

Copper-catalysed oxidative Csp³-H methylenation to terminal olefins using DMF

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1. General Information

All manipulations were carried out using standard Schlenk techniques. Unless otherwise stated, analytical grade solvents and commercially available reagents were used as received. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel in *n*-hexane. Gradient flash chromatography was conducted eluting with a continuous gradient from *n*-hexane to the ethyl acetate. All new compounds were characterized by ^1H NMR, ^{13}C NMR and HRMS. IR spectra were recorded on a Mettler Toledo React IRTM 15 spectrometer using a diamond comb.

2. General Procedures for Terminal Olefins of the Ketones

A mixture of ketones (0.50 mmol), $\text{Cu}(\text{TFA})_2 \cdot x\text{H}_2\text{O}$ (0.15 mmol), and $\text{K}_2\text{S}_2\text{O}_8$ (1.0 mmol) in DMF (2.0 mL) was stirred in N_2 at 100 °C for 24 h. After completion of the reaction, the solution was extracted with ethyl acetate (3×15 mL). The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column chromatography on silica gel to afford the desired product.

3. General Procedures for Substituent Benzylpyridines

A mixture of benzylpyridines (0.50 mmol), $\text{Cu}(\text{TFA})_2 \cdot x\text{H}_2\text{O}$ (0.15 mmol), and $\text{K}_2\text{S}_2\text{O}_8$ (2.0 mmol) in DMF (2.0 mL) was stirred in N_2 at 100 °C for 24 h. After completion of the reaction, the solution was extracted with ethyl acetate (3×15 mL). The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column chromatography on silica gel to afford the desired product.

4. Control Experiments for the mechanism

4.1 Copper-Catalyzed Oxidative Methylenation of 2-Phenylacetophenone and DMAc

A mixture of 2-phenylacetophenone (0.50 mmol), $\text{Cu}(\text{TFA})_2 \cdot x\text{H}_2\text{O}$ (0.15 mmol), and $\text{K}_2\text{S}_2\text{O}_8$ (1.0 mmol) in DMAc (2.0 mL) was stirred in N_2 at 100 °C for 24 h. After completion of the reaction, the solution was extracted with ethyl acetate (3×15 mL). The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column

chromatography on silica gel to afford the desired product.

4.2 Copper-Catalyzed Oxidative Methylenation of 2-Phenylacetophenone and Amide

A mixture of 2-phenylacetophenone (0.50 mmol), Cu(TFA)₂·xH₂O (0.15 mmol), and K₂S₂O₈ (1.0 mmol) in amide (2.0 mL) was stirred in N₂ at 100 °C for 24 h. After completion of the reaction, the solution was extracted with ethyl acetate (3×15 mL). The organic layers were combined, and dried over sodium sulfate. The residue was detected by GC-MS, no desired product was obtained.

4.3 Copper-Catalyzed Oxidative Methylenation of 2-Phenylacetophenone and *d*₇-DMF

A mixture of 2-phenylacetophenone (0.25 mmol), Cu(TFA)₂·xH₂O (0.075 mmol), and K₂S₂O₈ (0.50 mmol) in *d*₇-DMF (1.0 mL) was stirred in N₂ at 100 °C for 24 h. After completion of the reaction, the solution was extracted with ethyl acetate (3×15 mL). The organic layers were combined, and dried over sodium sulfate. The pure product was obtained by flash column chromatography on silica gel to afford the desired product (**Figure 1**).

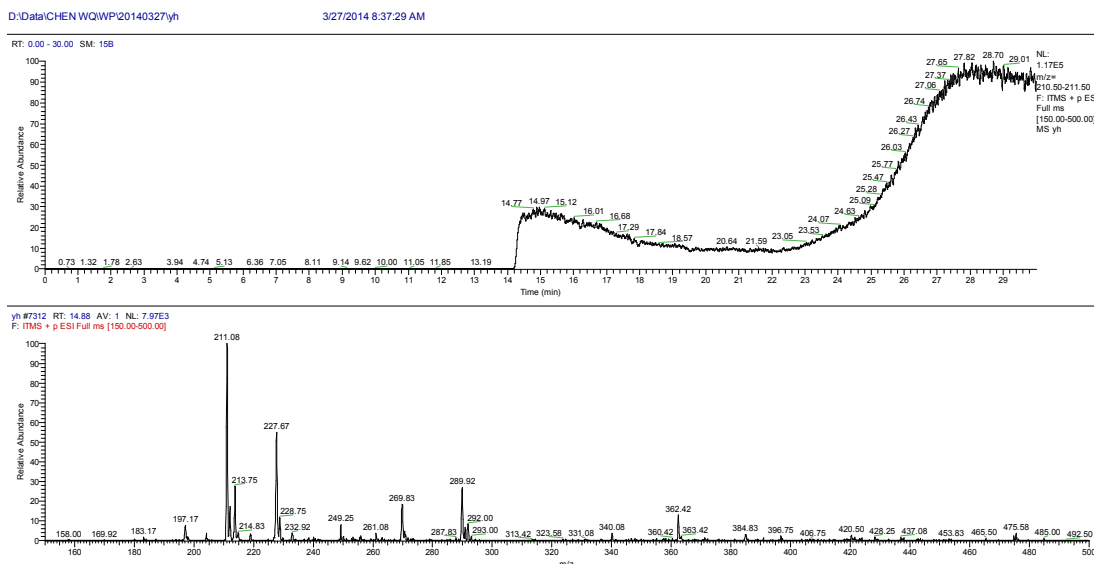


Figure S1: The MS data of *d*₂-1, 2-diphenylprop-2-en-1-one

4.4 Procedure for the IR Experiments of Copper-catalyzed Oxidative Methylenation of 2-Phenylacetophenone and DMF

A three necked reaction vessel was fitted with a magnetic stirring bar. The IR probe was inserted through an adapter into the middle neck; the other two necks were capped by septa for

injections and a nitrogen line. Following evacuation under vacuum and flushing with nitrogen for three times, the three necked vessel was charged with 2-phenylacetophenone (1.0 mmol), $\text{Cu}(\text{TFA})_2 \cdot x\text{H}_2\text{O}$ (0.15 mmol), and $\text{K}_2\text{S}_2\text{O}_8$ (2.0 mmol) in *N,N*-dimethylformamide (3.0 mL). The reaction mixture was stirred at 100 °C. After the temperature was stable, the data collection was started. IR spectra were recorded over the course of the reaction. The standard IR spectrums of **1a** and **2a** are shown in **Figure 2**.

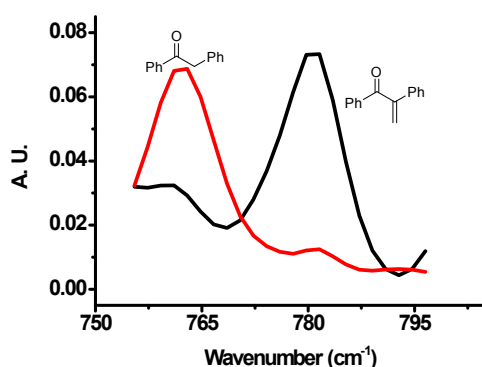


Figure S2: The standard spectrum of 2-phenylacetophenone and 1, 2-diphenylprop-2-en-1-one

5. The Proposed Mechanism of Copper-Catalyzed Oxidative Methylenation of 2-Phenylacetophenone and DMF

Based on the previous reports and our results,¹ a proposed mechanism is depicted in **Figure 3**. The iminium species was generated by the reaction between the DMF and $\text{K}_2\text{S}_2\text{O}_8$ in the presence of copper catalyst. The in situ generated enolate attacked the iminium species A to form the intermediate B, which then underwent elimination to give the product **2a**.

