Gold-catalyzed allene cycloisomerization for pyrrole synthesis: towards highly fluorinated BODIPY dyes

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Electronic Supplementary Information

Contents

1. General Information

All reactions were carried out under argon atmosphere in dried glassware. For air and moisture sensitive liquids syringes and septa were used. Solids were added in argon reverse flow. All reactions were performed in dry solvents, which were dried with the *MB-SPS-800* solvent system from *M. Braun*.

Chemicals were purchased from *ABCR*, *Acros Organics*, *Sigma Aldrich*, *Fluorochem* and *TCI*. They were directly used, if not otherwise noted. The ionic liquids were stirred at 80 °C in *vacuo* to remove gases or water. Ionic liquids and gold catalysts were ordered from the following suppliers:

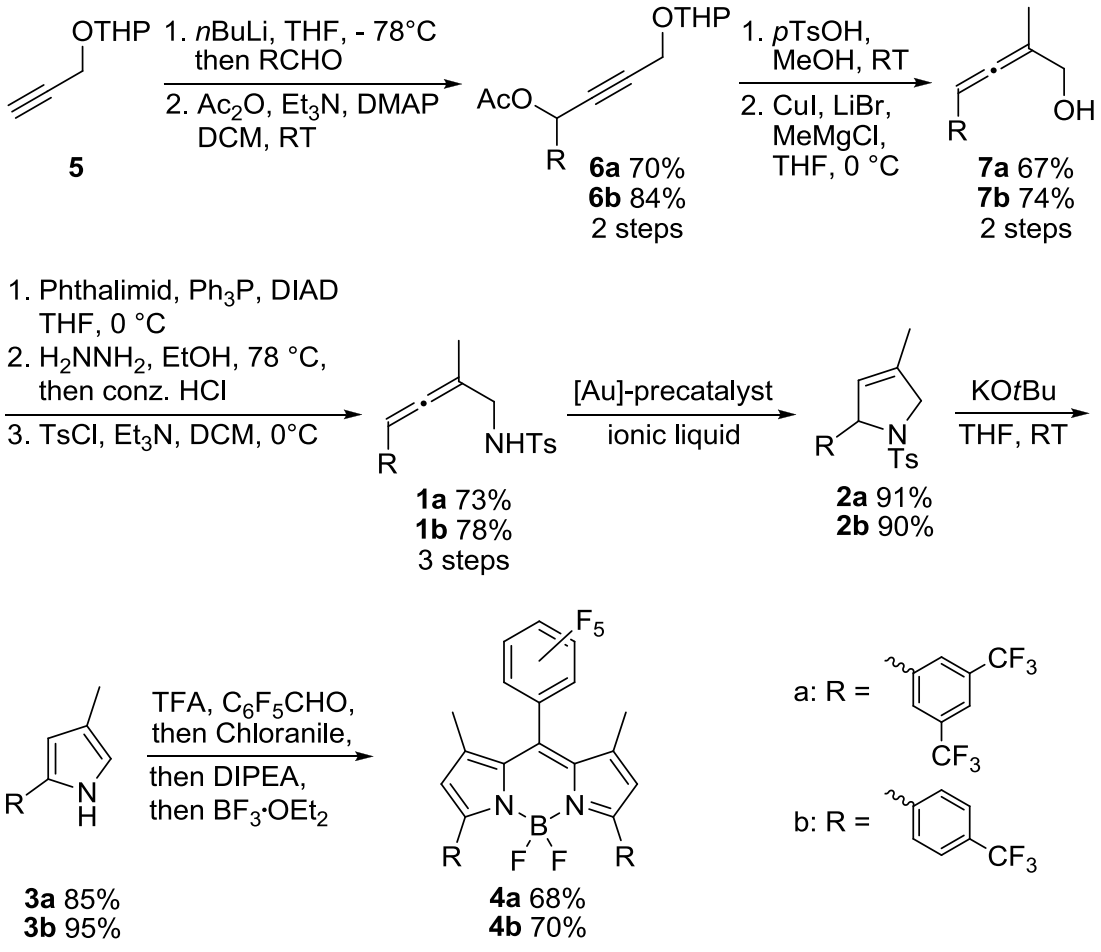
[BMIM][PF_6], [BMIM][BF_4], [BMIM][HSO_4], [EMIM][HSO_4]: Sigma Aldrich;

[EMIM][BF_4]: Alfa Aesar;

JohnPhosAu(MeCN)SbF_6, JohnPhosAuCl, Ph_3PAuCl, $Ph_3PAuNTf_2$: Sigma Aldrich;

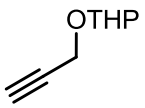
$AuBr_3$: Alfa Aesar; $AgSbF_6$: *Fluorochem*

2. Synthesis stragety



3. Synthesis of α-Aminoallenes

2-(2-Propynyloxy)-tetrahydro-2H-pyran (5)



A mixture of 6.0 ml (103.82 mmol) freshly distilled propargyl alcohol, 12.1 ml (134.96 mmol) DHP and 215 mg (1.04 mmol, 1 mol%) *p*-TsOH·H_2O were stirred for 1 h at 0 °C. The reaction mixture was directly purified by silica gel column chromatography (pentane:Et_2O, 30:1) to give 12.16 g (86.76 mmol, 84%) of **1** as a colorless clear oil (97% in Et_2O/pentane).

^{1}H-NMR (300.1 MHz, $CDCl_3$): δ (ppm) = 4.81 (t, J = 3.4 Hz, 1H), 4.25 (ddd, J = 27.4, 15.7, 2.4 Hz, 2 H), 3.83 (m, 1 H), 3.54 (m, 1 H), 2.40 (t, *J* = 2.4 Hz, 1 H), 1.87-1.79 (m, 2H), 1.63-1.52 (m,4 H).

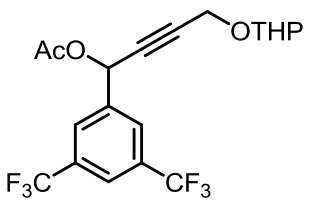
^{13}C-NMR (75.5 MHz, $CDCl_3$): δ (ppm) = 96.8, 79.7, 74.0, 61.9, 53.9, 30.2, 25.3, 19.0.

Known compound.[S1]

Synthesis of propargylic acetates (6)

n-BuLi (1.2 eq, 2.5 M in hexane) was slowly added to a stirred solution of alkine **5** (1 eq) in THF (1.3 ml/mmol) at –78 °C. After 30 min the aldehyde was dropped into the solution and stirred for 1 h. The mixture was allowed to warm up to –10 °C during this time. It was hydrolyzed and washed two times with sat. aq. NH_4Cl. The aqueous layers were extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was directly used in the acetylation reaction. For this purpose, it was dissolved in DCM (10 ml/mmol) before Ac_2O (1.2 eq), Et_3N (1.5 eq) and a catalytic amount of DMAP were added at RT. The solution was stirred for 16 h and successively washed with sat. aq. NH_4Cl and sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified via silica gel column chromatography (cyclohexane:EtOAc, 15:1 to 10:1).

1-(3,5-Bis-(trifluoromethyl)phenyl)-4-(tetrahydro-2H-pyran-2-yloxy)but-2-ynyl acetate (6a)



The reaction was carried out using 41 ml THF, 4.50 g (31.46 mmol, 97% purity) of alkine **5**, 15.1 ml (37.75 mmol) *n*-BuLi solution and 5.2 ml (31.46 mmol) of 3,5-bis(trifluoromethyl)-benzaldehyde. The acetylation was performed in 315 ml DCM with 3.6 ml (37.75 mmol) Ac_2O, 6.5 ml (47.15 mmol) Et_3N and a catalytic amount DMAP. After column chromatography 9.4 g (22.15 mmol, 70%) of the product **6a** were obtained as colorless oil.

^{1}H-NMR (300.1 MHz, $CDCl_3$): δ (ppm) = 7.96 (s, 2 H), 7.87 (s, 1 H), 6.57 (m, 1H), 4.78 (m, 1 H), 4.35 (m, 2 H), 3.82 (m, 1 H), 3.52 (m, 1 H), 2.15 (s, 3 H), 1.83-1.72 (m, 2 H), 1.65-1.53 (m, 4 H).

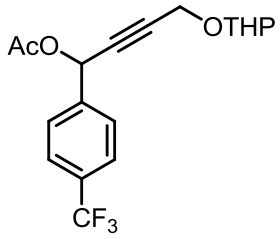
^{13}C-NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 169.4, 139.5, 132.1 (q, J_{CF} = 33.6 Hz), 127.9, 123.0 (q, J_{CF} = 272.8 Hz), 122.9 (m), 97.1, 85.1, 80.8/80.8*, 64.2, 62.0/62.0*, 54.1/54.0*, 30.1, 25.2, 20.9, 18.9/18.9*.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –62.1.

HR-MS (ESI): $C_{19}H_{18}O_4F_6$ (424.33), calculated: 447.10015 $[M+Na]^+$, found: 447.09961.

IR: ν (cm^{-1}) = 2942 (m, C–H), 2873 (w, C–H), 1747 (s, C=O), 1627 (w).

4-(Tetrahydro-2H-pyran-2-yloxy)-1-(4-(trifluoromethyl)phenyl)but-2-ynyl acetate (6b)



The reaction was carried out using 38 ml THF, 4.18 g (28.89 mmol, 97% purity) of alkine **5**, 13.9 ml (34.67 mmol) *n*-BuLi solution and 4.0 ml (28.89 mmol) of 4-(trifluoromethyl)-benzaldehyde. The acetylation was performed in 290 ml DCM with 3.3 ml (34.67 mmol) Ac_2O, 5.9 ml (43.34 mmol) Et_3N and a catalytic amount DMAP. After column chromatography 8.61 g (24.16 mmol, 84%) of the product **6b** were obtained as colourless oil.

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ (ppm) = 7.63 (s, 4 H), 6.54 (s, 1 H), 4.79 (q, J = 3.1 Hz, 1 H), 4.33 (m, 2 H), 3.82 (m, 1 H), 3.52 (m, 1 H), 2.11 (s, 3 H), 1.83-1.69 (m, 2 H), 1.64-1.52 (m, 4 H).

^{13}C-NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 169.5, 140.7, 131.0 (q, J_{CF} = 32.4 Hz), 127.9, 125.6 (q, J_{CF} = 3.7 Hz), 123.8 (q, J_{CF} = 272.3 Hz), 97.0/96.9*, 84.2, 81.6/81.6*, 64.8, 62.0/61.9*, 54.1/54.1*, 30.1, 25.3, 20.9, 18.9/18.9*.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –61.9.

HR-MS (ESI): $C_{18}H_{20}O_4F_3$ (356.34), calculated: 357.13082 $[M+H]^+$, found: 357.13054.

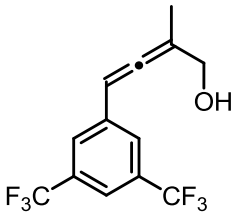
IR: ν (cm^{-1}) = 2923 (m, C–H), 2852 (w, C–H), 1738 (s, C=O).

Synthesis of *α*-hydroxyallenes (7)

The corresponding propargylic acetate **6** was dissolved in MeOH (1.2 ml/mmol) and 5 mol% *p*-TsOH·H_2O were added. The mixture was stirred for 3 h at RT, diluted with Et_2O and washed with sat. aq. $NaHCO_3$. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was directly used in the cupper mediated S_N'-reduction. For this purpose, a mixture of CuI (2 eq) and LiBr (2 eq) in THF (8 ml/mmol) was cooled to 0 °C before MeMgCl (3 eq, 3M in THF) was added. The mixture was stirred for 30 min at the

same temperature. The crude product was dissolved in a small amount of THF and dropped into the cuprate-mixture. After 1 h sat. aq. NH_4Cl (0.2 ml/mmol) was added and the solid filtered. The organic layer was washed with sat. aq. $NaHCO_3$ for several times, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified via silica gel column chromatography (cyclohexane:EtOAc, 10:1 to 4:1).

4-(3,5-Bis(trifluoromethyl)phenyl)-2-methylbuta-2,3-dien-1-ol (7a)



For the THP cleavage 26 ml MeOH, 9.32 g (21.96 mmol) of **6a** and 209 mg (1.10 mmol) *p*-TsOH·H_2O were used. The S_N'-reduction was performed in 180 ml THF with 8.36 g (43.92 mmol) CuI, 3.81 g (43.92 mmol) LiBr and 22.0 ml (65.88 mmol) MeMgCl. After column chromatography 4.33 g (14.62 mmol, 67%) of the product **7a** were obtained as pale yellow solid.

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ (ppm) = 7.68 (s, 1 H), 7.67 (s, 2 H), 6.33 (m, 1 H), 4.22 (ddd, J = 2.8 Hz, 13.3, 11.5 Hz, 2 H), 1.89 (d, J = 2.8 Hz, 3 H), 1.56 (s, 1 H).

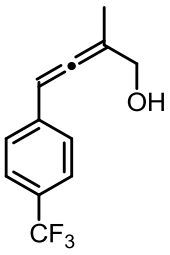
^{13}C-NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 202.1, 137.5, 131.9 (q, J_{CF} = 33,3 Hz), 126.4 (q, J_{CF} = 2,7 Hz), 123.3 (q, J_{CF} = 272,7 Hz), 120.4, 106.6, 95.1, 63.6, 15.2.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –62.2.

HR-MS (ESI): $C_{13}H_{10}F_6O$ (296.21), calculated: 297.07086 $[M+H]^+$, found: 297.07010.

IR: ν (cm^{-1}) = 3318 (br, OH), 2923 (w, C–H), 2869 (w, C–H), 1958 (w, C=C=C), 1738 (w), 1619 (w).

2-Methyl-4-(4-(trifluoromethyl)phenyl)buta-2,3-dien-1-ol (7b)



For the THP cleavage 29 ml MeOH, 8.60 g (24.13 mmol) of **6b** and 230 mg (1.21 mmol) *p*-TsOH·H_2O were used. The S_N'-reduction was performed in 180 ml THF with 9.19 g (48.26 mmol) CuI, 4.19 g (48.26 mmol) LiBr and 24.1 ml (72.39 mmol) MeMgCl. After column chromatography 4.09 g (17.92 mmol, 74%) of the product **7b** were obtained as white solid.

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ (ppm) = 7.54 (d, J = 8.1 Hz, 2 H), 7.37 (d, J = 8.1 Hz, 2 H), 6.29 (m, 1 H), 4.19 (ddd, J = 13.2 Hz, 7.5 Hz, 2.8 Hz, 2 H), 1.87 (d, J = 2.8 Hz, 3 H), 1.56 (s, 1 H).

^{13}C-NMR (75.5 MHz, $CDCl_3$): δ (ppm) = 202.0, 138.7, 128.8 (q, J_{CF} = 32,3 Hz), 126.8, 125.5 (q, J_{CF} = 3,8 Hz), 120.6 (q, J_{CF} = 271,8 Hz), 105.4, 96.0, 63.7, 15.2.

Known compound.[S2]

Synthesis of tosyl-protected *α*-aminoallenes (4)

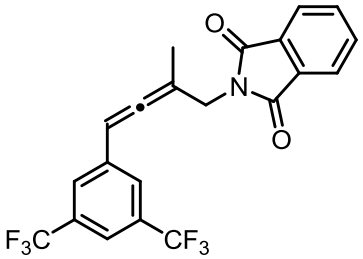
*1. Synthesis of Phthalimides (**8**)*

The *α*-hydroxyallene **7**, Ph_3P (1.5 eq) and phthalimide (1.5 eq) were dissolved in THF (8 ml/mmol). After cooling to 0 °C DIAD (1.5 eq) was added. The mixture was stirred for 1 h. Then the solvent was concentrated *in vacuo* and the crude product purified via silica gel column chromatography (cyclohexane:EtOAc, 20:1 to 10:1).

2. Hydrazinolysis and tosylation

The phthalimide **8** was dissolved in EtOH (4.4 ml/mmol). $H_2NNH_2 \cdot H_2O$ (2.1 eq) was added and the mixture was stirred at 80 °C for 3 h. Then conc. HCl (0.2 ml/mmol) was added at 0 °C and stirred for 15 min. The solid was filtered, washed with EtOAc and the filtrate extracted. For this purpose, water and 1 M NaOH were added to adjust the pH to 10. The aq. phase was extracted with EtOAc for three times. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was directly used in the tosylation reaction. It was dissolved in DCM (2.5 ml/mmol). Et_3N (2.5 eq) and TsCl (0.9 eq) were addet at 0 °C. The reaction was stirred for 20 h at RT. The organic phase was washed with sat. aq. NH_4Cl, dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified via silica gel column chromatography (cyclohexane:EtOAc, 20:1 to 8:1).

N-Phthalimido-4-(3,5-bis(trifluoromethyl)phenyl)-2-methyl-buta-2,3-dien-1-amine (8)



The reaction was performed in 117 ml THF using 4.33 g (14.62 mmol) of **7a**, 5.75 g (21.93 mmol) Ph_3P, 3.22 g phthalimide (21.93 mmol) and 4.43 ml DIAD (21.93 mmol). After column chromatography 5.80 g (13.64 mmol, 93%) of the product **8a** were obtained as white solid.

^{1}H-NMR (499.8 MHz, $CDCl_3$): δ (ppm) = 7.76 (m, 2 H), 7.66 (m, 2 H), 7.62 (s, 1 H), 7.56 (m, 2 H), 6.16 (m, 1 H), 4.37 (m, 2 H), 1.92 (d, J = 2.8 Hz, 3 H).

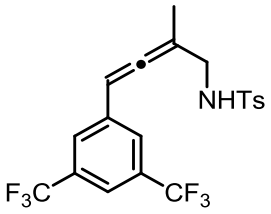
^{13}C-NMR (125.7 MHz, $CDCl_3$): δ (ppm) = 203.2, 167.7, 136.9, 134.0, 131.9, 131.7 (q, J_{CF} = 33,3 Hz), 126.7 (m), 123.3 (q, J_{CF} = 272,9 Hz), 120.4 (m), 102.3, 95.6, 40.1, 16.3.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –62.2.

