Supporting information

Design, synthesis and biological evaluation novel 3,4-dihydro-2(1*H*)-quinoline-*O*-carbamate derivatives as AChE/MAO-B dual inhibitors for the treatment of Alzheimer's disease

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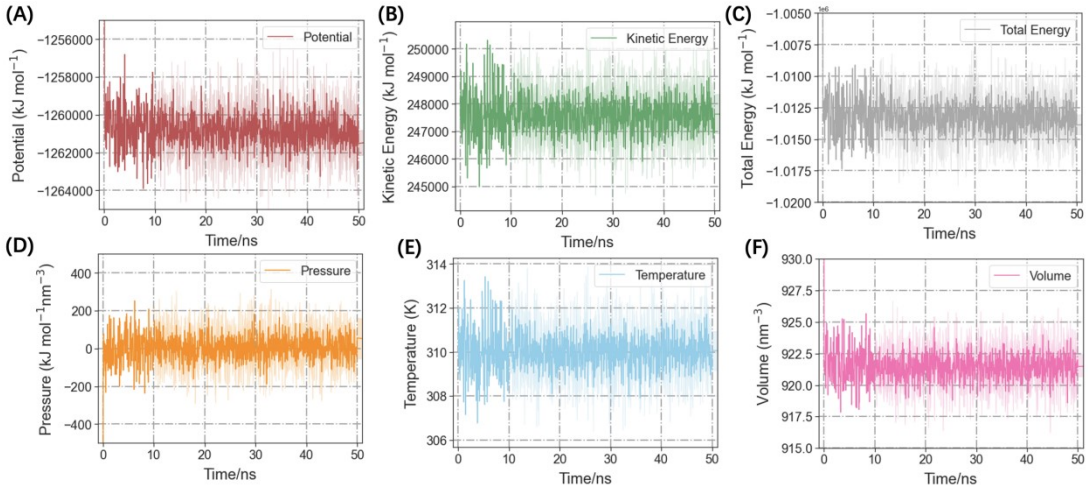


Figure S1. Energy fluctuations of AChE-3c complex during MD simulations. (A) Potential, (B) Kinetic energy, (C) Total energy, (D) Pressure, (E) Temperature and (F) Volume. Each simulation was repeated three times, and the error bars for the three simulations were represented with light shading.

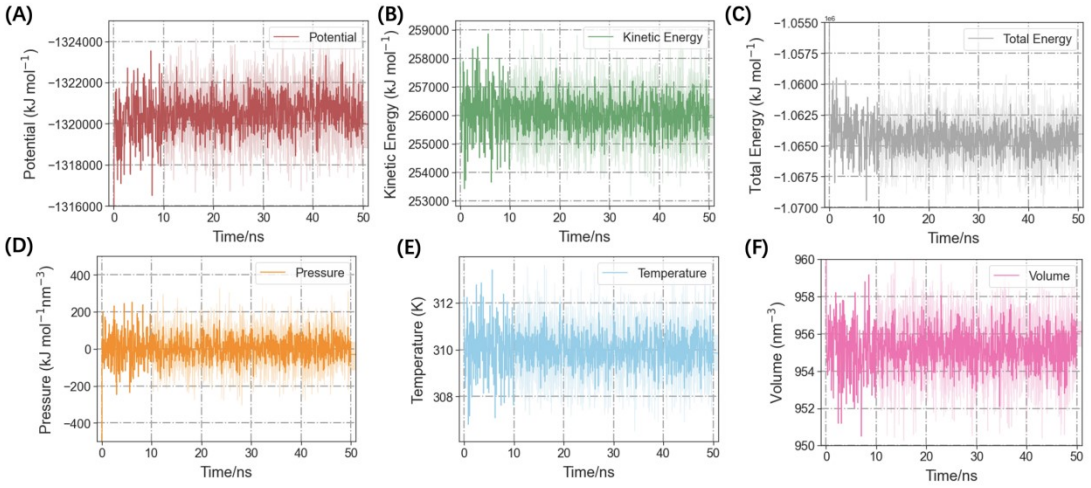


Figure S2. Energy fluctuations of MAOB-3c complex during MD simulations. (A) Potential, (B) Kinetic energy, (C) Total energy, (D) Pressure, (E) Temperature and (F) Volume. Each simulation was repeated three times, and the error bars for the three simulations were represented with light shading.

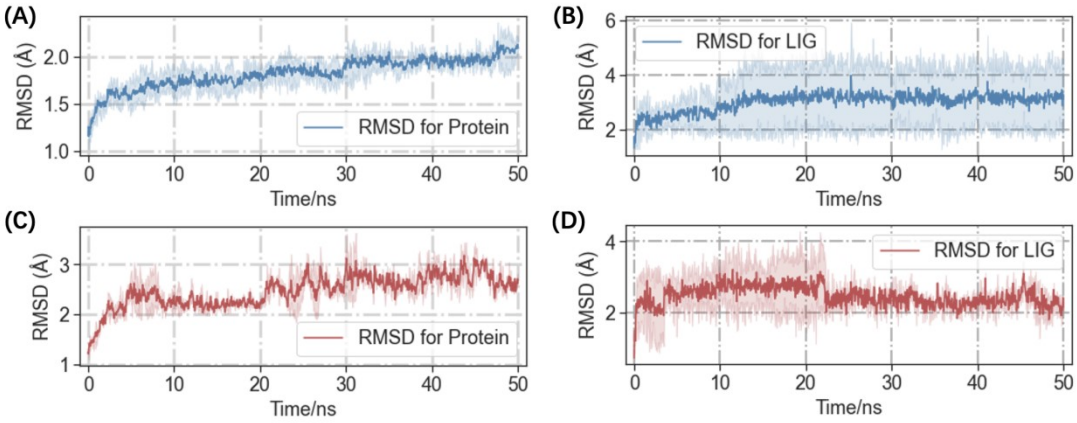
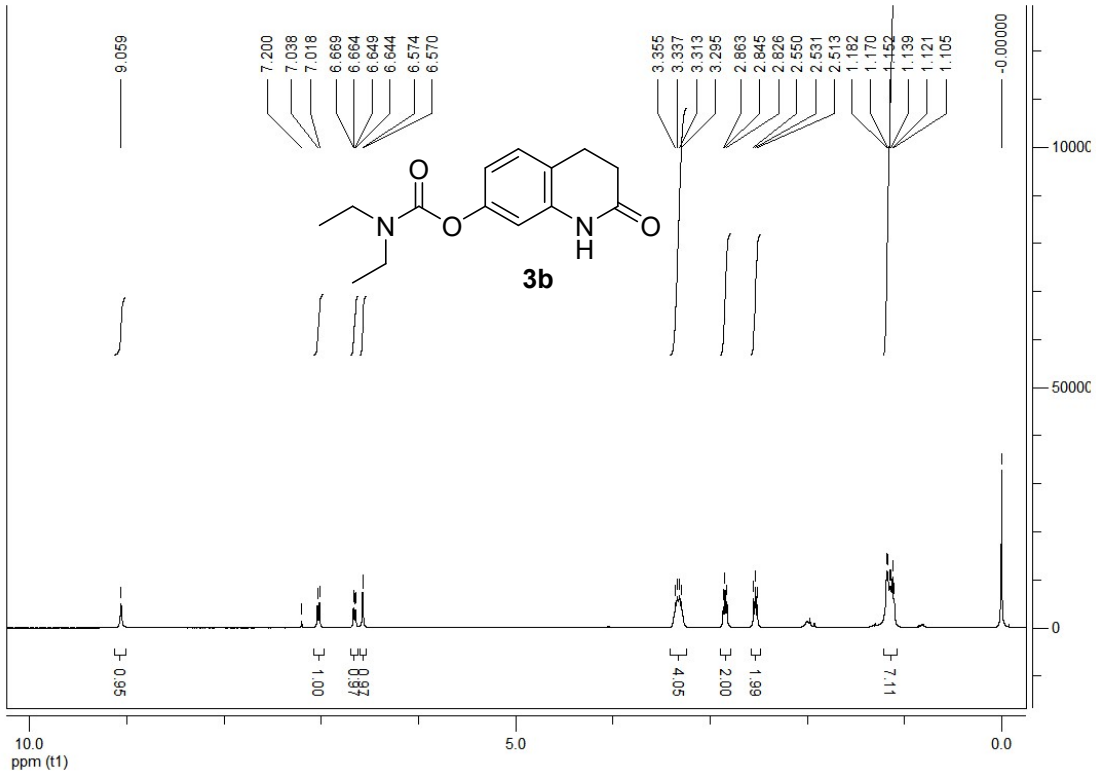
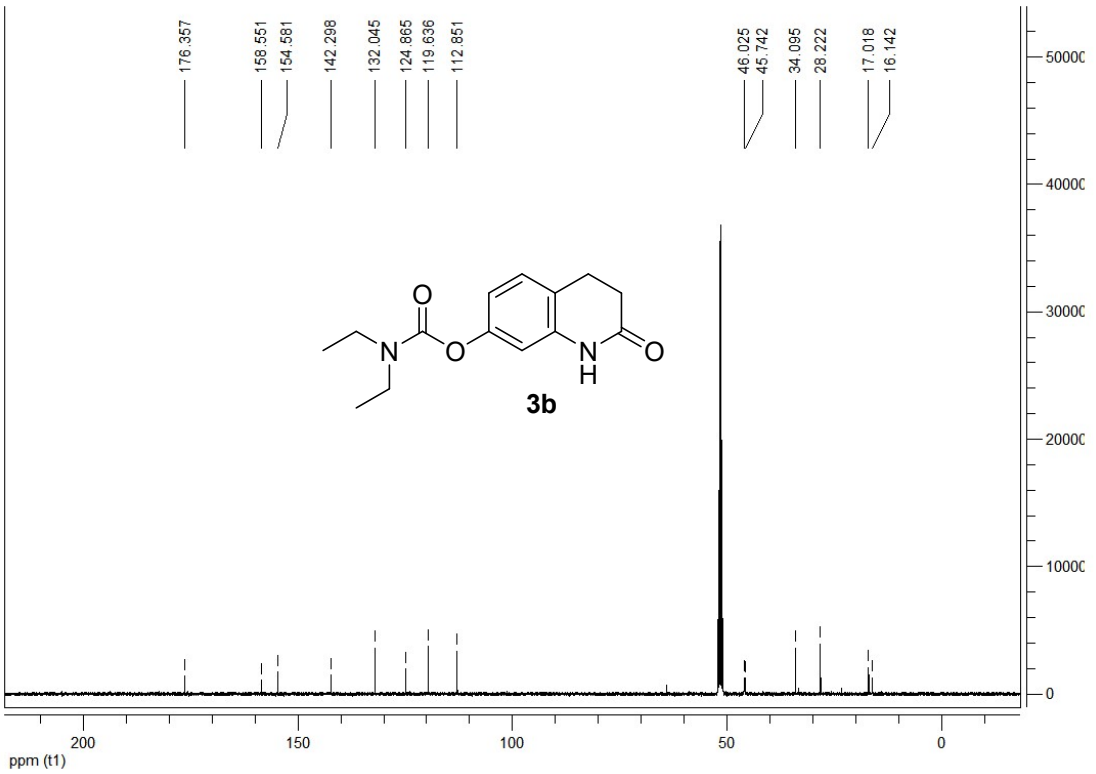
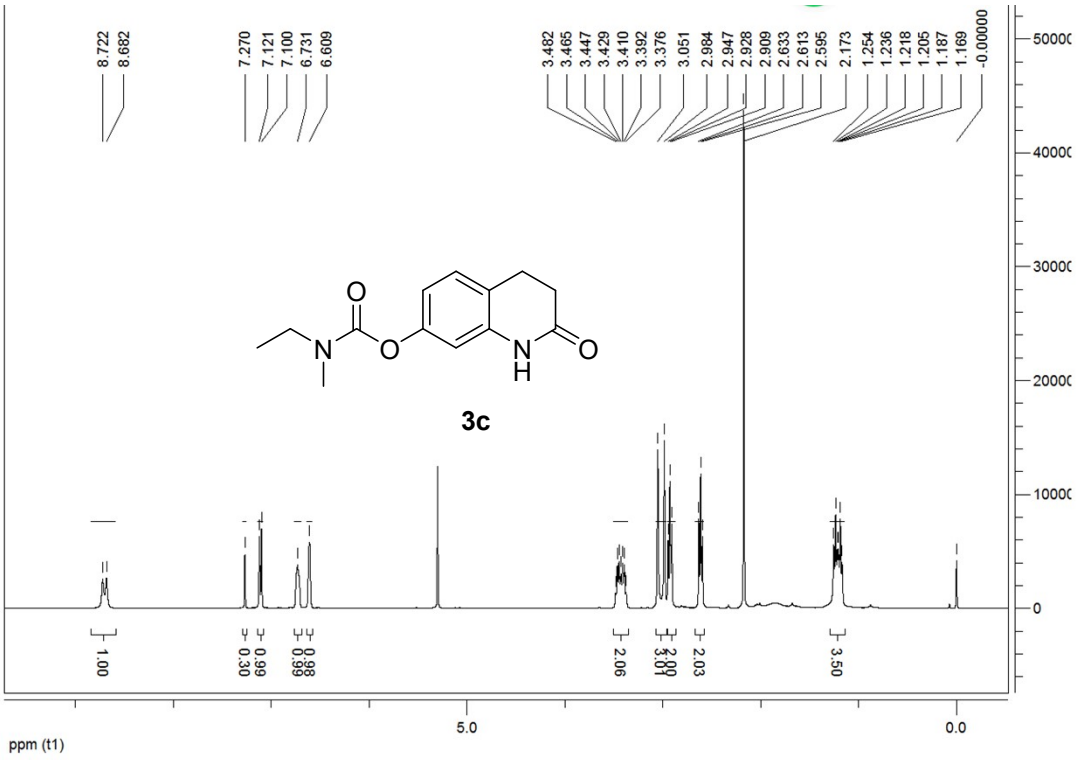


