Electronic Supplementary Material (ESI) for MedChemComm.

Supplementary Information

The Winding Road of the Uvaretin Class of Natural Products: From Total Synthesis to Bioactive Agent Discovery.

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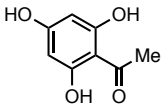
Table of Contents

Table S1: Attempting Conditions

Entry	Lewis acid	Conditions	Yields **15/16%**
1	$BF_3•Et_2O$ (1.3 eq.)	**14** & **Chalcone Compound** to dioxane, add L.A. in dioxane in four portions 10 min apart at RT	0%, 62%
2		**Chalcone Compound** in dioxane, add L.A and heat at 60 °C, dropwise addition of 14 in dioxane over 2.5 h	23%, 46%
3		**Chalcone Compound** in dioxane heated to 60 °C, dropwise addition of **14** & L.A. in dioxane over 2.5 h	0%, 73%
4		*Same as entry 1*, except stirred for 12 h, then heated to 60 °C, **14** dissolved in dioxane with L.A. in two portions 45 min apart, stirred for 12 h, and then refluxed for 48 h	0%, 68%
6	$FeCl_3$ (10% mol)	**14** and **Chalcone Compound** in CH_2Cl_2, L.A. added, stirred at RT for 8 h, then refluxed for 24 h	0%, 0%
7		**14** and **Chalcone Compound** in dioxane, L.A. added, heated at 60 °C for 48 h	31%, 0%
8		**14** and L.A. in dioxane, heated at 60 °C, **Chalcone Compound** in dioxane added dropwise over 18 h	0%, 0%

Table S2: Summary of all sole bioactive agents.



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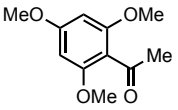

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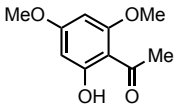

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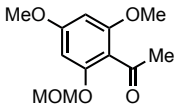

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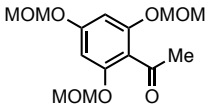

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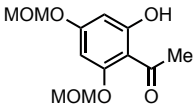

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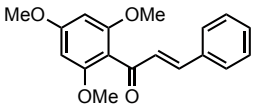
HeLa	>20	3.1 ± 1.0	18.7 ± 3.1	14.0 ± 1.0	>20	11.5 ± 1.1
A549	>20	9.8 ± 1.3	>20	16.9 ± 1.6	>20	8.4 ± 1.3
MIA PaCa-2	>20	14.3 ± 1.0	>20	>20	6.1 ± 1.6	11.8 ± 2.6
HCT-116	>20	>20	>20	>20	>20	>20



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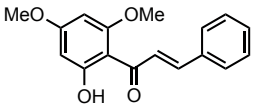

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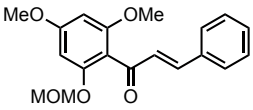

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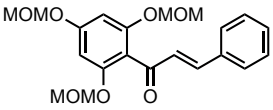

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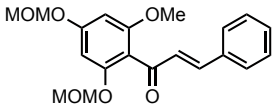
HeLa	5.2 ± 1.4	>20	4.8 ± 0.6	12.2 ± 0.9
A549	4.3 ± 0.9	19.7 ± 2.2	3.5 ± 0.8	>20
MIA PaCa-2	14.3 ± 1.0	18.2 ± 1.7	5.6 ± 0.7	>20
HCT-116	>20	>20	>20	>20



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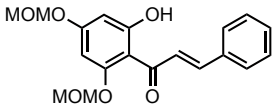

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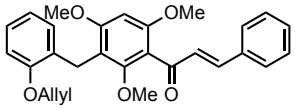
HeLa	9.7 ± 1.3	19.7 ± 0.6
A549	4.2 ± 1.9	>20
MIA PaCa-2	2.2 ± 0.6	7.8 ± 0.4
HCT-116	>20	>20



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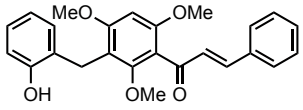

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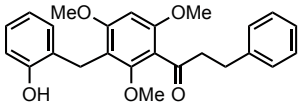

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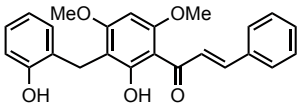
HeLa	5.8 ± 0.5	2.7 ± 0.6	>20
A549	8.5 ± 0.6	9.3 ± 1.1	>20
MIA PaCa-2	9.4 ± 1.3	4.1 ± 0.3	>20
HCT-116	>20	18.6 ± 2.5	>20



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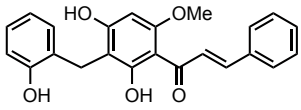

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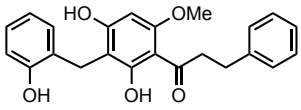

Uvaretin (1)

HeLa	3.1 ± 0.5	4.6 ± 1.4	3.7 ± 0.8
A549	5.8 ± 1.8	4.3 ± 2.1	2.2 ± 1.0
MIA PaCa-2	>20	5.1 ± 1.8	2.0 ± 1.1
HCT-116	>20	19.5 ± 3.1	>20

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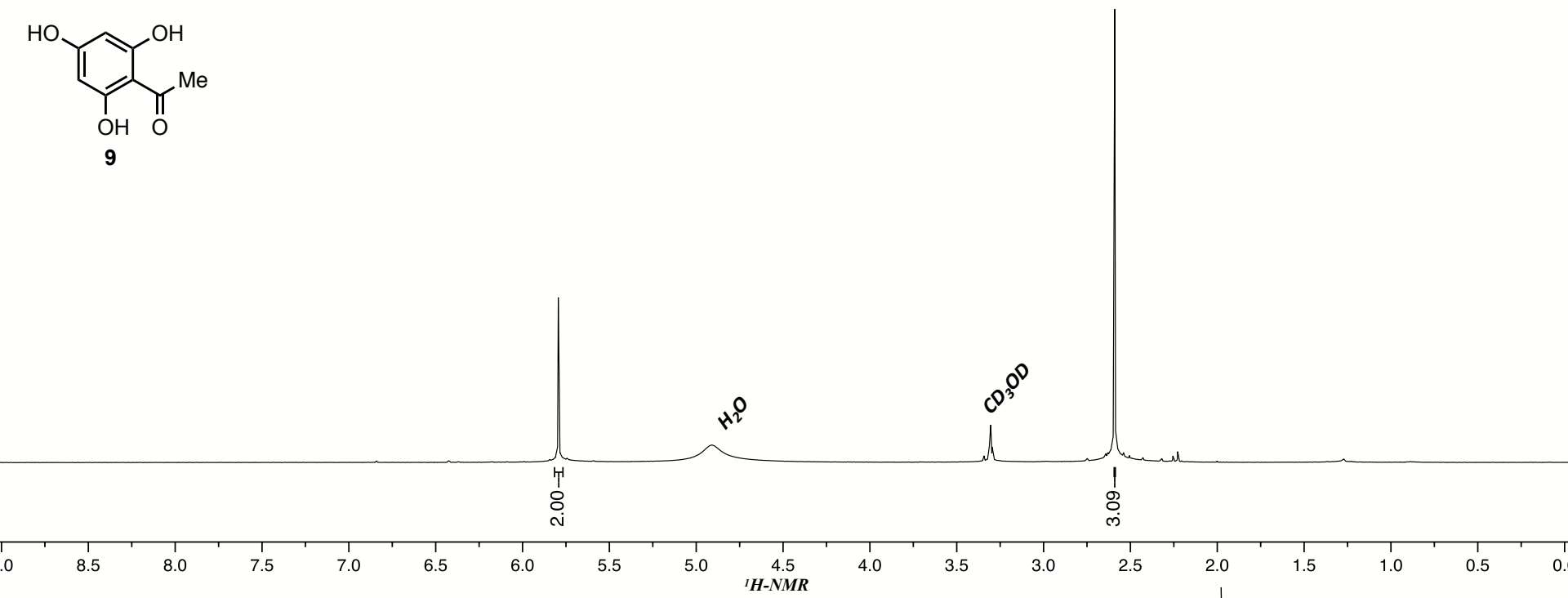

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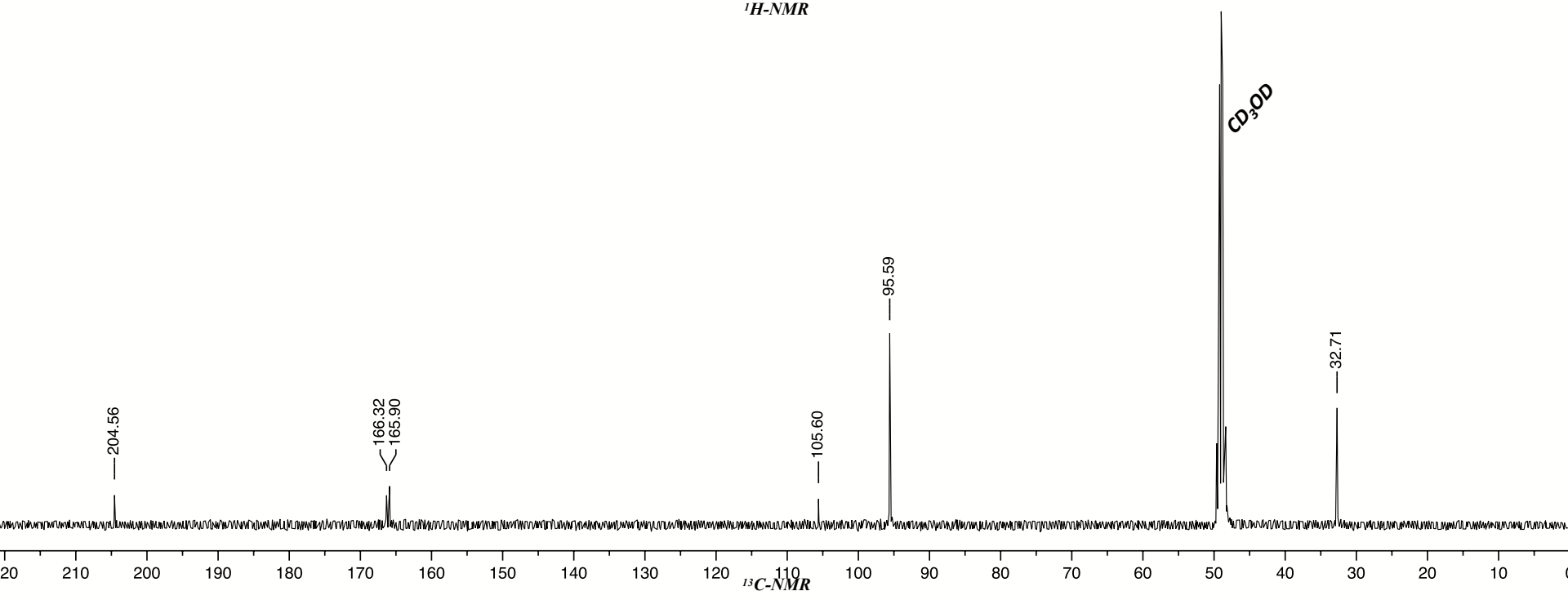

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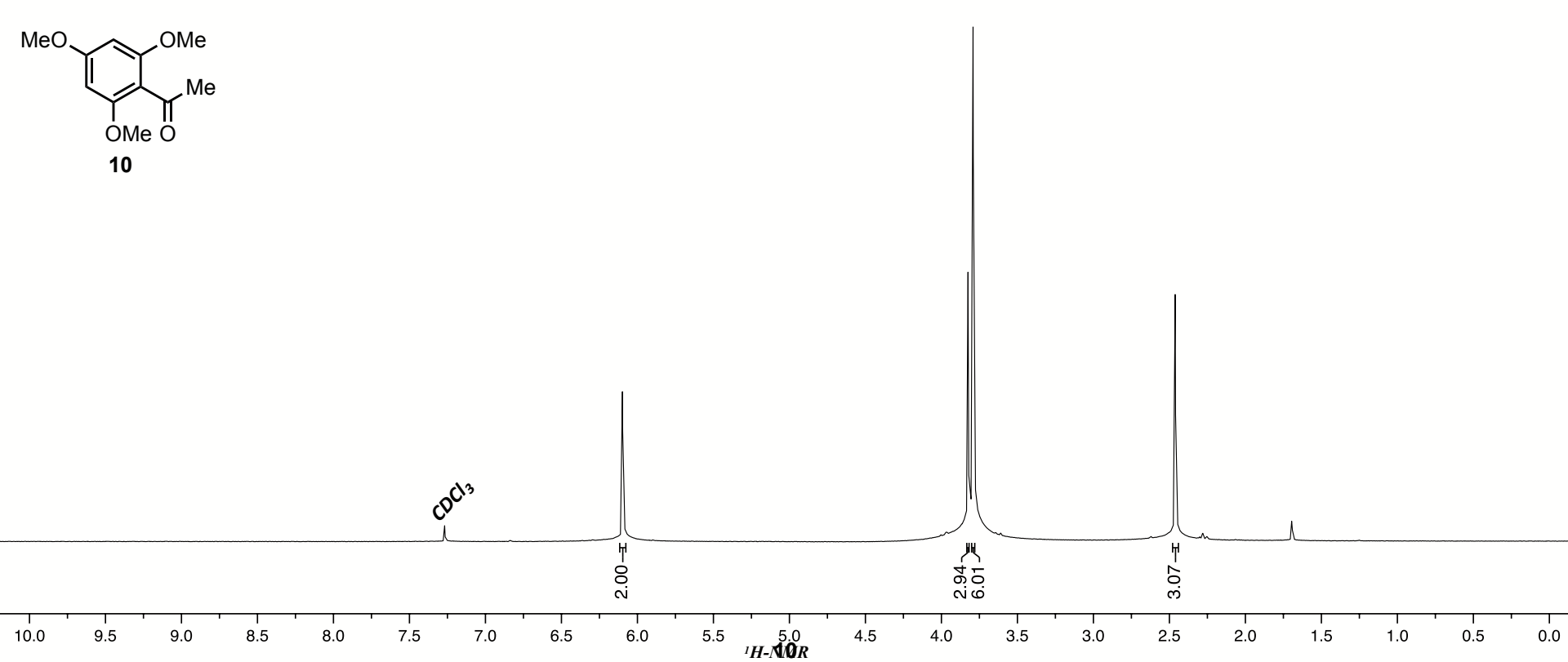

