Supporting Information

Cu_2O-Catalyzed Selective 1,2-Addition of Acetonitrile to α,β-Unsaturated Aldehydes

Fengrui Che,[a] Maorong Wang,[b] Chunzheng Yu,[a] Xiangyu Sun,[a] Donghua Xie,[a] Zonghua Wang*[a] and Yuexia Zhang*[a]

[a]College of Chemistry and Chemical Engineering, Shandong Sino-Japanese Center for Collaborative Research of Carbon Nanomaterials, Qingdao University, 308 Ningxia Road, Qingdao 266071, China

[b]State Key Laboratory of Bio-Fibers and Eco-Textiles, Qingdao University, 308 Ningxia Road, Qingdao 266071, China

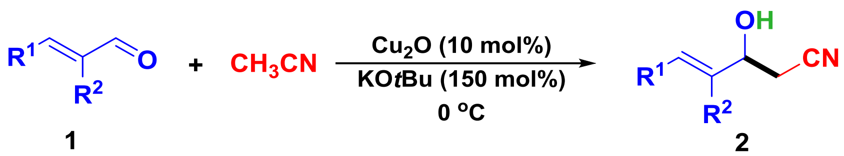
E-mail: zhangyx@qdu.edu.cn; wangzonghua@qdu.edu.cn

Table of contents

I. General information

All reagents and solvents were purchased from J&K Chemicals, Energy Chemical or other commercial suppliers and used as received without further purification. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a Bruker Avance III HD 400 (400 MHz) spectrometer，Bruker Avance 500 (500 MHz) spectrometer or Bruker Avance 600 (600 MHz) spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). ^{1}H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker Avance III HD 400 (100 MHz), Bruker Avance 500 (125 MHz) spectrometer or Bruker Avance 600 (150 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on an Ultima Global spectrometer with an ESI source. Flash chromatography was performed using Qingdao Haiyang silica gel 100 - 200 with distilled solvents. Visualization was performed using a UV lamp.

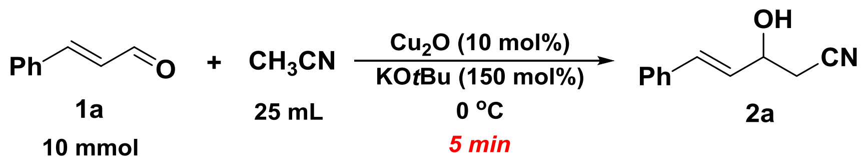
II. General procedure for 1,2-addition of acetonitrile to α,β-unsaturated aldehydes



To a 4 mL vial with a magnetic stir bar was added Cu_2O (5.7 mg, 0.04 mmol, 10 mol%), KO*t*Bu (67.2 mg, 0.6 mmol, 150 mol%) and CH_3CN (2.0 mL), the vial was cooled to 0 ℃. 0.4 mmol α,β-unsaturated aldehyde (**1**) was then added and the resulting mixture was stirred at 0 ℃ (in ice bath) for about 1 – 10 min. The mixture was purified immediately by silica gel column chromatography once complete consumption of α,β-unsaturated aldehyde as monitored by TLC to afford the desired product **2**.

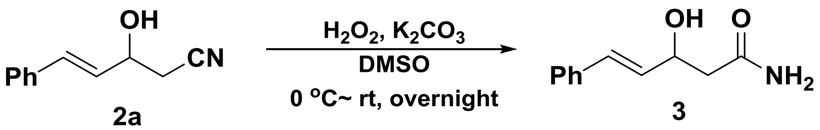
III. Gram scale synthesis of 2a and synthetic transformations of product 2a

1. Gram scale synthesis of 2a



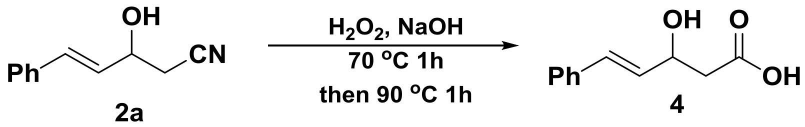
To a 50 mL round bottom flask equipped with a magnetic stir bar, was added Cu_2O (143.1 mg, 1.0 mmol, 10 mol%), KO*t*Bu (1683.0 mg, 15.0 mmol, 150 mol%) and CH_3CN (25 mL). The flask was then located in the ice bath to cool to 0 ℃ without stirring. After that, **1a** (1321.6 mg, 10.0 mmol) was added and the resulting mixture was stirred to 0 ℃ for 5 min. The mixture was concentrated under reduced pressure and purified by silica gel column chromatography (petroleum ether/ethyl acetate =3:1) to afford compound **2a** as a pale yellow oil, 1364.6 mg, 79% yield.

2. Hydrolysis of 2a to amide 3[1]



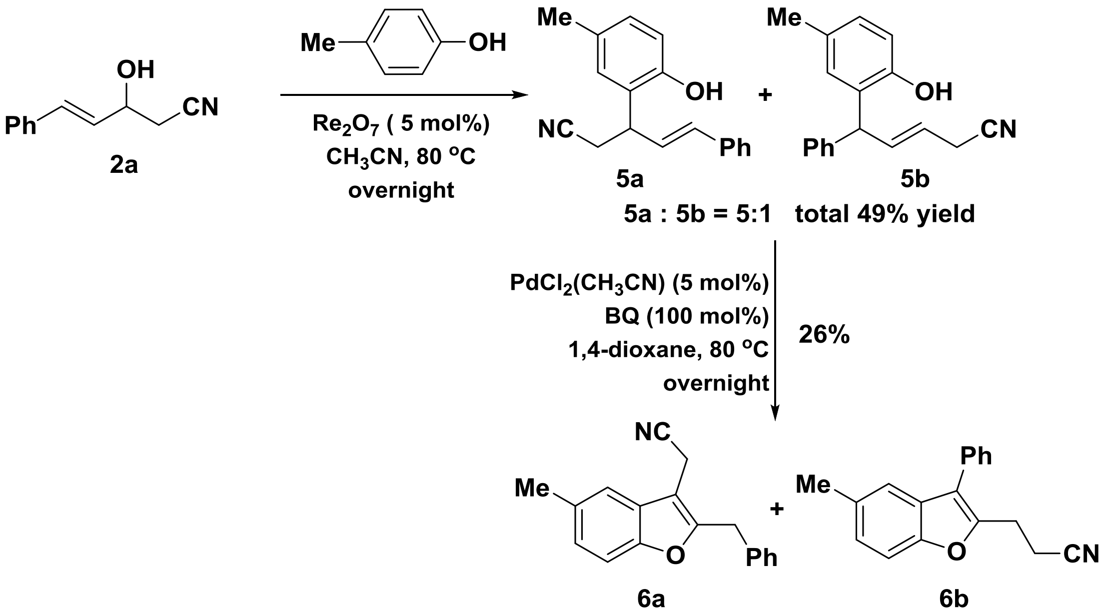
To a stirred solution of **2a** (86.5 mg, 0.5 mmol) in DMSO (1 mL), cooled in a ice bath, was added 30% H_2O_2 (200 uL) and K_2CO_3 (345.5 mg, 5.0 equiv), the mixture was allowed to warm up to room temperature. After 5 min, distilled water (20 mL) was added. The reaction mixture stirred at room temperature overnight until the completion of **2a** (monitored by TLC). The mixture was extracted with dichloromethane (3 × 20 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (petroleum ether/ethyl acetate/methanol = 3:1:0.2) to afford compound **3** as white solid, 91.0 mg, 95% yield.

3. Hydrolysis of 2a to acid 4[2]



To a 50 mL round bottom flask equipped with a magnetic stir bar, was added the **2a** (86.5 mg, 0.5 mmol), 3 M NaOH (3.7 mL), 30% H_2O_2 (1.3 mL). The reaction mixture was heated at 70 ℃ for 1 h and 90 ℃ for another 1 h, the reaction mixture was then cooled to room temperature. The solution was washed once with ethyl ether (3.0 mL). The aqueous solution was acidified with 2 M HCl (10 mL) and then extracted with dichloromethane (3 × 20 mL). The combined organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (petroleum ether/ethyl acetate =2:1) to afford compound **4** as a white solid, 89.4 mg, 93% yield.

4. Transformation of 2a to functionalized benzuo[*b*]furans[3]

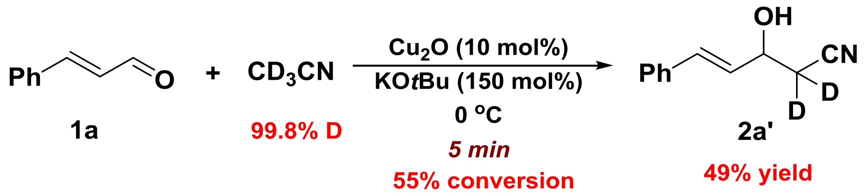


Step 1: To a 50 mL round bottom flask equipped with a magnetic stir bar, was added **2a** (86.5 mg, 0.5 mmol), *p*-cresol (59.5 mg, 1.1 equiv), Re_2O_7 (12.1 mg, 5 mol%) and CH_3CN (2.0 mL). A refluxed condenser was attached, and then the reaction mixture was stirred at 80 ℃ overnight until complete consumption of **2a** as monitored by TLC. The mixture was concentrated under reduced pressure and purified by silica gel

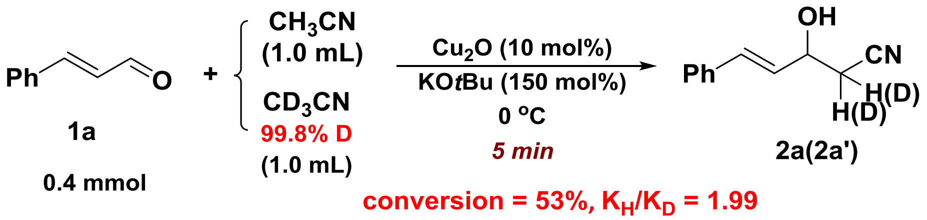
column chromatography (petroleum ether/ethyl acetate =10:1) to afford **5a** and **5b** as a mixture in 49% combined yield.

Step 2: To a 10 mL sealed tube equipped with a magnetic stir bar, was added mixed **5a** and **5b** obtained above (64.0 mg), $PdCl_2(CH_3CN)_2$ (3.2 mg, 5 mol%), benzoquinone (26.3 mg, 1.0 equiv). Then the mixture was dissolved in 1,4-dioxane (1.0 mL). The reaction mixture was placed in a preheated oil bath at 80 ℃ and stirred at 80 ℃ overnight. After consumption of **5a** and **5b** as monitored by TLC, the mixture was cooled to room temperature. Evaporation of the solvent followed by purification by silica gel column chromatography (petroleum ether/ethyl acetate =20:1) to afford **6a** and **6b** in 26% combined yield.

IV. Deuteration experiments

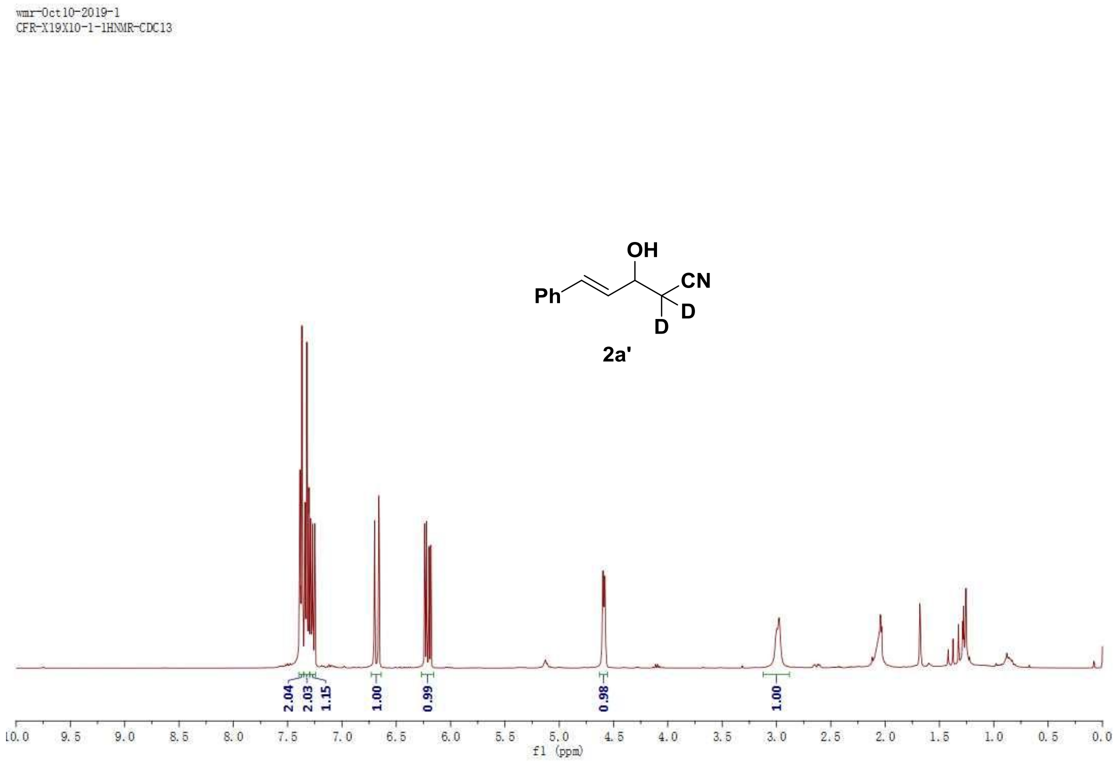


To a 4 mL vial with magnetic stir bar was added Cu_2O (5.7 mg, 0.04 mmol, 10 mol%), KO*t*Bu (0.6 mmol, 67.2 mg, 150 mol%) and CD_3CN (2.0 mL, 99.8% D), the vial was then cooled to 0 ℃. **1a** (52.9 mg, 0.4 mmol) was added and the resulting mixture was stirred at 0 ℃ (in ice bath) for 5 min. The mixture was purified immediately by silica gel column chromatography (petroleum ether/ethyl acetate =3:1) to afford **1a** 23.8 mg, **2a'** 34.3 mg**.**

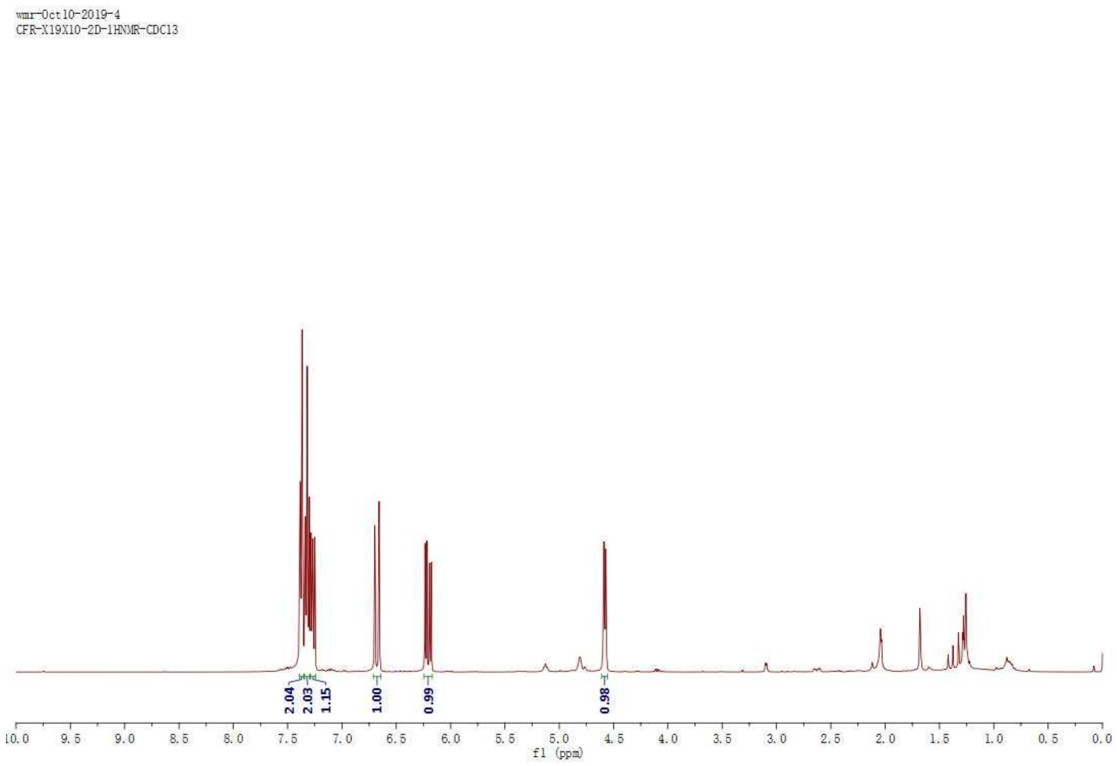


To a 4 mL vial with magnetic stir bar was added Cu_2O (5.7 mg, 0.04 mmol, 10 mol%), KO*t*Bu (0.6 mmol, 67.2 mg, 150 mol%) and 2.0 mL 1:1 mixture of CH_3CN and CD_3CN, the vial was then cooled to 0 ℃. **1a** (52.9 mg, 0.4 mmol) was added and the resulting mixture was stirred at 0 ℃ (in ice bath) for 5 min. The mixture was purified immediately by silica gel column chromatography (petroleum ether/ethyl acetate =3:1) to afford the mixture products of **2a** and **2a'**.

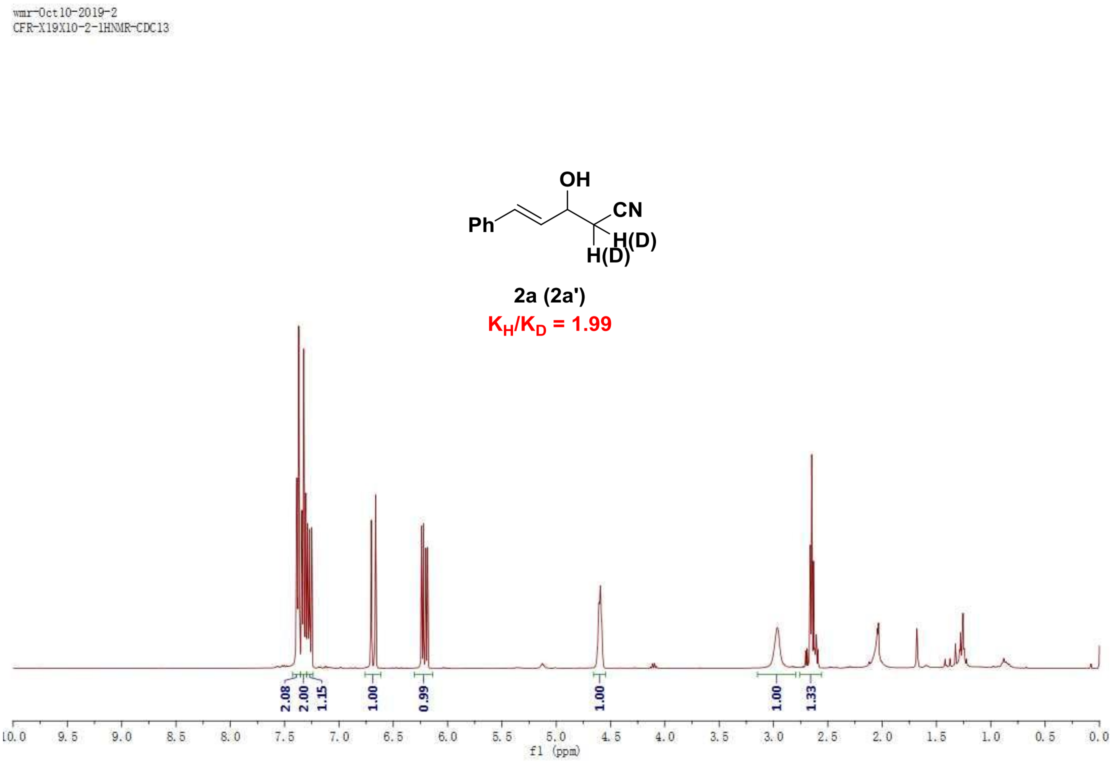
^{1}H NMR of 2a' (in $CDCl_3$)



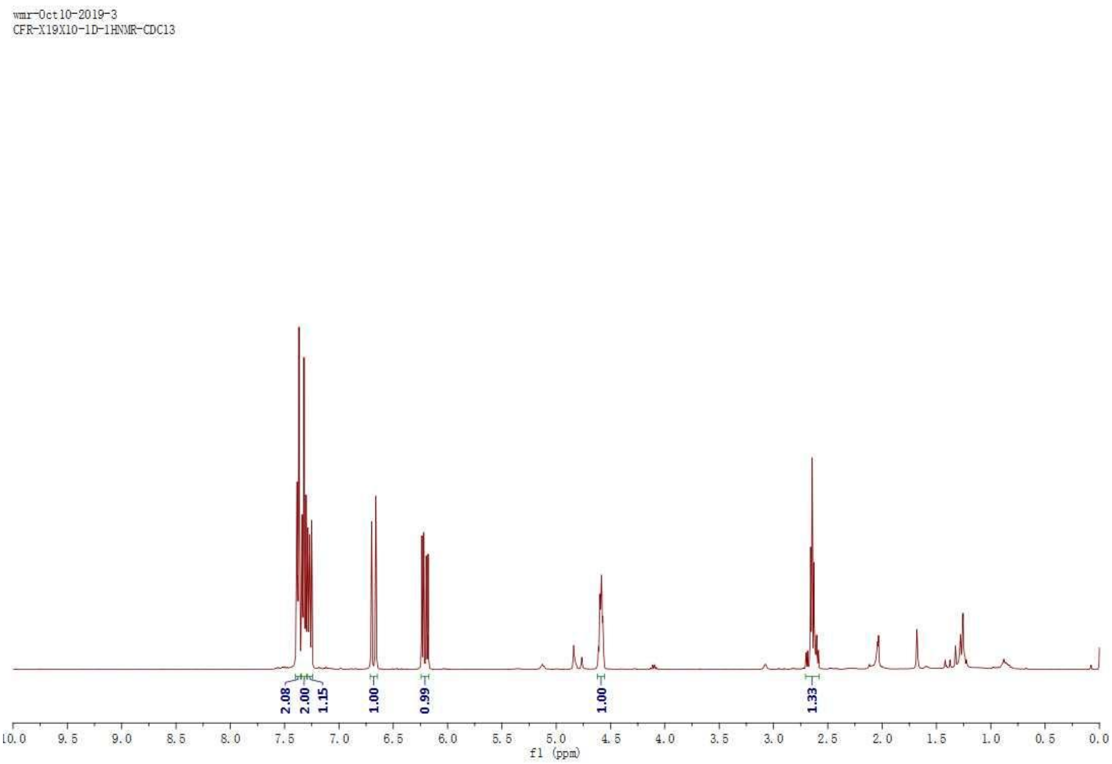
^{1}H NMR of 2a' after Hydrogen-Deuterium Exchange with D_2O (in $CDCl_3$)



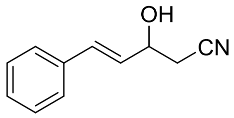
t=5min, Conversion = 53%, K_H/K_D = 1.99



After Hydrogen-Deuterium Exchange with D_2O



V. Characterizations data for all products



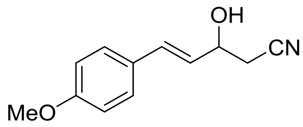
2a

(*E*)-3-hydroxy-5-phenylpent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 - 7.32 (m, 2H), 7.36 – 7.30 (m, 2H), 7.30 – 7.25 (m, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.23 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.65 – 4.60 (m, 1H), 2.73 – 2.61 (m, 2H), 2.41 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5, 133.0, 128.7, 128.4, 127.9, 126.7, 117.6, 68.7, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{11}NONa$ 196.0738; found 196.0736.



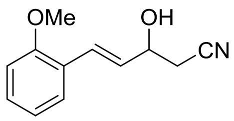
2b

(*E*)-3-hydroxy-5-(4-methoxyphenyl)pent-4-enenitrile: pale yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.4 Hz, 2H), 6.68 (d, *J* = 8.8 Hz, 2H), 6.44 (d, *J* = 15.6 Hz, 1H), 5.90 (dd, *J* = 15.6, 6.8 Hz, 1H), 4.40 (q, *J* = 5.6 Hz, 1H), 3.62 (s, 3H), 2.67 (s, 1H), 2.53 – 2.41 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 132.3, 128.2, 127.9, 125.7, 117.4, 114.0, 68.7, 55.2, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{12}H_{13}NO_2Na$ 226.0844; found 226.0850.



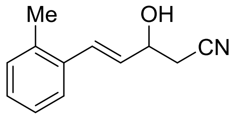
2c

(*E*)-3-hydroxy-5-(2-methoxyphenyl)pent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.25 – 7.20 (m, 1H), 6.98 (d, *J* = 16.0 Hz, 1H), 6.92 – 6.84 (m, 2H), 6.24 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.59 (q, *J* = 6.4 Hz, 1H), 3.81 (s, 3H), 2.70– 2.58 (m, 2H), 2.39 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 129.8, 128.9, 128.4, 127.6, 124.7, 120.9, 117.6, 111.2, 69.5, 55.7, 26.6.

HRMS (ESI-TOF) [M+Na]$^+$ calcd. for $C_{12}H_{13}NO_2Na$ 226.0844; found 226.0851.



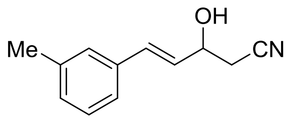
2d

(*E*)-3-hydroxy-5-(o-tolyl)pent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.41 (m, 1H), 7.19 – 7.15 (m, 3H), 6.94 (d, *J* = 15.6 Hz, 1H), 6.11 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.67 – 4.61 (m, 1H), 2.74 – 2.62 (m, 3H), 2.35 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8, 134.7, 130.9, 130.4, 129.4, 128.3, 126.2, 125.8, 117.1, 68.9, 26.4, 19.7.

HRMS (ESI-TOF) [M+Na]$^+$ calcd. for $C_{12}H_{13}NONa$ 210.0895; found 210.0905.



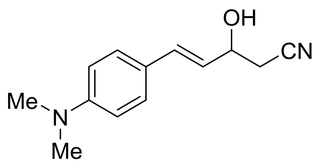
2e

(*E*)-3-hydroxy-5-(m-tolyl)pent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.17 (m, 3H), 7.10 (d, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 15.6, 6.4 Hz, 1H), 4.64 – 4.57 (m, 1H), 2.72 – 2.64 (m, 2H), 2.58 (s, 1H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 136.7, 133.8, 131.6, 127.7, 126.9, 126.1, 125.8, 122.3, 115.5, 67.2, 24.7, 19.7.

