Electronic Supplementary Material (ESI) for Chemical Communications

Tandem indole C-H alkenylation / arylation for tetra-substituted alkene synthesis

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Supporting Information

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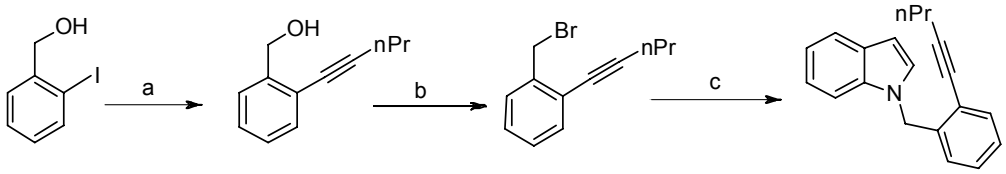
1. General Experimental

Reagents were purchased from Sigma-Aldrich or Fisher Scientific and used without further purification unless otherwise noted. $Pd(OAc)_2$ was purchased from STREM Chemicals. Solvents used were ACS reagent or HPLC grade. Melting point measurements were obtained from a Griffin melting point apparatus and are uncorrected. IR spectra were recorded either on a JASCO 400 IR apparatus (preparing the sample as a film on a NaCl disc or as a solid solution mixed with KBr) or on a SHIMADZU IRAffinity-1 apparatus (neat compound). ^{1}H-NMR and ^{13}C NMR were recorded either on a Brüker Avance III 400MHz or on a Brüker Avance III 500 MHz instrument from the University of Edinburgh. The products were dissolved in deuterated chloroform ($CDCl_3$) with residual $CHCl_3$ peak as internal reference. The following abbreviation have been used: δ (chemical shift), J (coupling constant), s (singlet), bs (broad singlet), d (doublet), dd (double doublet), ddd (doublet of doublet of doublets), dt (double triplet), t (triplet), td (triplet of doublets), q (quartet), sext (sextet), sept (septet), m (multiplet), quat (quaternary carbon). HPLC/MS data was obtained from a 1200 Series Agilent Technologies apparatus with a WATERS Atlantis dC18.3µm (3.0x2.0 mm IS) column. High resolution mass spectrometry was performed by EPSRC National Mass Spectrometry Service Centre at Swansea using either of the following ionisation techniques: Electron Ionisation (EI), Electrospray Ionisation (ESI) or Atmospheric Pressure Chemical Ionisation (APCI). A Biotage 2.5 Initiator Microwave Synthesiser was used for reactions requiring microwave irradiation as specified. Reactions were monitored by thin layer chromatography (TLC) using Merck $60F_{254}$ silica plates, visualised by UV light (λ=254 nm) and / or stained in anisaldehyde solution. All compounds were purified by wet flash chromatography using Merck Kieselogel 60 silica (particle size 35-70) under positive pressure.

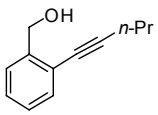
2. Experimental procedures: Synthesis of starting materials



The starting materials were prepared *via* a) Sonagashira coupling [1-pentyne (1.2 equiv), $Pd(PPh_3)Cl_2$ (1 mol%), CuI (2 mol%), toluene:piperidine, 1:1, r.t.]; b) bromination using the procedure of Shashida *et. al.*[4] for the synthesis of *o*-ethynylbenzyl bromides [PBr_3 (1.1 equiv), pyridine (1.3 equiv), $CHCl_3$, 0 ºC - r.t.]; c) indole *N*-alkylation [indole (1 equiv), NaH (1.1 equiv), DMF, r.t.].

Representative procedure for the synthesis of 2-ethynylbenzyl alcohols (step a)

2-Pent-1-ynylbenzyl alcohol: 2-Iodobenzyl alcohol (1.0 g, 4.28 mmol) was weighed in a dried flask containing a stirrer bar. Piperidine and dry toluene (12 mL, 1:1) were added and the mixture was degassed with a stream of N_2 for 10 min. $Pd_2Cl_2(PPh_3)_2$ (28 mg, 0.04 mmol) and CuI (15 mg, 0.08 mmol) were then added. The flask was capped with a rubber septum and 1-pentyne (450 µL, 4.62 mmol) was added *via* syringe. The reaction was left stirring at r.t. (approx. 20 °C) under N_2 atmosphere for 6 h aftewhich time no starting material was seen by TLC. Water and EtOAc were added (15 mL each) and the two layers separated. The aqueous layer was extracted twice with EtOAc (15 mL × 2) and the combined organic layers washed with sat. NH_4Cl aqueous solution (15 mL × 2) and brine (15 mL × 2). Drying over $MgSO_4$, filtration and concentration *in vacuo* gave a crude solid that was purified



using silica gel column chromatography (hexane:CH_2Cl_2, 1:1), affording 682 mg (93%) of a colourless oil. Spectroscopic data was in accordance with the literature values.[5]

5-Fluoro-2-pent-1-ynylbenzyl alcohol. The product was synthesised through a Sonogashira coupling between 2-bromo-5-fluorobenzyl alcohol (0.97 mmol) and 1-pentyne. The general procedure was followed but the reaction was carried out at 100 ºC (instead of r.t.) for 36 h. Aqueous work-up and purification afforded the product as a colourless oil in 50% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.05 (3H, t, *J*= 7.4 Hz), 1.63 (2H, sext, *J*= 7.2 Hz), 2.41 (2H, t, *J*= 7.0 Hz), 4.77 (2H, bs), 6.90 (1H, td, *J*= 2.7, 8.4 Hz), 7.14 (1H, dd, *J*= 2.7, 9.4 Hz), 7.35 (1H, dd, *J*= 5.6, 8.4 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.52 (CH_3), 21.40 (CH_2), 22.16 (CH_2), 63.48 (CH_2), 77.17 (quat), 94.97 (quat, d, J_{C-F}= 1.6 Hz), 113.91 (CH, d, J_{C-F}= 25.0 Hz), 114.14 (CH, d, J_{C-F}= 22.1 Hz), 117.64 (quat, d, J_{C-F}= 3.3 Hz), 133.74 (CH, d, J_{C-F}= 8.2 Hz), 145.10 (quat, d, J_{C-F}= 7.3 Hz), 162.23 (quat, d, J_{C-F}= 248.7 Hz); **IR** (neat): 3296(b), 2962, 2933, 1581, 1487, 1463, 1440, 1409, 1230, 1147, 1064, 1024 cm^{-1}; **HRMS:** (APCI) calculated for $C_{12}H_{17}ONF$ [MNH_4^+] : 210.1289, found: 210.1285.

2-(3-Cyclohexylprop-1-ynyl)benzyl alcohol. The product was obtained as colourless oil in 98% yield after 15 h reaction using 2-iodobenzyl alcohol (2.13 mmol). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.03-1.33 (5H, m), 1.65-1.89 (5H, m), 2.35 (2H, d, *J*= 6.6 Hz), 4.80 (2H, s), 7.22 (1H, td, *J*= 1.5, 7.5 Hz), 7.28 (1H, td, *J*= 1.5, 7.6 Hz), 7.38-7.42 (2H, m); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.12 (CH_2), 26.23 (2 × CH_2), 27.35 (CH_2), 32.77 (CH_2), 37.47 (CH), 64.31 (CH_2), 78.96 (quat), 94.44 (quat), 122.24 (quat), 127.21 (CH), 127.37 (CH), 127.88 (CH), 132.25 (CH), 142.32 (quat); **IR** (neat): 3352 (bs), 2920, 2848, 2220, 1448 cm^{-1}; **HRMS:** (EI) calculated for $C_{16}H_{20}O$ [M^+]: 228.15087, found: 228.15073.

2-Cyclohexylethynylbenzyl alcohol. The general procedure afforded the product in 78% yield after 15 h (2.13 mmol scale). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.35-1.44 (3H, m), 1.52-1.58 (3H, m), 1.73-1.77 (2H, m), 1.88-1.91 (2H, m), 2.62-2.66 (1H, m), 4.80 (2H, s), 7.22 (1H, td, *J*= 1.3, 7.4 Hz), 7.29 (1H, dd, *J*= 1.3, 7.5 Hz), 7.37-7.42 (2H, m); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 24.83 (CH_2), 25.85 (2 × CH_2), 29.75 (CH), 32.66 (2 × CH_2), 64.36 (CH_2), 78.06 (quat), 99.65 (quat), 122.20 (quat), 127.21 (CH), 127.37 (CH), 127.88 (CH), 132.12 (CH), 142.39 (quat); **IR** (neat): 3354 (b), 2927, 2852, 2224, 1483, 1448, 1037, 1008 cm^{-1}; **HRMS:** (EI) calculated for $C_{15}H_{18}O$ [M^+]: 214.13522, found: 214.13531.

General procedure for the synthesis of 2-ethynylbenzyl bromides (step b)

The synthesis of 2-ethynylbenzyl bromides was carried out using Shashida and co-workers' procedure[4]. The preparation of **2-pent-1-ynylbenzyl bromide** is described as an example. To a solution of 2-pent-1-ynylbenzyl alcohol (590 mg, 3.4 mmol) and pyridine (360 µL, 4.34 mmol) in $CHCl_3$ (3.4 mL) at 0 ºC was slowly added phosphorus tribromide (350 µL, 3.69 mmol). The mixture was left to react at r.t. for 2 h, and then poured into ice-water. The aqueous phase was extracted twice with CH_2Cl_2 (15mL × 2) and the combined organic layer was washed with 5% H_2SO_4 (15mL × 2), sat. $NaHCO_3$ (15mL × 2), and brine (15mL × 2) and then dried with $MgSO_4$. The solvent was evaporated under reduced pressure and the crude material purified using silica gel column chromatography (hexane:CH_2Cl_2, 9:1) to give 630 mg of a clear oil (79%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.09 (3H, t, *J*= 7.4 Hz), 1.68 (2H, sext. *J*= 7.0 Hz), 2.46 (2H, t, *J*= 7.0 Hz), 4.67 (2H, *s*), 7.21-7.27 (2H, m), 7.39-7.41 (2H, m); **^{13}C**

NMR (150 MHz, $CDCl_3$): δ 13.62 (CH_3), 21.63 (CH_2), 22.14 (CH_2), 32.32 (CH_2), 77.83 (quat), 96.43 (quat), 124.00 (quat), 127.98 (CH), 128.34 (CH), 129.56 (CH), 132.49 (CH), 138.96 (quat); **IR** (neat): 2963, 2933, 2871, 2234, 1600, 1485, 1450, 1338, 1265, 1222, 759, 608 cm^{-1}; **HRMS:** (EI) calculated for $C_{12}H_{13}Br^{79}$ [M^+]: 236.01951, found: 236.01939.

5-Fluoro-2-pent-1-ynylbenzyl bromide. Starting from 5-fluoro-2-pent-1-ynylbenzyl alcohol (0.45 mmol), the general procedure (2 h reaction time) gave the named product as a colourless oil in 62% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.08 (3H, t, *J*=7.4 Hz), 1.67 (2H, sext, *J*= 7.2 Hz), 2.44 (3H, t, *J*= 7.0 Hz), 4.61 (2H, s), 6.94 (1H, td, *J*= 2.7, 8.4 Hz), 7.12 (1H, dd, *J*= 2.7, 9.1 Hz), 7.38 (1H, dd, *J*= 5.7, 8.6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.60 (CH_3), 21.56 (CH_2), 22.11 (CH_2), 31.25 (CH_2, d, $J_{C\text{-}F}$= 1.7 Hz), 76.87 (quat), 96.00 (quat, d, $J_{C\text{-}F}$=1.6 Hz), 115.64 (CH, d, $J_{C\text{-}F}$= 21.9 Hz), 116.50 (CH, d, $J_{C\text{-}F}$= 22.7 Hz), 119.97 (quat, d, $J_{C\text{-}F}$= 3.4 Hz), 134.15 (CH, d, $J_{C\text{-}F}$= 8.3 Hz), 141.19 (quat, d, $J_{C\text{-}F}$= 7.9 Hz), 161.72 (quat, d, $J_{C\text{-}F}$= 249.2 Hz); **IR** (neat): 3257 (b), 2958, 2933, 2908, 2837, 1604, 1502, 1463, 1438, 1382, 1259, 1153 cm^{-1}; **HRMS:** (EI) calculated for C12H12Br^{79}F: 254.0101, found: 254.0100.

2-(3-Cyclohexylprop-1-ynyl)benzyl bromide. The general procedure (8 h reaction time, 1.74 mmol scale) afforded the desired product in 69% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.09-1.16 (3H, m), 1.25-1.31 (3H, m), 1.65-1.69 (1H, m), 1.74-1.77 (2H, m), 1.88-1.91 (2H, m), 2.38 (2H, d, *J*= 6.5 Hz), 4.67 (2H, s), 7.24 (2H, ddd, *J*= 1.7, 5.1, 7.4 Hz), 7.37-7.41 (2H, m); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.16 (2 × CH_2), 26.25 (CH_2), 27.46 (CH_2), 32.36 (CH_2), 32.79 (2 × CH_2), 37.49 (CH), 78.58 (quat), 95.54 (quat), 124.09 (quat), 127.93 (CH), 128.33 (CH), 129.57 (CH), 132.53 (CH), 138.96 (quat); **IR** (neat): 2922, 2850, 2222, 1485, 1448, 1263, 1220 cm^{-1}; **HRMS:** (ESI) calculated for $C_{16}H_{19}Br^{79}$ [M^+]:290.0665, found: 290.0662.

2-Cyclohexylethynylbenzyl bromide. The general procedure (4 h reaction time, 1.66 mmol scale) afforded the desired product in 45% yield. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.37-1.40 (3H, m), 1.58-1.65 (2H, m), 1.76-1.82 (2H, m), 1.90-1.93 (2H, m), 2.66-2.71 (1H, m), 4.67 (2H, s), 7.22-7.25 (2H, m), 7.38-7.41 (2H, m); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 24.80 (CH_2), 25.92 (2 × CH_2), 29.82 (CH), 32.41 (2 × CH_2), 32.52 (CH_2), 77.69 (quat), 100.66 (quat), 124.09 (quat), 127.92 (CH), 128.34 (CH), 129.52 (CH), 132.38 (CH), 138.99 (quat); **IR** (neat): 2933, 2856, 2198, 1485, 1448, 1263, 1220, 1053 cm^{-1}; **HRMS:** (EI) calculated for $C_{15}H_{17}Br^{79}$ [MH^+]: 276.05081, found: 276.05080.

General procedure for the *N*-alkylation of indole derivatives with 2-ethynylbenzyl bromides[6] (step c)

The indole derivative (8.5 mmol) was weighed in an oven dried 100 mL round bottomed flask and dissolved in dry DMF (50 mL) under N_2 atmosphere. NaH (60% in mineral oil, 9.3 mmol) was added portionwise and the mixture was stirred for 1 h at r.t. A solution of 2-ethynylbenzyl bromide (9.3 mmol) dissolved in DMF (5 mL) was then added via cannula under N_2. The reaction was left stirring for 3-15 h until no indole starting material was seen by TLC. The mixture was then quenched with EtOAc (30 mL) and water (30 mL), and the two layers separated. The aqueous layer was extracted with EtOAc (30 mL × 2), and the combined organic layers washed with brine (30 mL × 2), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was chromatographed on silica gel (hexane:CH_2Cl_2 mixtures).

[The indoles, **5**, prepared using this procedure are not individually numbered in the paper. Accordingly, they are labelled here in the order in which they appear in Schemes 2 and 3 of the paper (**5a**, **5b** etc.]

1-(2-Pent-1-ynylbenzyl)-*1H*-indole, 5a. The general *N*-alkylation procedure afforded the named product in 88% yield as a colourless oil, solidifying on standing. **m.p.**: 36-38 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): 1.07 (3H, t, *J*= 7.5 Hz), 1.66 (2H, qt, *J*= 4.5 Hz), 2.46 (2H, t, *J*= 7.0 Hz), 5.49 (2H, s), 6.57 (1H, d, *J*= 3.0 Hz), 6.67 (1H, d, *J*= 8.0 Hz), 7.09-7.19 (5H, m), 7.31 (1H, d, *J*= 8.0 Hz), 7.45 (1H, d, *J*= 8.0 Hz), 7.66 (1H, d, *J*= 8.1 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.62 (CH_3), 21.57 (CH_2), 22.21 (CH_2), 48.56 (CH_2), 78.23 (quat), 96.19 (quat), 101.60 (CH), 109.76 (CH), 119.46 (CH), 120.88 (CH), 121.62 (CH), 122.29 (quat), 126.40 (CH), 127.20 (CH), 128.01 (CH), 128.41 (CH), 128.51 (quat), 132.16 (CH), 136.35 (quat), 138.97 (quat) **IR** (neat): 3096, 2999, 2997, 2253, 1711, 1501, 1437 cm^{-1}; **HRMS**: (ESI) calculated for $C_{20}H_{20}N$ [MH^+]: 274.1590, found: 274.1596.

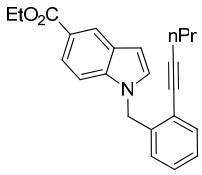
3-Methyl-1-(2-pent-1-ynylbenzyl)-*1H*-indole, 5b. *N*-alkylation of 3-methylindole (2.2 mmol) with 2-pent-1-ynylbenzyl bromide afforded the desired product in 88% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.08 (3H, t, *J*= 7.3 Hz), 1.67 (2H, sext, *J*= 7.3 Hz), 2.36 (3H, d, *J*= 1.0 Hz), 2.46 (2H, t, *J*= 7.0 Hz), 5.43 (2H, s), 6.70 (1H, dd, *J*= 0.6, 7.7 Hz), 6.93 (1H, d, *J*= 1.0 Hz), 7.08-7.20 (4H, m), 7.26-7.28 (1H, m), 7.45 (1H, dd, *J*= 1.0, 7.5 Hz), 7.6 (1H, dd, *J*= 2.0, 7.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 9.64 (CH_3), 13.61 (CH_3), 21.58 (CH_2), 22.21 (CH_2), 48.23 (CH_2), 78.31 (quat), 96.08 (quat), 109.53 (CH), 110.76 (quat), 118.70 (CH), 118.93 (CH), 121.54 (CH), 122.22 (quat), 125.99 (CH), 126.45 (CH), 127.08 (CH), 127.97 (CH), 128.79 (quat), 132.12 (CH), 136.68 (quat), 139.32 (quat); **IR** (neat): 3056, 3030,2962, 2931, 2871, 2232, 1614, 1482, 1466, 1352, 1331 cm^{-1}; **HRMS**: (ESI) calculated for $C_{21}H_{22}N$ [MH^+]: 288.1747, found: 288.1750.

5-Methoxy-1-(2-pent-1-ynylbenzyl)-*1H*-indole, 5c. *N*-alkylation of 5-methoxyindole (1.4 mmol) afforded a colourless oil (75%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.06 (3H, t, *J*= 7.4 Hz), 1.65 (2H, sext, *J*= 7.2 Hz), 2.45 (2H, t, *J*= 7.0 Hz), 3.85 (3H, s), 5.44 (2H, s), 6.48 (1H, d, *J*= 2.9 Hz), 6.65 (1H, d, *J*= 7.7 Hz), 6.82 (1H, dd, *J*= 2.5, 7.7 Hz), 7.10-7.14 (3H, m), 7.18 (2H, d, *J*= 8.1 Hz), 7.44 (1H, d, *J*= 7.4 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.63 (CH_3), 21.58 (CH_2), 22.22 (CH_2), 48.75 (CH_2), 55.85 (CH_3), 78.22 (quat), 96.18 (quat), 101.11 (CH), 102.48 (CH), 110.54 (CH), 111.96 (CH), 122.22 (quat), 126.32 (CH), 127.18 (CH), 128.02 (CH), 128.93 (quat), 128.99 (CH), 131.67 (quat), 132.15 (CH), 139.06 (quat), 154.07 (quat); **IR** (neat): 2965, 2837, 2252, 1623, 1488, 1449, 1239, 1151, 1033 cm^{-1}; **HRMS:** (ESI) calculated for $C_{21}H_{22}ON$ [MH^+]: 304.1696, found: 304.1693.

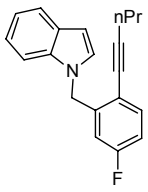
6-Fluoro-1-(2-pent-1-ynylbenzyl)-*1H*-indole, 5d. N-Alkylation of 6-fluoroindole (1.5 mmol) with 2-pent-1-ynylbenzyl bromide afforded **5d** (48%) as a pale brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.09 (3H, t, *J*= 7.4 Hz), 1.68 (2H, sext, *J*= 7.2 Hz), 2.48 (2H, t, *J*= 7.0 Hz), 5.44 (2H, s), 6.56 (1H, dd, *J*= 0.8, 3.2 Hz), 6.74 (1H, dd, *J*= 0.6, 7.7 Hz), 6.90 (1H, ddd, *J*= 2.3, 8.7, 9.6 Hz), 7.02 (1H, dd, *J*= 2.2, 9.9 Hz), 7.14-7.18 (2H, m), 7.22 (1H, td, *J*= 1.3, 7.6 Hz), 7.46 (1H, dd, *J*= 1.3, 7.6 Hz), 7.57 (1H, dd, *J*= 5.4, 8.6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.61 (CH_3), 21.56 (CH_2), 22.18 (CH_2), 48.74 (CH_2), 78.20 (quat), 96.25 (CH, d, $J_{C\text{-}F}$= 26.2 Hz), 96.33 (quat), 101.80 (CH), 108.28 (CH, d, $J_{C\text{-}F}$= 24.4 Hz), 121.58 (CH, d, $J_{C\text{-}F}$= 10.0 Hz), 122.53 (quat), 125.03 (quat), 126.52 (CH), 127.44 (CH), 128.04 (CH), 128.80 (CH, d, $J_{C\text{-}F}$= 3.6 Hz), 132.33 (CH), 136.41 (quat, d, $J_{C\text{-}F}$=

23.4 Hz), 138.39 (quat), 159.80 (quat, d, J_{C-F}=237.4 Hz); **IR** (neat): 2962, 2872, 2231, 1620, 1487, 1465, 1452, 1330, 1251, 1166 cm^{-1}; **HRMS:** (APCI) calculated for $C_{20}H_{19}NF$ [MH^+]: 292.1496, found: 292.1500.

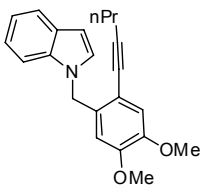
1-(2-Pent-1-ynylbenzyl)-*1H*-indole-5-carboxylic acid ethyl ester, 5e. The general *N*-alkylation reaction between *1H*-indole-5-carboxylic acid (3.1 mmol) and 2-pent-1-ynylbenzyl bromide (2.2 equiv) afforded the dialkylated product. The crude obtained after the usual aqueous work-up and solvent evaporation was dissolved in EtOH (50 mL) and LiOH (223 mg, 9.3 mmol) was added. The mixture was left stirring overnight and then the solvent was evaporated under vacuum. The crude was partitioned between EtOAc and water (15 mL each), the layers were separated and the aqueous one was further extracted with EtOAc (15mL × 3). The combined organic layers were washed with brine (15 mL × 3), then dried over $MgSO_4$, filtered and the solvent evaporated. The residue was purified through flash chromatography on silica (hexane:CH_2Cl_2, 6:4) to give **5f** as a colourless oil in 37% yield after two steps. (46% of 2-pent-1-ynylbenzyl alcohol was recovered). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.05 (3H, t, *J*= 7.4 Hz), 1.41 (3H, t, *J*= 7.1 Hz), 1.63 (2H, sext, *J*= 7.2 Hz), 2.43 (2H, t, *J*= 7.0 Hz), 4.39 (2H, q, *J*= 7.12 Hz), 5.49 (2H, s), 6.65 (1H, dd, *J*= 0.7, 3.2 Hz), 6.69 (1H, dd, *J*= 0.6, 7.7 Hz), 7.12 (1H, td, *J*= 1.3, 7.6 Hz), 7.18-7.22 (2H, m), 7.33 (1H, d, *J*= 8.7 Hz), 7.46 (1H, dd, *J*= 1.1, 7.6 Hz),7.89 (1H, dd, *J*= 1.6, 8.7 Hz), 8.42 (1H, dd, *J*= 0.4, 1.6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.60 (CH_3), 14.46 (CH_3), 21.55 (CH_2), 22.17 (CH_2), 48.80 (CH_2), 60.49 (CH_2), 78.12 (quat), 96.38 (quat), 103.23 (CH), 109.35 (CH), 121.96 (quat), 122.55 (quat), 123.05 (CH), 123.89 (CH), 126.50 (CH), 127.50 (CH), 128.05 (CH), 128.11 (quat), 129.71 (CH), 132.35 (CH), 138.26 (quat), 138.83 (quat), 167.71 (CO); **IR** (neat): 2927, 2933, 2228, 1707, 1612, 1308, 1254, 1184 cm^{-1}; **HRMS:** (ESI) calculated for $C_{23}H_{24}O_2N$ [MH^+]: 346.1802, found: 346.1798.



1-(5-Fluro-2-pent-1-ynylbenzyl)-*1H*-indole, 5f. General procedure for *N*-alkylation between indole (1.2 mmol) and 5-fluoro-2-pent-1-ynylbenzyl bromide gave the desired product in 82% yield after 4 h reaction. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.07 (3H, t, *J*= 7.4 Hz), 1.66 (2H, sext, *J*= 7.0 Hz), 2.45 (2H, t, *J*= 7.0 Hz), 5.45 (2H, s), 6.33 (1H, dd, *J*= 2.6, 9.5 Hz), 6.58 (1H, d, *J*= 3.0 Hz), 6.87 (1H, td, *J*= 2.6, 8.3 Hz), 7.12 (1H, t, *J*= 7.3 Hz), 7.15 (1H, d, *J*= 3.2 Hz), 7.18 (1H, td, *J*= 1.0, 7.5 Hz), 7.27 (1H, d, *J*= 6.3 Hz), 7.42 (1H, dd, *J*= 5.6, 8.5 Hz), 7.67 (1H, d, *J*= 7.8 Hz); **^{13}C NMR:** (125 MHz, $CDCl_3$): δ 13.63 (CH_3), 21.52 (CH_2), 22.19 (CH_2), 48.37 (CH_2), 77.25 (quat), 95.86 (quat), 102.08 (CH), 109.57 (CH), 113.57 (CH, d, J_{C-F}= 23.4 Hz), 114.47 (CH, d, J_{C-F}= 22.1 Hz), 118.09 (quat, d, J_{C-F}= 3.4 Hz), 119.68 (CH), 121.03 (CH), 121.86 (CH), 128.24 (CH), 128.64 (quat), 133.88 (CH, d, J_{C-F}= 8.2 Hz), 136.21 (quat), 141.85 (quat, d, J_{C-F}= 7.2 Hz), 162.3 (quat, d, J_{C-F}= 251.3 Hz); **IR** (neat): 2962, 2931, 2220, 1606, 1583, 1512, 1485, 1462, 1433, 1317, 1267, 1186 cm^{-1}; **HRMS:** (APCI) calculated for $C_{20}H_{19}NF$ [MH^+]: 292.1496, found: 292.1497.

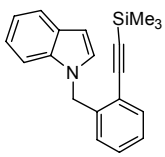


1-(4,5-Dimethoxy-2-pent-1-ynylbenzyl)-*1H*-indole, 5g. This compound was prepared using an alternative ordering of the steps in the general procedure. Accordingly, 2-bromo-4,5-dimethoxybenzyl bromide[8] was synthesised first from 2-bromo-4,5-dimethoxybenzyl alcohol (1 g, 4.04 mmol) in 81% yield following the general bromination procedure. Next, *N*-alkylation of indole (2.92 mmol) with the bromide according to the general alkylation procedure afforded **1-(2-Bromo-4,5-dimethoxybenzyl)-*1H*-indole** as a white solid in 75% yield. [**m.p.:** 66-68 ºC **^{1}H NMR** (400 MHz, $CDCl_3$): δ 3.52 (3H, s), 3.86 (3H, s), 5.32 (2H, s), 6.16 (1H, s), 6.57 (1H, d, *J*= 3.1 Hz), 7.06 (1H, s), 7.11-7.14 (2H, m), 7.18-7.21 (1H, m), 7.29 (1H, d, *J*= 8.2 Hz), 7.66 (1H, d, *J*= 7.9 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 49.79 (CH_2), 55.81



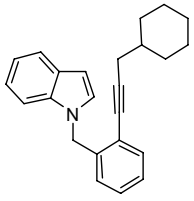
(CH_3), 56.20 (CH_3), 101.96 (CH), 109.65 (CH), 111.12 (CH), 112.41 (quat), 115.47 (CH), 119.66 (CH), 120.10 (CH), 121.83 (CH), 128.09 (CH), 128.53 (quat), 128.65 (quat), 136.28 (quat), 148.77 (quat), 149.00 (quat) **IR** (neat): 3053, 3003, 2933, 2908, 1600, 1504, 1462, 1435, 1382, 1313, 1259, 1209, 1159 cm^{-1}; **HRMS:** (ESI) calculated for $C_{17}H_{17}O_2NBr^{79}$ [MH^+]: 346.0437, found: 346.0442]. 1-(2-Bromo-4,5-dimethoxybenzyl)-*1H*-indole (400 mg, 1.15 mmol) was dissolved in diisopropylamine (14 mL) and bubbled with N_2 for 10 min. Meanwhile $Pd(OAc)_2$ (13.4 mg, 0.06 mmol), CuI (21mg, 0.11 mmol), PPh_3 (60.2 mg, 0.23 mmol) and 1-pentyne (120 µL, 1.26 mmol) were added. The mixture was heated up to 100 ºC and left stirring under a N_2 atmosphere for 15 h. After this time the reaction was cooled down to r.t. and the crude material filtered through a silica pad eluting with EtOAc. The solvent was evaporated *in vacuo*. The residue was purified by flash chromatography on silica (hexane:EtOAc, 6:4) giving 188 mg of a colourless oil (51%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.05 (3H, t, *J*= 7.4 Hz), 1.64 (2H, sext, *J*= 7.2 Hz), 2.43 (2H, t, *J*= 7.0 Hz), 3.59 (3H, s), 3.86 (3H, s), 5.41 (2H, s), 6.30 (1H, s), 6.54 (1H, dd, *J*= 0.8, 3.1 Hz), 6.94 (1H, s), 7.1 (1H, ddd, *J*= 1.0, 7.0, 8.0 Hz), 7.15 (2H, d, *J*= 3.2 Hz), 7.18 (1H, td, *J*= 1.1, 2.2 Hz), 7.37 (1H, dd, *J*= 0.8, 8.2 Hz), 7.64 (1H, m); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.65 (CH_3), 21.55 (CH_2), 22.29 (CH_2), 48.28 (CH_2), 55.72 (CH_3), 55.96 (CH_3), 78.27 (quat), 94.20 (quat), 101.55 (CH), 109.76 (CH), 110.03 (CH), 114.55 (CH), 114.67 (quat), 119.42 (CH), 120.89 (CH), 121.58 (CH), 128.17 (CH), 128.63 (quat), 132.04 (quat), 136.37 (quat), 147.97 (quat), 149.12 (quat); **IR** (neat): 2960, 2931, 2870, 2223, 1512, 1462, 1265, 1224, 1207 cm^{-1}; **HRMS:** (ESI) calculated for $C_{22}H_{24}O_2N$ [MH^+]: 334.1802, found: 334.1806.

1-(2-Trimethylsilanylethynylbenzyl)-*1H*-indole, 5h. 2-Ethynylbenzyl-*1H*-indole (200 mg, 0.86 mmol) was weighed in an oven-dried flask and dissolved in dry THF (3 mL) under N_2 atmosphere. The flask was put in a -78 ºC dry ice/acetone bath and nBuLi (1.6 M, 1.04 mmol) was added dropwise during 15 min. The mixture was stirred 30 min. at -78 ºC and then 30 min. at r.t. After that it was cooled again at -78 ºC and trimethylsilyl chloride (1.29 mmol) was added dropwise



via syringe. The reaction was left to warm up to r.t. during 2h. After this time EtOAc and water (5 mL each) were added, the two phases were separated. The aqueous layer was further extracted with EtOAc (5mL × 2), the combined organic layers were washed with brine (5 mL × 2), dried over $MgSO_4$, filtered and concentrated under vacuum. The residue was purified through a silica column (hexane:CH_2Cl_2, 8:2) to give **5i** as a white solid (99%). **m.p.:**102-104 ºC **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.27 (9H, s), 5.49 (2H, s), 6.56 (1H, d, *J*=2.5 Hz), 6.70 (1H, d, *J*= 7.1 Hz), 7.10-7.21 (5H, m), 7.32 (1H, dd, *J*= 0.5, 8.2 Hz), 7.51 (1H, dd, *J*= 1.3, 7.6 Hz), 7.66 (1H, d, *J*= 7.9 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ -0.05 (3xCH_3), 48.44 (CH_2), 100.39 (quat), 101.7 (CH), 102.37 (quat), 109.77 (CH), 119.53 (CH), 120.93 (CH), 121.35 (quat), 121.70 (CH), 126.51 (CH), 127.24 (CH), 128.44 (CH), 128.61 (quat), 129.03 (CH), 132.49 (CH), 136.30 (quat), 139.57 (quat); **IR** (KBr): 3090, 2960, 2918, 2160, 1463, 1247 cm^{-1}; **HRMS:** (ESI) calculated for $C_{20}H_{22}NSi$ [MH^+]: 304.1516, found: 304.1520.

1-[2-(3-Cyclohexylprop-1-ynyl)-benzyl]-*1H*-indole, 5i. The general procedure for the *N*-alkylation of indole (0.73



mmol) and 2-(3-cyclohexylprop-1-ynyl)-benzyl bromide afforded 158 mg (91%) of the desired product. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.09-1.17 (3H, m), 1.18-1.32 (3H, m), 1.58-1.64 (1H, m), 1.71-1.76 (2H, m), 1.85-1.89 (2H, m), 2.37 (2H, d, *J*= 6.6 Hz), 5.48 (2H, s), 6.56 (1H, dd, *J*= 0.8, 3.1 Hz),6.68 (1H, d, *J*= 7.7 Hz), 7.08-7.13 (2H, m), 7.15-7.19 (3H, m), 7.31 (1H, dd, *J*= 0.7, 8.1 Hz), 7.45 (1H, dd, *J*= 1.2, 7.6 Hz), 7.66 (1H, d, *J*= 7.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.11 (2 × CH_2), 26.24 (CH_2), 27.42 (CH_2), 32.83 (2 × CH_2), 37.47 (CH), 48.59 (CH_2), 78.97 (quat), 95.26 (quat), 101.58 (CH), 109.77 (CH), 119.47 (CH), 120.88 (CH), 121.63 (CH), 122.43 (quat), 126.46 (CH), 127.21 (CH), 127.97 (CH), 128.39

(CH), 128.60 (quat), 132.23 (CH), 136.36 (quat), 138.90 (quat); **IR** (neat): 2920, 2848, 2220, 1612, 1512, 1483, 1462, 1448, 1350, 1317, 1192, 1178 cm^{-1}; **HRMS:** (ESI) calculated for $C_{24}H_{26}N$ [MH^+]: 328.2060, found: 328.2063.

1-(2-Cyclohexylethynylbenzyl)-*1H*-indole, 5j. The general procedure for the *N*-alkylation of indole (0.67 mmol) and 2-cyclohexylethynylbenzyl bromide gave 180 mg (86%) of a colourless oil. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.34-1.42 (3H, m), 1.52-1.61 (3H, m), 1.73-1.80 (2H, m), 1.88-1.92 (2H, m), 2.64-2.70 (1H, m), 5.48 (2H, s), 6.57 (1H, dd, *J*= 0.7, 3.1 Hz), 6.68 (1H, d, *J*= 7.5 Hz), 7.08-7.13 (2H, m),7.16-7.20 (3H, m), 7.32 (1H, d, *J*= 8.1 Hz), 7.45 (1H, dd, *J*= 1.2, 7.6 Hz), 7.66 (1H, d, *J*= 7.6 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 24.88 (CH_2), 25.86 (2 × CH_2), 29.84 (CH), 32.69 (2 × CH_2), 48.56 (CH_2), 78.04 (quat), 100.46 (quat), 101.58 (CH), 109.78 (CH), 119.46 (CH), 120.88 (CH), 121.62 (CH), 122.33 (quat), 126.40 (CH), 127.18 (CH), 127.96 (CH), 128.41 (CH), 128.59 (quat), 132.09 (CH), 136.34 (quat), 138.91 (quat); **IR** (neat): 3055, 2927, 2852, 2223, 1512, 1483, 1462, 1448, 1350, 1317, 1178 cm^{-1}; **HRMS:** (ESI) calculated for $C_{23}H_{24}N$ [MH^+]: 314.1903, found: 314.1906.

2-(Indol-1-ylmethylphenyl)-propynoic acid methyl ester, 5k. 1-(2-ethynylbenzyl)-*1H*-indole (150 mg, 0.65 mmol) was weighed in a dry flask, dissolved in dry THF (2 mL) and purged with N_2. The flask was put in a -78 ºC dry ice/acetone bath and *n*-BuLi (1.6 M, 440 µL, 0.72 mmol) was added dropwise *via* syringe. After the addition the mixture was left for 30 min at -78 ºC and 30 min at r.t., then recooled to -78 ºC when methyl chloroformate (60 µL, 0.78 mmol) was added dropwise. The final mixture was allowed to warm slowly to r.t. and left o/n. EtOAc and water (2 mL each) were added, the two phases were separated. The aqueous layer was further extracted with EtOAc (2mL × 2), the combined organic layers were washed with brine (2mL × 2), dried over $MgSO_4$, filtered and concentrated at reduced pressure. The residue was chromatographed on a silica column (hexane:CH_2Cl_2, 6:4) to give a white solid (76%) **m.p.:** 116-118 ºC **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.94 (3H, s), 5.62 (2H, s), 6.66 (1H, d, *J*= 3.1 Hz), 6.78-6.80 (1H, m), 7.20 (1H, td, *J*= 1.0, 7.5 Hz), 7.24-7.27 (2H, m), 7.33-7.36 (3H, m), 7.70-7.72 (1H, m), 7.74 (1H, d, *J*= 8.0 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 48.26 (CH_2), 52.93 (CH_3), 83.60 (quat), 85.56 (quat), 102.09 (CH), 109.62 (CH), 117.57 (quat), 119.68 (CH), 121.00 (CH), 121.86 (CH), 126.78 (CH), 127.59 (CH), 128.44 (CH), 128.67 (quat), 131.29 (CH), 133.79 (CH), 136.23 (quat), 141.41 (quat), 154.24 (CO); **IR** (neat): 3182, 3153, 2988, 2224, 1705, 1515, 1427, 1298, 1203 cm^{-1}; **HRMS**: (ESI) calculated for $C_{19}H_{16}O_2N$ [MH^+]: 290.1176, found: 290.1172.

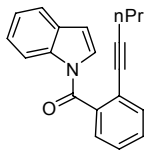
1-(2-Pent-1-ynylbenzyl)-*1H*-pyrrole, 5l. Alkylation of pyrrole (3.7 mmol) and 2-pent-1-ynylbenzyl bromide using the general procedure afforded the desired product in 55% yield as colourless oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.07 (3H, t, *J*= 7.5 Hz), 1.67 (2H, sext, *J*= 7.2 Hz), 2.46 (2H, t, *J*= 7.0 Hz), 5.23 (2H, s), 6.19 (2H, t, *J*= 2.0 Hz), 6.73 (2H, t, *J*= 2.0 Hz), 6.79 (1H, dd, *J*= 3.7, 5.4 Hz), 7.19 (2H, dd, *J*= 3.4, 5.7), 7.41 (1H, dd, *J*= 3.6, 5.5 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.63 (CH_3), 21.55 (CH_2), 22.21 (CH_2), 51.81 (CH_2), 78.23 (quat), 95.73 (quat), 108.34 (2 × CH), 121.30 (2 × CH), 122.30 (quat), 126.74 (CH), 127.26 (CH), 128.07 (CH), 132.05 (CH), 139.85 (quat); **IR** (neat): 2963, 2931, 2231, 1708, 1496, 1450,1429, 1290, 1274, 1085 cm^{-1}; **HRMS:** (ESI) calculated for $C_{16}H_{18}N$ [MH^+]: 224.1434, found: 224.1436.

1-(2-Pent-1-ynylphenyl)-*1H*-indole, 5m. The named product was synthesised by a Sonogashira coupling from 1-(2-iodophenyl)-*1H*-indole (180 mg, 1.57 mmol, obtained following the procedure described by Larock *et al.*[9]) and 1-pentyne. The aryliodide was dissolved in Et_3N (5 mL) bubbled with N_2 for 10 min. and $PdCl_2(PPh_3)_2$ (4.3mg, 0.006 mmol), CuI (2.3mg, 0.012 mmol) and 1-pentyne (190 µL, 1.89 mmol) were added. The mixture was heated at 60 ºC for 20 h. Then the crude was filtered through a silica pad, eluting with EtOAc and the solvent was evaporated under vacuum. The residue was purified through a silica column (hexane:CH_2Cl_2, 8:2) affording 220 mg of colourless oil (54% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.75 (3H, t, *J*= 7.4 Hz), 1.31 (2H, sext, *J*= 7.0 Hz), 2.13 (2H, t, *J*= 7.0 Hz), 6.64 (1H, d, *J*= 3.2 Hz), 7.14 (1H, td, *J*= 1.1, 7.4 Hz), 7.18 (1H, td, *J*= 1.5, 8.0 Hz), 7.30 (1H, dd, *J*= 1.0, 8.7 Hz), 7.34 (1H, dd, *J*= 1.6, 7.4 Hz), 7.38-7.44 (3H, m), 7.58 (1H, dd, *J*= 1.4, 7.7 Hz), 7.67 (1H, d, *J*= 7.2 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.26 (CH_3), 21.36 (CH_2), 21.62 (CH_2), 95.83 (quat), 102.49 (CH), 111.02 (CH), 119.96 (CH), 120.67 (CH), 121.59 (quat), 121.76 (CH), 126.93 (CH), 127.00 (CH), 128.26 (CH), 128.76 (quat), 129.04 (CH), 133.61 (CH), 136.45 (quat), 140.58 (quat); **IR** (neat): 2960, 2931, 2870, 2230, 1514, 1492, 1458, 1330, 1211, 1136, 1012 cm^{-1}; **HRMS:** (APCI) calculated for $C_{19}H_{18}N$ [MH^+]: 260.1434, found: 260.1439.

1-[2-(2-Pent-1ynylphenyl)-ethyl]-*1H*-indole, 5n. 2-(2-Iodophenyl)-ethanol was synthesised according to the procedure described by Buchwald and Minatti[10] from the commercially available 2-iodophenylacetic acid. Sonogashira coupling according to the general procedure for benzyl alcohols and alkynes afforded 2-(pent-1-ynylphenyl)-ethanol[5] in 83% yield from 2-(2-iodophenyl)-ethanol (2.0 mmol) and pentyne (1.1 equiv). The alkynylphenyl ethanol was converted to the sulfonate[11] as follows: the alcohol (370 mg, 1.5 mmol) was dissolved in dry CH_2Cl_2 (2 mL) at r.t., DABCO (350mg, 3.12 mmol) and *p*-toluenesulfonyl chloride (440mg, 2.31 mmol) were added and the mixture was left stirring for 5 h. Usual aqueous work up and purification through a silica column (hexane: EtOAc, 1:1) afforded 514 mg of **toluene-4-sulfonic acid 2-(2-pent-1-ynylphenyl)-ethyl ester** (87%) as colourless oil [**^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.02 (3H, t, *J*= 7.4 Hz), 1.58 (2H, sext, *J*= 7.2 Hz), 2.35 (2H, t, *J*= 7.0 Hz), 2.43 (3H, s), 3.12 (2H, t, *J*= 7.2 Hz), 4.26 (2H, t, *J*= 7.2 Hz), 7.10-7.17 (3H, m), 7.27 (2H, d, *J*= 8.0 Hz), 7.31 (1H, dd, *J*= 2.0, 7.0 Hz), 7.68 (2H, d, *J*= 8.3 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.57 (CH_3), 21.42 (CH_3), 21.61 (CH_2), 22.18 (CH_2), 34.32 (CH_2), 69.63 (CH_2), 78.45 (quat), 94.76 (quat), 123.83 (quat), 126.80 (CH), 127.71 (CH), 127.80 (2 × CH), 129.68 (CH), 129.70 (2 × CH), 132.29 (CH), 133.07 (quat), 137.58 (quat), 144.47 (quat); **IR**: 2964, 2231, 1554, 1544, 1406, 1361, 1195 cm^{-1}; **HRMS:** (EI) calculated for $C_{20}H_{22}O_3S$: 342.1284, found: 342.1287]. The general *N*-alkylation failed to give the desired product (elimination product was obtained instead). So the method described by Guida and Mathre[12] for *N*-indole alkylation was followed. To a stirred solution of 18-crown-6 (29 mg, 0.11 mmol) in diethyl ether (2 mL), potassium tert-butoxide (123 mg, 1.1. mmol) and indole (118 mg, 1.0 mmol) were added in one portion. The mixture was purged with N_2 and stirred for 1 h at r.t. After this time toluene-4-sulfonic acid 2-(pent-1-ynylphenyl)-ethyl ester (398 mg, 1.16 mmol) dissolved in diethyl ether (2 mL) was added dropwise through a cannula under N_2 atm. The mixture was left to react for 20 h. Water (2 mL) and Et_2O (2 mL) were added and the layers were separated. The aqueous layer was extracted with Et_2O (2 mL × 2) and the combined organic solution was washed with brine (2 mL × 2), dried ($MgSO_4$), filtered and evaporated under vacuum. The crude was purified through a silica column (hexane:CH_2Cl_2, 8:2) to afford 95 mg of the desired product as a colourless oil (33% yield, 55% elimination product obtained). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.08 (3H, t, *J*= 7.4 Hz), 1.67 (2H, sext, *J*= 7.2 Hz), 2.45 (2H, t, *J*= 7.0 Hz), 3.27 (2H, t, *J*= 7.5 Hz), 4.39 (2H, t, *J*= 7.5 Hz), 6.45 (1H, d, *J*= 3.1 Hz), 6.96 (1H, d, *J*= 3.1 Hz), 7.00 (1H, dd, *J*= 1.5, 6.5 Hz), 7.11 (1H, t, *J*= 7.4 Hz), 7.14 (1H, dd, *J*= 1.5, 7.4 Hz), 7.17 (1H, dd, *J*= 1.7, 7.3 Hz), 7.20 (1H, t, *J*= 7.0 Hz), 7.44

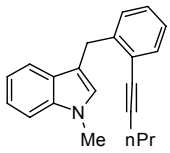
(2H, d, *J*= 8.2 Hz), 7.63 (1H, d, *J*= 7.9 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.67 (CH_3), 21.58 (CH_2), 22.31 (CH_2), 35.85 (CH_2), 46.96 (CH_2), 79.04 (quat), 94.25 (quat), 100.95 (CH), 109.38 (CH), 119.20 (CH), 120.91 (CH), 121.28 (CH), 123.68 (quat), 126.60 (CH), 127.80 (CH), 127.81 (CH), 128.60 (quat), 129.34 (CH), 132.52 (CH), 135.85 (quat), 139.97 (quat); **IR** (neat): 3051, 2962, 2872, 2231, 1485, 1265 cm^{-1}; **HRMS:** (ESI) calculated for $C_{21}H_{22}N$ [MH^+]: 288.1747, found: 288.1741.

1-(2-Pent-1-ynylbenzoyl)-*1H*-indole, 5o. The general *N*-alkylation procedure between indole (8.5 mmol) and 2-



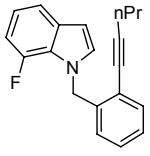
iodobenzoyl chloride afforded the known product 1-(2-iodobenzoyl)-1H-indole[7] as colourless prisms in 72% yield. 500 mg of this product (1.44 mmol) were weighed in a dry reaction tube with a screw cap. Diisopropylamine (5 mL) was added *via* syringe and the mixture was bubbled with N_2 for 10 min. Meanwhile $PdCl_2(PPh_3)$ (10mg, 0.014 mmol) and CuI (5.3mg, 0.028 mmol) were added followed by 1-pentyne (170 µL, 1.72 mmol). The mixture was purged with N_2, the tube was capped and heated up to 60 ºC. After 4 h of reaction the tube was left to cool down to r.t. and the content was filtered through a silica pad, eluting with EtOAc. The crude was concentrated and purified through a silica column (hexane:CH_2Cl_2, 6:4) giving 292 mg (71%) of a yellow oil. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.65 (3H, t, *J*= 7.4 Hz), 1.16 (2H, sext, *J*= 7.0 Hz), 2.07 (2H, t, *J*= 6.9 Hz), 6.56 (1H, d, *J*= 3.8 Hz), 7.05 (1H, d, *J*= 3.2 Hz), 7.30 (1H, t, *J*= 7.4 Hz), 7.36 (1H, t, *J*= 7.6 Hz), 7.42 (1H, td, *J*= 1, 7.5 Hz), 7.47 (1H, td, *J*= 1.4, 7.6 Hz), 7.51 (2H, d, *J*= 7.6 Hz), 7.57 (1H, d, *J*= 7.7 Hz), 8.40 (1H, bs); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.08 (CH_3), 21.19 (CH_2), 21.53 (CH_2), 77.32 (quat), 96.11 (quat), 108.80 (CH), 116.40 (CH), 120.66 (CH), 122.34 (quat), 123.92 (CH), 124.86 (CH), 127.40 (CH), 127.52 (CH), 127.69 (CH), 130.25 (CH), 130.95 (quat), 132.31 (CH), 135.54 (quat), 137.85 (quat), 168.14 (CO); **IR** (neat): 2962, 2930, 2233, 1687, 1536, 1451, 1380, 1344, 1207 cm^{-1}; **HRMS:** (ESI) calculated for $C_{20}H_{18}ON$ [MH^+]: 288.1383, found: 288.1386.

1-Methyl-3-(2-pent-1-ynylbenzyl)-*1H*-indole, 5p. The Friedel-Crafts reaction between indole and benzylbromides



described by De Rosa and Soriente.[16] was followed for the synthesis of this compound. Methylindole (75 µL, 0.6 mmol) and 2-pent-1-ynylbenzyl bromide (117 mg, 0.5 mmol) were added to a 5 mL biotage microwave tube, deionised water (1mL) was added, the tube was capped and placed in the microwave cavity were it was heated at 150 ºC under microwave irradiation for 10 min. After the vial was cooled down EtOAc (1 mL) was added and usual aqueous work up was done. The resulting crude was purified by a silica column (hexane:CH_2Cl_2. 95:5) affording 61 mg (43%) of the product. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.02 (3H, t, *J*= 7.4 Hz), 1.61 (2H, sext, *J*= 7.5 Hz), 2.42 (2H, t, *J*= 7.0 Hz), 3.74 (3H, s), 4.27 (2H, s), 6.80 (1H, s), 7.06-7.09 (1H, m), 7.11-7.18 (3H, m), 7.21 (1H, t, *J*= 7.0 Hz), 7.29 (1H, d, *J*= 8.2 Hz), 7.42 (1H, dd, *J*= 1.8, 7.1 Hz), 7.58 (1H, d, *J*= 7.9 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.54 (CH_3), 21.61 (CH_2), 22.28 (CH_2), 29.68 (CH_3), 39.60 (CH_2), 79.62 (quat), 94.40 (quat), 109.03 (CH), 113.75 (quat), 118.66 (CH), 119.33 (CH), 121.42 (CH), 123.73 (quat), 125.63 (CH), 127.23 (CH), 127.60 (CH), 127.97 (quat), 128.77 (CH), 132.04 (CH), 137.06 (quat), 143.13 (quat); **IR** (neat): 2960, 2931, 2872, 2233, 1560, 1473, 1448, 1373 cm^{-1}; **HRMS:** (ESI) calculated for $C_{21}H_{22}N$ [MH^+]: 288.1747, found: 288.1743.

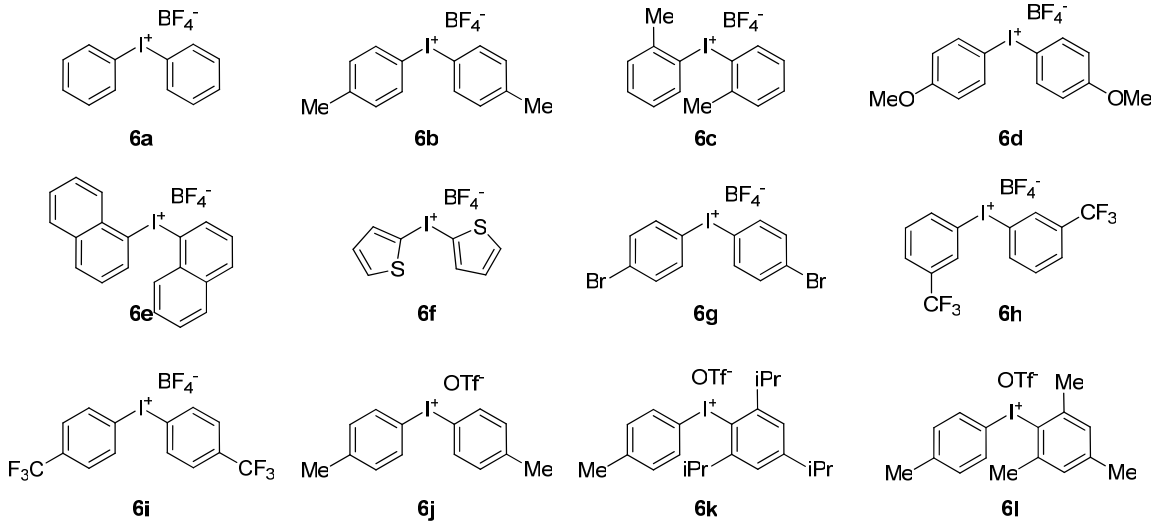
7-Fluoro-1-(2-pent-1-ynylbenzyl)-*1H*-indole (not in table). *N*-alkylation reaction of 7-indole (1.5 mmol) afforded a



pale brown oil in 53% yield after 2h reaction. The reaction flask was covered with aluminium foil as 7-fluoroindole is light sensitive. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.05 (3H, t, *J*= 7.4 Hz), 1.64 (2H, sext, *J*= 7.3 Hz), 2.43 (2H, t, *J*= 7.0 Hz), 5.66 (2H, s), 6.55 (1H, dd, *J*= 2.4, 3.0 Hz), 6.73 (1H, d, *J*= 7.4 Hz), 6.85

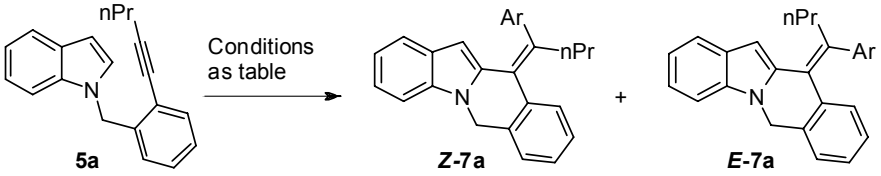
(1H, ddd, *J*= 0.6, 7.8, 12.8 Hz), 6.97-7.01 (1H, m), 7.11 (1H, d, *J*= 3.1 Hz), 7.13 (1H, td, *J*= 1.4, 7.6 Hz), 7.19 (1H, td, *J*= 1.3, 7.5 Hz), 7.39 (1H, d, *J*= 7.9 Hz), 7.44 (1H, dd, *J*= 1.3, 7.6 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.57 (CH_3), 21.54 (CH_2), 21.19 (CH_2), 50.65 (CH_2), 78.25 (quat), 95.88 (quat), 102.59 (CH), 107.34 (CH, d, J_{C-F}= 18.0 Hz), 116.70 (CH, d, J_{C-F}= 3.5 Hz), 119.67 (CH, d, J_{C-F}= 6.5 Hz), 122.25 (CH), 124.38 (quat, d, J_{C-F}=9.4 Hz), 126.40 (quat), 127.23 (CH), 128.01 (CH), 129.71 (CH), 132.20 (CH), 135.60 (quat, d, J_{C-F}= 5.5 Hz), 139.77 (quat), 150.28 (quat, d, J_{C-F}= 243.8 Hz); **IR**: 2960, 2929, 2229, 1573, 1490, 1452, 1313, 1238, 1190, 1178, 1029 cm^{-1}; **HRMS:** (APCI) calculated for $C_{20}H_{19}NF$ [MH^+]: 292.1496, found: 292.1496.