HR-MS (ESI): $C_{21}H_{13}F_6NO_2$ (425.32), calculated: 426.09232 $[M+H]^+$, found: 426.09178.

IR: ν (cm^{-1}) = 2998 (w, C–H), 2970 (w, C–H), 2924 (w, C–H), 1960 (w, C=C=C), 1771 (m), 1730 (s, C=O), 1617 (m).

N-(*p*-Toluolsulfonyl)-4-(3,5-bis(trifluormethyl)phenyl)-2-methyl-buta-2,3-dien-1-amin (1a)



1.60 g (3.76 mmol) of the corresponding phthalimide **8a**, 17 ml ethanol, 390 µl (7.90 mmol) $H_2NNH_2 \cdot H_2O$ and 1.8 ml conc. HCl were used. The crude product was dissolved in 9 ml DCM and 1.3 ml Et_3N (9.40 mmol) and 645 mg TsCl (3.38 mmol) used for the tosylation. After column chromatography 1.32 g (2.95 mmol, 78%) of the product **1a** were obtained as white solid.

^{1}H-NMR (499.8 MHz, $CDCl_3$): δ (ppm) = 7.71 (d, J = 8.3 Hz, 1 H), 7.67 (s, 1 H), 7.59 (s, 2 H), 7.24 (d, J = 8.0 Hz, 2 H), 6.19 (m, 1 H), 4.97 (t, J = 6.1 Hz, 1 H), 3.65 (m, 2 H), 2.39 (s, 3 H), 1.85 (d, J = 2.8 Hz, 3 H).

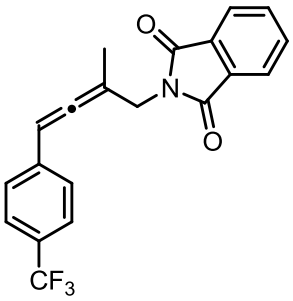
^{13}C-NMR (125.7 MHz, $CDCl_3$): δ (ppm) = 202.6, 143.6, 137.1, 136.8, 131.9 (q, J_{CF} = 33,3 Hz), 129.7, 127.0, 126.6 (m), 123.2 (q, J_{CF} = 272.9 Hz), 120.6 (m), 110.0, 102.9, 95.5, 45.3, 21.4, 16.3.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –62.2.

HR-MS (ESI): $C_{20}H_{17}F_6NO_2S$ (449.41), calculated: 450.09570 $[M+H]^+$, found: 450.09555.

IR: ν (cm^{-1}) = 3281 (br, NH), 2970 (w, C–H), 2925 (w, C–H), 2865 (w, C–H), 1959 (C=C=C), 1738 (s), 1618 (w), 1599 (w).

N-Phthalimido-2-methyl-4-(4-(trifluoromethyl)phenyl)-buta-2,3-dien-1-amine (8b)



The reaction was performed in 140 ml THF using 4.00 g (17.53 mmol) of **7b**, 6.90 g (26.30 mmol) Ph_3P, 3.87 g phthalimide (26.30 mmol) and 5.18 ml DIAD (26.30 mmol). After column chromatography 5.71 g (15.98 mmol, 91%) of the product **8b** were obtained as white solid.

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ (ppm) = 7.75 (m, 2 H), 7.66 (m, 2 H), 7.46 (d, J = 8.2 Hz, 2 H), 7.24 (d, J = 8.2 Hz, 2 H), 6.12 (m, 1 H), 4.35 (m, 2 H), 1.89 (d, J = 2.8 Hz, 3 H).

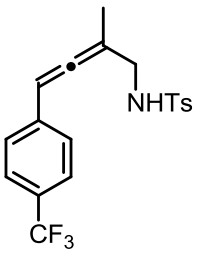
^{13}C-NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 202.7, 167.7, 138.0, 133.9, 131.8, 128.6 (q, J_{CF} = 32,3 Hz), 126.9, 125.3 (q, J_{CF} = 3,8 Hz), 124.1 (q, J_{CF} = 271,9 Hz), 123.2, 101.0, 96.5, 40.1, 16.2.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –61.6.

HR-MS (ESI): $C_{20}H_{14}F_3NO_2$ (357.33), calculated: 358.10494 $[M+H]^+$, found: 358.10408.

IR: ν (cm^{-1}) = 2980 (w, C–H), 2922 (w, C–H), 1953 (w, C=C=C), 1771 (m), 1716 (s, C=O), 1615 (m).

N-(*p*-Toluolsulfonyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)-buta-2,3-dien-1-amine (1b)



1.00 g (2.80 mmol) of the corresponding phthalimide **8b**, 12 ml ethanol, 285 µl (5.55 mmol) $H_2NNH_2 \cdot H_2O$ and 1.4 ml conc. HCl were used. The crude product was dissolved in 7 ml DCM and 970 µl Et_3N (7.00 mmol) and 480 mg TsCl (2.52 mmol) used for the tosylation. After column chromatography 0.92 g (2.41 mmol, 86%) of **1b** were obtained as glass-like pale yellow substance.

^{1}H-NMR (499.8 MHz, $CDCl_3$): δ (ppm) = 7.73 (d, J = 8.2 Hz, 1 H), 7.51 (d, J = 8.2 Hz, 2 H), 7.26 (m, 4 H), 6.16 (m, 1 H), 4.84 (t, J = 5.9 Hz, 1 H), 3.63 (m, 2 H), 2.42 (s, 3 H), 1.80, (d, J = 2.8 Hz, 3 H).

^{13}C-NMR (125.7 MHz, $CDCl_3$): δ (ppm) = 202.6, 143.5, 138.2 (q, J_{CF} = 1,3 Hz), 136.8, 129.7, 129.0 (q, J_{CF} = 32,5 Hz), 128.5, 127.0, 125.5 (q, J_{CF} = 3,9 Hz), 124.1 (q, J_{CF} = 271,6 Hz), 101.5, 96.3, 45.4, 21.5, 16.3.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –61.6.

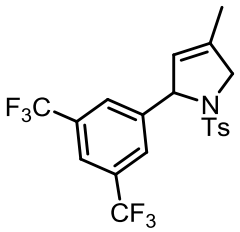
4. Cycloisomerization and Recycling

Gold-catalyzed cycloisomerization in ionic liquids and recycling

Under optimized conditions the α-aminoallene (0.125 mmol) **1** was added to a solution of 2 mg $Ph_3PAuNTf_2$ (2.5 µmol, 2 mol%) in 0.5 ml of the ionic liquid [BMIM][PF_6]. A film of 100 µl toluene was added as co-solvent. The conversion was determined by NMR spectroscopy. For this purpose small samples of the reaction were taken and extracted with Et_2O. The solvent was removed in *vacuo* and the sample dissolved in $CDCl_3$. After complete conversion the product was extracted with toluene (4 x 3 ml) and pipetted into a flask. After removing the solvent in *vacuo*, the crude product was filtered through a small silica column (cyclohexane:EtOAc, 4:1) and concentrated in *vacuo*.

The ionic liquid/catalyst system was reused by addition of another α-aminoallene.

2-(3,5-bis(trifluoromethyl)phenyl)-4-methyl-1-tosyl-3-pyrroline (2a)



56 mg (0.125 mmol) of allene **1a** were stirred for 5 min. 54 mg (0.120 mmol, 96%) of **2a** were obtained as white solid.

^{1}H-NMR (400.1 MHz, $CDCl_3$): δ (ppm) = 7.72 (s, 1 H), 7.64 (s, 2 H), 7.51 (d, J = 8.2 Hz, 2 H), 7.20 (d, J = 8.1, 2 H), 5.55 (m, 1 H), 5.25 (m, 1 H), 4.24 (m, 2 H), 2.38 (s, 3 H), 1.78 (s, 3 H).

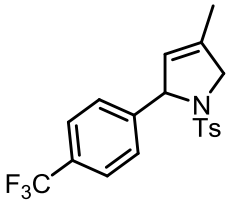
^{13}C-NMR (100.6 MHz, $CDCl_3$): δ (ppm) = 143.9, 143.8, 136.3, 135.0, 131.6 (q, J_{CF} = 33.4 Hz), 129.6, 127.3 (m), 127.1, 123.2, 123.2 (q, J_{CF} = 272.2 Hz), 121.6 (m), 69.6, 58.4, 21.4, 14.0.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –62.0.

HR-MS (ESI): $C_{20}H_{17}F_6NO_2S$ (449.41), calculated: 450.09570 $[M+H]^+$, found: 450.09546.

IR: ν (cm^{-1}) = 2970 (w, C–H), 2924 (w, C–H), 2865 (w, C–H), 1738 (m), 1598 (w).

4-Methyl-1-tosyl-2-(4-(trifluormethyl)phenyl)-3-pyrroline (2b)



48 mg (0.125 mmol) of allene **1b** were stirred for 5 min. 43 mg (0.113 mmol, 90%) of **2b** were obtained as white solid.

^{1}H-NMR (499.8 MHz, $CDCl_3$): δ (ppm) = 7.68 (m, 4 H), 7.34 (d, J = 8.0 Hz, 2 H), 7.19 (d, J = 8.4 Hz, 2 H), 5.49 (m, 1 H), 5.25 (m, 1 H), 4.21 (m, 2 H), 2.39 (s, 3 H), 1.75 (s, 3 H).

^{13}C-NMR (125.7 MHz, $CDCl_3$): δ (ppm) = 145.1 (q, J_{CF} = 1.2 Hz), 143.4, 135.3, 135.2, 129.8 (q, J_{CF} = 32,3 Hz), 129.5, 127.5, 127.2, 125.3 (q, J_{CF} = 3,7 Hz), 124.1 (q, J_{CF} = 272,0 Hz), 124.0, 70.0, 58.4, 21.4, 13.9.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –61.7.

HR-MS (ESI): $C_{19}H_{18}F_3NO_2S$ (381.41), calculated: 382.10831 $[M+H]^+$, found: 382.10888.

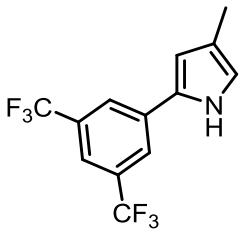
IR: ν (cm^{-1}) = 3020 (w, C–H), 2920 (w, C–H), 2862 (w, C–H), 1738 (m), 1618 (w).

5. Synthesis of BODIPY Dyes

Synthesis of pyrroles

The pyrroline **2** was solved in THF (5 ml/mmol) and KO^{t}Bu (3 eq) was added at 0 °C. The mixture was stirred for 30 min. After hydrolysis with sat. aq. NH_4Cl the aqueous phase was extracted with EtOAc. The combined organic layers were dried over $MgSO_4$, concentrated *in vacuo* and the crude product purified via silica gel column chromatography (cyclohexane:EtOAc, 20:1 to 10:1).

2-(3,5-Bis(trifluoromethyl)phenyl)-4-methyl-1-tosyl-1H-pyrrole (3a)



200 mg (0.45 mmol) of **2a** in 2.3 ml THF and 151 mg (1.35 mmol) KO^{t}Bu gave 121 mg (0.41 mmol, 93%) of **3a** as white solid.

^{1}H-NMR (300.1 MHz, $CDCl_3$): δ (ppm) = 8.26 (s, 1H), 7.79 (s, 2 H), 7.63 (s, 1 H), 6.70 (s, 1 H), 6.52 (d, J = 2.5 Hz, 1 H), 2.15 (s, 3 H).

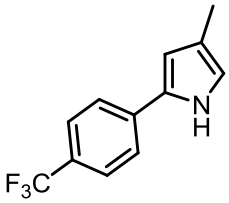
^{13}C-NMR (75.5 MHz, $CDCl_3$): δ (ppm) = 134.7, 131.1 (q, J = 33.1 Hz), 129.0, 123.3 (q, J = 272.7 Hz), 123.0 (m), 121.6, 118.9 (m), 118.8 (m), 110.0, 11.8.

^{19}F-NMR (282.4 MHz, $CDCl_3$): δ (ppm) = –62.3.

HR-MS (ESI): $C_{13}H_9F_6N$ (293.21), calculated: 294.07120 $[M+H]^+$, found: 294.07095.

IR: ν (cm^{-1}) = 3490 (br, NH), 2933 (w, C–H), 1708 (w), 1620 (m).

4-Methyl-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole (3b)



200 mg (0.52 mmol) of **2b** in 2.6 ml THF and 175 mg (1.56 mmol) KO^{t}Bu gave 112 mg (0.50, 95%) of **3b** as white solid.

^{1}H-NMR (500.1 MHz, $CDCl_3$): δ (ppm) = 8.23 (br s, 1H), 7.58 (d, J = 8.34 Hz, 2 H), 7.51 (d, J = 8.3 Hz, 2 H), 6.68 (s, 1 H), 6.47 (m, 1 H), 2.16 (s, 3 H).

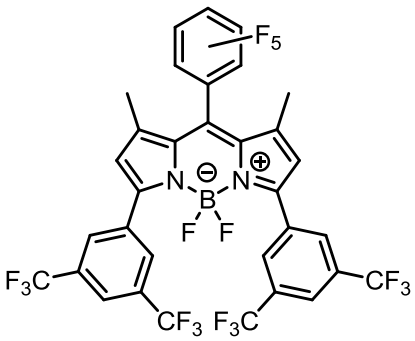
^{13}C-NMR (125.8 MHz, $CDCl_3$): δ (ppm) = 136.0, 130.4, 127.4 (q, J = 32.6 Hz), 125.8 (q, J = 3.8 Hz), 124.2 (q, J = 271.5 Hz), 123.3, 121.2, 118.1, 109.2, 11.8.

Known compound.[S3]

Synthesis of BODIPY dyes (4)

The pyrrole **3** (2 eq) and pentafluorobenzaldehyde (1 eq) were solved in DCM (25 ml/mmol) and a catalytic amount of TFA was added. After 30 min *p*-chloranil (1.2 eq) was added. The mixture was stirred for 40 min, then DIPEA (7 eq) was added and stirred for another 5 min before $BF_3 \cdot Et_2O$ (9 eq) was dropped into the reaction. The mixture was washed with water, dried over $MgSO_4$, concentrated *in vacuo* and dissolved in DCM again. Then DIPEA and $BF_3 \cdot Et_2O$ (same manner and amounts like before) were added. The reaction mixture was washed with water and the crude product purified via silica gel column chromatography (pentane:EtOAc, 40:1 to 10:1).

4,4-Difluoro-4-bora-3,5-bis-(3,5-bis(trifluoromethyl)phenyl)-1,7-dimethyl-3a,4a-diaza-s-indacene-8-yl)-pentafluorobenzole (4a)



390 mg (1.33 mmol) of pyrrole **3a** dissolved in 28 ml DCM, 131 mg (0.67 mmol) pentafluorbenzaldehyde, 4 drops TFA, 196 mg (0.80 mmol) chloranile, 837 µl (4.69 mmol) DIPEA (2 times) and 764 µl (6.03 mmol) $BF_3 \cdot Et_2O$ (2 times) were used. 366 mg (0.45 mmol, 68%) of the dye **4a** were observed as dark shining crystals.

^{1}H-NMR (300.1 MHz, $CDCl_3$): δ (ppm) = 8.31 (d, J = 1.1 Hz, 4 H), 7.90 (s, 2 H), 6.52 (s, 2 H), 1.78 (s, 6 H).

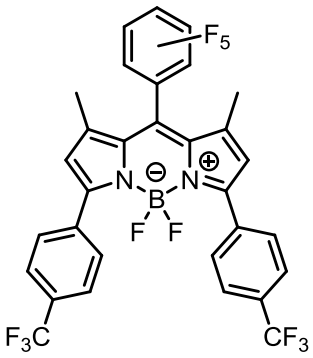
^{13}C-NMR(150.8 MHz, $CDCl_3$): δ (ppm) = 155.3, 143.7, 133.5, 133.4, 131.7 (q, J = 33.8 Hz), 129.4 (m), 127.9, 126.9, 123.6 (m), 123.4 (m), 123.0 (q, J = 272.9 Hz), 14.1.

^{19}F-NMR (282.4 MHz, $CDCl_3$): *δ* (ppm) = –62.4, –129.6 (q, J = 32.5), –137.9 (m), –147.7 (t, J = 21.0), 157.4 (m).

HR-MS (ESI): $C_{33}H_{14}N_2{}^{11}BF_{19}$ (810.09), calculated: 810.09412 $[M]^+$, found: 810.09343.

IR: ν (cm^{-1}) = 2928 (w, C–H), 2857 (w, C–H), 1733 (w), 1654 (w), 1629 (w).

4,4-Difluoro-4-bora-3,5-bis-(4-(trifluoromethyl)phenyl)-1,7-dimethyl-3a,4a-diaza-s-indacene-8-yl-pentafluorobenzole (4b)



300 mg (1.33 mmol) of pyrrole **3b** dissolved in 28 ml DCM, 131 mg (0.67 mmol) pentafluorbenzaldehyde, 4 drops TFA, 196 mg (0.80 mmol) chloranile, 837 µl (4.69 mmol) DIPEA (2 times) and 764 µl (6.03 mmol) $BF_3 \cdot Et_2O$ (2 times) were used. 316 mg (0.47 mmol, 70%) of the dye **4b** were observed as dark shining crystals.

^{1}H-NMR (400 MHz, $CDCl_3$): δ (ppm) = 7.91 (d, $^3J_{HH}$ = 7,3 Hz, 4 H), 7.67 (d, J = 8.2 Hz, 4 H), 6.44 (s, 2 H), 1.76 (s, 6 H).

^{13}C-NMR(100 MHz, $CDCl_3$): δ (ppm) = 157.1, 142.6, 135.2, 133.1, 131.5 (q, J = 32.7 Hz), 129.7 (t, J = 3.8 Hz), 125.8, 125.2 (m), 124.9 (q, J = 272.4 Hz), 124.0 (m), 14.0.

