

An *anti*-Carbopalladation/Amination Cascade with Alkynes: Access to Tetrasubstituted Enamines and Pyrroles

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1) General Experimental

All solvents were dried and stored over molecular sieves under Argon atmosphere unless otherwise stated. Air- and moisture-sensitive reactions were carried out in oven-dried or flame-dried glassware, septum-capped under atmospheric pressure of argon. Commercially available compounds were used without further purification unless otherwise stated.

Proton (^1H), carbon (^{13}C) and fluorine (^{19}F) NMR spectra were recorded on a Bruker AV300, Bruker AVIII400, Bruker AVIIIHD500 or Bruker AVII600 instrument using the residual signals from CHCl_3 , $\delta = 7.26$ ppm and $\delta = 77.16$ ppm, as internal reference for ^1H and ^{13}C chemical shifts, respectively. Additionally, tetramethylsilane (TMS; $\delta = 0.00$ ppm; 0.03%) was added to NMR samples. The following abbreviations were used for NMR chemical shifts: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and combinations thereof. ESI-HRMS mass spectrometry was carried out on an FTICR instrument. GC-HRMS mass spectrometry was carried out on an Agilent 6890 gas chromatograph coupled to a JMS-T100GC (GC AccuTOF, JEOL, Japan) time of flight mass spectrometer in electron ionization (EI) mode. IR spectra were recorded on an ATR spectrometer Tensor 27 from Bruker. Melting Points were recorded with a Büchi SMP-20 melting point meter and are uncorrected.

2) General procedures (GP)

GP1: Synthesis of Tosylate

To a solution of alcohol (1.0 equiv) in CH_2Cl_2 (10.0 mL/mmol) was added triethylamine (1.4-3.0 equiv) and 4-dimethylaminopyridine (catalytic amount) at 0 °C. Afterwards tosyl chloride (1.1-1.6 equiv) was added in several portions. The mixture was stirred overnight at ambient temperature. To the reaction mixture was added NaOH-solution (2M) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3×). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by silica gel column chromatography.

GP2: Synthesis of Amine (A)

The tosylate (1.0 equiv) was dissolved in DMF (4 mL/mmol). To the solution were added potassium iodide (catalytic amount), amine (1.4-2.5 equiv) and potassium carbonate (2.8-3.2 equiv) and the mixture was stirred at 90 °C (oil bath) until TLC showed full conversion of the starting material. To the reaction mixture was added NH_4Cl -solution and the layers were separated. The aqueous layer was extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by Silica gel column chromatography.

GP3: Pd-catalyzed Domino Reaction

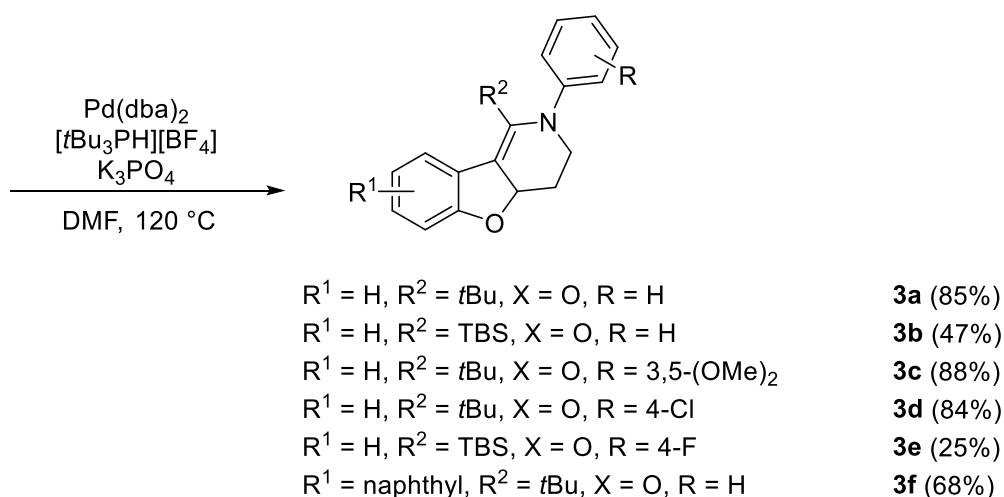
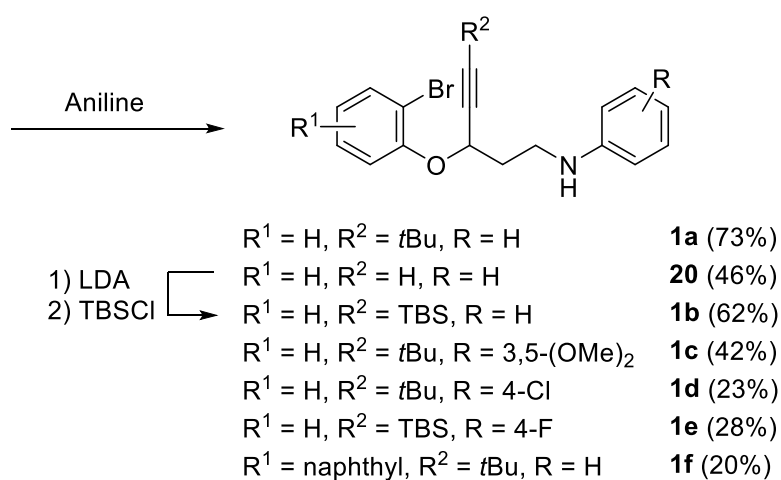
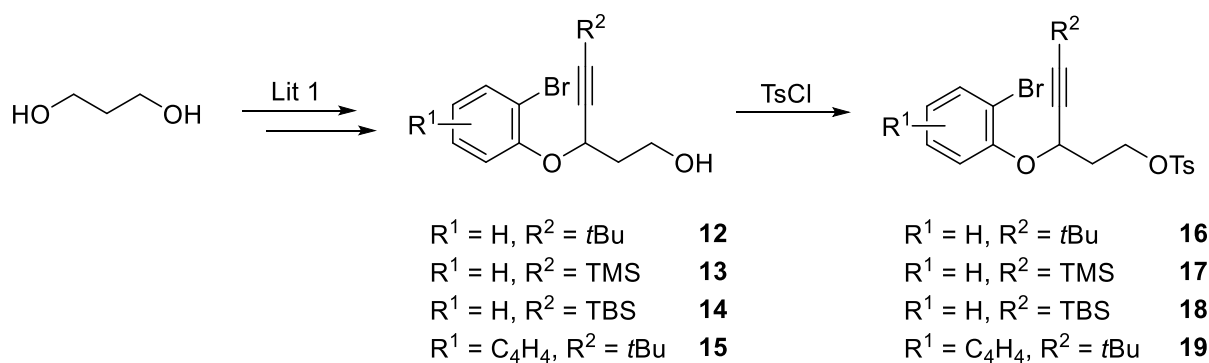
The domino precursor (1.0 equiv) was dissolved in DMF (3.0 mL/100 μmol). The solution was degassed with argon for 10 min. Afterwards base (5.0 equiv), ligand (10 mol %) and Pd-catalyst (5 mol %) were added in that order. The mixture was stirred 30 min at rt and afterwards at 120 °C (oil bath) until TLC showed full conversion of the starting material. After cooling to rt, water was added to the reaction mixture. The layers were separated and the aqueous layer was extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by silica gel column chromatography.

GP4: Synthesis of Amine (B)

The alcohol (1.0 equiv) was dissolved in CH_2Cl_2 (10 mL/mmol). To the solution were added *N,N*-diisopropylethylamine (1.3-2.0 equiv) and triflic anhydride (1.1-1.7 equiv) at 0 °C. The reaction mixture was stirred 30 min at 0 °C. Afterwards the amine (1.7-2.9 equiv) was added.

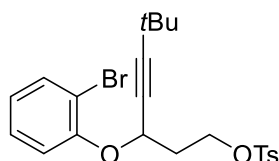
The reaction mixture was stirred at rt until TLC showed full conversion of the starting material. To the reaction mixture was added NH_4Cl -solution and the layers were separated. The aqueous layer was extracted with EtOAc (3×). The combined organic layers were washed with brine, dried over Na_2SO_4 , and concentrated *in vacuo*. The residue was purified by Silica gel column chromatography.

3) Syntheses of Precursors of Type 1 and Domino Products of Type 3



3a) Syntheses of Tosylates

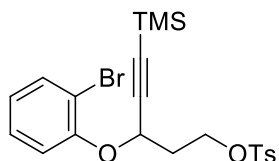
3-(2-Bromophenoxy)-6,6-dimethylhept-4-yn-1-yl 4-methylbenzenesulfonate (**16**)



The alcohol **12**¹ (952 mg, 3.06 mmol), triethylamine (580 μ L, 4.23 mmol) and tosyl chloride (646 mg, 3.39 mmol) were reacted according to GP1 (Synthesis of Tosylate). The reaction mixture was stirred 15 h at rt. After extraction, compound **16** (1.42 g, 3.05 mmol, 100%) was obtained as colorless oil.

The product was used without further purification in the next step.

3-(2-Bromophenoxy)-5-(trimethylsilyl)pent-4-yn-1-yl 4-methylbenzenesulfonate (**17**)



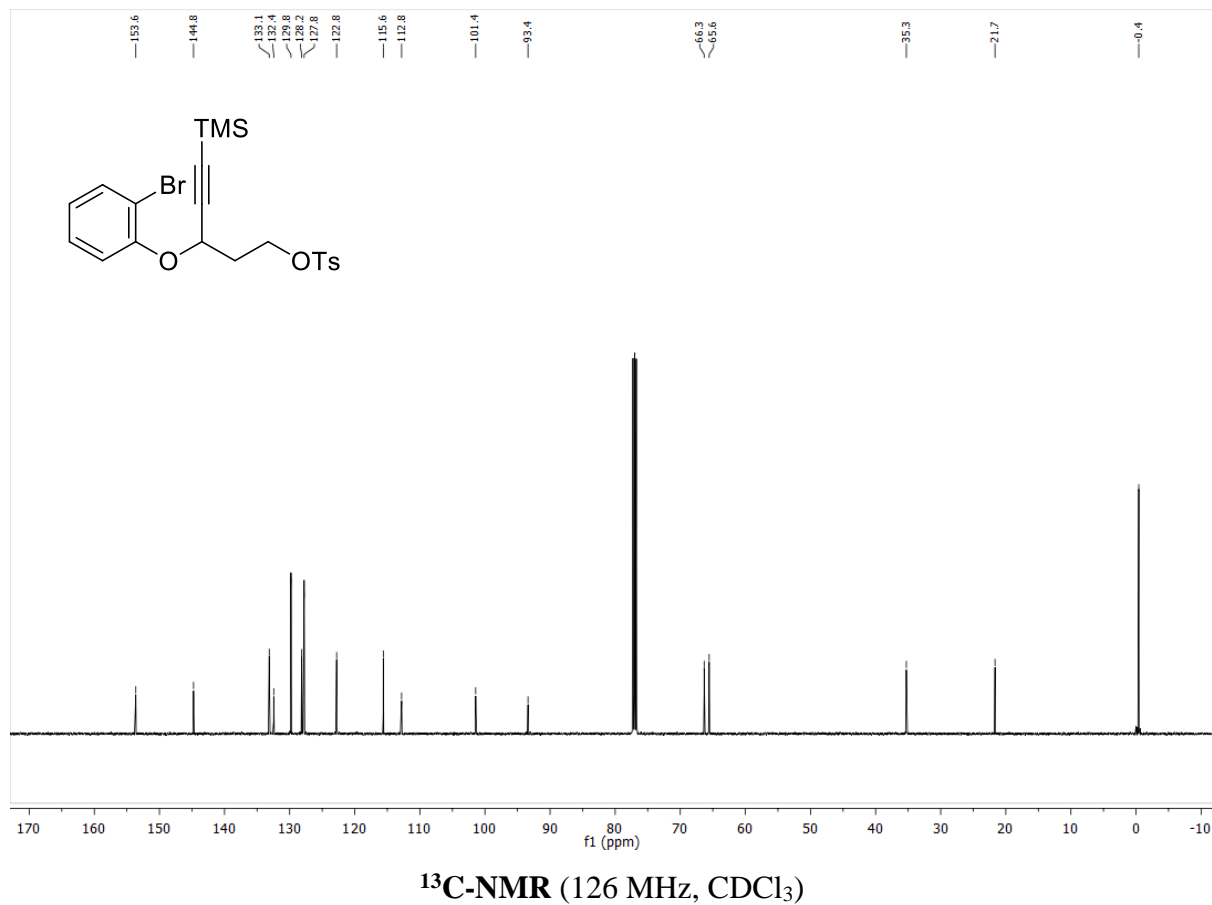
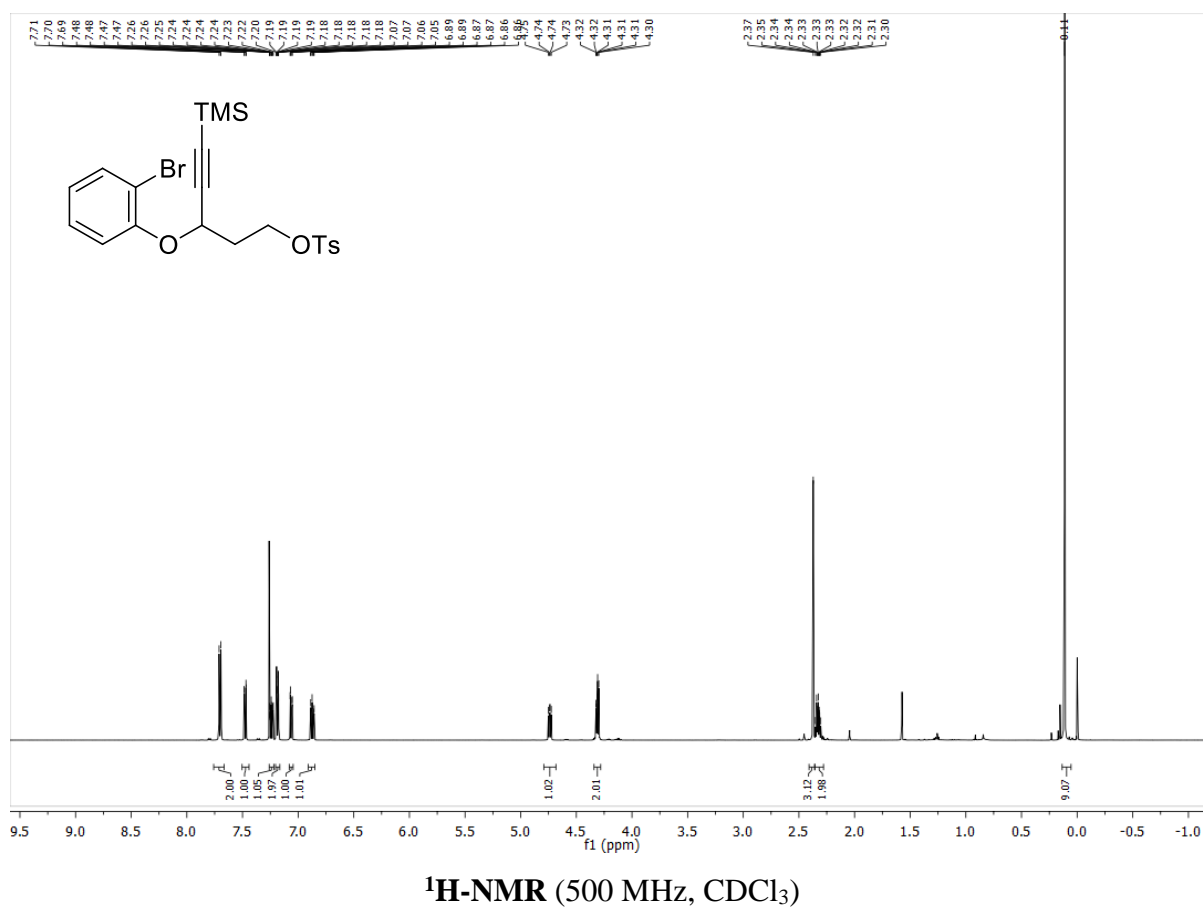
The alcohol **13**¹ (2.56 g, 7.82 mmol), triethylamine (2.20 mL, 15.9 mmol) and tosyl chloride (1.81 g, 9.49 mmol) were reacted according to GP1 (Synthesis of Tosylate). Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded product **17** (3.73 g, 7.74 mmol, 99%) as colorless oil.

¹H-NMR (500 MHz, CDCl₃): δ = 0.11 (s, 9H), 2.28–2.36 (m, 2H), 2.37 (s, 3H), 4.28–4.34 (m, 2H), 4.74 (dd, J = 8.0, 5.1 Hz, 1H), 6.85–6.91 (m, 1H), 7.06 (dd, J = 8.3, 1.4 Hz, 1H), 7.16–7.20 (m, 2H), 7.24 (ddd, J = 8.2, 7.3, 1.7 Hz, 1H), 7.48 (dd, J = 7.8, 1.6 Hz, 1H), 7.70 (d, J = 8.3 Hz, 2H).

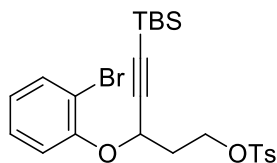
¹³C-NMR (126 MHz, CDCl₃): δ = -0.4, 21.7, 35.3, 65.6, 66.3, 93.4, 101.4, 112.8, 115.6, 122.8, 127.8, 128.2, 129.8, 132.4, 133.1, 144.8, 153.6.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3064 (w), 2962 (w), 2902 (w), 1474 (m), 1363 (m), 1244 (m), 1180 (s).

HRMS-ESI: C₂₁H₂₅BrO₄SSi m/z calcd. [M+Na⁺]: 503.0318 found 503.0320.



3-(2-Bromophenoxy)-5-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl 4-methylbenzenesulfonate (18)



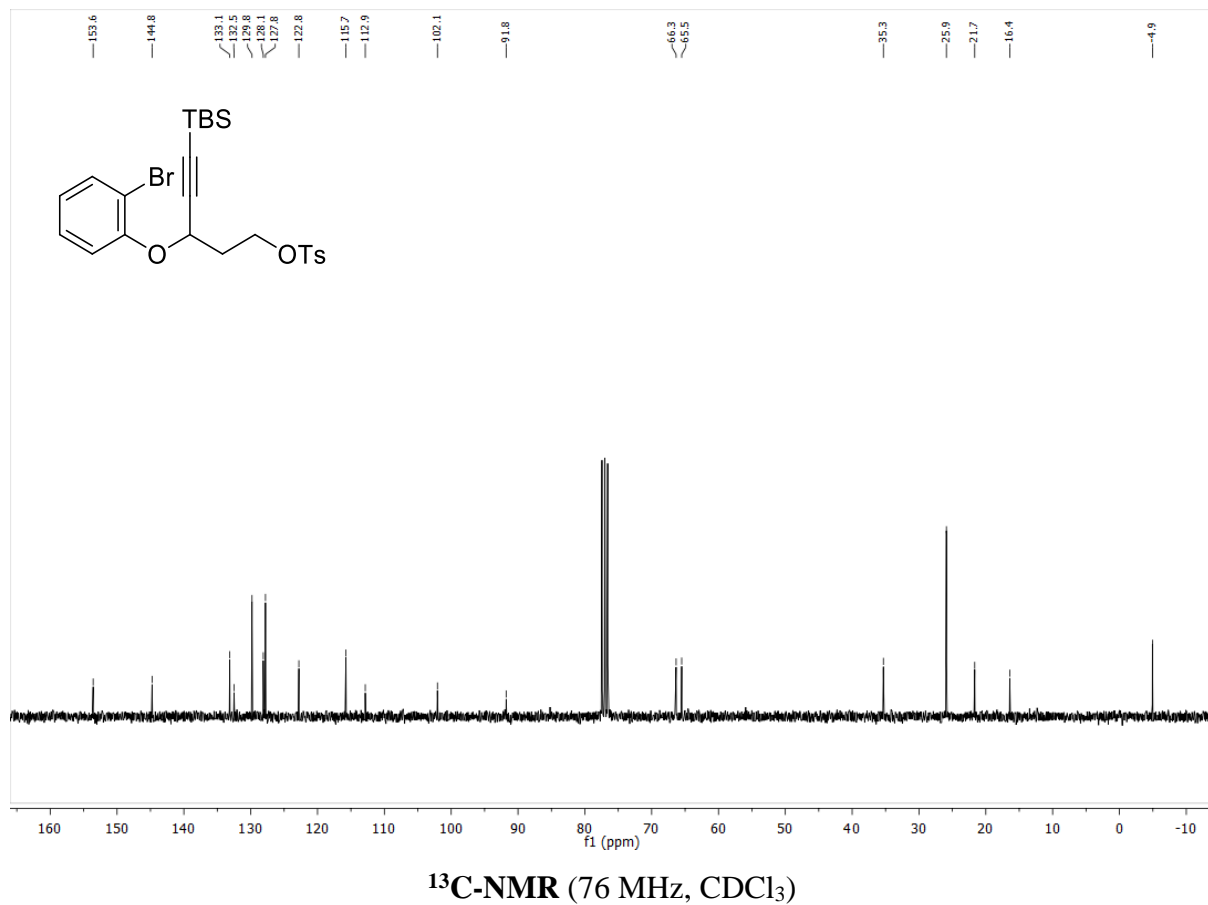
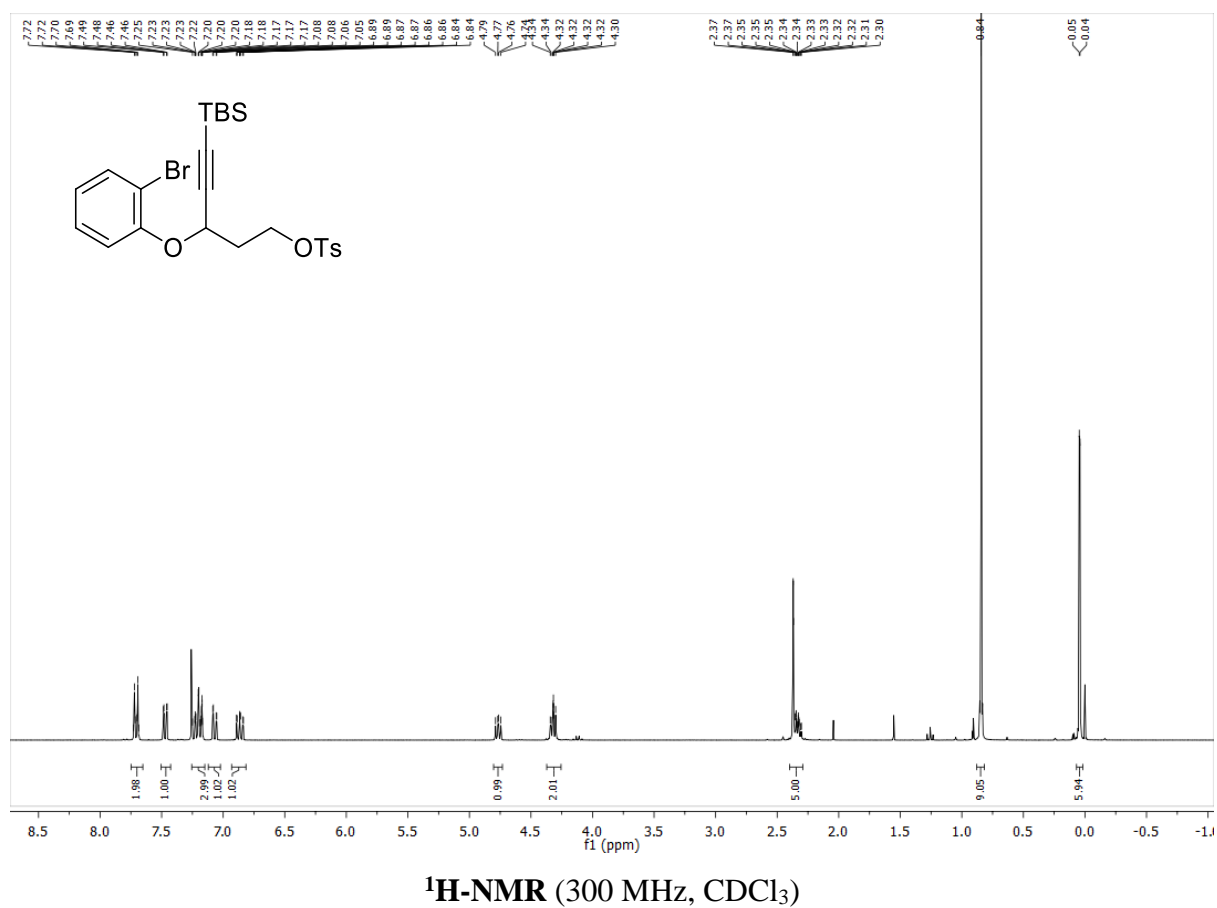
The alcohol **14**² (3.81 g, 10.3 mmol), triethylamine (4.20 mL, 30.3 mmol) and tosyl chloride (2.33 g, 12.2 mmol) were reacted according to GP1 (Synthesis of Tosylate). The reaction mixture was stirred 14 h at rt. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded product **18** (5.30 g, 10.1 mmol, 98%) as colorless oil.

¹H-NMR (300 MHz, CDCl₃): δ = 0.04 (d, J = 1.7 Hz, 6H), 0.84 (s, 9H), 2.29–2.40 (m, 5H), 4.26–4.37 (m, 2H), 4.77 (dd, J = 7.4, 5.6 Hz, 1H), 6.86 (ddd, J = 7.9, 7.3, 1.5 Hz, 1H), 7.07 (dd, J = 8.3, 1.4 Hz, 1H), 7.15–7.26 (m, 3H), 7.47 (dd, J = 7.9, 1.6 Hz, 1H), 7.65–7.75 (m, 2H).

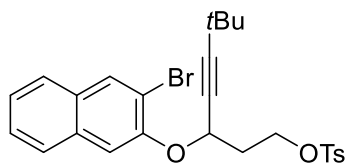
¹³C-NMR (76 MHz, CDCl₃): δ = -4.9, 16.4, 21.7, 25.9, 35.3, 65.5, 66.3, 91.8, 102.1, 112.9, 115.7, 122.8, 127.8, 128.1, 129.8, 132.5, 133.1, 144.8, 153.6.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 2934 (m), 2892 (m), 2858 (m), 1589 (w), 1472 (m), 1365 (m), 1244 (m), 1180 (s).

HRMS-ESI: C₂₄H₃₁BrO₄SSi m/z calcd. [M+Na⁺]: 545.0788 found 545.0792.



**3-((3-Bromonaphthalen-2-yl)oxy)-6,6-dimethylhept-4-yn-1-yl 4-methylbenzenesulfonate
(19)**

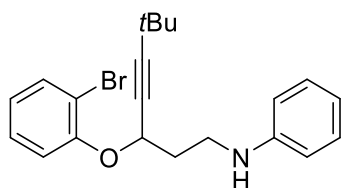


The alcohol **15**¹ (162 mg, 447 μ mol), triethylamine (150 μ L, 1.08 mmol) and tosyl chloride (135 mg, 708 μ mol) were reacted according to GP1 (Synthesis of Tosylate). The reaction mixture was stirred 15 h at rt. After extraction compound **19** (195 mg, 447 μ mol, 100%) was obtained as colorless oil.

The product was used without further purification in the next step.

3b) Syntheses of Precursors of Type 1

N-(3-(2-Bromophenoxy)-6,6-dimethylhept-4-yn-1-yl)aniline (**1a**)



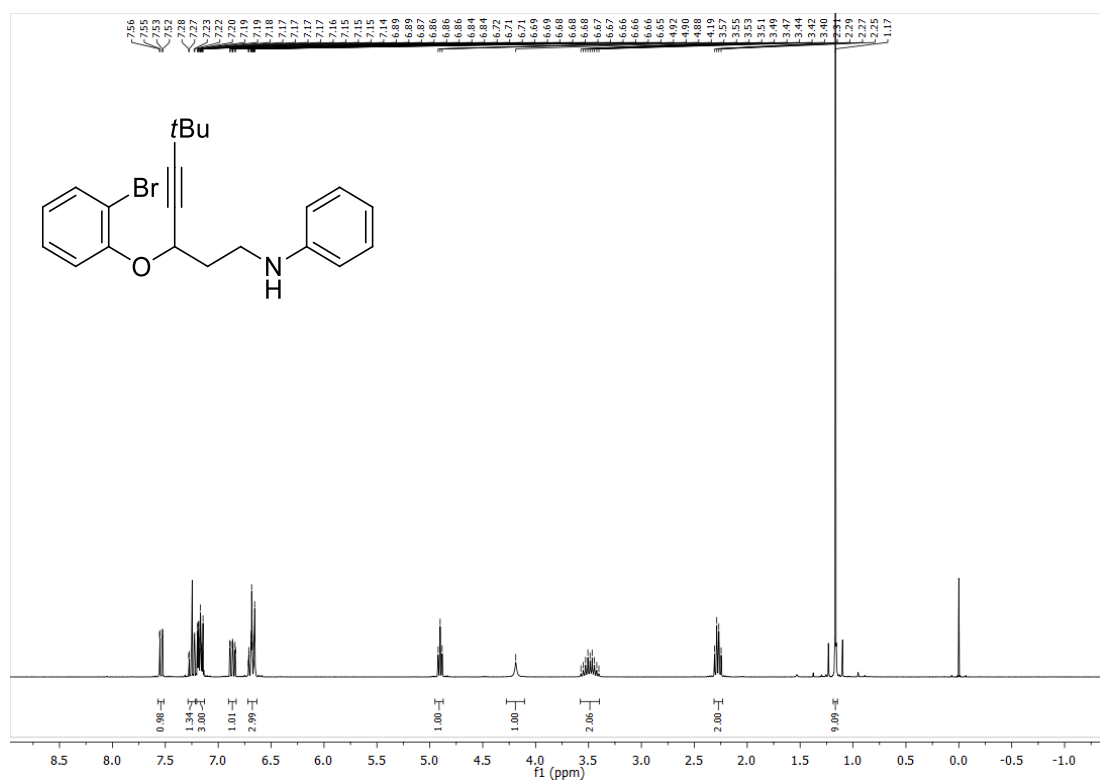
The tosylate **15** (1.42 g, 3.05 mmol) was reacted with potassium iodide (54.2 mg, 327 μ mol), aniline (420 μ L, 428 mg, 4.60 mmol) and potassium carbonate (1.26 g, 9.12 mmol) according to GP2 (Synthesis of Amine (A)). The reaction mixture was stirred 19 h. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded product **1a** (868 mg, 2.25 mmol, 73%) as yellow oil.

¹H-NMR (300 MHz, CDCl₃): δ = 1.17 (s, 9H), 2.23–2.31 (m, 2H), 3.49 (qt, J = 12.8, 6.4 Hz, 2H), 4.19 (s, 1H), 4.90 (t, J = 5.7 Hz, 1H), 6.64–6.72 (m, 3H), 6.86 (ddd, J = 7.9, 7.2, 1.7 Hz, 1H), 7.13–7.20 (m, 3H), 7.25 (dd, J = 15.5, 1.6 Hz, 1H), 7.54 (dd, J = 7.9, 1.6 Hz, 1H).

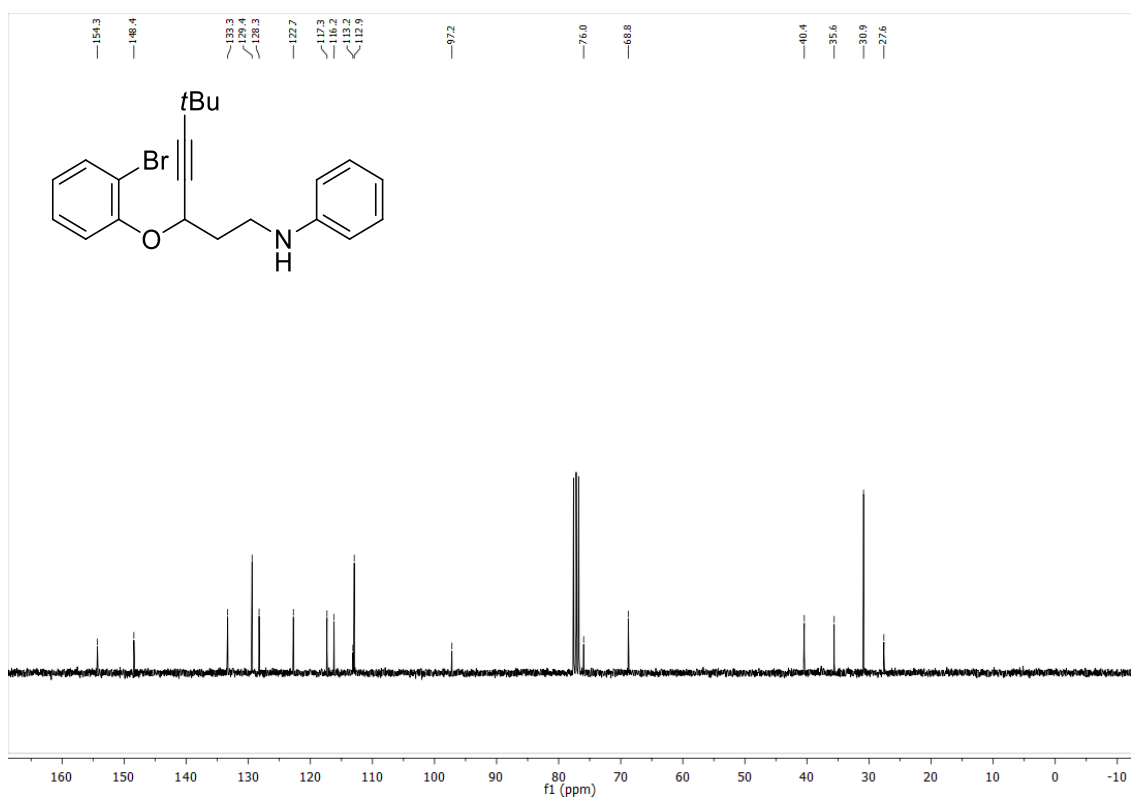
¹³C-NMR (76 MHz, CDCl₃): δ = 27.6, 30.9, 35.6, 40.4, 68.8, 76.0, 97.2, 112.9, 113.2, 116.2, 117.3, 122.7, 128.3, 129.4, 133.3, 148.4, 154.3.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3412 (w), 2968 (m), 2928 (w), 2899 (w), 2867 (w), 1603 (m), 1507 (m), 1475 (s), 1239 (m).

HRMS-ESI: C₂₁H₂₄BrNO m/z calcd. [M+Na⁺]: 408.0933 found 408.0939.

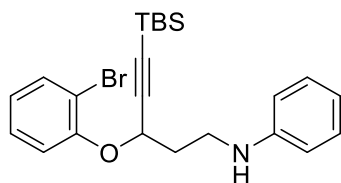


¹H-NMR (300 MHz, CDCl₃)

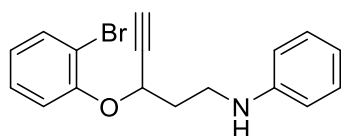


¹³C-NMR (76 MHz, CDCl₃)

***N*-(3-(2-Bromophenoxy)-5-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)aniline (**1b**)**



The tosylate **17** (1.16 g, 2.41 mmol) was reacted with potassium iodide (52.0 mg, 313 μ mol), aniline (350 μ L, 3.83 mmol) and potassium carbonate (1.43 g, 6.74 mmol) according to GP2 (Synthesis of Amines (A)). The reaction mixture was stirred 16 h at rt. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded terminal alkyne **20** (365 mg, 1.11 mmol, 46%) as yellow oil.



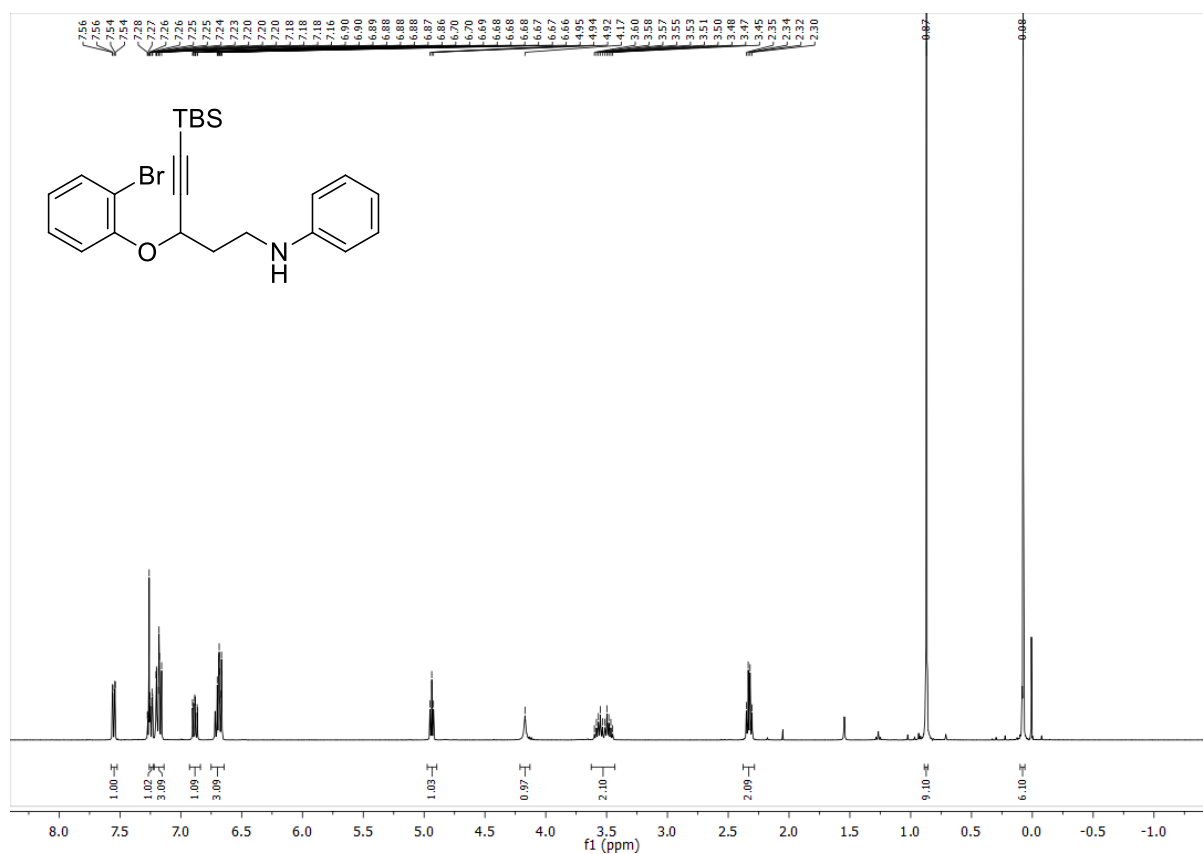
The terminal alkyne **20** (365 mg, 1.11 mmol) was dissolved in THF (10 mL). The reaction mixture was cooled to -78 °C. Afterwards LDA (1 M, 1.30 mL, 1.30 mmol) was added dropwise over 30 min. The reaction mixture was stirred 1 h at -78 °C. A solution of TBSCl (212 mg, 1.41 mmol) in THF (2.0 mL) was added dropwise over 10 min and the mixture was slowly warmed up to rt. The reaction was quenched with sat. NH₄Cl solution. The aqueous layer was extracted with EtOAc (3 \times). The combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded product **1b** (308 mg, 693 μ mol, 62%) as yellow oil.

¹H-NMR (400 MHz, CDCl₃): δ = 0.08 (s, 6H), 0.87 (s, 9H), 2.33 (q, J = 6.3 Hz, 2H), 3.43–3.63 (m, 2H), 4.17 (s, 1H), 4.94 (t, J = 5.8 Hz, 1H), 6.64–6.75 (m, 3H), 6.88 (ddd, J = 7.9, 7.3, 1.6 Hz, 1H), 7.14–7.22 (m, 3H), 7.22–7.28 (m, 1H), 7.55 (dd, J = 7.9, 1.6 Hz, 1H).

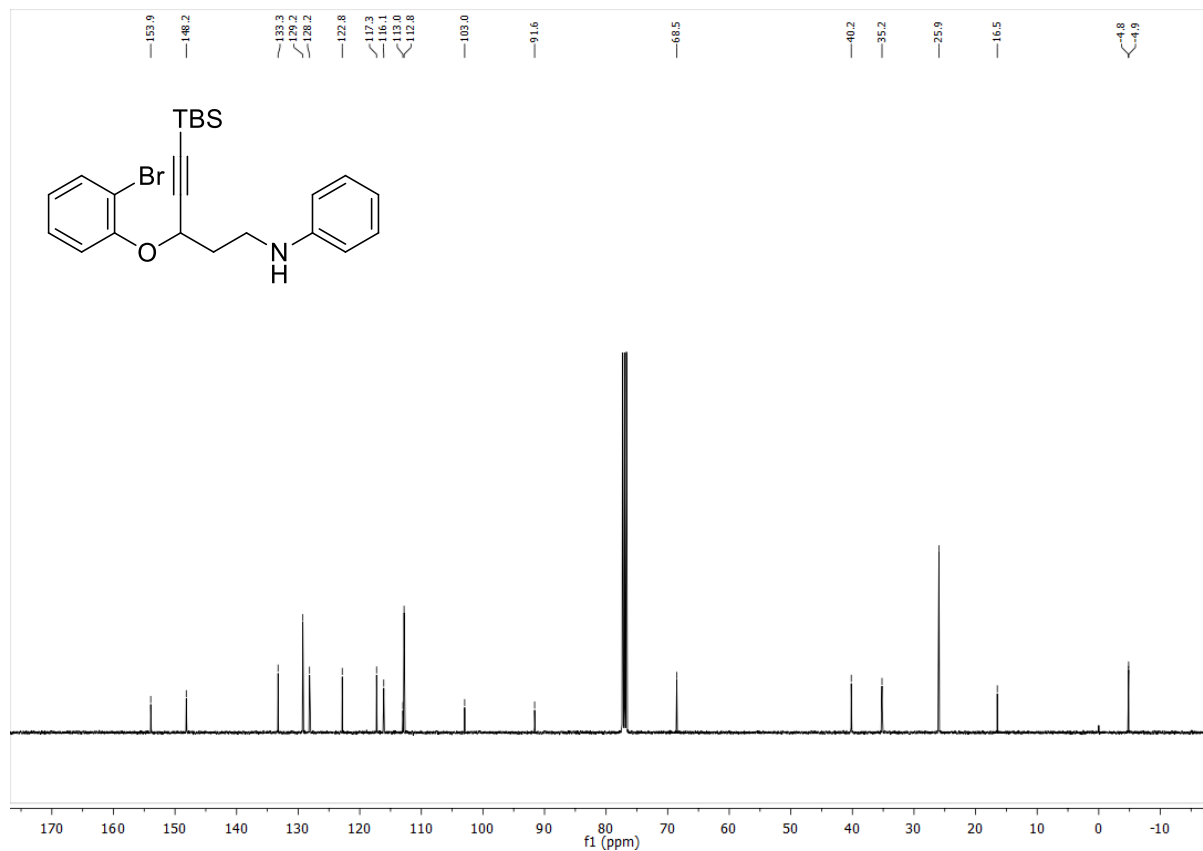
¹³C-NMR (101 MHz, CDCl₃): δ = -4.9, -4.8, 16.5, 25.9, 35.2, 40.2, 68.5, 91.6, 103.0, 112.8, 113.0, 116.1, 117.3, 122.8, 128.2, 129.2, 133.3, 148.2, 153.9.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3413 (w), 2952 (m), 2934 (m), 2890 (w), 2857 (m), 1061 (m), 1507 (m), 1473 (s), 1243 (m), 1038 (w).

HRMS-ESI: C₂₃H₃₀BrNOSi m/z calcd. [M+H⁺]: 444.1353 found 444.1364.

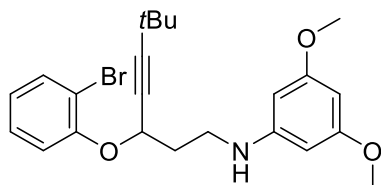


¹H-NMR (400 MHz, CDCl₃)



¹³C-NMR (101 MHz, CDCl₃)

***N*-(3-(2-Bromophenoxy)-6,6-dimethylhept-4-yn-1-yl)-3,5-dimethoxyaniline (**1c**)**



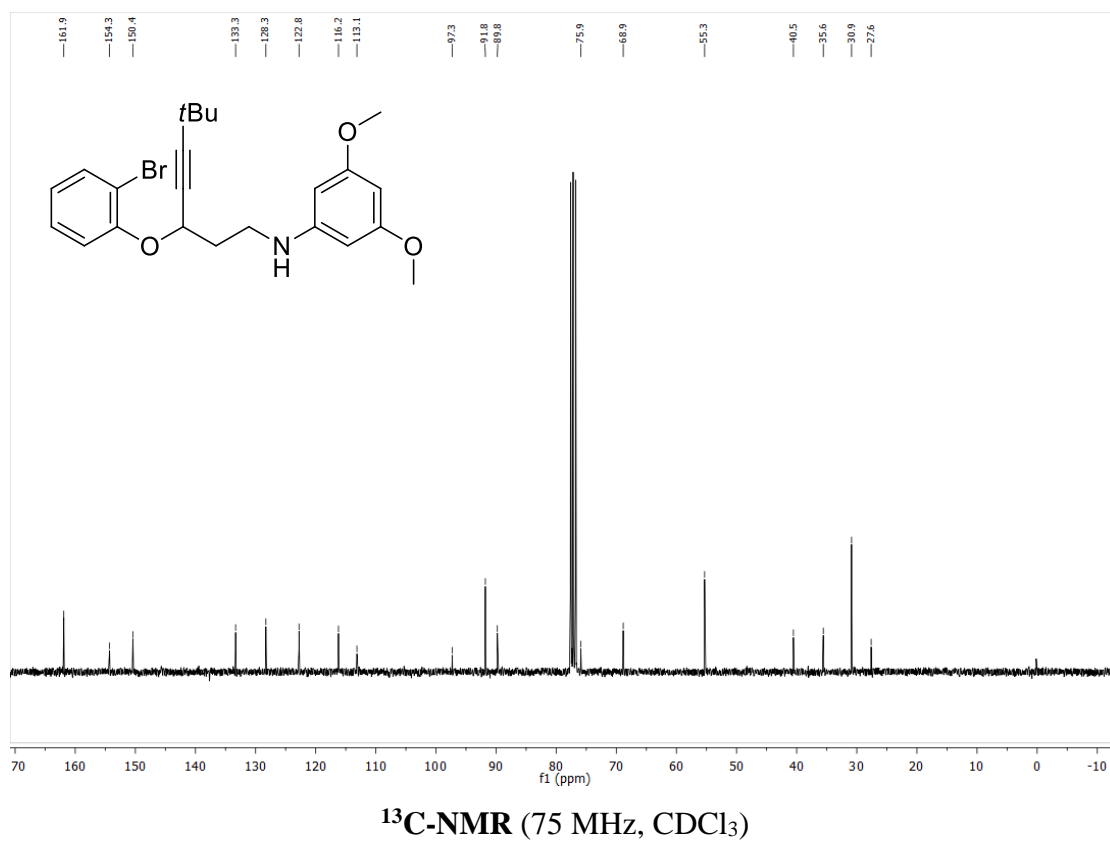
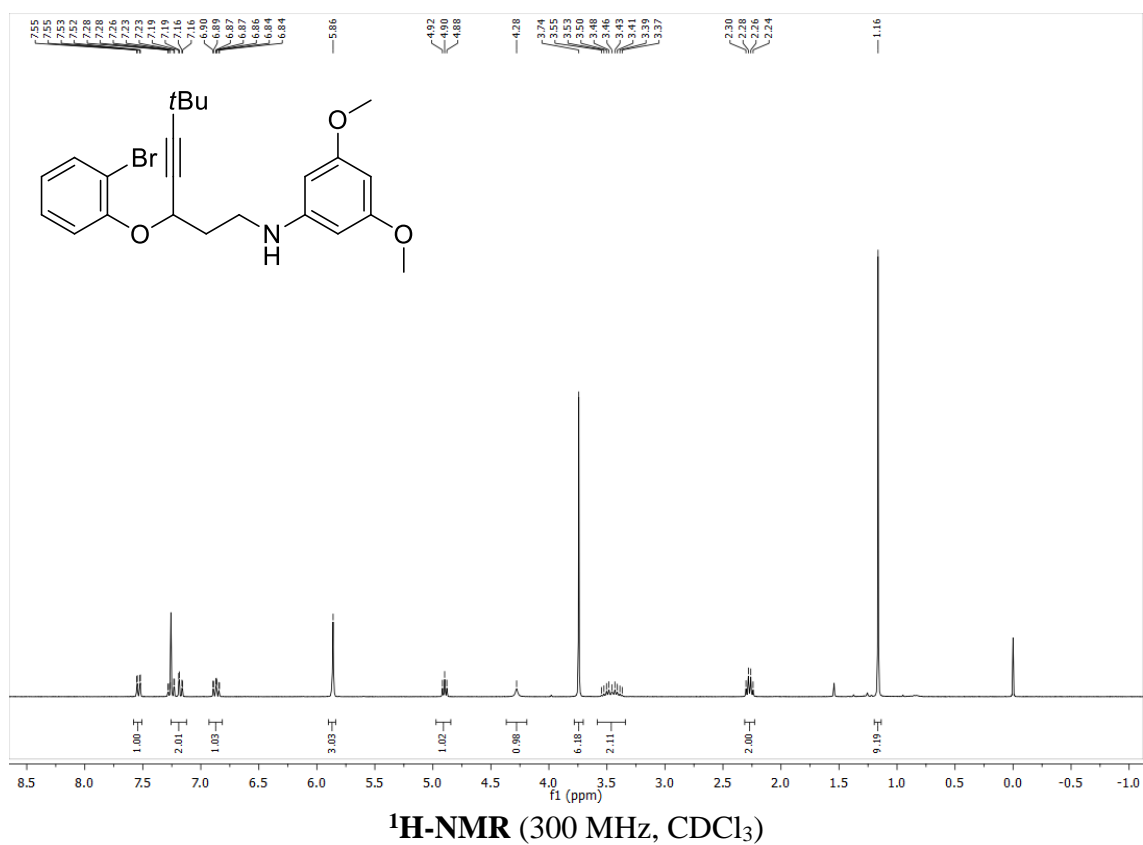
The tosylate **16** (230 mg, 495 μ mol) was reacted with potassium iodide (15 mg, 90.4 μ mol), aniline (119 mg, 777 μ mol) and potassium carbonate (219 mg, 1.58 mmol) according to GP2 (Synthesis of Amine (A)). The reaction mixture was stirred 19 h at 90 °C. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded product **1c** (93.5 mg, 209 μ mol, 42%) as yellow oil.