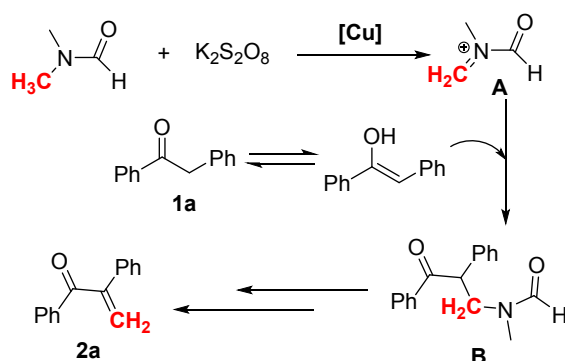
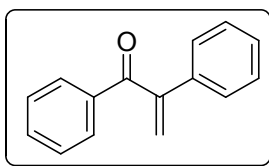


Figure S3. The proposed mechanism of copper-catalyzed oxidative methylenation of 2-phenylacetophenone and DMF

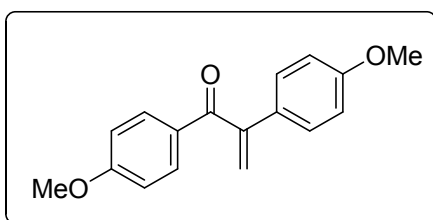
6. Characterization of Products

1, 2-diphenylprop-2-en-1-one (2a)



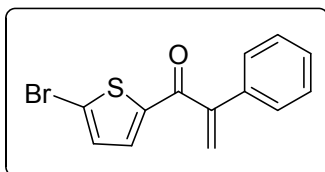
^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.0 Hz, 2H), 7.55 (d, J = 8.0 Hz, 1H), 7.46-7.42 (m, 4H), 7.36-7.34 (m, 3H), 6.08 (s, 1H), 5.65 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.6, 148.3, 137.1, 137.0, 133.1, 130.0, 128.7, 128.4, 127.1, 121.0. HRMS, calculated for $\text{C}_{15}\text{H}_{13}\text{O}$ [$\text{M}+\text{H}^+$]: 209.0961, found: 209.0961.

1, 2-bis(4-methoxyphenyl)prop-2-en-1-one (2b)



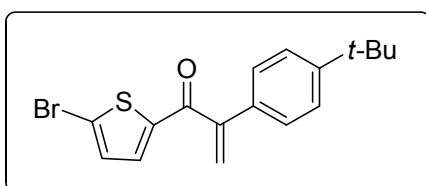
^1H NMR (400 MHz, CDCl_3) δ 7.92 (d, J = 8.0 Hz, 2H), 7.35 (d, J = 12.0 Hz, 2H), 6.91-6.85 (m, 4H), 5.90 (s, 1H), 5.45 (s, 1H), 3.85 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.7, 163.7, 159.8, 147.9, 132.5, 129.9, 129.7, 128.1, 117.0, 114.0, 113.7, 55.5, 55.3. HRMS, calculated for $\text{C}_{17}\text{H}_{17}\text{O}_3$ [$\text{M}+\text{H}^+$]: 269.1172, found: 269.1172.

1-(5-bromothiophen-2-yl)-2-phenylprop-2-en-1-one (2c)



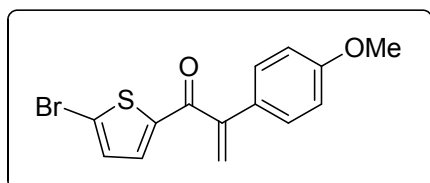
^1H NMR (400 MHz, CDCl_3) δ 7.47-7.45 (m, 2H), 7.40-7.38 (m, 3H), 7.35 (d, J = 4.0 Hz, 1H), 7.09 (d, J = 4.0 Hz, 1H), 6.03 (s, 1H), 5.80 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 188.1, 147.4, 145.4, 136.5, 135.2, 131.3, 128.8, 128.7, 127.1, 124.0, 120.6. HRMS, calculated for $\text{C}_{13}\text{H}_9\text{BrSNaO}$ [$\text{M}+\text{Na}^+$]: 316.9429, found: 316.9433.

1-(5-bromothiophen-2-yl)-2-(4-(tert-butyl)phenyl)prop-2-en-1-one (2d)



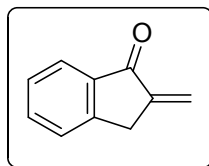
^1H NMR (400 MHz, CDCl_3) δ 7.44-7.39 (m, 4H), 7.38 (d, $J = 4.0$ Hz, 1H), 7.09 (d, $J = 4.0$ Hz, 1H), 6.02 (s, 1H), 5.74 (s, 1H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, CDCl_3) δ 188.4, 151.9, 147.1, 145.5, 135.1, 133.5, 131.3, 126.8, 125.7, 123.9, 119.7, 34.7, 31.3. HRMS, calculated for $\text{C}_{17}\text{H}_{17}\text{BrSNaO}$ $[\text{M}+\text{Na}^+]$: 373.0056, found: 373.0059.

1-(5-bromothiophen-2-yl)-2-(4-methoxyphenyl)prop-2-en-1-one (2e)



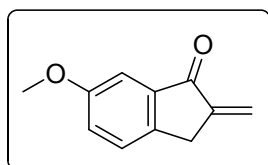
^1H NMR (400 MHz, CDCl_3) δ 7.40-7.38 (m, 2H), 7.36 (d, $J = 4.0$ Hz, 1H), 7.08 (d, $J = 4.0$ Hz, 1H), 6.92-6.90 (m, 2H), 5.93 (s, 1H), 5.69 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 188.5, 160.0, 146.8, 145.4, 135.1, 131.3, 128.9, 128.4, 123.8, 118.8, 114.1, 55.4. HRMS, calculated for $\text{C}_{14}\text{H}_{11}\text{BrSNaO}_2$ $[\text{M}+\text{Na}^+]$: 346.9535, found: 346.9538.

2-methylene-2,3-dihydro-1H-inden-1-one (2f)



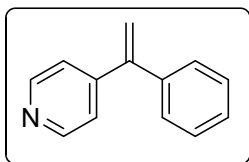
^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 8.0$ Hz, 1H), 7.65-7.61 (m, 1H), 7.52 (d, $J = 8.0$ Hz, 1H), 7.45-7.41 (m, 1H), 6.39 (s, 1H), 5.67 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 193.5, 149.9, 143.3, 138.3, 134.9, 127.6, 126.4, 124.7, 119.3, 31.8. HRMS, calculated for $\text{C}_{10}\text{H}_8\text{NaO}$ $[\text{M}+\text{Na}^+]$: 167.0467, found: 167.0469.

6-methoxy-2-methylene-2,3-dihydro-1H-inden-1-one (2g)



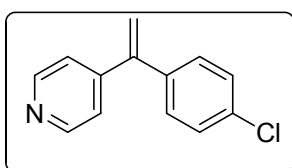
^1H NMR (400 MHz, CDCl_3) δ 7.40 (d, $J = 8.0$ Hz, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.23-7.20 (m, 1H), 6.33 (s, 1H), 5.59 (s, 1H), 3.87 (s, 3H), 3.69 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 193.5, 159.5, 144.1, 142.8, 139.4, 127.2, 124.4, 119.2, 105.8, 55.6, 31.1. HRMS, calculated for $\text{C}_{11}\text{H}_{10}\text{NaO}_2$ $[\text{M}+\text{Na}^+]$: 197.0573, found: 197.0576.

4-(1-phenylvinyl)pyridine (4a)



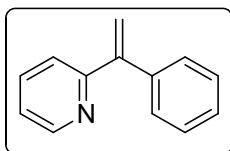
^1H NMR (400 MHz, CDCl_3) δ 8.58 (d, $J = 4.0$ Hz, 2H), 7.37-7.35 (m, 3H), 7.30-7.28 (m, 2H), 7.25-7.23 (m, 2H), 5.61 (s, 1H), 5.60 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 148.9, 147.9, 139.8, 128.5, 128.3, 128.2, 122.8, 117.0. HRMS, calculated for $\text{C}_{13}\text{H}_{11}\text{N}$ [$\text{M}+\text{H}^+$]: 182.0964, found: 182.0970.

4-(1-(4-chlorophenyl)vinyl)pyridine (4b)



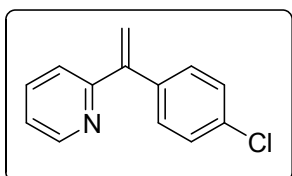
^1H NMR (400 MHz, CDCl_3) δ 8.58 (d, $J = 4.0$ Hz, 2H), 7.33-7.30 (m, 2H), 7.22-7.20 (m, 4H), 5.61 (s, 1H), 5.58 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 149.9, 148.4, 146.9, 138.2, 134.2, 129.5, 128.7, 122.7, 117.4. HRMS, calculated for $\text{C}_{13}\text{H}_{11}\text{ClN}$ [$\text{M}+\text{H}^+$]: 216.0575, found: 216.0574.

