Asymmetric Synthesis of Chloroisothreonine Derivatives *via syn*-Stereoselective Mannich-type Additions across *N*-Sulfinyl-α-chloroimines

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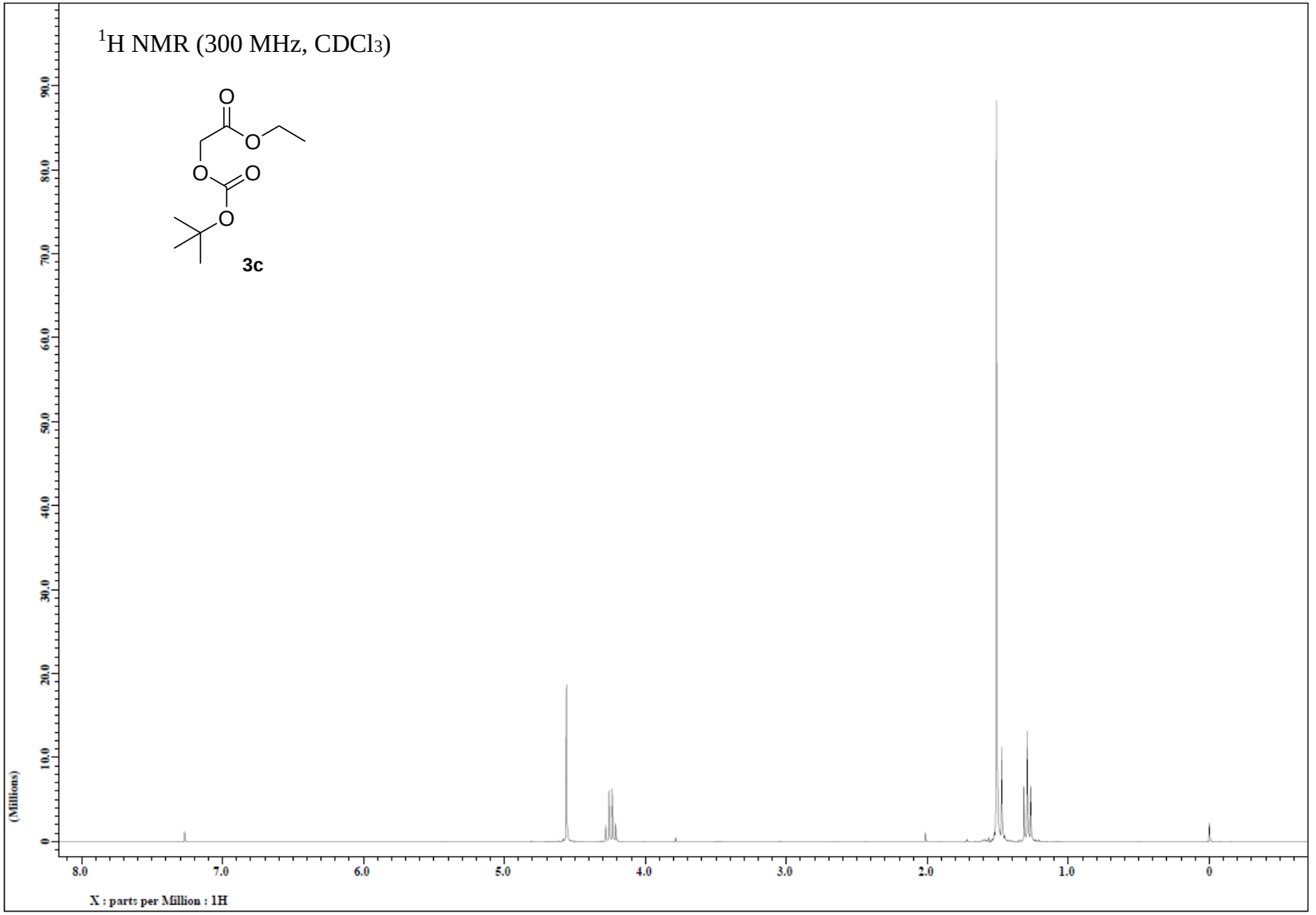
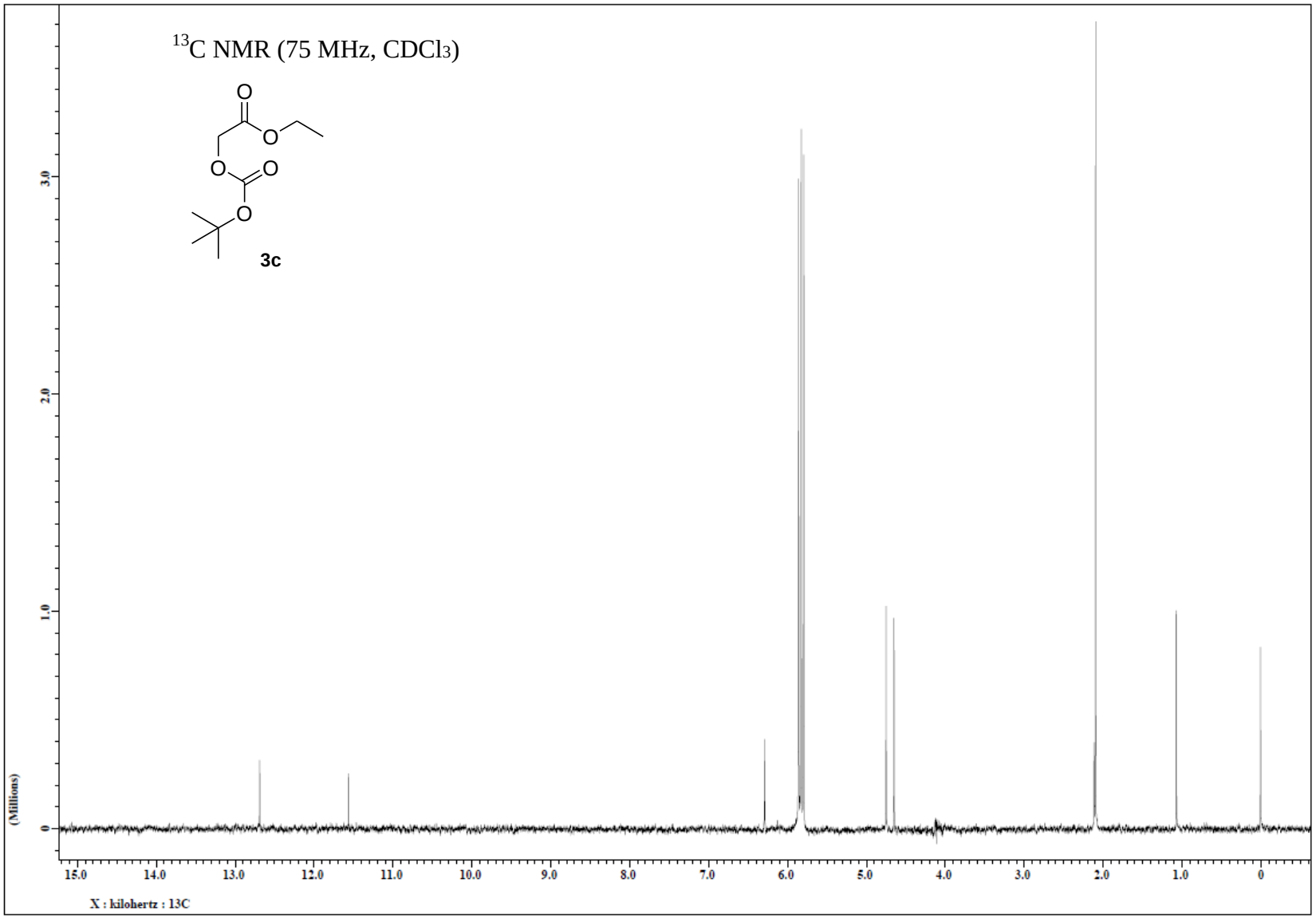
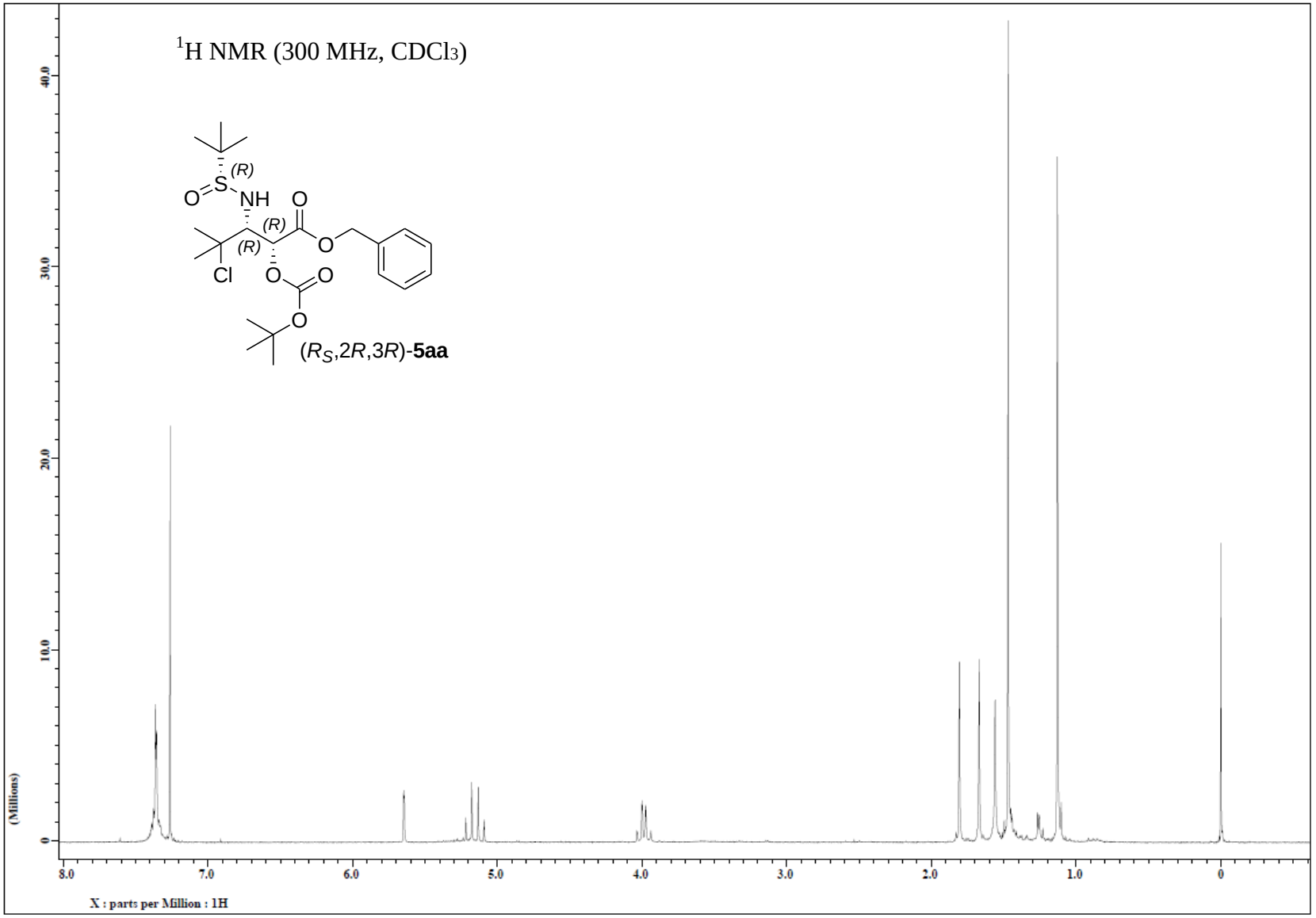
I. General methods

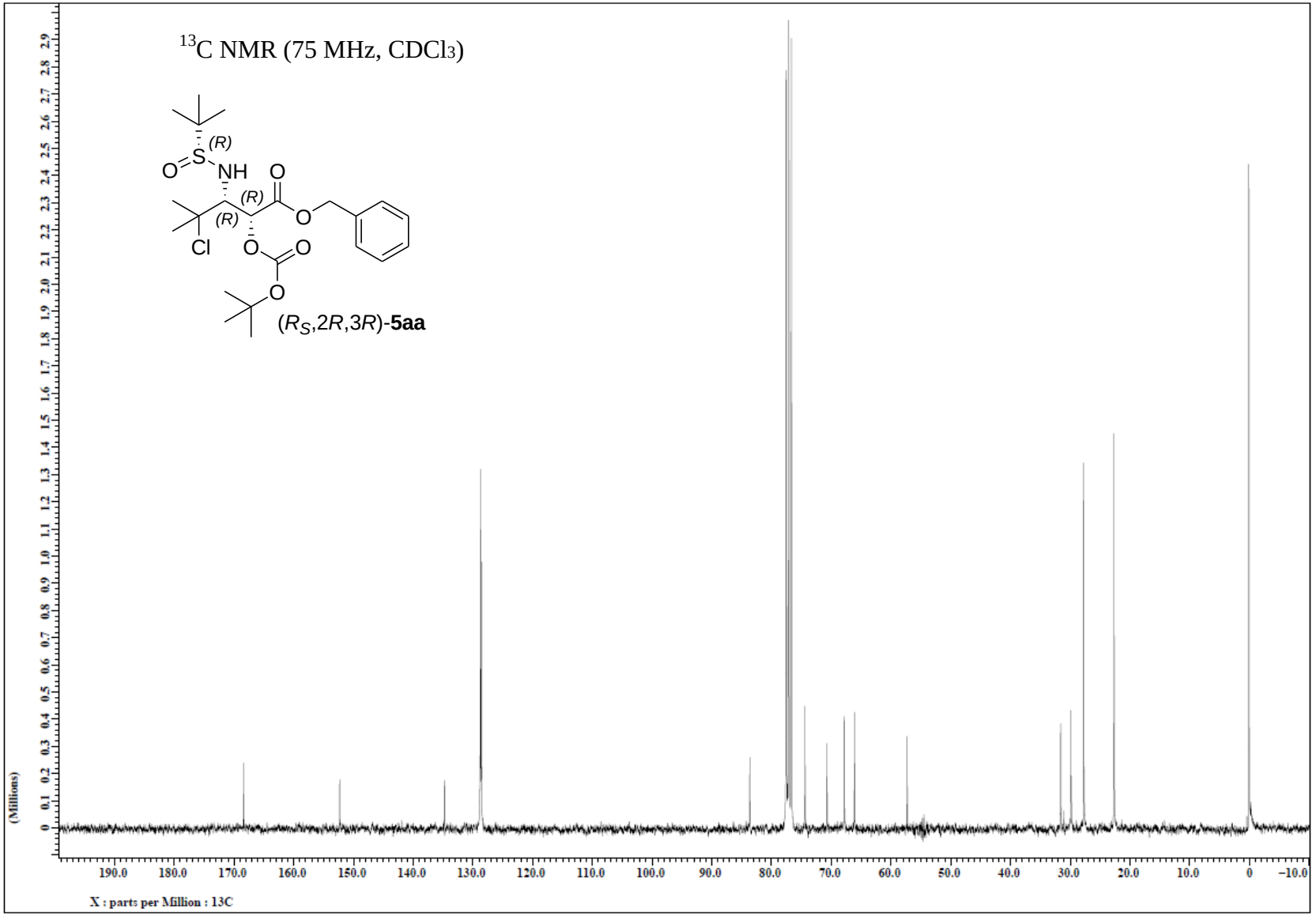
Flame-dried glassware was used for all non-aqueous reactions. Commercially available solvents and reagents were purchased from common chemical suppliers and used without further purification, unless stated otherwise. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled under a nitrogen atmosphere from sodium/benzophenone ketyl, whereas dichloromethane (CH_2Cl_2) was distilled from calcium hydride. Petroleum ether refers to the 40-60 °C boiling fraction. ^{1}H NMR (300 MHz), ^{13}C NMR (75 MHz) spectra were recorded in deuterated solvents with tetramethylsilane (TMS, $\delta = 0$ ppm) as internal standard unless specified otherwise. Mass spectra were recorded using a direct inlet system (ESI, 4000 V). IR spectra were obtained from samples in neat form with an ATR (Attenuated Total Reflectance) accessory. Elementary analyses were performed using a CHNS/O elementary analyzer. HRMS analysis was performed using a HPLC coupled to a TOF-Mass Spectrometer equipped with ESI/APCI-multimode source. Melting points of crystalline compounds were determined in open-end capillary tubes using a hot stage apparatus and were not corrected. Optical rotations were determined at a wavelength of 589 nm. The purification of the reaction mixtures was performed by column chromatography with silica gel (particle size 0.035-0.070 mm, pore diameter ca. 6 nm). Thin layer chromatography (TLC) was performed on glass plates coated with silica gel 60 F_{254}, using UV and $KMnO_4$ as a visualizing agent. The enantiopure reagents (S_S)-*p*-toluenesulfinamide and (R_S)- and (S_S)-*tert*-butanesulfinamide were commercially available (ee > 98%).

