

Aqueous Suzuki couplings mediated by a hydrophobic catalyst

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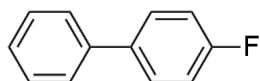
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Experimental section

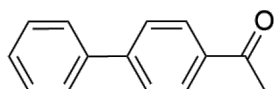
General procedures. All coupling reactions were performed under aerobic conditions. Compounds **2a** and **2b** were prepared following the procedures reported previously.^{1,2} All other chemicals and reagent grade solvents were used as received from commercial vendors. The Suzuki coupling reactions were analyzed by GCMS on Shimadzu GCMS-QP2010 SE equipped with a Restek Rtx-5MS capillary column. The identity of the cross-coupling products was confirmed by comparison with authentic samples. GC yields were determined by integration against dodecane as an internal standard. All NMR spectra were recorded at room temperature on JEOL JNM-ECZS or JEOL ECZ600R. Chemical shifts (δ) are listed as parts per million downfield from tetramethylsilane. Coupling constants (J) are listed in hertz. ¹H NMR spectra are referenced using the solvent residual signal at δ 7.26 for CDCl₃. ¹³C NMR spectra are referenced using the internal solvent signal at δ 77.16 for CDCl₃. The signal assignment of the carbon atoms is based on the DEPT ¹³C NMR spectroscopy. High resolution mass spectra were recorded on a JEOL JMS-T200GC AccuTOF GCx mass spectrometer.

Procedures of Suzuki reactions. A Schlenk tube was sequentially charged with a palladium complex (0.1 mol%), aryl halide (0.15 mmol), arylboronic acid (1.5 equiv), base (2.0 equiv), solvent (2 mL), and a Teflon-coated magnetic stir bar. The Schlenk tube was sealed with a Teflon stopper and heated in an oil bath at prescribed temperatures with stirring. After being heated for 12 hours, the reaction mixture was cooled to room temperature. All organic compounds were extracted by diethyl ether (3 mL x 3) or dichloromethane (3 mL x 3). The organic solution was separated from the aqueous layer, dried over MgSO₄, filtered, evaporated to dryness under reduced pressure, and subject to flash column chromatography on silica gel to afford the desired product.

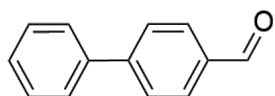
Experimental details of competitive reactions (Figure 2). A Schlenk tube was charged with **2a** (0.15 mmol), aryl bromides (0.03 mmol each), phenylboronic acid (0.23 mmol), K₃CO₃ (0.30 mmol), 2/1 (v/v) H₂O/*n*BuOH (2 mL), and a Teflon-coated magnetic stir bar. The Schlenk tube was capped with a Teflon stopper and heated in an oil bath prescribed at 100 °C with stirring for 2 hours. An aliquot was taken with a syringe, worked up with standard procedures, and subject to GCMS analysis. Yields were determined against dodecane as an internal standard, affording the Hammett plot.



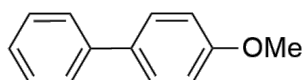
4-Fluorobiphenyl. Elution with EtOAc/*n*-hexane (1/4) yielded the product as a pale yellow solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.56 (m, 4, Ar), 7.44 (t, 2, $J = 7.71$, Ar), 7.35 (t, 1, $J = 7.41$, Ar), 7.13 (t, 2, $J = 8.70$, Ar). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 162.5 (d, $^1J_{\text{CF}} = 244.9$, CF), 140.3 (s, C), 137.3 (d, $^4J_{\text{CF}} = 3.2$, C), 128.8 (s, CH), 128.7 (d, $^3J_{\text{CF}} = 7.9$, CH), 127.3 (s, CH), 127.0 (s, CH), 115.6 (d, $^2J_{\text{CF}} = 21.3$, CH). $^{19}\text{F}\{^1\text{H}\}$ NMR (CDCl_3 , 564 MHz) δ -117.16. HRMS (EI): calcd for $\text{C}_{12}\text{H}_9\text{F}$ m/z 172.0694, found m/z 172.0692.



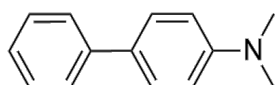
4-Acetylbiphenyl. Elution with EtOAc/*n*-hexane/ CH_2Cl_2 (1/4/1) yielded the product as colorless needle crystals. ^1H NMR (CDCl_3 , 600 MHz) δ 8.04 (d, 2, $J = 8.70$, Ar), 7.70 (d, 2, $J = 8.70$, Ar), 7.64 (d, 2, $J = 8.28$, Ar), 7.48 (t, 2, $J = 7.38$, Ar), 7.41 (t, 1, $J = 7.38$, Ar), 2.65 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 197.8 (C=O), 145.8 (C), 139.9 (C), 135.9 (C), 128.96 (CH), 128.92 (CH), 128.2 (CH, para), 127.28 (CH), 127.23 (CH), 26.7 (CH₃). HRMS (EI): calcd for $\text{C}_{14}\text{H}_{12}\text{O}$ m/z 196.0894, found m/z 196.0890.



4-Phenylbenzaldehyde. Elution with EtOAc/*n*-hexane/ CH_2Cl_2 (1/4/1) yielded the product as a colorless oil. ^1H NMR (CDCl_3 , 600 MHz) δ 10.07 (s, 1, CHO), 7.97 (d, 2, $J = 8.28$, Ar), 7.77 (d, 2, $J = 7.28$, Ar), 7.65 (d, 2, $J = 8.10$, Ar), 7.49 (t, 2, $J = 7.56$, Ar), 7.43 (t, 1, $J = 7.35$, Ar). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 191.9 (C=O), 147.2 (C), 139.7 (C), 135.2 (C), 130.3 (CH), 129.0 (CH), 128.5 (CH), 127.7 (CH), 127.4 (CH). HRMS (EI): calcd for $\text{C}_{13}\text{H}_{10}\text{O}$ m/z 182.0737, found m/z 182.0731.

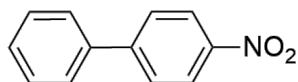


4-Methoxybiphenyl. Elution with EtOAc/*n*-hexane (1/4) yielded the product as an off-white solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.57 (d, 2, $J = 7.20$, Ar), 7.54 (d, 2, $J = 8.82$, Ar), 7.43 (t, 2, $J = 7.38$, Ar), 7.32 (t, 1, $J = 7.38$, Ar), 6.99 (d, 2, $J = 8.76$, Ar), 3.86 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 159.1 (C), 140.8 (C), 133.8 (C), 128.7 (CH), 128.2 (CH), 126.74 (CH), 126.65 (CH), 114.2 (CH), 55.3 (Me). HRMS (EI): calcd for $\text{C}_{13}\text{H}_{12}\text{O}$ m/z 184.0894, found m/z 184.0892.

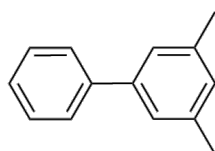


4-(Dimethylamino)biphenyl. Elution with EtOAc/*n*-hexane/ CH_2Cl_2 (1/4/1) yielded the product as an off-white solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.56 (d, 2, $J = 8.46$, Ar),

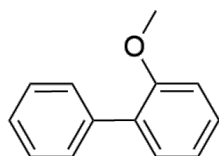
7.51 (d, 2, $J = 8.82$, Ar), 7.39 (t, 2, $J = 7.38$, Ar), 7.25 (t, 1, $J = 7.38$, Ar), 6.81 (d, 2, $J = 8.64$, Ar), 2.99 (s, 6, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 150.1 (C), 141.3 (C), 129.4 (C), 128.7 (CH), 127.8 (CH), 126.41 (CH), 126.10 (CH), 112.9 (CH), 40.7 (Me). HRMS (EI): calcd for $\text{C}_{14}\text{H}_{15}\text{N}$ m/z 197.1210, found m/z 197.1204.



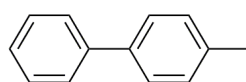
4-Nitrobiphenyl. Elution with $\text{EtOAc}/n\text{-hexane}/\text{CH}_2\text{Cl}_2$ (1/4/1) yielded the product as pale yellow needle crystals. ^1H NMR (CDCl_3 , 600 MHz) δ 8.31 (d, 2, $J = 8.94$, Ar), 7.75 (d, 2, $J = 9.00$, Ar), 7.64 (d, 2, $J = 6.96$ Ar), 7.51 (t, 2, $J = 7.14$, Ar), 7.46 (t, 1, $J = 7.20$, Ar). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 147.6 (C), 147.1 (C), 138.8 (C), 129.2 (CH), 128.9 (CH), 127.8 (CH), 127.4 (CH), 124.1 (CH). HRMS (EI): calcd for $\text{C}_{12}\text{H}_9\text{NO}_2$ m/z 199.0639, found m/z 199.0640.



3,5-Dimethylbiphenyl. Elution with $n\text{-hexane}$ yielded the product as a pale yellow oil. ^1H NMR (CDCl_3 , 600 MHz) δ 7.60 (d, 2, $J = 8.40$, Ar), 7.45 (t, 2, $J = 7.92$, Ar), 7.35 (t, 1, $J = 7.38$, Ar), 7.24 (s, 2, Ar), 7.03 (s, 1, Ar), 2.41 (s, 6, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 141.5 (C), 141.3 (C), 138.2 (C), 128.9 (CH), 128.6 (CH), 127.2 (CH), 127.1 (CH), 125.1 (CH), 21.4 (CH_3). HRMS (EI): calcd for $\text{C}_{13}\text{H}_{12}\text{O}$ m/z 184.0894, found m/z 184.0888.

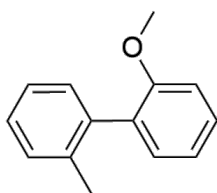


2-Methoxybiphenyl. Elution with $n\text{-hexane}$ yielded the product as a yellow oil. ^1H NMR (CDCl_3 , 600 MHz) δ 7.56 (d, 2, $J = 7.08$, Ar), 7.44 (t, 2, $J = 7.44$, Ar), 7.35 (m, 3, Ar), 7.06 (t, 1, $J = 7.44$, Ar), 7.02 (d, 1, $J = 7.44$, Ar), 3.84 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 156.4 (C), 138.5 (C), 130.9 (CH), 130.7 (C), 129.5 (CH), 128.6 (CH), 128.0 (CH), 126.9 (CH), 120.8 (CH), 111.2 (CH), 55.5 (CH_3). HRMS (EI): calcd for $\text{C}_{14}\text{H}_{14}$ m/z 182.1101, found m/z 182.1096.

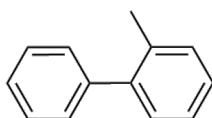


4-Methylbiphenyl. Elution with $\text{EtOAc}/n\text{-hexane}$ (1/4) yielded the product as a pale pink solid. ^1H NMR (CDCl_3 , 600 MHz) δ 7.61 (d, 2, $J = 8.28$, Ar), 7.53 (d, 2, $J = 8.16$, Ar), 7.46 (t, 2, $J = 7.38$, Ar), 7.35 (t, 1, $J = 7.38$, Ar), 7.28 (d, 2, $J = 7.80$, Ar), 2.43 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 141.1 (C), 138.3 (C), 137.0 (C), 129.5 (CH), 128.7 (CH), 126.98 (CH), 126.96 (CH), 21.1 (CH_3). HRMS (EI): calcd for $\text{C}_{13}\text{H}_{12}$ m/z 168.0944, found

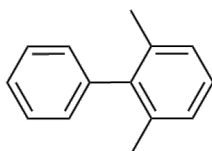
m/z 168.0943.



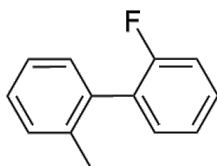
2-Methoxy-2'-methylbiphenyl. Elution with *n*-hexane yielded the product as a pale yellow oil. ^1H NMR (CDCl_3 , 600 MHz) δ 7.37 (ddd, 1, $J = 8.28, 7.44, 1.80$, Ar), 7.29 (m, 1, Ar), 7.28 (m, 1, Ar), 7.26 (m, 1, Ar), 7.21 (d, 1, $J = 7.20$, Ar), 7.17 (dd, 1, $J = 7.38, 1.70$, Ar), 7.04 (td, 1, $J = 7.41, 1.24$, Ar), 6.99 (dd, 1, $J = 8.28, 0.96$, Ar), 3.79 (s, 3, OMe), 2.17 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 156.7 (C), 138.7 (C), 136.9 (C), 131.1 (CH), 130.9 (C), 130.1 (CH), 129.7 (CH), 128.6 (CH), 127.4 (CH), 125.5 (CH), 120.5 (CH), 110.7 (CH), 55.5 (OCH₃), 20.0 (CH₃). HRMS (EI): calcd for $\text{C}_{14}\text{H}_{14}\text{O}$ m/z 198.1050, found m/z 198.1052.



2-Methylbiphenyl. Elution with *n*-hexane yielded the product as a colorless oil. ^1H NMR (CDCl_3 , 600 MHz) δ 7.44 (m, 2, Ar), 7.36 (m, 3, Ar), 7.29 (m, 2, Ar), 7.27 (m, 2, Ar), 2.30 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 142.0 (C), 141.9 (C), 135.3 (C), 130.3 (CH), 129.8 (CH), 129.2 (CH), 128.0 (CH), 127.2 (CH), 126.7 (CH), 125.7 (CH), 20.4 (CH₃). HRMS (EI): calcd for $\text{C}_{13}\text{H}_{12}$ m/z 168.0944, found m/z 168.0943.

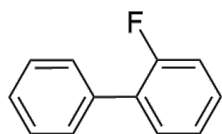


2,6-Dimethylbiphenyl. Elution with *n*-hexane yielded the product as a colorless oil. ^1H NMR (CDCl_3 , 600 MHz) δ 7.47 (t, 2, $J = 7.53$, Ar), 7.38 (t, 1, $J = 6.78$, Ar), 7.20 (m, 3, Ar), 7.16 (d, 2, $J = 7.50$, Ar), 2.08 (s, 6, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 141.9 (C), 141.1 (C), 136.0 (C), 129.0 (CH), 128.4 (CH), 127.3 (CH), 127.0 (CH), 126.6 (CH), 20.8 (CH₃). HRMS (EI): calcd for $\text{C}_{14}\text{H}_{14}$ m/z 182.1101, found m/z 182.1096.