2-(1-phenylvinyl)pyridine (4c)



^1H NMR (400 MHz, CDCl_3) δ 8.66 (s, 1H), 7.65 (d, $J = 4.0$ Hz, 1H), 7.39-7.37 (m, 5H), 7.24 (d, $J = 8.0$ Hz, 1H), 6.02 (s, 1H), 5.63 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.5, 149.4, 149.1, 140.4, 136.4, 128.5, 128.3, 127.9, 122.9, 122.5, 117.9. HRMS, calculated for $\text{C}_{13}\text{H}_{11}\text{N}$ [$\text{M}+\text{H}^+$]: 182.0964, found: 182.0966.

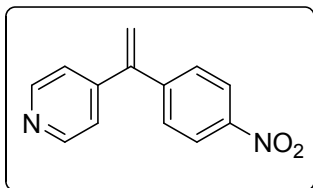
2-(1-(4-chlorophenyl)vinyl)pyridine (4d)



^1H NMR (400 MHz, CDCl_3) δ 8.66 (d, $J = 4.0$ Hz, 1H), 7.69-7.65 (m, 1H), 7.38-7.29 (m, 5H), 7.24-7.23 (m, 1H), 5.98 (s, 1H), 5.62 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.2, 149.4, 148.2, 138.8, 136.5, 133.8, 129.8, 128.5, 122.8, 122.7, 118.1. HRMS, calculated for $\text{C}_{13}\text{H}_{11}\text{ClN}$ [$\text{M}+\text{H}^+$]:

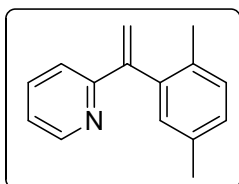
216.0575, found: 216.0571.

4-(1-(4-nitrophenyl)vinyl)pyridine (4e)



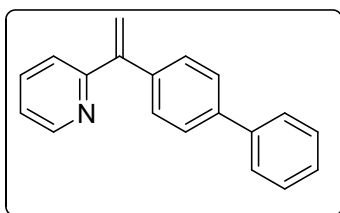
^1H NMR (400 MHz, CDCl_3) δ 8.69 (s, 2H), 8.27 (d, $J = 8.0$ Hz, 2H), 7.48-7.46 (m, 4H), 5.94 (s, 1H), 5.89 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 149.6, 148.1, 147.7, 146.1, 146.0, 129.0, 123.9, 122.8, 120.3. HRMS, calculated for $\text{C}_{13}\text{H}_{11}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}^+]$: 227.815, found: 227.0820.

2-(1-(2,5-dimethylphenyl)vinyl)pyridine (4f)



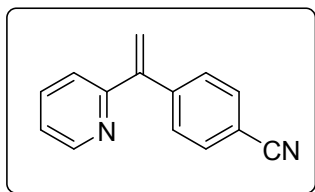
^1H NMR (400 MHz, CDCl_3) δ 8.65 (d, $J = 4.0$ Hz, 1H), 7.66 (dd, $J = 8.0, 4.0$ Hz, 1H), 7.28 (d, $J = 8.0$ Hz, 1H), 7.23 (d, $J = 4.0$ Hz, 1H), 6.98-6.96 (m, 3H), 5.96 (s, 1H), 5.58 (s, 1H), 2.32 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.7, 149.3, 149.3, 140.3, 137.8, 136.4, 129.6, 126.3, 122.9, 122.4, 117.5, 21.3. HRMS, calculated for $\text{C}_{15}\text{H}_{16}\text{N}$ $[\text{M}+\text{H}^+]$: 270.1277, found: 210.1275.

2-(1-([1,1'-biphenyl]-4-yl)vinyl)pyridine (4g)



^1H NMR (400 MHz, CDCl_3) δ 8.70 (d, $J = 4.0$ Hz, 1H), 7.72 (t, $J = 8.0$ Hz, 1H), 7.65-7.61 (m, 4H), 7.49-7.45 (m, 4H), 7.40-7.38 (m, 2H), 6.01 (s, 1H), 5.71 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 158.6, 149.3, 148.7, 140.8, 140.8, 139.2, 136.5, 128.8, 128.8, 127.4, 127.1, 123.0, 122.6, 117.9. HRMS, calculated for $\text{C}_{19}\text{H}_{16}\text{N}$ $[\text{M}+\text{H}^+]$: 258.1277, found: 258.1273.

4-(1-(pyridin-2-yl)vinyl)benzonitrile (4h)

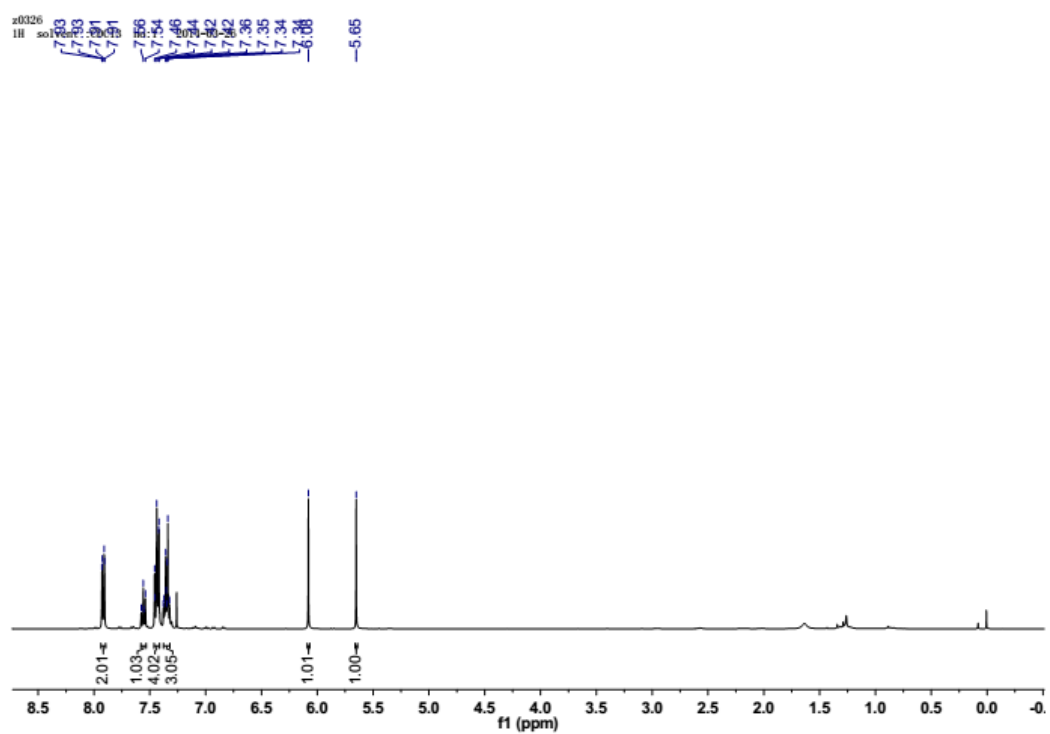
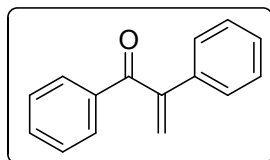


