

Supporting Information

Copper-Catalyzed Nucleophilic Trifluoromethylation of Propargylic Halides

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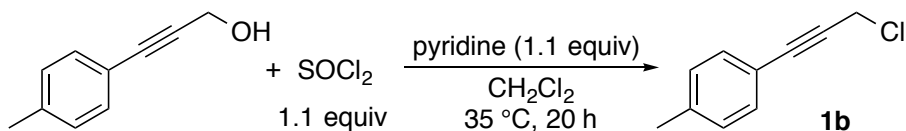
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General Methods.

¹H NMR (270 MHz) and ¹³C NMR (67.8 MHz) spectra were measured on a JEOL Excalibur 270 spectrometer using CDCl₃ as solvent unless otherwise noted. ¹⁹F NMR (471 MHz) spectra were recorded on a JEOL JNM-ECP 500 spectrometer. HPLC analyses were performed on Hitachi L-7100 and apparatus equipped with a UV detector using 25 cm x 4.6 mm DAICEL Chiralpak OJ-H columns. Elemental analyses were performed at Microanalytical Center of The University of Tokyo. Mass spectra were measured on a JEOL JMS-700 mass spectrometer. Weight of reagents were measured on Mettler Toledo AL204 Laboratory Balance

All reactions were carried out under dry nitrogen atmosphere. Solvents were dried by the usual methods, then distilled under N₂ and degassed before use. CF₃SiMe₃ is commercially available and was distilled before use. Potassium fluoride (KF) was dried under vacuum at 190 °C overnight and stored in a glove box. Copper (I) thiophene 2-carboxylate (CuTC) was prepared according to the reported method.^{S1} 3-Phenylpropargyl chloride (**1a**) was prepared by the reaction of the corresponding propargylic alcohol with PCl₃ and pyridine.^{S2} Other primary propargylic alcohols were prepared by the reaction of the corresponding propargylic alcohol with SOCl₂ and pyridine as described below. Secondary propargylic chlorides were prepared from corresponding alcohols and PPh₃ in CCl₄.^{S3} Trifluoromethylated products such as **2a**,^{S4} **2b**,^{S4} **2d**,^{S4} **2h**,^{S4} **2k**,^{S4} **2l**^{S2} and **3l**^{S2} were known compounds.

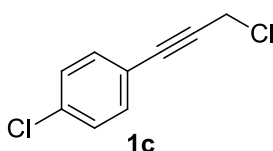
Preparation of Primary Propargylic Halides (1b-1k)



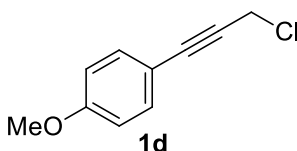
A typical experimental procedure for the preparation of 1-(3-chloroprop-1-yn-1-yl)-4-methylbenzene (**1b**). In a 50 mL Schlenk flask was placed 3-(*p*-tolyl)prop-2-yn-1-ol (732.6 mg, 5.0 mmol). Anhydrous and degassed CH₂Cl₂ (10 mL) and pyridine (440 μL, 5.5 mmol) were added. After the addition of SOCl₂ (400 μL, 5.5 mmol) at

0 °C, the reaction flask was kept 35 °C for 20 h. The solution was poured into water (20 mL) and the resulting mixture was extracted with CH₂Cl₂ (15 mL x 3). The combined extracts were washed with brine, and dried over anhydrous MgSO₄. After the concentration under reduced pressure, the resulting residue was purified by column chromatography (SiO₂, eluent: hexane) to give **1b** as yellow oil (584.3 mg, 3.55 mmol, 71% isolated yield).^{S5}

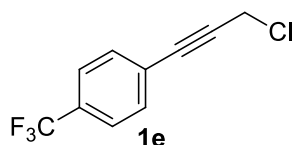
Spectroscopic data of other products are as follows.



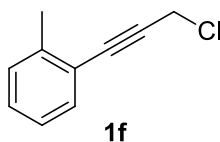
1c:^{S6} A pale yellow oil. ¹H NMR δ 7.38 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H), 4.36 (s, 2H). ¹³C NMR δ 135.0, 133.1, 128.7, 120.5, 85.1, 84.7, 30.9.



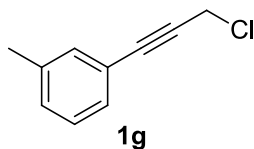
1d:^{S6} A yellow oil. ¹H NMR δ 7.39 (d, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 4.38 (s, 2H), 3.82 (s, 3H). ¹³C NMR δ 160.1, 133.4, 114.1, 114.0, 86.4, 82.5, 55.3, 31.5.



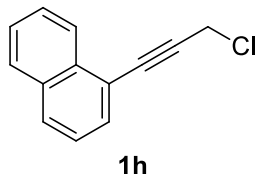
1e: A yellow oil. ¹H NMR δ 7.53-7.61 (m, 4H), 4.38 (s, 2H). ¹³C NMR δ 132.1, 130.6 (q, ²*J*_{C-F} = 32.7 Hz), 125.8 (q, ⁴*J*_{C-F} = 1.5 Hz), 125.3 (q, ³*J*_{C-F} = 3.7 Hz), 123.8 (q, ¹*J*_{C-F} = 272 Hz), 86.2, 84.8, 30.6. HRMS (EI) Calcd for C₁₀H₆ClF₃ [M]: 218.0110. Found: 218.0117.



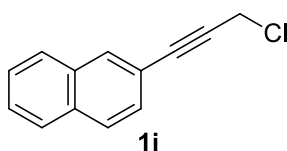
1f: A yellow oil. ¹H NMR δ 7.41 (d, *J* = 7.3 Hz, 1H), 7.10-7.26 (m, 3H), 4.42 (s, 2H), 2.43 (s, 3H). ¹³C NMR δ 140.6, 132.2, 129.5, 128.9, 125.5, 121.8, 87.6, 85.4, 31.3, 20.6. HRMS (EI) Calcd for C₁₀H₉Cl [M]: 164.0393. Found: 164.0387.



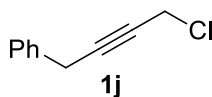
1g:^{S6} A pale yellow oil. ¹H NMR δ 7.13-7.30 (m, 4H), 4.37 (s, 2H), 2.33 (s, 3H). ¹³C NMR δ 138.0, 132.4, 129.8, 128.9, 128.2, 121.8, 86.5, 83.4, 31.2, 21.2.



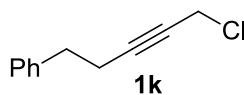
1h: A yellow oil. ¹H NMR δ 8.28-8.32 (m, 1H), 7.84-7.87 (m, 2H), 7.67-7.70 (m, 1H), 7.49-7.62 (m, 2H), 7.40-7.45 (m, 1H), 4.53 (s, 2H). ¹³C NMR δ 133.3, 133.1, 130.9, 129.4, 128.3, 127.0, 126.5, 126.0, 125.1, 119.7, 88.5, 84.6, 31.3. HRMS (EI) Calcd for C₁₃H₉Cl [M]: 200.0393. Found: 200.0395.