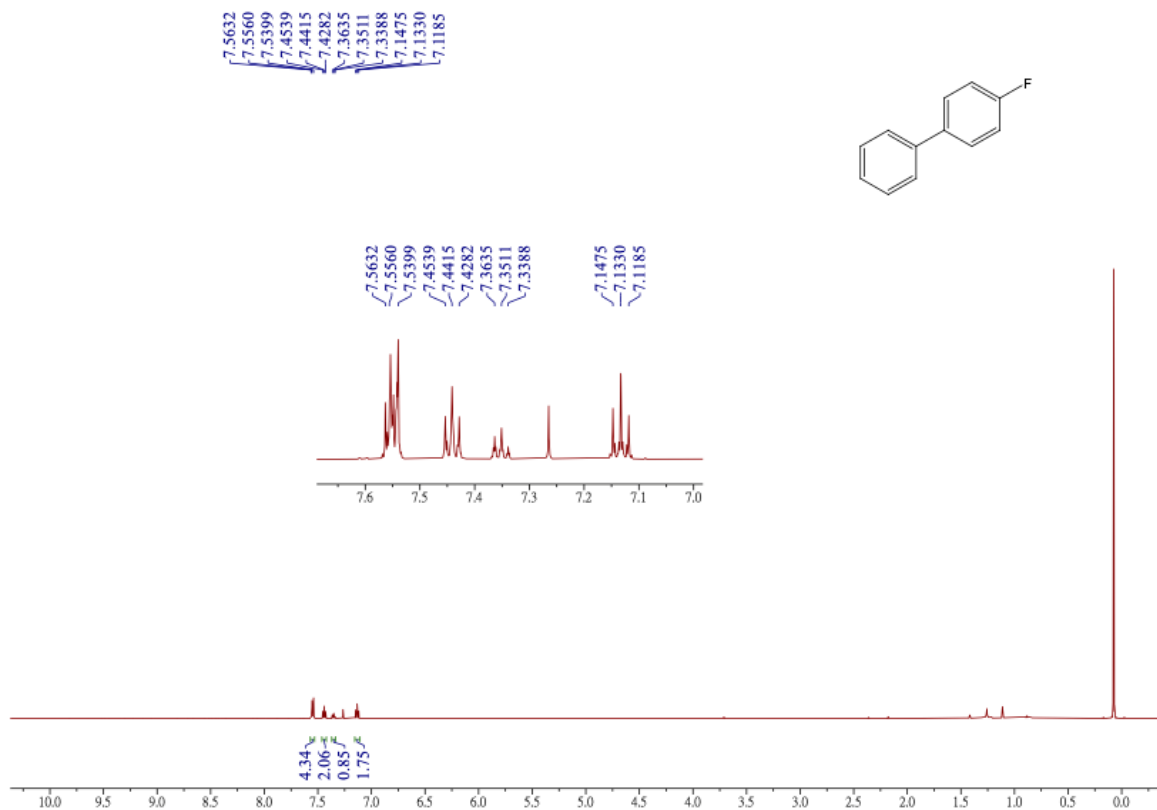


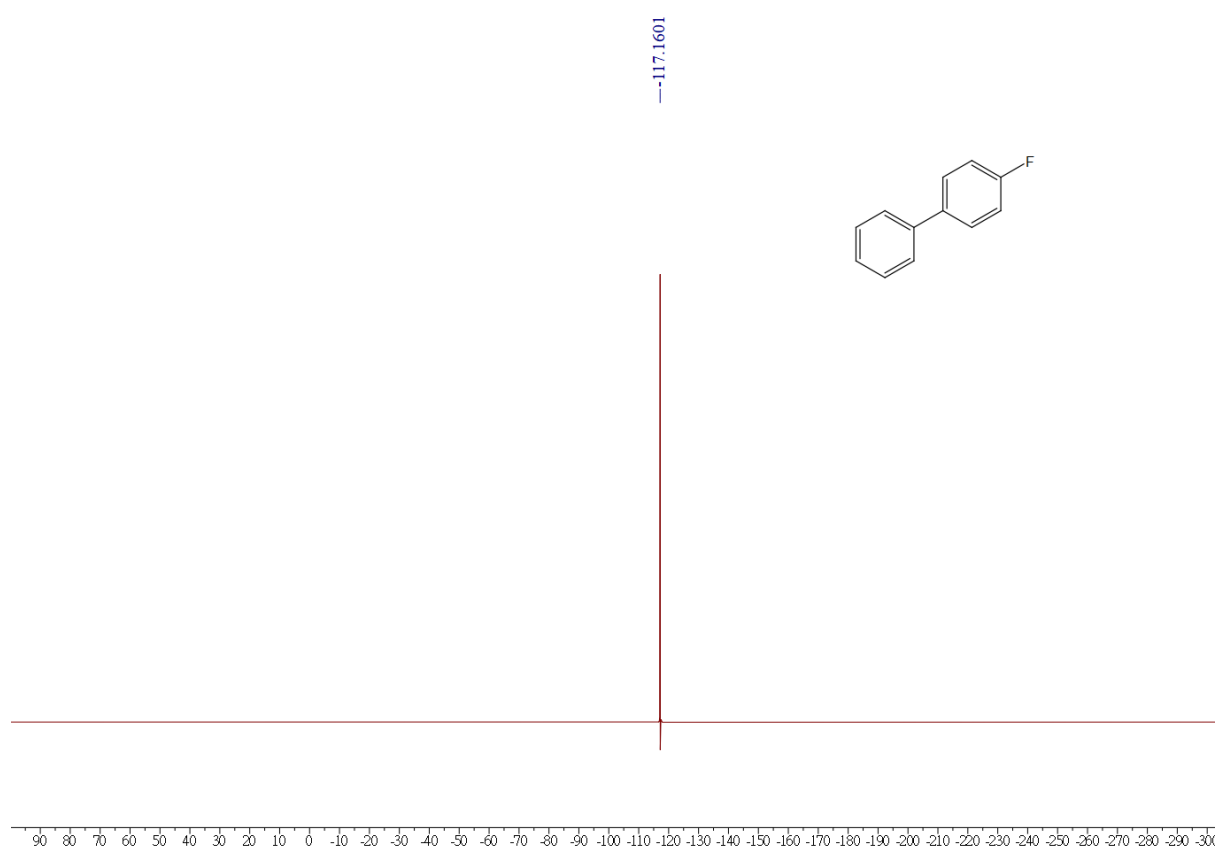
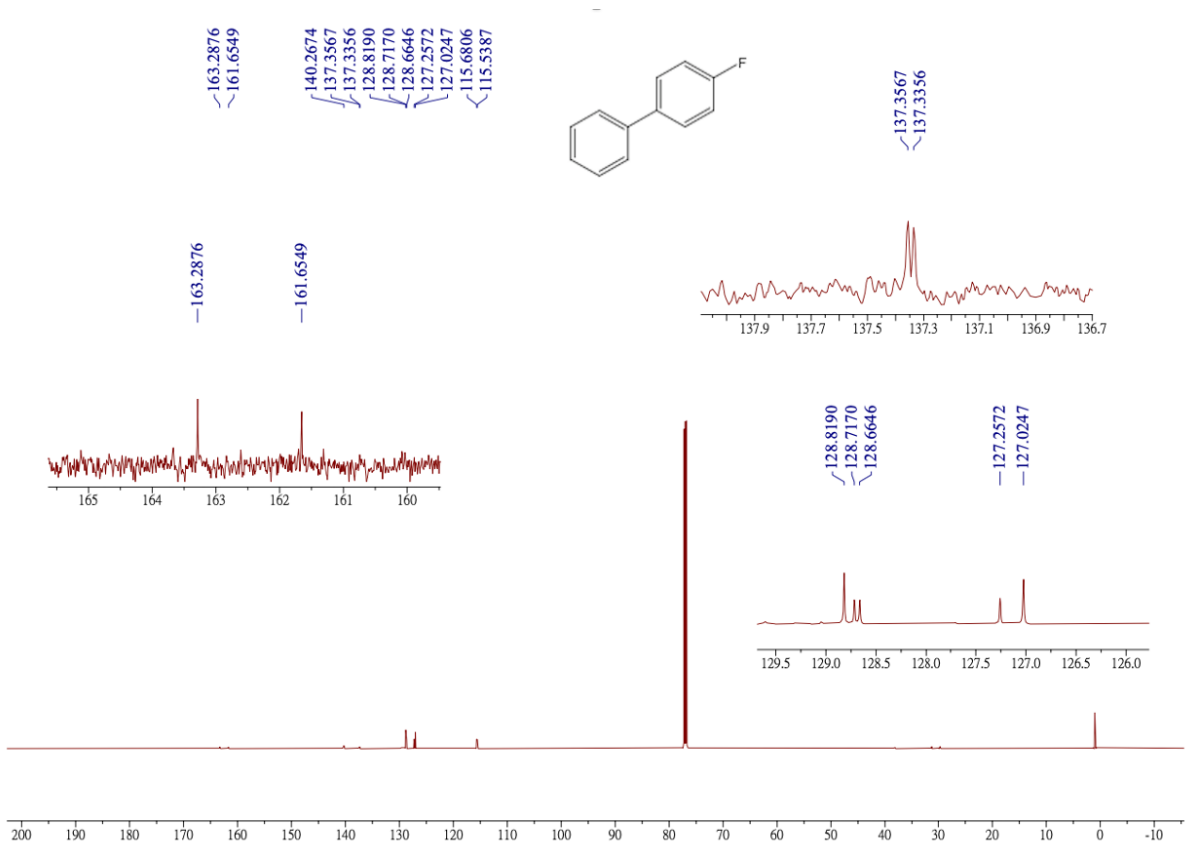
2-Fluoro-2'-methylbiphenyl. Elution with *n*-hexane yielded the product as an off-white solid. ^1H NMR (CDCl_3 , 400 MHz) δ 7.39 (m, 1, Ar), 7.34 (m, 2, Ar), 7.30 (m, 2, Ar), 7.28 (m, 1, Ar), 7.24 (m, 1, Ar), 7.18 (t, 1, $J = 9.03$, Ar), 2.26 (s, 3, Me). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 150 MHz) δ 159.6 (d, $^1J_{\text{CF}} = 244.3$, C), 136.6 (s, C), 135.7 (s, C), 131.5 (d, $J_{\text{CF}} = 3.7$, CH),