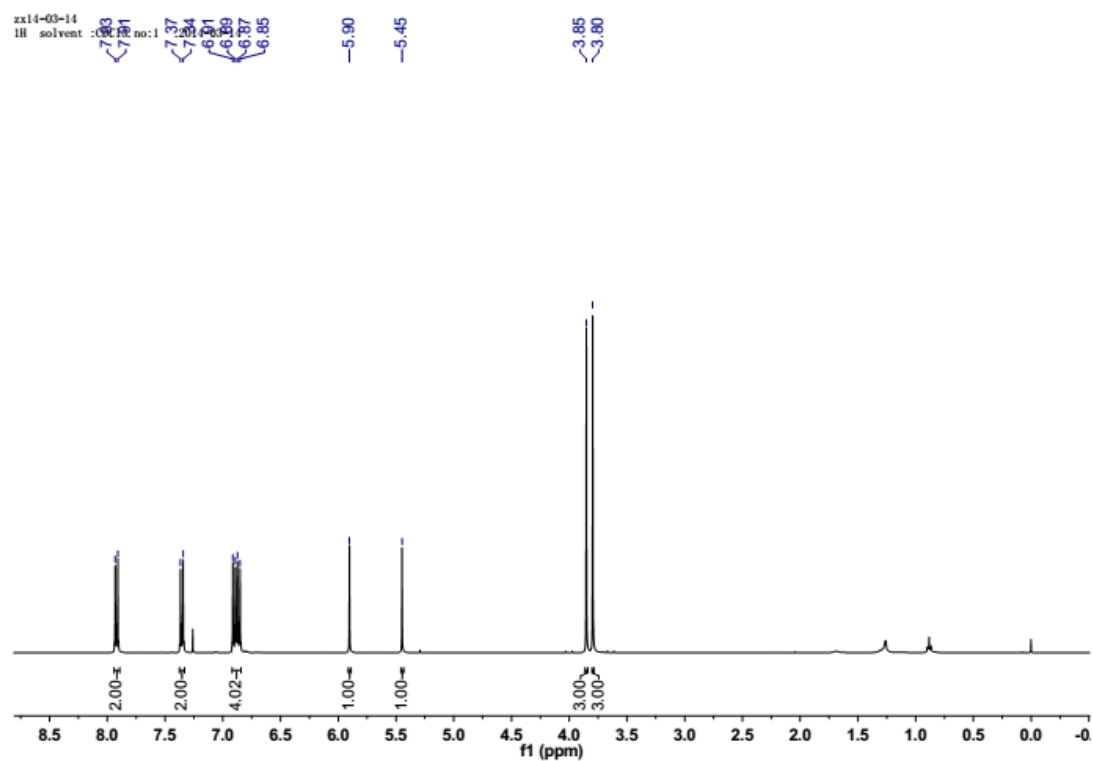
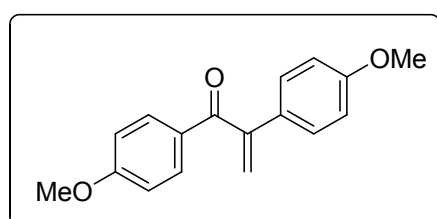
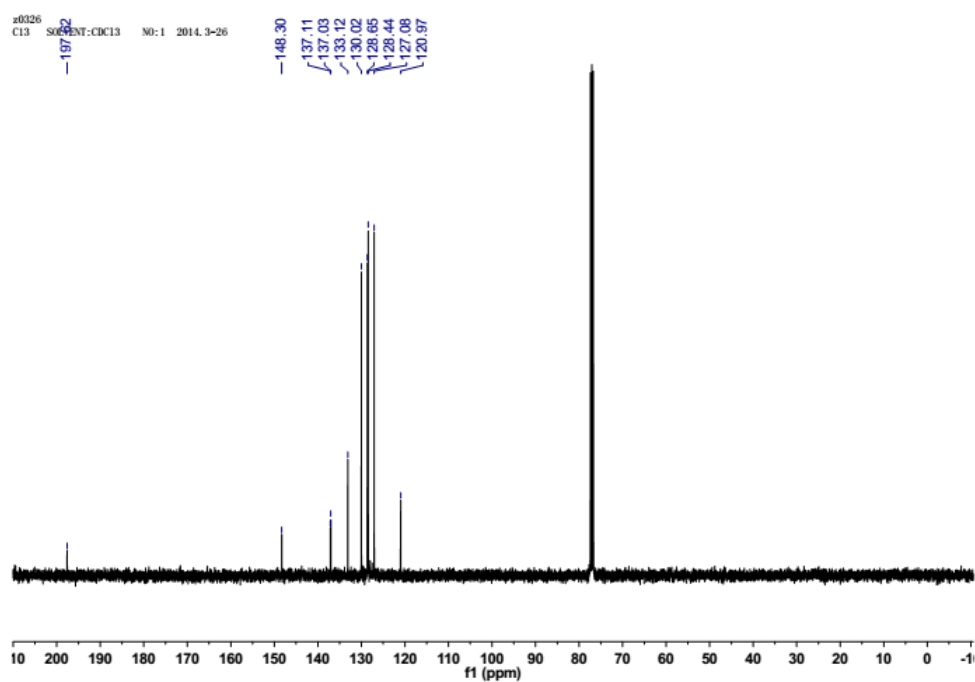
^1H NMR (400 MHz, CDCl_3) δ 8.63 (ddd, $J = 5.1, 1.9, 1.0$ Hz, 1H), 7.70 (td, $J = 7.7, 1.8$ Hz, 1H), 7.65 (dd, $J = 8.4, 1.8$ Hz, 2H), 7.49-7.43 (m, 2H), 7.35-7.31 (m, 1H), 7.26 (td, $J = 4.9, 2.5$ Hz, 1H), 6.04 (s, 1H), 5.71 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 157.5, 147.9, 144.9, 136.8, 132.1, 129.1, 122.9, 122.7, 119.9, 118.9, 115.3, 111.5. HRMS, calculated for $\text{C}_{14}\text{H}_{11}\text{N}$ $[\text{M}+\text{H}^+]$: 207.0917, found: 209.0920.

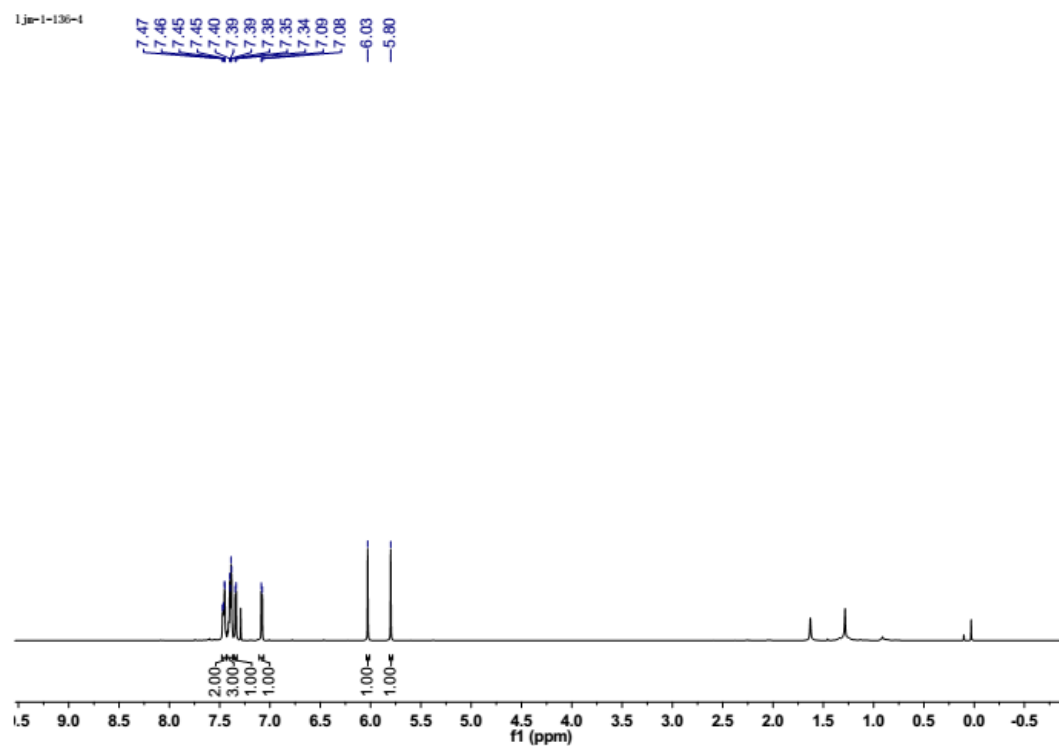
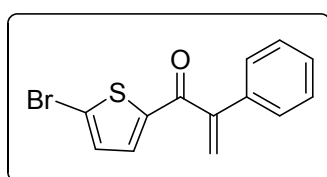
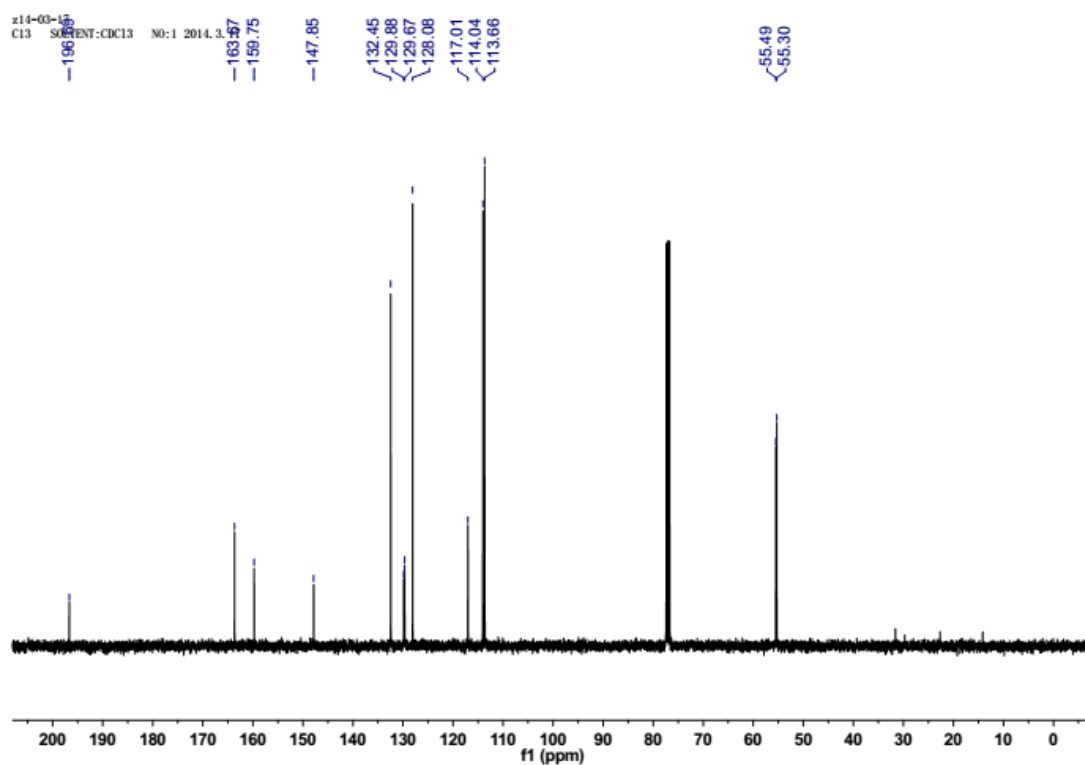
References