II. Copies of ^{1}H NMR and ^{13}C NMR spectra of 3c, 5, 6, 7, 9, 10 and 11

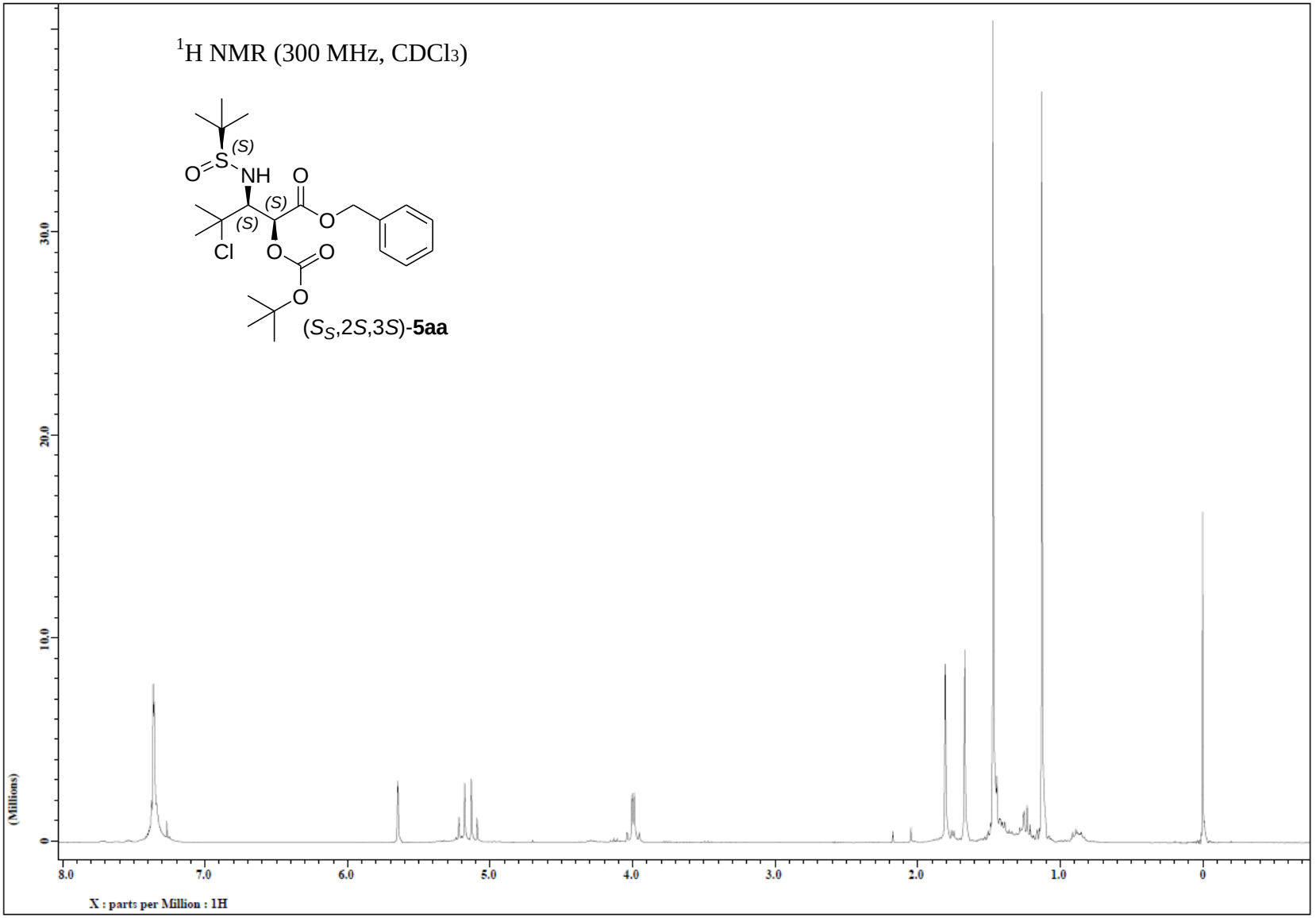



^{13}C NMR (75 MHz, CDCl$_3$)
3c
(Millions)
3.0
2.0
1.0
0
15.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : kilohertz : 13C

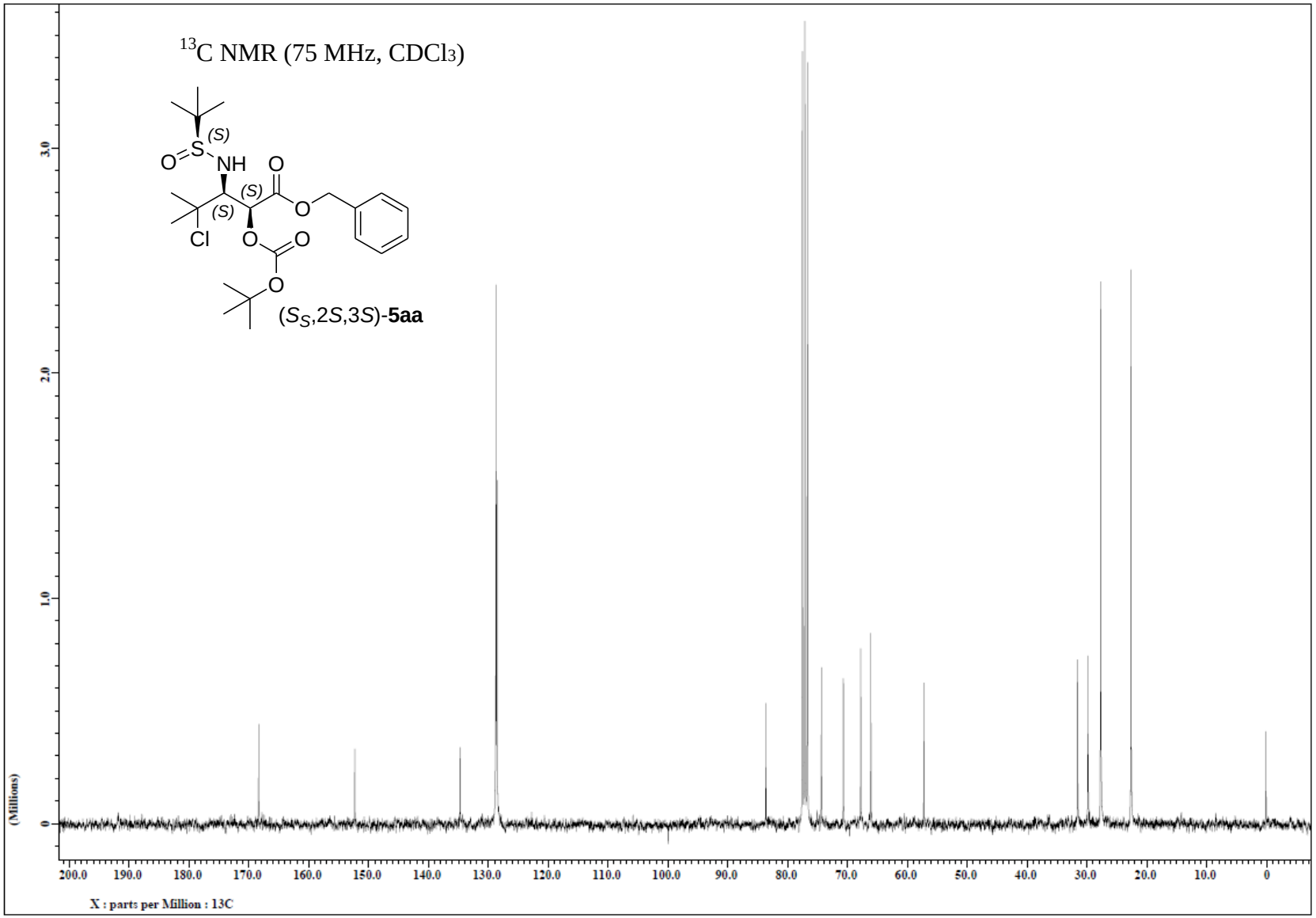

^{1}H NMR (300 MHz, CDCl$_3$)
(R)
S
O
NH
O
(R)
(R)
O
Cl
O
O
O
(R_S,2R,3R)-**5aa**
40.0
30.0
20.0
10.0
0
(Millions)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H


13C NMR (75 MHz, CDCl3)
(R)
O
S
NH
O
(R)
(R)
O
Cl
O
O
O
(RS,2R,3R)-5aa
(Millions)
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
-10.0
X : parts per Million : 13C

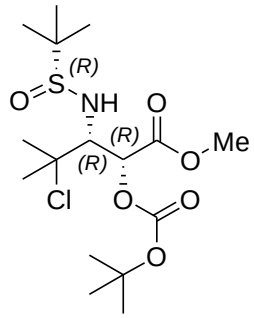
^{1}H NMR (300 MHz, $CDCl_3$)



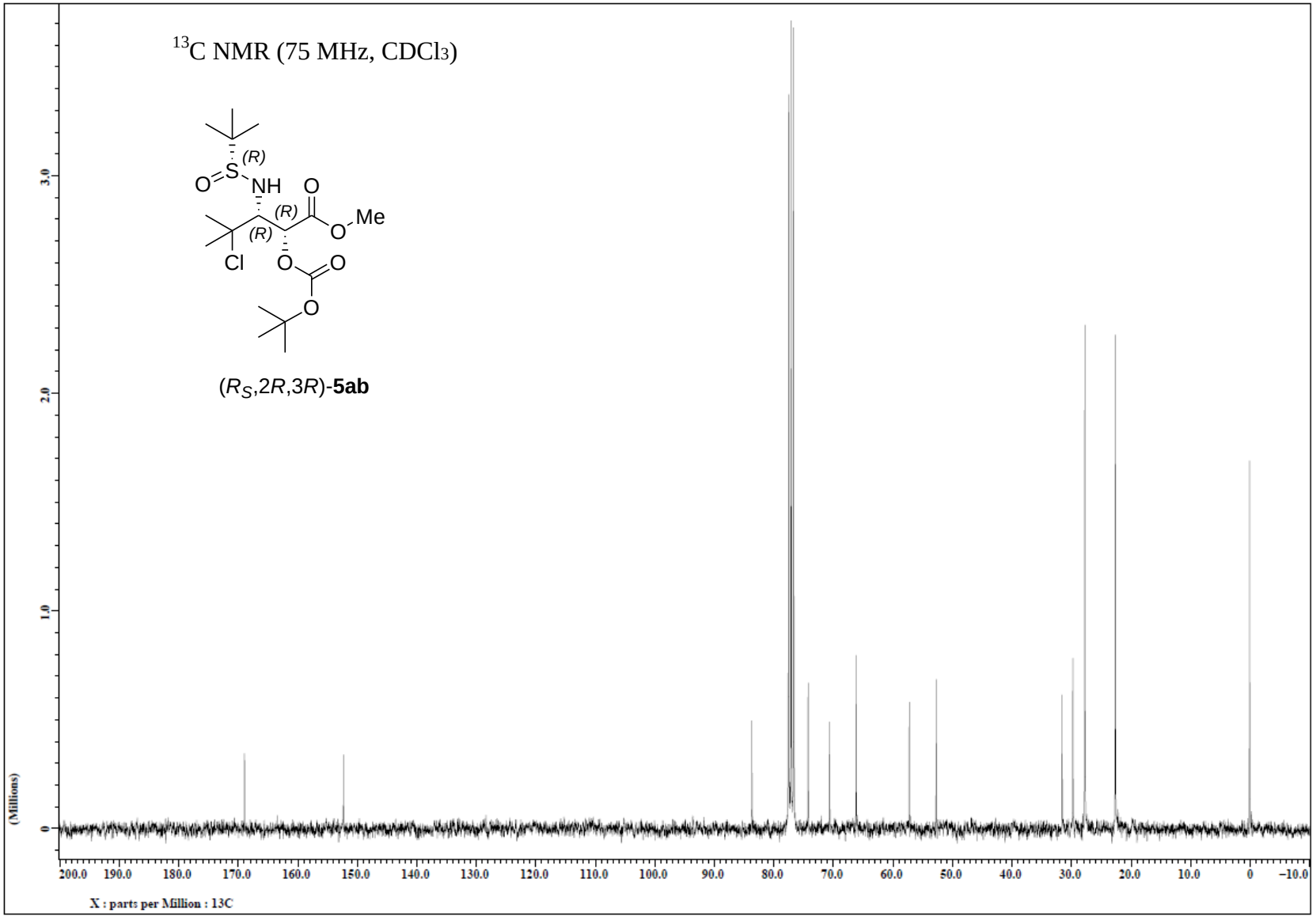
(S_S,2*S*,3*S*)-**5aa**


13C NMR (75 MHz, CDCl3)
(S)
O
S
NH
O
(S)
(S)
O
Cl
O
O
O
(SS,2S,3S)-5aa
(Millions)
3.0
2.0
1.0
0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : 13C

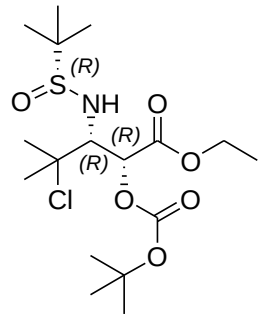
^{1}H NMR (300 MHz, $CDCl_3$)



(R_S,2*R*,3*R*)-**5ab**

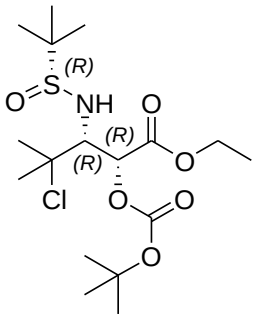

13C NMR (75 MHz, CDCl3)
(R)
S
O
NH
O
(R)
O
Me
(R)
Cl
O
O
O
(RS,2R,3R)-5ab
(Millions)
3.0
2.0
1.0
0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)

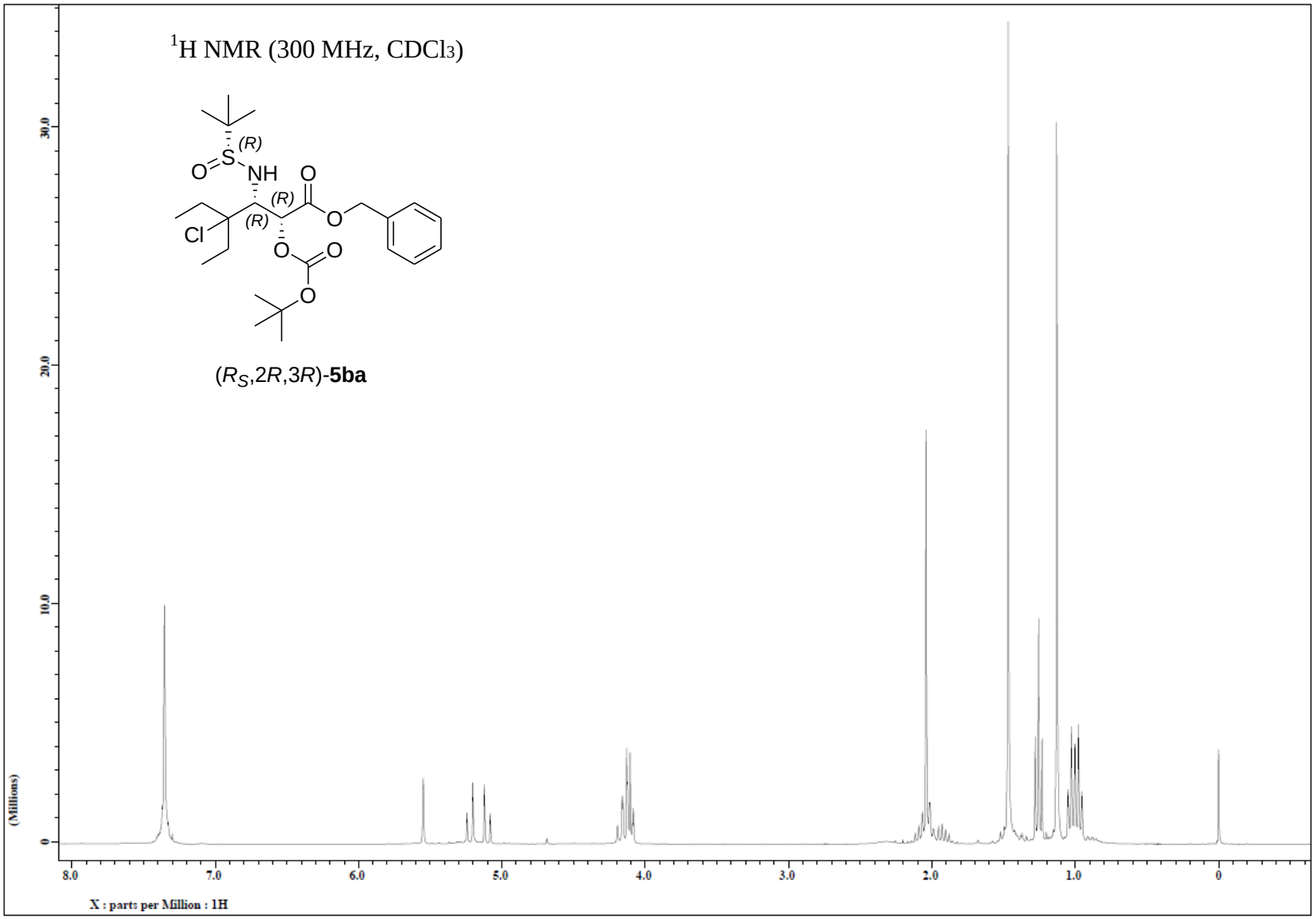


(R_S,2*R*,3*R*)-**5ac**

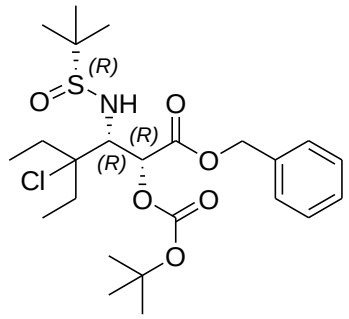
^{13}C NMR (75 MHz, $CDCl_3$)



