Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

NHC-Catalyzed Enantioselective Synthesis of Dihydropyran-4-Carbonitriles bearing All-Carbon Quaternary Centers

Qiuju Wu,[†] Chengcheng Li,[†] Weihong Wang, Hongling Wang, Dingwu Pan, Pengcheng Zheng*

Laboratory Breeding Base of Green Pesticide and Agricultural Bioengineering, Key Laboratory of Green Pesticide and Agricultural Bioengineering Ministry of Education, Guizhou University, Huaxi District, Guiyang 550025, China.

E-mail: zhengpc1986@163.com

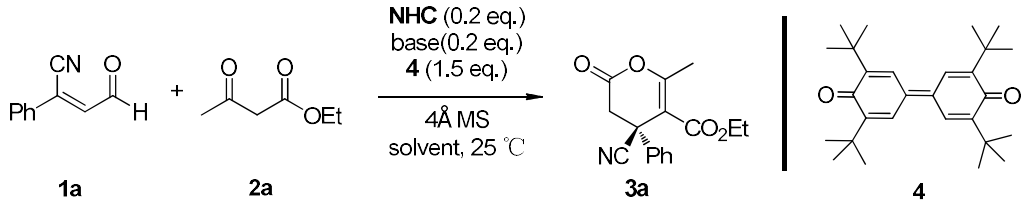
Ⅰ General Information

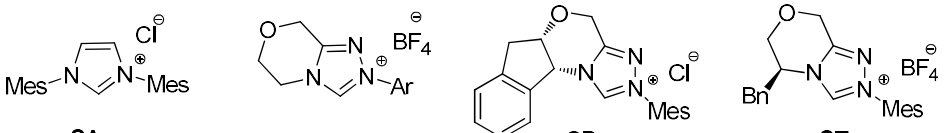
Commercially available materials purchased from Innochem and J&K were used as received. THF was distilled from Na and used directly. Unless otherwise specified, all reactions were carried out under an atmosphere of argon in 10 mL Schlenk tube. NMR spectra were measured either on a Bruker ASCEND 400 (400 MHz) or on a JEOL-ECX-500 (500 MHz) spectrometer. The chemical shift δ values were corrected to 7.26 ppm (^{1}H NMR) and 77.16 ppm (^{13}C NMR) for $CHCl_3$. ^{1}H NMR splitting patterns are designated as singlet (s), double (d), triplet (t), quartet (q), dd (doublet of doublets), m (multiplets), and etc. All first-order splitting patterns were assigned on the base of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). High resolution mass spectrometer analysis (HRMS) was performed on Thermo Fisher Q Exactive mass spectrometer. HPLC analyses were measured on Waters systems with Empower3 system controller, Alliance column heater, and 2998 Diode Array Waters 2489 UV/Vis detector. Chiralcel brand chiral columns from Daicel Chemical Industries were used with models AD-H, or IB in 4.6 x 250 mm size. Absolute configuration of the products was determined by X-ray crystallography. The racemic products used to determine the *er* values were synthesized using racemic catalyst. Optical rotations were measured on a Insmark IP-digi Polarimeter in a 1 dm cuvette at 20˚C. The concentration (c) is given in g/100 mL. Analytical thin-layer chromatography (TLC) was carried out on pre-coated silica gel plate (0.2 mm thickness). Melting Point (MP): Melting points were measured on a Beijing Tech XT-4 micro melting point apparatus and are uncorrected. Visualization was performed with short wave UV light.

Ⅱ General procedure

a) Condition optimization

Table S1. **Screening of NHCs and bases for the reaction of 1a and 2a.**





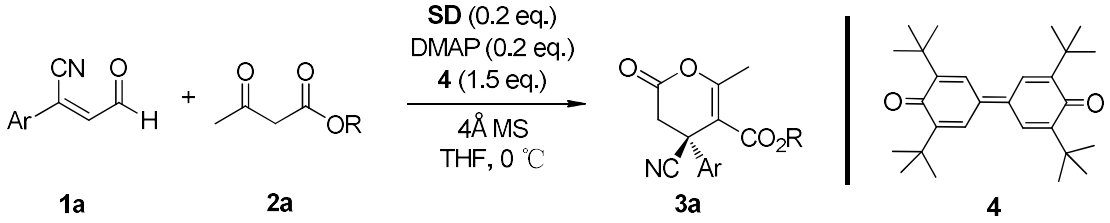
SA SB:Ar=Ph SC:Ar=Mes SD SE

entry	catalyst	base	additive	yield **3a** (%)[b]	er **3a**[c]
1	SA	Cs_2CO_3	-	36	-
2	SB	Cs_2CO_3	-	11	-
3	SC	Cs_2CO_3	-	31	-
4	SD	Cs_2CO_3	-	52	80:20
5	SE	Cs_2CO_3	-	61	86:14
6	SD	Cs_2CO_3	LiCl	82	93:7
7[d]	SD	Cs_2CO_3	$Sc(OTf)_3$	<5%	-
8	SD	Cs_2CO_3	$Mg(OTf)_2$	42	85:15
9	SE	Cs_2CO_3	LiCl	85	90:10
10	SD	K_2CO_3	LiCl	80	92:8
11	SD	KOAc	LiCl	74	94:6
12	SD	DIEA	LiCl	42	94:6
13	SD	Et_3N	LiCl	51	89:11
14	SD	DABCO	LiCl	39	92:8
15	SD	DMAP	LiCl	89	94:6
16	SD	DBU	LiCl	55	93:7

17	SD	-	LiCl	81	93:7
18[e]	SD	DMAP	LiCl	25	88:12
19[f]	SD	DMAP	LiCl	56	91:9
20[g]	SD	DMAP	LiCl	90	97:3

[a] 1.5 Equiv. **1a**, 1 equiv. **2a** (0.1 mmol), 20 mol% NHC, 20 mol% base, 1 eq of additive, 1.5 eq of **4**, 2 mL THF, RT, 18 h. [b] Yields were isolated yields after column chromatography. [c] e.r. was determined via HPLC using a chiral stationary phase. [d] 0.2 0.2 Equiv. of additive was used. [e] With DCM instead of THF. [f] With 1,4 dioxane instead of THF. [g] The reactions were performed at 0 ℃.

b) General procedure for the catalytic reactions of aldehydes (1) with 1,3-dicarbony compounds (2) to synthesize product 3:



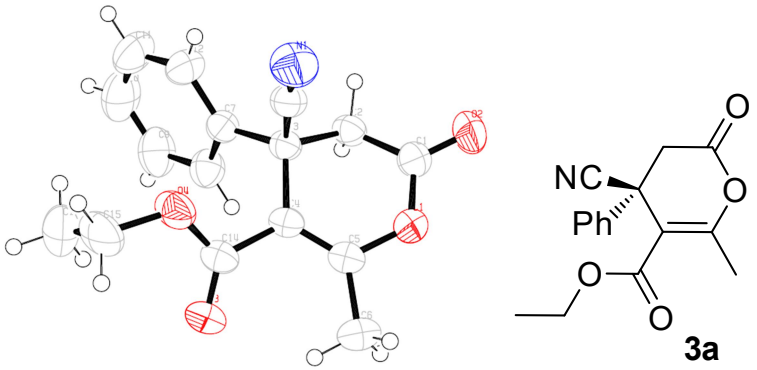
To a dry Schlenk tube equipped with a magnetic stir bar, was added aldehydes **1** (0.15 mmol), 1,3-dicarbonyl compounds **2** (0.10 mmol), triazolium salt **SD** (0.02 mmol), and DMAP (0.02 mmol). The tube was closed with a septum, evacuated, and refilled with nitrogen. Freshly distilled THF (2 mL) was added and the reaction mixture was then stirred at 0 ℃ till **2** was completely consumed (monitored by TLC). The mixture was concentrated under reduced pressure. The resulting crude residue was purified *via* column chromatography on silica gel (6:1 petroleum ether/EtOAc) to afford the desired product **3**, which was confirmed by ^{1}H NMR, ^{13}C NMR spectrum, and enantio ratio was determined by chiral HPLC.

Note: NHC **F** was prepared according to literature procedure.[1]

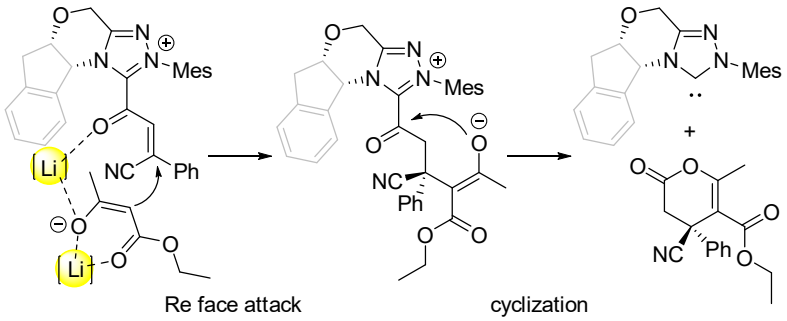
c) Stereochemistry determination 3a *via* X-ray crystallographic analysis

Product **3a** was crystallized as a colorless crystal *via* vaporization of a petrollium

ether/ethyl acetate solution, and its absolute configuration was determined by x-ray structure analysis. CCDC 1559727 contains the supplementary crystallographic data that can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data request/cif.

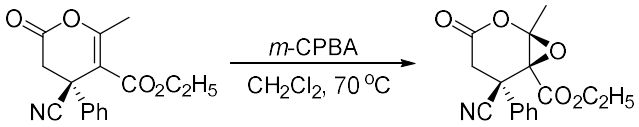


d) Proposed reaction mechanism for chirality control.



The formation of the acylazolium intermediate has been well demonstrated in literatures.[2] LiCl has good affinities for carbonyl oxygens and carboxylates. It is likely involved in multisite coordination to activate the β-ketoester electrophile through formation of a cyclic enolate intermediate and bring the electrophile to close proximity with the acylium intermediate. After enantioselective Re face attack and intramolecular lacton formation, the desired product could be afforded and the catalyst was released for another catalytic cycle.

e) Synthetic transformations of catalytic reaction products 3a



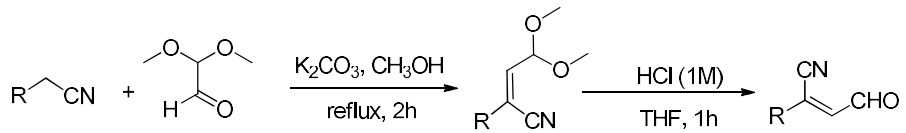
3a
97:3 e.r.

5a, 55%
95:5 e.r., 1:1 d.r.

To a solution of **1a** (28.6 mg, 0.1 mmol) in CH_2Cl_2 (1.5 mL) was added *m*-CPBA (55%, 221.0 mg, 0.7 mmol). After 48 h of stirring at 70 °C, the solution was cooled down to room temperature. A known quantity (12.8 mg) of 1,3,5-trimethoxybenzene was added as an internal standard, and a part of the mixture was analyzed by ^{1}H NMR spectroscopy in $CDCl_3$.

III. Characterizations of substrates and products, reference

a) Preparations and characterizations of substrates



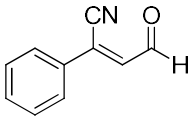
S1 **S2** **S3** **1**

To a stirred suspension of substituted phenyl acetonitrile **S1** (20 mmol, 1.0 eq) and glyoxal dimethyl acetal **S2** (2.51 g, 3.62 mL, 24.0 mmol, 1.20 eq, 60% aq. soln) in MeOH (50 mL), K_2CO_3(4.15 g, 30.0 mmol, 1.50 eq) was added at rt. The mixture was heated to reflux for 2 h. Cooling to rt and poured water (70 mL) into the mixture. The mixture was extracted with EA (3× 60 mL), the combined organic layers were washed with brine and dried over Na_2SO_4.The residual solvents were removed under reduced pressure to afford the product (Z)-4,4-dimethoxy-2-phenylbut-2-enenitrile as colorless liquid without further purification.

To a stirred suspension of (Z)-4,4-dimethoxy-2-phenylbut-2-enenitrile in THF (50 mL) was added 1N HCl (50 mL). The mixture was stirred at rt for 1h until material completion as judged by TLC. The mixture was extracted with EA (3× 50 mL). The organic layers were washed with brine and treated with anhydrous Na_2SO_4. The

solvent was evaporated and the product (Z)-4-oxo-2-phenylbut-2-enenitrile were purified by flash chromatography (Petroleum ether /EtOAc, 20:1) to afford the substrate as solid.

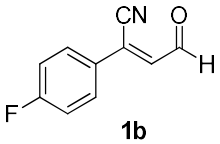
(*Z*)-4-oxo-2-phenylbut-2-enenitrile (1a)



1a

Light yellow solid, yield: 1.41 g (45%). **^{1}H NMR** (400 MHz, CDCl3): δ=10.25 (d, *J* = 7.6 Hz, 1H), 7.79 – 7.76 (m, 2H), 7.60 – 7.50 (m, 3H), 7.06 (d, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, CDCl3): δ=190.11, 135.99, 132.77, 131.60, 130.69, 129.64, 127.11, 114.09.

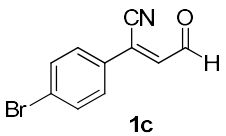
(*Z*)-2-(4-fluorophenyl)-4-oxobut-2-enenitrile (1b)



1b

Yellow solid, yield:1.56 g (44%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.23 (d, *J* = 7.6 Hz, 1H), 7.79 (dd, *J* = 9.0, 5.0 Hz, 2H), 7.26 – 7.20 (m, 2H), 7.00 (d, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=189.93, 165.31 (d, *J* = 256.3 Hz), 135.71 (d, *J* = 2.4 Hz), 130.37, 126.91 (d, *J* = 3.4 Hz), 117.17, 116.94, 113.96.

(*Z*)-2-(4-bromophenyl)-4-oxobut-2-enenitrile (1c)

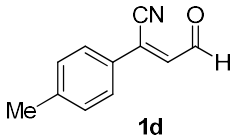


1c

Yellow solid, yield:2.23 g (47%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ=10.24 (d, *J* = 7.5 Hz, 1H), 7.65 (dd, *J* = 21.3, 8.2 Hz, 4H), 7.05 (d, *J* = 7.5 Hz, 1H); **^{13}C NMR** (125

MHz, $CDCl_3$): δ=189.93, 136.19, 133.05, 130.50, 129.66, 128.49, 127.81, 113.82.

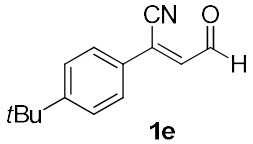
(*Z*)-4-oxo-2-(p-tolyl)but-2-enenitrile (1d)



1d

Yellow solid, yield: 1.80 g (52%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.22 (d, *J* = 7.7 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.32 (d, *J* = 8.1 Hz, 2H), 7.02 (d, *J* = 7.7 Hz, 1H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=190.27, 143.92, 134.86, 131.62, 130.37, 127.95, 127.10, 114.21, 21.64.

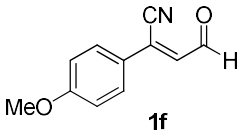
(*Z*)-2-(4-(tert-butyl)phenyl)-4-oxobut-2-enenitrile (1e)



1e

Brown solid, 2.5 g (48%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.24 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.54 (d, *J* = 8.7 Hz, 2H), 7.04 (d, *J* = 7.7 Hz, 1H), 1.36 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=190.31, 156.96, 134.97, 131.57, 127.89, 127.03, 126.68, 114.20, 35.23, 31.03.

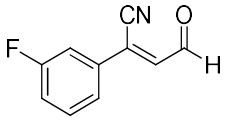
(*Z*)-2-(4-methoxyphenyl)-4-oxobut-2-enenitrile (1f)



1f

Yellow solid, yield: 3.15 g (84%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ=10.20 (d, *J* = 7.9 Hz, 1H), 7.77 – 7.69 (m, 2H), 7.06 – 6.97 (m, 2H), 6.94 (d, *J* = 7.8 Hz, 1H), 3.90 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=190.33, 163.49, 133.45, 131.28, 129.13, 123.21, 115.17, 114.35, 55.78.

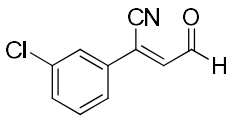
(*Z*)-2-(3-fluorophenyl)-4-oxobut-2-enenitrile (1g)



1g

Yellow solid, 0.82 g (23%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ=10.25 (d, *J* = 7.5 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.53 (td, *J* = 8.0, 5.6 Hz, 1H), 7.48 – 7.43 (m, 1H), 7.29 (dd, *J* = 8.1, 2.5 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=189.87, 164.16, 162.17, 136.96, 132.78, 131.49, 130.34, 123.07, 119.89, 113.97.

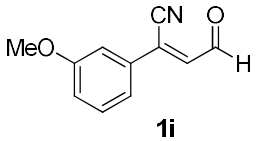
(*Z*)-2-(3-chlorophenyl)-4-oxobut-2-enenitrile (1h)



1h

Brown solid, 1.10 g (28%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.25 (d, *J* = 7.5 Hz, 1H), 7.74 (t, *J* = 1.8 Hz, 1H), 7.66 (ddd, *J* = 7.7, 1.8, 1.1 Hz, 1H), 7.55 (ddd, *J* = 8.0, 1.9, 1.1 Hz, 1H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=189.67, 136.95, 135.94, 132.65, 132.41, 130.87, 130.05, 127.00, 125.25, 113.69 .

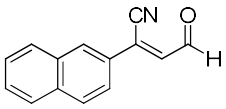
(*Z*)-2-(3-methoxyphenyl)-4-oxobut-2-enenitrile (1i)



1i

Yellow solid, yield:0.50 g (13%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ=10.25 (d, *J* = 6.3 Hz, 1H), 7.47 – 7.34 (m, 2H), 7.26 – 7.23 (m, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.04 (d, *J* = 6.1 Hz, 1H), 3.88 (s, 3H); **^{13}C NMR** (125 MHz,$CDCl_3$): δ=190.26, 160.38, 136.23, 132.02, 131.59, 130.78, 119.66, 118.66, 114.19, 112.24, 55.65.

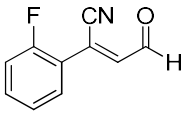
(*Z*)-2-(naphthalen-2-yl)-4-oxobut-2-enenitrile (1j)



1j

The title compound was prepared according to the general procedure on 10 mmol scale. Yellow solid, yield: 1.15 g(55%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.29 (d, *J* = 7.6 Hz, 1H), 8.33 (s, 1H), 8.00 – 7.86 (m, 3H), 7.70 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.62 (m, 2H), 7.14 (d, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=190.15, 135.65, 135.03, 132.91, 131.52, 129.71, 129.57, 129.33, 129.00, 127.95, 127.72, 121.70, 114.19.

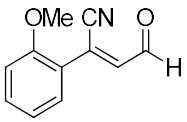
(*Z*)-2-(2-fluorophenyl)-4-oxobut-2-enenitrile (1k)



1k

Light yellow solid, 0.56 g (16%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ=10.28 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.78 (t, *J* = 7.8 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.34 (t, *J* = 7.7 Hz, 1H), 7.26 – 7.21 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=190.52, 160.72 (d, *J* = 257.0 Hz), 140.57 (d, *J* = 13.4 Hz), 134.00 (d, *J* = 9.4 Hz), 130.48, 126.40, 125.31 (d, *J* = 3.6 Hz), 119.24 (d, *J* = 9.8 Hz), 117.24 (d, *J* = 22.1 Hz), 113.71.

(*Z*)-2-(2-methoxyphenyl)-4-oxobut-2-enenitrile (1l)

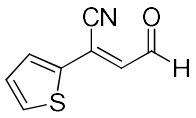


1l

Yellow solid, yield: 1.05 g (28%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.27 (d, *J* = 7.9 Hz, 1H), 7.69 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.50 (ddd, *J* = 8.9, 7.5, 1.6 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 7.09 (td, *J* = 7.7, 1.0 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 1H), 3.95 (s, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ=191.66, 158.39, 139.84, 133.54, 130.79, 129.12, 121.33, 120.05, 114.50, 111.95, 55.82.

(*E*)-4-oxo-2-(thiophen-2-yl)but-2-enenitrile (1m)

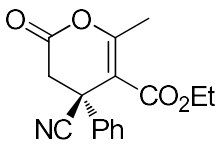


1m

Brown solid, yield: 1.35 g (38%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ=10.14 (d, *J* = 7.6 Hz, 1H), 7.71 (dd, *J* = 3.8, 0.9 Hz, 1H), 7.62 (dd, *J* = 5.1, 1.0 Hz, 1H), 7.20 (dd, *J* = 5.1, 3.8 Hz, 1H), 6.81 (d, *J* = 7.6 Hz, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=189.38, 136.19, 132.85 (d, *J* = 3.8 Hz), 132.22, 129.22, 125.08, 113.20.

b) Characterizations of products

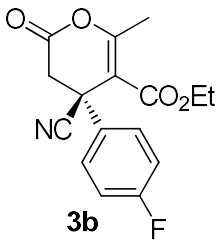
(*R*)-ethyl-4-cyano-6-methyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (3a)



3a

White solid, yield: 25.8 mg (90%); mp: 90-91 ℃; $[\alpha]_D^{20}$=26.5 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.44 – 7.35 (m, 5H), 4.08 – 3.98 (m, 2H), 3.31 (d, *J* = 15.9 Hz, 1H), 3.09 (d, *J* = 15.9 Hz, 1H), 2.48 (s, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.99, 162.22, 161.35, 137.02, 129.58, 128.98, 124.82, 119.03, 107.81, 61.51, 43.00, 42.79, 18.86, 13.48; **HRMS** (ESI) calcd for $C_{16}H_{16}NO_4(M+H)^+$: 286.1073, Found: 286.1070; 97:3 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 16.98 min, t_r (major) = 22.76min.

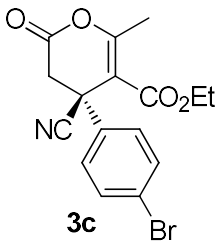
(*R*)-ethyl-4-cyano-4-(4-fluorophenyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3b)



3b

White solid, yield: 26.4 mg (87%); mp: 85-86 ℃; $[\alpha]_D^{20}$=38.3 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.39 (dd, *J* = 8.8, 4.8 Hz, 2H), 7.11 (t, *J* = 8.5 Hz, 2H), 4.24 – 3.88 (m, 2H), 3.32 (d, *J* = 15.8 Hz, 1H), 3.08 (d, *J* = 15.9 Hz, 1H), 2.48 (s, 3H), 1.03 (t, *J* = 7.1 Hz, 3H).; **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.83, 163.73, 162.36, 161.15, 132.71, 126.88 (d, *J* = 8.4 Hz), 118.94, 116.62 (d, *J* = 22.3 Hz), 107.58, 61.65, 42.77, 42.49, 18.93, 13.60; **HRMS** (ESI) calcd for $C_{16}H_{15}FNO_4$ $(M+H)^+$: 304.0979, Found: 304.0978; 96:4 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 15.25 min, t_r (major) = 20.59min.

(*R*)-ethyl-4-(4-bromophenyl)-4-cyano-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3c)

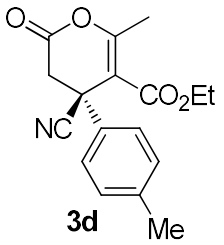


3c

Yellow solid, yield: 23.1 mg (63%); mp: 51-52 ℃; $[\alpha]_D^{20}$= 46.7 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.55 (d, *J* = 8.8 Hz, 2H), 7.28 (d, *J* = 8.8 Hz, 2H), 4.28 – 3.76 (m, 2H), 3.31 (d, *J* = 15.9 Hz, 1H), 3.06 (d, *J* = 15.9 Hz, 1H), 2.48 (s, 3H), 1.04 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.83, 162.72, 161.10, 136.19,

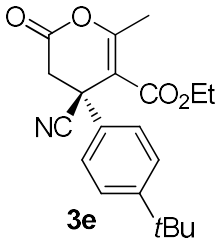
132.85, 126.72, 123.29, 118.77, 107.36, 61.81, 42.81, 42.57, 19.06, 13.71; **HRMS** (ESI) calcd for $C_{16}H_{15}BrNO_4$ $(M+H)^+$: 364.0184, Found: 364.0181; 96:4 *er* as determined by HPLC (Daicel Chralcel IB, 80:20 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 12.40 min, t_r (major) = 26.82 min.

(*R*)-ethyl-4-cyano-6-methyl-2-oxo-4-(p-tolyl)-3,4-dihydro-2H-pyran-5-carboxylat e (3d)



White solid, yield: 23.3 mg (78%); mp: 84-85℃; $[\alpha]_D^{20}$= 28.5 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.27 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.5 Hz, 2H), 4.32 – 3.78 (m, 2H), 3.29 (d, *J* = 15.8 Hz, 1H), 3.07 (d, *J* = 15.9 Hz, 1H), 2.47 (s, 3H), 2.35 (s, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=164.07, 161.95, 161.54, 138.98, 133.85, 130.17, 124.73, 119.21, 107.92, 61.52, 42.84, 42.68, 21.01, 18.85, 13.55; **HRMS** (ESI) calcd for $C_{17}H_{18}NO_4$ $(M+H)^+$: 300.1230, Found: 300.1232; 97:3 *er* as determined by HPLC (Daicel Chralcel IB, 80:20 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 10.33 min, t_r (major) = 24.09min.

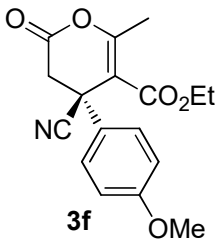
(*R*)-ethyl-4-(4-(tert-butyl)phenyl)-4-cyano-6-methyl-2-oxo-3,4-dihydro-2H-pyran -5-carboxylate (3e)



White solid, yield: 34.1 mg (88%); mp: 104-105 ℃; $[\alpha]_D^{20}$= 32.4 (c 1.0, $CHCl_3$); **^{1}H**

NMR (500 MHz, $CDCl_3$): δ=7.41 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 4.14 – 3.94 (m, 2H), 3.30 (d, *J* = 15.9 Hz, 1H), 3.10 (d, *J* = 15.9 Hz, 1H), 2.46 (s, 3H), 1.30 (s, 9H), 0.94 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=164.10, 161.88, 161.61, 152.16, 133.74, 126.45, 124.58, 119.17, 108.07, 61.43, 42.72, 42.56, 34.61, 31.17, 18.85, 13.43; **HRMS** (ESI) calcd for $C_{20}H_{24}NO_4$ $(M+H)^+$: 342.1699, Found: 342.1698; 99:1 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254 nm, t_r (minor) = 8.65 min, t_r (major) = 12.81 min.

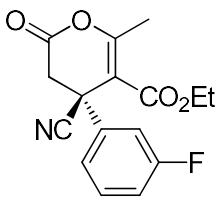
(*R*)-ethyl-4-cyano-4-(4-methoxyphenyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3f)



3f

White solid, yield: 25.2 mg (80%); mp: 40-41 ℃; $[\alpha]_D^{20}$= 29.5 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.30 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.13 – 4.03 (m, 2H), 3.81 (s, 1H), 3.09 (d, *J* = 15.8 Hz, 1H), 2.46 (s, 3H), 1.04 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=164.20, 161.91, 161.70, 159.99, 128.60, 126.32, 119.40, 114.90, 108.10, 61.65, 55.51, 43.02, 42.44, 18.95, 13.73; **HRMS** (ESI) calcd for $C_{17}H_{18}NO_5$ $(M+H)^+$: 316.1179, Found: 316.1173; 95:5 *er* as determined by HPLC (Daicel Chralcel IB, 70:30 hexanes/ *i*-PrOH, 0.8 mL/min), λ=254nm, t_r (minor) = 11.22 min, t_r (major) = 25.33 min.

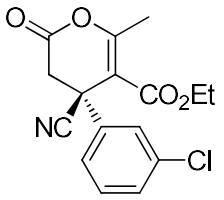
(*R*)-ethyl-4-cyano-4-(3-fluorophenyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3g)



3g

White solid, yield: 19.4 mg (60%); mp: 60-61 ℃; $[\alpha]_D^{20}$= 42.8 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.41 (dd, *J* = 13.9, 8.0 Hz, 1H), 7.22 – 7.17 (m, 1H), 7.15 – 7.05 (m, 2H), 4.14 – 4.04 (m, 2H), 3.33 (d, *J* = 15.9 Hz, 1H), 3.08 (d, *J* = 15.9 Hz, 1H), 2.49 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.72, 163.12 (d, *J* = 249.1 Hz), 162.74, 139.49 (d, *J* = 7.1 Hz), 131.40 (d, *J* = 8.4 Hz), 120.57, 118.66, 116.16 (d, *J* = 21.1 Hz), 112.51 (d, *J* = 24.0 Hz), 107.21, 61.66, 42.79, 42.47, 18.96, 13.56; **HRMS** (ESI) calcd for $C_{16}H_{15}FNO_4$ $(M+H)^+$: 304.0979, Found: 304.0988; >99:1 *er* as determined by HPLC (Daicel Chralcel AD-H, 95:5 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 13.65 min, t_r (major) = 15.31min.

(*R*)-ethyl-4-(3-chlorophenyl)-4-cyano-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3h)

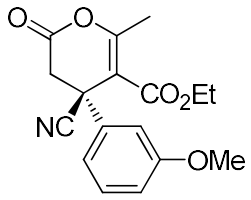


3h

White solid, yield: 25.2 mg (79%); mp: 47-48 ℃; $[\alpha]_D^{20}$= 20.5 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.42 – 7.35 (m, 3H), 7.31 – 7.27 (m, 1H), 4.27 – 3.55 (m, 2H), 3.33 (d, *J* = 16.0 Hz, 1H), 3.08 (d, *J* = 15.8 Hz, 1H), 2.50 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.67, 162.80, 160.95, 139.01, 135.62, 130.90, 129.34, 125.30, 123.02, 118.57, 107.13, 61.68, 42.73, 42.44, 18.98, 13.56; **HRMS** (ESI) calcd for $C_{16}H_{15}ClNO_4$ $(M+H)^+$: 337.0949, Found: 337.0946; 95:5 *er* as

determined by HPLC (Daicel Chralcel AD-H, 90:10 hexanes/ *i*-PrOH, 0.8 mL/min), λ=254nm, t_r (minor) = 11.46 min, t_r (major) = 13.81min.

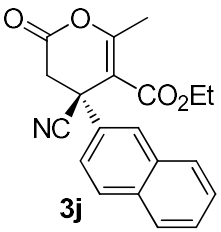
(*R*)-ethyl-4-cyano-4-(3-methoxyphenyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3i)



3i

White solid, yield: 18.7 mg (59%); mp: 57-58 ℃; $[\alpha]_D^{20}$=28.3 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.33 (t, *J* = 7.9 Hz, 1H), 6.99 – 6.82 (m, 3H), 4.16 – 3.97 (m, 2H), 3.82 (s, 3H), 3.31 (d, *J* = 15.8 Hz, 1H), 3.09 (d, *J* = 15.8 Hz, 1H), 2.48 (s, 3H), 1.00 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=164.00, 162.21, 161.39, 160.36, 138.48, 130.73, 119.02, 116.86, 113.94, 111.14, 107.70, 61.53, 55.43, 42.95, 42.6, 18.87,13.54; **HRMS** (ESI) calcd for $C_{17}H_{18}NO_5$ $(M+H)^+$: 316.1179, Found: 316.1176; 91:9 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 0.8 mL/min), λ=254nm, t_r (minor) = 21.85 min, t_r (major) = 31.78 min.

(*R*)-ethyl-4-cyano-6-methyl-4-(naphthalen-2-yl)-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3j)

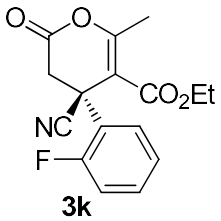


3j

Yellow, yield: 27.5 mg (77%); mp: 77-78 ℃; $[\alpha]_D^{20}$= 59.3 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.93 – 7.89 (m, 2H), 7.88 – 7.84 (m, 2H), 7.61 – 7.50 (m, 2H),

7.42 (dd, *J* = 8.6, 2.1 Hz, 1H), 4.09 – 3.90 (m, 2H), 3.37 (d, *J* = 16.0 Hz, 1H), 3.19 (d, *J* = 16.0 Hz, 1H), 2.53 (s, 3H), 0.87 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=164.03, 162.37, 161.36, 134.01, 133.09, 132.99, 129.92, 128.18, 127.70, 127.18 (d, *J* = 6.9 Hz), 124.62, 121.61, 119.12, 107.72, 61.52, 43.12, 42.64, 18.95, 13.47; **HRMS** (ESI) calcd for $C_{20}H_{18}NO_4$ $(M+H)^+$: 336.1230, Found: 336.1229; 97:3 *er* as determined by HPLC (Daicel Chralcel IB, 75:25 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 17.30 min, t_r (major) = 35.22min.

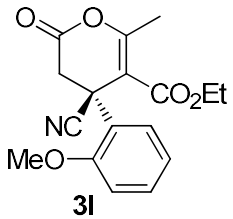
(*S*)-ethyl-4-cyano-4-(2-fluorophenyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3k)



3k

White solid, yield: 14.3 mg (47%); mp: 71-72 ℃; $[\alpha]_D^{20}$= 20.1 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.54 (t, *J* = 8.1 Hz, 1H), 7.44 – 7.35 (m, 1H), 7.22 (t, *J* = 7.7 Hz, 1H), 7.13 (dd, *J* = 11.9, 8.2 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.40 (d, *J* = 16.2 Hz, 1H), 3.29 (d, *J* = 16.1 Hz, 1H), 2.47 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.80, 161.85, 161.50, 159.45 (d, *J* = 248.6 Hz), 131.26 (d, *J* = 8.5 Hz), 128.69, 124.87 (d, *J* = 3.2 Hz), 123.33 (d, *J* = 9.9 Hz), 118.24, 117.09 (d, *J* = 21.6 Hz), 106.55, 61.50, 40.51, 39.45, 19.11, 13.59; **HRMS** (ESI) calcd for $C_{16}H_{15}FNO_4$ $(M+H)^+$: 304.0979, Found: 304.0991; 95:5 *er* as determined by HPLC (Daicel Chralcel AD-H, 90:10 hexanes/ *i*-PrOH, 0.8 mL/min), λ=254nm, t_r (minor) = 11.99 min, t_r (major) = 13.78min.

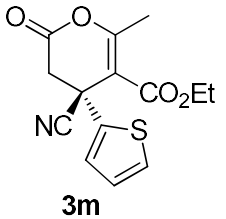
(*R*)-ethyl-4-cyano-4-(2-methoxyphenyl)-6-methyl-2-oxo-3,4-dihydro-2H-pyran-5-carboxylate (3l)



3l

White solid, yield: 23.2 mg (74%); mp: 104-105 ℃; $[\alpha]_D^{20}$=87.3 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.60 (d, *J* = 7.8 Hz, 1H), 7.35 (t, *J* = 7.9 Hz, 1H), 7.01 (t, *J* = 7.7 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 4.13 – 4.04 (m, 2H), 3.79 (s, 3H), 3.44 (d, *J* = 16.3 Hz, 1H), 3.25 (d, *J* = 16.6 Hz, 1H), 2.44 (s, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=164.36, 162.24, 161.10, 155.87, 130.50, 128.89, 124.00, 120.93, 119.89, 111.68, 105.85, 61.28, 54.84, 41.92, 38.87, 19.42, 13.71; **HRMS** (ESI) calcd for $C_{17}H_{18}NO_5$ $(M+H)^+$: 316.1179, Found: 316.1183; 95:5 *er* as determined by HPLC (Daicel Chralcel AD-H, 90:10 hexanes/ *i*-PrOH, 0.8 mL/min), λ=254nm, t_r (minor) = 12.08 min, t_r (major) = 16.36min.

(*R*)-ethyl-4-cyano-6-methyl-2-oxo-4-(thiophen-2-yl)-3,4-dihydro-2H-pyran-5-carboxylate (3m)

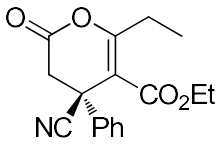


3m

Yellow solid, yield: 19.6 mg (67%); mp: 45-46 ℃; $[\alpha]_D^{20}$= 30.7 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.30 (d, *J* = 5.1 Hz, 1H), 7.16 – 7.12 (m, 1H), 7.02 – 6.96 (m, 1H), 4.30 – 4.13 (m, 2H), 3.39 (d, *J* = 15.9 Hz, 1H), 3.33 (d, *J* = 15.9 Hz, 1H), 2.45 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.75, 162.24, 161.33, 140.04, 127.59, 126.58, 126.12, 118.72, 108.43, 61.95, 43.07, 39.45, 19.16, 13.83; **HRMS** (ESI) calcd for $C_{14}H_{14}SNO_4$ $(M+H)^+$: 292.0638, Found: 292.0608; 98:2 *er* as determined by HPLC (Daicel Chralcel AD-H, 90:10 hexanes/

i-PrOH, 0.8 mL/min), λ=254nm, t_r (minor) = 19.58 min, t_r (major) = 27.24min.