Synthesis of Diaryliodonium salts



All the diaryliodonium salts were synthesised from literature procedures. Diphenyliodonium tetrafluoroborate (**6a**) was obtained by oxidative anion metathesis from the commercially available diphenyliodonium bromide and fluoroboric acid as described by Skulski and Kazmierczak[17]. Salts **6b, 6c**, **6d**, **6e**, **6g**, **6h** and **6i** were prepared by the one-pot synthesis described by Olofsson and co-workers[18] from the corresponding arylboronic acids and the aryl iodides. **6f** was synthesised from 2-(Diacetoxyiodo)thiophene[19] and thiophene-2-boronic acid as described by Ochiai and co-workers[20]. Finally salts **6j, 6k** and **6l** were prepared from *p*-iodotoluene and the corresponding arene in the presence of mCPBA and TfOH[21].

3. Optimisation of tetra-substituted alkene synthesis.



5a **Z-7a** **E-7a**

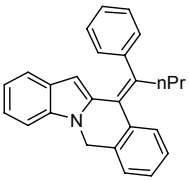
Entry	Catalyst (5 mol%)	Ar-I (1.2 equiv)	Ligand	Base	Solvent (0.1 M)	T (°C)	t (h)	Results[a]
1	$Pd(OAc)_2$	PhI	PPh_3, 10 mol%	-	Toluene	100	15	n.r.
2[b]	$Pd(OAc)_2$	PhBr	di-Prpf, 7 mol%	DABCO 2 equiv	NMP (0.5 M)	120	15	traces
3	$Pd(OAc)_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	80	15	47% **7a**, *Z:E*, 5:1[c]
4	$Pd(OAc)_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.[d]	24	57%, only *Z*-**7a**
5	$Pd(CNPh)_2Cl_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	40%, only *Z*-**7a**
7	$Pd_2(dba)_3$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	10%, only *Z*-**7a**
8	$Pd(C_5H_7O_2)_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	55%, only *Z*-**7a**
9	Pd(dppf)$_2$.DCM	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	traces
10	$FeCl_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	n.r.[e]
11	$Rh(C_5H_7O_2)_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	n.r.
12	$Ir(C_5H_7O_2)_2$	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	n.r.
13	-	Ph_2IBF_4	-	-	CF_3CH_2OH	r.t.	24	n.r.
14	$Pd(OAc)_2$	-	-	-	CF_3CH_2OH	r.t.	24	n.r.
15	$Pd(OAc)_2$	PhI	-	-	CF_3CH_2OH	r.t.	24	n.r.
16	$Pd(OAc)_2$	Ph_2IBF_4	PPh_3, 10 mol%	-	CF_3CH_2OH	r.t.	24	12%[f]
17	$Pd(OAc)_2$	Ph_2IBF_4	P(*o*Tol)$_3$, 10 mol%	-	CF_3CH_2OH	r.t.	24	52%[f]
18	$Pd(OAc)_2$	Ph_2IBF_4	1,10-phen, 10 mol%	-	CF_3CH_2OH	r.t.	24	26%[f]
19	$Pd(OAc)_2$	Ph_2IBF_4	IMes.HCl, 10 mol%	LiO^tBu (1 eq)	CF_3CH_2OH	r.t.	24	46%, only *Z*-**7a**
20	$Pd(OAc)_2$	Ph_2IBF_4	SIMes.HCl, 10 mol%	LiO^tBu (1 eq)	CF_3CH_2OH	r.t.	24	59%, only *Z*-**7a**
21	$Pd(OAc)_2$	Ph_2IBF_4	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	CF_3CH_2OH	r.t.	24	62%, only *Z*-**7a**
22	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	CF_3CH_2OH	30	8	78%, only *Z*-**7a**
23	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	CH_2Cl_2	30	3	92%, **7a**, *Z:E*, 3:1[c]
24	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	DCE	30	24	63%, **7a**, *Z:E,* 1.3:1[c]
25	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	MeOH	30	24	79%, only *Z*-**7a**
26	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	MeCN	30	2	93%, only *Z*-**7a**[g]
27	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	Cs_2CO_3 (1 eq)	Chlorobenzene	30	3	86%, only *Z*-**7a**
28	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	SIMes.HCl, 10 mol%	-	MeCN	30	24	53%, only *Z*-**7a**
29	$Pd(OAc)_2$	Ph_2IBF_4 1.05 eq	-	Cs_2CO_3 (1 eq)	MeCN	30	2	52% only *Z*-**7a**

All reaction carried out with 0.3 mmol of **5a**. [a] Isolated yields. [b] Reaction conditions used in the 5-*exo*-dig annulation of *o*-alkynylbiaryls by Gevorgyan and co-workers.[1] [c] NMR ratio. [d] ~ 20 °C. [e] n.r.: no reaction, starting material recovered. [f] HPLC yield. [g] Whilst highly efficient for **5a**, MeCN afforded lower *Z*-selectivities than chlorobenzene when the reaction was extended to other indoles.

General procedure for the annulation tandem reaction between alkyne-tethered indoles and diaryliodonium salts

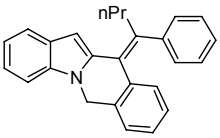
Cs_2CO_3, SIMes.HCl and the diaryliodonium salt were dried in an oven at 100 ºC under vacuum for 1 h prior to the reaction. The alkyne-tethered indole (0.3 mmol) was weighed in a 5 mL glass screwed cap vial (previously dried in the oven at 100 ºC) and dissolved in chlorobenzene (3 mL, ACS reagent grade). Cs_2CO_3 (98 mg, 0.3 mmol), SIMes.HCl (10.2 mg, 0.03 mmol), $PdOAc_2$ (3.4 mg, 0.015 mmol) and the diaryliodonium salt (0.32 mmol) were added in this order and the mixture was flushed with N_2. The vial was capped and put into an aluminium bloc previously heated at 30 ºC. The reaction was followed by TLC till no starting material remained. The mixture was then diluted with toluene and filtered through a silica + 3% Et_3N pad, eluting with toluene. To the filtrate was added some silica + 3% Et_3N and the solvent evaporated under vacuum in a rotary evaporator (water bath at 30 ºC). The product adsorbed on silica was purified through a silica + 3% Et_3N column eluting with hexane:CH_2Cl_2 mixtures.

11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, *Z*-7a. White solid in 86% yield from **5a**, and **6a**.



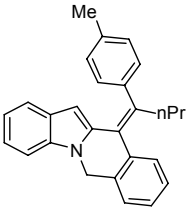
m.p.: 188-190 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.87 (3H, t, *J*= 7.0 Hz), 1.46 (2H, m), 2.80 (2H, t, *J*= 8.0 Hz), 5.16 (2H, s), 5.45 (1H, s), 6.95 (1H, td, *J*= 1.0, 7.5 Hz), 7.11 (1H, td, *J*= 1.5, 8.0 Hz), 7.17 (1H, d, *J*= 1.5 Hz), 7.19 (1H, d, *J*= 1.5 Hz), 7.28-7.42 (8H, m), 7.68 (1H, d, *J*= 7.5 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.95 (CH_3), 21.71 (CH_2), 38.32 (CH_2), 45.38 (CH_2), 100.45 (CH), 108.23 (CH), 119.13 (CH), 120.64 (CH), 120.79 (CH), 125.39 (quat), 126.29 (CH), 126.72 (CH), 126.79 (CH), 126.86 (CH), 128.19 (2 × CH), 128.40 (quat), 128.72 (CH), 128.82 (2 × CH), 129.02 (CH), 134.60 (2xquat), 135.39 (quat), 136.66 (quat), 142.62 (quat), 143.20 (quat); **IR** (KBr): 2954, 2925, 2865, 1452, 1385, 1368, 1264 cm^{-1}; **HRMS**: (ESI) calculated for $C_{26}H_{24}N$ [MH^+]: 350.1903, found: 350.1906.

11-[1-Phenylbut-(*E*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, *E*-7a. Reaction of **5a** with **6a** using the general procedure but with CH_2Cl_2 as reaction solvent gave 97 mg of **7a** as a mixture of isomers (92% yield, *Z*:*E*, 3:1). Further purification through a silica + 10% $AgNO_3$[22] column enabled partial separation of the minor *E* isomer for characterisation purposes. 22 mg (22 %) of the *E* isomer was obtained as a slightly yellow gum.



^{1}H NMR (500 MHz, $CDCl_3$): δ 0.86 (3H, t, *J*= 7.3 Hz), 1.41 (2H, m), 3.05-3.08 (2H, m), 5.20 (2H, s), 6.69 (1H, s), 6.73 (1H, d, *J*= 7.9 Hz), 6.82 (1H,t, *J*= 7.6 Hz), 7.05 (1H, t, *J*= 7.4 Hz), 7.12-7.15 (1H, m), 7.17 (2H, d, *J*= 6.5 Hz), 7.23-7.29 (5H, m), 7.44 (1H, d, *J*= 8.2 Hz), 7.68 (1H, d, *J*= 7.9 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.79 (CH_3), 21.45 (CH_2), 37.15 (CH_2), 45.49 (CH_2), 100.14 (CH), 108.47 (CH), 119.51 (CH), 120.66 (CH), 121.25 (CH), 125.10 (quat), 125.55 (CH), 125.93 (CH), 126.08 (CH), 126.73 (CH), 128.08 (2 × CH), 128.44 (quat), 129.41 (2 × CH), 129.90 (CH), 134.03 (quat), 135.06 (quat), 135.99 (quat), 136.10 (quat), 142.40 (quat), 142.86 (quat); **IR** (neat): 2933, 2947, 2858, 1421, 1265 cm^{-1}; **HRMS**: (ESI) calculated for $C_{26}H_{24}N$ [MH^+]: 350.1903, found: 350.1901.

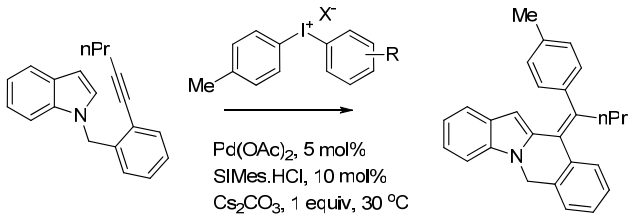
11-[1-*p*-Tolylbut-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, 7b. White solid in 90% yield from **5a** and **6b**.



m.p.: 190-192 ºC **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.86 (3H, t, *J*= 7.3 Hz), 1.46 (2H, sext, *J*= 7.3 Hz), 2.39 (3H, s), 2.78 (2H, m), 5.15 (2H, s), 5.47 (2H, s), 6.96 (1H, td, *J*= 0.9, 7.7 Hz), 7.07 (2H, d, *J*= 8 Hz), 7.11 (1H, td, *J*= 1.2, 7.2 Hz), 7.15 (2H, d, *J*= 7.7 Hz), 7.30-7.33 (3H, m), 7.37 (1H, dt, *J*= 1.4, 7.6 Hz), 7.40 (1H, d, *J*= 7.4 Hz), 7.67 (1H, dd, *J*= 0.8, 7.7 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.9 (CH_3), 21.29 (CH_3), 21.76 (CH_2), 31.58 (CH_2), 38.43 (CH_2), 45.37 (CH_2), 100.41 (CH), 108.22 (CH),

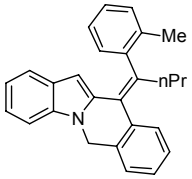
119.08 (CH), 120.61 (CH), 120.71 (CH), 125.31 (quat), 126.25 (CH), 126.69 (CH), 126.77 (CH), 128.42 (quat), 128.64 (2 × CH), 128.70 (CH), 128.88 (2 × CH), 134.59 (2xquat), 135.52 (quat), 136.27 (quat), 136.79 (quat), 139.57 (quat), 143.33 (quat); **IR** (neat)**:** 2904, 1496, 1452, 1280, 1195, 1033, 1022 cm^{-1}; **HRMS:** (ESI) calculated for $C_{27}H_{26}N$ [MH^+]: 364.2060, found: 364.2066.

Reaction with different tolyliodonium salts

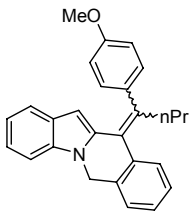


Entry[a]	R	X^-	Solvent (0.1 M)	Results[b]
1	1,3,5-iPr, **6k**	OTf	MeCN	n.r.[c]
2	1,3,5-iPr, **6k**	OTf	CF_3CH_2OH	50%
3	1,3,5-iPr, **6k**	OTf	Chlorobenzene	69%
4	1,3,5-Me, **6l**	OTf	Chlorobenzene	75%
5	4-Me, **6j**	OTf	Chlorobenzene	90%
5	4-Me, **6b**	BF_4	Chlorobenzene	90%

[a] 0.3 mmol scale reaction. 1.05 equiv. of diaryliodonium salt used. [b] Isolated yield [c] n.r. = no reaction, starting material recovered.

11-[1-*o*-Tolylbut-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, 7c. Light brown oil in 83% yield from **5a** and **6c** after 3 h. 

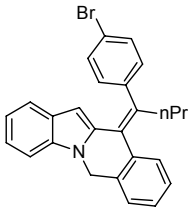
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.91 (3H, t, *J*= 7.3 Hz), 1.47-1.62 (2H, m), 2.07 (3H, s), 2.57-2.63 (1H, m), 2.88-2.92 (1H, m), 5.10 (1H, d, *J*= 14.6 Hz), 5.20 (1H, d, *J*= 14.6 Hz), 5.34 (1H, s), 6.96 (1H, t, *J*= 7.4 Hz), 7.11 (1H, t, *J*= 7.5 Hz), 7.16-7.18 (2H, m), 7.24 (1H, d, *J*= 3.4 Hz), 7.25 (1H, d, *J*= 3.8 Hz), 7.29-7.35 (3H, m), 7.39 (1H, d, *J*= 7.5 Hz), 7.42 (1H, d, *J*= 7.9 Hz), 7.7 (1H, d, *J*= 7.6 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 14.30 (CH_3), 19.26 (CH_3), 21.72 (CH_2), 38.13 (CH_2), 45.29 (CH_3), 100.03 (CH), 108.24 (CH), 119.13 (CH), 120.67 (CH), 120.81 (CH), 125.53 (CH), 125.74 (quat), 126.31 (CH), 126.77 (CH), 126.90 (CH), 126.98 (CH), 128.60 (CH), 128.68 (CH), 129.21 (CH), 129.70 (quat), 130.29 (CH), 134.47 (quat), 134.55 (quat), 134.79 (quat), 135.24 (quat), 136.61 (quat), 141.74 (quat), 142.00 (quat); **IR** (neat): 2956, 2857, 1612, 1597, 1454, 1317, 1234, 1141 cm^{-1}; **HRMS:** (ESI) calculated for $C_{27}H_{26}N$ [MH^+]: 364.2060, found: 364.2062.

11-[1-(4-Methoxyphenyl)but-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, *Z*-7d and **11-[1-(4-Methoxyphenyl)but-(*E*)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, *E*-7d**. White solid (86 mg, 75%, $Z_{(a)}$:$E_{(b)}$ = 1:2) from **5a** and **6d**. 

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.84 ($3H_b$, t, *J*= 7.3 Hz), 0.86 ($3H_a$, t, *J*= 7.3 Hz), 1.35-1.43 ($2H_b$, m), 1.43-1.49 ($2H_a$, m), 2.77-2.80 ($2H_a$, m), 3.02-3.05 ($2H_b$, m), 3.81 ($3H_b$, s), 3.84 ($3H_a$, s), 5.15 ($2H_a$, s), 5.18 ($2H_b$, s), 5.49 ($1H_a$, s), 6.66 ($1H_b$, s), 6.76 ($1H_b$, d, *J*= 7.9 Hz), 6.80 ($2H_b$, d, *J*= 8.7 Hz), 6.85 ($1H_b$, t, *J*= 7.6 Hz), 6.89 ($2H_a$, d, *J*= 8.7 Hz), 6.95-6.98 ($1H_a$, m), 7.03-7.13 ($2H_a$, $4H_b$, m), 7.16-7.18 ($2H_a$, m), 7.21-7.24 ($1H_b$, m), 7.27 ($1H_b$, d, *J*= 8.8 Hz), 7.30-7.34 ($2H_a$, m), 7.37 ($1H_a$, td, *J*= 1.4, 7.6 Hz), 7.40 ($1H_a$, d, *J*= 7.7 Hz), 7.42 ($1H_b$, d, *J*= 8.3 Hz), 7.66 ($1H_a$, d, *J*= 7.1 Hz), 7.67 ($1H_b$, d, *J*= 7.9 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.77 (CH_3), 13.92 (CH_3), 21.49 (CH_2), 21.74 (CH_2), 37.17 (CH_2), 38.45 (CH_2), 45.39 (CH_2), 45.50 (CH_2), 55.17 (CH_3), 55.20 (CH_3), 100.07 (CH), 100.37 (CH), 108.22 (CH), 108.43 (CH),

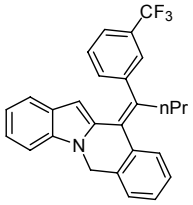
113.49 (2 × CH), 113.61 (2x CH), 114.15 (quat), 116.34 (quat), 119.12 (CH), 119.47 (CH), 120.63 (CH), 120.66 (CH), 120.73 (CH), 121.17 (CH), 124.85 (CH), 125.55 (CH), 125.80 (CH), 126.17 (CH), 126.25 (CH), 126.69 (CH), 126.78 (CH), 128.43 (quat), 128.46 (quat), 128.73 (CH), 129.90 (2 × CH), 130.07 (CH), 130.55 (2 × CH), 134.05 (quat), 134.59 (quat), 134.60 (quat), 134.87 (quat), 135.03 (quat), 135.54 (quat), 136.27 (quat), 136.37 (quat), 136.84 (quat), 138.18 (quat), 142.49 (quat), 142.96 (quat), 158.41 (quat), 158.43 (quat); **IR** (neat): 2956, 2933, 2873, 1604, 1508, 1465, 1448, 1246, 1178 cm^{-1}; **HRMS:** (ESI) calculated for $C_{27}H_{26}ON$ $[MH^+]$: 380.2009, found: 380.2017.

11-[1-(4-Bromophenyl)but-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, 7e. White solid in 81 % yield from



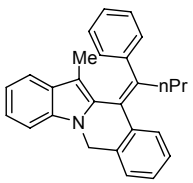
5a and **6g**. **m.p.:** 170-172 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.85 (3H, t, *J*= 7.3 Hz), 1.41 (2H, m), 2.76-2.80 (2H, m), 5.15 (2H, s), 5.46 (1H, s), 6.98 (1H, t, *J*= 7.4 Hz), 7.07 (2H, d, *J*= 8.2 Hz), 7.13 (1H, t, *J*= 7.4 Hz), 7.32-7.42 (5H, m), 7.47 (2H, d, *J*= 8.2 Hz), 7.66 (1H, d, *J*= 7.5 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.87 (CH_3), 21.63 (CH_2), 37.98 (CH_2), 45.38 (CH_2), 100.71 (CH), 108.27 (CH), 119.30 (CH), 120.75 (quat), 120.79 (CH), 121.05 (CH), 125.91 (quat), 126.35 (CH), 126.76 (CH), 127.04 (CH), 128.29 (quat), 128.63 (CH), 130.69 (2 × CH), 131.43 (2 × CH), 134.61 (quat), 134.65 (quat), 135.11 (quat), 135.26 (quat), 141.51 (quat), 141.58 (quat) **IR** (neat): 2957, 2870, 1485, 1452, 1319, 1240, 1009 cm^{-1}; **HRMS:** (ESI) calculated for $C_{26}H_{23}NBr^{79}$ $[MH^+]$: 428.1008, found: 428.1011.

11-[1-(3-Trifluoromethylphenyl)but-(Z)-ylidene]-6,11-dihydro-indolo[1,2*b*]isoquinoline, 7f. White solid in 86%



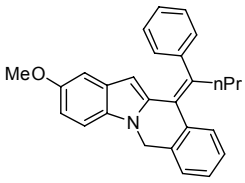
yield from **5a** and **6h**. **m.p.:** 128-130 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.88 (3H, t, *J*= 7.3 Hz), 1.39-1.46 (2H, m), 2.80-2.83 (2H, m), 5.17 (2H, s), 5.33 (1H, s), 6.97 (1H, t, *J*= 7.4 Hz), 7.13 (1H, m), 7.29-7.35 (4H, m), 7.38-7.44 (3H, m), 7.53 (1H, s), 7.58 (1H, d, *J*= 7.8 Hz), 7.68 (1H, d, *J*= 7.5 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.87 (CH_3), 21.66 (CH_2), 38.02 (CH_2), 45.38 (CH_2), 100.72 (CH), 108.28 (CH), 119.33 (CH), 121.26 (CF_3, q, $J_{C\text{-}F}$= 263 Hz), 120.76 (CH), 121.14 (CH), 123.72 (CH, q, $J_{C\text{-}F}$= 3.7 Hz), 125.62 (CH, q, $J_{C\text{-}F}$= 3.7 Hz), 126.39 (CH), 126.84 (CH), 127.18 (CH), 128.25 (quat), 128.63 (CH), 128.74 (CH), 130.60 (quat, q, $J_{C\text{-}F}$= 32.2 Hz), 132.61 (CH), 134.64 (quat), 134.69 (quat), 134.95 (quat), 136.00 (quat), 141.13 (quat), 143.34 (quat); **IR** (neat): 2966, 2941, 2883, 1589, 1454, 1332, 1319, 1165, 1107, 1070 cm^{-1}; **HRMS:** (ESI) calculated for $C_{27}H_{23}NF_3$ $[MH^+]$: 418.1777, found: 418.1776.

12-Methyl-11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, 7g. Yellow solid in 76% yield from

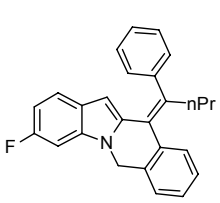


5b, and **6a**. **m.p.**: 158-160 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.70 (3H, t, 7.3 Hz), 1.07-1.19 (1H, m), 1.23-1.33 (1H, m), 1.38 (3H, s), 2.69-2.82 (1H, m), 3.17-3.30 (1H, m), 5.06-5.18 (1H, m), 5.23-5.26 (1H, m), 6.98 (1H, td, *J*= 1.0, 8.0 Hz), 7.13-7.24 (7H, m), 7.29-7.37 (4H, m), 7.64-7.65 (1H, d, *J*= 7.0 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 9.06 (CH_3), 13.28 (CH_3), 21.49 (CH_2), 35.64 (CH_2), 45.81 (CH_2), 106.36 (quat), 107.86 (CH), 118.22 (CH), 118.93 (CH), 120.81 (CH), 125.94 (CH), 126.18 (quat), 126.37 (CH), 126.39 (CH), 126.59 (CH), 127.96 (2 × CH), 128.34 (CH), 129.11 (quat), 129.23 (2 × CH), 133.88 (quat), 135.17 (quat), 135.74 (quat), 137. 44 (quat), 142.03 (quat), 142.56 (quat); **IR** (neat): 2953, 2906, 2858, 1490, 1465, 1444, 1375, 1247, 1028 cm^{-1}; **HRMS**: (ESI) calculated for $C_{26}H_{24}N$ $[MH^+]$: 350.1903, found: 350.1906.

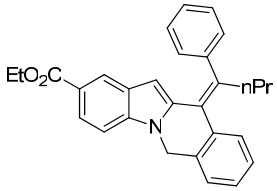
2-Methoxy-11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, 7h. White solid in 88% yield from **5c** and **6a**. **m.p.:** 192-194 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.87 (3H, t, *J*= 7.0 Hz), 1.42-1.55 (2H, m), 2.77-2.88 (2H, m), 3.75 (3H, s), 5.11 (2H, s), 5.32 (1H, s), 6.76 (1H, s), 6.77 (1H, dd, *J*= 2.5, 9.9 Hz), 7.17-7.21 (3H, m), 7.30-7.41 (6H, m), 7.68 (1H, dd, *J*= 1.0, 8.0 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.96 (CH_3), 21.73 (CH_2), 38.42 (CH_2), 45.46 (CH_2), 55.78 (CH_3), 100.17 (CH), 102.21 (CH), 108.93 (CH), 111.19 (CH), 125.36 (quat), 126.27 (CH), 126.67 (CH), 126.76 (CH), 126.82 (CH), 128.20 (2 × CH), 128.60 (quat), 128.70 (CH), 128.82 (2 × CH), 130.07 (quat), 134.60 (quat), 135.26 (quat), 137.22 (quat), 142.72 (quat), 142.97 (quat), 153.81 (quat); **IR** (neat): 2956, 2933, 1620, 1482, 1217, 1152, 1034, 786 cm^{-1}; **HRMS:** (ESI) calculated for $C_{27}H_{26}O_1N_1$: 380.2009, found: 380.2008.



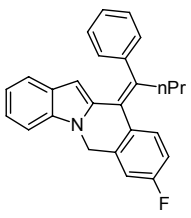
3-Fluoro-11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, 7i. White solid in 78% yield from **5d** and **6a**. **m.p.:** 74-76 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.87 (3H, t, *J*= 7.3 Hz), 1.42-1.50 (2H, m), 2.77-2.80 (2H, m), 5.08 (2H, s), 5.37 (1H, s), 6.71 (1H, ddd, *J*= 2.3, 8.7, 9.7 Hz), 6.98 (1H, dd, *J*= 2.1, 9.9 Hz), 7.16-7.19 (3H, m), 7.31-7.41 (6H, m), 7.68 (1H, d, *J*= 7.7 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.95 (CH_3), 21.70 (CH_2), 38.33 (CH_2), 45.59 (CH_2), 94.78 (CH, d, $J_{C\text{-}F}$= 26.2 Hz), 100.38 (CH), 107.80 (CH, d, $J_{C\text{-}F}$= 24.2 Hz), 121.23 (CH, d, $J_{C\text{-}F}$= 9.9 Hz), 124.99 (quat, d, $J_{C\text{-}F}$= 38.9 Hz), 126.32 (CH), 126.85 (2 × CH), 126.97 (CH), 127.48 (quat), 128.23 (2 × CH), 128.74 (CH), 128.75 (2 × CH), 134.23 (quat), 134.52 (quat, d, $J_{C\text{-}F}$= 12.1 Hz), 135.26 (quat), 137.15 (quat, $J_{C\text{-}F}$= 3.7 Hz), 142.57 (quat), 143.20 (quat), 159.38 (quat, d, $J_{C\text{-}F}$= 235.6 Hz); **IR** (neat): 3054, 2985, 1421, 1265 cm^{-1}; **HRMS:** (APCI) calculated for $C_{26}H_{23}NF$ [MH^+]: 368.1809, found: 368.1811.



11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline-2-carboxylic acid ethyl ester, 7j. White solid in 52% yield (17% SM recovered, brsm yield = 63%) from **5f**, and **6a** (30 h reaction time). **m.p.**: 112-114 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.88 (3H, t, *J*= 6.48 Hz), 1.38 (3H, t, *J*= 7.2 Hz), 1.43-1.53 (2H, m), 2.79-2.83 (2H, m), 4.34 (2H, q, *J*= 7.1 Hz), 5.18 (2H, s), 5.50 (1H, s), 7.18 (2H, dd, *J*= 1.7, 7.7 Hz), 7.31-7.43 (8H, m), 7.70 (1H, d, *J*= 7.8 Hz), 7.84 (1H, dd, *J*= 1.6, 8.7 Hz), 8.06 (1H, d, *J*= 1.2 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.94 (CH_3), 14.43 (CH_3), 21.65 (CH_2), 38.27 (CH_2), 45.63 (CH_2), 60.40 (CH_2), 101.73 (CH), 107.86 (CH), 121.48 (quat), 122.31 (CH), 123.49 (CH), 124.98 (quat), 126.37 (CH), 126.97 (CH), 127.0 (CH), 127.07 (CH), 127.87 (quat), 128.27 (2 × CH), 128.67 (2 × CH), 128.74 (CH), 134.09 (quat), 135.06 (quat), 136.92 (quat), 138.04 (quat), 142.32 (quat), 144.25 (quat), 167.75 (CO) **IR** (neat): 2958, 2870, 1701, 1608, 1444, 1354, 1300, 1249, 1165, 1085 cm^{-1}; **HRMS:** (ESI) calculated for $C_{29}H_{28}O_2N$ [MH^+]: 422.2115, found: 422.2115.

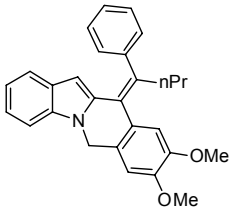


8-Fluoro-11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, 7k. Off-white solid in 49% yield (62% brsm, 43% SM recovered) from **5g**, and **6a**. **m.p.:** 138-140 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.87 (3H, t, *J*= 7.3Hz), 1.42-1.49 (2H, m), 2.75-2.78 (2H, m), 5.13 (2H, s), 5.40 (1H, s), 6.97 (1H, t, *J*= 7.5 Hz), 7.06-7.18 (5H, m), 7.29-7.37 (5H, m), 7.65 (1H, dd, *J*= 5.5, 8.5 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.95 (CH_3), 21.64 (CH_2), 38.34 (CH_2), 45.20 (CH_2), 100.66 (CH), 108.19 (CH), 113.29 (CH, d, $J_{C\text{-}F}$= 22.2 Hz), 113.65 (CH, d, $J_{C\text{-}F}$= 21.3 Hz), 119.32 (CH), 120.72 (CH), 120.99 (CH), 124.52 (quat), 126.88 (CH), 128.24 (2 × CH), 128.37 (quat), 128.76 (2 × CH), 130.37 (CH, d, $J_{C\text{-}F}$= 8.7 Hz), 131.43

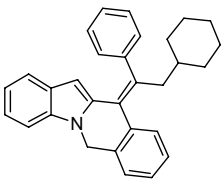


(quat, d, $J_{C\text{-}F}$= 3.3 Hz), 134.56 (quat), 134.41 (quat), 136.76 (quat, d, $J_{C\text{-}F}$= 7.6 Hz), 142.40 (quat), 143.11 (quat), 161.25 (quat, d, $J_{C\text{-}F}$= 247.6 Hz); **IR** (neat): 2958. 2870, 1614, 1581, 1492, 1450, 1238 cm^{-1}; **HRMS:** (ESI) calculated for $C_{26}H_{23}NF$ [MH^+]: 368.1809, found: 368.1813.

8,9-Dimethoxy-11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline, 7l. Tan solid in 78% yield from **5h** and **6a**. **m.p.:** 148-150 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.91 (3H, t, *J*= 7.3 Hz), 1.52-1.56 (2H, m), 2.78-2.81 (2H, m), 3.96 (3H, s), 3.97 (3H, s), 5.10 (2H, s), 5.39 (1H, s), 6.92 (1H, s), 6.95 (1H, t, *J*= 7.5 Hz), 7.10 (1H, t, *J*= 7.5 Hz), 7.18-7.19 (2H, m), 7.23 (1H, s), 7.28-7.37 (5H, m); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 14.15 (CH_3), 21.91 (CH_2), 38.93 (CH_2), 45.02 (CH_2), 56.03 (CH_3), 56.07 (CH_3), 101.34 (CH), 108.18 (CH), 109.39 (CH), 112.13 (CH), 119.13 (CH), 120.64 (CH), 120.78 (CH), 125.24 (quat), 126.79 (CH), 127.32 (quat), 127.71 (quat), 128.24 (2 × CH), 128.32 (quat), 128.88 (2 × CH), 134.62 (quat), 136.67 (quat), 141.86 (quat), 142.88 (quat), 147.23 (quat), 147.88 (quat); **IR** (neat): 2959, 2931, 1608, 1514, 1454, 1315, 1213, 1117 cm^{-1}; **HRMS:** (ESI) calculated for $C_{28}H_{28}O_2N$ [MH^+]: 410.2115, found: 410.2112.

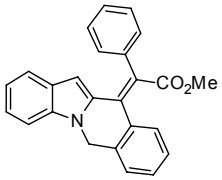


11-[2-Cyclohexyl-1-phenyleth-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, 7m. White solid in 71% yield (8h reaction) from **5j**, and **6a**. **m.p.:** 156-158 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.71-0.78 (2H, m), 1.00-1.03 (3H, m), 1.14-1.22 (1H, m), 1.51-1.54 (3H, m), 1.60-1.62 (2H, m), 2.86 (2H, d, *J*= 7.0 Hz), 5.14 (2H, s), 5.34 (1H, s), 6.93-6.96 (1H, m), 7.10 (1H, ddd, *J*= 1.1, 7.0, 8.2 Hz), 7.17 (2H, dd, *J*= 1.8, 7.6 Hz), 7.27-7.32 (6H, m), 7.36 (1H, td, *J*= 1.3, 7.6 Hz), 7.40 (1H, d, *J*= 7.4 Hz), 7.72 (1H, d, *J*= 7.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 26.03 (2 × CH_2), 26.34 (CH_2), 32.99 (2 × CH_2), 35.31 (CH), 42.63 (CH_2), 45.45 (CH_2), 100.22 (CH), 108.19 (CH), 119.05 (CH), 120.64 (CH), 120.69 (CH), 126.25 (CH), 126.48 (quat), 126.65 (CH), 126.66 (CH), 126.74 (CH), 128.10 (2 × CH), 128.42 (quat), 128.85 (2 × CH), 129.12 (CH), 134.52 (quat), 134.88 (quat), 135.79 (quat), 136.94 (quat), 141.74 (quat), 142.36 (quat) **IR** (neat): 2924, 1475, 1448, 1421, 1350, 1315, 1263, 1236, 1165 cm^{-1}; **HRMS:** (ESI) calculated for $C_{30}H_{30}N$ [MH^+]: 404.2373, found: 404.2373.

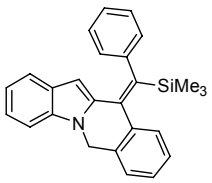


11-[1-Cyclohexyl-1-phenylmeth-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, 7n. White solid in 71% yield from **5k** and **6a** (8h reaction time). **m.p.:** 228-230 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 1.25-1.33 (5H, m), 1.59-1.61 (1H, m), 1.72-1.74 (2H, m), 1.82-1.83 (2H, m), 3.21-3.26 (1H, m), 5.14 (2H, s), 5.20 (1H, d, *J*= 0.7 Hz), 6.93 (1H, ddd, *J*= 0.9, 7.1, 7.5 Hz), 7.07-7.10 (3H, m), 7.24-7.26 (1H, m), 7.29-7.34 (5H, m), 7.38 (1H, td, *J*= 1.4, 7.6 Hz), 7.41 (1H, d, *J*= 7.4 Hz), 7.66 (1H, d, *J*= 6.9 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 25.78 (CH_2), 26.07 (2 × CH_2), 32.18 (2 × CH_2), 42.33 (CH), 45.38 (CH_2), 100.62 (CH), 108.16 (CH), 119.04 (CH), 120.60 (CH), 120.71 (CH), 124.97 (quat), 126.35 (CH), 126.67 (CH), 126.75 (CH), 126.87 (CH), 127.74 (2 × CH), 128.42 (quat), 128.54 (CH), 129.74 (2 × CH), 134.43 (quat), 134.78 (quat), 135.30 (quat), 136.79 (quat), 140.22 (quat), 147.89 (quat); **IR** (neat): 2929, 2850, 1487, 1448, 1317, 1238 cm^{-1}; **HRMS:** (ESI) calculated for $C_{29}H_{28}N$ [MH^+]: 390.2216, found: 390.2210.

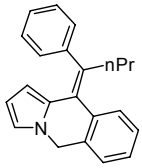
[6*H*-Indolo[1,2-*b*]isoquinolin-(11E)-ylidene]-phenyl-acetic acid methyl ester, 7o. Yellow solid in 79% from **5l** and **6a** (4h reaction time). **m.p.:** 190-192 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 3.68 (3H, s), 5.27 (2H, s), 5.63 (1H, s), 7.01 (1H, t, *J*= 7.8 Hz), 7.17-7.21 (1H, m), 7.32-7.44 (8H, m), 7.47-7.49 (2H, m), 7.69 (1H, dd, *J*= 1.1, 7.6 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): 42.25 (CH_2), 52.36 (CH_3), 102.75 (CH), 108.72 (CH), 119.85 (CH), 121.26 (CH), 122.08 (CH), 126.57 (CH), 126.91 (CH), 127.34 (CH), 128.02 (quat), 128.26 (CH), 128.42 (CH), 128.74 (2 × CH), 129.47 (2 × CH), 129.90 (quat), 131.94 (quat), 133.18 (quat), 133.28 (quat), 133.32 (quat), 135.39 (quat), 136.69 (quat), 170.36 (CO); **IR** (neat): 3053, 2947, 1724, 1448, 1435, 1319, 1261, 1215, 1132 cm^{-1}; **HRMS**: (ESI) calculated for $C_{25}H_{20}O_2N$ [MH^+]: 366.1489, found: 366.1489.

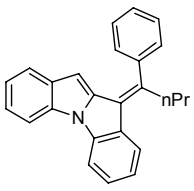


11-[1-Phenyl-1-trimethylsilanylmeth-(*E*)-ylidene]-6,11-dihydro-indolo[1,2*b*]isoquinoline, 7p. White solid in 42% yield (42% of SM recovered, 71% brsm) from **5i** and **6a** (36 hr reaction time). **m.p.:** 158-160 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.07 (9H, s), 5.18 (2H, s), 5.23 (1H, s), 6.96 (1H, td, *J*= 1.0, 7.5 Hz), 7.0 (2H, dd, *J*= 1.0, 7.5 Hz), 7.14 (1H, ddd, *J*= 1.1, 7.0, 8.2 Hz), 7.27-7.38 (8H, m), 7.78 (1H, dd, *J*= 1.9, 6.8 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 1.17 (3xCH_3), 45.18 (CH_2), 101.85 (CH), 108.45 (CH), 119.28 (CH), 120.98 (CH), 121.35 (CH), 125.70 (CH), 125.88 (CH), 126.73 (CH), 127.88 (2 × CH), 127.93 (CH), 128.18 (quat), 128.36 (2 × CH), 128.94 (CH), 134.00 (quat), 134.61 (quat), 136.41 (quat), 137.05 (quat), 138.68 (quat), 144.86 (quat), 145.35 (quat) **IR** (neat): 3059, 3016, 2947, 2858, 1583, 1483, 1446, 1665, 1317, 1250, 1199 cm^{-1}; **HRMS:** (APCI) calculated for $C_{26}H_{26}NSi$ [MH^+]: 380.1829, found: 380.1830.



10-[1-Phenylbut-(*Z*)-ylidene]-5,10-dihydropyrrolo[1,2*b*]isoquinoline, 7q. White solid in 70% yield from **5m** and **6a** (reaction temperature was maintained between 15-18 ºC for 2 h to avoid double bond isomerisation). **m.p.:** 148-150 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.86 (3H, t, *J*= 7.3 Hz), 1.45 (2H, sext, *J*= 7.4 Hz), 2.72-2.76 (2H, m), 4.96 (2H, s), 5.05 (1H, dd, *J*= 1.5, 3.7 Hz), 5.82 (1H, dd, *J*= 2.7, 3.6 Hz), 6.59 (1H, dd, *J*= 1.7, 2.4 Hz), 7.17-7.19 (2H, m), 7.26-7.32 (3H, m), 7.33-7.38 (3H, m), 7.65 (1H, d, *J*= 7.6 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.97 (CH_3), 21.83 (CH_2), 38.26 (CH_2), 49.10 (CH_2), 107.58 (CH), 107.85 (CH), 117.90 (CH), 125.15 (quat), 125.98 (CH), 126.51 (2 × CH), 126.56 (CH), 128.09 (2 × CH), 128.62 (CH), 128.99 (2 × CH), 130.46 (quat), 134.64 (quat), 135.80 (quat), 139.44 (quat), 143.23 (quat); **IR** (neat): 2954, 2924, 2868, 1490, 1475, 1458, 1436, 1323, 1190, 1082, 1070, 1026 cm^{-1}; **HRMS:** (ESI) calculated for $C_{22}H_{22}N$ [MH^+]: 300.1747, found: 300.1750.

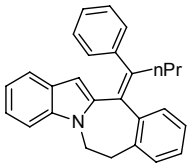




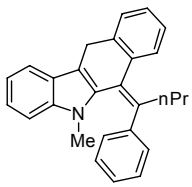
10-[1-Phenylbut-(*Z*)-ylidene]-*10H*-indolo[1,2*a*]indole, 7r. Yellow solid in 78% yield from **5n** and **6a** (50 ºC overnight). **m.p.:** 130-132 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.09 (3H, t, *J*= 7.3 Hz) ,1.73 (2H, sext., *J*= 7.4 Hz), 2.97-3.00 (2H, m), 5.14 (1H, s), 7.04 (1H, td, *J*=1.0, 7.5 Hz), 7.16 (2H, td, *J*= 1.0, 7.7 Hz), 7.20 (1H, ddd, *J*= 1.0, 7.2, 8.2 Hz), 7.34-7.37 (3H, m), 7.40 (1H,t d, *J*= 1.0, 7.8 Hz), 7.48 (1H, *J*= 1.9, 4.7Hz), 7.52-7.55 (2H, m), 7.60 (1H, d, *J*= 7.8 Hz), 7.67 (1H, dd, *J*= 0.6, 8.2 Hz), 7.83 (1H, d, *J*= 7.7 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 14.27 (CH_3), 20.95 (CH_2), 38.49 (CH_2), 98.39 (CH), 110.48 (CH), 110.52 (CH), 120.53 (CH), 121.49 (CH), 122.31 (CH), 122.42 (CH), 124.51 (quat), 124.96 (CH), 127.65 (2 × CH), 127.79 (CH), 128.36 (CH), 129.36 (2 × CH), 130.65 (quat), 131.15 (quat), 132.92 (quat), 140.90 (quat), 141.04 (quat),

143.82 (quat), 145.17 (quat); **IR** (neat): 3059, 2953, 2929, 2870, 1599, 1489, 1469, 1450, 1328, 1230 cm^{-1}; **HRMS:** (ESI) calculated for $C_{25}H_{22}N$ [MH^+]: 336.1747, found: 336.1746

11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydro-*5H*-4b-aza-dibenzo[*a*,*f*]azulene, 7s. White solid in 52% yield from **5o** and **6a** (50 ºC for 20 h). **m.p.:** 194-196 ºC; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.68 (3H, t, *J*= 7.3 Hz), 1.07-1.14 (1H, m), 1.23-1.29 (1H, m), 2.43-2.49 (1H, m), 2.66-2.72 (1H, m), 3.11 (1H, dt, *J*= 3.4, 14.0 Hz), 3.91 (1H, td, *J*= 4.4, 13.8 Hz), 4.15 (1H, td, *J*= 3.5, 13.5 Hz), 4.49 (1H, dt, *J*= 3.9, 11.9 Hz), 5.69 (1H, s), 6.94 (1H, t, *J*= 7.8 Hz), 7.04-7.07 (1H, m), 7.18-7.20 (2H, m), 7.20-7.23 (3H, m), 7.24-7.27 (4H, m), 7.33-7.35 (2H, m); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.64 (CH_3), 20.55 (CH_2), 31.22 (CH_2), 36.44 (CH_2), 46.27 (CH_2), 103.22 (CH), 108.59 (CH), 119.30 (CH), 120.17 (CH), 120.73 (CH), 125.29 (quat), 126.41 (CH), 126.72 (CH), 127.53 (CH), 127.58 (quat), 127.83 (CH), 127.92 (2 × CH), 128.22 (quat), 128.54 (CH), 128.95 (2 × CH), 129.03 (quat), 137.02 (quat), 137.11 (quat), 138.10 (quat), 141.06 (quat), 142.01 (quat), 143.07 (quat); **IR** (neat): 2958, 2925, 2870, 1487, 1454, 1350, 1313, 1261 cm^{-1}; **HRMS:** (EI) calculated for $C_{27}H_{26}N$ [MH^+]: 364.2060, found: 364.2059



11-[1-Phenyl-but-(Z)-ylidene]-11*H*-indolo[1,2-*b*]isoquinolin-6-one, *Z*-7t and **11-[1-Phenyl-but-(*E*)-ylidene]-11*H*-indolo[1,2-*b*]isoquinolin-6-one, *E*-7t**. Light yellow gum in 46% yield ($Z_{(a)}$:$E_{(b)}$ ratio = 1:1.6) from **5p** and **6a** (36 h at 50 ºC). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.94 ($3H_a$, t, *J*= 7.3 Hz), 0.94 ($3H_b$, t, *J*= 7.3 Hz), 1.51-1.61 ($2H_a$, $2H_b$, m), 2.76-2.79 ($2H_a$, m), 2.90-2.93 ($2H_b$, m), 5.37 ($1H_a$, s), 6.79 ($1H_b$, d, *J*= 8.0 Hz), 6.85 ($1H_b$, s), 7.01 ($1H_b$, ddd, *J*= 1.5, 7.3, 8.1 Hz), 7.10-7.15 ($1H_a$ $3H_b$, m), 7.19 ($1H_a$, t, *J*= 7.9 Hz), 7.24-7.31 ($4H_b$, m), 7.34 ($2H_a$, t, *J*= 7.5Hz), 7.38-7.45 ($2H_a$, $1H_b$, m), 7.54 ($1H_a$, t, *J*= 7.5 Hz), 7.64-7.67 ($1H_a$, $1H_b$, m), 7.80 ($1H_a$, d, *J*= 7.8 Hz), 8.26 ($1H_b$, dd, *J*= 1.1, 7.8 Hz), 8.41 ($1H_a$, dd, *J*= 1.3, 7.8 Hz), 8.55 ($1H_a$, dd, *J*= 0.8, 8.2 Hz), 8.66 ($1H_b$, dd, *J*= 0.7, 8.1 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 14.00 (CH_3), 14.09 (CH_3), 21.47 (CH_2), 21.86 (CH_2), 39.10 (CH_2), 40.0 (CH_2), 108.44 (CH), 108.64 (CH), 115.94 (CH), 116.08 (CH), 120.33 (CH), 120.45 (CH), 122.11 (quat), 122.69 (quat), 123.83 (CH), 124.13 (CH), 124.53 (CH), 125.02 (CH), 126.97 (CH), 127.28 (CH), 127.40 (CH), 127.91 (2 × CH), 127.95 (CH) 128.02 (CH), 128.07 (CH), 128.21 (CH), 128.62 (2 × CH), 128.72 (2 × CH), 128.80 (CH), 128.94 (2 × CH), 129.20 (quat), 129.33 (quat), 129.59 (CH), 130.72 (CH), 131.62 (quat), 134.77 (quat), 134.42 (quat), 134.94 (quat), 135.09 (quat), 135.11 (quat),136.57 (quat), 137.37 (quat), 142.92 (quat) 142.95 (quat), 147.97 (quat), 148.55 (quat), 161.66 (CO), 162.06 (CO); **IR** (neat): 3059, 2985, 1687, 1421, 1265 cm^{-1}; **HRMS:** (ESI) calculated for $C_{26}H_{22}ON$ [MH^+]: 364.1696, found: 364.1697.



5-Methyl-6-[1-phenylbut-(Z)-ylidene]-6,11-dihydro-5*H*-benzo[*b*]carbazole, 7u. Pale yellow solid in 64 % yield from **5q** and **6a** (50 ºC for 5 h). **m.p.:** 128-130 °C; **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.66 (3H, t, *J*= 7.3 Hz), 1.07-1.13 (1H, m), 1.26-1.28 (1H, m), 2.74 (3H, s), 2.74-2.78 (1H, s), 3.25-3.31 (1H, m), 4.05 (1H, s), 4.07 (1H, s), 6.98-7.00 (1H, m), 7.07-7.11 (3H, m), 7.18-7.25 (6H, m), 7.43 (1H, d, *J*= 7.0 Hz), 7.57-7.59 (1H, m), 7.64 (1H, dd, *J*= 1.0, 7.4 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.21 (CH_3), 21.71 (CH_2), 28.90 (CH_2), 30.88 (CH_3), 35.66 (CH_2), 109.45 (CH), 111.93 (quat), 117.68 (CH), 119.03 (CH), 120.90 (CH), 124.63 (CH), 125.76 (quat), 125.88 (CH), 126.16 (quat), 126.60 (CH), 127.87 (CH), 127.95 (2 × CH), 128.41 (CH), 129.27 (CH), 137.64 (quat), 138.36 (quat), 138.49 (quat), 139.05 (quat), 140.03 (quat), 142.26 (quat); **IR** (neat): 2954, 1635, 1554, 1544, 1442, 1409, 1373 cm^{-1}; **HRMS:** (ESI) calculated for $C_{27}H_{26}N$ [MH^+]: 364.2060, found: 364.2060.

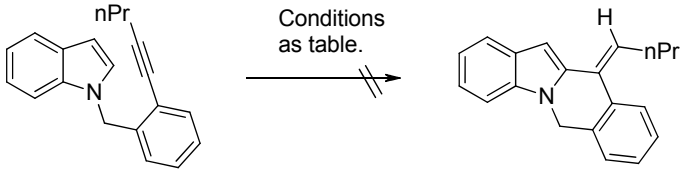
11-[1-Naphthalen-1-ylbut-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline (not in table). Pale brown solid in 50 % yield (64% yield brsm) from **5a** and **6e**. **m.p.:** 94-96 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 0.86 (3H, t, *J*= 7.3 Hz), 1.40-1.51 (2H, m), 2.72-2-88 (1H, m), 2.98-3.04 (1H, m), 5.18 (3H, bs), 6.85 (1H, t, , *J*= 7.1 Hz), 7.05 (1H, td, *J*= 1.0, 7.0 Hz), 7.11 (1H, d, *J*= 7.9 Hz), 7.26-7.30 (2H, m), 7.35-7.40 (2H, m), 7.43-7.49 (4H, m), 7.82-7.88 (3H, m), 7.92 (1H, d, *J*= 8.3 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 14.16 (CH_3), 22.47 (CH_2), 38.94 (CH_2), 45.35 (CH_2), 100.16 (CH), 108.13 (CH), 118.99 (CH), 120.60 (CH), 120.76 (CH), 125.19 (CH), 125.34 (CH), 125.69 (CH), 126.04 (CH), 126.38 (CH), 126.39 (CH), 126.85 (CH), 127.06 (CH), 127.20 (quat), 127.26 (CH), 128.34 (quat), 128.48 (CH), 128.72 (CH), 131.61 (quat), 133.72 (quat), 134.55 (quat), 134.63 (quat), 135.37 (quat), 136.41 (quat), 139.96 (quat), 141.16 (quat); **IR** (neat): 3055, 2956, 2868, 1612, 1589, 1504, 1479, 1446, 1317, 1234, 1141 cm^{-1}; **HRMS:** (ESI) calculated for $C_{30}H_{26}N$ [MH^+]: 400.2060, found: 400.2054.

11-[1-Thiophen-2-ylbut-(Z)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline, and **11-[1-Thiophen-2-ylbut-(*E*)-ylidene]-6,11-dihydro-indolo[1,2-*b*]isoquinoline (not in table)**. Pale yellow solid in 51 % yield ($Z_{(a)}$:$E_{(b)}$ = 1:1.9) from **5a** and **6f**. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.91 ($3H_a$, t, *J*= 7.3 Hz), 0.97 ($3H_b$, t, *J*= 7.3 Hz), 1.57-1.67 ($2H_a$, $2H_b$, m), 2.76-2.79 ($2H_a$, m), 2.95-2.98 ($2H_b$, m), 5.17 ($2H_a$, s), 5.19 ($2H_b$, s), 5.82 ($1H_a$, s), 6.66 ($1H_b$, s), 6.78 ($1H_b$, dd, *J*= 1.0, 3.4 Hz), 6.90-6.92 ($1H_b$, $1H_a$, m), 6.95 ($1H_b$, t, *J*= 7.6 Hz), 7.00 ($1H_a$, t, J= 7.5 Hz), 7.02 ($1H_a$, t, *J*= 3.4, 5.0 Hz), 7.07 ($1H_b$, d, *J*= 7.9 Hz), 7.11-7.16 ($1H_a$, $2H_b$, m), 7.22-7.26 ($4H_a$, $1H_b$, m), 7.29-7.43 ($2H_a$, $3H_b$), 7.65-7.68 ($1H_a$, $1H_b$, m); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.82 (CH_3, CH_3), 22.04 (CH_3, CH_3), 38.37 (CH_2), 38.90 (CH_2), 45.40 (CH_2), 45.40 (CH_2), 100.17 (CH), 100.33 (CH), 108.35 (CH), 108.53 (CH), 119.29 (CH), 119.62 (CH), 120.80 (CH), 121.07 (CH), 121.52 (CH), 124.90 (CH), 125.23 (CH), 125.29 (quat), 125.70 (CH), 126.31 (CH), 126.42 (CH), 126.67 (CH), 126.72 (CH), 126.77 (CH), 127.14 (2xCH), 127.23 (CH), 128.21 (quat), 128.37 (CH), 128.46 (quat), 128.60 (CH), 128.86 (quat), 129.02 (quat), 129.54 (CH), 134.17 (quat), 134.69 (quat), 134.85 (quat), 135.14 (quat), 135.23 (quat), 135.54 (quat), 136.10 (quat), 136.22 (quat), 143.50 (quat), 144.69 (quat); **IR** (neat): 2953, 2926, 2868, 1722, 1674, 1610, 1448, 1371, 1354, 1240 cm^{-1}; **HRMS:** (ESI) calculated for $C_{24}H_{22}NS$ [MH^+]: 356.1468, found: 356.1465.

