Supplementary Information

Synthesis of β- and γ-carbolines via ruthenium and rhodium catalysed [2+2+2] cycloadditions of yne-ynamides with methylcyanoformate

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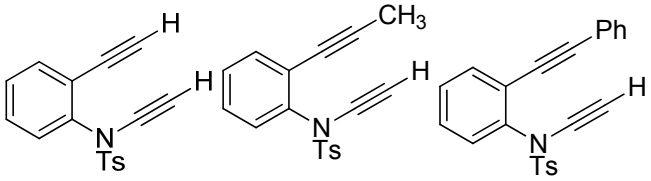
General: All reactions were performed under an atmosphere of dry nitrogen. Commercially available reagents were used without further purification. Solvents (THF, toluene, diethyl ether, CH_2Cl_2) were purified by an Innovative Technology Pure Solvent Device (activated alumina column containing a copper catalyst and molecular sieves) and were degassed. Reactions were magnetically stirred and monitored by thin layer chromatography on Merck silica gel 60-F54 coated 0.25 mm plates. Flash chromatography was performed with Merck silica gel 60 (particle size 40-60 μm). Yields reported refer to isolated and purified compounds. IR spectra were recorded on a Perkin Elmer spectrometer with an ATR set-up. NMR spectra were recorded using a 400 or 500 MHz Bruker Avance III spectrometer, or a Bruker AC300, ARX400, or AMX400 spectrometer. Mass spectra were obtained on a Q-TOF Micro WATERS under electron spray ionisation (ESI) and a Varian MAT 311 spectrometer. Microanalyses were recorded using a Vario Micro Cube from Elementar. Melting points are uncorrected. $Cp^*RuCl(cod)$[1] and 3-iodo-1-[(4-methylphenyl)sulphonyl]-1H-indole[2] were prepared according to literature procedures.

[1] N. Oshima, H. Suzuki, Y. Moro-oka, *Chem. Lett.* 1984, 1161-1164.
[2] B. Witulski, N. Buschmann, U. Bergsträßer, *Tetrahedron* 2000, ***56***, 8473-8480.

I. Synthesis of substituted yne-ynamides:

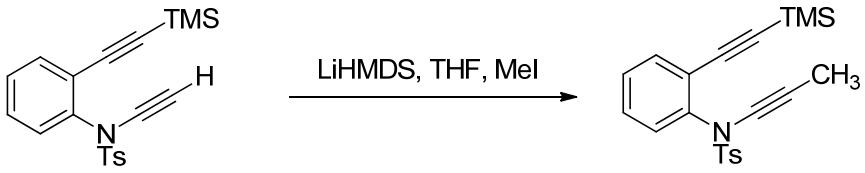
The following yne-ynamides were synthesized as described previously,[3]



9 **12** **16**

Ia via methylation (compounds **2**, **3**, and **4**)

4-Methyl-*N*-prop-1-ynyl-*N*-(2-trimethylsilanylethynyl-phenyl)-benzenesulfonamide (2)

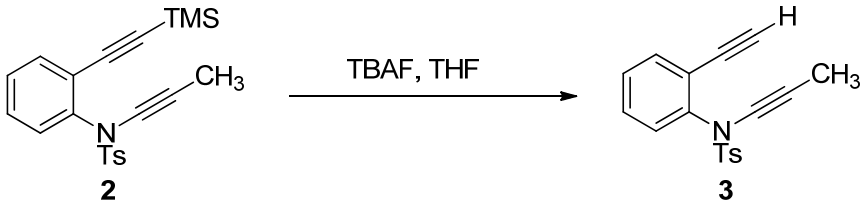


1 **2**

To a solution of **1** (463 mg, 1.26 mmol) in dry THF (16 mL) was added LiHMDS (3.8 mL of a 0.5 *M* solution in THF) under N_2 at –78 °C. The reaction mixture was gradually taken to –40 °C and kept at this temperature for 1 h. Then a solution of MeI (314 µL, 5 mmol) in dry THF (6.5 mL) was added at –40 °C. The temperature was slowly raised to –5 °C and then the cold bath was replaced by an ice bath and the reaction mixture was allowed to warm up to room temperature overnight. The reaction mixture was worked up by the addition of diethyl ether and brine, separation of the layers and extraction of the aqueous layer with diethyl ether. The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. The obtained residue was purified by flash chromatography (9:1 pentane/diethyl ether) to afford **2** (466 mg, 97% yield) as a white solid, mp 81 °C.

^{1}H NMR (300 MHz; $CDCl_3$): δ_H 0.17 (9 H, s), 1.89 (3 H, s), 2.44 (3 H, s), 7.23–7.30 (5 H, m), 7.45–7.48 (1 H, m), 7.69 (2 H, d, J = 8.4 Hz). ^{13}C NMR (75 MHz; $CDCl_3$): δ_C –0.3 (q), 3.3 (q), 21.6 (q), 65.4 (s), 72.1 (s), 100.2 (s), 100.9 (s), 122.3 (d), 128.4 (d), 128.8 (d), 129.0 (d), 129.4 (d, 2 peaks), 133.9 (d), 134.9 (s), 139.8 (d), 144.3 (s); IR (KBr): $\tilde{\nu}_{max}$/cm^{-1} = 3060, 2963, 2916, 2362, 2259, 2159, 1597, 1481, 1446, 1365, 1247, 1166, 1091, 926. MS [ESI (+)]: *m*/*z* (%) = 382 ([M+H]$^+$, 36), 102 (100); HRMS [ESI (+)]: Mass calcd for $C_{21}H_{23}NO_2SSiNa$ [M+Na]$^+$, 404.1111; found, 404.1139.

***N*-(2-Ethynyl-phenyl)-4-methyl-*N*-prop-1-ynyl-benzenesulfonamide (3)**



2 **3**

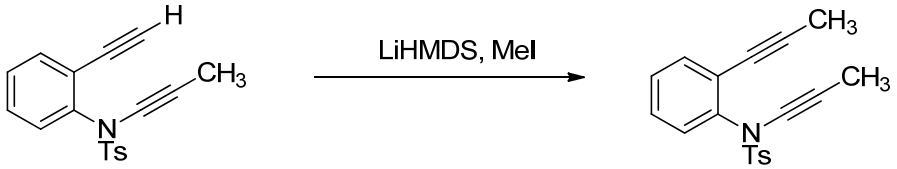
A solution of **2** (226 mg, 0.59 mmol) in THF (15 mL) was purged by bubbling N_2 through it for 15 min then cooled down to 0 °C. A 1 *M* solution of TBAF in THF (0.77 mL, 0.77 mmol) was added dropwise. After 15 min

[3] B. Witulski, C. Alayrac, *Angew. Chem. Int. Ed.* **2002**, *41*, 3281-3284.

the reaction mixture was worked up by addition of Et_2O and brine, separation of the layers and extraction of the aqueous layer with Et_2O. The combined organic layers were drying with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the obtained residue by flash chromatography (pentane/Et_2O) afforded **3** (164 mg, 90% yield) as white solid, mp 111 °C, R_f 0.8 (1:2 pentane/Et_2O).

^{1}H NMR (400 MHz; $CDCl_3$): δ_H 1.88 (3 H, s), 2.45 (3 H, s), 3.08 (1 H, s), 7.13–7.15 (1 H, m), 7.29–7.32 (4 H, m), 7.49–7.52 (1 H, m), 7.70 (2 H, d, J = 8.4 Hz). ^{13}C NMR (100 MHz; $CDCl_3$): δ_C 3.2 (q), 21.6 (q), 65.3 (s), 72.1 (s), 79.4 (s), 82.7 (s), 122.4 (s), 128.4 (d), 128.7 (d), 129.4 (d), 129.4 (d), 129.5 (d), 134.0 (d), 134.3 (s), 140.3 (s), 144.6 (s); IR (KBr): $\tilde{\nu}_{max}$/cm^{-1} = 3256, 2255, 2109, 1595, 1483, 1444, 1366, 1297, 1172, 1090, 930. MS (EI): *m*/*z* (%) = 309 (M^+, 7%), 271 (15), 245 (7), 213 (4), 198 (3), 154 (100), 128 (44), 101 (33), 91 (32), 57 (16). Anal calcd for $C_{18}H_{15}NO_2S$ (309.38 g mol^{-1}); C, 69.88; H, 4.89; N, 4.5; Found: C, 69.76; H, 4.68; N, 4.36.

4-Methyl-*N*-prop-1-ynyl-*N*-(2-prop-1-ynyl-phenyl)-benzenesulfonamide (4)



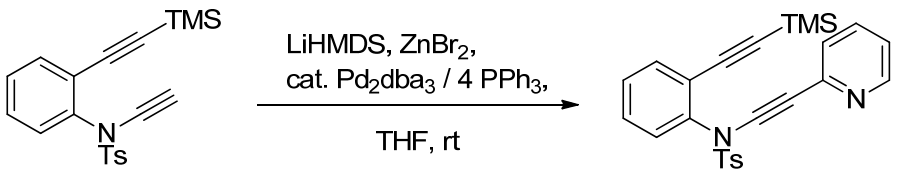
3 **4**

To a solution of **3** (103 mg, 0.33 mmol) in dry THF (4.2 mL) at –78 °C was added dropwise a 0.5 M solution of LiHMDS in THF (1.0 mL, 0.5 mmol). The reaction mixture was gradually taken to –40 °C and kept at this temperature for 1 h. Then a solution of MeI (83 µL, 1.33 mmol) in dry THF (1.7 mL) was added dropwise at –40 °C. The temperature was slowly raised to –5 °C and then the reaction mixture was allowed to warm up to rt overnight. The reaction mixture was worked up by addition of diethyl ether and brine, separation of the layers and extraction of the aqueous layer with diethyl ether and then drying of the combined organic layers with $MgSO_4$. Purification by flash chromatography (7:3 pentane/diethyl ether) afforded **4** as a colourless solid (98 mg, 0.30 mmol, 92% yield); mp 90-91 °C (Et_2O/hexane); R_f 0.35 (7:3 pentane/Et_2O).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2 H), 7.39-7.37 (m, 1 H), 7.31 (d, J = 8.3 Hz, 2 H), 7.27-7.19 (m, 3 H), 2.46 (s, 3 H), 1.91 (s, 3 H), 1.84 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4 (s), 139.7 (s), 135.0 (s), 133.5 (d), 129.5 (d), 129.3 (d), 128.8 (d), 128.6 (d), 128.3 (d), 123.9 (s), 92.3 (s), 75.6 (s), 72.4 (s), 65.3 (s), 21.8 (q), 4.6 (q), 3.5 (q); IR (neat): $\tilde{\nu}_{max}$/cm^{-1} = 2916, 2256, 1596, 1488, 1443, 1364, 1169, 1085, 910, 666; MS [ESI (+)]: m/z = 324 (100, M+1), 169 (50), 155 (80); HRMS [ESI (+)]: Mass calcd for $C_{19}H_{18}NO_2S$ (MH^+) 324.1058; found 324.1051.

Ib) via Negishi reactions (compounds **5a-d** and **6a-d**)

General procedure for Negishi reactions with yne-ynamide 1:

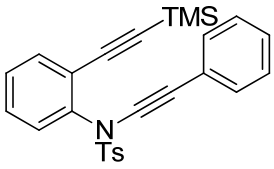


1 **5c**

Freshly prepared LiHMDS (0.8 mL of a 0.5 M solution in THF, 0.40 mmol) was added to a solution of **1** (98 mg, 0.27 mmol) in dry THF (3.4 mL) at -78 °C and stirred for 40 min at -40 °C. Thereafter, a solution of $ZnBr_2$ (66 mg, 0.29 mmol, 1.1 equiv.) in THF (0.2 mL) was added and the reaction mixture was stirred without cooling for

20 min and then transferred via canula to a solution of [$Pd_2(dba)_3$] (11.4 mg, 0.012 mmol, 5 mol%), PPh_3 (13.7 mg, 0.052 mmol, 20 mol%) and 2-iodopyridine (66 mg, 0.32 mmol) in dry THF (2.5 mL). After stirring for 12 h at room temperature, brine was added and the aqueous phase extracted with Et_2O. The combined organic layers were dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the obtained residue by flash chromatography (7:3 to 6:4 pentane/ethyl acetate) afforded yne-ynamide **5c** (104 mg, 0.23 mmol, 87% yield) as a viscous yellow oil; R_f 0.3 (7:3 pentane/ethyl acetate).

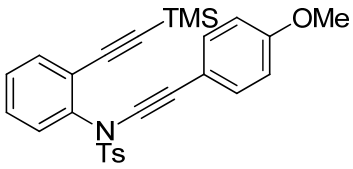
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (ddd, *J* = 4.9 Hz, *J* = 1.7 Hz, *J* = 0.9 Hz, 1 H), 7.76 (d, *J* = 8.4 Hz, 2 H), 7.58 (ddd, *J* = 7.8 Hz, *J* = 7.7 Hz, *J* = 1.8 Hz, 1 H), 7.51-7.47 (m, 1 H), 7.34-7.30 (m, 6 H), 7.12 (ddd, *J* = 7.6 Hz, *J* = 4.9 Hz, *J* = 1.2 Hz, 1 H), 2.44 (s, 3 H), 0.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9 (d), 145.0 (s), 143.9 (s), 138.9 (s), 135.9 (d), 134.7 (s), 134.2 (d), 129.9 (d), 129.27 (d), 129.25 (d), 129.1 (d), 128.7 (d), 126.2 (d), 123.2 (s), 121.9 (d), 101.7 (s), 99.8 (s), 83.0 (s), 71.3 (s), 21.9 (q), -0.3 (q); IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 3064, 2960, 2237, 2163, 1583, 1483, 1469, 1445, 1373, 1171, 1083, 842; MS [ESI (+)]: m/z = 445 (50, M+1), 306 (100); HRMS [ESI (+)]: Mass calcd for $C_{25}H_{25}N_2O_2SSi$ (M+H) 445.1406; found 445.1395.



5a

Yne-ynamide **5a** (110 mg, 0.25 mmol, 91% yield) was obtained after flash chromatography (97:3 cyclohexane /ethyle acetate) as an oil; R*f* 0.1 (95:5 cyclohexane/ethyle acetate).

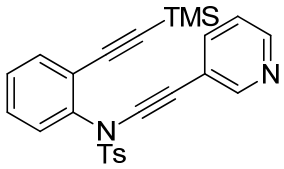
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.53 (m, 1H), 7.38 – 7.25 (m, 9H), 2.46 (s, 3H), 0.10 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$) δ 144.8 (s), 139.4 (s), 134.7 (s), 134.2 (d), 131.2 (d), 129.8 (d), 129.3 (2 d), 129.3 (d), 128.9 (d), 128.7 (d), 128.2 (d), 127.6 (d), 123.2 (s), 122.9 (s), 101.5 (s), 99.9 (s), 82.6 (s), 70.7 (s), 21.9 (q), -0.3 (q); IR (neat) $\tilde{\nu}_{max}$/cm^{-1} = 3064, 3034, 2960, 2899, 2240, 2163, 1598, 1483, 1444, 1374, 1249, 1171, 1091; MS [ESI (+)]: m/z (%) = 444 (100%, M+H$^+$), 289 (30), 288 (10), 216 (70); HRMS [ESI (+)]:Mass calcd for $C_{26}H_{26}NO_2SSi$ (M+H), 444.1454; found 444.1437.



5b

Yne-ynamide **5b** (100 mg, 0.25 mmol, 92% yield) was obtained after flash chromatography (9:1 cyclohexane /ethyle acetate) as an oil; R*f* : 0.15 (9:1 cyclohexane /ethyle acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.3 Hz, 2H), 7.53 (m, 1H), 7.33 – 7.29 (m, 8H),3.79 (s, 3H), 2.45 (s, 3H), 0.12 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.4 (s), 144.7 (s), 139.7 (s), 134.9 (s), 134.3 (s), 133.3 (d), 129.7 (d), 129.3 (d), 129.2 (d), 128.8 (s), 128.7 (d), 123.1 (d), 115.2 (d), 113.9 (d), 101.4 (s), 100.2 (s), 81.2 (s), 70.2 (s), 55.4 (q), 21.9 (q), -0.1 (q); MS [ESI (+)]: m/z (%) = 474 (100, [M+H]$^+$) 319 (61), 146 (85); HRMS [ESI (+)]: Mass Calcd for $C_{27}H_{27}NO_3SSi$ (M+H) 474.1559; found 474.1542.



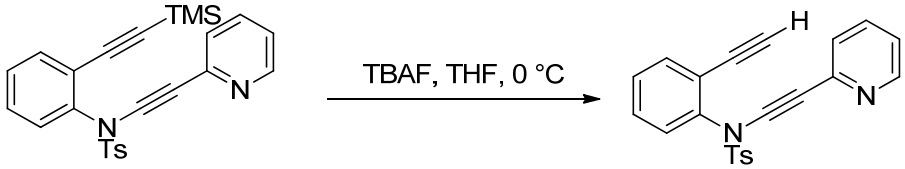
5d

5d (96 mg, 0.22 mmol, 81% yield) was obtained after flash chromatography (1:1 pentane/ethyl acetate) as a pale yellow solid (mp 77-79 °C), R_f 0.4 (1:1 pentane/ethyl acetate).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (dd, *J* = 2.1 Hz, *J* = 0.8 Hz, 1 H), 8.45 (dd, *J* = 4.9 Hz, *J* = 1.7 Hz, 1 H), 7.73 (d, *J* = 8.4 Hz, 2 H), 7.62 (ddd, *J* = 8.2 Hz, *J* = 2.0 Hz, *J* = 1.8 Hz, 1 H), 7.52-7.50 (m, 1 H), 7.39-7.30 (m, 5 H), 7.19 (ddd, *J* = 7.9 Hz, *J* = 4.9 Hz, *J* = 0.9 Hz, 1 H), 2.45 (s, 3 H), 0.06 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8 (d), 148.0 (d), 145.1 (s), 138.9 (s), 137.9 (d), 134.6 (s), 134.3 (d), 129.9 (d), 129.4 (d), 129.3 (d), 129.1 (d), 128.7 (d), 123.0 (d), 122.9 (s), 120.6 (s), 101.7 (s), 99.8 (s), 85.7 (s), 67.8 (s), 21.9 (q), -0.2 (q); IR (neat): $\tilde{\nu}_{max}$/cm^{-1} = 3031, 2960, 2238, 2165, 1595, 1481, 1444, 1405, 1365, 1171, 1079, 843; MS [ESI (+)]: m/z = 445 (90, M+H), 231 (100); HRMS [ESI (+)]: MS calcd for $C_{25}H_{25}N_2O_2SSi$ (M+H) 445.1406; found 445.1423.

General procedure for the desilylation reaction of silylated ynamides:

***N*-(2-Ethynyl-phenyl)-4-methyl-*N*-pyridin-2-ylethynyl-benzenesulfonamide (6c)**

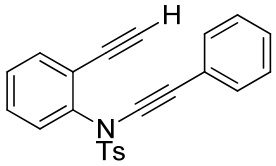


5c **6c**

A 1 M solution of TBAF in THF (0.2 mL, 0.20 mmol) was added to a solution of **5c** (67 mg, 0.15 mmol) in THF (3 mL) at 0 °C. After 15 min, the reaction mixture was worked up by addition of diethyl ether and brine. Separation of the layers and extraction of the aqueous layer with diethyl ether was followed by drying the combined organic layers with $MgSO_4$. After removal of the solvants under reduced pressure the obtained crude product was purified by flash chromatography (1:1 silica gel, pentane/ethyl acetate) to afford **6c** (51 mg, 0.14 mmol, 90% yield) as a white solid; R_f 0.4 (1:1 pentane/ethyl acetate); mp 113-114 °C ($CHCl_3$/pentane).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (ddd, *J* = 4.9 Hz, *J* = 1.7 Hz, *J* = 0.9 Hz, 1 H), 7.77 (d, *J* = 8.3 Hz, 2 H), 7.59 (td, *J* = 7.8 Hz, *J* = 1.8 Hz, 1 H), 7.54-7.51 (m, 1 H), 7.37-7.31 (m, 5 H), 7.27-7.24 (m, 1 H), 7.14 (ddd, *J* = 7.6 Hz, *J* = 4.9 Hz, *J* = 1.2 Hz, 1 H), 3.06 (s, 1 H), 2.45 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9 (d), 145.3 (s), 143.6 (s), 139.4 (s), 136.0 (d), 134.3 (d), 134.2 (s), 129.83 (d), 129.76 (d), 129.4 (d), 129.2 (d), 128.7 (d), 126.6 (d), 122.6 (s), 122.2 (d), 83.3 (d), 82.9 (s), 78.8 (s), 70.7 (s), 21.8 (q); IR (neat): $\tilde{\nu}_{max}$/cm^{-1} 3255, 2242, 1588, 1482, 1469, 1443, 1376, 1173, 1114, 1080, 921; MS [ESI (+)]: m/z (%) = 373 (100, M+H), 347 (20), 234 (45), 218 (75); HRMS [ESI (+)]: Mass calcd for $C_{22}H_{17}N_2O_2S$ (M+H), 373.1011; found, 373.1015.