1i: A white solid, m.p. 41.4-42.3 °C. ¹H NMR δ 7.99 (s, 1H), 7.77-7.84 (m, 3H), 7.47-7.52 (m, 3H), 4.43 (s, 2H). ¹³C NMR δ 133.0, 132.8, 132.0, 128.2, 128.0, 127.8, 127.7, 127.0, 126.6, 119.3, 86.7, 84.0, 31.2. Anal Calcd for C₁₃H₉Cl: C, 77.81; H, 4.52. Found: C, 77.75; H, 4.66.

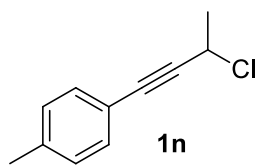


1j:^{S7} A yellow oil. ¹H NMR δ 7.22-7.33 (m, 5H), 4.20 (t, *J* = 2.3 Hz, 2H), 3.66 (t, *J* = 2.3 Hz, 2H). ¹³C NMR (C₆D₆) δ 136.3, 128.7, 128.1, 126.9, 85.2, 77.6, 30.8, 25.1.

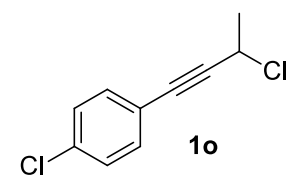


1k:^{S8} A yellow oil. ¹H NMR δ 7.20-7.33 (m, 5H), 4.13 (t, *J* = 2.3 Hz, 2H), 2.84 (t, *J* = 7.5 Hz, 2H), 2.53 (tt, *J* = 7.5 and 2.3 Hz, 2H). ¹³C NMR δ 140.3, 128.4, 126.4, 86.8, 75.7, 34.7, 31.1, 21.0.

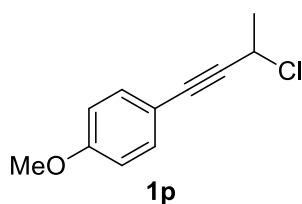
Spectroscopic data of secondary propargylic chlorides are as follows.



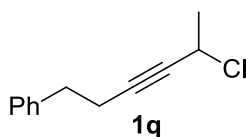
1n: A colorless oil. $^1\text{H NMR}$ δ 7.33 (d, $J = 8.0$ Hz, 2H), 7.12 (d, $J = 8.0$ Hz, 2H), 4.89 (q, $J = 6.8$ Hz, 1H), 2.35 (s, 3H), 1.84 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ δ 138.9, 131.7, 129.0, 119.0, 87.7, 85.0, 44.8, 26.7, 21.5. HRMS (EI) Calcd for $\text{C}_{11}\text{H}_{11}\text{Cl}$ [M]: 178.0549. Found: 178.0542.



1o: A white solid. $^1\text{H NMR}$ δ 7.37 (d, $J = 8.6$ Hz, 2H), 7.29 (d, $J = 8.6$ Hz, 2H), 4.87 (q, $J = 6.8$ Hz, 1H), 1.84 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ δ 134.9, 133.0, 128.7, 120.6, 89.3, 84.2, 44.3, 26.5. Anal Calcd for $\text{C}_{10}\text{H}_8\text{Cl}_2$: C, 60.38; H, 4.05. Found: C. 60.22; H. 4.15.

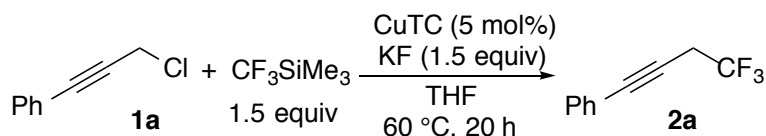


1p: A colorless oil. $^1\text{H NMR}$ δ 7.38 (d, $J = 8.8$ Hz, 2H), 6.84 (d, $J = 8.8$ Hz, 2H), 4.89 (q, $J = 6.8$ Hz, 1H), 3.81 (s, 3H), 1.84 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ δ 160.0, 133.3, 114.1, 113.9, 87.1, 85.4, 55.3, 45.0, 26.7. HRMS (EI) Calcd for $\text{C}_{11}\text{H}_{11}\text{ClO}$ [M]: 194.0498. Found: 194.0502.



1q: A colorless oil. $^1\text{H NMR}$ δ 7.19-7.33 (m, 5H), 4.64 (qt, $J = 6.8$ and 2.2 Hz, 1H), 2.83 (t, 7.5 Hz, 2H), 2.52 (dt, $J = 7.5$ and 2.2 Hz, 2H), 1.70 (d, $J = 6.8$ Hz, 3H). $^{13}\text{C NMR}$ δ 140.4, 128.5, 128.4, 126.3, 85.7, 80.5, 44.7, 34.8, 26.9, 21.0. HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{13}\text{Cl}$ [M]: 192.0706. Found: 192.0707.

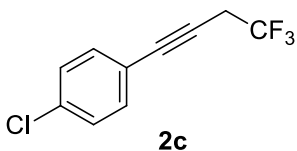
Copper-Catalyzed Trifluoromethylation of Propargylic Halides (1)



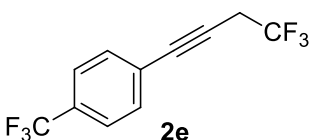
A typical experimental procedure for the reaction of 3-phenyl propargyl chloride (**1a**) with CF_3SiMe_3 is described below. In a 20 mL Schlenk flask were placed CuTC (4.7 mg, 0.025 mmol) and KF (43.8 mg, 0.75 mmol). Anhydrous and degassed THF (3.0 mL) was added, and then the mixture was magnetically stirred at room temperature. After the addition of **1a** (75.6 mg, 0.50 mmol) and CF_3SiMe_3 (110 μL , 0.74 mmol), the reaction flask was kept at 60 °C for 20 h. The solution was poured into water (5 mL) and the resulting mixture was extracted with diethyl ether (30 mL x 3). The combined extracts were washed with brine, and dried over anhydrous MgSO_4 . After the concentration under reduced pressure, the resulting residue was purified by column chromatography (SiO_2 , eluent: hexane) to give **2a** as a colorless oil (67.6 mg, 0.367 mmol, 73% isolated yield)^{S4}

In all of the reactions noted in Table 2, the formation of only a small amount (less than 5%) of the allenyl compounds **3b-3k** was confirmed in the crude products.

Isolated yields and spectroscopic data of other products **2** are as follows.