4-Fluoro-11-[1-Phenylbut-(*Z*)-ylidene]-6,11-dihydroindolo[1,2*b*]isoquinoline (not in table). Reddish gum in 54% yield from **5e** and **6a**. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 0.86 (3H, t, *J*= 7.3 Hz), 1.41-1.49 (2H, m), 2.79-2.82 (2H, m), 5.43 (1H, d, *J*= 2.4 Hz), 5.46 (2H, s), 6.71-6.83 (3H, m), 7.02 (1H, d, *J*= 7.8 Hz), 7.18 (1H, t, *J*= 1.4 Hz), 7.20 (1H, d, *J*= 1.6 Hz), 7.31-7.30 (4H, m), 7.39 (1H, td, *J*= 1.4, 7.8 Hz), 7.42 (1H, td, *J*= 1.0, 7.4 Hz), 7.68 (1H, d, *J*= 7.7 Hz); **^{13}C NMR** (150 MHz, $CDCl_3$): δ 13.90 (CH_3), 21.64 (CH_2), 38.18 (CH_2), 47.80 (CH_2, d, $J_{C\text{-}F}$= 6.5 Hz), 101.43 (CH, d, $J_{C\text{-}F}$= 6.0 Hz), 106.38 (CH, d, $J_{C\text{-}F}$= 72.2 Hz), 116.35 (CH, d, $J_{C\text{-}F}$= 3.2 Hz), 119.05 (CH, d, $J_{C\text{-}F}$= 6.6 Hz), 122.61 (quat, d, *J*= 9.0 Hz), 125.07 (quat), 126.34 (CH), 126.82 (CH), 126.88 (CH), 126.96 (CH), 128.22 (2 × CH), 128.52 (CH), 128.73 (2 × CH), 132.09 (quat), 132.13 (quat), 135.09 (quat, d, $J_{C\text{-}F}$= 5.5 Hz), 138.08 (quat), 142.40 (quat), 143.80 (quat), 149.72 (quat, d, $J_{C\text{-}F}$= 248.1 Hz); **IR** (neat): 2960, 2931, 2872, 1691, 1578, 1492, 1442, 1263, 1236 cm^{-1}; **HRMS:** (APCI) calculated for $C_{26}H_{23}NF$ [MH^+]: 368.1809, found: 368.1804.

4. Mechanistic Studies

Trapping Experiments 1. Hydroarylation (cyclisation in the absence of iodonium salt)

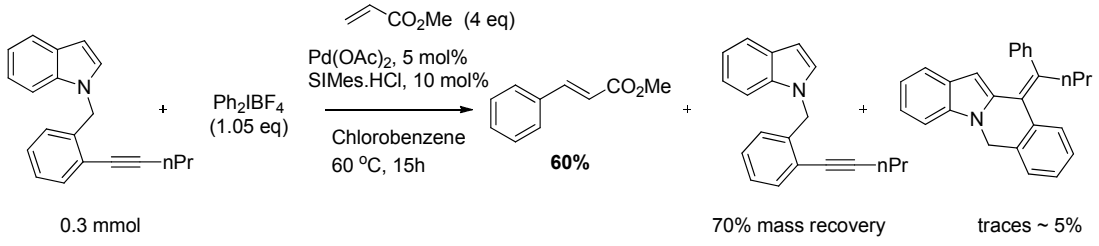


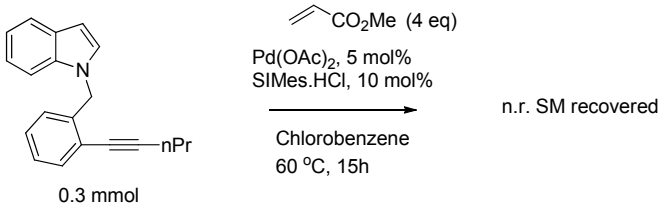
Entry	Pd cat. 5 mol%	Ligand	Additive	Base	Solvent	T (°C)	t (h)	Results
1[a]	$Pd(OAc)_2$	di-Prpf, 7 mol%	-	-	Toluene (0.5 M)	120	15	n.r.[b]
2	$Pd(OAc)_2$	-	-	-	Toluene/ AcOH (0.1M)	100	15	n.r.
3[c]	$Pd(OAc)_2$, 10 mol%	-	-	-	AcOH (0.2M)	r.t.[d]	20	n.r.
4	$Pd(OAc)_2$, 10 mol%	-	-	-	DCM/ TFA, 3/1 (0.2 M)	r.t.	15	Messy reaction, some product of Friedel-Crafts acylation with TFA detected
5	$Pd(CNMe)_4(BF_4)_2$	-	-	-	CF_3CH_2OH (0.1M)	r.t.	20	n.r.
6	$Pd(OAc)_2$	SIMes.HCl 10 mol%	$Cu(OAc)_2$, 2 equiv	Cs_2CO_3, 1 equiv	CH_2Cl_2 (0.1M)	30	24	n.r.
7	$Pd(OAc)_2$	-	$PhI(OAc)_2$, 1equiv	-	Chlorobenzene	30	24	Some 3-acetoxyindole detected but no desired product
8	$Pd(OAc)_2$	-	$PhI(OAc)_2$, 1equiv	-	AcOH	30	24	decomp.

[a] Reaction conditions used for the hydroarylation of *o*-alkynyl biaryls by Gevorgyan and co-workers.[2] [b] n.r.: no reaction, starting material recovered. [c] Reaction conditions used for indole addition to C-C triple bonds by Fujiwara and co-workers.[3] [d] ~ 20 °C

Intramolecular hydroarylation was unsuccessful under a range of conditions.

Trapping Experiments 2. Addition of a competitive Heck acceptor.

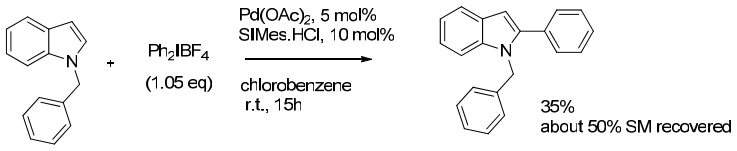




A Heck acceptor was added to the reaction in order to trap out the proposed palladated indole intermediate(s) (*e.g.* **8** and / or **9** in Scheme 4 in the paper). Under the standard reaction conditions in the presence of iodonium salt **6a** simple Heck coupling was observed to produce the methyl cinnamate. In the absence of iodonium salt there was no observable reaction.

Trapping Experiments 3. Arylation under the reaction conditions.

Arylation of N-benzylindole with **6a** was attempted to assess whether indole palladation was viable under the reaction conditions. A low yield of 2-phenyl-N-benzylindole was recorded.



Kinetic Isotope Effect (KIE) studies

KIEs were determined by studying the initial rate of reactions for 1-(2-pent-1-ynylbenzyl)-*1H*- indole, **5a,** 2-deutero-1-(2-pent-1-ynylbenzyl)-*1H*-indole, ***2d*-5a**, and 3-deutero-1-(2-pent-1-ynylbenzyl)-*1H*-indole**,** ***3d*-5a**. The deuterated starting materials were synthesised as follows:

2-Deutero-1-(2-pent-1-ynylbenzyl)-*1H*-indole, *2d*-5a. 2*d*-Indole (2.8 mmol, synthesised from 1-(phenylsulfonyl)indole as described by Maresh *et al.*[23]) was dissolved in dry DMF (9 mL) under N_2 atmosphere and NaH (60%, 3.1 mmol) was added portionwise at r.t. The mixture was stirred for 1 h, after this time 2-pent-1-ynylbenzyl bromide (3.1 mmol dissolved in 4 mL of dry DMF) was added dropwise. Monitoring by TLC showed no starting material was left after 4 h. EtOAc and water (10 mL each) were added and the solvent was partially evaporated before adding more EtOAc and water (10 mL) and the two layers were separated. The aqueous phase was extracted twice with EtOAc (5 mL) and the combined organic layers were washed with brine (5 mL × 2), dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the crude was purified through silica column (Hexane:CH_2Cl_2, 8:2) affording the named product as a colourless oil in 85% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ 01.06 (3H, t, *J*= 7.4 Hz), 1.65 (2H, sext, *J*= 7.2 Hz), 2.45 (2H, t, *J*= 7.0 Hz), 5.48 (2H, s), 6.56 (1H, s), 6.67 (1H, d, 7.8 Hz), 7.08-7.13 (2H, m), 7.15-7.20 (2H, m), 7.31 (1H, d, *J*= 8.1 Hz), 7.45 (1H, dd, *J*= 1.0, 7.6 Hz), 7.66 (1H, d, *J*= 7.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.62 (CH_3), 21.58 (CH_2), 22.21 (CH_2), 48.53 (CH_2), 78.24 (quat), 96.19 (quat), 101.43 (CH), 109.76 (CH), 119.46 (CH), 120.89 (CH), 121.61 (CH), 122.31 (quat), 126.42 (CH), 127.20 (CH), 128.01 (CH), 128.17 (quat, t, $J_{C\text{-}D}$= 20.5 Hz), 128.59 (quat), 132.17 (CH), 136.33 (quat), 138.96 (quat); **IR** (neat): 2964, 2231, 1541, 1460, 1406, 1265, 1012 cm^{-1}; **HRMS:** (APCI) calculated for $C_{20}H_{19}{}^2H_1N$ [MH^+]: 275.1653, found: 275, 1647.

3-Deutero-1-(2-pent-1-ynylbenzyl)-*1H*-indole, *3d*-5a. 1-(2-Pent-1-ynylbenzyl)-*1H*-indole, **5a** (100 mg, 0.37 mmol) was weighed in a microwave vial and D_2O (1 mL) and CD_3OD (1mL) added together with DCl (0.01 M)[24] and the mixture heated at 150 ºC under microwave irradiation for 30 min. After cooling to r.t. the residue was extracted with hexane (5 mL × 3), the combined organic layers were dried over anh. Na_2SO_4, filtered and the solvent evaporated under reduced pressure to afford a pale orange oil in 91% yield. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 1.06 (3H, t, *J*= 7.4 Hz), 1.65 (2H, sext, *J*= 7.2 Hz), 2.45 (2H, t, *J*= 7.0 Hz), 5.48 (2H, s), 6.67 (1H, d, 7.7 Hz), 7.08-7.13 (2H, m), 7.15-7.19 (3H, m), 7.31 (1H, d, *J*= 8.1 Hz), 7.45 (1H, dd, *J*= 1.0, 7.6 Hz), 7.66 (1H, d, *J*= 7.8 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$): δ 13.62 (CH_3), 21.58 (CH_2), 22.21 (CH_2), 48.57 (CH_2), 78.24 (quat), 96.19 (quat), 101.40 (quat, t, $J_{C\text{-}D}$= 26.2 Hz), 109.76 (CH), 119.46 (CH), 120.86 (CH), 121.62 (CH), 122.31 (quat), 126.42 (CH), 127.20 (CH), 128.01 (CH), 128.32 (CH), 128.51 (quat), 132.17 (CH), 136.36 (quat), 138.98 (quat); **IR** (neat): 2962, 2936, 2873, 2231, 1483, 1461, 1429, 1329 cm^{-1}; **HRMS:** (EI) calculated for $C_{20}H_{19}{}^2H_1N$ [MH$^+$]: 275.1650, found: 275, 1649

For the KIE experiments the general procedure was used: **5a** (82 mg, 0.03 mmol) was weighed in an oven-dried 5 mL vial, dissolved in 3 mL of chlorobenzene and then Cs_2CO_3 (98 mg, 0.3 mmol), SIMes.HCl (10.2 mg, 0.03 mmol), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol) and diphenyliodonium tetrafluoroborate (116mg, 0.32 mmol) were added in this order and the mixture was flushed with N_2. The vial was capped and put into an aluminium bloc at 20 ºC (the vial was not heated in order to slow down the reaction and make it easier to follow). During the first half an hour of the reaction aliquots of 50 µL were taken every 4 min. Each aliquot was dissolved in 2 mL of DMSO containing 0.002M of benzanilide (used as Internal Standard) and then MeOH was added till a final volume of 10 mL in a volumetric flask (final [IS]= 0.0004). Every sample was analysed using HPLC/MS and the response was measured by Single Ion Monitoring (SIM). The comparison between SIM of the product being formed and SIM of the internal standard gave a response vs time rate of the reaction. Three different kinetic experiments were done and the rate represented comes from the average data of the three runs.

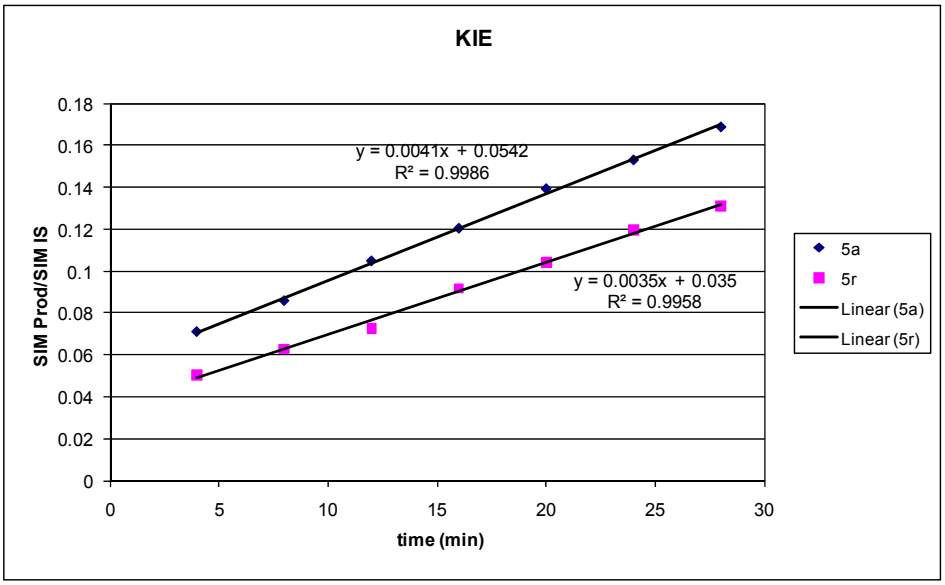
Time (min)	SIM Prod/SIM IS (i)	SIM Prod/SIM IS (ii)	SIM Prod/SIM IS (iii)	Average
4	0.064565419	0.075597673	0.072477683	0.070880259
8	0.074861166	0.087512677	0.09473584	0.085703228
12	0.089929217	0.114318842	0.110074207	0.104774089
16	0.11605677	0.121721737	0.123452228	0.120410245
20	0.132013869	0.13911516	0.146913759	0.139347596
24	0.141504644	0.163390948	0.154556341	0.153150645
28	0.158149378	0.175954253	0.172782273	0.168961968

Exactly the same procedure was followed using the 2-deuterated substrate **5r**

Time (min)	SIM Prod/SIM IS (i)	SIM Prod/SIM IS (ii)	SIM Prod/SIM IS (iii)	Average
4	0.057184782	0.050831516	0.042782923	0.050266407
8	0.052079604	0.070364242	0.065702653	0.0627155
12	0.074748186	0.079299271	0.063962703	0.072670053
16	0.09072035	0.080839404	0.103733762	0.091764505
20	0.097119972	0.107556504	0.108276724	0.104317733

24	0.110460093	0.129079515	0.119525546	0.119688385
28	0.122846136	0.135727089	0.133946523	0.130839916

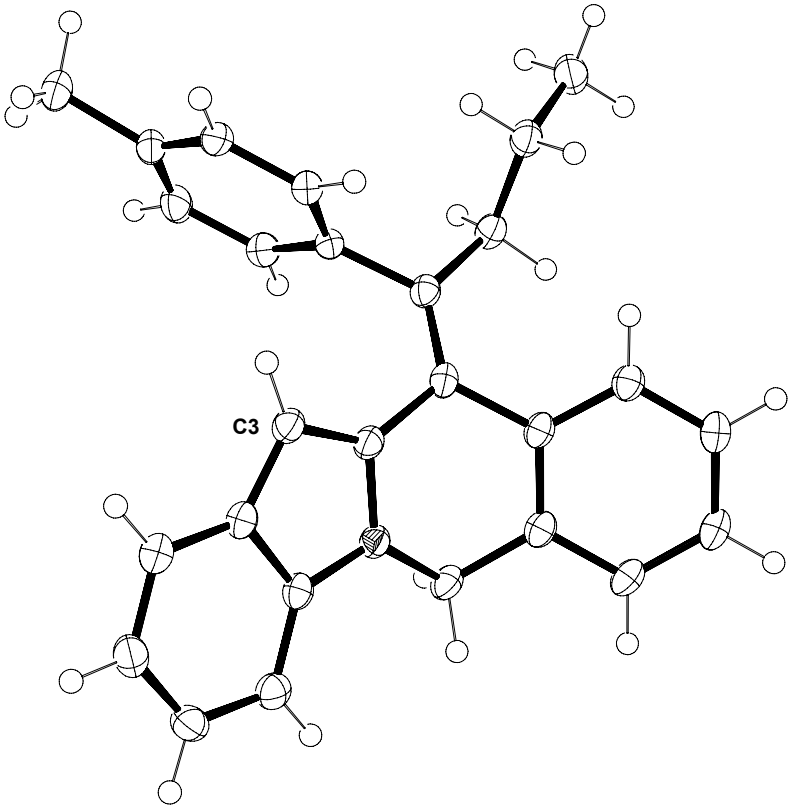
Finally the two reaction rates where compared giving a $\mathbf{k_H/k_D}$ = 1.2



The same procedure was followed for ***3d*-5a**. However, a non-linear relationship was observed when plotting product formation response against time. This can be due to H/D exchange taking place during the sampling phase of the reaction. ^{1}H NMR of the crude reaction mixture after 30 min showed a 20% conversion, with the product having a H:D ratio of 1:1 at the indole C3-position.

5. X-Ray Structure.

X-Ray Structure of **7b** (thermal ellipsoid probability = 50%).



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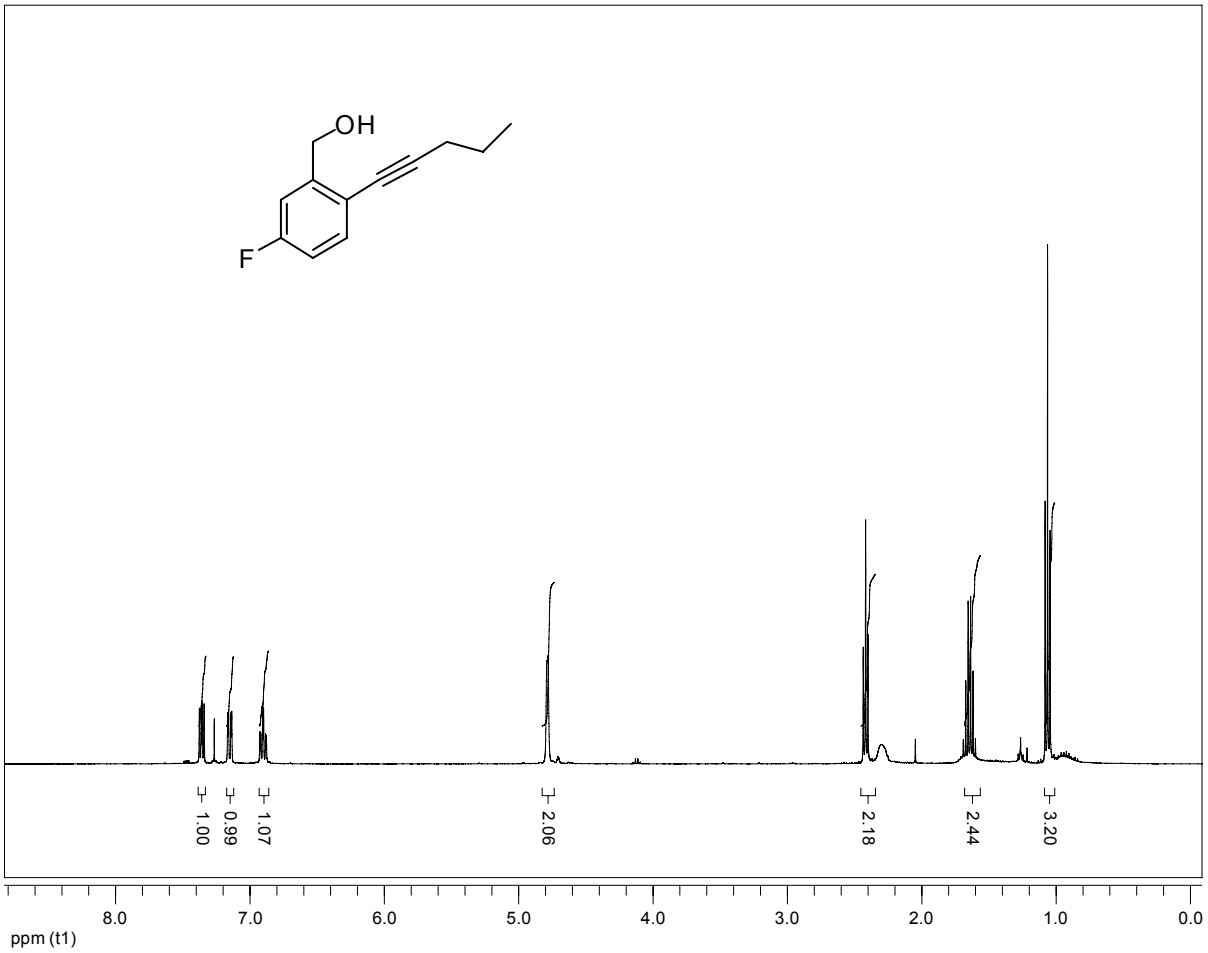
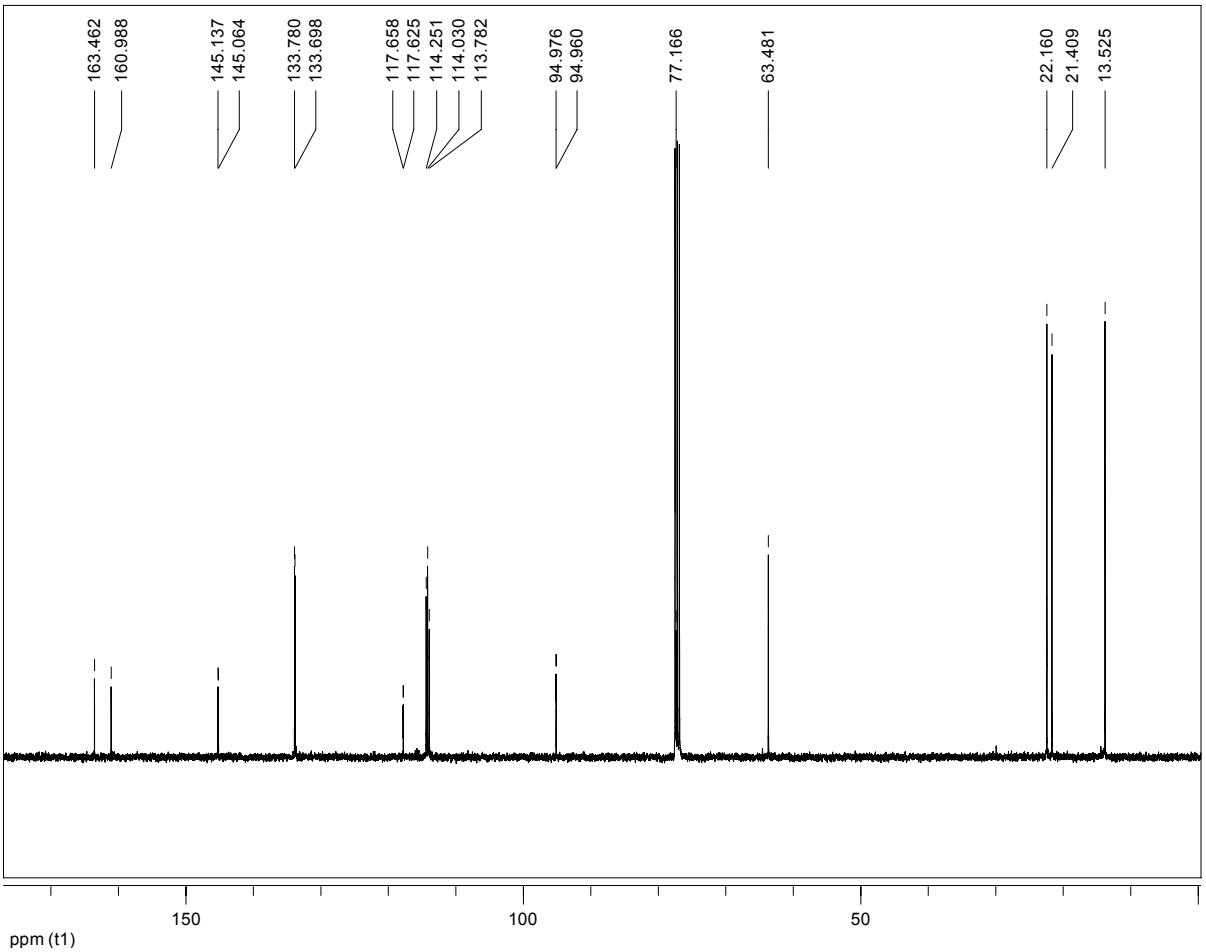
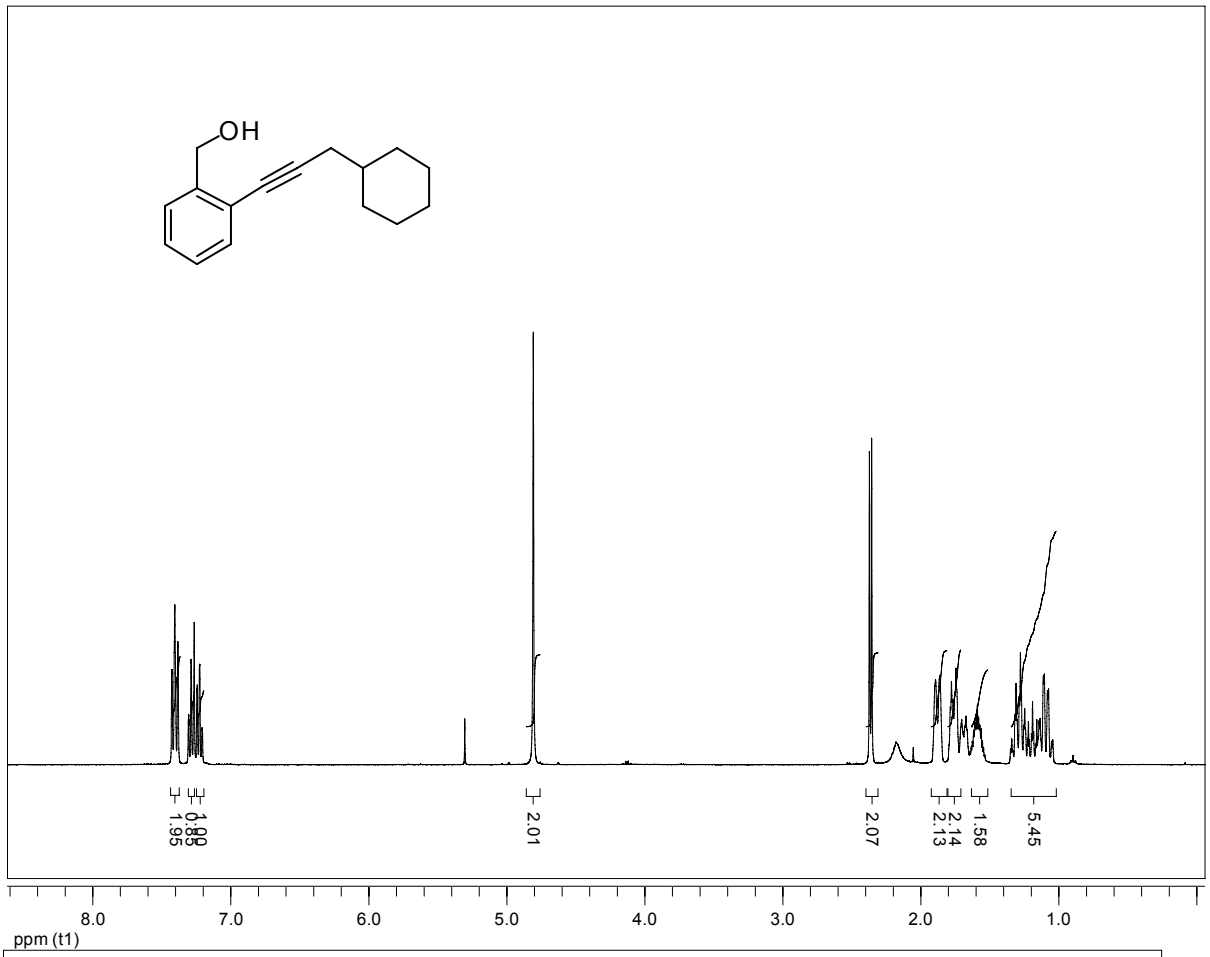
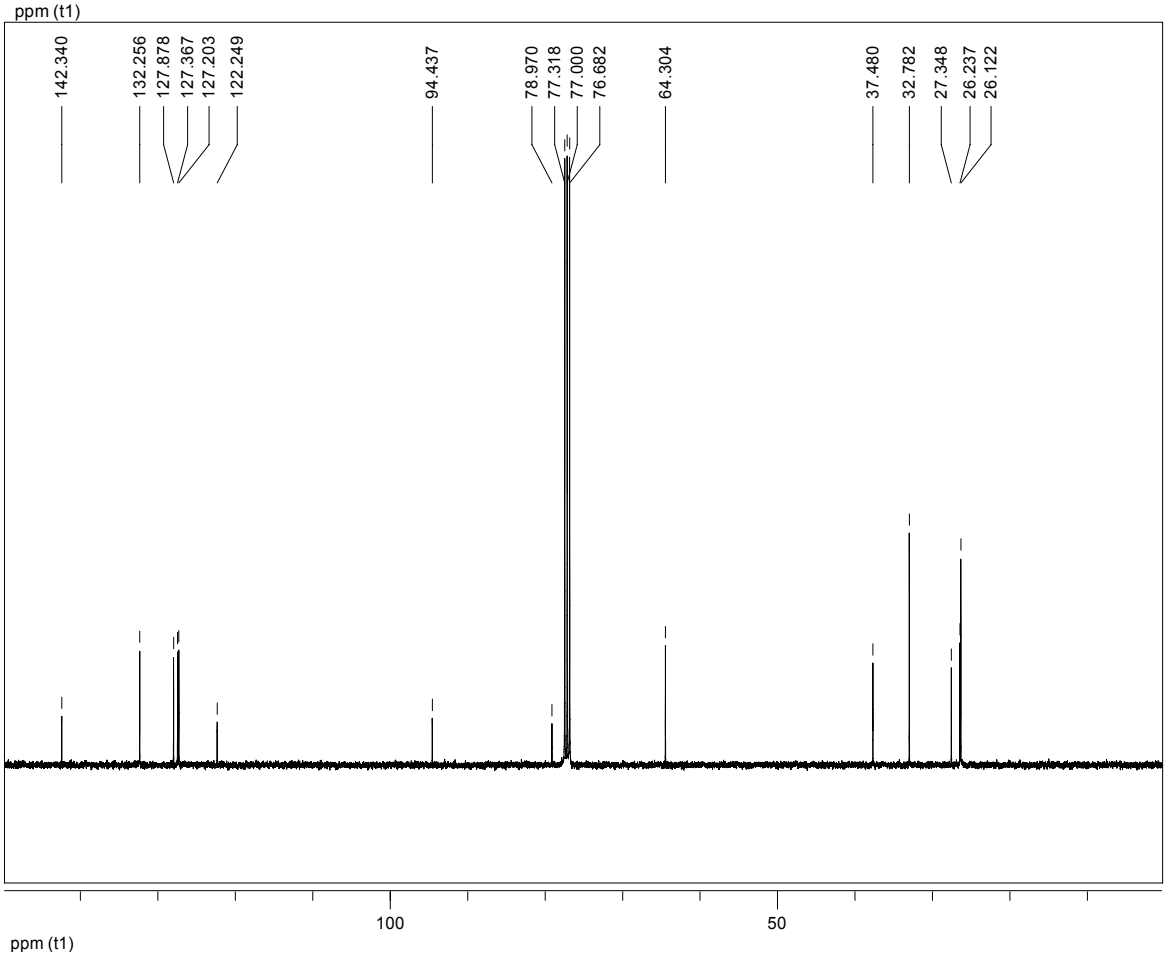
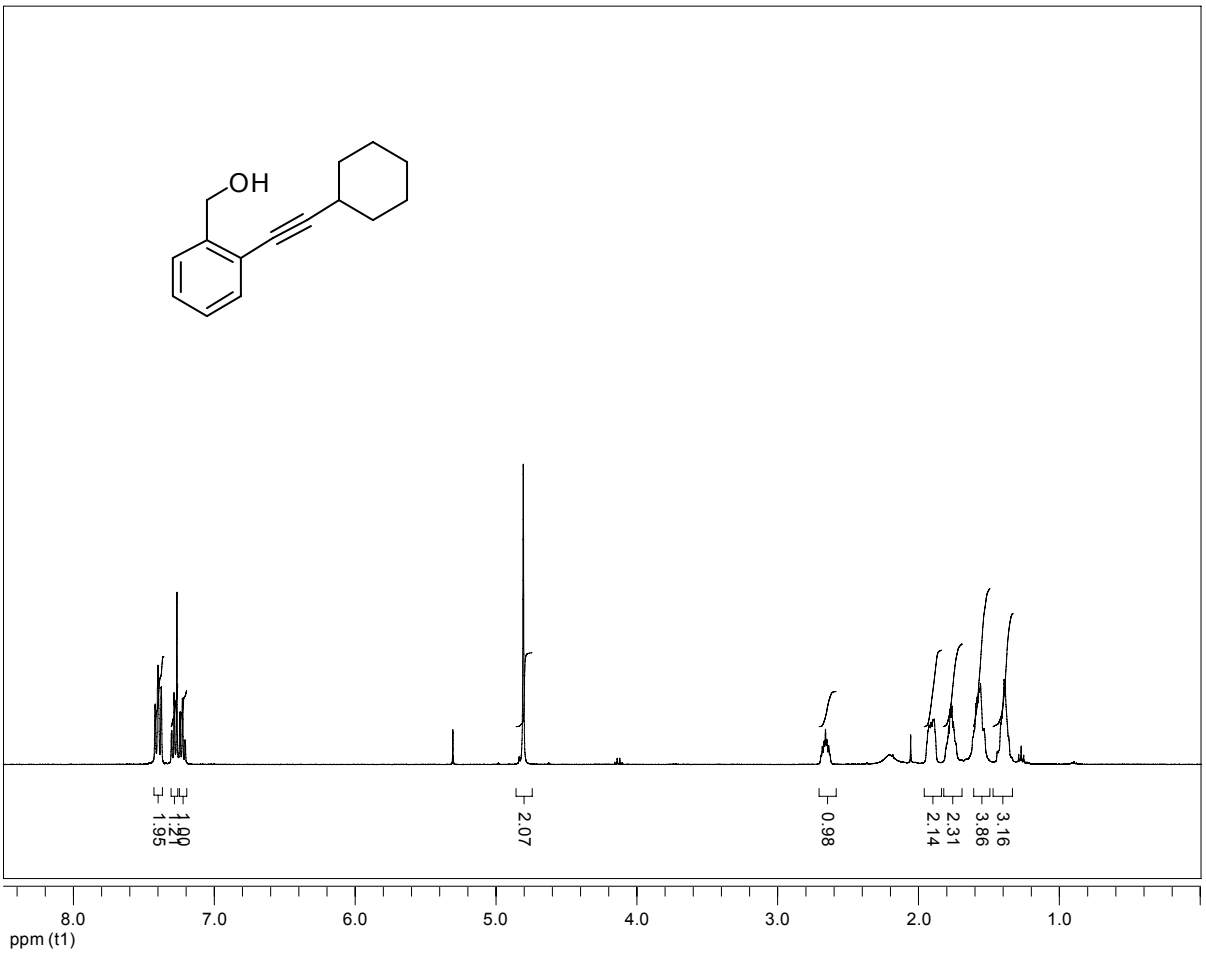
25. CCDC 813229 and 813230 contain the crystallographic data for structures **7b** and **7h**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.







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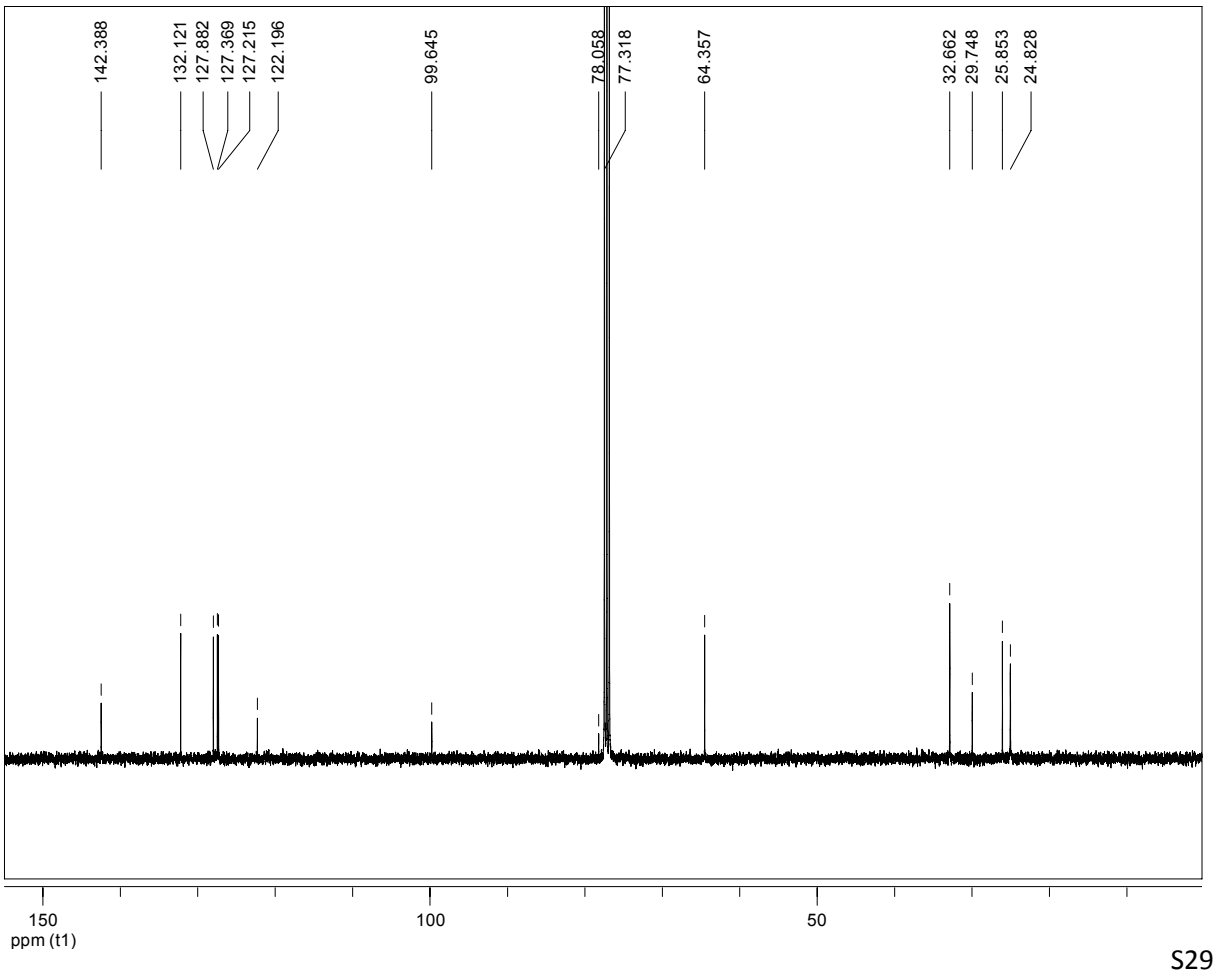
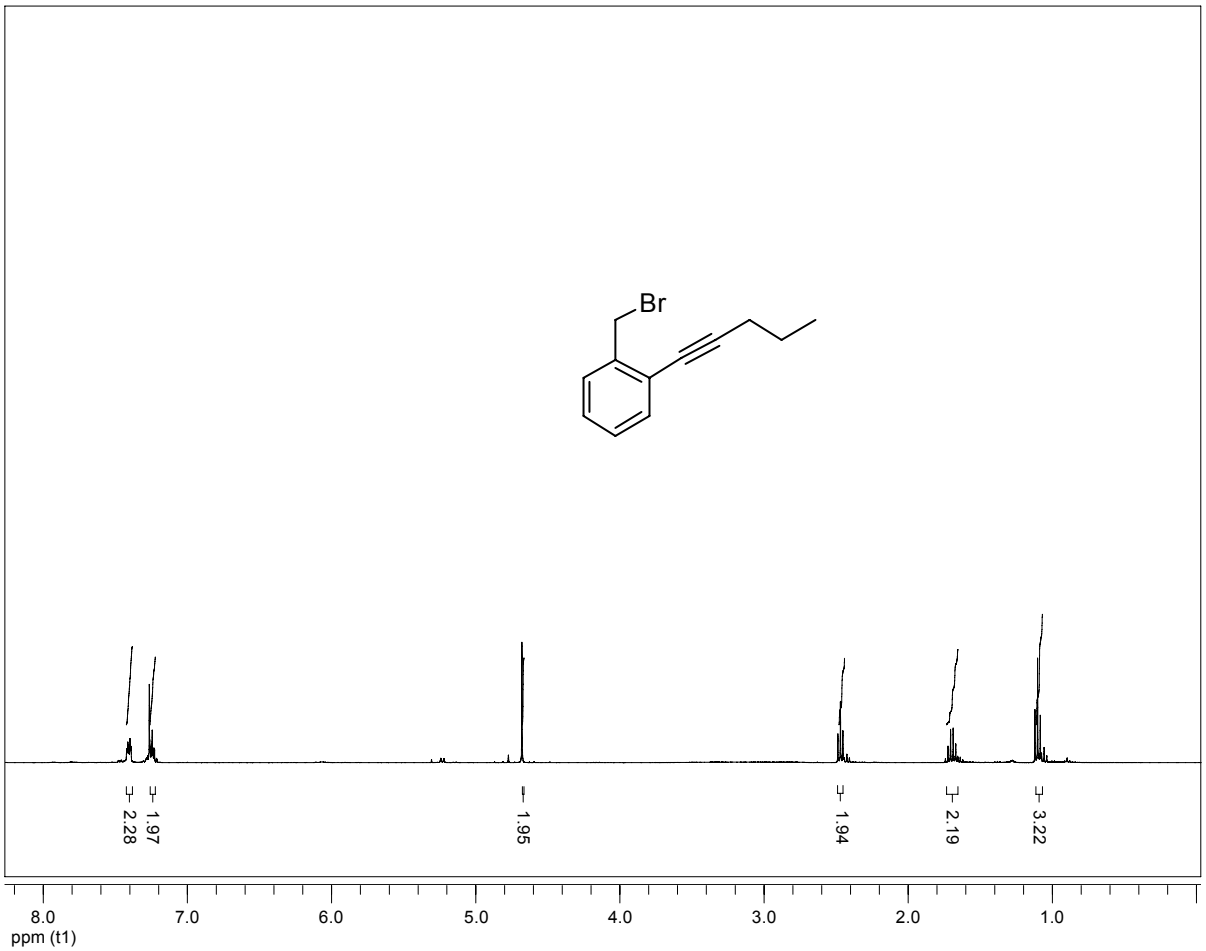
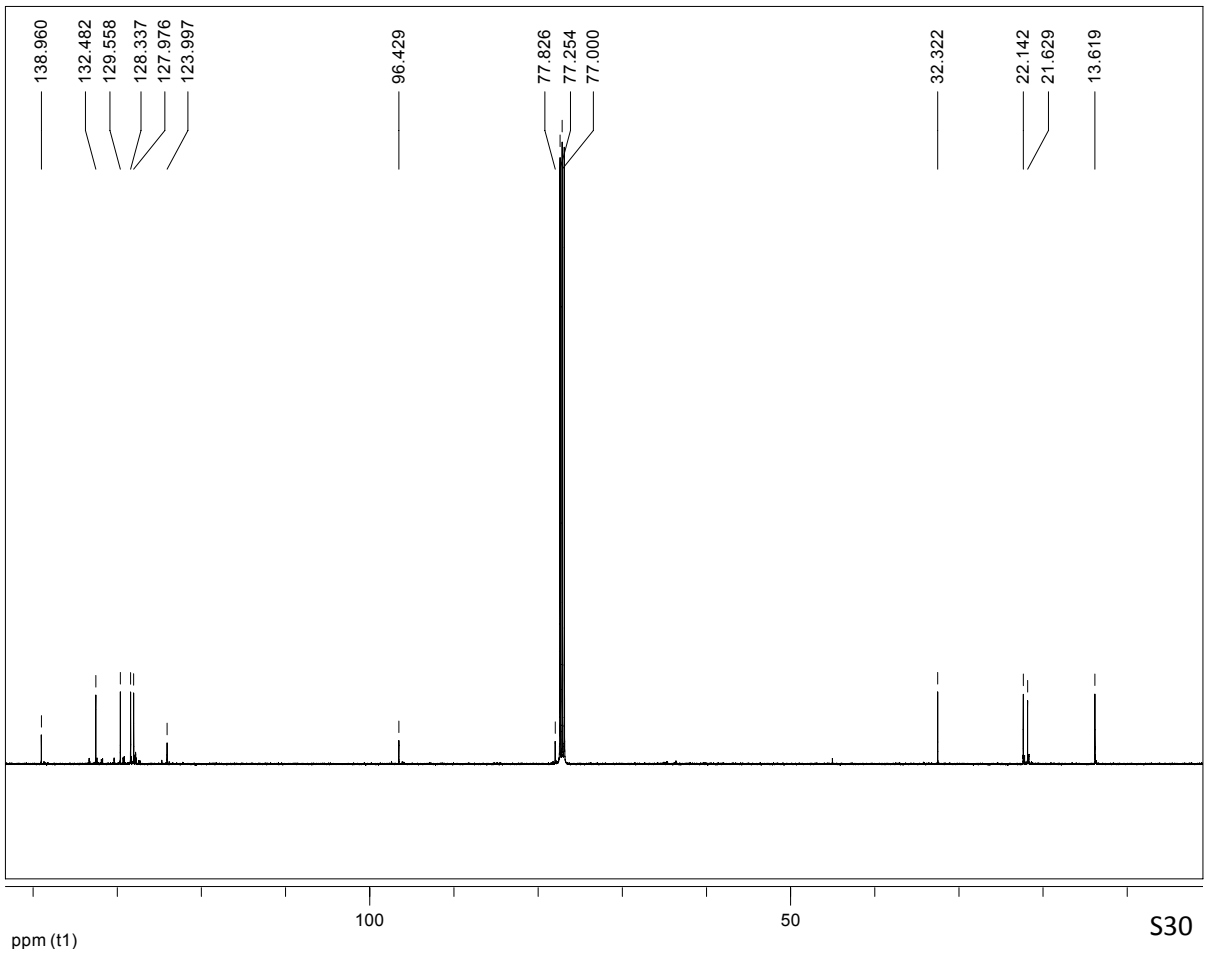
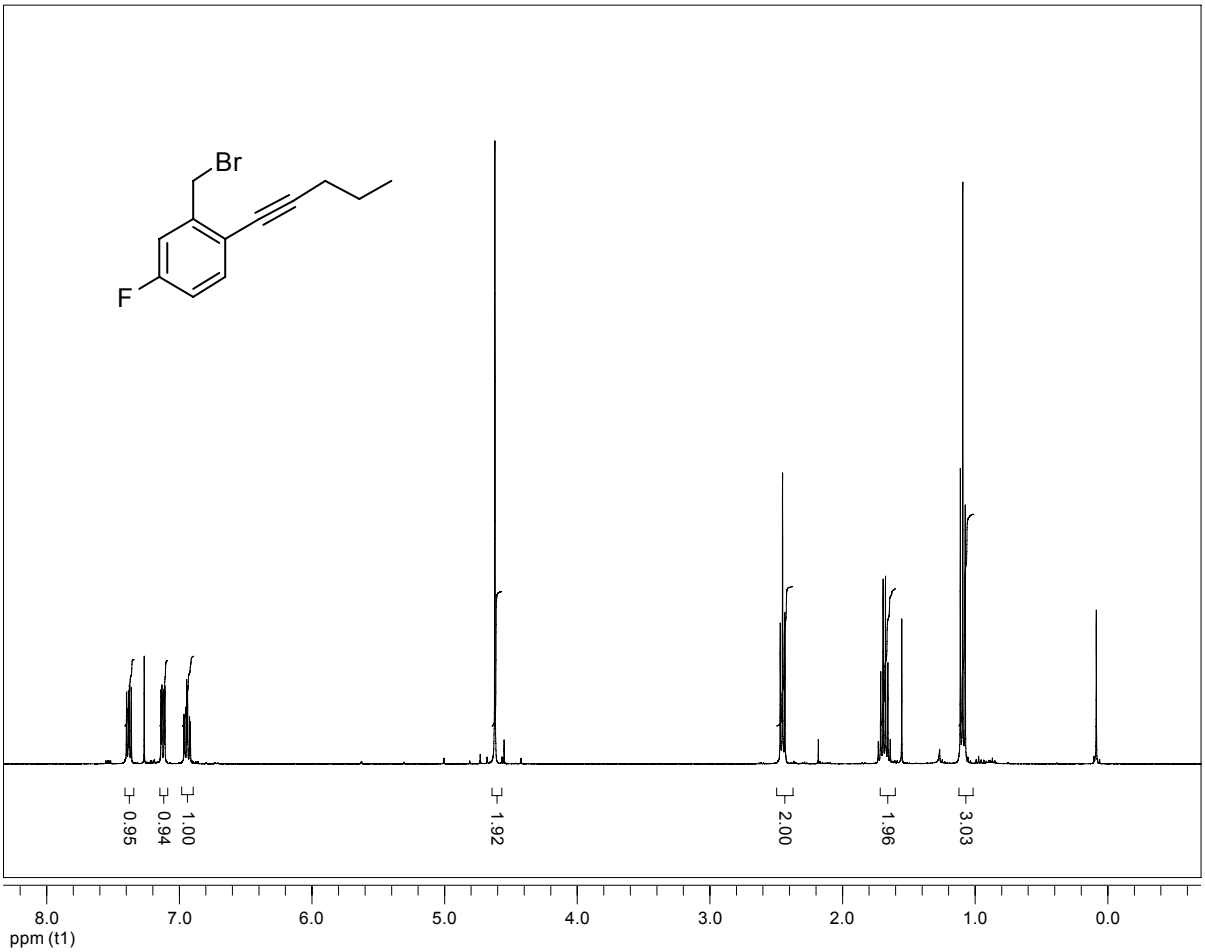
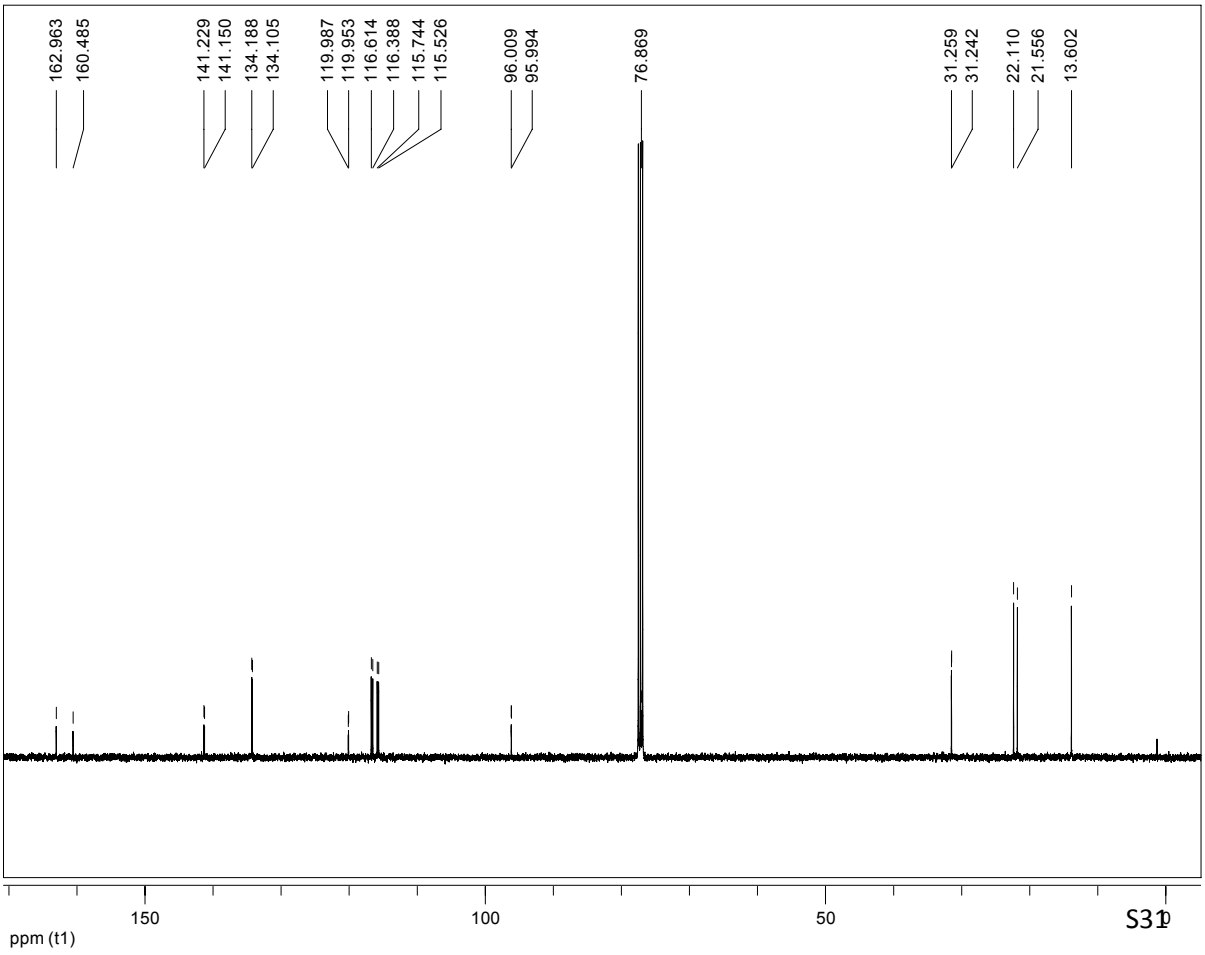
1.65
1.90
2.07
0.98
2.14
2.31
3.86
3.16
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