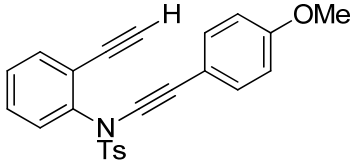
***N*-(2-Ethynyl-phenyl)-4-methyl-*N*-phenylethynyl-benzenesulfonamide (6a)**



6a

Yne-ynamide **6a** (270 mg, 0.73 mmol, 87%) was obtained after flash chromatography (6:1 pentane/diethyl ether) as a solid, R_f 0.51 (1:1 pentane/diethyl ether);, mp 132-133 °C (pentane/$CHCl_3$).
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 8.3 Hz, 2H), 7.53-7.51 (m, 1H), 7.38-7.24 (m, 10H), 3.04 (s, 1H), 2.44 (s, 3H; ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1 (s), 140.0 (s), 134.4 (d), 134.2 (s), 131.6 (d), 129.7 (d), 129.3 (d), 129.1 (d), 128.8 (d), 128.3 (d), 128.0 (d), 127.4 (d), 123.0 (s), 122.3 (s), 83.2 (d), 82.7 (s), 79.0 (s), 70.4 (s), 21.9 (q); IR (KBr): $\tilde{\nu}_{max}$/cm^{-1} = 3265, 2236, 1596, 1486, 1441, 1369, 117; MS [ESI (+)]: m/z = 371 (100, M^+); HRMS [ESI (+)]: Mass calcd for $C_{23}H_{18}NO_2S$ (M+H), 372.1058; found, 372.1049.

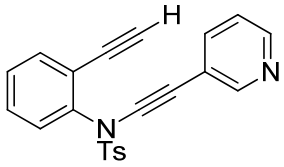
***N*-(2-Ethynyl-phenyl)-*N*-(4-methoxy-phenylethynyl)-4-methyl-benzenesulfonamide (6b)**



6b

Yne-ynamide **6b** (100 mg, 0.25 mmol, 80% yield) was obtained after flash chromatography (8:2 cyclohexane /ethyl acetate) as a solid; R_f 0.27 (8:2 cyclohexane /ethyl acetate), mp 106 °C (pentane/$CHCl_3$).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.54 – 7.51 (m, 1H), 7.39 – 7.27 (m, 7H), 6.81 (d, J = 8.3 Hz, 2H), 3.80 (s, 3H), 3.05 (s, 1H), 2.47 (s, 3H); ^{13}C NMR (100MHz, $CDCl_3$) δ 159.7 (s), 145.0 (s), 140.3 (s), 134.4 (d), 134.3 (d), 133.7 (d), 129.7 (d), 129.6 (d) , 129.3 (d), 129.0 (d), 128.8 (d), 122.4 (s), 114.9 (s), 114.0 (d), 83.1 (s), 81.3 (s), 79.1 (s), 70.1 (s), 55.4 (q), 21.9 (q); IR (neat): $\tilde{\nu}_{max}$/cm^{-1} = 3263, 2235, 2114, 1602, 1509, 1478, 1362, 1246, 1163, 1087, 1031, 916; MS [ESI (+)] m/z (%) = 402 (100, $M+H^+$), 247 (50); HRMS [ESI (+)]: Mass calcd for $C_{24}H_{20}NO_3S$ (M+H), 402.1164; found 402.1167.

***N*-(2-Ethynyl-phenyl)-4-methyl-*N*-pyridin-3-ylethynyl-benzenesulfonamide (6d)**

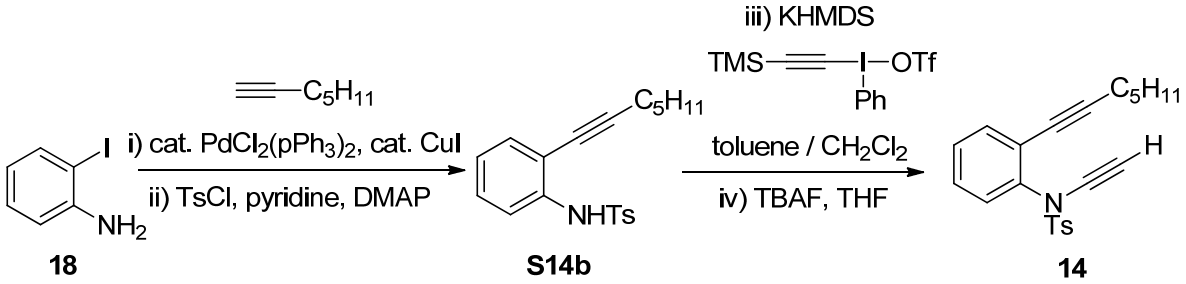


6d

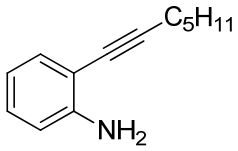
6d (41 mg, 0.11 mmol, 92% yield) was obtained after flash chromatography (1:1 pentane/ethyl acetate) as a white solid; R_f 0.3 (1:1 pentane/ethyl acetate), mp 111-112 °C ($CHCl_3$/pentane).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (d, J = 1.4 Hz, 1 H), 8.47 (dd, J = 4.8 Hz, J = 1.5 Hz, 1 H) 7.74 (d, J = 8.3 Hz, 2 H), 7.65 (ddd, J = 7.9 Hz, J = 2.0 Hz, J = 1.8 Hz, 1 H), 7.54-7.52 (m, 1 H), 7.40-7.31 (m, 5 H), 7.20 (ddd, J = 7.9 Hz, J = 4.9 Hz, J = 0.8 Hz, 1 H), 3.02 (s, 1 H), 2.46 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3 (d), 148.3 (d), 145.4 (s), 139.5 (s), 138.4 (d), 134.4 (d), 134.1 (s), 129.84 (d), 129.83 (d), 129.4 (d), 129.3 (d), 128.7 (d), 123.1 (d), 122.2 (s), 120.3 (s), 85.7 (s), 83.3 (d), 78.8 (s), 67.5 (s), 21.9 (q); IR (neat): $\tilde{\nu}_{max}$/cm^{-1} = 3261,

2233, 1595, 1485, 1442, 1371, 1173, 1109, 1087, 1069, 911, 803; MS [ESI (+)]: m/z (%) = 373 (100, M+H), 234 (20), 218 (60); HRMS [ESI (+)]: Mass calcd for $C_{22}H_{17}N_2O_2S$ (M+H), 373.1011; found, 373.1007.

Ic) Synthesis of yne-ynamide **14**



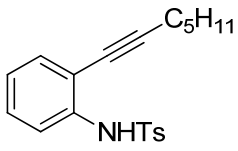
2-Hept-1-ynyl-phenylamine (S14a)



S14a

1-heptyne (1.392 g, 14.50 mmol) was added to a solution of 2-iodoaniline **18** (2.65 g, 12.10 mmol), $PdCl_2(PPh_3)_2$ (410 mg, 0.61 mmol) and CuI (224 mg, 1.210 mmol) in DMF (14 mL) and NEt_3 (25 mL) and was stirred at room temperature over night. The solvent was removed under reduced pressure and H_2O and CH_2Cl_2 were added to the obtained residue. The product was extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. Flash chromatography (10:1 pentane/diethyl ether) afforded **S14a** (1.930 g, 10.30 mmol, 85%) as a colourless oil, R_f 0.19 (10:1 pentane/diethyl ether).
^{1}H NMR (400 MHz, $CDCl_3$): δ 1.01 (t, J = 7.4 Hz, 3H), 1.46 (m, 2H), 1.53 (m, 2H), 1.73 (m, 2H), 2.54 (t, J = 7.1 Hz, 2H), 4.23 (s, 2H), 6.72-6.77 (m, 2H), 7.15 (m, 1H), 7.33 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6 (s), 131.9 (d), 128.7 (d), 117.7 (d), 114.1 (d), 108.9 (s), 95.7 (s), 77.0 (s), 31.1 (t), 28.6 (t), 22.2 (t), 19.5 (t), 13.9 (q). IR (neat): $\tilde{\nu}_{max}$/cm^{-1} = 3475, 3380, 3029, 2931, 2859, 1614, 1493, 1456, 1306, 748. MS [ESI (+)]: m/z = 188 $[M+H]^+$.

***N*-(2-Hept-1-ynyl-phenyl)-4-methyl-benzenesulfonamide (S14b)**

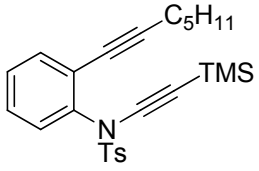


S14b

Tosylchloride (2.150 g, 11.30 mmol) was added to a solution of **S14a** (1.760 g, 9.40 mmol) in dry THF (40 mL) and dry pyridine (20 mL) and the resulting mixture was stirred at room temperature over night. Thereafter, H_2O (200 mL) and CH_2Cl_2 (30 mL) were added and the product was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried with $MgSO_4$, filtered and the solvent was removed under reduced pressure. Flash chromatography (4:1 pentane/diethyl ether) afforded **S14b** (2.420 g, 7.10 mmol, 75 % yield) as a solid, R_f 0.55 (6:1 pentane/diethyl ether), mp 66-67 °C (pentane/CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94 (d, J = 6.9 Hz, 3H), 1.36-1.45 (m, 4H), 1.55-1.64 (m, 2H), 2.35 (s, 3H), 2.40 (t, J = 7.1 Hz, 2H), 6.96 (m, 1H), 7.26-7.16 (m, 5H), 7.56 (d, J = 8.3 Hz, 1H), 7.66 (d, J = 8.3 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9 (s), 137.7 (s), 136.3 (s), 131.9 (d), 129.6 (d), 128.8 (d), 127.3 (d), 124.2 (d), 119.3 (d), 114.9 (s), 98.0 (s), 75.4 (s), 31.2 (t), 28.4 (t), 22.2 (q), 21.5 (t), 19.6 (t), 14.0 (q). IR (KBr): $\tilde{\nu}_{max}$/cm^{-1} = 3264, 2957, 2937, 2870, 1496, 1399, 1340, 1165, 918. MS [ESI (+)]: m/z = 364 $[M+Na]^+$. HRMS [ESI (+)]: Mass calcd for $C_{20}H_{23}NO_2SNa$ $[M+Na]^+$, 364.1347, found, 364.1358.

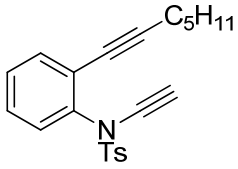
***N*-(2-Hept-1-ynyl-phenyl)-4-methyl-*N*-trimethylsilanylethynyl-benzenesulfonamide (S14c)**



S14c

KHMDS (3.5 mL of 0.5 M solution in toluene) was added dropwise to a solution of **S14b** (500 mg, 1.50 mmol) in dry toluene (150 mL) at 0 °C. After 15 min a solution of (trimethylsilyl)ethynyl phenyliodonium triflate (878 mg, 1.95 mmol) in dry CH_2Cl_2 (60 mL) was added and the resulting reaction mixture was stirred over night at room temperature. After completion of reaction the solvents were removed under reduced pressure and H_2O and CH_2Cl_2 were added to the obtained residue. The product was extracted with CH_2Cl_2 and the combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under reduced pressure. The obtained crude product was purified by flash chromatography (4:1 pentane/diethyl ether) to afford **S14c** (320 mg, 0.7 mmol, 50% yield) as colourless oil, R_f 0.3 (15:1 pentane/diethyl ether).
^{1}H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 9H), 0.91 (t, J = 6.9 Hz, 3H), 1.25-1.37 (m, 4H), 1.45-1.53 (m, 2H), 2.15 (t, J = 6.5 Hz, 2H), 2.45 (s, 3H), 7.23-7.28 (m, 5H), 7.28-7.40 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.4, 138.6, 134.7, 133.4, 129.2, 128.9, 128.7, 128.6, 128.0, 123.8, 96.9, 94.7, 76.0, 72.5, 31.2, 28.2, 22.1, 21.5, 19.5, 13.9, 0.03; HRMS [ESI (+)]: Mass calcd for $C_{25}H_{31}NO_2SSiNa$ $[M+Na]^+$, 460.1742; found, 460.1742.

***N*-Ethynyl-*N*-(2-hept-1-ynyl-phenyl)-4-methyl-benzenesulfonamide (14)**

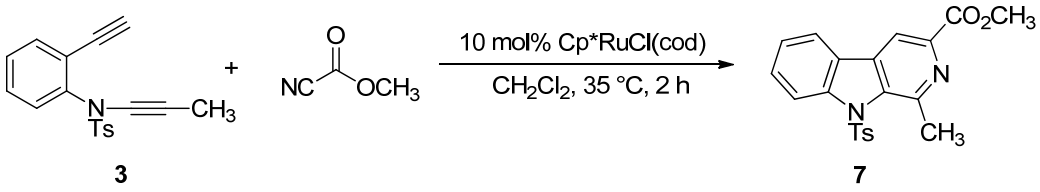


14

To a solution of **S14c** (2.210 g, 5.00 mmol) in THF (20 mL) was added TBAF (6.6 mL of 1 M solution in THF) at 0 °C. After 15 min stirring at 0 °C diethyl ether and brine were added. The product was extracted with diethyl ether, the combined organic layers dried with $MgSO_4$, filtrated and concentrated under reduced pressure. The obtained crude product was purified with flash chromatography (13:1 pentane/diethyl ether) to afford yne-ynamide **14** (1.530 g, 4.20 mmol, 83% yield) as a colourless oil, R_f 0.18 (15:1 pentane/diethyl ether).
^{1}H NMR (400 MHz, $CDCl_3$): δ 0.91 (t, J = 7.1 Hz, 3H), 1.25-1.37 (m, 4H), 1.40-1.51 (m, 2H), 2.17 (t, J = 6.5 Hz, 2H), 2.45 (s, 3H), 2.81 (s, 1H), 7.16-7.33 (m, 5H), 7.40 (m, 1H), 7.73 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.6, 138.3, 134.8, 133.4, 129.4, 129.1, 128.9, 128.4, 128.1, 123.9, 97.2, 75.9, 75.9, 58.4, 31.0, 28.0, 22.1, 21.5, 19.5, 13.9; HRMS [ESI (+)]: Mass calcd for $C_{22}H_{23}NO_2SNa$ $[M+Na]^+$, 388.1347; found, 388.1320.

*General procedures for the [2+2+2] cycloaddition reactions of yne-ynamides with methylcyanoformate to afford β- or γ-carbolines (compounds 7, **8a-e**, **10**, **11**, **13**, **15**, and **17**)*

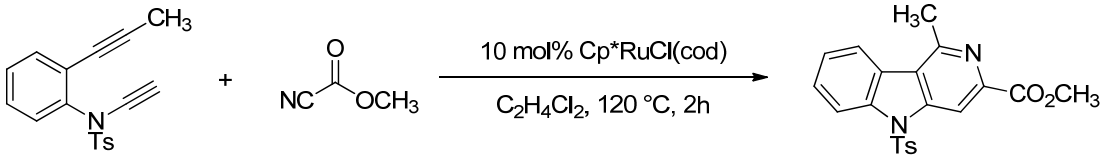
Method A:



3 **7**

To a solution of Cp*RuCl(cod) (9.8 mg, 0.026 mmol, 10 mol%) in dry with nitrogen purged CH_2Cl_2 (1 mL) was added methylcyanoformate (0.4 μL, 0.05 mmol, 2 equiv.). To the resulting mixture was added a solution of diyne **3** (80 mg, 0.26 mmol) in CH_2Cl_2 (10 mL) during 1-2 h via syringe-pump at 35 °C. After completion of the addition the reaction mixture was stirred additional 30 min (monitored by TLC). Thereafter the solvent was removed under reduced pressure and the resulting residue was purified by flash chromatography (2:1 diethyl ether/pentane) to afford β-carboline **7** (94 mg, 0.24 mmol, 92% yield) as a colourless solid.

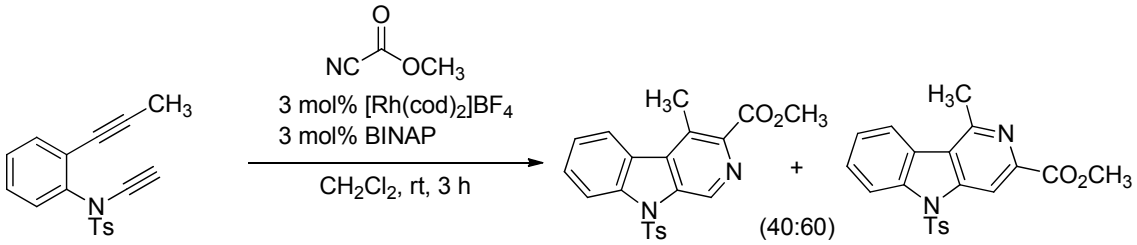
Method B:



12 **13**

In a Schlenk tube were introduced Cp*RuCl(cod) (9.8 mg, 0.026 mmol, 10 mol%), methylcyanoformate (200 μL, 2.50 mmol) and dry dichloroethane (20 mL) and the resulting solution was purged with nitrogen. A solution of diyne **12** (80 mg, 0.26 mmol) in dichloroethane (4 mL) was added and the reaction mixture was heated at 120 °C for 1.5 h (monitored by TLC). Thereafter, the solvent was removed by evaporation under reduced pressure and the resulting residue was purified by flash chromatography (1:1 petroleum ether/ethyl acetate) to afford γ-carboline **13** (46 mg, 0.12 mmol, 46% yield) as a colourless solid.

Method C:

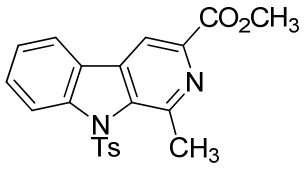


12 **S13** **13**

In a Schlenk tube were dissolved $[Rh(cod)_2]BF_4$ (2.6 mg, 3 mol%) and BINAP (4.2 mg, 3 mol%) in dry CH_2Cl_2 (1.0 mL) and the mixture was stirred for 5 min. Hydrogen gas was introduced to the resulting solution under ambient pressure and the reaction mixture was stirred for 20 min at room temperature. Thereafter, the solution was concentrated to dryness in vacuum. The residue was dissolved in CH_2Cl_2 (1.2 mL) and methylcyanoformate (175 μL, 2.2 mmol) and a solution of diyne **12** (68 mg, 0.22 mmol) in CH_2Cl_2 (1.0 mL) was added. The mixture was stirred at room temperature for 3 h (monitored by TLC). Thereafter, the solvent was removed by evaporation under reduced pressure and the resulting residue was purified by flash chromatography (4:1 petroleum

ether/ethyl acetate) to furnish β-carboline **S13** (29 mg, 0.07 mmol, 33% yield) and γ-carboline **13** (43 mg, 0.11 mmol, 50% yield) as colourless solids.

1-Methyl-9-(toluene-4-sulfonyl)-*9H*-β-carboline-3-carboxylic acid methyl ester (7)

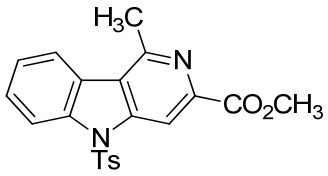


7

Following **Method A** β-carboline **7** (94 mg, 0.24 mmol, 92% yield) was obtained after flash chromatography (1:1 petroleum ether/ethyl acetate) as a colourless solid; R_f 0.27 (1:2 petroleum ether/diethyl ether), mp 183-184 °C (pentane/CH_2Cl_2).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.21 (s, 3H), 3.14 (s, 3H), 4.05 (s, 3H), 6.91 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.2 Hz, 2H), 7.41 (t, J = 7.4 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 8.30 (d, J = 8.4 Hz, 1H), 8.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 165.6 (s), 150.7 (s), 145.0 (s), 143.0 (s), 142.2 (s), 138.0 (s), 137.8 (s), 132.6 (s), 130.1 (d), 129.1 (d), 126.6 (d), 126.5 (s), 125.9 (d), 121.2 (d), 119.2 (d), 114.1 (d), 53.0 (q), 26.0 (q), 21.4 (q); IR (KBr): $\tilde{\nu}_{max}$/cm^{-1} = 2948, 1746, 1614, 1594, 1573, 1171, 686. MS [ESI (+)]: m/z = 417 $[M+Na]^+$; HRMS [ESI (+)]: Mass calcd for $C_{21}H_{19}N_2O_4S$ $[M+H]^+$, 395.1065; found, 395.1072. Anal calcd for $C_{21}H_{18}N_2O_4S$ (394.44 g mol^{-1}): C, 63.94; H, 4.60; N, 7.10; Found C, 63.89; H, 4.59; N, 7.05.

1**-Methyl-5-(toluene-4-sulfonyl)-*5H*-pyrido[4,3-*b*]indole-3-carboxylic acid methyl ester (13)**

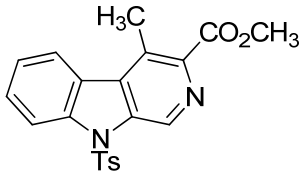


13

Following **Method B** γ-carboline **13** (46 mg, 0.11 mmol, 46% yield) was obtained after flash chromatography (4:1 petroleum ether/ethyl acetate) as a colourless solid; R_f 0.06 (4:1 petroleum ether/ethyl acetate), mp 246-247 °C (pentane/CH_2Cl_2).