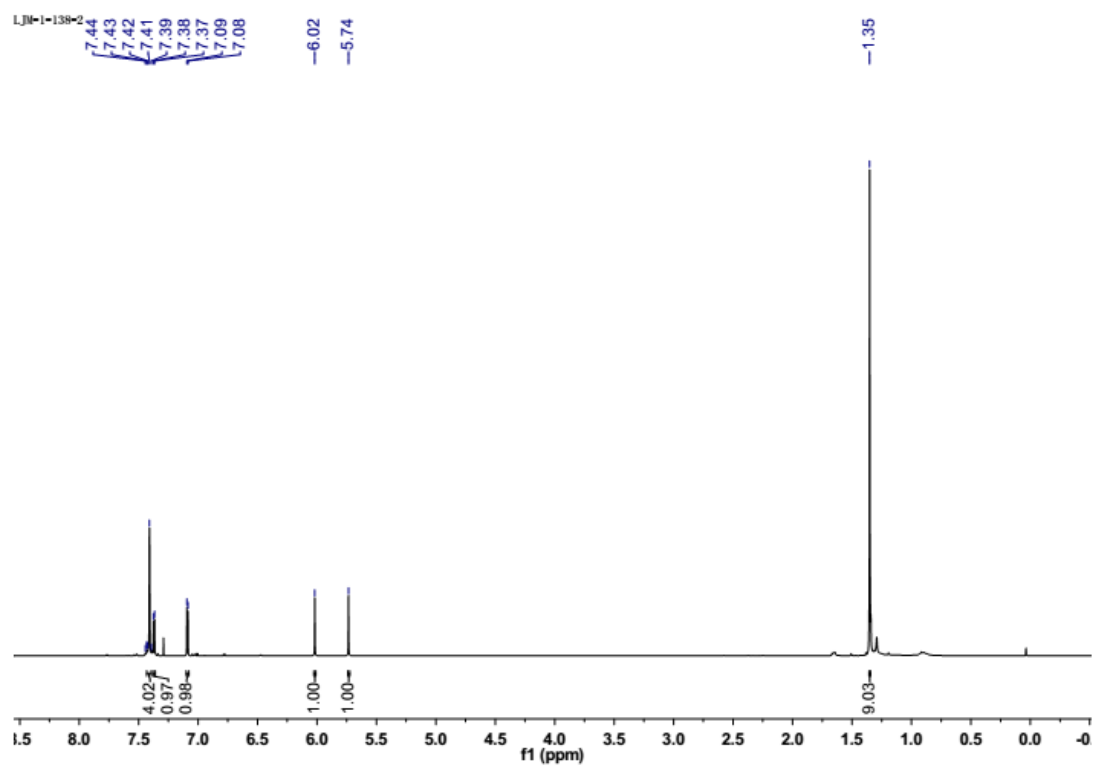
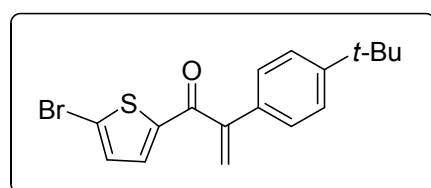
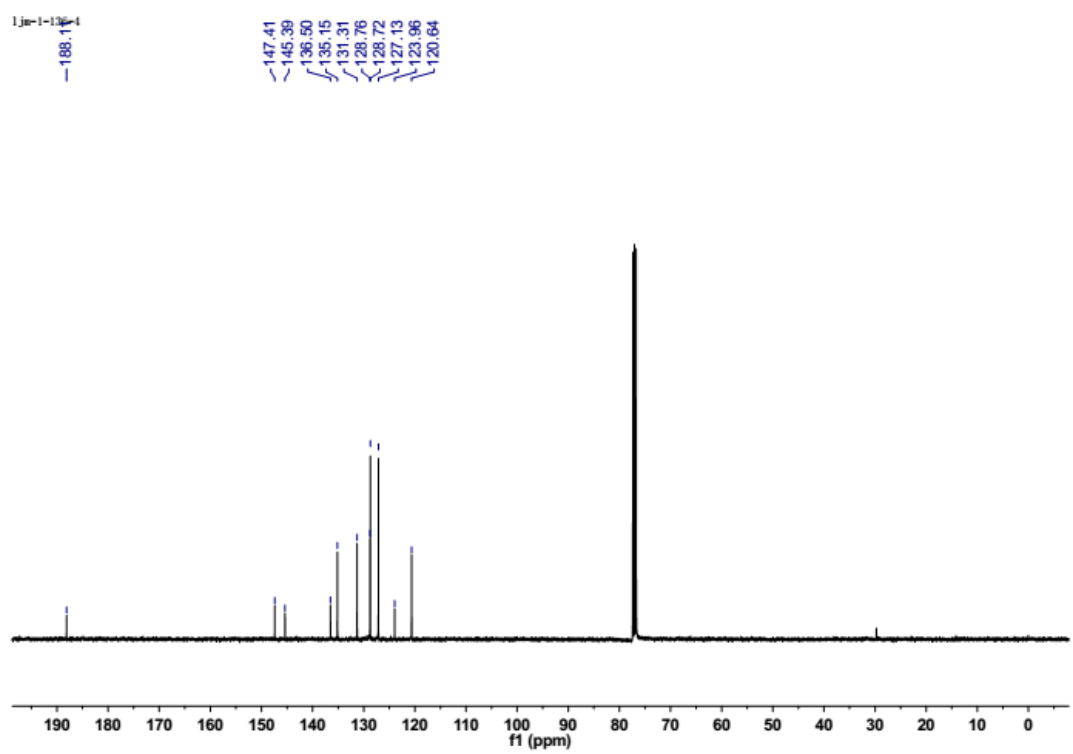
- (a) Y. Li, D. Xue, W. Lu, C. Wang, Z.-T. Liu, and J. Xiao, *Org. Lett.*, 2014, **16**, 66-69. (b) M. Itoh, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2014, **16**, 2050-2053. (c) S.-J. Lou, D.-Q. Xu, D.-F. Shen, Y.-F. Wang, Y.-K. Liu and Z.-Y. Xu, *Chem. Commun.*, 2012, **48**, 11993-11995; (d) Y. Li, F. Guo, Z. Zha and Z. Wang, *Chem. Asian. J.*, 2013, **8**, 534-537.