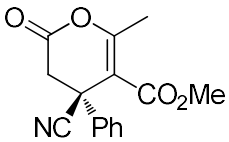
(*R*)-ethyl-4-cyano-6-ethyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (3n)



3n

White solid, yield: 28.0 mg (93%); mp: 101-102 ℃; $[\alpha]_D^{20}$= 36.1 (c 1.0, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.45 – 7.35 (m, 5H), 4.09 – 3.99 (m, 2H), 3.31 (d, *J* = 15.9 Hz, 1H), 3.08 (d, *J* = 15.9 Hz, 1H), 2.90 – 2.75 (m, 2H), 1.31 (t, *J* = 7.5 Hz, 3H), 0.96 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=166.45, 163.89, 161.66, 136.89, 129.59, 128.98, 124.83, 119.09, 107.18, 61.52, 42.94, 42.76, 25.52, 13.46, 11.64; **HRMS** (ESI) calcd for $C_{17}H_{18}NO_4$ $(M+H)^+$: 300.1230, Found: 300.1232; 96:4 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 10.73 min, t_r (major) = 14.89min.

(*R*)-methyl-4-cyano-6-methyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (3o)

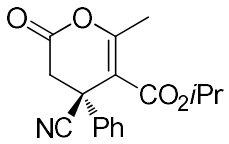


3o

White solid, yield: 21.6 mg (80%); mp: 78-79 ℃; $[\alpha]_D^{20}$= 50.5 (c 1.0, $CHCl_3$); **^{1}H NMR** (400 MHz, $CDCl_3$): δ=7.51 – 7.33 (m, 5H), 3.58 (s, 3H), 3.33 (d, *J* = 15.8 Hz, 1H), 3.11 (d, *J* = 15.8 Hz, 1H), 2.49 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=164.56, 162.47, 161.36, 136.58, 129.68, 129.10, 124.81, 119.13, 107.66, 52.13, 43.00, 42.75, 19.00; **HRMS** (ESI) calcd for $C_{15}H_{14}NO_4$ $(M+H)^+$: 272.0917, Found: 272.0918;

97:3 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 15.45 min, t_r (major) = 18.89min.

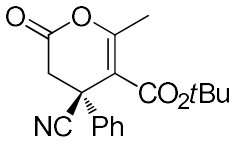
(*R*)-isopropyl-4-cyano-6-methyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (3p)



3p

White solid, yield: 24.9 mg (83%); mp: 91-92 ℃; $[\alpha]_D^{20}$= 13.8 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.43 – 7.34 (m, 5H), 4.87 (m, *J* = 12.5, 6.2 Hz, 1H), 3.30 (d, *J* = 16.0 Hz, 1H), 3.06 (d, *J* = 16.0 Hz, 1H), 2.47 (s, 3H), 1.17 (d, *J* = 6.3 Hz, 3H), 0.72 (d, *J* = 6.2 Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.45, 161.97, 161.42, 137.35, 129.54, 128.89, 124.84, 118.96, 107.98, 69.65, 42.95, 42.81, 21.41, 20.77, 18.76; **HRMS** (ESI) calcd for $C_{17}H_{18}NO_4$ $(M+H)^+$:300.1230, Found: 300.1228; 93:7 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 14.21min, t_r (major) = 21.08min.

(*R*)-tert-butyl-4-cyano-6-methyl-2-oxo-4-phenyl-3,4-dihydro-2H-pyran-5-carboxylate (3q)

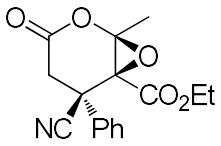


3q

White solid, yield: 33.12 mg (87%); mp: 77-78 ℃; $[\alpha]_D^{20}$= 28.6 (c 0.5, $CHCl_3$); **^{1}H NMR** (500 MHz, $CDCl_3$): δ=7.50 – 7.30 (m, 5H), 3.27 (d, *J* = 16.0 Hz, 1H), 3.03 (d, *J* = 16.0 Hz, 1H), 2.43 (s, 3H), 1.18 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$): δ=163.02, 161.56, 161.11, 137.45, 129.50, 128.87, 124.97, 118.99, 108.95, 83.21, 43.07, 42.83,

27.49, 18.45; **HRMS** (ESI) calcd for $C_{18}H_{20}NO_4$ $(M+H)^+$: 314.1386, Found: 314.1381; 98:2 *er* as determined by HPLC (Daicel Chralcel IB, 90:10 hexanes/ *i*-PrOH, 1 mL/min), λ=254nm, t_r (minor) = 10.66 min, t_r (major) = 16.58min.

(1R,5S,6S)-ethyl 5-cyano-1-methyl-3-oxo-5-phenyl-2,7-dioxabicyclo[4.1.0]heptane-6-carboxylate (5a)



5a

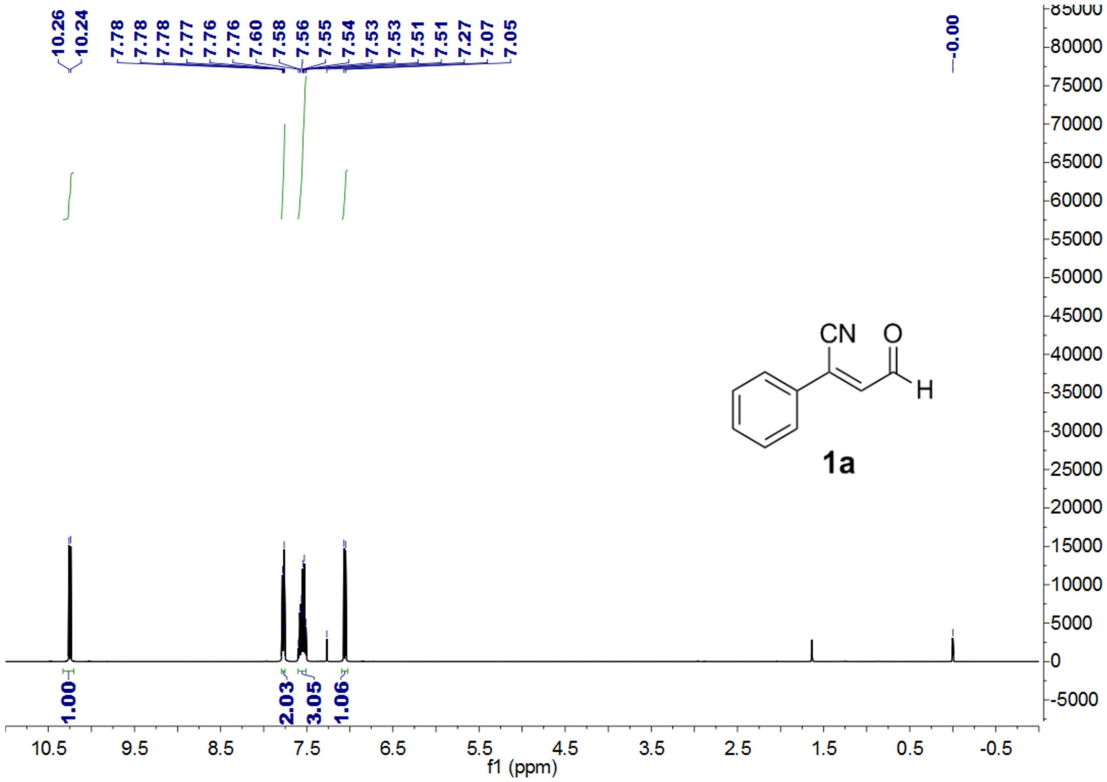
^{1}H NMR (400 MHz, $CDCl_3$): δ=7.44 (dd, *J* = 13.5, 5.5 Hz, 5H), 4.33 – 4.00 (m, 2H), 3.37 (d, *J* = 16.0 Hz, 1H), 2.92 (d, *J* = 16.0 Hz, 1H), 2.00 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$): δ=163.48, 162.87, 161.88, 161.19, 134.98, 133.49, 129.87, 129.51, 129.51, 125.55, 125.08, 117.74, 86.92, 63.32, 41.89, 17.08, 13.57.

c) References

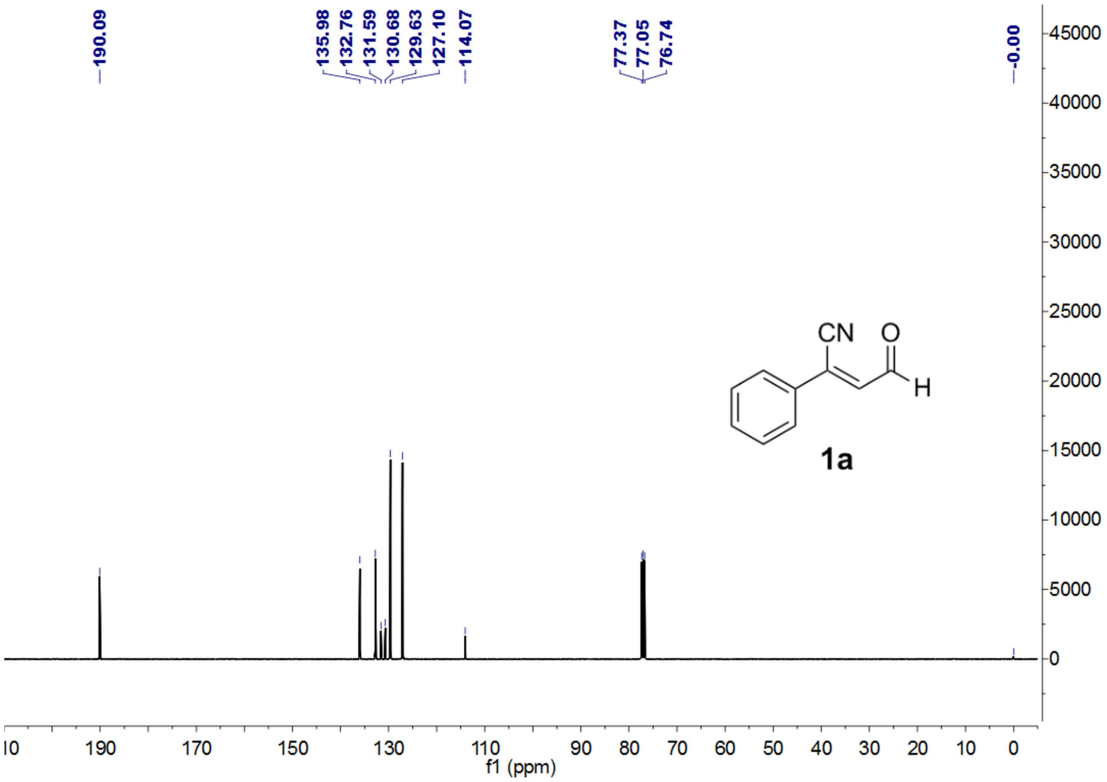
[1] J. R. Struble, Y. Lian, J. W. Bode, *Org. Synth.* 2010, **87**, 362.

[2] a) S. De Sarkar and A. Studer, *Angew. Chem. Int. Ed.* 2010, **49**, 9266; b) A. Biswas, S. D. Sarkar, R. Frohlich, A. Studer, *Org. Lett.* 2011, **13**, 4080; c) Z.-Q. Rong, M.-Q. Jia, S.-L. You, *Org. Lett.* 2011, **13**, 4966; d) F.-G. Sun, L-H. Sun, S. Ye, *Adv. Synth. Catal.* 2011, **353**, 3134; e) C. Yao, D. Wang, J. Lu, T. Li, W. Jiao, C. Yu, *Chem. Eur. J.* 2012, **18**, 1914; f) D. Xie, D. Shen, Q. Chen, J. Zhou, X. Zeng, G. Zhong, *J. Org. Chem.* 2016, **81**, 6136; g) A. Axelsson, E. Hammarvid, L. Ta, H. Sunden, *Chem. Commun*. 2016, **52**, 11571; h) X. Wu, Y. Zhang, Y. Wang, J. Ke, M. Jeret, R. N. Reddi, S. Yang, B.-A. Song, Y. R. Chi, *Angew. Chem. Int. Ed.* 2017, **56**, 2942.

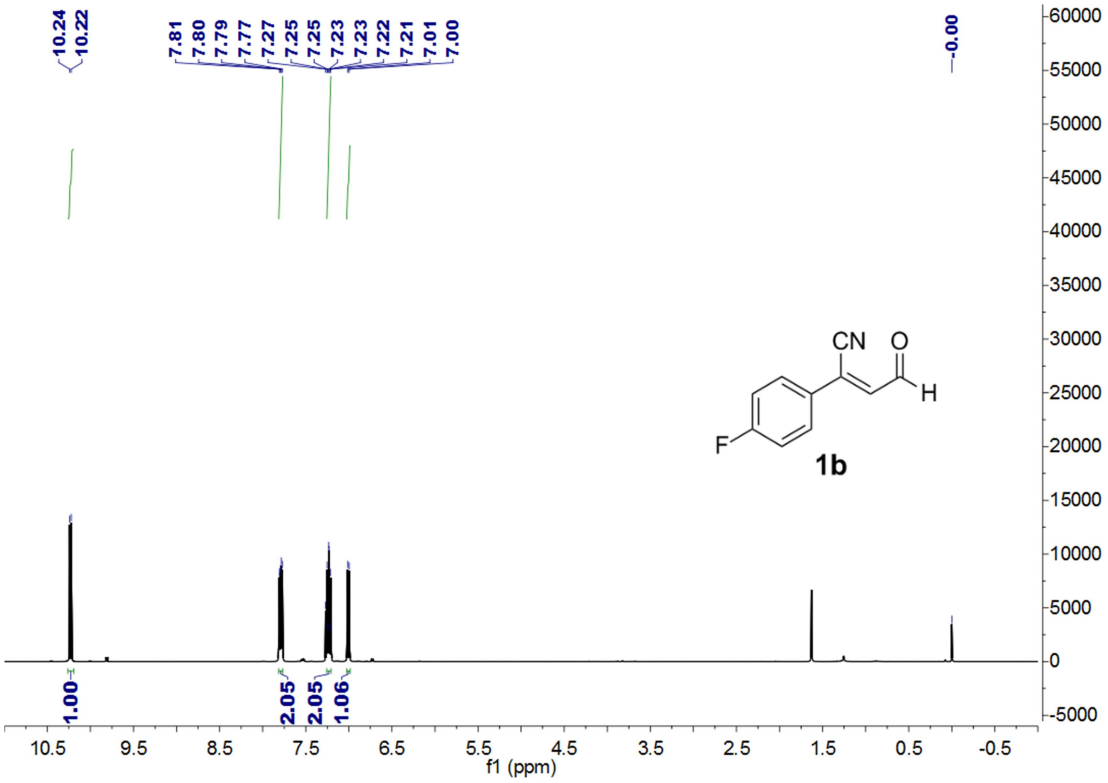
Ⅳ ^{1}H, ^{13}C NMR spectra



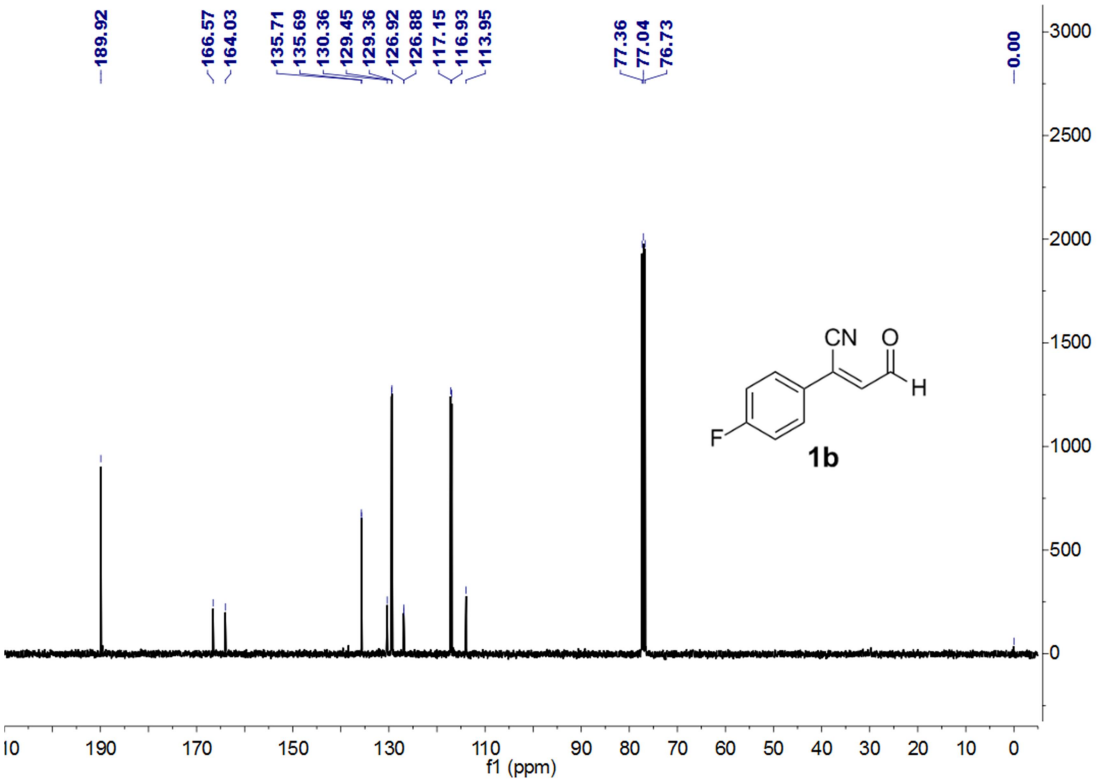
^{1}H NMR spectrum of **1a** (400 MHz, $CDCl_3$)



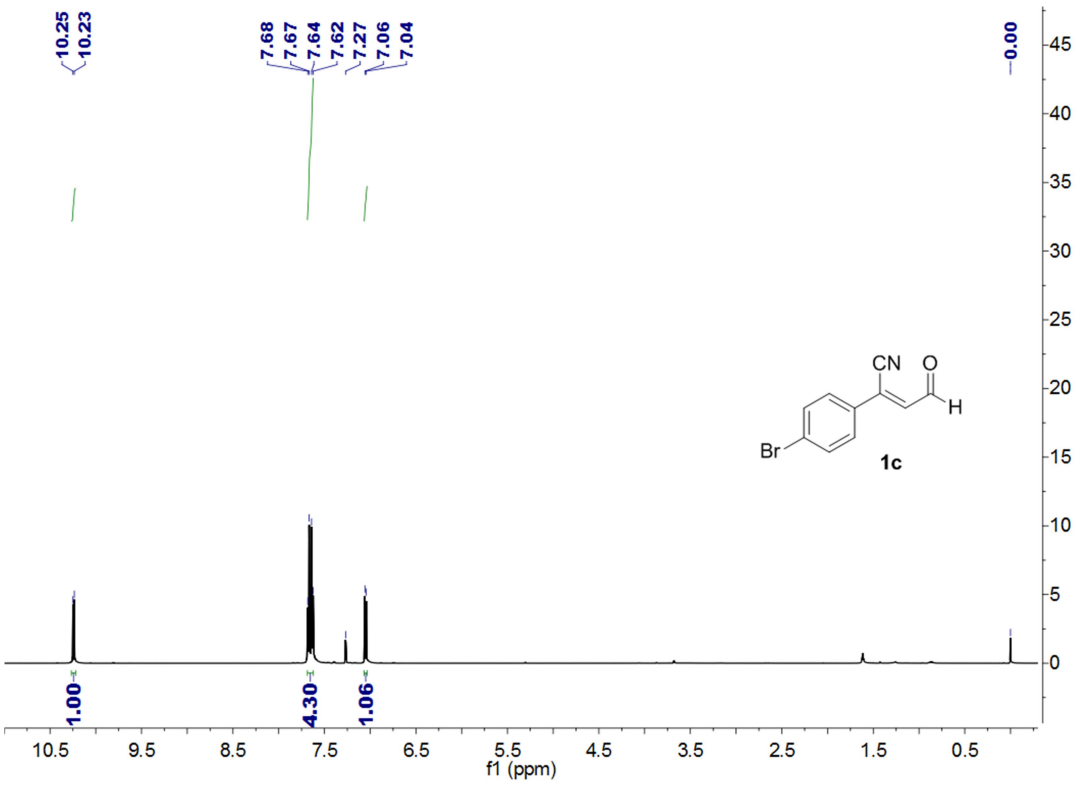
^{13}C NMR spectrum of **1a** (100 MHz, $CDCl_3$)



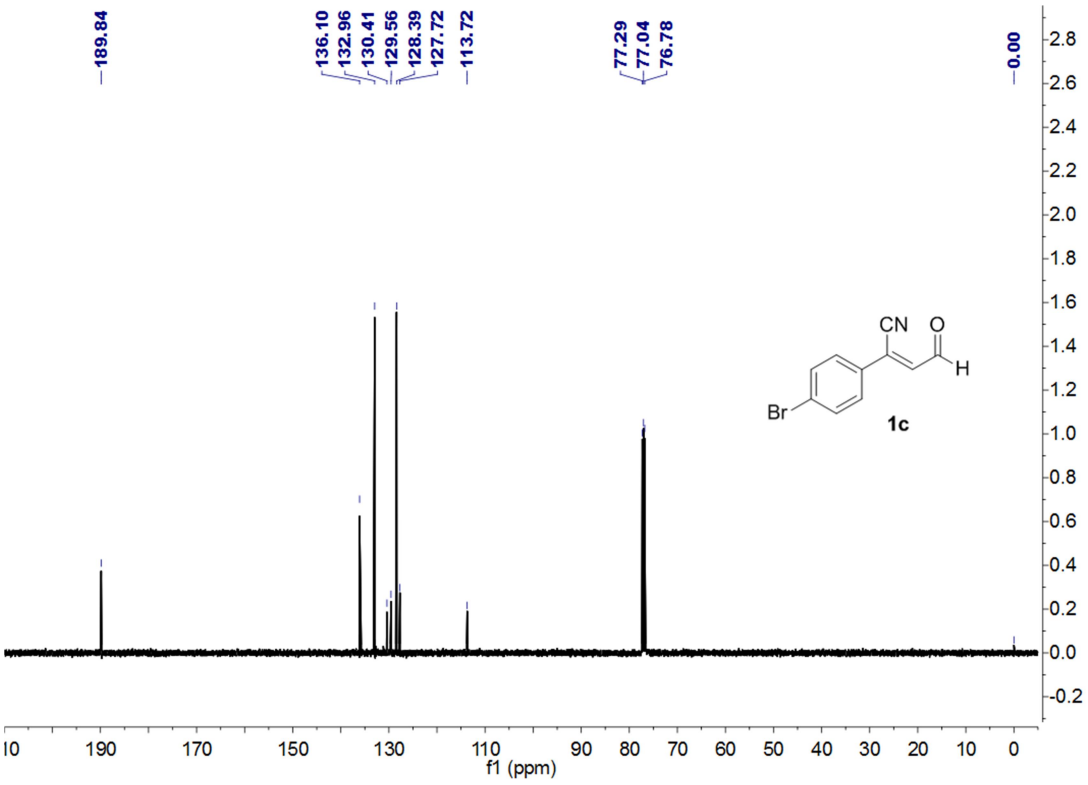
^{1}H NMR spectrum of **1b** (400 MHz, $CDCl_3$)



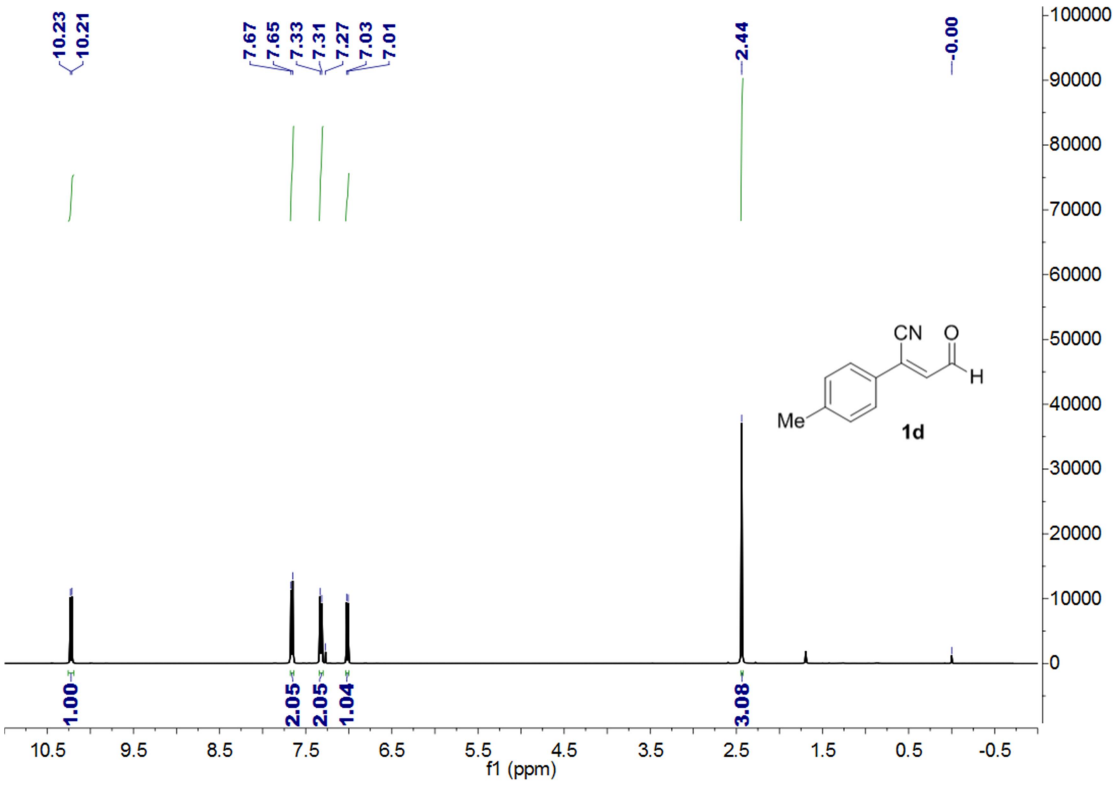
^{13}C NMR spectrum of **1b** (100 MHz, $CDCl_3$)



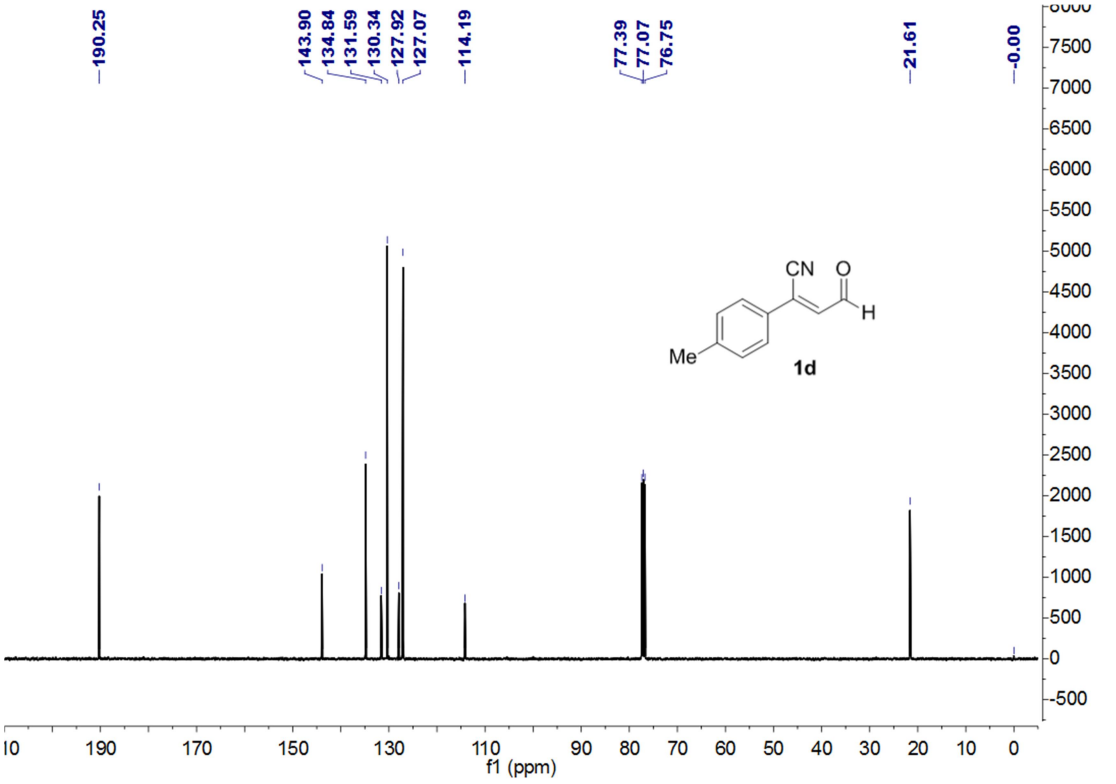
^{1}H NMR spectrum of **1c** (500 MHz, $CDCl_3$)



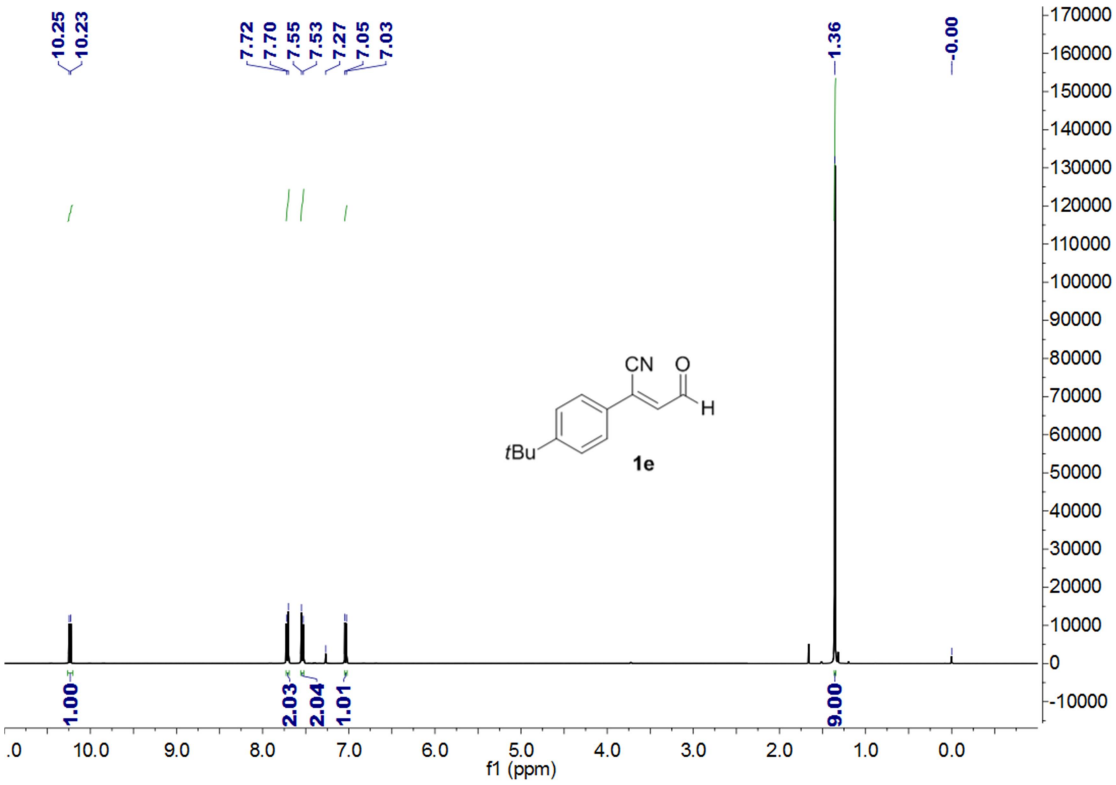
^{13}C NMR spectrum of **1c** (125 MHz, $CDCl_3$)



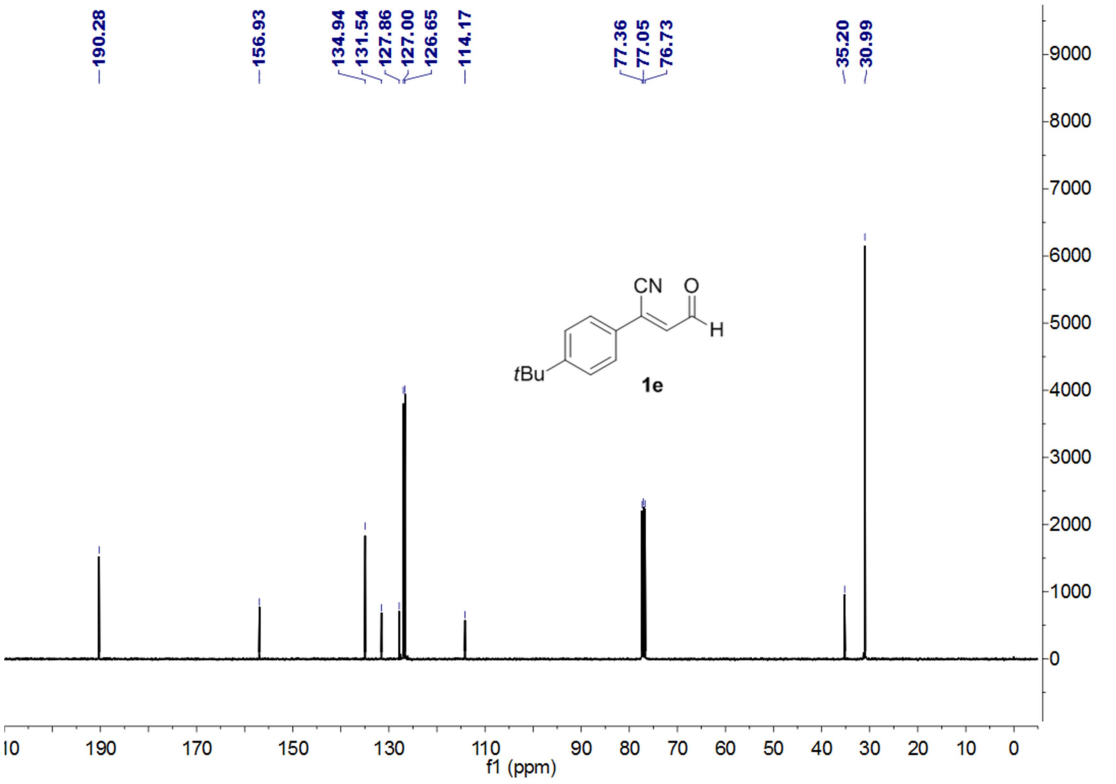
^{1}H NMR spectrum of **1d** (400 MHz, $CDCl_3$)



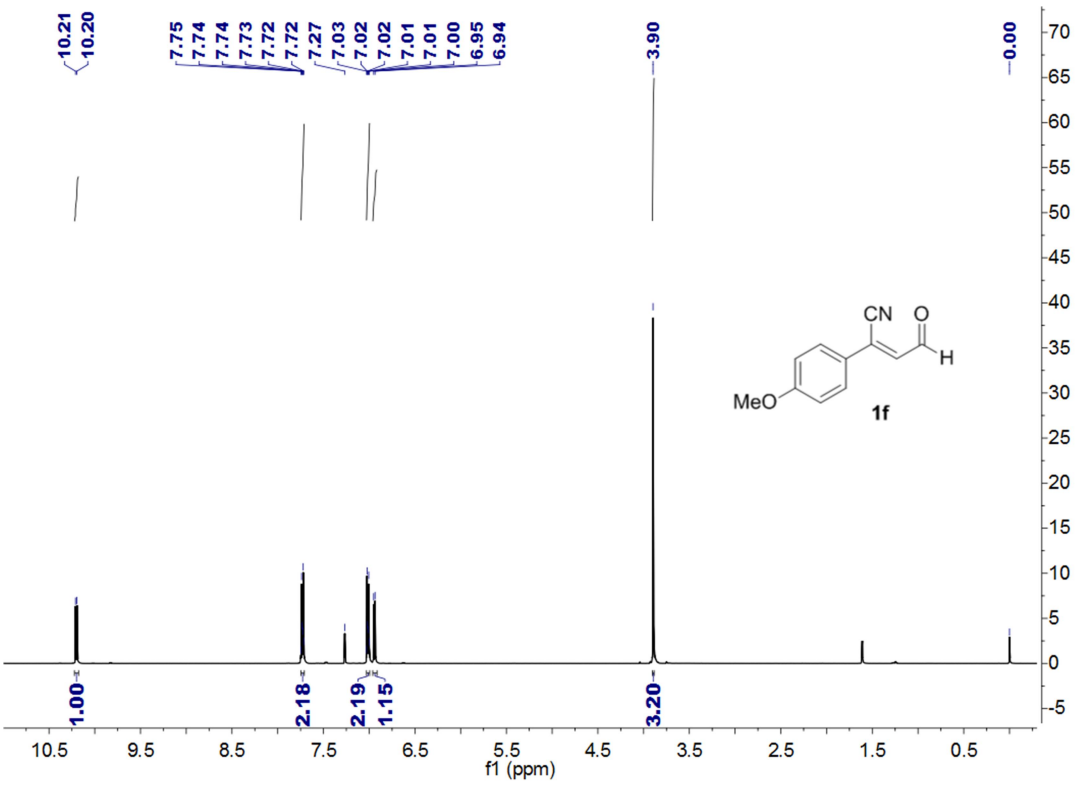
^{13}C NMR spectrum of **1d** (100 MHz, $CDCl_3$)