HRMS (ESI-TOF) [M+Na]$^+$ calcd. for $C_{12}H_{13}NONa$ 210.0895; found 210.0897.



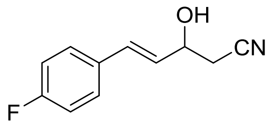
2f

(*E*)-5-(4-(dimethylamino)phenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 8.8 Hz, 2H), 6.66 (d, *J* = 8.8 Hz, 2H), 6.57 (d, *J* = 15.6 Hz, 1H), 6.00 (dd, *J* = 15.6, 7.2 Hz, 1H), 4.58 – 4.52 (m, 1H), 2.96 (s, 6H), 2.70 – 2.61 (m, 2H), 2.50 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 133.5, 128.1, 123.9, 123.7, 117.7, 112.5, 69.5, 40.7, 26.7.

HRMS (ESI-TOF) $[M+H]^+$ calcd. for $C_{13}H_{17}N_2O$ 217.1336; found 217.1339.



2g

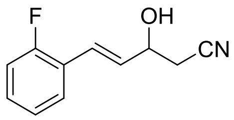
(*E*)-5-(4-fluorophenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.32 (m, 2H), 7.04 – 6.98 (m, 2H), 6.66 (d, *J* = 16.0 Hz, 1H), 6.14 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.64 – 4.58 (m, 1H), 2.86 (s, 1H), 2.73 – 2.61 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, $J_{C\text{-}F}$ = 246.5 Hz), 131.7 (d, $J_{C\text{-}F}$ = 3.3 Hz), 131.6, 128.3 (d, $J_{C\text{-}F}$ = 8.0 Hz), 127.7 (d, $J_{C\text{-}F}$ = 2.1 Hz), 117.3, 115.6 (d, $J_{C\text{-}F}$ = 21.6 Hz), 68.4, 26.3.

^{19}F NMR (377 MHz, $CDCl_3$) δ -112.86.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{10}FNONa$, 214.0644 found, 214.0651.



2h

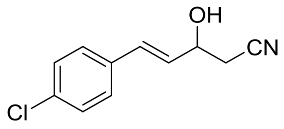
(*E*)-5-(2-fluorophenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 1H), 7.31 – 7.24 (m, 1H), 7.15 – 7.04 (m, 2H), 6.88 (d, *J* = 16.0 Hz, 1H), 6.35 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.67 (q, *J* = 5.6 Hz, 1H), 2.77 – 2.65 (m, 2H), 2.62 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (d, $J_{C\text{-}F}$ = 248.6 Hz), 130.3 (d, $J_{C\text{-}F}$ = 5.2 Hz), 129.4 (d, $J_{C\text{-}F}$ = 8.5 Hz), 127.5 (d, $J_{C\text{-}F}$ = 3.4 Hz), 125.1 (d, $J_{C\text{-}F}$ = 3.3 Hz), 123.9 (d, $J_{C\text{-}F}$ = 3.6 Hz), 123.0 (d, $J_{C\text{-}F}$ = 12.0 Hz), 116.9, 115.5 (d, $J_{C\text{-}F}$ = 21.9 Hz), 68.3, 25.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -117.33.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{10}FNONa$ 214.0644; found 214.0645.



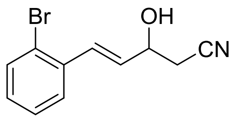
2i

(*E*)-5-(4-chlorophenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 4H), 6.64 (d, *J* = 15.6 Hz, 1H), 6.19 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.61 (q, *J* = 5.6 Hz, 1H), 2.82 (s, 1H), 2.73 – 2.60 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.1, 133.0, 130.5, 127.9, 127.7, 126.9, 116.3, 67.4, 25.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{10}ClNONa$ 230.0349; found 230.0347.



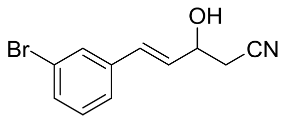
2j

(*E*)-5-(2-bromophenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.52 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.19 – 7.14 (m,1H), 7.08 (d, *J* = 16.0 Hz, 1H), 6.22 (dd, *J* = 15.6, 6.4 Hz, 1H), 4.80 – 4.65 (m, 1H), 2.79 – 2.67 (m, 2H), 2.57 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 132.6, 130.2, 128.9, 128.1, 126.8, 124.8, 124.4, 121.0, 114.2, 65.6, 23.4.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{10}BrNONa$ 273.9843; found 273.9850.



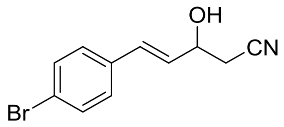
2k

(*E*)-5-(3-bromophenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.43 (dd, *J* = 8.4, 0.6 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 6.67 (d, *J* = 15.6 Hz, 1H), 6.26 (dd, *J* = 15.6, 6.6 Hz, 1H), 4.69 – 4.64 (m, 1H), 3.01 (s, 1H), 2.76 – 2.66 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 137.8, 131.3, 131.2, 130.3, 129.7, 129.6, 125.5, 122.9, 117.3, 68.3, 26.4.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{10}BrNONa$ 273.9843; found 273.9852.



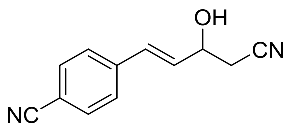
2l

(*E*)-5-(4-bromophenyl)-3-hydroxypent-4-enenitrile: white solid

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.13 (dd, *J* = 16.0, 6.8 Hz, 1H),4.60 – 4.45 (m, 1H), 2.85 (s, 1H), 2.66 – 2.53 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 134.1, 131.4, 131.2, 128.4, 127.9, 121.9, 116.9, 68.0, 25.9.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_{10}BrNONa$ 273.9843; found 273.9825.



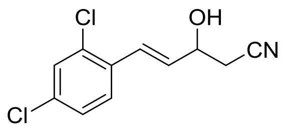
2m

(*E*)-4-(4-cyano-3-hydroxybut-1-en-1-yl)benzonitrile: brown solid

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 6.70 (d, *J* = 16.0 Hz, 1H), 6.31 (dd, *J* = 16.0, 6.4 Hz, 1H), 4.66 – 4.60 (m, 1H), 2.71 – 2.59 (m, 2H), 2.35 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3, 132.6, 132.4, 128.7, 126.9, 118.9, 110.8, 63.1, 29.7.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{12}H_{10}N_2ONa$ 221.0691; found 221.0712.



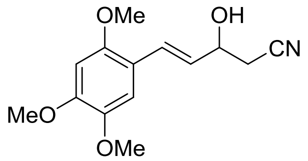
2n

(*E*)-5-(2,4-dichlorophenyl)-3-hydroxypent-4-enenitrile: pale yellow solid

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 (d, *J* = 8.4 Hz, 1H), 7.33 (d, *J* = 2.4 Hz, 1H), 7.17 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.99 (d, *J* = 15.6 Hz, 1H), 6.18 (dd, *J* = 15.6, 6.6 Hz, 1H), 4.68 – 4.60 (m, 1H), 2.80 (s, 1H), 2.72 – 2.62 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 134.1, 133.6, 132.1, 131.1, 129.2, 127.7, 127.5, 127.1, 116.7, 68.0, 25.9.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{11}H_9Cl_2NONa$ 263.9959; found 263.9959.



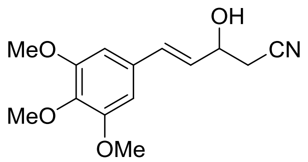
2o

(*E*)-3-hydroxy-5-(2,4,5-trimethoxyphenyl)pent-4-enenitrile: yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 – 6.92 (m, 2H), 6.51 (s, 1H), 6.14 (dd, *J* = 16.0, 7.2 Hz, 1H), 4.62 (q, *J* = 6.0 Hz, 1H), 3.93 – 3.84 (m, 9H), 2.79 – 2.65 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 150.1, 143.2, 127.3, 126.2, 117.4, 116.0, 110.0, 97.3, 69.2, 56.5, 56.4, 55.9, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{14}H_{17}NO_4Na$ 286.1055; found 286.1063.



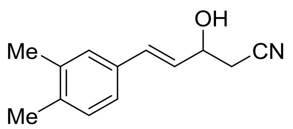
2p

(*E*)-3-hydroxy-5-(3,4,5-trimethoxyphenyl)pent-4-enenitrile: yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.64 – 6.56 (m, 3H), 6.14 (dd, *J* = 16.0, 6.8 Hz, 1H), 4.62 (q, *J* = 5.6 Hz, 1H), 3.87 (s, 6H), 3.85 (s, 3H), 2.76 – 2.63 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 153.2, 138.2, 132.8, 131.3, 127.5, 117.2, 103.8, 68.6, 60.9, 56.1, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{14}H_{17}NO_4Na$ 286.1055; found 286.1060.



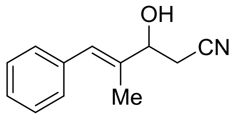
2q

(*E*)-5-(3,4-dimethylphenyl)-3-hydroxypent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1H), 7.14 – 7.07 (m, 2H), 6.62 (d, *J* = 15.6 Hz, 1H), 6.16 (dd, *J* = 15.6, 6.8 Hz, 1H), 4.58 (q, *J* = 5.6 Hz, 1H), 2.72 (s, 1H), 2.70 – 2.62 (m, 2H), 2.25 (s, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 137.0, 136.8, 133.1, 132.9, 129.9, 127.9, 126.8, 124.2, 117.3, 68.7, 26.3, 19.7, 19.5.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{13}H_{15}NONa$ 224.1051; found 224.1056.



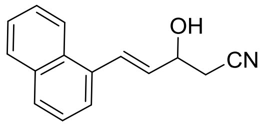
2r

(*E*)-3-hydroxy-4-methyl-5-phenylpent-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 2H), 7.31 – 7.25 (m, 3H), 6.66 (s, 1H), 4.54 (t, *J* = 6.4 Hz, 1H), 2.77 – 2.65 (m, 3H), 1.91 (d, *J* = 1.2 Hz, 3H).

^{13}C NMR (100MHz,$CDCl_3$) δ 134.8, 134.6, 127.1, 126.4, 125.8, 125.1, 115.7, 71.3, 22.8, 11.4.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{12}H_{13}NONa$ 210.0895; found 210.0899.



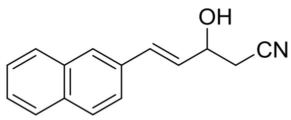
2s

(*E*)-3-hydroxy-5-(naphthalen-1-yl)pent-4-enenitrile: pale yellow solid

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.0 Hz, 1H), 7.87 – 7.79 (m, 2H), 7.59 – 7.42 (m, 5H), 6.26 (dd, *J* = 15.6, 6.8 Hz, 1H), 4.74 (q, *J* = 6.0 Hz, 1H), 2.79 – 2.67 (m, 2H), 2.51 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 133.6, 133.4, 131.3, 131.1, 130.3, 128.8, 128.7, 126.4, 126.0, 125.6, 124.3, 123.6, 117.2, 68.8, 26.5.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{15}H_{13}NONa$ 246.0895; found 246.0898.



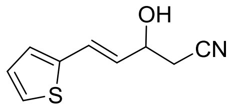
2t

(*E*)-3-hydroxy-5-(naphthalen-2-yl)pent-4-enenitrile: pale yellow solid

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.73 (m, 3H), 7.69 (s, 1H), 7.54 – 7.51 (m, 1H), 7.45 – 7.43 (m, 2H), 6.79 (d, *J* = 16.2 Hz, 1H), 6.29 (dd, *J* = 16.2, 6.6 Hz, 1H), 4.65 – 4.58 (m, 1H), 2.94 (s, 1H), 2.69 – 2.60 (m, 2H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 133.3, 133.2, 132.9, 132.8, 128.3, 128.2, 128.0, 127.6, 127.1, 126.4, 126.2, 123.3, 117.4, 68.5, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{15}H_{13}NONa$ 246.0895; found 246.0900.



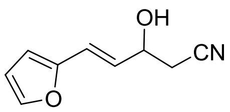
2u

(*E*)-3-hydroxy-5-(thiophen-2-yl)pent-4-enenitrile：brown oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 4.8 Hz, 1H), 7.01 (d, *J* = 3.2 Hz, 1H), 6.97 (dd, *J* = 4.8, 3.6 Hz, 1H), 6.84 (d, *J* = 15.6 Hz, 1H), 6.05 (dd, *J* = 15.6, 6.4 Hz, 1H), 4.62 – 4.57 (m, 1H), 2.73 – 2.61 (m, 2H), 2.26 (s, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 140.4, 127.5, 127.2, 127.1, 126.1, 125.4, 117.0, 68.5, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for C_9H_9NOSNa 202.0303; found 202.0305.



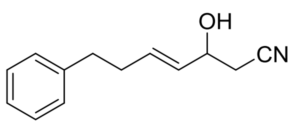
2v

(*E*)-5-(furan-2-yl)-3-hydroxypent-4-enenitrile: brown oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 1.6 Hz, 1H), 6.46 (dd, *J* = 16.0, 0.8 Hz, 1H), 6.31 (dd, *J* = 3.2, 2.0 Hz, 1H), 6.24 (d, *J* = 3.6 Hz, 1H), 6.08 (dd, *J* = 16.0, 6.4 Hz, 1H), 4.55 - 4.49 (m,1H), 2.64 – 2.52 (m, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 151.3, 142.6, 126.3, 120.7, 117.2, 111.5, 109.7, 68.1, 26.3.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_9H_9NO_2Na$ 186.0531; found 186.0534.



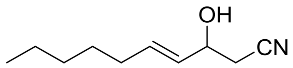
2w

(*E*)-3-hydroxy-7-phenylhept-4-enenitrile: pale yellow oil

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30 – 7.23 (m, 2H), 7.21 – 7.16 (m, 3H), 5.87 – 5.81 (m, 1H), 5.53 (dd, *J* = 15.0, 6.6 Hz, 1H), 4.38 (q, *J* = 6.0 Hz, 1H), 2.72 (t, *J* = 7.8Hz, 2H), 2.58 – 2.49 (m, 2H), 2.42 – 2.37 (m, 2H), 2.09 (s, 1H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 141.2, 133.9, 129.9, 128.4, 128.3, 126.0, 117.2, 68.5, 35.1, 33.7, 26.2.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{13}H_{15}NONa$, 224.1051 found, 224.1056.



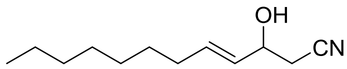
2x

(*E*)-3-hydroxydec-4-enenitrile: pale yellow oil

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 – 5.79 (m, 1H), 5.54 (dd, *J* = 15.5, 7.0 Hz, 1H), 4.45 – 4.38 (m, 1H), 2.63 – 2.53 (m, 2H), 2.09 – 2.03 (m, 3H), 1.43 – 1.36 (m, 6H), 0.95 – 0.90 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 135.9, 129.7, 117.9, 69.3, 32.6, 31.9, 29.1, 26.9, 23.0, 14.6.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{10}H_{17}NONa$ 190.1208; found 190.1218.



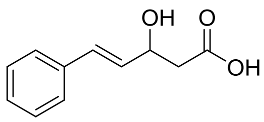
2y

(*E*)-3-hydroxydodec-4-enenitrile: pale yellow oil

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.87 – 5.79 (m, 1H), 5.58 – 5.51 (m, 1H), 4.48 – 4.38 (m, 1H), 2.64 – 2.53 (m, 2H), 2.20 – 2.00 (m, 3H), 1.44 – 1.28 (m, 10H), 0.89 (t, *J* = 6.4 Hz, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 135.4, 129.1, 117.3, 68.7, 32.0, 31.7, 29.1, 28.8, 26.3, 22.6, 14.1.

HRMS (ESI-TOF) $[M+Na]^+$ calcd. for $C_{12}H_{21}NONa$ 218.1521; found 218.1525.

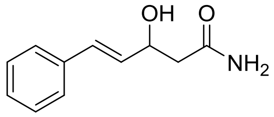


3

(*E*)-3-hydroxy-5-phenylpent-4-enoic acid: white solid

^{1}H NMR (500 MHz, CD_3CN) δ 7.41 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.27 – 7.23 (m, 1H), 6.63 (d, *J* = 16.5 Hz, 1H), 6.30 (dd, *J* = 16.0, 6.0 Hz, 1H), 4.65 – 4.60 (m, 1H), 3.49 (s, 1H), 2.59 (dd, *J* = 15.5, 4.5 Hz, 1H), 2.51 (dd, *J* = 15.5, 8.5 Hz, 1H).

^{13}C NMR (125 MHz, CD_3CN) δ 173.2, 137.8, 132.3, 130.5, 129.6, 128.6, 127.3, 69.4, 42.4.

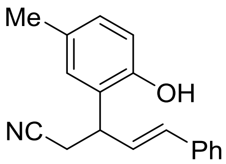


4

(*E*)-3-hydroxy-5-phenylpent-4-enamide: white solid

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.42 – 7.38 (m, 2H), 7.32 (t, *J* = 7.2 Hz, 3H), 7.22 (t, *J* = 7.2 Hz, 1H), 6.83 (s, 1H), 6.54 (d, *J* = 16.0 Hz, 1H), 6.30 (dd, *J* = 15.6, 5.2 Hz, 1H), 5.12 (d, *J* = 4.8 Hz, 1H), 4.55 – 4.48 (m, 1H), 2.34 – 2.23 (m, 2H).

^{13}C NMR (100 MHz, DMSO-d_6) δ 172.8, 137.3, 133.9, 129.1, 128.5, 127.8, 126.7, 68.7, 44.1.

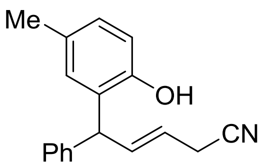


5a

(*E*)-3-(2-hydroxy-5-methylphenyl)-5-phenylpent-4-enenitrile: pale yellow gum

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.5 Hz, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.26 – 7.21 (m, 1H), 7.00 (s, 1H), 6.93 (dd, *J* = 8.0, 1.0 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.57 (d, *J* = 16.0 Hz, 1H), 6.48 (dd, *J* = 16.0, 7.5 Hz, 1H), 5.10 (s, 1H), 4.13 (q, J = 7.0 Hz, 1H), 2.90 (d, *J* = 7.0 Hz, 2H), 2.26 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 150.7, 136.9, 131.9, 130.5, 128.6, 128.5, 128.4, 127.7, 126.7, 126.5, 118.7, 115.8, 40.1, 22.7, 20.6.

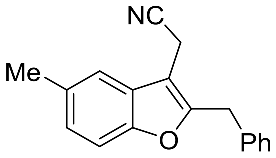


5b

(*E*)-5-(2-hydroxy-5-methylphenyl)-5-phenylpent-3-enenitrile: pale yellow gum

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.5 Hz, 2H), 7.26 – 7.21 (m, 2H), 7.19 (d, *J* = 7.0 Hz, 2H), 6.88 (s, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.35 (dd, *J* = 15.5, 7.0 Hz, 1H), 5.34 – 5.27 (m, 1H), 5.00 (d, *J* = 7.0 Hz, 1H), 4.69 (s, 1H), 3.14 (d, *J* = 5.5 Hz, 2H), 2.26 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 150.8, 141.6, 137.1, 130.0, 129.9, 129.2, 129.0, 128.6, 128.5, 127.9, 126.8, 126.5, 119.4, 115.9, 47.3, 20.6, 20.4.

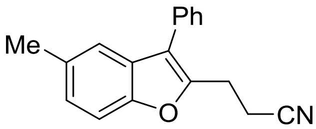


6a

2-(2-benzyl-5-methylbenzofuran-3-yl)acetonitrile: pale yellow gum

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 4H), 7.26 – 7.22 (m, 3H), 7.09 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.14 (s, 2H), 3.60 (s, 2H), 2.45 (s, 3H).

^{13}C NMR (150 MHz, $CDCl_3$) δ 154.1, 152.3, 136.4, 132.6, 128.8, 128.5, 127.6, 125.3, 120.6, 118.3, 110.8, 104.5, 32.8, 21.3, 12.6.



6b

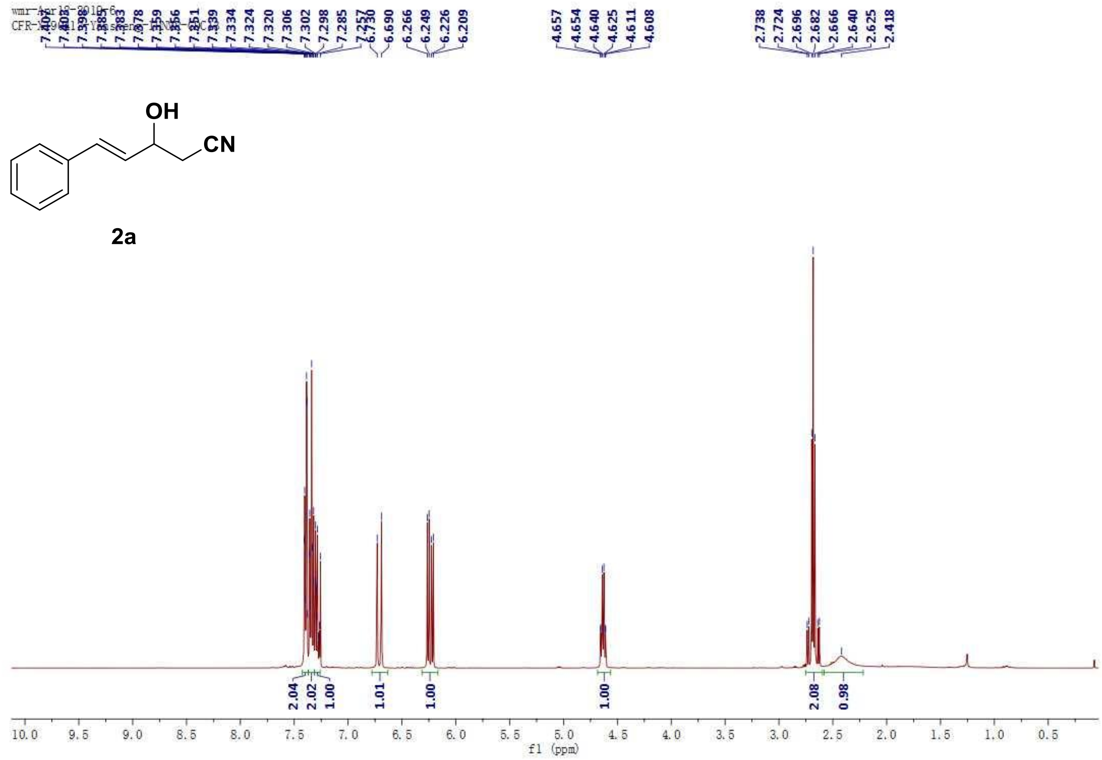
3-(5-methyl-3-phenylbenzofuran-2-yl)propanenitrile: pale yellow gum

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 4H), 7.27 – 7.21 (m, 2H), 7.06 (dd, *J* = 8.5, 1.0 Hz, 1H), 6.48 (s, 1H), 3.11 (t, *J* = 7.5 Hz, 2H), 2.76 (t, *J* = 7.5 Hz, 2H), 2.42 (s, 3H).

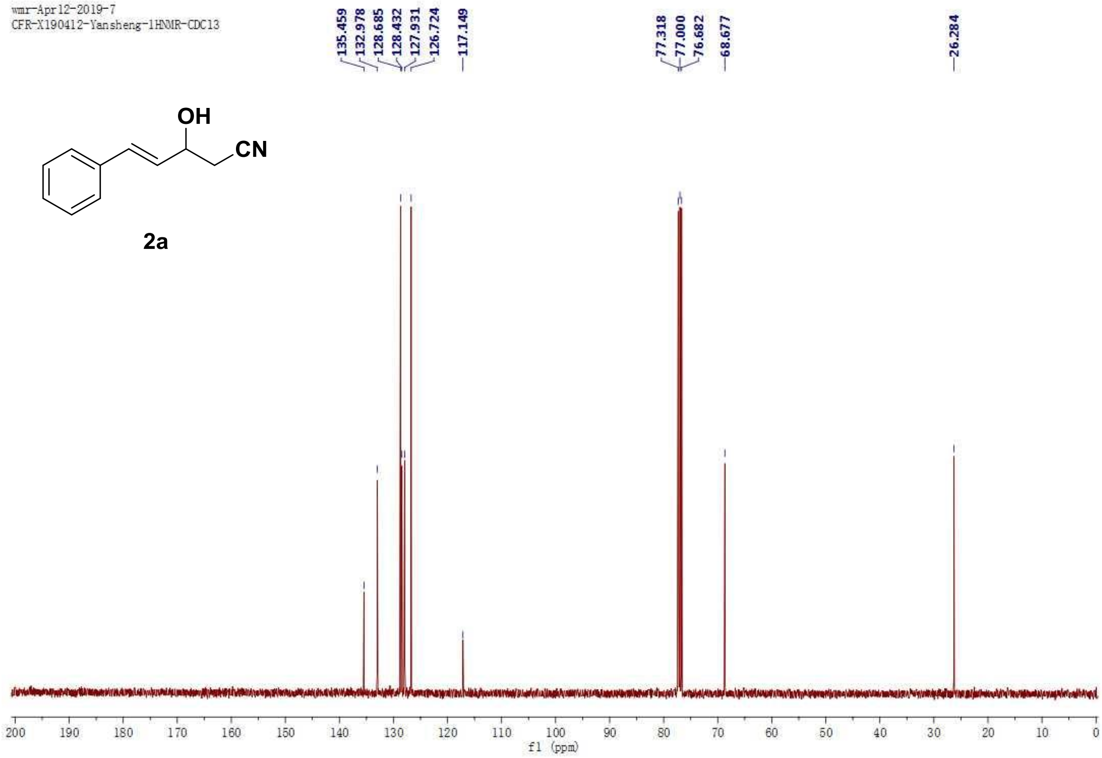
^{13}C NMR (150 MHz, $CDCl_3$) δ 154.1, 153.2, 136.4, 132.3, 128.3, 126.9, 125.7, 118.5, 116.8, 110.4, 103.6, 24.8, 21.2, 16.2.

