N-Heterocyclic Carbene-catalyzed Homoenolate addition Reaction to 3-Cyano-2-imino-2*H*-chromenes: Synthesis of C_4-Functionalized 2-Amino-3-cyano-4*H*-chromene

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Experimental Section

General

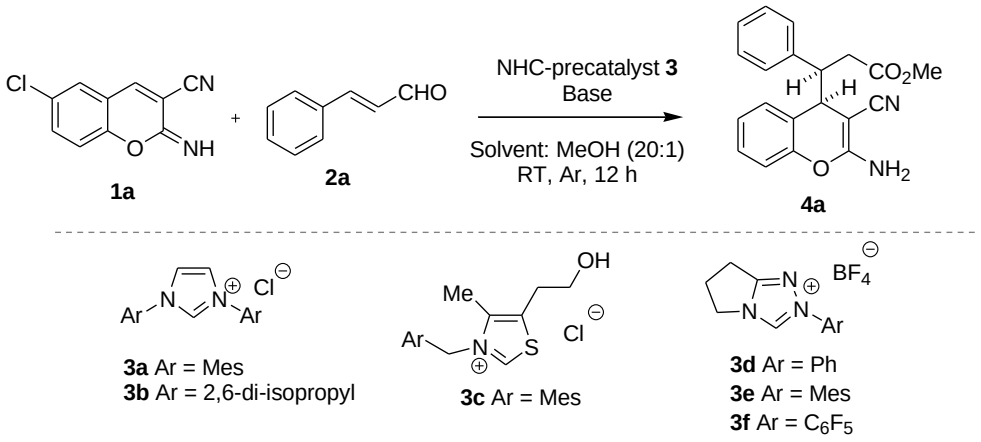
All reactions were conducted using oven-dried glassware under an atmosphere of Argon (Ar). Commercial AR-grade reagents were used without further purification. Solvents were dried and distilled following usual protocols. Flash column chromatography was performed in all cases using the indicated solvent system on silica gel (230-400 mesh). Analytical thin layer chromatography (TLC) was performed on aluminum-backed plates coated with Silica gel 60 with F_{254} indicator (Merck). The ^{1}H-NMR spectra were measured with 400 MHz, and ^{13}C-NMR spectra were recorded with 400 (100 MHz), using $CDCl_3$ as solvent. ^{1}H-NMR chemical shifts are expressed in parts per million (δ) downfield to $CHCl_3$ (δ = 7.26), ^{13}C-NMR chemical shifts are expressed in parts per million (δ) relative to the central $CDCl_3$ resonance (δ = 77.0). Coupling constants in ^{1}H-NMR are in Hz. The following abbreviations classify the multiplicity: s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, dd = doublet of doublets, td = triplet of doublet. Electro spray ionization (ESI) mass spectrometry (MS) experiments were performed on Agilent Technologies 6530 Accurate-Mass Q-TOF LC/MS. IR spectra were recorded using NICOLET IS5 FTIR with KBr window. Melting point was determined by Labtronics LT-115 digital melting/boiling point apparatus (Indian make).

All salicylaldehyde derivatives, inorganic reagents and solvents were used as received. (*Z*)-6-chloro-2-(phenylimino)-2*H*-chromene-3-carbonitrile was prepared according to reported literature procedure.[1]

1. Mandal, P.S., Vijay Kumar, A., *Tetrahedron Lett.* **2019**, *60*, 150940.

Optimization Study: Screening of Catalyst, Base Solvent and reaction conditions for diastereoselective synthesis

Table **1** Evaluation of NHC catalysts and optimization of reaction conditions[a]

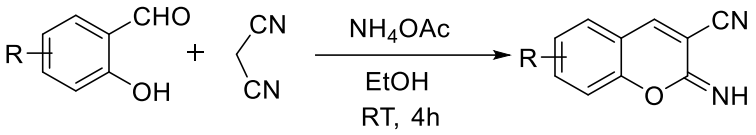


Entry	NHC **3**	Base	Solvent	Yield (%)[b]of **4a**	d.r.[c]of **4a**
1	**3a-3b**	$KHCO_3$	Toluene	<10	ND
2	**3c**	$KHCO_3$	Toluene	15	1:1
3	**3d**	$KHCO_3$	Toluene	NR	-
4	**3e**	$KHCO_3$	Toluene	58	1:1
5	**3f**	$KHCO_3$	Toluene	NR	-
6	**3e**	K_2CO_3	Toluene	46	1:1
7	**3e**	Et_3N/DBU	Toluene	<10	ND
8	**3e**	NaOAc	Toluene	43	1.2:1
9	**3e**	K_3PO_4	Toluene	62	1:1
10	**3e**	K_3PO_4	THF	51	1:1
11	**3e**	K_3PO_4	Et_2O	43	1:1
12	**3e**	K_3PO_4	1,4-Dioxane	42	1:1
13	**3e**	K_3PO_4	DMF	52	4:1
14	**3e**	K_3PO_4	$CHCl_3$	51	1.1:1
15	**3e**	K_3PO_4	Acetonitrile	73	7:1
16	**3e**	K_3PO_4	DCM	44	1:1
17[d]	**3e**	K_3PO_4	Acetonitrile	72	7:1
18[e]	**3e**	K_3PO_4	Acetonitrile	56	7:1

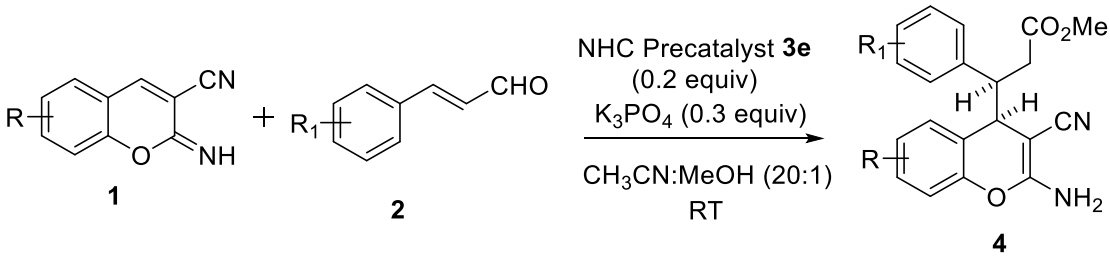
[a]Unless indicated otherwise, the reaction of **1a** (75 mg, 0.366 mmol, 1.0 equiv) and **2a** (72 mg, 68.5 µL, 0.550 mmol, 1.5 equiv) was carried out in mixed solvent 2.4 mL (0.15 M) at room temperature in the presence of NHC catalyst **3** (20 mol%) and base (30 mol%) for 12 h. [b] Isolated yield. [c] d.r. value is determined from the ^{1}H-NMR of the crude reaction mixture. [d]Sodium 2-Chloro benzoate (1.0 equiv) was added as an additive. [e] Base K_3PO_4 was used 100 mol%.

*General Procedure **I** "Preparation of 3-cyano-2H-imonochrome derivatives*[2]

In an oven dried RBF, To a stirred solution of the specific salicylaldehyde (1.0 *equiv*) in ethanol (1 mL/mmol), Malononitrile (1.0 *equiv*) and NH_4OAc (0.6 *equiv*) were added under nitrogen atmosphere at rt and stirred for 4 hours resulting in precipitation. On complete consumption of salicylaldehyde derivative (checked via TLC), the resulting precipitate was filtered and washed with ethanol, followed by drying under vacuum to afford pure product as yellow solid.



*General Procedure **II** "NHC catalyzed synthesis of 2-Amino-3-cyano-4H-chromenes via homoenolate intermediate*

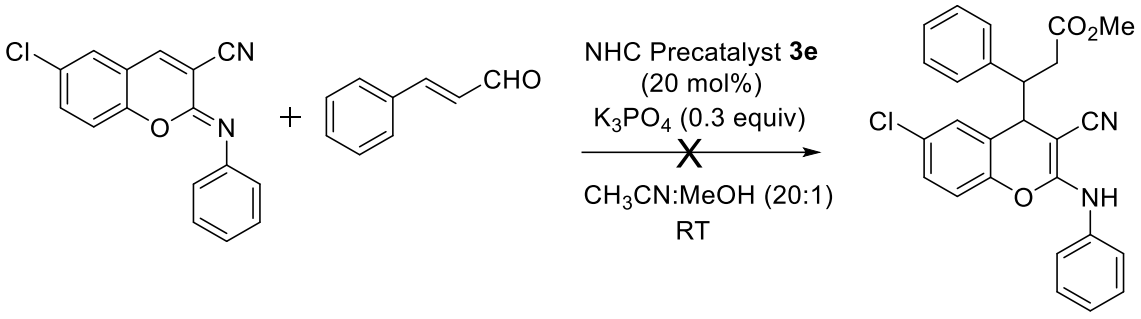


A solution of 3-cyano-2*H*-iminochromene **1** (1.0 *equiv*), cinnamaldehyde derivative **2** (1.5 *equiv*), K_3PO_4 (0.3 *equiv*), and NHC precatalyst **3e** (20 mol%) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature under nitrogen atmosphere. After complete consumption of 3-cyano-2*H*-iminochromene solvent was evaporated under reduced pressure. The residue was then subjected to purification by flash column chromatography using EtOAc and petroleum- ether mixture as an eluent to yield the desired product **4**.

2. Li, W., Liu, H., Jiang, X., Wang, J. *ACS Catal.* **2012**, *2*, 1535-1538.

Control Experiments and Mechanism investigation:

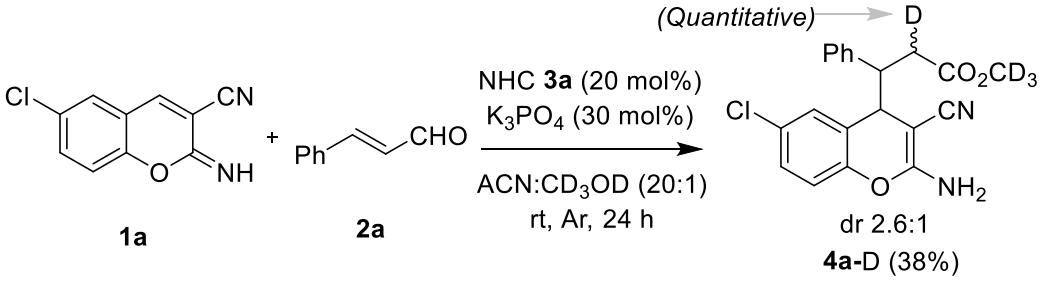
a) Attempt to explore *N*-arylated 3-cyano-2*H*-iminochromene as Substrate for 'Homoenolate addition' strategy



yield = 0%

A solution of (*Z*)-2-(phenylimino)-2*H*-chromene-3-carbonitrile[1] (100 mg, 0.356 mmol, 1.0 *equiv*), cinnamaldehyde (70 mg, 67.2 µL, 0.534 mmol, 1.5 *equiv*), K_3PO_4 (0.3 *equiv*), and NHC precatalyst **3e** (20 mol%) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature under nitrogen atmosphere. After overnight stirring no desired product formation was observed.

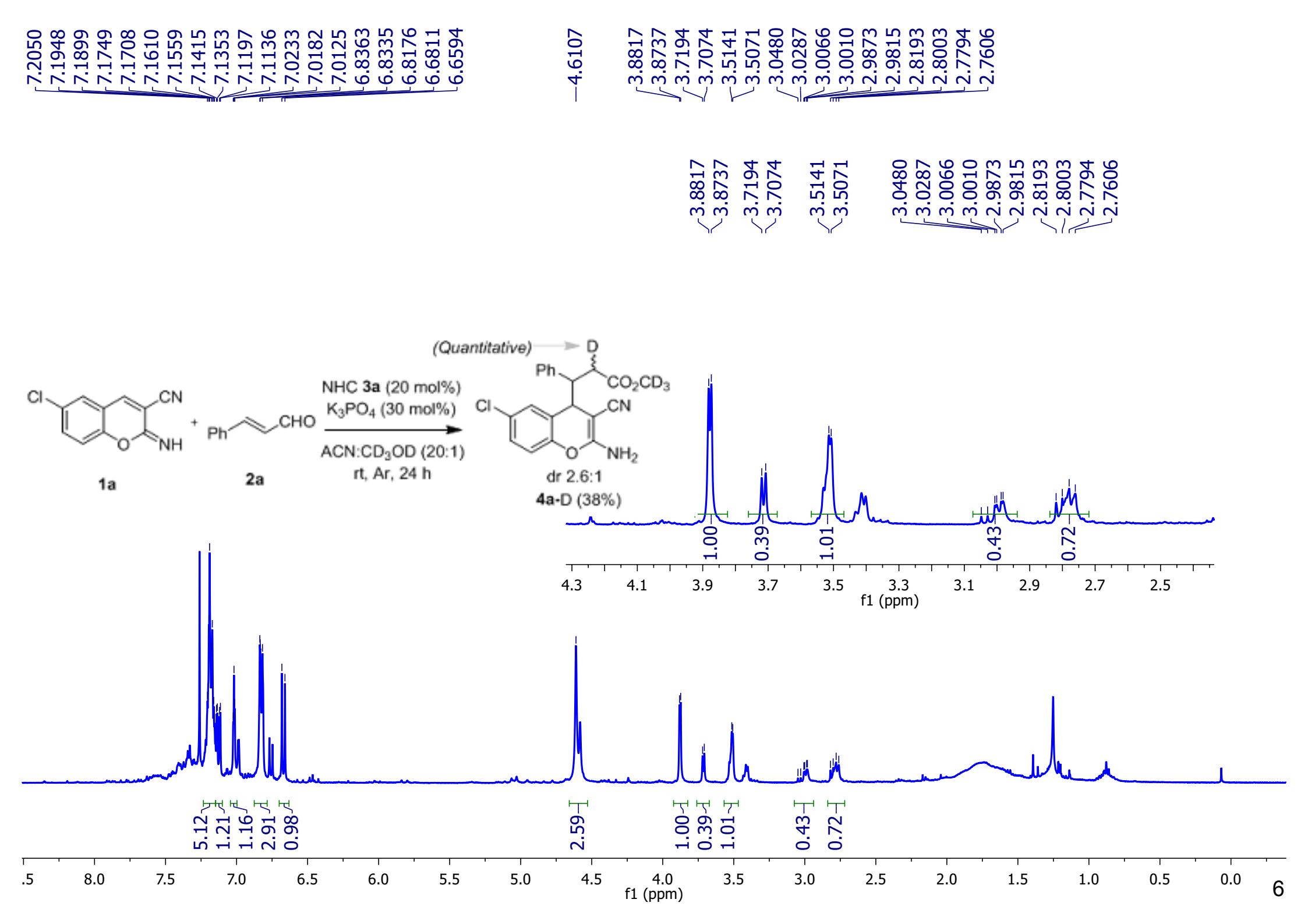
b) Isotope labeling experiment using MeOH-d_4



A solution of 3-cyano-2*H*-iminochromene **1a** (75 mg, 0.366 mmol, 1.0 *equiv*), cinnamaldehyde derivative **2a** (72 mg, 0.550 mmol, 1.5 *equiv*), K_3PO_4 (0.3 *equiv*), and NHC precatalyst **3e** (20 mol%) in CH_3CN (anhydrous):MeOH-d_4 (20:1) (2.4 mL: 0.12 mL) (0.15 M) was stirred for 24 hours at room temperature under nitrogen atmosphere. After complete consumption of 3-cyano-2*H*-iminochromene solvent was evaporated under reduced pressure. The residue was then subjected to purification by flash column chromatography using EtOAc and petroleum- ether

mixture as an eluent to yield the desired product **4a-**D (yield= 38%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); dr = 2.5:1.

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.20-7.15 (m, 3H), 7.12 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.02 (d, *J* = 2.0 Hz, 1H), 6.83-6.81 (m, 2H), 6.67 (d, *J* = 8.7 Hz, 1H), 4.61 (s, 2H), 3.87 (d, *J* = 3.1 Hz, 1H), 3.51 (d, *J* = 2.8 Hz, 1H), 3.01-2.98 (m, 0.43H), 2.78 (dd, *J* = 16.0, 7.6 Hz, 0.72H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 161.9, 148.6, 138.4, 129.8, 128.5, 128.47, 128.3, 128.0, 127.3, 124.3, 120.8, 117.2, 54.7, 49.9, 41.0.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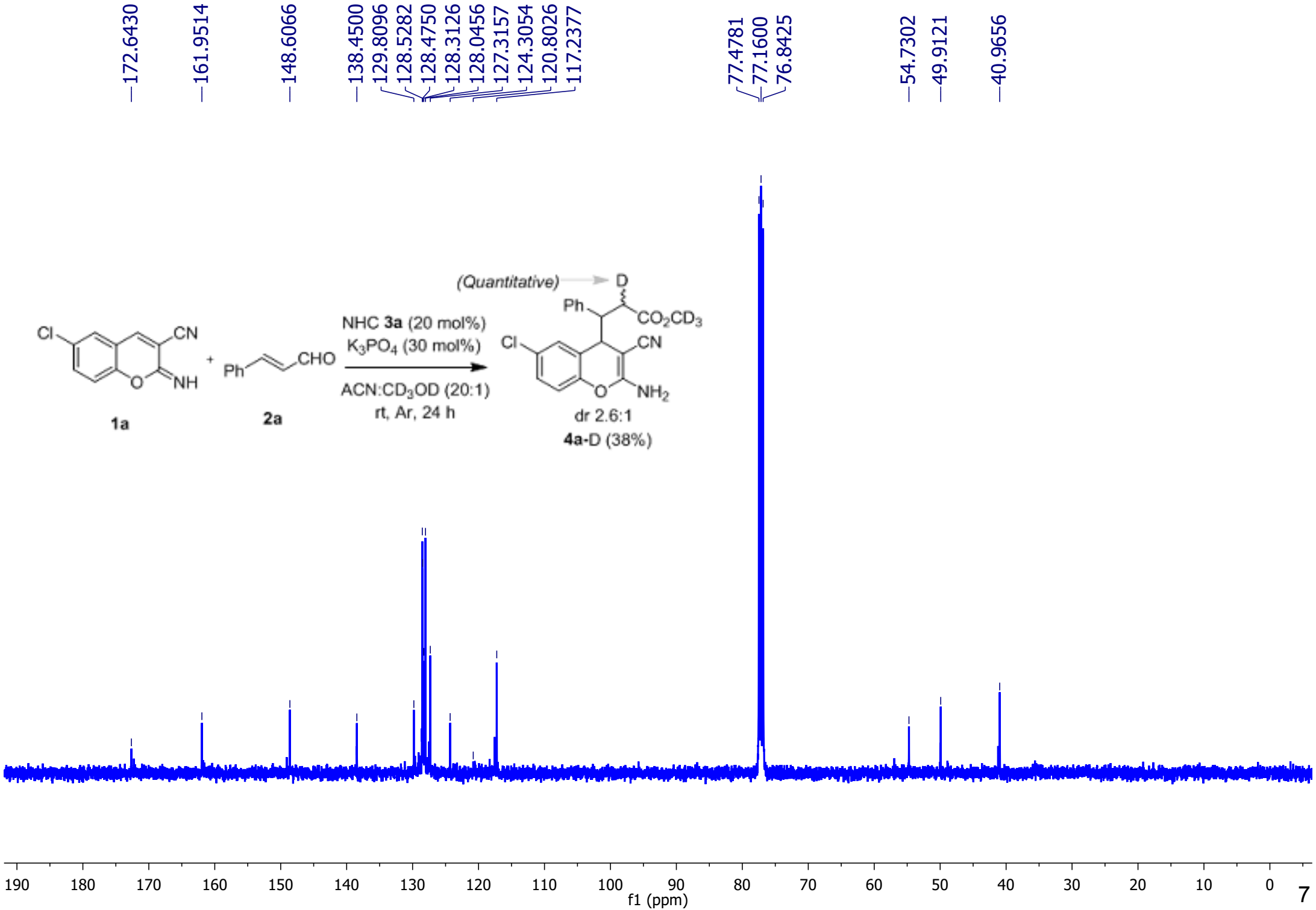
7.1899
7.1749
7.1708
7.1610
7.1559
7.1415
7.1353
7.1197
7.1136
7.0233
7.0182
7.0125
6.8363
6.8335
6.8176
6.6811
6.6594
4.6107
3.8817
3.8737
3.7194
3.7074
3.5141
3.5071
3.0480
3.0287
3.0066
3.0010
2.9873
2.9815
2.8193
2.8003
2.7794
2.7606
(Quantitative)
D
Ph
CO2CD3
Cl
CN
NH2
O
NHC 3a (20 mol%)
K3PO4 (30 mol%)
ACN:CD3OD (20:1)
rt, Ar, 24 h
Cl
CN
NH
O
Ph
CHO
1a
2a
dr 2.6:1
4a-D (38%)
1.00
0.39
1.01
0.43
0.72
4.3
4.1
3.9
3.7
3.5
3.3
3.1
2.9
2.7
2.5
f1 (ppm)
5.12
1.21
1.16
2.91
0.98
2.59
1.00
0.39
1.01
0.43
0.72
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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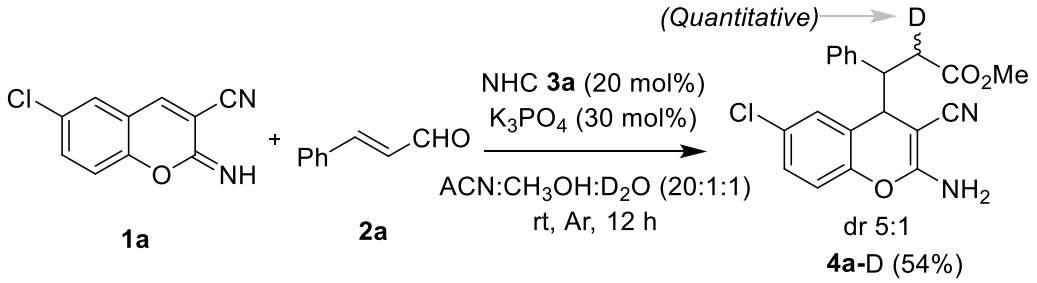
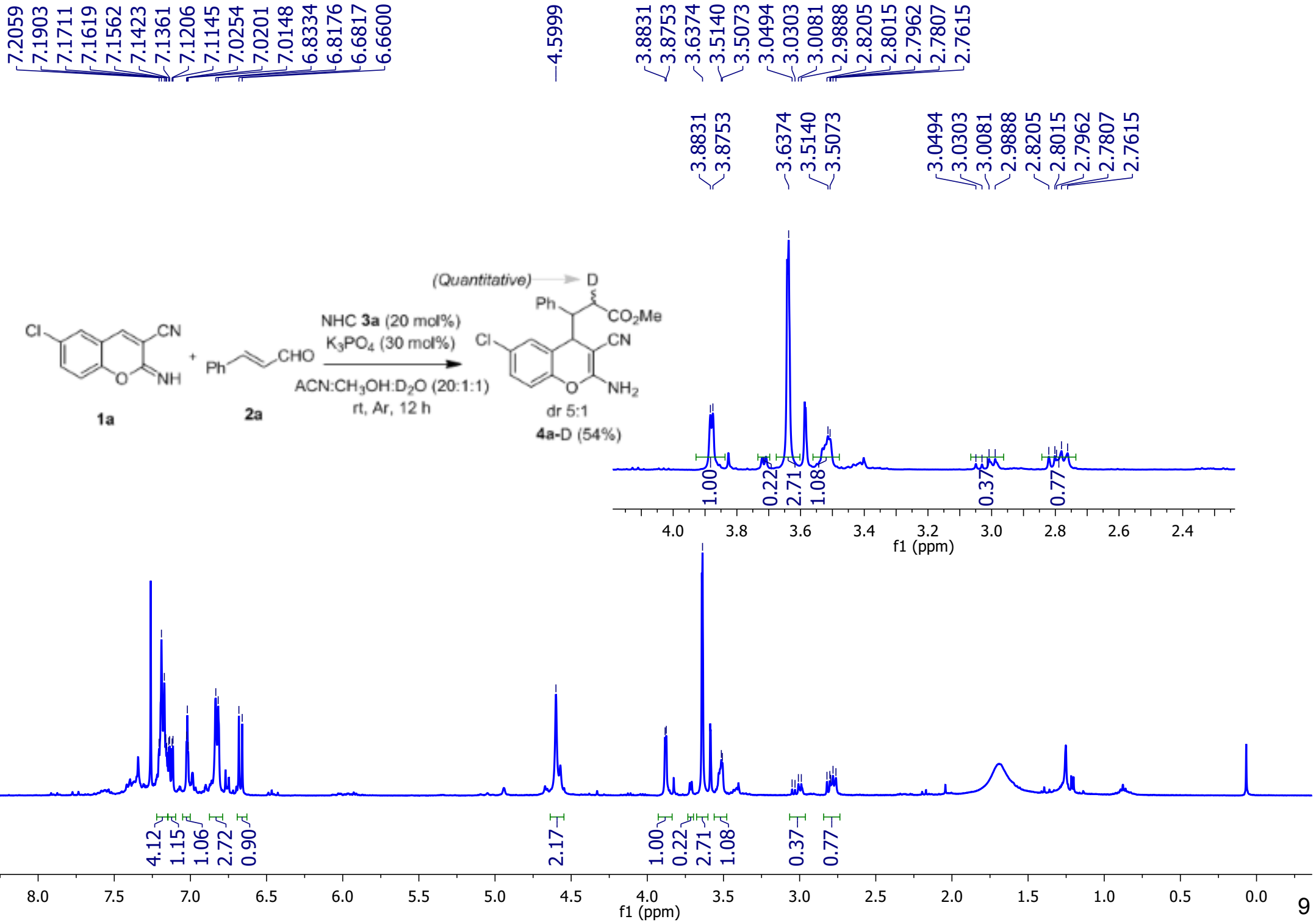
148.6066
138.4500
129.8096
128.5282
128.4750
128.3126
128.0456
127.3157
124.3054
120.8026
117.2377
77.4781
77.1600
76.8425
54.7302
49.9121
40.9656
Cl
CN
NH
O
1a
+
Ph
CHO
2a
NHC 3a (20 mol%)
K3PO4 (30 mol%)
ACN:CD3OD (20:1)
rt, Ar, 24 h
(Quantitative)
D
Ph
CO2CD3
Cl
CN
O
NH2
dr 2.6:1
4a-D (38%)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

c) Isotope labelling experiment using D_2O as additive



A solution of 3-cyano-2*H*-iminochromene **1a** (75 mg, 0.366 mmol, 1.0 *equiv*), cinnamaldehyde derivative **2a** (72 mg, 0.550 mmol, 1.5 *equiv*), K_3PO_4 (0.3 *equiv*), and NHC precatalyst **3e** (20 mol%) in CH_3CN(anhydrous):MeOH:D_2O (20:1:1) (2.4 mL: 0.12 mL : 0.12 mL) (0.15 M) was stirred for 12 hours at room temperature under nitrogen atmosphere. After complete consumption of 3-cyano-2*H*-iminochromene solvent was evaporated under reduced pressure. The residue was then subjected to purification by flash column chromatography using EtOAc and petroleum-ether mixture as an eluent to yield the desired product **4a**-D (yield= 54%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); dr = 5:1.

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.20-7.15 (m, 3H), 7.13 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.02 (d, *J* = 4.2 Hz, 1H), 6.83-6.81 (m, 2H), 6.67 (d, *J* = 8.7 Hz, 1H), 4.56 (s, 2H), 3.88 (d, *J* = 3.1 Hz, 1H), 3.63 (s, 3H), 3.52-3.50 (m, 1H), 3.01 (dd, *J* = 16.5, 7.6 Hz, 0.37H), 2.78 (dd, *J* = 15.9, 9.7 Hz, 0.77H).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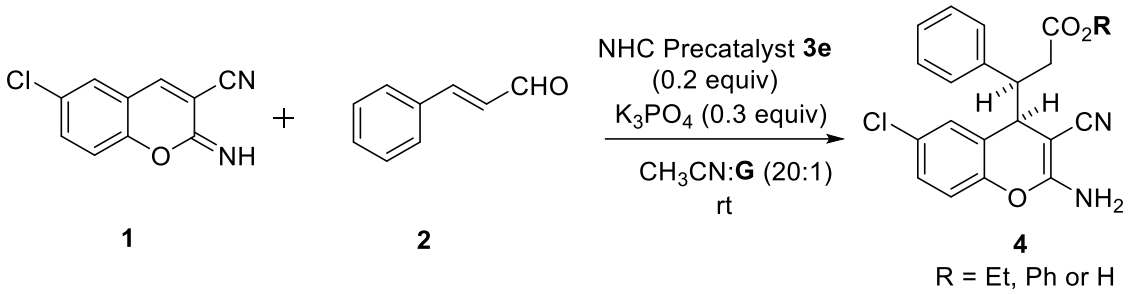
7.1903
7.1711
7.1619
7.1562
7.1423
7.1361
7.1206
7.1145
7.0254
7.0201
7.0148
6.8334
6.8176
6.6817
6.6600
4.5999
3.8831
3.8753
3.6374
3.5140
3.5073
3.0494
3.0303
3.0081
2.9888
2.8205
2.8015
2.7962
2.7807
2.7615
(Quantitative)
D
NHC 3a (20 mol%)
K3PO4 (30 mol%)
ACN:CH3OH:D2O (20:1:1)
rt, Ar, 12 h
dr 5:1
4a-D (54%)
1a
2a
1.00
0.22
2.71
1.08
0.37
0.77
f1 (ppm)
4.12
1.15
1.06
2.72
0.90
2.17
1.00
0.22
2.71
1.08
0.37
0.77
f1 (ppm)

Attempt to explore some protic solvents other than methanol in developed reaction strategy:



1 **2** **4**

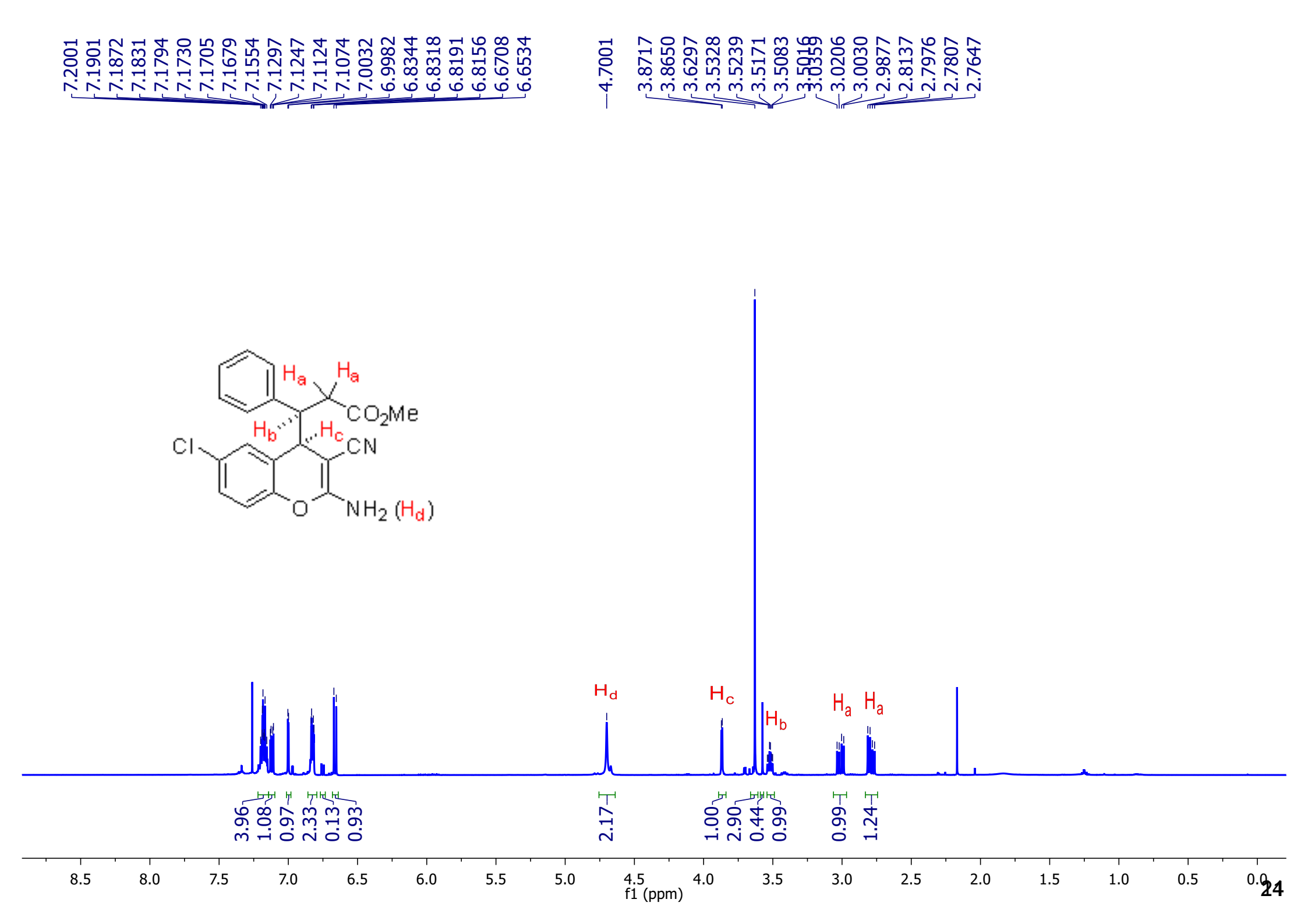
R = Et, Ph or H

S.No.	G (Protic Solvent)	Time (hour)	Result
1	EtOH	24	Messy RM
2	PhOH	24	Messy RM
3	H_2O	24	No Reaction

A solution of 3-cyano-2*H*-iminochromene **1a** (75 mg, 0.366 mmol, 1.0 *equiv*), cinnamaldehyde derivative **2a** (72 mg, 0.550 mmol, 1.5 *equiv*), K_3PO_4 (0.3 *equiv*), and NHC precatalyst **3e** (20 mol%) in CH_3CN:EtOH/PhOH/H_2O (20:1) (0.15 M) was stirred for 24 hours at room temperature under nitrogen atmosphere. In case of EtOH/PhOH incomplete conversion was observed as starting material was not fully consumed. Further, in case of water no reaction was initiated.