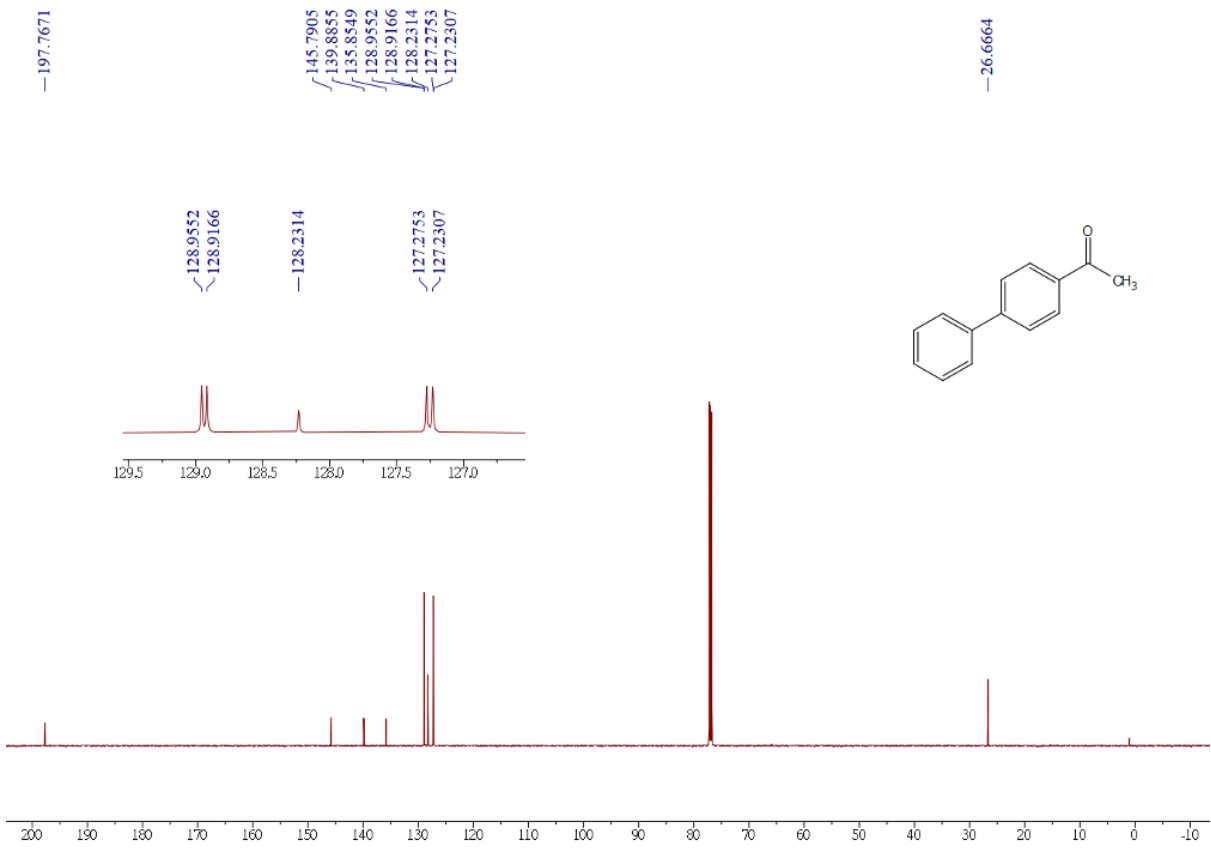
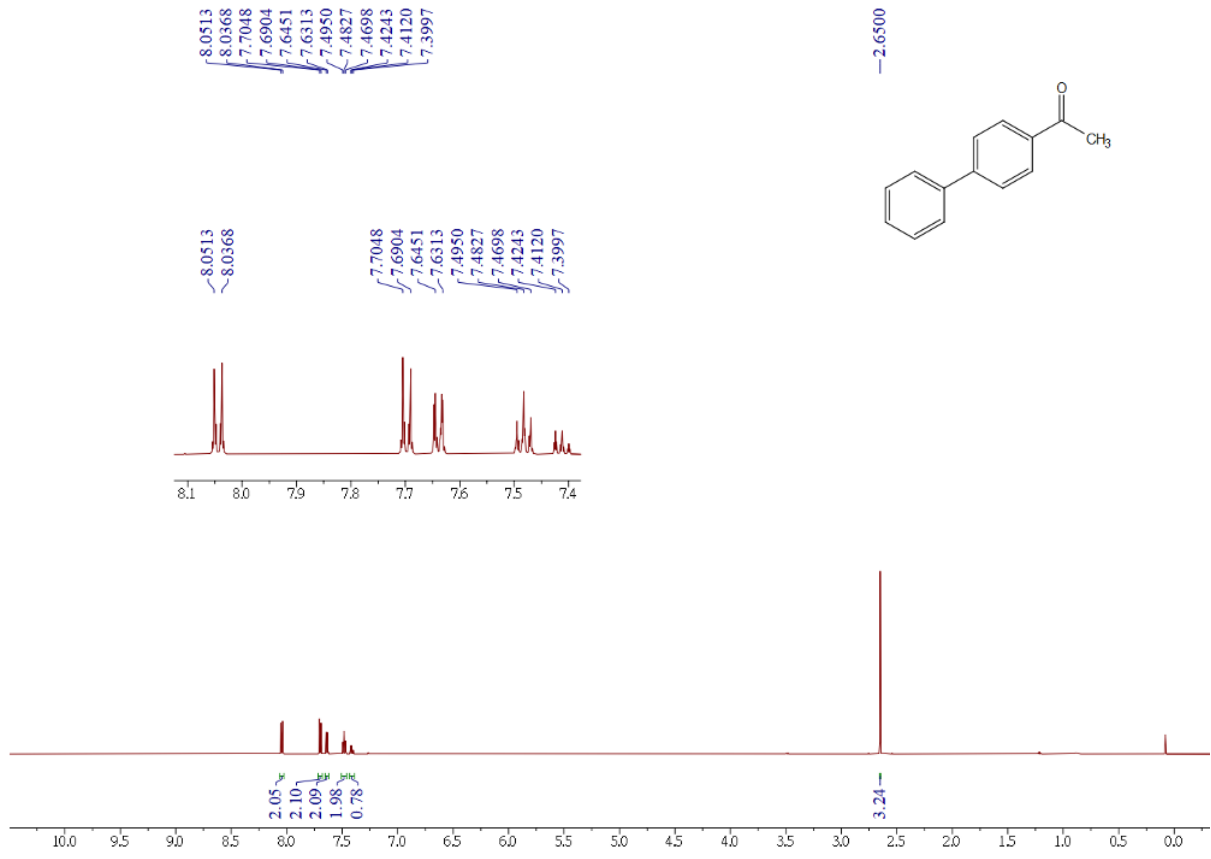
130.1 (s, CH), 129.9 (s, CH), 129.3 (d, $J_{CF} = 16.4$, C), 129.0 (d, $J_{CF} = 7.9$, CH), 128.0 (s, CH), 125.6 (s, CH), 124.0 (d, $J_{CF} = 3.6$, CH), 115.5 (d, $J_{CF} = 22.5$, CH), 19.9 (d, $J_{CF} = 2.9$, CH₃). $^{19}\text{F}\{^1\text{H}\}$ NMR (CDCl₃, 564 MHz) δ -116.12. HRMS (EI): calcd for C₁₃H₁₁F m/z 186.0850, found m/z 186.0851.

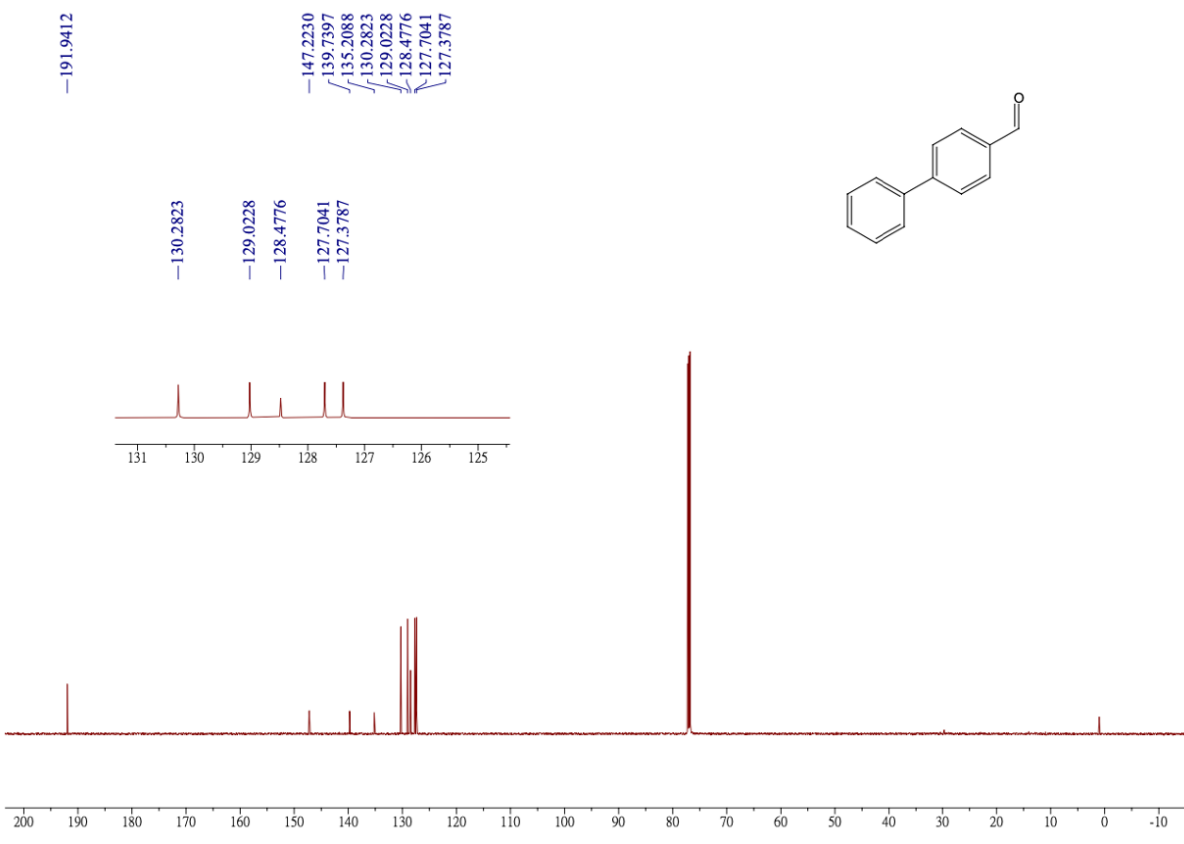
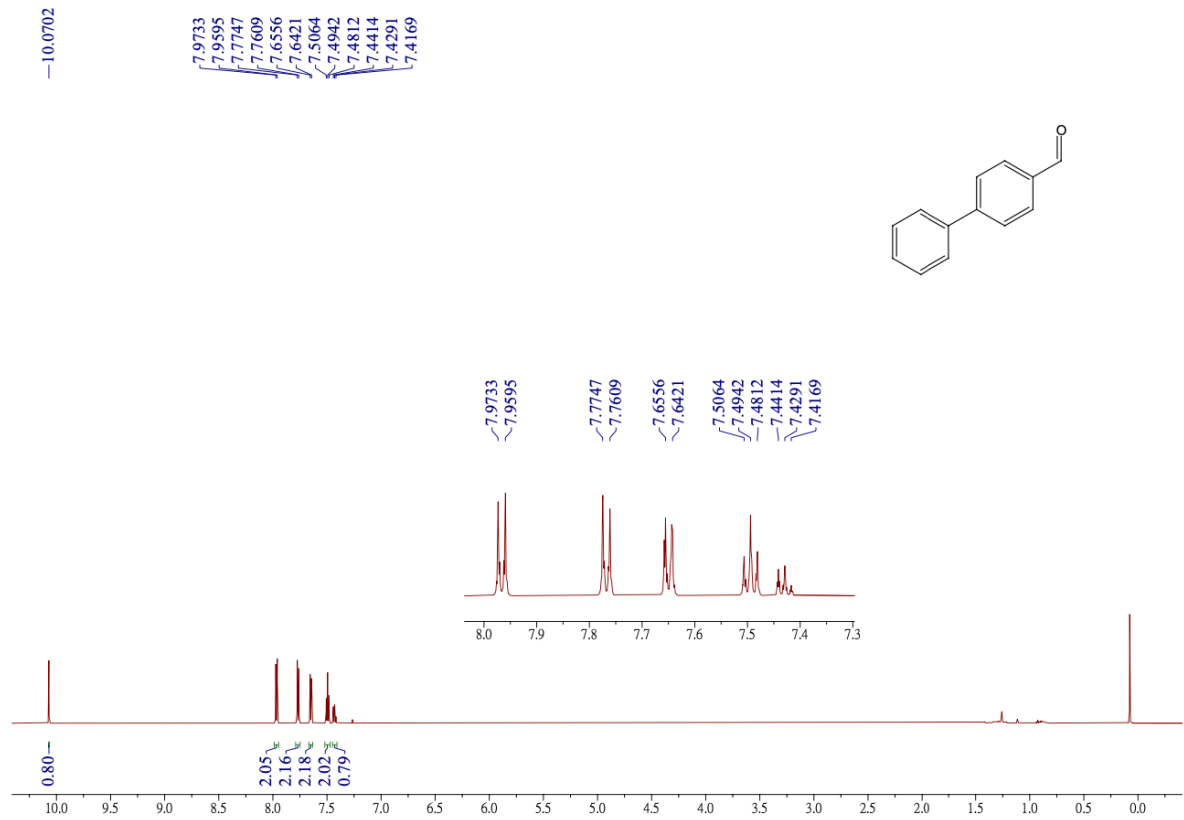


