Supporting Information

Pd-Catalyzed Asymmetric Allylic Substitution Cascade via An Asymmetric Desymmetrization for the Synthesis of Bicyclic Dihydrofurans

Kai Xu,[a] Hao Liu,[a] Yilin Hou,[a] Jiefeng Shen,*[,a] Delong Liu*[,a] and Wanbin Zhang[a,b]

[a]Shanghai Key Laboratory for Molecular Engineering of Chiral Drugs, School of Pharmacy, [b]School of Chemistry and Chemical Engineering, Shanghai Jiao Tong University, 800 Dongchuan Road, Shanghai 200240, P. R. China

Contents

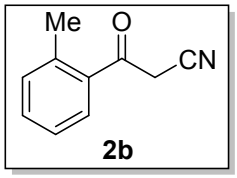
1. General Details

The NMR spectra were recorded on Bruker Advance III HD 400 (400 MHz, ^{1}H; 100 MHz, ^{13}C) or Bruker Advance III HD 500 (500 MHz, ^{1}H; 125 MHz, ^{13}C) and dealed with the software MestReNova. HRMS was performed on a Waters Micromass Q-TOF Premier Mass Spectrometer at the Instrumental Analysis Center of Shanghai Jiao Tong University. Melting points were measured with SGW X-4 micro melting point apparatus. X-Ray crystallography data were collected using an Xcalibur Atlas Gemini ultra diffractometer. Enantioselectivity was measured by high performance liquid chromatography (HPLC) using Daicel Chiralcel OD-H, AS-H, IC-3 and OJ-H columns with *n*-hexane/*i*-PrOH as an eluent. Column chromatography was performed using 100–200 mesh silica gel. The commercially available reagents were used without further purification.

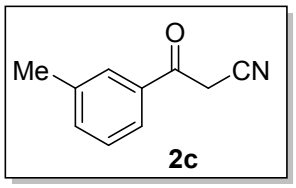
2. Preparation of 3-Oxo-nitrile Substrates

General Procedure A: To a solution of ester (10 mmol, 1.0 equiv) in THF (20 mL) under a nitrogen atmosphere was added NaH (15 mmol, 60 % dispersion in mineral oil, 1.5 equiv) at r.t and the mixture was stirred for 30 min. Acetonitrile (20 mL) was added dropwise and the reaction mixture was stirred at 60 °C for 12 h. The reaction was quenched with H_2O and the solvent was removed in vacuo. The water phase was extracted with ethyl acetate (3×25 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether : ethyl acetate = 3:1) to obtain the corresponding 3-oxo-3-propanenitrile.

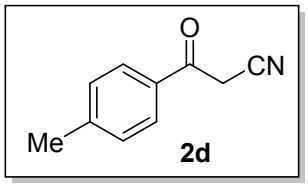
General Procedure B: To a solution of *n*-BuLi (25 mmol, 2.5 M solution in hexane, 2.5 equiv) in THF (20 mL) in a three-neck round bottom flask was added dropwise acetonitrile (30 mmol, 3.0 equiv) at -78 °C, and the reaction mixture was stirred for 1 h. Then a solution of ethyl benzoate (10 mmol, 1.0 equiv) in THF (10 mL) was added slowly, and the reaction mixture was stirred for another 2 h at -78 °C. The reaction was quenched with H_2O (20 mL) and the solvent was removed in vacuo. The resulting mixture was diluted with EtOAc (20 mL) and the organic layer was separated. The water layer was extracted with EtOAc (3×20 mL), and the combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (petroleum ether : ethyl acetate = 3:1) to obtain the corresponding 3-oxo-3-propanenitrile.



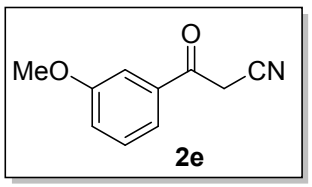
3-Oxo-3-(*o*-tolyl)propanenitrile (2b):[1] General procedure **A** was followed on a 10.0 mmol scale. The product **2b** was obtained as a yellow solid (1.1 g, 70%). Mp: 81~82 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.6 Hz, 1H), 7.50 (t, J = 7.6 Hz, 1H), 7.34 (t, J = 7.6 Hz, 2H), 4.08 (s, 2H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 140.4, 133.8, 133.3, 132.8, 129.3, 126.2, 114.2, 31.5, 21.8. HRMS (ESI) calcd for $C_{10}H_{10}NO$ $[M+H]^+$ 160.0762, found 160.0766.



3-Oxo-3-(*m*-tolyl)propanenitrile (2c):[1] General procedure **A** was followed on a 10.0 mmol scale. The product **2c** was obtained as a yellow solid (0.6 g, 37%). Mp: 68~69 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.68 (m, 2H), 7.48 (d, J = 7.6 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 4.10 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4, 139.2, 135.5, 134.3, 129.0, 128.9, 125.7, 114.0, 29.4, 21.3. HRMS (ESI) calcd for $C_{10}H_{10}NO$ $[M+H]^+$ 160.0762, found 160.0763.

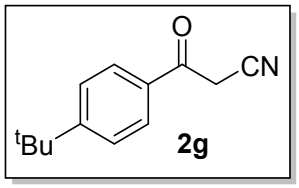


3-Oxo-3-(*p*-tolyl)propanenitrile (2d):[1] General procedure **A** was followed on a 10.0 mmol scale. The product **2d** was obtained as a yellow solid (1.8 g, 84%). Mp: 99~100 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 4.08 (s, 2H), 2.49 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.74 145.99 131.86 129.83 128.60 114.02 29.29 21.80. HRMS (ESI) calcd for $C_{10}H_{10}NO$ $[M+H]^+$ 160.0762, found 160.0765.

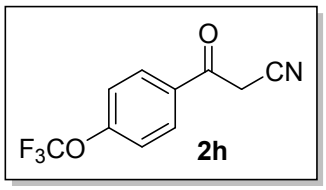


3-Oxo-3-(*p*-tolyl)propanenitrile (2e):[2] General procedure **A** was followed on a 10.0 mmol scale. The product **2e** was obtained as a yellow solid (0.7 g, 35%). Mp: 87~88 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.40 (m, 3H), 7.24–7.18 (m, 1H), 4.10 (s, 2H), 3.88 (s, 3H). ^{13}C NMR (125 MHz,

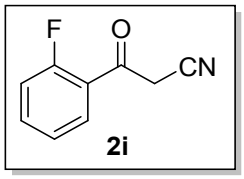
$CDCl_3$) δ 187.0, 160.1, 135.5, 130.1, 121.2, 120.9, 113.8, 112.6, 55.5, 29.5. HRMS (ESI) calcd for $C_{10}H_9NNaO_2$ $[M+Na]^+$ 198.0531, found 198.0536.



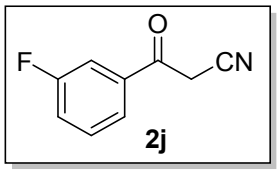
3-(4-(Tert-butyl)phenyl)-3-oxopropanenitrile (2g):[3] General procedure **B** was followed on a 10.0 mmol scale. The product **2g** was obtained as a yellow solid (0.9 g, 40%). Mp: 73~74 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94–7.82 (m, 2H), 7.62–7.48 (m, 2H), 4.09 (s, 2H), 1.37 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7, 158.8, 131.7, 128.5, 126.1, 114.0, 35.3, 30.9, 29.3. HRMS (ESI) calcd for $C_{13}H_{15}NNaO$ $[M+Na]^+$ 224.1051, found 224.1051.



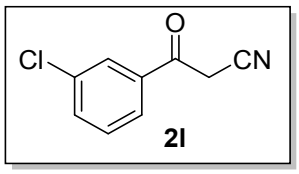
3-Oxo-3-(4-(trifluoromethoxy)phenyl)propanenitrile (2h):[4] General procedure **B** was followed on a 10.0 mmol scale. The product **2h** was obtained as a yellow solid (1.61 g, 64%). Mp: 72~73 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08–7.95 (m, 2H), 7.37 (d, J = 8.0 Hz, 2H), 4.11 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.7, 153.7, 132.3, 130.6, 123.2, 120.2 (q, J = 8.1 Hz), 113.4, 29.4. ^{19}F NMR (471 MHz, $CDCl_3$): δ –57.6. HRMS (ESI) calcd for $C_{10}H_6F_3NNaO_2$ $[M+Na]^+$ 252.0248, found 252.0253.



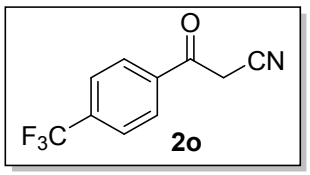
3-(2-Fluorophenyl)-3-oxopropanenitrile (2i):[1] General procedure **B** was followed on a 20.0 mmol scale. The product **2i** was obtained as a yellow solid (1.1 g, 69.9%). Mp: 60–61 °C , ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (td, J = 7.6, 2.0 Hz, 1H), 7.68–7.63 (m, 1H), 7.38–7.29 (m, 1H), 7.26–7.17 (m, 1H), 4.12 (d, J = 2.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.1 (d, J = 3.8 Hz), 162.2 (d, J = 3.8 Hz), 253.3 (d, J = 9.5 Hz), 131.13 (d, J = 1.6 Hz), 125.18 (d, J = 3.3 Hz), 122.75 (d, J = 12.3 Hz), 116.9 (d, J = 23.4 Hz), 113.53 (d, J = 3.8 Hz), 33.66 (d, J = 11.6 Hz). ^{19}F NMR (471 MHz, $CDCl_3$): δ –109.1. HRMS (ESI) calcd for C_9H_7FNO $[M+H]^+$ 164.0512, found 164.0510.



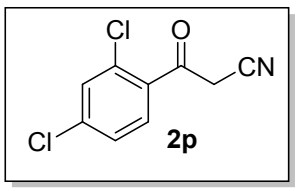
3-(3-Fluorophenyl)-3-oxopropanenitrile (2j):[5] General procedure **A** was followed on a 10.0 mmol scale. The product **2j** was obtained as a yellow solid (1.1 g, 84.0%). Mp: 71~72 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 7.8 Hz, 1H), 7.66–7.61 (m, 1H), 7.54 (td, J = 8.0, 5.5 Hz, 1H), 7.39 (td, J = 8.2, 2.5 Hz, 1H), 4.12 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.1 (d, J = 2.4 Hz), 162.9 (d, J = 248.3 Hz), 136.1 (d, J = 6.6 Hz), 130.9 (d, J = 7.7 Hz), 124.2 (d, J = 3.1 Hz), 121.9 (d, J = 21.2 Hz), 115.2 (d, J = 22.6 Hz), 113.50 (s), 29.65 (s). ^{19}F NMR (471 MHz, $CDCl_3$): δ –110.4. HRMS (ESI) calcd for C_9H_7FNO $[M+H]^+$ 164.0512, found 164.0515.



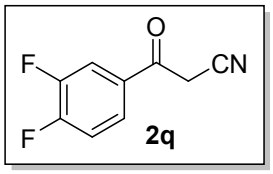
3-(3-Chlorophenyl)-3-oxopropanenitrile (2l):[1] General procedure **A** was followed on a 10.0 mmol scale. The product **2m** was obtained as a yellow solid (1.1 g, 60%). **1**H NMR (500 MHz, $CDCl_3$) δ 7.91 (t, J = 1.6 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.69–7.63 (m, 1H), 7.50 (t, J = 7.9 Hz, 1H), 4.11 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 186.1, 135.7, 135.6, 134.7, 130.5, 128.5, 126.5, 113.4, 29.6. HRMS (ESI) calcd for $C_9H_6F_2NO$ $[M+H]^+$ 182.0417, found 182.0423.



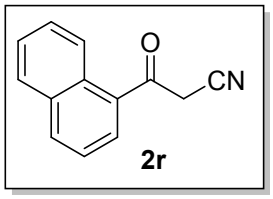
3-Oxo-3-(4-(trifluoromethyl)phenyl)propanenitrile (2o):[6] General procedure **A** was followed on a 10.0 mmol scale. The product **2o** was obtained as a yellow solid (1.0 g, 48%). Mp: 143~144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 4.15 (d, J = 1.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.3, 136.8, 135.9 (q, J = 52.6 Hz), 128.8, 126.2 (q, J = 29.0 Hz), 123.5 (q, J = 271.4 Hz), 122.1, 119.9, 113.1, 29.6. ^{19}F NMR (471 MHz, $CDCl_3$): δ –63.4. HRMS (ESI) calcd for $C_{10}H_7F_3NO$ $[M+H]^+$ 213.0474, found 213.0470.



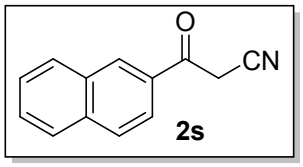
3-(2,4-Dichlorophenyl)-3-oxopropanenitrile (2p):[7] General procedure **A** was followed on a 10.0 mmol scale. The product **2p** was obtained as a yellow solid (1.1 g, 50%). Mp: 52~53 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.4 Hz, 1H), 7.54–7.51 (m, 1H), 7.43–7.39 (m, 1H), 4.16 (d, J = 0.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.1, 139.9, 133.7, 132.9, 131.7, 130.9, 128.0, 113.1, 33.0. HRMS (ESI) calcd for $C_9H_6Cl_2NO$ $[M+H]^+$ 213.9826, found 213.9827.



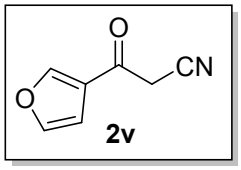
3-(3,4-Difluorophenyl)-3-oxopropanenitrile (2q):[8] General procedure **B** was followed on a 10.0 mmol scale. The product **2q** was obtained as a yellow solid (0.9 g, 50%). Mp: 65~66 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86–7.77 (m, 1H), 7.75–7.71 (m, 1H), 7.38–7.32 (m, 1H), 4.11 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.9, 144.5 (dd, J = 258.8, 12.8 Hz), 150.6 (dd, J = 251.4, 13.1 Hz), 131.3 (t, J = 4.5 Hz), 125.75 (q, J = 7.7 Hz), 118.2 (d, J = 18.1 Hz), 117.9 (dd, J = 18.3, 2.1 Hz), 113.3, 29.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ –126.1 (d, J = 21.0 Hz), –134.3 (d, J = 26.7 Hz). HRMS (ESI) calcd for $C_9H_6F_2NO$ $[M+H]^+$ 182.0417, found 182.0423.



3-(Naphthalen-1-yl)-3-oxopropanenitrile (2r):[9] General procedure **A** was followed on a 10.0 mmol scale. The product **2r** was obtained as a yellow solid (1.1 g, 58%). Mp: 92~93 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.96–7.85 (m, 2H), 7.71–7.65 (m, 1H), 7.63–7.59 (m, 1H), 7.55 (t, J = 8.0 Hz, 1H), 4.22 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.6, 135.2, 134.0, 131.4, 130.3, 129.6, 128.7, 127.1, 125.6, 124.2, 114.2, 31.8. HRMS (ESI) calcd for $C_{13}H_{10}NO$ $[M+H]^+$ 196.0762, found 196.0763.

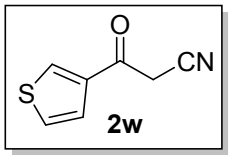


3-(Naphthalen-2-yl)-3-oxopropanenitrile (2s):[1] General procedure **B** was followed on a 10.0 mmol scale. The product **2s** was obtained as a yellow solid (1.2 g, 61%). Mp:119~120 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 8.00–7.90 (m, 4H), 7.77–7.52 (m, 2H), 4.23 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.1, 136.1, 132.2, 131.6, 130.7, 129.7, 129.5, 127.9, 127.4, 123.3, 114.0, 29.4. HRMS (ESI) calcd for $C_{13}H_{10}NO$ $[M+H]^+$ 196.0762, found 196.0767.



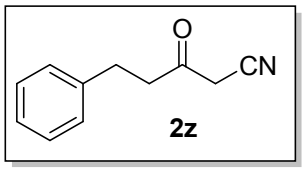
3-(Furan-3-yl)-3-oxopropanenitrile (2v):[1] General procedure **B** was followed on a 10.0 mmol

scale. The product **2v** was obtained as a yellow solid (0.6 g, 39%). Mp: 71~72 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.61–7.41 (m, 1H), 6.81 (d, J = 2.5 Hz, 1H), 4.00–3.73 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.3, 148.3, 148.2, 145.0, 125.6, 113.6, 108.5, 30.3. HRMS (ESI) calcd for $C_7H_5NNaO_2$ $[M+Na]^+$ 158.0218, found 158.0220.



2w

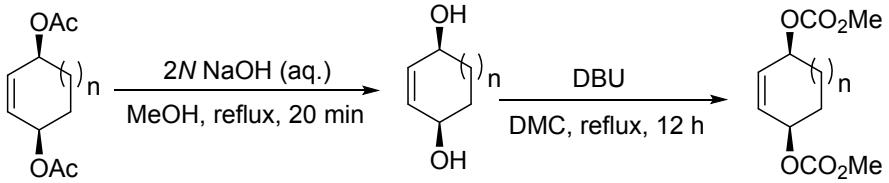
3-Oxo-3-(thiophen-3-yl)propanenitrile (2w):[1] General procedure **B** was followed on a 10.0 mmol scale. The product **2w** was obtained as a yellow solid (0.8 g, 53%). Mp: 82~83 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28–8.08 (m, 1H), 7.67–7.52 (m, 1H), 7.42 (q, J = 5.1, 2.8 Hz, 1H), 4.03 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.1, 139.2, 134.1, 127.6, 126.8, 113.9, 30.2. HRMS (ESI) calcd for C_7H_6NOS $[M+Na]^+$ 152.0170, found 152.0168.



2z

3-Oxo-5-phenylpentanenitrile (2z):[10] General procedure **A** was followed on a 10.0 mmol scale. The product **2z** was obtained as a yellow solid (0.8 g, 47%). Mp: 231~232 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, J = 7.5 Hz, 2H), 7.25 (d, J = 7.0 Hz, 1H), 7.22 (t, J = 7.0 Hz, 2H), 3.43 (s, 2H), 3.01–2.89 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.0, 196.9, 139.7, 128.7, 128.3, 126.6, 113.8, 113.7, 43.6, 32.2, 29.4. HRMS (ESI) calcd for $C_{11}H_{12}NO$ $[M+Na]^+$ 174.0919, found 174.0920.

3. General Procedure for the Preparation of Allyl Biscarbonates



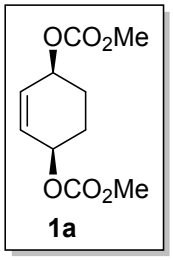
n = 0 (cis-1,4-Diacetoxy-2-cyclopentene) **1b:** n = 0

n = 1 (cis-1,4-Diacetoxy-2-cyclohexene) **1a:** n = 1

n = 2 (cis-1,4-Diacetoxy-2-cycloheptene) **1c:** n = 2

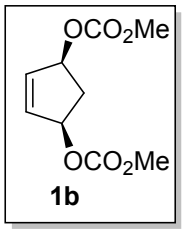
A representative procedure for the hydrolysis of these acetylated compounds to **1** was as follows: To a solution of a mixture of allylic bisacetates[11] (10 mmol) in methanol (50 mL), 2N NaOH aq. (12 mL) was added. The mixture was stirred at reflux for 30 min. After cooling to r.t., the MeOH was removed under reduced pressure and extracted with ethyl acetate six times. The combined organic layer was dried over Na_2SO_4, filtered and concentrated to give the crude product, which was

used in the next step without further purification. The mixture of the crude allylic bisalcohols and DBU (10 mmol) in dimethyl carbonate (20 mL) was stirred under reflux for 12 h. The mixture was evaporated in vacuo to remove dimethyl carbonate. The residue was purified by flash silica gel column chromatography (PE/EA = 10/1) to give **1**.



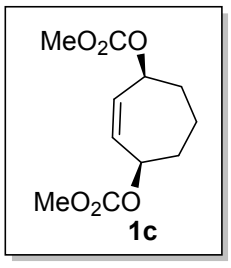
1a

***cis*-1,4-Dimethylcarbonate-2-cyclohexene (1a)**: General procedure was followed on a 10.0 mmol scale. The product **1a** was obtained as a colorless oil (1.0 g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (s, 2H), 5.10 (d, J = 1.2 Hz, 2H), 3.79 (s, 6H), 2.03–1.89 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 130.0, 70.9, 54.7, 24.6. IR (KBr) (v/cm^{-1}): 2959, 1343, 1314, 1053, 939, 916, 758. HRMS (ESI) calcd for $C_{10}H_{14}NaO_6$ $[M+Na]^+$ 253.0683, found 253.0691.



1b

***cis*-1,4-Dimethylcarbonate-2-cyclopentene (1b)**: General procedure was followed on a 10.0 mmol scale. The product **1b** was obtained as a colorless oil (0.4 g, 19%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.14 (d, J = 0.8 Hz, 2H), 5.51–5.39 (m, 2H), 3.89–3.68 (m, 6H), 3.00–2.82 (m, 1H), 1.99–1.82 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 134.5, 79.7, 54.7, 36.8. IR (KBr) (v/cm^{-1}): 2959, 1746, 1338, 1255, 792. HRMS (ESI) calcd for $C_9H_{12}NaO_6$ $[M+Na]^+$ 239.0526, found 239.0531.



1c

***cis*-1,4-Dimethylcarbonate-2-cycloheptene (1c)**: General procedure was followed on a 10.0 mmol scale. The product **1c** was obtained as a white solid (0.6 g, 25%). Mp: 89~90 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (s, 2H), 5.26–5.21 (m, 2H), 3.80 (s, 6H), 2.09–2.03 (m, 1H), 2.01–1.95 (m, 2H), 1.86–1.76 (m, 1H), 1.69–1.64 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 132.0, 77.5,

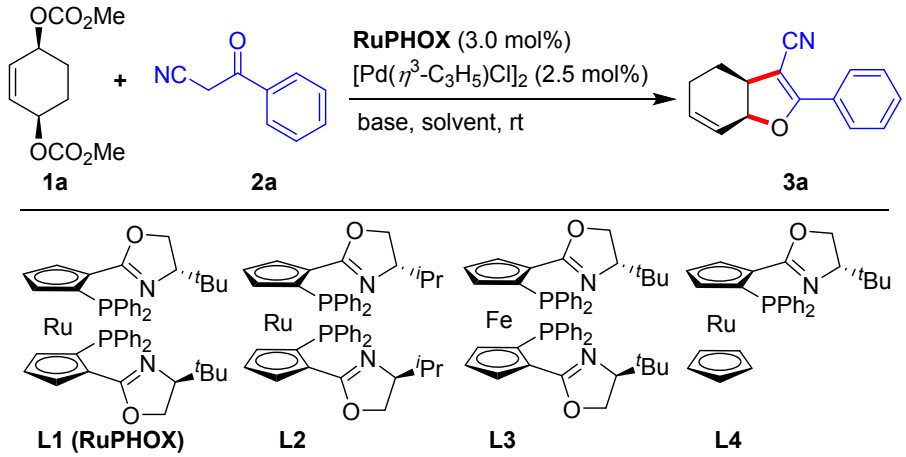
54.8, 32.2, 22.8. IR (KBr) (v/cm^{-1}): 2956, 1747, 1631, 1443, 1328, 973. HRMS (ESI) calcd for $C_{11}H_{16}NaO_6$ [M+Na]$^+$ 267.0839, found 267.0943.

4. General Procedure for the Pd-Catalyzed Asymmetric Allylic Substitution

4.1 Optimization of the reaction conditions

At the outset, *cis*-cyclohex-2-ene-1,4-diyl dicarbonate (**1a**) and benzoylacetonitrile (**2a**) were chosen as the model substrates to investigate the reaction conditions. In the presence of 2.5 mol% $[Pd(C_3H_5)Cl]_2$, 3.0 mol% of **L1**, and 2.0 equiv of DBU,[11h] the reaction of **1a** and **2a** in dioxane for 24 h gave chiral bicyclic dihydrofuran **3a** in 71% yield and 93% ee (Table 1, entry 1). Encouraged by these results, further optimization of the reaction conditions was carried out. When the leaving group of **2a** was re-placed by an Ac substituent, the reaction proceeded but with a decline in both yield and enantioselectivity (entry 2). Next, the effect of different solvents on the reaction was investigated, and dioxane was found to be the solvent of choice (entry 1 and entries 3−7). Surprisingly, when the loading of DBU was lowered to 1.0 equiv, the yield of **3a** further increased (85% isolated yield, entry 8) and was accompanied by a slight increase in ee (94% ee). Notably, the reaction also occurred with a slightly increased yield and ee in the absence of base (entry 9). Careful investigations of a variety of metallocene-based planar chiral ligands (**L1~4**) were finally carried out. It was shown that ^{t}Bu-**RuPHOX** (**L1**) was the most efficient ligand for this reaction, which afforded **3a** in 87% yield and with 95% ee (entries 9−12). According to observations in the optimization studies, the best reaction conditions were identified as the following: reaction of **1a** and **2a** in dioxane with 2.5 mol% of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$, 3.0 mol% of **RuPHOX** at rt for 24 h.

Table S1. Optimization of the Reaction Conditions.[a]

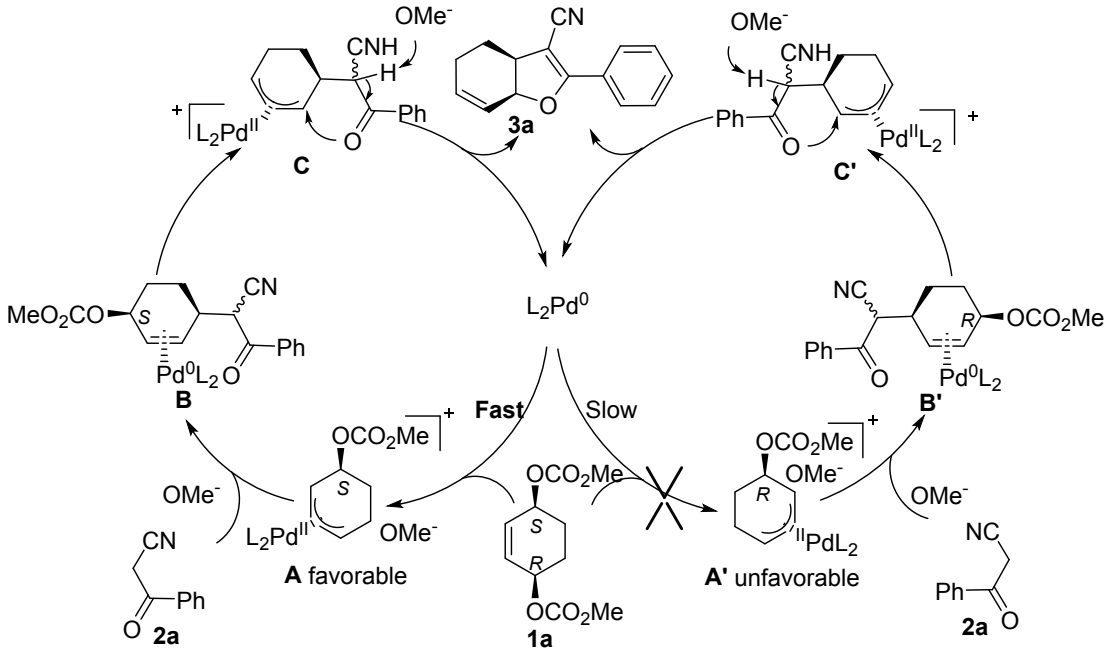


Entry	L*	base	solvent	yield (%)[b]	ee[c]
1	**L1**	DBU	dioxane	71	93
2[d]	**L1**	DBU	dioxane	56	90
3	**L1**	DBU	THF	49	95

4	**L1**	DBU	DCE	63	89
5	**L1**	DBU	CH_2Cl_2	54	92
6	**L1**	DBU	toluene	trace	--
7	**L1**	DBU	MeCN	trace	--
8[e]	**L1**	DBU	dioxane	85	94
9[f]	**L1**	--	dioxane	87	95
10	**L2**	--	dioxane	72	78
11	**L3**	--	dioxane	83	92
12	**L4**	--	dioxane	87	79

[a]Reaction conditions: **1a** (0.24 mmol), **2a** (0.2 mmol), $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (2.5 mol%), ligand (3.0 or 6.0 mol%), DBU (2.0 equiv) in dioxane (2 mL) at rt for 24 h. [b]Isolated yield; All of the reactions afforded >20:1 dr. [c]Determined by chiral HPLC analysis using OD-H chiral column. The absolute configuration of **3a** was determined according to X-ray analysis of **3f** and is shown in Supporting Information.[14] [d]Ac instead of CO_2Me [e]DBU (1.0 equiv). [f]Without a base.

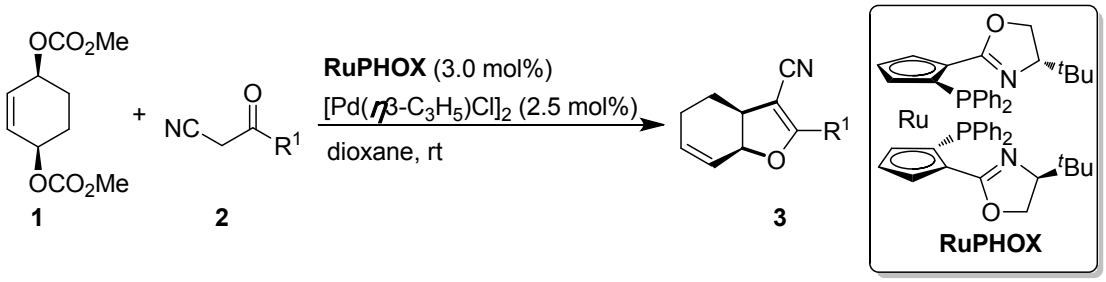
Scheme S1. Proposed Reaction Mechanism[12]



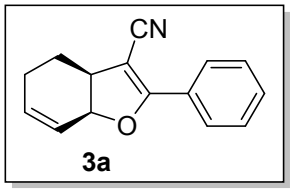
Scheme S1. Proposed Reaction Mechanism

A plausible catalytic cycle for the formation of chiral bicyclic dihydrofuran **3a** is depicted in Scheme S1. Obviously, **3a** is constructed via an allylic alkylation followed by an intramolecular *O*-allylic alkylation. First, combination of *cis*-**1a** with L_2Pd^0 provide allyl-Pd complex **A**. The process represents an asymmetric desymmetrization of *cis*-**1a** because L_2Pd^0 prefers to attack the *R*-chiral carbon of **1a** in the presence of a chiral catalyst. Complex **A** then reacts with nucleophile **2a** to give alkylated intermediate **B**. Finally, **B** takes part in the next intramolecular *O*-allylic alkylation, giving the chiral bicyclic dihydrofuran **3a** in high yield as well as excellent dr via allyl-Pd complex **C**.

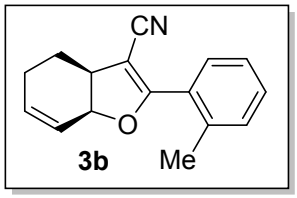
4.2 General procedure for the Pd-catalyzed asymmetric allylic substitution



General procedure: A flame-dried Schlenk tube equipped with a magnetic stirring bar, was charged with a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (1.83 mg, 2.5 mol%) and **L1** (5.1 mg, 3.0 mol%). After being evacuated and backfilled with nitrogen three times, 1,4-dioxane (2 mL) was added to the Schlenk tube and the mixture was stirred at room temperature under a N_2 atmosphere for 1 h. Allylic biscarbonate **1** (0.24 mmol, 1.2 equiv) was added via a syringe followed by addition of benzoyl acetonitrile **2** (0.2 mmol) under a N_2 atmosphere. The reaction mixture was allowed to stir under a N_2 atmosphere at room temperature for 24 h. 1,4-dioxane was evaporated in vacuo and the residue was purified by flash silica gel column chromatography (PE/EA = 20/1) to give product **3**.

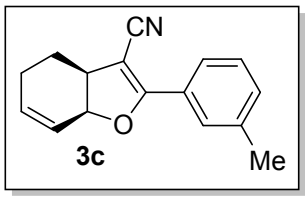


(*3aS,7aS*)-2-Phenyl-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3a): Colorless oil (39.0 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02–7.90 (m, 2H), 7.56–7.40 (m, 3H), 6.30–6.13 (m, 1H), 5.94 (ddt, J = 10.1, 3.6, 1.9 Hz, 1H), 5.15–5.06 (m, 1H), 3.40 (td, J = 8.9, 4.6 Hz, 1H), 2.33–2.19 (m, 1H), 2.01 (dddt, J = 8.1, 6.8, 5.5, 3.4 Hz, 2H), 1.80–1.65 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 134.6, 131.3, 128.6, 128.4, 127.1, 122.9, 117.7, 84.7, 78.7, 42.0, 29.7, 23.9, 22.0. IR (KBr) (v/cm^{-1}): 2932, 2199, 1578, 1221, 1048, 917, 700. HRMS (ESI) calcd for $C_{15}H_{14}NO$ $[M+H]^+$ 224.1075, found 224.1077.HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 0.8 mL/min) t_{R1} = 8.766 min (minor) and t_{R2} = 9.493 min (major), ee = 95%. $[\alpha]_D^{25}$ = –98.7 (*c* 0.4, $CHCl_3$).



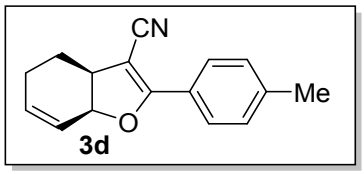
(*3aS,7aS*)-2-(*o*-Tolyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3b): Colorless oil (42.4 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56–7.49 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.29–7.24

(m, 2H), 6.28–6.21 (m, 1H), 5.93–5.90 (m, 1H), 5.21–5.11 (m, 1H), 3.42 (td, J = 8.5, 4.5 Hz, 1H), 2.42 (s, 3H), 2.32–2.21 (m, 1H), 2.10–1.94 (m, 2H), 1.81–1.69 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 137.2, 134.5, 130.9, 130.7, 129.2, 128.1, 125.8, 123.0, 116.8, 88.5, 79.6, 41.3, 24.0, 21.9, 20.1. IR (KBr) (v/cm^{-1}): 2922, 2360, 2204, 1631, 1582, 1345, 792, 723. HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 238.1232, found 238.1234. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 16.481 min (minor) and t_{R2} = 22.916 min (major), ee = 93%. $[\alpha]_D^{25}$ = –101.8 (*c* 0.20, $CHCl_3$).



3c

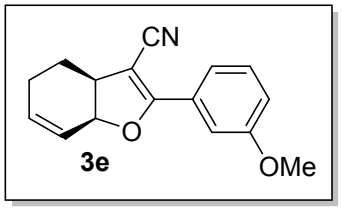
(*3aS,7aS*)-2-(*m*-Tolyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3c): Colorless oil (43.5 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88–7.68 (m, 2H), 7.41–7.22 (m, 2H), 6.33–6.17 (m, 1H), 5.95–5.92 (m, 1H), 5.15–5.01 (m, 1H), 3.39 (td, J = 8.5, 5.0 Hz, 1H), 2.41 (s, 3H), 2.30–2.16 (m, 1H), 2.06–1.96 (m, 2H), 1.72–1.65 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 138.4, 134.5, 132.1, 128.5, 128.3, 127.5, 124.3, 122.9, 117.7, 84.5, 78.6, 41.9, 23.9, 22.0, 21.4. IR (KBr) (v/cm^{-1}): 2922, 2793, 2359, 2199, 1194, 918, 794, 699. HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 238.1232, found 238.1234. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 10.964 min (minor) and t_{R2} = 13.685 min (major), ee = 97%. $[\alpha]_D^{25}$ = –150.7 (*c* 0.22, $CHCl_3$).



3d

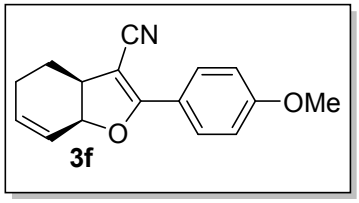
(*3aS,7aS*)-2-(*p*-Tolyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3d): Colorless oil (44.8 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.92 (m, 2H), 6.97–6.93 (m, 2H), 6.27–6.16 (m, 1H), 5.93 (ddt, J = 10.1, 3.6, 1.9 Hz, 1H), 5.07–5.05 (m, 1H), 3.87 (s, 3H), 3.37 (td, J = 8.9, 4.6 Hz, 1H), 2.29–2.20 (m, 1H), 2.06–1.93 (m, 2H), 1.72–1.61 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 141.8, 134.5, 129.3, 127.1, 125.6, 122.9, 117.9, 83.8, 78.6, 41.9, 31.4, 29.7, 23.9, 22.0, 21.6. IR (KBr) (v/cm^{-1}): 2920, 2846, 2341, 1495, 1020, 767, 690, 609. HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 238.1232, found 238.1235. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 10.964 min (minor) and t_{R2} = 13.685 min (major), ee = 96%.

$[\alpha]_D^{25}$ = –79.2 (*c* 0.30, $CHCl_3$).



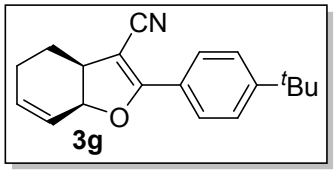
3e

(*3aS,7aS*)-2-(3-Methoxyphenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3e): Colorless oil (46.4 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 1H), 7.51–7.44 (m, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.05–6.99 (m, 1H), 6.24–6.20 (m, 1H), 5.93 (ddd, J = 10.0, 3.5, 2.0 Hz, 1H), 5.09 (dd, J = 9.0, 2.0 Hz, 1H), 3.86 (s, 3H), 3.39 (td, J = 9.0, 4.5 Hz, 1H), 2.30–2.18 (m, 1H), 2.09–1.93 (m, 2H), 1.72–1.65 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7, 159.6, 134.5, 129.6, 129.5, 122.9, 119.5, 117.8, 117.6, 111.6, 84.9, 78.7, 55.4, 41.9, 23.8, 22.0. IR (KBr) (v/cm^{-1}): 3854, 3036, 1593, 1462, 1187, 987, 875, 730. HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 254.1181, found 254.1187. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 94/6, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 14.148 min (minor) and t_{R2} = 15.523 min (major), ee = 96%. $[\alpha]_D^{25}$ = –132.8 (*c* 0.26, $CHCl_3$).



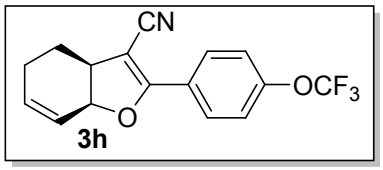
3f

(*3aS,7aS*)-2-(4-Methoxyphenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3f): White solid (44.0 mg, 88%). Mp: 85–86 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95–7.92 (m, 2H), 7.02–6.93 (m, 2H), 6.24–6.20 (m, 1H), 5.93 (ddt, J = 10.1, 3.6, 1.9 Hz, 1H), 5.07–5.05 (m, 1H), 3.87 (s, 3H), 3.37 (td, J = 8.8, 4.4 Hz, 1H), 2.29–2.20 (m, 1H), 2.05–1.99 (m, 2H), 1.72–1.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 161.9, 134.5, 128.9, 123.0, 121.0, 118.2, 113.9, 82.5, 78.5, 55.4, 41.8, 24.0, 22.1. IR (KBr) (v/cm^{-1}): 3800, 2966, 1593, 1460, 1185, 976, 855, 732. HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 254.1181, found 254.1182. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 17.617 min (minor) and t_{R2} = 26.526 min (major), ee = 96%. $[\alpha]_D^{25}$ = –150.6 (*c* 1.00, $CHCl_3$).



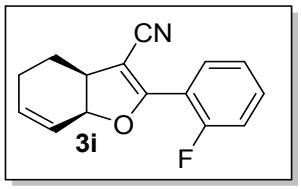
3g

(*3aS,7aS*)-2-(4-(Tert-butyl)phenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3g): Colorless oil (50.4 mg, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 8.5 Hz, 2H), 7.47 (d, J = 8.5 Hz, 2H), 6.23–6.20 (m, 1H), 5.94–5.91 (m, 1H), 5.08 (d, J = 8.5 Hz, 1H), 3.39 (td, J = 8.5, 4.5 Hz, 1H), 2.32–2.16 (m, 1H), 2.10–1.93 (m, 2H), 1.77–1.64 (m, 1H), 1.35 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 154.9, 134.4, 126.9, 125.6, 125.5, 123.0, 117.8, 83.9, 78.6, 41.8, 35.0, 31.1, 23.9, 21.9. IR (KBr) (v/cm^{-1}): 2960, 21198, 1922, 1457, 1363, 1119, 918, 776. HRMS (ESI) calcd for $C_{19}H_{22}NO$ $[M+H]^+$ 280.1701, found 280.1704. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 9.500 min (minor) and t_{R2} = 10.274 min (major), ee = 96%. [α] $^{25}_{D}$ = –129.2 (*c* 0.36, $CHCl_3$).



3h

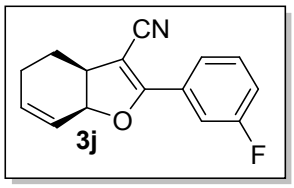
(*3aS,7aS*)-2-(4-(Trifluoro(oxo)-l6-methyl)phenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3h): Colorless oil (56.0 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12–7.93 (m, 2H), 7.40–7.20 (m, 2H), 6.31–6.11 (m, 1H), 5.92 (ddt, J = 10.0, 3.6, 2.0 Hz, 1H), 5.22–5.01 (m, 1H), 3.42 (td, J = 9.2, 4.8 Hz, 1H), 2.37–2.19 (m, 1H), 2.15–1.93 (m, 2H), 1.74–1.66 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.3, 151.0 (d, J = 7.2 Hz), 134.7, 128.9, 126.8, 122.7, 12.7, 120.3 (q, J = 205.5 Hz), 117.2, 85.4, 78.9, 41.9, 23.8, 21.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ –57.6. IR (KBr) (v/cm^{-1}): 2931, 2360, 2201, 1618, 1508, 1212, 1169, 917, 856, 662. HRMS (ESI) calcd for $C_{16}H_{13}F_3NO_2$ $[M+H]^+$ 308.0898, found 308.0898. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 8.213 min (minor) and t_{R2} = 8.679 min (major), ee = 97%. [α] $^{25}_{D}$ = –109.5 (*c* 0.12, $CHCl_3$).



3i

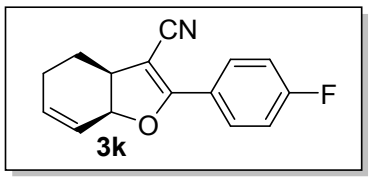
(*3aS,7aS*)-2-(2-Fluorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3i): White solid (43.0 mg, 85%). Mp: 88–89 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (td, J = 7.6, 2.0 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.24–7.15 (m, 2H), 6.27–6.23 (m, 1H), 5.95–5.91 (m, 1H), 5.20–5.07 (m, 1H), 3.43 (td, J = 8.8, 4.4 Hz, 1H), 2.32–2.23 (m, 1H), 2.09–1.96 (m, 2H), 1.77–1.68 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J = 2.6 Hz), 161.1, 158.6, 134.7, 132.8 (d, J = 8.6 Hz), 129.7 (d, J = 2.2 Hz), 124.2 (d, J = 3.7 Hz), 122.7, 116.7 (dd, J = 39.1, 21.5 Hz), 116.1 (d, J = 1.3 Hz), 89.4 (d, J = 2.2 Hz), 79.2, 41.9, 23.8, 21.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ –107.4. IR (KBr) (v/cm^{-1}): 2920,

2207, 1489, 1268, 914, 738. HRMS (ESI) calcd for $C_{15}H_{13}FNO$ $[M+H]^+$ 242.0981, found 242.0980. HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 10.601 min (minor) and t_{R2} = 11.731 min (major), ee = 94%. [α] $^{25}_{D}$ = –163.4 (*c* 0.11, $CHCl_3$).



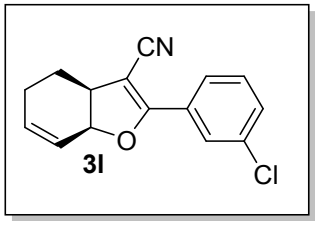
3j

(*3aS,7aS*)-2-(3-Fluorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3j): Colorless oil (40.0 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.0 Hz, 1H), 7.63–7.60 (m, 1H), 7.43 (td, J = 8.0, 6.0 Hz, 1H), 7.18 (td, J = 8.4, 2.4 Hz, 1H), 6.26–6.22 (m, 1H), 5.95–5.91 (m, 1H), 5.13–5.10 (m, 1H), 3.42 (td, J = 9.2, 4.8 Hz, 1H), 2.30–2.22 (m, 1H), 2.07–1.97 (m, 2H), 1.74–1.65 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4 (d, J = 1.9 Hz), 163.5, 161.5, 134.7, 130.3 (d, J = 8.1 Hz), 122.9 (d, J = 2.3 Hz), 122.7, 118.2 (d, J = 16.8 Hz), 117.1, 114.0 (d, J = 19.0 Hz), 85.9, 78.8, 42.0, 23.8, 21.9. **^{19}F NMR** (376 MHz, $CDCl_3$): δ –111.6. IR (KBr) (v/cm^{-1}): 2848, 2341, 1949, 1447, 1020, 936, 603. HRMS (ESI) calcd for $C_{15}H_{13}FNO$ $[M+H]^+$ 242.0981, found 242.0986. HPLC (Daicel Chiralcel IC-3, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 0.8 mL/min) t_{R1} = 21.611 min (minor) and t_{R2} = 22.905 min (major), ee = 94%. [α] $^{25}_{D}$ = –163.4 (*c* 0.29, $CHCl_3$).

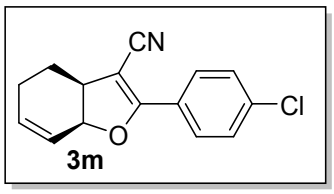


3k

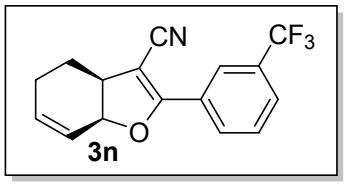
(*3aS,7aS*)-2-(4-Fluorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3k): Colorless oil (46.3 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00–7.96 (m, 2H), 7.16–7.10 (m, J = 2H), 6.24–6.21 (m, 1H), 5.94–5.90 (m, 1H), 5.10–5.08 (m, 1H), 3.40 (td, J = 8.9, 4.6 Hz, 1H), 2.30–2.21 (m, 1H), 2.07–1.95 (m, 2H), 1.73–1.64 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8, 165.2, 163.2, 134.6, 129.4 (d, J = 8.8 Hz), 124.6 (d, J = 3.3 Hz), 122.8, 117.59, 115.88, 115.7, 84.4 (d, J = 1.5 Hz), 78.80, 41.9, 23.8, 21.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ –107.0. IR (KBr) (v/cm^{-1}): 2929, 2200, 1594, 1361, 957, 743. HRMS (ESI) calcd for $C_{15}H_{13}FNO$ $[M+H]^+$ 242.0981, found 242.0984. HPLC (Daicel Chiralcel IC-3, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 0.8 mL/min) t_{R1} = 18.201 min (minor) and t_{R2} = 19.316 min (major), ee = 96%. [α] $^{25}_{D}$ = –164.7 (*c* 0.28, $CHCl_3$).



(*3aS,7aS*)-2-(3-Chlorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3l): Colorless oil (42.0 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (dd, J = 8.0, 1.0 Hz, 1H), 7.88 (d, J = 2.0 Hz, 1H), 7.45 (dd, J = 8.0, 1.0 Hz, 1H), 7.41–7.37 (m, 1H), 6.25–6.22 (m, 1H), 5.94–5.91 (m, 1H), 5.11 (d, J = 9.0 Hz, 1H), 3.41 (td, J = 9.0, 4.0 Hz, 1H), 2.26–2.22 (m, 1H), 2.10–1.93 (m, 2H), 1.72–1.65 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 134.8, 134.7, 131.2, 130.0, 129.9, 127.0, 125.2, 122.7, 117.0, 85.9, 78.8, 42.0, 23.8, 21.9. IR (KBr) (v/cm^{-1}): 3448, 2930, 2201, 1616, 1430, 1145, 917, 813, 704, 626. HRMS (ESI) calcd for $C_{15}H_{13}ClNO$ $[M+H]^+$ 258.0686, found 258.0687. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 11.685 min (minor) and t_{R2} = 14.326 min (major), ee = 96%. $[\alpha]_D^{25}$ = –119.8 (*c* 0.16, $CHCl_3$).

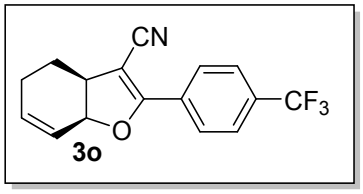


(*3aS,7aS*)-2-(4-Chlorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3m): Colorless oil (50.0 mg, 97%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dt, J = 8.4, 2.4 Hz,, 2H), 7.91 (dt, J = 8.4, 2.4 Hz,, 2H), 6.54–6.21 (m, 1H), 5.89–5.94 (m, 1H), 5.11–5.09 (m, 1H), 3.40 (td, J = 9.2, 4.8 Hz, 1H), 2.37–2.15 (m, 1H), 2.07–1.95 (m, 2H), 1.73–1.62 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 137.3, 134.7, 128.9, 128.4, 126.8, 122.8, 117.4, 85.2, 78.8, 41.9, 23.8, 21.9. IR (KBr) (v/cm^{-1}): 3035, 2359, 1633, 1552, 1343, 996, 794, 625. HRMS (ESI) calcd for $C_{15}H_{13}ClNO$ $[M+H]^+$ 258.0686, found 258.0688. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 10.700 min (minor) and t_{R2} = 11.514 min (major), ee = 97%. $[\alpha]_D^{25}$ = –149.0 (*c* 0.26, $CHCl_3$).

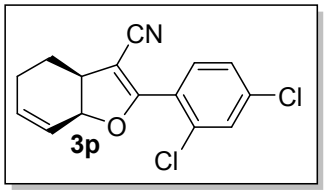


(*3aS,7aS*)-2-(3-(Trifluoromethyl)phenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3n): Colorless oil (50.4 mg, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 7.5 Hz, 1H), 8.14 (s, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.60 (t, J = 8.0 Hz, 1H), 6.27–6.24 (m, 1H), 5.96–5.94 (m, 1H),

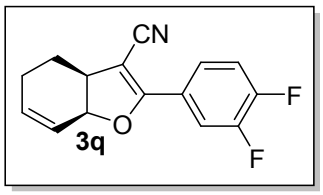
5.14 (d, J = 9.0 Hz, 1H), 3.44 (td, J = 9.0, 5.0 Hz, 1H), 2.33–2.21 (m, 1H), 2.10–1.96 (m, 2H), 1.74–1.66 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.07, 134.8, 131.2 (q, J = 32.6 Hz), 130.24, 129.2 (d, J = 13.2 Hz), 127.7 (q, J = 3.6 Hz), 124.7, 123.87 (q, J = 3.9 Hz), 123.6 (d, J = 270.8 Hz), 116.9, 86.4, 79.0, 42.0, 23.7, 21.9. ^{19}F NMR (471 MHz, $CDCl_3$): δ –65.0. IR (KBr) (v/cm^{-1}): 2933, 1923, 1436, 1367, 1324, 1179, 916, 695. HRMS (ESI) calcd for $C_{16}H_{13}F_3NO$ $[M+H]^+$ 292.0949, found 292.0948. HPLC (Daicel Chiralcel IC-3, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 11.770 min (minor) and t_{R2} = 12.678 min (major), ee = 95%. $[\alpha]_D^{25}$ = –140.6 (*c* 0.20, $CHCl_3$).



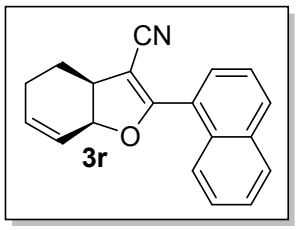
(*3aS,7aS*)-2-(4-(Trifluoromethyl)phenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3o)： Colorless oil (48.5 mg, 83%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, J = 8.5 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 6.30–6.19 (m, 1H), 6.01–5.87 (m, 1H), 5.14 (d, J = 9.0 Hz, 1H), 3.44 (td, J = 9.0, 4.5 Hz, 1H), 2.28–2.23 (m, 1H), 2.08–2.04 (m, 2H), 1.74–1.70 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 134.8 (dd, J = 32.5 Hz), 131.6, 127.4, 125.6 (q, J = 3.8 Hz), 123.6 (d, J = 274.7 Hz), 122.5, 116.9, 86.9, 79.0, 42.0, 23.7, 21.9. ^{19}F NMR (471 MHz, $CDCl_3$): δ –63.1. IR (KBr) (v/cm^{-1}): 2933, 2202, 1991, 1324, 1128, 916, 668. HRMS (ESI) calcd for $C_{16}H_{13}F_3NO$ $[M+H]$+ 292.0949, found 292.0953. HPLC (Daicel Chiralcel IC-3, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 0.8 mL/min) t_{R1} = 15.512 min (minor) and t_{R2} = 16.629 min (major), ee = 96%. $[\alpha]_D^{25}$ = –136.7 (*c* 0.26, $CHCl_3$).



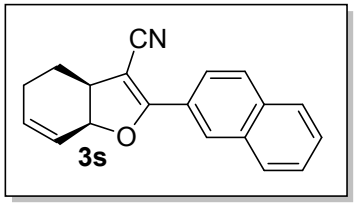
(*3aS,7aS*)-2-(2,4-Dichlorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3p): Colorless oil (48 mg, 82%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J = 2.0 Hz, 1H), 7.47 (d, J = 8.5 Hz, 1H), 7.33 (dd, J = 8.0, 2.0 Hz, 1H), 6.28–6.24 (m, 1H), 5.92 (ddt, J = 10.0, 3.5, 2.0 Hz, 1H), 5.17 (dd, J = 8.5, 2.6 Hz, 1H), 3.46–3.37 (m, 1H), 2.33–2.22 (m, 1H), 2.11–1.95 (m, 2H), 1.79–1.67 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 137.4, 134.8, 134.0, 131.5, 130.4, 127.2, 126.5, 122.6, 115.7, 91.0, 80.1, 41.6, 23.9, 21.9. IR (KBr) (v/cm^{-1}): 2929, 2208, 1633, 1473, 1120, 931, 794. HRMS (ESI) calcd for $C_{15}H_{12}Cl_2NO$ $[M+H]^+$ 292.0296, found 292.0300. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 15.190 min (minor) and t_{R2} = 21.269 min (major), ee = 93%. $[\alpha]_D^{25}$ = –92.1 (*c* 0.26, $CHCl_3$).



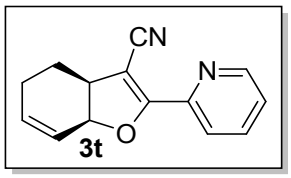
(*3aS,7aS*)-2-(3,4-Difluorophenyl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3q): Colorless oil (48.0 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85–7.70 (m, 2H), 7.31–7.19 (m, 1H), 6.29–6.20 (m, 1H), 5.96–5.87 (m, 1H), 5.15–5.07 (m, 1H), 3.41 (td, J = 9.0, 5.0 Hz, 1H), 2.31–2.18 (m, 1H), 2.10–1.95 (m, 2H), 1.74–1.65 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4, 151.9 (dd, J = 229.9, 12.9 Hz), 150.0 (dd, J = 211.6, 12.9 Hz), 134.8, 125.3 (dd, J = 6.5, 3.9 Hz), 123.9 (dd, J = 6.9, 3.8 Hz), 122.6, 117. (d, J = 17.8 Hz), 117.0, 116.4 (d, J = 19.3 Hz), 85.6 (d, J = 1.7 Hz), 78.9, 42.03, 23.78, 21.93. ^{19}F NMR (471 MHz, $CDCl_3$): δ –131.9 (d, J = 16.9 Hz), –135.9 (d, J = 16.9 Hz). IR (KBr) (v/cm^{-1}): 2926, 2360, 2202, 1619, 1519, 1192, 916, 734. HRMS (ESI) calcd for $C_{15}H_{12}F_2NO$ $[M+H]^+$ 260.0887, found 260.0890. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 10.643 min (minor) and t_{R2} = 13.684 min (major), ee = 96%. [α] $^{25}_{D}$ = –163.2 (*c* 0.23, $CHCl_3$).