Structure determination of 2-amino-3-cyano-4*H*-chromenes **4**

The structure of 2-amino-3-cyano-4*H*-chromenes **4** was determined by the 2D-NMR of **4a** and X-ray crystallographic analysis of the product **4n** (CCDC 2195418) and the structure of all other 2-amino-3-cyano-4*H*-chromene derivatives were assigned consequently.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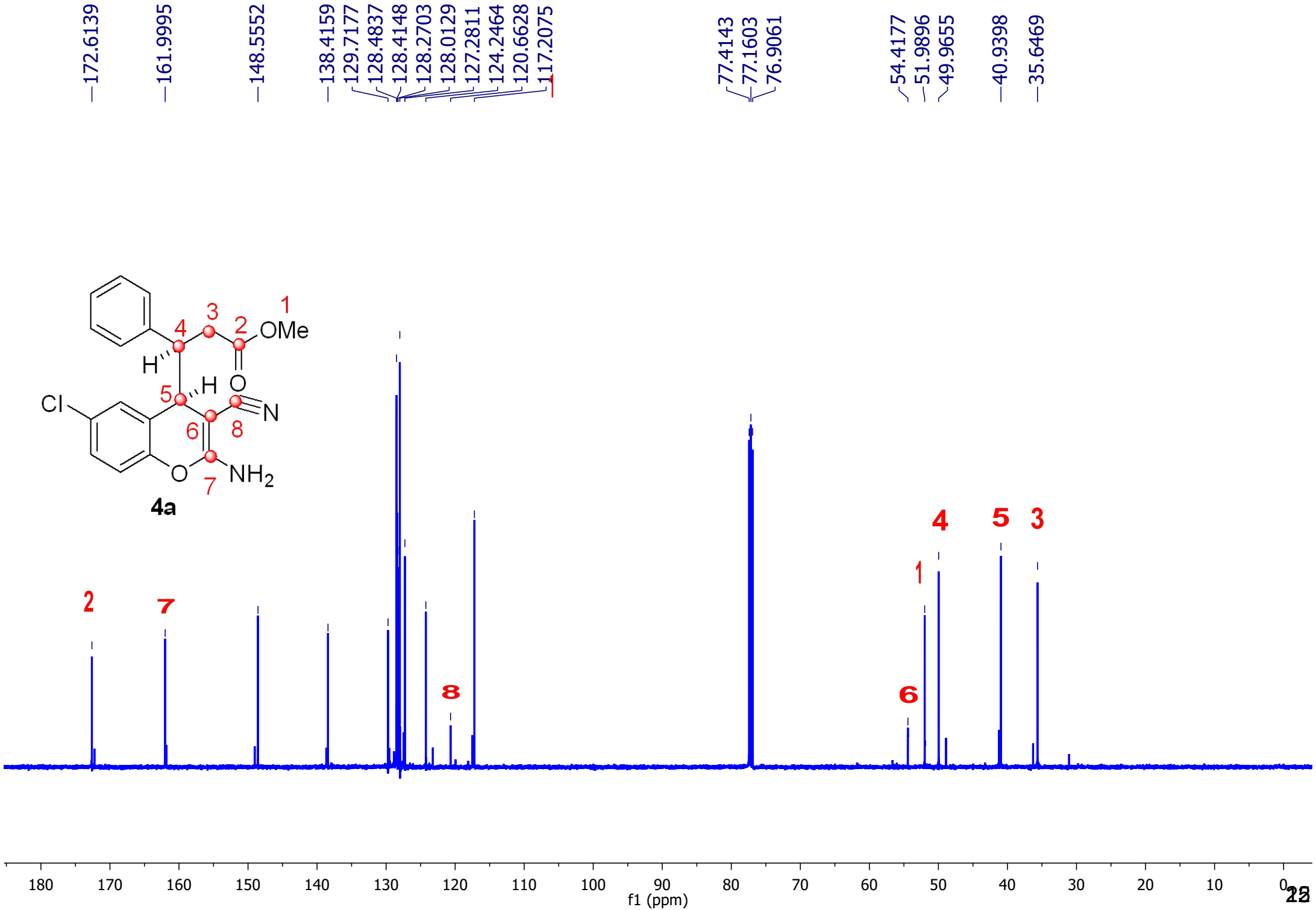
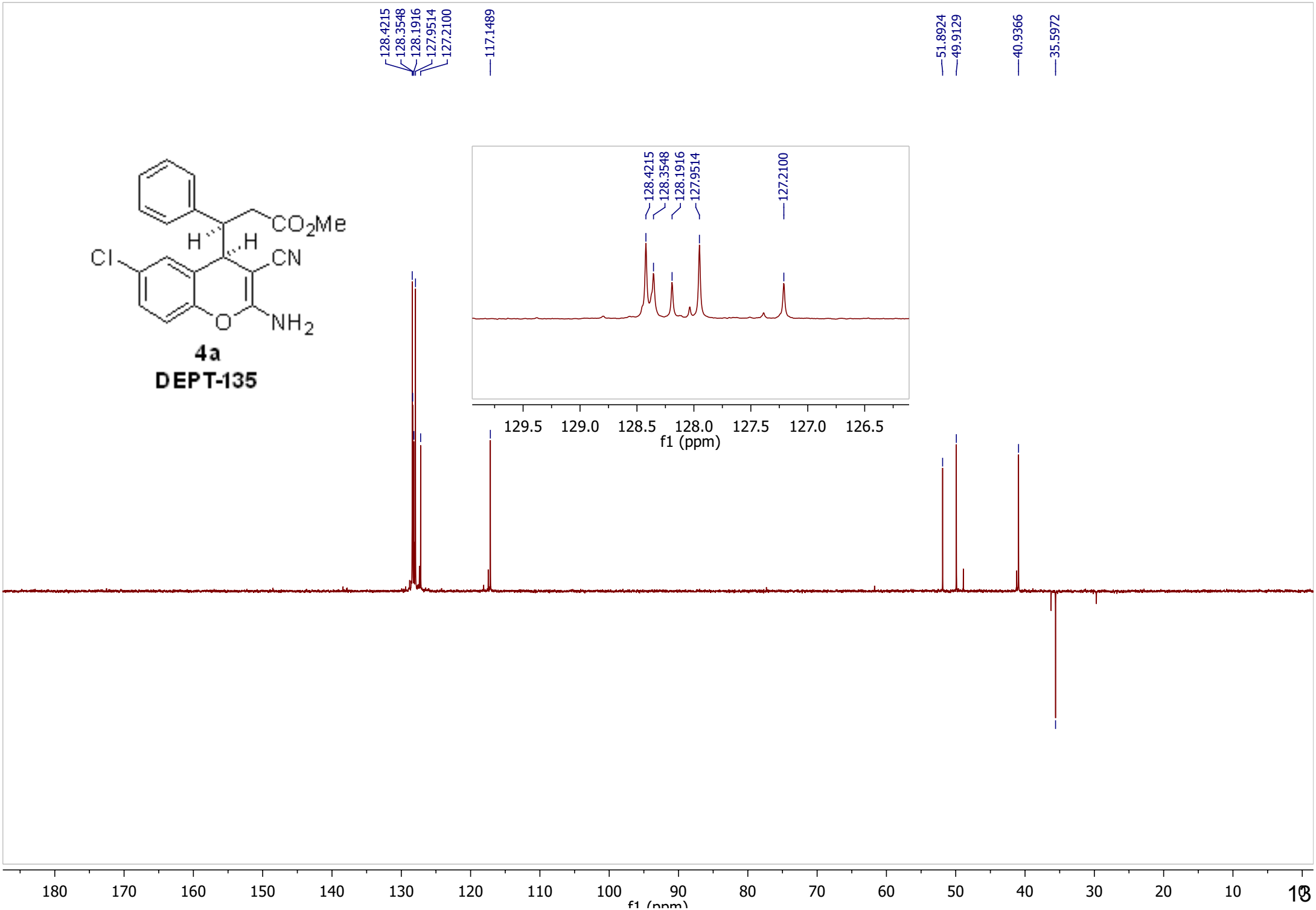
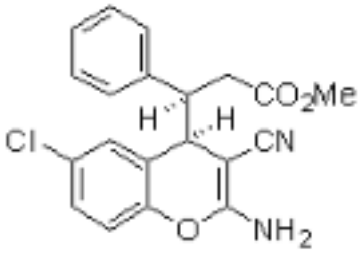
7.1831
7.1794
7.1730
7.1705
7.1679
7.1554
7.1297
7.1247
7.1124
7.1074
7.0032
6.9982
6.8344
6.8318
6.8191
6.8156
6.6708
6.6534
4.7001
3.8717
3.8650
3.6297
3.5328
3.5239
3.5171
3.5083
3.0206
3.0030
2.9877
2.8137
2.7976
2.7807
2.7647
Ha
Ha
CO2Me
Hb
Hc
CN
Cl
O
NH2 (Hd)
Hd
Hc
Hb
Ha
Ha
3.96
1.08
0.97
2.33
0.13
0.93
2.17
1.00
2.90
0.44
0.99
0.99
1.24
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

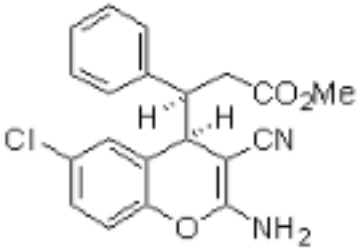

172.6139
161.9995
148.5552
138.4159
129.7177
128.4837
128.4148
128.2703
128.0129
127.2811
124.2464
120.6628
117.2075
77.4143
77.1603
76.9061
54.4177
51.9896
49.9655
40.9398
35.6469
OMe
Cl
N
NH2
H
O
4a
2
7
8
6
1
4
5
3
f1 (ppm)


128.4215
128.3548
128.1916
127.9514
127.2100
117.1489
51.8924
49.9129
40.9366
35.5972
CO2Me
H
H
Cl
CN
O
NH2
4a
DEPT-135
129.5
129.0
128.5
128.0
127.5
127.0
126.5
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

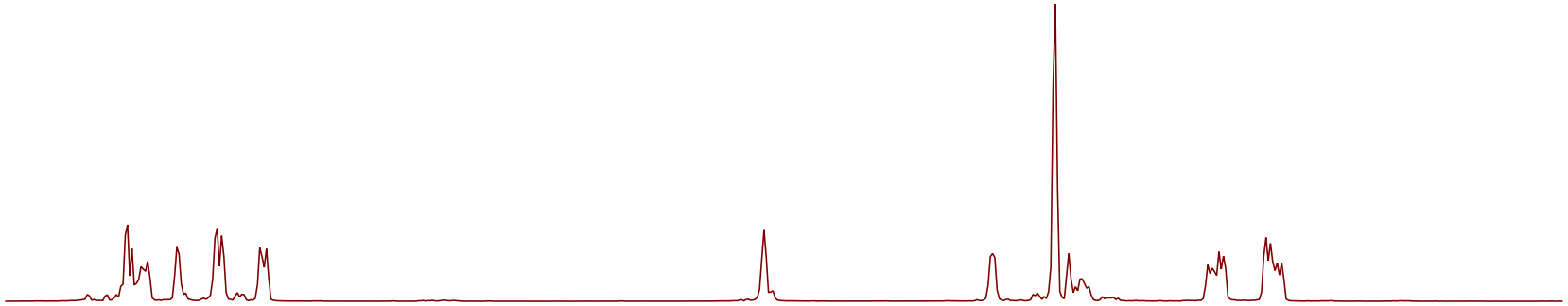

CO2Me
H
H
Cl
CN
O
NH2

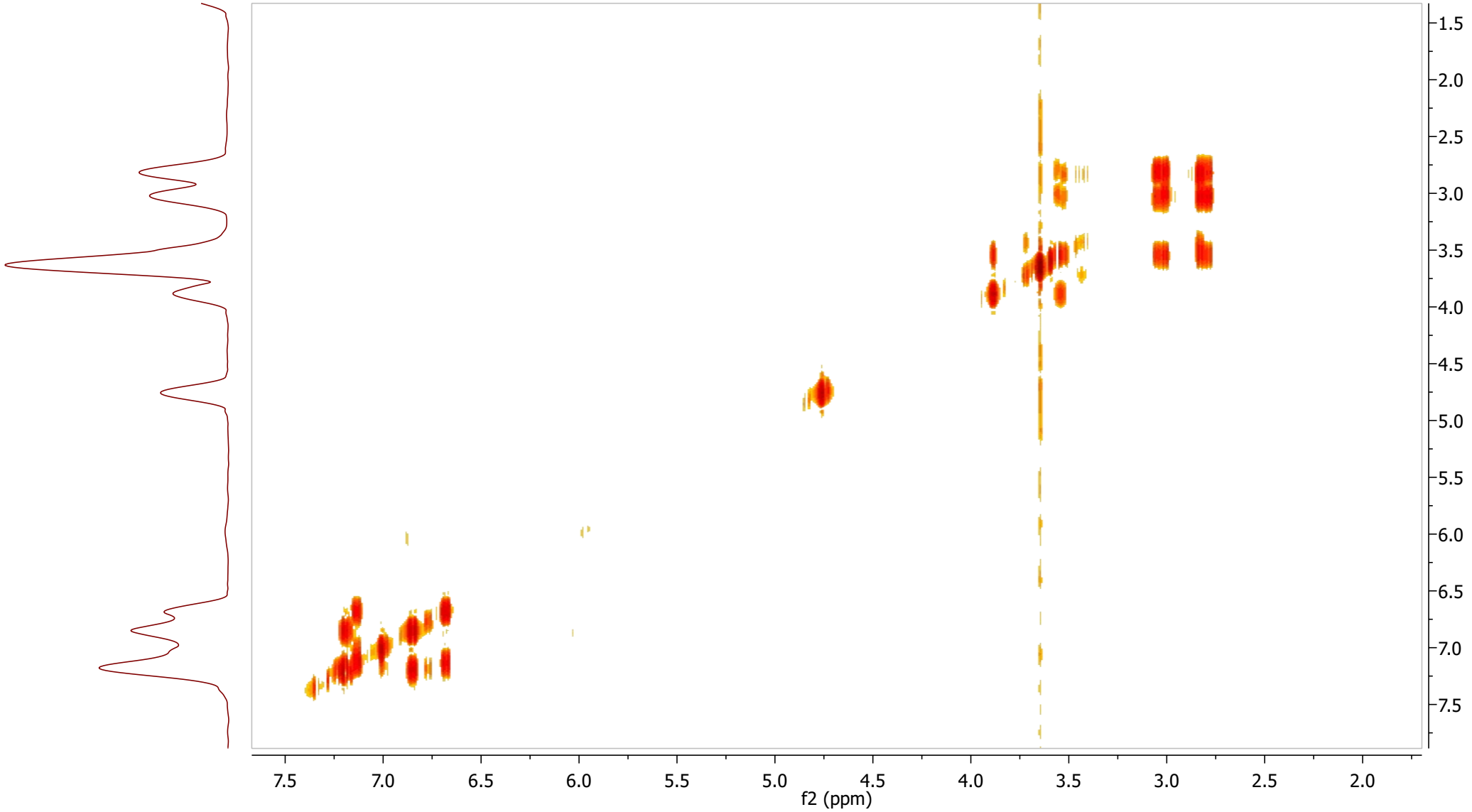
4a
COSY

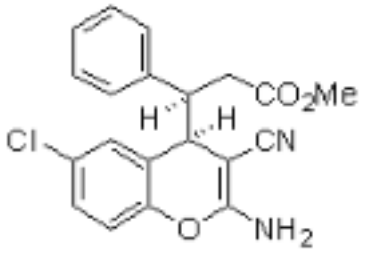
f2 (ppm)
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
1
2
3
4
5
6
7
8


CO2Me
H
H
CN
Cl
O
NH2

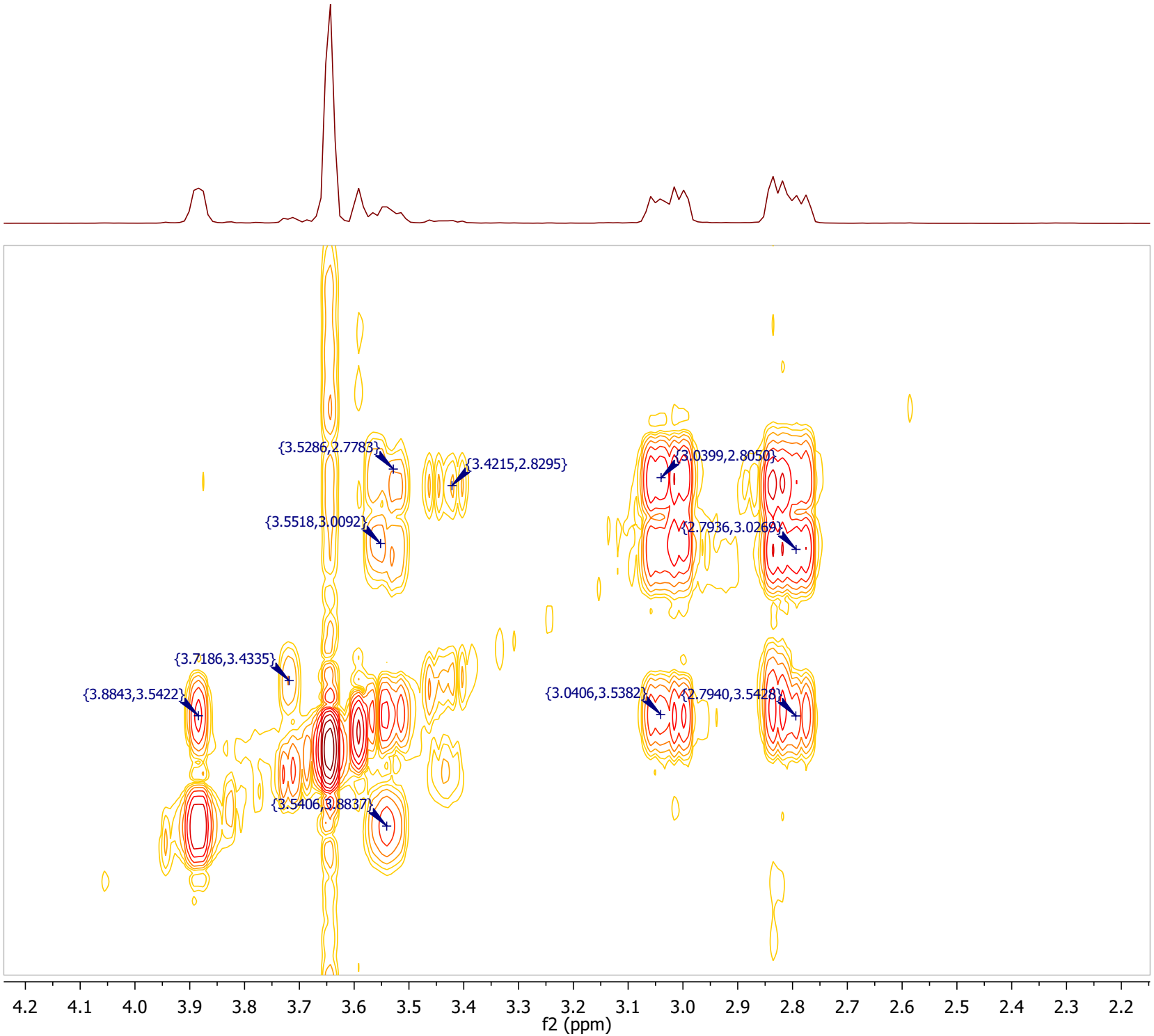
4a
COSY

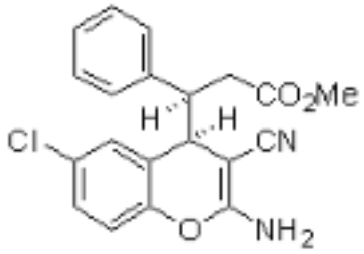



1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f2 (ppm)


CO2Me
H
H
CN
Cl
O
NH2

4a
COSY


{3.5286,2.7783}
{3.4215,2.8295}
{3.0399,2.8050}
{3.5518,3.0092}
{2.7936,3.0269}
{3.7186,3.4335}
{3.8843,3.5422}
{3.0406,3.5382}
{2.7940,3.5428}
{3.5406,3.8837}
f2 (ppm)
f1 (ppm)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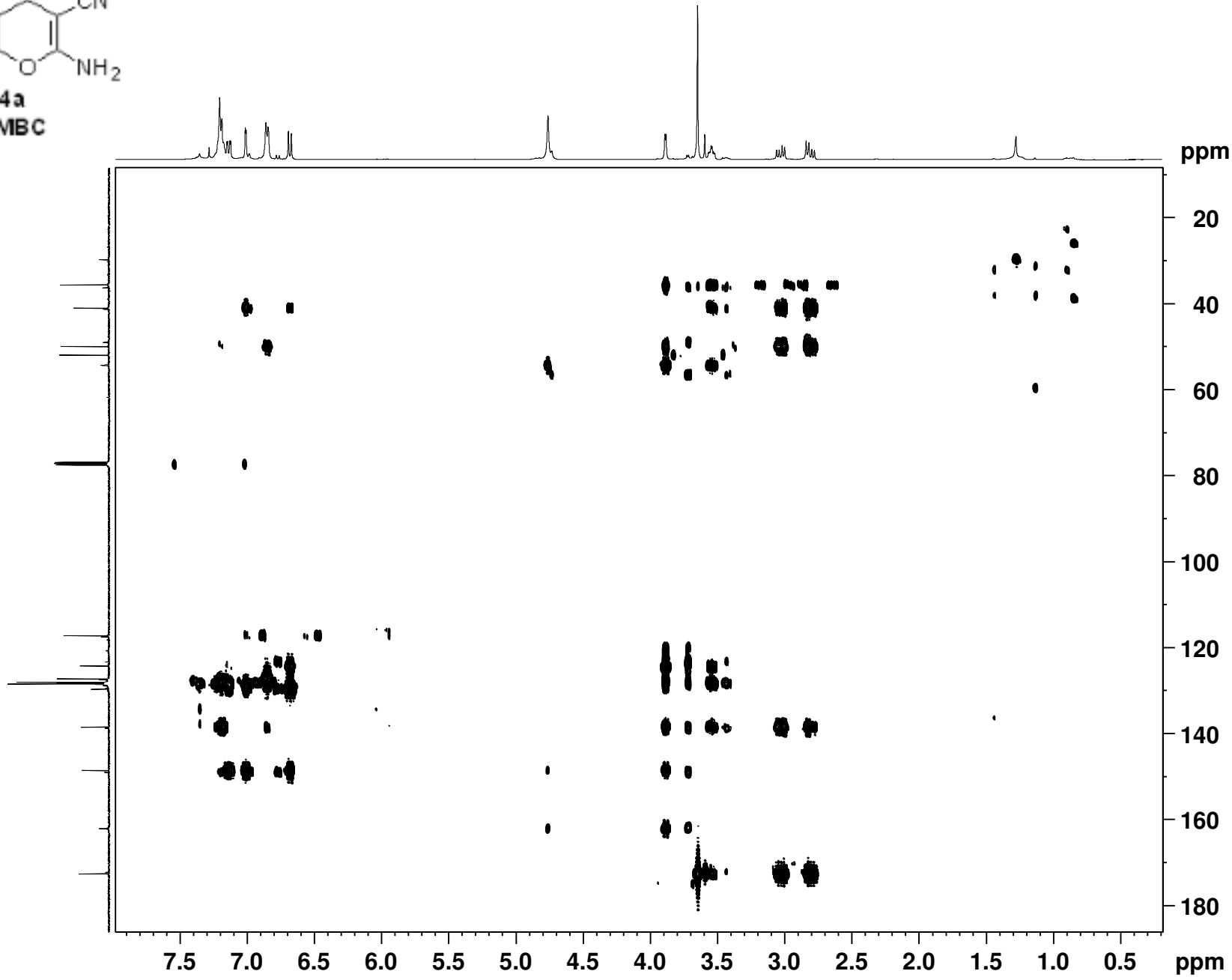
CN
Cl
O
NH2

4a
HMBC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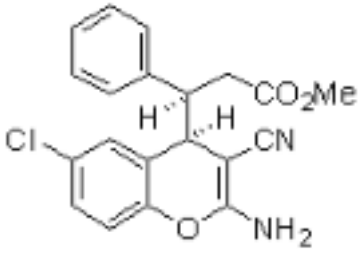
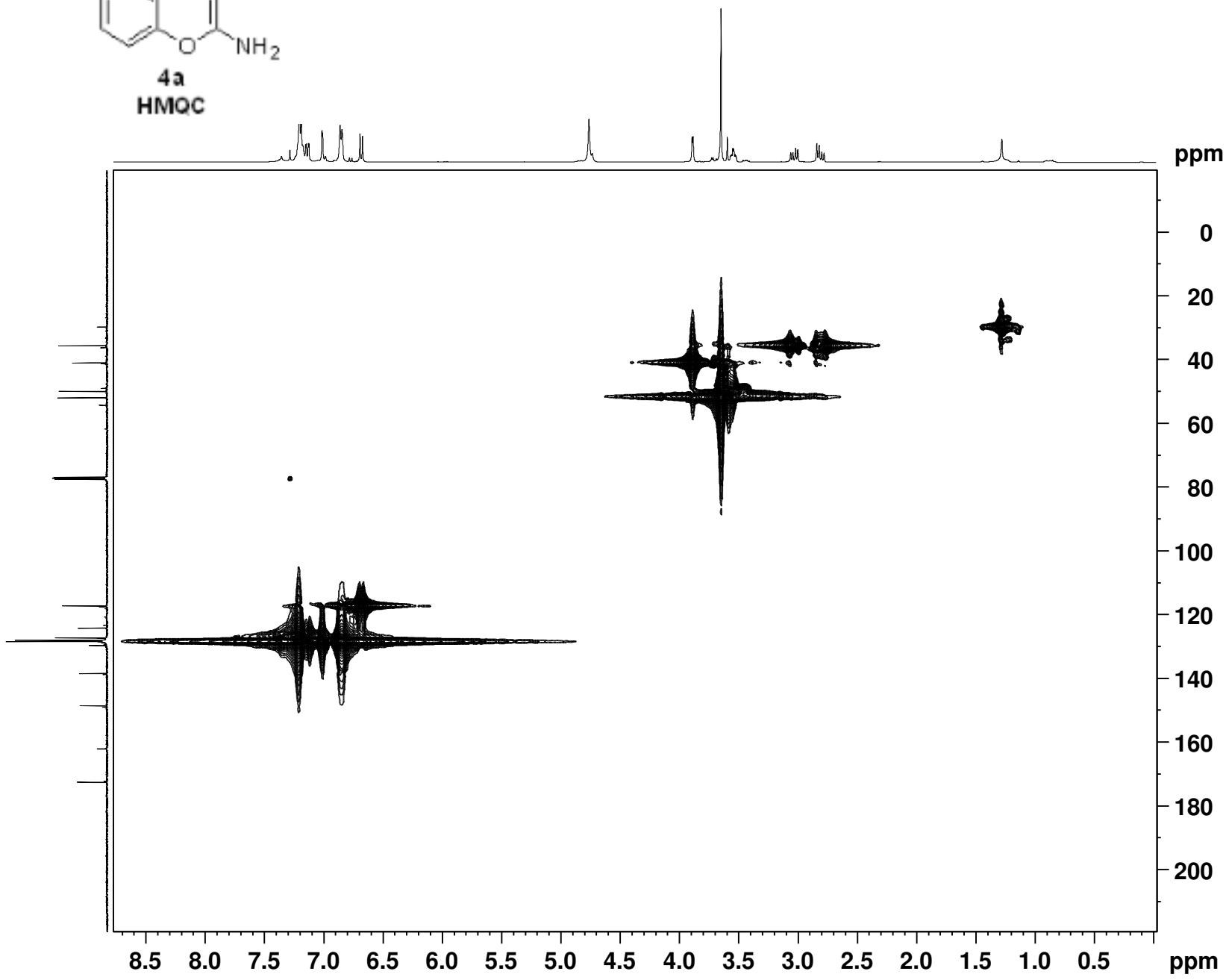


4a

HMQC

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CPDPRG[2             garp
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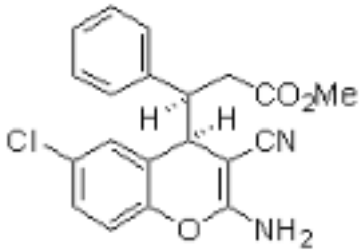
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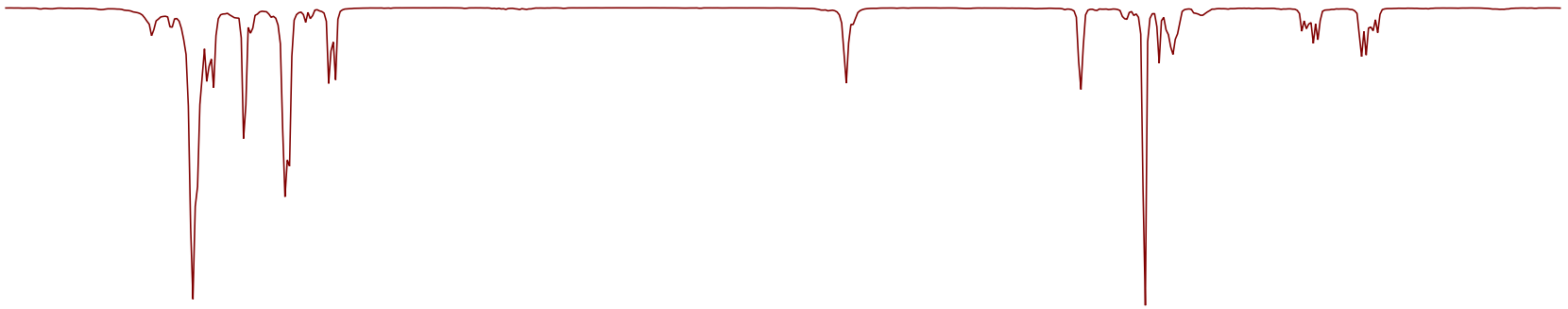
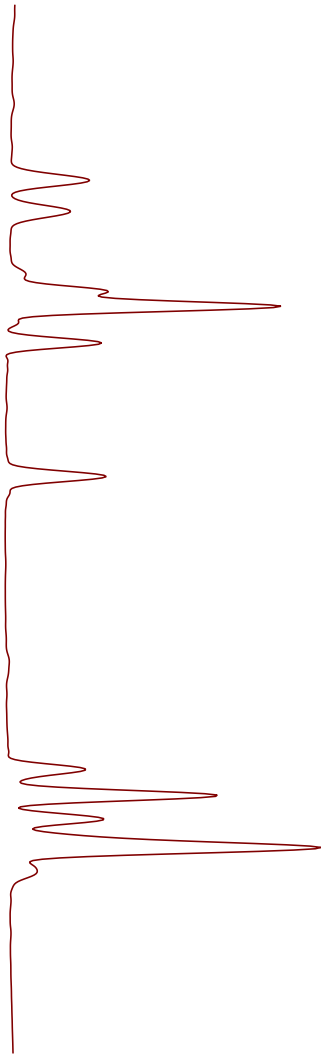
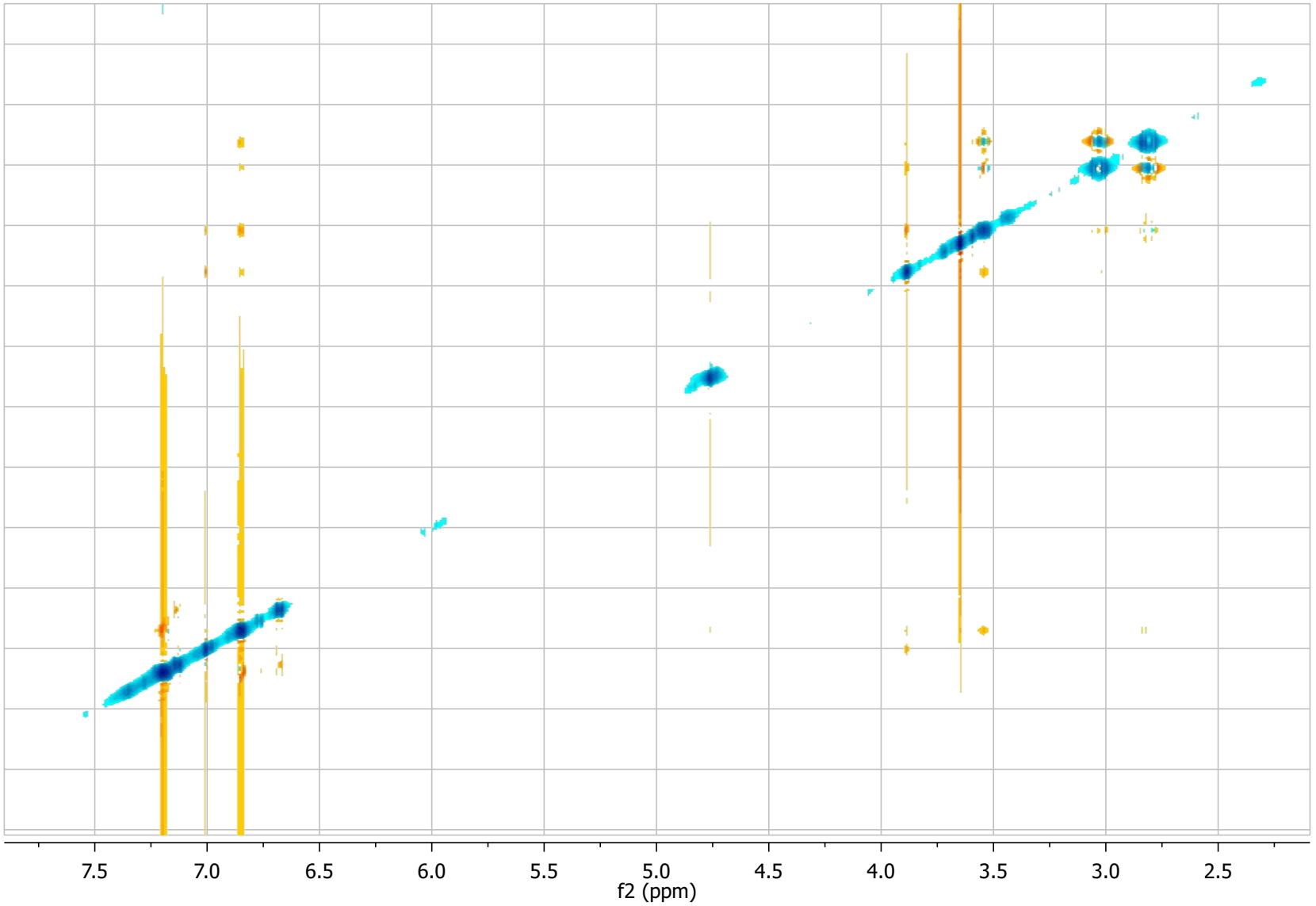
CN
Cl
O
NH2