Figure S3. The stability of AChE-3c (A-B) and MAOB-3c (C-D) complexes. The root mean square deviation (RMSD) of the AChE (A) and compound **3c** (B) during 50ns MD simulations. The root mean square deviation (RMSD) of the MAO-B (C) and compound **3c** (D) during 50ns MD simulations. Each simulation was repeated three times, and the error bars for the three simulations were represented with light shading.

➢ The representative ^{1}H, ^{13}C NMR spectra for the synthesized compounds



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3.376
3.051
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2.947
2.928
2.909
2.633
2.613
2.595
2.173
1.254
1.236
1.218
1.205
1.187
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1.00
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2.00
2.03
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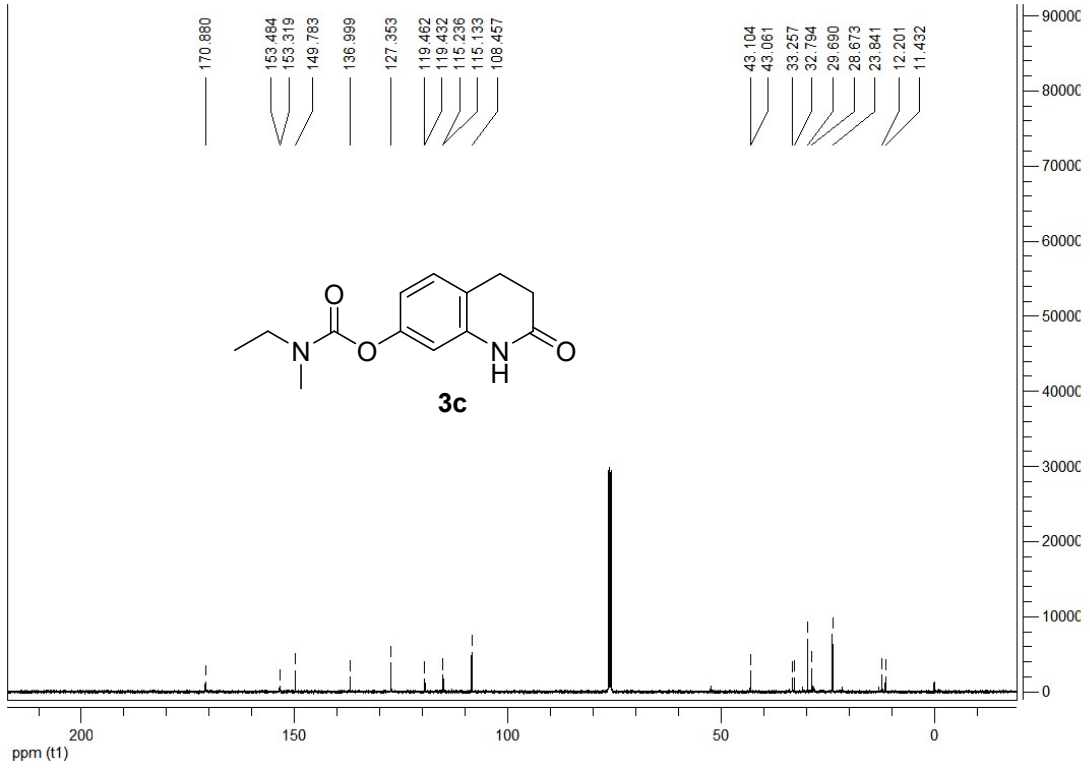
0.0
ppm (t1)
3c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ppm (t1)
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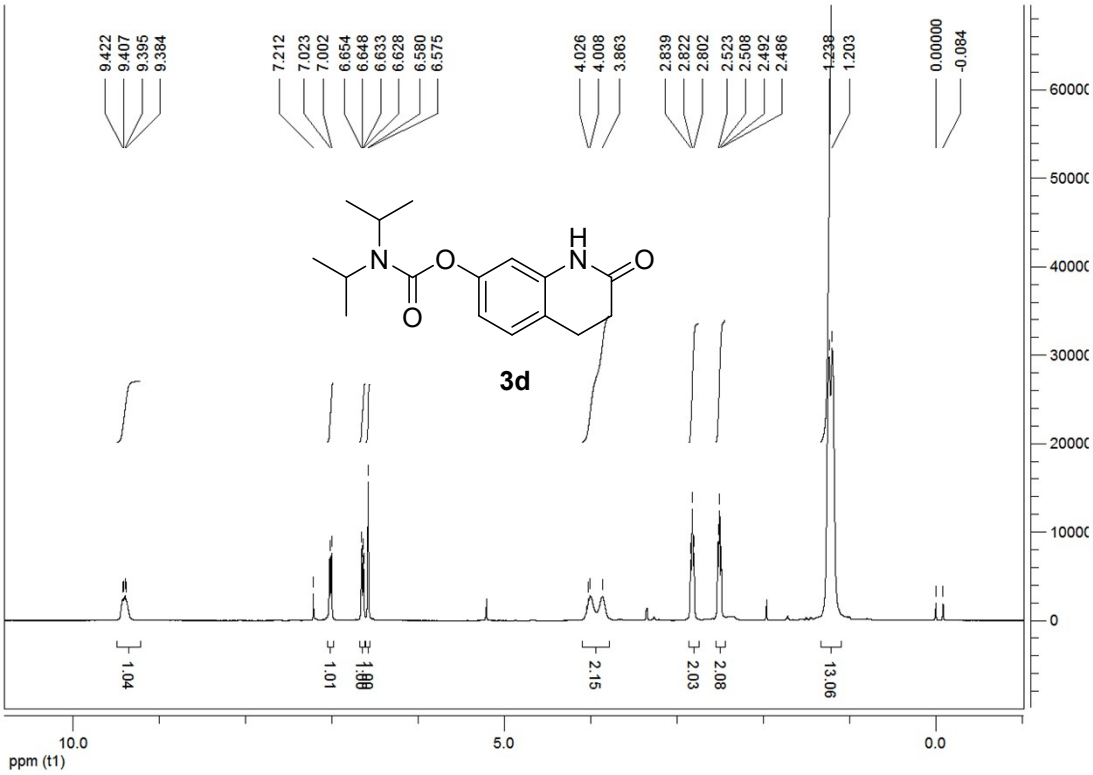
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4.026
4.008
3.863
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2.802
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2.492
2.486
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1.04
1.01
1.00
2.15
2.03
2.08
13.06
10.0
5.0
0.0
ppm (t1)