(*3aS,7aS*)-2-(Naphthalen-1-yl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3r): Colorless oil (48.6 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 8.5 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.82 (d, J = 7.0 Hz, 1H), 7.66–7.50 (m, 3H), 6.36–6.26 (m, 1H), 6.06–5.99 (m, 1H), 5.30 (d, J = 9.0 Hz, 1H), 3.52 (td, J = 9.0, 5.0 Hz, 1H), 2.38–2.25 (m, 1H), 2.15–1.98 (m, 2H), 1.89–1.77 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 134.8, 133.6, 131.6, 130.5, 128.5, 128.2, 127.0, 126.4, 125.9, 125.2, 124.9, 123.0, 116.7, 89.5, 80.0, 41.4, 24.1, 21.9. IR (KBr) (v/cm^{-1}): 3420, 29224, 2203, 1507, 1386, 1349, 739. HRMS (ESI) calcd for $C_{19}H_{16}NO$ $[M+H]^+$ 274.1232, found 274.1236. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 94/6, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 24.591 min (minor) and t_{R2} = 32.434 min (major), ee = 96%. [α] $^{25}_{D}$ = –56.4 (*c* 0.13, $CHCl_3$).

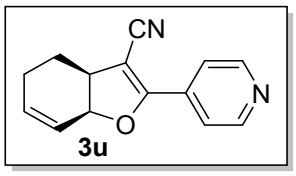


(*3aS,7aS*)-2-(Naphthalen-2-yl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3s): Colorless oil (51.8 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.10 (dd, J = 8.7, 1.8 Hz, 1H), 7.94–7.85 (m, 3H), 7.64–7.48 (m, 2H), 6.27–6.23 (m, 1H), 5.99 (ddt, J = 12.5, 4.5, 2.5 Hz, 1H), 5.20–5.10 (m, 1H), 3.44 (td, J = 8.9, 4.7 Hz, 1H), 2.34–2.20 (m, 1H), 2.12–1.96 (m, 2H), 1.81–1.69 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 134.6, 134.4, 132.6, 129.0, 128.3, 127.8, 127.7, 126.7, 125.6, 123.4, 122.9, 117.7, 85.1, 78.7, 42.1, 23.9, 22.0. IR (KBr) (v/cm^{-1}): 2929, 2198, 1922, 1435, 1193, 877, 750, 473. HRMS (ESI) calcd for $C_{19}H_{16}NO$ $[M+H]^+$ 274.1232, found 274.1231. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 92/8, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 14.086 min (minor) and t_{R2} = 24.599 min (major), ee = 96%. [α] $^{25}_{D}$ = –78.4 (*c* 0.28, $CHCl_3$).



3t

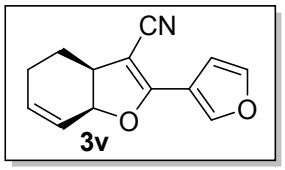
(*3aS,7aS*)-2-(Pyridin-2-yl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3t): Colorless oil (42.0 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80–8.71 (m, 1H), 7.84–7.73 (m, 2H), 7.40–7.32 (m, 1H), 6.30–6.17 (m, 1H), 6.00–5.91 (m, 1H), 5.22–5.13 (m, 1H), 3.43 (td, J = 8.8, 4.4 Hz, 1H), 2.32–2.20 (m, 1H), 2.13–1.93 (m, 2H), 1.80–1.67 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 149.9, 147.2, 136.6, 134.7, 125.2, 122.8, 121.9, 116.9, 88.4, 79.4, 77.3, 77.0, 76.8, 42.0, 31.4, 30.2, 29.7, 23.7, 22.0. IR (KBr) (v/cm^{-1}): 3822, 2036, 2848, 1593, 1382, 1187, 855, 811, 736. HRMS (ESI) calcd for $C_{14}H_{13}N_2O$ $[M+H]^+$ 225.1028, found 225.1021. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 95/5, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 21.803 min (minor) and t_{R2} = 26.914 min (major), ee = 95%. [α] $^{25}_{D}$ = –172.3 (*c* 0.27, $CHCl_3$).



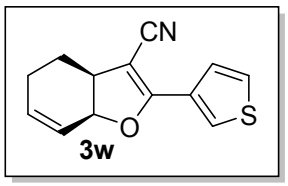
3u

(*3aS,7aS*)-2-(Pyridin-4-yl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3u): Colorless oil (43.5 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (dd, J = 4.8, 1.2 Hz, 2H), 7.79 (dd, J = 4.8, 1.2 Hz, 2H), 6.31–6.17 (m, 1H), 5.98–5.83 (m, 1H), 5.18–5.08 (m, 1H), 3.43 (td, J = 9.2, 4.8 Hz, 1H), 2.36–2.17 (m, 1H), 2.11–1.94 (m, 2H), 1.77–1.58 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1, 150.3, 135.4, 134.9, 122.5, 120.5, 116.4, 88.8, 79.2, 42.1, 23.6, 21.9. IR (KBr) (v/cm^{-1}): 3085, 2359, 1654, 1482, 1159, 853, 744, 489. HRMS (ESI) calcd for $C_{14}H_{13}N_2O$ $[M+H]^+$ 225.1028, found 225.1026. HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 95/5, UV = 254 nm, flow rate = 1.0

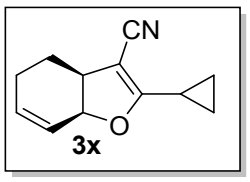
mL/min) t_{R1} = 12.119 min (major) and t_{R2} = 13.792 min (minor), ee = 97%. [α] $^{25}_{D}$ = –199.7 (*c* 0.14, $CHCl_3$).



(*3aS,7aS*)-2-(Furan-3-yl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3v): Colorless oil (44.3 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.48 (t, *J* = 2.0 Hz, 1H), 6.96 (d, *J* = 1.5 Hz, 1H), 6.28–6.17 (m, 1H), 5.90 (ddt, *J* = 10.0, 3.5, 2.0 Hz, 1H), 5.05 (d, *J* = 9.0 Hz, 1H), 3.32 (td, *J* = 9.0, 4.5 Hz, 1H), 2.28–2.14 (m, 1H), 1.99–1.98 (m, 2H), 1.66–1.58 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 143.9, 143.8, 134.6, 122.8, 117.1, 116.0, 108.2, 84.3, 79.1, 41.2, 24.0, 22.0. IR (KBr) (v/cm^{-1}): 2848, 2200, 1646, 1456, 1367, 1170, 914, 873, 599. HRMS (ESI) calcd for $C_{13}H_{11}NNaO_2$ $[M+H]^+$ 236.0687, found 236.0690. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 12.988 min (minor) and t_{R2} = 14.658 min (major), ee = 96%. [α] $^{25}_{D}$ = –116.5 (*c* 0.12, $CHCl_3$).

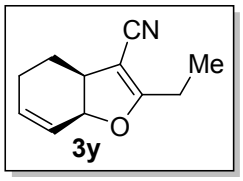


(*3aS,7aS*)-2-(Thiophen-3-yl)-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3w): Yellow oil (41.0 mg, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 3.2, 1.2 Hz, 1H), 7.70 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.38 (dd, *J* = 5.2, 3.2 Hz, 1H), 6.24–6.19 (m, 1H), 5.94–5.90 (m, 1H), 5.08–5.06 (m, 1H), 3.36 (td, *J* = 9.2, 4.8 Hz, 1H), 2.28–2.19 (m, 1H), 2.05–1.95 (m, 2H), 1.70–1.61 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 134.6, 130.2, 128.0, 126.5, 125.9, 122.9, 117.6, 83.7, 78.9, 41.6, 24.0, 22.0. IR (KBr) (v/cm^{-1}): 2926, 2359, 2198, 1617, 915, 792, 689. HRMS (ESI) calcd for $C_{13}H_{12}NOS$ $[M+H]^+$ 230.0640, found 230.0644. HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 9.410 min (minor) and t_{R2} = 10.727 min (major), ee = 96%. [α] $^{25}_{D}$ = –123.8 (*c* 0.35, $CHCl_3$).

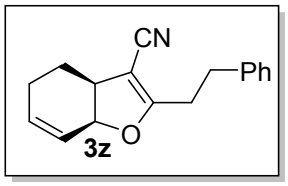


(*3aS,7aS*)-2-Cyclopropyl-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3x): Colorless oil (30.0 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19–6.15 (m, 1H), 5.77 (ddt, *J* = 10.0, 3.6, 2.0 Hz,

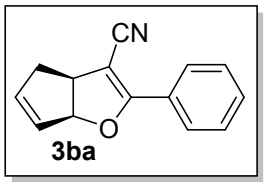
1H), 4.88–4.78 (m, 1H), 3.17 (td, J = 9.2, 4.8 Hz, 1H), 2.27–2.12 (m, 1H), 2.00–1.81 (m, 3H), 1.59–1.45 (m, 1H), 1.05–0.83 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 134.5, 122.9, 117.4, 84.8, 79.1, 40.7, 24.2, 22.0, 9.7, 7.5, 7.1. IR (KBr) (v/cm^{-1}): 3394, 3036, 2848, 2205, 1593, 1219, 913, 811. HRMS (ESI) calcd for $C_{12}H_{14}NO$ $[M+H]^+$ 188.1075, found 188.1078. HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 10.530 min (minor) and t_{R2} = 12.588 min (major), ee = 95%. [α] $^{25}_{D}$ = –185.7 (*c* 0.10, $CHCl_3$).



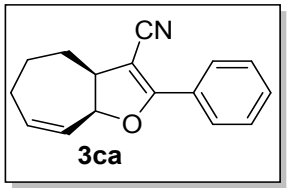
(*3aS,7aS*)-2-Ethyl-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3y): Colorless oil (26.7 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.23–6.16 (m, 1H), 5.85 (ddt, J = 10.0, 3.5, 2.0 Hz, 1H), 4.93 (d, J = 8.9 Hz, 1H), 3.17 (td, J = 9.0, 4.6 Hz, 1H), 2.45–2.35 (m, 2H), 2.24–2.15 (m, 1H), 2.01–1.87 (m, 2H), 1.55–1.44 (m, 1H), 1.18 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 134.4, 122.9, 116.8, 85.8, 79.4, 40.6, 24.3, 22.0, 21.8, 10.8. IR (KBr) (v/cm^{-1}): 3394, 2922, 2205, 1634, 1593, 1026, 987, 738. HRMS (ESI) calcd for $C_{11}H_{14}NO$ $[M+H]^+$ 176.1075, found 176.1078. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 7.529 min (minor) and t_{R2} = 8.431 min (major), ee = 91%. [α] $^{25}_{D}$ = –206.9 (*c* 0.11, $CHCl_3$).



(*3aS,7aS*)-2-Phenethyl-3a,4,5,7a-tetrahydrobenzofuran-3-carbonitrile (3z): Colorless oil (36.0 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.28 (m, 2H), 7.27–7.17 (m, 3H), 6.20–6.17 (m, 1H), 5.85 (ddt, J = 10.0, 3.5, 2.0 Hz, 1H), 4.97–4.89 (m, 1H), 3.15 (td, J = 9.5, 4.5 Hz, 1H), 2.95–2.85 (m, 2H), 2.78–2.64 (m, 2H), 2.14–2.08 (m, 1H), 1.95–1.82 (m, 2H), 1.50–1.38 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.0, 139.7, 134.5, 128.5, 128.4, 126.4, 122.9, 116.5, 87.4, 79.5, 40.6, 32.3, 29.9, 24.1, 21.9. IR (KBr) (v/cm^{-1}): 3394, 3029, 2927, 1603, 1246, 912, 699. HRMS (ESI) calcd for $C_{17}H_{18}NO$ $[M+H]^+$ 252.1388, found 252.1387. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 0.8 mL/min) t_{R1} = 23.391 min (major) and t_{R2} = 25.118 min (minor), ee = 91%. [α] $^{25}_{D}$ = –106.1 (*c* 0.19, $CHCl_3$).



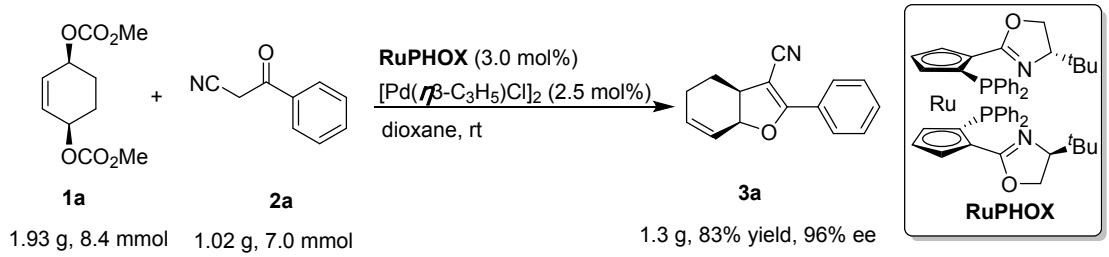
(*3aS,6aS*)-2-Phenyl-4,6a-dihydro-3aH-cyclopenta[*b*]furan-3-carbonitrile (3ba): Colorless oil (36.0 mg, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.0 Hz, 2H), 7.52–7.40 (m, 3H), 6.15 – 6.14 (m, 1H), 5.95–5.84 (m, 2H), 4.01 (t, J = 8.5 Hz, 1H), 2.80 (dd, J = 17.5, 7.5 Hz, 1H), 2.71 (d, J = 17.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.2, 136.0, 131.2, 128.6, 128.2, 127.1, 118.0, 92.6, 84.8, 45.6, 38.6. IR (KBr) (v/cm^{-1}): 3262, 2919, 2848, 2199, 1494, 1353, 690. HRMS (ESI) calcd for $C_{14}H_{12}NO$ $[M+H]^+$ 210.0919, found 210.0922. HPLC (Daicel Chiralcel IC-3, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 16.876 min (minor) and t_{R2} = 18.971 min (major), ee = 71%. $[\alpha]_D^{25}$ = –44.1 (*c* 0.19, $CHCl_3$).



(*3aS,8aS*)-2-Phenyl-4,5,6,8a-tetrahydro-3aH-cyclohepta[*b*]furan-3-carbonitrile (3ca): Colorless oil (44.0 mg, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.96 (m, 2H), 7.52–7.41 (m, 3H), 5.89–5.74 (m, 2H), 5.57 (d, J = 10.0 Hz, 1H), 3.38 (td, J = 10.5, 3.0 Hz, 1H), 2.31–2.11 (m, 2H), 1.97–1.85 (m, 1H), 1.85–1.77 (m, 1H), 1.70–1.62 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.3, 131.2, 129.6, 128.6, 128.0, 127.1, 126.7, 117.7, 85.2, 84.6, 45.9, 26.9, 26.4, 21.3. IR (KBr) (v/cm^{-1}): 3422, 2926, 2360, 2202, 1701, 1448, 1075, 691. HRMS (ESI) calcd for $C_{16}H_{16}NO$ $[M+H]^+$ 238.1232, found 238.1230. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 99/1, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 7.561 min (minor) and t_{R2} = 9.307 min (major), ee = 79%. $[\alpha]_D^{25}$ = –26.8 (*c* 0.19, $CHCl_3$).

5. Transformations

5.1 Procedure for the gram-scale synthesis of 3a



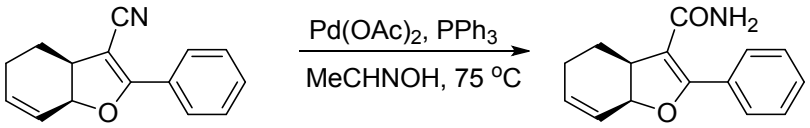
1a 1.93 g, 8.4 mmol

2a 1.02 g, 7.0 mmol

3a 1.3 g, 83% yield, 96% ee

A flame-dried Schlenk tube equipped with a magnetic stirring bar, was charged with a mixture of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (64.1 mg, 2.5 mol%) and **L1** (178.5 mg, 3.0 mol%). After being evacuated and backfilled with nitrogen three times, 1,4-dioxane (20 mL) was added to the Schlenk tube and the mixture was stirred at room temperature under a N_2 atmosphere for 1 h. Allylic biscarbonates **1a** (8.4 mmol, 1.2 equiv) was added via a syringe followed by addition of benzoyl acetonitrile **2a** (7.0 mmol) under a N_2 atmosphere. The reaction mixture was allowed to stir under a N_2 atmosphere at room temperature for 24 h. 1,4-dioxane was evaporated in vacuo and the residue was purified by flash silica gel column chromatography (PE/EA = 20/1) to give product **3a**.

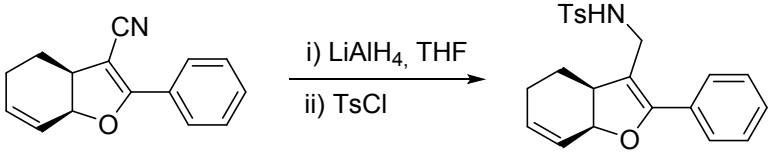
5.2 Procedure for synthesis of 4 and characterization data[13]



3a **4**

(*3aS,7aS*)-2-phenyl-3a,4,5,7a-tetrahydrobenzofuran-3-carboxamide (4): To a glass tube were added diacetoxypalladium (0.02 mmol, 4.6 mg), triphenylphosphine (0.04 mmol, 10.6 mg), and EtOH / H_2O (1.6 mL / 0.4 mL). Then, **3a** (22.3 mg, 0.1 mmol), and acetaldehyde oxime (0.8 mmol, 47.2 mg) were added and the mixture was stirred at 75 °C. After 12 hours, the mixture was cooled down to room temperature and then directly subjected to silica gel column chromatography (EA/PE =1/3 to EA/PE =1/1) to give pure product **4** as white gummy oil (15.2 mg, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64–7.57 (m, 2H), 7.48–7.38 (m, 3H), 6.28–6.19 (m, 1H), 6.00 (d, J = 10.0 Hz, 1H), 5.69 (brs, 1H), 5.25 (brs, 1H), 4.91 (d, J = 8.5 Hz, 1H), 3.34–3.18 (m, 1H), 2.27–2.09 (m, 2H), 2.03–1.92 (m, 1H), 1.53 (ddd, J = 15.0, 11.0, 3.5 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 160.8, 134.6, 130.5, 130.3, 129.0, 128.7, 123.1, 11.3, 77.8, 42.3, 24.9, 23.2. IR (KBr) (v/cm^{-1}): 3393, 3057, 2925, 2359, 1654, 1592, 1437, 1264, 1180, 1119, 694, 540. HRMS (ESI) calcd for $C_{15}H_{15}NNaO_2$ $[M+Na]^+$ 264.1000, found 264.1003. HPLC (Daicel Chiralcel OJ-H, *n*-hexane/*i*-PrOH = 90/10, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 8.253 min (major) and t_{R2} = 14.790 min (minor), ee = 95%. [α] $\overset{25}{D}$ = –107.8 (*c* 0.10, $CHCl_3$).

5.3 Procedure for synthesis of 5 and characterization data[14]



3a **5**

4-Methyl-*N*-(((*3aS,7aS*)-2-phenyl-3a,4,5,7a-tetrahydrobenzofuran-3-yl)methyl)benzenesulfonamide (5): Under N_2 atmosphere, **3a** (22.3 mg, 0.1 mmol) in dry THF (0.5 mL) was added dropwise

to a stirred suspension of lithium aluminum hydride (1 M in THF, 0.2 mL) in dry THF (0.5 mL) at 0 °C. The resulting solution was then allowed to warm slowly to room temperature and stirred for ca. 3 h, and the mixture was quenched by the addition of a 10% sodium hydroxide solution (2.0 mL). The mixture was then filtered through Celite, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude primary amine as a colorless oil, which was used in the next step without further purification. TsCl (23.0 mg, 0.1 mmol) in dry CH_2Cl_2 (0.5 mL) was added to a solution of crude primary amine and Et_3N (28 μL, 0.2 mmol) in dry CH_2Cl_2 (1.0 mL) at 0 °C under an atmosphere of N_2. The resulting solution was then allowed to warm slowly to room temperature and stirred for 24 h. The residue was purified by flash silicagel column chromatography (PE:EA = 3:1) to afford the desired product **5** as a colorless oil (32.5 mg, 89% yield for two steps). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.5 Hz, 2H), 7.32 –7.25 (m, 7H), 6.19–6.09 (m, 1H), 5.96–5.94 (m, 1H), 4.73–4.61 (m, 2H), 3.92 (dd, J = 13.5, 4.5 Hz, 1H), 3.78 (dd, J = 13.5, 7.0 Hz, 1H), 2.94–2.85 (m, 1H), 2.50–2.42 (m, 3H), 2.12–2.04 (m, 1H), 1.92–1.78 (m, 2H), 1.34–1.30 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.1, 143.5, 136.6, 133.2, 130.6, 129.7, 128.8, 128.3, 127.3, 127.2, 124.2, 75.8, 42.2, 39.5, 24.0, 22.9, 21.5. IR (KBr) (v/cm^{-1}): 3775, 3405, 2927, 2359, 2341, 1493, 1383, 1350, 1060, 935, 740, 698. HRMS (ESI) calcd for $C_{22}H_{24}NO_3S$ $[M+H]^+$ 382.1471, found 382.1474. HPLC (Daicel Chiralcel IC-3, *n*-hexane/*i*-PrOH = 90/10, UV = 210 nm, flow rate = 0.8 mL/min) t_{R1} = 44.865 min (major) and t_{R2} = 48.359 min (minor), ee = 98%. $[\alpha]_D^{25}$ = –54.7 (*c* 0.35, $CHCl_3$).

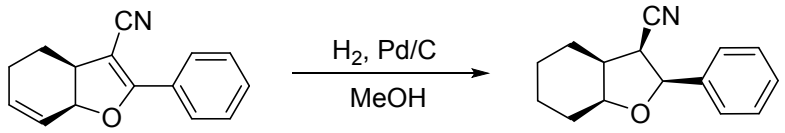
5.4 Procedure for synthesis of 6 and characterization data[15]

3a **6**

(*2R,3S,3aS,7aS*)-2-Phenyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-carbonitrile (6): Under N_2 atmosphere, **3a** (22.3 mg, 0.1 mmol) and $BF_3{\cdot}Et_2O$ (28 μL, 0.22 mol)were added to a solution of Et_3SiH (32 μL, 0.2 mmol) in anhydrous DCM (2 mL) and the reaction mixture was stirred at -20 °C for 20 h. The mixture was quenched with 10% $NaHCO_3$ solution and the mixture was extracted with DCM (6 mL × 3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silicagel column chromatography (PE:EA = 20:1) to afford the desired product **6** as a colorless oil (21 mg, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2H), 7.44–7.40 (m, 2H), 7.37–7.34 (m, 1H), 6.20–6.11 (m, 1H), 5.96 (dd, J = 9.5, 1.0 Hz, 1H), 5.20 (d, J = 9.5 Hz, 1H), 4.63 (s, 1H), 3.22 (dd, J = 9.0, 1.5 Hz, 1H), 2.70–2.64 (m, 1H), 2.37–2.33 (m, 1H), 2.14–2.02 (m, 2H), 1.75–1.63 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.7, 132.6, 128.8, 128.5, 125.4, 117.6, 80.7, 75.0, 43.5, 39.9, 23.5, 21.6. IR (KBr) (v/cm^{-1}):

3451, 3281, 2924, 1598, 1327, 1093, 1037, 814, 699, 569, 550. HRMS (ESI) calcd for $C_{15}H_{16}NO$ $[M+H]^+$ 226.1226, found 226.1228. HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 99/1, UV = 210 nm, flow rate = 1.0 mL/min) t_{R1} = 14.492 min (minor) and t_{R2} = 15.396 min (major), ee = 97%. $[\alpha]_D^{25}$ = –67.1 (*c* 0.24, $CHCl_3$).

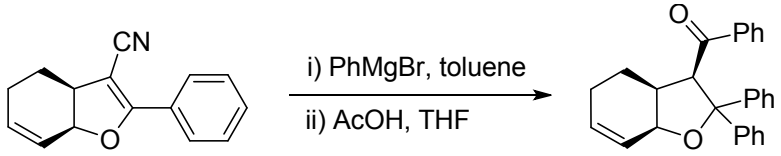
5.5 Procedure for synthesis of 7 and characterization data



3a **7**

(*2R,3S,3aS,7aS*)-2-Phenyloctahydrobenzofuran-3-carbonitrile (7): 3a (22.3 mg, 0.1 mmol) was treated with Pd/C (10 mol%) in MeOH, the mixture was stirred under H_2 (40 bar) at r.t. in a stainless-steel autoclave for 24 h. Then Pd/C was filtered and the organic layer was concentrated under reduced pressure. The residue was purified by flash silicagel column chromatography (PE:EA = 10:1) to afford the desired product **7** as a white solid (20.0 mg, 90%). Mp: 89–90 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44–7.38 (m, 4H), 7.35–7.31 (m, 1H), 5.12 (d, J = 9.6 Hz, 1H), 4.01 (dd, J = 6.6, 3.2 Hz, 1H), 3.63 (dd, J = 9.6, 7.3 Hz, 1H), 2.37 (ddd, J = 11.2, 6.6, 4.2 Hz, 1H), 2.25–2.19 (m, 1H), 1.86–1.77 (m, 2H), 1.73–1.65 (m, 2H), 1.59 (dd, J = 6.6, 2.4 Hz, 1H), 1.48 (ddd, J = 25.2, 12.6, 3.6 Hz, 1H), 1.28–1.23 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.2, 128.5, 128.4, 126.3, 117.5, 79.7, 77.6, 41.5, 40.2, 27.7, 26.0, 24.2, 20.3. IR (KBr) (v/cm^{-1}):2925, 1600, 1395, 771, 760, 427. HRMS (ESI) calcd for $C_{22}H_{24}NO_3S$ $[M+NH_4]^+$ 245.1648, found 245.1649. HPLC (Daicel Chiralcel AS-H, *n*-hexane/*i*-PrOH = 90/10, UV = 210 nm, flow rate = 1.0 mL/min) t_{R1} = 10.658 min (major) and t_{R2} = 13.604 min (minor), ee = 94%. $[\alpha]_D^{25}$ = –46.3 (*c* 0.11, $CHCl_3$).

5.6 Procedure for synthesis of 8 and characterization data[14]

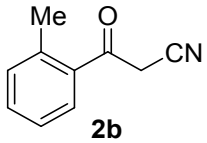


3a **8**

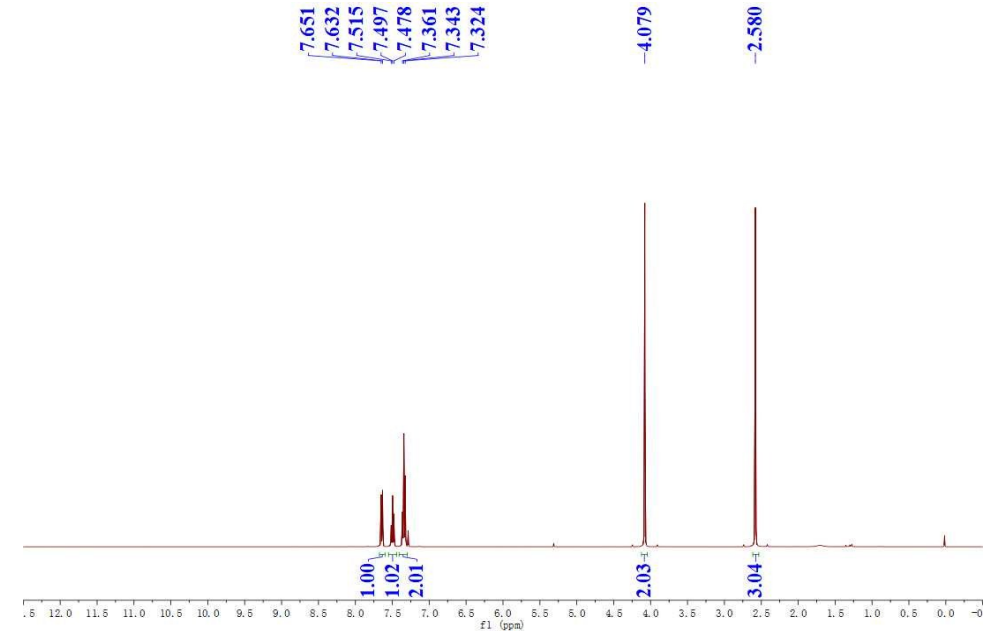
((*3R,3aS,7aS*)-2,2-Diphenyl-2,3,3a,4,5,7a-hexahydrobenzofuran-3-yl)(phenyl)methanone (8): Phenylmagnesium bromide (0.1 mL, 0.3 mmol; 3M solution in tetrahydrofuran) was added dropwise to a stirred solution of **3a** (22.3 mg, 0.1 mmol) in toluene (2.0 mL) at room temperature under an atmosphere of N_2 and the resulting yellow solution heated to 110 °C for 12 hours. The mixture was then allowed to cool to room temperature and quenched with water (2 mL). A solution of acetic acid, tetrahydrofuran and water (4:1:1; 10 mL) was then added and the resulting biphasic mixture stirred vigorously for ca. 4 hours. The mixture was then partitioned between ethyl acetate (10 mL) and 2M sodium hydroxide solution (20 mL). The organic layers were combined, washed

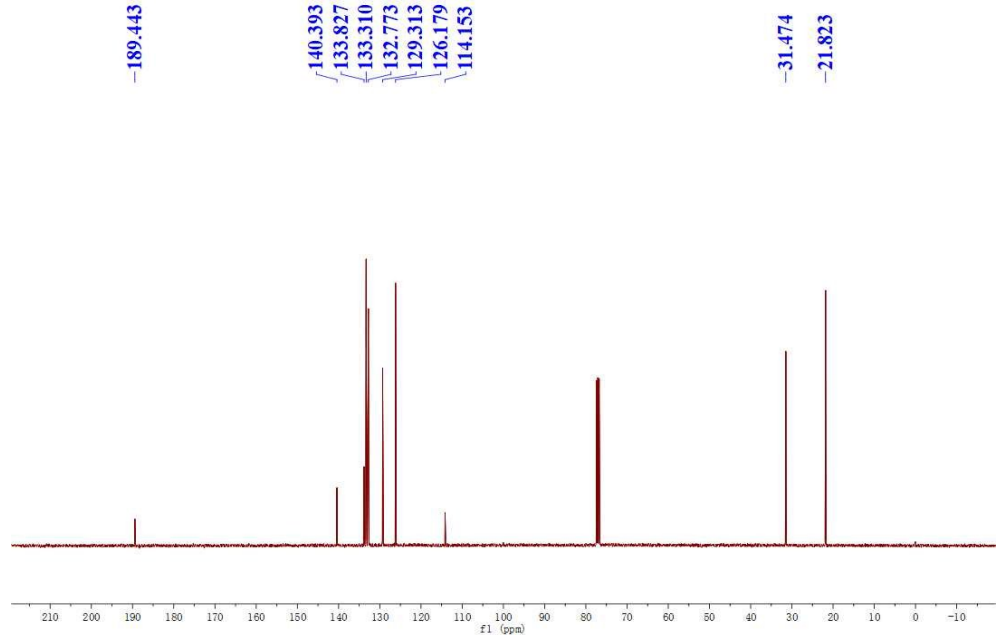
with a saturated aqueous sodium bicarbonate solution, saturated aqueous sodium chloride solution, dried (anhyd. $MgSO_4$), filtered and concentrated in vacuo to afford the crude product. Purification by flash column chromatography (PE:EA = 10:1) afforded the aryl ketone (19.7 mg, 52%) as a colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44–7.38 (m, 4H), 7.35–7.31 (m, 1H), 5.12 (d, J = 9.6 Hz, 1H), 4.01 (dd, J = 6.6, 3.0 Hz, 1H), 3.63 (dd, J = 9.6, 7.2 Hz, 1H), 2.37 (ddd, J = 11.4, 6.6, 4.2 Hz, 1H), 2.25–2.19 (m, 1H), 1.86–1.77 (m, 2H), 1.73–1.65 (m, 2H), 1.59 (dd, J = 6.6, 2.4 Hz, 1H), 1.48 (ddd, J = 25.2, 12.0, 3.6 Hz, 1H), 1.28–1.23 (m, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.4, 144.2, 137.3, 136.4, 133.5, 133.2, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 126.7, 58.4, 44.9, 42.8, 29.7, 23.8, 21.4. IR (KBr) (v/cm^{-1}): 3446, 2830, 1631, 1362, 1076, 786. HRMS (ESI) calcd for $C_{22}H_{24}NO_3S$ $[M+H]^+$ 381.1849, found 381.1847. HPLC (Daicel Chiralcel OD-H, *n*-hexane/*i*-PrOH = 92/8, UV = 254 nm, flow rate = 1.0 mL/min) t_{R1} = 4.759 min (major) and t_{R2} = 5.271 min (minor), ee = 96%. $[\alpha]_D^{25}$ = 10.8 (*c* 0.5, $CHCl_3$).

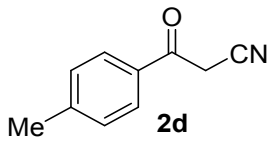
6. NMR Spectra



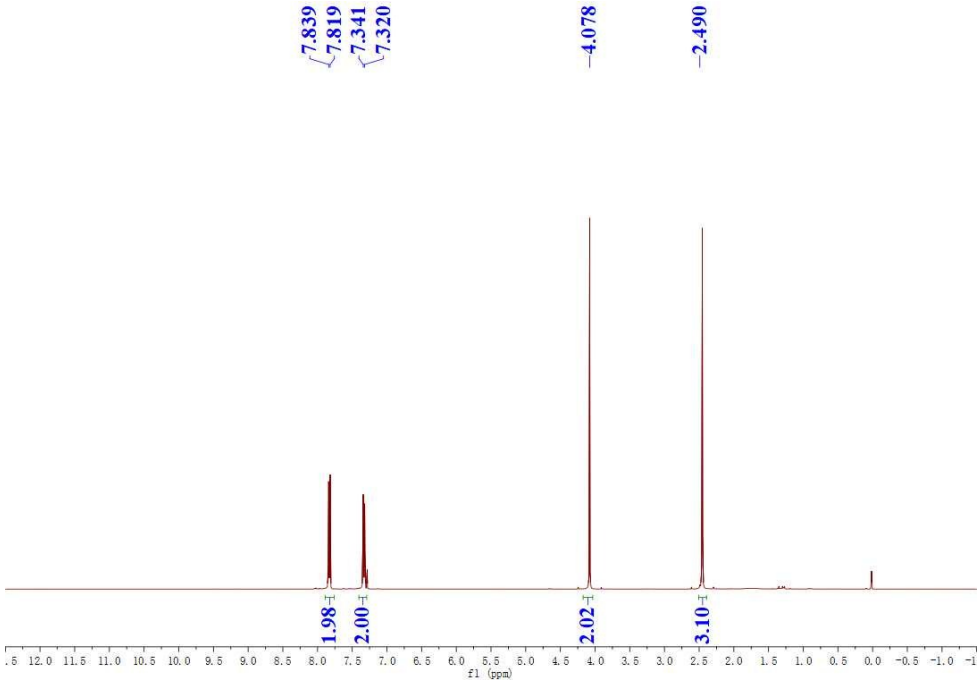
2b

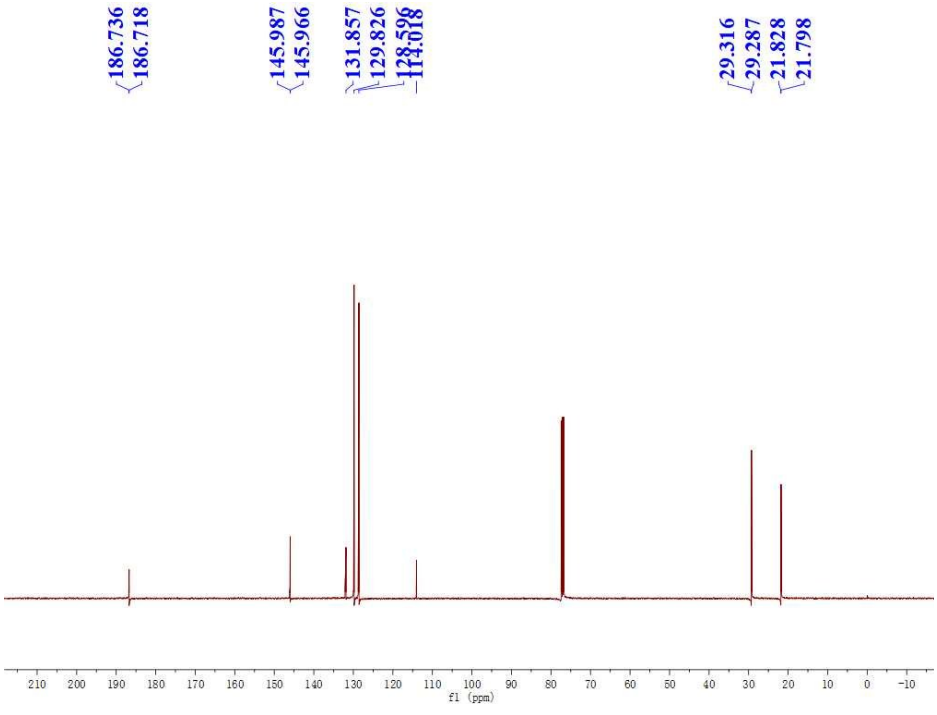


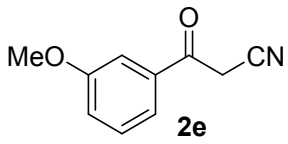



O
CN
Me

2d

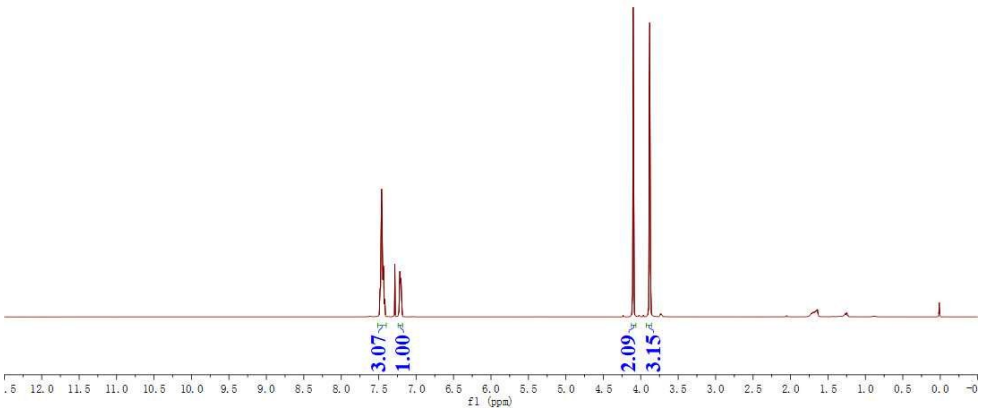

7.839
7.819
7.341
7.320
4.078
2.490
1.98
2.00
2.02
3.10
f1 (ppm)

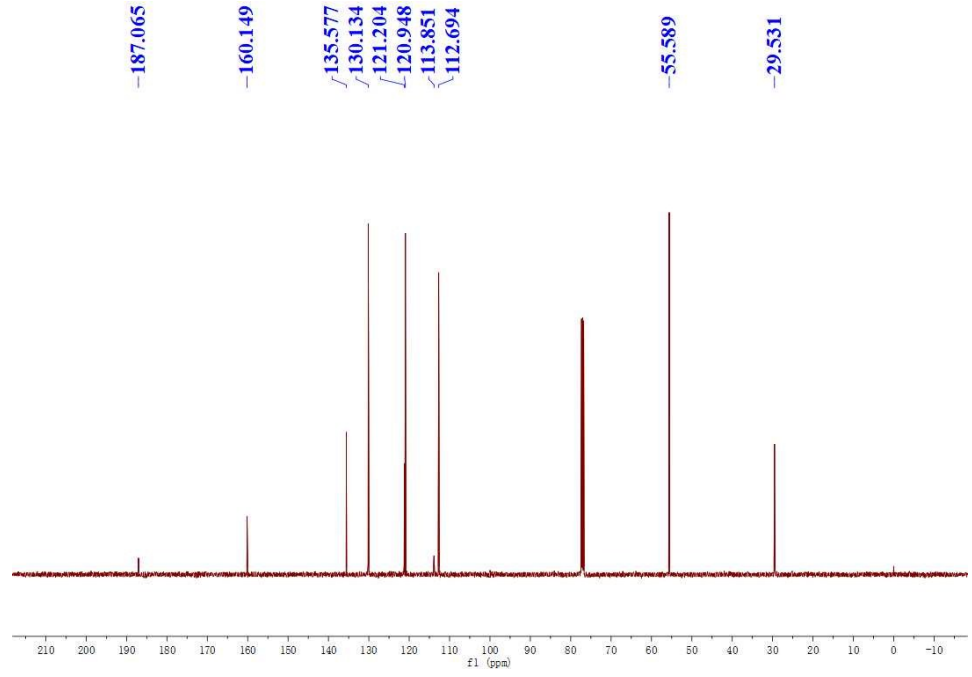

186.736
186.718
145.987
145.966
131.857
129.826
128.596
114.018
29.316
29.287
21.828
21.798
f1 (ppm)

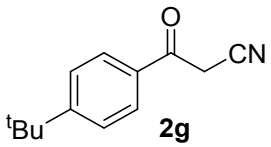

O
MeO
CN

2e

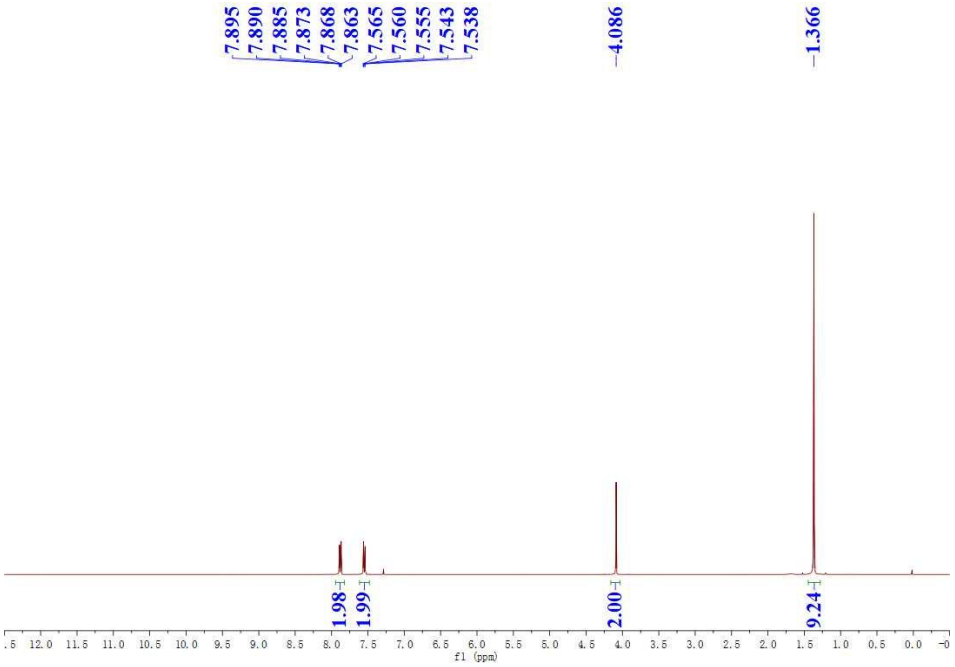

7.480
7.476
7.465
7.462
7.461
7.459
7.454
7.449
7.441
7.437
7.433
7.225
7.222
7.220
7.217
7.215
7.212
7.209
7.207
7.204
7.201
7.199
4.102
4.098
3.886
3.884
3.880
3.874

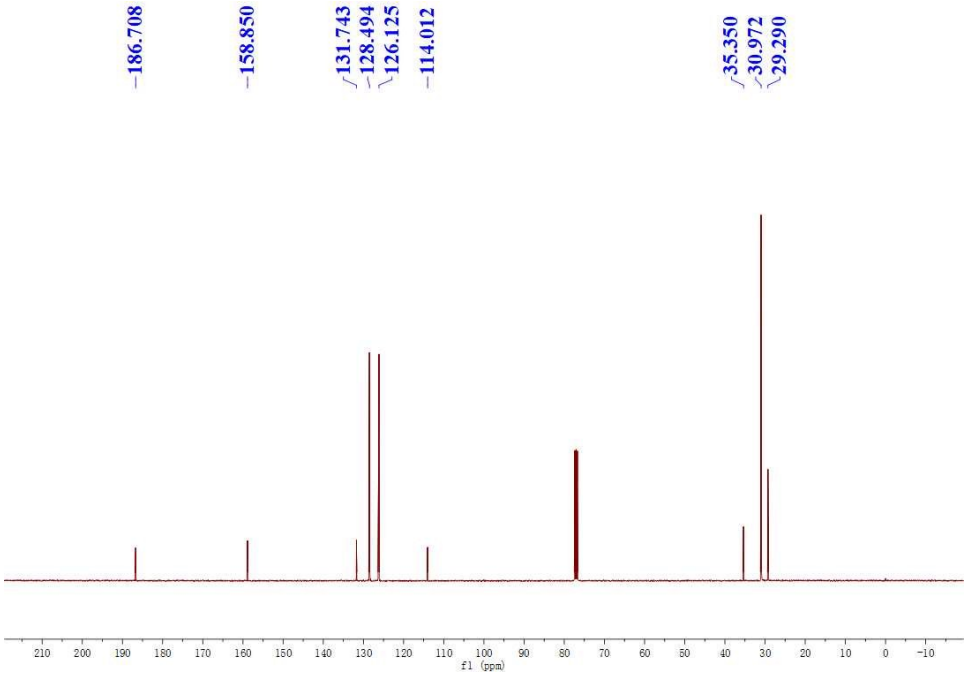

3.07
1.00
2.09
3.15
f1 (ppm)

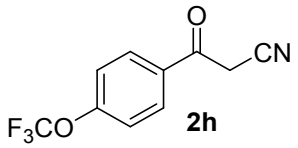

187.065
160.149
135.577
130.134
121.204
120.948
113.851
112.694
55.589
29.531
f1 (ppm)


O
CN
tBu

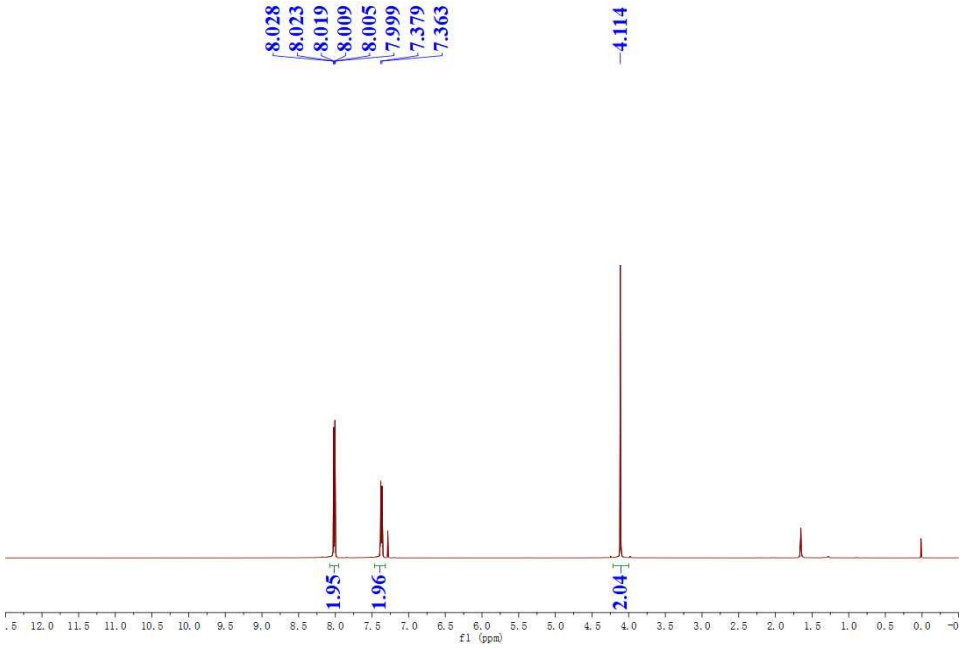
2g

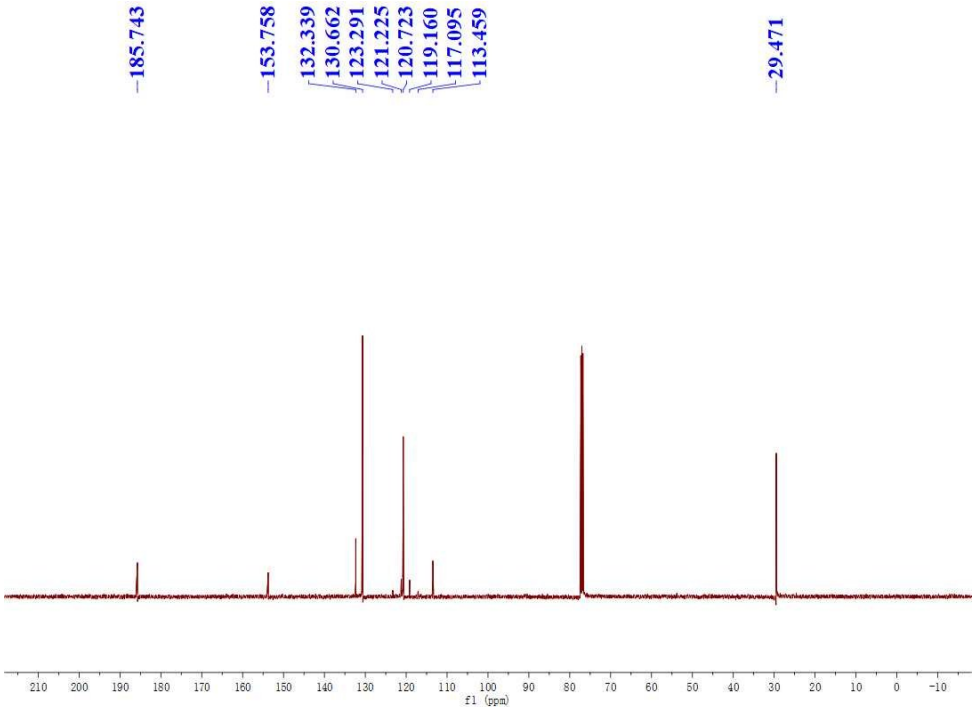

7.895
7.890
7.885
7.873
7.868
7.863
7.565
7.560
7.555
7.543
7.538
4.086
1.366
1.98
1.99
2.00
9.24
f1 (ppm)

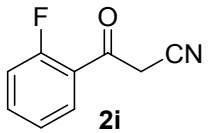

186.708
158.850
131.743
128.494
126.125
114.012
35.350
30.972
29.290
f1 (ppm)


O
CN
F3CO

2h

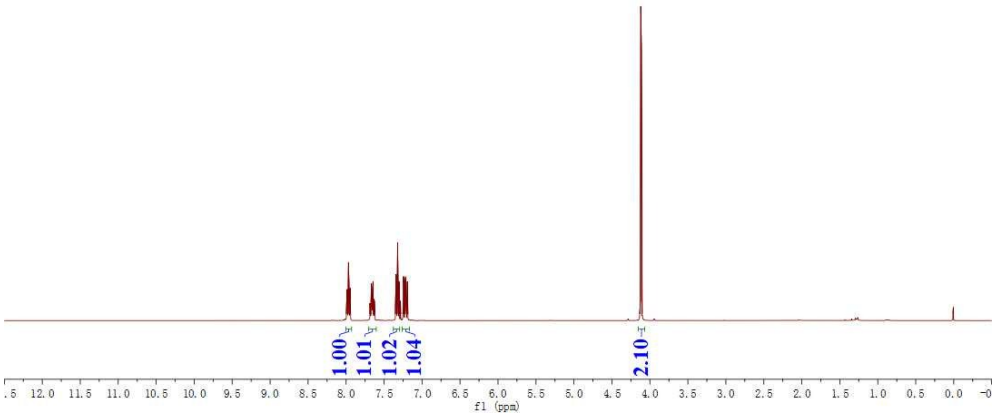

8.028
8.023
8.019
8.009
8.005
7.999
7.379
7.363
4.114
1.95
1.96
2.04
f1 (ppm)

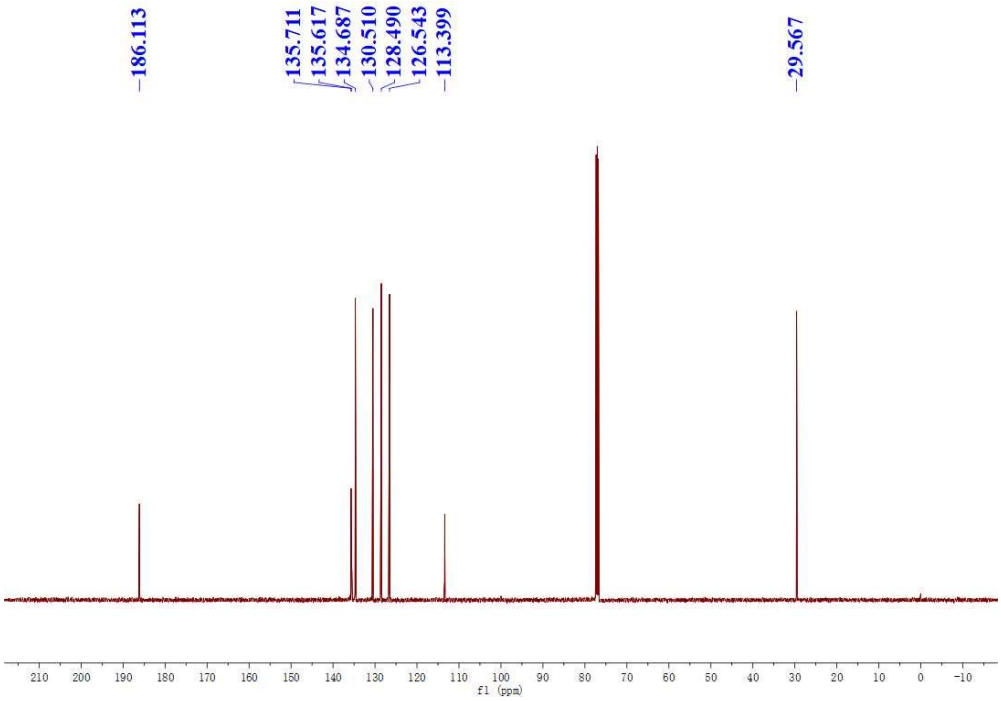

185.743
153.758
132.339
130.662
123.291
121.225
120.723
119.160
117.095
113.459
29.471
f1 (ppm)

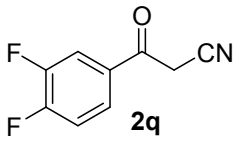

F
O
CN

2i


7.988
7.983
7.968
7.964
7.949
7.945
7.666
7.663
7.661
7.653
7.650
7.648
7.645
7.341
7.339
7.322
7.303
7.301
7.242
7.222
7.220
7.214
7.193
7.191
4.120
4.113

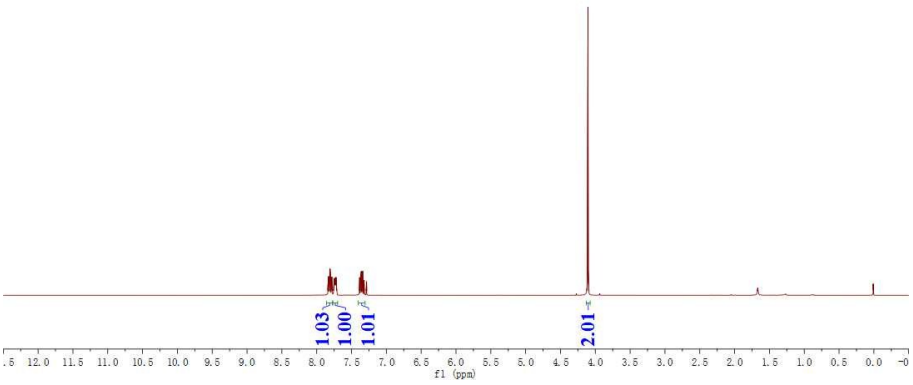

1.00
1.01
1.02
1.04
2.10
f1 (ppm)