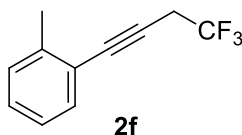


2c: 71% yield. A pale yellow oil. ^1H NMR 7.35-7.39 (m, 2H), 7.28-7.32 (m, 2H), 3.27 (q, $J = 9.5$ Hz, 2H). ^{13}C NMR δ 134.8, 133.1, 128.7, 124.1 (q, $^1J_{\text{C-F}} = 277$ Hz), 120.6, 82.3, 78.5 (q, $^3J_{\text{C-F}} = 5.2$ Hz), 26.8 (q, $^2J_{\text{C-F}} = 34.8$ Hz). ^{19}F NMR δ -68.6 (t, $J = 11.5$ Hz). HRMS (EI) Calcd for $\text{C}_{10}\text{H}_6\text{ClF}_3$ [M]: 218.0110 Found 218.0005.

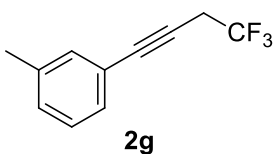


2e: 75% yield. A colorless oil. ^1H NMR δ 7.53-7.60 (br m, 4H), 3.30 (q, $J = 9.5$ Hz, 2H). ^{13}C NMR δ 132.1, 130.5 (q, $^2J_{\text{C-F}} = 32.7$ Hz), 126.0 (q, $^4J_{\text{C-F}} = 1.5$ Hz), 125.3 (q, $^3J_{\text{C-F}} = 3.9$ Hz), 124.0 (q, $^1J_{\text{C-F}} = 276$ Hz), 123.8 (q, $^1J_{\text{C-F}} = 271$ Hz), 83.1, 80.1 (q, $^3J_{\text{C-F}} = 5.0$ Hz), 26.8 (q, $^2J_{\text{C-F}} = 34.8$ Hz).

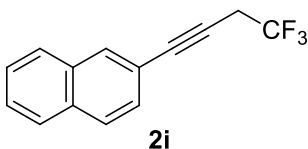
^{19}F NMR δ -65.2, -68.6 (t, J = 11.5 Hz). HRMS (EI) Calcd for $\text{C}_{11}\text{H}_6\text{F}_6$ [M]: 252.0374 Found 252.0375.



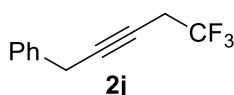
2f: 84% yield. A colorless oil. ^1H NMR δ 7.40 (d, J = 7.6 Hz, 1H), 7.11-7.26 (m, 3H), 3.31 (q, J = 9.6 Hz, 2H), 2.42 (s, 3H). ^{13}C NMR δ 140.6, 132.0, 129.5, 128.7, 125.5, 124.3 (q, $^1J_{\text{C-F}}$ = 276 Hz), 122.0, 83.3, 81.3 (q, $^3J_{\text{C-F}}$ = 4.8 Hz), 26.9 (q, $^2J_{\text{C-F}}$ = 34.6 Hz), 20.4. HRMS (EI) Calcd for $\text{C}_{11}\text{H}_9\text{F}_3$ [M]: 198.0656. Found: 198.0648.



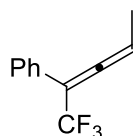
2g: 70% yield. A colorless oil. ^1H NMR δ 7.13-7.27 (m, 4H), 3.26 (q, J = 9.5 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (C_6D_6) δ 138.2, 132.8, 129.7, 129.2, 128.5, 124.9 (q, $^1J_{\text{C-F}}$ = 276 Hz), 122.5, 85.1, 77.6 (q, $^3J_{\text{C-F}}$ = 5.2 Hz), 26.3 (q, $^2J_{\text{C-F}}$ = 34.4 Hz), 20.9. HRMS (EI) Calcd for $\text{C}_{11}\text{H}_9\text{F}_3$ [M]: 198.0656. Found: 198.0653.



2i: 72% yield. A white solid, m.p. 48.0-49.0 °C. ^1H NMR δ 7.98 (s, 1H), 7.77-7.83 (m, 3H), 7.46-7.53 (m, 3H), 3.32 (q, J = 9.5 Hz, 2H). ^{13}C NMR δ 133.0, 132.8, 131.9, 128.3, 128.0, 127.7, 126.8, 126.6, 124.3 (q, $^1J_{\text{C-F}}$ = 276 Hz), 119.4, 84.7, 77.7 (q, $^3J_{\text{C-F}}$ = 5.0 Hz), 26.9 (q, $^2J_{\text{C-F}}$ = 34.8 Hz). ^{19}F NMR δ -68.7 (t, J = 11.5 Hz). Anal Calcd for $\text{C}_{14}\text{H}_9\text{F}_3$: C, 71.79; H, 3.87. Found: C, 71.64; H, 4.07.

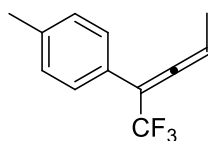


2j: 80% yield. A pale yellow oil. ^1H NMR δ 7.22-7.34 (m, 5H), 3.62 (t, J = 2.6 Hz, 2H), 3.22 (qt, J = 9.6 and 2.6 Hz, 2H). ^{13}C NMR δ 136.2, 128.6, 127.8, 126.7, 124.4 (q, $^1J_{\text{C-F}}$ = 276 Hz), 82.4, 70.5 (q, $^3J_{\text{C-F}}$ = 5.2 Hz), 26.2 (q, $^2J_{\text{C-F}}$ = 34.6 Hz), 24.9. ^{19}F NMR δ -69.1 (t, J = 11.5 Hz).



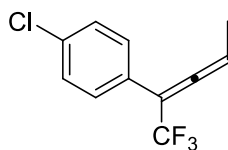
3m

3m: 89% yield. A colorless oil. ^1H NMR δ 7.29-7.44 (m, 5H), 5.88-5.95 (m, 1H), 1.88 (d, $J = 7.3$ Hz, 3H). ^{13}C NMR δ 205.1 (q, $^3J_{\text{C-F}} = 4.1$ Hz), 130.3, 128.6, 127.9, 127.0, 123.5 (q, $^1J_{\text{C-F}} = 273$ Hz), 101.2 (q, $^2J_{\text{C-F}} = 34.2$ Hz), 94.7, 13.3. ^{19}F NMR δ -62.8. HRMS (EI) Calcd for $\text{C}_{11}\text{H}_9\text{F}_3$ [M]: 198.0656. Found: 198.0652.