3d


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138.044
128.373
120.357
116.256
109.571
77.390
77.072
76.754
47.005
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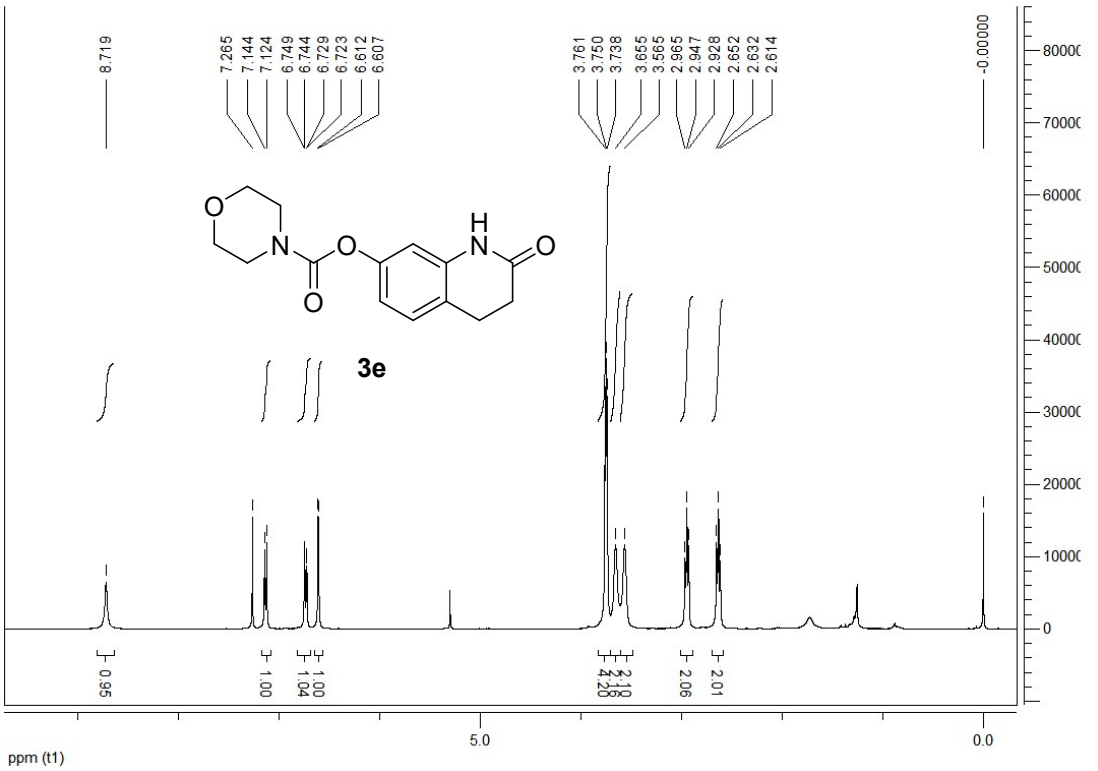
ppm (t1)

3d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3.738
3.655
3.565
2.965
2.947
2.928
2.652
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2.614
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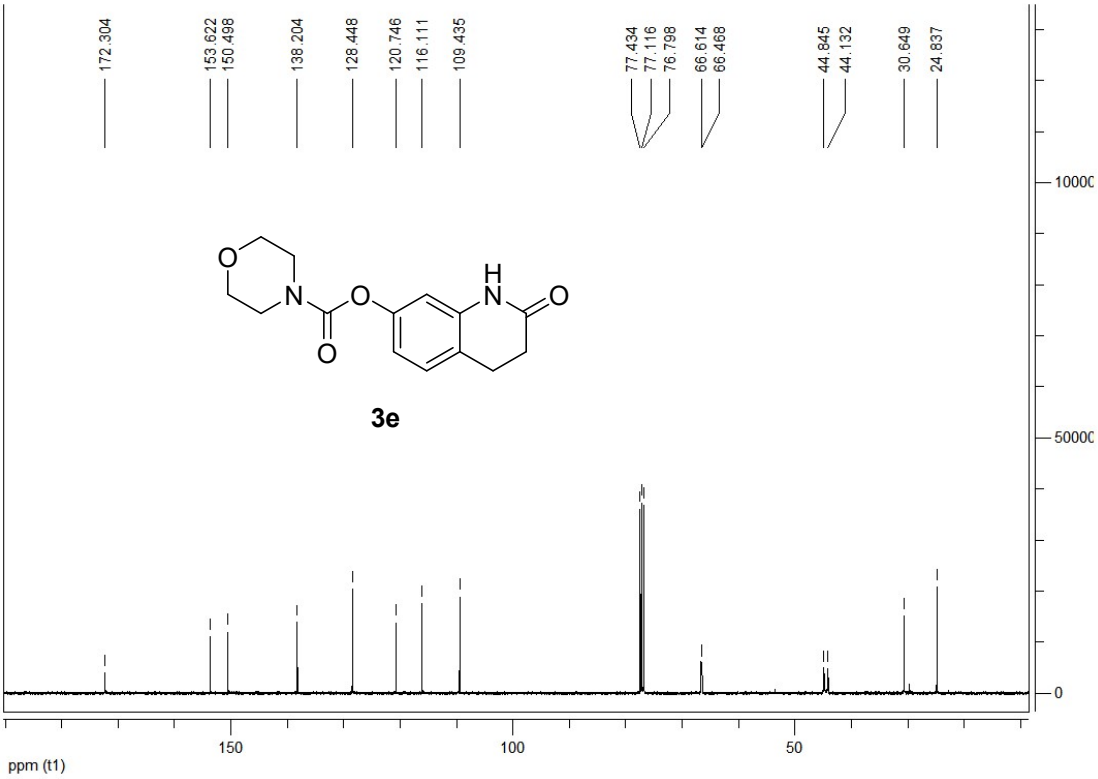
ppm (t1)

3e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44.845
44.132
30.649
24.837
150
100
50
ppm (t1)

3e


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7.334
7.328
7.319
7.304
7.299
7.214
7.210
7.195
7.027
7.006
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6.733
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6.658
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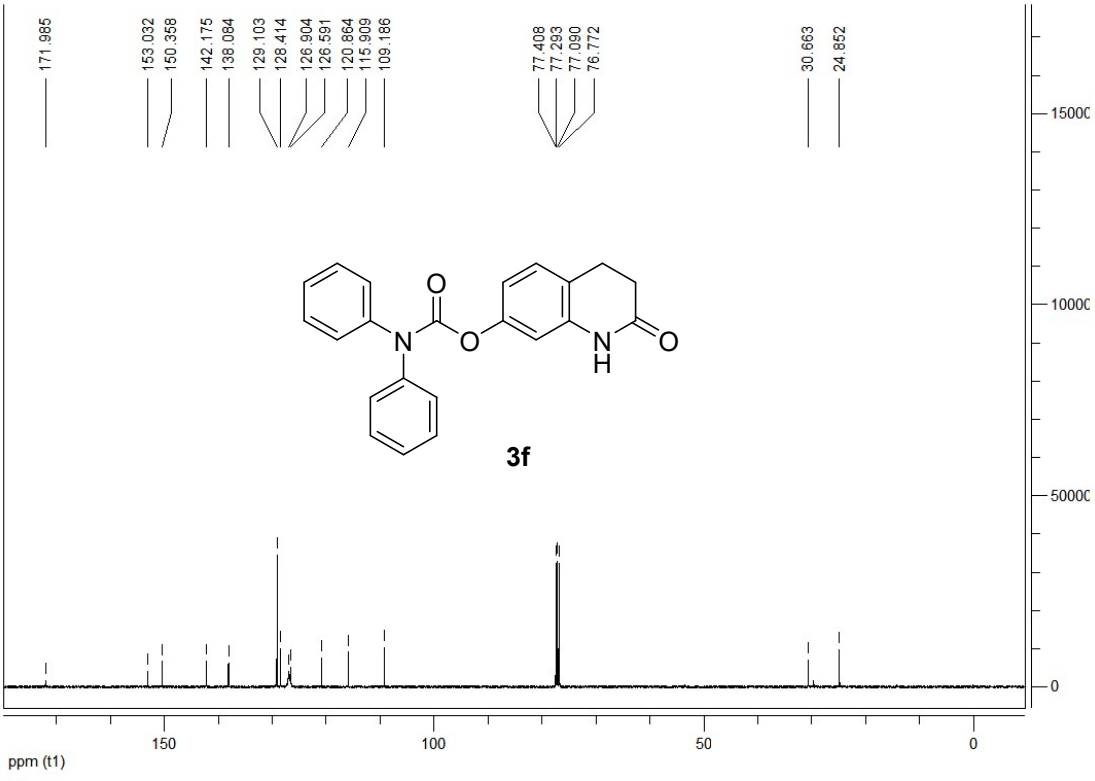
ppm (t1)

