Electronic Supplementary Information

Regioselective Oxidative Cleavage of Conjugated Dienes to Access Substituted Acrylonitriles

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CONTENT

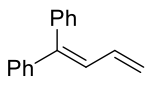
1. General information and starting materials

1.1 General information

Unless otherwise noted, all materials were purchased from commercial suppliers. Dichloromethane (DCM), acetonitrile and chlorobenzene were refluxed over CaH_2; tetrahydrofuran (THF) and toluene were refluxed over lithium aluminum hydride. The solvents were freshly distilled prior to use. Column chromatography was performed on silica gel (normal phase, 200-300 mesh) from Anhui Liangchen Silicon Material Co., Ltd, with petroleum ether (PE, bp. 60 – 90 °C) and ethyl acetate (EtOAc) as eluent. Reactions were monitored by thin-layer chromatography (TLC) on GF_{254} silica gel plates (0.2 mm) from Anhui Liangchen Silicon Material Co., Ltd. The plates were visualized by UV light. ^{1}H, ^{19}F and ^{13}C NMR, ^{15}N NMR spectra were recorded on Bruker 400 MHz spectrometer, Bruker Avance Neo 600 and Bruker Neo 700, usually in $CDCl_3$ as an internal standard, and the chemical shifts (δ) were reported in parts per million (ppm). Multiplicities are indicated as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), dd (doublet of doublet), ddd (doublet of doublet of doublet), m (multiplet), and dq (doublet of quartet). Coupling constants (J) are reported in Hertz (Hz). HRMS measurements were carried out on an Agilent LC/MSD TOF mass spectrometer (ESI-HRMS) and Bruker Compact (EI-HRMS). GC-MS measurements were carried out on a Trace 1300 GC/ISQ QD mass spectrometer. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. IR spectra [KBr pellets, v (cm^{-1})] were taken on a Bruker Tensor 27 spectrometer.

1.2 General information for the Starting materials: conjugated diene 1

All dienes in manuscript are listed below:



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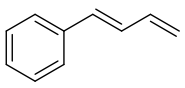

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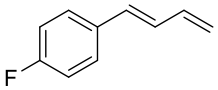

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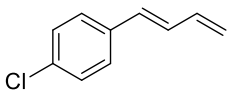

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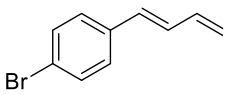

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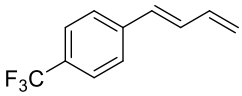

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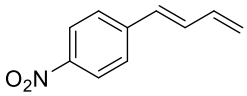

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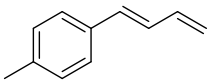

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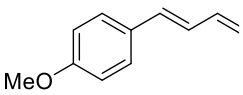

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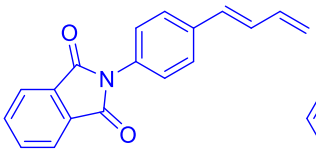

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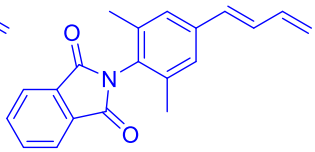

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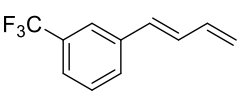

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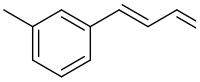

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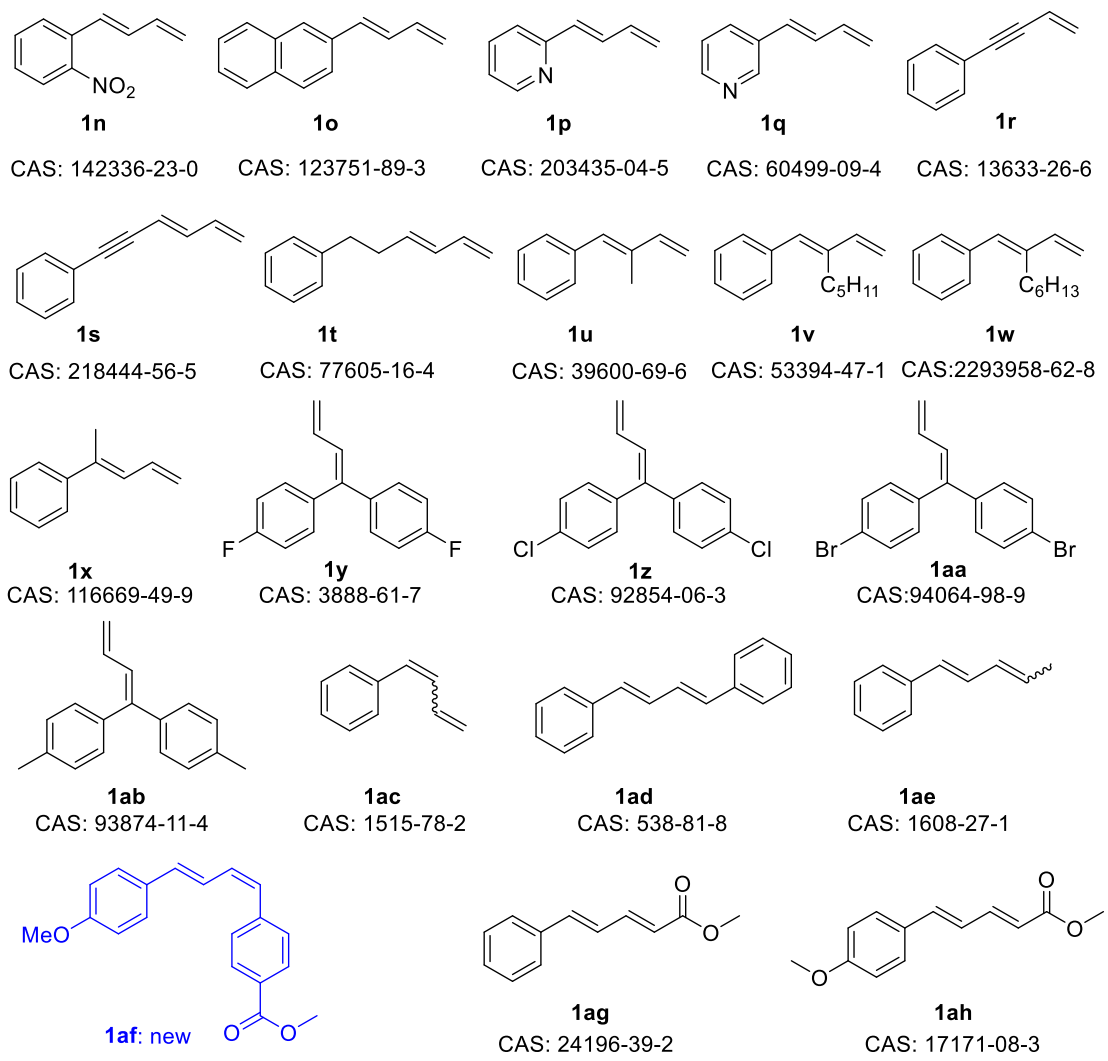
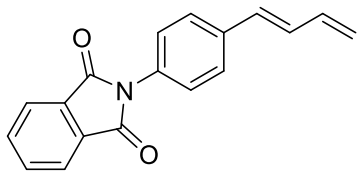


Figure S1 The dienes substrates

Conjugated dienes **1** were synthesized according to literatures[1].

Compound characterization data of three new compounds are listed below：

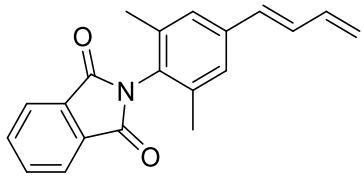
(E)-2-(4-(buta-1,3-dien-1-yl)phenyl)isoindoline-1,3-dione (**1j**):



[1] (a) W. Sun, M. P. Li and L. J. Li, Q. Huang, M. Y. Hua and S. F. Zhu, Ligands with 1,10-phenanthroline scaffold for highly regioselective iron-catalyzed alkene hydrosilylation *Nature Commun.* 2018, **9**, 211–231. (b) H. Cui, Y. Li and S. L. Zhang, *Org. Biomol. Chem.*, 2012, **10**, 2862–2869. (c) O. Halter, J. Spielmann, Y. Kanai and H. Plenio, Monitoring Ligand Substitution in (Catalytically Active) Metal Complexes with Bodipy-Tagged Diimines and NHC Ligands *Organometallics*, 2019, **38**, 2138–2149. (d) C. Z. Chen, S. Y. Fang, Z. Y. Dong, J. X. Xu and Z. H. Yang, Catalytic Diastereospecific and Enantioselective (3+2) Transannulations of 1,2,3-Thiadiazoles with Strained Norbornene Derivatives. *Org. Lett.*, 2022, **24**, 2110–2114. (e) X. L. Peng, J. Xu, T. T. Li, Y. R. Chi, and Z. C. Jin, Chemo-selective cross reaction of two enals via carbene-catalyzed dual activation. *Chem. Sci*., 2020, **11**, 12533–12539.

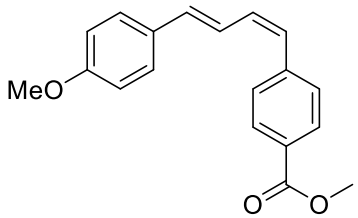
The new diene **1j** was synthesized according to the method reported in literature [1] and was purified by column chromatography (PE/EtOAc = 5:1). **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm): 7.99-7.94 (m, 2H), 7.93-7.89 (m, 2H), 7.63 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.8 Hz, 2H), 6.99 (dd, J = 16.0, 10.8 Hz, 1H), 6.70 (d, J = 15.6 Hz, 1H), 6.56 (dt, J = 16.8, 10.4 Hz, 1H), 5.42 (d, J = 16.8 Hz, 1H), 5.24 (d, J = 10.4 Hz, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ (ppm): 167.4, 137.6, 136.9, 135.2, 132.3, 132.0, 131.5, 131.0, 127.9, 127.1, 123.9, 119.2. HRMS (EI) calcd. for $C_{18}H_{13}NO_2$ [$M^{+\bullet}$]: 275.0946, found: 275.0958; $[M-H]^+$ 274.0863, found: 274.0863.

(*E*)-2-(4-(buta-1,3-dien-1-yl)-2,6-dimethylphenyl)isoindoline-1,3-dione (**1k**):



The new diene **1k** was synthesized according to the method reported in literature [1] and was purified by column chromatography (PE/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.96 (dd, J = 5.6, 3.2 Hz, 2H), 7.79 (dd, J = 5.6, 3.2 Hz, 2H), 7.22 (s, 2H), 6.80 (dd, J = 15.6, 10.4 Hz, 1H), 6.56-6.45 (m, 2 H), 5.35 (d, J = 16.4 Hz, 1H), 5.19 (d, J = 9.6 Hz, 1H), 2.15 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 167.3, 138.3, 137.1, 137.0, 134.4, 132.0, 130.7, 129.1, 126.5, 123.8, 118.2, 18.2. **HRMS** (ESI) calcd for [M+H, $C_{20}H_{18}NO_2$]$^+$: 304.1333, found 304.1332.

Methyl 4-((1*Z*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)benzoate (**1af**):



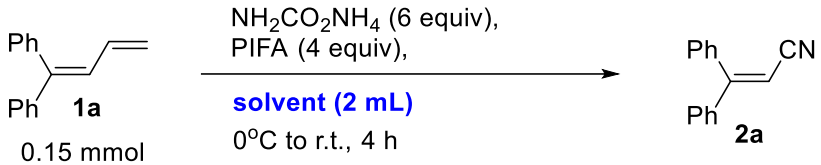
The new diene **1af** was synthesized according to the method reported in literature [1] and was purified by column chromatography (PE/EtOAc = 10:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.03 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.17 (ddd, J = 15.6, 8.8, 1.6 Hz, 1H), 6.85 (d, J = 8.8 Hz, 2H), 6.70 (d, J = 15.6 Hz, 1H), 6.52-6.42 (m, 2 H), 3.92 (s, 3H), 3.80 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 166.9, 159.6, 142.1, 134.2, 132.1, 130.4, 123.0, 129.9, 128.5, 127.9, 126.8, 126.0, 114.2, 55.4, 52.1. **HRMS** (ESI) calcd for $C_{19}H_{19}O_3^+$ $[M+H]^+$: 295.1329, found 295.1330.

2. Detailed information for all optimization conditions

2.1 solvents investigation

Various solvents were tested and the results are presented in Table S2-1. In general, alcoholic solvents (entries 1-11) showed better reaction transformations compared to other solvents. Methanol and ethanol produced the desired acrylonitrile **2a** with yields of 36% and 35%, respectively. Remarkably, the yield of **2a** significantly increased to 75% when trifluoroethanol (TFE) was used as the solvent (entry 4). This improvement in yield can be attributed to the more nucleophilic nature of these solvents, which stabilizes and deactivates the electrophilic nitrene iodonium intermediate (Scheme 1-**I**) through strong solvation. However, when the reaction was performed in dehydrated TFE under N_2 gas protection, the yield dropped to only 30%, indicating that trace amounts of water may greatly promote the current reaction. Acrylonitrile **2a** was not detected when hexafluoroisopropanol, dichloromethane, toluene, and dioxane were used as solvents (entries 6-9). Additionally, only 10% and 21% yields of **2a** were obtained with tetrahydrofuran and acetonitrile, respectively (entries 10-11). The major by-products in these reactions were diphenylketone **3a** and *N*-phenyl benzoamide **4a**.

Table S2-1 Solvent optimization



Entry	Solvent	Yield/%[a]
1	MeOH	36
2	EtOH	35
3	*i*-PrOH	13
4[b]	wet CF_3CH_2OH	75
5[c]	CF_3CH_2OH absolute	30
6	$(CF_3)_2CHOH$	trace
7	DCM	trace
8	PhMe	trace
9	dioxane	trace
10	THF	10
11	MeCN	21

[a.] NMR yield was obtained with trimethoxybenezene as internal standard

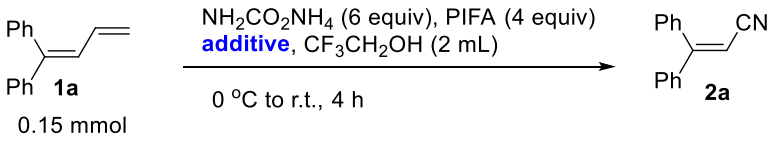
[b.] Trifluoroethanol was not dehydrated.

[c.] The current condition was performed with the protection of N_2 gas.

2.2 investigation of water and other additives.

In Table S2-1, we observed that trace amounts of water significantly enhanced the reaction conversion. Therefore, a series of reactions with varying amounts of water, ranging from 1 to 10 equiv. (entries 1-7), were investigated, and the best conversion was achieved when 2 equiv. of water were added (entry 3). However, the yield dramatically decreased to only 10% when 1 mL of water was added. There are two potential reasons why water promotes the reaction. Firstly, water can increase the solubility of ammonium carbamate ($H_2NCO_2NH_4$) in CF_3CH_2OH (TFE). Secondly, water can act as a nucleophile to attack the in-situ generated aziridium intermediate, thereby accelerating the reaction. To verify this possibility, methanol was added instead of water in 1, 2, and 5 equiv. (entries 8-10), and moderate to good yields of **2a** were obtained. However, when sodium azide (NaN_3) was used instead of water (entry 11), **2a** was obtained in a yield of only 17%. This result indicates that the main effect of water is to assist the solubility of inorganic salts.

Table S2-2 Optimization of nucleophiles



Entry	Additive (loading)	Yield/%[a]
1	H_2O (1 equiv)	64
2	H_2O (1.5 equiv)	71
3	H_2O (2 equiv)	78
4	H_2O (2.5 equiv)	68
5	H_2O (3 equiv)	60
6	H_2O (4 equiv)	60
7	H_2O (10 equiv)	58
8	MeOH (1 equiv)	54
9	MeOH (2 equiv)	67
10	MeOH (5 equiv)	49
11	NaN_3 (2 equiv)	18

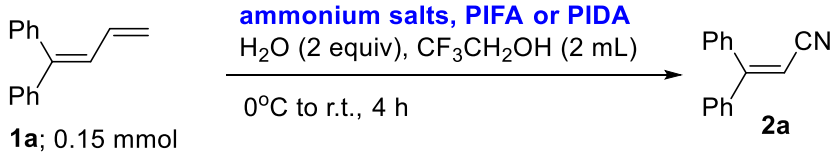
[a] NMR yield was obtained with trimethoxybenezene as internal standard

2.3 investigation of ammonium salts and hypervalent iodine reagent.

The loading of ammonium carbamate was initially investigated ranging from 2 to 8 equiv. (Table S2-3, entries 1-4), with 6 equiv. of ammonium carbamate providing the

highest yield (entry 3). The loading of PIFA has a significant impact on the current transformation. The yield initially increased as the loading of PIFA increased from 2 to 4 equiv. (entries 5-6 vs entry 3). However, further increasing the loading of PIFA noticeably inhibited the yield of **2a**, accompanied by an increase in the formation of amides **4a** as observed by TLC (entries 7-9). Other ammonium salts was also investigated. Ammonium acetate (NH_4OAc) gave desired product in only 16%, beside amide **4a**, some biacetoxy product **X** was also detected from crude ^1H NMR and MS (entry 10). Ammonium chloride (NH_4Cl), however, gave a very complicated system, benzonitriles, benzaldehyde, amide **4a** and a series of chlorinated molecules including chlorinated benzonitriles were generated according to GC-MS. Besides that, some high polar molecules, probably polymers, were generated according to TLC. Notably, changing the oxidants of PIFA to PIDA gave **4a** in yield of 55%, which will be discussed later in Table S4-1, page S20. Ammonia in methanol (2 mol/) is another choice for current transformation, gave **4a** in 70% yield, slightly less than $NH_4CO_2NH_4$ (entry 12).

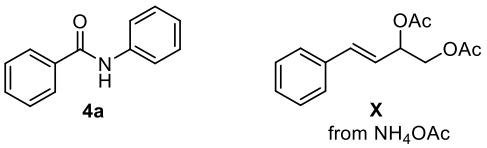
Table S2-3 Optimization of ammonium salt and hypervalent iodine reagent



Entry	Ammonium salts /equiv	Hypervalent iodium(III)/equiv.	Yield/%[a]
1	$NH_2CO_2NH_4$ / 2	PIFA / 4	13
2	$NH_2CO_2NH_4$ / 4	PIFA /4	53
3	$NH_2CO_2NH_4$ / 6	PIFA /4	78
4	$NH_2CO_2NH_4$ / 8	PIFA /4	72
5	$NH_2CO_2NH_4$ / 6	PIFA /2	34
6	$NH_2CO_2NH_4$ / 6	PIFA /3	53
7	$NH_2CO_2NH_4$ / 6	PIFA /5	53
8	$NH_2CO_2NH_4$ / 6	PIFA /6	47
9	$NH_2CO_2NH_4$ / 6	PIFA /7	29
10	NH_4OAc / 6	PIFA /4	16
11	NH_4Cl / 6	PIFA /4	trace
12	NH_3/MeOH 6	PIFA /4	70

a. NMR yield was obtained with 1,3,5-trimethoxybenzene as internal standard.

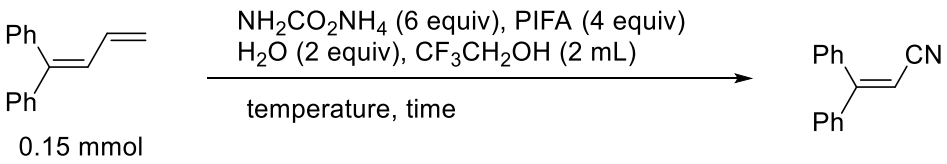
By-products with different ammonium source



2.4 investigation of temperature and time

The reaction is sensitive to temperature. Prior to the addition of PIFA, the entire system should be cooled to 0 °C using an ice-water bath. After the addition of PIFA, the reaction should be gradually allowed to reach room temperature to give the best result (Table S2-4, entry 1). When the reaction was conducted at 0 °C for 4 h, only 54% of **2a** was produced (Table S2-4, entry 2). The yields increased to 65% when the reaction time was extended to 6 h (Table S2-4, entry 3). Further extension of the reaction time to 8 hours did not yield any noticeable improvement (Table S2-4, entry 4), likely due to the complete consumption of the oxidant and ammonium salt. When the reaction was carried out at room temperature (~20 °C), the addition of PIFA resulted in a significant heat release and the reaction color suddenly turned dark brown. The reaction system became highly complex, and only 19% of the desired **2a** was generated (entry 5). Time screening revealed that the optimal reaction time is 4 h (entries 7-11).

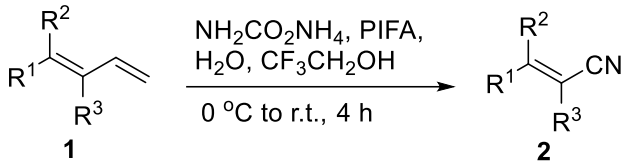
Table S2-4 Optimization of temperature and time



Entry	Tempreture	Time/h	Yield/%[a]
1	0 °C to r.t	4	78
2	0 °C	4	54
3	0 °C	6	64
4	0 °C	8	65
5	r.t.	4	19
6	0 °C then 50 °C	4	15
7	0 °C to r.t.	1	30
8	0 °C to r.t.	2	46
9	0 °C to r.t.	3	62
10	0 °C to r.t.	5	73
11	0 °C to r.t.	6	73

[a].NMR yield was obtained with 1,3,5-trimethoxybenzene as internal standard.

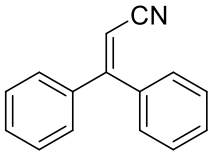
3. Synthesis of substituted acrylonitriles 2 from ammouniun carbamate ($NH_2CO_2NH_4$)



3.1 General experimental procedures and compound characterization data in Scheme 2:

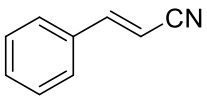
Conjugated diene **1** (0.5 mmol, 1.0 equiv), $NH_2CO_2NH_4$ (234 mg, 3.0 mmol, 6.0 equiv), H_2O (18 mg, 1.0 mmol, 2.0 equiv), and 6 mL CF_3CH_2OH were added to a 15 mL pressure-resistant reaction tube equipped with a magnetic stirring bar. The tube was then cooled to 0 °C, and PIFA (860 mg, 2.0 mmol, 4.0 equiv) was added. After sealing the tube with a rubber septum, the mixture was allowed to return to room temperature and stirred for 4 h. The system was then quenched with water (10 mL) and extracted with CH_2Cl_2 (5 mL×2). The organic layers were collected, dried over Na_2SO_4, and filtered. After removing the solvent under vacuum, the residue was purified by column chromatography on silica gel to obtain pure product 2.

3,3-diphenylacrylonitrile (**2a**): [CAS: 3531-24-6][2]



The product was purified by column chromatography (PE/EtOAc = 20:1), light yellow liquid, 69.7 mg, 68%. R_f = 0.29 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.50–7.41 (m, 6H), 7.37 (t, J = 7.6 Hz, 2H), 7.32–7.27 (m, 2H), 5.74 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 163.2, 139.0, 137.1, 130.4, 130.1, 129.6, 128.7, 128.6, 128.5, 117.9, 94.9.

Cinnamonitrile (**2b**): [CAS: 1885-38-7][3]



The product was purified by column chromatography (pentene/Et_2O = 30:1). Light yellow liquid, 52.1 mg, 80%. R_f= 0.5 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.48-7.36 (m, 6H), 5.88 (d, J = 16.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 150.6, 133.5, 131.2, 129.1, 127.4, 118.2, 96.4.

4-Fluorocinnamonitrile (**2c**): [CAS: 27530-50-3][3]

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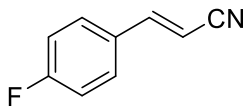
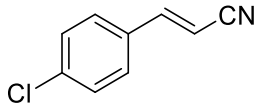
[2] G. S. Kumar, P. S. Shinde, H. Chen, K. Muralirajan, R. Kancherla, and M. Rueping, Paired Electrolysis for Decarboxylative Cyanation: 4-CN-Pyridine, a Versatile Nitrile Source. *Org. Lett*. 2022, **24**, 6357–6363.

[3] G. Zhang, C. Zhang, Y. Tian and F. Chen, Fe-Catalyzed Direct Synthesis of Nitriles from Carboxylic Acids with Electron-Deficient N-Cyano-N-aryl–arylsulfonamide. *Org. Lett*. 2023, **25**, 917–922.



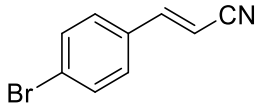
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless solid, 45 mg, 61%. R_f = 0.21 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.46 (ddt, *J* = 8.8, 5.2, 3.2 Hz, 2H), 7.37 (d, *J* = 16.4 Hz, 1H), 7.11 (tt, *J* = 8.8, 2.8 Hz, 2H), 5.81 (dd, *J* = 16.4, 0.8 Hz, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ (ppm): -107.8. **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 164.4 (d, *J* = 253.5 Hz), 149.2, 129.9, 129.4 (d, *J* = 9.1 Hz), 118.0, 116.4 (d, *J* = 22.2 Hz), 96.1.

(*E*)-3-(4-chlorophenyl)acrylonitrile (**2d**): [CAS: 14378-04-2][4]



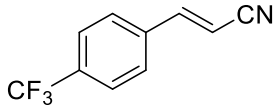
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless solid 39 mg, 48%. R_f = 0.22 (PE : EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.39 (app. s, 4H), 7.36 (d, *J* = 16.8 Hz, 1H), 5.86 (d, *J* = 16.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 149.1, 137.3, 132.0, 129.5, 128.6, 117.8, 97.0.

(*E*)-3-(4-bromophenyl)acrylonitrile (**2e**): [CAS: 27549-93-5][3]



The product was purified by column chromatography (pentene/Et_2O = 30:1). 0.2 mmol, Colorless solid 30 mg, 71%. R_f = 0.4 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.55 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 16.4 Hz, 1H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.86 (d, *J* = 16.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 149.2, 132.4, 128.7, 127.3, 125.7, 117.8, 97.1.

(*E*)-3-(4-(trifluoromethyl)phenyl)acrylonitrile (**2f**): [CAS: 51791-29-8][4]



The product was purified by column chromatography (PE/EtOAc = 30:1). Colorless solid, 74 mg, 75%. R_f = 0.32 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.68 (d, *J* = 8.2 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 16.6 Hz, 1H), 5.99 (d, *J* = 16.6 Hz, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ (ppm): -63.0. **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 148.8, 136.7, 132.6 (q, *J* = 32.3 Hz), 127.6, 126.1 (q, *J* = 4.0 Hz), 123.6 (q, *J* = 273.7 Hz), 117.4, 99.3.

(*E*)-3-(4-nitrophenyl)acrylonitrile (**2g**): [CAS: 29246-70-6][5]

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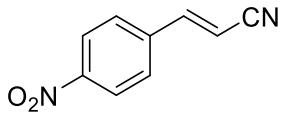
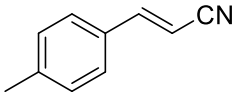
[4] R. Ye, M. Zhu, X. Yan, Y. Long, Y. Xia and X. Zhou, Pd(II)-catalyzed C=C bond cleavage by a formal group-exchange reaction. *ACS Catal.* 2021, **11**, 8678–8683.

[5] Chatterjee, B.; Jena, S.; CHugh, V.; Weyhermuller, T.; Werle, C. A Molecular Iron-Based System for Divergent Bond Activation: Controlling the Reactivity of Aldehydes. *ACS Catal.* 2021, **11**, 7176–7185.



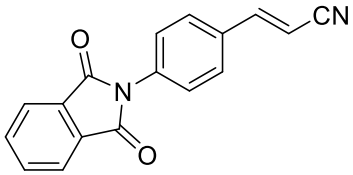
The product was purified by column chromatography (PE/EtOAc = 30:1). Colorless solid, 52 mg, 60%. R_f = 0.5 (PE:EtOAc = 5:1). **^{1}H NMR** (400 MHz, DMSO-d_6) δ (ppm): 8.29 (d, J = 8.8 Hz, 2H), 7.93 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 16.6 Hz, 1H), 6.74 (d, J = 16.6 Hz, 1H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ (ppm): 148.9, 148.7, 140.3, 129.4, 124.5, 118.6, 101.8.

(*E*)-3-(p-tolyl)acrylonitrile (**2h**): [CAS: 35121-93-8] [4]



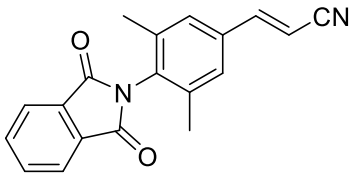
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless solid 15 mg, 21%. R_f = 0.30 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.37 (d, J = 16.4 Hz, 1H), 7.34 (d, J = 8.0 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 5.82 (d, J = 16.8 Hz, 1H), 2.39 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 150.5, 141.8, 130.9, 129.8, 127.3, 108.1, 95.1, 21.5.

(*E*)-3-(4-(1,3-dioxoisoindolin-2-yl)phenyl)acrylonitrile (**2j**)：[CAS: 59244-47-2]



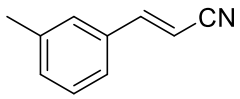
The product was purified by column chromatography (PE/EtOAc = 3:1). 0.2 mmol, creamy white solid 27 mg, 49%. R_f = 0.54 (PE:EtOAc = 3:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.04–7.92 (m, 2H), 7.88–7.76 (m, 2H), 7.67–7.50 (m, 4H), 7.44 (d, J = 16.6 Hz, 1H), 5.92 (d, J = 16.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 166.8, 149.4, 134.7, 134.2, 132.8, 131.6, 128.0, 126.7, 124.0, 117.9, 97.3.

(*E*)-3-(4-(1,3-dioxoisoindolin-2-yl)-3,5-dimethylphenyl)acrylonitrile (**2k**)：



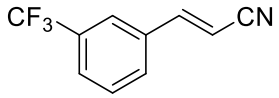
The product was purified by column chromatography (PE/EtOAc = 5:1). 0.25 mmol, Light yellow solid 48 mg, 63%. R_f = 0.50 (PE:EtOAc = 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.97 (dd, J = 5.6, 3.2 Hz, 2H), 7.83 (dd, J = 5.6, 3.2 Hz, 2H), 7.37 (d, J = 16.8 Hz, 1H), 7.27 (s, 2H), 5.90 (d, J = 16.4 Hz, 1H), 2.19 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 166.8, 149.7, 138.1, 134.6, 134.5, 132.5, 131.9, 127.4, 124.0, 117.9, 97.5, 18.2. EI-HRMS calcd. For $C_{19}H_{14}O_2N_2$: 302.1055 [$M^{+\bullet}$], found 302.1048.

(*E*)-3-(m-tolyl)acrylonitrile (**2l**): [CAS: 30116-00-8] [4]



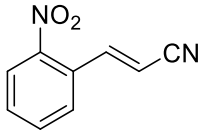
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless liquid 21 mg, 36%. R_f= 0.38 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.37 (d, *J* = 16.8 Hz, 1H), 7.30–7.22 (m, 4H), 5.86 (d, *J* = 16.8 Hz, 1H), 2.38 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 150.8, 138.9, 133.5, 132.1, 129.0, 128.0, 124.6, 118.3, 96.1, 21.3.

(*E*)-3-(3-(trifluoromethyl)phenyl)acrylonitrile (**2m**): [CAS: 51791-29-8][6]



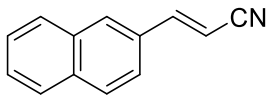
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless solid, 75 mg, 76%. R_f= 0.35 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.74-7.69 (m, 2H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 16.8 Hz, 1H), 6.01 (d, *J* = 16.8 Hz, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ (ppm): -63.0. **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 148.8, 134.2, 131.7 (q, *J* = 33.7 Hz), 130.4, 129.8, 127.6 (q, *J* = 3.7 Hz), 124.0 (q, *J* = 4.1 Hz), 123.6 (q, *J* = 273.5 Hz), 117.4, 98.7. **IR** (KBr) ν (cm^{-1}): 2220.18.

(*E*)-3-(2-nitrophenyl)acrylonitrile (**2n**): [CAS: 51991-49-2][7]



The product was purified by column chromatography (PE/EtOAc = 40:1). Colorless solid 68 mg, 65%. R_f= 0.58 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.13 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.97 (d, *J* = 16.4 Hz, 1H), 7.73 (t, *J* = 7.6 Hz, 1H), 7.64 (dt, *J* = 1.6, 7.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 5.86 (d, *J* = 16.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 147.5, 146.6, 134.1, 131.4, 129.7, 128.7, 125.3, 116.9, 101.5.

(*E*)-3-(naphthalen-2-yl)acrylonitrile (**2o**): [CAS: 301660-67-3] [4]



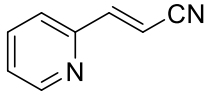
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless solid 60.7 mg, 67%. R_f= 0.28 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm):

6 G. Xing, Z. Zhi, C. Yi, J. Zou, X. Jing, A. Y. Woo, B. Lin, L. Pan, Y. Zhang and M. Cheng, 8-Hydroxyquinolin-2(1H)-one analogues as potential β2-agonists: Design, synthesis and activity study. *Eur. J. Med. Chem*. 2021, **224**, 113697.

7 Q. Wu, Y. Luo, A. Lei and J. You, Aerobic Copper-Promoted Radical-Type Cleavage of Coordinated Cyanide Anion: Nitrogen Transfer to Aldehydes to Form Nitriles. *J. Am. Chem. Soc*. 2016, **138**, 2885–2888.

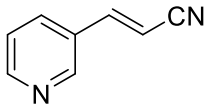
7.90-7.81 (m, 4H), 7.59-7.50 (m, 4H), 5.96 (dd, *J* = 16.8, 1.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 150.6, 134.5, 133.1, 131.0, 129.7, 129.1, 128.7, 127.9, 127.8, 127.1, 122.2, 118.3, 96.3.

(*E*)-3-(pyridin-2-yl)acrylonitrile (**2p**): [CAS: 39077-59-3][8]



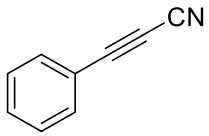
The product was purified by column chromatography (pentene/Et_2O = 4:1). Light yellow solid 32 mg, 49%. The yield could be increased up to 70% when extra 2 equiv. of $NH_2CO_2NH_4$ and 1 equiv. of PIFA was added for another 2h (total 6 h). R_f = 0.45 (PE:EtOAc = 4:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.64 (d, *J* = 3.2 Hz, 1H), 7.75 (dt, *J* = 1.6, 7.8 Hz, 1H), 7.40 (d, *J* = 16.0 Hz, 1H), 7.34 (dd, *J* = 7.8, 3.2 Hz, 1H), 7.33 (d, *J* = 7.8 Hz, 1H), 6.59 (d, *J* = 16.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 151.1, 150.3, 148.7, 137.1, 125.2, 124.3, 118.0, 100.8.

(*E*)-3-(pyridin-3-yl)acrylonitrile (**2q**): [CAS: 54356-27-3][9]



The product was purified by column chromatography (pentene/Et_2O = 4:1). Colorless solid 36 mg, 55%. R_f = 0.12 (PE:EtOAc = 3:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 8.71 (s, 1H), 8.67 (d, *J* = 4.8 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 16.4 Hz, 1H), 7.38 (dd, *J* = 8.0, 4.8 Hz, 1H), 6.00 (d, *J* = 16.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 151.9, 149.0, 147.0, 133.5, 129.3, 123.9, 117.4, 98.8.

3-phenylpropiolonitrile (**2r**): [CAS:935-02-4][10]



The product was purified by column chromatography (pentene/Et_2O = 30:1). Yellow solid 32 mg, 50%. R_f = 0.6 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.64–7.59 (m, 2H), 8.54 (tt, *J* = 7.6, 1.6 Hz, 1H), 7.42 (t, *J* = 8.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 133.5, 132.0, 128.9, 117.6, 105.5, 83.0, 63.1.

(*E*)-5-phenylpent-2-en-4-ynenitrile (**2s**): [CAS: 49840-80-4][11]

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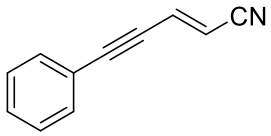
[8] Q. Wu, N. Chen and J. Xu, Chemoselectivity in the Transannulation of 1,2,3-Thiadiazoles and Alk-2-enenitriles: Specific Synthesis of 3-(Alk-1-enyl)isothiazoles. *ChemistrySelect* 2022, **7**, e202103943.

[9] K. Sun, H. Shan, H. Neumann, G.-P. Lu and M Beller, Efficient iron single-atom catalysts for selective ammoxidation of alcohols to nitriles. *Nature Commun*. 2022, **13**, 1848(1-9).

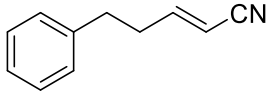
[10] M. Kumar and G. Avijit, Tunable Regio- and Stereoselective Synthesis of Z-Acrylonitrile Indoles and 3-Cyanoquinolines from 2-Alkynylanilines and Alkynylnitriles. *Org. Lett.* 2023, **25**, 3254–3259.

[11] B. Li, Z. Li, K. You, A. Qin and B. Z. Tang, Responsive hyperbranched poly(formyl-1,2,3-triazole)s toward quadruple-modal information security protection. *Sci. China Chem*. 2022, **65**, 771–777.



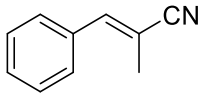
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless liquid, 52 mg, 64%. R_f = 0.54 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.48 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.43-7.32 (m, 3H), 6.67 (d, *J* = 16.2 Hz, 1H), 5.77 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 132.1, 131.0, 130.0, 128.6, 121.3, 117.1, 108.0, 100.7, 85.4.

(*E*)-5-phenylpent-2-enenitrile (**2t**): [CAS: 5320-30-9][12]



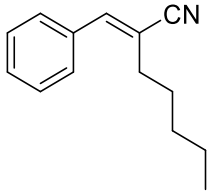
The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless liquid 52 mg, 66%. R_f = 0.35 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.30 (t, *J* = 7.6 Hz, 2H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.14 (d, *J* = 7.6 Hz, 2H), 6.70 (dt, *J* = 16.4, 7.6 Hz, 1H), 5.30 (dt, *J* = 16.4, 1.6 Hz, 1H), 2.75 (t, *J* = 7.6 Hz, 2H), 7.14 (dq, *J* = 1.2, 7.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 154.7, 139.8, 128.7, 128.3, 126.5, 117.4, 100.5, 34.9, 33.9.

(*E*)-2-methyl-3-phenyl-2-Propenenitrile (**2u**): [CAS: 53587-72-7] [13]



The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless liquid, 50 mg, 69%. R_f = 0.45 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.44–7.36 (m, 3H), 7.34–7.30 (m, 2H), 7.21 (q, *J* = 1.6 Hz, 2H), 2.14 (d, *J* = 1.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 144.5, 134.1, 129.4, 129.3, 128.7, 121.3, 109.7, 16.9.

(*E*)-2-(Phenylmethylene)heptanenitrile (**2v**): [CAS: 2757913-85-0][13]



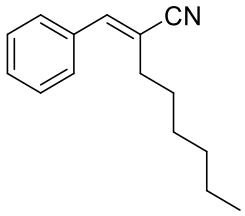
The product was purified by column chromatography (PE/EtOAc = 30:1). Colorless liquid, 60 mg, 60%. R_f = 0.56 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.44–7.34 (m, 3H), 7.31–7.27 (m, 2H), 7.21 (s, 1H), 2.45 (dt, *J* = 1.6, 8.0 Hz, 2H), 1.67 (quint, *J* = 8.4 Hz, 2H), 1.37-1.26 (m, 4H), 0.89 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101

[12] S. Arai, K. Nakazawa, X.-F. Yang and A. Nishida, Nickel-catalyzed regioselective hydrocyanation of terminal alkynes by assistance of a tosyl group. *Tetrahedron* 2019, **75**, 2482–2485

[13] Z. Zhu, B. Liu, W. Tang, H. Tong and X. Xu, Preparation method of nitrile compounds. China patent, **2021**, CN113861069.

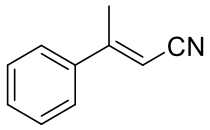
MHz, $CDCl_3$) δ (ppm):144.0, 134.2, 129.2, 129.1, 128.7, 120.4, 116.2, 31.2, 29.4, 27.9, 22.3, 13.9.

(*E*)-2-(Phenylmethylene)octanenitrile (**2w**): [CAS: 2232880-31-6][14]



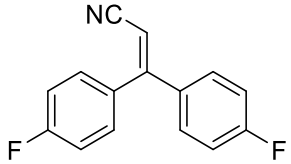
The product was purified by column chromatography (PE/EtOAc = 30:1). Colorless liquid, 61 mg, 57%. R_f= 0.55 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.44–7.34 (m, 3H), 7.31–7.27 (m, 2H), 7.21 (s, 1H), 2.45 (dt, *J* = 1.2, 7.6 Hz, 2H), 1.66 (quint, *J* = 7.6 Hz, 2H), 1.40-1.25 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 144.0, 134.2, 129.2, 129.1, 128.7, 120.4, 116.2, 31.4, 29.4, 28.7, 28.2, 22.5, 14.0.

(*E*)-3-phenylbut-2-enenitrile (**2x**): [CAS: 14799-78-1][15]



The product was purified by column chromatography (PE/EtOAc = 30:1). Colorless liquid, 31 mg, 43%. R_f= 0.33 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.50–7.35 (m, 5H), 5.61 (s, 1H), 2.46 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 159.8, 138.2, 130.3, 128.9, 125.9, 117.6, 95.6, 20.2.

3,3-bis(4-fluorophenyl)acrylonitrile (**2y**): [CAS: 50775-35-4][16]



The product was purified by column chromatography (PE/EtOAc = 20:1). 0.2 mmol, colorless liquid 35 mg, 29%. R_f= 0.37 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.43 (ddt, *J* = 8.8, 5.2, 3.2 Hz, 2H), 7.28 (ddt, *J* = 9.5, 5.2, 2.4 Hz, 2H), 7.15 (tt, *J* = 8.8, 2.8 Hz, 2H), 7.08 (tt, *J* = 8.8, 2.8 Hz, 2H), 5.68 (s, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ (ppm): -109.4, -109.7. **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 164.2 (d, *J* = 253.2 Hz), 161.9 (d, *J* = 252.5 Hz), 160.9, 134.9 (d, *J* = 3.0 Hz), 132.9 (d, *J* = 3.0 Hz),

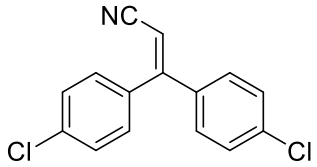
[14] P. Maity, D. Kundu, T. Ghosh and B. C. Ranu, Copper catalyzed cyanation through C=C bond cleavage of gem-aryl dibromide followed by second cyanation of iodoarene by a released CN unit. *Org. Chem. Front.* 2018, **5**, 1586–1599.

[15] M. Li and Z. Jing, Iron-Catalyzed Deoxynitrogenation of Carboxylic Acids with Cyanamides to Access Nitriles. *Chem. Eur. J.* 2023, **29**, e202300217

[16] Y. Wang, J.-X. Zhang, and W. Shu, W. Cu-Catalyzed Remote Transarylation of Amines via Unstrained C-C Functionalization. *Acs, Catal*. 2020, **10**, 15065–15070.

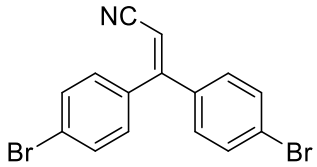
131.6 (d, *J* = 8.1 Hz), 130.4 (d, *J* = 8.1 Hz), 117.6, 116.0 (d, *J* = 6.1 Hz), 115.8 (d, *J* = 6.1 Hz), 94.9.

3,3-bis(4-chlorophenyl)acrylonitrile (**2z**): [CAS: 1071466-43-7][16]



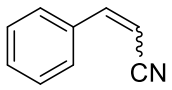
The product was purified by column chromatography (PE/EtOAc = 20:1). Light yellow liquid 57.5 mg, 42%. R_f = 0.38 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.44 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.36 (dt, *J* = 8.4, 2.0 Hz, 4H), 7.22 (dt, *J* = 8.8, 2.4 Hz, 2H), 5.73 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 160.6, 137.0, 136.9, 136.5, 135.0, 130.9, 129.7, 129.11, 129.07, 117.4, 95.7.

3,3-bis(4-bromophenyl)acrylonitrile (**2aa**): [CAS: 100914-54-3] [16]



The product was purified by column chromatography (PE/EtOAc = 20:1). Light yellow liquid 47 mg, 26%. R_f = 0.38 (PE:EtOAc = 20:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.60 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.52 (dt, *J* = 8.8, 2.4 Hz, 2H), 7.29 (dt, *J* = 8.4, 2.4 Hz, 2H), 7.15 (dt, *J* = 8.8, 2.4 Hz, 2H), 5.74 (s, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 160.7, 137.3, 135.4, 132.1, 132.0, 131.1, 129.9, 125.4, 124.9, 117.3, 95.7.

(*Z*)-/(*E*)-3-phenyl-2-propenenitrile (**2ac**): [CAS: 4360-47-8][17]

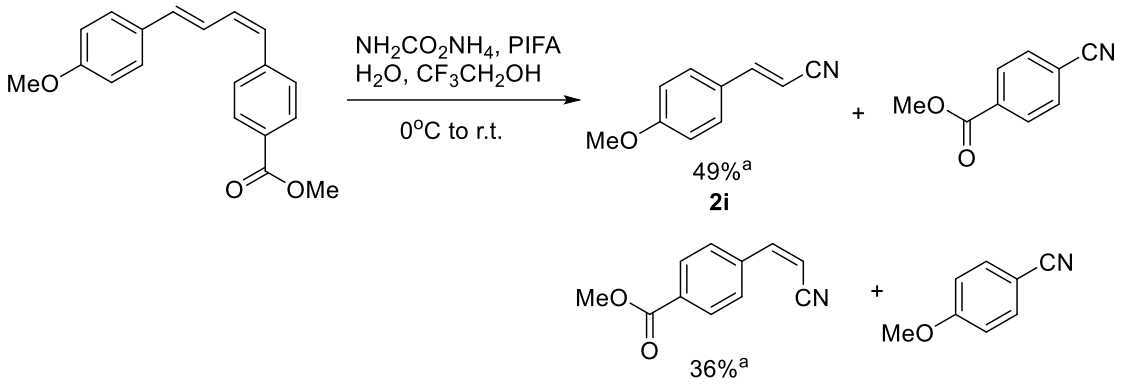


The product was purified by column chromatography (pentene/Et_2O = 30:1). Colorless liquid, 46 mg, 71% (*Z*/*E* = 3/1). This mixture comes from the mixture raw materials (Z/E=3:1). (*Z*)-3-phenyl-2-propenenitrile: **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.84-7.75 (m, 2H), 7.50-7.36 (m, 3H), 7.11 (d, *J* = 12.2 Hz, 3H), 5.42 (d, *J* = 12.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 148.8, 133.6, 129.04, 128.96, 127.4, 117.4, 95.1. ^{1}H NMR and ^{13}C NMR of (*E*)-isomer are same with **2b**.

[17] N. A. Stini, P. L. Gkizis and C. G. Kokotos, Cyrene: a bio-based solvent for the Mizoroki-Heck reaction of aryl iodides. *Org. Biomol. Chem.* 2023, **21**, 351–358.