¹H-NMR (300 MHz, CDCl₃): δ = 1.16 (s, 9H), 2.27 (q, J = 6.1 Hz, 2H), 3.46 (dtd, J = 19.0, 13.0, 6.3 Hz, 2H), 3.74 (s, 6H), 4.28 (s, 1H), 4.90 (t, J = 5.7 Hz, 1H), 5.86 (s, 3H), 6.81–6.93 (m, 1H), 7.12–7.26 (m, 2H), 7.54 (dd, J = 7.9, 1.6 Hz, 1H).

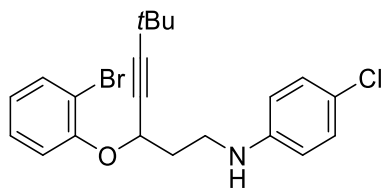
¹³C-NMR (75 MHz, CDCl₃) δ = 27.6, 30.9, 35.6, 40.5, 55.3, 68.9, 75.9, 89.8, 91.8, 97.3, 113.1, 116.2, 122.8, 128.3, 133.3, 150.4, 154.3, 161.9.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3410 (w), 2966 (m), 2931 (w), 2901 (w), 2867 (w), 2840 (w), 1614 (m), 1591 (m), 1474 (m), 1239 (m), 1201 (m), 1149 (s).

HRMS-ESI: C₂₃H₂₈BrNO₃ m/z calcd. [M+H⁺]: 446.1325 found 446.1336.



***N*-(3-(2-Bromophenoxy)-6,6-dimethylhept-4-yn-1-yl)-4-chloroaniline (1d)**



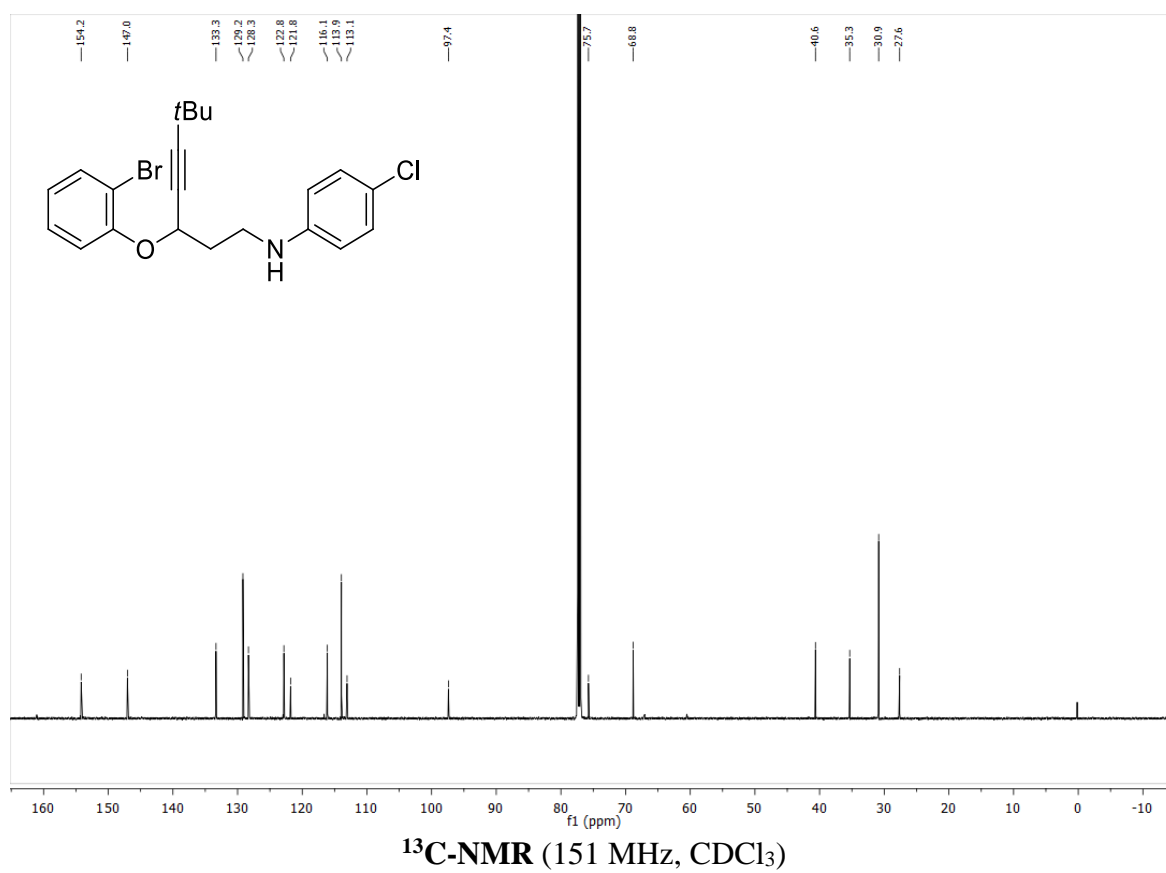
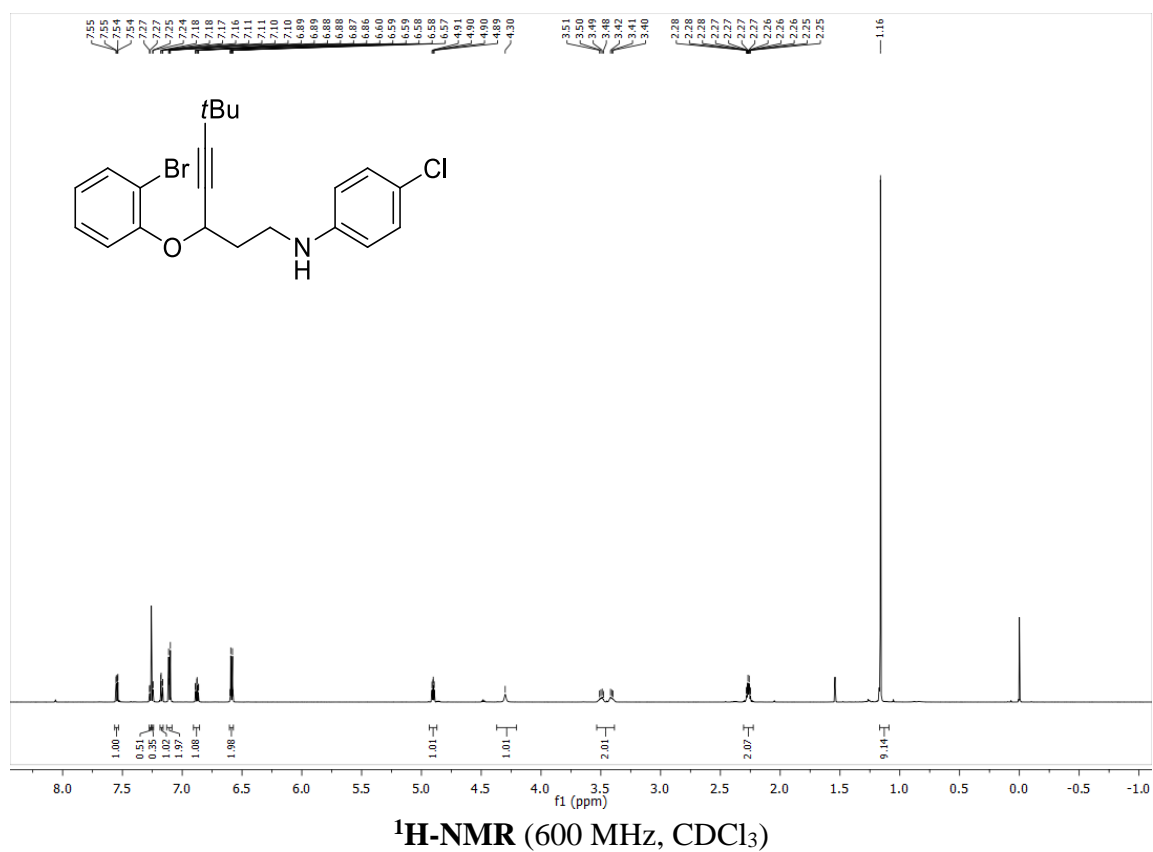
The tosylate **16** (261 mg, 560 μmol) was reacted with potassium iodide (30 mg, 180 μmol), 4-chloroaniline (107 mg, 839 μmol) and potassium carbonate (248 mg, 1.79 mmol) according to GP2 (Synthesis of Amine (A)). The reaction mixture was stirred 14 h at 90 °C. Silica gel column chromatography (EtOA:*n*-pentane = 1:50) afforded product **1d** (53.4 mg, 127 μmol , 23%) as yellow oil.

^1H -NMR (600 MHz, CDCl_3): δ = 1.16 (s, 9H), 2.23–2.31 (m, 2H), 3.39–3.53 (m, 2H), 4.30 (s, 1H), 4.90 (dd, J = 6.2, 4.9 Hz, 1H), 6.57–6.61 (m, 2H), 6.88 (td, J = 7.6, 1.5 Hz, 1H), 7.09–7.13 (m, 2H), 7.17 (dd, J = 8.3, 1.5 Hz, 1H), 7.24–7.27 (m, 1H), 7.55 (dd, J = 7.9, 1.7 Hz, 1H).

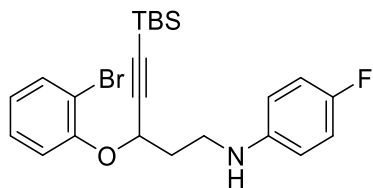
^{13}C -NMR (151 MHz, CDCl_3) δ = 27.6, 30.9, 35.3, 40.6, 68.8, 75.7, 97.4, 113.1, 113.9, 116.1, 121.8, 122.8, 128.3, 129.2, 133.3, 147.0, 154.2.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3411 (w), 2969 (m), 2928 (w), 2899 (w), 2867 (w), 2840 (w), 1601 (m), 1503 (m), 1475 (s), 1240 (m), 1049 (w), 1031 (w).

HRMS-ESI: $\text{C}_{21}\text{H}_{23}\text{BrClNO}$ m/z calcd. $[\text{M}+\text{Na}^+]$: 442.0544 found 442.0547.



***N*-(3-(2-Bromophenoxy)-5-(*tert*-butyldimethylsilyl)pent-4-yn-1-yl)-4-fluoroaniline (1e)**



The tosylate **18** (272 mg, 520 μ mol) was reacted with potassium iodide (36 mg, 217 μ mol), 4-fluoroaniline (72 μ L, 750 μ mol) and potassium phosphate (222 mg, 1.05 mmol) according to GP2 (Synthesis of Amine (A)). The reaction mixture was stirred 14 h at 90 °C. Silica gel column chromatography (EtOAc:*n*-pentane =1:40) afforded product **1e** (67.7 mg, 146 μ mol, 28%) as yellow oil.

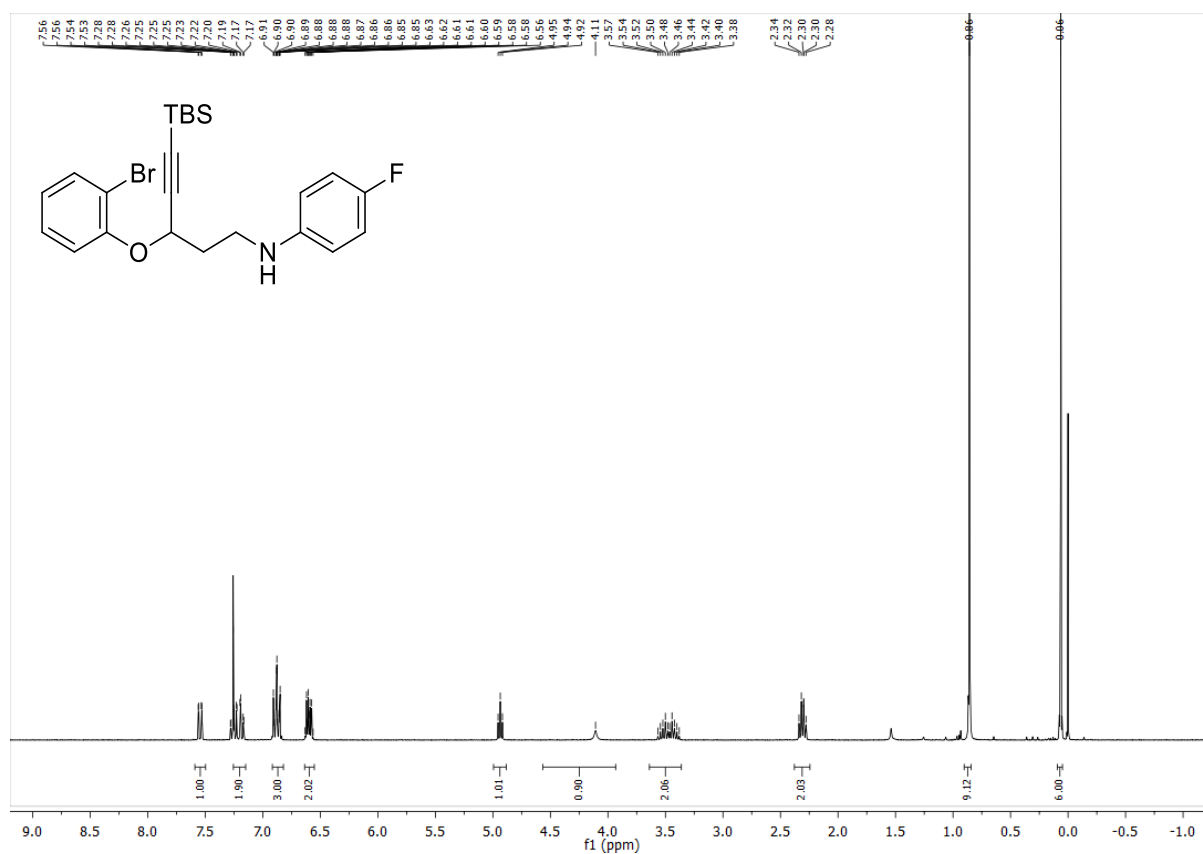
¹H-NMR (300 MHz, CDCl₃): δ = 0.06 (s, 6H), 0.86 (s, 9H), 2.24–2.38 (m, 2H), 3.36–3.64 (m, 2H), 4.11 (s, 1H), 4.94 (t, J = 5.7 Hz, 1H), 6.55–6.64 (m, 2H), 6.82–6.92 (m, 3H), 7.15–7.28 (m, 2H), 7.55 (dd, J = 7.9, 1.6 Hz, 1H).

¹³C-NMR (76 MHz, CDCl₃) δ = -4.9, -4.8, 16.5, 25.9, 35.0, 40.9, 68.6, 91.7, 102.8, 112.9, 113.59 (d, J = 7.4 Hz), 115.91 (d, J = 20.6 Hz), 116.0, 122.9, 128.2, 133.3, 144.56 (d, J = 1.8 Hz), 153.9, 154.2.

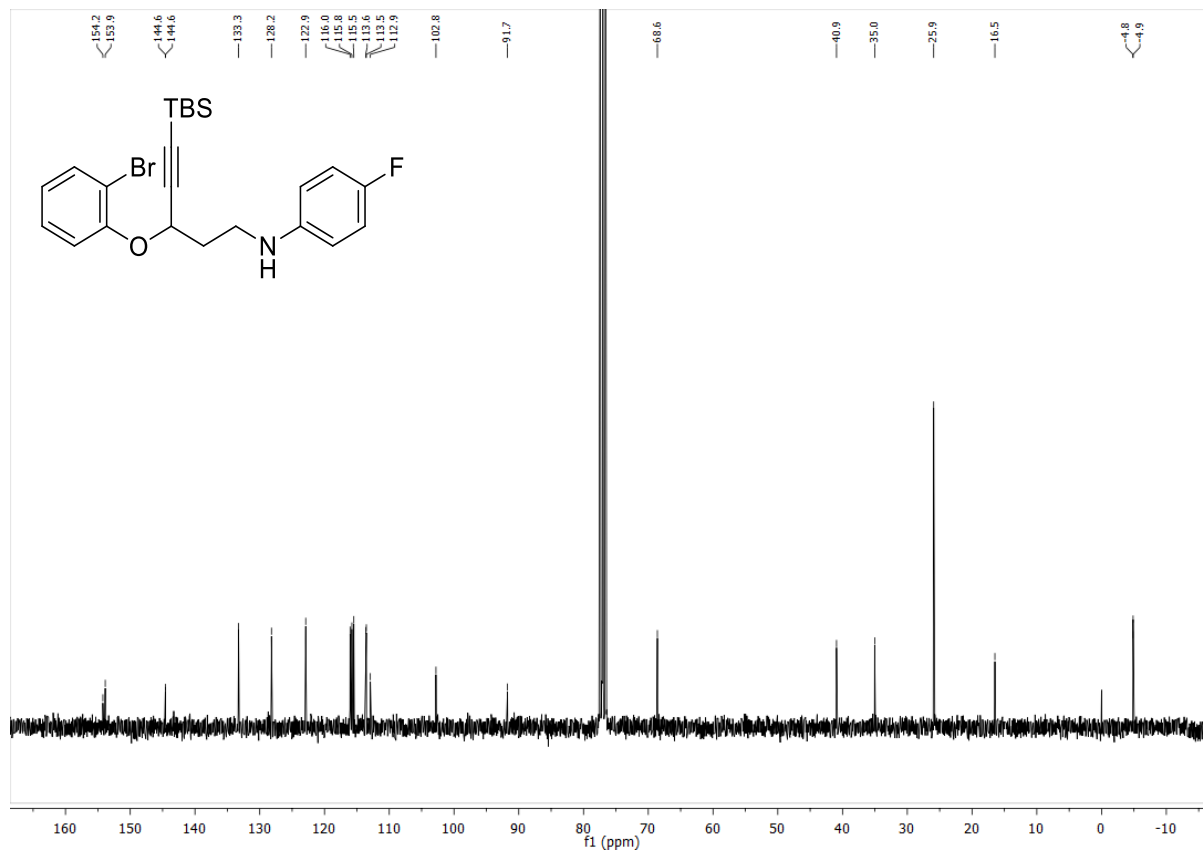
¹⁹F-NMR (283 MHz, CDCl₃): δ = -128.78.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3410 (w), 2952 (m), 2934 (m), 2890 (w), 2857 (m), 1513 (s), 1473 (m), 1228 (m), 1039 (m).

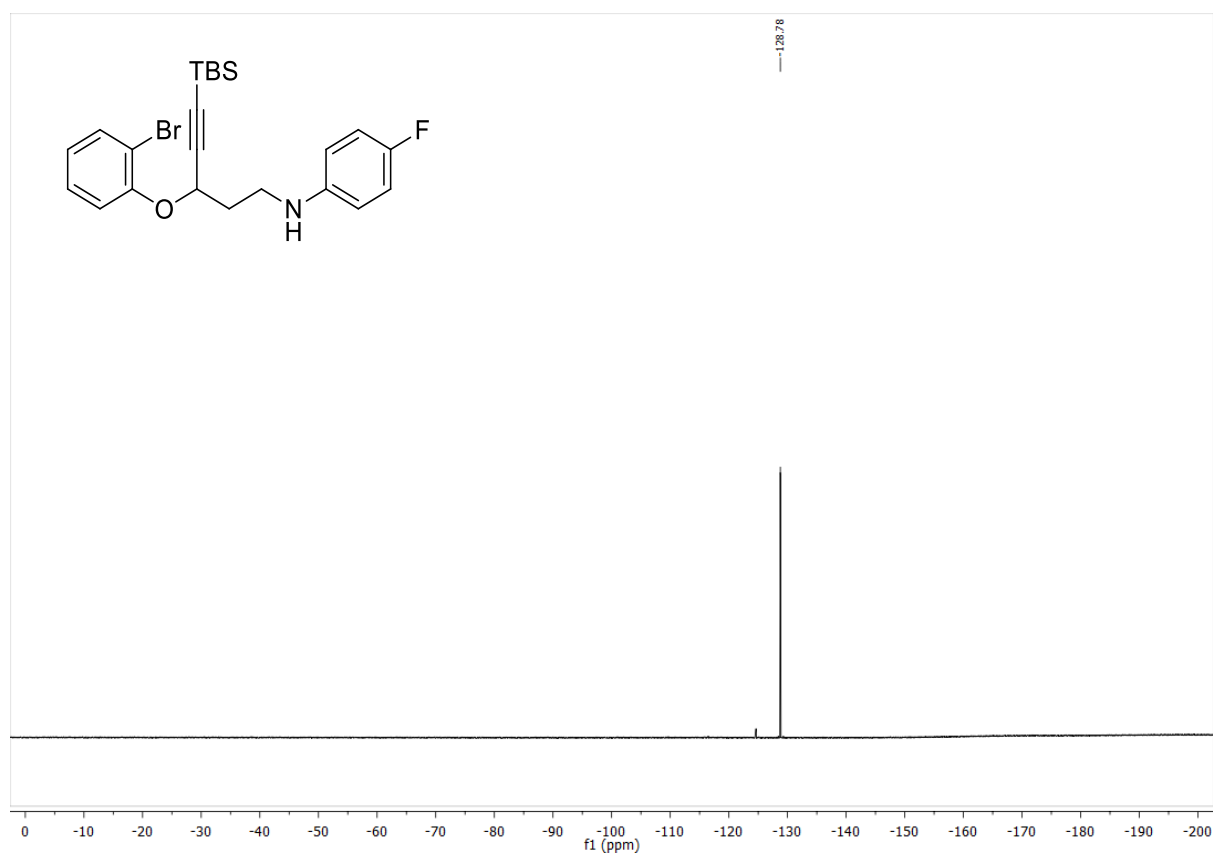
ESI-HRMS: C₂₃H₂₉BrFNOSi m/z calcd. [M+H⁺]: 462.1259 found 462.1264.



¹H-NMR (300 MHz, CDCl₃)

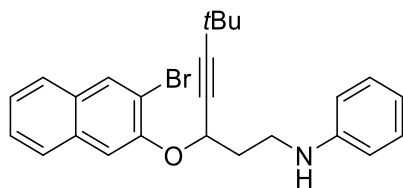


¹³C-NMR (76 MHz, CDCl₃)



^{19}F -NMR (283 MHz, CDCl_3)

***N*-(3-((3-Bromonaphthalen-2-yl)oxy)-6,6-dimethylhept-4-yn-1-yl)aniline (1f)**



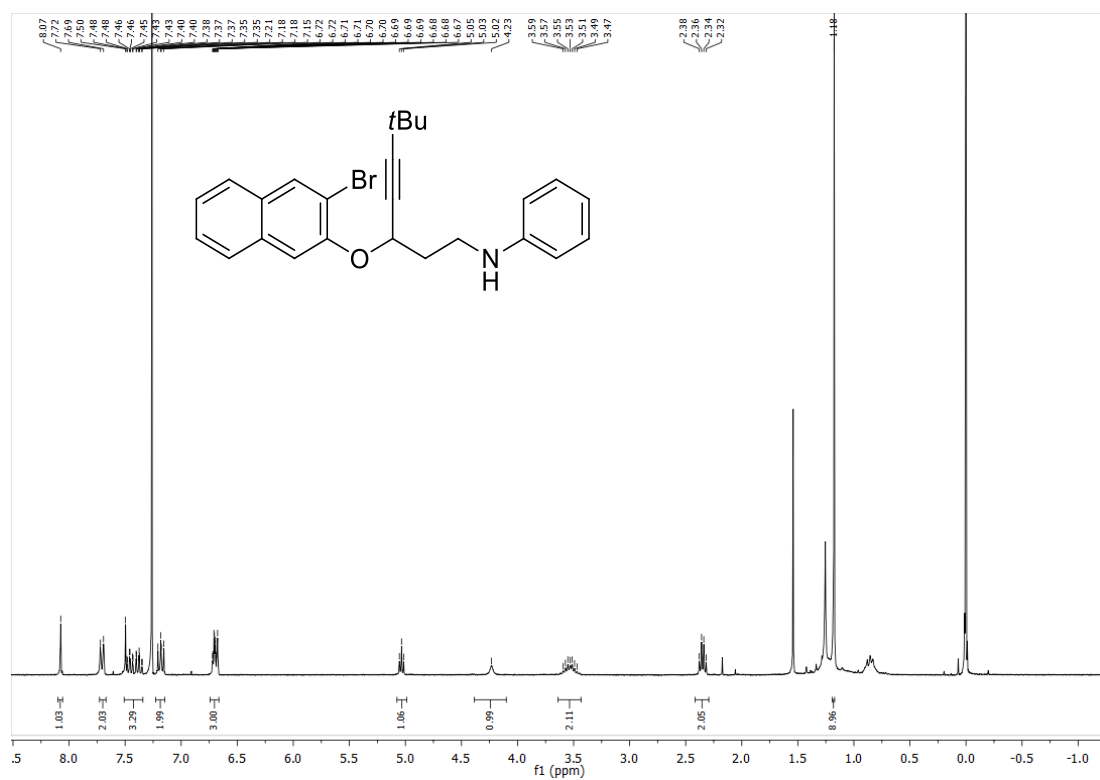
The tosylate **19** (230 mg, 447 μmol) was reacted with potassium iodide (20 mg, 120 μmol), aniline (100 μL , 102 mg, 1.10 mmol) and potassium carbonate (136 mg, 984 μmol) according to GP2 (Synthesis of Amine (A)). The reaction mixture was stirred 19 h at 90 °C. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded product **1f** (39.2 mg, 89.8 μmol , 20%) as colorless oil.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.18 (s, 9H), 2.35 (q, J = 6.3 Hz, 2H), 3.53 (tt, J = 12.9, 6.5 Hz, 2H), 4.23 (s, 1H), 5.03 (t, J = 5.7 Hz, 1H), 6.66–6.74 (m, 3H), 7.18 (dd, J = 8.6, 7.3 Hz, 2H), 7.34–7.51 (m, 3H), 7.71 (d, J = 8.2 Hz, 2H), 8.07 (s, 1H).

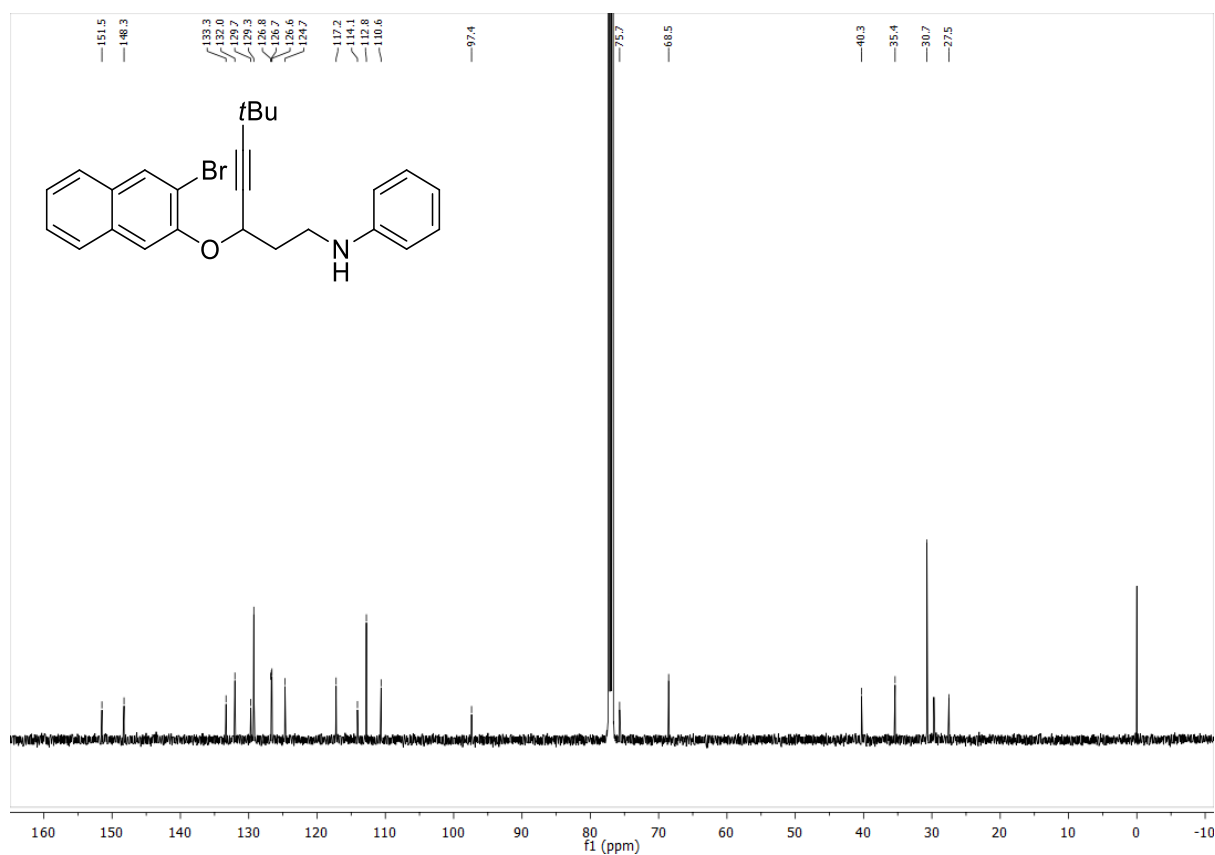
$^{13}\text{C-NMR}$ (126 MHz, CDCl_3): δ = 27.7, 30.9, 35.6, 40.5, 68.7, 75.9, 97.6, 110.8, 112.9, 114.3, 117.4, 124.9, 126.8, 126.9, 127.0, 129.4, 129.9, 132.2, 133.5, 148.4, 151.7.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3411 (w), 2964 (m), 2923 (m), 2853 (m), 1602 (m), 1506 (m), 1455 (s), 1244 (m), 1215 (m), 1182 (m).

HRMS-ESI: $\text{C}_{25}\text{H}_{26}\text{BrNO}$ m/z calcd. $[\text{M}+\text{H}^+]$: 436.1271 found 436.1278.



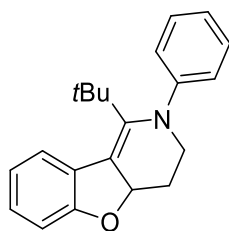
¹H-NMR (300 MHz, CDCl₃)



¹³C-NMR (126 MHz, CDCl₃)

3c) Syntheses of Domino Products of Type 3

Domino product 3a



The domino precursor **1a** (38.3 mg, 99.1 μmol), potassium phosphate (105 mg, 495 μmol), [*t*Bu₃PH][BF₄] (3.0 mg, 10.3 μmol) and Pd(dba)₂ (3.5 mg, 6.1 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 °C. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded domino product **3a** (19.6 mg, 90.6 μmol , 85%) as yellow solid.

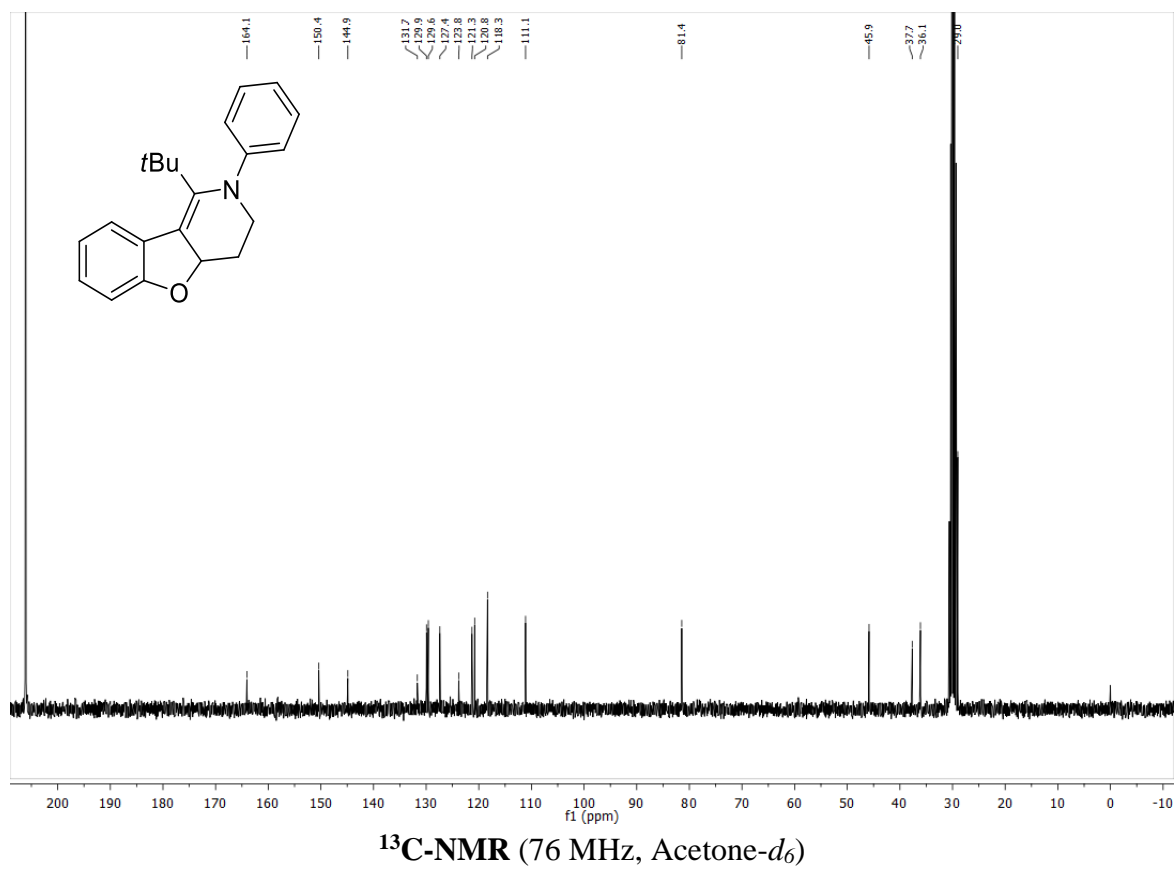
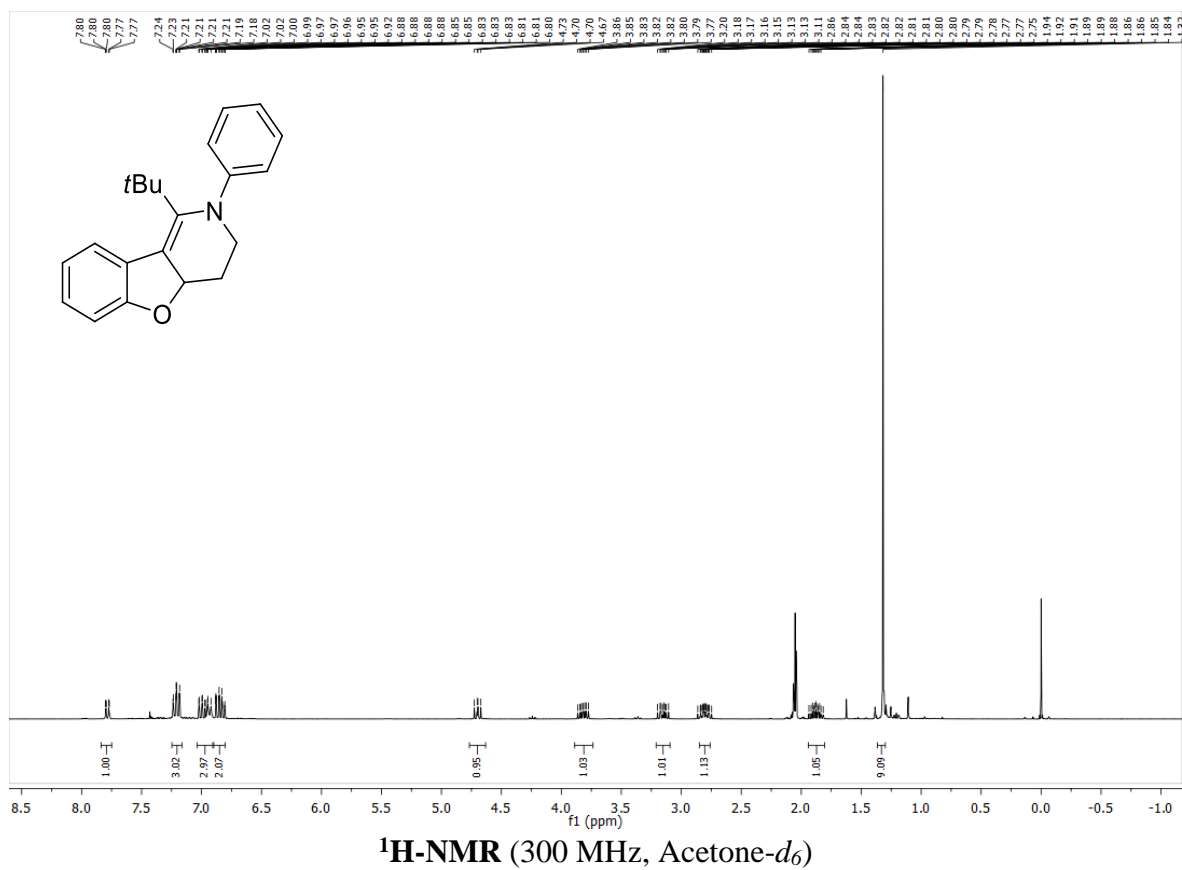
¹H-NMR (300 MHz, Acetone-*d*₆): δ = 1.32 (s, 9H), 1.88 (dtd, J = 12.2, 8.9, 5.5 Hz, 1H), 2.76–2.85 (m, 1H), 3.15 (ddd, J = 12.5, 8.8, 6.3 Hz, 1H), 3.82 (ddd, J = 12.5, 8.7, 5.5 Hz, 1H), 4.70 (dd, J = 9.1, 7.3 Hz, 1H), 6.80–6.90 (m, 2H), 6.91–7.04 (m, 3H), 7.21 (ddd, J = 8.0, 7.3, 1.3 Hz, 3H), 7.75–7.84 (m, 1H).

¹³C-NMR (76 MHz, Acetone-*d*₆) δ = 29.0, 36.1, 37.7, 45.9, 81.4, 111.1, 118.3, 120.8, 121.3, 123.8, 127.4, 129.6, 129.9, 131.7, 144.9, 150.4, 164.1.

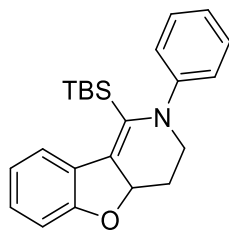
IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 2955 (w), 2932 (w), 2871 (w), 1595 (m), 1492 (m), 1459 (m), 1330 (m), 1225 (m), 1215 (m).

M.p.: 91–96 °C.

GC-HRMS (EI): C₂₁H₂₃NO m/z calcd. [M⁺]: 305.1780 found 305.1797.



Domino product 3b



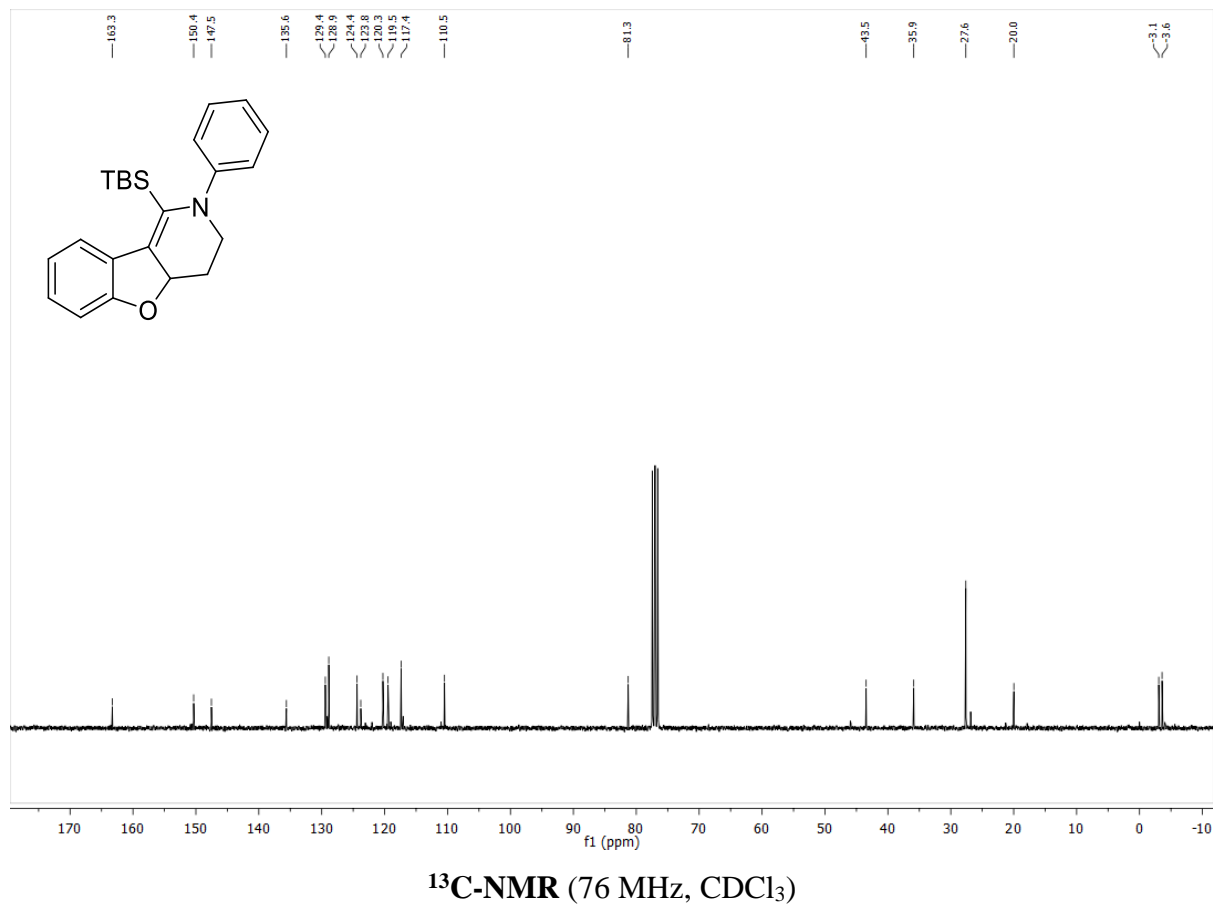
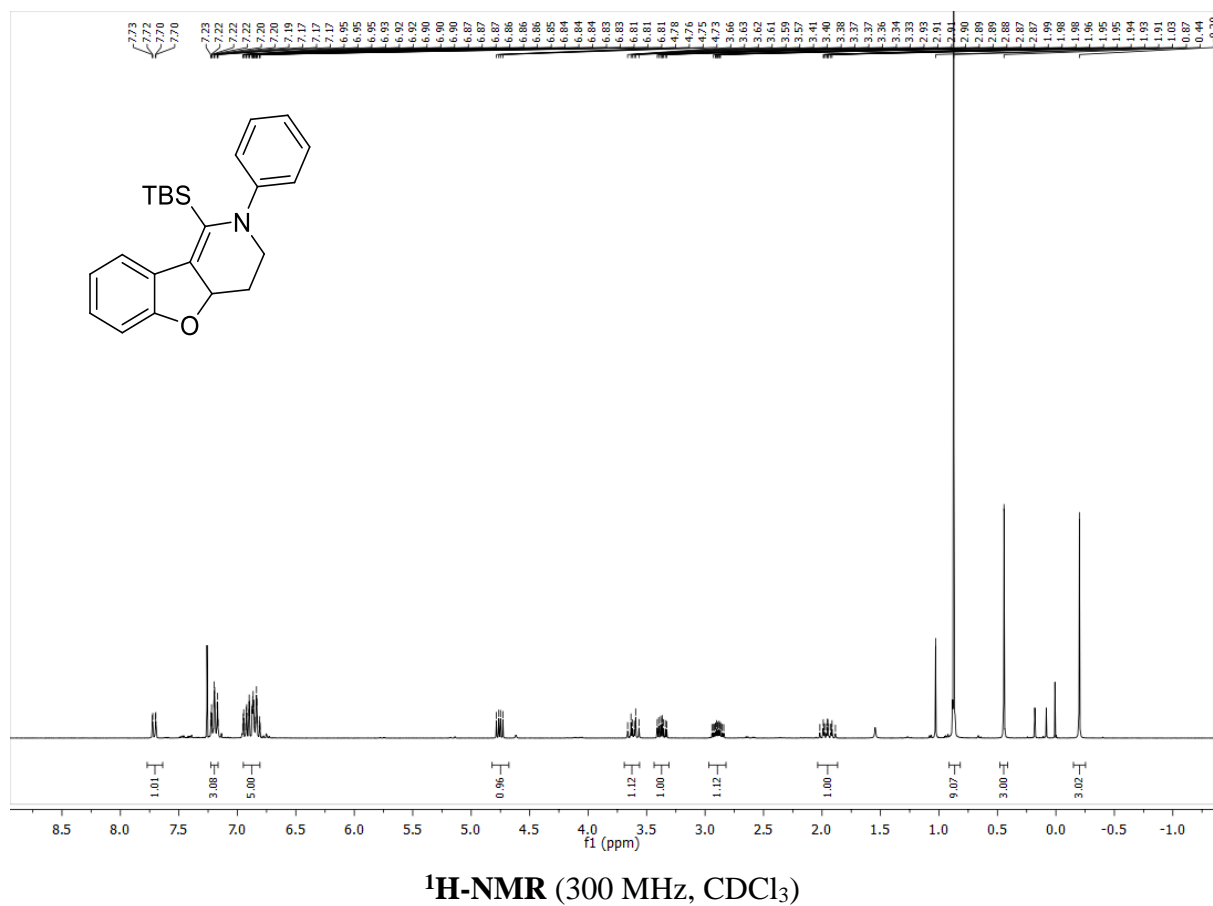
The domino precursor **1b** (47.2 mg, 106 μmol), potassium phosphate (105 mg, 495 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.9 mg, 10.0 μmol) and $\text{Pd}(\text{dba})_2$ (3.0 mg, 5.2 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **3b** (18.1 mg, 49.8 μmol , 47%) as yellow oil.

