310, 815 cm^{-1}.

2-(2-Pyridinylethynyl)aniline (**2c**):[3] yellow needles, 57%; Mp.: 110-112 °C (*n*-hexane); Lit.: 113-115 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.58 (d, *J* = 3.7 Hz, 1 H), 7.60 - 7.79 (m, 1 H), 7.44 - 7.60 (m, 1 H), 7.31 - 7.44 (m, 1 H), 7.18 - 7.31 (m, 1 H), 7.14 (t, *J*=7.7 Hz, 1 H), 6.59 - 6.81 (m, 2 H), 4.58 ppm (br. s., 2 H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 149.5, 148.7, 143.2, 136.5, 132.6, 130.6, 127.0, 122.6, 117.7, 114.4, 106.3, 93.7, 87.1 ppm; IR: 3379, 3306, 2207, 1636, 1558, 1454, 772 cm^{-1}.

2-Decynylaniline (**2d**): yellow oil, 90%; ^{1}H NMR ($CDCl_3$, 600 MHz): δ = 7.18 (d, *J* = 7.2 Hz, 1 H), 6.97 - 7.09 (m, 1 H), 6.66 (d, *J* = 8.3 Hz, 1 H), 6.62 (t, *J* = 7.4 Hz, 1 H), 4.42 (br. s., 2 H), 2.38 (t, *J* = 7.2 Hz, 2 H), 1.54 (quin, *J* = 7.4 Hz, 2 H), 1.30 - 1.43 (m, 2 H), 1.01 - 1.30 (m, 8 H), 0.81 ppm (t, *J* = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 151 MHz): δ = 146.8, 132.1, 128.8, 118.4, 114.7, 109.6, 96.1, 77.3, 31.9, 29.2, 29.2, 29.1, 29.0, 29.0, 22.7, 19.7, 14.1 ppm; IR: 3471, 3380, 2927, 2854, 1734, 1611, 1492, 1456, 1305.

2-(Trimethylsilylethynyl)aniline (**2e**):[4] yellowish oil, 85%; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.29 (d, *J* = 7.3 Hz, 8 H), 7.10 (t, *J* = 7.7 Hz, 7 H), 6.53 - 6.77 (m, 14 H), 4.40 (br. s., 9 H), 0.27 ppm (s, 62 H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ = 148.2, 132.2, 129.8, 117.7, 114.1, 107.7, 101.8, 99.7, 0.1 ppm; IR: 3482, 3385, 2959, 2145, 1613, 1490, 1249, 745 cm^{-1}.

Representative procedure for the indole synthesis in a ball mill

The milling beakers (V = 45 ml, hardened steel) were filled with six milling balls (d = 15 mm, hardened steel) and afterwards NaCl (7 g), 2-(phenylethynyl)aniline (**2a**; 1 mmol, 193 mg) and $ZnBr_2$ (1 mmol, 225 mg) were added sequentially. Milling was performed at 800 rpm for 30 min. After cooling to room temperature, the crude products were extracted with ethyl acetate (50 ml). The resulting filtrate was analyzed by GC-FID and GC-MS. To isolate the products, the ethyl acetate is evaporated in vacuo and the crude product is purified by column chromatography and recrystallization.

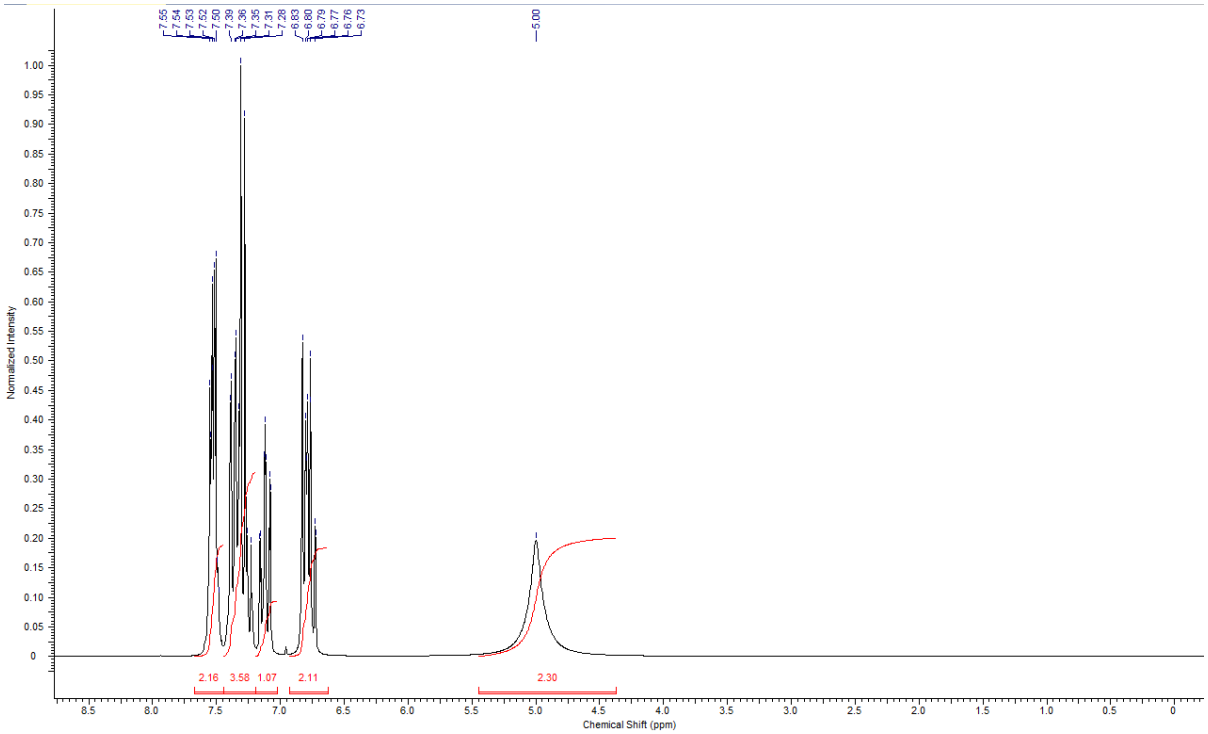
2-Phenyl-1*H*-indole (**3a**):[5] white solid, 82%; Mp.: 186-187 °C (*n*-hexane); Lit.: 187-188 °C; ^{1}H NMR (acetone-D_6, 400 MHz): δ = 10.75 (br. s., 1 H), 7.88 (d, *J* = 7.3 Hz, 2 H), 7.58 (d, *J* = 7.9 Hz, 1 H), 7.39 - 7.52 (m, 3 H), 7.32 (t, *J* = 7.4 Hz, 1 H), 7.12 (t, *J* = 8.0 Hz, 1 H), 7.04 (t, *J* = 7.8 Hz, 1 H), 6.91 ppm (d, *J* = 1.2 Hz, 1 H); ^{13}C NMR (acetone-D_6, 101 MHz): δ = 138.0, 137.6, 132.7, 129.3, 128.9, 127.4, 125.0, 121.8, 120.2, 119.6, 111.2, 99.0 ppm; IR: 3440, 3049, 1480, 1457, 1447, 4351, 1298, 763 cm^{-1}; HR-MS: $[C_{14}H_{11}N+H]^+$, calc. 194.0964, found 194.0974.