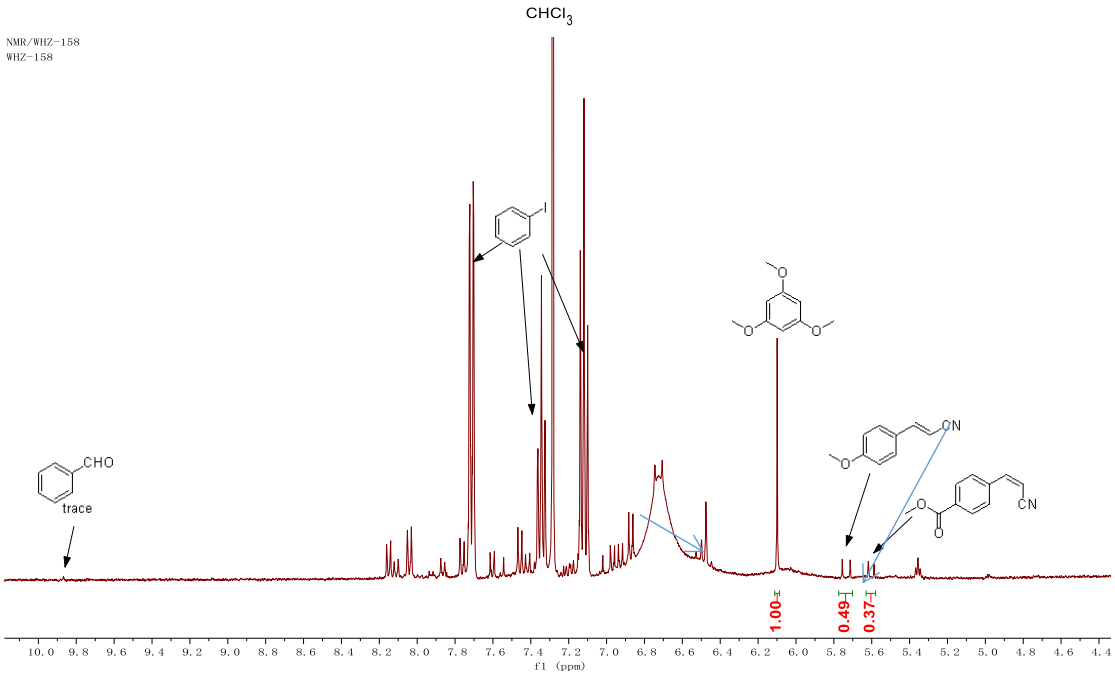
3.2 Reactions System analysis of **1ae, 1ag** and **1ah (Scheme 3)**

a) Reaction system of **1ae**

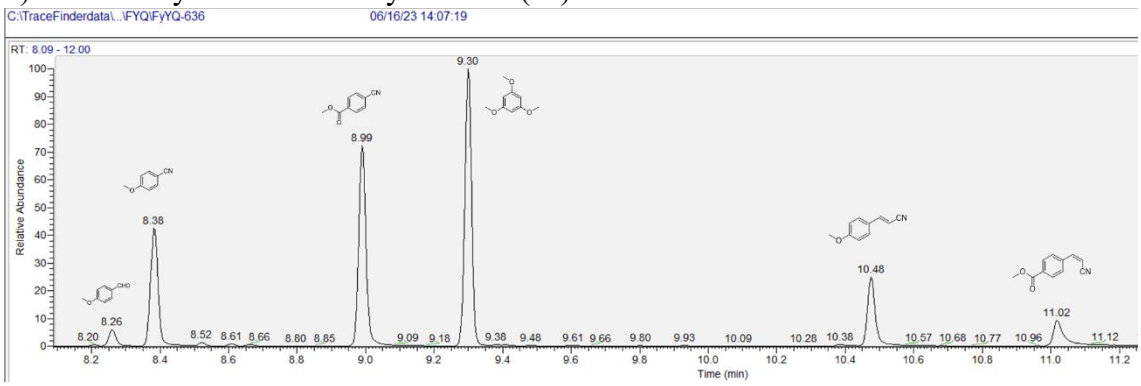


[a] ^{1}H NMR yield

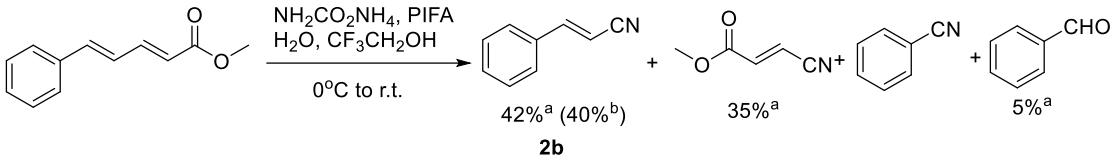
Reaction system checked by ^{1}H NMR



b) Reaction system checked by GC-MS (EI)



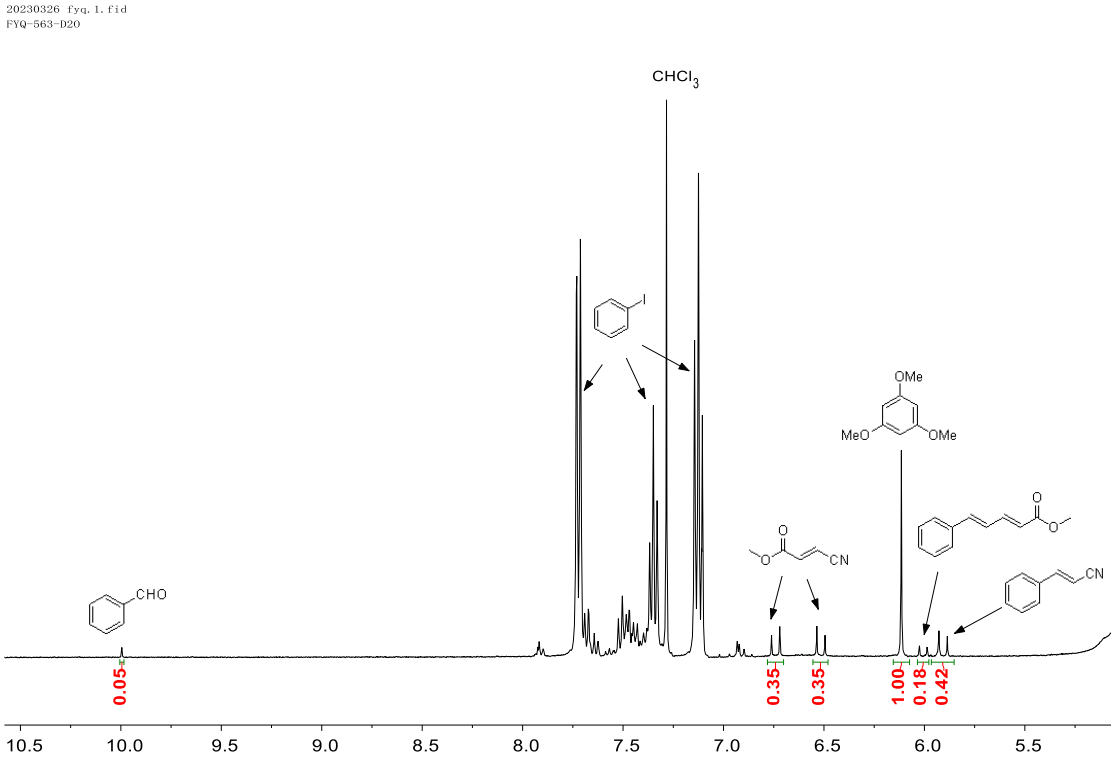
c) Reaction system of **1ag**



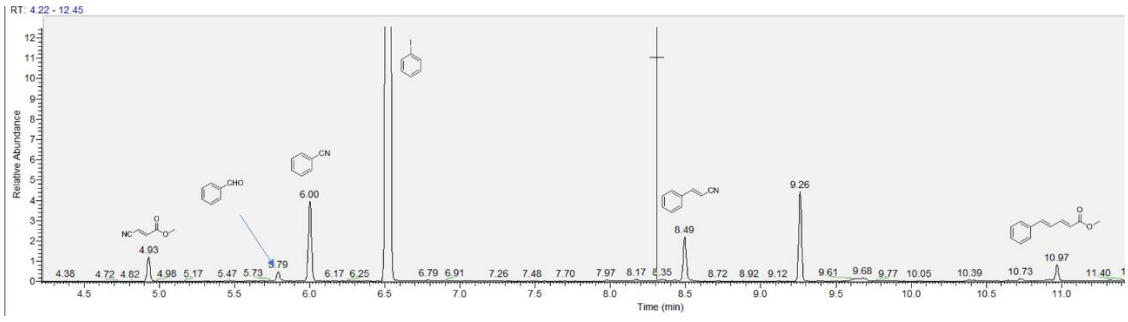
2b

[a] ^{1}H NMR yield [b] isolated yield

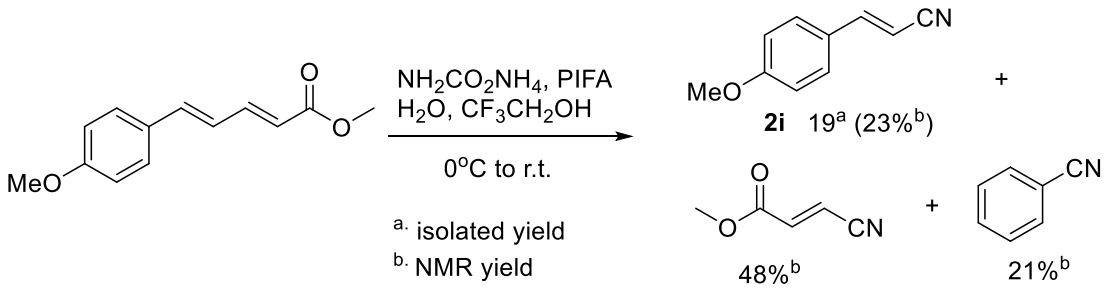
Reaction system checked by ^{1}H NMR



Reaction system checked by GC-MS (EI)

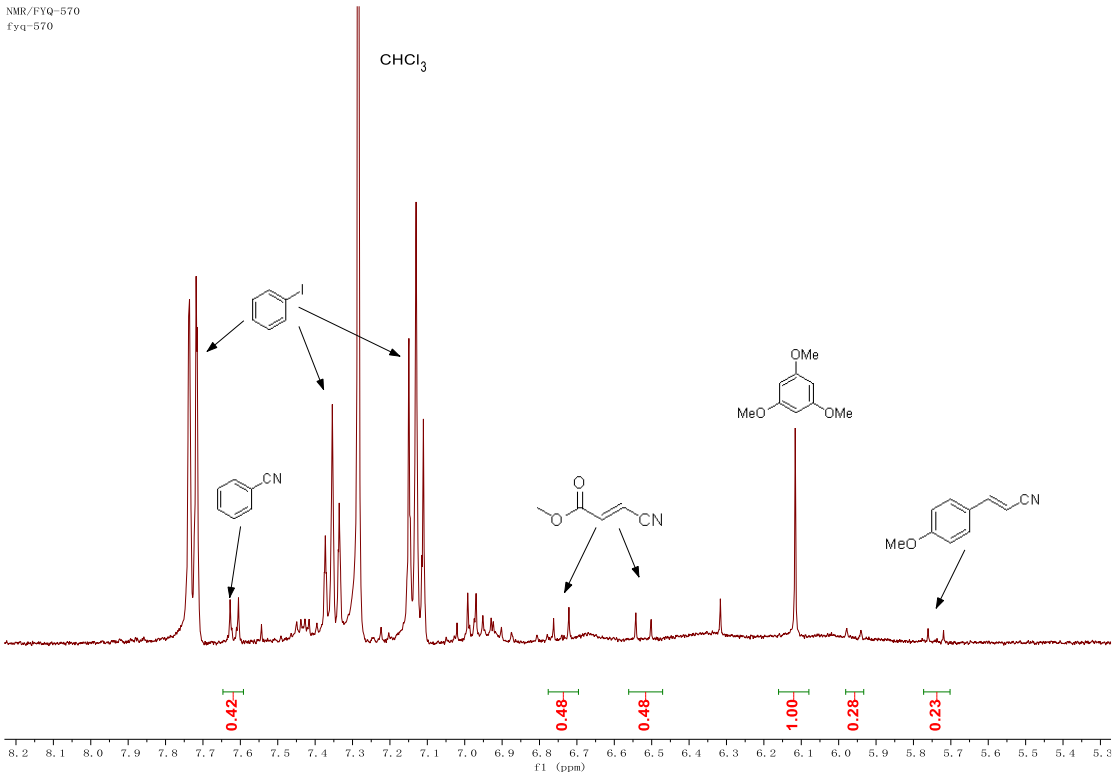


Reaction system of **1ah**

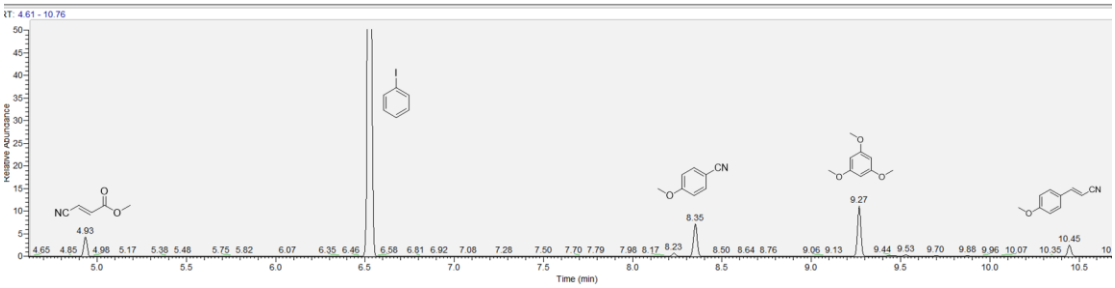


[a] ^{1}H NMR yield [b] isolated yield

Reaction system checked by ^{1}H NMR



Reaction system by GC-MS (EI)

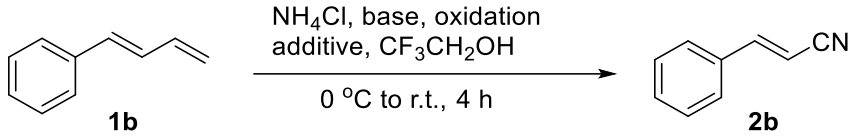


4. Reactions with ammonium chloride and *N*-15 atom labeled ammouniun chloride

4.1 Detailed optimization of reactions with ammouniun chloride

Initially, we attempted the reaction using NH_4Cl and PIFA as the oxidant, but unfortunately, no desired product **2b** was generated (Table S4-1, entry 1). Furthermore, the reaction system proved to be very complex, as indicated by GC-MS analysis. In an attempt to improve the system, we added extra K_2CO_3 as the base, but this resulted in an even worse outcome (entry 2). The complex mixture obtained from the reaction contained benzonitriles, benzaldehyde, as well as a series of chlorinated benzonitriles and chloroiodobenzenes. The presence of chlorinated products led us to hypothesize that PIFA might be too strong of an oxidant, potentially oxidizing the chloride to chlorine or its cation.

Table S4-1. Optimization of the reaction conditions



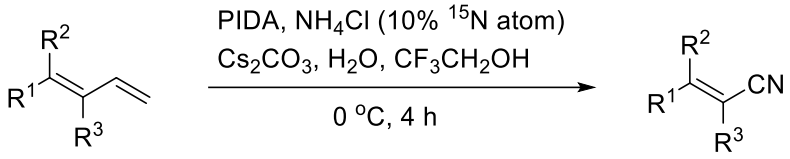
Entry	Base	Oxidation	additive	Yield/%[a]
1	-	PIFA	H_2O	0
2	K_2CO_3	PIFA	H_2O	trace[b]
3	K_2CO_3	PIDA	H_2O	10[c]
4	K_2CO_3	PIDA	H_2O	52
5	NaOH	PIDA	H_2O	27
6	NaOAc	PIDA	H_2O	trace
7	NaH	PIDA	MeOH	36
8	*t*-BuOK	PIDA	MeOH	62
9	Cs_2CO_3	PIDA	H_2O	70 (58%[d])

[a] Reaction condition: **1b** (0.2 mmol, 26 mg), NH_4Cl (0.4 mmol, 21.2 mg), base (0.4 mmol, 140 mg), PIDA or PIFA (0.4 mmol), H_2O (0.4 mmol, 7.2 μL/mg), CF_3CF_2OH (1.5 mL). NMR yields were obtained. [b] Very complicated reaction system [c] The reaction performed at 0 °C for 4h. [d]Yields obtained from isolated compounds.

To investigate this further, we conducted the reaction at a continuous low temperature of 0 °C. 10% yield of the desired product **2b** was observed and the system remained complicated (entry 3). In order to address these challenges, we decided to replace PIFA with the less reactive PIDA. Fortunately, this modification led to the successful formation of **2b** in a 52% NMR yield. We then proceeded to

investigate various bases (entries 4-9), and ultimately found that Cs2CO3 provided the most favorable results (entry 9).

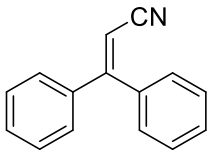
4.2 General information for the synthesis of substituted acrylonitriles **2** from NH_4Cl and *N*-15 atom labeled NH_4Cl (Scheme 4 & Scheme 5a)



General Procedure:

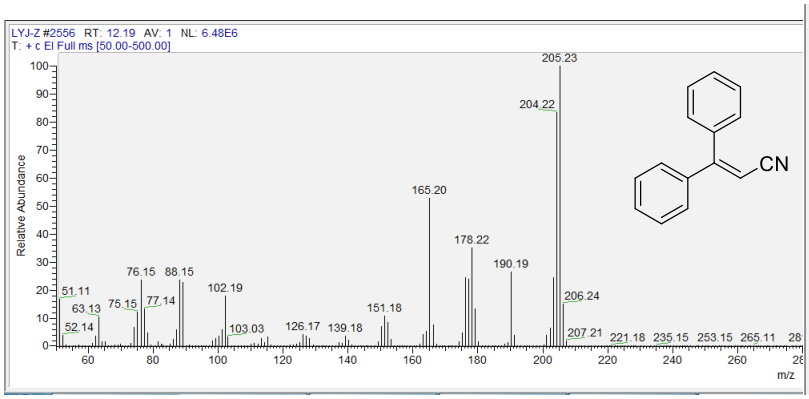
To a pressure resistant reaction tube equipped with a magnetic stirring bar was added conjugated diene **1** (0.5 mmol, 1.0 equiv), 10% N-15 NH_4Cl (53 mg, 1.0 mmol, 2.0 equiv), Cs_2CO_3 (326 mg, 1.0 mmol, 2.0 equiv), H_2O (18 mg, 1.0 mmol, 2.0 equiv.) and 6 mL CF_3CH_2OH. The tube was cooled to 0 °C and then PIDA (322 mg, 1.0 mmol, 2.0 equiv) was added. The mixture was stired for 4 h at 0 °C. The reaction mixture was quenched with water (10 mL), and then extracted with CH_2Cl_2 (5 mL×2). The organic layers were collected, dried over Na_2SO_4. After removing the solvent in vacuo, the residue was purified by flash column chromatography on silica gel to obtain the pure product **2**. The ^1H NMR and ^{13}C NMR 10% *N*-15 atom labeled α,β–unsaturated nitriles (**2a***) was almost same with natural abundance α,β–unsaturated nitriles, so EI-MS was attached to verify the nitrogen abundance.

3,3-diphenylacrylonitrile (**2a***):



0.7 mmol scale, light yellow liquid 82 mg, 57%.

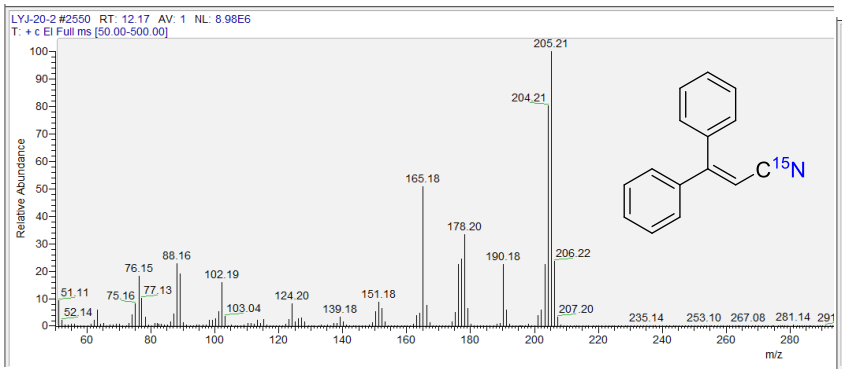
EI-MS of 3,3-diphenylacrylonitrile (**2a**):



LYJ-Z#2556 RT: 12.19
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
51.11	1082029.0	16.70
63.13	676908.2	10.45
75.15	784506.0	12.11
76.15	1531128.1	23.63
77.14	868119.3	13.40
88.15	1527884.9	23.58
89.18	1480240.5	22.84
102.19	1162816.8	17.94
151.18	696215.8	10.74
152.19	552819.1	8.53
165.20	3422158.0	52.81
176.21	1595376.5	24.62
177.21	1556885.4	24.02
178.22	2267755.0	34.99
179.22	868028.4	13.39
190.19	1724095.5	26.61
203.22	1580678.4	24.39
204.22	5419346.0	83.63
205.23	6480338.5	100.00
206.24	974646.0	15.04

EI-MS of 10% *N*-15 atom labeled 3,3-diphenylacrylonitrile (**2a***):

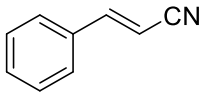


LYJ-20-2#2550 RT: 12.17
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
51.11	842276.7	9.38
75.16	738933.7	8.23
76.15	1644241.1	18.31
77.13	912149.4	10.16
88.16	2038302.9	22.70
89.15	1702219.4	18.95
102.19	1422414.1	15.84
124.20	731390.9	8.14
151.18	795094.0	8.85
152.19	583742.1	6.50
165.18	4567220.5	50.86
166.20	672970.4	7.49
176.20	2012766.4	22.41
177.20	2189540.8	24.38
178.20	2989329.5	33.29
190.18	2026839.6	22.57
203.20	2021922.8	22.52
204.21	7205704.0	80.24
205.21	8980324.0	100.00
206.22	2116444.8	23.57

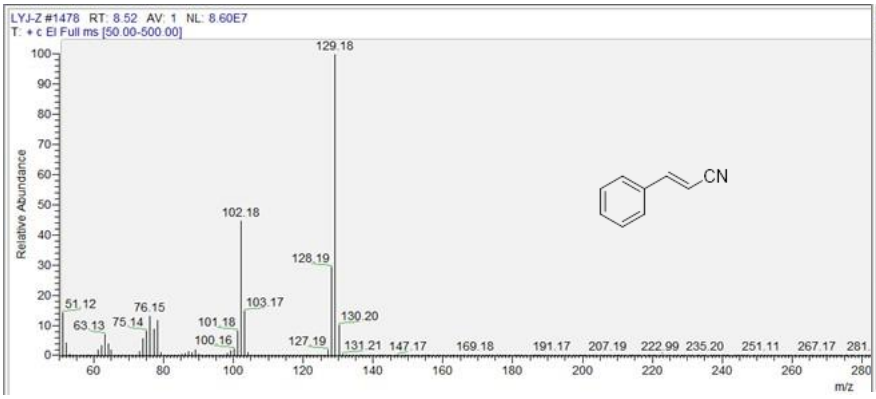
	2a	10% N-15 atom labeled **2a***
[M+1]/[M]	15.04 %	23.57 %

Cinnamonitrile (**2b***):



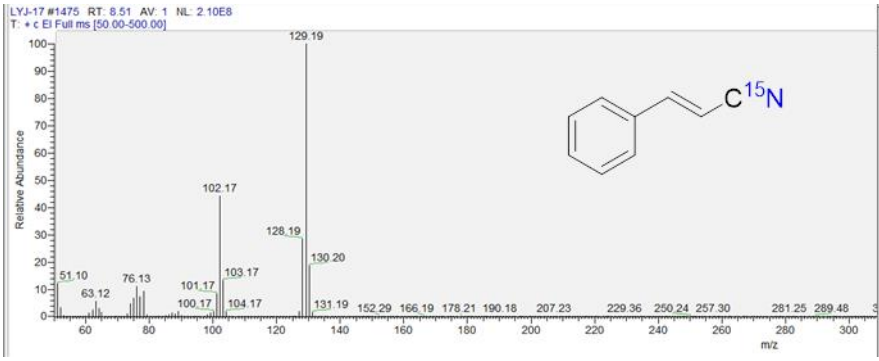
0.5 mmol scale; light yellow liquid 38 mg, 58%。

EI-MS of cinnamonitrile (**2b**):



LYJ-Z#1478 RT: 8.52 T: + c EI Full ms [50.00-500.00] m/z= 50.00-499.97		
m/z	Intensity	Relative
50.22	6529432.5	7.60
51.12	12250173.0	14.25
52.11	3688204.0	4.29
62.12	2924731.5	3.40
63.13	5914023.5	6.88
64.17	3448431.3	4.01
64.98	1628855.9	1.89
74.13	4827084.5	5.62
75.14	7107730.5	8.27
76.15	11326435.0	13.18
77.15	7391361.5	8.60
78.16	10005806.0	11.64
100.16	1764448.4	2.05
101.18	6907811.0	8.04
102.18	38232992.0	44.47
103.17	12707206.0	14.78
127.19	1652034.6	1.92
128.19	25331504.0	29.47
129.18	85966848.0	100.00
130.20	8866378.0	10.31

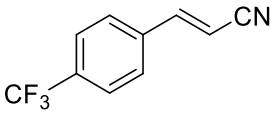
EI-MS of 10% *N*-15 atom labeled cinnamonitrile (**2b***):



LYJ-17#1475 RT: 8.51 T: + c EI Full ms [50.00-500.00] m/z= 50.00-499.97		
m/z	Intensity	Relative
50.21	12167109.0	5.79
51.10	25273718.0	12.03
52.09	7087988.5	3.38
62.10	5401525.5	2.57
63.12	11985397.0	5.71
64.16	6487291.5	3.09
74.11	9840649.0	4.69
75.12	14052861.0	6.69
76.13	23151666.0	11.02
77.14	15318663.0	7.29
78.14	19636510.0	9.35
100.17	4164106.8	1.98
101.17	17509158.0	8.34
102.17	93134448.0	44.35
103.17	28207340.0	13.43
104.17	4126691.5	1.97
127.19	4046388.0	1.93
128.19	60033324.0	28.59
129.19	210006496.0	100.00
130.20	39612784.0	18.86

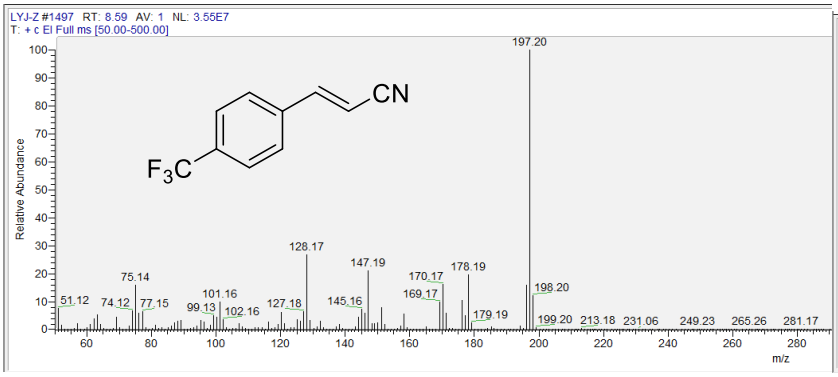
	2b	10% *N*-15 atom labeld **2b***
[M+1]/[M]	10.05%	18.86 %

(*E*)-3-(4-(trifluoromethyl)phenyl)acrylonitrile (**2f***):



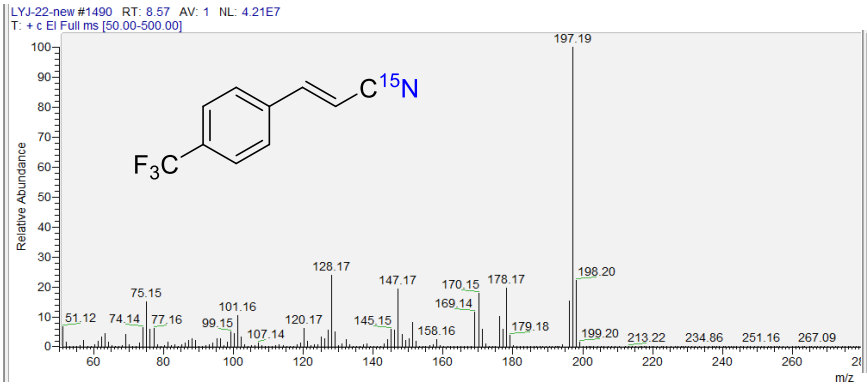
0.7 mmol scale, colorless solid 85 mg, 62%.

EI-MS of (*E*)-3-(4-(trifluoromethyl)phenyl)acrylonitrile (**2f**)



m/z	Intensity	Relative
50.22	2105810.5	5.93
51.12	2708303.5	7.63
74.12	2343637.0	6.60
75.14	5631535.5	15.87
77.15	2259946.3	6.37
101.16	3478148.0	9.80
120.16	2196025.5	6.19
127.18	2288396.0	6.45
128.17	9465012.0	26.67
145.16	2556667.8	7.20
147.19	7512520.5	21.17
151.17	2767351.5	7.80
169.17	3552143.8	10.01
170.17	5715528.0	16.11
171.16	2126347.0	5.99
176.16	3673154.3	10.35
178.19	7000128.0	19.73
196.20	5612613.5	15.82
197.20	35486976.0	100.00
198.20	4348453.0	12.25

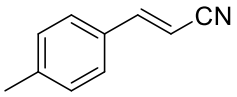
EI-MS of 10% *N*-15 atom labeled (*E*)-3-(4-(trifluoromethyl)phenyl)acrylonitrile (**2f***):



m/z	Intensity	Relative
51.12	2874774.3	6.83
74.14	2661834.3	6.33
75.15	6270673.0	14.90
76.12	2442949.5	5.81
77.16	2637806.0	6.27
101.16	4392503.5	10.44
120.17	2625561.8	6.24
128.17	10111469.0	24.03
145.15	2508904.5	5.96
147.17	8132985.0	19.33
151.16	3480697.3	8.27
169.14	4881118.0	11.60
170.15	7585652.5	18.03
171.15	2520314.5	5.99
176.15	4323790.5	10.27
177.18	2473127.8	5.88
178.17	8261890.0	19.63
196.15	6509237.5	15.47
197.19	42083292.0	100.00
198.20	9298612.0	22.10

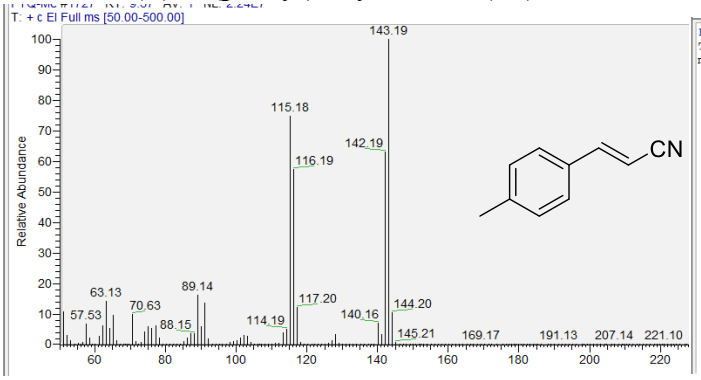
	2f	10% *N*-15 atom labeled **2f***
[M+1]/[M]	12.25%	22.10 %

(*E*)-3-(p-tolyl)acrylonitrile (**2h***):



0.5 mmol scale, colorless solid 35.8 mg, 50%.

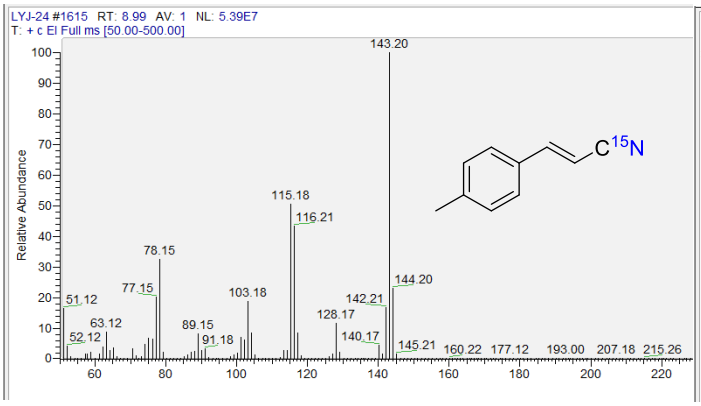
EI-MS of (*E*)-3-(p-tolyl)acrylonitrile (**2h**):



FYQ-Me#1727 RT: 9.37
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.22	1302435.0	5.80
51.12	2408176.3	10.73
57.53	1483017.4	6.61
62.15	1405888.1	6.26
63.13	3165983.0	14.10
65.14	2158905.8	9.62
70.63	2220857.3	9.89
75.11	1324719.1	5.90
76.13	1187435.4	5.29
77.14	1394408.8	6.21
89.14	3634458.3	16.19
90.16	1348444.5	6.01
91.17	3035234.8	13.52
115.18	16818024.0	74.91
116.19	12899036.0	57.46
117.20	2719437.0	12.11
140.16	1551158.1	6.91
142.19	14156888.0	63.06
143.19	22449670.0	100.00
144.20	2361041.5	10.52

10% *N*-15 atom labeled (*E*)-3-(p-tolyl)acrylonitrile (**2h***)

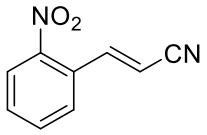


LYJ-24#1618 RT: 9.00
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

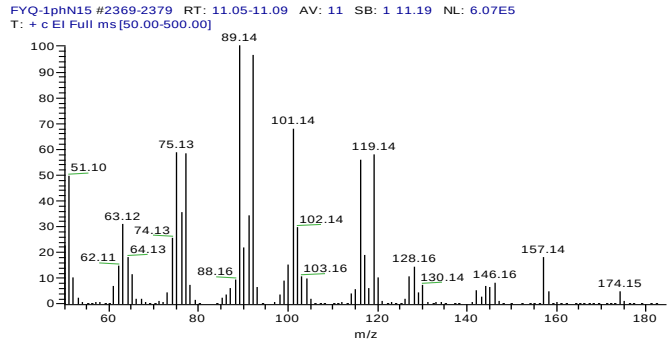
m/z	Intensity	Relative
50.21	1949384.5	7.83
51.11	5090299.0	20.45
63.13	2504222.3	10.06
74.13	1451760.8	5.83
75.13	1737214.6	6.98
76.15	1849557.6	7.43
77.15	5901923.5	23.71
78.16	9383902.0	37.70
89.16	2202056.5	8.85
101.17	1747418.3	7.02
102.18	1600612.8	6.43
103.17	4938910.0	19.84
104.18	2084343.9	8.37
115.19	13016398.0	52.29
116.21	11180105.0	44.91
117.20	2133844.0	8.57
128.17	2732630.3	10.98
142.19	3722474.0	14.95
143.19	24893740.0	100.00
144.20	5084593.0	20.43

	2h	10% *N*-15 atom labeled **2h***
[M+1]/[M]	10.52%-*	20.43 %

(*E*)-3-(2-Nitrophenyl)-2-propenenitrile (**2n***)



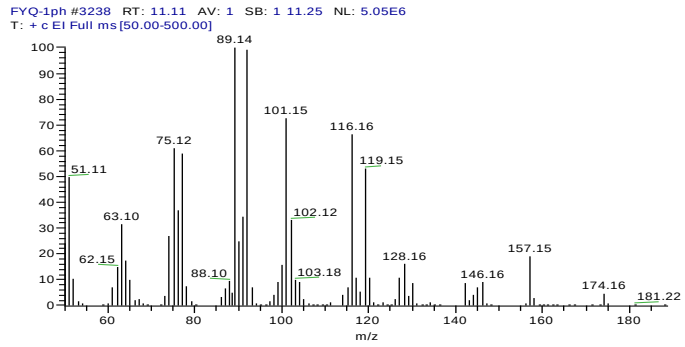
0.7 mmol scale, colorless solid 71 mg, 49%.
EI-MS of
(*E*)-3-(2-Nitrophenyl)-2-propenenitrile (2n)



FYQ-1phN15#2369-2379 RT: 11.
SB: 1 11.19
T: + c EI Full ms [50.00-50(
m/z= 121.72-192.67

m/z	Intensity	Relative
134.16	4589.4	4.22
141.19	4125.2	3.80
142.16	32703.2	30.09
143.18	16448.9	15.14
144.18	40328.6	37.11
145.18	38852.7	35.75
146.16	47906.5	44.08
147.14	6109.3	5.62
157.14	108674.8	100.00
158.15	28325.9	26.06
174.15	28861.3	26.56
175.14	5986.1	5.51

EI-MS of *N*-15 atom labeled (*E*)-3-(2-Nitrophenyl)-2-propenenitrile (2n)

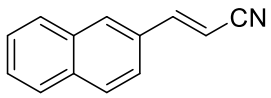


FYQ-1ph#3238 RT: 11.11
SB: 1 11.25
T: + c EI Full ms [50.00-500.
m/z= 122.89-184.00

m/z	Intensity	Relative
134.16	46039.9	4.87
142.16	432445.3	45.72
143.18	97800.5	10.34
144.16	202049.3	21.36
145.15	350829.2	37.09
146.16	446537.8	47.21
147.19	32543.1	3.44
156.31	41442.4	4.38
157.15	945865.1	100.00
158.21	127436.2	13.47
174.16	222414.1	23.51
175.16	23777.6	2.51

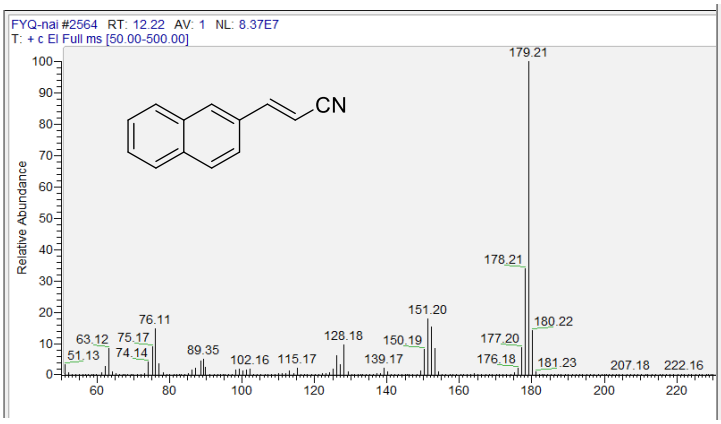
	2n	10% *N*-15 atom labeled **2n***
[M+1]/[M]	10.67% (2.51/23.51)	20.74% (5.51/26.56)

(*E*)-3-(naphthalen-2-yl)acrylonitrile (**2o***):



Colorless solid 63 mg, 70%.

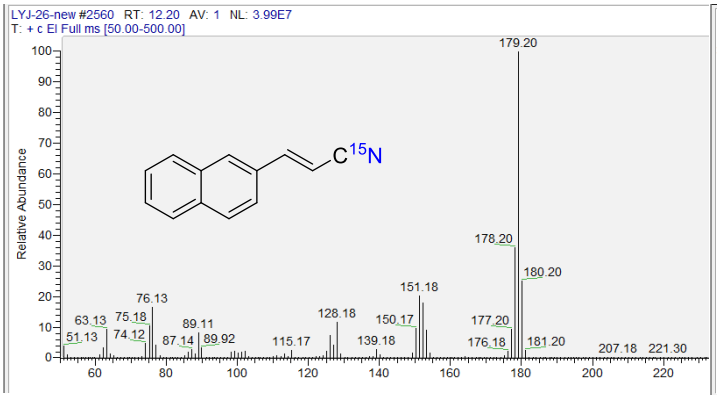
EI-MS of (*E*)-3-(naphthalen-2-yl)acrylonitrile (**2o**)



FYQ-nai#2564 RT: 12.22
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
51.13	2768456.8	3.31
62.12	2165552.0	2.59
63.12	6961490.5	8.32
74.14	3542210.5	4.23
75.17	7536592.5	9.00
76.11	12347860.0	14.75
77.10	3038119.5	3.63
88.63	3704559.0	4.43
89.35	4149986.5	4.96
126.17	5082957.0	6.07
127.18	2864273.5	3.42
128.18	7923430.5	9.47
150.19	6853838.5	8.19
151.20	15091981.0	18.03
152.20	12937532.0	15.46
153.19	7176686.0	8.57
177.20	7431360.0	8.88
178.21	28331552.0	33.85
179.21	83699768.0	100.00
180.22	11783247.0	14.08

10% *N*-15 atom labeled (*E*)-3-(naphthalen-2-yl)acrylonitrile (**2o***)

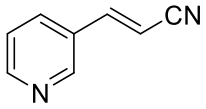


LYJ-26-new#2558 RT: 12.20
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
51.13	831563.9	3.84
62.13	670213.6	3.09
63.13	2066075.0	9.53
74.13	1014175.4	4.68
75.18	2202868.0	10.16
76.13	3469569.3	16.00
77.10	890792.0	4.11
88.87	1069536.8	4.93
89.57	1358651.1	6.27
126.18	1494906.5	6.90
127.18	937242.4	4.32
128.18	2353554.3	10.86
150.18	2071347.8	9.55
151.17	4538301.0	20.93
152.19	3879313.3	17.89
153.19	2007300.6	9.26
177.19	2009851.8	9.27
178.20	7772882.0	35.85
179.20	21679762.0	100.00
180.21	5268746.5	24.30

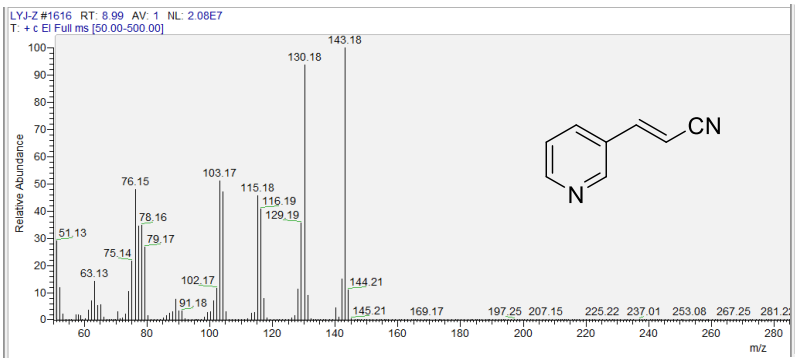
	2o	*N*-15 atom labeled **2o***
[M+1]/[M]	14.08%	24.30%

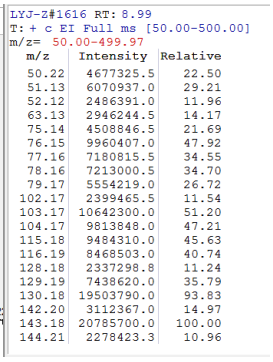
(*E*)-3-(pyridin-3-yl)acrylonitrile (**2p***):



0.5 mmol scale, colorless solid 20 mg, 31%

EI-MS of (*E*)-3-(pyridin-3-yl)acrylonitrile (**2p**):

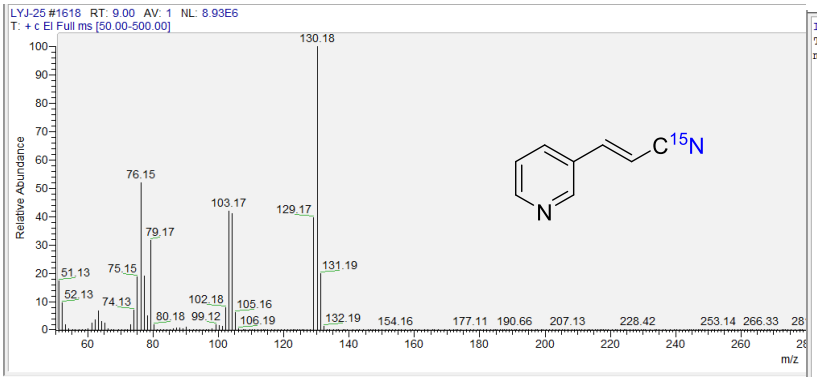


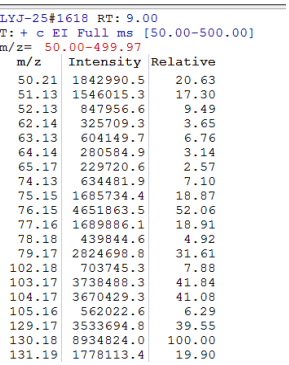


LYJ-Z#1616 RT: 8.99
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.22	4677325.5	22.50
51.13	6070937.0	29.21
52.12	2486391.0	11.96
63.13	2946244.5	14.17
75.14	4508846.5	21.69
76.15	9960407.0	47.92
77.16	7180815.5	34.55
78.16	7213000.5	34.70
79.17	5554219.0	26.72
102.17	2399465.5	11.54
103.17	10642300.0	51.20
104.17	9813848.0	47.21
115.18	9484310.0	45.63
116.19	8468503.0	40.74
128.18	2337298.8	11.24
129.19	7438620.0	35.79
130.18	19503790.0	93.83
142.20	3112367.0	14.97
143.18	20785700.0	100.00
144.21	2278423.3	10.96

EI-MS of 10% *N*-15 atom labeled (*E*)-3-(pyridin-3-yl)acrylonitrile (**2p***):



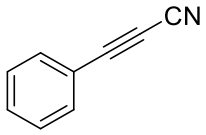


LYJ-25#1618 RT: 9.00
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.21	1842990.5	20.63
51.13	1546015.3	17.30
52.13	847956.6	9.49
62.14	325709.3	3.65
63.13	604149.7	6.76
64.14	280584.9	3.14
65.17	229720.6	2.57
74.13	634481.9	7.10
75.15	1685734.4	18.87
76.15	4651863.5	52.06
77.16	1689886.1	18.91
78.18	439844.6	4.92
79.17	2824698.8	31.61
102.18	703745.3	7.88
103.17	3738488.3	41.84
104.17	3670429.3	41.08
105.16	562022.6	6.29
129.17	3533694.8	39.55
130.18	8934824.0	100.00
131.19	1778113.4	19.90

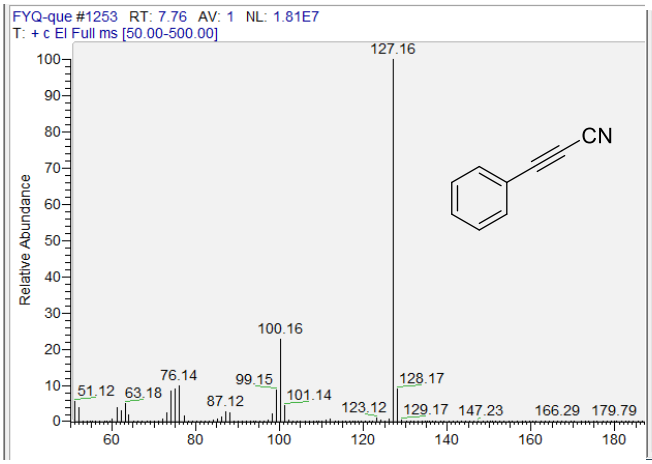
	2p	*N*-15 atom labeled **2p***
[M+1]/[M]	10.96 %	19.9 %

3-phenylpropiolonitrile (**2r***):



0.5 mmol scale, yellow solid 30 mg, 47%.