VI. ^{1}H and ^{13}C NMR

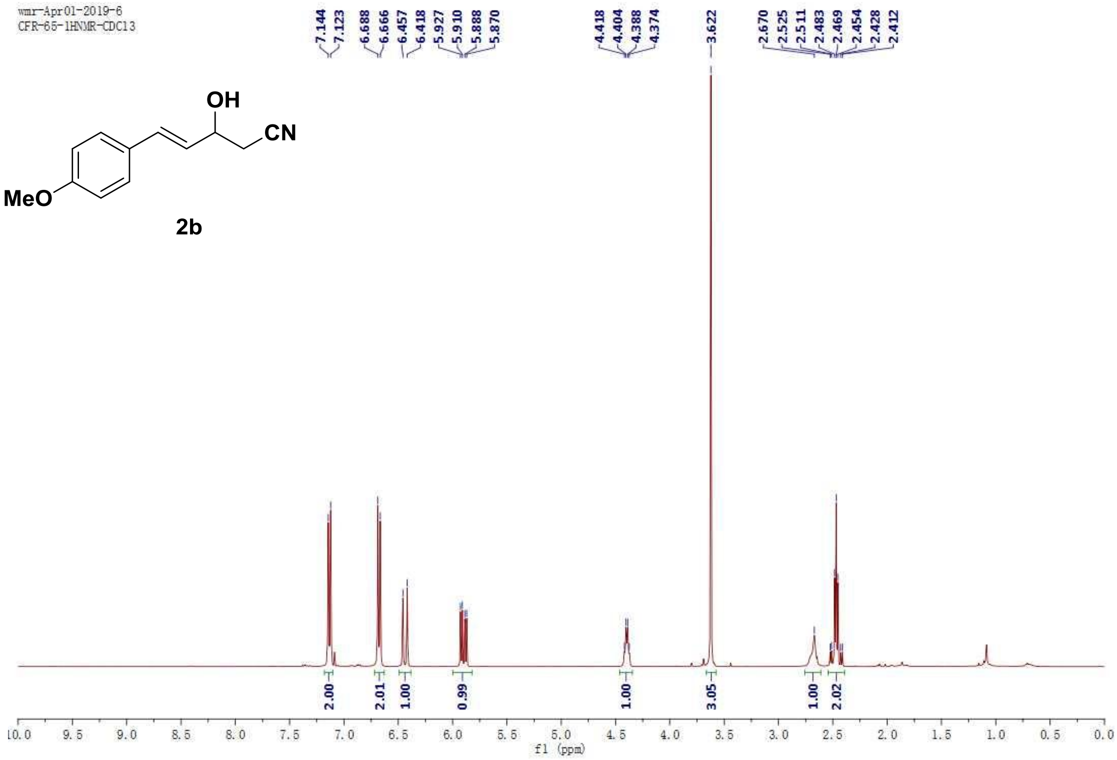
2a-^{1}H NMR



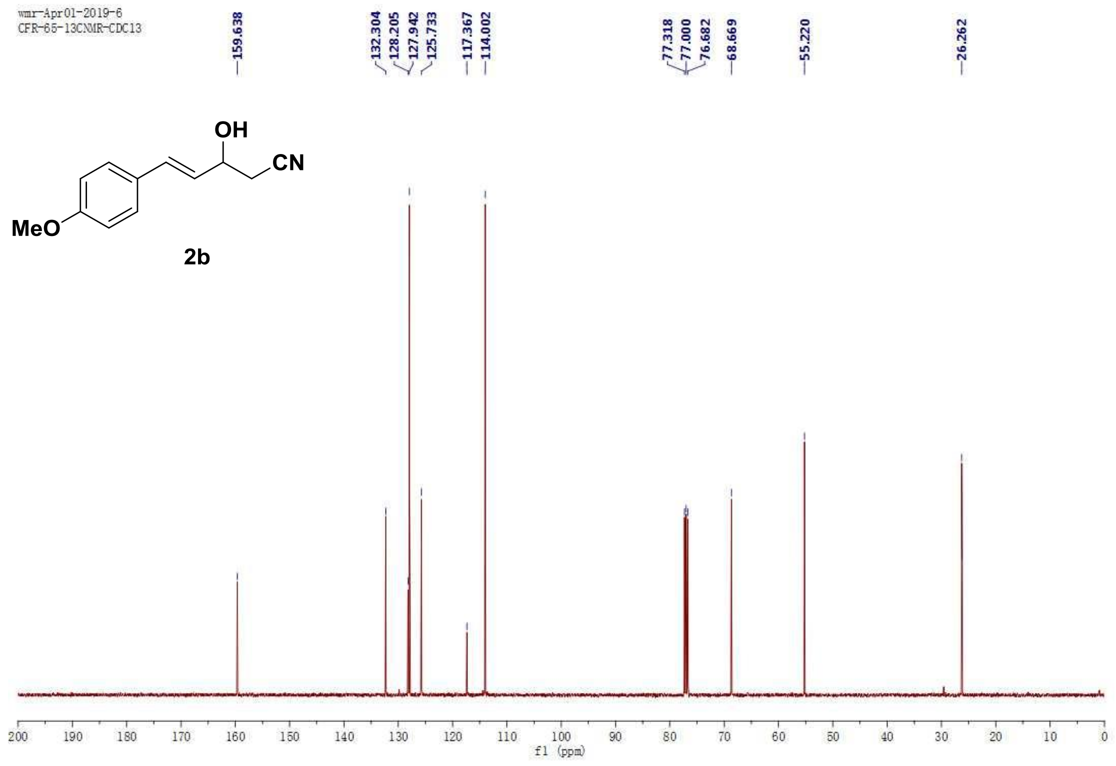
2a-^{13}C NMR



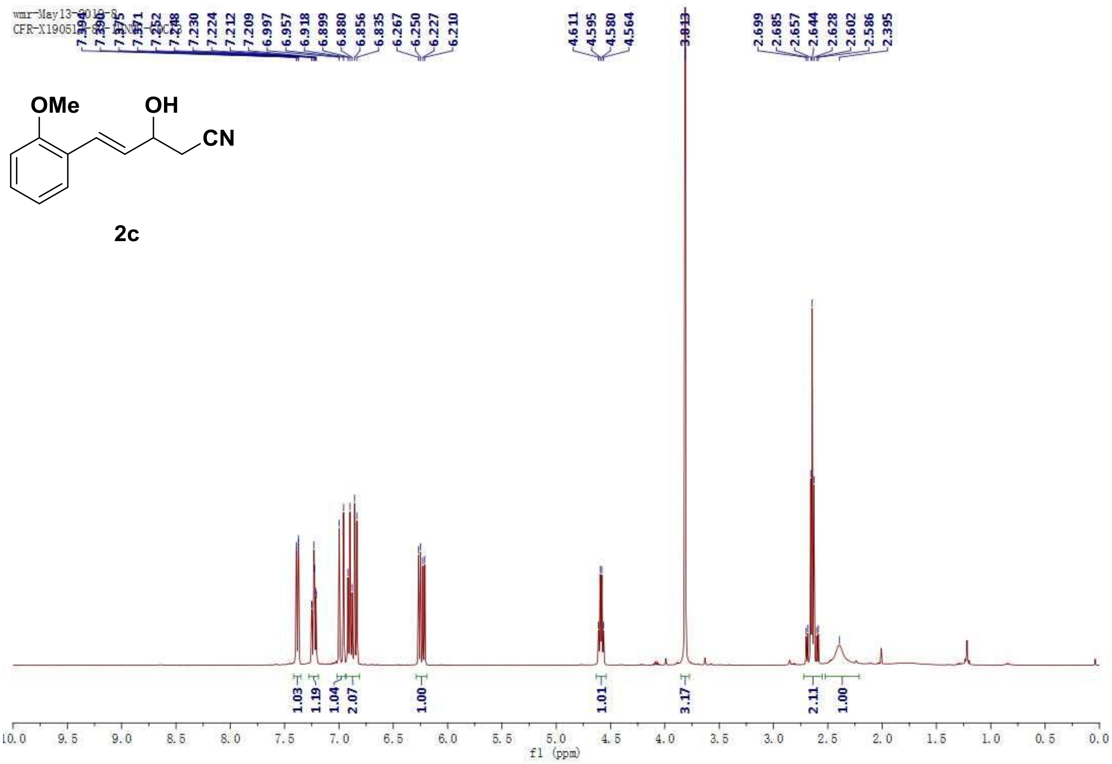
2b-^{1}H NMR



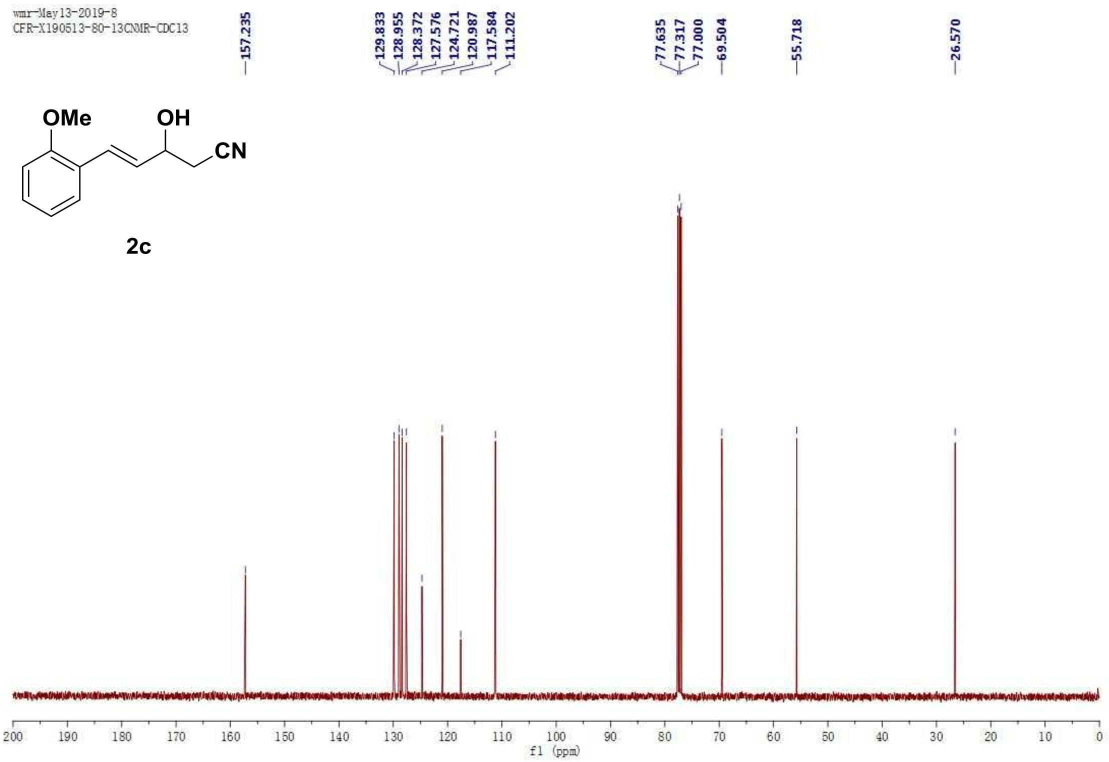
2b-^{13}C NMR



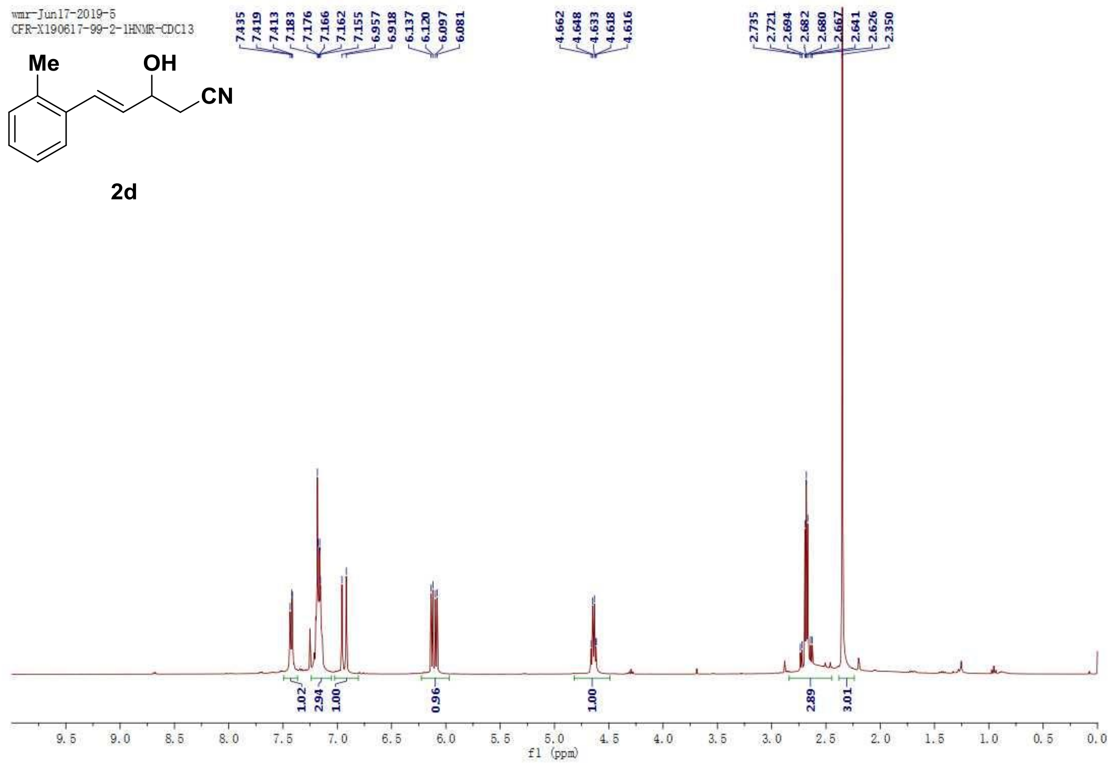
2c-^{1}H NMR



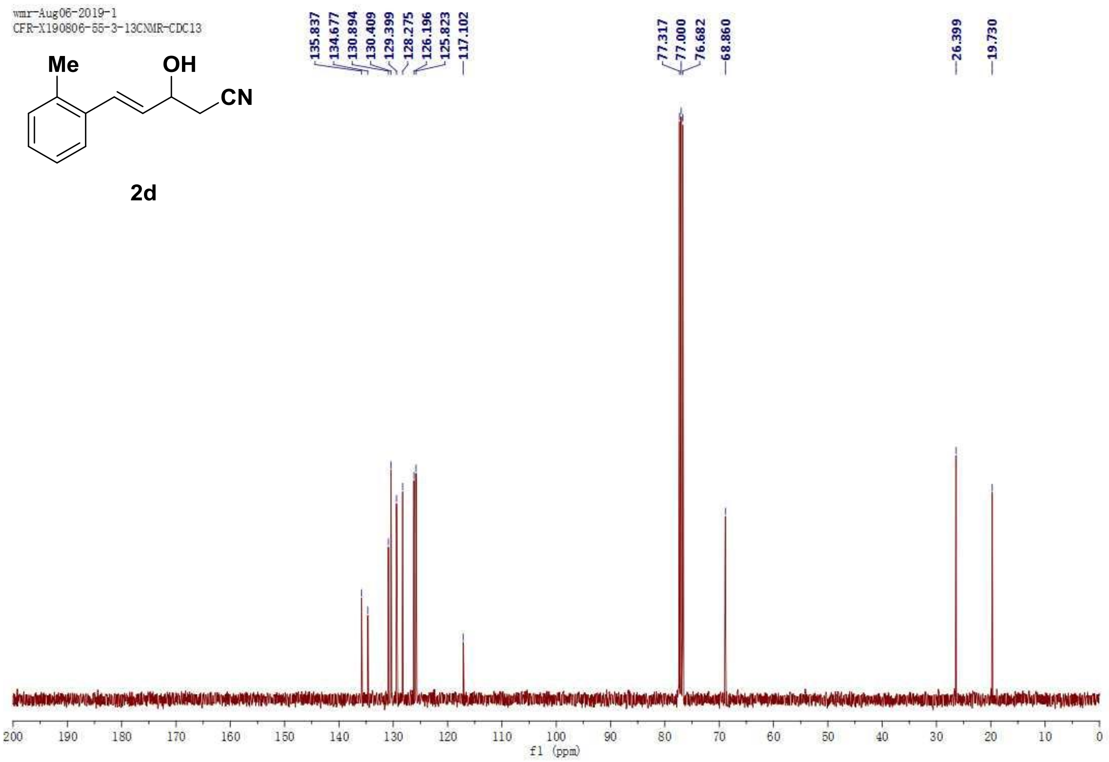
2c-^{13}C NMR



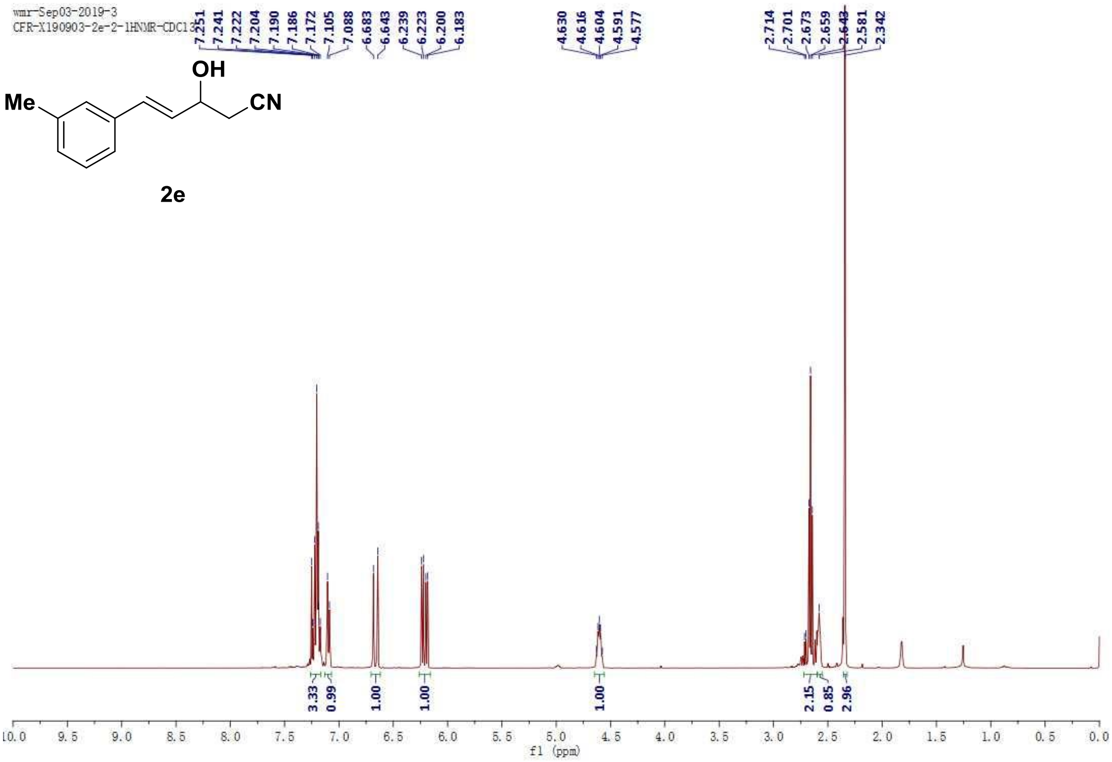
2d-[1]H NMR



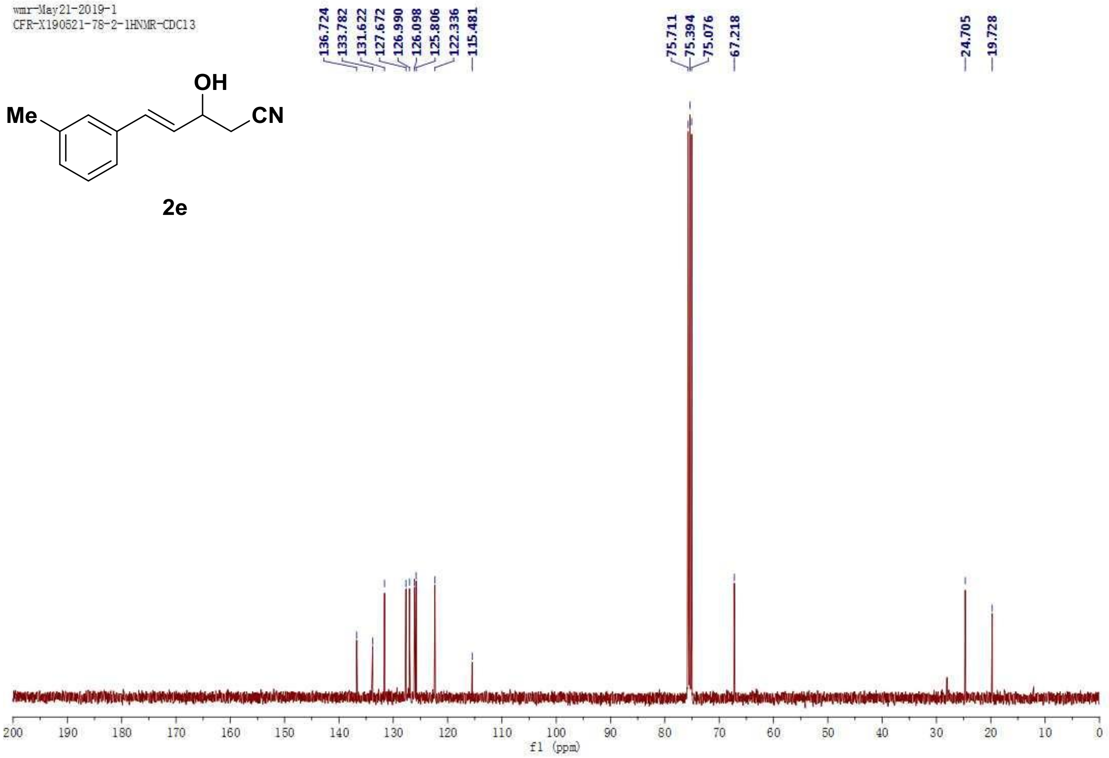
2d-[13]C NMR



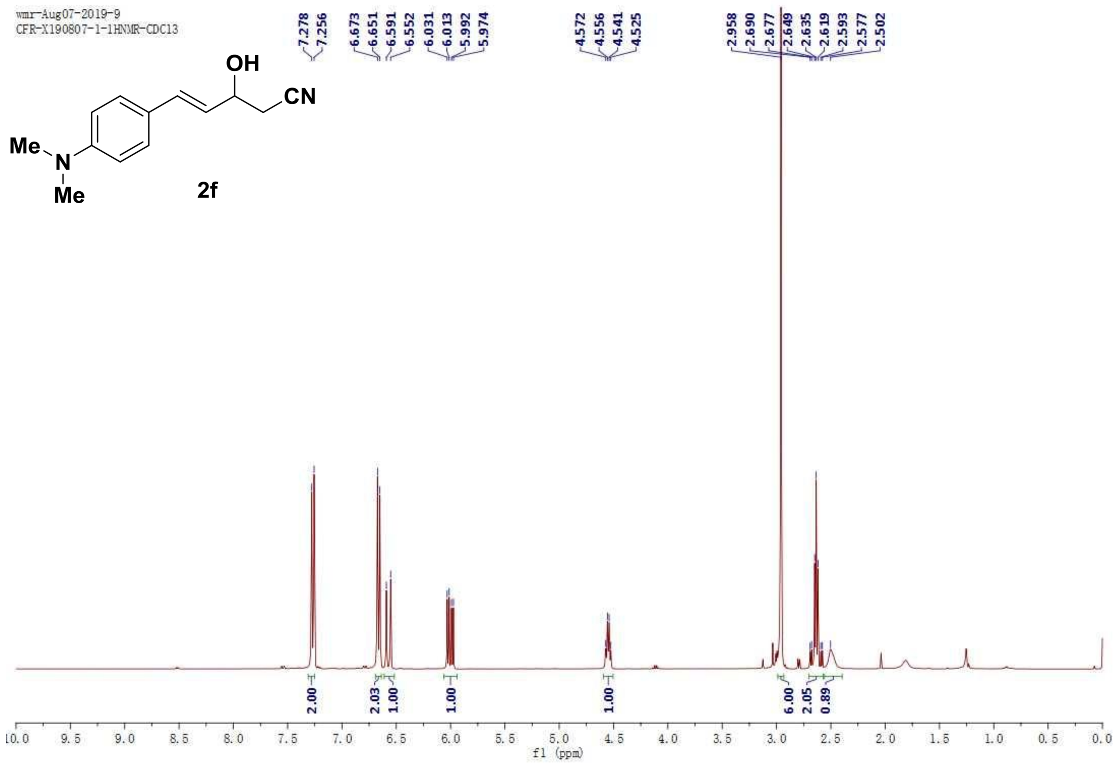
2e-^{1}H NMR



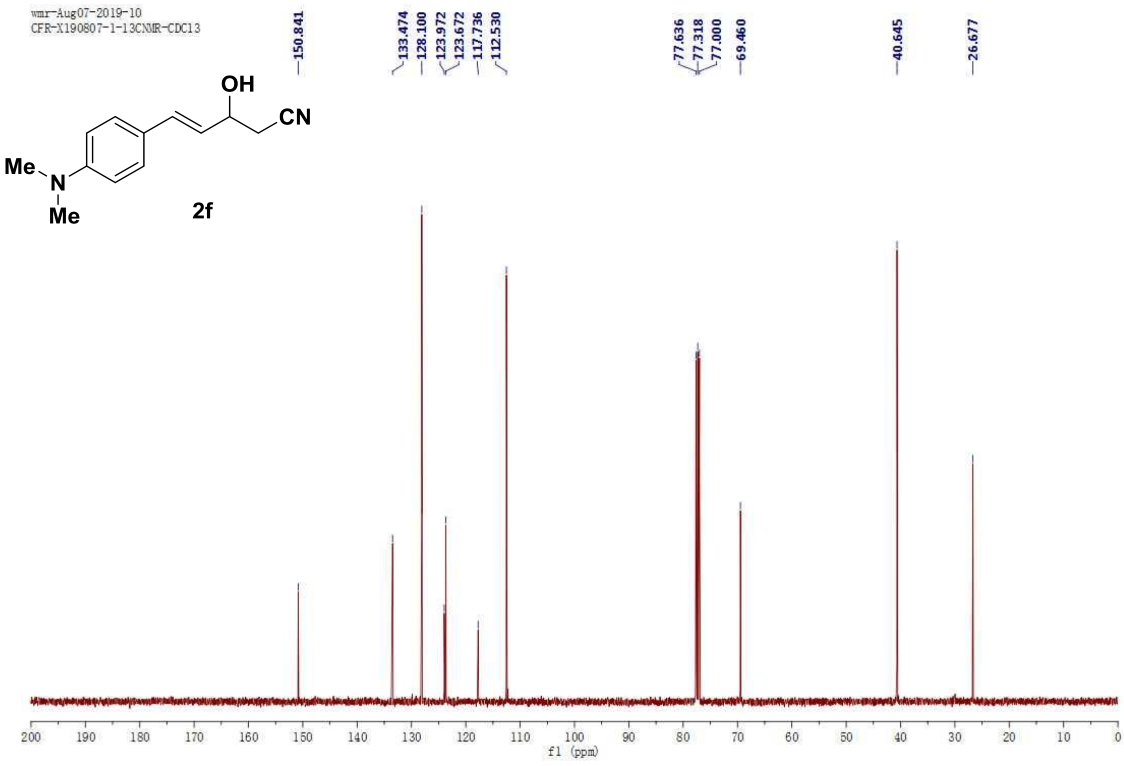
2e-^{13}C NMR



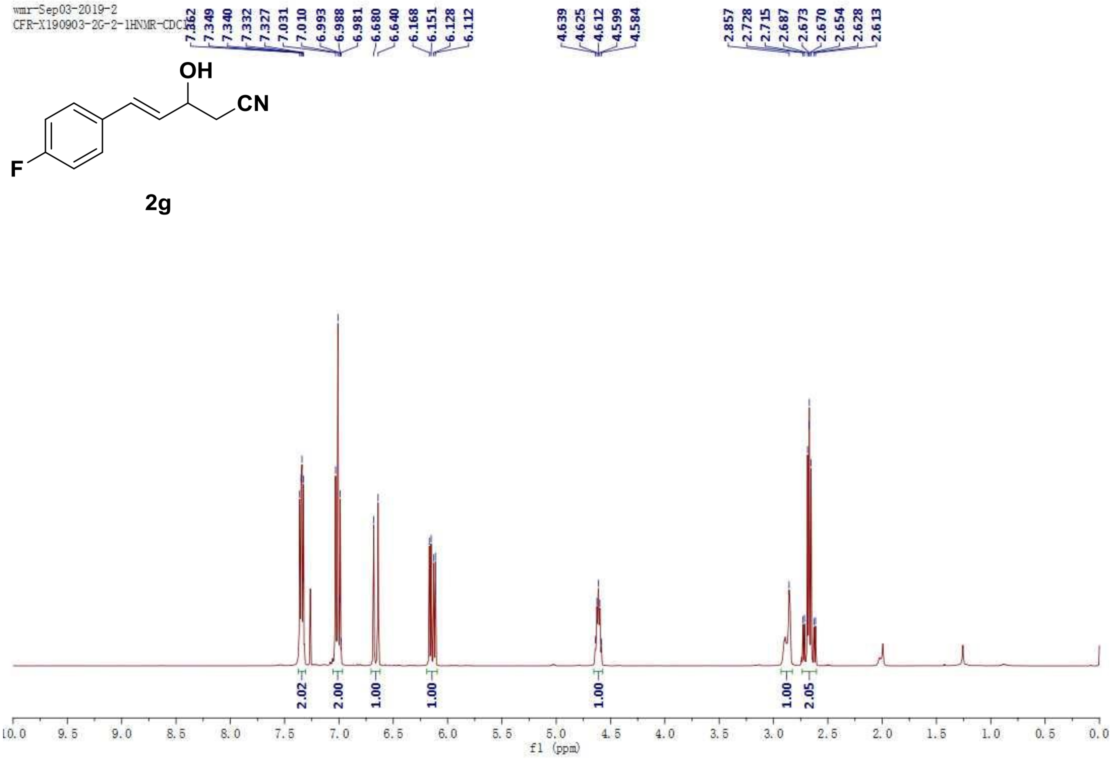