^{19}F-NMR (282.4 MHz, $CDCl_3$): *δ* (ppm) = –62.1, –130.1 (q, J = 31.7), –137.9 (m), –148.4 (t, J = 21.0), 157.8 (m).

HR-MS (ESI): $C_{31}H_{16}N_2{}^{11}BF_{13}$ (674.26), calculated: 674.11935 $[M]^+$, found: 674.11837.

IR: ν (cm^{-1}) = 2961 (w, C–H), 2929 (w, C–H), 2858 (w, C–H), 1653 (w), 1619 (w).

6. X-Ray structure analysis, X-Ray diffraction.

The X-ray data collection was performed on a Bruker Kappa Apex four circle-CCD diffractometer using graphite monochromatized Mo-Kα radiation (λ = 0.71070 Å). Data reduction (Lorentz-Polarization correction) was carried out using the SMART/SAINT program [S4]. The SADABS program was used for empirical absorption correction [S5]. Crystal structures were solved by direct methods. Structure solution, refinement and data output were carried out with the SHELXTL program [S6,S7]. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were placed in geometrically calculated positions by using a riding model. Images and hydrogen bonding interactions were created in the crystal lattice with DIAMOND and MERCURY software packages [S8,S9]. The crystallographic data (excluding structure factors) for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 1040186 and 1040187. (Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, fax: +44 1223336033 or e-mail: deposit@ccdc.cam.ac.uk).

Table S1 Crystal data and structure refinement for **4a**,**b**

Compound reference	**4a**	**4b**
Chemical formula	$C_{33}H_{14}BF_{19}N_2$	$C_{31}H_{16}BF_{13}N_2$
Formula Mass	810.27	674.27
Crystal system	Monoclinic'	Triclinic'
a/Å	10.9506(5)	7.3337(12)
b/Å	19.9674(9)	9.9719(16)
c/Å	15.2675(9)	10.1280(16)
α/°	90.00	93.269(5)
β/°	110.711(2)	99.210(5)
γ/°	90.00	110.524(4)
Unit cell volume/Å^3	3122.6(3)	679.57(19)
Temperature/K	150(2)	150(2)
Space group	*P*2(1)/*c*	*P*1
No. of formula units per unit cell, *Z*	4	1
Radiation type	Mo-Kα	Mo-Kα
Absorption coefficient, μ/mm^{-1}	0.181	0.159
No. of reflections measured	75746	4958
No. of independent reflections	7800	4958
R_{int}	0.0366	0.0000
Final R_1 values ($I > 2\sigma(I)$)	0.0605	0.0637
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1506	0.1738
Final R_1 values (all data)	0.0719	0.0646
Final $wR(F^2)$ values (all data)	0.1592	0.1747
Goodness of fit on F^2	1.045	1.095
CCDC number	1040186	1040187

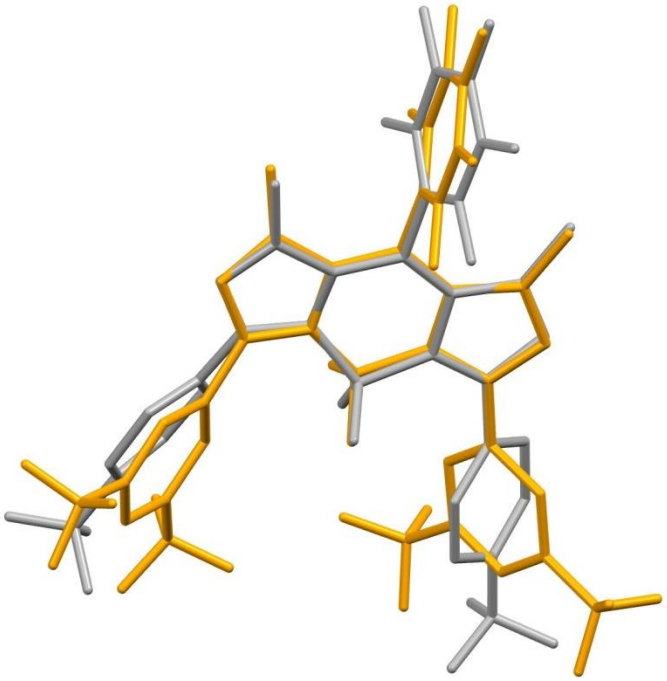


Figure S1. Overlay of **4a** (yellow) and **4b** (grey).

7. Optical Spectroscopy, Experimental and Data

UV-vis absorption spectra were recorded on an Analytik Jena Specord 210 Plus spectrophotometer. Steady-state fluorescence measurements were carried out on a Horiba Jobin–Yvon FluoroMax-4P spectrofluorometer, using standard 10 mm quartz cells. Fluorescence lifetimes were determined with a unique customized laser impulse fluorometer with picoseconds time resolution described elsewhere.[S10,S11] The fluorescence lifetime profiles were analyzed using the Horiba Scientific software package DAS 6.

The photostability experiments were carried out with a Nd:YVO_4 laser (Millennia, Spectra Physics) with a stabilized output power, directed onto a disposable ultra-micro cuvette (Eppendorf UVette, 10 mm path length) containing 60 µL of the dye with the absorbance adjusted to 0.1 at 532 nm for all dyes. The fluorescence was recorded with a fibre spectrometer (HR4000, OceanOptics). The absorption was measured prior and after photobleaching to verify that the reduced fluorescence is in agreement with the reduction in absorption. No changes of the structures of the absorption (>300 nm) or emission bands were noted after bleaching. All solvents employed for the spectroscopic measurements were of UV spectroscopic grade (Aldrich). Radiative (k_f) and nonradiative (k_{nr}) rate constants in Table S1 and S2 have been calculated according to $k_f = \Phi_f/\tau_f$ and $k_{nr} = (1 - \Phi_f)/\tau_f$.

Table S2. Spectroscopic properties and photophysical data of **4a** in selected solvents at 298 K.

Solvent	λ_{abs} [nm]	λ_{em} [nm]	$\Delta\nu_{abs\text{-}em}$[cm^{-1}]	Φ_f	τ_f [ns]	k_f [10^8 s^{-1}]	k_{nr} [10^8 s^{-1}]
Hex	558	584	798	0.91	5.44	1.68	0.16
Tol	566	595	861	0.93	4.88	1.90	0.15
Bu_2O	560	587	821	0.89	5.26	1.70	0.20
Et_2O	558	586	856	0.91	5.67	1.60	0.17
THF	560	589	879	0.89	5.19	1.70	0.22
MeCN	556[a]	587	950	0.91	5.80	1.57	0.16
EtOH	558[a]	589	943	0.90	5.46	1.64	0.19
MeOH	556	584	862	0.91	5.67	1.60	0.16

[a] Representative molar absorption coefficients (at λ_{max}) were determined to 49000±1000 (EtOH) and 46600±700 (acetonitrile).

Table S3. Spectroscopic properties and photophysical data of **4b** in selected solvents at 298 K.

Solvent	λ_{abs} [nm]	λ_{em} [nm]	$\Delta\nu_{abs\text{-}em}$[cm^{-1}]	Φ_f	τ_f [ns]	k_f [10^8 s^{-1}]	k_{nr} [10^8 s^{-1}]
Hex	558	588	914	0.86	5.36	1.60	0.27
Tol	563	598	1040	0.95	4.75	2.00	0.10
Bu_2O	559	590	940	0.93	5.14	1.81	0.14
Et_2O	556	589	1008	0.93	5.48	1.69	0.13
THF	557	593	1090	0.92	5.13	1.80	0.15
MeCN	550[a]	587	1146	0.94	5.57	1.69	0.11
EtOH	555[a]	586	953	0.86	5.25	1.63	0.27
MeOH	553	587	1047	0.89	5.39	1.65	0.21

[a] Representative molar absorption coefficients (at λ_{max}) were determined to 58000±3000 (Ethanol) and 58100±800 (acetonitrile)**.**

8. Computational Details and Results

The optimization of the S_0 ground-state geometries in the gas phase was performed with the density functional theory (DFT) method employing the hybrid functional B3LYP with a 6-311G(d,p) basis set and energy minimized as implemented in Gaussian 03.[S12] The excitation energies and the oscillator strengths were obtained using the time-dependent density functional theory (TD-DFT) method at the same level of theory on the B3LYP / 6-311G(d,p) optimized geometries.

Table S4. Calculated properties for the vertical excitation of the most stable energy-minimized ground-state geometries of the title dyes by TD-DFT (for calculation details, see above).

	$\lambda_{S_n \leftarrow S_0}$ (n)[a] /nm	f [b]	$\Delta\mu_{S_n - S_0}$ [c] /D	Orbitals (coefficients) [d]
4a	478.3 (1) [e]	0.637	–2.2	HOMO–LUMO (0.596)
	384.3 (2)	0.020	1.5	HOMO–1–LUMO (0.675)
	360.2 (3)	0.014	0.4	HOMO–2–LUMO (0.663) HOMO–3–LUMO (0.131)
	341.9 (4)	0.003	27.2	HOMO–4–LUMO (0.703)
	336.7 (5)	0.196	–5.8	mixed [g]
4b	483.7 (1) [f]	0.644	–4.0	HOMO–LUMO (0.596)
	381.0 (2)	0.015	0.0	HOMO–1–LUMO (0.655) HOMO–2–LUMO (–0.167)
	359.0 (3)	0.004	–4.9	HOMO–2–LUMO (0.397) HOMO–3–LUMO (0.161) HOMO–5–LUMO (0.515)
	355.2 (4)	0.047	1.2	mixed
	345.6 (6) [h]	0.189	–2.6	mixed

[a] Wavelength of the transition. [b] Oscillator strength of the transition. [c] Dipole moment difference between ground (μ_0) and respective excited (μ_n) state; μ_0 **7a** = 7.9 D, μ_0 **7b** = 7.4 D. [d] MOs involved in the transitions. [e] $\Delta_{S_1-T_1}$ = 1.25 eV. [f] $\Delta_{S_1-T_1}$ = 1.24 eV. [g] mixed = more than three transitions involved. [h] Transition 5 is also oscillator-weak and involves HOMO–3–LUMO and HOMO–5–LUMO transitions.

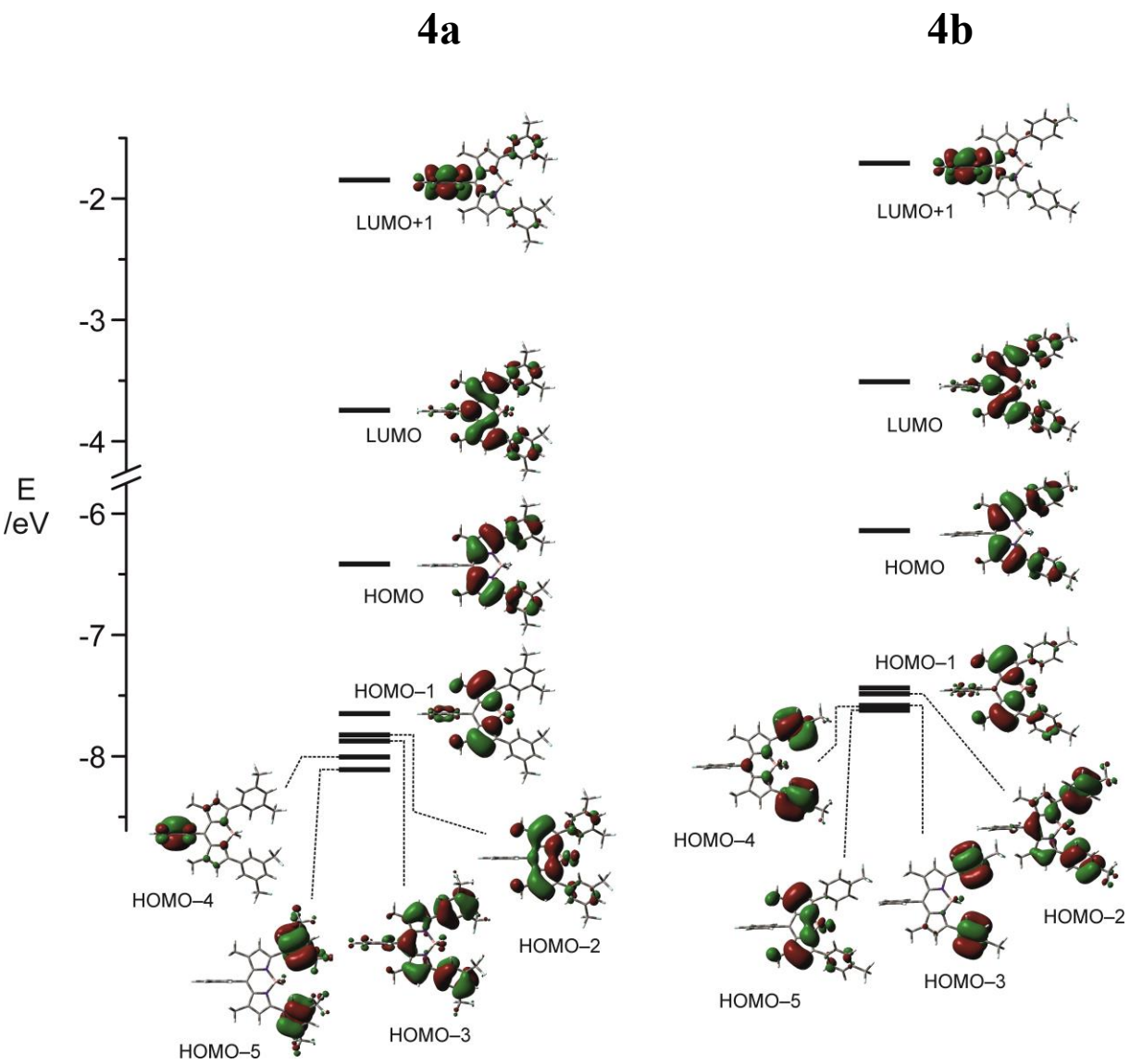


Figure S2. Frontier molecular orbitals HOMO–5,–4,–3,–2,–1, HOMO, LUMO and LUMO+1 of **4a** and **4b**.