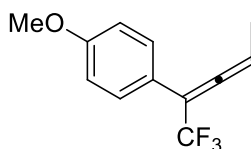
3n

3n: 79% yield. A colorless oil. ^1H NMR δ 7.31 (d, $J = 8.0$ Hz, 2H), 7.17 (d, $J = 8.0$ Hz, 2H), 5.86-5.95 (m, 1H), 2.35 (s, 3H), 1.87 (d, $J = 7.3$ Hz, 3H). ^{13}C NMR δ 204.8 (q, $^3J_{\text{C-F}} = 4.1$ Hz), 137.9, 129.3, 127.3, 127.0 (q, $^3J_{\text{C-F}} = 1.5$ Hz), 123.5 (q, $^1J_{\text{C-F}} = 273$ Hz), 101.1 (q, $^2J_{\text{C-F}} = 34.2$ Hz), 94.5, 21.1, 13.3 (q, $^5J_{\text{C-F}} = 1.5$ Hz). HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{11}\text{F}_3$ [M]: 212.0813. Found: 212.0812



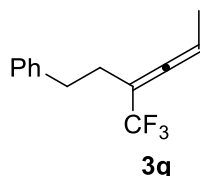
3o

3o: 81% Yield. A colorless oil. ^1H NMR δ 7.33-7.35 (br m, 4H), 5.89-5.99 (m, 1H), 1.88 (d, $J = 7.3$ Hz, 3H). ^{13}C NMR δ 205.0 (q, $^3J_{\text{C-F}} = 4.1$ Hz), 133.9, 128.82, 128.77, 128.3 (q, $^3J_{\text{C-F}} = 1.5$ Hz), 123.3 (q, $^1J_{\text{C-F}} = 273$ Hz), 100.5 (q, $^2J_{\text{C-F}} = 34.8$ Hz), 95.2, 13.2. ^{19}F NMR δ -63.0. HRMS (EI) Calcd for $\text{C}_{11}\text{H}_8\text{ClF}_3$ [M]: 232.0267. Found: 232.0262.



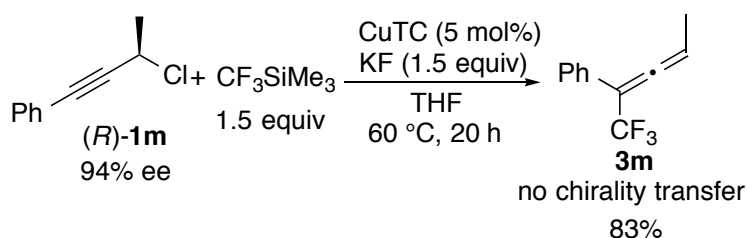
3p

3p: 77% Yield. A colorless oil. ^1H NMR δ 7.35 (d, $J = 8.6$ Hz, 2H), 6.86-6.92 (m, 2H), 5.82-5.93 (m, 1H), 3.81 (s, 3H), 1.86 (d, $J = 7.3$ Hz, 3H). ^{13}C NMR δ 204.5 (q, $^3J_{\text{C-F}} = 4.3$ Hz), 159.4, 128.3 (q, $^3J_{\text{C-F}} = 1.5$ Hz), 123.6 (q, $^1J_{\text{C-F}} = 273$ Hz), 122.4, 114.1, 100.7 (q, $^2J_{\text{C-F}} = 34.2$ Hz), 94.5, 55.2, 13.4 (q, $^5J_{\text{C-F}} = 1.5$ Hz). HRMS (EI) Calcd for $\text{C}_{12}\text{H}_{11}\text{F}_3\text{O}$ [M]: 228.0762. Found: 228.0757.



3q: 71% Yield. A colorless oil. ^1H NMR δ 7.26-7.32 (m, 2H), 7.18-7.21 (m, 3H), 5.49-5.58 (m, 1H), 2.77 (t, J = 7.6 Hz, 2H), 2.40-2.47 (m, 2H), 1.64 (d, J = 7.0 Hz, 3H). ^{13}C NMR δ 203.2 (q, $^3J_{\text{C-F}}$ = 4.1 Hz), 140.8, 128.43, 128.37, 126.1, 124.0 (q, $^1J_{\text{C-F}}$ = 273 Hz), 97.5 (q, $^2J_{\text{C-F}}$ = 33.8 Hz), 93.7, 33.5, 27.8, 13.4 (q, $^3J_{\text{C-F}}$ = 1.5 Hz). ^{19}F NMR δ -66.5. HRMS (EI) Calcd for $\text{C}_{13}\text{H}_{13}\text{F}_3$ [M]: 226.0969. Found: 226.0979

Copper-Catalyzed Trifluoromethylation of (*R*)-**1m**

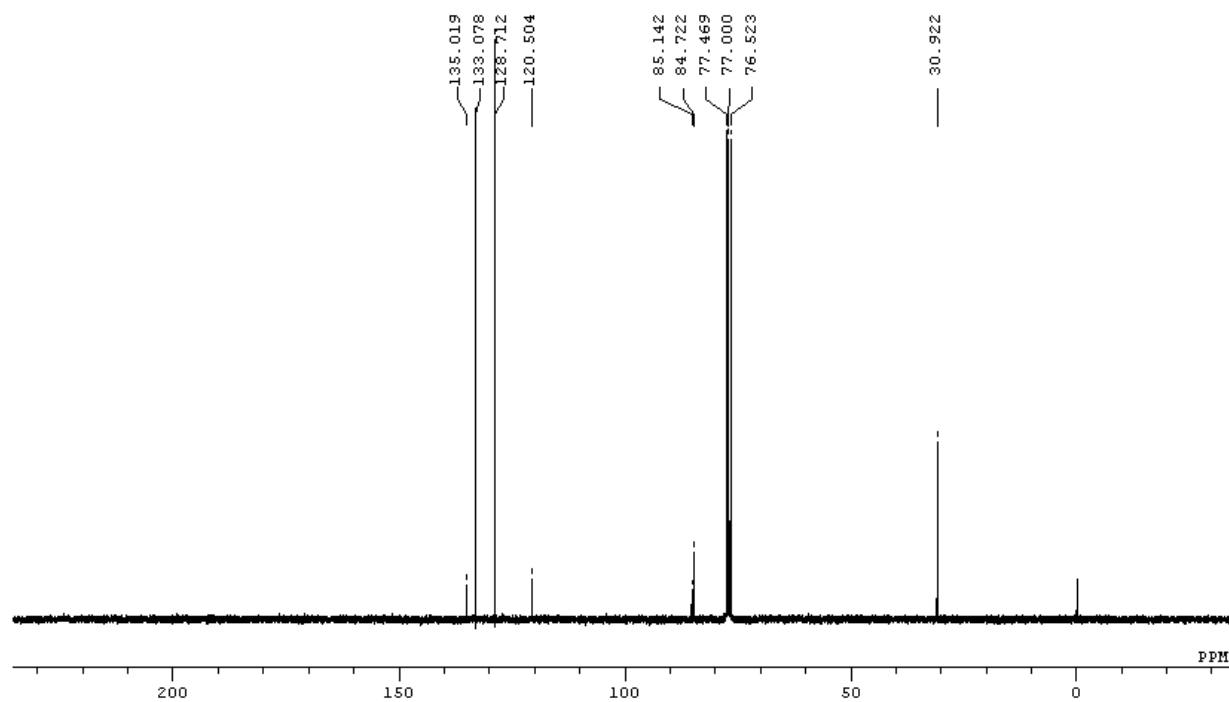
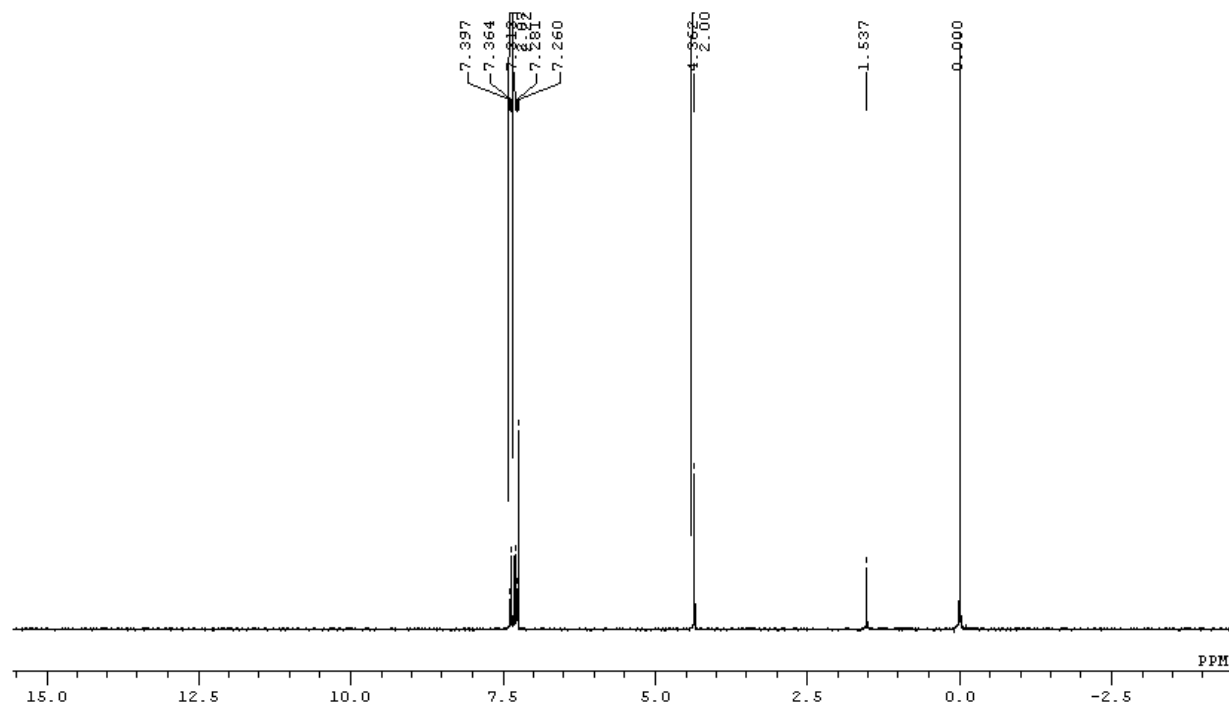
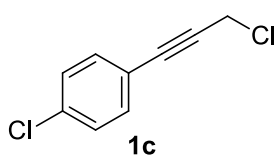