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.29 (s, 3H), 3.06 (s, 3H), 4.08 (s, 3H), 7.17 (d, J = 8.3 Hz, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.6 Hz, 1H), 7.77 (d, J = 8.3 Hz, 2H), 8.10 (d, J = 7.8 Hz, 1H), 8.41 (d, J = 8.4 Hz, 1H), 8.97 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (s), 153.9 (s), 145.9 (s), 144.5 (s), 143.8 (s), 139.1 (s), 134.7 (s), 130.2 (d), 128.8 (s), 126.8 (d), 124.9 (d), 124.1 (s), 123.2 (d), 122.8 (d), 114.9 (d), 109.9 (d), 53.2 (q), 24.5 (q), 21.7 (q); IR (neat): $\tilde{\nu}$/cm^{-1} = 1735, 1574, 1428, 1370, 1328, 1219, 1171, 939. MS [ESI (+)]: m/z = 417 $[M+Na]^+$. Anal calcd for $C_{21}H_{18}N_2O_4S$ (394.10 g mol^{-1}): C, 63.94; H, 4.60; N, 7.10; Found: C, 63.85; H, 4.49; N, 7.09.

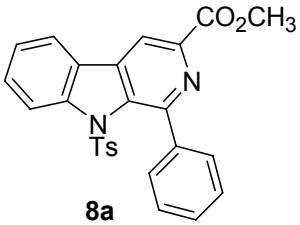
4-Methyl-9-(toluene-4-sulfonyl)-*9H*-β-carboline-3-carboxylic acid methyl ester (S13)



S13

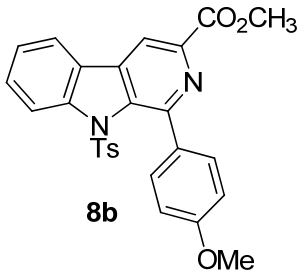
Following **Method C** the carbolines **13** and **S13** were obtained in a ratio of 40:60 (83% yield). The regioisomers were separated by flash chromatography (4:1 petroleum ether/ethyl acetate). β-carboline **S13** was obtained as a solid, R_f 0.12 (SiO_2, petroleum ether/ethyl acetate = 4:1 (v/v)), mp 195-197 °C (petroleum ether/CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.46 (d, J = 8.7 Hz, 1H), 8.20 (d, J = 7.2 Hz, 1H), 7.74 (d, J = 8.5 Hz, 2H), 7.66-7.70 (m, 1H), 7.45-7.50 (m, 1H), 7.14 (d, J = 8.5 Hz, 2H), 4.04 (s, 3H), 3.02 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 167.0 (s), 145.9 (s), 142.2 (s), 139.2 (s), 135.3 (s), 134.4 (s), 134.2 (s), 132.3 (s), 130.4 (s), 130.1 (d), 129.7 (d), 126.7 (d), 125.0 (s), 124.7 (d), 124.3 (d), 115.2 (d), 52.9 (q), 21.7 (q), 16.4 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 2950, 1716, 1594, 1436, 1370, 1308, 1296, 1251, 1228, 1172, 1071, 936. FD-MS: m/z (%) = 394 (100) [M^+]. HRMS [ESI (+)]: Mass calcd for $C_{21}H_{18}N_2NaO_4S$ $[M+Na]^+$, 417.0879; found 417.0858.

1-Phenyl-9-(toluene-4-sulfonyl)-*9H*-β-carboline-3-carboxylic acid methyl ester (8a)



8a

Following **Method A** β-carboline **8a** (59 mg, 0.13 mmol, 61% yield) was obtained after flash chromatography (3:1 petroleum ether/ethyl acetate) as a colourless solid; R_f 0.29 (1:2 petroleum ether/diethyl ether), mp 212-213 °C (pentane/CH_2Cl_2). **Method C** provided a mixture of β-(**8a**) and γ-carboline in a ratio of 92:8 (95% yield) from which isomeric pure β-carboline **8a** was obtained after flash chromatography.
^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18 (s, 3H), 4.04 (s, 3H), 6.84 (d, J = 8.4 Hz, 2H), 6.97 (d, J = 8.4 Hz, 2H), 7.37-7.56 (m, 4H), 7.61 (dt, J = 7.9 Hz, J = 1.2 Hz, 1H), 7.84 (d, J = 7.9 Hz, 2H), 8.08-8.15 (m, 2H), 8.28 (d, J = 8.4 Hz, 2H), 8.42 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8 (s), 151.2 (s), 144.8 (s), 143.8 (s), 142.4 (s), 140.3 (s), 139.2 (s), 136.6 (s), 132.0 (s), 130.2 (d), 128.9 (d), 128.7 (d), 128.3 (d), 126.8 (s), 126.7 (d), 126.0 (d), 121.4 (d), 119.4 (d), 114.5 (d), 53.0 (q), 21.4 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 2952, 2925, 1714, 1614, 1593, 1564, 1378, 1359, 1275, 1240, 1173, 1149, 933. MS: m/z (%) = 456 (100) [M^+]. HRMS: Mass calcd for $C_{26}H_{21}N_2O_4S$ $[(M+H)]^+$, 457.1222; found 457.1222.

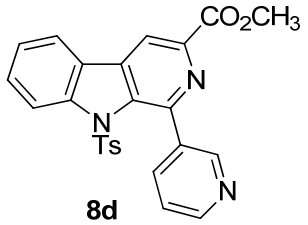


8b

Following **Method B** β-carboline **8b** (60 mg, 0.12 mmol, 60% yield) was obtained after flash chromatography (8:2 pentane/ethyl acetate) as a colourless solid; R_f 0.16 (8:2 pentane/diethyl ether).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (S, 1H), 8.27 (d, *J* = 4.3 Hz, 1H), 8.12 (d, *J* = 8.8 Hz, 2H), 7.81 (d, J = 7.7 Hz, 1H), 7.59 (dd, *J* = 7.3 Hz, *J* = 3.9 Hz, 1H), 7.41 (dd, *J* = 7.3 Hz, *J* = 3.9 Hz, 1H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.96 (d, *J* = 8.36 Hz, 2H), 6.83 (d, *J* = 8.20 Hz, 2H), 4.04 (s, 3H), 3,89 (s, 3H), 2,18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9 (s), 160.5 (s), 151.1 (s), 144.9 (s), 143.9 (s), 142.5 (s), 139.4 (s), 136.4 (s), 132.9 (s), 131.9 (s), 130.1 (d), 130.2 (s), 129.0 (d), 127.1 (s), 126.8 (d), 126.1 (d), 121.4 (d), 119.6 (d), 114.0 (d), 113.8 (d), 55.3 (q), 53.0 (q), 21.5 (q); HRMS [ESI (+)]: Mass clacd for $C_{27}H_{23}N_2O_5S$ (M+H), 487.1328; found, 487.1311.

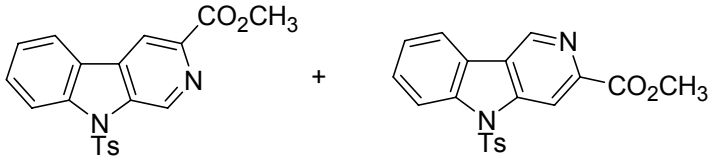
1-Pyridin-3-yl-9-(toluene-4-sulfonyl)-*9H*-β-carboline-3-carboxylic acid methyl ester (8d)



8d

Following **Method A** β-carboline **8d** (37 mg, 0.08 mmol, 70% yield) was obtained after flash chromatography (1:2 petroleum ether/ethyl acetate) as a solid; R_f 0.39 (ethyl acetate), mp 210-215 °C (pentane/CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.20 (s, 3H), 4.06 (s, 3H), 6.86 (d, *J* = 8.2 Hz, 2H), 6.96 (d, *J* = 8.2 Hz, 2H), 7.43-7.50 (m, 2H), 7.66 (dt, *J* = 7.8 Hz, *J* = 1.2 Hz, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 8.31 (d, *J* = 8.2 Hz, 1H), 8.41 (dt, *J* = 7.9 Hz, *J* = 1.9 Hz, 1H), 8.48 (s, 1H), 8.66 (dd, *J* = 4.9 Hz, *J* = 1.5 Hz, 1H), 9.27 (d, *J* = 1.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5 (s), 149.7 (d), 149.6 (d), 148.2 (s), 145.2 (s), 144.0 (s), 142.3 (s), 139.5 (s), 136.8 (s), 136.3 (s), 135.9 (d), 131.7 (s), 130.6 (d), 129.1 (d), 126.7 (d), 126.6 (d), 126.3 (d), 123.2 (s), 121.5 (d), 119.5 (d), 115.2 (d), 53.1 (q), 21.5 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 2957, 2899, 2836, 2232, 2161, 1620, 1595, 1482, 1373, 1229, 1172, 1081, 1028, 920. FD-MS: m/z (%) = 457 (100) [M^+]; Anal calcd for $C_{25}H_{19}N_3O_4S$ (457.50 g mol^{-1}): C, 65.63; H, 4.19; N, 9.18; Found: C, 65.59; H, 4.22; N, 9.06.

9-(Toluene-4-sulfonyl)-*9H*-β-carboline-3-carboxylic acid methyl ester (10) and
5-(Toluene-4-sulfonyl)-5*H*-γ-carboline-3-carboxylic acid methyl ester (S10)

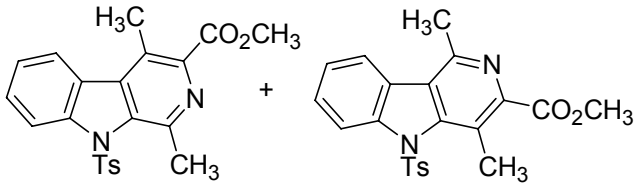


10 **S10**

Following **Method A** the carbolines **10** and **S10** were obtained in a ratio of 30:70 (72 mg, 0.19 mmol, 70% yield). The regioisomers **10** and **S10** were separated by flash chromatography (1:1 petroleum ether/ethyl acetate).
Following **Method C** the carbolines **10** and **S10** were obtained in a ratio of 40:60 (38 mg, 0.10 mmol, 40% yield).
β-carboline **10** was obtained as a solid, R_f 0.29 (1:1 petroleum ether/ethyl acetate), mp 166-167 °C (pentane/CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (s, 1H), 8.71 (s, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.06 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.67-7.72 (m, 1H), 7.45-7.50 (m, 1H), 7.15 (d, *J* = 8.2 Hz, 2H), 4.06 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.9 (s), 146.0 (s), 142.3 (s), 139.6 (s), 137.0 (d), 136.5 (s), 134.6 (s), 133.3 (s), 130.8 (d), 130.2 (d), 126.8 (d), 124.9 (d), 124.1 (s), 122.0 (d), 117.1 (d), 115.4 (d), 53.1 (q), 21.7 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 3066, 3013, 2946, 1716, 1622, 1595, 1437, 1289, 1173. FD-MS: m/z (%) = 380 (100) [M^+].

γ-carboline **S10** was obtained as a solid, R_f 0.12 (1:1 petroleum ether/ethyl acetate), mp 206-207 °C (pentane/CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 9.04 (s, 1H), 8.34 (d, J = 8.6 Hz, 1H), 8.07 (d, J = 7.7 Hz, 1H), 7.78 (d, J = 8.4 Hz, 2H), 7.62 (m, 1H), 7.46 (m, 1H), 7.17 (d, J = 8.4 Hz, 2H), 4.08 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9 (s), 146.0 (s), 145.6 (s), 143.8 (s), 142.6 (d), 139.3 (s), 134.7 (s), 130.2 (d), 129.6 (d), 126.8 (d), 125.0 (d), 124.7 (s), 123.2 (s), 121.3 (d), 115.1 (d), 111.7 (d), 53.2 (q), 21.7 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 2948, 1719, 1589, 1457, 1433, 1294, 1170, 971. MS: m/z (%) = 380 (100) [M$^+$]. Anal calcd for $C_{20}H_{16}N_2O_4S$ (380.08 g mol^{-1}): C, 63.14; H, 4.24; N, 7.36; Found, C, 63.08; H, 4.30; N, 7.22.

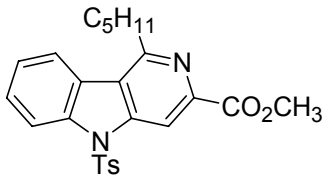
1,4-Dimethyl-9-(toluene-4-sulfonyl)-*9H*-β-carboline-3-carboxylic acid methyl ester (11) and 1,4-Dimethyl-5-(toluene-4-sulfonyl)-5*H*-γ-carboline-3-carboxylic acid methyl ester (S11)



11 **S11**

Following **Method B** the carbolines **11** and **S11** were obtained in a ratio of 50:50 (69 mg, 0.17 mmol, 87% yield). The regioisomers **11** and **S11** were separated by flash chromatography (2:1 petroleum ether/ethyl acetate).
β-carboline **11** was obtained as a solid, R_f 0.26 (2:1 petroleum ether/ethyl acetate), mp 166-167 °C (pentane/CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 8.4 Hz, 1H), 7.96 (d, J = 8,0 Hz, 1H), 7.54-7.61 (m, 1H), 7.36-7.43 (m, 1H), 7.09 (d, J = 8.4 Hz, 2H), 6.91 (d, J = 8.4 Hz, 2H), 4,03 (s, 3H), 3.07 (s, 3H), 2.81 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2 (s), 147.9 (s), 145.0 (s), 142.2 (s), 137.1 (s), 137.0 (s), 132.6 (s), 129.3 (d), 129.2 (d), 127.9 (s), 126.9 (d), 126.1 (s), 125.9 (d), 123.8 (d), 119.4 (d), 53.0 (q), 25.7 (q), 21.6 (q), 15.8 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 2950, 2930, 1727, 1596, 1573, 1439, 1422, 1372, 1172, 1140. MS: m/z (%) = 409 (100) [M+H]$^+$. Anal calcd for $C_{22}H_{20}N_2O_4S$ (408.11 g mol^{-1}): C, 64.69; H, 4.94; N, 6.86; Found, C, 64.54; H, 4.93; N, 6.84.
γ-carboline **S11** was obtained as a solid, R_f 0.10 (1:2 pentane/diethyl ether), mp 167-168 °C (pentane/CH_2Cl_2).
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.3 Hz, 1H), 7.82 (d, J = 7.8 Hz, 1H), 7.48-7.54 (m, 1H), 7.36-7.23 (m, 1H), 7.07 (d, J = 8.3 Hz, 2H), 6.90 (d, J = 8.3 Hz, 2H), 4.04 (s, 3H), 2.91 (s, 3H), 2.87 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2 (s), 150.1 (s), 147.7 (s), 147.1 (s), 145.0 (s), 142.1 (s), 132.6 (s), 129.1 (d), 128.2 (d), 127.2 (s), 126.9 (d), 126.4 (s), 126.1 (d), 124.6 (s), 122.7 (d), 119.3 (d), 53.0 (q), 23.7 (q), 21.6 (q), 18.9 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 2949, 2925, 1739, 1721, 1597, 1565, 1438, 1366, 1323, 1173, 1059. MS: m/z (%) = 409 (100) [M+H]$^+$. Anal calcd for $C_{22}H_{20}N_2O_4S$ (408.11 g mol^{-1}): C, 64.69; H, 4.94; N, 6.86; Found, C, 64.63; H, 5.02; N, 6.75.

1-Pentyl-5-(toluene-4-sulfonyl)-*5H*-γ-carboline-3-carboxylic acid methyl ester (15)

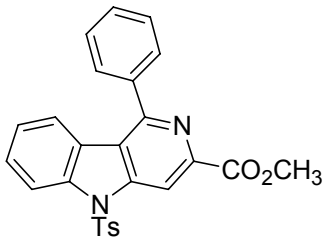


15

Following **Method B** γ-carboline **15** (32 mg, 0.07 mmol, 52% yield) was obtained after flash chromatography (3:1 petroleum ether/ethyl acetate) as a solid; R_f 0.13 (2:1 pentane/diethyl ether), mp 167-169 °C (pentane/CH_2Cl_2).

^{1}H NMR (600 MHz, $CDCl_3$): δ 8.96 (s, 1H), 8.43 (d, J = 8.6 Hz, 1H), 8.04 (d, J = 7.9 Hz, 1H), 7.79 (d, J = 8.5 Hz, 2H), 7.62 (dt, J = 7.9 Hz, J = 1.2 Hz, 1H), 7.50 (dt, J = 7.5 Hz, J = 0.9 Hz, 1H), 7.18 (d, J = 8.3 Hz, 2H), 4.08 (s, 3H), 3.35 (m, 2H), 2.31 (s, 3H), 1.80-1.86 (m, 2H), 1.51 (m, 2H), 1.39 (m, 2H), 0.91 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (s), 158.1 (s), 145.8 (s), 144.6 (s), 144.1 (s), 139.0 (s), 134.6 (s), 130.0 (d), 128.6 (d), 126.7 (d), 124.8 (d), 123.6 (s), 123.0 (d), 122.0 (s), 114.8 (d), 109.7 (d), 53.08 (q), 37.4 (t), 32.1 (t), 28.1 (t), 22.6 (t), 21.6 (q), 14.0 (q); IR (KBr): $\tilde{\nu}$ /cm^{-1} = 2951, 2924, 1714, 1372, 1333, 1176. MS [ESI (+)]: m/z = 473 [M+Na]$^+$, 923 [2 M+Na]$^+$. HRMS (ESI (+)]: Mass calcd for $C_{25}H_{26}N_2O_4SNa$ [M+Na]$^+$, 473.1511; found, 473.1507.

1-Phenyl-5-(toluene-4-sulfonyl)-*5H*-γ-carboline-3-carboxylic acid methyl ester (17)



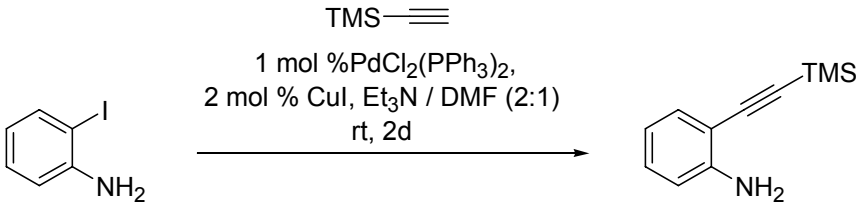
17

Following **Method B** γ-carboline **17** (61 mg, 0.13 mmol, 67% yield) was obtained after flash chromatography (4:1 petroleum ether/ethyl acetate) as a solid; R_f 0.14 (2:1 pentane/diethyl ether), mp 198-199 °C (pentane/$CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.1 (s, 1H), 8.38 (d, J = 8.4 Hz, 1H), 7.84 (d, J = 8.4 Hz, 2H), 7.64-7.68 (m, 2H), 7.51-7.59 (m, 4H), 7.42 (d, J = 7.5 Hz, 1H), 7.17-7.23 (m, 3H), 4.07 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (s), 155.2 (s), 145.9 (s), 144.9 (s), 144.4 (s), 139.1 (s), 139.0 (s), 134.6 (s), 130.1 (s), 129.3 (d), 129.0 (d), 128.7 (d), 126.7 (s), 124.2 (s), 123.4 (s), 123.0 (d), 122.1 (s), 114.5 (d), 110.1 (d), 53.1 (q), 21.6 (q); IR (KBr): $\tilde{\nu}$ /cm^{-1} = 2951, 1740, 1715, 1564, 1371, 1229, 1174, 752, 667. MS [ESI (+)]: m/z = 457 [M+H]$^+$. Anal calcd for $C_{26}H_{20}N_2O_4S$ (456.51 g mol^{-1})**:** C, 68.41; H, 4.42; N, 6.14; Found: C, 68.31; H, 4.42; N, 6.03.

II. Synthesis of the marine alkaloid eudistomin U (22)

2-Trimethylsilanylethynyl-phenylamine (S18a)

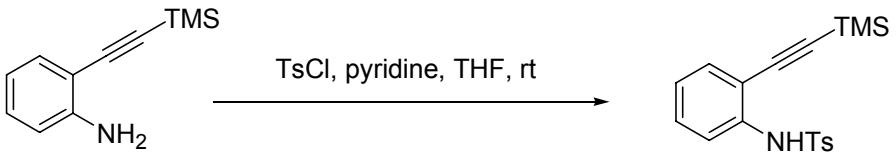


18 **S18a**

Into a flame dried Schlenk tube were introduced 2-iodoaniline (**18**) (5.90 g, 26.94 mmol), $PdCl_2(PPh_3)_2$ (188 mg, 0.27 mmol),CuI (102 mg, 0.54 mmol), dry Et_3N (62.8 mL), dry DMF (27 mL), and trimethylsilylacetylene (5.20 mL, 35.02 mmol). The Schlenk tube was sealed with a screw cap and the resulting reaction mixture stirred at room temperature for 1 day. Thereafter, water and CH_2Cl_2 were added and the product extracted with CH_2Cl_2 and washed with brine. The combined organic layers were dried with $MgSO_4$ filtered and concentrated. Flash chromatography (9:1 cyclohexane/ethyl acetate) of the obtained residue afforded **S18a** (5.04 g, 26.67 mmol, 99% yield) as an oil, R_f 0.43.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.3 Hz, 1H), 7.12 (dd, J = 6.6 Hz, J = 1.2 Hz, 2H), 6.67 (dd, J =6.6 Hz, J = 1.2 Hz, 2H), 4.23 (bs, 2H), 0.28 (s, 9H); ^{13}C NMR (100MHz, $CDCl_3$) δ 148.4 (s), 132.4 (d), 130.0 (d), 117.9 (d), 114.3 (d), 108.0 (s), 102.0 (s), 99.9 (s), 0.3 (q); MS [ESI (+)]: m/z (%) = 190 (100, $[M+H]^+$), 168 (10), 162 (20), 91 (80).