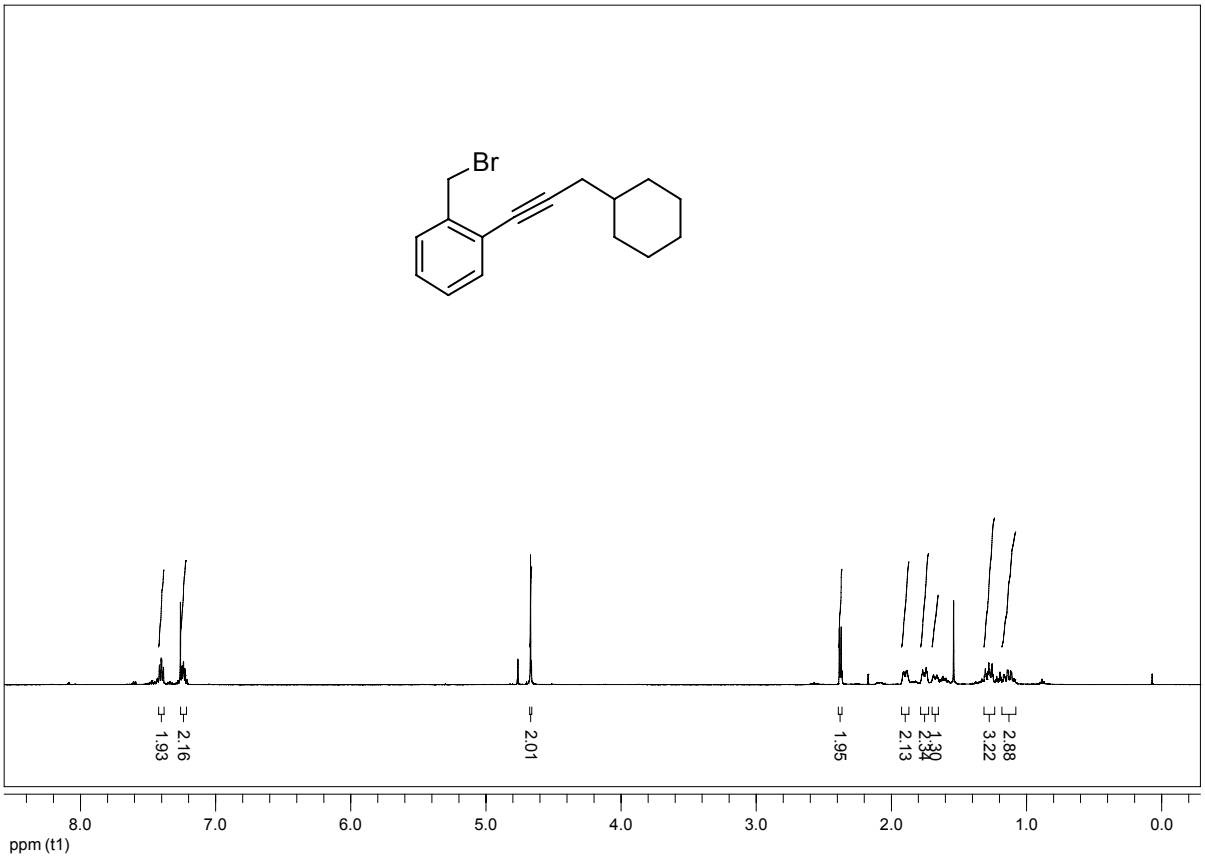

142.388
132.121
127.882
127.369
127.215
122.196
99.645
78.058
77.318
64.357
32.662
29.748
25.853
24.828
150
100
50
ppm (t1)

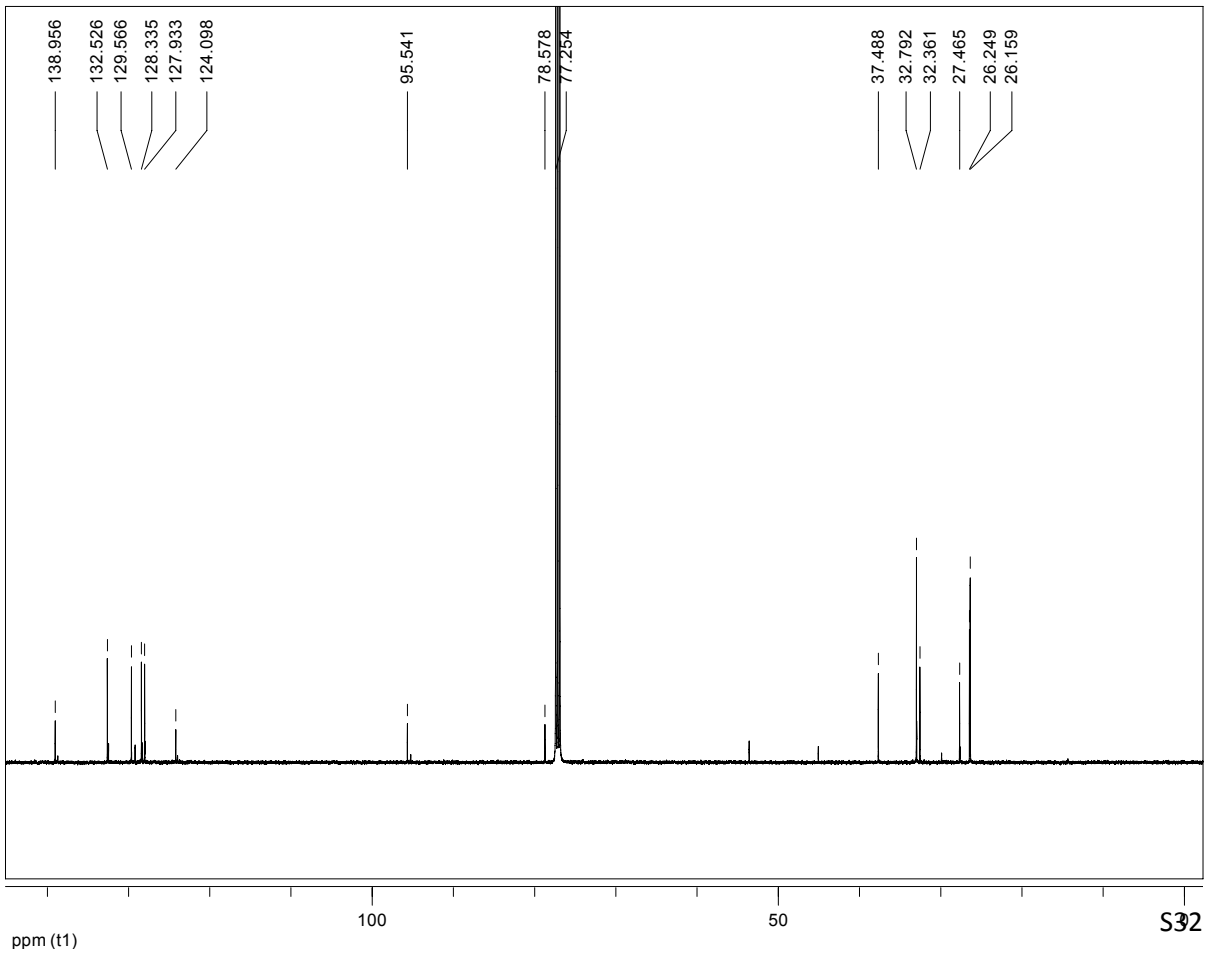


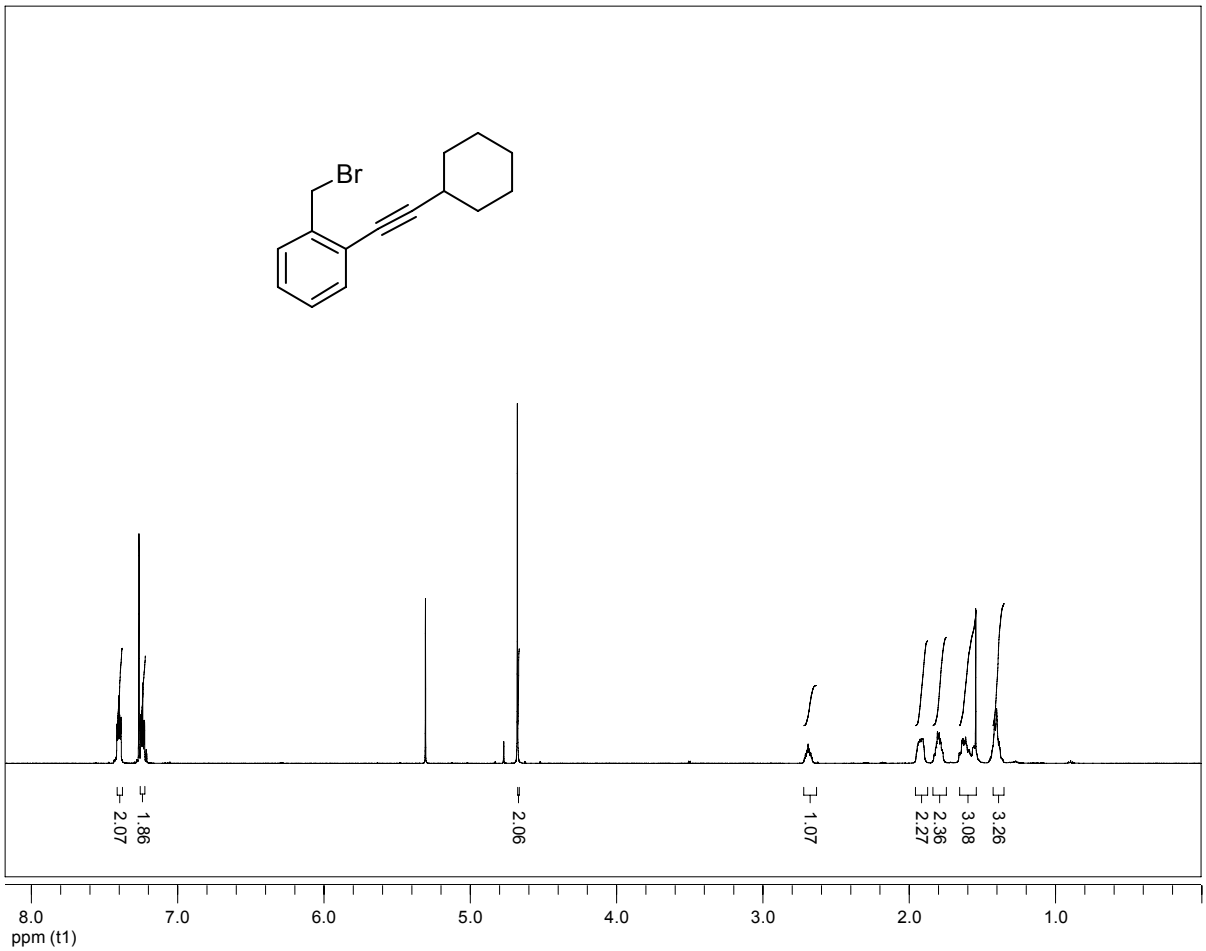


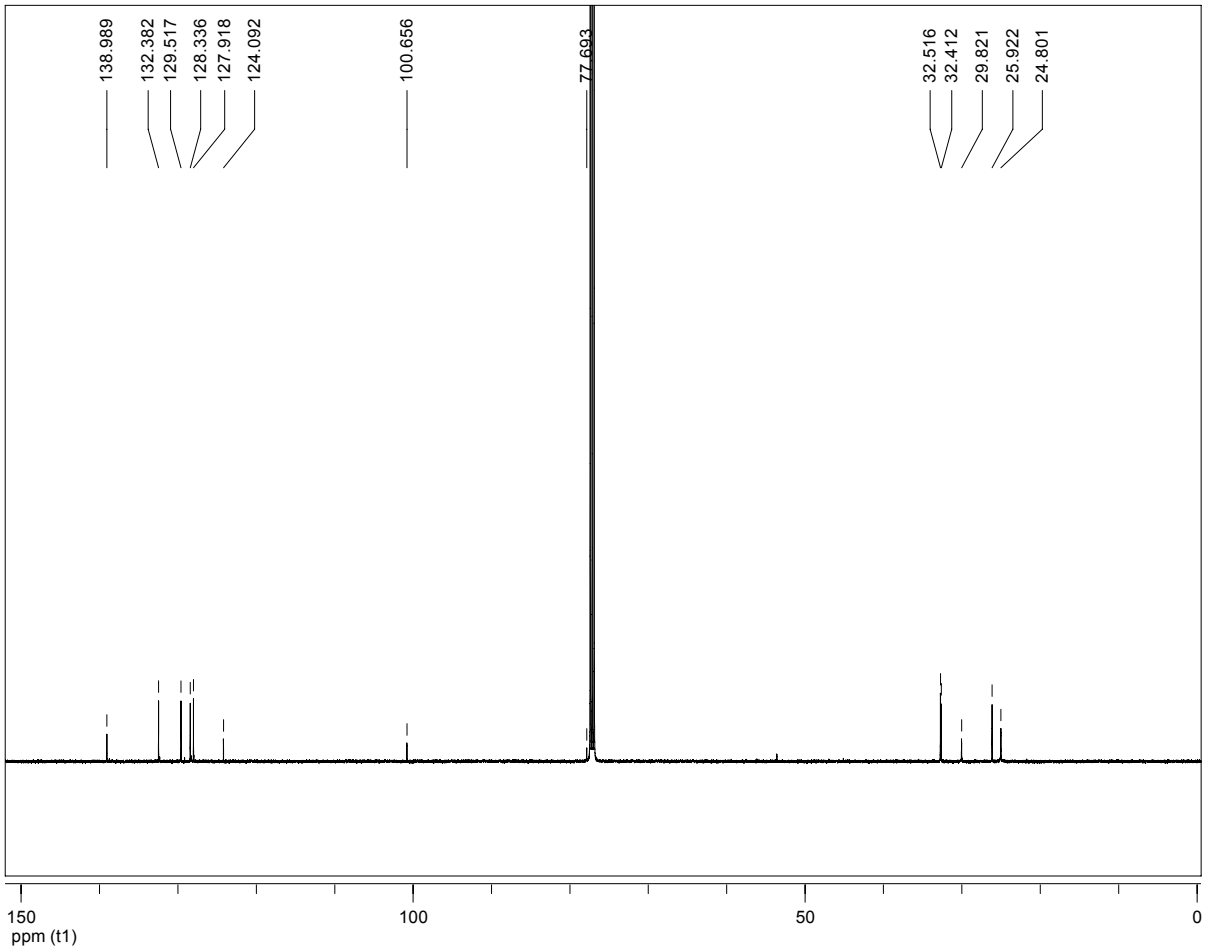


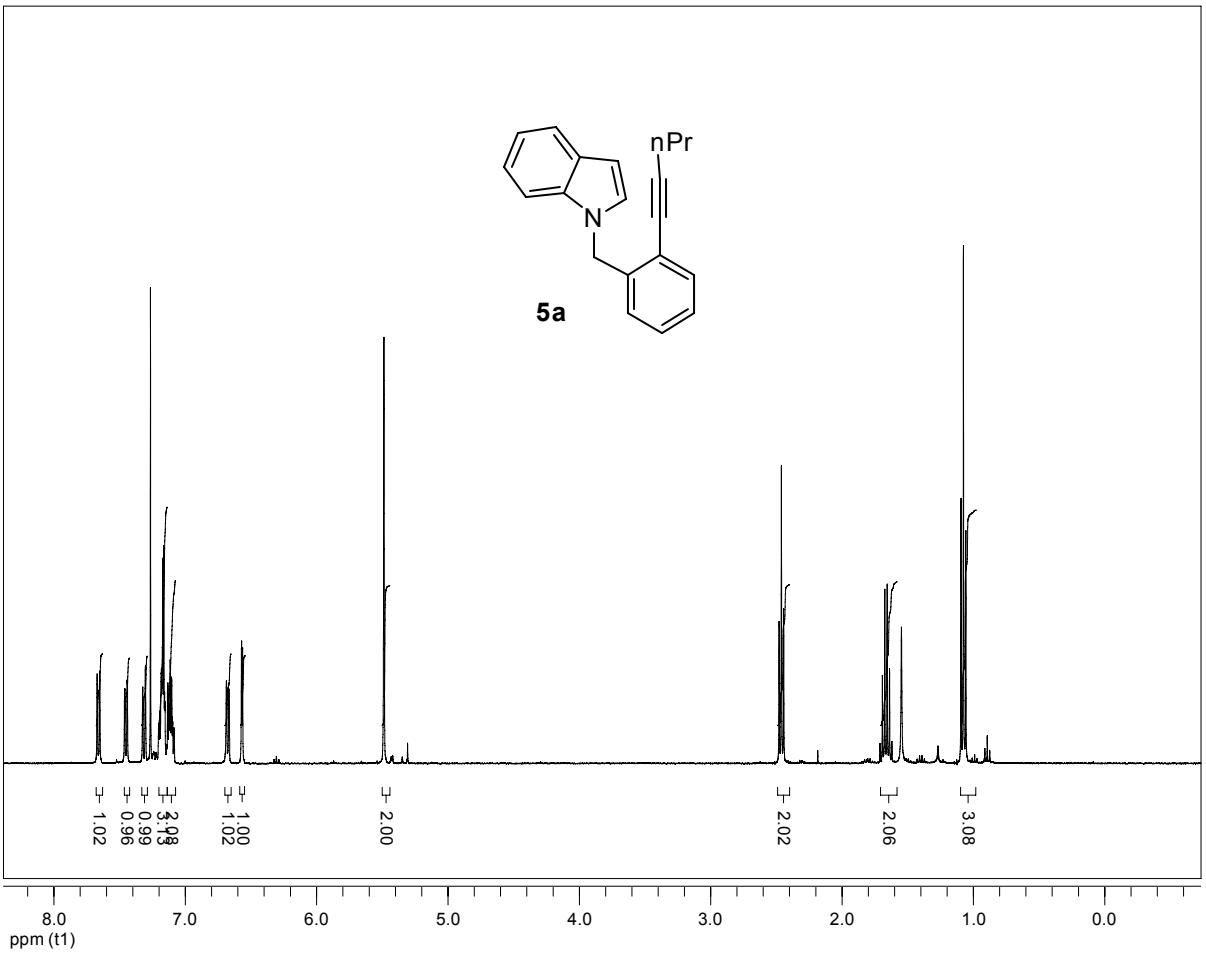


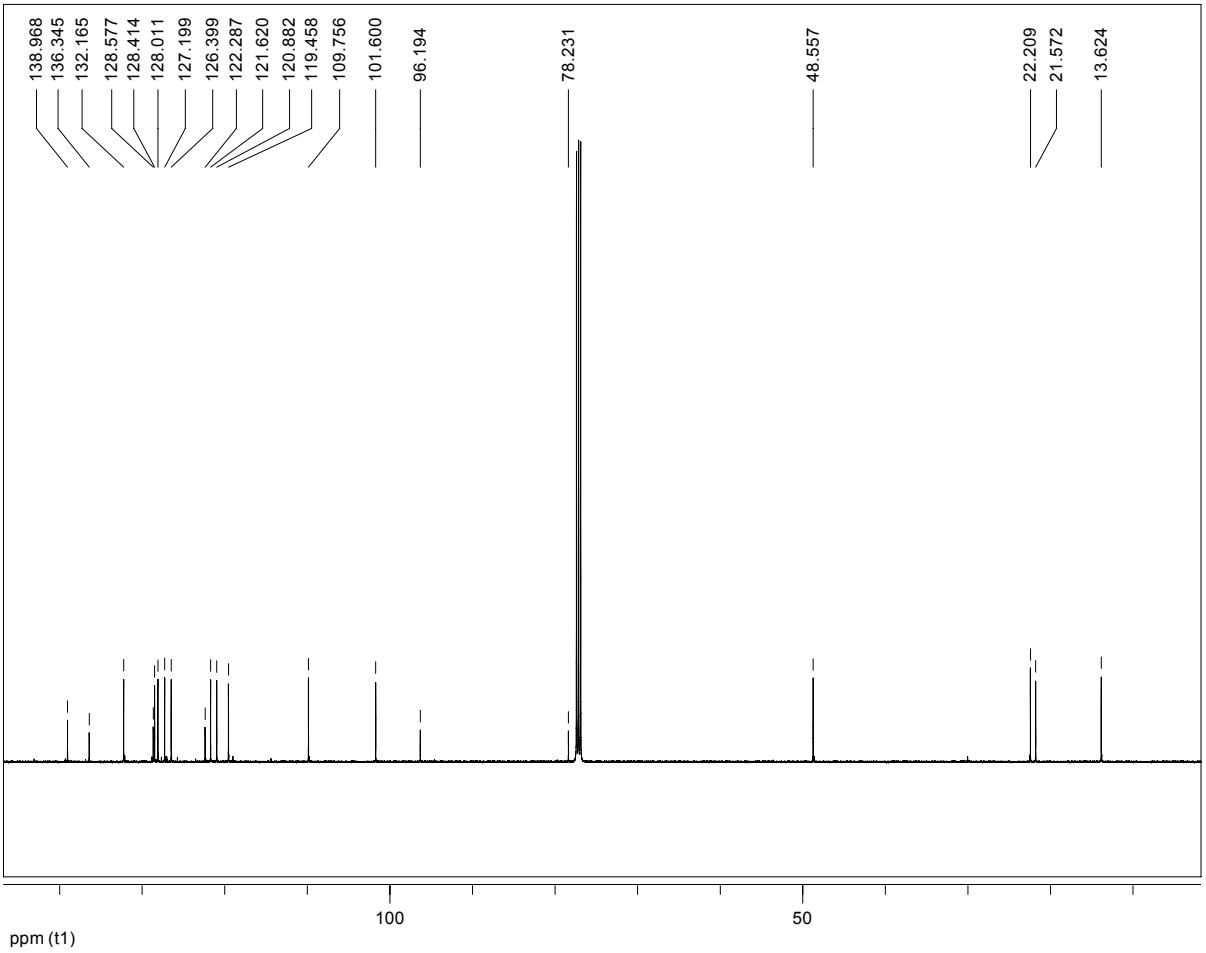









nPr
N
5a
1.02
0.96
0.99
2.13
2.08
1.00
1.02
2.00
2.02
2.06
3.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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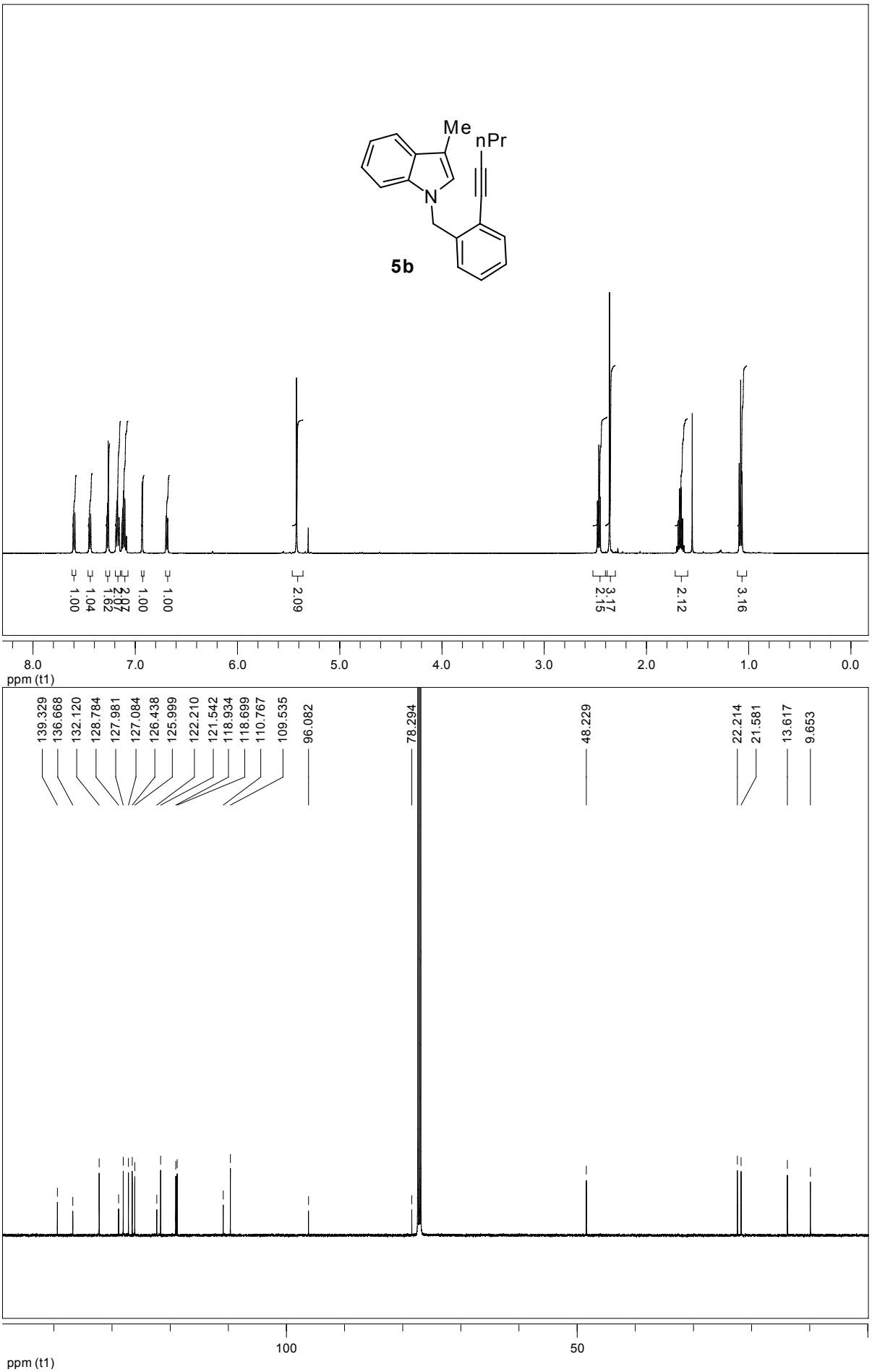
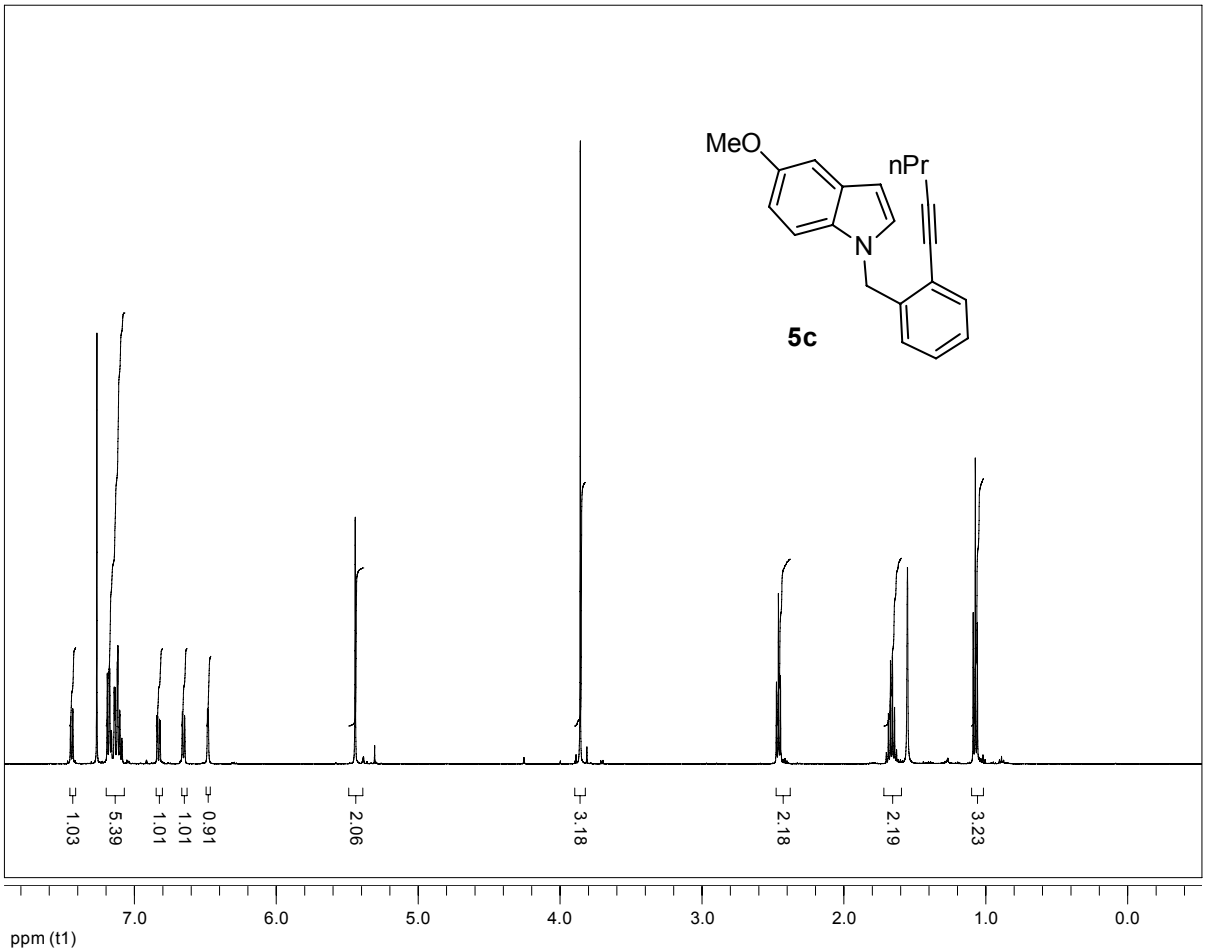
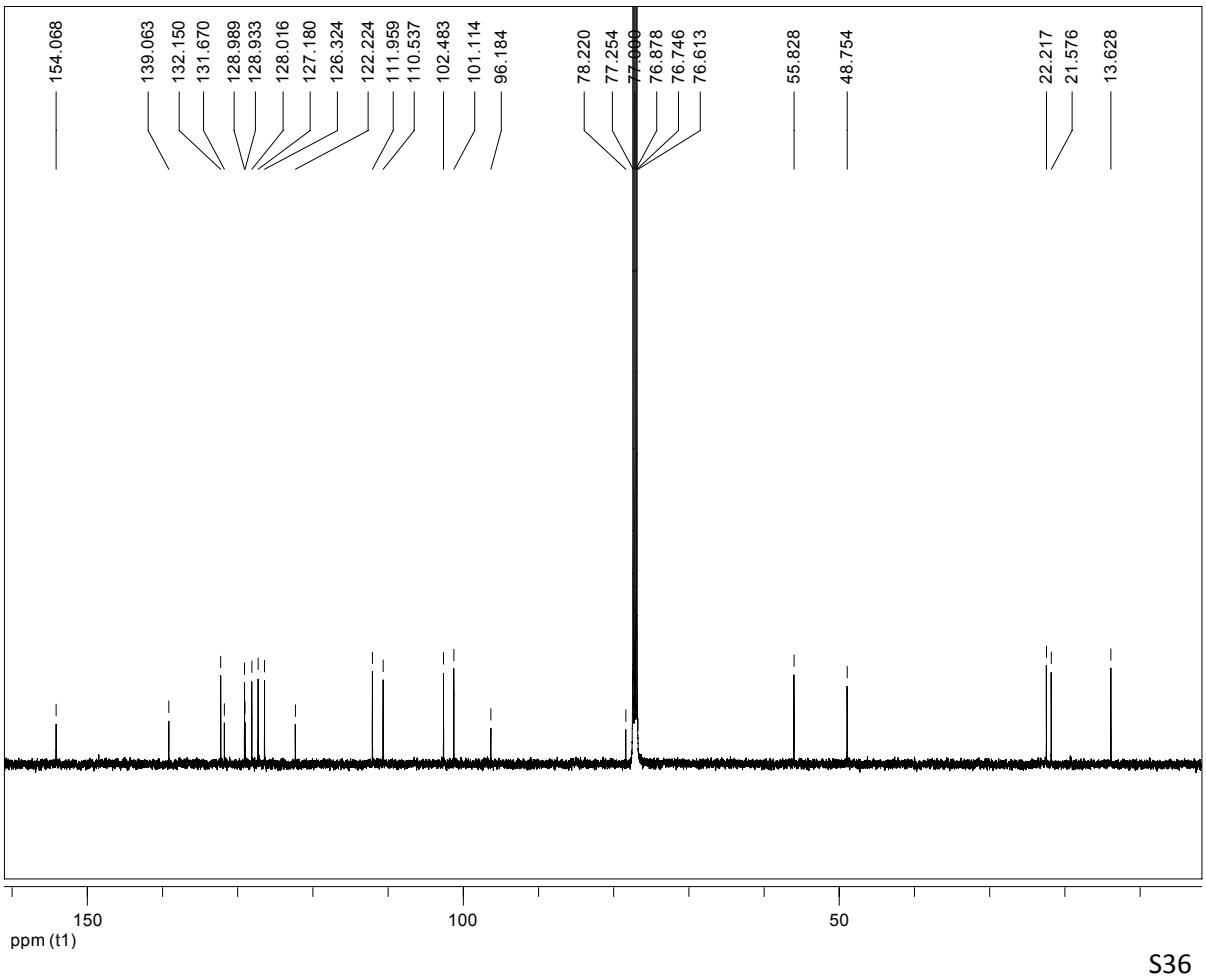
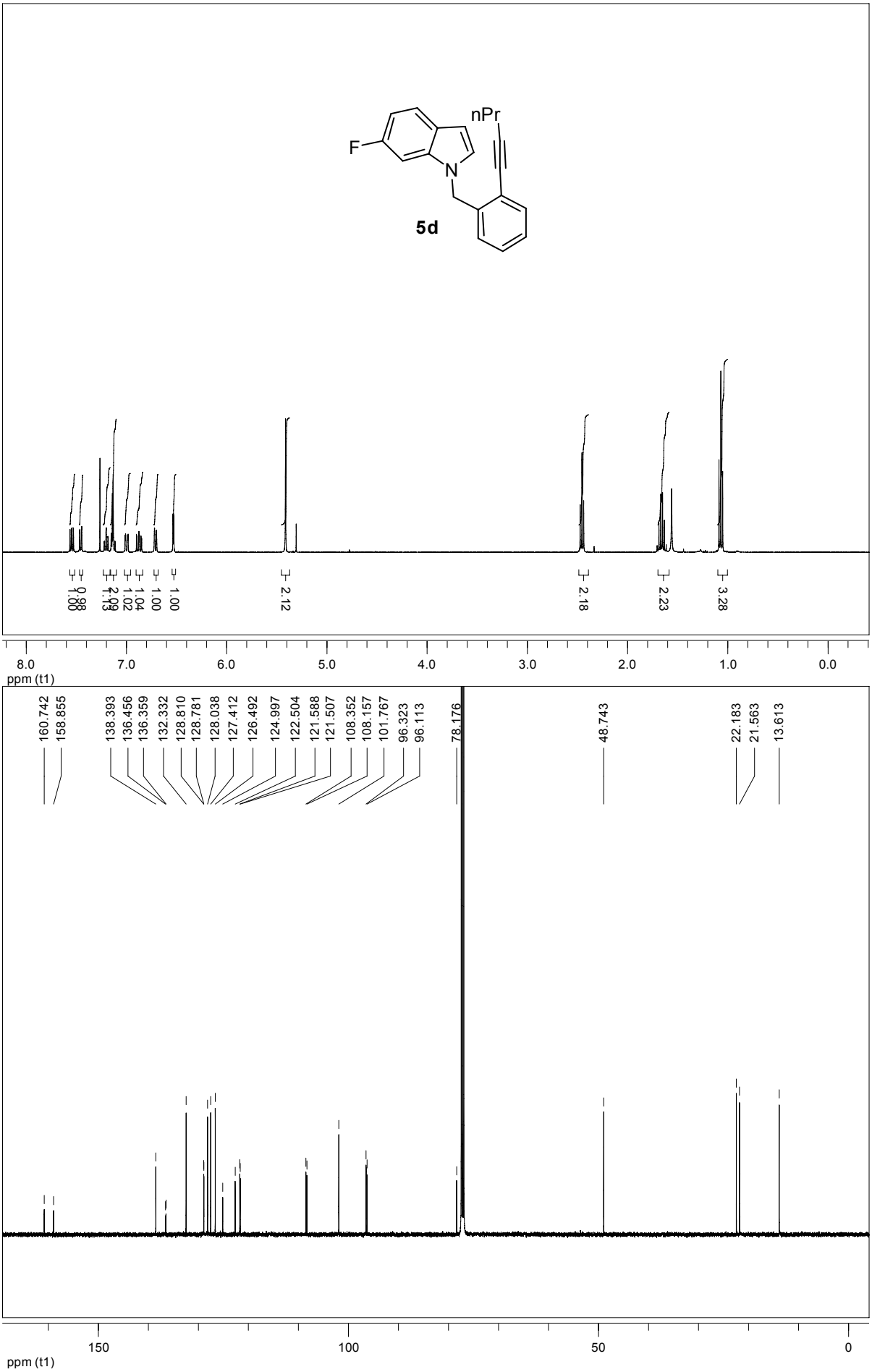
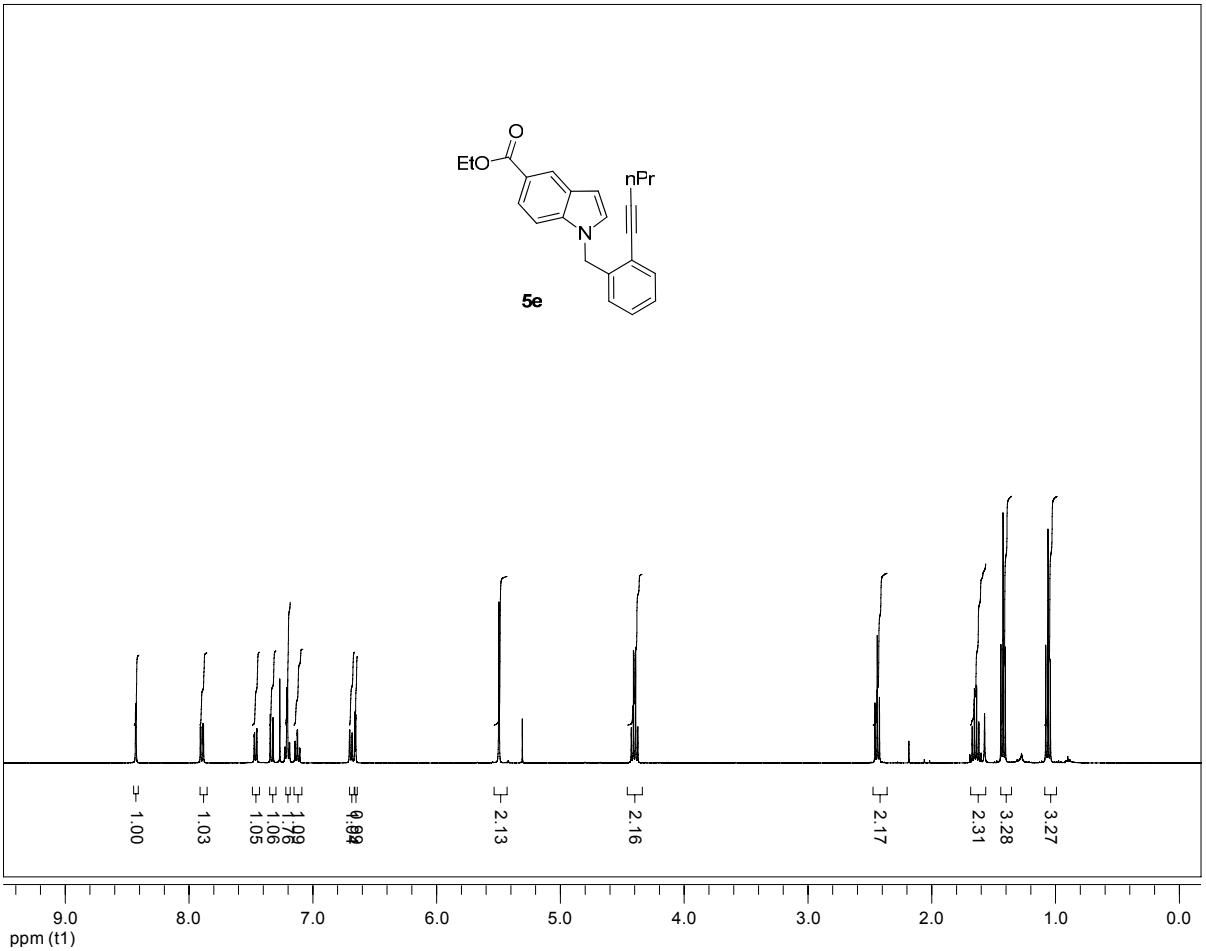
132.165
128.577
128.414
128.011
127.199
126.399
122.287
121.620
120.882
119.458
109.756
101.600
96.194
78.231
48.557
22.209
21.572
13.624
100
50
ppm (t1)

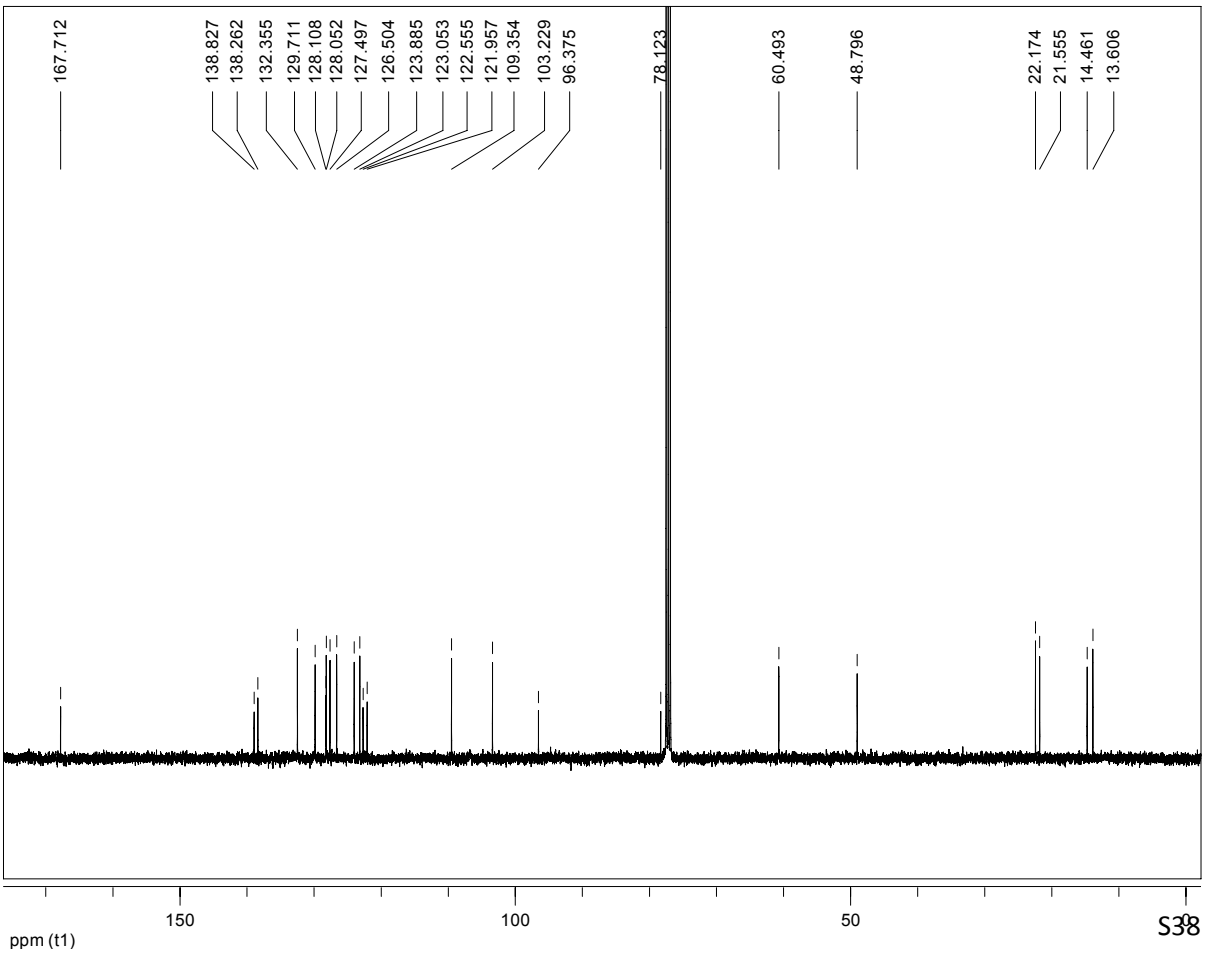







nPr
F
N
5d
1.00
1.04
1.02
2.09
4.13
0.88
2.12
2.18
2.23
3.28
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
160.742
158.855
138.393
136.456
136.359
132.332
128.810
128.781
128.038
127.412
126.492
124.997
122.504
121.588
121.507
108.352
108.157
101.767
96.323
96.113
78.176
48.743
22.183
21.563
13.613
150
100
50
0
ppm (t1)