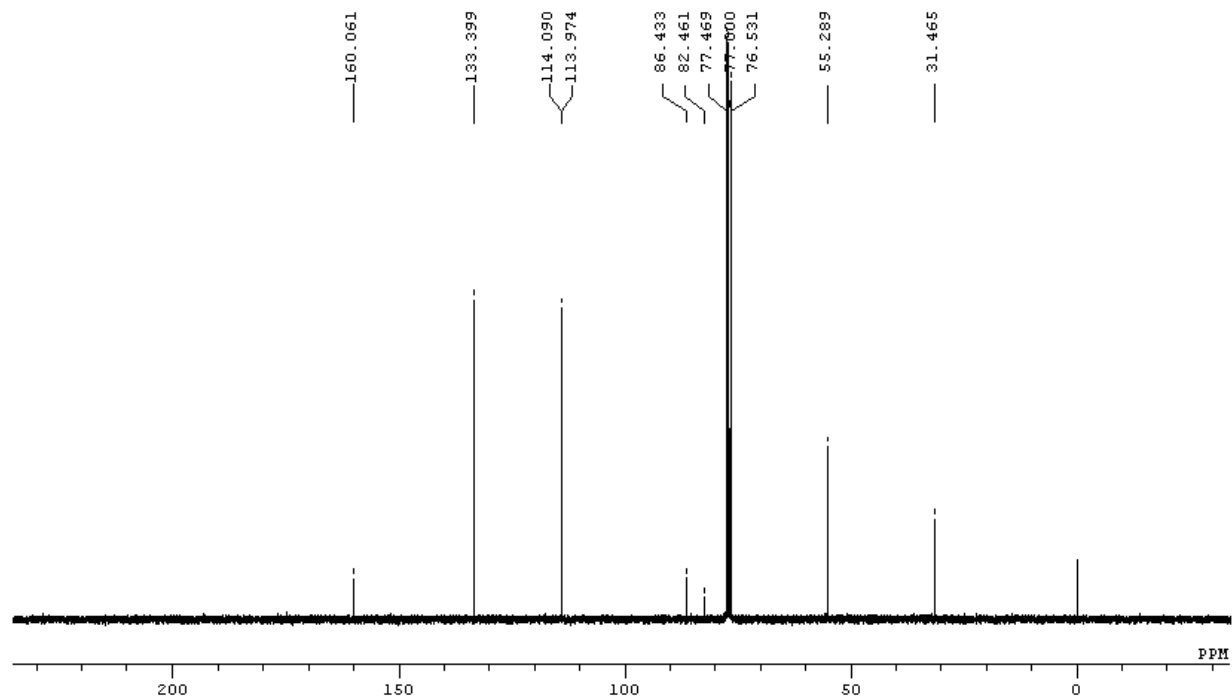
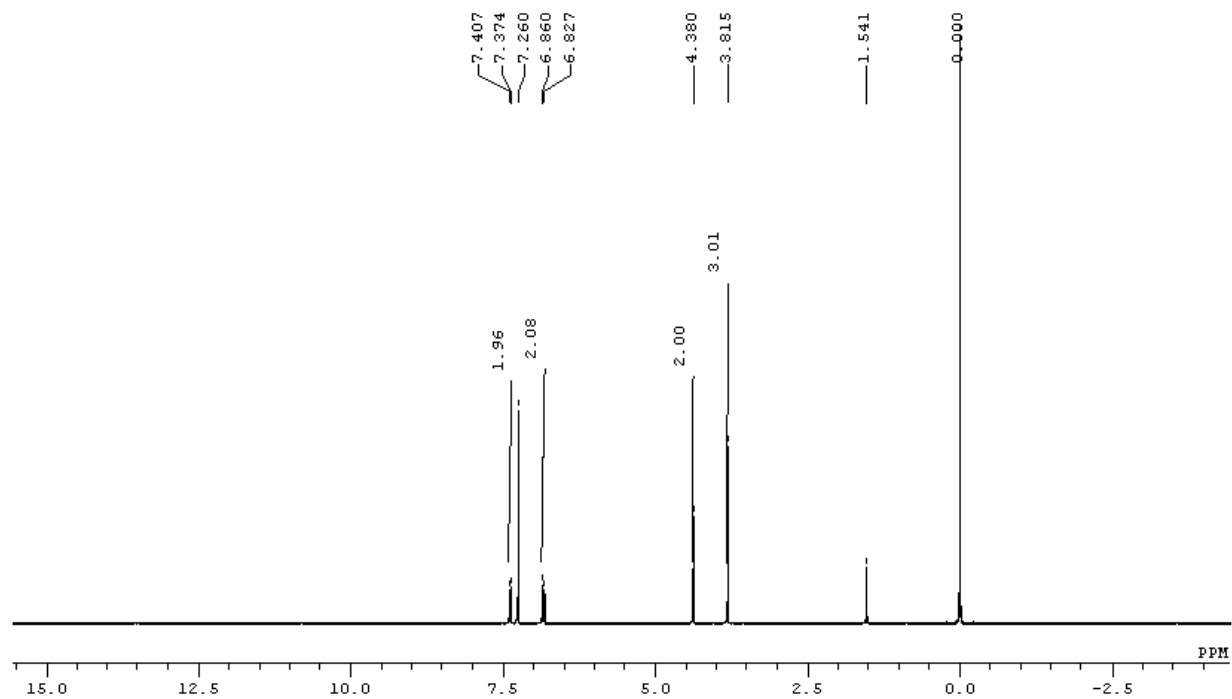
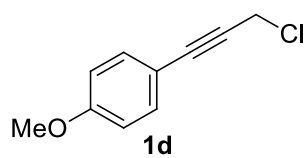
In a 20 mL Schlenk flask were placed CuTC (4.9 mg, 0.026 mmol) and KF (43.3 mg, 0.75 mmol). Anhydrous and degassed THF (3.0 mL) was added, and then the mixture was magnetically stirred at room temperature. After the addition of (*R*)-**1m**^{S3} (82.5 mg, 0.50 mmol, 94% ee) and CF_3SiMe_3 (110 μL , 0.74 mmol), the reaction flask was kept at 60 °C for 20 h. The solution was poured into water (5 mL) and the resulting mixture was extracted with diethyl ether (30 mL x 3). The combined extracts were washed with brine, and dried over anhydrous MgSO_4 . After the concentration under reduced pressure, the resulting residue was purified by column chromatography (SiO_2 , eluent: hexane) to give **3m** as a colorless oil (82.0 mg, 0.413 mmol, 83% isolated yield). The optical purity of **3m** was determined by HPLC analysis; DAICEL Chiralpak OJ-H (x2), hexane/*i*PrOH = 98 /2, flow rate 0.5 mL/min, λ = 254 nm, retention time 19.0 min and 19.8 min, 4% ee.