4-Methyl-*N*-(2-trimethylsilanylethynyl-phenyl)-benzenesulfonamide (S18b):

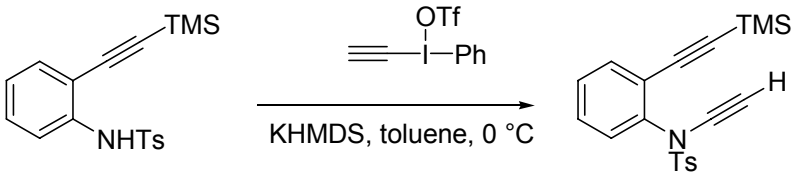


S18a **S18b**

Into a round bottom flask were introduced aniline **S18a** (5.04 g, 26.60 mmol), tosylchloride (11.14 g, 58.60 mmol), and dry pyridine (88 mL). The resulting reaction mixture was stirred at room temperature until completion. Thereafter, water and CH_2Cl_2 were added and the product was extracted with CH_2Cl_2. The combined layers were washed with brine, dried with $MgSO_4$, filtered and concentrated. Flash chromatography (9:1 pentane/diethyl ether) afforded **S18b** (8.600 g, 25.07 mmol, 94% yield) as colourless solid; mp 81 °C pentane/CH_2Cl_2, R_f 0.4.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 8.3 Hz, 1H), 7.30-7.24 (m, 2H), 7.20 (s, 1H), 7.19 (d, J = 8.3 Hz, 2H), 7.00 (m, 1H), 2.36 (s, 3H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1 (s), 138.2 (s), 136.2 (s), 132.1 (d), 129.9 (d), 129.7 (d), 127.4 (d), 124.4 (d), 119.8 (d), 114.3 (s), 102.4 (s), 99.6 (s), 21.6 (q), 0.0 (q); IR (neat): $\tilde{\nu}$ /cm^{-1} = 3258, 2959, 2158, 1488, 1450, 1400, 1339, 1246, 1170, 1095, 909; MS [ESI (+)]: m/z (%) = 366 (100, $[M+Na]^+$). HRMS [ESI (+)]: Mass calcd for $C_{18}H_{21}NNaO_2SSi$, 366.0960, found 366.0975; Anal. calcd for $C_{18}H_{21}NO_2SSi$ (343.52): C, 62.94; H, 6.16; N, 4.08. Found: C, 62.70, H, 6.06, N, 3.95.

***N*-Ethynyl-4-methyl-*N*-(2-trimethylsilanylethynyl-phenyl)-benzenesulfonamide (1)**

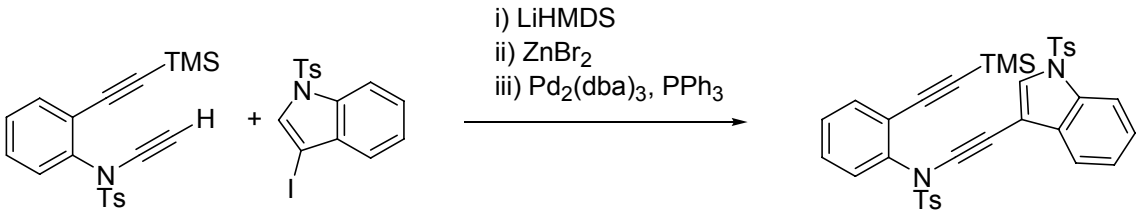


S18b **1**

To a solution of **S18b** (715 mg, 2.08 mmol) in dry toluene (100 mL) was added KHMDS (5 mL of a 0.5 M solution in toluene) at 0 °C. After 30 min of stirring at 0 °C, a solution of ethynylphenyliodonium triflate (1.18 g, 3.12 mmol, 1.5 equiv.) in dry CH_2Cl_2 (70 mL) was added. The reaction mixture was stirred at room temperature overnight. Concentration of the solution was followed by addition of CH_2Cl_2 and water. The product was extracted with CH_2Cl_2 and the combined organic layers were dried with $MgSO_4$, filtrated and concentrated under reduced pressure. Purification of the obtained residue by flash chromatography (9:1 petroleum ether/diethyl ether) afforded **1** (648 mg, 85% yield) as a pale yellow solid, mp 92–93 °C (pentane/$CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J = 8.2 Hz, 2 H), 7.49 (m, 1 H), 7.33-7.26 (m, 5 H), 2.82 (s, 1 H), 2.45 (s, 3 H), 0.17 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 144.8 (s), 138.7 (s), 134.7 (s), 133.9 (d), 129.6 (d), 129.1 (d), 129.0 (d), 128.9 (d), 128.5 (d), 123.0 (s), 101.5 (s), 99.8 (s), 75.6 (s), 58.9 (s), 21.7 (q), -0.3 (q).

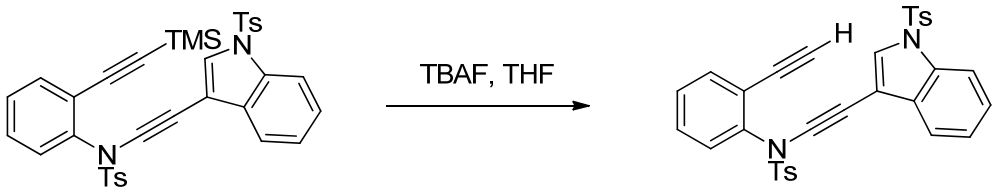
IR (KBr): $\tilde{\nu}_{max}$/cm^{-1} = 3269, 2961, 2894, 2163, 2125, 1596, 1480, 1366, 1252, 1212, 1174, 1120, 1077, 1037, 929. MS (EI, 70 eV): *m/z* (%) = 367 (M^+, 16), 352 (12), 302 (33), 288 (17), 212 (100), 197 (12), 184 (16), 182 (21), 91 (14). Anal calcd for $C_{20}H_{21}NO_2SSi$ (367.53 g mol^{-1}): C, 65.36; H, 5.76; N, 3.81; Found: C, 65.21; H, 5.76; N, 3.86.



1 **S19**

Freshly prepared LiHMDS (3.3 mL of a 0.5 *M* solution in THF) was added to a solution of **1** (400 mg, 1.09 mmol) in dry THF at −78 °C and stirred for 40 min at −40 °C. Thereafter, a solution of $ZnBr_2$ (270 mg, 1.20 mmol) in THF (0.8 mL) was added and the reaction mixture was stirred without cooling for 20 min and then transferred via canula to a solution of $Pd_2(dba)_3$ (50 mg, 0.05 mmol), PPh_3 (55 mg, 0.21 mmol) and 3-iodo-1-tosylindole (519 mg, 1.30 mmol) in dry THF (10 mL). After stirring for 12 h at room temperature, water was added and the aqueous phase extracted with Et_2O. The combined organic layers were washed with brine, dried with $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the obtained residue with flash chromatography (petroleum ether/ ethyl acetate) afforded **S19** (635 mg, 0.99 mmol, 92% yield) as a solid, R_f 0.56 (2:1 petroleum ether/ethyl acetate), mp 61 °C.

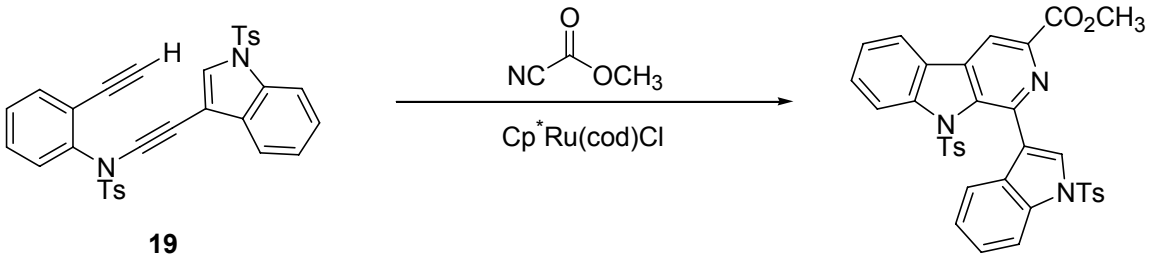
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 7.1 Hz, 2H), 7.74 (d, J = 7.1 Hz, 2H), 7.63 (s, 1H), 7.53 (m, 2H), 7.29-7.36 (m, 6H), 7.18-7.27 (m, 3H), 2.46 (s, 3H), 2.32 (s, 3H), 0.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7 (s), 145.3 (s), 139.7 (s), 135.4 (s), 135.2 (s), 134.7 (d), 131.6 (s), 130.4 (d), 130.2 (d), 129.7 (d), 129.5 (d), 129.4 (d), 129.0 (d), 128.8 (d), 127.4 (d), 125.8 (d), 124.0 (d), 123.5 (s), 121.3 (d), 114.0 (d), 105.5 (s), 101.9 (s), 100.5 (s), 86.6 (s), 62.0 (s), 22.2 (q), 22.1 (q), 0.2 (q); IR (KBr): $\tilde{\nu}$/cm^{-1} = 3065, 2959, 2361, 2242, 2161, 1711, 1597, 1483, 1447, 1374 , 1174, 1129, 1089, 860. MS: m/z (%) = 636 (100, M^+).



S19 **19**

TBAF (1.3 mL of 1 *M* solution in THF) was added to a solution of **S19** (639 mg, 0.99 mmol) in THF (50 mL) at 0 °C. After 20 min, the reaction mixture was quenched by the addition of diethyl ether and water. The aqueous phase was extracted with diethyl ether. The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated under reduced pressure. The obtained residue was purified by flash chromatography (3:1 heptane/diethyl ether) to afford yne-ynamide **19** (474 mg, 0.84 mmol, 85% yield) as a colourless solid; R_f 0.38 (2:1 heptane/ethyl acetate), mp 80-82 °C (pentane/CH_2Cl_2).

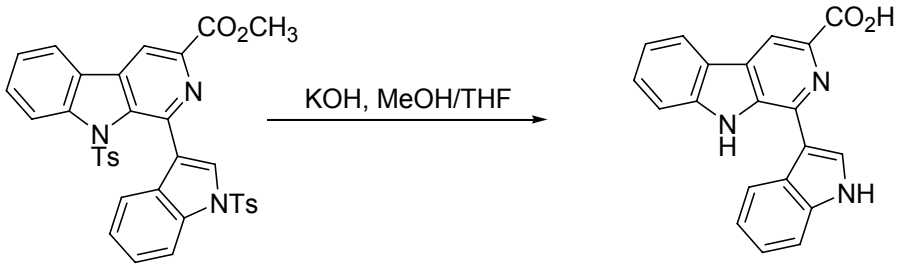
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 8.4 Hz, 1H), 7.76 (d, J = 8.4 Hz, 4H), 7.68 (s, 1H), 7.50-7.56 (m, 2H), 7.30-7.41 (m, 6H), 7.18-7.27 (m, 3H), 3.06 (s, 1H), 2.46 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3 (s), 145.1 (s), 139.7 (s), 134.8 (s), 134.3 (d), 134.1 (s), 131.2 (s), 130.0 (d), 129.70 (d), 129.65 (d), 129.2 (d), 129.1 (d), 128.6 (d), 126.9 (d), 125.4 (d), 123.6 (d), 122.1 (s), 120.6 (d), 113.5 (d), 104.6 (s), 86.0 (s), 83.2 (d), 78.9 (s), 61.3 (s), 21.7 (q), 21.6 (q); IR (KBr): $\tilde{\nu}$ /cm^{-1} = 3276, 2242, 1596, 1483, 1447, 1374, 1189, 1174, 1130, 1088, 959. MS: m/z (%) = 564.1 (100) [M^+]; HRMS [ESI (+)]: Mass calcd for $C_{32}H_{25}N_2O_4S_2$ ($M+H^+$), 565.1256, found, 565.1252.



19 **20**

To a solution of Cp*RuCl(cod) (9.8 mg, 0.026 mmol, 10 mol%) in dry CH_2Cl_2 (1 mL) was added methyl cyanoformiate (410 µL, 0.52 mmol). Thereafter, a solution of yne-ynamide **19** (40 mg, 0.07 mmol) in CH_2Cl_2 (10 mL) was added over a period of 1-2 h using a syringe-pump at 40 °C. The reaction was completed within 2 h (monitored by TLC). The solvent was removed by evaporation under reduced pressure and the resulting residue was purified by column chromatography (2:1 heptane/ethyl acetate) to provide β-carboline **20** (43 mg, 94%) as a solid; R_f 0.26, mp 224-225 °C (pentane/CH_2Cl_2).

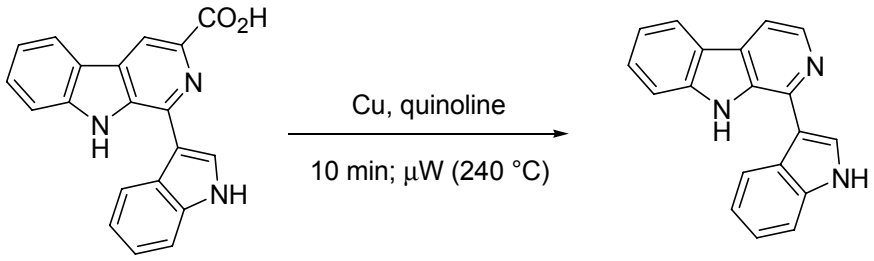
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 1H), 8.39 (s, 1H), 8.29-8.36 (m, 2H), 7.98-8.04 (m, 1H), 7.93 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 7.6 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.35-7.40 (m, 2H), 7.23 (d, J = 8.3 Hz, 2H), 6.92 (d, J = 8.3 Hz, 2H), 6.83 (d, J = 8.3 Hz, 2H), 4.05 (s, 3H), 2.30 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9 (s), 145.3 (s), 145.14 (s), 145.09 (s), 143.9 (s), 142.7 (s), 139.4 (s), 137.1 (s), 135.2 (s), 135.0 (s), 131.9 (s), 130.4 (d), 130.0 (d), 129.5 (s), 129.1 (d), 127.9 (d), 127.5 (d), 127.1 (s), 126.8 (d), 126.3 (d), 124.9 (d), 124.1 (d), 122.2 (d), 121.5 (d), 121.3 (s), 119.9 (d), 114.4 (d), 113.4 (d), 53.1 (q), 21.64 (q), 21.60 (q); IR (KBr): $\tilde{\nu}$ /cm^{-1} = 2954, 2924, 1708, 1615, 1596, 1575, 1371, 1176, 1268. MS: m/z (%) = 649.2 (100) [M^+], 650.2 (39) [M^+]. HRMS [ESI (+)]: Mass calcd for $C_{35}H_{28}N_3O_6S_2$ ($M+H^+$), 650.1420, found, 650.1415. Anal. calcd for $C_{35}H_{27}N_3O_6S_2$ (649.74 g mol^{-1})**:** C, 64.70; H, 4.19; N, 6.47; found, C, 64.39; H, 4.28; N, 6.46.



20 **21**

KOH (200 mg, 3.6 mmol) was added to a solution of **20** (233 mg, 0.36 mmol) in MeOH/THF (6 mL, 1:1 5 (v/v)) and the resulting mixture was stirred at 80 °C for 3 h. Thereafter the solvent was removed under reduced pressure and the obtained residue was taken up in water. The aqueous phase was washed with CH_2Cl_2 and adjusted to pH 6 with conc. HCl. The resulting precipitate was isolated by filtration and dried under reduced pressure to give **21** (113 mg, 0.35 mmol, 96% yield) as a solid, mp 299-300 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ 11.80 (s, 1H), 11.69 (s, 1H), 8.85 (d, J = 7.6 Hz, 1H), 8.76 (s, 1H), 8.43 (d, J = 2.5 Hz, 1H), 8.38 (d, J = 8.0 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.56-7.63 (m, 1H), 7.53 (d, J = 8.0 Hz, 1H), 7.29-7.35 (m, 1H), 7.21-7.27 (m, 1H), 7.15-7.21 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.4 , 141.3, 139.7, 136.9, 136.6, 133.3, 128.5, 128.3, 126.7, 126.3, 122.9, 122.4, 121.8, 121.6, 120.4, 120.3, 114.3, 112.9, 112.6, 111.6; IR (neat): $\tilde{\nu}$ /cm^{-1} = 3136, 1623, 1581, 1534, 1499, 1445, 13364, 1339, 1265, 1227, 1103, 1018, 733. MS: m/z (%) = 327 (100) [M$^+$]; HRMS [ESI (+)]: Mass calcd for $C_{20}H_{13}N_3O_2Na$ (M+Na), 350.0905, found, 350.0901.



21 **22**

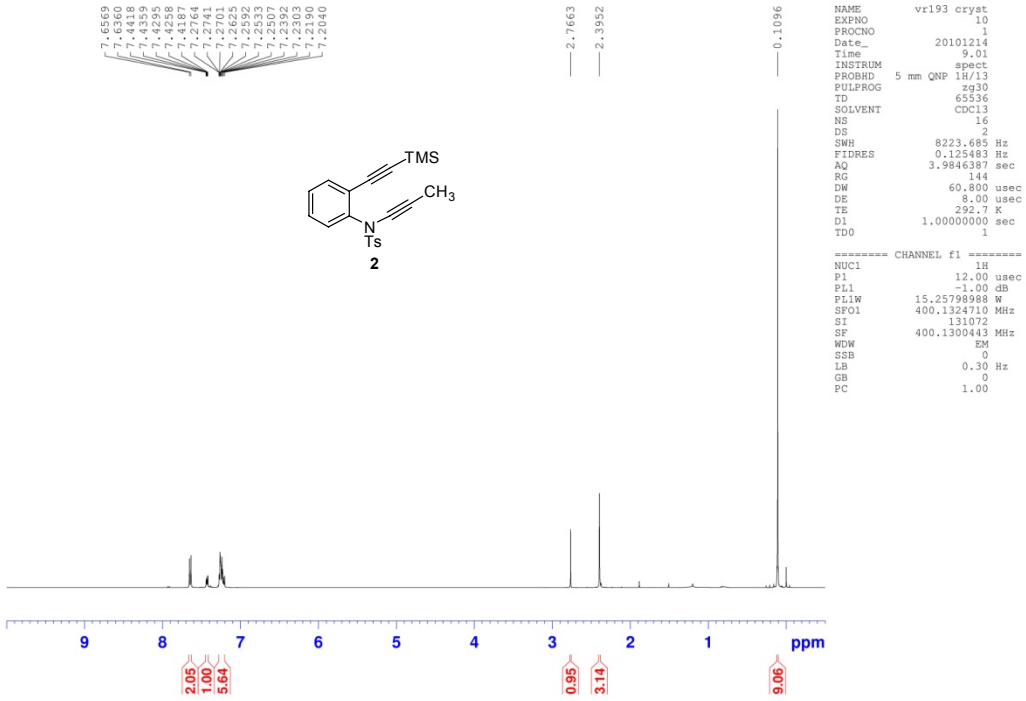
A solution of **21** (26 mg, 0.08 mmol) in quinoline (5 mL) containing copper powder (1.5 mg) was sealed under nitrogen in a reaction vial and irradiated in a microwave reactor for 10 min at 240 °C. Thereafter, the solvent was removed under reduced pressure and the obtained residue purified by column chromatography (Al_2O_3, 1:1 petroleum ether/ethyl acetate) to afford eudistomin U (**22**) (21 mg, 0.07 mmol, 88%) as a solid, R_f 0.29 (Al_2O_3, 1:1 petroleum ether/ethyl acetate), mp 235-236 °C.

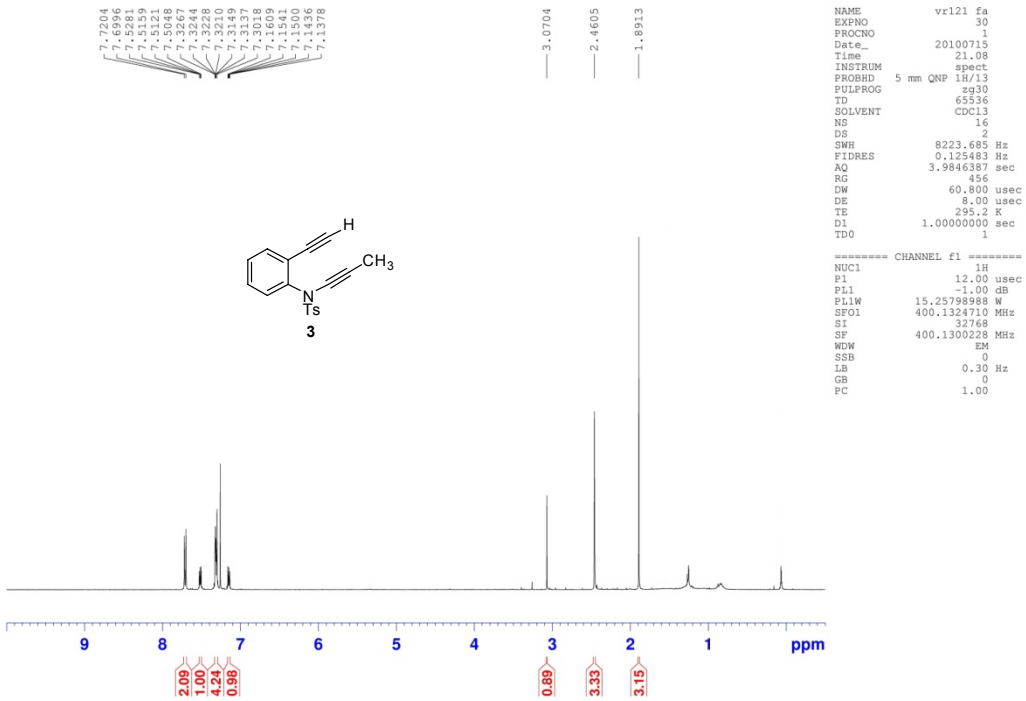
^{1}H NMR (400 MHz, DMSO-d_6): δ 11.70 (s, 1H), 11.28 (s, 1H), 8.56 (d, J = 8.0 Hz, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.29 (d, J = 2.5 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 5.2 Hz, 1H), 7.69 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 7.9 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.21 (t, J = 7.9 Hz, 1H), 7.13 (t, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 140.7 (s), 140.4 (s), 138.0 (d), 136.5 (s), 132.0 (s), 128.1 (s), 127.7 (d), 126.2 (s), 125.9 (d), 122.4 (d), 122.0 (d), 121.3 (d), 121.2 (s), 119.8 (d), 119.4 (d), 113.3 (s), 112.4 (d), 111.5 (d), 111.5 (d); ^{15}N NMR (40.5 MHz, DMSO-d_6) δ 114.0 (NH), 135.7 (NH), 298.8; IR (neat): $\tilde{\nu}$ /cm^{-1} = 3406, 3056, 2967, 2927, 1721, 1624, 1563, 1454, 1235, 1042, 739. MS: m/z (%) = 283 (100) [M$^+$].