2f-[1]H NMR



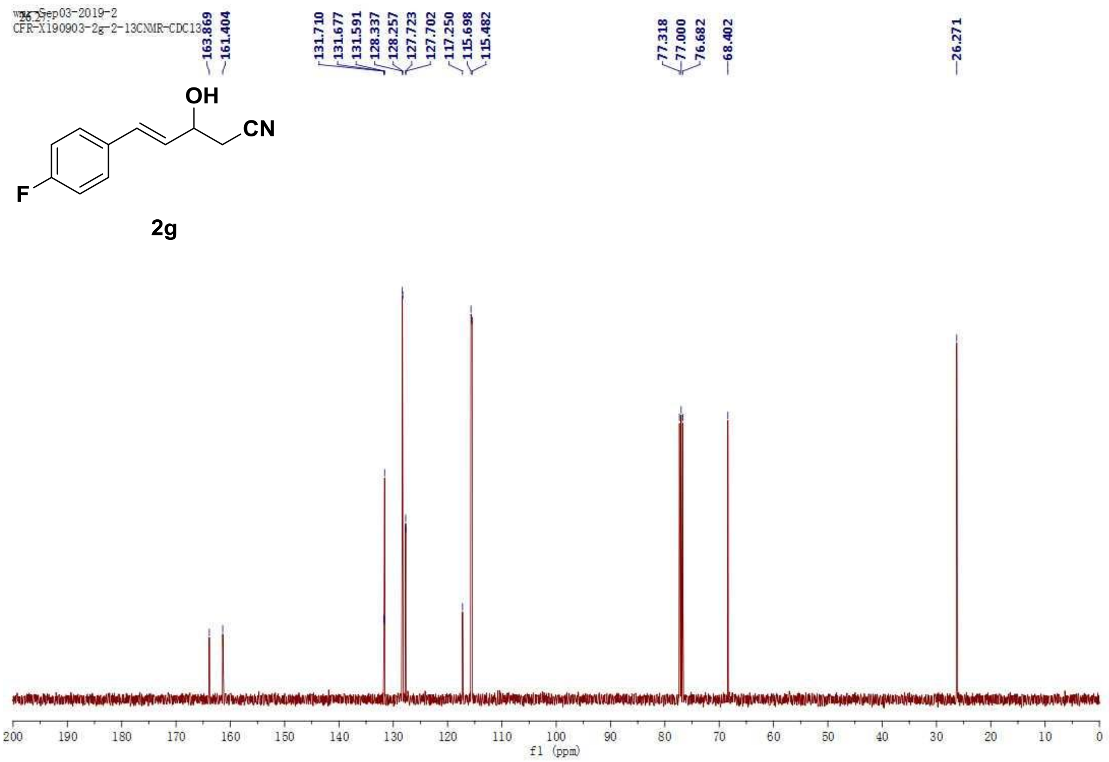
2f-[13]C NMR



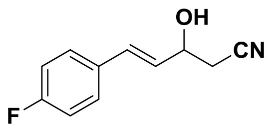
2g-^{1}H NMR



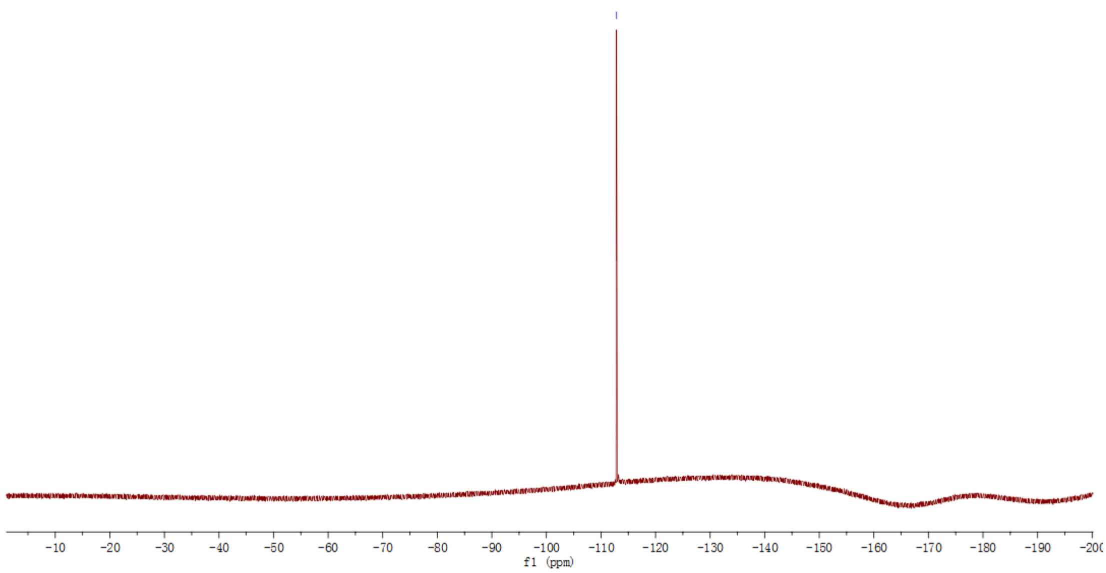
2g-^{13}C NMR



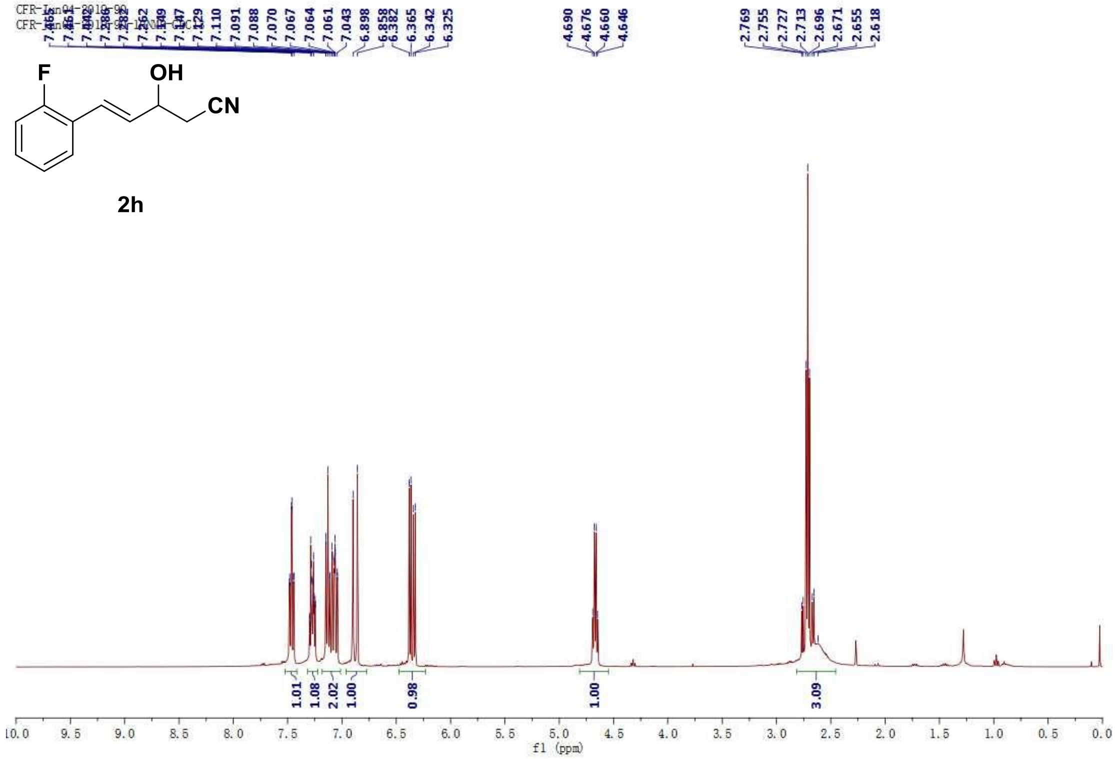
2g-^{19}F NMR



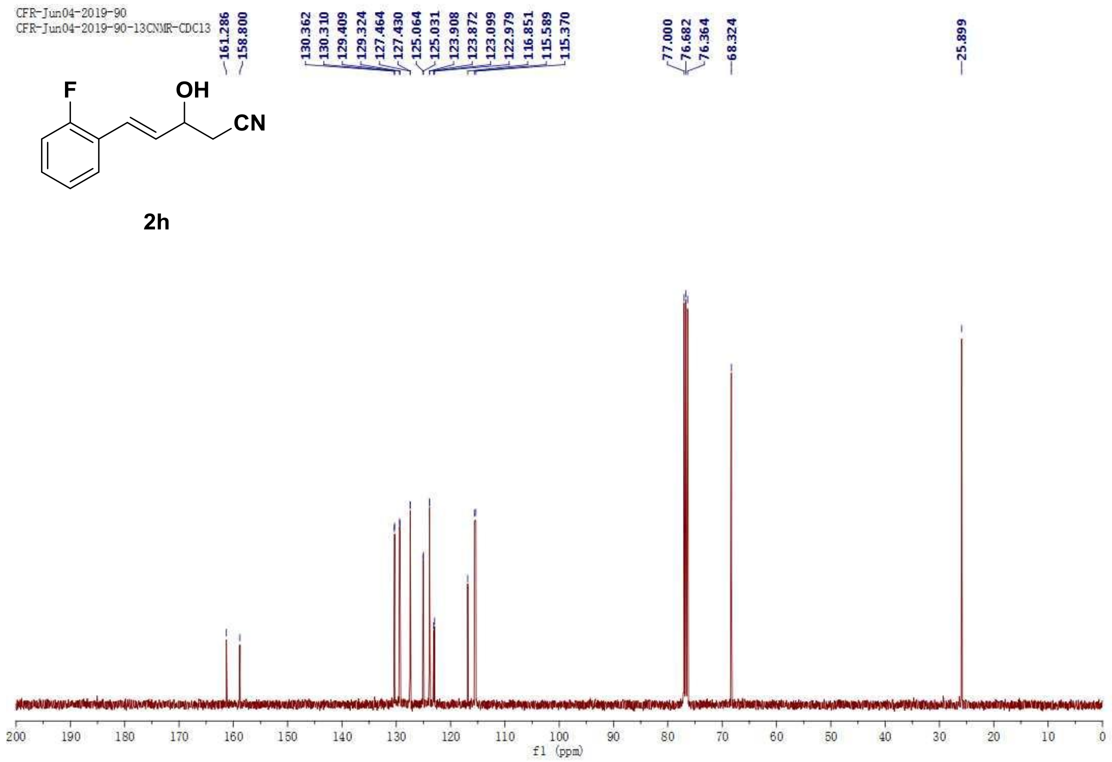
2g


-112.859
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

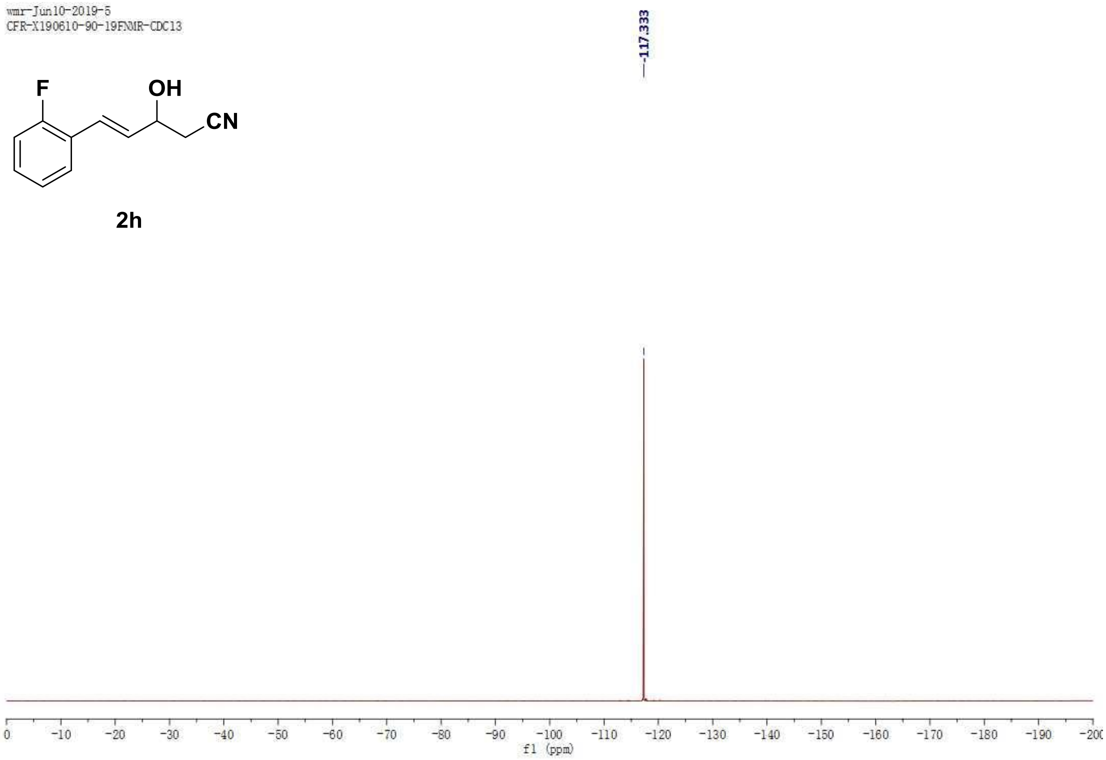
2h-[1]H NMR



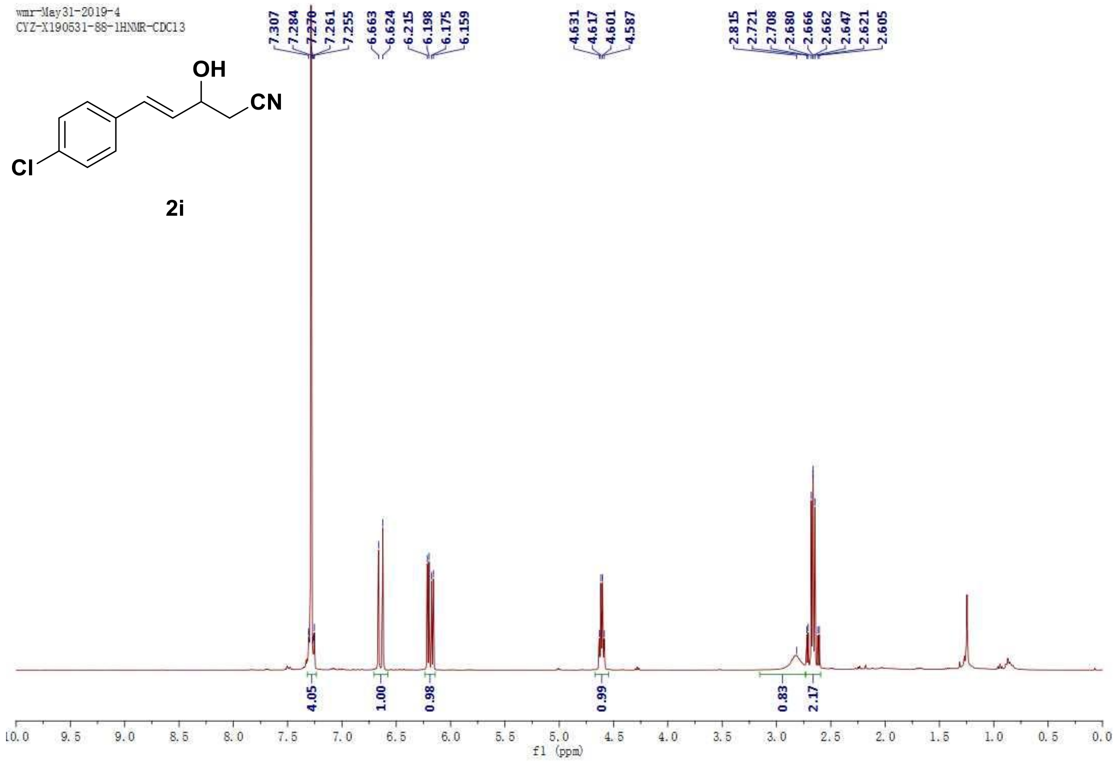
2h-[13]C NMR



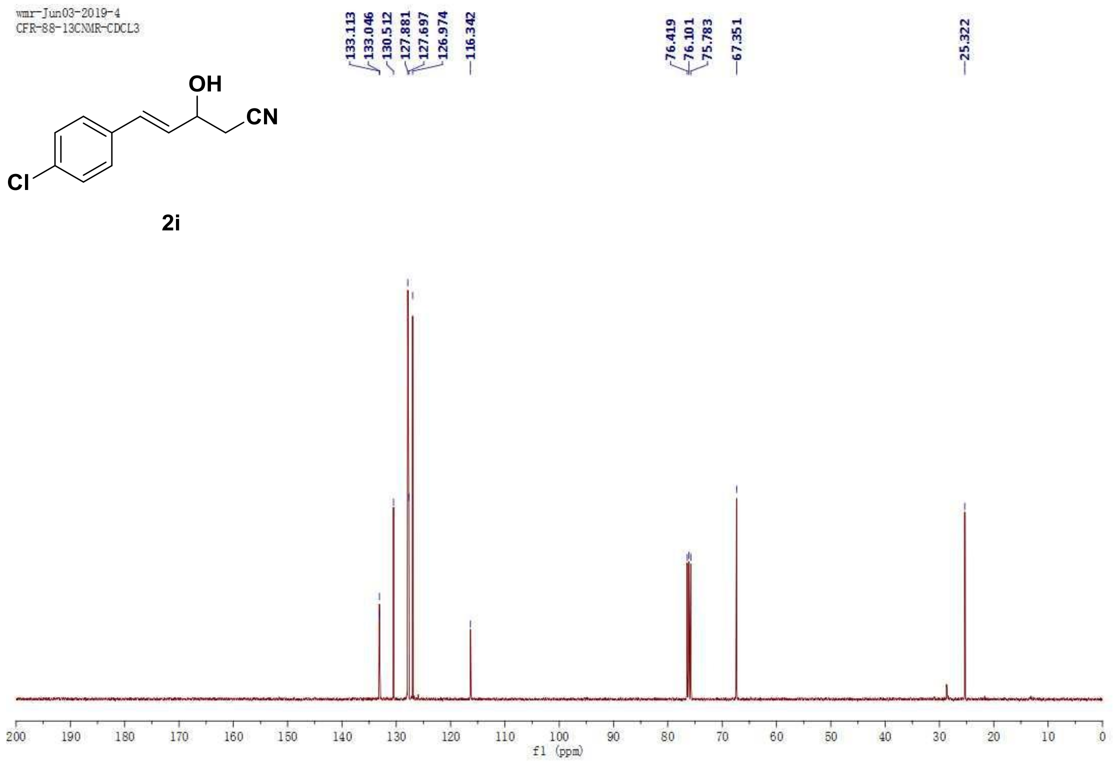
2h-^{19}F NMR


wmr-Jun10-2019-5
CFR-X190610-90-19FNMR-CDCl3
-117.333
F
OH
CN
2h
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