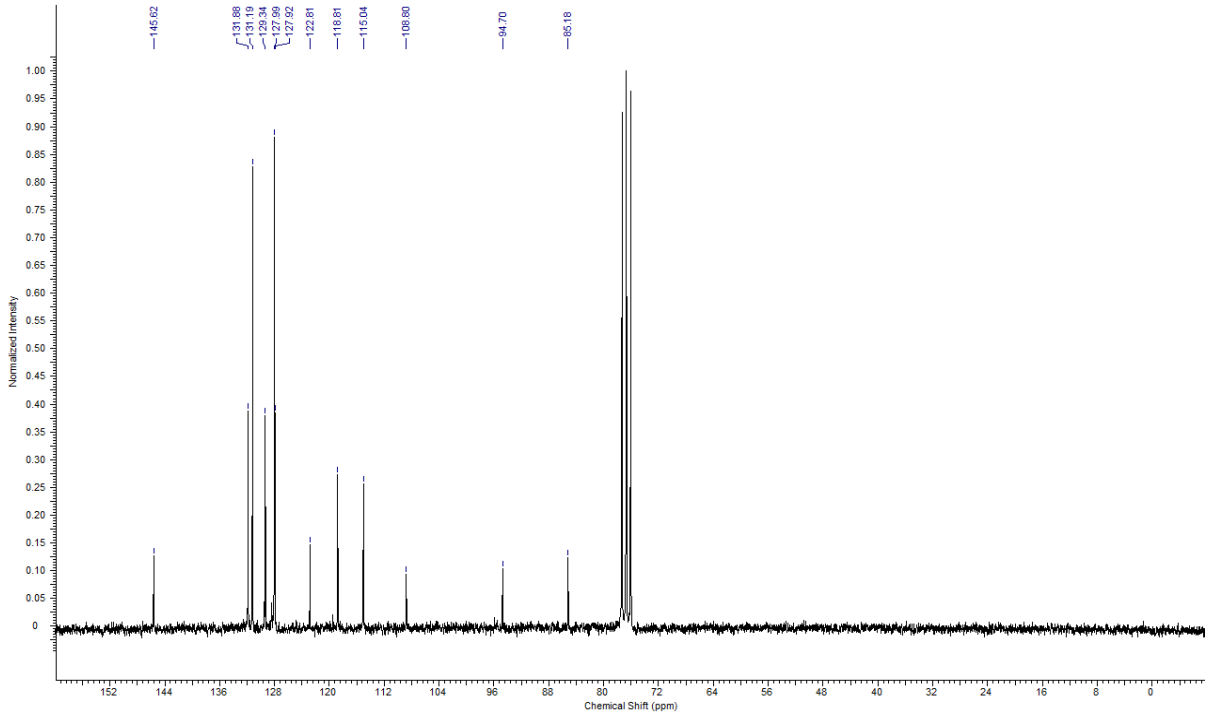
2-(4-Tolyl)-1*H*-indole (**3b**):[6] greyish solid, 80%; Mp.: 210-212 °C (*n*-hexane) Lit.: 212-213 °C; ^{1}H NMR (acetone-D_6, 400 MHz): δ = 10.68 (br. s., 1 H), 7.76 (d, *J* = 8.2 Hz, 2 H), 7.56 (d, *J* = 7.6 Hz, 1 H), 7.42 (d, *J* = 7.9 Hz, 1 H), 7.27 (d, *J* = 7.9 Hz, 2 H), 7.10 (t, *J* = 7.5 Hz, 1 H), 7.02 (t, *J* = 7.3 Hz, 1 H), 6.85 (s, 1 H), 2.36 ppm (s, 3 H); ^{13}C NMR (acetone-D_6, 101 MHz): δ = 138.1, 137.4, 137.1, 130.0, 129.5, 129.4, 125.0, 121.5, 120.1, 119.5, 111.1, 98.4, 20.3 ppm; IR: 3435, 3052, 2914, 1547, 1453, 1298, 822, 734 cm^{-1}; HR-MS: $[C_{16}H_{13}N+H]^+$, calc. 208.1121, found 208.1116.

2-(2-Pyridinyl)-1*H*-indole (**3c**):[7] yellow solid, 71%; Mp.: 155 °C (methanol); Lit.: 153-154 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 10.19 (br. s., 1 H), 8.62 (d, *J* = 4.9 Hz, 1 H), 7.85 (d, *J* = 7.8 Hz, 1 H), 7.63 - 7.80 (m, 2 H), 7.39 (d, *J* = 8.1 Hz, 0 H), 7.11 - 7.32 (m, 2 H), 7.08 ppm (s, 1 H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 150.5, 149.1, 136.8, 136.7, 129.1, 123.2, 122.0, 121.2, 120.1, 120.0, 111.5, 100.7 ppm; IR: 3417, 3060, 1596, 1560, 1442, 1305, 778 cm^{-1}; HR-MS$[C_{13}H_{10}N_2+H]^+$, calc. 195.0917, found 195.0932.

2-Octyl-1*H*-indole (**3d**):[8] white solid, 81%; Mp.: 50 °C (petrol ether 40-60 °C); Lit.: 50-51 °C; ^{1}H NMR ($CDCl_3$, 400 MHz,): δ ppm 7.82 (br s, 1 H), 7.42 - 7.61 (d, *J* = 7.0 Hz, 1 H), 7.19 - 7.37 (d, *J* = 7.6 Hz, 1 H), 6.99 - 7.16 (dt, *J* = 7.8 Hz, 2 H), 6.23 (s, 1 H) 2.74 (t, *J* = 7.6 Hz, 2 H), 1.71 (quin, *J* = 7.5 Hz, 2 H), 1.12 - 1.46 (m, 10 H) 0.88 (t, *J* = 4.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 140.0, 135.8, 128.8, 120.9, 119.7, 119.5, 110.2, 99.4, 77.3, 77.2, 77.0, 76.7, 31.9, 29.4, 29.3, 29.2, 29.2, 28.3, 22.7, 14.1 ppm; IR: 3411, 3053, 2922, 1456, 1407, 1294, 747, 735 cm^{-1}; HR-MS: $[C_{16}H_{23}N+H]^+$, calc. 230.1903, found 230.1901.

2-(Phenylethynyl)aniline (**2a**)





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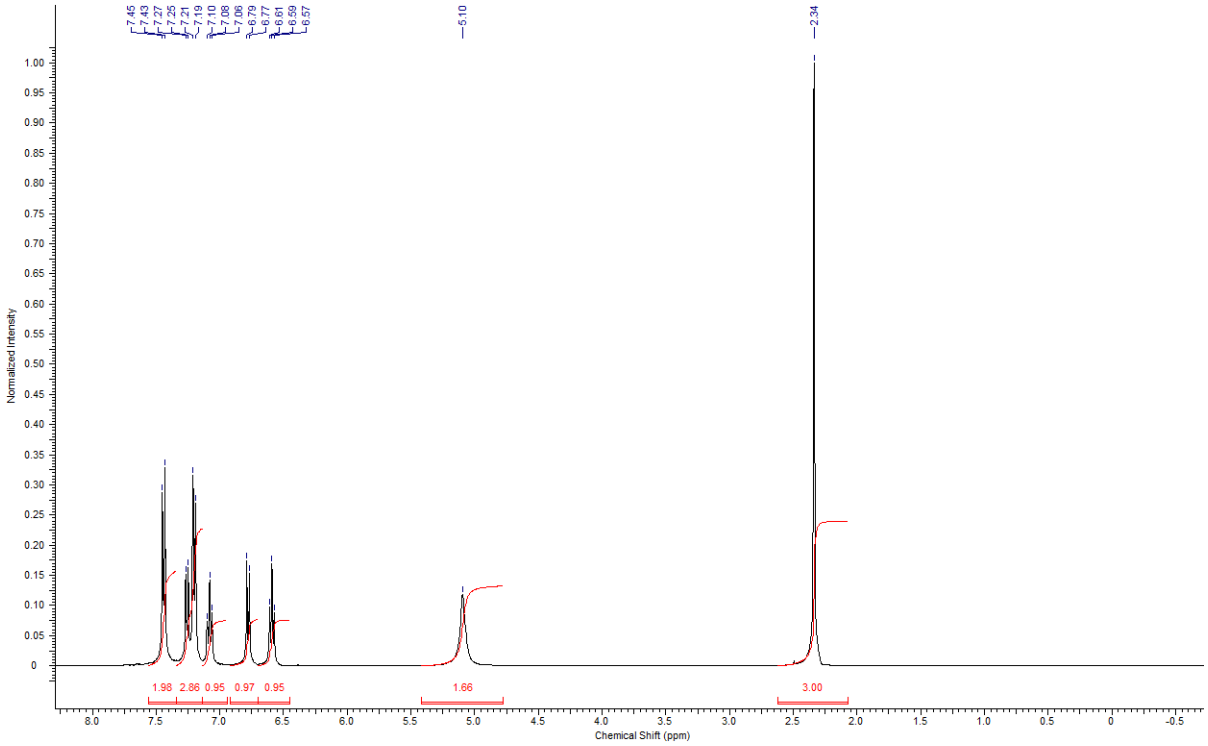