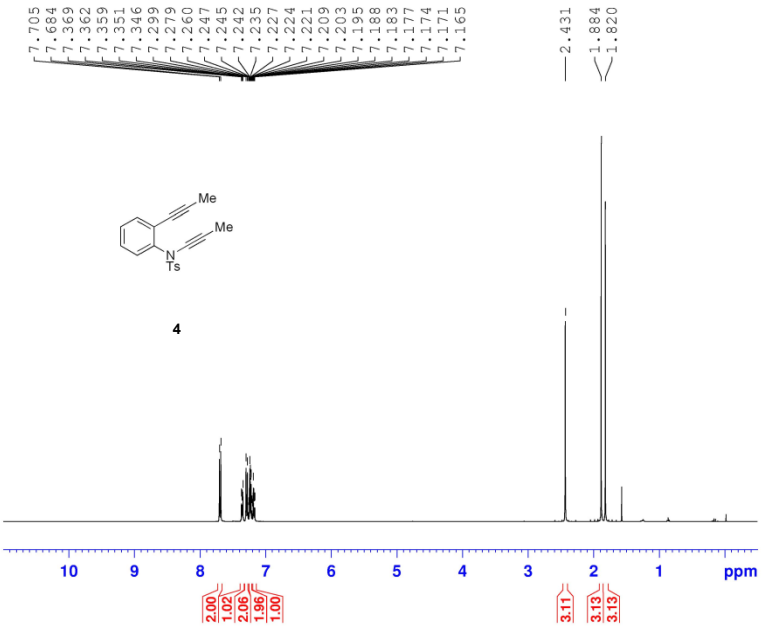
Spectroscopic and analytical data are in agreement with those reported from eudistomin U isolated from the carribean ascidian *lissoclinum fragile*.[4]

[4] A. Badre, A. Boulanger, E. Abou-Mansour, B. Banaigs, G. Combaut, C. Francisco, *J. Nat. Prod.*, 1994, **57**, 528.

IV Selected NMR spectra





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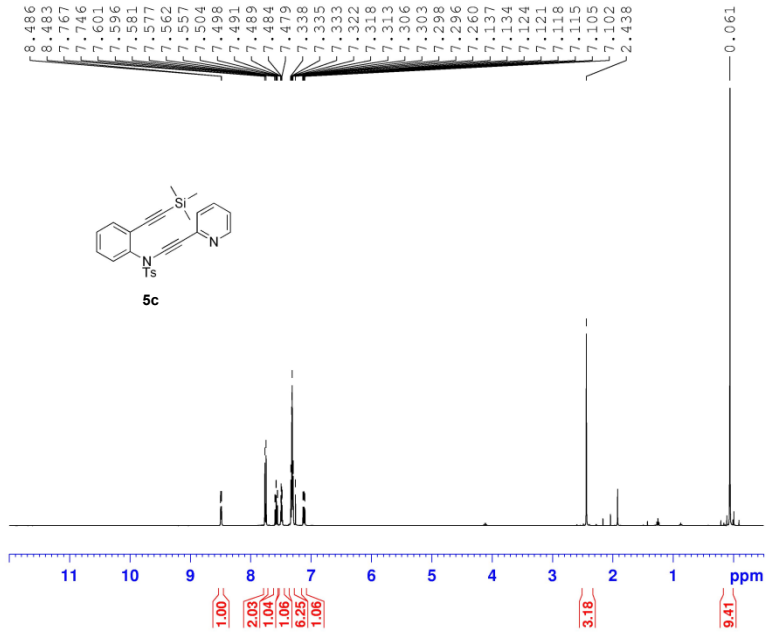


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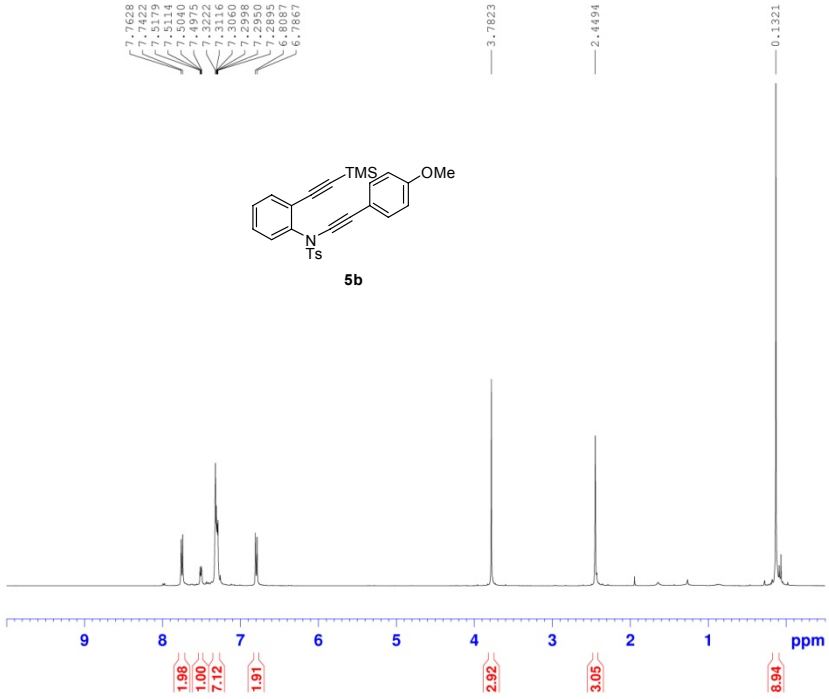


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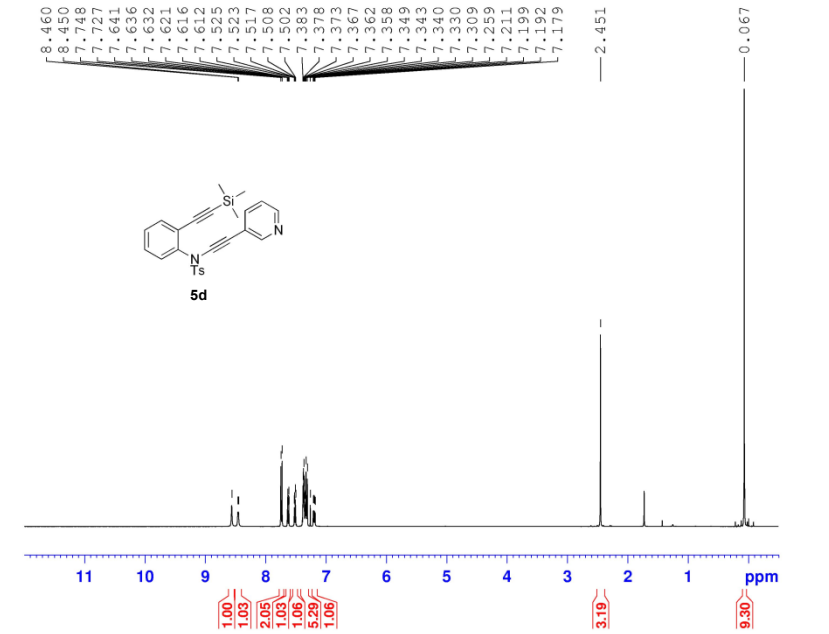


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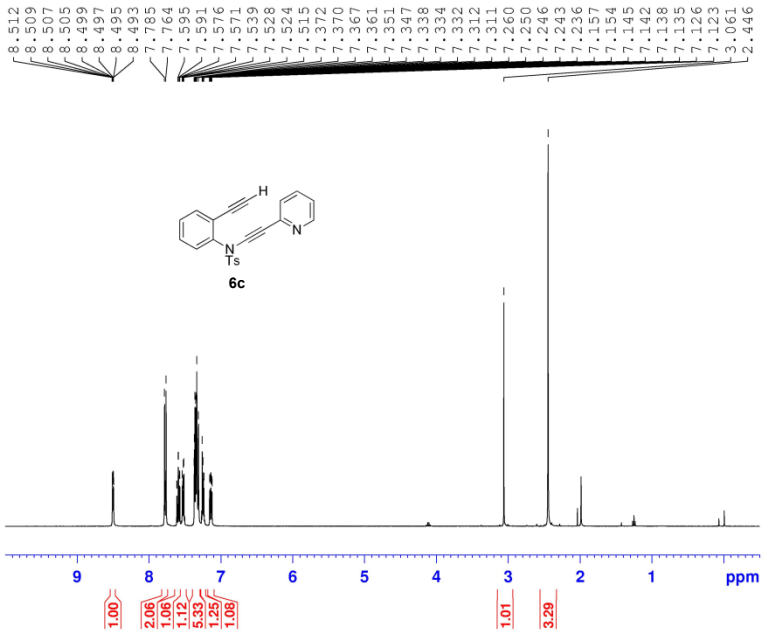

6c

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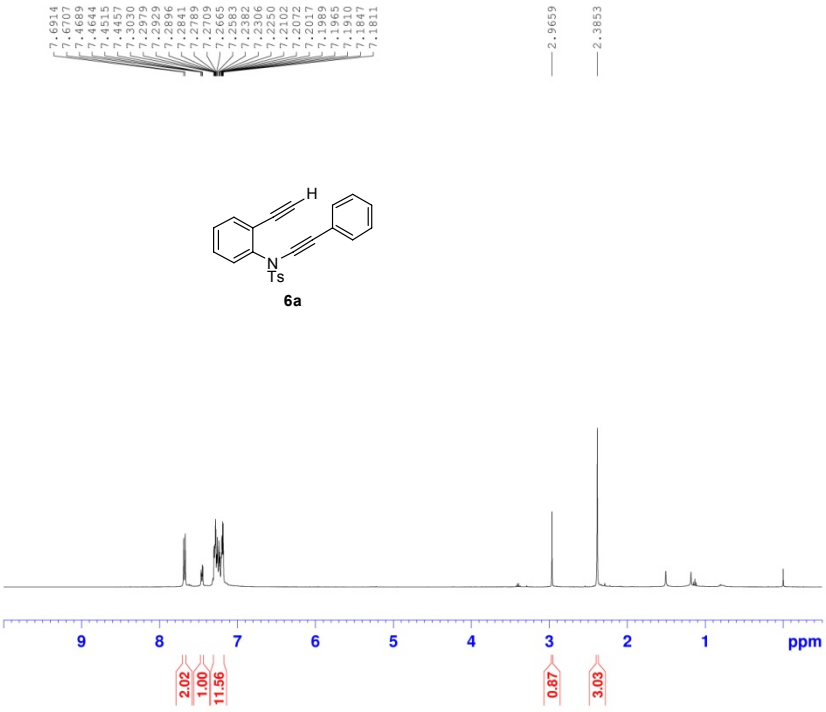

6a

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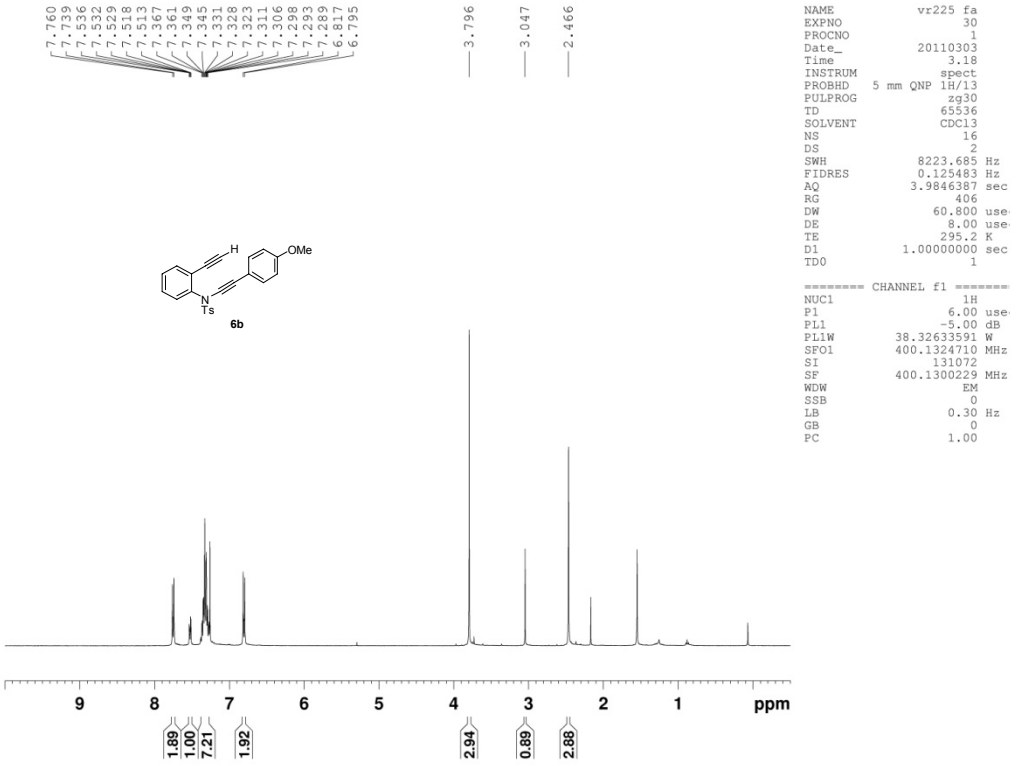


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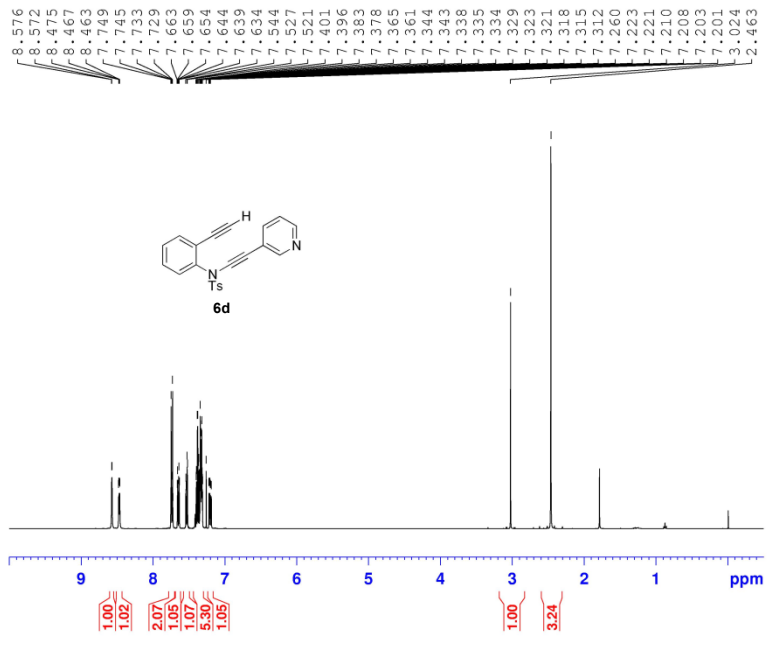


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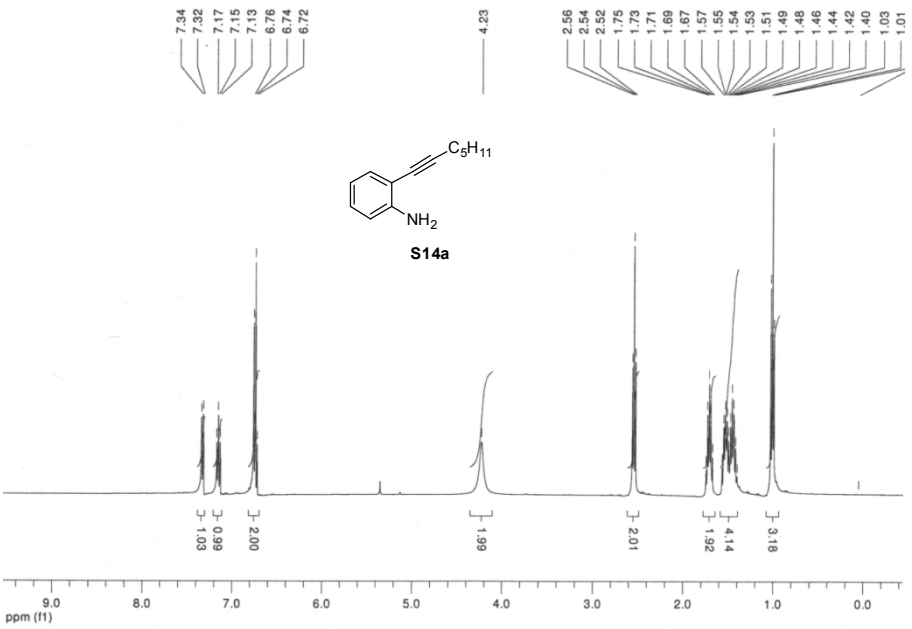
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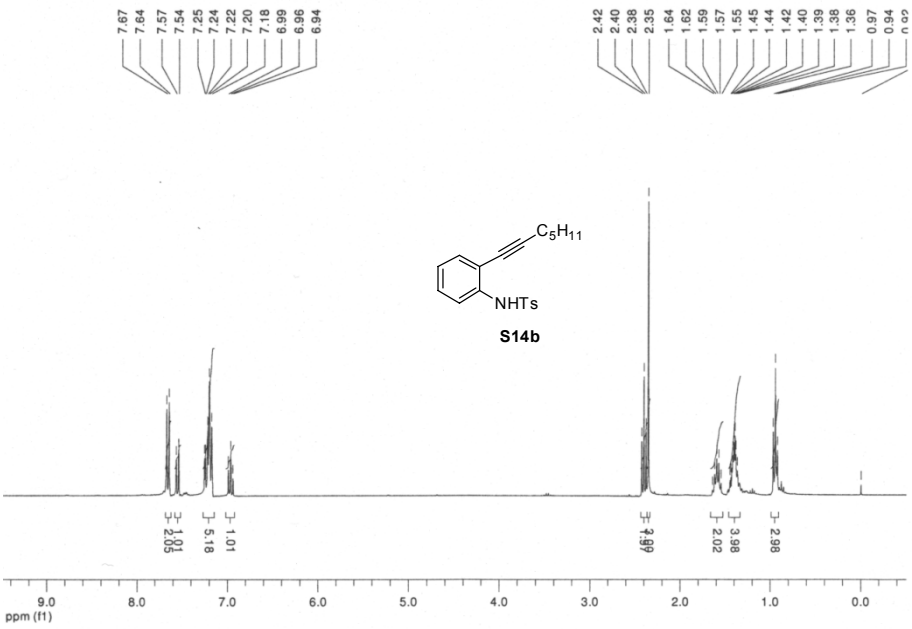
S14a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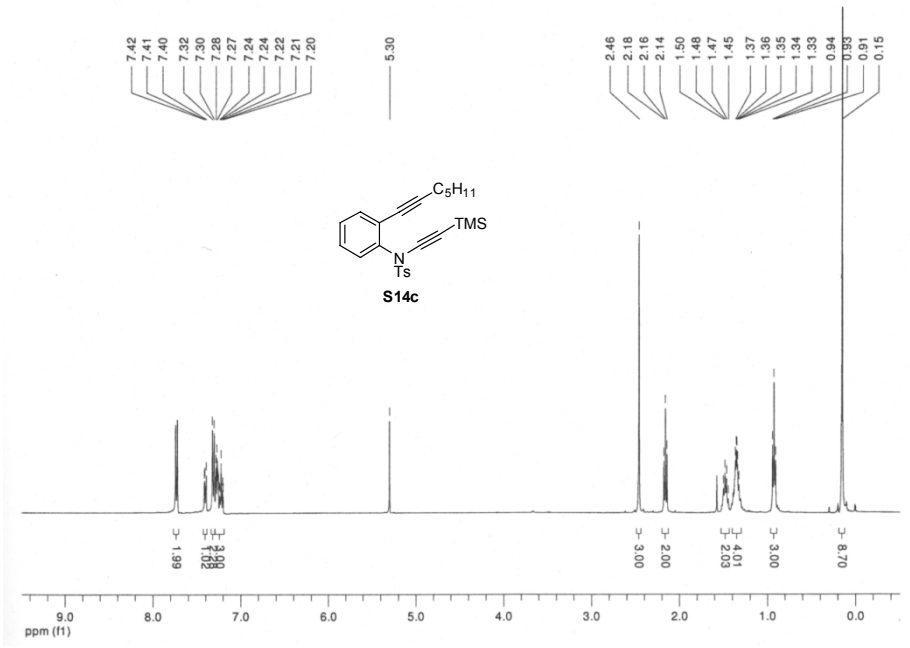
S14b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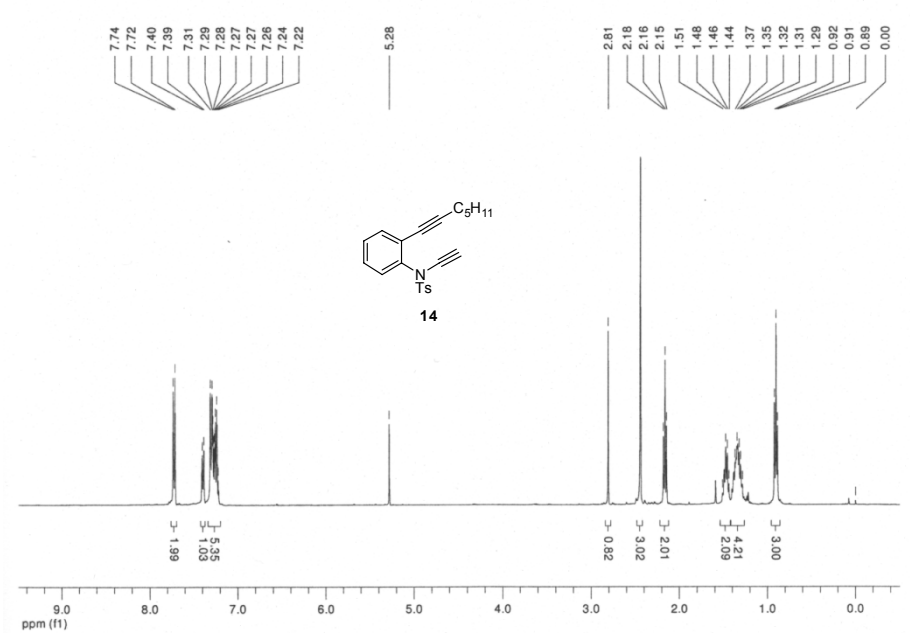
ppm (f1)