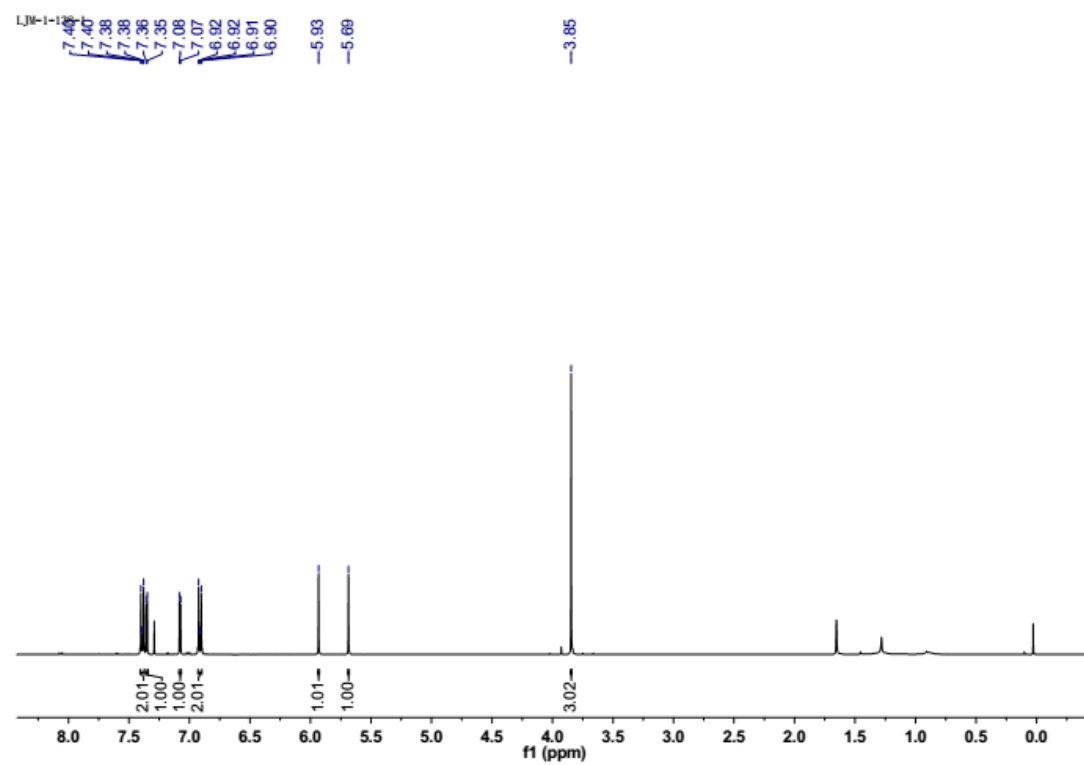
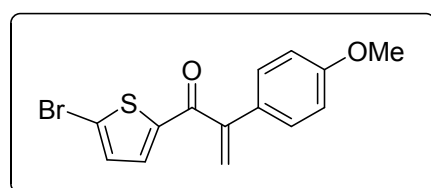
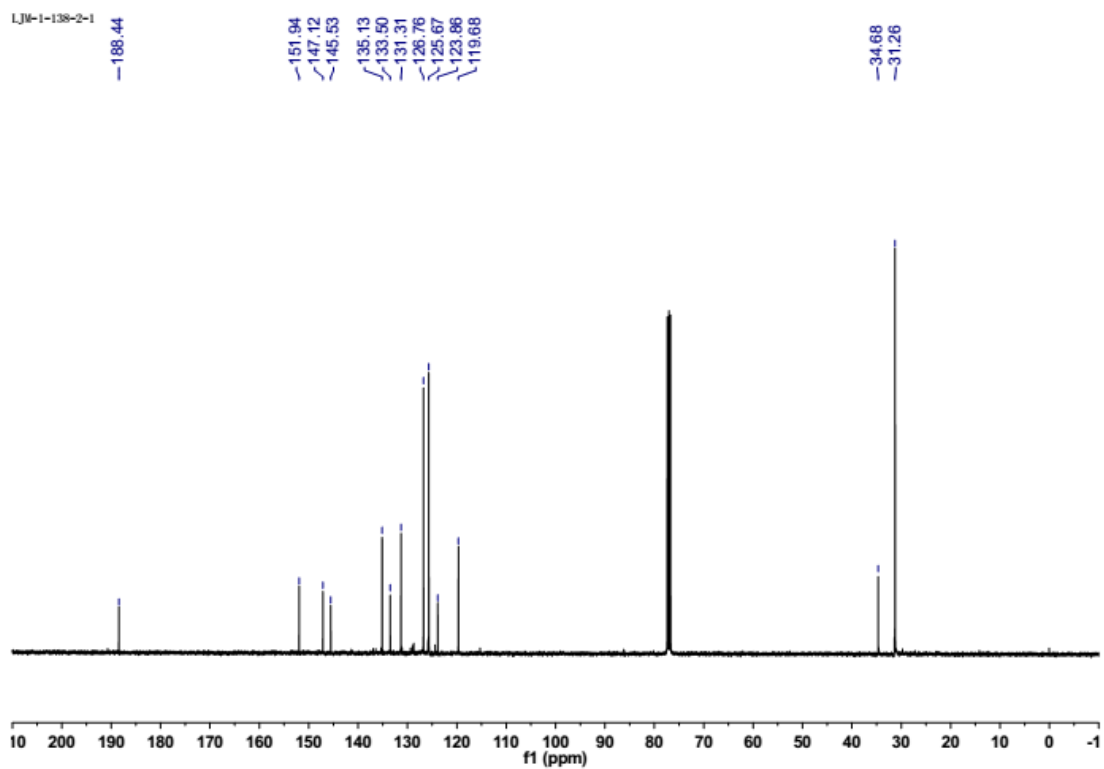
7. NMR Spectra of Products

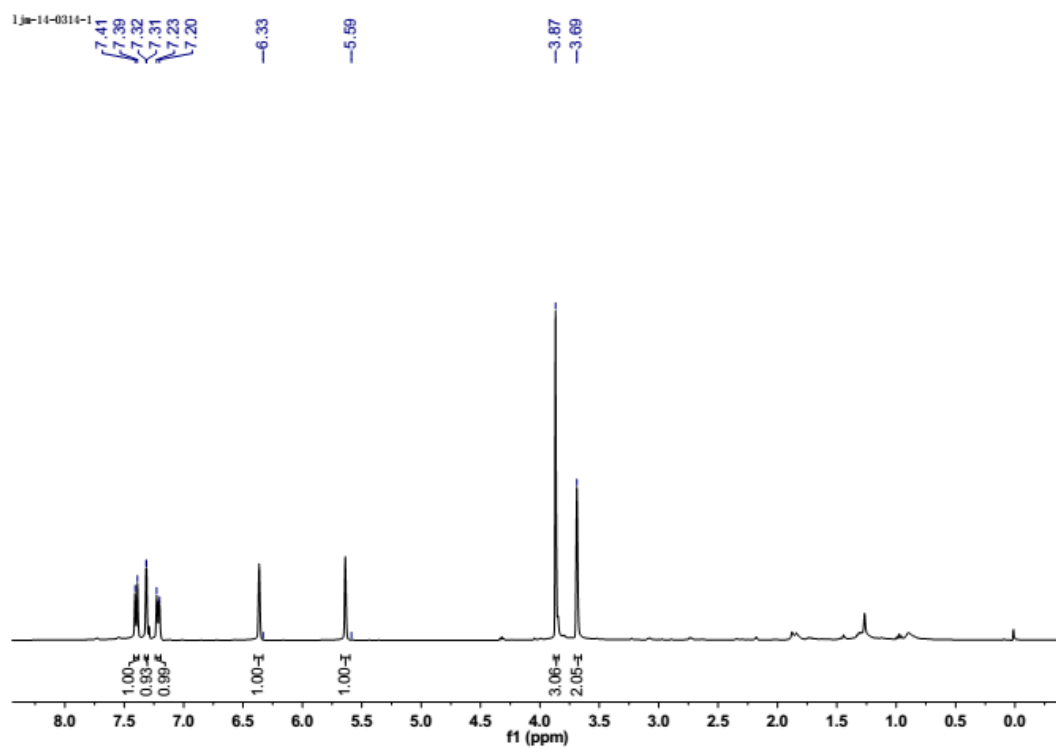
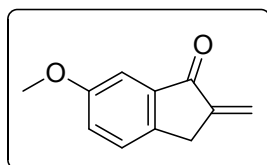
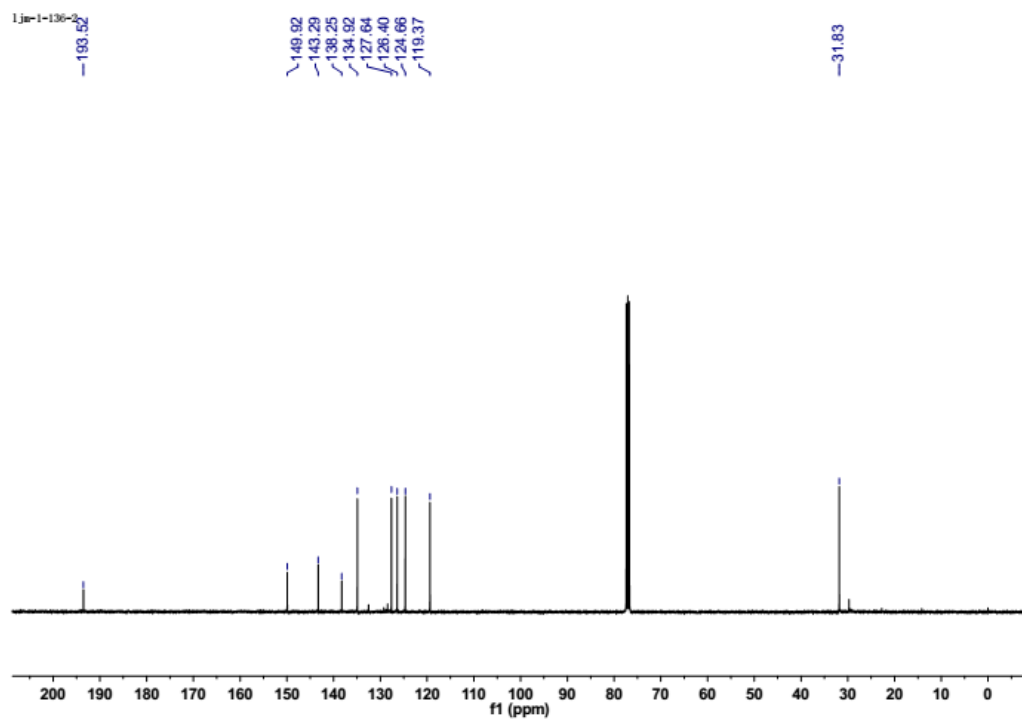