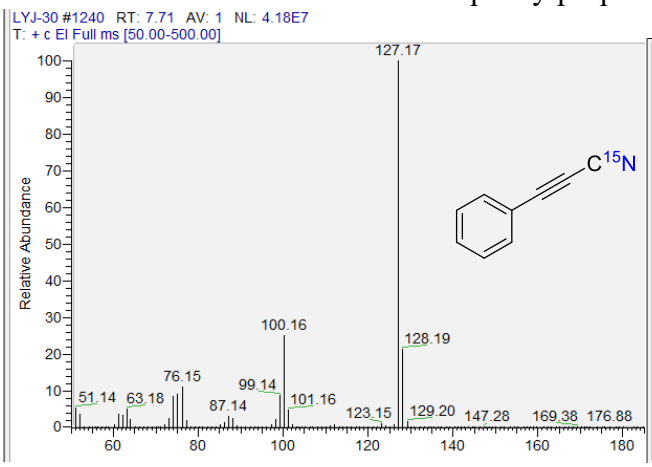
EI-MS of 3-phenylpropiolonitrile (**2r**):



FYQ-que#1253 RT: 7.76
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.22	1569391.5	8.65
51.12	1027511.1	5.67
52.12	717907.4	3.96
61.12	683824.4	3.77
62.13	561768.9	3.10
63.18	889477.0	4.90
63.92	328349.0	1.81
73.13	450898.3	2.49
74.12	1555700.4	8.58
75.12	1649141.4	9.09
76.14	1777400.6	9.80
77.14	266625.5	1.47
87.12	509660.3	2.81
88.13	463970.6	2.56
98.15	374413.8	2.06
99.15	1603525.3	8.84
100.16	4141589.5	22.83
101.14	822735.1	4.54
127.16	18137424.0	100.00
128.17	1636343.0	9.02

EI-MS of 10% *N*-15 atom labeled 3-phenylpropiolonitrile (**2r***):

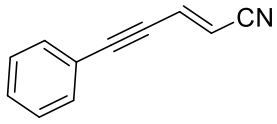


LYJ-30#1232 RT: 7.69
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.21	17491.9	6.56
51.17	11360.2	4.26
57.24	6966.8	2.61
61.10	9486.5	3.56
62.04	9999.2	3.75
63.23	9007.0	3.38
63.96	5544.8	2.08
71.21	5559.0	2.09
73.20	8284.9	3.11
74.19	16552.3	6.21
75.16	22509.8	8.45
76.16	25339.2	9.51
77.15	6061.8	2.27
87.13	7432.4	2.79
88.14	4621.9	1.73
99.14	20393.6	7.65
100.16	56585.9	21.23
101.18	12305.0	4.62
127.16	266485.4	100.00
128.18	51020.7	19.15

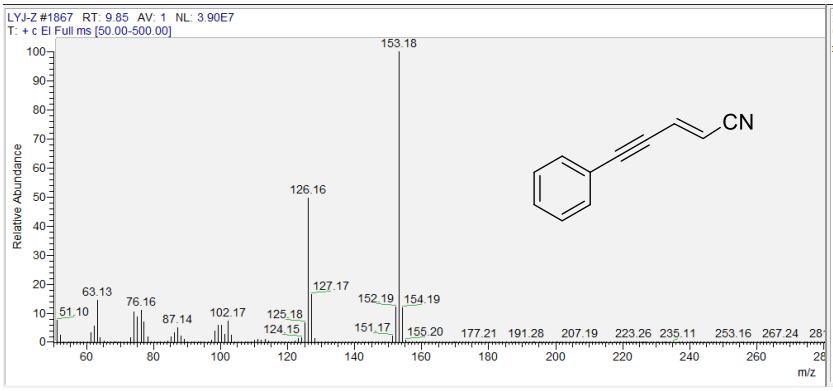
	2r	*N*-15 atom labeled **2r***
[M+1]/[M]	9.02 %	19.15 %

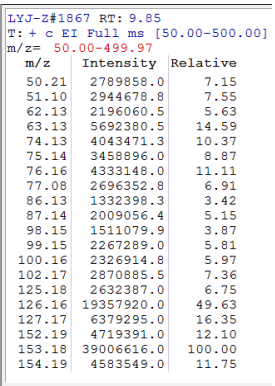
(*E*)-5-phenylpent-2-en-4-ynenitrile (**2s***):



0.5 mmol scale, colorless liquid 31 mg, 40%.

EI-MS of (*E*)-5-phenylpent-2-en-4-ynenitrile (**2s**):

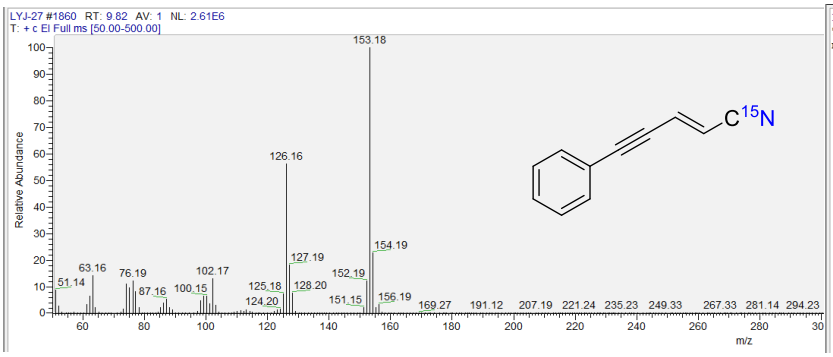


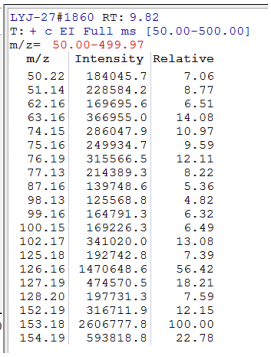


LYJ-Z#1867 RT: 9.85
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.21	2789858.0	7.15
51.10	2944678.8	7.55
62.13	2196060.5	5.63
63.13	5692380.5	14.59
74.13	4043471.3	10.37
75.14	3458896.0	8.87
76.16	4333148.0	11.11
77.08	2696352.8	6.91
86.13	1332398.3	3.42
87.14	2009056.4	5.15
98.15	1511079.9	3.87
99.15	2267289.0	5.81
100.16	2326914.8	5.97
102.17	2870885.5	7.36
125.18	2632387.0	6.75
126.16	19357920.0	49.63
127.17	6379295.0	16.35
152.19	4719391.0	12.10
153.18	39006616.0	100.00
154.19	4583549.0	11.75

EI-MS of *N*-15 atom labeled (*E*)-5-phenylpent-2-en-4-ynenitrile (**2s***):



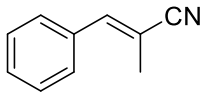


LYJ-27#1860 RT: 9.82
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.22	184045.7	7.06
51.14	228584.2	8.77
62.16	169695.6	6.51
63.16	366955.0	14.08
74.15	286047.9	10.97
75.16	249934.7	9.59
76.19	315566.5	12.11
77.13	214389.3	8.22
87.16	139748.6	5.36
98.13	125568.8	4.82
99.16	164791.3	6.32
100.15	169226.3	6.49
102.17	341020.0	13.08
125.18	192742.8	7.39
126.16	1470648.6	56.42
127.19	474570.5	18.21
128.20	197731.3	7.59
152.19	316711.9	12.15
153.18	2606777.8	100.00
154.19	593818.8	22.78

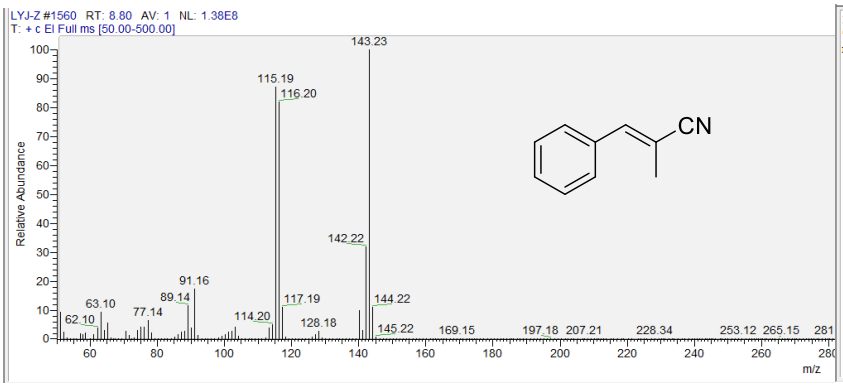
	2s	*N*-15 atom labeled **2s***
[M+1]/[M]	11.75 %	22.78 %

(*E*)-2-methyl-3-phenylacrylonitrile (**2u***):



0.5 mmol scale, light yellow liquid 40 mg, 55 %.

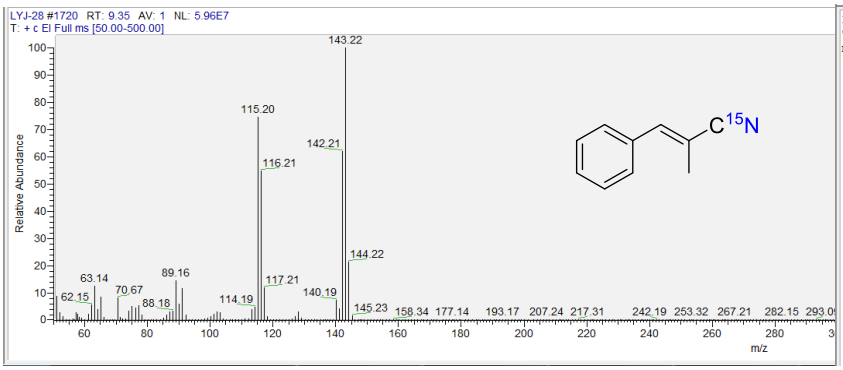
EI-MS of (*E*)-2-methyl-3-phenylacrylonitrile (**2u**):



LYJ-Z#1560 RT: 8.80
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
51.10	12773541.0	9.28
62.10	5364565.5	3.90
63.10	12964172.0	9.42
65.12	7588909.5	5.51
75.12	5535984.5	4.02
76.13	5868199.5	4.26
77.14	8700054.0	6.32
89.14	15841779.0	11.51
90.18	5137777.5	3.73
91.16	23873624.0	17.34
103.17	5680321.0	4.13
113.17	5504251.0	4.00
114.20	6891138.0	5.00
115.19	120265840.0	87.35
116.20	112890600.0	81.99
117.19	15253567.0	11.08
140.17	13655350.0	9.92
142.22	43937468.0	31.91
143.23	137690048.0	100.00
144.22	15331339.0	11.13

EI-MS of 10% *N*-15 atom labeled (*E*)-2-methyl-3-phenylacrylonitrile (**2u***):

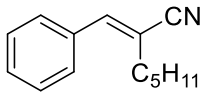


LYJ-28#1720 RT: 9.35
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.23	2890860.3	4.85
51.13	5227264.5	8.77
62.15	3267565.3	5.48
63.14	7395739.0	12.41
65.15	5067453.5	8.51
70.67	4805160.5	8.07
75.15	3020068.0	5.07
76.16	2731222.3	4.58
77.16	3173889.0	5.33
89.16	8544452.0	14.34
90.20	3432521.0	5.76
91.19	6927127.0	11.63
114.19	2789699.5	4.68
115.20	44401200.0	74.53
116.21	32699848.0	54.89
117.21	7163994.0	12.03
140.19	4393261.5	7.37
142.21	36996008.0	62.10
143.22	59575264.0	100.00
144.22	12757036.0	21.41

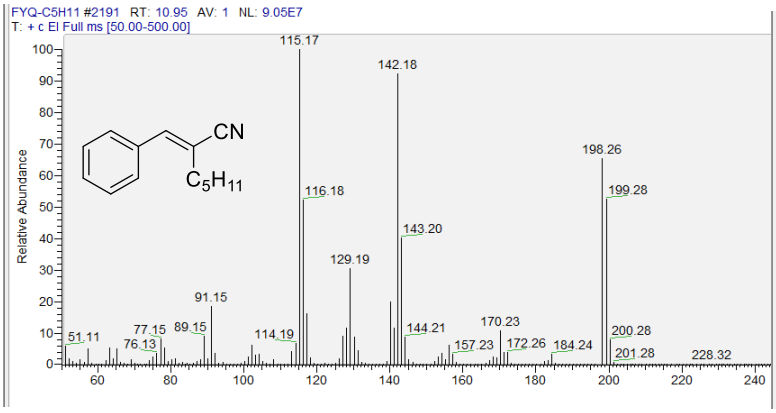
	2u	*N*-15 atom labeled **2u***
[M+1]/[M]	11.13 %	21.41 %

(2*E*)-2-(Phenylmethylene)heptanenitrile (**2v***)



0.5 mmol scale, colorless solid 65 mg, 65%.

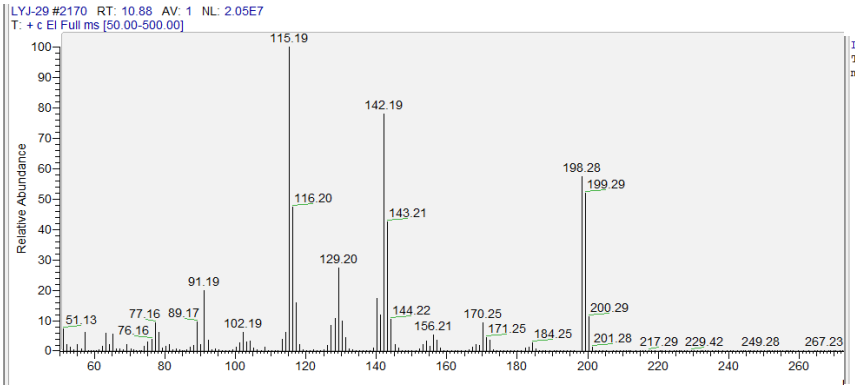
EI-MS of (2*E*)-2-(Phenylmethylene)heptanenitrile (**2v**):



FYQ-C5H11#2191 RT: 10.95
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
77.15	7283930.5	8.05
89.15	8171151.0	9.03
91.15	16810746.0	18.58
114.19	6110678.5	6.75
115.17	90487344.0	100.00
116.18	47205956.0	52.17
117.20	14717449.0	16.26
127.17	8156459.5	9.01
128.19	10379402.0	11.47
129.19	27521930.0	30.42
130.21	7929508.0	8.76
140.17	18076344.0	19.98
141.20	10568534.0	11.68
142.18	83523464.0	92.30
143.20	36557760.0	40.40
144.21	7869942.0	8.70
170.23	9629702.0	10.64
198.26	59298184.0	65.53
199.28	47527664.0	52.52
200.28	7118887.5	7.87

10% *N*-15 atom labeled (2*E*)-2-(Phenylmethylene)heptanenitrile (**2v***):

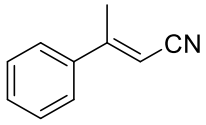


LYJ-29#2169 RT: 10.87
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

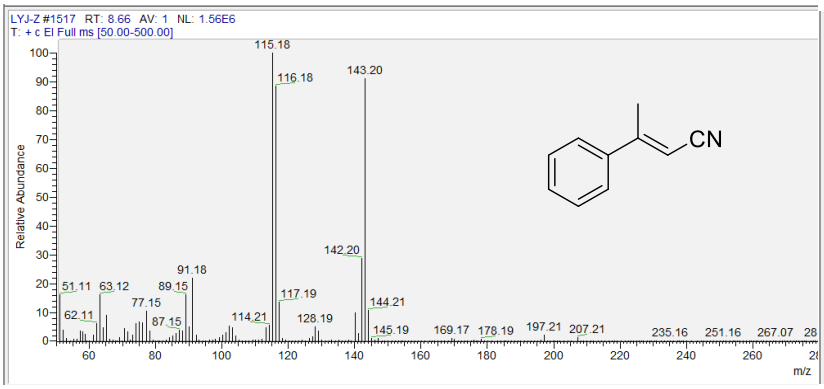
m/z	Intensity	Relative
51.12	740658.4	7.37
77.16	950927.2	9.47
89.18	958348.8	9.54
91.19	2001364.0	19.92
115.19	10044955.0	100.00
116.21	4704674.0	46.84
117.21	1674813.6	16.67
127.20	855534.6	8.52
128.21	1147937.5	11.43
129.20	2798458.3	27.86
130.21	1015567.2	10.11
140.19	1745706.0	17.38
141.20	1190415.1	11.85
142.19	8021220.5	79.85
143.20	4396561.5	43.77
144.22	1052944.9	10.48
170.24	931395.9	9.27
198.27	5818134.5	57.92
199.28	5088091.0	50.65
200.27	1218288.5	12.13

	2v	*N*-15 atom labeled **2v***
[M+1]/[M]	14.98% (7.87/52.52)	23.94% (12.13/50.65)

(*E*)-3-phenylbut-2-enenitrile (**2x***):



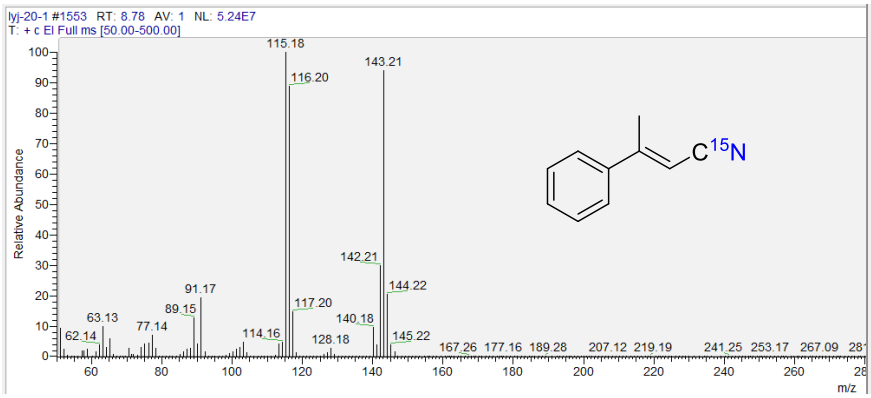
0.5 mmol scale, colorless liquid 41 mg, 55%.
EI-MS of (*E*)-3-phenylbut-2-enenitrile (**2x**):



LYJ-Z#1517 RT: 8.66
T: + c EI Full ms [50.00-500.00]
m/z= 50.00-499.97

m/z	Intensity	Relative
50.21	108552.1	6.97
51.11	254108.0	16.31
62.11	97468.0	6.26
63.12	252239.0	16.19
65.14	138568.6	8.89
74.15	93918.8	6.03
75.14	106150.7	6.81
76.14	100622.9	6.46
77.15	161790.7	10.38
89.15	251492.7	16.14
91.18	341815.0	21.94
102.16	82735.4	5.31
114.21	88826.2	5.70
115.18	1558012.9	100.00
116.18	1379831.5	88.56
117.19	212001.1	13.61
140.18	152436.0	9.78
142.20	446436.1	28.65
143.20	1423573.0	91.37
144.21	167952.3	10.78

EI-MS of 10% *N*-15 atom labeled (*E*)-3-phenylbut-2-enenitrile (**2x***):



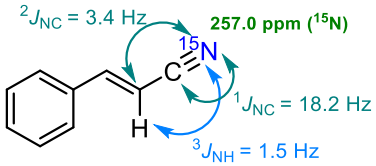
lyj-20-1#1553 RT: 8.78
T: + c EI Full ms [50.00-500.00]
m/z= 129.68-317.91

m/z	Intensity	Relative
130.24	31119.3	0.06
131.17	109784.5	0.22
132.26	11019.9	0.02
133.27	9211.3	0.02
135.14	18012.6	0.04
136.21	7616.9	0.02
137.31	8358.9	0.02
138.20	51209.9	0.10
139.14	101279.7	0.21
140.18	5077806.5	10.29
141.21	1971933.4	4.00
142.21	15681328.0	31.78
143.21	49344492.0	100.00
144.22	10790287.0	21.87
145.22	2062540.3	4.18
146.21	819588.5	1.66
147.20	76289.3	0.15
148.21	9305.7	0.02
177.16	8222.1	0.02
207.12	12771.1	0.03

	2x	*N*-15 atom labeled **2x***
[M+1]/[M]	10.78 %	21.87 %

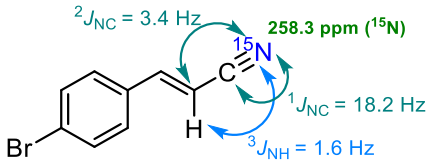
4.3 Spectroscopic data of 99% N-15 atom labeled cinnamonitriles and their spectroscopic characteristics

^{15}N-Cinnamonitrile (**2b-N**): [CAS: 2007073-64-3][18]



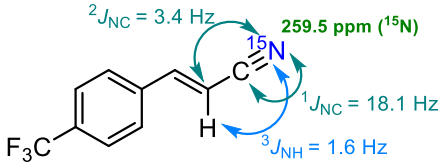
The product was purified by column chromatography (pentene/Et_2O = 10:1). Light yellow liquid 38 mg, 58%. **HRMS** (EI) calcd for [$M^{+\cdot}$, $C_9H_7{}^{15}N$]: 130.0549, found 130.0542. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.48-7.35 (m, 6H), 5.87 (dd, J = 16.8, 1.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 150.6, 133.5, 131.2, 129.1, 127.4, 118.1 (d, J = 18.2 Hz), 96.3 (d, J = 3.4 Hz). **^{15}N NMR** (71 MHz, $CDCl_3$) δ (ppm): 257.0. **IR** (KBr) ν (cm^{-1}): 2189.9.

^{15}N-(*E*)-3-(4-bromophenyl)acrylonitrile (**2e-N**):



The product was purified by column chromatography (pentene/Et_2O = 10:1). 5 mmol, colorless solid 428 mg, 41%. **HRMS** (EI) calcd for [$M^{+\cdot}$, $C_9H_6Br{}^{15}N$]: 207.9654, found 207.9648. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.54 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 16.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 2H), 5.88 (dd, J = 16.4, 1,6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 149.2, 132.4, 128.7, 125.7, 117.8 (d, J = 18.2 Hz), 97.1 (d, J = 3.4 Hz). **^{15}N NMR** (71 MHz, $CDCl_3$) δ (ppm): 258.3. **IR** (KBr) ν (cm^{-1}): 2290.8

^{15}N-(*E*)-3-(3-(trifluoromethyl)phenyl)acrylonitrile (**2m-N**):



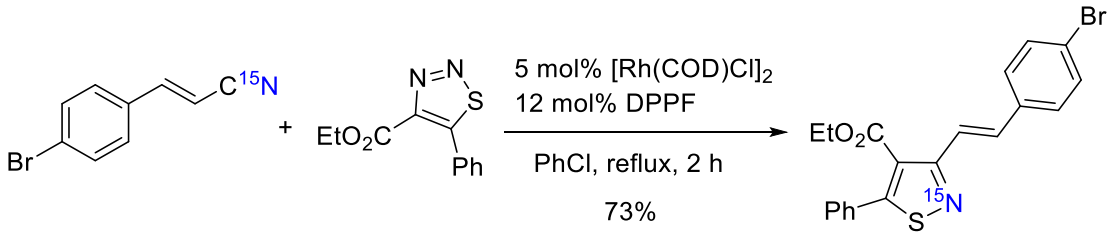
The product was purified by column chromatography (pentene/Et_2O = 10:1). Colorless liquid 45 mg, 45%. **HRMS** (EI) calcd for [$M^{+\cdot}$, $C_{10}H_6F_3{}^{15}N$]: 198.0423, found 198.0416. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.73-7.67 (m, 2H), 7.64 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 8.0 Hz, 1H), 7.43 (d, J = 16.8 Hz, 1H), 5.98 (dd, J = 16.8, 1.6 Hz, 1H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ (ppm): -63.0. **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 148.8, 134.2, 131.7 (q, J = 32.8 Hz), 130.4, 129.8, 127.6 (q, J = 4.1 Hz), 124.0 (q, J = 4.1 Hz), 123.5 (q, J = 273.4 Hz), 117.4 (d, J = 18.1 Hz), 98.6 (d, J = 3.4 Hz).

[18] M. M. Guru, T. Shima and Z. Hou, Conversion of Dinitrogen to Nitriles at a Multinuclear Titanium Framework. *Angew. Chem. Int. Ed.* 2016, **55**, 12316–12320.

^{15}N NMR (71 MHz, $CDCl_3$) δ (ppm): 259.5. **IR** (KBr) ν (cm^{-1}): 2194.3.

Generally, for the 99% *N*-15 atom labeled cinnamonitriles, the chemical shift of ^{15}N in cinnamonitriles is approximately 255-260 ppm (^{15}N NMR). In ^{1}H NMR, the α-H of cyano in ^{15}N-cinnamonitrile (**2b-N**) was observed to be split into a double of doublet (dd). The coupling between the ^{15}N in cyano and the α-H is only 1.5 Hz ($^3J_{N\text{-}H}$), in contrast to the trans olefinic $^3J_{H\text{-}H}$ coupling (16.7 Hz). Moreover, in ^{13}C NMR, the $^1J_{N\text{-}C}$ in the cyano group is only 18.2 Hz, while the $^2J_{N\text{-}C}$ between the ^{15}N and the adjacent α-C is 3.4 Hz. The gyro-magnetic ratio of ^{15}N (-4.36 MHz/T) is approximately one-tenth of ^{1}H (42.67 MHz/T), which results in much lower coupling constants between ^{15}N and ^{1}H or ^{13}C than H-H and C-H coupling constants.

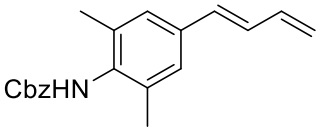
5. Synthesis of isothiazole 5e-*N** (Scheme 5b) [8]



To a pre-dried vial were added ethyl 5-phenyl-1,2,3-thiadiazole-4-carboxylate (47 mg, 0.2 mmol, 1.0 equiv), ^{15}N-(*E*)-3-(4-bromophenyl)acrylonitrile (**2e-N**) (84 mg, 0.4 mmol, 2.0 equiv), $[Rh(COD)Cl]_2$ (5 mg, 0.01 mmol, 5 mol%), DPEphos (13 mg, 0.024 mmol, 12 mol%), and 1.0 mL of chlorobenzene as solvent under N_2 atmosphere. The solution was stirred reflux in a heating module for 2 hours. The vial was cooled down to room temperature when the reaction was finished. The suspension was directly purified through silica gel column chromatography with a mixture of petroleum ether and ethyl acetate (200:1, v/v) as the eluent to afford product **5e-N**, 61 mg, 73%. **HRMS** (ESI) calcd for $C_{20}H_{16}BrS^{15}NO_2^+$, $[M+H]^+$: 415.0129, found: 415.0126. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.70–7.64 (m, 2H), 7.53–7.40 (m, 9H), 4.21 (q, J = 7.2 Hz, 2H), 1.01 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 172.2, 165.2, 163.4, 135.5, 134.3 (d, J = 3.3 Hz), 131.9, 130.4, 129.7, 128.8, 128.4, 125.5 (d, J = 2.5 Hz), 122.6, 121.3 (d, J = 6.2 Hz), 61.2, 13.8. **^{15}N NMR** (71 MHz, $CDCl_3$) δ (ppm): 274.8.

6. Synthesis of 99% *N*-15 atom labeled Rilpivirine (Scheme 5c)

Conjugated dienes **6** were synthesized according to literatures[19].
benzyl (E)-(4-(buta-1,3-dien-1-yl)-2,6-dimethylphenyl)carbamate (**6**):

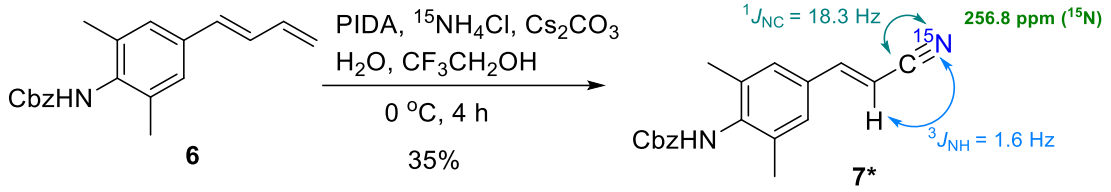


6

[19] A. Bhowmik and R. A. Fernandes, Iron(III)/O_2-Mediated Regioselective Oxidative Cleavage of 1-Arylbutadienes to Cinnamaldehydes *Org. Lett*. 2019, **21**, 9203–9207.

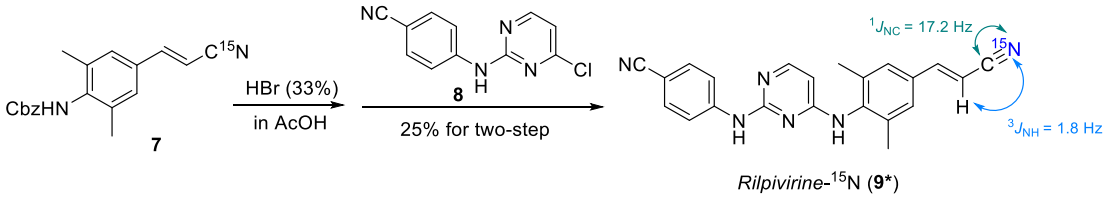
The product was purified by column chromatography (pentene/Et_2O = 10:1). Colorless solid. **HRMS** (ESI) calcd for $C_{20}H_{22}NO_2$, $[M+H]^+$: 308.1646, found 308.1653. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.45–7.15 (m, 5H, Ph), 7.01 (s, 2H), 6.73 (dd, J = 15.6, 10.4 Hz, 1H), 6.54-6.41 (m, 2H), 6.15 (br s, 1H, NH), 5.31 (d, J = 16.8 Hz, 1H), 5.22–5.10 (m, 3H), 2.21 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 154.3, 137.2, 136.4, 136.0, 135.92, 135.88, 133.0, 132.3, 129.8, 128.6, 128.2, 126.3, 117.6, 67.1, 18.4.

Benzyl (*E*)-(4-(2-(cyano-^{15}N)vinyl)-2,6-dimethylphenyl)carbamate (**7***):



To a pressure resistant reaction tube equipped with a magnetic stirring bar was added Cbz-protected diene **6** (215 mg, 0.7 mmol, 1.0 equiv), $^{15}NH_4Cl$ (76 mg, 1.4 mmol, 2.0 equiv), Cs_2CO_3 (456 mg, 1.4 mmol, 2.0 equiv), H_2O (25 mg, 1.4 mmol, 2.0equiv) and 9 mL CF_3CH_2OH. The tube was cooled to 0 °C and then PIDA (451 mg, 1.4 mmol, 2.0 equiv) was added. After sealing with a rubber septum, the mixture was stirred for 4 h at 0 °C. The reaction mixture was quenched with water (15 mL), and then extracted with CH_2Cl_2 (8 mL×2). The organic layers were combined, dried over Na_2SO_4 and filtered. After removing the solvent in vacuo, the residue was purified by flash column chromatography (PE/EtOAc = 20:1) on silica gel to obtain the pure product **7***, colorless solid 85 mg, 35%. R_f = 0.45 (PE:EtOAc = 4:1). **HRMS** (ESI) calcd for $C_{19}H_{18}N^{15}NO_2^+$, $[M+H]^+$: 308.1412, found 308.1413. **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm): 7.45–7.30 (m, 5H), 7.28 (d, J = 16.6 Hz, 1H), 7.14 (s, 2H), 6.26 (s, 1H), 5.79 (dd, J = 16.6, 1.6 Hz, 1H), 5.18 (s, 2H), 2.25 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ (ppm): 154.2, 150.0, 136.53, 136.48, 136.1, 132.1, 128.6, 128.4, 128.2, 127.3, 118.2 (d, J = 18.3 Hz), 96.2, 67.4, 18.5. **^{15}N NMR** (71 MHz, $CDCl_3$) δ (ppm): 256.8.

Rilpivirine-15N (**9***):



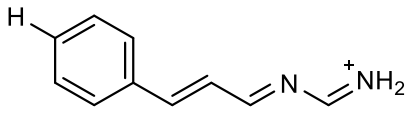
A solution of the Cbz-protected amine **7*** (71 mg, 0.23mmol) in 33 % hydrobromic acid in acetic acid (0.52 mL) and glacial acetic acid (0.31 mL) was stirred at rt for 1.5 h under an atmosphere of nitrogen.[20] The reaction system was filtered and the residue was washed with ethyl acetate to obtain the 4-amino-2,6-dimethyl cinnamonitrile as gray solid 30 mg, 52%. The solid was dissolved in 1 mL of CH_3CN in a 10 mL microwave vial and then a solution of **8** (24 mg, 0.10 mmol) in 1 mL CH_3CN was added

[20] A. Bertram, and G. Pattenden, Dendroamide A, Nostocyclamide and Related Cyclopeptides from Cyanobacteria. Total Synthesis, together with Organised and Metal-templated Assembly from Oxazole and Thiazole-based Amino Acids *Heterocycles*, 2002, **58**, 521–561.

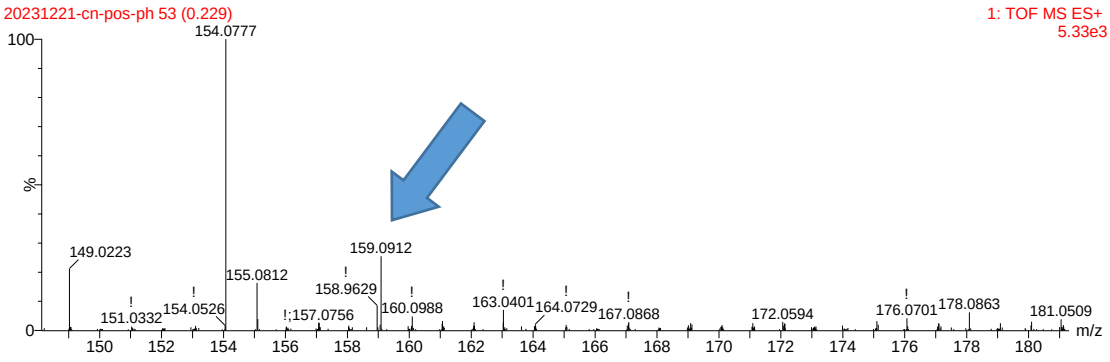
into. The reaction was heated at 140 °C for 2 h under microwave irradiation. After cooling to r.t., 10% K_2CO_3 solution was added dropwise to the vial to adjust the pH to 8-9 and filtered.[21] The filtrate was washed with CH_3CN to obtain the target molecule N-15 atom labeled rilpivirine **9*** as a white solid, 21 mg, yield 25% (two-step). Mp: 175–177 °C. **HRMS** (ESI) calcd for $C_{22}H_{19}N_5{}^{15}N^+$, $[M+H]^+$: 368.1636; found 368.1639. **^{1}H NMR** (600 MHz, DMSO-d_6) δ (ppm): 9.60 (br s, 1H), 9.02 (br s, 1H), 8.02 (d, J = 6 Hz, 1H), 7.80–7.60 (m, 1H), 7.64 (d, J = 16.8 Hz, 1H), 7.49 (s, 2H), 7.42 (br s, 2H), 6.47 (dd, J = 16.8, 1.8 Hz, 1H), 6.40 (br s, 1H), 2.17 (s, 6H). **^{13}C NMR** (151 MHz, DMSO-d_6) δ (ppm): 162.2, 159.6, 150.8, 146.0, 137.0, 133.6, 133.0, 127.9, 120.2, 119.5 (d, J = 17.2 Hz), 119.2, 118.5, 118.3, 101.8, 99.0, 96.6, 18.8. **^{15}N NMR** (61 MHz, DMSO-d_6) δ (ppm): 258.9.

7. In-situ HRMS of the reaction with 1b, 1e and 1h at 1 hour

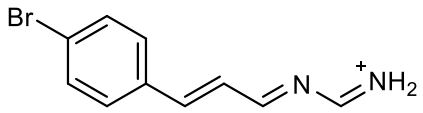
The HRMS (ESI-positive) was detected directly when the reaction of **1b**, **1e** and **1h** were performed at 1 hour.



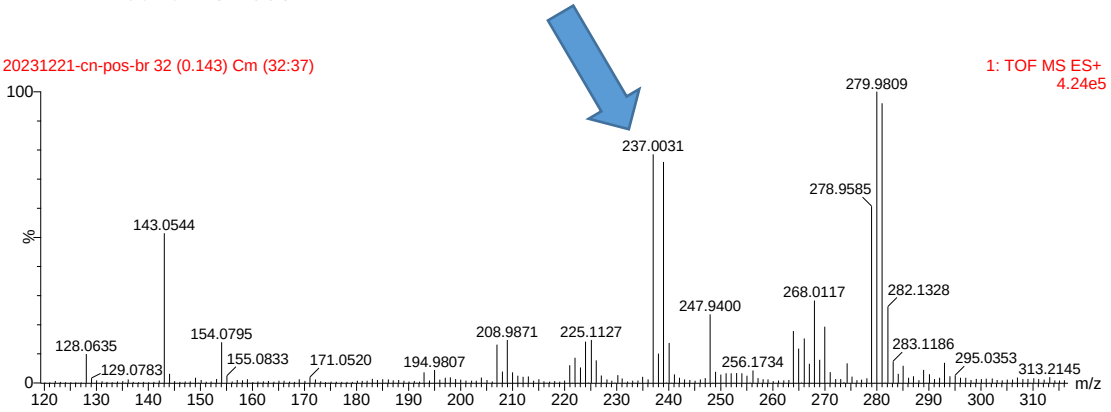
Chemical Formula: $C_{10}H_{11}N_2^+$
Exact Mass: 159.0917
found: 159.0912

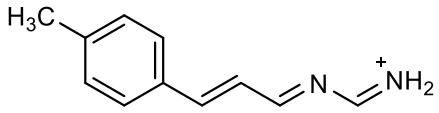


[21] T. Zhang, J. P. Yang, Z. X. Zhou, Z. P. Fu, S. Cherukupalli, D. W. Kang, P. Zhan and X. Y. Liu, The development of an effective synthetic route of rilpivirine. *BMC Chemistry*, **2021**, *15*, 22–30.

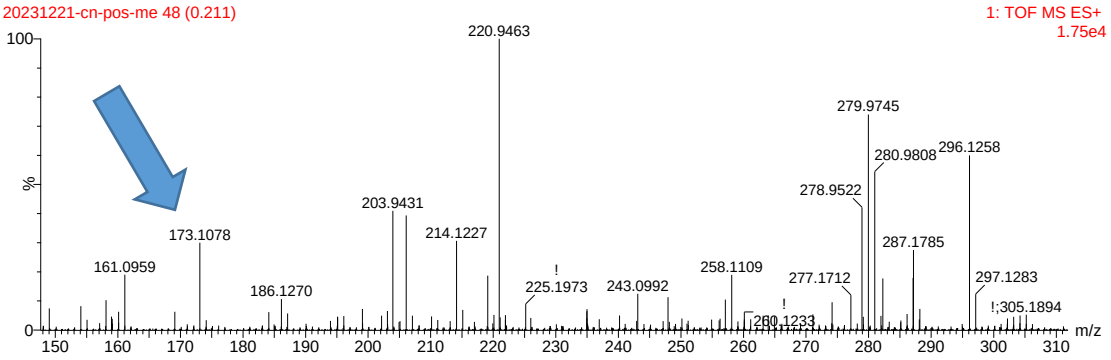


Chemical Formula: $C_{10}H_{10}BrN_2^+$
Exact Mass: 237.0022
found: 237.0031





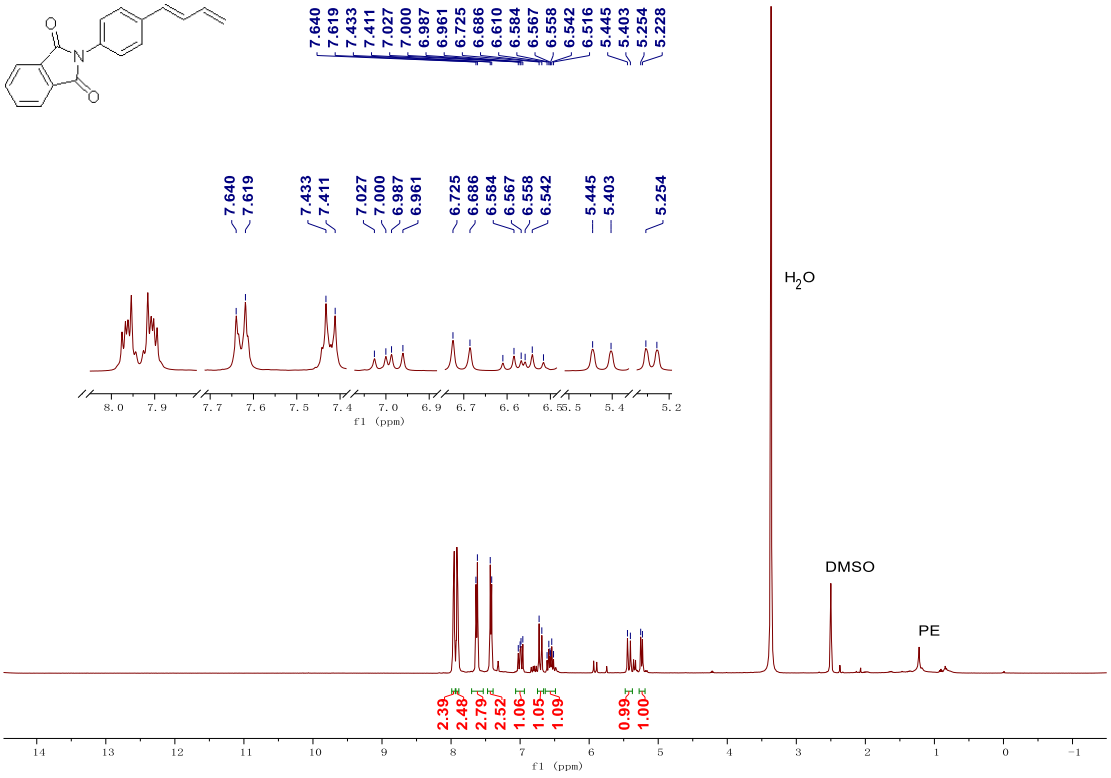
Chemical Formula: $C_{11}H_{13}N_2^+$
Exact Mass: 173.1073
Found: 173.1078



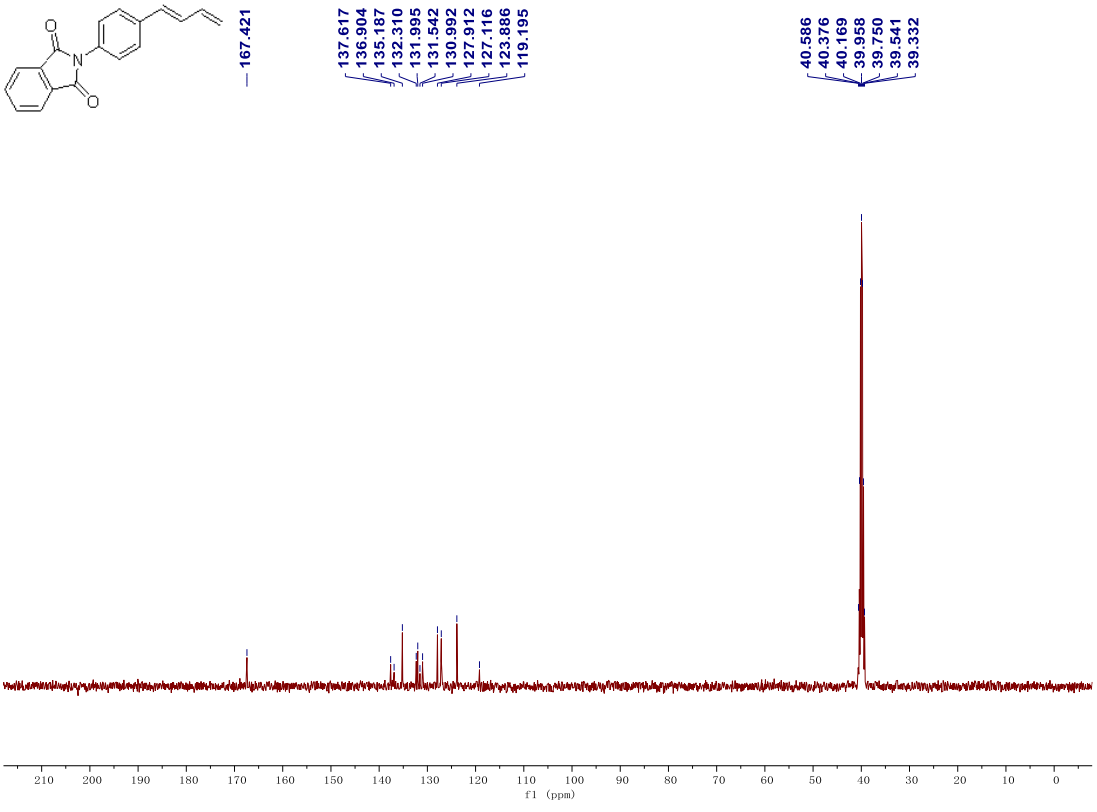
8. Spectra Copies of Unknown dienes and all α,β-unsaturated nitrile 2

(*E*)-2-(4-(buta-1,3-dien-1-yl)phenyl)isoindoline-1,3-dione (**1j**)

^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm)

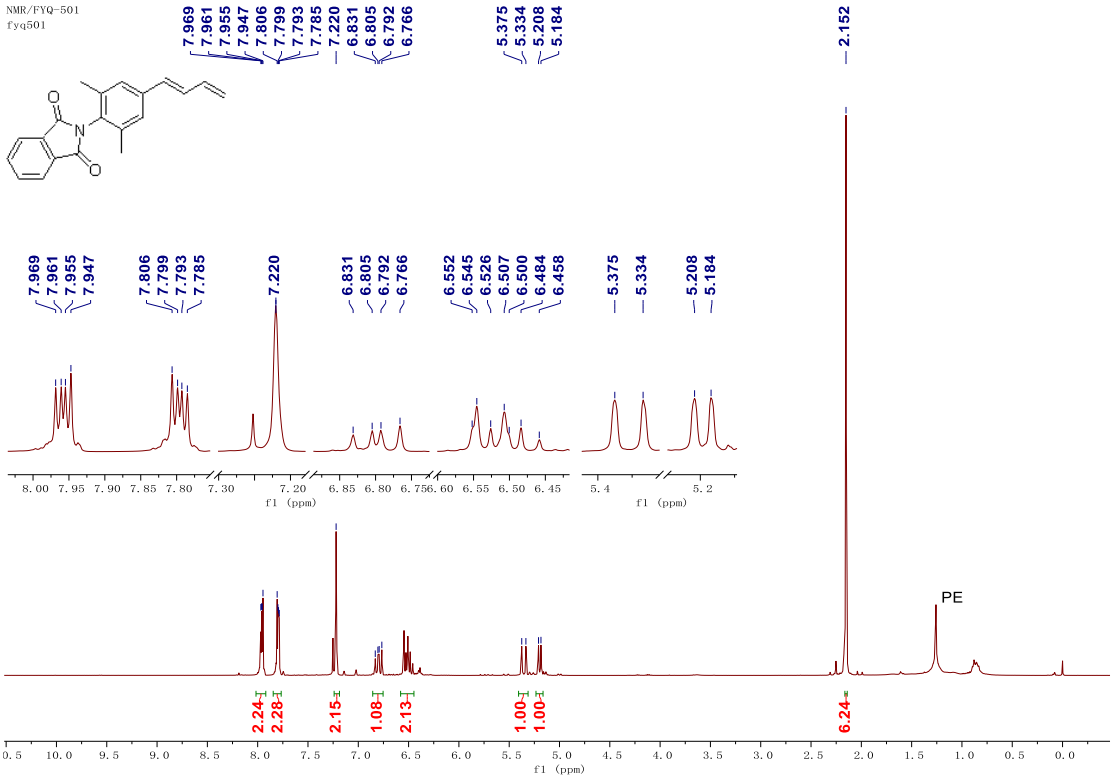


^{13}C NMR (101 MHz, DMSO-d_6)