9. References

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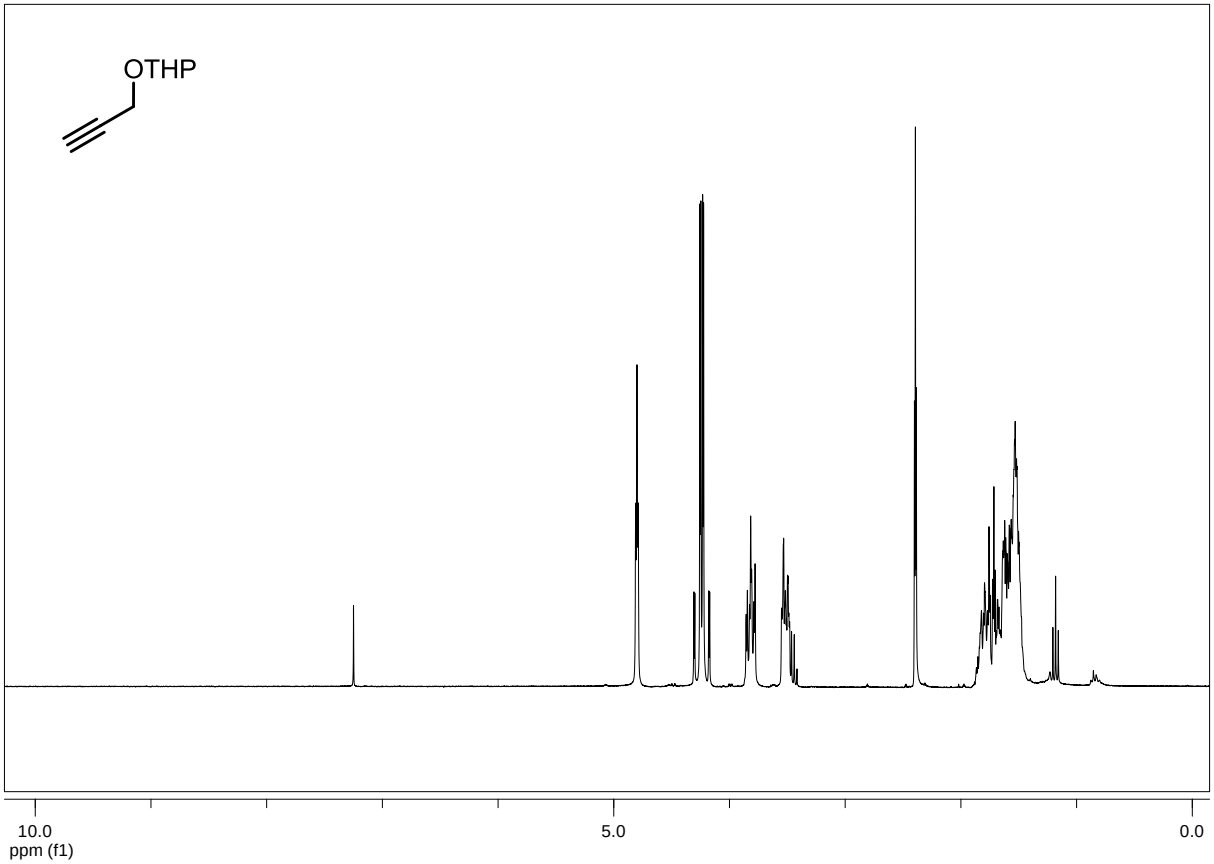
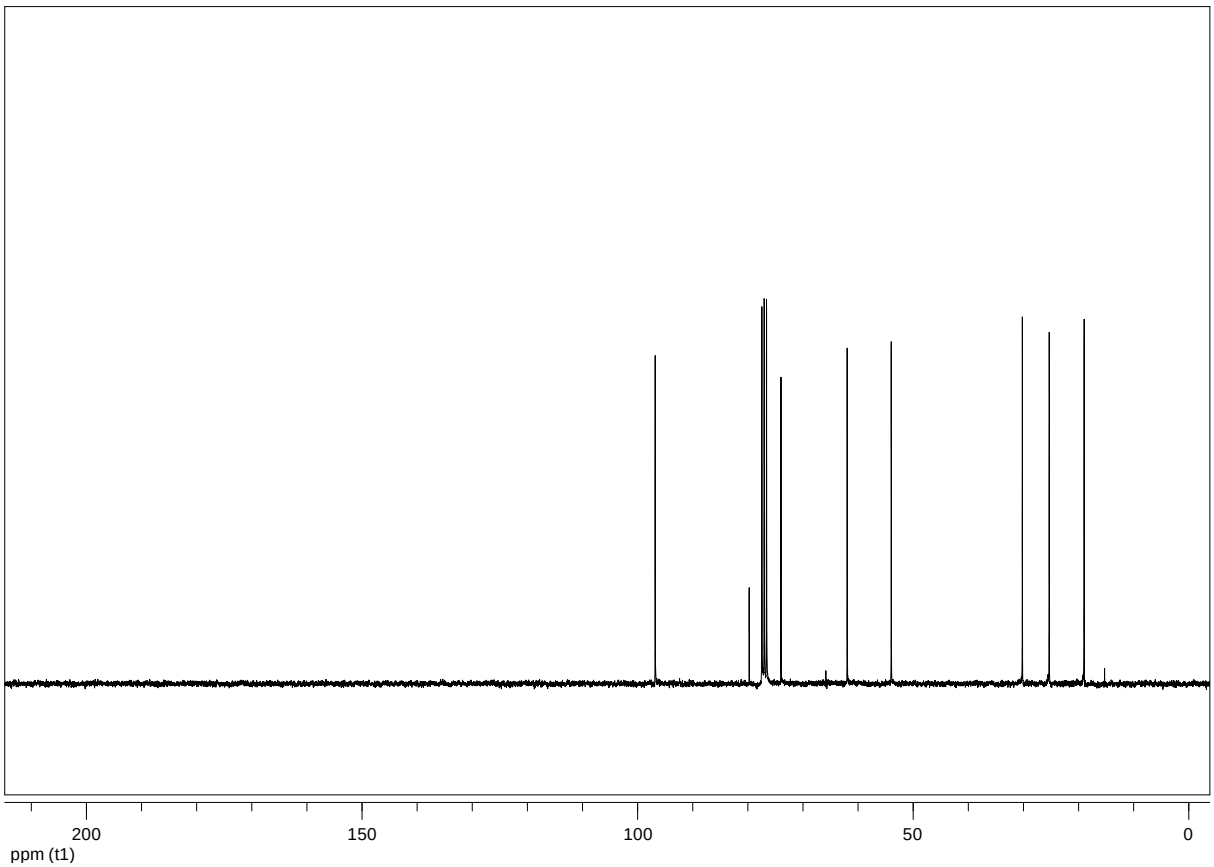
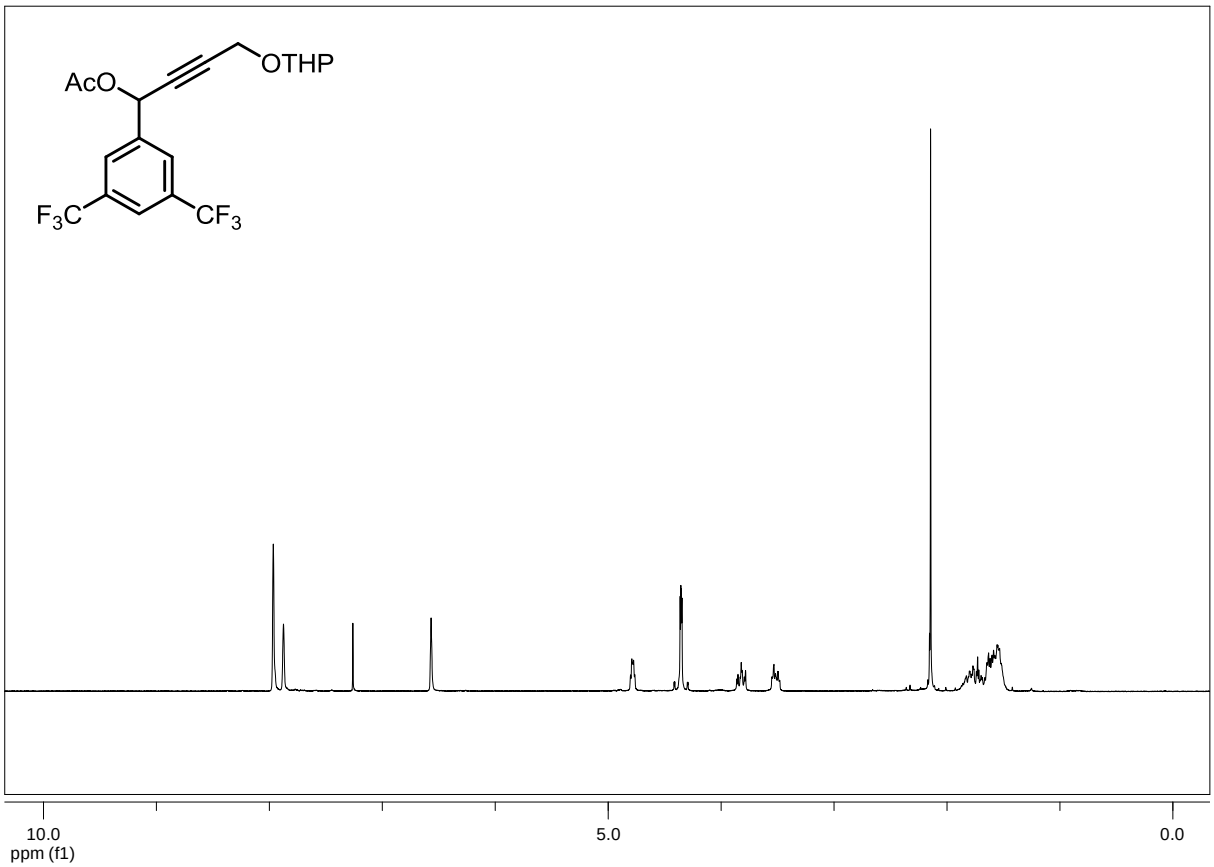
10.NMR Spectra

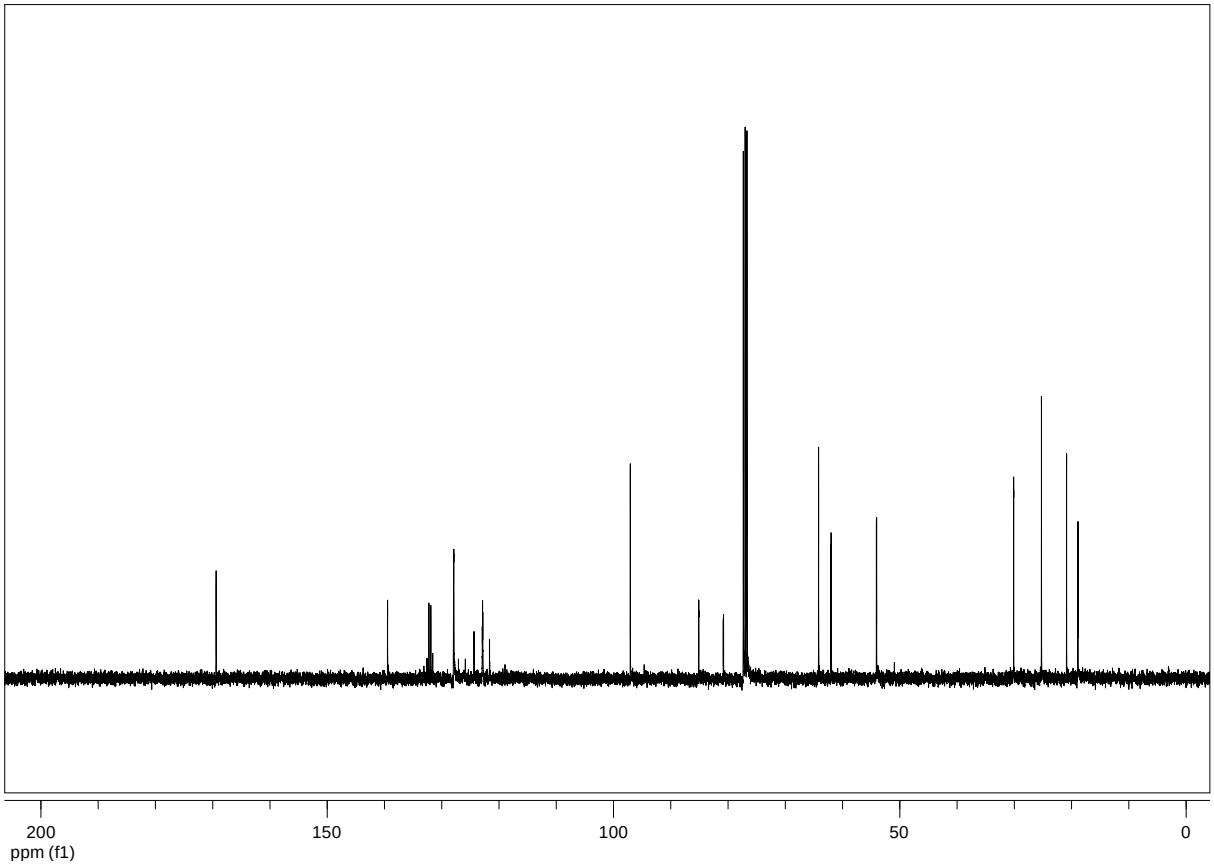
2-(2-Propynyloxy)-tetrahydro-2H-pyran (5)



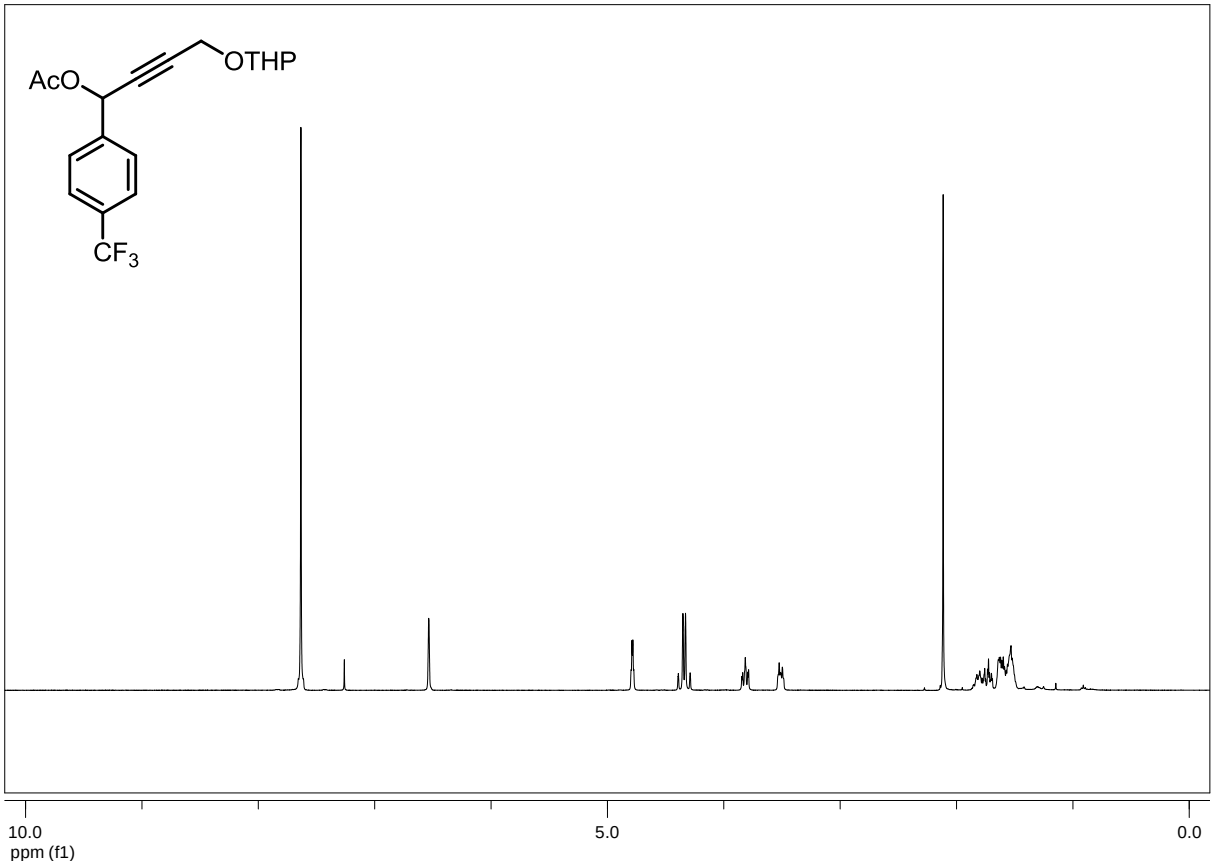


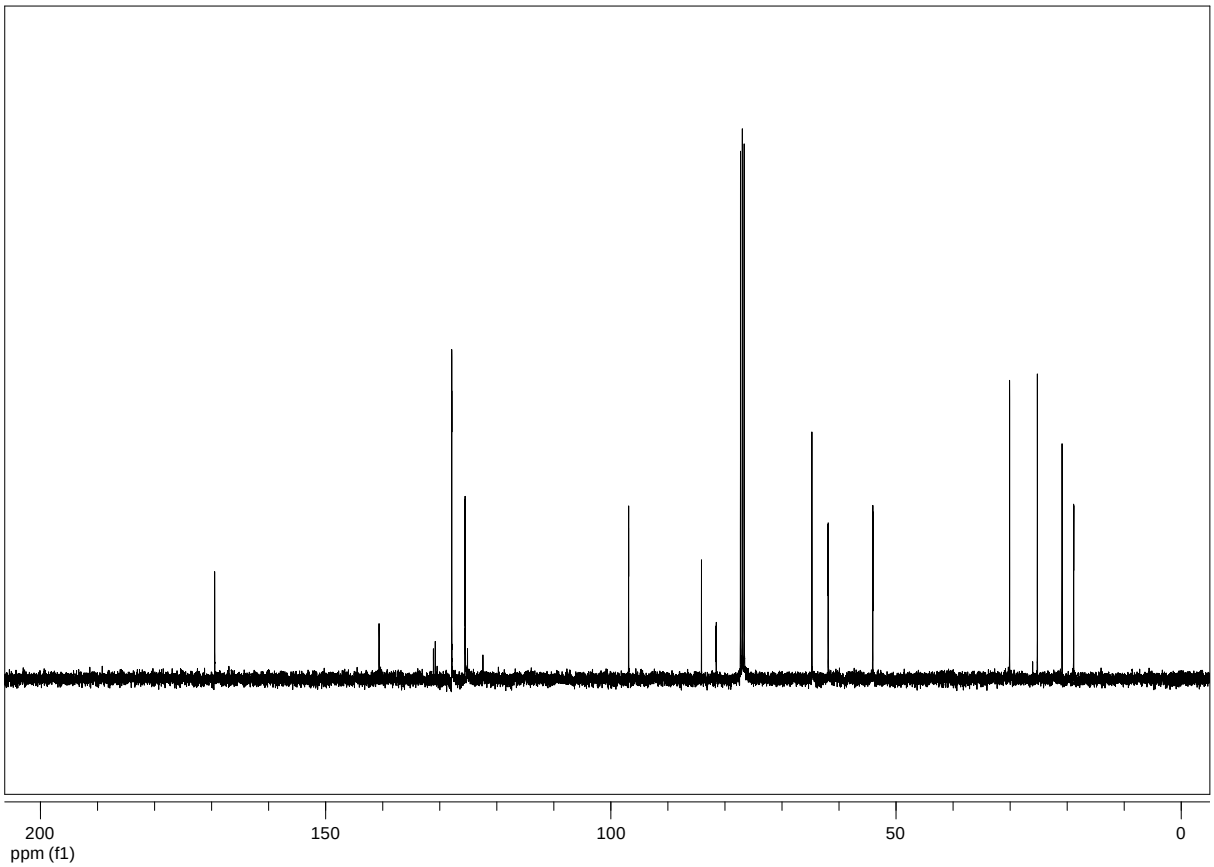
1-(3,5-Bis-(trifluoromethyl)phenyl)-4-(tetrahydro-2H-pyran-2-yloxy)but-2-ynyl acetate (6a)