^1H -NMR (300 MHz, CDCl_3): δ = -0.20 (s, 3H), 0.44 (s, 3H), 0.87 (s, 9H), 1.87–2.04 (m, 1H), 2.82–2.97 (m, 1H), 3.37 (ddd, J = 11.9, 8.8, 3.7 Hz, 1H), 3.61 (dt, J = 11.9, 8.6 Hz, 1H), 4.76 (dd, J = 10.6, 6.1 Hz, 1H), 6.81–6.95 (m, 5H), 7.16–7.23 (m, 3H), 7.71 (dd, J = 7.8, 1.3 Hz, 1H).

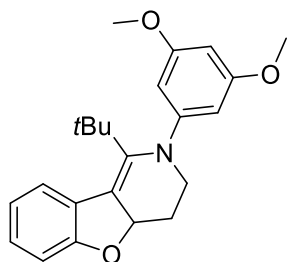
^{13}C -NMR (76 MHz, CDCl_3) δ = -3.6, -3.1, 20.0, 27.6, 35.9, 43.5, 81.3, 110.5, 117.4, 119.5, 120.3, 123.8, 124.4, 128.9, 129.4, 135.6, 147.5, 150.4, 163.3.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2951 (m), 2933 (m), 2858 (m), 1596 (m), 1492 (m), 1460 (m), 1218 (m), 1035 (m).

GC-HRMS (EI): $\text{C}_{23}\text{H}_{29}\text{NOSi}$ m/z calcd. $[\text{M}^+]$: 363.2018 found 363.2037.



Domino product 3c



The domino precursor **1c** (43.5 mg, 97.4 μmol), potassium phosphate (100 mg, 471 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.7 mg, 9.3 μmol) and $\text{Pd}(\text{dba})_2$ (2.9 mg, 5.0 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **3c** (31.5 mg, 86.2 μmol , 88%) as yellow solid.

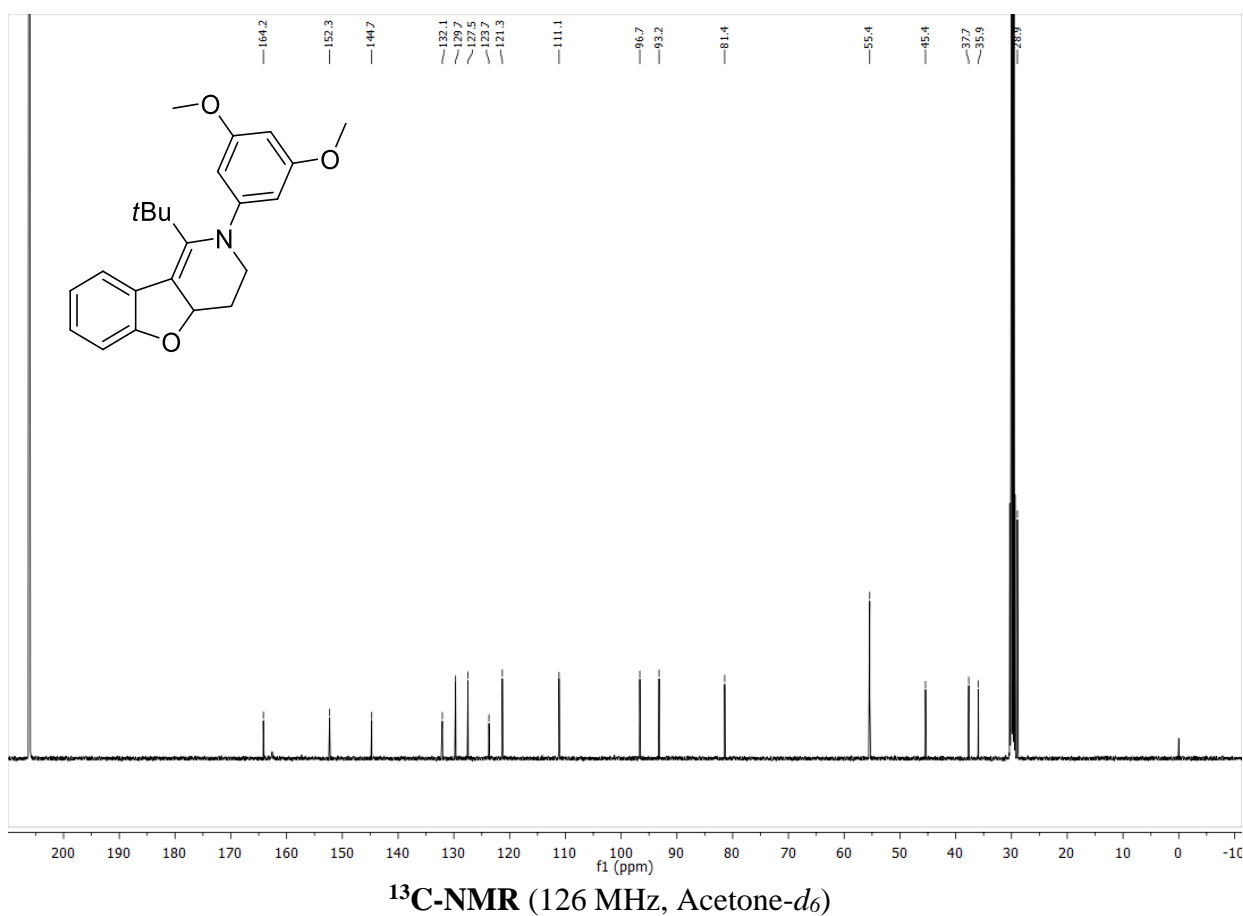
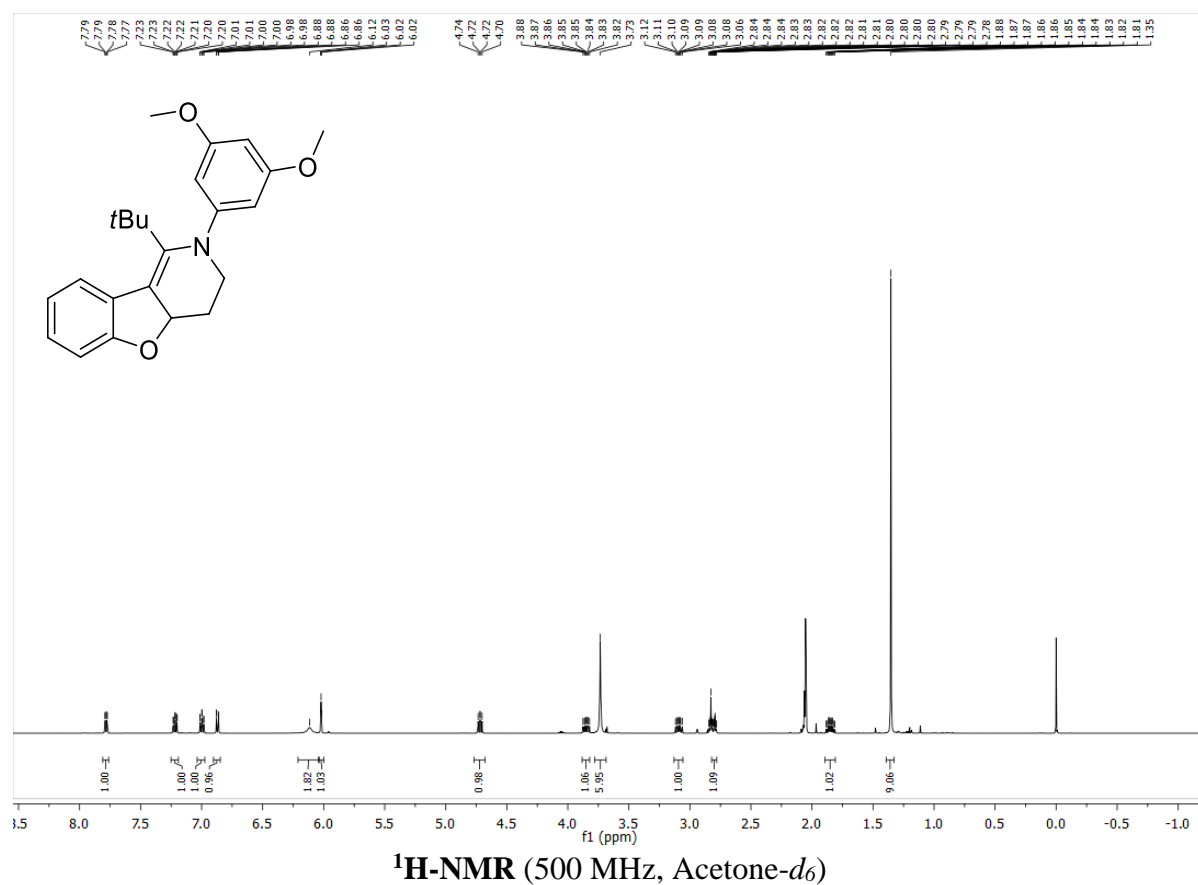
^1H -NMR (500 MHz, Acetone- d_6): δ = 1.35 (s, 9H), 1.81–1.89 (m, 1H), 2.78–2.82 (m, 1H), 3.09 (ddd, J = 12.6, 8.9, 6.3 Hz, 1H), 3.73 (s, 6H), 3.85 (ddd, J = 12.7, 8.8, 5.4 Hz, 1H), 4.72 (dd, J = 9.2, 7.3 Hz, 1H), 6.02 (t, J = 2.1 Hz, 1H), 6.12 (s, 2H), 6.87 (dd, J = 8.1, 1.2 Hz, 1H), 7.00 (td, J = 7.5, 1.0 Hz, 1H), 7.19–7.25 (m, 1H), 7.78 (dd, J = 8.0, 1.3 Hz, 1H).

^{13}C -NMR (126 MHz, Acetone- d_6) δ = 28.9, 35.9, 37.7, 45.4, 55.4, 81.4, 93.2, 96.7, 111.1, 121.3, 123.7, 127.5, 129.7, 132.1, 144.7, 152.3, 164.2.

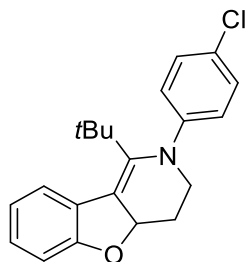
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2957 (m), 2874 (w), 2842 (w), 1593 (s), 1459 (m), 1205 (m), 1156 (m).

M.p.: 99–102 $^\circ\text{C}$.

GC-HRMS (EI): $\text{C}_{23}\text{H}_{27}\text{NO}_3$ m/z calcd. $[\text{M}^+]$: 365.1991 found 365.1971.



Domino product **3d**



The domino precursor **1d** (45.6 mg, 108 μ mol), potassium phosphate (106 mg, 499 μ mol), [*t*Bu₃PH][BF₄] (4.0 mg, 13.8 μ mol) and Pd(dba)₂ (3.1 mg, 5.4 μ mol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 °C. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **3d** (31.0 mg, 90.9 μ mol, 84%) as yellow oil.

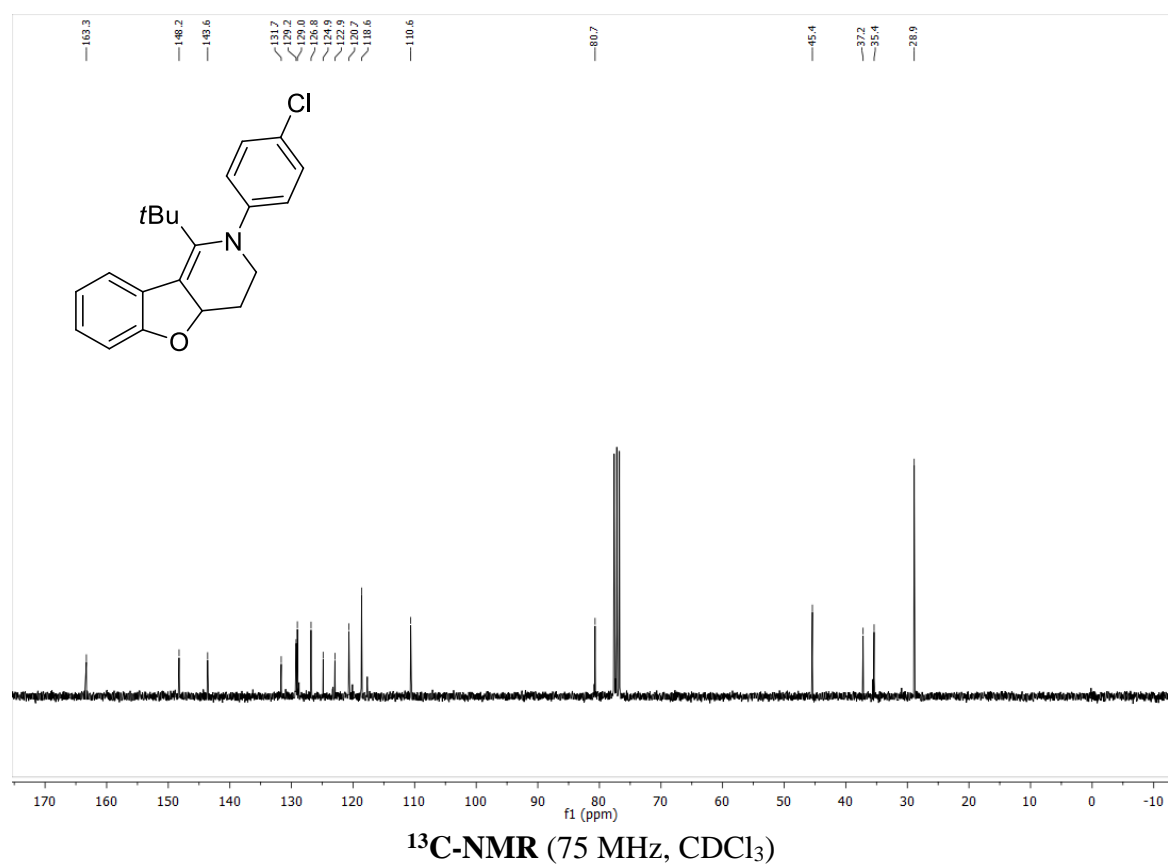
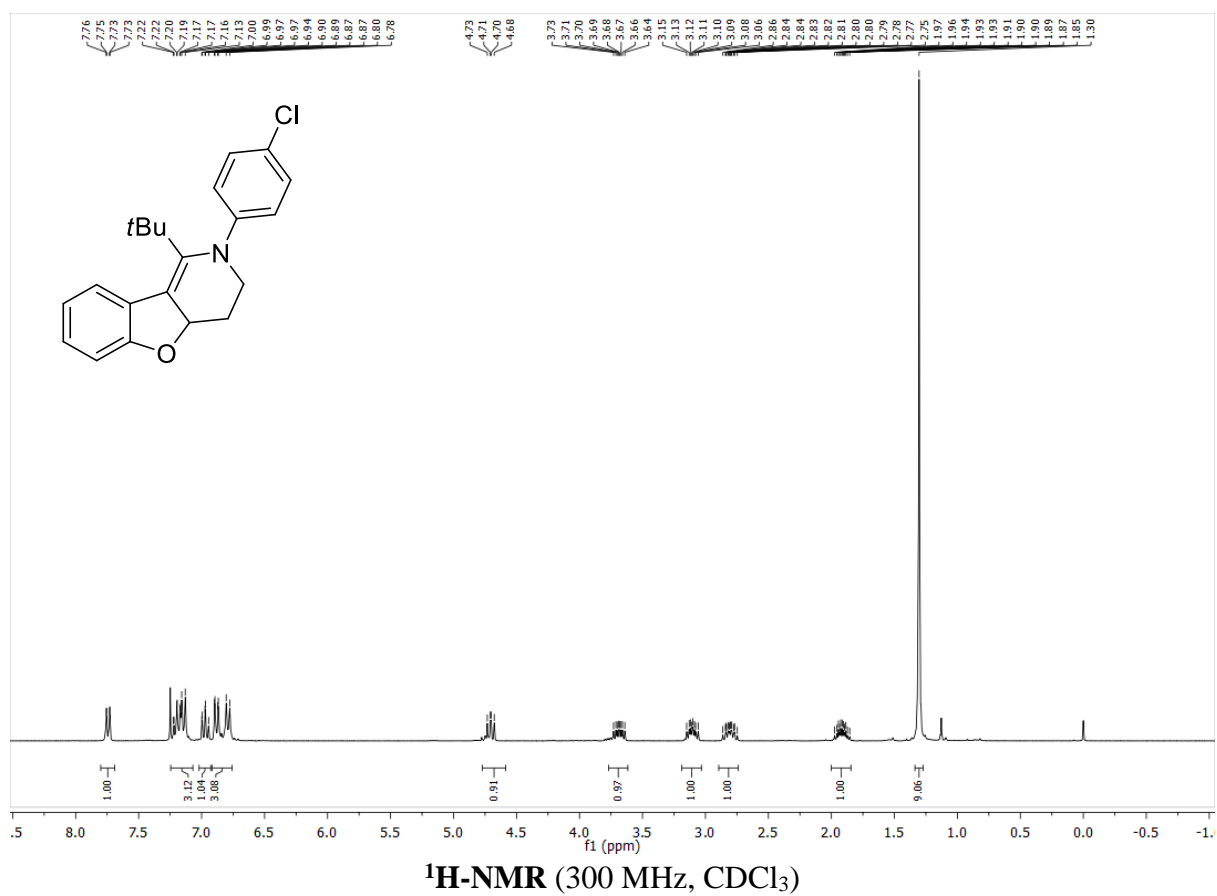
¹H-NMR (300 MHz, CDCl₃): δ = 1.30 (s, 9H), 1.91 (dtd, *J* = 12.2, 9.1, 5.6 Hz, 1H), 2.81 (dtd, *J* = 13.1, 8.6, 7.9, 6.3 Hz, 1H), 3.10 (ddd, *J* = 12.6, 9.0, 6.1 Hz, 1H), 3.69 (ddd, *J* = 12.5, 8.8, 5.6 Hz, 1H), 4.70 (dd, *J* = 9.3, 7.2 Hz, 1H), 6.76–6.92 (m, 3H), 6.93–7.02 (m, 1H), 7.07–7.25 (m, 3H), 7.74 (dd, *J* = 7.8, 1.4 Hz, 1H).

¹³C-NMR (75 MHz, CDCl₃): δ = 28.9, 35.4, 37.2, 45.4, 80.7, 110.6, 118.6, 120.7, 122.9, 124.9, 126.8, 129.0, 129.2, 131.7, 143.6, 148.2, 163.3.

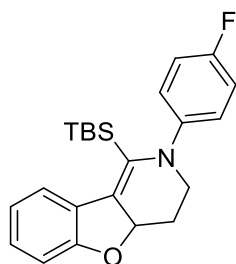
IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 2956 (m), 2873 (w), 1591 (m), 1488 (s), 1460 (m), 1328 (m), 1220 (m), 1047 (m).

M.p.: 99–102 °C.

GC-HRMS (EI): C₂₁H₂₂ClNO *m/z* calcd. [M⁺]: 339.1390 found 339.1411.



Domino product 3e



The domino precursor **1e** (58.3 mg, 126 μmol), potassium phosphate (102 mg, 480 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (3.6 mg, 12.4 μmol) and $\text{Pd}(\text{dba})_2$ (3.6 mg, 6.3 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (100% *n*-pentane) afforded domino product **3e** (12.1 mg, 31.7 μmol , 25%) as yellow oil.

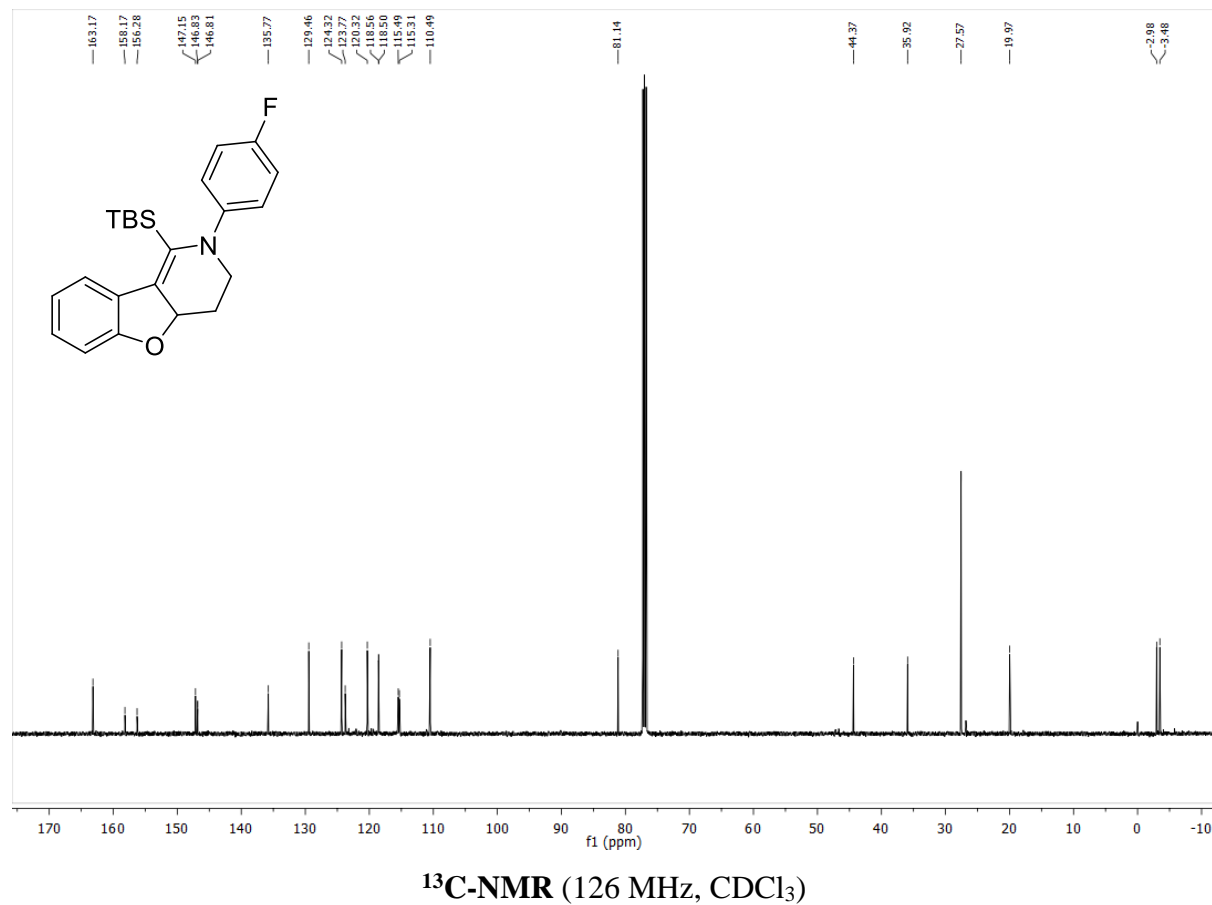
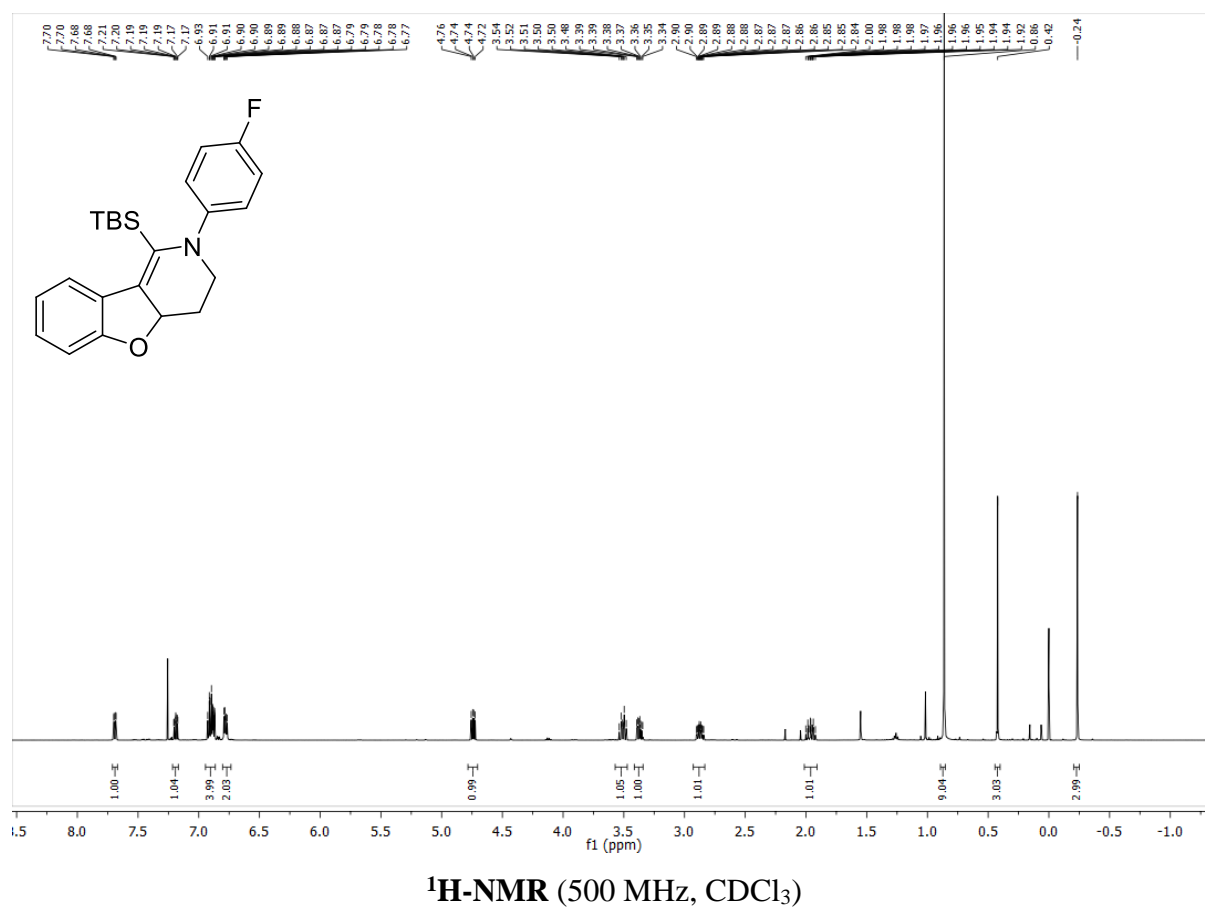
^1H -NMR (500 MHz, CDCl_3): δ = -0.24 (s, 3H), 0.42 (s, 3H), 0.86 (s, 9H), 1.91 – 2.01 (m, 1H), 2.83 – 2.93 (m, 1H), 3.34 – 3.41 (m, 1H), 3.51 (dt, J = 11.8, 8.5 Hz, 1H), 4.74 (dd, J = 10.4, 6.1 Hz, 1H), 6.78 (dd, J = 9.0, 4.7 Hz, 2H), 6.86 – 6.94 (m, 4H), 7.19 (ddd, J = 8.5, 7.3, 1.3 Hz, 1H), 7.69 (dd, J = 8.0, 1.3 Hz, 1H).

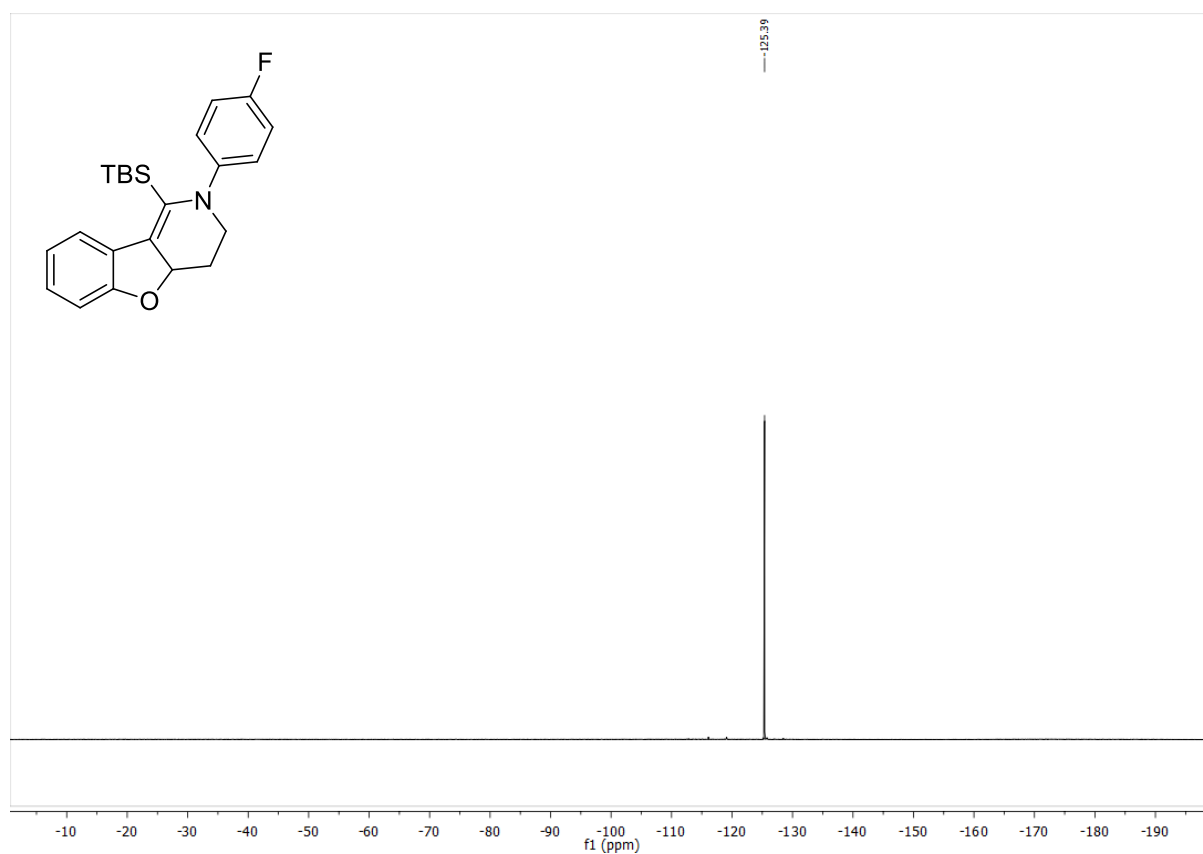
^{13}C -NMR (126 MHz, CDCl_3): δ = -3.5, -3.0, 20.0, 27.6, 35.9, 44.4, 81.1, 110.5, 115.4 (d, J = 22.1 Hz), 118.5 (d, J = 7.6 Hz), 120.3, 123.8, 124.3, 129.5, 135.8, 146.8 (d, J = 2.2 Hz), 147.2, 157.2 (d, J = 238.4 Hz), 163.2.

^{19}F -NMR (377 MHz, CDCl_3): δ = -125.4.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2952 (m), 2934 (m), 2888 (w), 2859 (m), 1670 (m), 1505 (s), 1460 (m), 1219 (m), 1038 (m).

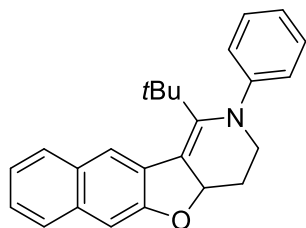
GC-HRMS (EI): $\text{C}_{23}\text{H}_{28}\text{FNOSi}$ m/z calcd. $[\text{M}^+]$: 381.1924 found 381.1907.





^{19}F -NMR (377 MHz, CDCl_3)

Domino product (3f)



The domino precursor **1f** (39.2 mg, 89.8 μmol), potassium phosphate (94 mg, 443 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.6 mg, 9.0 μmol) and $\text{Pd}(\text{dba})_2$ (2.0 mg, 3.5 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane= 1:20) afforded domino product **3f** (21.6 mg, 60.8 μmol , 68%) as brown solid.

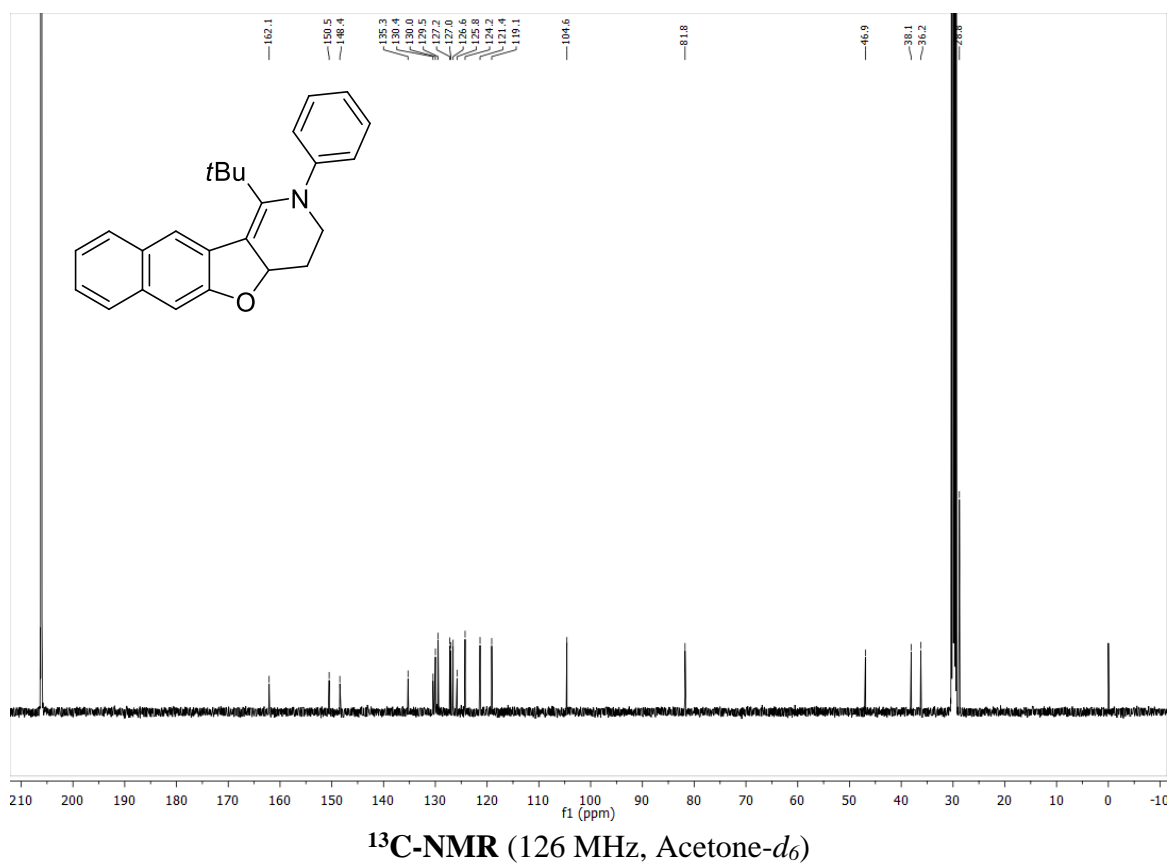
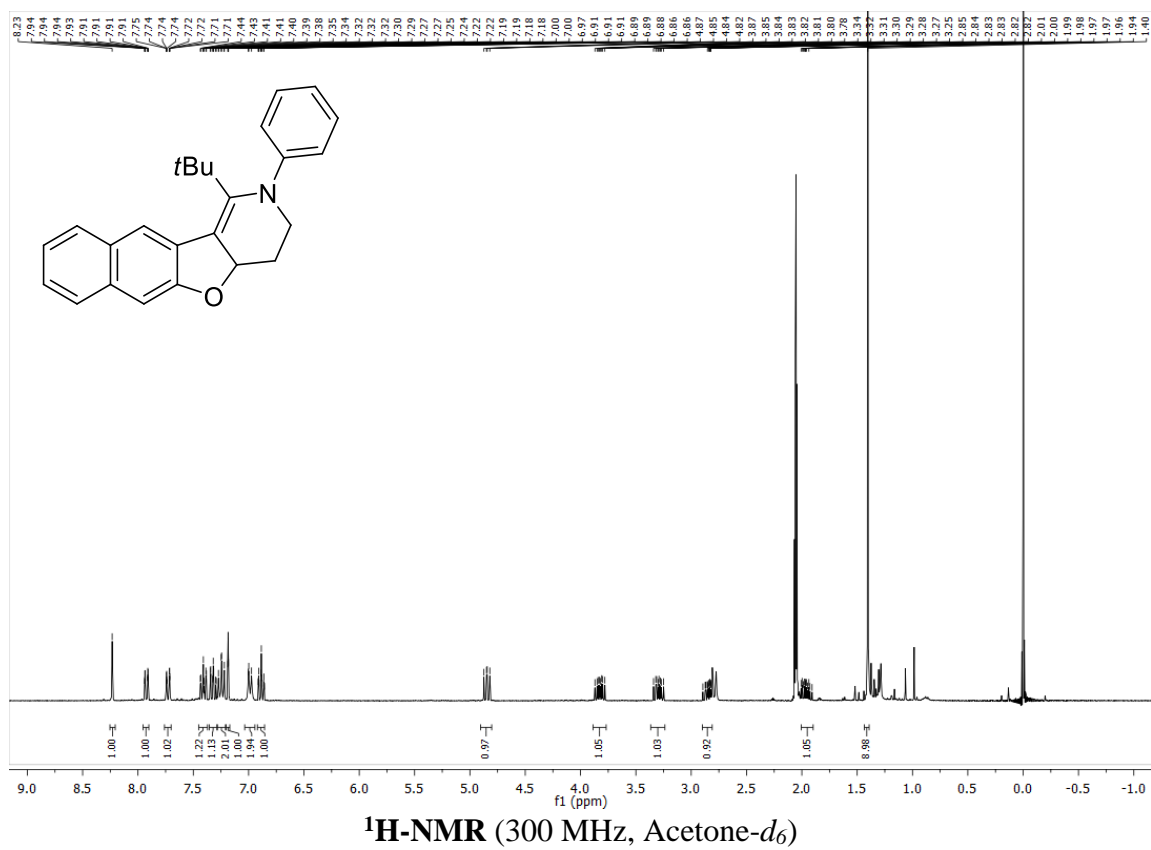
^1H -NMR (300 MHz, Acetone- d_6): δ = 1.40 (s, 9H), 1.90–2.01 (m, 1H), 2.81–2.90 (m, 1H), 3.30 (ddd, J = 12.4, 8.6, 6.2 Hz, 1H), 3.83 (ddd, J = 12.5, 8.6, 5.9 Hz, 1H), 4.85 (dd, J = 9.0, 7.1 Hz, 1H), 6.89 (tt, J = 7.3, 1.1 Hz, 1H), 6.94–7.04 (m, 2H), 7.18 (q, J = 0.6 Hz, 1H), 7.25 (td, J = 7.4, 1.0 Hz, 2H), 7.32 (ddd, J = 8.1, 6.9, 1.4 Hz, 1H), 7.41 (ddd, J = 8.3, 6.8, 1.4 Hz, 1H), 7.73 (ddd, J = 8.1, 1.3, 0.6 Hz, 1H), 7.92 (ddd, J = 8.1, 1.4, 0.7 Hz, 1H), 8.23 (s, 1H).

^{13}C -NMR (126 MHz, Acetone- d_6) δ = 28.8, 36.2, 38.1, 46.9, 81.8, 104.6, 119.1, 121.4, 124.2, 125.8, 126.6, 127.0, 127.2, 129.5, 130.0, 130.4, 135.3, 148.4 150.5, 162.1.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2953 (w), 2928 (w), 2869 (w), 1592 (m), 1490 (m), 1444 (m), 1233 (m), 1219 (m), 1155 (m).

M.p.: 174–177 $^\circ\text{C}$.

GC-HRMS (EI): $\text{C}_{25}\text{H}_{25}\text{NO}$ m/z calcd. $[\text{M}^+]$: 355.1936 found 355.1949.



4) Syntheses of Precursors of Type 2

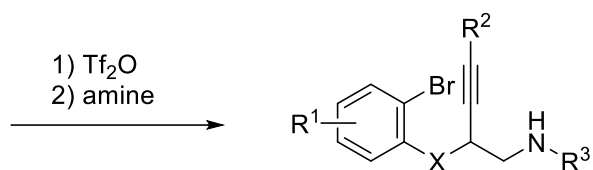


$R^1 = \text{H}, R^2 = t\text{Bu}, X = \text{O}$ **21**

$R^1 = \text{C}_6\text{H}_4, R^2 = t\text{Bu}, X = \text{O}$ **22**

$R^1 = \text{H}, R^2 = \text{TMS}, X = \text{NTs}$ **23**

$R^1 = \text{H}, R^2 = \text{TBS}, X = \text{NTs}$ **24**



$R^1 = \text{H}, R^2 = t\text{Bu}, R^3 = \text{Ph}, X = \text{O}$ **2a** (84%)

$R^1 = \text{H}, R^2 = t\text{Bu}, R^3 = 3,5\text{-(OMe)}_2\text{-Ph}, X = \text{O}$ **2b** (40%)

$R^1 = \text{H}, R^2 = t\text{Bu}, R^3 = 4\text{-Cl-Ph}, X = \text{O}$ **2c** (38%)

$R^1 = \text{naphthyl}, R^2 = t\text{Bu}, R^3 = \text{Ph}, X = \text{O}$ **2d** (80%)

$R^1 = \text{H}, R^2 = t\text{Bu}, R^3 = 2,4,6\text{-Me}_3\text{-Ph}, X = \text{O}$ **2e** (67%)

$R^1 = \text{H}, R^2 = \text{TMS}, R^3 = 2,4,6\text{-Me}_3\text{-Ph}, X = \text{NTs}$ **2f** (42%)

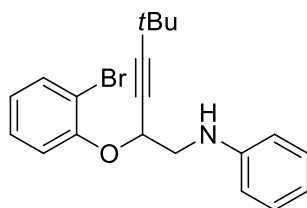
$R^1 = \text{H}, R^2 = \text{TMS}, R^3 = \text{Ph}, X = \text{NTs}$ **2g** (44%)

$R^1 = \text{H}, R^2 = \text{TBS}, R^3 = \text{Ph}, X = \text{NTs}$ **2h** (73%)

$R^1 = \text{H}, R^2 = t\text{Bu}, R^3 = i\text{Pr}, X = \text{O}$ **2i** (65%)

$R^1 = \text{H}, R^2 = t\text{Bu}, R^3 = \text{Bn}, X = \text{O}$ **2j** (79%)

***N*-(2-(2-Bromophenoxy)-5,5-dimethylhex-3-yn-1-yl)aniline (**2a**)**



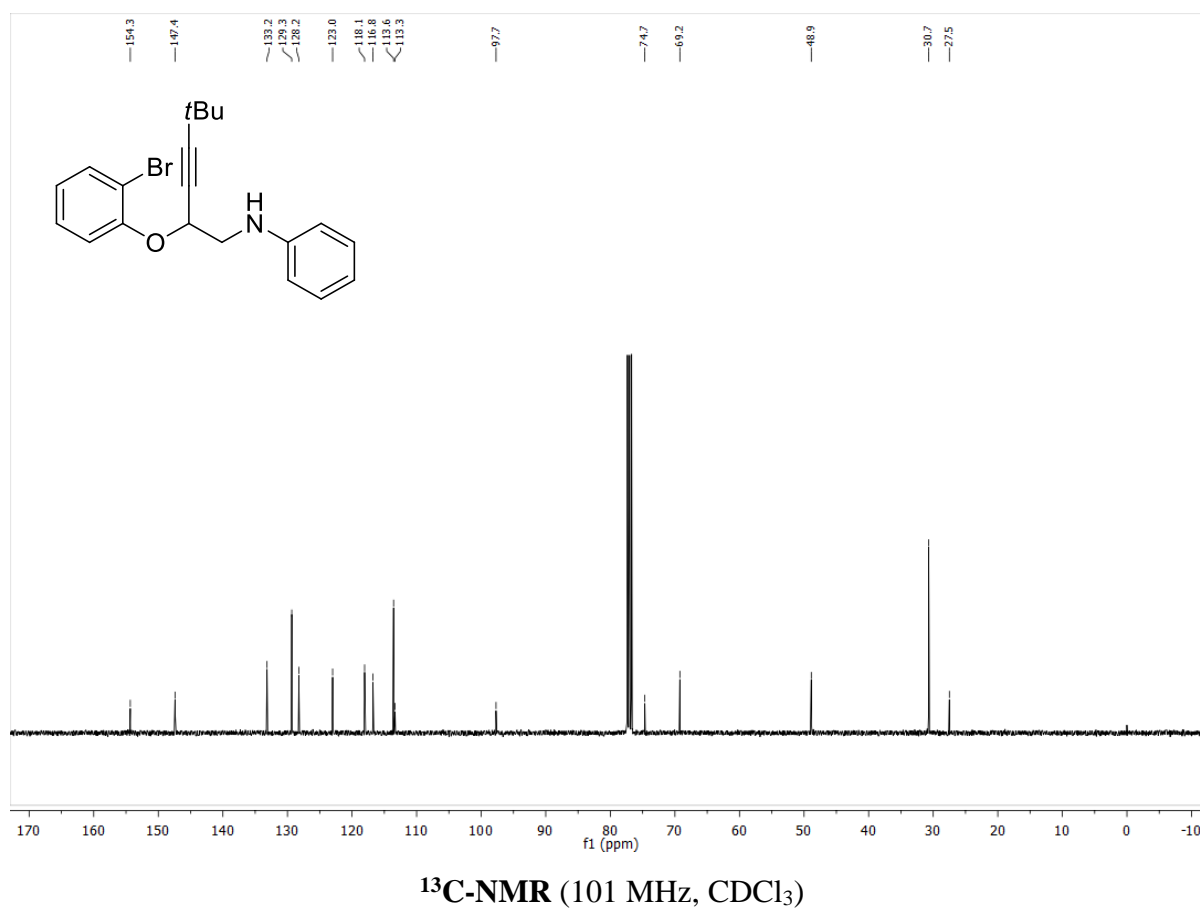
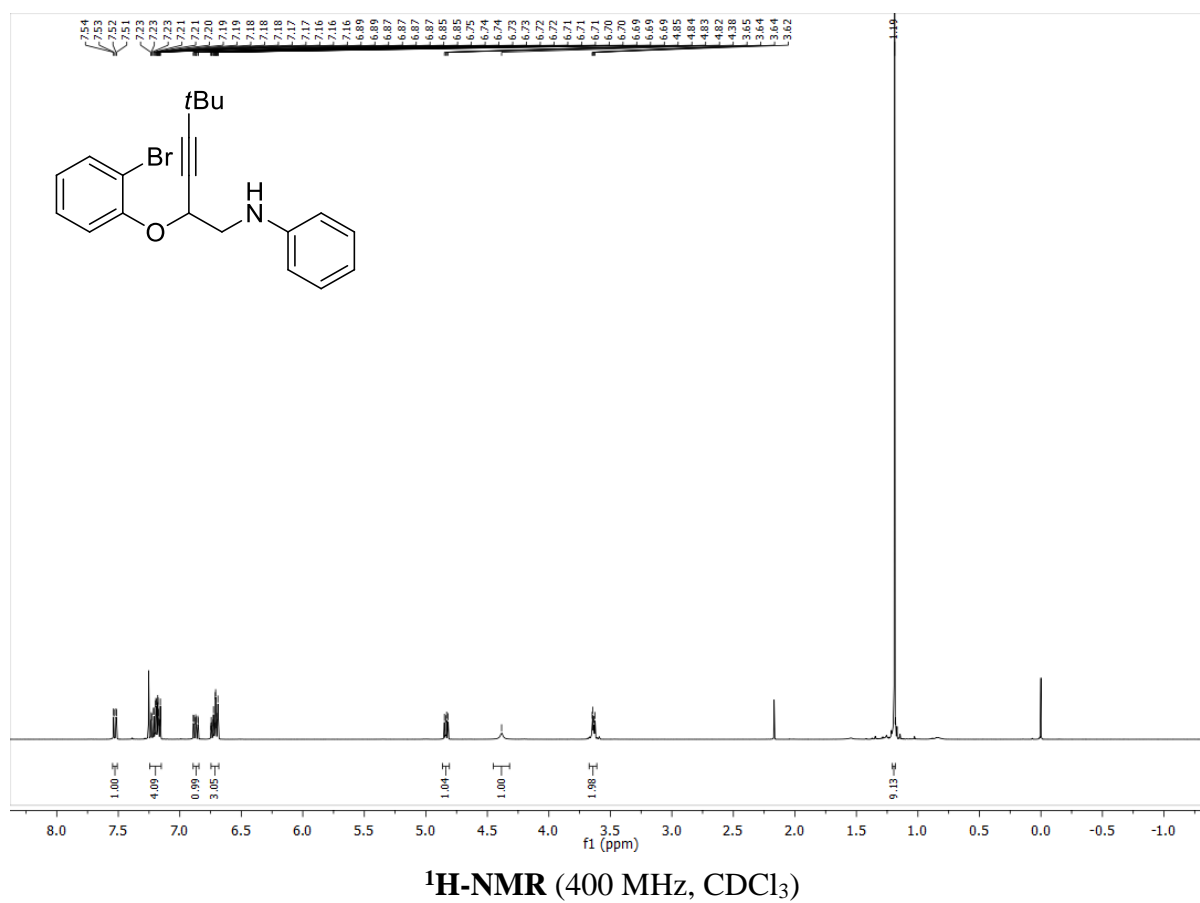
Alcohol **21**³ (1.18 g, 3.96 mmol) was reacted with DIPEA (900 μ L, 5.17 mmol), TiF_2O (750 μ L, 4.57 mmol) and aniline (600 μ L, 6.57 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded compound **2a** (1.24 g, 3.33 mmol, 84%) as colorless oil.