O
EtO
nPr
N
5e
1.00
1.03
1.05
1.06
1.07
1.09
2.13
2.16
2.17
2.31
3.28
3.27
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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138.262
132.355
129.711
128.108
128.052
127.497
126.504
123.885
123.053
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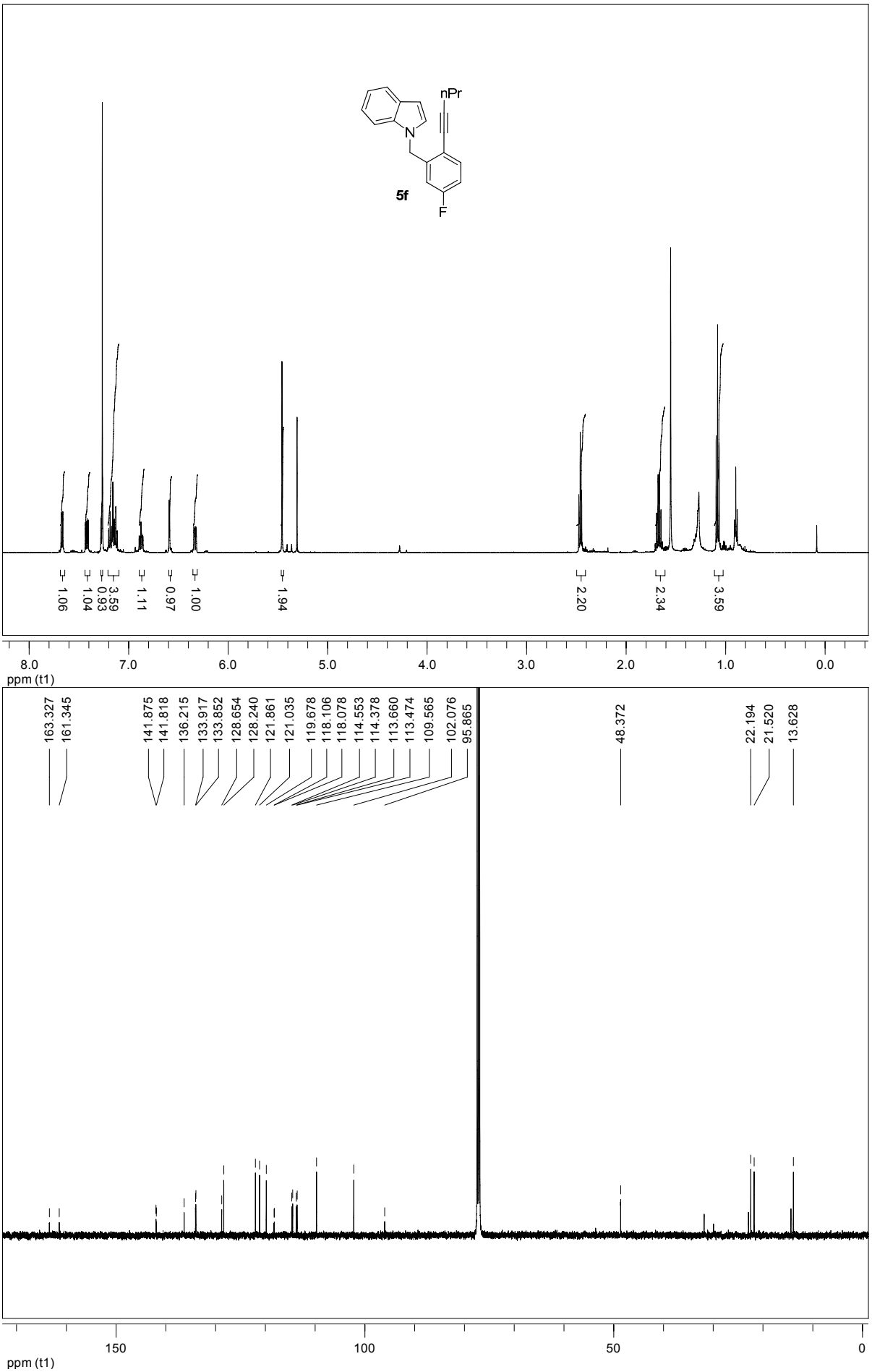
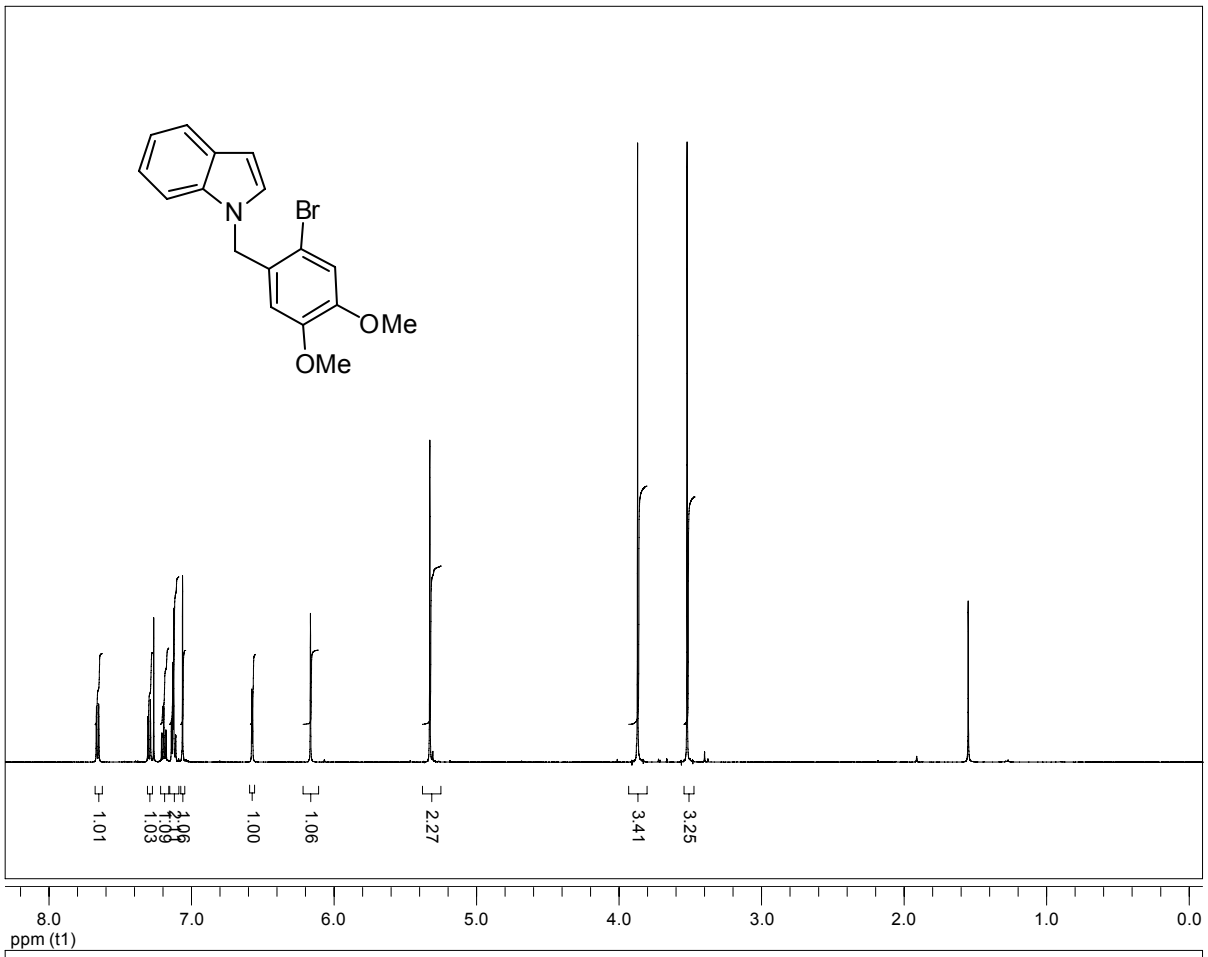
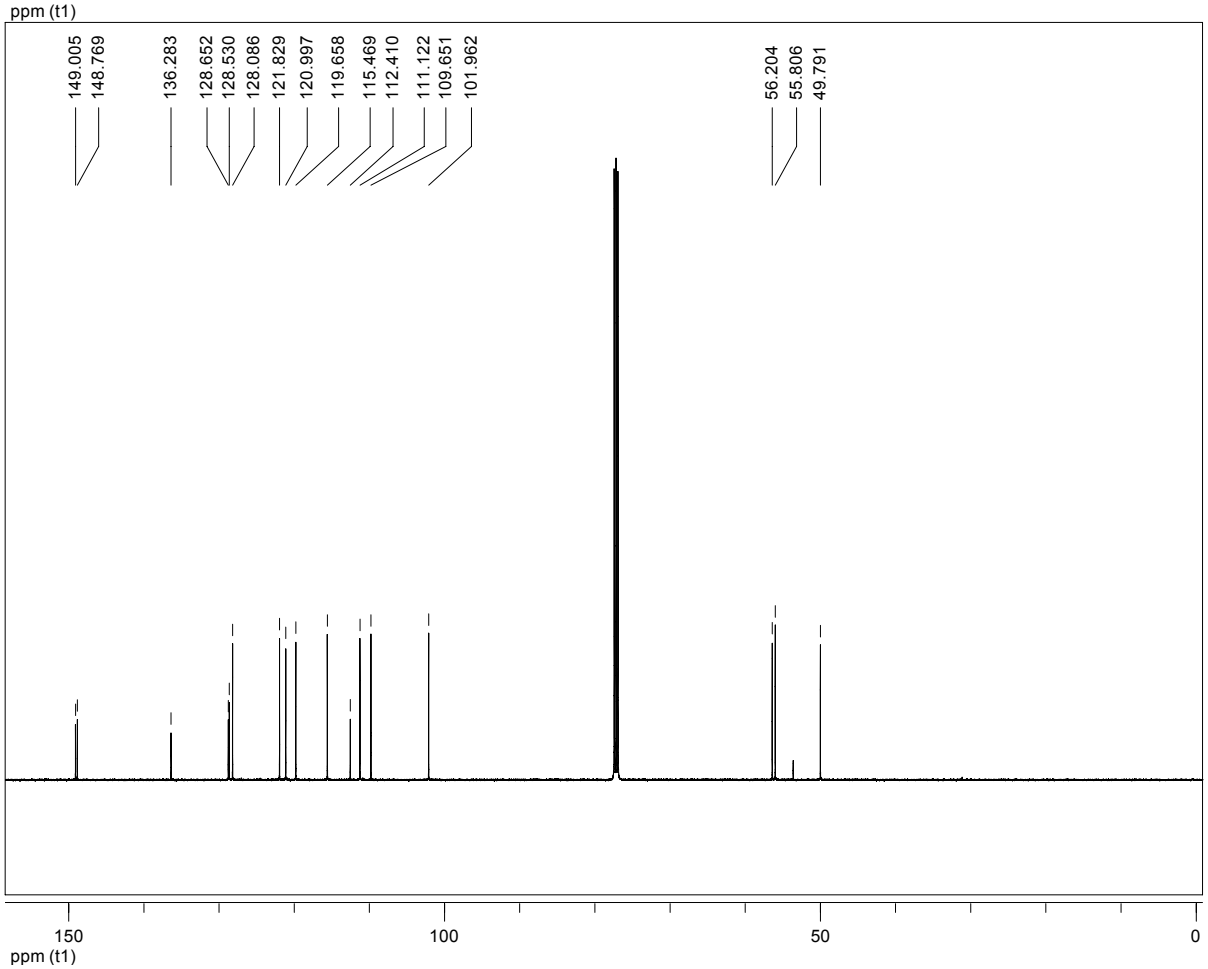
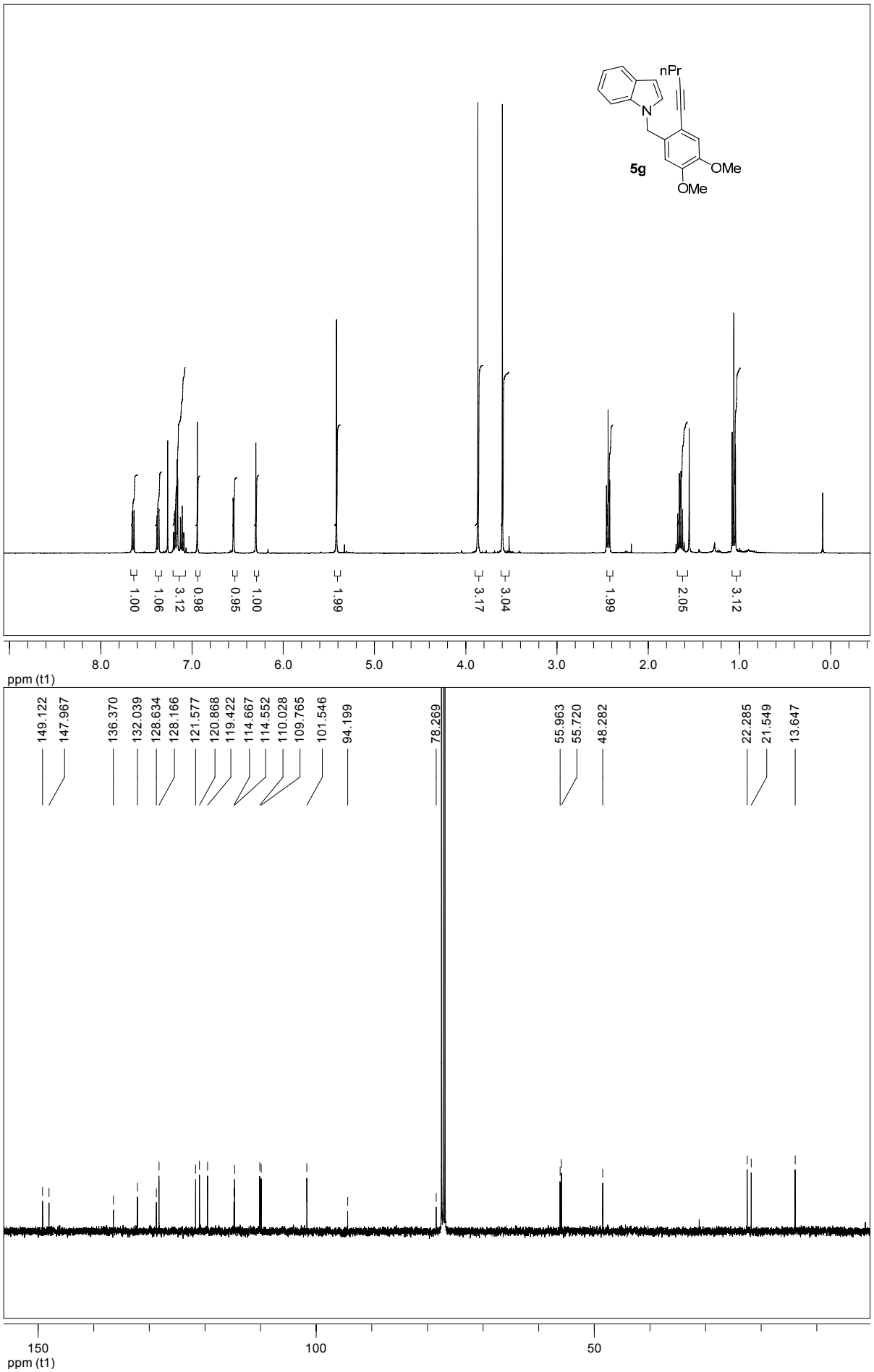
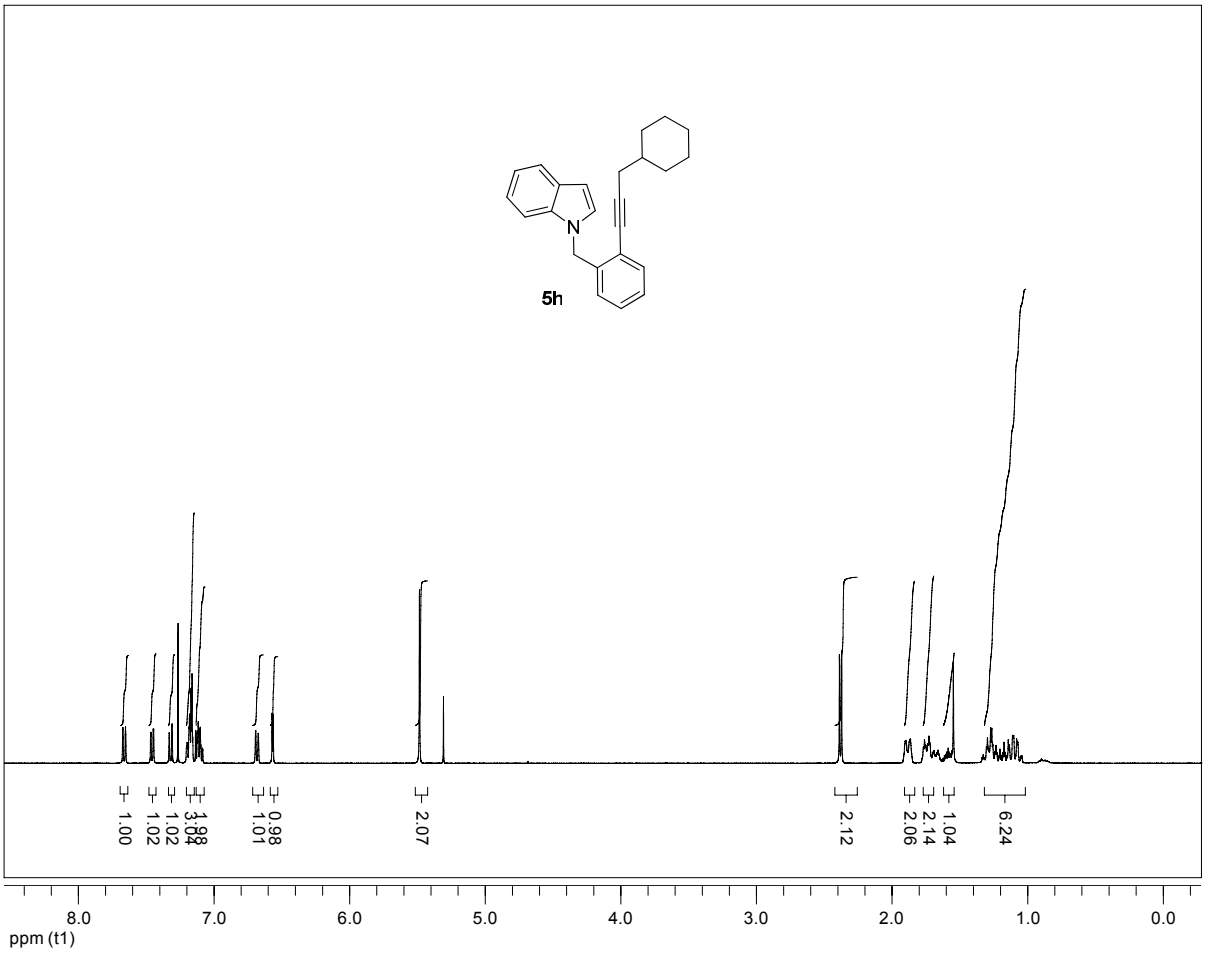
121.957
109.354
103.229
96.375
78.123
60.493
48.796
22.174
21.555
14.461
13.606
150
100
50
ppm (t1)

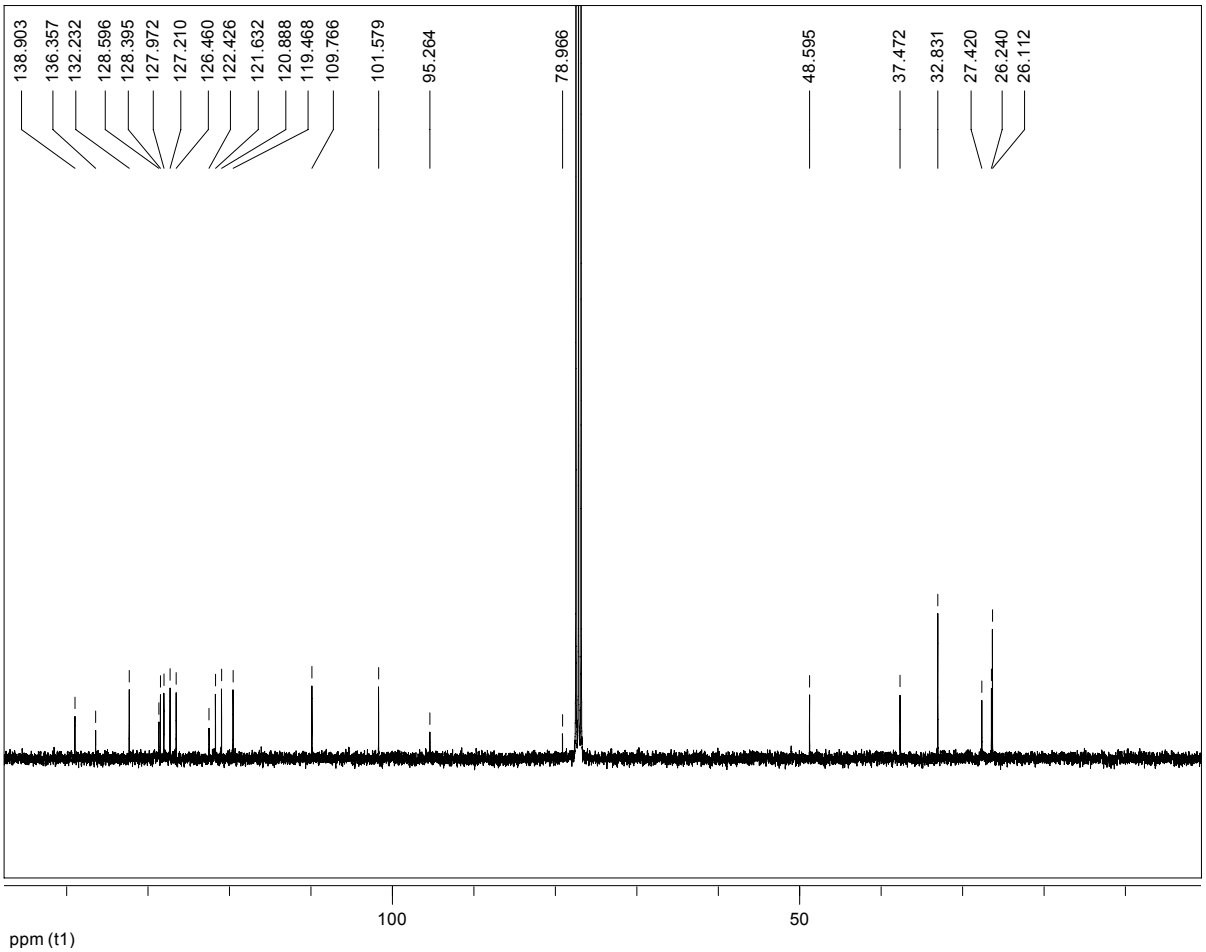


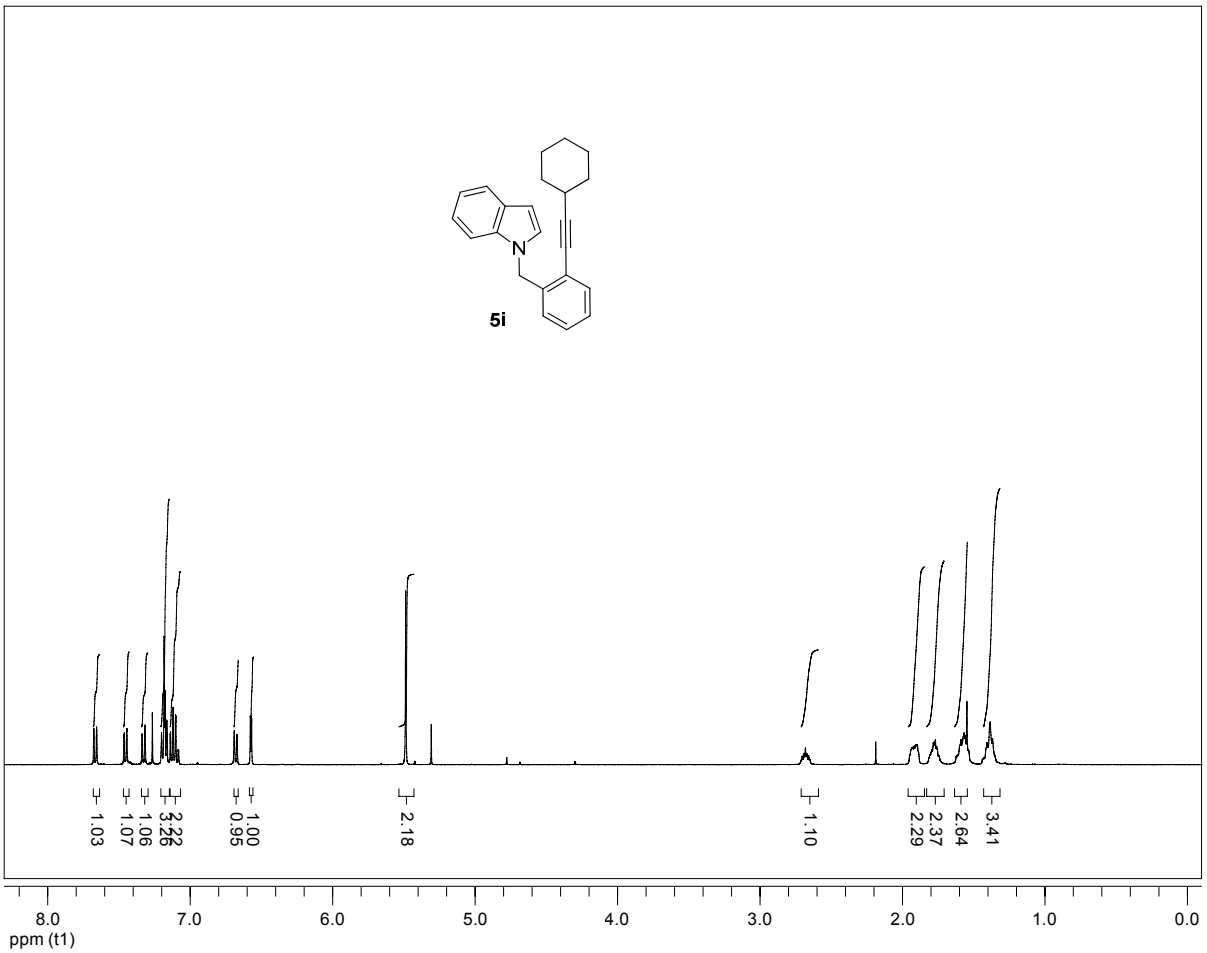


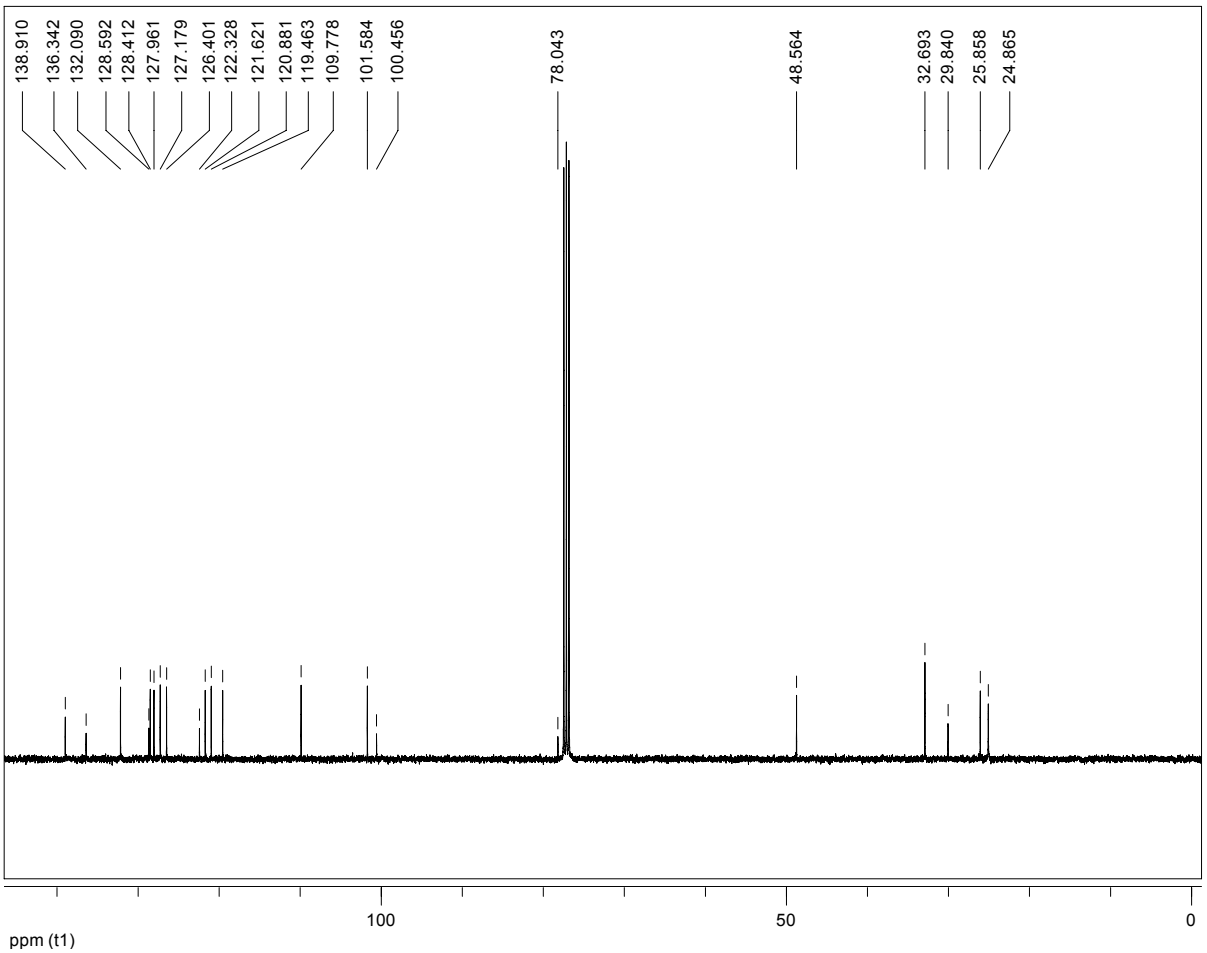



nPr
N
OMe
OMe
5g
1.00
1.06
3.12
0.98
0.95
1.00
1.99
3.17
3.04
1.99
2.05
3.12
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
149.122
147.967
136.370
132.039
128.634
128.166
121.577
120.868
119.422
114.667
114.552
110.028
109.765
101.546
94.199
78.269
55.963
55.720
48.282
22.285
21.549
13.647
150
100
50
ppm (t1)






5i
1.03
1.07
1.06
3.22
3.26
1.00
0.95
2.18
1.10
2.29
2.37
2.64
3.41
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)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128.412
127.961
127.179
126.401
122.328
121.621
120.881
119.463
109.778
101.584
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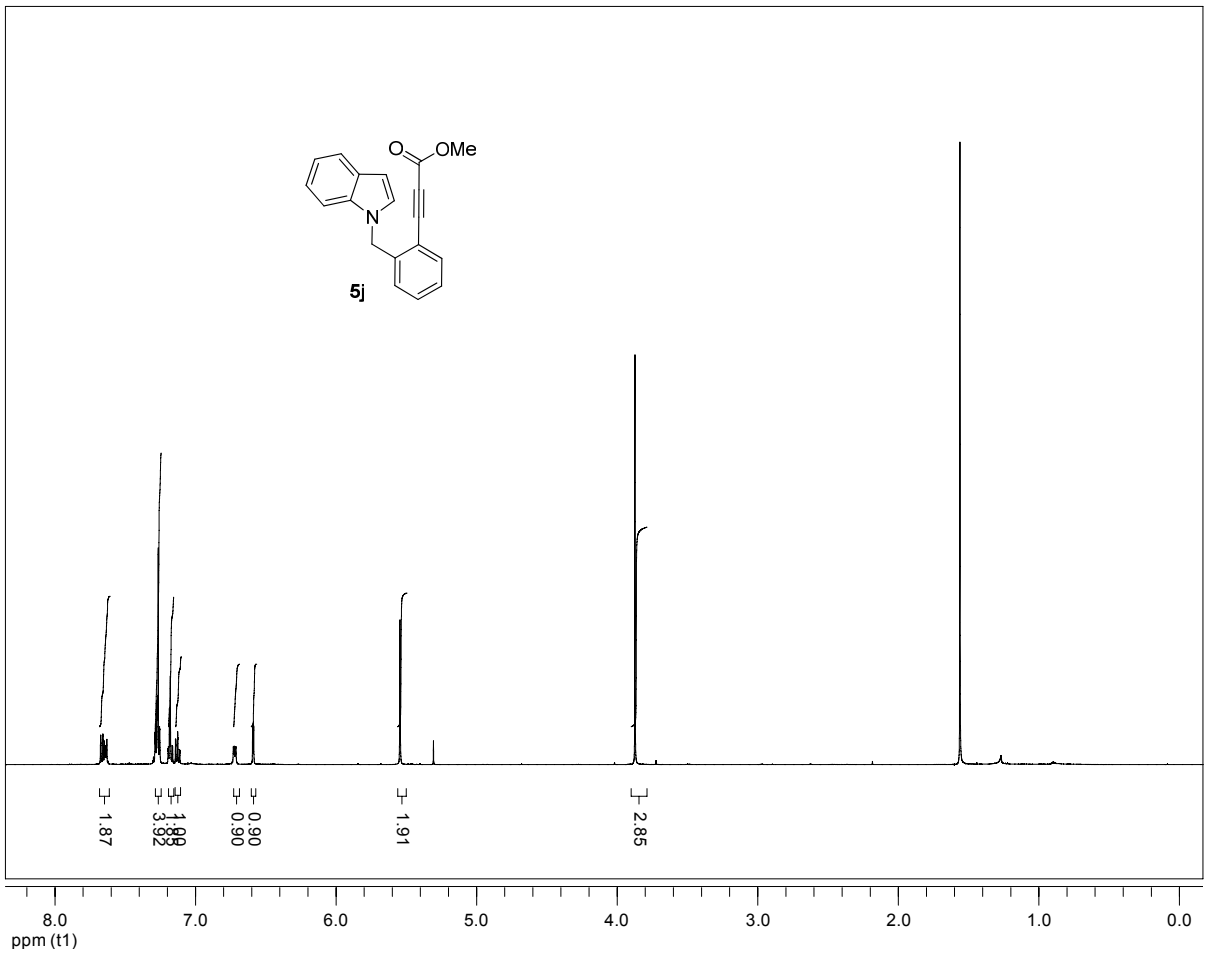
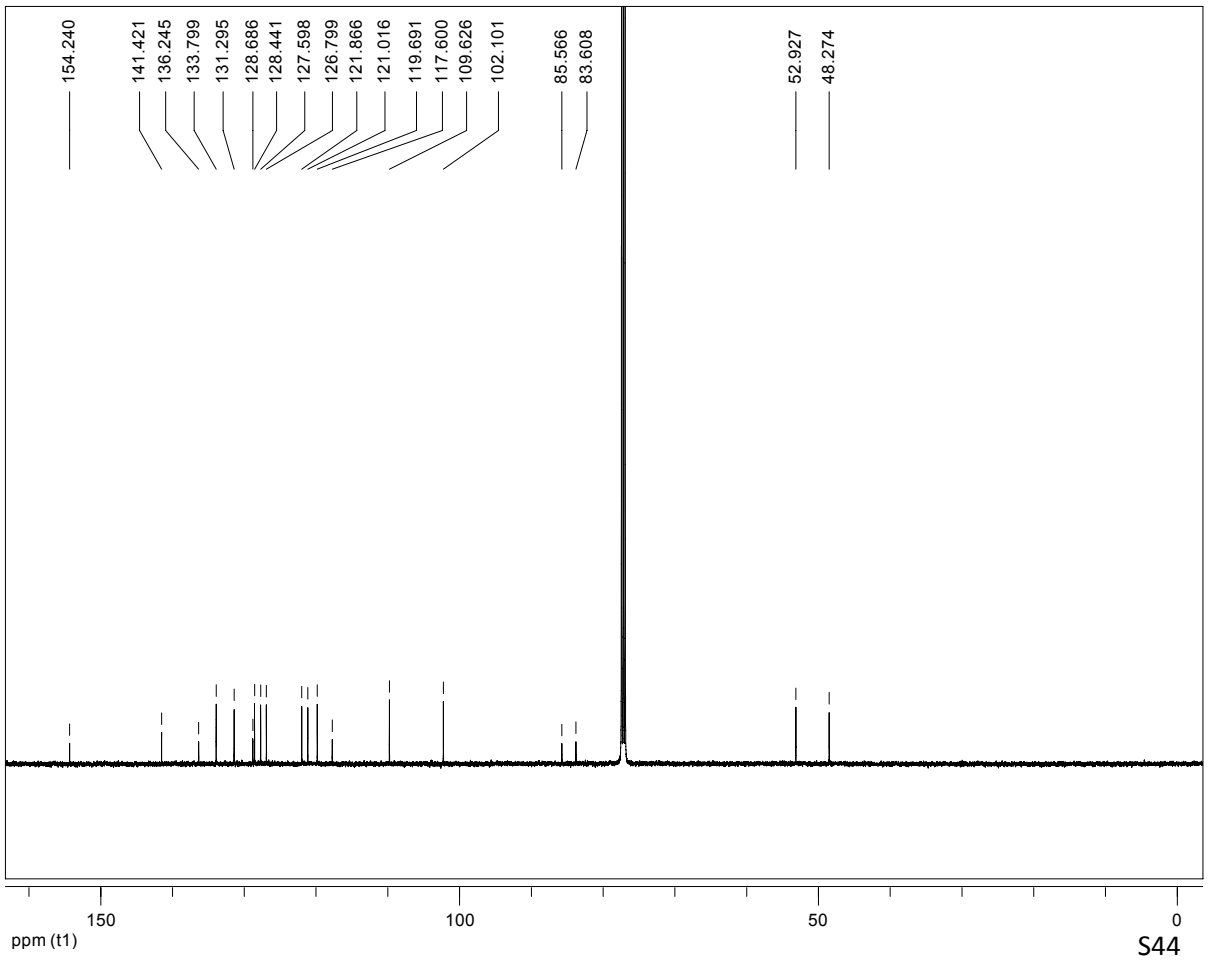
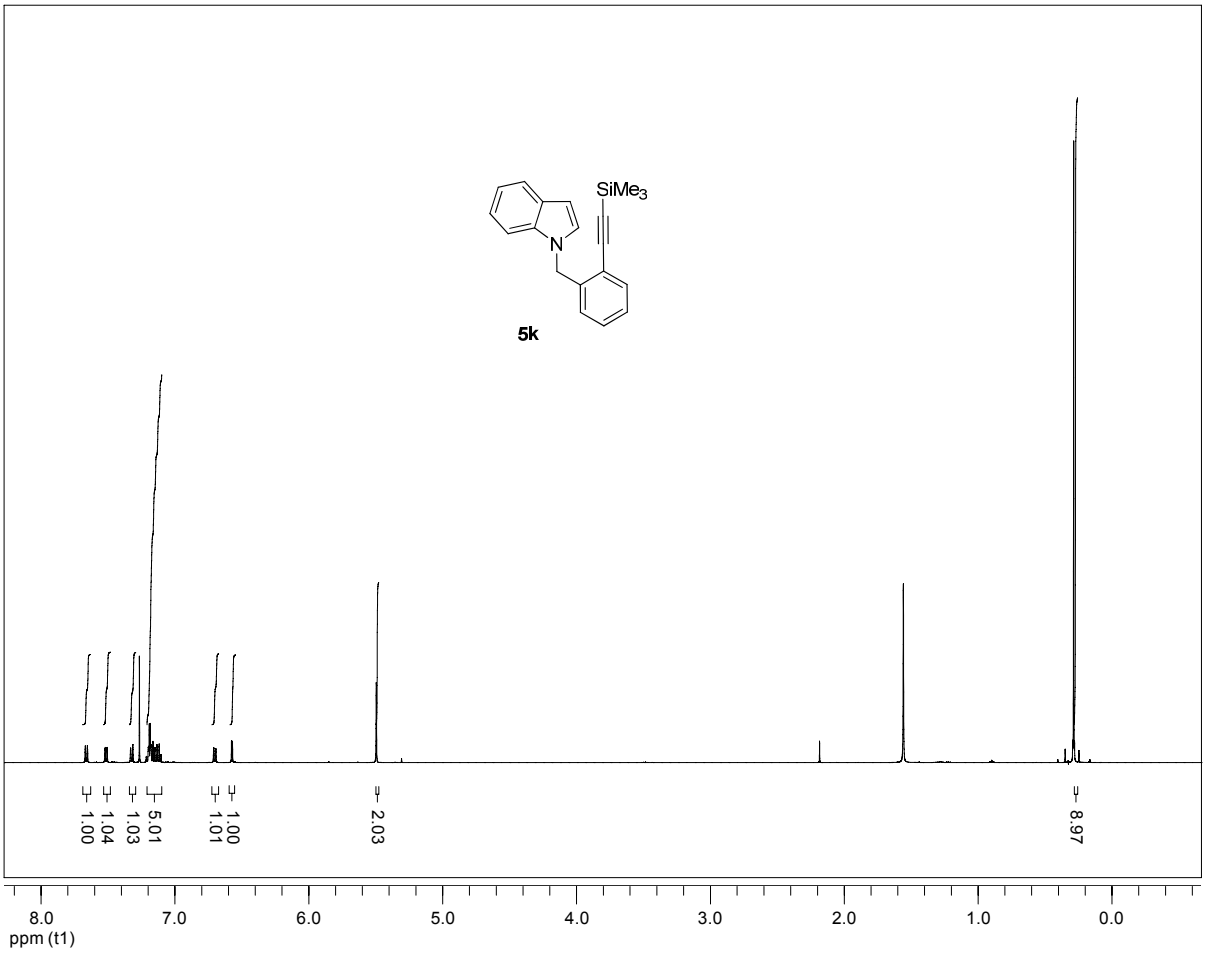
78.043
48.564
32.693
29.840
25.858
24.865
100
50
0
ppm (t1)






SiMe3
N
5k
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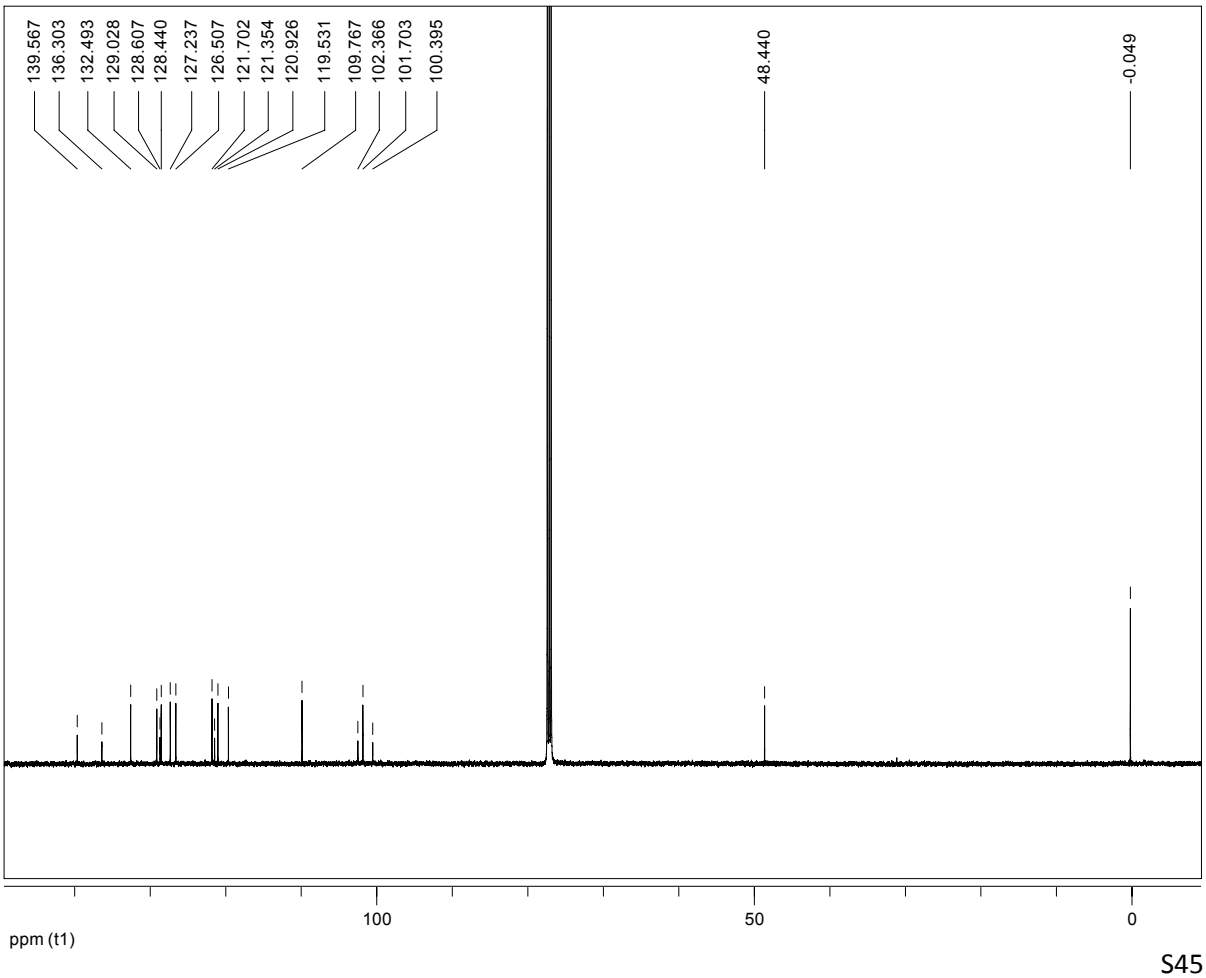
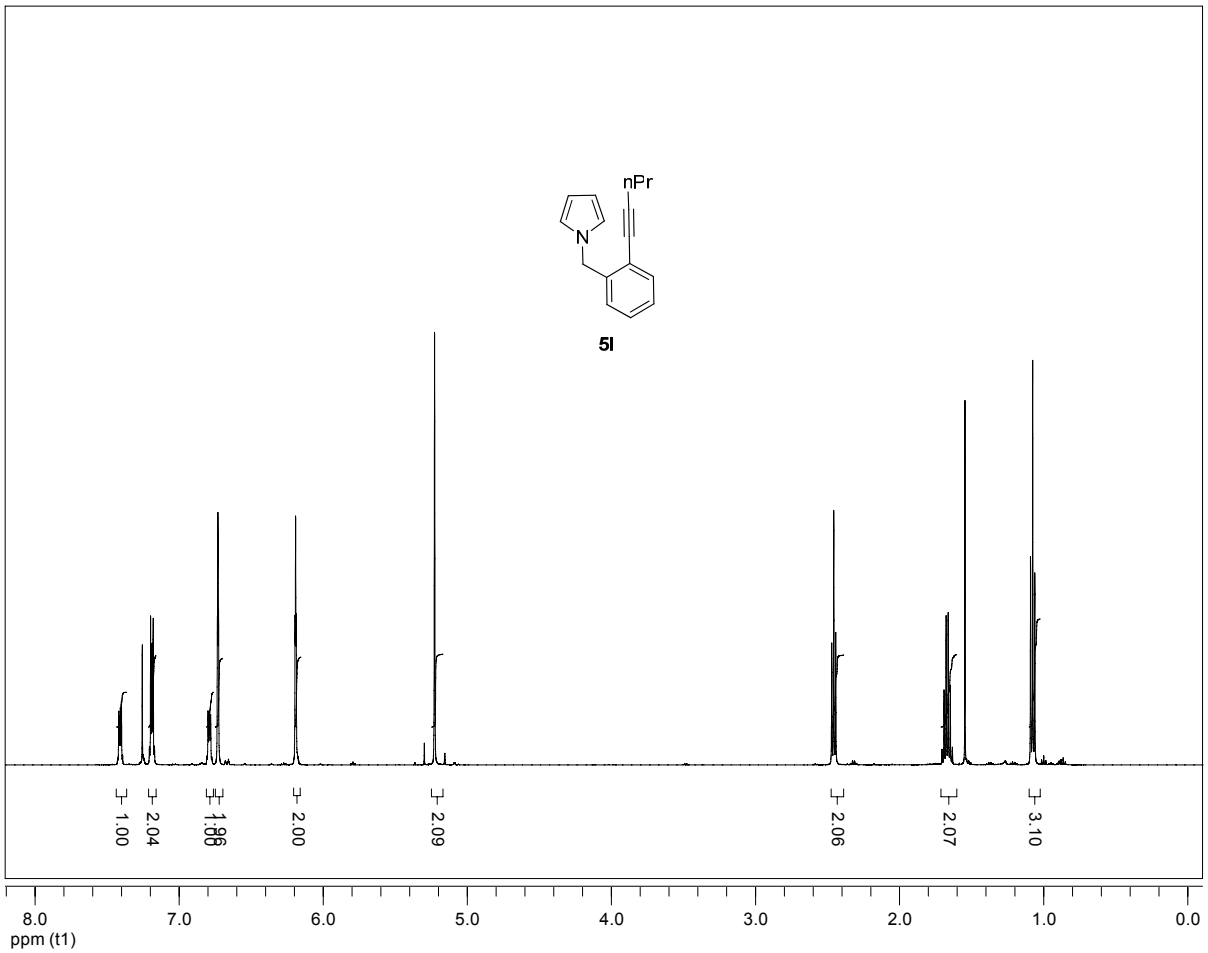
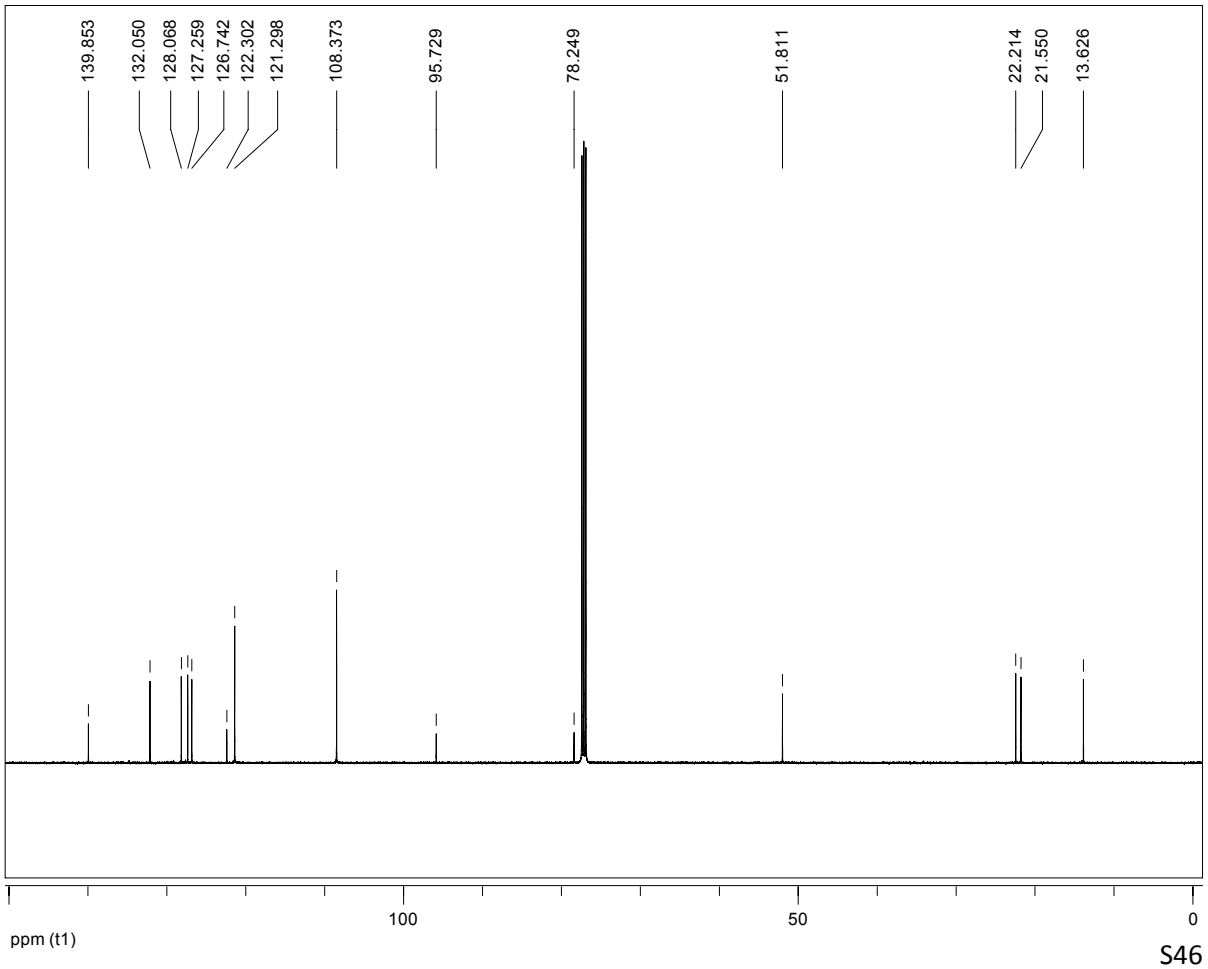
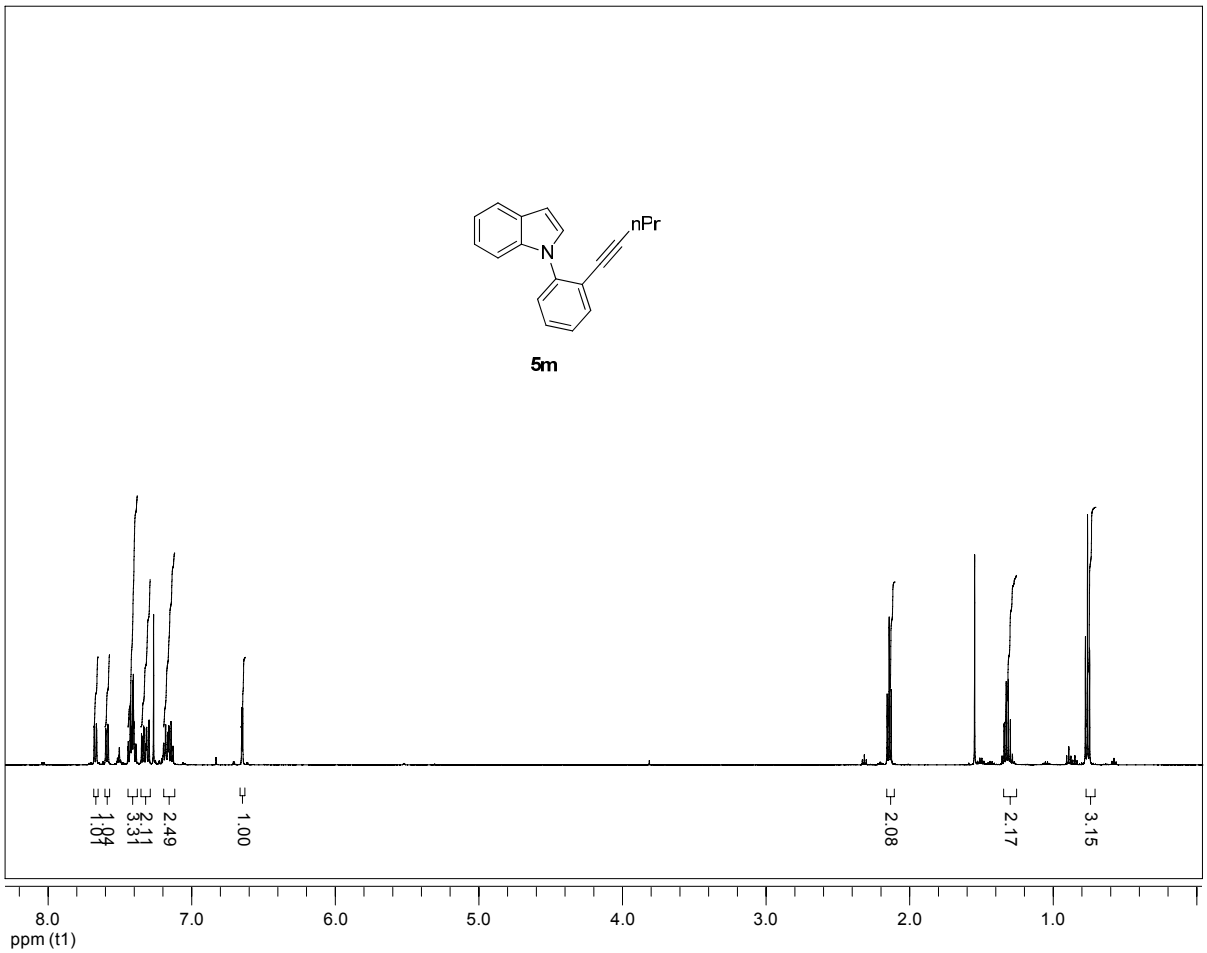
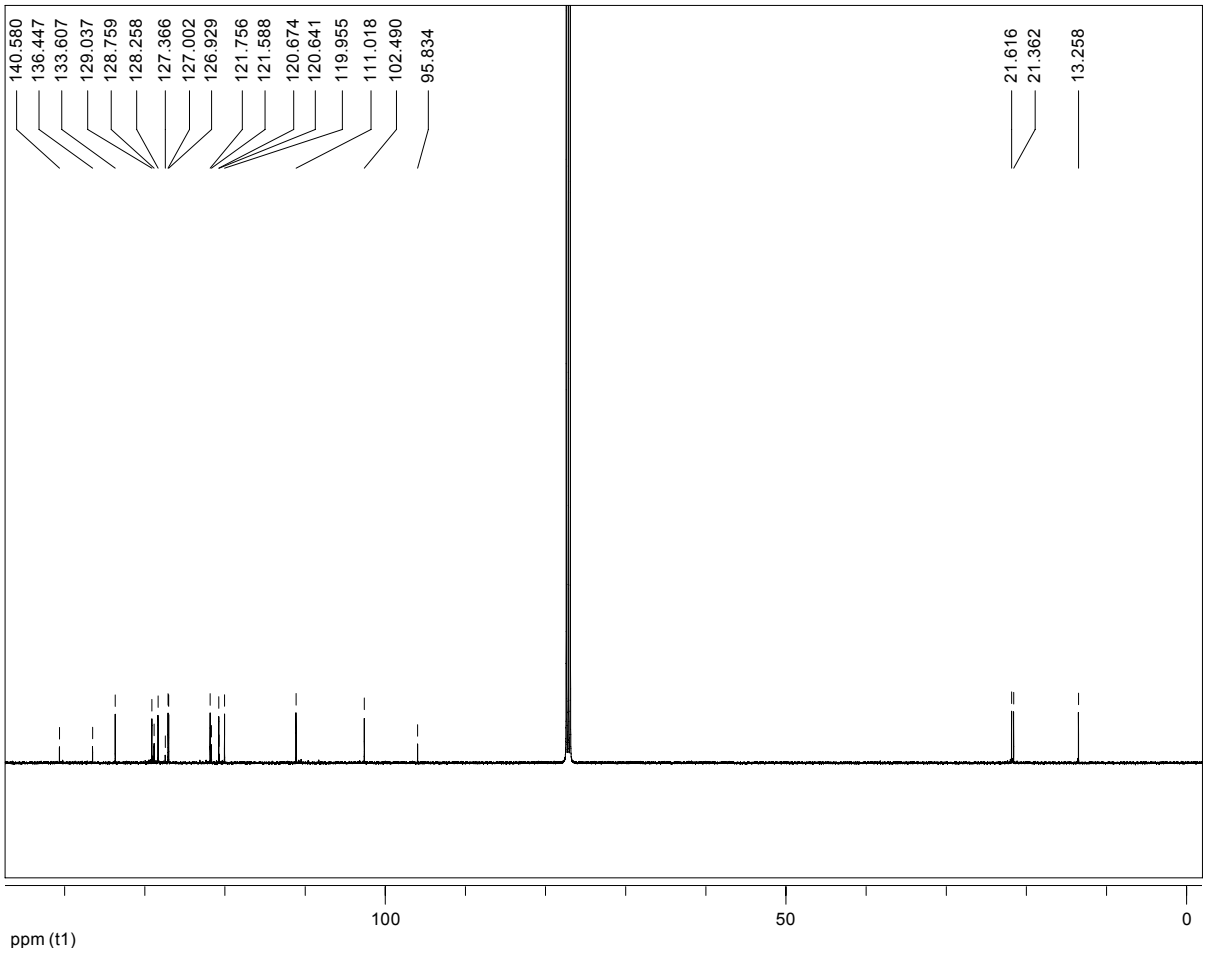
1.04
1.03
5.01
1.01
1.00
2.03
8.97
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