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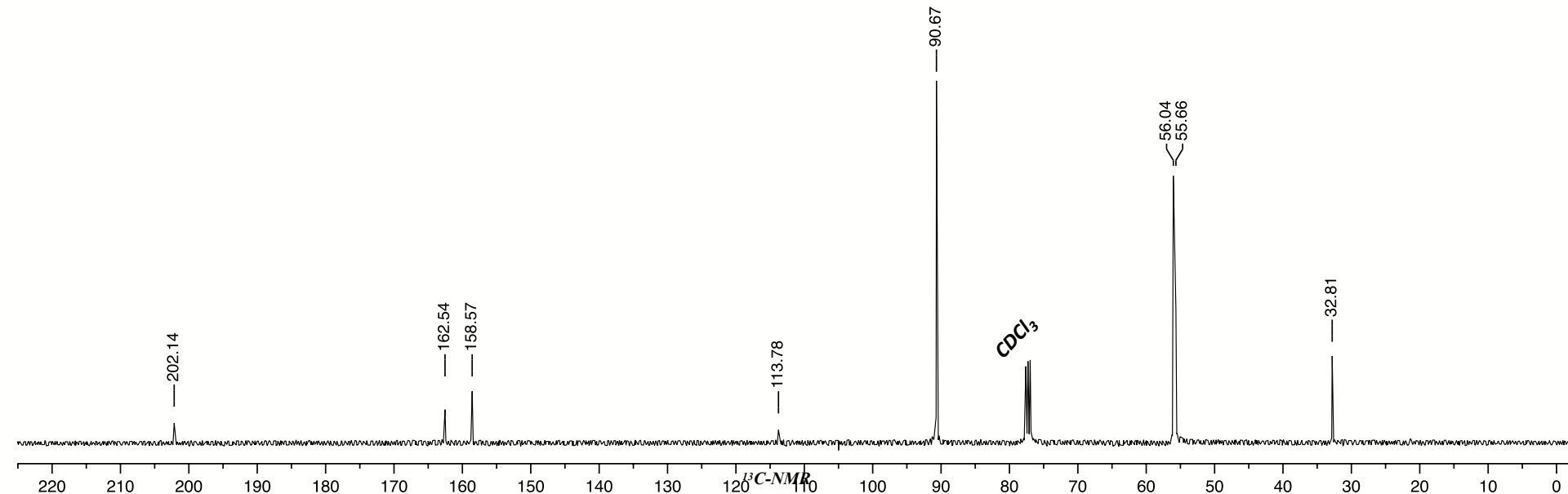

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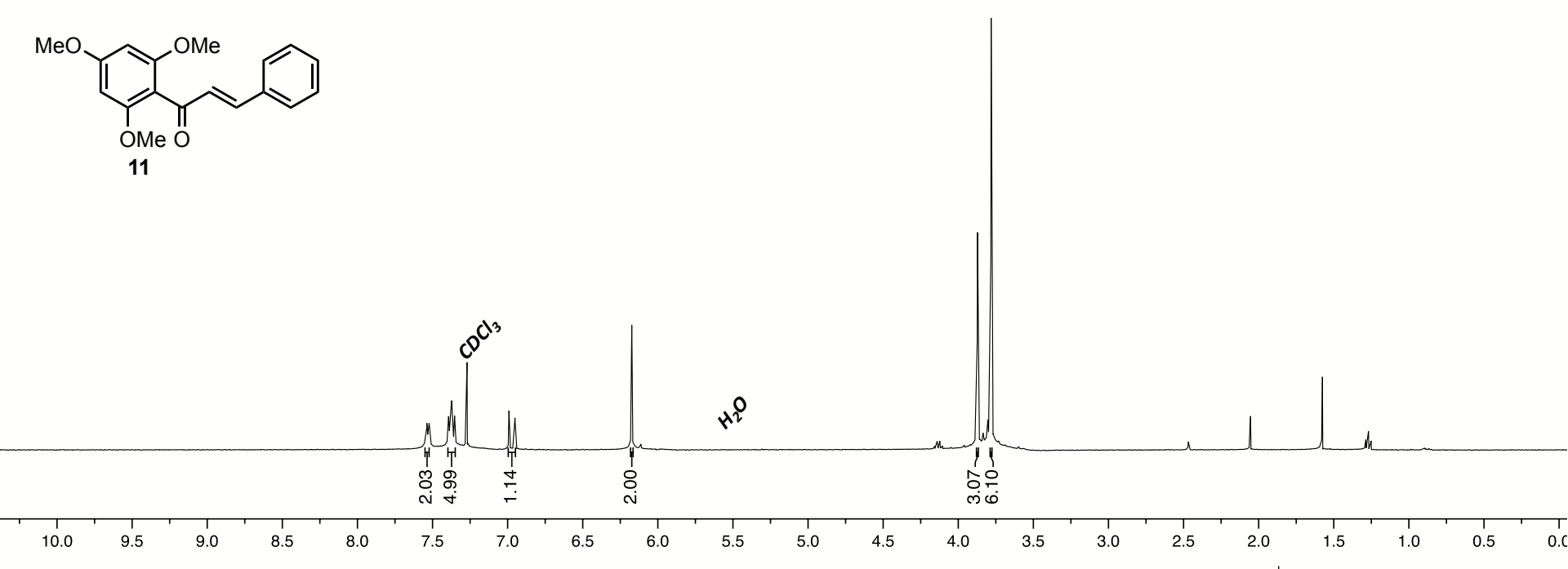

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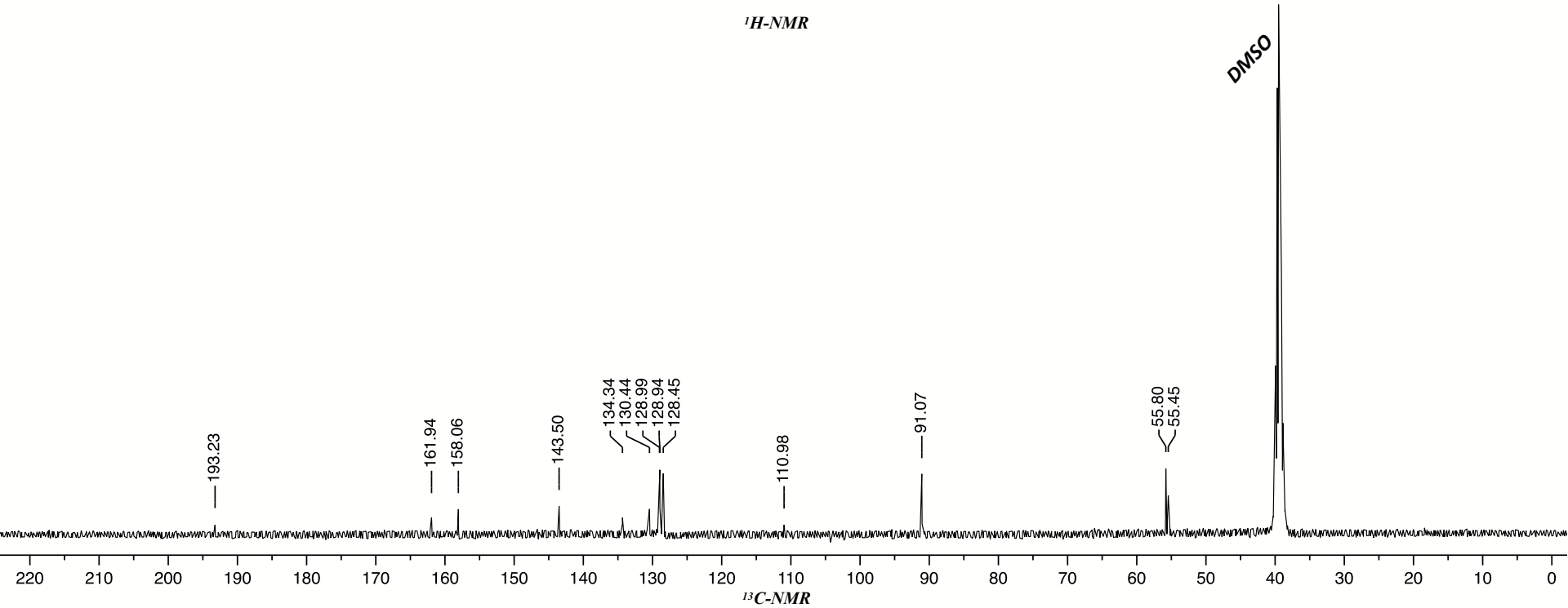

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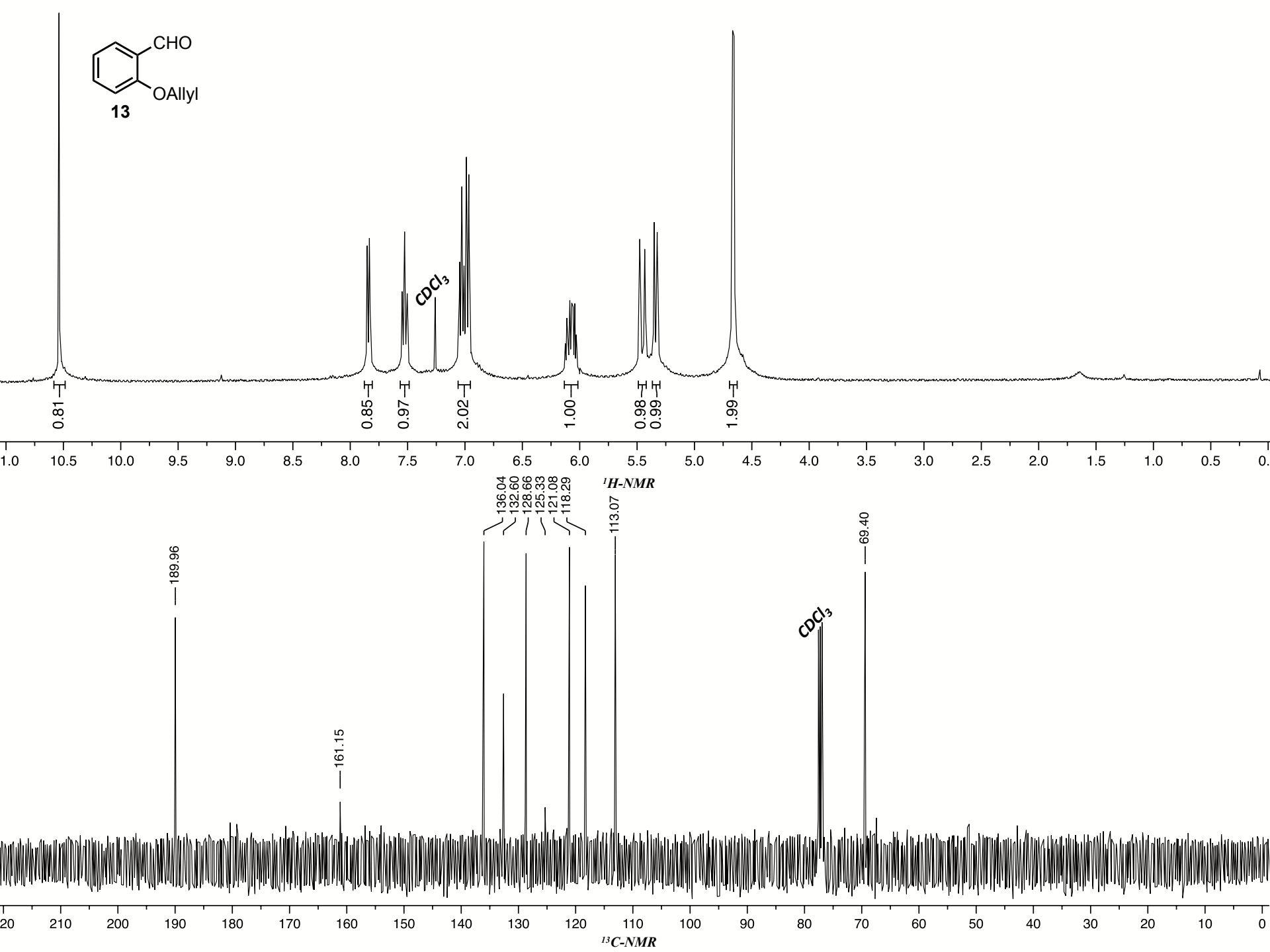
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1.99
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125.33
121.08
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113.07
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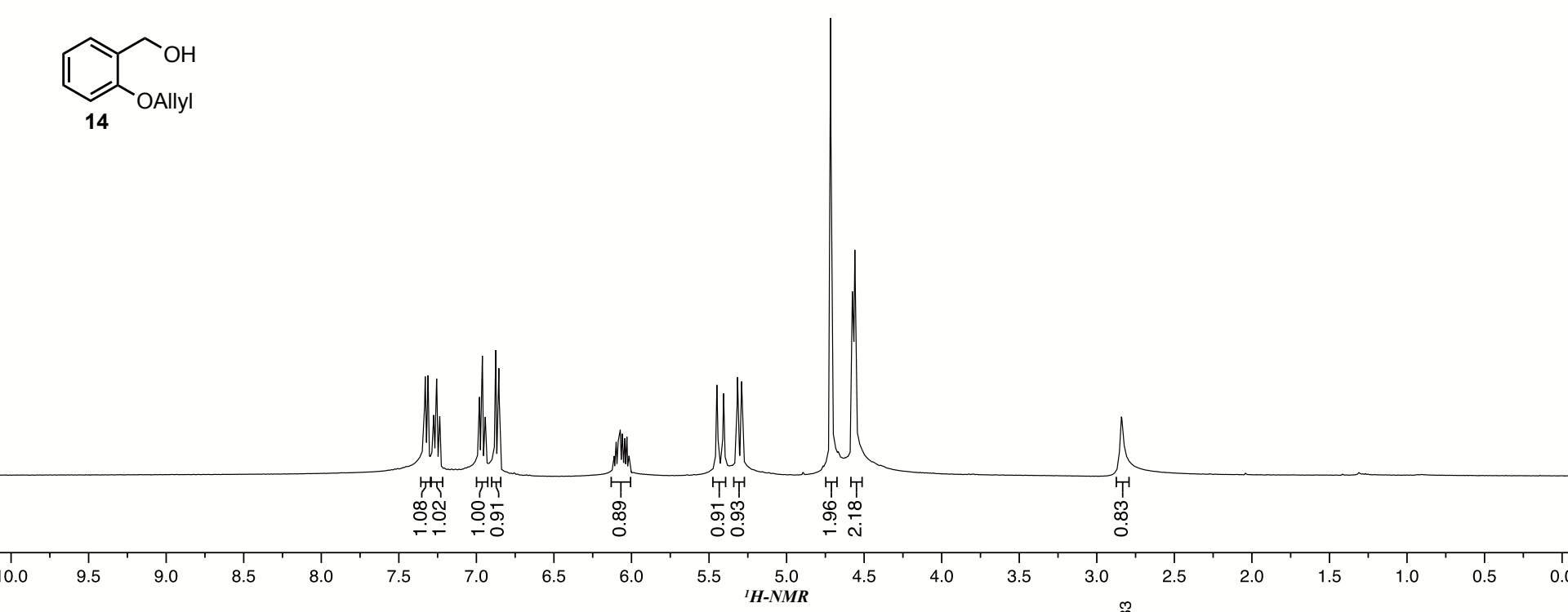
161.15
69.40
CDCl3
13C-NMR