3f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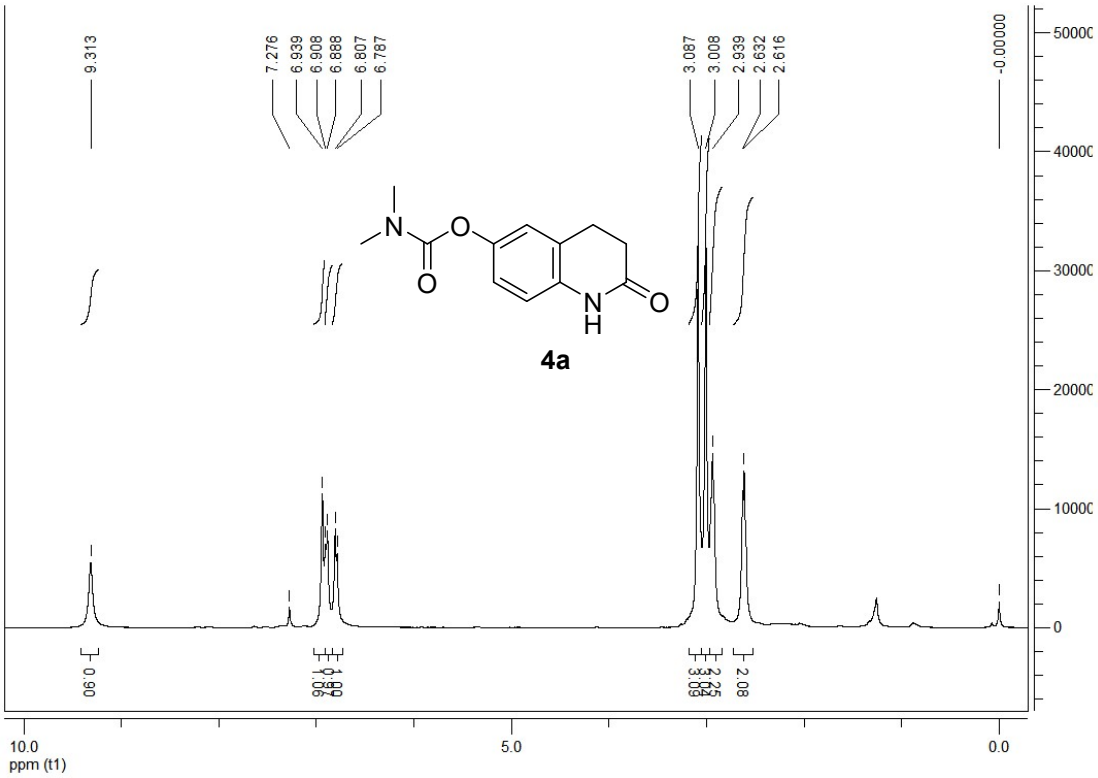
ppm (t1)