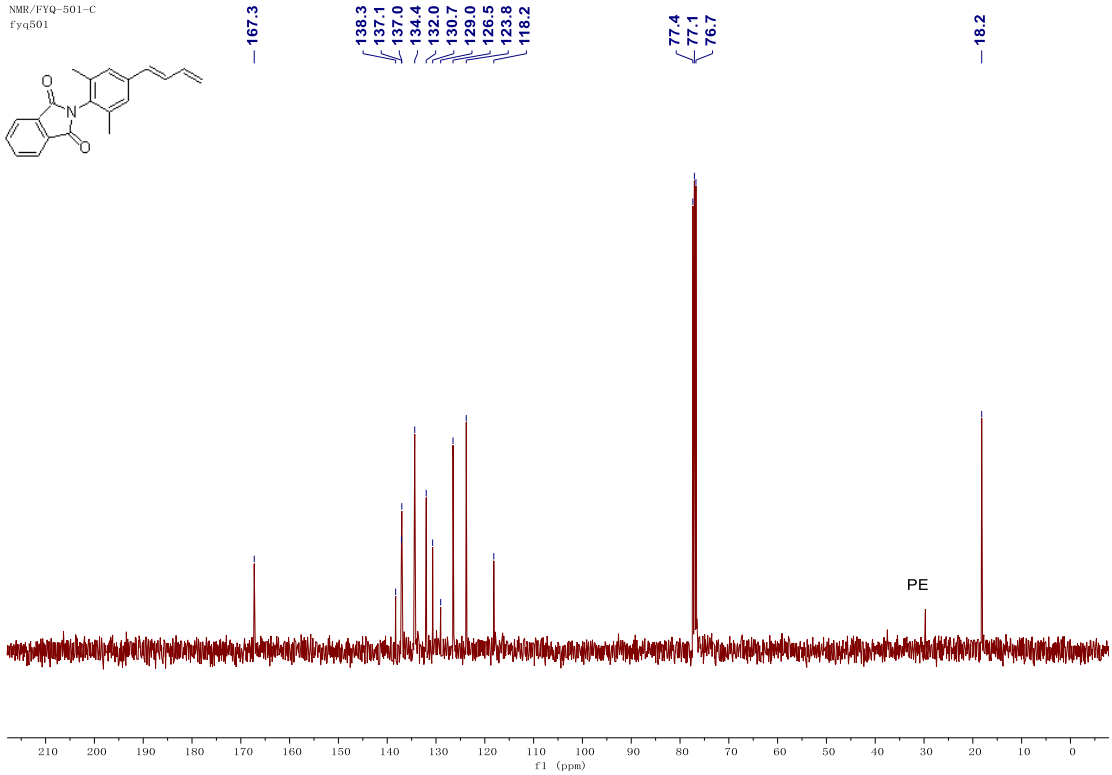


(*E*)-2-(4-(buta-1,3-dien-1-yl)-2,6-dimethylphenyl)isoindoline-1,3-dione (**1k**)

^{1}H NMR (400 MHz, $CDCl_3$)

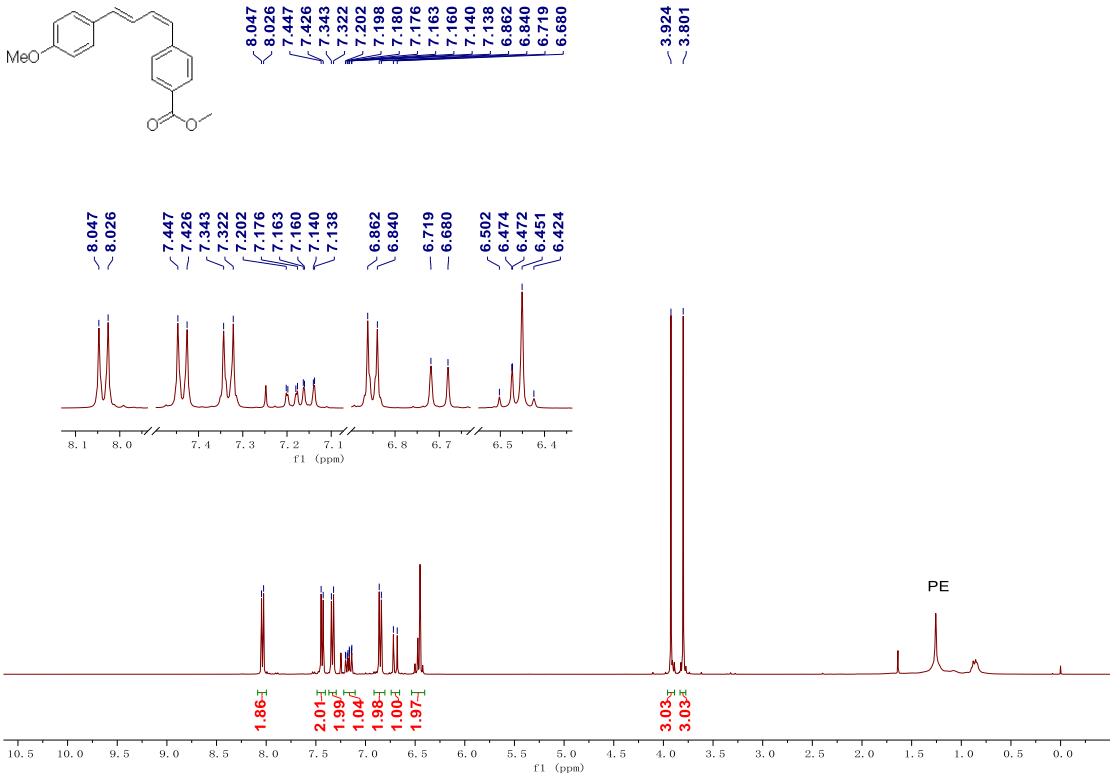


^{13}C NMR (101 MHz, $CDCl_3$)

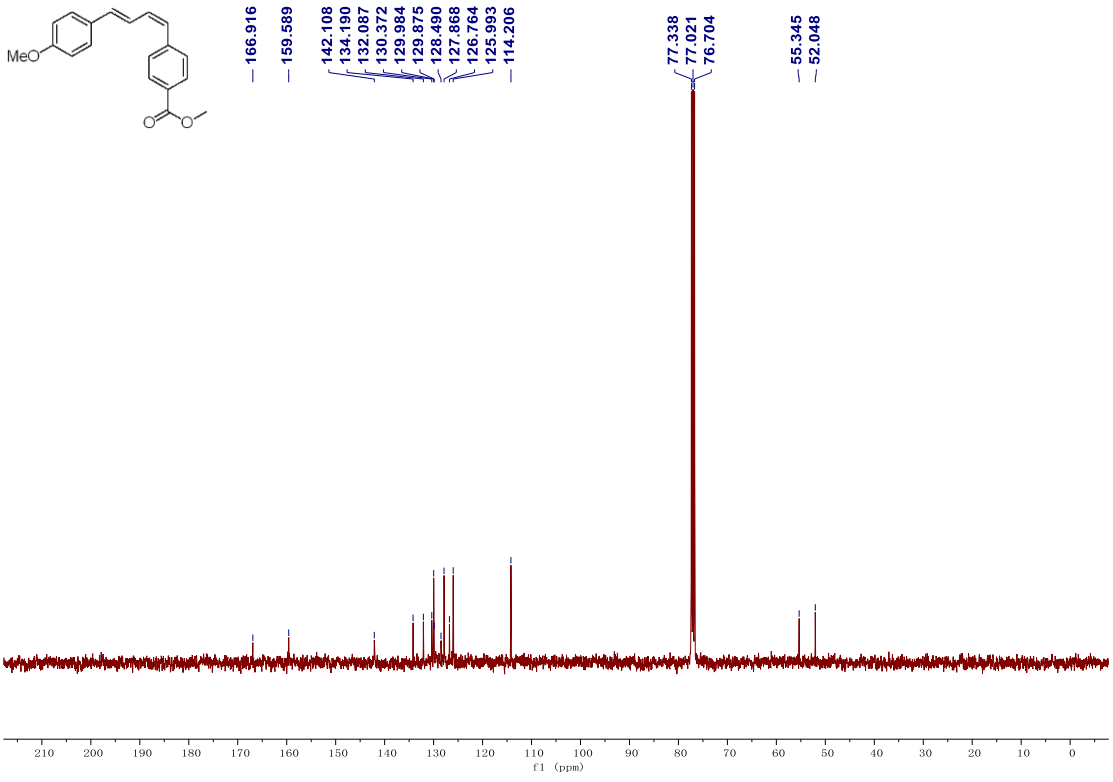


Methyl 4-((1*Z*,3*E*)-4-(4-methoxyphenyl)buta-1,3-dien-1-yl)benzoate (**1af**):

^{1}H NMR (400 MHz, $CDCl_3$)

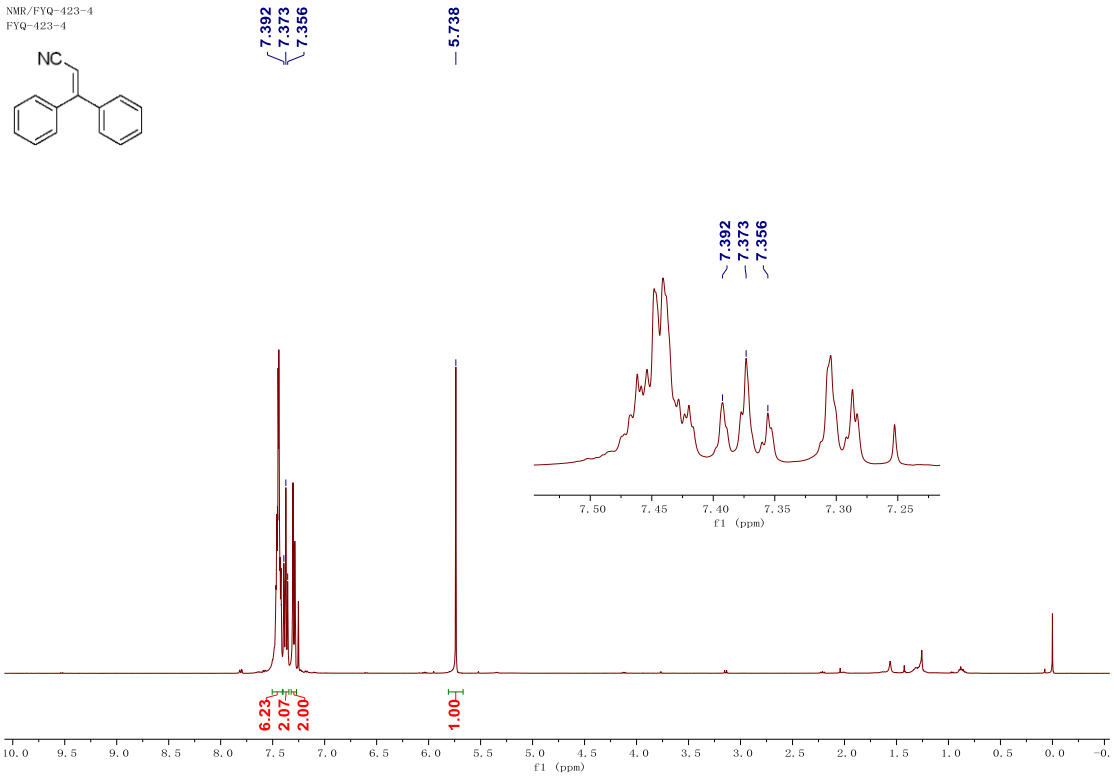


^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm)

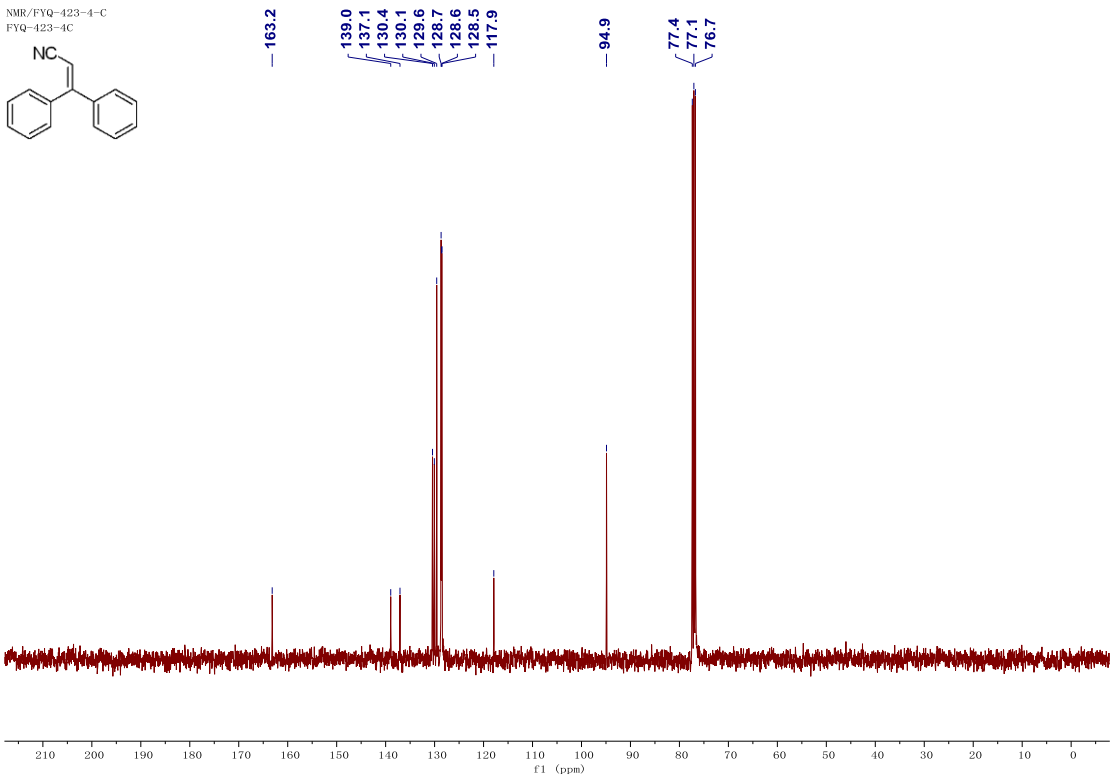


3,3-diphenylacrylonitrile (**2a**) [CAS: 3531-24-6]

^{1}H NMR (400 MHz, $CDCl_3$)

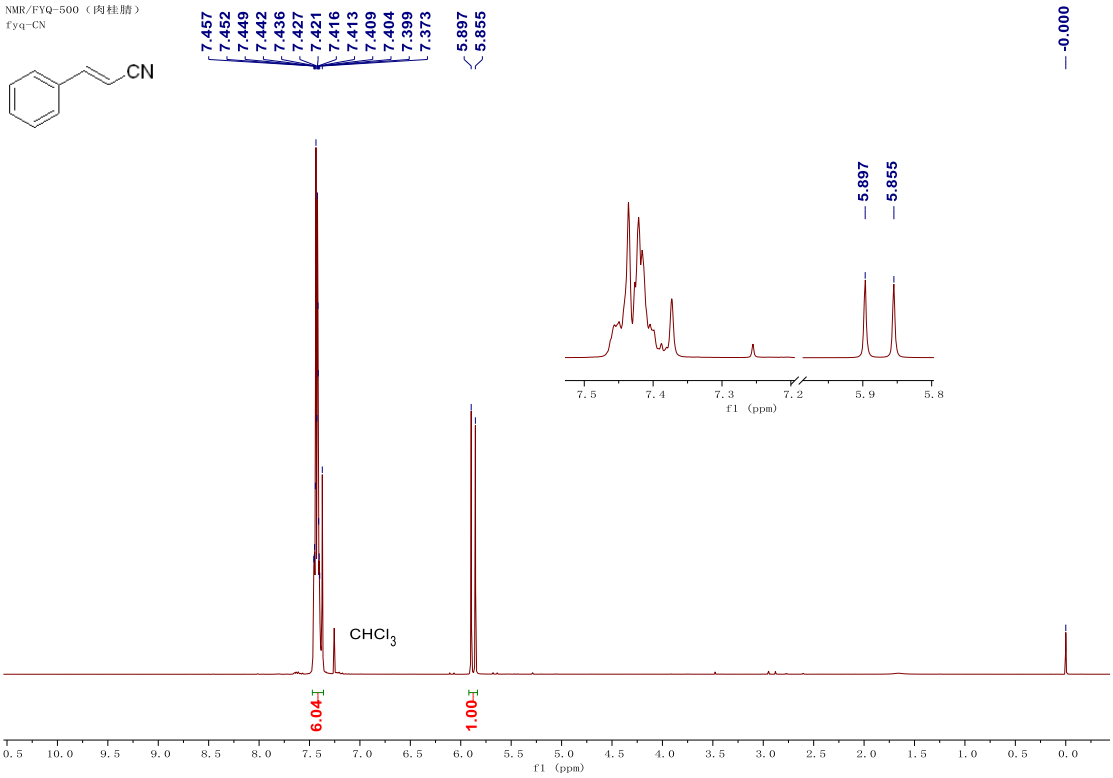


^{13}C NMR (101 MHz, $CDCl_3$)

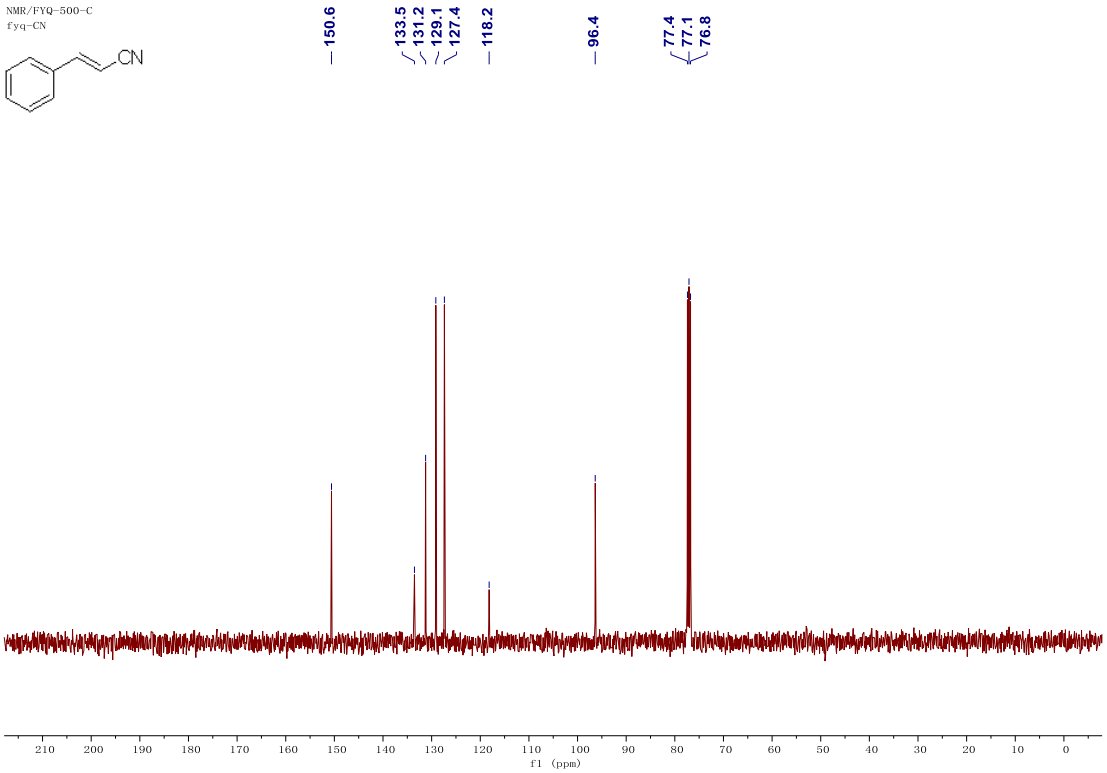


Cinnamonitrile (**2b**) [CAS: 1885-38-7]

^{1}H NMR (400 MHz, $CDCl_3$)

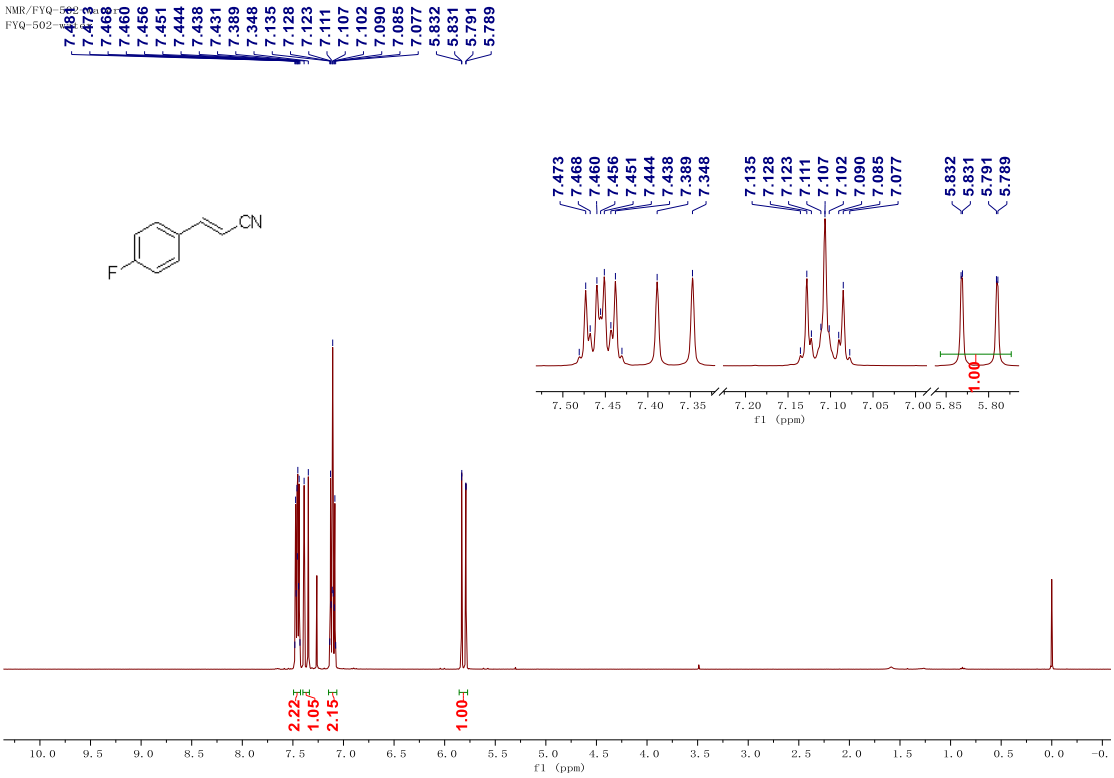


^{13}C NMR (101 MHz, $CDCl_3$)

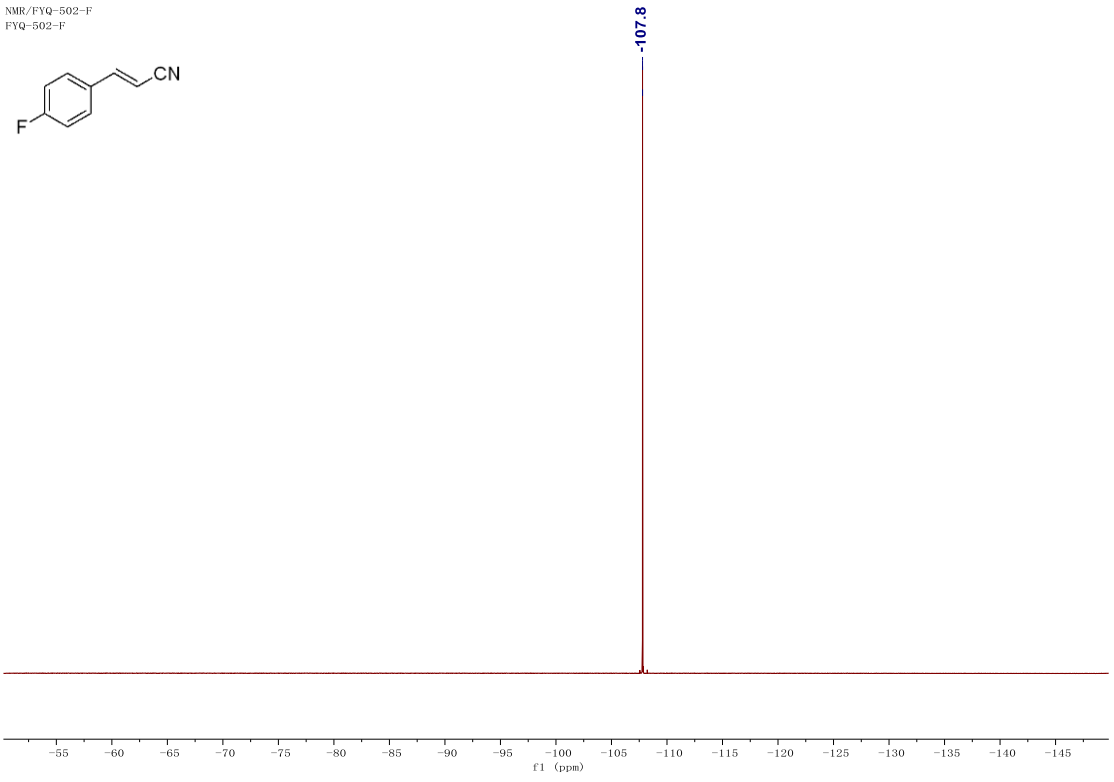


4-Fluorocinnamonitrile (**2c**)

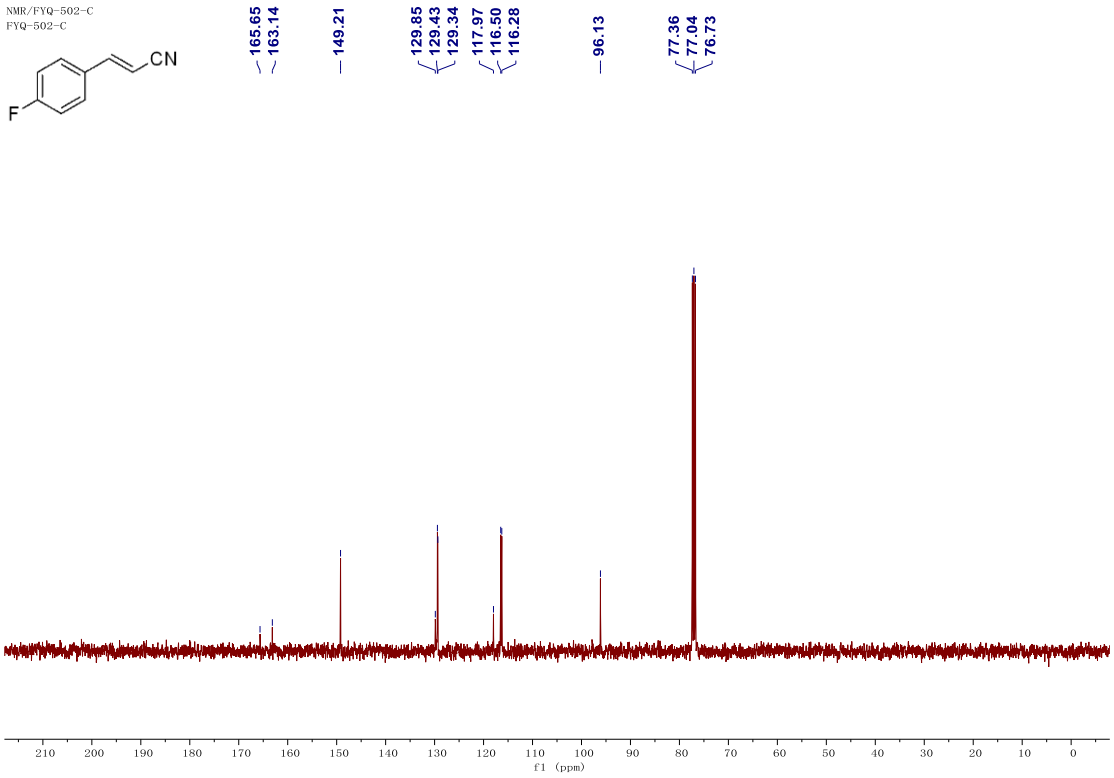
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

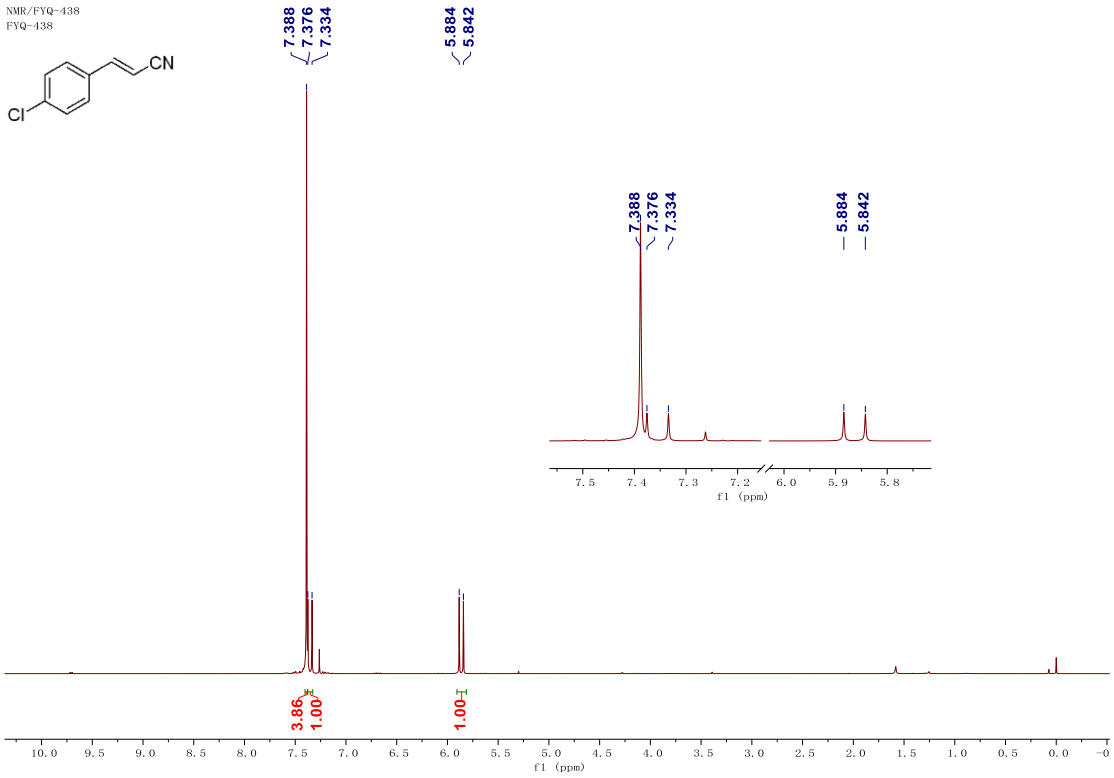


^{13}C NMR (101 MHz, $CDCl_3$)

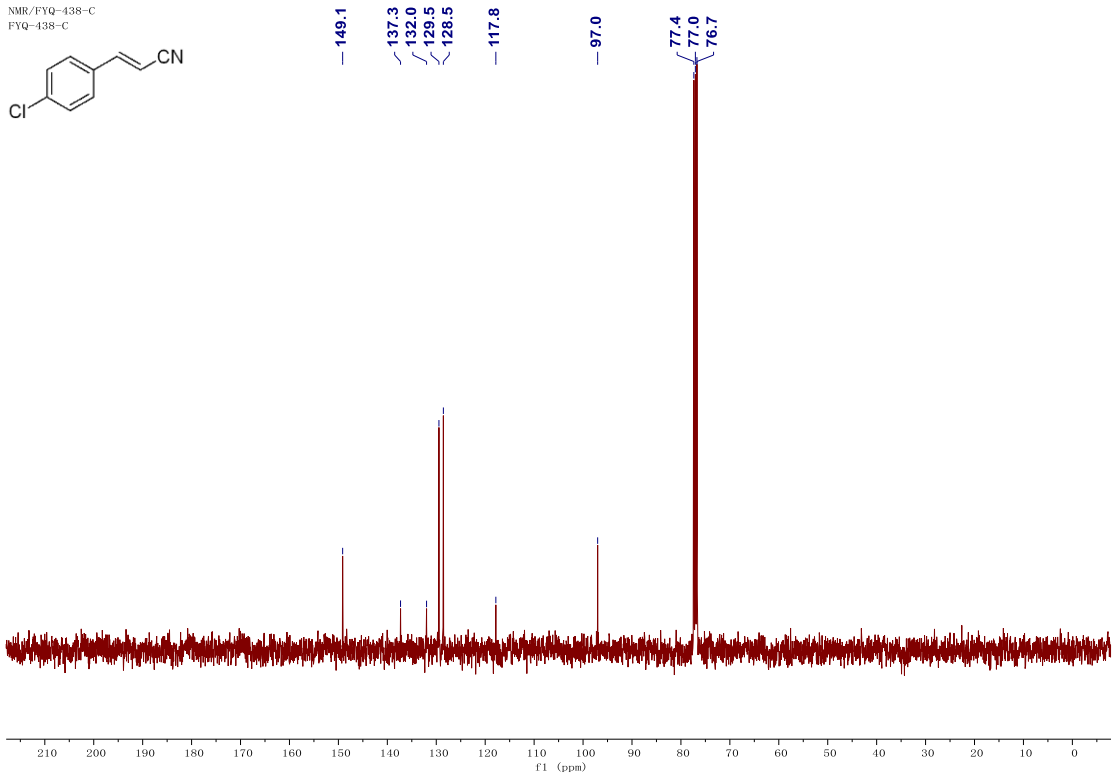


(*E*)-3-(4-chlorophenyl)acrylonitrile (**2d**)

^{1}H NMR (400 MHz, $CDCl_3$)

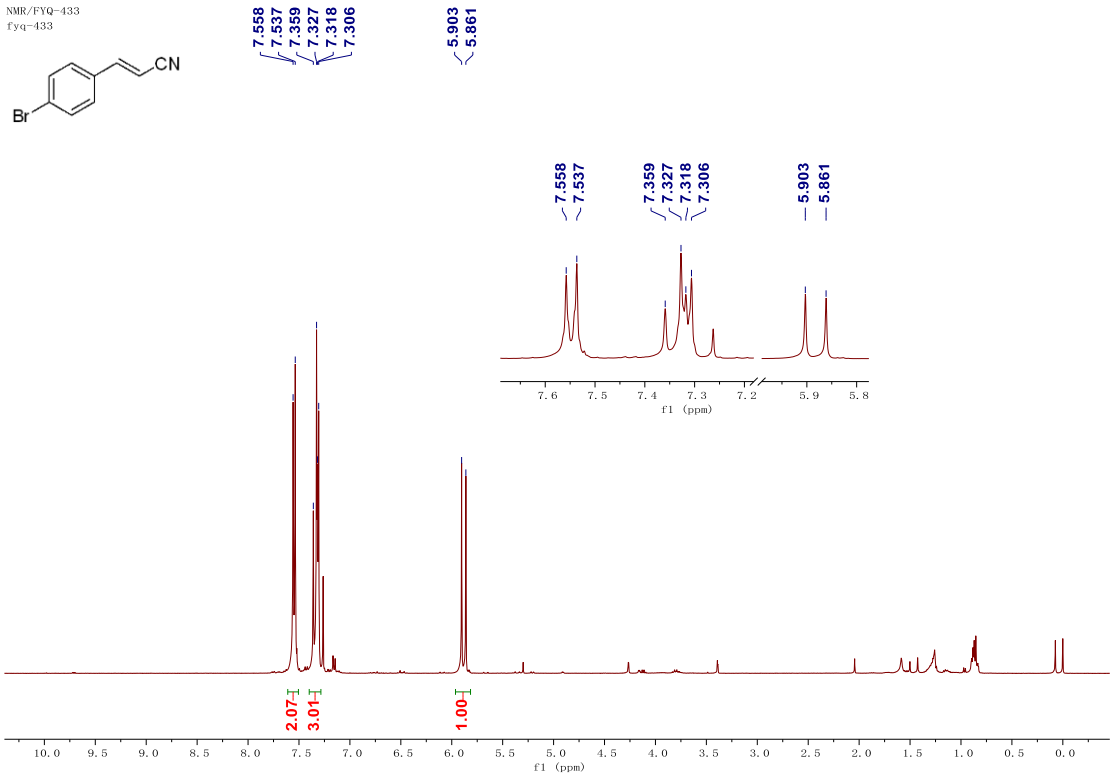


^{13}C NMR (101 MHz, $CDCl_3$)

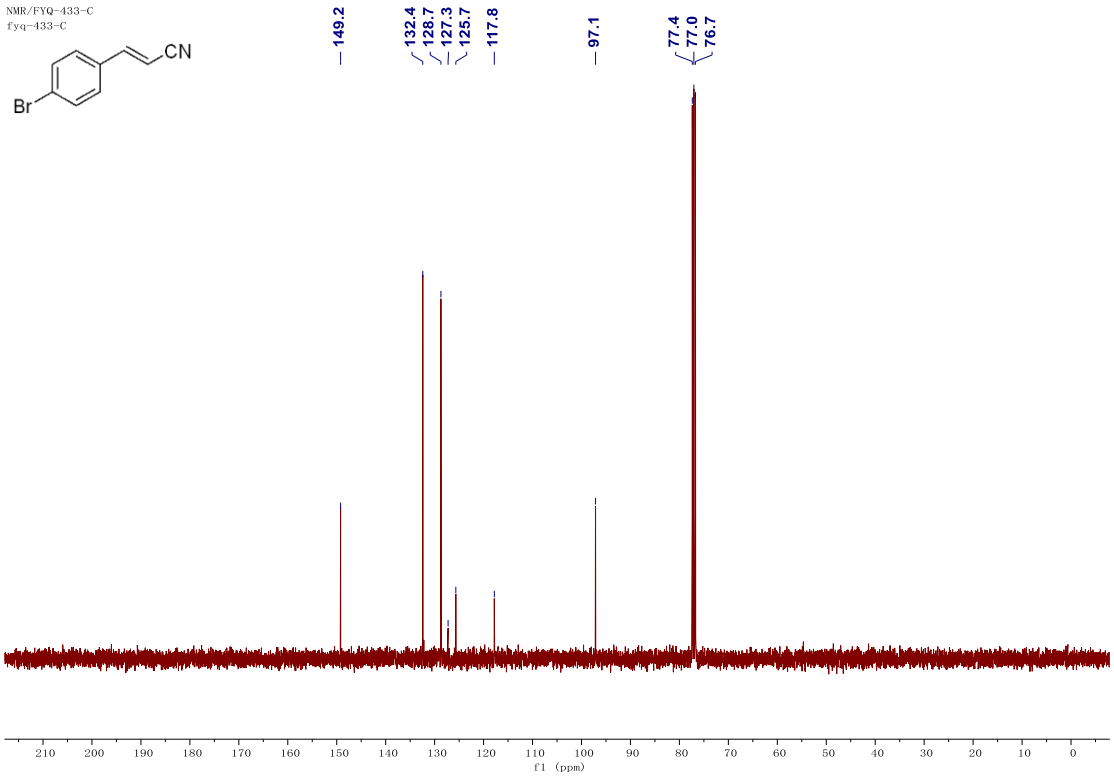


(*E*)-3-(4-bromophenyl)acrylonitrile (**2e**)

^{1}H NMR (400 MHz, $CDCl_3$)

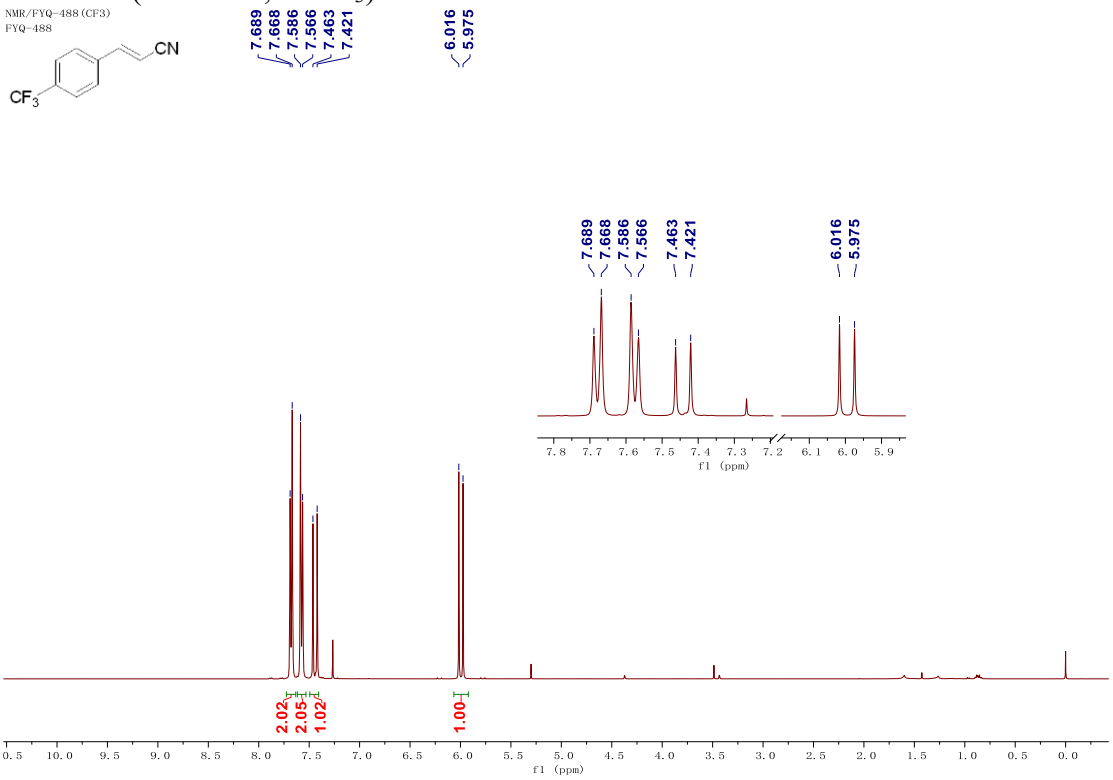


^{13}C NMR (101 MHz, $CDCl_3$)

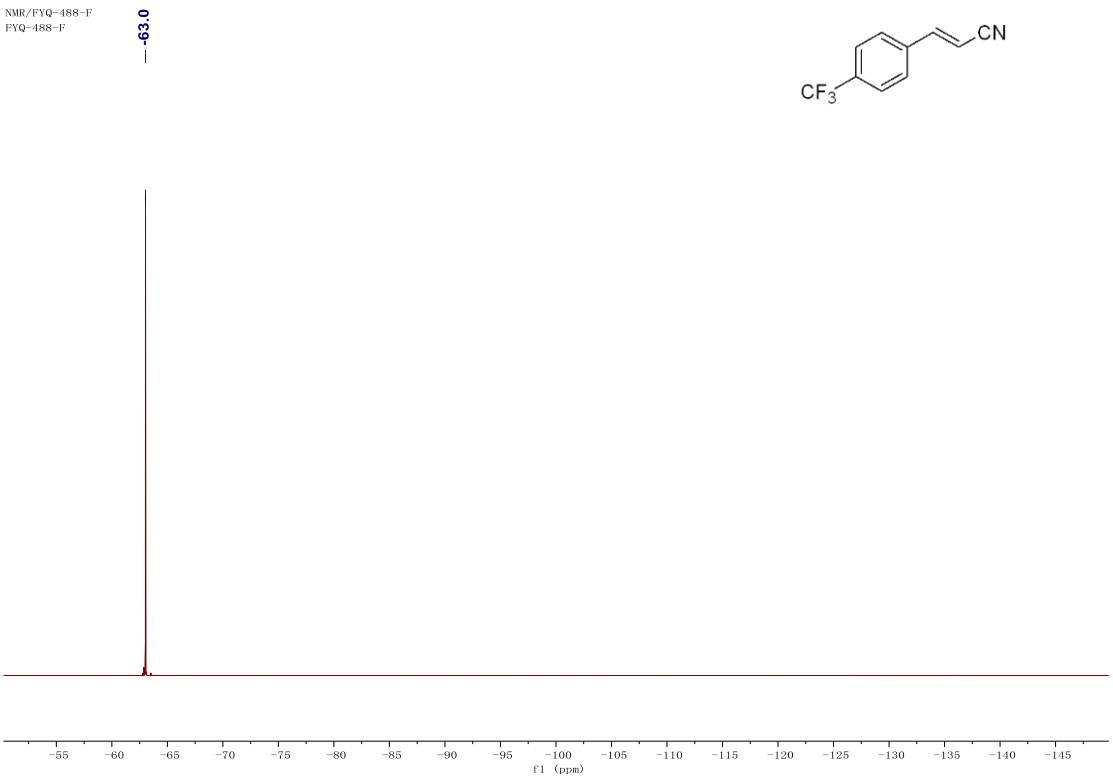


(*E*)-3-(4-(trifluoromethyl)phenyl)acrylonitrile (**2f**):

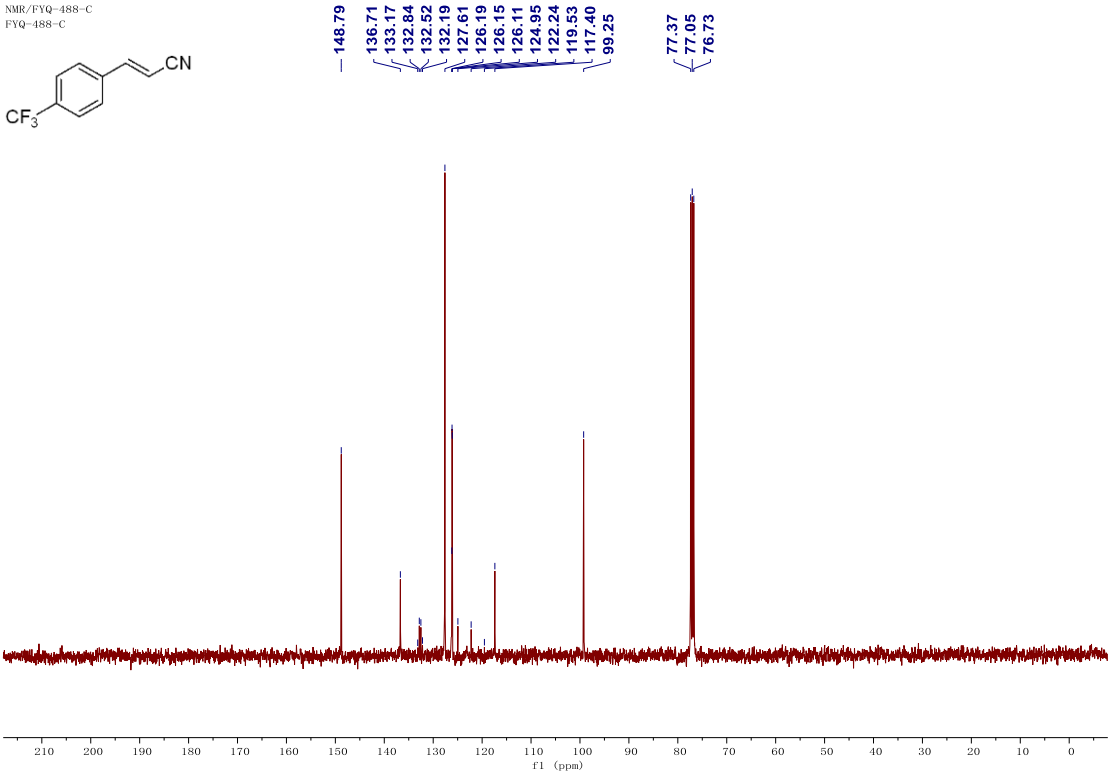
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