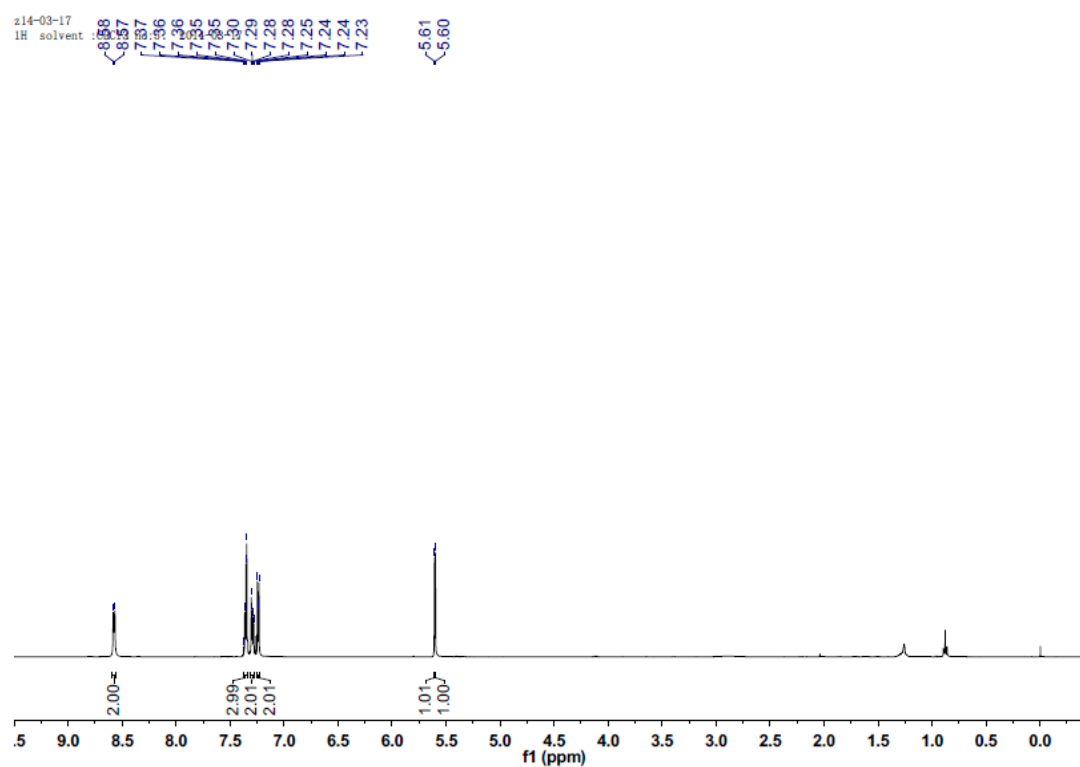
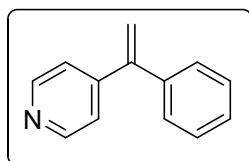
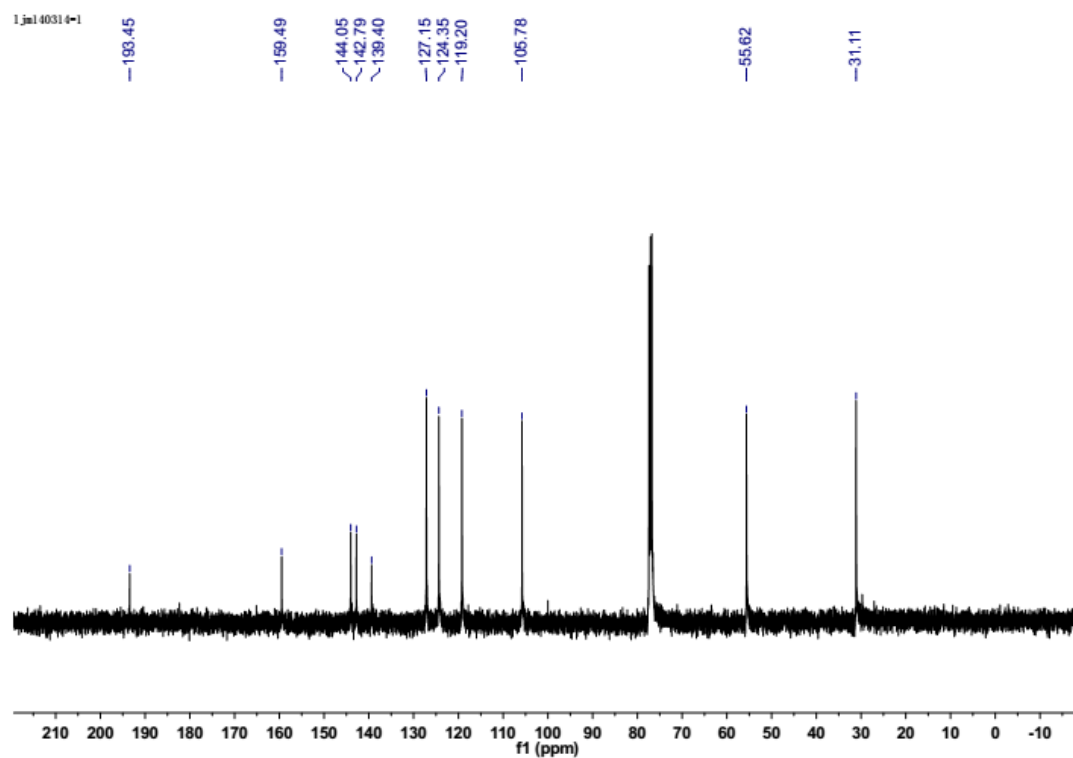


