# Supporting Information

# Base promoted one pot solvent free version of Ramachary reductive coupling/alkylation reaction for the synthesis of 2,2-disubstituted ethyl cyanoacetates

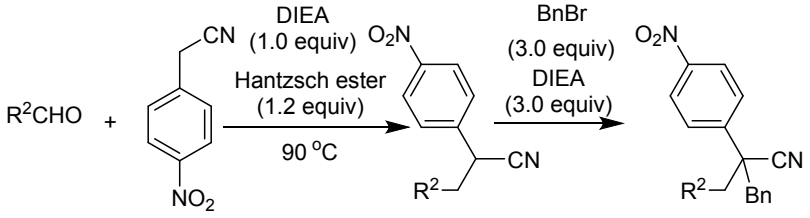
Guangyou Jiang[a#], Min Liu[a#], Dongmei Fang[b], Ping Tan[a], Min Huang[a], Taiping Zhou[a], Zhenju Jiang[a], Zhihong Xu*[a], Zhouyu Wang*[a]

[a] Department of Chemistry, Xihua University, Chengdu, 610039, China. E-mail: zhouyuwang77@163.com, xzh1966@163.com
[b] Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu, 610041, China.
[#]These authors contributed equally to this work and should be considered co-first authors.
Fax: +86-028-8772-3006; Tel: +86-028-8772-9463

**General Methods:** All starting materials were of the commercially available (analytical grade) and used without further purification. All the solvents are used after redistillation. Reactions were monitored by thin layer chromatography using silica gel HSGF254 plates. Flash chromatography was performed using silica gel HG/T2354-92. Melting points were measured with SGW X-4 melting point apparatus. $^1$H NMR (400 MHz) spectra were recorded in $CDCl_3$ or DMSO. $^1$H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, δ = 7.26 ppm； DMSO, δ = 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constants (Hz) and integration.$^{13}$C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, 77.0 ppm; DMSO, 39.5 ppm). Chemical yields refer to pure isolated substances. ESIMS spectra were recorded on BioTOF Q. All products were prepared according to the general procedure. Except for **1f** and **1i**, all the products are unknown compounds.

**General experimental procedure for preparing 2, 2-disubstituted ethyl cyanoacetates:** Under solvent-free conditions, the mixture of aldehydes (0.25 mmol), ethyl 2-cyanoacetate (0.30 mmol), benzyl bromide (0.75 mmol), DIEA (0.50 mmol) and Hantzsch esters (0.30 mmol) was stirred at 90 ℃ for 2 h. After the completion of the K/H/A process and the reaction mixtures were cooled to room temperature. Then the residue was purified through column chromatograph on silica gel to give the pure products**.**

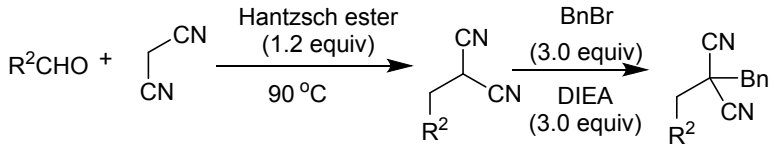
**General experimental procedure for preparing 2, 2-disubstituted 2-(4-nitrophenyl)-acetonitrile:** Under solvent-free conditions, the mixture of aldehydes (0.25 mmol), 2-(4-nitrophenyl)-acetonitrile (0.25 mmol), DIEA (0.25 mmol) and Hantzsch esters (0.30 mmol) was stirred at 90 ℃ for 2 h. After the completion of the K/H process and the reaction mixtures were cooled to room temperature. Without any work up process, the benzyl bromide (0.75 mmol) with DIEA (0.75 mmol) were added and the stirring was maintained at 90 ℃ for 2 h. The reaction mixtures were cooled to room temperature. The residue was purified through column chromatograph（Petroleum ether : EtOAc ，80:1→15:1） onto silica gel to give the crude products. Finally, all the crude products are purified through the silica gel plate (200 mm × 200 mm, Petroleum ether : $CH_2Cl_2$ = 1: 1).



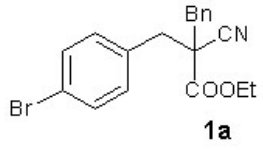

| Entry | $R^2$ | Yield (%) |
|---|---|---|
| 1 | $C_6H_5$ | 90 |
| 2 | 4-$BrC_6H_4$ | 86 |
| 3 | 4-$ClC_6H_4$ | 76 |
| 4 | 4-$FC_6H_4$ | 85 |
| 5 | 4-$MeC_6H_4$ | 95 |
| 6 | 4-$MeOC_6H_4$ | 76 |
| 7 | 4-$NCC_6H_4$ | 88 |
| 8 | 1-Naphthyl | 83 |
| 9 | 2-furyl | 62 |

| | | |
|---|---|---|
| 10 | 2-thienyl | 68 |

**General experimental procedure for preparing 2, 2-disubstituted malononitrile:** Under solvent-free conditions, the mixture of aldehydes (0.25 mmol), malononitrile(0.25 mmol) and Hantzsch esters (0.30 mmol) was stirred at 90 ℃ for 2 h. After the completion of the self-catalyzed K/H process and the reaction mixtures were cooled to room temperature. Without any work up process, the benzyl bromide (0.75 mmol) with DIEA (0.75 mmol) were added and stirred at 90 ℃ for 2 h. The reaction mixtures were cooled to room temperature. The residue was purified through column chromatograph（Petroleum ether : EtOAc ， 80:1→15:1） onto silica gel to give the crude products. Finally, all the crude products are purified through the silica gel plate (200 mm × 200 mm, Petroleum ether : $CH_2Cl_2$ = 1: 1).

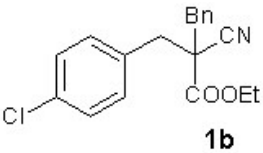



| Entry | $R^2$ | Yield (%) |
|---|---|---|
| 1 | $C_6H_5$ | 86 |
| 2 | 4-$BrC_6H_4$ | 93 |
| 3 | 4-$ClC_6H_4$ | 93 |
| 4 | 4-$FC_6H_4$ | 80 |
| 5 | 4-$MeC_6H_4$ | 88 |
| 6 | 4-$MeOC_6H_4$ | 94 |
| 7 | 4-$NCC_6H_4$ | 61 |
| 8 | 4-$NO_2C_6H_4$ | 80 |
| 9 | 1-Naphthyl | 92 |
| 10 | 2-furyl | 80 |
| 11 | 2-thienyl | 90 |



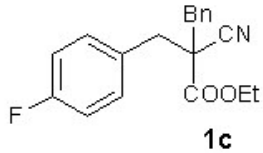

**1a**

**ethyl 2-benzyl-3-(4-bromophenyl)-2-cyanopropanoate (1a):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1a** as yellow liquid with 92% yield. $^1$H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, $J$ = 8.32 Hz, 2H), 7.32 - 7.34 (m, 5H), 7.20 (d, $J$ = 8.32 Hz, 2H), 4.03 (q, $J$ = 7.12 Hz, 2H), 3.34, 3.32 (AB system, $J_{AB}$ = 13.40 Hz, 2H), 3.13, 3.08 (AB system, $J_{AB}$ = 13.44 Hz, 2H), 1.03 (t, $J$ = 7.12 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ 167.9, 149.4, 143.5, 134.9, 130.3, 128.9, 128.2, 118.6, 111.1, 109.4, 62.9, 52.0, 42.2, 35.5, 14.2. ESI HRMS exact mass calcd. for $(C_{19}H_{18}BrNO_2 + Na)^+$ requires m/z 394.04099, found m/z 394.04089.



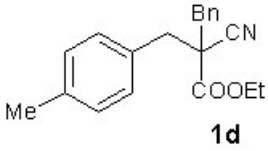

**1b**

**ethyl 2-benzyl-3-(4-chlorophenyl)-2-cyanopropanoate (1b):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1b** as yellow oily liquid with 96% yield. $^1$H NMR (400 MHz, DMSO) δ 7.25 - 7.45 (m, 9 H), 4.04 (q, $J$ = 7.12 Hz, 2H), 3.36, 3.33 (AB system, $J_{AB}$ = 11.32 Hz, 2H), 3.27, 3.23 (AB system, $J_{AB}$ = 13.56 Hz, 2H), 1.01 (t, $J$ = 7.12 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ168.1, 135.1, 135.0, 134.1, 133.0, 132.1, 130.3, 128.9, 128.1, 118.9, 62.8, 54.0, 42.8, 41.8, 14.1. ESI HRMS exact mass calcd. for $(C_{19}H_{18}ClNO_2 + Na)^+$ requires m/z 350.09168, found m/z 350.09172.