(R_S,2*R*,3*R*)-**5ac**

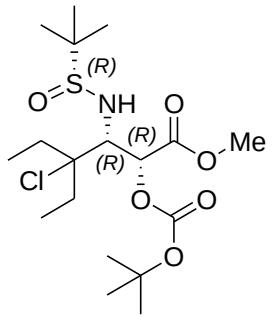

^{1}H NMR (300 MHz, CDCl$_3$)
(R)
S
O
NH
O
(R)
(R)
O
Cl
O
O
O
(R_S,2R,3R)-**5ba**
30.0
20.0
10.0
0
(Millions)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

^{13}C NMR (75 MHz, $CDCl_3$)



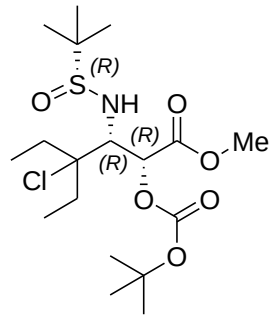
(R_S,2*R*,3*R*)-**5ba**

^{1}H NMR (300 MHz, $CDCl_3$)



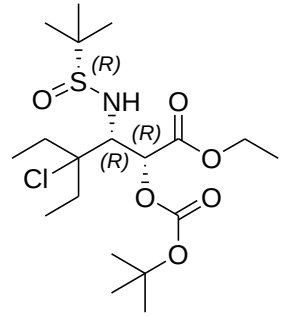
(R_S,2*R*,3*R*)-**5bb**

^{13}C NMR (75 MHz, $CDCl_3$)



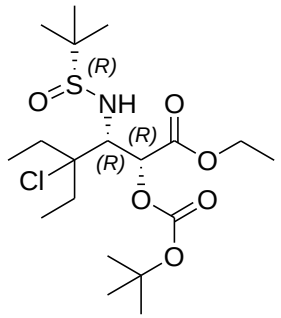
(R_S,2*R*,3*R*)-**5bb**

^{1}H NMR (300 MHz, $CDCl_3$)



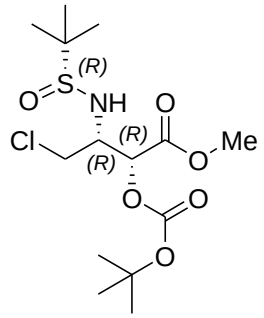
(R_S,2*R*,3*R*)-**5bc**

^{13}C NMR (75 MHz, $CDCl_3$)



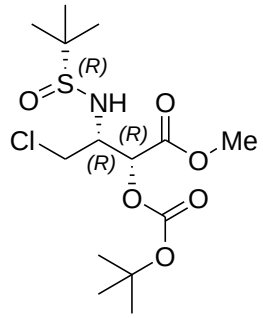
(R_S,2*R*,3*R*)-**5bc**

^{1}H NMR (300 MHz, $CDCl_3$)



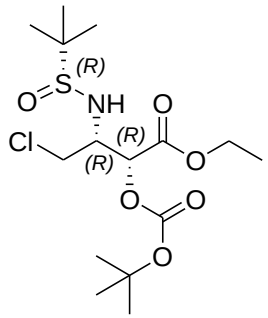
(R_S,2*R*,3*R*)-**5cb**

^{13}C NMR (75 MHz, $CDCl_3$)



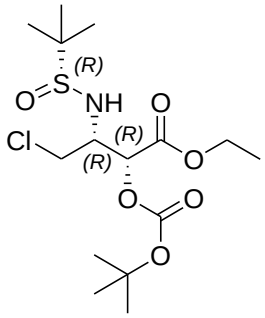
(R_S,2*R*,3*R*)-**5cb**

^{1}H NMR (300 MHz, $CDCl_3$)

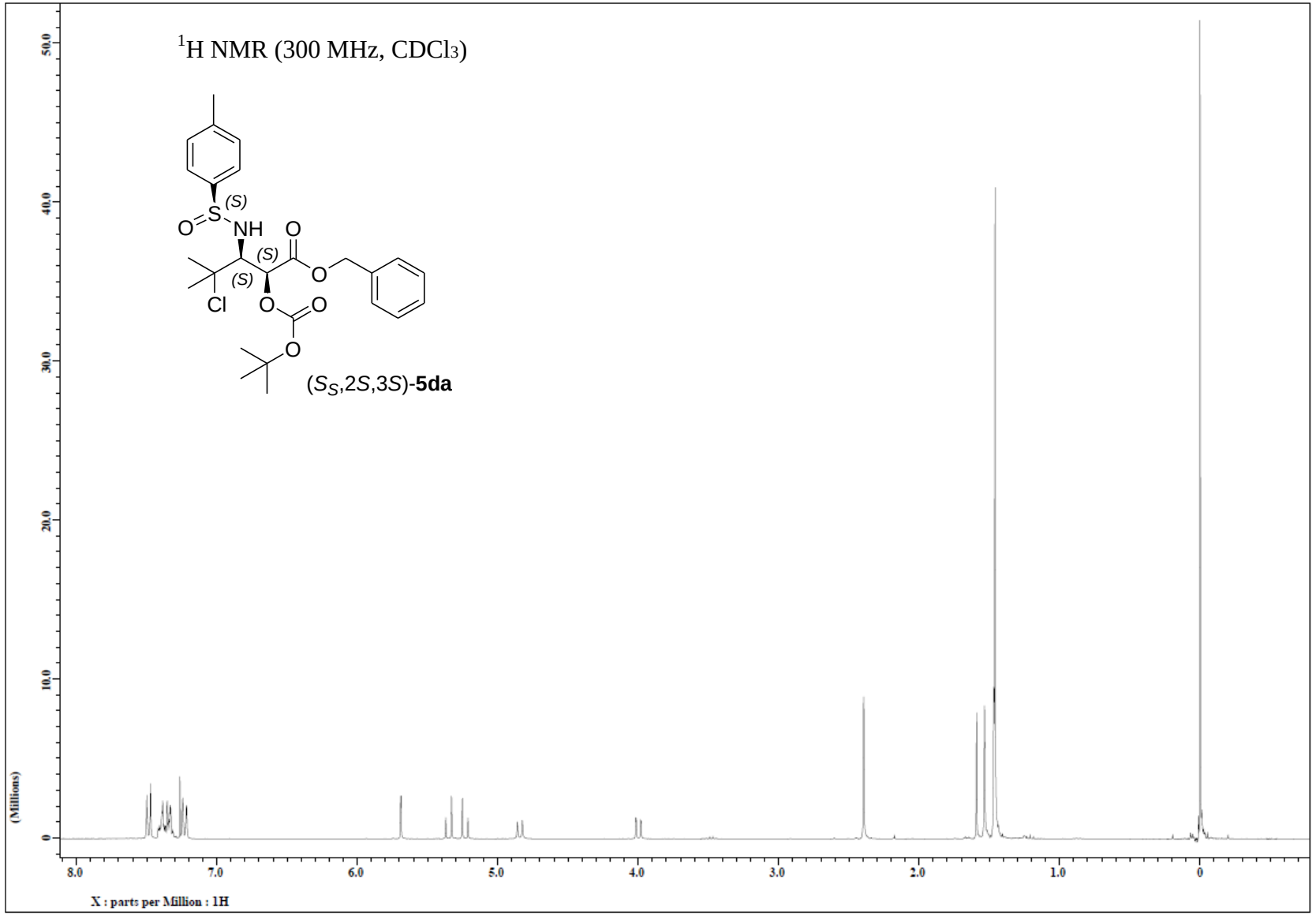


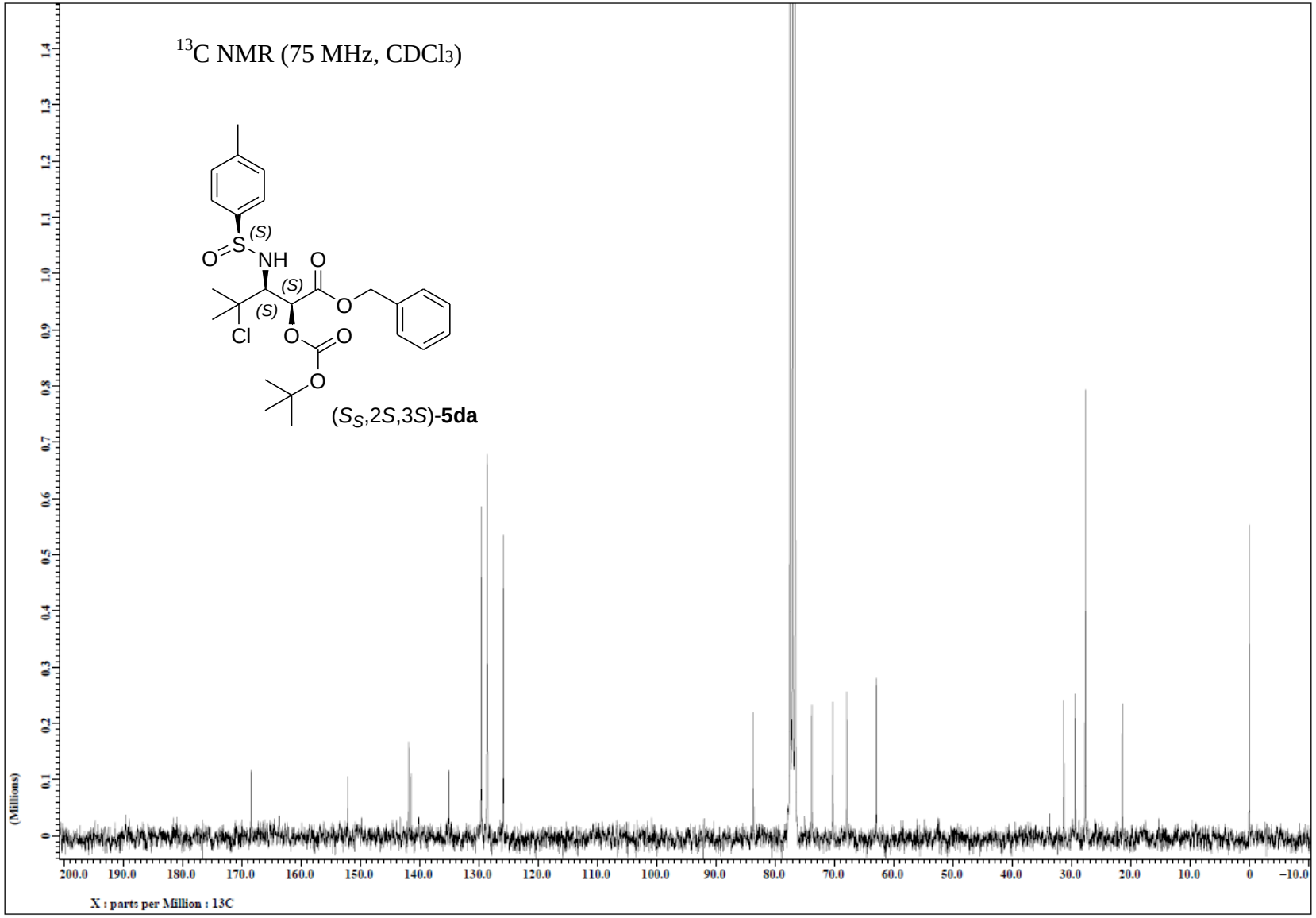
(R_S,2*R*,3*R*)-**5cc**

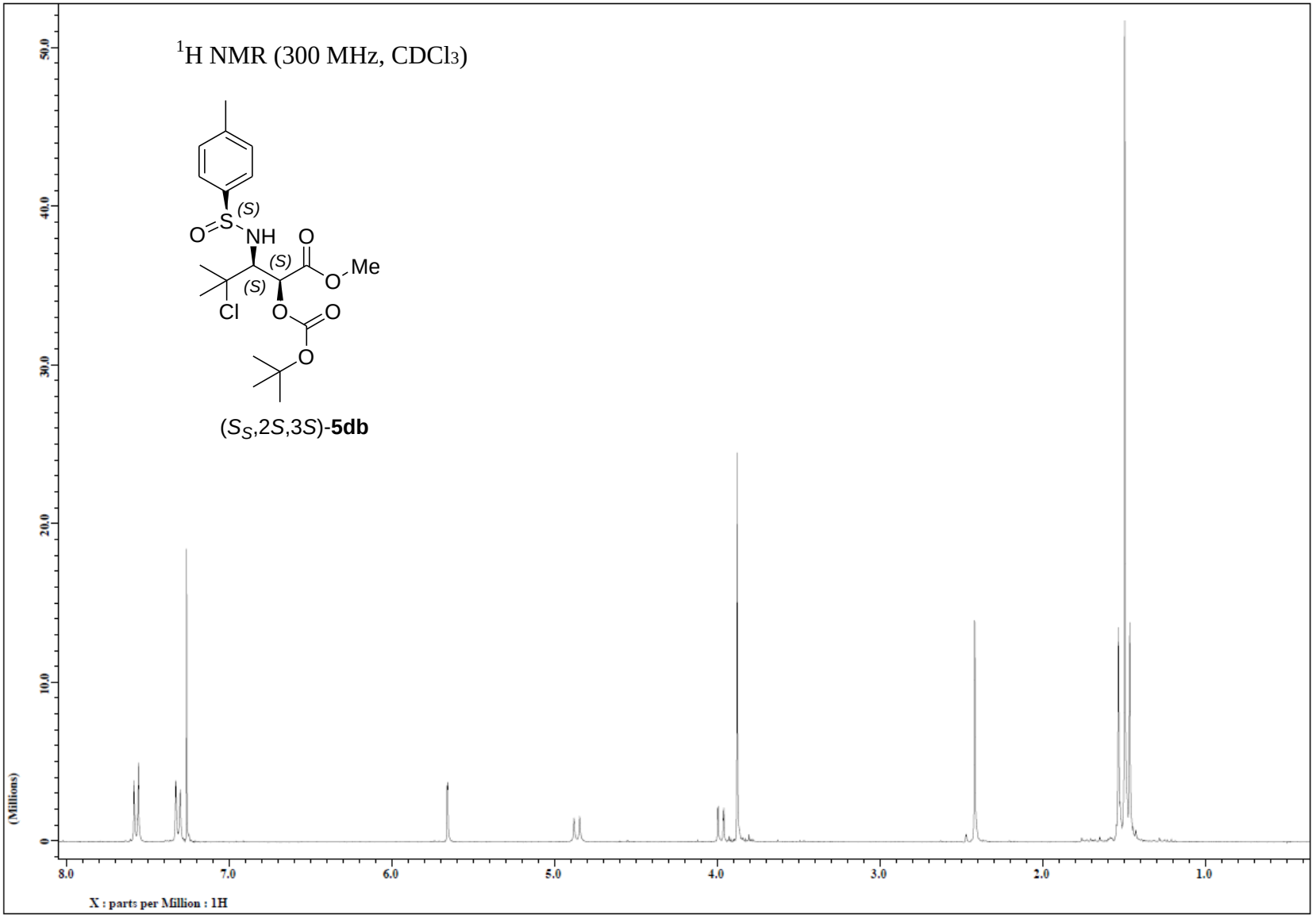
^{13}C NMR (75 MHz, $CDCl_3$)