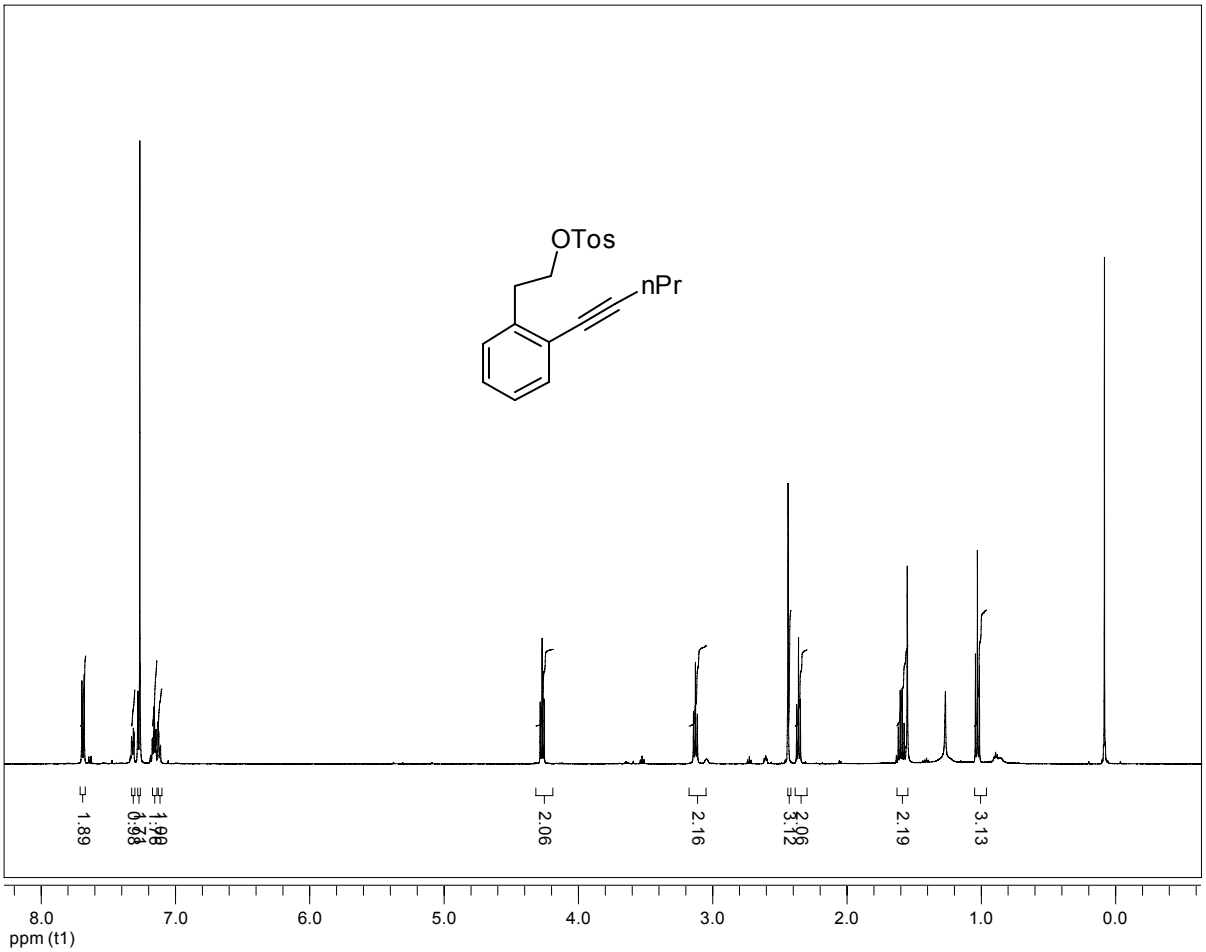

139.567
136.303
132.493
129.028
128.607
128.440
127.237
126.507
121.702
121.354
120.926
119.531
109.767
102.366
101.703
100.395
48.440
-0.049
100
50
0
ppm (t1)

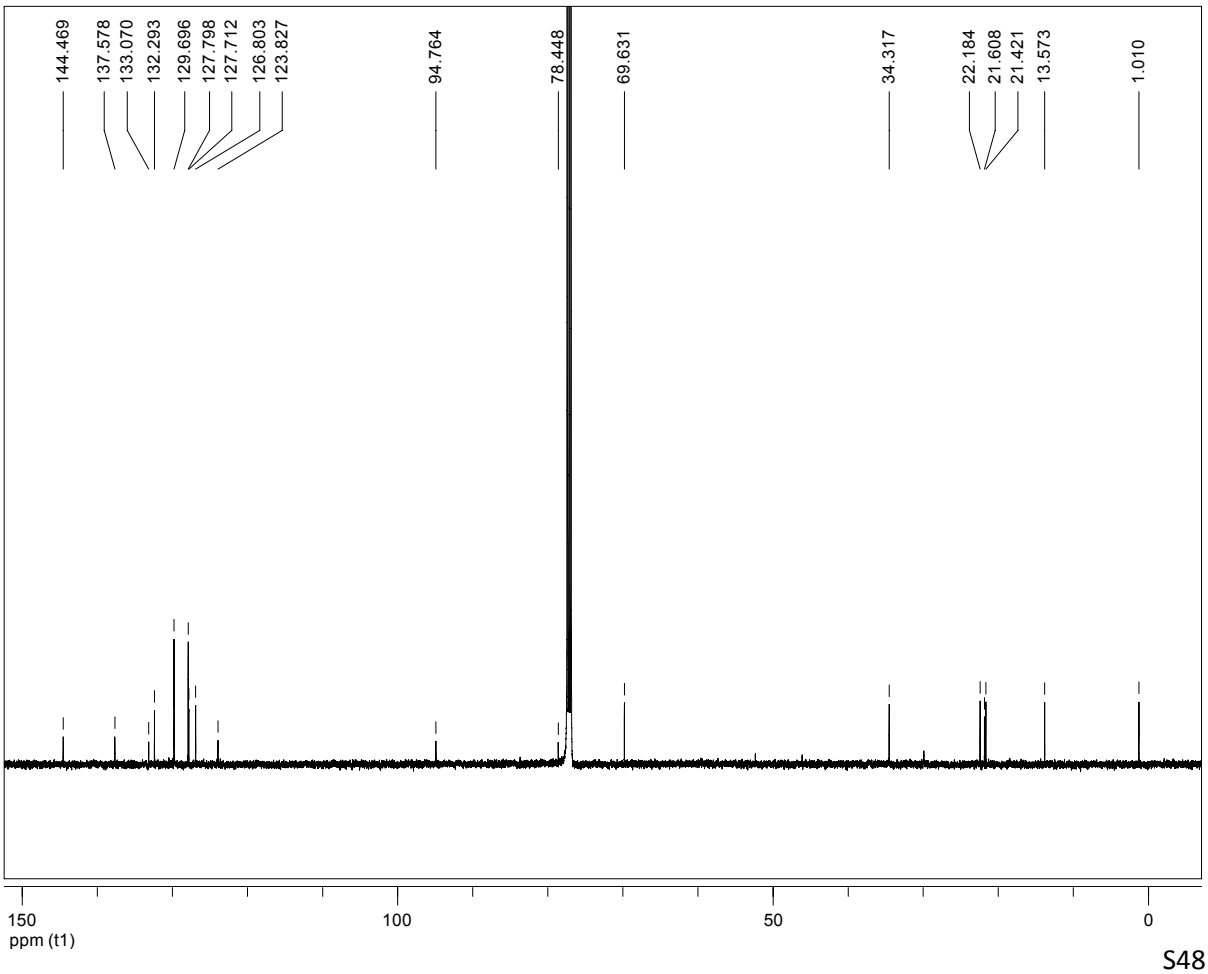


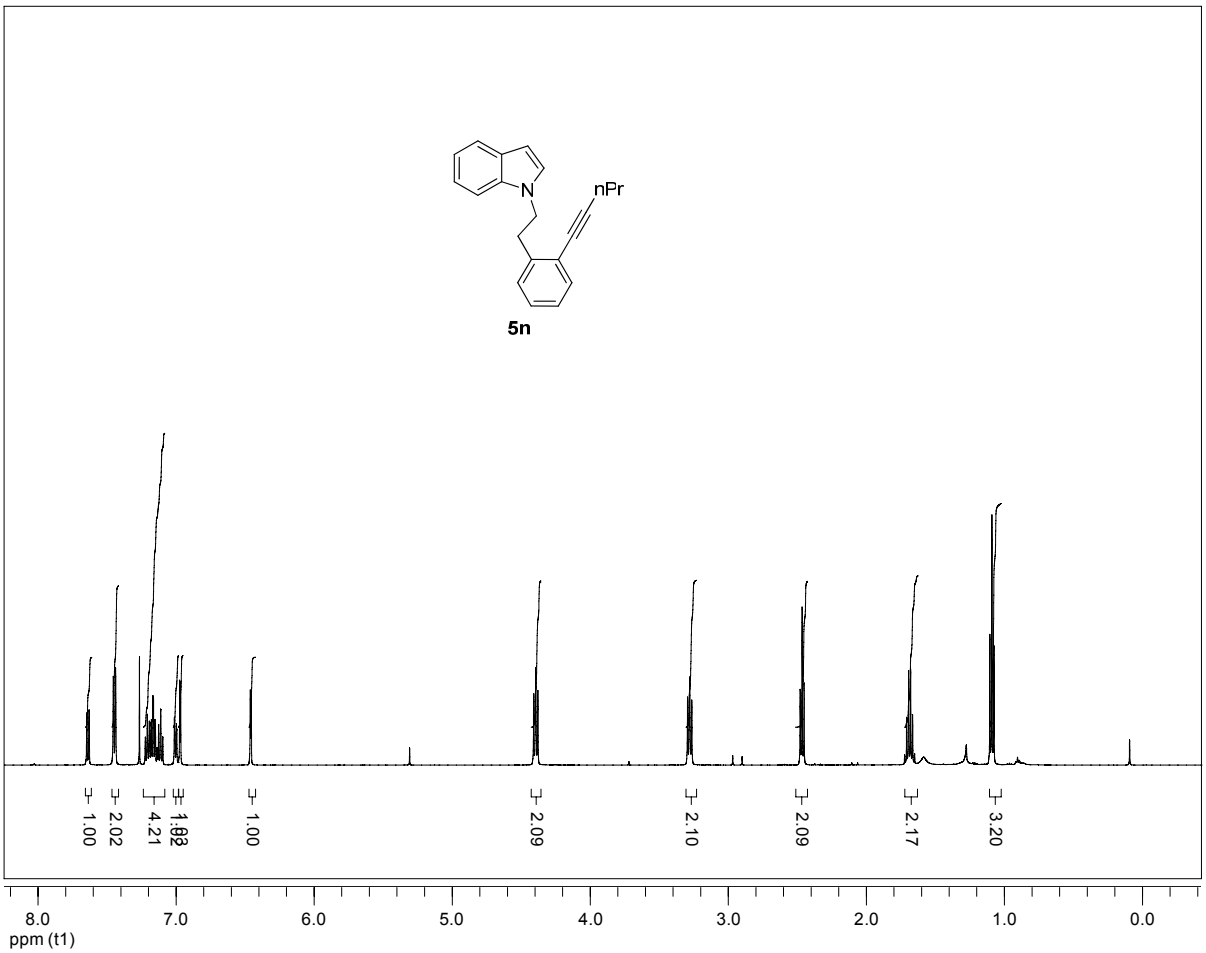


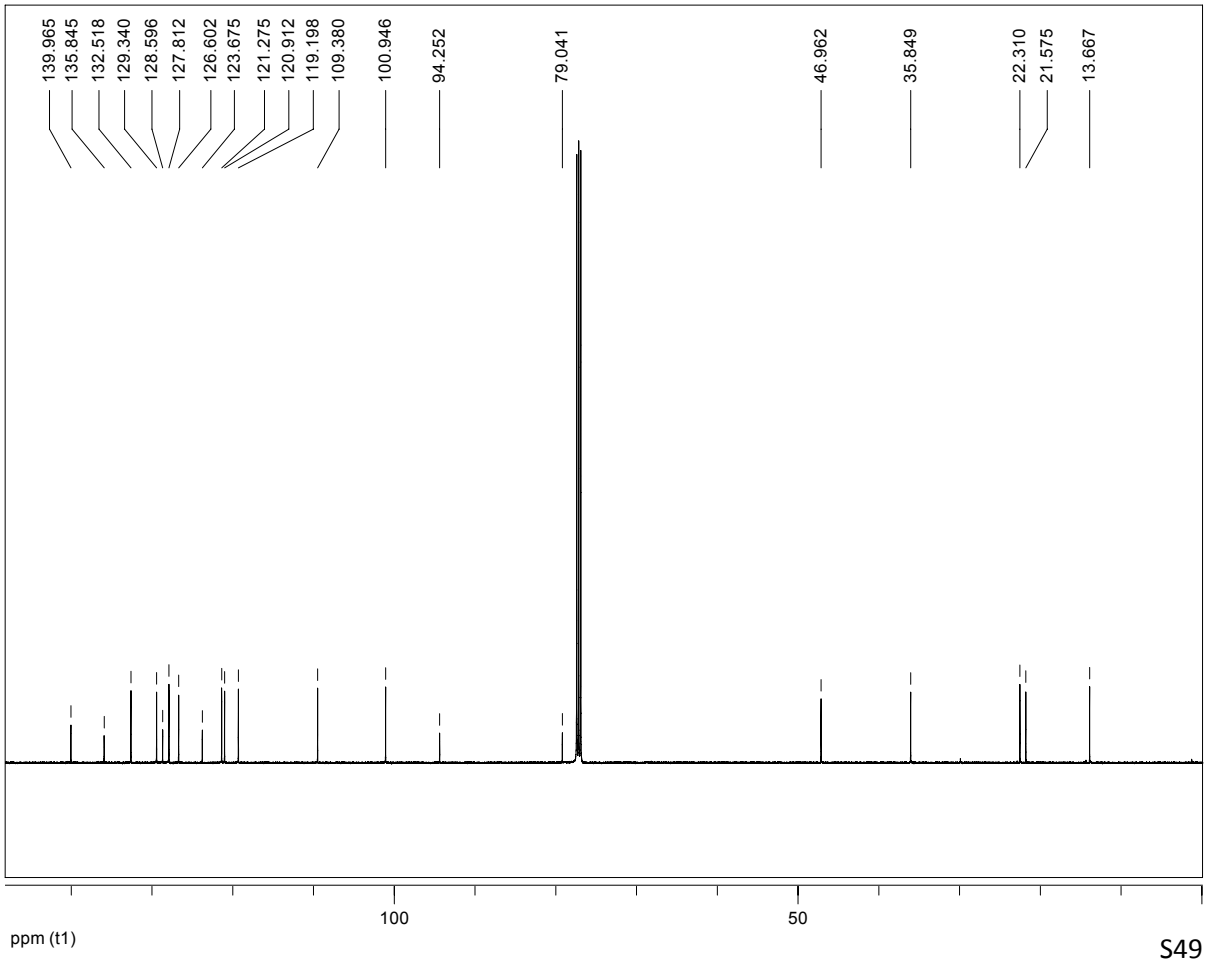


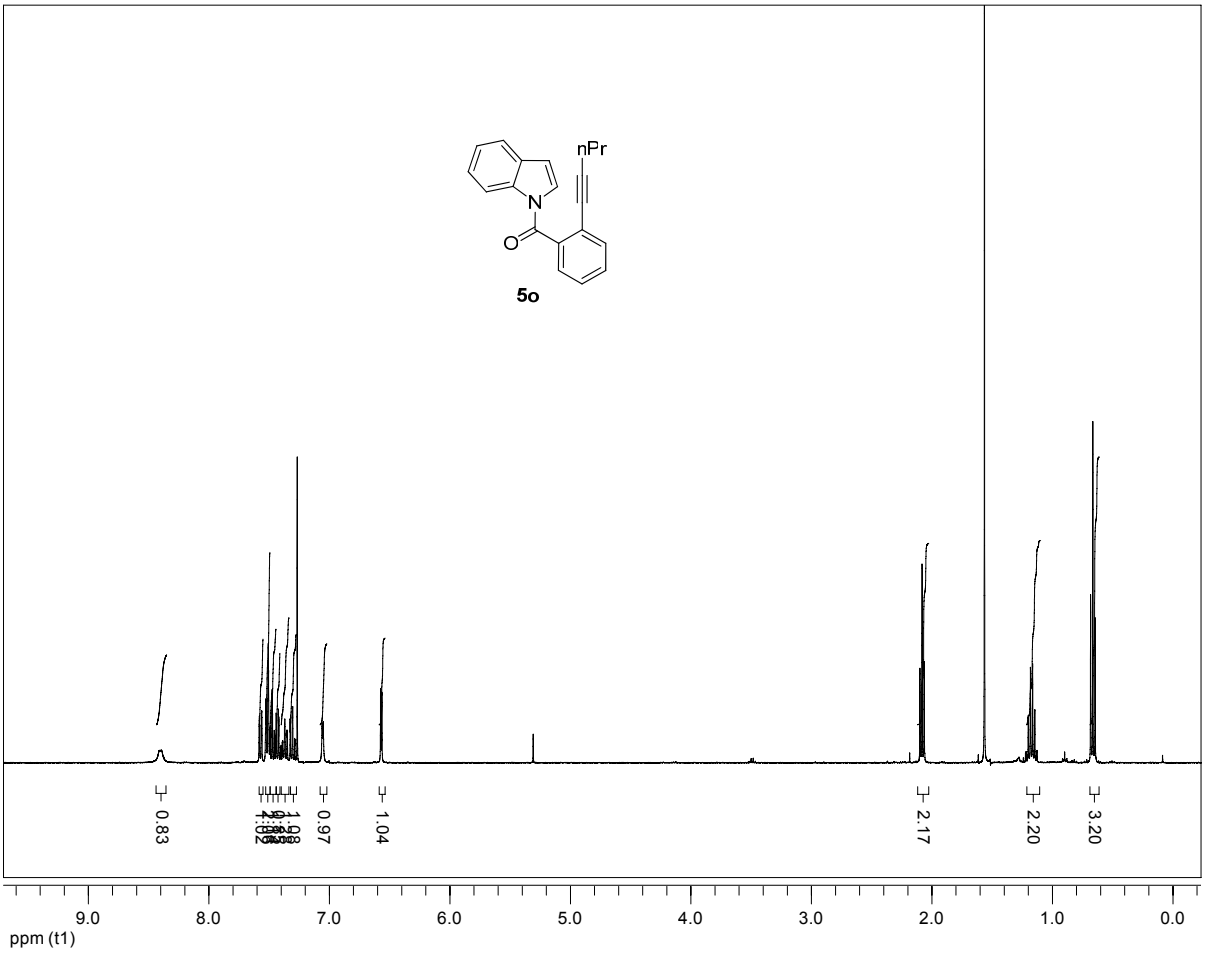


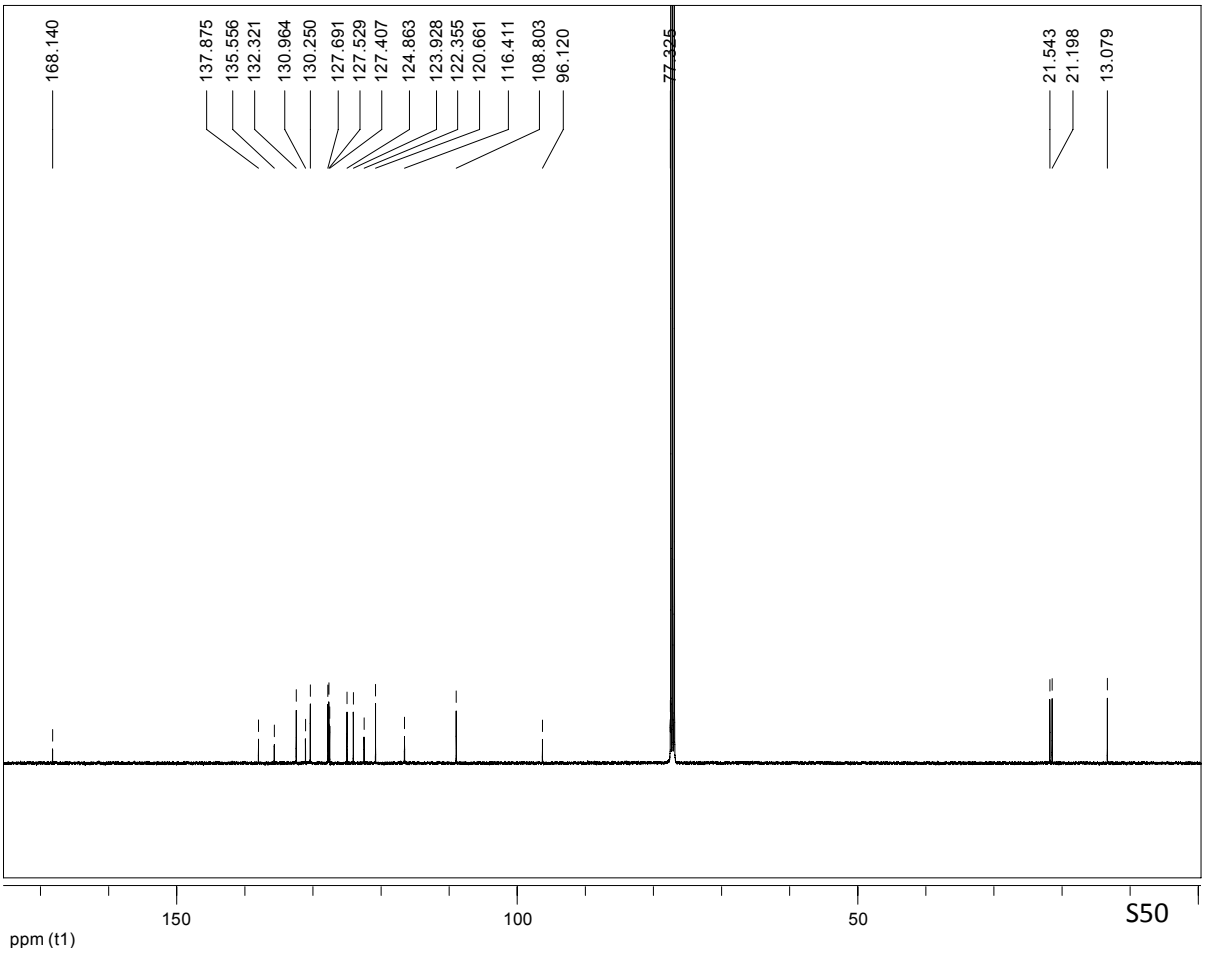


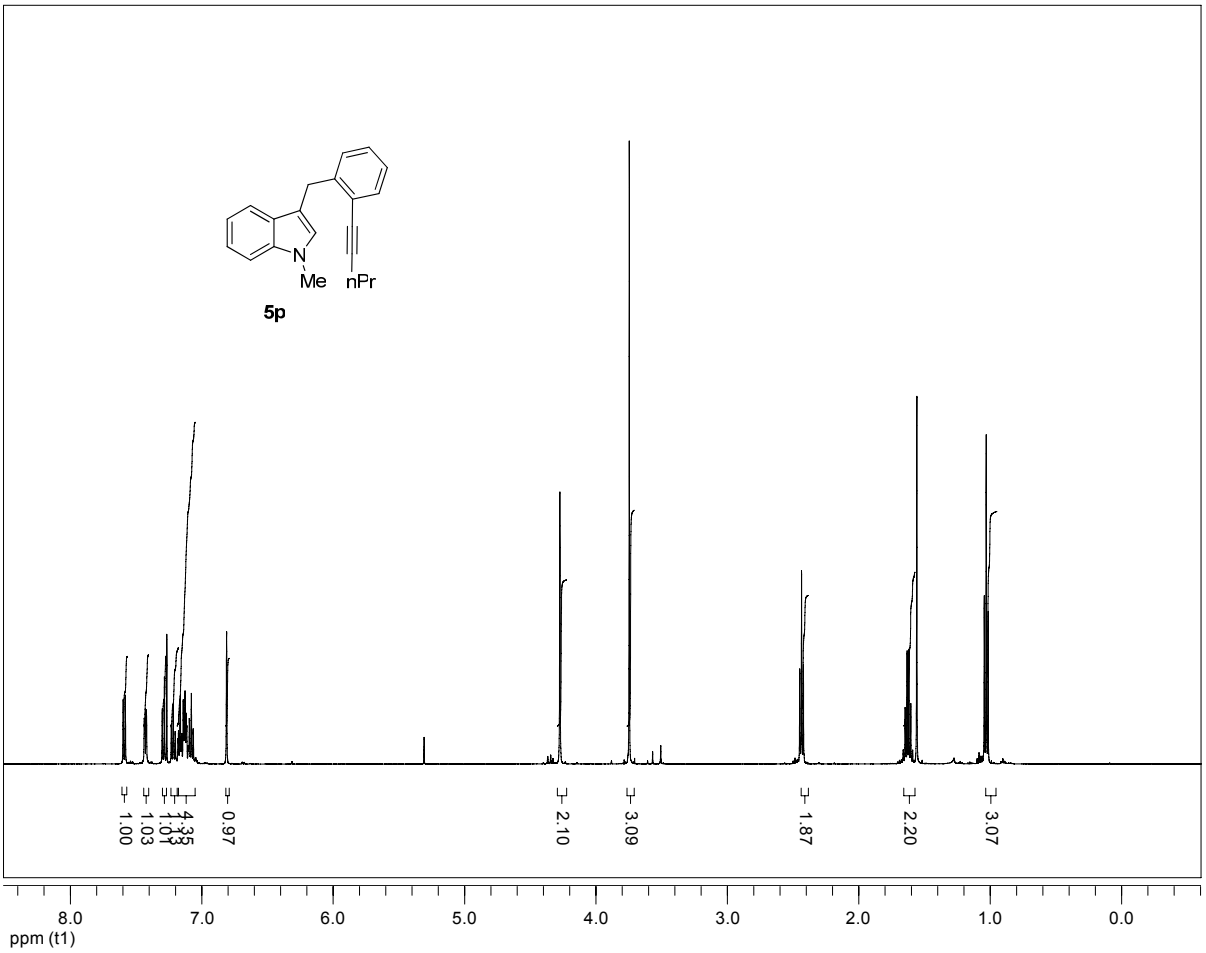


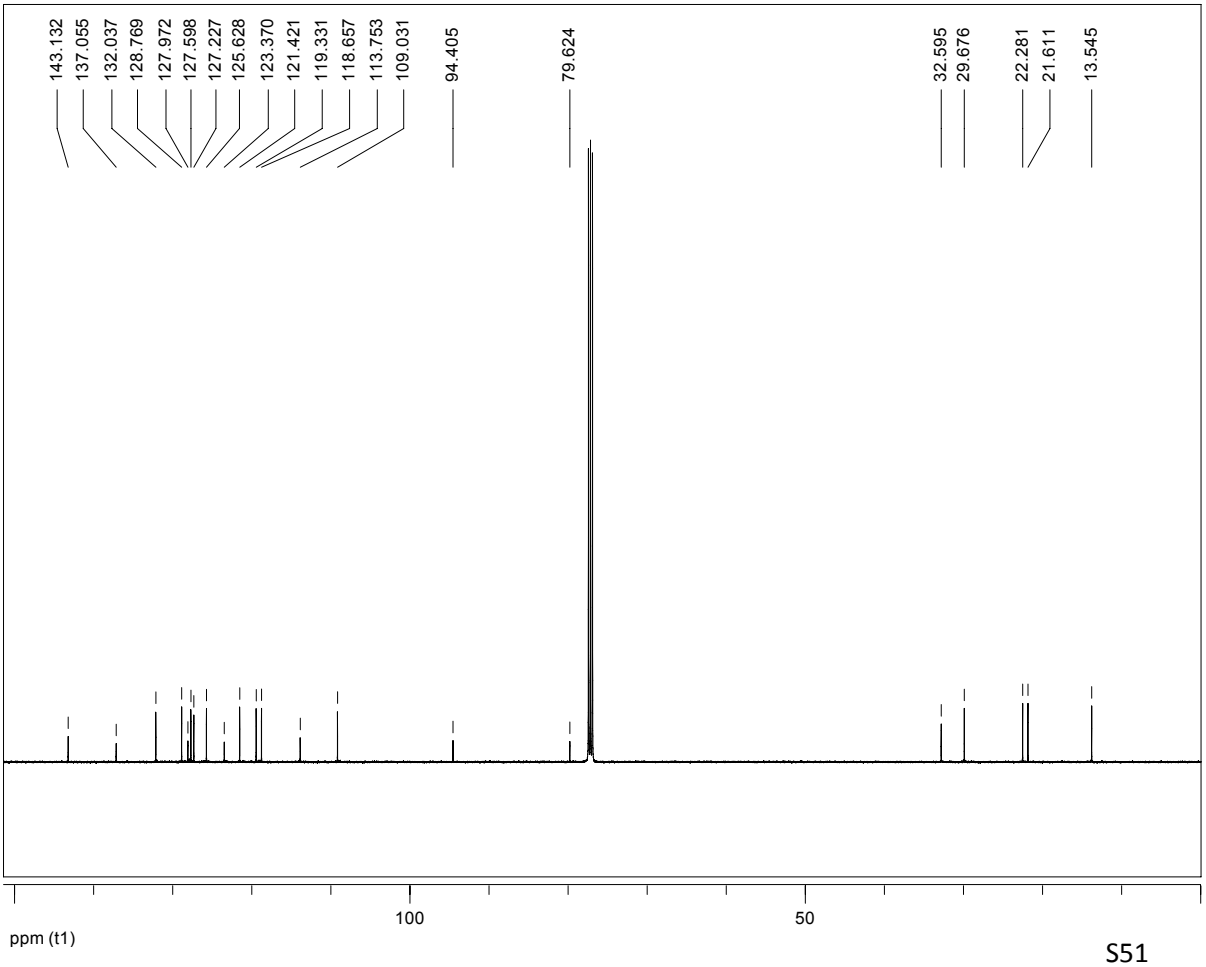


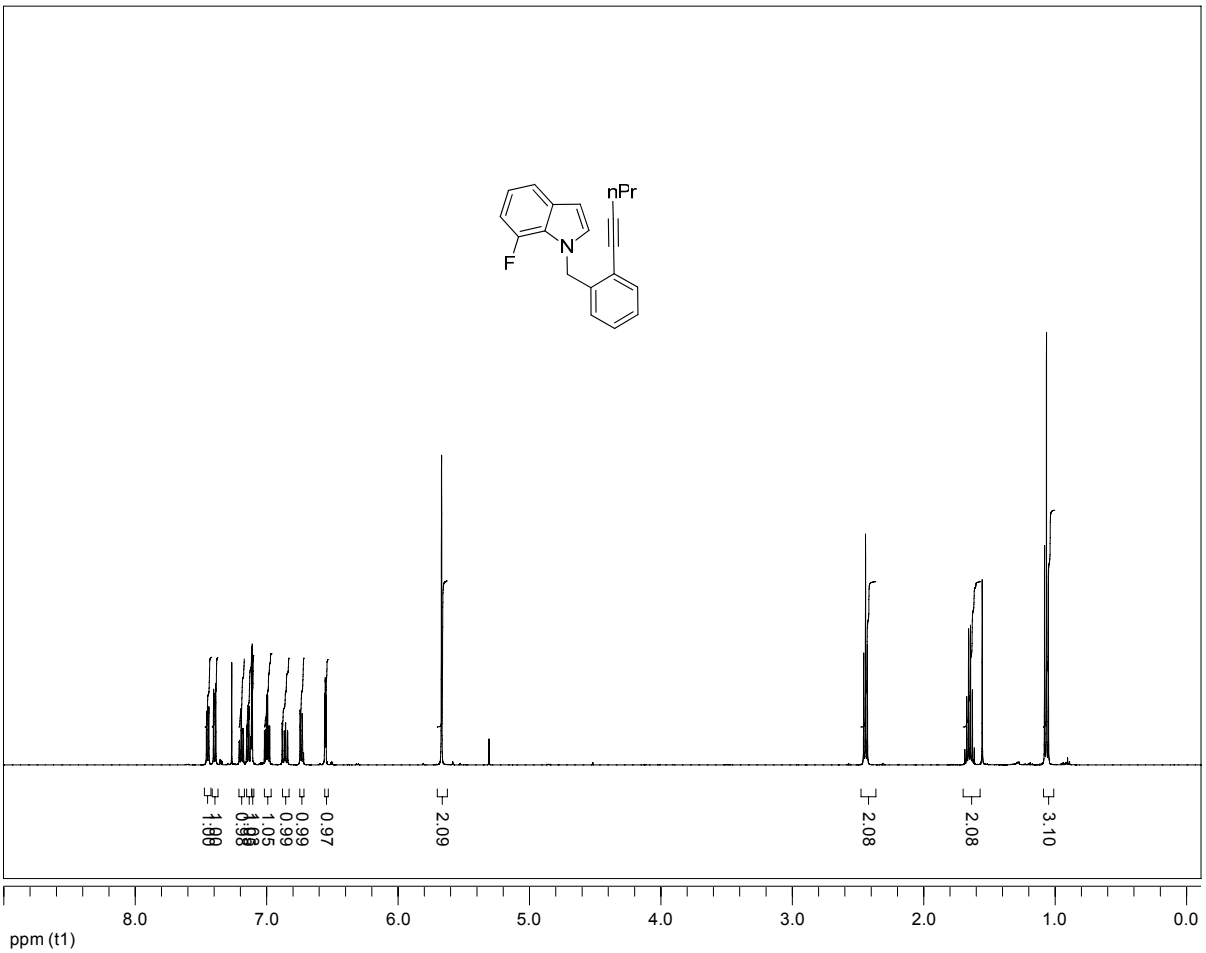


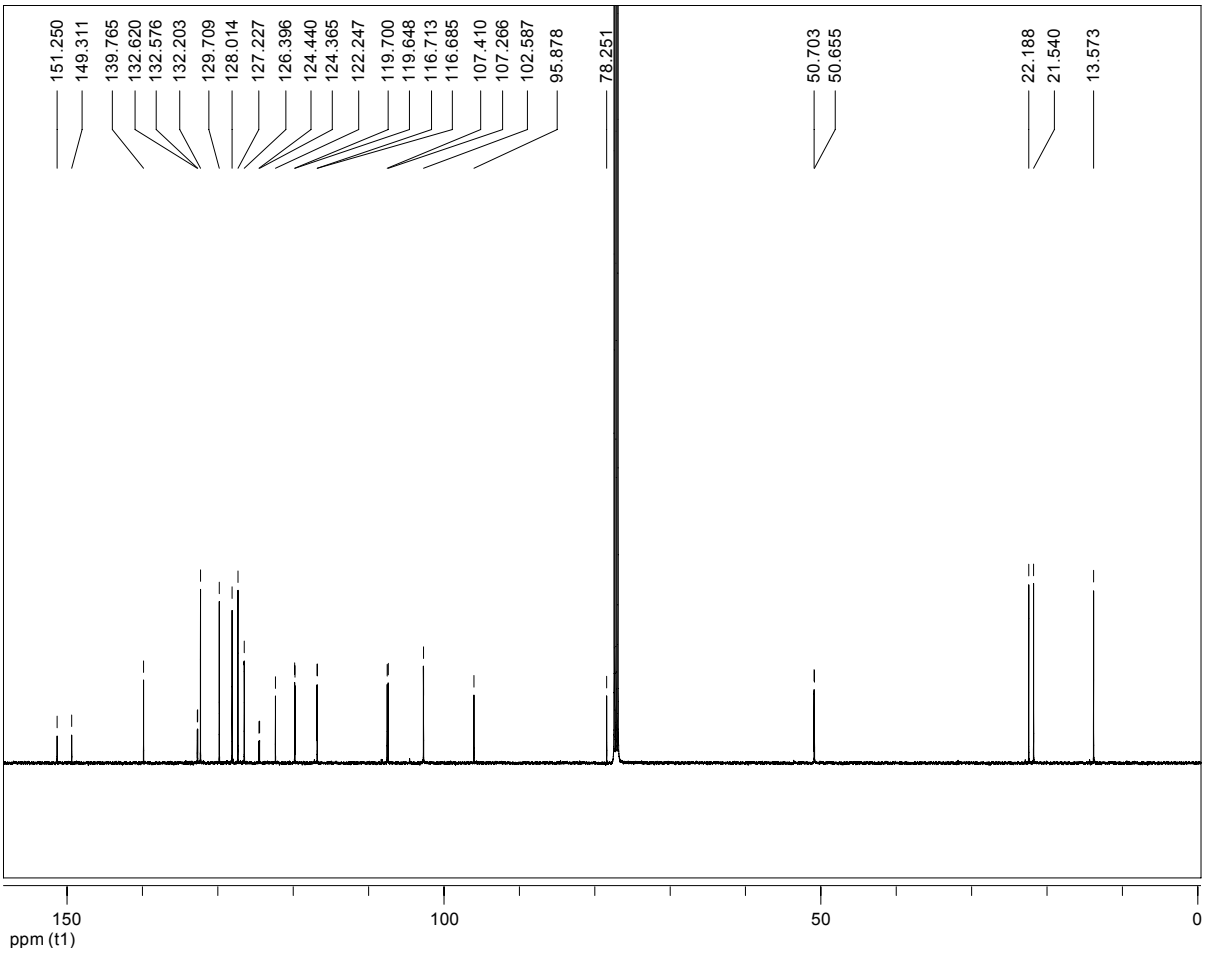


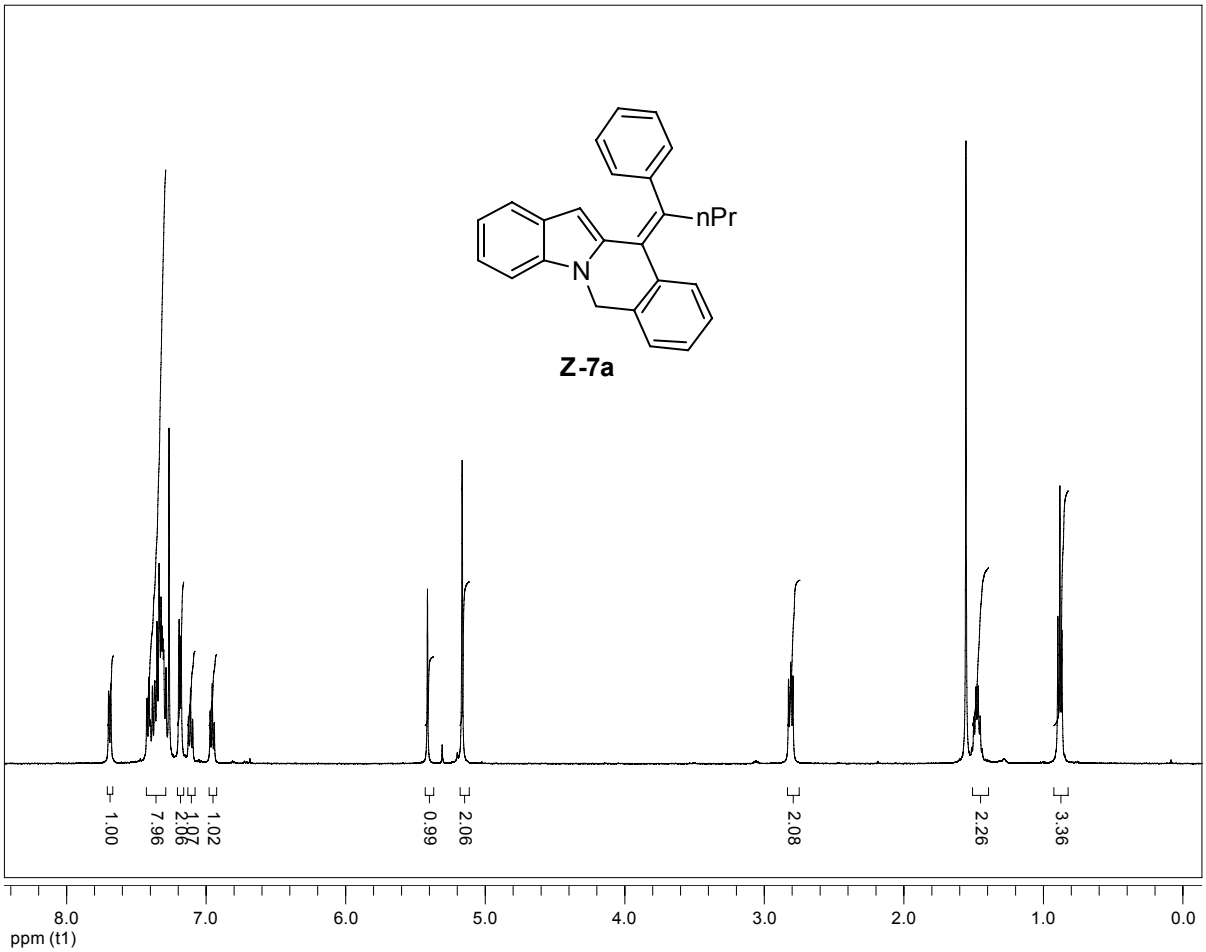


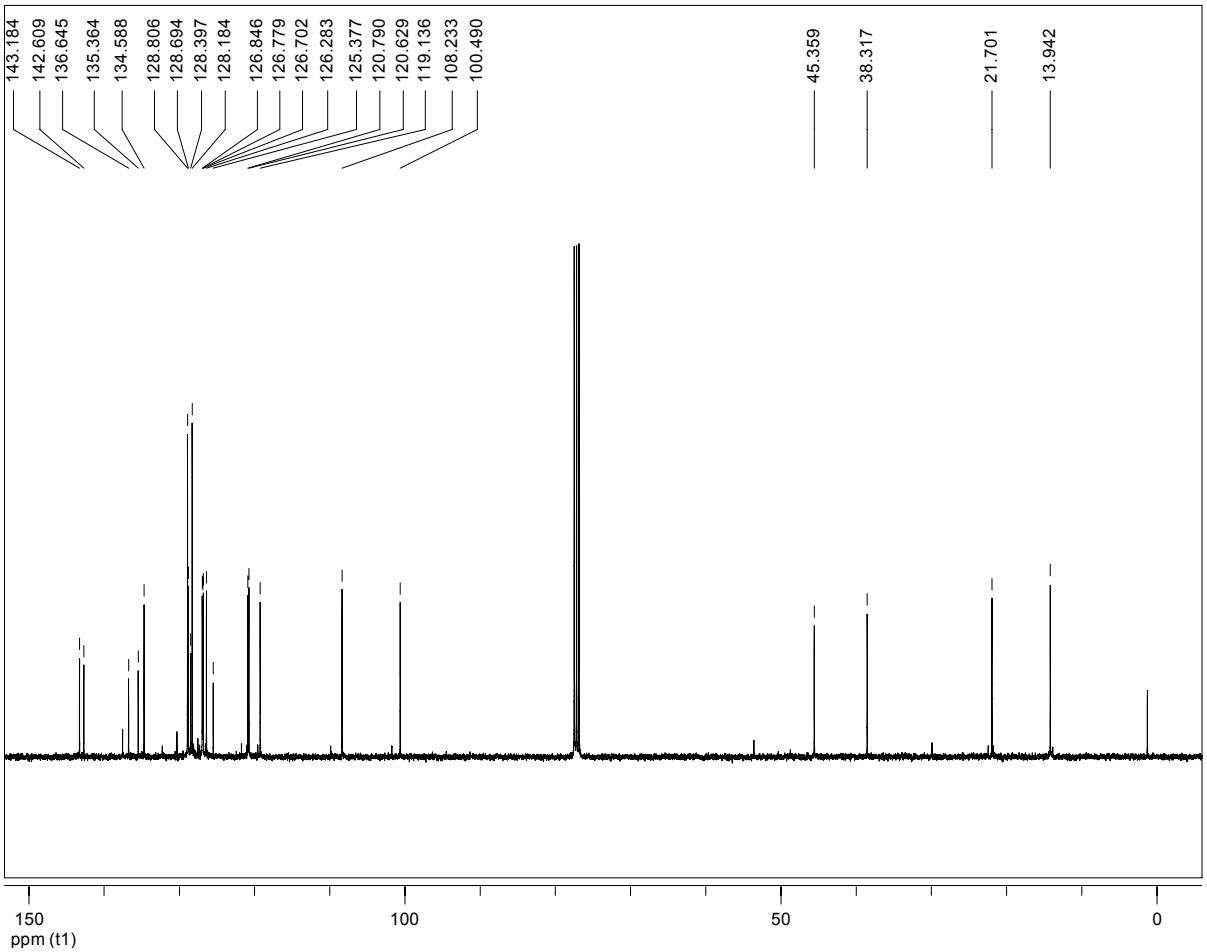

N
Me
nPr
5p
1.00
1.03
4.35
0.67
2.10
3.09
1.87
2.20
3.07
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

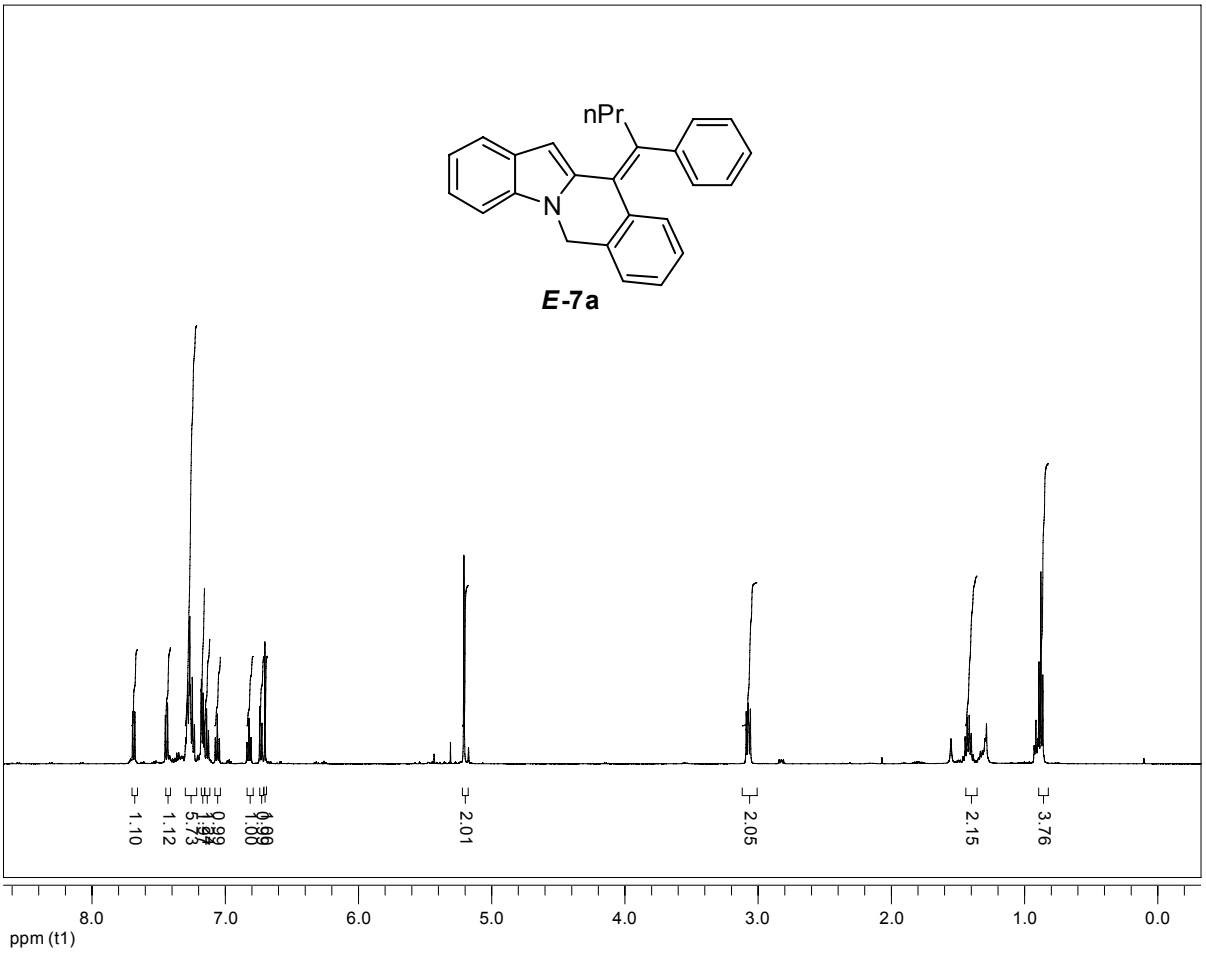

143.132
137.055
132.037
128.769
127.972
127.598
127.227
125.628
123.370
121.421
119.331
118.657
113.753
109.031
94.405
79.624
32.595
29.676
22.281
21.611
13.545
100
50
ppm (t1)

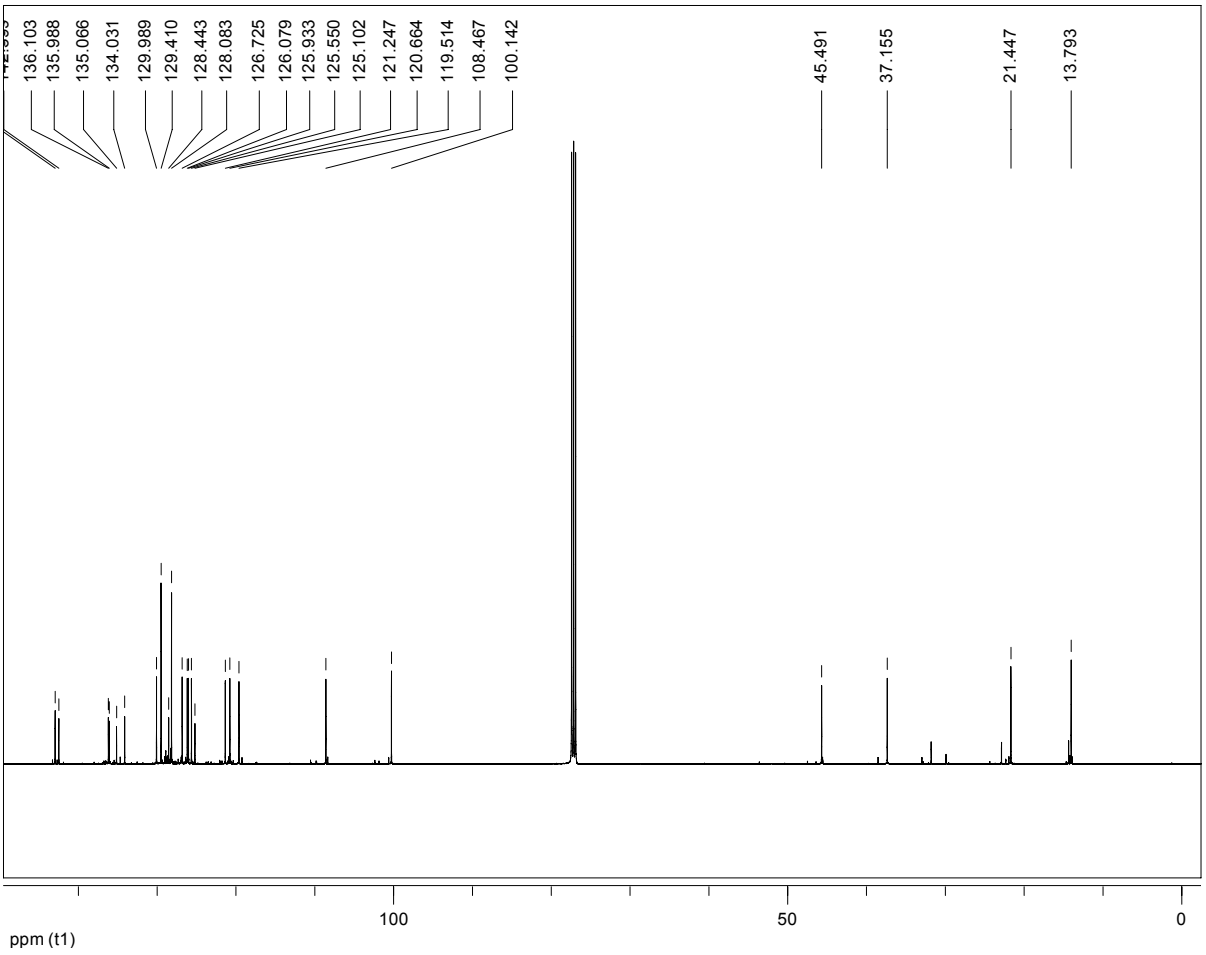

nPr
F
N
1.00
1.08
1.08
1.05
0.99
0.97
2.09
2.08
2.08
3.10
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

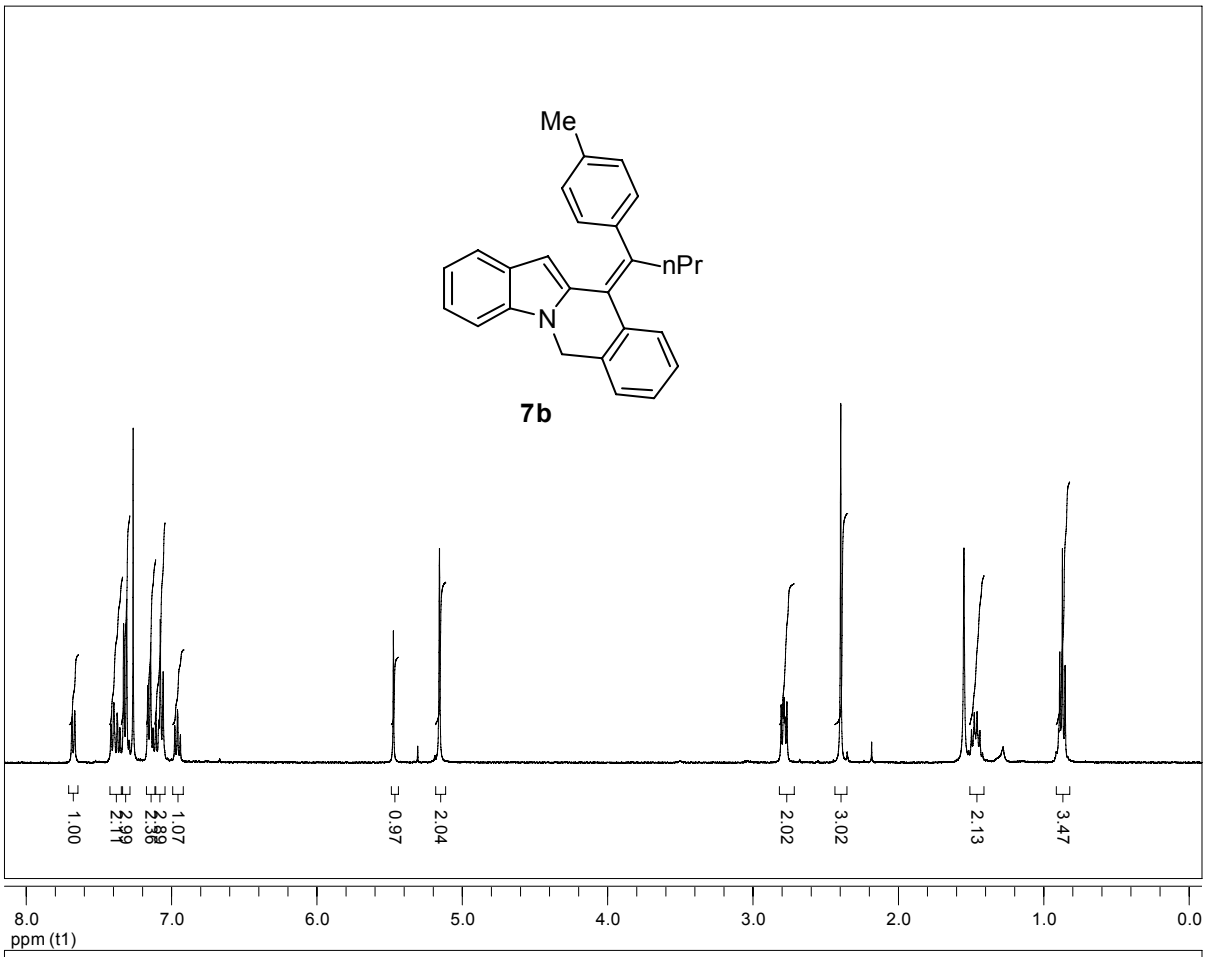

151.250
149.311
139.765
132.620
132.576
132.203
129.709
128.014
127.227
126.396
124.440
124.365
122.247
119.700
119.648
116.713
116.685
107.410
107.266
102.587
95.878
78.251
50.703
50.655
22.188
21.540
13.573
150
100
50
0
ppm (t1)