4a
NOESY



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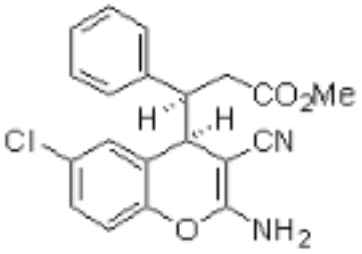
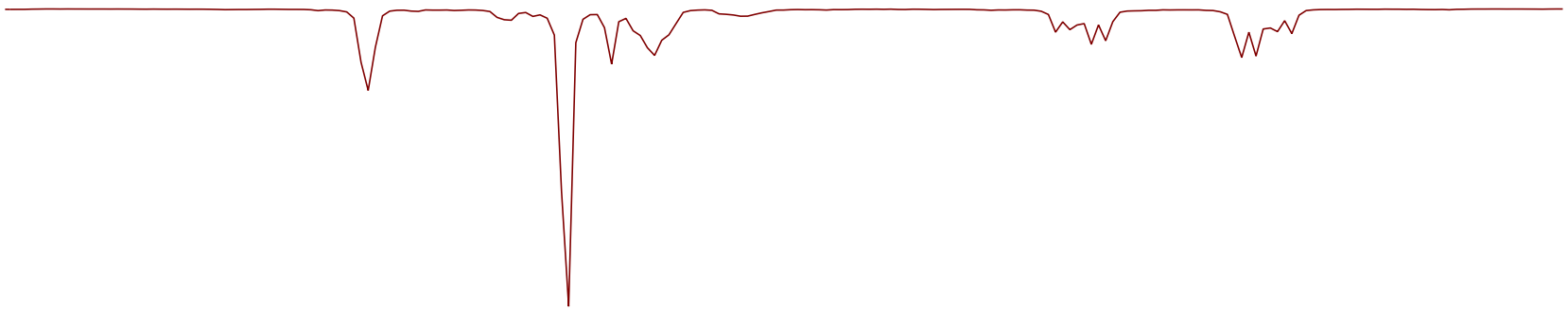
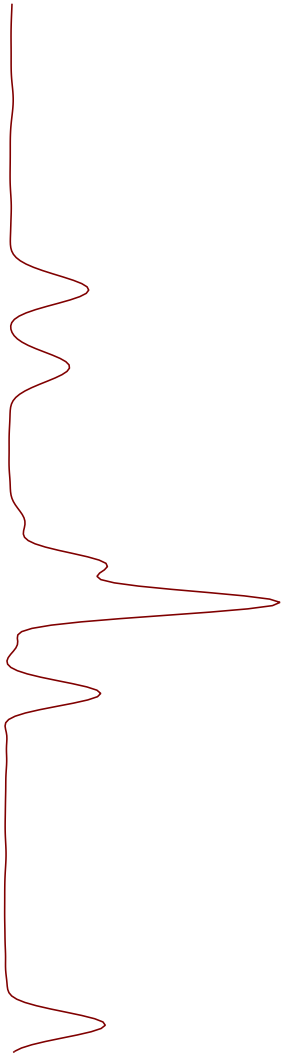
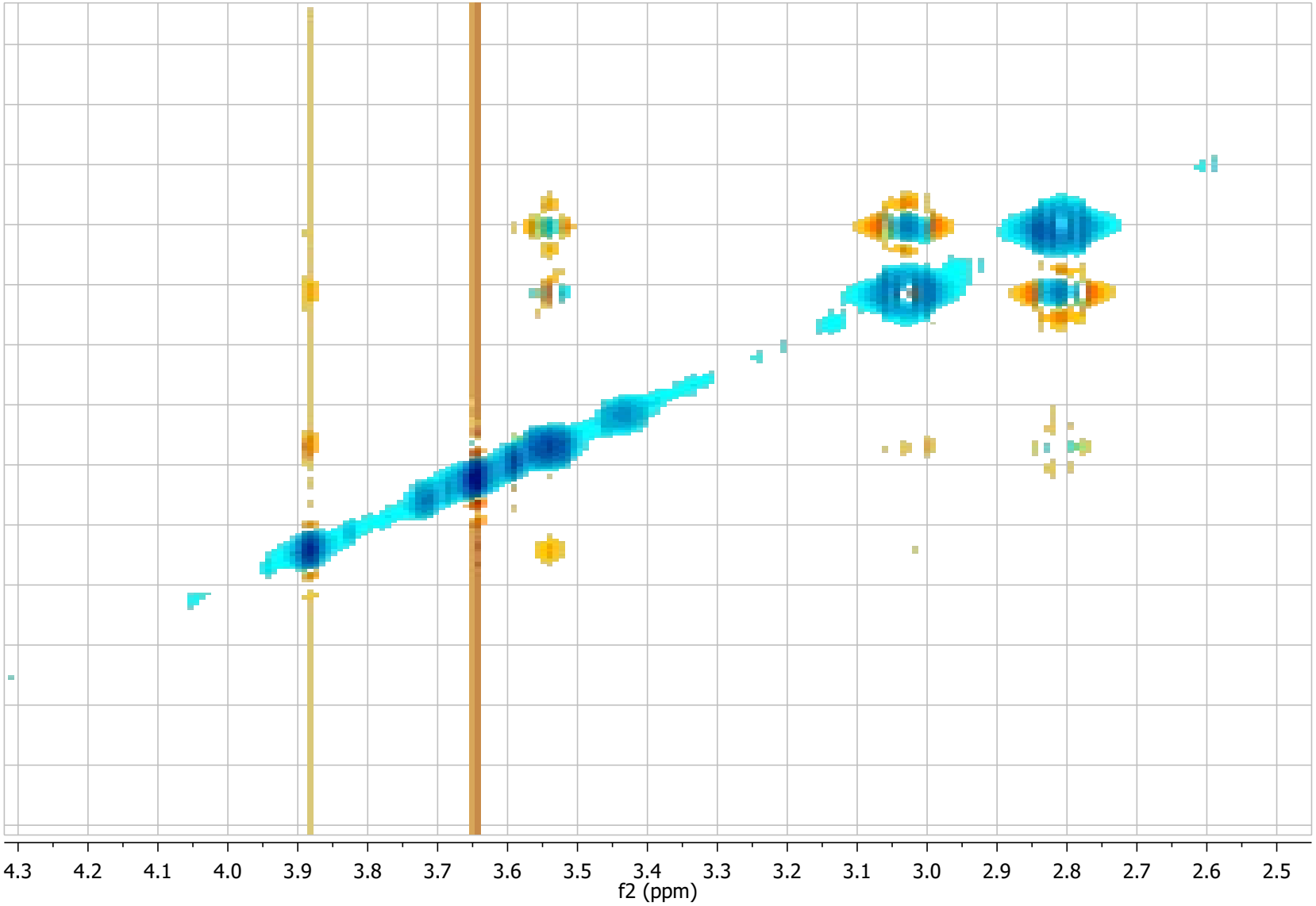

CO2Me
H
H
CN
Cl
O
NH2

4a
NOESY



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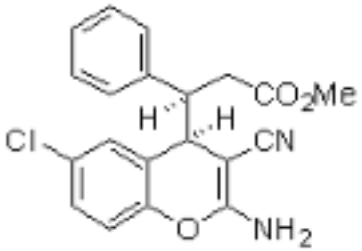
f1 (ppm)


CO2Me
H
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CN
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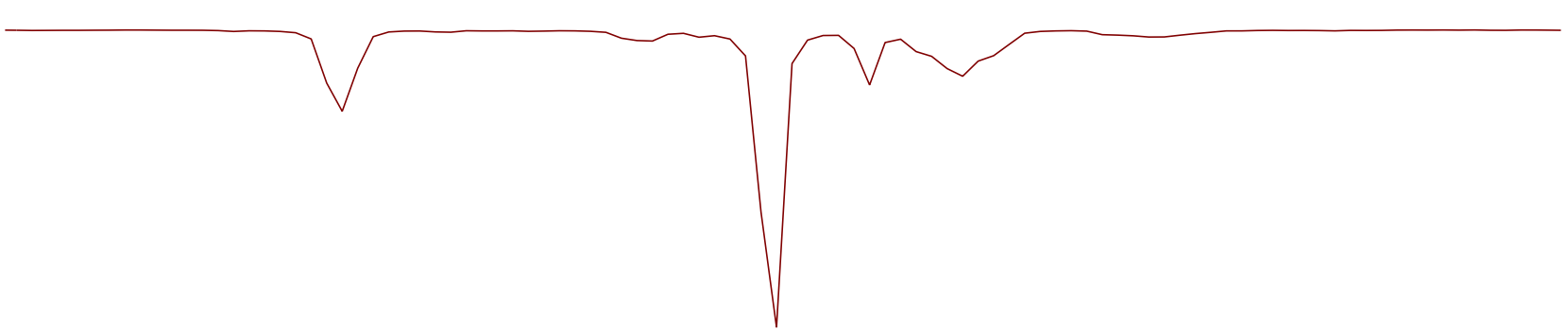
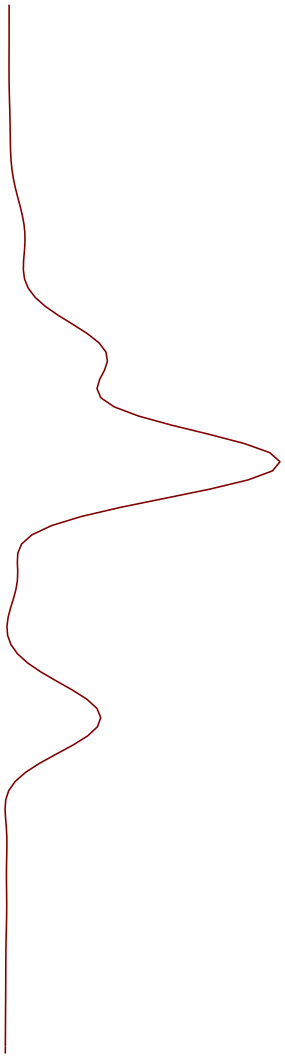
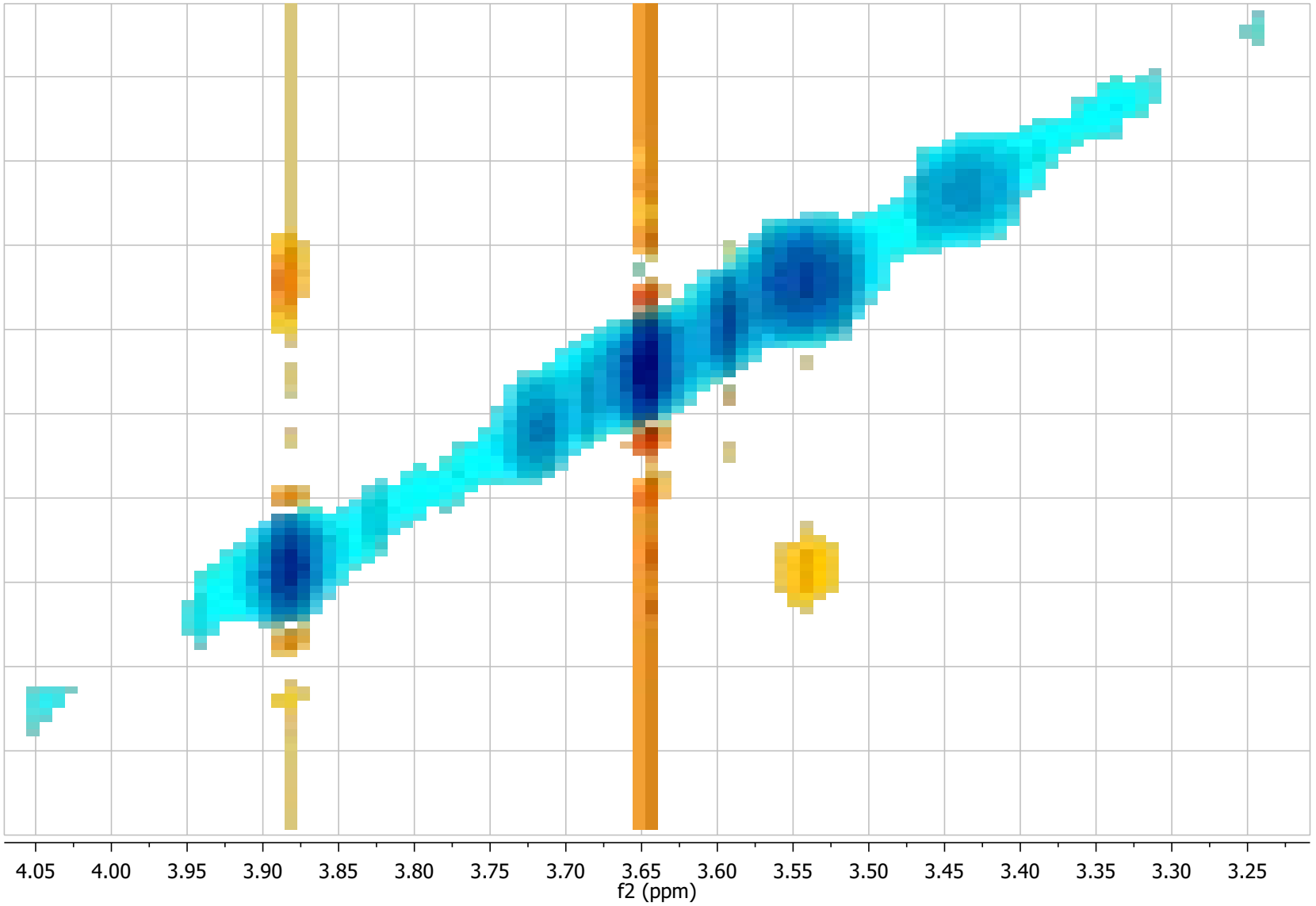
NH2

4a
NOESY



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3.9
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4.1
f1 (ppm)

checkCIF/PLATON report

Structure factors have been supplied for datablock(s) f1

THIS REPORT IS FOR GUIDANCE ONLY. IF USED AS PART OF A REVIEW PROCEDURE FOR PUBLICATION, IT SHOULD NOT REPLACE THE EXPERTISE OF AN EXPERIENCED CRYSTALLOGRAPHIC REFEREE.

No syntax errors found. CIF dictionary Interpreting this report

Datablock: f1

```
Bond precision:   C-C = 0.0055 A          Wavelength=0.71073

Cell:             a=13.486(3)     b=14.311(3)          c=24.277(6)
                  alpha=90        beta=99.610(13)      gamma=90
Temperature:      100 K
```

	Calculated	Reported
Volume	4619.7(18)	4620(2)
Space group	C 2/c	C 1 2/c 1
Hall group	-C 2yc	-C 2yc
Moiety formula	C24 H19 Br N2 O3, 0.5(C2 H2 Cl2)	C24 H19 Br N2 O3, C H Cl
Sum formula	C25 H20 Br Cl N2 O3	C25 H20 Br Cl N2 O3
Mr	511.78	511.79
Dx,g cm-3	1.472	1.472
Z	8	8
Mu (mm-1)	1.925	1.925
F000	2080.0	2080.0
F000'	2079.67	
h,k,lmax	18,19,32	18,19,32
Nref	5991	5977
Tmin,Tmax		0.488,0.746
Tmin'		

```
Correction method= # Reported T Limits: Tmin=0.488 Tmax=0.746
AbsCorr = NONE

Data completeness= 0.998            Theta(max)= 28.719

R(reflections)= 0.0589( 4087)                    wR2(reflections)=
                                                 0.1455( 5977)
S = 1.037                  Npar= 281
```

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C

```
CRYSC01_ALERT_1_C The word below has not been recognised as a standard
           identifier.
           whiteish
RINTA01_ALERT_3_C  The value of Rint is greater than 0.12
           Rint given   0.133
PLAT053_ALERT_1_C Minimum Crystal Dimension Missing (or Error) ...     Please Check
PLAT054_ALERT_1_C Medium  Crystal Dimension Missing (or Error) ...     Please Check
PLAT055_ALERT_1_C Maximum Crystal Dimension Missing (or Error) ...     Please Check
PLAT202_ALERT_3_C Isotropic non-H Atoms in Anion/Solvent .........          2 Check
             Cl1     C0AA
PLAT906_ALERT_3_C Large K Value in the Analysis of Variance ......      2.677 Check
PLAT911_ALERT_3_C Missing FCF Refl Between Thmin & STh/L=    0.600         11 Report
PLAT913_ALERT_3_C Missing # of Very Strong Reflections in FCF ....          8 Note
PLAT976_ALERT_2_C Check Calcd Resid. Dens.  0.60Ang From C0AA    .      -0.80 eA-3
PLAT976_ALERT_2_C Check Calcd Resid. Dens.  0.60Ang From C0AA    .      -0.66 eA-3
PLAT976_ALERT_2_C Check Calcd Resid. Dens.  0.89Ang From N006    .      -0.42 eA-3
PLAT977_ALERT_2_C Check Negative Difference Density on H0AA      .      -0.37 eA-3
```