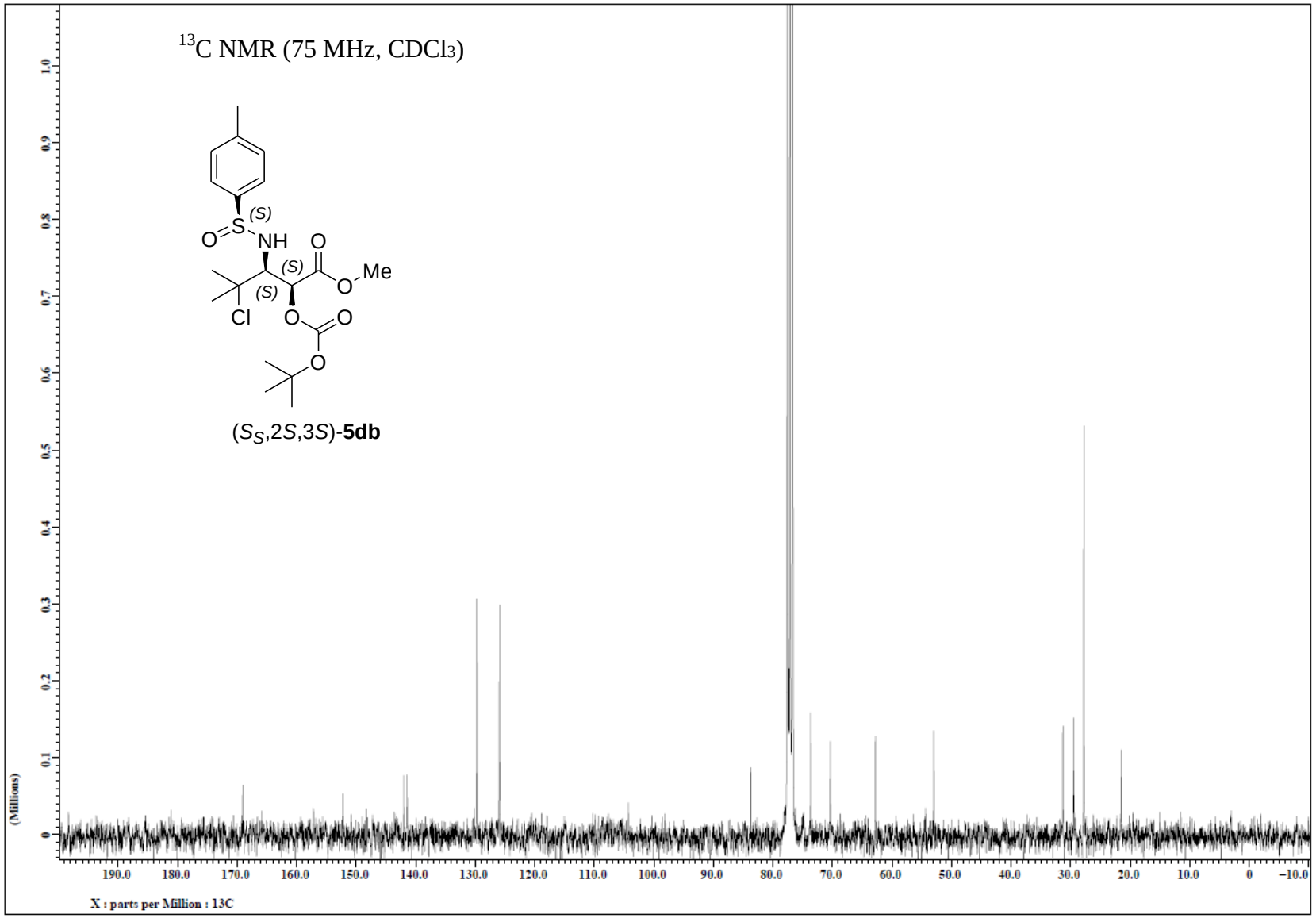


(R_S,2*R*,3*R*)-**5cc**

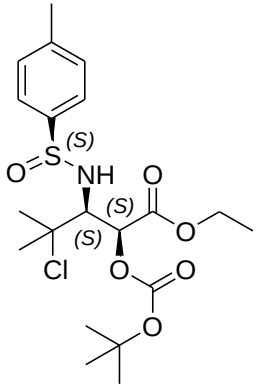

^{1}H NMR (300 MHz, CDCl$_3$)
(S)
S
O
NH
O
(S)
(S)
O
Cl
O
O
O
(S_S,2S,3S)-**5da**
50.0
40.0
30.0
20.0
10.0
0
(Millions)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H


13C NMR (75 MHz, CDCl3)
(S)
O
S
NH
O
(S)
(S)
Cl
O
O
O
O
(SS,2S,3S)-5da
(Millions)
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0
X : parts per Million : 13C


^{1}H NMR (300 MHz, CDCl3)
(S)
O
S
NH
O
(S)
O
Me
(S)
Cl
O
O
O
(S,2S,3S)-5db
50.0
40.0
30.0
20.0
10.0
0
(Millions)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
X : parts per Million : 1H

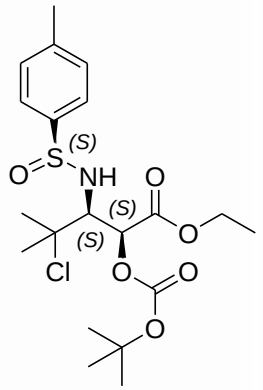

13C NMR (75 MHz, CDCl3)
(S)
O
S
NH
O
(S)
O
Me
(S)
Cl
O
O
O
(SS,2S,3S)-5db
(Millions)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)

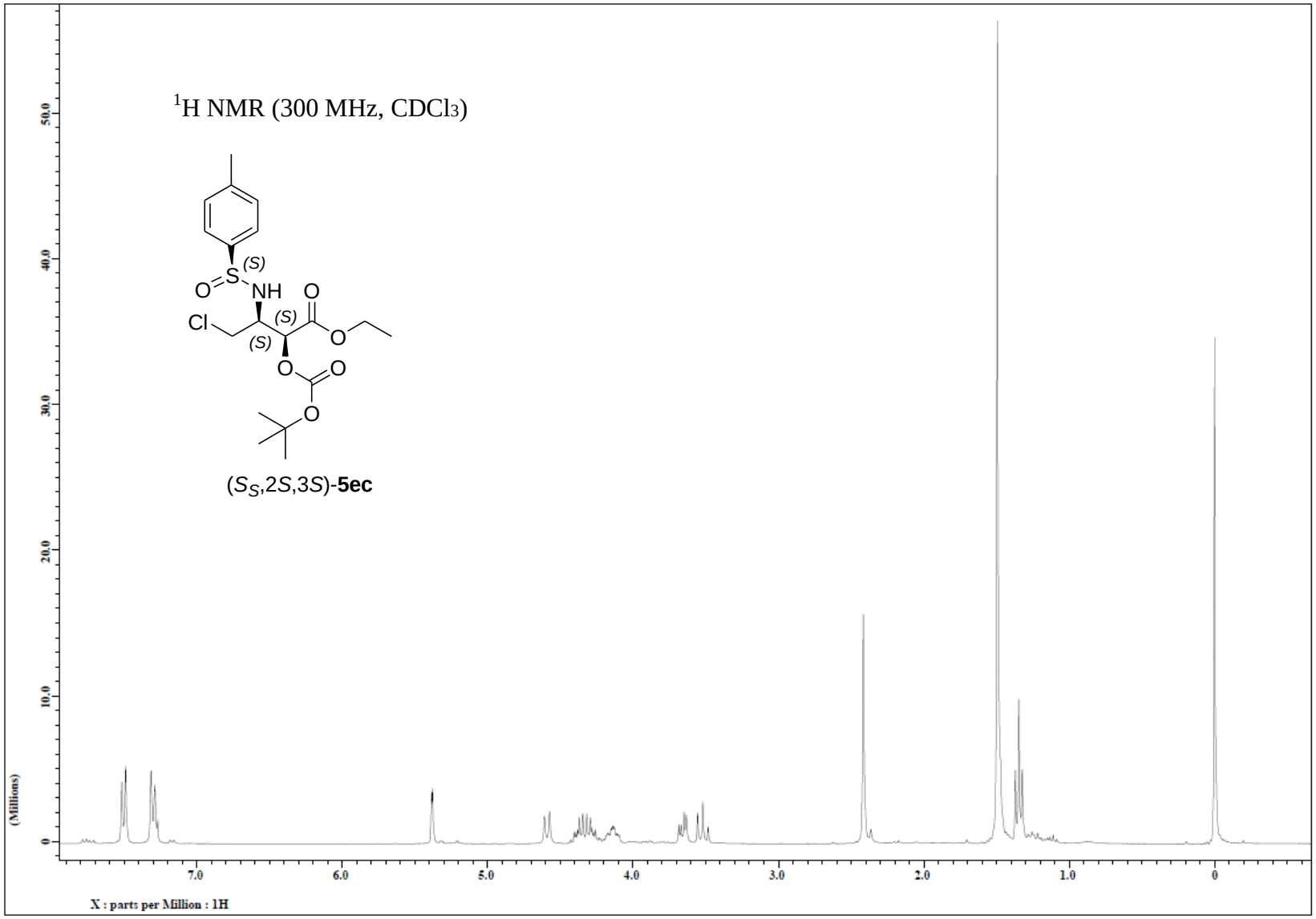


(S_S,2*S*,3*S*)-**5dc**

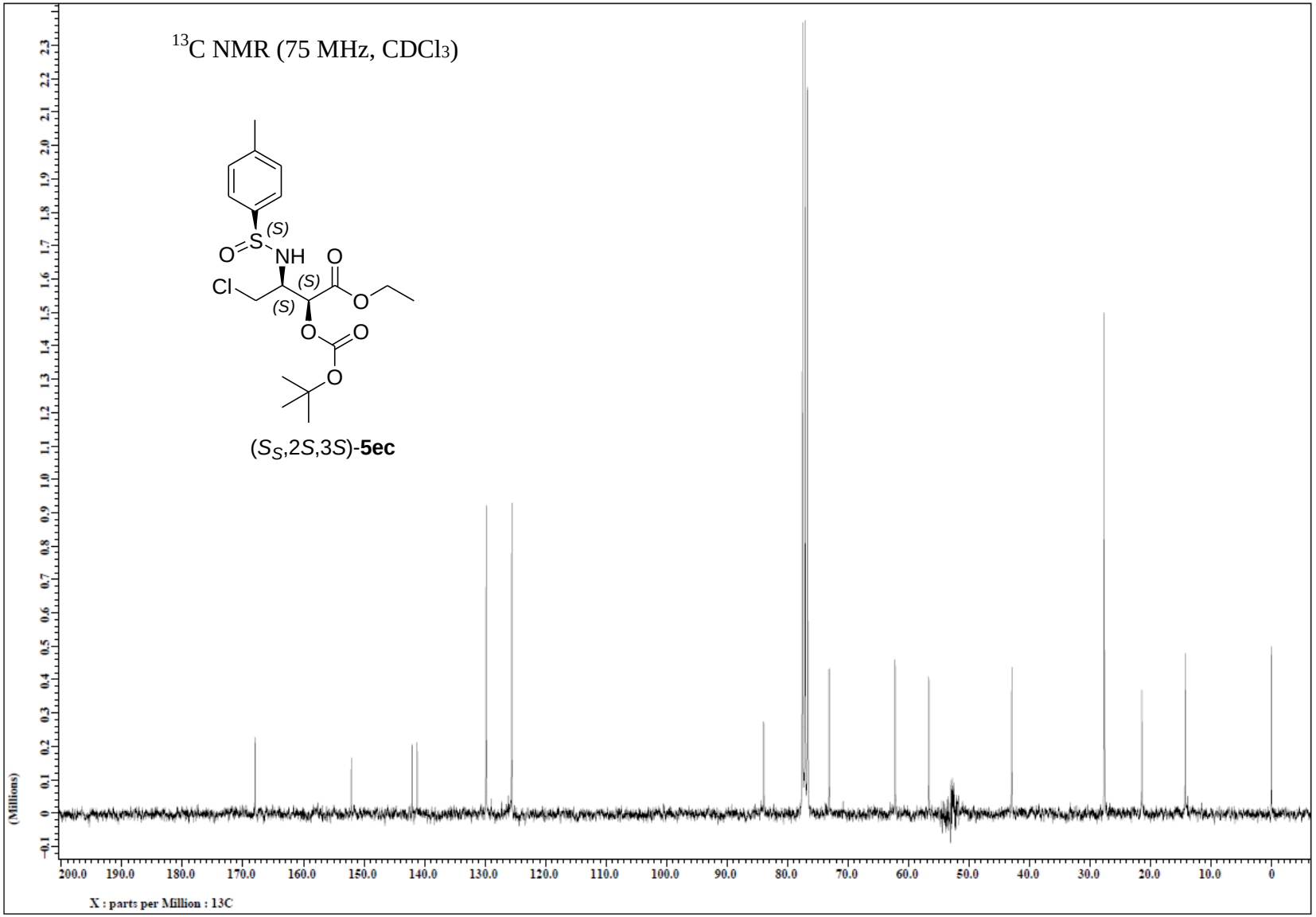
^{13}C NMR (75 MHz, $CDCl_3$)



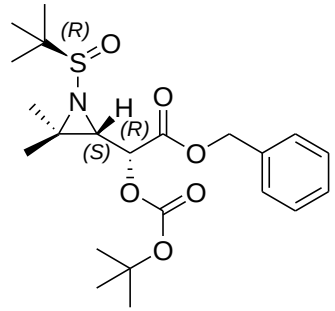
(S_S,2*S*,3*S*)-**5dc**


^{1}H NMR (300 MHz, CDCl$_3$)
(S)
O
S
NH
O
Cl
(S)
(S)
O
O
O
O
(Millions)
50.0
40.0
30.0
20.0
10.0
0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

(S_S,2*S*,3*S*)-**5ec**

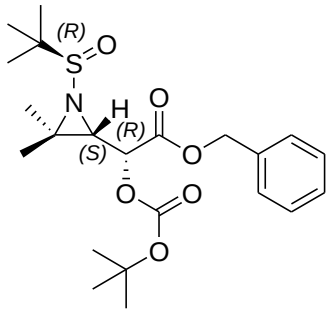

13C NMR (75 MHz, CDCl3)
(S)
O
S
NH
O
Cl
(S)
(S)
O
O
O
O
(SS,2S,3S)-5ec
(Millions)
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)



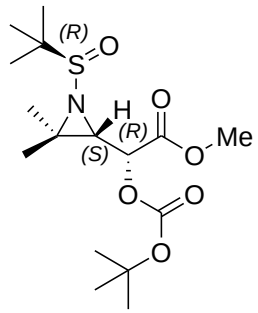
(R_S,2*R*,2'*S*)-**6aa**

^{13}C NMR (75 MHz, $CDCl_3$)



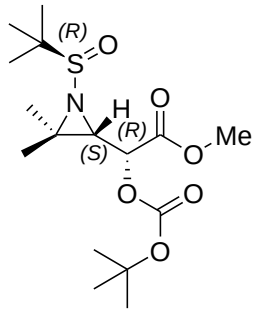
(R_S,2*R*,2'*S*)-**6aa**

^{1}H NMR (300 MHz, $CDCl_3$)



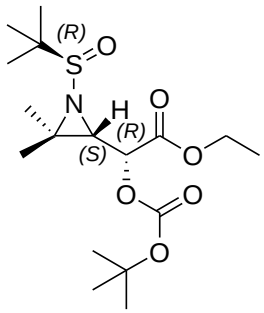
(R_S,2*R*,2'*S*)-**6ab**

^{13}C NMR (75 MHz, $CDCl_3$)



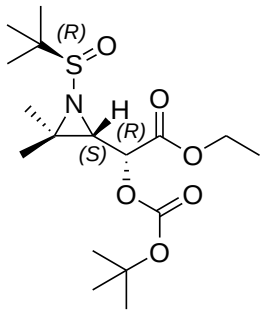
(R_S,2*R*,2'*S*)-**6ab**

^{1}H NMR (300 MHz, $CDCl_3$)



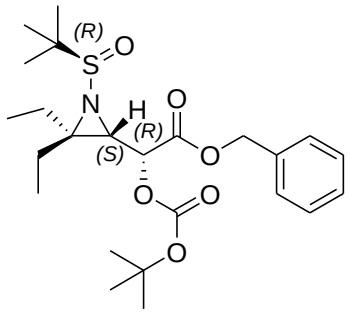
(R_S,2*R*,2'*S*)-**6ac**

^{13}C NMR (75 MHz, $CDCl_3$)



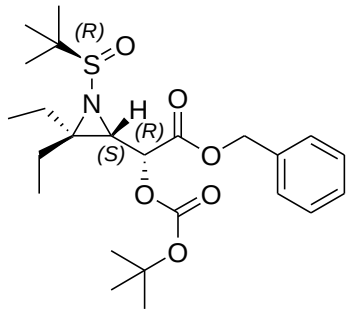
(R_S,2*R*,2'*S*)-**6ac**

^{1}H NMR (300 MHz, $CDCl_3$)