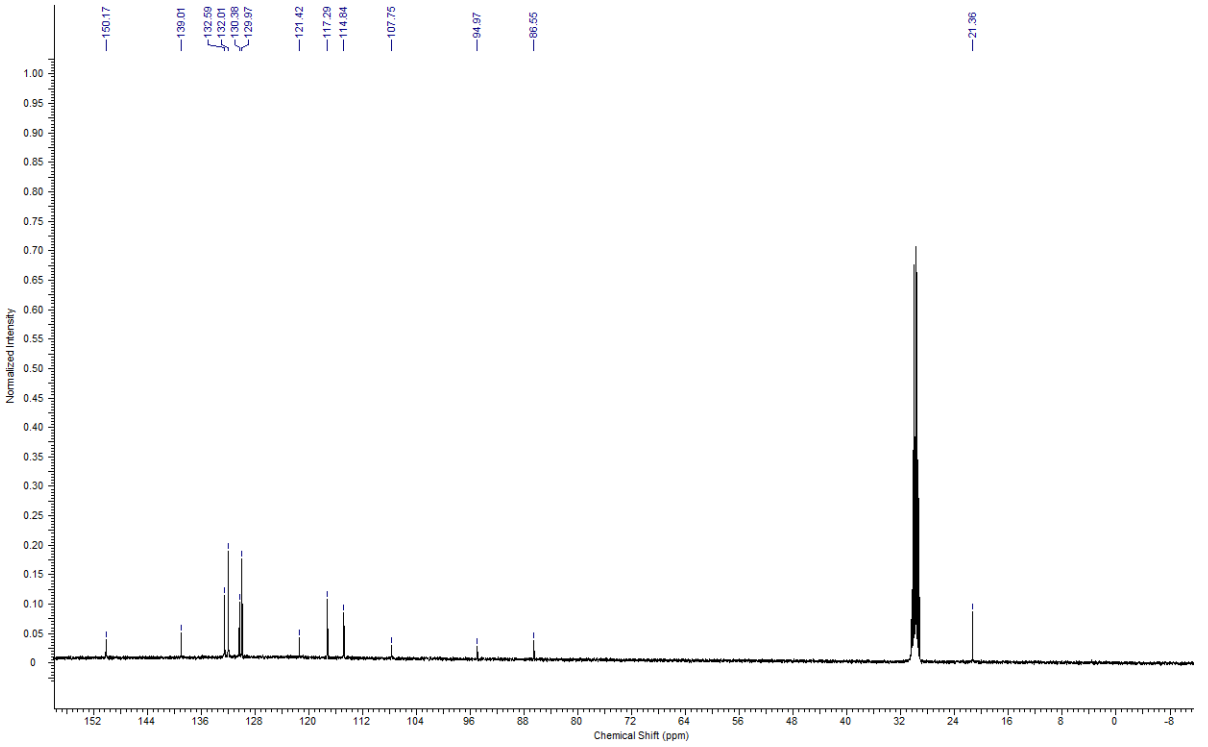

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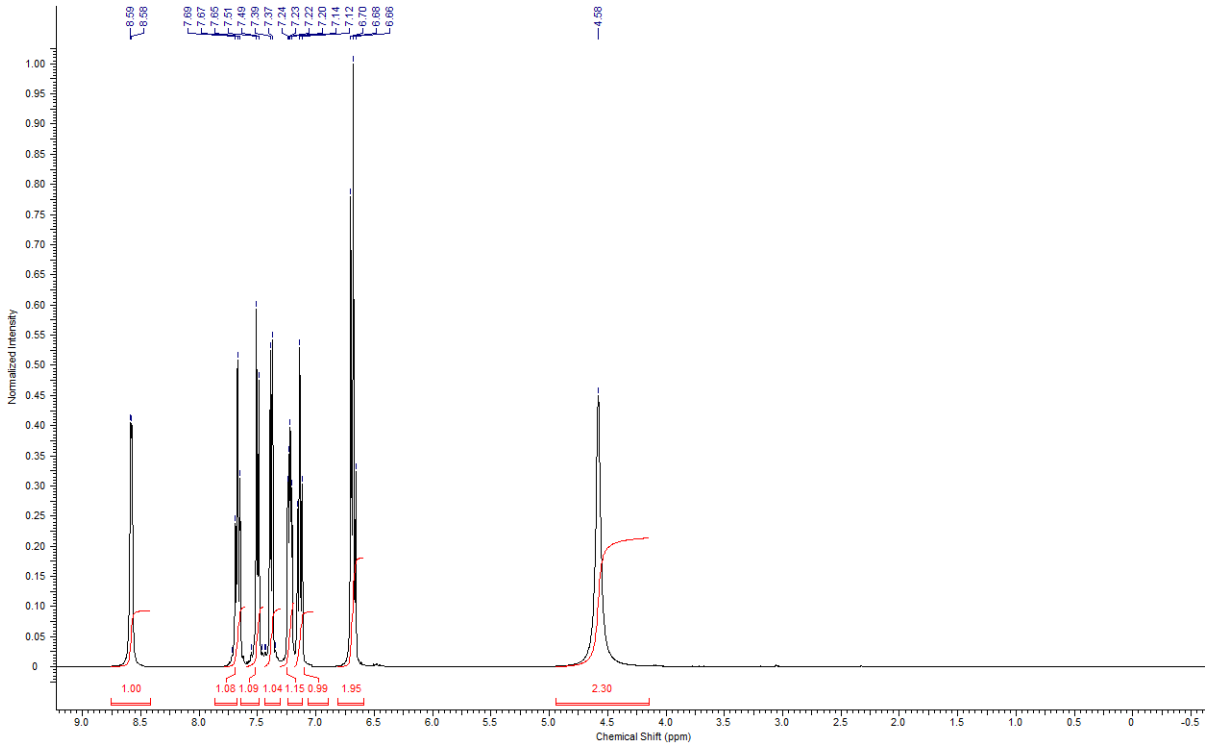