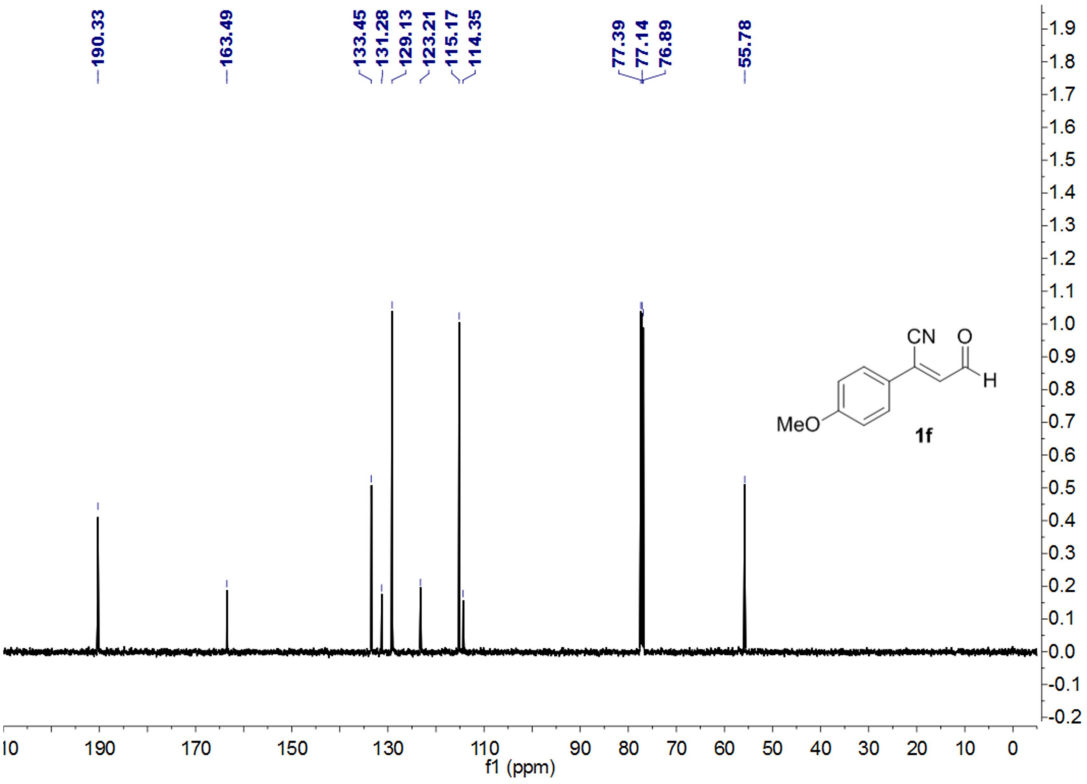
^{1}H NMR spectrum of **1e** (400 MHz, $CDCl_3$)



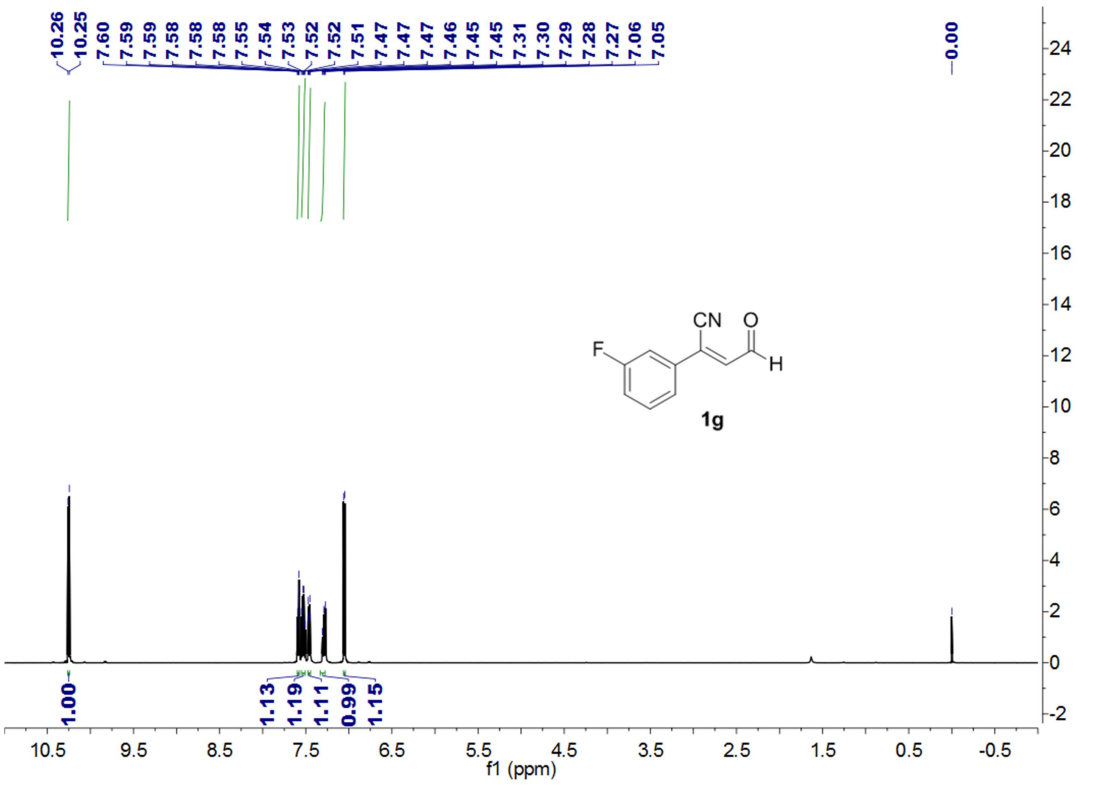
^{13}C NMR spectrum of **1e** (100 MHz, $CDCl_3$)



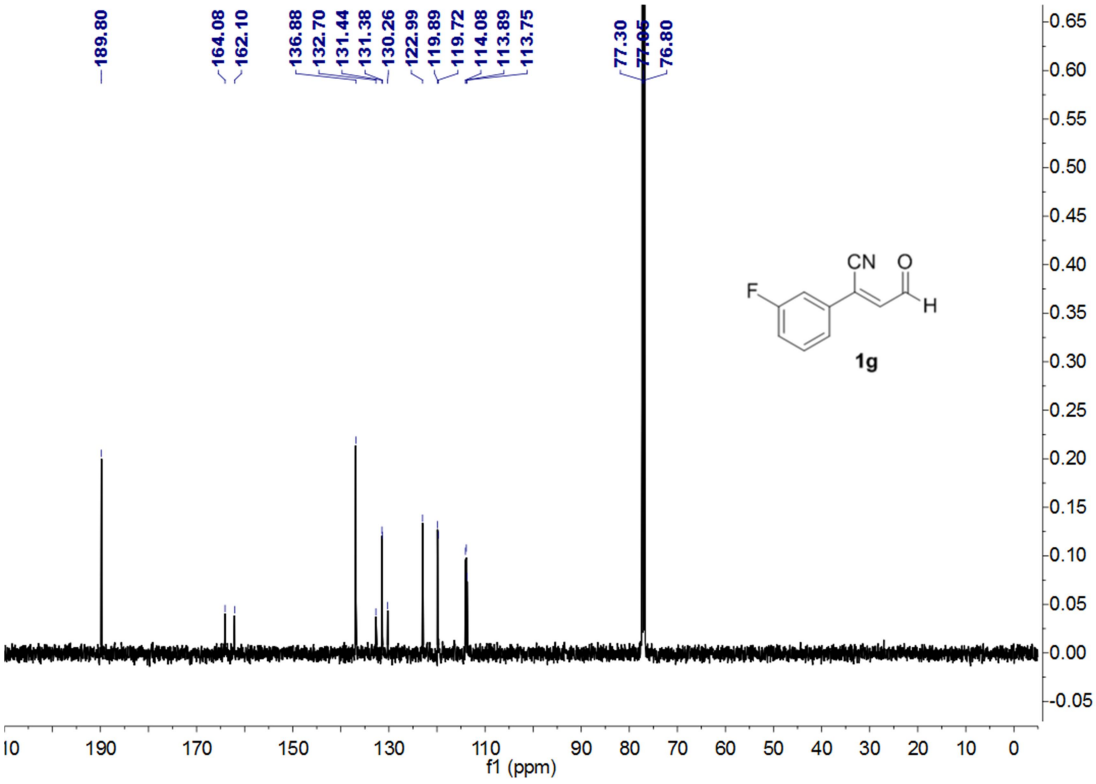
^{1}H NMR spectrum of **1f** (500 MHz, $CDCl_3$)



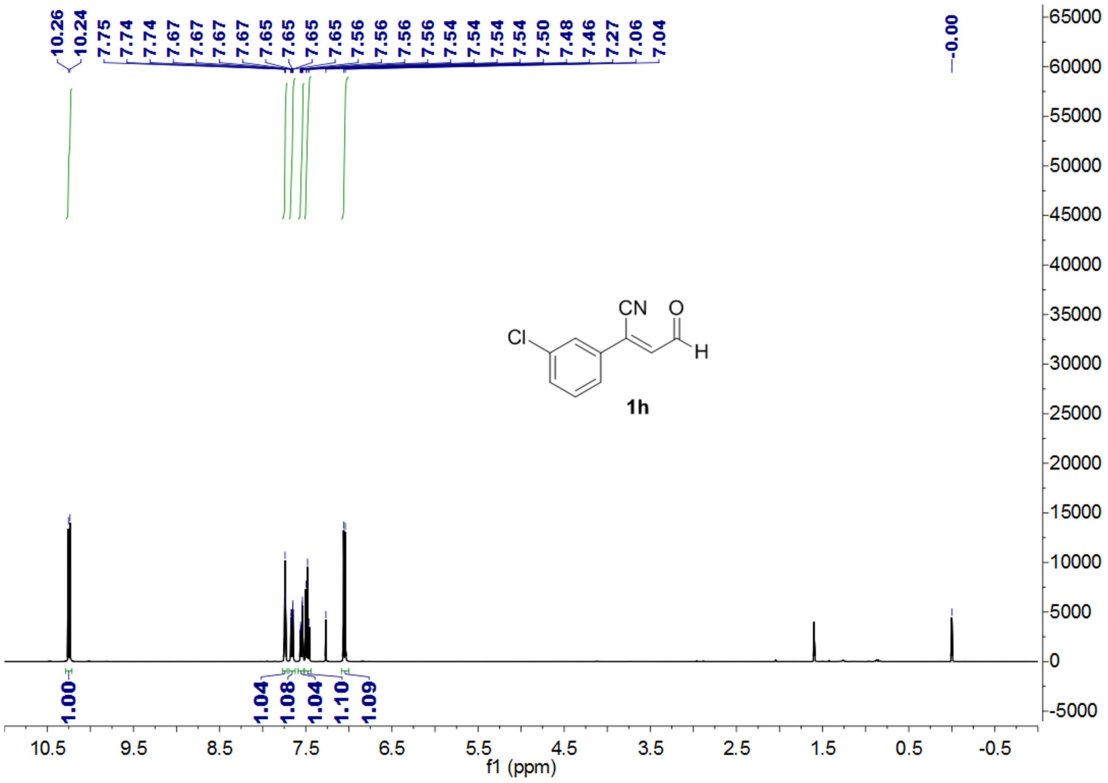
^{13}C NMR spectrum of **1f** (125 MHz, $CDCl_3$)



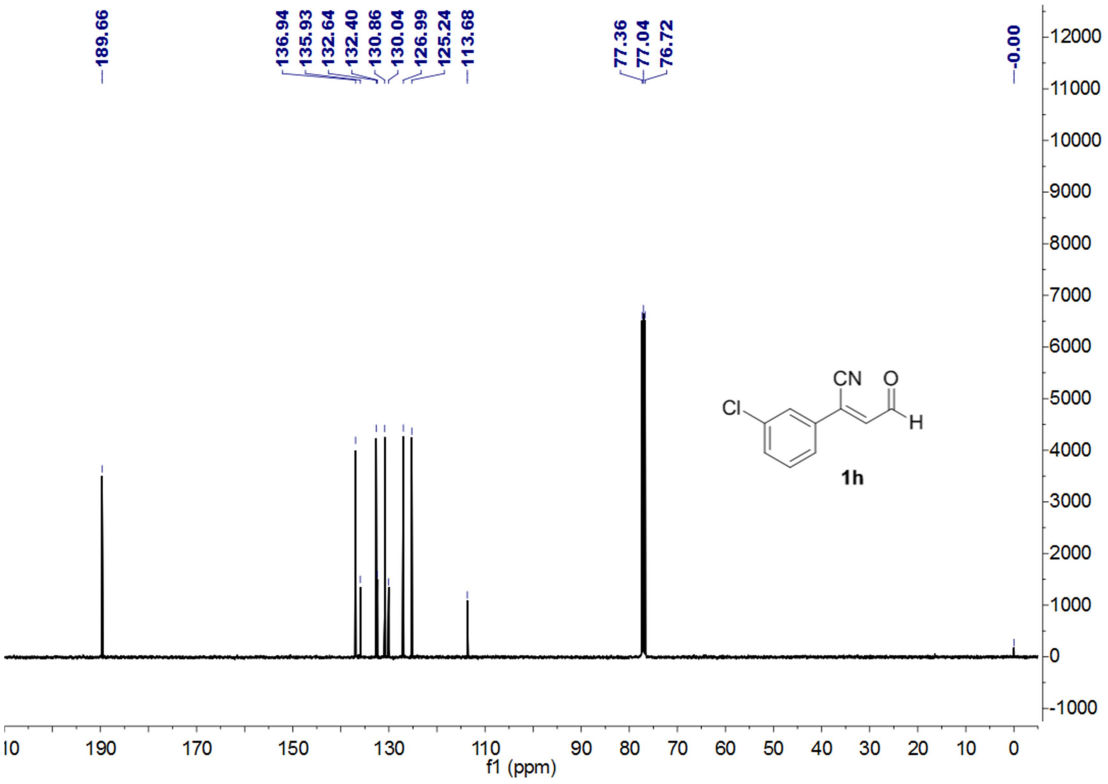
^{1}H NMR spectrum of **1g** (500 MHz, $CDCl_3$)



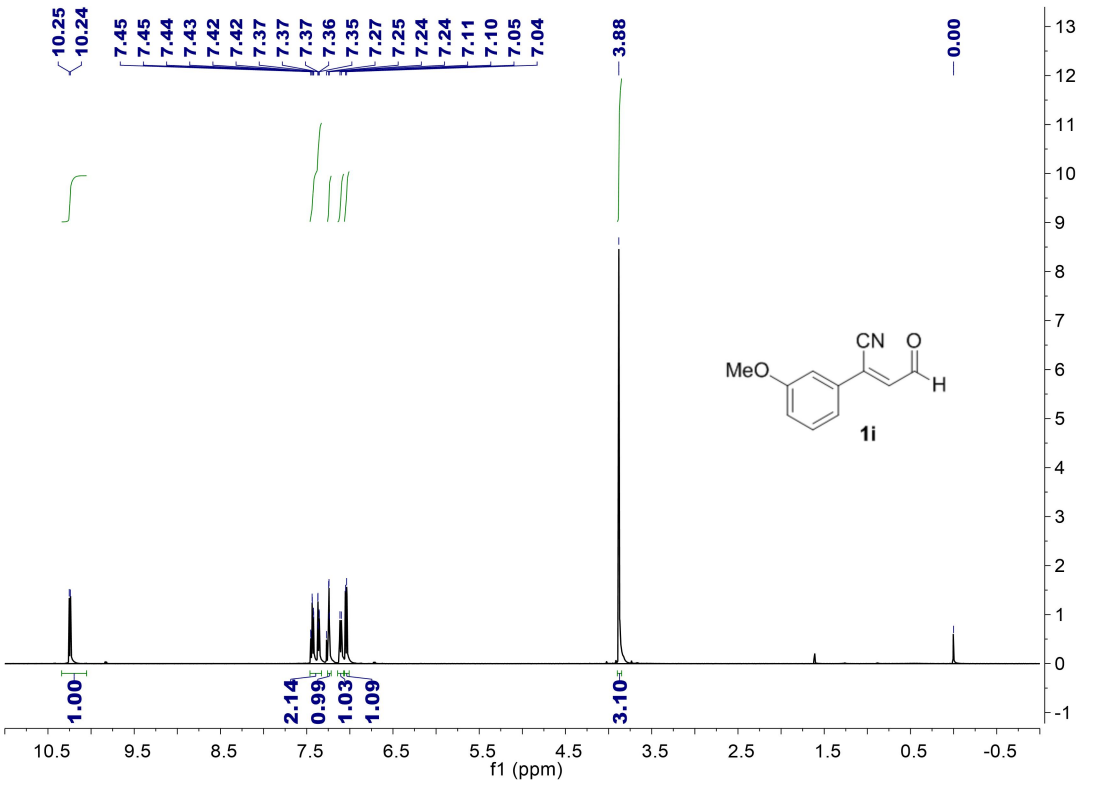
^{13}C NMR spectrum of **1g** (125 MHz, $CDCl_3$)



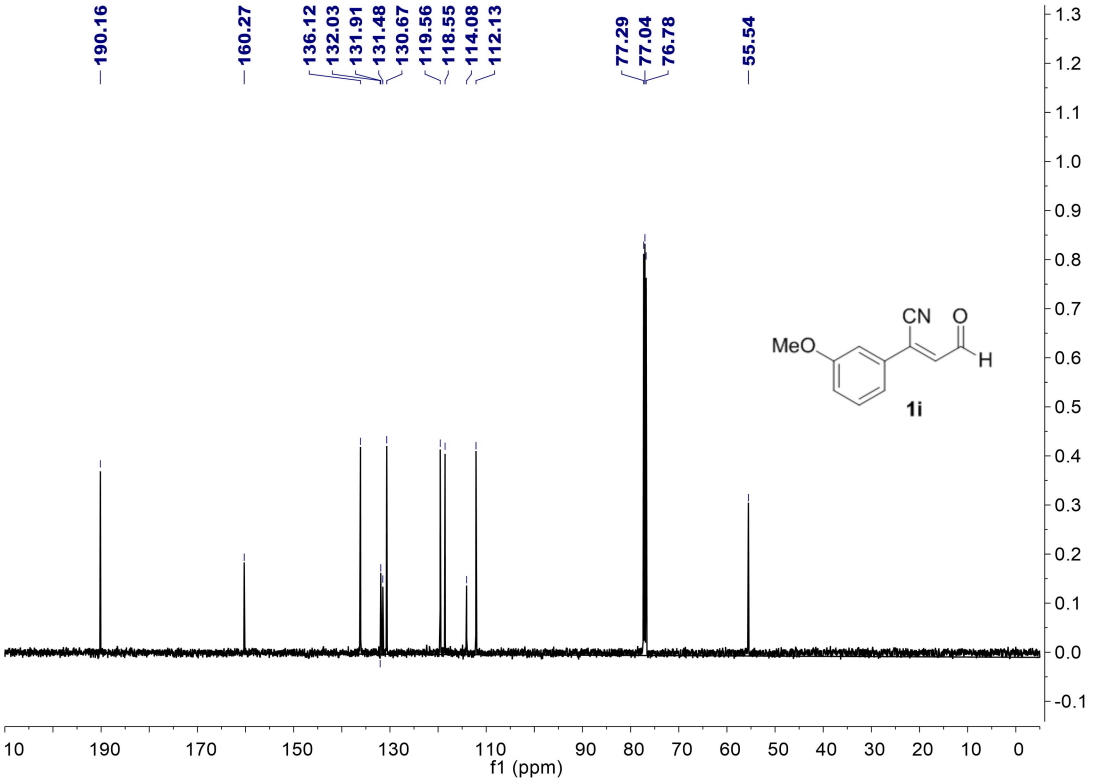
^{1}H NMR spectrum of **1h** (400 MHz, $CDCl_3$)



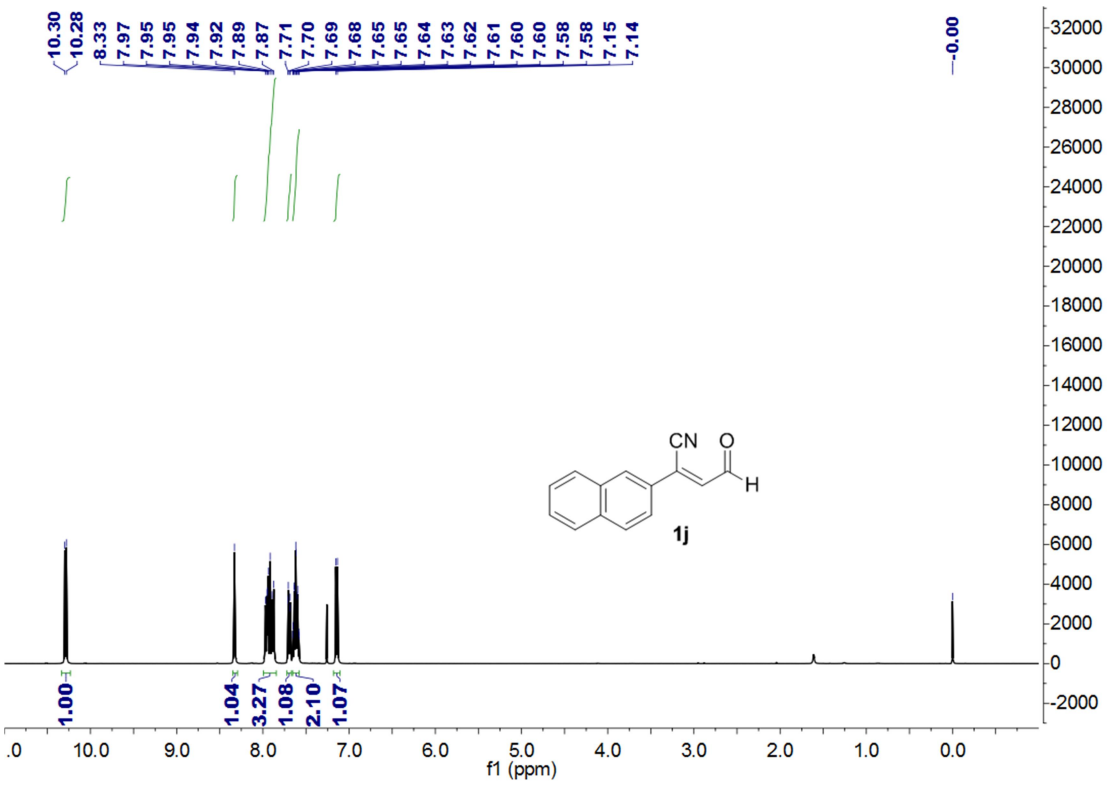
^{13}C NMR spectrum of **1h** (100 MHz, $CDCl_3$)



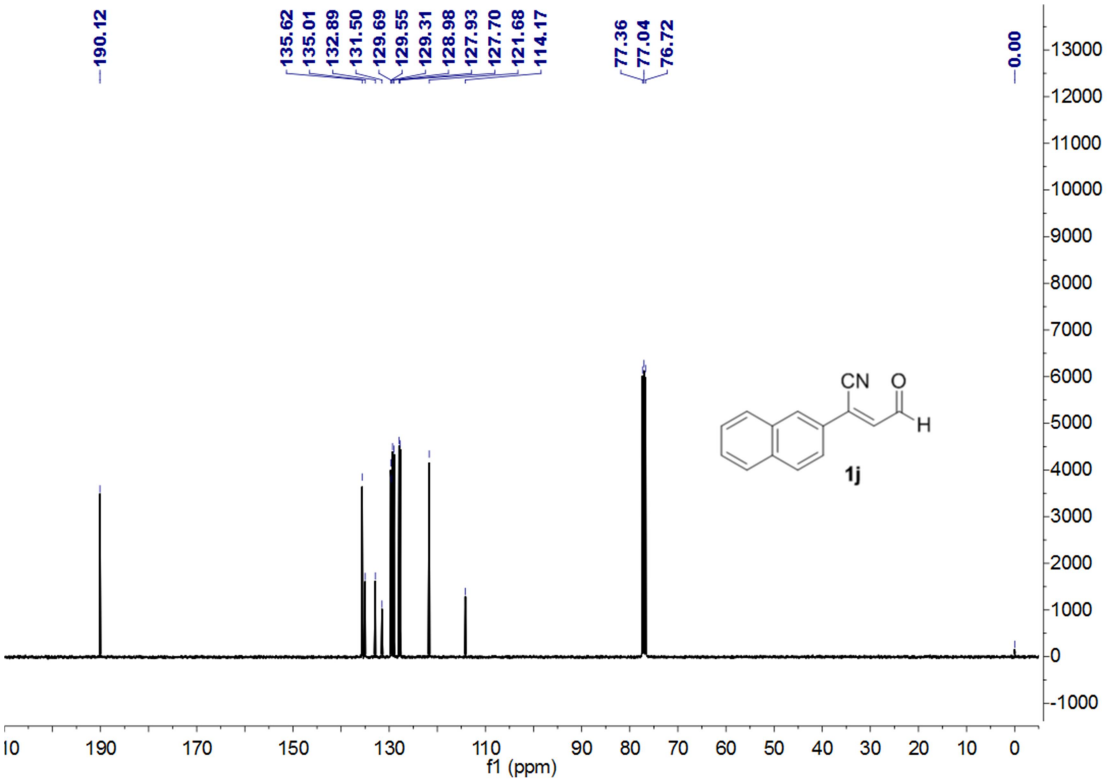
^{1}H NMR spectrum of **1i** (500 MHz, $CDCl_3$)



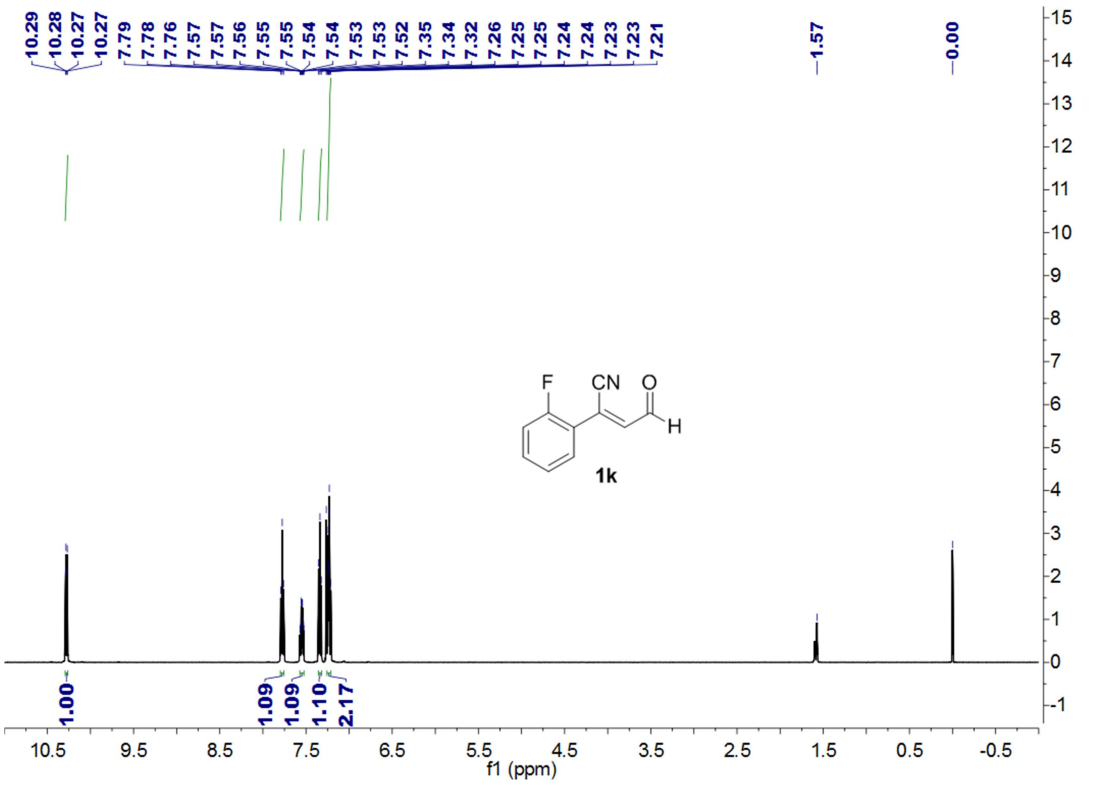
^{13}C NMR spectrum of **1i** (125 MHz, $CDCl_3$)



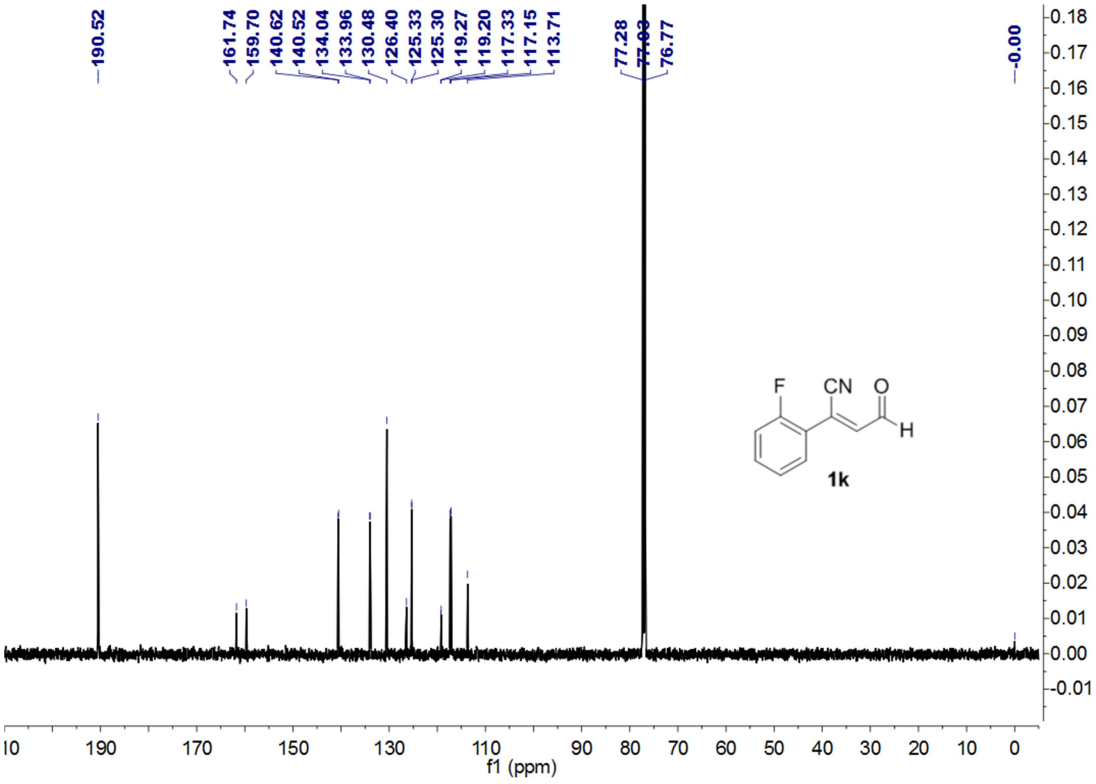
^{1}H NMR spectrum of **1j** (400 MHz, $CDCl_3$)



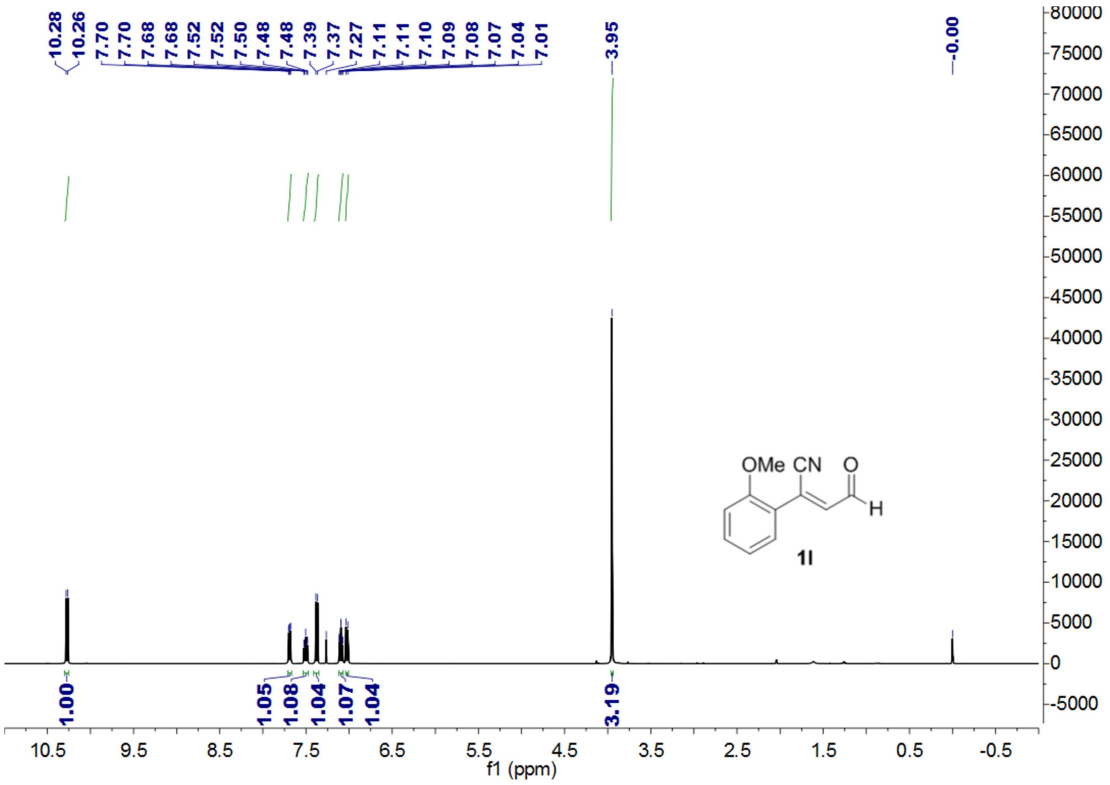
^{13}C NMR spectrum of **1j** (100 MHz, $CDCl_3$)