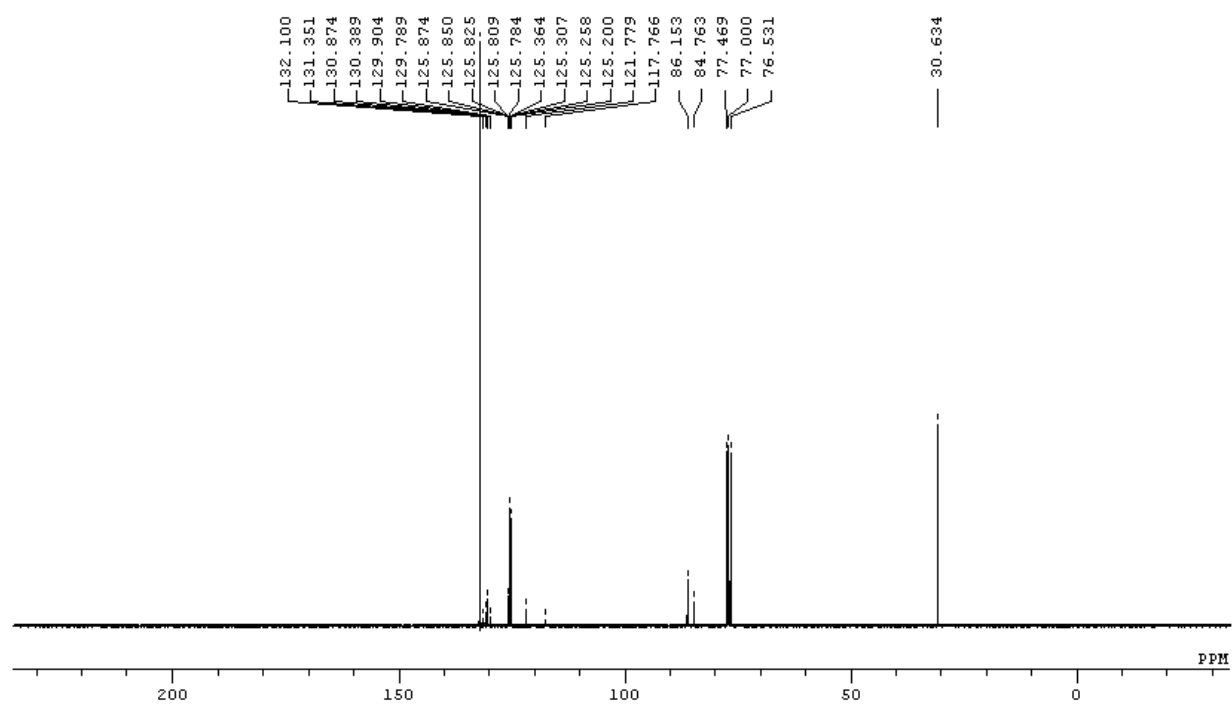
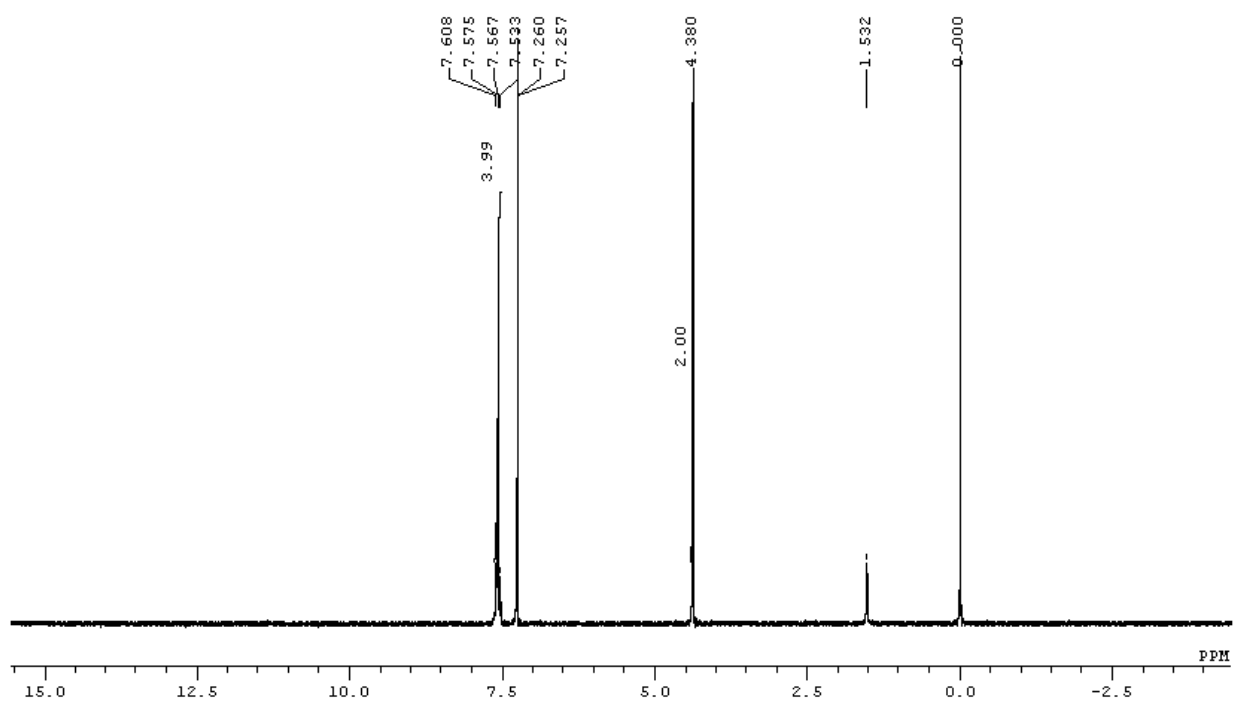
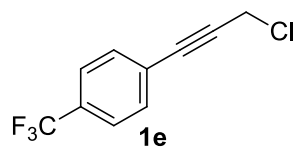
References and Notes