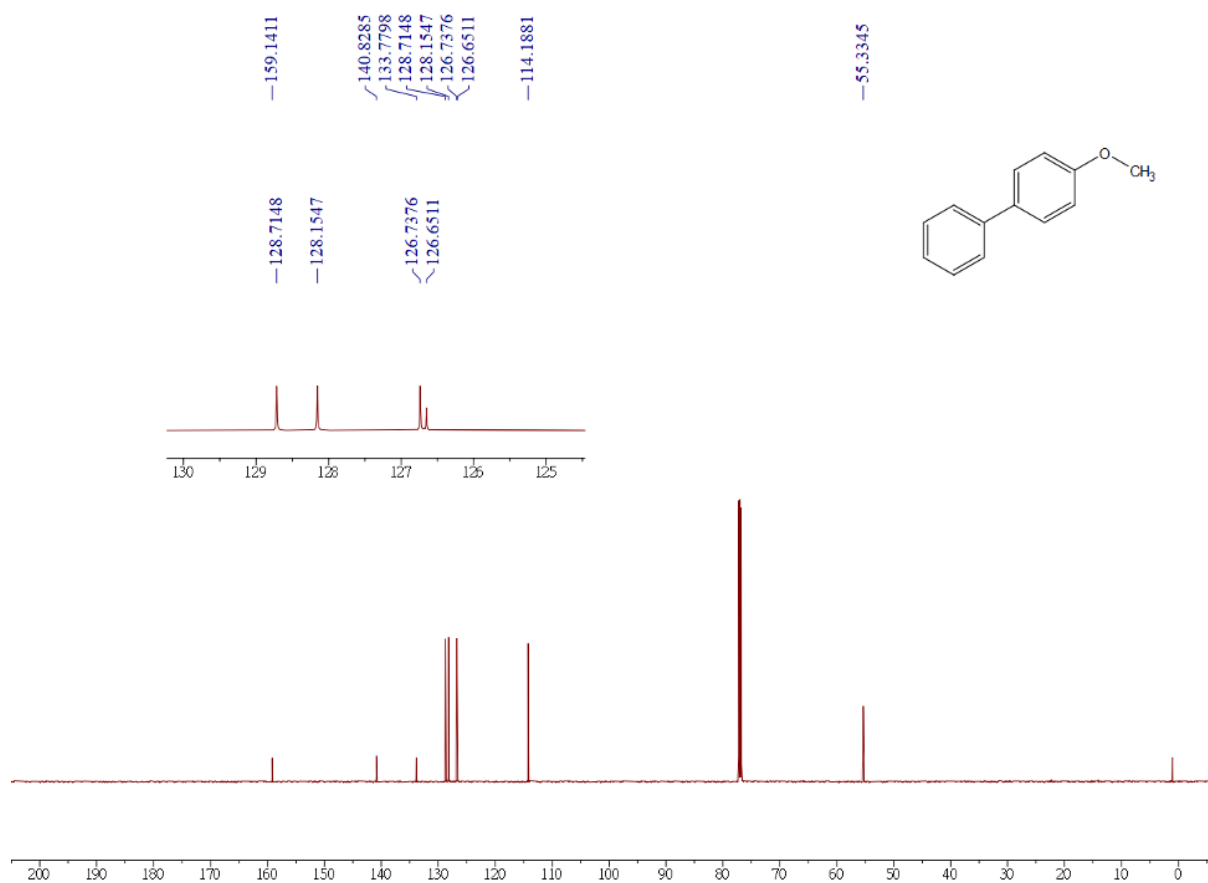
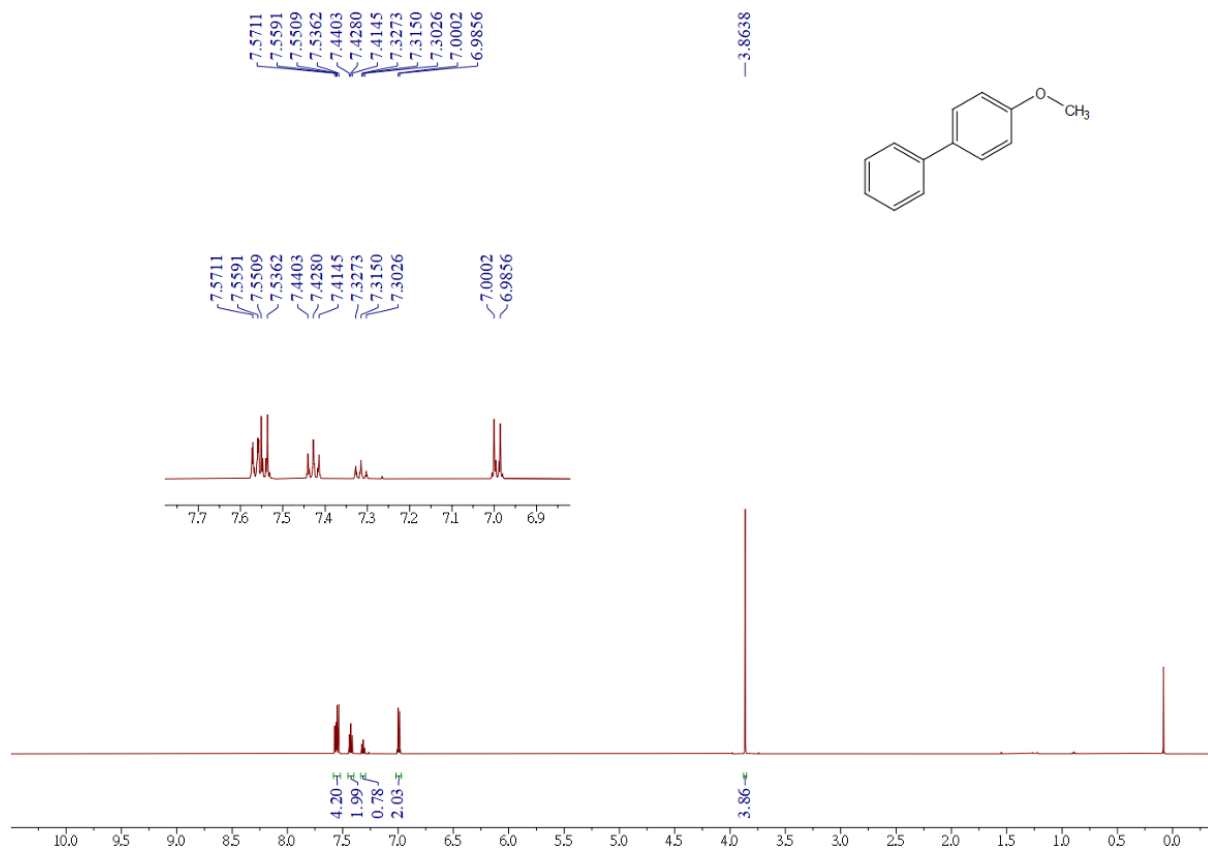
2-Fluorobiphenyl. Elution with *n*-hexane/CH₂Cl₂ (10/1) yielded the product as colorless crystals. ^1H NMR (CDCl₃, 400 MHz) δ 7.57 (m, 2, Ar), 7.46 (m, 3, Ar), 7.38 (m, 1, Ar), 7.32 (m, 1, Ar), 7.22 (t, 1, $J = 7.52$, Ar), 7.16 (m, 1, Ar). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl₃, 150 MHz) δ 159.8 (d, $^1J_{CF} = 246.4$, C), 135.8 (s, C), 130.8 (d, $J_{CF} = 3.6$, CH), 129.0 (d, $J_{CF} = 2.8$, CH), 128.9 (d, $J_{CF} = 8.2$, CH), 128.4 (s, CH), 127.6 (s, CH), 127.2 (s, C), 124.3 (d, $J_{CF} = 3.7$, CH), 116.1 (d, $J_{CF} = 22.4$, CH). $^{19}\text{F}\{^1\text{H}\}$ NMR (CDCl₃, 564 MHz) δ -119.38. HRMS (EI): calcd for C₁₂H₉F m/z 172.0694, found m/z 172.0688.