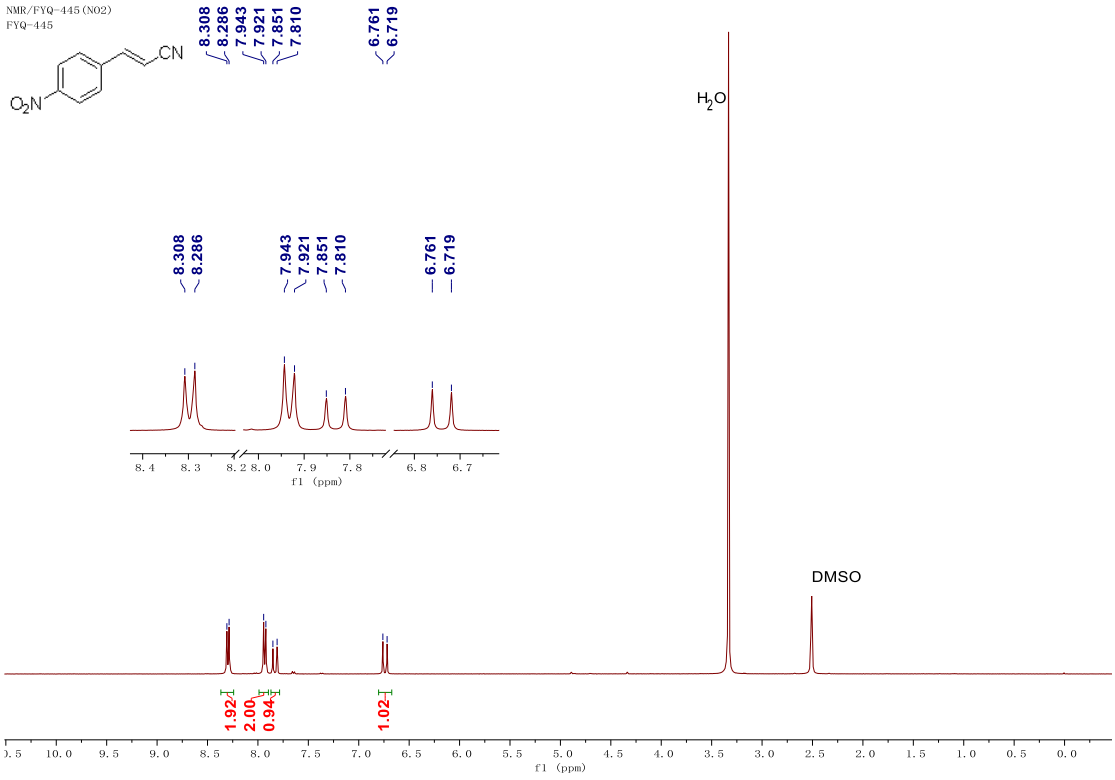


^{13}C NMR (101 MHz, $CDCl_3$)

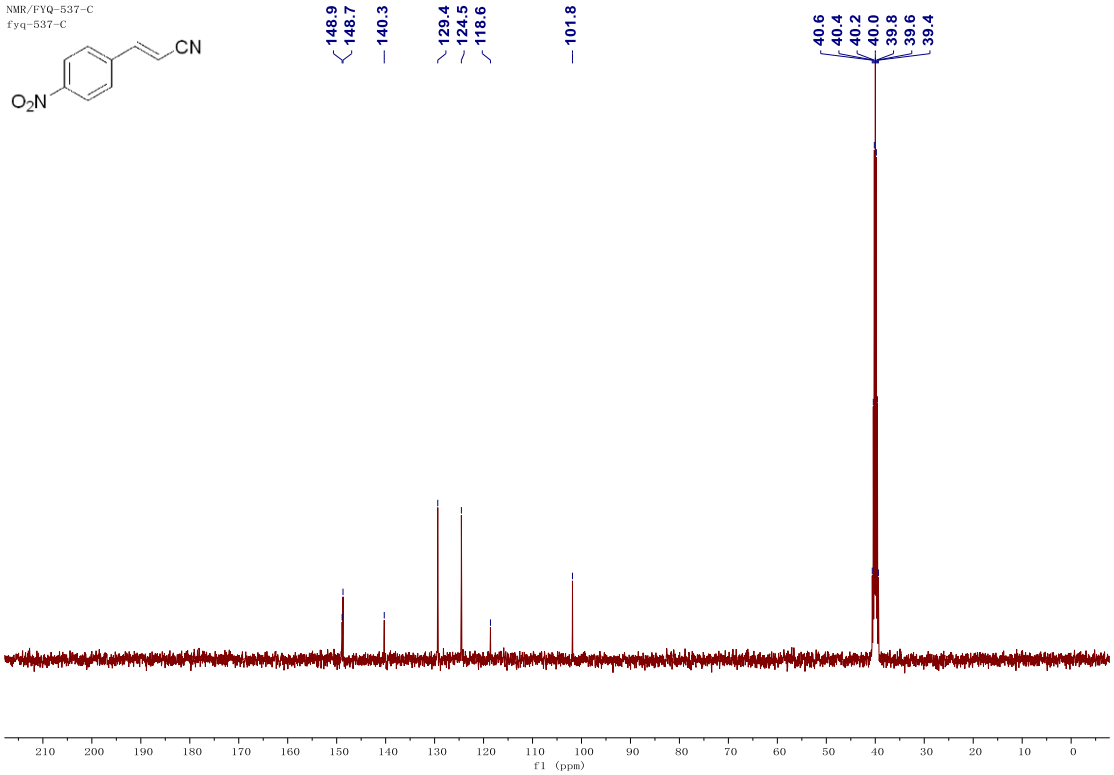


(*E*)-3-(4-nitrophenyl)acrylonitrile (**2g**):

^{1}H NMR (400 MHz, DMSO-d_6)

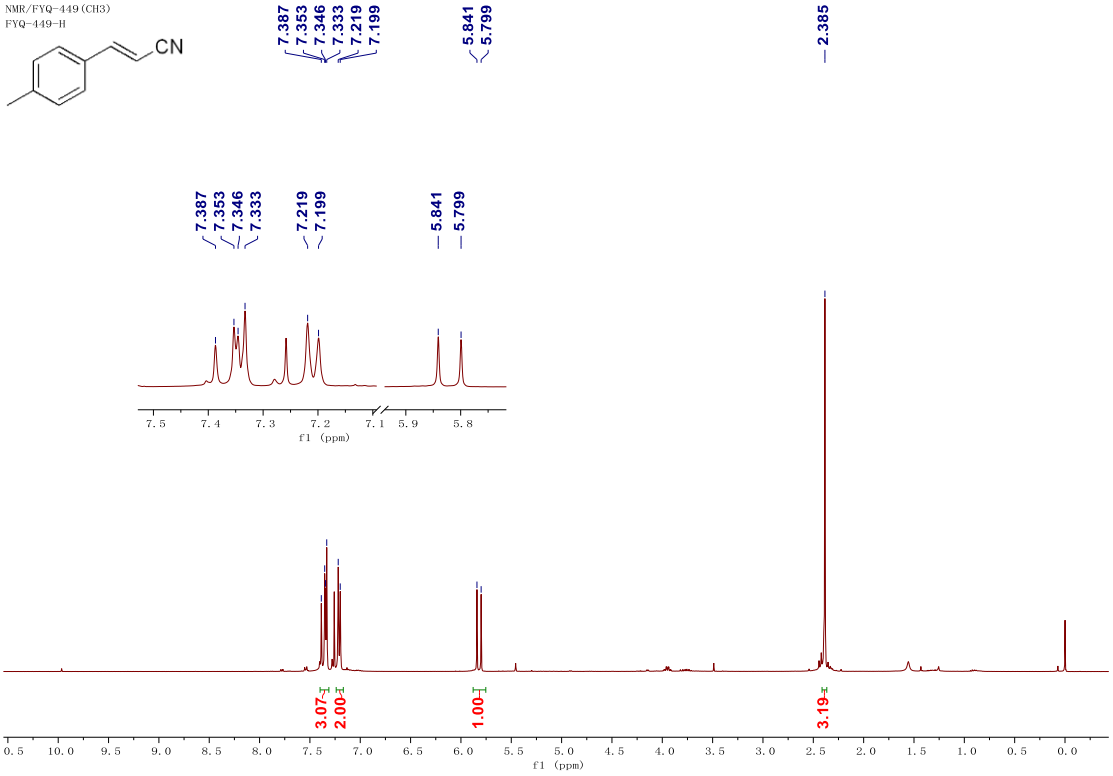


^{13}C NMR (101 MHz, DMSO-d_6)

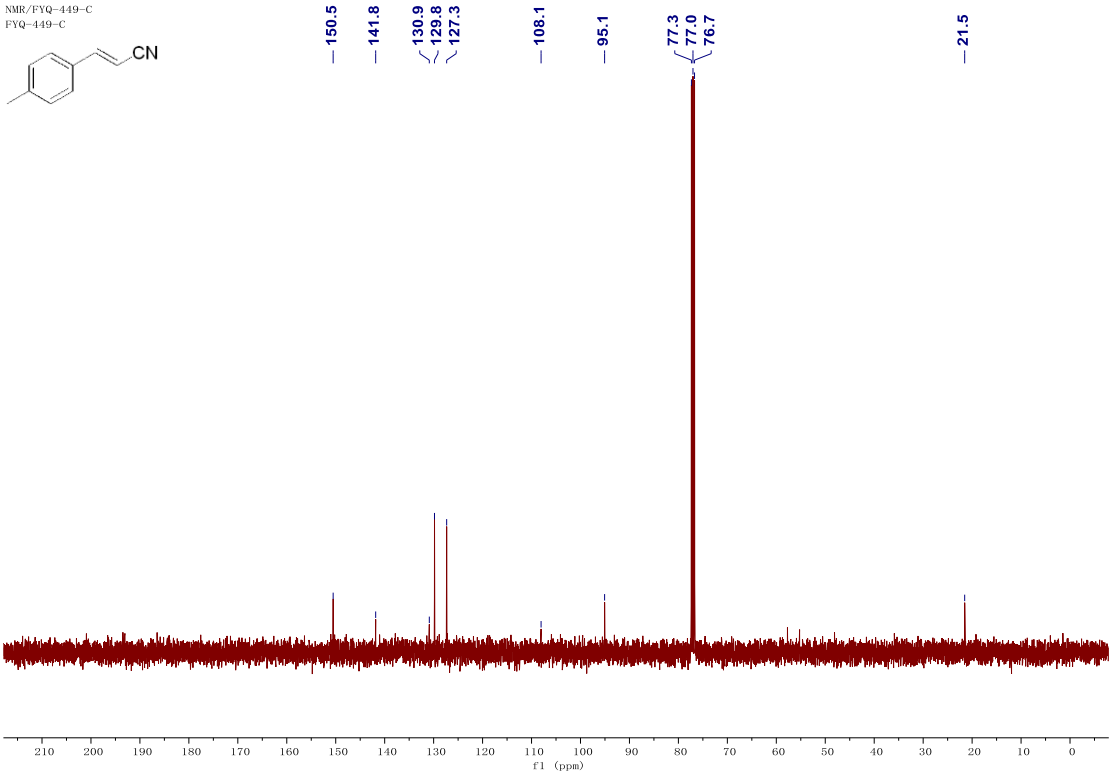


(*E*)-3-(p-tolyl)acrylonitrile (**2h**):

^{1}H NMR (400 MHz, $CDCl_3$)

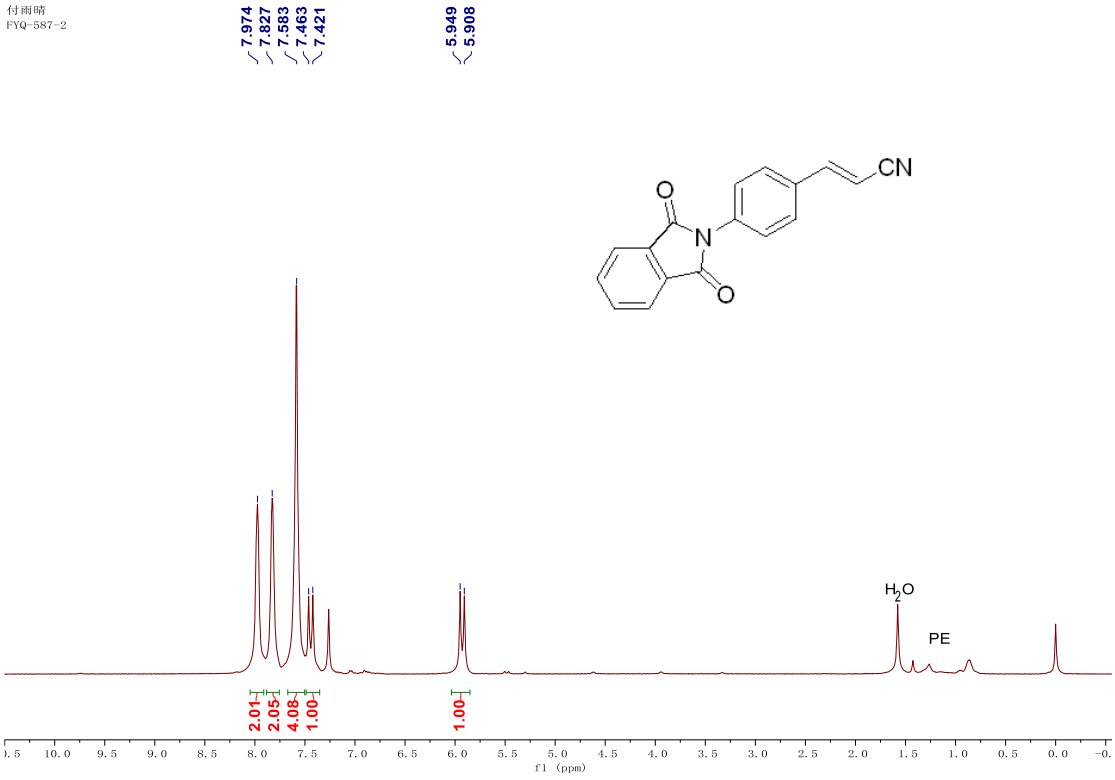


^{13}C NMR (101 MHz, $CDCl_3$)

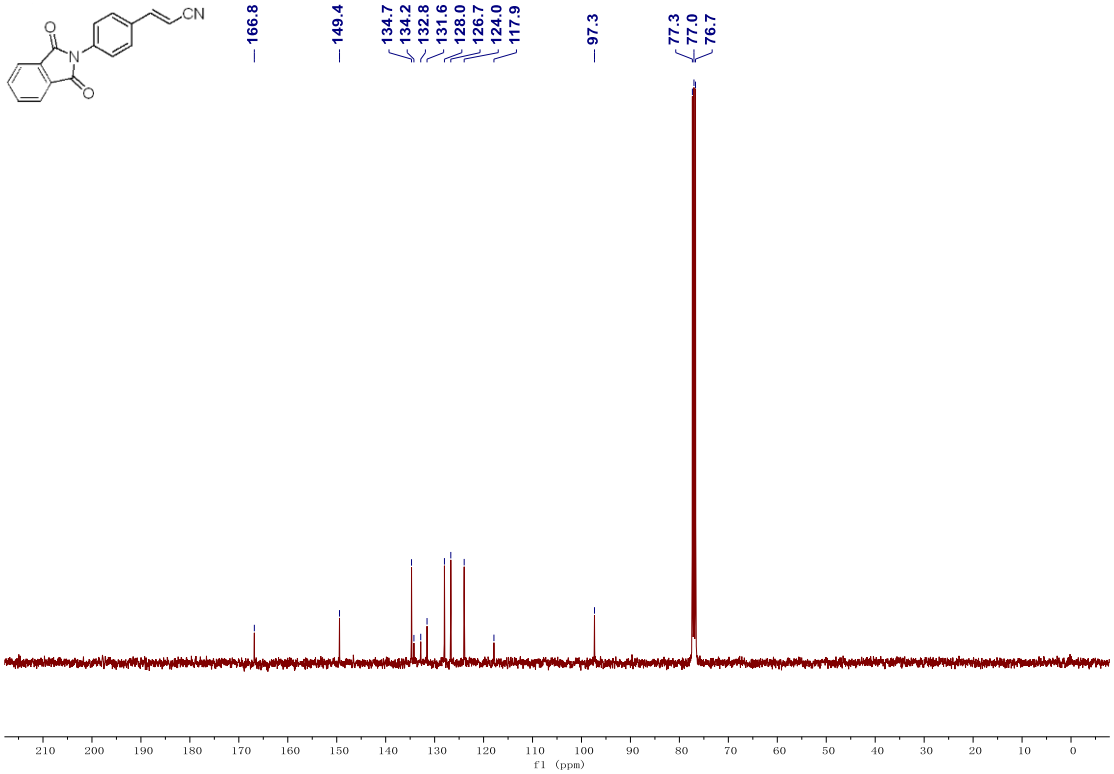


(*E*)-3-(4-(1,3-dioxoisoindolin-2-yl)phenyl)acrylonitrile (**2j**):

^{1}H NMR (400 MHz, $CDCl_3$)

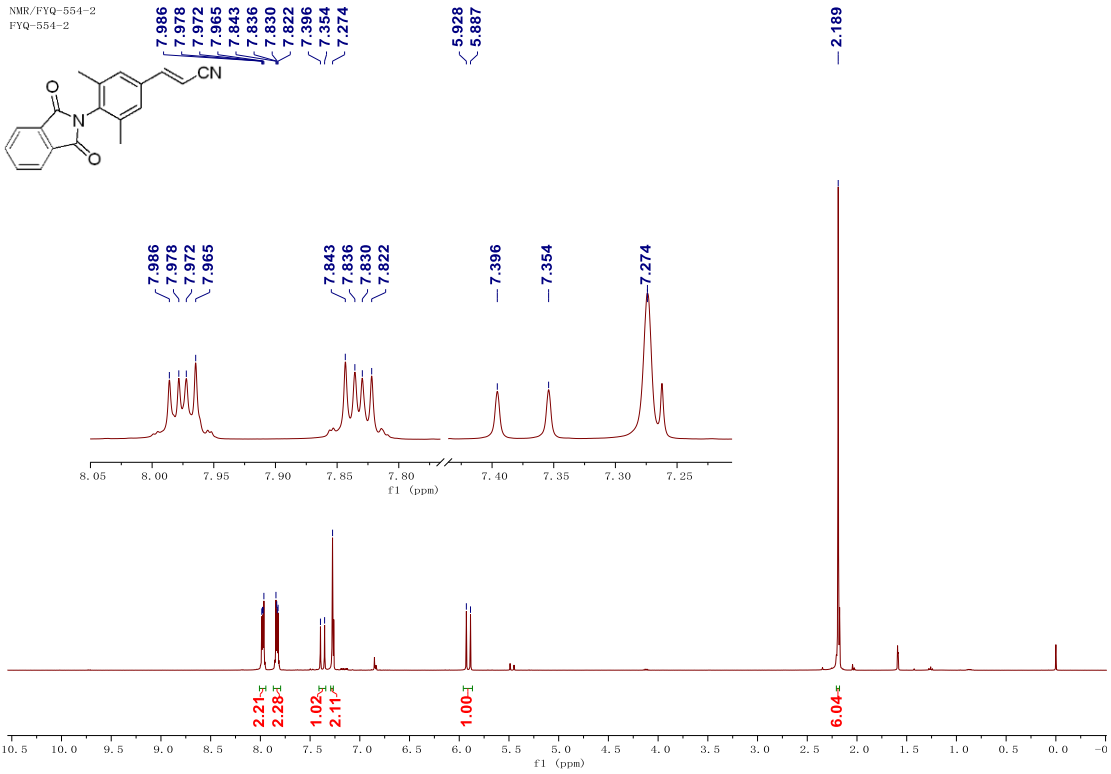


^{13}C NMR (101 MHz, $CDCl_3$)

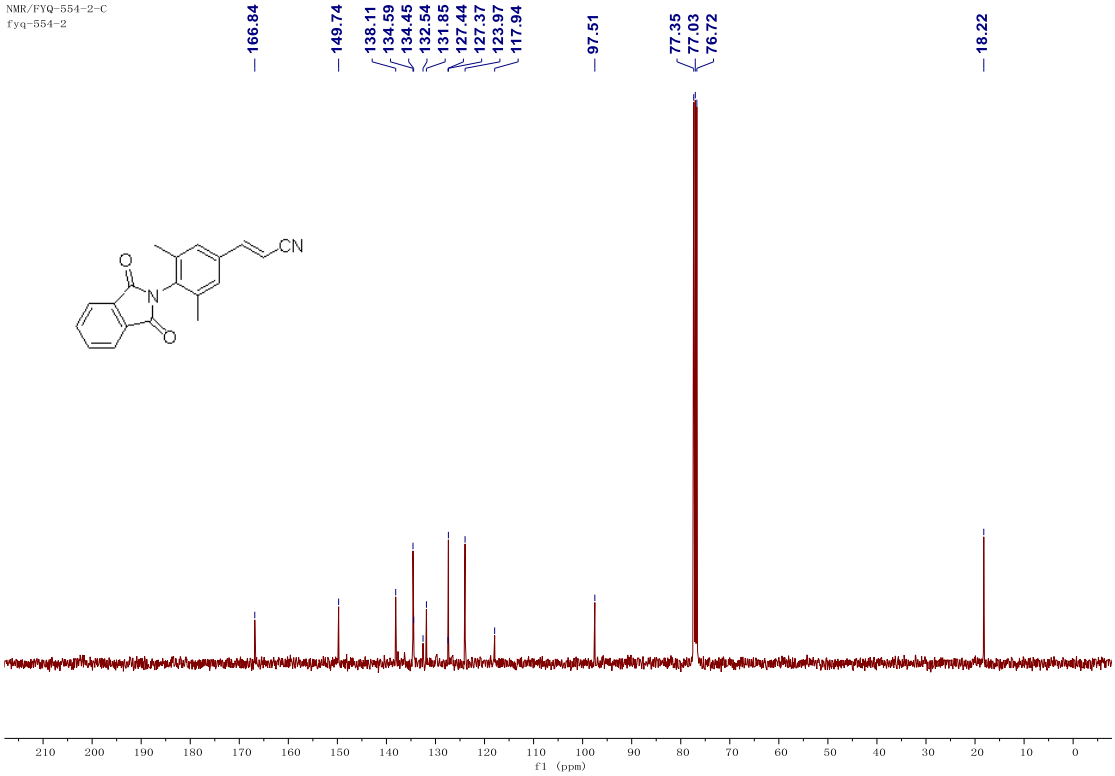


(*E*)-3-(4-(1,3-dioxoisoindolin-2-yl)-3,5-dimethylphenyl)acrylonitrile (**2k**):

^{1}H NMR (400 MHz, $CDCl_3$)

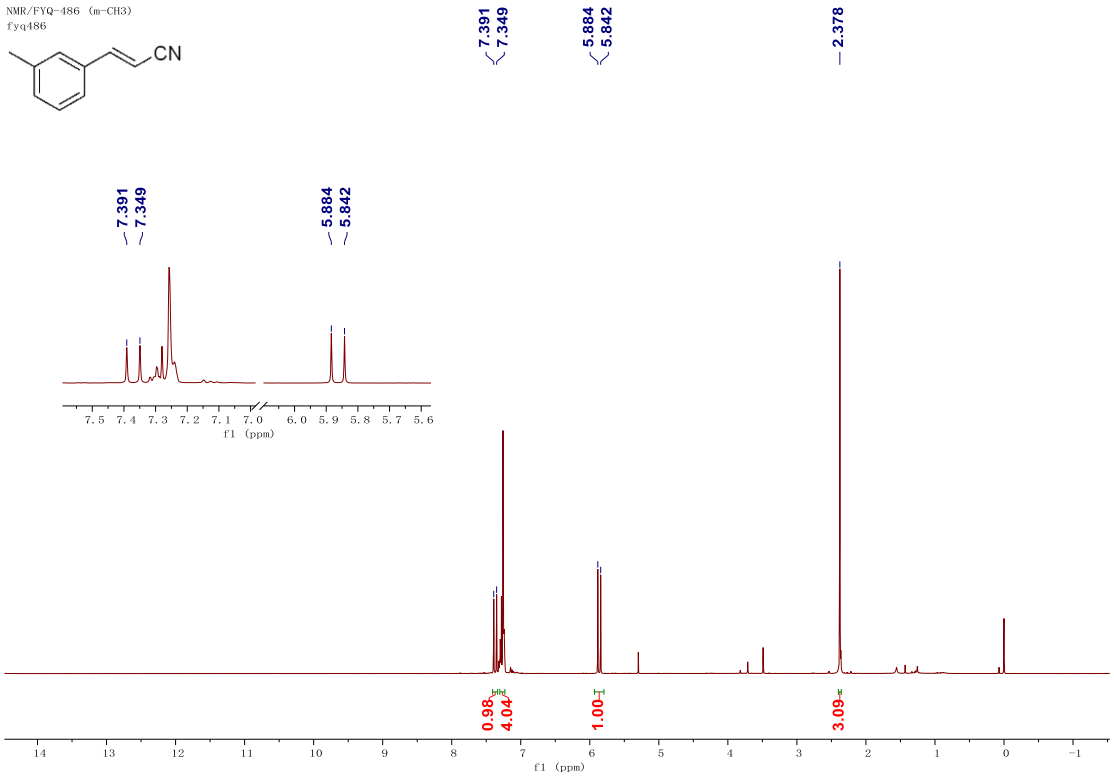


^{13}C NMR (101 MHz, $CDCl_3$)

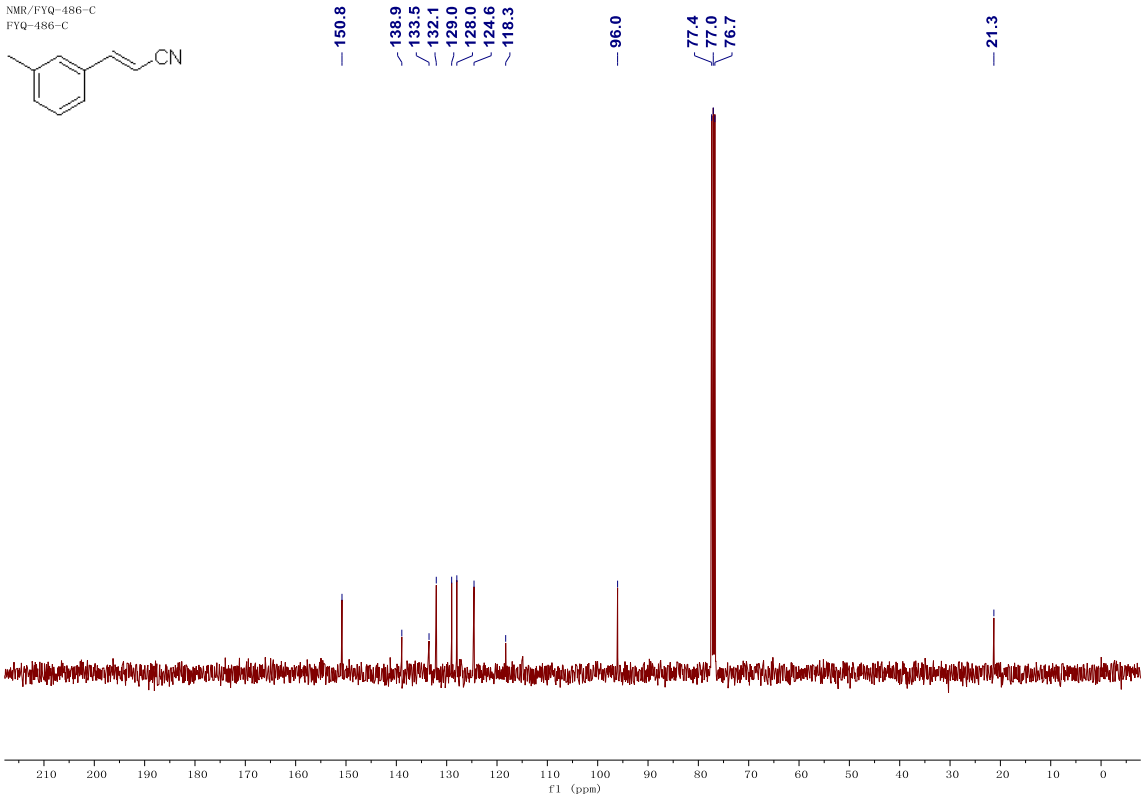


(*E*)-3-(m-tolyl)acrylonitrile (**2l**):

^{1}H NMR (400 MHz, $CDCl_3$)

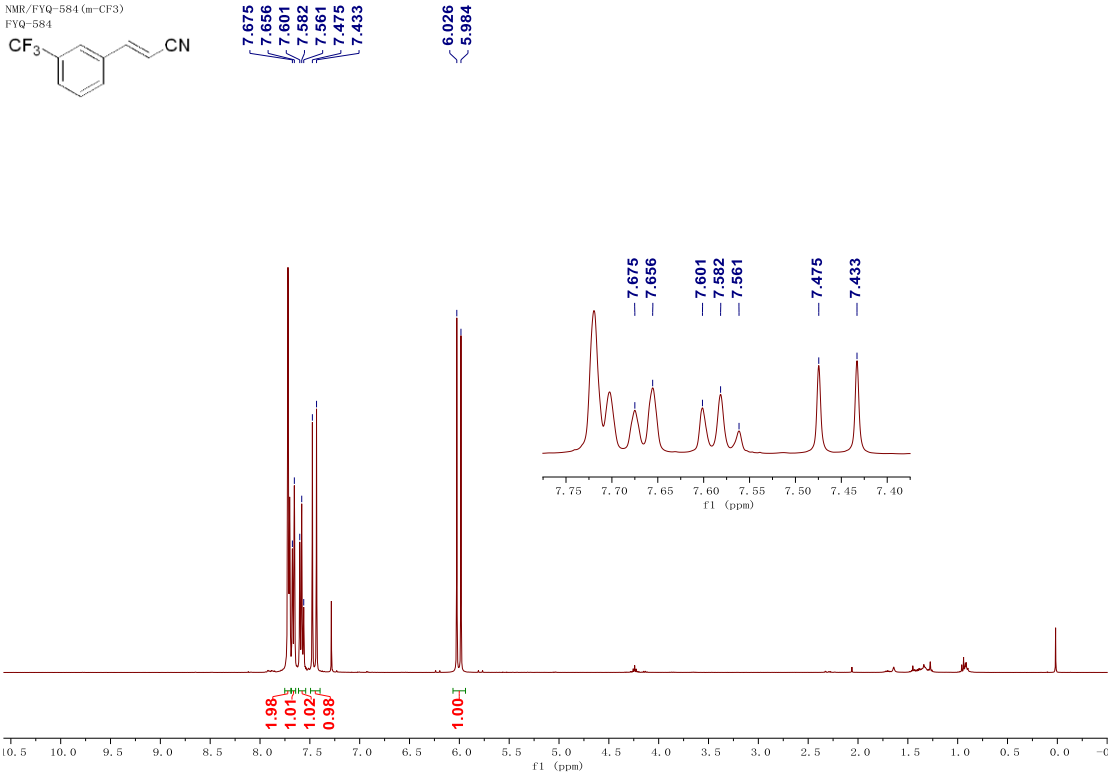


^{13}C NMR (101 MHz, $CDCl_3$)

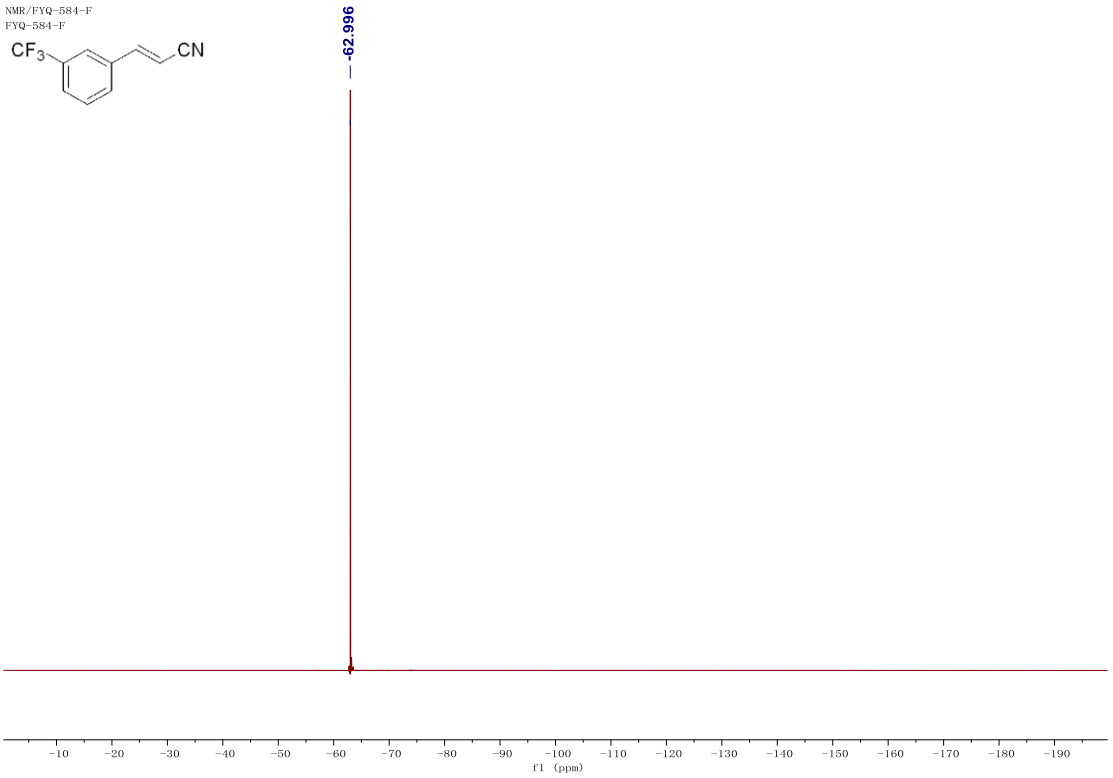


(*E*)-3-(3-(trifluoromethyl)phenyl)acrylonitrile (**2m**):

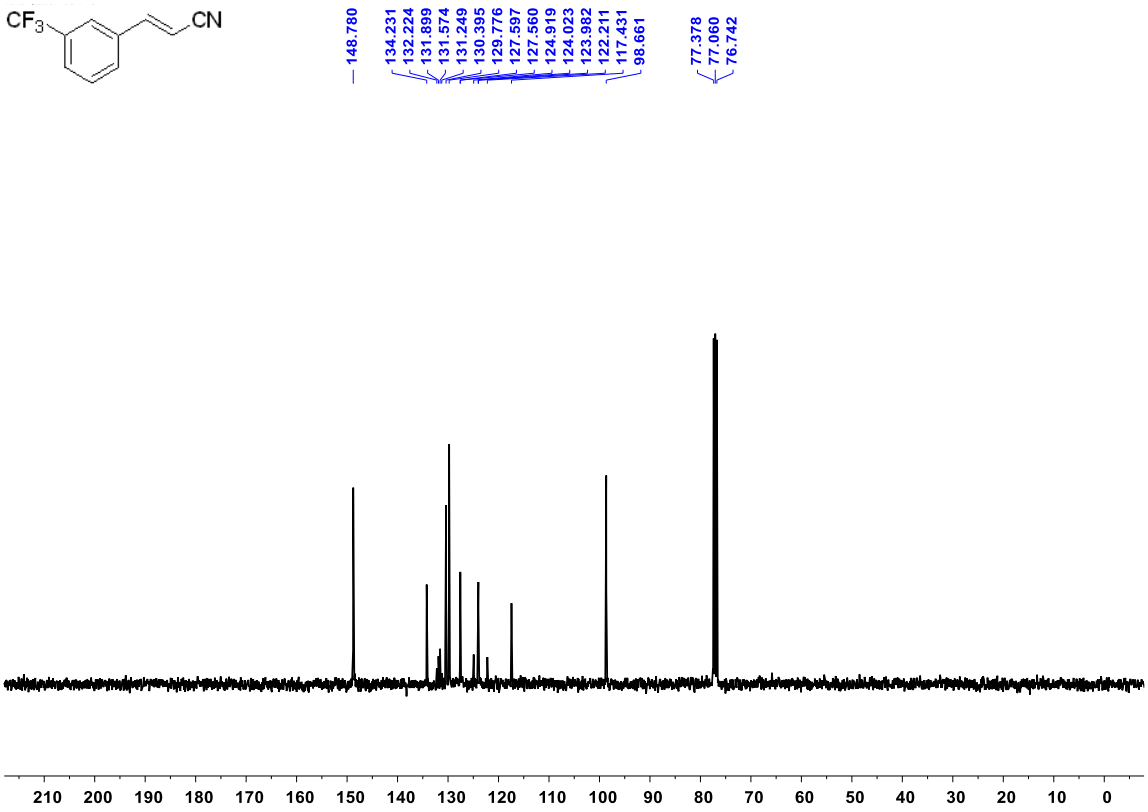
^{1}H NMR (400 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

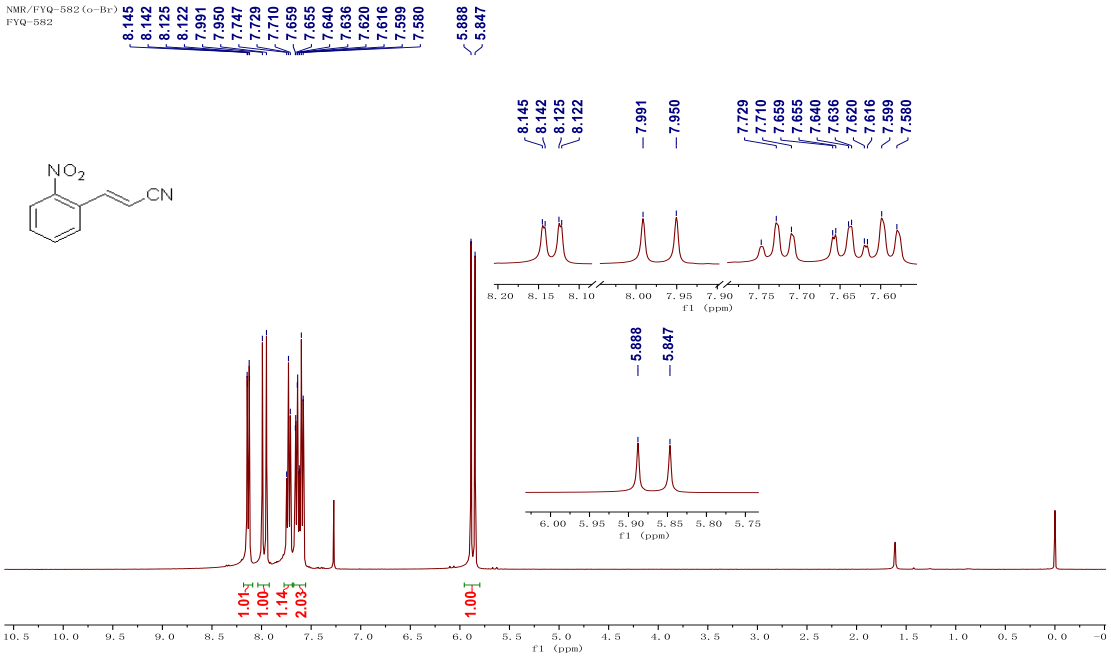


^{13}C NMR (101 MHz, $CDCl_3$)

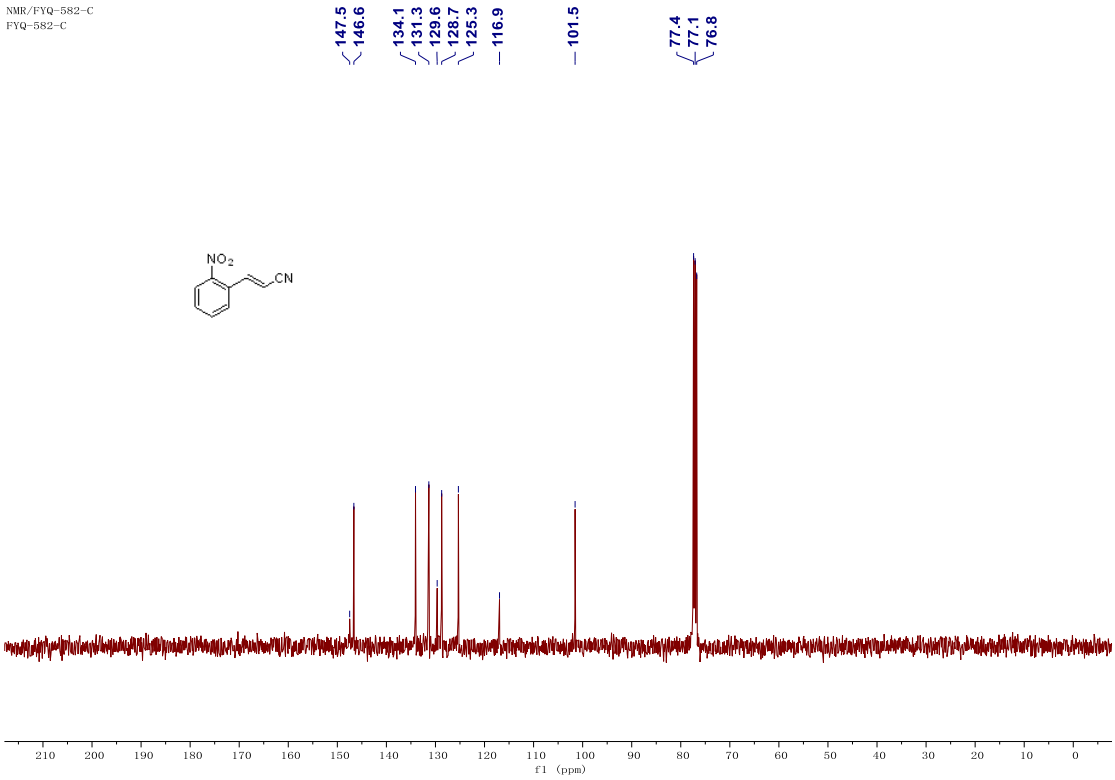


(*E*)-3-(2-bromophenyl)acrylonitrile (**2n**):

^{1}H NMR (400 MHz, $CDCl_3$)

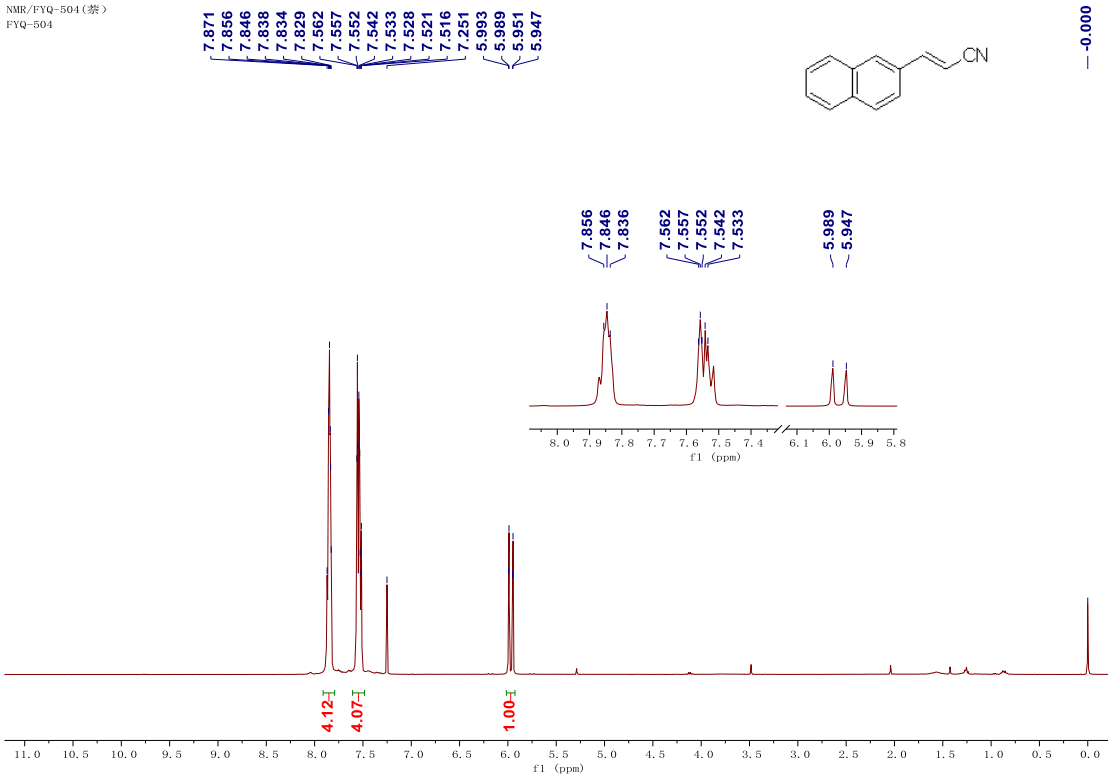


^{13}C NMR (101 MHz, $CDCl_3$)

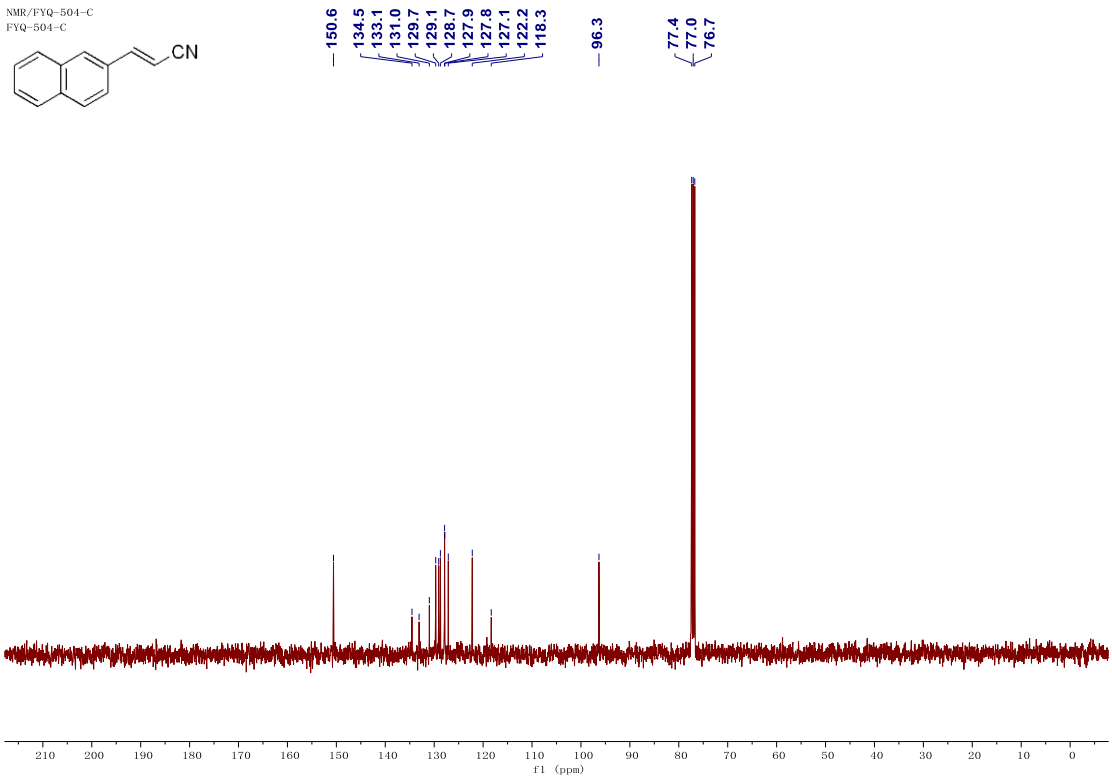


(*E*)-3-(naphthalen-2-yl)acrylonitrile (**2o**)