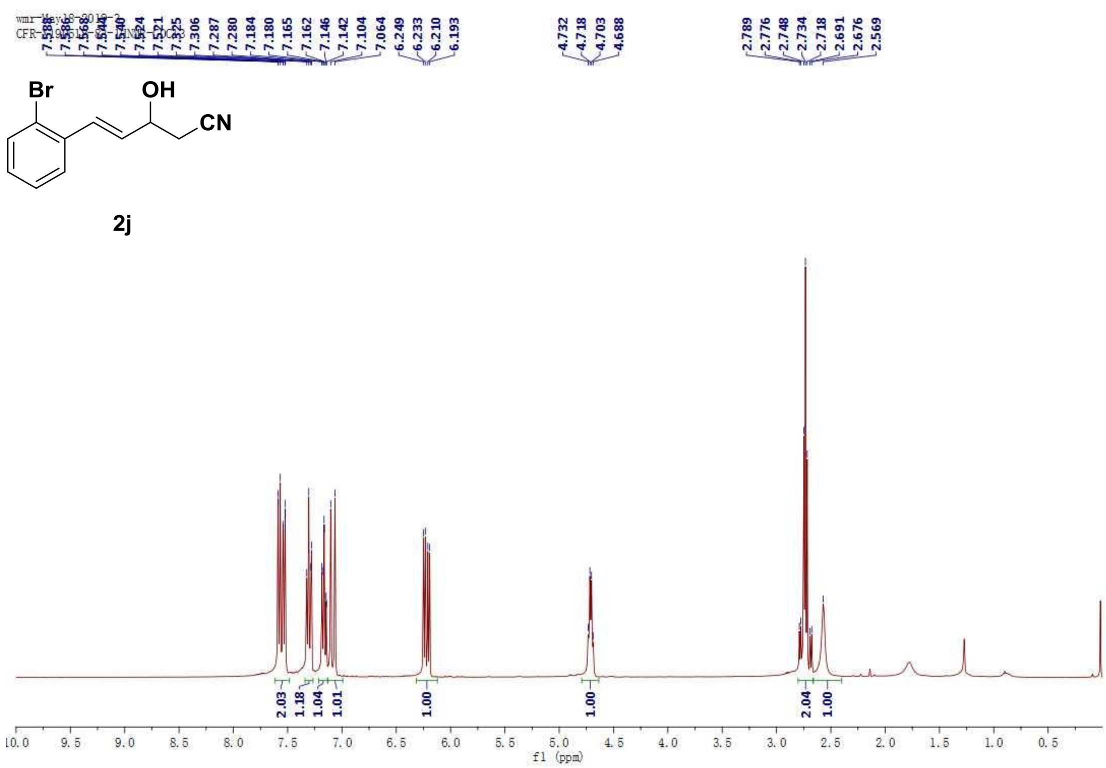
2i-^{1}H NMR



2i-^{13}C NMR

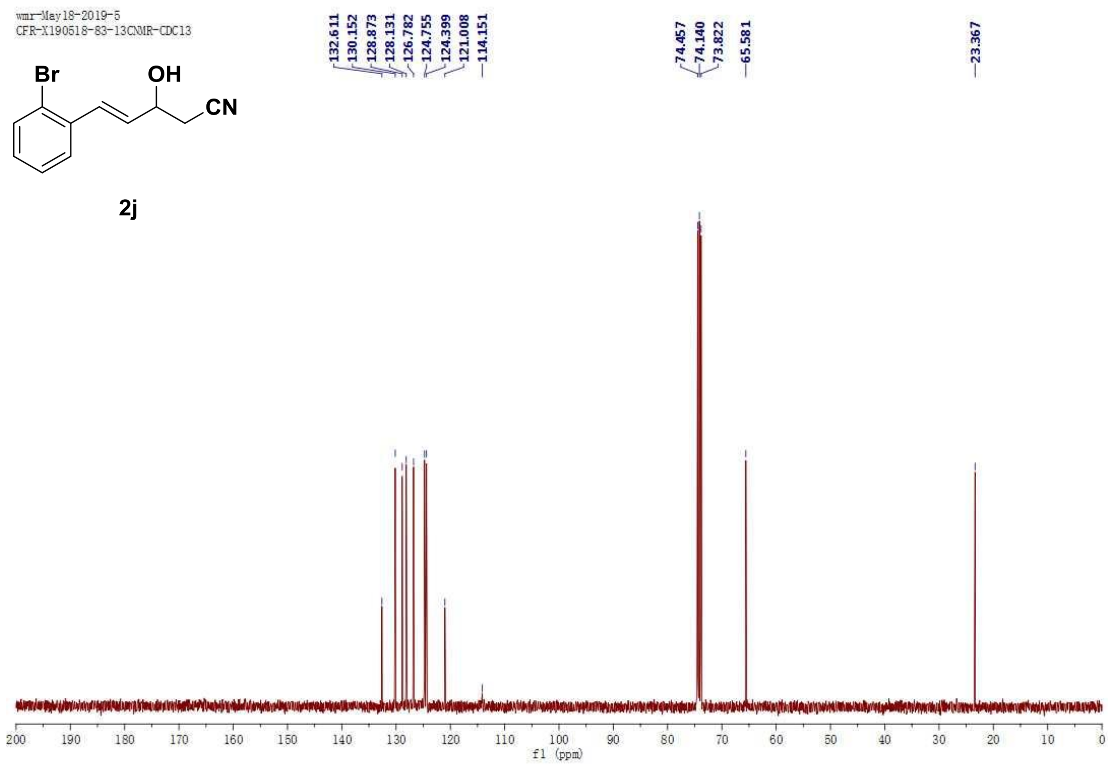


2j-^{1}H NMR



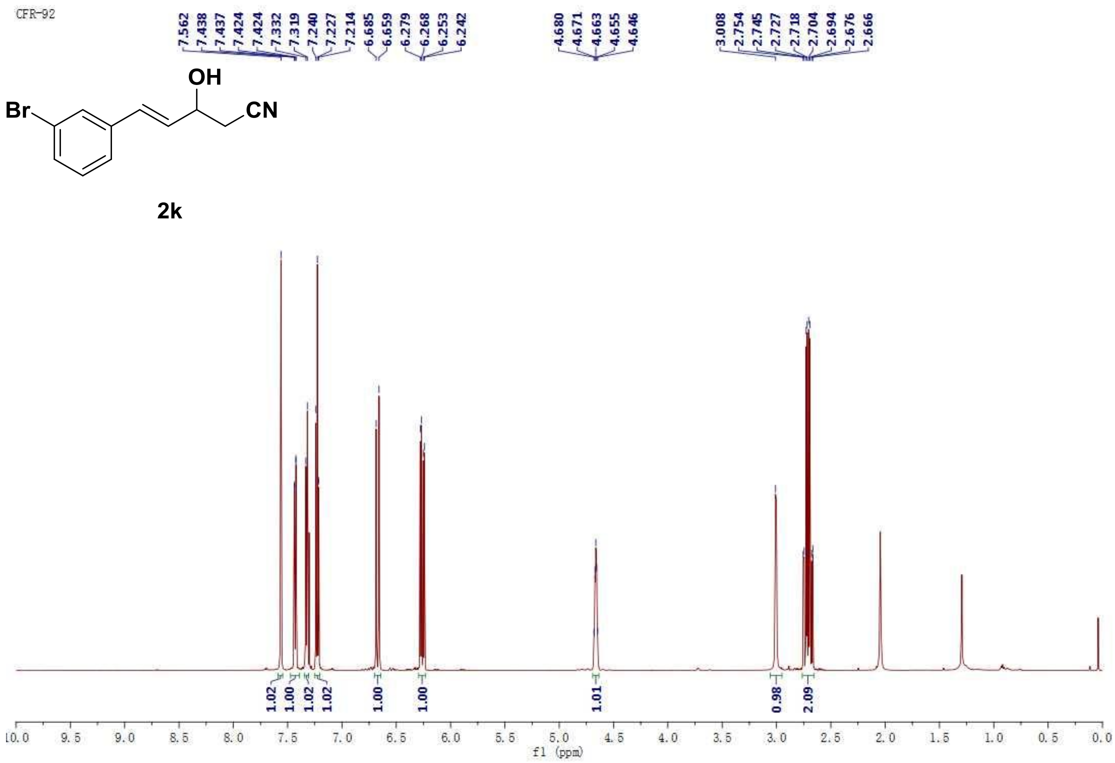
2j

2j-^{13}C NMR

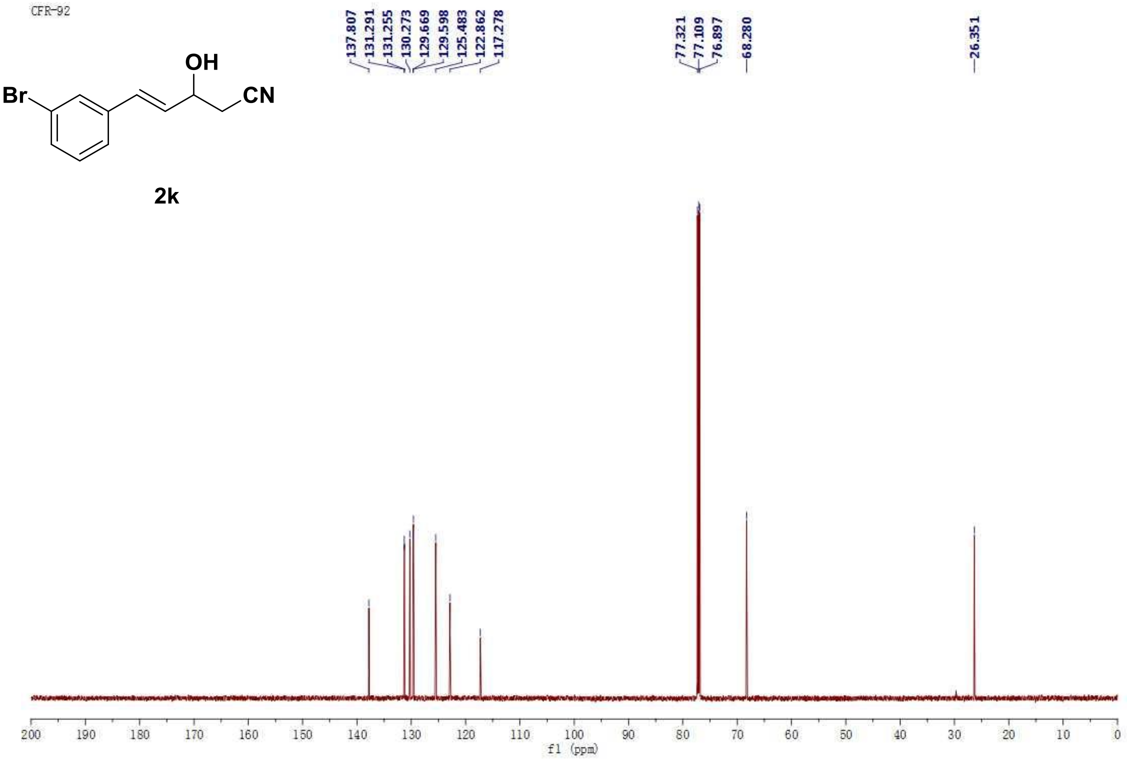


2j

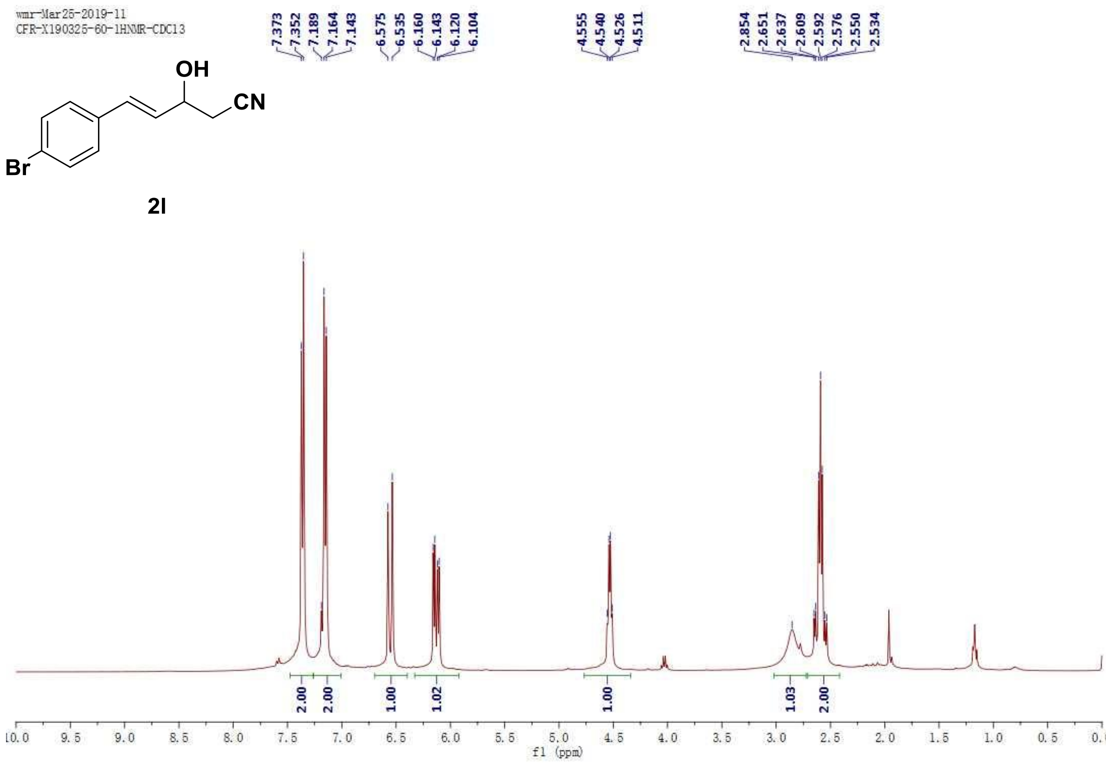
2k-^{1}H NMR



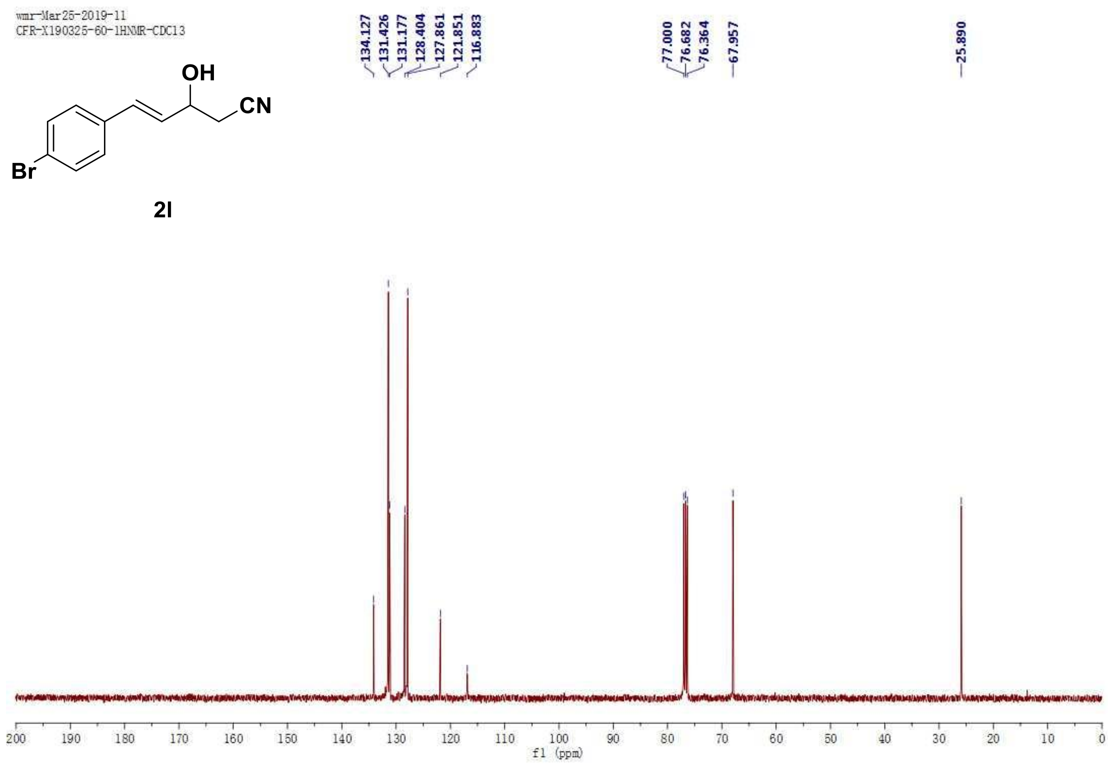
2k-^{13}C NMR



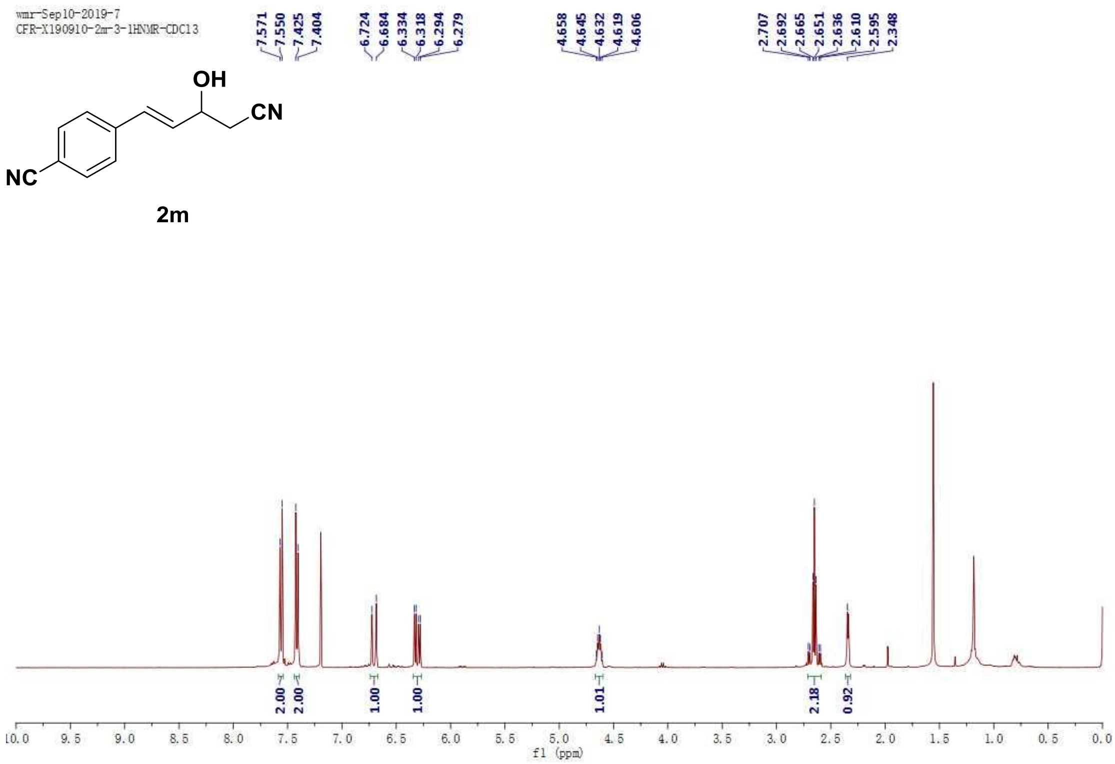
2l-[1]H NMR



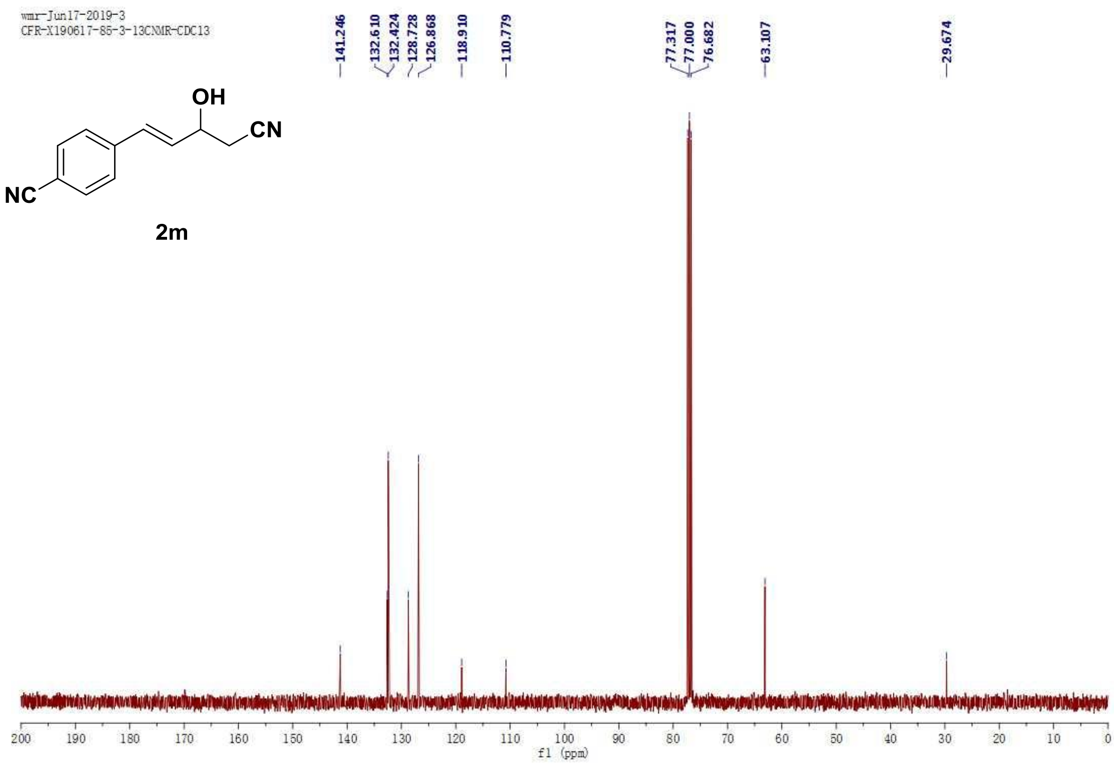
2l-[13]C NMR



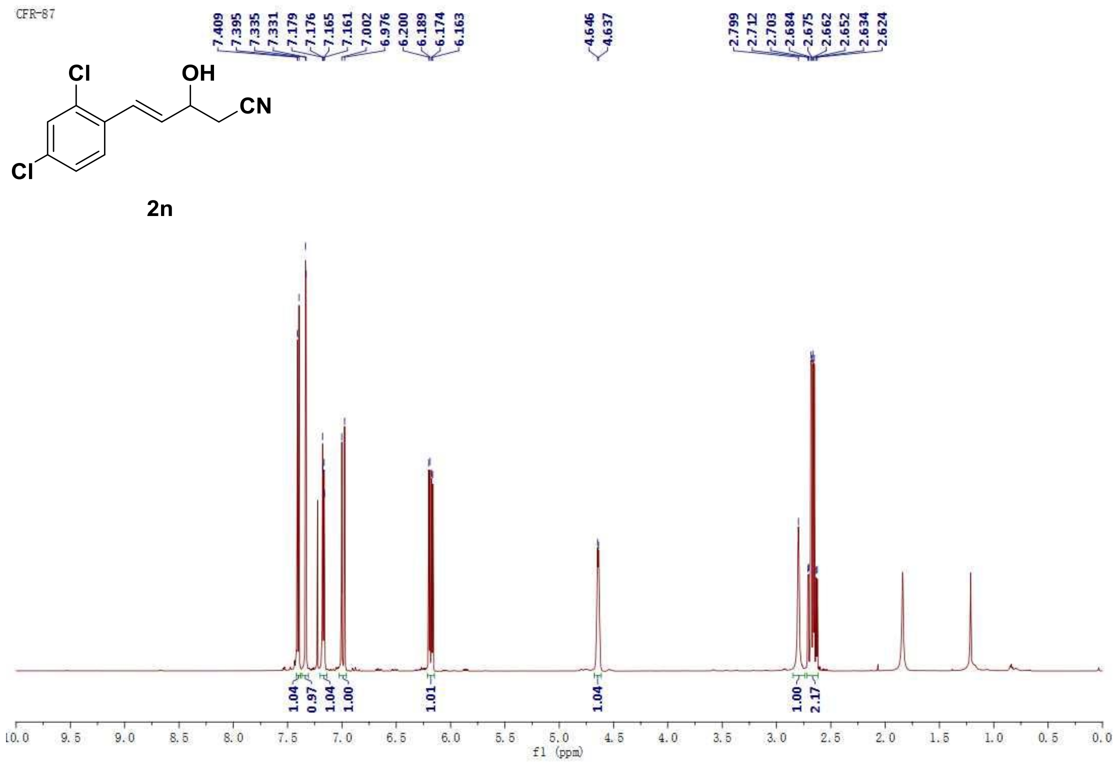
2m-[1]H NMR



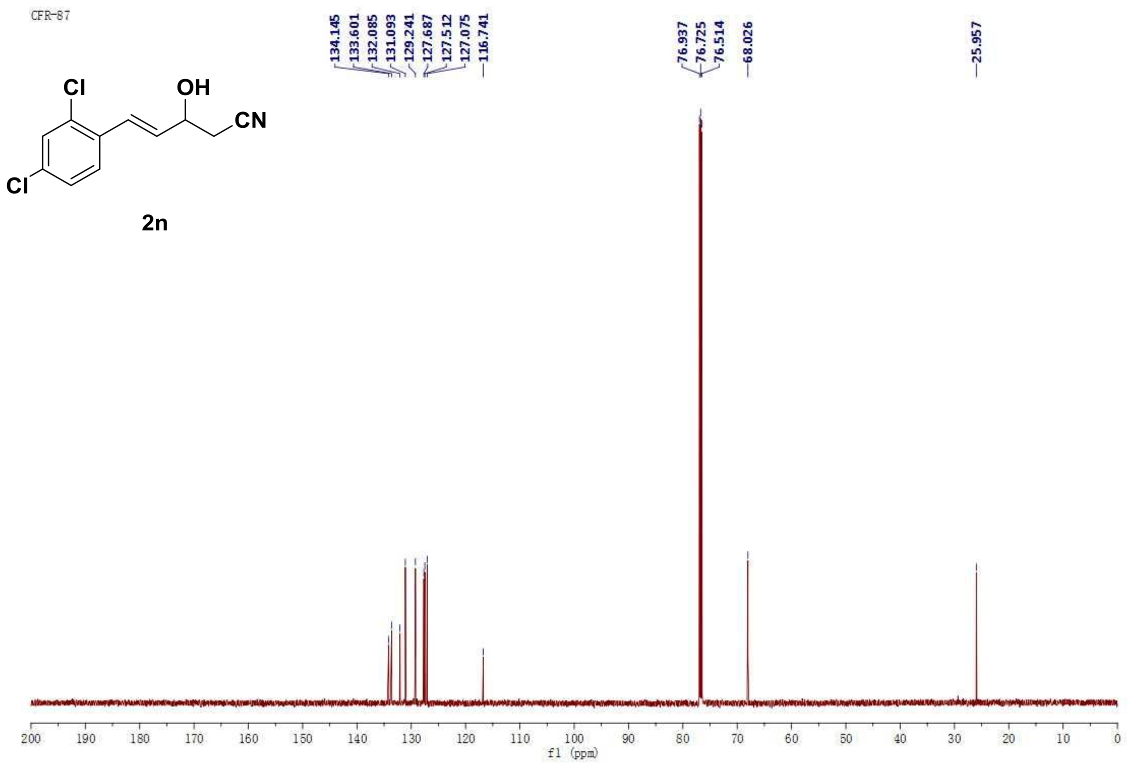
2m-[13]C NMR



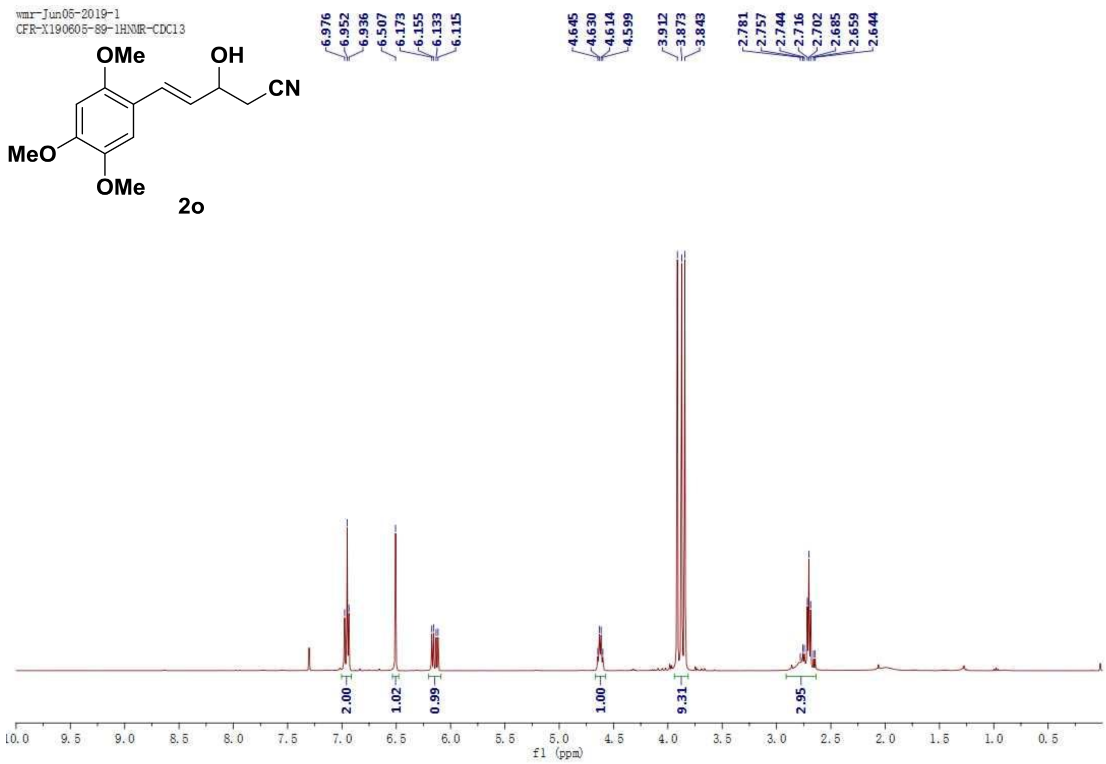
2n-^{1}H NMR



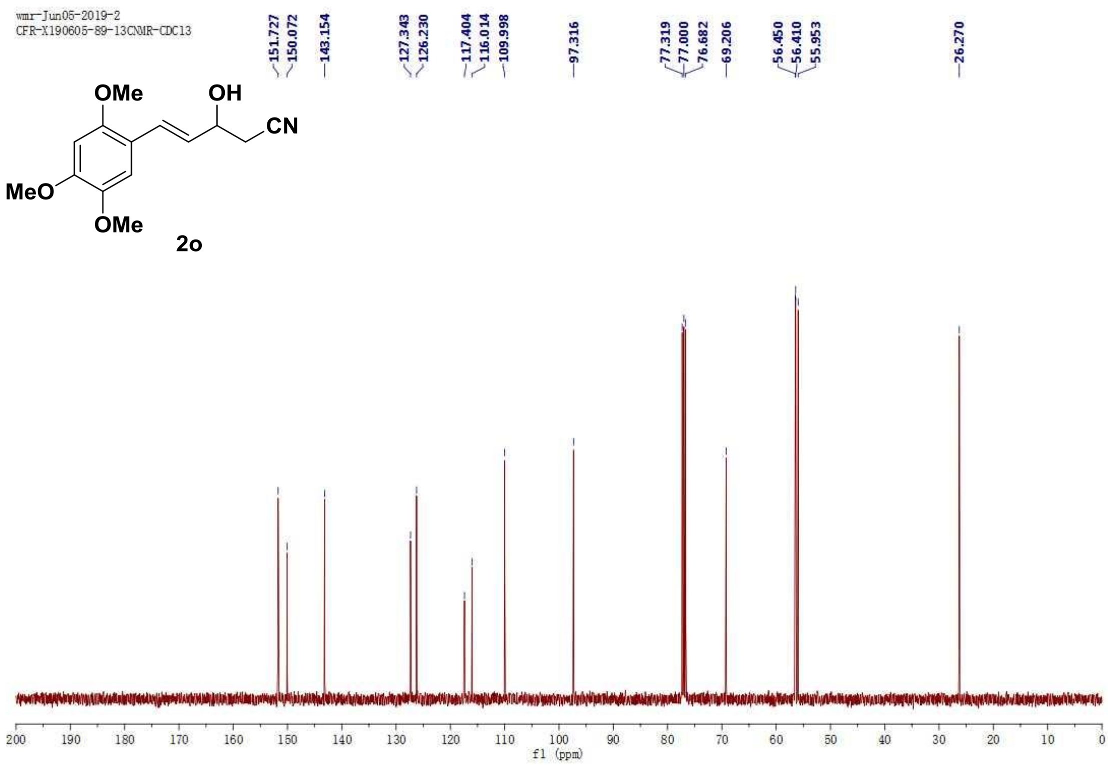