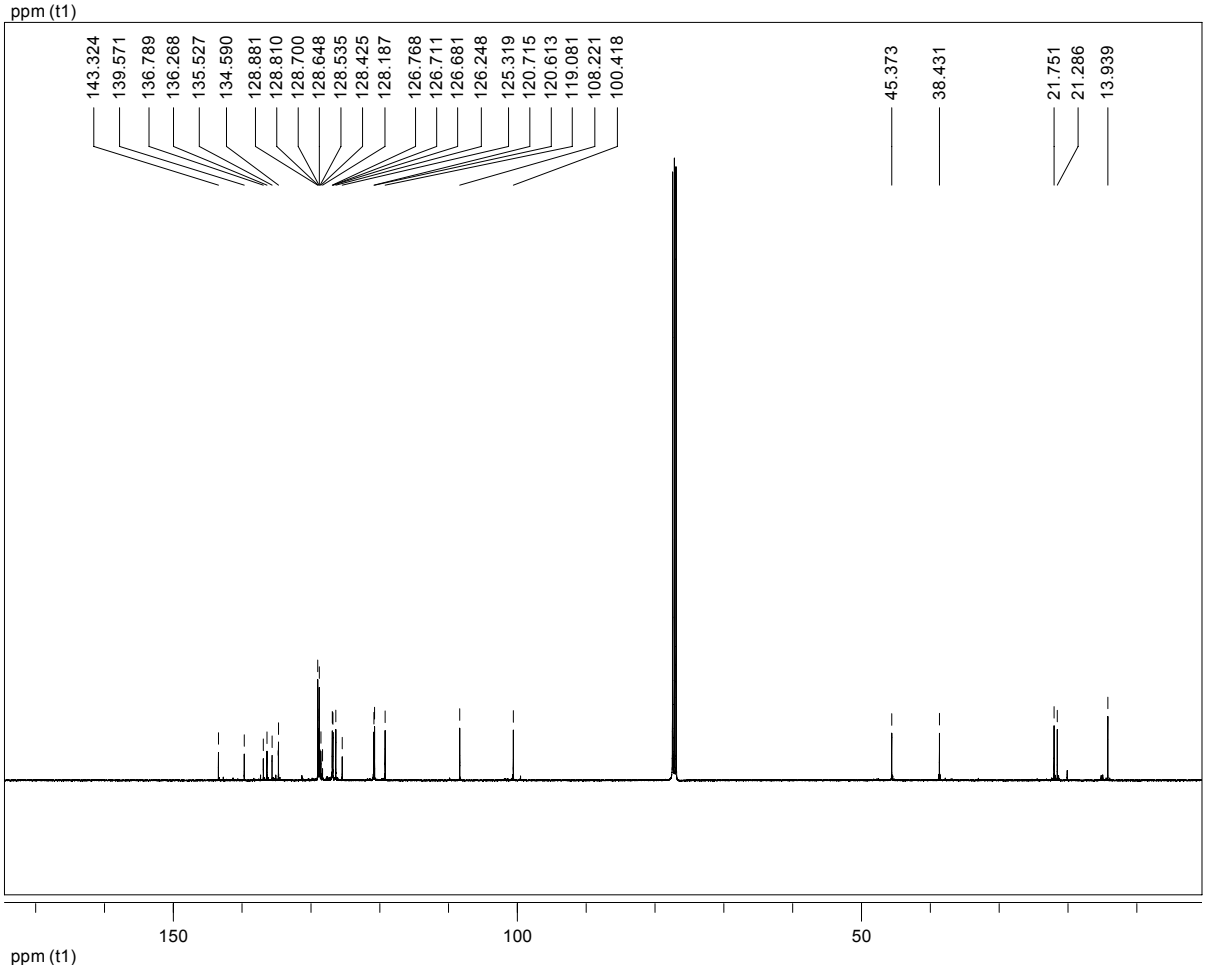

nPr
N
Z-7a
1.00
7.96
2.07
1.02
0.99
2.06
2.08
2.26
3.36
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

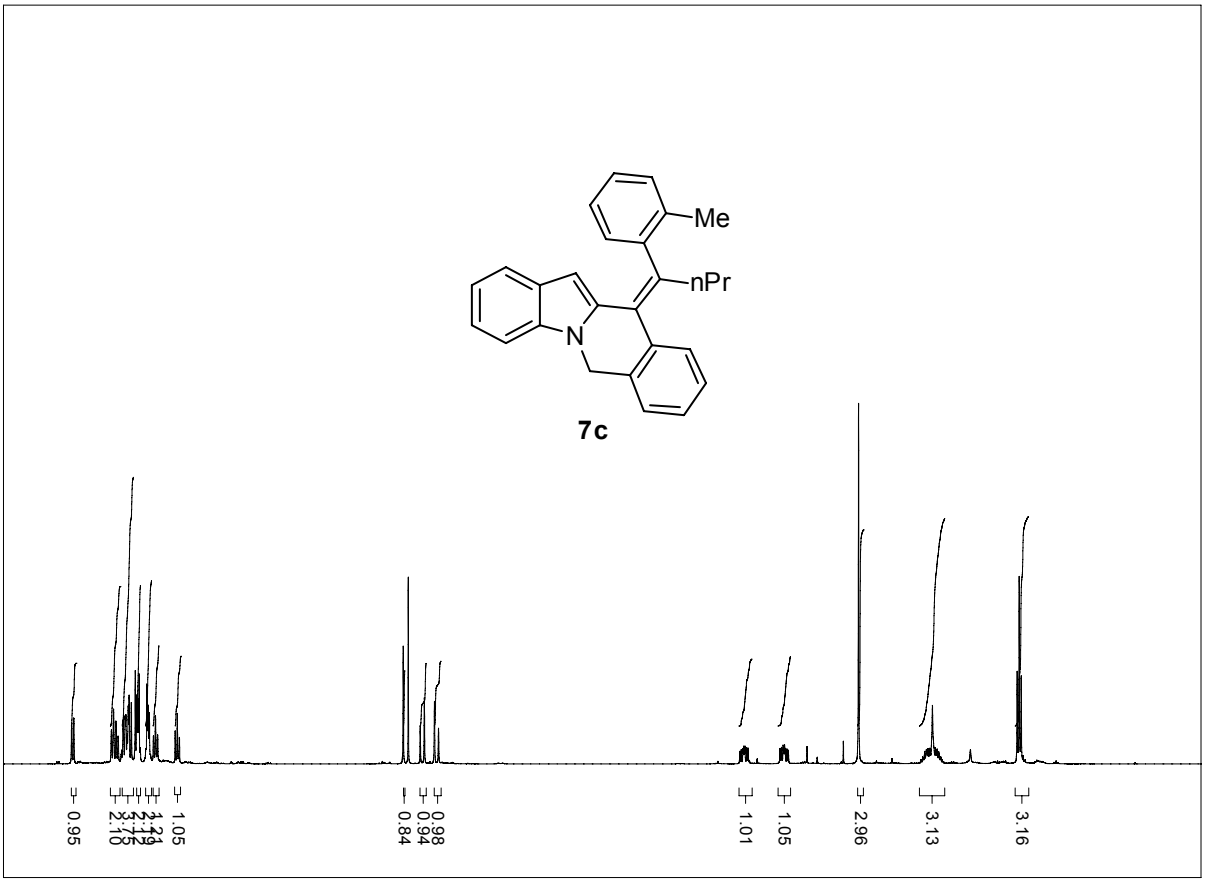

143.184
142.609
136.645
135.364
134.588
128.806
128.694
128.397
128.184
126.846
126.779
126.702
126.283
125.377
120.790
120.629
119.136
108.233
100.490
45.359
38.317
21.701
13.942
150
100
50
0
ppm (t1)

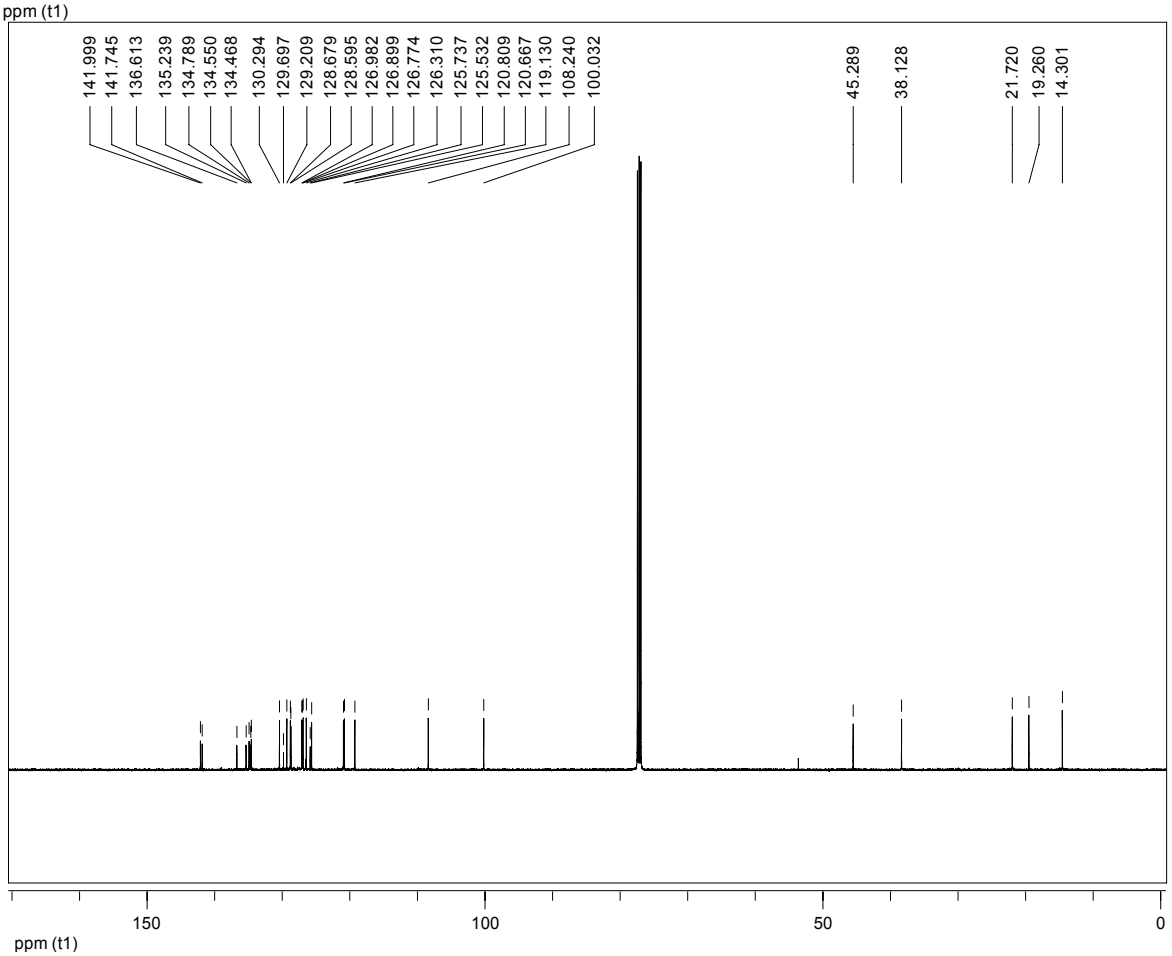

nPr
N
E-7a
1.10
1.12
5.73
2.01
2.05
2.15
3.76
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

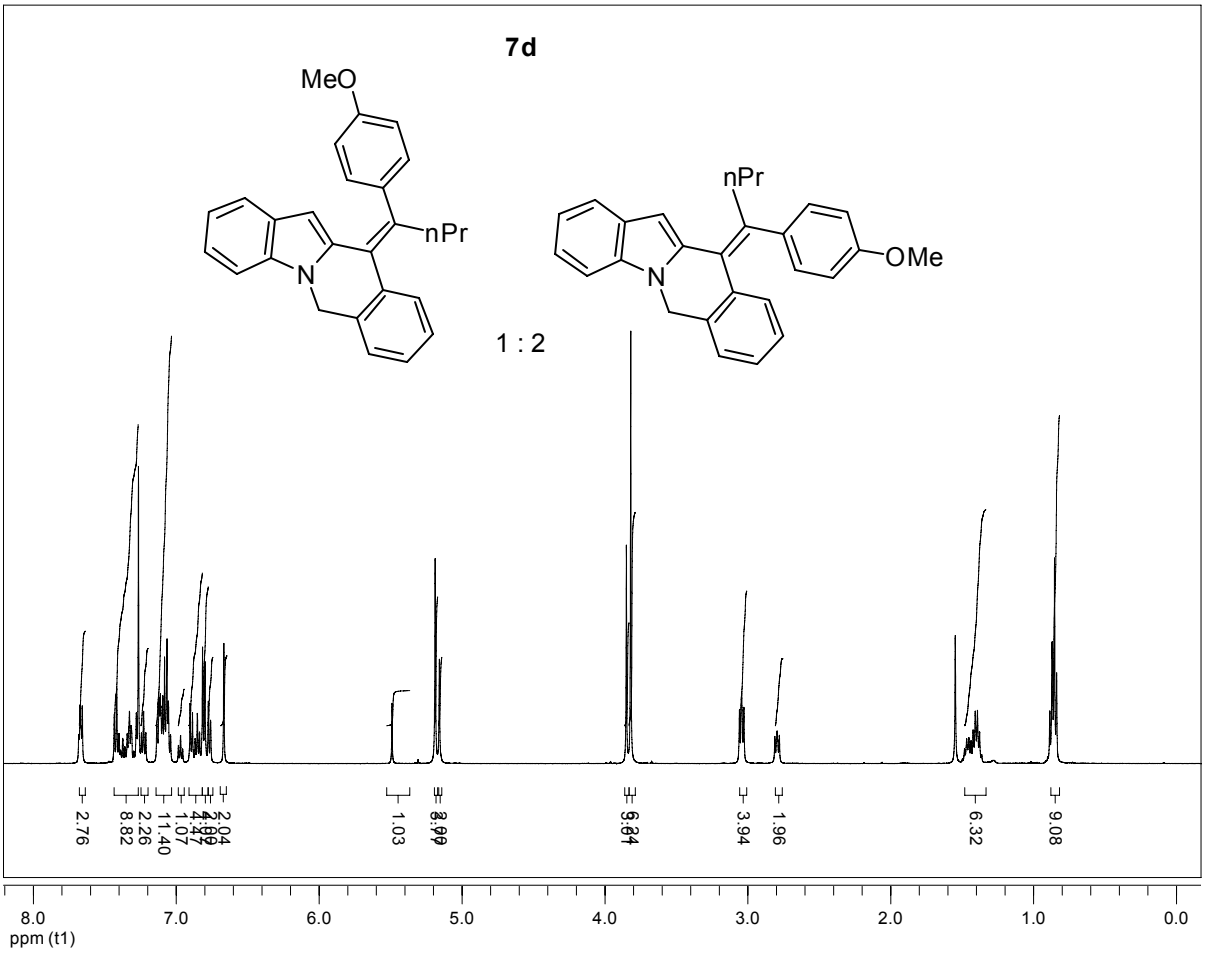

136.103
135.988
135.066
134.031
129.989
129.410
128.443
128.083
126.725
126.079
125.933
125.550
125.102
121.247
120.664
119.514
108.467
100.142
45.491
37.155
21.447
13.793
100
50
0
ppm (t1)

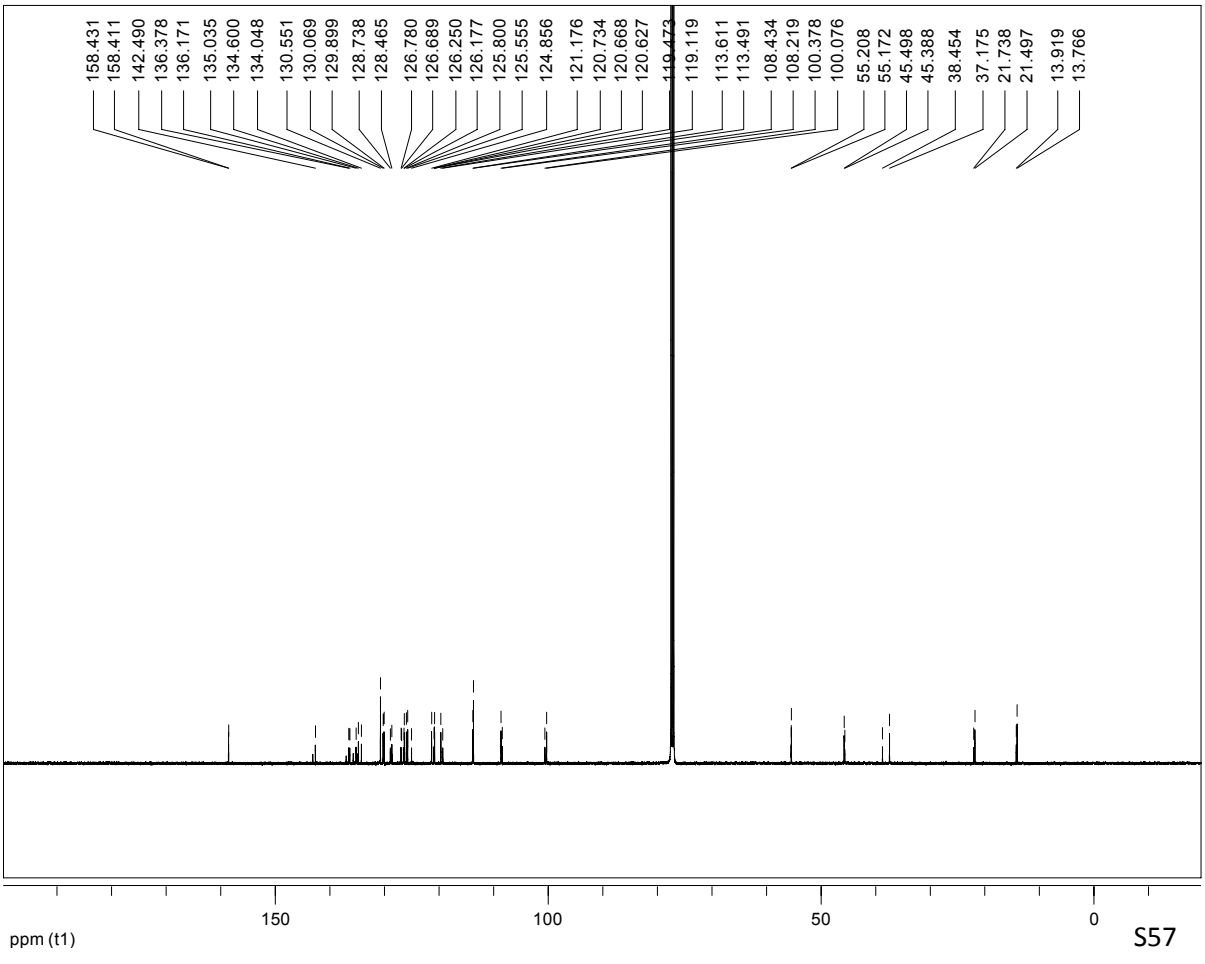


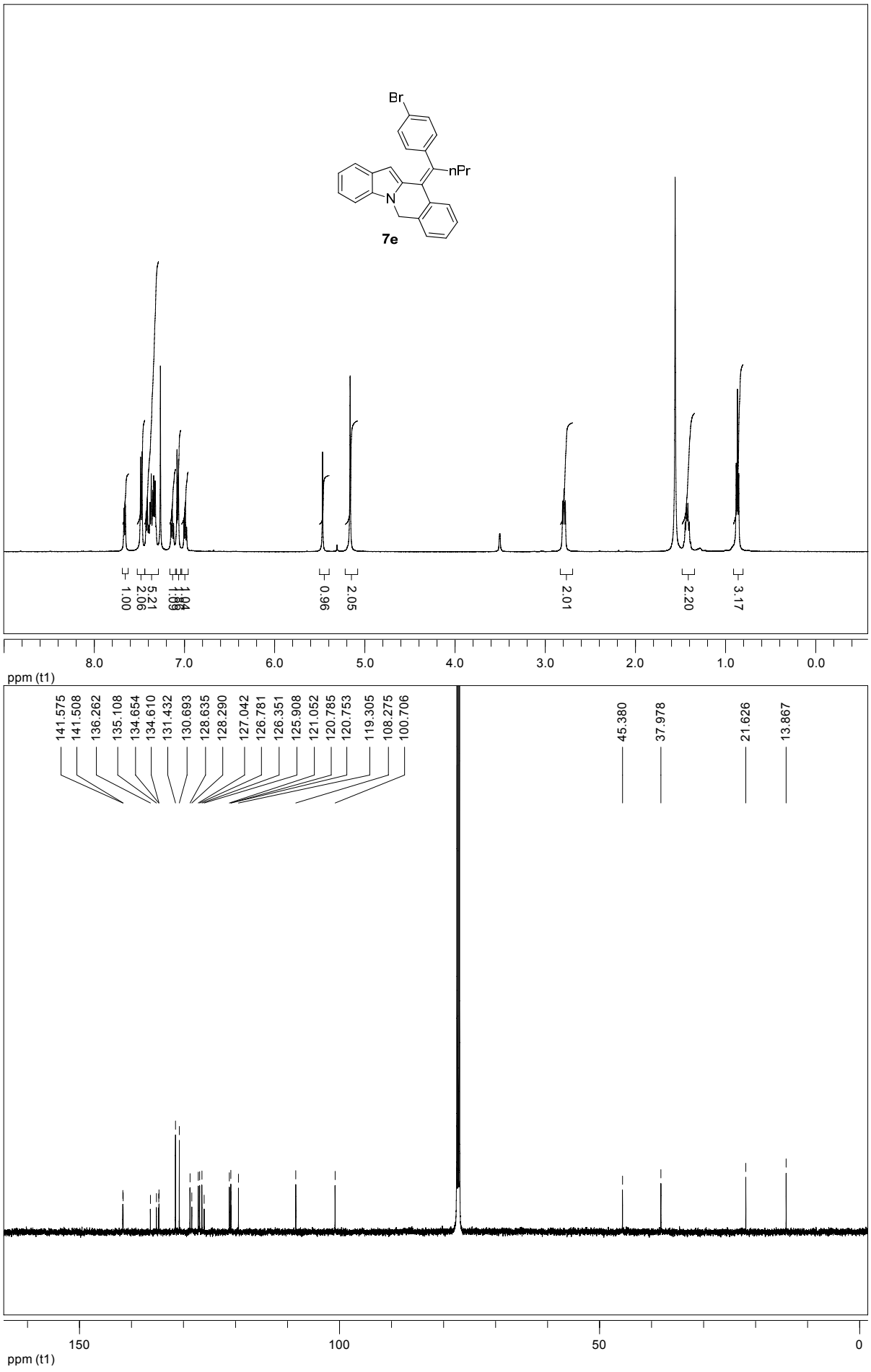


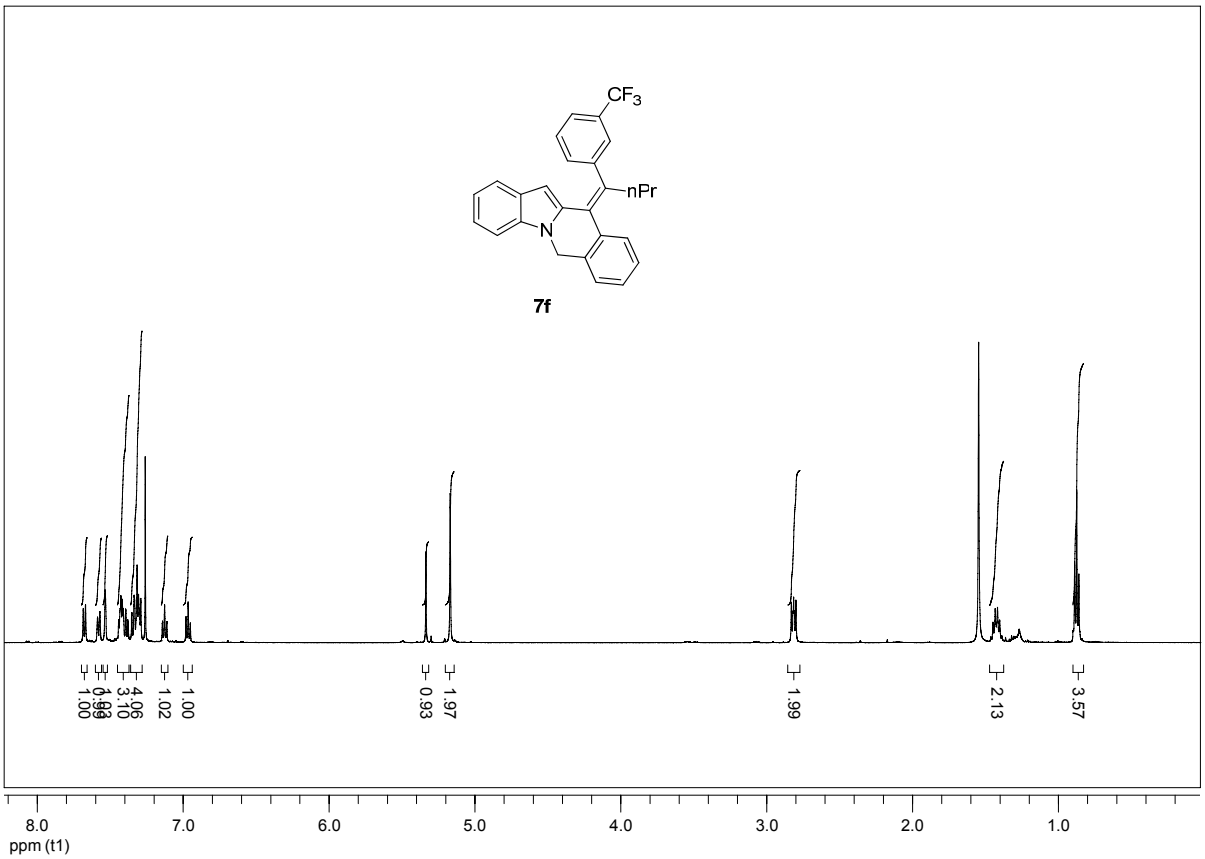

Me
nPr
N
7c
0.95
2.10
1.05
0.84
0.94
0.98
1.01
1.05
2.96
3.13
3.16
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

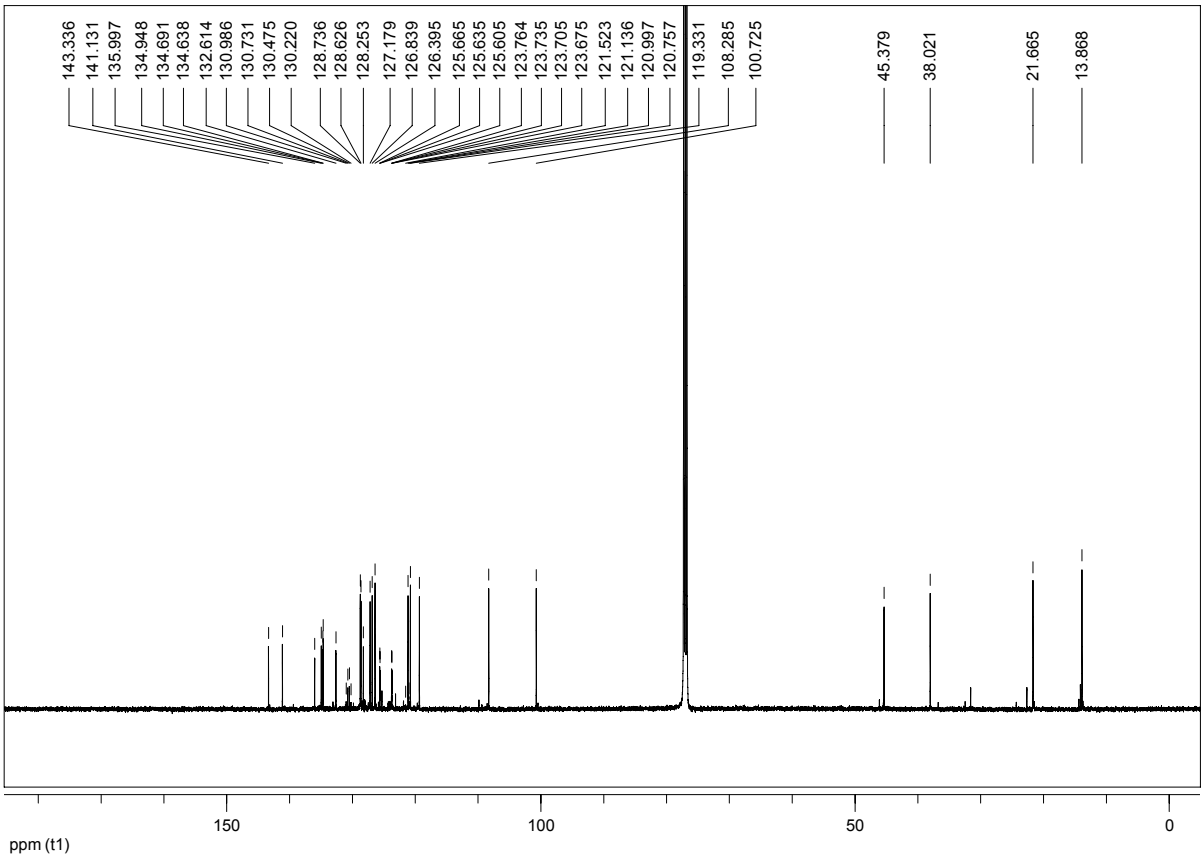

141.999
141.745
136.613
135.239
134.789
134.550
134.468
130.294
129.697
129.209
128.679
128.595
126.982
126.899
126.774
126.310
125.737
125.532
120.809
120.667
119.130
108.240
100.032
45.289
38.128
21.720
19.260
14.301
150
100
50
0
ppm (t1)

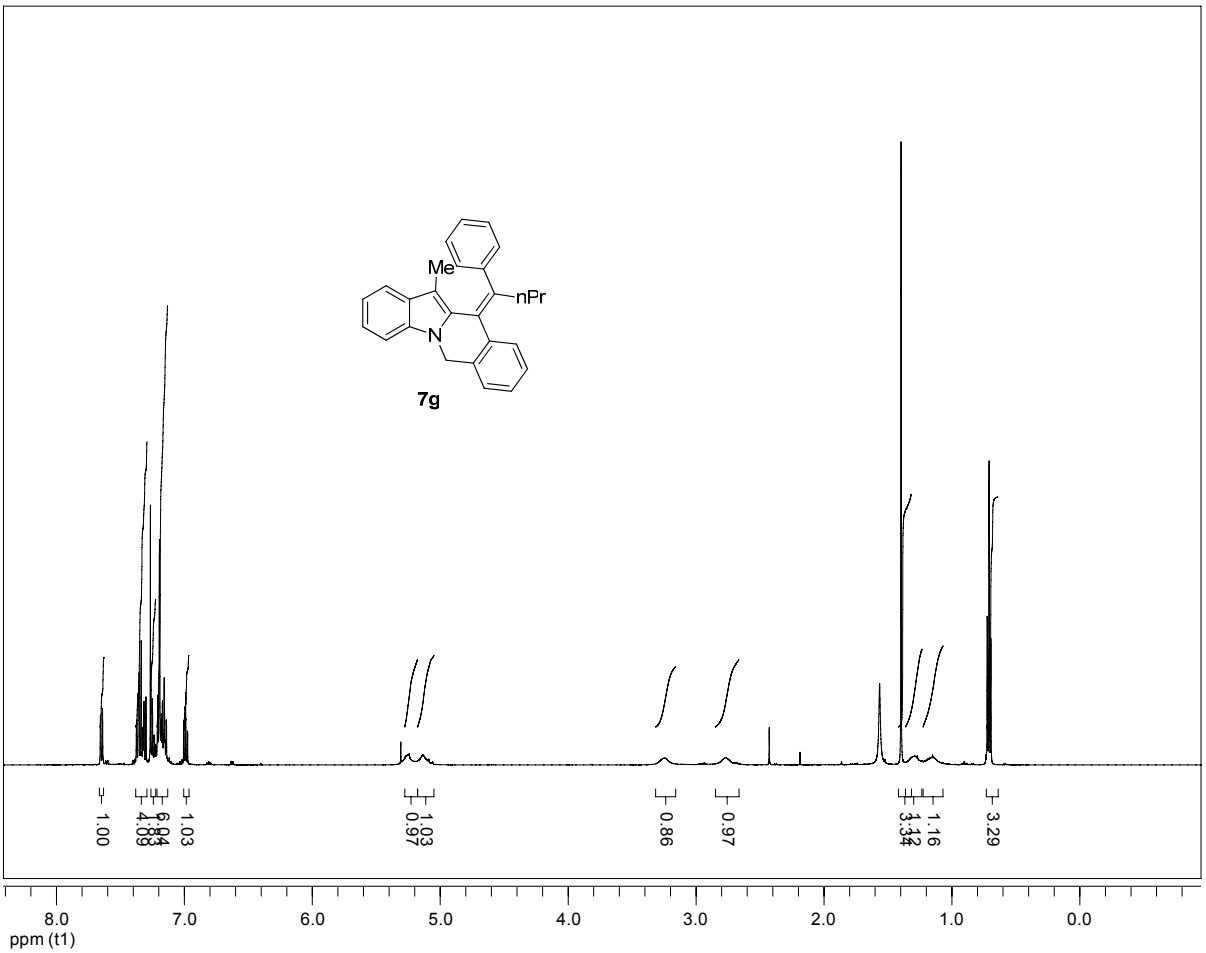

7d
MeO
nPr
N
nPr
OMe
N
1 : 2
2.76
8.82
2.26
11.40
1.07
2.04
1.03
6.04
3.94
1.96
6.32
9.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

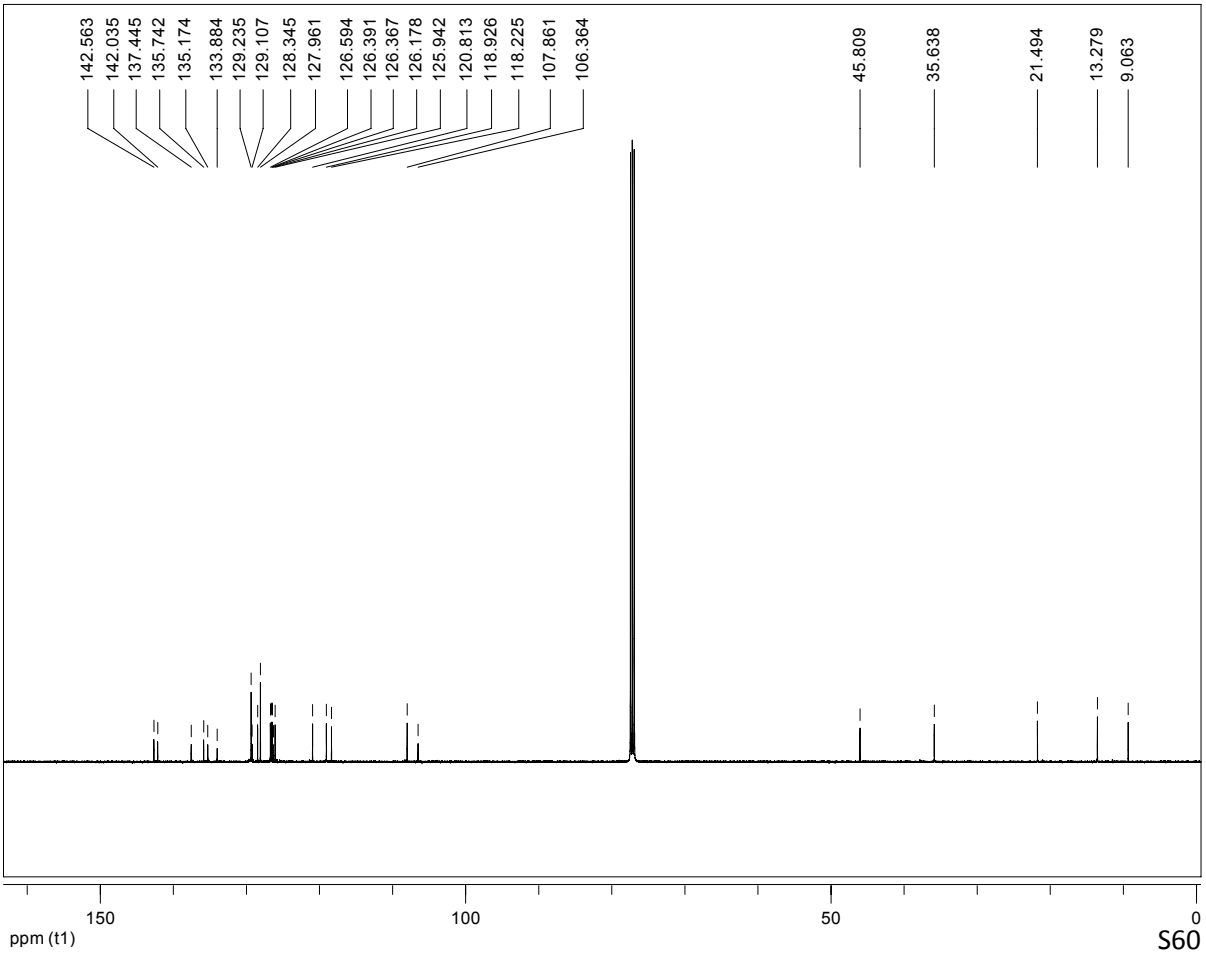

158.431
158.411
142.490
136.378
136.171
135.035
134.600
134.048
130.551
130.069
129.899
128.738
128.465
126.780
126.689
126.250
126.177
125.800
125.555
124.856
121.176
120.734
120.668
120.627
119.473
119.119
113.611
113.491
108.434
108.219
100.378
100.076
55.208
55.172
45.498
45.388
38.454
37.175
21.738
21.497
13.919
13.766
150
100
50
0
ppm (t1)

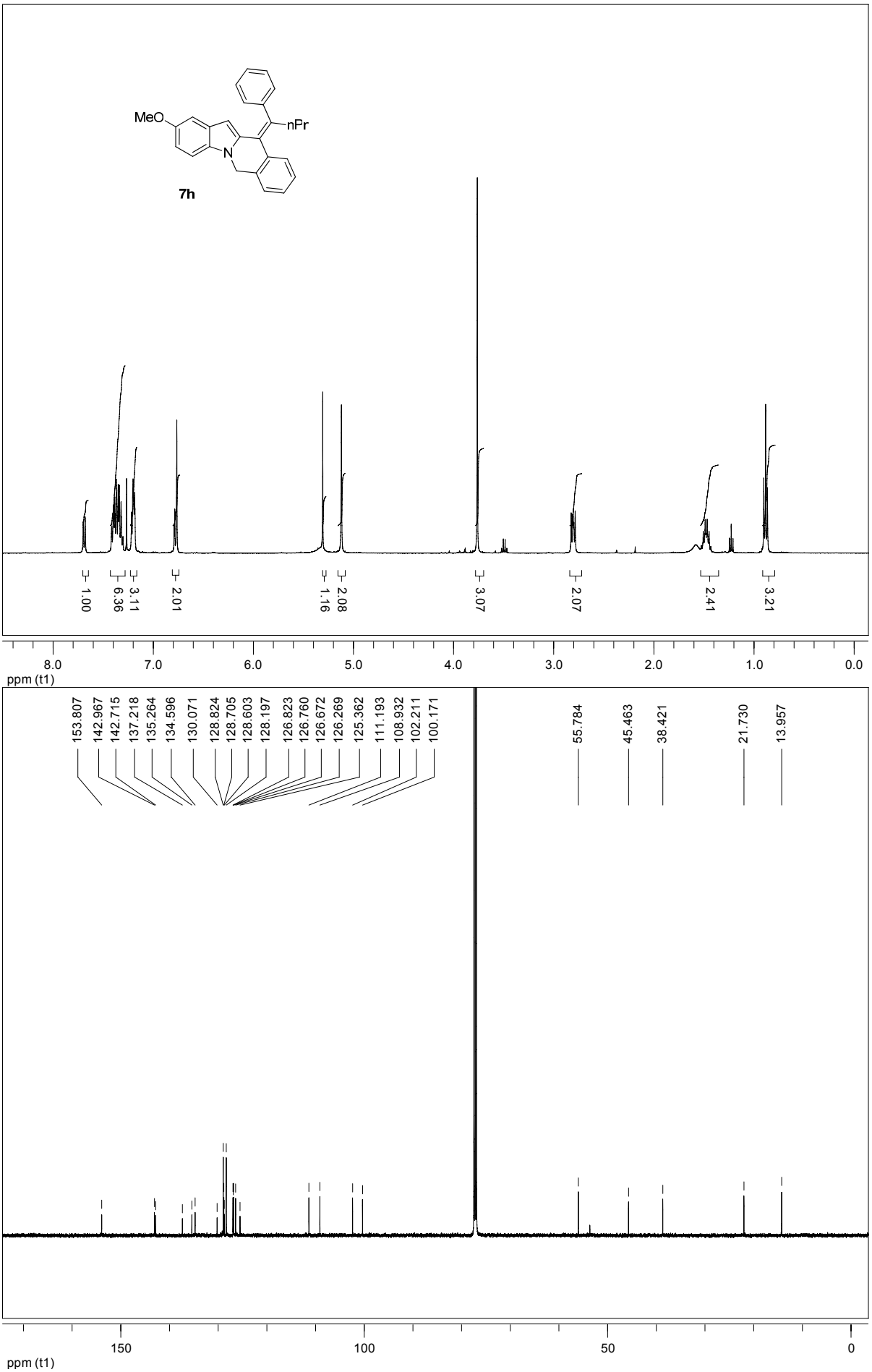

Br
nPr
N
7e
1.00
2.06
5.21
0.96
2.05
2.01
2.20
3.17
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
141.575
141.508
136.262
135.108
134.654
134.610
131.432
130.693
128.635
128.290
127.042
126.781
126.351
125.908
121.052
120.785
120.753
119.305
108.275
100.706
45.380
37.978
21.626
13.867
150
100
50
0
ppm (t1)

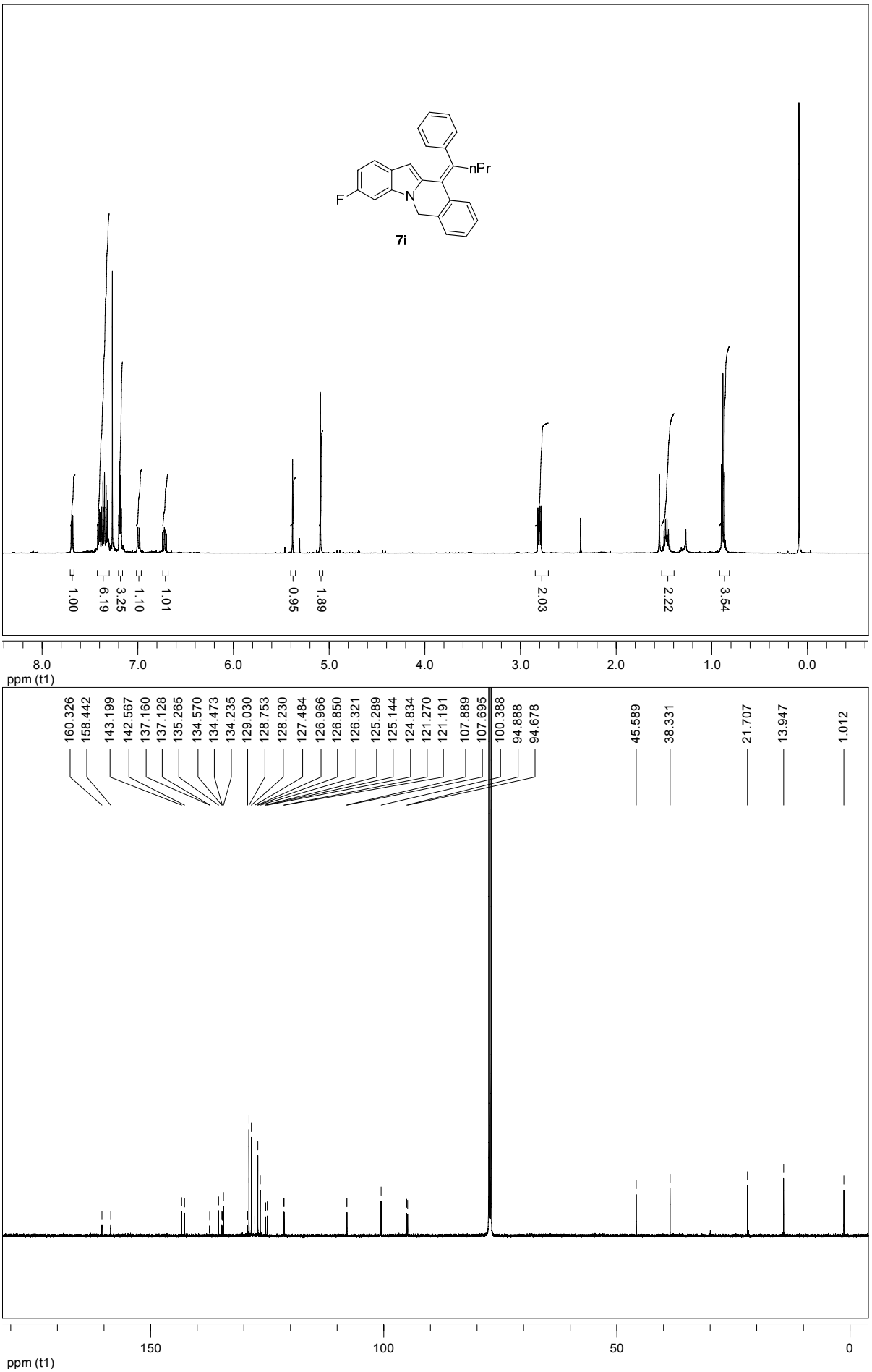

CF3
nPr
N
7f
1.00
0.93
3.10
4.06
1.02
1.00
0.93
1.97
1.99
2.13
3.57
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

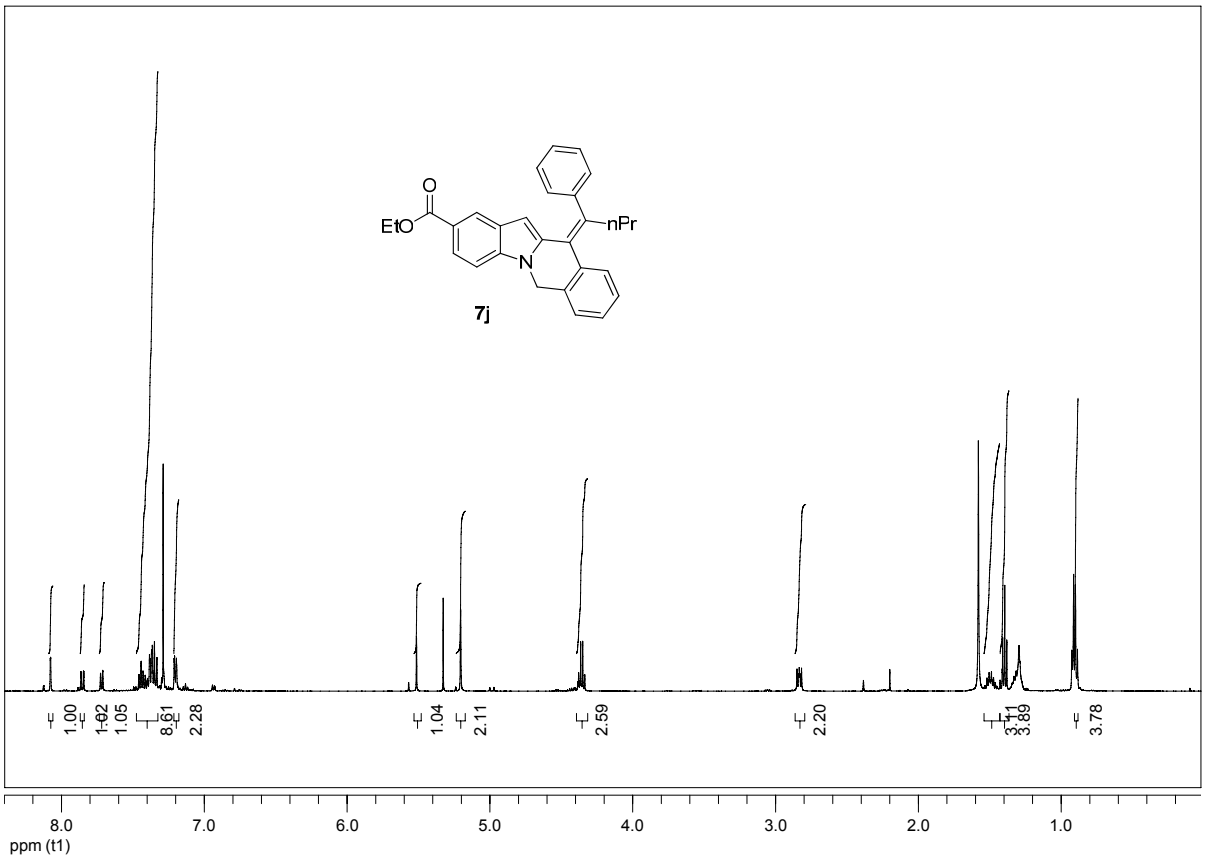

143.336
141.131
135.997
134.948
134.691
134.638
132.614
130.986
130.731
130.475
130.220
128.736
128.626
128.253
127.179
126.839
126.395
125.665
125.635
125.605
123.764
123.735
123.705
123.675
121.523
121.136
120.997
120.757
119.331
108.285
100.725
45.379
38.021
21.665
13.868
150
100
50
0
ppm (t1)