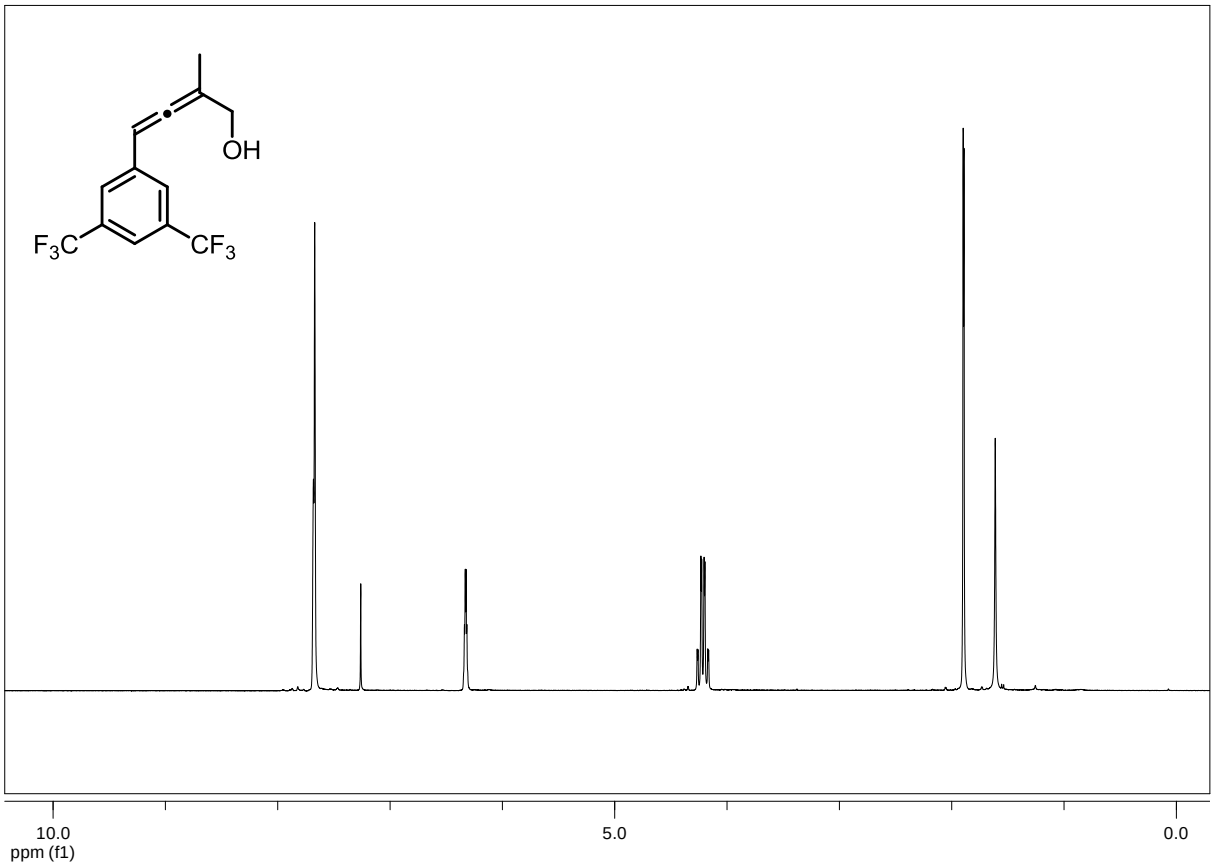


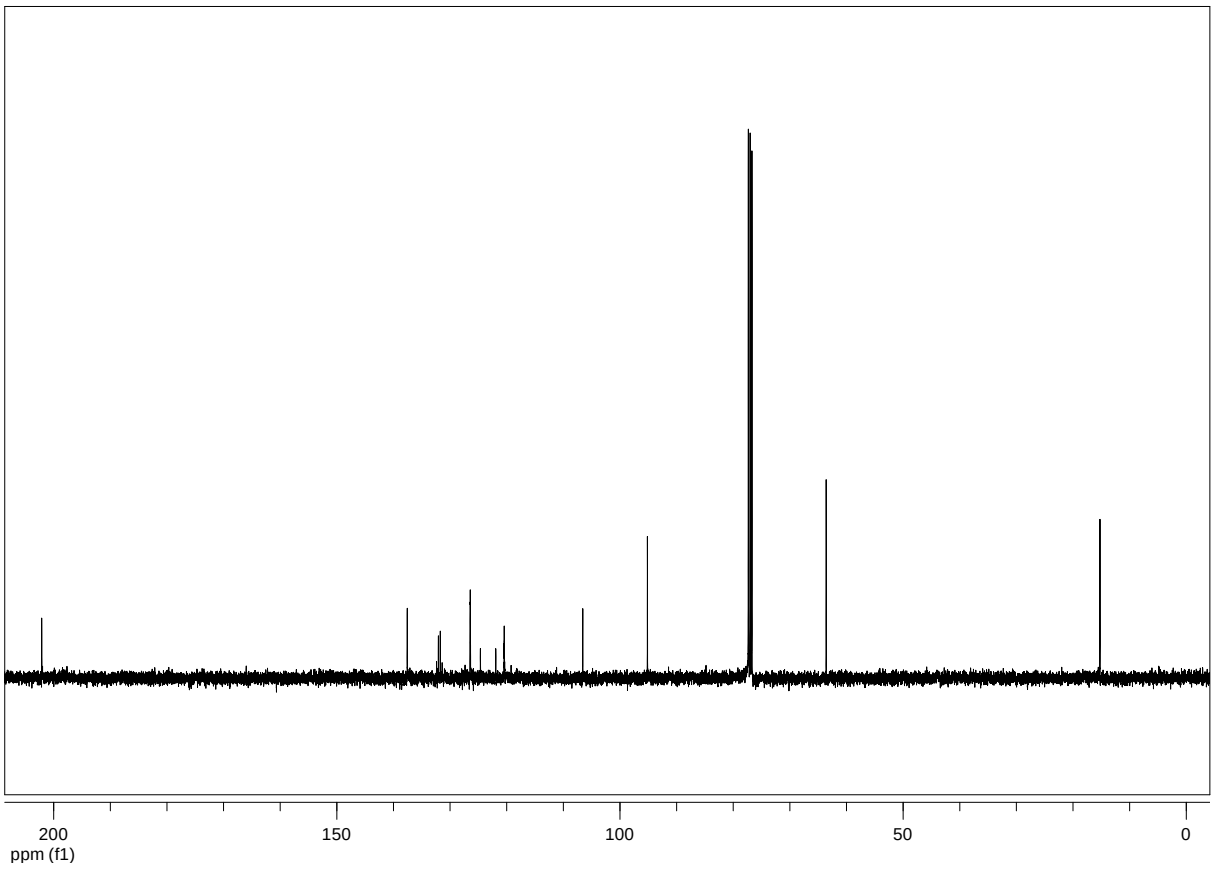
4-(Tetrahydro-2H-pyran-2-yloxy)-1-(4-(trifluoromethyl)phenyl)but-2-ynyl acetate (6b)



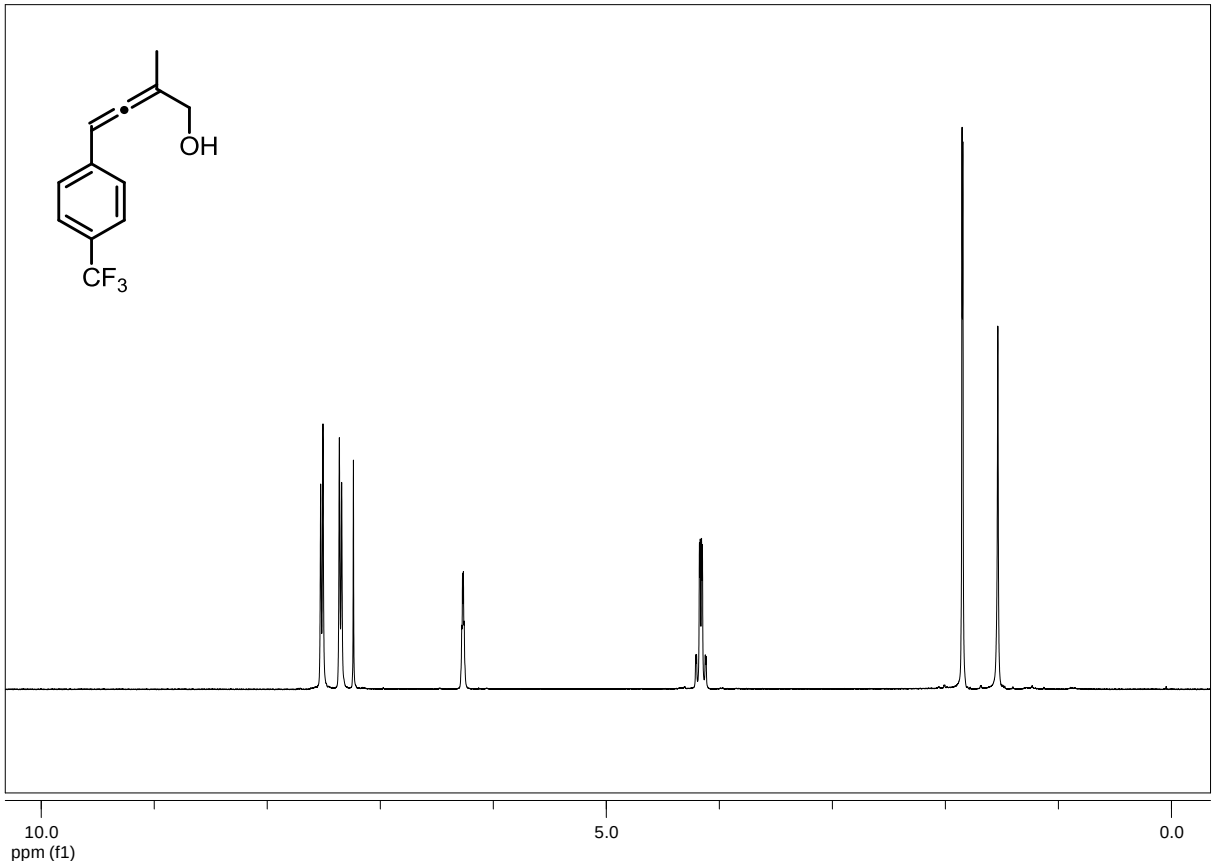


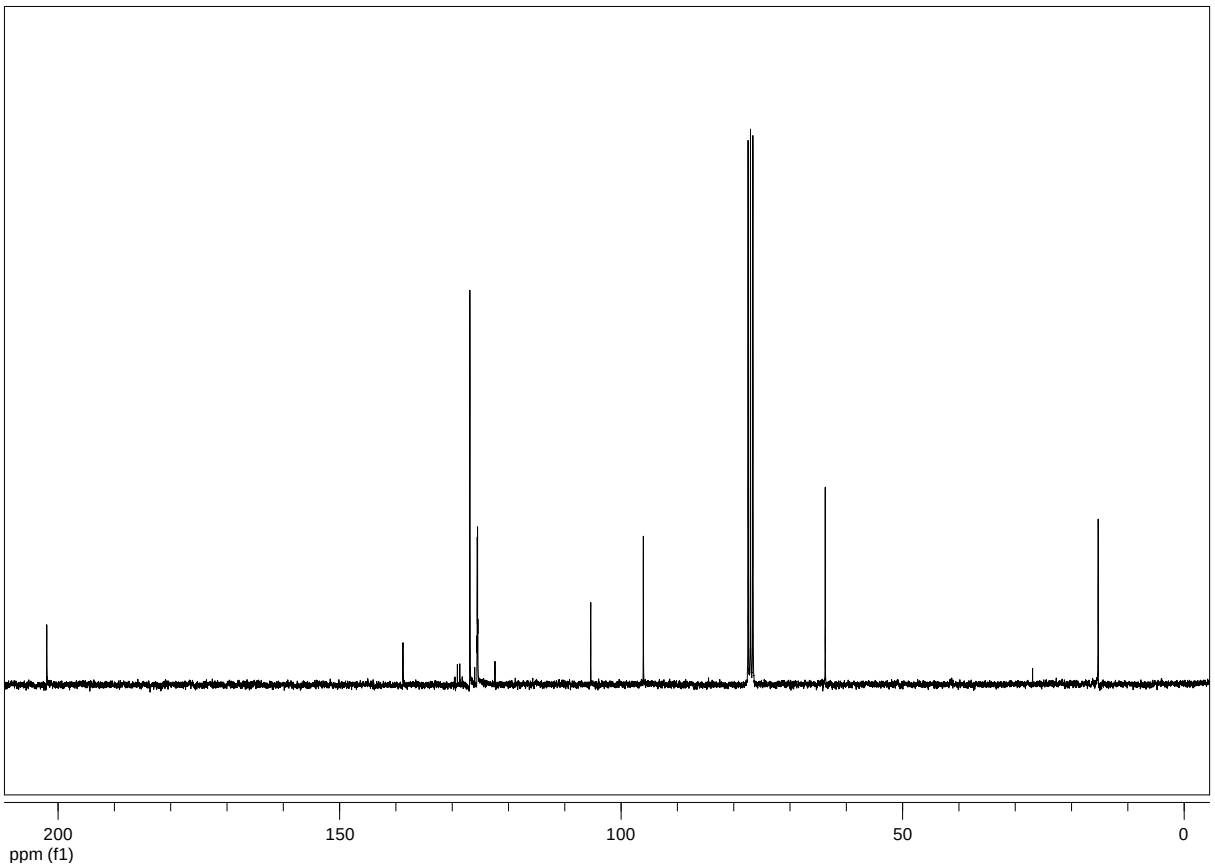
4-(3,5-Bis(trifluoromethyl)phenyl)-2-methylbuta-2,3-dien-1-ol (7a)



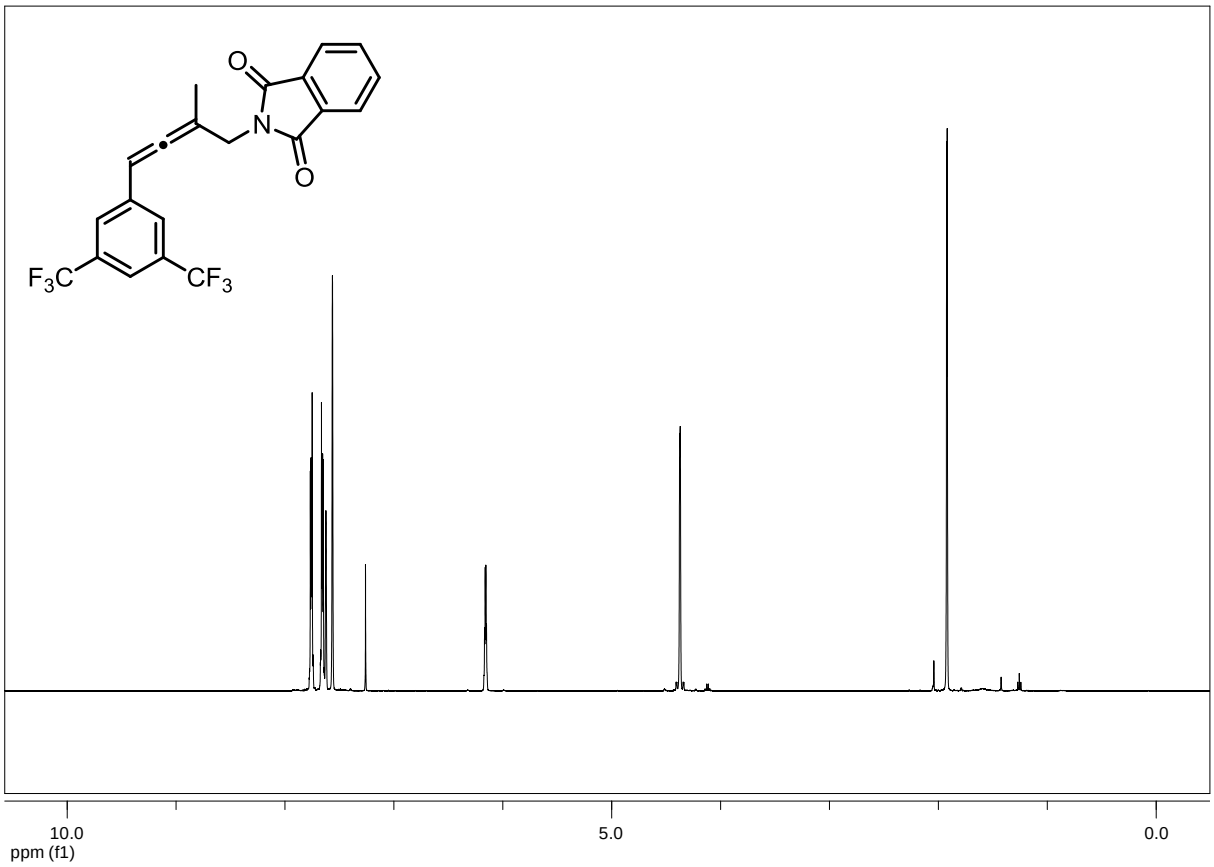


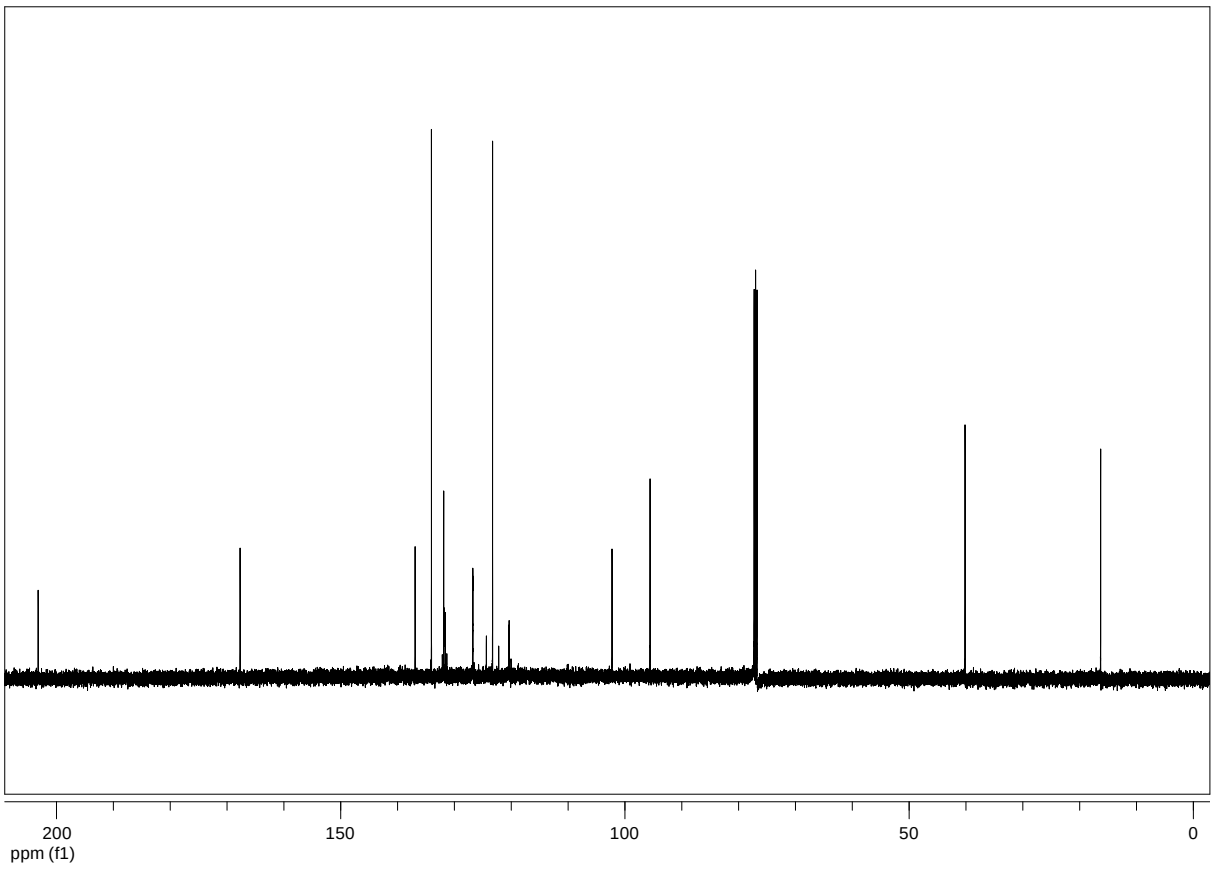
2-Methyl-4-(4-(trifluoromethyl)phenyl)buta-2,3-dien-1-ol (7b)