2n-^{13}C NMR



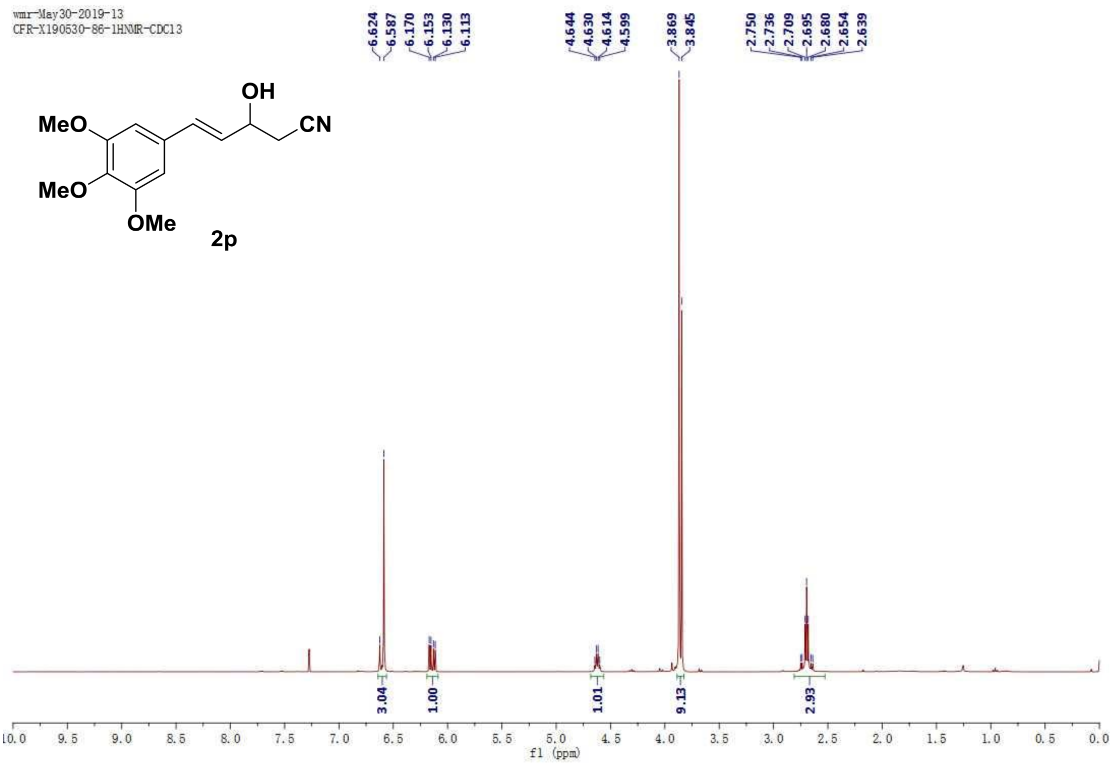
2o-^{1}H NMR



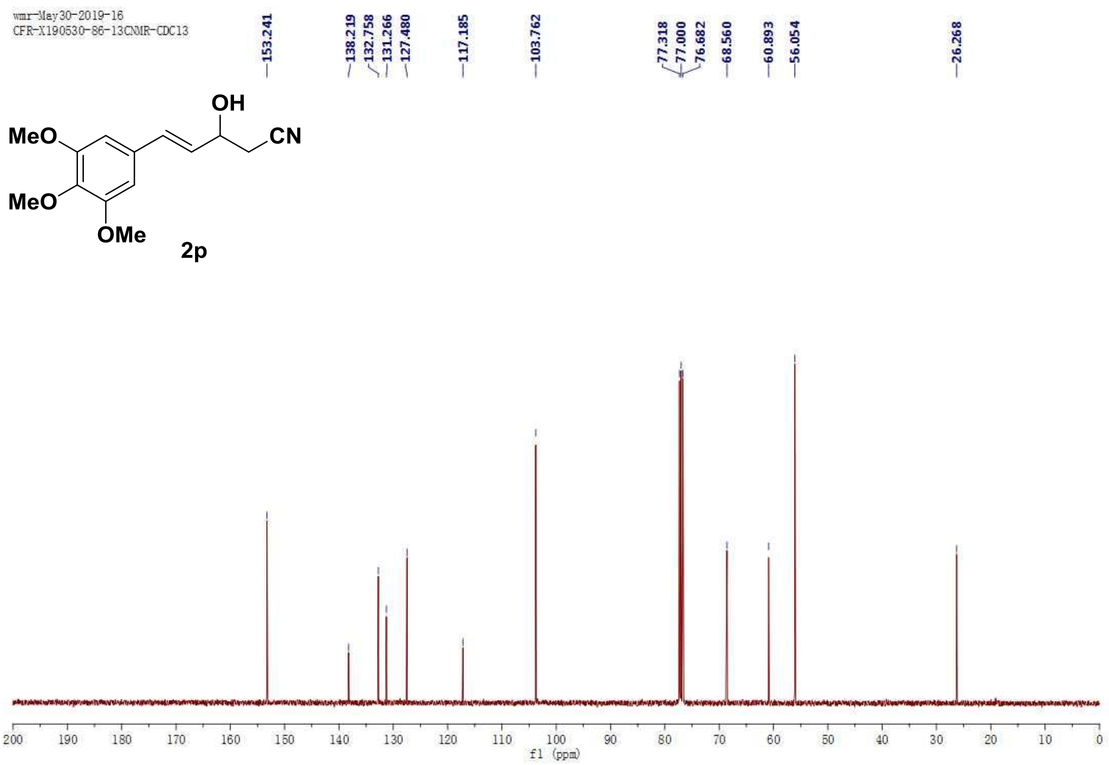
2o-^{13}C NMR



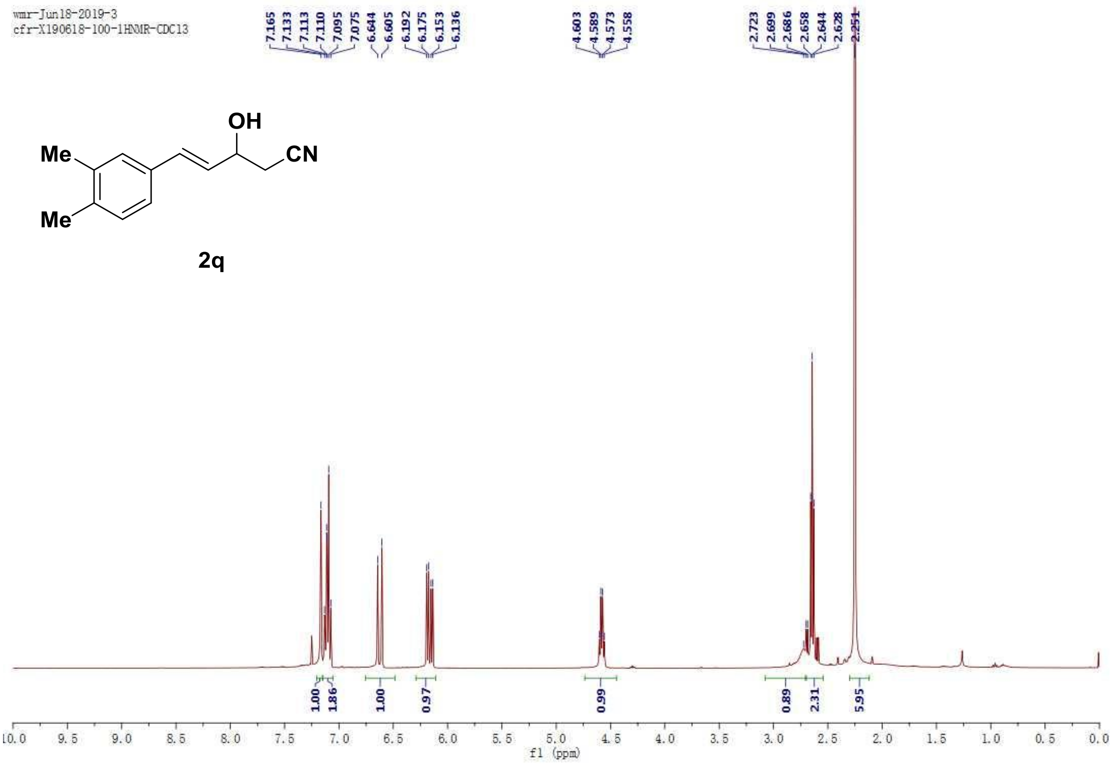
2p-^{1}H NMR



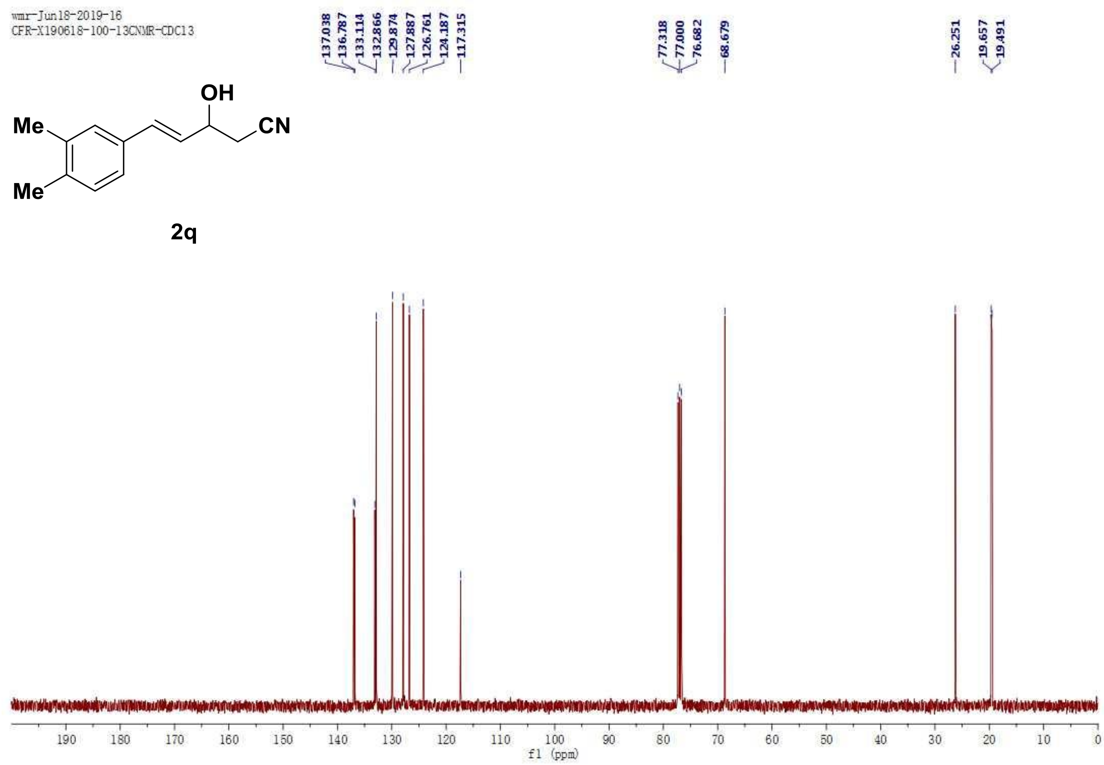
p-^{13}C NMR



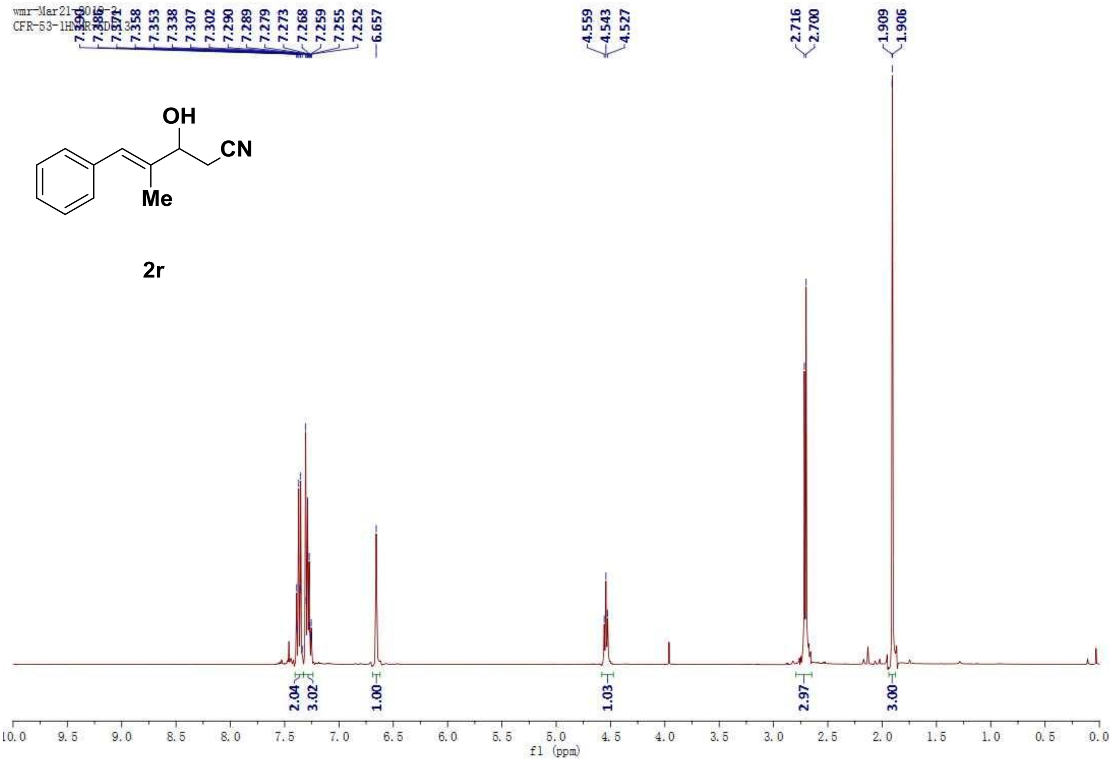
2q-^{1}H NMR



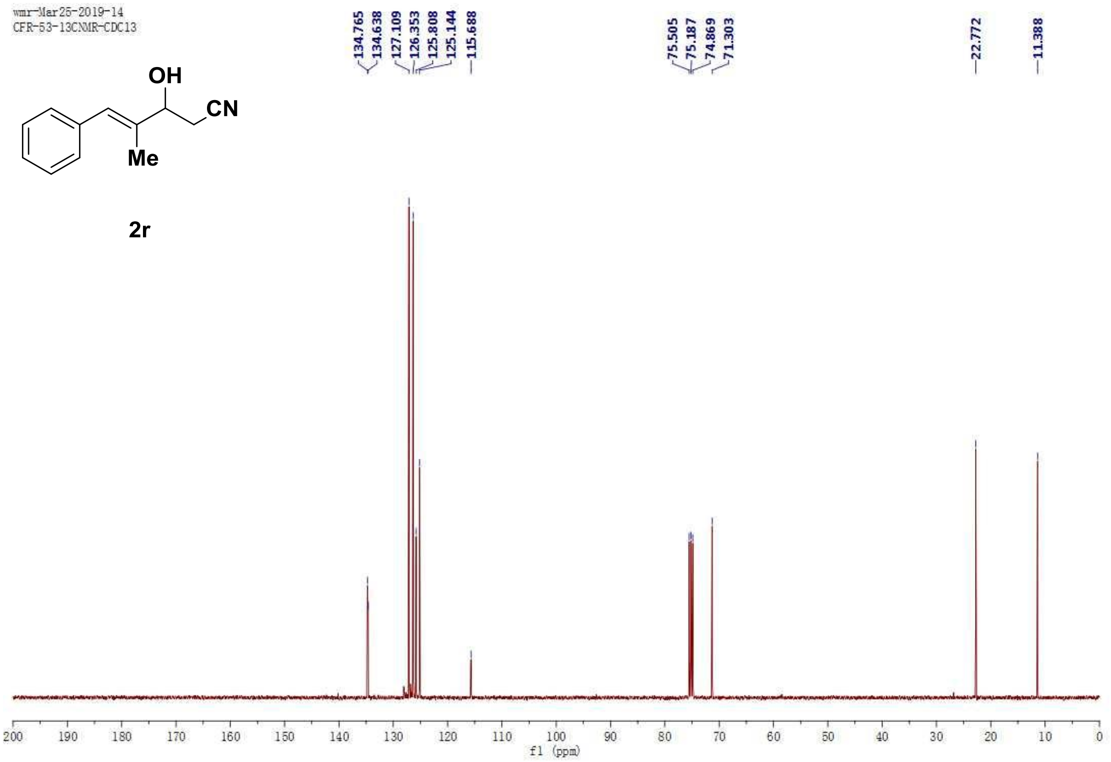
2q-^{13}C NMR



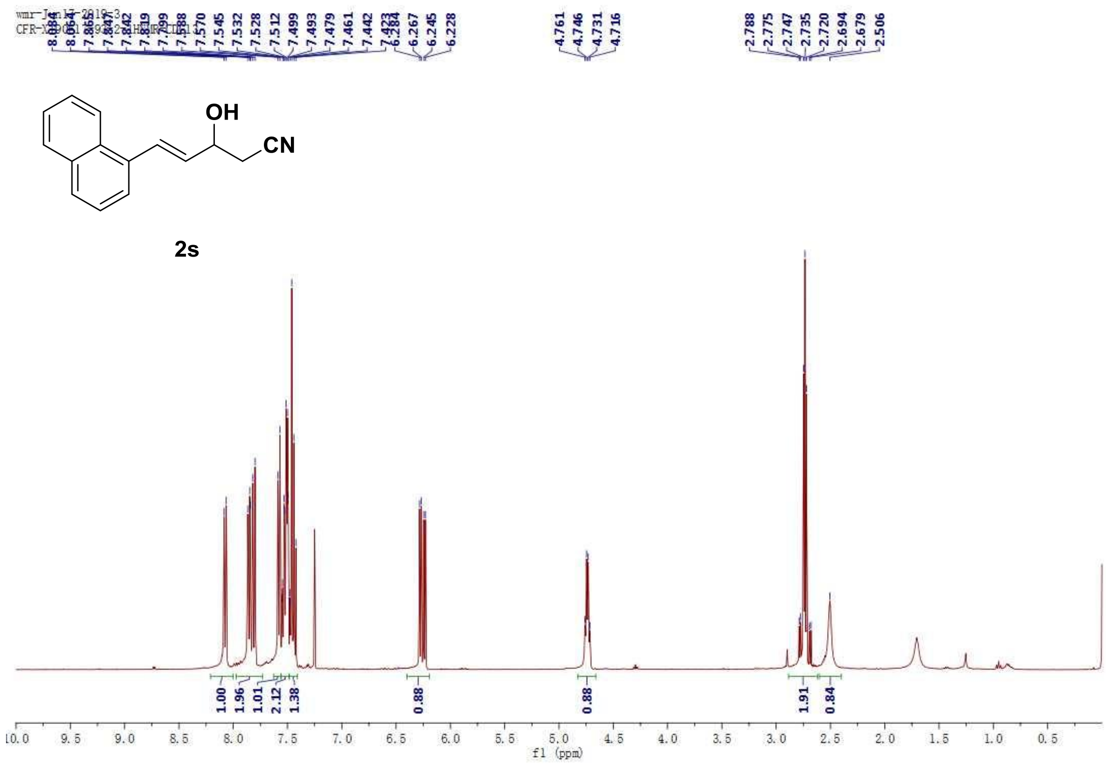
2r-^{1}H NMR



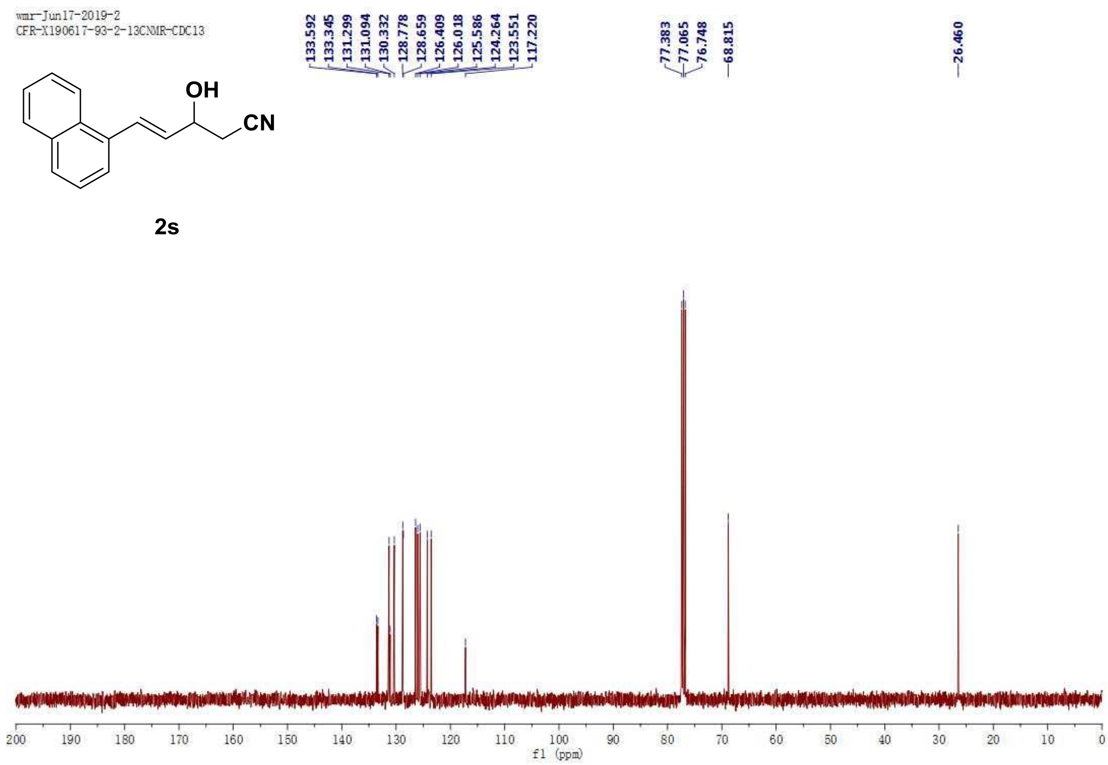
2r-^{13}C NMR



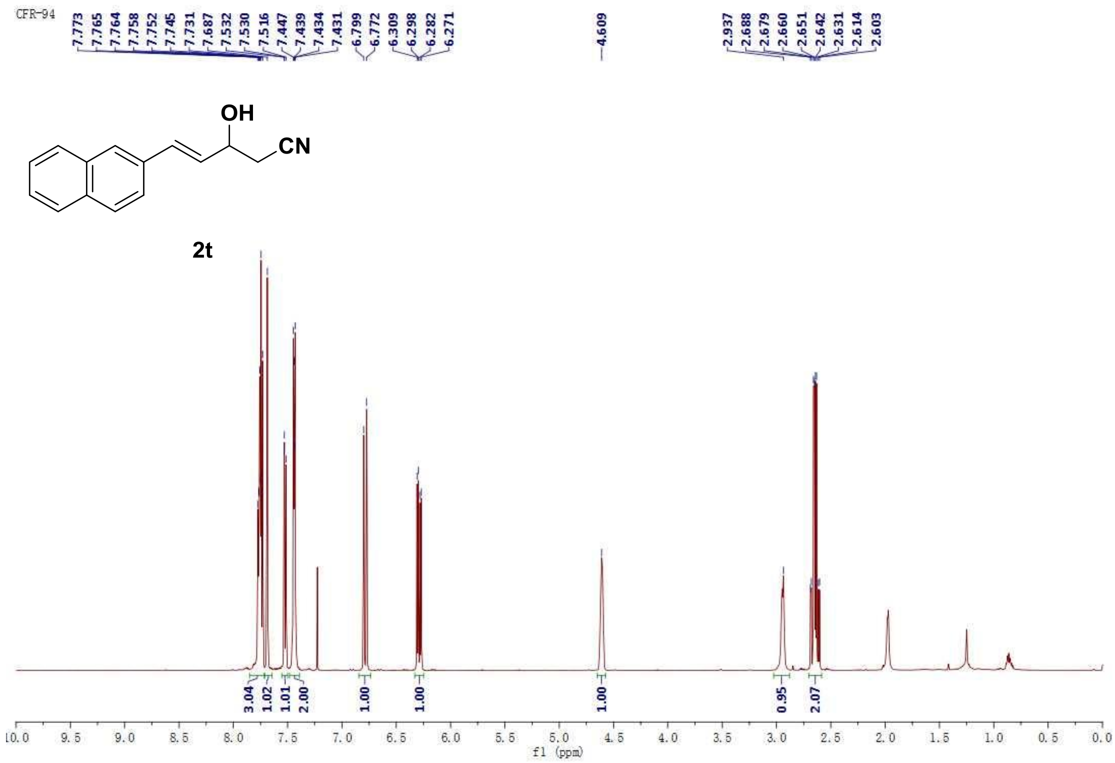
2s-^{1}H NMR



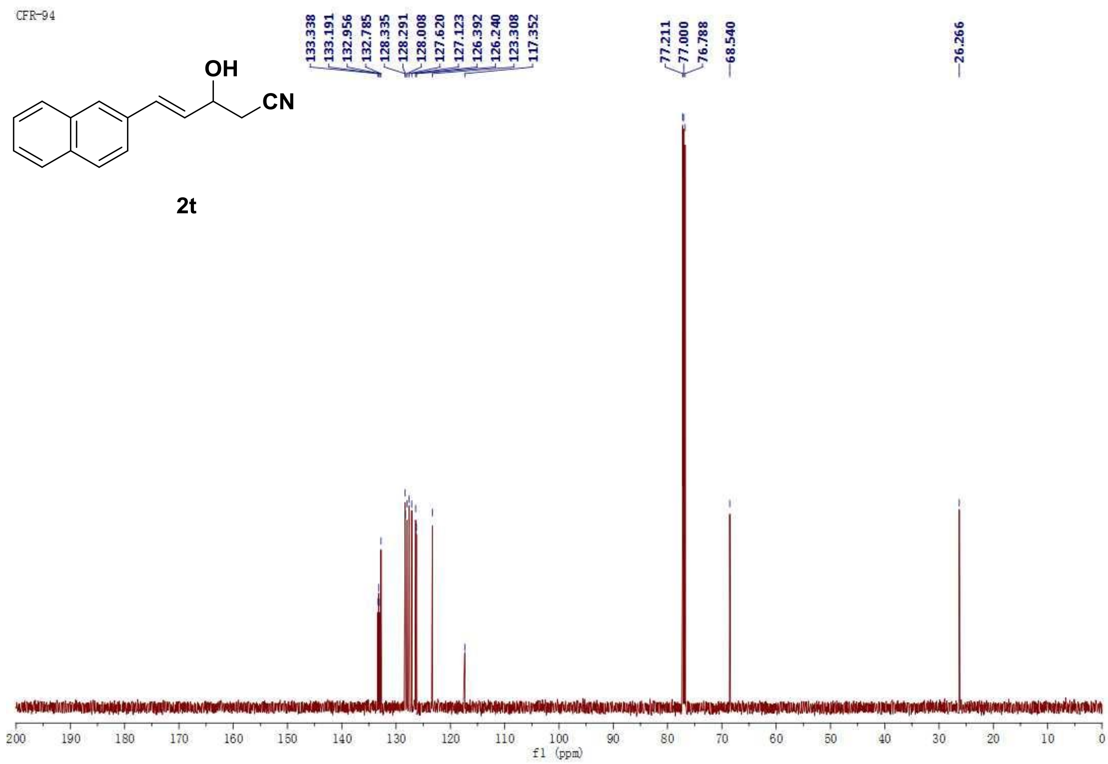
2s-^{13}C NMR



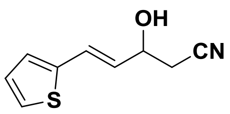
2t-[1]H NMR



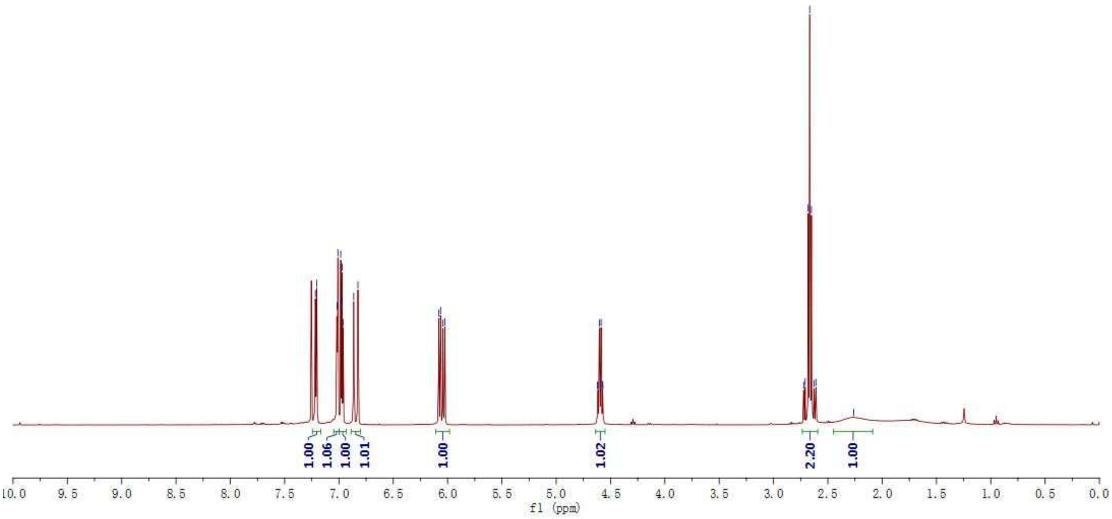