^1H -NMR (400 MHz, CDCl_3): δ = 1.19 (s, 9H), 3.61–3.67 (m, 2H), 4.38 (s, 1H), 4.83 (dd, J = 7.4, 4.9 Hz, 1H), 6.68–6.75 (m, 3H), 6.87 (ddd, J = 8.0, 7.1, 1.7 Hz, 1H), 7.15–7.24 (m, 4H), 7.53 (dd, J = 7.9, 1.6 Hz, 1H).

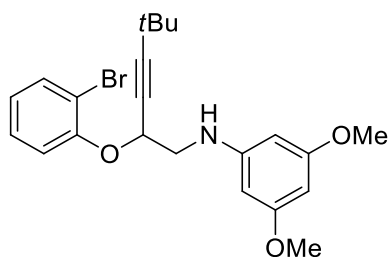
^{13}C -NMR (101 MHz, CDCl_3) δ = 27.5, 30.7, 48.9, 69.2, 74.7, 97.7, 113.3, 113.6, 116.8, 118.1, 123.0, 128.2, 129.3, 133.2, 147.4, 154.3.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3411 (w), 3054 (w), 3023 (w), 2969 (m), 2928 (m), 2901 (m), 2867 (m), 1603 (m), 1475 (s), 1262 (m), 1241 (m), 1030 (m).

GC-HRMS (EI): $\text{C}_{20}\text{H}_{22}\text{BrNO}$ m/z calcd. [M^+]: 371.0885 found 371.0895.



***N*-(2-(2-Bromophenoxy)-5,5-dimethylhex-3-yn-1-yl)-3,5-dimethoxyaniline (**2b**)**



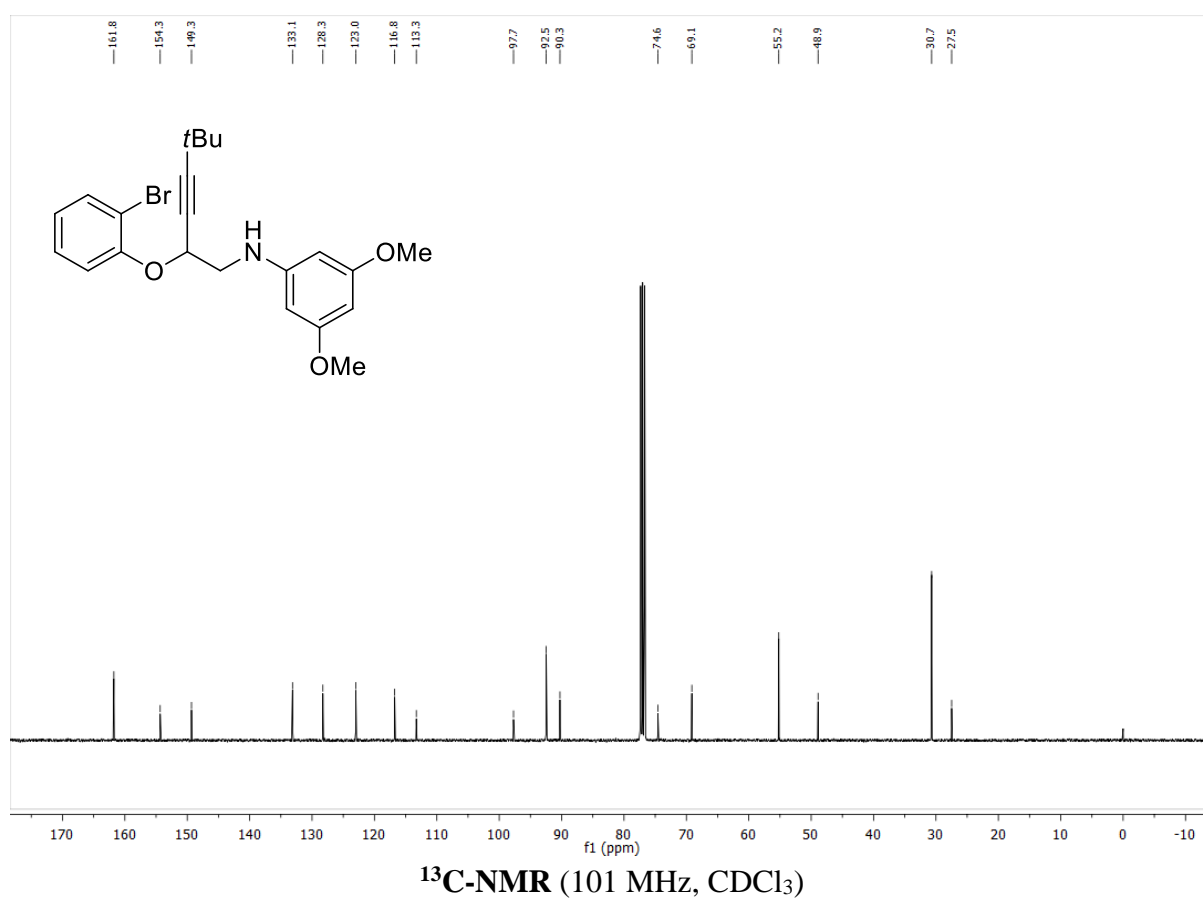
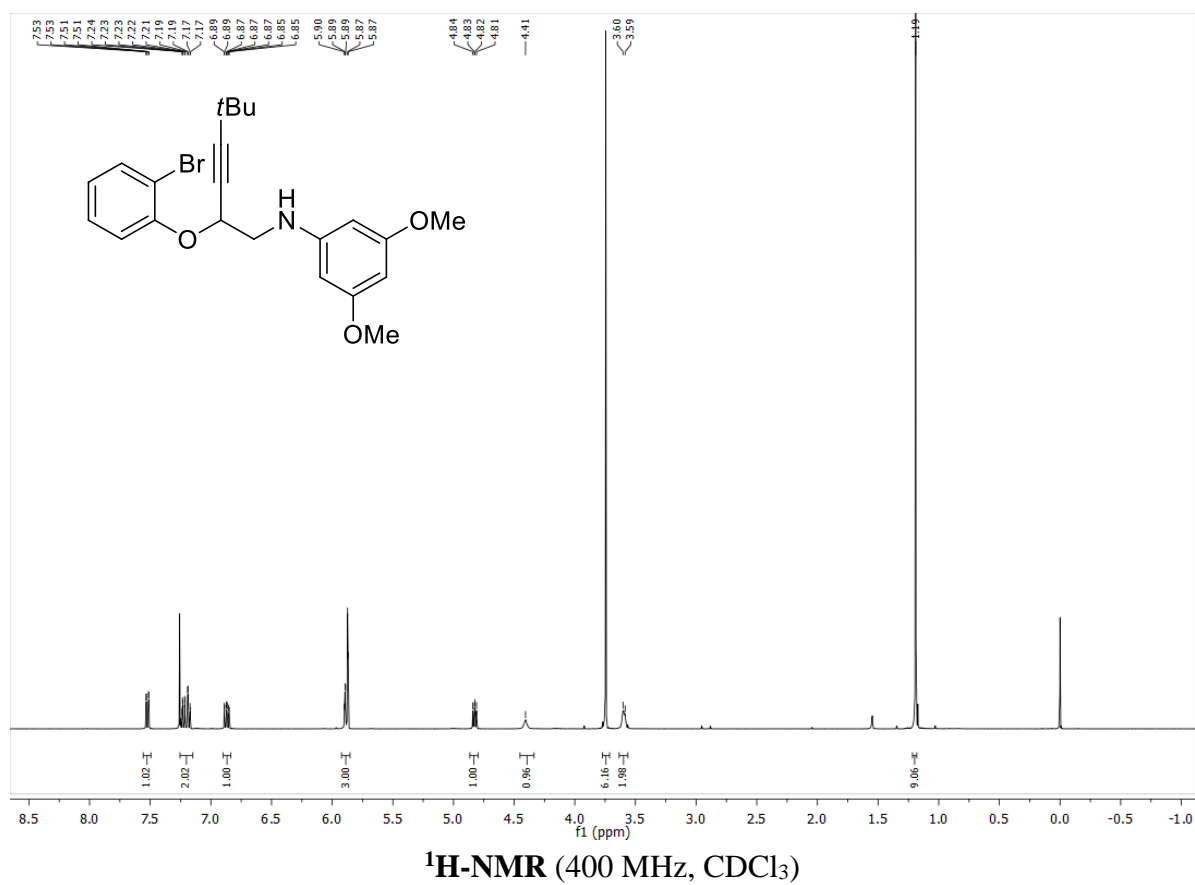
Alcohol **21**³ (225 mg, 757 μ mol) was reacted with DIPEA (180 μ L, 1.03 mmol), TiF_2O (140 μ L, 854 μ mol) and 3,5-dimethoxyaniline (226 mg, 1.47 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:15) afforded compound **2b** (130 mg, 300 μ mol, 40%) as colorless oil.

^1H -NMR (400 MHz, CDCl_3): δ = 1.19 (s, 9H), 3.56–3.63 (m, 2H), 3.74 (s, 6H), 4.41 (s, 1H), 4.83 (dd, J = 7.1, 5.2 Hz, 1H), 5.85–5.92 (m, 3H), 6.84–6.90 (m, 1H), 7.15–7.25 (m, 2H), 7.52 (dd, J = 7.9, 1.6 Hz, 1H).

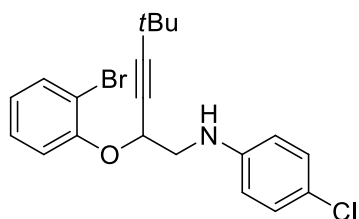
^{13}C -NMR (101 MHz, CDCl_3): δ = 27.5, 30.7, 48.9, 55.2, 69.1, 74.6, 90.3, 92.5, 97.7, 113.3, 116.8, 123.0, 128.3, 133.1, 149.3, 154.3, 161.8.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3407 (w), 2967 (m), 2905 (m), 2867 (w), 2841 (w), 1611 (s), 1474 (m), 1238 (m), 1203 (s), 1153 (s).

ESI-HRMS: $\text{C}_{22}\text{H}_{26}\text{BrNO}_3$ m/z calcd. $[\text{M}+\text{H}^+]$: 432.1169 found 432.1174.



***N*-(2-(2-Bromophenoxy)-5,5-dimethylhex-3-yn-1-yl)-4-chloroaniline (2c)**



Alcohol **21**³ (148 mg, 498 μ mol) was reacted with DIPEA (140 μ L, 804 μ mol), TiF_2O (100 μ L, 610 μ mol) and 4-chloroaniline (128 mg, 1.00 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:25) afforded compound **2c** (77.8 mg, 191 μ mol, 38%) as yellow oil.

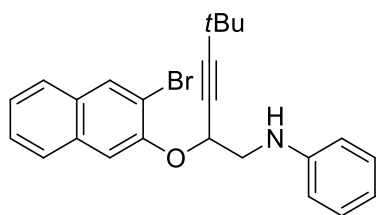
$^1\text{H-NMR}$ (500 MHz, CDCl_3): δ = 1.18 (s, 9H), 3.57–3.63 (m, 2H), 4.41 (s, 1H), 4.81 (dd, J = 6.8, 5.4 Hz, 1H), 6.60–6.64 (m, 2H), 6.86–6.92 (m, 1H), 7.09–7.14 (m, 2H), 7.18 (dd, J = 8.3, 1.6 Hz, 1H), 7.22–7.26 (m, 1H), 7.53 (dd, J = 7.9, 1.5 Hz, 1H).

$^{13}\text{C-NMR}$ (126 MHz, CDCl_3): δ = 27.5, 30.7, 49.0, 69.1, 74.4, 97.9, 113.3, 114.6, 116.8, 122.6, 123.2, 128.3, 129.1, 133.2, 146.0, 154.2.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3405 (w), 2969 (m), 2927 (w), 2902 (w), 2868 (w), 1598 (m), 1502 (s), 1474 (s), 1238 (s), 1028 (m).

ESI-HRMS: $\text{C}_{20}\text{H}_{21}\text{BrClNO}$ m/z calcd. $[\text{M}+\text{H}^+]$: 406.0568 found 406.0571.

***N*-(2-((3-Bromonaphthalen-2-yl)oxy)-5,5-dimethylhex-3-yn-1-yl)aniline (2d)**



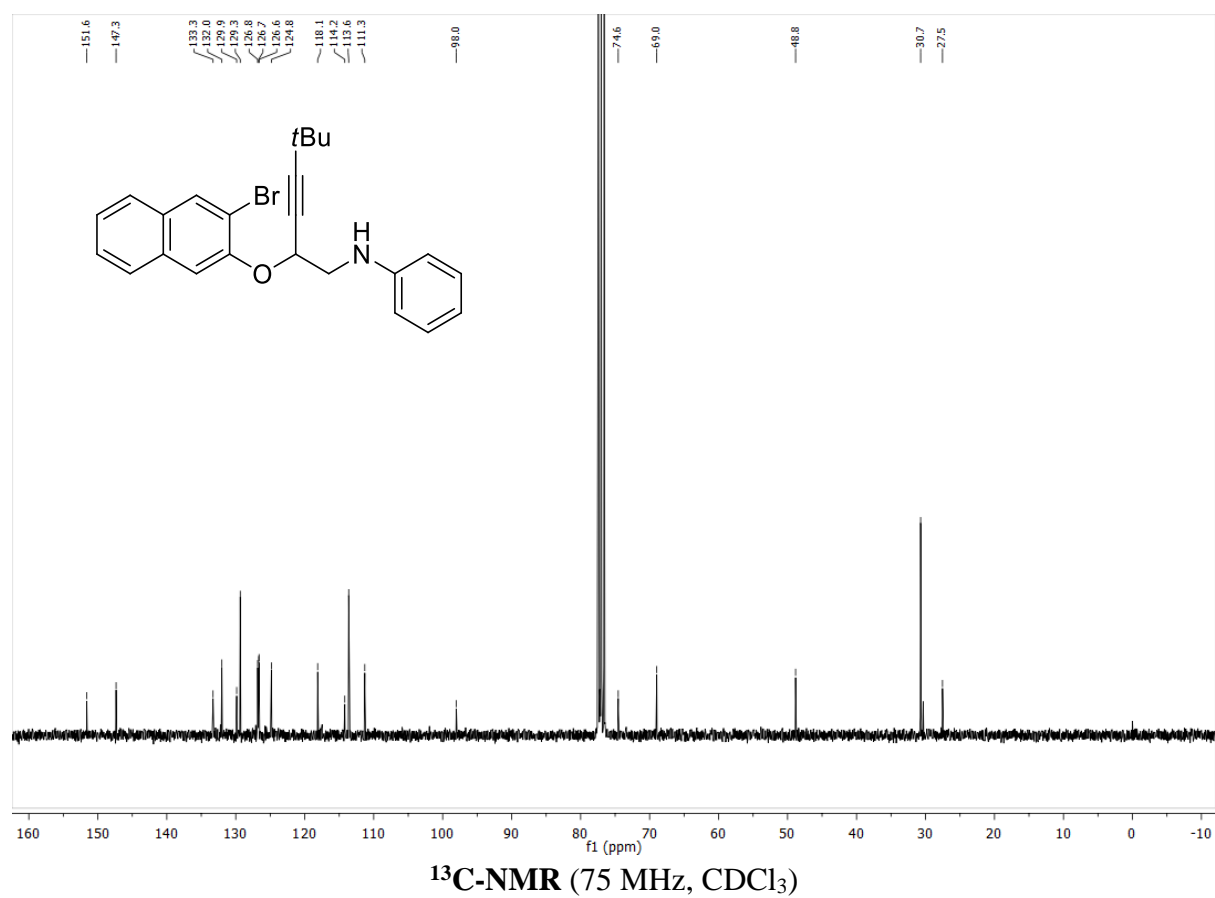
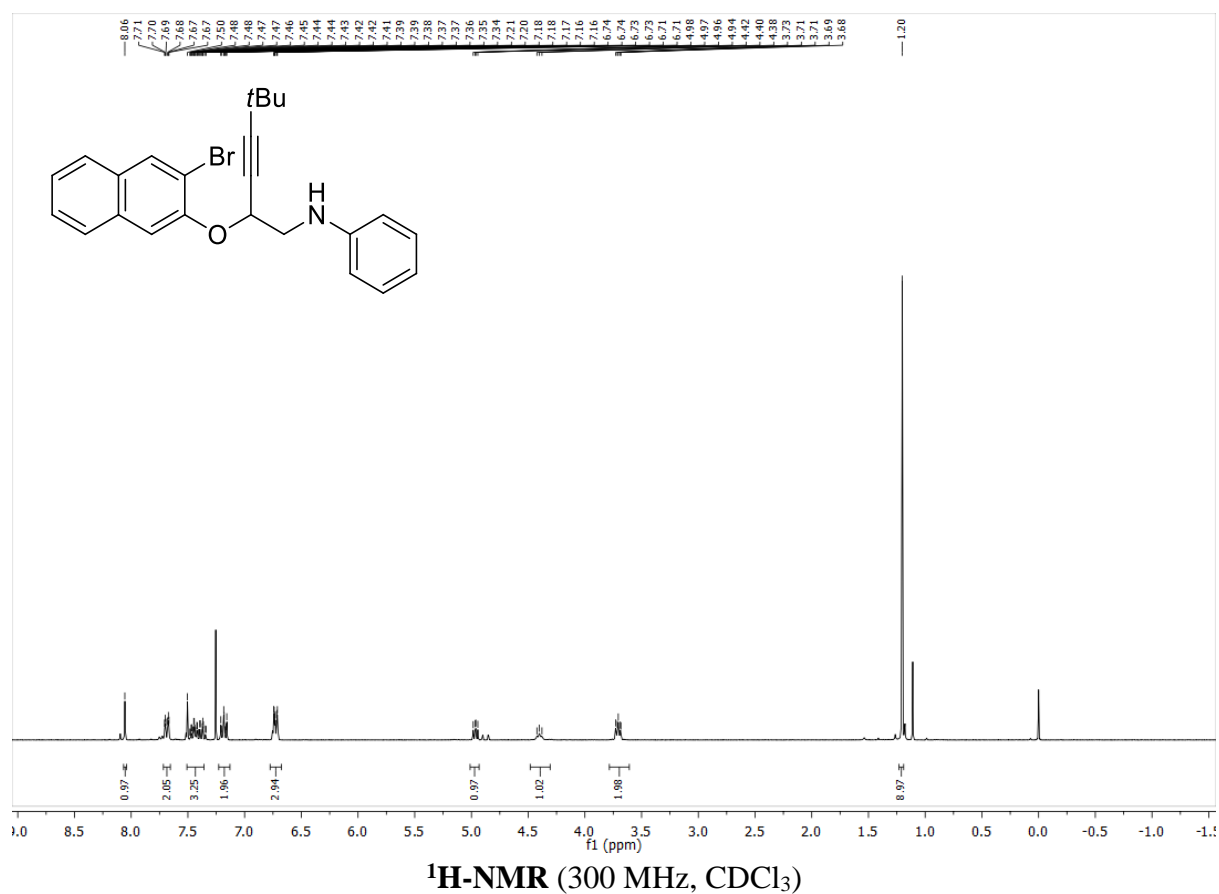
Alcohol **22**³ (173 mg, 499 μ mol) was reacted with DIPEA (130 μ L, 746 μ mol), TiF_2O (130 μ L, 793 μ mol) and aniline (92 μ L, 1.01 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:25) afforded compound **2d** (149 mg, 401 μ mol, 80%) as yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.20 (s, 9H), 3.61–3.78 (m, 2H), 4.40 (t, J = 6.7 Hz, 1H), 4.96 (dd, J = 7.1, 5.3 Hz, 1H), 6.68–6.77 (m, 3H), 7.13–7.23 (m, 2H), 7.36–7.51 (m, 3H), 7.65–7.72 (m, 2H), 8.06 (s, 1H) .

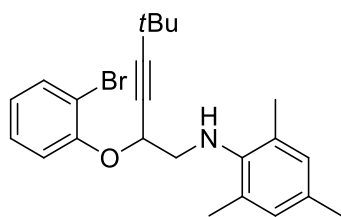
$^{13}\text{C-NMR}$ (75 MHz, CDCl_3): δ = 27.5, 30.7, 48.8, 69.0, 74.6, 98.0, 111.3, 113.6, 114.2, 118.1, 124.8, 126.6, 126.7, 126.8, 129.3, 129.9, 132.0, 133.3, 147.3, 151.6.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3405 (w), 3055 (w), 2969 (m), 2928 (m), 2902 (m), 2868 (w), 1599 (s), 1504 (s), 1454 (s), 1245 (s), 1216 (s), 1024 (m).

ESI-HRMS: $\text{C}_{24}\text{H}_{24}\text{BrNO}$ m/z calcd. $[\text{M}+\text{Na}^+]$: 444.0933 found 444.0939.



***N*-(2-(2-Bromophenoxy)-5,5-dimethylhex-3-yn-1-yl)-2,4,6-trimethylaniline (2e)**



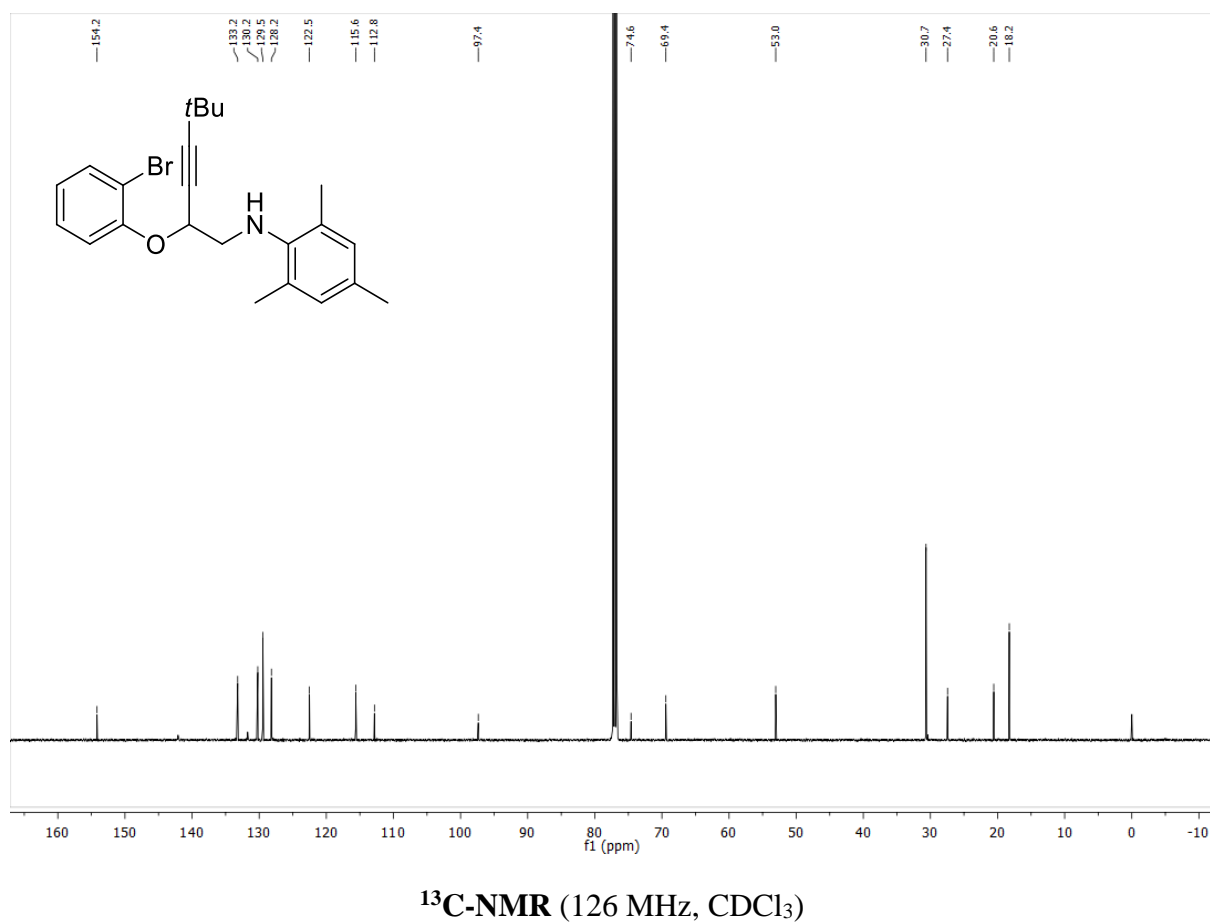
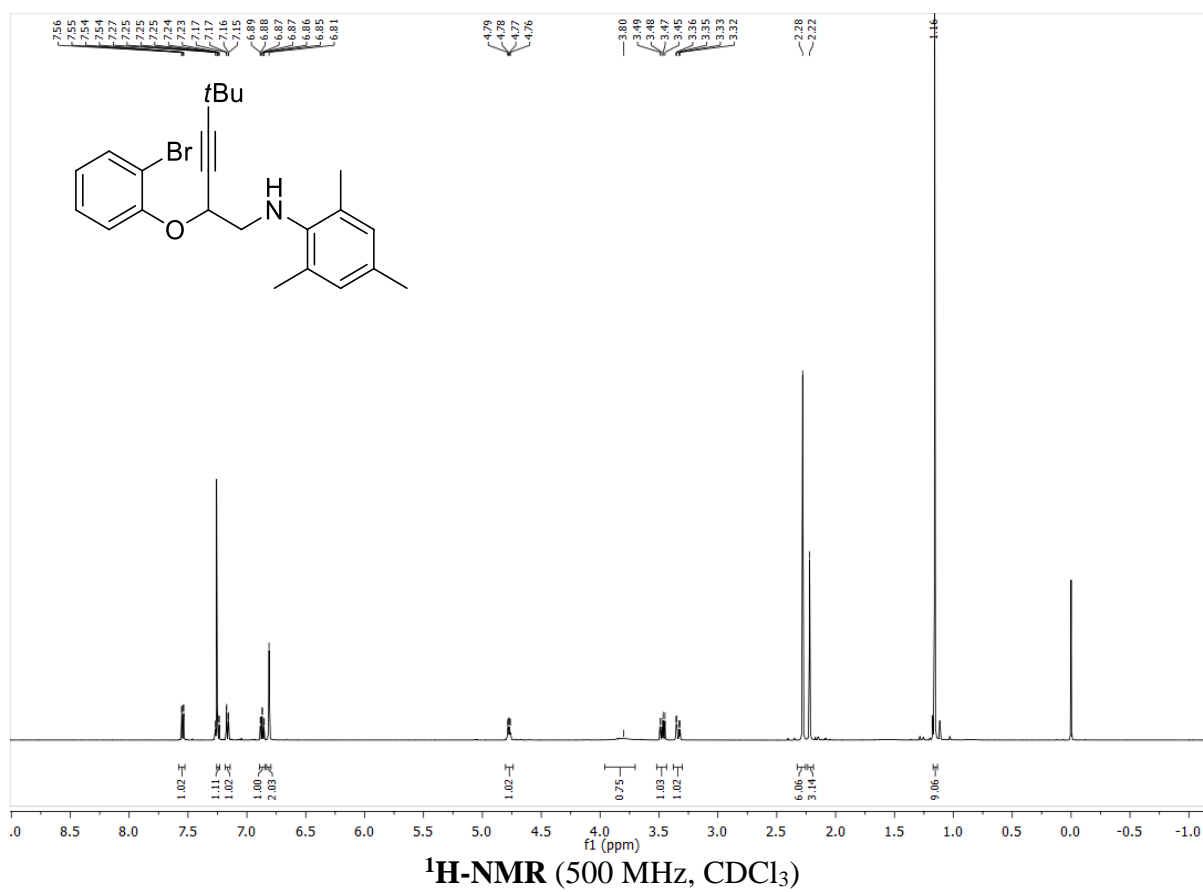
Alcohol **21**³ (147 mg, 495 μ mol) was reacted with DIPEA (120 μ L, 689 μ mol), TiF_2O (100 μ L, 610 μ mol) and 2,4,6-trimethylaniline (150 μ L, 1.07 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded compound **2e** (138 mg, 333 μ mol, 67%) as yellow oil.

¹H-NMR (500 MHz, CDCl_3): δ = 1.16 (s, 9H), 2.22 (s, 3H), 2.28 (s, 6H), 3.34 (dd, J = 13.1, 3.9 Hz, 1H), 3.47 (dd, J = 13.2, 8.0 Hz, 1H), 3.80 (s, 1H), 4.77 (dd, J = 8.0, 3.7 Hz, 1H), 6.81 (s, 2H), 6.87 (td, J = 7.6, 1.5 Hz, 1H), 7.16 (dd, J = 8.4, 1.4 Hz, 1H), 7.23–7.26 (m, 1H), 7.55 (dd, J = 7.8, 1.6 Hz, 1H).

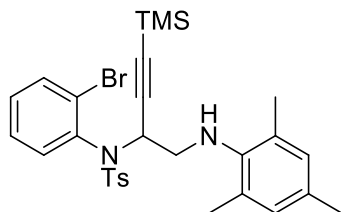
¹³C-NMR (126 MHz, CDCl_3): δ = 18.2, 20.6, 27.4, 30.7, 53.0, 69.4, 74.6, 97.4, 112.8, 115.6, 122.5, 128.2, 129.5, 130.2, 133.2, 154.2.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3379(w), 2969 (m), 2923 (m), 2865 (w), 1477 (s), 1280 (m), 1238 (s), 1028 (m).

ESI-HRMS: $\text{C}_{23}\text{H}_{28}\text{BrNO}$ m/z calcd. $[\text{M}+\text{H}^+]$: 414.1427 found 414.1434.



***N*-(2-Bromophenyl)-*N*-(1-(mesitylamino)-4-(trimethylsilyl)but-3-yn-2-yl)-4-methylbenzenesulfonamide (**2f**)**



Alcohol **23**³ (232 mg, 497 μ mol) was reacted with DIPEA (270 μ L, 1.55 mmol), TiF_2O (140 μ L, 854 μ mol) and 2,4,6-trimethylaniline (142 μ L, 1.01 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography ($\text{EtOAc}:\text{n-pentane} = 1:15$) afforded compound **2f** (122 mg, 209 μ mol, 42%) as yellow solid.

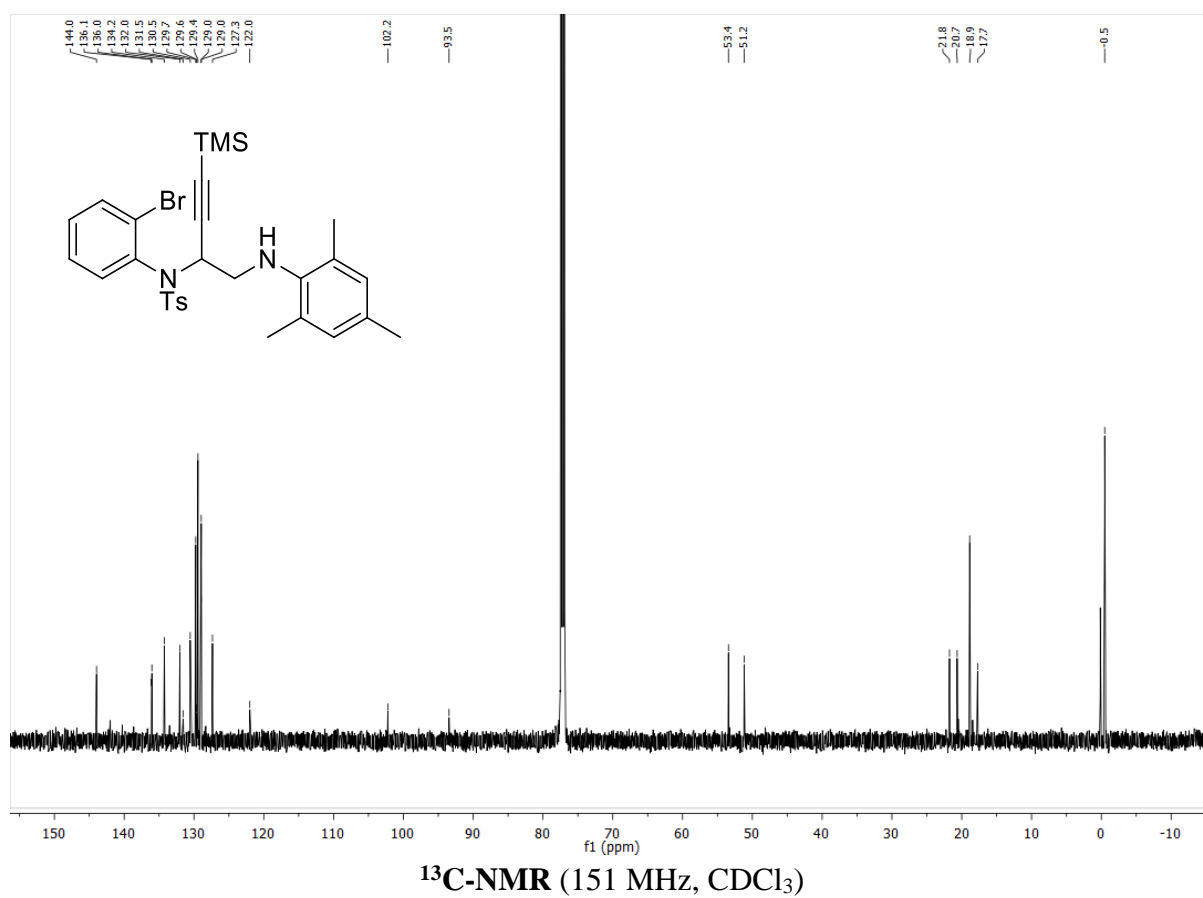
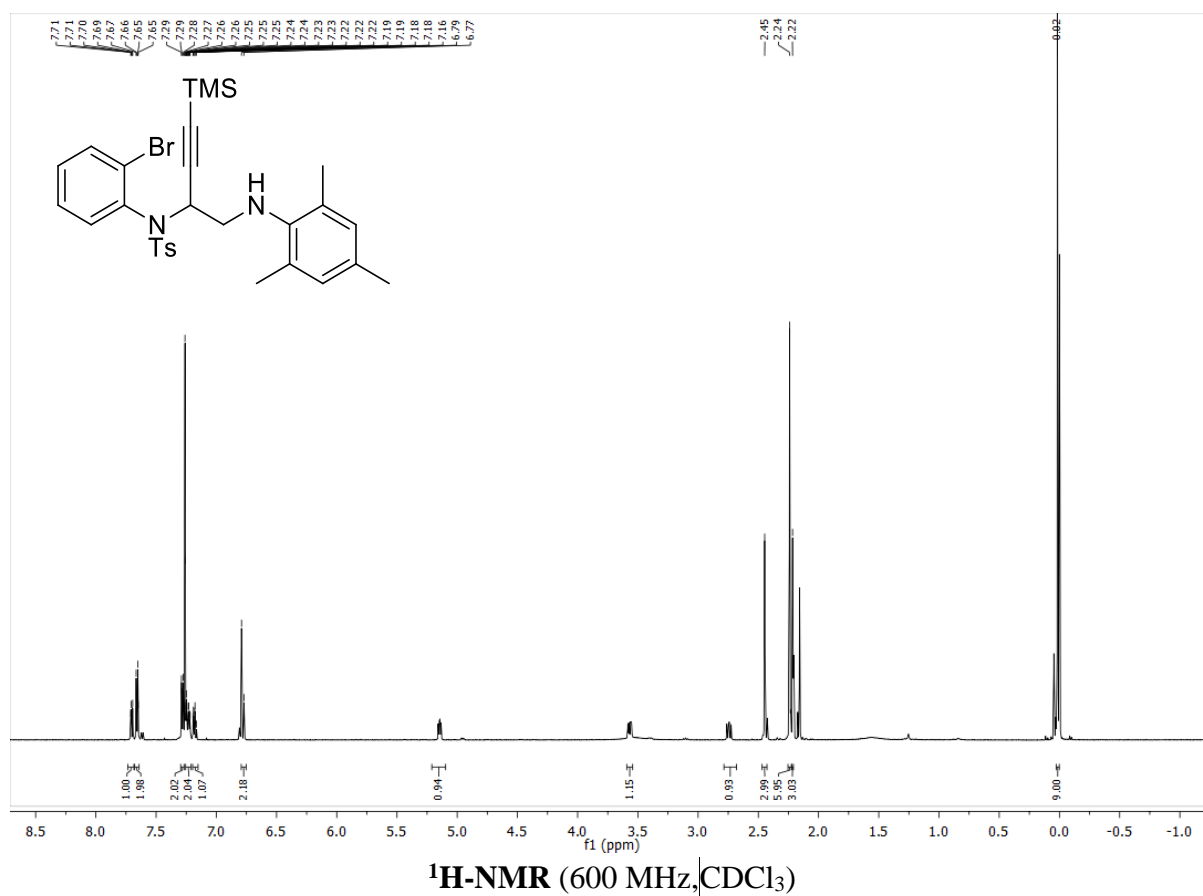
$^1\text{H-NMR}$ (600 MHz, CDCl_3): $\delta = 0.02$ (s, 9H), 2.22 (s, 3H), 2.24 (s, 6H), 2.45 (s, 3H), 2.74 (dd, $J = 12.2, 8.8$ Hz, 1H), 3.57 (dd, $J = 12.3, 5.6$ Hz, 1H), 5.15 (dd, $J = 8.7, 5.6$ Hz, 1H), 6.78 (d, $J = 12.4$ Hz, 2H), 7.15–7.21 (m, 1H), 7.20–7.27 (m, 1H), 7.26–7.31 (m, 2H), 7.66 (d, $J = 8.2$ Hz, 2H), 7.70 (dd, $J = 8.0, 1.6$ Hz, 1H).

$^{13}\text{C-NMR}$ (151 MHz, CDCl_3): $\delta = -0.5, 17.7, 18.9, 20.7, 21.8, 51.2, 53.4, 93.5, 102.2, 122.0, 127.3, 129.0, 129.0, 129.4, 129.6, 129.7, 130.5, 131.5, 132.0, 134.2, 136.0, 136.1, 144.0$.

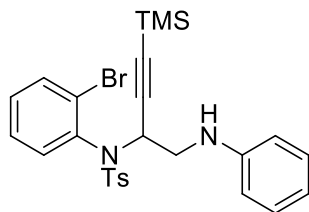
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3396 (w), 2959 (w), 2920 (w), 2858 (w), 1480 (m), 1358 (m), 1250 (m), 1165 (s), 1068 (m).

M.p.: 122–125 $^{\circ}\text{C}$.

ESI-HRMS: $\text{C}_{29}\text{H}_{35}\text{BrN}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 583.1445 found 583.1449.



***N*-(2-Bromophenyl)-4-methyl-*N*-(1-(phenylamino)-4-(trimethylsilyl)but-3-yn-2-yl)-benzenesulfonamide (2g)**



Alcohol **23**³ (103 mg, 221 μ mol) was reacted with DIPEA (130 μ L, 746 μ mol), Tf₂O (50 μ L, 305 μ mol) and aniline (42 μ L, 460 μ mol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded compound **2g** (52.7 mg, 97.3 μ mol, 44%) as yellow solid.

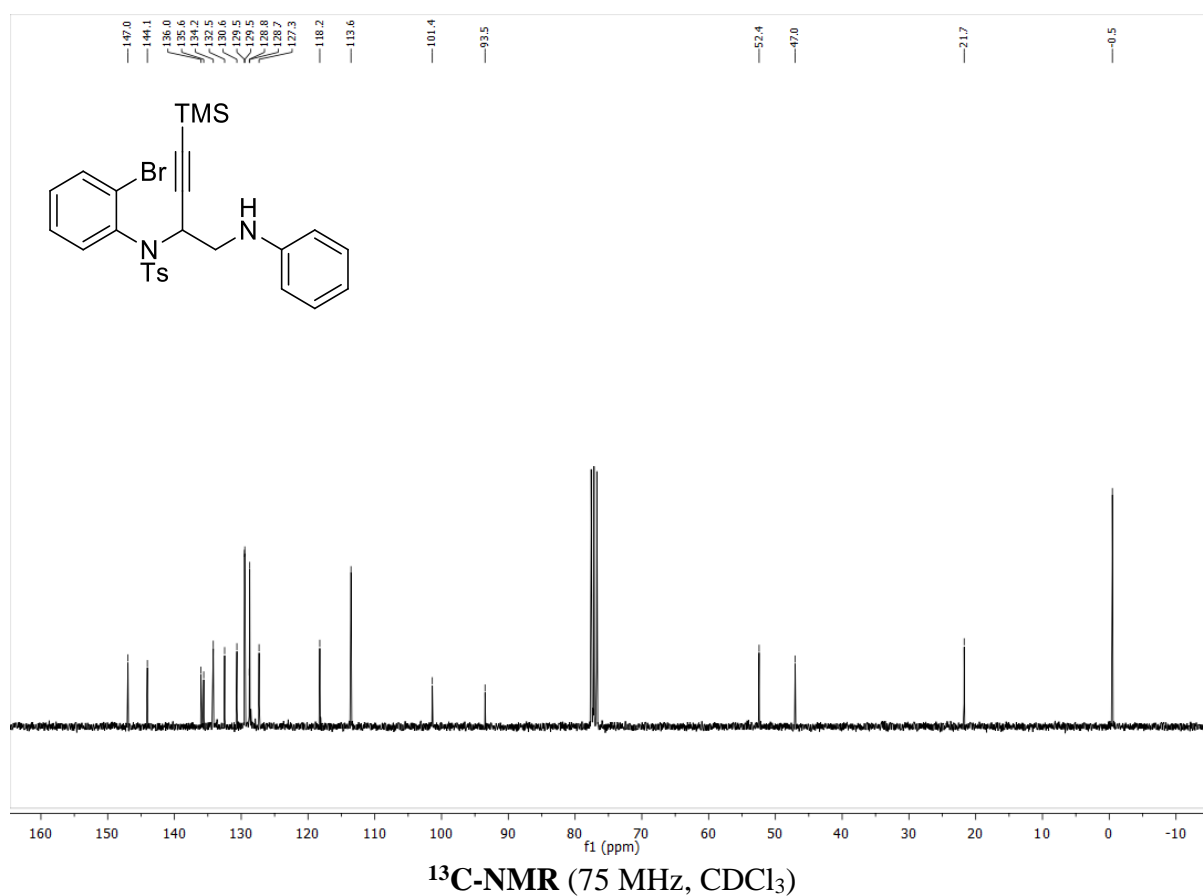
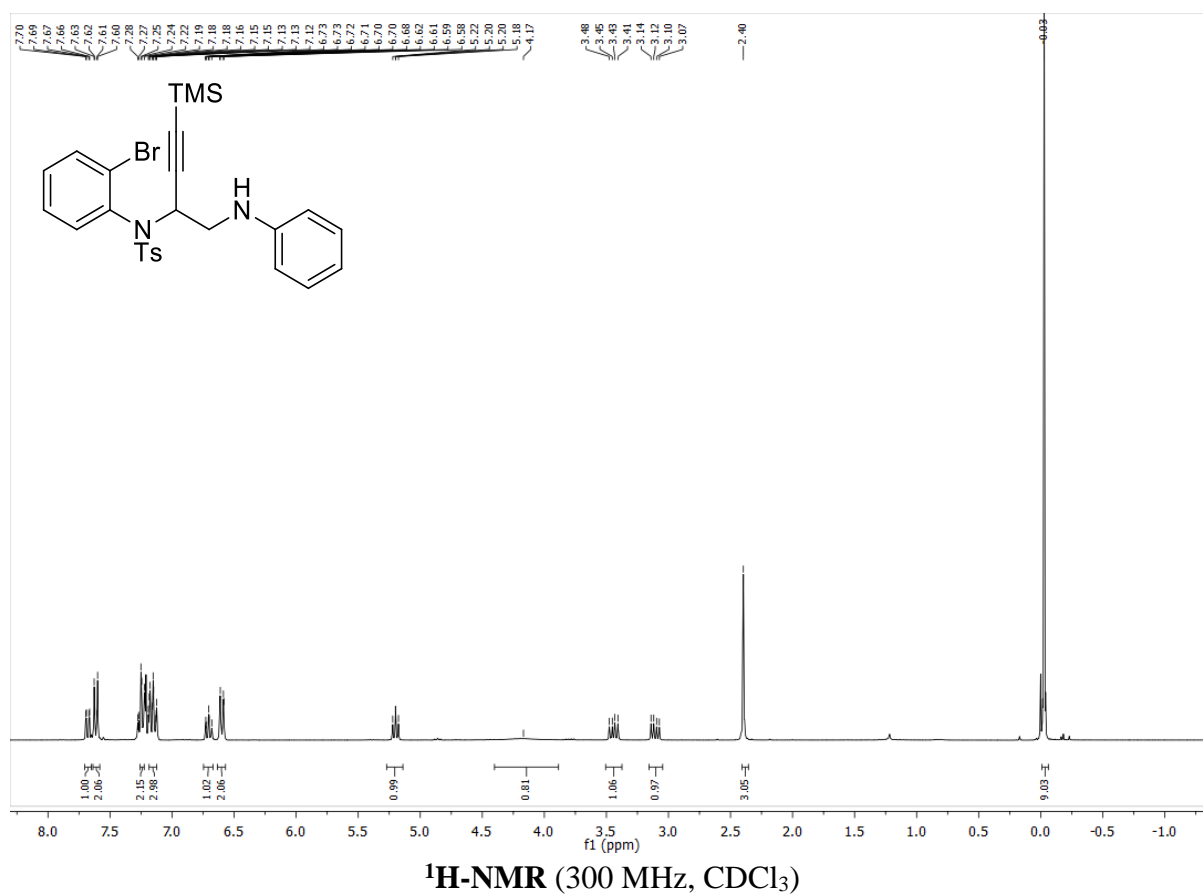
¹H-NMR (300 MHz, CDCl₃): δ = -0.03 (s, 9H), 2.40 (s, 3H), 3.11 (dd, *J* = 13.5, 6.6 Hz, 1H), 3.44 (dd, *J* = 13.5, 7.5 Hz, 1H), 4.17 (s, 1H), 5.20 (dd, *J* = 7.4, 6.5 Hz, 1H), 6.57–6.64 (m, 2H), 6.67–6.75 (m, 1H), 7.12–7.18 (m, 3H), 7.25 (d, *J* = 1.9 Hz, 2H), 7.58–7.64 (m, 2H), 7.68 (dd, *J* = 7.7, 1.8 Hz, 1H).