Alert level G

```
PLAT007_ALERT_5_G Number of Unrefined Donor-H Atoms ..............          2 Report
PLAT020_ALERT_3_G The Value of Rint is Greater Than 0.12 .........      0.133 Report
PLAT042_ALERT_1_G Calc. and Reported Moiety Formula Strings Differ     Please Check
PLAT083_ALERT_2_G SHELXL Second Parameter in WGHT  Unusually Large      20.97 Why ?
PLAT152_ALERT_1_G The Supplied and Calc. Volume s.u. Differ by ...         -2 Units
PLAT344_ALERT_2_G Unusual           Angle Range in Solvent/Ion for       C0AA Check
PLAT720_ALERT_4_G Number of Unusual/Non-Standard Labels ..........         51 Note
PLAT767_ALERT_4_G INS Embedded LIST 6 Instruction Should be LIST 4     Please Check
PLAT779_ALERT_4_G Suspect or Irrelevant (Bond) Angle(s) in CIF ...      40.30 Deg.
             C0AA -CL1  -C0AA    1_555   1_555   2_656 ......     #    48 Check
PLAT793_ALERT_4_G Model has Chirality at C00C        (Centro SPGR)          R Verify
PLAT793_ALERT_4_G Model has Chirality at C00J        (Centro SPGR)          S Verify
PLAT910_ALERT_3_G Missing # of FCF Reflection(s) Below Theta(Min).          1 Note
PLAT912_ALERT_4_G Missing # of FCF Reflections Above STh/L=  0.600          3 Note
PLAT978_ALERT_2_G Number C-C Bonds with Positive Residual Density.          6 Info
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
  13 ALERT level C = Check. Ensure it is not caused by an omission or oversight
  14 ALERT level G = General information/check it is not something unexpected

   6 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   7 ALERT type 2 Indicator that the structure model may be wrong or deficient
   7 ALERT type 3 Indicator that the structure quality may be low
   6 ALERT type 4 Improvement, methodology, query or suggestion
   1 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

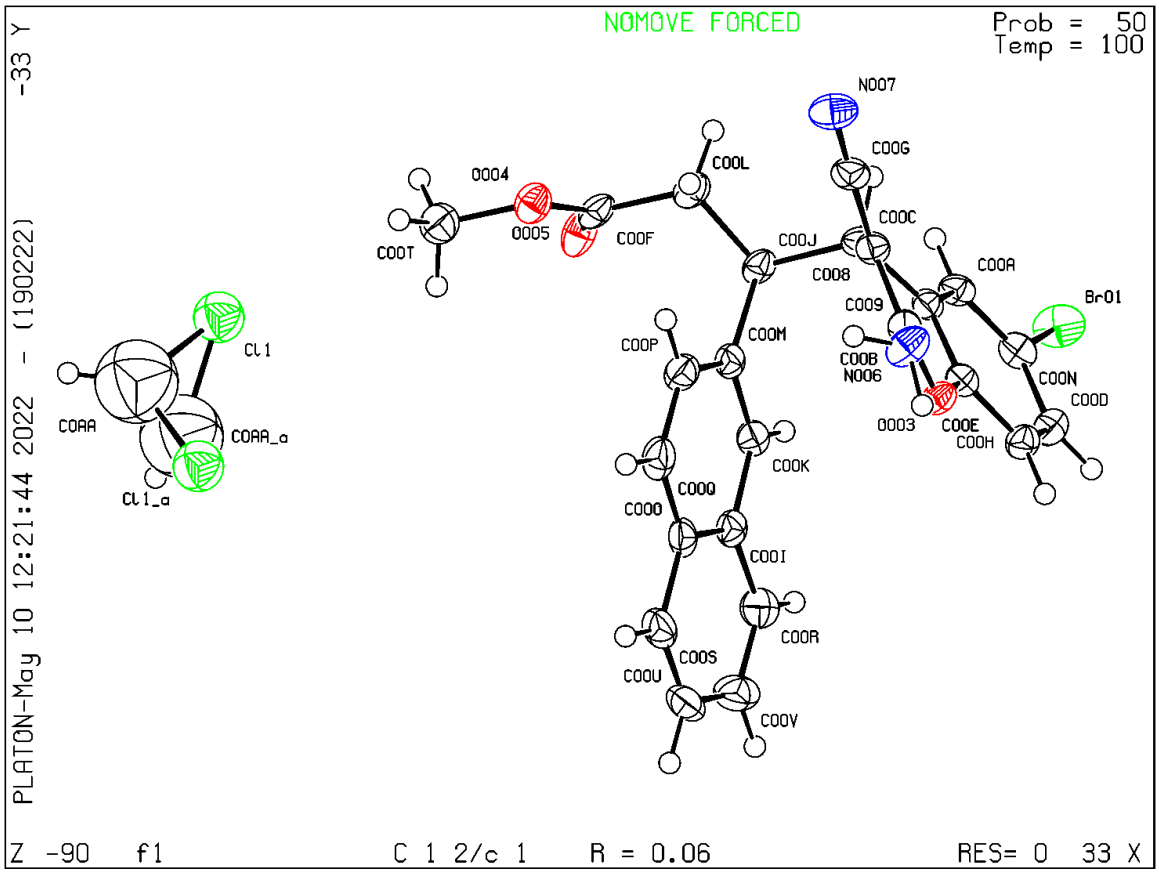
A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

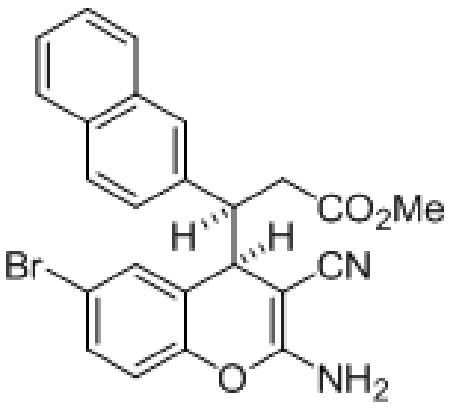
Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 19/02/2022; check.def file version of 19/02/2022

Datablock f1 - ellipsoid plot

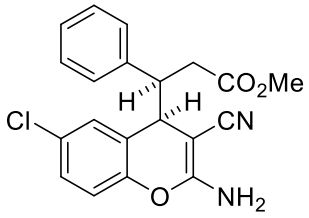




4n

CCDC 2195418

Spectroscopic Details of all 3-cyano-4*H*-chromenes:

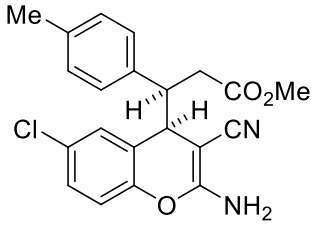


methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-phenylpropanoate **(4a)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-Cinnamaldehyde (72 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4a** (98 mg, 73%) as yellow solid (Petroleum ther/ethyl acetate = 3:1); m.p. = 97-99 °C; *d.r.* = 7:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.20-7.15 (m, 3H), 7.11 (dd, *J* = 7.2, 2.0 Hz, 1H), 7.00 (d, *J* = 2.0 Hz, 1H), 6.83-6.81 (m, 2H), 6.66 (d, *J* = 7.2 Hz, 1H), 4.70 (s, 2H), 3.86 (d, *J* = 2.8 Hz, 1H), 3.63 (s, 3H), 3.57 (td, *J* = 7.5, 2.8 Hz, 1H), 3.01 (dd, *J* = 13.2, 6.0 Hz, 1H), 2.78 (dd, *J* = 13.2, 6.4 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 162.0, 148.5, 138.4, 129.7, 128.5, 128.41, 128.3, 128.0, 127.3, 124.2, 120.7, 117.2, 54.4, 52.0, 50.0, 40.9, 35.6.

HRMS (EI) calcd for $C_{20}H_{17}ClN_2O_3$, 391.0825 *m/z* $(M+Na)^+$; Found, 391.0821 *m/z*.

FTIR (cm^{-1}): 2359, 2183, 1737, 1636, 1418, 1260, 1224, 809, 754.

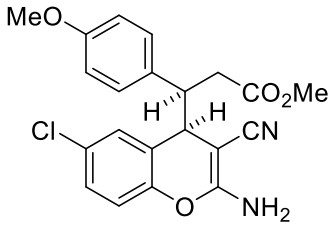


methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(*p*-tolyl)propanoate **(4b)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(*p*-tolyl)acrylaldehyde (80 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) was stirred overnight at room temperature to obtain **4b** (100 mg, 72%) as off yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 91-93 °C; *d.r.* = 9:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.10 (dd, *J* = 8.7, 2.3 Hz, 1H), 6.96 (d, *J* = 7.6 Hz, 3H), 6.72-6.65 (m, 3H), 4.71 (s, 2H), 3.83 (d, *J* = 3.2 Hz, 1H), 3.61 (s, 3H), 3.48 (td, *J* = 7.8, 3.30 Hz, 1H), 2.97 (dd, *J* = 16.4, 7.5 Hz, 1H), 2.74 (dd, *J* = 16.3, 8.0 Hz, 1H), 2.27 (s, 3H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 162.0, 148.6, 136.8, 135.4, 129.6, 128.7, 128.4, 128.3, 128.2, 124.3, 120.7, 117.2, 54.6, 51.9, 49.6, 41.0, 35.7, 21.2.

HRMS (EI) calcd for $C_{21}H_{19}ClN_2O_3$, 405.0982 *m/z* $(M+Na)^+$; Found, 405.0977 *m/z*.

FTIR (cm^{-1}): 3392, 3229, 3209, 2360, 2341, 2192, 1721, 1660, 1611, 1414, 1232, 1163, 1028, 817.

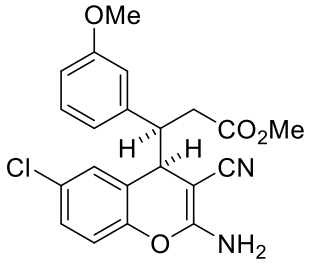


methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(4-methoxyphenyl)propanoate **(4c)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1 *equiv*) and (*E*)-3-(4-methoxyphenyl)acrylaldehyde (89 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4c** (100 mg, 69%) as yellow solid (Petroleum ether/ethyl acetate = 2.5:1); m.p. = 87-89 °C; *d.r.* = 6:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.10 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.01 (s, 1H), 6.73-6.64 (m, 5H), 4.70 (s, 2H), 3.82 (d, *J* = 2.9 Hz, 1H), 3.73 (s, 3H), 3.61 (s, 3H), 3.45 (td, *J* = 7.8, 3.2 Hz, 1H), 2.97 (dd, *J* = 16.4, 7.5 Hz, 1H), 2.75 (dd, *J* = 16.0, 8.1 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 162.0, 158.8, 148.6, 130.3, 129.7, 129.4, 128.4, 128.2, 124.4, 120.7, 117.2, 113.4, 55.2, 54.3, 51.9, 49.3, 41.0, 36.0.

HRMS (EI) calcd for $C_{21}H_{19}ClN_2O_4$, 421.0931 *m/z* $(M+Na)^+$; Found, 421.0906 *m/z*.

FTIR (cm^{-1}): 3326, 2952, 2184, 1726, 1643, 1511, 1417, 1248, 1178, 1030, 817.

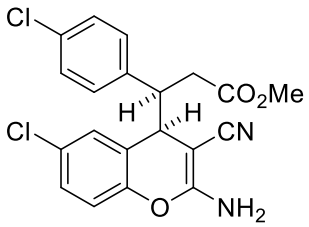


methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(3-methoxyphenyl)propanoate **(4d)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(3-methoxyphenyl)acrylaldehyde (89 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4d** (85 mg, 58%) as yellow oil (Petroleum ether/ethyl acetate = 2.5:1); *d.r.* = 6:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.14-7.07 (m, 2H), 6.99 (d, *J* = 2.2 Hz, 1H), 6.74 (dd, *J* = 8.5, 2.4 Hz, 1H), 6.68 (d, *J* = 8.7 Hz, 1H), 6.45 (d, *J* = 7.6 Hz, 1H), 6.33 (s, 1H), 4.67 (s, 2H), 3.87 (d, *J* = 3.2 Hz, 1H), 3.67 (s, 3H), 3.63 (s, 3H), 3.49 (td, *J* = 7.8, 3.2 Hz, 1H), 2.97 (dd, *J* = 16.5, 7.6 Hz, 1H), 2.76 (dd, *J* = 16.6, 8.0 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 161.9, 159.3, 148.6, 140.1, 129.7, 129.0, 128.5, 128.3, 124.2, 120.8, 120.5, 117.2, 113.9, 113.2, 55.3, 54.8, 52.0, 49.9, 40.9, 35.6.

HRMS (EI) calcd for $C_{21}H_{19}ClN_2O_4$, 421.0931 *m/z* $(M+Na)^+$; Found, 421.0917 *m/z*.

FTIR (cm^{-1}): 3312, 2927, 2203, 1732, 1658, 1542, 1420, 1352, 1229, 1117, 1032, 857.



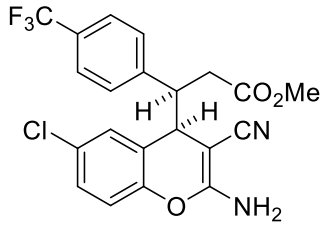
methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(4-chlorophenyl)propanoate **(4e)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(4-chlorophenyl)acrylaldehyde (91 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4e**

(115 mg, 78%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 143-145 °C; *d.r.* = 8:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.14-7.10 (m, 4H), 6.74 (d, *J* = 8.2 Hz, 2H), 6.67 (d, *J* = 8.6 Hz, 1H), 4.70 (s, 2H), 3.87 (d, *J* = 2.9 Hz, 1H), 3.63 (s, 3H), 3.48 (td, *J* = 7.7, 3.0 Hz, 1H), 3.02 (dd, *J* = 16.5, 7.4 Hz, 1H), 2.79 (dd, *J* = 16.6, 8.2 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.3, 162.1, 148.5, 136.9, 133.2, 130.0, 129.8, 128.5, 128.2, 128.1, 124.2, 120.6, 117.4, 53.9, 52.0, 49.7, 40.7, 35.9.

HRMS (EI) calcd for $C_{20}H_{16}Cl_2N_2O_3$, 425.0436 *m/z* $(M+Na)^+$; Found, 425.0435 *m/z*.

FTIR (cm^{-1}): 3457, 3331, 2357, 2180, 1742, 1634, 1480, 1419, 1185, 1090, 823.

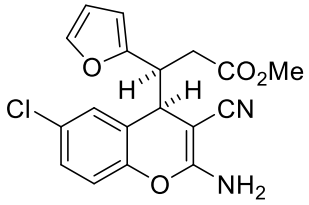


methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(4-(trifluoromethyl)phenyl)propanoate **(4f)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(4-(trifluoromethyl)phenyl)acrylaldehyde (110 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4f** (127 mg, 80%) as off yellow solid (Petroleum ether/ethyl acetate = 3:1); Major isomer was separated during column chromatography, dr is based on NMR of crude reaction mixture; m.p. = 113-115 °C; *d.r.* = 10:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.41 (d, *J* = 8.0 Hz, 2H), 7.14 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.09 (s, 1H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 8.7 Hz, 1H), 4.72 (s, 2H), 3.91 (d, *J* = 3.0 Hz, 1H), 3.63 (s, 3H), 3.58 (td, *J* = 7.8, 3.2 Hz, 1H), 3.06 (dd, *J* = 16.6, 7.4 Hz, 1H), 2.84 (dd, *J* = 16.6, 8.2 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.2, 162.1, 148.5, 142.6, 130.1, 128.9, 128.6, 128.2, 124.9, 124.8, 124.0, 120.5, 117.4, 53.8, 52.1, 50.1, 40.7, 35.7.