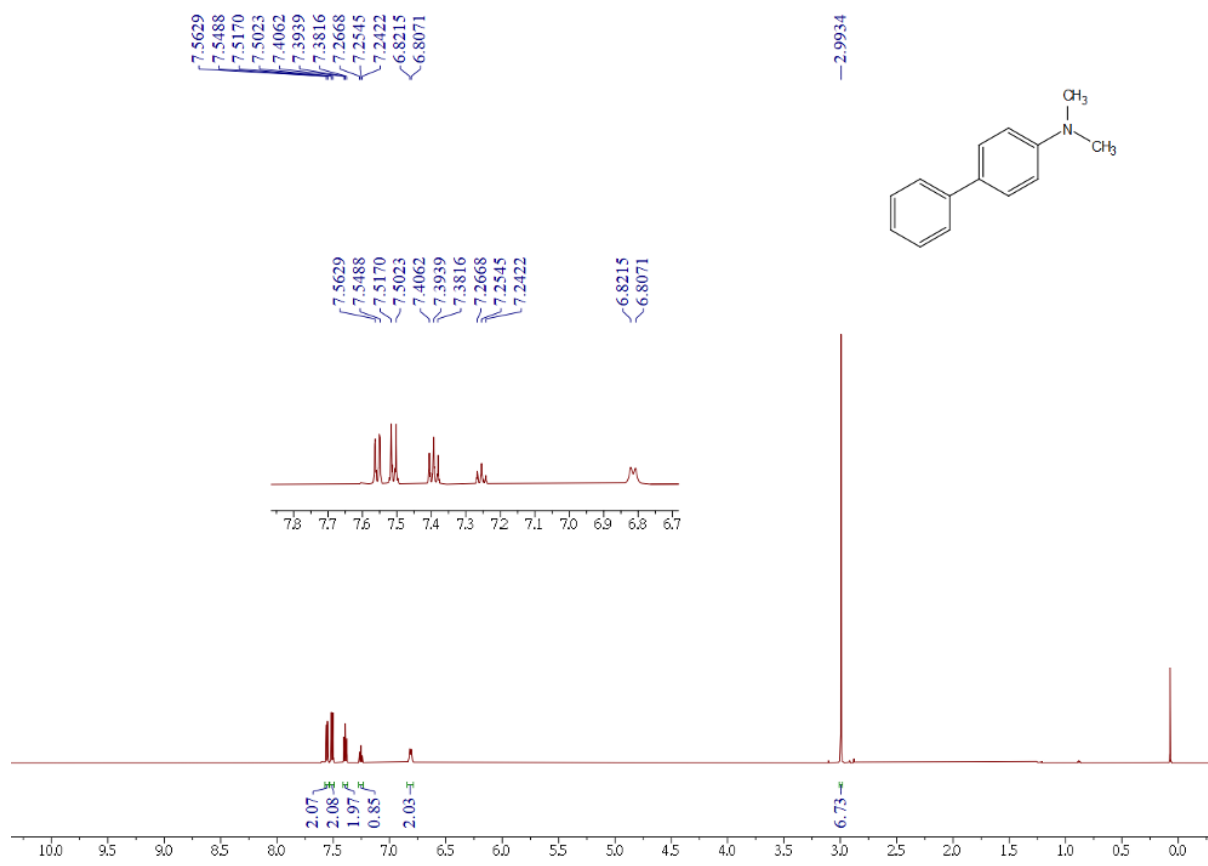


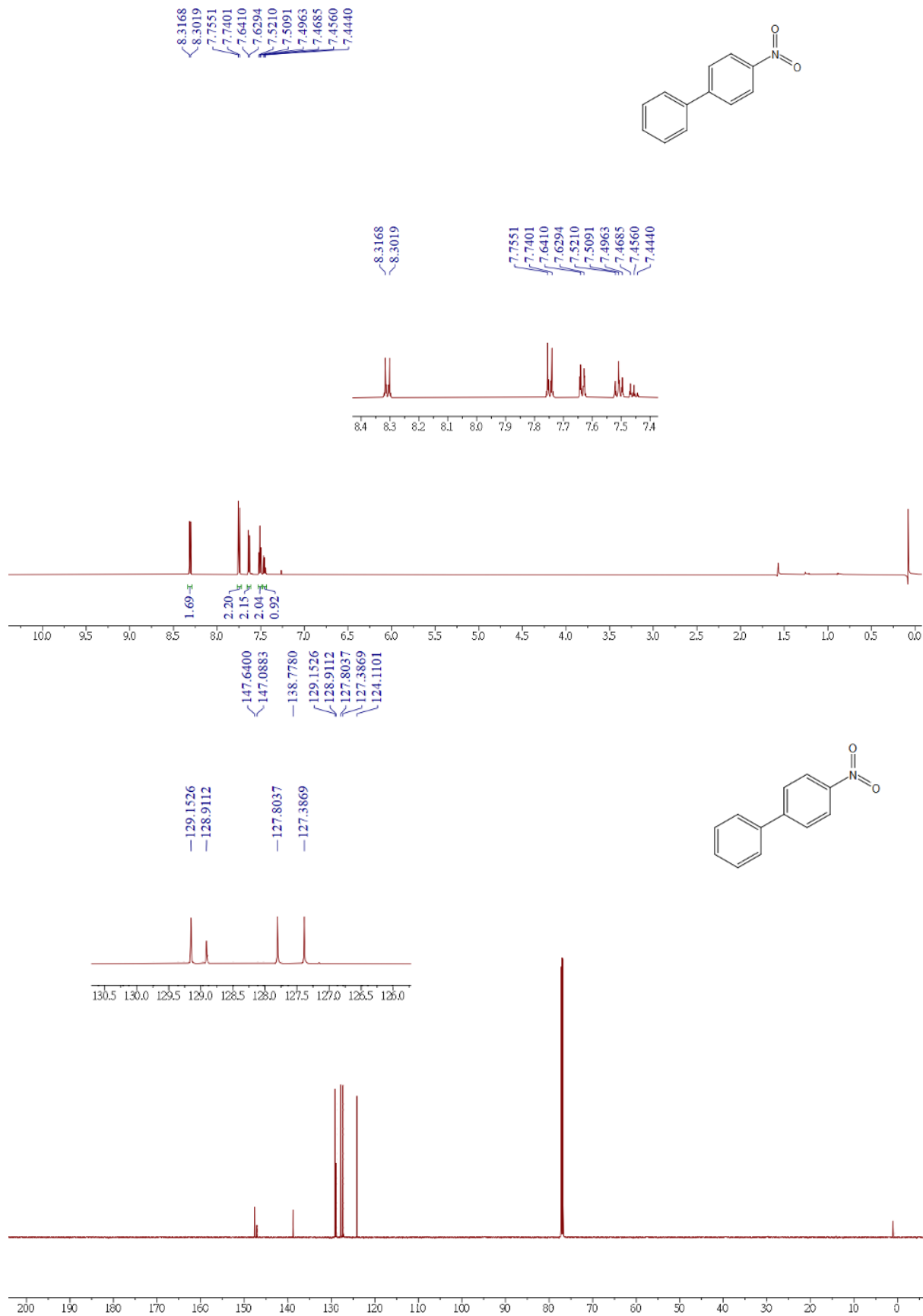


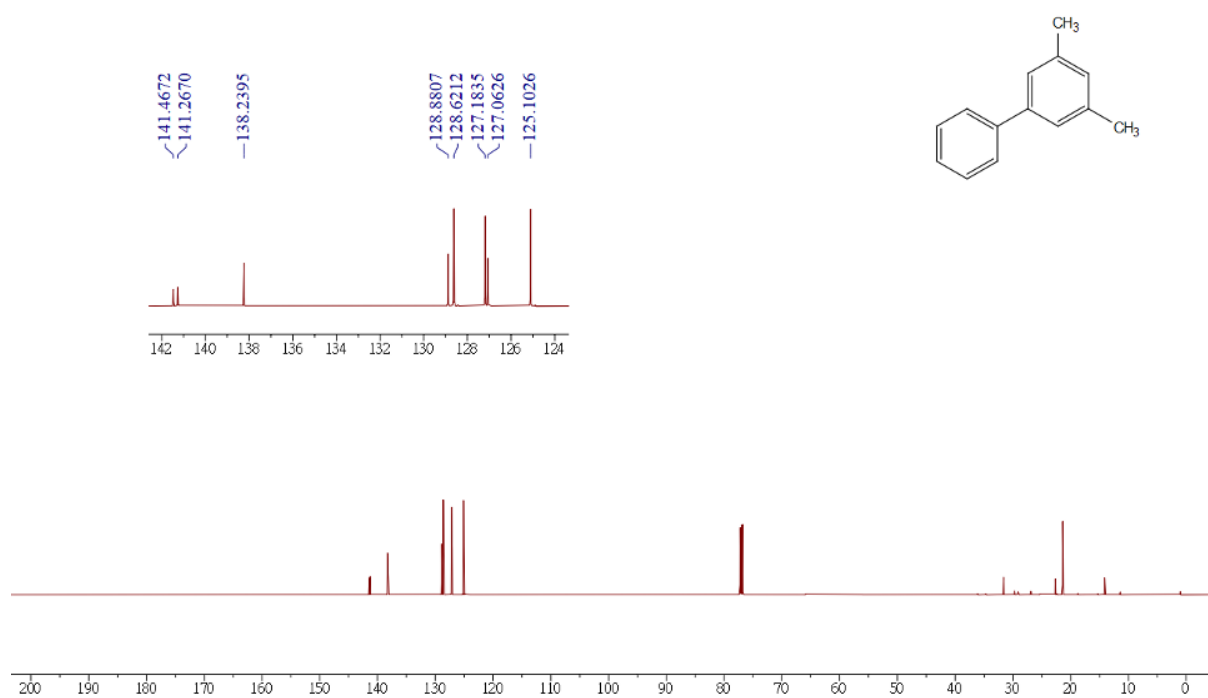
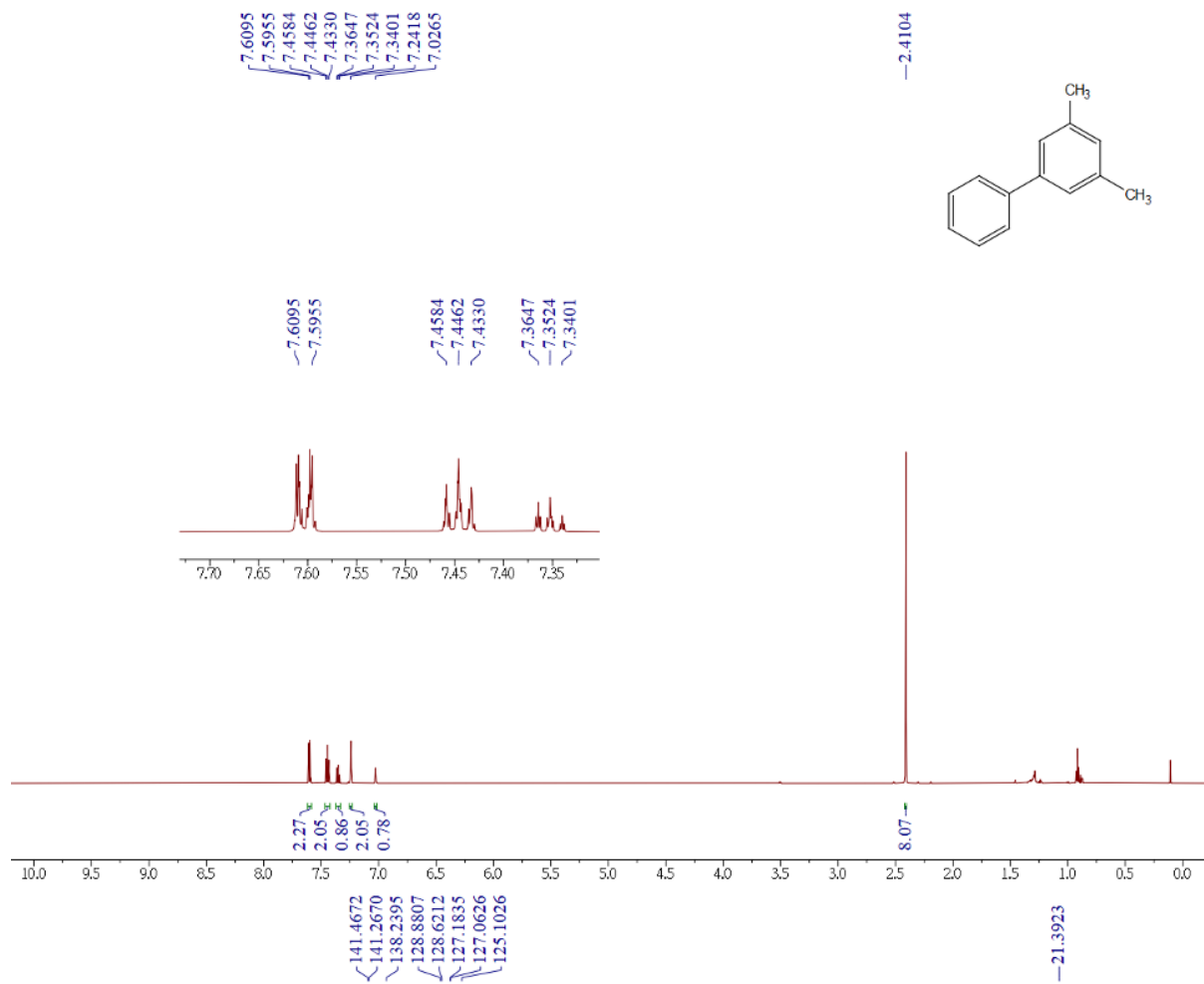


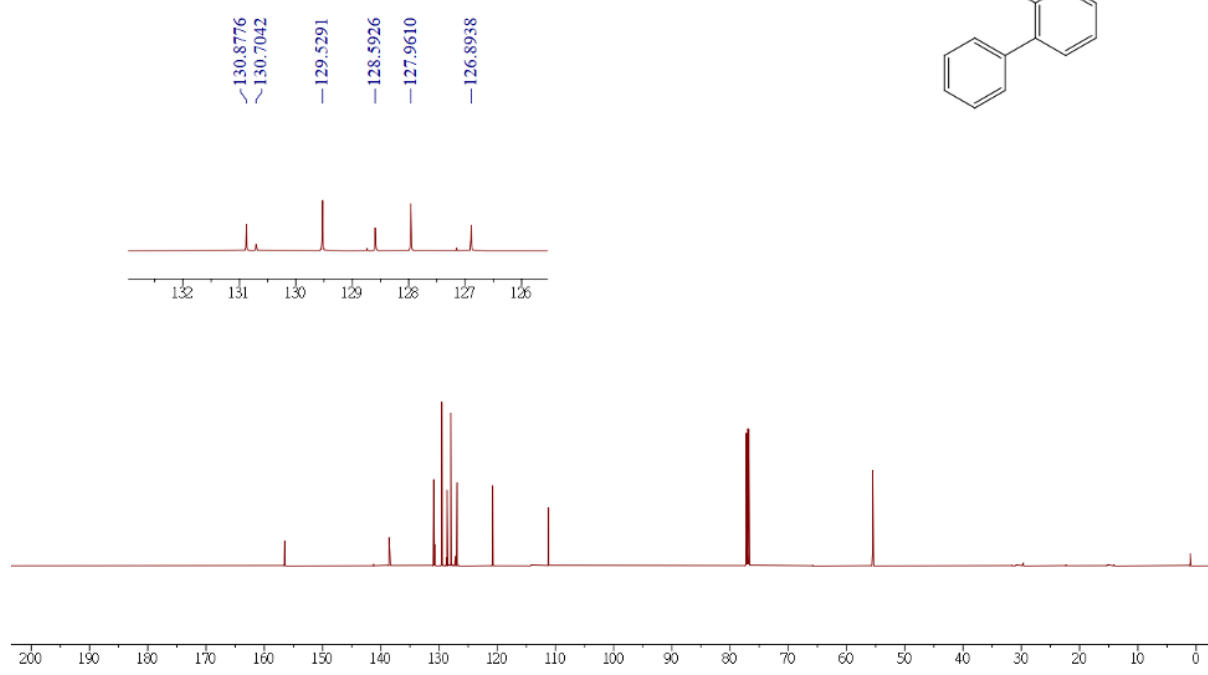
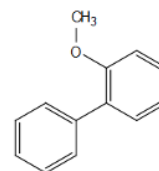
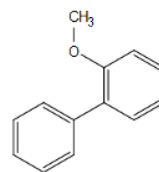
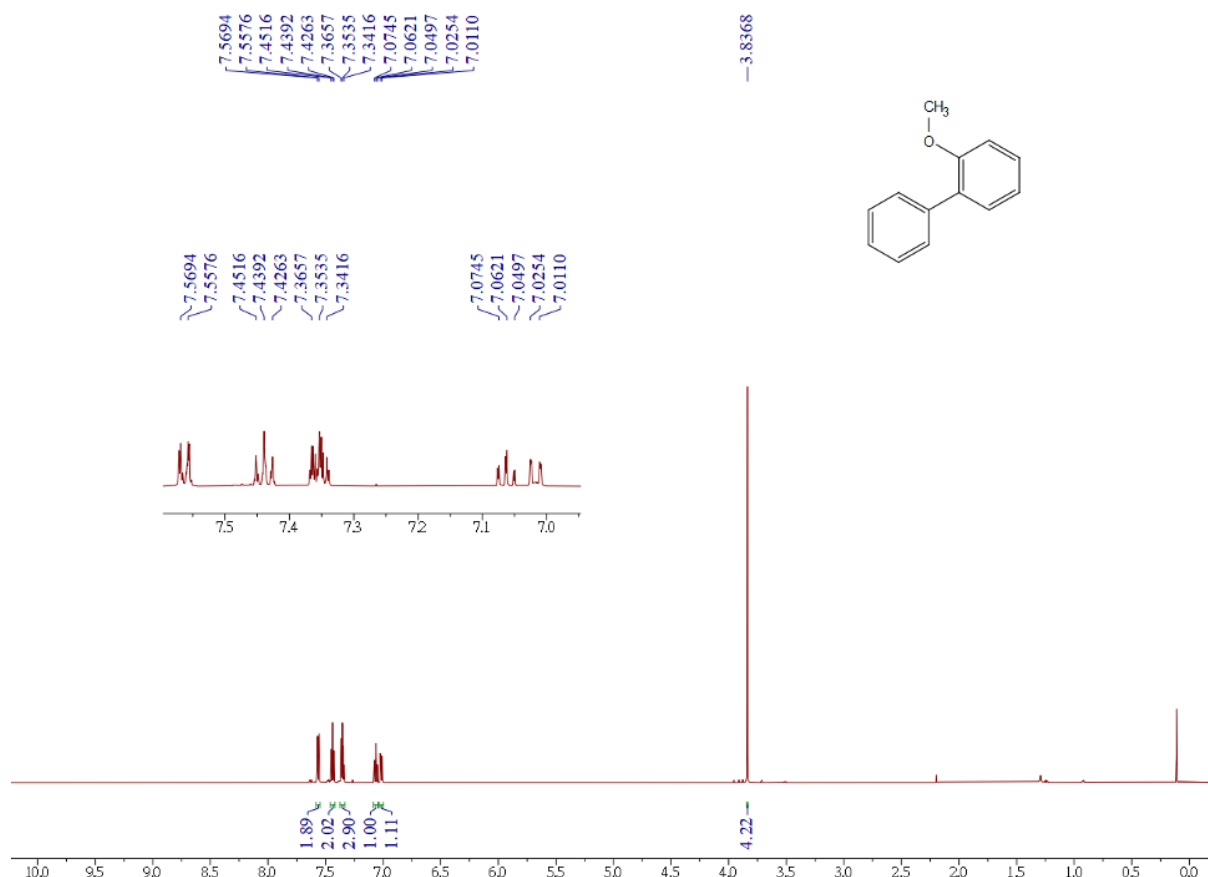


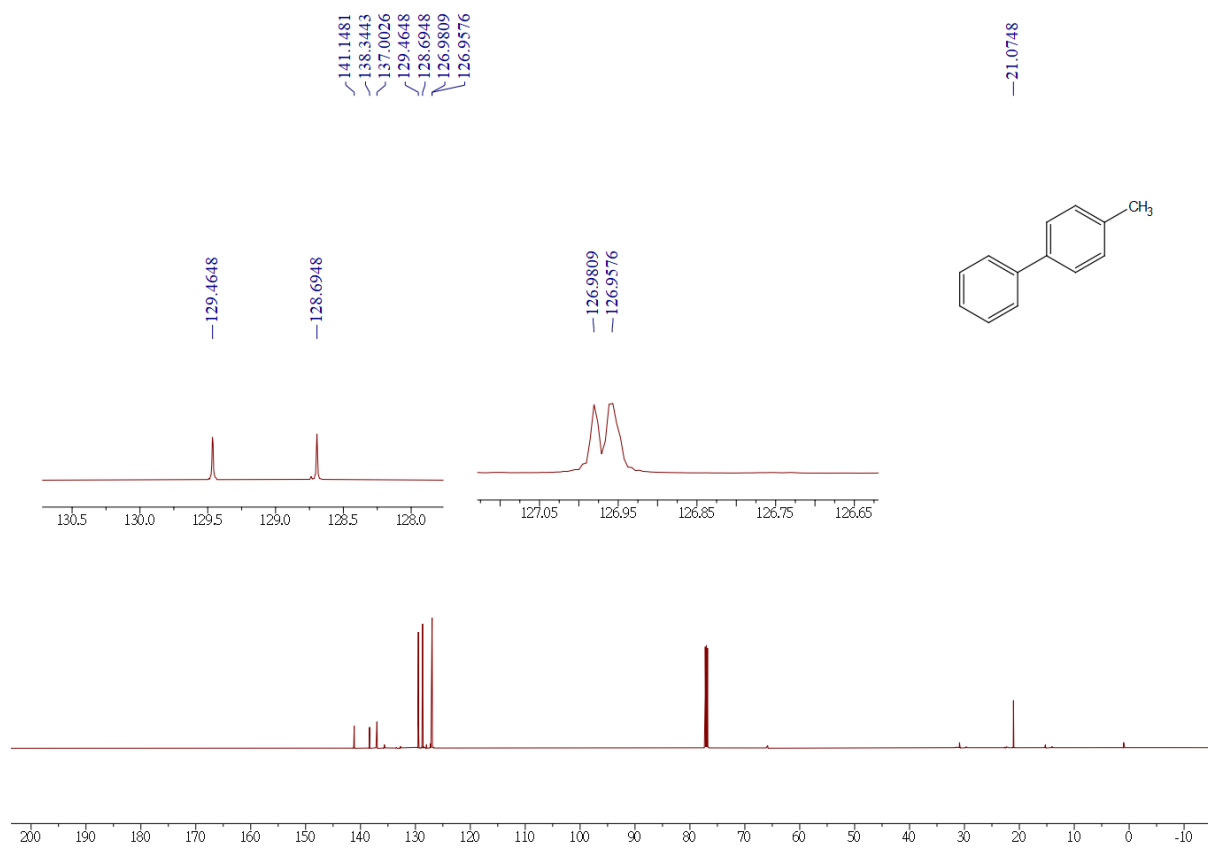
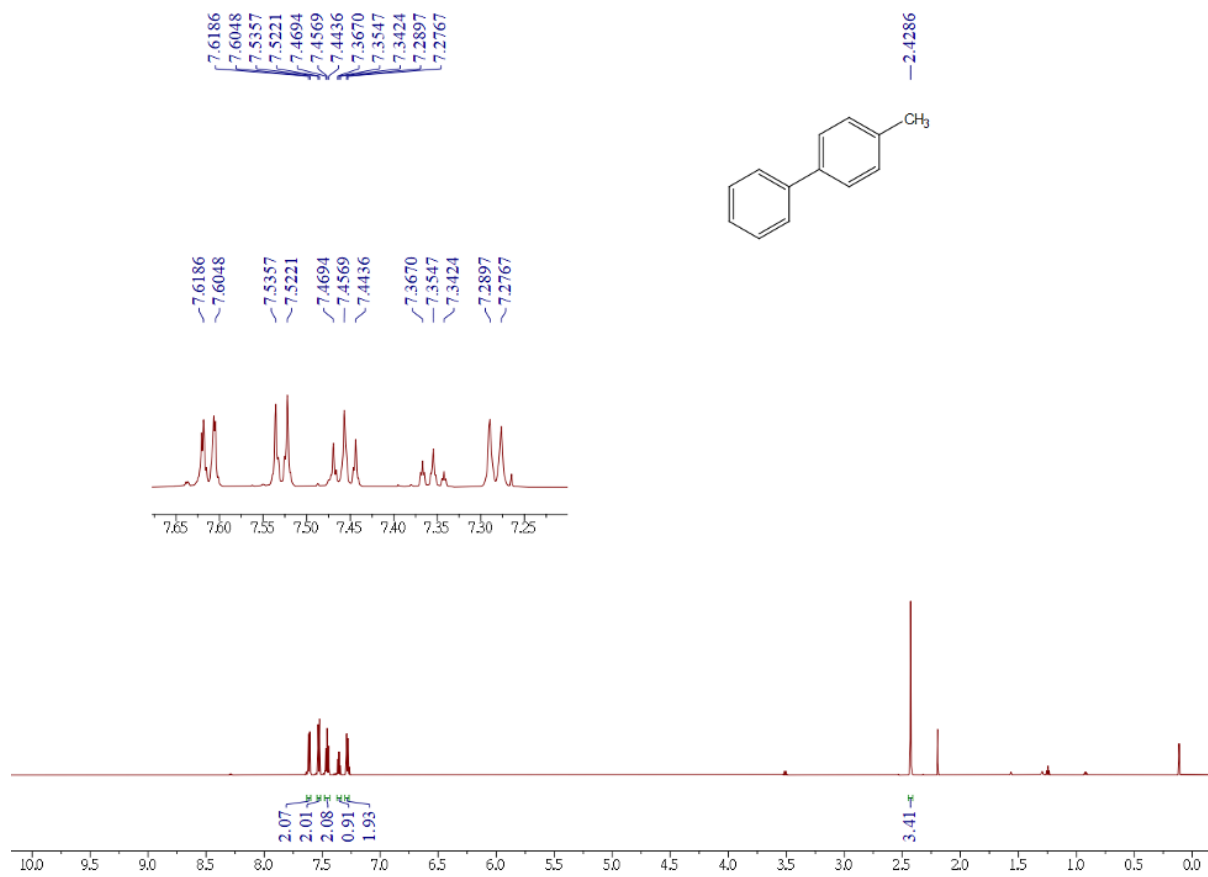