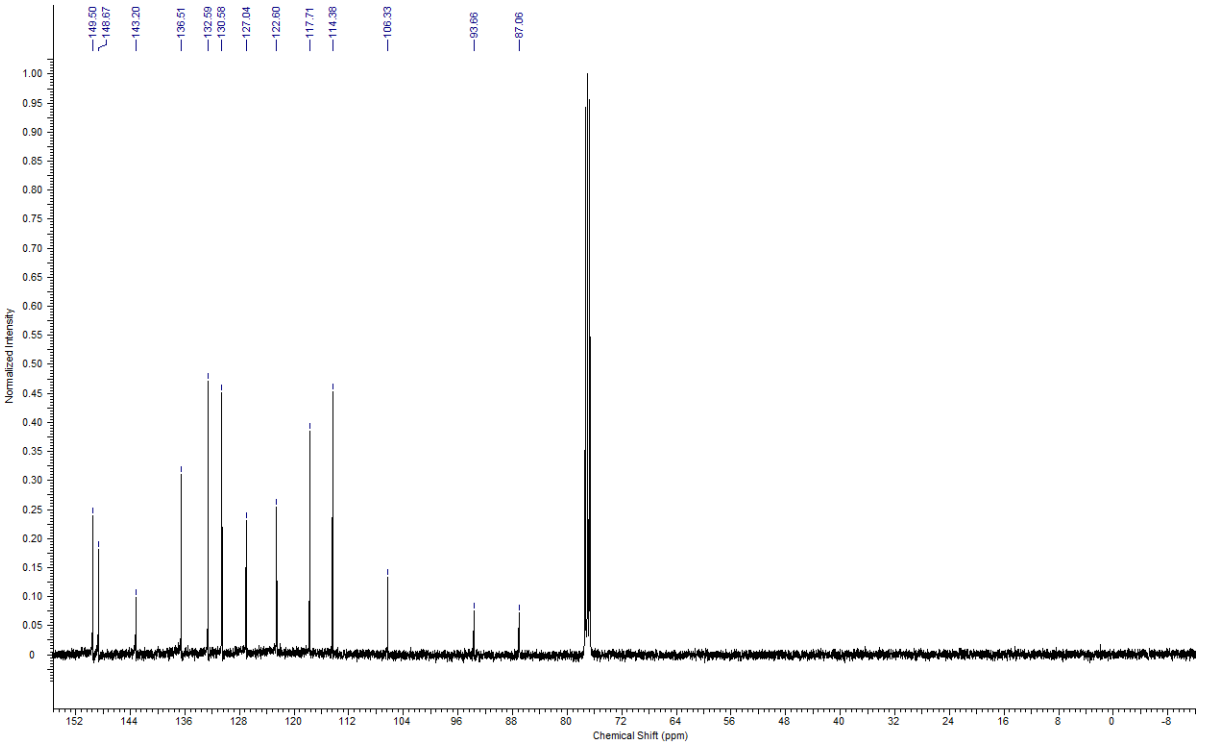
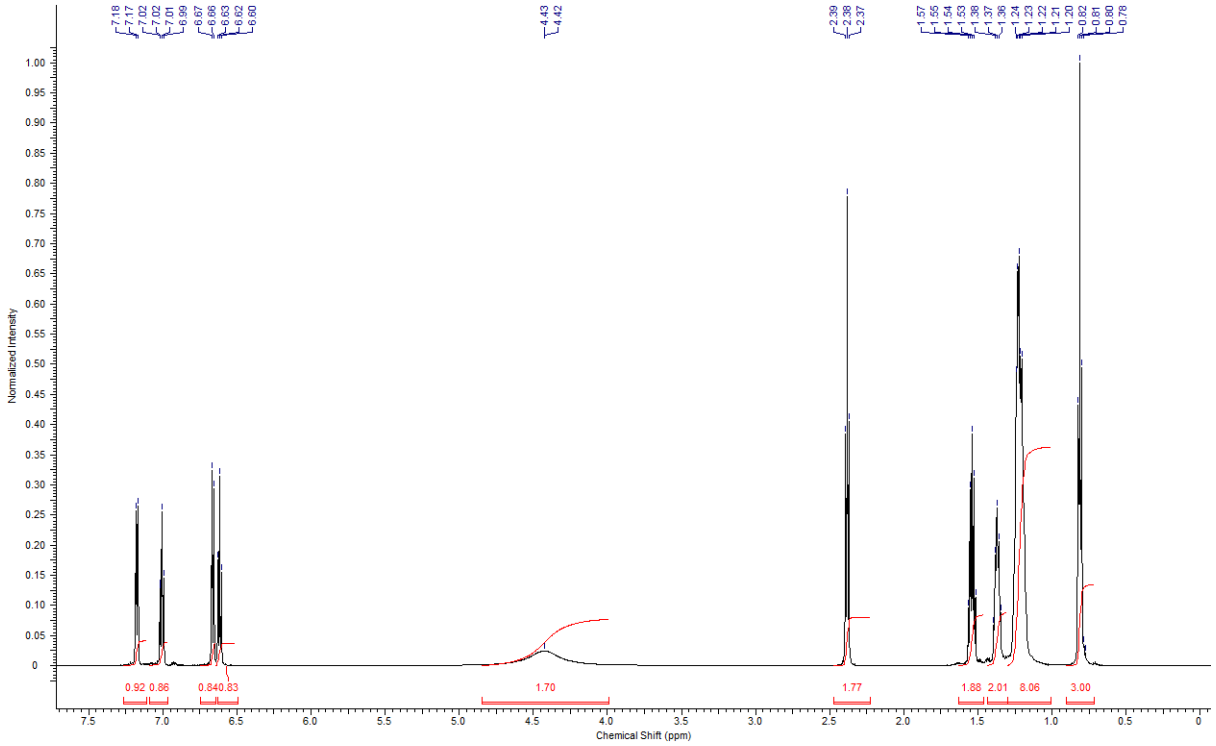
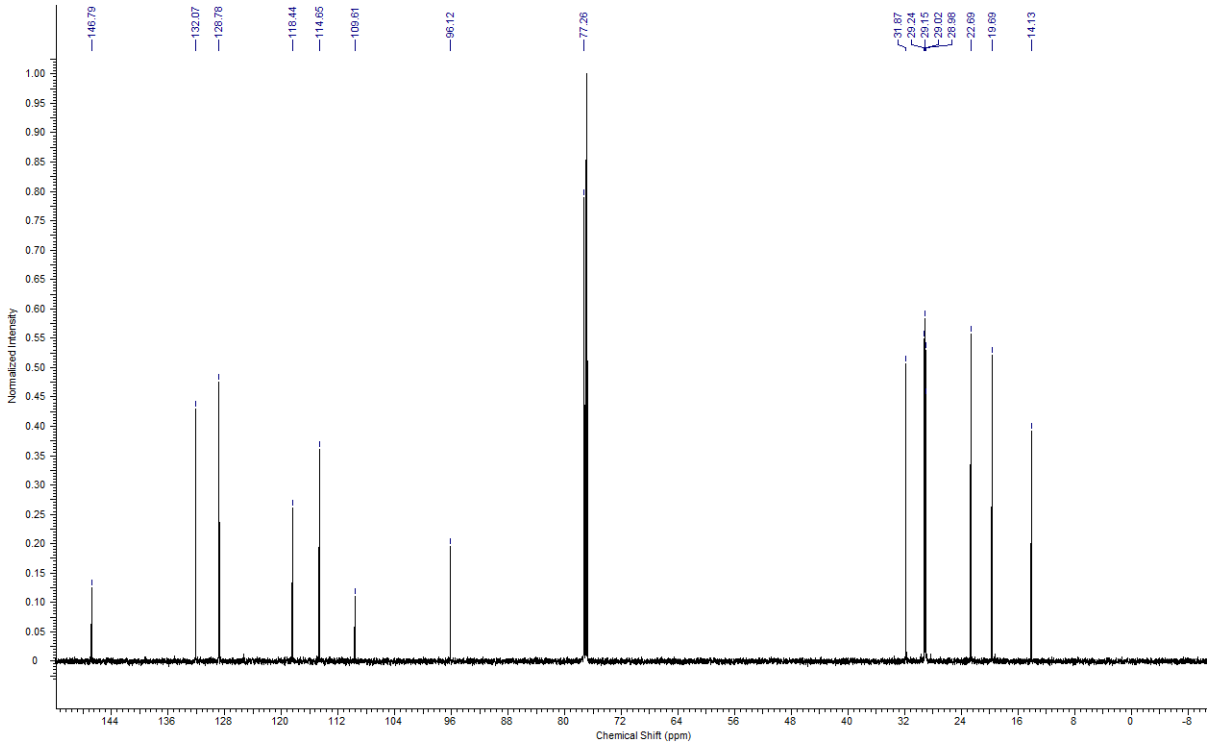