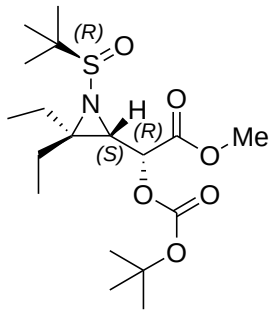
(*R*$_S$,2*R*,2'*S*)-**6ba**

^{13}C NMR (75 MHz, $CDCl_3$)



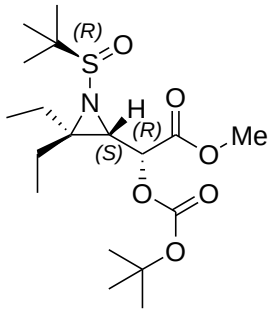
(R_S,2*R*,2'*S*)-**6ba**

^{1}H NMR (300 MHz, $CDCl_3$)

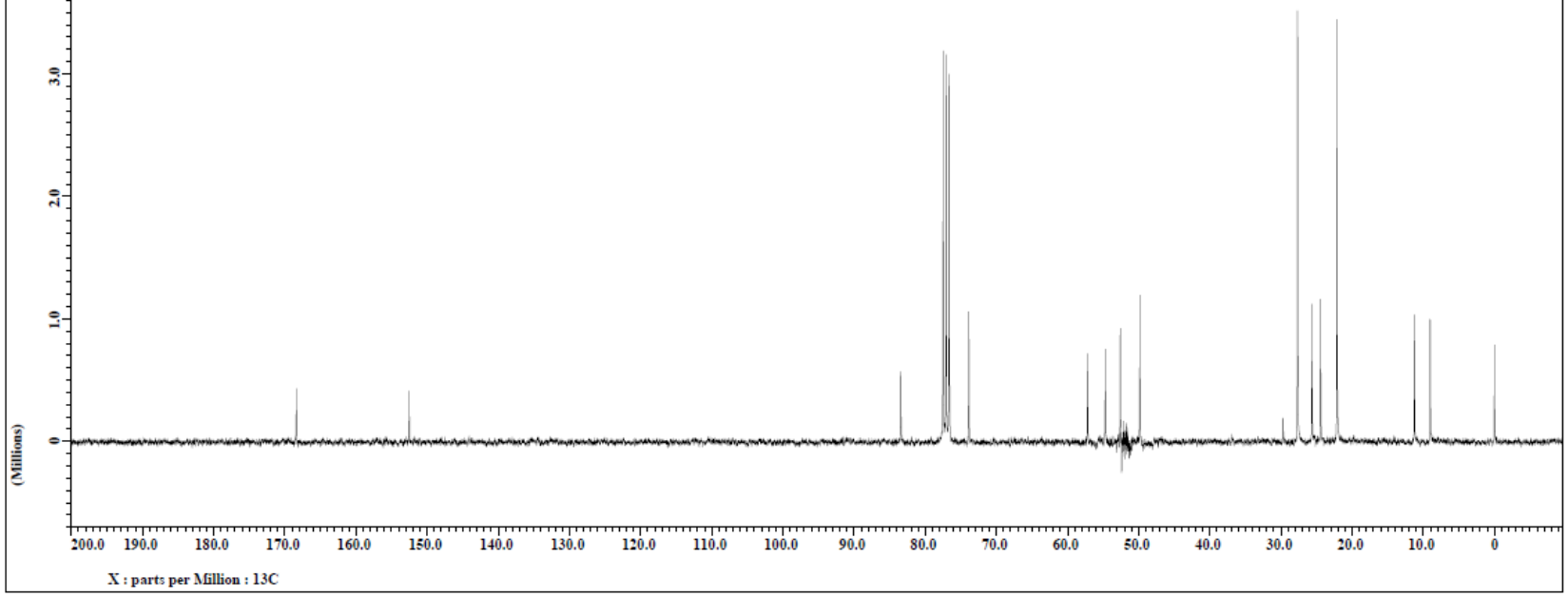


(R_S,2*R*,2'*S*)-**6bb**

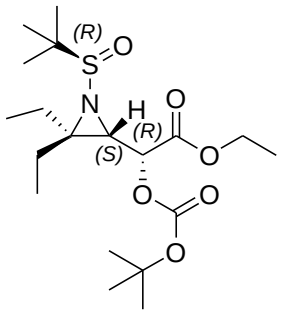
^{13}C NMR (75 MHz, $CDCl_3$)



(R_S,2*R*,2'*S*)-**6bb**

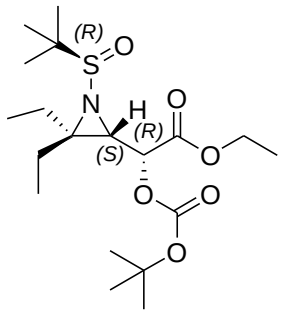


^{1}H NMR (300 MHz, $CDCl_3$)



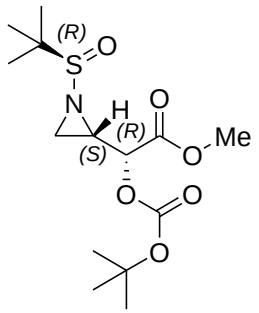
(R_S,2*R*,2'*S*)-**6bc**

^{13}C NMR (75 MHz, $CDCl_3$)



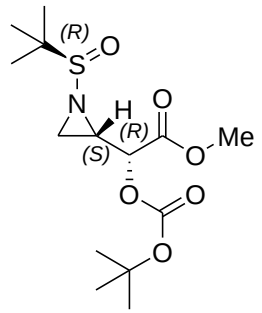
(R_S,2*R*,2'*S*)-**6bc**

^{1}H NMR (300 MHz, $CDCl_3$)



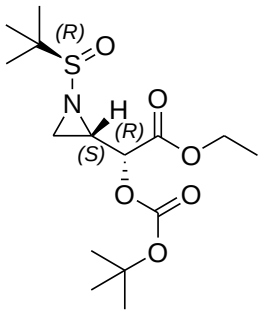
(R_S,2*R*,2'*S*)-**6cb**

^{13}C NMR (75 MHz, $CDCl_3$)



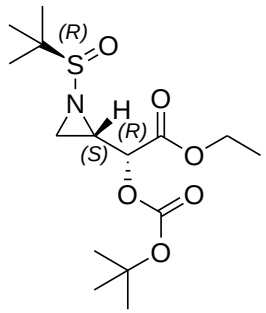
(R_S,2*R*,2'*S*)-**6cb**

^{1}H NMR (300 MHz, $CDCl_3$)

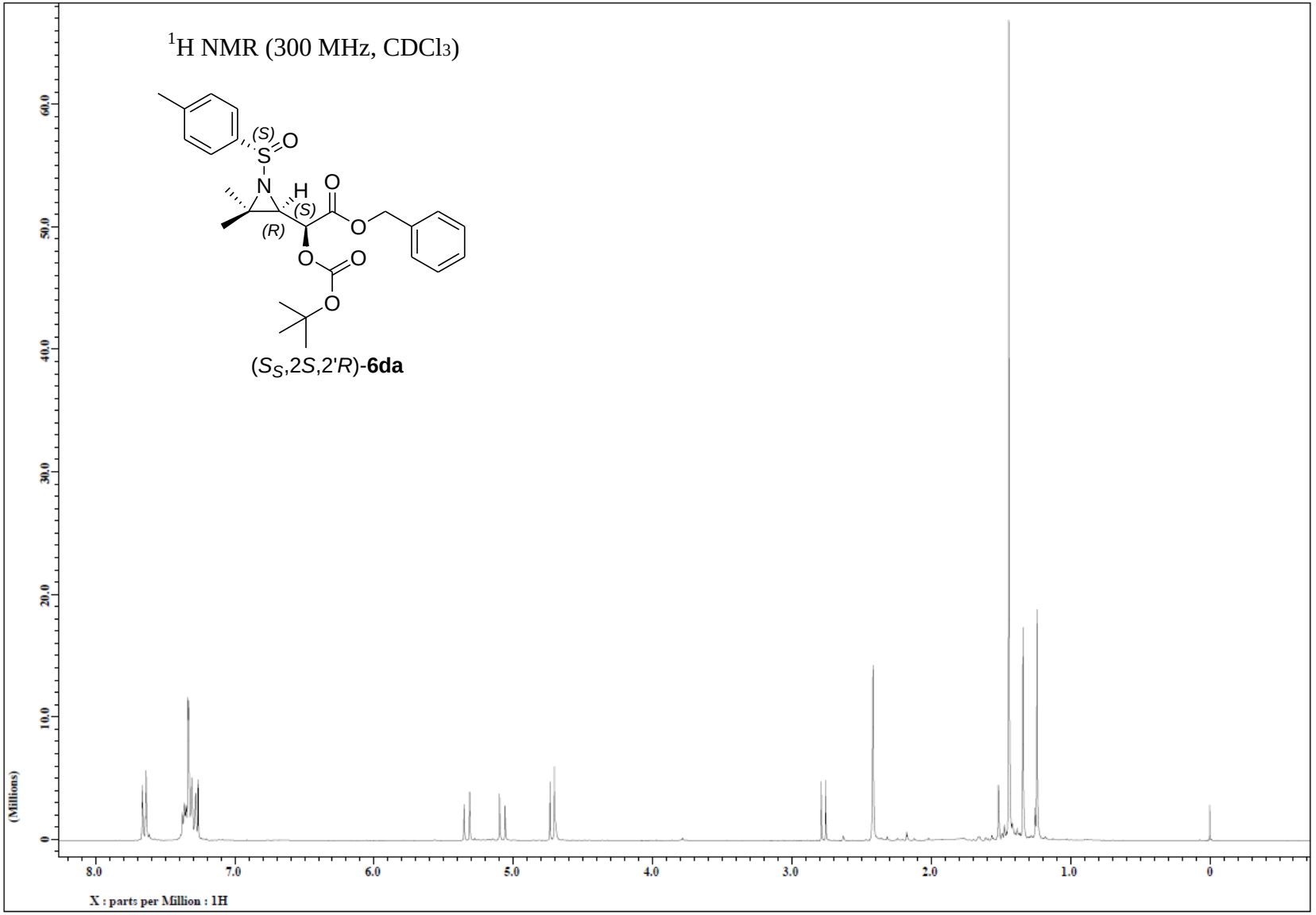


(R_S,2*R*,2'*S*)-**6cc**

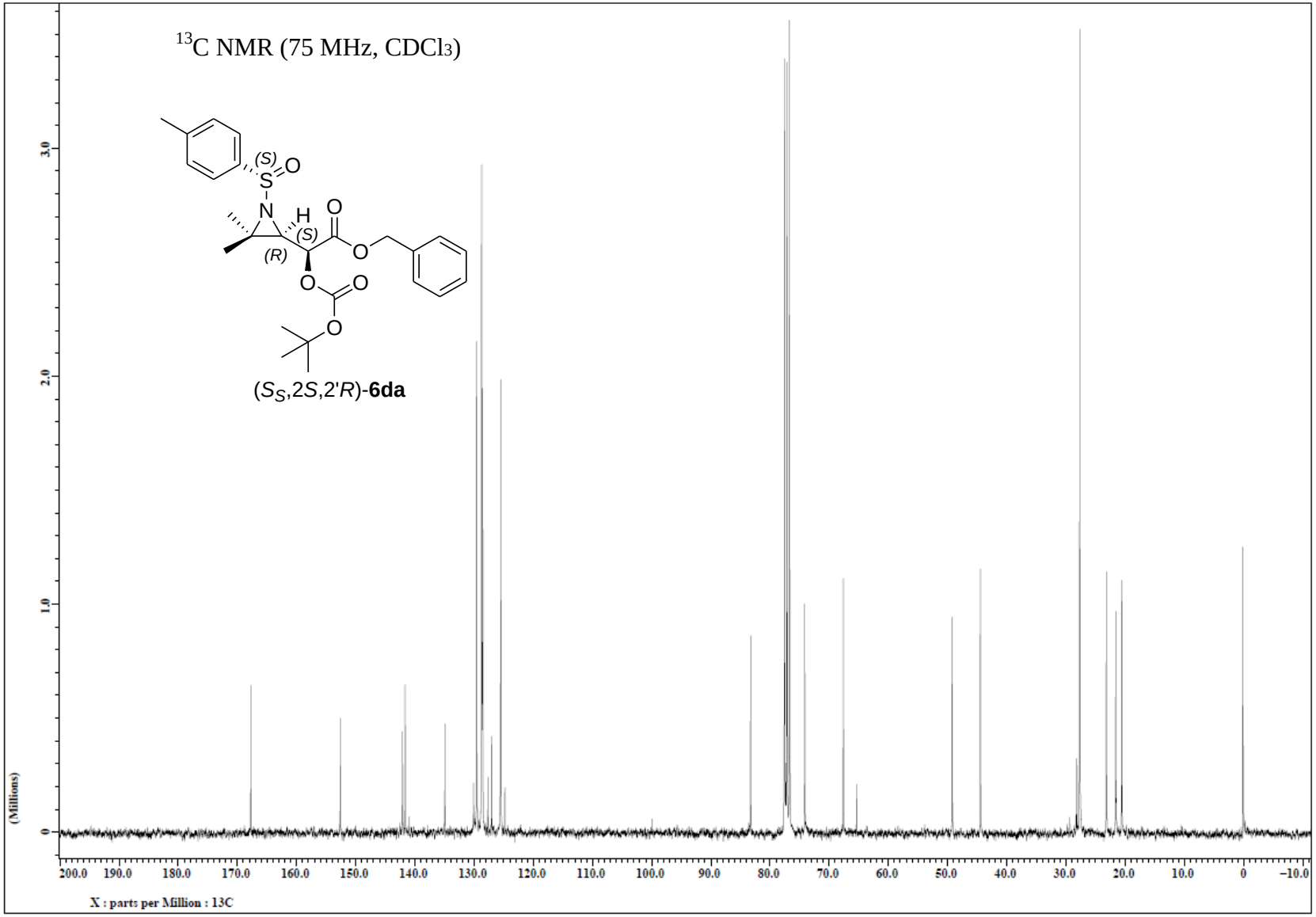
^{13}C NMR (75 MHz, $CDCl_3$)



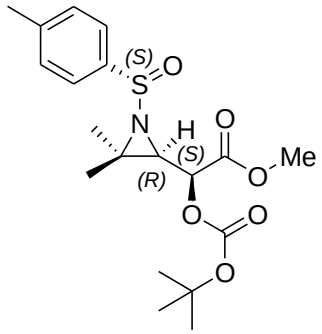
(R_S,2*R*,2'*S*)-**6cc**


^{1}H NMR (300 MHz, CDCl3)
(S)
O
S
N
H
O
(S)
(R)
O
O
O
O
(Millions)
60.0
50.0
40.0
30.0
20.0
10.0
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

(S_S,2*S*,2'*R*)-**6da**

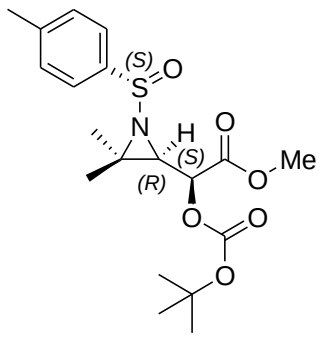

13C NMR (75 MHz, CDCl3)
(S)
O
S
N
H
O
(S)
(R)
O
O
O
O
(SS,2S,2'R)-6da
(Millions)
3.0
2.0
1.0
0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)



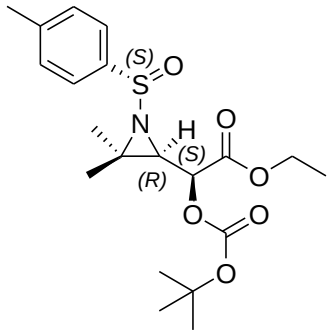
(*S*$_S$,2*S*,2'*R*)-**6db**

^{13}C NMR (75 MHz, $CDCl_3$)