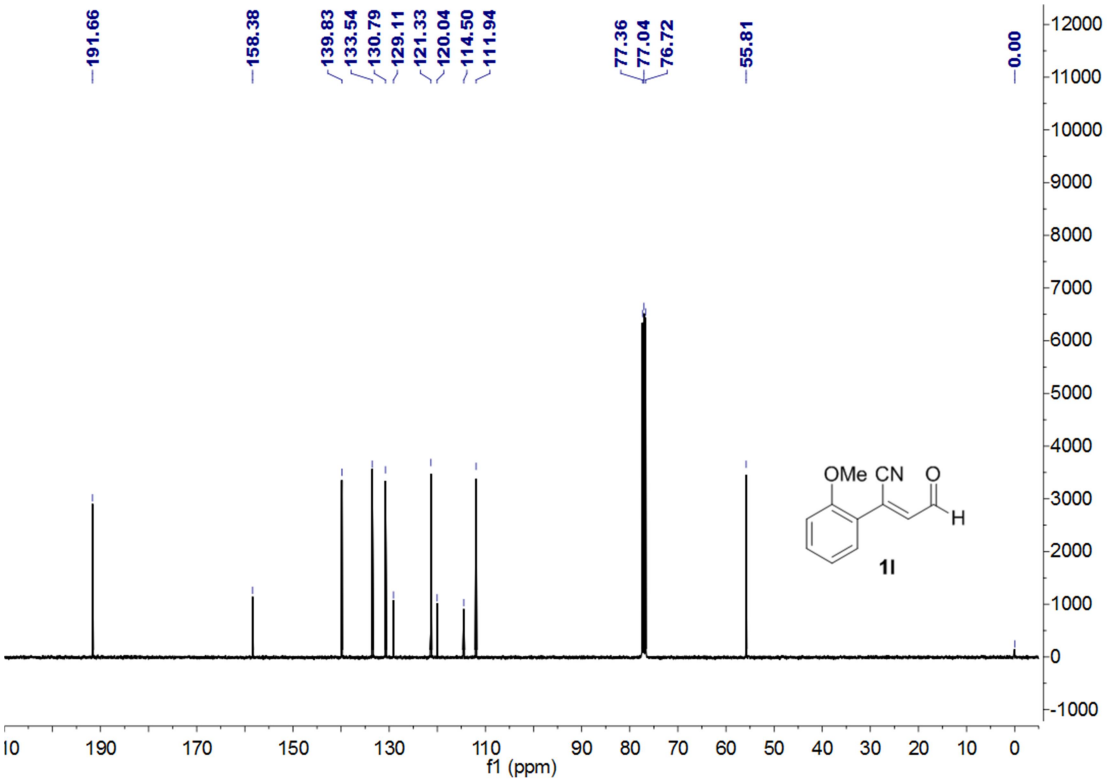
^{1}H NMR spectrum of **1k** (500 MHz, $CDCl_3$)



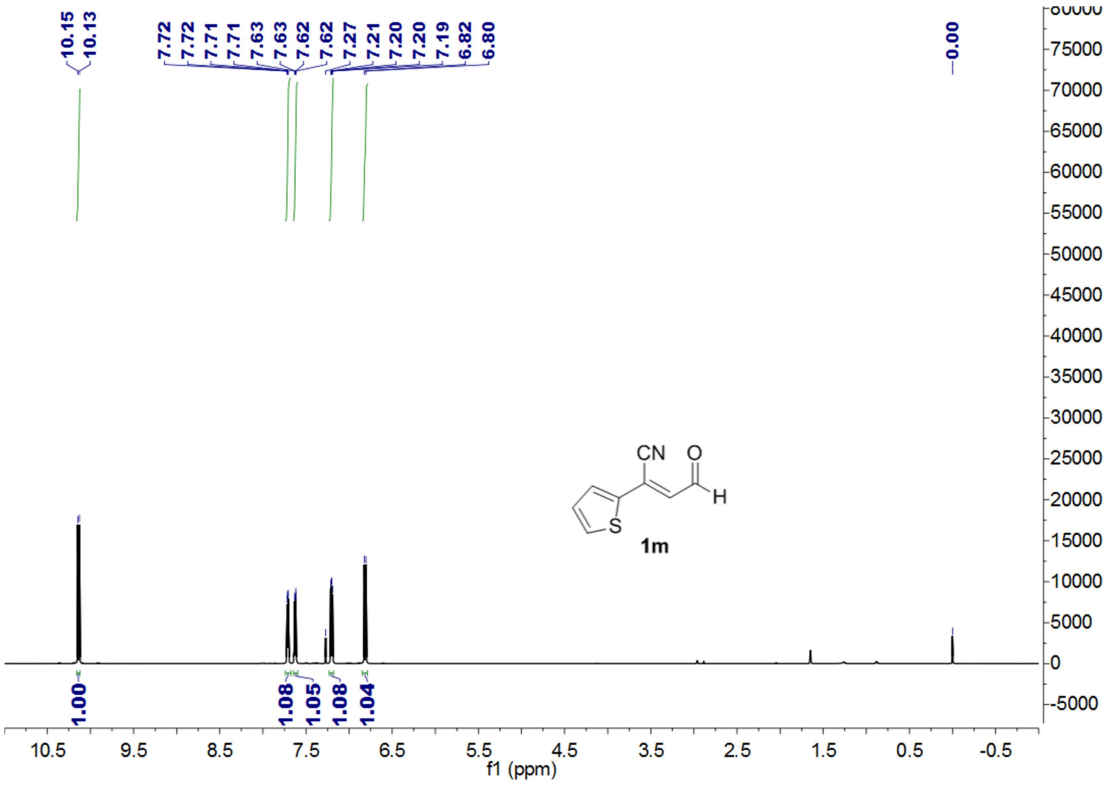
^{13}C NMR spectrum of **1k** (125 MHz, $CDCl_3$)



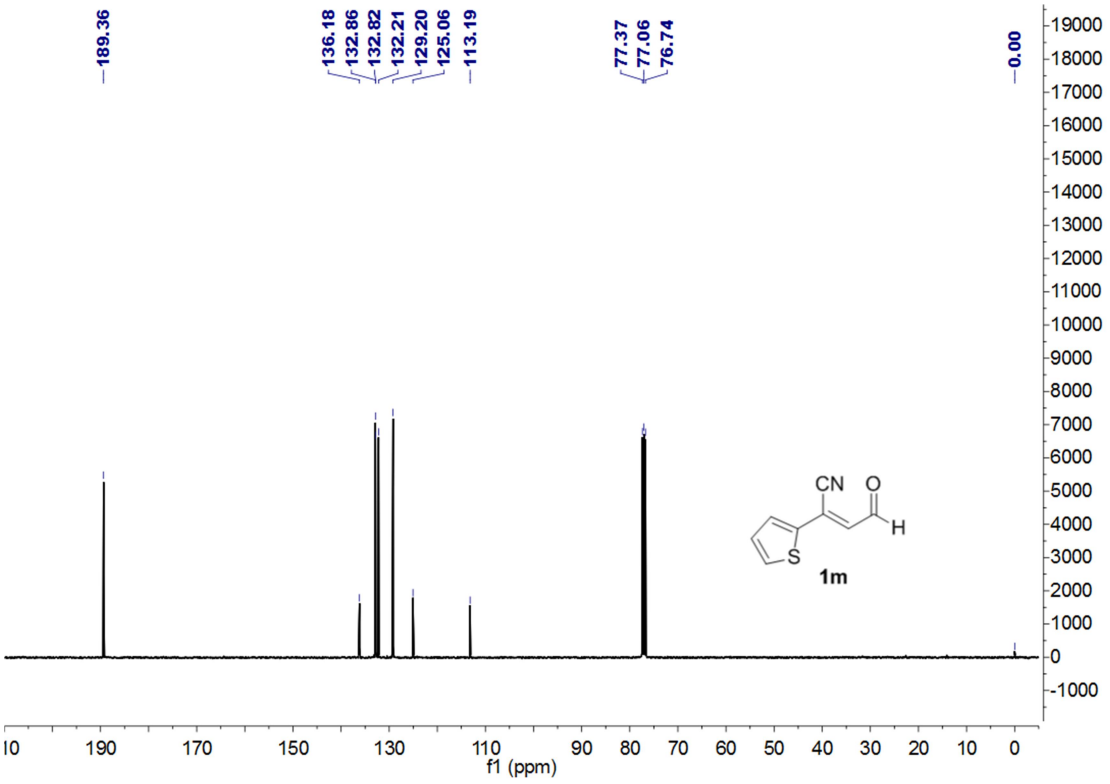
^{1}H NMR spectrum of **1l** (400 MHz, $CDCl_3$)



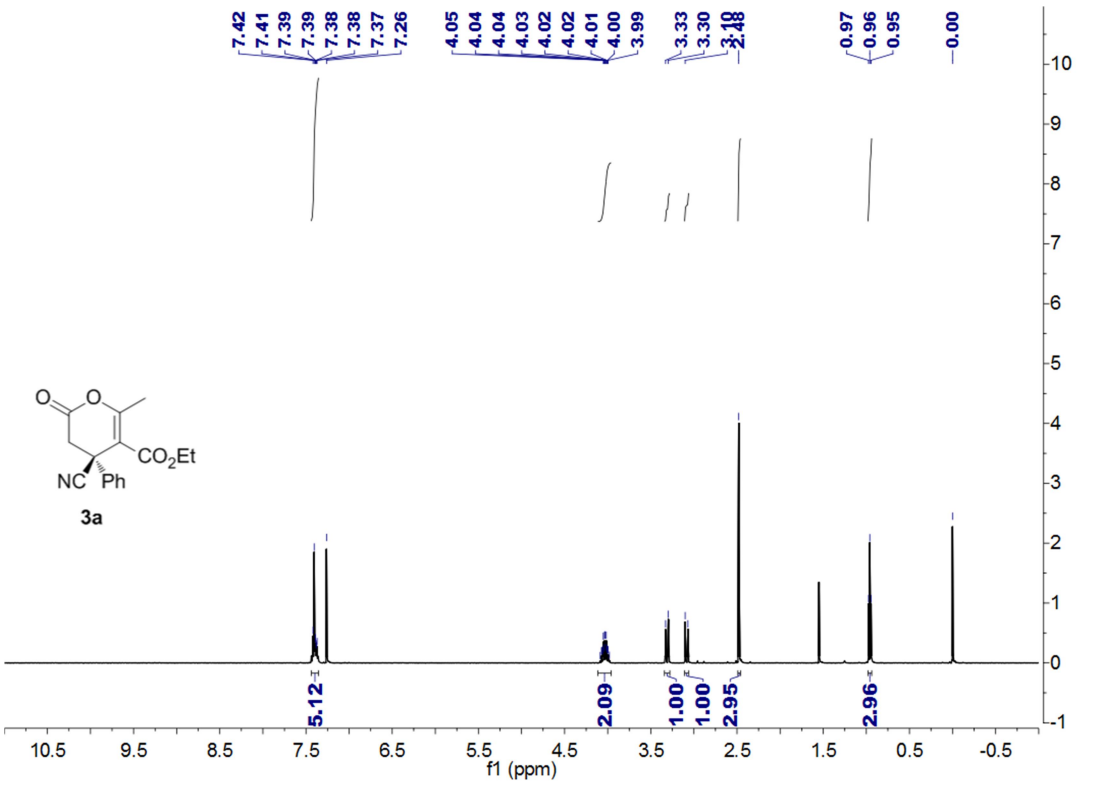
^{13}C NMR spectrum of **1l** (100 MHz, $CDCl_3$)



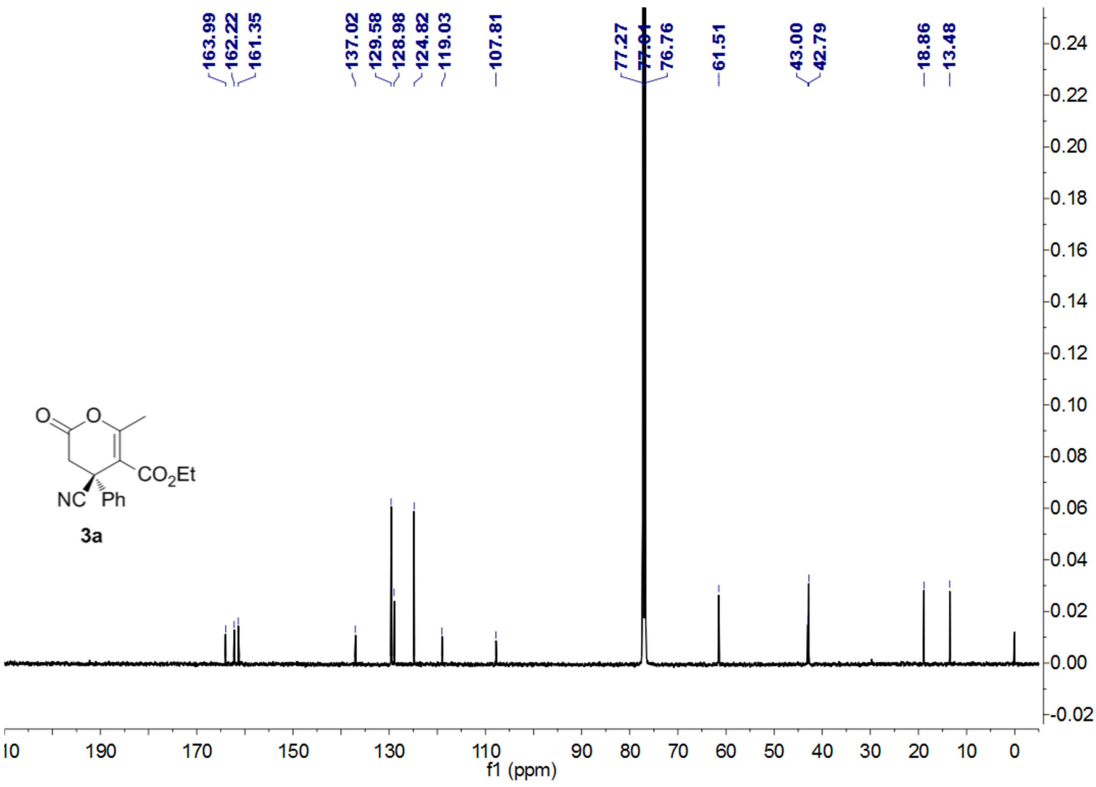
^{1}H NMR spectrum of **1m** (400 MHz, $CDCl_3$)



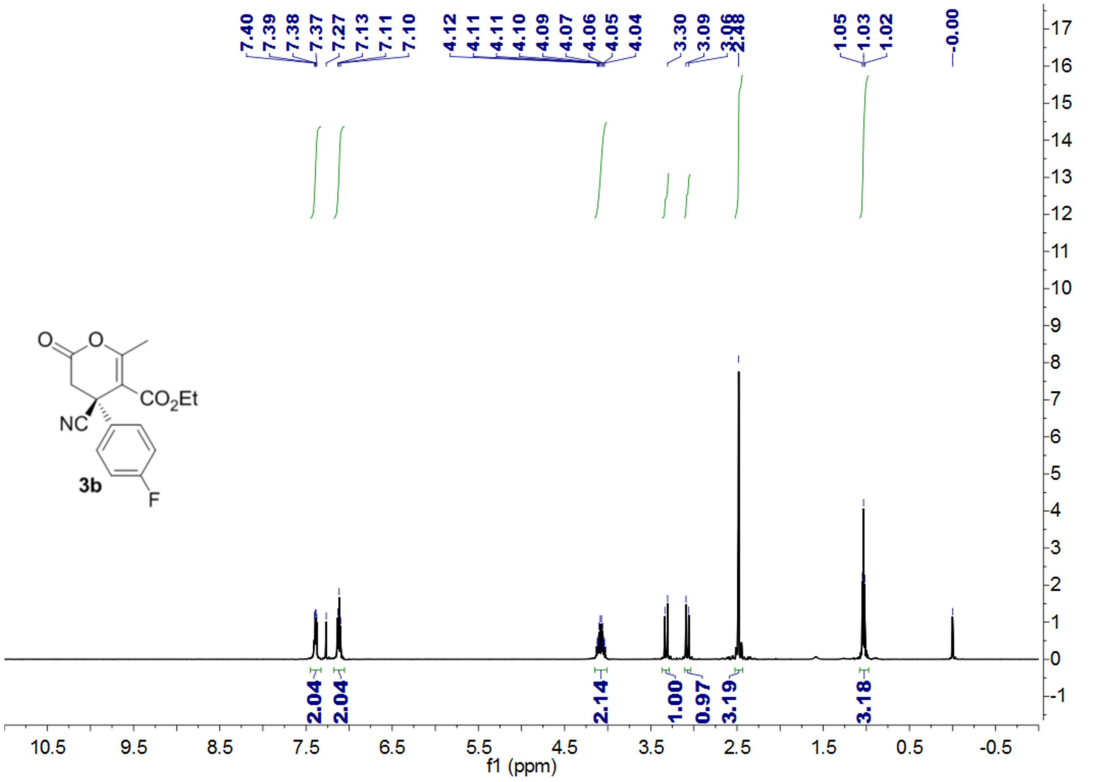
^{13}C NMR spectrum of **1m** (100 MHz, $CDCl_3$)



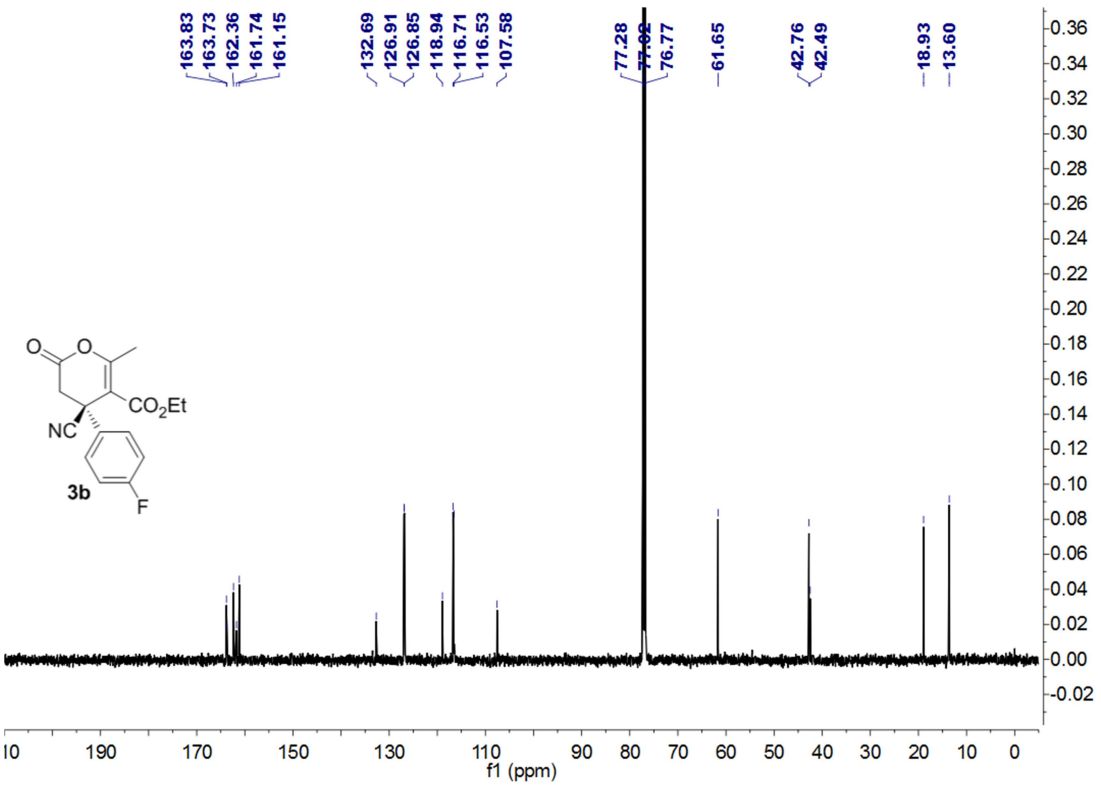
^{1}H NMR spectrum of **3a** (500 MHz, $CDCl_3$)



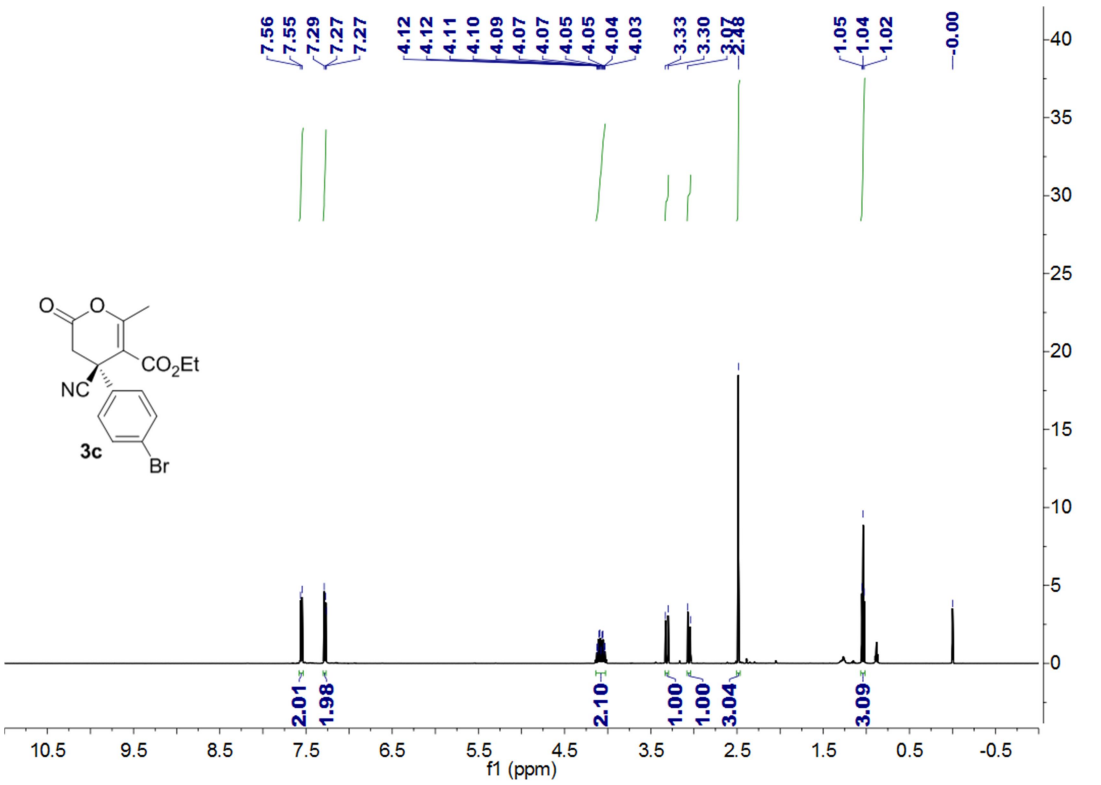
^{13}C NMR spectrum of **3a** (125 MHz, $CDCl_3$)



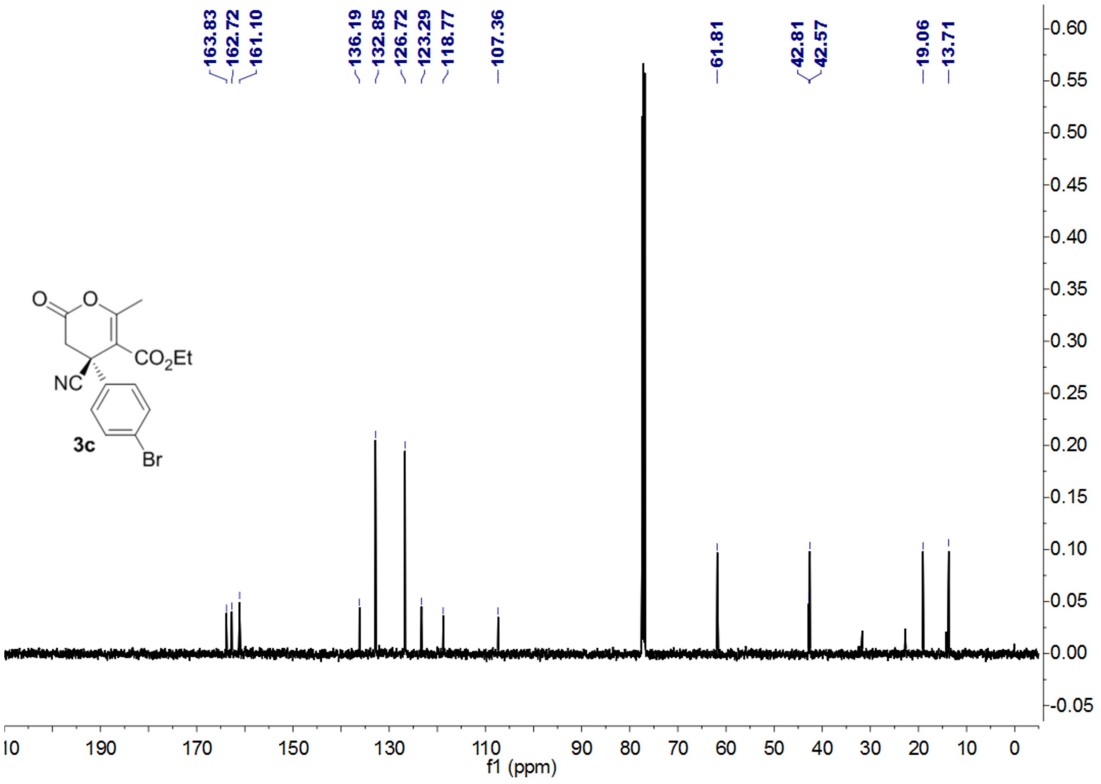
^{1}H NMR spectrum of **3b** (500 MHz, $CDCl_3$)



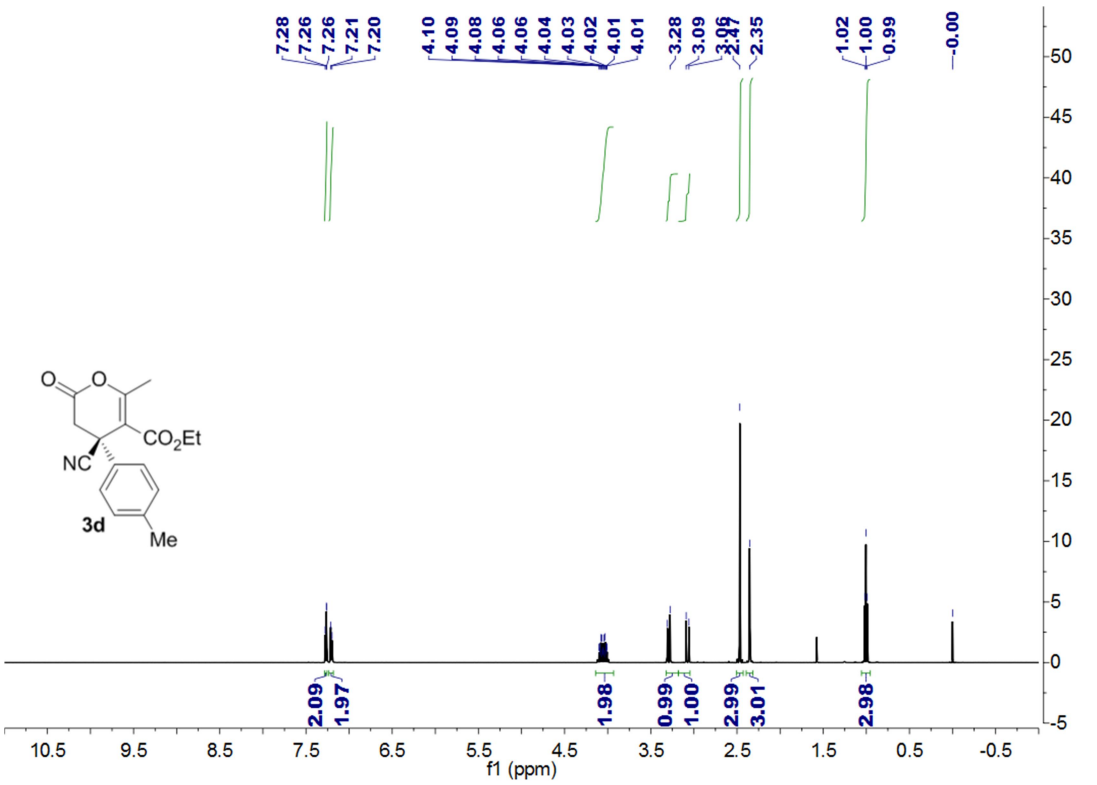
^{13}C NMR spectrum of **3b** (125 MHz, $CDCl_3$)



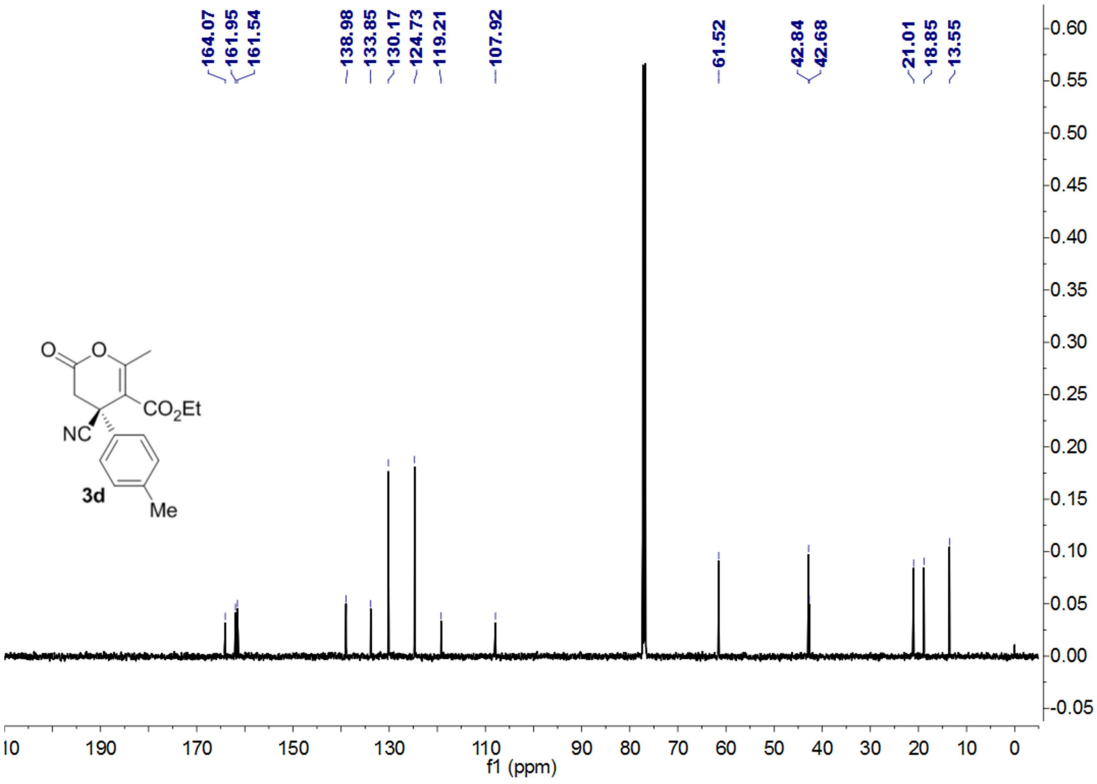
^{1}H NMR spectrum of **3c** (500 MHz, $CDCl_3$)



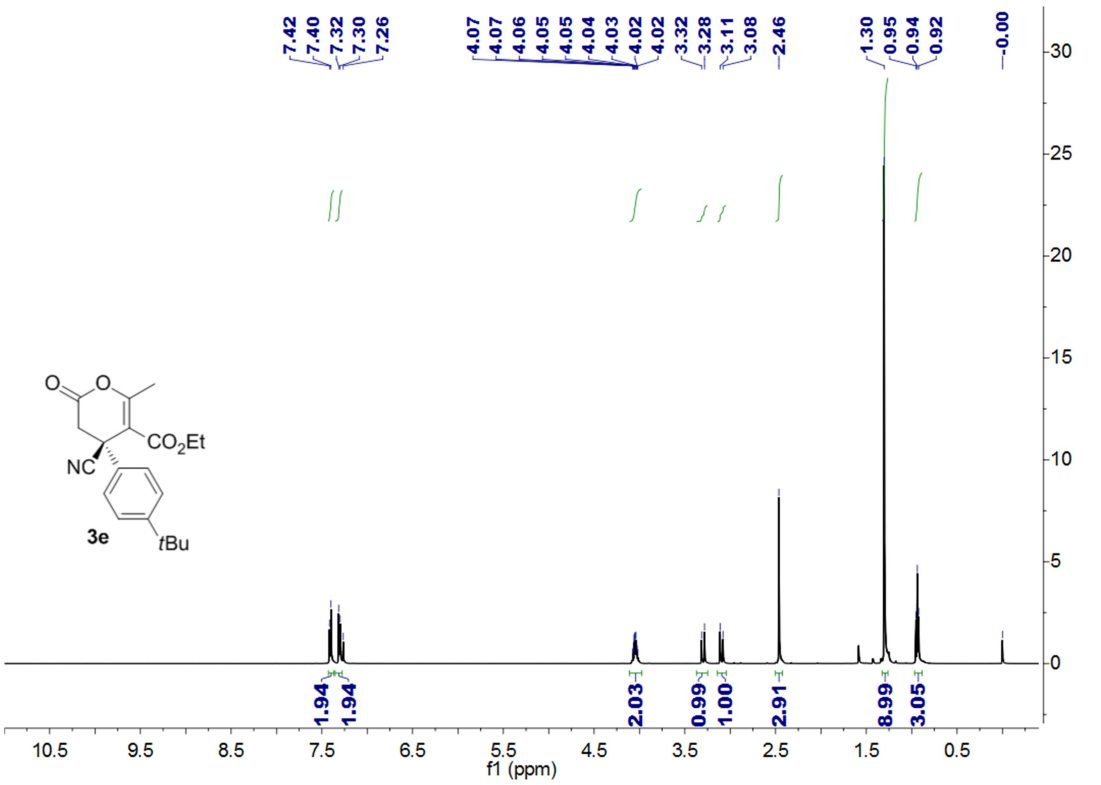
^{13}C NMR spectrum of **3c** (125 MHz, $CDCl_3$)



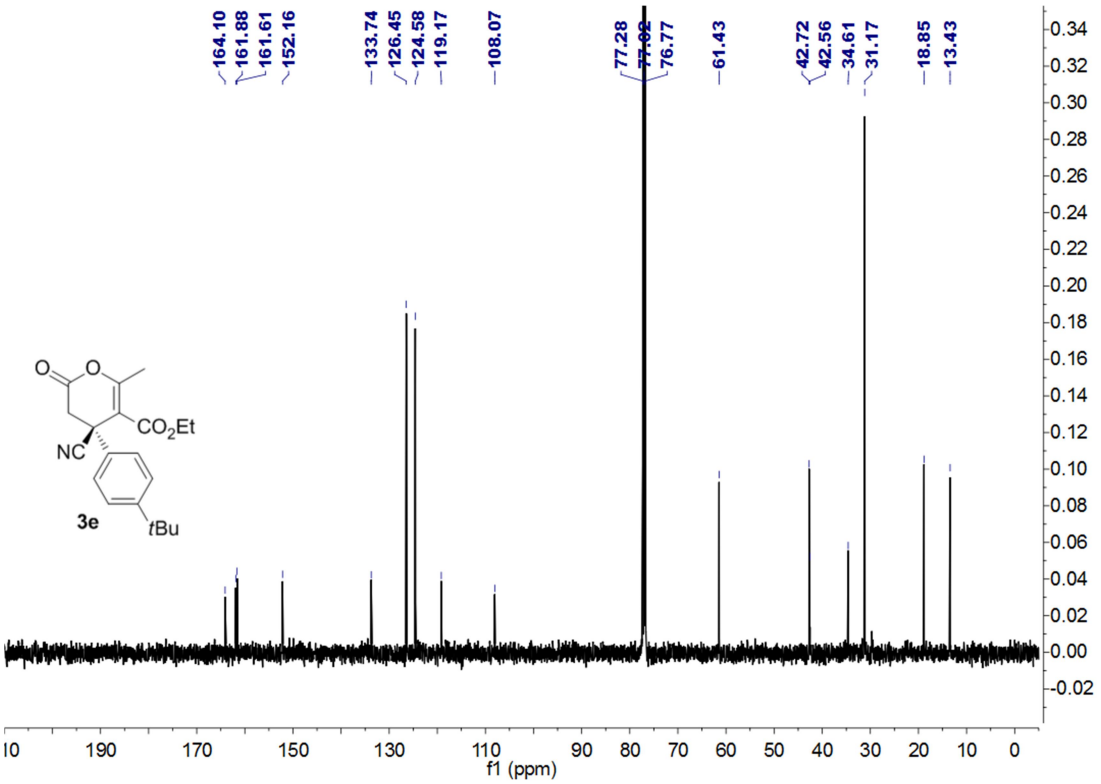
^{1}H NMR spectrum of **3d** (500 MHz, $CDCl_3$)