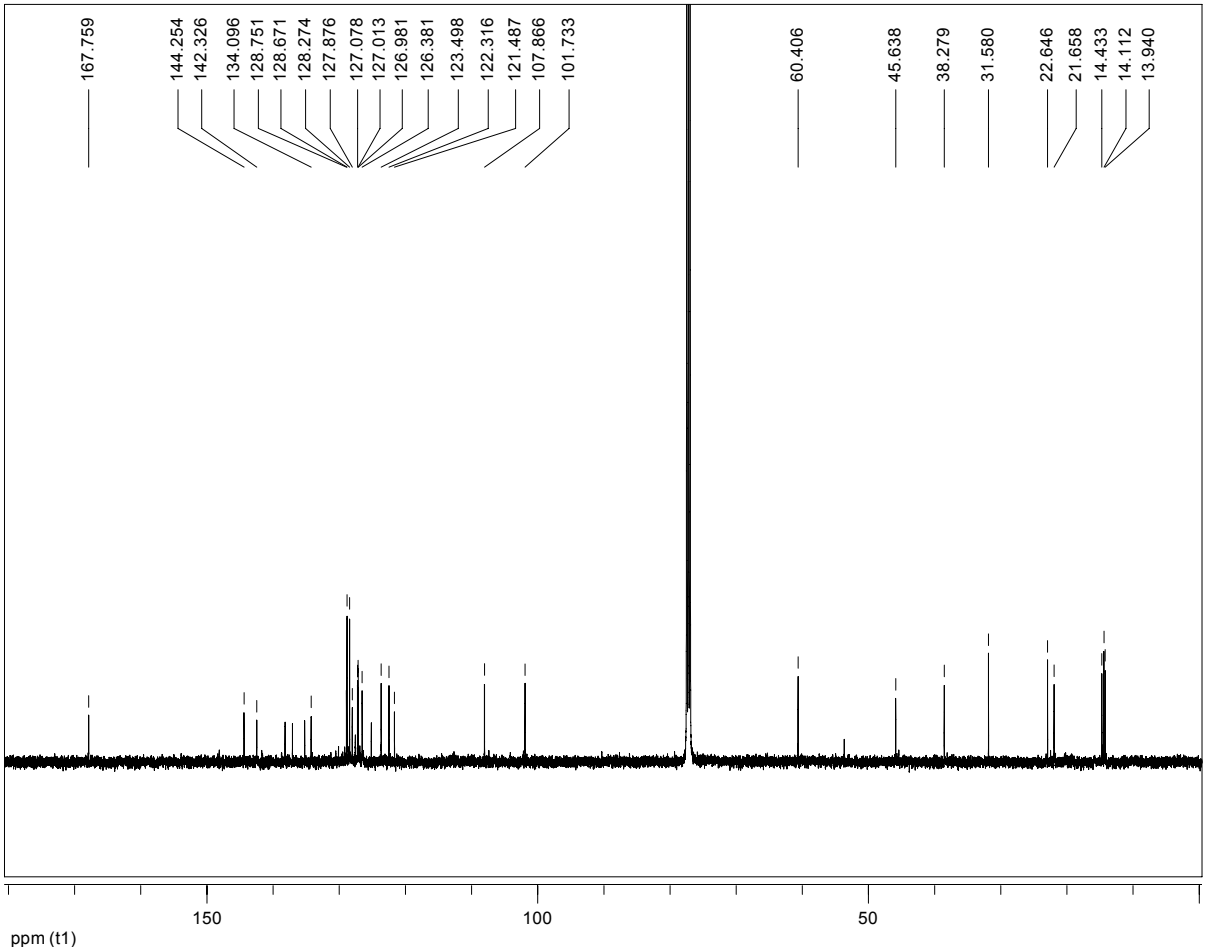


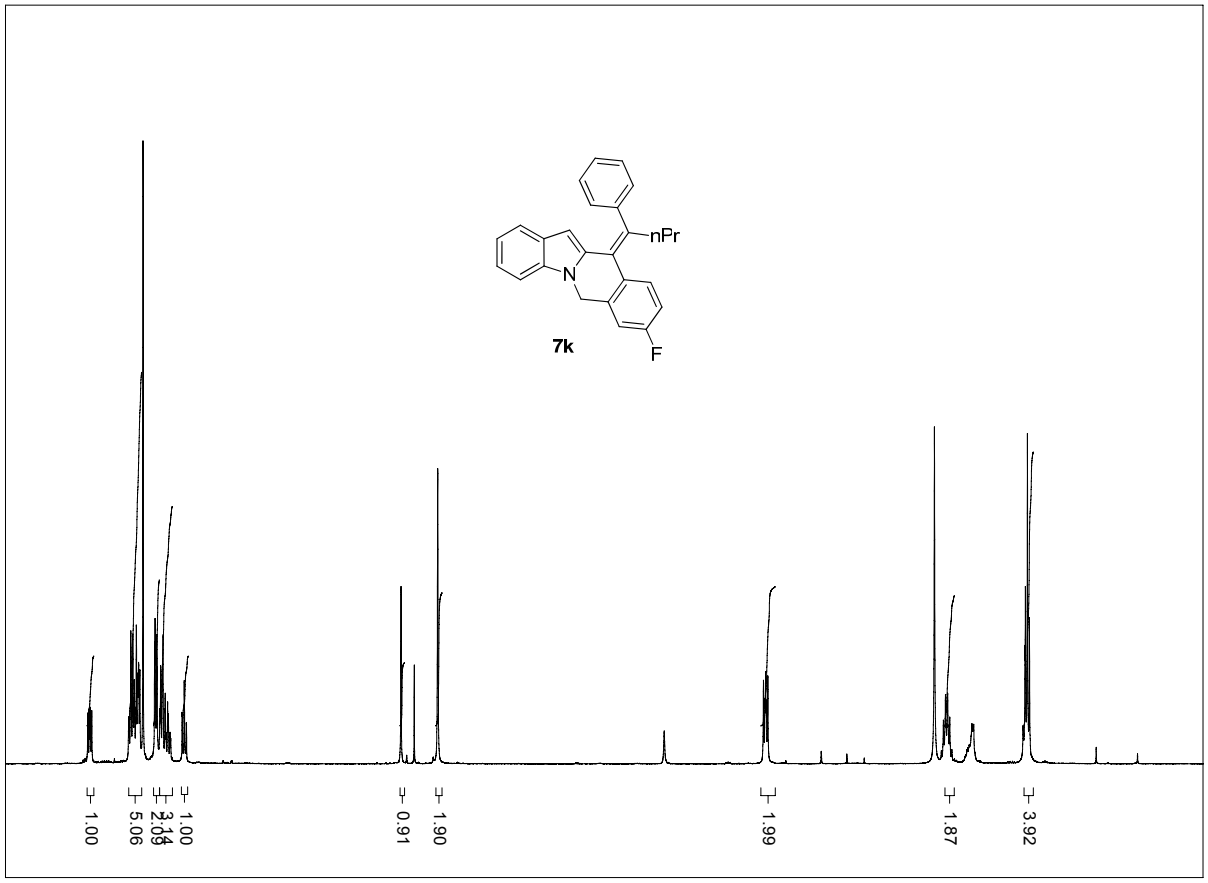


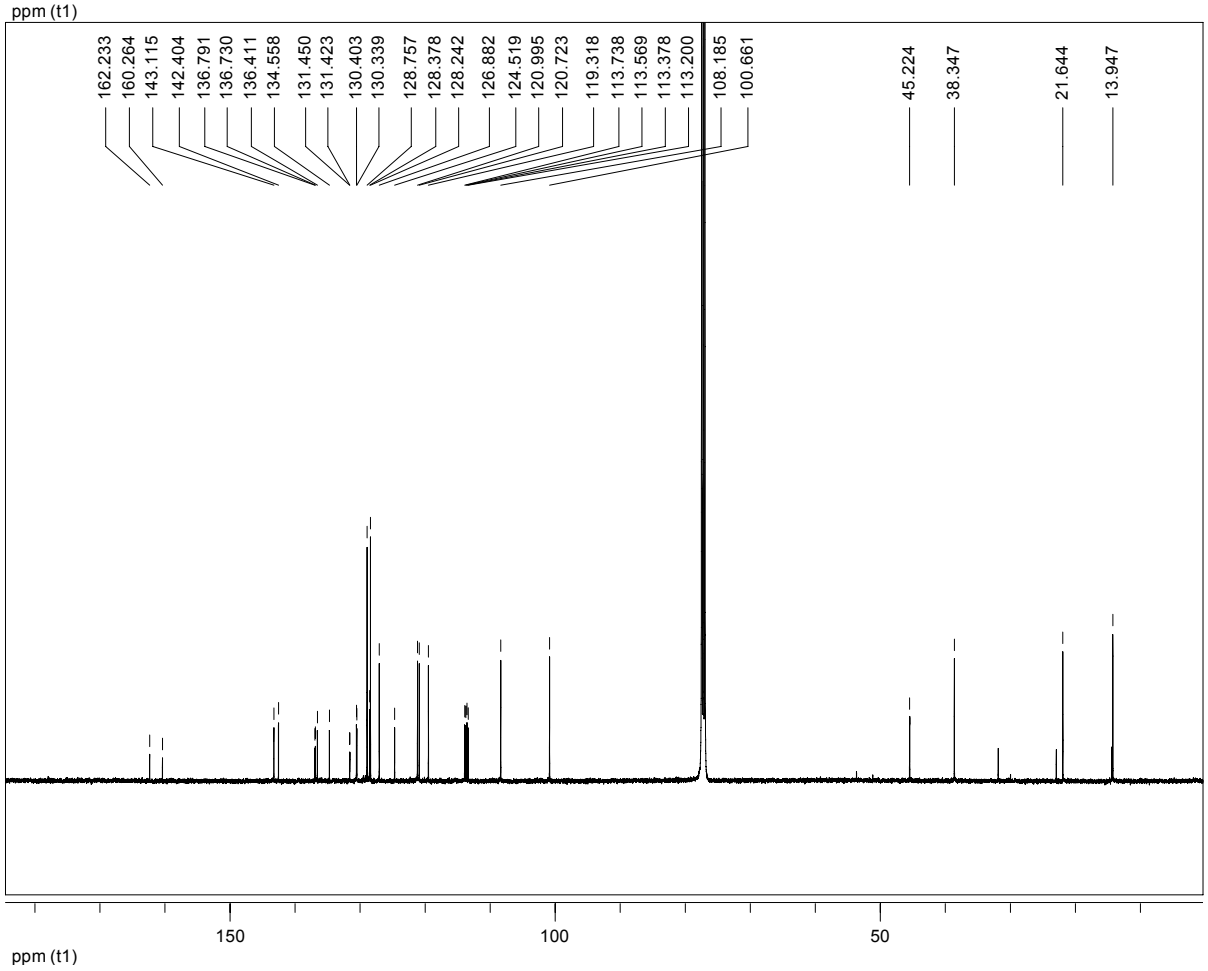

MeO
nPr
N
7h
1.00
6.36
3.11
2.01
1.16
2.08
3.07
2.07
2.41
3.21
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
153.807
142.967
142.715
137.218
135.264
134.596
130.071
128.824
128.705
128.603
128.197
126.823
126.760
126.672
126.269
125.362
111.193
108.932
102.211
100.171
55.784
45.463
38.421
21.730
13.957
150
100
50
0
ppm (t1)

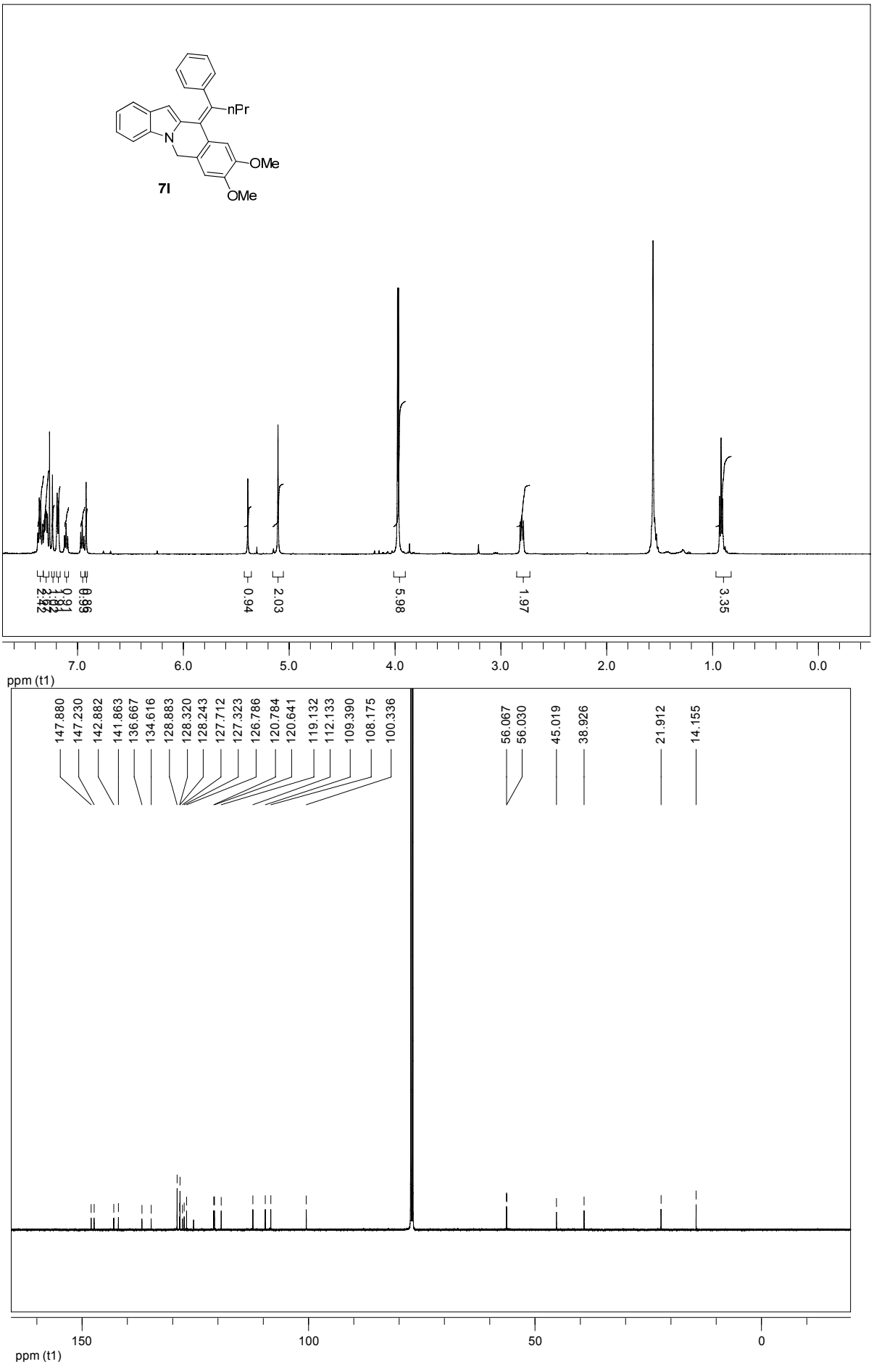

nPr
F
N
7i
1.00
6.19
3.25
1.10
1.01
0.95
1.89
2.03
2.22
3.54
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
160.326
158.442
143.199
142.567
137.160
137.128
135.265
134.570
134.473
134.235
129.030
128.753
128.230
127.484
126.966
126.850
126.321
125.289
125.144
124.834
121.270
121.191
107.889
107.695
100.388
94.888
94.678
45.589
38.331
21.707
13.947
1.012
150
100
50
0
ppm (t1)

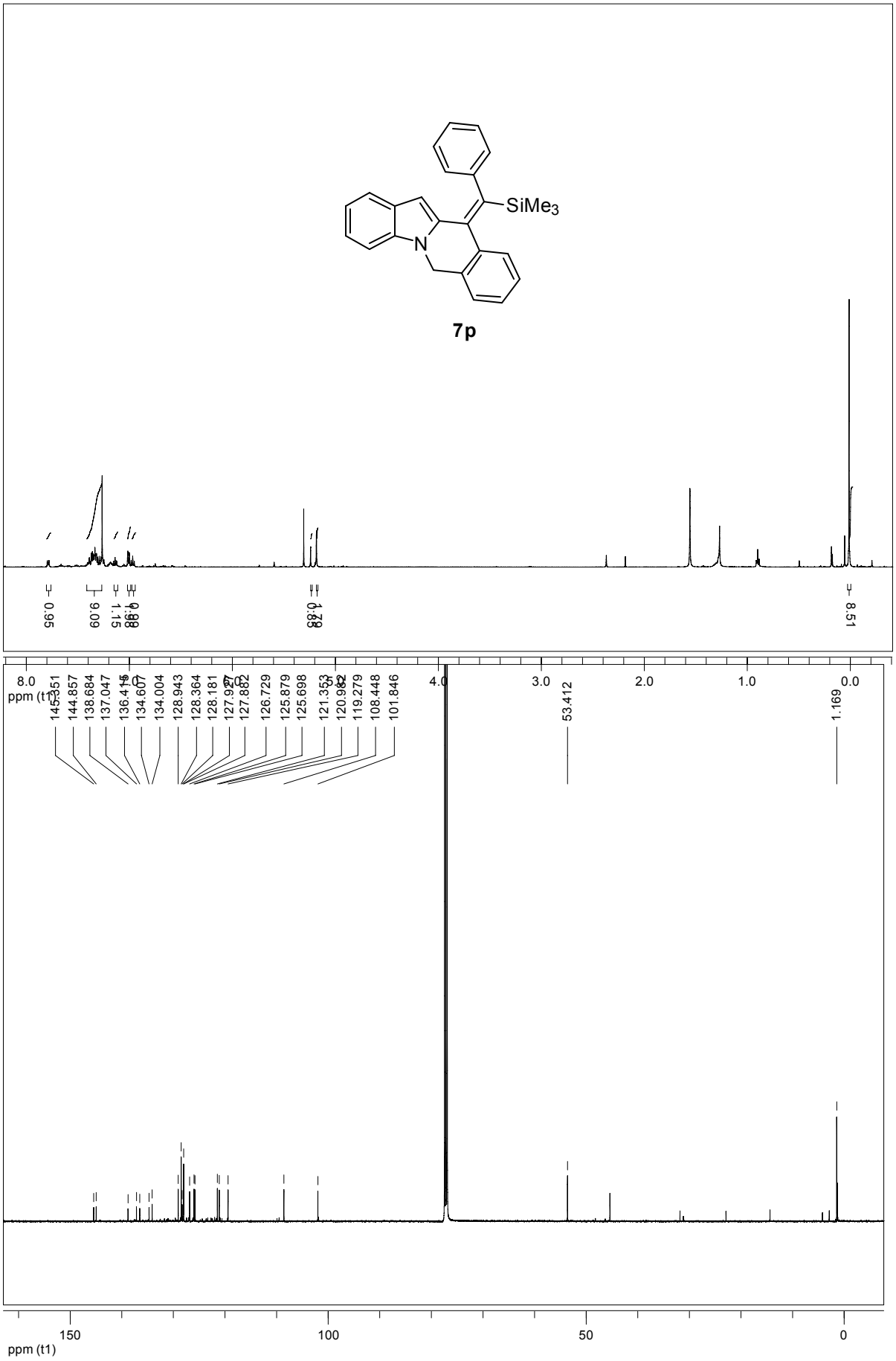

O
EtO
nPr
N
7j
1.00
1.02
1.05
8.61
2.28
1.04
2.11
2.59
2.20
3.11
3.89
3.78
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

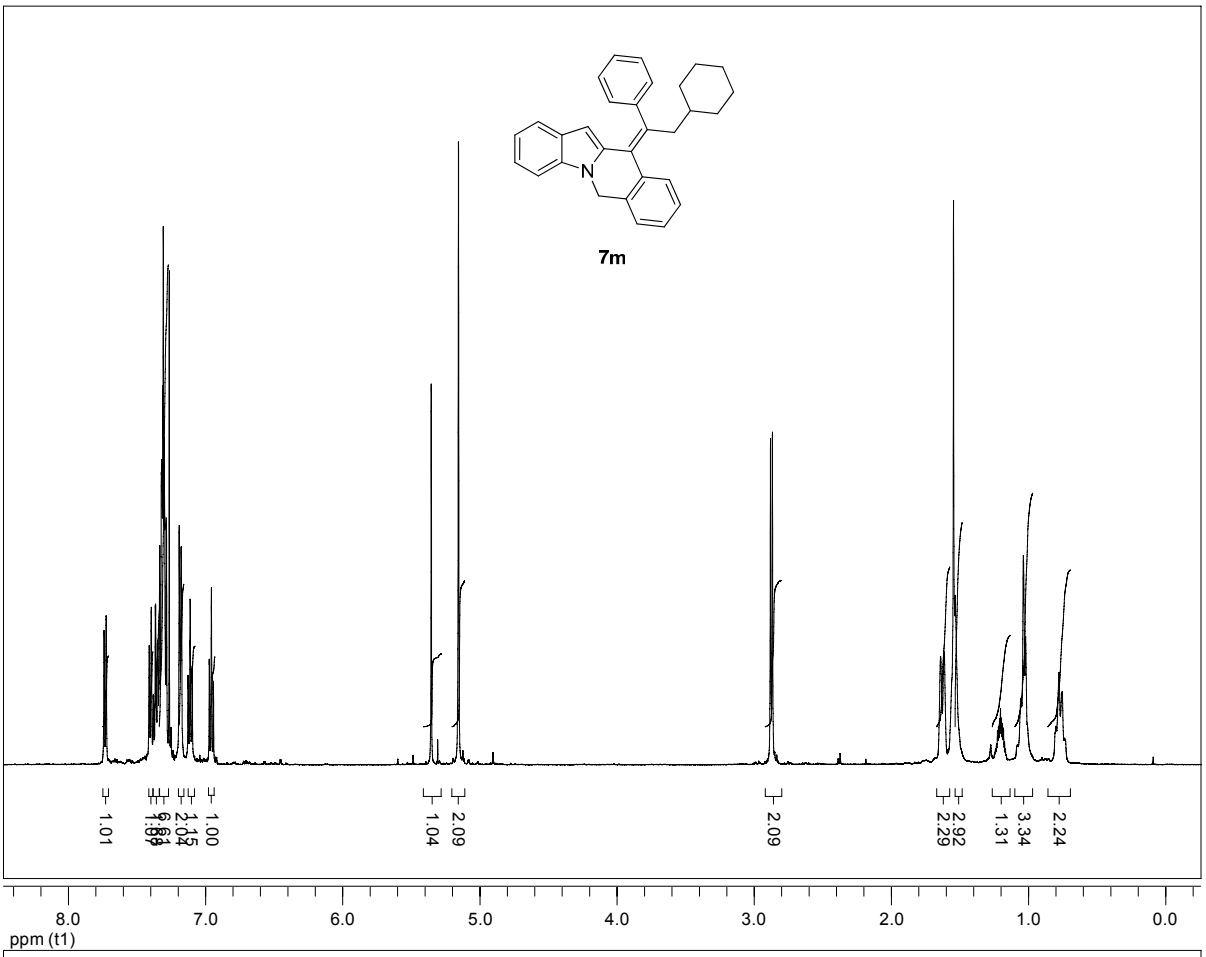

167.759
144.254
142.326
134.096
128.751
128.671
128.274
127.876
127.078
127.013
126.981
126.381
123.498
122.316
121.487
107.866
101.733
60.406
45.638
38.279
31.580
22.646
21.658
14.433
14.112
13.940
150
100
50
ppm (t1)

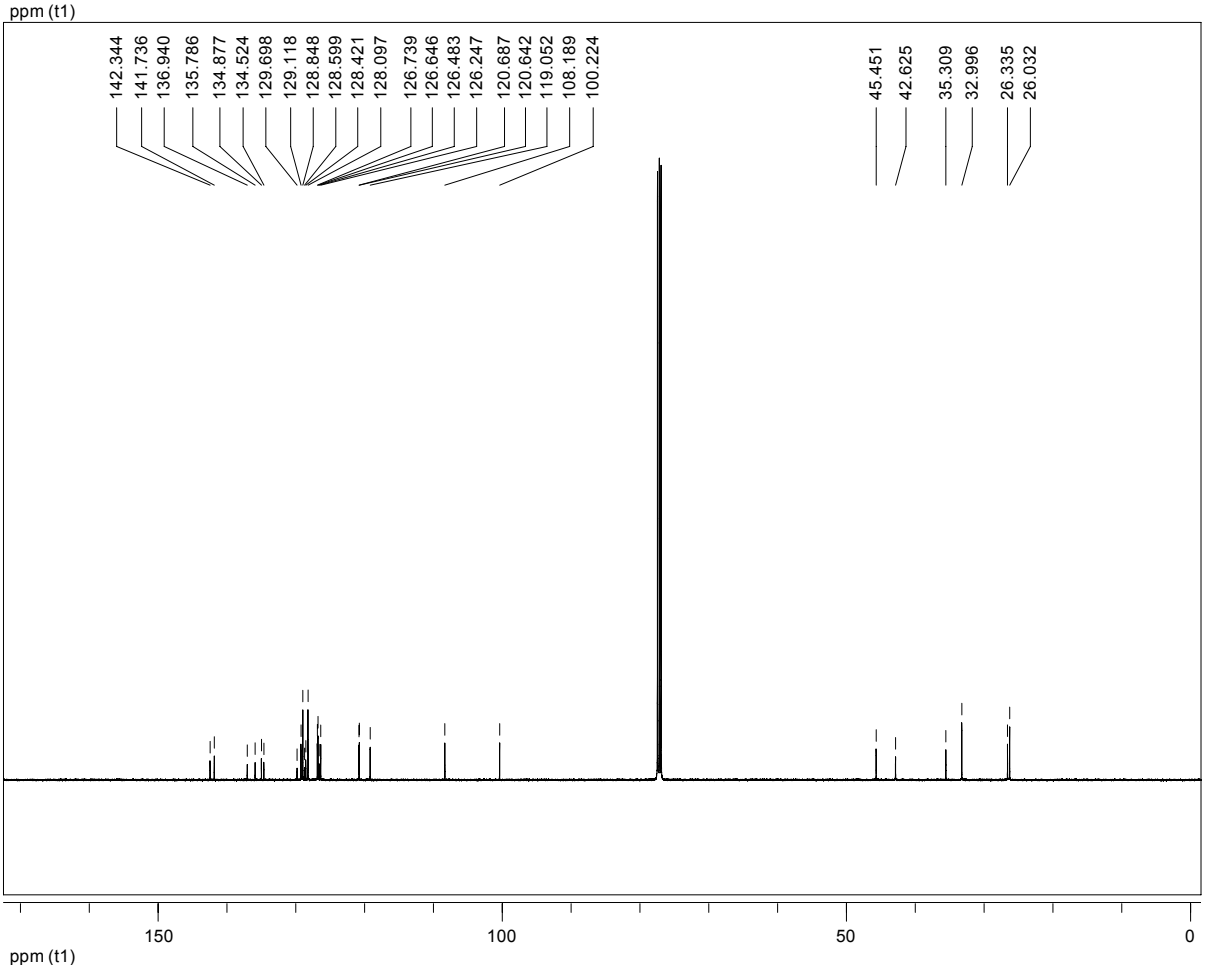

nPr
N
F
7k
1.00
5.06
3.14
3.09
1.00
0.91
1.90
1.99
1.87
3.92
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

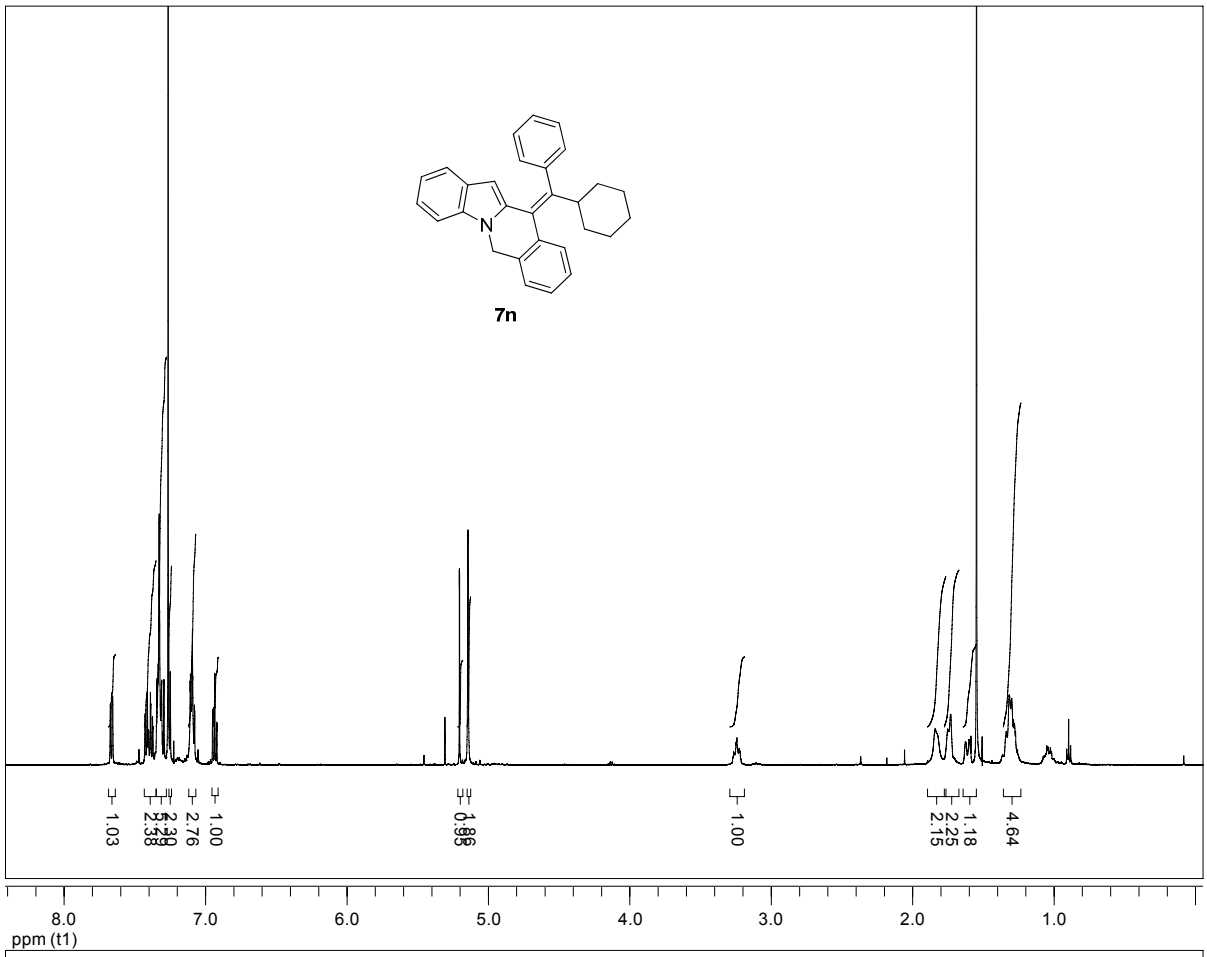

162.233
160.264
143.115
142.404
136.791
136.730
136.411
134.558
131.450
131.423
130.403
130.339
128.757
128.378
128.242
126.882
124.519
120.995
120.723
119.318
113.738
113.569
113.378
113.200
108.185
100.661
45.224
38.347
21.644
13.947
150
100
50
ppm (t1)

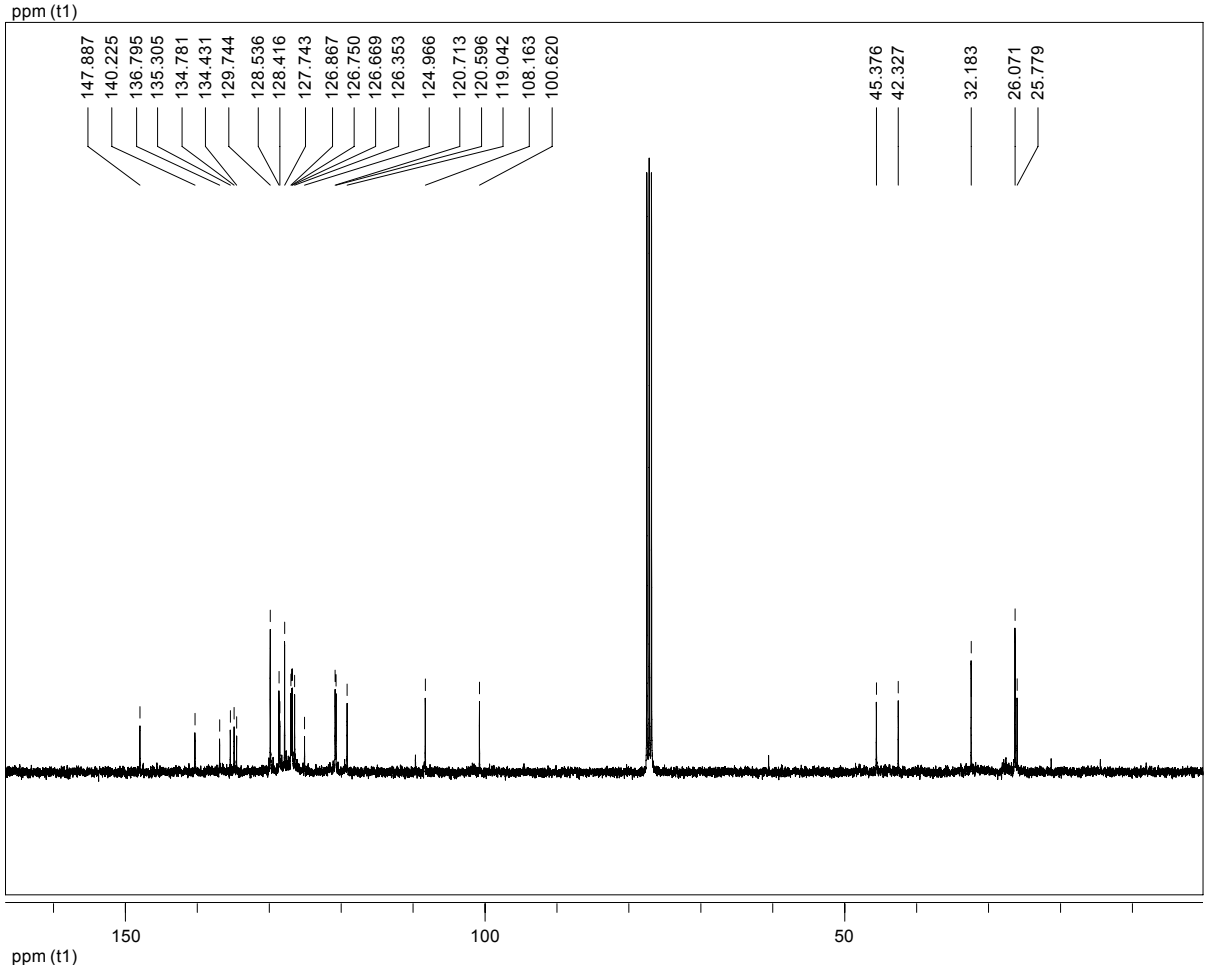

nPr
N
OMe
OMe
7l
0.94
2.03
5.98
1.97
3.35
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
147.880
147.230
142.882
141.863
136.667
134.616
128.883
128.320
128.243
127.712
127.323
126.786
120.784
120.641
119.132
112.133
109.390
108.175
100.336
56.067
56.030
45.019
38.926
21.912
14.155
150
100
50
0
ppm (t1)

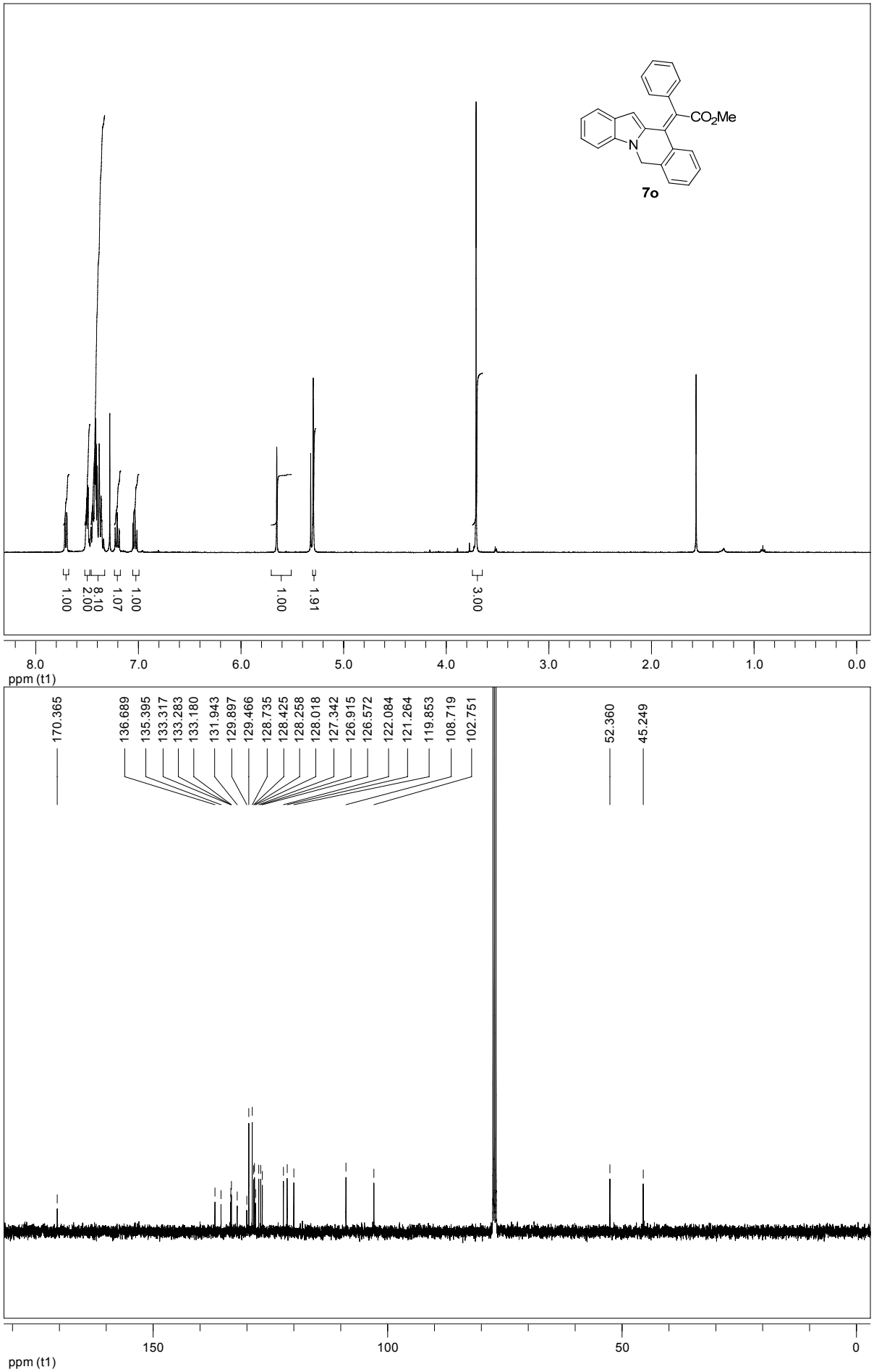

SiMe3
N
7p
0.95
9.09
1.15
0.88
1.27
8.51
8.0
ppm (t1)
4.0
3.0
2.0
1.0
0.0
145.351
144.857
138.684
137.047
136.415
134.607
134.004
128.943
128.364
128.181
127.927
127.882
126.729
125.879
125.698
121.353
120.982
119.279
108.448
101.846
53.412
1.169
150
100
50
0
ppm (t1)

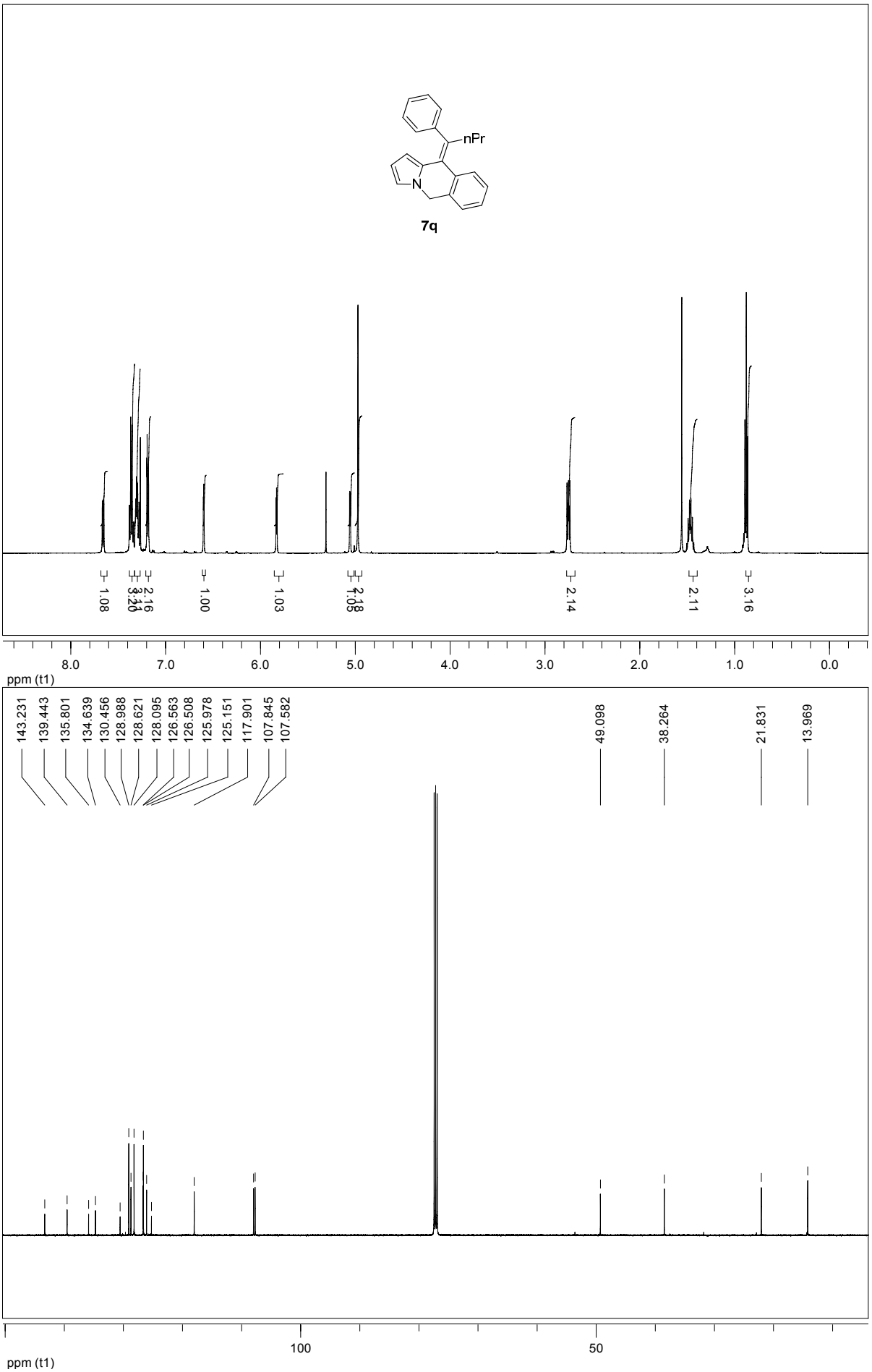


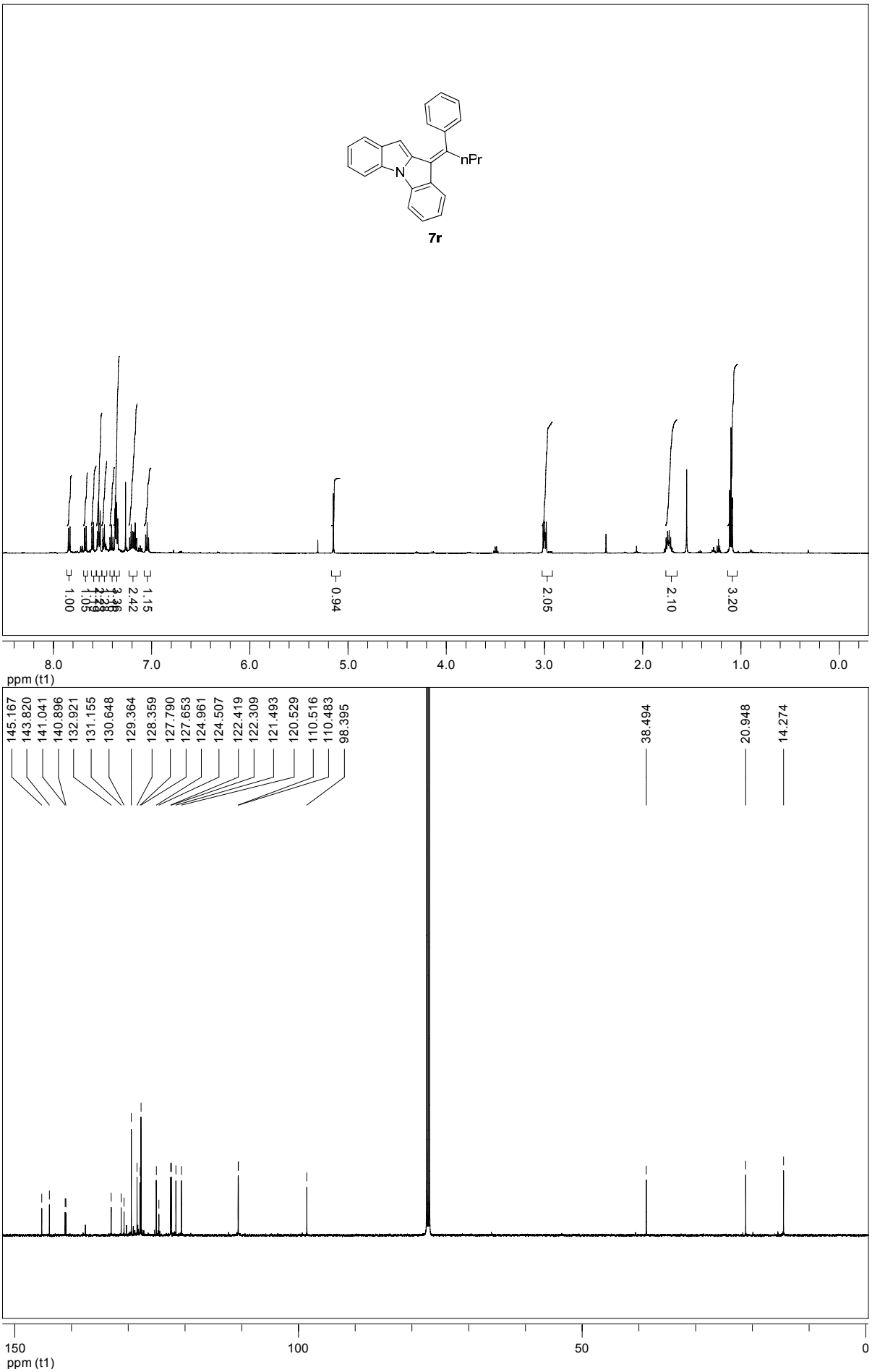


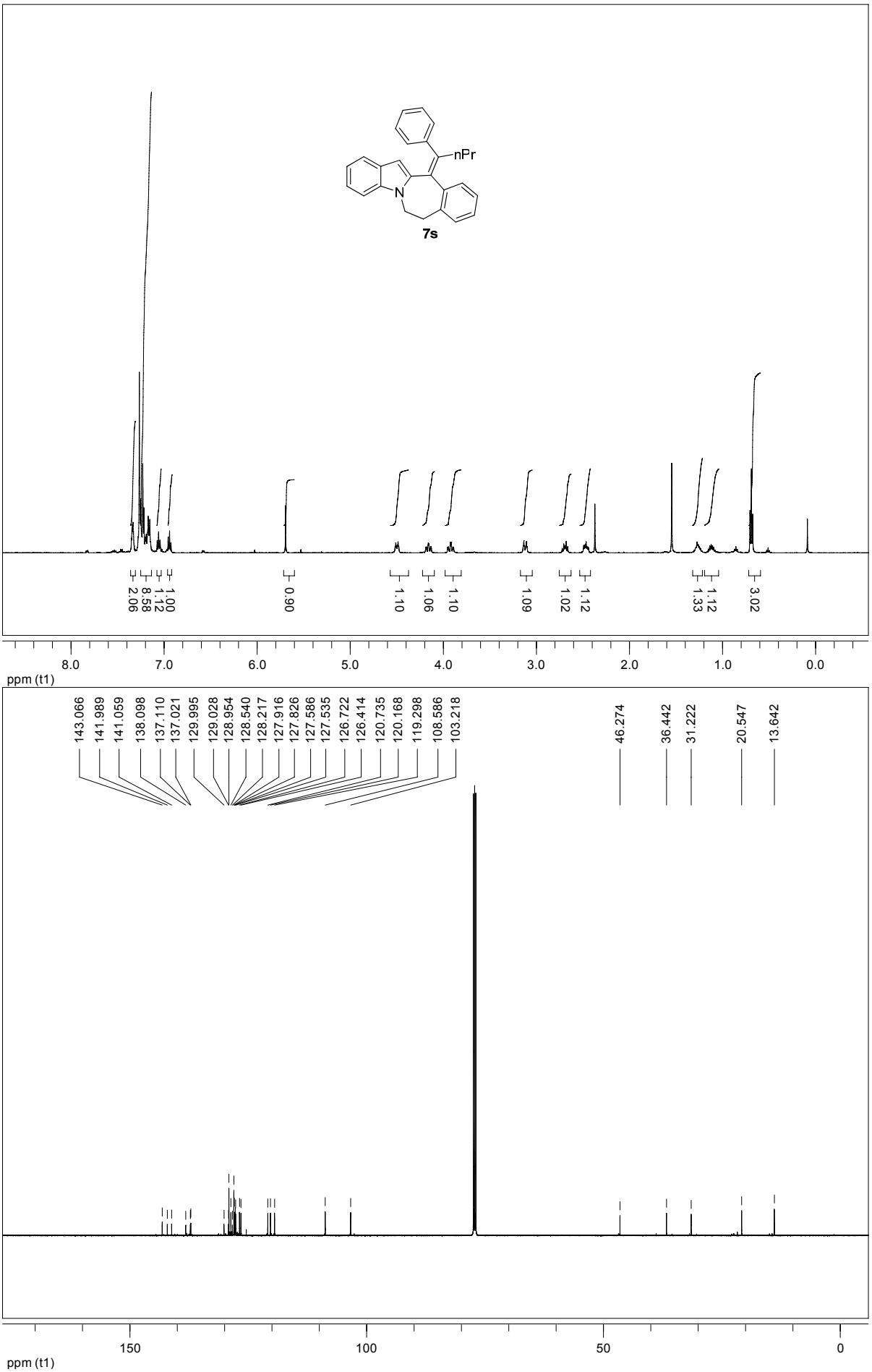


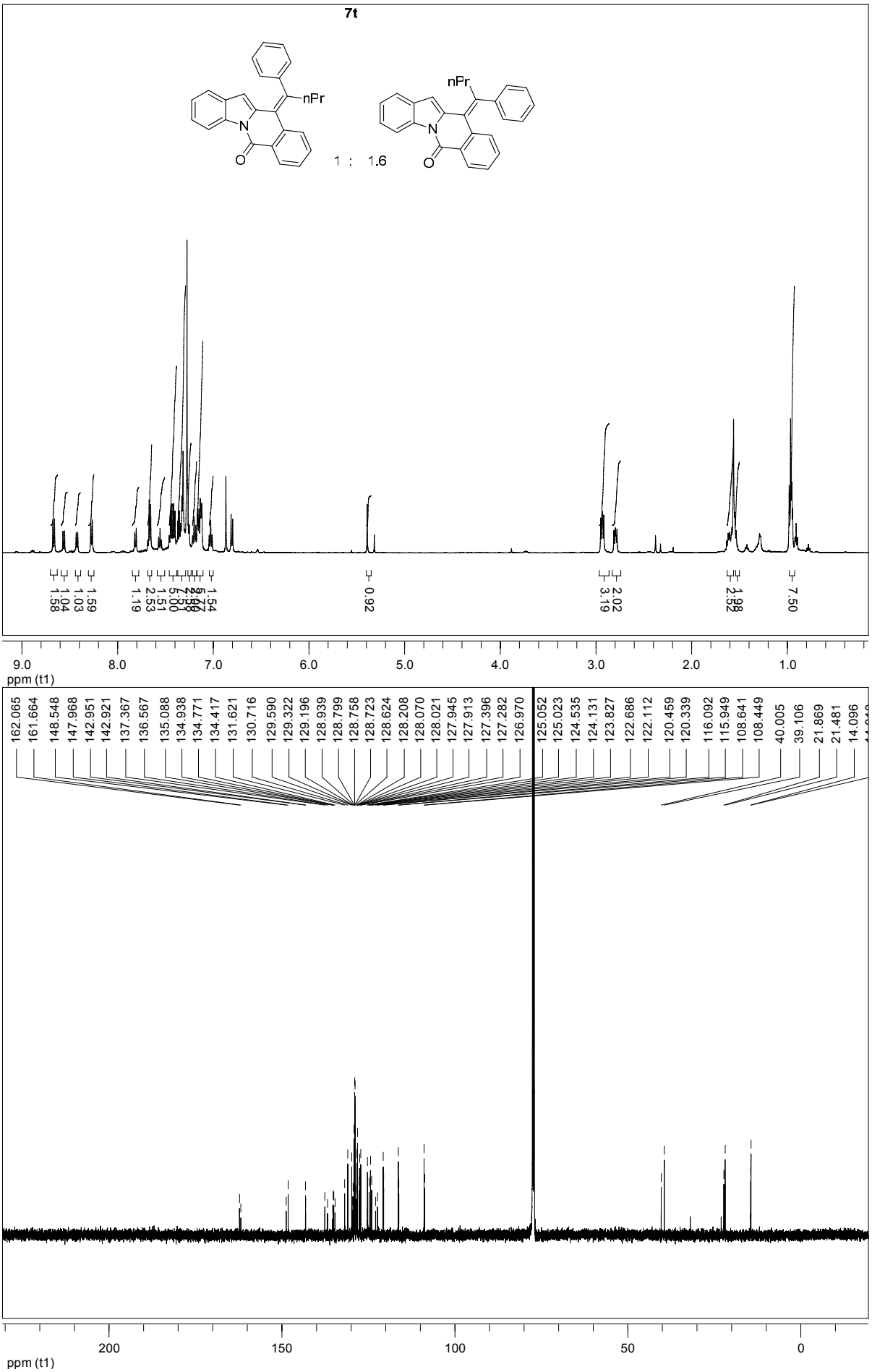


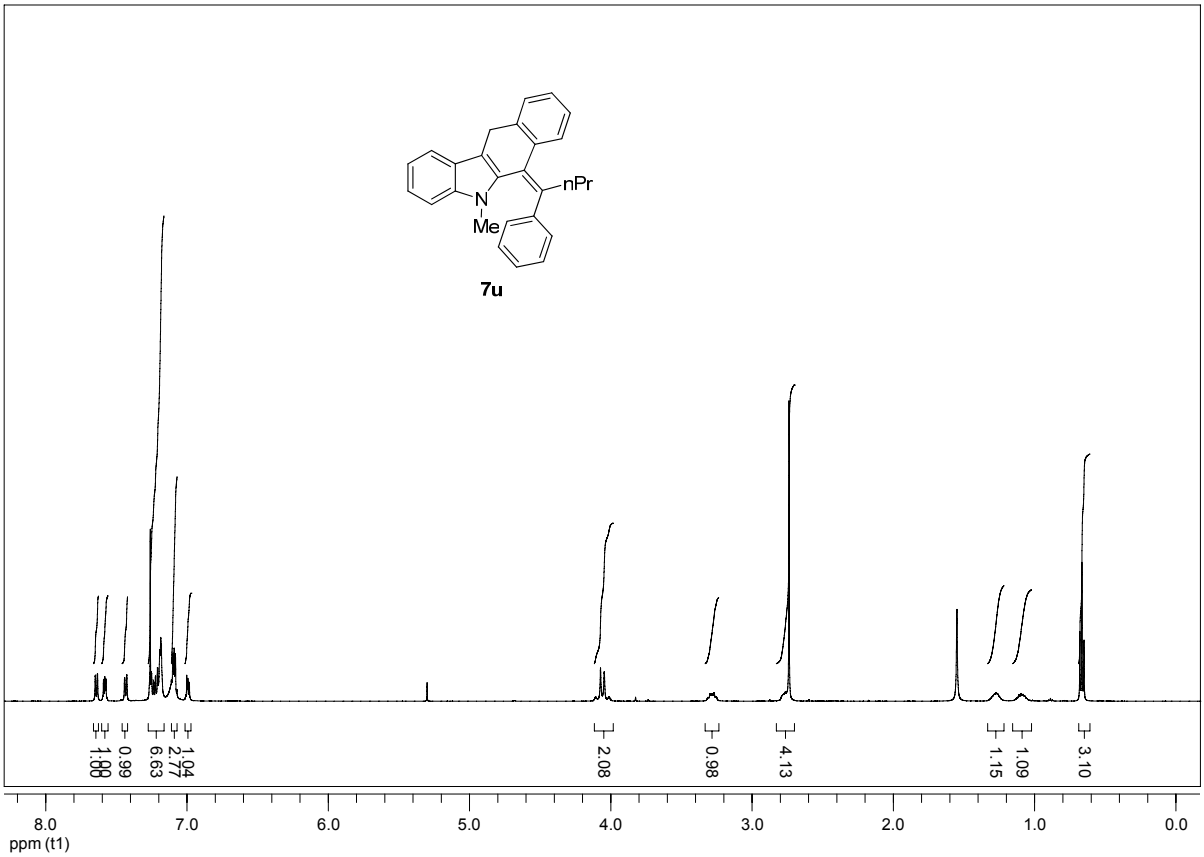

CO2Me
N
7o
1.00
2.00
8.10
1.07
1.00
1.00
1.91
3.00
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)
170.365
136.689
135.395
133.317
133.283
133.180
131.943
129.897
129.466
128.735
128.425
128.258
128.018
127.342
126.915
126.572
122.084
121.264
119.853
108.719
102.751
52.360
45.249
150
100
50
0
ppm (t1)








7t
nPr
nPr
1 : 1.6
1.58
1.04
1.03
1.59
1.19
2.53
1.51
1.54
0.92
3.19
2.02
2.38
7.50
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)
162.065
161.664
148.548
147.968
142.951
142.921
137.367
136.567
135.088
134.938
134.771
134.417
131.621
130.716
129.590
129.322
129.196
128.939
128.799
128.758
128.723
128.624
128.208
128.070
128.021
127.945
127.913
127.396
127.282
126.970
125.052
125.023
124.535
124.131
123.827
122.686
122.112
120.459
120.339
116.092
115.949
108.641
108.449
40.005
39.106
21.869
21.481
14.096
200
150
100
50
0
ppm (t1)



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