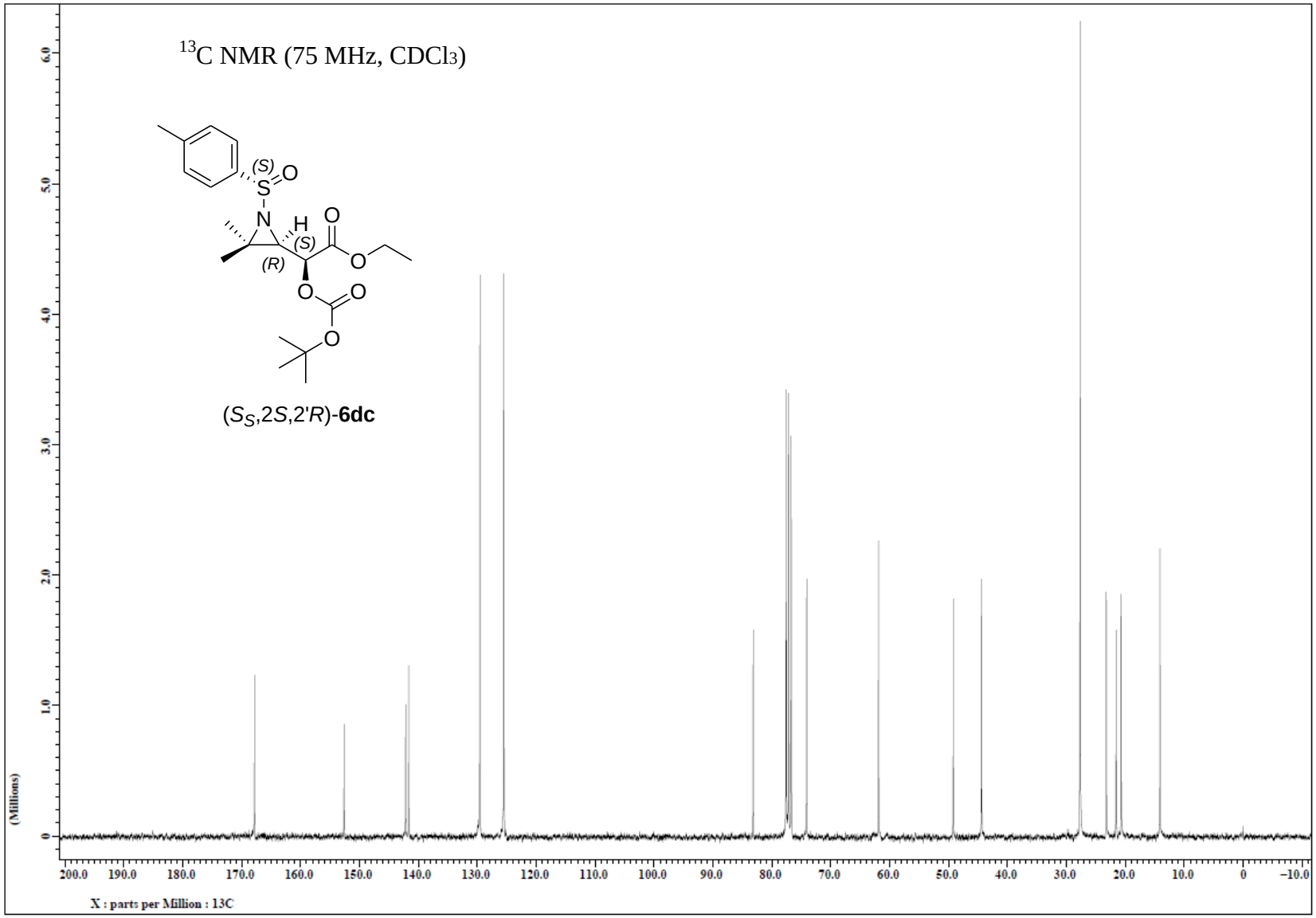


(S_S,2*S*,2'*R*)-**6db**

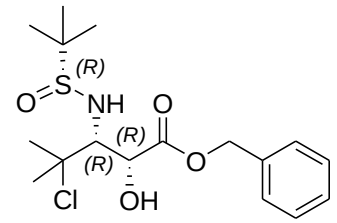
^{1}H NMR (300 MHz, $CDCl_3$)



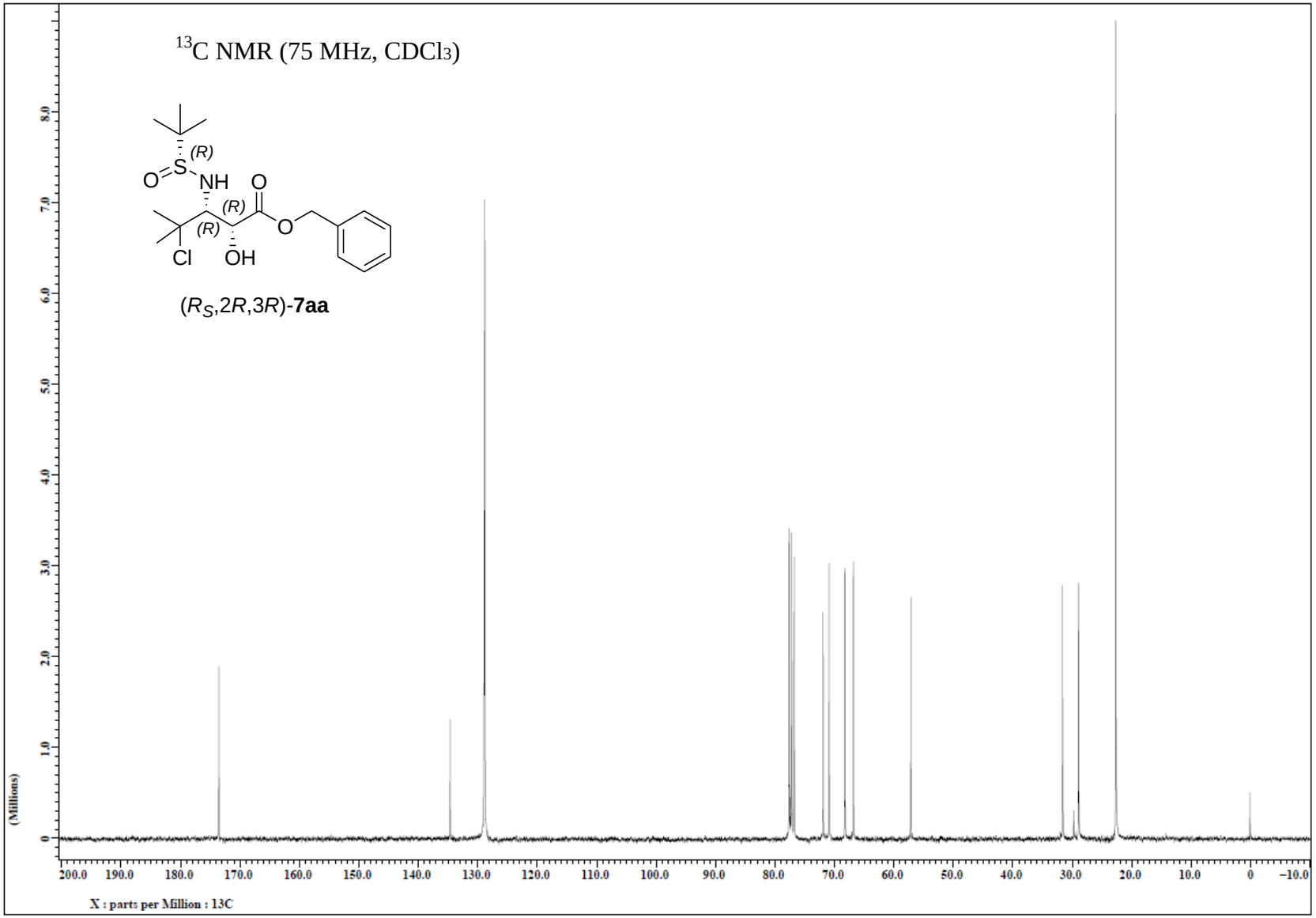
(S_S,2*S*,2'*R*)-**6dc**


13C NMR (75 MHz, CDCl3)
(S)
O
S
N
H
O
(S)
(R)
O
O
O
O
(SS,2S,2'R)-6dc
(Millions)
6.0
5.0
4.0
3.0
2.0
1.0
0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
X : parts per Million : 13C

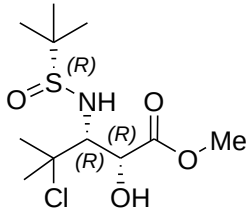
^{1}H NMR (300 MHz, $CDCl_3$)



(R_S,2*R*,3*R*)-**7aa**

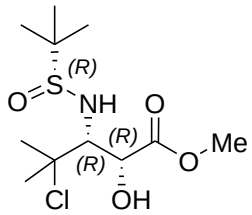

13C NMR (75 MHz, CDCl3)
(R)
O
S
NH
O
(R)
(R)
O
Cl
OH
(RS,2R,3R)-7aa
(Millions)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)



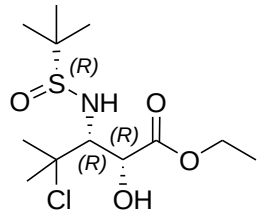
(R_S,2*R*,3*R*)-**7ab**

^{13}C NMR (75 MHz, $CDCl_3$)



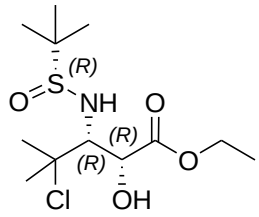
(R_S,2*R*,3*R*)-**7ab**

^{1}H NMR (300 MHz, $CDCl_3$)



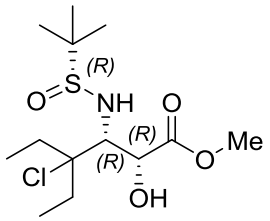
(R_S,2*R*,3*R*)-**7ac**

^{13}C NMR (75 MHz, $CDCl_3$)



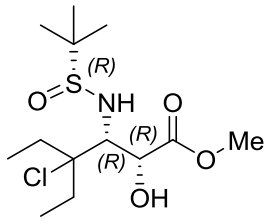
(R_S,2*R*,3*R*)-**7ac**

^{1}H NMR (300 MHz, $CDCl_3$)

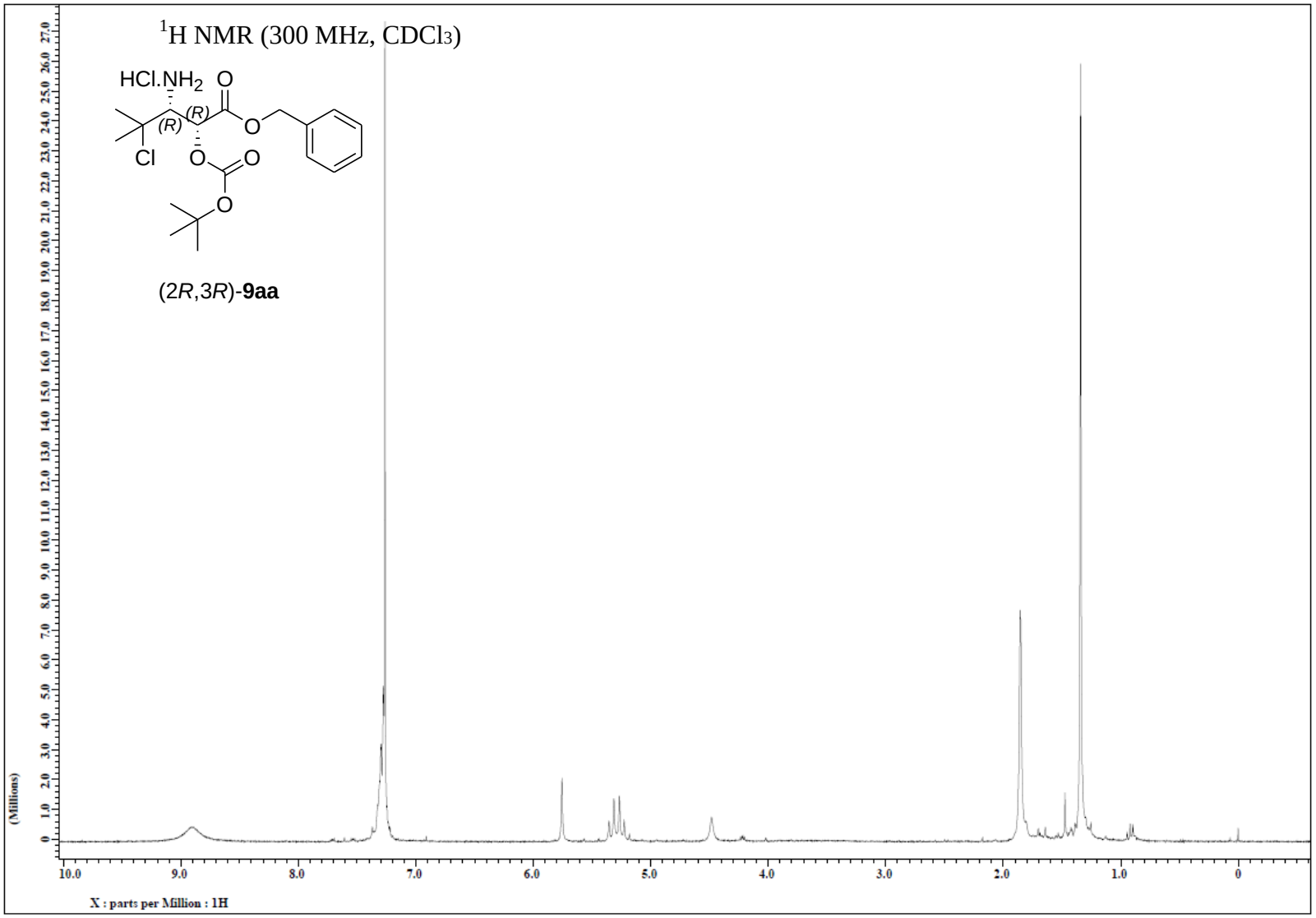


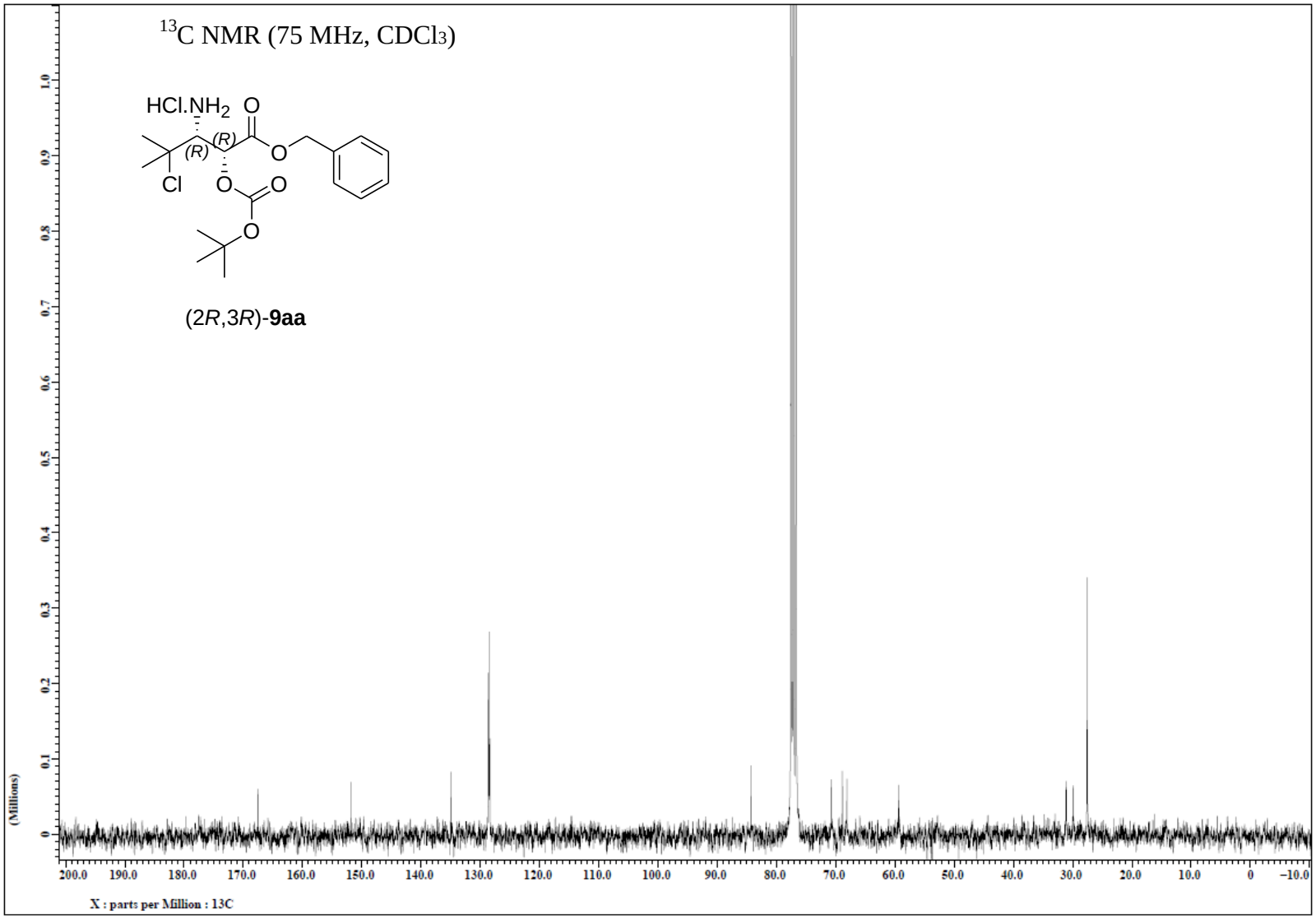
(R_S,2*R*,3*R*)-**7bb**

^{13}C NMR (75 MHz, $CDCl_3$)