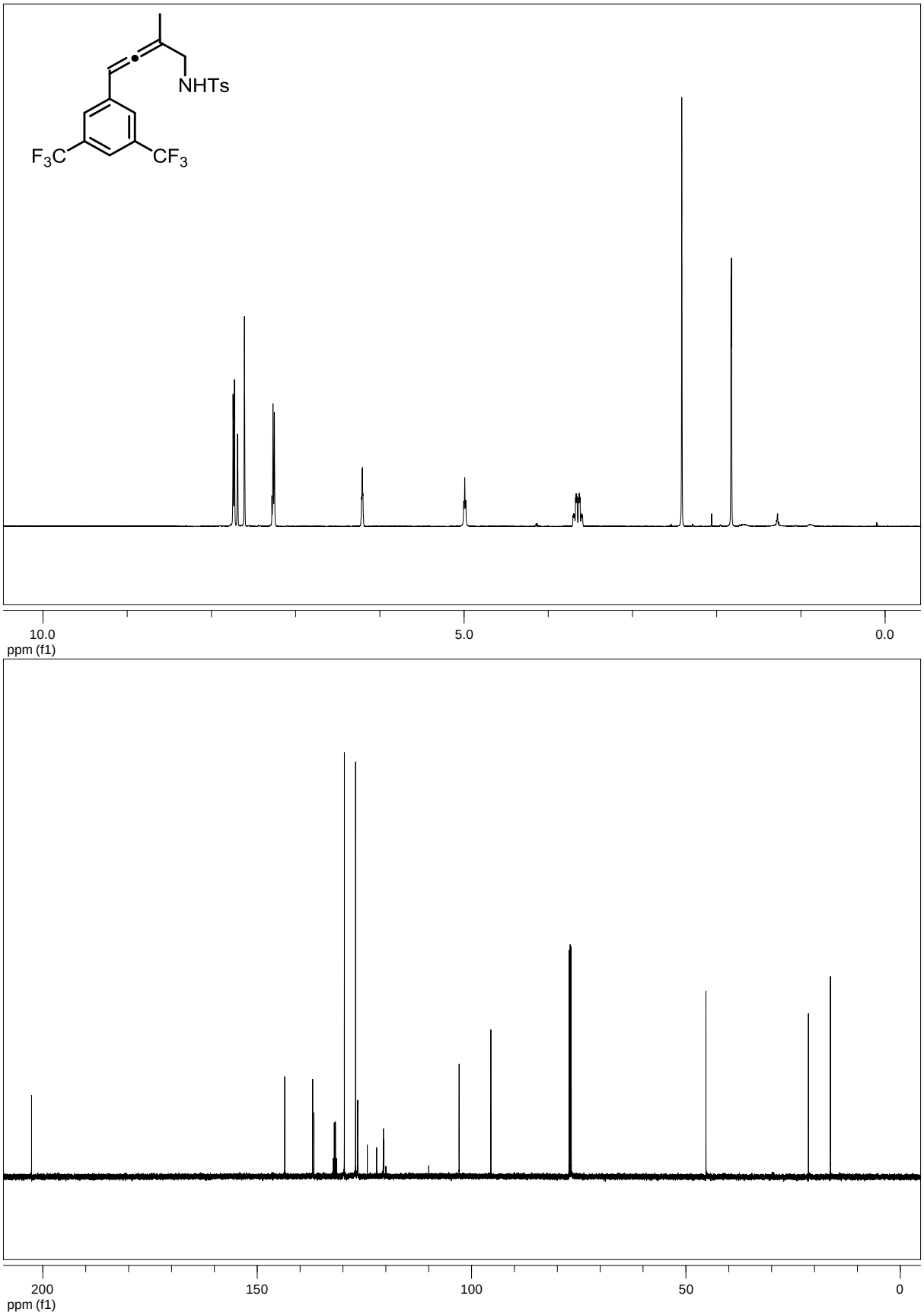


N-Phthalimido-4-(3,5-bis(trifluoromethyl)phenyl)-2-methyl-buta-2,3-dien-1-amine (8a)

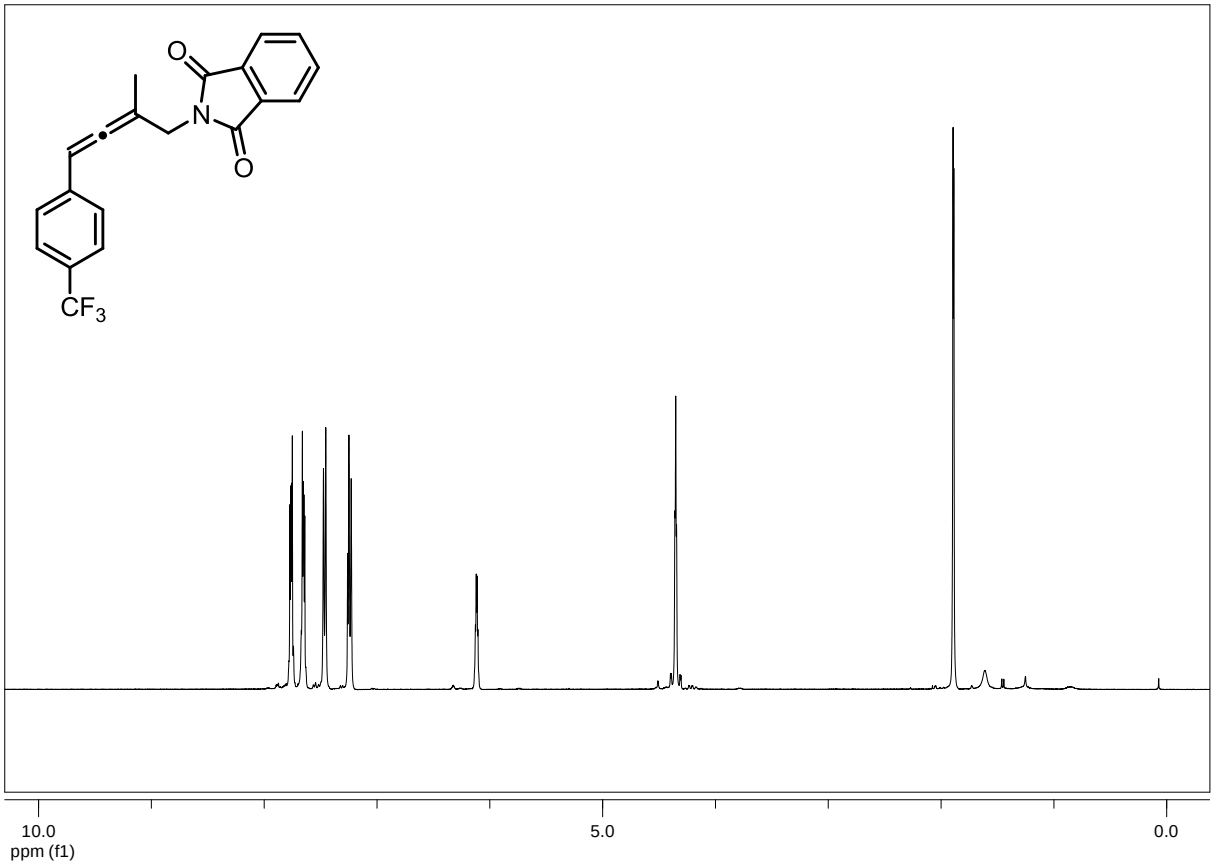


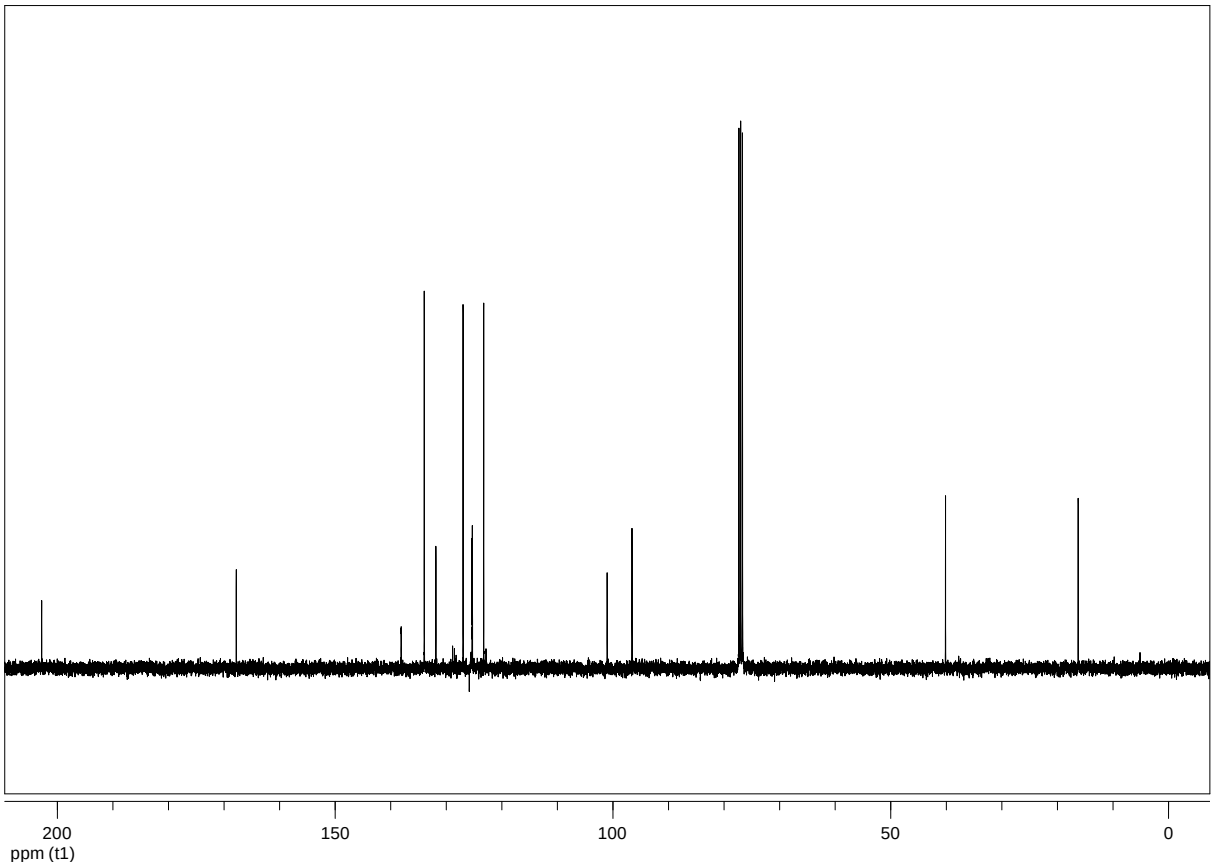


N-(*p*-Toluolsulfonyl)-4-(3,5-bis(trifluormethyl)phenyl)-2-methyl-buta-2,3-dien-1-amin (1a)

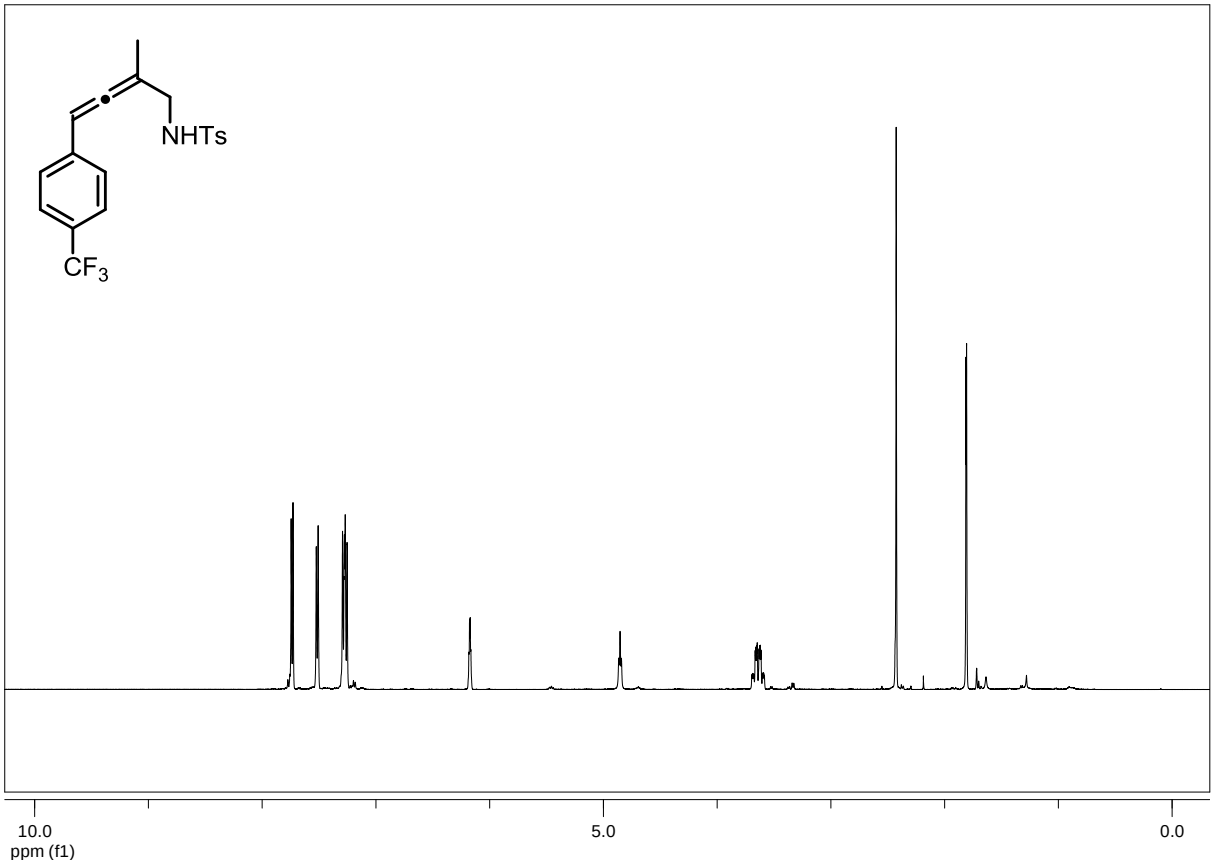


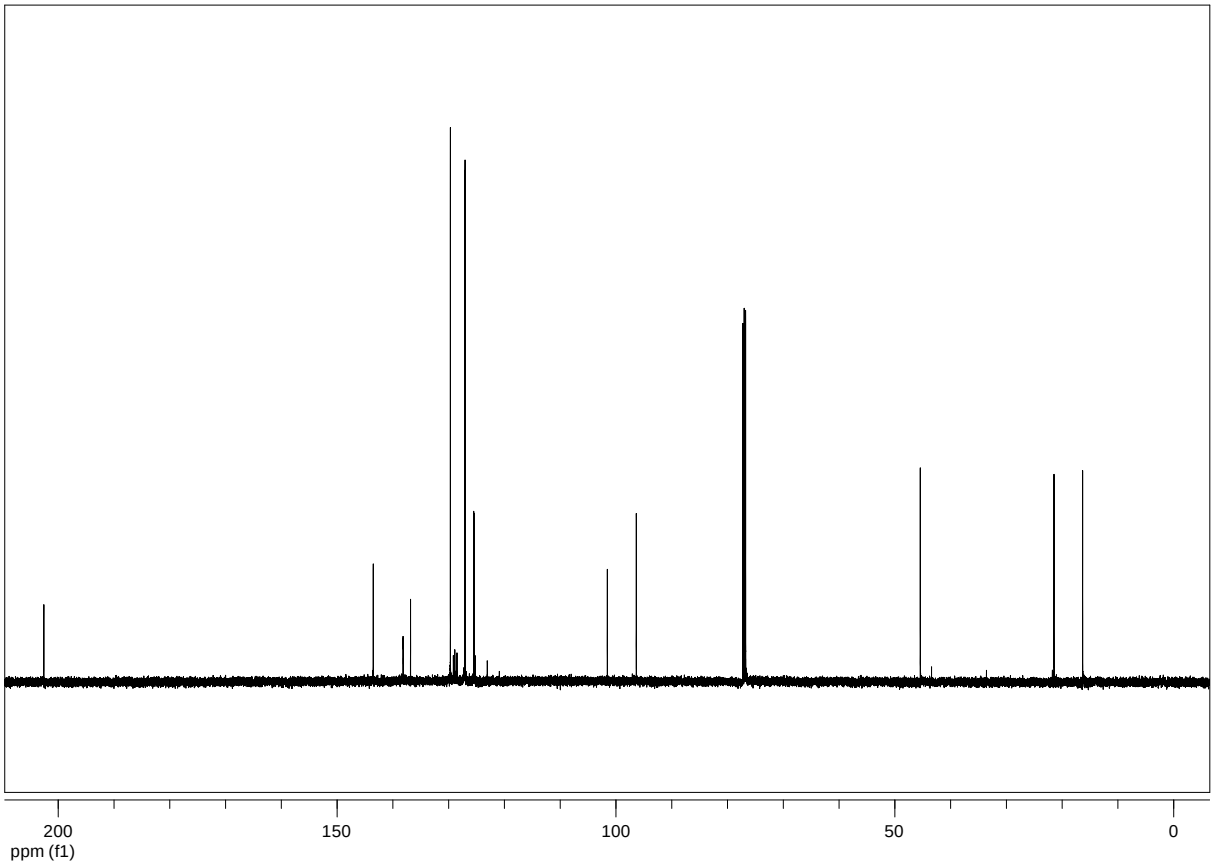
N-Phthalimido-2-methyl-4-(4-(trifluoromethyl)phenyl)-buta-2,3-dien-1-amine (8b)