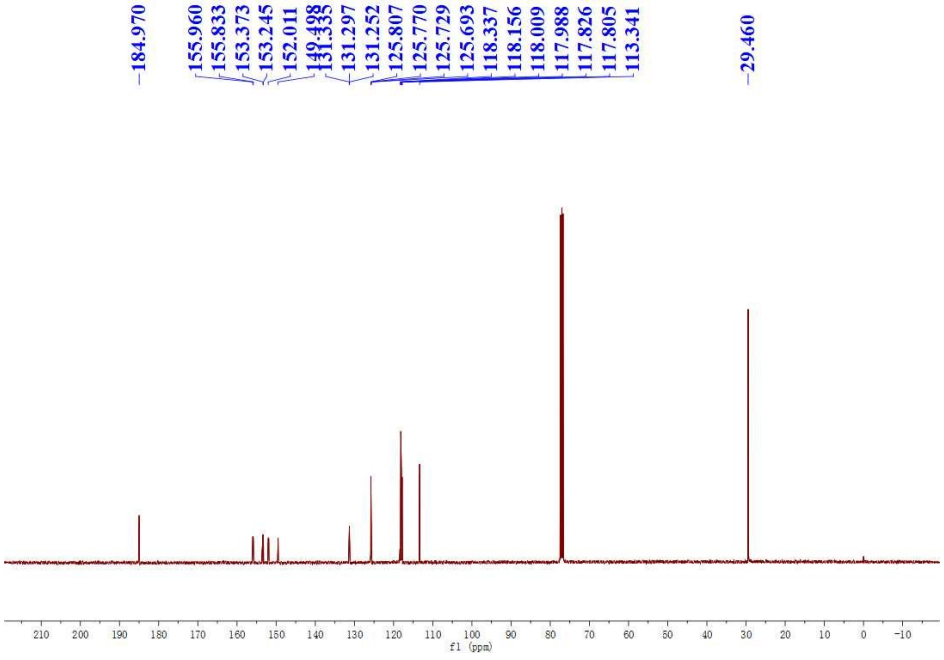

186.113
135.711
135.617
134.687
130.510
128.490
126.543
113.399
29.567
f1 (ppm)

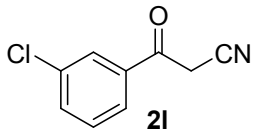

O
F
CN
F

2q

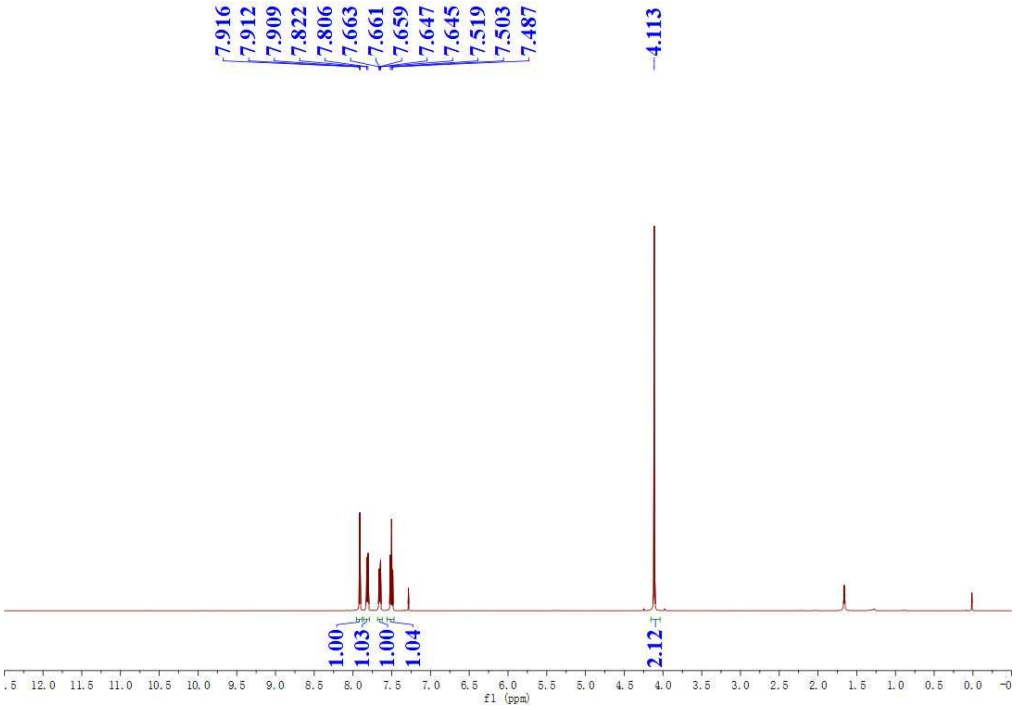

7.834
7.828
7.815
7.809
7.802
7.789
7.784
7.751
7.744
7.740
7.738
7.735
7.733
7.729
7.727
7.723
7.719
7.383
7.364
7.361
7.360
7.342
7.341
7.338
4.105

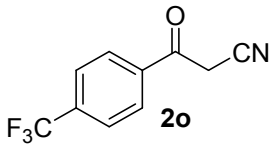

1.03
1.00
1.01
2.01
f1 (ppm)


184.970
155.960
155.833
153.373
153.245
152.011
131.335
131.297
131.252
125.807
125.770
125.729
125.693
118.337
118.156
118.009
117.988
117.826
117.805
113.341
29.460
f1 (ppm)

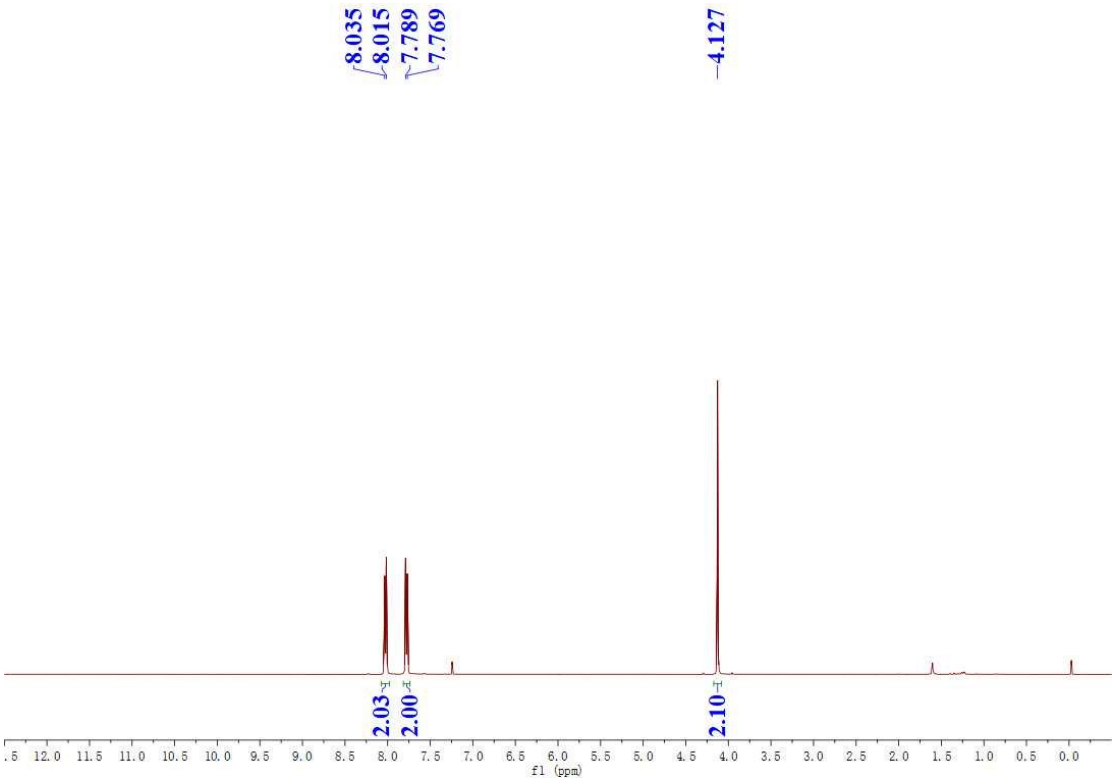

O
Cl
CN

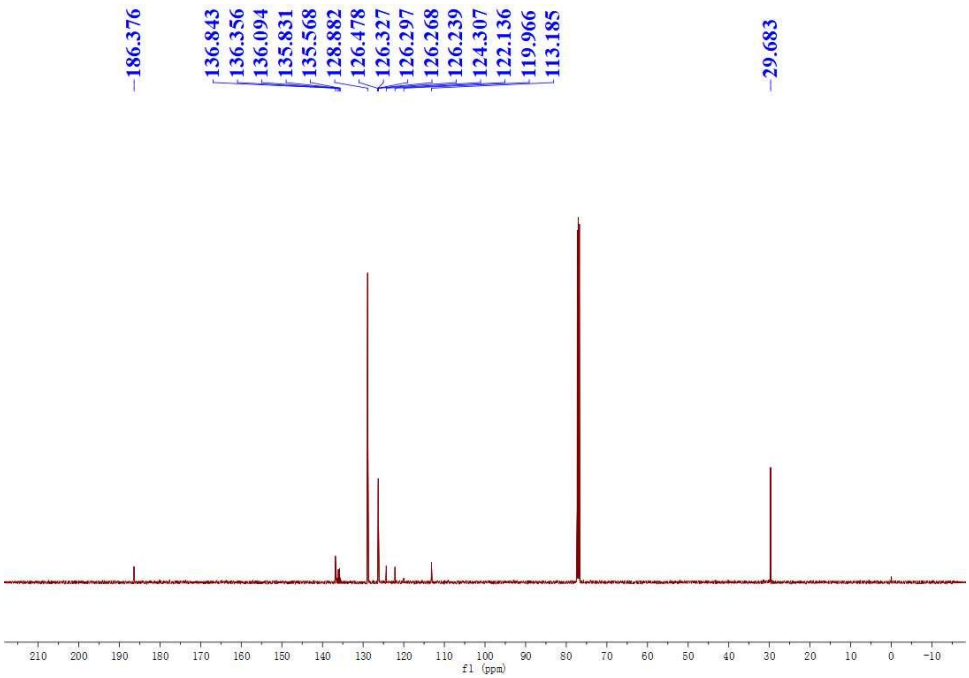
2l

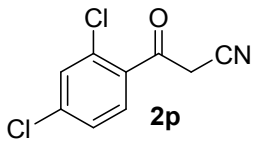

7.916
7.912
7.909
7.822
7.806
7.663
7.661
7.659
7.647
7.645
7.519
7.503
7.487
4.113
1.00
1.03
1.00
1.04
2.12
f1 (ppm)

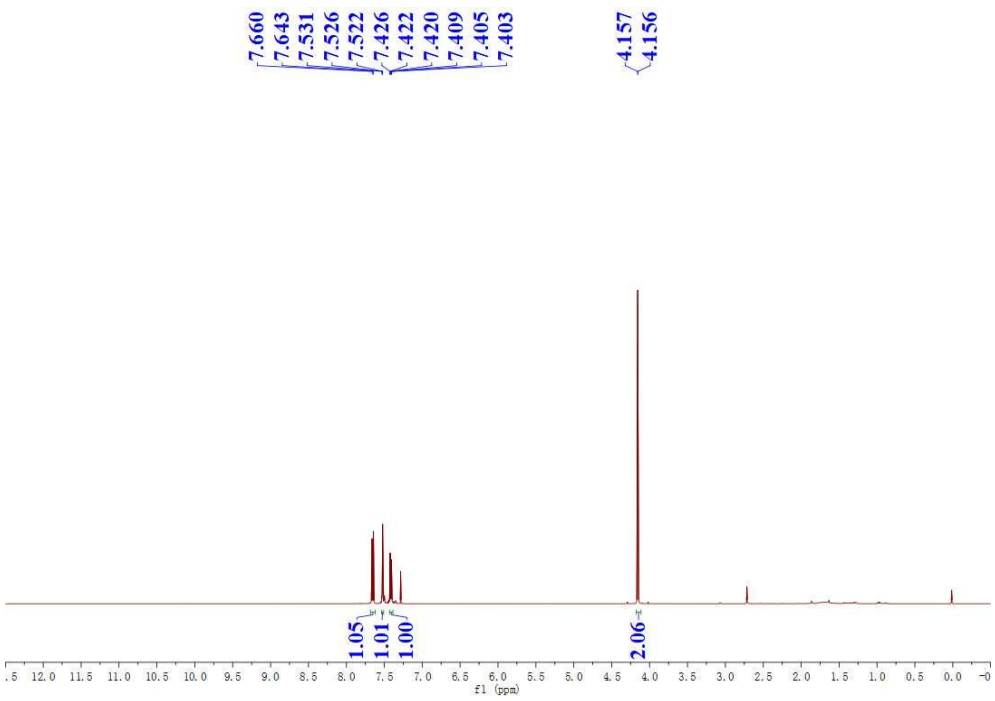

O
CN
F3C

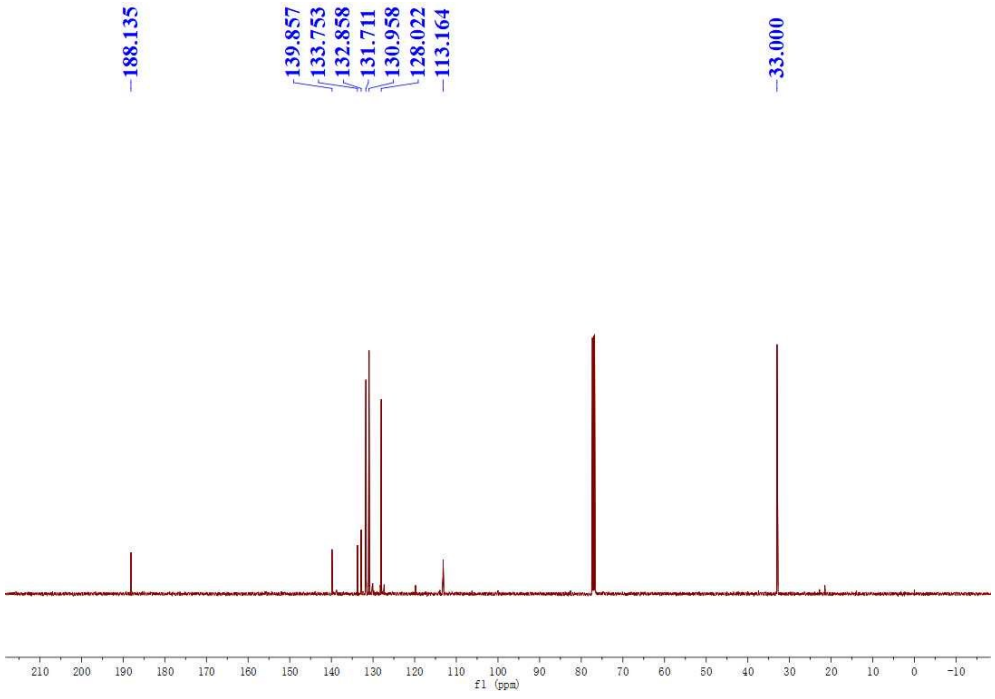
2o

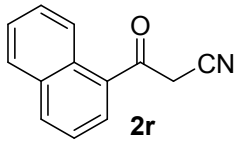

8.035
8.015
7.789
7.769
4.127
2.03
2.00
2.10
f1 (ppm)


186.376
136.843
136.356
136.094
135.831
135.568
128.882
126.478
126.327
126.297
126.268
126.239
124.307
122.136
119.966
113.185
29.683
f1 (ppm)

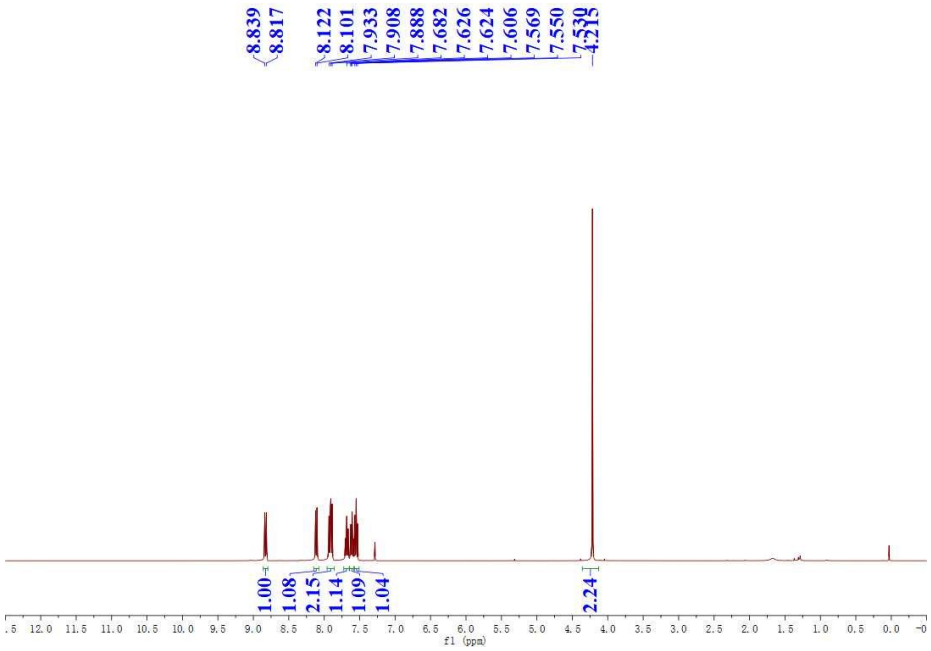

Cl
O
CN
Cl
2p

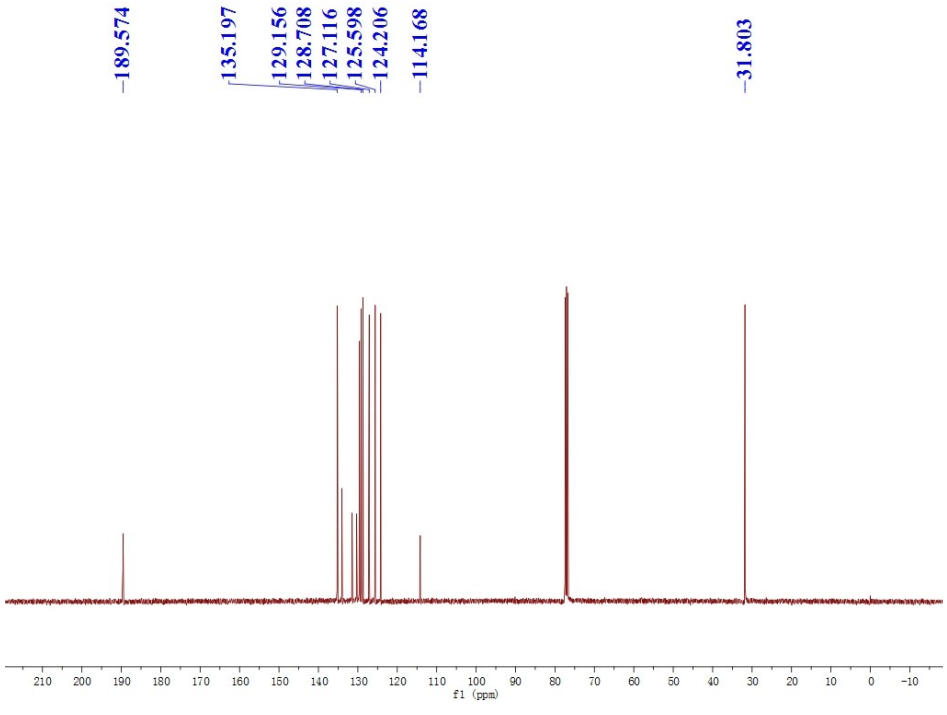

7.660
7.643
7.531
7.526
7.522
7.426
7.422
7.420
7.409
7.405
7.403
4.157
4.156
1.05
1.01
1.00
2.06
f1 (ppm)

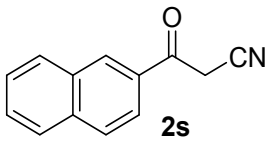

188.135
139.857
133.753
132.858
131.711
130.958
128.022
113.164
33.000
f1 (ppm)


O
CN

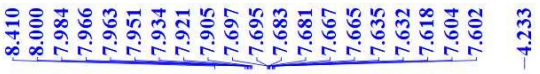
2r

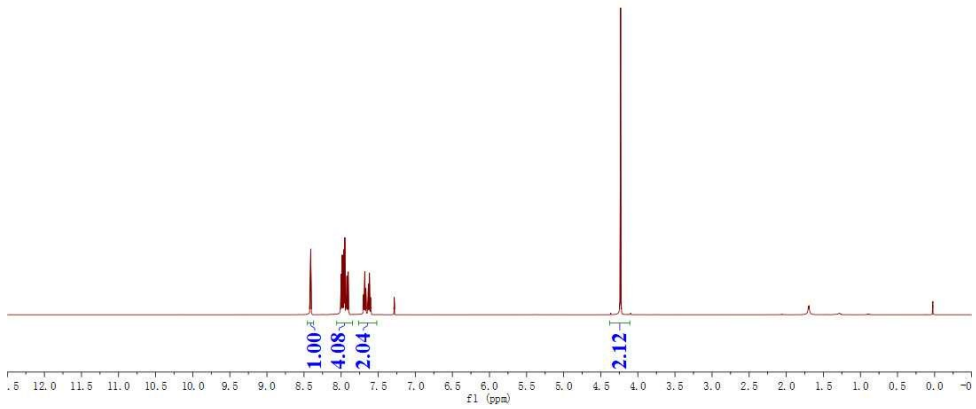

8.839
8.817
8.122
8.101
7.933
7.908
7.888
7.682
7.626
7.624
7.606
7.569
7.550
7.530
4.215
1.00
1.08
2.15
1.14
1.09
1.04
2.24
f1 (ppm)


189.574
135.197
129.156
128.708
127.116
125.598
124.206
114.168
31.803
f1 (ppm)

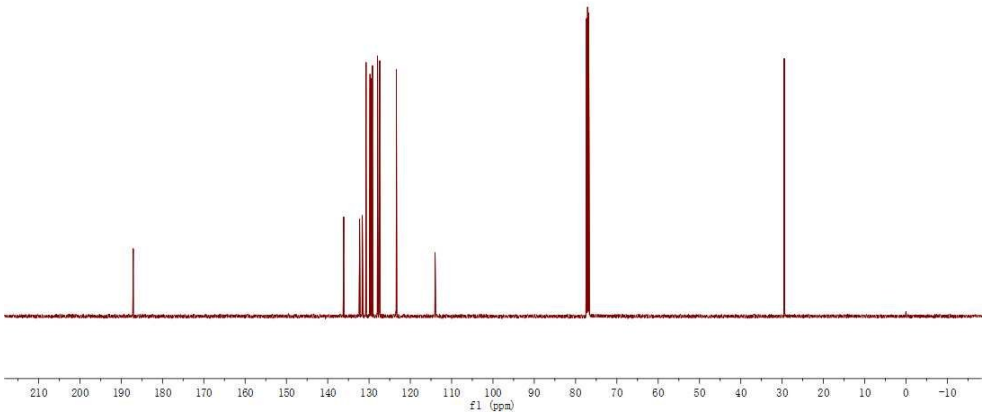

O
CN

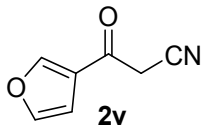
2s


8.410
8.000
7.984
7.966
7.963
7.951
7.934
7.921
7.905
7.697
7.695
7.683
7.681
7.667
7.665
7.635
7.632
7.618
7.604
7.602
4.233

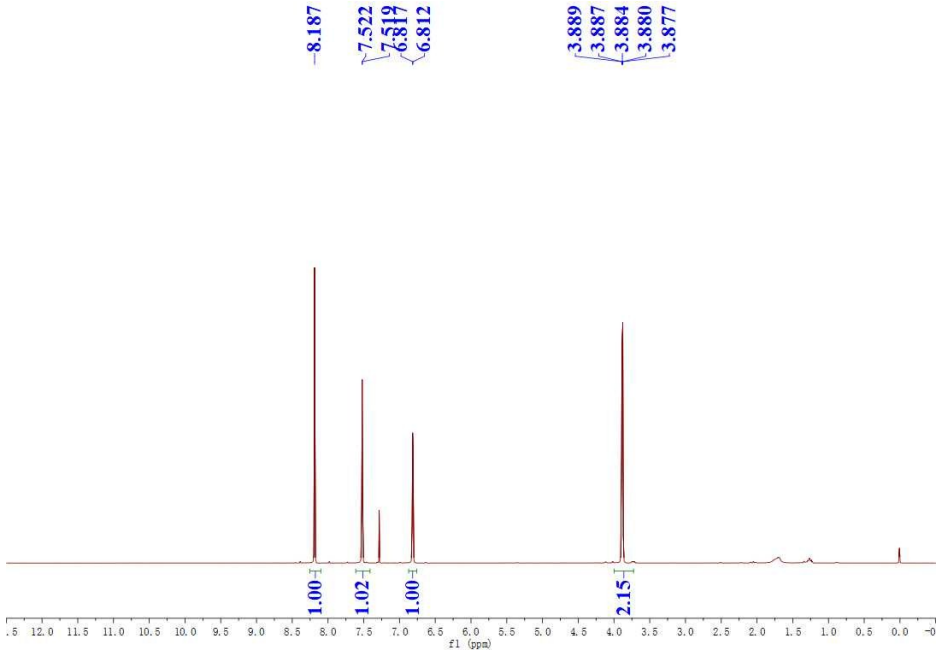

1.00
4.08
2.04
2.12
f1 (ppm)

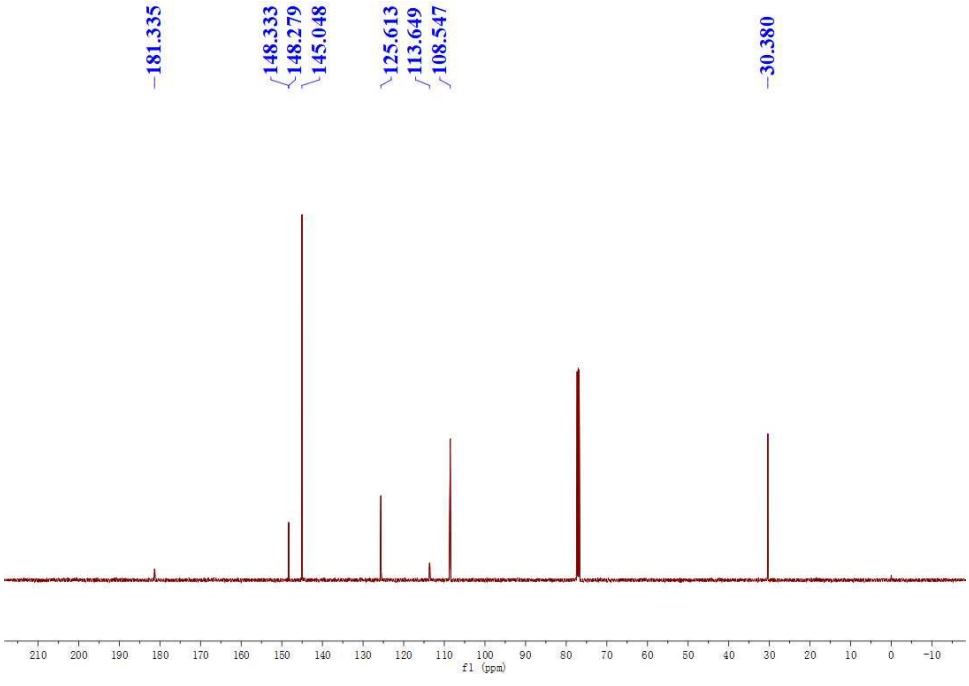

187.093
136.147
132.276
131.632
130.733
129.749
129.532
129.187
127.938
127.429
123.382
114.004
29.486

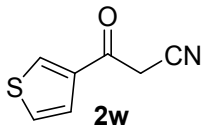

f1 (ppm)


O
CN
O

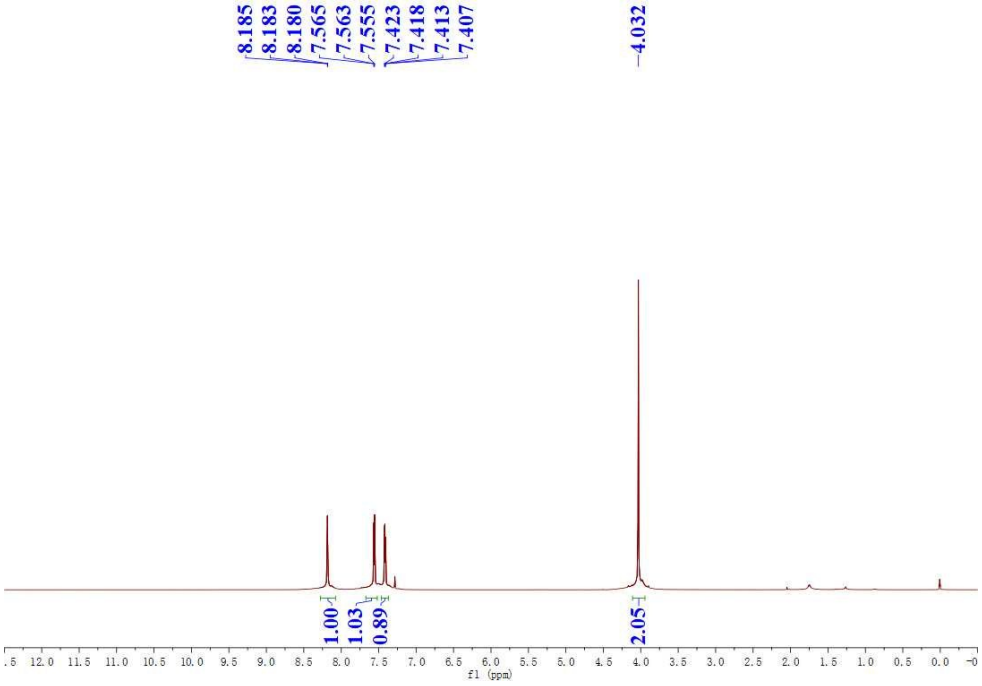
2v

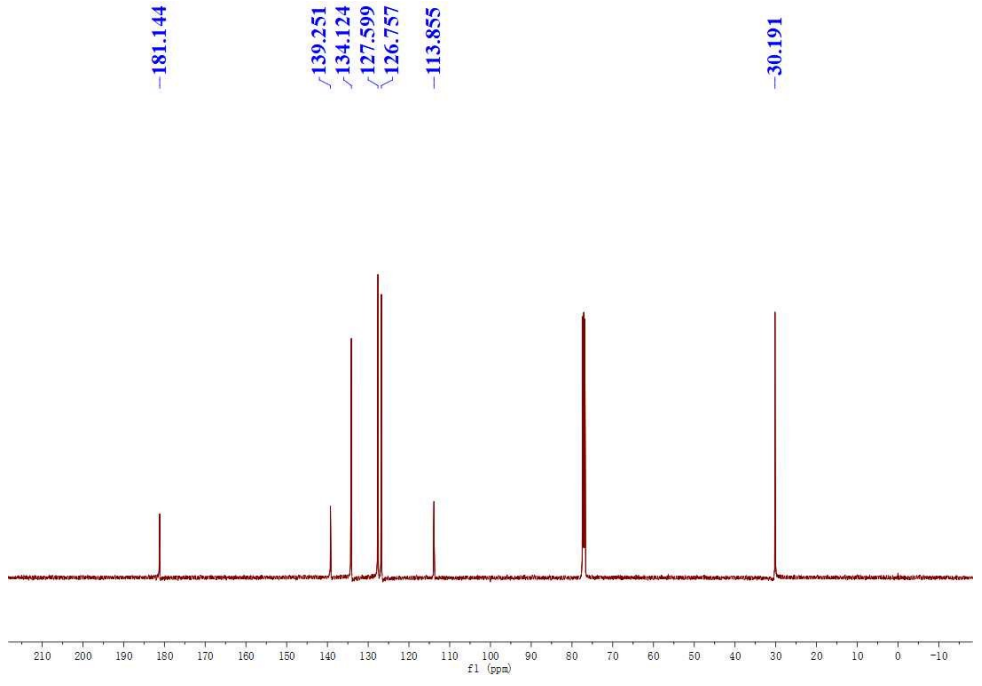

8.187
7.522
7.519
6.817
6.812
3.889
3.887
3.884
3.880
3.877
1.00
1.02
1.00
2.15
f1 (ppm)

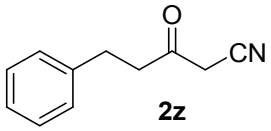

181.335
148.333
148.279
145.048
125.613
113.649
108.547
30.380
f1 (ppm)


O
CN
S

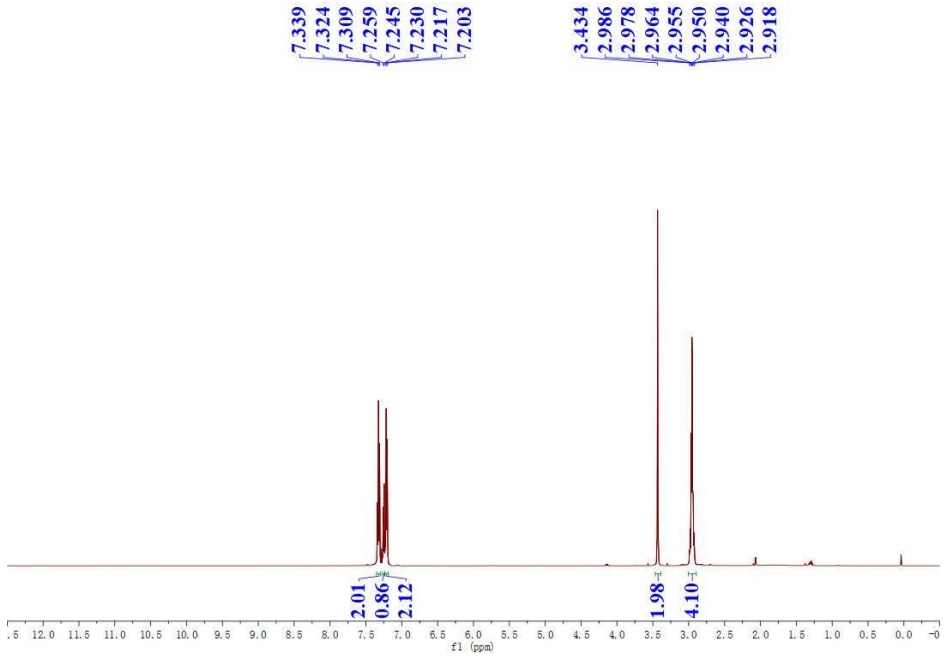
2w

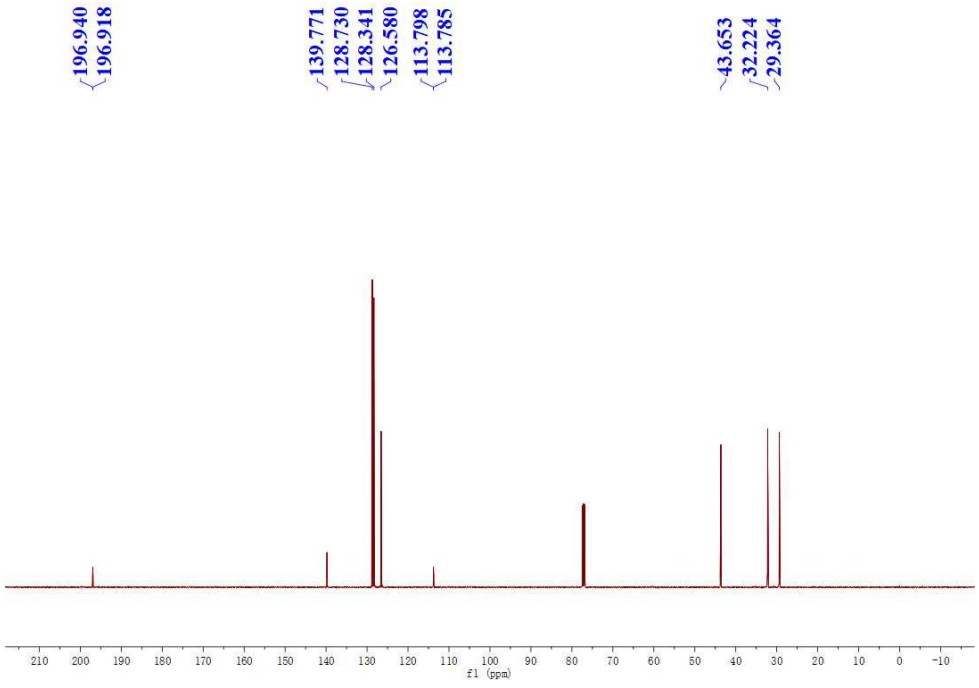

8.185
8.183
8.180
7.565
7.563
7.555
7.423
7.418
7.413
7.407
4.032
1.00
1.03
0.89
2.05
f1 (ppm)

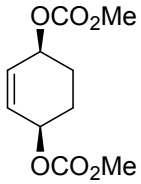

181.144
139.251
134.124
127.599
126.757
113.855
30.191
f1 (ppm)


O
CN

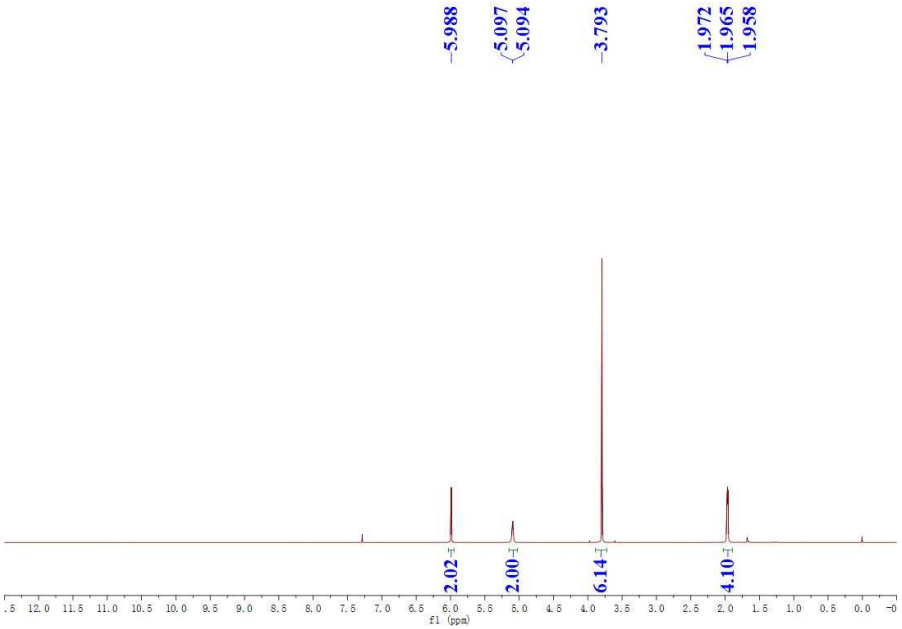
2z

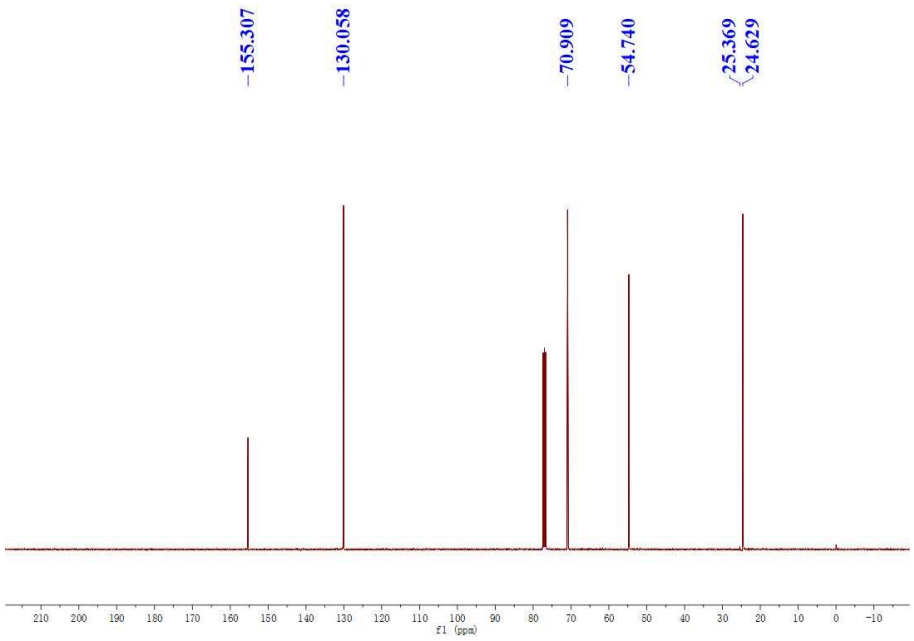

7.339
7.324
7.309
7.259
7.245
7.230
7.217
7.203
3.434
2.986
2.978
2.964
2.955
2.950
2.940
2.926
2.918
2.01
0.86
2.12
1.98
4.10
f1 (ppm)

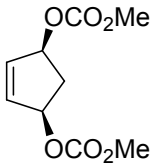

196.940
196.918
139.771
128.730
128.341
126.580
113.798
113.785
43.653
32.224
29.364
f1 (ppm)


OCO2Me
OCO2Me

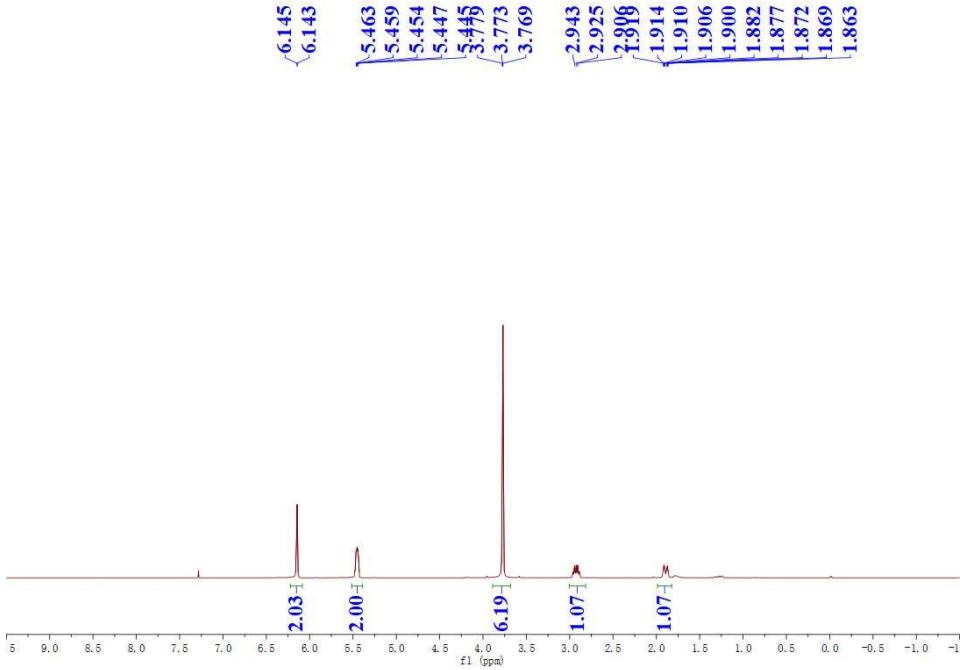
1a

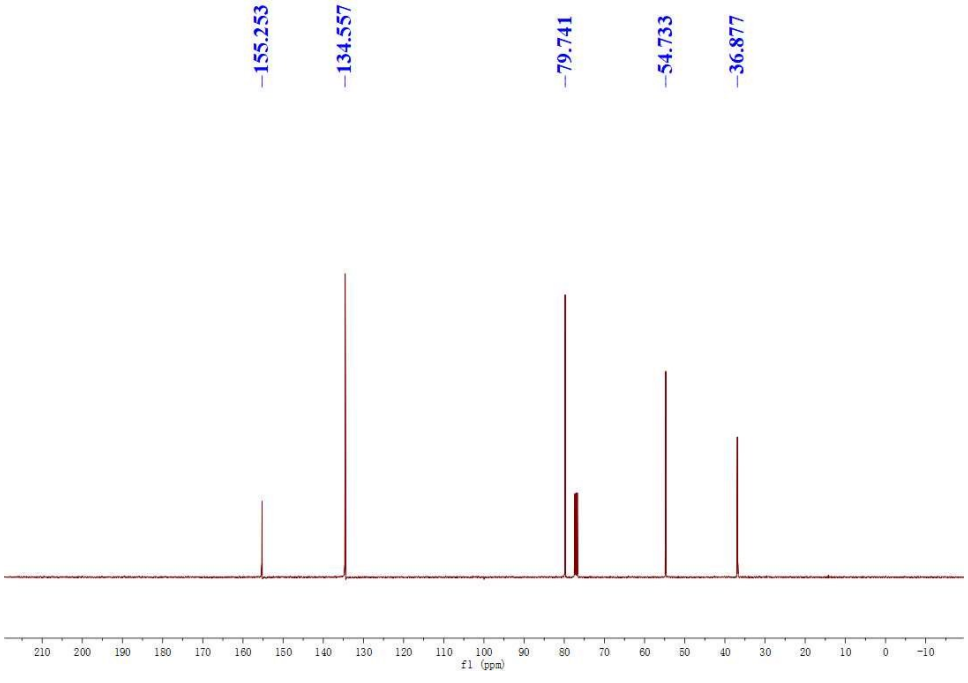

5.988
5.097
5.094
3.793
1.972
1.965
1.958
2.02
2.00
6.14
4.10
f1 (ppm)

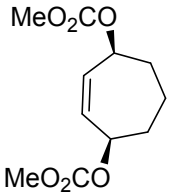

155.307
130.058
70.909
54.740
25.369
24.629
f1 (ppm)


OCO2Me
OCO2Me

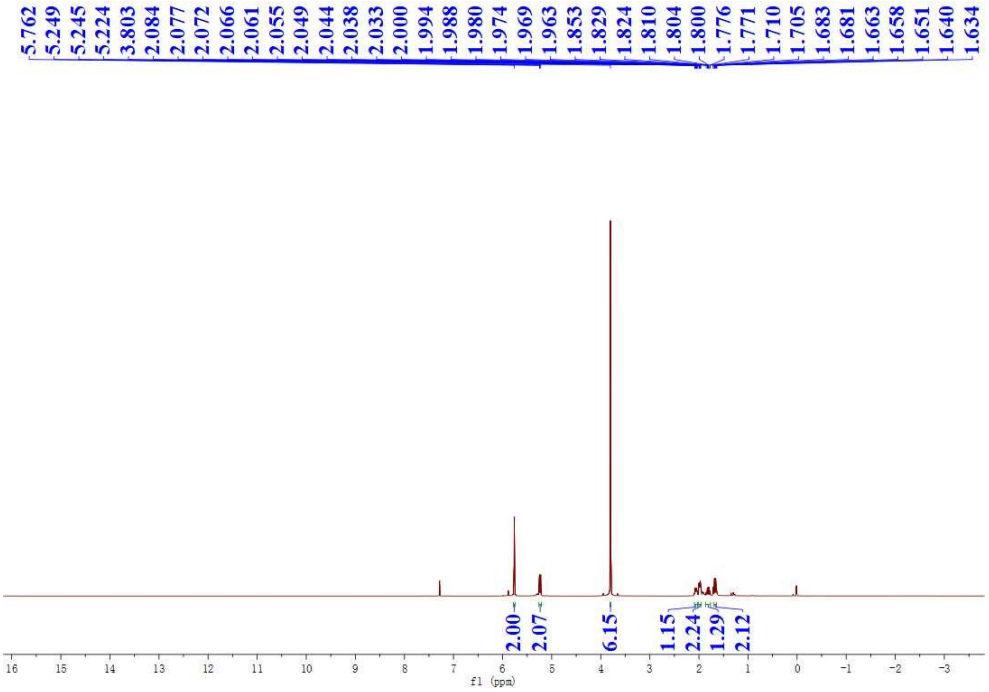
1b

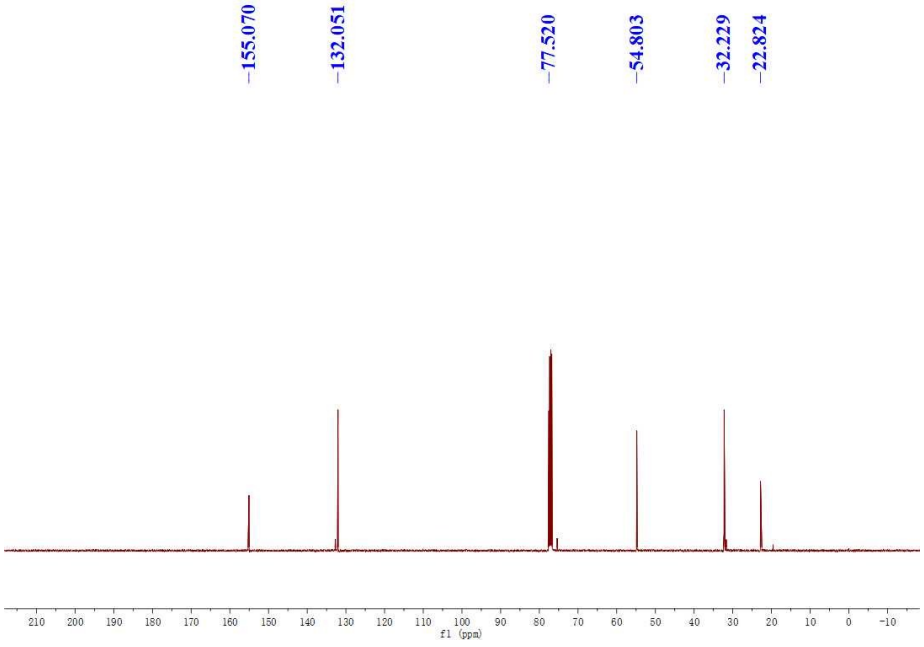

6.145
6.143
5.463
5.459
5.454
5.447
3.773
3.769
2.943
2.925
1.914
1.910
1.906
1.900
1.882
1.877
1.872
1.869
1.863
2.03
2.00
6.19
1.07
1.07
f1 (ppm)

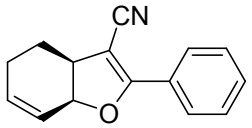

155.253
134.557
79.741
54.733
36.877
f1 (ppm)


MeO2CO
MeO2CO

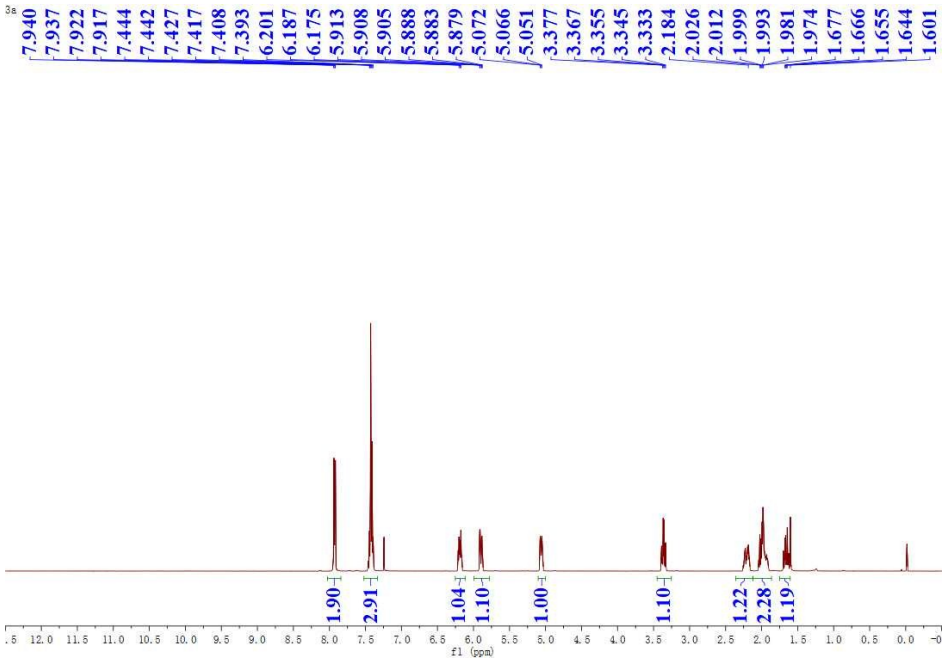
1c

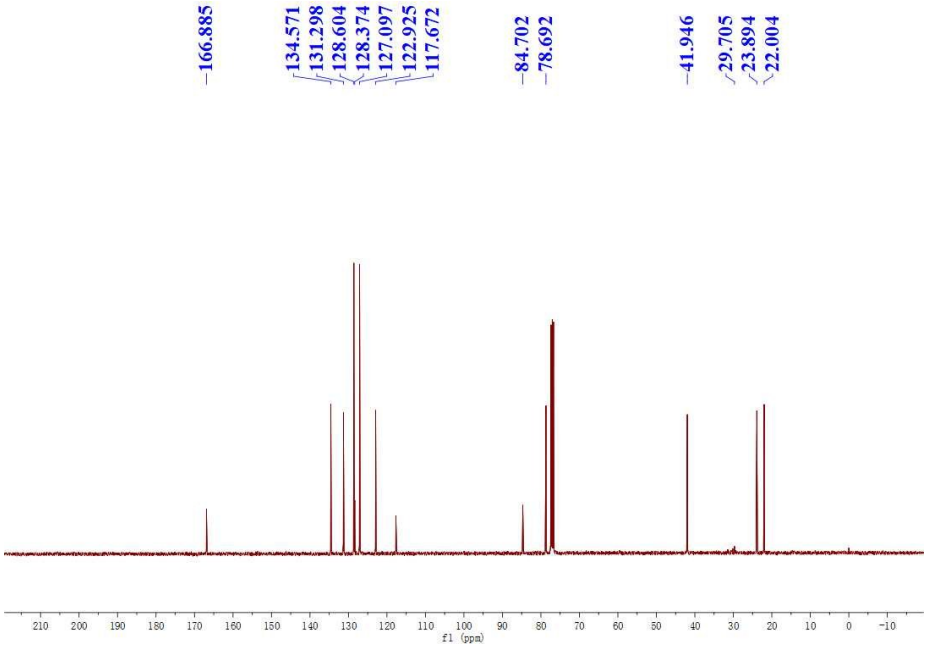

5.762
5.249
5.245
5.224
3.803
2.084
2.077
2.072
2.066
2.061
2.055
2.049
2.044
2.038
2.033
2.000
1.994
1.988
1.980
1.974
1.969
1.963
1.853
1.829
1.824
1.810
1.804
1.800
1.776
1.771
1.710
1.705
1.683
1.681
1.663
1.658
1.651
1.640
1.634
2.00
2.07
6.15
1.15
2.24
1.29
2.12
f1 (ppm)

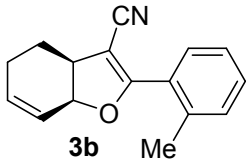

155.070
132.051
77.520
54.803
32.229
22.824
f1 (ppm)