^{1}H NMR (400 MHz, $CDCl_3$)

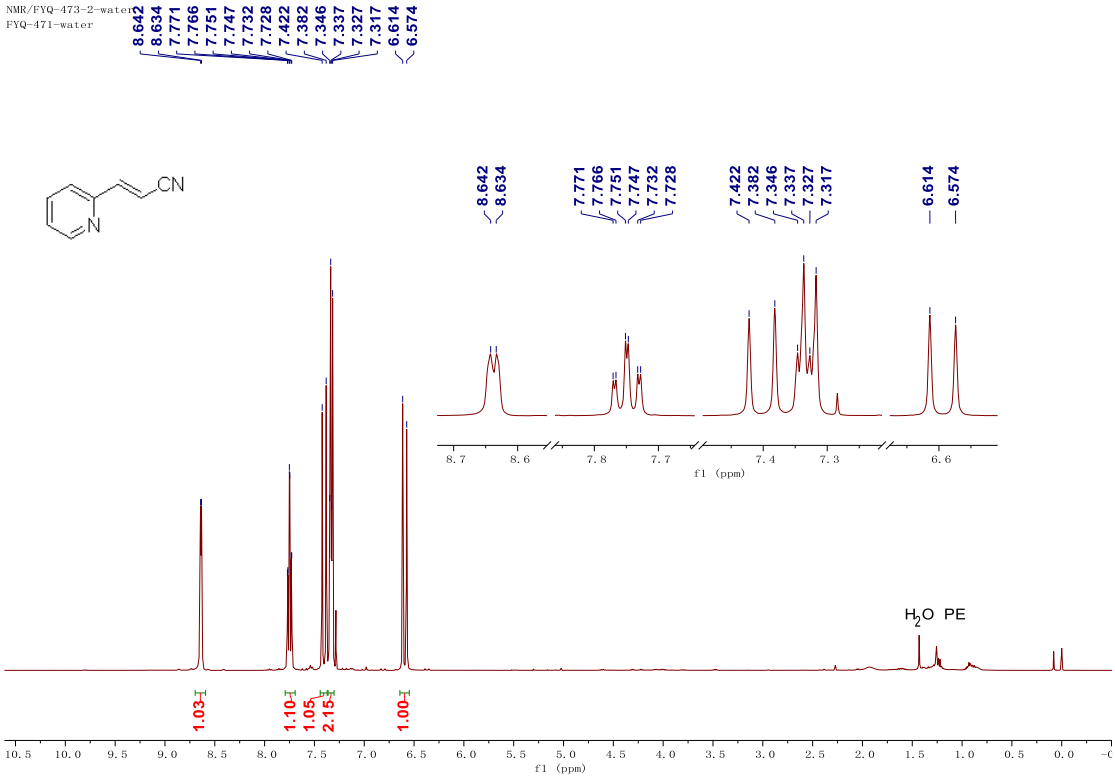


^{13}C NMR (101 MHz, $CDCl_3$)

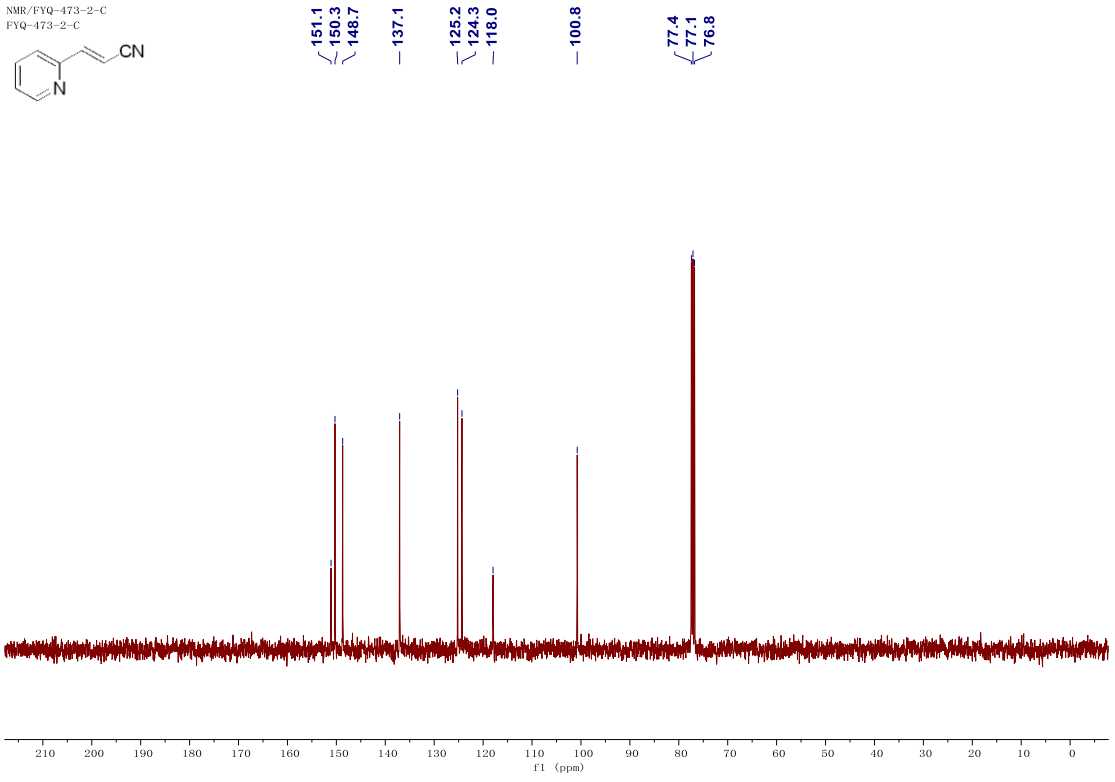


(*E*)-3-(pyridin-2-yl)acrylonitrile (**2p**)

^{1}H NMR (400 MHz, $CDCl_3$)

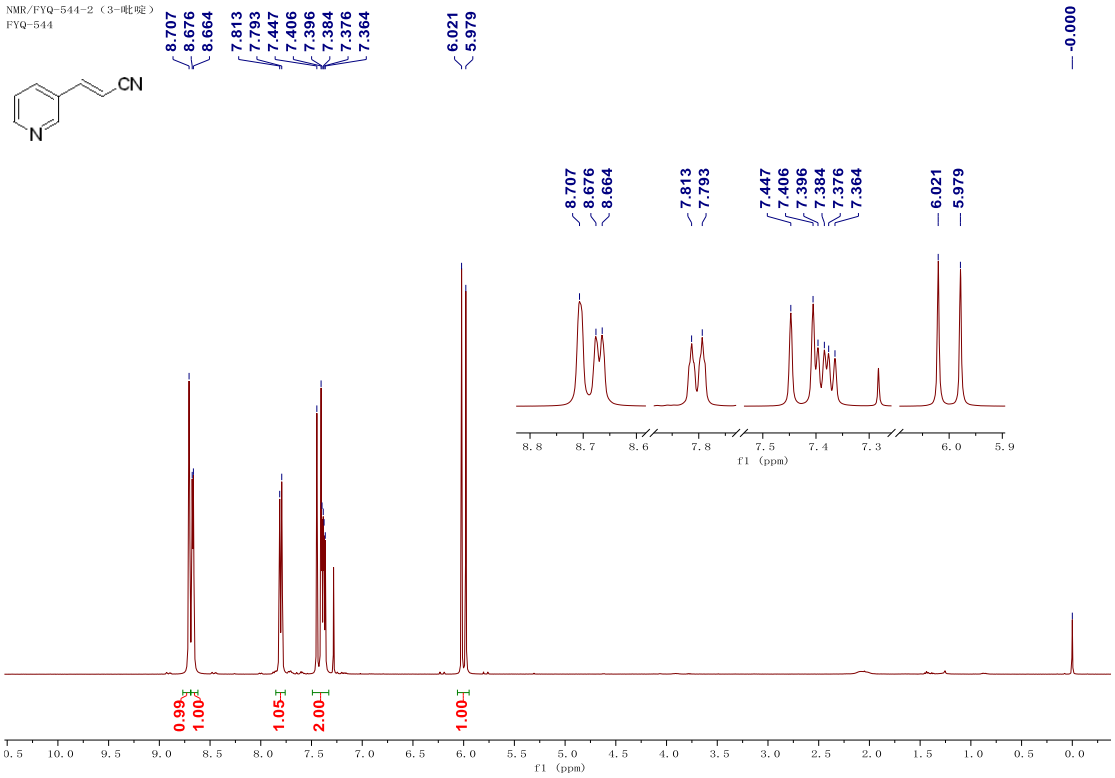


^{13}C NMR (101 MHz, $CDCl_3$)

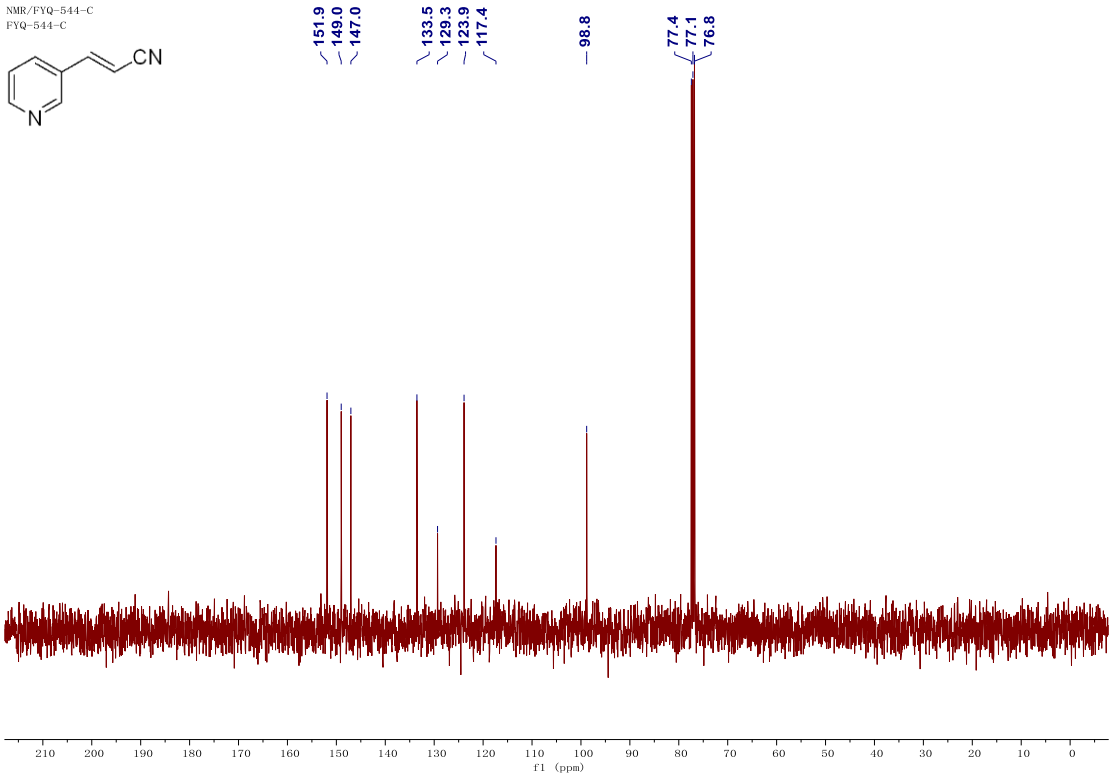


(*E*)-3-(pyridin-3-yl)acrylonitrile (**2q**)

^{1}H NMR (400 MHz, $CDCl_3$)

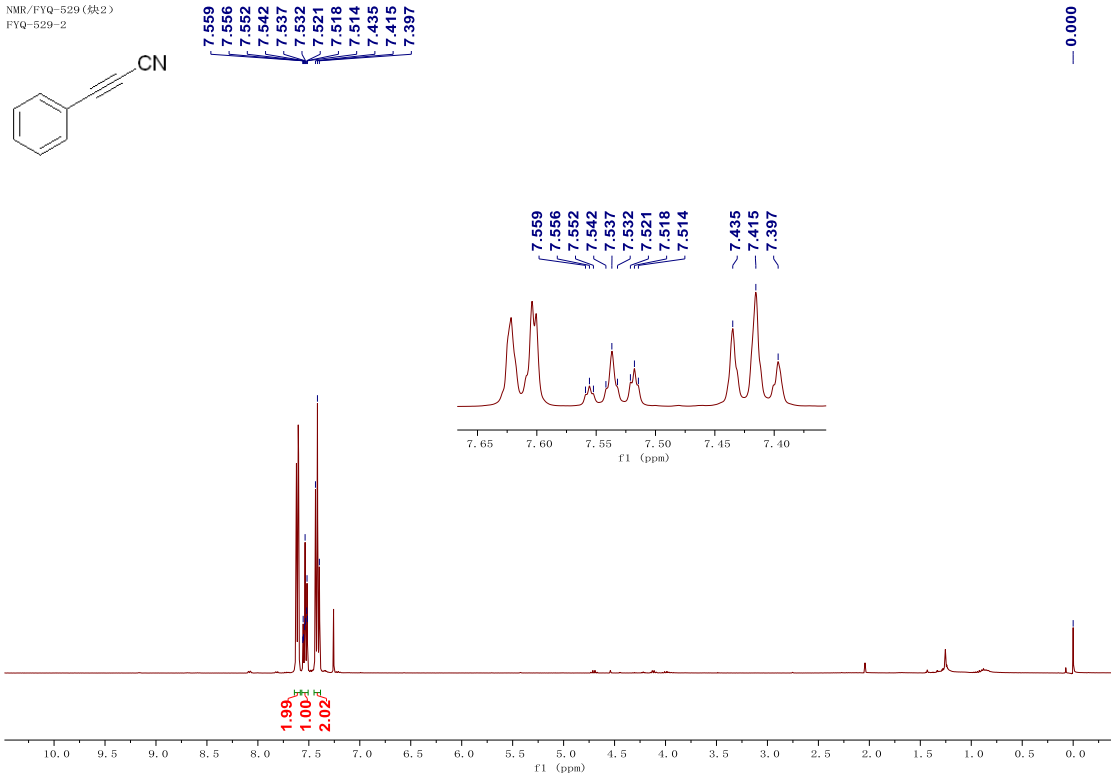


^{13}C NMR (101 MHz, $CDCl_3$)

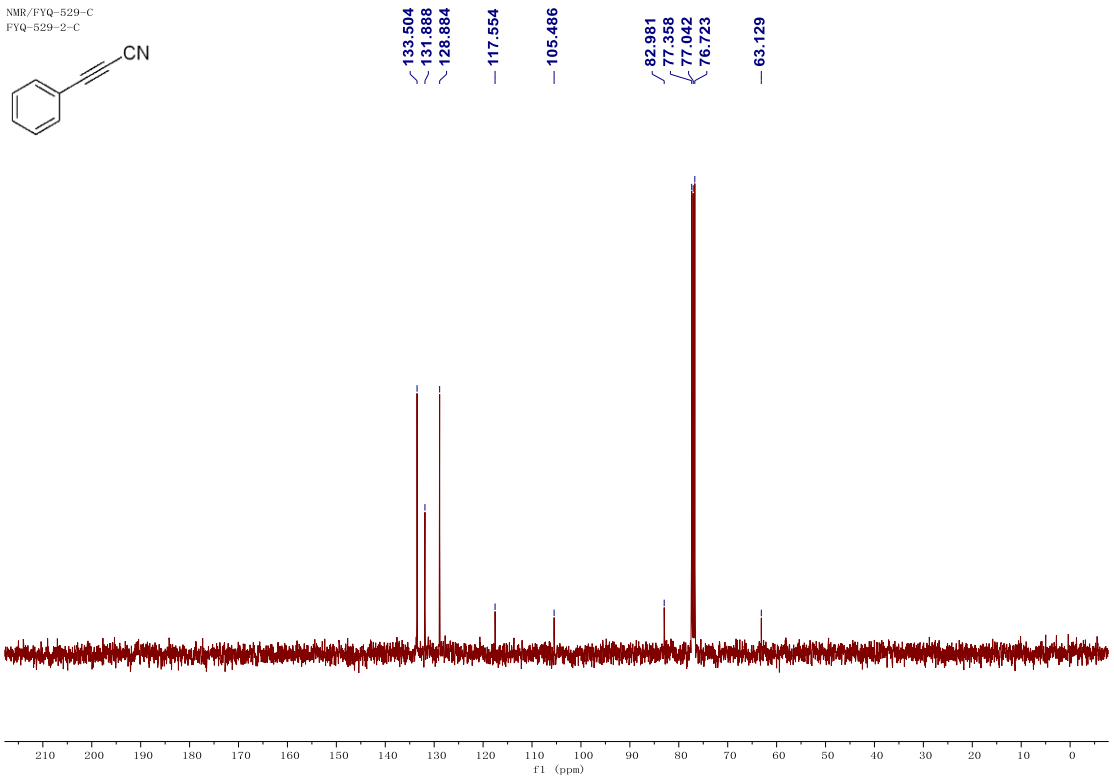


3-phenylpropiolonitrile (**2r**):

^{1}H NMR (400 MHz, $CDCl_3$)

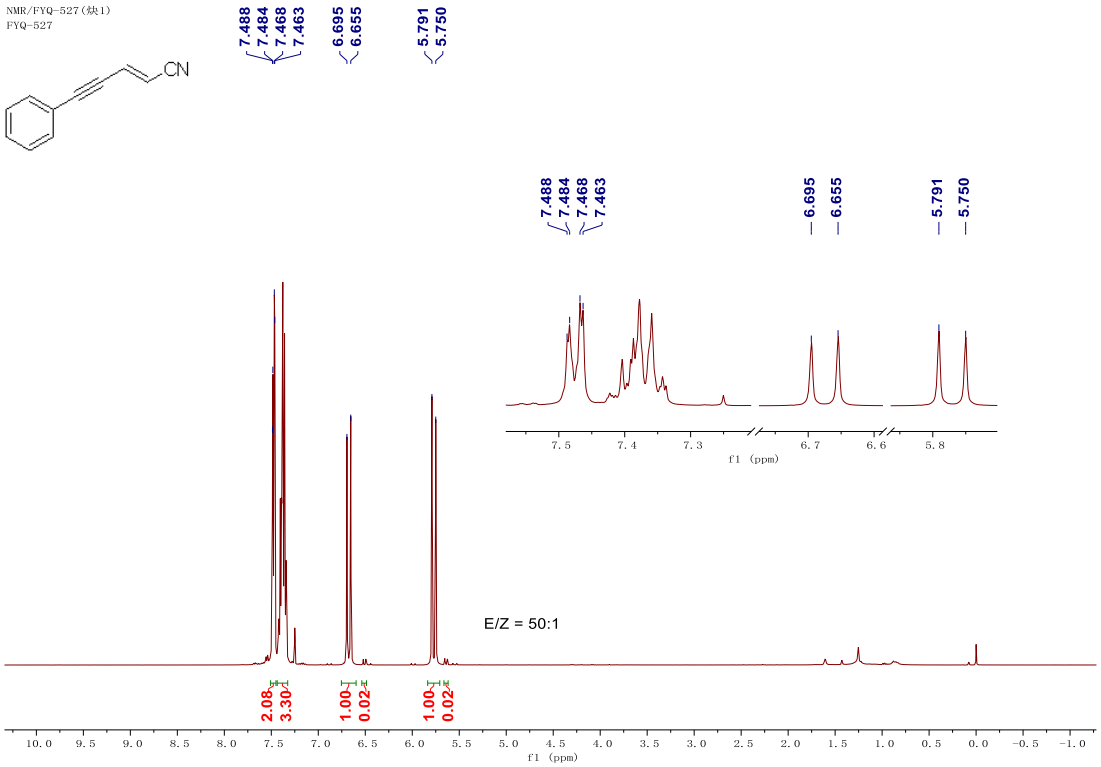


^{13}C NMR (101 MHz, $CDCl_3$)

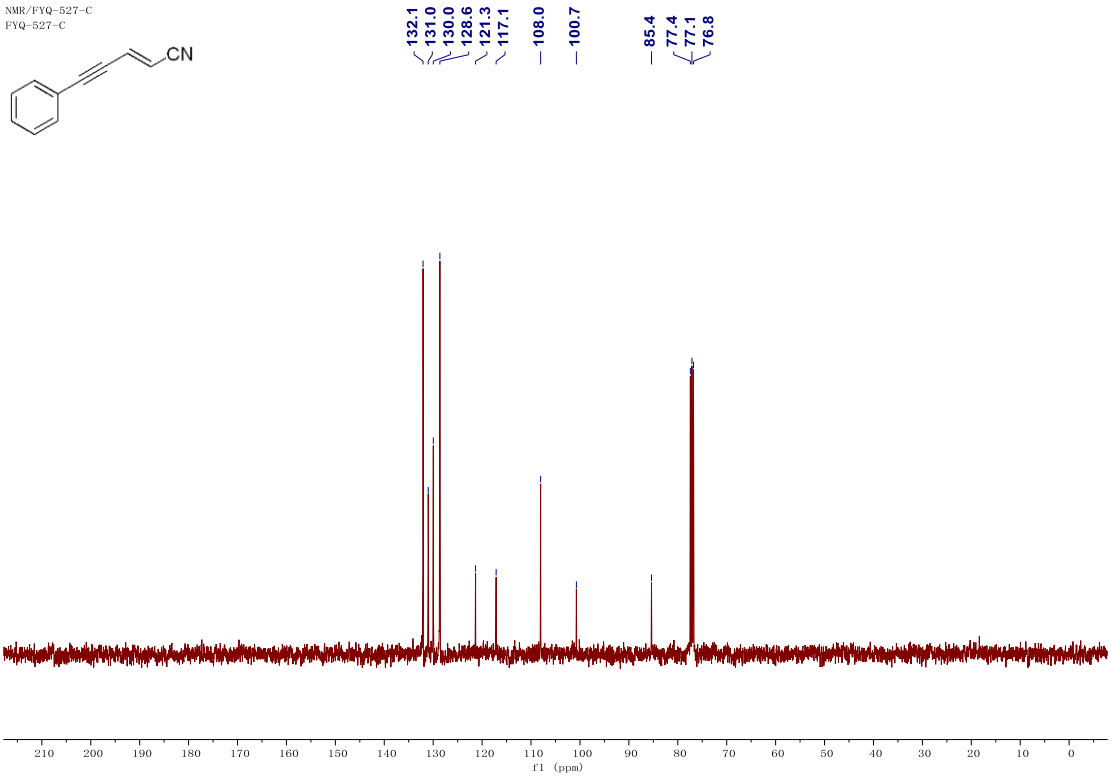


(*E*)-5-phenylpent-2-en-4-ynenitrile (**2s**):

^{1}H NMR (400 MHz, $CDCl_3$)

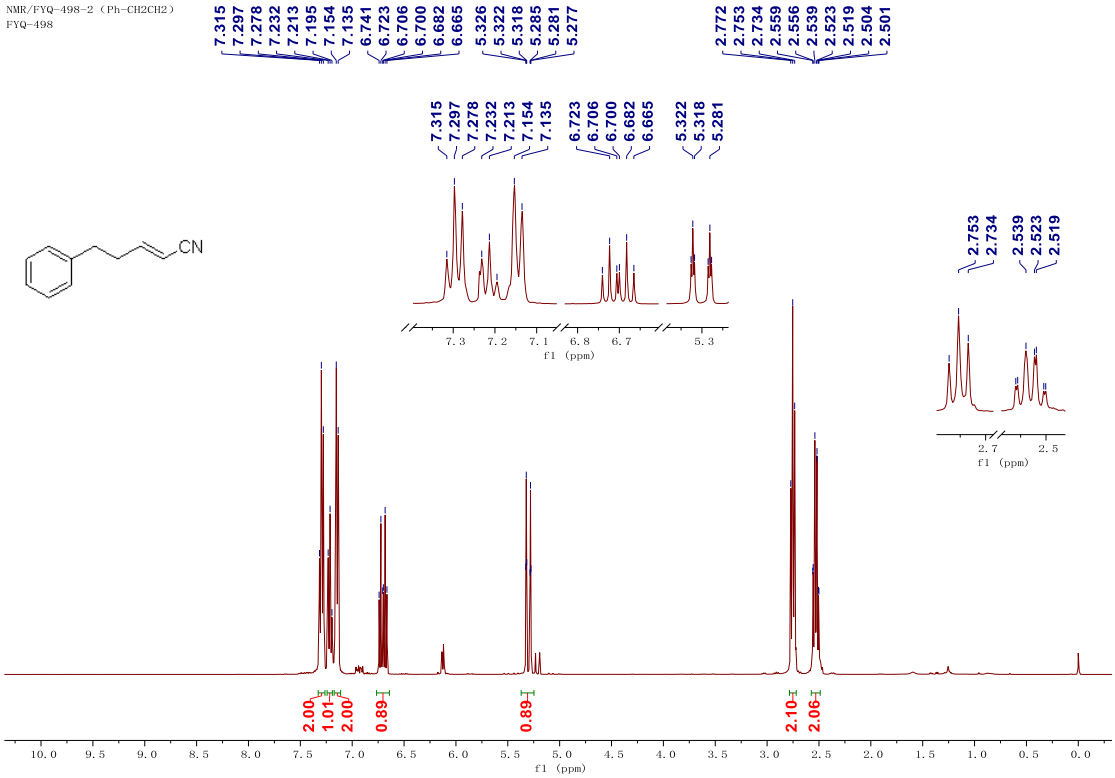


^{13}C NMR (101 MHz, $CDCl_3$)

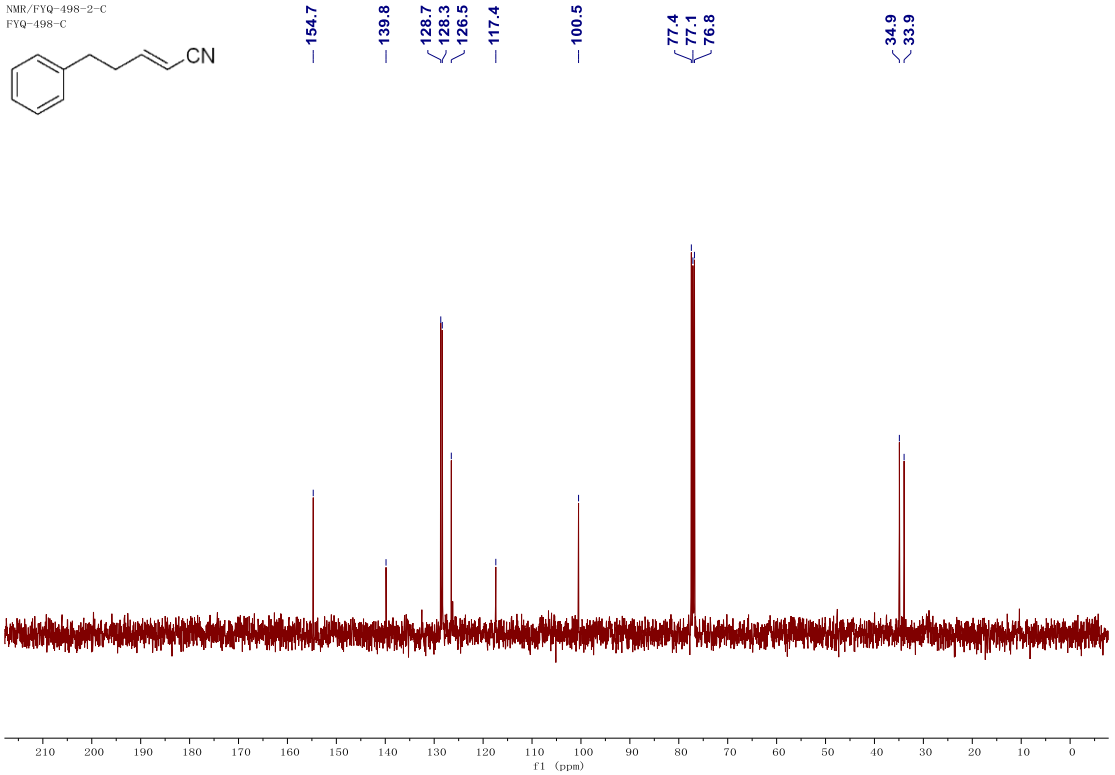


(*E*)-5-phenylpent-2-enenitrile (**2t**):

^{1}H NMR (400 MHz, $CDCl_3$)

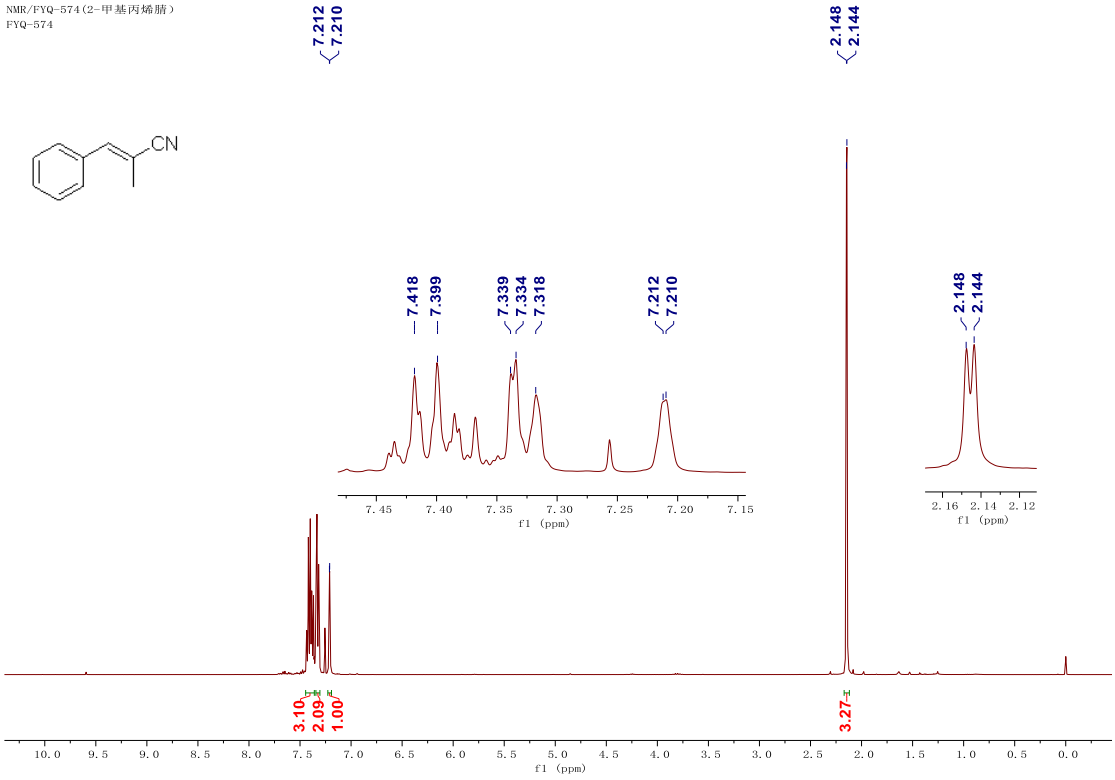


^{13}C NMR (101 MHz, $CDCl_3$)

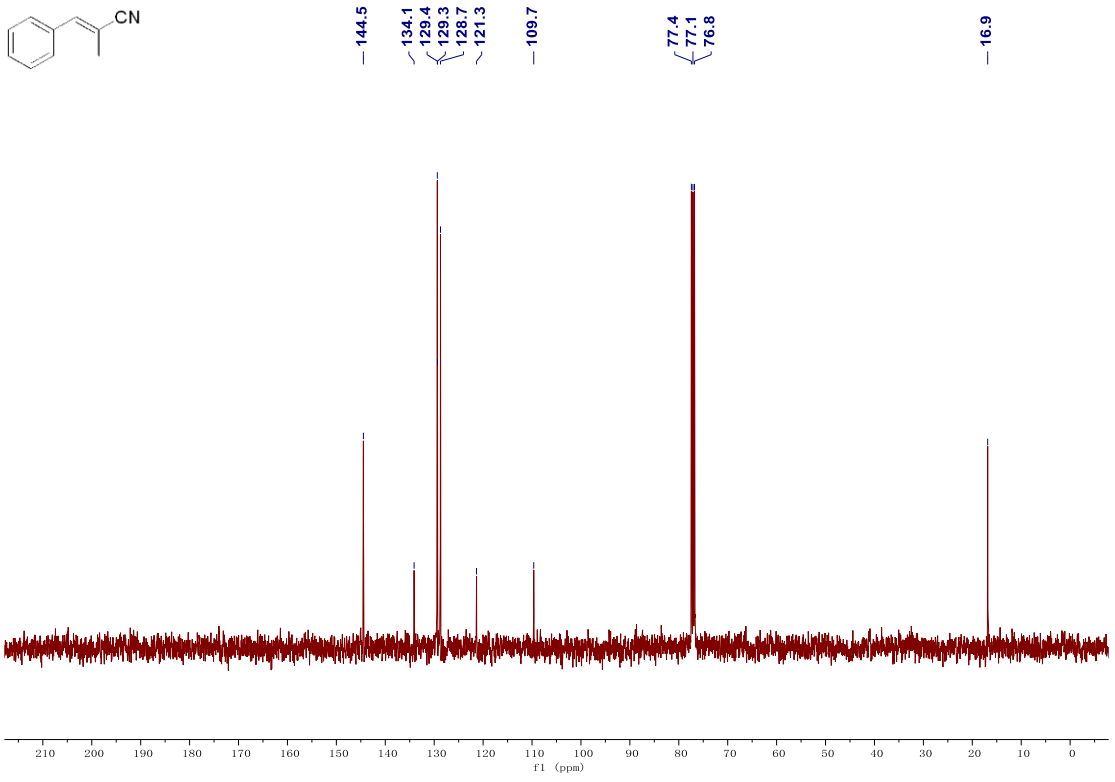


(*E*)-2-methyl-3-phenyl-2-Propenenitrile (**2u**):

^{1}H NMR (400 MHz, $CDCl_3$)

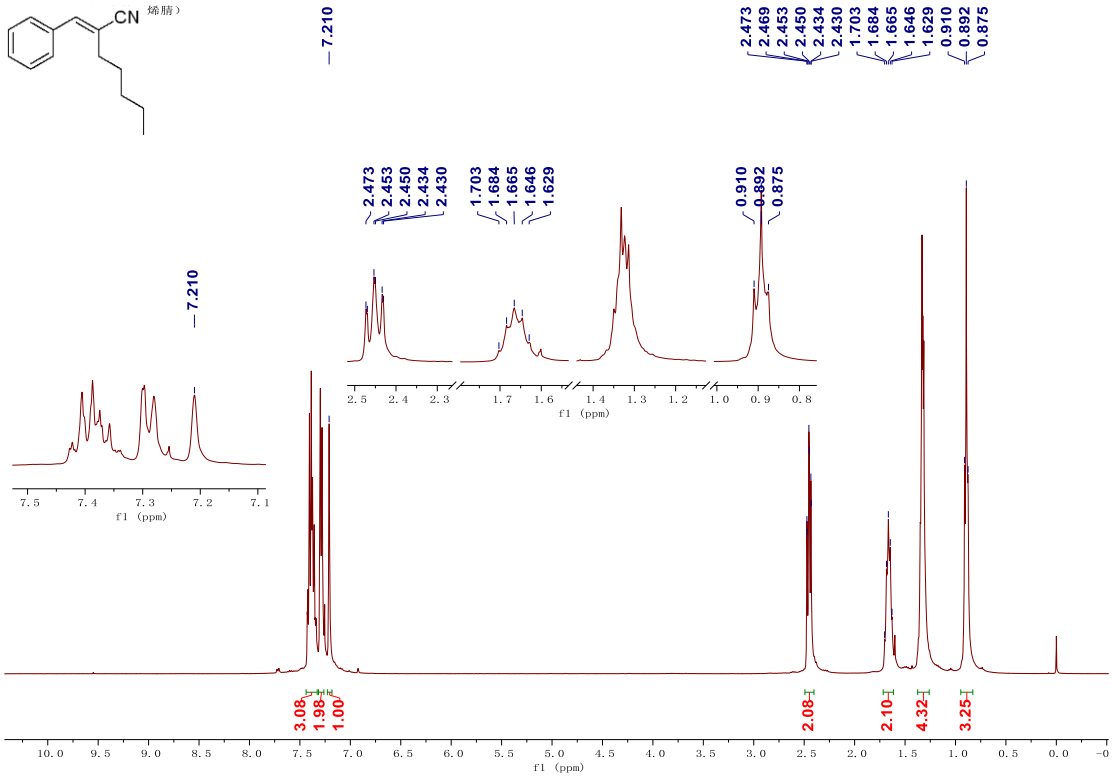


^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm):

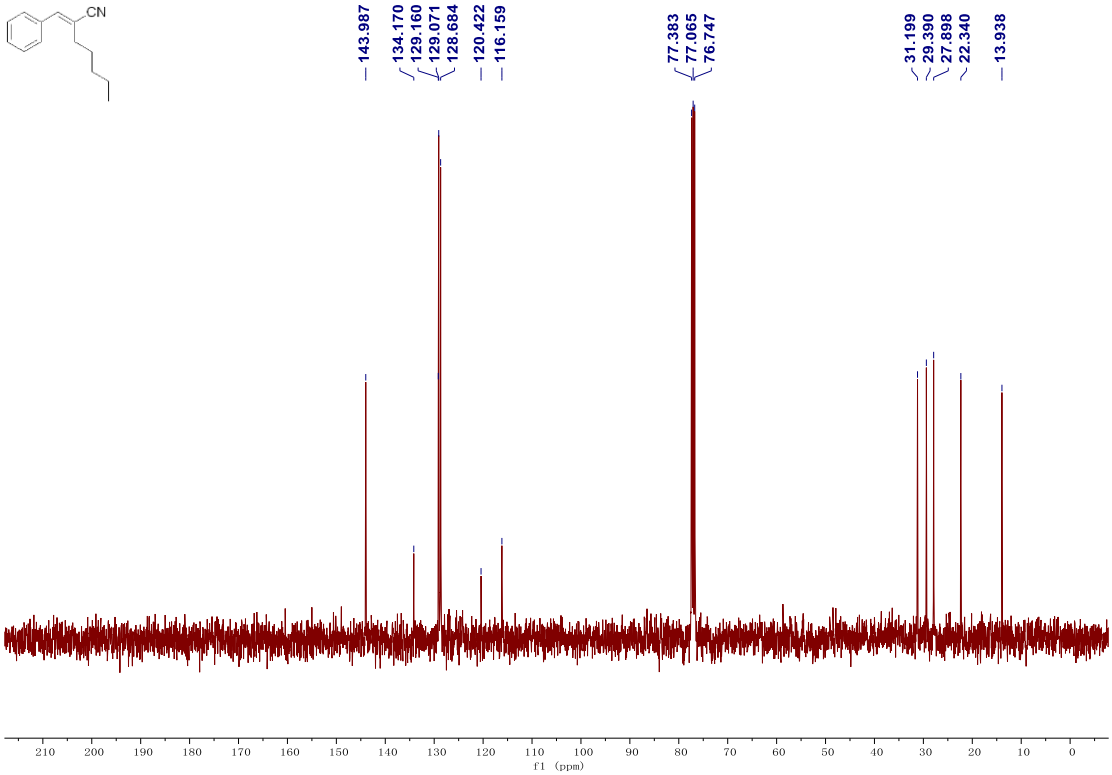


(2*E*)-2-(Phenylmethylene)heptanenitrile (**2v**)

^{1}H NMR (400 MHz, $CDCl_3$)

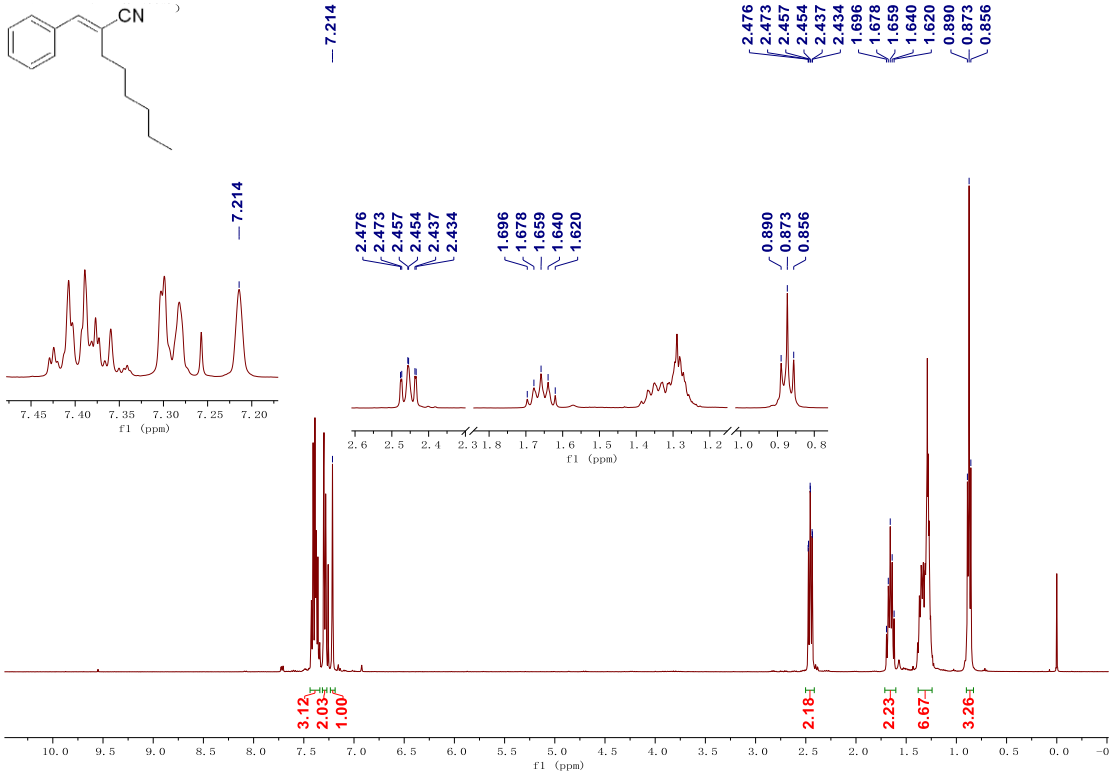


^{13}C NMR (101 MHz, $CDCl_3$)

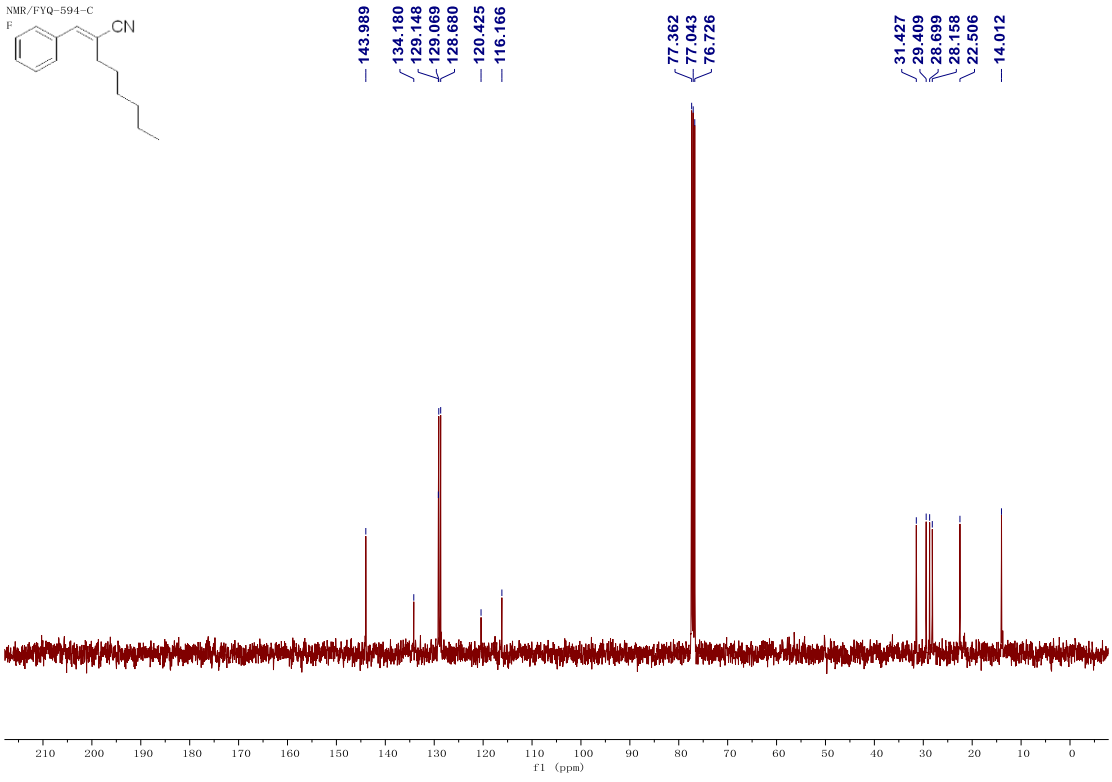


(2*E*)-2-(Phenylmethylene)octanenitrile (**2w**)

^{1}H NMR (400 MHz, $CDCl_3$)

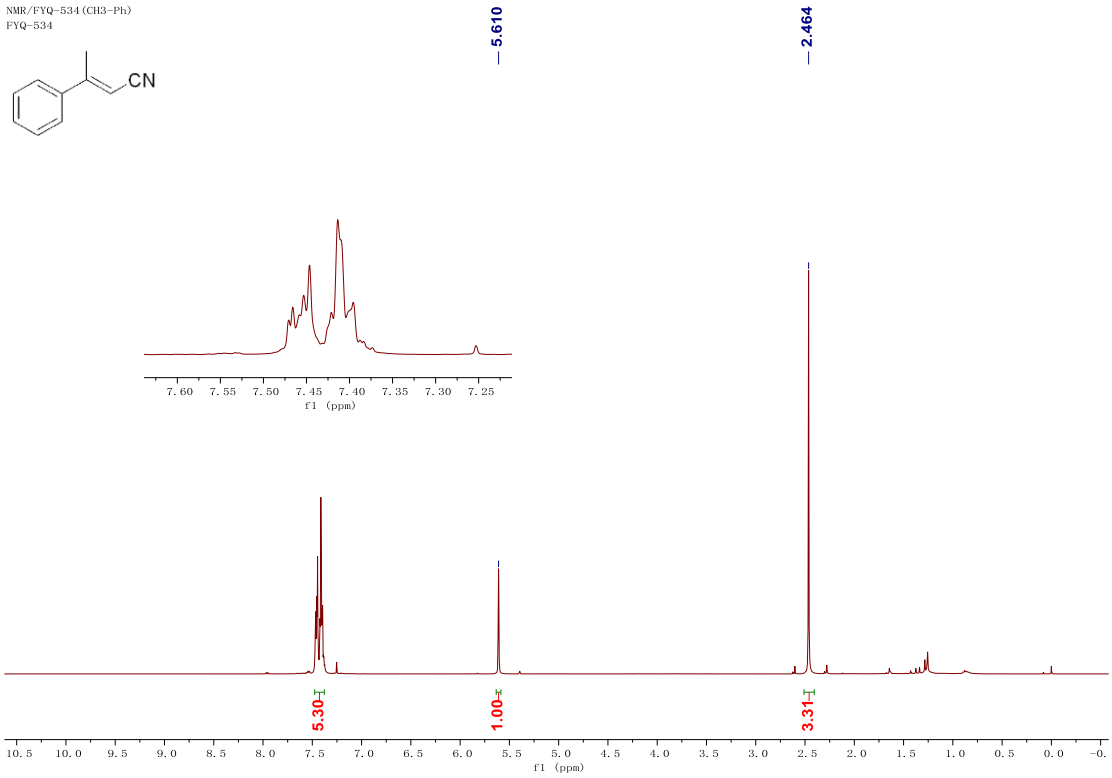


^{13}C NMR (101 MHz, $CDCl_3$)