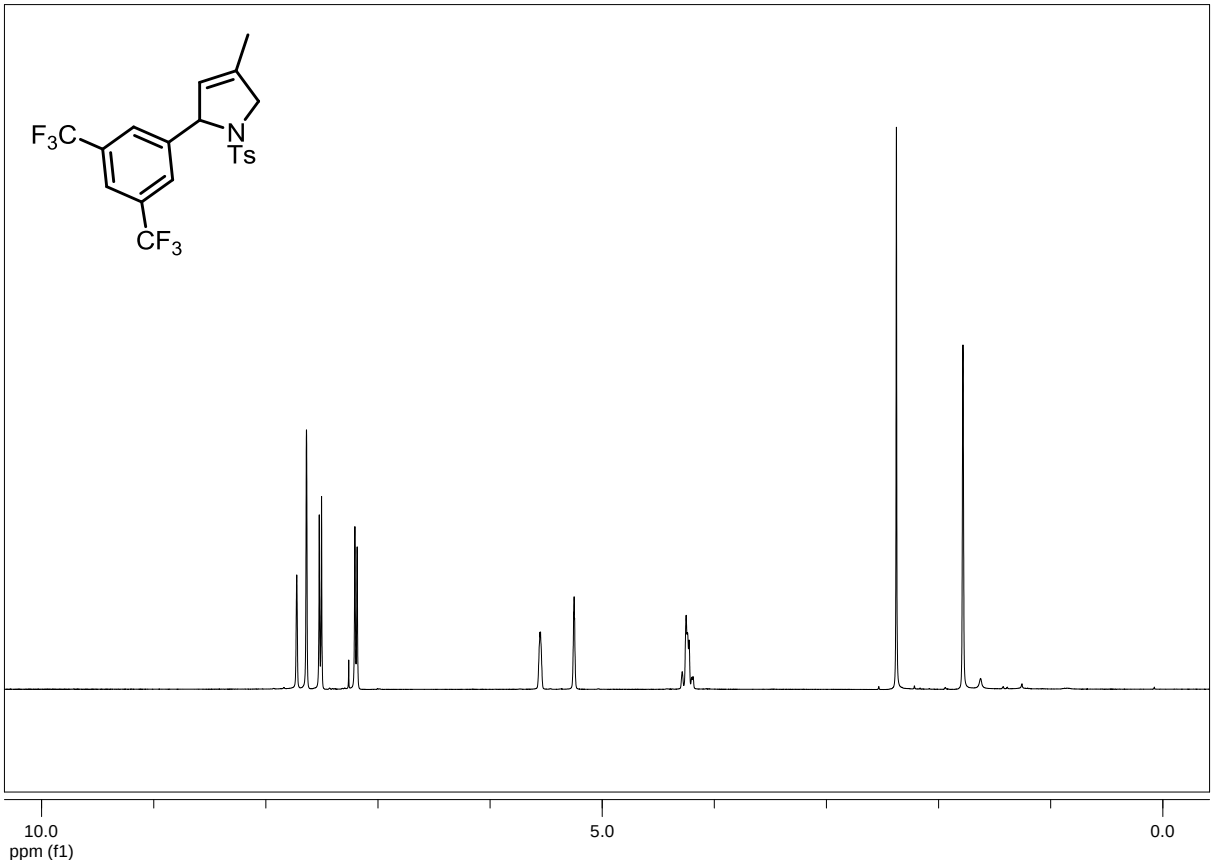


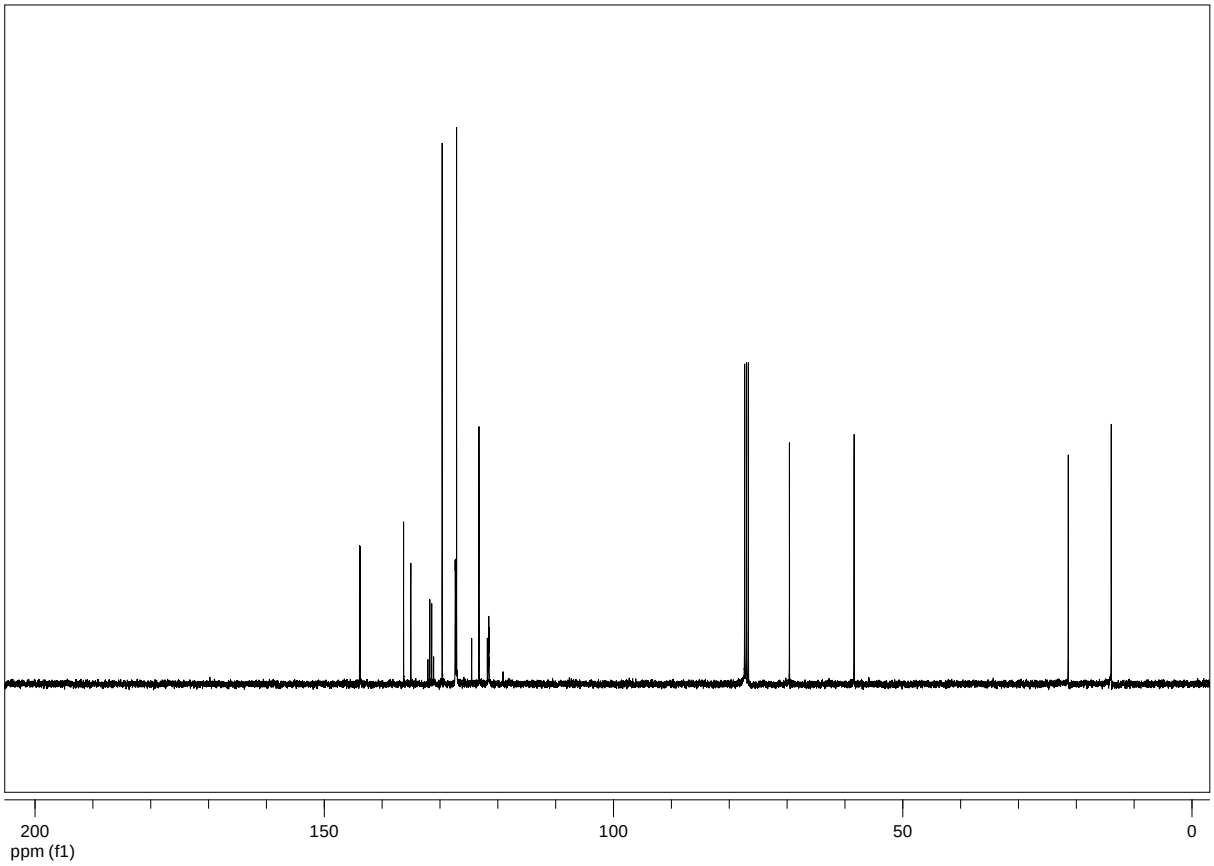
N-(*p*-Toluolsulfonyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)-buta-2,3-dien-1-amine (1b)



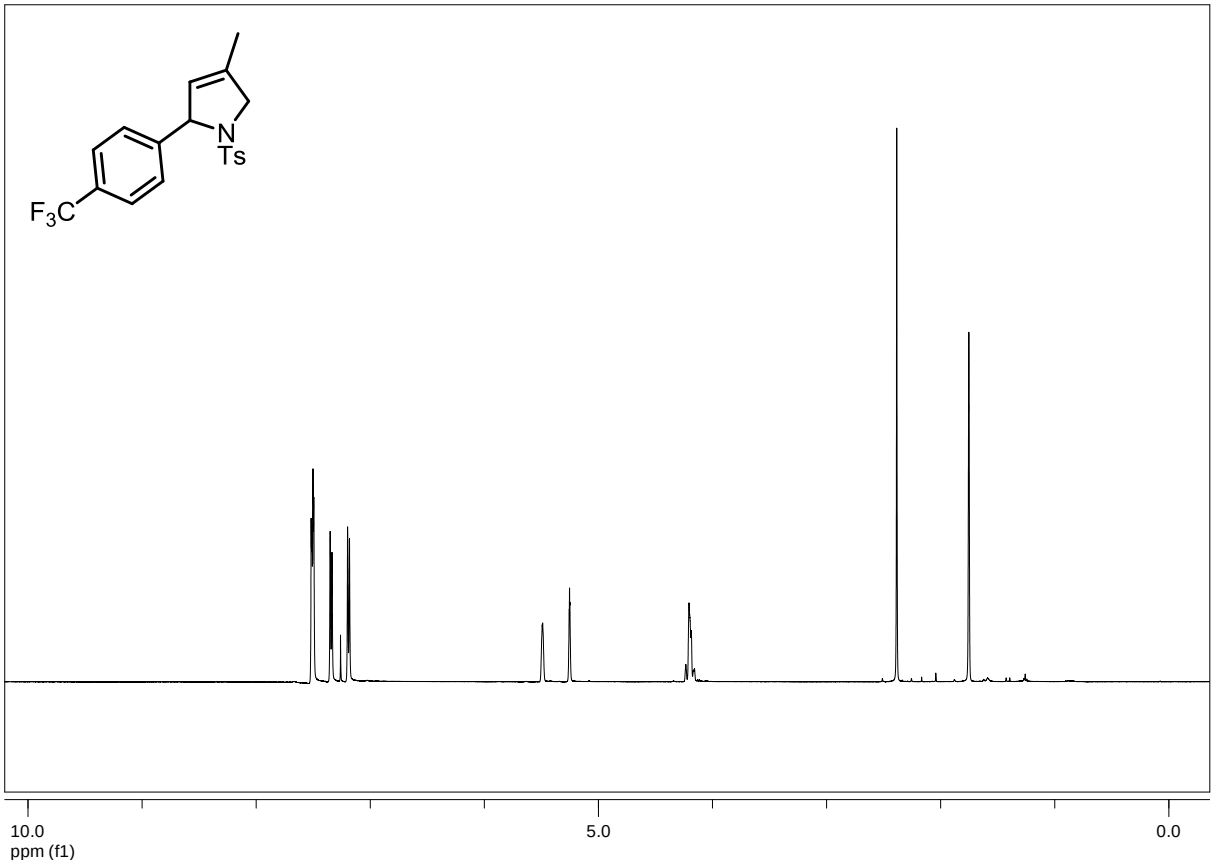


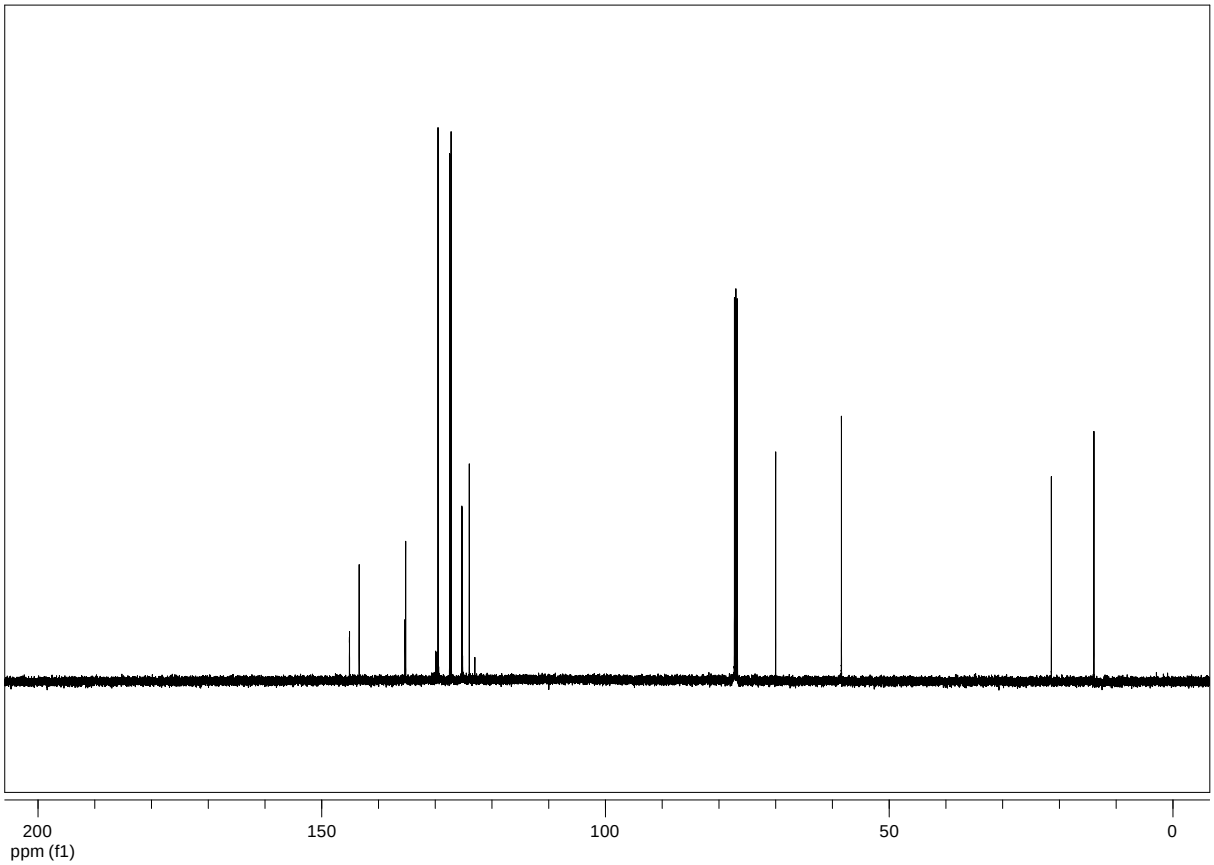
2-(3,5-bis(trifluoromethyl)phenyl)-4-methyl-1-tosyl-3-pyrroline (2a)