3f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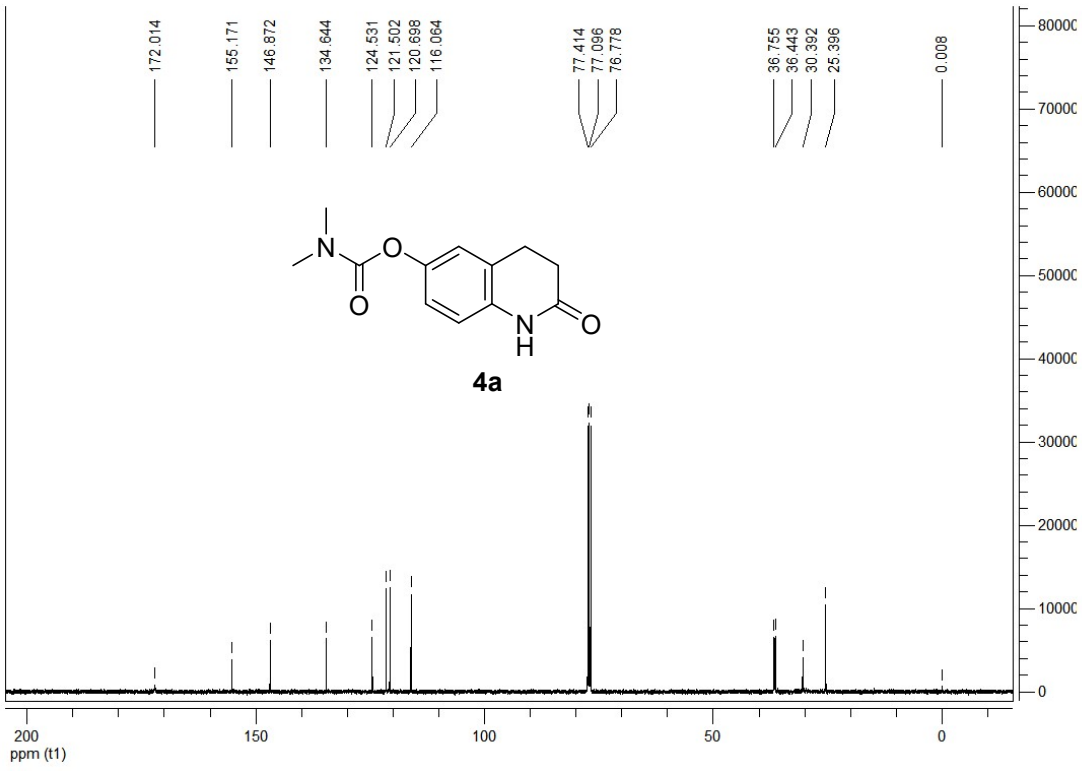
4a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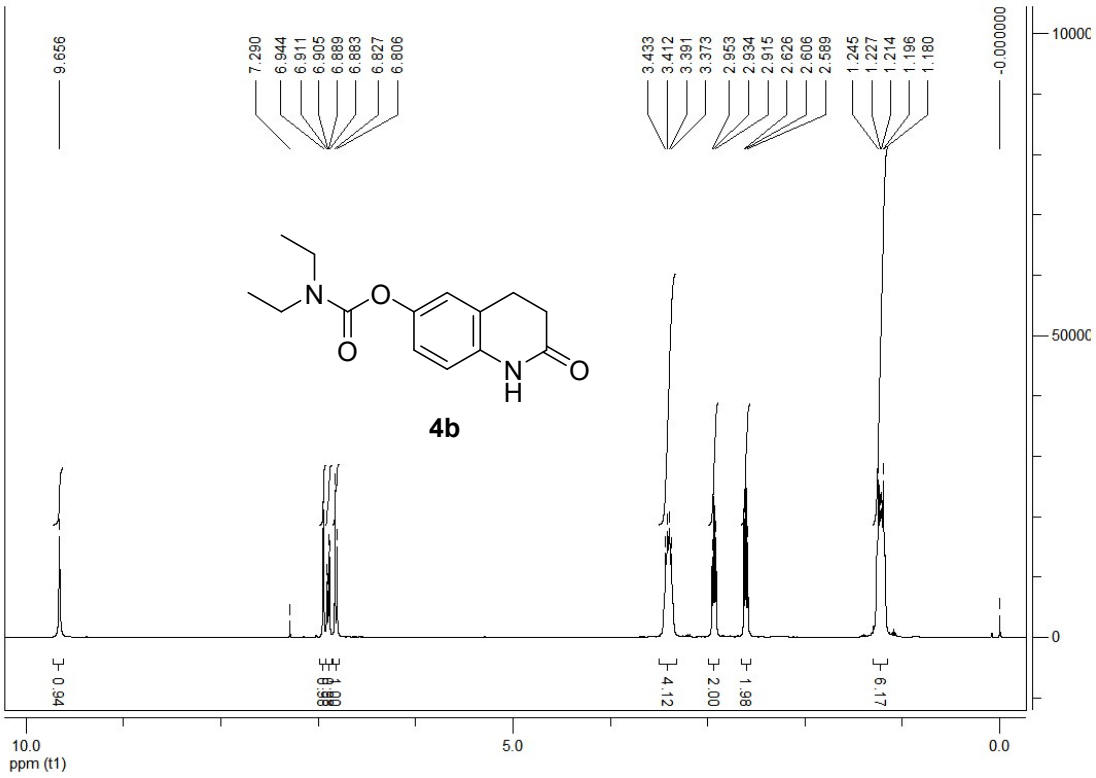
4a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3.373
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2.934
2.915
2.626
2.606
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1.214
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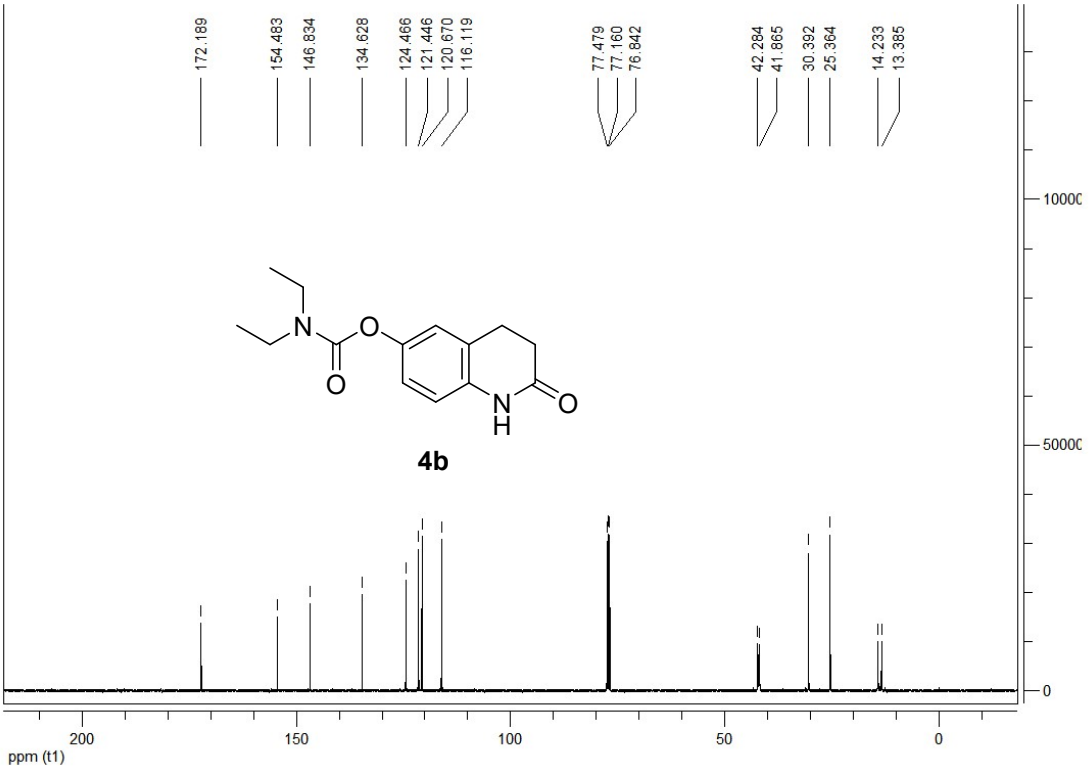
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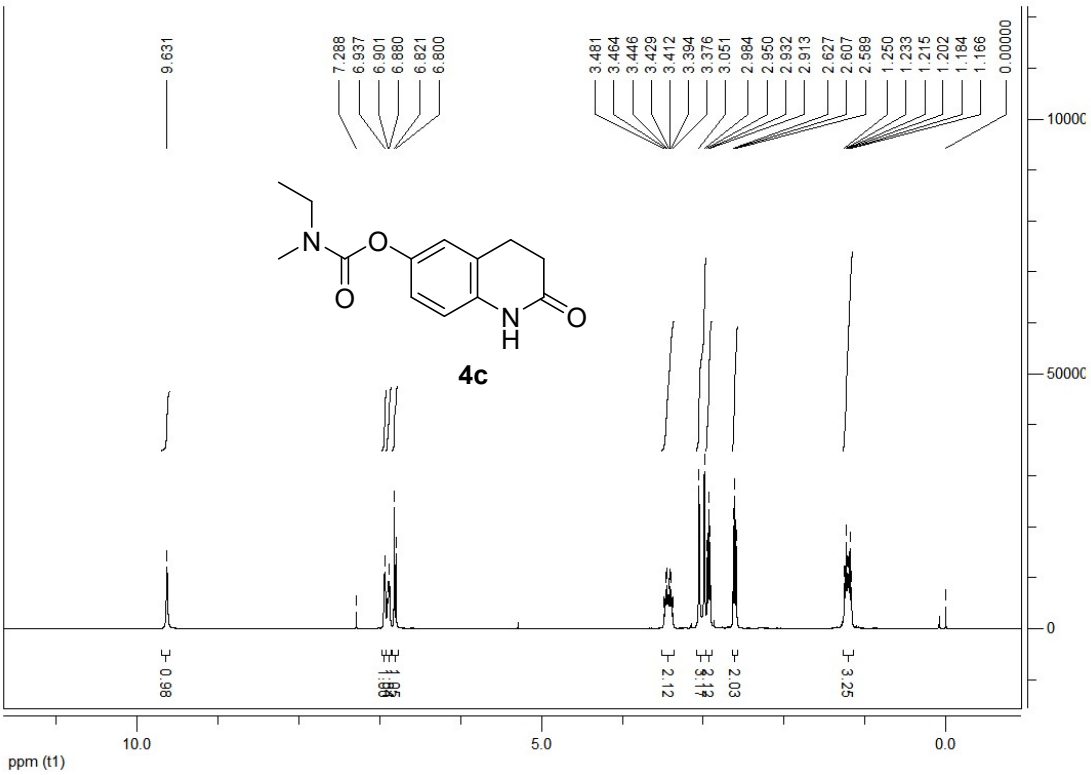
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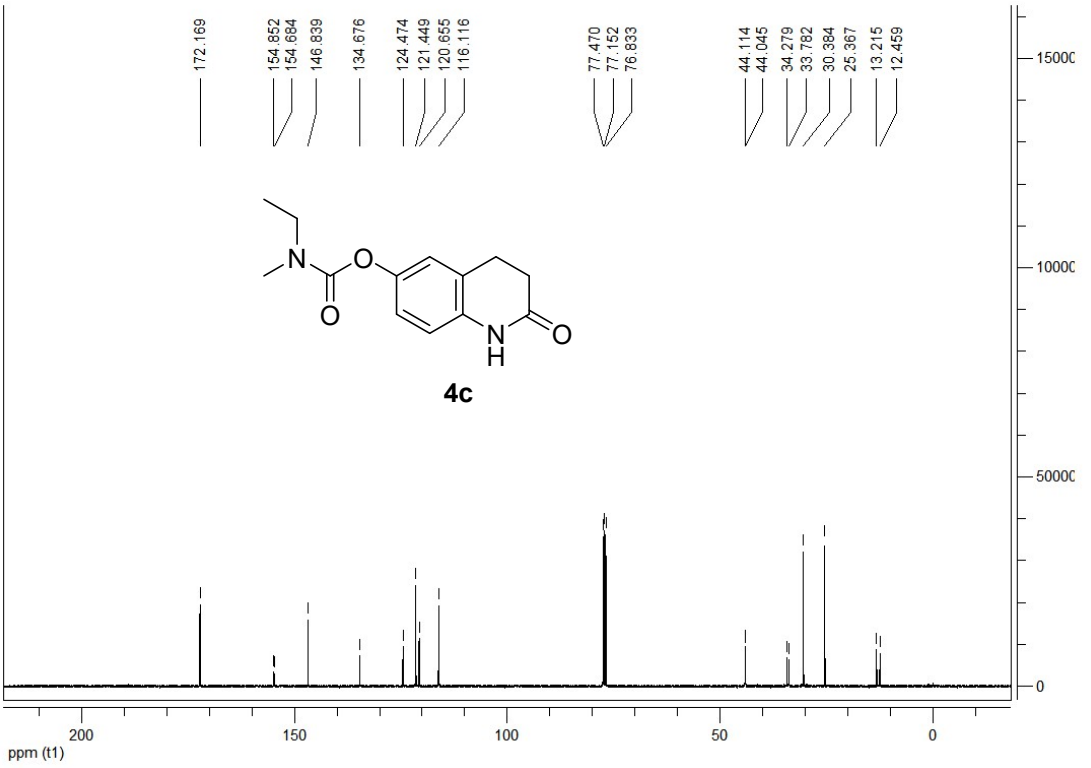