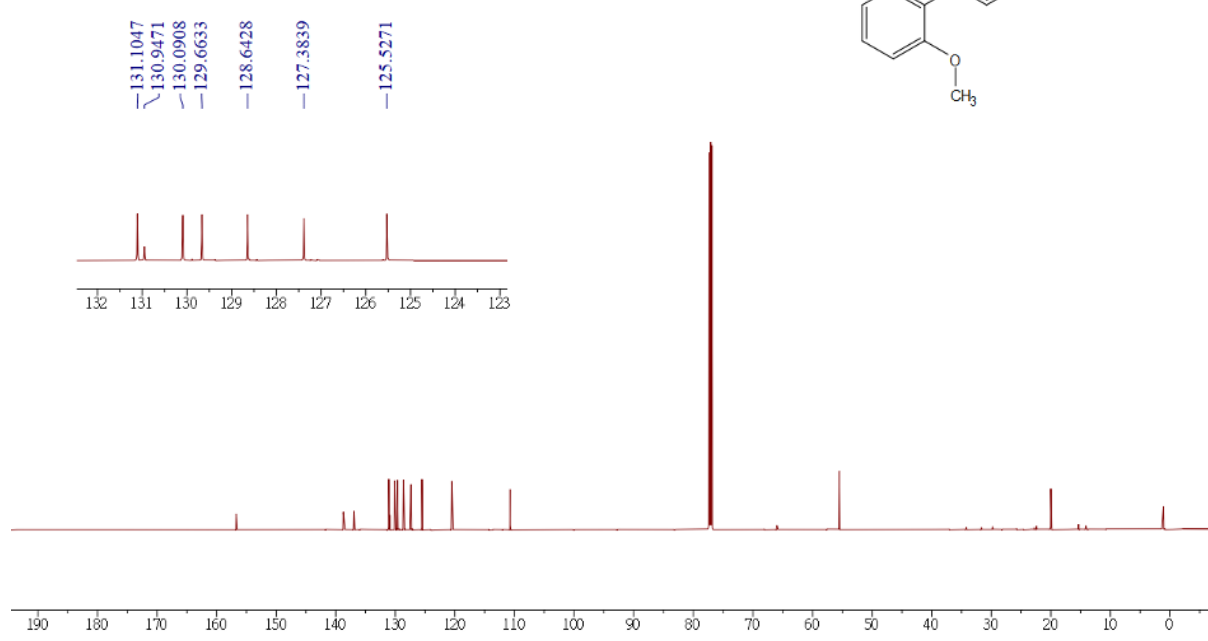
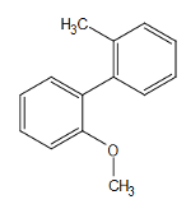
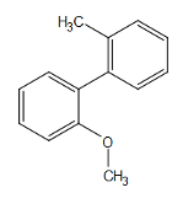
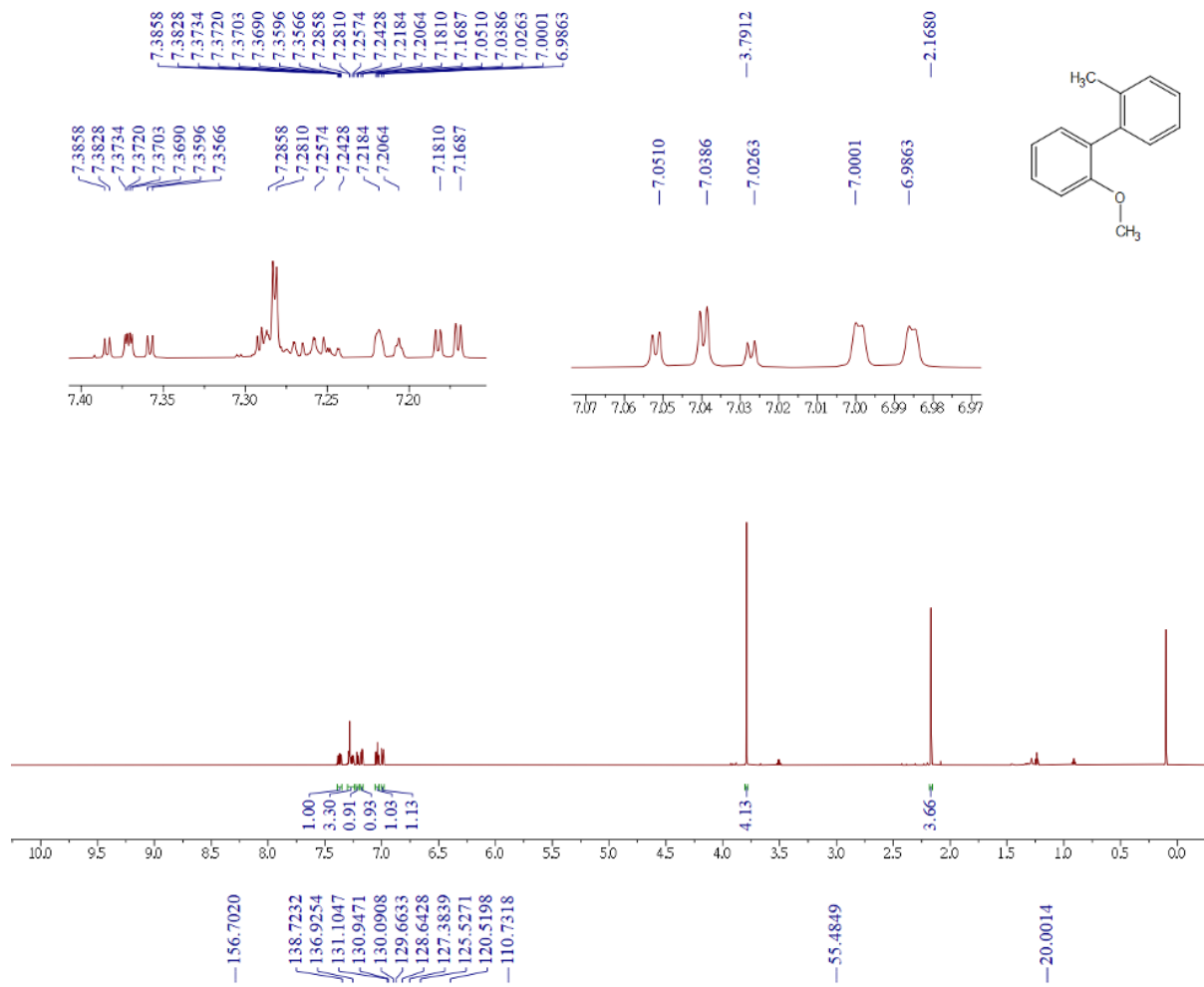


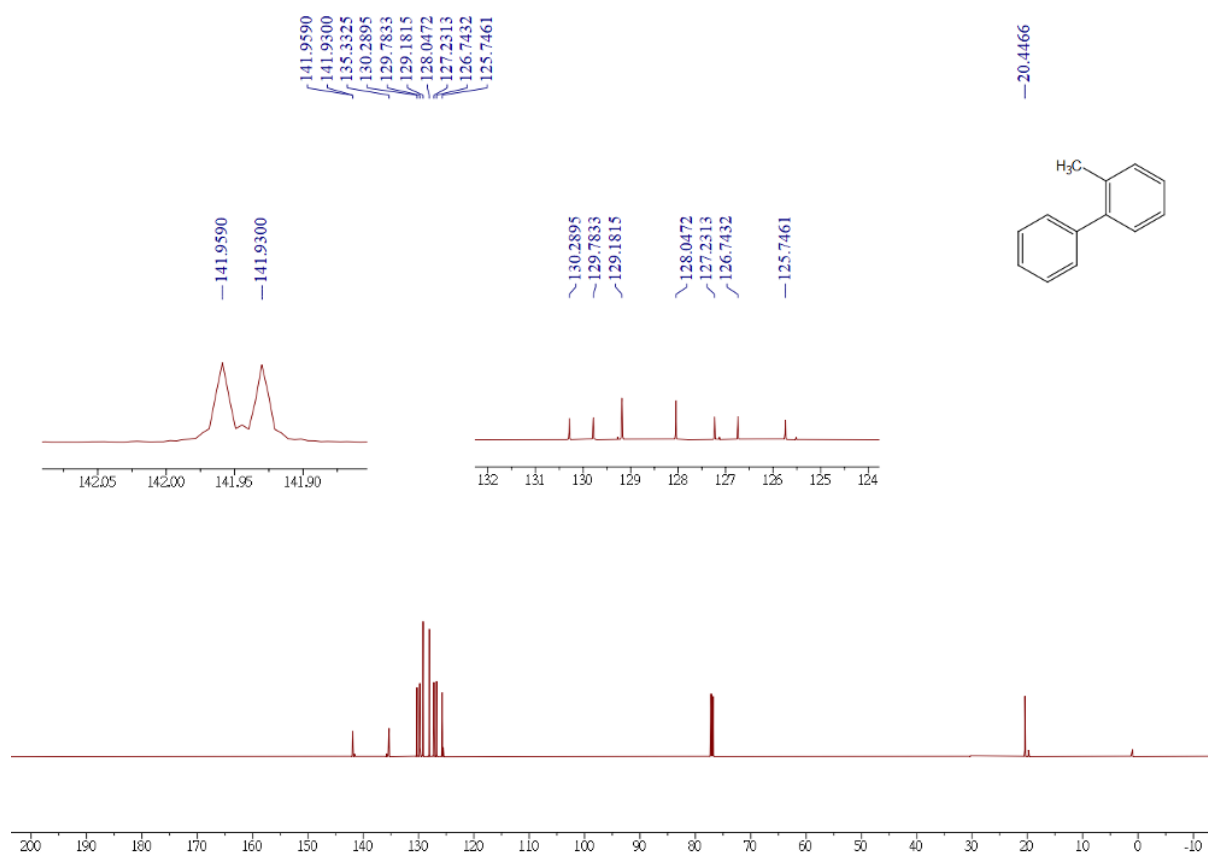
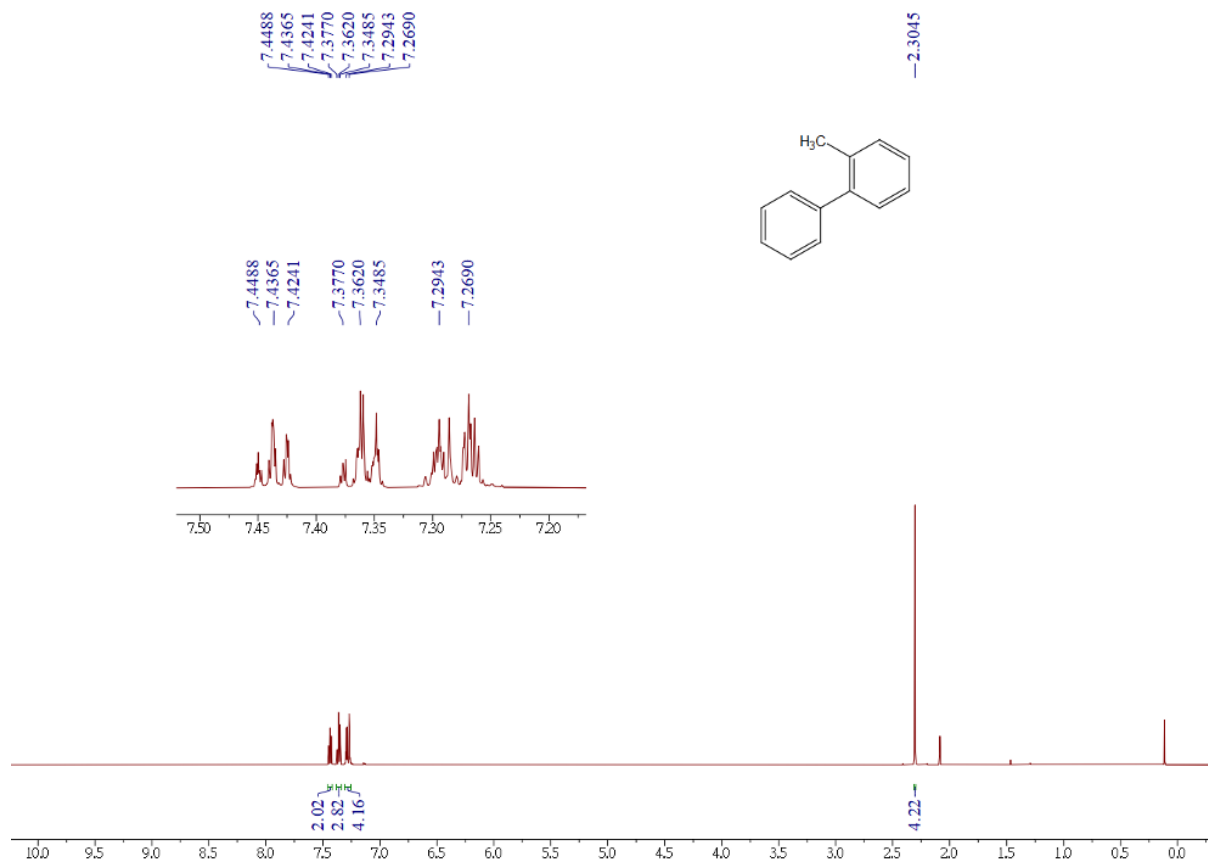