HRMS (EI) calcd for $C_{21}H_{16}ClF_3N_2O_3$, 459.0699 *m/z* $(M+Na)^+$; Found, 459.0702 *m/z*.

FTIR (cm^{-1}): 3321, 2358, 2190, 1714, 1652, 1481, 1419, 1321, 1159, 1112, 1067, 833, 811.

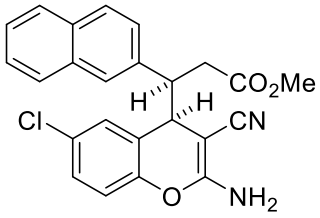


methyl 3-(2-amino-6-chloro-3-cyano-4H-chromen-4-yl)-3-(furan-2-yl)propanoate **(4g)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(furan-2-yl)acrylaldehyde (67 mg, 0.55 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4g** (120 mg, 92%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 103-105 ˚C; *d.r.* = 4:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.27 (d, *J* = 5.4 Hz, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 6.74 (d, *J* = 8.7 Hz, 1H), 6.47 (s, 1H), 6.19 (s, 1H), 5.79 (d, *J* = 2.3 Hz, 1H), 4.71 (s, 2H), 3.88 (d, *J* = 3.2 Hz, 1H), 3.57 (s, 4H), 2.65 (dd, *J* = 16.2, 6.0 Hz, 1H), 2.44 (dd, *J* = 16.2, 9.0 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.2, 161.7, 153.3, 148.6, 141.9, 129.7, 128.5, 128.4, 122.7, 119.9, 117.3, 110.5, 107.5, 55.6, 52.1, 43.2, 39.4, 33.5.

HRMS (EI) calcd for $C_{18}H_{15}ClN_2O_4$, 381.0618 *m/z* $(M+Na)^+$; Found, 381.0611 *m/z*.

FTIR (cm^{-1}): 3179, 2359, 2192, 1705, 1650, 1574, 1504, 1483, 1421, 1222, 1152, 1004, 895, 826.



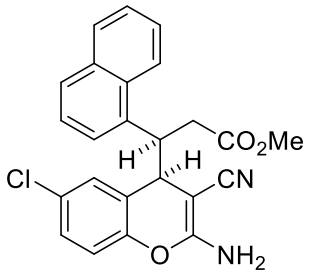
methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(naphthalen-2-yl)propanoate **(4h)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(naphthalen-2-yl)acrylaldehyde (100 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4h**

(136 mg, 89%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 110-112 °C; *d.r.* = 10:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.76-7.75 (m, 1H), 7.67-7.63 (m, 2H), 7.43-7.41 (m, 2H), 7.27 (d, *J* = 9.6 Hz, 1H), 7.10 (dd, *J* = 8.7, 2.2 Hz, 1H), 7.06 (s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.56 (d, *J* = 8.6 Hz, 1H), 4.65 (s, 2H), 3.95 (d, *J* = 3.0 Hz, 1H), 3.70 (td, *J* = 7.5, 4.8 Hz, 1H), 3.60 (s, 3H), 3.11 (dd, *J* = 16.4, 7.4 Hz, 1H), 2.92 (dd, *J* = 16.2, 8.2 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.5, 162.0, 148.5, 136.0, 133.1, 132.6, 129.8, 128.4, 128.3, 127.9, 127.6, 127.5, 127.4, 126.7, 126.0, 125.8, 124.3, 120.7, 117.2, 54.3, 52.0, 50.2, 41.0, 35.9.

HRMS (EI) calcd for $C_{24}H_{19}ClN_2O_3$, 441.0982 *m/z* $(M+Na)^+$; Found, 441.0984 *m/z*.

FTIR (cm^{-1}): 3319, 2360, 2183, 1725, 1648, 1422, 1350, 1259, 1150, 814, 746.

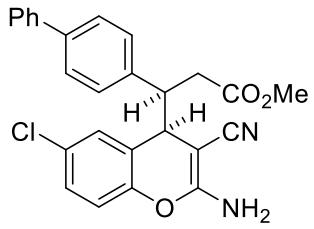


methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-(naphthalen-1-yl)propanoate **(4i)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-(naphthalen-1-yl)acrylaldehyde (100 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight room temperature to obtain **4i** (110 mg, 72%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 103-105 °C; *d.r.* = 5:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 8.06 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.53-7.46 (m, 2H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.07-7.02 (m, 2H), 6.69 (d, *J* = 8.7 Hz, 1H), 6.16 (s, 1H), 4.71 (s, 2H), 4.55 (m, 1H), 3.95 (d, *J* = 3.0 Hz, 1H), 3.57 (s, 3H), 2.92 (dd, *J* = 16.0, 9.0 Hz, 1H), 2.64 (dd, *J* = 16.0, 9.1 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.5, 161.7, 148.8, 135.1, 134.0, 131.6, 129.4, 129.2, 129.1, 128.4, 128.3, 126.5, 125.8, 124.9, 124.8, 122.7, 112.2, 119.9, 117.2, 57.0, 52.0, 43.1, 40.2, 34.6.

HRMS (EI) calcd for $C_{24}H_{19}ClN_2O_3$, 441.0982 *m/z* $(M+Na)^+$; Found, 441.0972 *m/z*.

FTIR (cm^{-1}): 3329, 2359, 2184, 1731, 1653, 1480, 1420, 1241, 1026, 771.

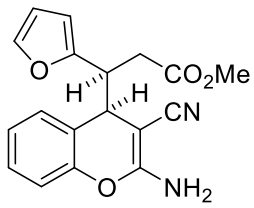


methyl 3-([1,1'-biphenyl]-4-yl)-3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)propanoate **(4j)**: According to the general reaction procedure **II** 6-chloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.366 mmol, 1.0 *equiv*) and (*E*)-3-([1,1'-biphenyl]-4-yl)acrylaldehyde (115 mg, 0.550 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4j** (122 mg, 75%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 125-127 $^{\circ}$C; *d.r.* = 7:1;

^{1}H-NMR (DMSO-d_6, 400 MHz**):** δ 7.62 (d, *J* = 7.5 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 6.94 (m, 2H), 6.90 (d, *J* = 8.1 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 1H), 3.90 (d, *J* = 3.9 Hz, 1H), 3.48 (s, 2H), 3.41-3.36 (m, 1H), 3.33 (s, 3H), 2.90-2.87 (m, 2H); **^{13}C-NMR (**DMSO-d_6, 100 MHz**):** δ 171.6, 162.7, 148.7, 139.5, 138.2, 138.1, 128.9, 128.8, 128.0, 127.8, 127.3, 126.4, 125.7, 125.3, 121.2, 117.3, 51.4, 50.2, 49.5, 40.7, 35.9.

HRMS (EI) calcd for $C_{26}H_{21}ClN_2O_3$, 467.1138 *m/z* $(M+Na)^+$; Found, 467.1137 *m/z*.

FTIR (cm^{-1}): 3237, 2357, 2119, 1726, 1648, 1524, 1423, 1222, 1183, 1004, 942, 824, 763.



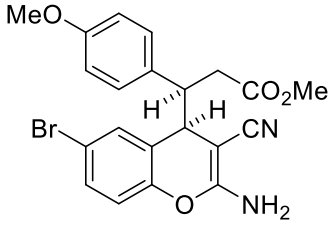
methyl 3-(2-amino-3-cyano-4*H*-chromen-4-yl)-3-(furan-2-yl)propanoate **(4l)**: According to the general reaction procedure **II** 2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.440 mmol, 1.0 *equiv*) and (*E*)-3-(furan-2-yl)acrylaldehyde (80 mg, 0.660 mmol, 1.5 *equiv*) in CH_3CN:MeOH

(20:1) (0.15 M) was stirred overnight at room temperature to obtain **4l** (91 mg, 64%) as yellow oil (Petroleum ther/ethyl acetate = 3:1); *d.r.* = 3:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.33 (s, 1H), 7.19 (d, *J* = 5.9 Hz, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.25 (s, 1H), 5.82 (d, *J* = 3.0 Hz, 1H), 4.70 (s, 2H), 4.01 (d, *J* = 3.6 Hz, 1H), 3.71-3.59 (m, 1H), 3.63 (s, 3H), 2.73 (dd, *J* = 16.2, 6.0 Hz, 1H), 2.51 (dd, *J* = 16.1, 9.1 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.4, 161.8, 153.8, 150.1, 141.8, 128.8, 128.4, 124.8, 121.0, 120.2, 116.0, 110.4, 107.3, 56.2, 52.0, 43.3, 39.4, 33.6.

HRMS (EI) calcd for $C_{18}H_{16}N_2O_4$, 347.1008 *m/z* $(M+Na)^+$; Found, 347.1000 *m/z.*

FTIR (cm^{-1}): 3312, 2398, 2157, 1738, 1645, 1423, 1241, 1217, 812, 722.

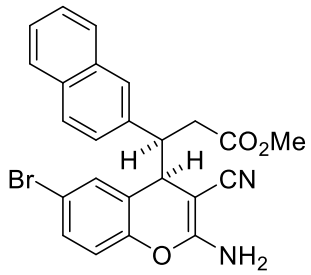


methyl 3-(2-amino-6-bromo-3-cyano-4*H*-chromen-4-yl)-3-(4-methoxyphenyl)propanoate **(4m)**: According to the general reaction procedure **II** 6-bromo-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.301 mmol, 1.0 *equiv*) and (*E*)-3-(4-methoxyphenyl)acrylaldehyde (73 mg, 0.451 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4m** (93 mg, 70%) as yellow solid (Petroleum ether/ethyl acetate = 2.5:1); m.p. = 137-139 $^{\circ}$C; *d.r.* = 9:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.18 (dd, *J* = 7.8, 2.0 Hz, 1H), 6.08 (d, *J* = 1.8 Hz, 1H), 6.64 (dd, *J* = 13.2, 9.0 Hz, 4H), 6.53 (d, *J* = 8.6 Hz, 1H), 4.66 (s, 2H), 3.75 (d, *J* = 3.1 Hz, 1H), 3.74 (s, 3H), 3.67 (s, 3H), 3.39 (td, *J* = 7.8, 3.2 Hz, 1H), 2.89 (dd, *J* = 16.3, 7.4 Hz, 1H), 2.67 (dd, *J* = 16.4, 8.2 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 161.9, 158.7, 149.1, 131.3, 131.1, 130.3, 129.4, 124.8, 120.7, 117.6, 117.1, 113.4, 55.2, 54.4, 51.9, 49.3, 40.9, 35.9.

HRMS (EI) calcd for $C_{21}H_{19}{}^{81}BrN_2O_4$, 467.0405 *m/z* $(M+Na)^+$; Found, 467.0389 *m/z.*

FTIR (cm^{-1}): 3378, 3317, 2963, 2208, 1732, 1635, 1497, 1421, 1232, 1105, 1032, 815, 763.

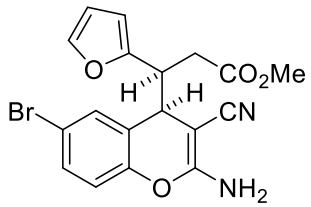