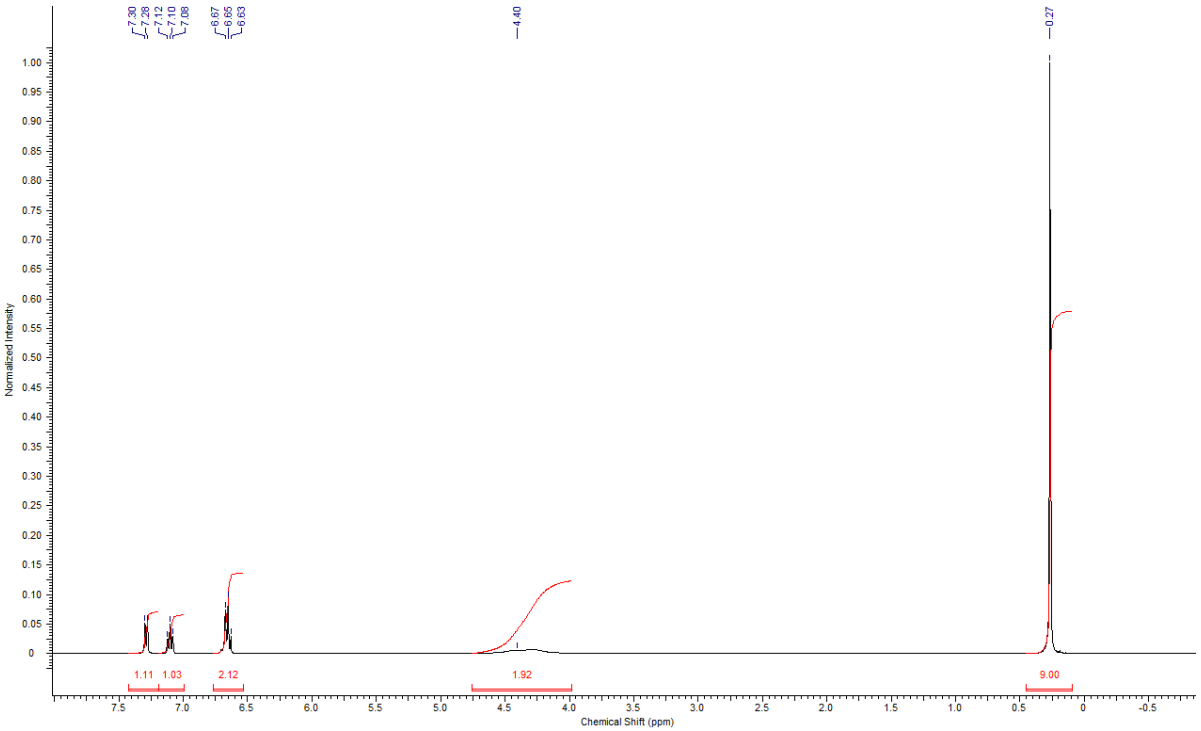


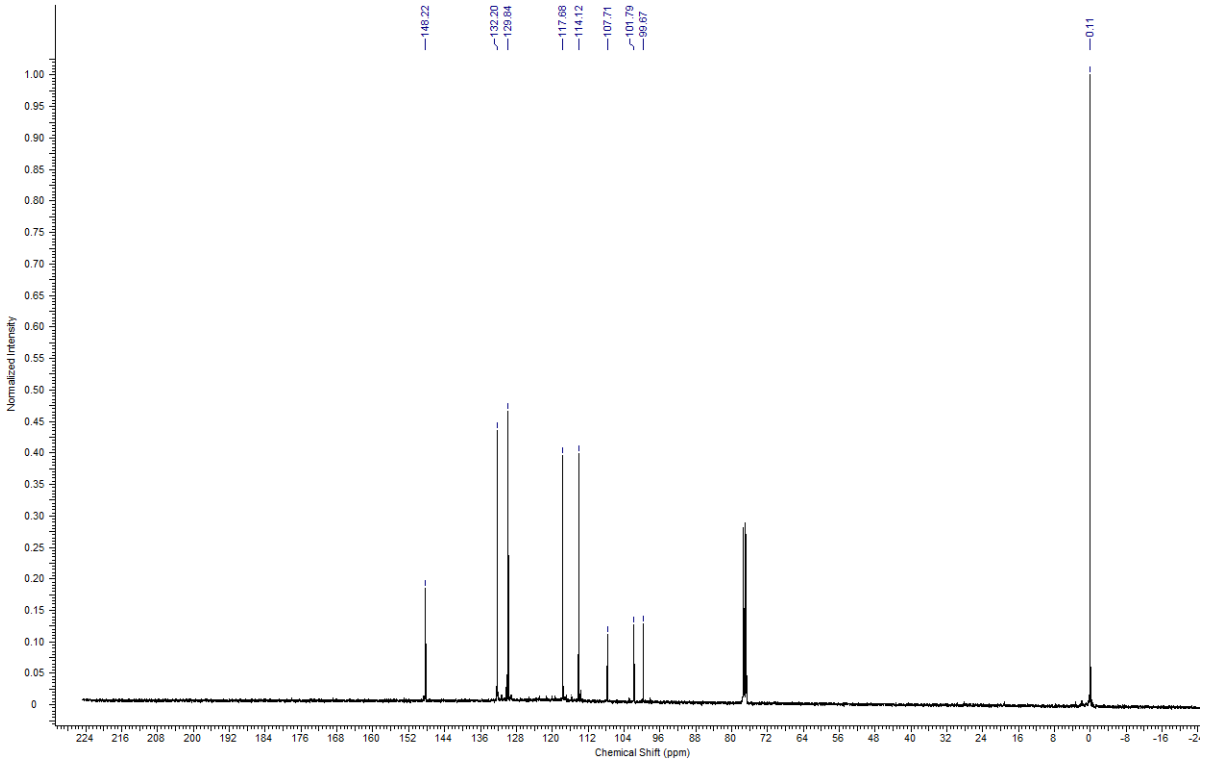
2-Decynylaniline (**2d**)