7.74
7.72
7.40
7.39
7.31
7.29
7.28
7.27
7.27
7.26
7.24
7.22
5.28
2.81
2.18
2.16
2.15
1.51
1.48
1.46
1.44
1.37
1.35
1.32
1.31
1.29
0.92
0.91
0.89
0.00
C5H11
N
Ts
14
1.99
5.35
1.03
0.82
3.02
2.01
4.21
2.09
3.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
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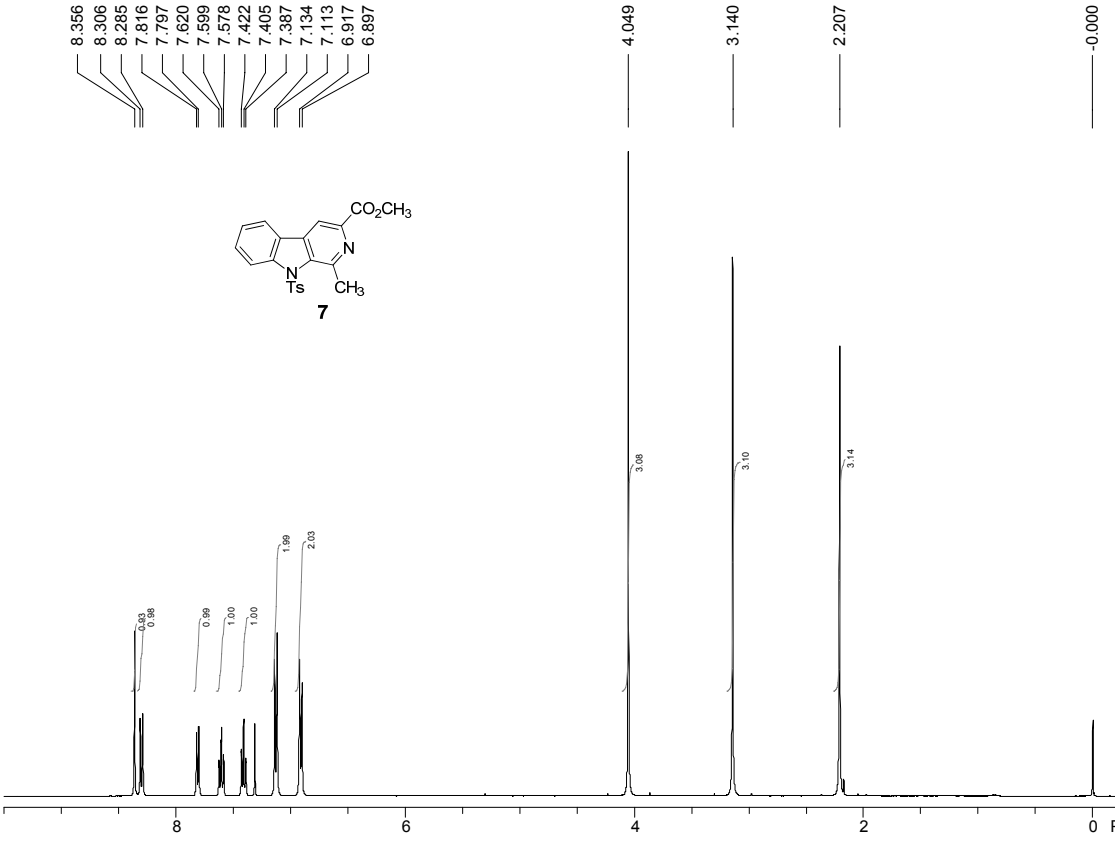
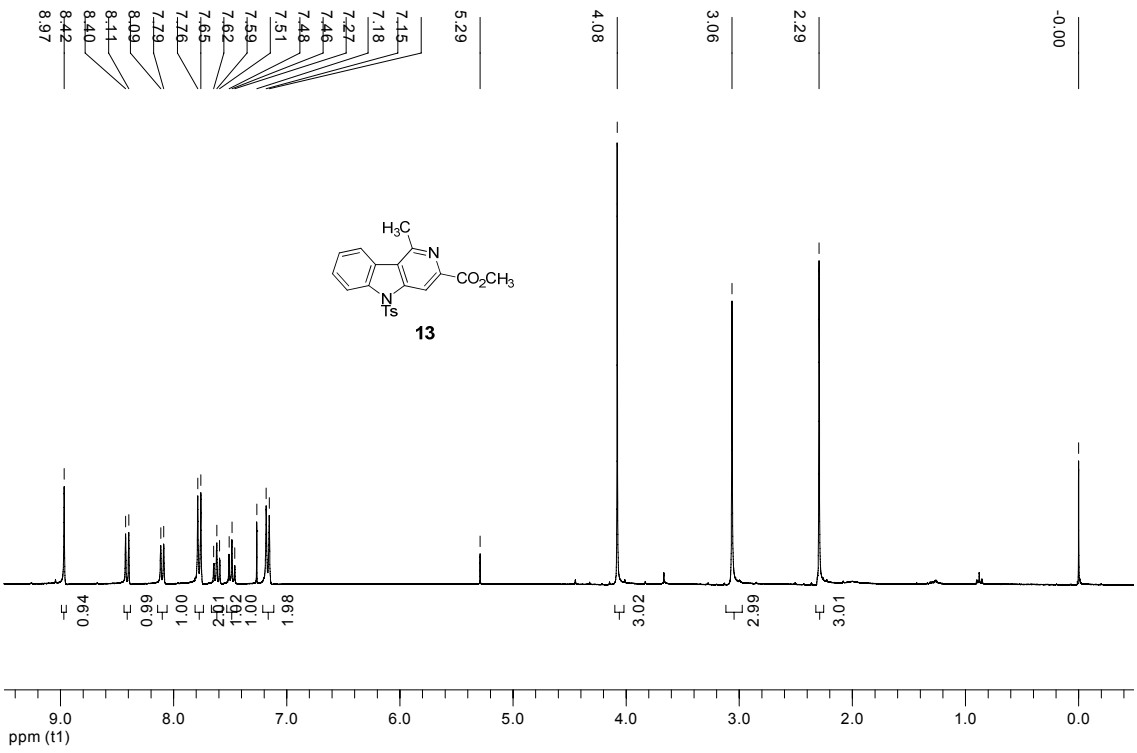
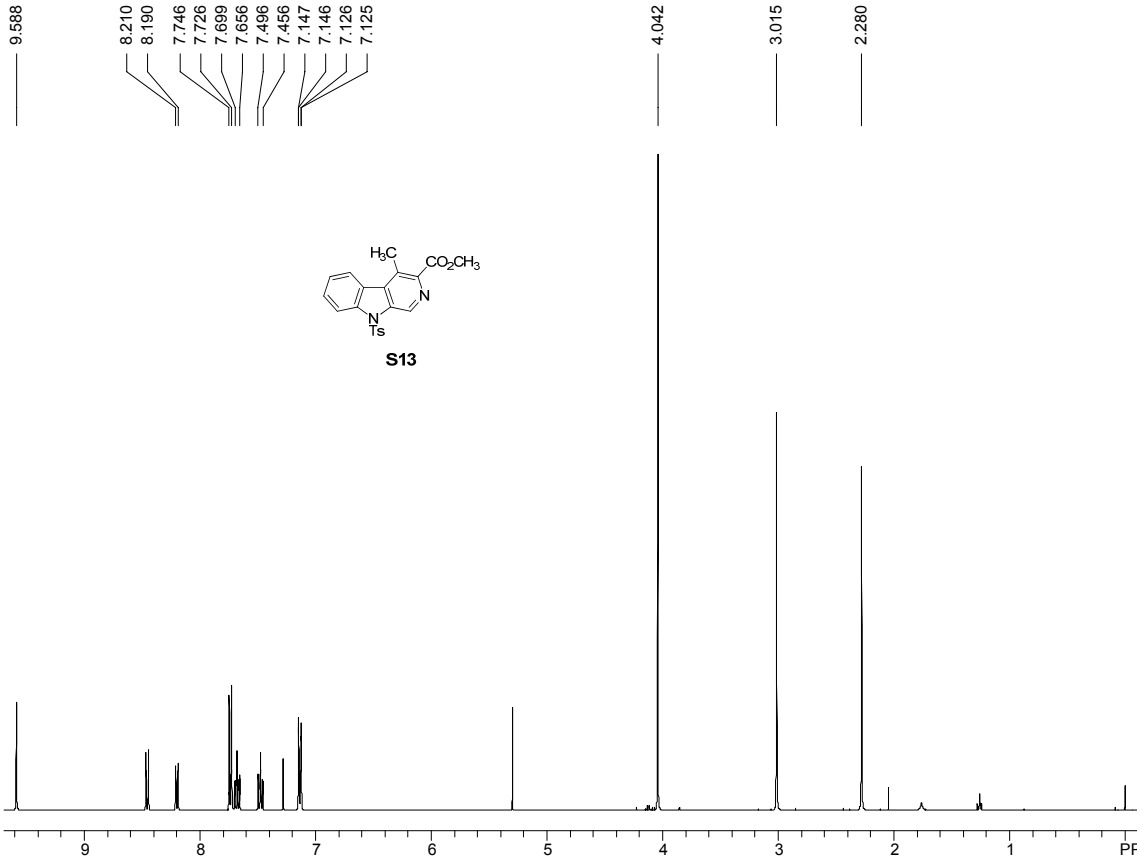
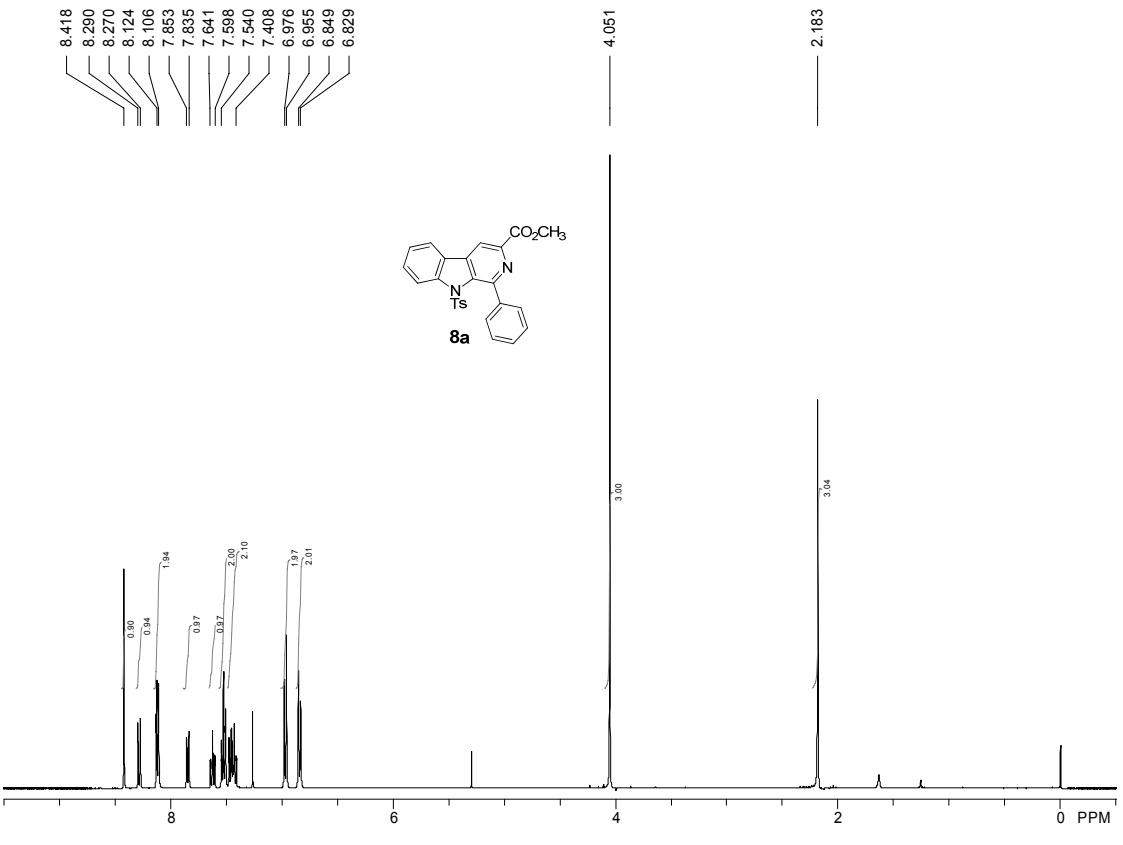
0.0
ppm (f1)


8.356
8.306
8.285
7.816
7.797
7.620
7.599
7.578
7.422
7.405
7.387
7.134
7.113
6.917
6.897
4.049
3.140
2.207
-0.000
CO2CH3
N
N
Ts
CH3
7
3.08
3.10
3.14
1.99
2.03
0.83
0.98
0.99
1.00
1.00
8
6
4
2
0

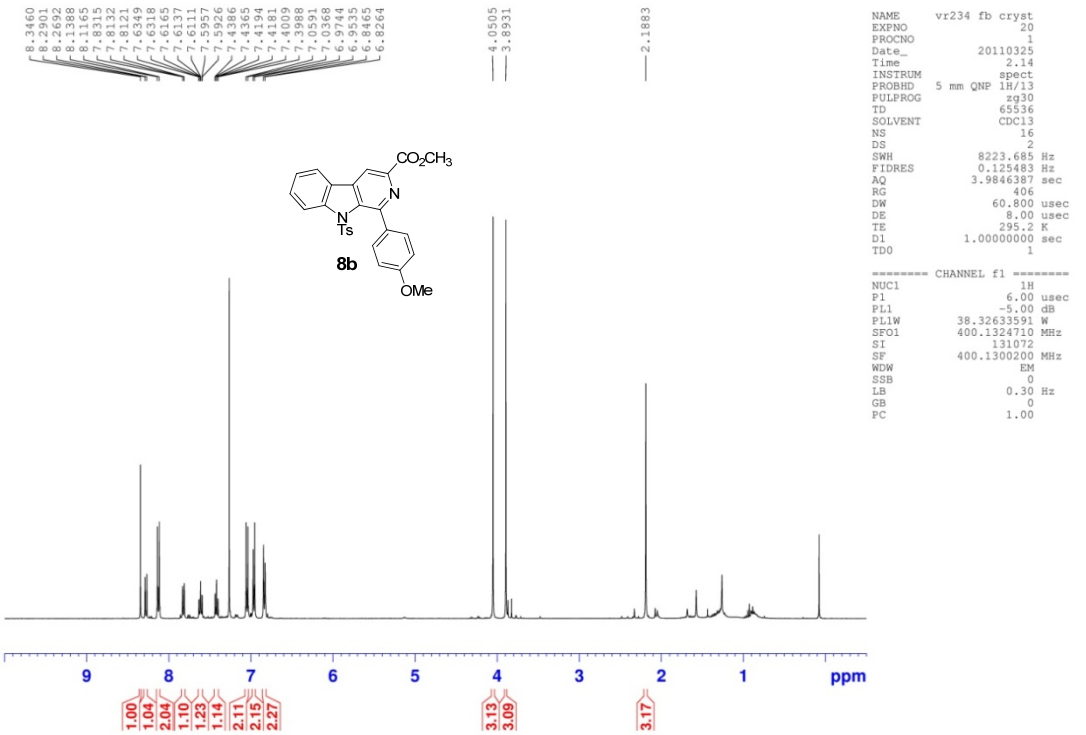

8.97
8.42
8.40
8.11
8.09
7.79
7.76
7.65
7.62
7.59
7.51
7.48
7.46
7.27
7.18
7.15
5.29
4.08
3.06
2.29
-0.00
H3C
N
CO2CH3
N
Ts
13
0.94
0.99
1.00
2.01
1.22
1.00
1.98
3.02
2.99
3.01
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

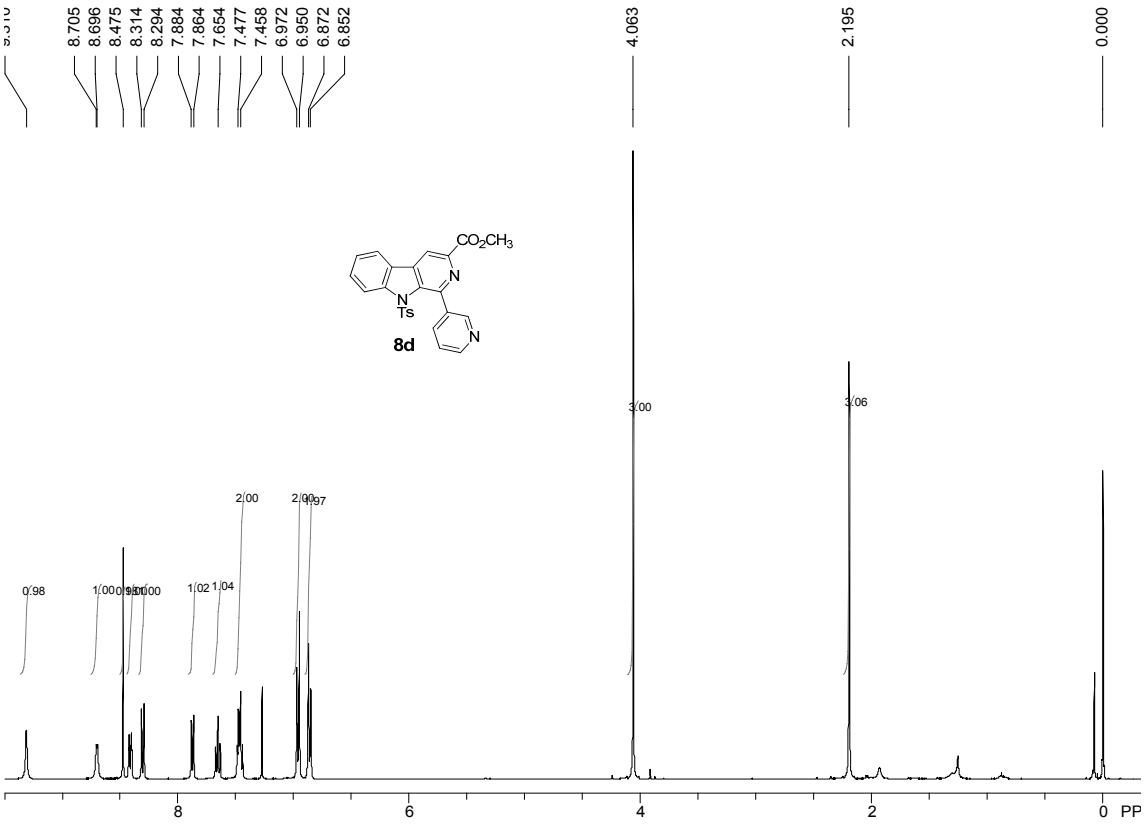

9.588
8.210
8.190
7.746
7.726
7.699
7.656
7.496
7.456
7.147
7.146
7.126
7.125
4.042
3.015
2.280
H3C
CO2CH3
N
N
Ts
9
8
7
6
5
4
3
2
1
PF