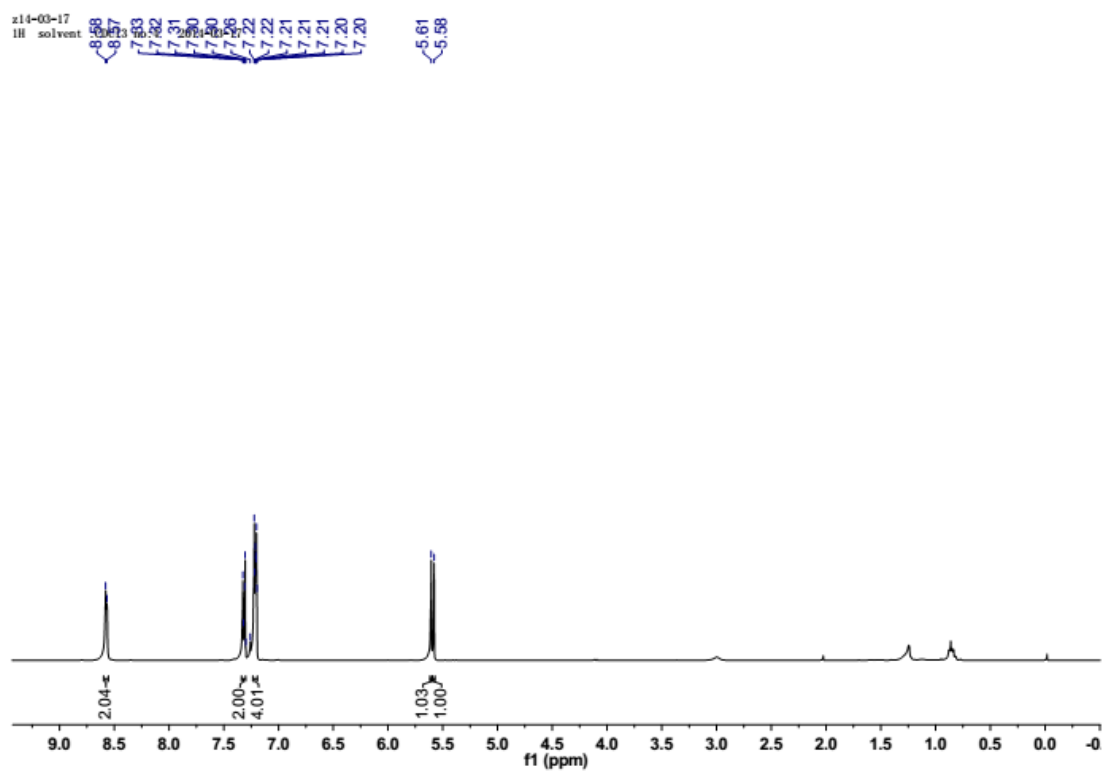
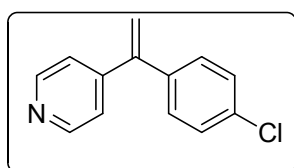
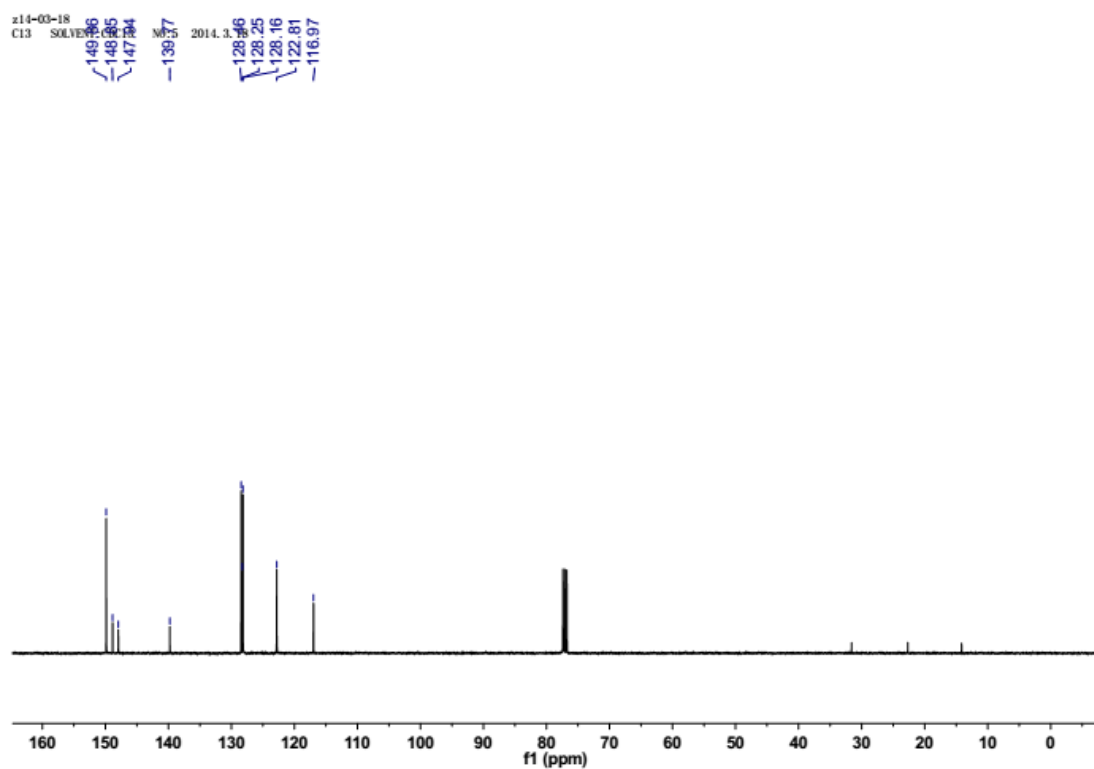




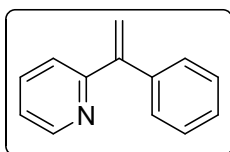
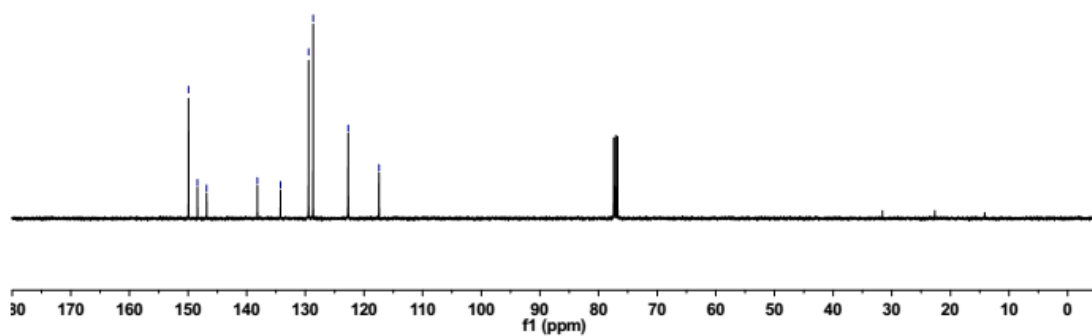




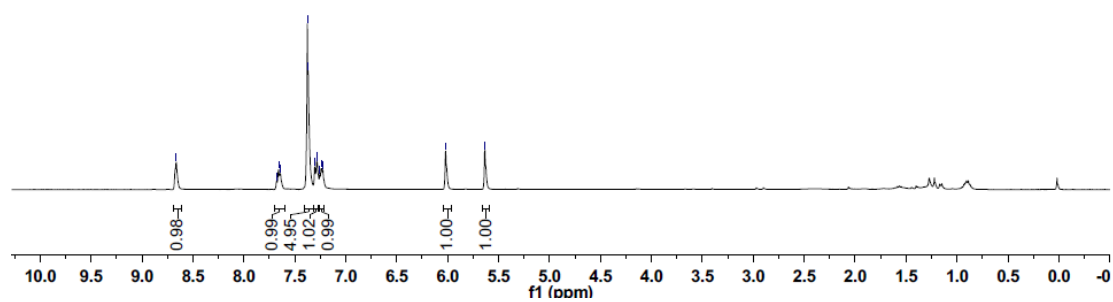




z14-03-18
C13 SOLVENT:CDCl3 NO: 148.92 148.90 148.85 138.19 134.24 129.45 128.68 122.70 117.43



z14-02-25
1H solvent:CDCl3 NO: 8.66 7.68 7.66 7.64 7.38 7.37 7.30 7.28 7.28 7.25 7.24 7.24 7.22 6.02 5.63



xx14-02-28
C13 SOLVENT:CDCl3