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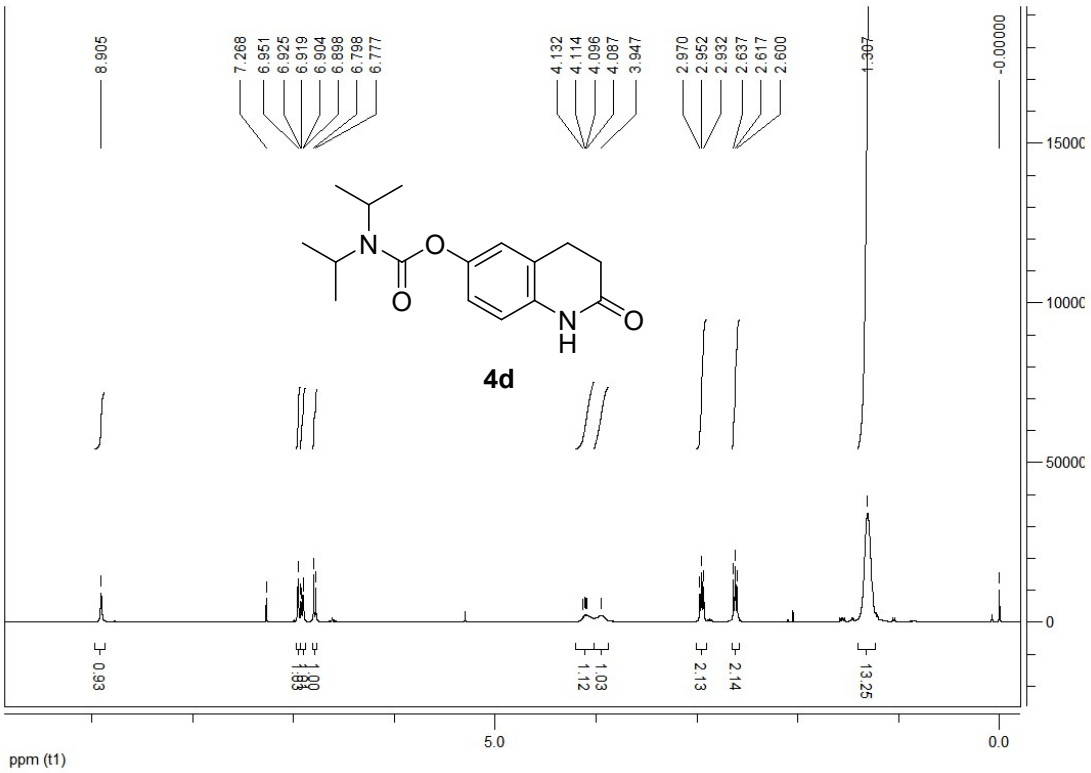
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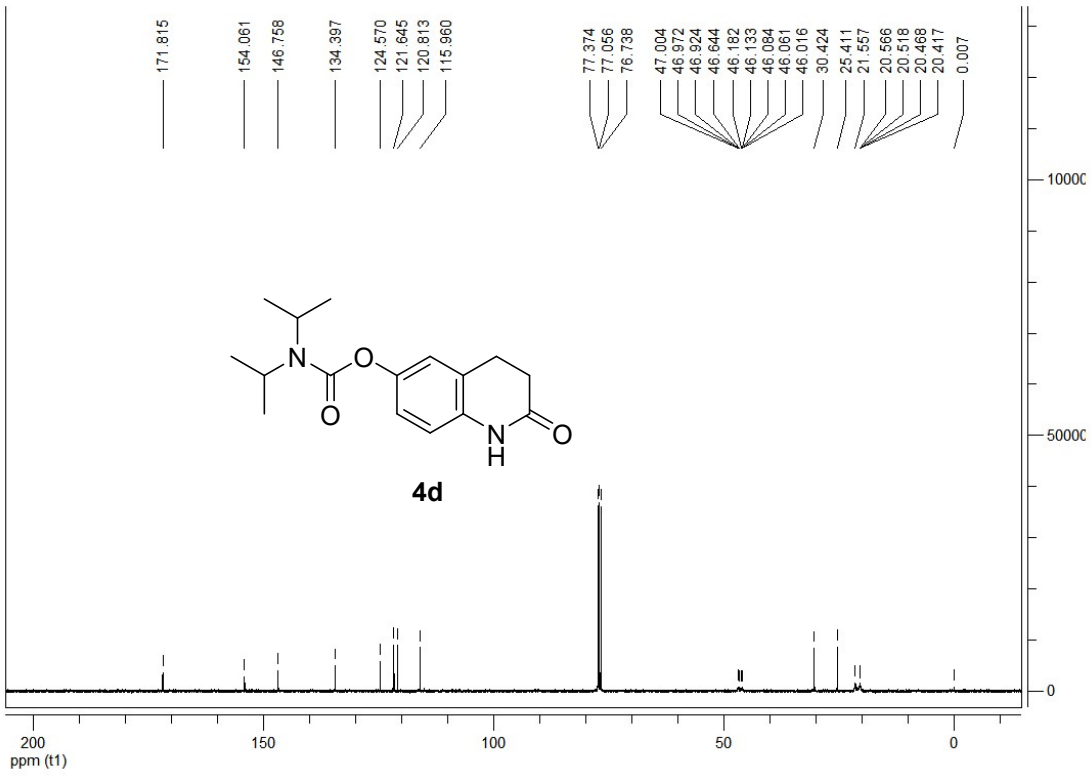
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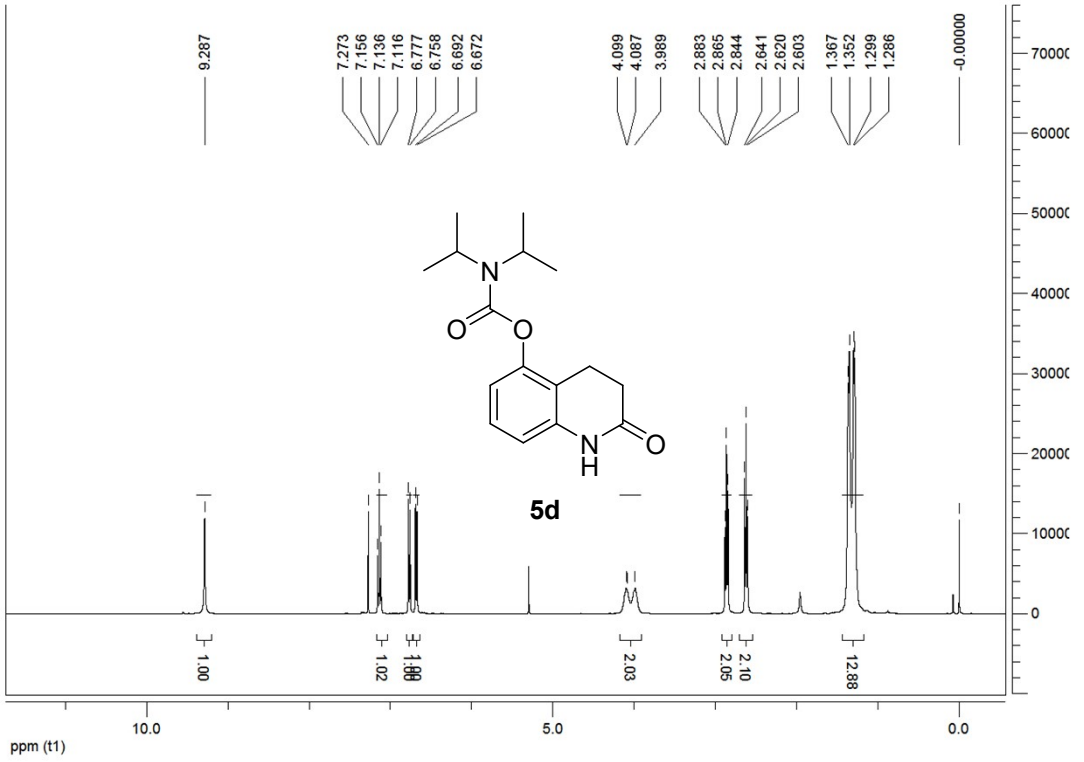
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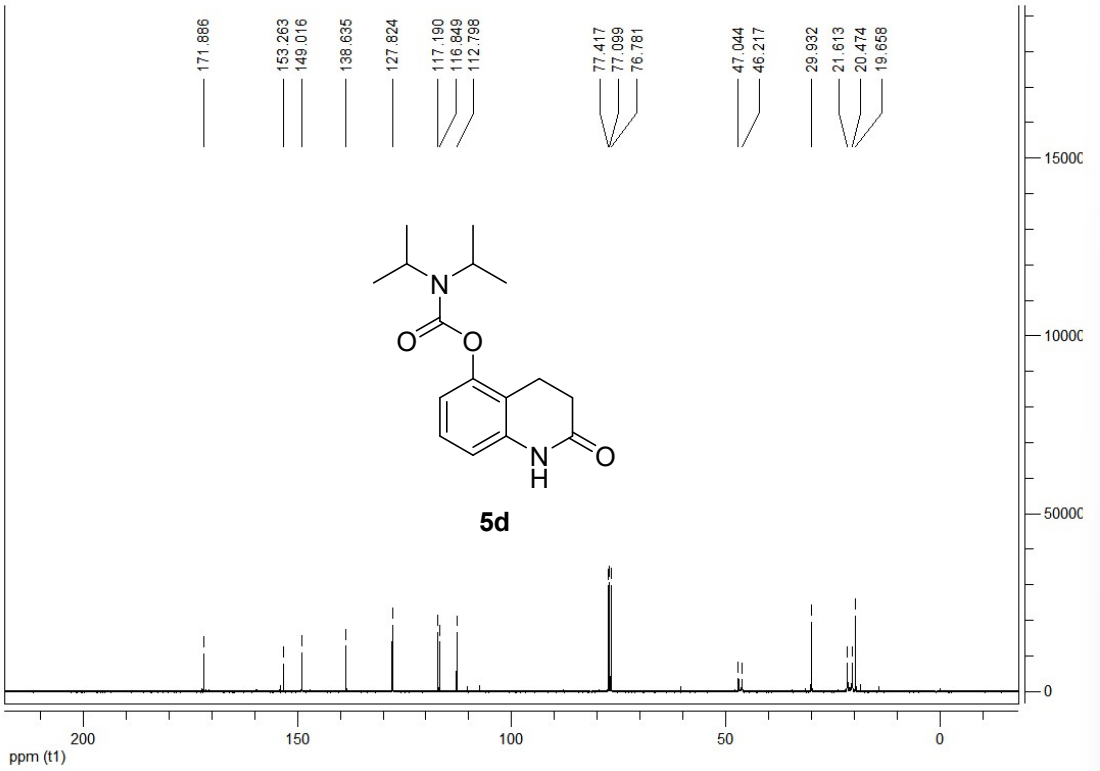
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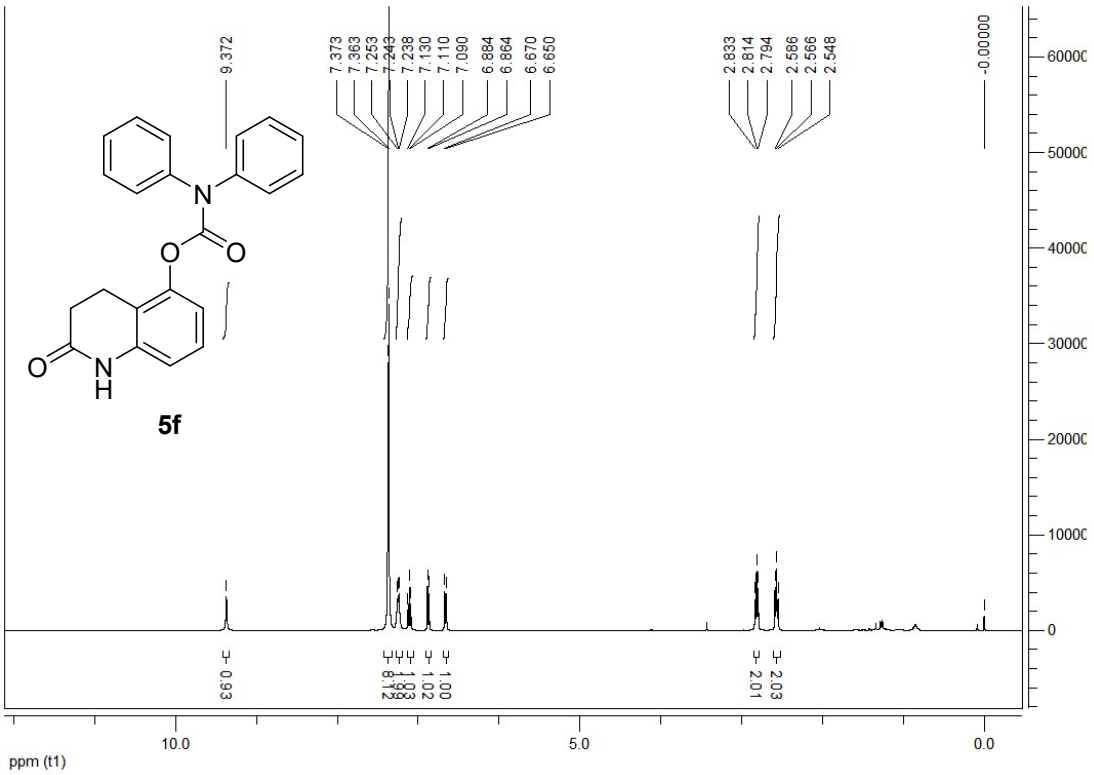
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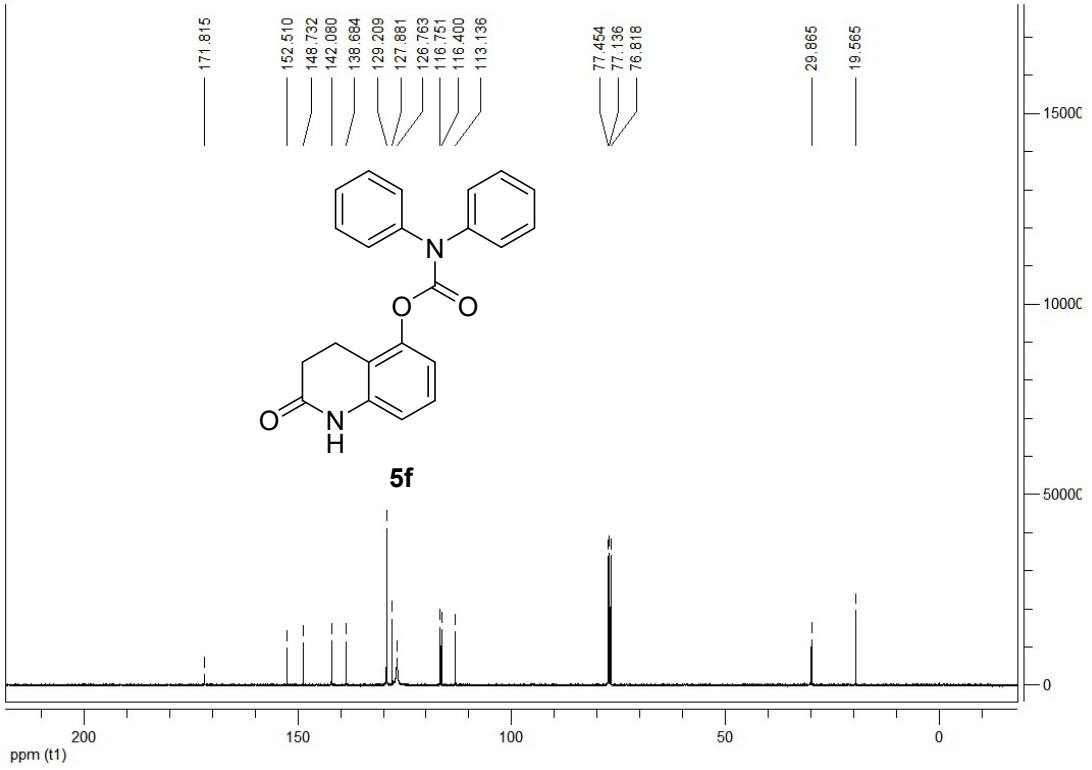
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200
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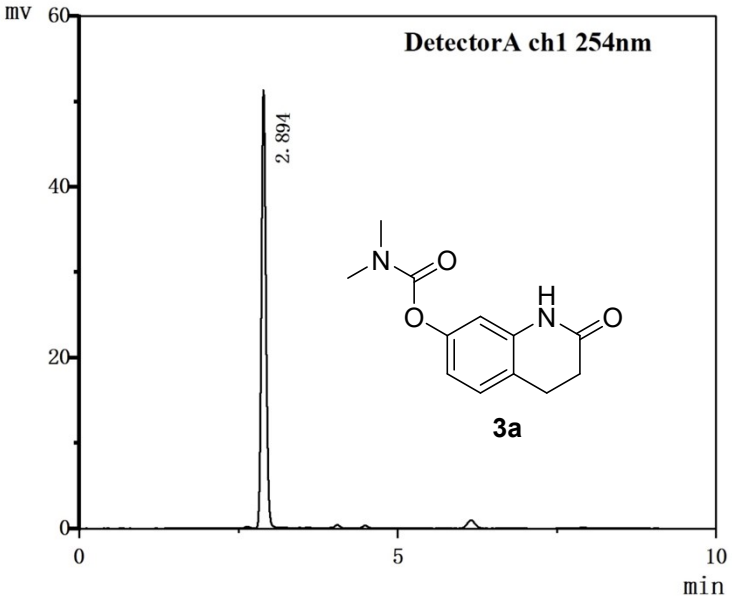
100
50
0
ppm (t1)
5f