14



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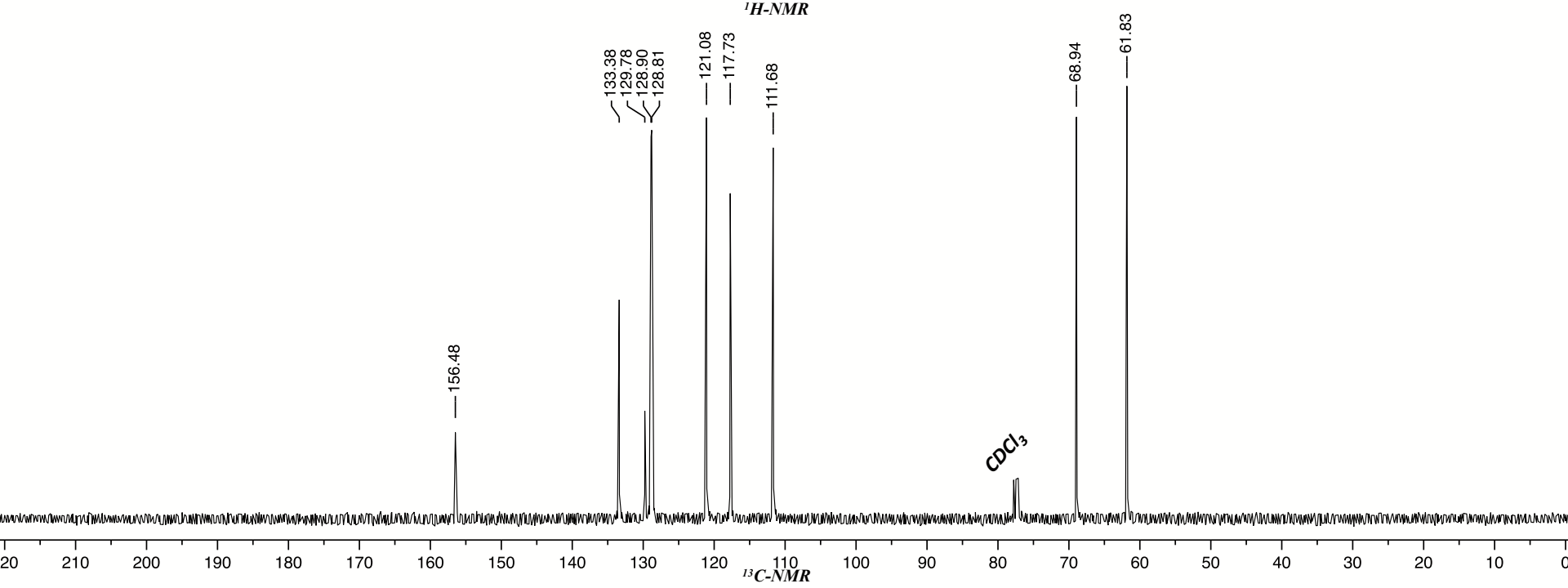

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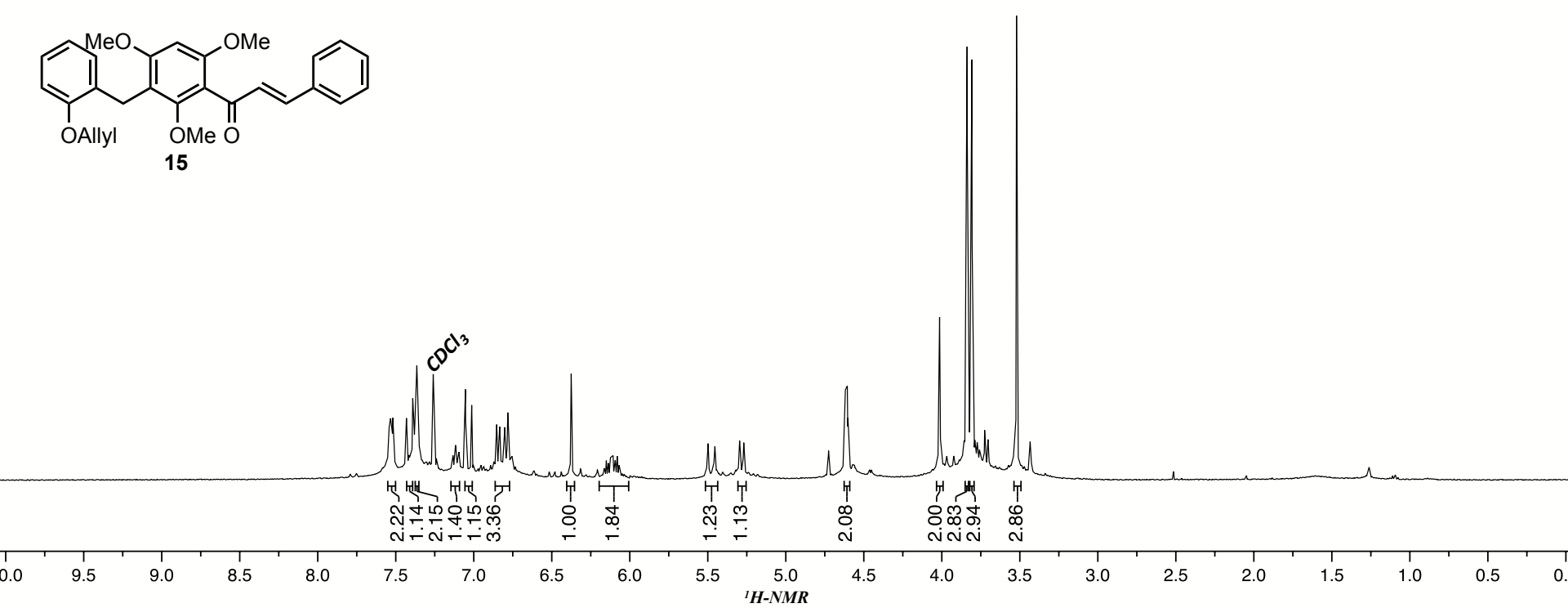

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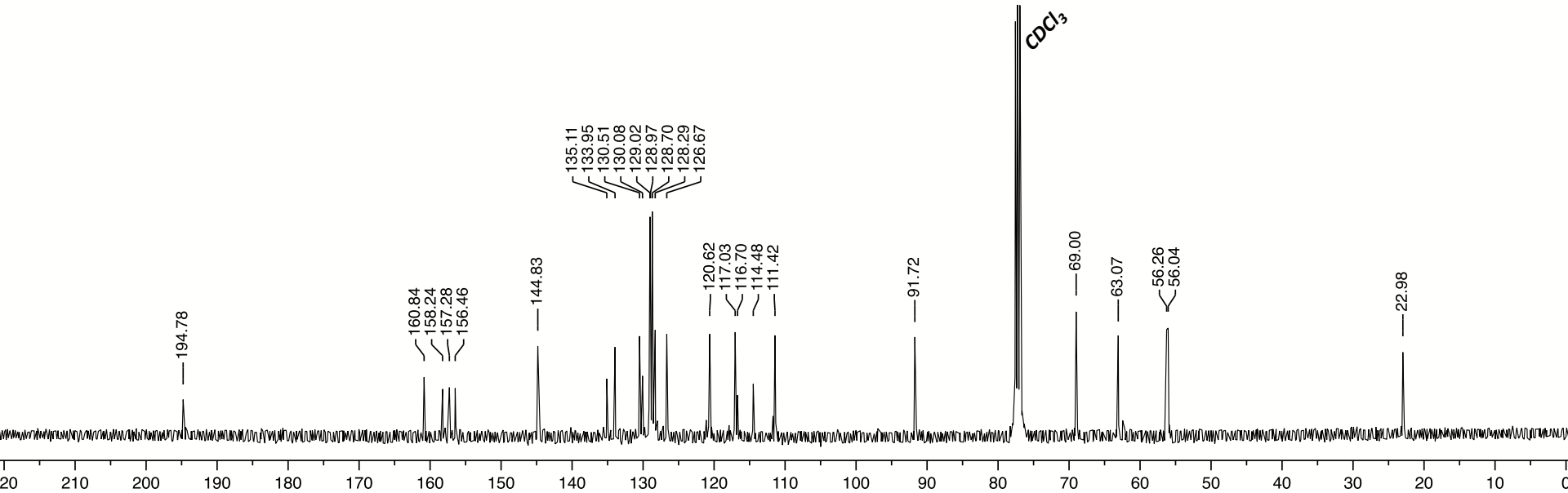

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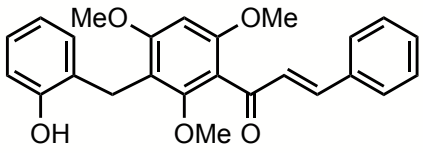

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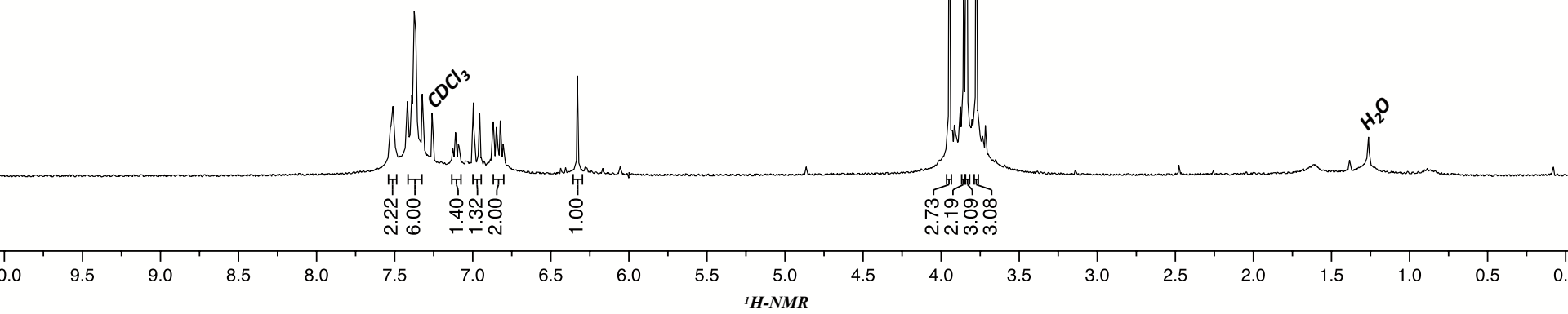

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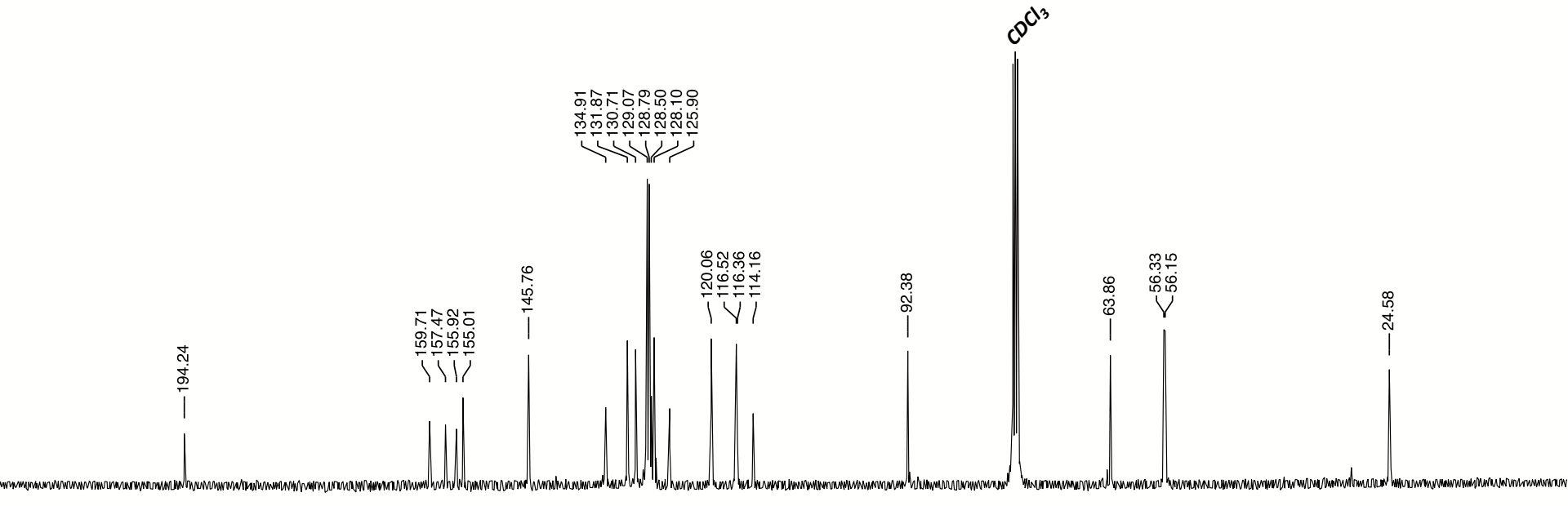

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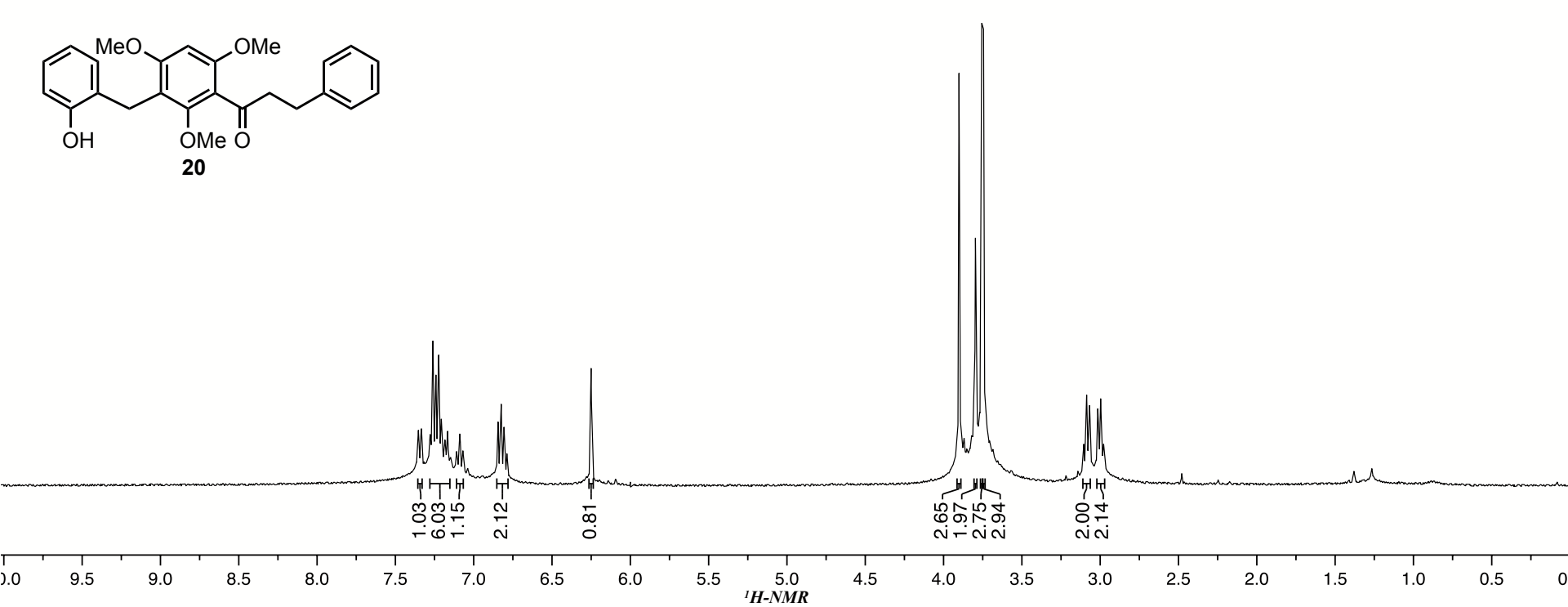