CN
O

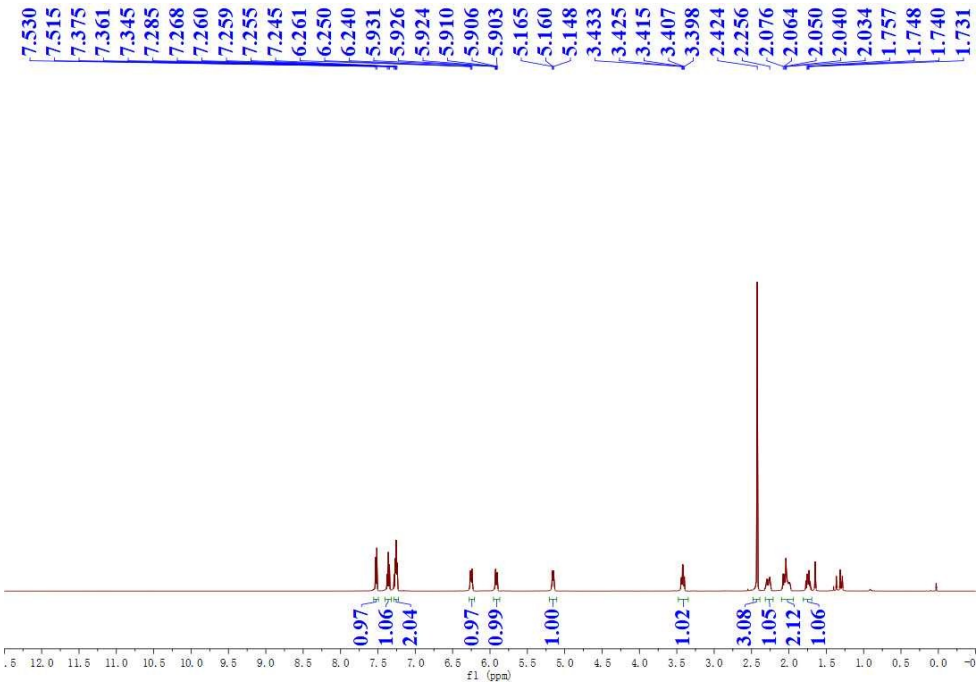
3a

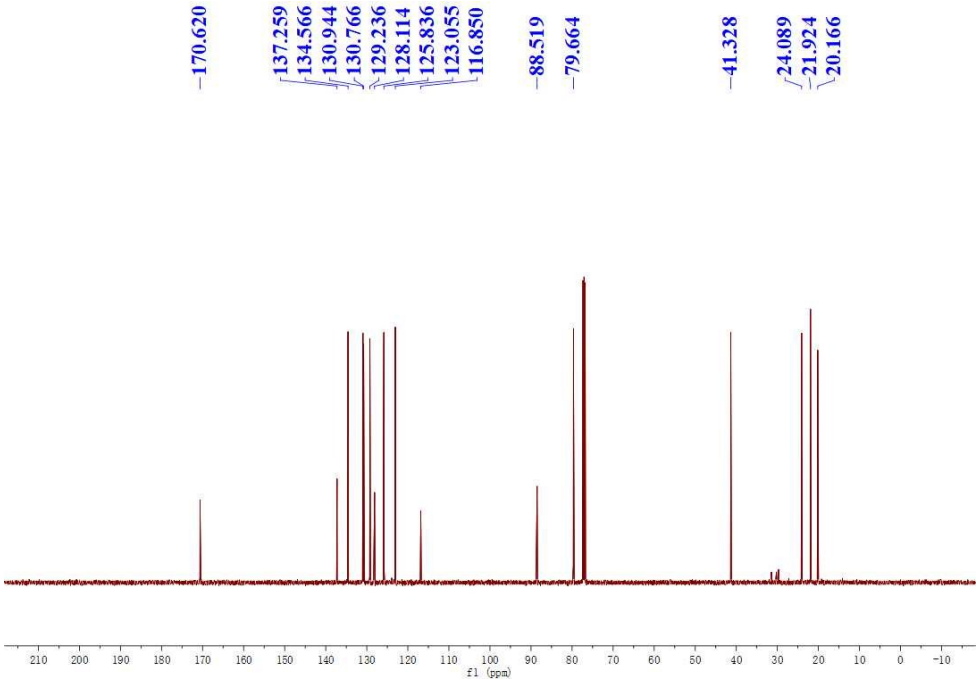

3a
7.940
7.937
7.922
7.917
7.444
7.442
7.427
7.417
7.408
7.393
6.201
6.187
6.175
5.913
5.908
5.905
5.888
5.883
5.879
5.072
5.066
5.051
3.377
3.367
3.355
3.345
3.333
2.184
2.026
2.012
1.999
1.993
1.981
1.974
1.677
1.666
1.655
1.644
1.601
1.90
2.91
1.04
1.10
1.00
1.10
1.22
2.28
1.19
f1 (ppm)

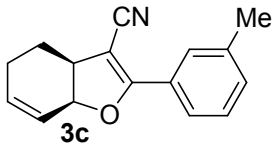

166.885
134.571
131.298
128.604
128.374
127.097
122.925
117.672
84.702
78.692
41.946
29.705
23.894
22.004
f1 (ppm)


CN
O
Me

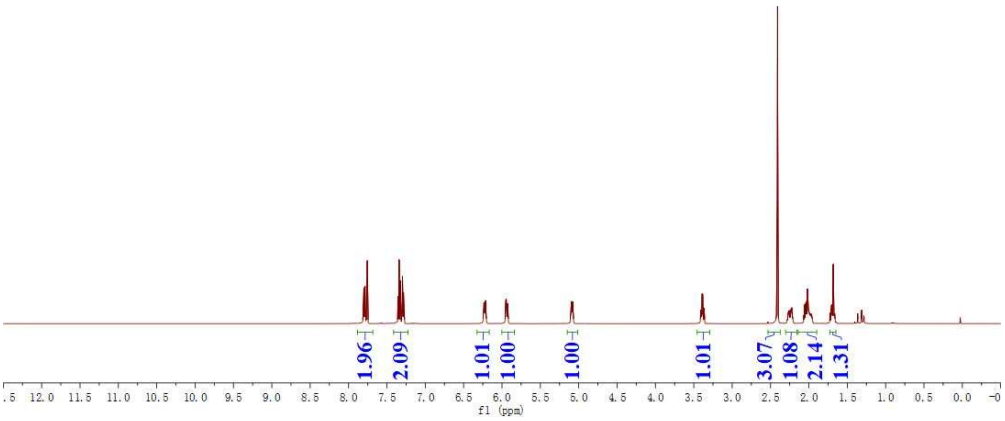
3b


7.530
7.515
7.375
7.361
7.345
7.285
7.268
7.260
7.259
7.255
7.245
6.261
6.250
6.240
5.931
5.926
5.924
5.910
5.906
5.903
5.165
5.160
5.148
3.433
3.425
3.415
3.407
3.398
2.424
2.256
2.076
2.064
2.050
2.040
2.034
1.757
1.748
1.740
1.731
0.97
1.06
2.04
0.97
0.99
1.00
1.02
3.08
1.05
2.12
1.06
f1 (ppm)

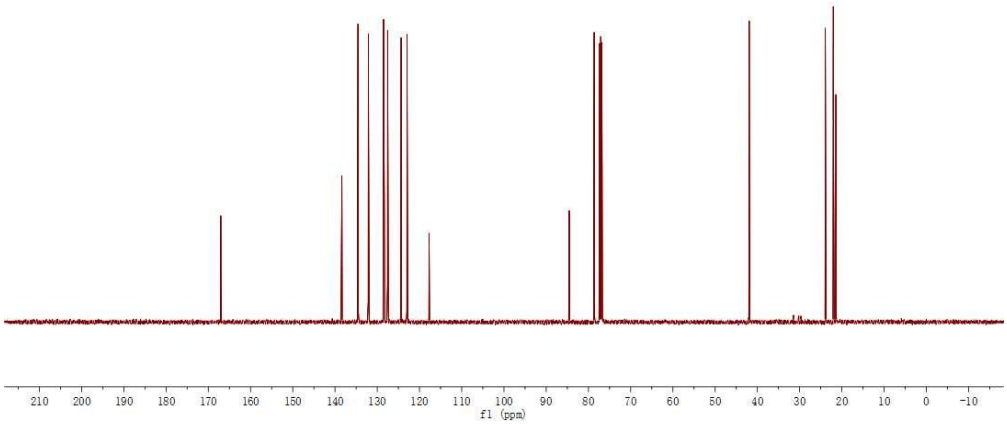

170.620
137.259
134.566
130.944
130.766
129.236
128.114
125.836
123.055
116.850
88.519
79.664
41.328
24.089
21.924
20.166
f1 (ppm)

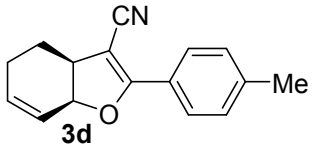


7.800
7.785
7.756
7.356
7.341
7.325
7.296
7.283
6.243
6.235
6.224
6.215
5.951
5.947
5.944
5.940
5.931
5.926
5.924
5.096
5.079
5.073
3.401
3.392
3.383
3.375
3.365
2.409
2.234
2.223
2.055
2.044
2.034
2.029
2.019
2.013
1.707
1.698
1.689

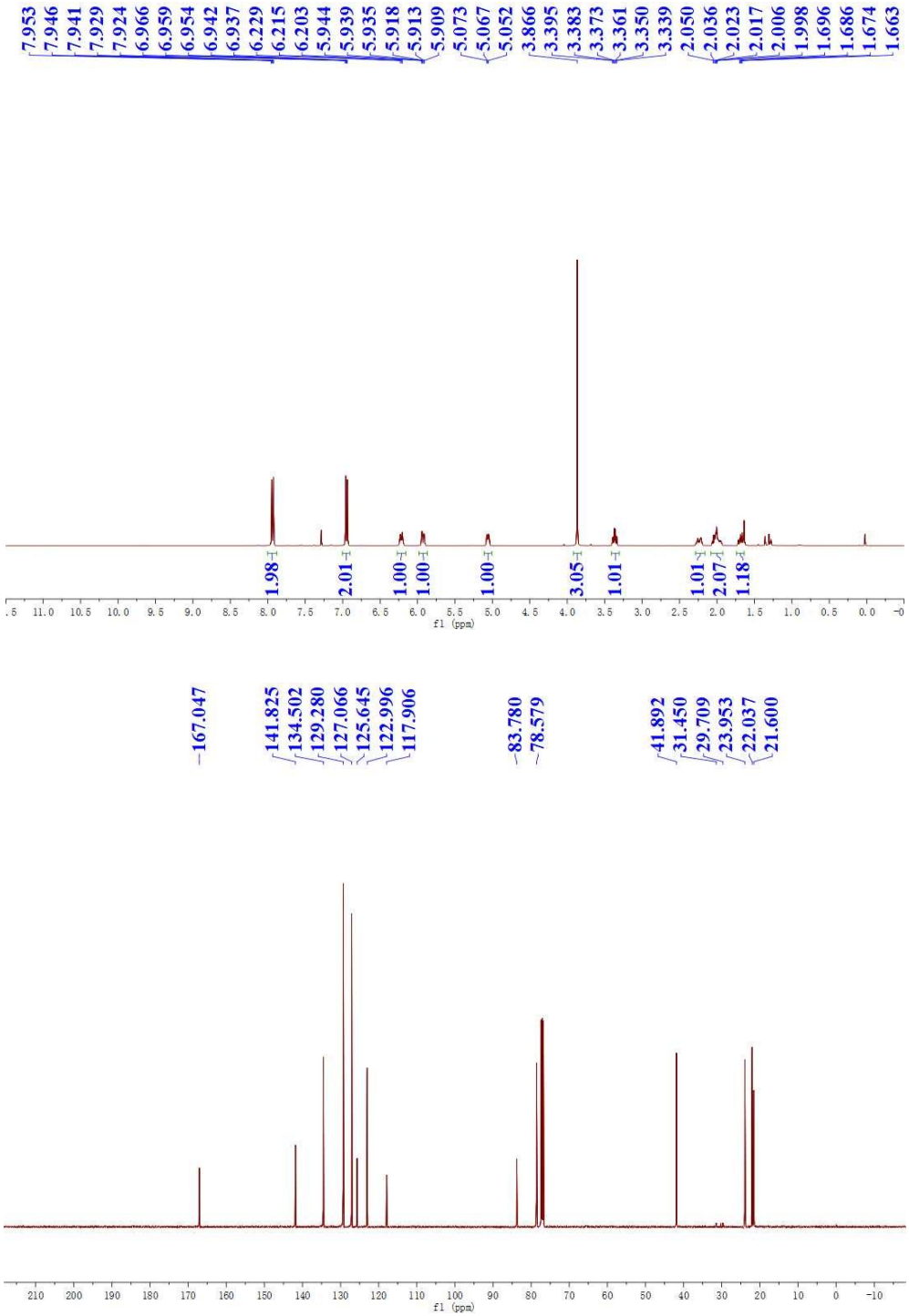


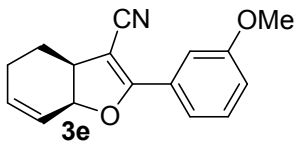
167.057
138.374
134.548
132.109
128.526
128.316
127.546
124.325
122.959
117.722
84.545
78.634
41.936
23.909
22.015
21.397

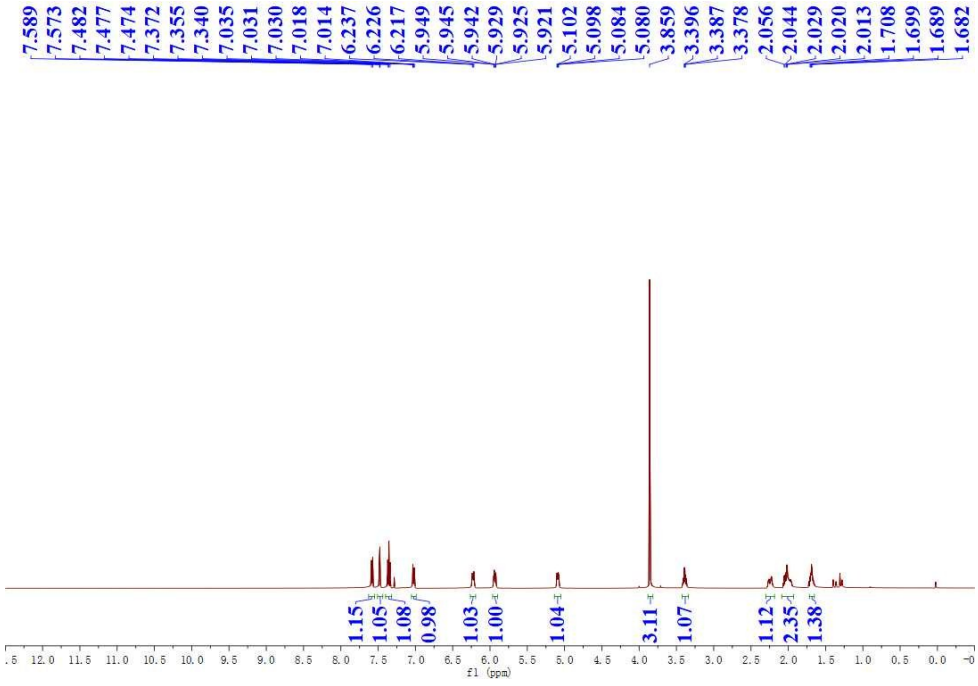


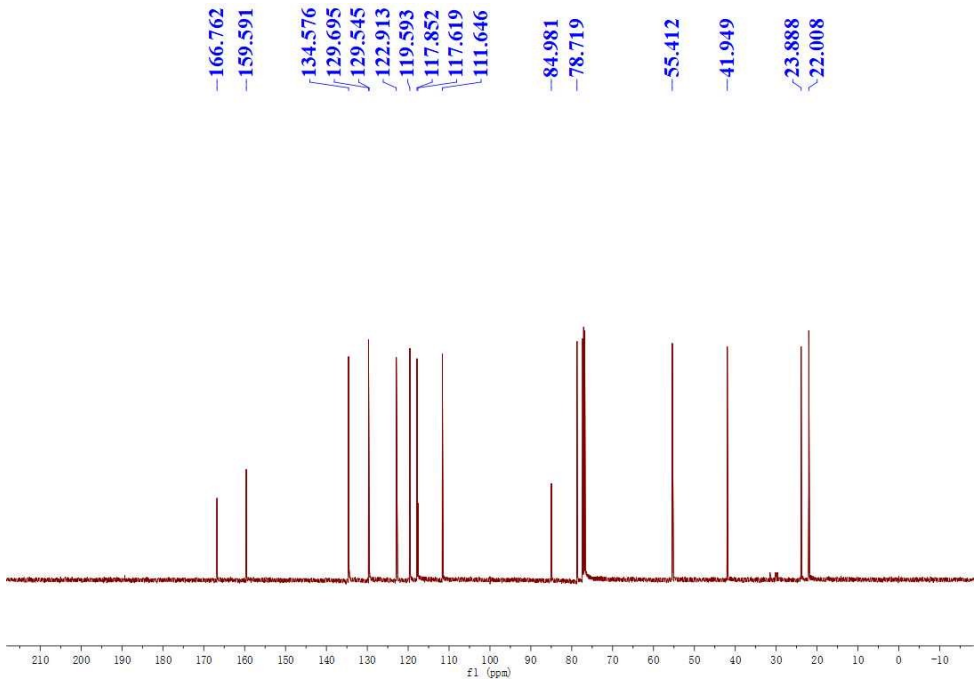

CN
Me
O

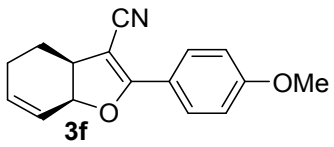
3d


7.953
7.946
7.941
7.929
7.924
6.966
6.959
6.954
6.942
6.937
6.229
6.215
6.203
5.944
5.939
5.935
5.918
5.913
5.909
5.073
5.067
5.052
3.866
3.395
3.383
3.373
3.361
3.350
3.339
2.050
2.036
2.023
2.017
2.006
1.998
1.696
1.686
1.674
1.663
1.98
2.01
1.00
1.00
1.00
3.05
1.01
1.01
2.07
1.18
f1 (ppm)
167.047
141.825
134.502
129.280
127.066
125.645
122.996
117.906
83.780
78.579
41.892
31.450
29.709
23.953
22.037
21.600
f1 (ppm)

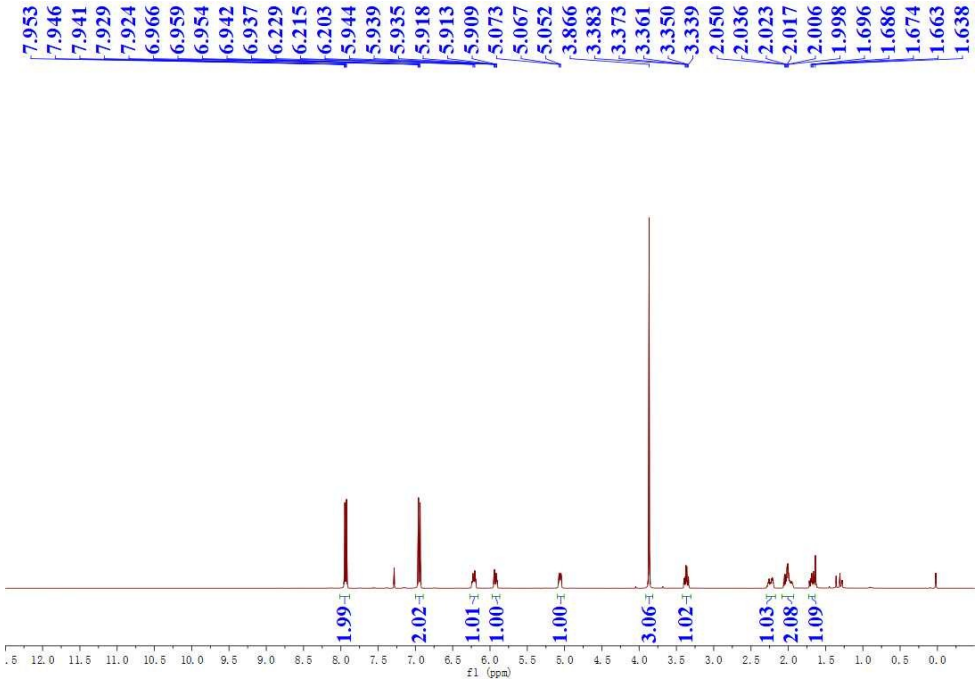

CN
OMe
O
3e

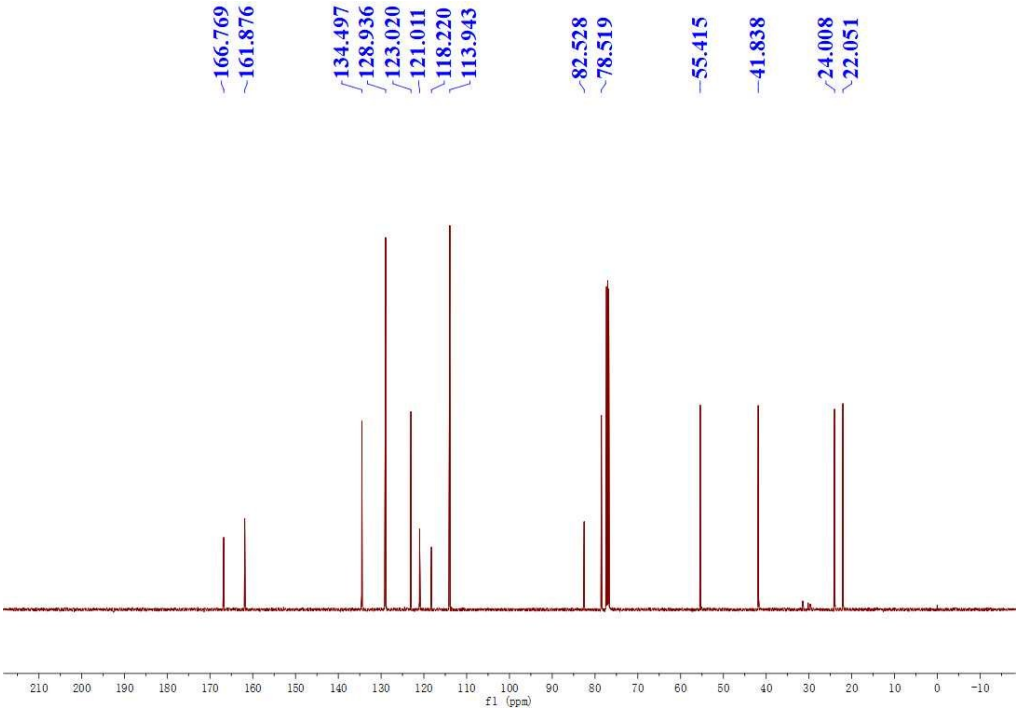

7.589
7.573
7.482
7.477
7.474
7.372
7.355
7.340
7.035
7.031
7.030
7.018
7.014
6.237
6.226
6.217
5.949
5.945
5.942
5.929
5.925
5.921
5.102
5.098
5.084
5.080
3.859
3.396
3.387
3.378
2.056
2.044
2.029
2.020
2.013
1.708
1.699
1.689
1.682
1.15
1.05
1.08
0.98
1.03
1.00
1.04
3.11
1.07
1.12
2.35
1.38
f1 (ppm)

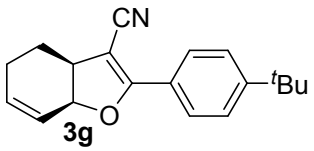

166.762
159.591
134.576
129.695
129.545
122.913
119.593
117.852
117.619
111.646
84.981
78.719
55.412
41.949
23.888
22.008
f1 (ppm)


CN
OMe
O

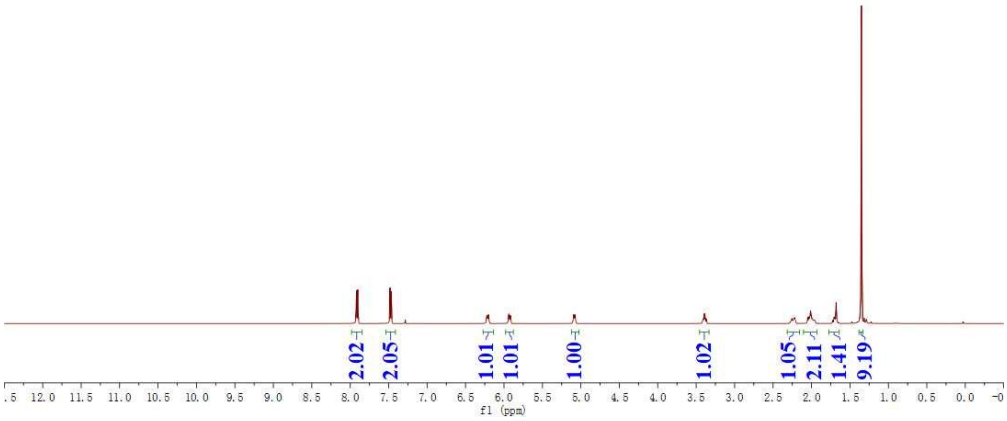
3f

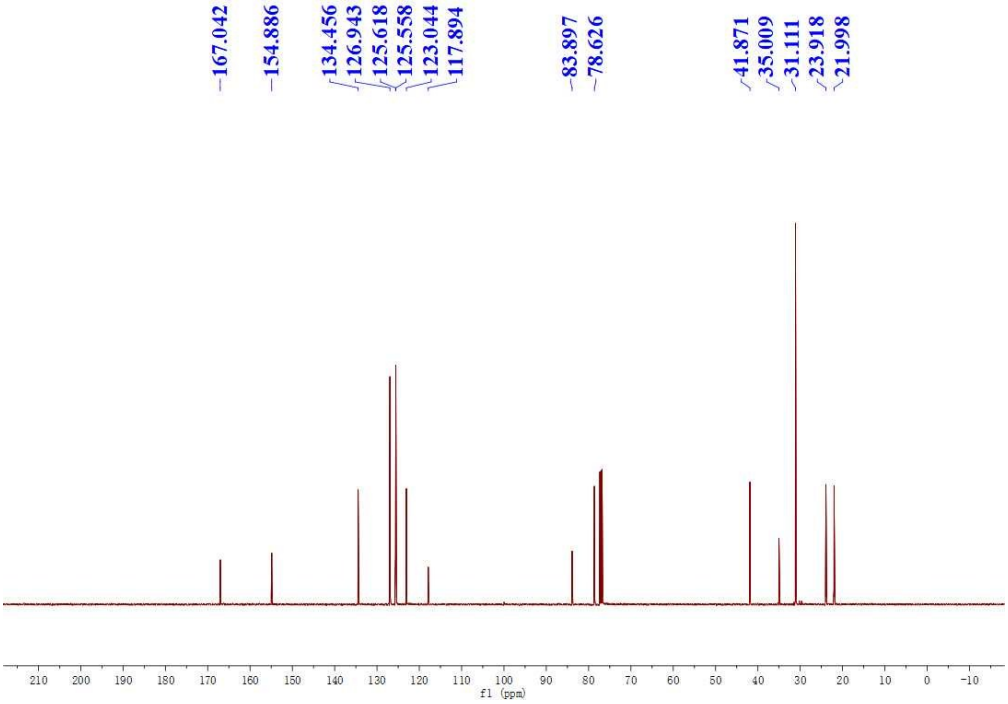

7.953
7.946
7.941
7.929
7.924
6.966
6.959
6.954
6.942
6.937
6.229
6.215
6.203
5.944
5.939
5.935
5.918
5.913
5.909
5.073
5.067
5.052
3.866
3.383
3.373
3.361
3.350
3.339
2.050
2.036
2.023
2.017
2.006
1.998
1.696
1.686
1.674
1.663
1.638
1.99
2.02
1.01
1.00
1.00
3.06
1.02
1.03
2.08
1.09
f1 (ppm)

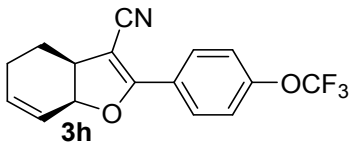

166.769
161.876
134.497
128.936
123.020
121.011
118.220
113.943
82.528
78.519
55.415
41.838
24.008
22.051
f1 (ppm)


CN
tBu
O
3g

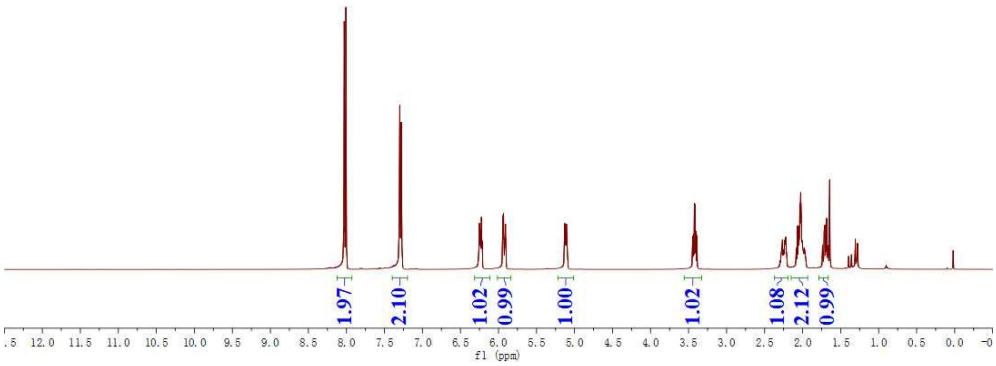

7.919
7.902
7.483
7.466
6.230
6.222
6.212
6.202
5.941
5.937
5.921
5.917
5.093
5.076
3.413
3.404
3.395
3.386
3.378
3.369
2.262
2.254
2.240
2.229
2.219
2.049
2.038
2.032
2.023
2.013
2.008
1.966
1.962
1.724
1.707
1.698
1.689
1.663
1.351


2.02
2.05
1.01
1.01
1.00
1.02
1.05
2.11
1.41
9.19
f1 (ppm)

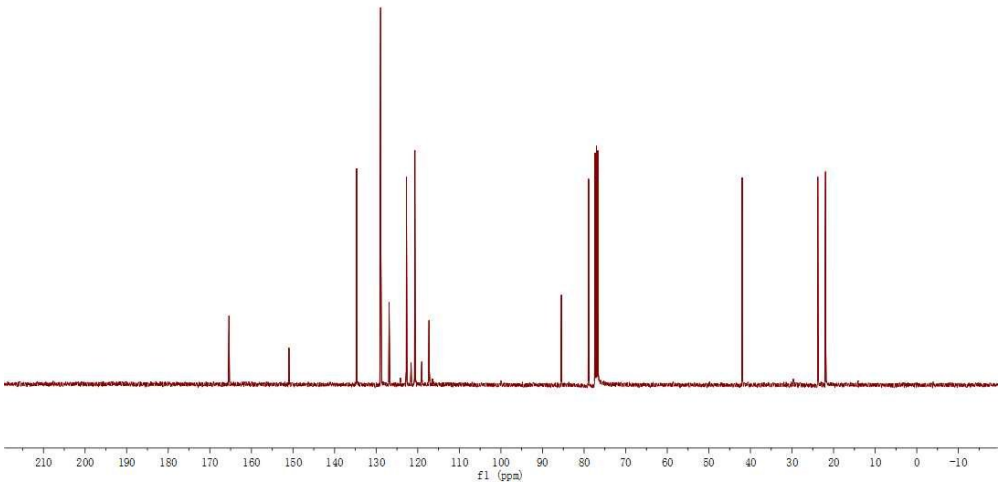

167.042
154.886
134.456
126.943
125.618
125.558
123.044
117.894
83.897
78.626
41.871
35.009
31.111
23.918
21.998
f1 (ppm)

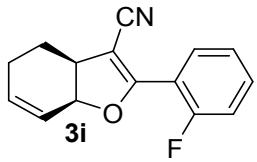


8.036
8.029
8.024
8.012
8.007
8.000
7.299
7.284
7.278
6.250
6.237
6.225
5.942
5.937
5.933
5.916
5.912
5.908
5.128
5.122
5.106
3.446
3.435
3.424
3.413
3.402
3.390
2.223
2.070
2.056
2.049
2.044
2.037
2.026
2.018
1.717
1.706
1.695
1.684



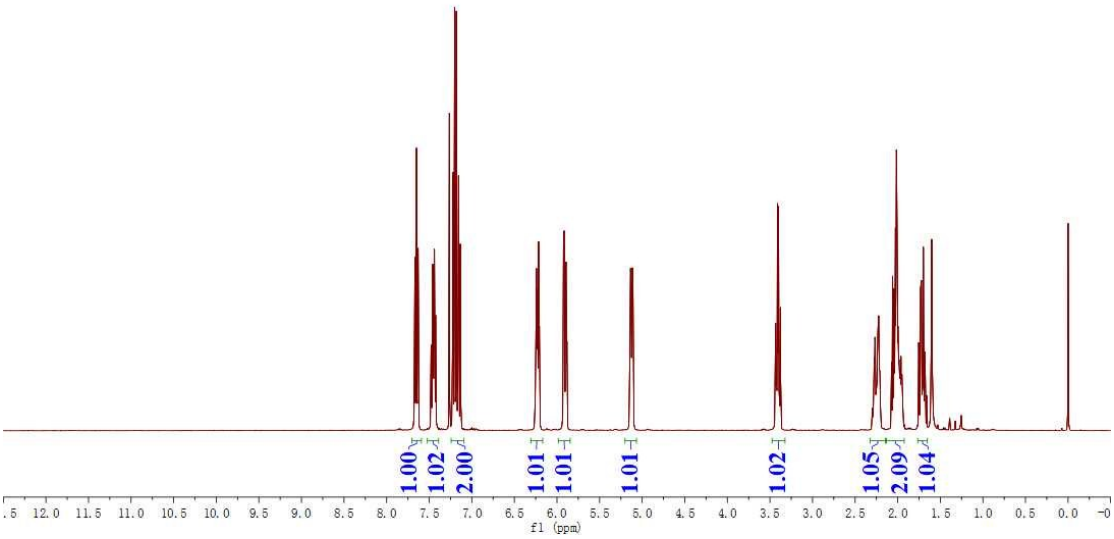
165.383
151.000
150.982
134.715
128.919
126.886
124.170
122.732
121.601
120.700
119.033
117.280
85.443
78.924
41.989
23.805
21.931

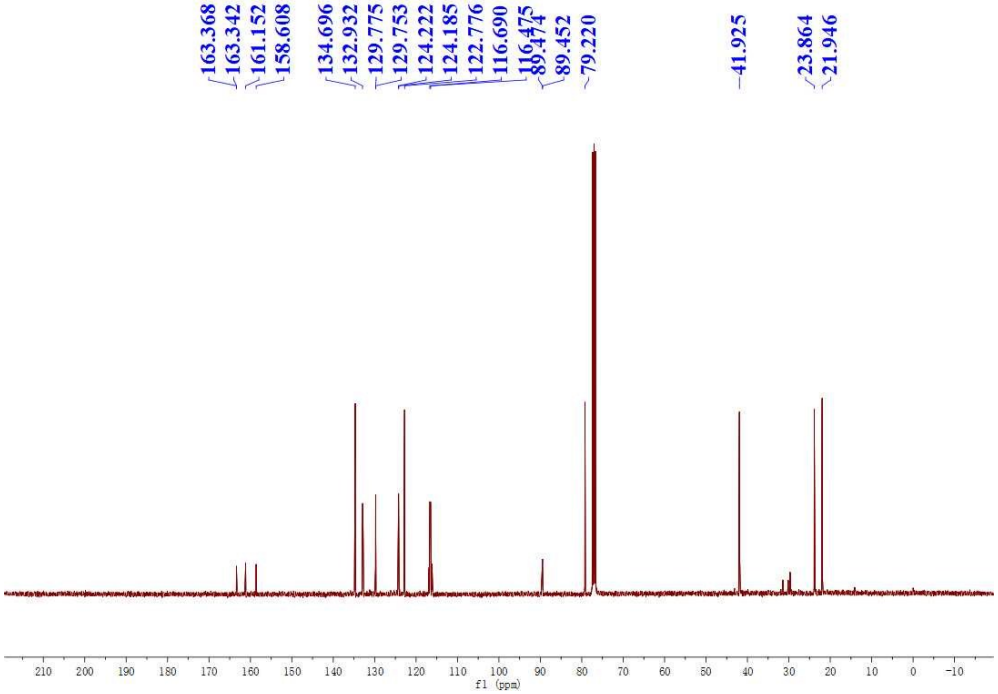


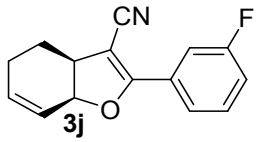

CN
O
F

3i

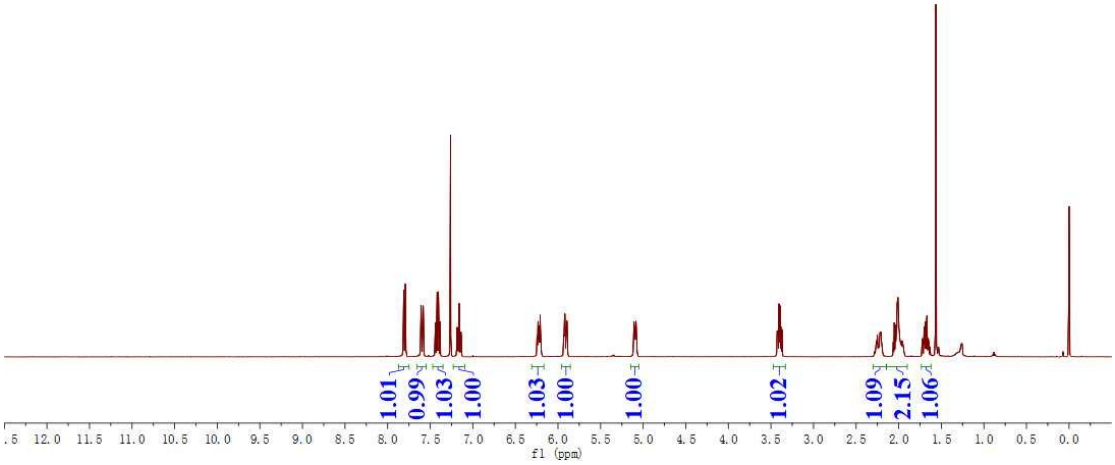

7.676
7.667
7.652
7.649
7.634
7.630
7.459
7.442
7.439
7.263
7.223
7.220
7.203
7.201
7.182
7.161
7.158
7.156
7.153
7.135
7.132
6.242
6.216
5.923
5.918
5.914
5.898
5.893
5.889
5.136
5.115
3.411
3.399
2.060
2.027
2.015
2.011
2.007
1.699


1.00
1.02
2.00
1.01
1.01
1.01
1.02
1.05
2.09
1.04
f1 (ppm)

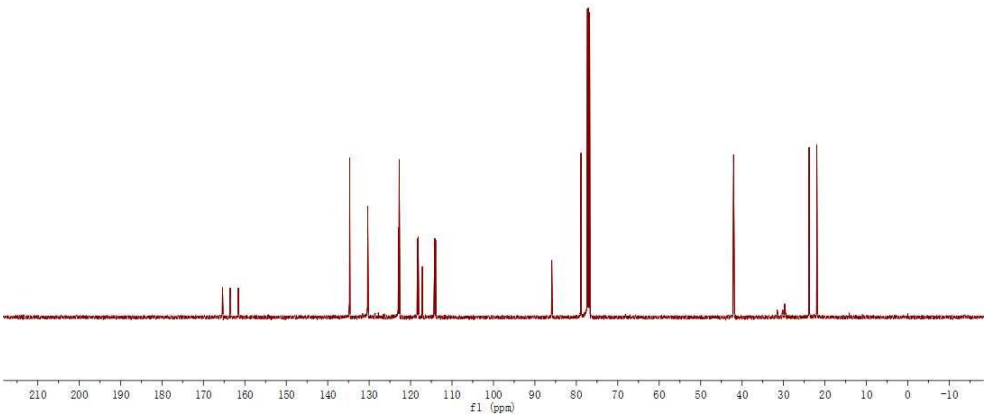

163.368
163.342
161.152
158.608
134.696
132.932
129.775
129.753
124.222
124.185
122.776
116.690
116.475
89.474
89.452
79.220
41.925
23.864
21.946
f1 (ppm)

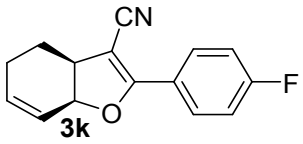

CN
F
O
3j

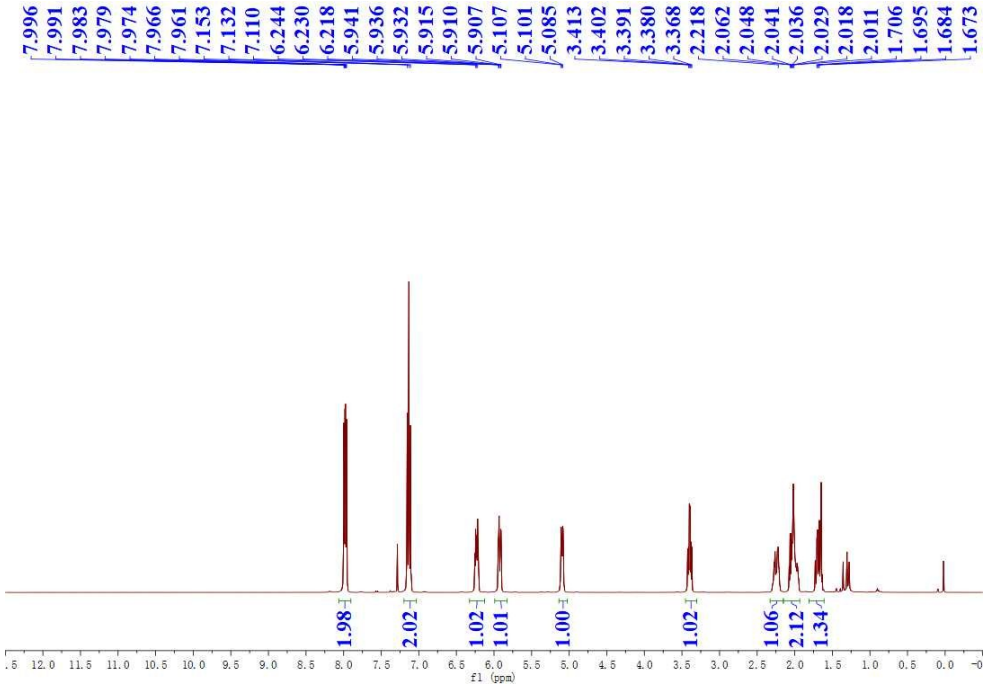

7.812
7.792
7.611
7.607
7.601
7.584
7.582
7.577
7.439
7.424
7.418
7.404
7.398
7.384
6.234
6.221
6.209
5.927
5.922
5.918
5.902
5.897
5.893
5.108
5.101
5.085
3.405
3.393
3.383
3.371
2.052
2.038
2.026
2.019
2.008
2.001
1.702
1.691
1.668

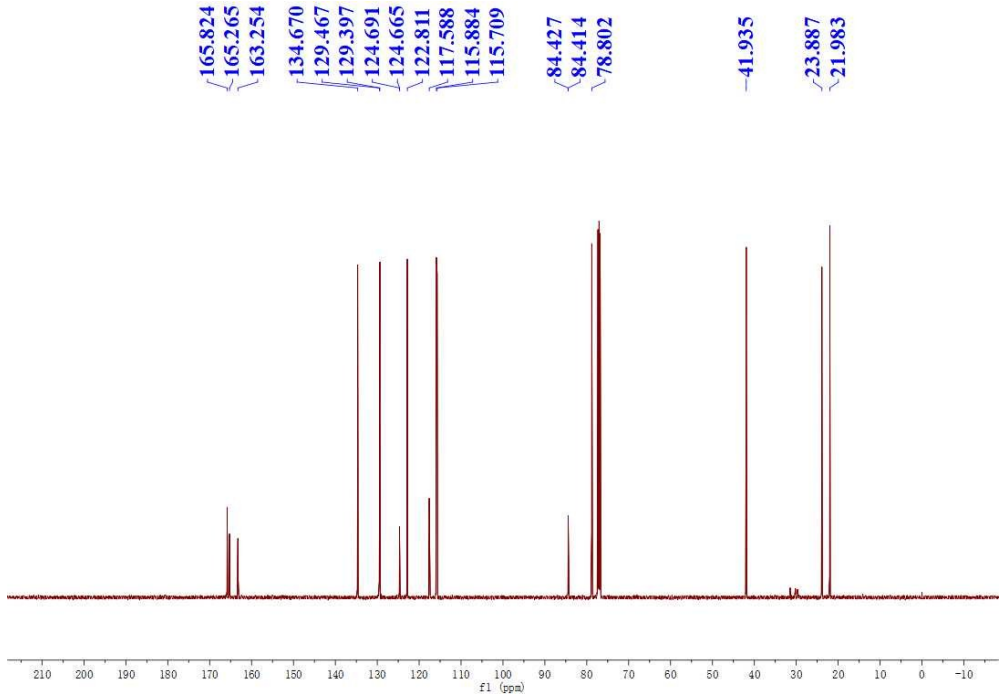

1.01
0.99
1.03
1.00
1.03
1.00
1.00
1.02
1.09
2.15
1.06
f1 (ppm)

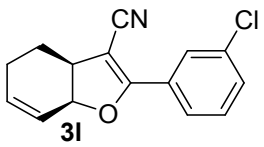

165.394
163.548
161.583
134.714
130.357
130.292
122.927
122.904
122.748
118.336
118.168
117.142
114.152
113.962
85.925
78.864
42.033
23.796
21.953

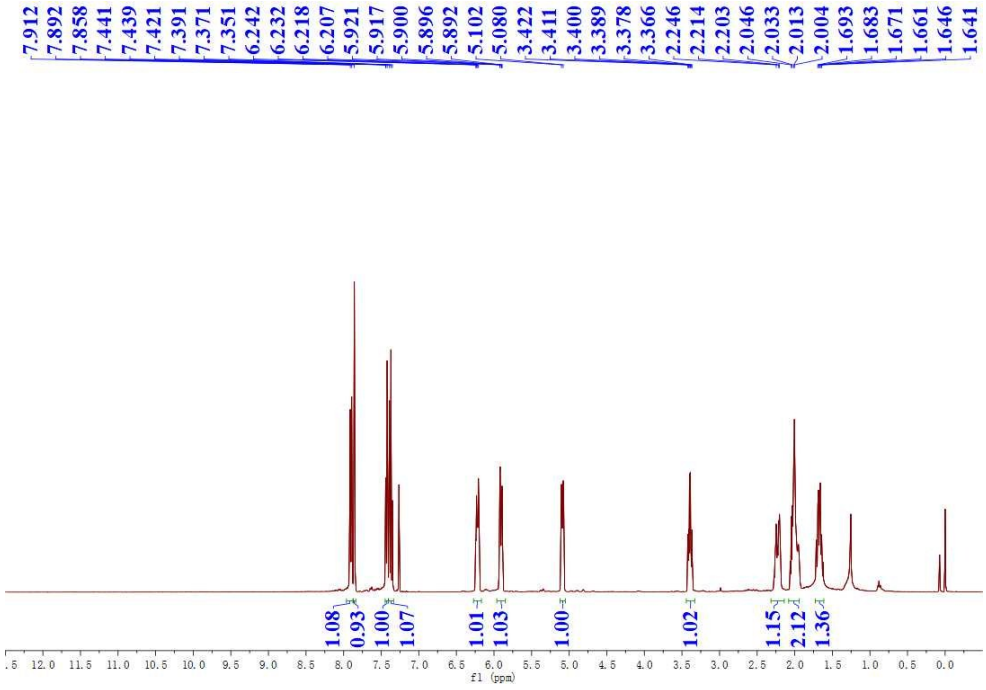

f1 (ppm)

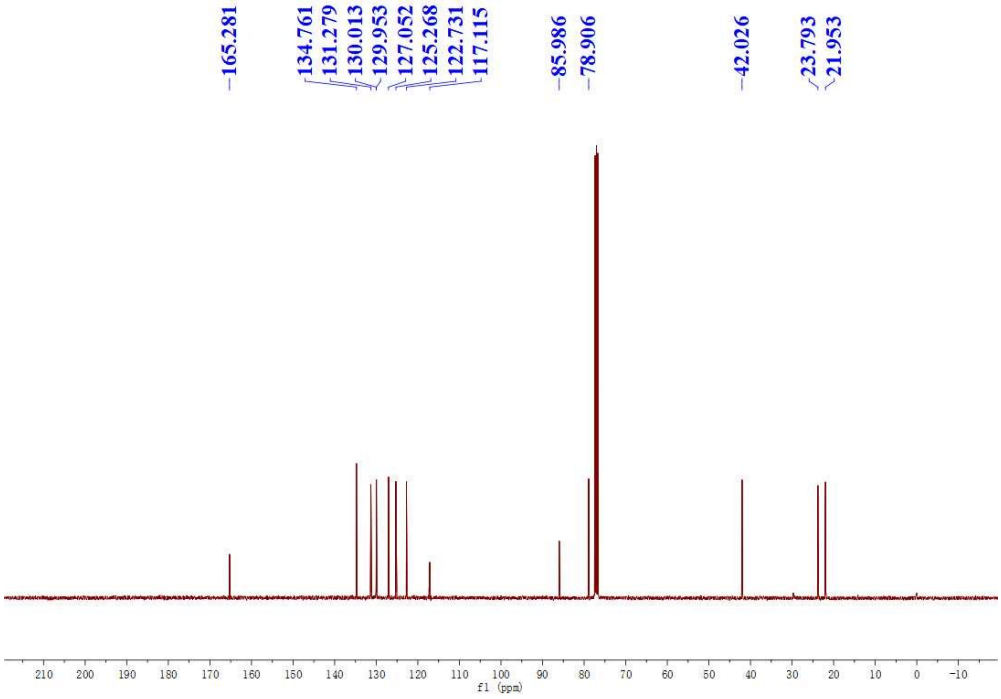

CN
F
O
3k

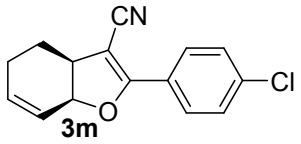

7.996
7.991
7.983
7.979
7.974
7.966
7.961
7.153
7.132
7.110
6.244
6.230
6.218
5.941
5.936
5.932
5.915
5.910
5.907
5.107
5.101
5.085
3.413
3.402
3.391
3.380
3.368
2.218
2.062
2.048
2.041
2.036
2.029
2.018
2.011
1.706
1.695
1.684
1.673
1.98
2.02
1.02
1.01
1.00
1.02
1.06
2.12
1.34
f1 (ppm)

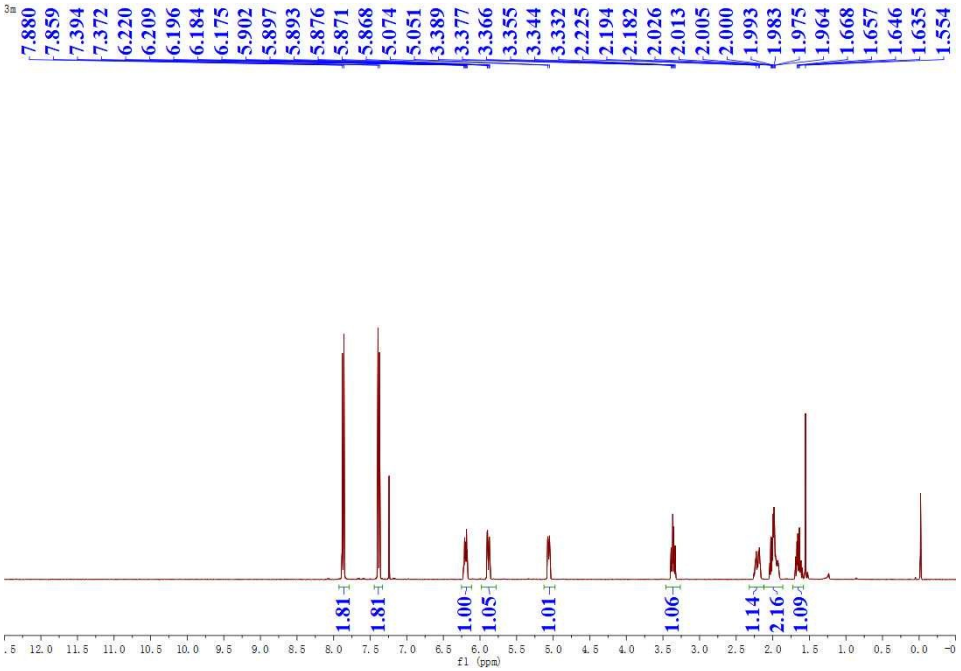

165.824
165.265
163.254
134.670
129.467
129.397
124.691
124.665
122.811
117.588
115.884
115.709
84.427
84.414
78.802
41.935
23.887
21.983
f1 (ppm)

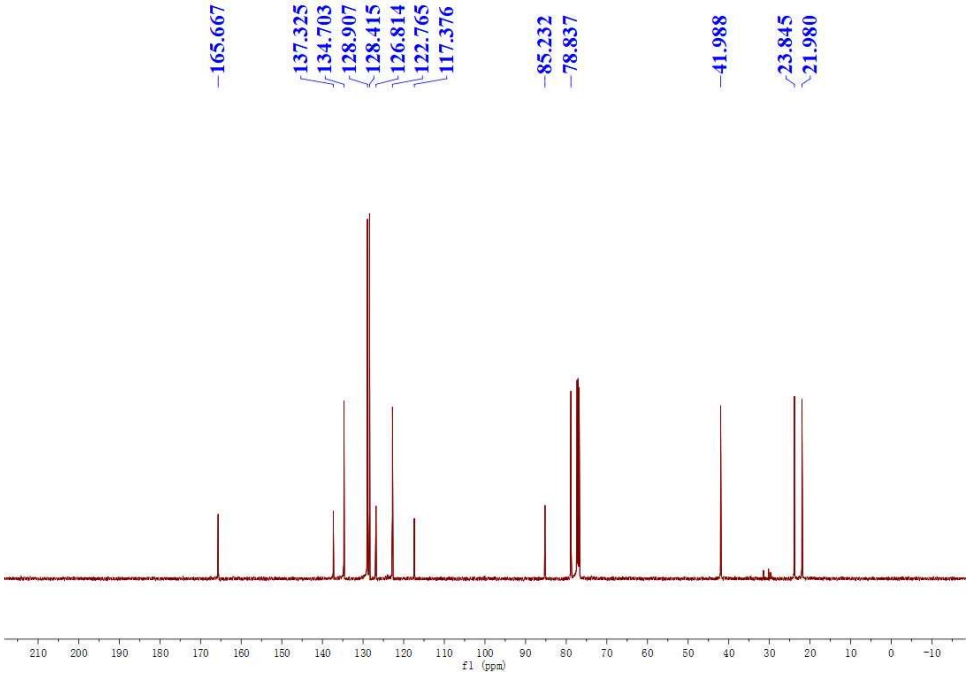

CN
Cl
O
3l

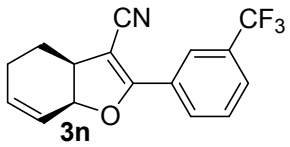

7.912
7.892
7.858
7.441
7.439
7.421
7.391
7.371
7.351
6.242
6.232
6.218
6.207
5.921
5.917
5.900
5.896
5.892
5.102
5.080
3.422
3.411
3.400
3.389
3.378
3.366
2.246
2.214
2.203
2.046
2.033
2.013
2.004
1.693
1.683
1.671
1.661
1.646
1.641
1.08
0.93
1.00
1.07
1.01
1.03
1.00
1.02
1.15
2.12
1.36
f1 (ppm)

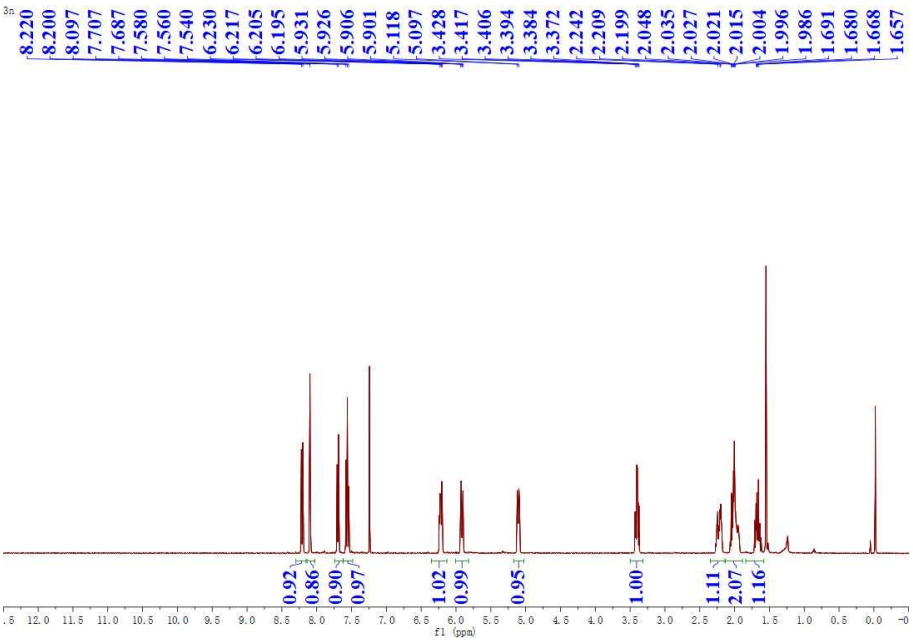

165.281
134.761
131.279
130.013
129.953
127.052
125.268
122.731
117.115
85.986
78.906
42.026
23.793
21.953
f1 (ppm)