methyl 3-(2-amino-6-bromo-3-cyano-4*H*-chromen-4-yl)-3-(naphthalen-2-yl)propanoate **(4n)**: According to the general reaction procedure **II** 6-bromo-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.301 mmol, 1.0 *equiv*) and (*E*)-3-(naphthalen-2-yl)acrylaldehyde (82 mg, 0.451 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4n** (105 mg, 76%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 123-125 °C; *d.r.* = 12:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.77-7.75 (m, 1H), 7.68 (dd, *J* = 6.1, 2.4 Hz, 1H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.43-7.41 (m, 2H), 7.27-7.24 (m, 2H), 7.21 (d, *J* = 2.3 Hz, 1H), 6.95 (dd, *J* = 8.5, 1.6 Hz, 1H), 6.52 (d, *J* = 8.6 Hz, 1H), 4.57 (s, 2H), 3.95 (d, *J* = 3.2 Hz, 1H), 3.69 (td, *J* = 8.9, 3.2 Hz, 1H), 3.61 (s, 3H), 3.10 (dd, *J* = 16.4, 7.4 Hz, 1H), 2.91 (dd, *J* = 16.4, 8.2 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 161.9, 149.0, 136.0, 133.2, 132.6, 131.4, 131.2, 127.9, 127.6, 127.5, 127.4, 126.7, 126.1, 125.9, 124.7, 120.7, 117.6, 117.3, 54.6, 52.0, 50.2, 40.9, 35.9.

HRMS (EI) calcd for $C_{24}H_{19}{}^{81}BrN_2O_3$, 487.0456 *m/z* $(M+Na)^+$; Found, 487.0451 *m/z*.

FTIR (cm^{-1}): 3359, 3342, 2312, 2178, 1735, 1642, 1412, 1343, 1244, 1098, 854, 783.



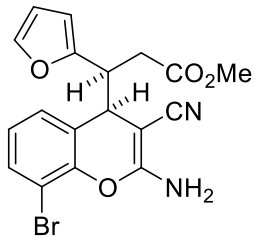
methyl 3-(2-amino-6-bromo-3-cyano-4*H*-chromen-4-yl)-3-(furan-2-yl)propanoate **(4o)**: According to the general reaction procedure **II** 6-bromo-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.301 mmol, 1.0 *equiv*) and (*E*)-3-(furan-2-yl)acrylaldehyde (55 mg, 0.451 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4o**

(106 mg, 88%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 113-115 °C; *d.r.* = 4:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.26-7.20 (m, 1H), 7.18 (d, *J* = 7.1 Hz, 1H), 6.68 (d, *J* = 8.7 Hz, 1H), 6.62 (d, *J* = 1.9 Hz, 1H), 6.19 (s, 1H), 5.79 (d, *J* = 3.2 Hz, 1H), 4.67 (s, 2H), 3.88 (d, *J* = 3.5 Hz, 1H), 3.57 (s, 3H), 3.57- 3.54 (m, 1H), 2.65 (dd, *J* = 16.2, 6.1 Hz, 1H), 2.44 (dd, *J* = 16.1, 9.0 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.2, 161.6, 153.3, 149.1, 141.9, 131.5, 131.4, 123.2, 119.8, 117.7, 117.2, 110.5, 107.6, 55.7, 52.1, 43.3, 39.4, 33.5.

HRMS (EI) calcd for $C_{18}H_{15}{}^{81}BrN_2O_4$, 427.0092 *m/z* $(M+Na)^+$; Found, 427.0084 *m/z*.

FTIR (cm^{-1}): 3178, 2922, 2192, 1704, 1643, 1416, 1221, 1151, 1008, 822, 727.

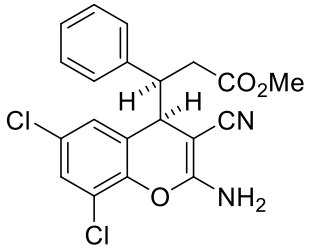


methyl 3-(2-amino-8-bromo-3-cyano-4*H*-chromen-4-yl)-3-(furan-2-yl)propanoate **(4p)**: According to the general reaction procedure **II** 8-bromo-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.301 mmol, 1.0 *equiv*) and (*E*)-3-(furan-2-yl)acrylaldehyde (55 mg, 0.451 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4p** (82 mg, 68%) as Yellow wax (Petroleum ether/ethyl acetate = 3:1); *d.r.* = 5:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.41 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.33 (d, *J* = 1.1 Hz, 1H), 6.90 (t, *J* = 7.9 Hz, 1H), 6.58 (d, *J* = 7.7 Hz, 1H), 6.26-6.25 (m, 1H), 5.84 (d, *J* = 3.2 Hz, 1H), 4.84 (s, 2H), 4.02 (d, *J* = 3.6 Hz, 1H), 3.64 (s, 3H), 3.64- 3.60 (m, 1H), 2.75 (dd, *J* = 16.2, 6.0 Hz, 1H), 2.52 (dd, *J* = 16.2, 9.4 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.2, 161.6, 153.3, 146.9, 141.9, 132.3, 127.9, 125.5, 123.2, 119.6, 110.5, 110.1, 107.5, 56.4, 52.1, 43.4, 40.0, 33.6.

HRMS (EI) calcd for $C_{18}H_{15}{}^{81}BrN_2O_4$, 427.0092 *m/z* $(M+Na)^+$; Found, 427.0094 *m/z*.

FTIR (cm^{-1}): 3342, 3159, 2893, 2184, 1723, 1635, 1496, 1219, 1168, 1046, 872, 748.

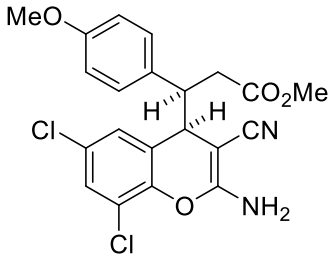


methyl 3-(2-amino-6,8-dichloro-3-cyano-4*H*-chromen-4-yl)-3-phenylpropanoate **(4q)**: According to the general reaction procedure **II** 6,8-dichloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.313 mmol, 1.0 *equiv*) and (*E*)-cinnamaldehyde (62 mg, 0.470 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4q** (88 mg, 70%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 115-117 ˚C; *d.r.* = 6:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.19-7.10 (m, 4H), 6.87 (d, *J* = 2.0 Hz, 1H), 6.74 (d, *J* = 7.0 Hz, 2H), 4.71 (s, 2H), 3.82 (d, *J* = 3.3 Hz, 1H), 3.57 (s, 3H), 3.42 (td, *J* = 7.7, 3.4 Hz, 1H), 2.95 (dd, *J* = 16.6, 7.8 Hz, 1H), 2.71 (dd, *J* = 16.6, 7.8 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.5, 161.6, 144.8, 138.0, 129.6, 128.7, 128.4, 128.1, 127.6, 126.9, 125.8, 122.1, 120.0, 54.8, 52.0, 50.0, 41.3, 35.5.

HRMS (EI) calcd for $C_{20}H_{16}Cl_2N_2O_3$, 425.0436 *m/z* $(M+Na)^+$; Found, 425.0436 *m/z*.

FTIR (cm^{-1}): 3371, 2392, 2142, 1703, 1640, 1435, 1269, 1207, 872, 823, 746, 699.



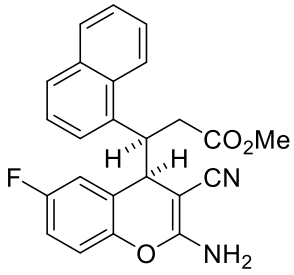
methyl 3-(2-amino-6,8-dichloro-3-cyano-4*H*-chromen-4-yl)-3-(4-methoxyphenyl)propanoate **(4r)**: According to the general reaction procedure **II** 6,8-dichloro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.313 mmol, 1.0 *equiv*) and (*E*)-3-(4-methoxyphenyl)acrylaldehyde (76 mg, 0.470 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room

temperature to obtain **4r** (99 mg, 73%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 121-123 °C; *d.r.* = 10:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 7.19-7.17 (m, 1H), 6.90 (d, *J* = 2.0 Hz, 1H), 6.65 (m, 4H), 4.67 (s, 2H), 3.79 (d, *J* = 3.0 Hz, 1H), 3.69 (s, 3H), 3.57 (s, 3H), 3.56 (td, *J* = 7.8, 3.2 Hz, 1H), 2.92 (dd, *J* = 16.5, 7.8 Hz, 1H), 2.67 (dd, *J* = 16.4, 7.9 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 161.6, 159.0, 144.8, 129.9, 129.6, 129.4, 128.7, 126.9, 126.1, 122.1, 120.1, 113.5, 55.4, 54.8, 52.0, 49.4, 41.4, 35.9.

HRMS (EI) calcd for $C_{21}H_{18}Cl_2N_2O_4$, 455.0541 *m/z* $(M+Na)^+$; Found, 455.0432 *m/z*.

FTIR (cm^{-1}): 3357, 2373, 2192, 1712, 1673, 1412, 1253, 883, 809, 763, 6



methyl 3-(2-amino-3-cyano-6-fluoro-4*H*-chromen-4-yl)-3-(naphthalen-1-yl)propanoate **(4s)**: According to the general reaction procedure **II** 6-fluoro-2-imino-2*H*-chromene-3-carbonitrile (75 mg, 0.398 mmol, 1.0 *equiv*) and (*E*)-3-(naphthalen-1-yl)acrylaldehyde (108 mg, 0.597 mmol, 1.5 *equiv*) in CH_3CN:MeOH (20:1) (0.15 M) was stirred overnight at room temperature to obtain **4s** (112 mg, 70%) as yellow solid (Petroleum ether/ethyl acetate = 3:1); m.p. = 129-131 °C; *d.r.* = 8:1;

^{1}H-NMR ($CDCl_3$, 400 MHz**):** δ 8.08 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.78 (d, *J* = 8.2 Hz, 1H), 7.53-7.44 (m, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.2 Hz, 1H), 6.80 (td, *J* = 9.0, 2.9 Hz, 1H), 6.72 (dd, *J* = 8.9, 4.7 Hz, 1H), 5.87 (d, *J* = 8.2 Hz, 1H), 4.85 (s, 2H), 4.55 (m, 1H), 3.97 (d, *J* = 3.1 Hz, 1H), 3.55 (s, 3H), 2.92 (dd, *J* = 16.0, 6.2 Hz, 1H), 2.63 (dd, *J* = 16.0, 9.3 Hz, 1H); **^{13}C-NMR (**$CDCl_3$, 100 MHz**):** δ 172.6, 161.9, 158.5 (J_{C-F} = 242.2 Hz), 146.3 (J_{C-F} = 2.2 Hz), 135.2, 134.0, 131.5, 129.1, 128.2, 126.5, 125.8, 124.8, 122.7, 122.2 (J_{C-F} = 7.9 Hz),

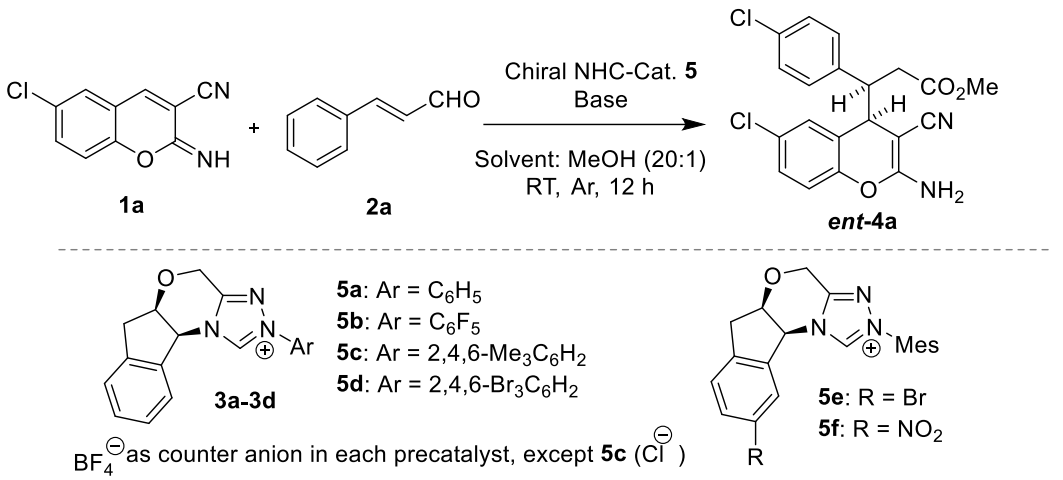
120.1, 117.1 ($J_{C\text{-}F}$ = 8.5 Hz), 115.9 ($J_{C\text{-}F}$ = 24.0 Hz), 115.2 ($J_{C\text{-}F}$ = 23.6 Hz), 56.5, 52.0, 43.1, 40.4, 34.4.

HRMS (EI) calcd for $C_{24}H_{19}FN_2O_3$, 425.1277 *m/z* $(M+Na)^+$; Found, 425.1274 *m/z*.

FTIR (cm^{-1}): 3340, 2187, 1721, 1648, 1488, 1402, 1189, 1010, 822, 778.

Optimization Study: Initial study to synthesize enantioenriched 3-cyano-4*H*-Chromenes

Table **2** Optimization of reaction conditions

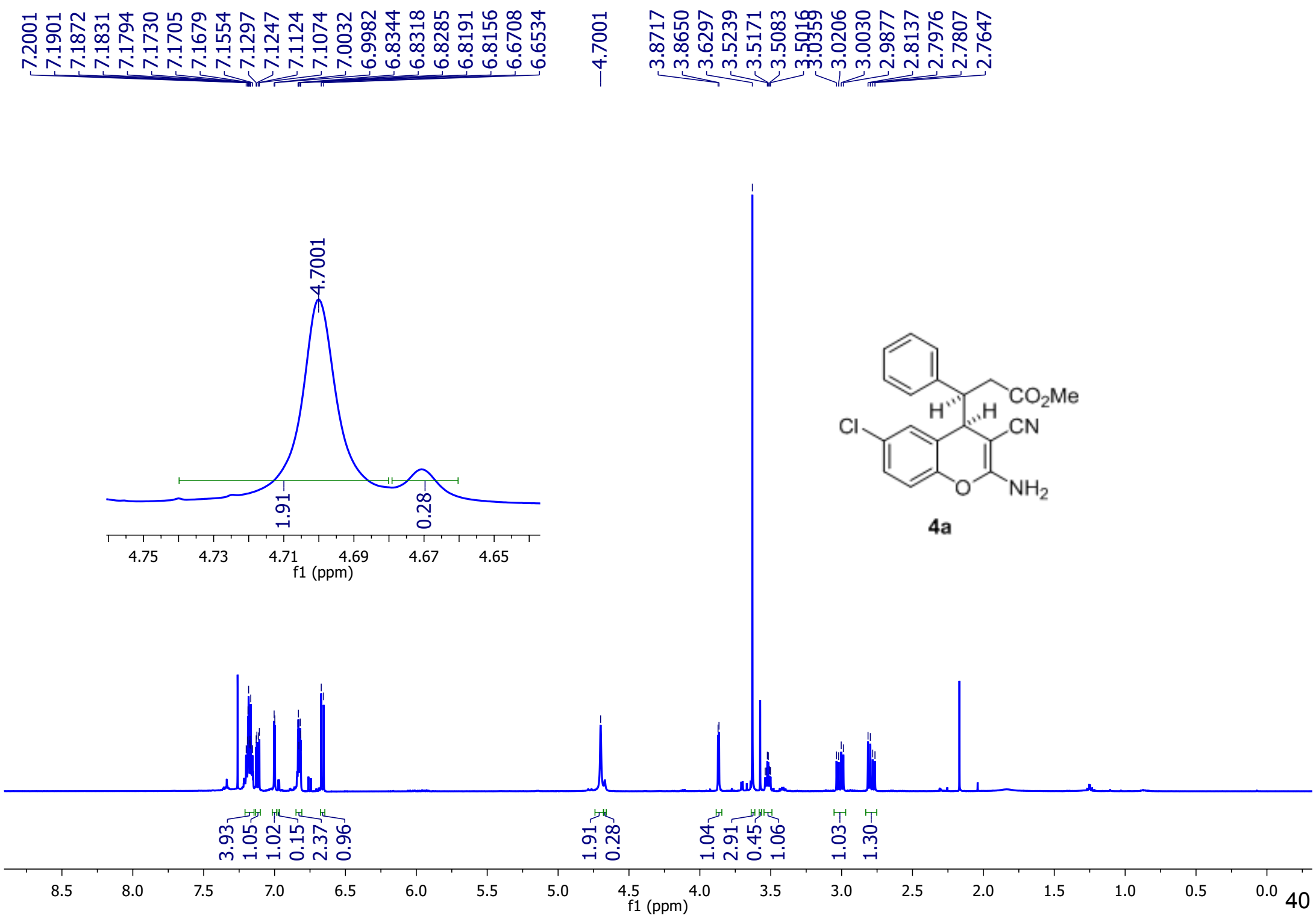


Entry	NHC-Cat. **5**	Base	Solvent	Yield (%)[b] of **4a**	dr[c] of *ent*-**4a**	ee[d] (%)
1	**5a-5b**	$KHCO_3$	Toluene	<10	ND	ND
2	**5c**	$KHCO_3$	Toluene	56	1:1.1	38/35
3	**5d**	$KHCO_3$	Toluene	11	1:1	41/34
4	**5e**	$KHCO_3$	Toluene	23	1:1	37/32
5	**5f**	$KHCO_3$	Toluene	NR	-	-
6	**5c**	Et_3N/DBU	Toluene	<10	1:1	ND
7	**5c**	NaOAC	Toluene	52	1:1.2	51/55
8	**5c**	$PhCO_2K$	Toluene	14	1:1	ND
9	**5c**	K_3PO_4	Toluene	59	1:1	34/31
10	**5c**	NaOAC	DMF	45	4:1	16/7
11	**5c**	NaOAC	Acetonitrile	67	7.5:1	14/0
12	**5c**	K_3PO_4	1,4-Dioxane	42	1:1	37/38

[a]Unless indicated otherwise, the reaction of **1a** (75 mg, 0.366 mmol, 1.0 equiv) and **2a** (72 mg, 68.5 µL, 0.550 mmol, 1.5 equiv) was carried out in mixed solvent 2.4 mL (0.15 M) at room temperature in the presence of chiral NHC cat. **5** (20 mol%) and base (30 mol%) for 12