¹³C-NMR (75 MHz, CDCl₃): δ = -0.5, 21.7, 47.0, 52.4, 93.5, 101.4, 113.6, 118.2, 127.3, 128.7, 128.8, 129.5, 129.5, 130.6, 132.5, 134.2, 135.6, 136.0, 144.1, 147.0.

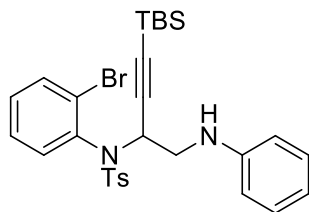
IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3416 (w), 3056 (w), 3026 (w), 2958 (w), 2901 (w), 2866 (w), 1602 (m), 1506 (m), 1470 (m), 1354 (m), 1252 (m), 1164 (s), 1071 (m).

M.p.: 51–54 °C.

ESI-HRMS: C₂₆H₂₉BrN₂O₂SSi *m/z* calcd. [M+H⁺]: 541.0975 found 541.0982.



***N*-(2-Bromophenyl)-*N*-(4-(*tert*-butyldimethylsilyl)-1-(phenylamino)but-3-yn-2-yl)-4-methylbenzenesulfonamide (2h)**



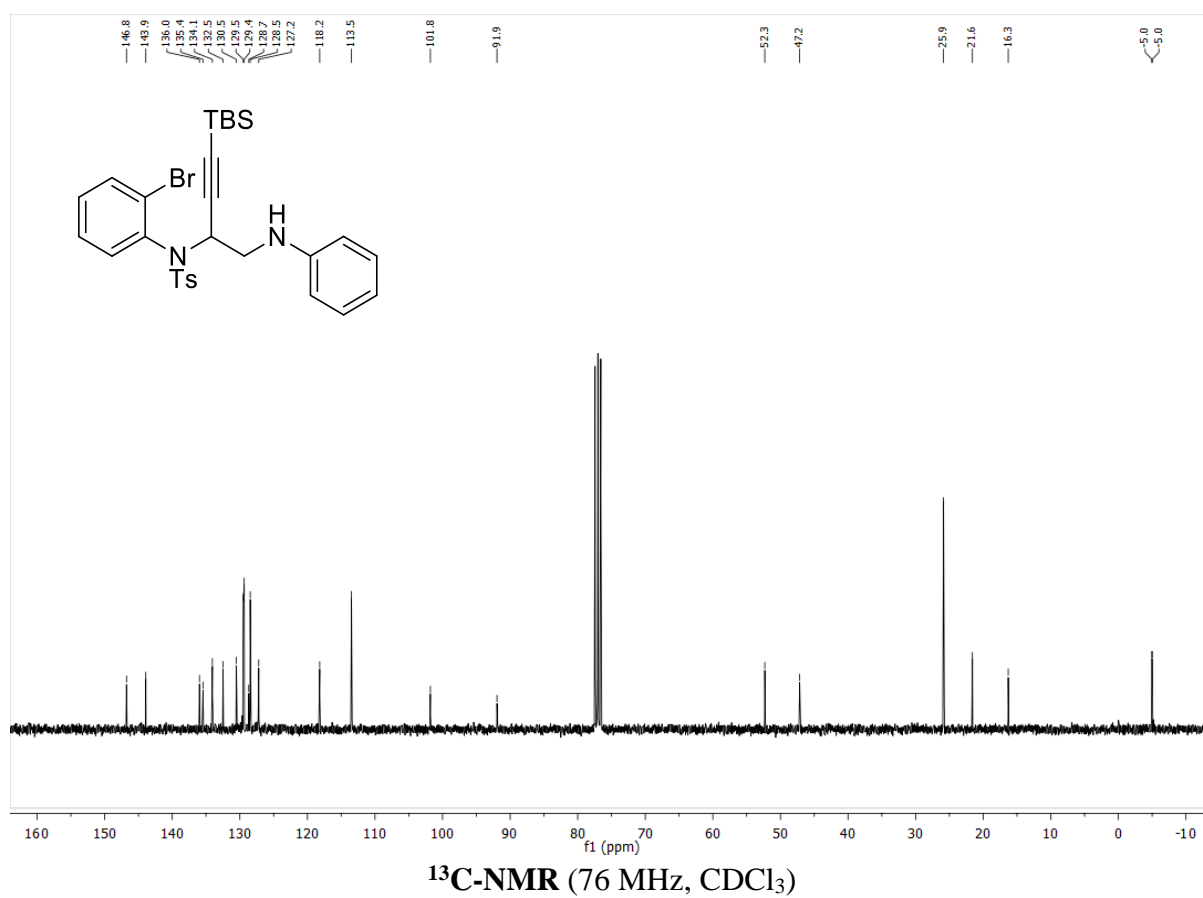
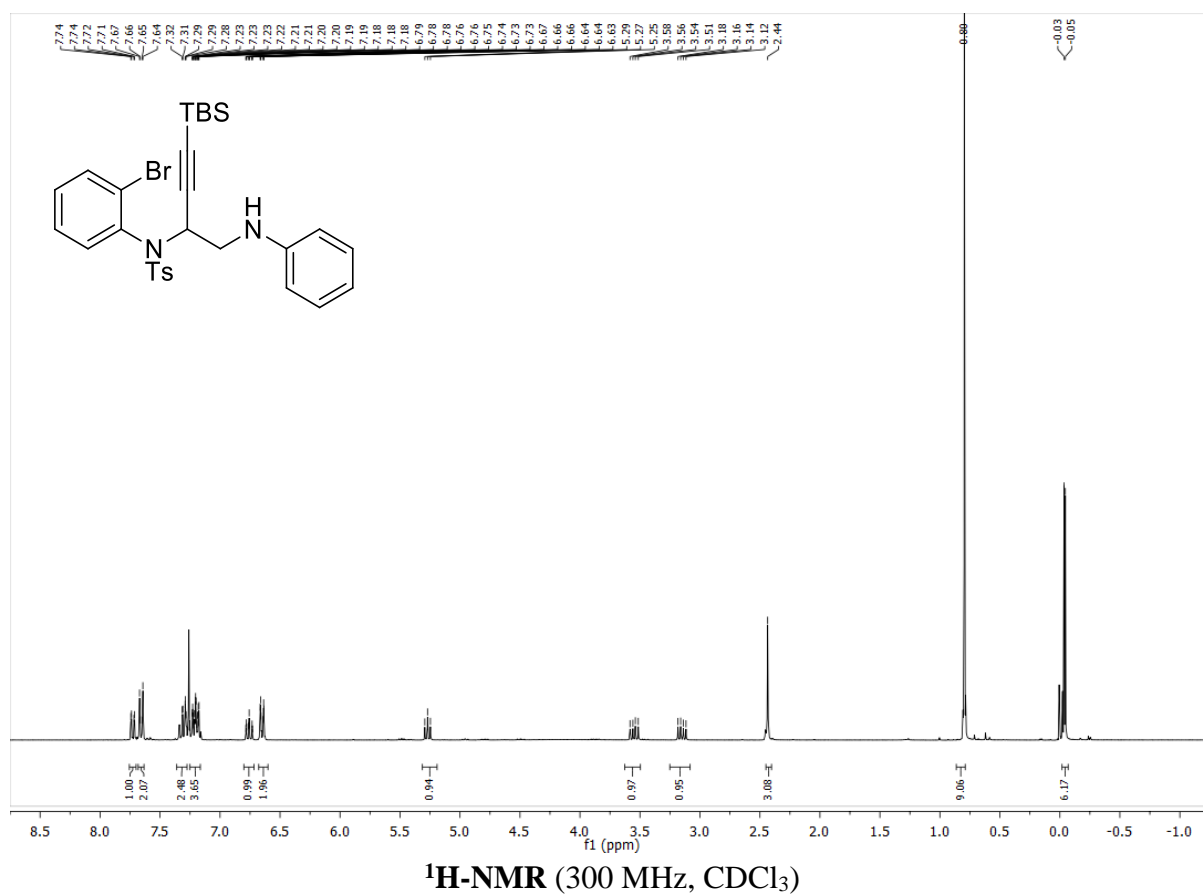
Alcohol **24**⁴ (1.02 g, 2.01 mmol) was reacted with DIPEA (700 μ L, 4.12 mmol), TiF_2O (470 μ L, 2.80 mmol) and aniline (420 μ L, 4.60 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded compound **2h** (855 mg, 1.47 mmol, 73%) as yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = -0.04 (d, J = 3.3 Hz, 6H), 0.80 (s, 9H), 2.44 (s, 3H), 3.15 (dd, J = 13.4, 6.8 Hz, 1H), 3.55 (dd, J = 13.4, 7.3 Hz, 1H), 5.27 (t, J = 7.0 Hz, 1H), 6.65 (dt, J = 7.9, 1.1 Hz, 2H), 6.76 (tt, J = 7.4, 1.1 Hz, 1H), 7.16–7.25 (m, 4H), 7.27–7.36 (m, 3H), 7.63–7.68 (m, 2H), 7.73 (dd, J = 7.8, 1.7 Hz, 1H).

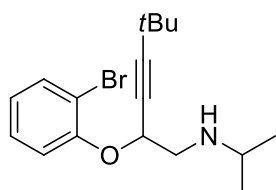
$^{13}\text{C-NMR}$ (76 MHz, CDCl_3) δ = 5.0, -5.0, 16.3, 21.6, 25.9, 47.2, 52.3, 91.9, 101.8, 113.5, 118.2, 127.2, 128.5, 128.7, 129.4, 129.5, 130.5, 132.5, 134.1, 135.4, 136.0, 143.9, 146.8.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3413 (w), 2933 (m), 2891 (w), 2857 (m), 1602 (m), 1506 (m), 1468 (m), 1356 (m), 1253 (m), 1164 (s), 1080 (m).

ESI-HRMS: $\text{C}_{29}\text{H}_{35}\text{BrN}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 583.1445 found 583.1447.



2-(2-Bromophenoxy)-*N*-isopropyl-5,5-dimethylhex-3-yn-1-amine (2i)



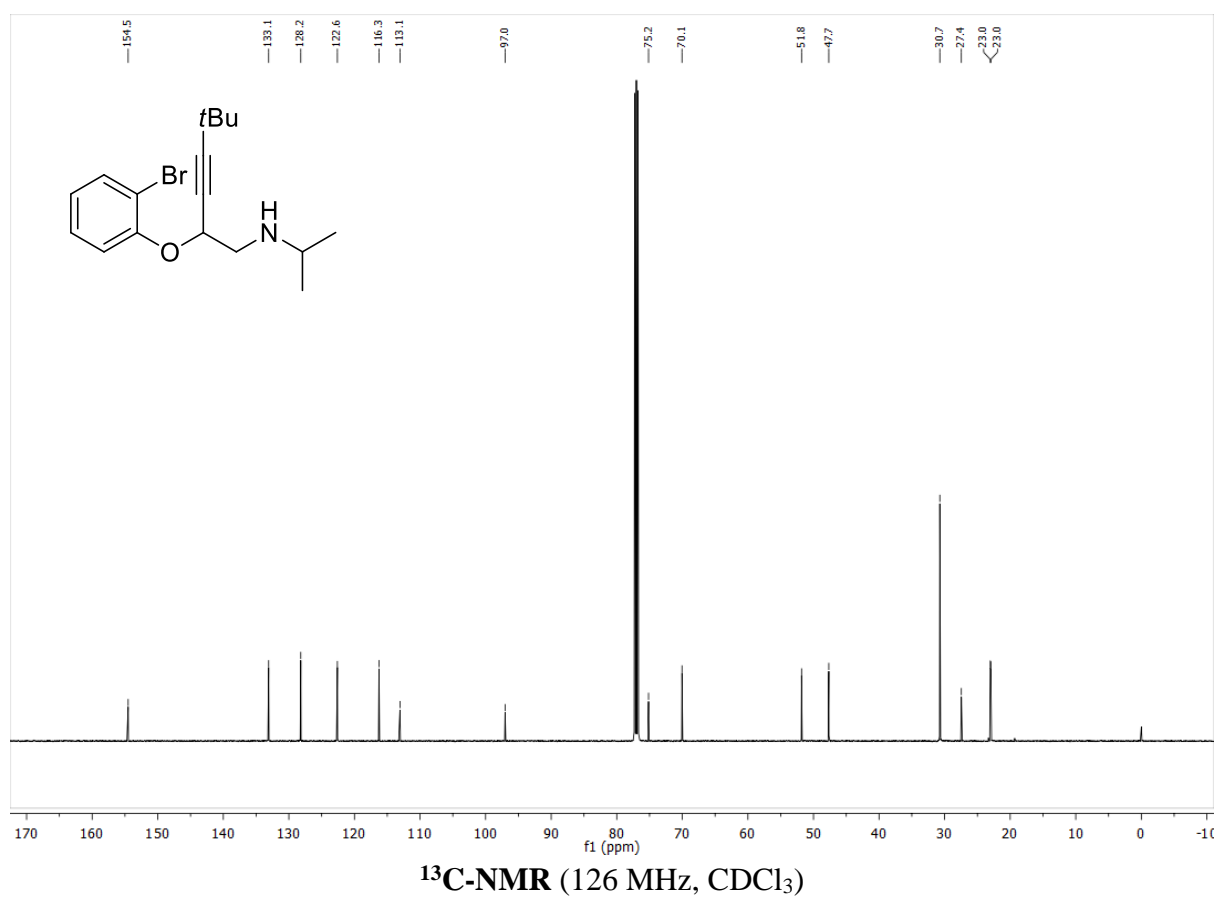
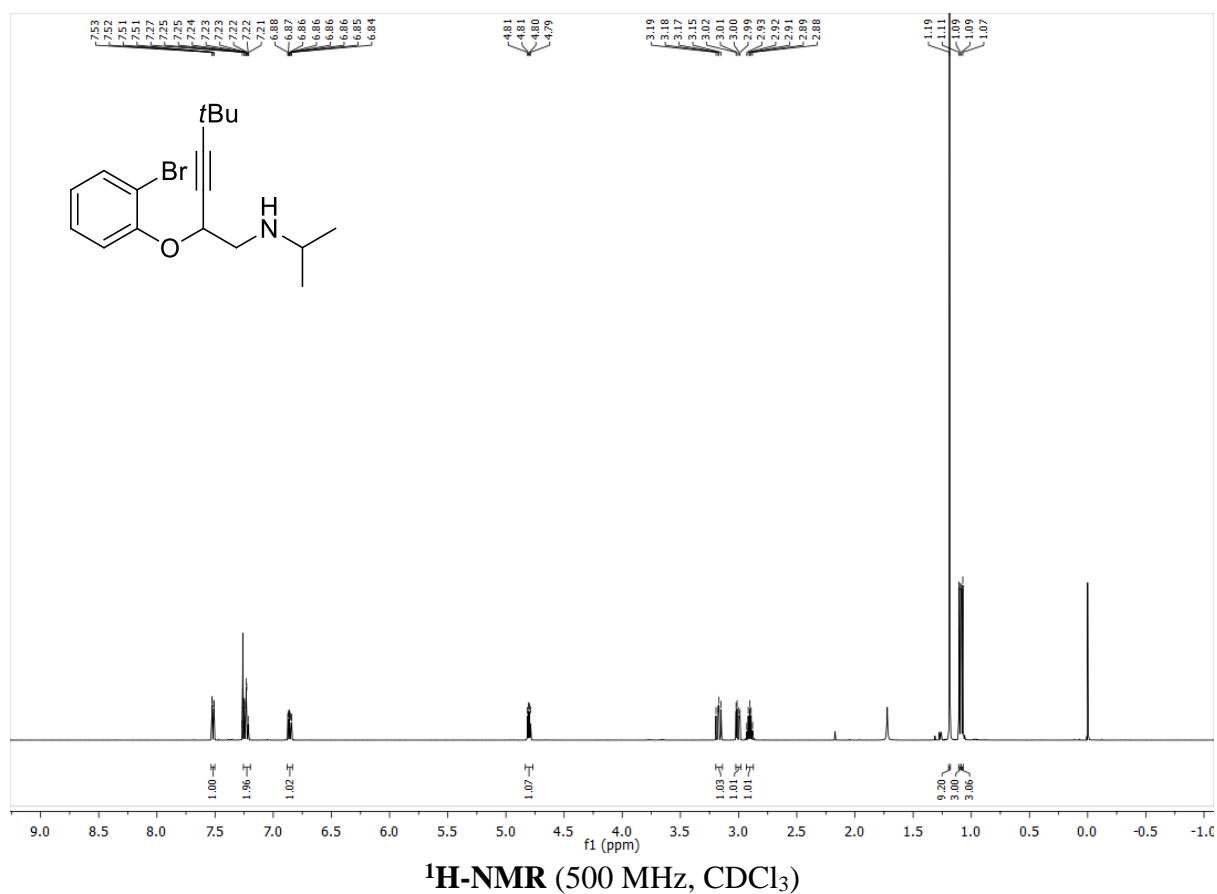
Alcohol **21**³ (297 mg, 1.00 mmol) was reacted with DIPEA (250 μ L, 1.44 mmol), TiF_2O (220 μ L, 1.34 mmol) and isopropylamine (250 μ L, 2.92 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:3) afforded compound **2i** (221 mg, 652 μ mol, 65%) as yellow oil.

$^1\text{H-NMR}$ (500 MHz, CDCl_3): δ = 1.08 (d, J = 6.2 Hz, 3H), 1.10 (d, J = 6.3 Hz, 3H), 1.19 (s, 9H), 2.91 (p, J = 6.2 Hz, 1H), 3.00 (dd, J = 12.7, 4.2 Hz, 1H), 3.17 (dd, J = 12.7, 8.8 Hz, 1H), 4.80 (dd, J = 8.8, 4.2 Hz, 1H), 6.86 (ddd, J = 7.7, 6.8, 2.0 Hz, 1H), 7.20–7.27 (m, 2H), 7.52 (dd, J = 7.9, 1.5 Hz, 1H).

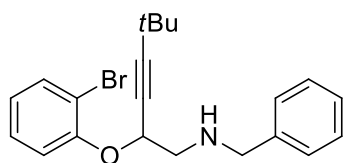
$^{13}\text{C-NMR}$ (126 MHz, CDCl_3) δ = 23.0, 23.0, 27.4, 30.7, 47.7, 51.8, 70.1, 75.2, 97.0, 113.1, 116.3, 122.6, 128.2, 133.1, 154.5.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3320 (w), 3067 (w), 2967 (m), 2929 (w), 2868 (w), 2837 (w), 1584 (w), 1475 (s), 1281 (m), 1240 (m), 1027 (m).

ESI-HRMS: $\text{C}_{17}\text{H}_{24}\text{BrNO}$ m/z calcd. $[\text{M}+\text{H}^+]$: 338.1114 found 338.1120.



***N*-Benzyl-2-(2-bromophenoxy)-5,5-dimethylhex-3-yn-1-amine (2j)**



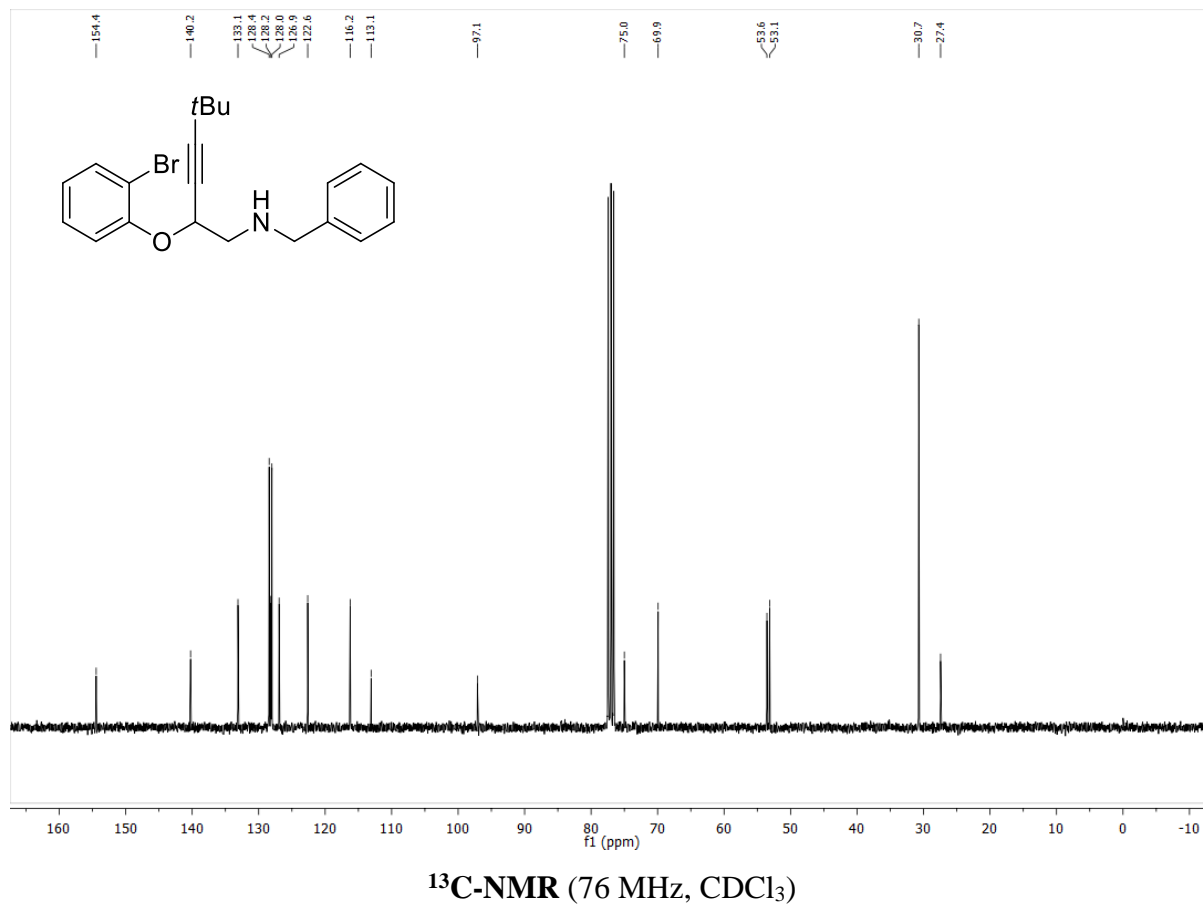
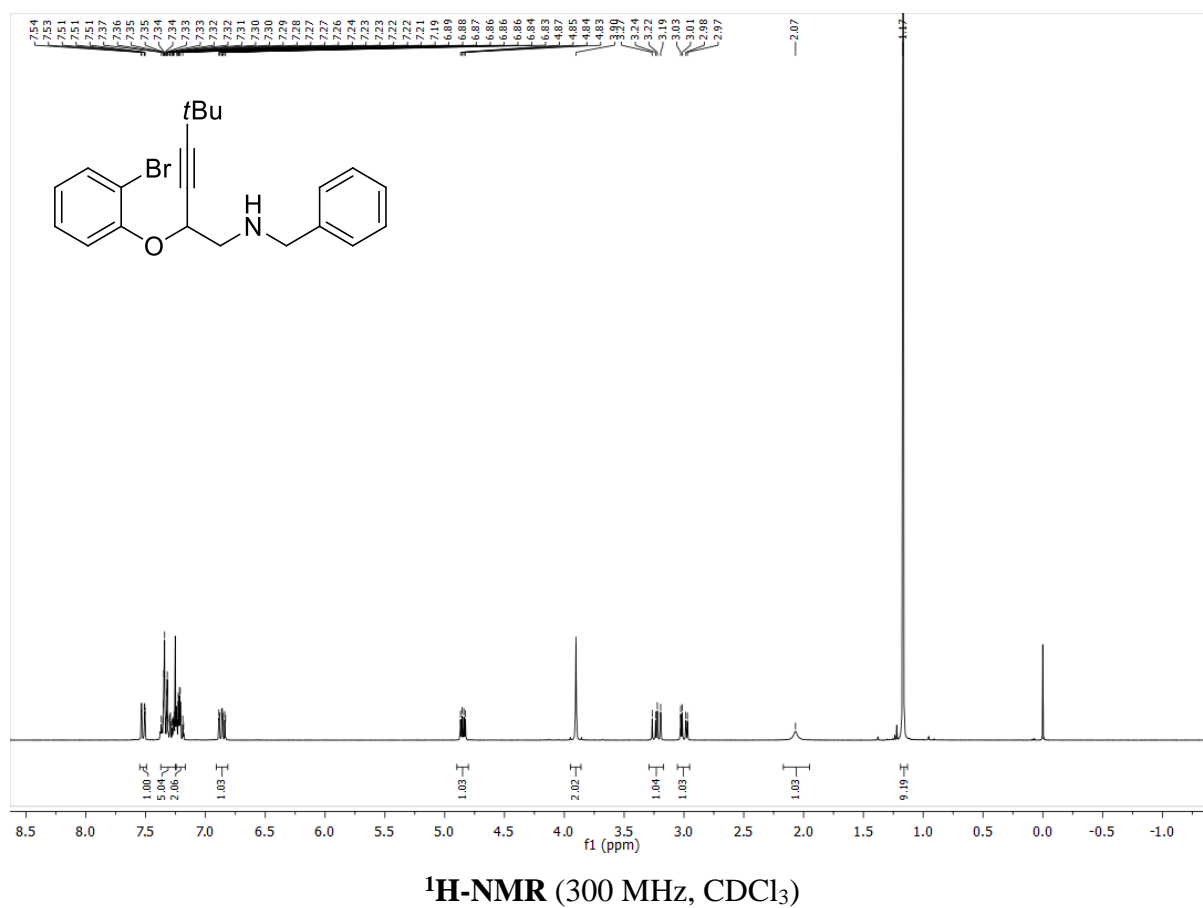
Alcohol **21**³ (297 mg, 1.00 mmol) was reacted with DIPEA (250 μ L, 1.44 mmol), TiF_2O (200 μ L, 1.22 mmol) and (300 μ L, 2.75 mmol) according to GP4 (Synthesis of Amine (B)). The reaction mixture was stirred at ambient temperature overnight. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded compound **2j** (304 mg, 786 μ mol, 79%) as yellow oil.

¹H-NMR (300 MHz, CDCl_3): δ = 1.17 (s, 9H), 2.07 (s, 1H), 3.00 (dd, J = 12.8, 4.1 Hz, 1H), 3.23 (dd, J = 12.8, 8.4 Hz, 1H), 3.90 (s, 2H), 4.85 (dd, J = 8.4, 4.0 Hz, 1H), 6.86 (ddd, J = 7.9, 6.9, 2.0 Hz, 1H), 7.17–7.25 (m, 2H), 7.25–7.37 (m, 5H), 7.49–7.55 (m, 1H).

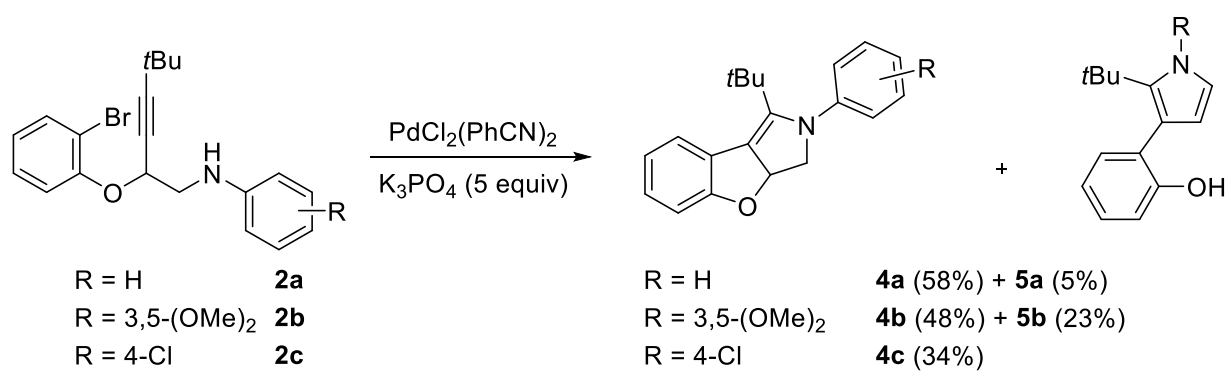
¹³C-NMR (76 MHz, CDCl_3) δ = 27.4, 30.7, 53.1, 53.6, 69.9, 75.0, 97.1, 113.1, 116.2, 122.6, 126.9, 128.0, 128.2, 128.4, 133.1, 140.2, 154.4.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3329 (w), 2969 (m), 2925 (w), 2902 (w), 2867 (w), 2837 (w), 1584 (w), 1474 (s), 1271 (m), 1239 (s), 1028 (m).

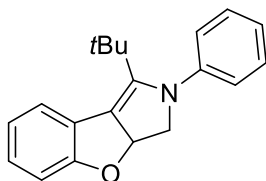
ESI-HRMS: $\text{C}_{21}\text{H}_{24}\text{BrNO}$ m/z calcd. $[\text{M}+\text{H}^+]$: 386.1114 found 386.1119.



5) Synthesis of Domino Products of Type 4



Domino product (4a)



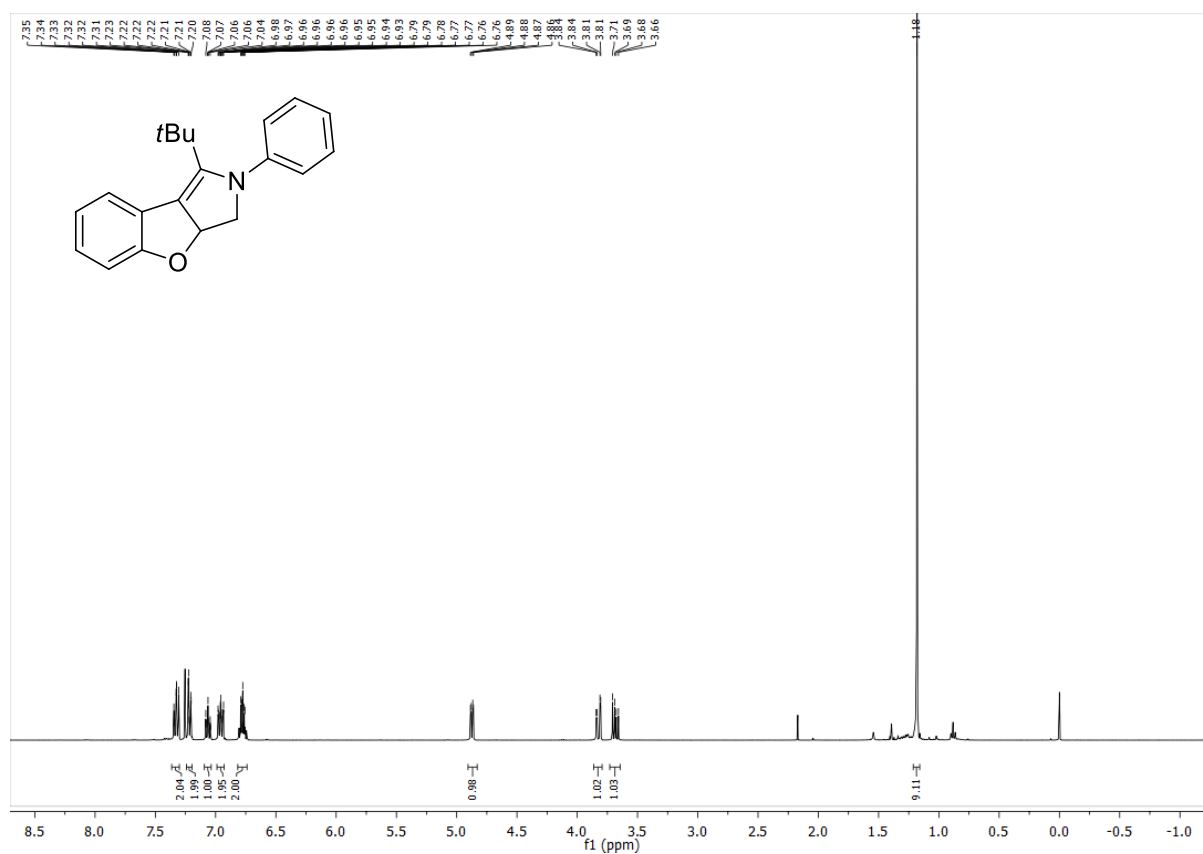
The domino precursor **2a** (37.2 mg, 100 μ mol), potassium phosphate (105 mg, 495 μ mol), [*t*Bu₃PH][BF₄] (2.9 mg, 10.0 μ mol) and PdCl₂(PhCN)₂ (2.0 mg, 5.21 μ mol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 °C. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **4a** (16.9 mg, 58.0 μ mol, 58%) as colorless oils and pyrrole **5a** (1.4 mg, 4.80 μ mol, 5%) as colorless oil.

¹H-NMR (400 MHz, CDCl₃): δ = 1.18 (s, 9H), 3.68 (dd, *J* = 12.7, 7.4 Hz, 1H), 3.82 (dd, *J* = 12.7, 2.5 Hz, 1H), 4.87 (dd, *J* = 7.4, 2.5 Hz, 1H), 6.74–6.82 (m, 2H), 6.93–6.99 (m, 2H), 7.06 (tt, *J* = 7.5, 1.2 Hz, 1H), 7.20–7.24 (m, 2H), 7.30–7.36 (m, 2H).

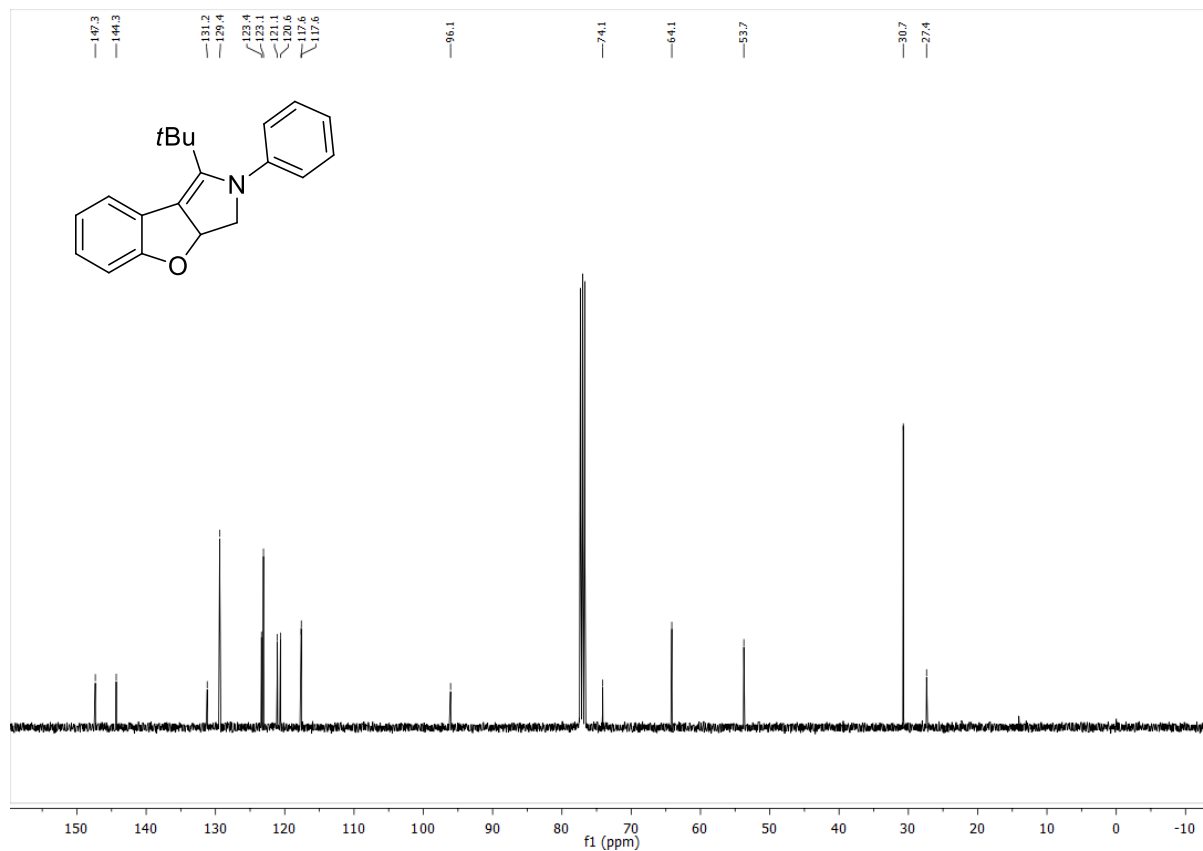
¹³C-NMR (101 MHz, CDCl₃): δ = 27.4, 30.7, 53.7, 64.1, 74.1, 96.1, 117.6, 117.6, 120.6, 121.1, 123.1, 123.4, 129.4, 131.2, 144.3, 147.3.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 2969 (m), 2926 (w), 2866 (w), 1592 (m), 1496 (s), 1352 (m), 1272 (m), 1248 (m).

GC-HRMS (EI): C₂₀H₂₁NO *m/z* calcd. [M⁺]: 291.1623 found 291.1613.

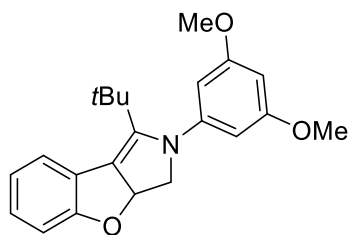


¹H-NMR (400 MHz, CDCl₃)



¹³C-NMR (101 MHz, CDCl₃)

Domino product (4b)



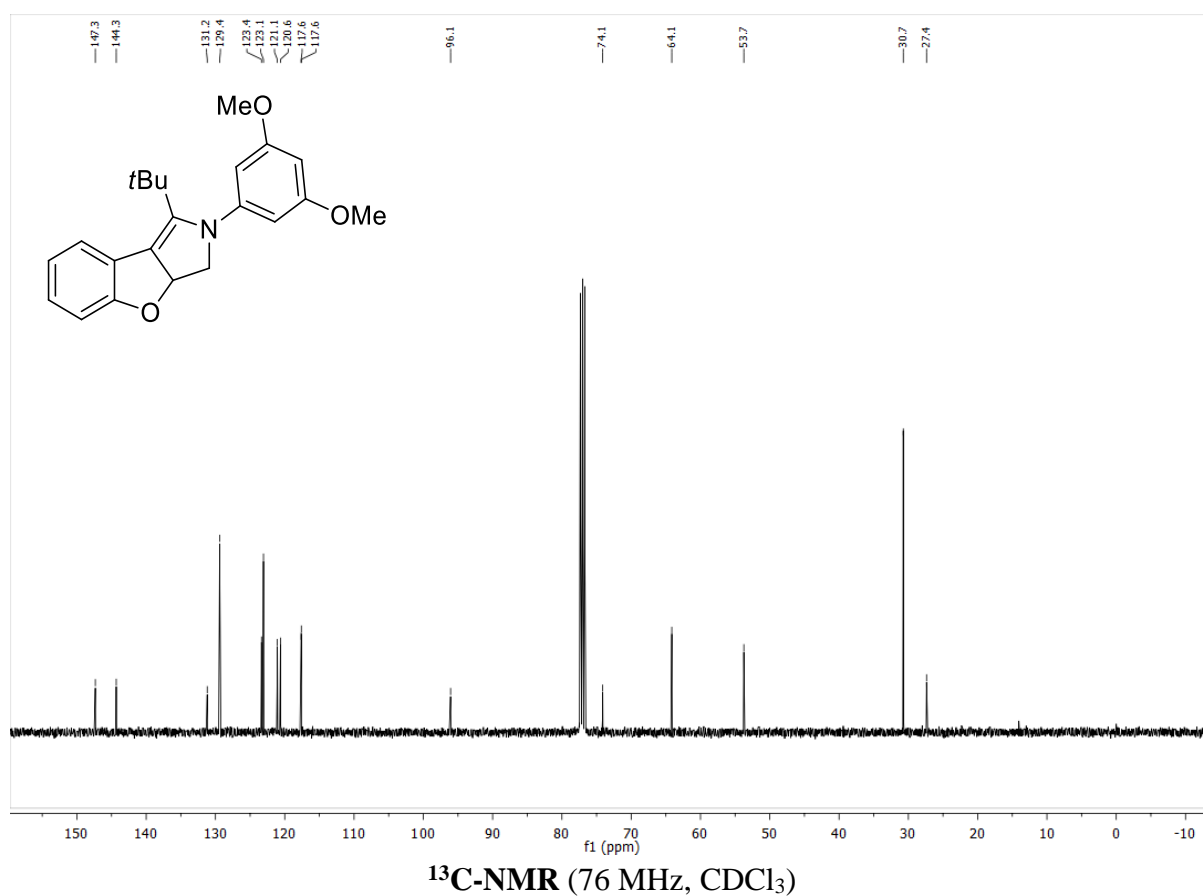
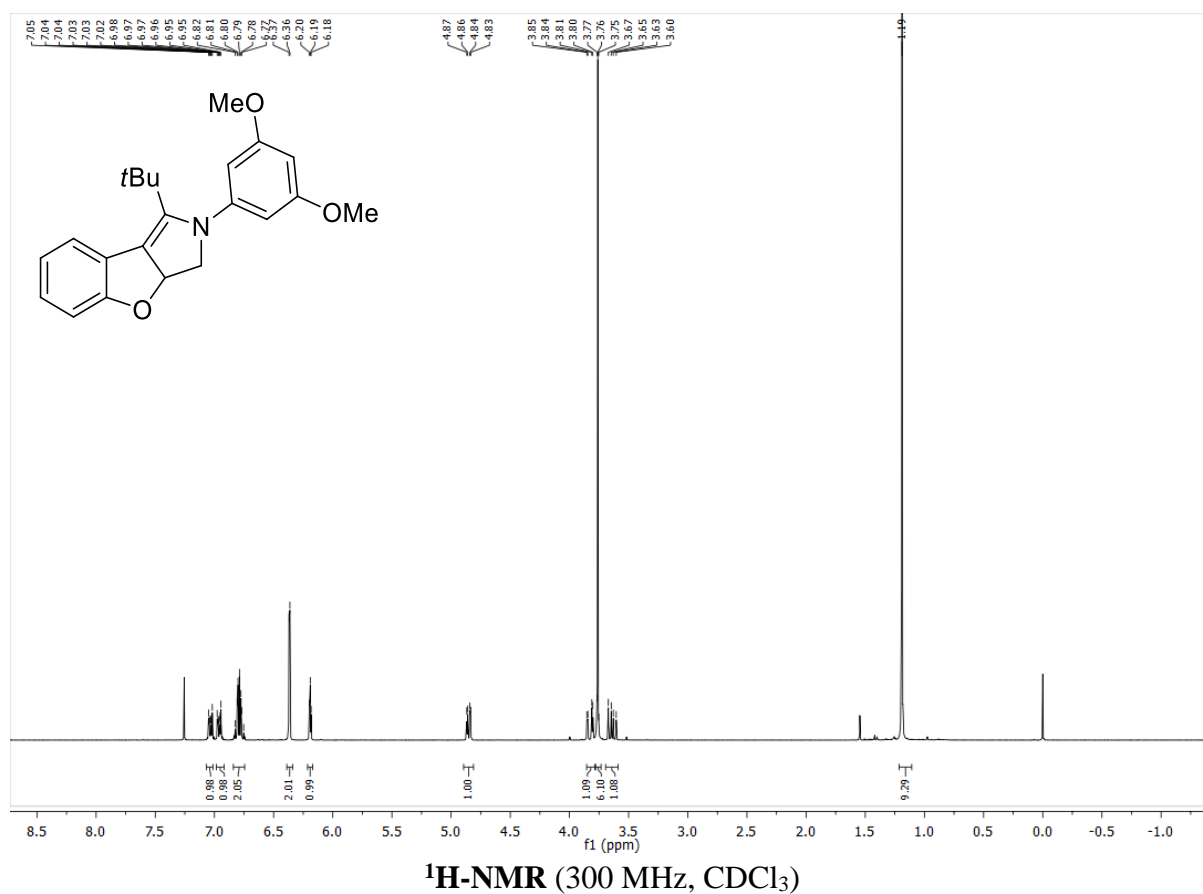
The domino precursor **2b** (41.4 mg, 95.8 μmol), potassium phosphate (102 mg, 480 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.9 mg, 10.0 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (2.0 mg, 5.21 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded domino product **4b** (16.3 mg, 46.4 μmol , 48%) as colorless oil and pyrrole **5b** (7.9 mg, 22.5 μmol , 23%) as yellow oil.

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.19 (s, 9H), 3.64 (dd, J = 12.7, 7.4 Hz, 1H), 3.76 (s, 6H), 3.83 (dd, J = 12.7, 2.5 Hz, 1H), 4.85 (dd, J = 7.5, 2.5 Hz, 1H), 6.19 (t, J = 2.2 Hz, 1H), 6.37 (d, J = 2.3 Hz, 2H), 6.74–6.84 (m, 2H), 6.92–6.98 (m, 1H), 7.01–7.07 (m, 1H).

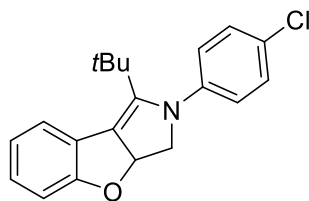
$^{13}\text{C-NMR}$ (76 MHz, CDCl_3): δ = 27.4, 30.7, 53.6, 55.4, 64.3, 74.0, 95.4, 96.1, 101.1, 117.6, 118.5, 121.0, 121.0, 130.7, 144.5, 149.3, 161.4.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2966 (m), 2866 (w), 2842 (w), 1589 (s), 1494 (m), 1455 (m), 1202 (s), 1153 (s), 1059 (m).

GC-HRMS (EI): $\text{C}_{22}\text{H}_{25}\text{NO}_3$ m/z calcd. $[\text{M}^+]$: 351.1834 found 351.1813.