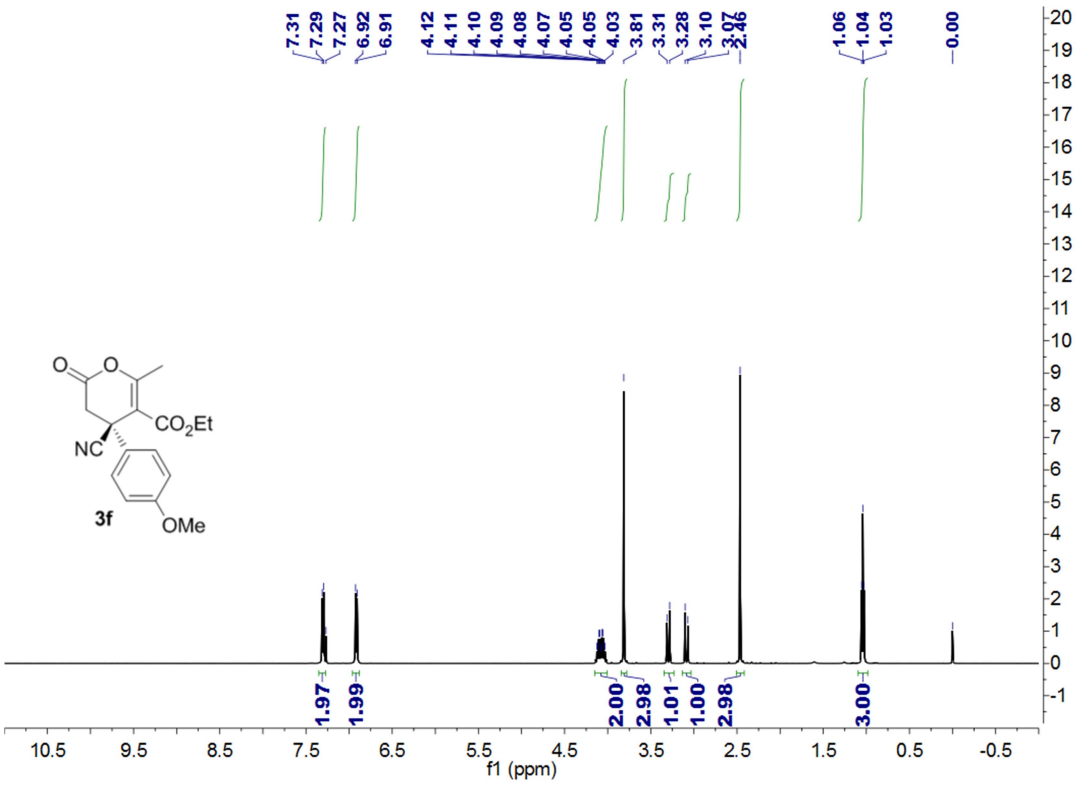
^{13}C NMR spectrum of **3d** (125 MHz, $CDCl_3$)



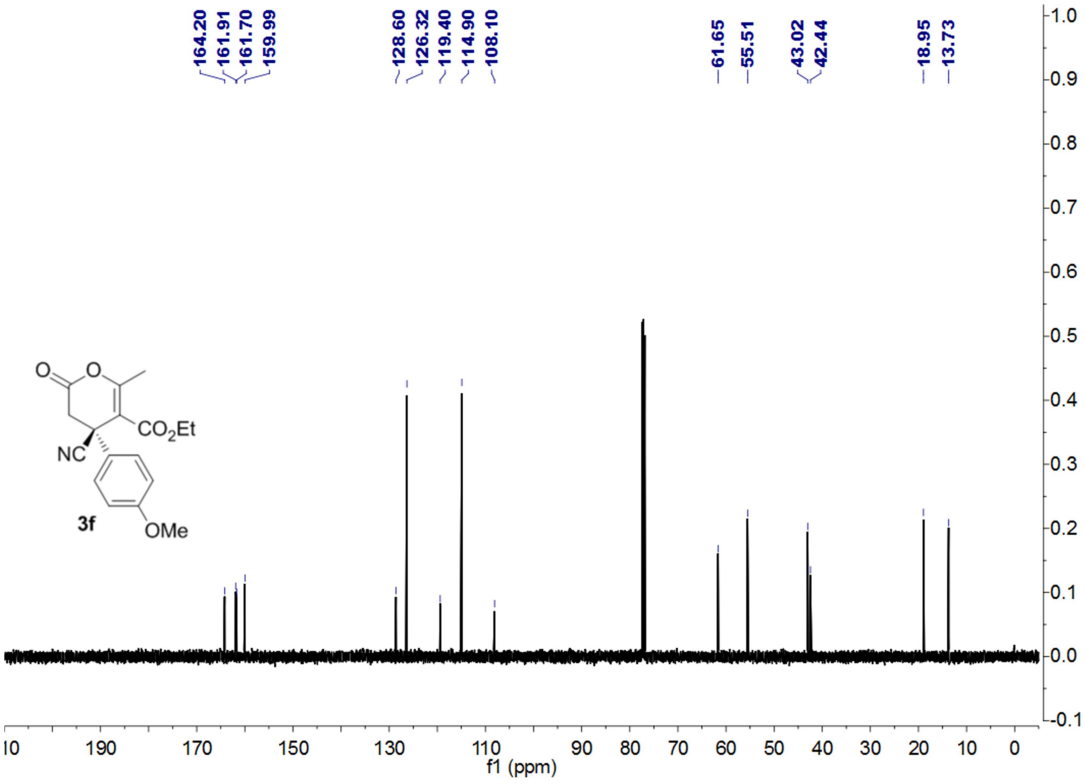
^{1}H NMR spectrum of **3e** (500 MHz, $CDCl_3$)



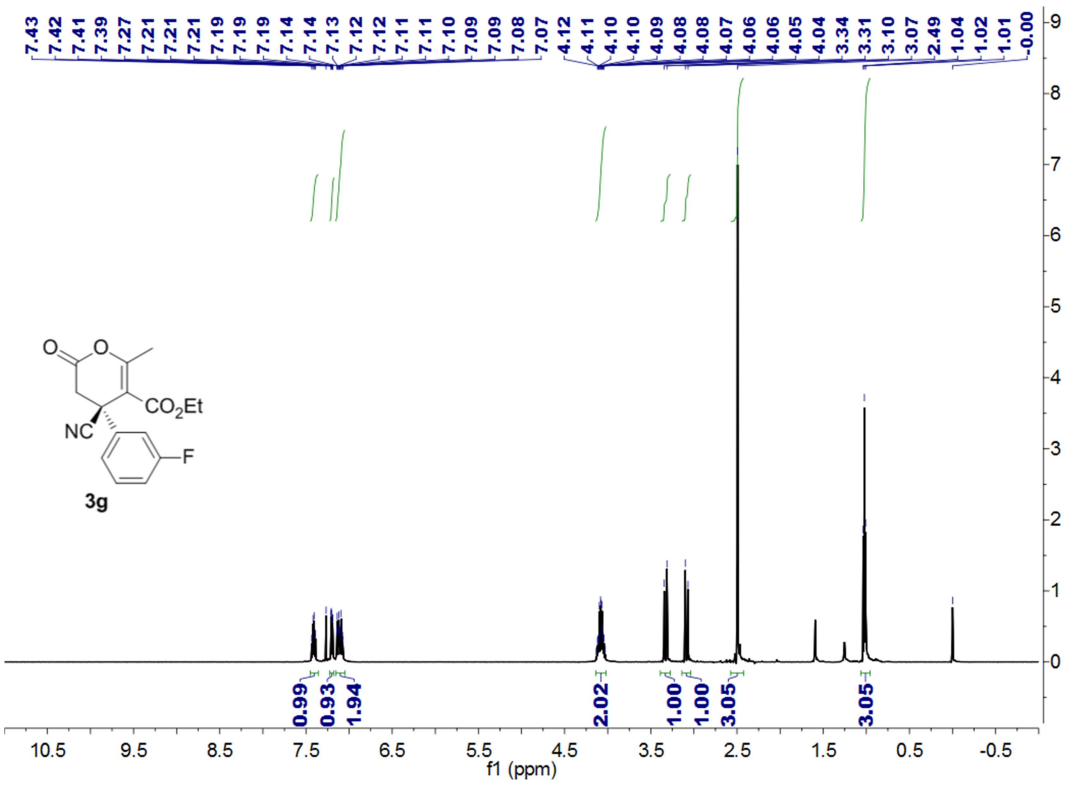
^{13}C NMR spectrum of **3e** (125 MHz, $CDCl_3$)



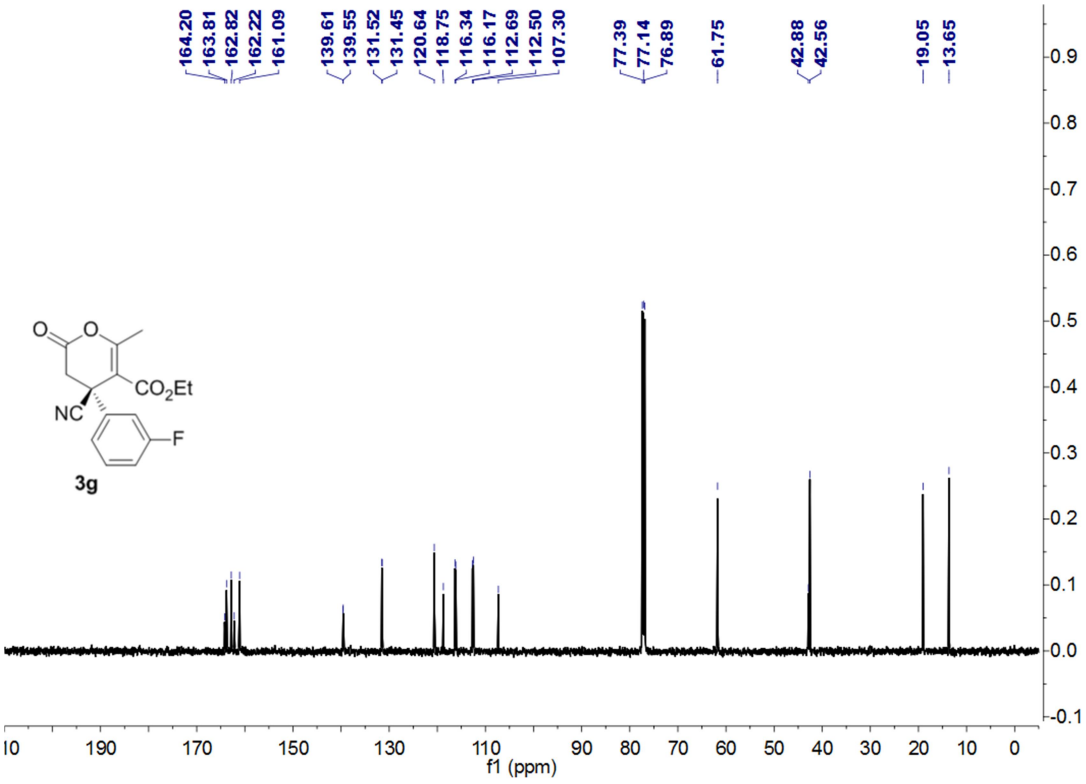
^{1}H NMR spectrum of **3f** (500 MHz, $CDCl_3$)



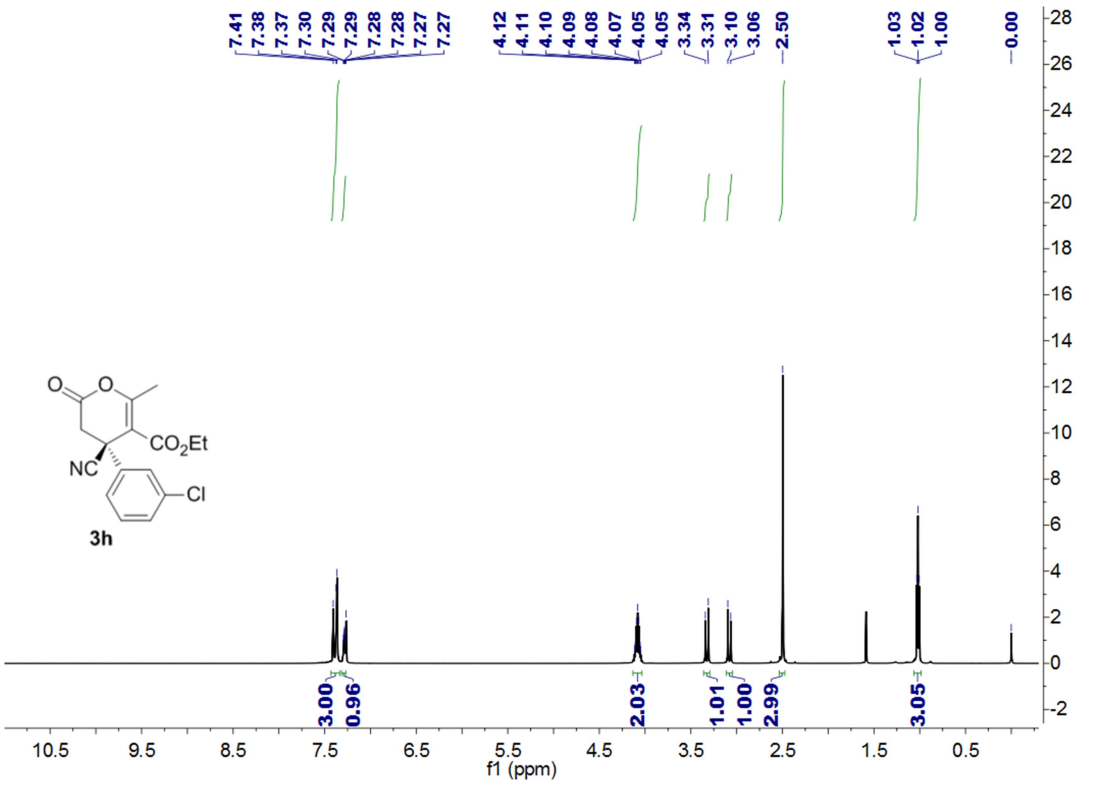
^{1}H NMR spectrum of **3f** (125 MHz, $CDCl_3$)



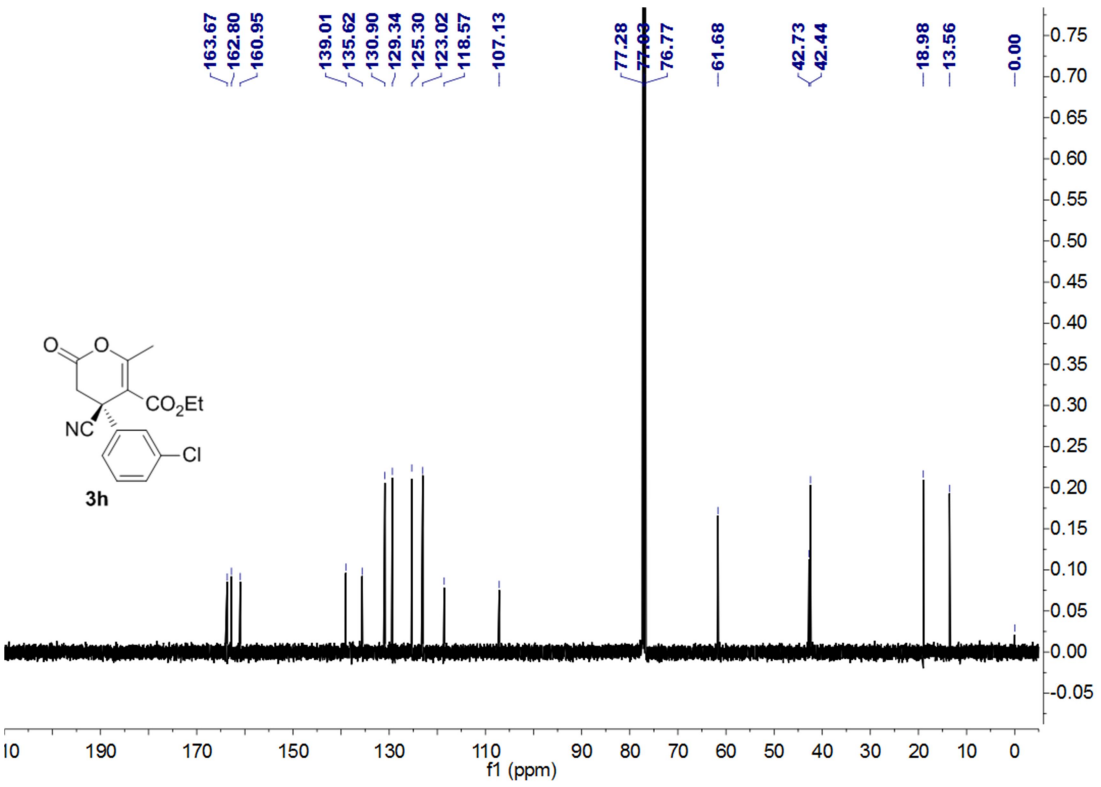
^{1}H NMR spectrum of **3g** (500 MHz, $CDCl_3$)



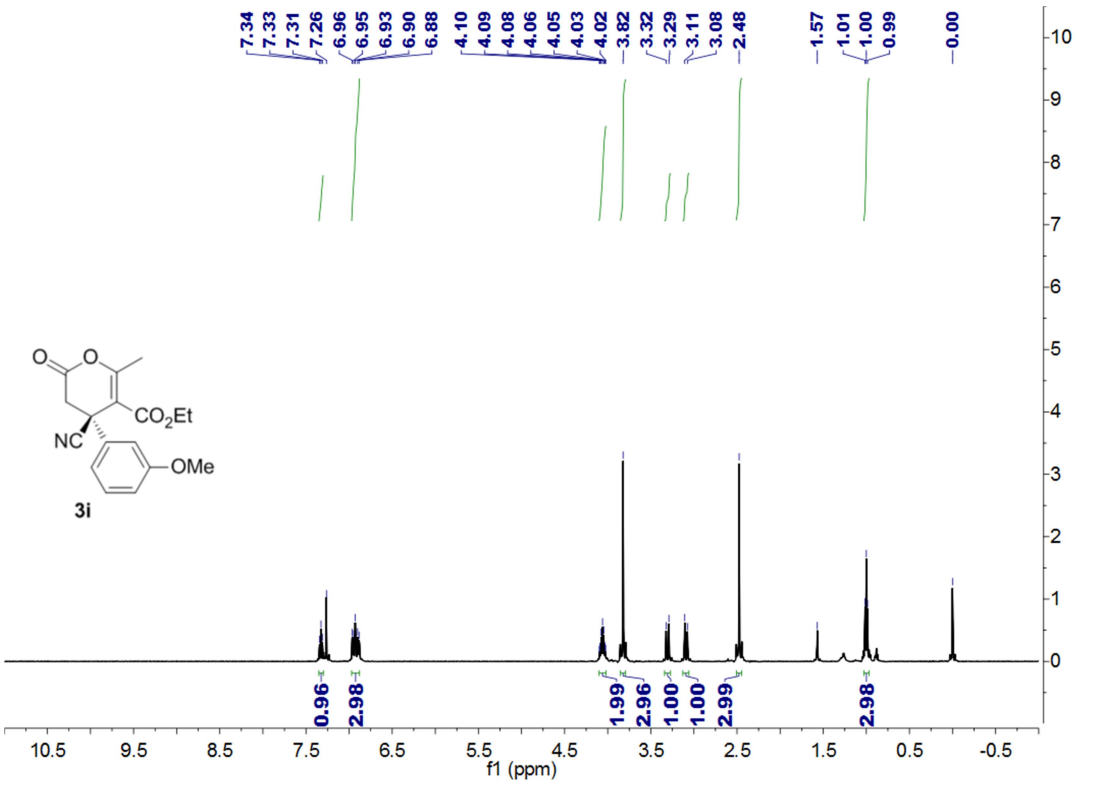
^{13}C NMR spectrum of **3g** (125 MHz, $CDCl_3$)



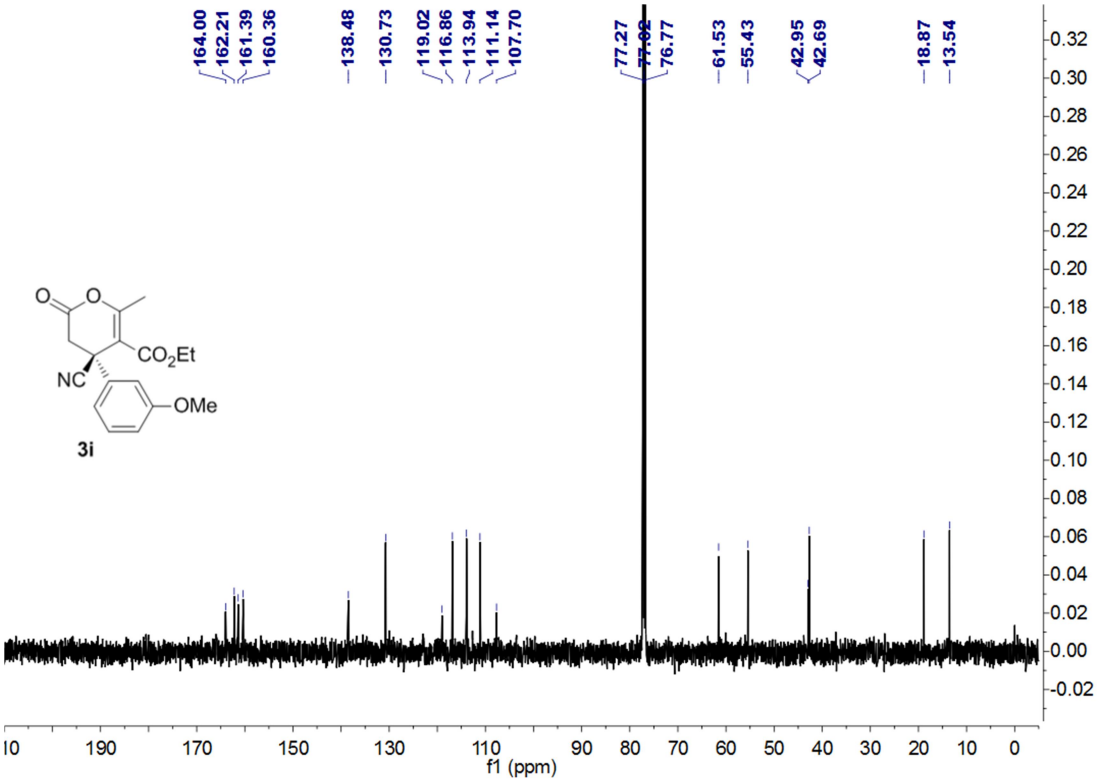
^{1}H NMR spectrum of **3h** (500 MHz, $CDCl_3$)



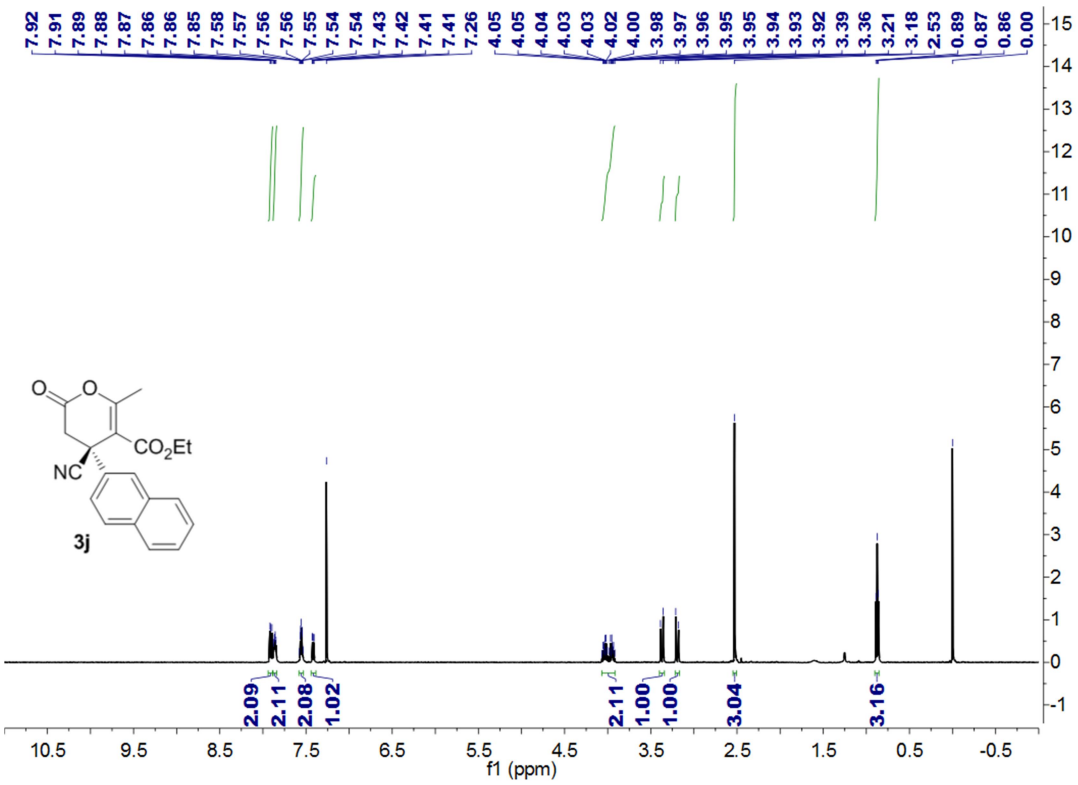
^{13}C NMR spectrum of **3h** (125 MHz, $CDCl_3$)



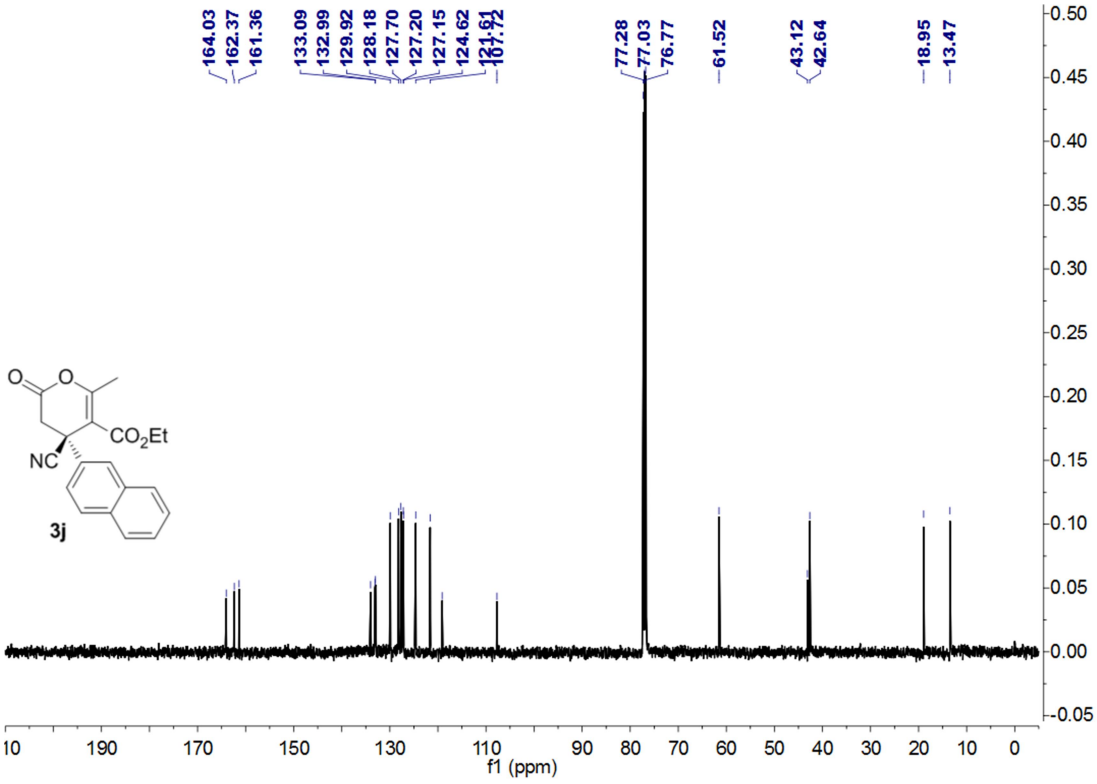
^{1}H NMR spectrum of **3i** (500 MHz, $CDCl_3$)



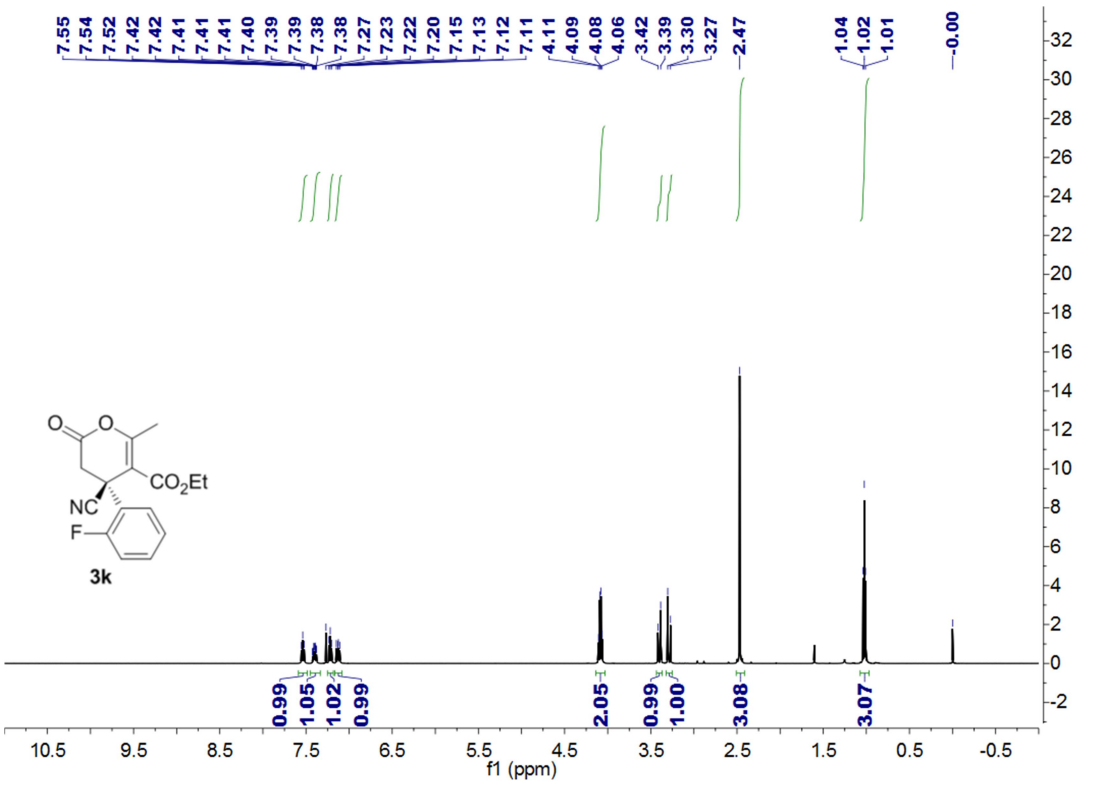
^{13}C NMR spectrum of **3i** (125 MHz, $CDCl_3$)



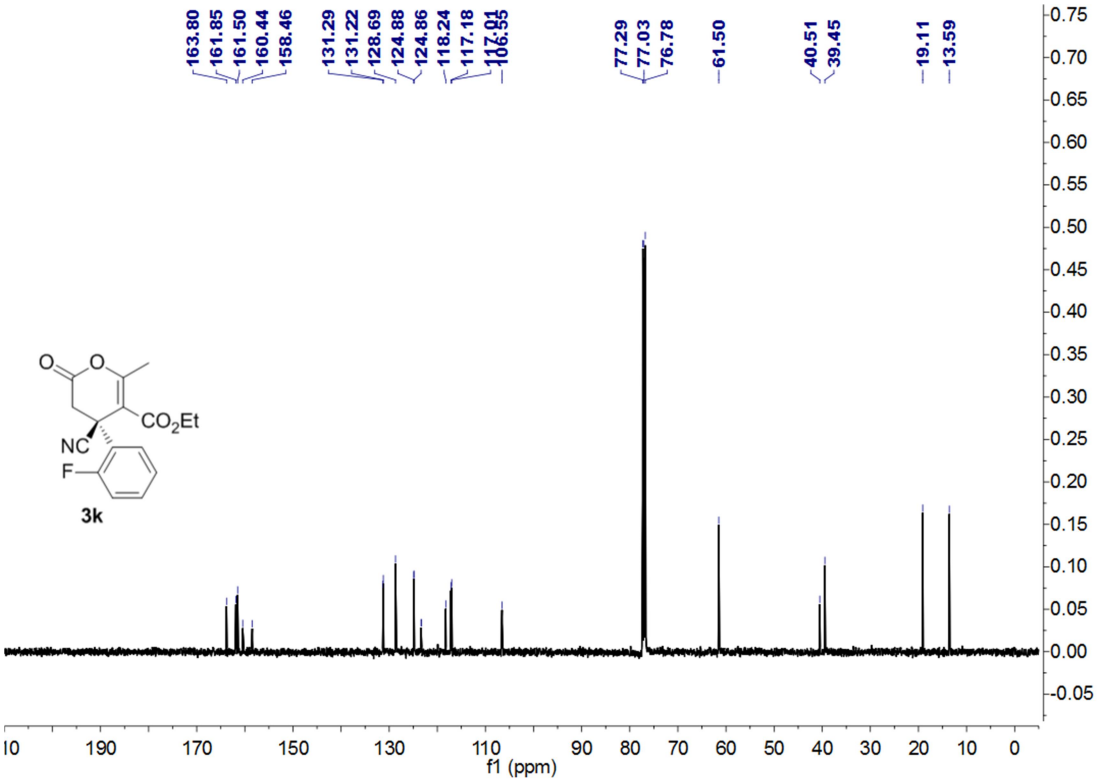
^{1}H NMR spectrum of **3j** (500 MHz, $CDCl_3$)



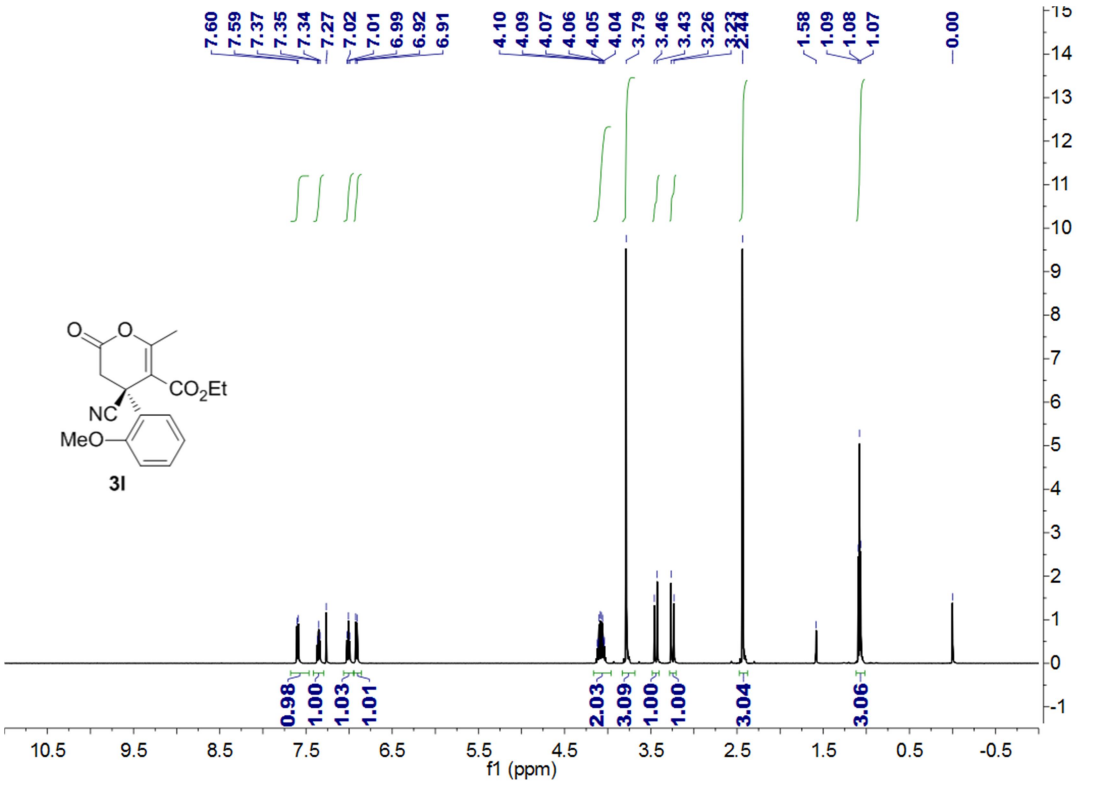
^{13}C NMR spectrum of **3j** (125 MHz, $CDCl_3$)