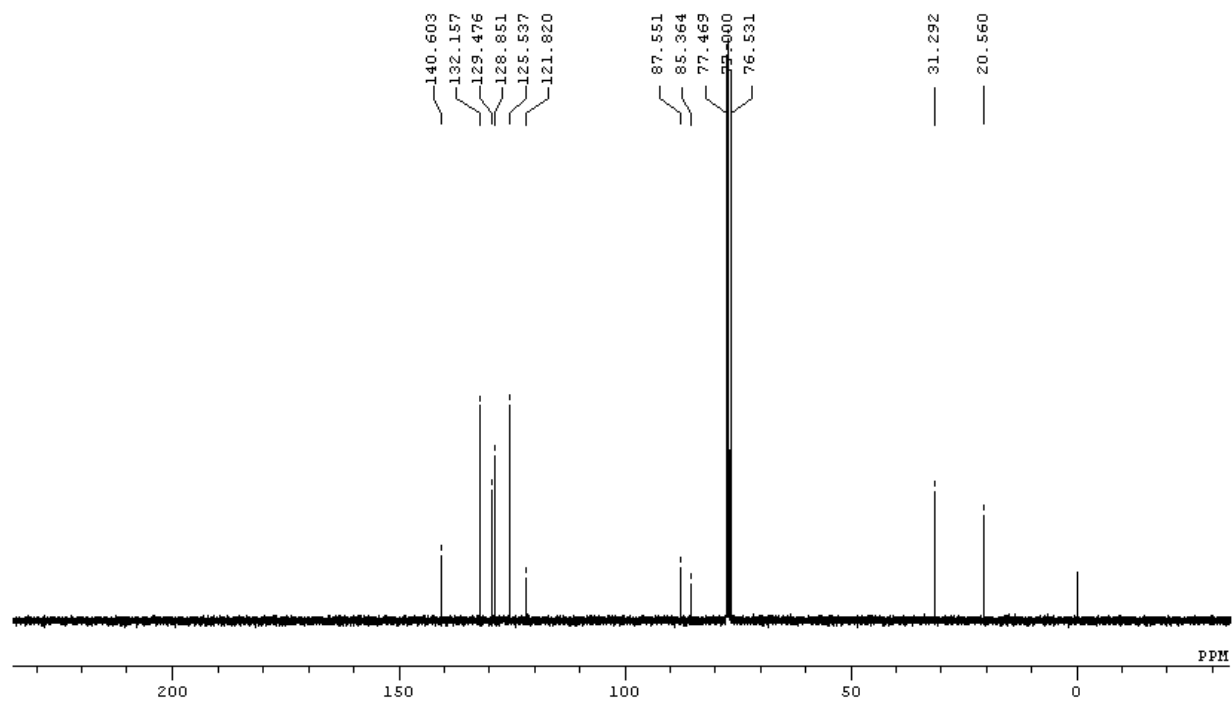
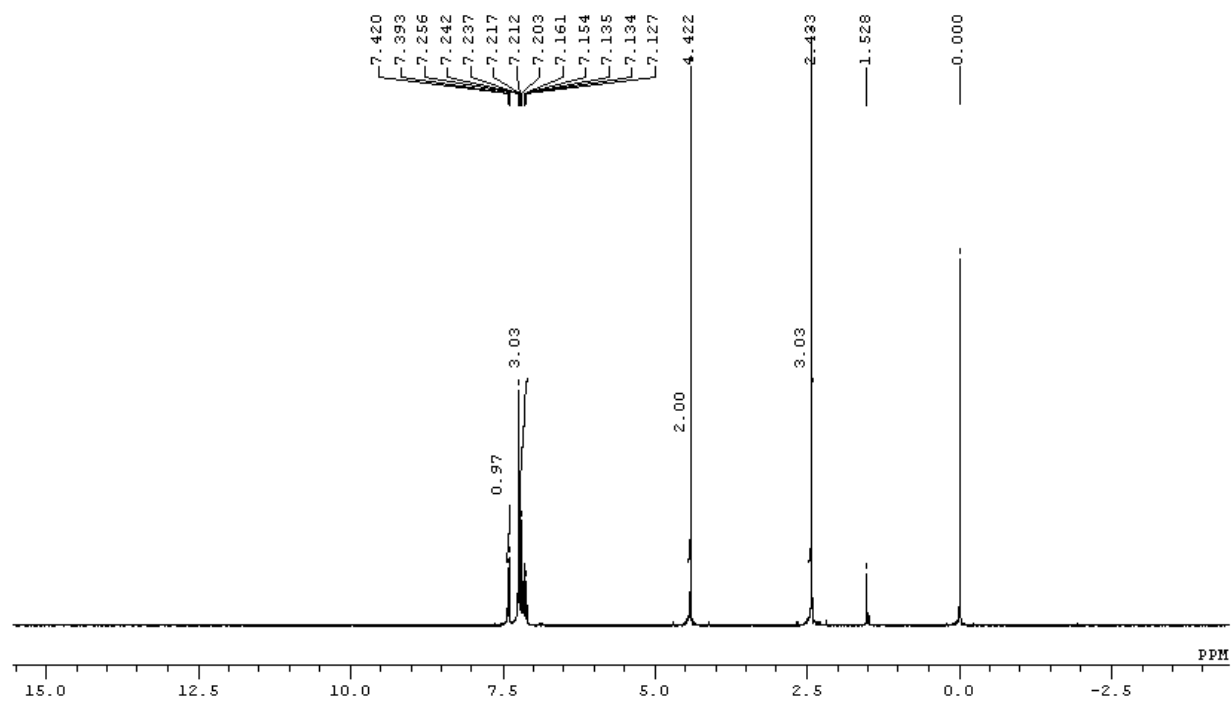
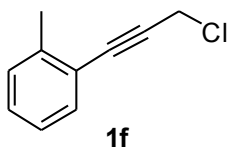
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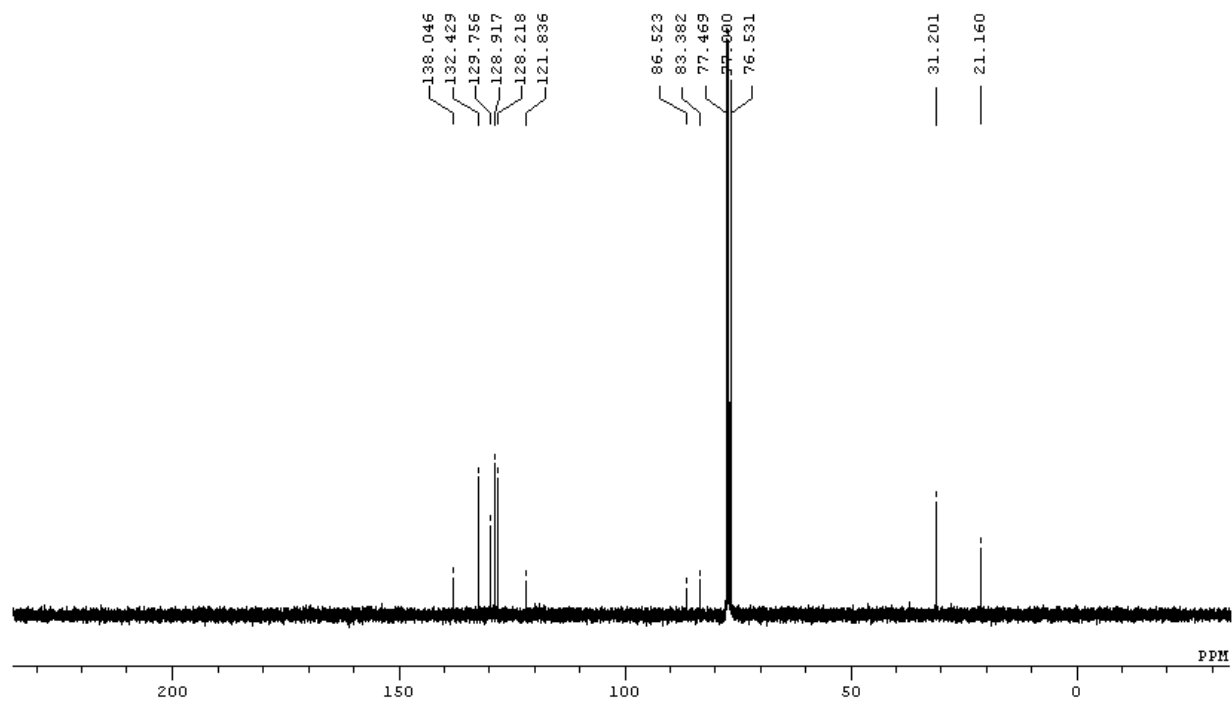