**1c**

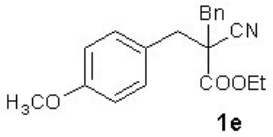
**ethyl 2-benzyl-2-cyano-3-(4-fluorophenyl)propanoate (1c):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1c** as yellow liquid with 95% yield.$^1$H NMR (400 MHz, DMSO) δ 7.18 - 7.38 (m, 9H), 4.04 (q, $J$ = 7.12 Hz, 2H), 3.37, 3.36 (AB system, $J_{AB}$ = 11.52 Hz, 2H), 3.29, 3.25 (AB system, $J_{AB}$ = 10.96 Hz, 2H), 1.01 (t, $J$ = 7.12 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ168.0, 163.4, 161.0, 135.1, 132.3, 131.3, 130.2, 128.9, 128.1, 118.8, 115.9, 62.8, 54.0, 42.6, 41.8, 14.1. ESI HRMS exact mass calcd. for $(C_{19}H_{18}FNO_2 + H)^+$ requires m/z 312.1394, found m/z 312.1382.




**1d**

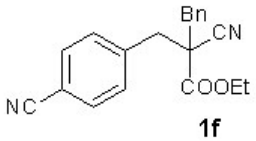
**ethyl 2-benzyl-2-cyano-3-p-tolylpropanoate (1d):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1d** as white colorless liquid 95% yield. $^1$H NMR

(400 MHz, DMSO) δ 7.13 - 7.38 (m, 9H), 4.04 (q, $J$ = 7.12 Hz, 2H), 3.18 - 3.35 (m, 4H), 2.29 (s, 3H), 1.03 (t, $J$ = 7.12 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ168.1, 137.3, 135.1, 132.0, 130.3, 130.1, 129.5, 128.9, 128.1, 118.9, 62.7, 54.1, 42.8, 42.4, 21.1, 14.2. ESI HRMS exact mass calcd. for $(C_{20}H_{21}NO_2 + H)^+$ requires m/z 308.1644, found m/z 308.1647.



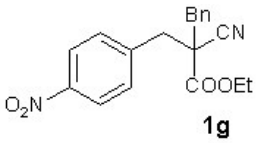
**1e**

**ethyl 2-benzyl-2-cyano-3-(4-methoxyphenyl)propanoate (1e):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1e** as colorless liquid with 73% yield. $^1$H NMR (400 MHz, DMSO) δ7.26-7.36 (m, 5H), 7.20 (d, $J$ = 8.64 Hz, 2H), 6.92 (d, $J$ = 8.64 Hz, 2H), 4.06 (q, $J$ = 7.08 Hz, 2H), 3.75 (s, 3H), 3.35, 3.31 (AB system, $J_{AB}$ = 13.32 Hz, 2H), 3.24, 3.22 (AB system, $J_{AB}$ = 14.00 Hz, 2H),, 1.02-1.05 (t, $J$ = 7.12 Hz，3H). $^{13}$C NMR (100 MHz, DMSO) δ 168.2, 159.2, 135.2, 131.4, 130.2, 128.9, 128.1, 126.9, 119.0, 114.3, 62.7, 55.5, 54.2, 42.7, 42.1, 14.2. ESI HRMS exact mass calcd. for $(C_{20}H_{21}NO_3 + H)^+$ requires m/z 324.1594, found m/z 324.1593.



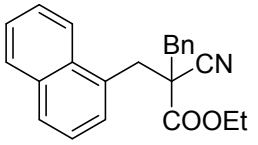
**1f**

**ethyl 2-benzyl-2-cyano-3-(4-cyanophenyl)propanoate (1f):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1f** as colorless liquid with 24% yield.$^1$H NMR (400 MHz, DMSO) δ 7.31 - 7.39 (m, 5H), 7.25 - 7.31 (m, 4H), 4.03 (q, $J$ = 7.12 Hz, 2H), 3.37, 3.34 (AB system, $J_{AB}$ = 13.56 Hz, 2H), 3.27, 3.24 (AB system, $J_{AB}$ = 13.56 Hz, 2H), 1.01 (t, $J$ = 7.12 Hz, 3H). See reference 16.



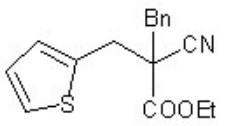
**1g**

**ethyl 2-benzyl-2-cyano-3-(4-nitrophenyl)propanoate (1g):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1g** as white solid with 76% yield. $^1$H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, $J$ = 8.72 Hz, 2H), 7.51 (d, $J$ = 8.72 Hz, 2H), 7.31 - 7.40 (m, 5H), 4.03 – 4.08 (m, 2H), 3.48, 3.45 (AB system, $J_{AB}$ = 13.40 Hz, 2H), 3.20, 3.16 (AB system, $J_{AB}$ = 13.48 Hz, 2H), 1.03 (t, $J$ = 7.16 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ167.8, 147.6, 143.0, 134.8, 131.7, 130.3, 129.0, 128.2, 124.0, 118.5, 63.1, 53.5, 42.7, 41.8, 14.1. ESI HRMS exact mass calcd. for $(C_{19}H_{18}N_2O_4 + H)^+$ requires m/z 338.1194, found m/z 338.1124.



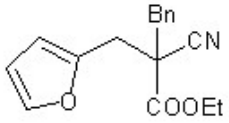
**1h**

**2-benzyl-2-((naphthalen-5-yl)methyl)malononitrile (1h):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1h** as colorless liquid with 92% yield.$^1$H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* =7.84 Hz, 1H), 7.90 - 7.97 (m, 2H), 7.37 - 7.60 (m, 4H), 7.31 - 7.35 (m,5H), 3.91 (q, *J* = 7.08 Hz, 2H), 3.87 (s, 2H), 3.52, 3.48 (AB system, $J_{AB}$ = 13.52 Hz, 2H), 0.88 (t, *J* = 7.12 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ168.3, 135.3, 134.0, 132.3, 131.6, 130.4, 129.0, 128.9, 128.5, 128.1, 126.4, 126.3, 125.7, 124.6, 119.0, 62.8, 53.4, 42.9, 38.4, 13.9. ESI HRMS exact mass calcd. for $(C_{23}H_{21}NO_2 + H)^+$ requires m/z 344.1604, found m/z 344.1602.



**1i**

**ethyl 2-benzyl-2-cyano-3-(thiophen-2-yl)propanoate (1i):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1i** as yellow liquid with 94% yield.$^1$H NMR (400 MHz, DMSO) δ 7.47 (d, *J* = 1.28 Hz, 1H), 7.33 - 7.46 (m, 3H), 7.25 - 7.27 (m, 2H), 7.00 - 7.03 (m, 2H), 4.09 (q, *J* = 7.12 Hz, 2H), 3.60, 3.53 (AB system, $J_{AB}$ = 14.72 Hz, 2H), 3.35 (s, 2H), 1.07 (t, *J* = 7.12 Hz, 3H).



**1j**

**ethyl 2-benzyl-2-cyano-3-(furan-2-yl)propanoate (1j):** The crude mixture was purified by column chromatography using Petroleum ether /EtOAc (60/1→15/1) to yield **1j** as colorless liquid with 88% yield.$^1$H NMR (400 MHz, DMSO) δ 7.61 (d, *J* = 1.04 Hz, 1H), 7.26 - 7.39 (m, 6H), 6.43 (d, *J* = 5.0 Hz, 1H), 6.30 (d, *J* = 3.16 Hz, 1H), 4.12 (q, *J* = 7.12 Hz, 2H), 3.22 - 3.41 (m, 4H), 1.10 (t, *J* = 7.12 Hz, 3H). $^{13}$C NMR (100 MHz, DMSO) δ167.8, 149.4, 143.5, 134.9, 130.3, 128.9, 128.2, 118.6, 111.1, 109.4, 62.9, 52.0, 42.2, 35.5, 14.1. ESI HRMS exact mass calcd. for $(C_{17}H_{17}NO_3 + H)^+$ requires m/z 284.1281, found m/z 284.1278.