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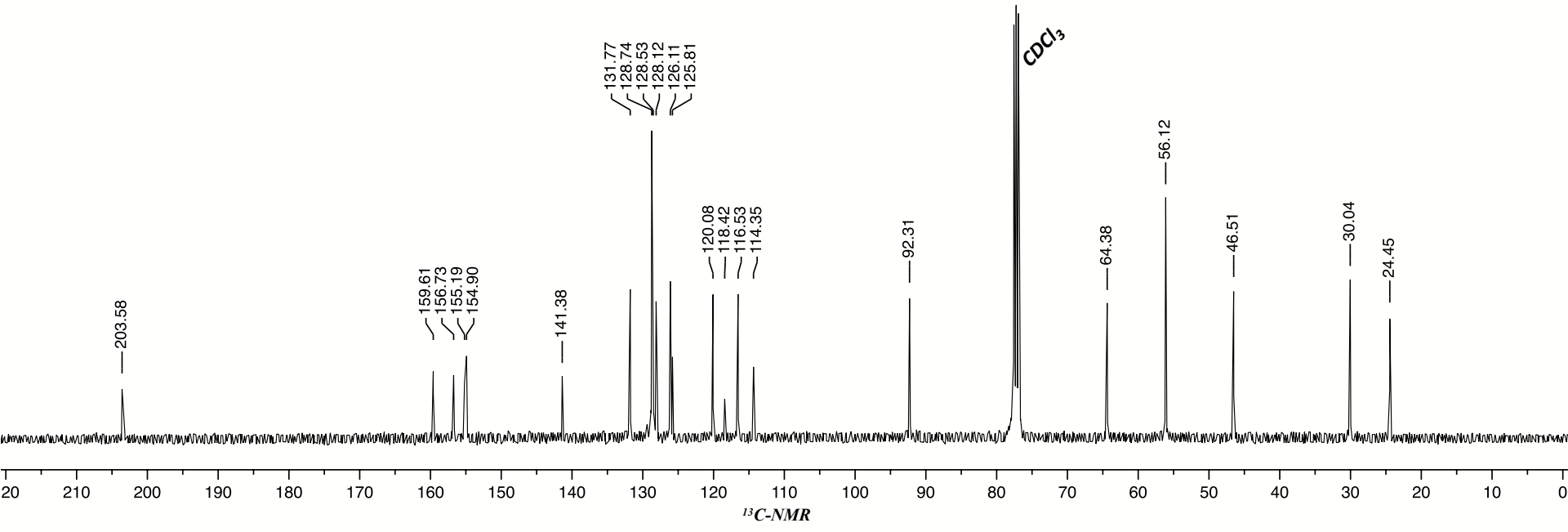

^{13}C-NMR

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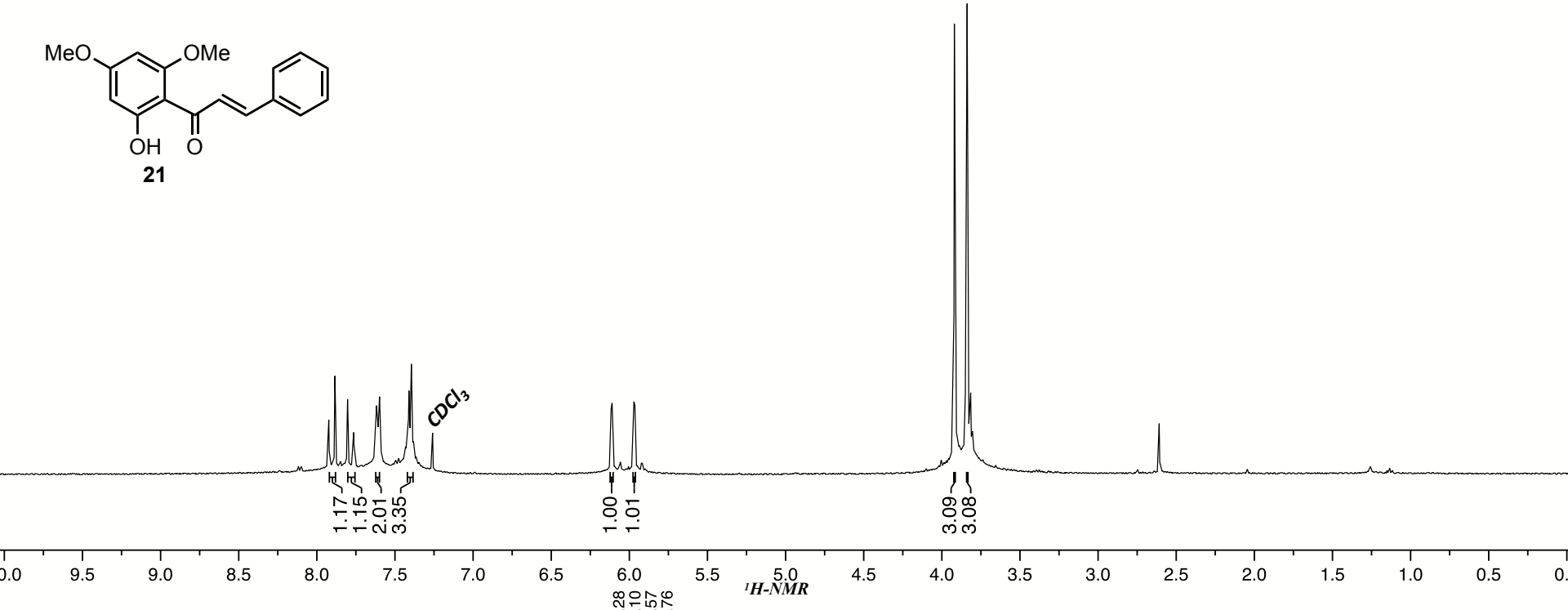
OMe
OH
O

21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8.0
7.5
7.0
6.5
6.0
5.5
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2.0
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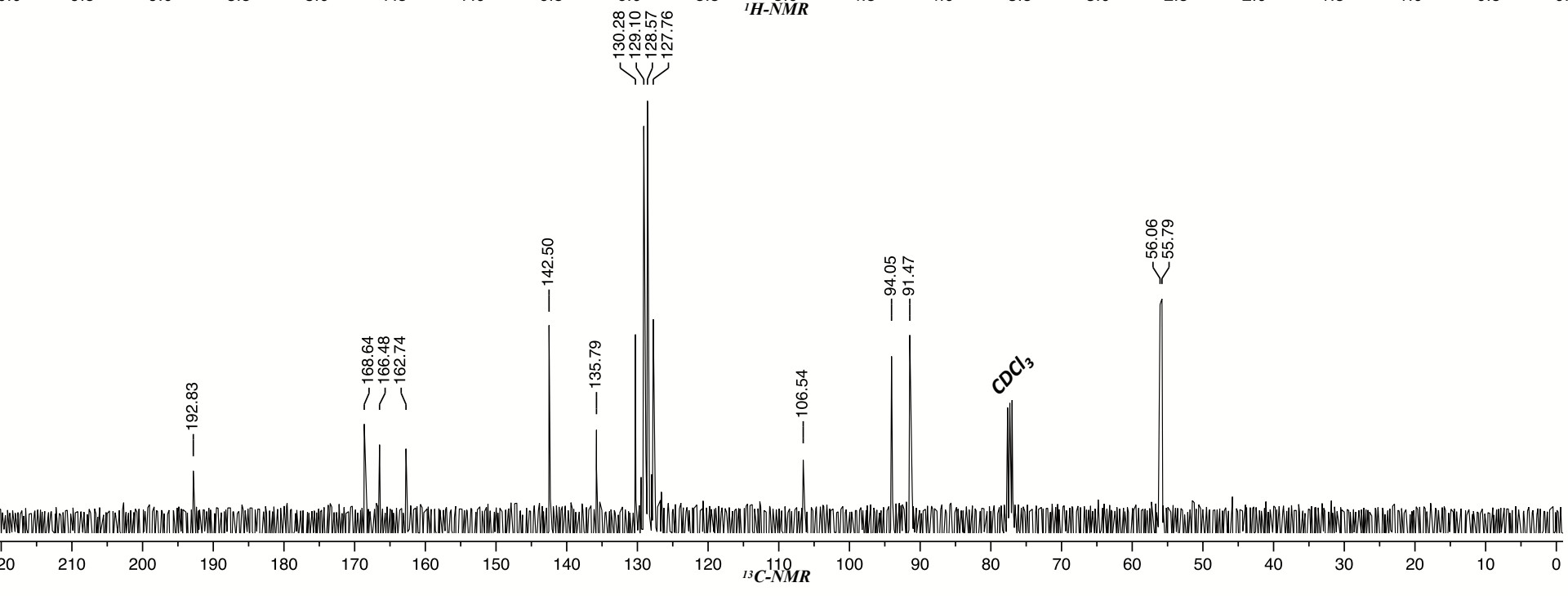
¹H-NMR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168.64
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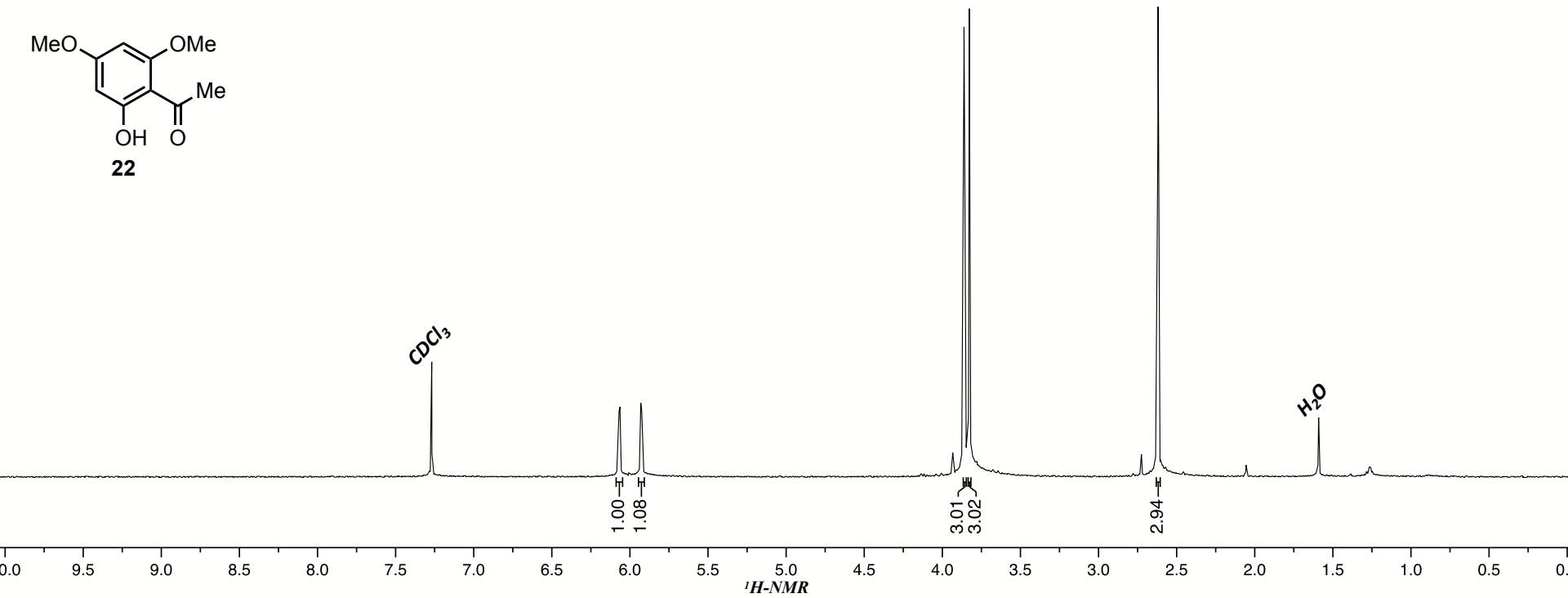
135.79
106.54
192.83
CDCl3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
¹³C-NMR

MeO
OMe
Me
OH
O

22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9.0
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8.0
7.5
7.0
6.5
6.0
5.5
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3.5
3.0
2.5
2.0
1.5
1.0
0.5
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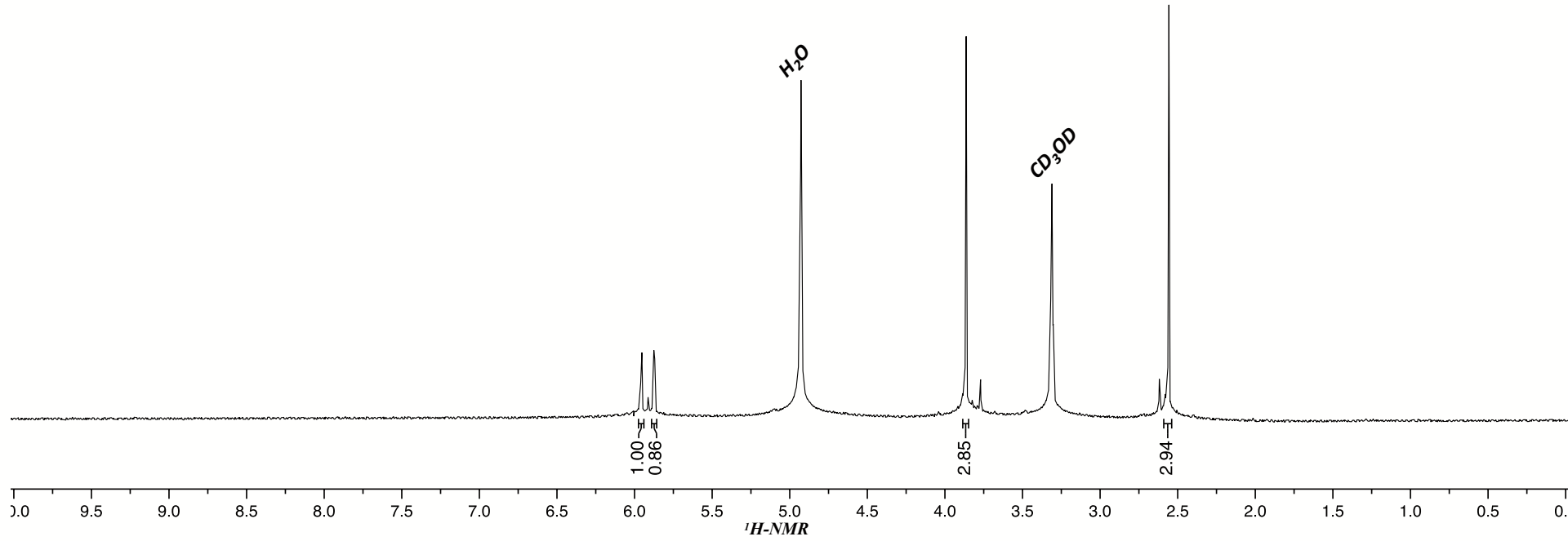
1H-NMR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6.5
6.0
5.5
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1.0
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1H-NMR