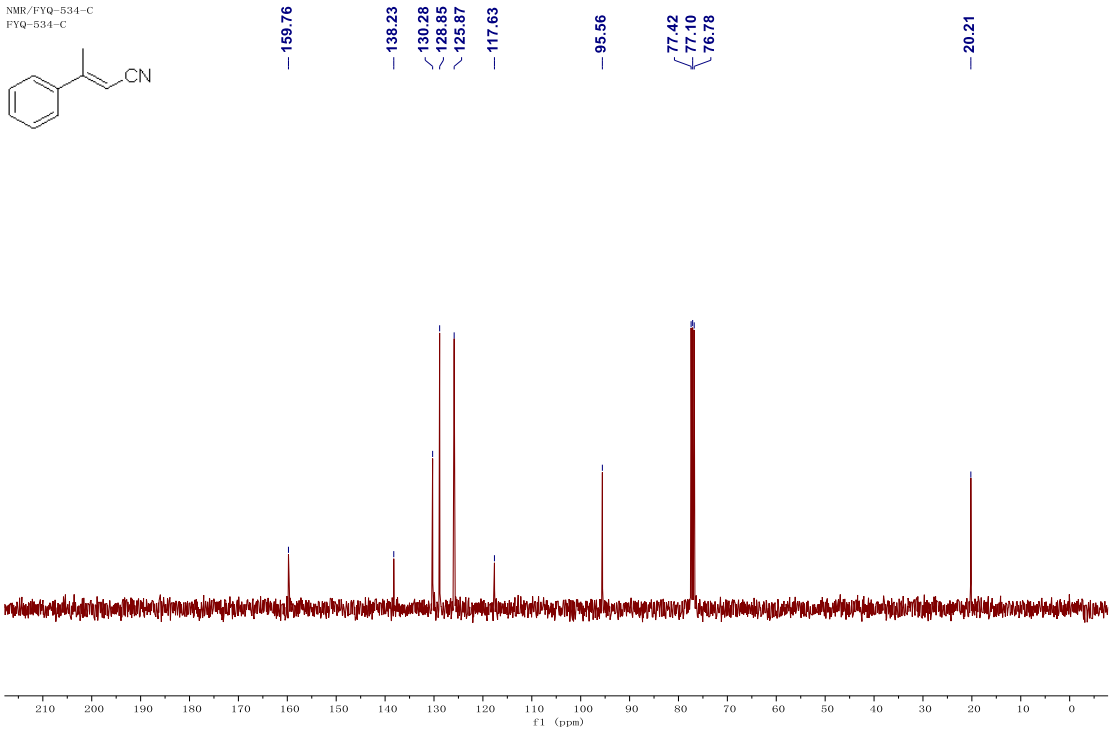


(*E*)-3-phenylbut-2-enenitrile (**2x**)

^{1}H NMR (400 MHz, $CDCl_3$)

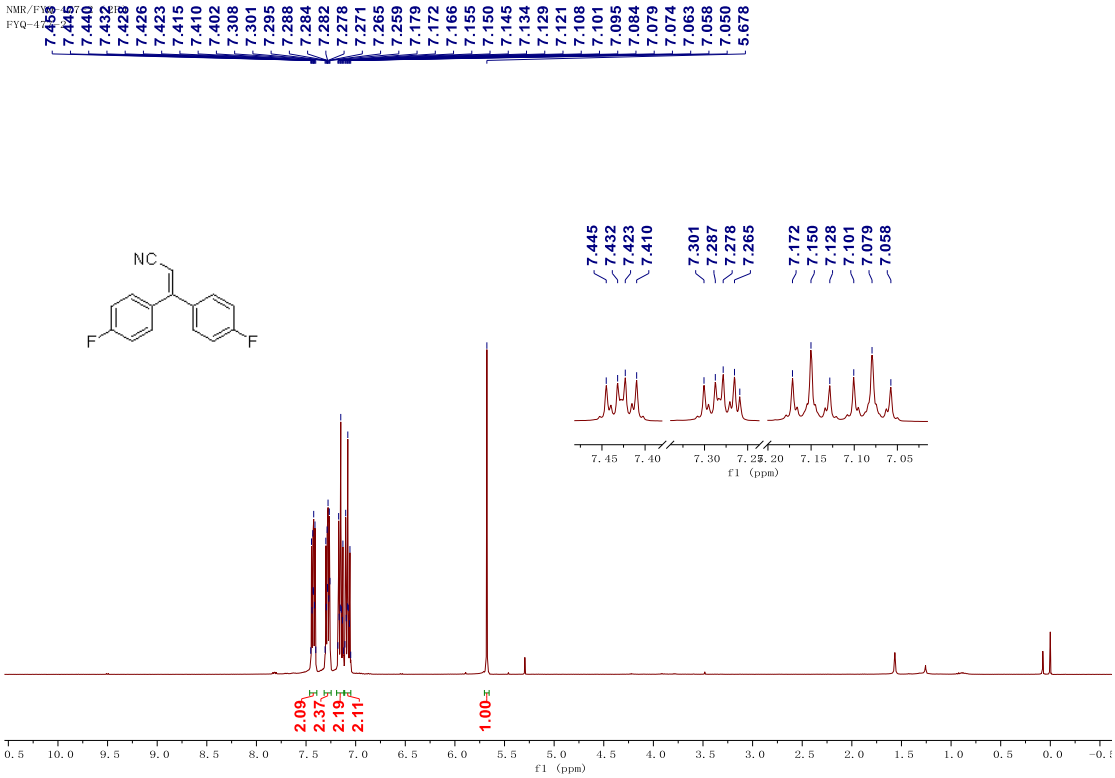


^{13}C NMR (101 MHz, $CDCl_3$)

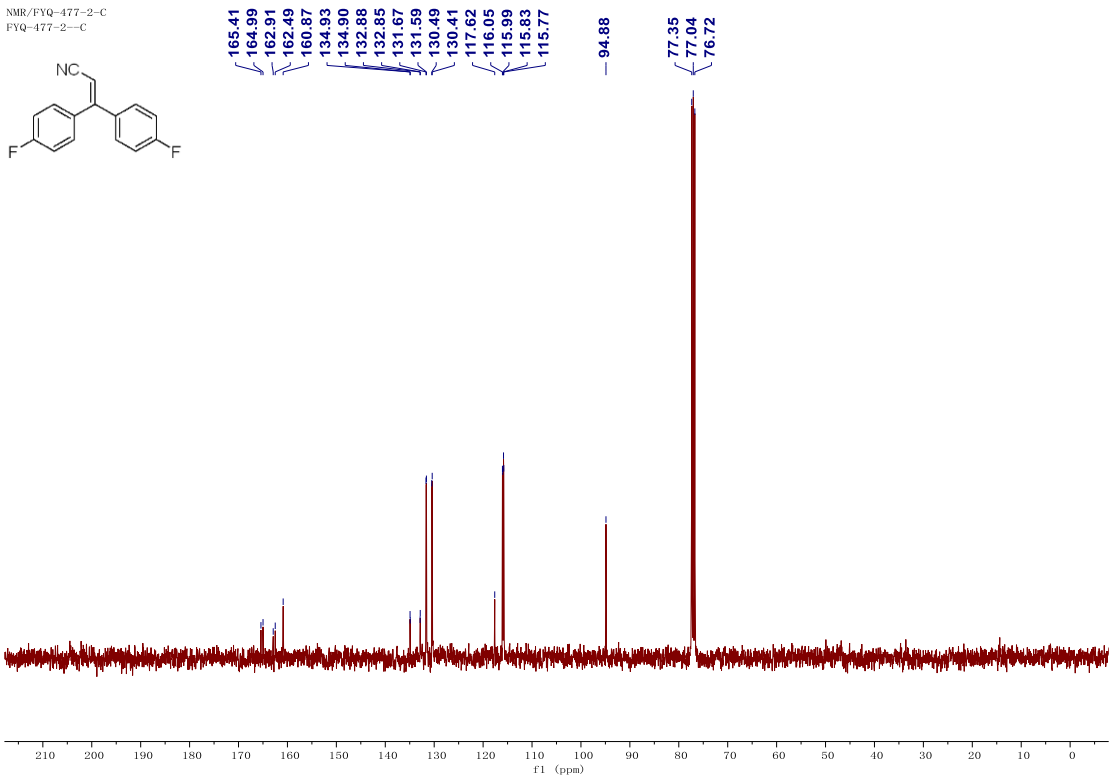


3,3-bis(4-fluorophenyl)acrylonitrile (**2y**):

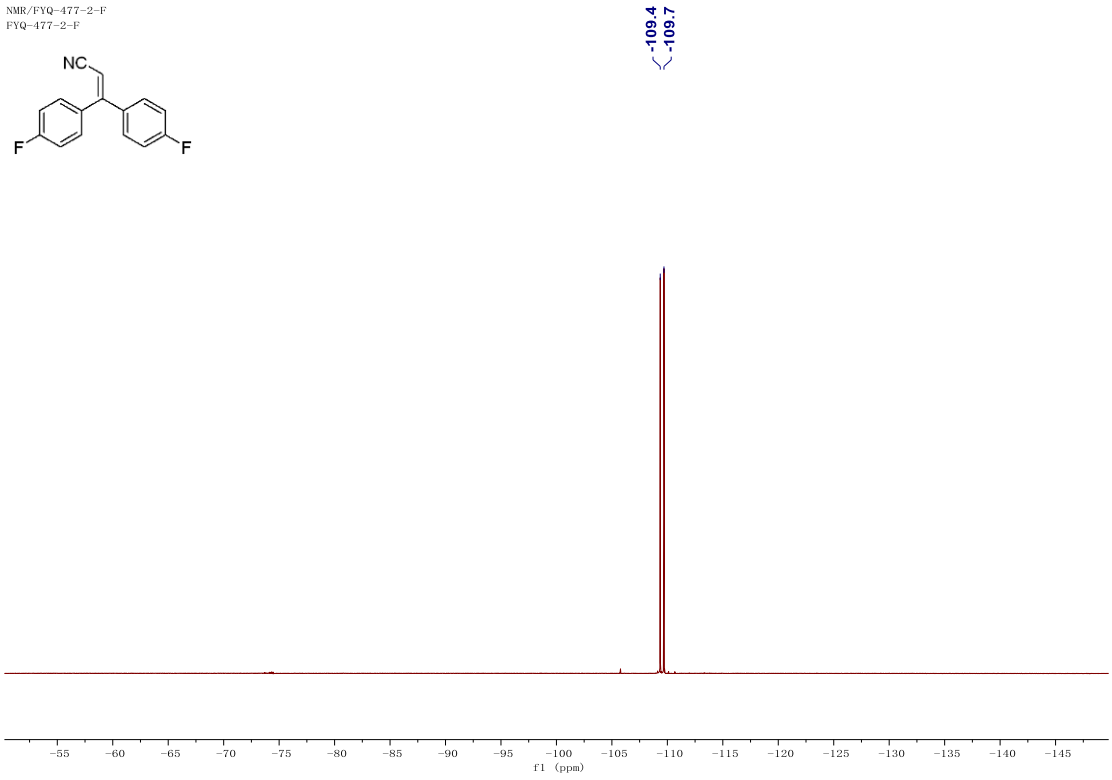
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

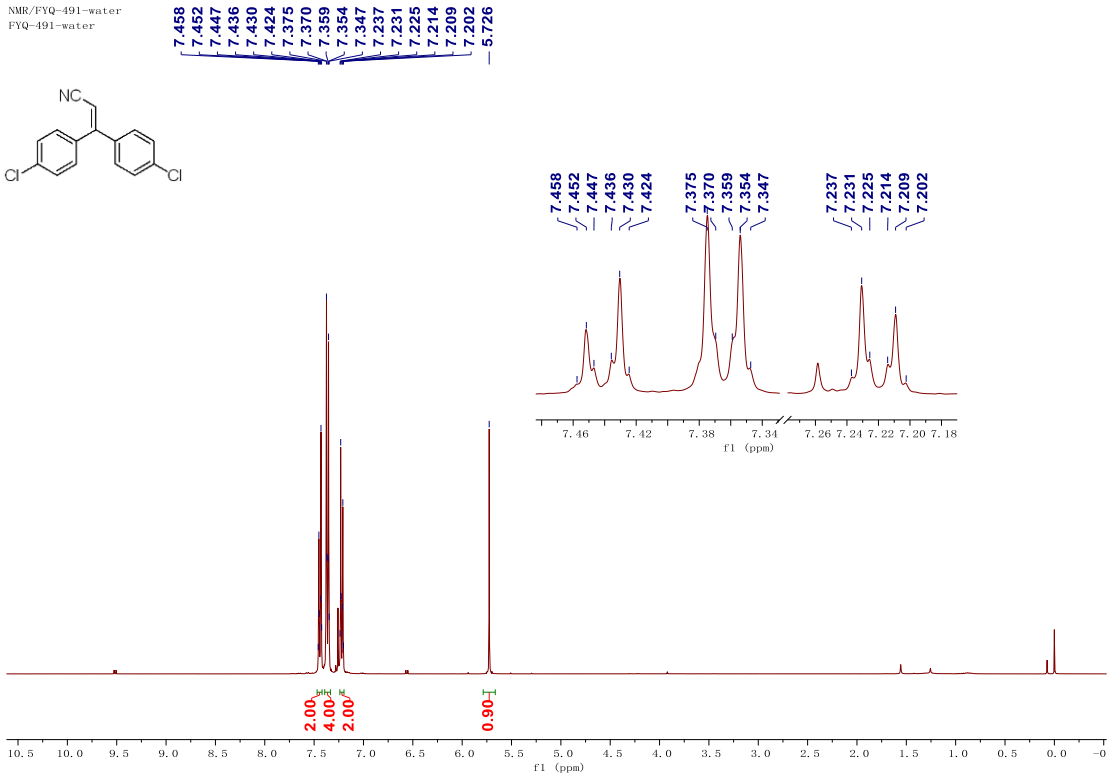


^{19}F NMR (377 MHz, $CDCl_3$)

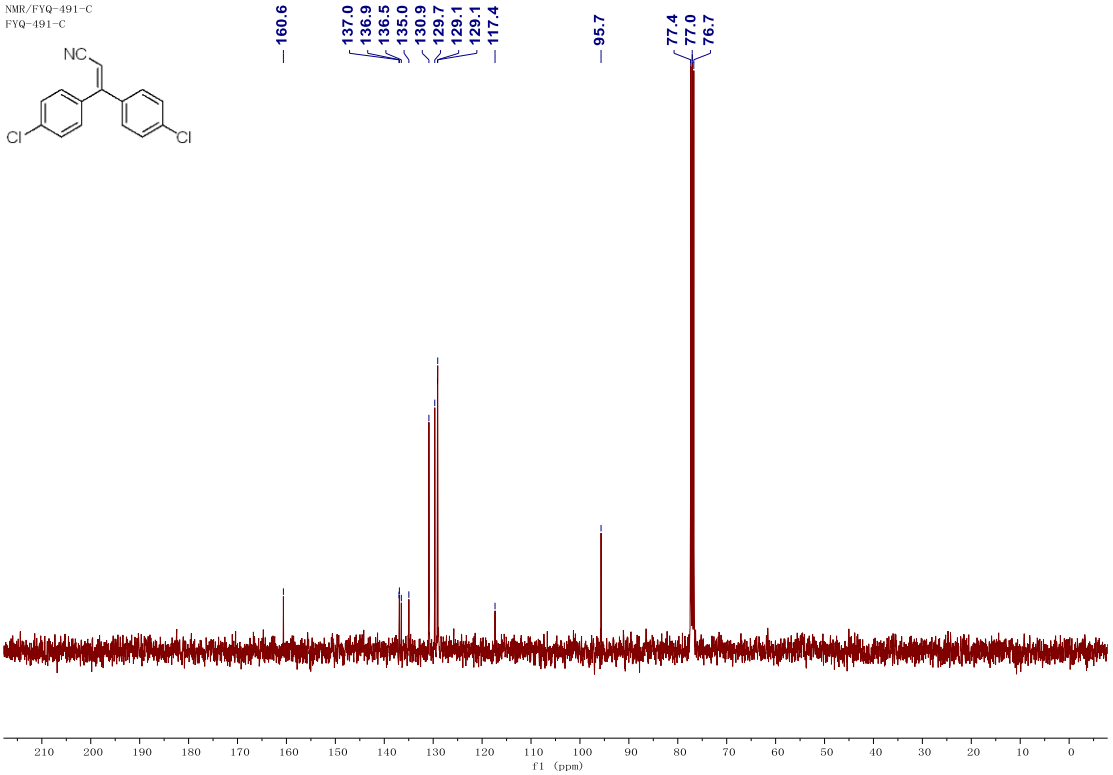


3,3-bis(4-chlorophenyl)acrylonitrile (**2z**)

^{1}H NMR (400 MHz, $CDCl_3$)

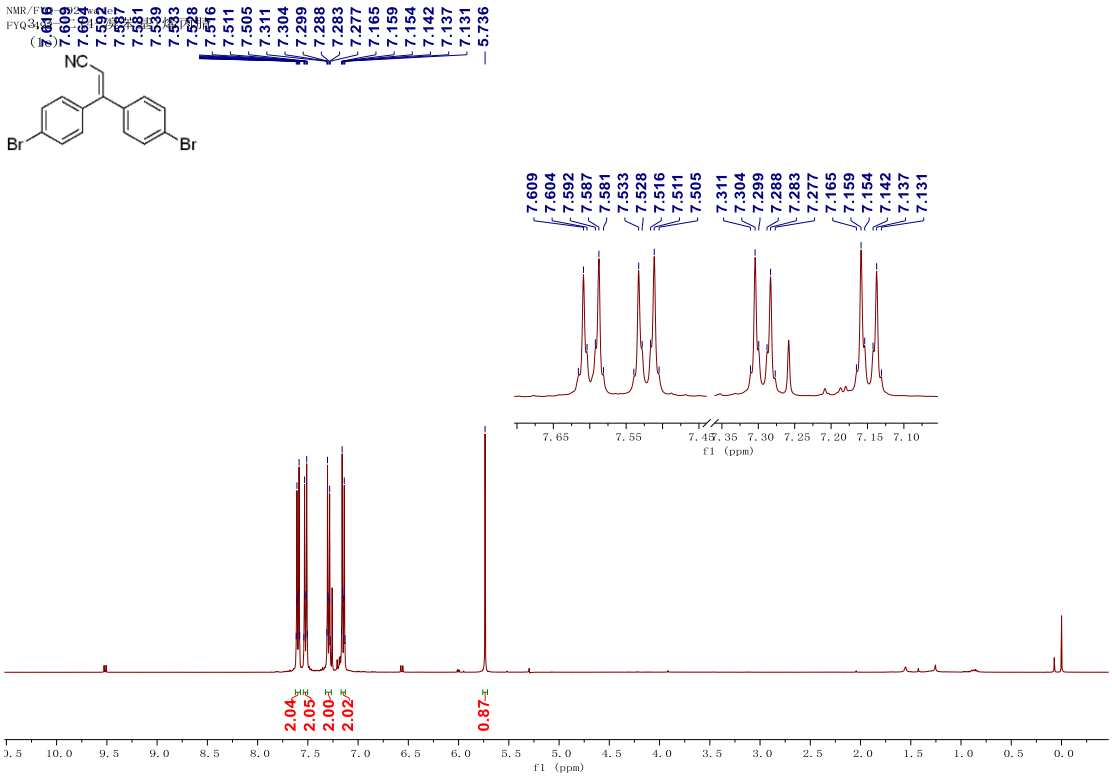


^{13}C NMR (101 MHz, $CDCl_3$)

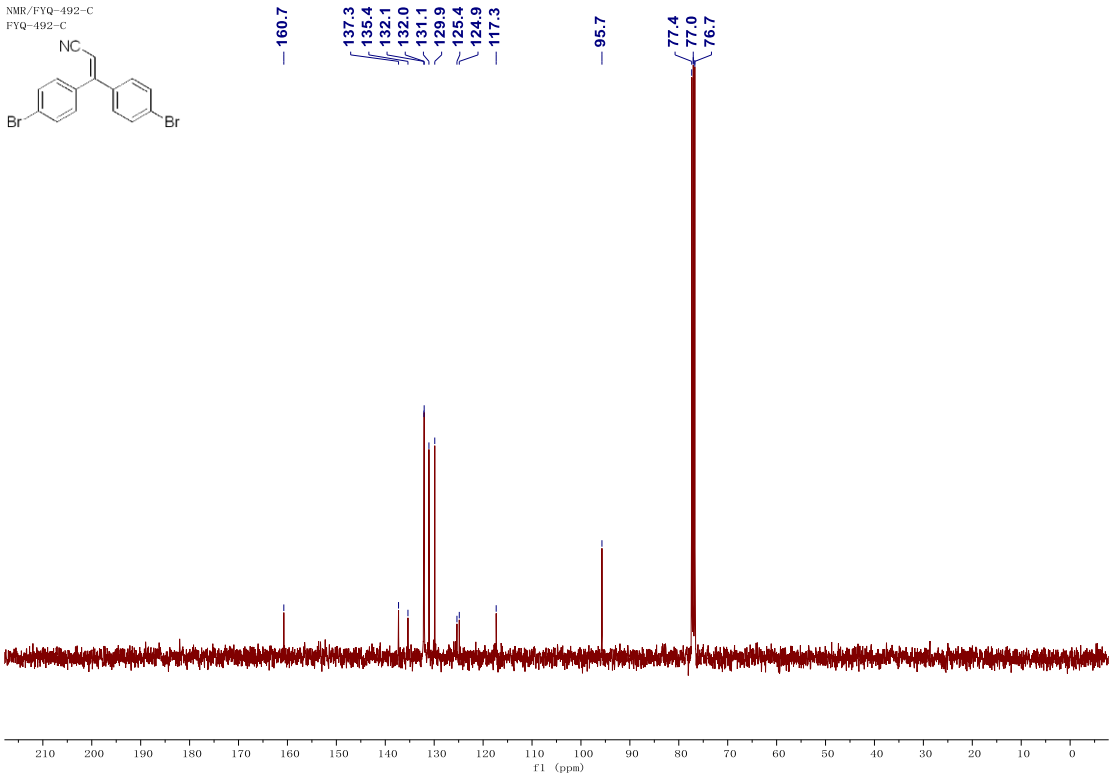


3,3-bis(4-bromophenyl)acrylonitrile (**2aa**)

^{1}H NMR (400 MHz, $CDCl_3$)

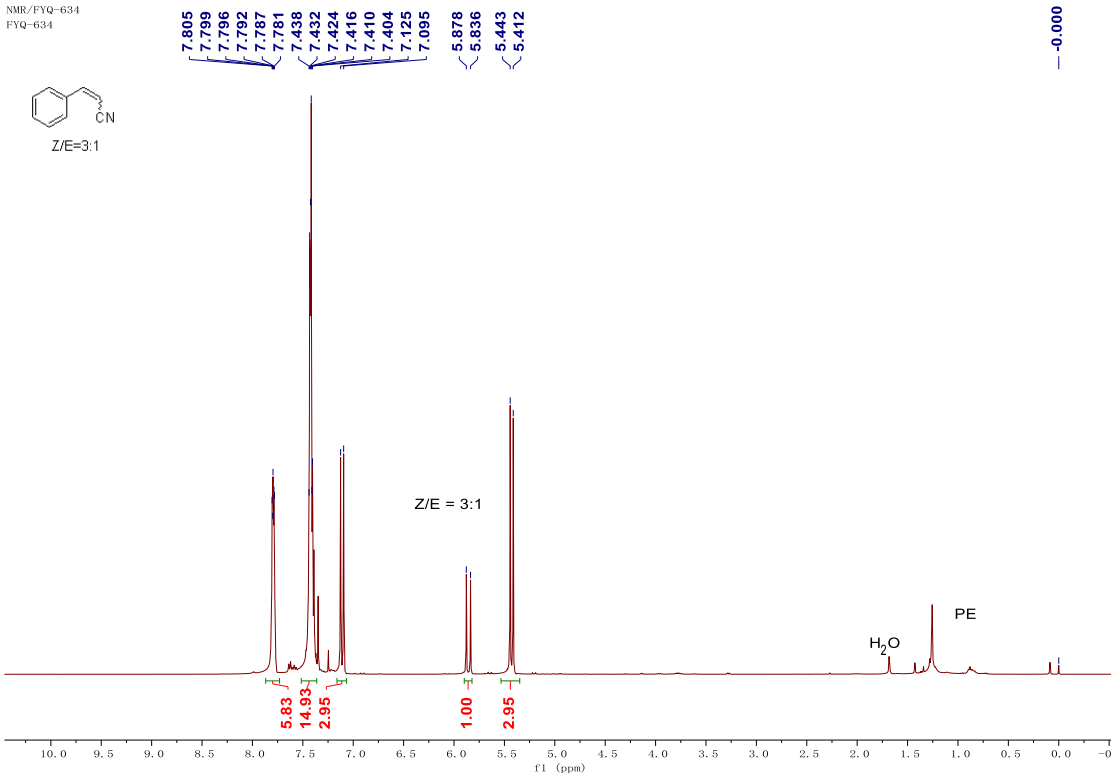


^{13}C NMR (101 MHz, $CDCl_3$)

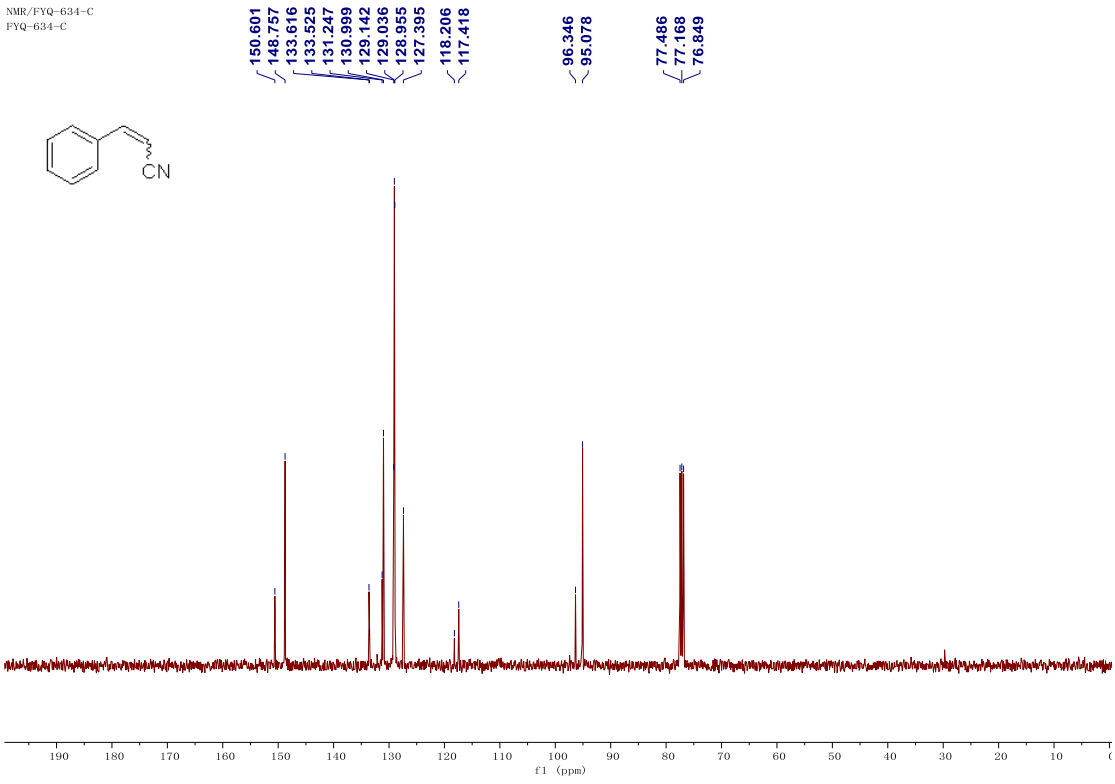


3-phenyl-2-propenenitril (**2ac**):

^{1}H NMR (400 MHz, $CDCl_3$)

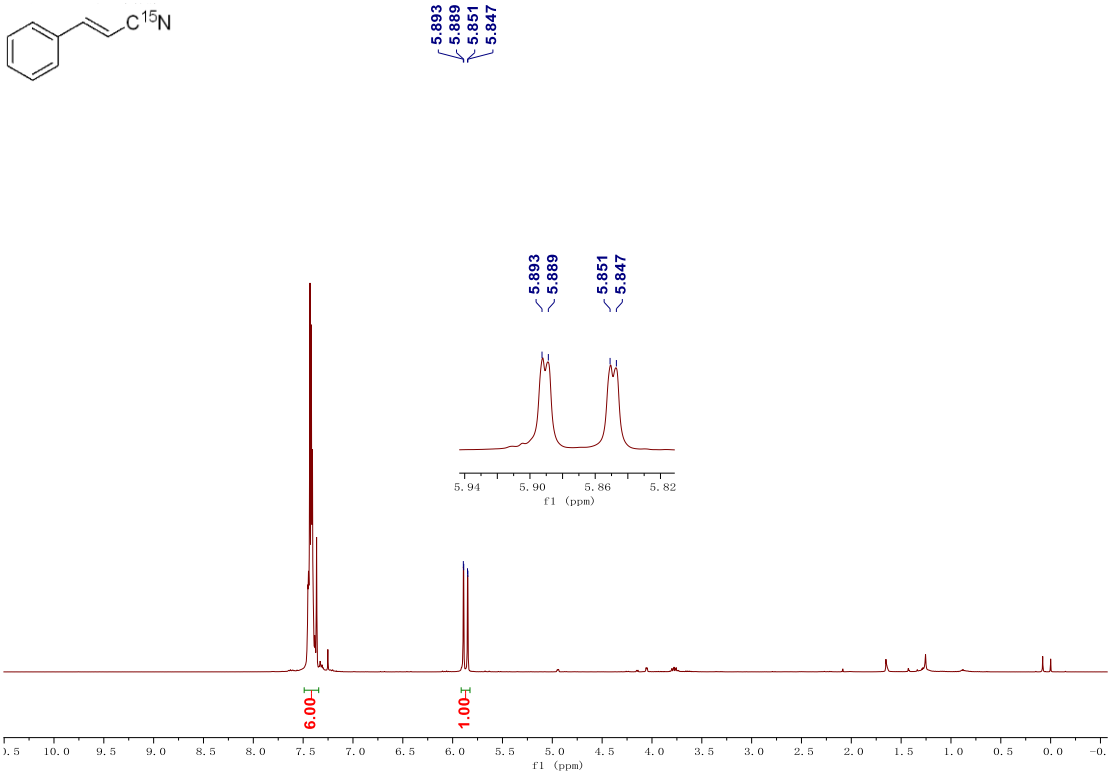


^{13}C NMR (101 MHz, $CDCl_3$)

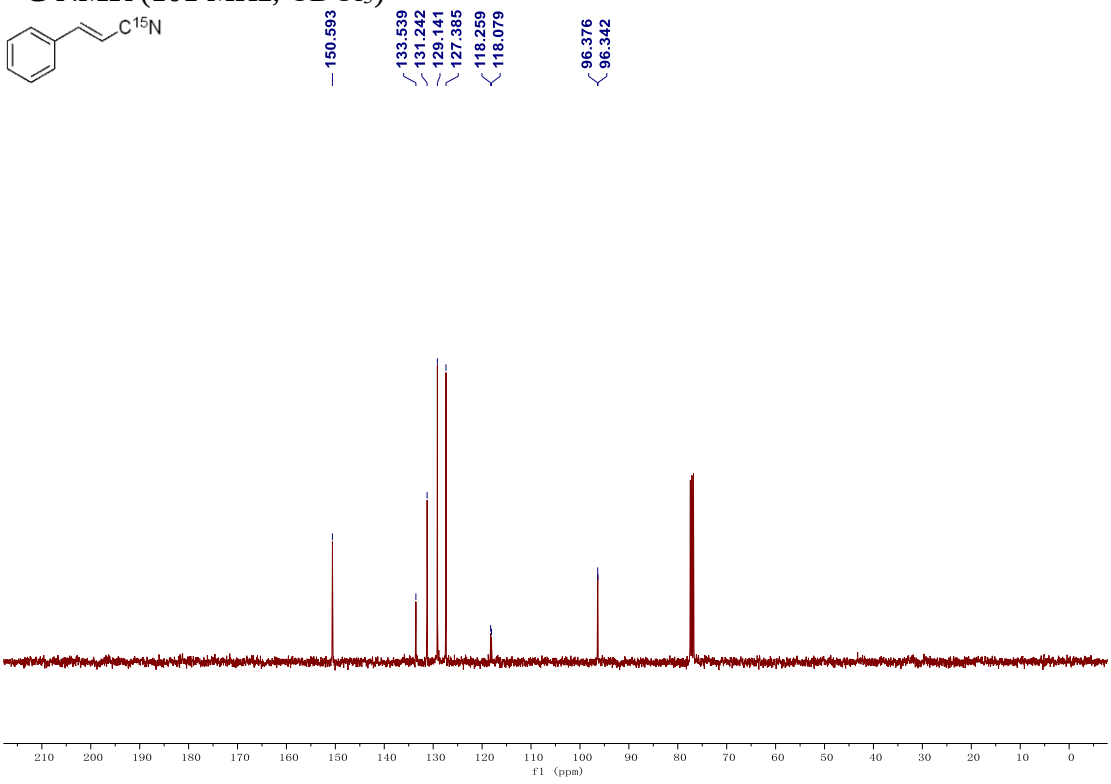


^{15}N-Cinnamonitrile (**2b-N**)

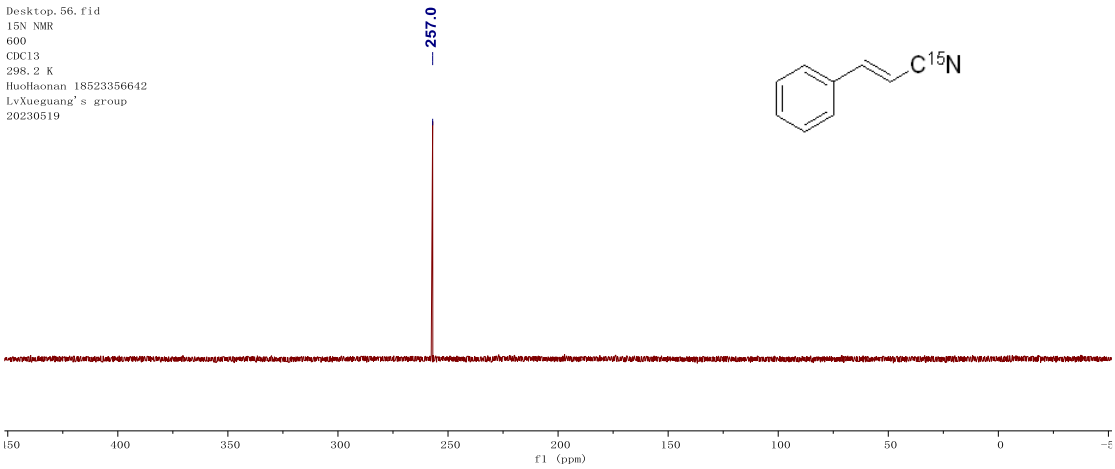
^{1}H NMR (400 MHz, $CDCl_3$)



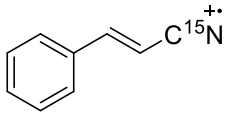
^{13}C NMR (101 MHz, $CDCl_3$)



^{15}N NMR (71 MHz, $CDCl_3$)



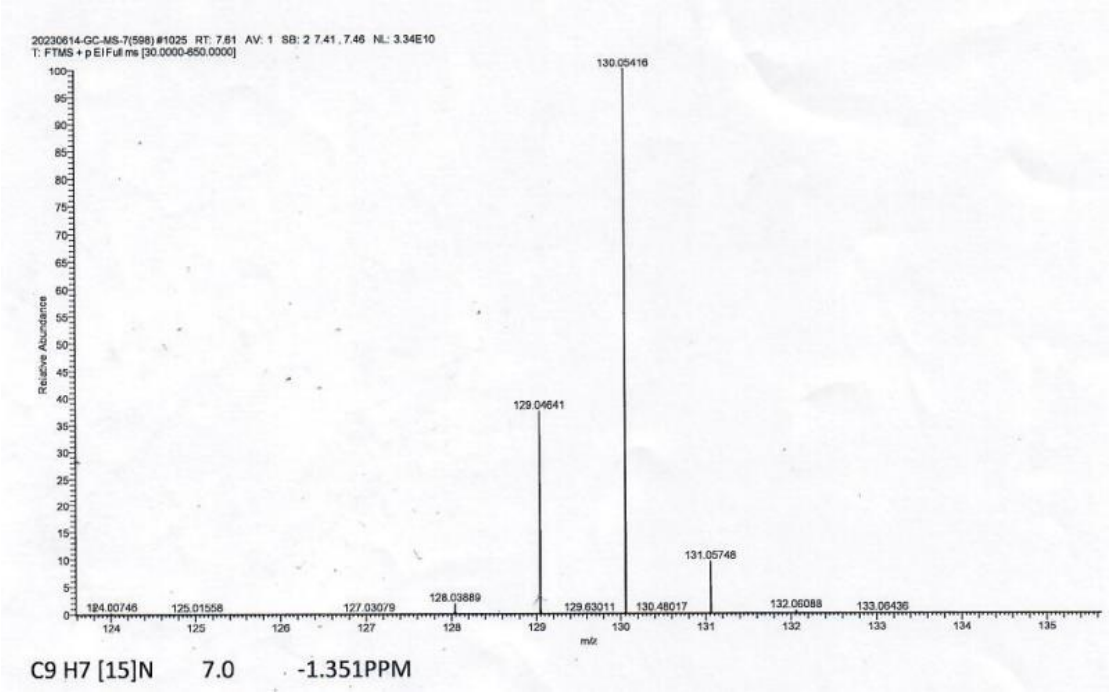
HRMS (EI)



Chemical Formula: $C_9H_7{}^{15}N^{\bullet+}$

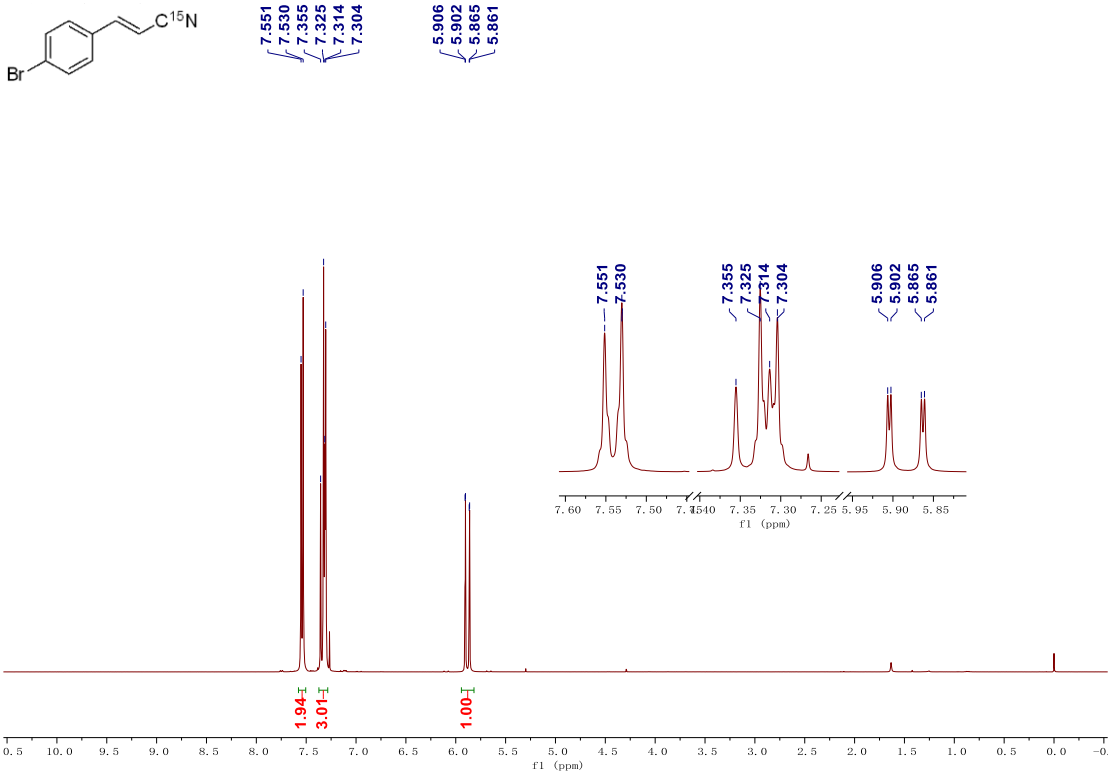
Exact Mass: 130.0543

m/z: 130.0543 (100.0%), 131.0577 (9.7%)

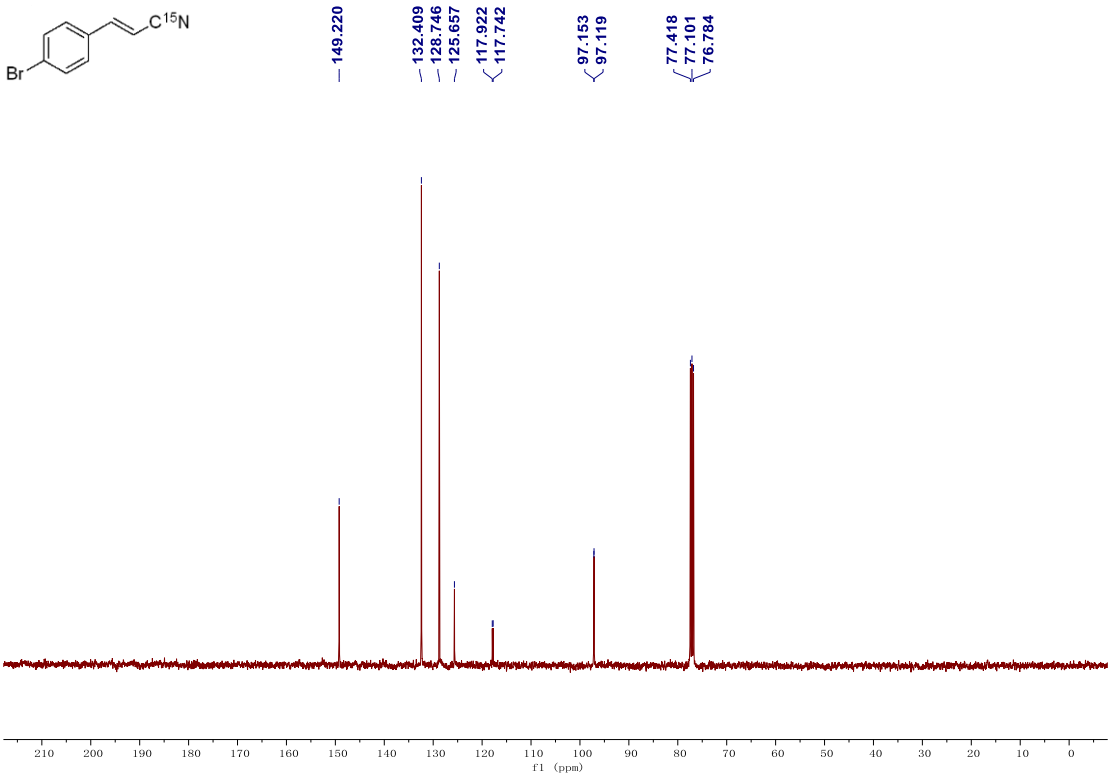


^{15}N-(*E*)-3-(4-bromophenyl)acrylonitrile (**2e-N**):

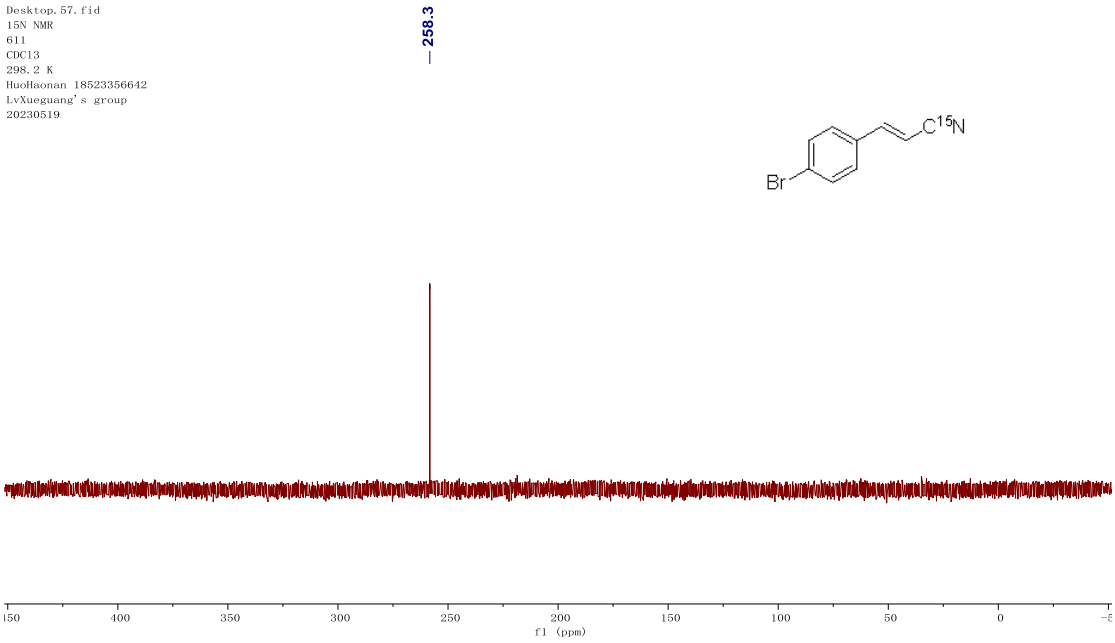
^{1}H NMR (400 MHz, $CDCl_3$)



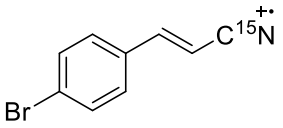
^{13}C NMR (101 MHz, $CDCl_3$)



^{15}N NMR (71 MHz, $CDCl_3$)