- The representative HPLC spectra for the synthesized compounds



Detector A Ch1 254nm

peak number	Retention time	Area	Height	Area%
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2	6.153	5993	814	2.324
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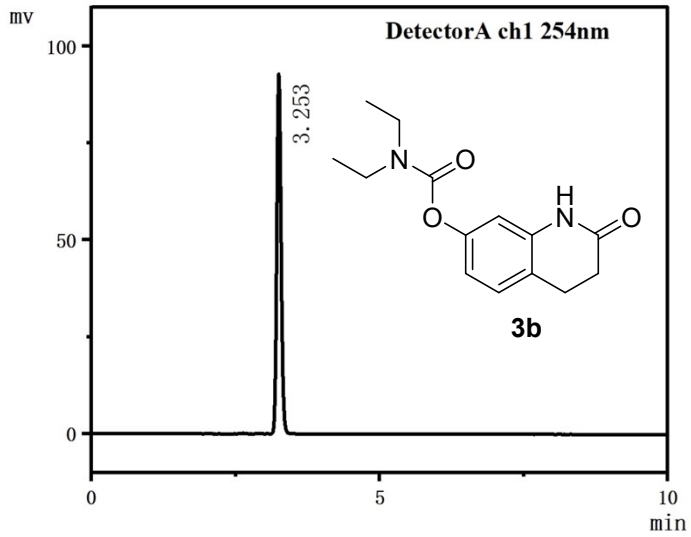
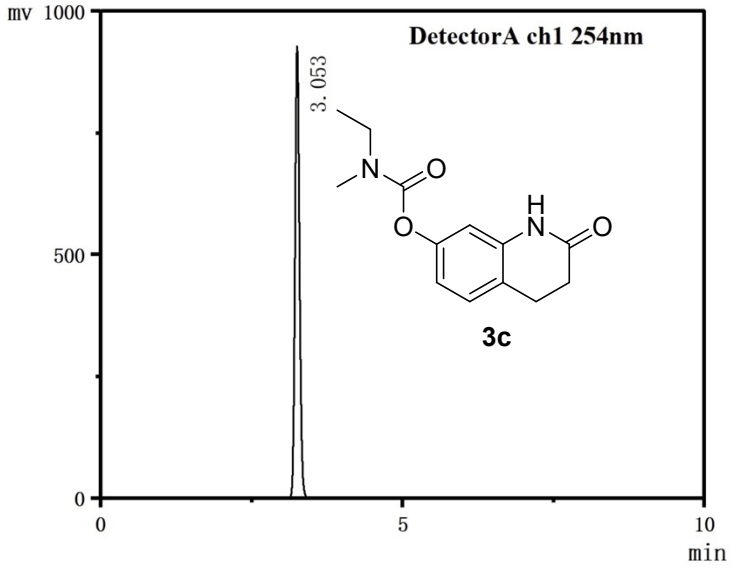