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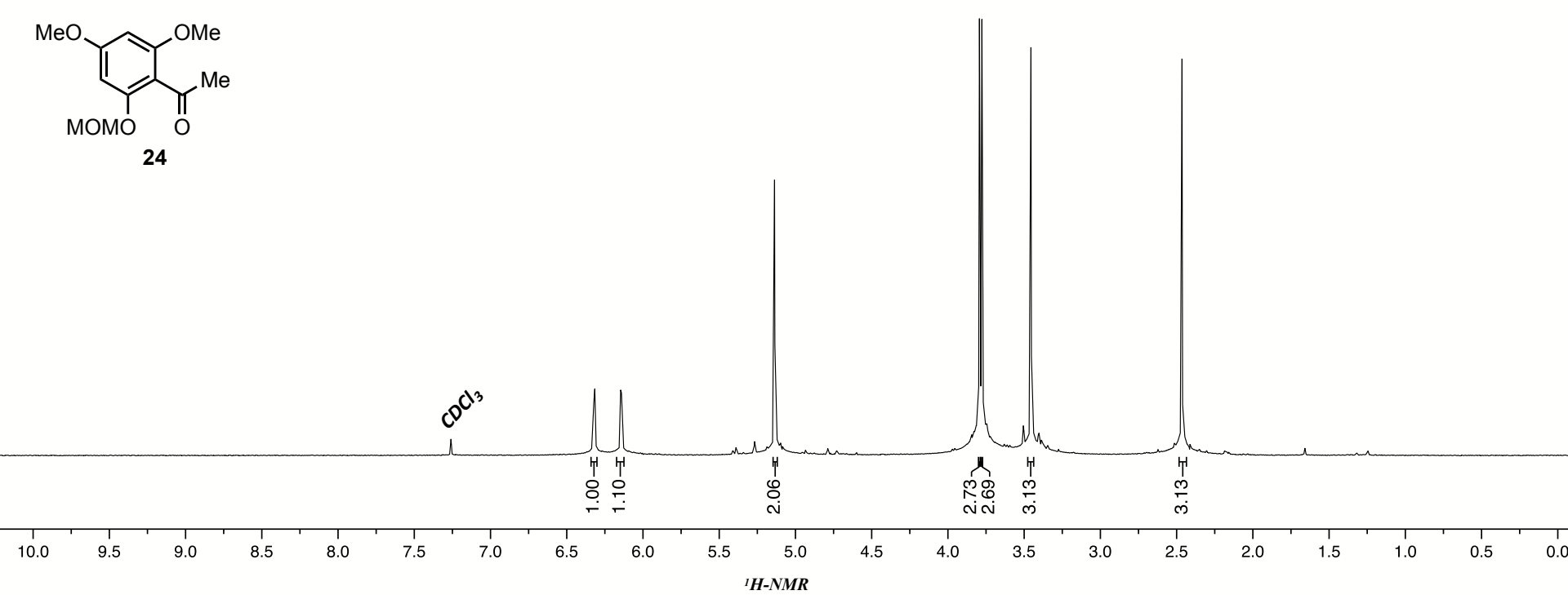

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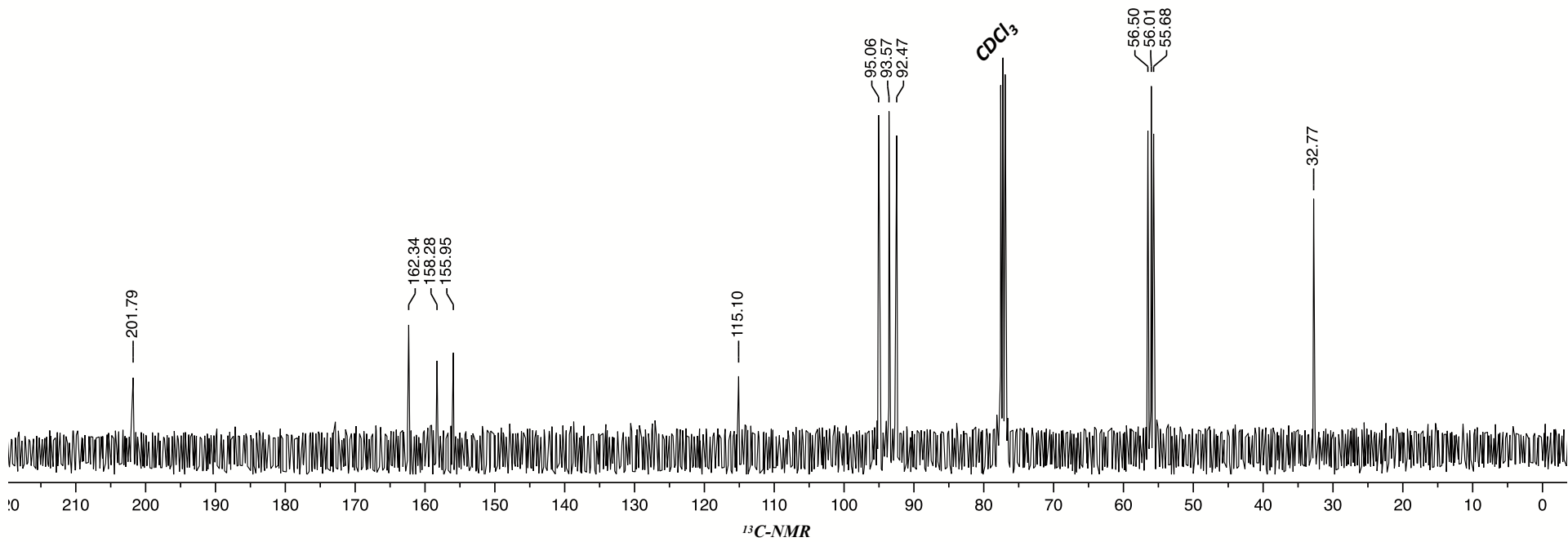

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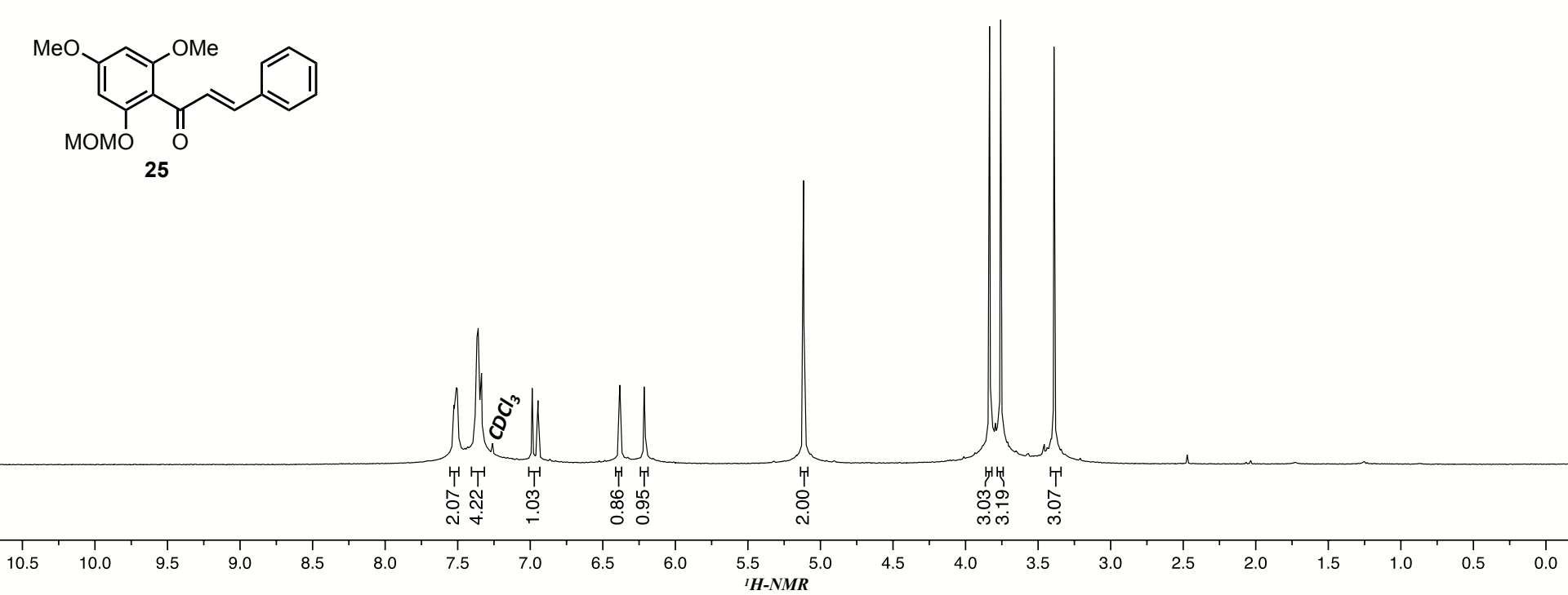

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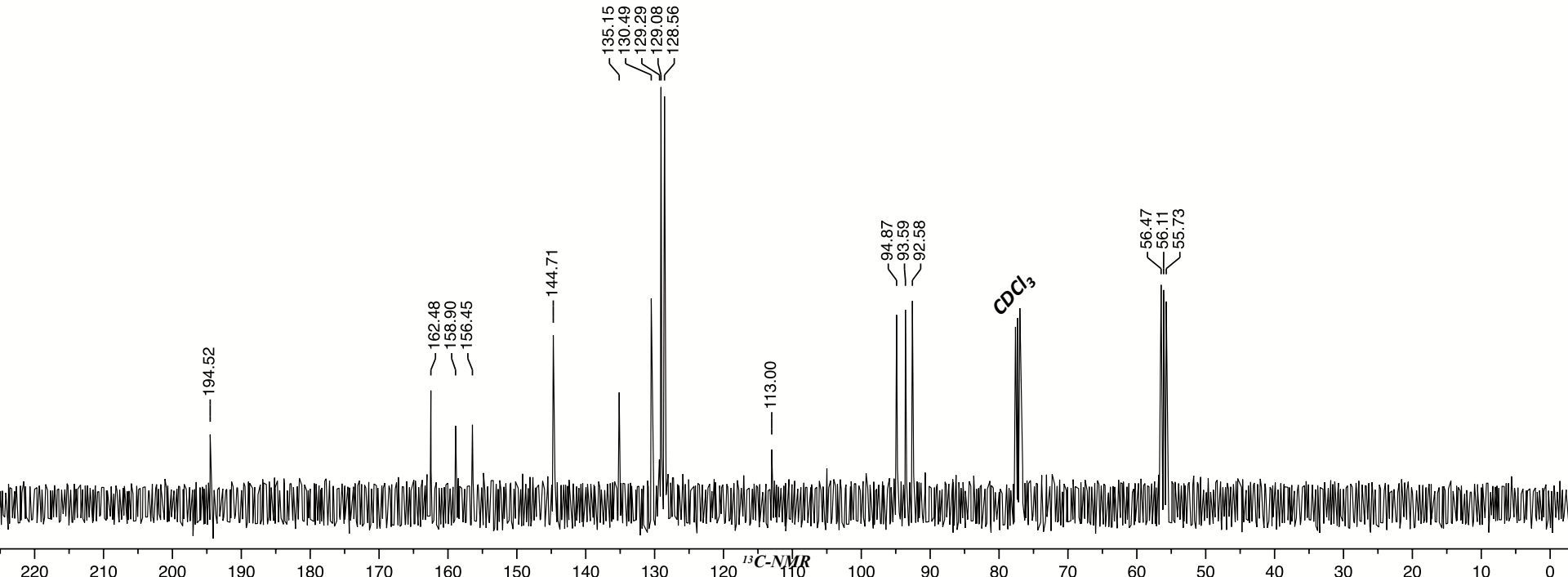

^{13}C-NMR

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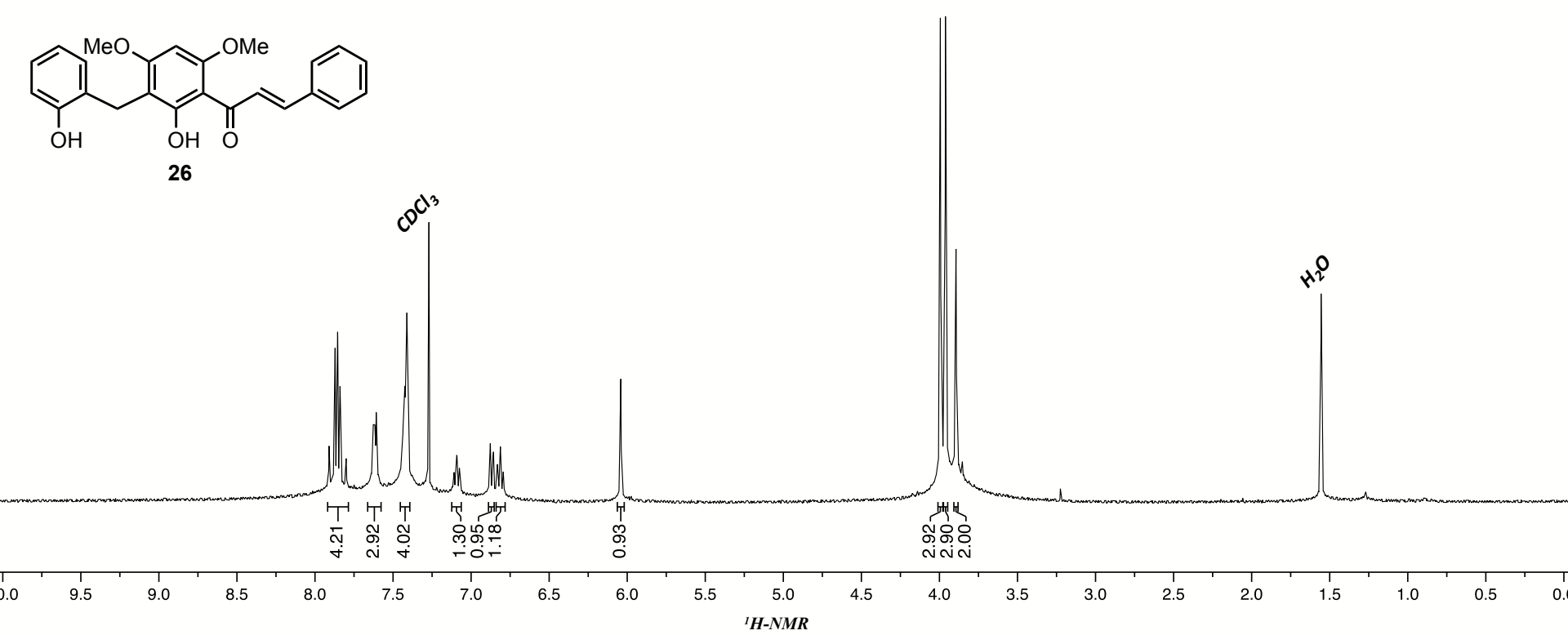