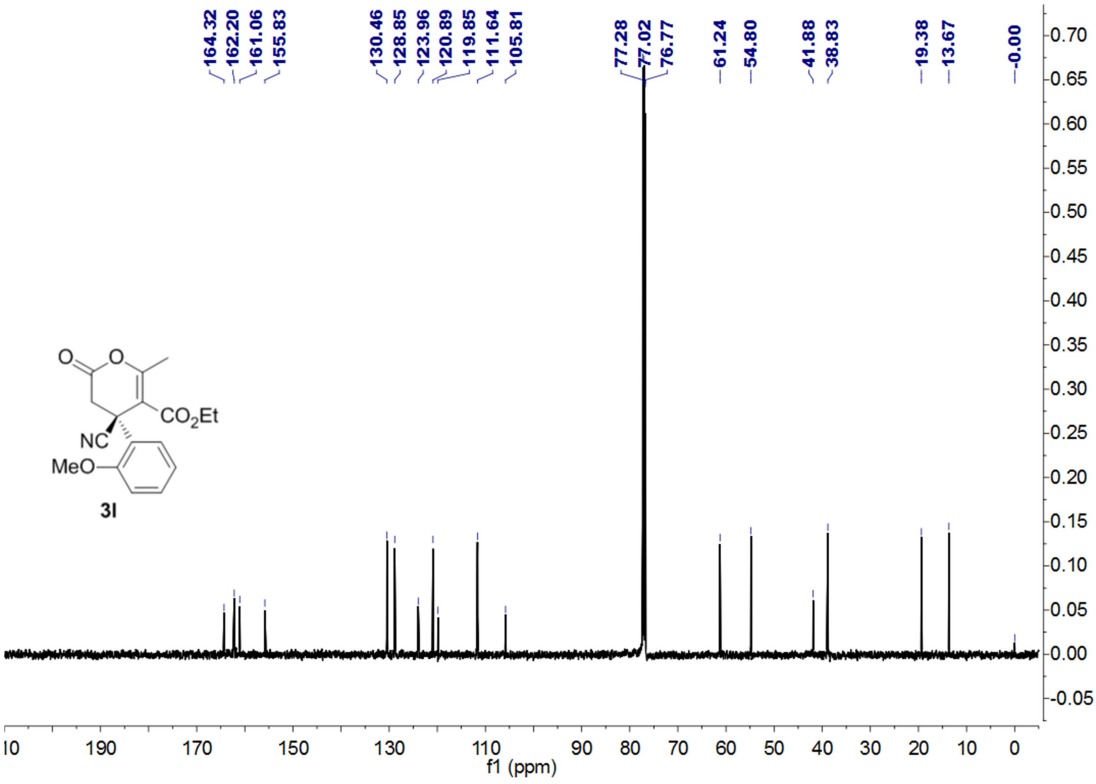
^{1}H NMR spectrum of **3k** (500 MHz, $CDCl_3$)



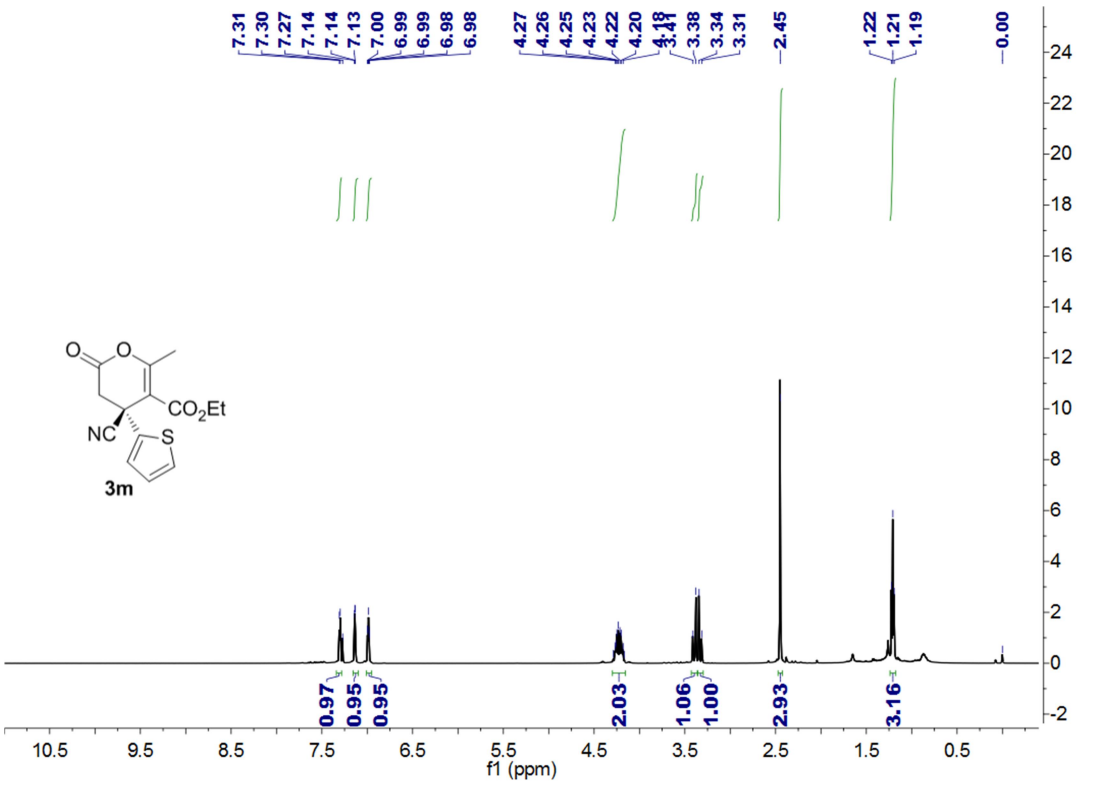
^{13}C NMR spectrum of **3k** (125 MHz, $CDCl_3$)



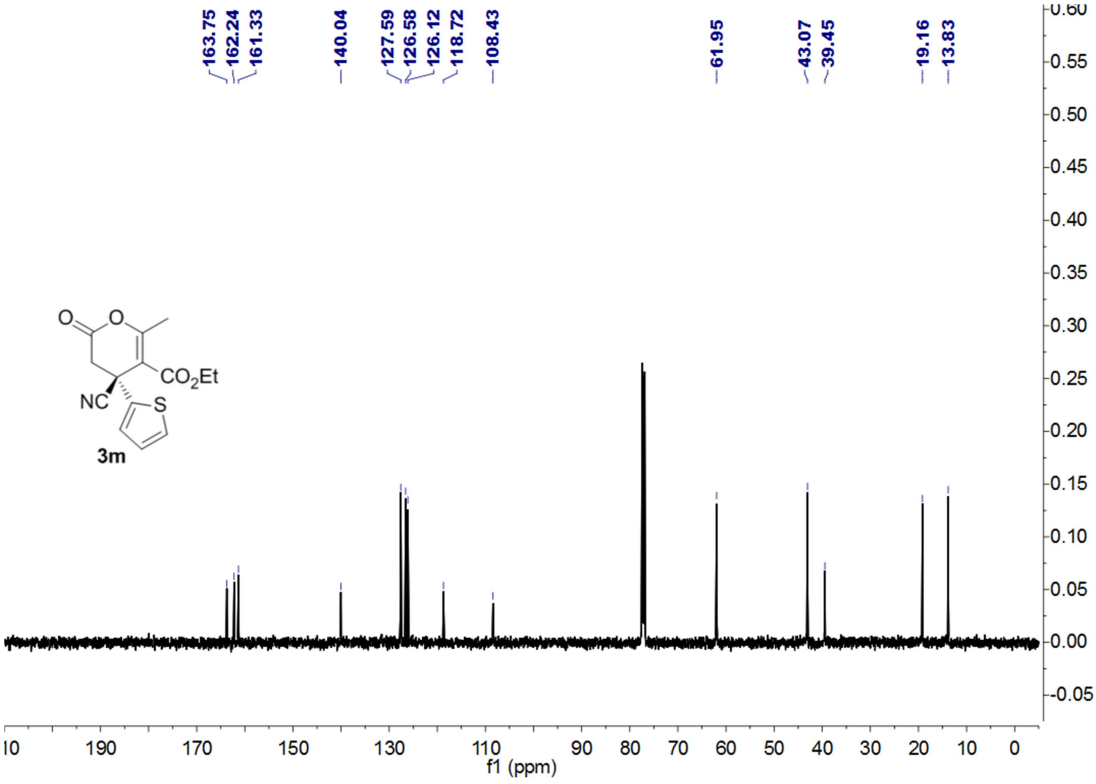
^{1}H NMR spectrum of **3l** (500 MHz, $CDCl_3$)



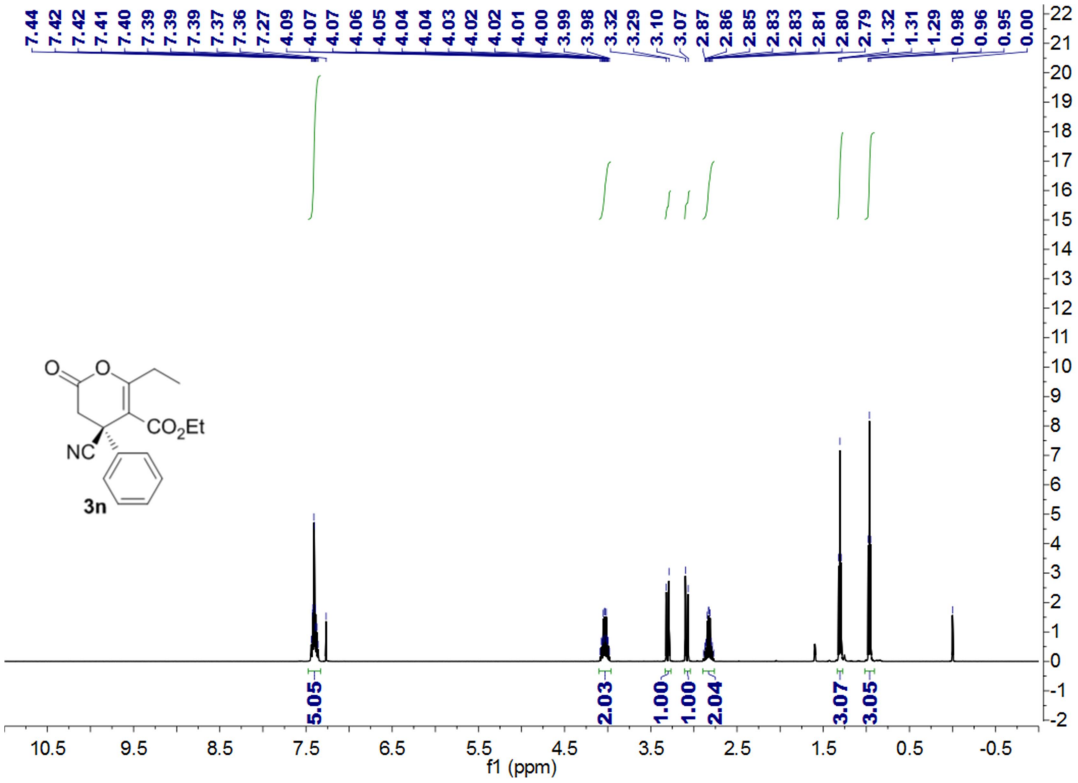
^{13}C NMR spectrum of **3l** (125 MHz, $CDCl_3$)



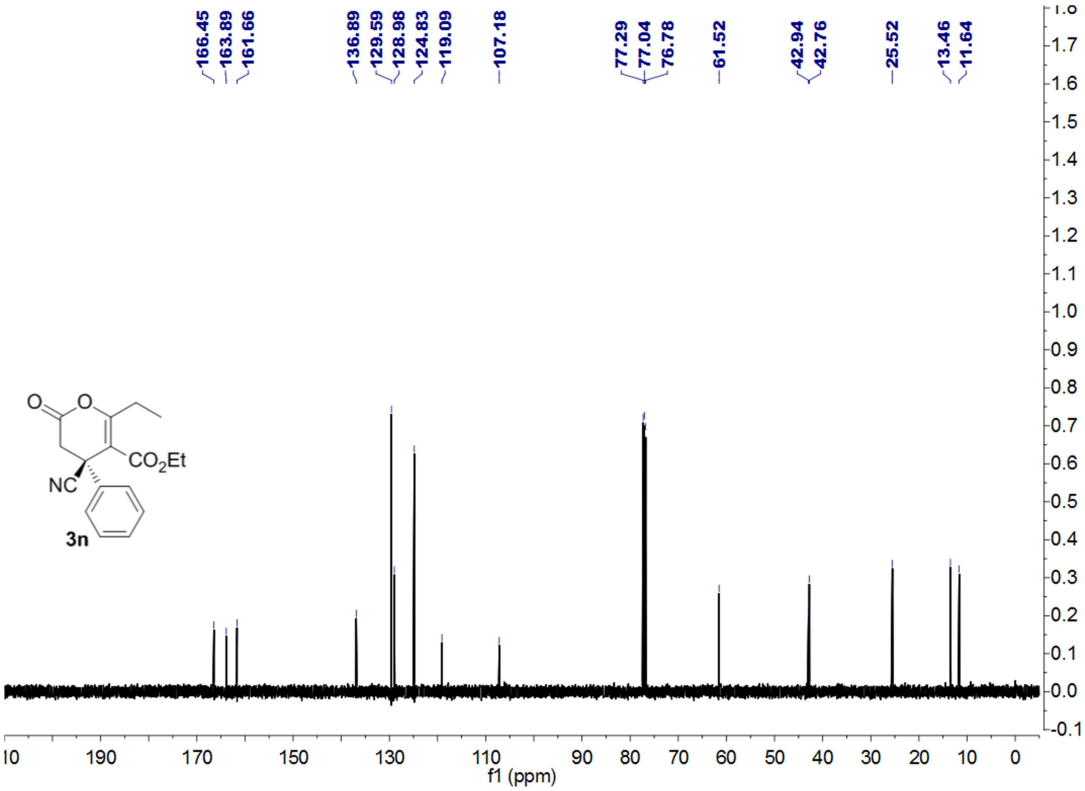
^{1}H NMR spectrum of **3m** (500 MHz, $CDCl_3$)



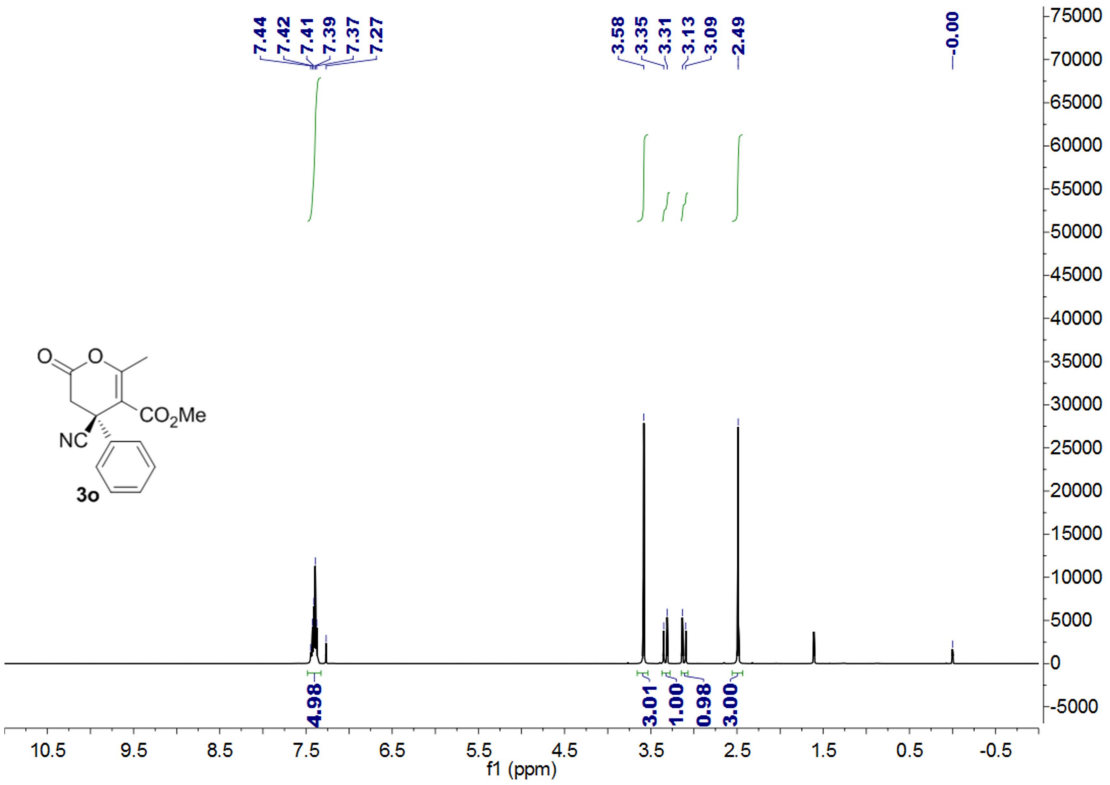
^{13}C NMR spectrum of **3m** (125 MHz, $CDCl_3$)



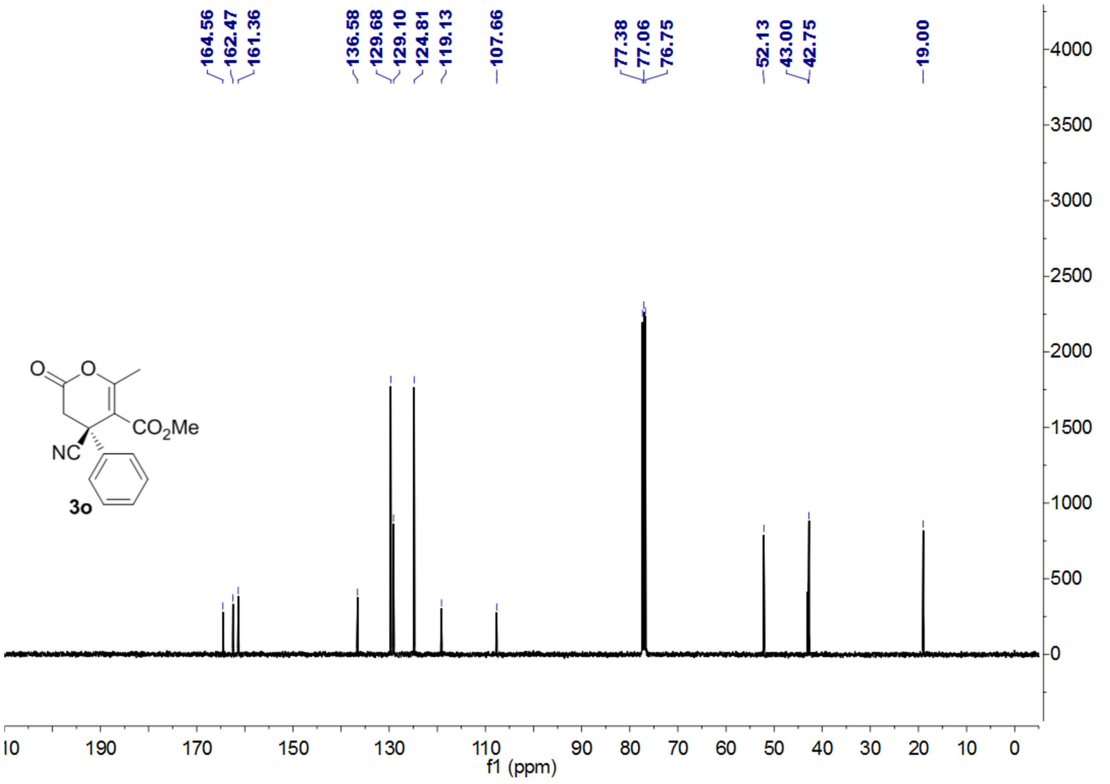
^{1}H NMR spectrum of **3n** (500 MHz, $CDCl_3$)



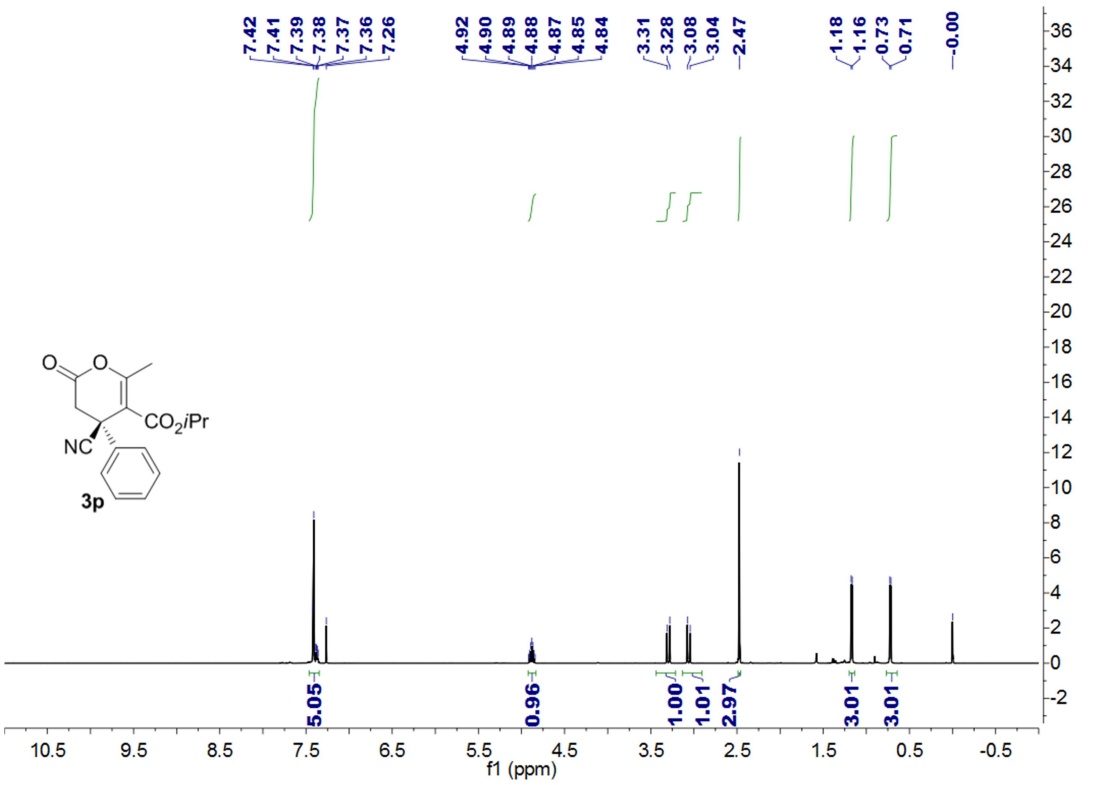
^{13}C NMR spectrum of **3n** (125 MHz, $CDCl_3$)



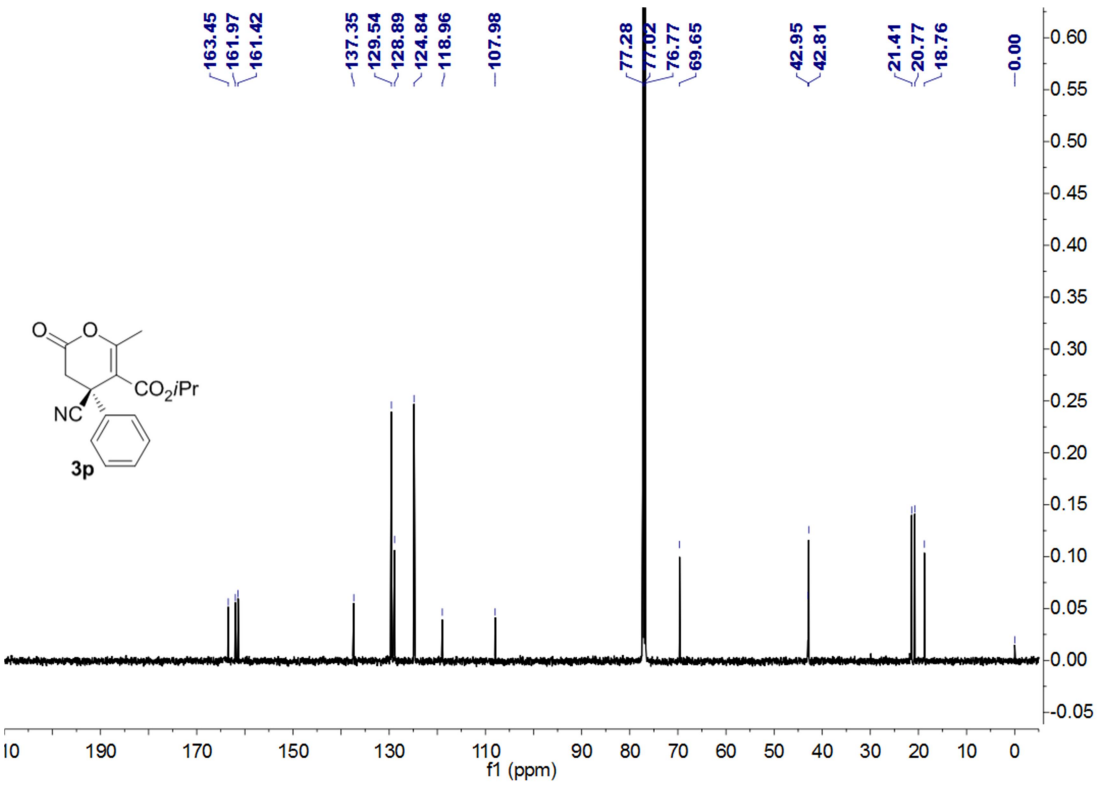
^{1}H NMR spectrum of **3o** (400 MHz, $CDCl_3$)



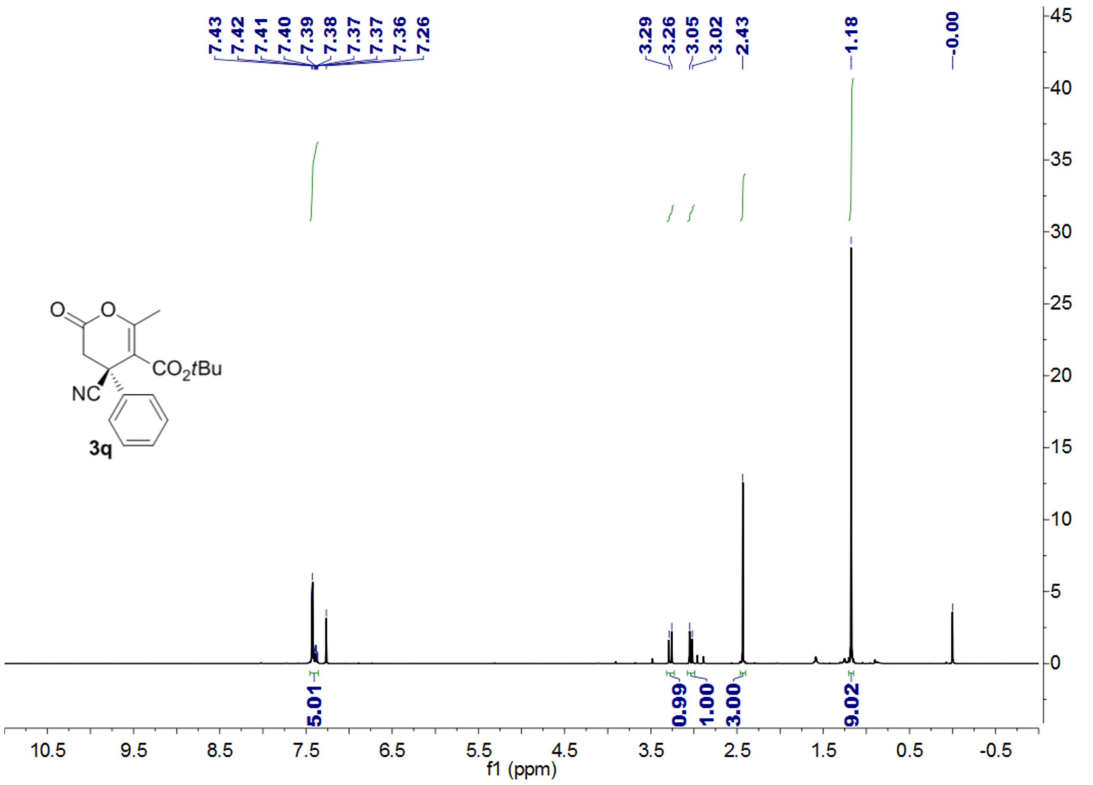
^{13}C NMR spectrum of **3o** (100 MHz, $CDCl_3$)



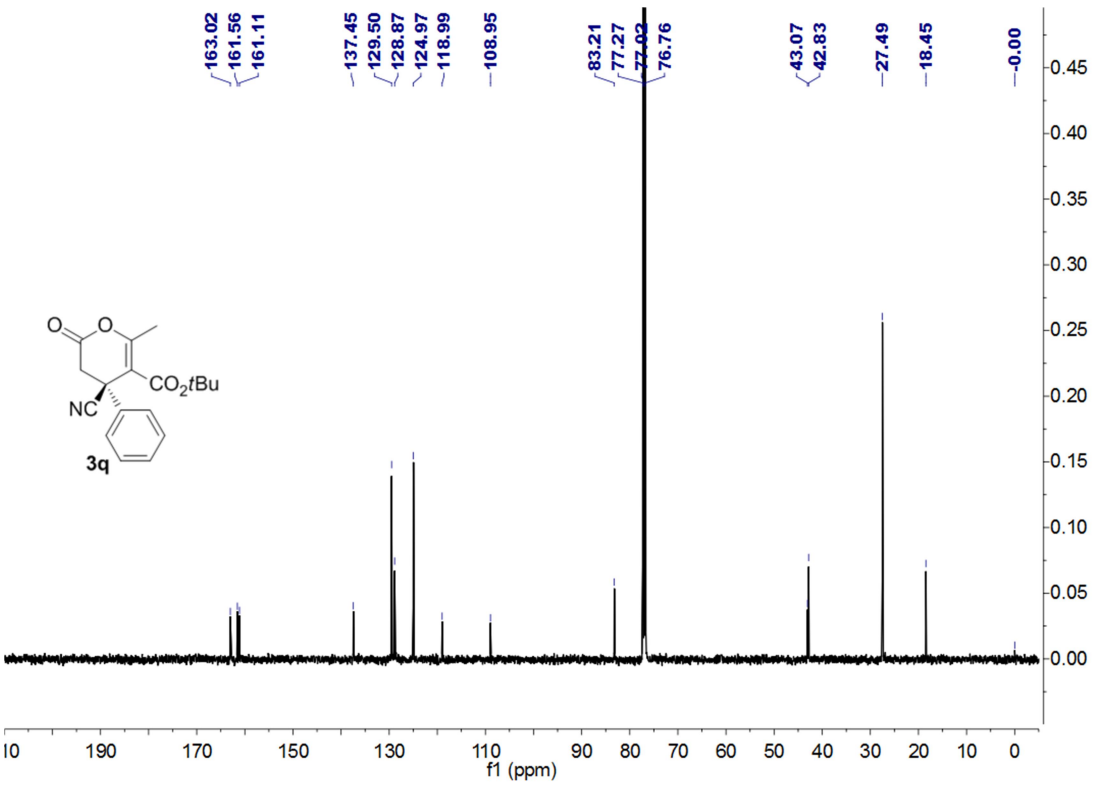
^{1}H NMR spectrum of **3p** (500 MHz, $CDCl_3$)



^{13}C NMR spectrum of **3p** (125 MHz, $CDCl_3$)

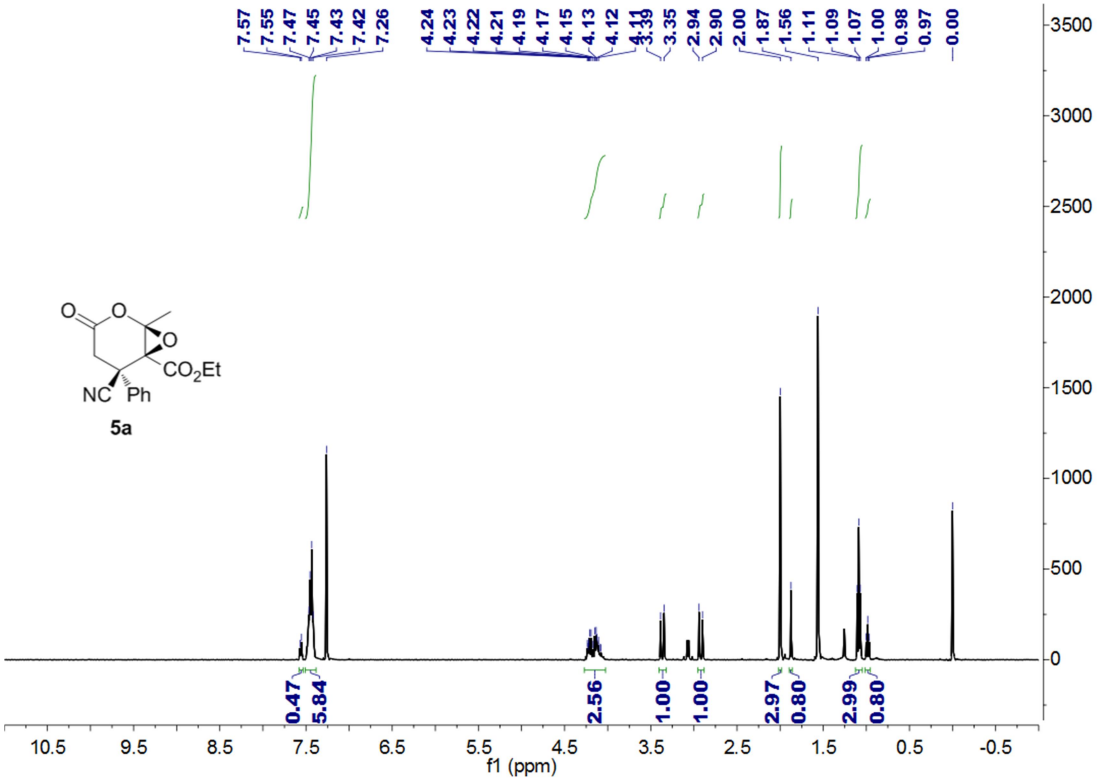


^{1}H NMR spectrum of **3q** (500 MHz, $CDCl_3$)

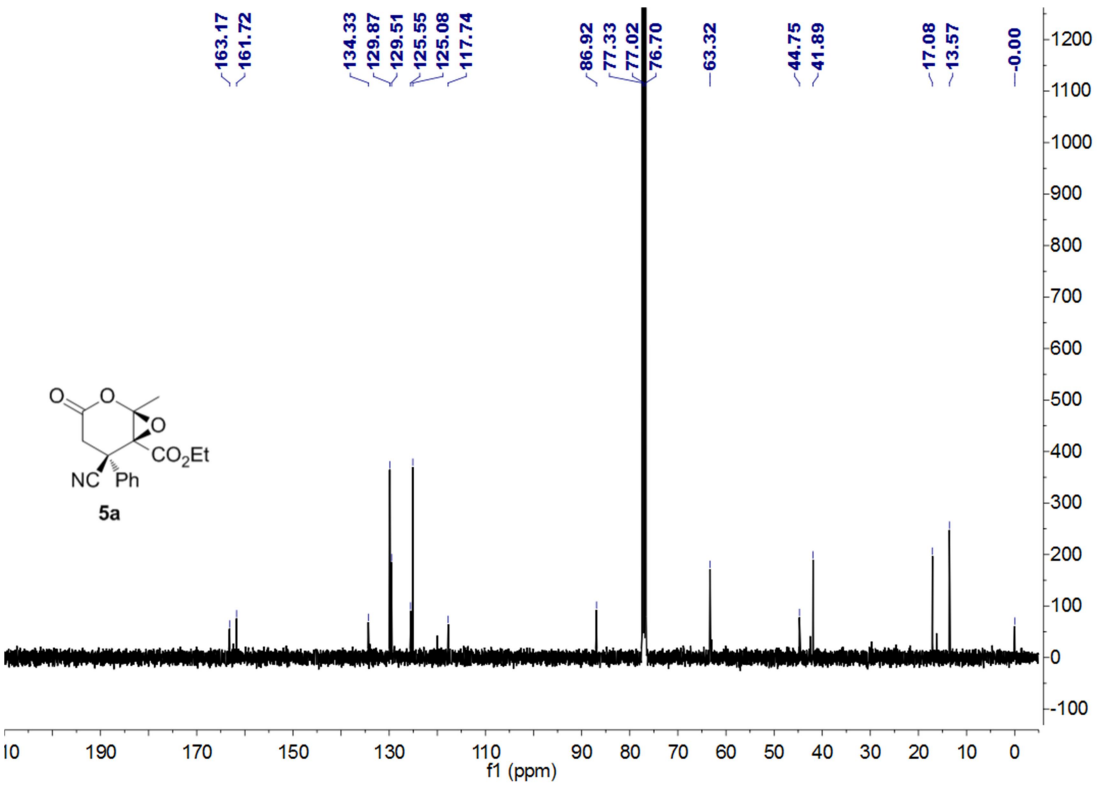


^{13}C NMR spectrum of **3q** (125 MHz, $CDCl_3$)