Domino product (4c)



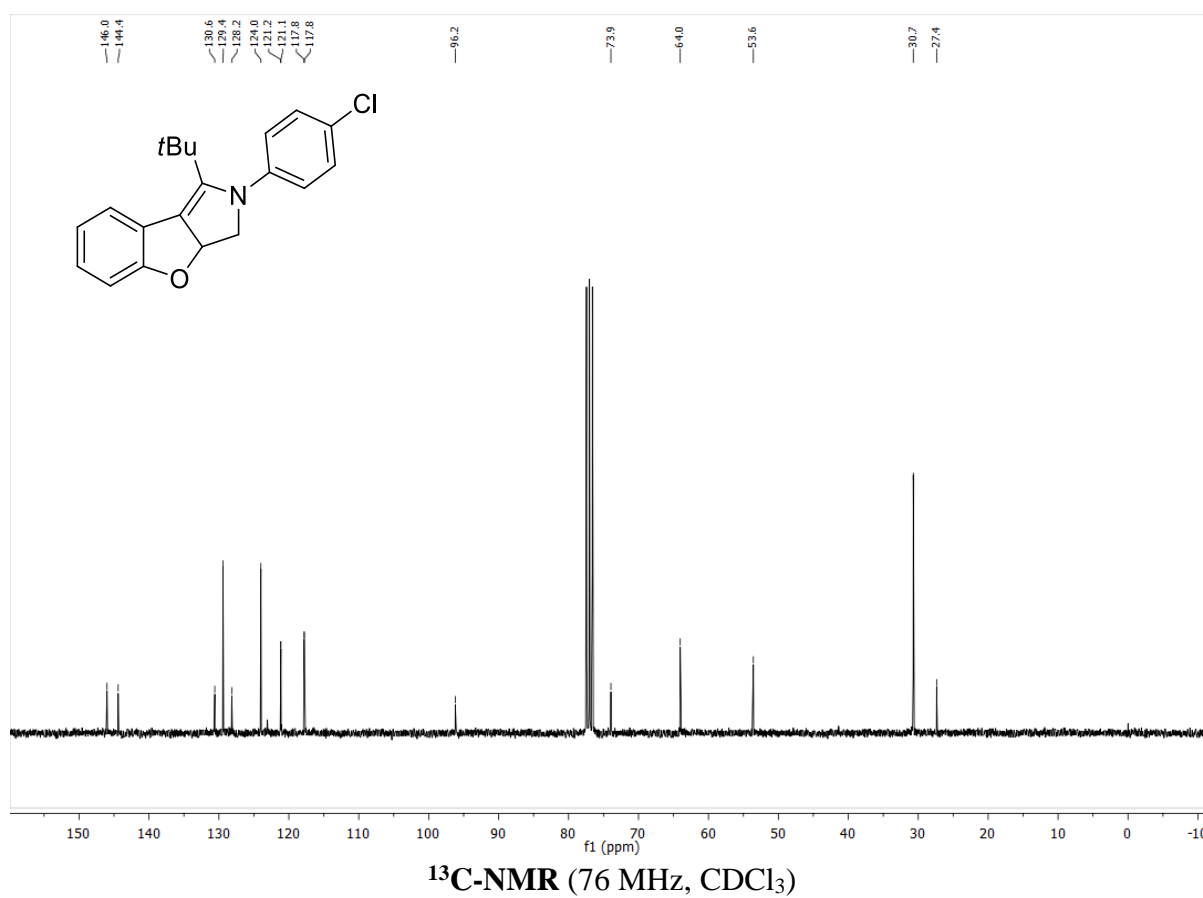
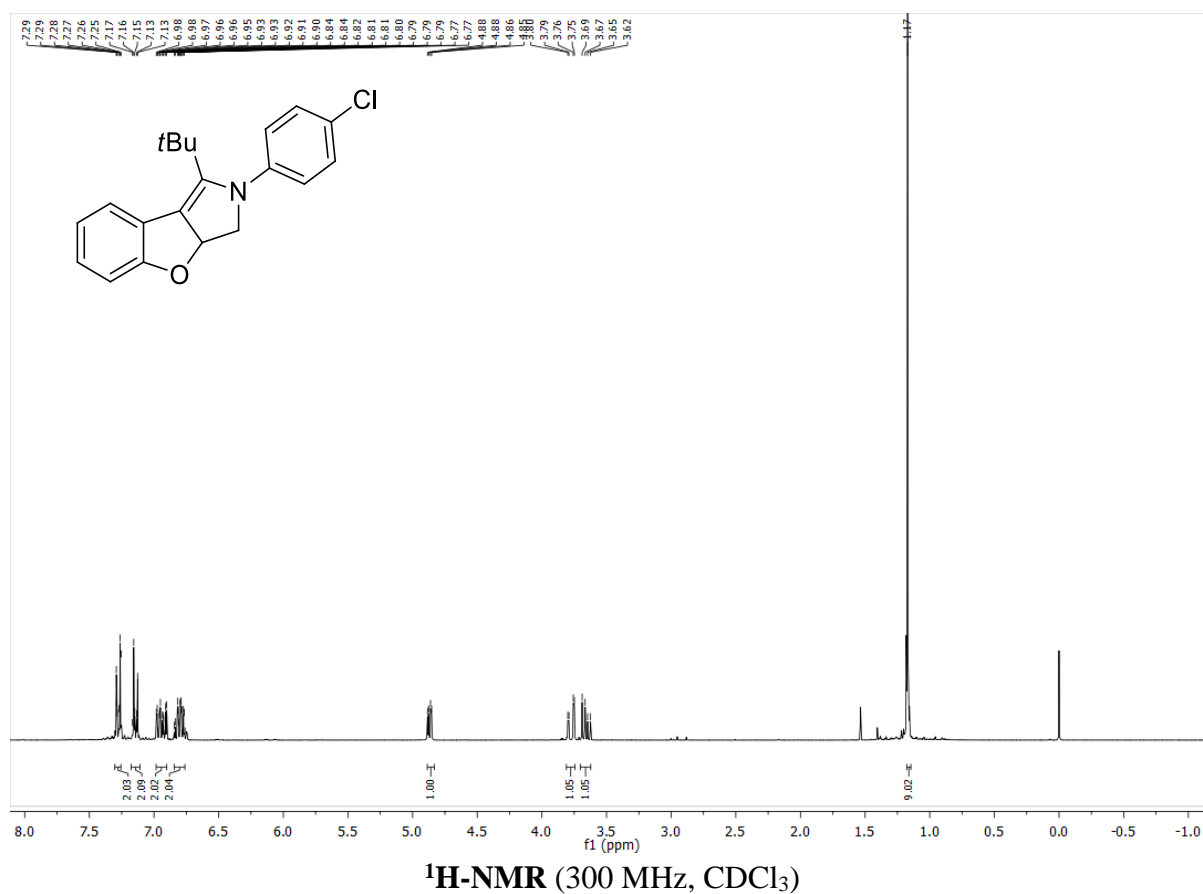
The domino precursor **2c** (48.8 mg, 120 μ mol), potassium phosphate (132 mg, 622 μ mol), $[t\text{Bu}_3\text{PH}][\text{BF}_4]$ (4.1 mg, 14.1 μ mol) and $\text{PdCl}_2(\text{PhCN})_2$ (2.3 mg, 6.0 μ mol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **4c** (13.3 mg, 40.8 μ mol, 34%) as colorless oil.

^1H -NMR (300 MHz, CDCl_3): δ = 1.17 (s, 9H), 3.66 (dd, J = 12.6, 6.9 Hz, 1H), 3.77 (dd, J = 12.7, 2.6 Hz, 1H), 4.87 (dd, J = 6.9, 2.6 Hz, 1H), 6.76–6.84 (m, 2H), 6.90–6.98 (m, 2H), 7.11–7.18 (m, 2H), 7.26–7.30 (m, 2H).

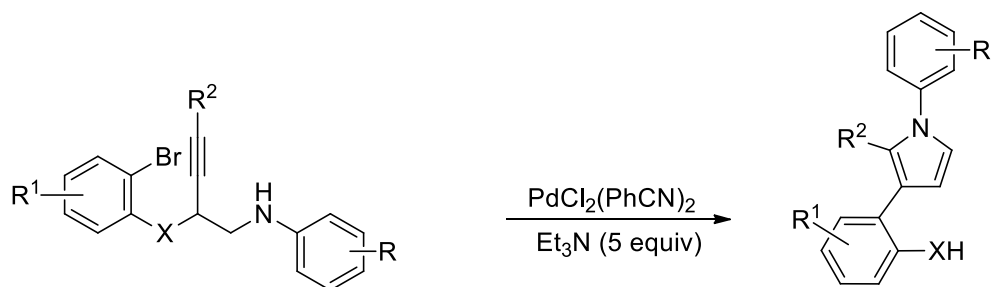
^{13}C -NMR (76 MHz, CDCl_3): δ = 27.4, 30.7, 53.6, 64.0, 73.9, 96.2, 117.8, 117.8, 121.1, 121.2, 124.0, 128.2, 129.4, 130.6, 144.4, 146.0.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2968 (m), 2927 (w), 2900 (w), 2866 (w), 1588 (m), 1490 (s), 1460 (m), 1246 (s), 1091 (m), 1058 (m).

GC-HRMS (EI): $\text{C}_{20}\text{H}_{20}\text{ClNO}$ m/z calcd. $[\text{M}^+]$: 325.1233 found 325.1213.

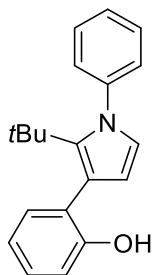


6) Synthesis of Domino Products of Type 5



R ¹ = H, R ² = <i>t</i> Bu, X = O, R = H	2a	5a (78%)
R ¹ = H, R ² = <i>t</i> Bu, X = O, R = 3,5-(OMe) ₂	2b	5b (80%)
R ¹ = H, R ² = <i>t</i> Bu, X = O, R = 4-Cl	2c	5c (64%)
R ¹ = naphthyl, R ² = <i>t</i> Bu, X = O, R = H	2d	5d (66%)
R ¹ = H, R ² = <i>t</i> Bu, X = O, R = 2,4,6-Me ₃	2e	5e (84%)
R ¹ = H, R ² = TMS, X = NTs, R = 2,4,6-Me ₃	2f	5f (50%)
R ¹ = H, R ² = TMS, X = NTs, R = H	2g	5g (58%)
R ¹ = H, R ² = TBS, X = NTs, R = H	2h	5h (94%)

Domino product (5a)



The domino precursor **2a** (37.2 mg, 100 μ mol), triethylamine (70 μ L, 505 μ mol), $[t\text{Bu}_3\text{PH}][\text{BF}_4]$ (2.9 mg, 10.0 μ mol) and $\text{PdCl}_2(\text{PhCN})_2$ (1.9 mg, 4.95 μ mol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **5a** (22.7 mg, 77.9 μ mol, 78%) as yellow solid.

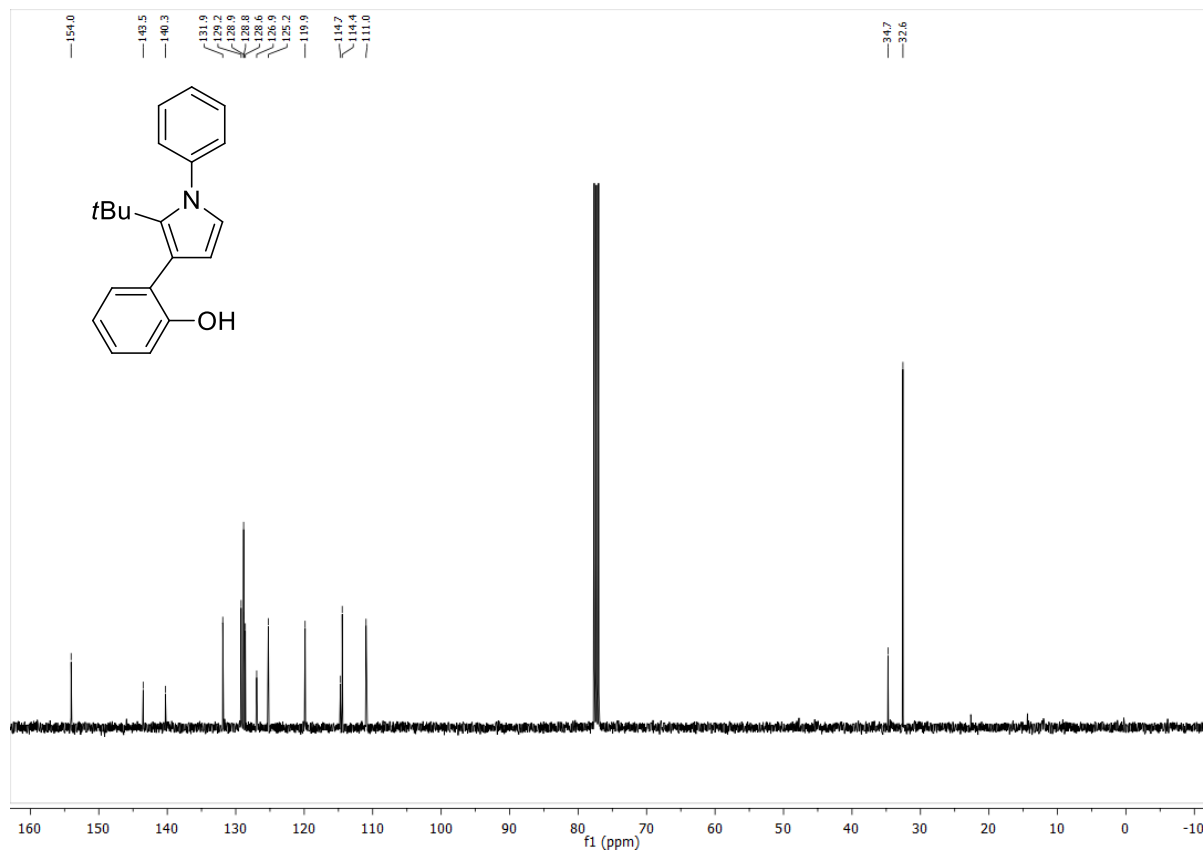
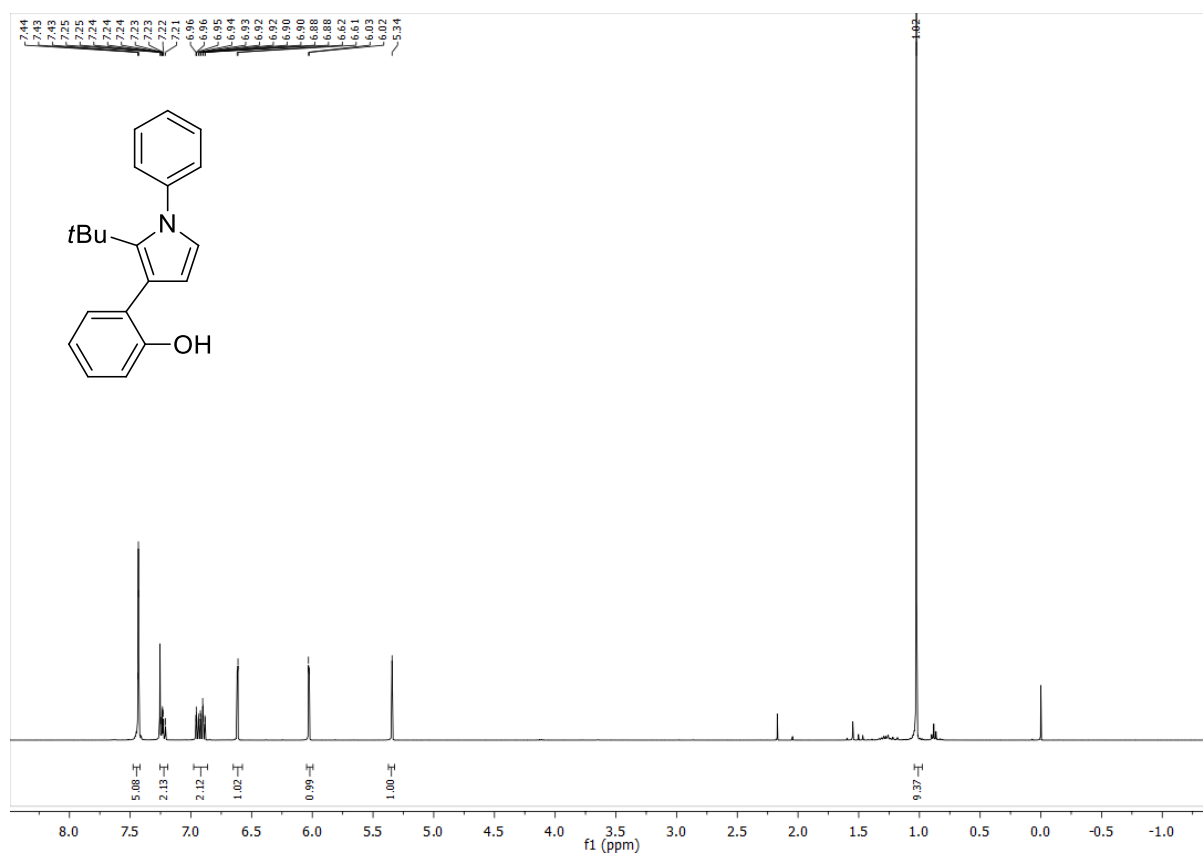
^1H -NMR (400 MHz, CDCl_3): δ = 1.02 (s, 9H), 5.34 (s, 1H), 6.03 (d, J = 2.8 Hz, 1H), 6.62 (d, J = 2.8 Hz, 1H), 6.86–6.98 (m, 2H), 7.19–7.25 (m, 2H), 7.42–7.44 (m, 5H).

^{13}C -NMR (101 MHz, CDCl_3): δ = 32.6, 34.7, 111.0, 114.4, 114.7, 119.9, 125.2, 126.9, 128.6, 128.8, 128.9, 129.2, 131.9, 140.3, 143.5, 154.0.

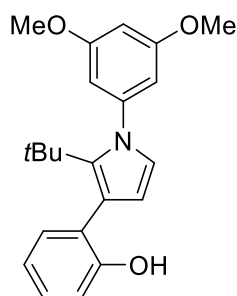
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3499 (m), 2994 (w), 2960 (m), 2907 (w), 2870 (w), 1597 (m), 1577 (m), 1463 (s), 1229 (m), 1184 (m).

M.p.: 107–109 $^\circ\text{C}$.

GC-HRMS (EI): $\text{C}_{20}\text{H}_{21}\text{NO}$ m/z calcd. $[\text{M}^+]$: 291.1623 found 291.1612.



Domino product (5b)



The domino precursor **2b** (42.5 mg, 98.3 μmol), triethylamine (70 μL , 505 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.8 mg, 9.65 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (2.2 mg, 5.74 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded domino product **5b** (27.6 mg, 78.5 μmol , 80%) as yellow solid.

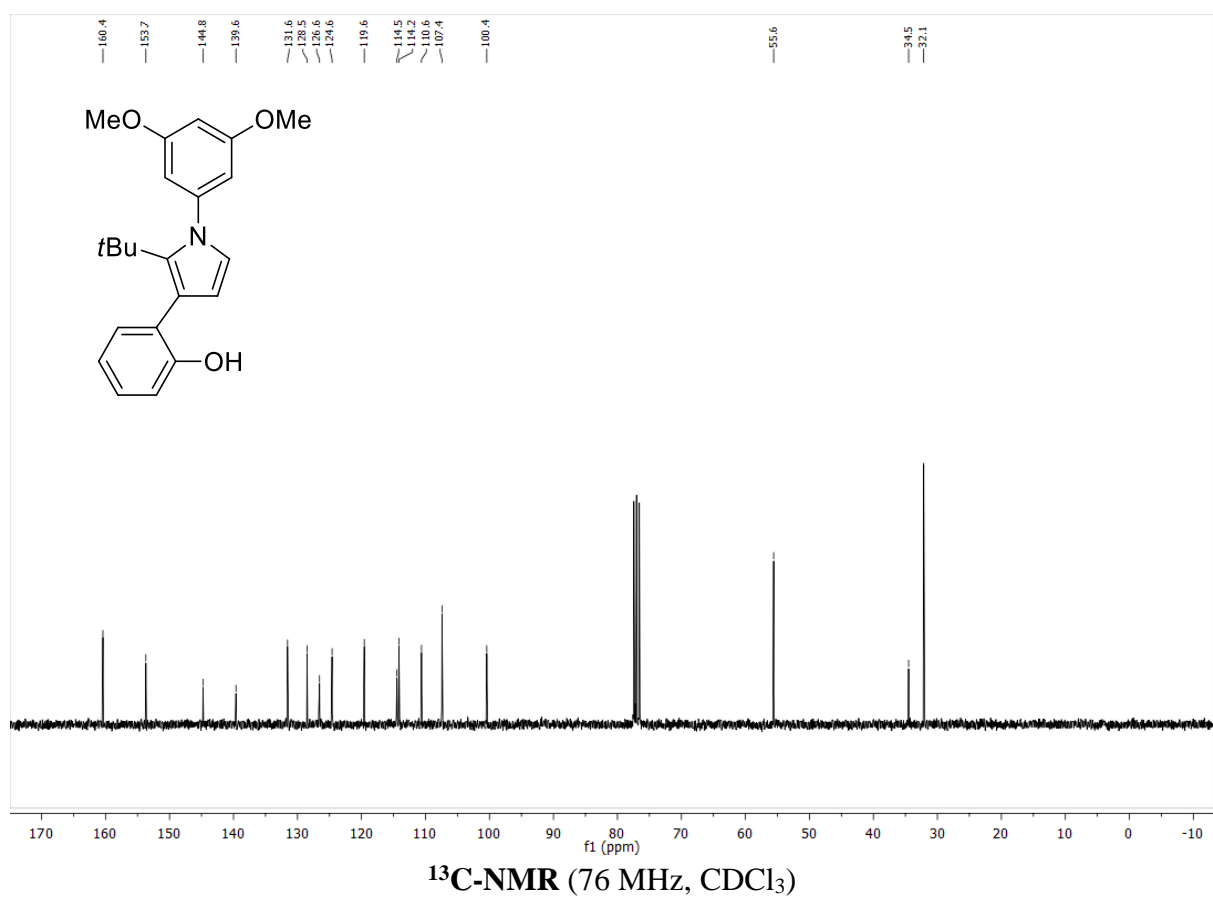
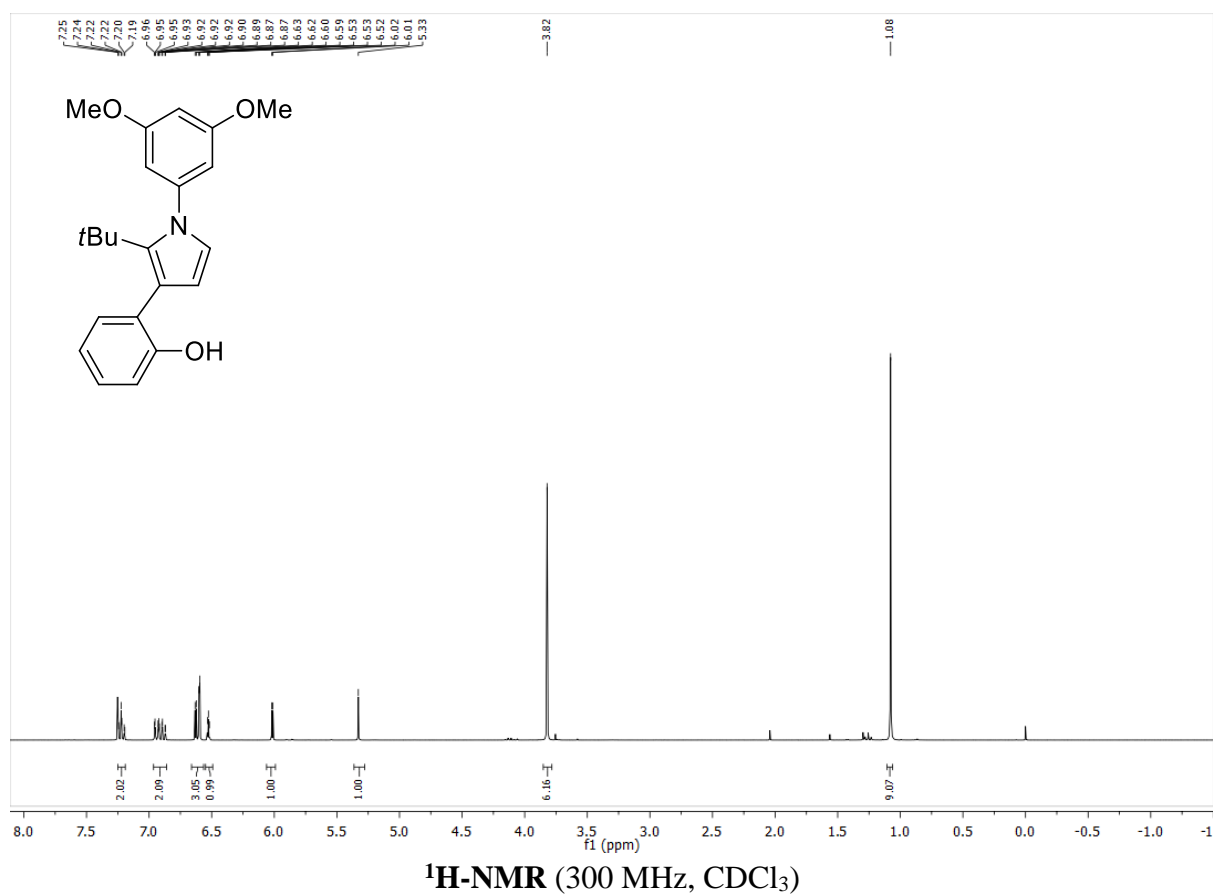
$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.08 (s, 9H), 3.82 (s, 6H), 5.33 (s, 1H), 6.02 (d, J = 2.8 Hz, 1H), 6.53 (t, J = 2.3 Hz, 1H), 6.56–6.66 (m, 3H), 6.86–6.96 (m, 2H), 7.19–7.25 (m, 2H).

$^{13}\text{C-NMR}$ (76 MHz, CDCl_3): δ = 32.1, 34.5, 55.6, 100.4, 107.4, 110.6, 114.2, 114.5, 119.6, 124.6, 126.6, 128.5, 131.6, 139.6, 144.8, 153.7, 160.4.

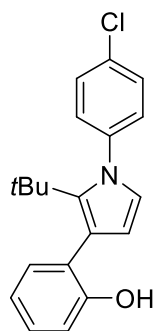
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3477 (m), 2996 (w), 2955 (m), 2904 (w), 2867 (w), 1595 (s), 1476 (m), 1460 (m), 1238 (m), 1200 (m), 1155 (s), 1057 (s).

M.p.: 151–154 $^\circ\text{C}$.

GC-HRMS (EI): $\text{C}_{22}\text{H}_{25}\text{NO}_3$ m/z calcd. $[\text{M}^+]$: 351.1834 found 351.1813.



Domino product (5c)



The domino precursor **2c** (48.8 mg, 120 μ mol), triethylamine (90 μ L, 649 μ mol), [*t*Bu₃PH][BF₄] (3.8 mg, 13.1 μ mol) and PdCl₂(PhCN)₂ (2.5 mg, 6.52 μ mol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 °C. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **5c** (25.0 mg, 76.7 μ mol, 64%) as yellow solid.

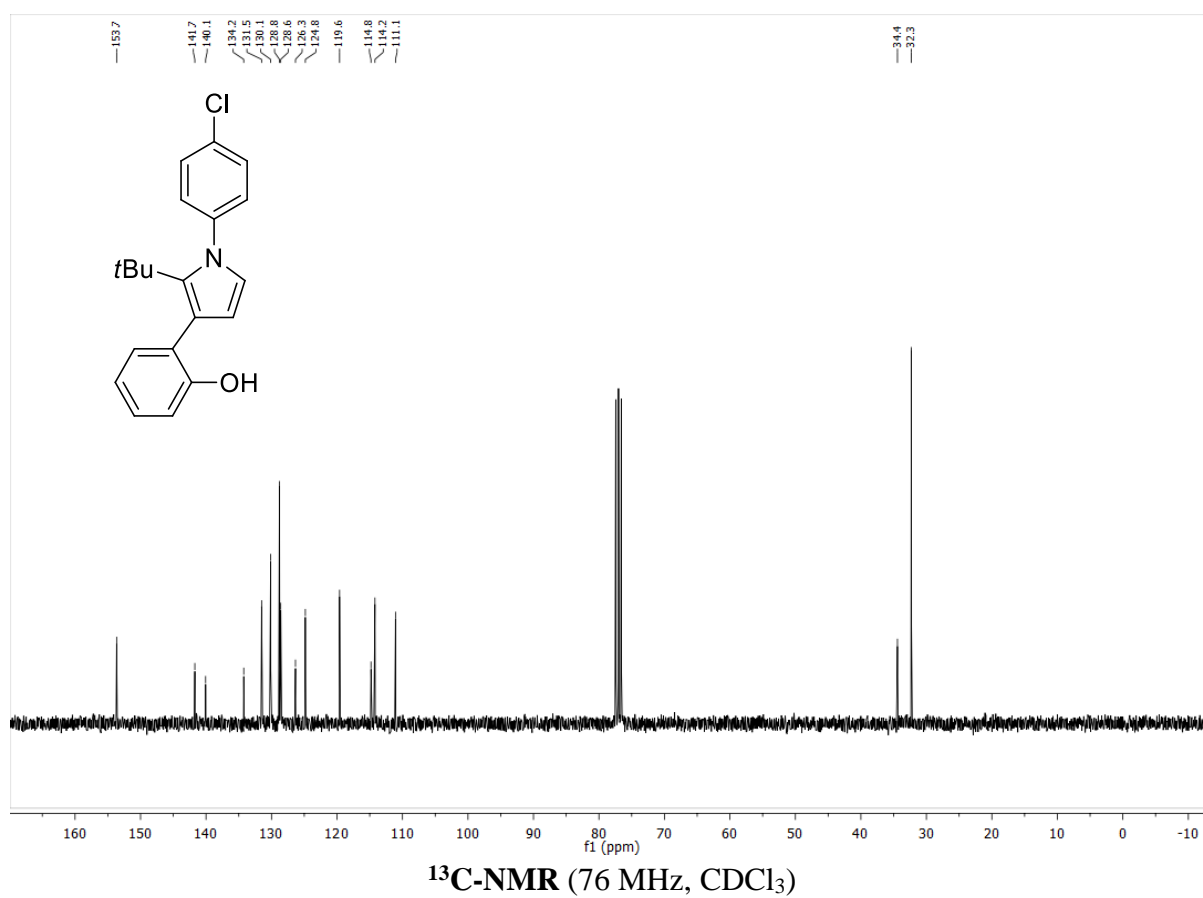
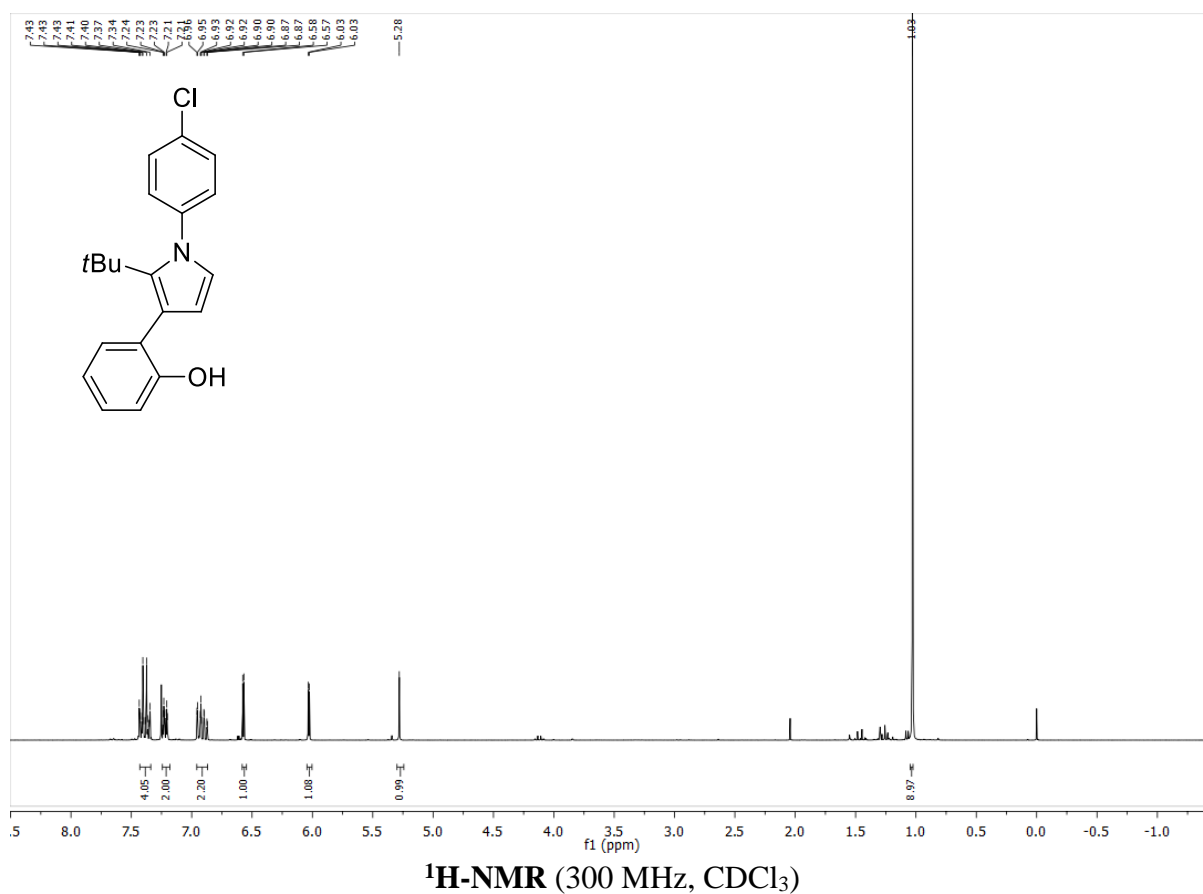
¹H-NMR (300 MHz, CDCl₃): δ = 1.03 (s, 9H), 5.28 (s, 1H), 6.03 (d, *J* = 2.8 Hz, 1H), 6.57 (d, *J* = 2.8 Hz, 1H), 6.87–6.96 (m, 2H), 7.22 (dt, *J* = 7.3, 1.5 Hz, 2H), 7.34–7.43 (m, 4H).

¹³C-NMR (76 MHz, CDCl₃) δ = 32.3, 34.4, 111.1, 114.2, 114.8, 119.6, 124.8, 126.3, 128.6, 128.8, 130.1, 131.5, 134.2, 140.1, 141.7, 153.7.

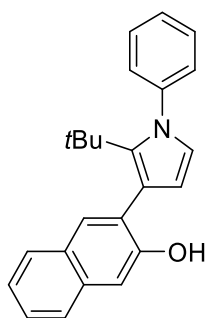
IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3500 (m), 2991 (w), 2962 (m), 2910 (w), 2871 (w), 1494 (s), 1539 (m), 1229 (m), 1182 (m).

M.p.: 112–116 °C.

GC-HRMS (EI): C₂₀H₂₀ClNO *m/z* calcd. [M⁺]: 325.1233 found 325.1209.



Domino product (5d)



The domino precursor **2d** (30.0 mg, 71.0 μmol), triethylamine (50 μL , 361 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.1 mg, 7.24 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (1.5 mg, 3.91 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography ($\text{EtOAc}:\text{n-pentane} = 1:20$) afforded domino product **5d** (16.0 mg, 46.9 μmol , 66%) as yellow oil.

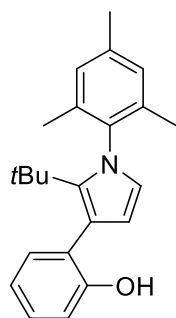
$^1\text{H-NMR}$ (500 MHz, CDCl_3): δ = 1.04 (s, 9H), 5.53 (s, 1H), 6.08 (d, J = 2.8 Hz, 1H), 6.65 (d, J = 3.0 Hz, 1H), 7.29–7.34 (m, 2H), 7.37–7.42 (m, 1H), 7.45 (s, 5H), 7.71–7.78 (m, 3H).

$^{13}\text{C-NMR}$ (126 MHz, CDCl_3): δ = 32.3, 34.5, 108.4, 111.0, 114.0, 123.3, 125.1, 125.9, 126.4, 127.6, 128.4, 128.4, 128.6, 128.9, 129.2, 130.3, 134.4, 140.3, 143.1, 152.3.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3487 (m), 2994 (w), 2961 (m), 2907 (w), 2870 (w), 1500 (s), 1453 (m), 1260 (m), 1244 (m), 1165 (m).

ESI-HRMS: $\text{C}_{24}\text{H}_{23}\text{NO}$ m/z calcd. $[\text{M}+\text{H}^+]$: 342.1852 found 342.1854.

Domino product (5e)



The domino precursor **2e** (78.0 mg, 188 μmol), triethylamine (130 μL , 938 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (5.5 mg, 19.0 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (3.6 mg, 9.39 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:50) afforded domino product **5e** (52.8 mg, 158 μmol , 84%) as colorless solid.

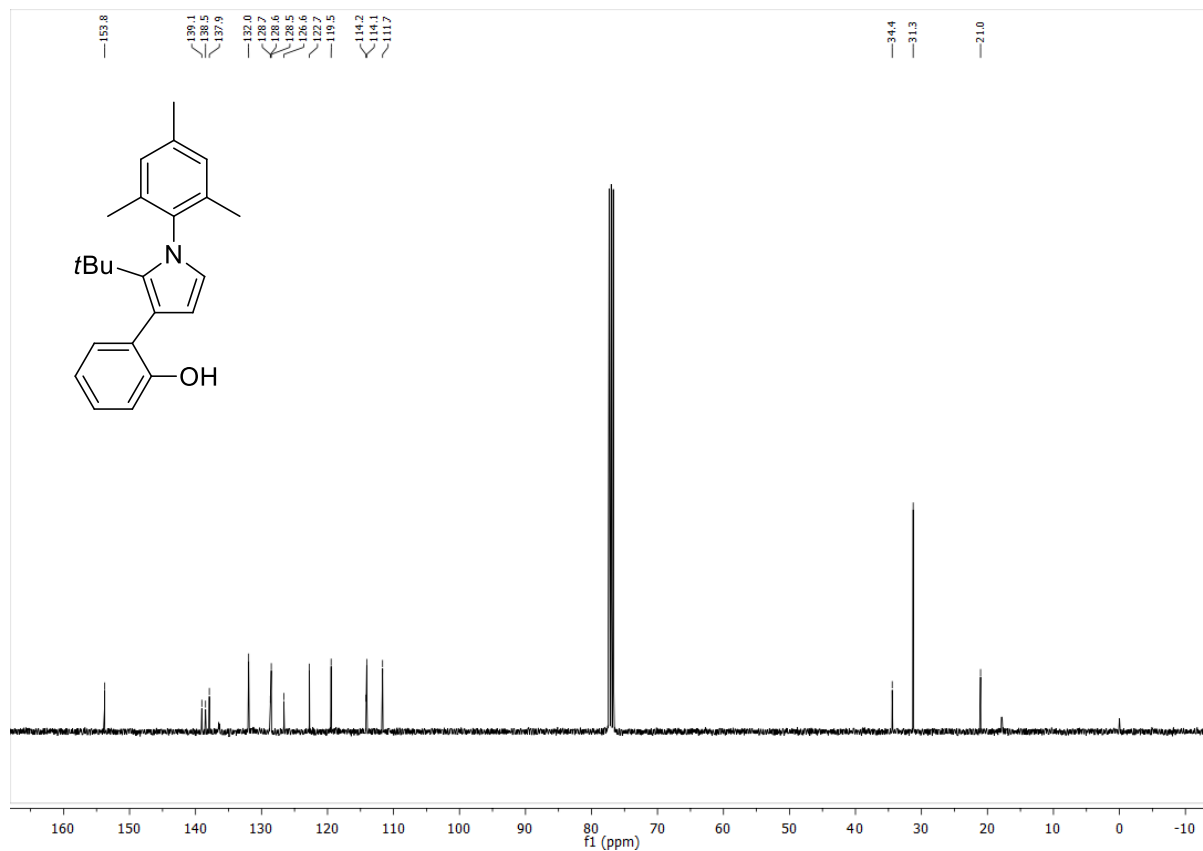
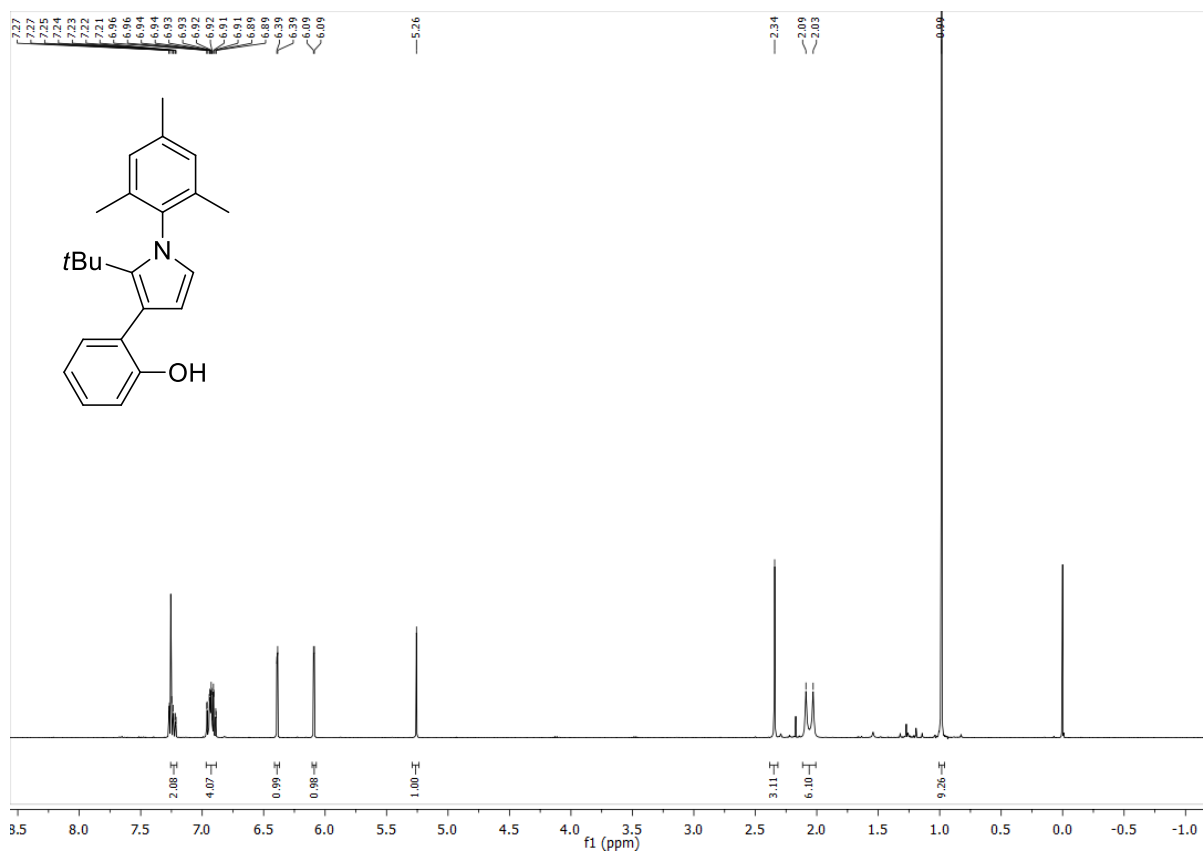
^1H -NMR (400 MHz, CDCl_3): δ = 0.99 (s, 9H), 2.06 (d, J = 23.5 Hz, 6H), 2.34 (s, 3H), 5.26 (s, 1H), 6.09 (d, J = 2.8 Hz, 1H), 6.39 (d, J = 2.8 Hz, 1H), 6.92 (dtd, J = 13.3, 7.8, 1.2 Hz, 4H), 7.21–7.27 (m, 2H).

^{13}C -NMR (101 MHz, CDCl_3): δ = 21.0, 31.3, 34.4, 111.7, 114.1, 114.2, 119.5, 122.7, 126.6, 128.5, 128.6, 128.7, 132.0, 137.9, 138.5, 139.1, 153.8.

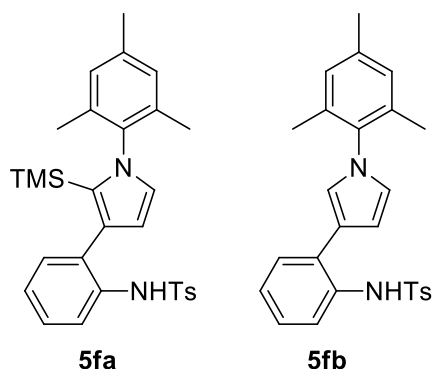
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3498 (m), 2991 (m), 2958 (m), 2917 (m), 2868 (m), 1493 (s), 1461 (m), 1227 (m), 1186 (m).

M.p.: 92–95 $^\circ\text{C}$.

GC-HRMS (EI): $\text{C}_{23}\text{H}_{27}\text{NO}$ m/z calcd. $[\text{M}^+]$: 333.2093 found 333.2079.



Domino product (5f)



The domino precursor **2f** (46.0 mg, 78.8 μmol), triethylamine (55 μL , 397 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.3 mg, 7.93 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (1.5 mg, 3.91 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography ($\text{EtOAc}:\text{n-pentane} = 1:20$) afforded a mixture of domino product **5fa** (19.7 mg, 39.2 μmol , 50%) as colorless oil and domino product **5fb** (9.6 mg, 22.3 μmol , 28%) as colorless oil.