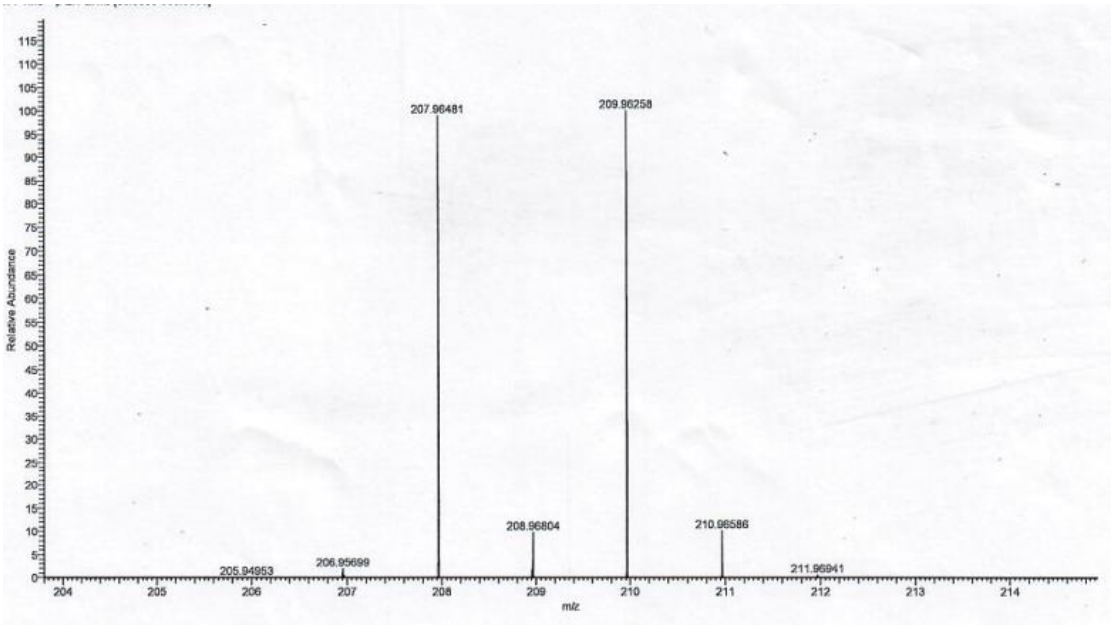
HRMS (EI)



Chemical Formula: $C_9H_6Br^{15}N^{\bullet+}$

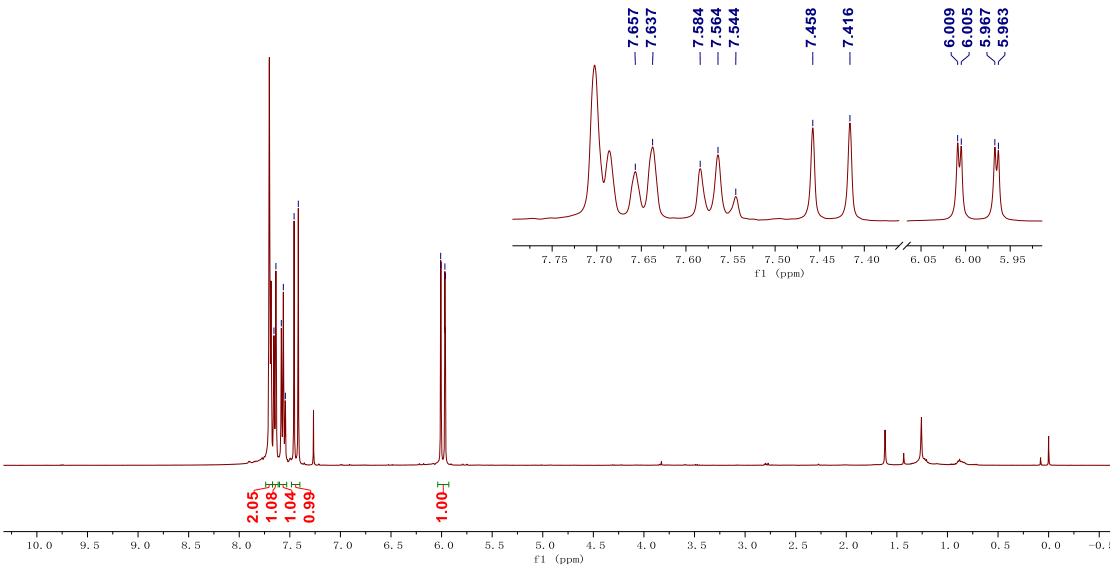
Exact Mass: 207.9648

m/z: 207.9648 (100.0%), 209.9628 (97.3%), 208.9682 (9.7%), 210.9662 (9.5%)

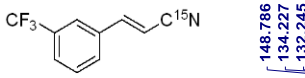


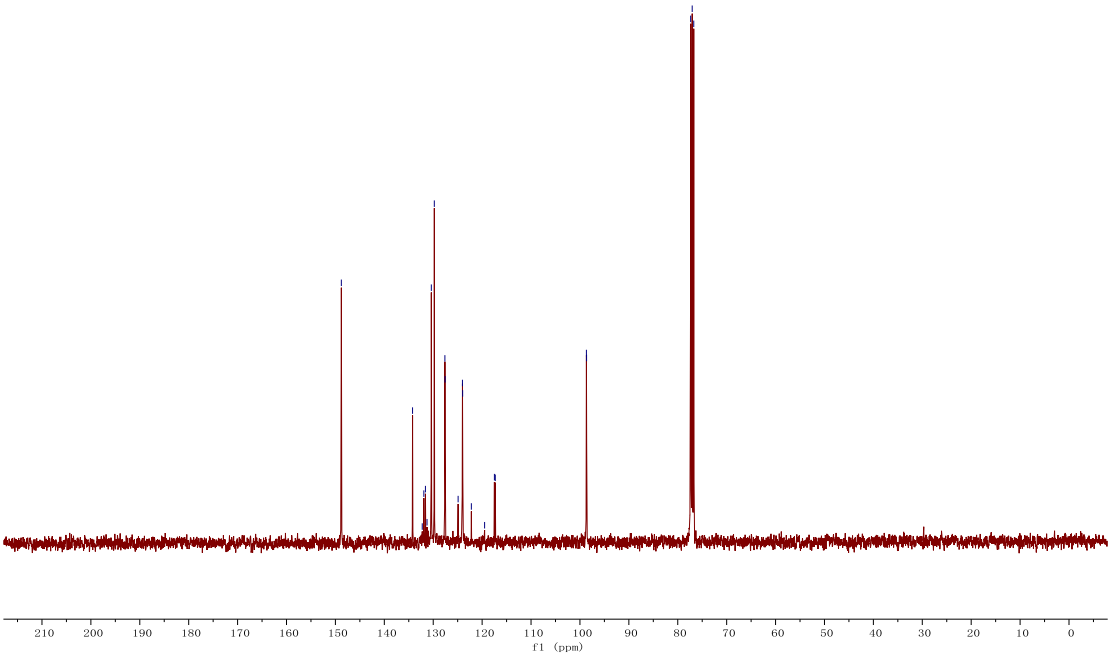
^{15}N-(*E*)-3-(3-(trifluoromethyl)phenyl)acrylonitrile (**2m-N**)

^{1}H NMR (400 MHz, $CDCl_3$)

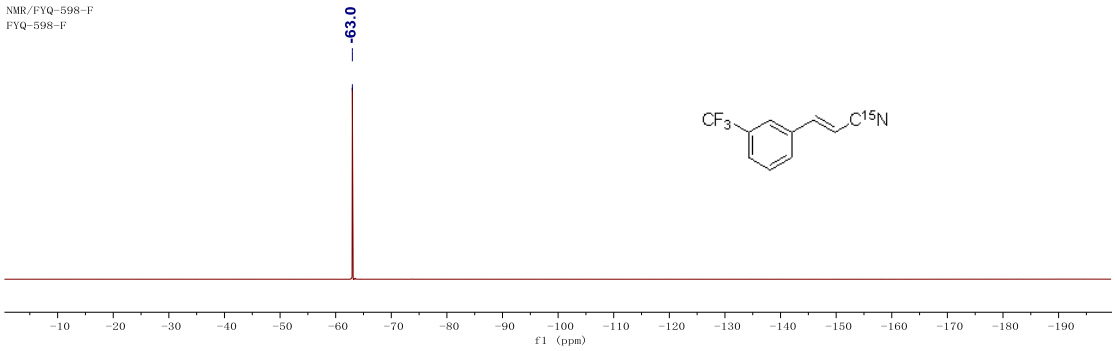


^{13}C NMR (101 MHz, $CDCl_3$)

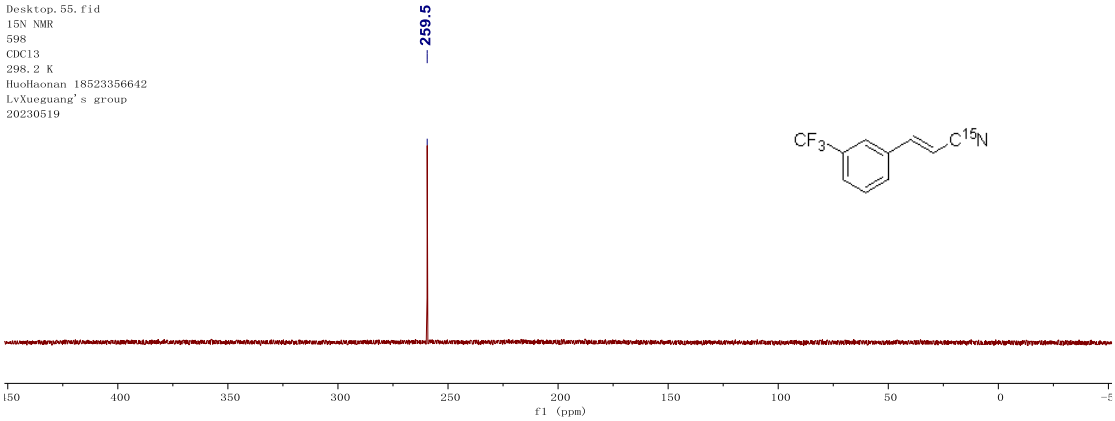




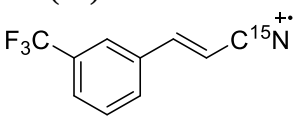
^{19}F NMR (377 MHz, $CDCl_3$)



^{15}N NMR (71 MHz, $CDCl_3$)

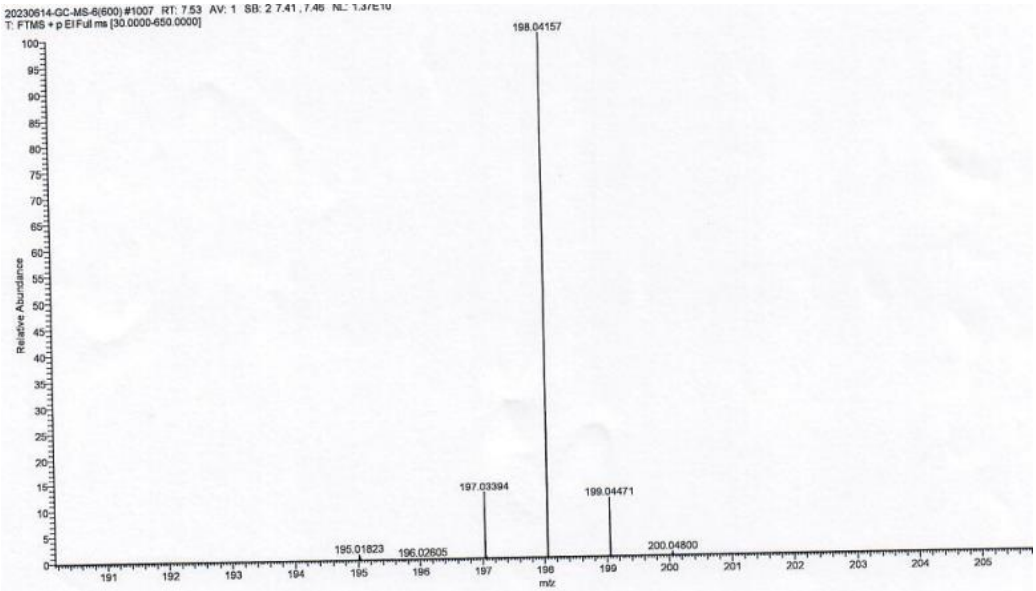


HRMS (EI)



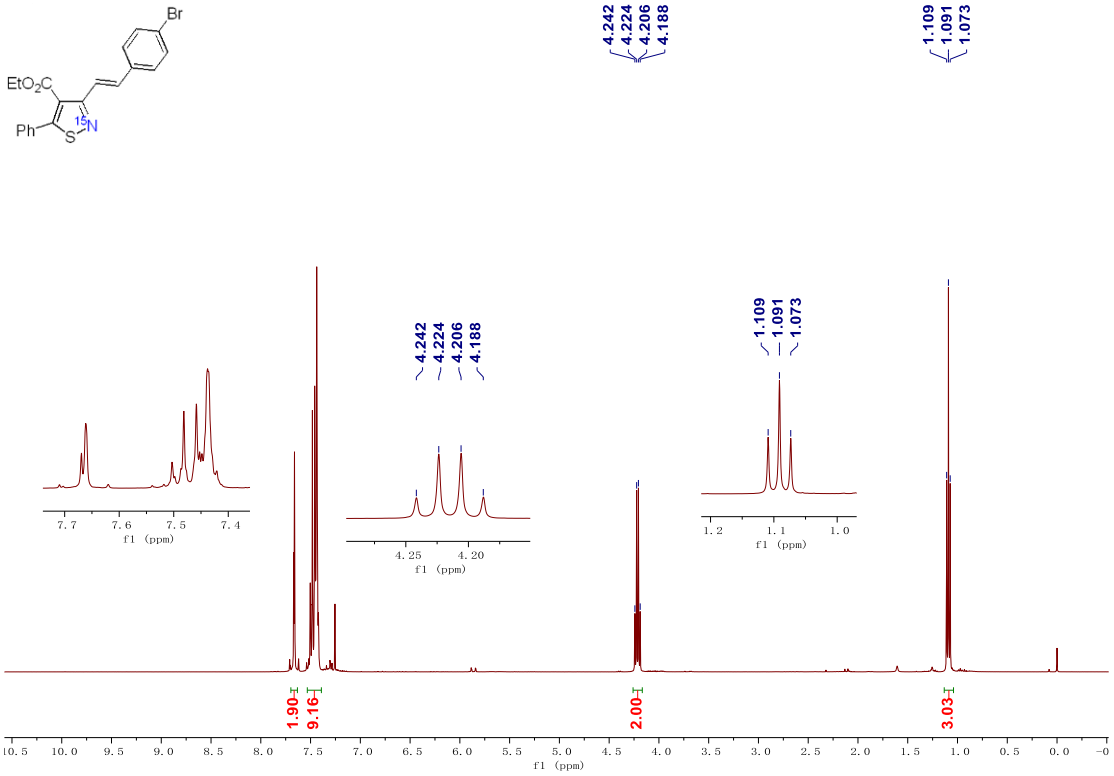
Chemical Formula: $C_{10}H_6F_3{}^{15}N^{\bullet+}$

Exact Mass: 198.0417

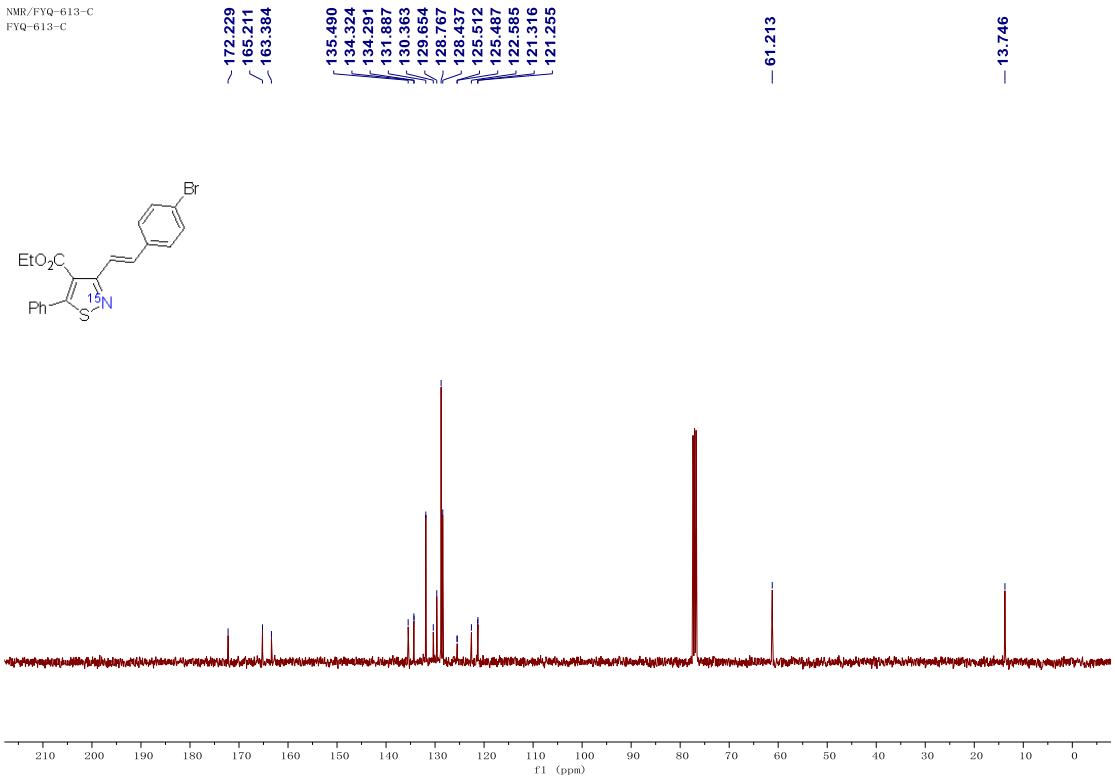


^{15}N-ethyl (E)-3-(4-bromostyryl)-5-phenylisothiazole-4-carboxylate

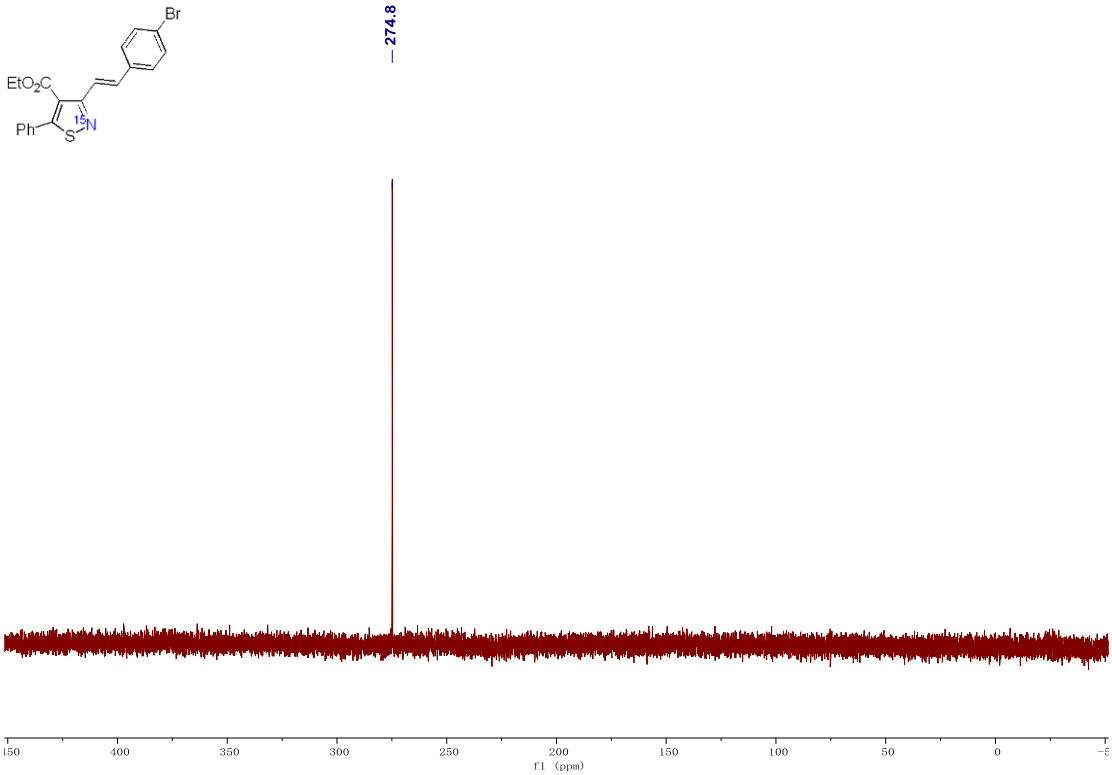
^{1}H NMR (400 MHz, $CDCl_3$)



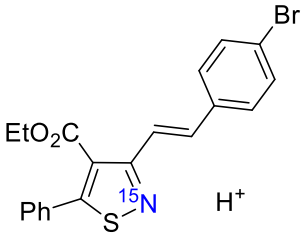
^{13}C NMR (101 MHz, $CDCl_3$)



^{15}N NMR (71 MHz, $CDCl_3$)

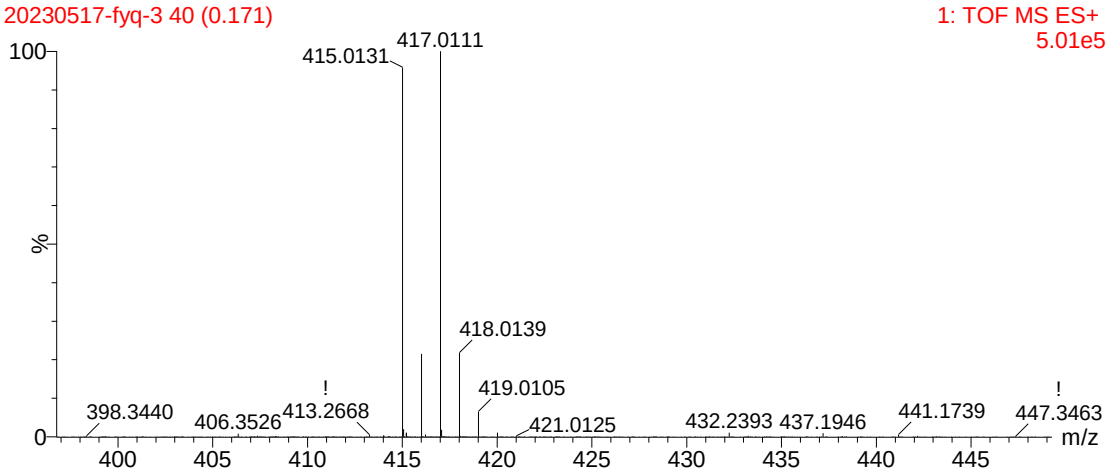


HRMS (ESI)



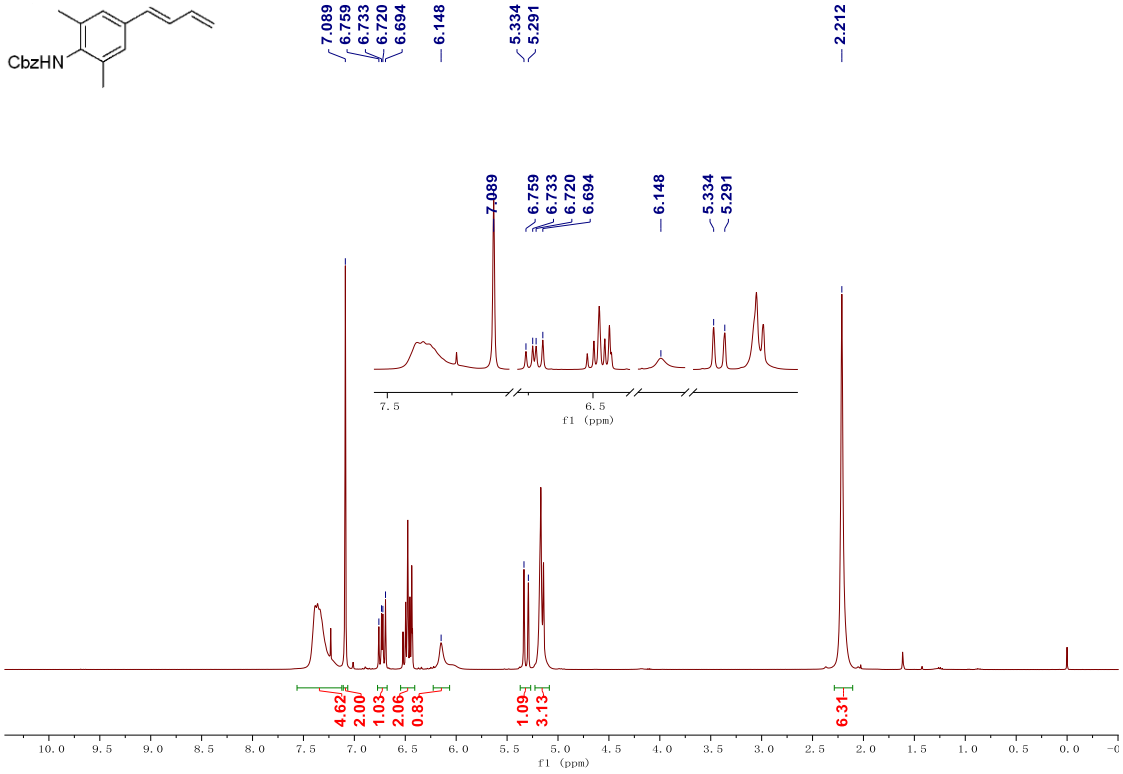
Chemical Formula: $C_{20}H_{17}Br^{15}NO_2S^+$

Exact Mass: 415.0128

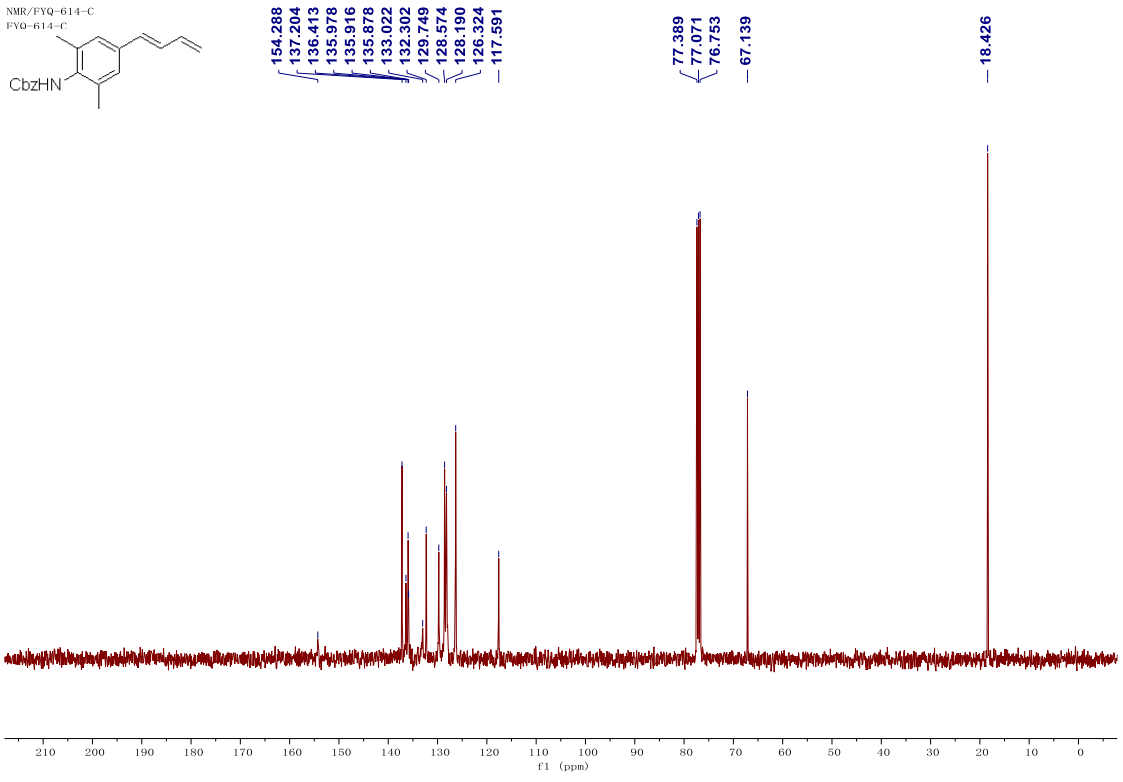


benzyl (E)-(4-(buta-1,3-dien-1-yl)-2,6-dimethylphenyl)carbamate (**6**):

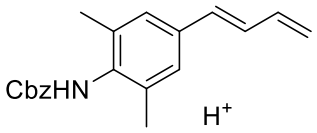
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

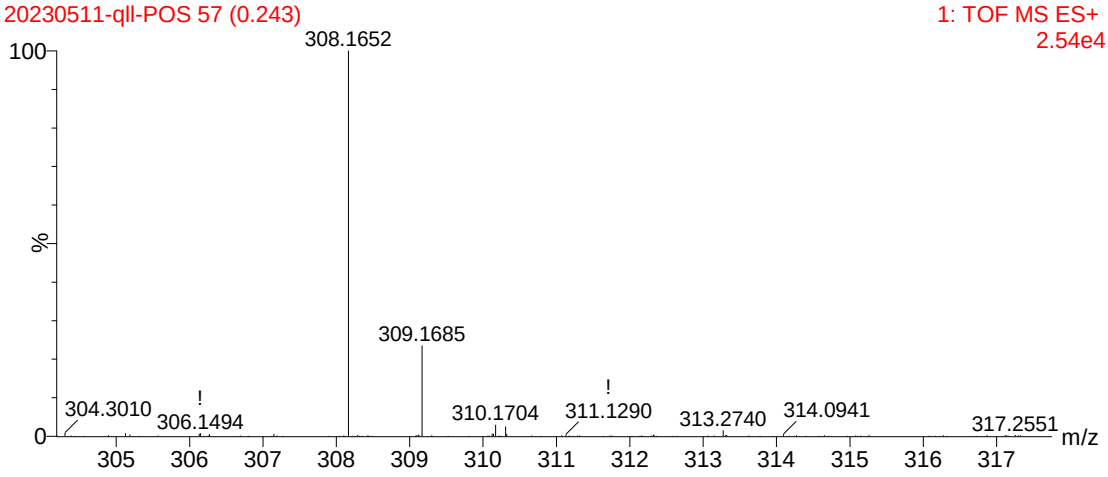


HRMS (ESI)



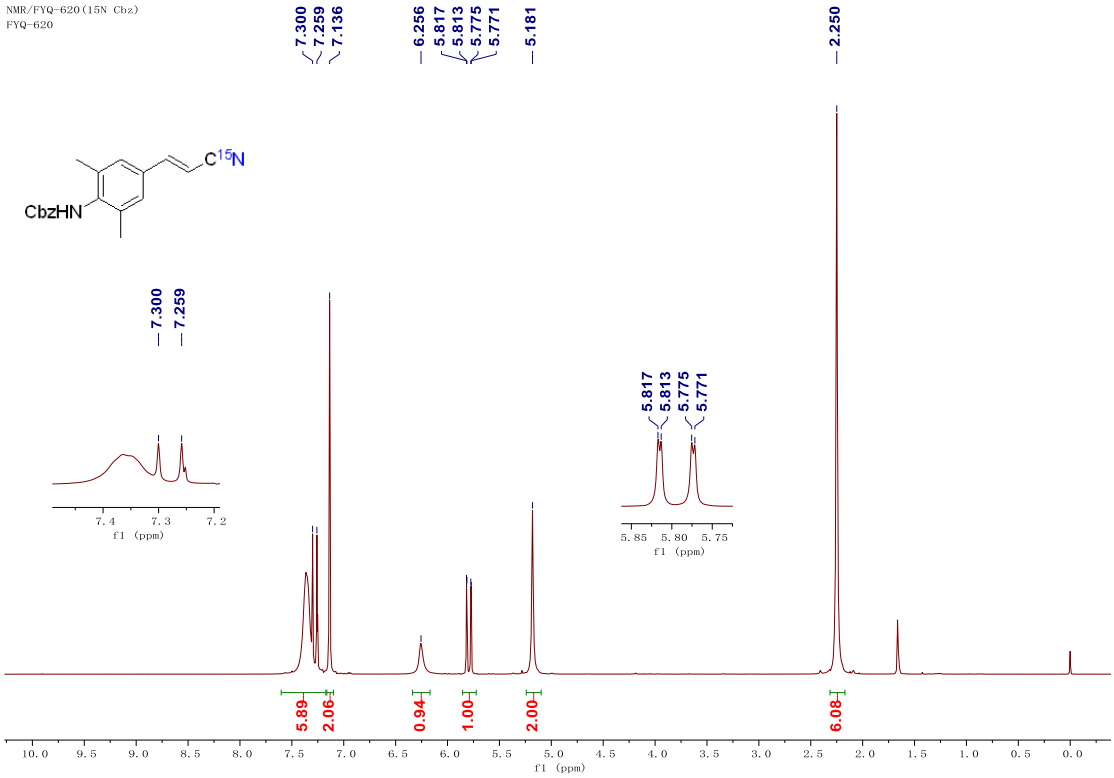
Chemical Formula: $C_{20}H_{22}NO_2^+$

Exact Mass: 308.1645

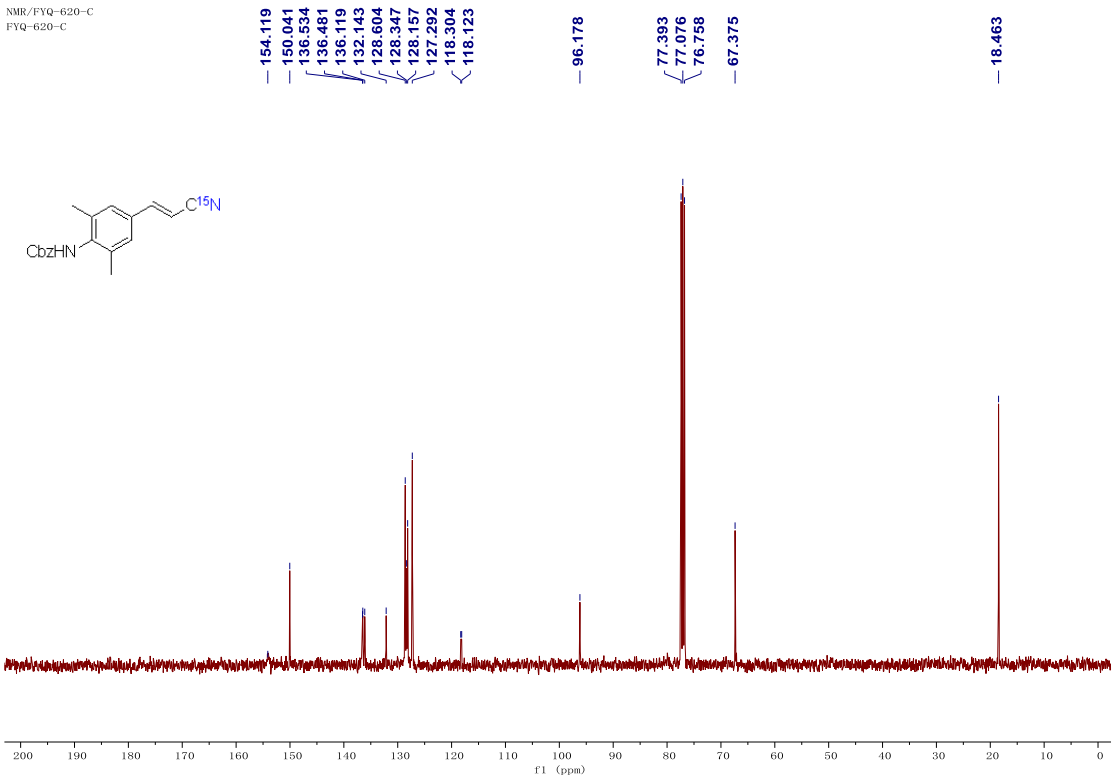


Benzyl (*E*)-(4-(2-(cyano-^{15}N)vinyl)-2,6-dimethylphenyl)carbamate (**7***)

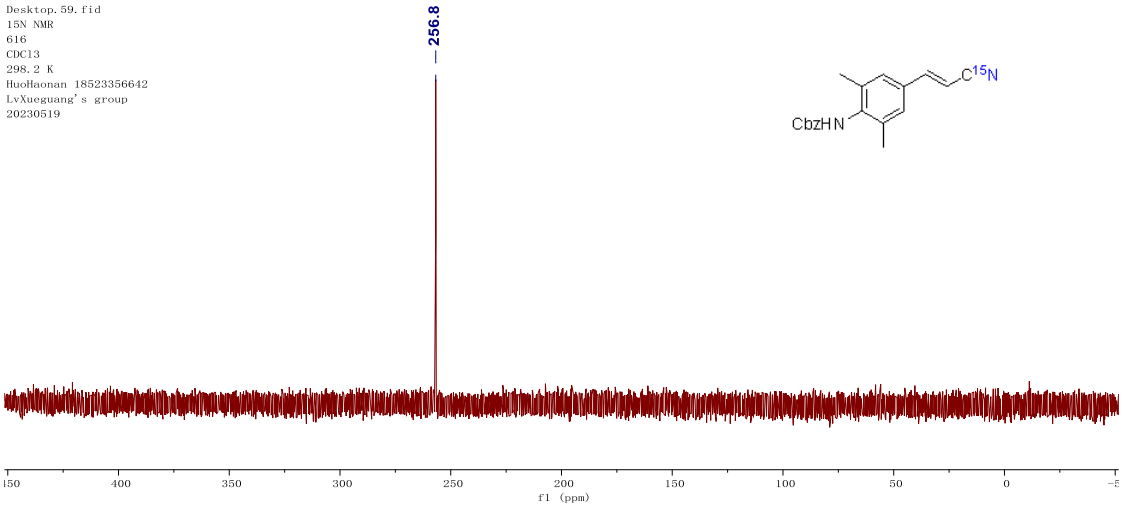
^{1}H NMR (400 MHz, $CDCl_3$)



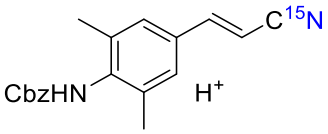
^{13}C NMR (101 MHz, $CDCl_3$)



^{15}N NMR (71 MHz, $CDCl_3$)

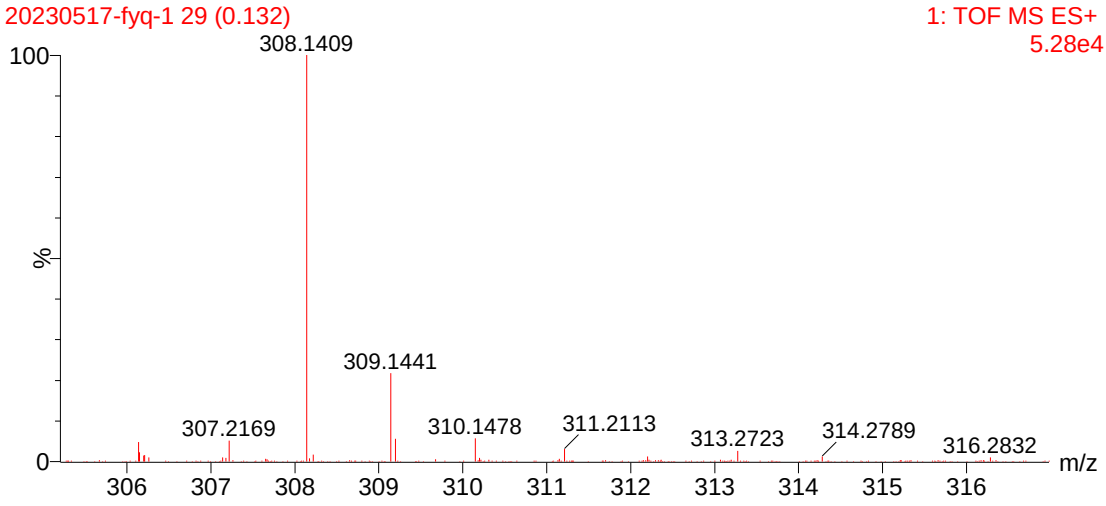


HRMS (ESI)



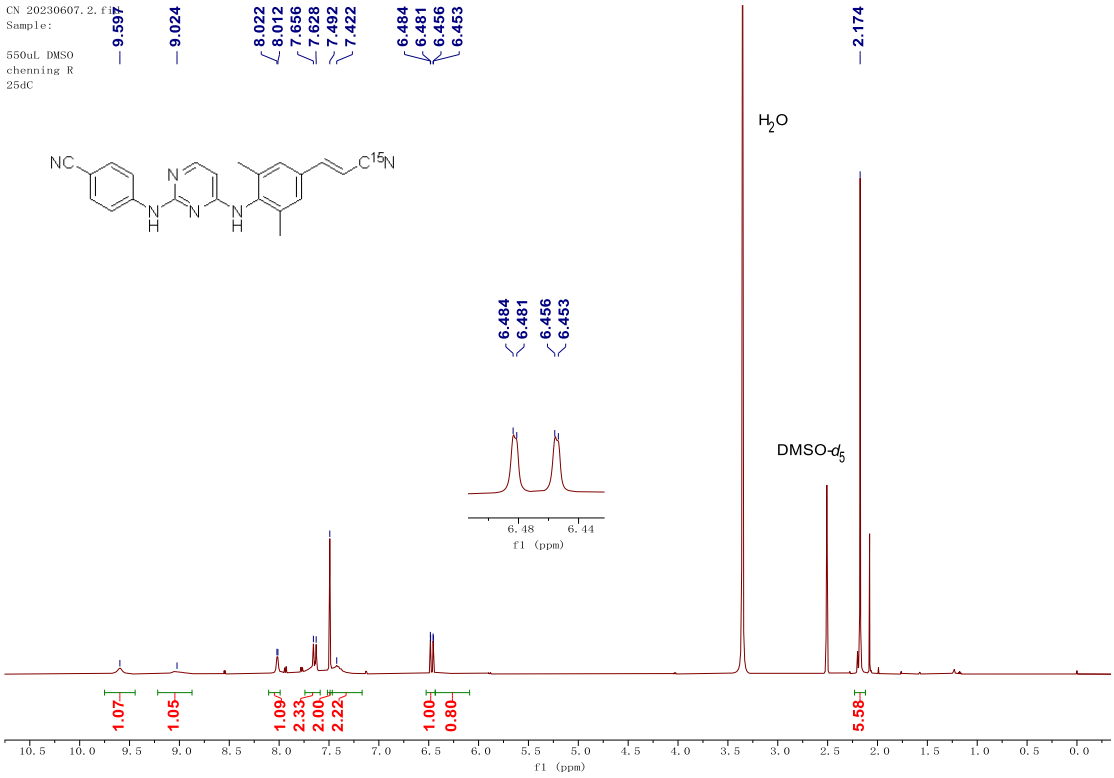
Chemical Formula: $C_{19}H_{19}N^{15}NO_2^+$

Exact Mass: 308.1411

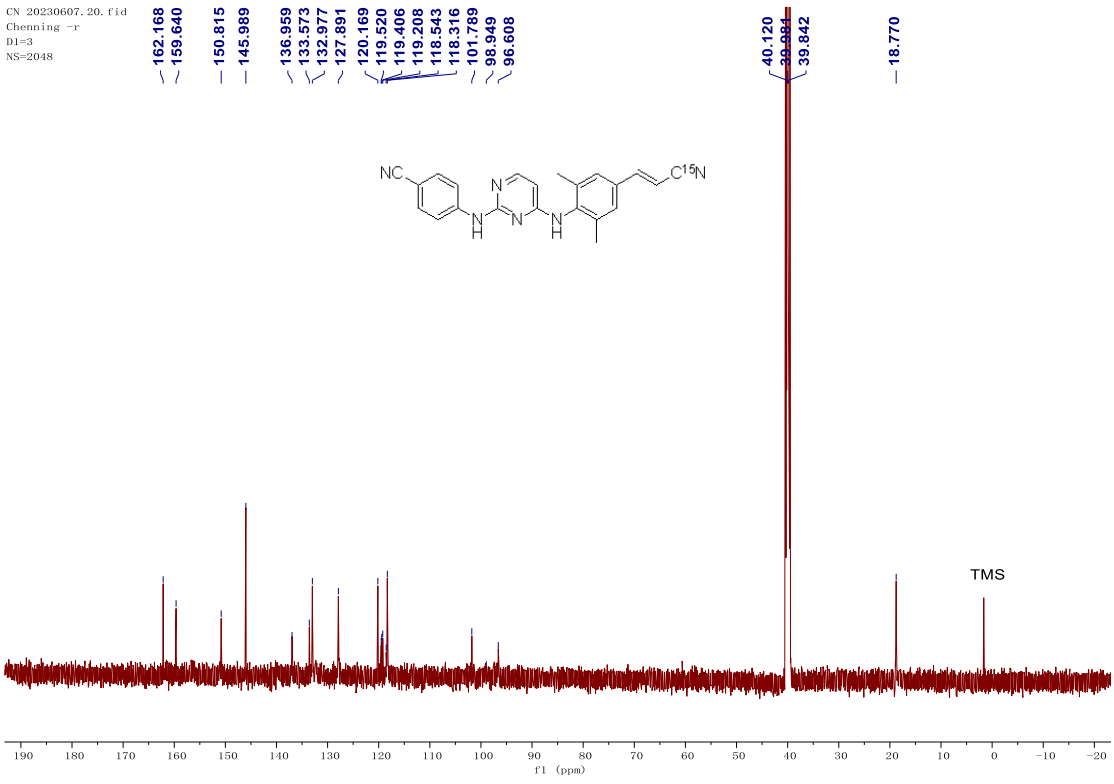


Rilpivirine-15N (**9***)

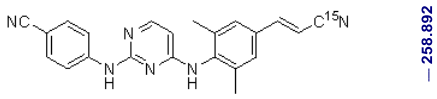
^{1}H NMR (600 MHz, DMSO-d_6)

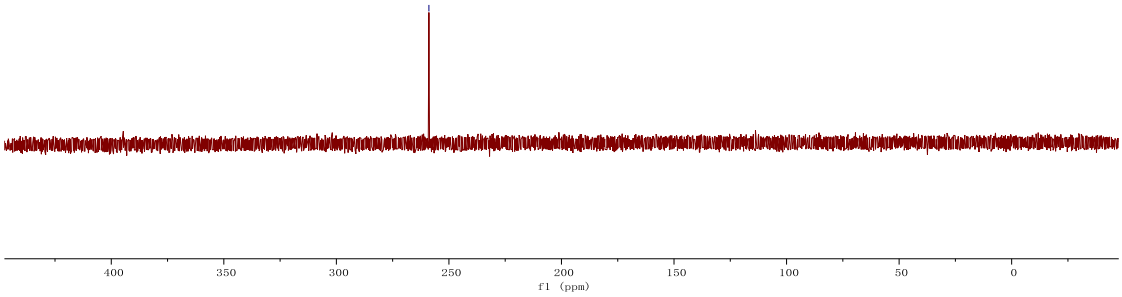


^{13}C NMR (151 MHz, DMSO-d_6)

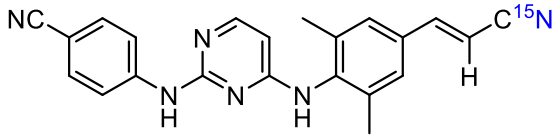


^{15}N NMR (61 MHz, DMSO-d_6)





HRMS (ESI)



***Rilpivirine*-^{15}N (9*)**

HMRS $[M+H]^+$ 368.1636 (calc.)

$[C_{22}H_{19}N_5{}^{15}N^+]$ 368.1639 (found)