**References**

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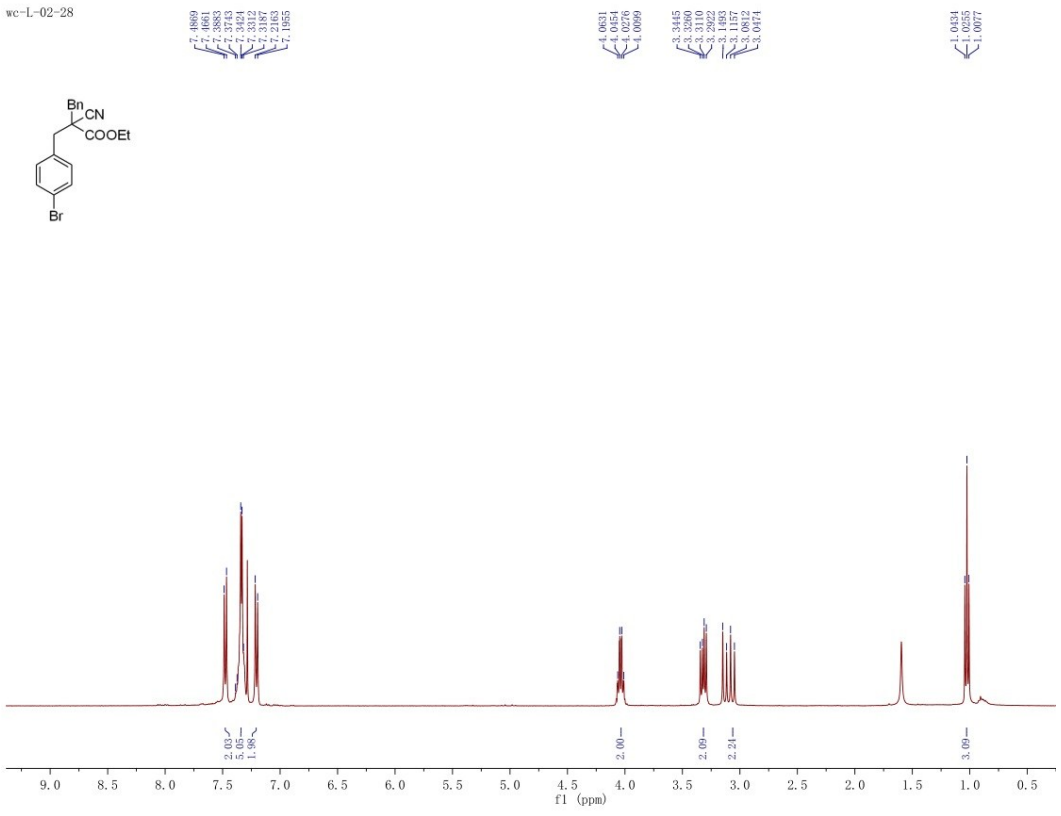
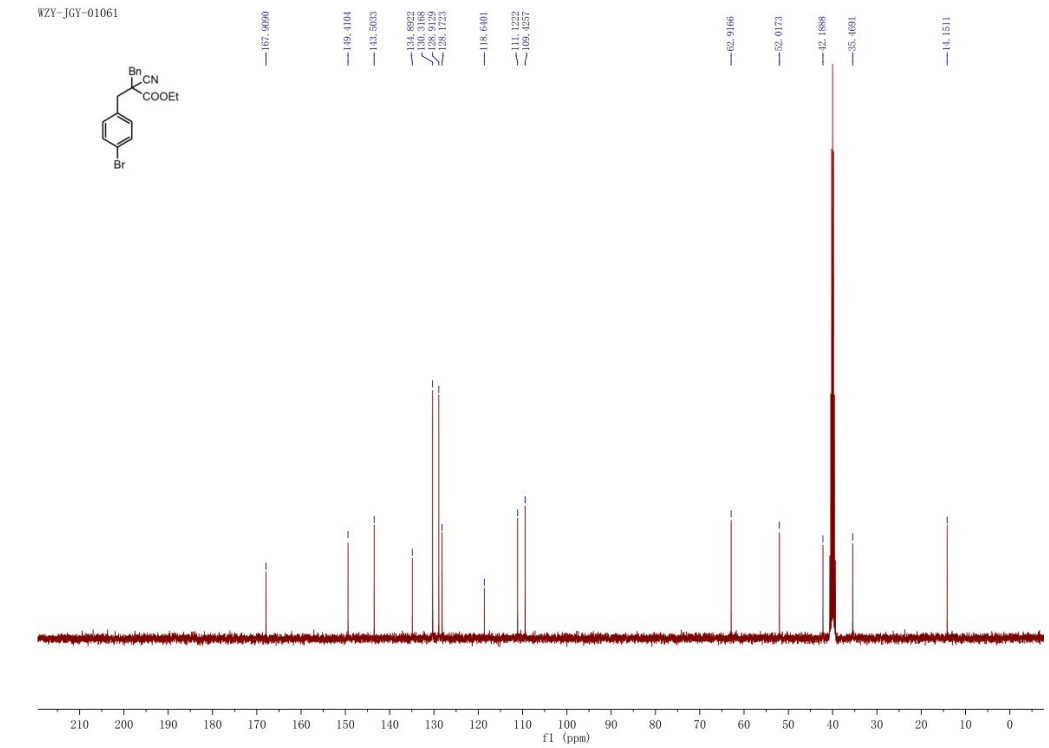
## $^{1}$H and $^{13}$C NMR Spectra:

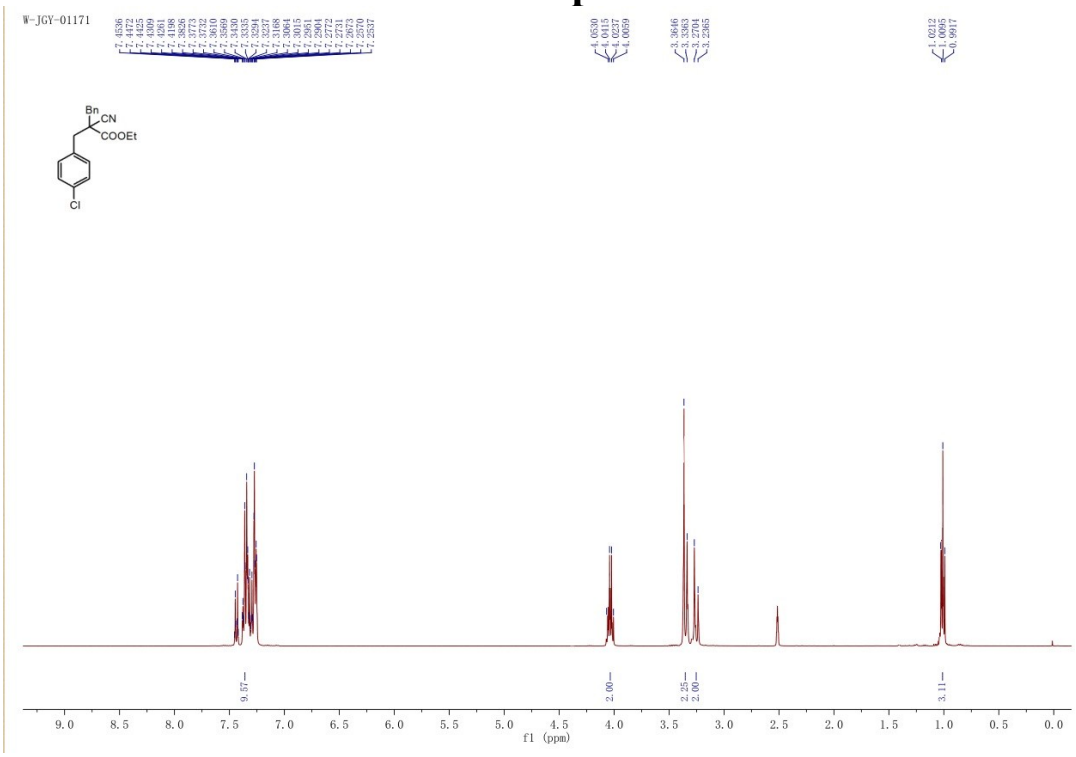
### The $^{1}$H NMR Spectra of 1a




### The $^{13}$C NMR Spectra of 1a




**The $^{1}$H NMR Spectra of 1b**

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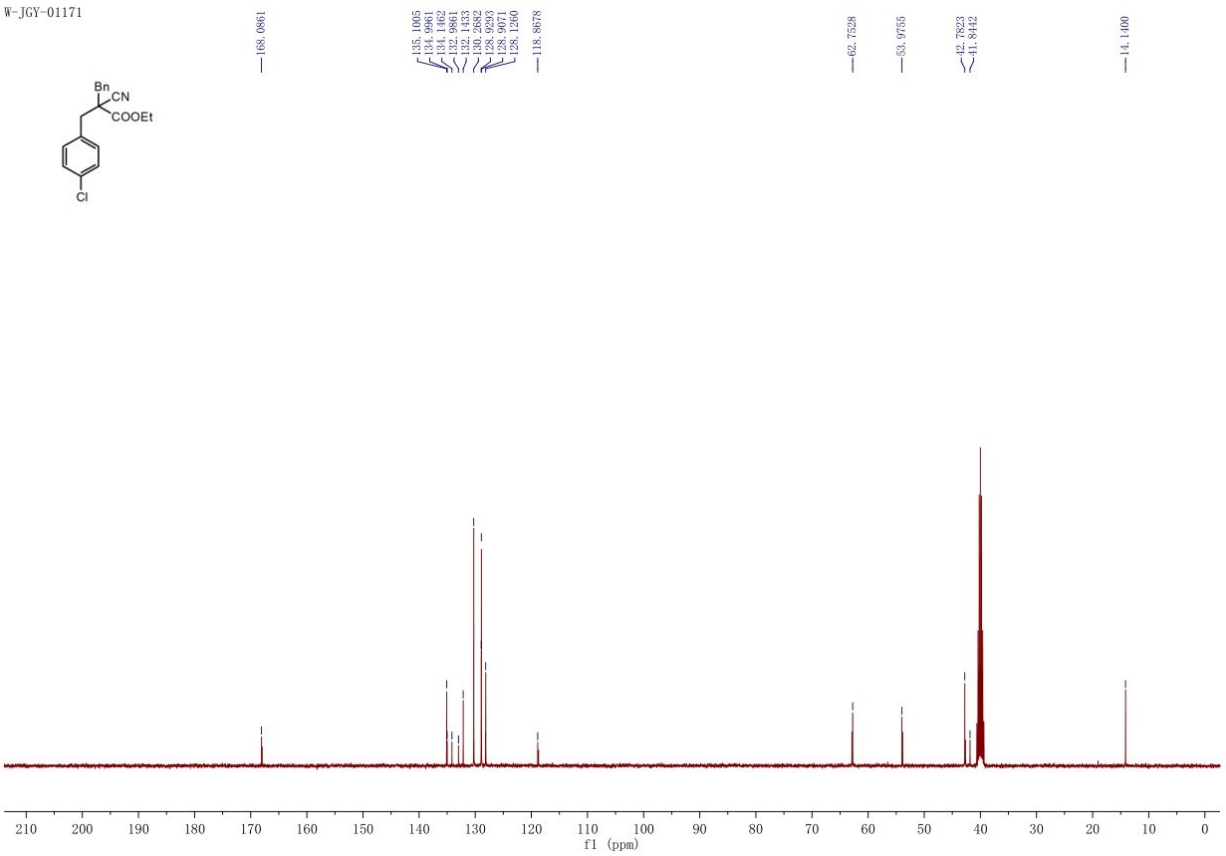
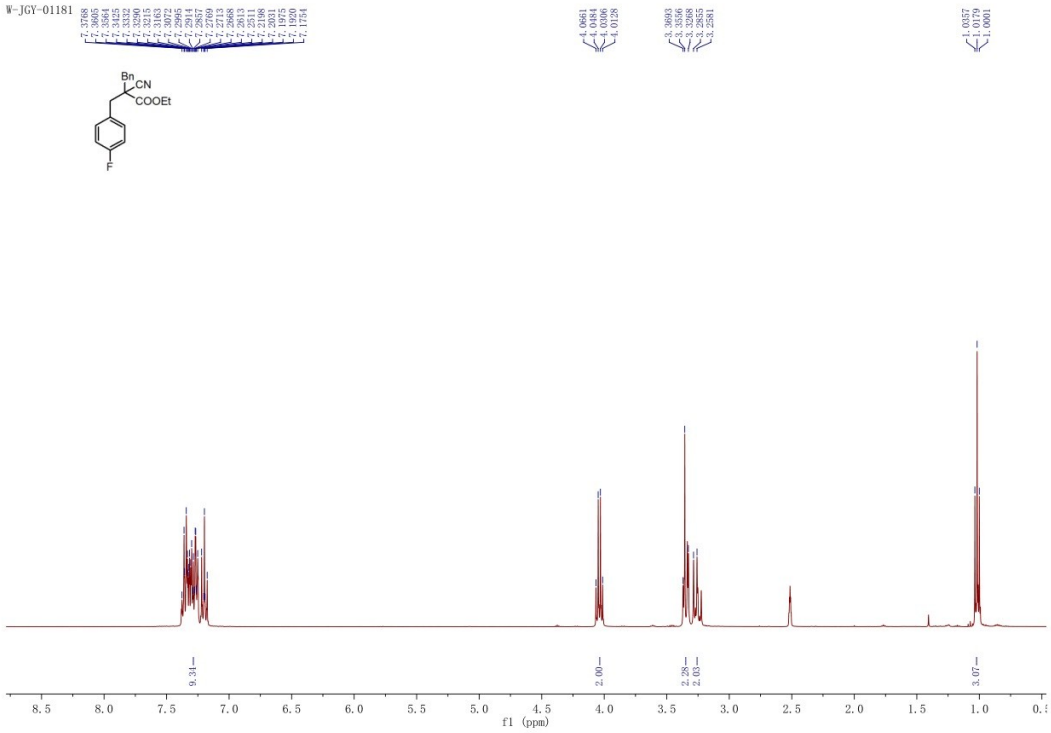