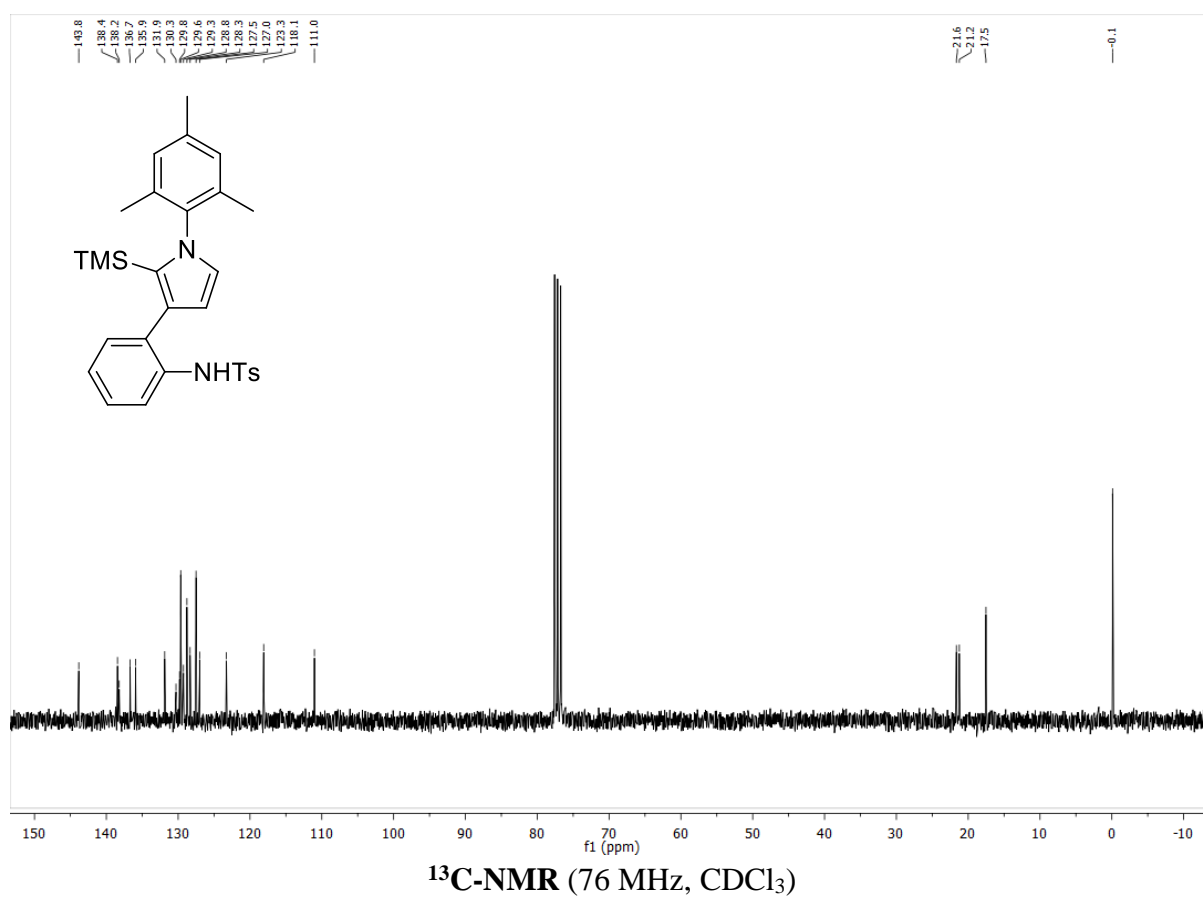
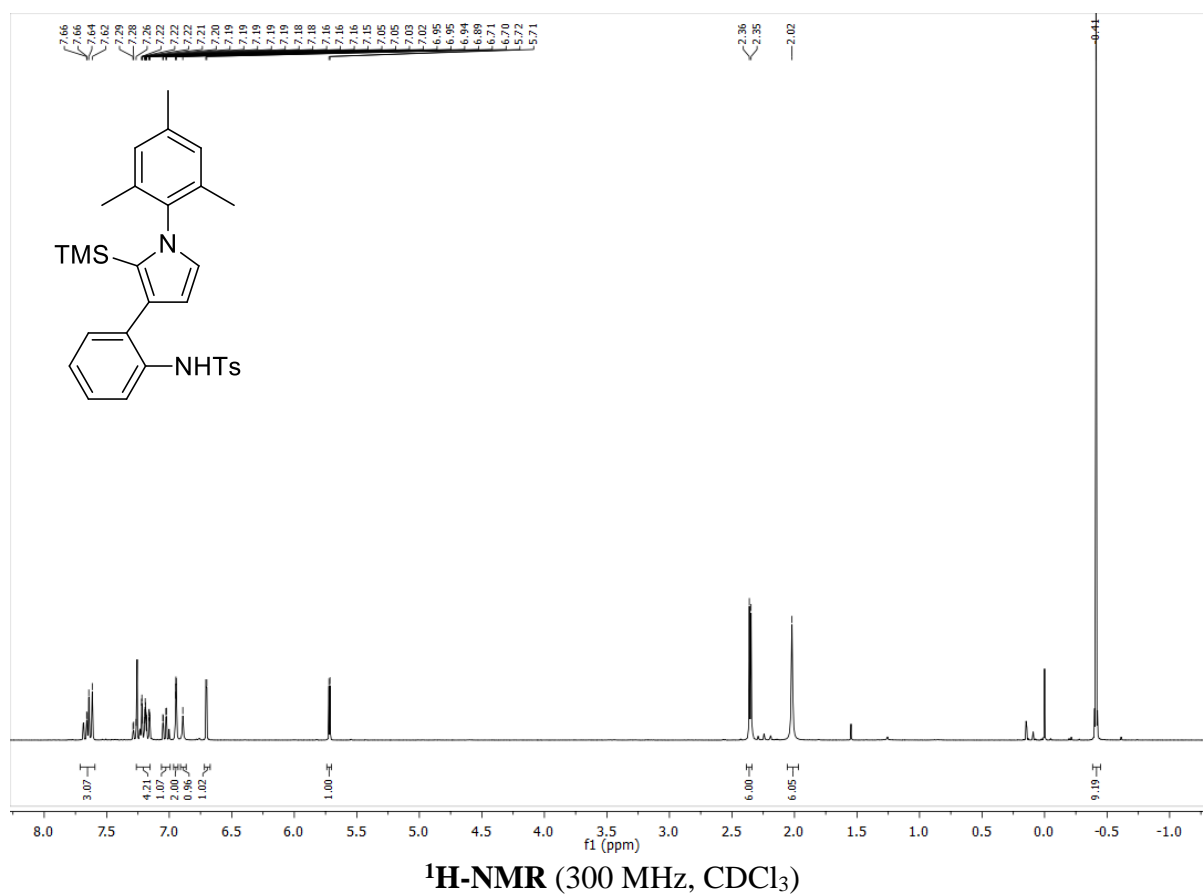
Analytical data of **5fa**:

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = -0.41$ (s, 9H), 2.02 (s, 6H), 2.35 (d, $J = 4.2$ Hz, 6H), 5.72 (d, $J = 2.4$ Hz, 1H), 6.70 (d, $J = 2.4$ Hz, 1H), 6.89 (s, 1H), 6.95 (s, 2H), 7.02 (td, $J = 7.4, 1.2$ Hz, 1H), 7.19–7.27 (m, 3H), 7.58–7.71 (m, 2H).

$^{13}\text{C-NMR}$ (76 MHz, CDCl_3) $\delta = -0.1, 17.5, 21.2, 21.6, 111.0, 118.1, 123.3, 127.0, 127.5, 128.3, 128.8, 129.3, 129.6, 129.8, 130.3, 131.9, 135.9, 136.7, 138.2, 138.4, 143.8$.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3309 (w), 2956 (w), 2922 (w), 2861 (w), 1492 (m), 1398 (m), 1338 (m), 1247 (m), 1164 (s), 1091 (m).

ESI-HRMS: $\text{C}_{29}\text{H}_{34}\text{N}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 503.2183 found 503.2186.



Analytical data of **5fb**:

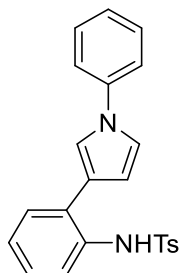
¹H-NMR (500 MHz, CDCl₃): δ = 2.03 (s, 6H), 2.33 (s, 3H), 2.35 (s, 3H), 6.08 (dd, J = 2.7, 1.8 Hz, 1H), 6.35 (t, J = 2.0 Hz, 1H), 6.64 (t, J = 2.4 Hz, 1H), 6.94–6.98 (m, 2H), 7.08 (td, J = 7.4, 1.2 Hz, 1H), 7.13–7.17 (m, 2H), 7.19–7.25 (m, 3H), 7.57–7.62 (m, 2H), 7.65 (dd, J = 8.2, 1.2 Hz, 1H).

¹³C-NMR (126 MHz, CDCl₃) δ = 17.3, 21.0, 21.5, 108.8, 119.9, 120.1, 120.1, 123.2, 124.4, 127.1, 127.5, 127.7, 128.8, 129.5, 130.4, 134.2, 135.5, 136.5, 136.7, 138.2, 143.7.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3316 (w), 3029 (w), 2953 (w), 2921 (w), 2859 (w), 1496 (m), 1400 (m), 1335 (m), 1161 (s), 1089 (m).

ESI-HRMS: C₂₆H₂₆N₂O₂S m/z calcd. [M+H⁺]: 431.1788 found 431.1791

Domino product (5g)



The domino precursor **2g** (51.6 mg, 95.3 μmol), triethylamine (70 μL , 505 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.8 mg, 9.65 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (1.8 mg, 4.69 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:15) afforded domino product **5g** (21.6 mg, 55.6 μmol , 58%) as yellow oil.

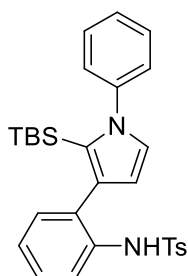
^1H -NMR (300 MHz, CDCl_3): δ = 2.31 (s, 3H), 6.11 (dd, J = 2.9, 1.8 Hz, 1H), 6.65 (t, J = 2.0 Hz, 1H), 7.04 (s, 1H), 7.08–7.17 (m, 4H), 7.22–7.37 (m, 5H), 7.43–7.51 (m, 2H), 7.53–7.61 (m, 2H), 7.65 (dd, J = 8.1, 1.2 Hz, 1H).

^{13}C -NMR (75 MHz, CDCl_3) δ = 21.5, 110.7, 117.9, 120.5, 120.5, 120.9, 121.7, 124.7, 126.2, 127.1, 127.8, 127.8, 129.5, 129.7, 130.3, 134.3, 136.5, 140.0, 143.7.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3320 (w), 3063 (w), 2955 (w), 2924 (w), 2857 (w), 1598 (m), 1506 (m), 1401 (m), 1334 (m), 1161 (s), 1090 (m).

GC-HRMS (EI): $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}_2\text{S}$ m/z calcd. $[\text{M}+\text{H}^+]$: 389.1318 found 389.1322.

Domino product (5h)



The domino precursor **2h** (117 mg, 200 μ mol), triethylamine (170 μ L, 1.23 mmol), $[t\text{Bu}_3\text{PH}][\text{BF}_4]$ (6.0 mg, 20.7 μ mol) and $\text{PdCl}_2(\text{PhCN})_2$ (4.0 mg, 10.4 μ mol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded domino product **5h** (94.0 mg, 187 μ mol, 94%) as yellow solid.

Scale-up: The domino precursor **2h** (584 mg, 1.00 mmol) was dissolved in DMF (30 mL). To the mixture were added triethylamine (700 μ L, 5.05 mmol), $[t\text{Bu}_3\text{PH}][\text{BF}_4]$ (29.0 mg, 100 μ mol) and $\text{PdCl}_2(\text{PhCN})_2$ (19.0 mg, 49.5 μ mol) in that order. The reaction flask was closed with a teflon cap and stirred 30 min at rt. Afterwards, the mixture was stirred 2 h at 120 $^\circ\text{C}$. The mixture was cooled to rt and water and EtOAc were added. The layers were separated and the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried over Na_2SO_4 and the solvent was removed *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded domino product **5h** (432 mg, 859 μ mol, 86%) as yellow solid.

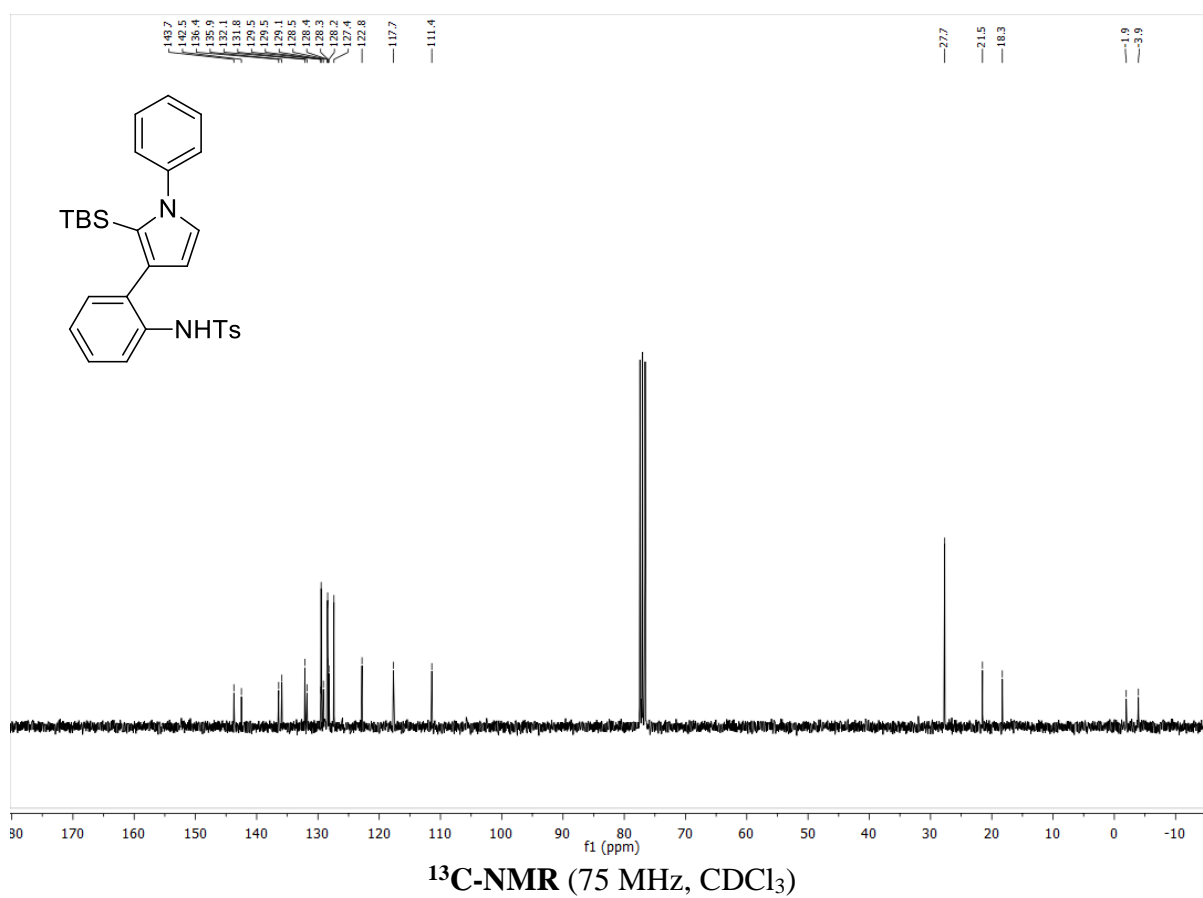
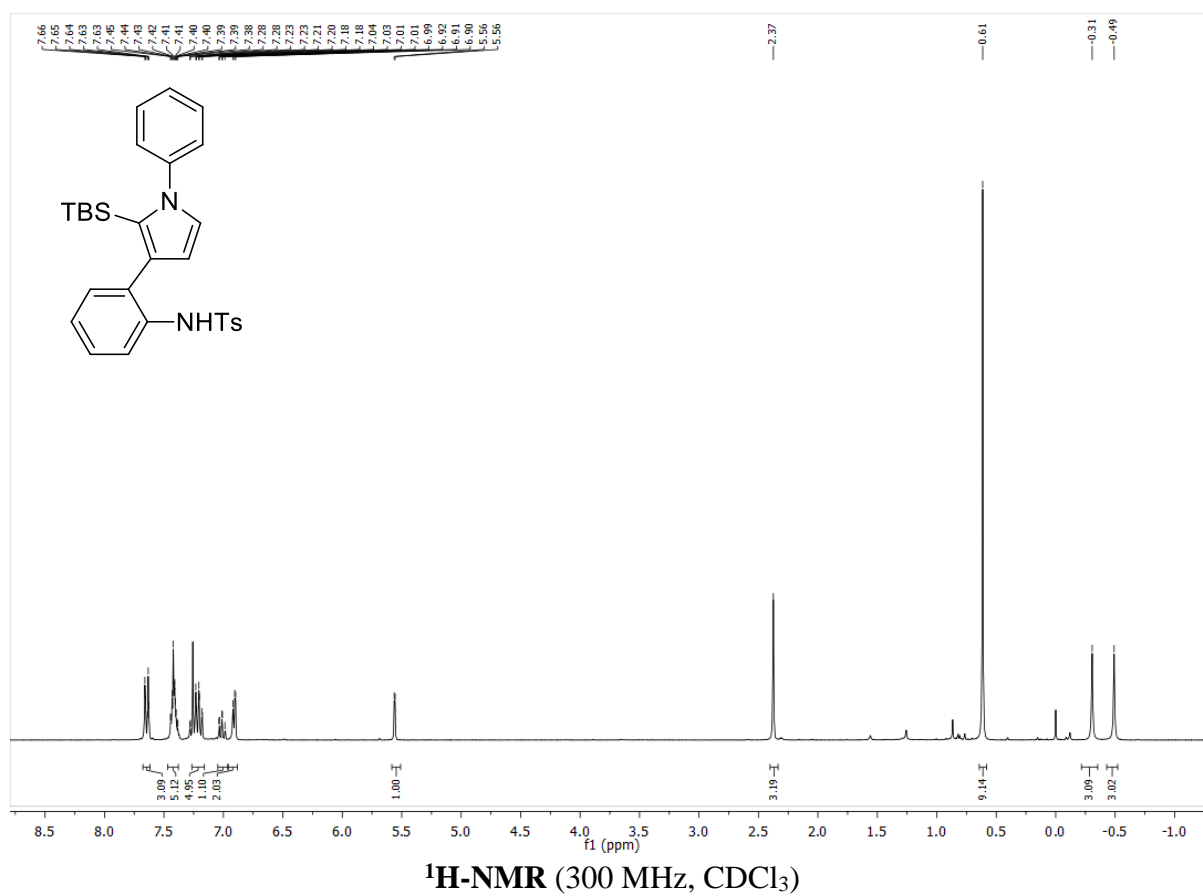
^1H -NMR (300 MHz, CDCl_3): δ = -0.49 (s, 3H), -0.31 (s, 3H), 0.61 (s, 9H), 2.37 (s, 3H), 5.56 (d, J = 2.4 Hz, 1H), 6.88–6.96 (m, 2H), 6.96–7.05 (m, 1H), 7.16–7.28 (m, 5H), 7.38–7.47 (m, 5H), 7.64 (dd, J = 8.4, 1.7 Hz, 3H).

^{13}C -NMR (75 MHz, CDCl_3) δ = -3.9, -1.9, 18.3, 21.5, 27.7, 111.4, 117.7, 122.8, 127.4, 128.2, 128.3, 128.4, 128.5, 129.1, 129.5, 129.5, 131.8, 132.1, 135.9, 136.4, 142.5, 143.7.

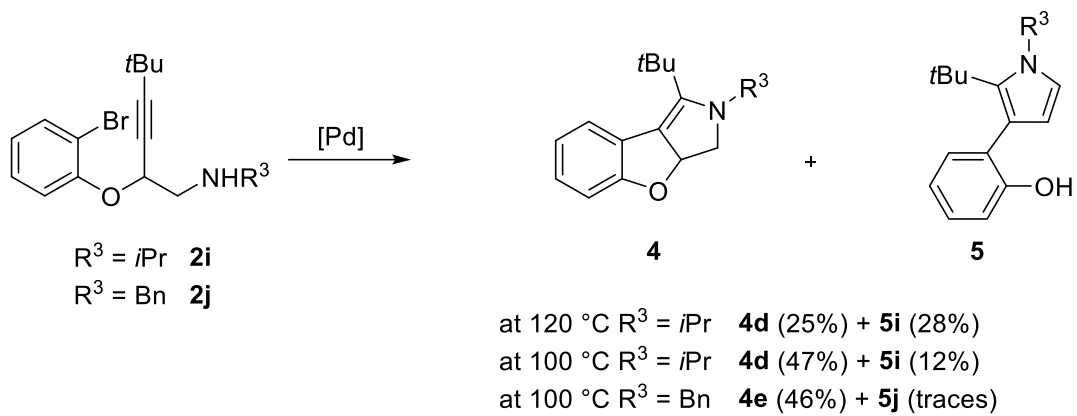
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3308 (w), 2954 (m), 2928 (m), 2892 (w), 2855 (w), 1497 (m), 1394 (m), 1334 (m), 1164 (s), 1092 (m).

M.p.: 127–130 $^\circ\text{C}$.

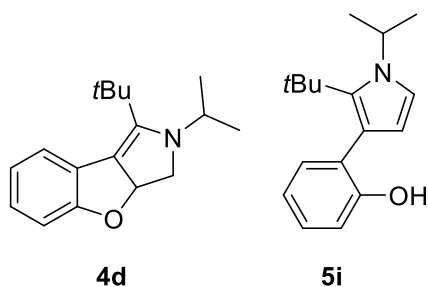
ESI-HRMS: $\text{C}_{29}\text{H}_{34}\text{N}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 503.2183 found 503.2182.



7) Termination with different Amines



Domino product 4d and Domino product 5i



The domino precursor **2i** (32.8 mg, 97.0 μmol), potassium phosphate (105 mg, 505 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (3.2 mg, 11.0 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (2.1 mg, 5.5 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 120 $^\circ\text{C}$. Silica gel column chromatography ($\text{EtOAc}:\text{n-pentane} = 1:20$) afforded a mixture of domino product **4d** (7.1 mg, 27.6 μmol , 28%) as yellow oil and domino product **5i** (6.3 mg, 24.5 μmol , 25%) as yellow oil.

The domino precursor **2i** (33.7 mg, 99.6 μmol), potassium phosphate (107 mg, 504 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (3.5 mg, 12.0 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (1.9 mg, 5.0 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 100 $^\circ\text{C}$. Silica gel column chromatography ($\text{EtOAc}:\text{n-pentane} = 1:20$) afforded a mixture of domino product **4d** (12.0 mg, 46.6 μmol , 47%) as yellow oil and domino product **5i** (3.0 mg, 11.7 μmol , 12%) as yellow oil.

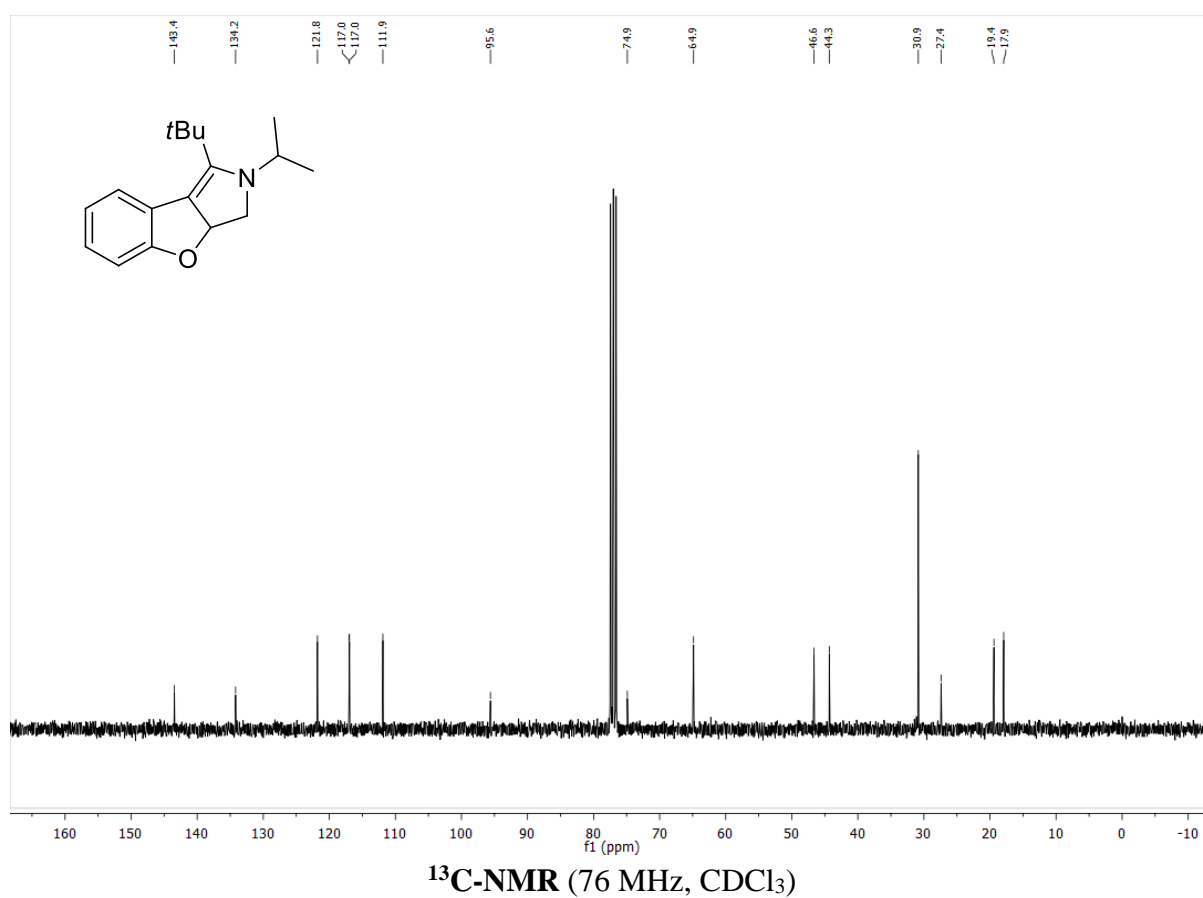
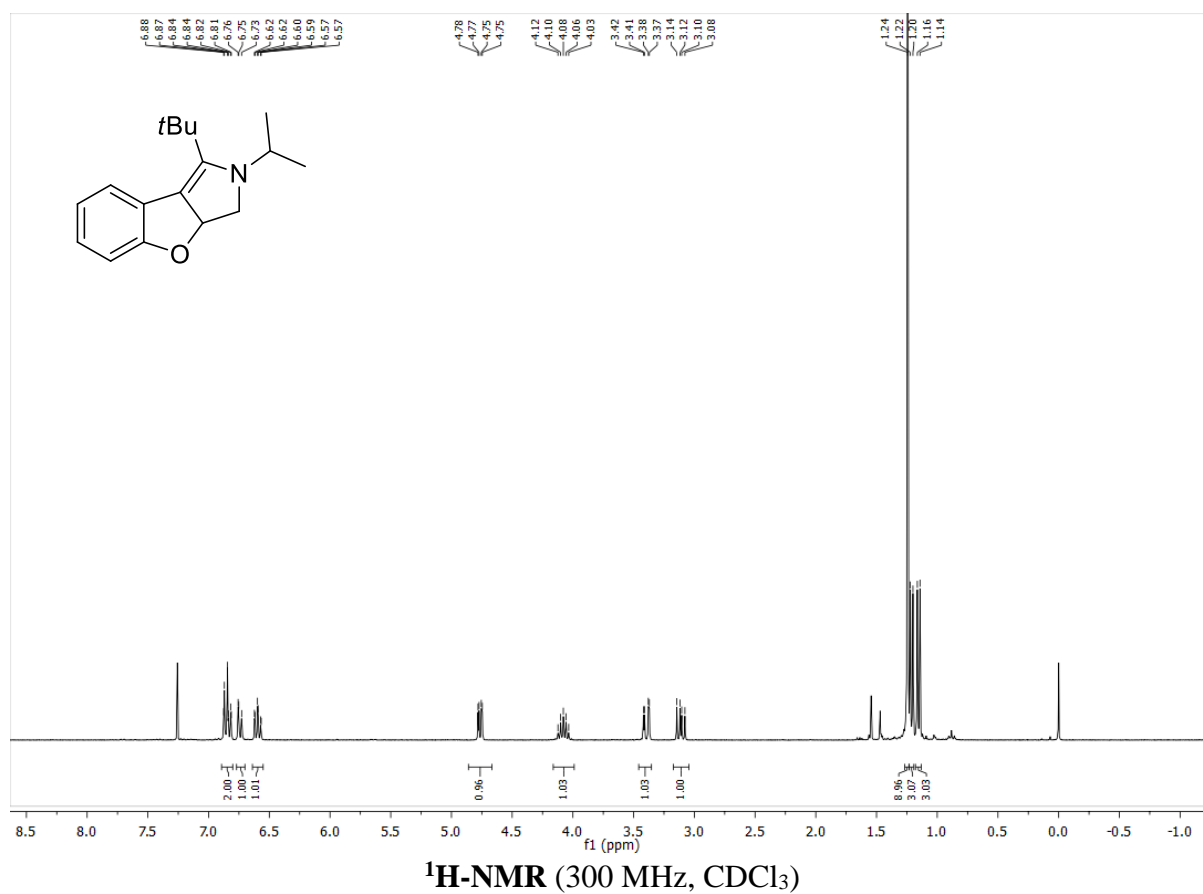
Analytical data for **4d**:

$^1\text{H-NMR}$ (300 MHz, CDCl_3): δ = 1.15 (d, J = 6.6 Hz, 3H), 1.21 (d, J = 6.6 Hz, 3H), 1.24 (s, 9H), 3.11 (dd, J = 12.0, 8.0 Hz, 1H), 3.39 (dd, J = 12.1, 2.6 Hz, 1H), 4.08 (p, J = 6.6 Hz, 1H), 4.76 (dd, J = 8.0, 2.6 Hz, 1H), 6.59 (td, J = 7.5, 1.6 Hz, 1H), 6.70–6.77 (m, 1H), 6.80–6.89 (m, 2H).

$^{13}\text{C-NMR}$ (76 MHz, CDCl_3) δ = 17.9, 19.4, 27.4, 30.9, 44.3, 46.6, 64.9, 74.9, 95.6, 111.9, 117.0, 117.0, 121.8, 134.2, 143.4.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2970 (m), 2929 (w), 2870 (w), 1605 (w), 1500 (s), 1461 (w), 1333 (m), 1264 (s), 1204 (m), 1081 (m).

GC-HRMS (EI): $\text{C}_{17}\text{H}_{23}\text{NO}$ m/z calcd. $[\text{M}^+]$: 257.1780 found 257.1790.



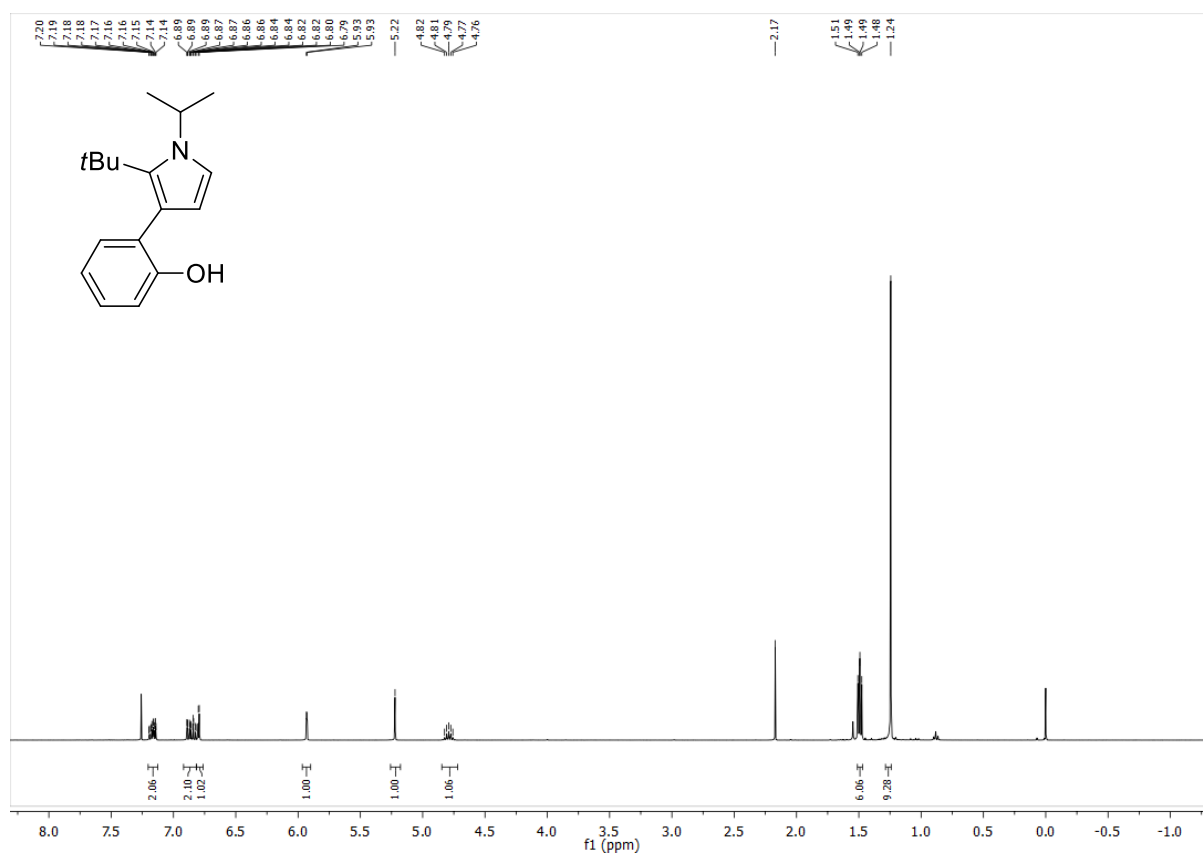
Analytical data for **5i**:

¹H-NMR (400 MHz, CDCl₃): δ = 1.24 (s, 9H), 1.49 (dd, J = 6.6, 5.9 Hz, 6H), 4.79 (p, J = 6.7 Hz, 1H), 5.22 (s, 1H), 5.93 (d, J = 3.0 Hz, 1H), 6.80 (d, J = 3.0 Hz, 1H), 6.82–6.92 (m, 2H), 7.13–7.20 (m, 2H).

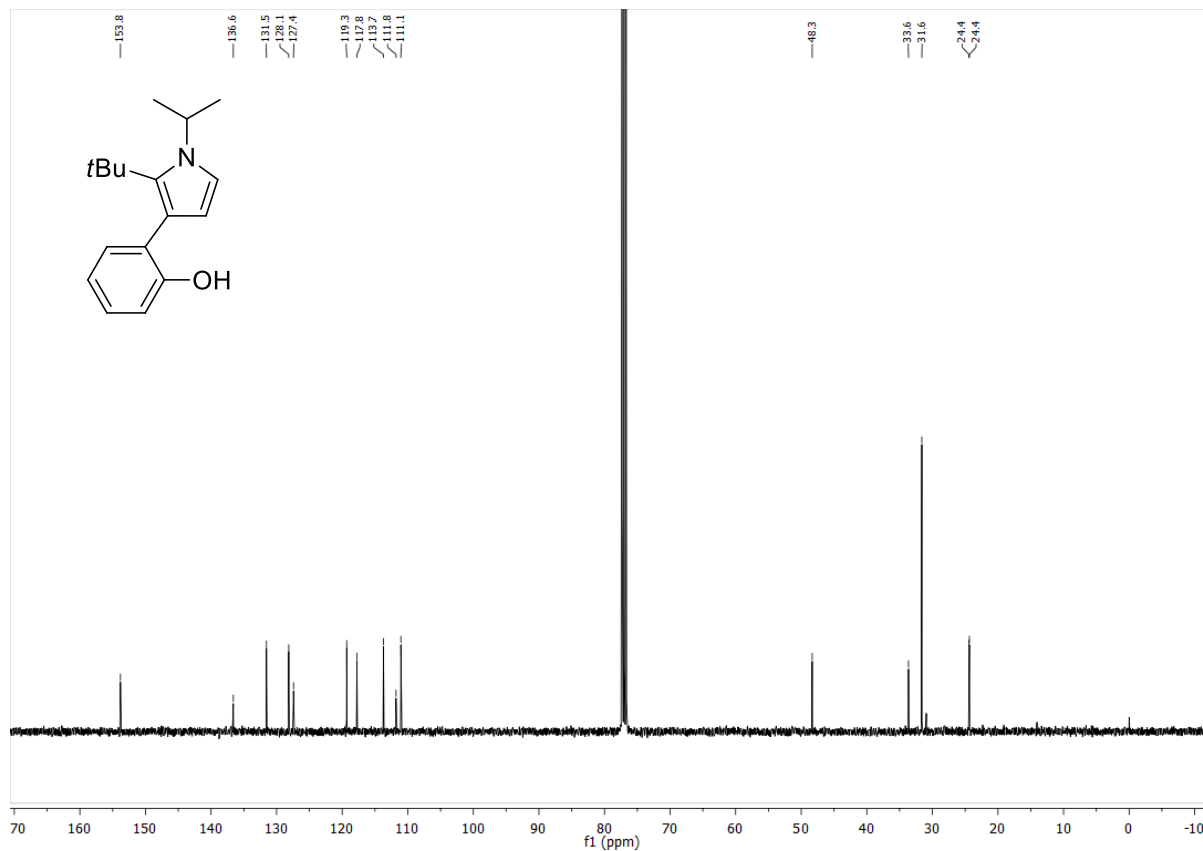
¹³C-NMR (101 MHz, CDCl₃) δ = 24.4, 24.4, 31.6, 33.6, 48.3, 111.1, 111.8, 113.7, 117.8, 119.3, 127.4, 128.1, 131.5, 136.6, 153.8.

IR (ATR): $\tilde{\nu}$ (cm⁻¹) = 3488 (m), 3035 (w), 2972 (m), 2875 (w), 1578 (w), 1501 (m), 1465 (m), 1243 (m), 1191 (s).

GC-HRMS (EI): C₁₇H₂₃NO m/z calcd. [M⁺]: 257.1180 found 257.1783.

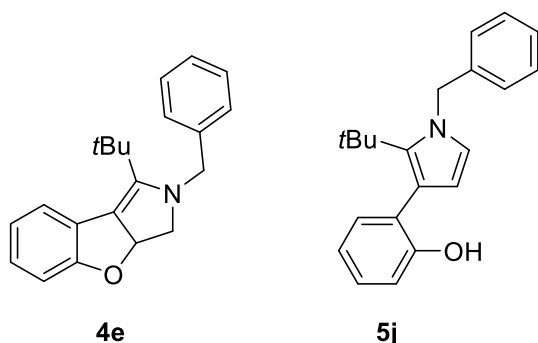


¹H-NMR (400 MHz, CDCl₃)



¹³C-NMR (101 MHz, CDCl₃)

Domino product 4e and Domino product 5j



The domino precursor **2j** (37.6 mg, 97.3 μmol), potassium phosphate (104 mg, 490 μmol), $[\text{tBu}_3\text{PH}][\text{BF}_4]$ (2.5 mg, 8.6 μmol) and $\text{PdCl}_2(\text{PhCN})_2$ (2.3 mg, 6.0 μmol) were reacted according to GP3 (Pd-catalyzed Domino Reaction). The mixture was stirred 2 h at 100 $^\circ\text{C}$. Silica gel column chromatography ($\text{EtOAc}:\text{n-pentane} = 1:20$) afforded domino product **4e** (13.6 mg, 44.6 μmol , 46%) as yellow oil and domino product **5j** only in traces.

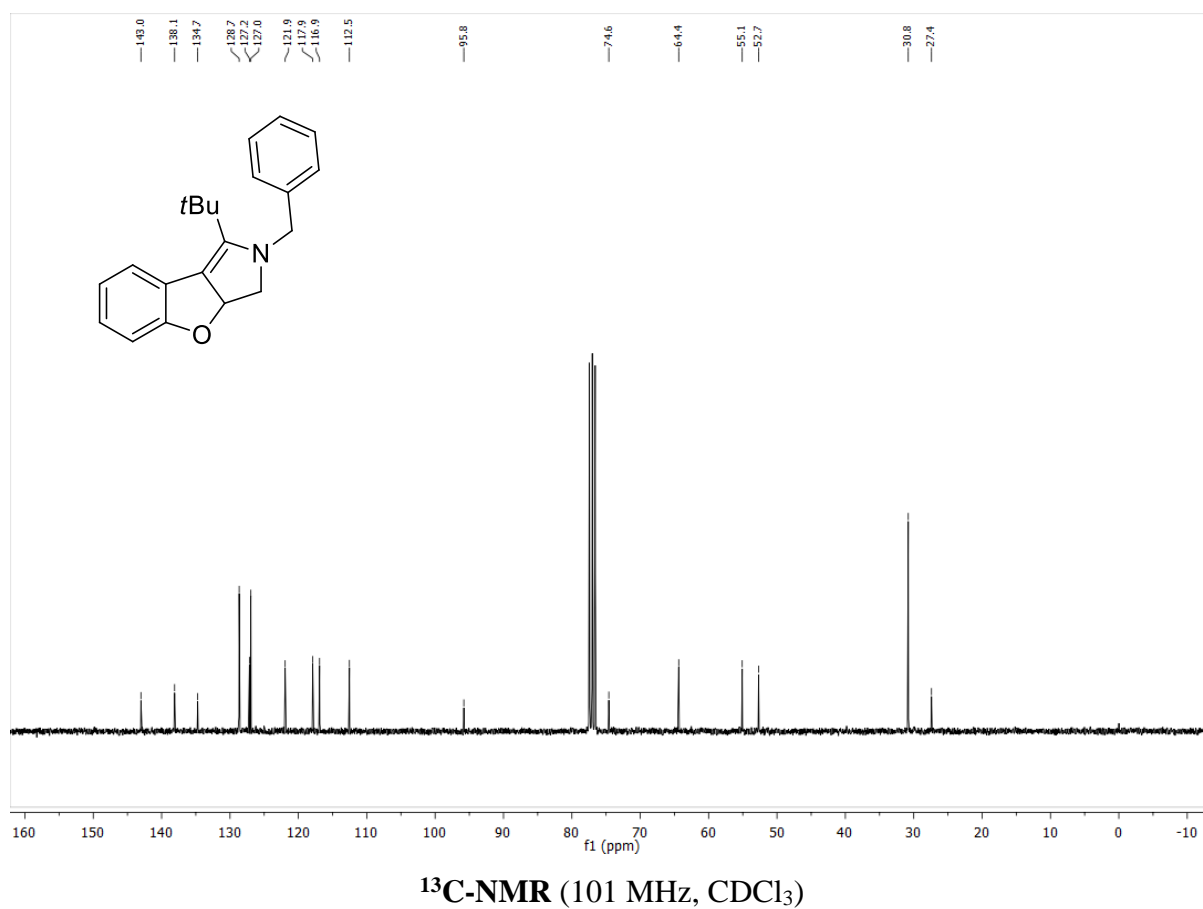
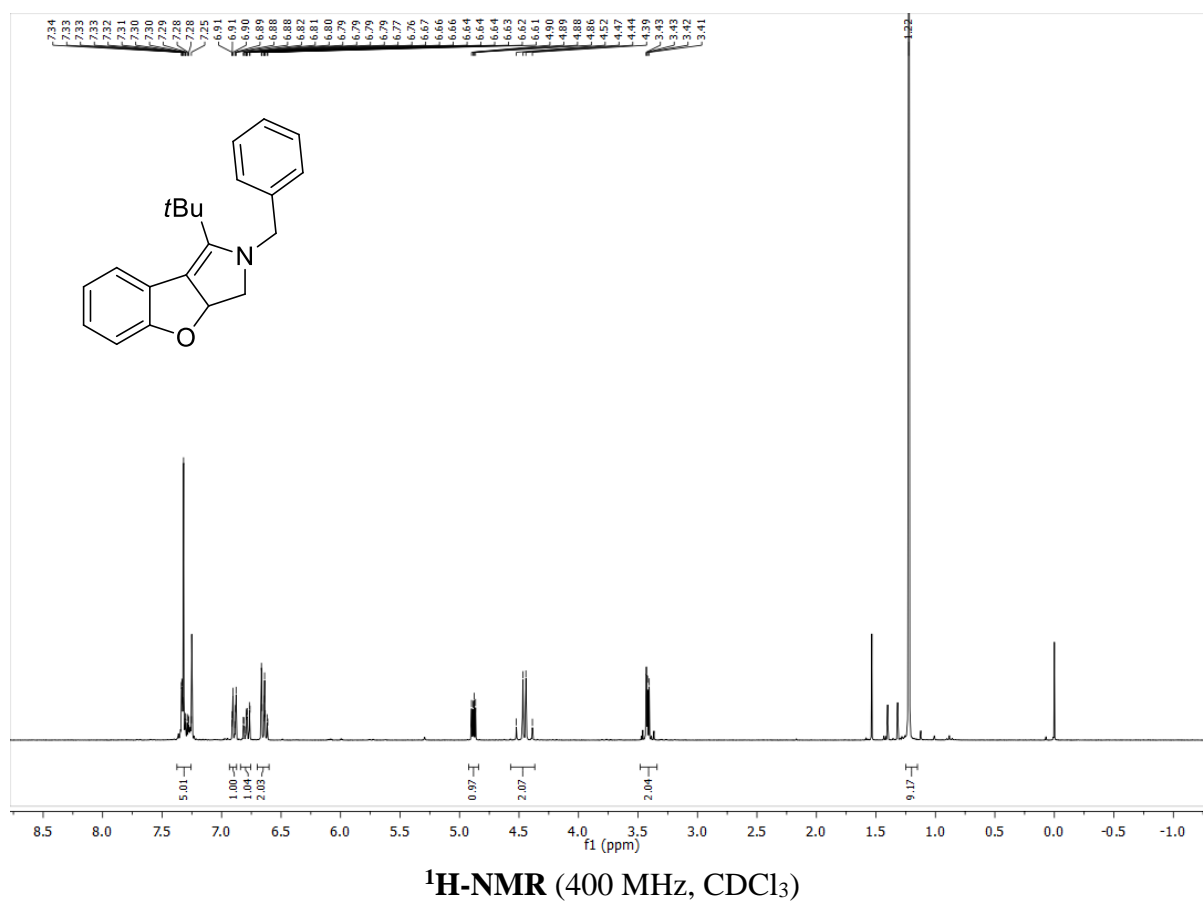
Analytical data for **4e**:

$^1\text{H-NMR}$ (300 MHz, CDCl_3): $\delta = 1.22$ (s, 9H), 3.34–3.48 (m, 2H), 4.37–4.57 (m, 2H), 4.88 (dd, $J = 6.6, 3.7$ Hz, 1H), 6.60–6.70 (m, 2H), 6.79 (ddd, $J = 8.2, 7.2, 1.6$ Hz, 1H), 6.89 (dd, $J = 8.1, 1.6$ Hz, 1H), 7.26–7.38 (m, 5H).

$^{13}\text{C-NMR}$ (76 MHz, CDCl_3) $\delta = 27.4, 30.8, 52.7, 55.1, 64.4, 74.6, 95.8, 112.5, 116.9, 117.9, 121.9, 127.0, 127.2, 128.7, 134.7, 138.1, 143.0$.

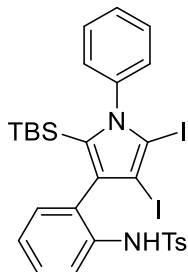
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2969 (m), 2926 (w), 2901 (w), 2866 (w), 1503 (s), 1357 (m), 1266 (m), 1212 (m), 1050 (w).

GC-HRMS (EI): $\text{C}_{21}\text{H}_{23}\text{NO}$ m/z calcd. $[\text{M}^+]$: 305.1780 found 305.1793.



8) Follow-up chemistry

N-(2-(2-(*tert*-Butyldimethylsilyl)-4,5-diiodo-1-phenyl-1*H*-pyrrol-3-yl)phenyl)-4-methylbenzenesulfonamide (**6**)



The pyrrole **5h** (13.2 mg, 26.3 μ mol) was dissolved in CH_2Cl_2 (500 μ L). NIS (12.0 mg, 53.3 μ mol) was added at 0 $^\circ\text{C}$ and the reaction mixture was stirred at ambient temperature overnight. To the reaction mixture was added silica gel and the solvent was evaporated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded compound **6** (15.6 mg, 20.7 μ mol, 79%) as colorless solid.

^1H -NMR (500 MHz, CH_2Cl_2): δ = -0.59 (s, 3H), -0.53 (s, 3H), 0.59 (s, 9H), 2.31 (s, 3H), 6.62 (s, 1H), 6.95 (td, J = 7.4, 1.1 Hz, 1H), 7.03 (dd, J = 7.5, 1.6 Hz, 1H), 7.18–7.28 (m, 5H), 7.39–7.46 (m, 4H), 7.73–7.78 (m, 2H).

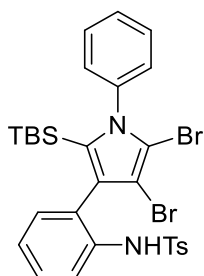
^{13}C -NMR (126 MHz, CH_2Cl_2) δ = 21.7, 28.0, 84.4, 93.2, 115.7, 122.5, 127.4, 128.0, 128.8, 129.0, 129.5, 130.1, 130.2, 130.8, 131.1, 133.7, 136.0, 136.8, 136.9, 137.0, 143.5, 144.7.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3256 (w), 2930 (w), 2854 (w), 1592 (w), 1385 (w), 1332 (m), 1253 (w), 1161 (m), 1090 (m).

M.p.: 210–212 $^\circ\text{C}$.

ESI-HRMS: $\text{C}_{29}\text{H}_{32}\text{I}_2\text{N}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 755.0116 found 755.0120.

***N*-(2-(4,5-Dibromo-2-(*tert*-butyldimethylsilyl)-1-phenyl-1*H*-pyrrol-3-yl)phenyl)-4-methylbenzenesulfonamide (7)**



The pyrrole **5h** (21.0 mg, 41.8 μ mol) was dissolved in CH_2Cl_2 (2.0 mL). NBS (24.0 mg, 135 μ mol) was added at 0 $^\circ\text{C}$ and the reaction mixture was stirred at ambient temperature overnight. To the reaction mixture was added silica gel and the solvent was evaporated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded compound **7** (25.1 mg, 38.0 μ mol, 91%) as colorless solid.