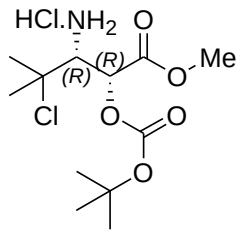


(R_S,2*R*,3*R*)-**7bb**


^{1}H NMR (300 MHz, CDCl3)
HCl.NH2
O
(R)
(R)
O
Cl
O
O
O
(2R,3R)-9aa
(Millions)
27.0
26.0
25.0
24.0
23.0
22.0
21.0
20.0
19.0
18.0
17.0
16.0
15.0
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

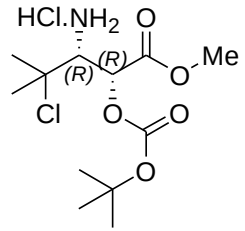

13C NMR (75 MHz, CDCl3)
HCl.NH2
O
(R)
(R)
O
Cl
O
O
O
(2R,3R)-9aa
(Millions)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
−10.0
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)



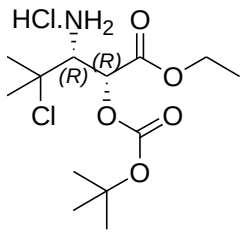
(2*R*,3*R*)-**9ab**

^{13}C NMR (75 MHz, $CDCl_3$)

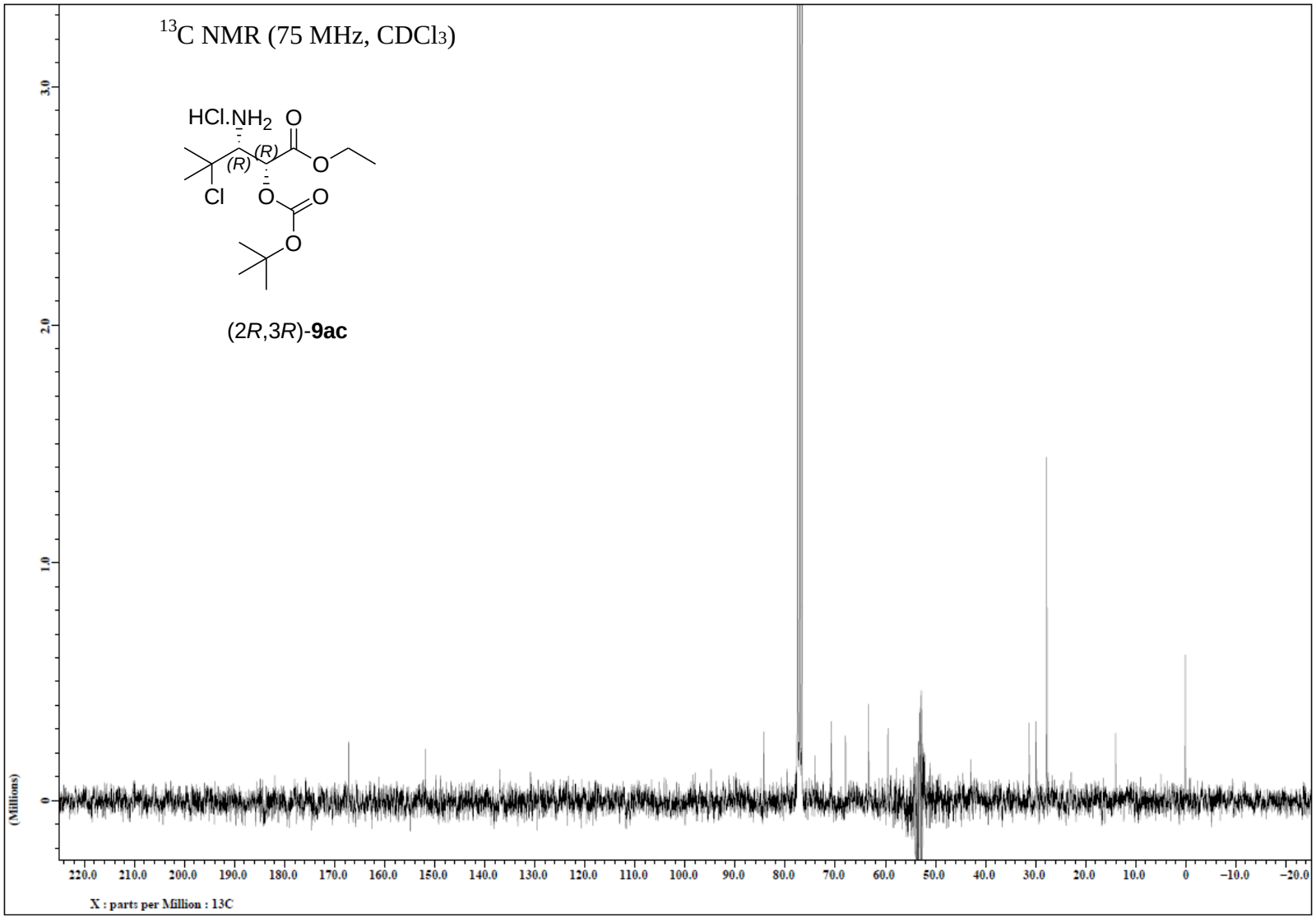


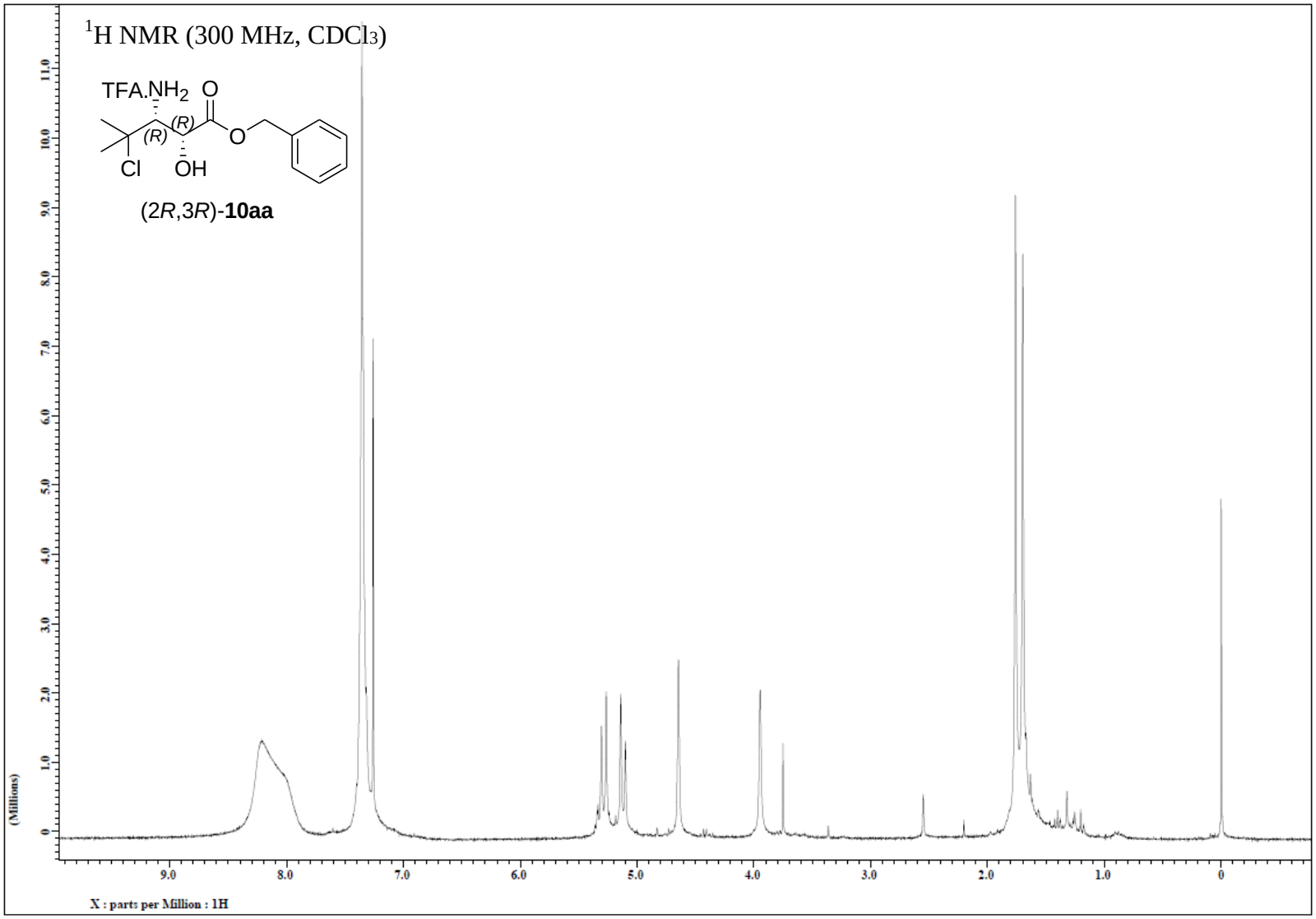
(2*R*,3*R*)-**9ab**

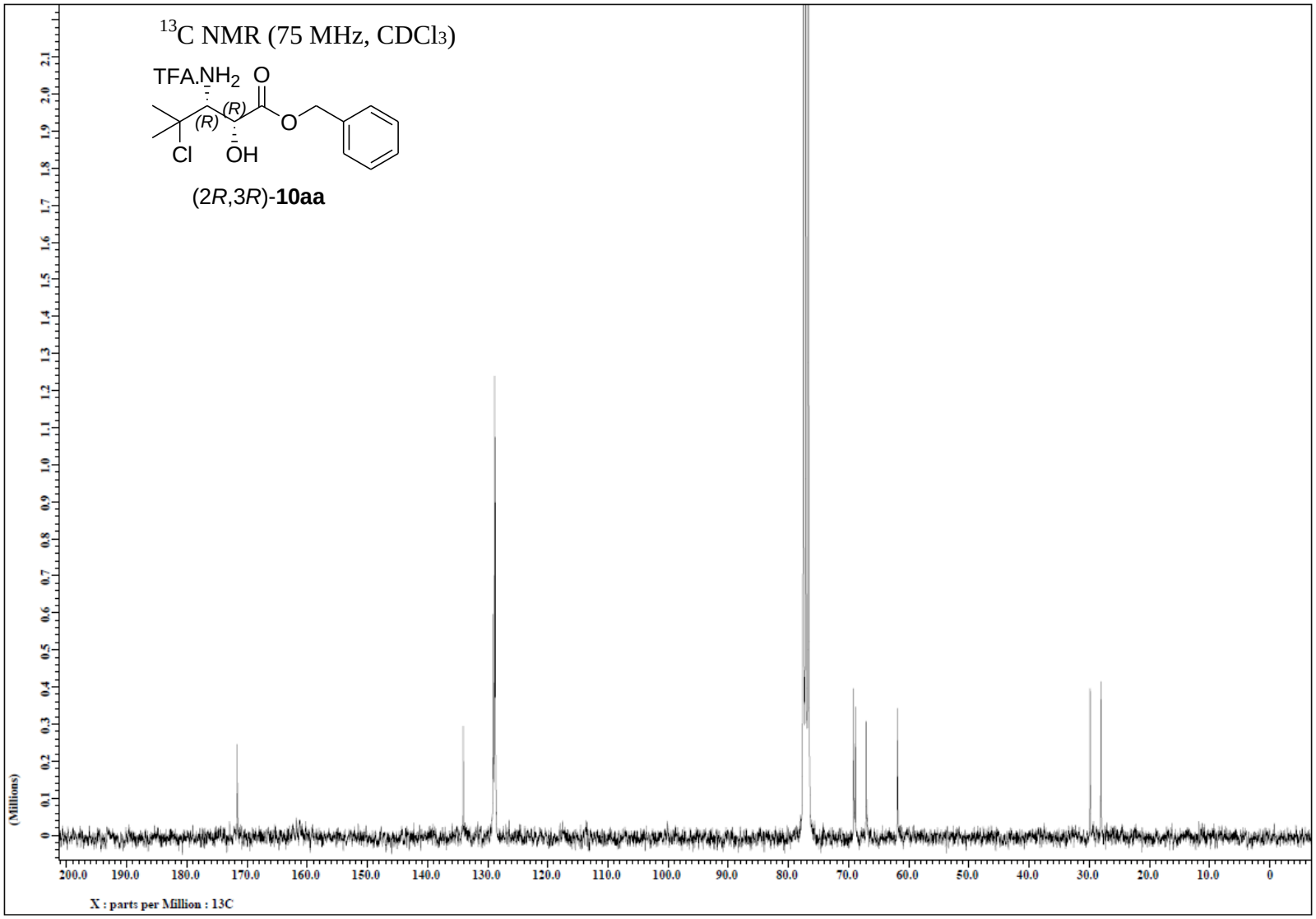
^{1}H NMR (300 MHz, $CDCl_3$)



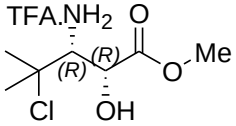
(2*R*,3*R*)-**9ac**


13C NMR (75 MHz, CDCl3)
HCl.NH2
O
(R)
(R)
O
Cl
O
O
O
(2R,3R)-9ac
3.0
2.0
1.0
0
(Millions)
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
X : parts per Million : 13C


^{1}H NMR (300 MHz, CDCl$_3$)
TFA.NH$_2$
O
(R)
(R)
O
Cl
OH
(2*R*,3*R*)-**10aa**
(Millions)
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

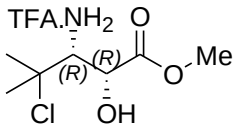

13C NMR (75 MHz, CDCl3)
TFA.NH2
O
(R)
(R)
O
Cl
OH
(2R,3R)-10aa
(Millions)
X : parts per Million : 13C

^{1}H NMR (300 MHz, $CDCl_3$)