**The [1] H NMR Spectra of 1c**

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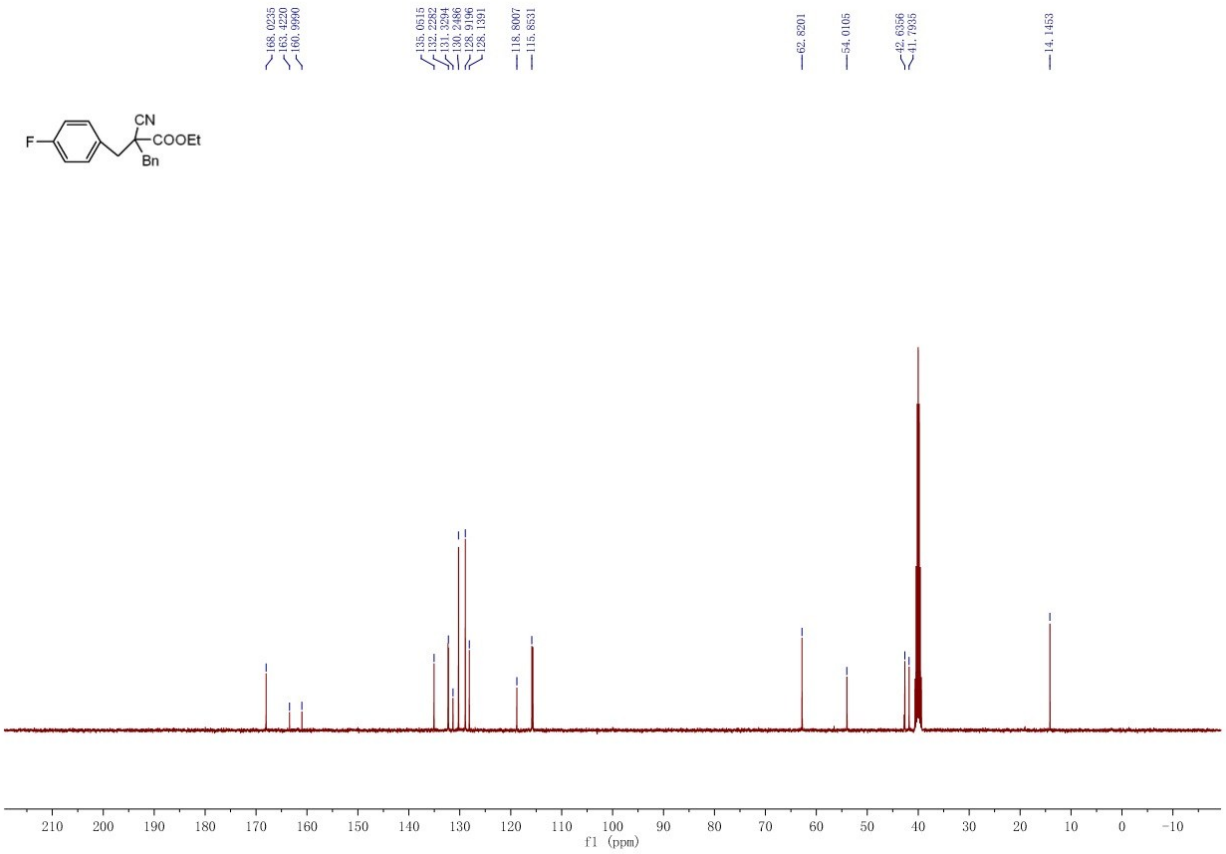
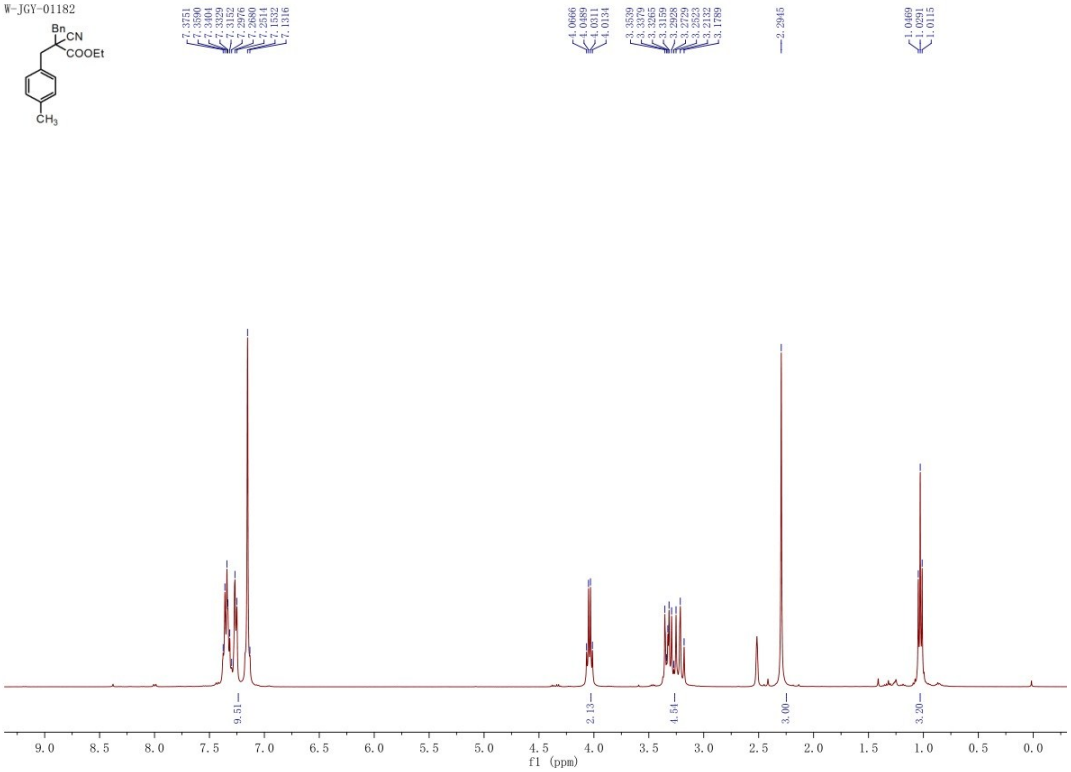
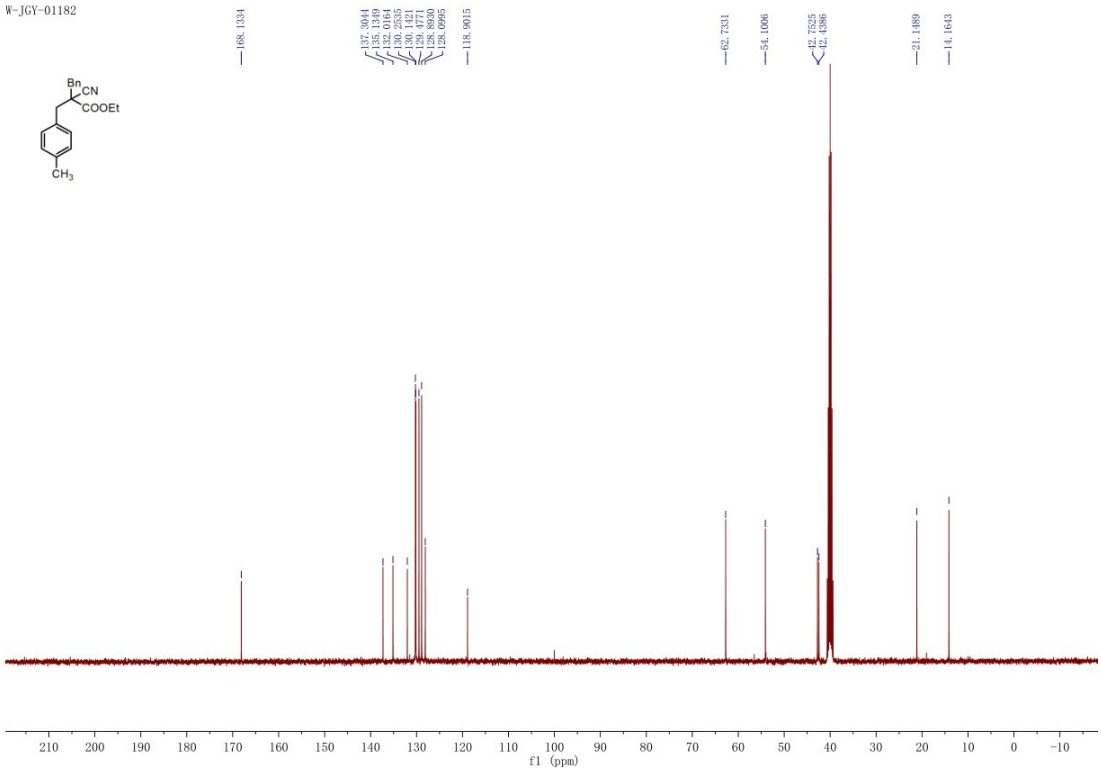