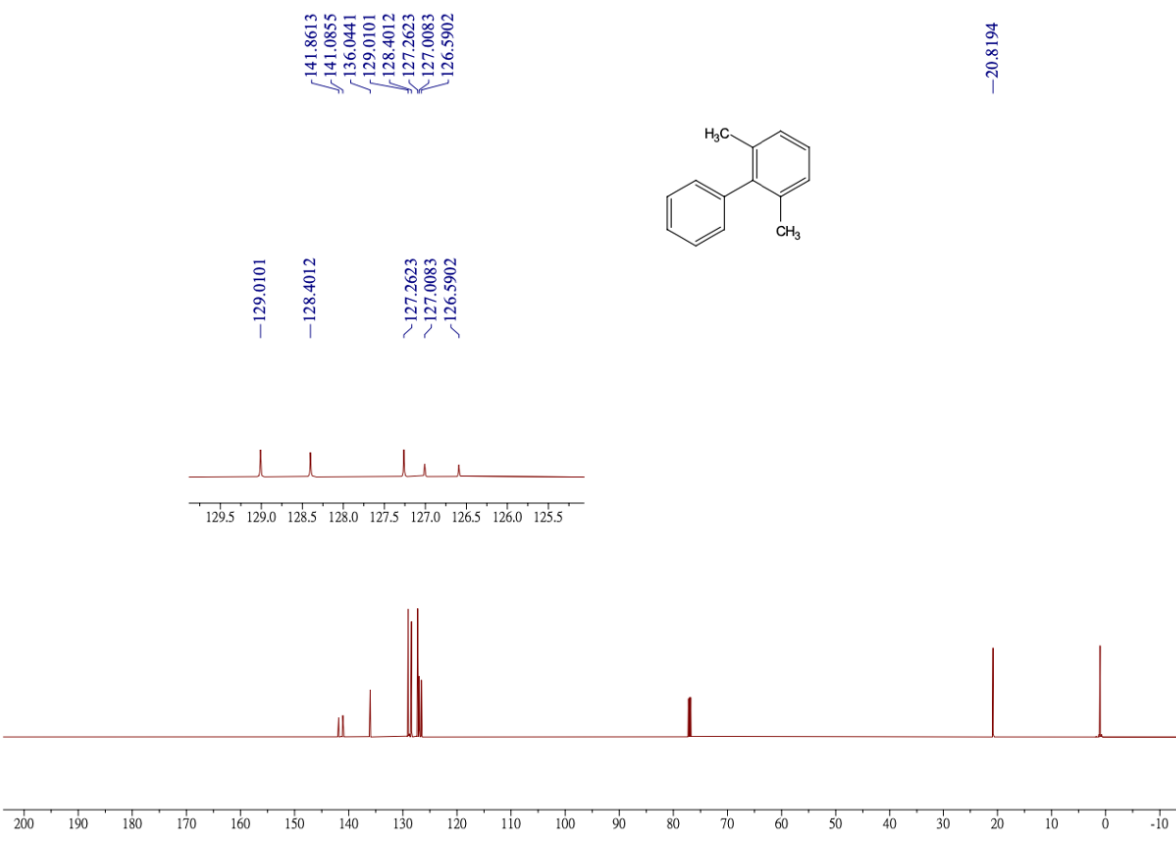
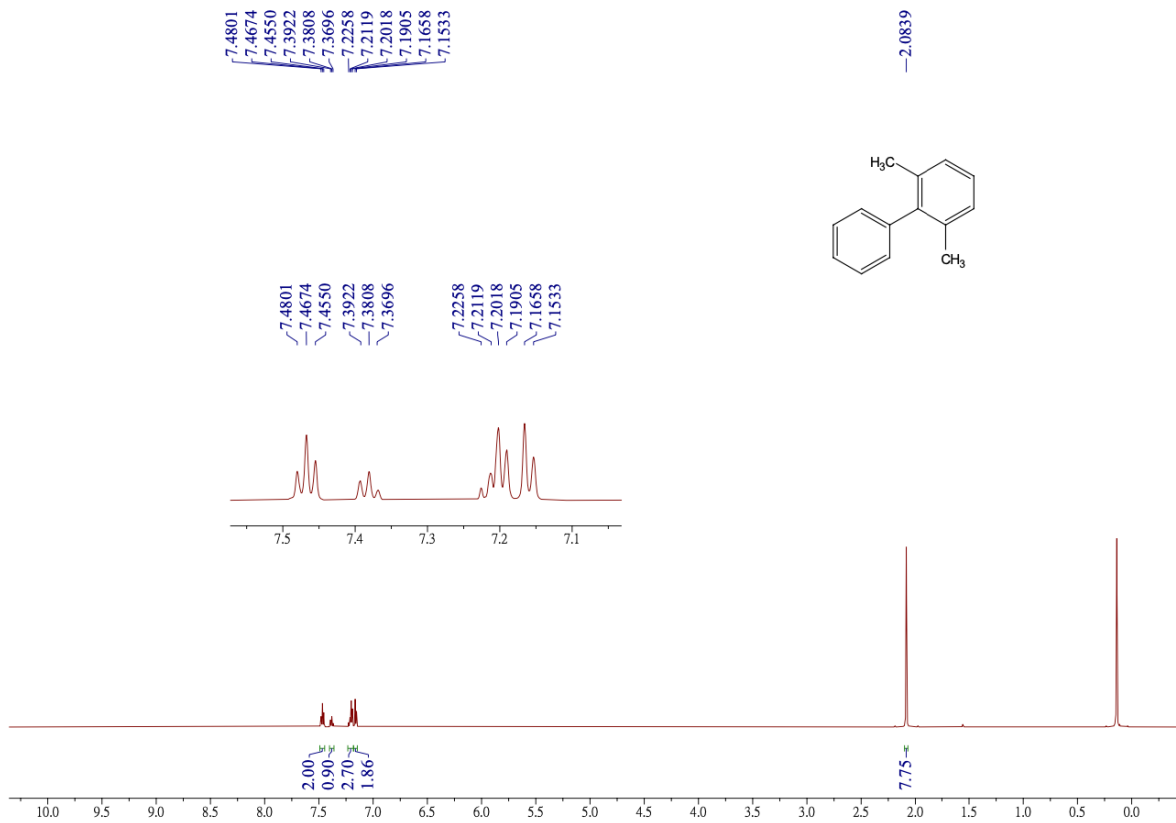


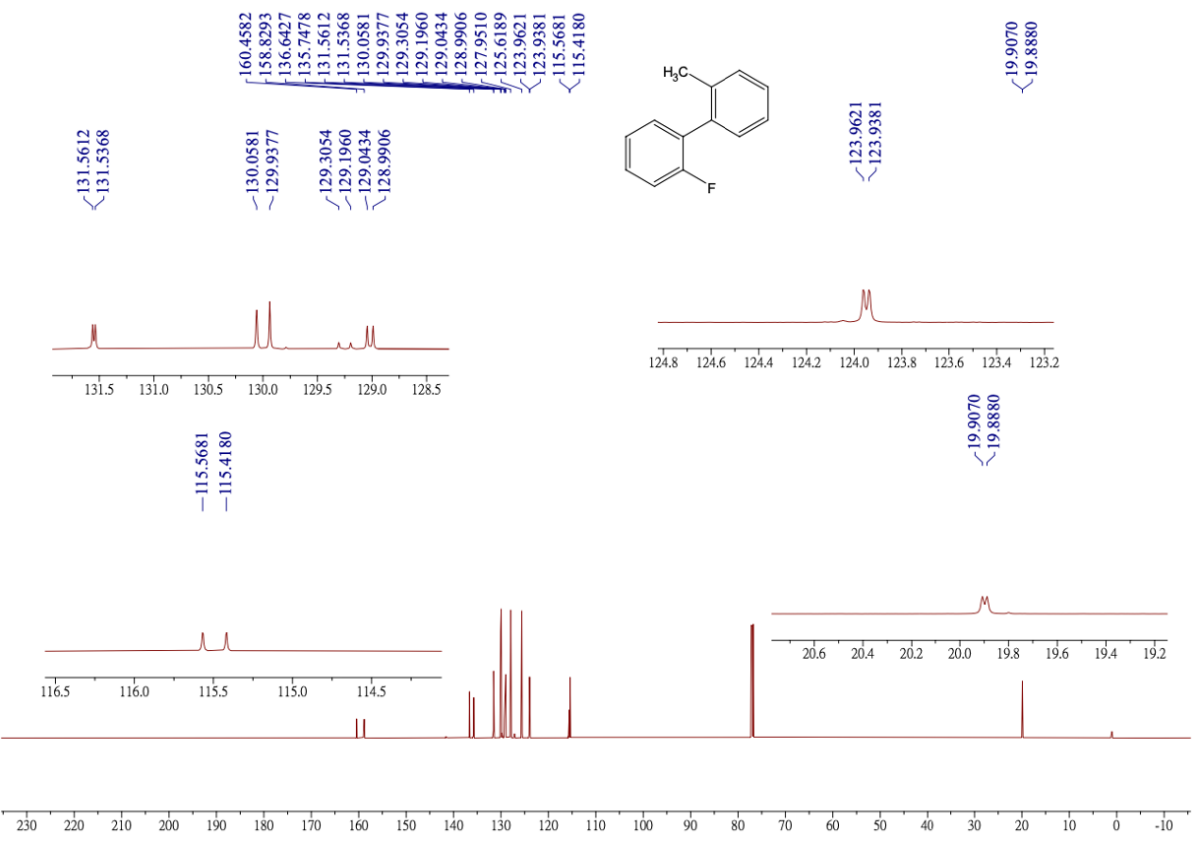
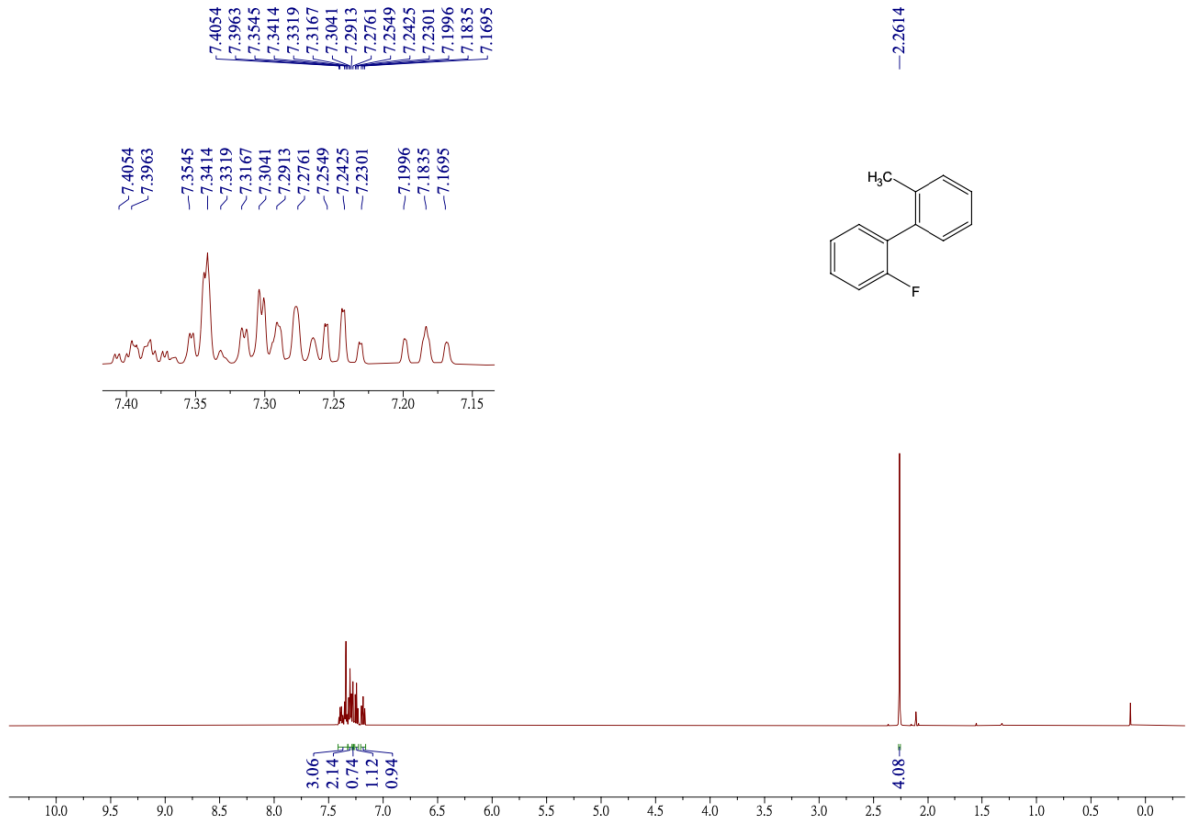