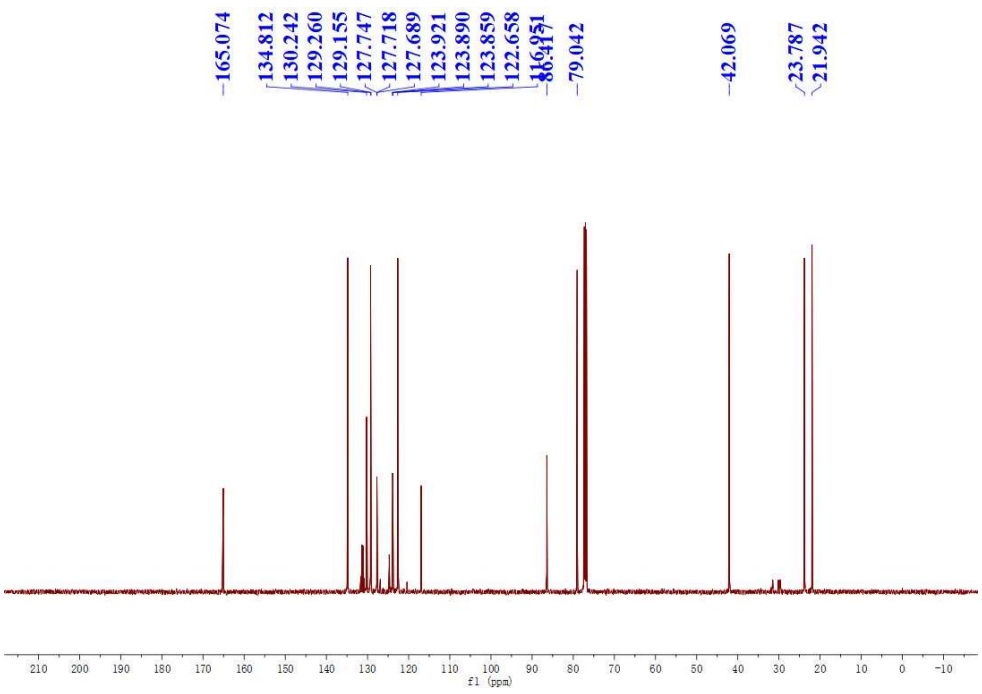

CN
Cl
O
3m

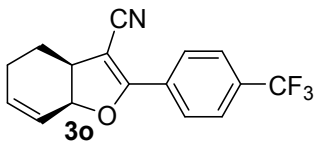

3m
7.880
7.859
7.394
7.372
6.220
6.209
6.196
6.184
6.175
5.902
5.897
5.893
5.876
5.871
5.868
5.074
5.051
3.389
3.377
3.366
3.355
3.344
3.332
2.225
2.194
2.182
2.026
2.013
2.005
2.000
1.993
1.983
1.975
1.964
1.668
1.657
1.646
1.635
1.554
1.81
1.81
1.00
1.05
1.01
1.06
1.14
2.16
1.09
f1 (ppm)


165.667
137.325
134.703
128.907
128.415
126.814
122.765
117.376
85.232
78.837
41.988
23.845
21.980
f1 (ppm)

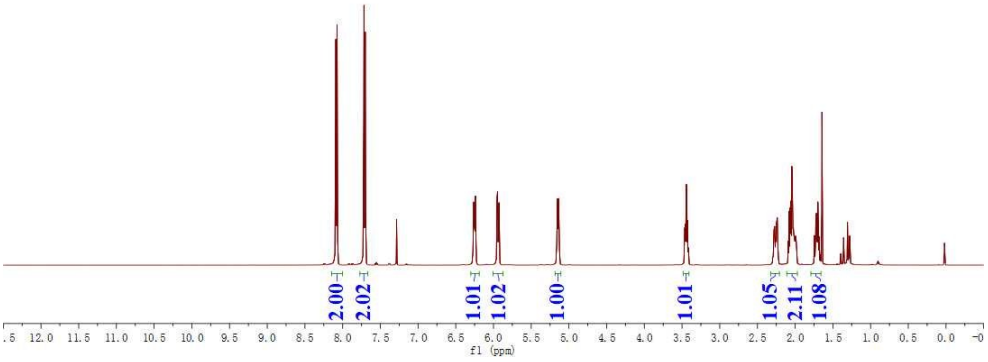

CN
CF3
O
3n


3n
8.220
8.200
8.097
7.707
7.687
7.580
7.560
7.540
6.230
6.217
6.205
6.195
5.931
5.926
5.906
5.901
5.118
5.097
3.428
3.417
3.406
3.394
3.384
3.372
2.242
2.209
2.199
2.048
2.035
2.027
2.021
2.015
2.004
1.996
1.986
1.691
1.680
1.668
1.657
0.92
0.86
0.90
0.97
1.02
0.99
0.95
1.00
1.11
2.07
1.16
f1 (ppm)

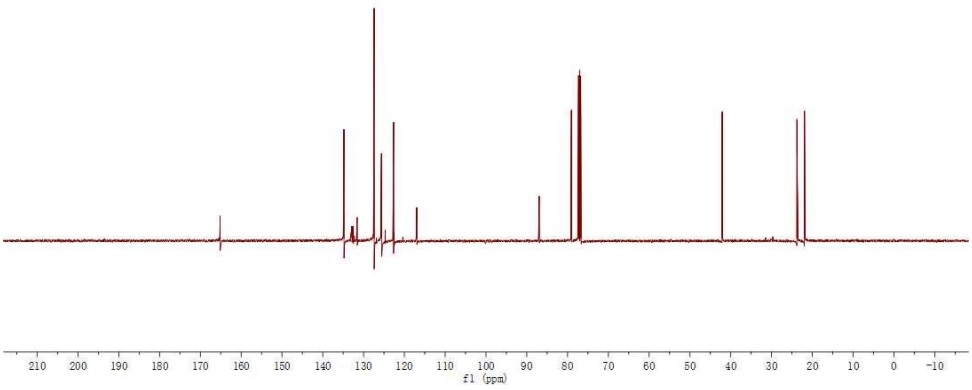

165.074
134.812
130.242
129.260
129.155
127.747
127.718
127.689
123.921
123.890
123.859
122.658
116.951
86.417
79.042
42.069
23.787
21.942
f1 (ppm)

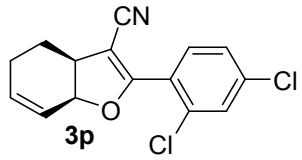


8.090
8.073
7.717
7.701
6.269
6.261
6.250
6.241
6.234
5.953
5.949
5.946
5.933
5.929
5.926
5.154
5.136
3.463
3.454
3.446
3.437
3.428
3.419
2.272
2.247
2.237
2.080
2.069
2.063
2.059
2.054
2.044
2.037
2.024
1.726
1.717
1.708
1.699
1.645



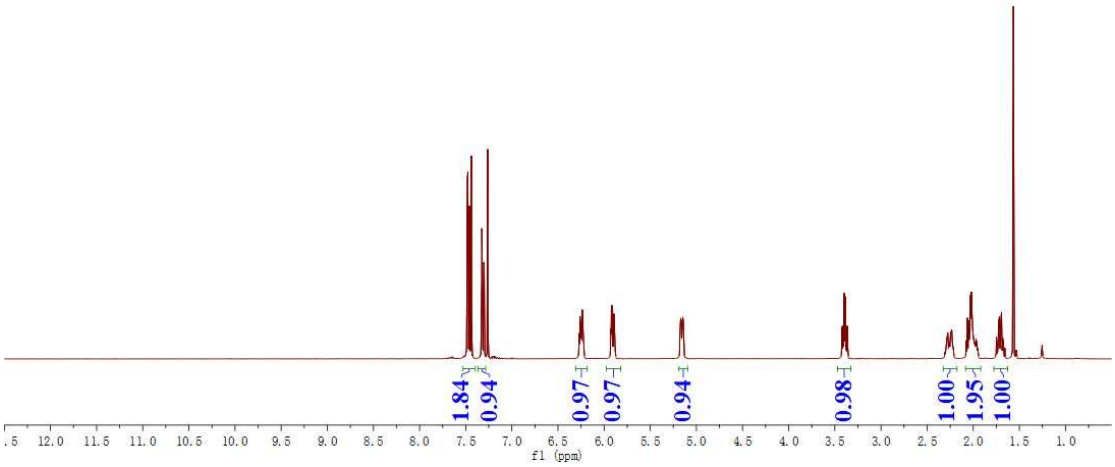
165.160
134.810
132.843
132.582
131.589
127.421
127.402
125.634
125.605
125.574
125.529
122.652
79.043
42.084
23.756
21.932

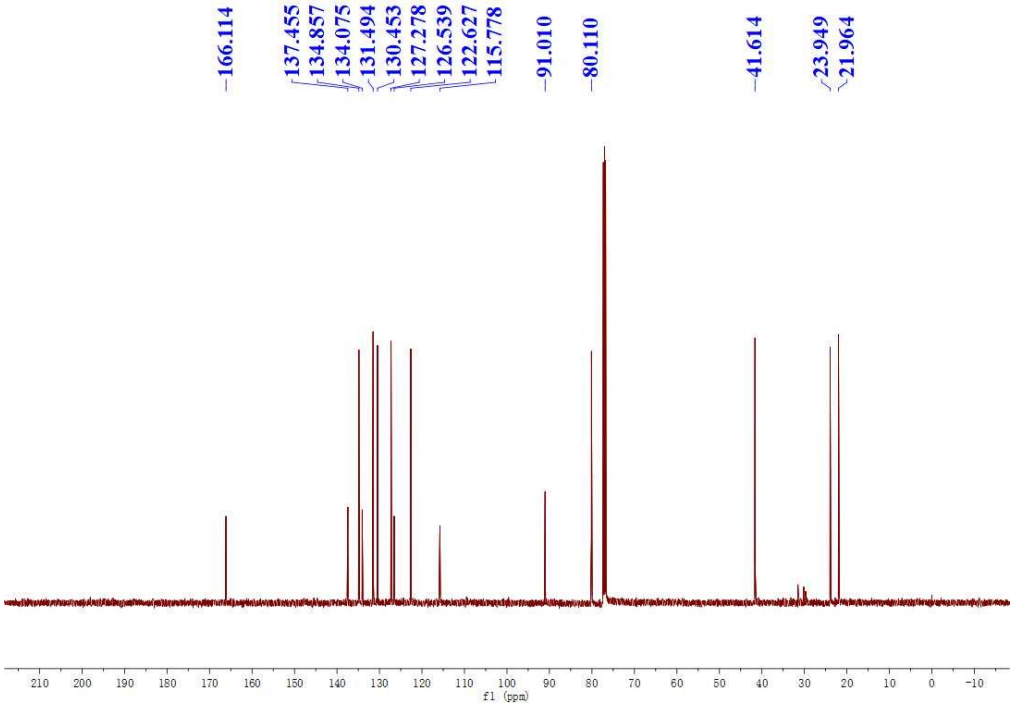


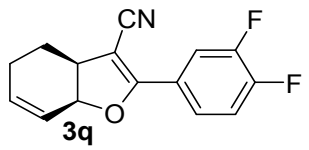

CN
Cl
O
Cl

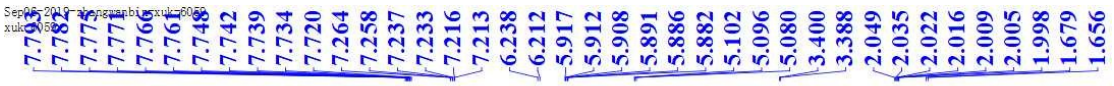
3p

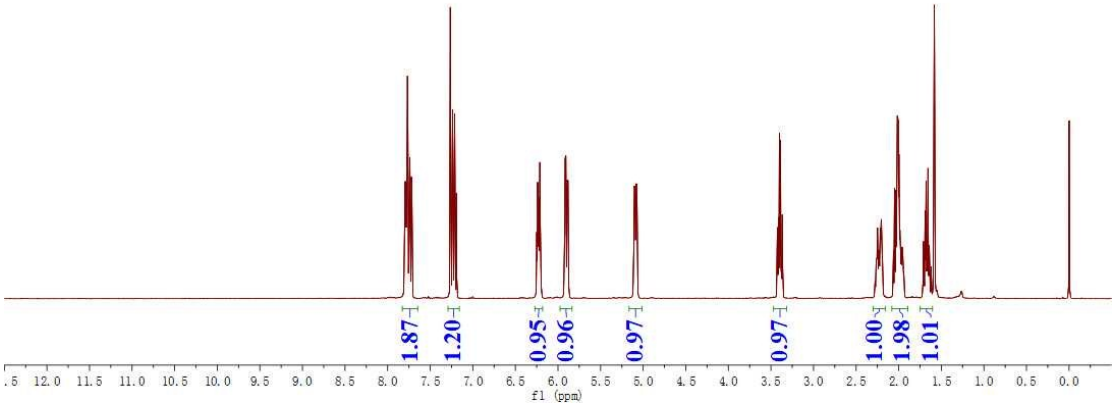

7.477
7.455
7.438
7.325
7.326
7.304
7.299
6.260
6.247
6.235
5.926
5.921
5.917
5.912
5.896
5.891
5.887
5.171
5.164
5.148
3.421
3.410
3.399
3.388
3.377
3.365
2.062
2.048
2.041
2.036
2.029
2.022
2.019
2.011
1.727
1.716
1.704
1.694

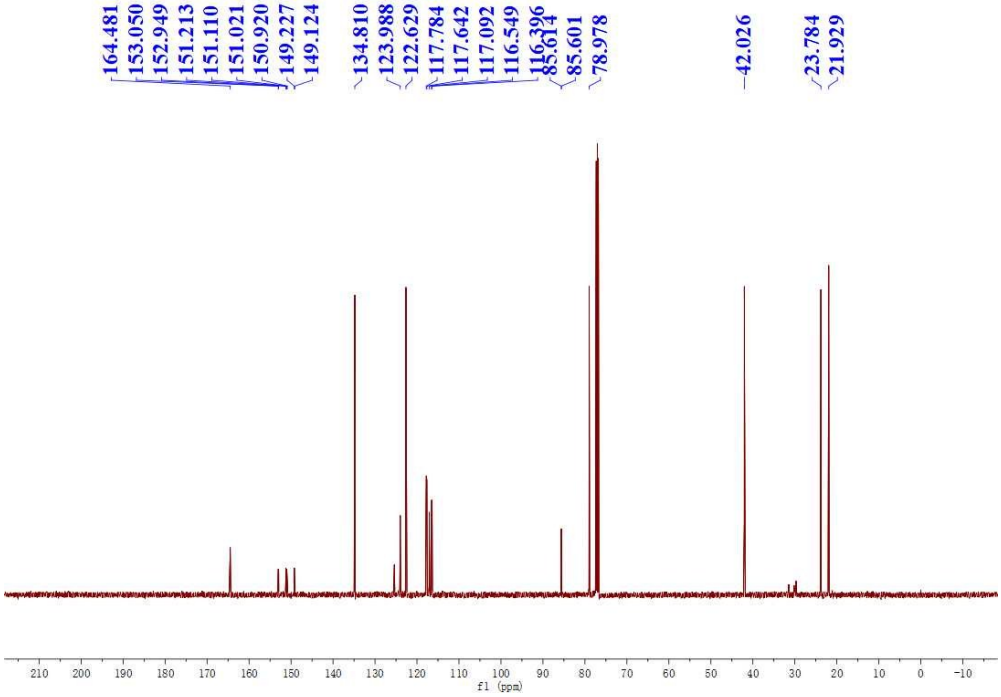

1.84
0.94
0.97
0.97
0.94
0.98
1.00
1.95
1.00
f1 (ppm)

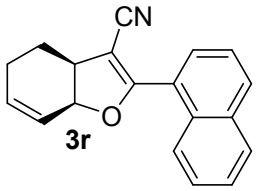

166.114
137.455
134.857
134.075
131.494
130.453
127.278
126.539
122.627
115.778
91.010
80.110
41.614
23.949
21.964
f1 (ppm)

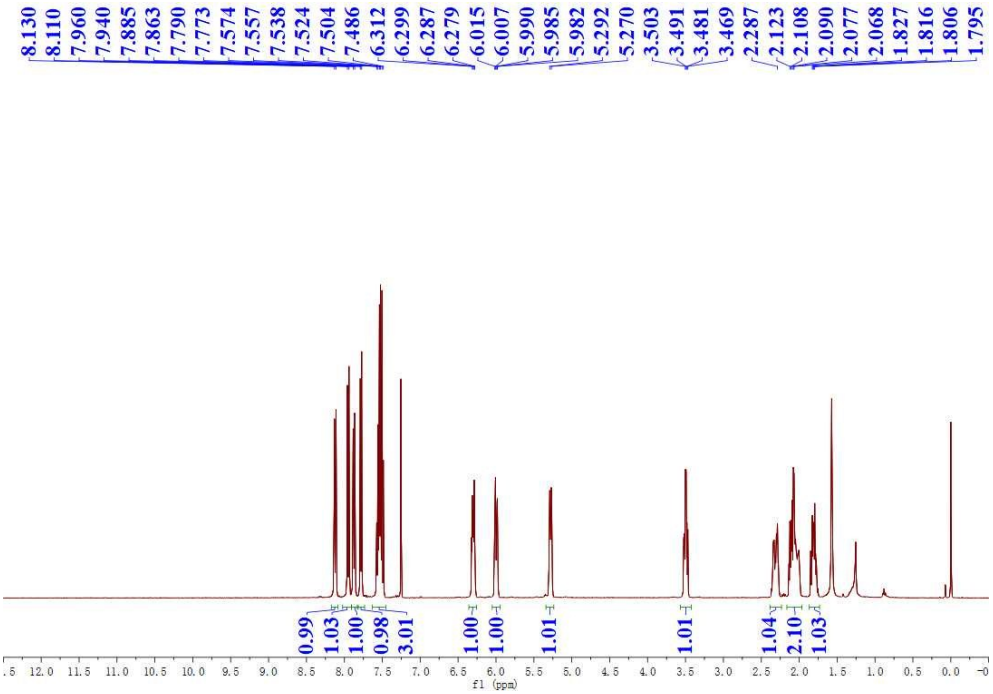

CN
F
F
O
3q

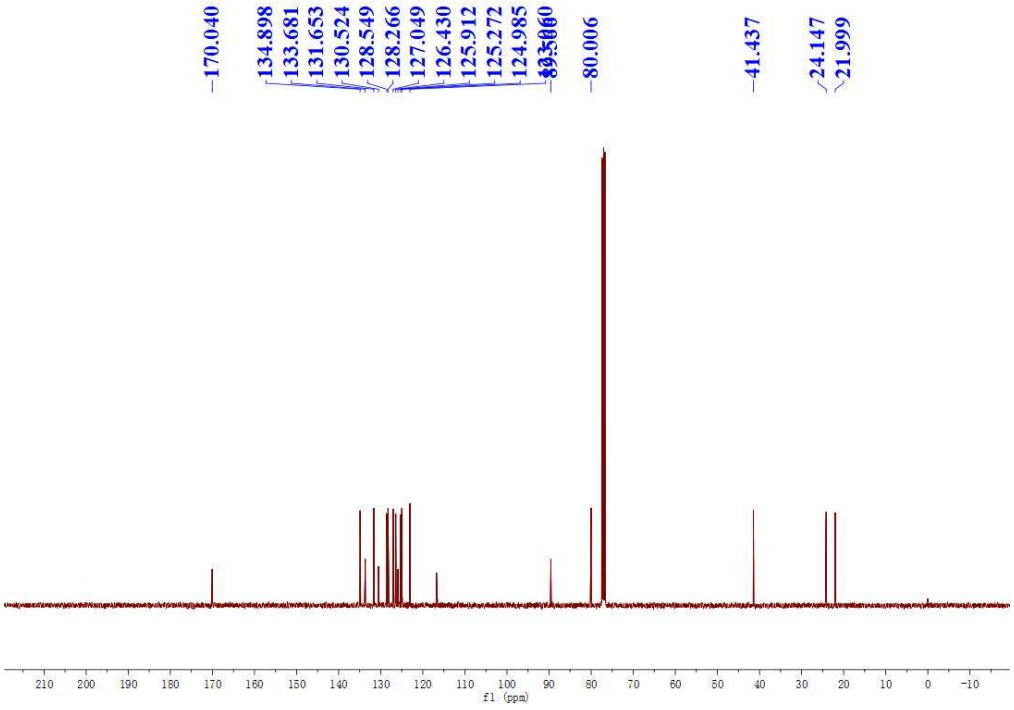

7.787
7.775
7.771
7.766
7.761
7.748
7.742
7.739
7.734
7.720
7.264
7.258
7.237
7.233
7.216
7.213
6.238
6.212
5.917
5.912
5.908
5.891
5.886
5.882
5.102
5.096
5.080
3.400
3.388
2.049
2.035
2.022
2.016
2.009
2.005
1.998
1.679
1.656

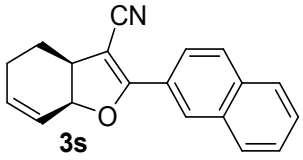

1.87
1.20
0.95
0.96
0.97
0.97
1.00
1.98
1.01
f1 (ppm)


164.481
153.050
152.949
151.213
151.110
151.021
150.920
149.227
149.124
134.810
123.988
122.629
117.784
117.642
117.092
116.549
116.396
85.614
85.601
78.978
42.026
23.784
21.929
f1 (ppm)

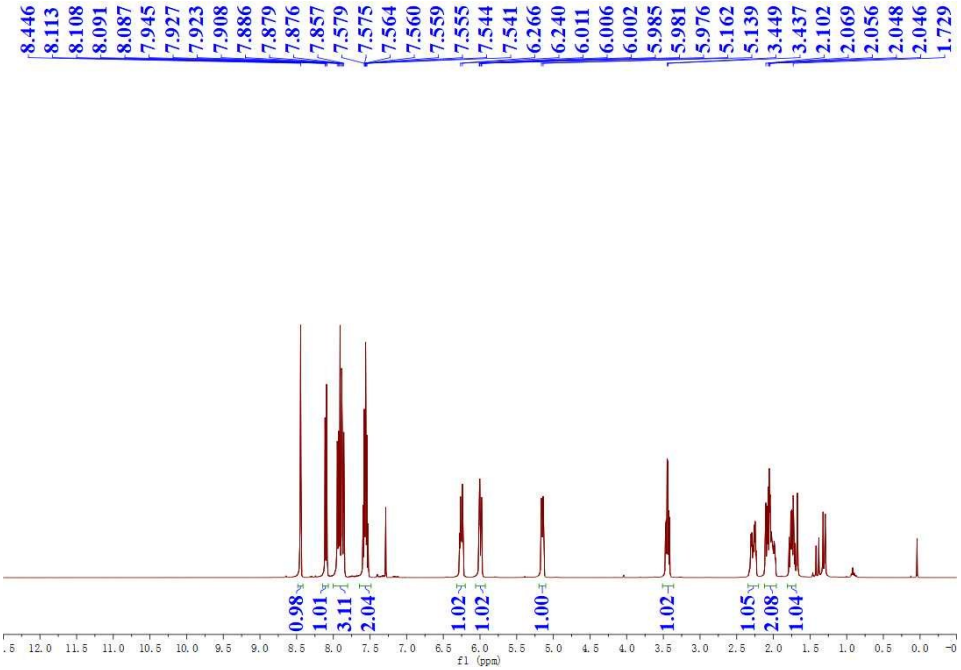

CN
O
3r

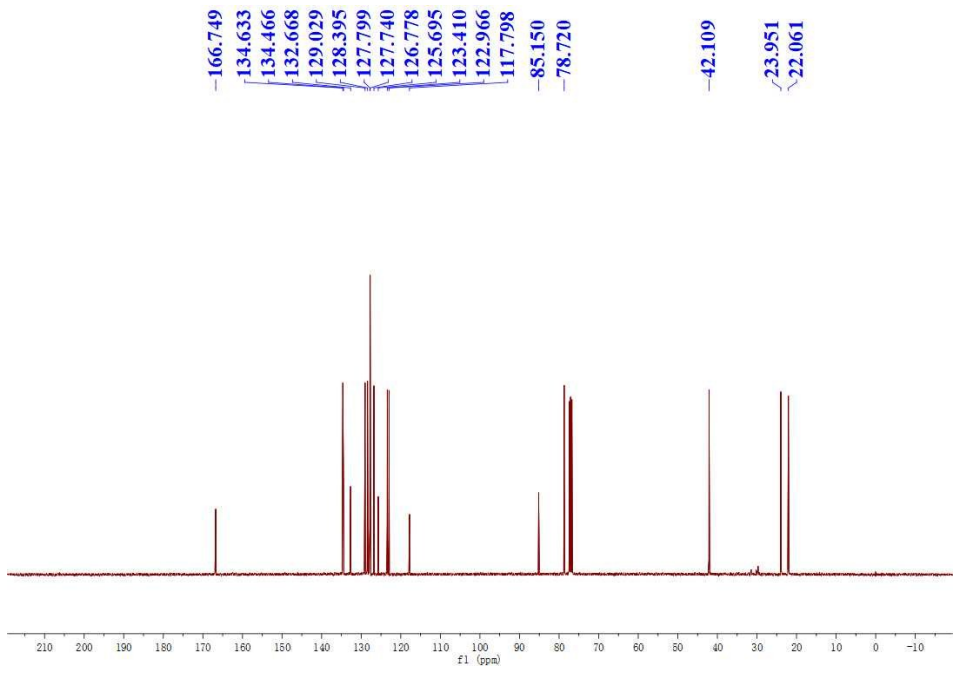

8.130
8.110
7.960
7.940
7.885
7.863
7.790
7.773
7.574
7.557
7.538
7.524
7.504
7.486
6.312
6.299
6.287
6.279
6.015
6.007
5.990
5.985
5.982
5.292
5.270
3.503
3.491
3.481
3.469
2.287
2.123
2.108
2.090
2.077
2.068
1.827
1.816
1.806
1.795
0.99
1.03
1.00
0.98
3.01
1.00
1.00
1.01
1.01
1.04
2.10
1.03
f1 (ppm)

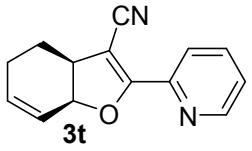

170.040
134.898
133.681
131.653
130.524
128.549
128.266
127.049
126.430
125.912
125.272
124.985
80.006
41.437
24.147
21.999
f1 (ppm)


CN
O

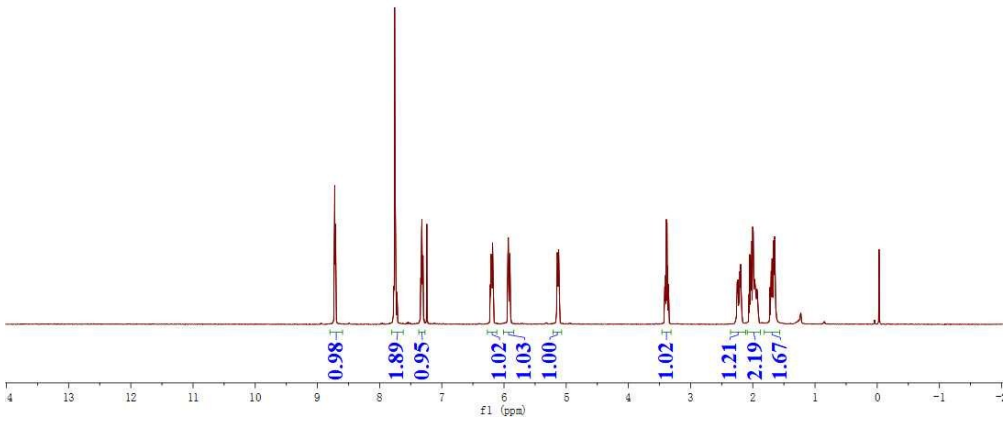
3s

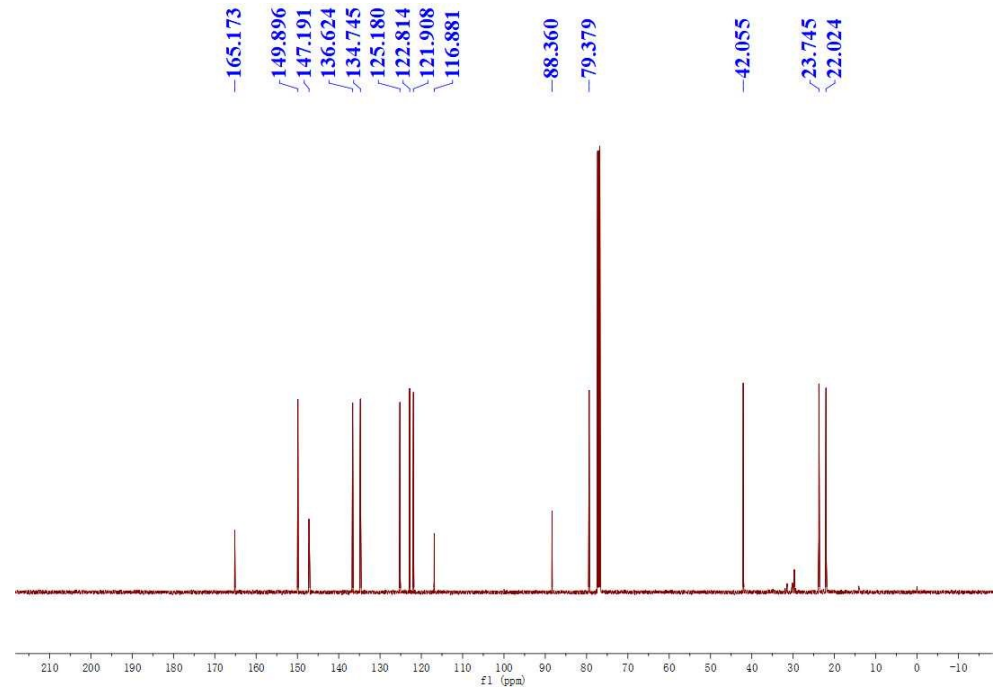

8.446
8.113
8.108
8.091
8.087
7.945
7.927
7.923
7.908
7.886
7.879
7.876
7.857
7.579
7.575
7.564
7.560
7.559
7.555
7.544
7.541
6.266
6.240
6.011
6.006
6.002
5.985
5.981
5.976
5.162
5.139
3.449
3.437
2.102
2.069
2.056
2.048
2.046
1.729
0.98
1.01
3.11
2.04
1.02
1.02
1.00
1.02
1.05
2.08
1.04
f1 (ppm)

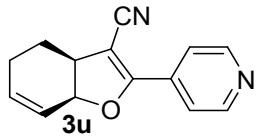

166.749
134.633
134.466
132.668
129.029
128.395
127.799
127.740
126.778
125.695
123.410
122.966
117.798
85.150
78.720
42.109
23.951
22.061
f1 (ppm)

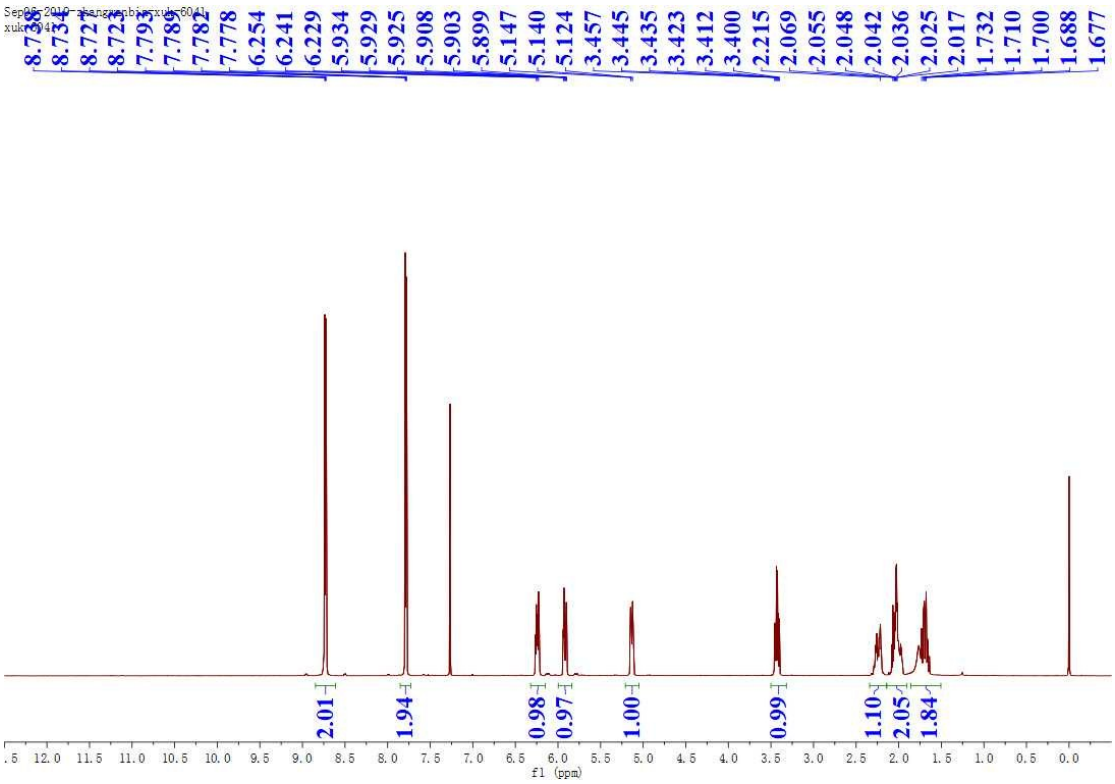

CN
O
N
3t

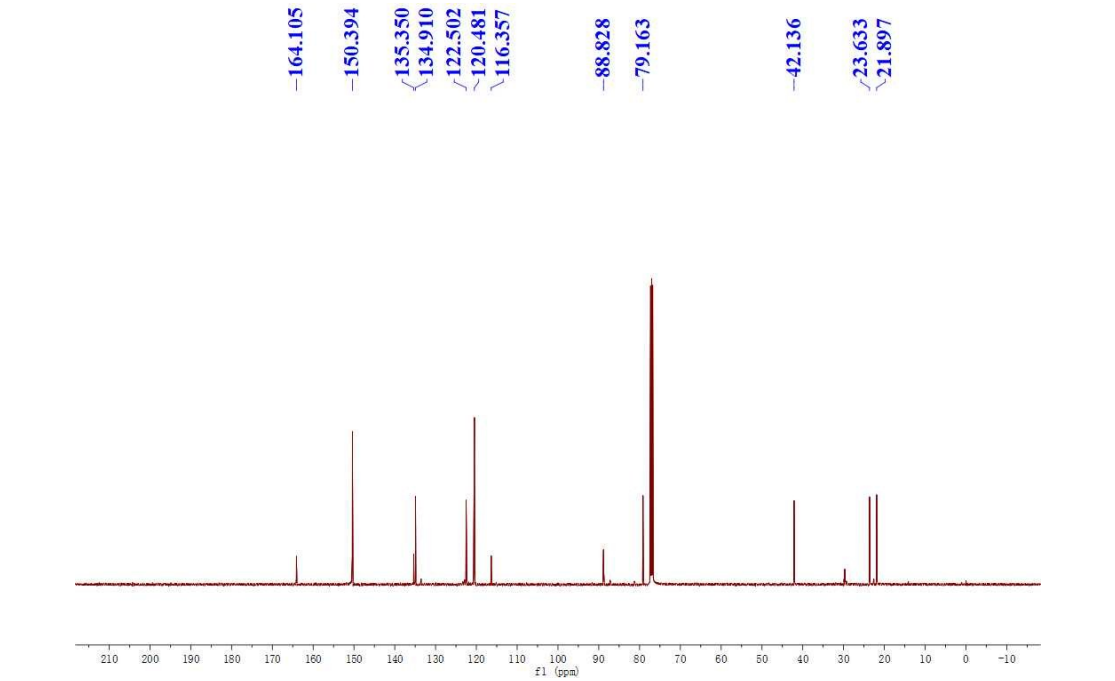

3t
8.723
8.711
7.759
7.756
7.743
7.739
7.336
7.330
7.324
7.320
7.314
7.308
7.302
6.209
6.196
6.184
5.936
5.931
5.927
5.911
5.906
5.902
5.144
5.121
3.391
3.380
3.369
2.196
2.048
2.034
2.015
2.003
1.993
1.703
1.691
1.680
1.669
1.656
1.648

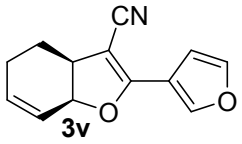

0.98
1.89
0.95
1.02
1.03
1.00
1.02
1.21
2.19
1.67
f1 (ppm)


165.173
149.896
147.191
136.624
134.745
125.180
122.814
121.908
116.881
88.360
79.379
42.055
23.745
22.024
f1 (ppm)

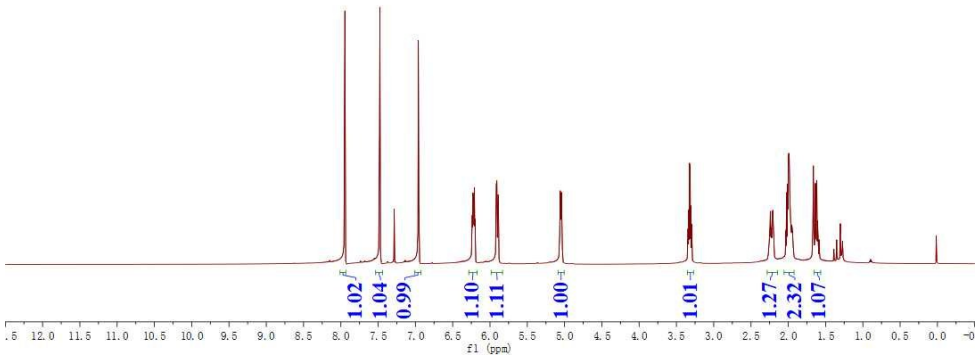

CN
N
O
3u


8.736
8.734
8.724
8.723
7.793
7.789
7.782
7.778
6.254
6.241
6.229
5.934
5.929
5.925
5.908
5.903
5.899
5.147
5.140
5.124
3.457
3.445
3.435
3.423
3.412
3.400
2.215
2.069
2.055
2.048
2.042
2.036
2.025
2.017
1.732
1.710
1.700
1.688
1.677
2.01
1.94
0.98
0.97
1.00
0.99
1.10
2.05
1.84
f1 (ppm)

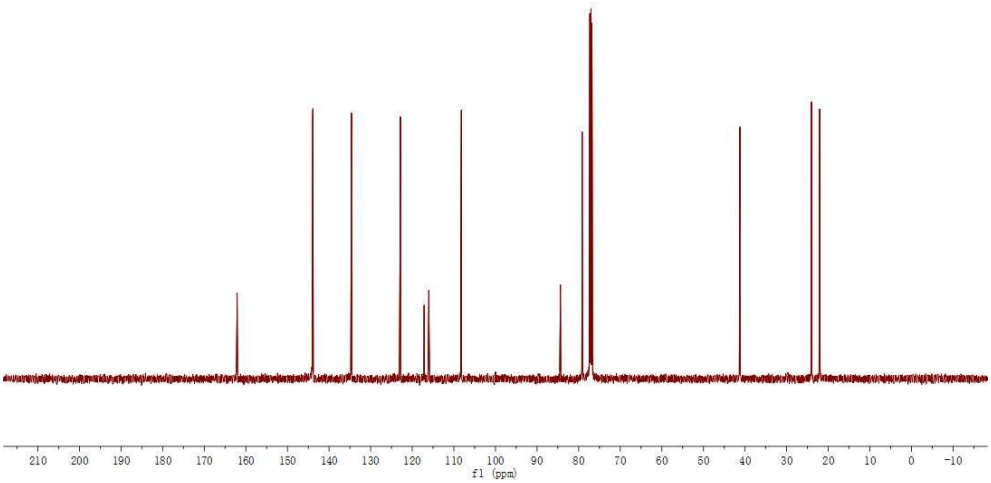

164.105
150.394
135.350
134.910
122.502
120.481
116.357
88.828
79.163
42.136
23.633
21.897
f1 (ppm)

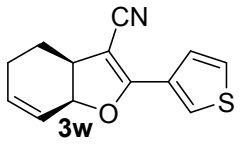


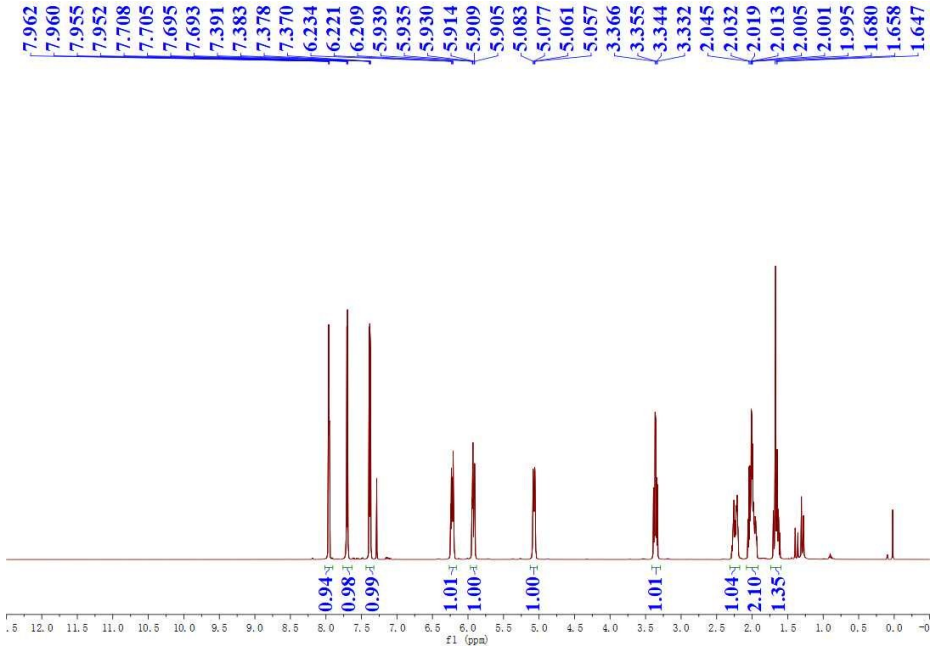
7.945
7.480
7.477
7.473
6.961
6.958
6.230
6.219
6.209
5.915
5.911
5.908
5.895
5.891
5.888
5.059
5.041
3.343
3.334
3.325
3.315
3.307
3.298
2.241
2.206
2.023
2.013
2.007
2.003
1.997
1.992
1.988
1.983
1.974
1.663
1.644
1.636
1.626
1.618

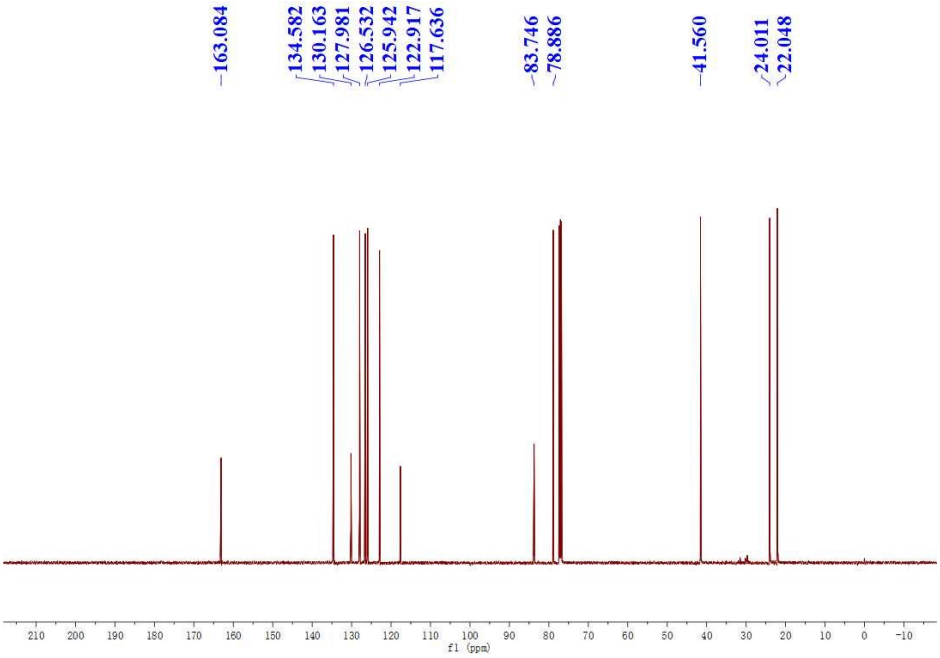


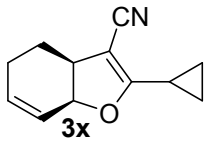
162.093
143.939
143.875
134.617
122.833
117.138
116.027
108.198
84.384
79.154
41.244
24.033
22.050



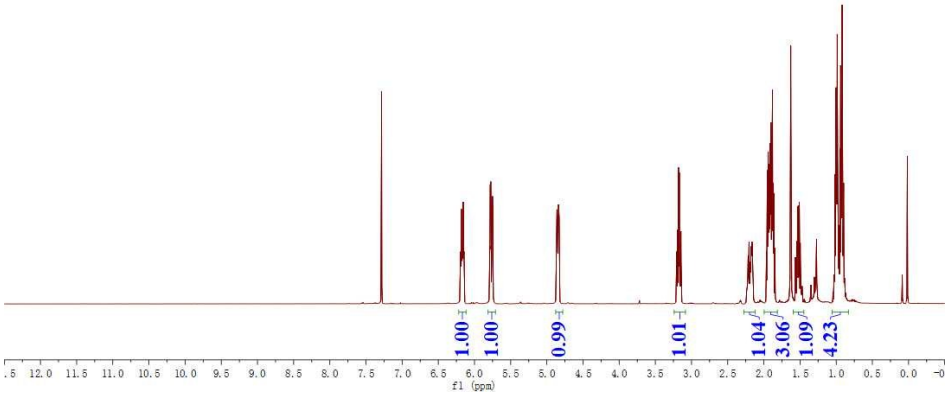

CN
O
S
3w


7.962
7.960
7.955
7.952
7.708
7.705
7.695
7.693
7.391
7.383
7.378
7.370
6.234
6.221
6.209
5.939
5.935
5.930
5.914
5.909
5.905
5.083
5.077
5.061
5.057
3.366
3.355
3.344
3.332
2.045
2.032
2.019
2.013
2.005
2.001
1.995
1.680
1.658
1.647
0.94
0.98
0.99
1.01
1.00
1.00
1.01
1.04
2.10
1.35
f1 (ppm)

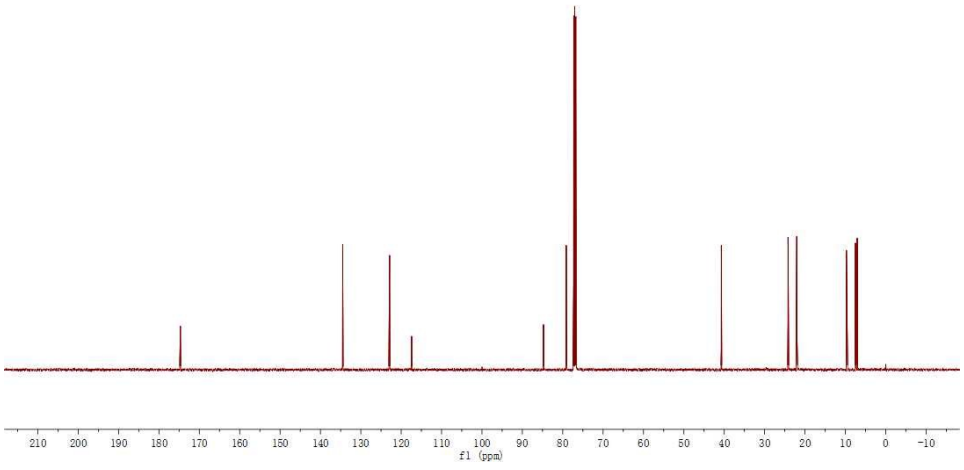

163.084
134.582
130.163
127.981
126.532
125.942
122.917
117.636
83.746
78.886
41.560
24.011
22.048
f1 (ppm)

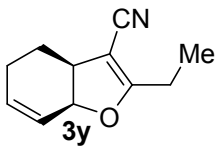


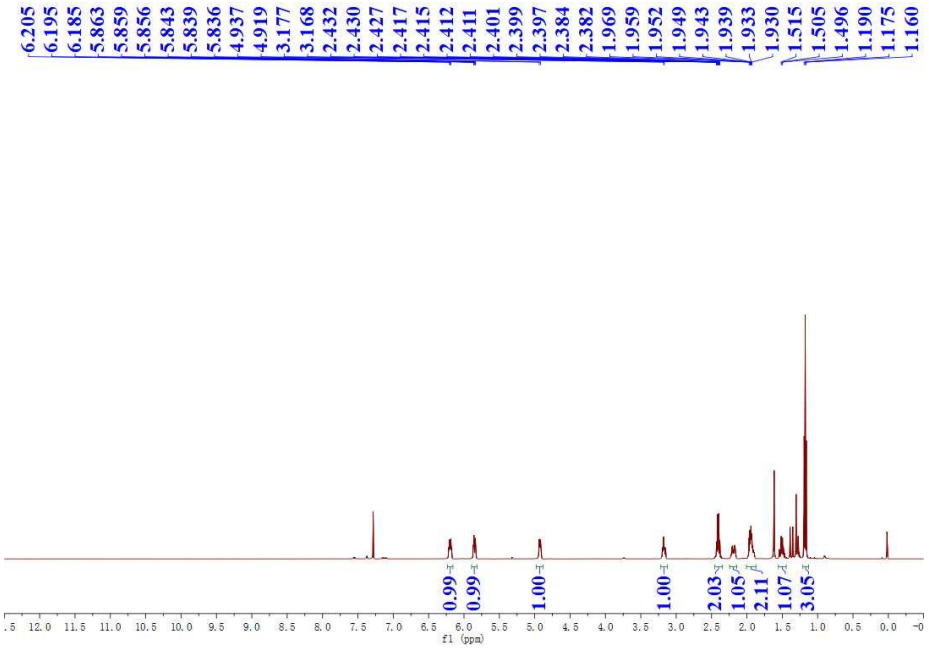
6.156
5.783
5.778
5.774
5.758
5.753
5.749
3.180
3.169
1.952
1.940
1.931
1.920
1.914
1.909
1.902
1.892
1.887
1.881
1.868
1.860
1.017
1.004
0.998
0.994
0.986
0.981
0.974
0.948
0.939
0.934
0.931
0.927
0.923
0.918
0.914
0.910
0.903
0.898

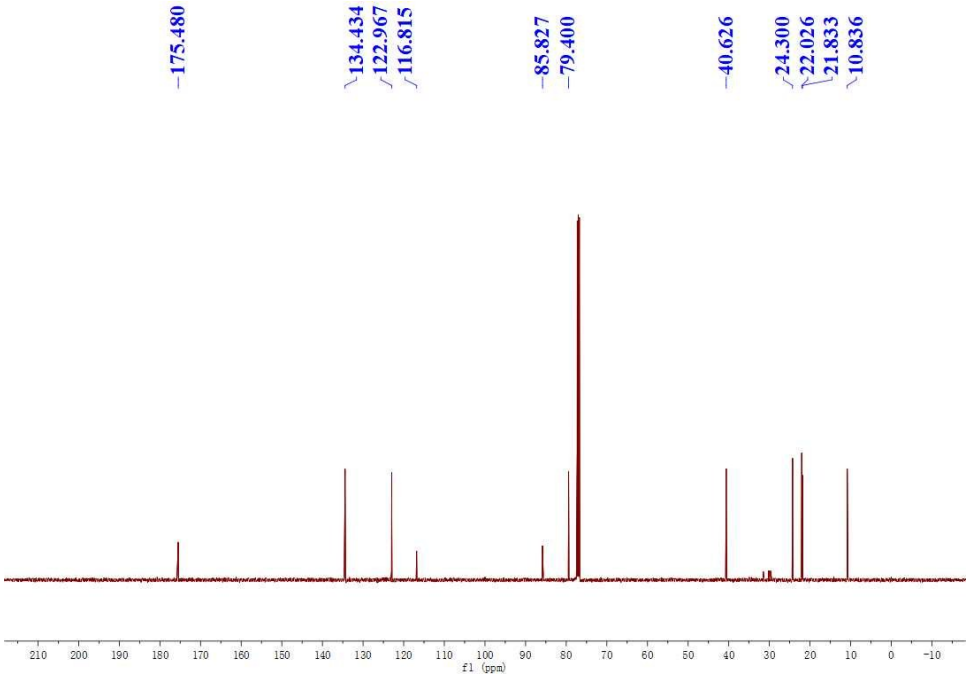


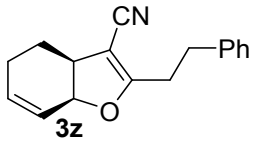
174.692
134.495
122.884
117.434
84.767
79.135
40.718
24.185
22.021
9.737
7.479
7.051



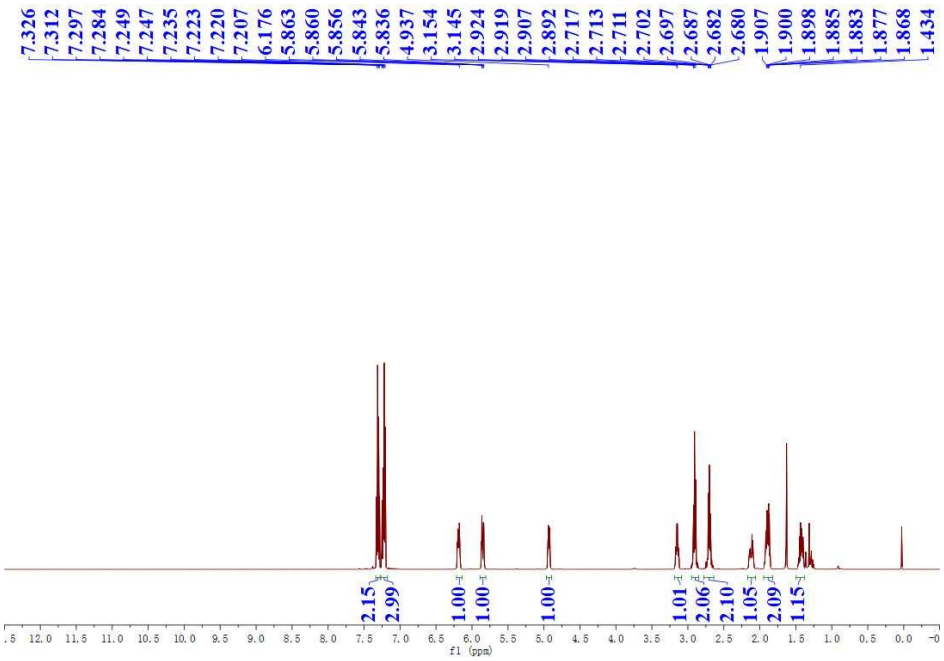

CN
Me
O
3y

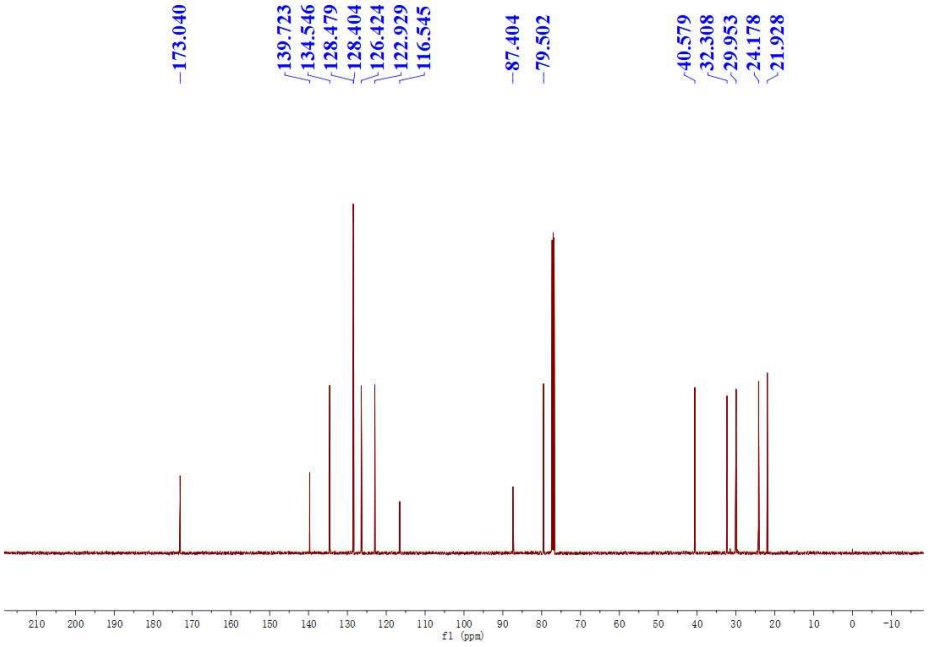

6.205
6.195
6.185
5.863
5.859
5.856
5.843
5.839
5.836
4.937
4.919
3.177
3.168
2.432
2.430
2.427
2.417
2.415
2.412
2.411
2.401
2.399
2.397
2.384
2.382
1.969
1.959
1.952
1.949
1.943
1.939
1.933
1.930
1.515
1.505
1.496
1.190
1.175
1.160
0.99
0.99
1.00
1.00
2.03
1.05
2.11
1.07
3.05
f1 (ppm)