**The $^{1}$H NMR Spectra of 1d**



## The $^{13}$C NMR Spectra of 1d

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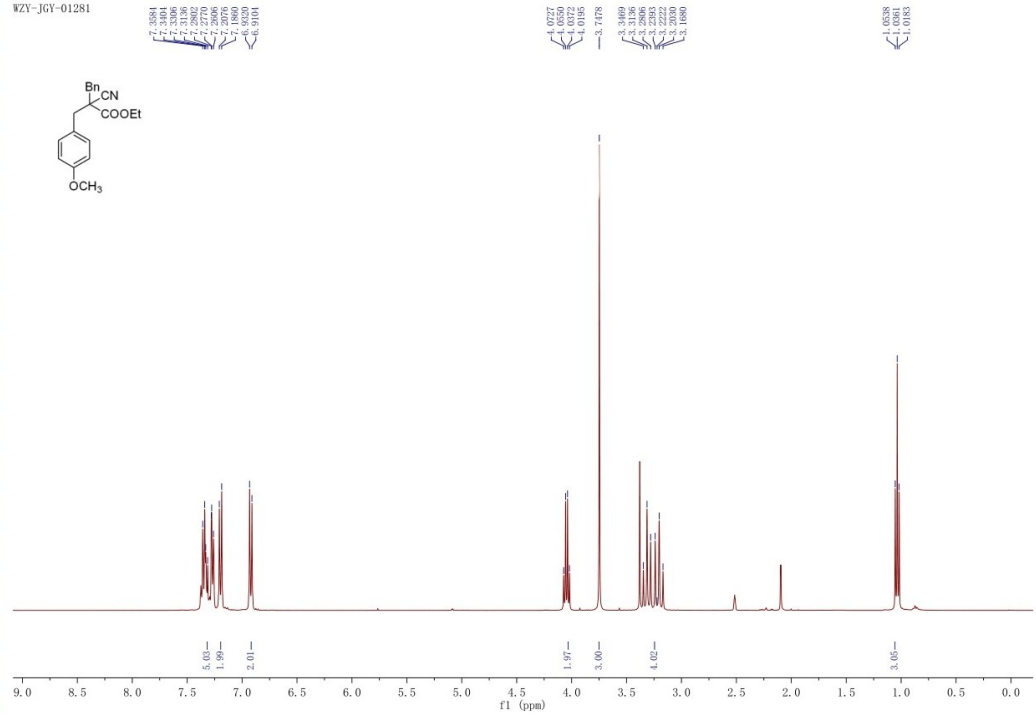
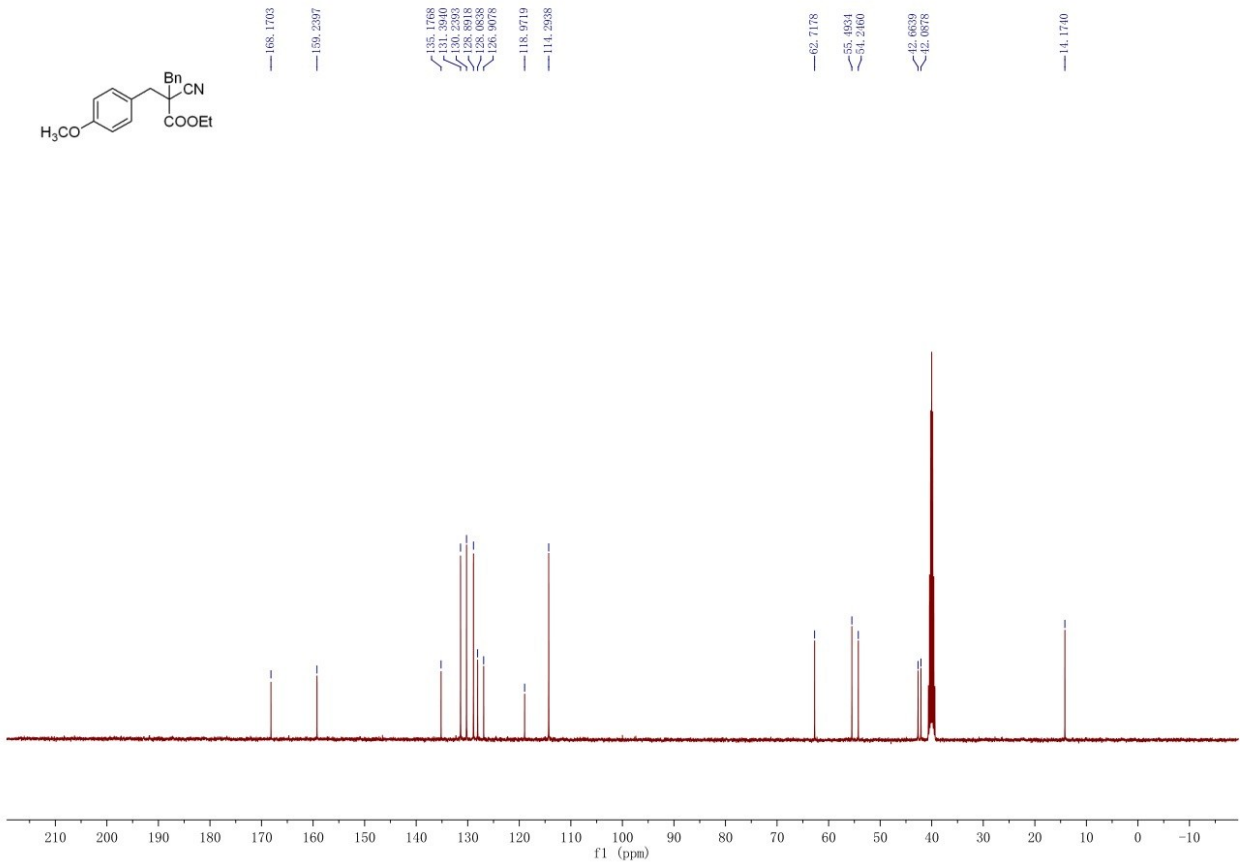
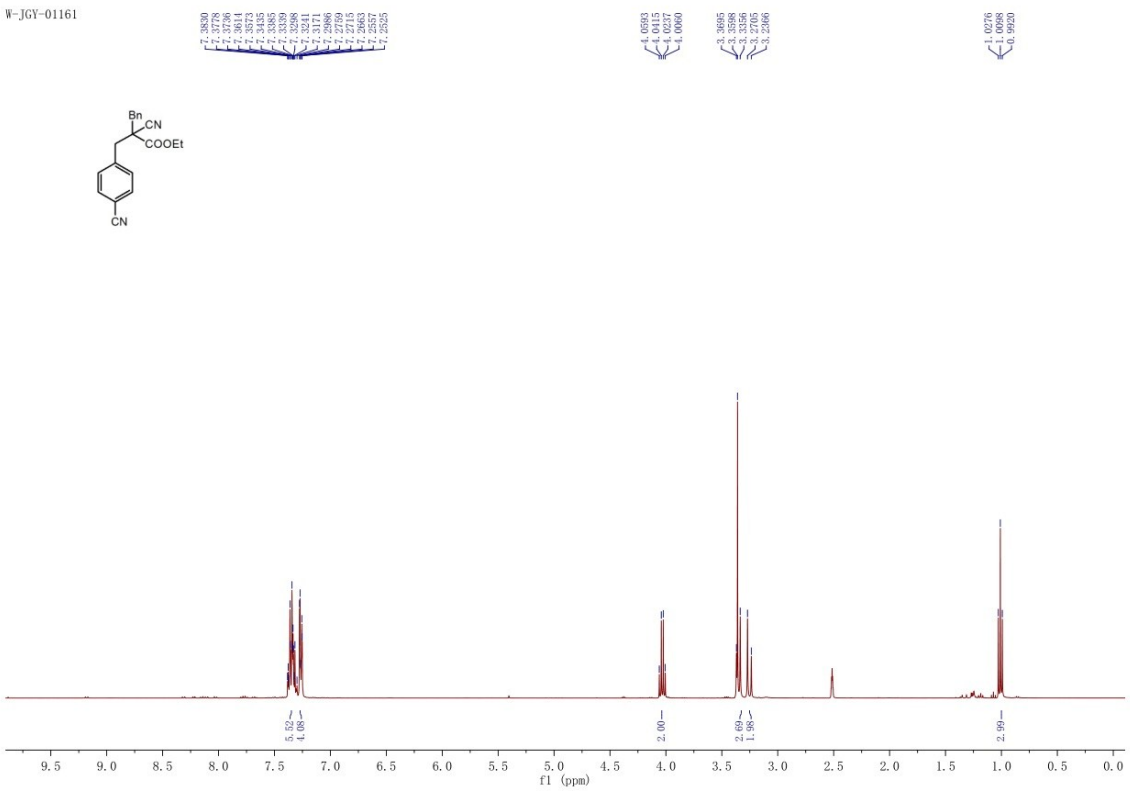