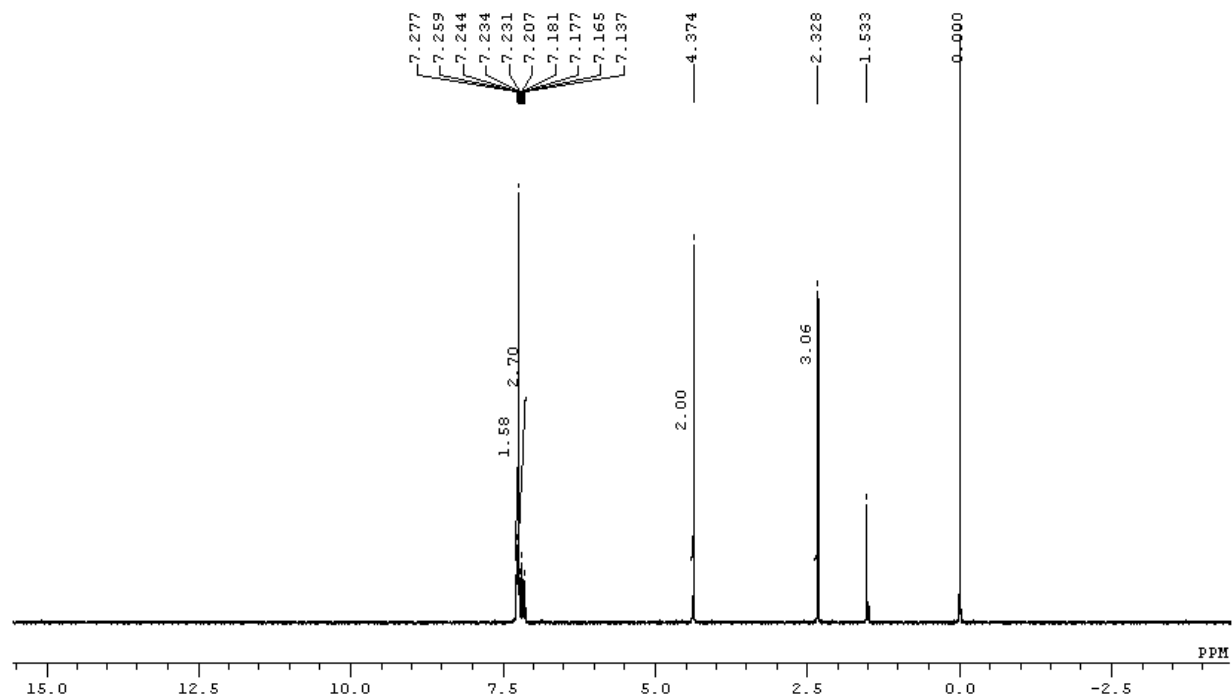
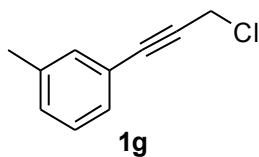
^1H , ^{13}C and ^{19}F NMR spectra

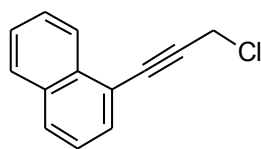












1h