2t-[13]C NMR



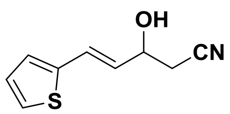
2u-¹H NMR



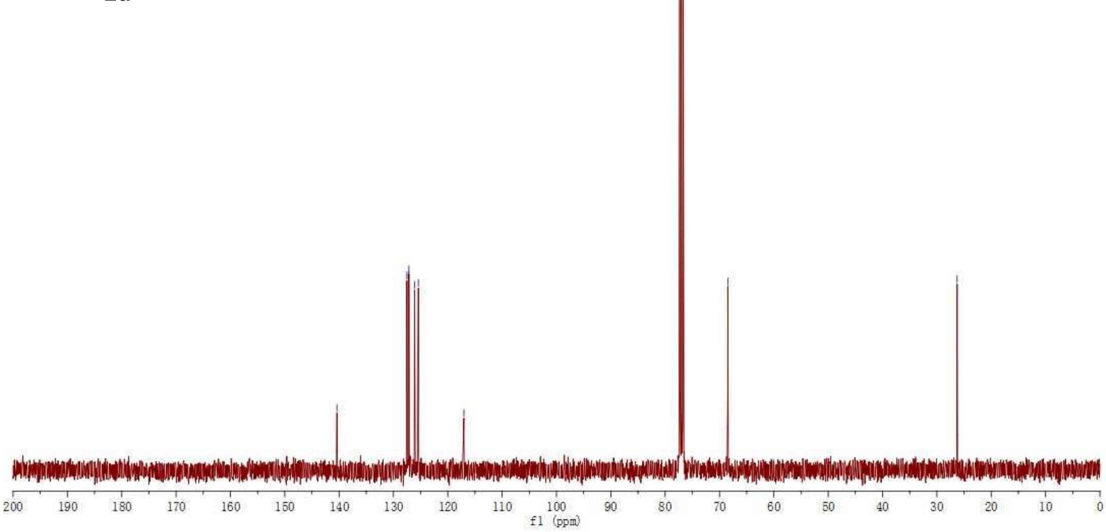
2u



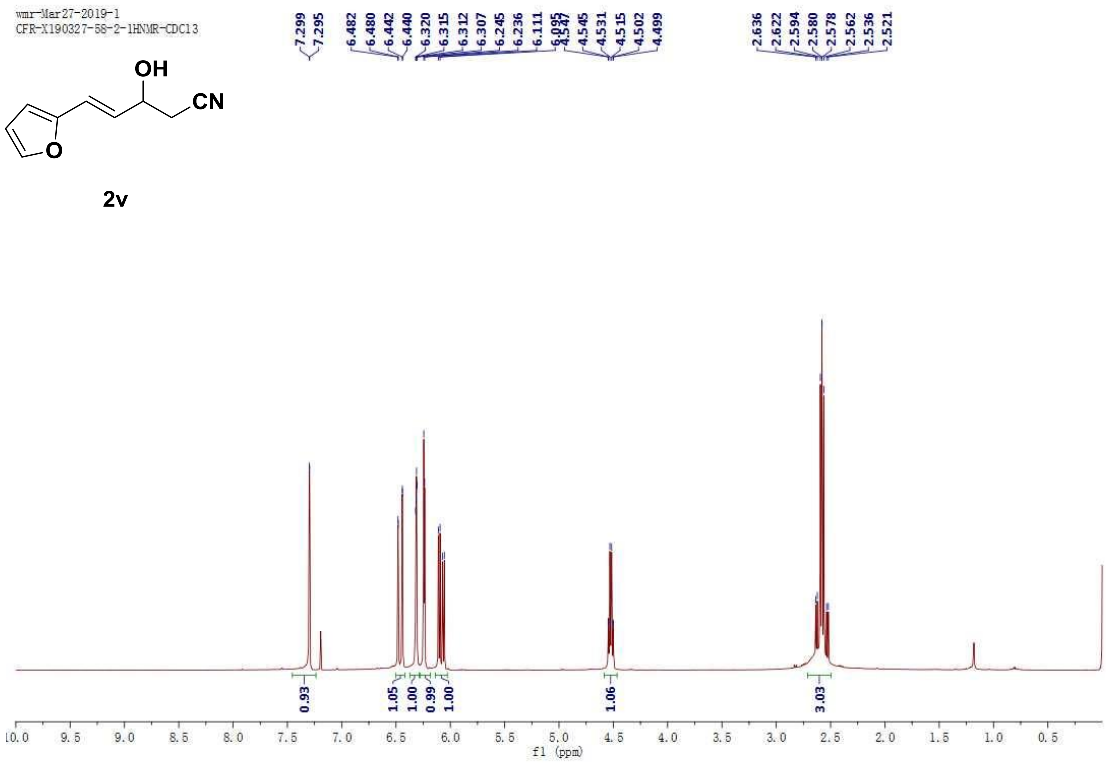
2u-¹³C NMR



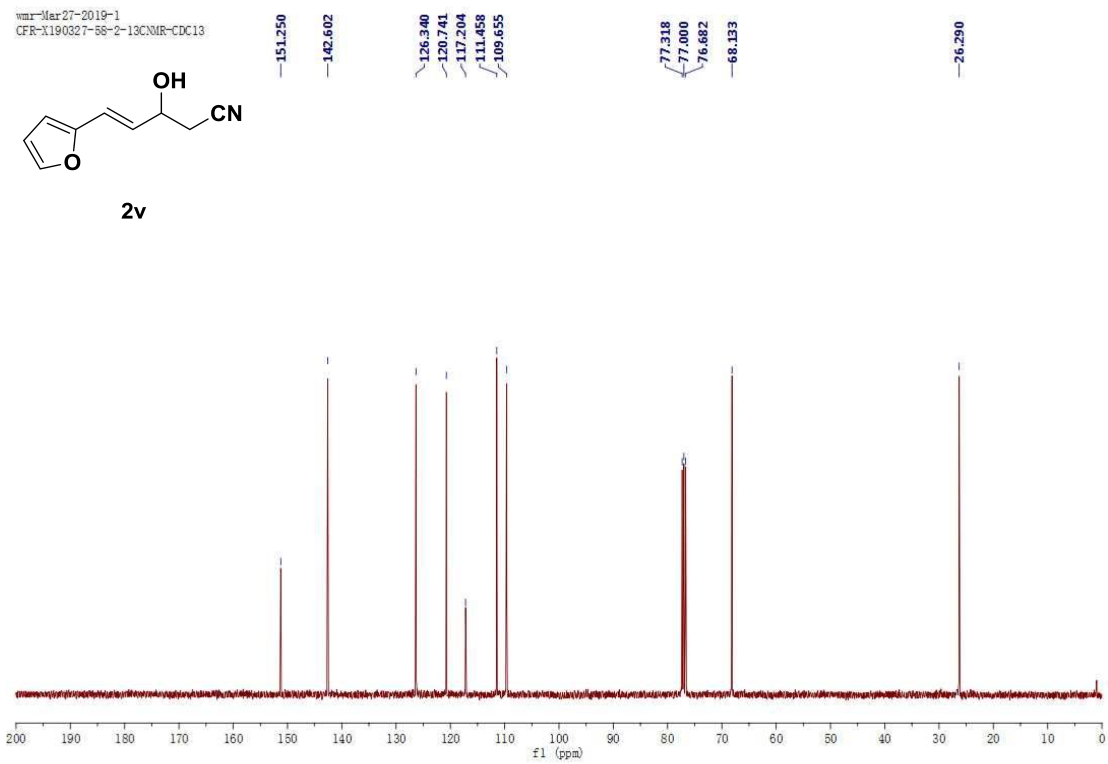
2u



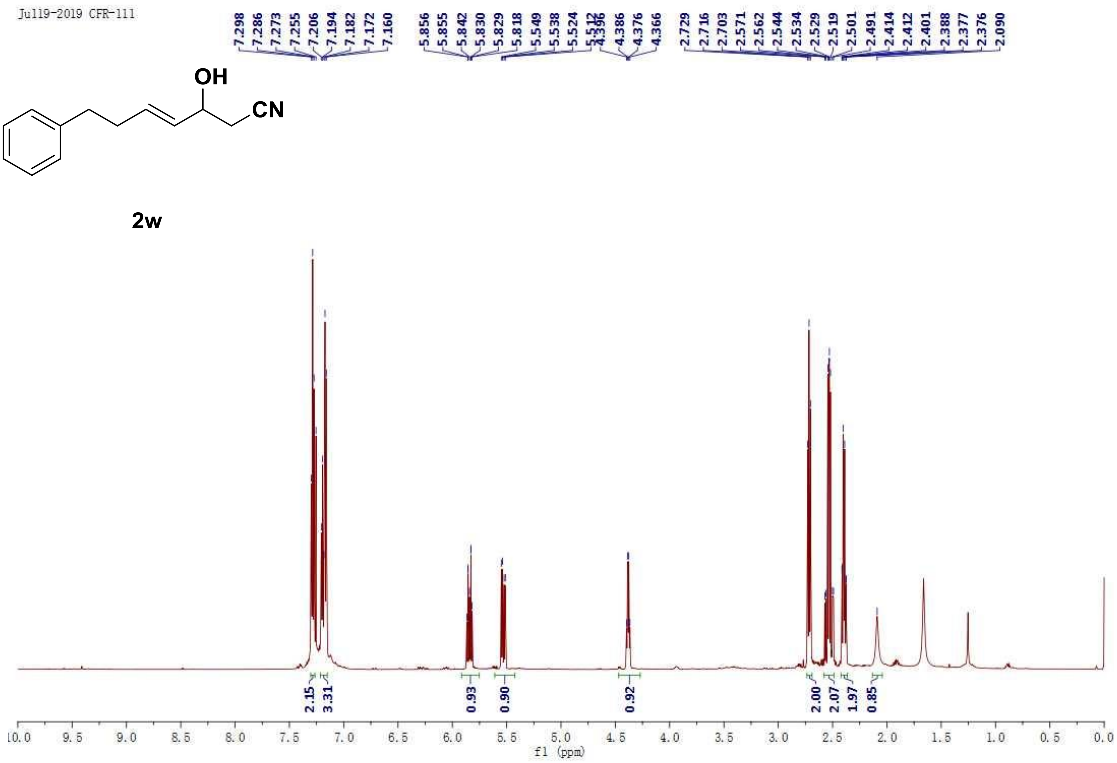
2v-^{1}H NMR



2v-^{13}C NMR

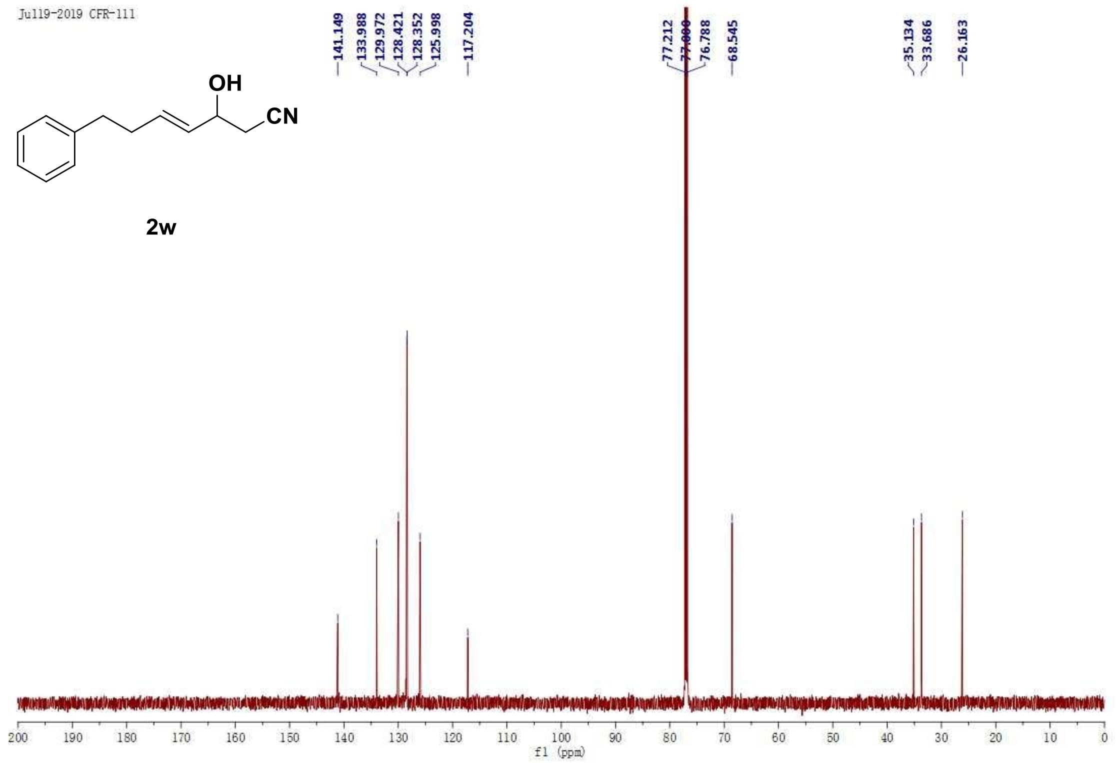


2w-^{1}H NMR



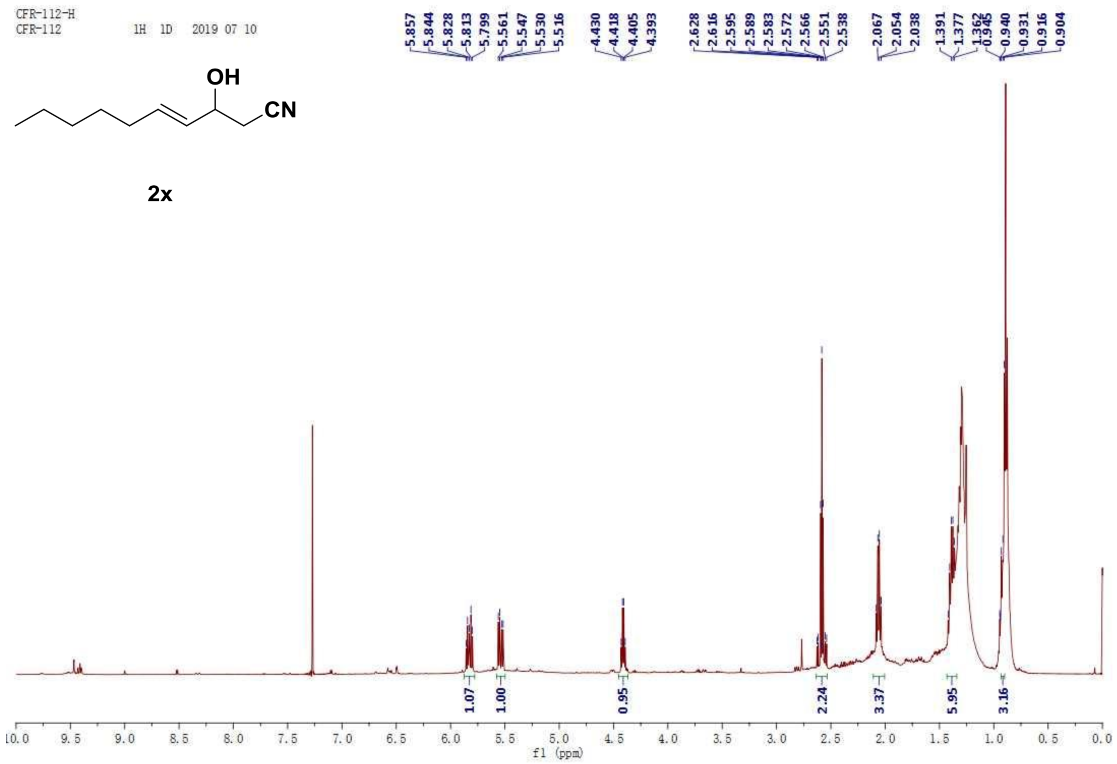
2w

2w-^{13}C NMR

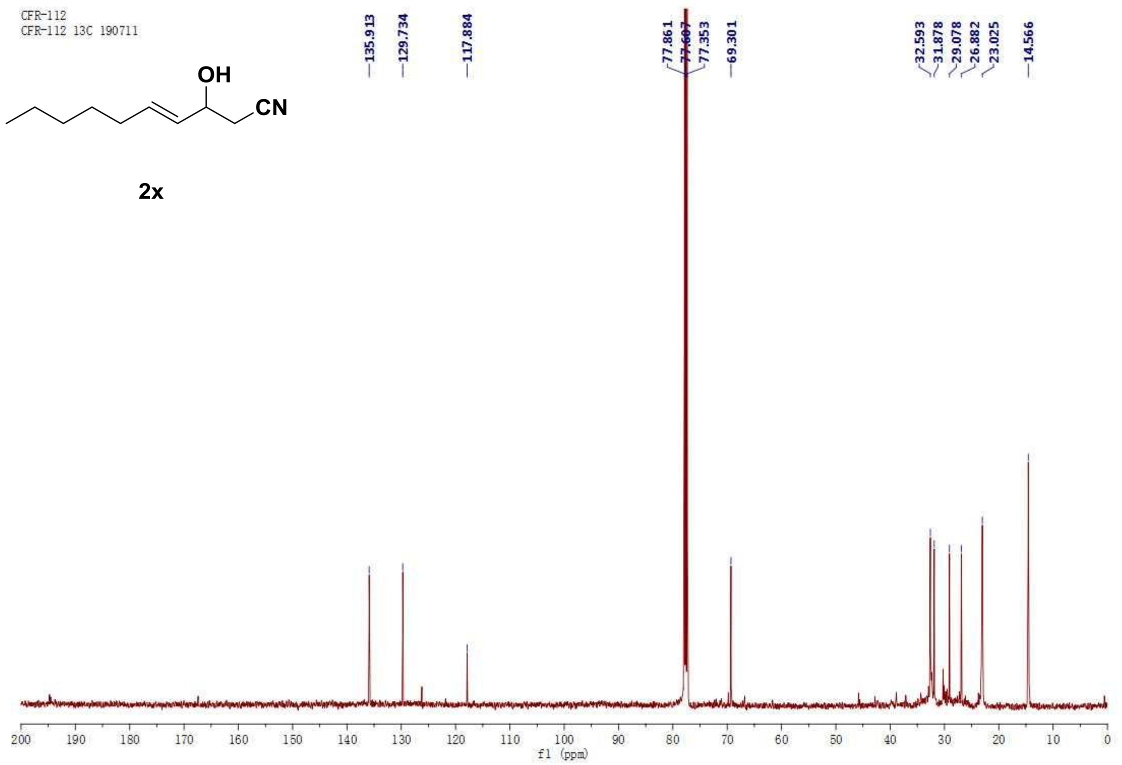


2w

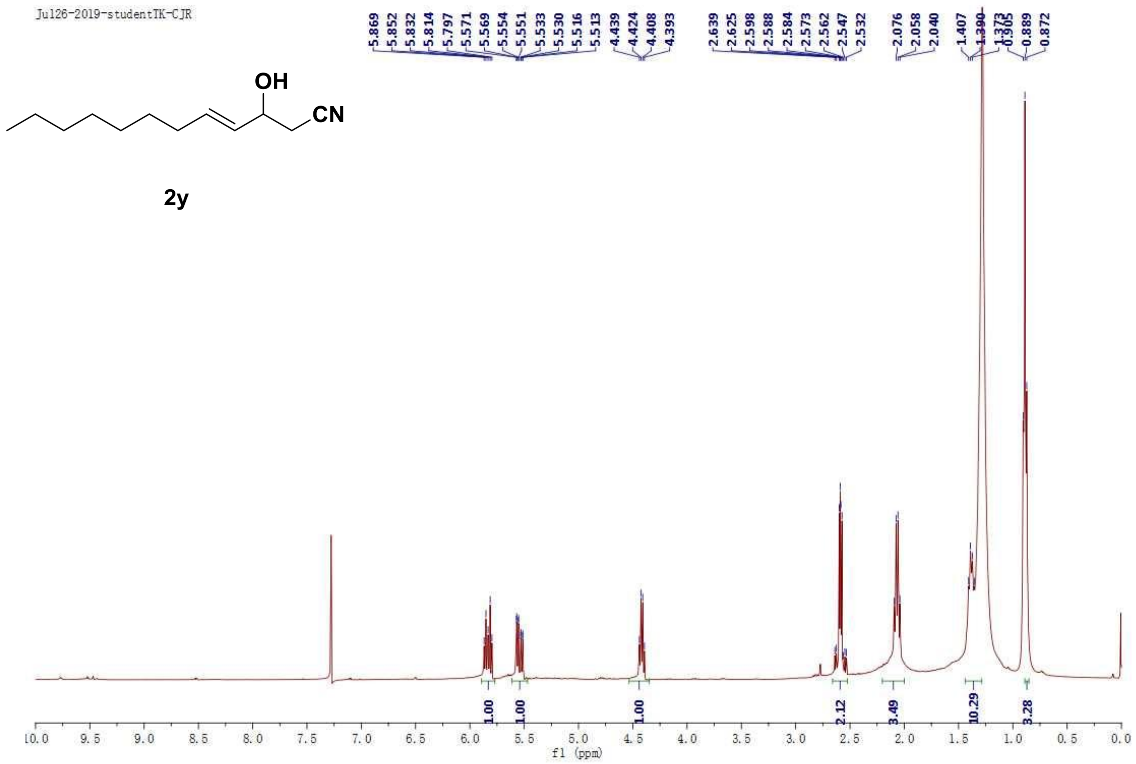
2x-[1]H NMR



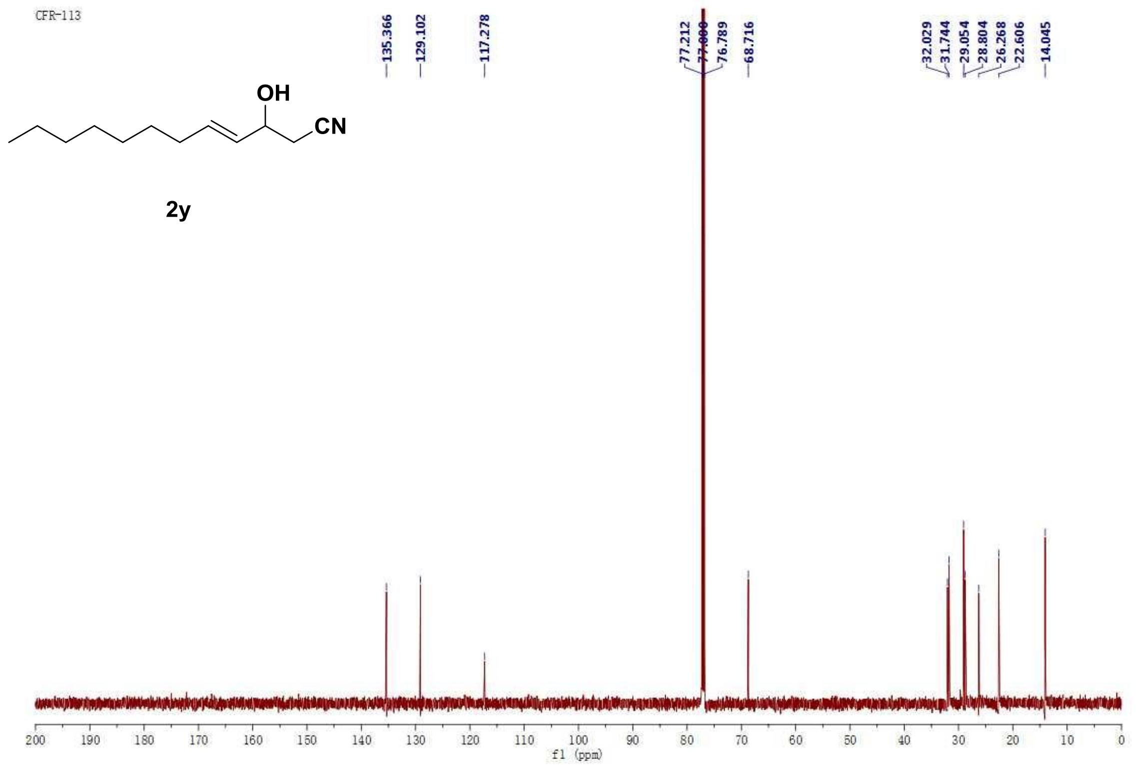
2x-[13]C NMR



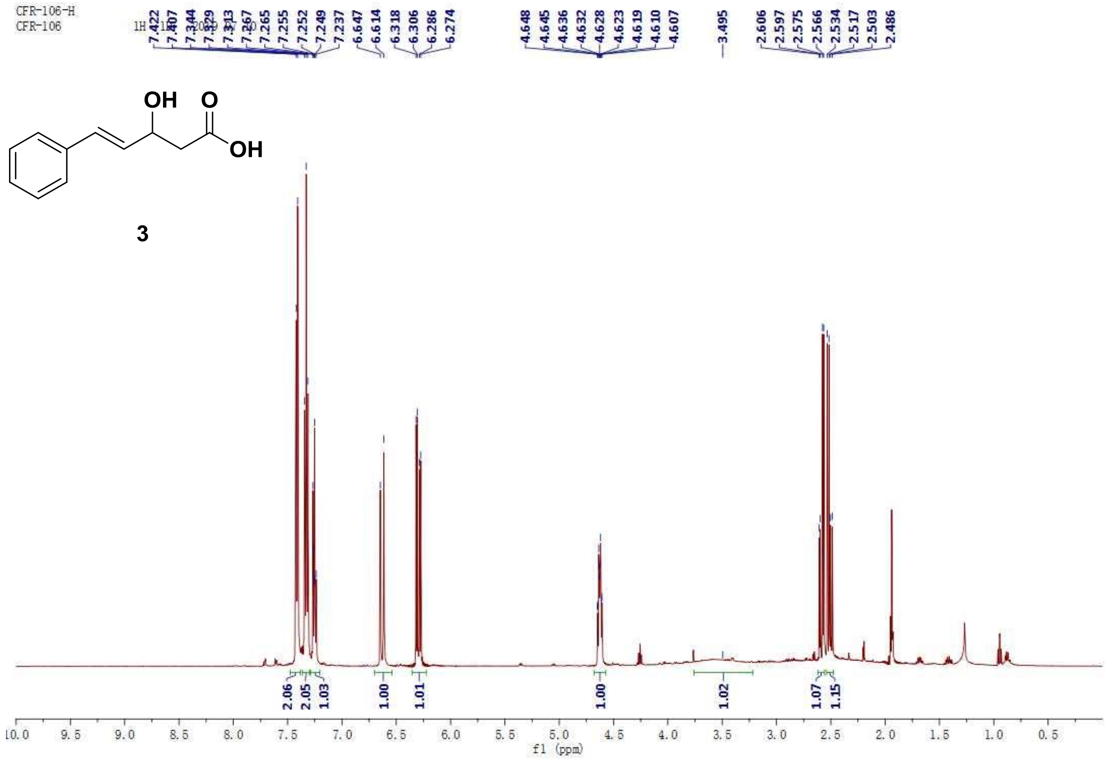
2y-^{1}H NMR



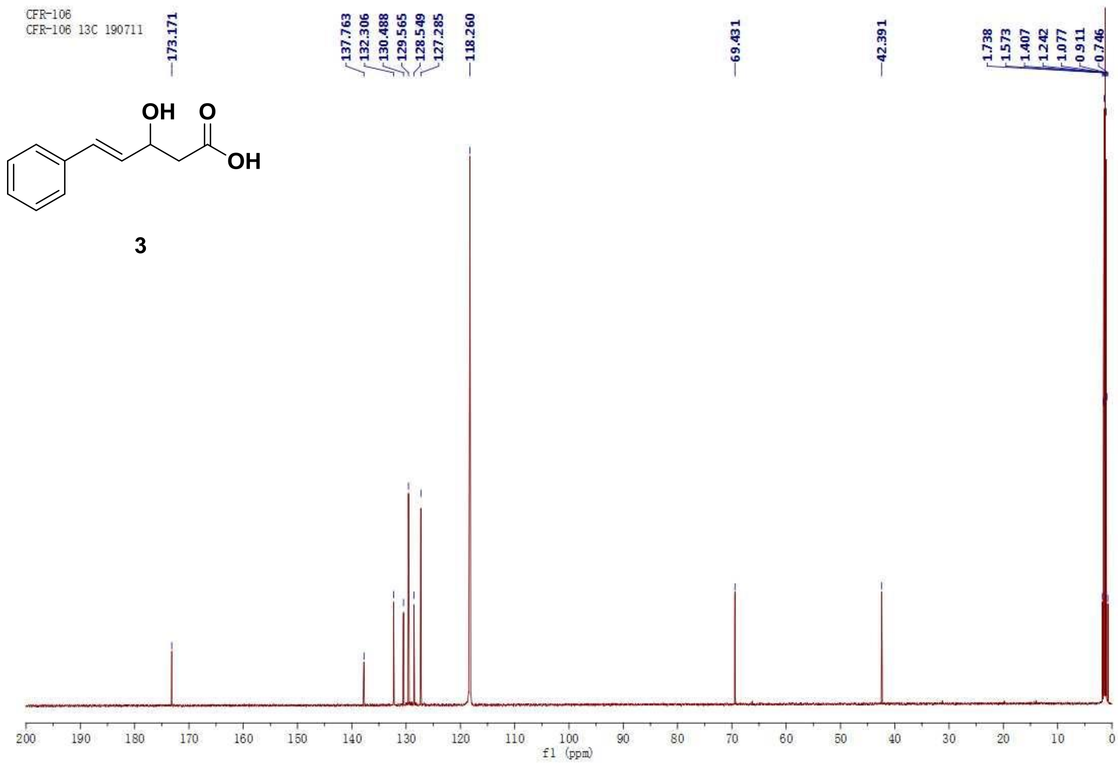