h. [b] Isolated yield. [c] dr value is determined from the ^{1}H-NMR of the crude reaction mixture. [d] ee was determined by HPLC using chiral stationary phase.

After successful development of diastereoselective method, we envisioned the same reaction would give enantioenriched homoenolate addition product *ent*-**4** in the presence of chiral NHC catalyst. Initially, the 2*H*-chromene substrate **1a** was reacted with cinnamaldehyde **2a** in the presence of chiral triazolium NHC catalysts **5a**-**5f**. After short screening of solvents and bases it was found that the mesityl-containing indanolamine-derived chiral triazolium carbene precatalyst **3c** in and NaOAc as base in toluene afforded the homoenolate addition product *ent*-**4a** in moderate yield (52%) and enantioselectivity (51/55%; entry 7). However, the diastereoselectivity was poor (dr = 1:1.2). While, In DMF *ent*-**4a** was formed in low yield (45%) and *ee* (16/7%) with similar diastereoselectivity as *rac*-**4a** (4:1) (Entry 10). In acetonitrile solvent, the 4*H*-chromene product *ent*-**4a** was formed in good yield (67%) and with good dr (~7.5:1) as similar as racemic version, but, the enantioselectivity of the major diastereoisomer *ent*-**4a** was very low (ee = 14%) (entry 11). In order to enhance the yield and selectivity of the desired homoenolate addition product *ent*-**4**, the further study of a suitable chiral NHCs, solvents and bases is still much needed for this reaction.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7.0032
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6.8318
6.8285
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4.65
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H
H
Cl
CN
O
NH2
4a
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0.96
1.91
0.28
1.04
2.91
0.45
1.06
1.03
1.30
8.5
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7.0
6.5
6.0
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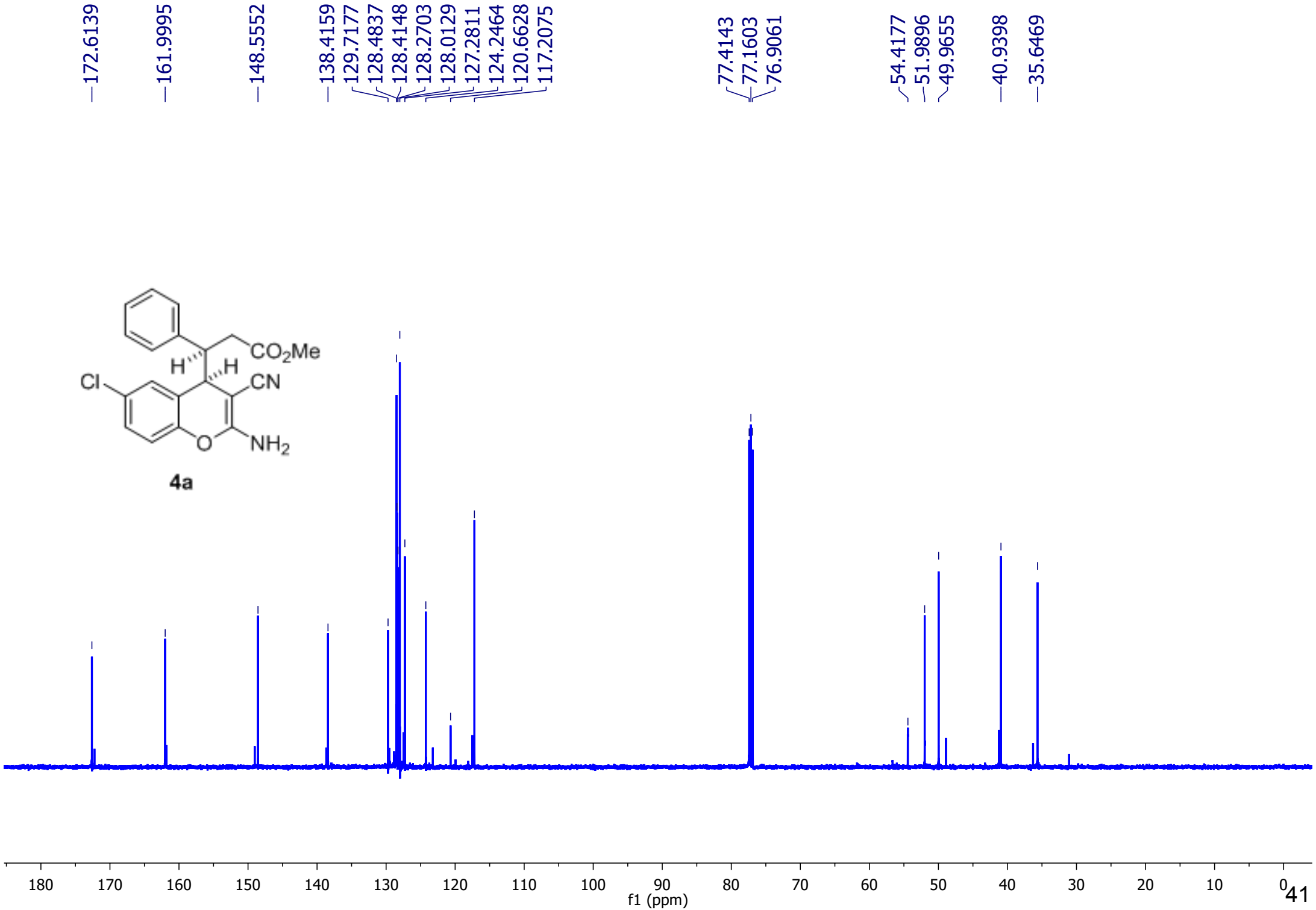
f1 (ppm)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O
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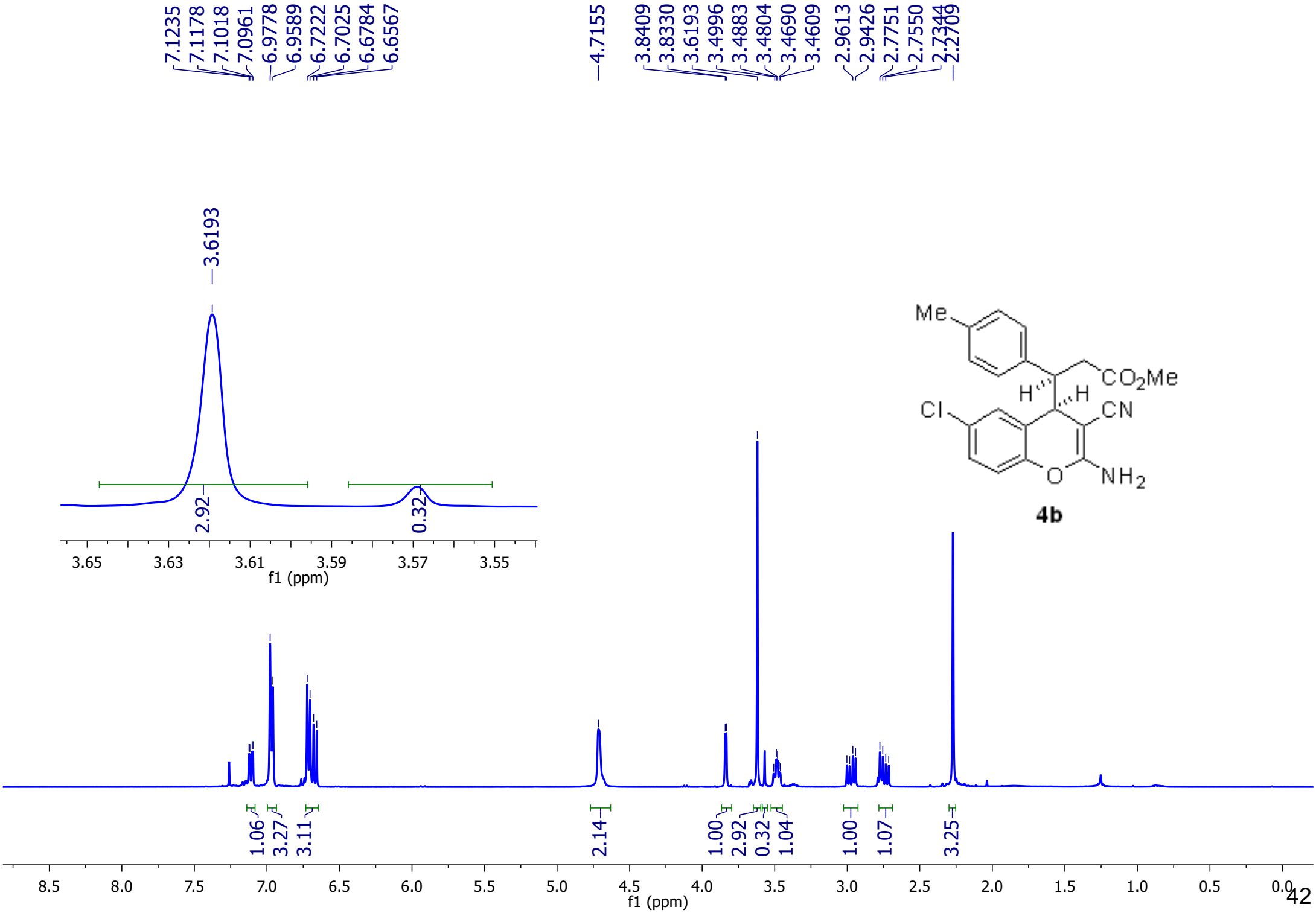
f1 (ppm)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H
H
Cl
CN
O
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1.00
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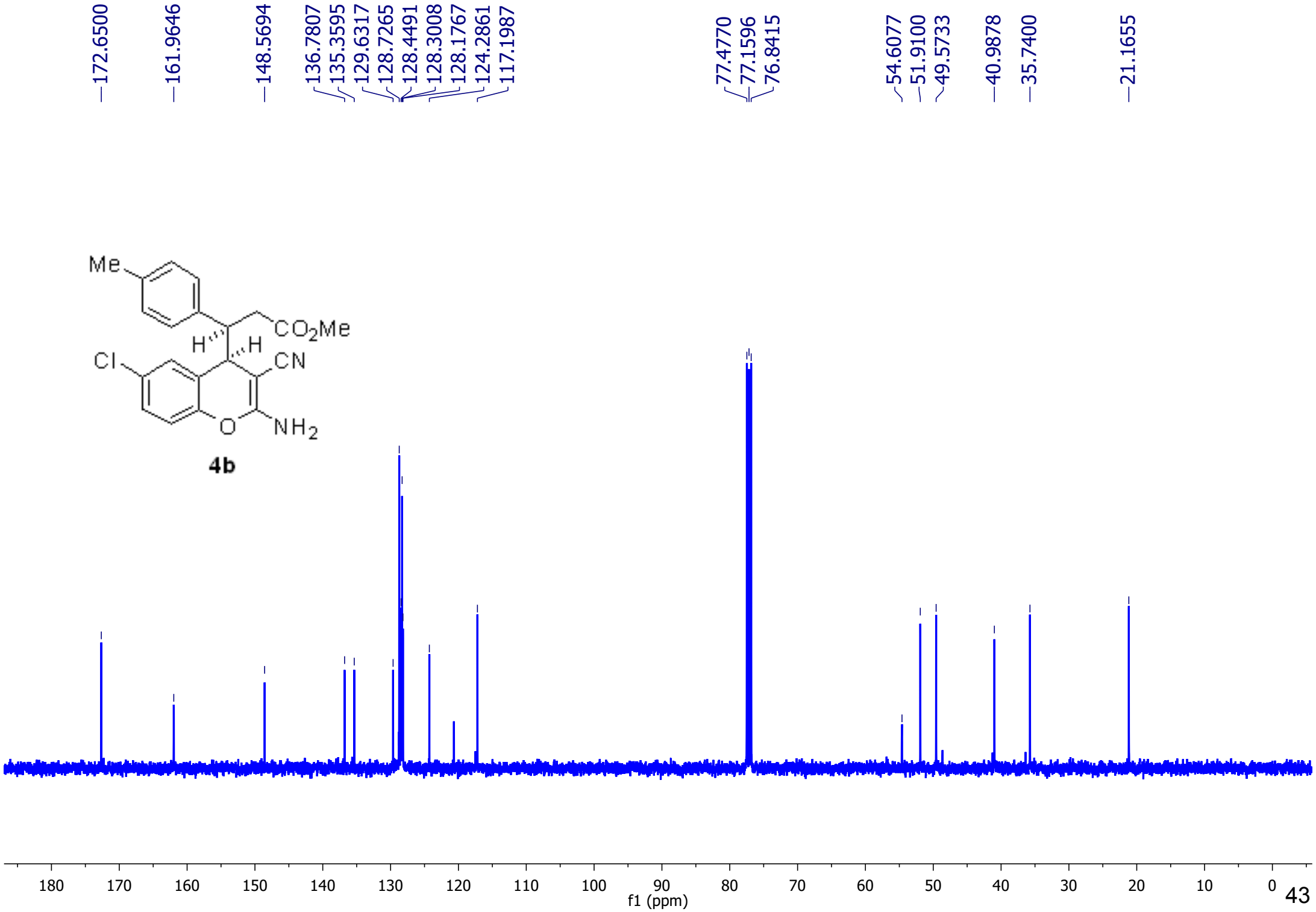
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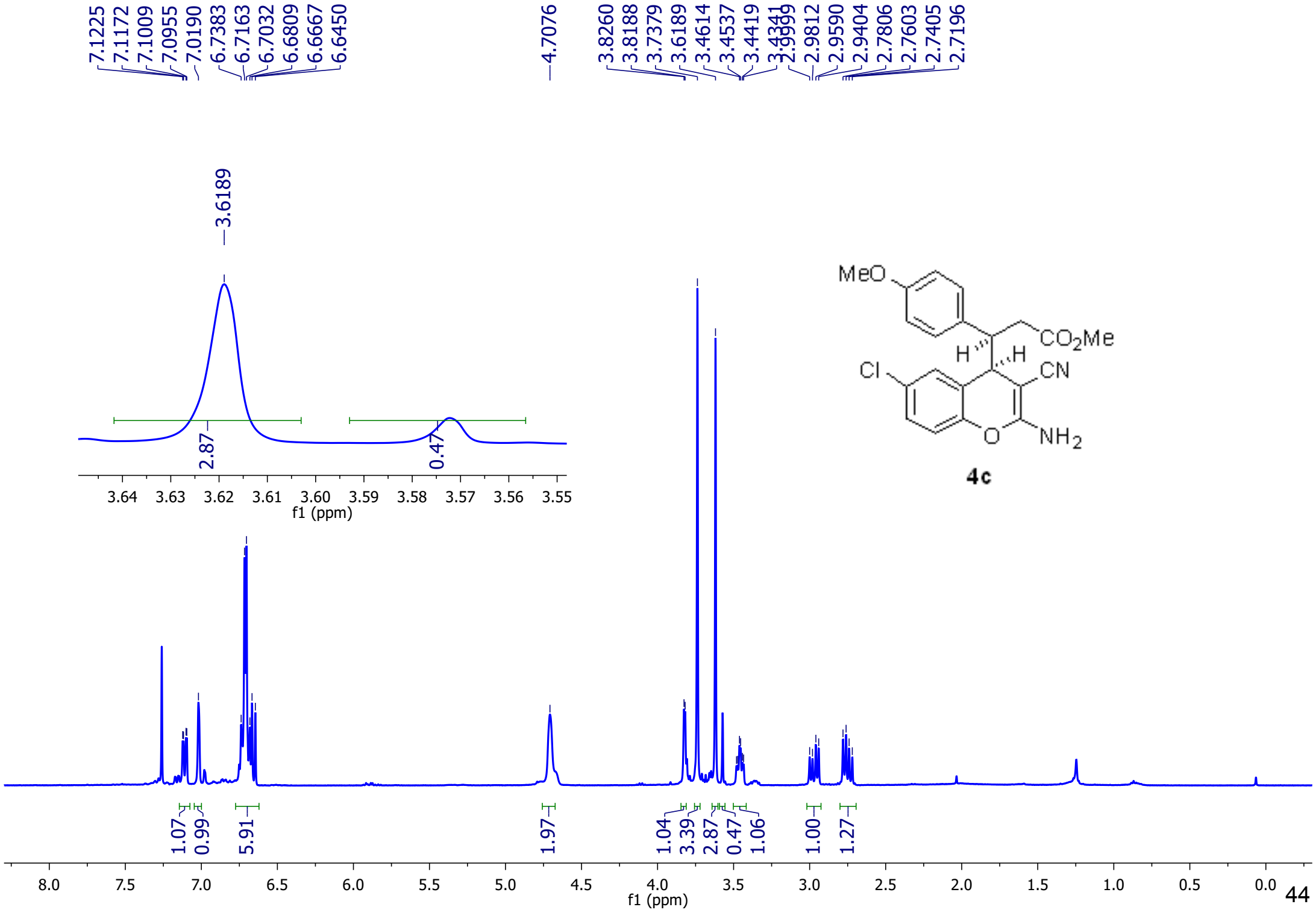
f1 (ppm)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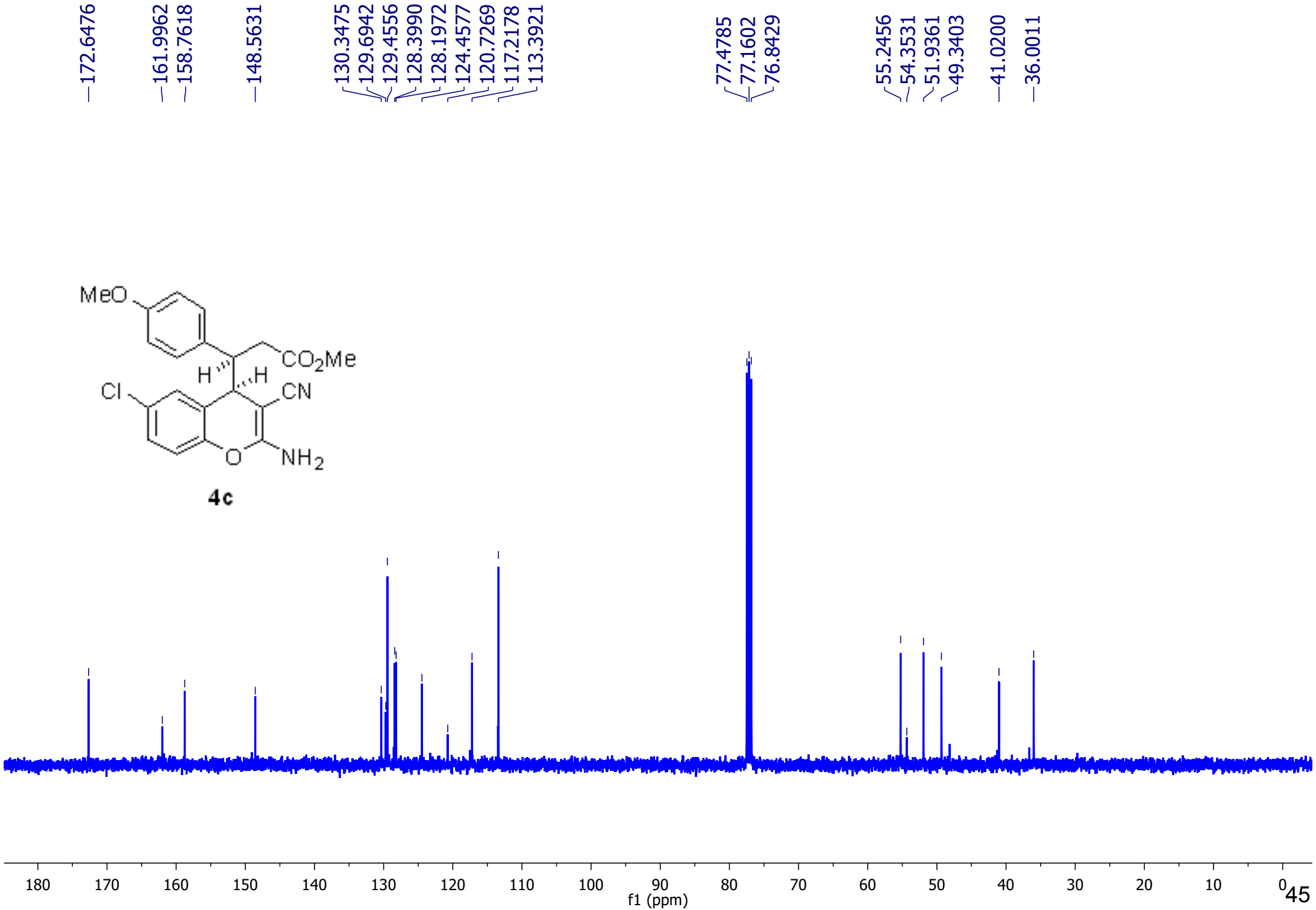
f1 (ppm)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O
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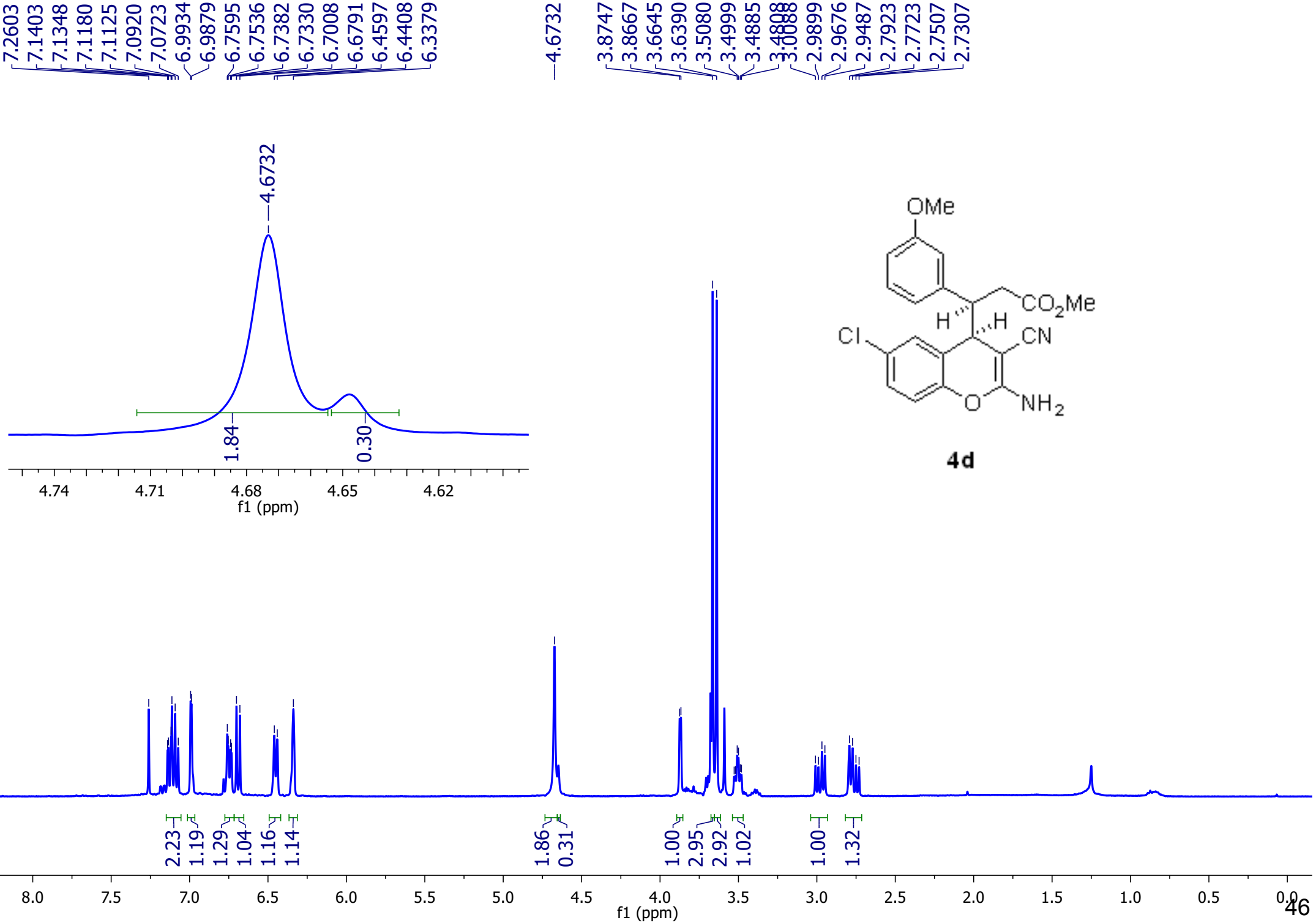
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f1 (ppm)

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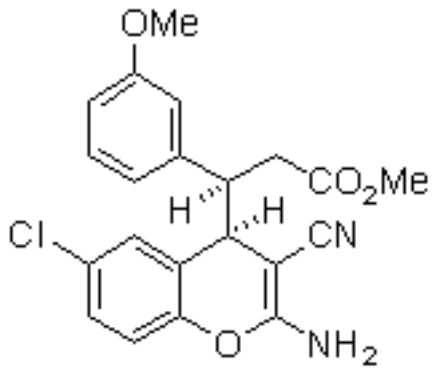

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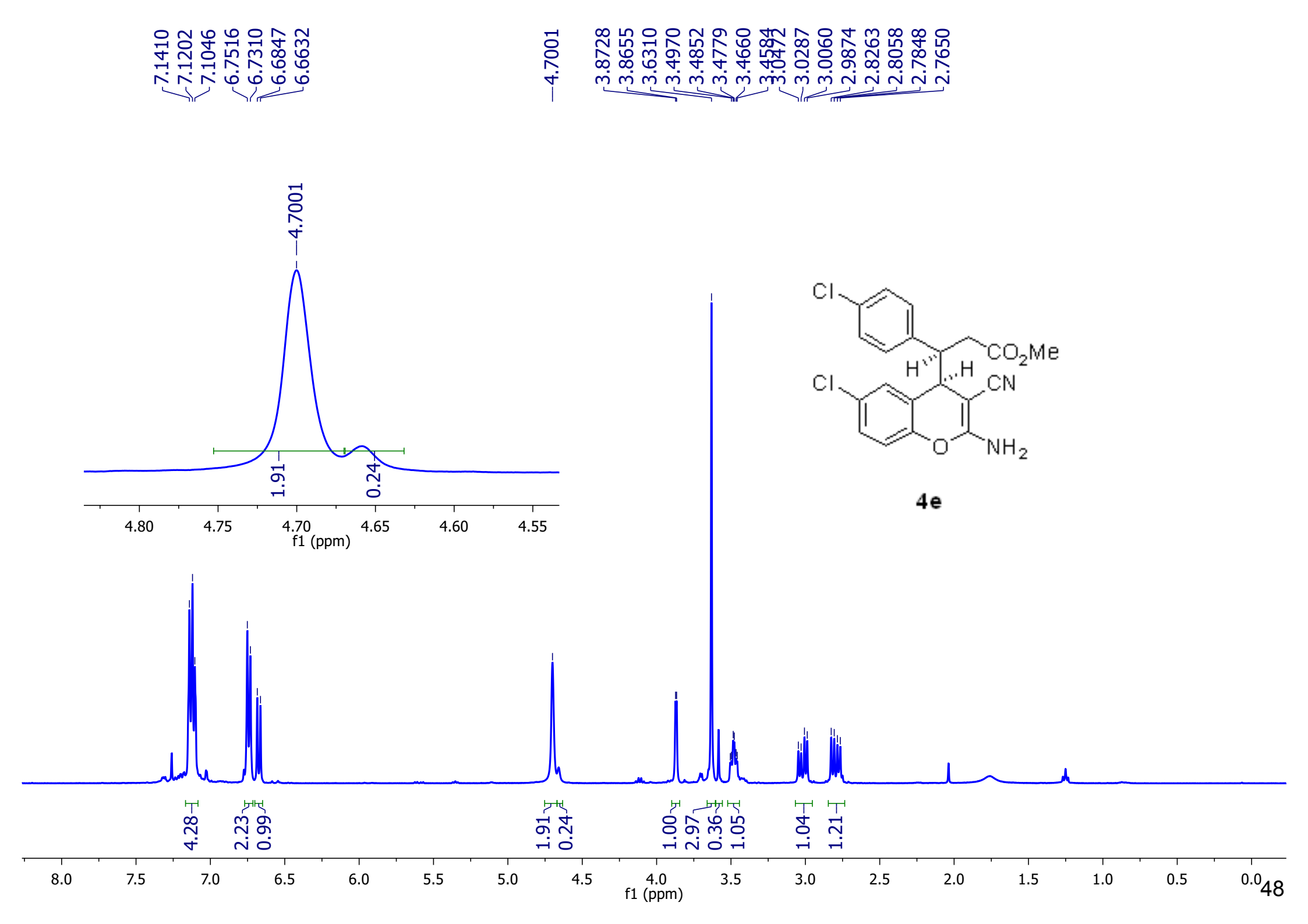
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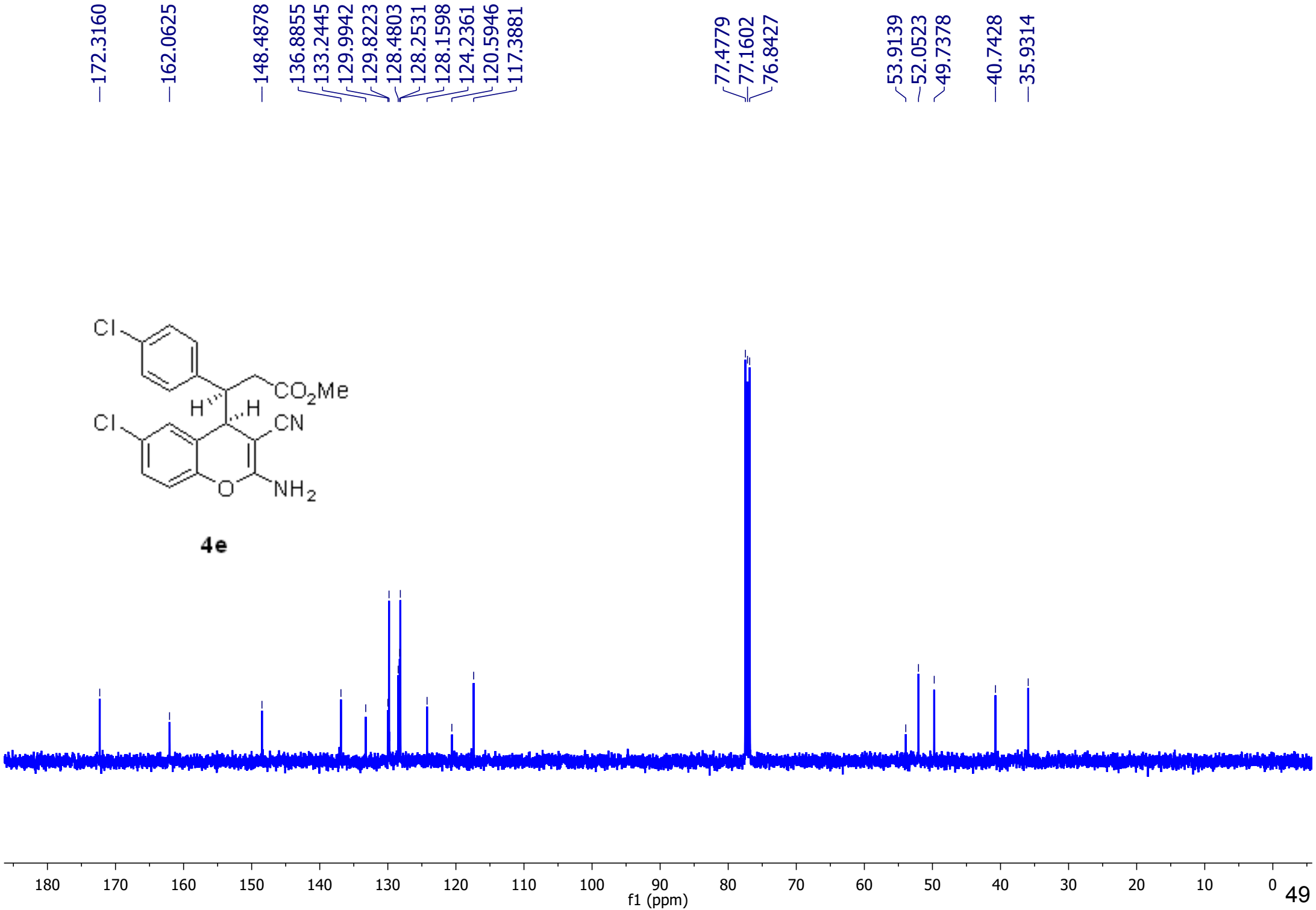
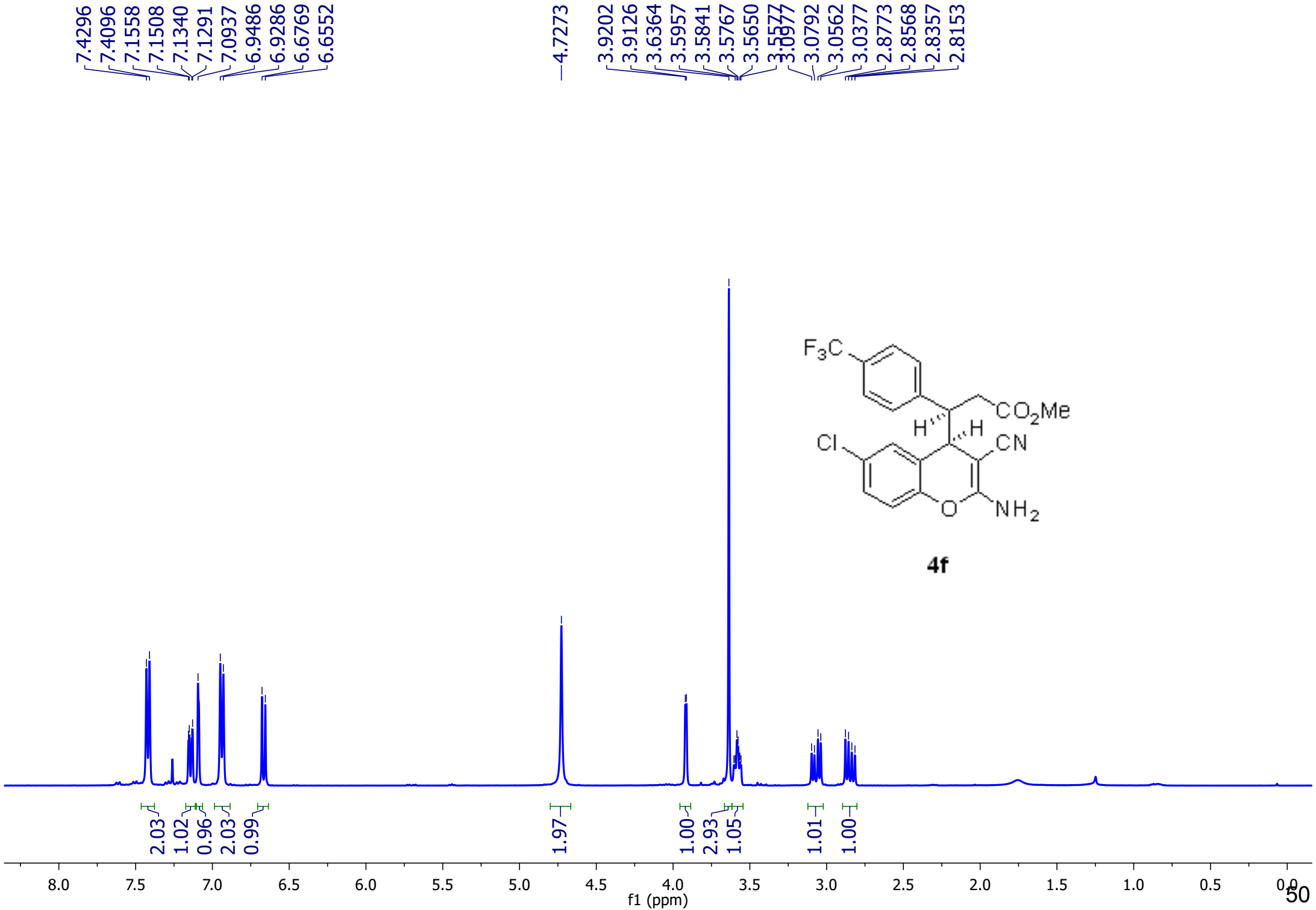
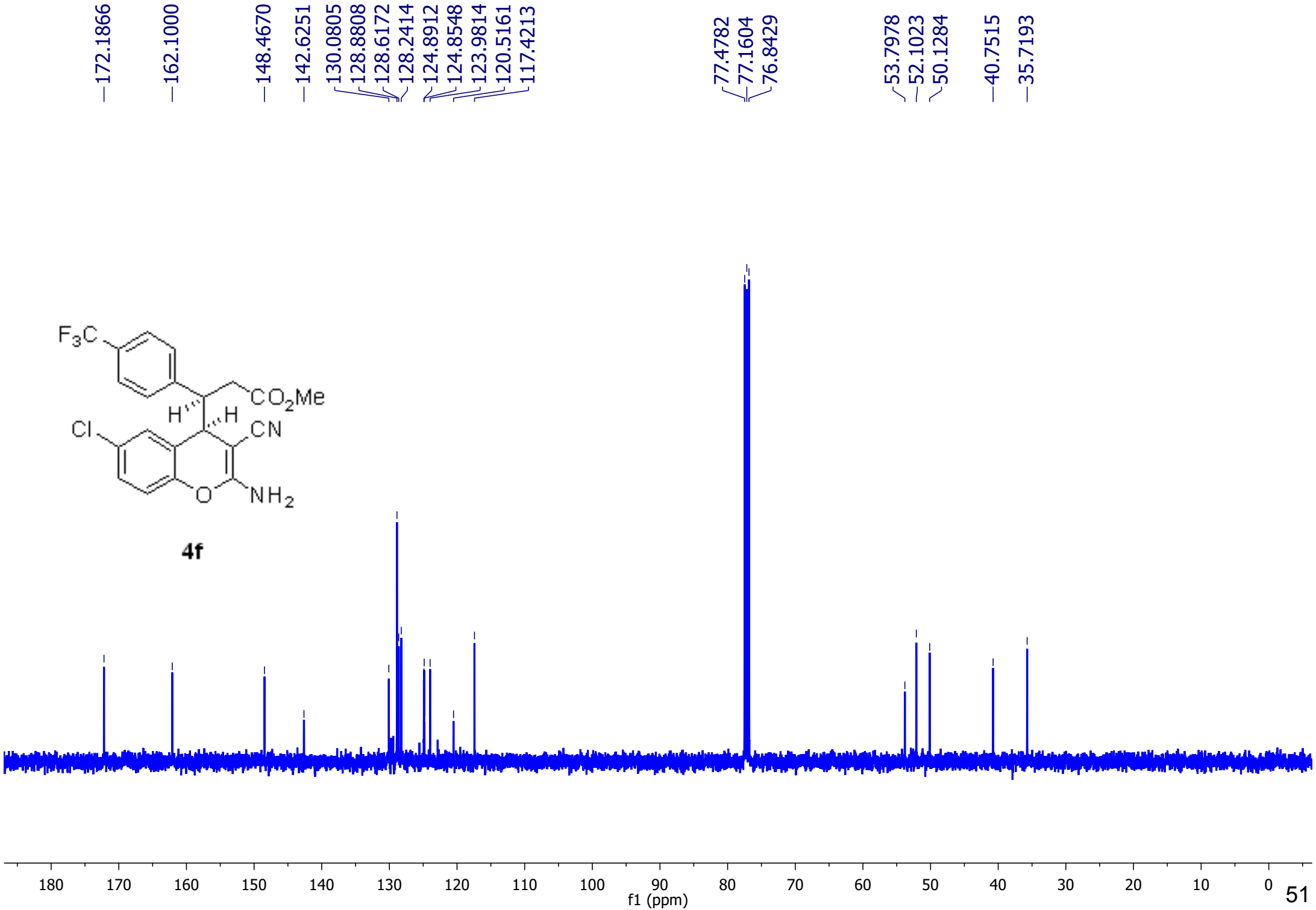
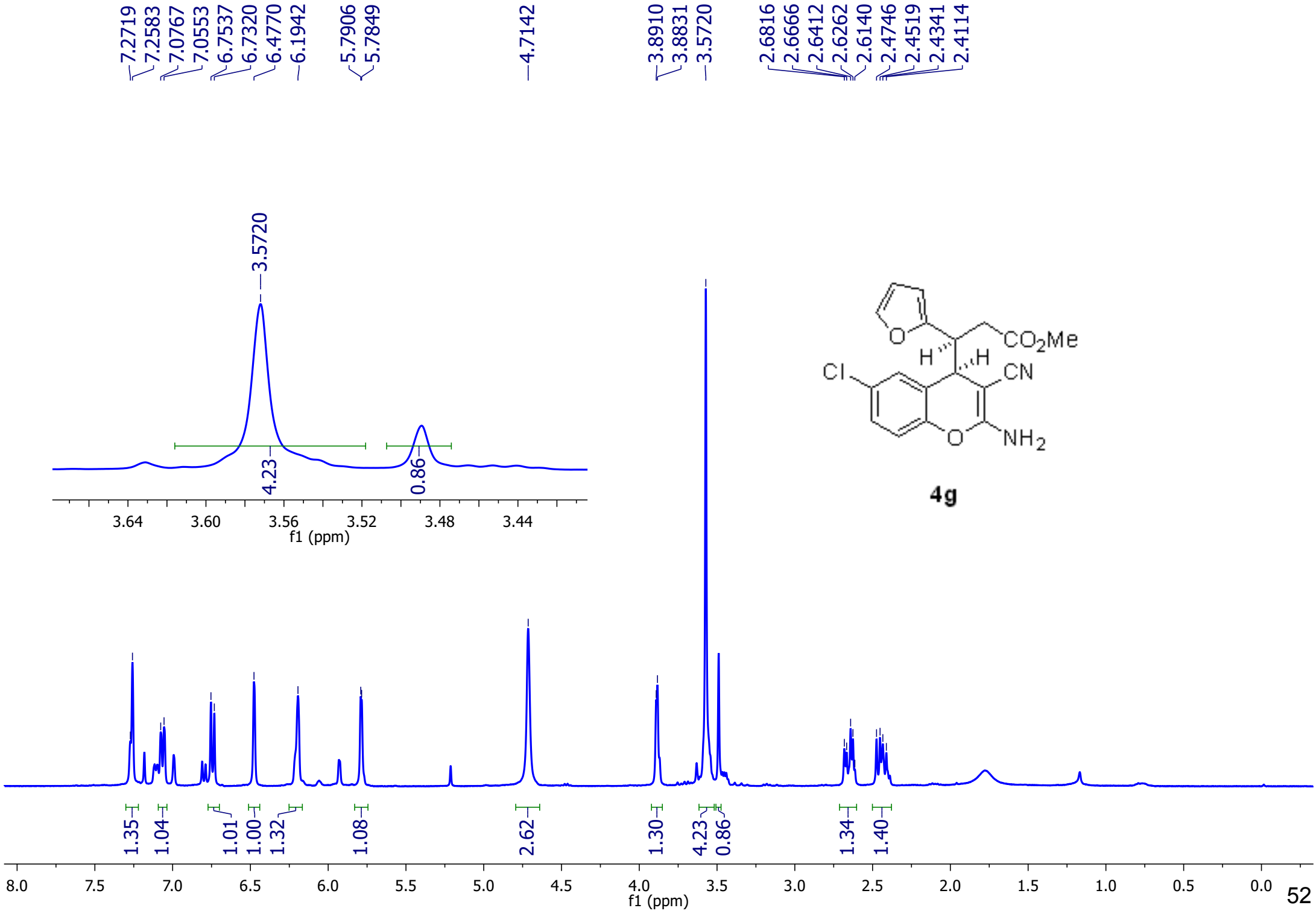
6.7310
6.6847
6.6632
4.7001
3.8728
3.8655
3.6310
3.4970
3.4852
3.4779
3.4660
3.0287
3.0060
2.9874
2.8263
2.8058
2.7848
2.7650
4.7001
1.91
0.24
4.80
4.75
4.70
4.65
4.60
4.55
f1 (ppm)
Cl
CO2Me
H
H
Cl
CN
O
NH2
4e
4.28
2.23
0.99
1.91
0.24
1.00
2.97
0.36
1.05
1.04
1.21
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

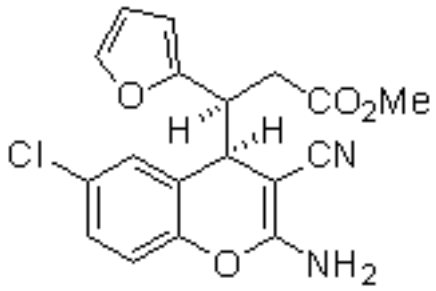

172.3160
162.0625
148.4878
136.8855
133.2445
129.9942
129.8223
128.4803
128.2531
128.1598
124.2361
120.5946
117.3881
77.4779
77.1602
76.8427
53.9139
52.0523
49.7378
40.7428
35.9314
Cl
CO2Me
H
H
Cl
CN
O
NH2
4e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.4296
7.4096
7.1558
7.1508
7.1340
7.1291
7.0937
6.9486
6.9286
6.6769
6.6552
4.7273
3.9202
3.9126
3.6364
3.5957
3.5841
3.5767
3.5650
3.0977
3.0792
3.0562
3.0377
2.8773
2.8568
2.8357
2.8153
F3C
CO2Me
H
H
Cl
CN
O
NH2
4f
2.03
1.02
0.96
2.03
0.99
1.97
1.00
2.93
1.05
1.01
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

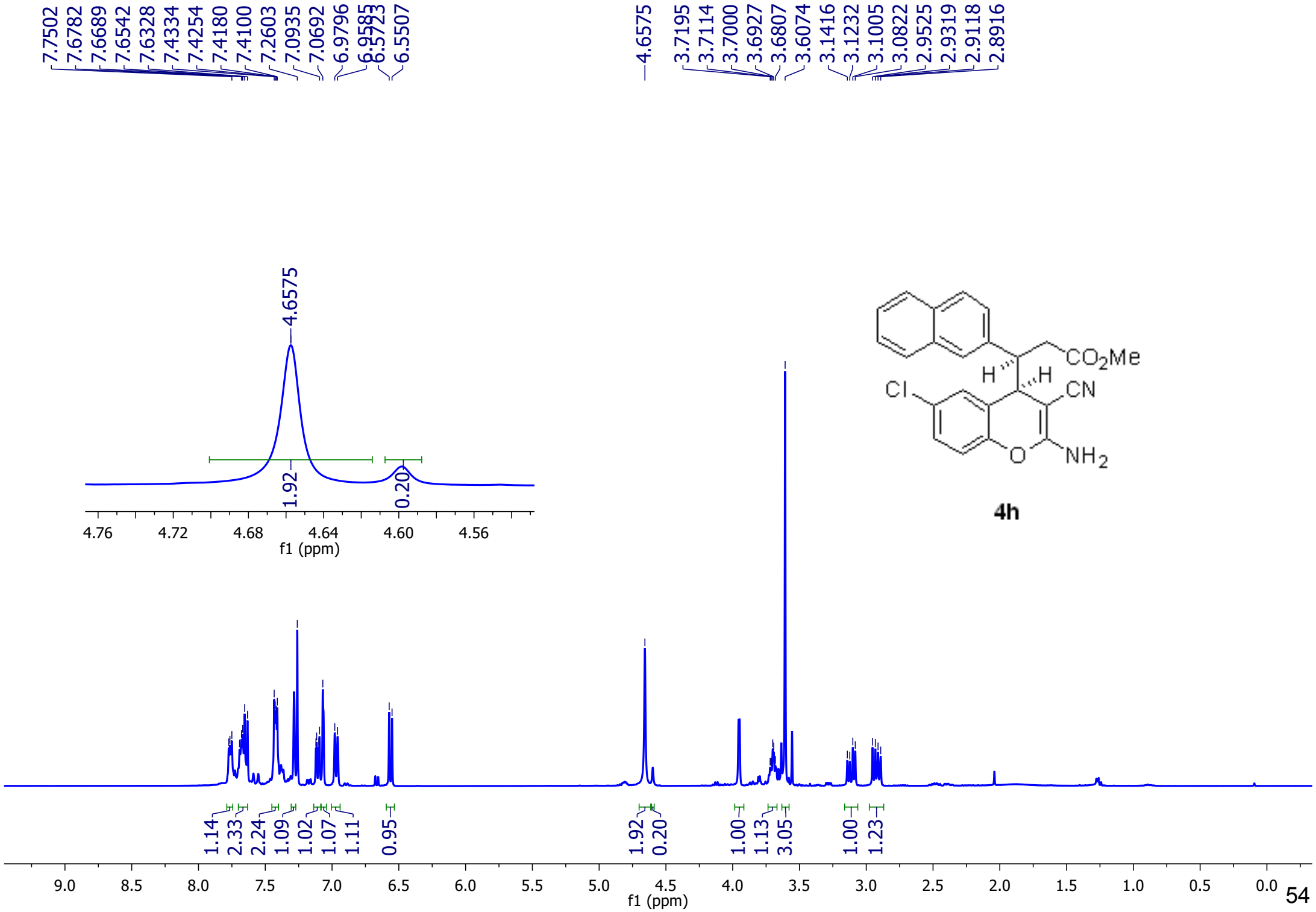

172.1866
162.1000
148.4670
142.6251
130.0805
128.8808
128.6172
128.2414
124.8912
124.8548
123.9814
120.5161
117.4213
77.4782
77.1604
76.8429
53.7978
52.1023
50.1284
40.7515
35.7193
F3C
CO2Me
H
H
Cl
CN
O
NH2
4f
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

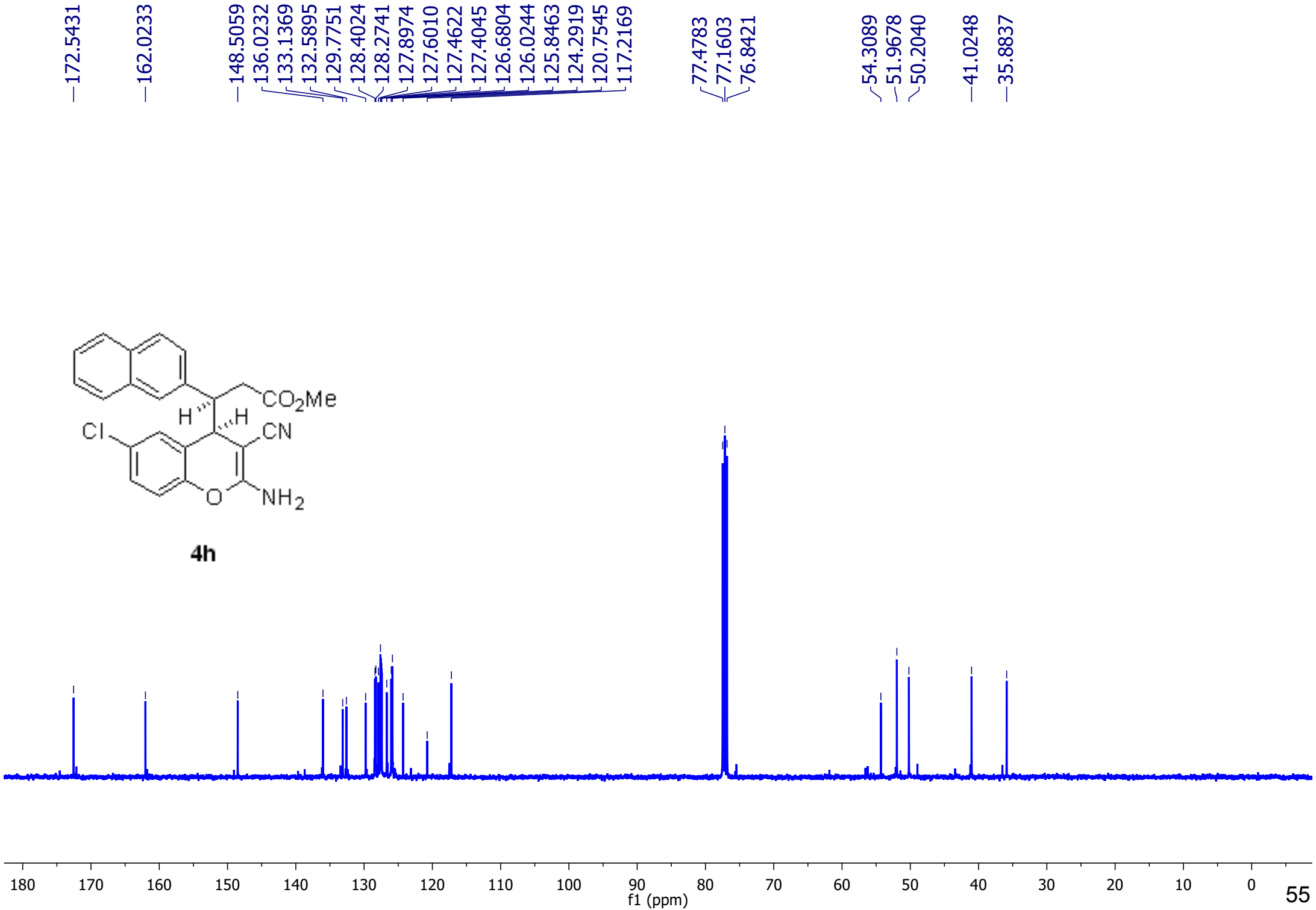

7.2719
7.2583
7.0767
7.0553
6.7537
6.7320
6.4770
6.1942
5.7906
5.7849
4.7142
3.8910
3.8831
3.5720
2.6816
2.6666
2.6412
2.6262
2.6140
2.4746
2.4519
2.4341
2.4114
3.5720
4.23
0.86
3.64
3.60
3.56
3.52
3.48
3.44
f1 (ppm)
O
H
H
CO2Me
Cl
CN
O
NH2
4g
1.35
1.04
1.01
1.00
1.32
1.08
2.62
1.30
4.23
0.86
1.34
1.40
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

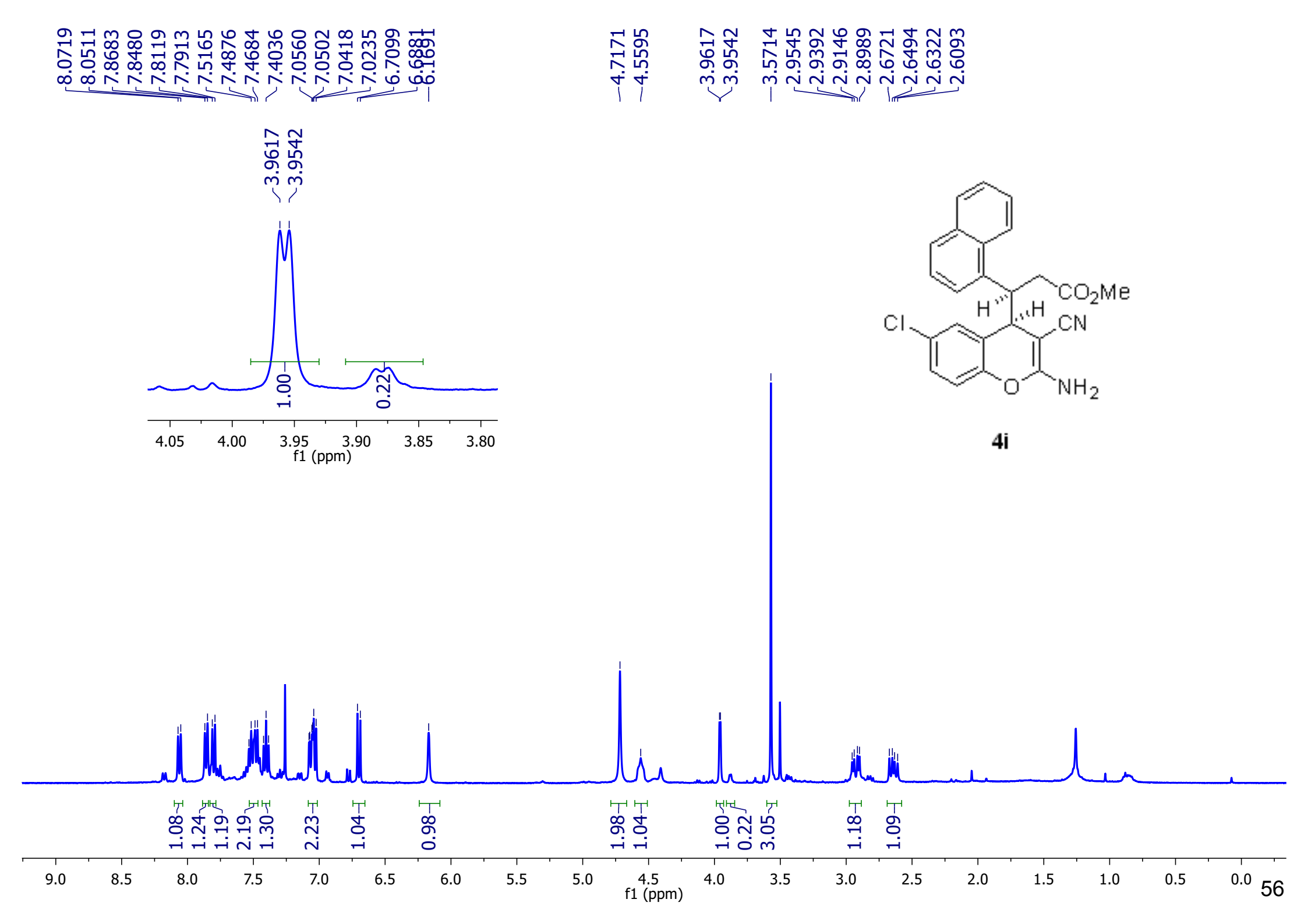
172.2212
161.6660
153.3274
148.5841
141.9160
129.7150
128.5197
128.4563
122.7510
119.8870
117.3223
110.5176
107.5566
77.4785
77.1603
76.8430
55.5849
52.1085
43.2281
39.4415
33.5307

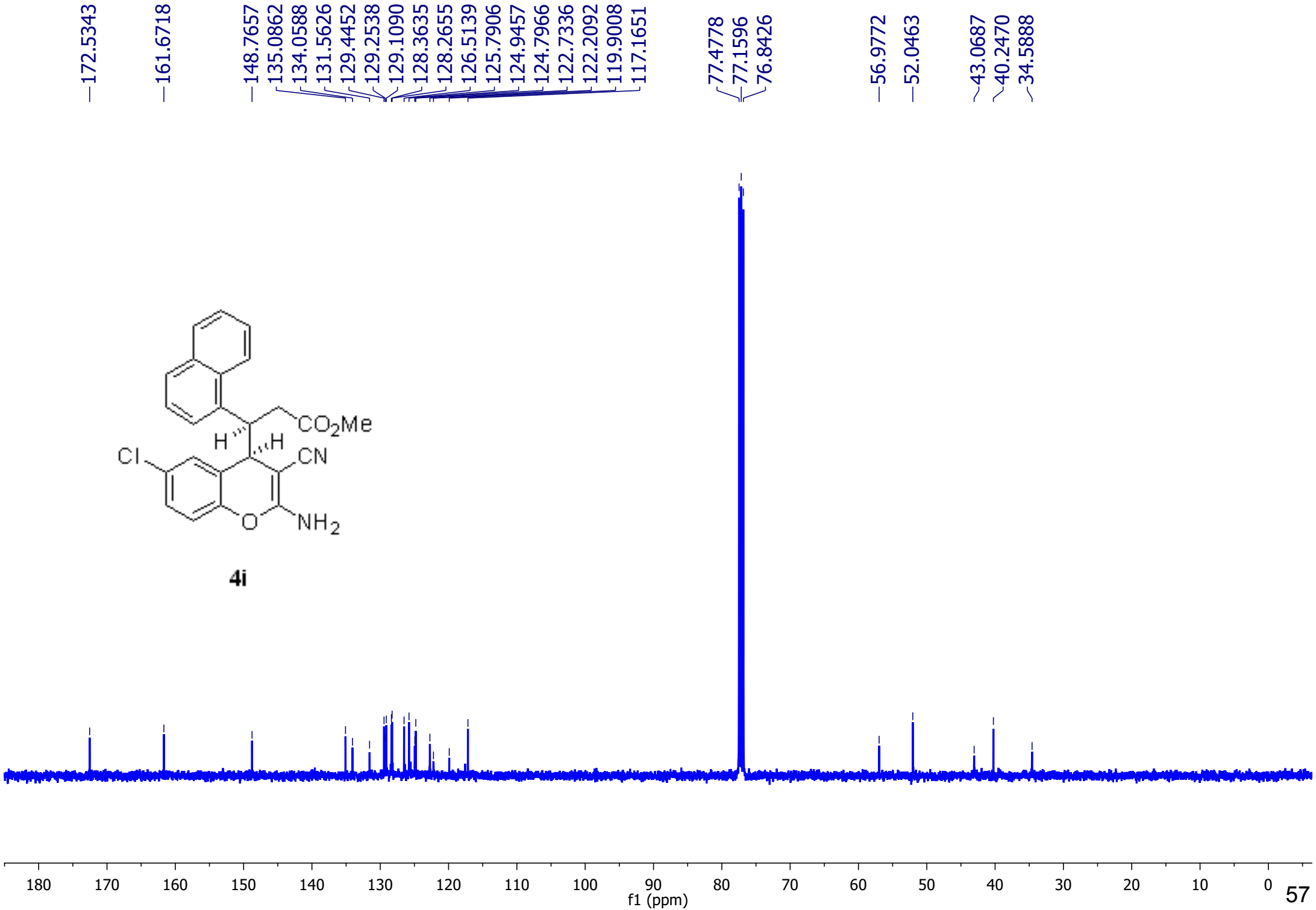


4g


7.7502
7.6782
7.6689
7.6542
7.6328
7.4334
7.4254
7.4180
7.4100
7.2603
7.0935
7.0692
6.9796
6.9585
6.5723
6.5507
4.6575
3.7195
3.7114
3.7000
3.6927
3.6807
3.6074
3.1416
3.1232
3.1005
3.0822
2.9525
2.9319
2.9118
2.8916
4.6575
1.92
0.20
4.76
4.72
4.68
4.64
4.60
4.56
f1 (ppm)
CO2Me
H
H
Cl
CN
O
NH2
4h
1.14
2.33
2.24
1.09
1.02
1.07
1.11
0.95
1.92
0.20
1.00
1.13
3.05
1.00
1.23
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.5431
162.0233
148.5059
136.0232
133.1369
132.5895
129.7751
128.4024
128.2741
127.8974
127.6010
127.4622
127.4045
126.6804
126.0244
125.8463
124.2919
120.7545
117.2169
77.4783
77.1603
76.8421
54.3089
51.9678
50.2040
41.0248
35.8837
CO2Me
H
H
Cl
CN
O
NH2
4h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.0719
8.0511
7.8683
7.8480
7.8119
7.7913
7.5165
7.4876
7.4684
7.4036
7.0560
7.0502
7.0418
7.0235
6.7099
6.6881
6.1891
4.7171
4.5595
3.9617
3.9542
3.5714
2.9545
2.9392
2.9146
2.8989
2.6721
2.6494
2.6322
2.6093
1.08
1.24
1.19
2.19
1.30
2.23
1.04
0.98
1.98
1.04
1.00
0.22
3.05
1.18
1.09
f1 (ppm)
CO2Me
H
H
Cl
CN
O
NH2
4i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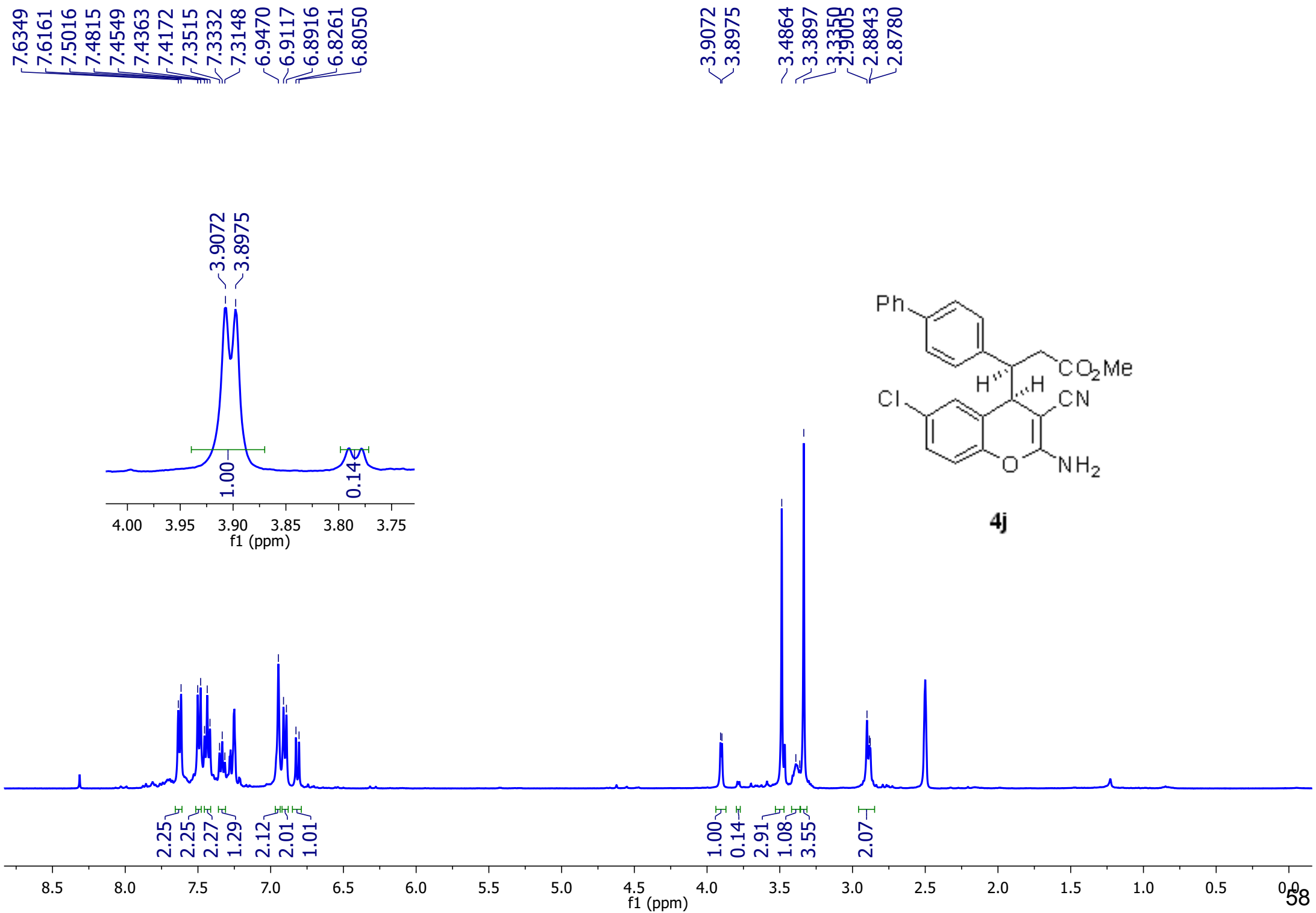
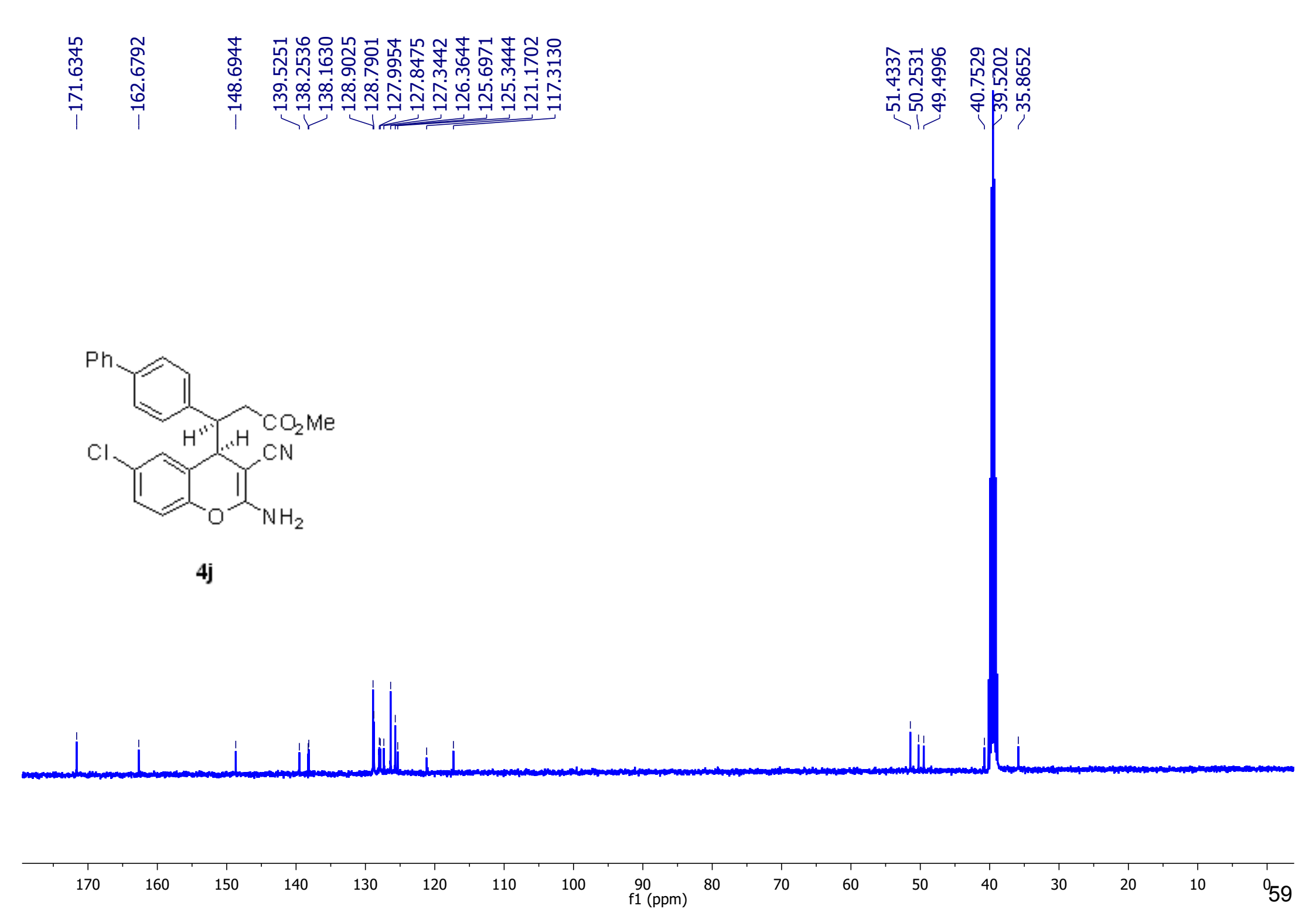
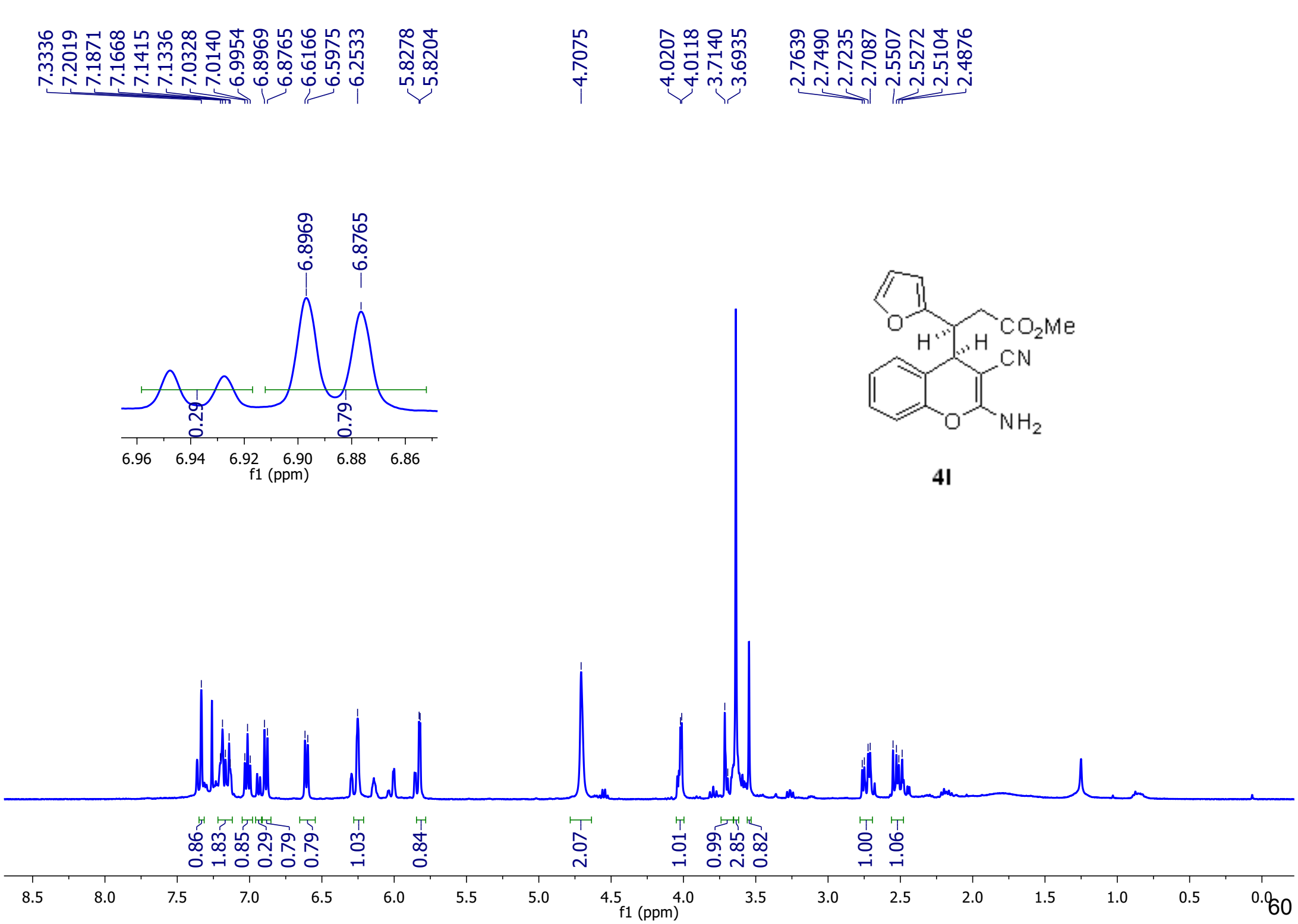
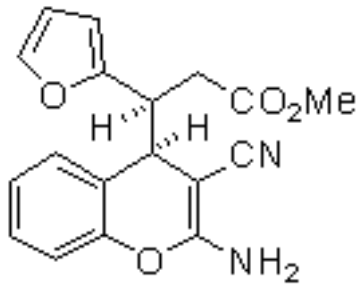
161.6718
148.7657
135.0862
134.0588
131.5626
129.4452
129.2538
129.1090
128.3635
128.2655
126.5139
125.7906
124.9457
124.7966
122.7336
122.2092
119.9008
117.1651
77.4778
77.1596
76.8426
56.9772
52.0463
43.0687
40.2470
34.5888
CO2Me
H
H
CN
Cl
O
NH2
4i
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.6349
7.6161
7.5016
7.4815
7.4549
7.4363
7.4172
7.3515
7.3332
7.3148
6.9470
6.9117
6.8916
6.8261
6.8050
3.9072
3.8975
3.4864
3.3897
3.3350
3.3005
2.8843
2.8780
3.9072
3.8975
1.00
0.14
4.00
3.95
3.90
3.85
3.80
3.75
f1 (ppm)
Ph
CO2Me
H
H
Cl
CN
O
NH2
4j
2.25
2.25
2.27
1.29
2.12
2.01
1.01
1.00
0.14
2.91
1.08
3.55
2.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

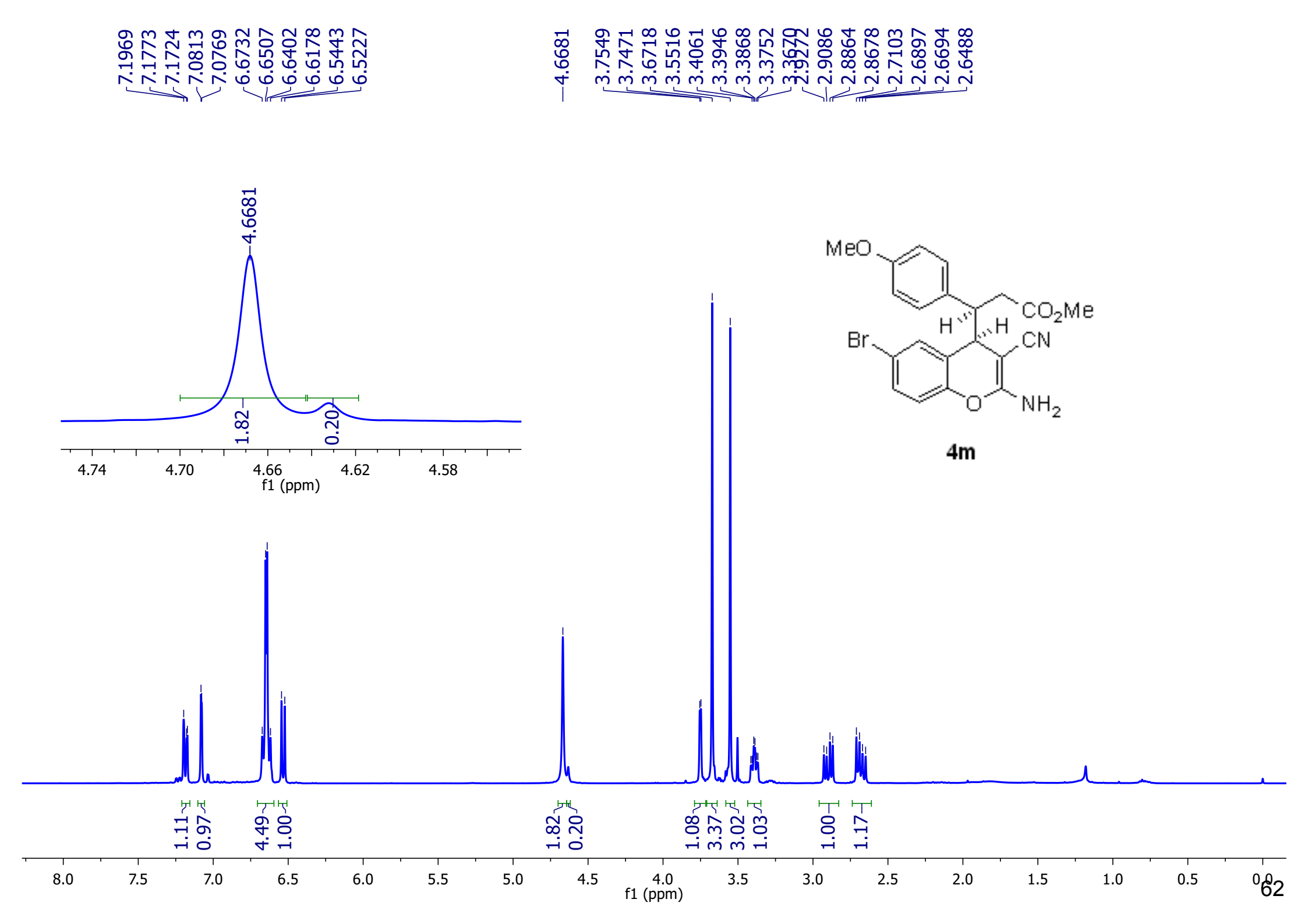

171.6345
162.6792
148.6944
139.5251
138.2536
138.1630
128.9025
128.7901
127.9954
127.8475
127.3442
126.3644
125.6971
125.3444
121.1702
117.3130
51.4337
50.2531
49.4996
40.7529
39.5202
35.8652
Ph
CO2Me
H
H
Cl
CN
O
NH2
4j
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

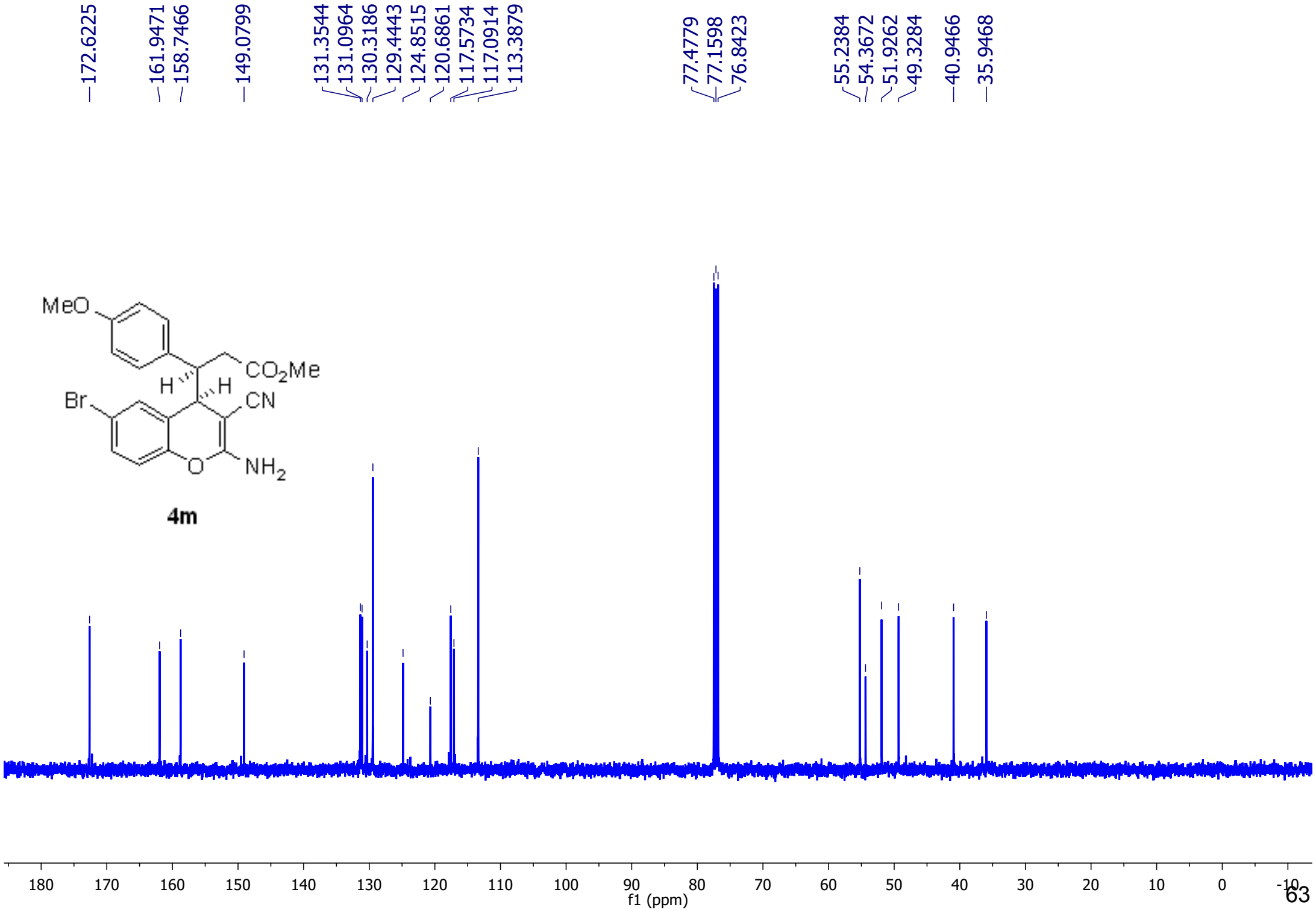

7.3336
7.2019
7.1871
7.1668
7.1415
7.1336
7.0328
7.0140
6.9954
6.8969
6.8765
6.6166
6.5975
6.2533
5.8278
5.8204
4.7075
4.0207
4.0118
3.7140
3.6935
2.7639
2.7490
2.7235
2.7087
2.5507
2.5272
2.5104
2.4876
6.8969
6.8765
0.29
0.79
6.96
6.94
6.92
6.90
6.88
6.86
f1 (ppm)
O
H
H
CO2Me
CN
O
NH2
4l
0.86
1.83
0.85
0.29
0.79
0.79
1.03
0.84
2.07
1.01
0.99
2.85
0.82
1.00
1.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

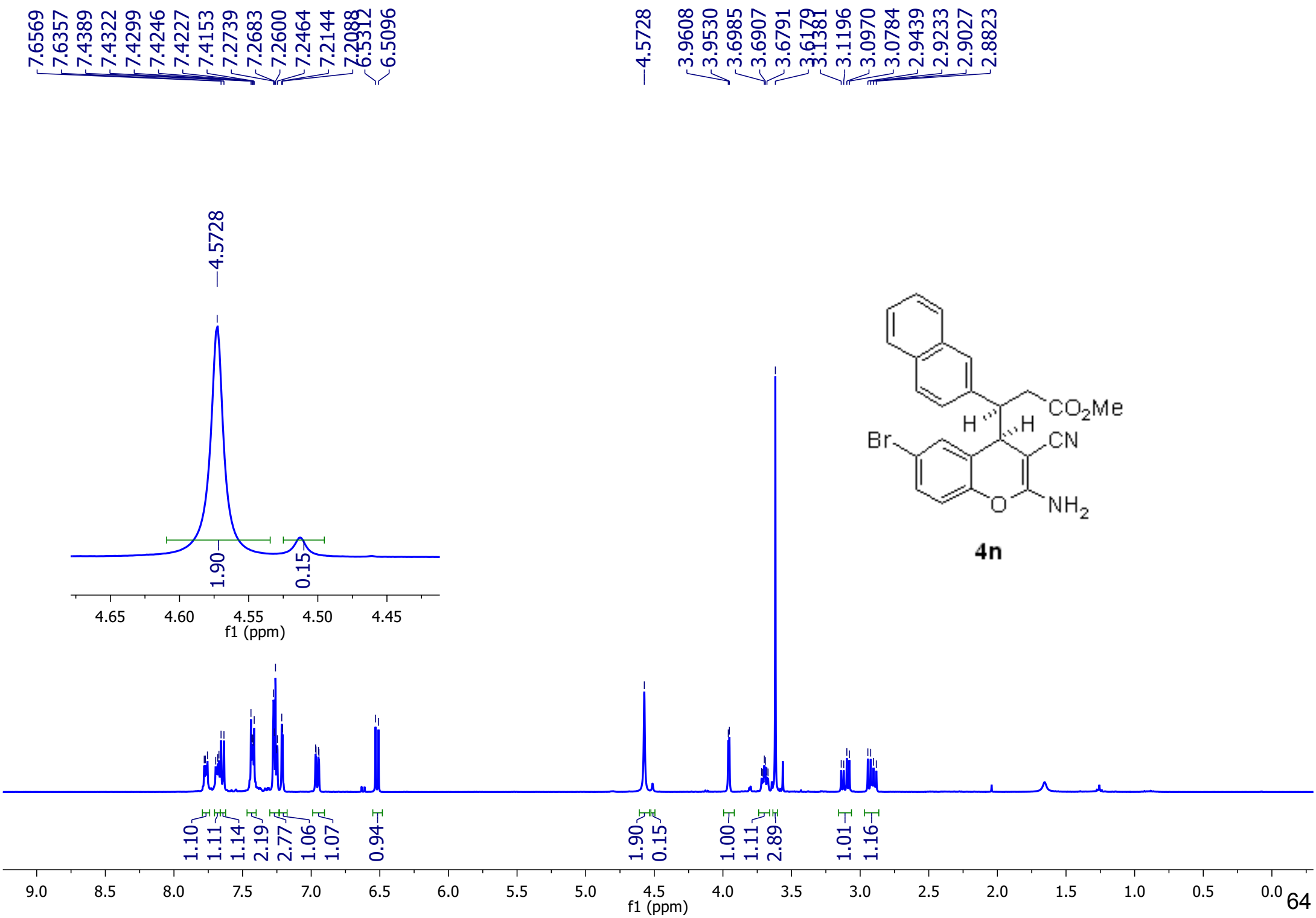
172.4040
161.8503
153.7924
150.0870
141.7645
128.8035
128.4369
124.7869
121.0224
120.1833
116.0366
110.4483
107.3251
77.4784
77.1601
76.8431
56.1847
52.0331
43.3581
39.4549
33.6373

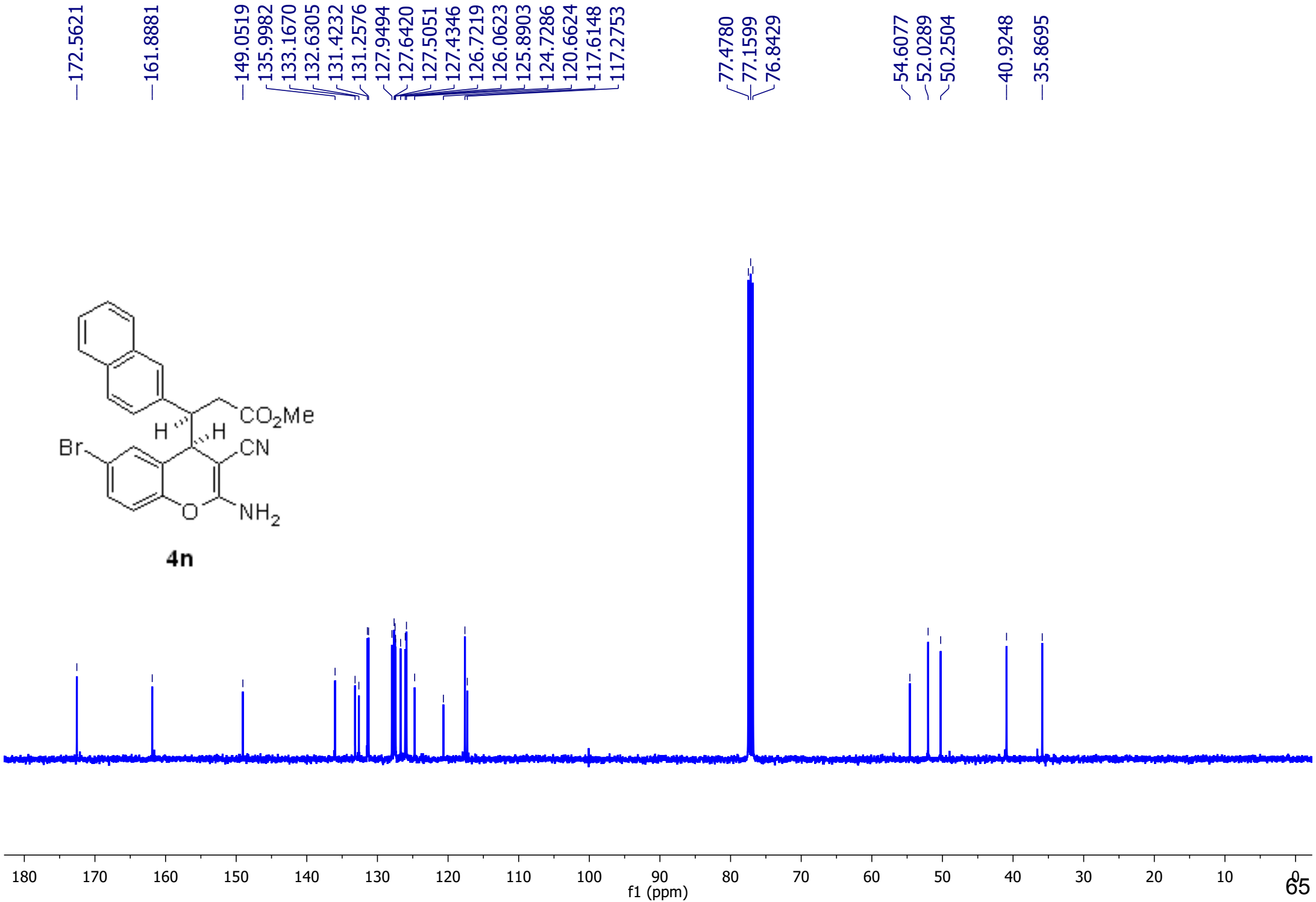