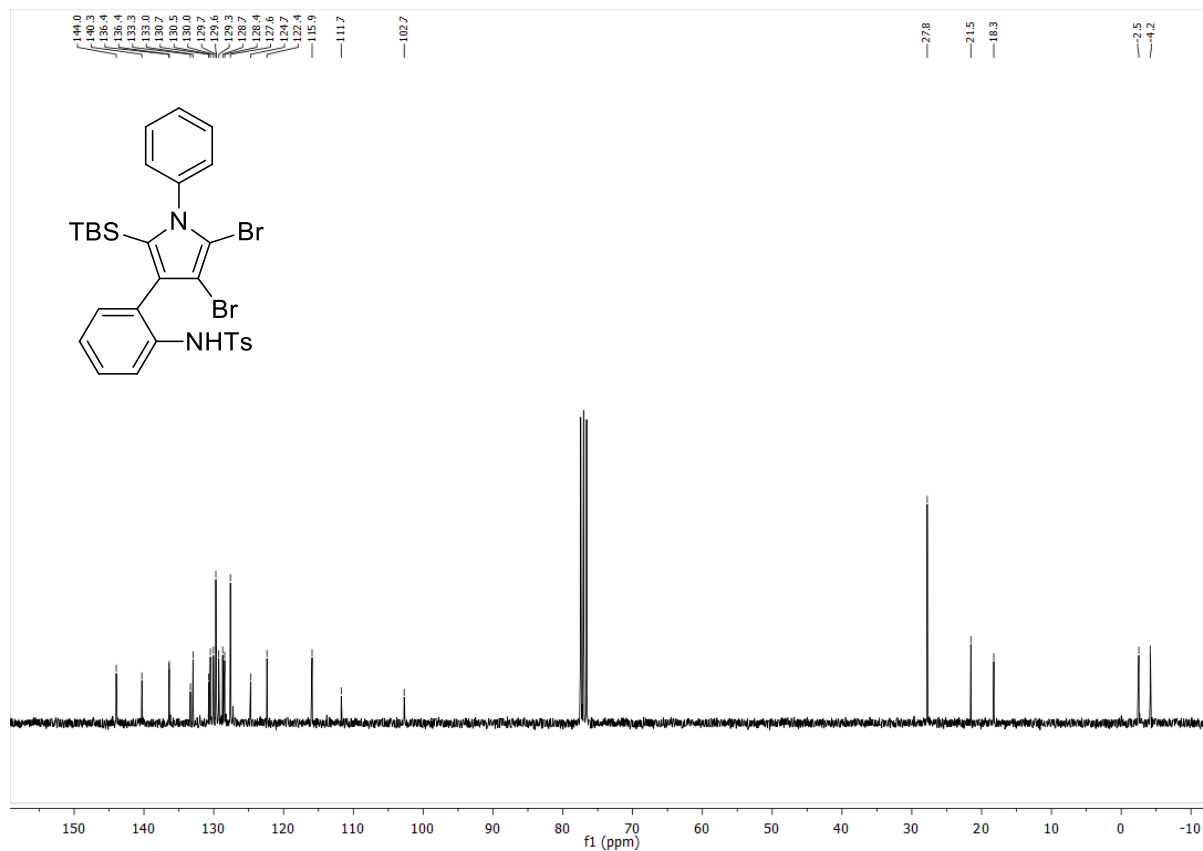
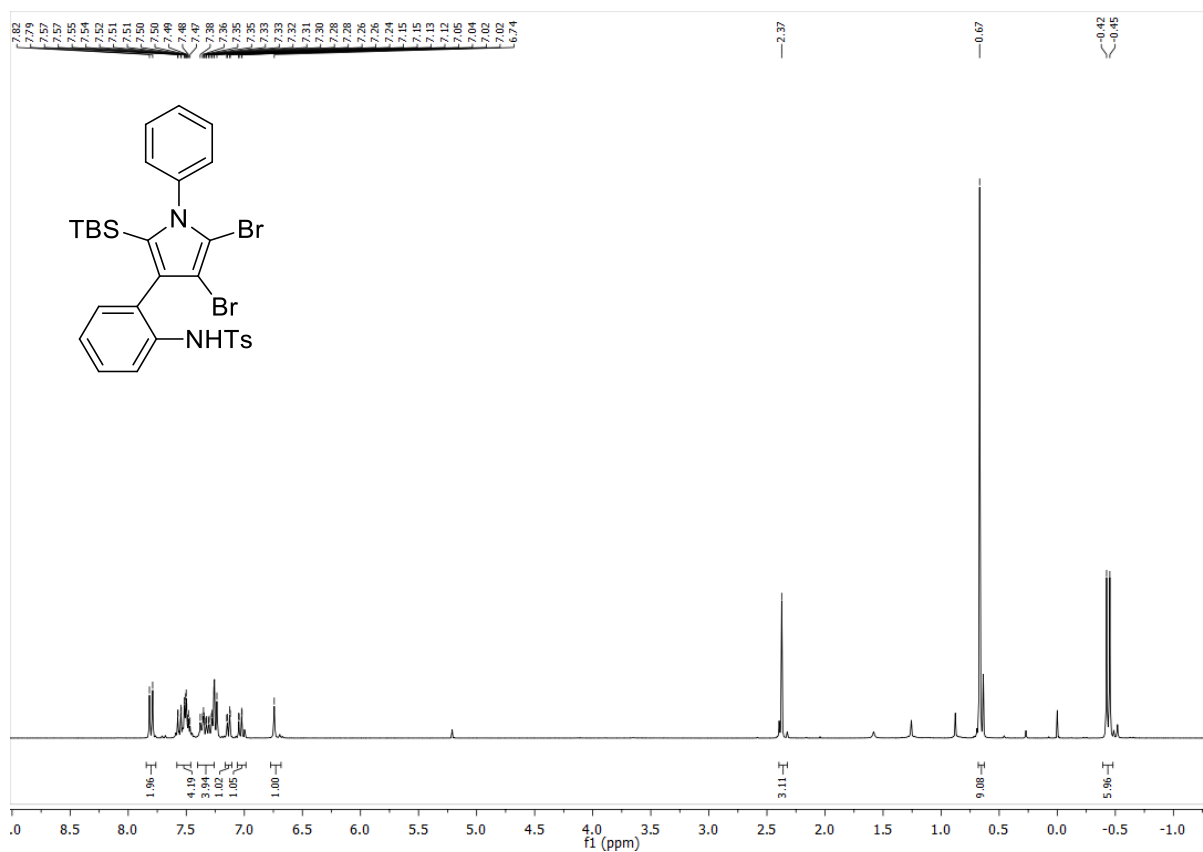
^1H -NMR (300 MHz, CDCl_3): δ = -0.44 (d, J = 8.4 Hz, 6H), 0.67 (s, 9H), 2.37 (s, 3H), 6.74 (s, 1H), 7.03 (dd, J = 7.5, 1.1 Hz, 1H), 7.14 (dd, J = 7.6, 1.6 Hz, 1H), 7.26–7.40 (m, 4H), 7.46–7.58 (m, 4H), 7.80 (d, J = 8.4 Hz, 2H).

^{13}C -NMR (75 MHz, CDCl_3) δ = -4.2, -2.5, 18.3, 21.5, 27.8, 102.7, 111.7, 115.9, 122.4, 124.7, 127.6, 128.4, 128.7, 129.3, 129.6, 129.7, 130.0, 130.5, 130.7, 133.0, 133.3, 136.4, 136.4, 140.3, 144.0.

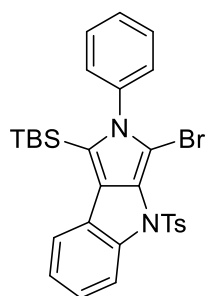
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3257 (m), 2956 (w), 2929 (w), 2893 (w), 2854 (w), 1493 (m), 1387 (m), 1333 (m), 1162 (s), 1089 (m).

M.p.: 220–222 $^\circ\text{C}$.

ESI-HRMS: $\text{C}_{29}\text{H}_{32}\text{Br}_2\text{N}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 659.0393 found 659.0400.



1-(*tert*-Butyldimethylsilyl)-2-phenyl-4-tosyl-2,4-dihydropyrrolo[3,4-*b*]indole (8)



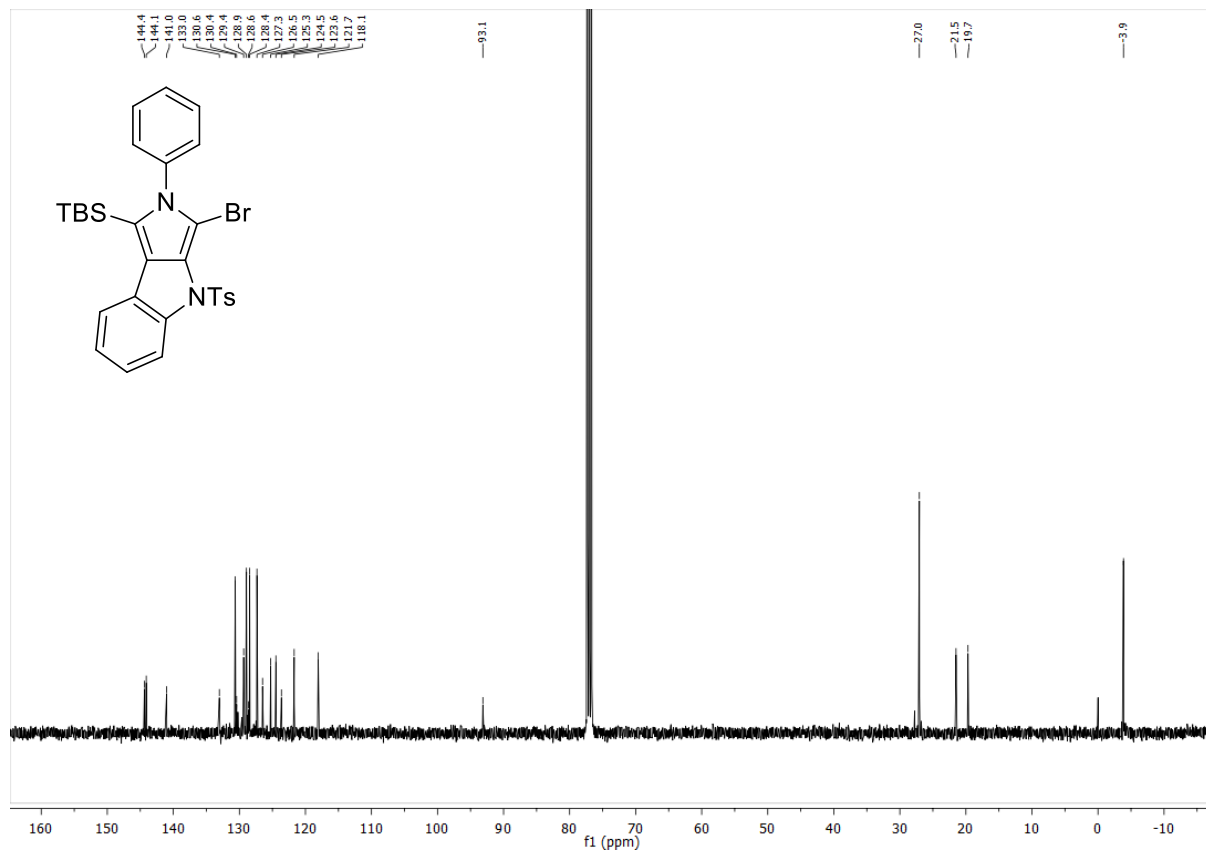
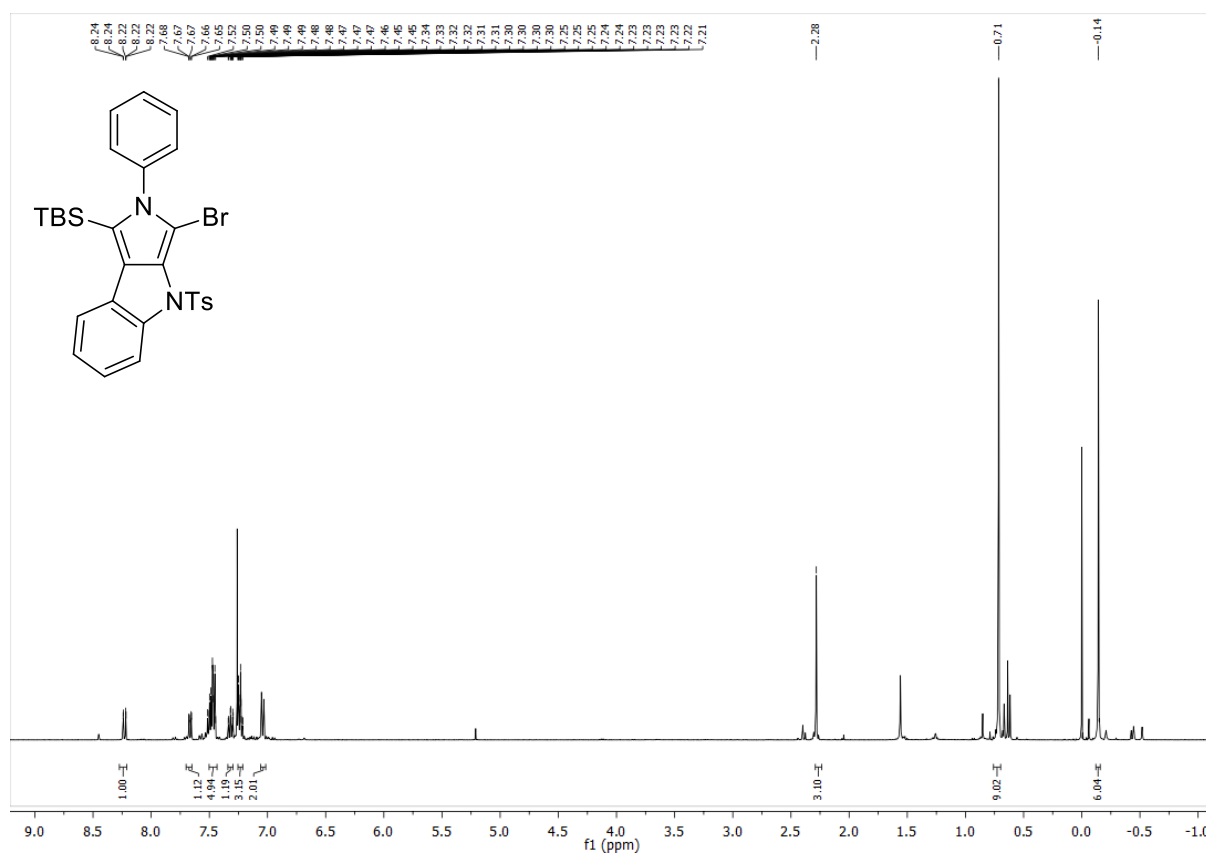
The bromide **7** (20 mg, 30.3 μmol) was diluted in DMF (1.0 mL). Afterwards triethylamine (1.0 mL), PPh_3 (2.1 mg, 8.0 μmol), and $\text{PdCl}_2(\text{PPh}_3)_2$ (5.6 mg, 8.0 μmol) were added. The mixture was stirred 16 h at 70 $^\circ\text{C}$. After cooling to rt, sat. NH_4Cl solution was added and the mixture was extracted with EtOAc (3 \times). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded domino product **8** (11.3 mg, 19.5 μmol , 64%) as yellow oil.

^1H -NMR (400 MHz, CDCl_3): δ = -0.14 (s, 6H), 0.71 (s, 9H), 2.28 (s, 3H), 7.02–7.06 (m, 2H), 7.21–7.25 (m, 3H), 7.30–7.34 (m, 1H), 7.43–7.50 (m, 5H), 7.65–7.70 (m, 1H), 8.21–8.27 (m, 1H).

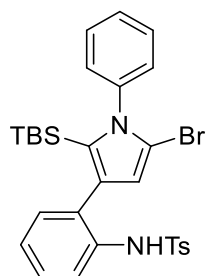
^{13}C -NMR (101 MHz, CDCl_3) δ = -3.9, 19.7, 21.5, 27.0, 93.1, 118.1, 121.7, 123.6, 124.5, 125.3, 126.5, 127.3, 128.4, 128.6, 128.9, 129.4, 130.4, 130.6, 133.0, 141.0, 144.1, 144.4.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 2931 (w), 2890 (w), 2856 (w), 1597 (w), 1493 (w), 1461 (w), 1369 (m), 1253 (w), 1176 (m), 1090 (w).

ESI-HRMS: $\text{C}_{29}\text{H}_{31}\text{BrN}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 579.1132 found 579.1135.



***N*-(2-(5-Bromo-2-(*tert*-butyldimethylsilyl)-1-phenyl-1*H*-pyrrol-3-yl)phenyl)-4-methylbenzenesulfonamide (9)**



The pyrrole **5h** (24.7 mg, 49.1 μ mol) was dissolved in CH_2Cl_2 (2.0 mL). NBS (9.5 mg, 53.3 μ mol) was added at 0 $^\circ\text{C}$ and the reaction mixture was stirred at ambient temperature overnight. To the reaction mixture was added silica gel and the solvent was evaporated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:20) afforded compound **8** (23.6 mg, 40.6 μ mol, 83%) as colorless solid.

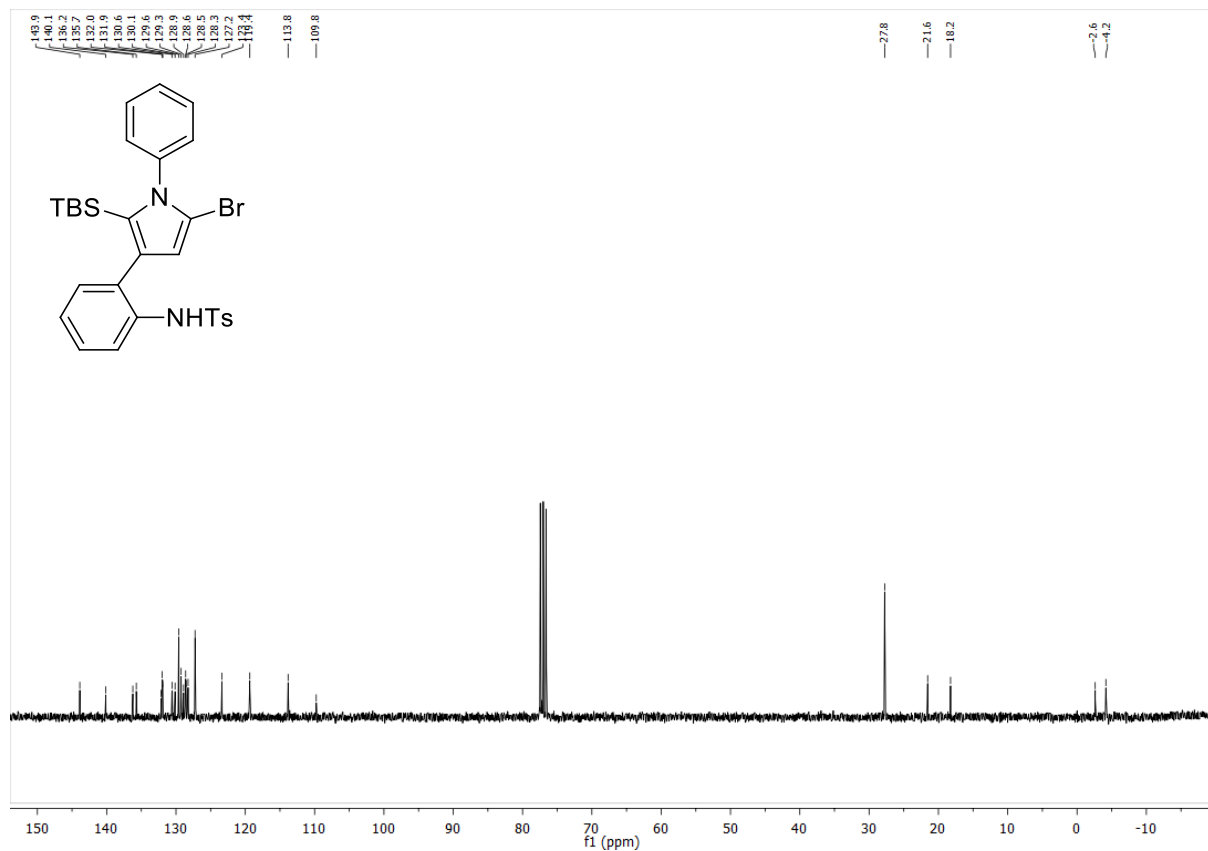
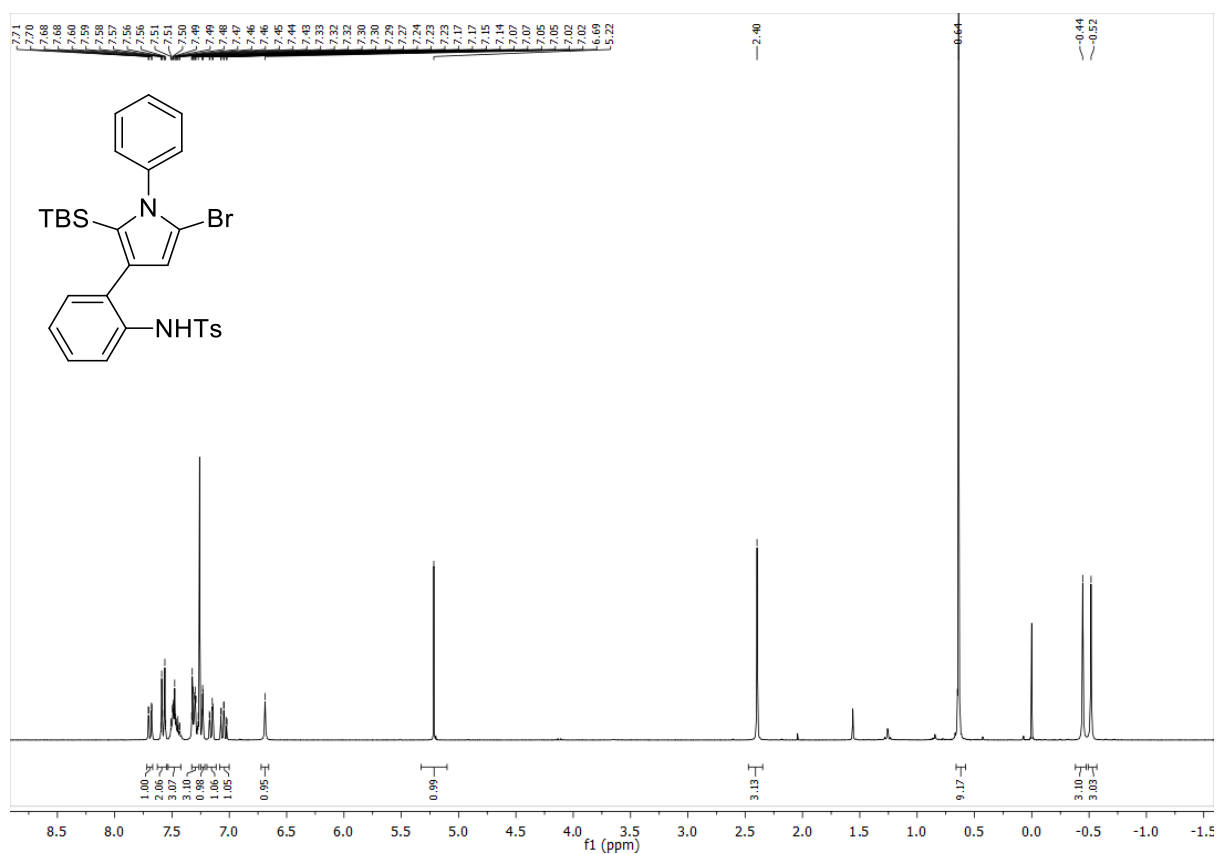
^1H -NMR (300 MHz, CDCl_3): δ = -0.52 (s, 3H), -0.44 (s, 3H), 0.64 (s, 9H), 2.40 (s, 3H), 5.22 (s, 1H), 6.69 (s, 1H), 7.05 (td, J = 7.4, 1.2 Hz, 1H), 7.16 (dd, J = 7.6, 1.6 Hz, 1H), 7.21–7.25 (m, 1H), 7.26–7.33 (m, 3H), 7.42–7.53 (m, 3H), 7.55–7.63 (m, 2H), 7.69 (dd, J = 8.2, 1.2 Hz, 1H).

^{13}C -NMR (76 MHz, CDCl_3) δ = -4.2, -2.6, 18.2, 21.6, 27.8, 109.8, 113.8, 119.4, 123.4, 127.2, 128.3, 128.5, 128.6, 128.9, 129.3, 129.6, 130.1, 130.6, 131.9, 132.0, 132.1, 135.7, 136.2, 140.1, 143.9.

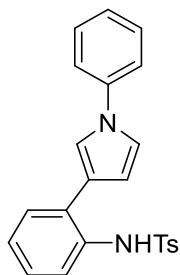
IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3298 (w), 2932 (w), 2891 (w), 2855 (w), 1490 (w), 1379 (m), 1332 (m), 1163 (s), 1091 (m).

M.p.: 190–192 $^\circ\text{C}$.

ESI-HRMS: $\text{C}_{29}\text{H}_{33}\text{BrN}_2\text{O}_2\text{SSi}$ m/z calcd. $[\text{M}+\text{H}^+]$: 581.1288 found 581.1294.



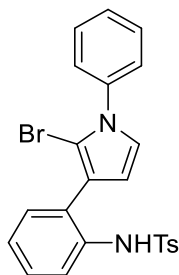
4-Methyl-*N*-(2-(1-phenyl-1*H*-pyrrol-3-yl)phenyl)benzenesulfonamide (5g)



The pyrrole **5h** (24.4 mg, 48.5 μmol) was dissolved in CH_2Cl_2 (5.0 mL). At 0 $^\circ\text{C}$, acetyl chloride (1 drop) and aluminium trichloride (8.0 mg, 60.0 μmol) were added and the reaction mixture was stirred at ambient temperature for 1h. To the reaction mixture was added water and the aqueous layer was extracted with EtOAc (3 \times). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded compound **5g** (15.7 mg, 36.5 μmol , 75%) as colorless solid.

For analytical data see page S80.

***N*-(2-(2-Bromo-1-phenyl-1*H*-pyrrol-3-yl)phenyl)-4-methylbenzenesulfonamide (10)**



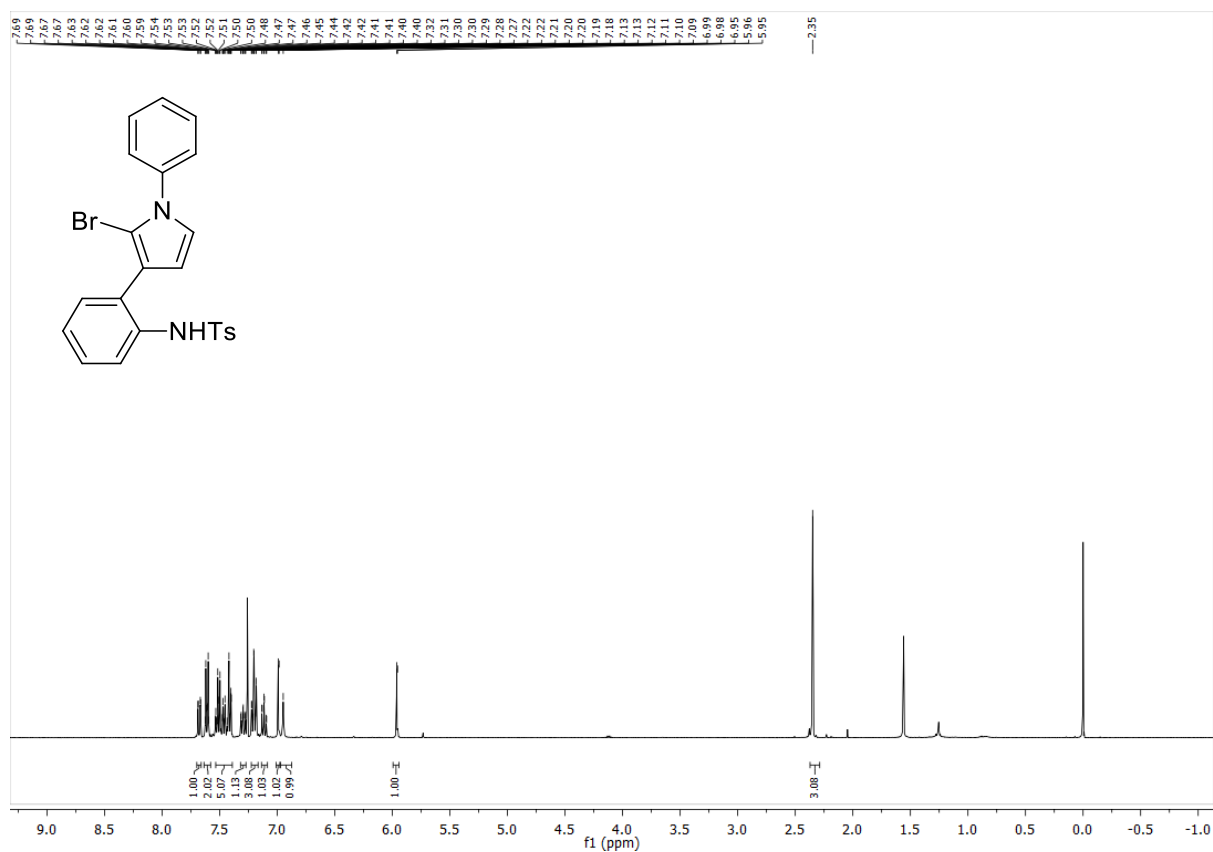
The pyrrole **5g** (13.0 mg, 33.5 μmol) was dissolved in CH_2Cl_2 (1.0 mL). At 0 $^\circ\text{C}$, NBS (6.2 mg, 34.8 μmol) was added and the reaction mixture was stirred at 0 $^\circ\text{C}$ for 1 h. To the reaction mixture was added silica gel and the solvent was evaporated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded compound **10** (9.3 mg, 19.9 μmol , 59%) as colorless oil.

^1H -NMR (400 MHz, CDCl_3): δ = 2.35 (s, 3H), 5.96 (d, J = 3.1 Hz, 1H), 6.95 (s, 1H), 6.99 (d, J = 3.1 Hz, 1H), 7.11 (td, J = 7.5, 1.2 Hz, 1H), 7.20 (td, J = 7.7, 1.8 Hz, 3H), 7.27–7.32 (m, 1H), 7.39–7.53 (m, 5H), 7.58–7.64 (m, 2H), 7.68 (dd, J = 8.3, 1.3 Hz, 1H).

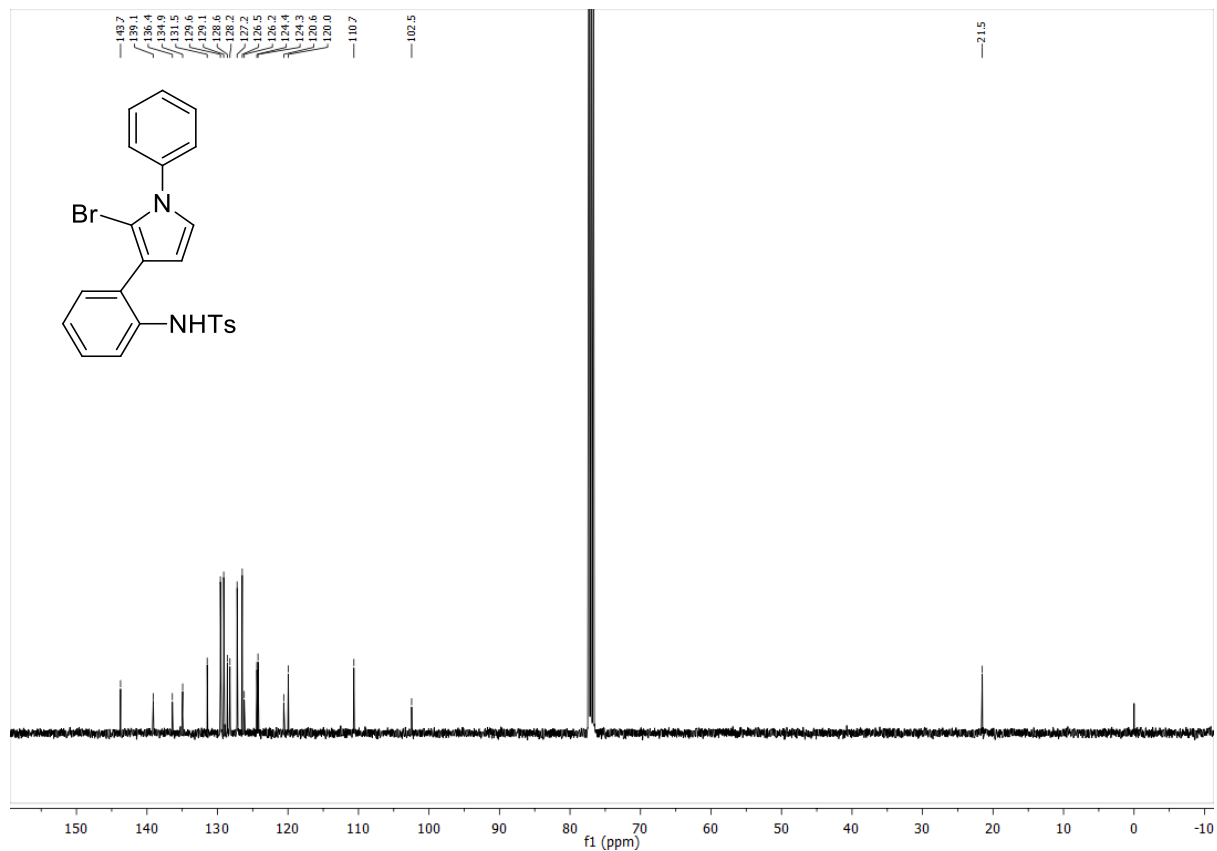
^{13}C -NMR (101 MHz, CDCl_3) δ = 21.5, 102.5, 110.7, 120.0, 120.6, 124.3, 124.4, 126.2, 126.5, 127.2, 128.2, 128.6, 129.1, 129.6, 131.5, 134.9, 136.4, 139.1, 143.7.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3331 (w), 2922 (w), 2857 (w), 1594 (w), 1497 (m), 1398 (m), 1334 (m), 1160 (s), 1088 (m).

ESI-HRMS: $\text{C}_{23}\text{H}_{19}\text{BrN}_2\text{O}_2\text{S}$ m/z calcd. $[\text{M}+\text{Na}^+]$: 489.0243 Found 489.0244.

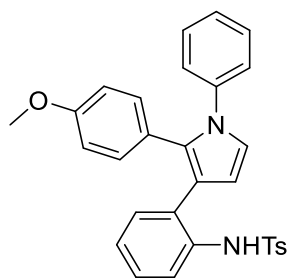


¹H-NMR (400 MHz, CDCl₃)



¹³C-NMR (101 MHz, CDCl₃)

***N*-(2-(2-(4-Methoxyphenyl)-1-phenyl-1*H*-pyrrol-3-yl)phenyl)-4-methylbenzenesulfonamide (11)**



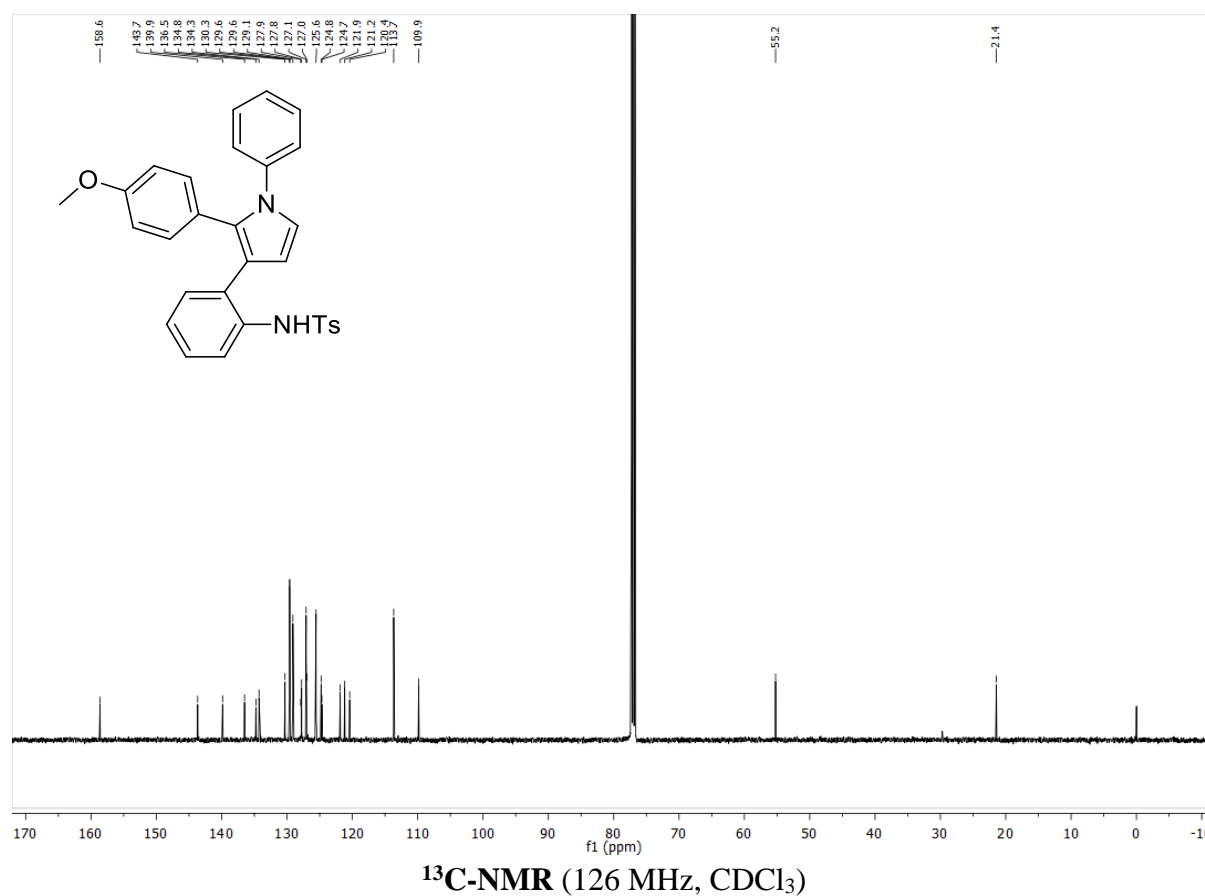
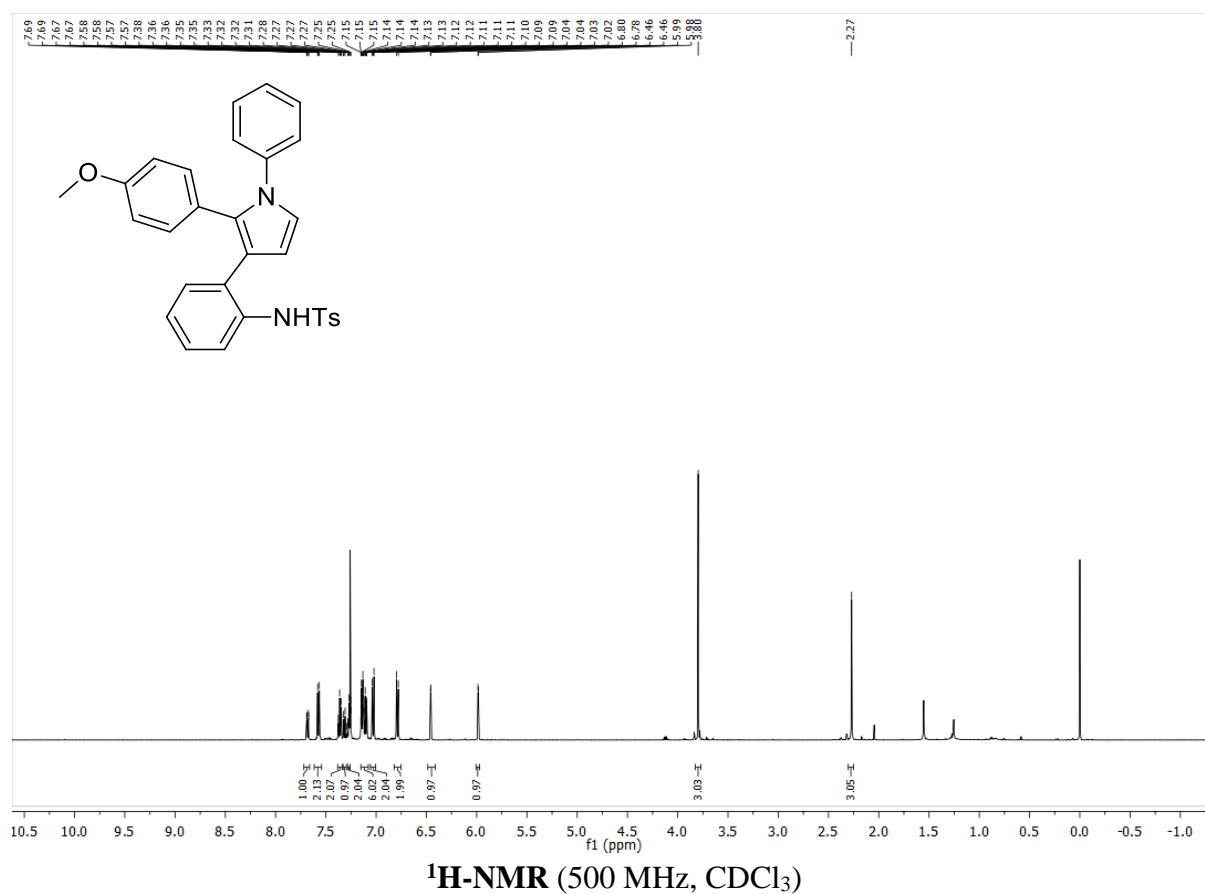
The pyrrole **5h** (24.9 mg, 49.5 μ mol) was dissolved in CH_2Cl_2 (2.0 mL). At 0 $^\circ\text{C}$, BCl_3 (1M in hexane, 60 μL , 60.0 μ mol) was added and the reaction mixture was stirred 30 minutes at 0 $^\circ\text{C}$. Afterwards the solvent was evaporated *in vacuo*. After drying under high vacuum for 30 minutes, the residue was dissolved in DME (2.0 mL). 4-Iodoanisole (37.7 mg, 161 μ mol), $\text{Pd}(\text{PPh}_3)_4$ (8.0 mg, 6.92 μ mol, 14 mol-%), and Na_2CO_3 -solution (2 M, 500 μL) were added. The reaction mixture was refluxed for 4h. After cooling to rt, sat. NH_4Cl solution was added. The aqueous layer was extracted with EtOAc (3 \times). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. Silica gel column chromatography (EtOAc:*n*-pentane = 1:10) afforded compound **11** (7.0 mg, 14.2 μ mol, 29% over two steps) as yellow oil.

^1H -NMR (500 MHz, CDCl_3): δ = 2.27 (s, 3H), 3.80 (s, 3H), 5.99 (d, J = 2.1 Hz, 1H), 6.46 (d, J = 1.9 Hz, 1H), 6.79 (d, J = 8.8 Hz, 2H), 7.00–7.06 (m, 2H), 7.08–7.15 (m, 6H), 7.26–7.28 (m, 2H), 7.30–7.33 (m, 1H), 7.34–7.38 (m, 2H), 7.54–7.62 (m, 2H), 7.68 (dd, J = 8.7, 1.3 Hz, 1H).

^{13}C -NMR (126 MHz, CDCl_3) δ = 21.4, 55.2, 109.9, 113.7, 120.4, 121.2, 121.9, 124.7, 124.8, 125.6, 127.0, 127.1, 127.8, 127.9, 129.1, 129.6, 129.6, 130.3, 134.3, 134.8, 136.5, 139.9, 143.7, 158.6.

IR (ATR): $\tilde{\nu}$ (cm^{-1}) = 3323 (w), 2957 (w), 2922 (w), 2836 (w), 1597 (m), 1493 (s), 1336 (m), 1248 (m), 1165 (s), 1092 (m).

ESI-HRMS: $\text{C}_{30}\text{H}_{26}\text{N}_2\text{O}_3\text{S}$ m/z calcd. $[\text{M}+\text{H}^+]$: 495.1737 found 495.1738.



9) Crystal Structure Determination of Compound 3f

A pale brown tablet-shaped crystal was mounted in inert oil on a glass fibre and transferred to the cold gas stream of an Oxford "Xcalibur E" diffractometer. Mo K α radiation was employed for the intensity measurements. An absorption correction was implemented on the basis of multi-scans. The structure was refined anisotropically on F^2 using the program SHELXL-2017.⁵ Hydrogen atoms were included using rigid methyl groups or a riding model starting from calculated positions.

Crystallographic data are summarized in Table S1. Additionally, complete data have been deposited with the Cambridge Crystallographic Data Centre under the number CCDC 1958050. Copies of the data can be obtained free of charge from www.ccdc.cam.ac.uk/data_request/cif.

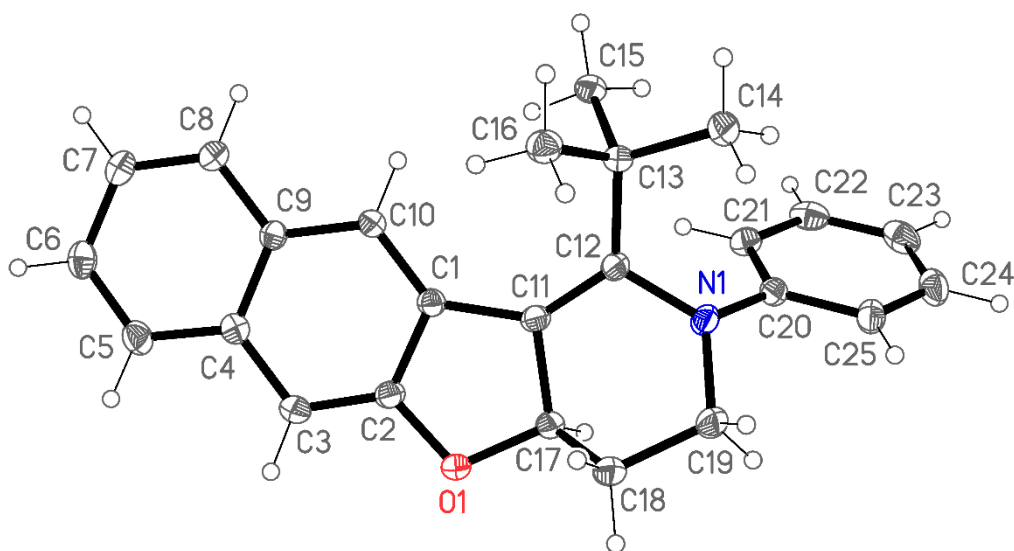


Figure S1. The structure of compound **3f** in the crystal. Ellipsoids represent 50% probability levels.

Table S1: Crystallographic data and structure refinement details.

Compound	3f
Formula	C ₂₅ H ₂₅ NO
M_r	355.46
Cryst. size (mm)	0.45 x 0.35 x 0.2
Crystal system	triclinic
Space group	$P(-1)$
Temperature (°C)	−163
a (Å)	8.3325(5)
b (Å)	9.7944(5)
c (Å)	12.6679(5)
α (°)	68.278(5)
β (°)	78.444(5)
γ (°)	86.722(5)
V (Å ³)	940.80
Z	2
D_x (Mg m ^{−3})	1.255
λ (Å)	0.71073
μ (mm ^{−1})	0.08
Transmissions	0.965 – 1.000
$F(000)$	380
$2\theta_{\max}$ (°)	60
Refl. measured	47793
Refl. indep.	5408
R_{int}	0.035
Parameters	247
$wR(F^2, \text{all refl.})$	0.123
$R(F, >4\sigma(F))$	0.046
S	1.03
Max. $\Delta\rho$ (e Å ^{−3})	0.40 / − 0.23

10) References

- [1] Schitter, T.; Jones, P. G.; Werz, D. B. *Chem. Eur. J.* **2018**, *24*, 13446.
- [2] The alcohol **14** was prepared by using a previously reported protocol (Schitter, T.; Jones, P. G.; Werz, D. B. *Chem. Eur. J.* **2018**, *24*, 13446.)
- [3] Schitter, T.; Roy, N. J.; Jones, P. G.; Werz, D. B. *Org. Lett.* **2019**, *21*, 640.
- [4] The alcohol **24** was prepared by using a previously reported protocol (Schitter, T.; Roy, N. J.; Jones, P. G.; Werz, D. B. *Org. Lett.* **2019**, *21*, 640.)
- [5] Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3.