2y-^{13}C NMR



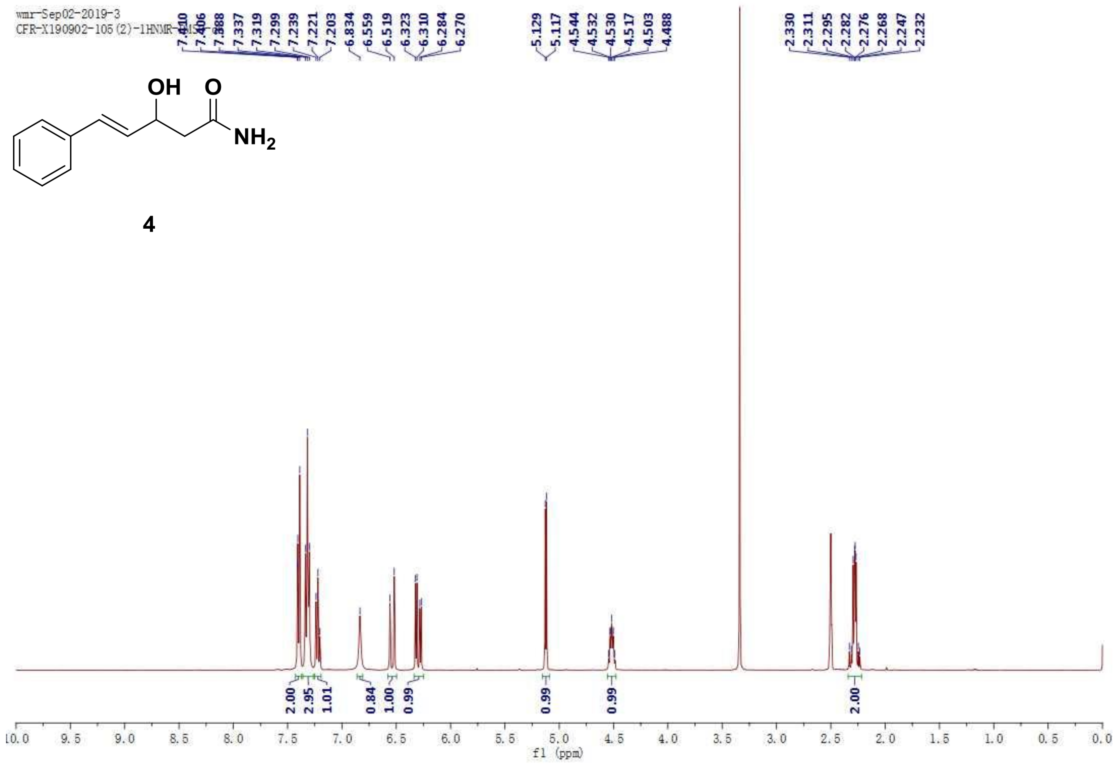
3-^{1}H NMR



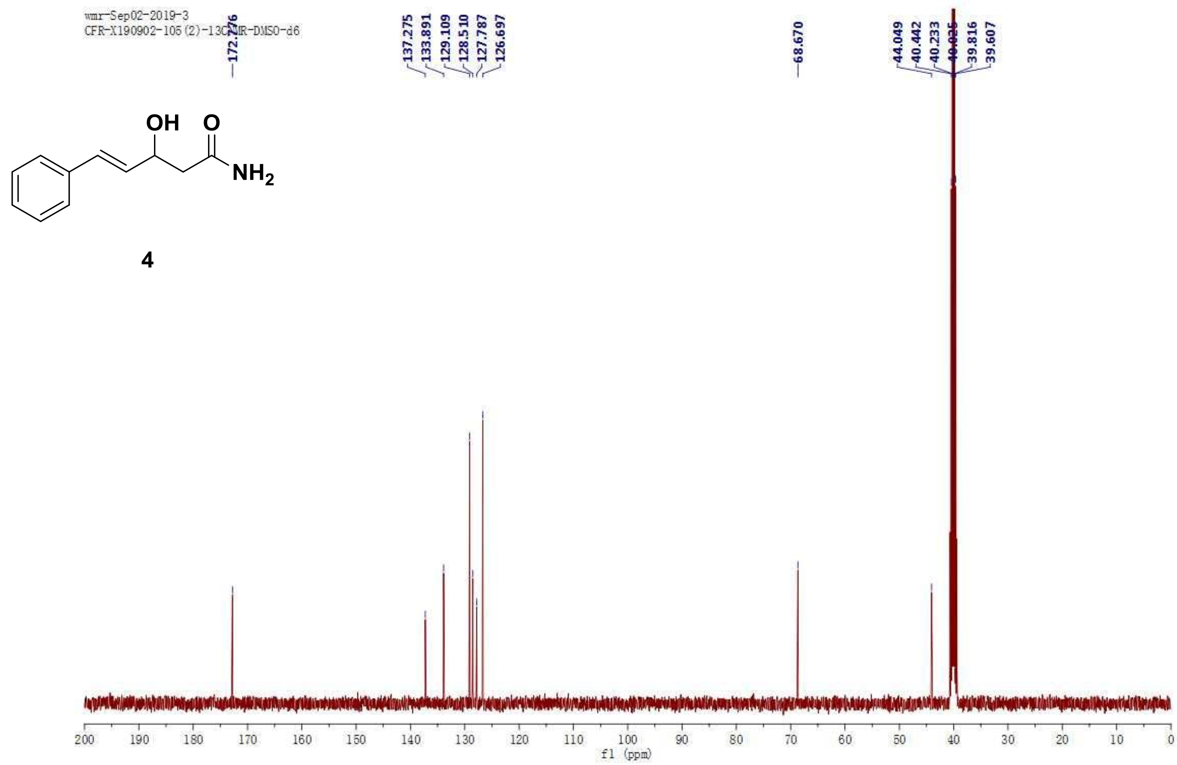
3-^{13}C NMR



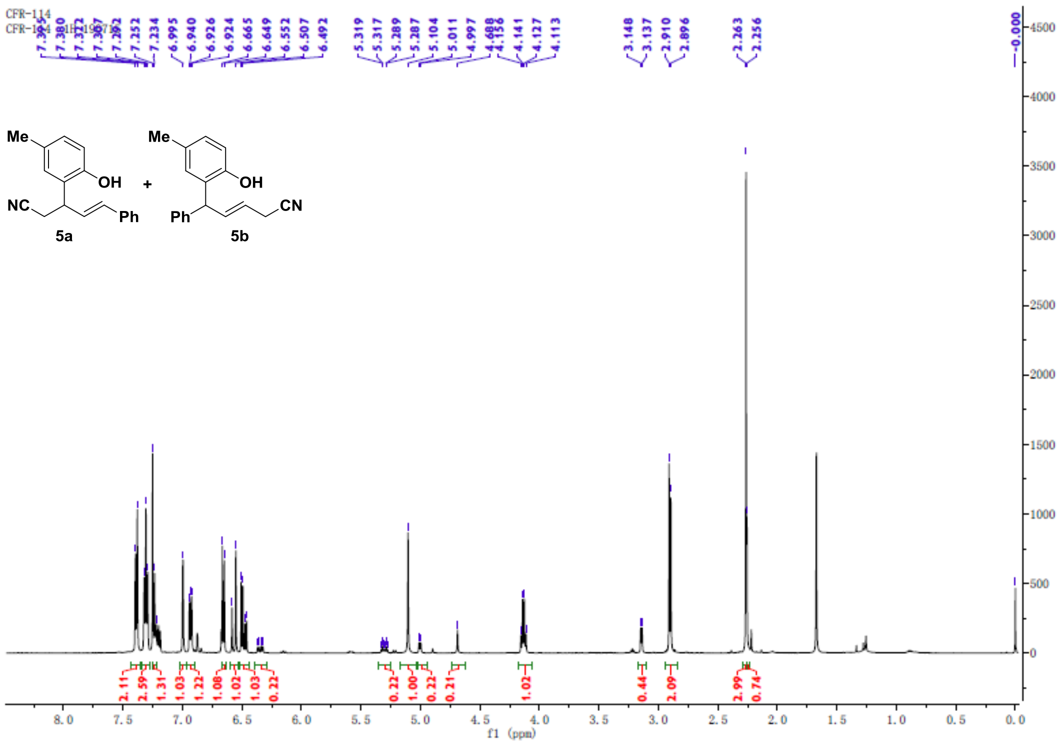
4-^{1}H NMR



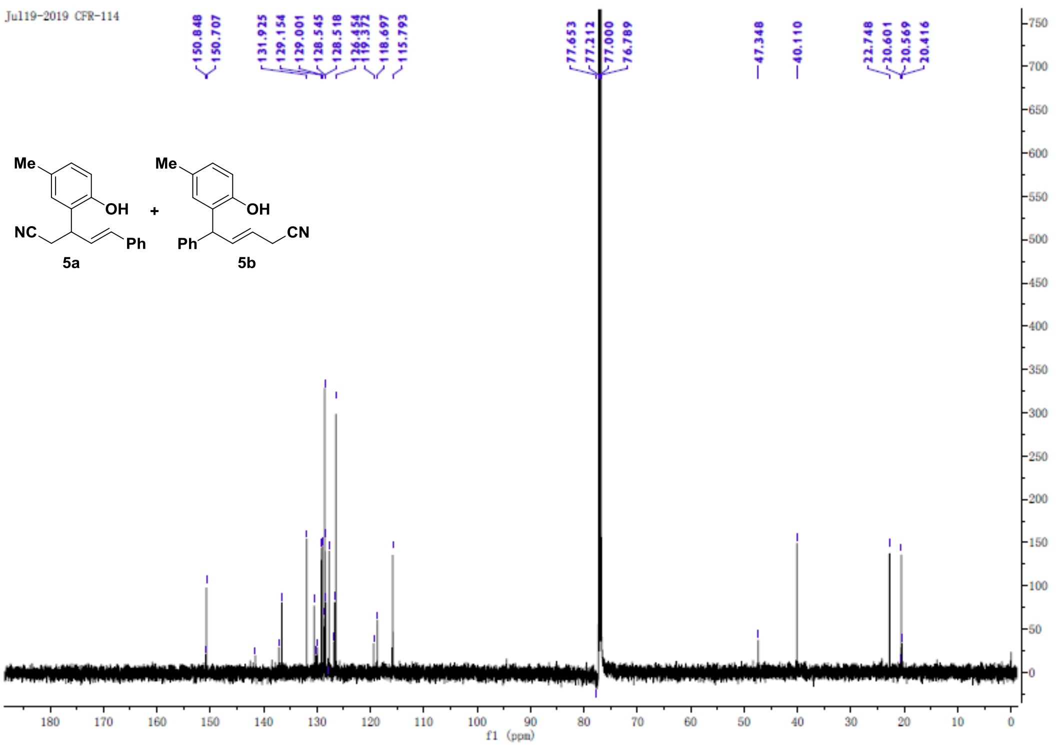
4-^{13}C NMR



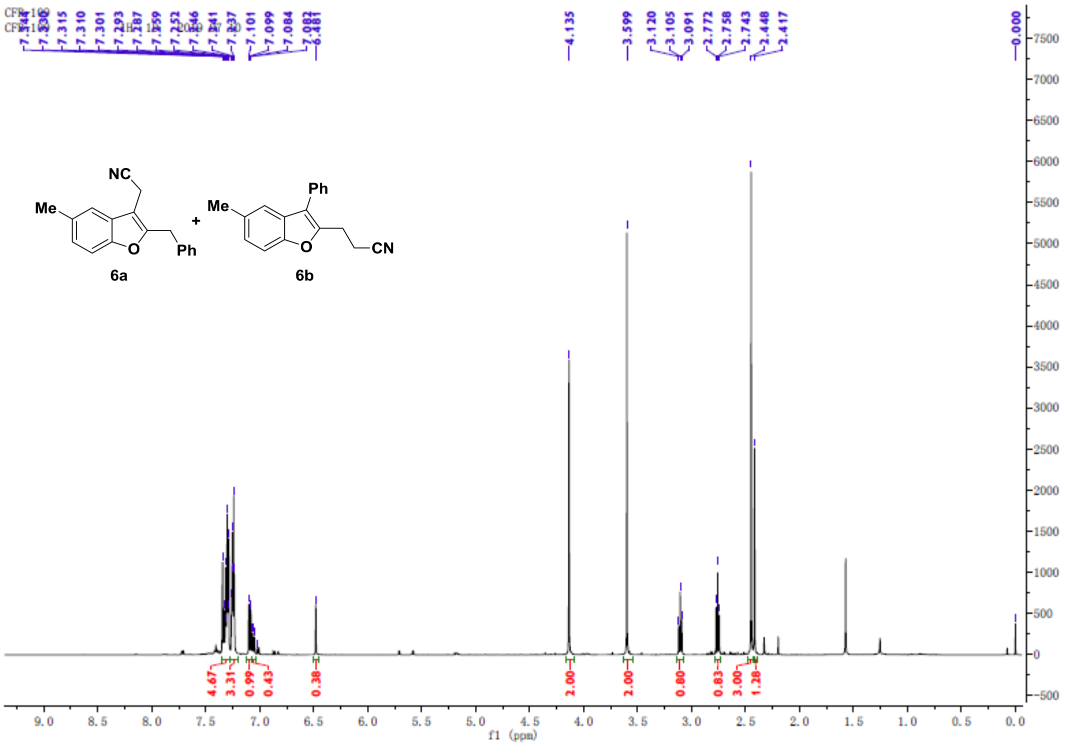
5a+5b ^{1}H NMR



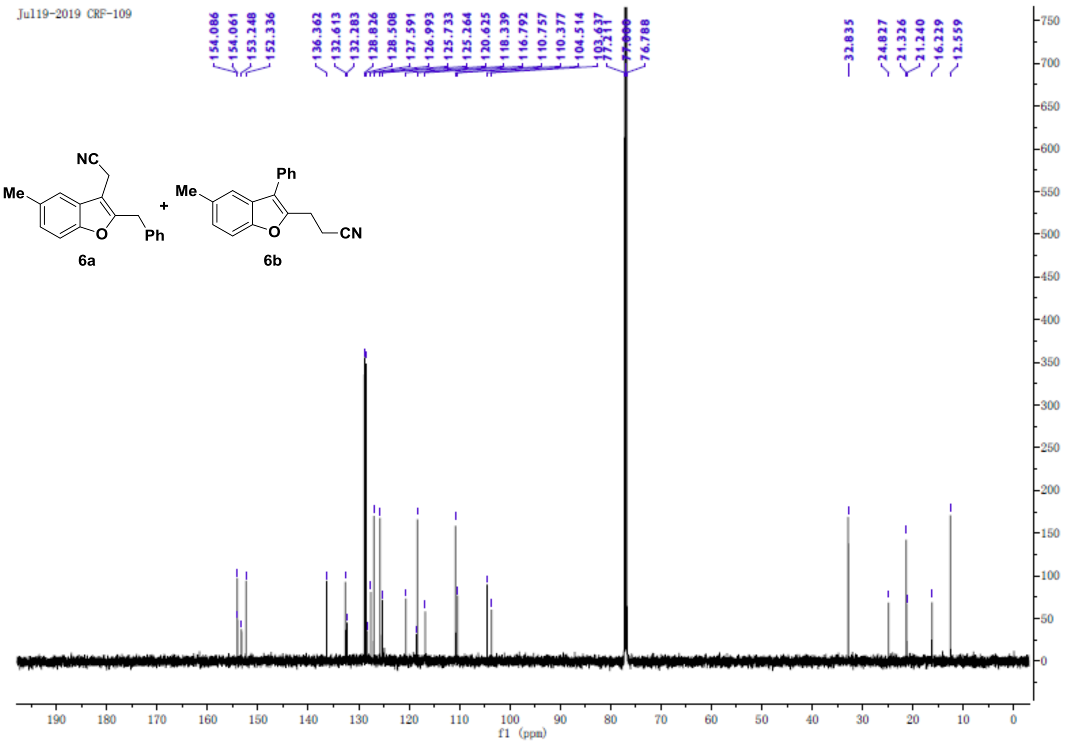
5a+5b ^{13}C NMR



6a+6b ^{1}H NMR



6a+6b ^{13}C NMR



VII. References

1. Katritzky, A. R.; Pilarski, B.; Urogdi, L. *Synthesis*, **1989**, 949-950.

2. Pamies, O.; Backvall, J.-E. *Adv. Synth. Catal*. **2002**, *344*, 947-952.

3. Rehan, M.; Nallagonda, R.; Das, B. G.; Meena, T.; Ghorai, P. *J. Org. Chem*. **2017**, *82*, 3411−3424.