5a



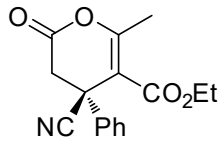
^{1}H NMR spectrum of **5a** (400 MHz, $CDCl_3$)



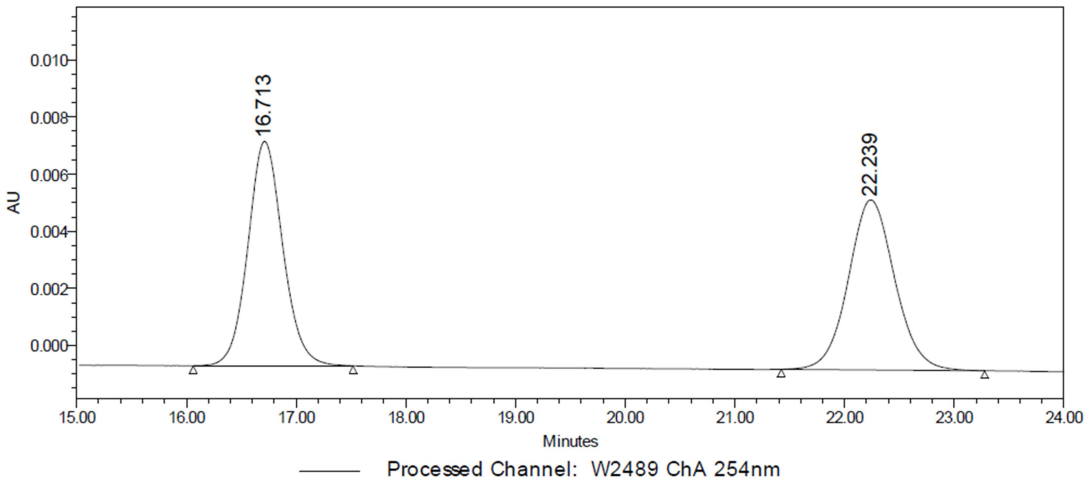
^{13}C NMR spectrum of **5a** (100 MHz, $CDCl_3$)

HPLC spectra of products

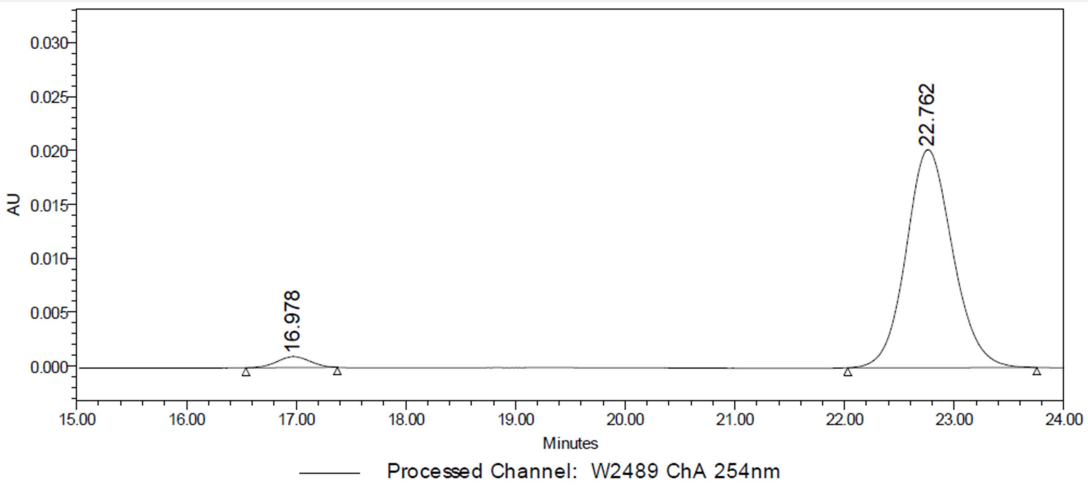
3a



3a

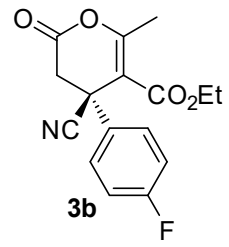


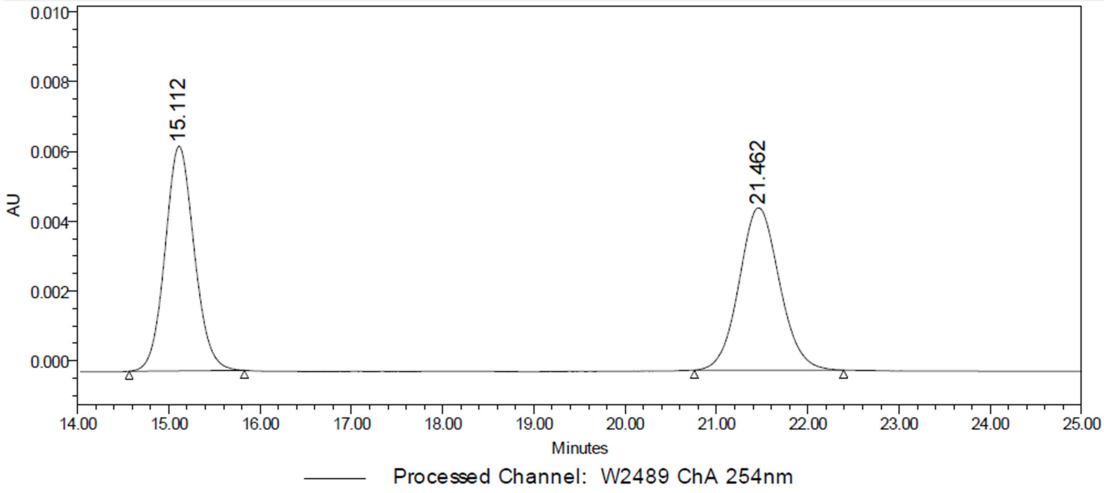
	RT	Area	% Area	Height	% Height
1	16.713	174278	49.88	7856	56.90
2	22.239	175121	50.12	5951	43.10
Sum		349398.9	100.0	13807.2	100.0



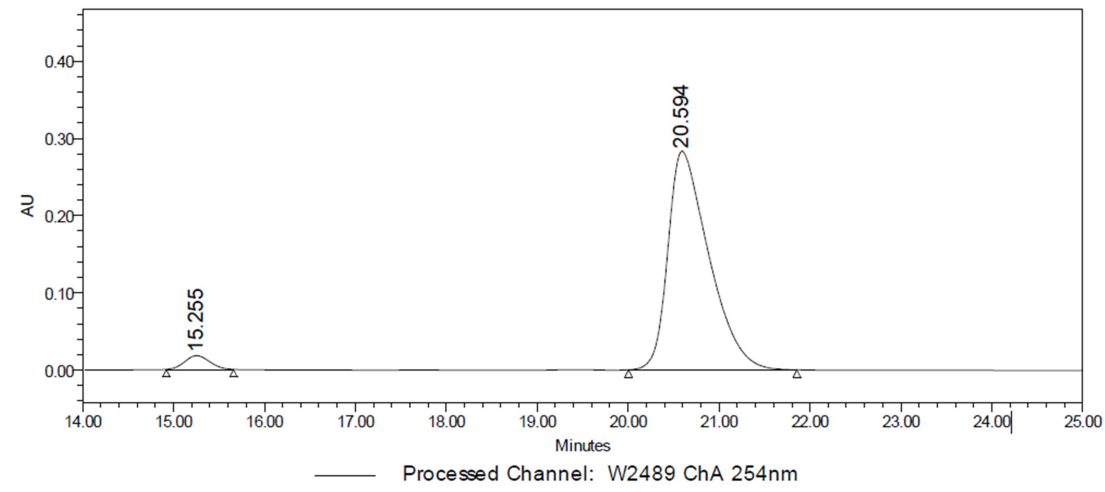
	RT	Area	% Area	Height	% Height
1	16.978	21177	3.42	1011	4.76
2	22.762	597447	96.58	20226	95.24
Sum		618623.7	100.0	21237.2	100.0

3b



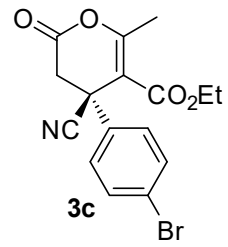


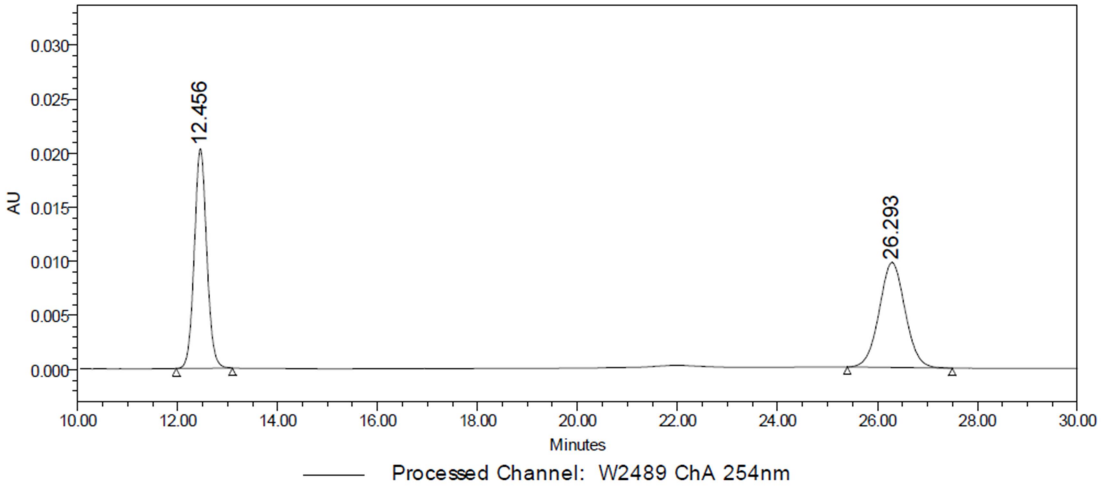
	RT	Area	% Area	Height	% Height
1	15.112	143503	50.05	6434	58.04
2	21.462	143211	49.95	4652	41.96
Sum		286714.7	100.0	11085.9	100.0



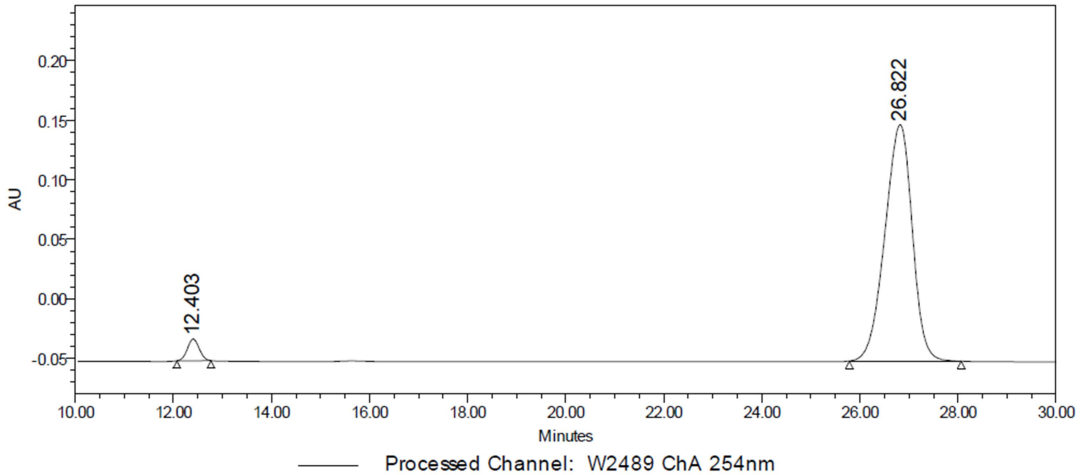
	RT	Area	% Area	Height	% Height
1	15.255	337398	3.67	17829	5.92
2	20.594	8854532	96.33	283096	94.08
Sum		9191929.1	100.0	300925.0	100.0

3c



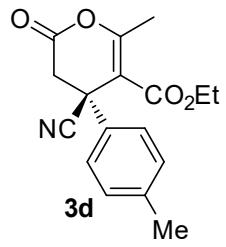


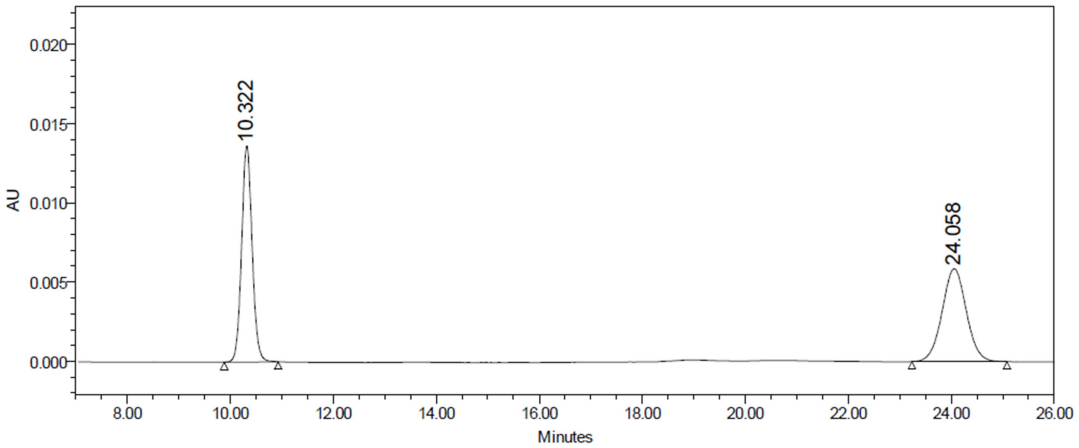
	RT	Area	% Area	Height	% Height
1	12.456	352580	50.20	20332	67.71
2	26.293	349754	49.80	9697	32.29
Sum		702334.2	100.0	30029.0	100.0



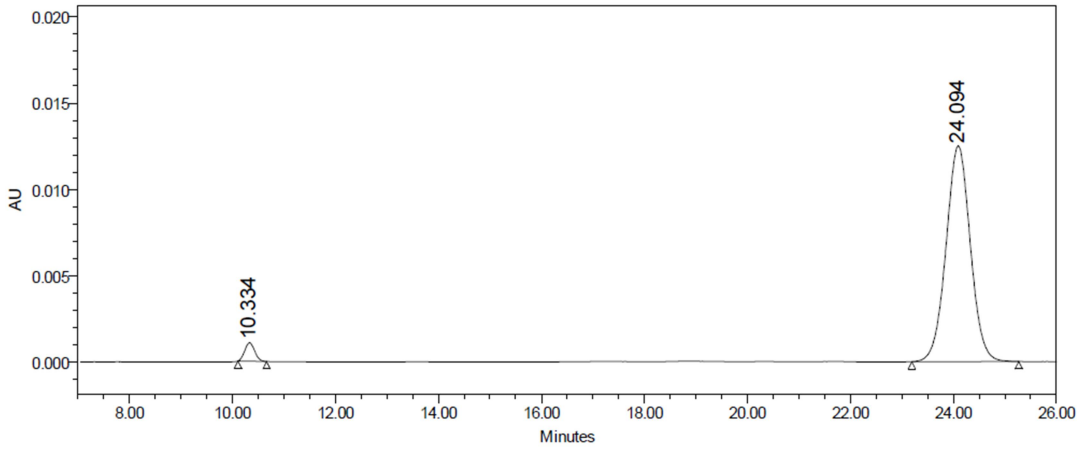
	RT	Area	% Area	Height	% Height
1	12.403	304884	3.80	18183	8.39
2	26.822	7711593	96.20	198655	91.61
Sum		8016476.8	100.0	216838.3	100.0

3d



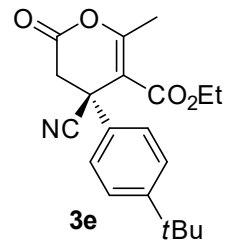


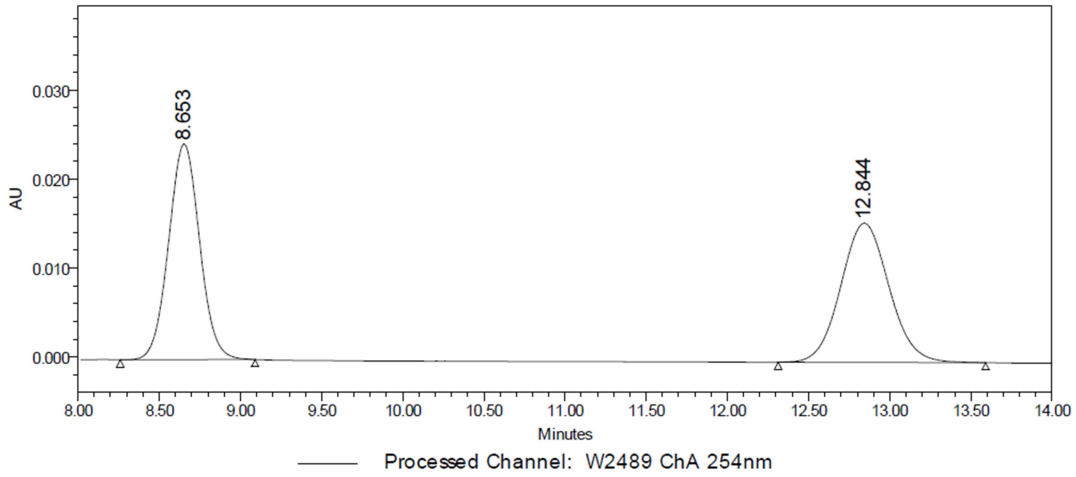
	RT	Area	% Area	Height	% Height
1	10.322	193475	50.18	13638	69.91
2	24.058	192075	49.82	5871	30.09
Sum		385550.4	100.0	19508.9	100.0



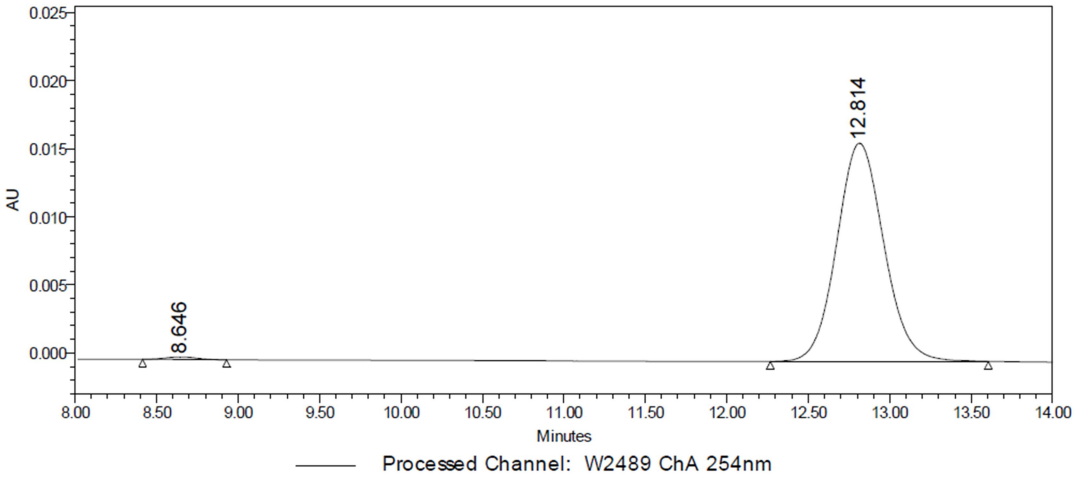
	RT	Area	% Area	Height	% Height
1	10.334	14224	3.36	1063	7.85
2	24.094	409638	96.64	12479	92.15
Sum		423862.3	100.0	13542.0	100.0

3e



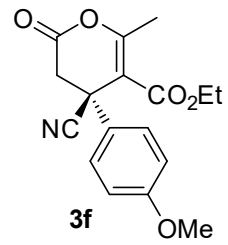


	RT	Area	% Area	Height	% Height
1	8.653	323098	49.87	24261	60.78
2	12.844	324759	50.13	15655	39.22
Sum		647856.8	100.0	39916.2	100.0

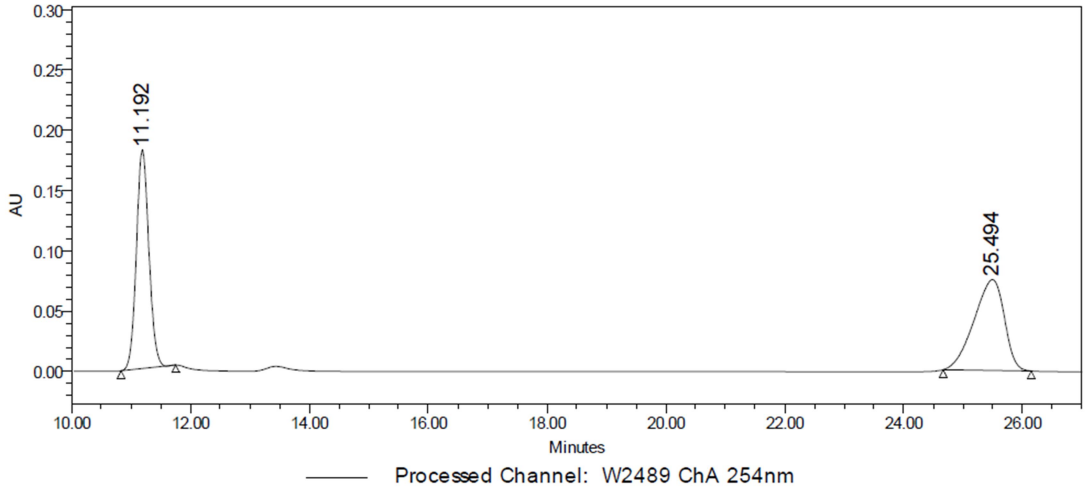


	RT	Area	% Area	Height	% Height
1	8.646	2347	0.72	189	1.17
2	12.814	322492	99.28	16024	98.83
Sum		324838.0	100.0	16213.3	100.0

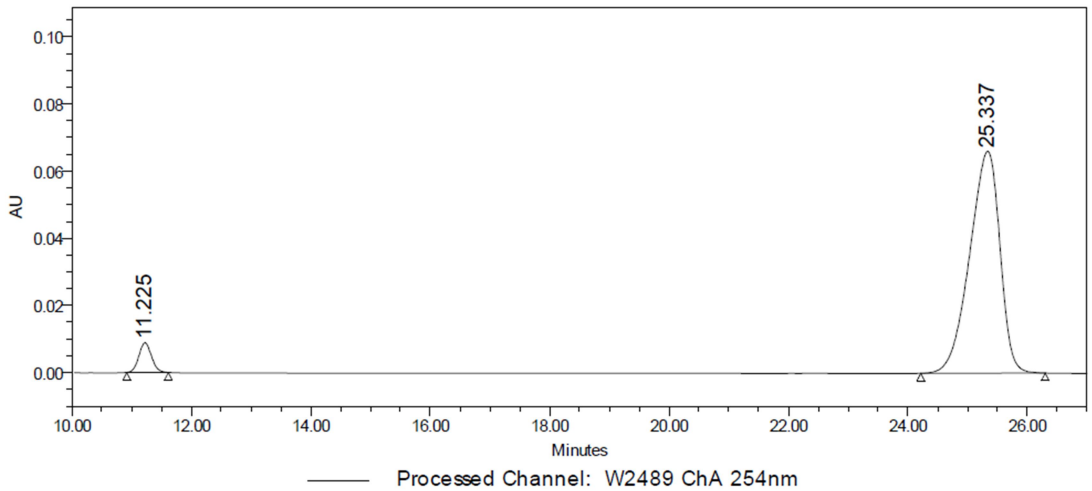
3f



3f

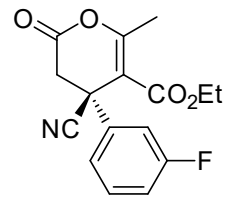


	RT	Area	% Area	Height	% Height
1	11.192	2654031	49.92	181460	70.69
2	25.494	2662036	50.08	75255	29.31
Sum		5316067.8	100.0	256714.6	100.0

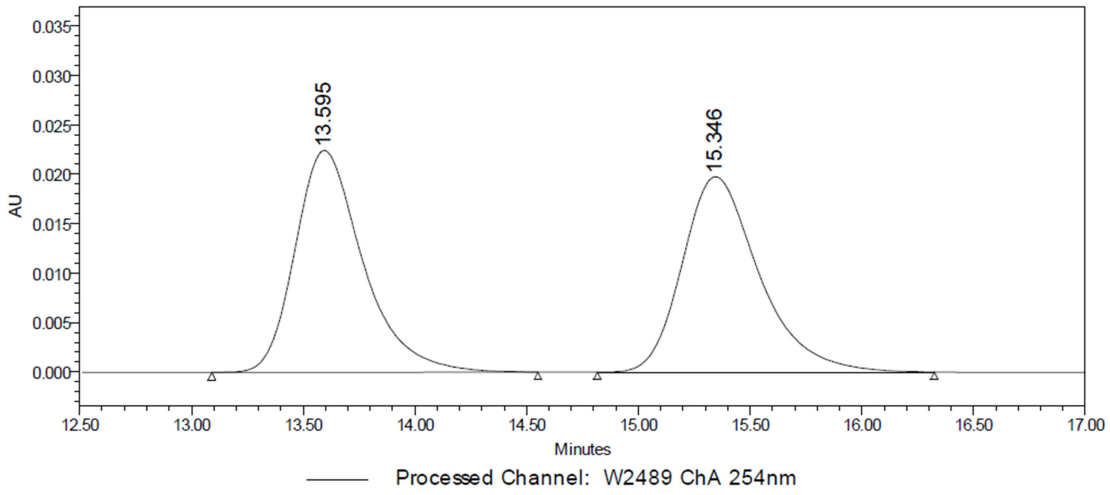


	RT	Area	% Area	Height	% Height
1	11.225	131193	5.34	8901	11.87
2	25.337	2326418	94.66	66079	88.13
Sum		2457610.2	100.0	74979.8	100.0

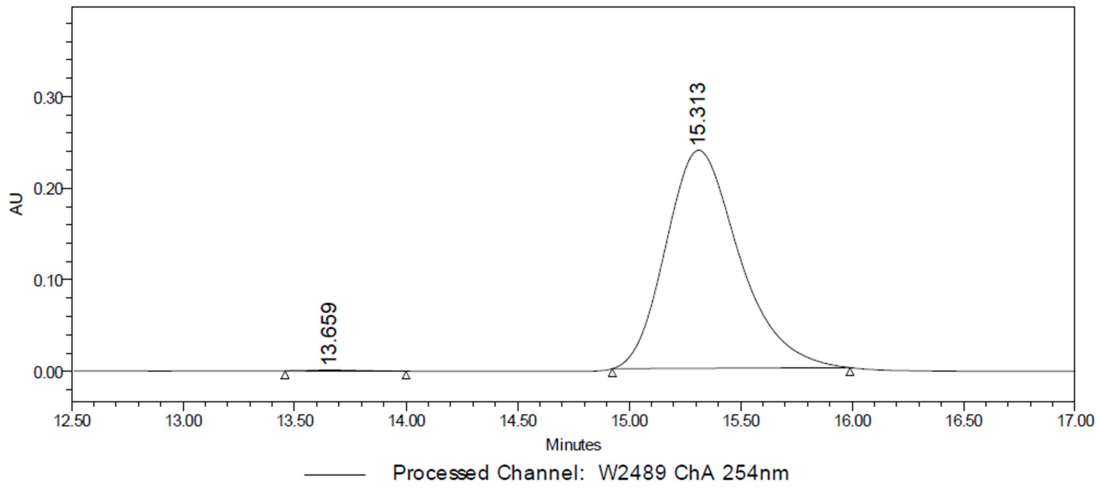
3g



3g

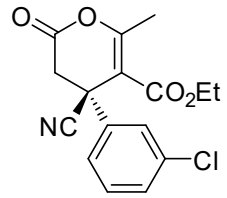


	RT	Area	% Area	Height	% Height
1	13.595	474432	50.00	22447	53.15
2	15.346	474340	50.00	19789	46.85
Sum		948771.8	100.0	42236.3	100.0

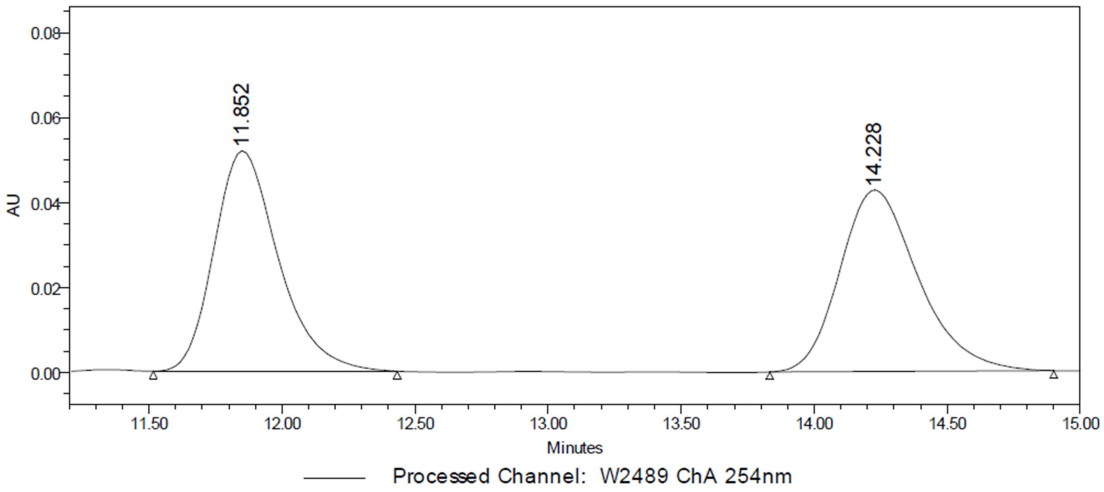


	RT	Area	% Area	Height	% Height
1	13.659	18635	0.34	1150	0.48
2	15.313	5462724	99.66	238270	99.52
Sum		5481359.2	100.0	239420.5	100.0

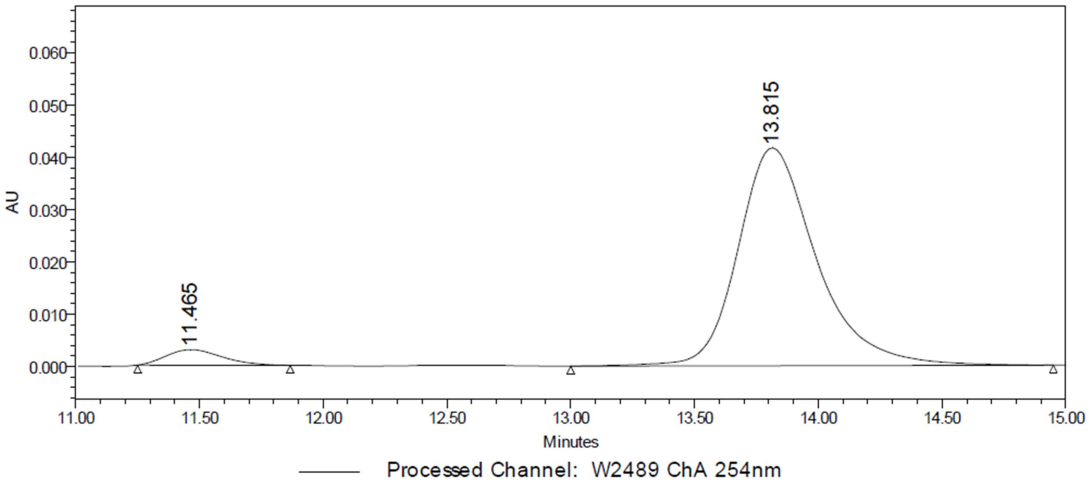
3h



3h

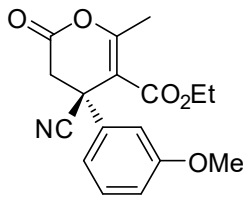


	RT	Area	% Area	Height	% Height
1	11.852	872041	49.94	51911	54.86
2	14.228	874108	50.06	42707	45.14
Sum		1746148.8	100.0	94617.8	100.0

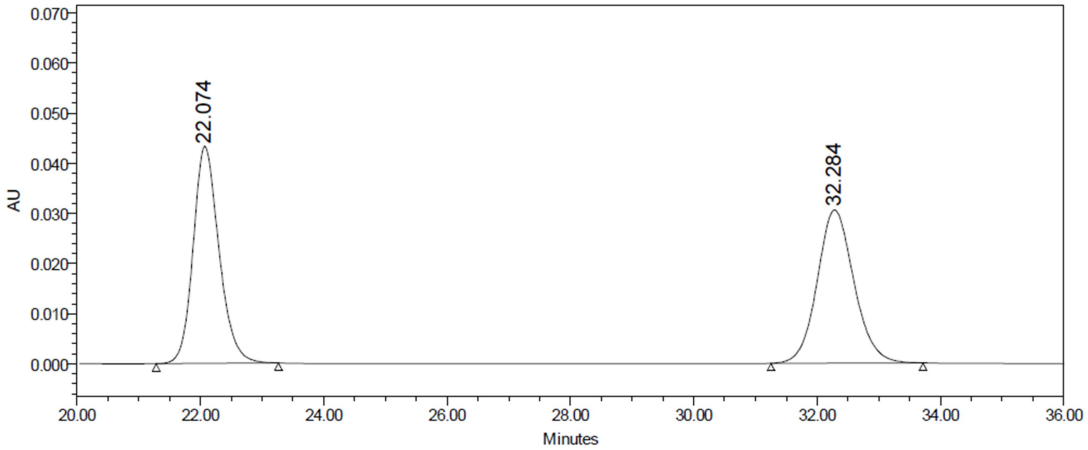


	RT	Area	% Area	Height	% Height
1	11.465	46340	4.80	2975	6.67
2	13.815	918350	95.20	41630	93.33
Sum		964690.2	100.0	44605.2	100.0

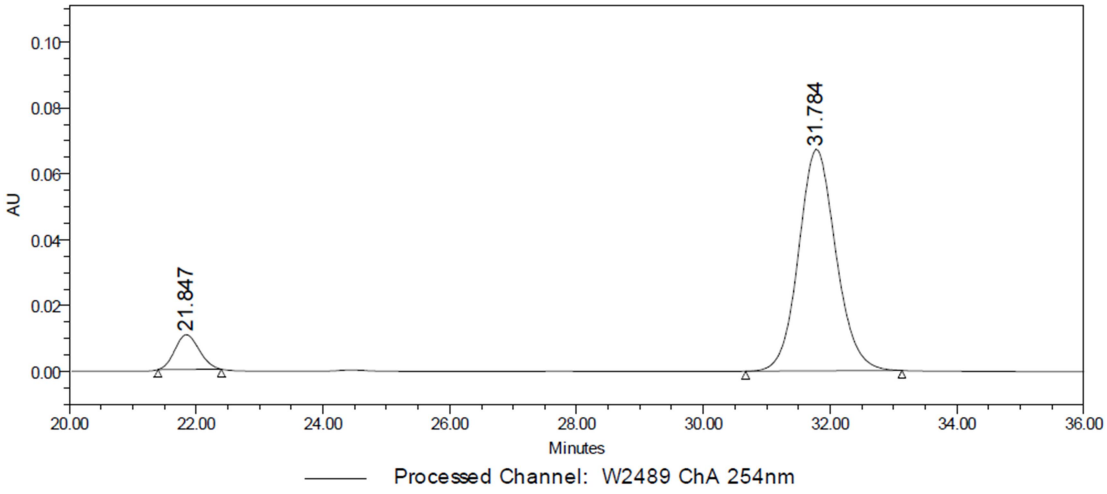
3i



3i

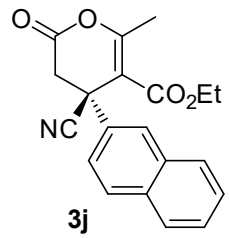


	RT	Area	% Area	Height	% Height
1	22.074	1265618	50.00	43301	58.63
2	32.284	1265838	50.00	30559	41.37
Sum		2531455.7	100.0	73860.0	100.0