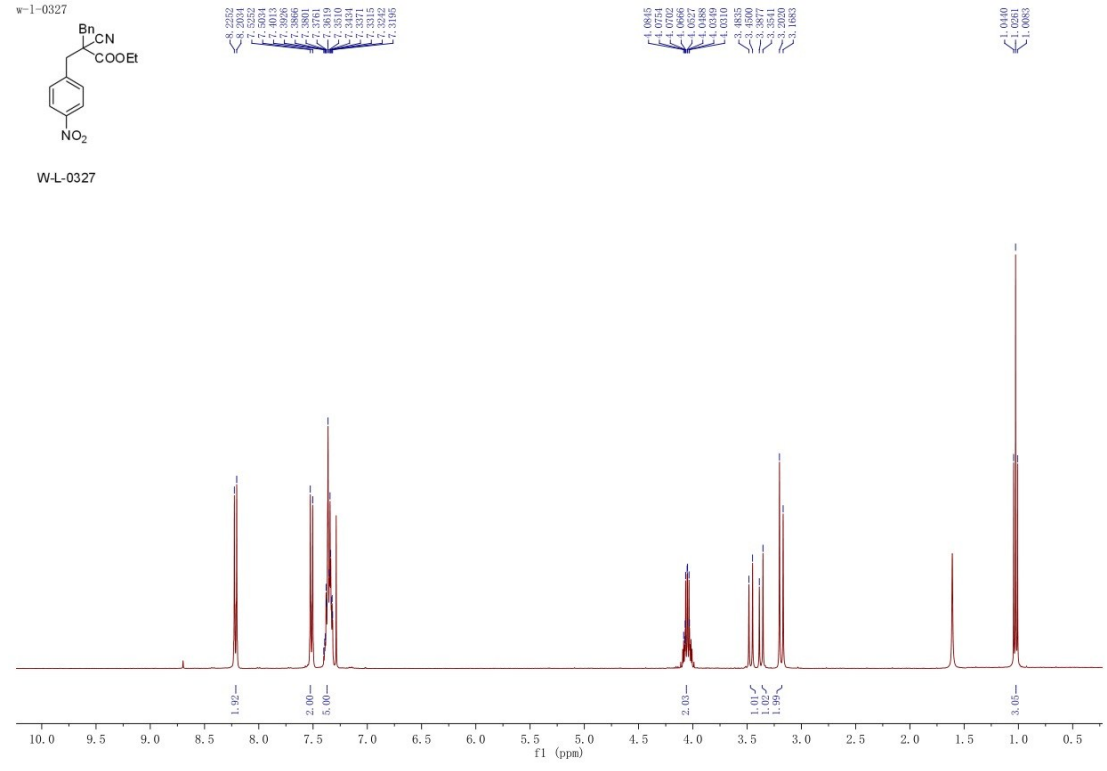

## The $^{13}$C NMR Spectra of 1e



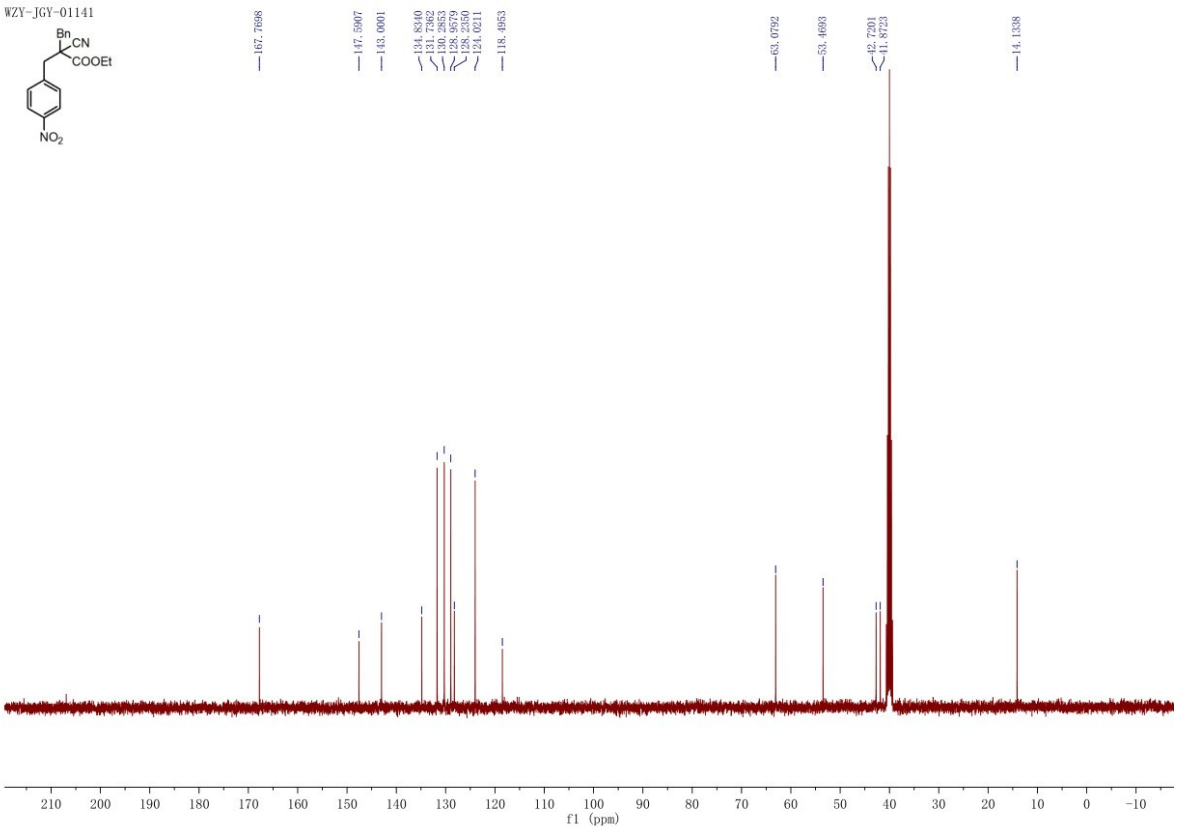

**The $^{1}$H NMR Spectra of 1f**



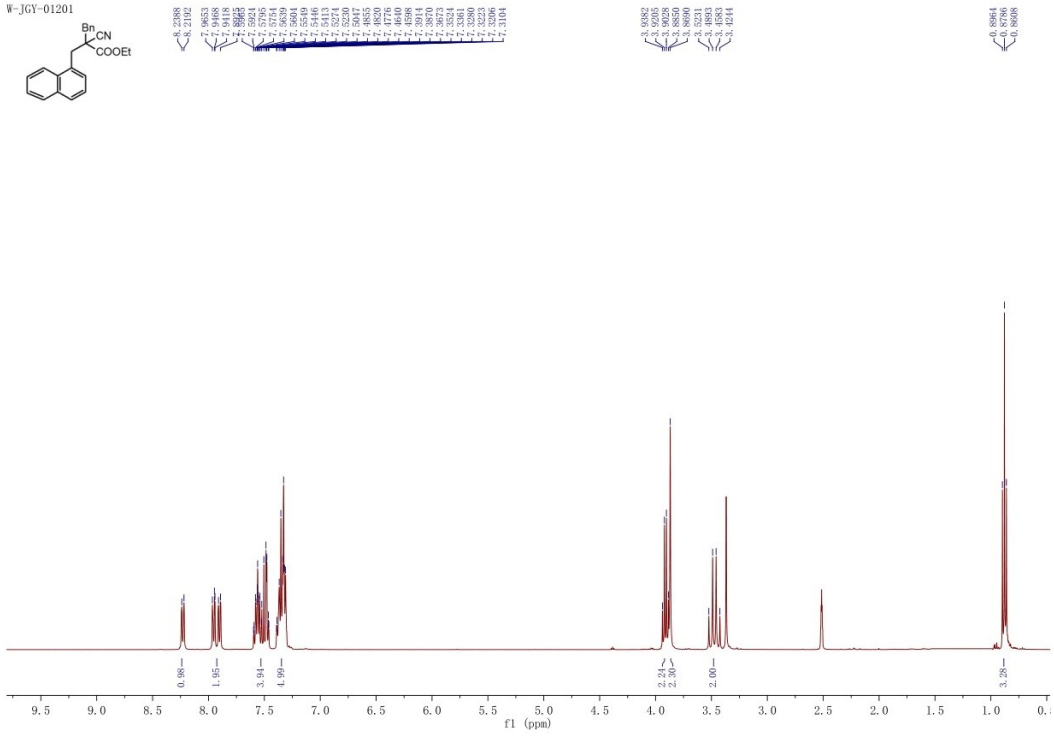

**The $^{1}$H NMR Spectra of 1g**



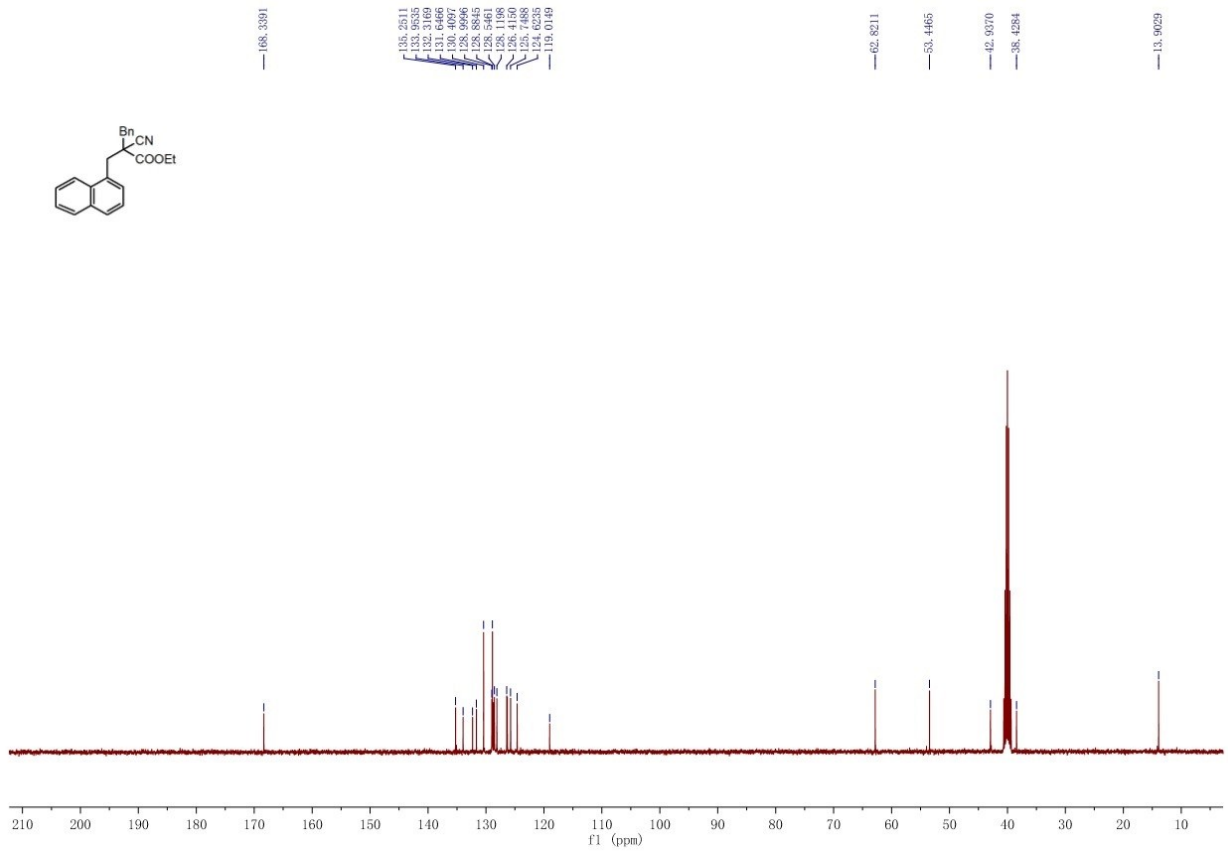