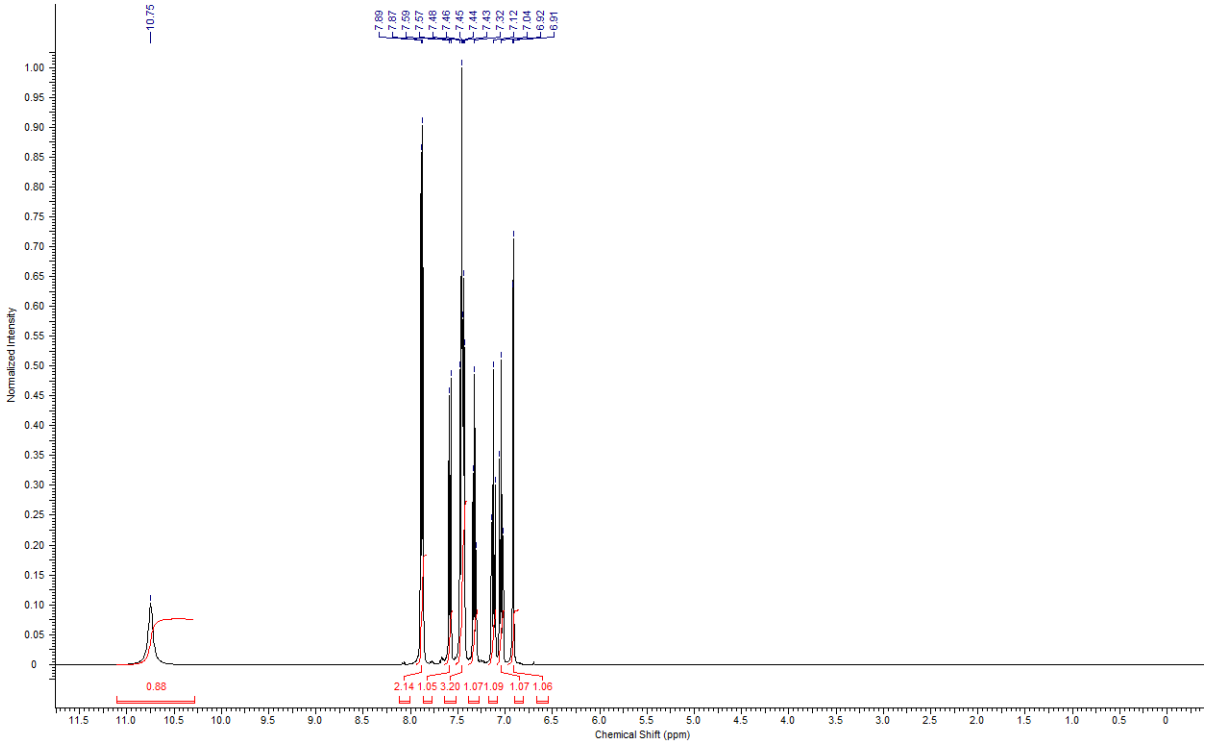


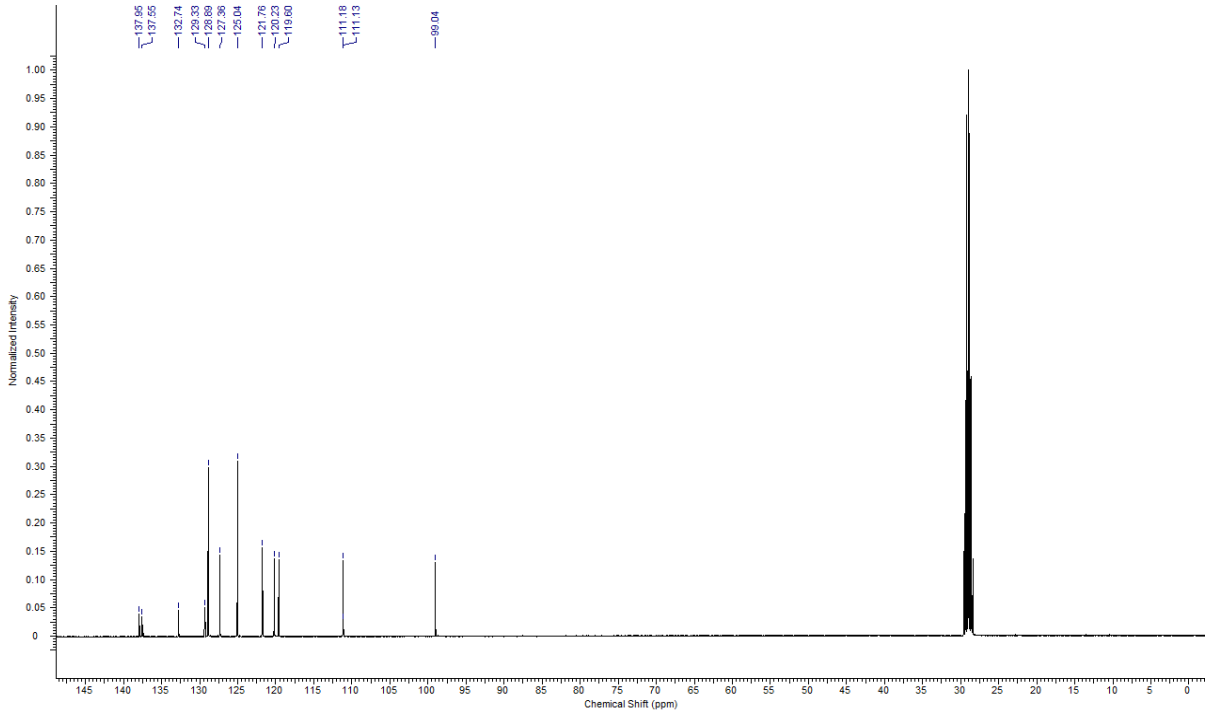
2-(Trimethylsilylethynyl)aniline (**2e**)