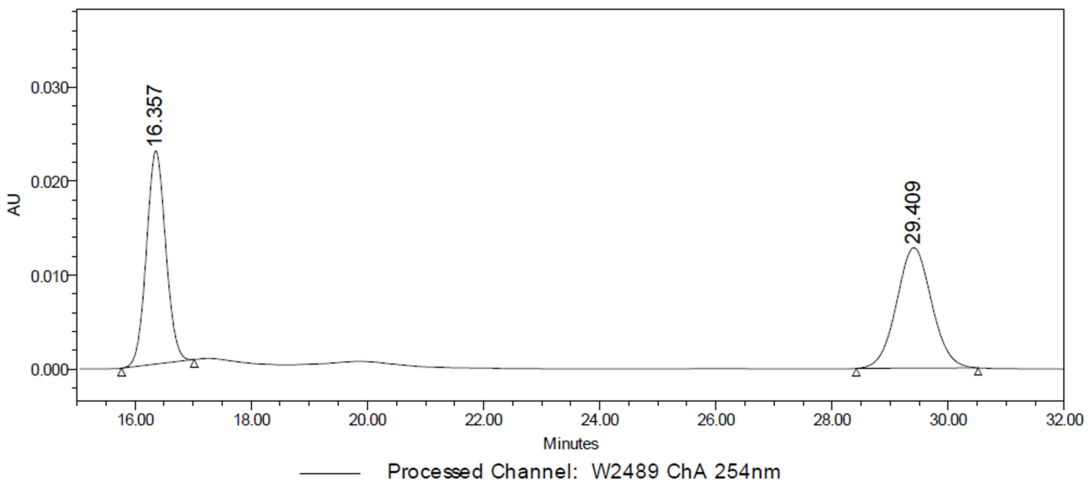


	RT	Area	% Area	Height	% Height
1	21.847	279820	9.22	10549	13.57
2	31.784	2756612	90.78	67218	86.43
Sum		3036432.6	100.0	77767.6	100.0

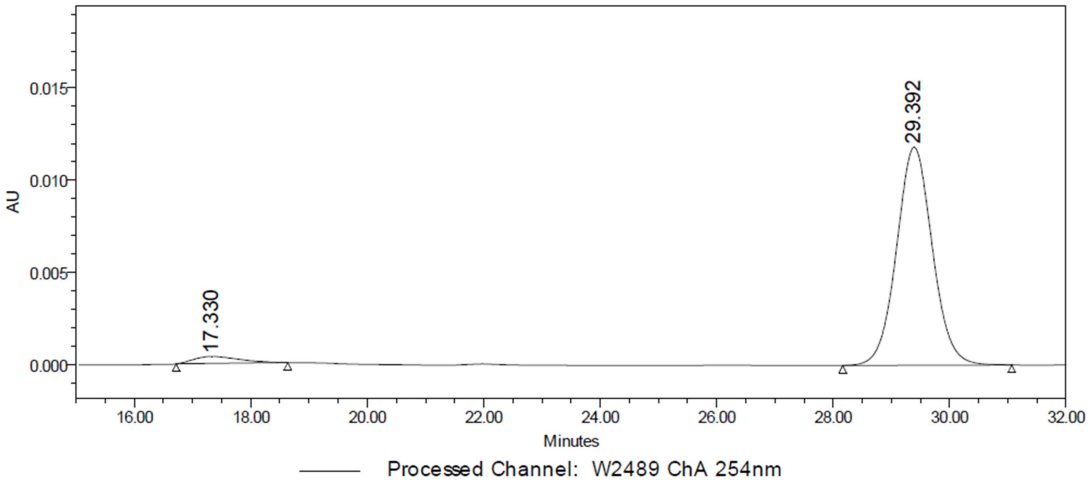
3j



3j

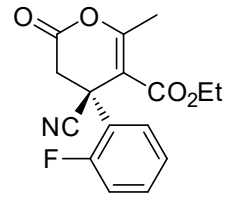


	RT	Area	% Area	Height	% Height
1	16.357	524036	49.35	22693	63.91
2	29.409	537831	50.65	12814	36.09
Sum		1061867.3	100.0	35506.7	100.0

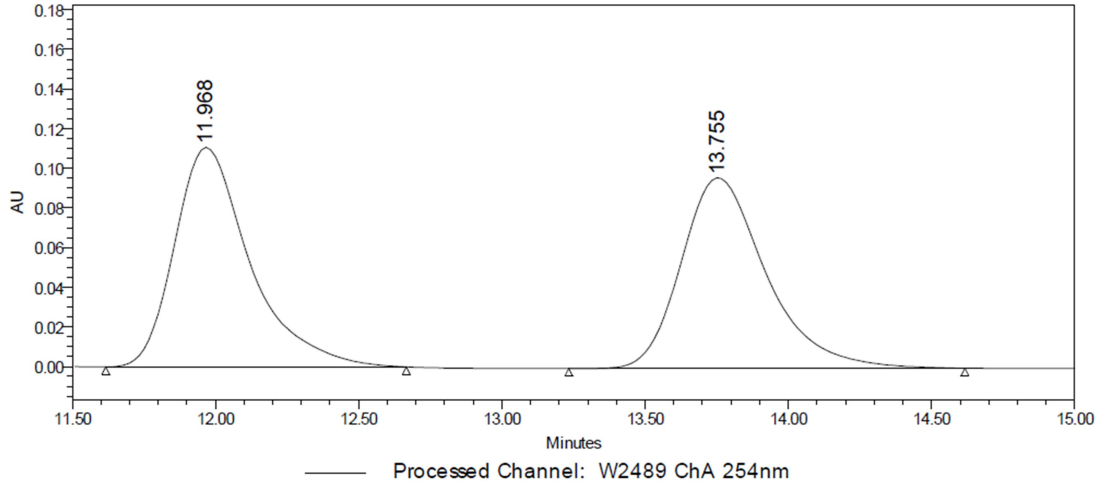


	RT	Area	% Area	Height	% Height
1	17.330	20744	3.94	378	3.10
2	29.392	505944	96.06	11837	96.90
Sum		526688.5	100.0	12214.7	100.0

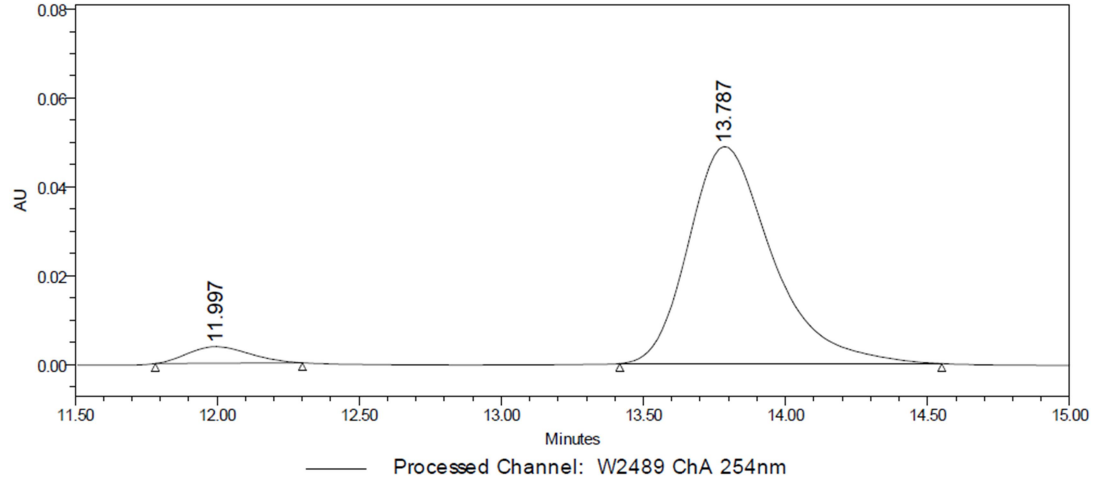
3k



3k

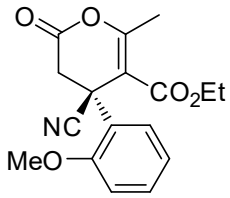


	RT	Area	% Area	Height	% Height
1	11.968	2023798	50.58	110677	53.52
2	13.755	1977672	49.42	96130	46.48
Sum		4001470.0	100.0	206806.9	100.0

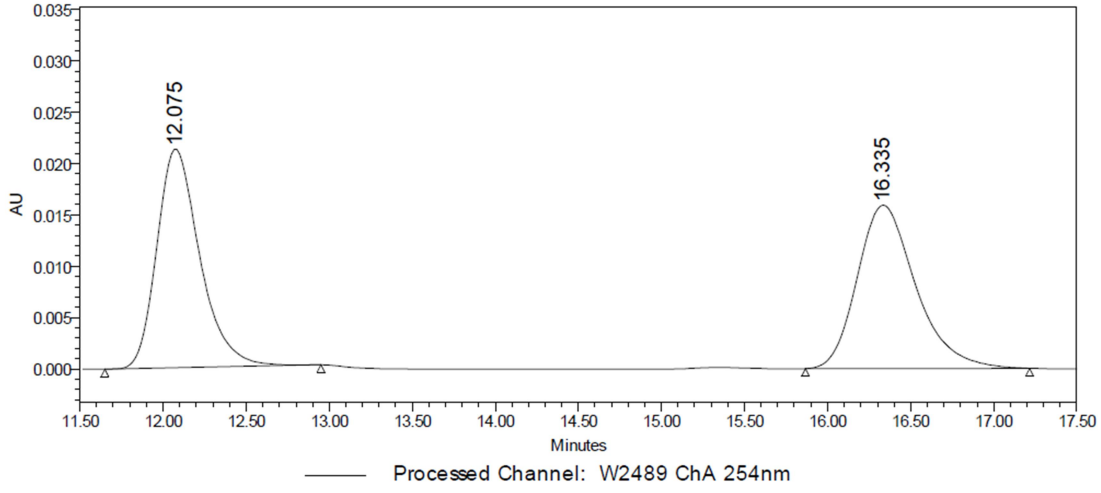


	RT	Area	% Area	Height	% Height
1	11.997	56005	5.29	3724	7.08
2	13.787	1002951	94.71	48906	92.92
Sum		1058956.1	100.0	52630.2	100.0

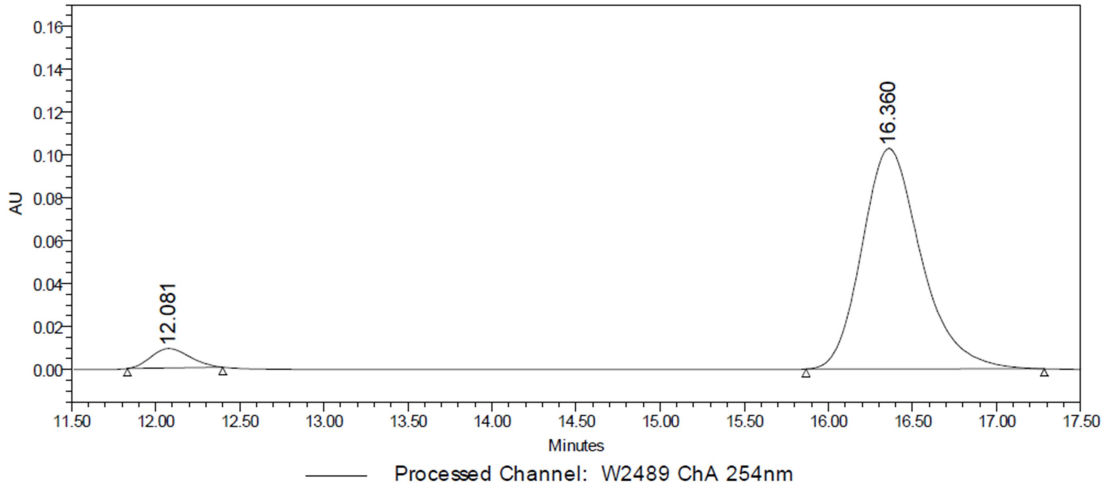
3l



3l

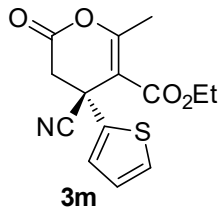


	RT	Area	% Area	Height	% Height
1	12.075	382746	49.57	21334	57.26
2	16.335	389419	50.43	15925	42.74
Sum		772165.2	100.0	37258.8	100.0

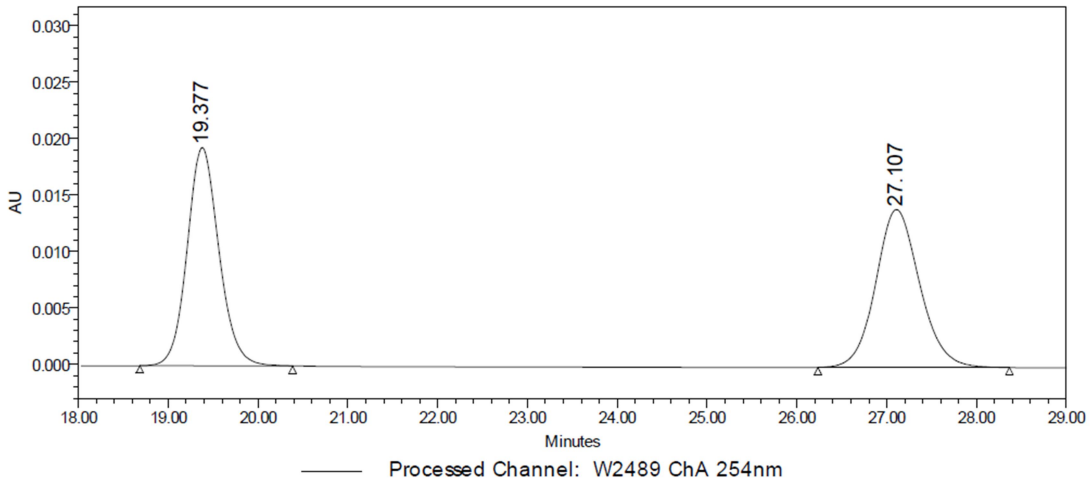


	RT	Area	% Area	Height	% Height
1	12.081	144278	5.41	9042	8.08
2	16.360	2521032	94.59	102893	91.92
Sum		2665309.2	100.0	111934.6	100.0

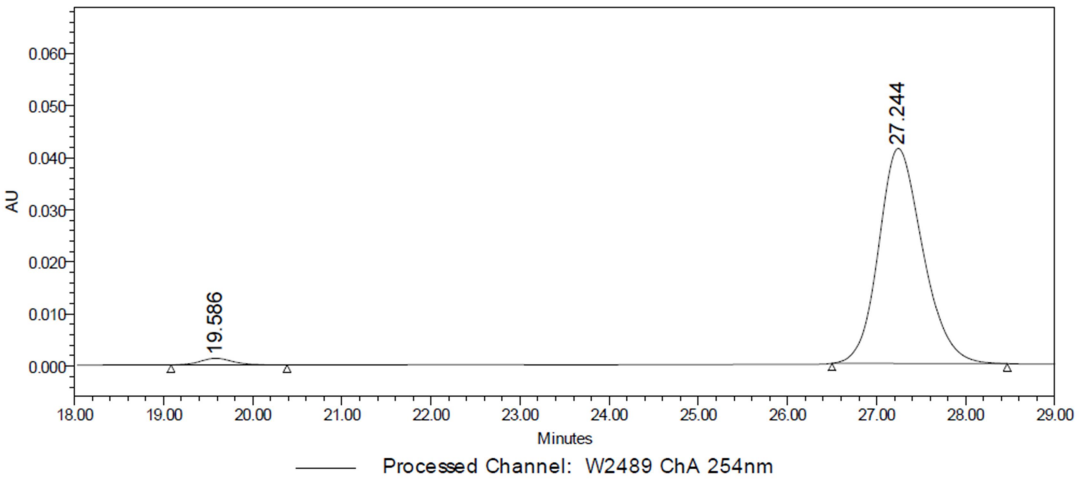
3m



3m

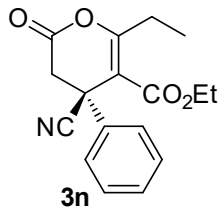


	RT	Area	% Area	Height	% Height
1	19.377	474775	49.92	19351	58.03
2	27.107	476268	50.08	13994	41.97
Sum		951042.8	100.0	33344.7	100.0

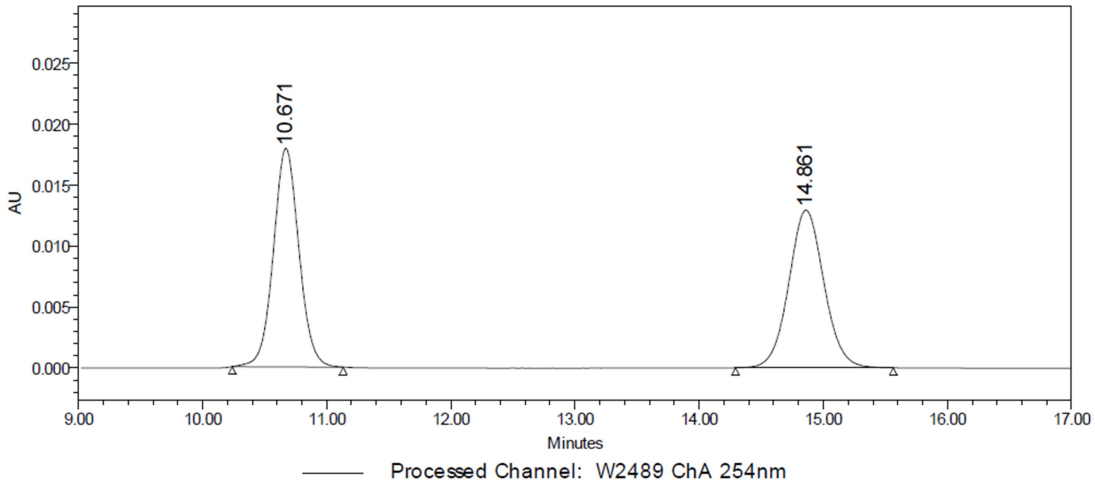


	RT	Area	% Area	Height	% Height
1	19.586	30348	2.08	1240	2.92
2	27.244	1425926	97.92	41273	97.08
Sum		1456274.0	100.0	42512.7	100.0

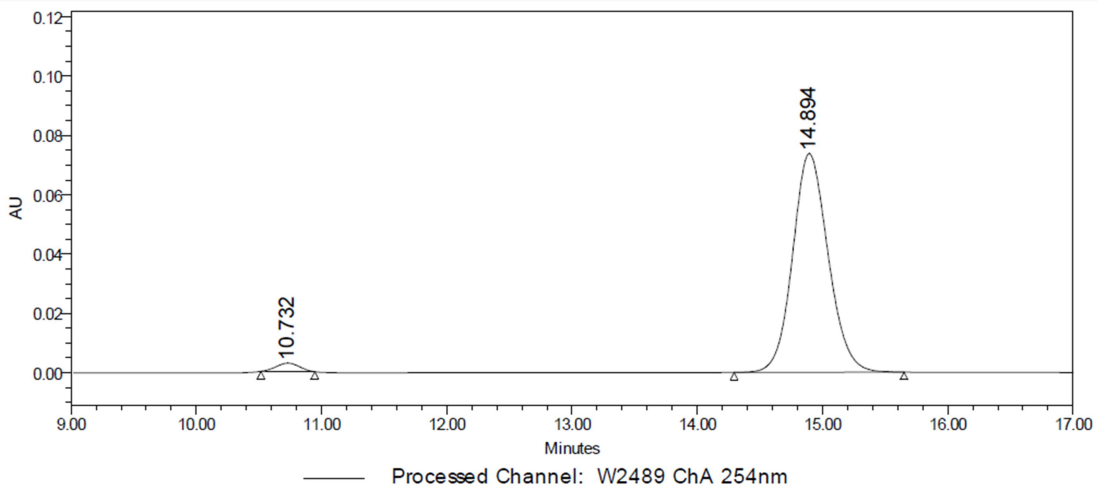
3n



3n

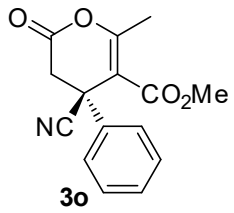


	RT	Area	% Area	Height	% Height
1	10.671	256787	50.18	17918	58.08
2	14.861	254912	49.82	12932	41.92
Sum		511698.4	100.0	30850.6	100.0

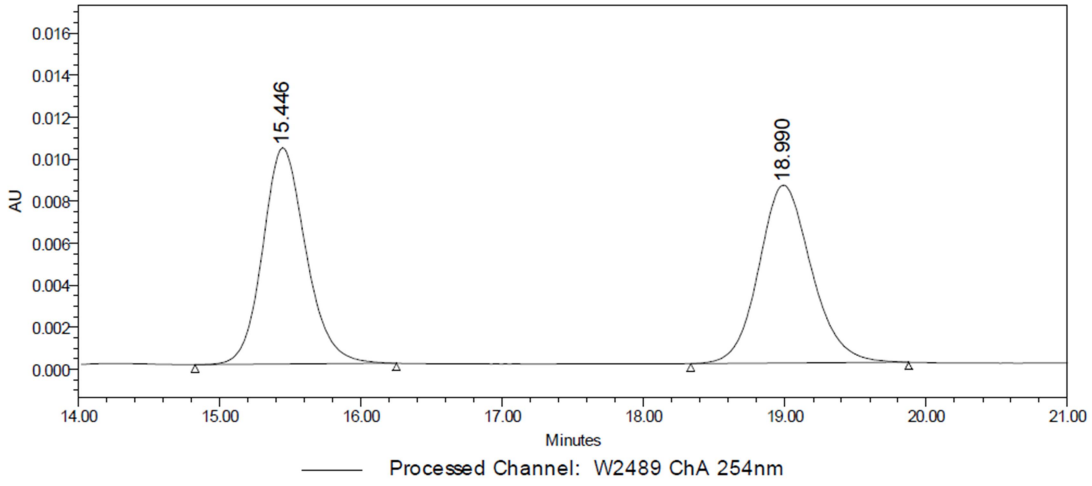


	RT	Area	% Area	Height	% Height
1	10.732	36383	2.44	2823	3.69
2	14.894	1456974	97.56	73740	96.31
Sum		1493356.6	100.0	76563.1	100.0

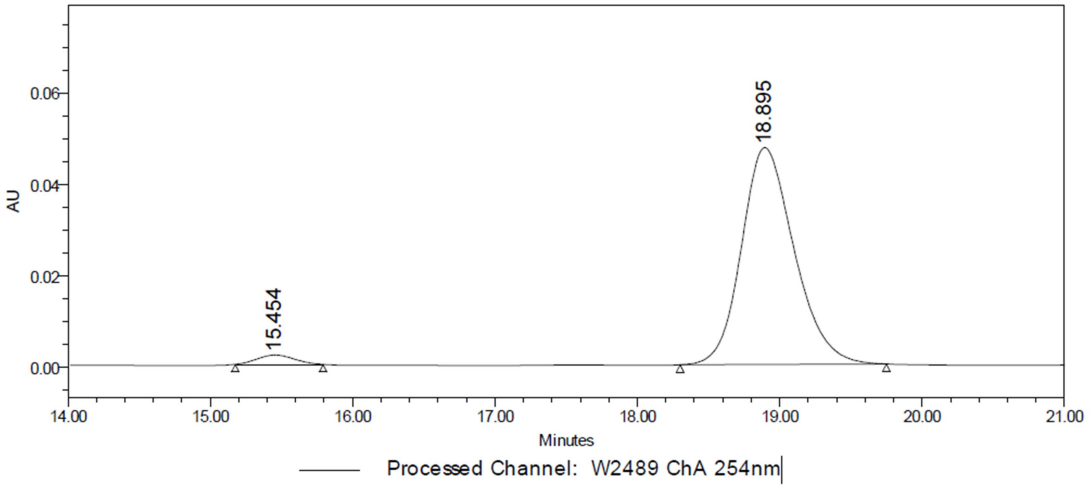
3o



3o

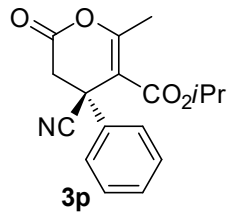


	RT	Area	% Area	Height	% Height
1	15.446	219272	49.95	10290	54.84
2	18.990	219704	50.05	8475	45.16
Sum		438975.4	100.0	18764.6	100.0

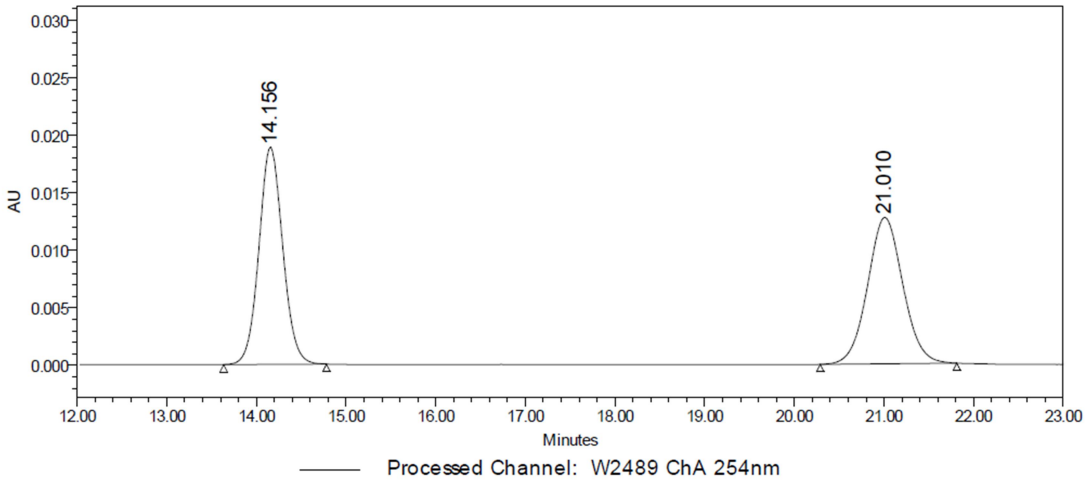


	RT	Area	% Area	Height	% Height
1	15.454	36918	2.93	2021	4.09
2	18.895	1223016	97.07	47439	95.91
Sum		1259933.6	100.0	49459.5	100.0

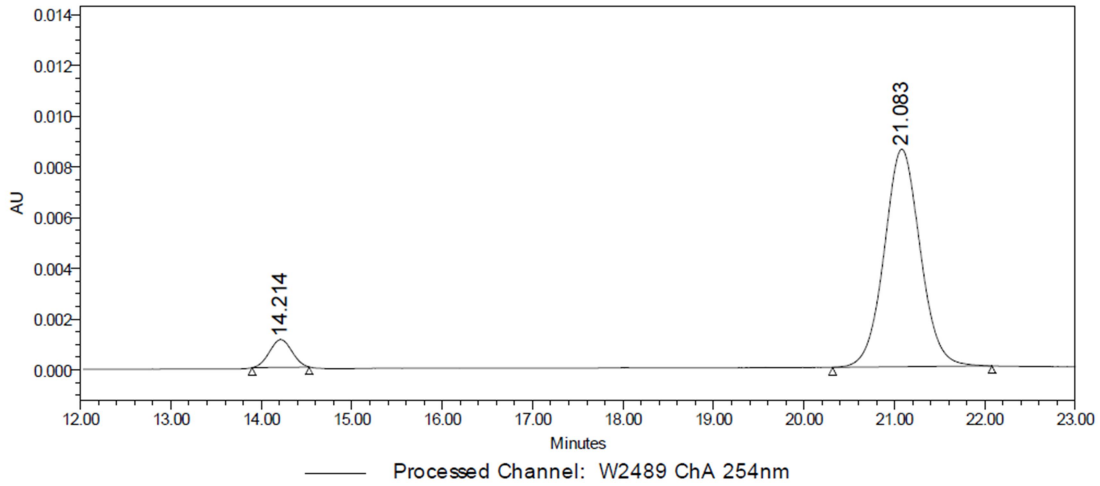
3p



3p

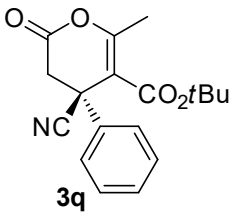


	RT	Area	% Area	Height	% Height
1	14.156	349045	50.05	18853	59.73
2	21.010	348289	49.95	12709	40.27
Sum		697334.0	100.0	31561.9	100.0

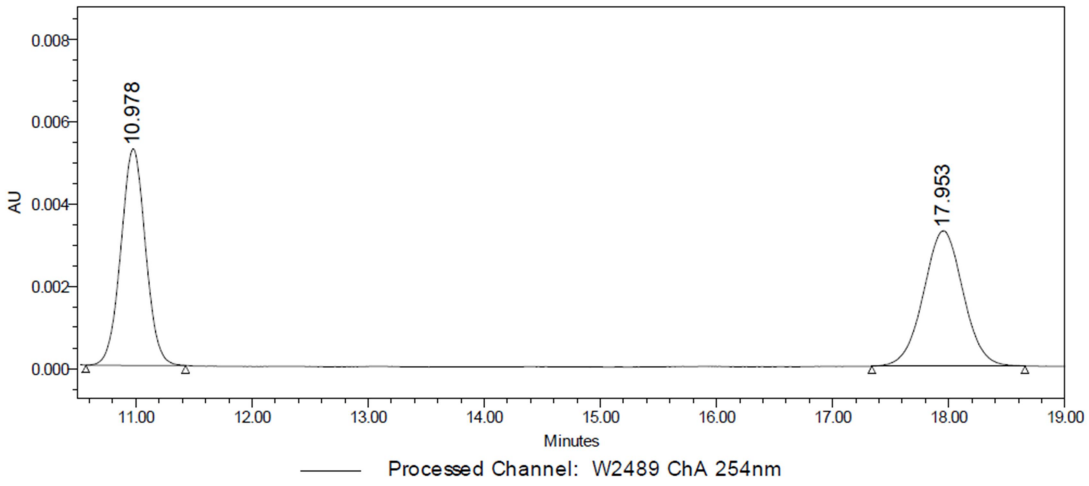


	RT	Area	% Area	Height	% Height
1	14.214	18713	7.30	1089	11.28
2	21.083	237558	92.70	8570	88.72
Sum		256271.1	100.0	9659.2	100.0

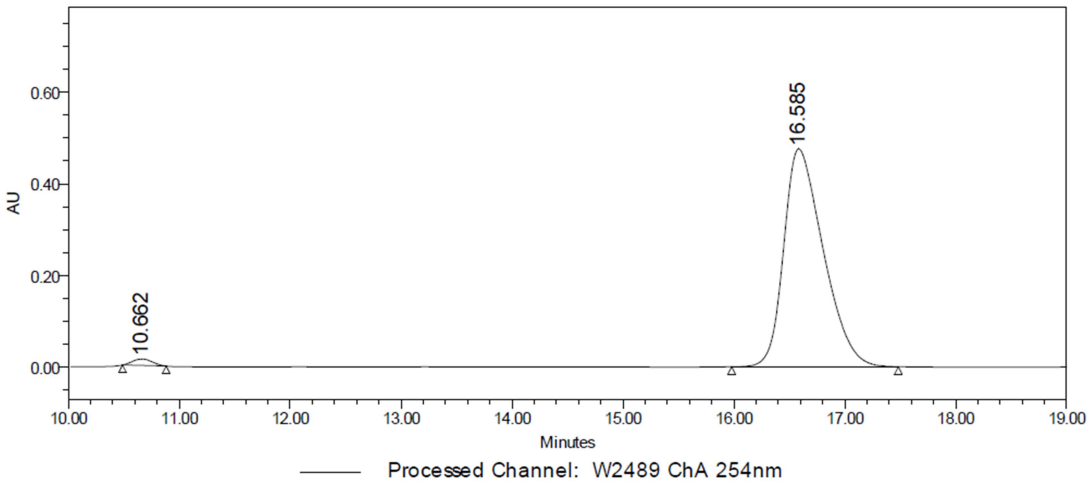
3q



3q

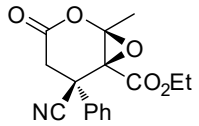


	RT	Area	% Area	Height	% Height
1	10.978	77800	49.92	5257	61.54
2	17.953	78035	50.08	3286	38.46
Sum		155834.8	100.0	8543.1	100.0

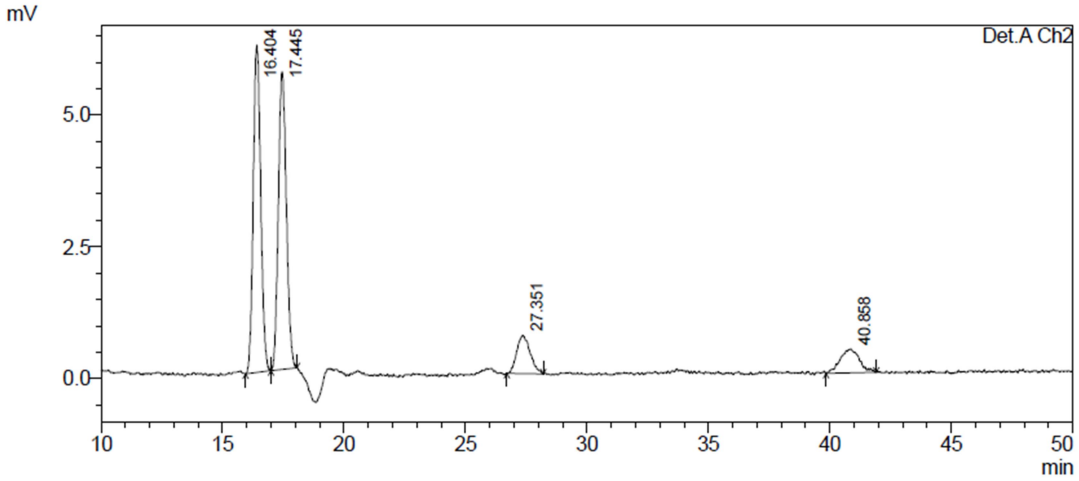


	RT	Area	% Area	Height	% Height
1	10.662	175317	1.47	14218	2.90
2	16.585	11776689	98.53	476012	97.10
Sum		11952005.8	100.0	490229.7	100.0

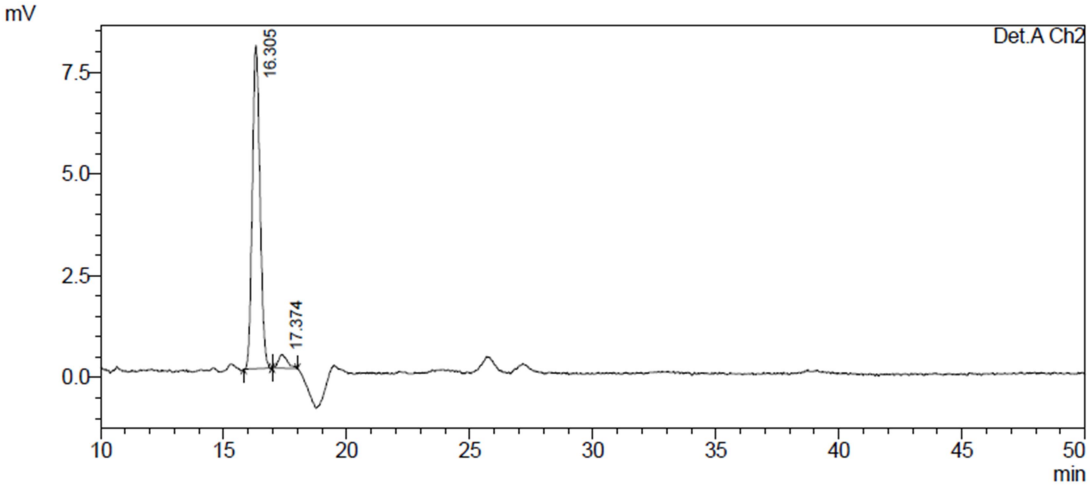
5a



5a



Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.404	132809	6220	42.079	47.613
2	17.445	129975	5661	41.181	43.340
3	27.351	27983	730	8.866	5.592
4	40.858	24854	451	7.875	3.456
Total		315620	13063	100.000	100.000



UV Detector Ch2 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.305	172179	7940	95.172	95.866
2	17.374	8734	342	4.828	4.134
Total		180913	8282	100.000	100.000