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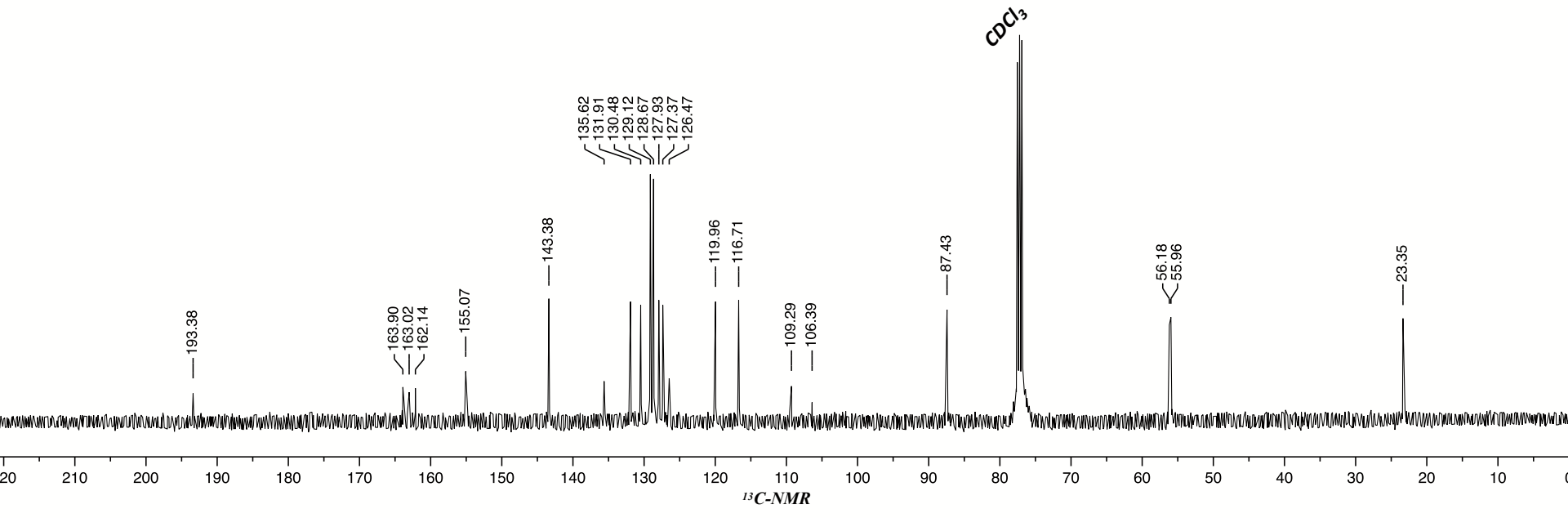

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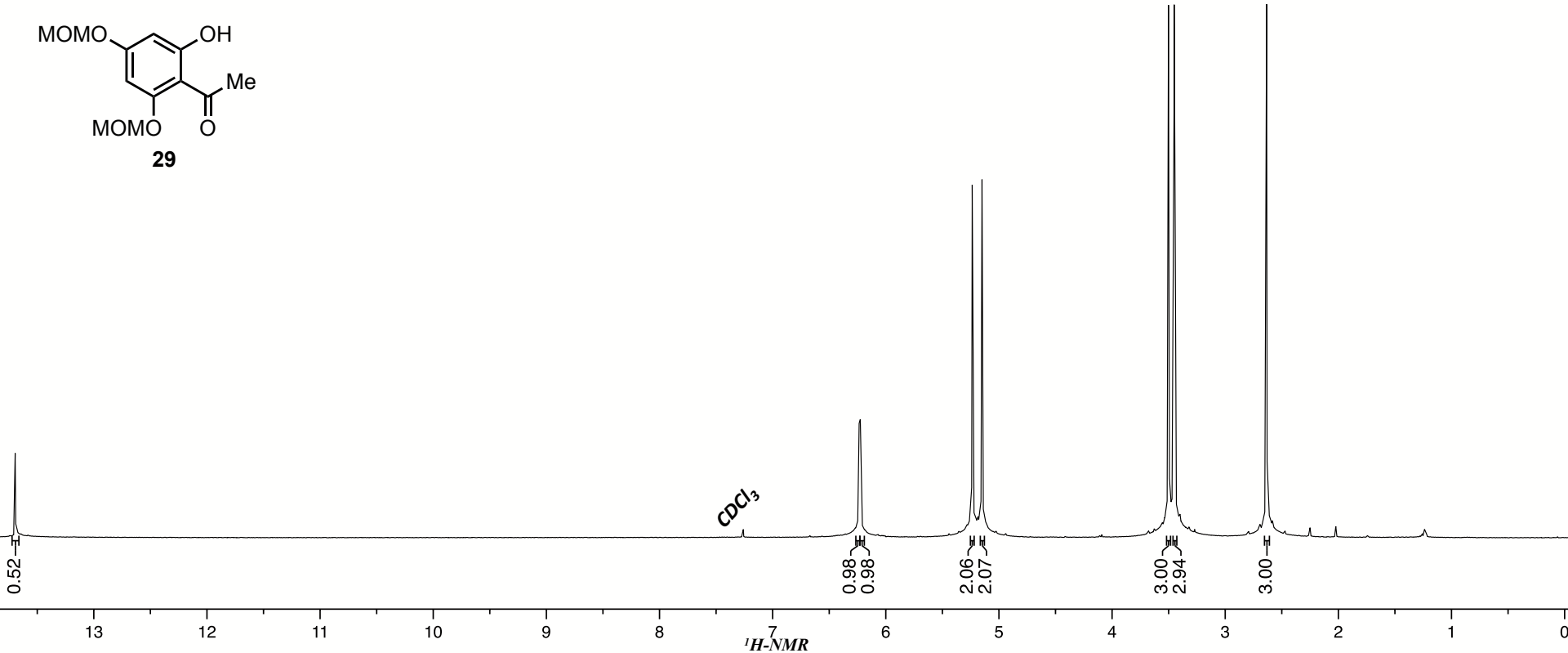

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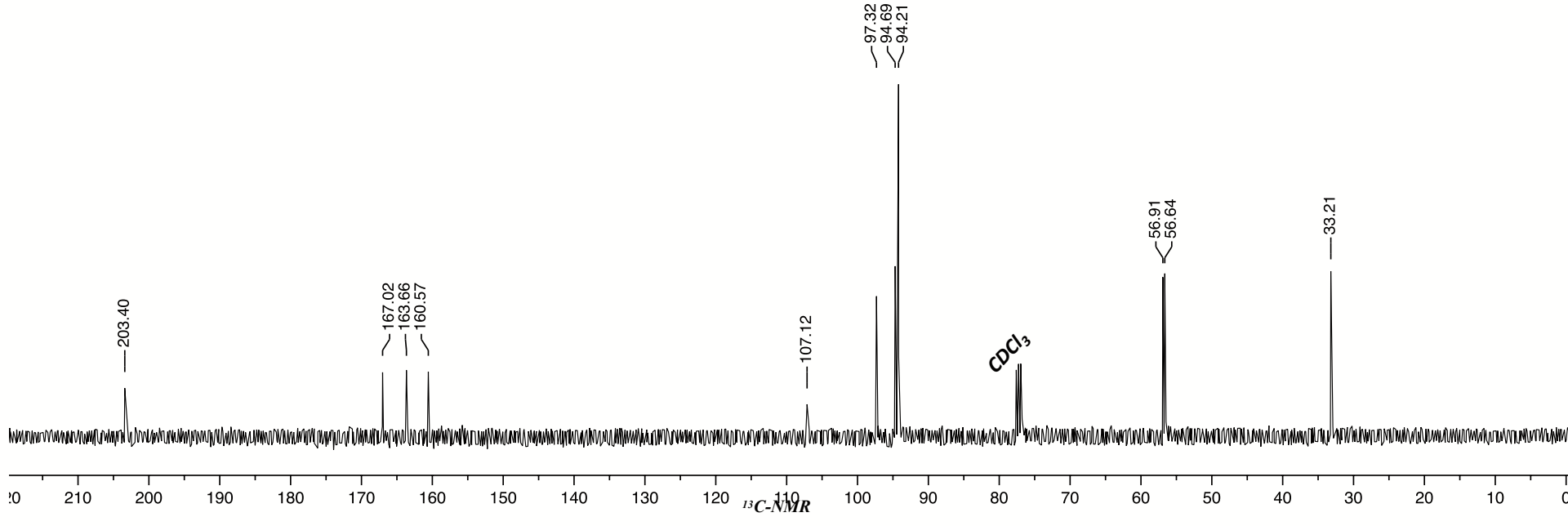

^{13}C-NMR

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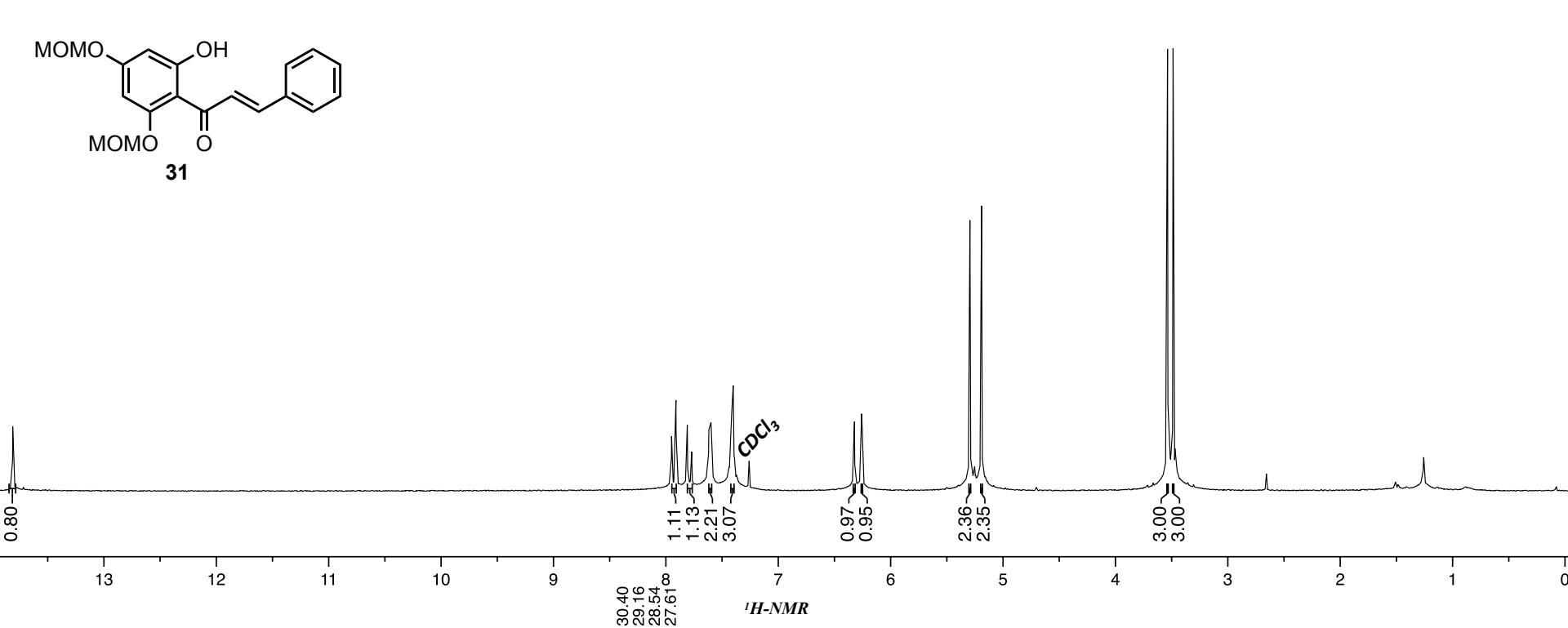
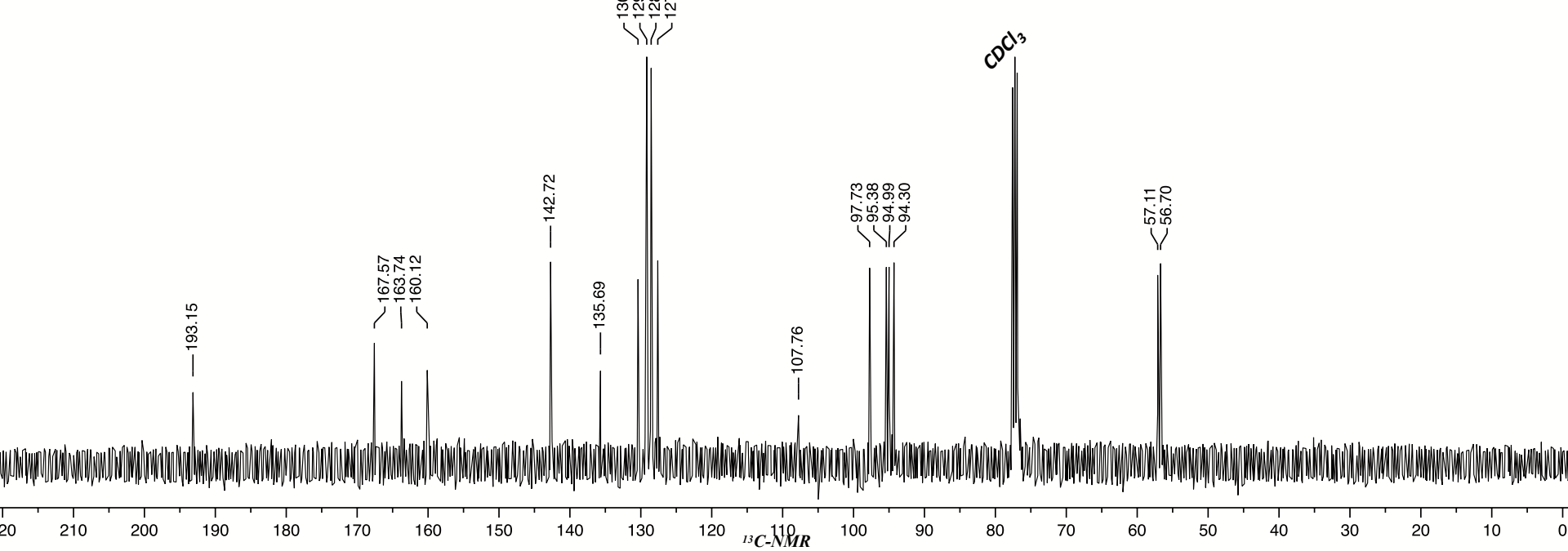
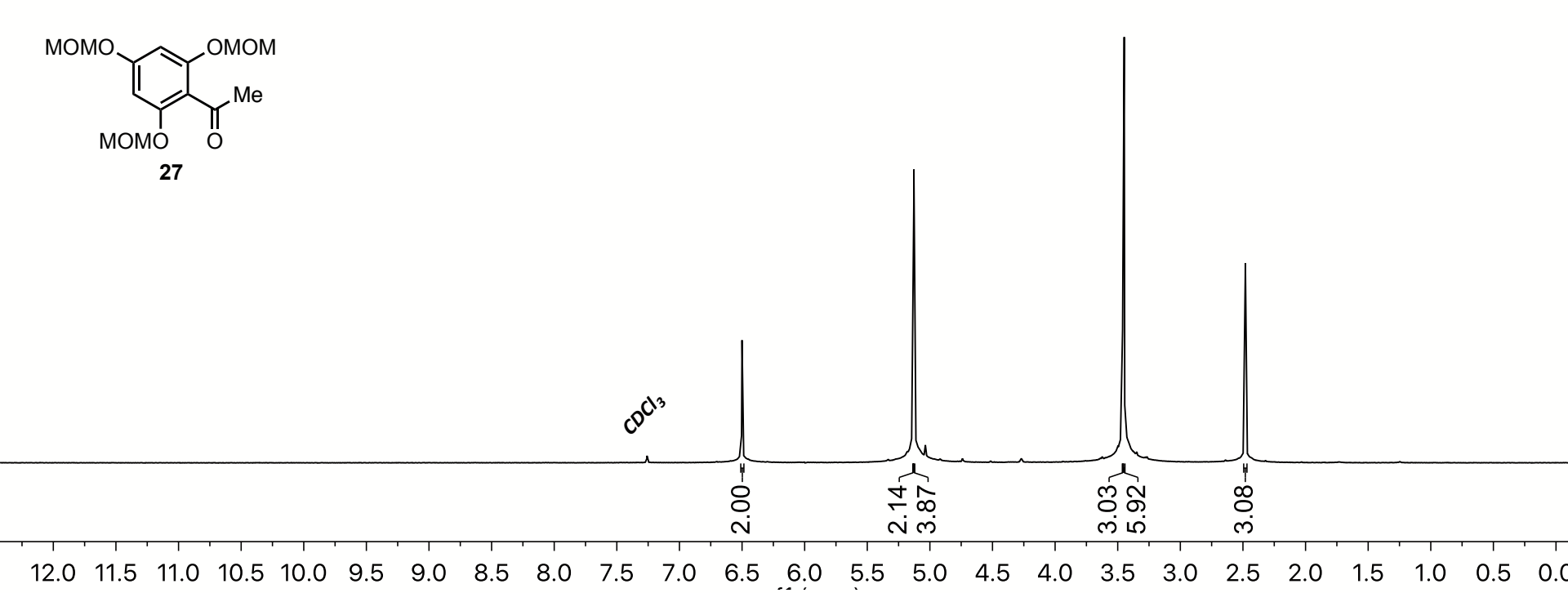