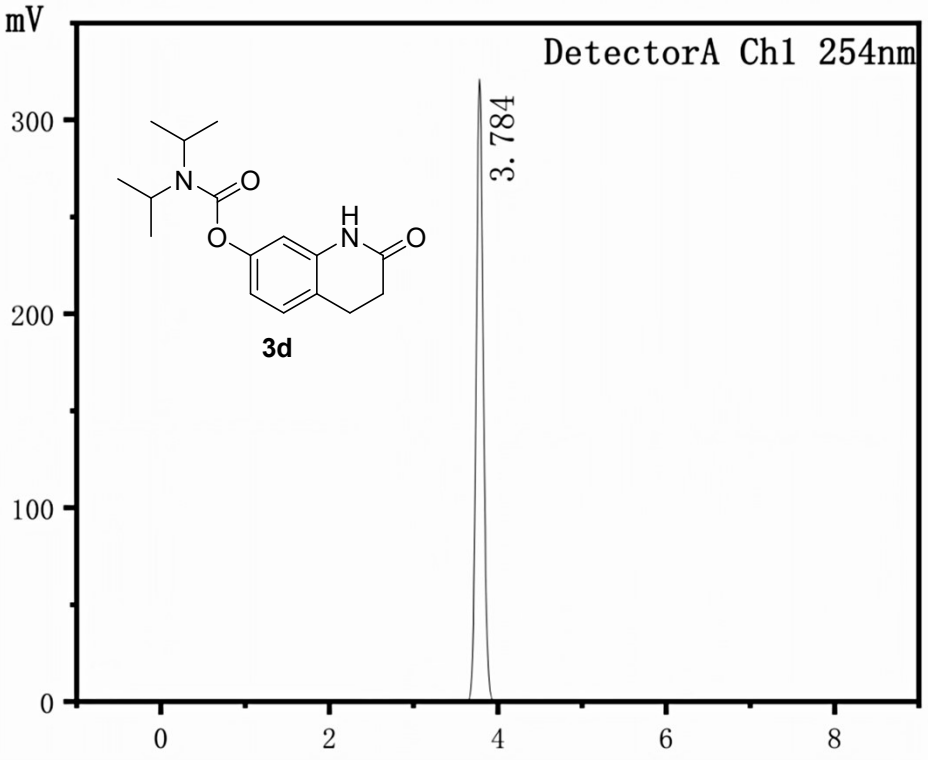
Detector A Ch1 254nm

peak number	Retention time	Area	Height	Area%
1	2.636	768	174	0.159
2	2.9	750	171	0.155
3	3.253	482234	92839	99.686
总计		483752	93185	100.000



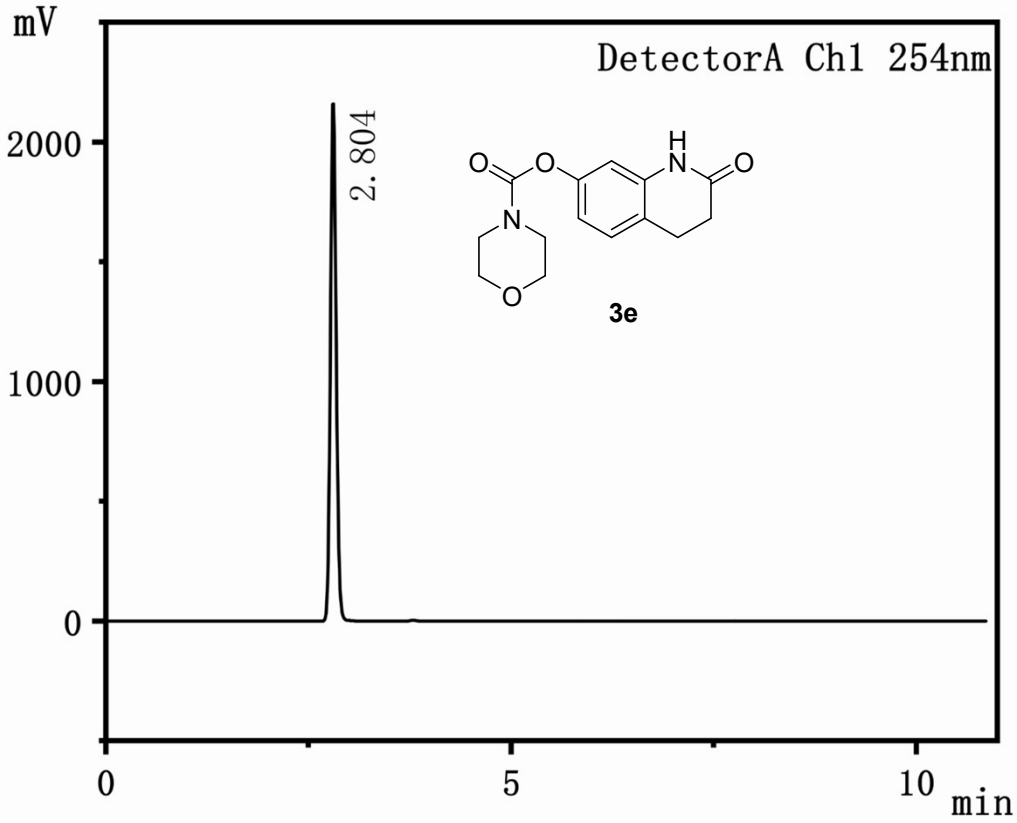
Detector A Ch1 254nm

peak number	Retention time	Area	Height	Area%
1	3.053	6569478	1301363	100.000
总计		6569478	1301363	100.000



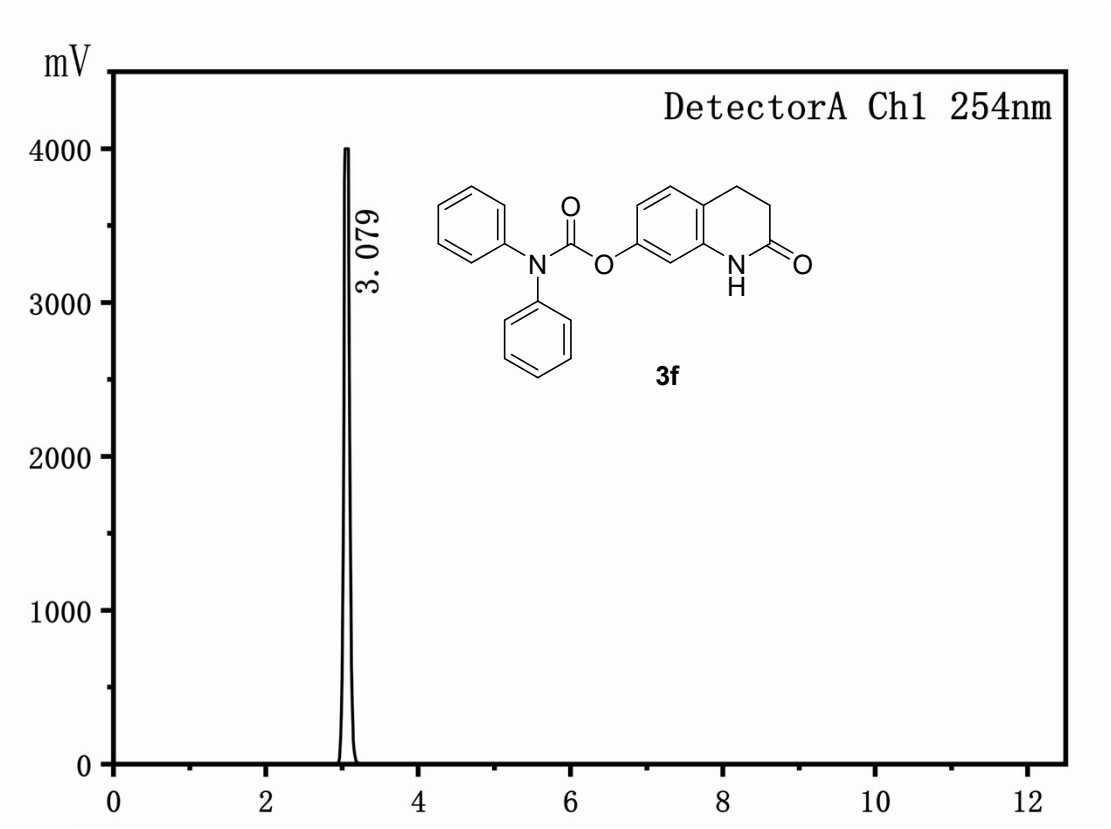
Detector A Ch1 254nm

Peak number	Retention time	Area	Height	Area%
1	0.273	1864	101	0.096
2	2.641	5098	1007	0.263
3	2.805	2094	329	0.108
4	2.900	2637	409	0.136
5	3.048	1175	173	0.061
6	3.249	2226	204	0.115
7	3.784	1907617	321479	98.518
8	4.483	2564	330	0.132
9	5.158	1540	165	0.080
10	5.278	2232	251	0.115
11	6.120	6194	663	0.320
12	6.862	1064	111	0.055
总计		1936305	325220	100.000



Detector A Ch1 254nm

Peak number	Retention time	Area	Height	Area%
1	2.804	10677870	2158385	99.742
2	3.791	16212	2602	0.151
3	4.042	1218	201	0.011
4	4.482	2131	321	0.020
5	6.139	6960	766	0.065
6	7.932	1145	108	0.011
总计		10705536	2162383	100.000



Detector A Ch1 254nm

Peak number	Retention time	Area	Height	Area%
1	1.217	2664	188	0.012
2	1.541	1288	108	0.006
3	2.125	5248	287	0.024
4	2.442	8825	721	0.040
5	2.517	4733	730	0.022
6	2.627	5877	749	0.027
7	3.079	21851391	4000393	99.800
8	4.123	3579	235	0.016
9	5.016	10091	306	0.046
10	11.431	1548	92	0.007
总计		21895246	4003810	100.000