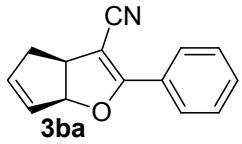

175.480
134.434
122.967
116.815
85.827
79.400
40.626
24.300
22.026
21.833
10.836
f1 (ppm)


CN
Ph
O

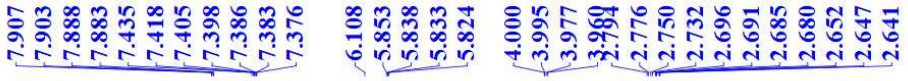
3z

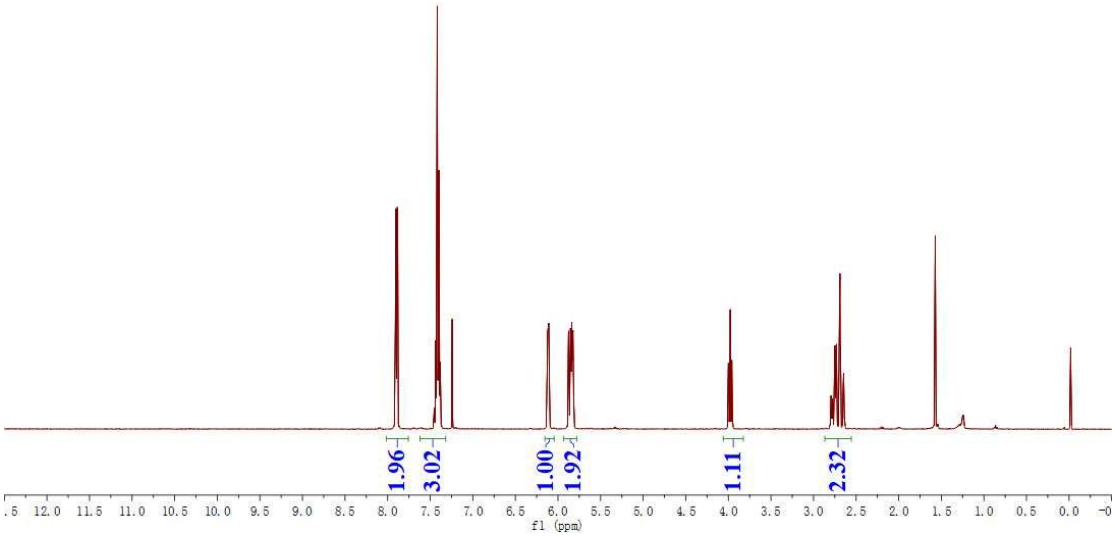

7.326
7.312
7.297
7.284
7.249
7.247
7.235
7.223
7.220
7.207
6.176
5.863
5.860
5.856
5.843
5.836
4.937
3.154
3.145
2.924
2.919
2.907
2.892
2.717
2.713
2.711
2.702
2.697
2.687
2.682
2.680
1.907
1.900
1.898
1.885
1.883
1.877
1.868
1.434
2.15
2.99
1.00
1.00
1.00
1.01
2.06
2.10
1.05
2.09
1.15
f1 (ppm)


173.040
139.723
134.546
128.479
128.404
126.424
122.929
116.545
87.404
79.502
40.579
32.308
29.953
24.178
21.928
f1 (ppm)

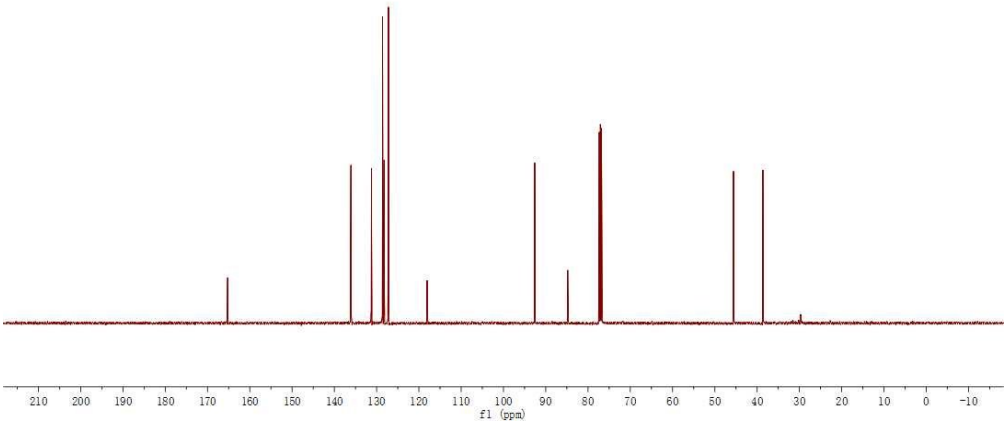

CN
O
3ba

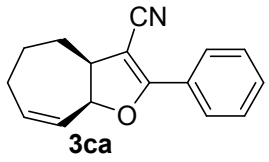
3ba


7.907
7.903
7.888
7.883
7.435
7.418
7.405
7.398
7.386
7.383
7.376
6.108
5.853
5.838
5.833
5.824
4.000
3.995
3.977
3.960
2.776
2.750
2.732
2.696
2.691
2.685
2.680
2.652
2.647
2.641

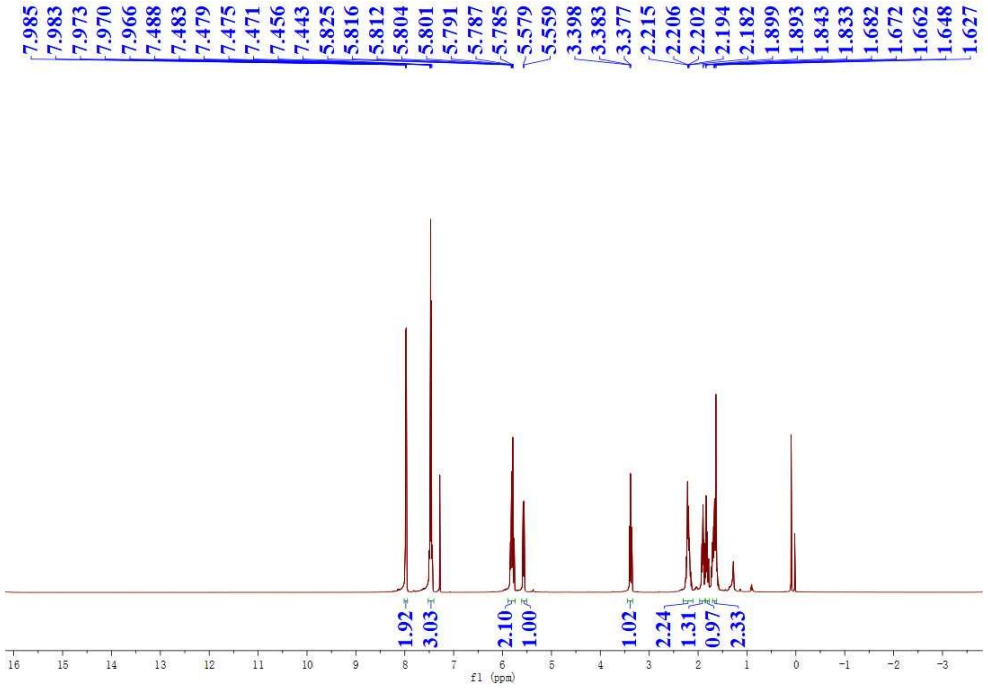

1.96
3.02
1.00
1.92
1.11
2.32
f1 (ppm)

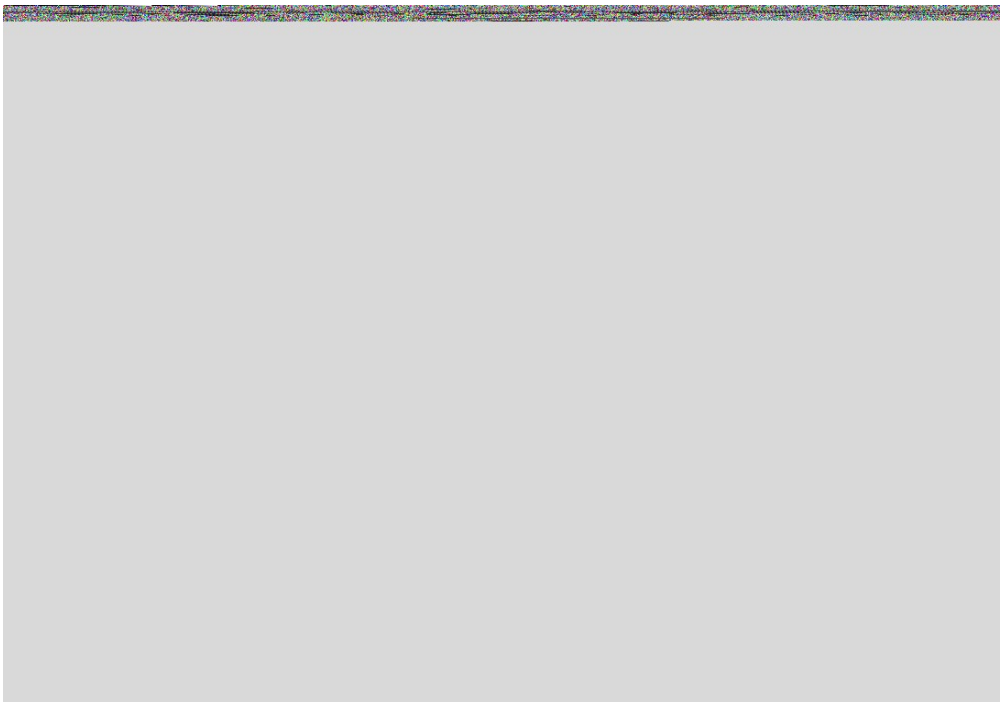

165.221
136.062
131.238
128.590
128.220
127.176
118.048
92.620
84.817
45.598
38.648

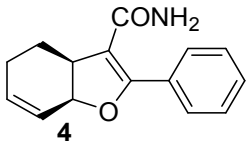

f1 (ppm)


CN
O

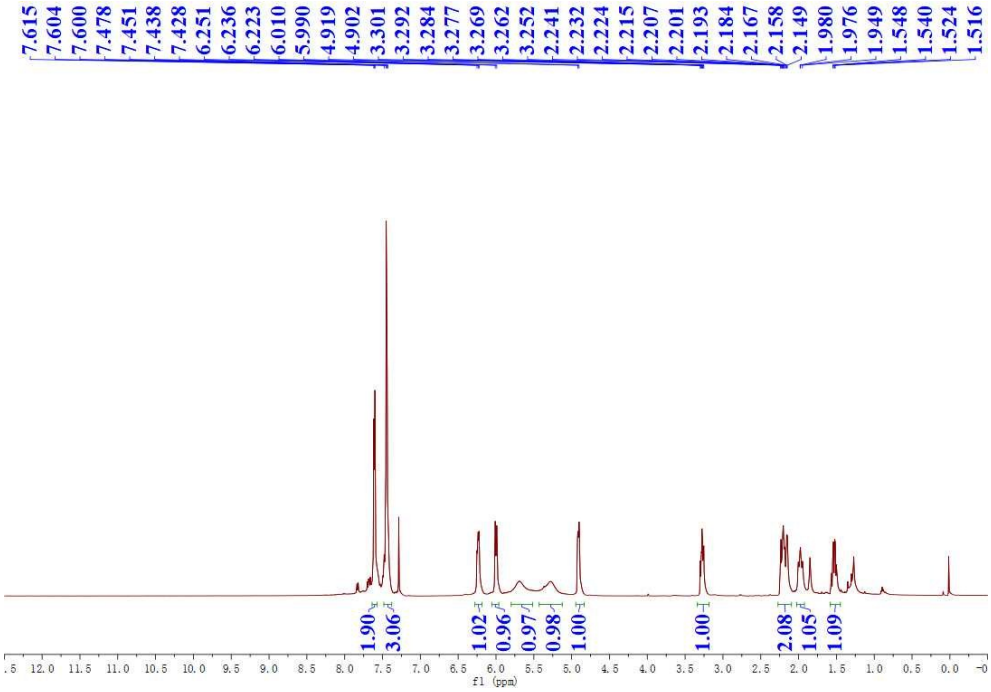
3ca

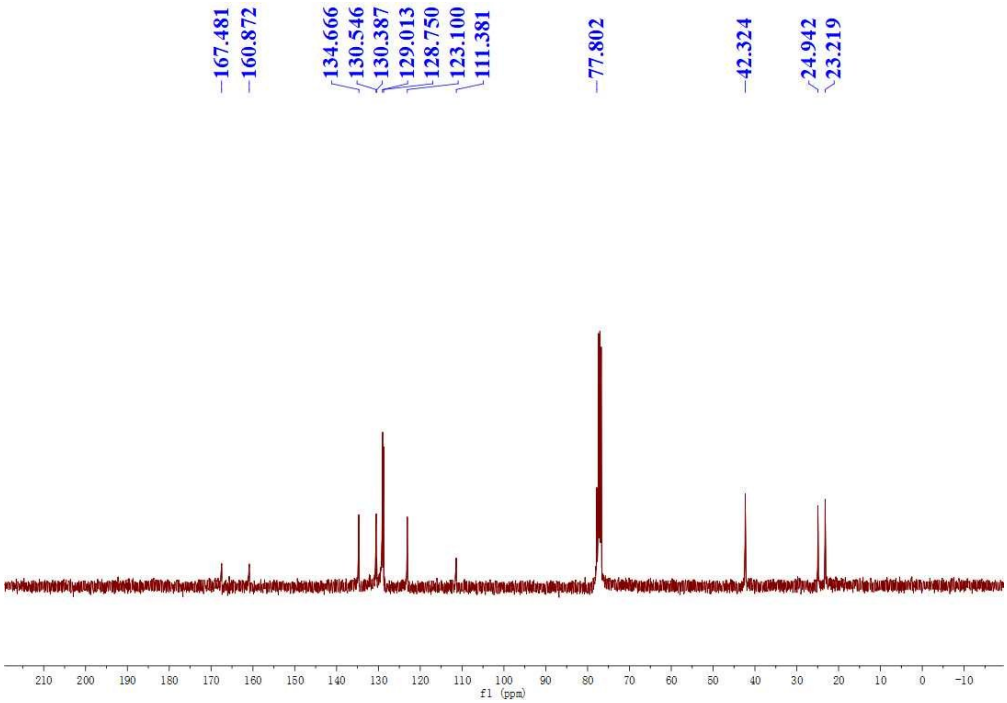

7.985
7.983
7.973
7.970
7.966
7.488
7.483
7.479
7.475
7.471
7.456
7.443
5.825
5.816
5.812
5.804
5.801
5.791
5.787
5.785
5.579
5.559
3.398
3.383
3.377
2.215
2.206
2.202
2.194
2.182
1.899
1.893
1.843
1.833
1.682
1.672
1.662
1.648
1.627
1.92
3.03
2.10
1.00
1.02
2.24
1.31
0.97
2.33
f1 (ppm)

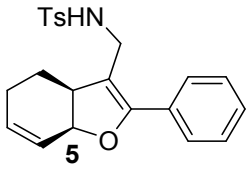


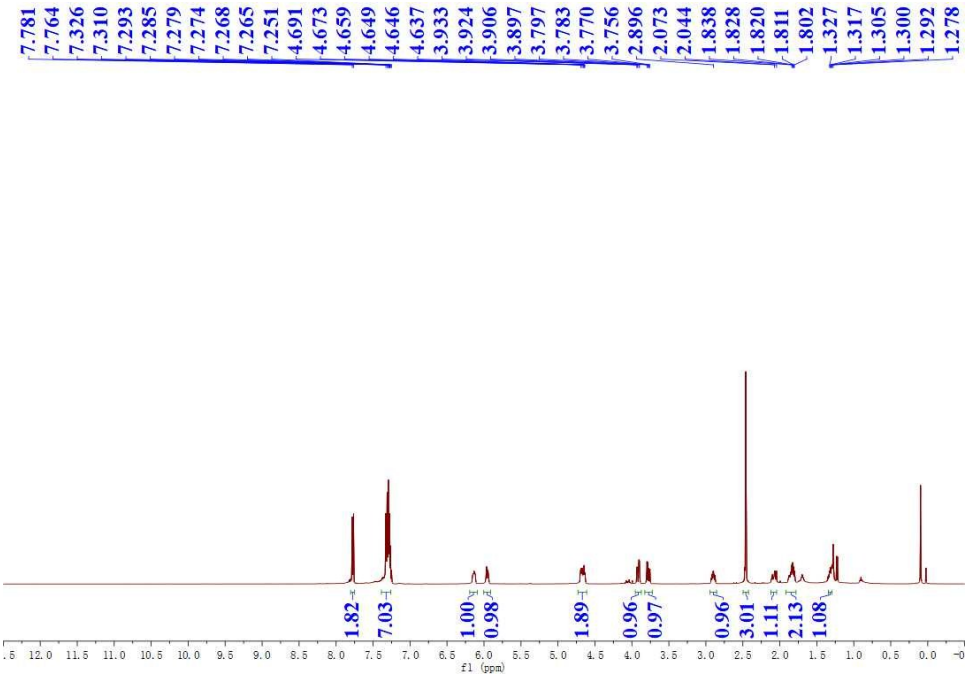

CONH2
O

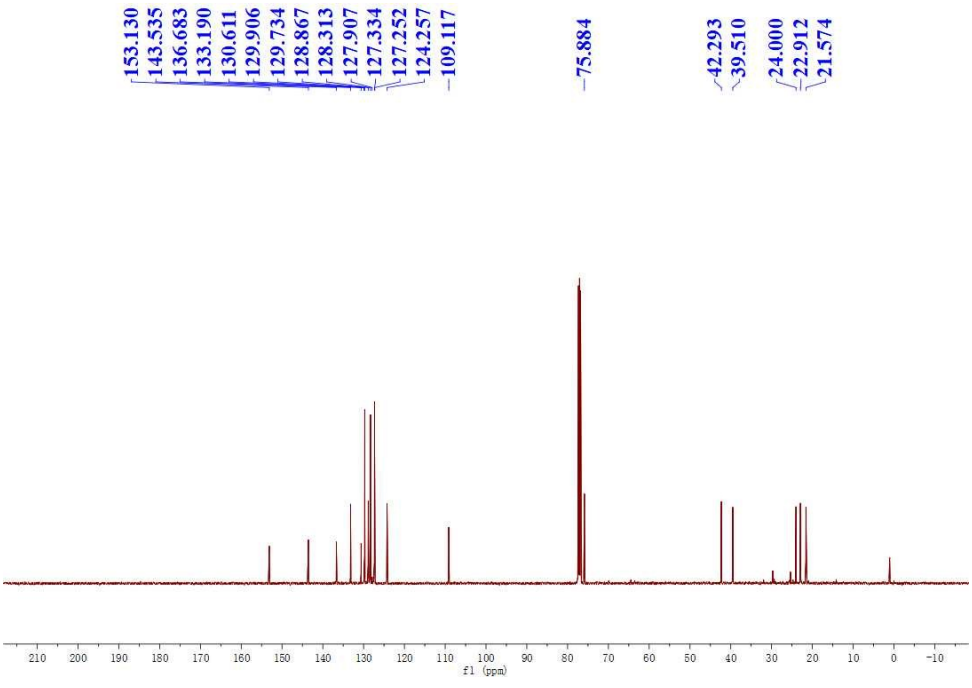
4

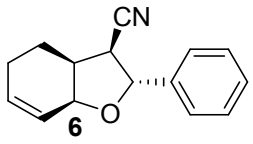

7.615
7.604
7.600
7.478
7.451
7.438
7.428
6.251
6.236
6.223
6.010
5.990
4.919
4.902
3.301
3.292
3.284
3.277
3.269
3.262
3.252
2.241
2.232
2.224
2.215
2.207
2.201
2.193
2.184
2.167
2.158
2.149
1.980
1.976
1.949
1.548
1.540
1.524
1.516
1.90
3.06
1.02
0.96
0.97
0.98
1.00
1.00
2.08
1.05
1.09
f1 (ppm)


167.481
160.872
134.666
130.546
130.387
129.013
128.750
123.100
111.381
77.802
42.324
24.942
23.219
f1 (ppm)

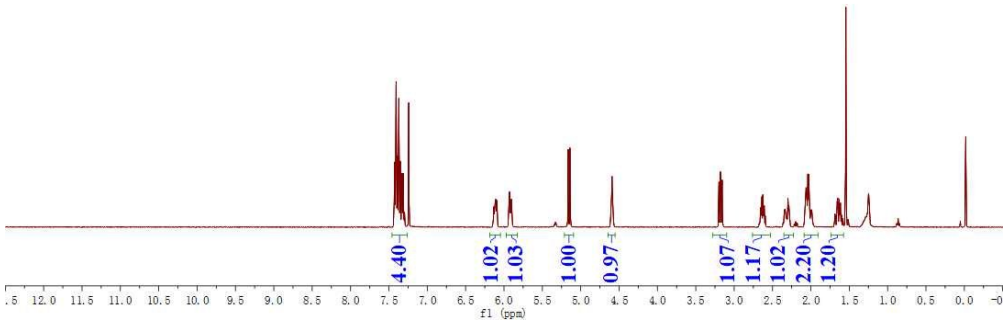

TsHN
O
5

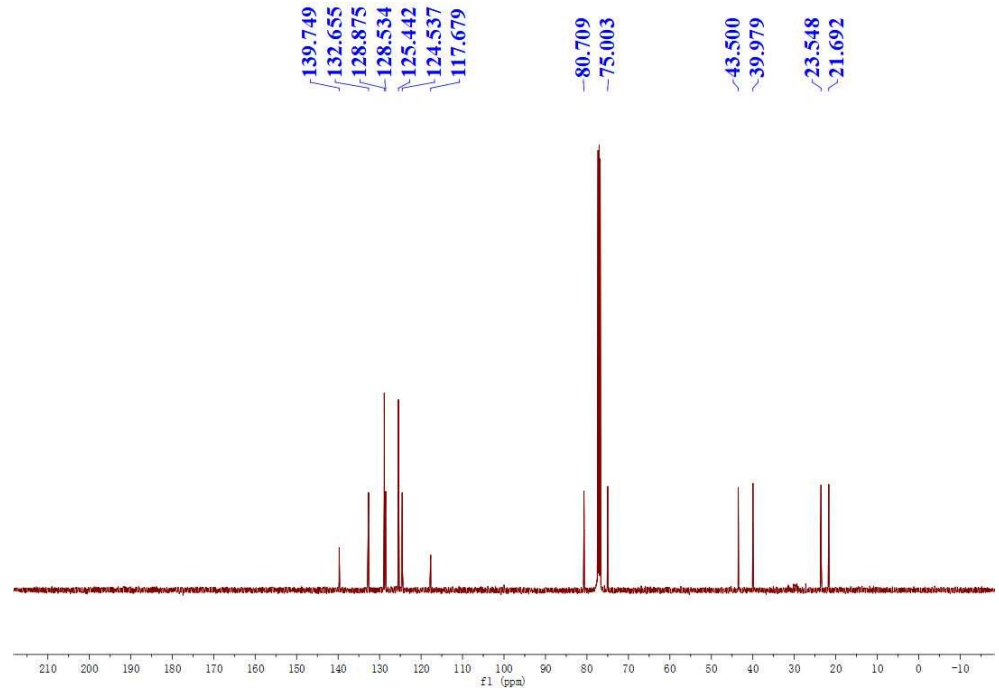

7.781
7.764
7.326
7.310
7.293
7.285
7.279
7.274
7.268
7.265
7.251
4.691
4.673
4.659
4.649
4.646
4.637
3.933
3.924
3.906
3.897
3.797
3.783
3.770
3.756
2.896
2.073
2.044
1.838
1.828
1.820
1.811
1.802
1.327
1.317
1.305
1.300
1.292
1.278
1.82
7.03
1.00
0.98
1.89
0.96
0.97
0.96
3.01
1.11
2.13
1.08
f1 (ppm)

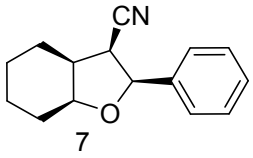

153.130
143.535
136.683
133.190
130.611
129.906
129.734
128.867
128.313
127.907
127.334
127.252
124.257
109.117
75.884
42.293
39.510
24.000
22.912
21.574
f1 (ppm)


CN
O
6


7.424
7.406
7.390
7.388
7.371
7.352
7.331
7.320
7.314
6.132
6.107
6.095
5.928
5.903
5.164
5.140
4.592
3.198
3.180
3.175
3.157
2.657
2.639
2.626
2.608
2.335
2.299
2.286
2.070
2.063
2.057
2.052
2.039
2.029
2.020
1.657
1.650
1.631
1.615

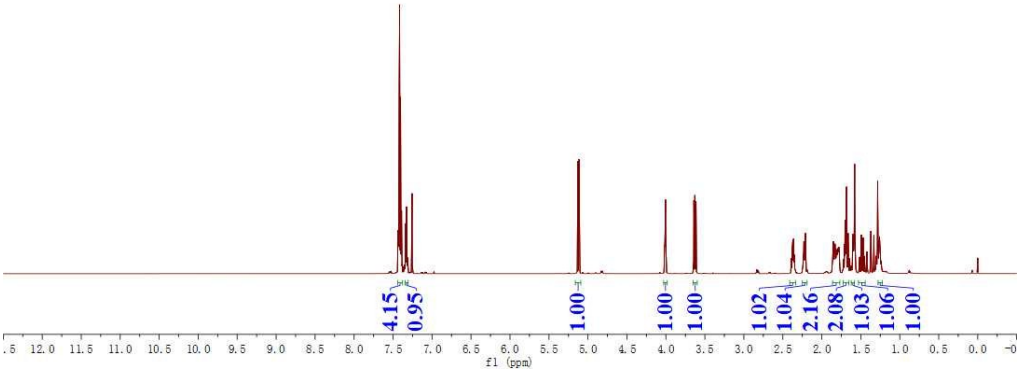

4.40
1.02
1.03
1.00
0.97
1.07
1.17
1.02
2.20
1.20
f1 (ppm)

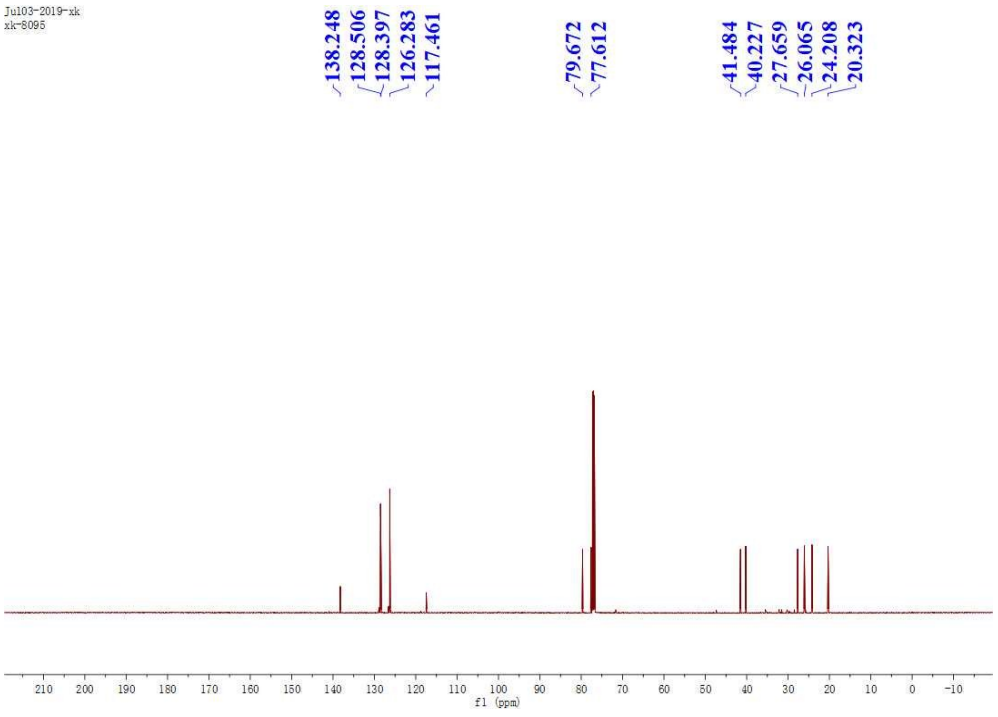

139.749
132.655
128.875
128.534
125.442
124.537
117.679
80.709
75.003
43.500
39.979
23.548
21.692
f1 (ppm)

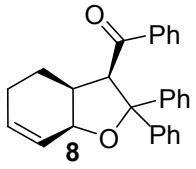

CN
O

7

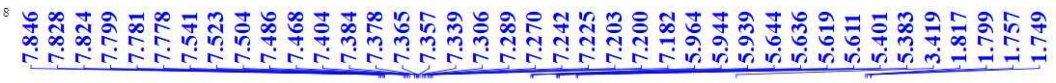

5.130
5.114
4.015
4.010
4.004
3.999
3.641
3.629
3.625
3.613
2.372
2.362
2.230
2.212
2.210
1.852
1.830
1.786
1.782
1.778
1.708
1.702
1.697
1.688
1.683
1.680
1.662
1.602
1.596
1.589
1.587
1.579
1.496
1.490
1.475
1.469
1.264
1.260
1.254

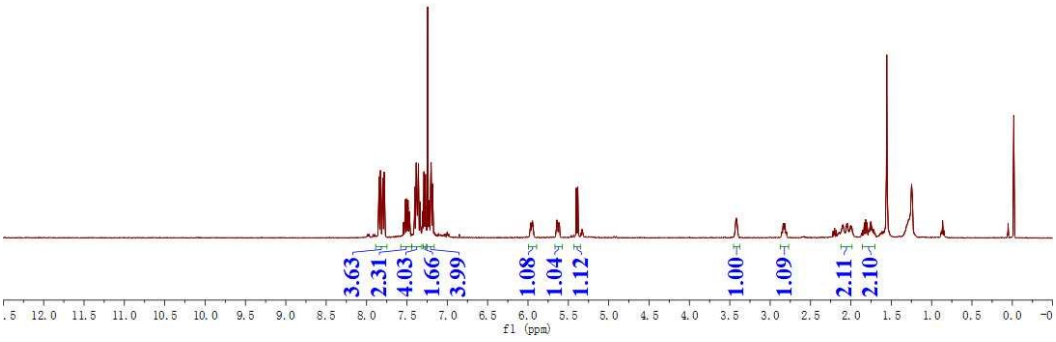

4.15
0.95
1.00
1.00
1.00
1.02
1.04
2.16
2.08
1.03
1.06
1.00
f1 (ppm)

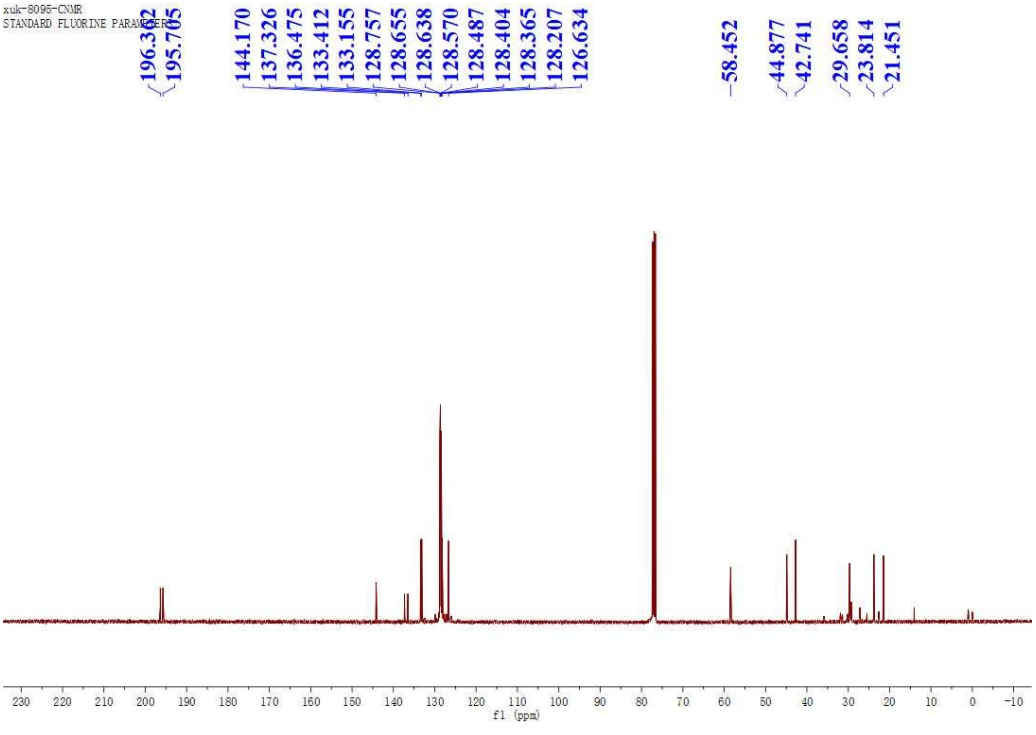

Jul03-2019-xk
xk-8095
138.248
128.506
128.397
126.283
117.461
79.672
77.612
41.484
40.227
27.659
26.065
24.208
20.323
f1 (ppm)

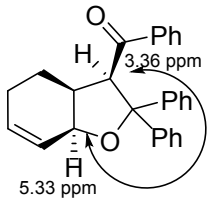

O
Ph
Ph
O
Ph

8


7.846
7.828
7.824
7.799
7.781
7.778
7.541
7.523
7.504
7.486
7.468
7.404
7.384
7.378
7.365
7.357
7.339
7.306
7.289
7.270
7.242
7.225
7.203
7.200
7.182
5.964
5.944
5.939
5.644
5.636
5.619
5.611
5.401
5.383
3.419
1.817
1.799
1.757
1.749

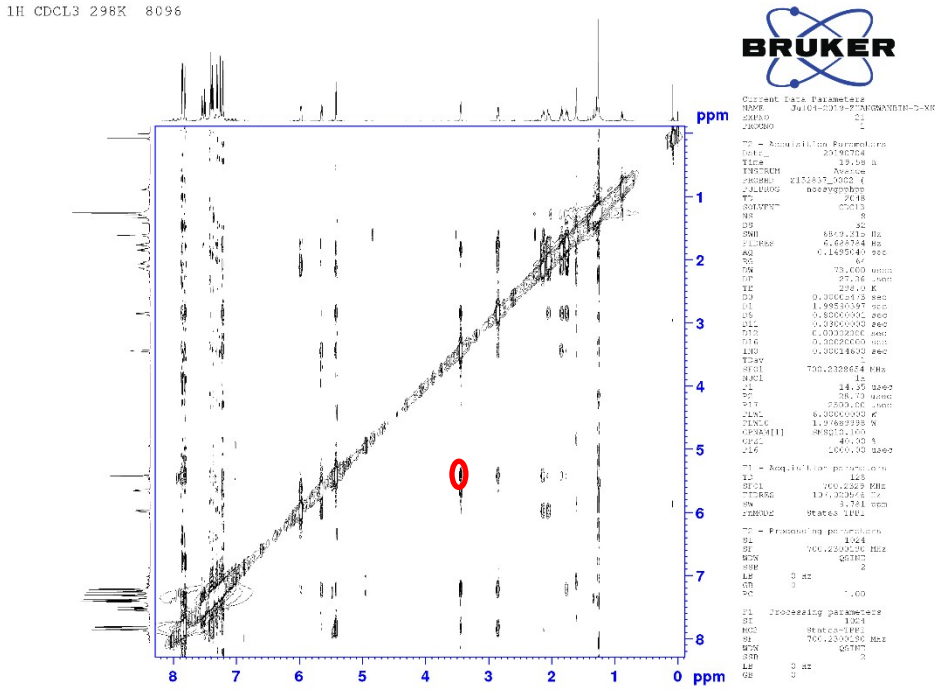

3.63
2.31
4.03
1.66
3.99
1.08
1.04
1.12
1.00
1.09
2.11
2.10
f1 (ppm)


xuk-8095-CNMR
STANDARD FLUORINE PARAMETER
196.362
195.705
144.170
137.326
136.475
133.412
133.155
128.757
128.655
128.638
128.570
128.487
128.404
128.365
128.207
126.634
58.452
44.877
42.741
29.658
23.814
21.451
f1 (ppm)

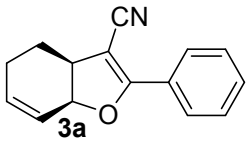


NOESY 8

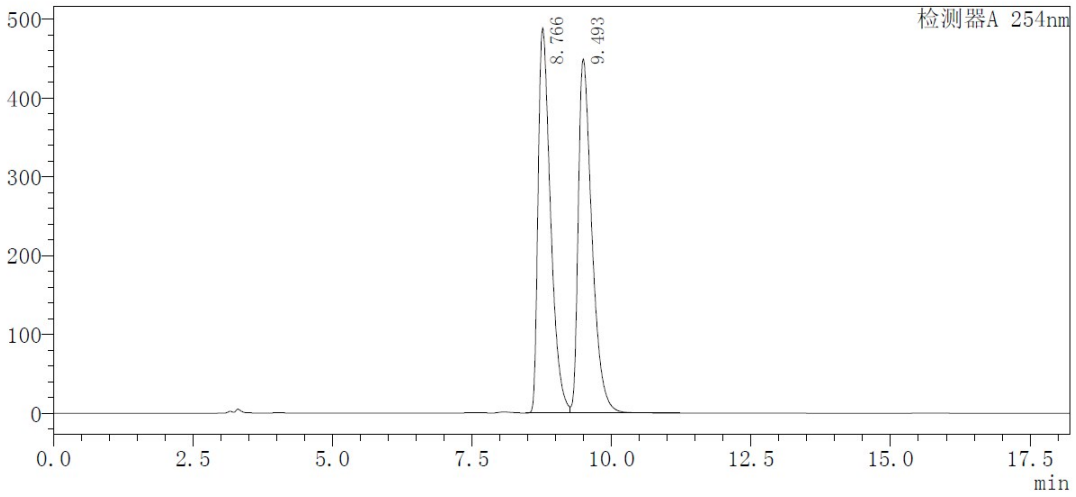
The relative stereochemistry of this compound was corroborated by NOE experiments (as indicated on the compound structure and the figure).



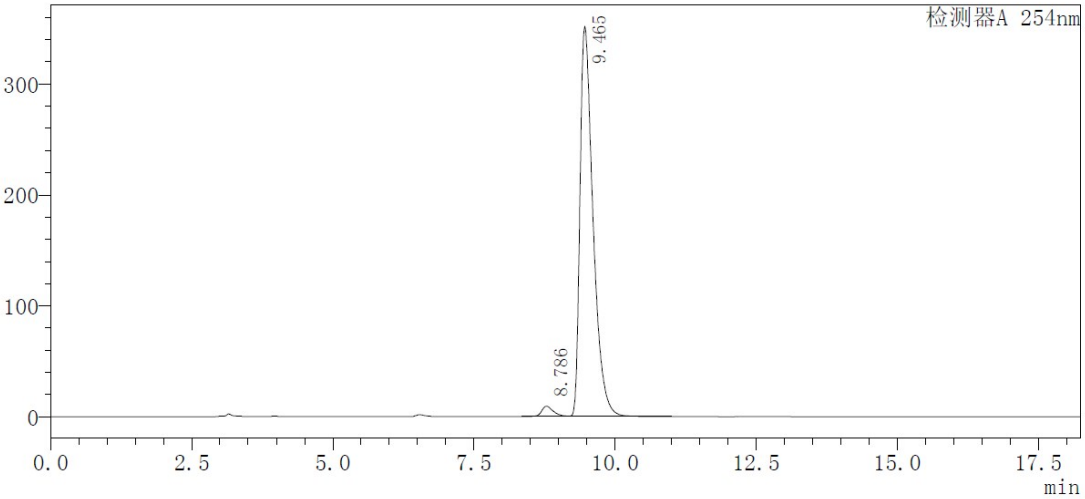
7. HPLC Data



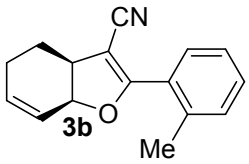
Racemate:



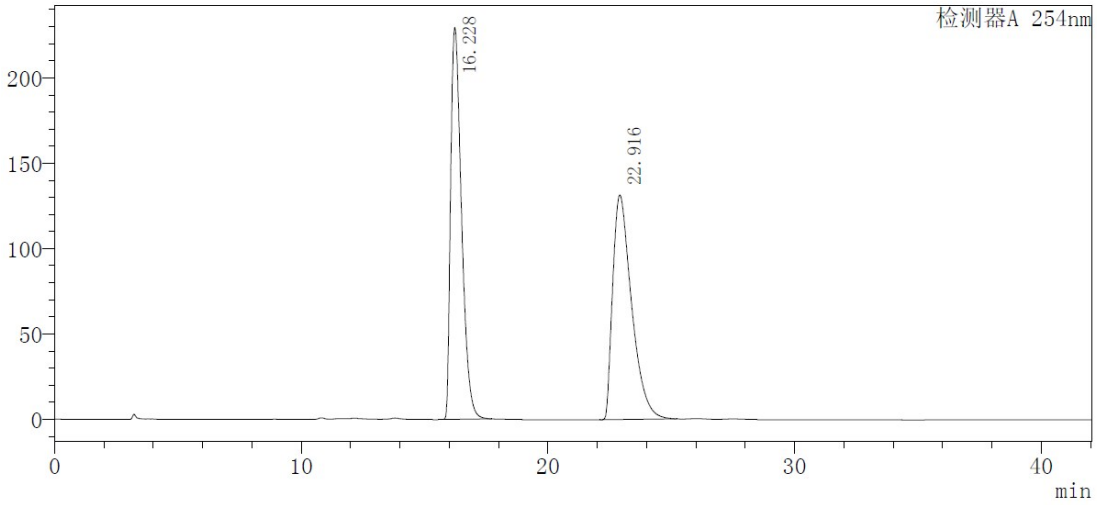
Chiral:



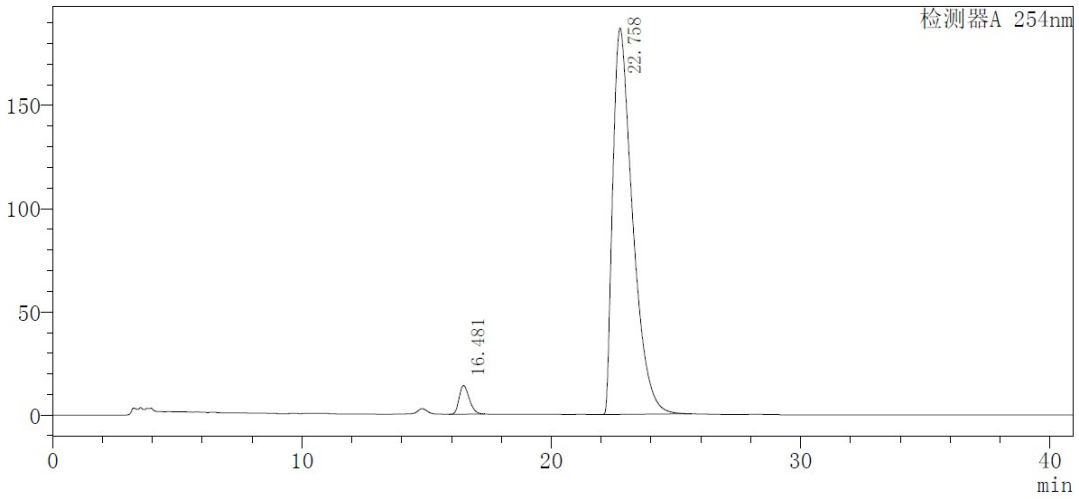
	Retention Time (min)	Area (%)	
Peak 1	8.786	2.366	**95% ee**
Peak 2	9.465	97.634	



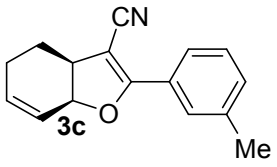
Racemate:



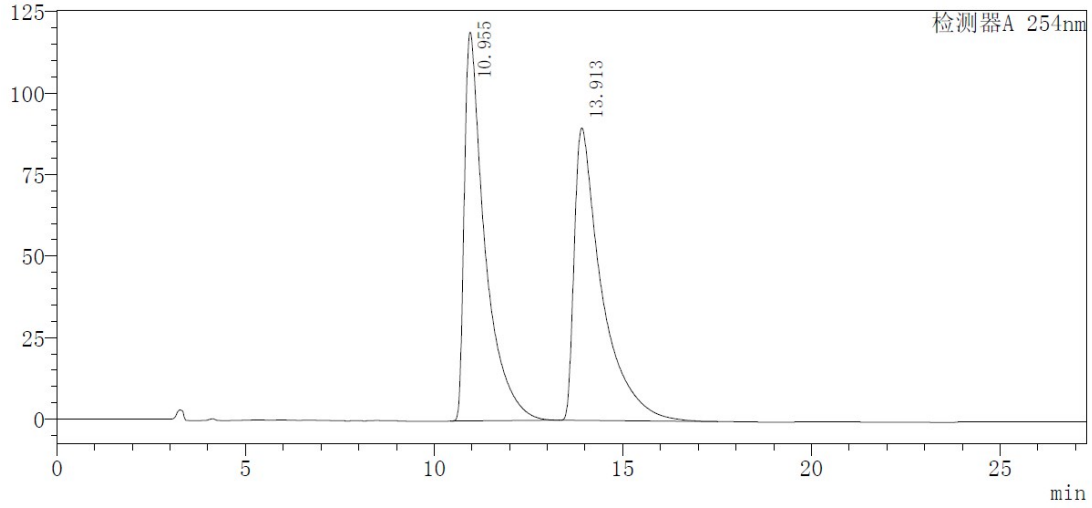
Chiral:



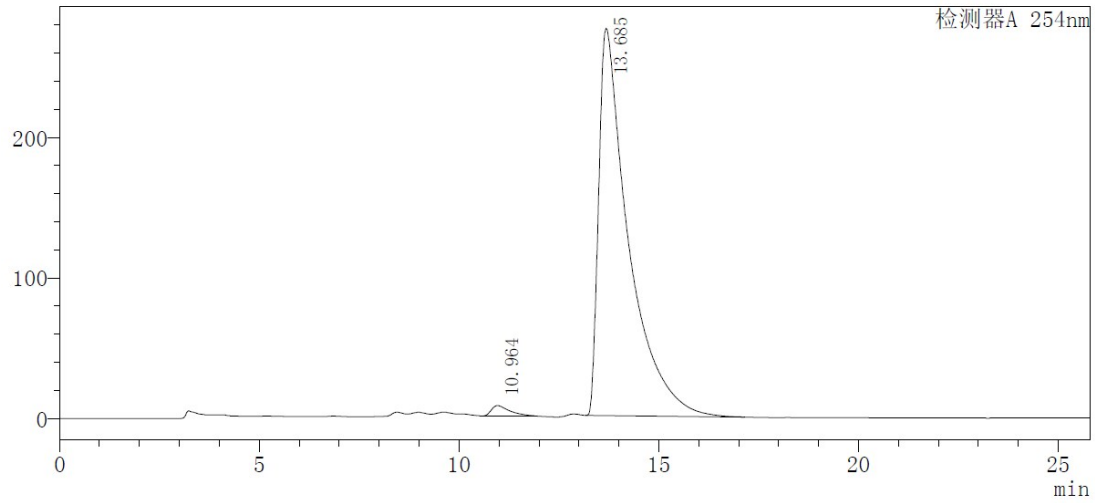
	Retention Time (min)	Area (%)	
Peak 1	16.481	3.643	**93% ee**
Peak 2	22.758	96.357	



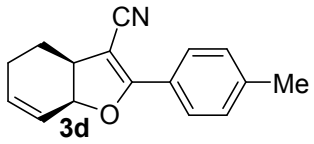
Racemate:



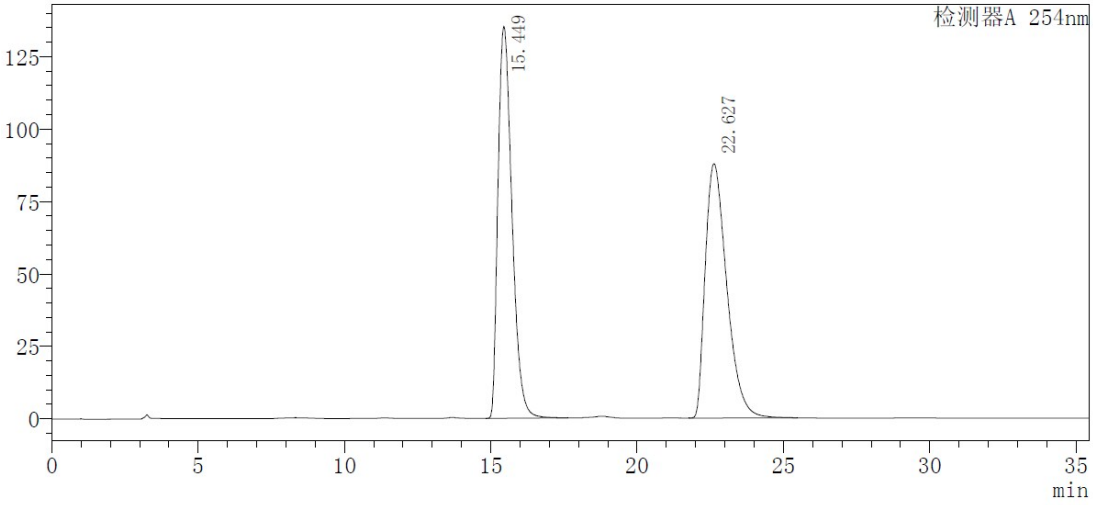
Chiral:



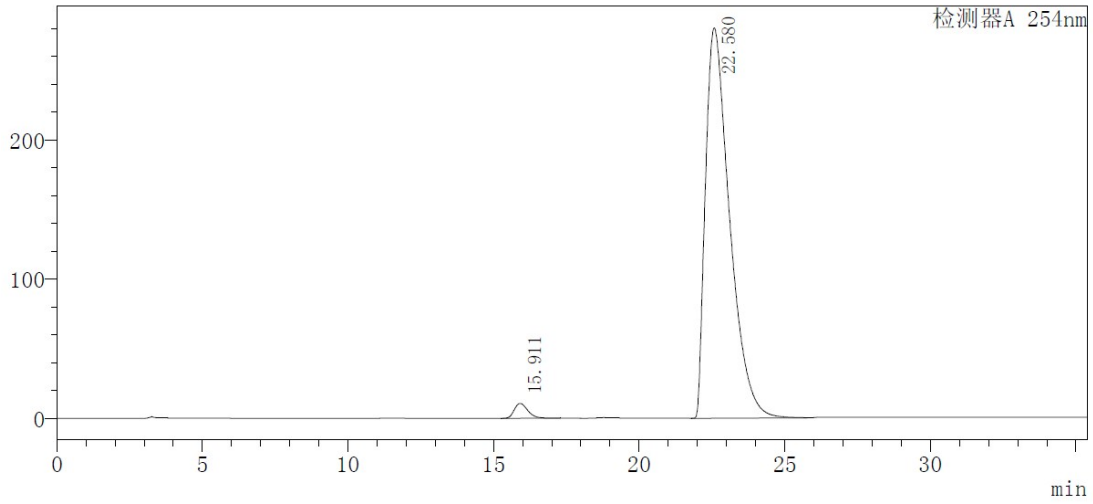
	Retention Time (min)	Area (%)	
Peak 1	10.964	1.607	**97% ee**
Peak 2	13.685	98.393	



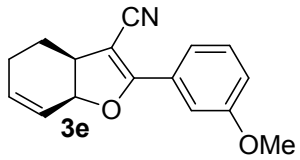
Racemate:



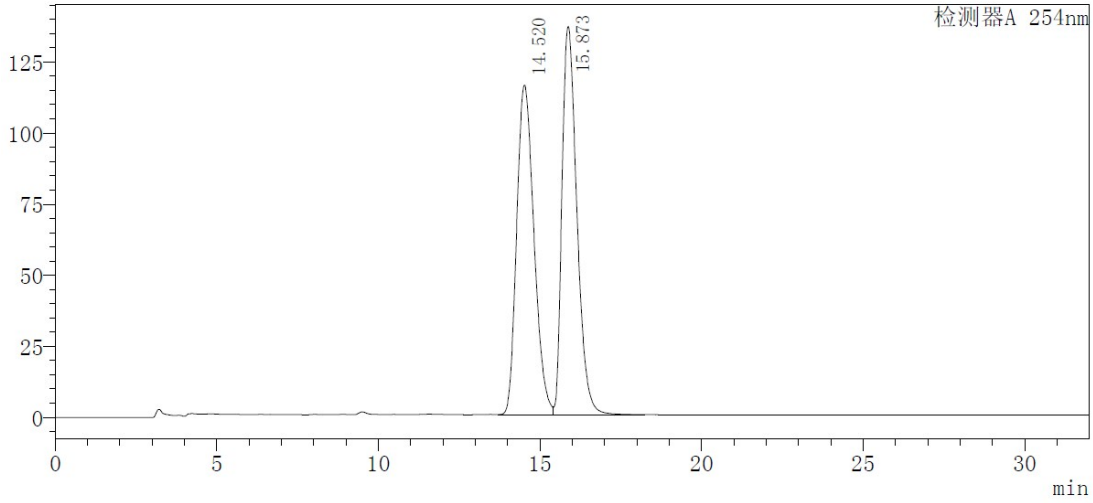
Chiral:



	Retention Time (min)	Area (%)	
Peak 1	15.911	2.076	**96% ee**
Peak 2	22.580	97.924	

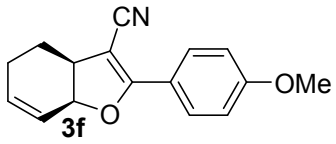


Racemate:

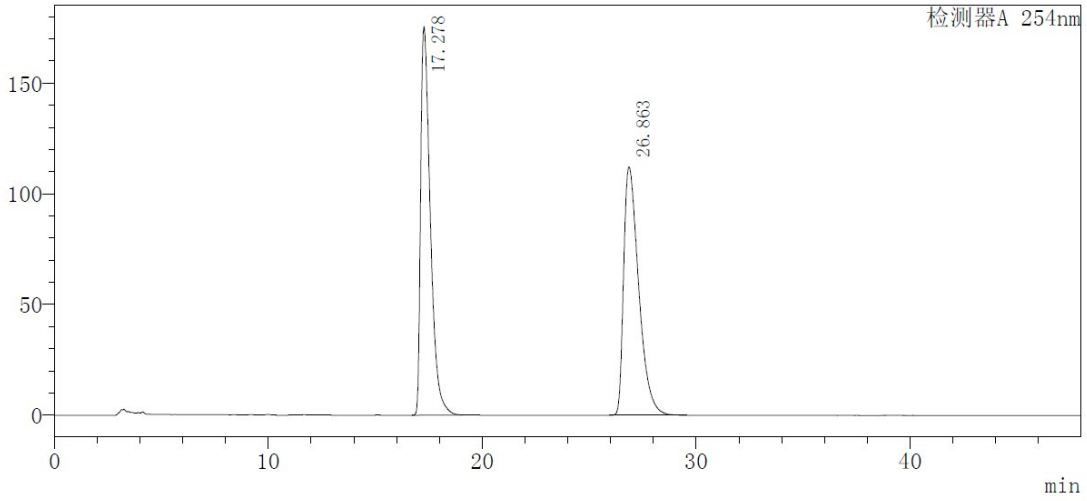


Chiral:

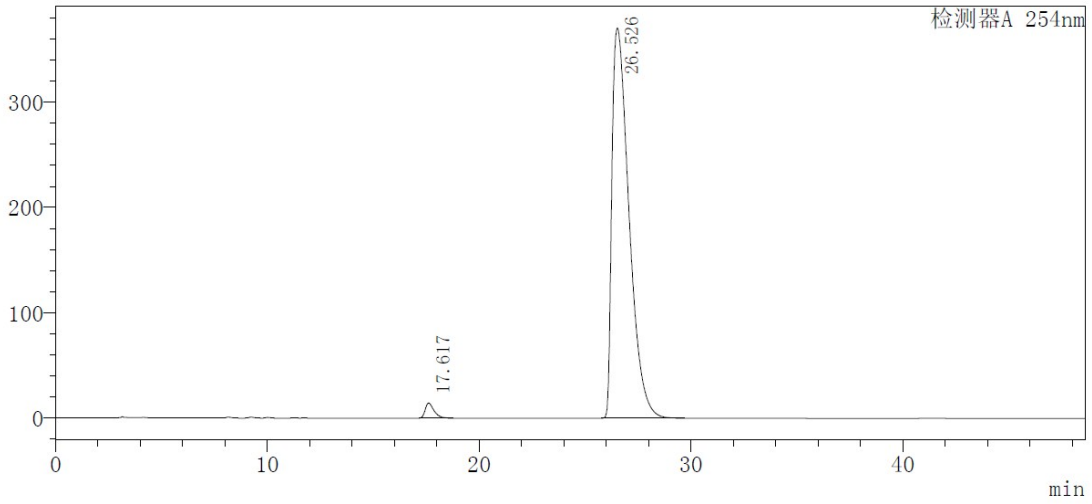
	Retention Time (min)	Area (%)	
Peak 1	14.148	1.791	**96% ee**
Peak 2	15.523	98.209	



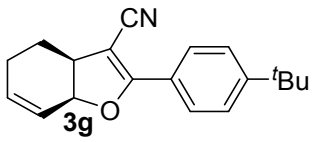
Racemate:



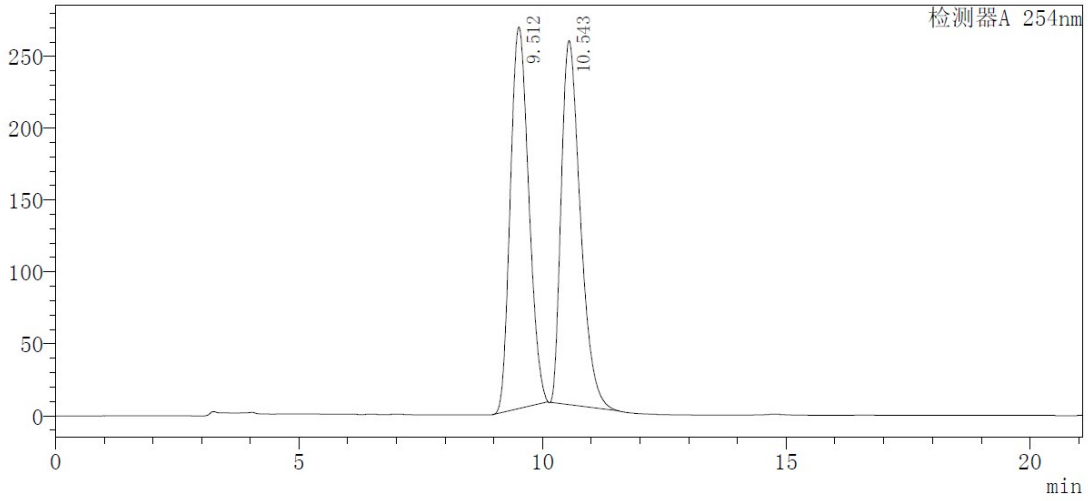
Chiral:



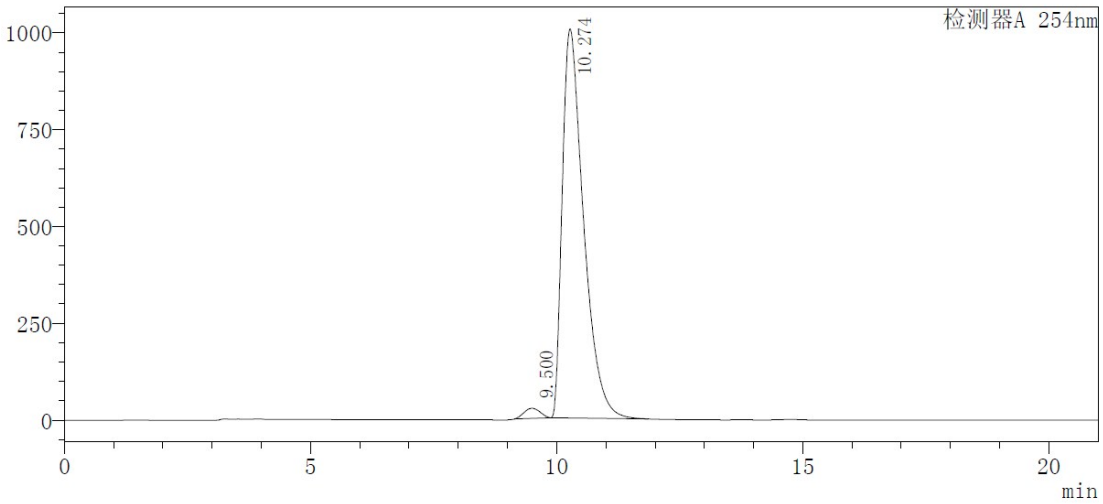
	Retention Time (min)	Area (%)	
Peak 1	17.617	1.951	**96% ee**
Peak 2	26.526	98.049	



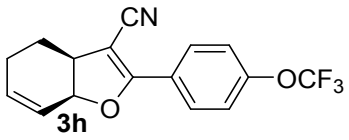
Racemate:



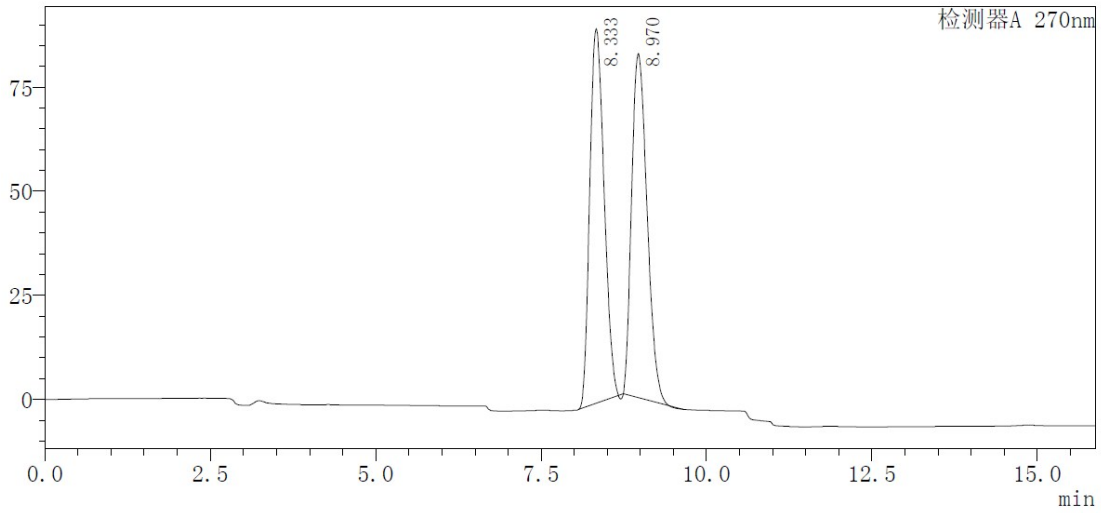
Chiral:



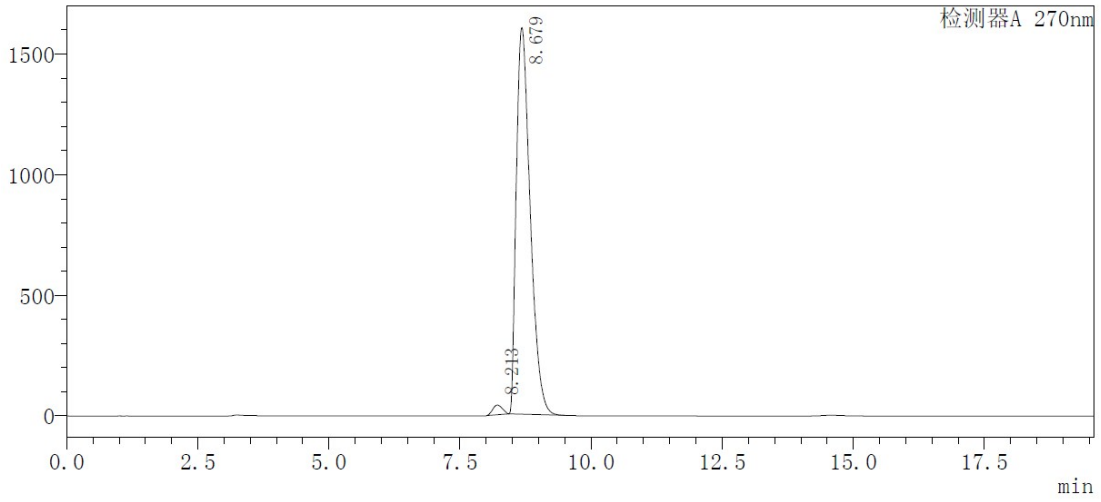
	Retention Time (min)	Area (%)	
Peak 1	9.500	1.934	**96% ee**
Peak 2	10.274	98.066	



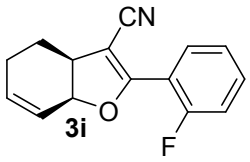
Racemate:



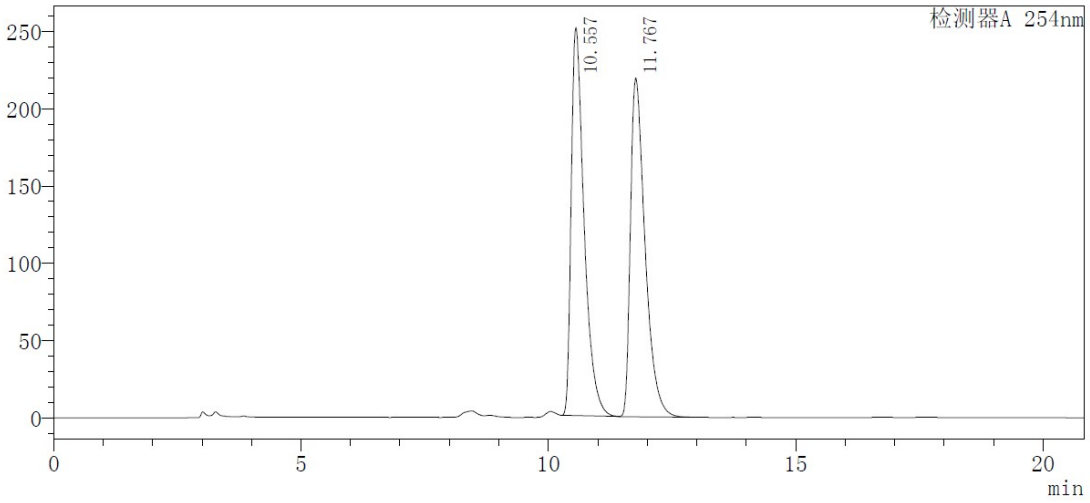
Chiral:



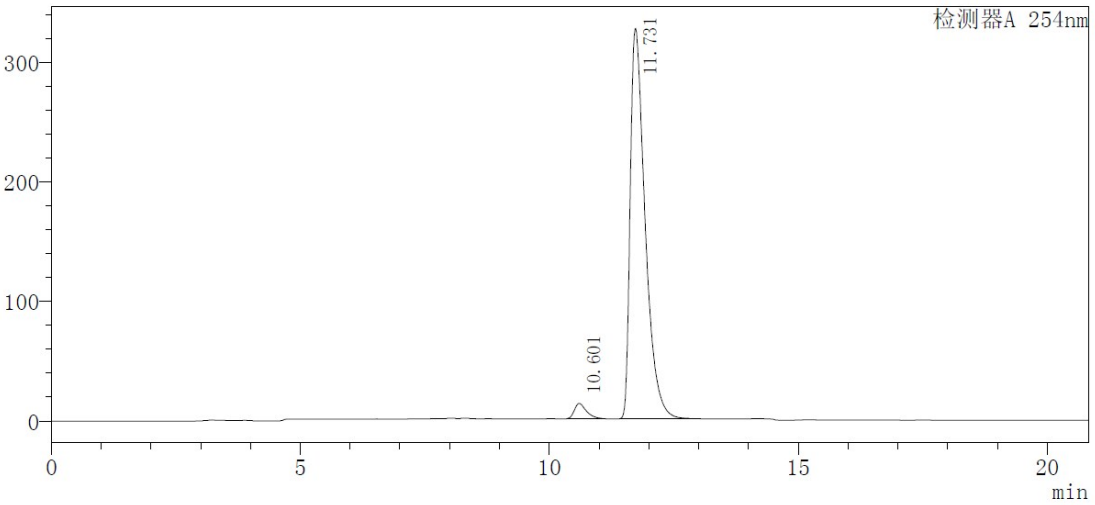
	Retention Time (min)	Area (%)	
Peak 1	8.213	1.704	**97% ee**
Peak 2	8.679	98.296	



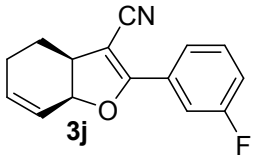
Racemate:



Chiral:

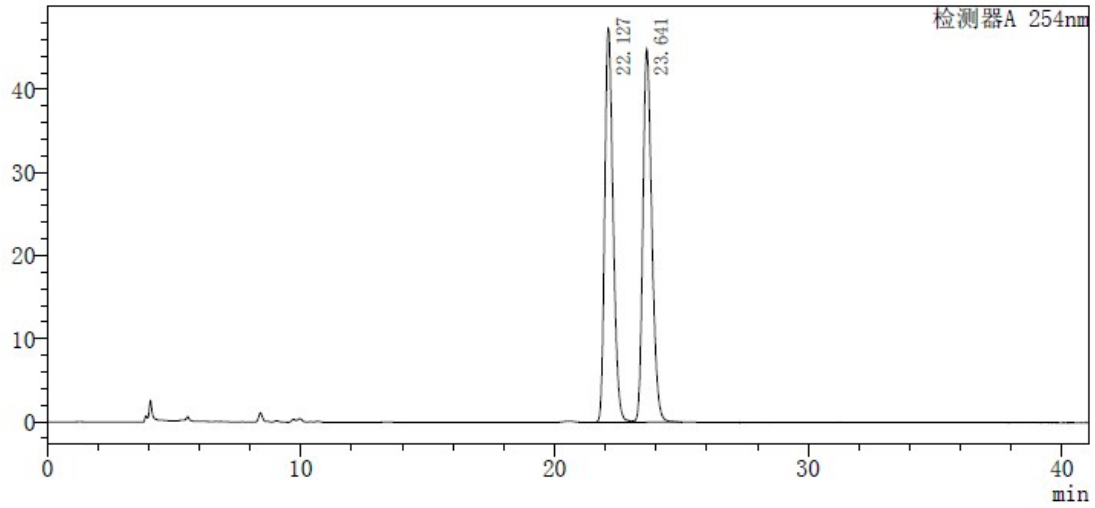


	Retention Time (min)	Area (%)	
Peak 1	10.601	2.901	**94% ee**
Peak 2	11.731	97.099	

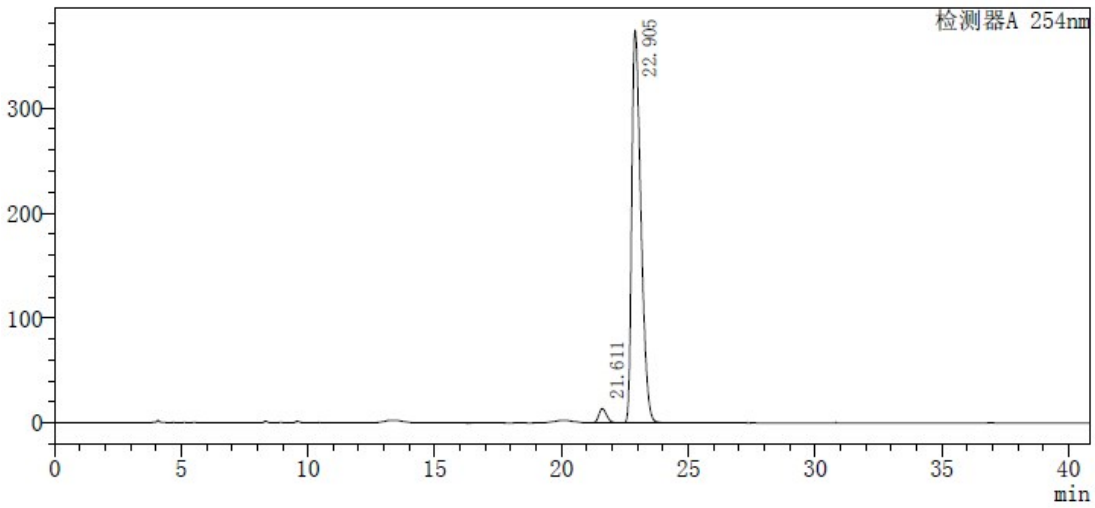


3j

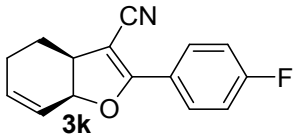
Racemate:



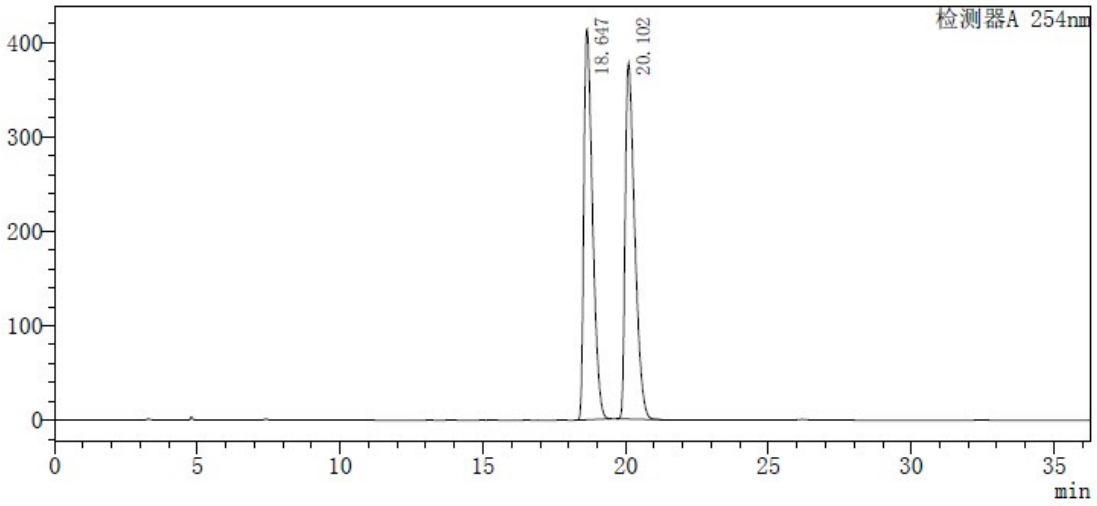
Chiral:



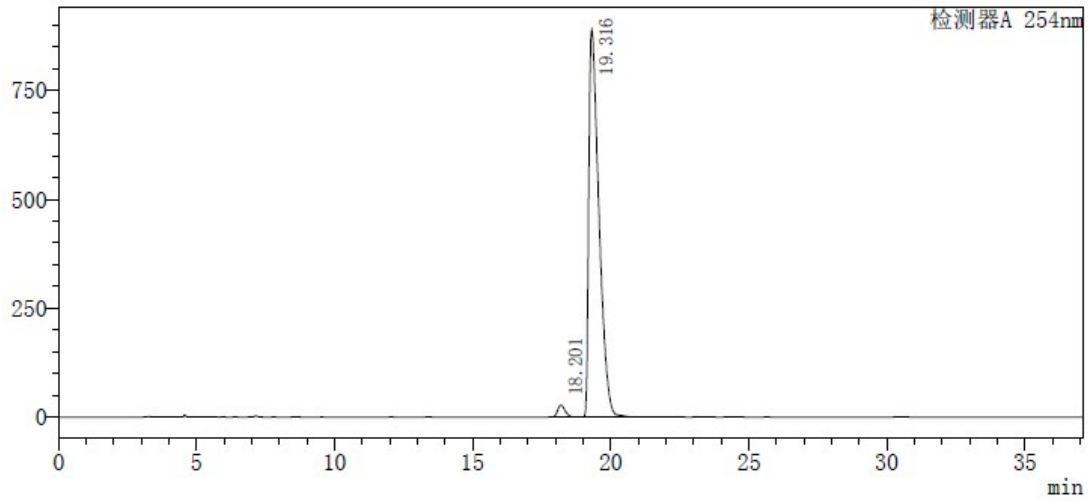
	Retention Time (min)	Area (%)	
Peak 1	21.611	2.961	**94% ee**
Peak 2	22.905	97.039	



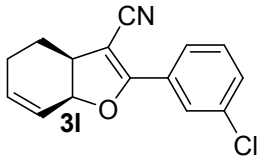
Racemate:



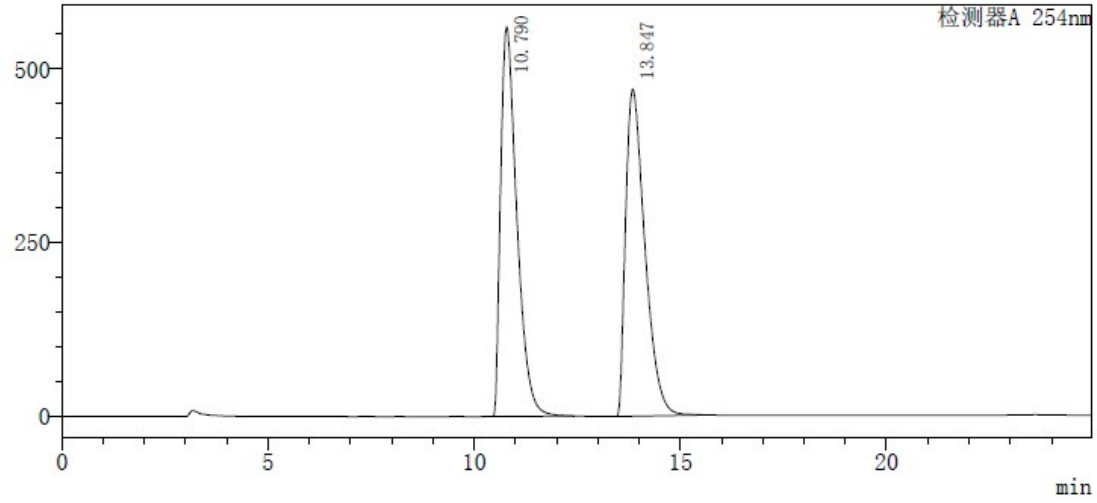
Chiral:



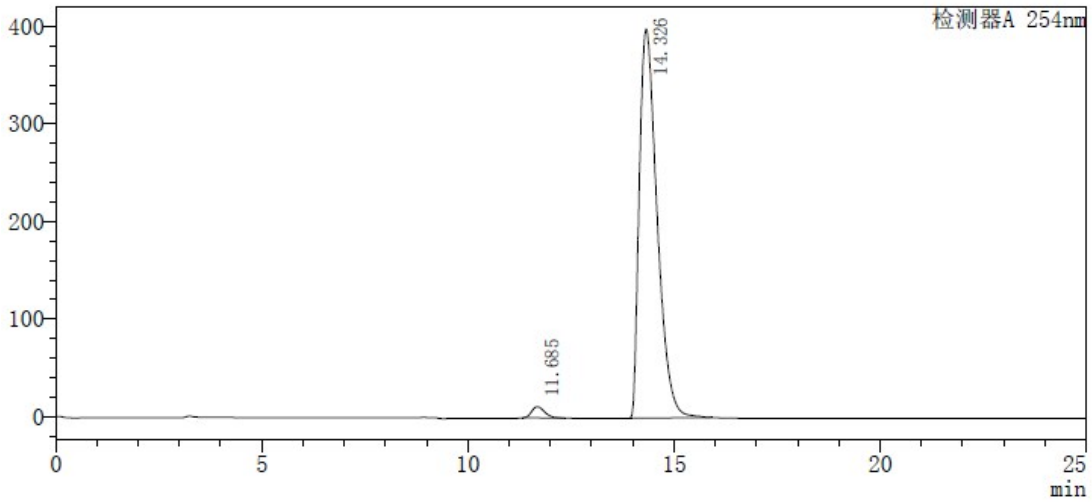
	Retention Time (min)	Area (%)	
Peak 1	18.201	2.134	**96% ee**
Peak 2	19.316	97.866	



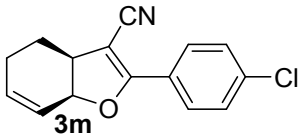
Racemate:



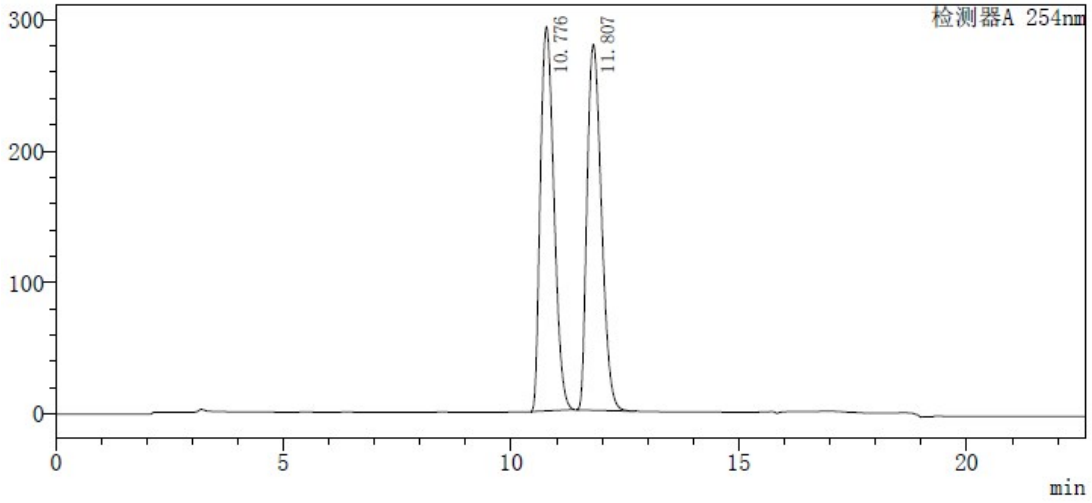
Chiral:



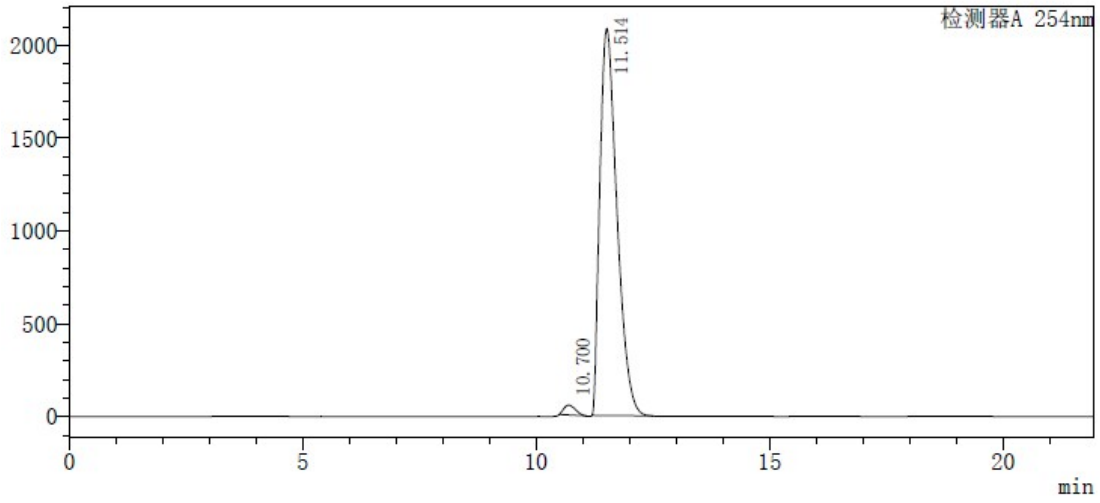
	Retention Time (min)	Area (%)	
Peak 1	11.685	2.032	**96% ee**
Peak 2	14.326	97.968	



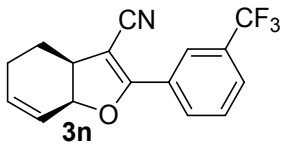
Racemate:



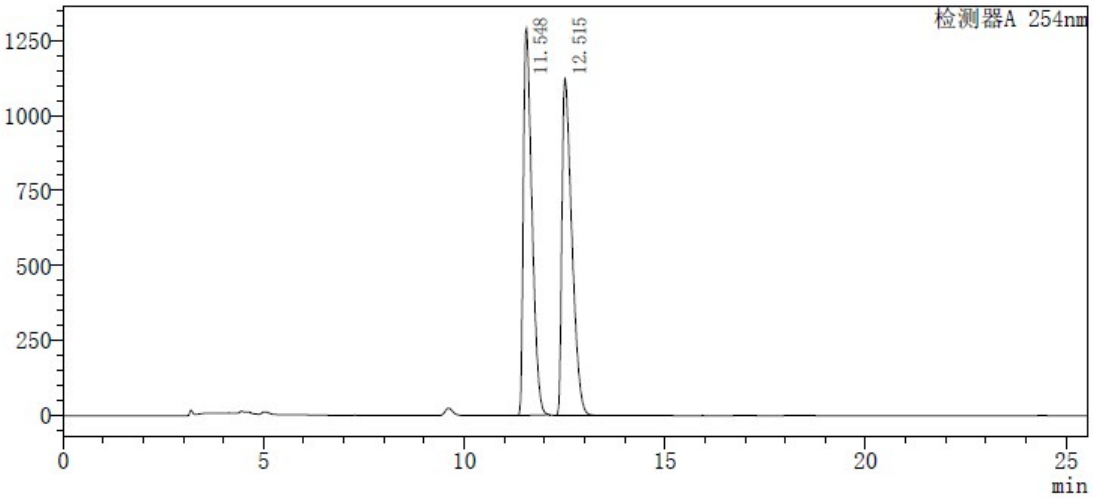
Chiral:



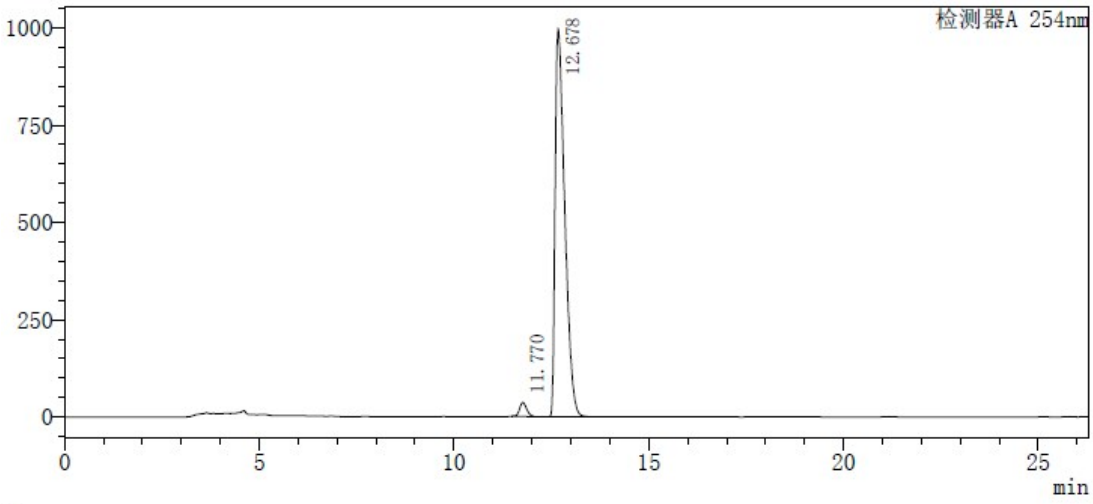
	Retention Time (min)	Area (%)	
Peak 1	10.700	1.690	**97% ee**
Peak 2	11.514	98.310	



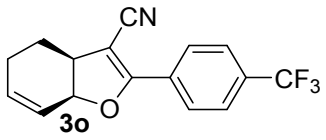
Racemate:



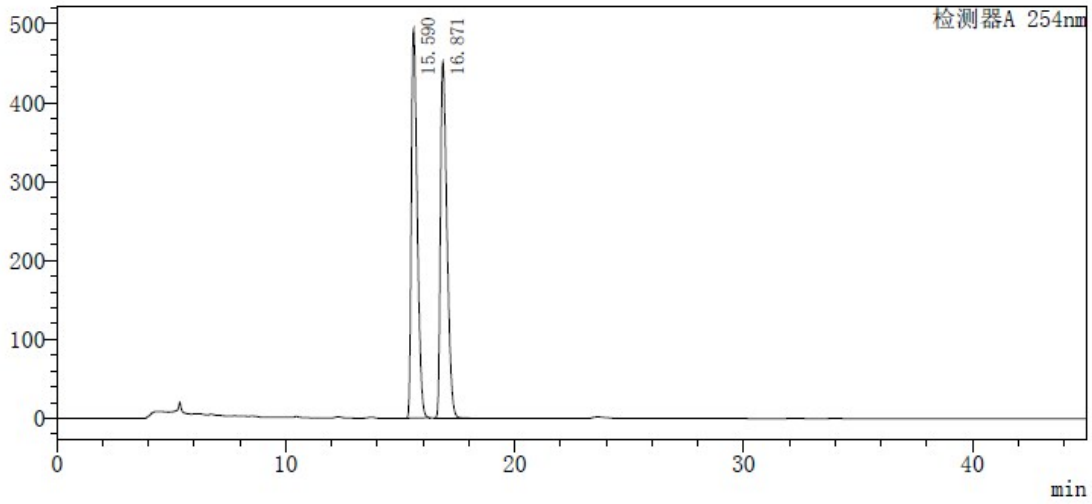
Chiral:



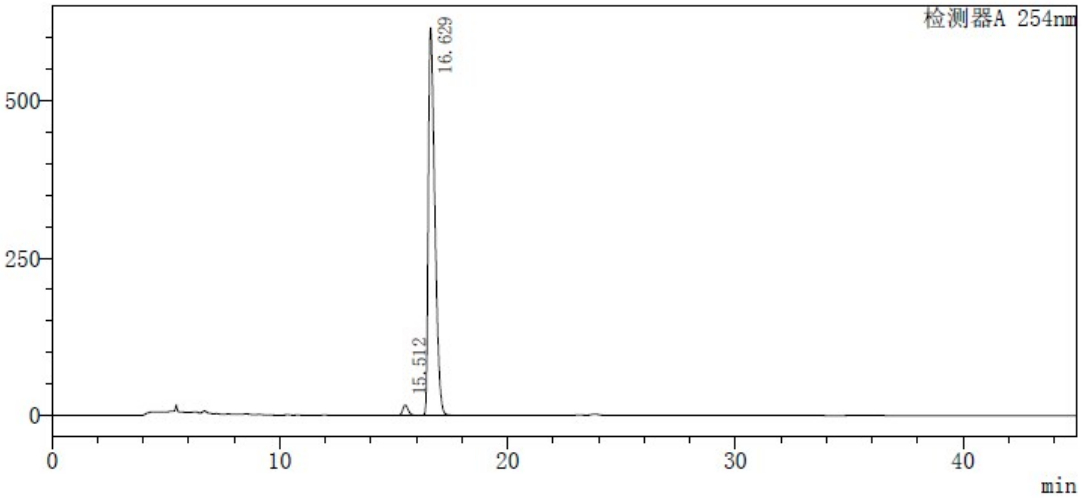
	Retention Time (min)	Area (%)	
Peak 1	11.770	2.575	**95% ee**
Peak 2	12.678	97.425	



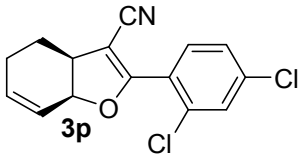
Racemate:



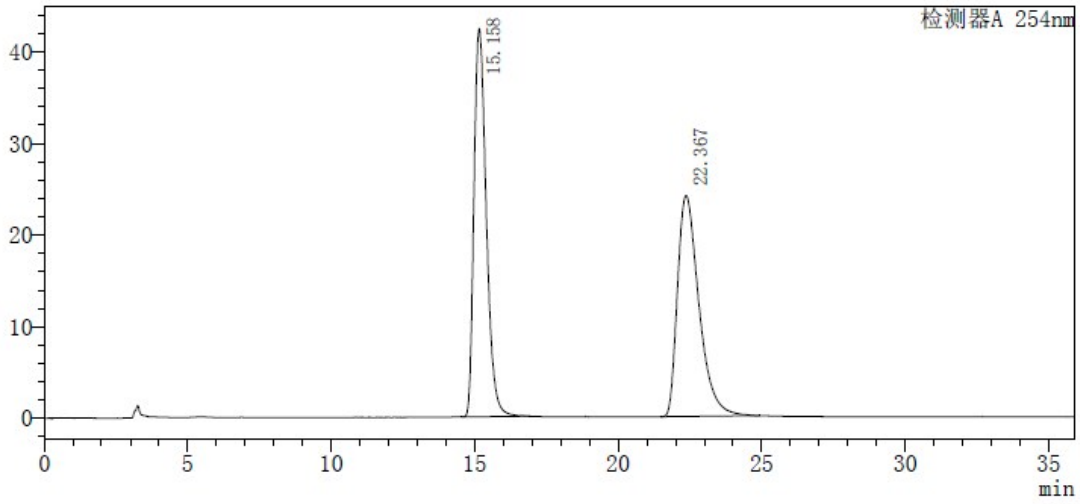
Chiral:



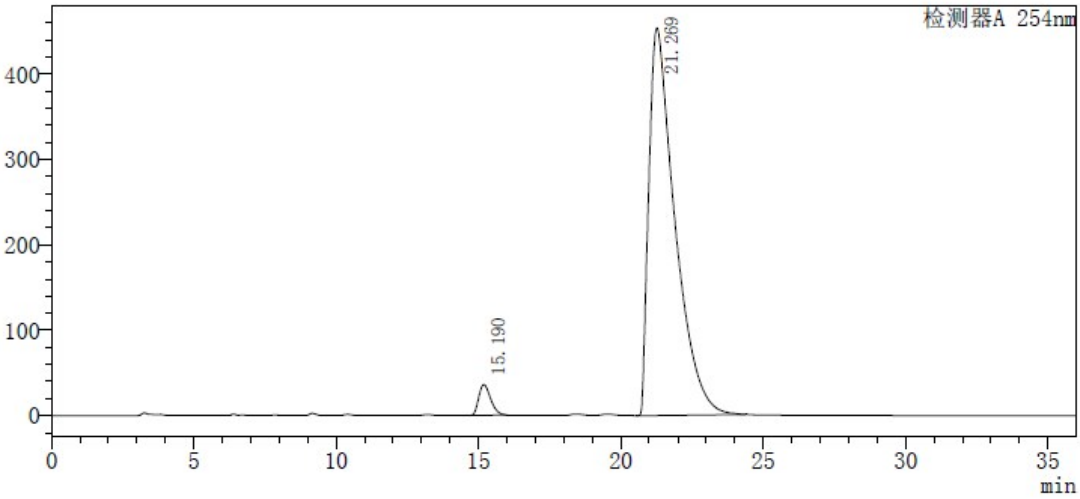
	Retention Time (min)	Area (%)	
Peak 1	15.512	2.127	**96% ee**
Peak 2	16.629	97.873	



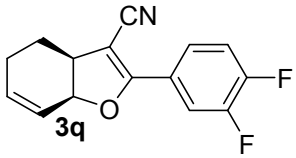
Racemate:



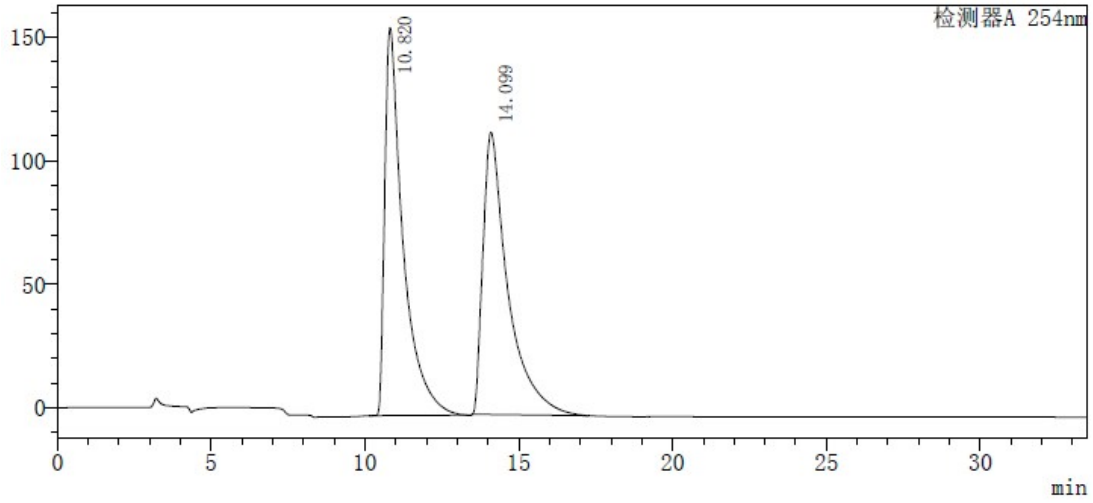
Chiral:



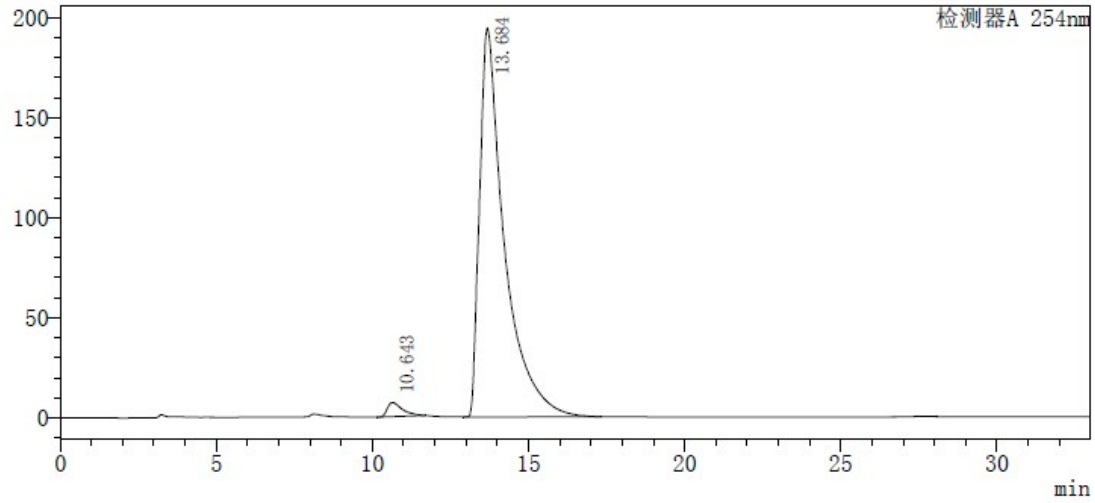
	Retention Time (min)	Area (%)	
Peak 1	15.190	3.501	**93% ee**
Peak 2	21.269	96.499	



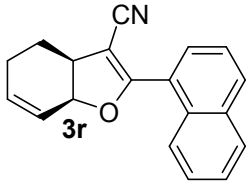
Racemate:



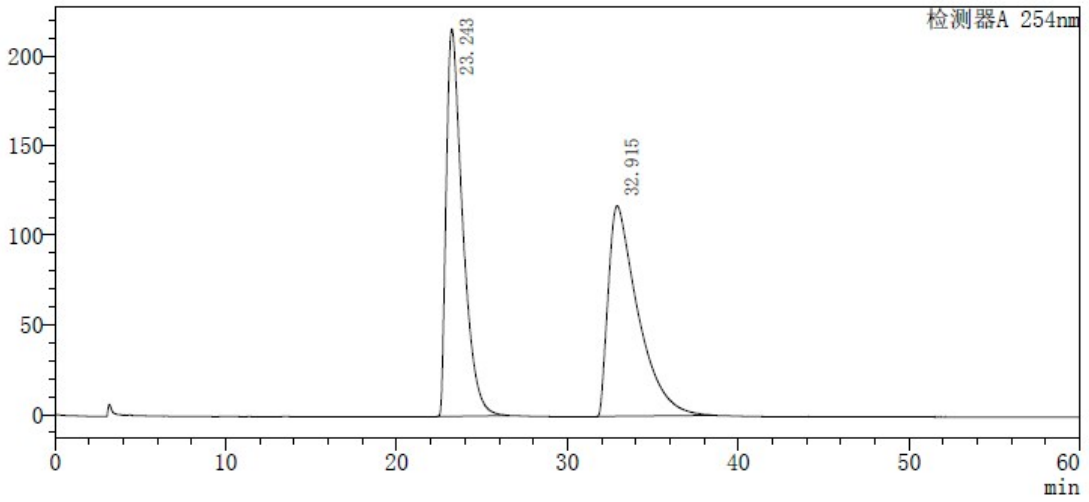
Chiral:



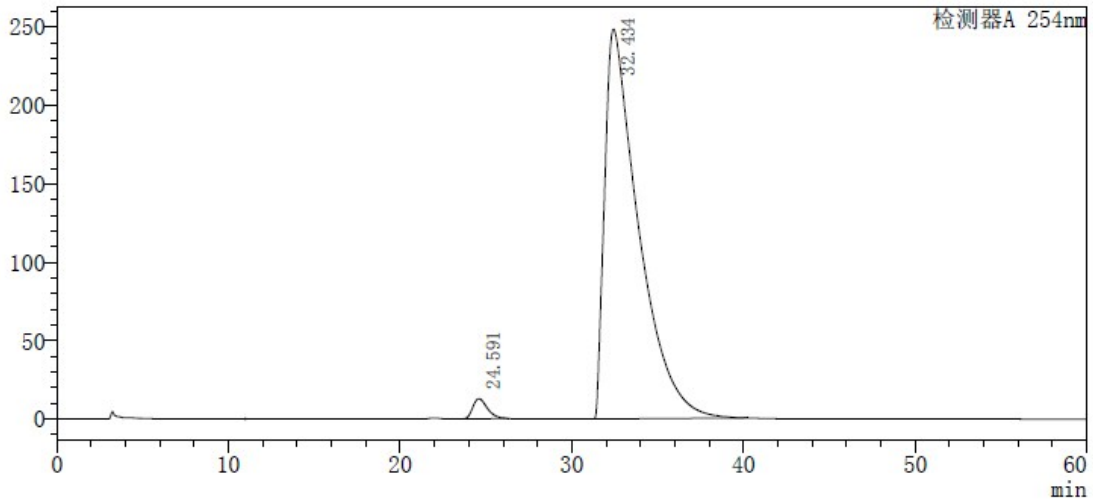
	Retention Time (min)	Area (%)	
Peak 1	10.643	2.167	**96% ee**
Peak 2	13.684	97.833	



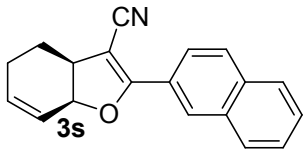
Racemate:



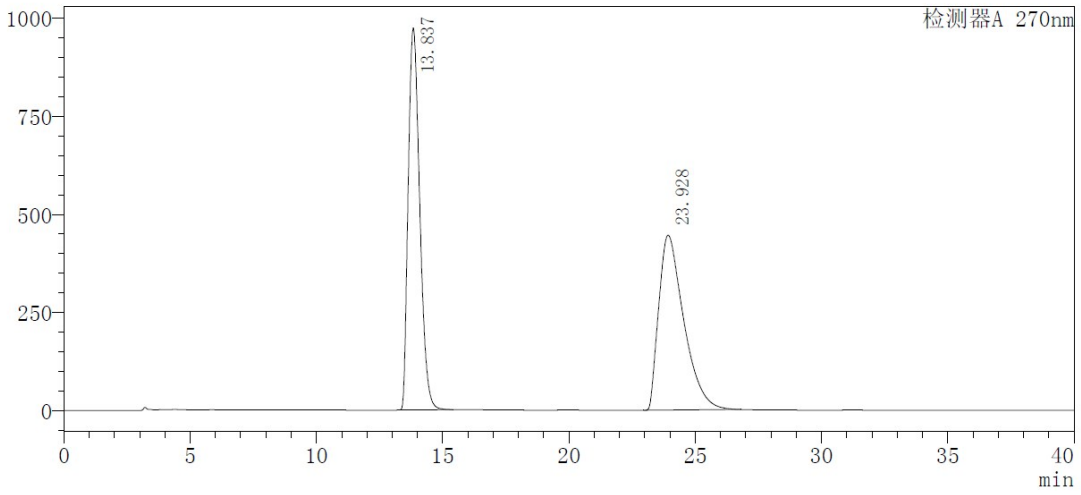
Chiral:



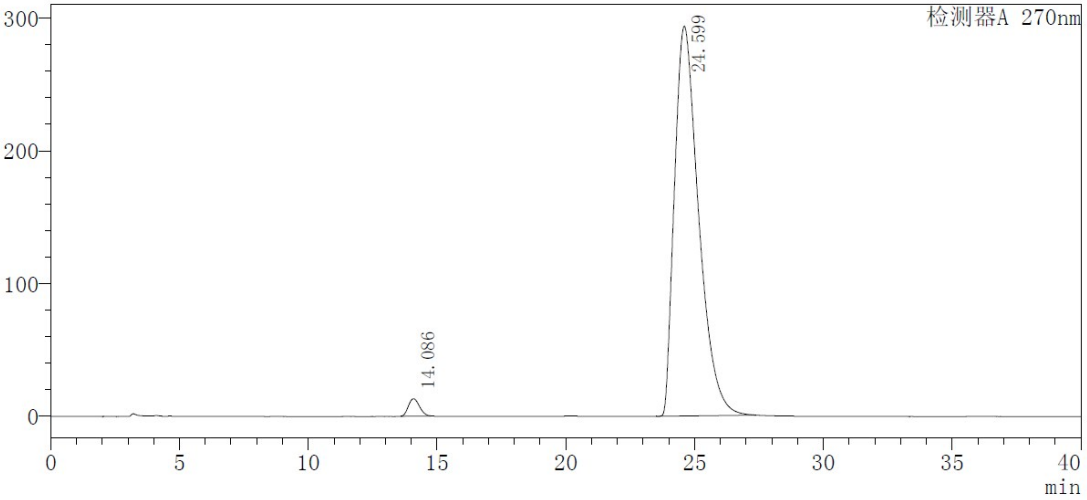
	Retention Time (min)	Area (%)	
Peak 1	24.591	2.167	**96% ee**
Peak 2	32.434	97.833	



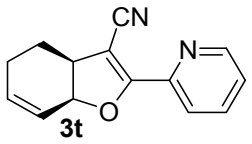
Racemate:



Chiral:

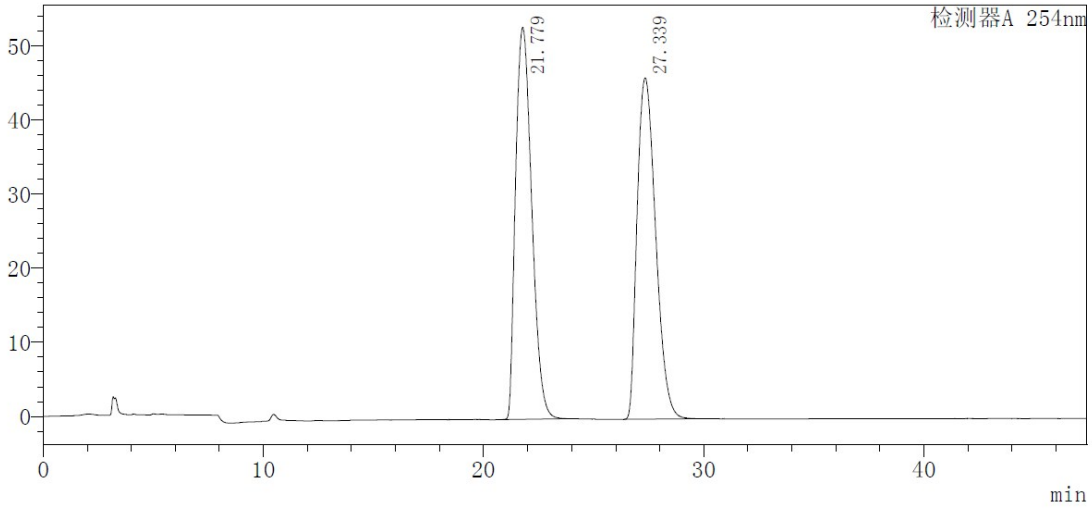


	Retention Time (min)	Area (%)	
Peak 1	14.086	2.014	**96% ee**
Peak 2	24.599	97.986	

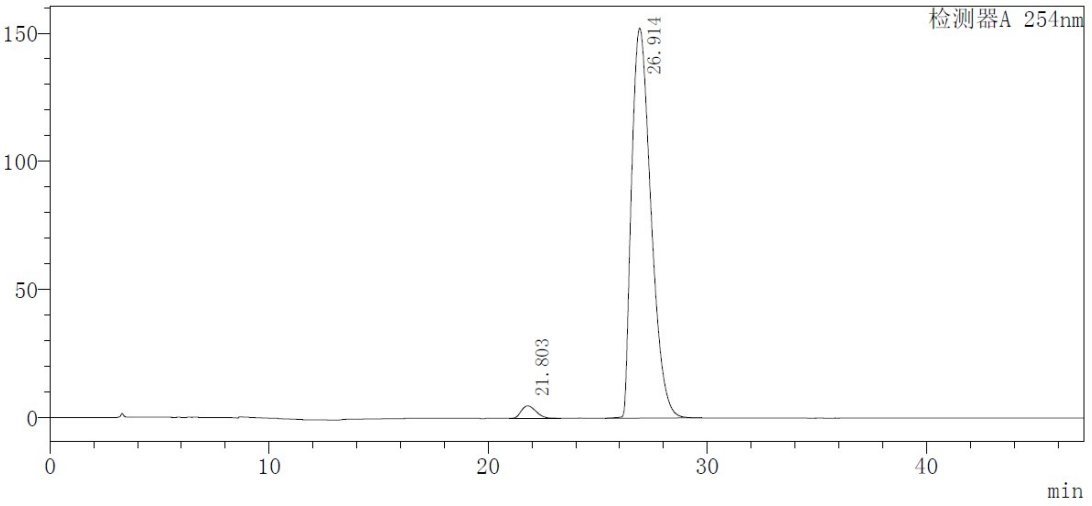


3t

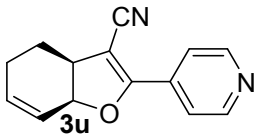
Racemate:



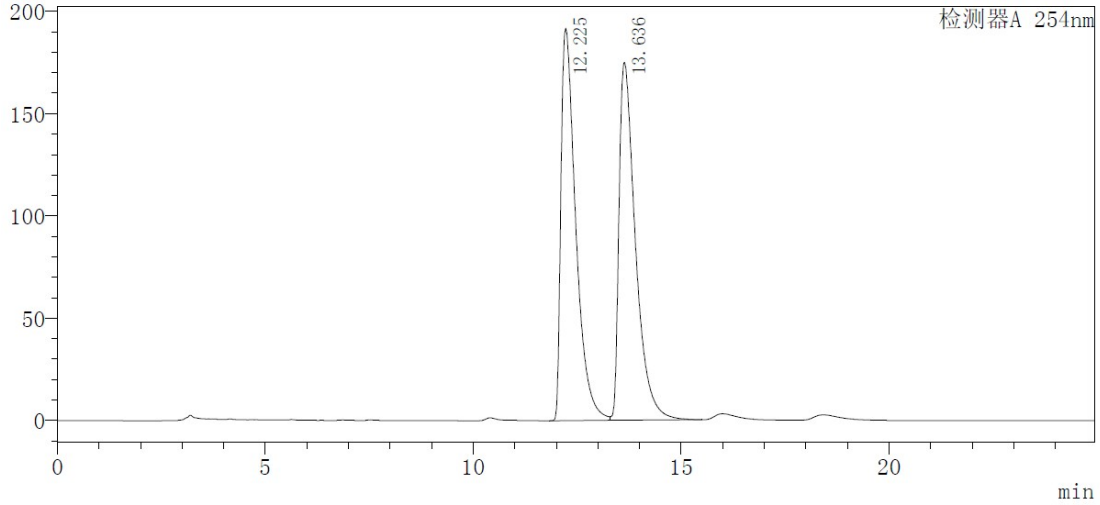
Chiral:



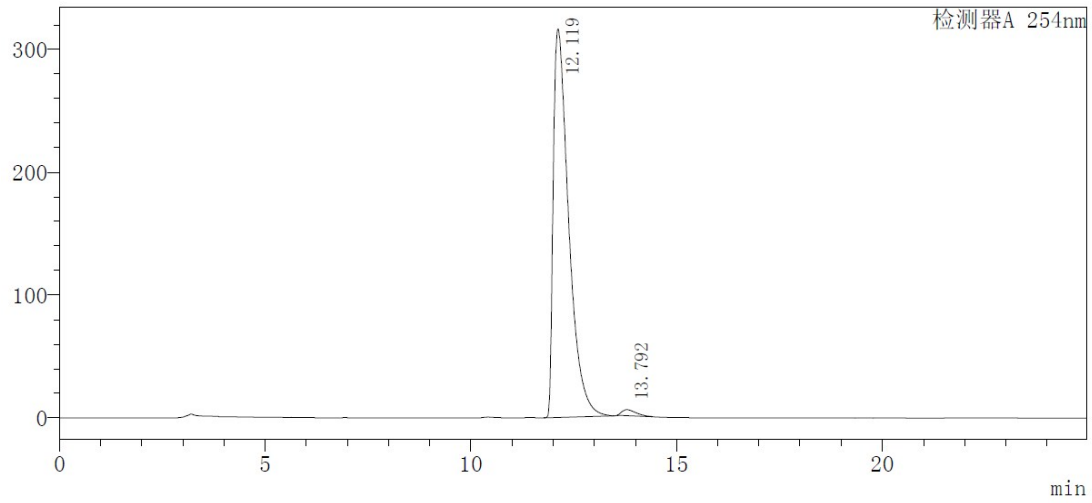
	Retention Time (min)	Area (%)	
Peak 1	21.803	2.368	**95% ee**
Peak 2	26.914	97.632	



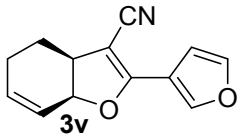
Racemate:



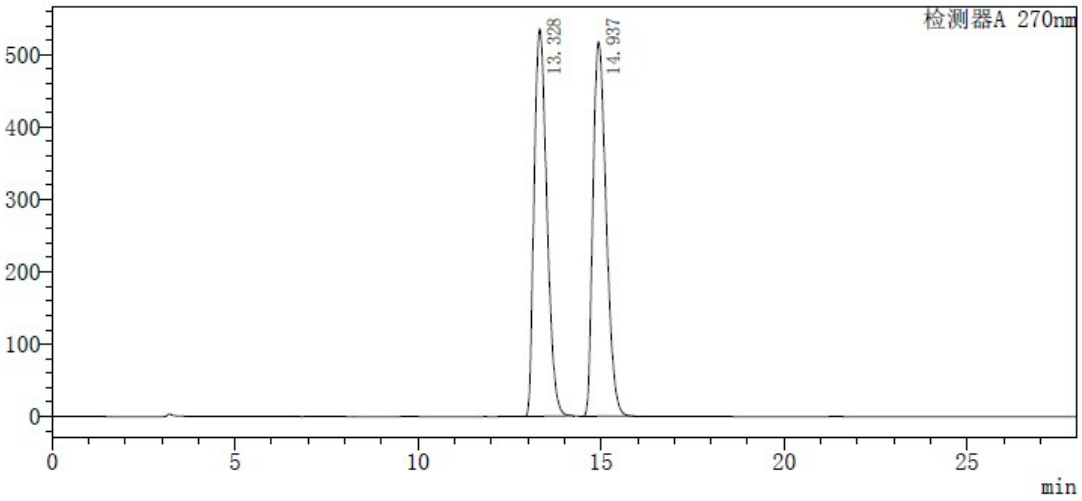
Chiral:



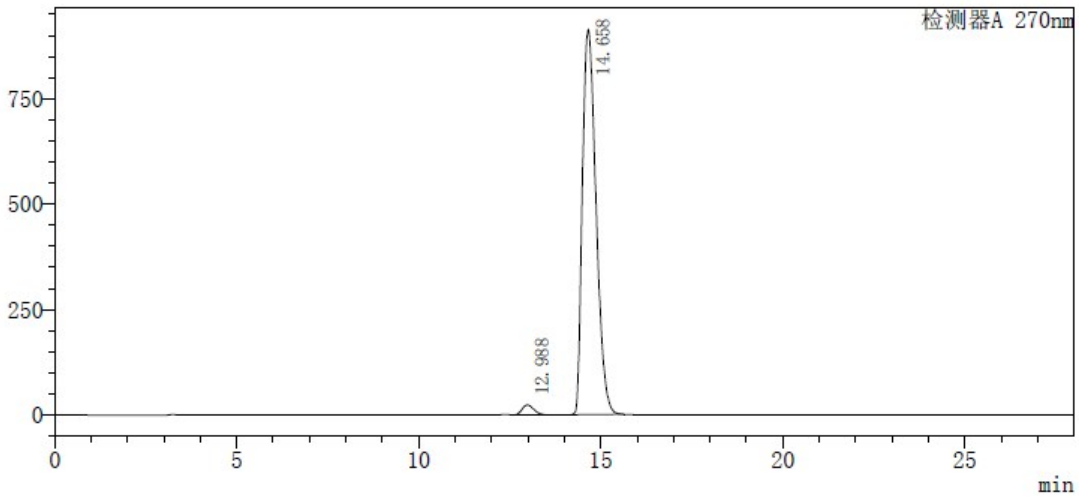
	Retention Time (min)	Area (%)	
Peak 1	12.119	98.646	**97% ee**
Peak 2	13.792	1.354	



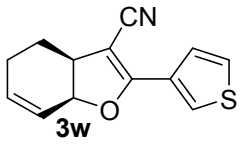
Racemate:



Chiral:

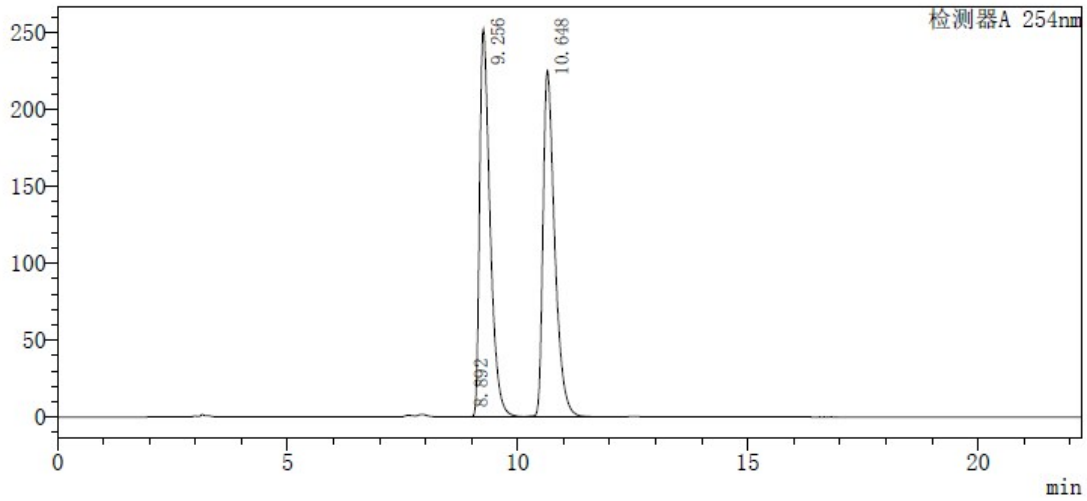


	Retention Time (min)	Area (%)	
Peak 1	12.988	2.121	**96% ee**
Peak 2	14.658	97.879	

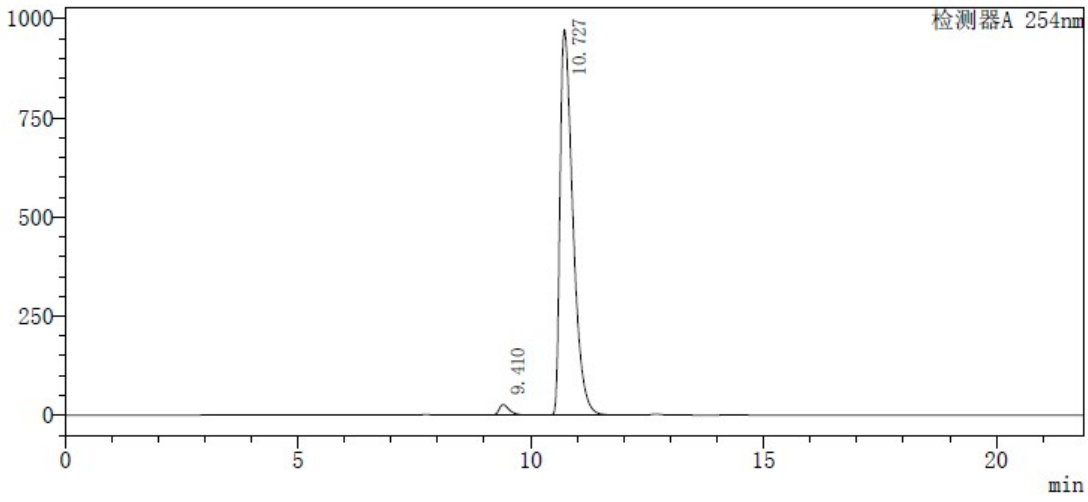


3w

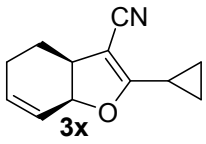
Racemate:



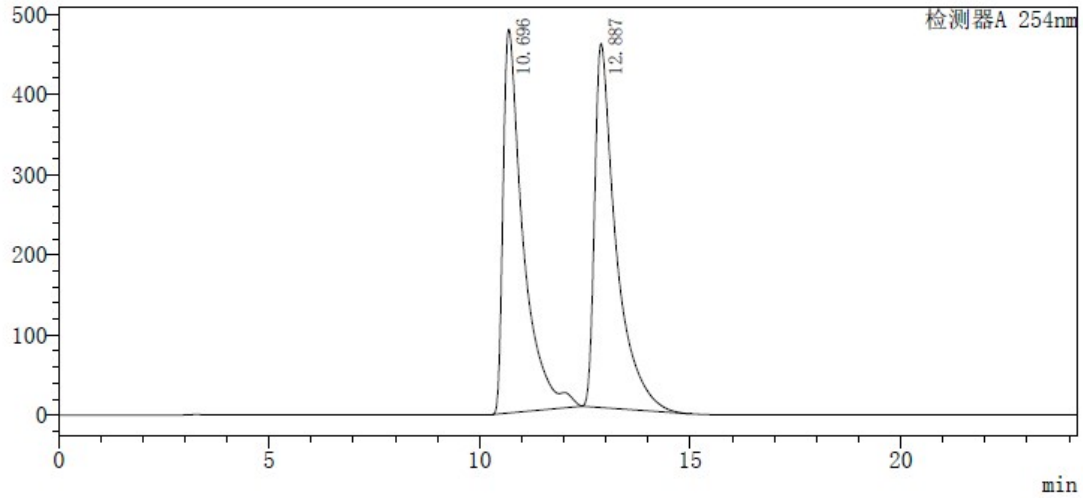
Chiral:



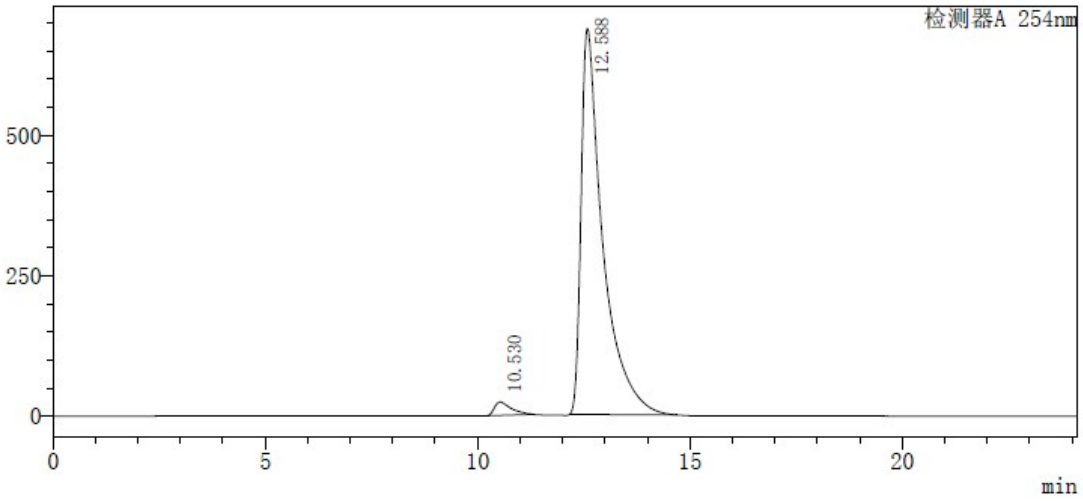
	Retention Time (min)	Area (%)	
Peak 1	9.410	2.069	**96% ee**
Peak 2	10.727	97.931	



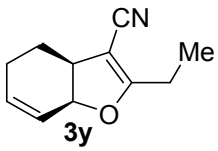
Racemate:



Chiral:

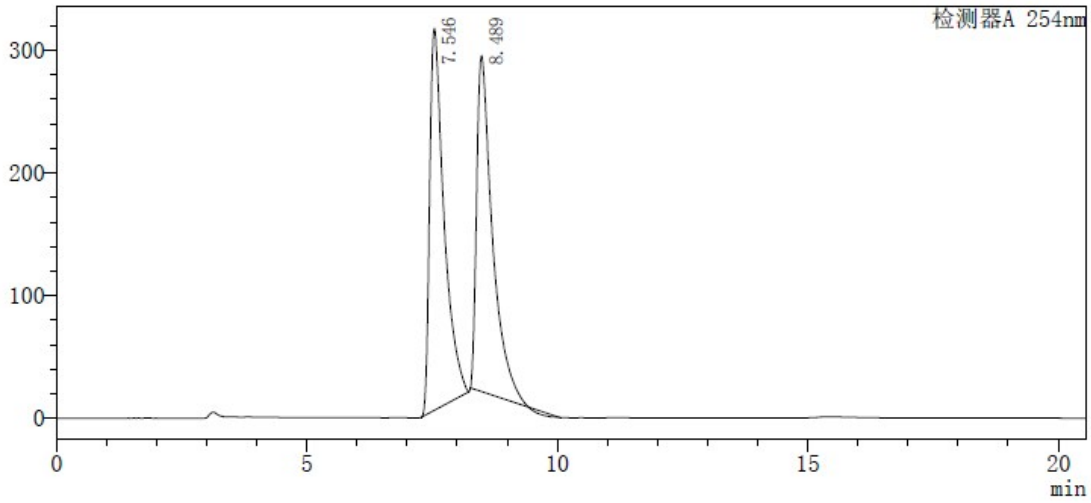


	Retention Time (min)	Area (%)	
Peak 1	10.530	2.636	**95% ee**
Peak 2	12.588	97.364	

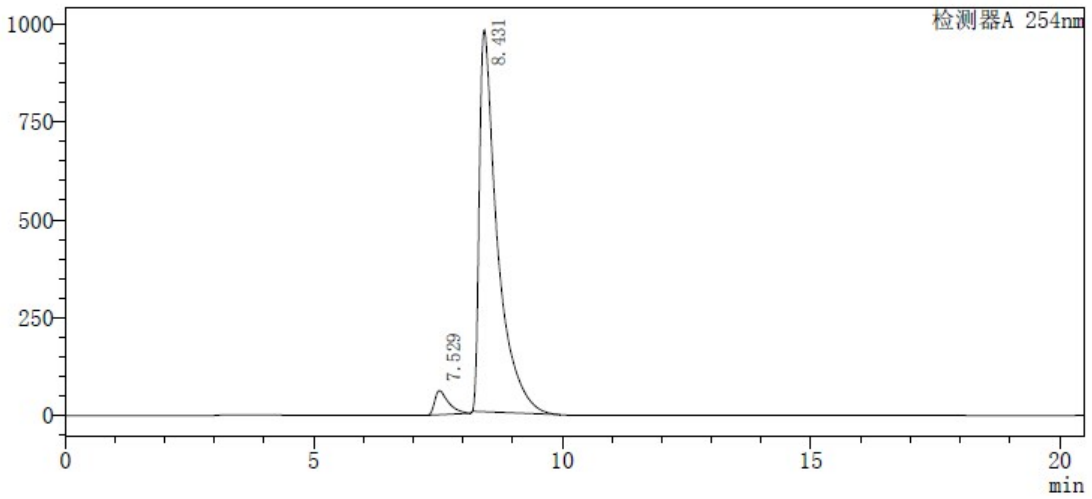


3y

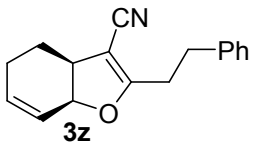
Racemate:



Chiral:

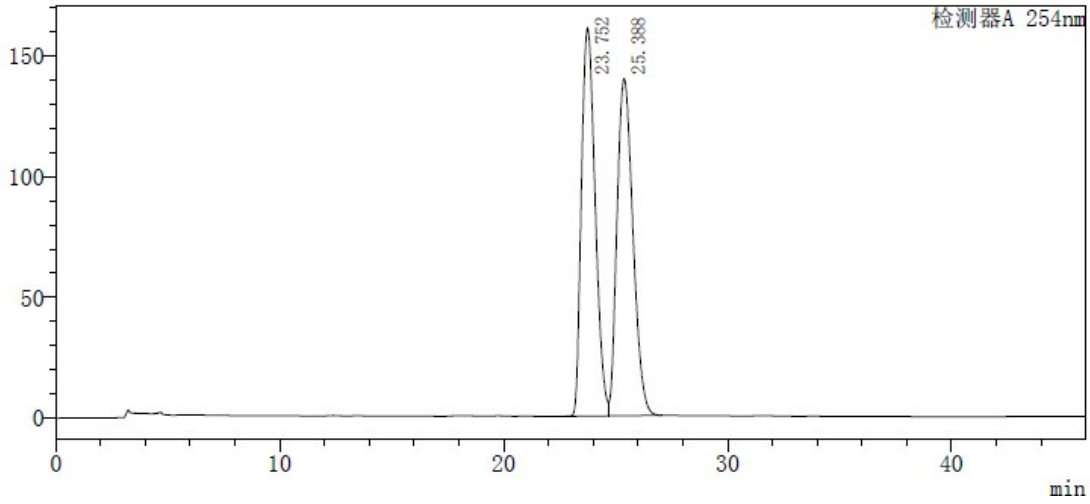


	Retention Time (min)	Area (%)	
Peak 1	7.529	4.565	**91% ee**
Peak 2	8.431	95.435	

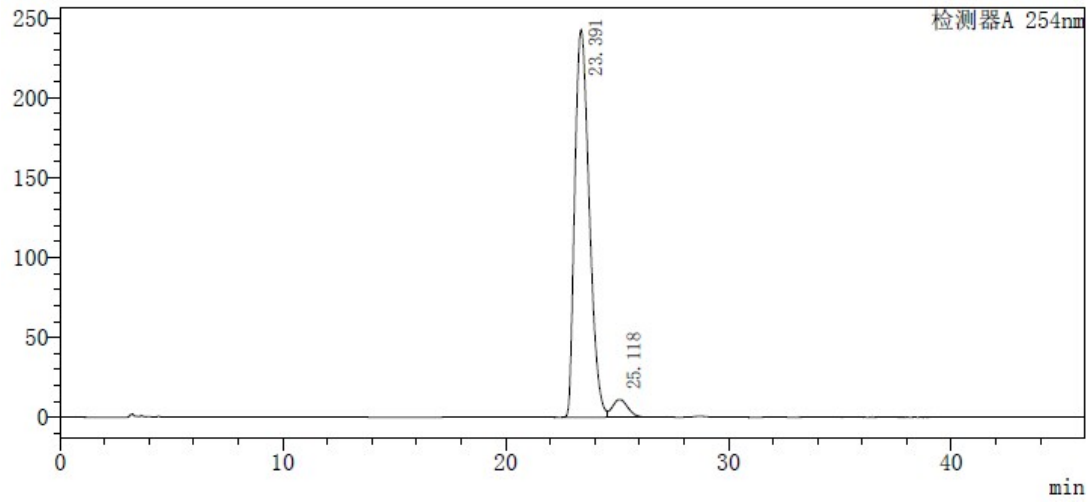


3z

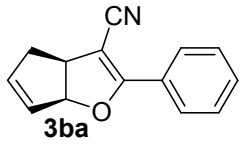
Racemate:



Chiral:

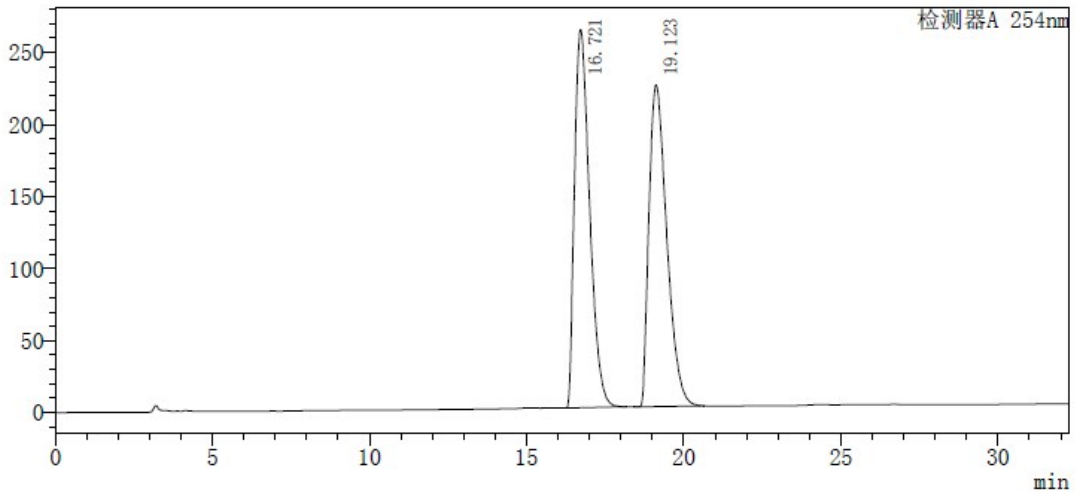


	Retention Time (min)	Area (%)	
Peak 1	23.391	95.487	**91% ee**
Peak 2	25.118	4.513	

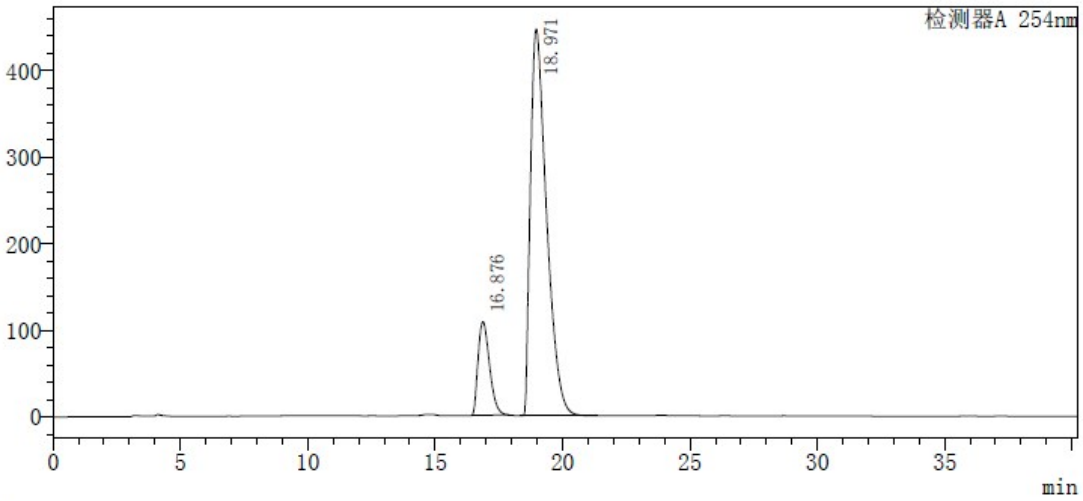


3ba

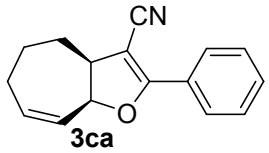
Racemate:



Chiral:

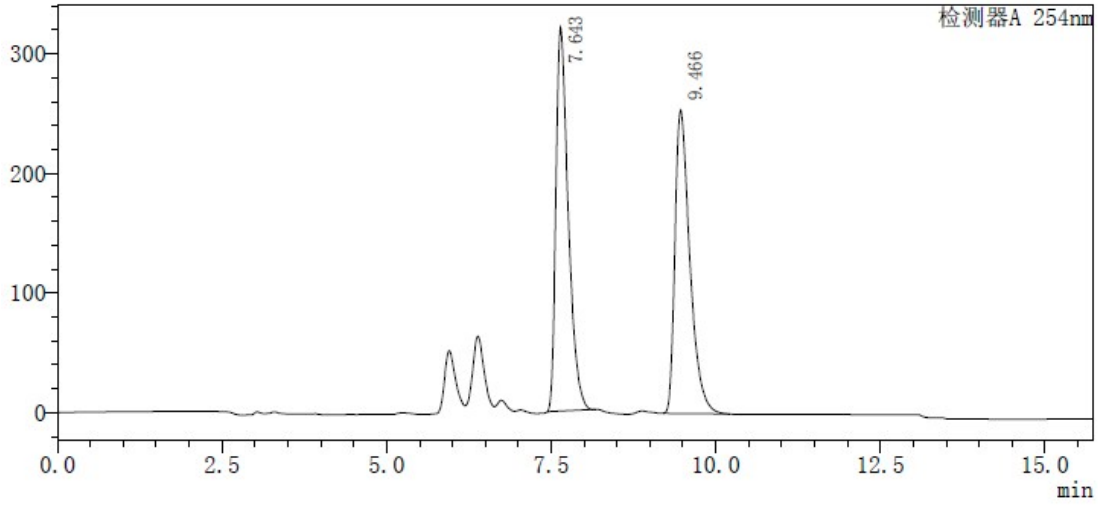


	Retention Time (min)	Area (%)	
Peak 1	16.876	14.648	**71% ee**
Peak 2	18.971	85.352	

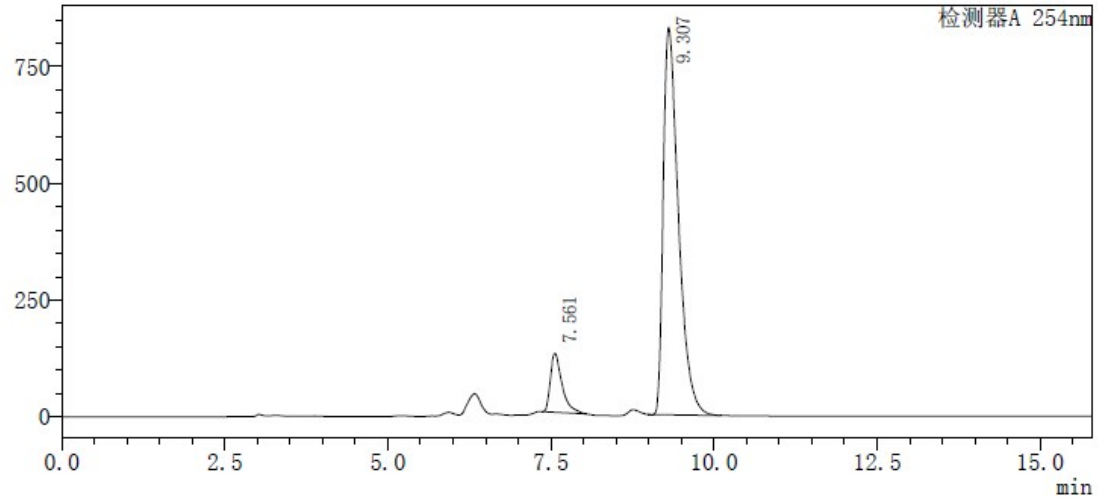


3ca

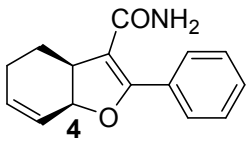
Racemate:



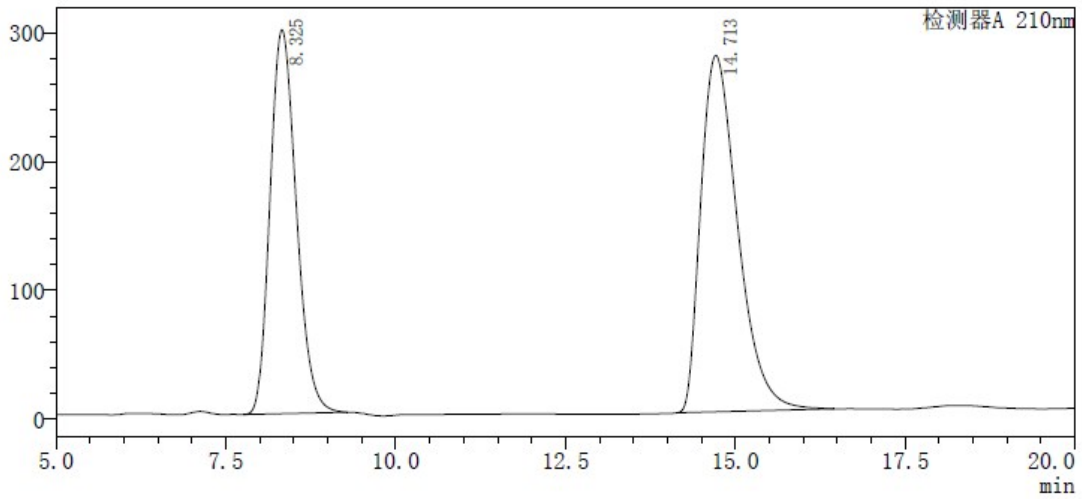
Chiral:



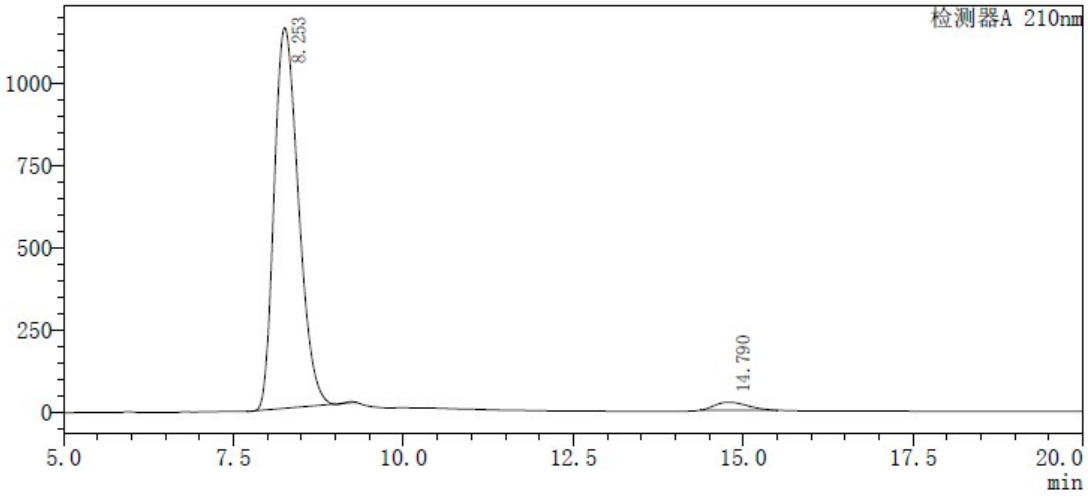
	Retention Time (min)	Area (%)	
Peak 1	7.561	10.440	**79% ee**
Peak 2	9.307	89.560	



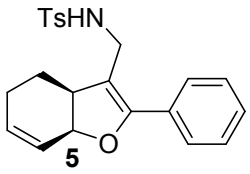
Racemate:



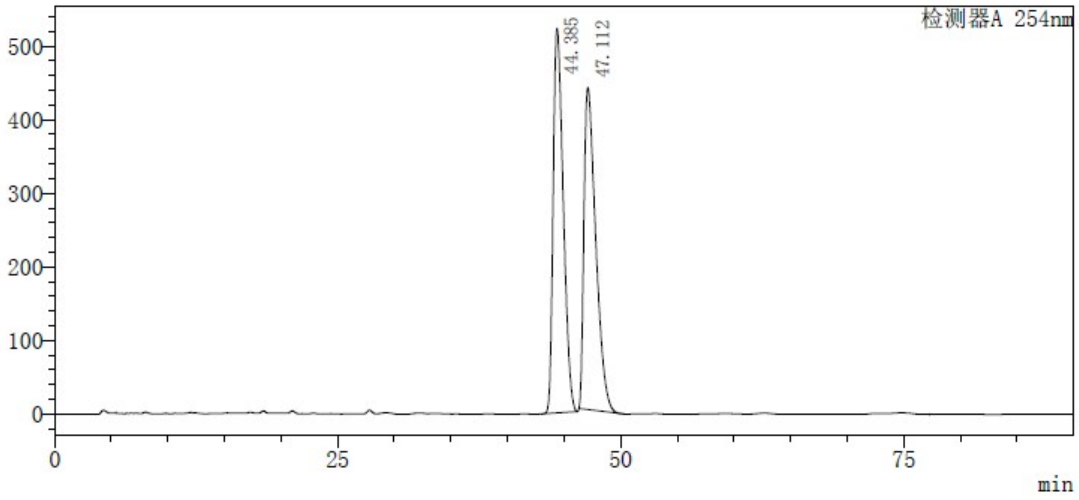
Chiral:



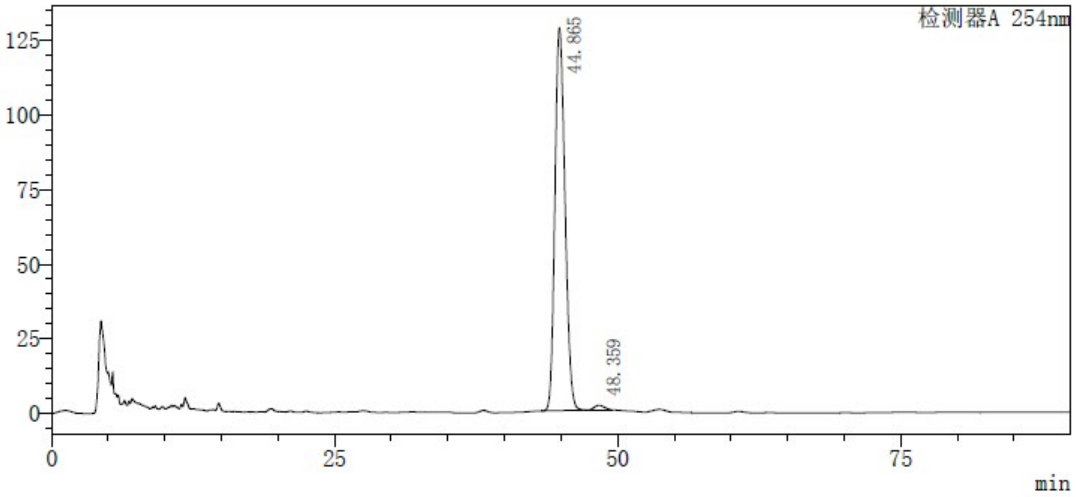
	Retention Time (min)	Area (%)	
Peak 1	8.253	97.579	**95% ee**
Peak 2	14.790	2.421	



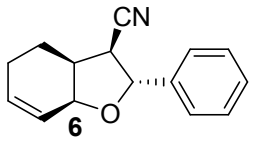
Racemate:



Chiral:

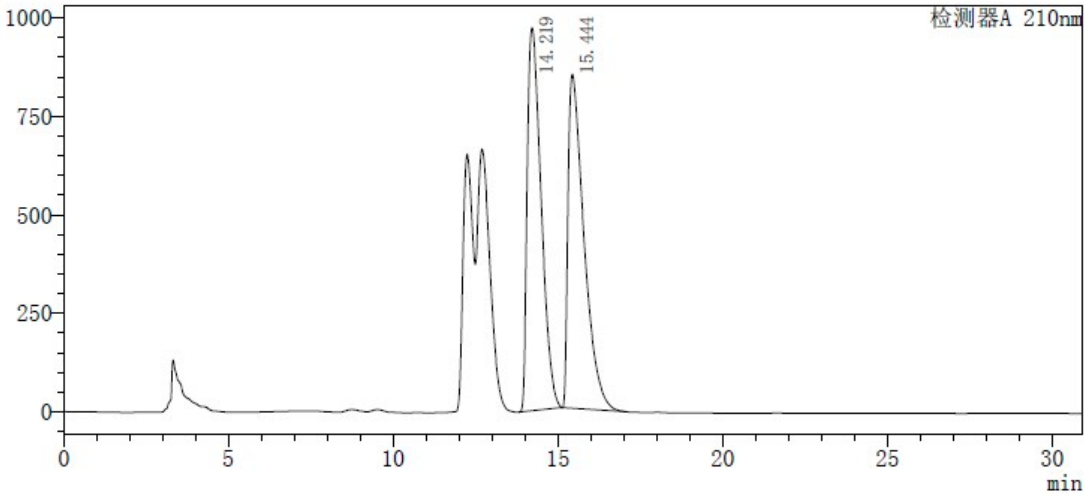


	Retention Time (min)	Area (%)	
Peak 1	44.865	98.793	**98% ee**
Peak 2	48.359	1.207	

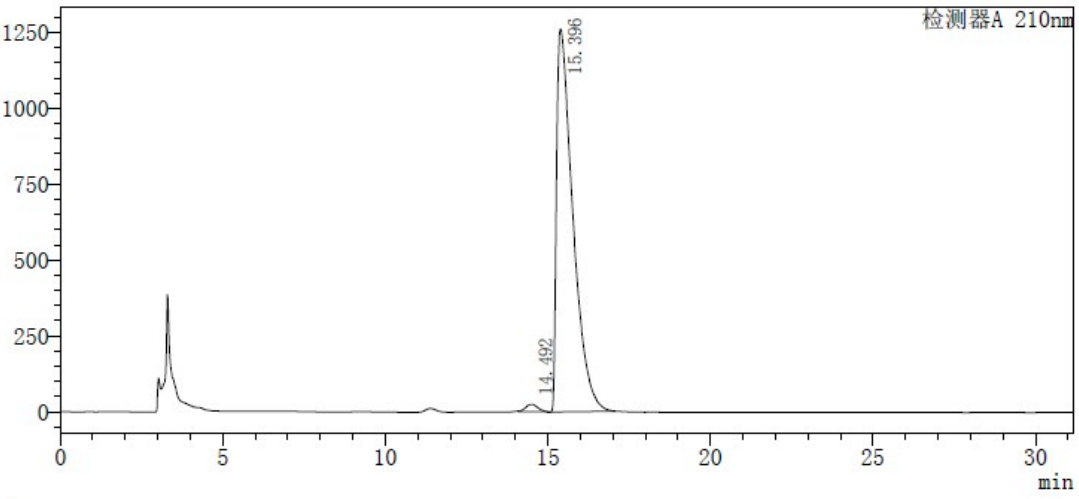


6

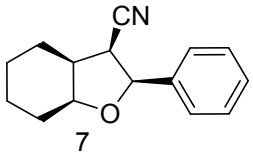
Racemate:



Chiral:

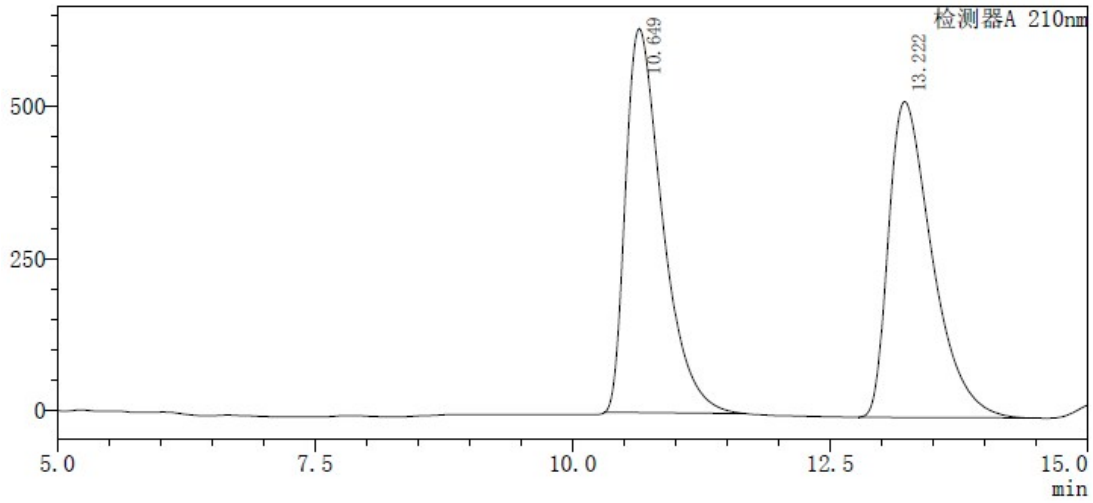


	Retention Time (min)	Area (%)	
Peak 1	14.492	1.328	**97% ee**
Peak 2	15.396	98.672	

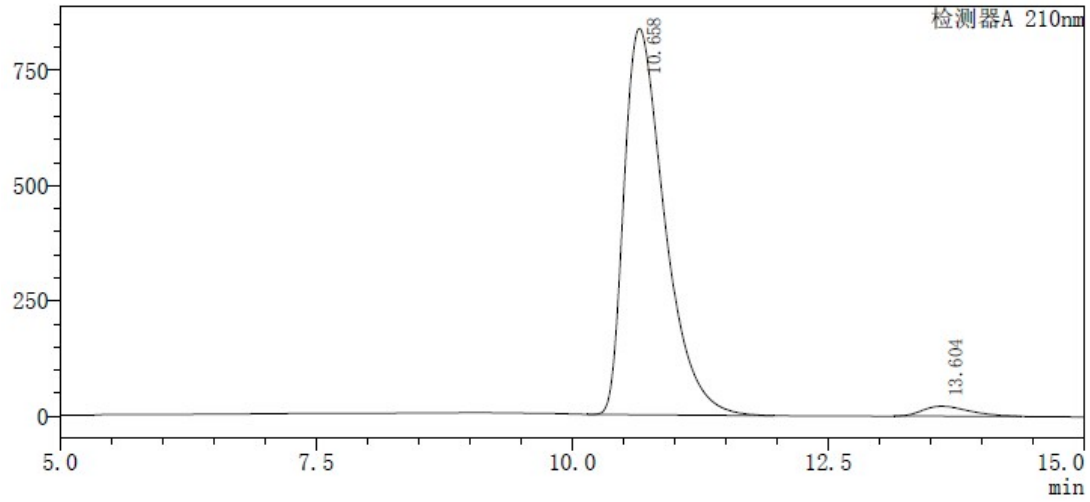


7

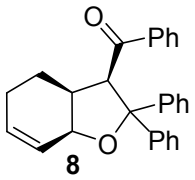
Racemate:



Chiral:

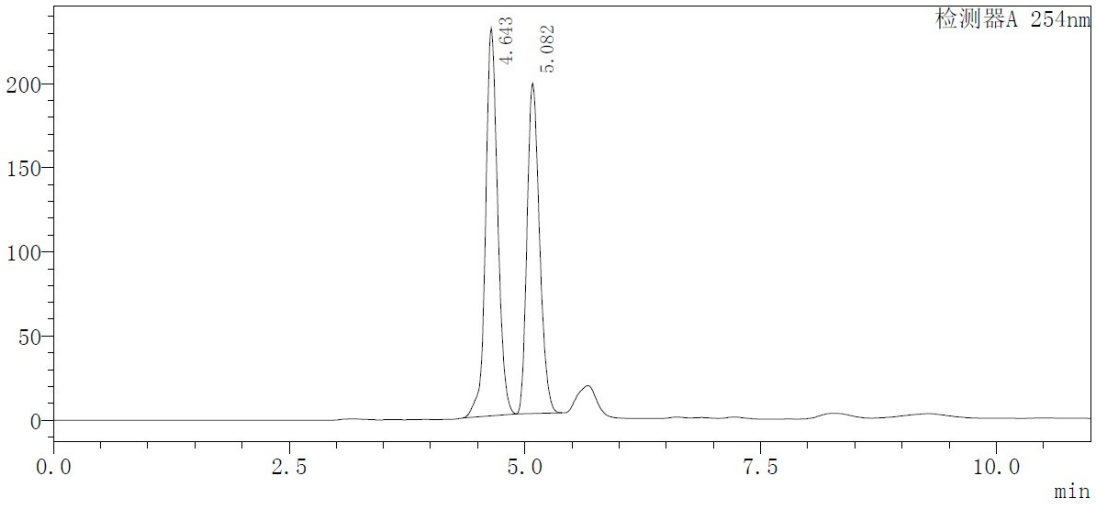


	Retention Time (min)	Area (%)	
Peak 1	10.658	97.197	**94% ee**
Peak 2	13.604	2.803	

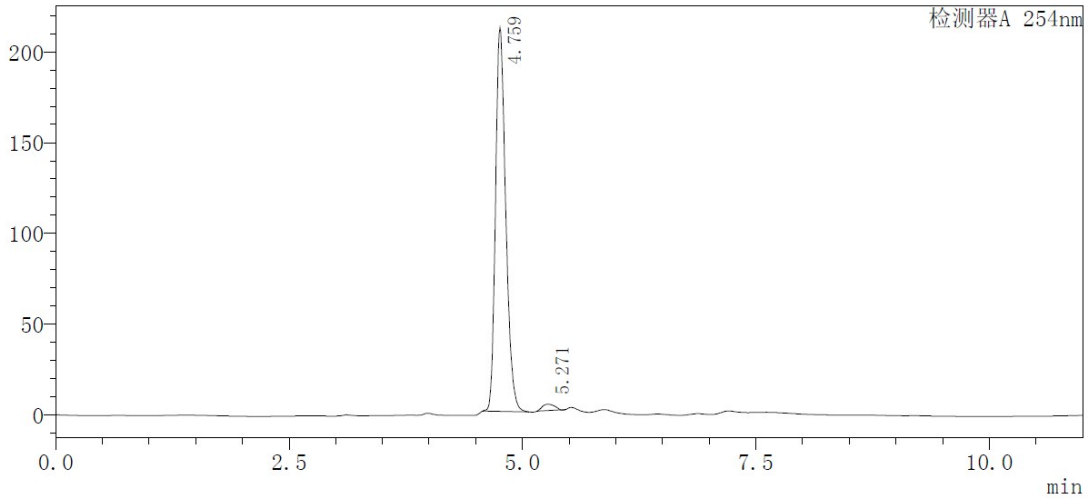


8

Racemate:



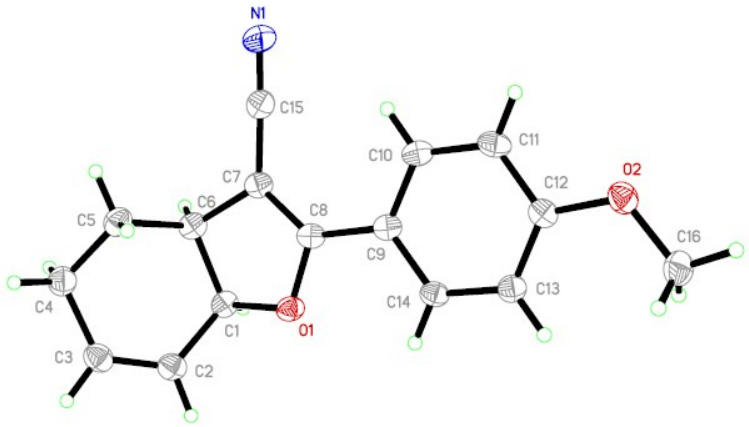
Chiral:



	Retention Time (min)	Area (%)	
Peak 1	4.759	98.074	**96% ee**
Peak 2	5.271	1.926	

8. X-ray Crystal Structure Analysis

X-Ray Crystallography Data for **3f** (CCDC 1940926): A colorless crystal suitable for X-ray crystallography was obtained from a *n*-hexane/dichloromethane solution at room temperature under air.



Bond precision: C-C = 0.0059 A Wavelength=1.54178

Cell: a=4.6461(6) b=11.4107(16) c=24.622(3)
alpha=90 beta=90 gamma=90
Temperature: 293 K

	Calculated	Reported
Volume	1305.3(3)	1305.3(3)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C16 H15 N O2	C16 H15 N O2
Sum formula	C16 H15 N O2	C16 H15 N O2
Mr	253.29	253.29
Dx,g cm-3	1.289	1.289
Z	4	4
Mu (mm-1)	0.683	0.683
F000	536.0	536.0
F000'	537.60	
h,k,lmax	5,13,28	5,13,28
Nref	2164[1310]	2155
Tmin,Tmax	0.872,0.903	0.519,0.753
Tmin'	0.872	

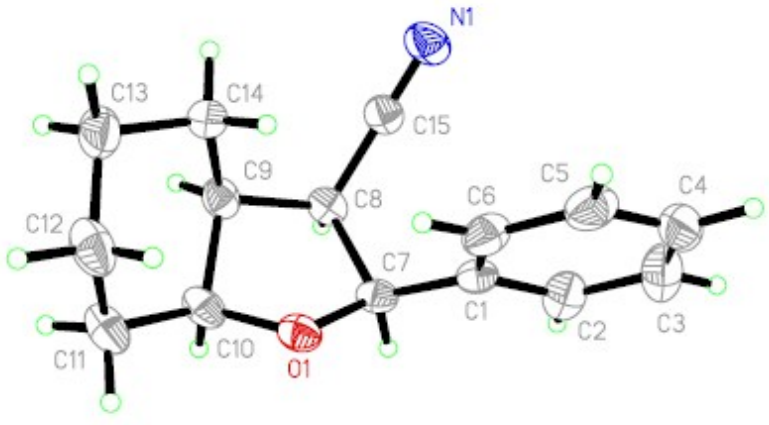
Correction method= # Reported T Limits: Tmin=0.519 Tmax=0.753
AbsCorr = ?

Data completeness= 1.65/1.00 Theta(max)= 63.758

R(reflections)= 0.0562(1913) wR2(reflections)= 0.1632(2155)

S = 1.158 Npar= 174

X-Ray Crystallography Data for **7** (CCDC 1945273): A colorless crystal suitable for X-ray crystallography was obtained from a *n*-hexane/dichloromethane solution at room temperature under air.



Bond precision: C-C = 0.0039 A Wavelength=1.54178

Cell: a=5.9300(1) b=8.7765(2) c=24.7421(6)
alpha=90 beta=90 gamma=90
Temperature: 297 K

	Calculated	Reported
Volume	1287.69(5)	1287.69(5)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C15 H17 N O	C15 H17 N O
Sum formula	C15 H17 N O	C15 H17 N O
Mr	227.30	227.29
Dx,g cm-3	1.172	1.172
Z	4	4
Mu (mm-1)	0.571	0.571
F000	488.0	488.0
F000'	489.33	
h,k,lmax	7,10,29	7,10,29
Nref	2364[1408]	2353
Tmin,Tmax	0.892,0.913	0.679,0.753
Tmin'	0.892	

Correction method= # Reported T Limits: Tmin=0.679 Tmax=0.753
AbsCorr = ?

Data completeness= 1.67/1.00 Theta(max)= 68.308

R(reflections)= 0.0387(2161) wR2(reflections)= 0.1079(2353)

S = 1.046 Npar= 154

9. References

1. J. X. Shen, D, J. Yang, Y. X. Liu and R. H. Liu, *Org. Lett*. 2014, **16**, 350.
2. H. Vzquez-Villa, S. Reber and M. A. Ariger, Carreira, E. M. *Angew. Chem. Int. Ed.* 2011, **50**, 8979.
3. A. D. Mamuye, L. Castoldi and V. Pace, *Org. Biomol. Chem.* 2015, **13**, 1969.
4. L. Joubran, W. R. Jackson, E. M. Campi and B. Jarrott, *Aust. J. Chem.* 2003, **56**, 597.
5. S. Y. Lee, T. Kim, B. H. Lee and K. Y. Yia, *Bioogr. Med. Chem. Lett.* 2007, **17**, 1291.
6. G. Rai, K. R. Brimacombe and B. T. Mott, *J. Med. Chem.* 2017, **60**, 9184.
7. R. Zanaletti, L. Bettinetti, C. Castaldo and M. Valacchi, *J. Med. Chem.* 2012, **55**, 4806.
8. S. Kamila, D. M. Zhu, E. R. Biehl and L. Hua, *Org. Lett.* 2006, **8**, 4429.
9. J. Zhou, X. H. Zhu and Y. Q. Wan, *Eur. J. Org. Chem.* 2017, **16**, 2317.
10. T. Nagata, H. Matsubara, K. Kiyokawa and S. Minakata, *Org. Lett.* 2017, **19**, 4672.
11. Q. An, D. Liu, J. Shen, Y. Liu and W. Zhang, *Org. Lett.* 2017, **19**, 238.
12. (a) J. Chiang and S. Bauer, *J. Am. Chem. Soc.*1969, **91**, 1898; (b) J. Fiaud and L. Aribi-Zouioueche, *J. Chem. Soc., Chem. Commun.* 1986, 390; (c) H.Yoshizaki, H. Satoh, Y. Sato, S. Nukui, M. Shibasaki and M. Mori, *J. Org. Chem.* 1995, **60**, 2016.
13. J. Feng, X. Yuan, W. Luo, L. Lin, X. Liu and X. Feng, *Chem. Eur. J.* 2016, **22**, 15650.
14. B. Turnbull and P. Evans, *J. Am. Chem. Soc.* 2015, **137**, 6156.
15. Q. An, J. Shen, N. Butt, D. Liu, Y. Liu and W. Zhang, *Adv. Synth. Catal.* 2015, **357**, 3627.