^{1}H-NMR

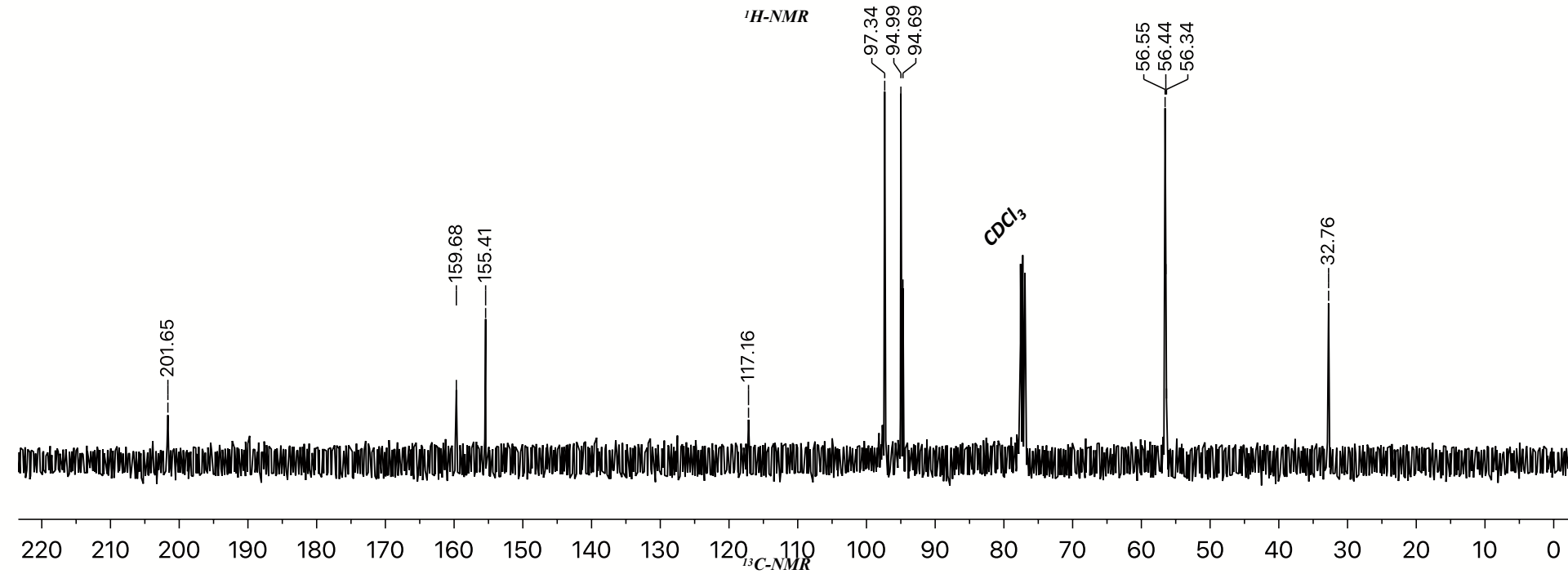


^{13}C-NMR

27



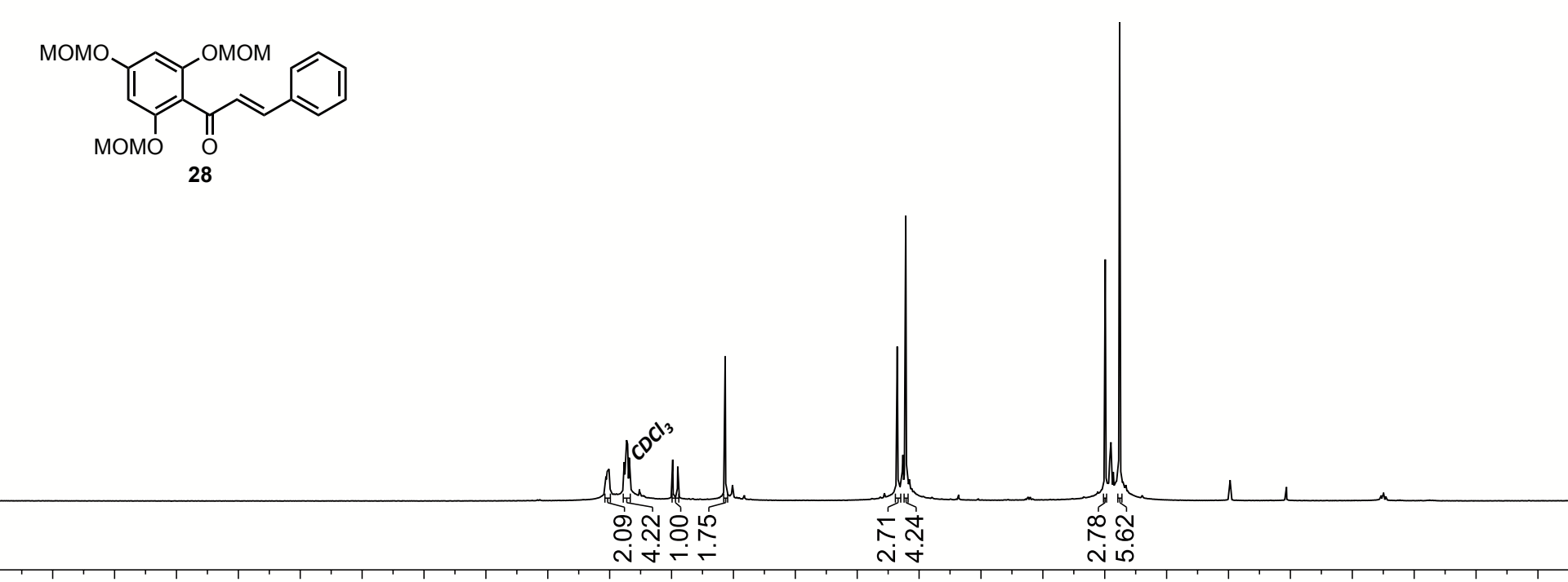
^{1}H-NMR



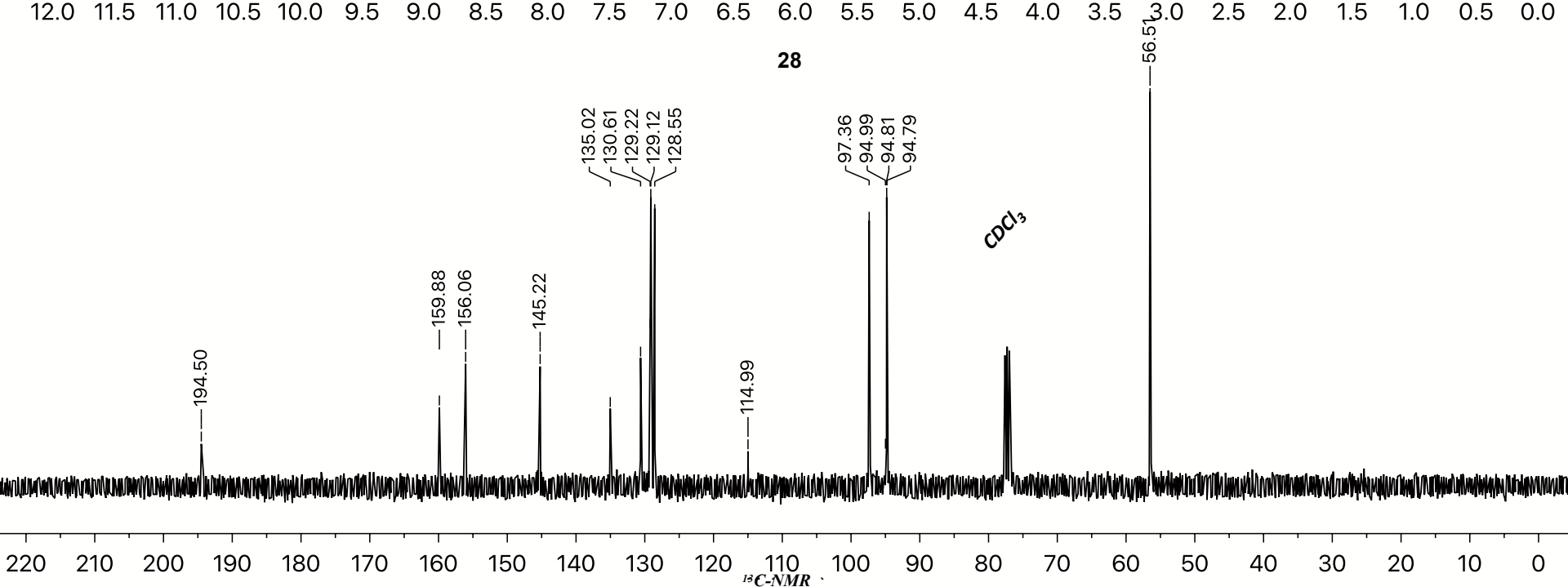
^{13}C-NMR

MOMO
OMOM
MOMO
O

28

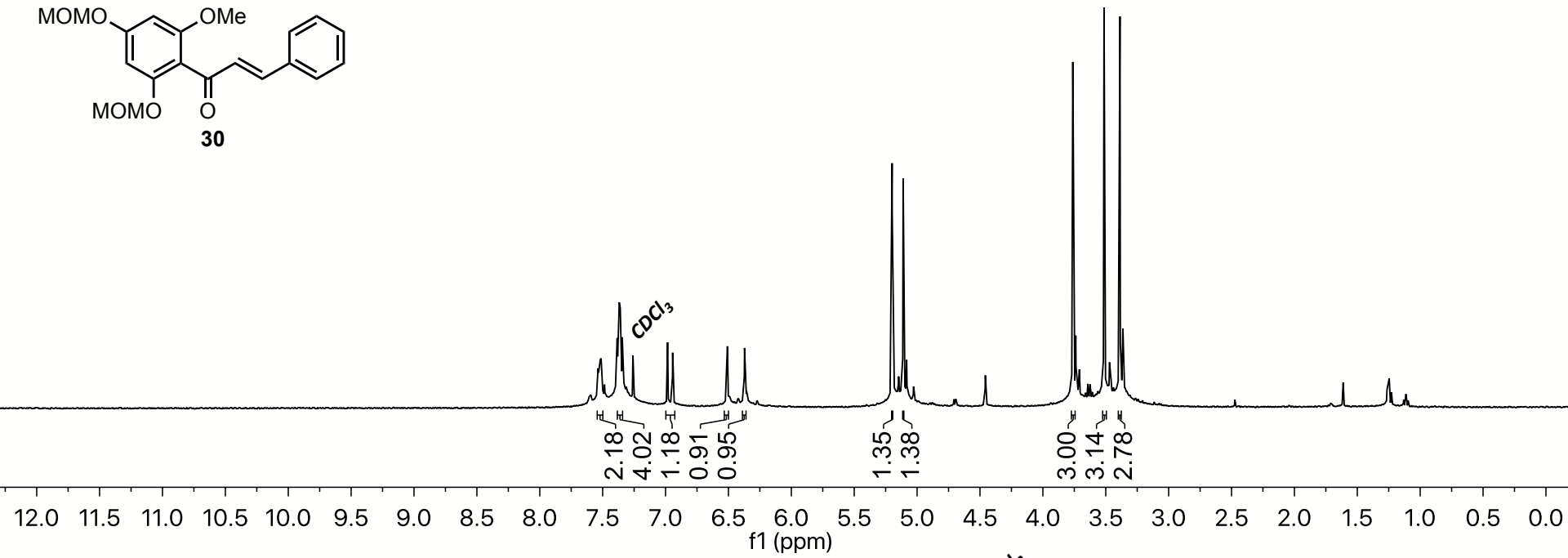

CDCl3
2.09
4.22
1.00
1.75
2.71
4.24
2.78
5.62
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