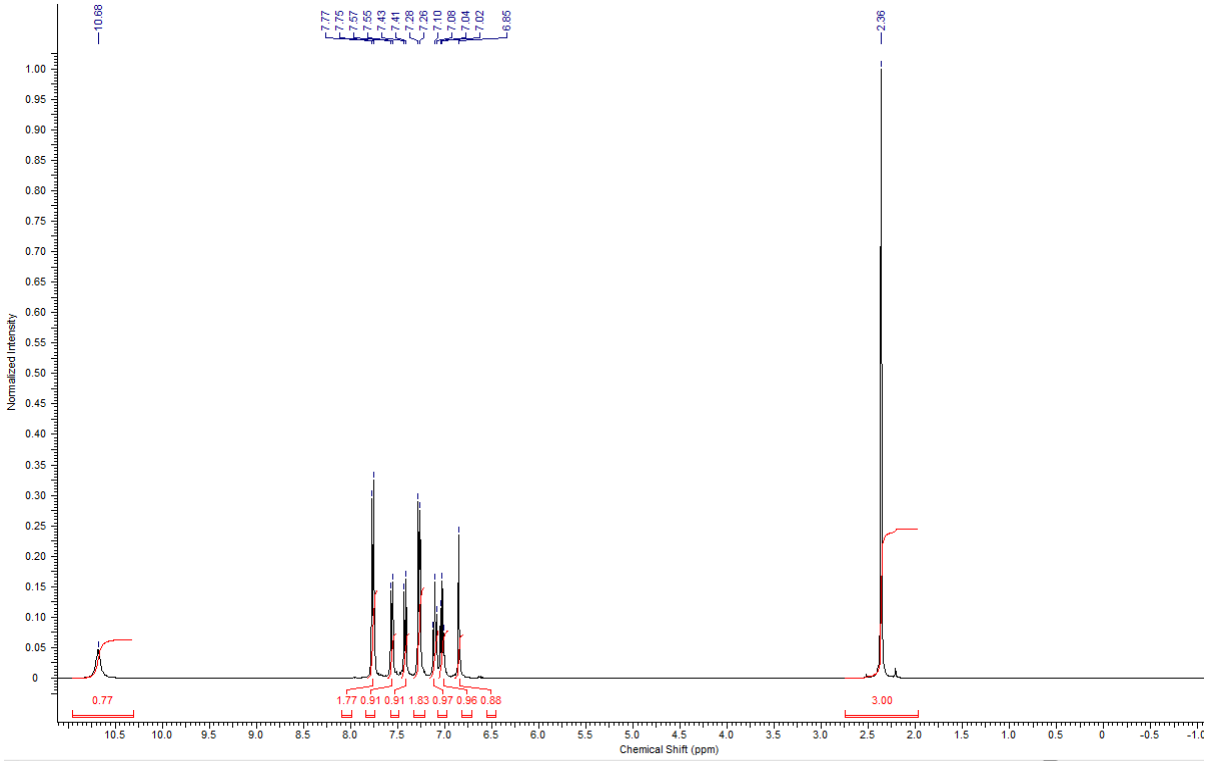


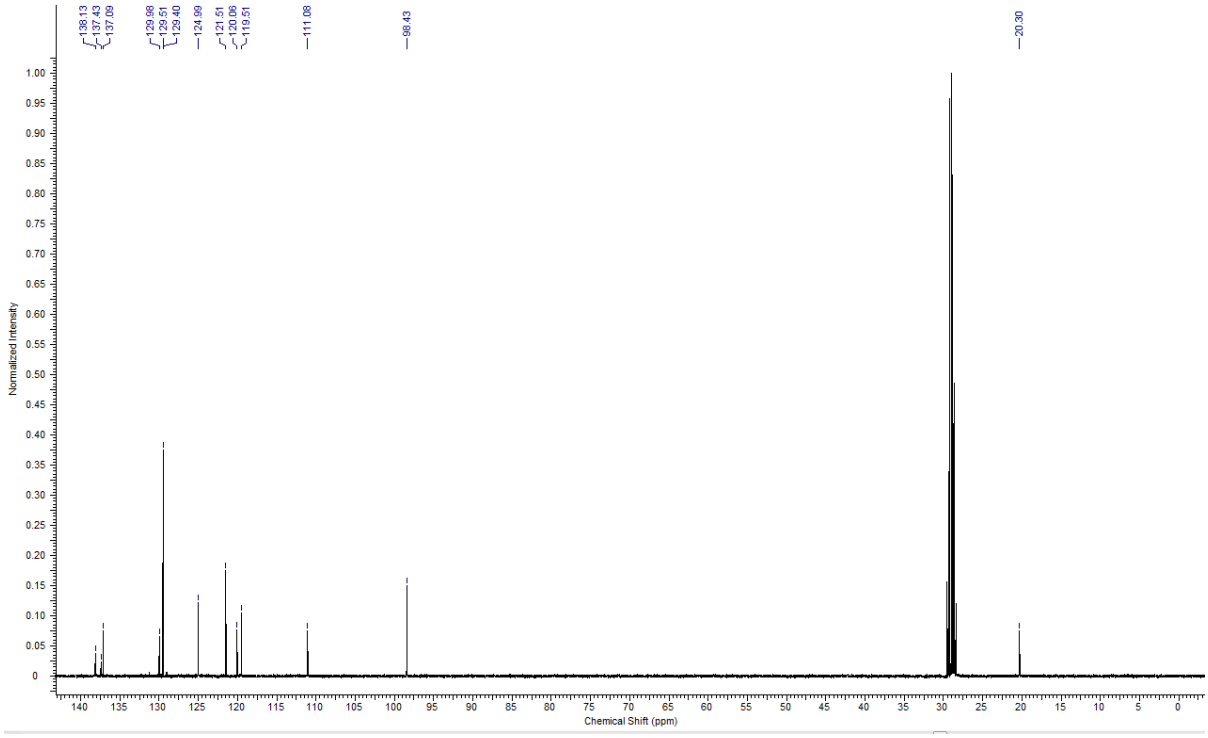
2-Phenyl-1*H*-indole (**3a**)



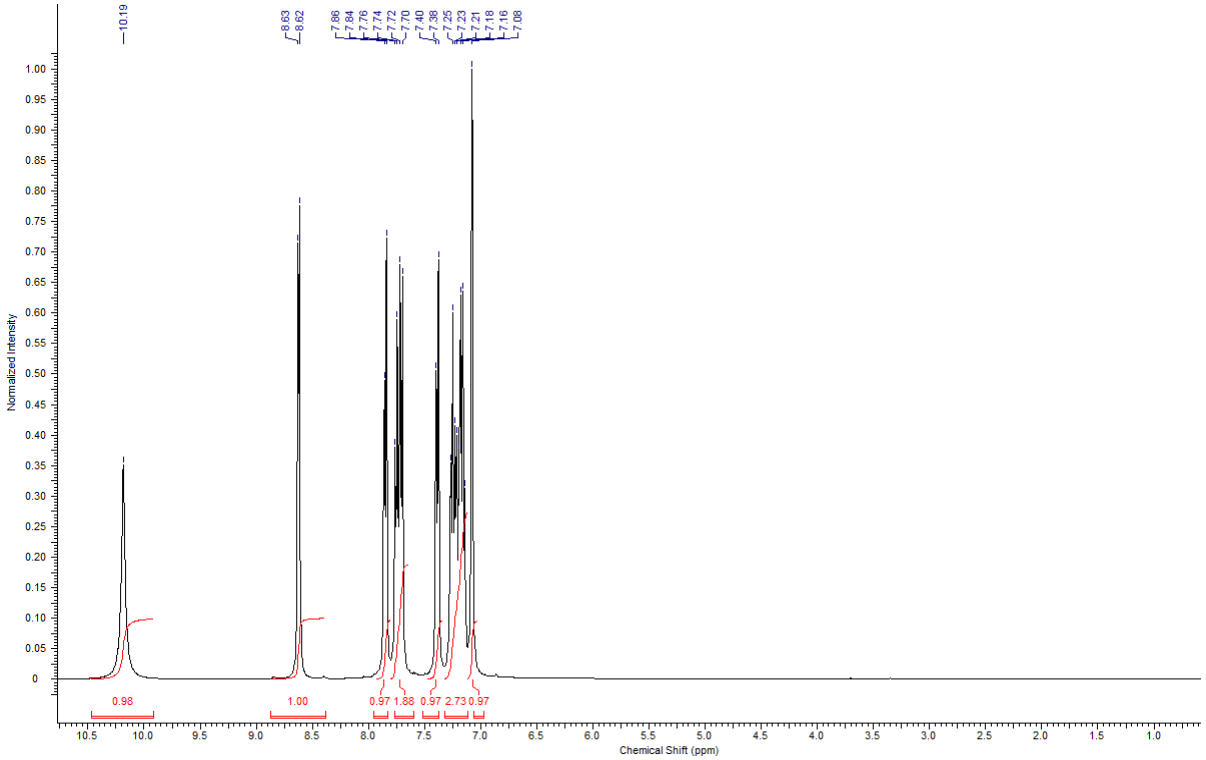


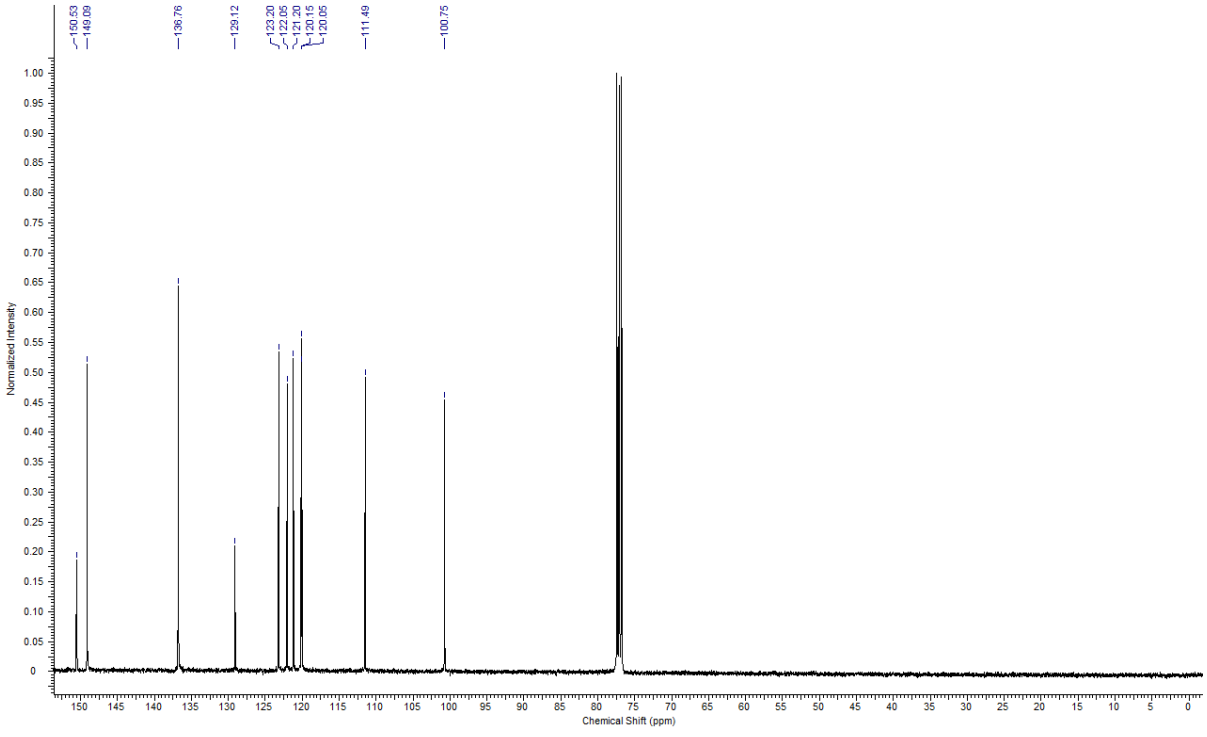
2-(4-Tolyl)-1*H*-indole (**3b**)