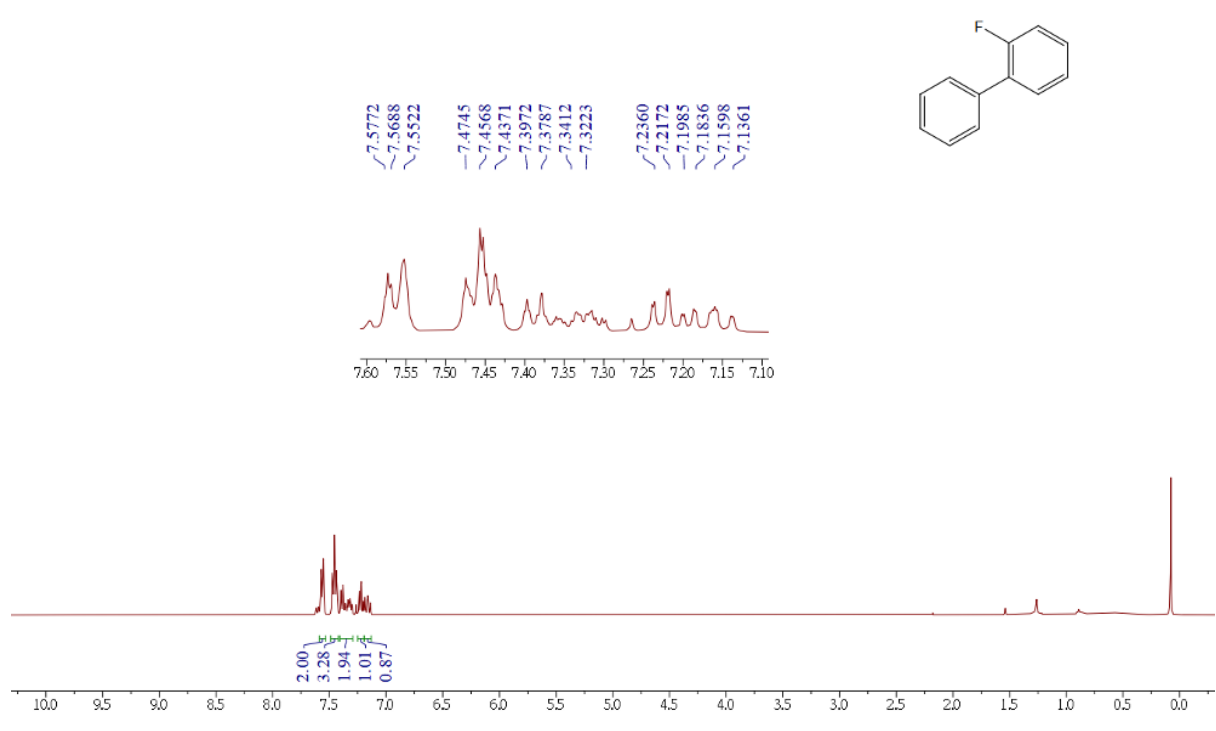
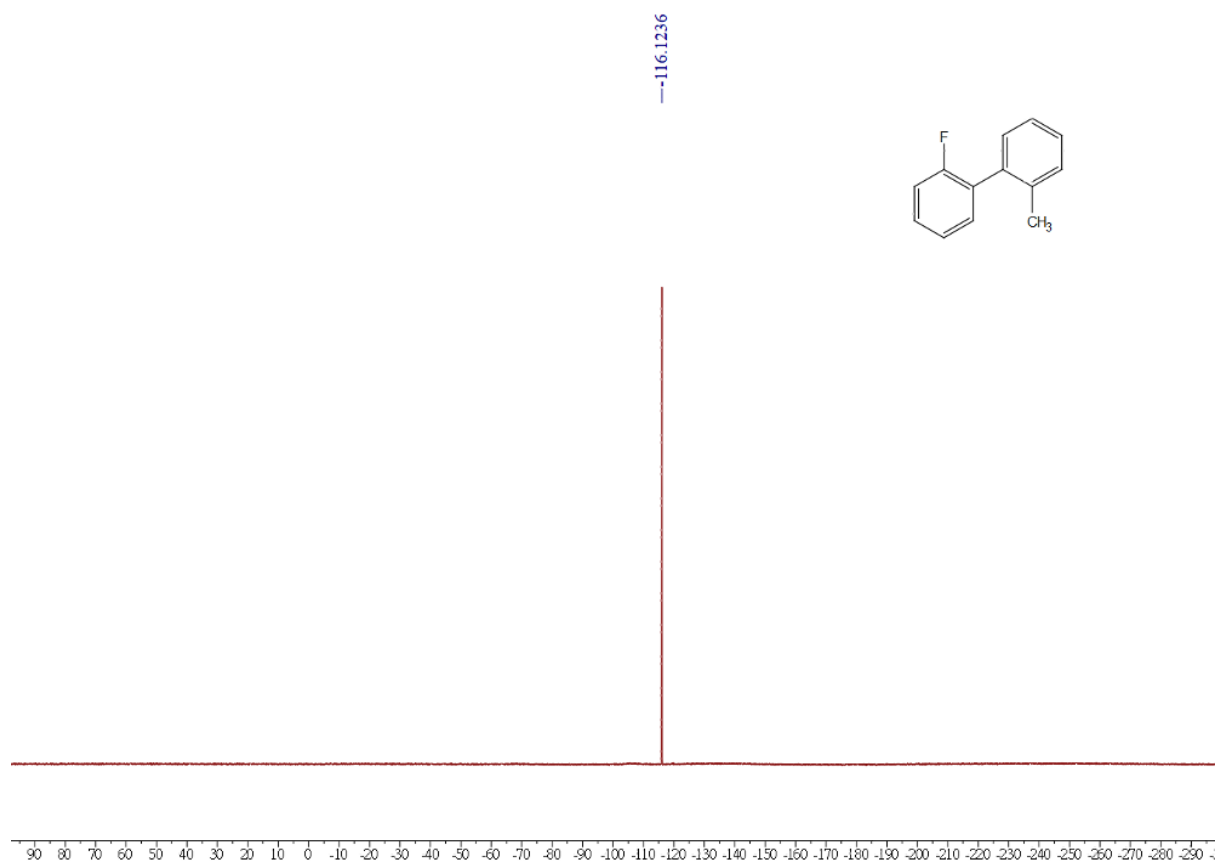


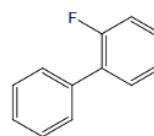
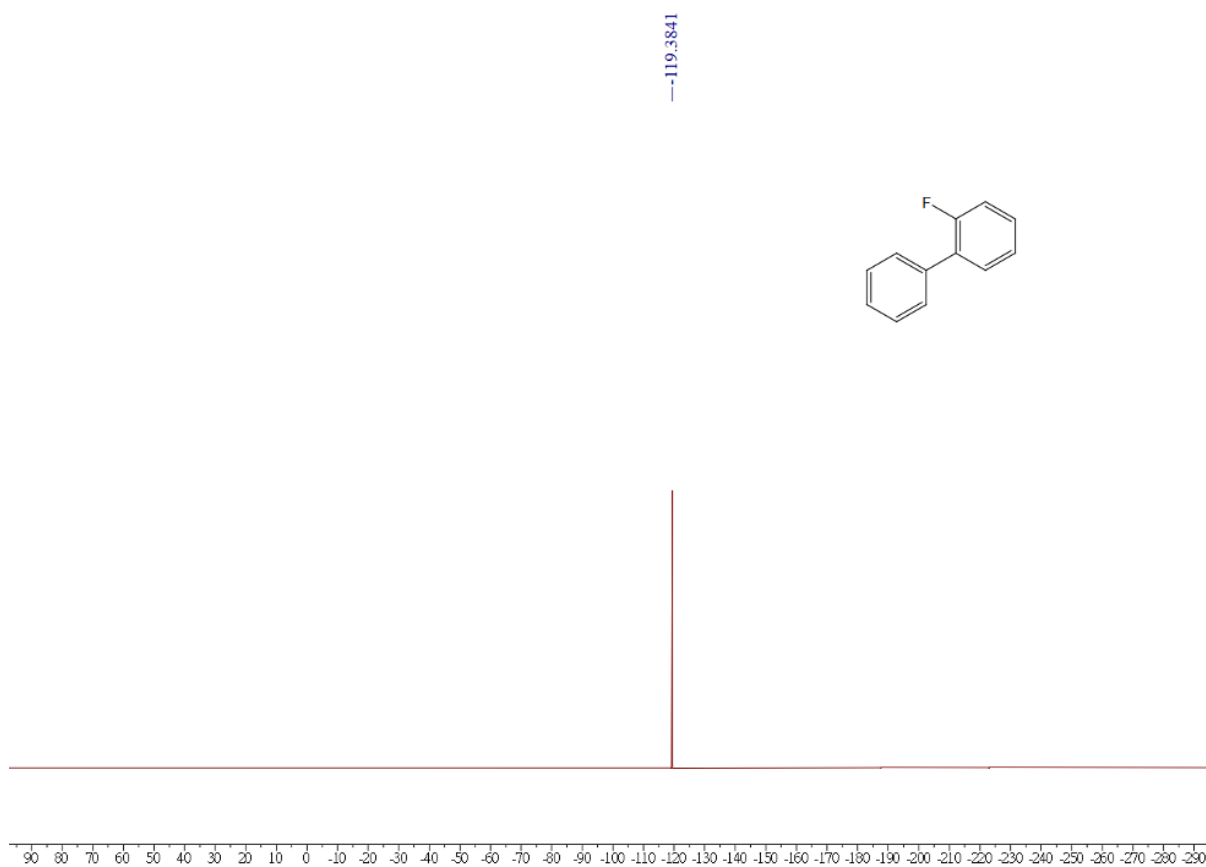
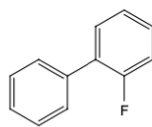
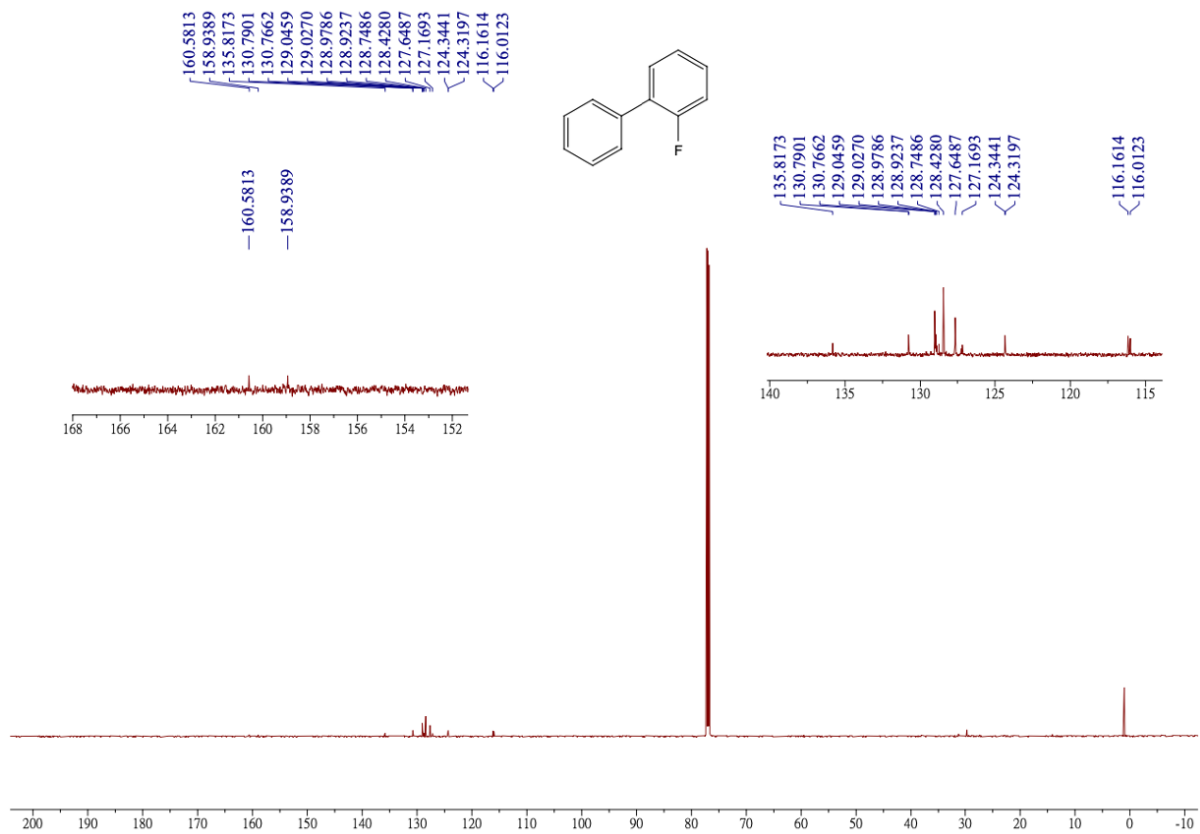












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