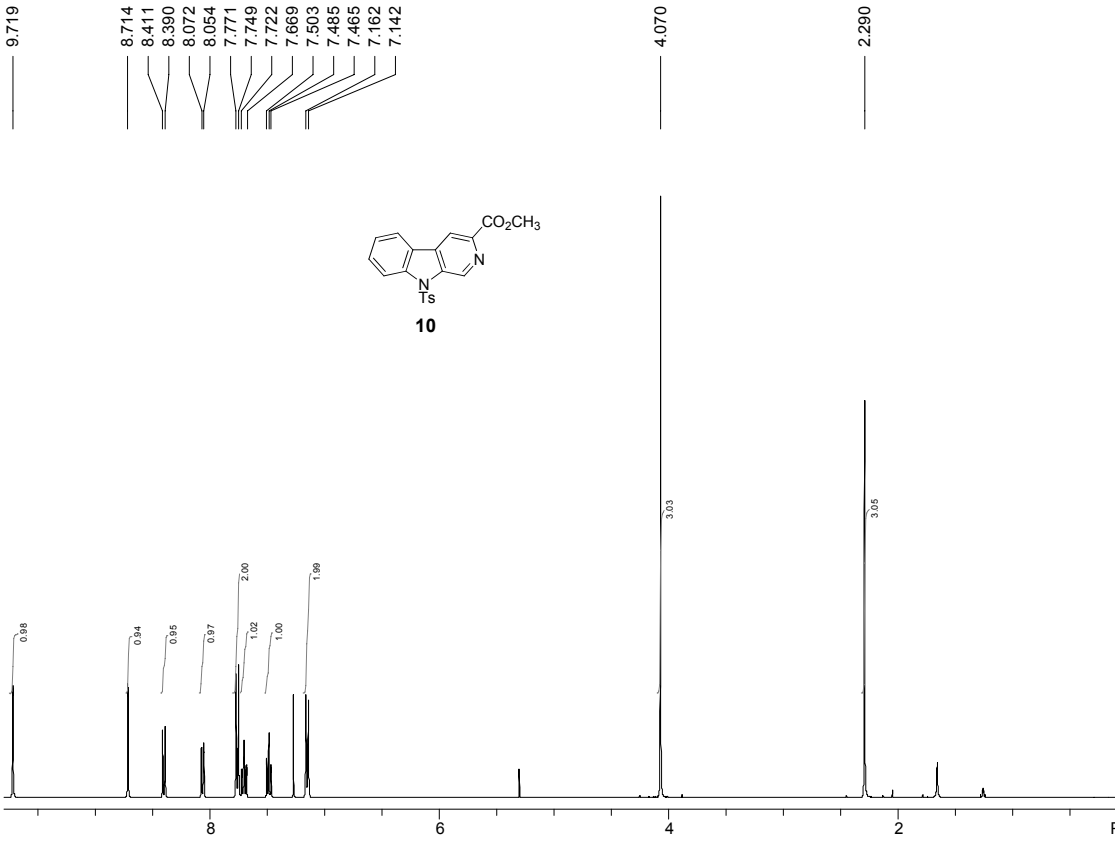
S13

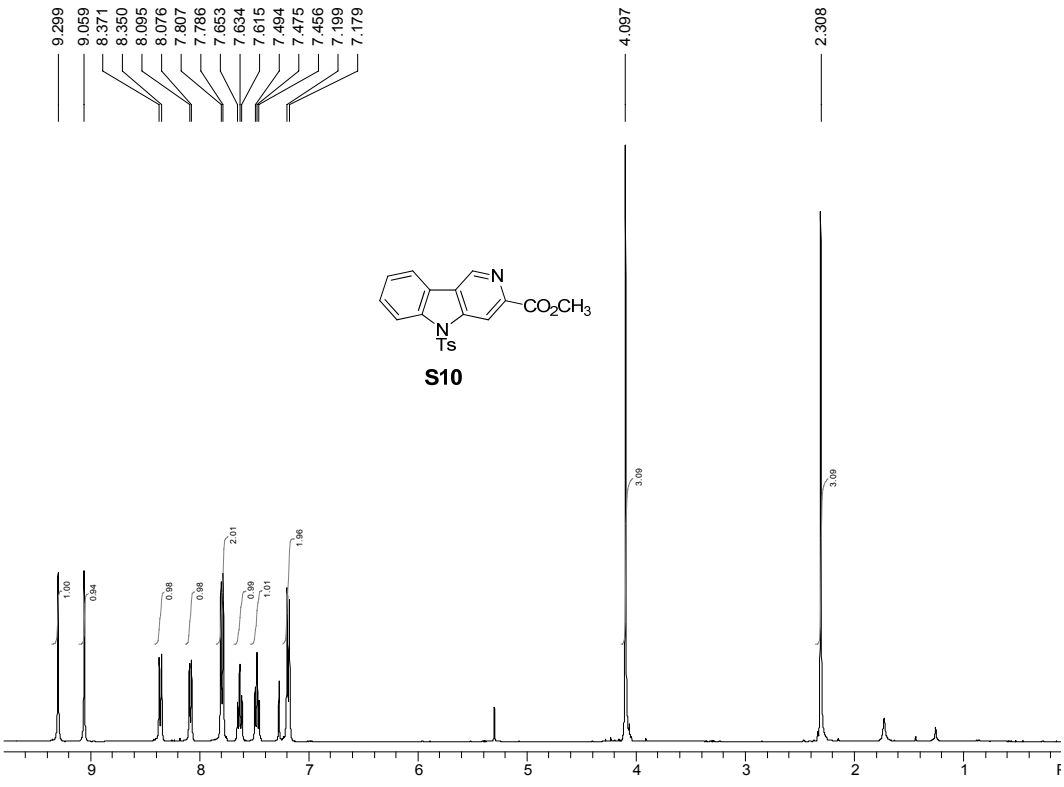

8.418
8.290
8.270
8.124
8.106
7.853
7.835
7.641
7.598
7.540
7.408
6.976
6.955
6.849
6.829
4.051
2.183
CO2CH3
N
N
Ts
3.00
3.04
0.90
0.94
1.94
0.97
0.97
2.00
2.10
1.97
2.01
8
6
4
2
0 PPM

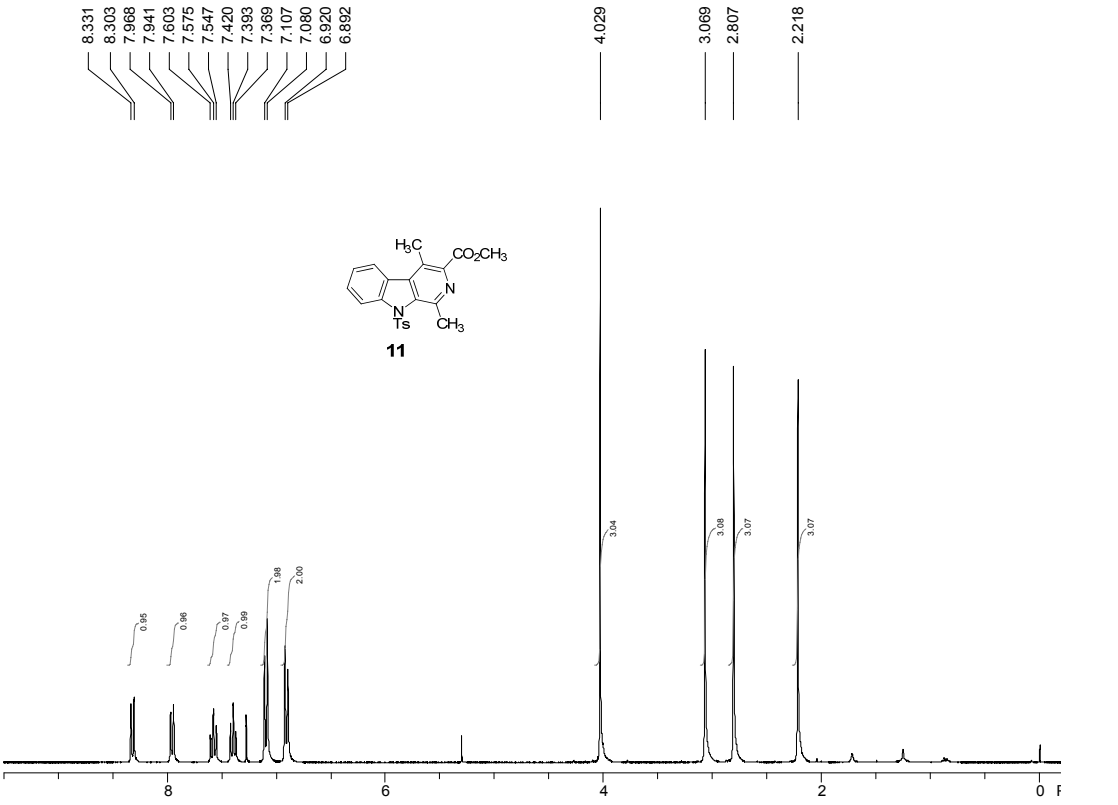
8a

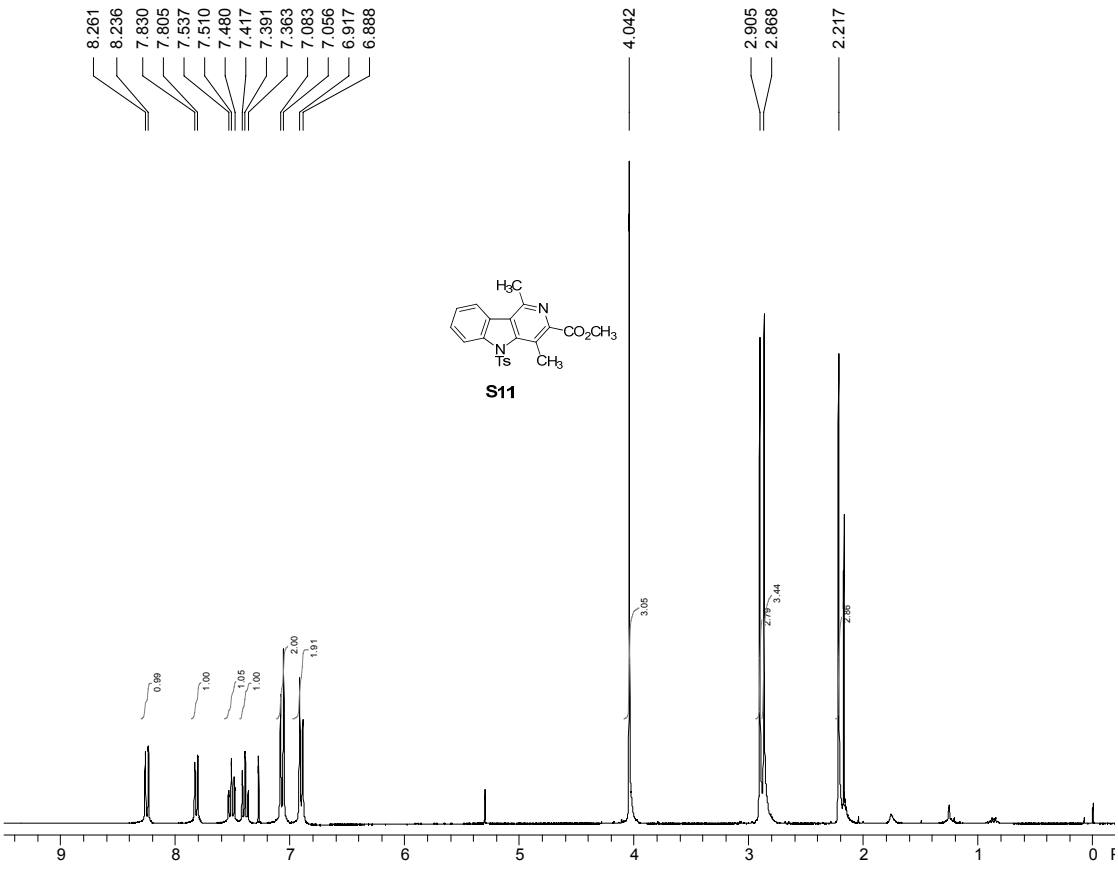

8.3460
8.2901
8.2692
8.1388
8.1165
7.8315
7.8132
7.8121
7.6349
7.6318
7.6165
7.6137
7.6111
7.5957
7.5926
7.4366
7.4195
7.4181
7.4009
7.3988
7.0591
7.0368
6.9744
6.9535
6.8465
6.8264
4.0505
3.8931
2.1883
CO2CH3
N
N
Ts
8b
OMe
NAME vr234 fb cryst
EXPNO 20
PROCNO 1
Date_ 20110325
Time 2.14
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 406
DW 60.800 usec
DE 8.00 usec
TE 295.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 6.00 usec
PL1 -5.00 dB
PL1W 38.32633591 W
SFO1 400.1324710 MHz
SI 131072
SF 400.1300200 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
ppm
1.00
1.04
2.04
1.10
1.23
1.14
2.11
2.15
2.27
3.13
3.09
3.17


8.705
8.696
8.475
8.314
8.294
7.884
7.864
7.654
7.477
7.458
6.972
6.950
6.872
6.852
4.063
2.195
0.000
CO2CH3
N
N
Ts
N
8d
3.00
3.06
2.00
2.00
0.98
1.00
1.02
1.04
8
6
4
2
0
PP


9.719
8.714
8.411
8.390
8.072
8.054
7.771
7.749
7.722
7.669
7.503
7.485
7.465
7.162
7.142
4.070
2.290
CO2CH3
N
N
Ts
10
0.98
0.94
0.95
0.97
2.00
1.02
1.00
1.99
3.03
3.05
8
6
4
2


9.299
9.059
8.371
8.350
8.095
8.076
7.807
7.786
7.653
7.634
7.615
7.494
7.475
7.456
7.199
7.179
4.097
2.308
N
CO2CH3
N
Ts
S10
1.00
0.94
0.98
0.98
2.01
0.99
1.01
1.96
3.09
3.09
9
8
7
6
5
4
3
2
1


8.331
8.303
7.968
7.941
7.603
7.575
7.547
7.420
7.393
7.369
7.107
7.080
6.920
6.892
4.029
3.069
2.807
2.218
H3C
CO2CH3
N
Ts
N
CH3
11
0.95
0.96
0.97
0.99
1.98
2.00
3.04
3.08
3.07
3.07
8
6
4
2
0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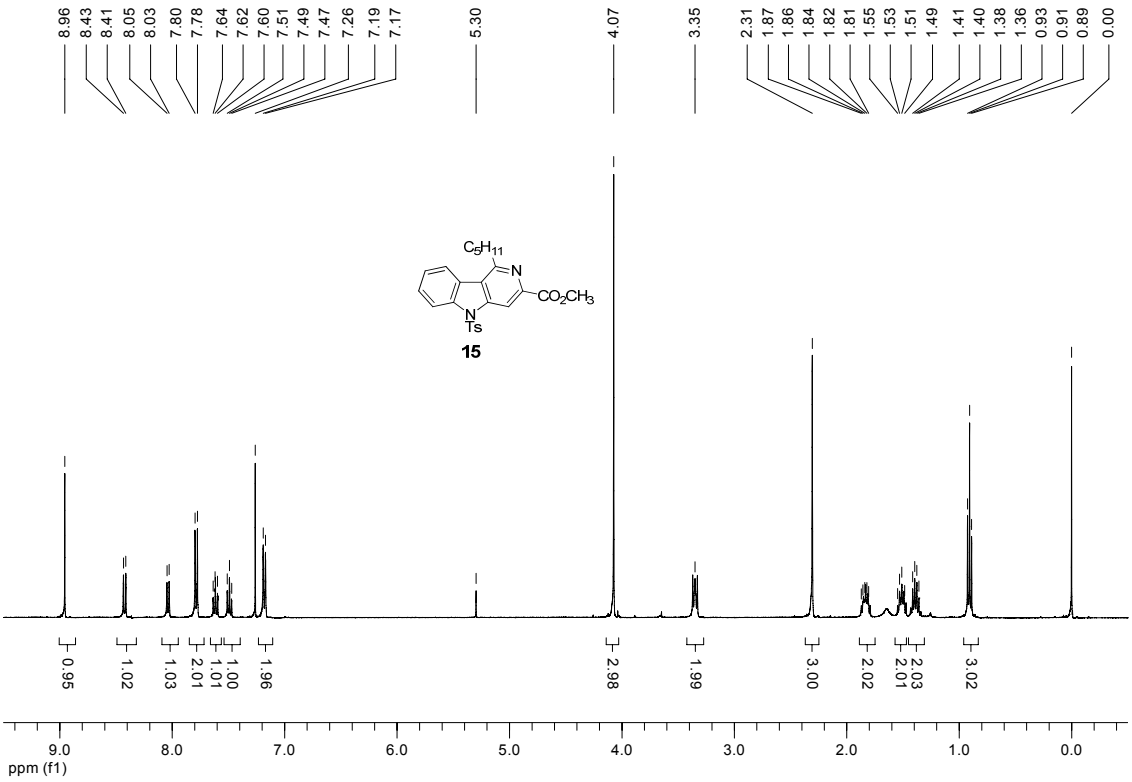
8.236
7.830
7.805
7.537
7.510
7.480
7.417
7.391
7.363
7.083
7.056
6.917
6.888
4.042
2.905
2.868
2.217
H3C
N
CO2CH3
N
Ts
CH3
S11
0.99
1.00
1.05
1.00
2.00
1.91
3.05
2.79
3.44
2.86
9
8
7
6
5
4
3
2
1
0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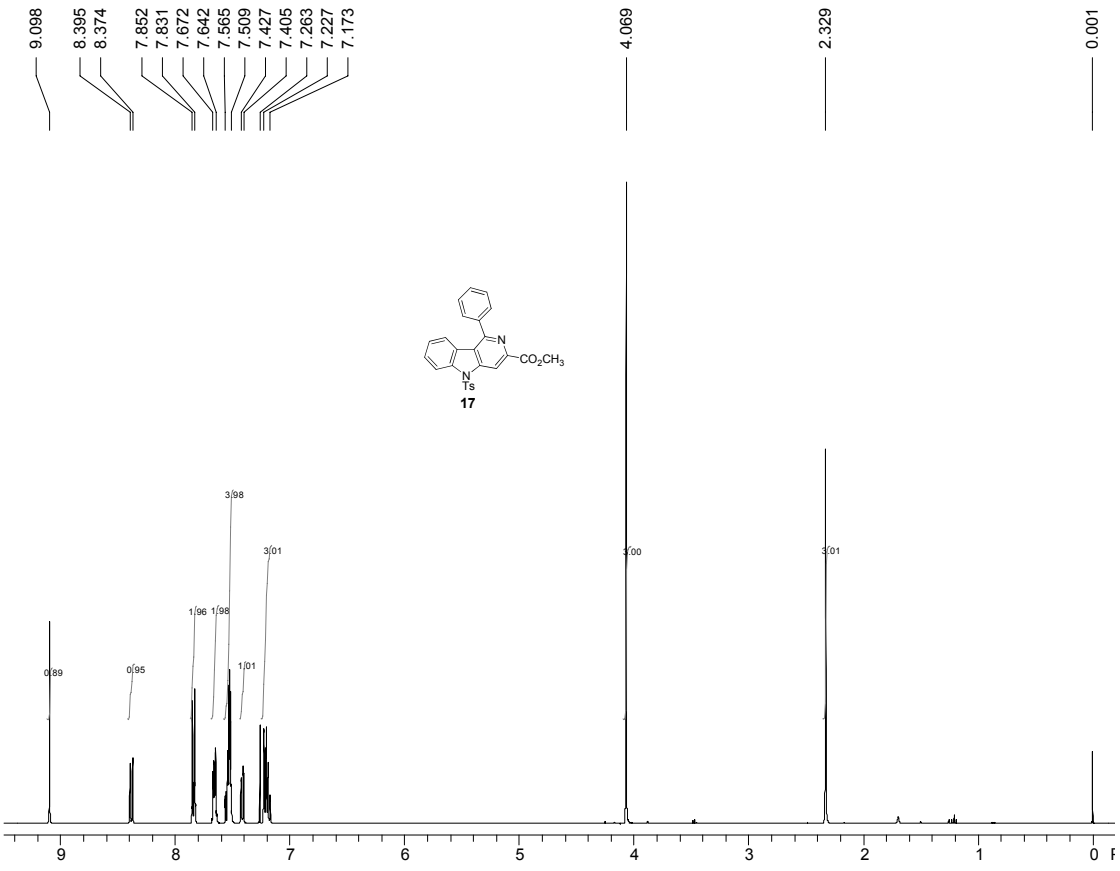
8.43
8.41
8.05
8.03
7.80
7.78
7.64
7.62
7.60
7.51
7.49
7.47
7.26
7.19
7.17
5.30
4.07
3.35
2.31
1.87
1.86
1.84
1.82
1.81
1.55
1.53
1.51
1.49
1.41
1.40
1.38
1.36
0.93
0.91
0.89
0.00
C5H11
N
CO2CH3
N
Ts
15
0.95
1.02
1.03
2.01
1.01
1.00
1.96
2.98
1.99
3.00
2.02
2.01
2.03
3.02
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (f1)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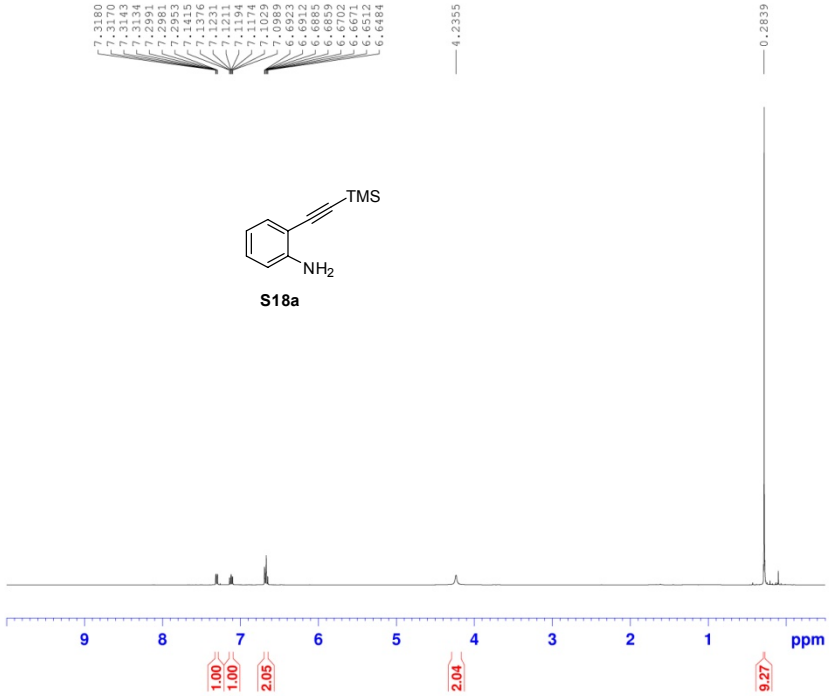
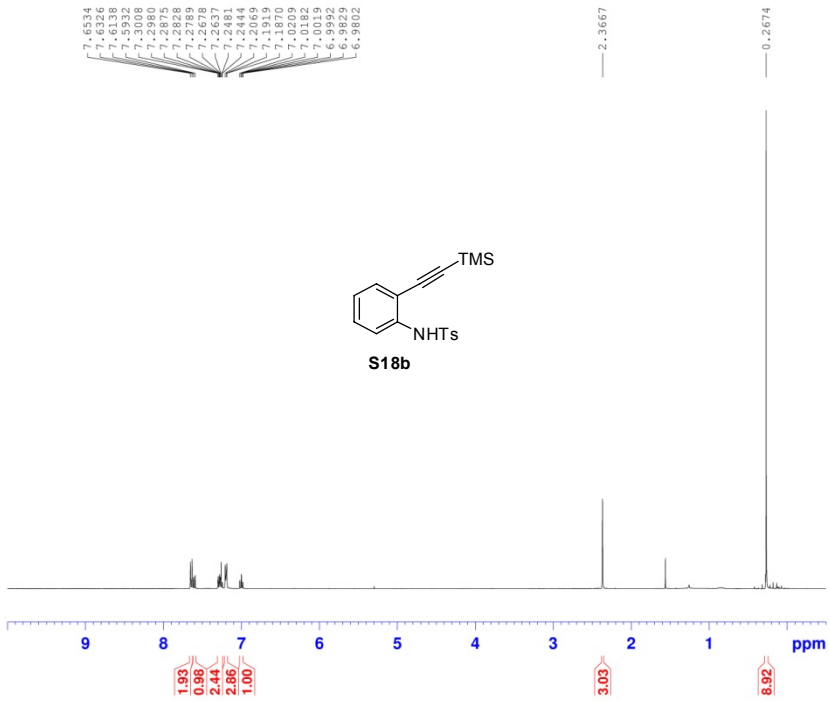
8.395
8.374
7.852
7.831
7.672
7.642
7.565
7.509
7.427
7.405
7.263
7.227
7.173
4.069
2.329
0.001
N
CO2CH3
N
Ts
17
3.98
3.01
1.96
1.98
1.01
0.89
0.95
3.00
3.01
9
8
7
6
5
4
3
2
1
0