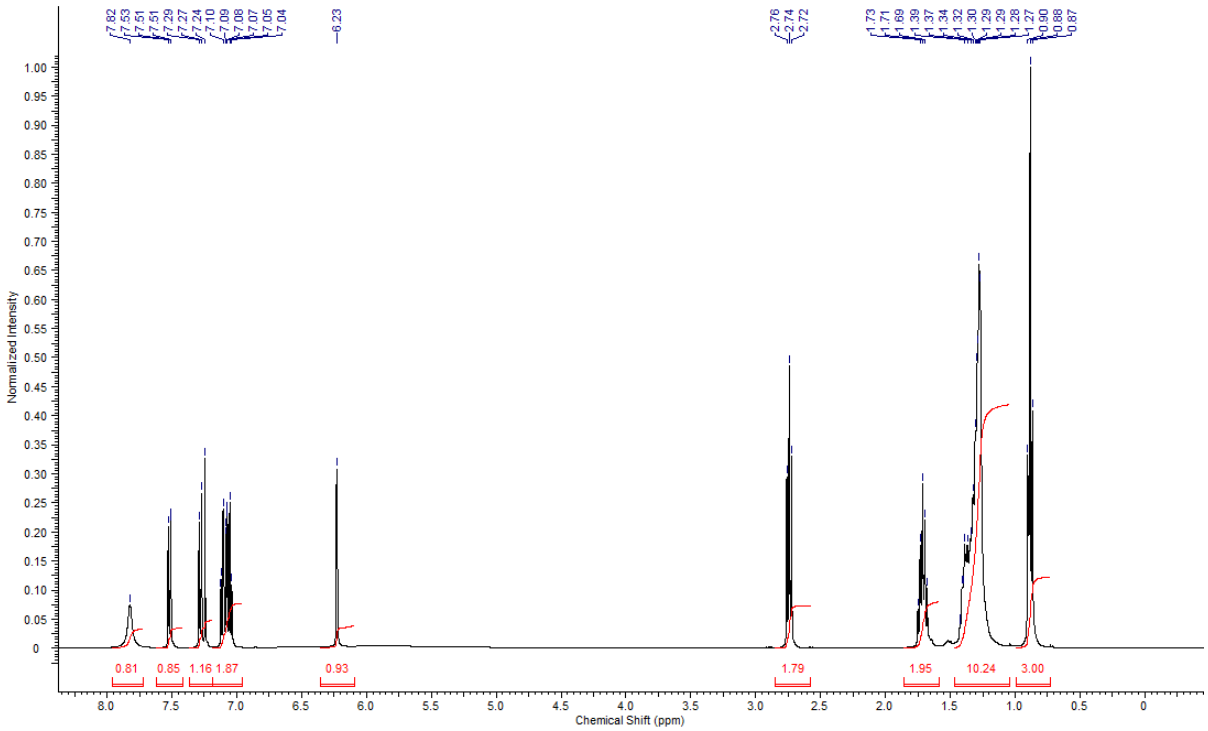


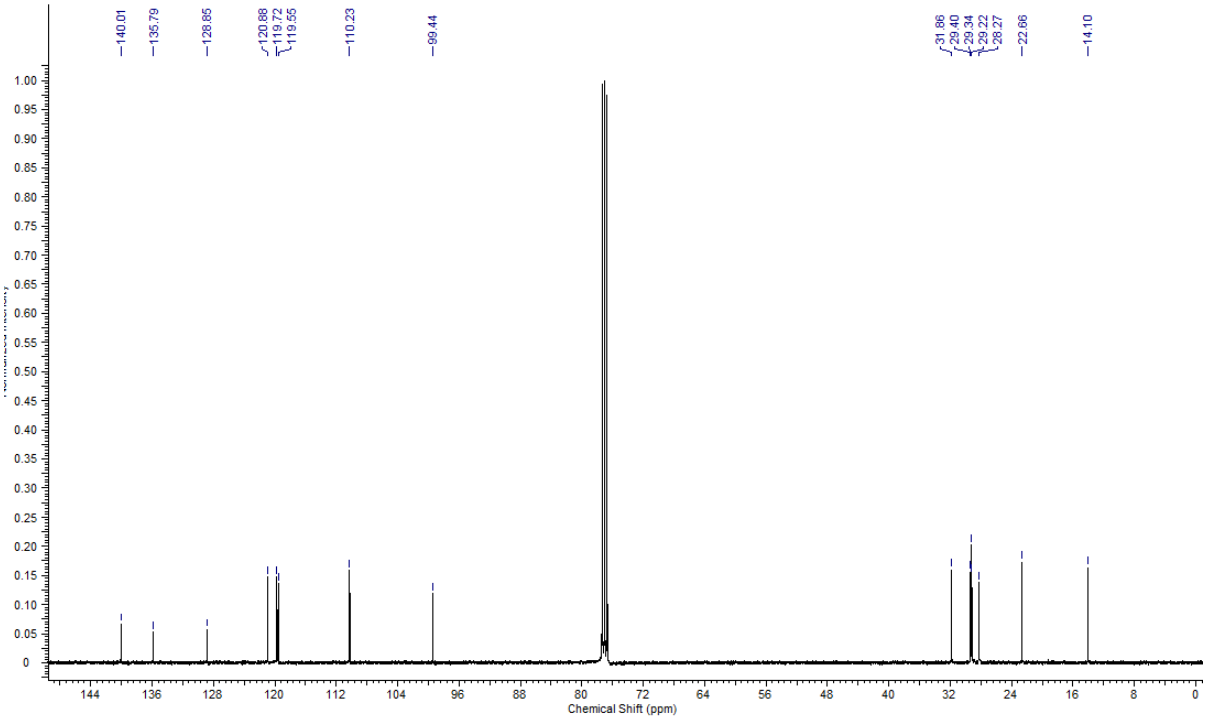
2-(2-Pyridinyl)-1*H*-indole (**3c**)





2-Octyl-1*H*-indole (**3d**)





References

1. R. Bernini, S. Cacchi, G. Fabrizi, G. Forte, F. Petrucci, A. Prastaro, S. Niembro, A. Shafir and A. Vallribera, *Green Chem.*, 2010, **12**, 150.
2. R. Alvarez, C. Martinez, Y. Madich, J. G. Denis, J. M. Aurrecoechea and A. R. de Lera, *Chemistry*, 2010, **16**, 12746-12753.
3. A. Carpita, A. Ribecai and P. Stabile, *Tetrahedron*, 2010, **66**, 7169-7178.
4. N. Sakai, K. Annaka and T. Konakahara, *J. Org. Chem.*, 2006, **71**, 3653-3655.
5. A. V. Butin, M. G. Uchuskin, A. S. Pilipenko, O. V. Serdyuk and I. V. Trushkov, *Tetrahedron Lett.*, 2011, **52**, 5255-5258.
6. H. Wang, Y. Li, L. Jiang, R. Zhang, K. Jin, D. Zhao and C. Duan, *Org. Biomol. Chem.*, 2011, **9**, 4983-4986.
7. T. Lipińska, E. Guibé-jampel, A. Petit and A. Loupy, *Synth. Commun.*, 1999, **29**, 1349-1354.
8. I. Ambrogio, A. Arcadi, S. Cacchi, G. Fabrizi and F. Marinelli, *Synlett*, 2007, 1775-1779.