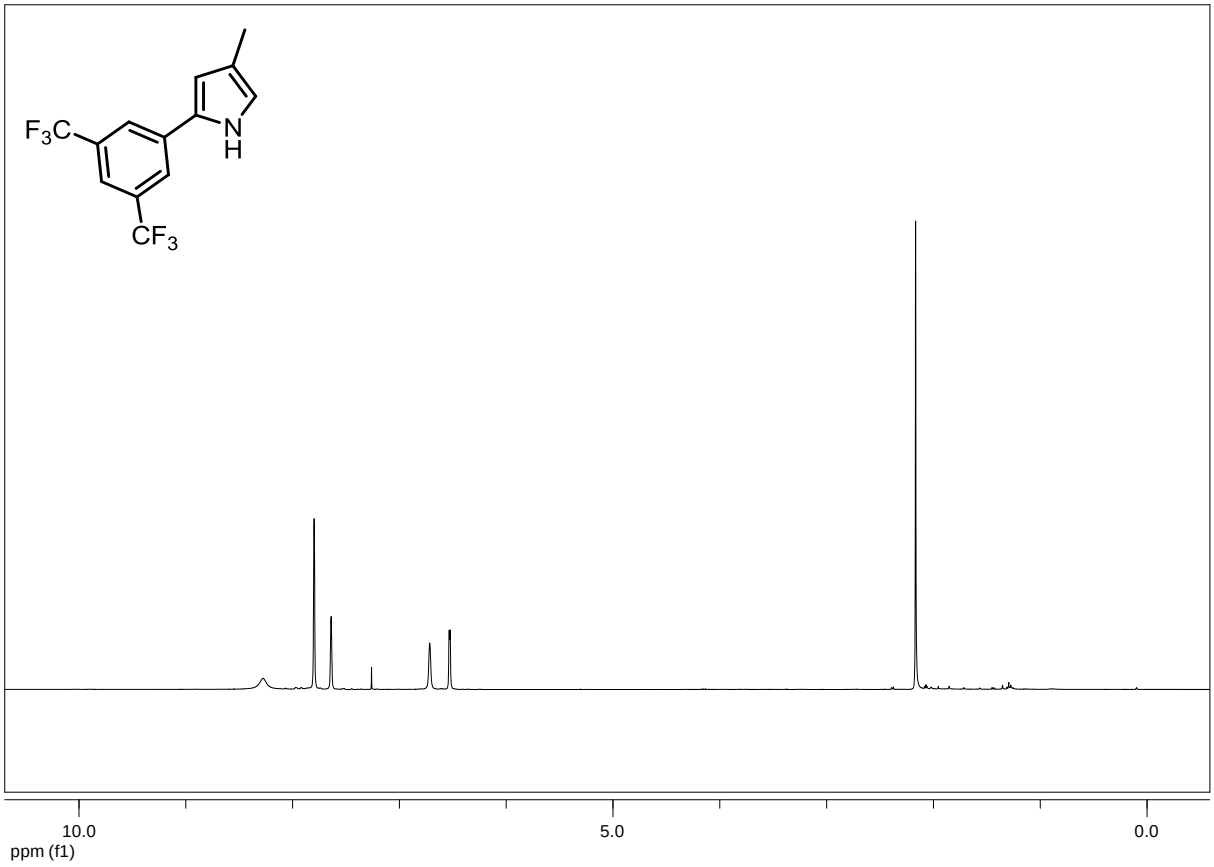


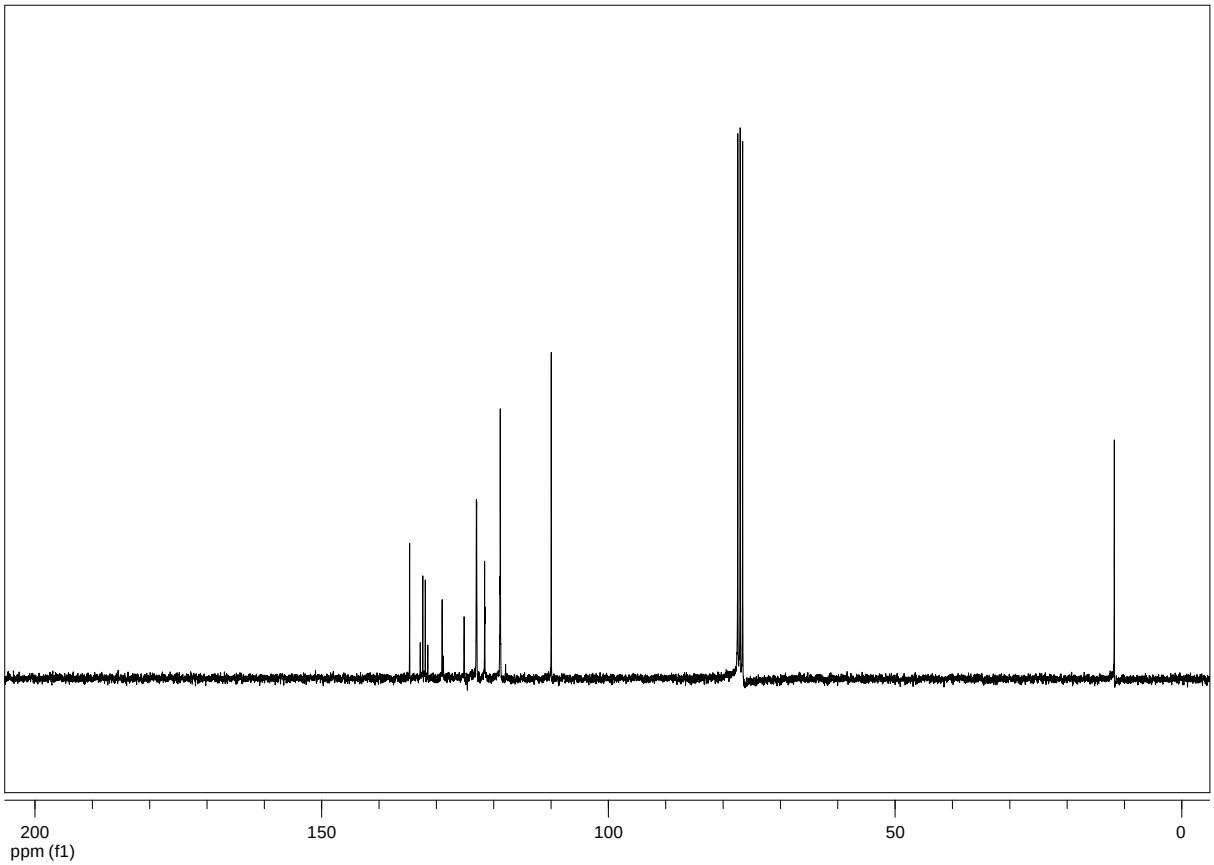
4-Methyl-1-tosyl-2-(4-(trifluormethyl)phenyl)-3-pyrroline (2b)



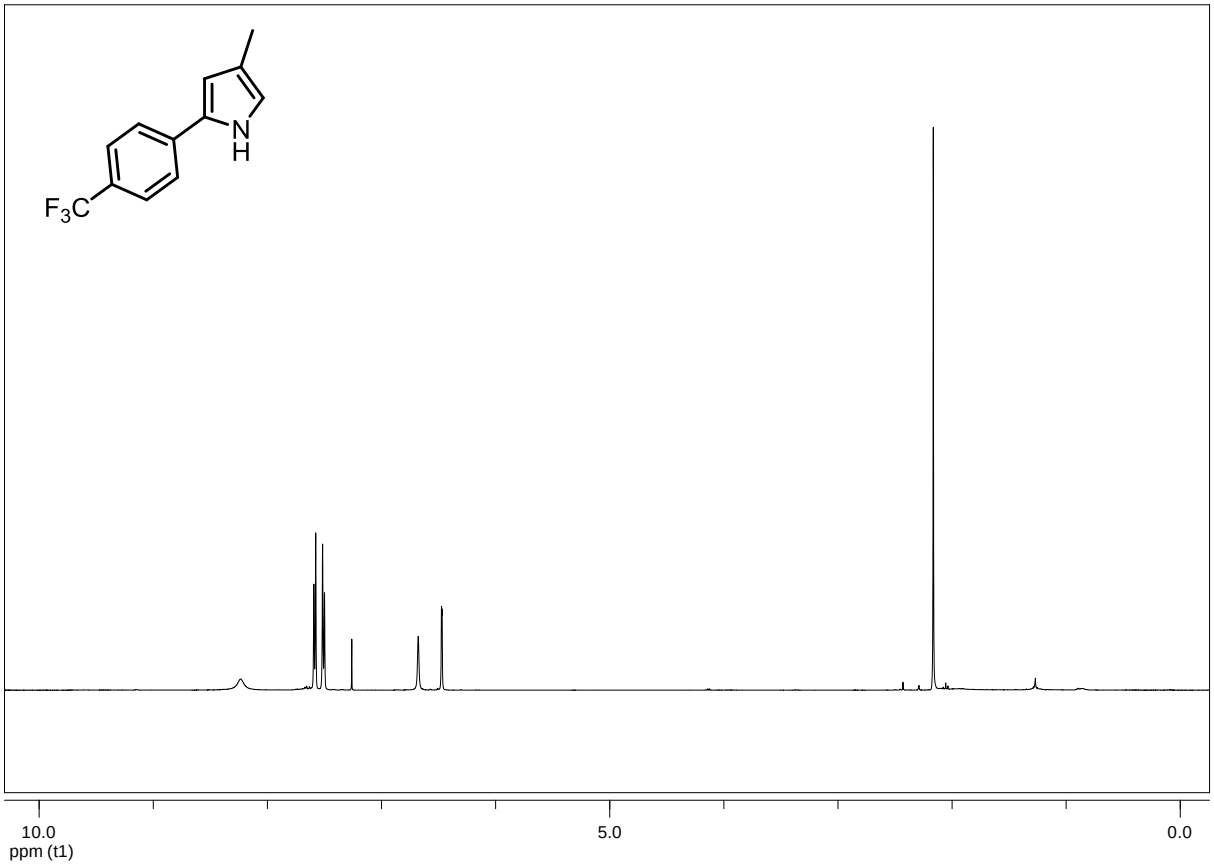


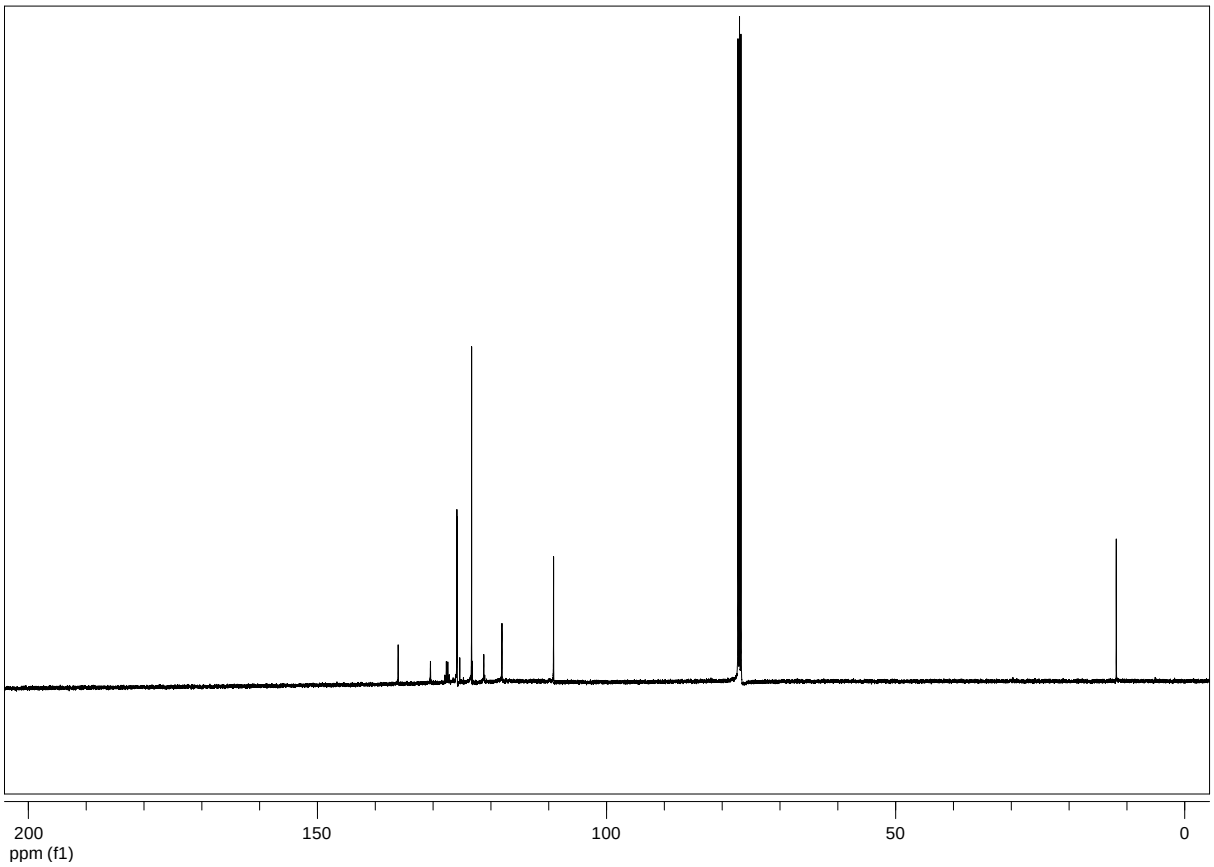
4-Methyl-2-(3,5-bis(trifluoromethyl)phenyl)-1H-pyrrole (3a)



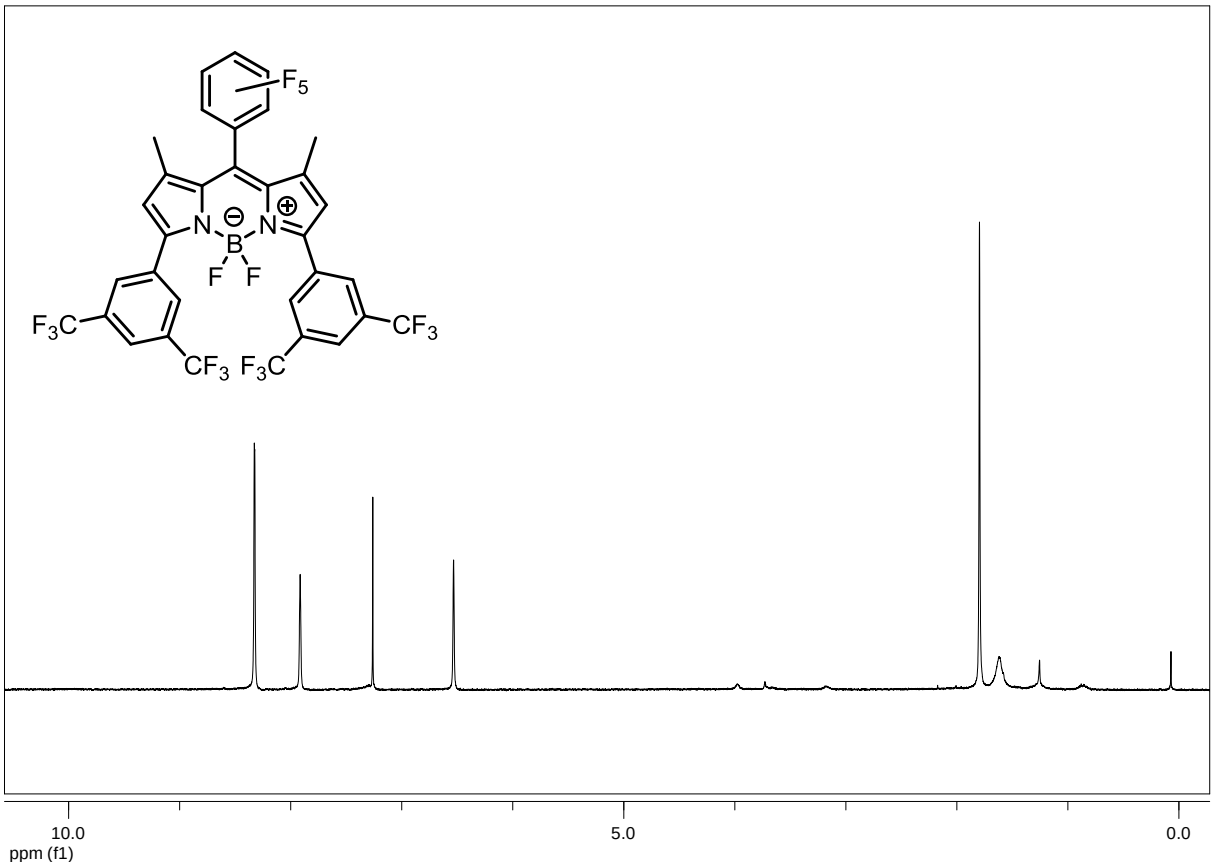


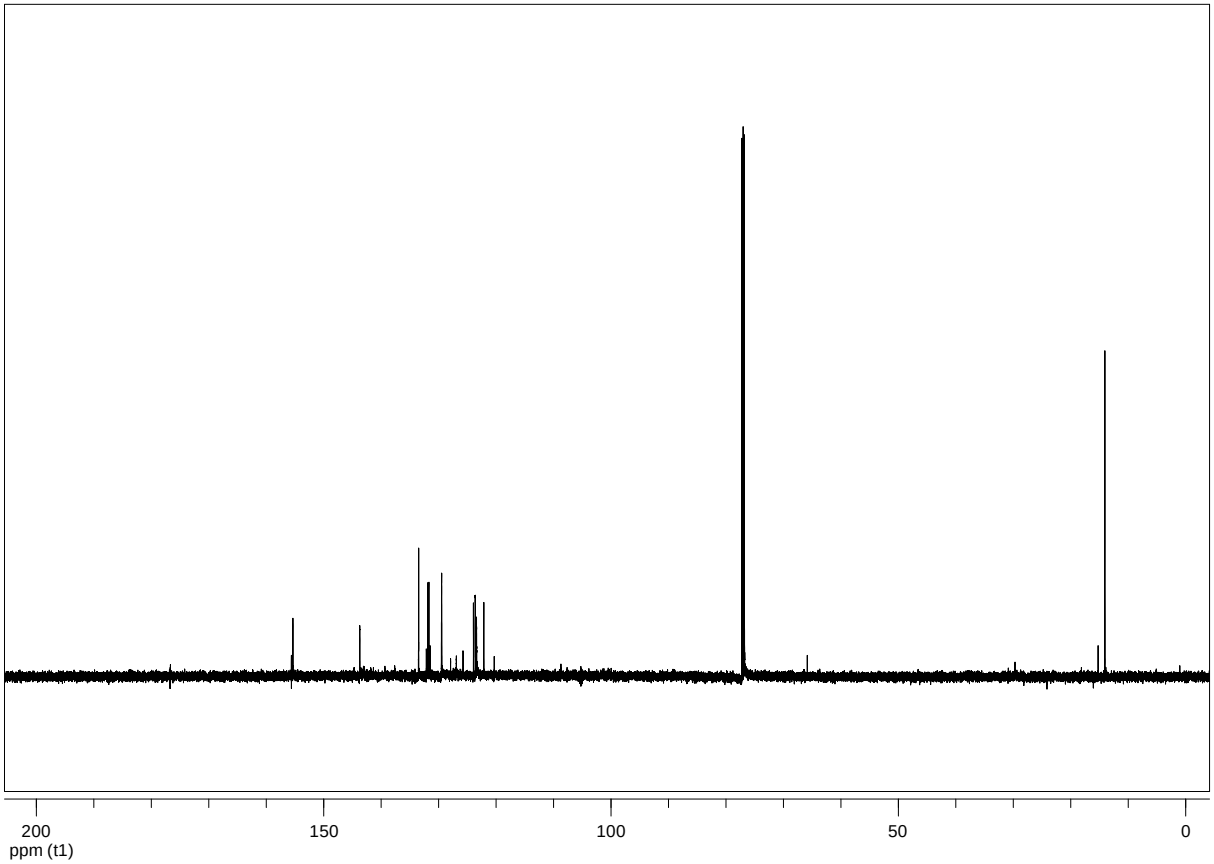
4-Methyl-2-(4-(trifluoromethyl)phenyl)-1H-pyrrole (3b)





4,4-Difluoro-4-bora-3,5-bis-(3,5-bis(trifluoromethyl)phenyl)-1,7-dimethyl-3a,4a-diaza-s-indacene-8-yl)-pentafluorobenzole (4a)





4,4-Difluoro-4-bora-3,5-bis-(4-(trifluoromethyl)phenyl)-1,7-dimethyl-3a,4a-diaza-s-indacene-8-yl-pentafluorobenzole (4b)