7.3190
7.3170
7.3143
7.3134
7.2991
7.2981
7.2953
7.1415
7.1376
7.1231
7.1211
7.1194
7.1074
7.1039
7.0989
6.6923
6.6912
6.6885
6.6859
6.6702
6.6671
6.6512
6.6484
4.2355
0.2839
TMS
NH2
S18a
NAME vr111 fb
EXPNO 10
PROCNO 1
Date_ 20100608
Time 16.29
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 32
DW 60.800 usec
DE 8.00 usec
TE 295.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.00 dB
PL1W 15.25798988 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300222 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9 8 7 6 5 4 3 2 1 ppm
1.00 1.00 2.05 2.04 9.27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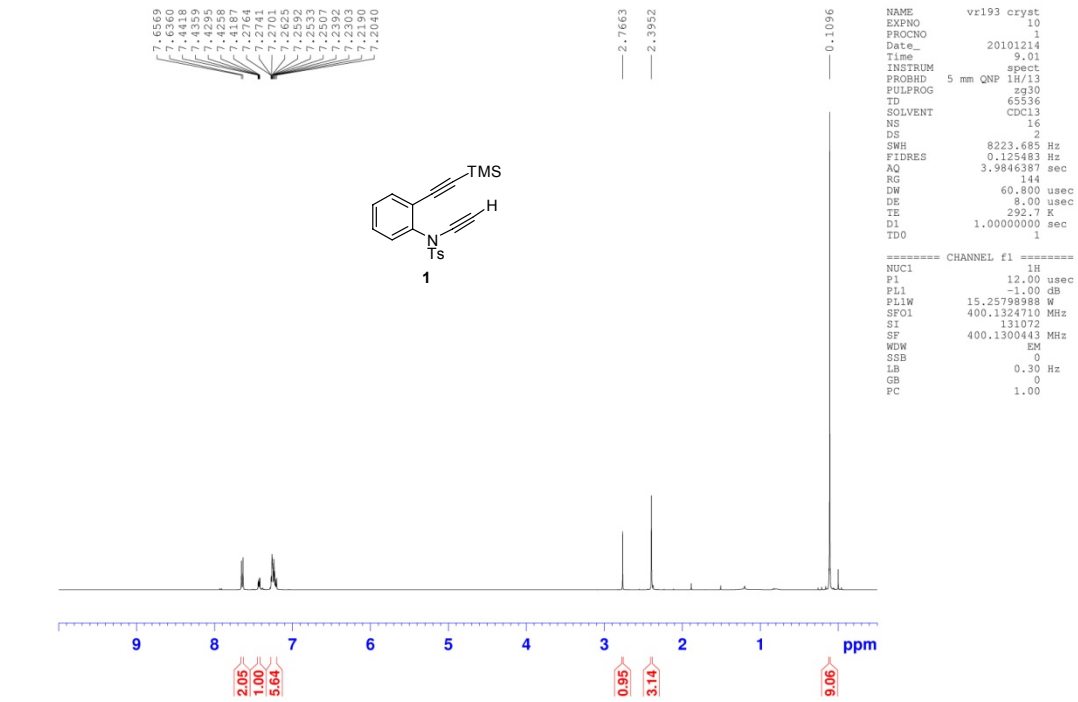
7.6326
7.6138
7.5922
7.5088
7.2990
7.2875
7.2828
7.2789
7.2678
7.2637
7.2481
7.2444
7.2069
7.1919
7.1870
7.1829
7.0182
7.0019
6.9992
6.9829
6.9802
2.3667
0.2674
TMS
NHTs
S18b
NAME vr217 fa
EXPNO 10
PROCNO 1
Date_ 20110218
Time 6.02
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 256
DW 60.800 usec
DE 8.00 usec
TE 293.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.00 dB
PL1W 15.25798988 W
SFO1 400.1324710 MHz
SI 131072
SF 400.1300219 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9 8 7 6 5 4 3 2 1 ppm
1.93 0.98 2.44 2.86 1.00 3.03 8.92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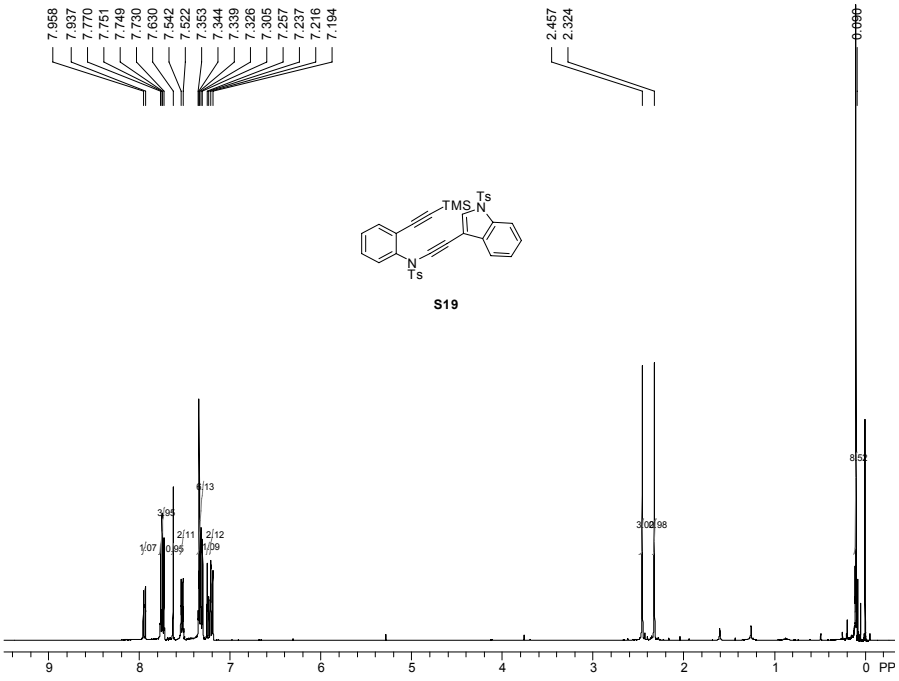
7.6360
7.4418
7.4359
7.4295
7.4258
7.3187
7.2764
7.2741
7.2701
7.2625
7.2592
7.2533
7.2507
7.2392
7.2303
7.2190
7.2040
2.7663
2.3952
0.1096
TMS
H
N
Ts
1
NAME vr193 cryst
EXPNO 10
PROCNO 1
Date_ 20101214
Time 9.01
INSTRUM spect
PROBHD 5 mm QNP 1H/13
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 144
DW 60.800 usec
DE 8.00 usec
TE 292.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 -1.00 dB
PL1W 15.25798988 W
SFO1 400.1324710 MHz
SI 131072
SF 400.1300443 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9 8 7 6 5 4 3 2 1 ppm
2.05 1.00 5.64 0.95 3.14 9.06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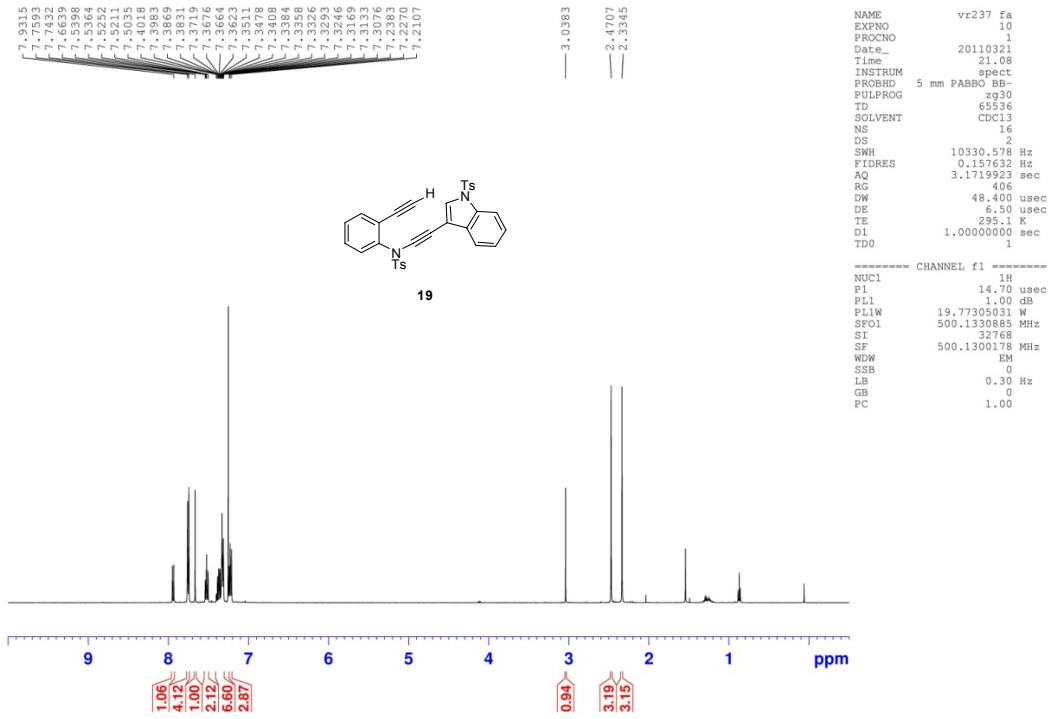
7.937
7.770
7.751
7.749
7.730
7.630
7.542
7.522
7.353
7.344
7.339
7.326
7.305
7.257
7.237
7.216
7.194
2.457
2.324
0.000
TMS
Ts
N
Ts
S19
3.95
6.13
2.11
2.12
1.07
0.95
1.09
3.00
2.98
8.52
9 8 7 6 5 4 3 2 1 0 PP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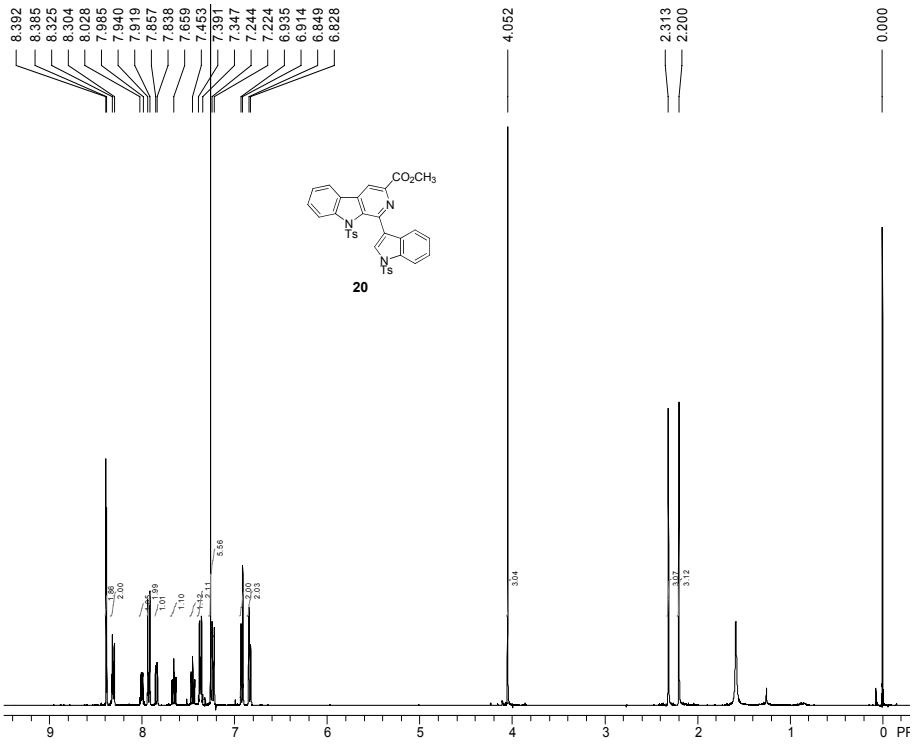
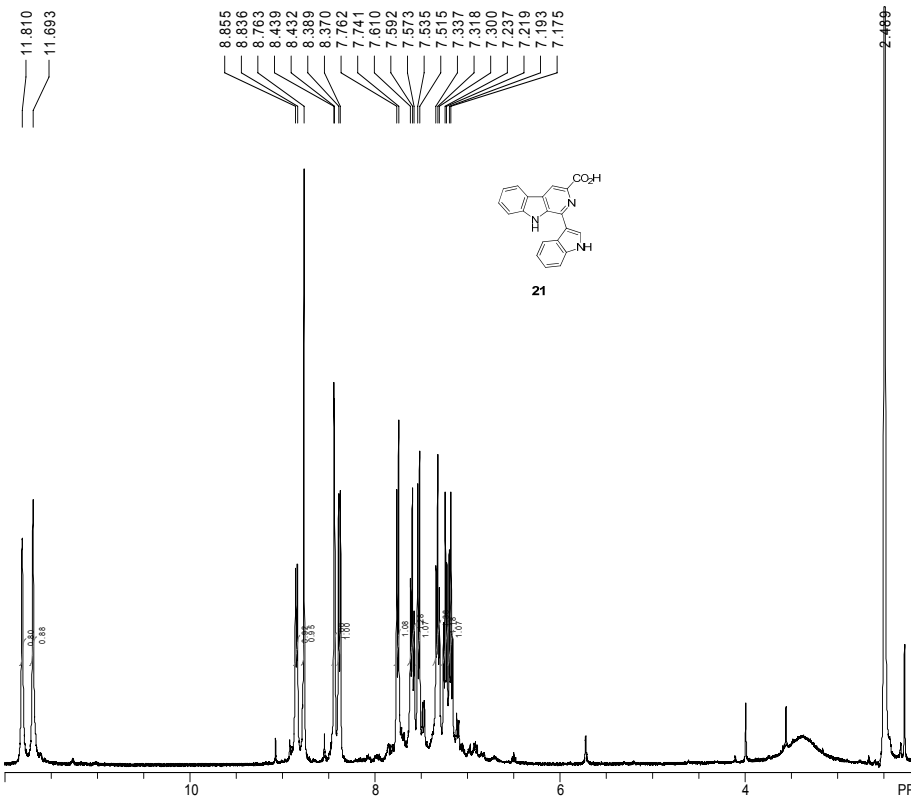
7.7593
7.7432
7.6639
7.5398
7.5364
7.5252
7.5211
7.5035
7.4018
7.3983
7.3869
7.3711
7.3719
7.3676
7.3664
7.3623
7.3511
7.3478
7.3408
7.3384
7.3358
7.3326
7.3293
7.3246
7.3169
7.3133
7.3076
7.2833
7.2270
7.2107
3.0383
2.4707
2.3345
Ts
H
N
N
Ts
19
NAME vr237 fa
EXPNO 10
PROCNO 1
Date_ 20110321
Time 21.08
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1719923 sec
RG 406
DW 48.400 usec
DE 6.50 usec
TE 295.1 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 1.00 dB
PL1W 19.77305031 W
SFO1 500.1330885 MHz
SI 32768
SF 500.1300178 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9
8
7
6
5
4
3
2
1
ppm
1.06
4.12
1.00
2.12
6.60
2.87
0.94
3.19
3.15


8.392
8.385
8.325
8.304
8.028
7.985
7.940
7.919
7.857
7.838
7.659
7.453
7.391
7.347
7.244
7.224
6.935
6.914
6.849
6.828
4.052
2.313
2.200
0.000
CO2CH3
N
N
Ts
N
Ts
20
9
8
7
6
5
4
3
2
1
0
PF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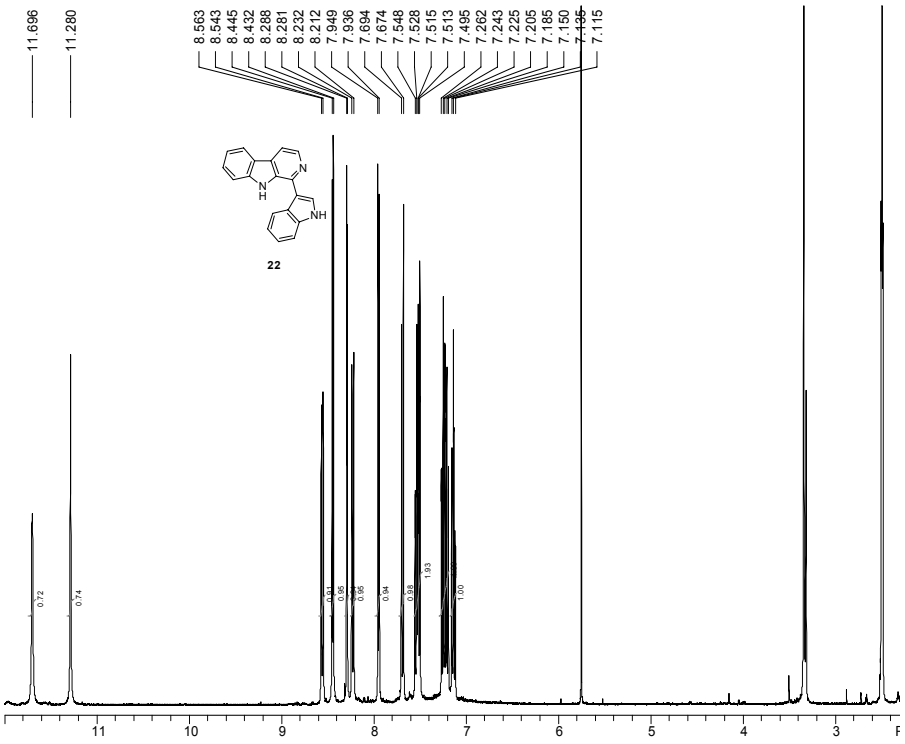
11.693
8.855
8.836
8.763
8.439
8.432
8.389
8.370
7.762
7.741
7.610
7.592
7.573
7.535
7.515
7.337
7.318
7.300
7.237
7.219
7.193
7.175
2.489
CO2H
N
H
NH
21
10
8
6
4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8.281
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7.694
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7.548
7.528
7.515
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7.495
7.262
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7.225
7.205
7.185
7.150
7.115
N
H
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22
11
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