4l


7.1969
7.1773
7.1724
7.0813
7.0769
6.6732
6.6507
6.6402
6.6178
6.5443
6.5227
4.6681
3.7549
3.7471
3.6718
3.5516
3.4061
3.3946
3.3868
3.3752
3.3670
2.9272
2.9086
2.8864
2.8678
2.7103
2.6897
2.6694
2.6488
4.6681
1.82
0.20
4.74
4.70
4.66
4.62
4.58
f1 (ppm)
MeO
CO2Me
H
H
Br
CN
O
NH2
4m
1.11
0.97
4.49
1.00
1.82
0.20
1.08
3.37
3.02
1.03
1.00
1.17
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.6225
161.9471
158.7466
149.0799
131.3544
131.0964
130.3186
129.4443
124.8515
120.6861
117.5734
117.0914
113.3879
77.4779
77.1598
76.8423
55.2384
54.3672
51.9262
49.3284
40.9466
35.9468
MeO
CO2Me
H
H
Br
CN
O
NH2
4m
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.6569
7.6357
7.4389
7.4322
7.4299
7.4246
7.4227
7.4153
7.2739
7.2683
7.2600
7.2464
7.2144
7.2088
6.5312
6.5096
4.5728
3.9608
3.9530
3.6985
3.6907
3.6791
3.6179
3.1381
3.1196
3.0970
3.0784
2.9439
2.9233
2.9027
2.8823
4.5728
1.90
0.15
4.65
4.60
4.55
4.50
4.45
f1 (ppm)
CO2Me
H
H
Br
CN
O
NH2
4n
1.10
1.11
1.14
2.19
2.77
1.06
1.07
0.94
1.90
0.15
1.00
1.11
2.89
1.01
1.16
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.5621
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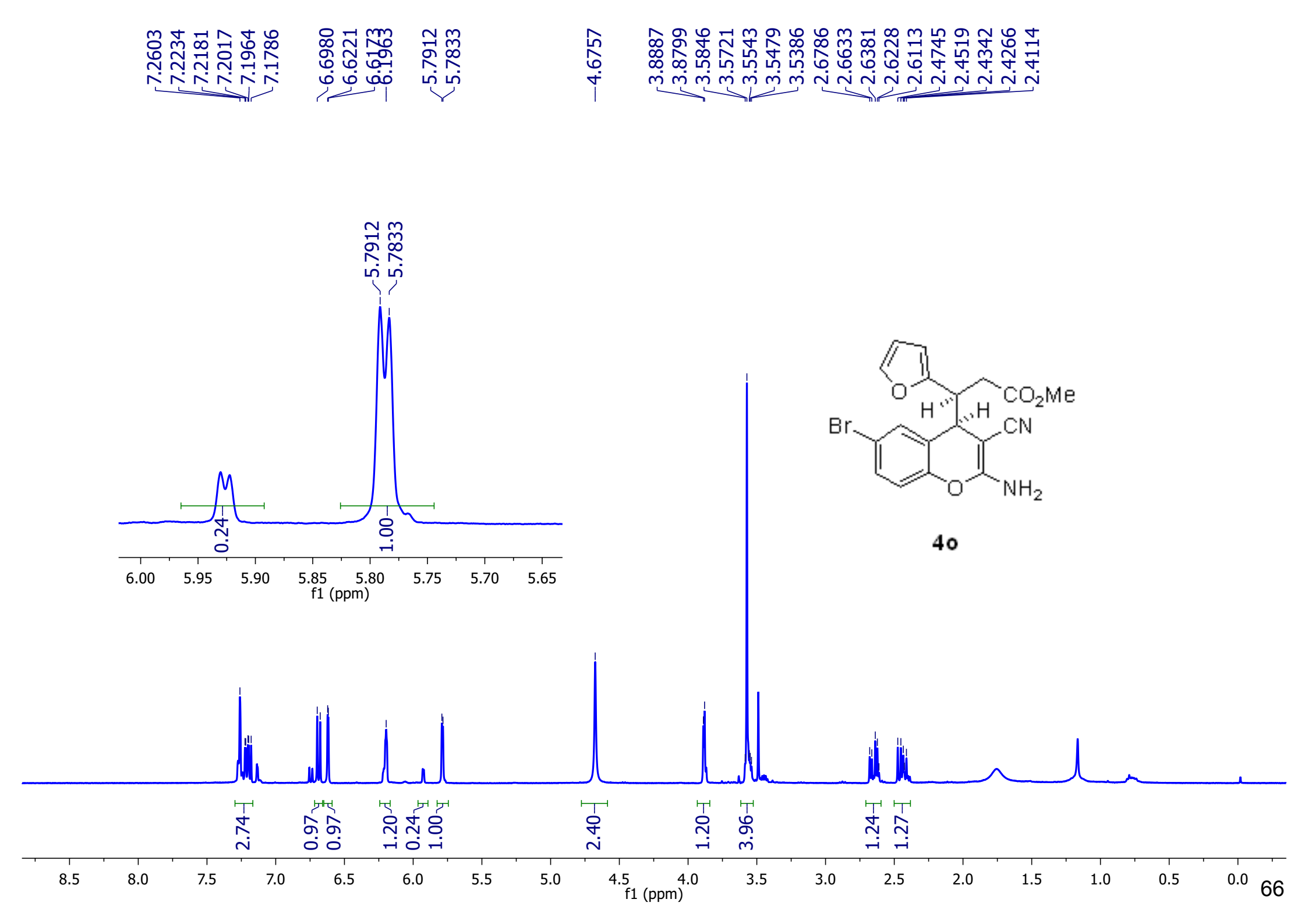
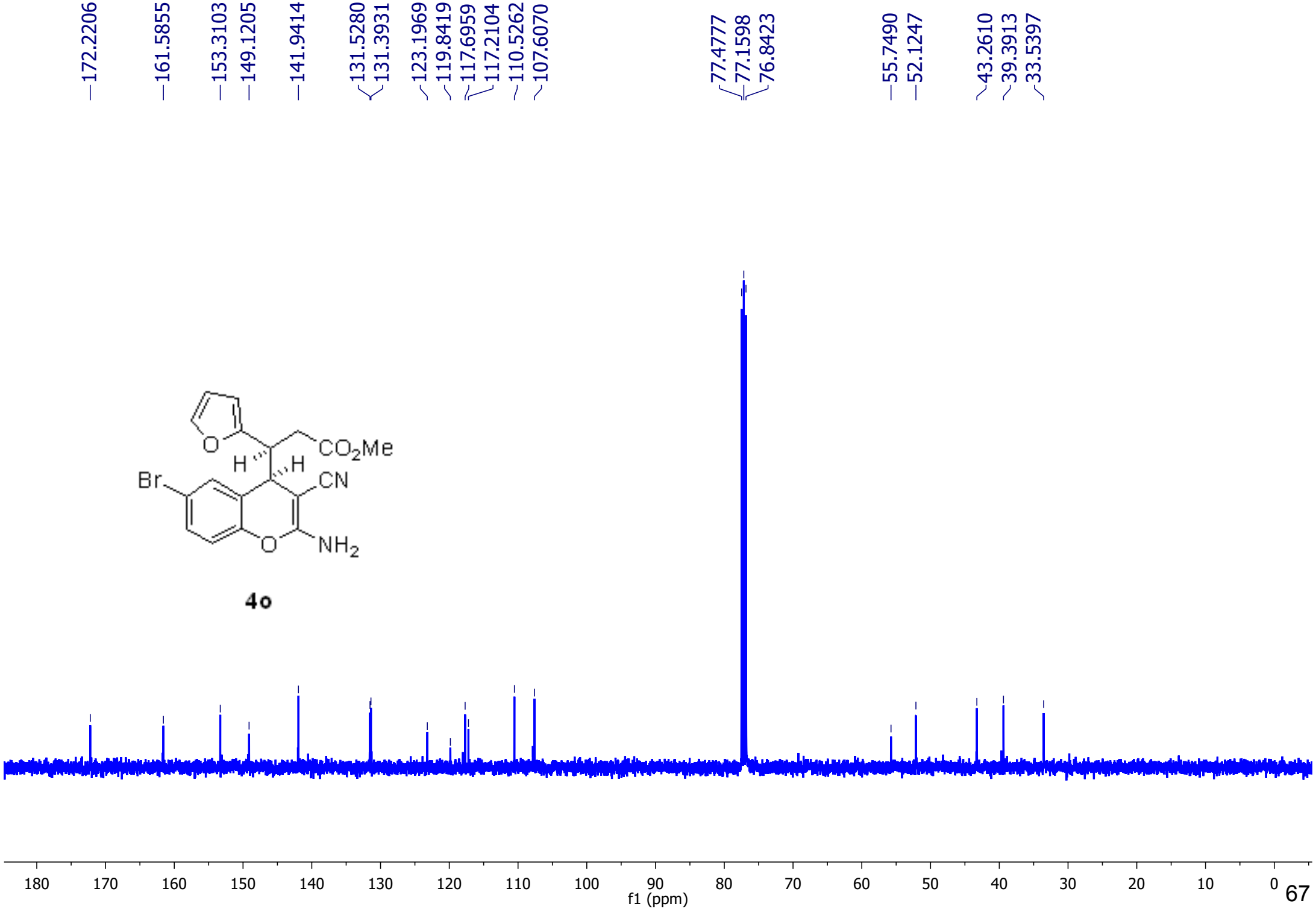
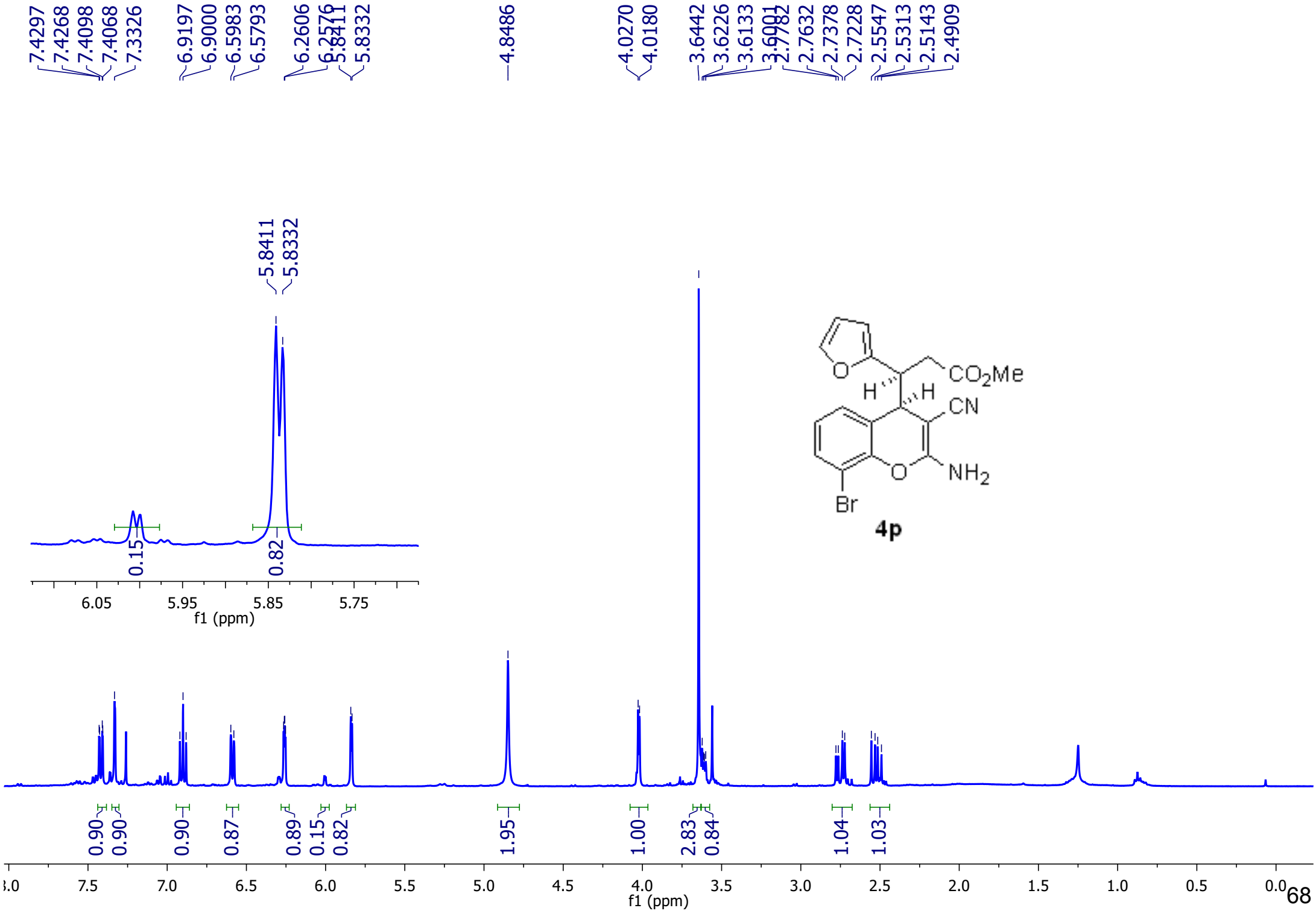
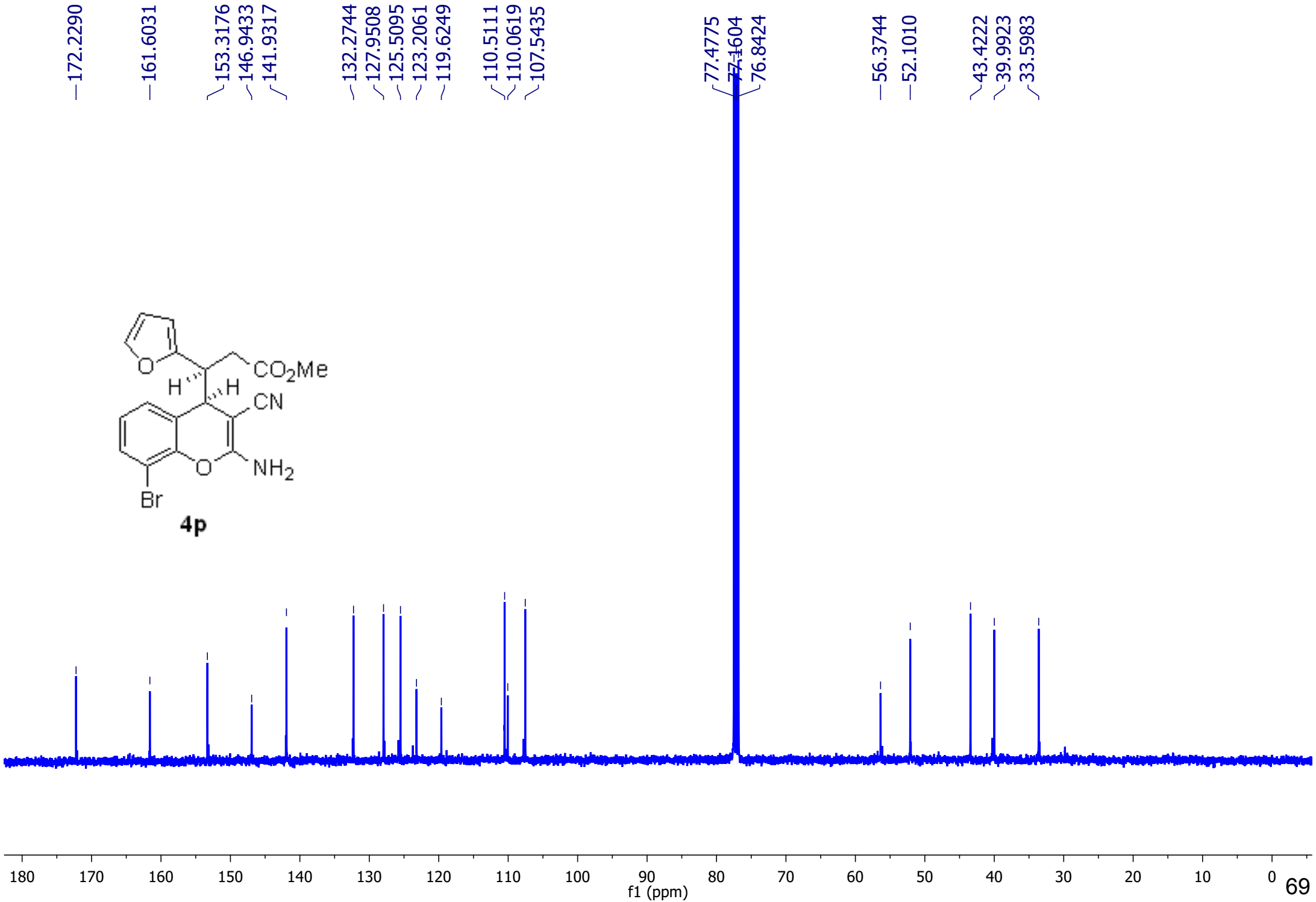
149.0519
135.9982
133.1670
132.6305
131.4232
131.2576
127.9494
127.6420
127.5051
127.4346
126.7219
126.0623
125.8903
124.7286
120.6624
117.6148
117.2753
77.4780
77.1599
76.8429
54.6077
52.0289
50.2504
40.9248
35.8695
CO2Me
H
H
Br
CN
O
NH2
4n
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.2603
7.2234
7.2181
7.2017
7.1964
7.1786
6.6980
6.6221
6.6173
6.1963
5.7912
5.7833
4.6757
3.8887
3.8799
3.5846
3.5721
3.5543
3.5479
3.5386
2.6786
2.6633
2.6381
2.6228
2.6113
2.4745
2.4519
2.4342
2.4266
2.4114
0.24
1.00
f1 (ppm)
Br
O
H
H
CO2Me
CN
NH2
4o
2.74
0.97
0.97
1.20
0.24
1.00
2.40
1.20
3.96
1.24
1.27
f1 (ppm)


172.2206
161.5855
153.3103
149.1205
141.9414
131.5280
131.3931
123.1969
119.8419
117.6959
117.2104
110.5262
107.6070
77.4777
77.1598
76.8423
55.7490
52.1247
43.2610
39.3913
33.5397
O
H
H
CO2Me
Br
CN
O
NH2
4o
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.4297
7.4268
7.4098
7.4068
7.3326
6.9197
6.9000
6.5983
6.5793
6.2606
6.2576
5.8411
5.8332
4.8486
4.0270
4.0180
3.6442
3.6226
3.6133
3.6001
2.7782
2.7632
2.7378
2.7228
2.5547
2.5313
2.5143
2.4909
5.8411
5.8332
0.15
0.82
6.05
5.95
5.85
5.75
f1 (ppm)
CO2Me
CN
NH2
Br
4p
0.90
0.90
0.90
0.87
0.89
0.15
0.82
1.95
1.00
2.83
0.84
1.04
1.03
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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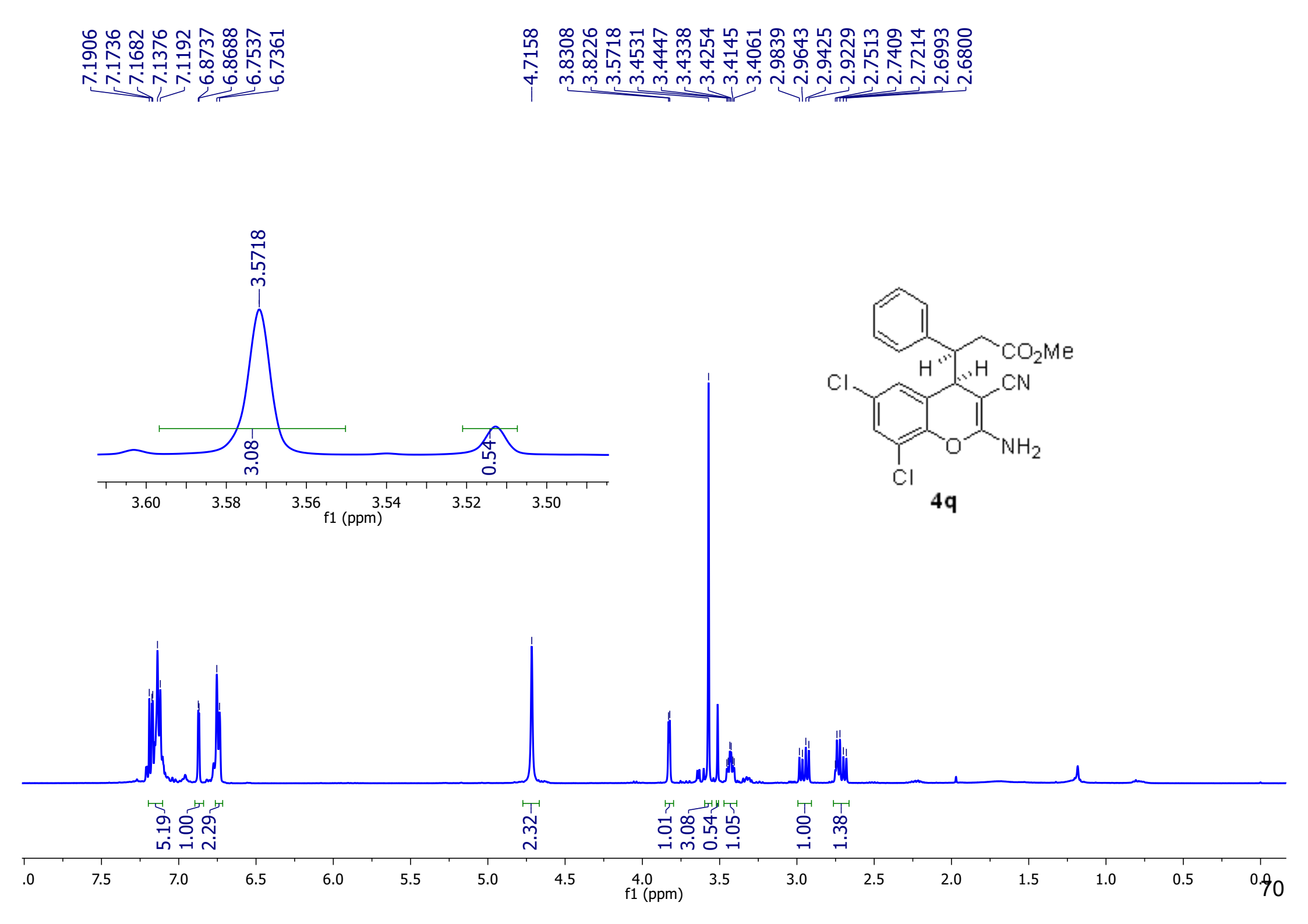
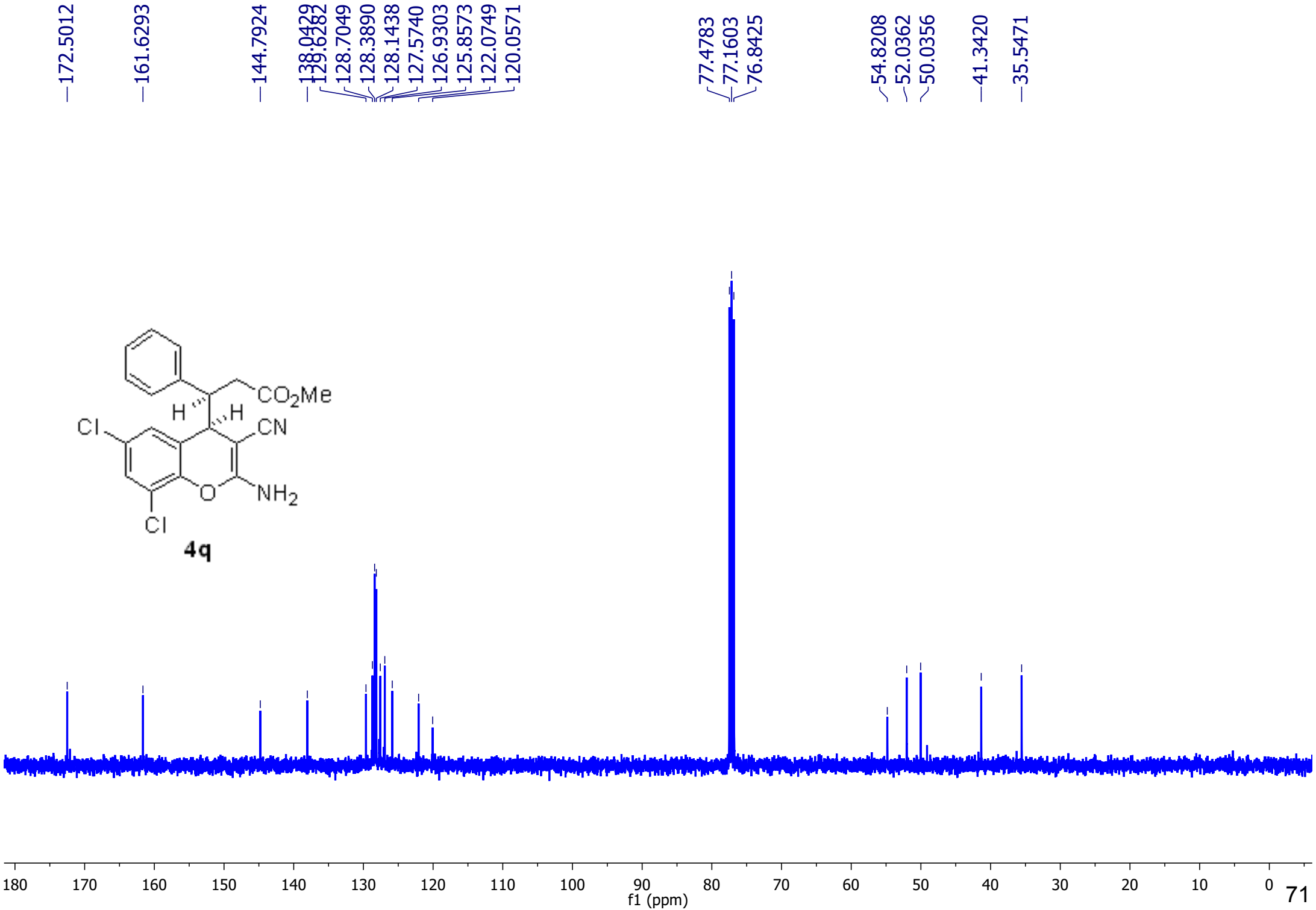
161.6031
153.3176
146.9433
141.9317
132.2744
127.9508
125.5095
123.2061
119.6249
110.5111
110.0619
107.5435
77.4775
77.1604
76.8424
56.3744
52.1010
43.4222
39.9923
33.5983
CO2Me
H
H
CN
NH2
O
O
Br
4p
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.1906
7.1736
7.1682
7.1376
7.1192
6.8737
6.8688
6.7537
6.7361
4.7158
3.8308
3.8226
3.5718
3.4531
3.4447
3.4338
3.4254
3.4145
3.4061
2.9839
2.9643
2.9425
2.9229
2.7513
2.7409
2.7214
2.6993
2.6800
3.5718
3.08
0.54
3.60
3.58
3.56
3.54
3.52
3.50
f1 (ppm)
CO2Me
H
H
CN
Cl
NH2
O
Cl
4q
5.19
1.00
2.29
2.32
1.01
3.08
0.54
1.05
1.00
1.38
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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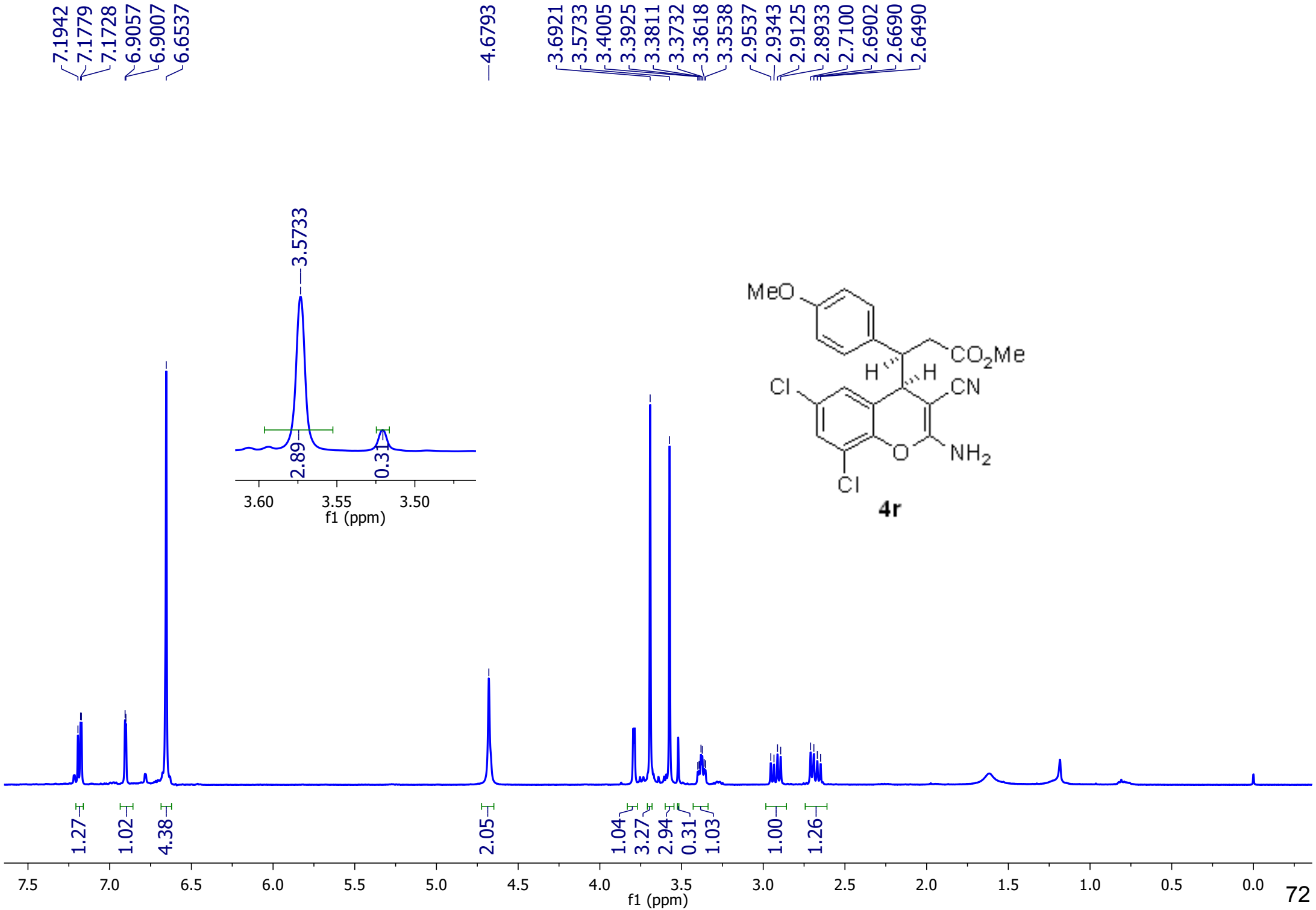
144.7924
138.0429
129.6282
128.7049
128.3890
128.1438
127.5740
126.9303
125.8573
122.0749
120.0571
77.4783
77.1603
76.8425
54.8208
52.0362
50.0356
41.3420
35.5471
CO2Me
H
H
CN
Cl
NH2
O
Cl
4q
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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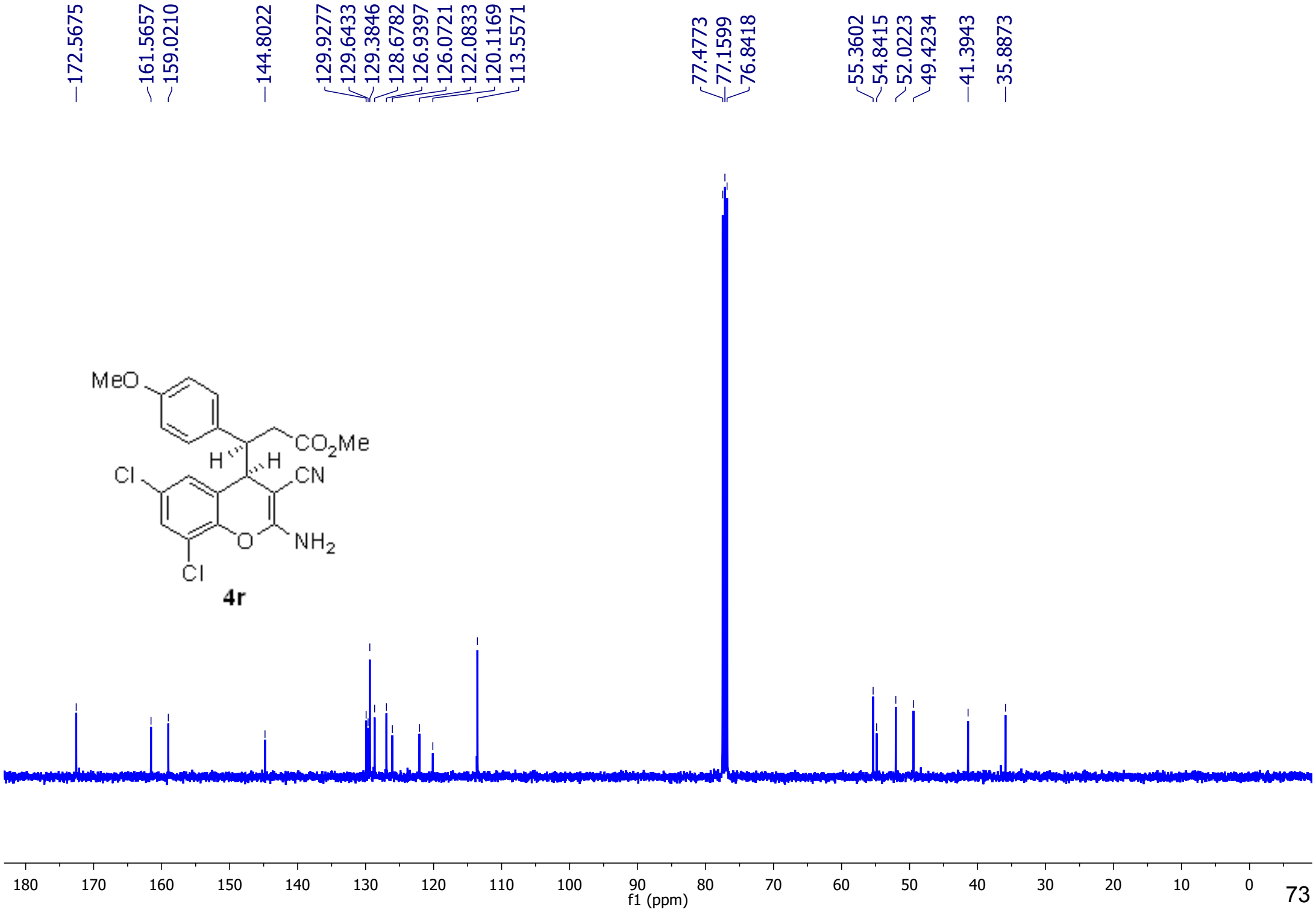
7.1779
7.1728
6.9057
6.9007
6.6537
4.6793
3.6921
3.5733
3.4005
3.3925
3.3811
3.3732
3.3618
3.3538
2.9537
2.9343
2.9125
2.8933
2.7100
2.6902
2.6690
2.6490
3.5733
2.89
0.31
3.60
3.55
3.50
f1 (ppm)
MeO
CO2Me
H
H
Cl
CN
O
NH2
Cl
4r
1.27
1.02
4.38
2.05
1.04
3.27
2.94
0.31
1.03
1.00
1.26
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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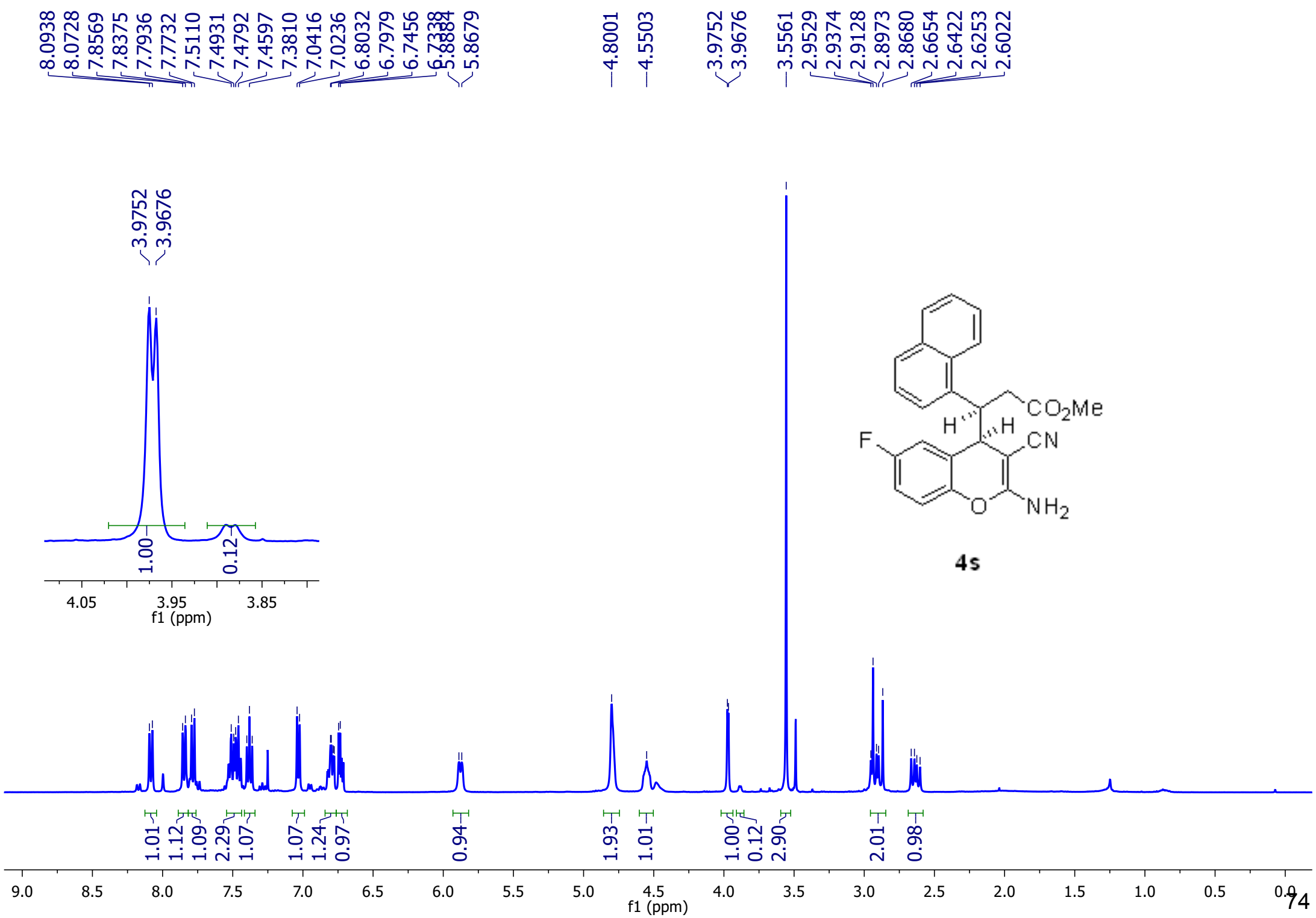
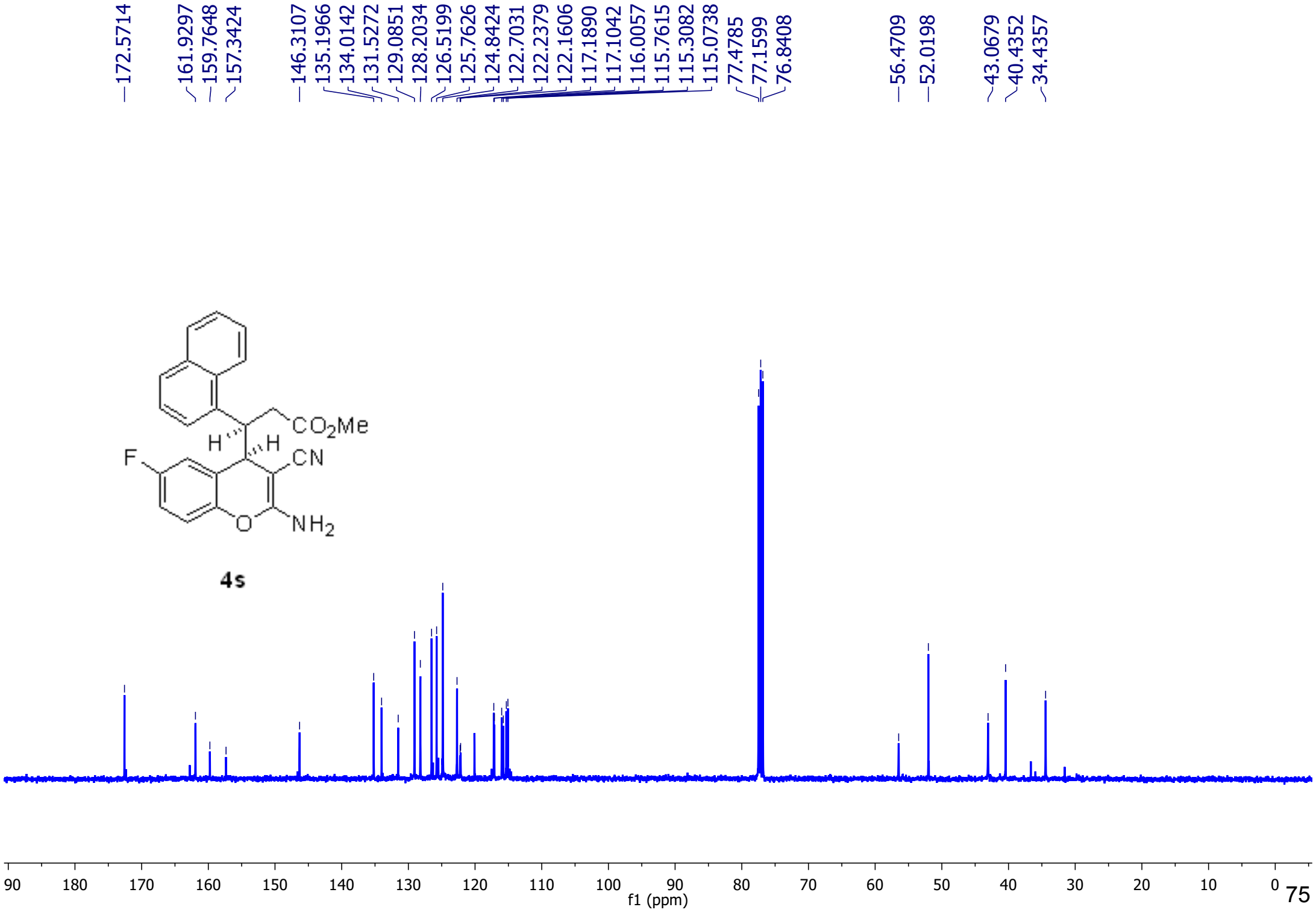
161.5657
159.0210
144.8022
129.9277
129.6433
129.3846
128.6782
126.9397
126.0721
122.0833
120.1169
113.5571
77.4773
77.1599
76.8418
55.3602
54.8415
52.0223
49.4234
41.3943
35.8873
MeO
CO2Me
H
H
Cl
CN
O
NH2
Cl
4r
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.0938
8.0728
7.8569
7.8375
7.7936
7.7732
7.5110
7.4931
7.4792
7.4597
7.3810
7.0416
7.0236
6.8032
6.7979
6.7456
6.7338
5.8884
5.8679
4.8001
4.5503
3.9752
3.9676
3.5561
2.9529
2.9374
2.9128
2.8973
2.8680
2.6654
2.6422
2.6253
2.6022
1.00
0.12
4.05
3.95
3.85
f1 (ppm)
CO2Me
H
H
CN
F
O
NH2
4s
1.01
1.12
1.09
2.29
1.07
1.07
1.24
0.97
0.94
1.93
1.01
1.00
0.12
2.90
2.01
0.98
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


172.5714
161.9297
159.7648
157.3424
146.3107
135.1966
134.0142
131.5272
129.0851
128.2034
126.5199
125.7626
124.8424
122.7031
122.2379
122.1606
117.1890
117.1042
116.0057
115.7615
115.3082
115.0738
77.4785
77.1599
76.8408
56.4709
52.0198
43.0679
40.4352
34.4357
CO2Me
H
H
CN
F
O
NH2
4s
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

HPLC Chromatogram of *rac*-**4a** *ent*-**4a**:

Preparation of *rac*-**4a**:

methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-phenylpropanoate **(4a)**:: A solution of 3-cyano-2*H*-iminochromene **1a** (75 mg, 0.366 mmol, 1.0 *equiv*), cinnamaldehyde derivative **2a** (72 mg, 68.5 µL, 0.550 mmol, 1.5 *equiv*), NaOAc (0.3 *equiv*), and NHC precatalyst **3e** (20 mol%) in DMF:MeOH (20:1) (0.15 M) was stirred overnight at room temperature under nitrogen atmosphere. After complete consumption of 3-cyano-2*H*-iminochromene solvent was evaporated under reduced pressure. The residue was then subjected to purification by flash column chromatography using EtOAc and petroleum- ether mixture as an eluent to yield the desired product *rac*-**4a**. 45% yield; *d.r.* = 4:1.

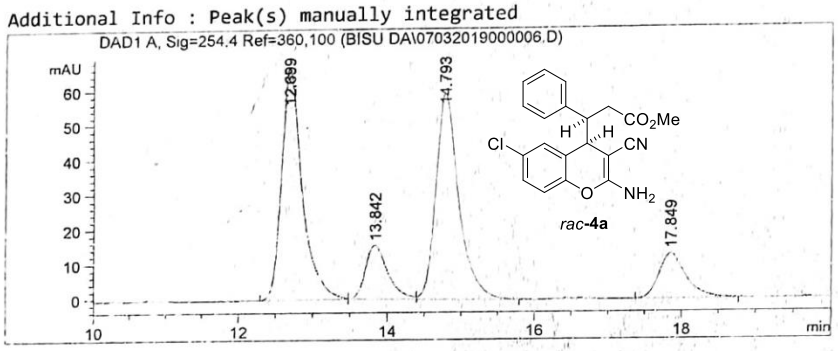
Preparation of *ent*-**4a**:

methyl 3-(2-amino-6-chloro-3-cyano-4*H*-chromen-4-yl)-3-phenylpropanoate **(4a)**:: A solution of 3-cyano-2*H*-iminochromene **1a** (75 mg, 0.366 mmol, 1.0 *equiv*), cinnamaldehyde derivative **2a** (72 mg, 68.5 µL, 0.550 mmol, 1.5 *equiv*), NaOAc (0.3 *equiv*), and NHC precatalyst **5c** (20 mol%) in Toluene:MeOH (20:1) (0.15 M) was stirred 6 hours at room temperature under nitrogen atmosphere. After complete consumption of 3-cyano-2*H*-iminochromene solvent was evaporated under reduced pressure. The residue was then subjected to purification by flash column chromatography using EtOAc and petroleum- ether mixture as an eluent to yield the desired product *ent*-**4a**. 52% yield; *d.r.* = 1.2:1.

HPLC analysis: 51/55% *ee* [Daicel CHIRALPAK IA-3 column, 10% i-PrOH/*n*-Hexane, 1.0 ml/min, 254 nm, (Major Diastereomer: Minor: 12.65 min, Major: 14.75 min; (Minor Diasteromer: Major: 13.75 min, 17.73 min)]; ^{1}H-NMR and ^{13}C-NMR spectral data of *ent*-**4a** obtained by enantioselective reaction and *rac*-**4a** are same.

Sample Info : BM-301-RAC
CHIRALPAK IA-3; 250 MM
IPA/HEXANE : 10/90
FLOW RATE: 1.0 mL/ min
254 nm

Additional Info : Peak(s) manually integrated

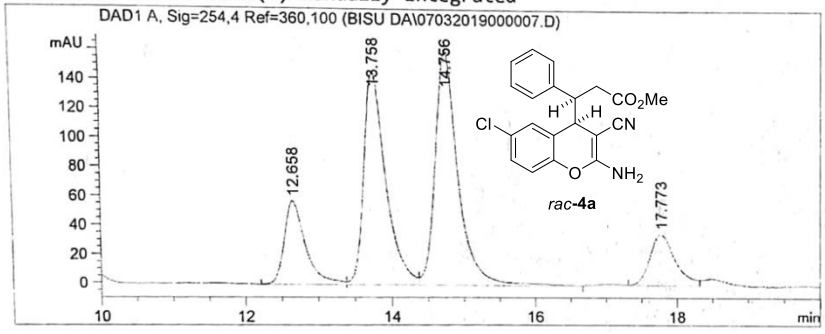


Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.699	BB	0.2899	1289.00293	66.58115	40.1384
2	13.842	BV	0.3018	313.65448	15.25743	9.7669
3	14.793	VB	0.3258	1276.82275	59.15871	39.7591
4	17.849	BB	0.3676	331.91837	12.92685	10.3356
Totals :				3211.39853	153.92414	

Sample Info : BM-302
CHIRALPAK IA-3; 250 MM
IPA/HEXANE : 10/90
FLOW RATE: 1.0 mL/ min
254 nm

Additional Info : Peak(s) manually integrated



Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.658	BV	0.3031	1171.19092	57.63941	13.4533
2	13.758	VV	0.3140	3062.64966	146.41205	35.1803
3	14.756	VB	0.3320	3588.78027	162.27850	41.2239
4	17.773	BV	0.3693	882.96930	35.85620	10.1426
Totals :				8705.59015	402.18617	