28

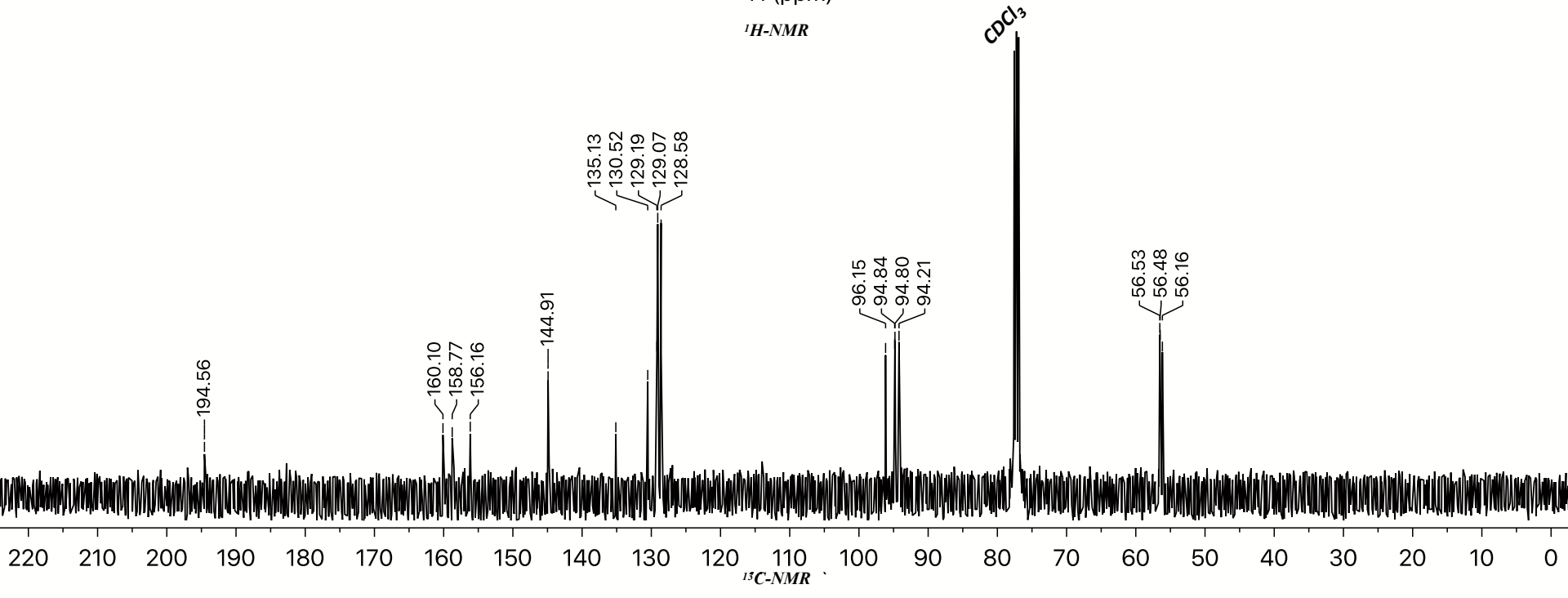

194.50
159.88
156.06
145.22
135.02
130.61
129.22
129.12
128.55
114.99
97.36
94.99
94.81
94.79
CDCl3
56.51
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

^{13}C-NMR

30

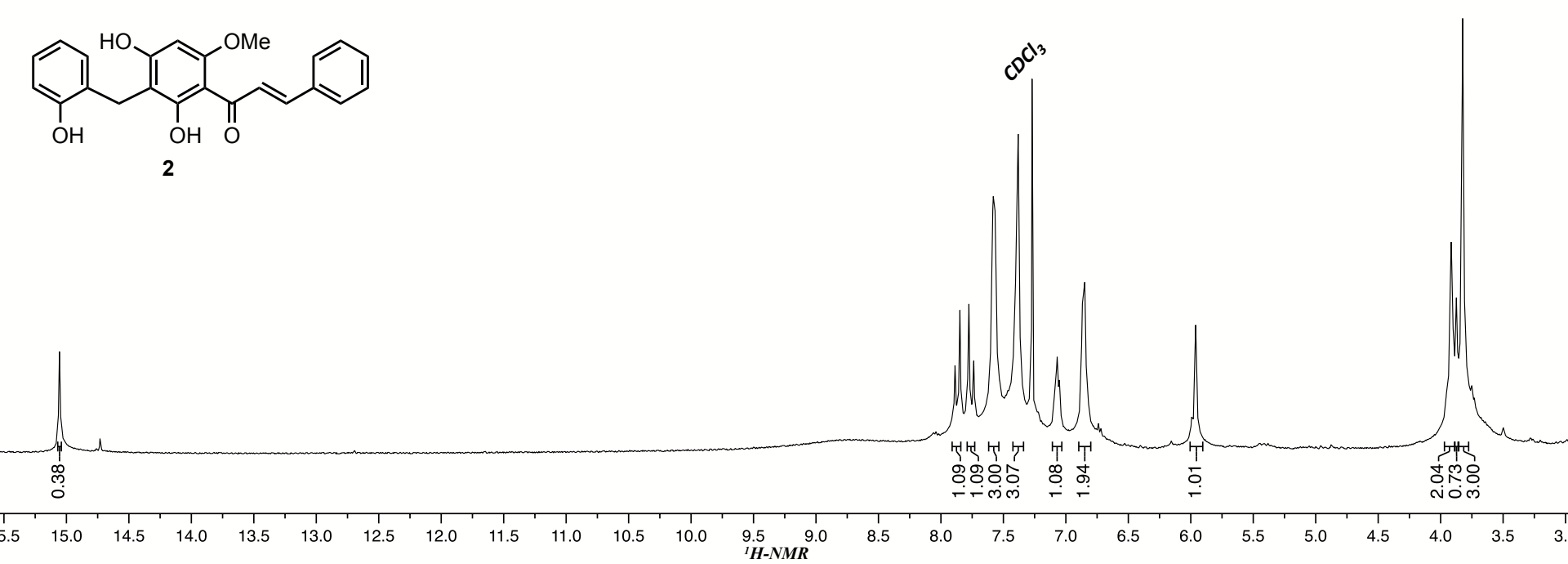


^{1}H-NMR

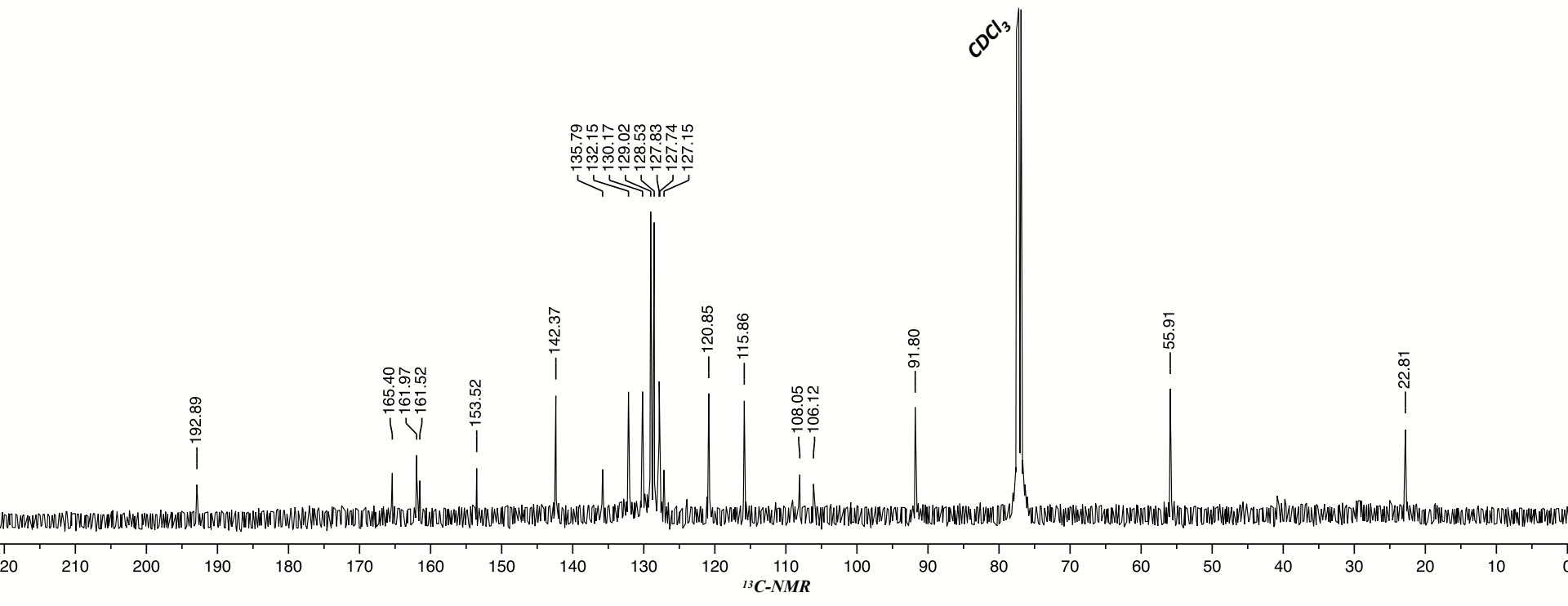


^{13}C-NMR

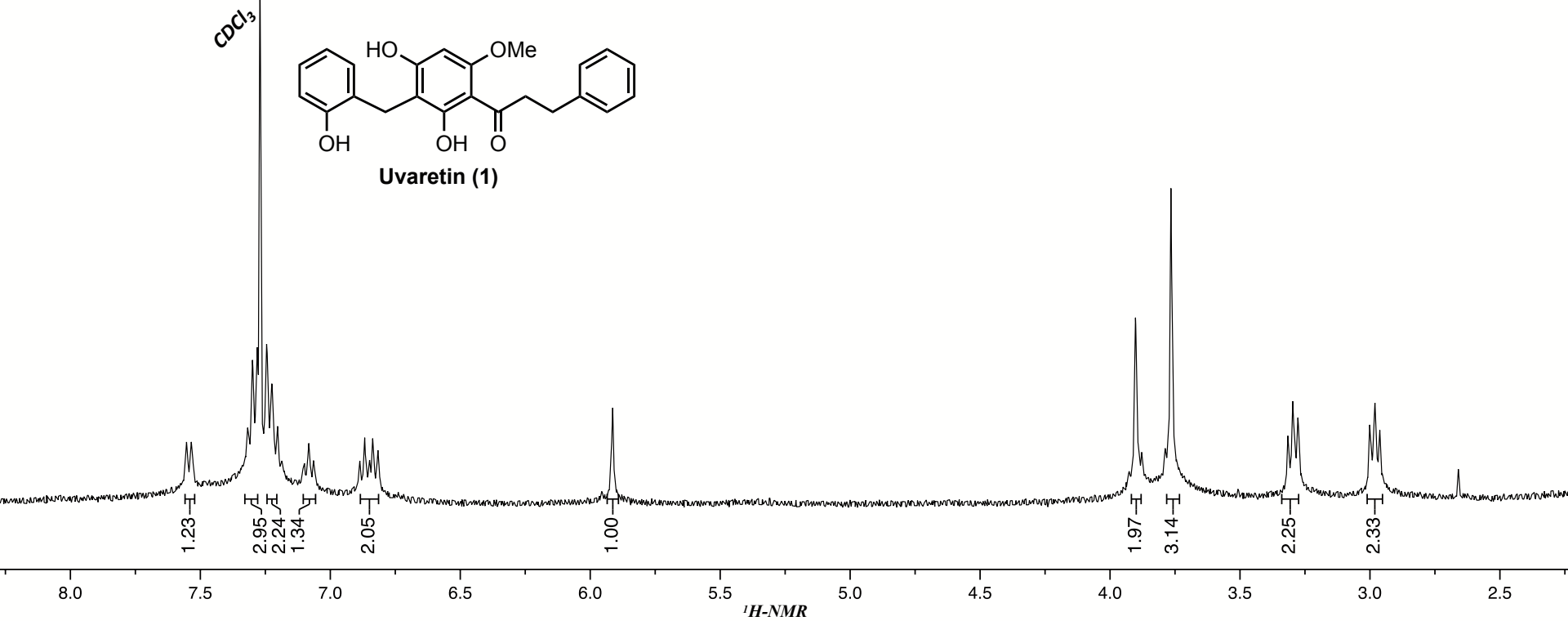
2

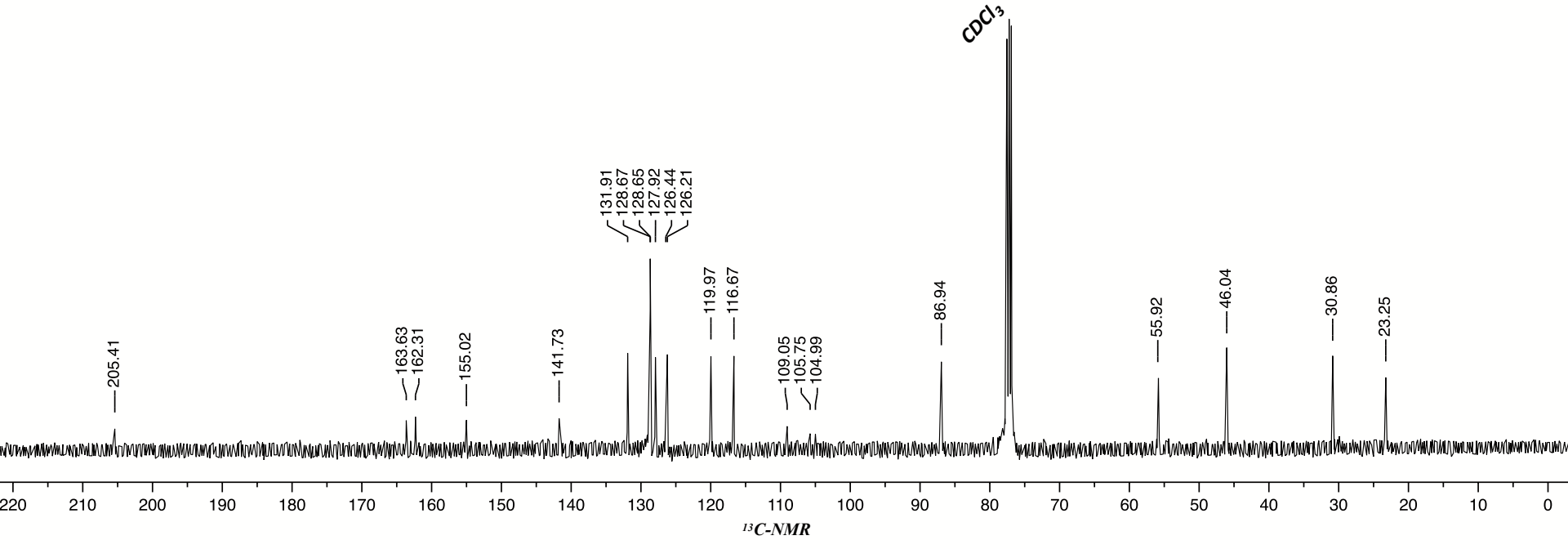


^{1}H-NMR



^{13}C-NMR


CDCl3
HO
OMe
OH
OH
O
Uvaretin (1)
1.23
2.95
2.24
1.34
2.05
1.00
1.97
3.14
2.25
2.33
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
1H-NMR


CDCl3
205.41
163.63
162.31
155.02
141.73
131.91
128.67
128.65
127.92
126.44
126.21
119.97
116.67
109.05
105.75
104.99
86.94
55.92
46.04
30.86
23.25
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
13C-NMR