**The $^{13}$C NMR Spectra of 1g**



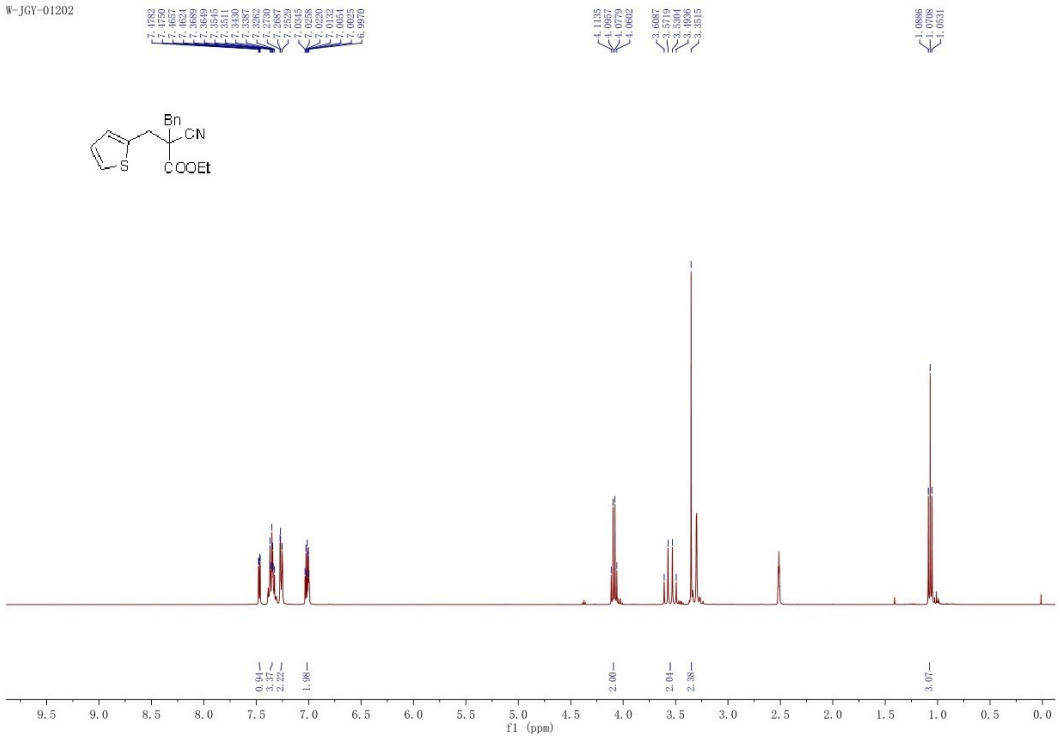

**The $^{1}$H NMR Spectra of 1h**



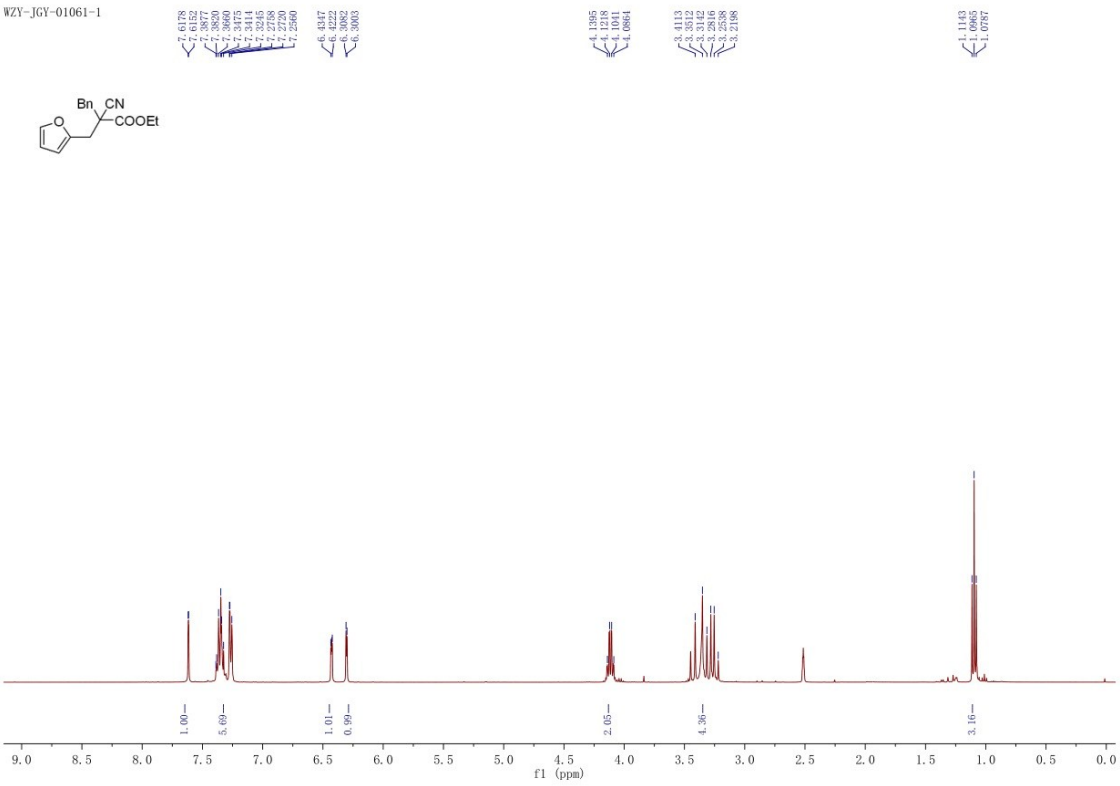

**The $^{13}$C NMR Spectra of 1h**




**The $^{1}$H NMR Spectra of 1i**



# The $^{1}$H NMR Spectra of 1j




# The $^{13}$C NMR Spectra of 1j