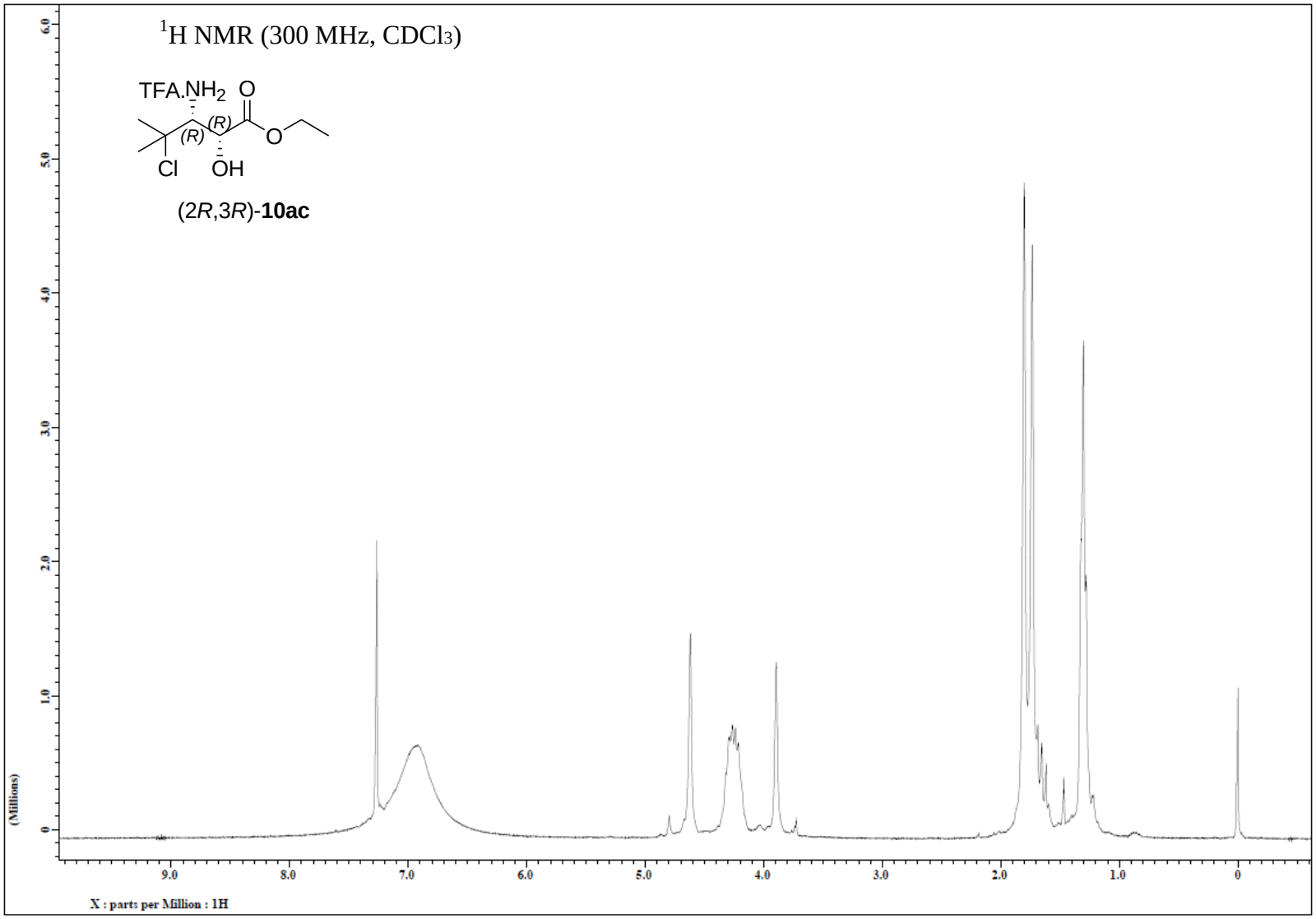


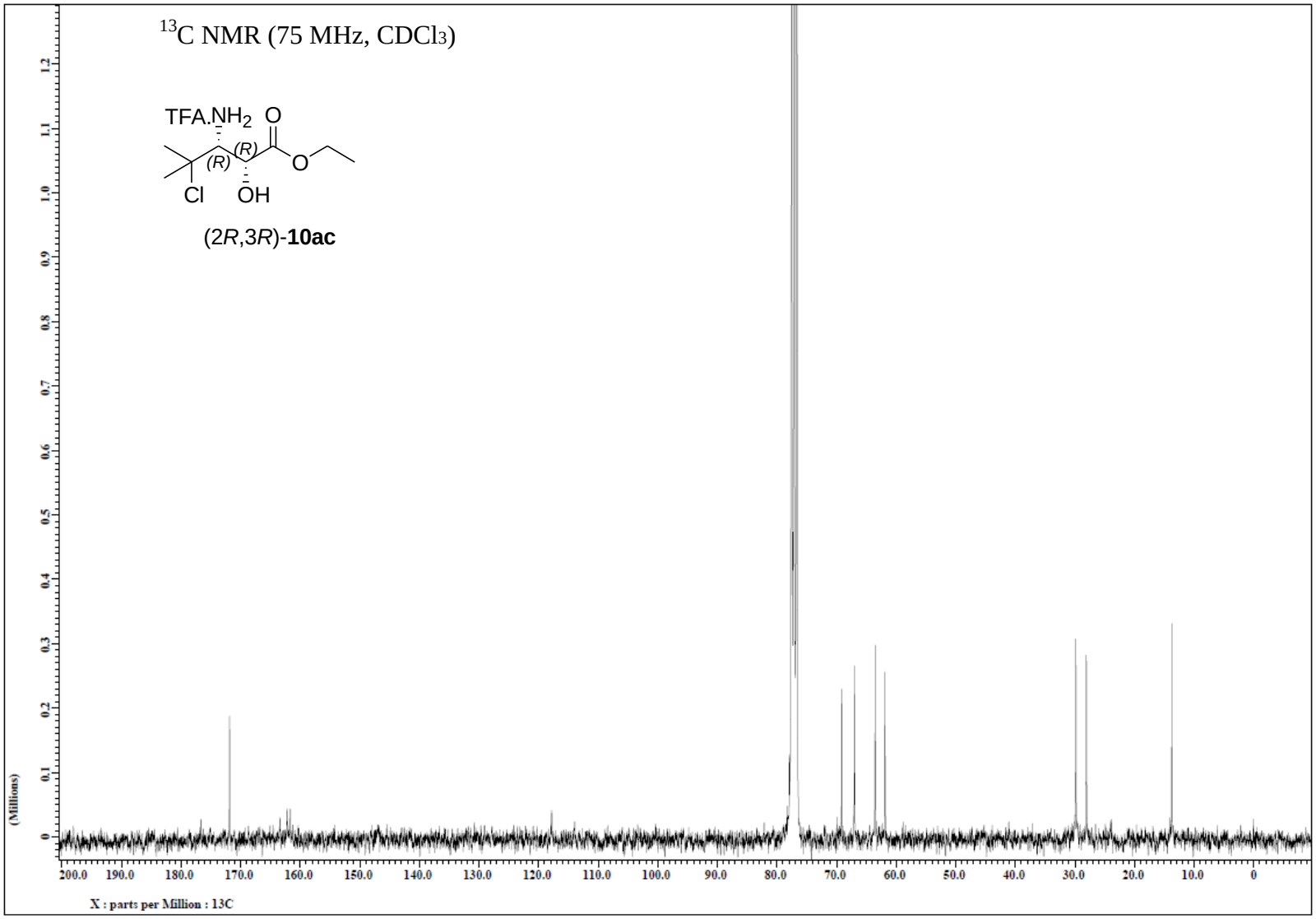
(2*R*,3*R*)-**10ab**

^{13}C NMR (75 MHz, $CDCl_3$)

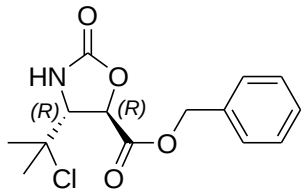


(2*R*,3*R*)-**10ab**

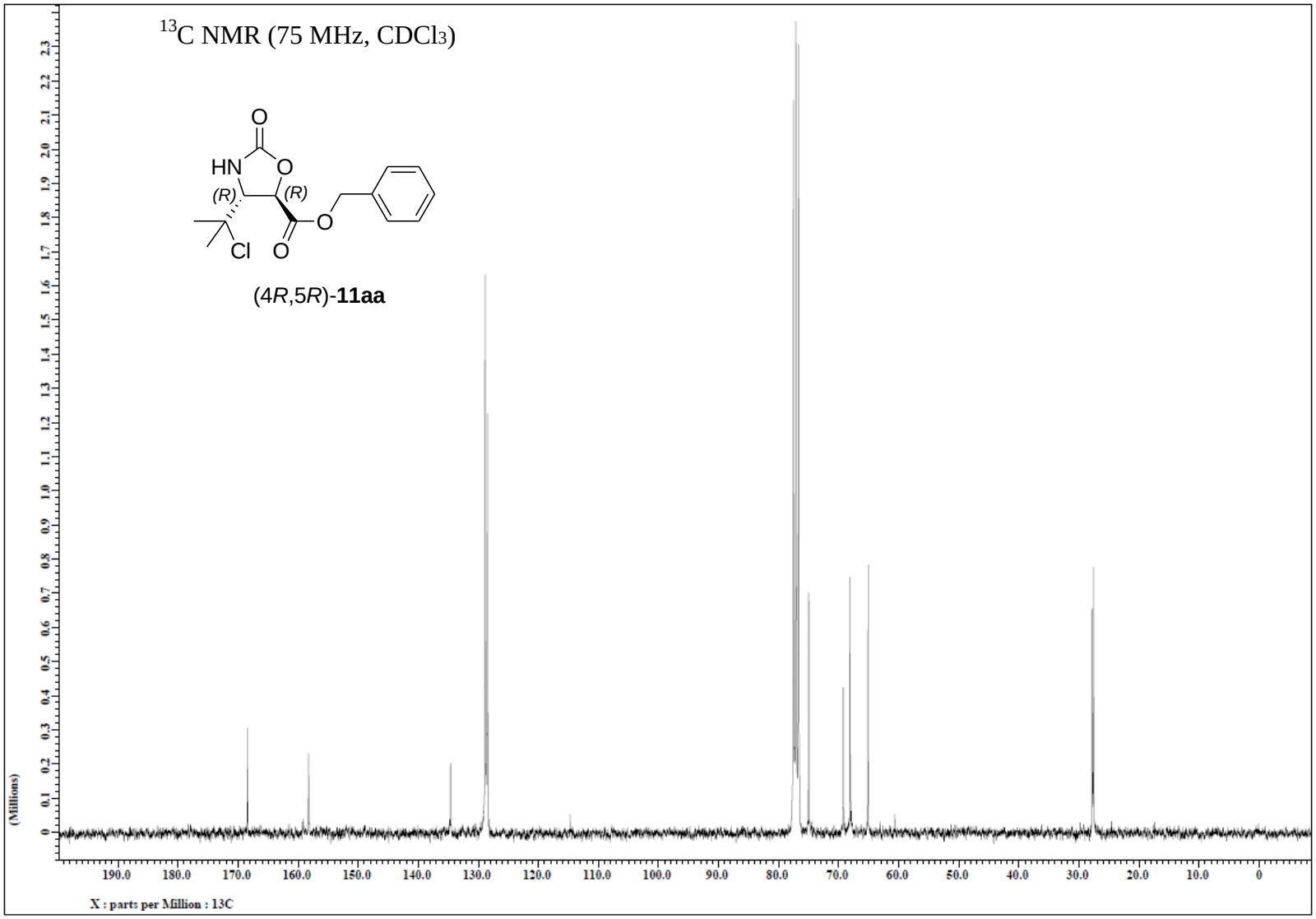

^{1}H NMR (300 MHz, CDCl$_3$)
TFA.NH$_2$
O
(R)
(R)
O
Cl
OH
(2*R*,3*R*)-**10ac**
(Millions)
6.0
5.0
4.0
3.0
2.0
1.0
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

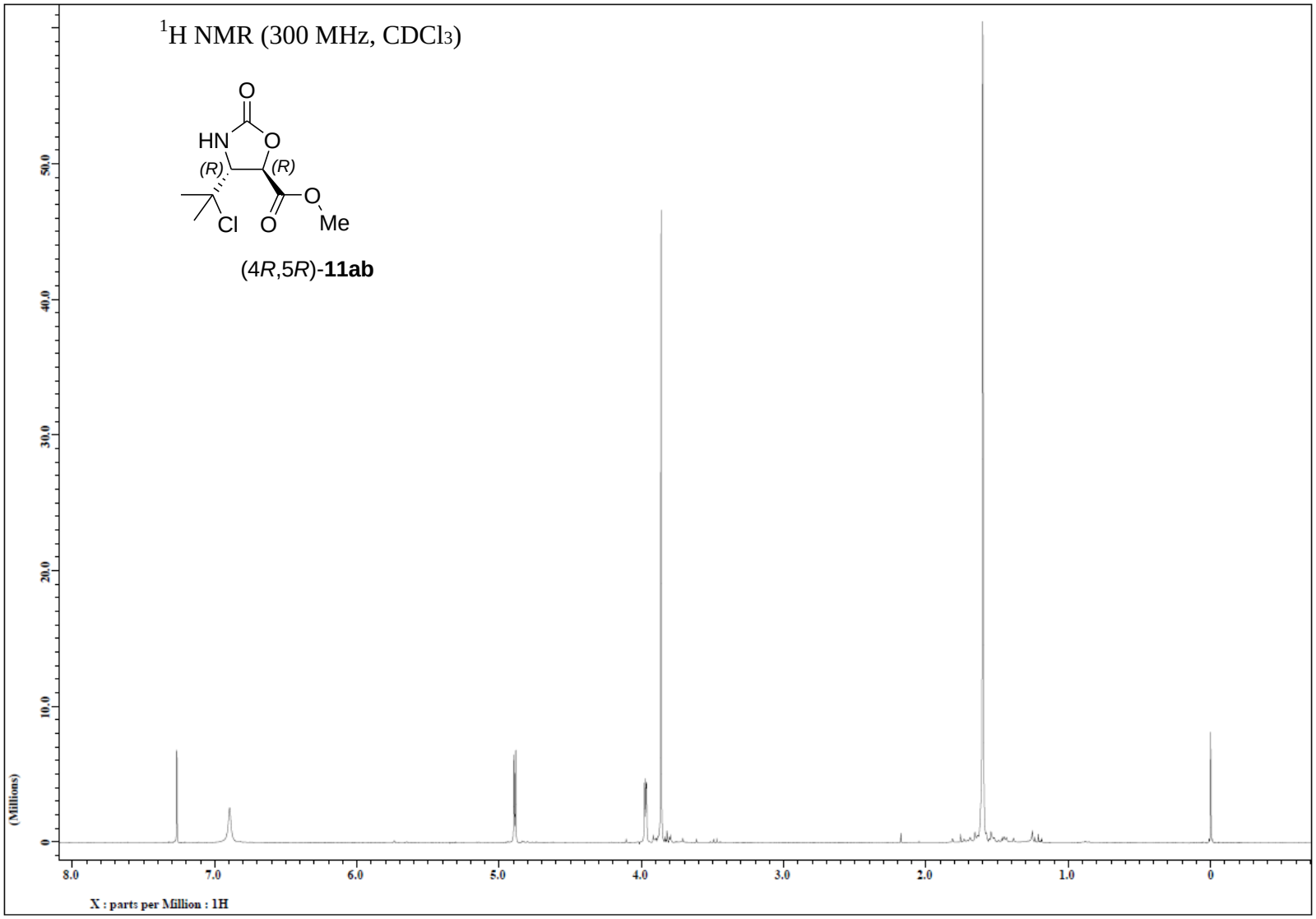

13C NMR (75 MHz, CDCl3)
TFA.NH2
O
(R)
(R)
O
Cl
OH
(2R,3R)-10ac
(Millions)
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : 13C

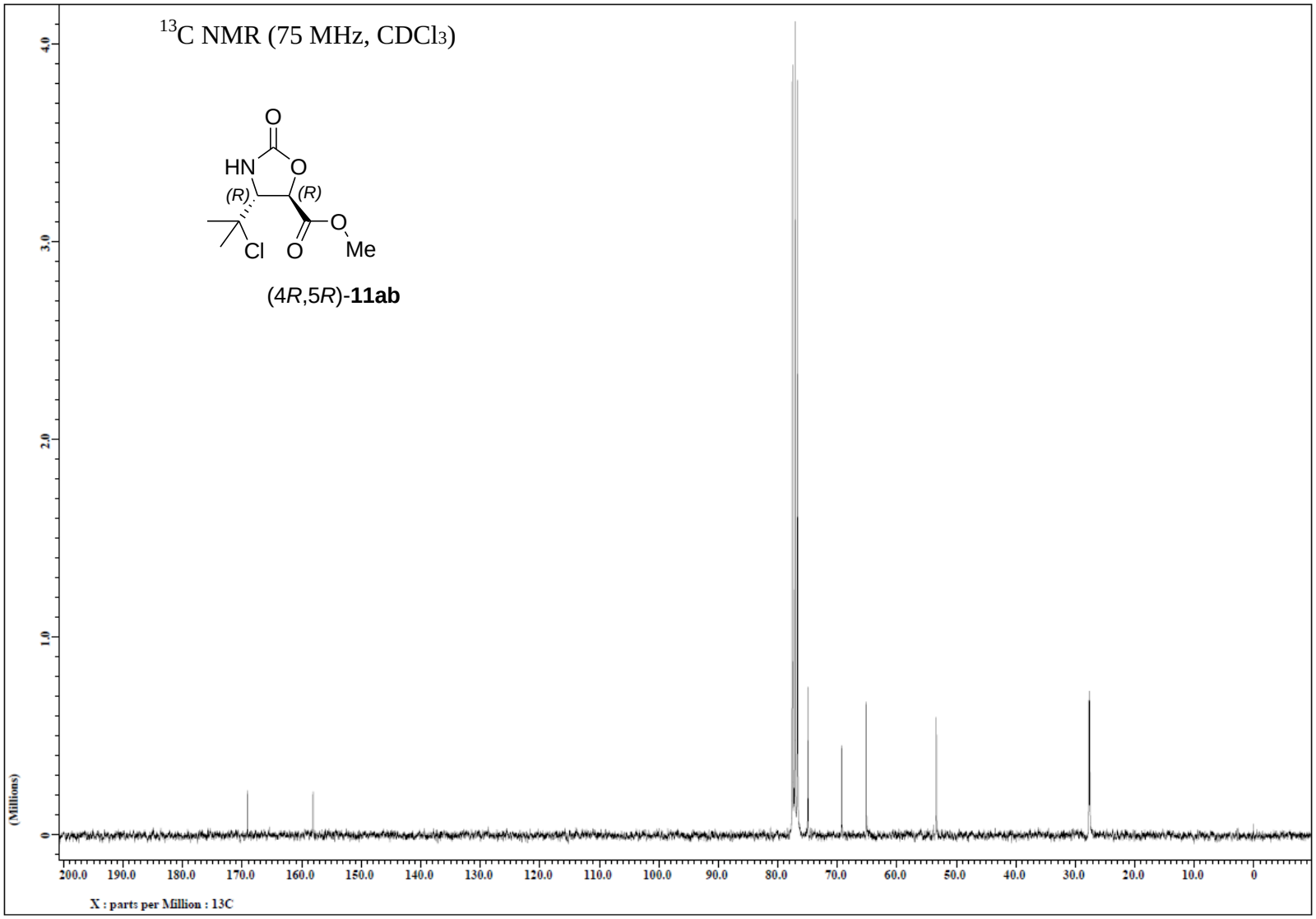
^{1}H NMR (300 MHz, $CDCl_3$)

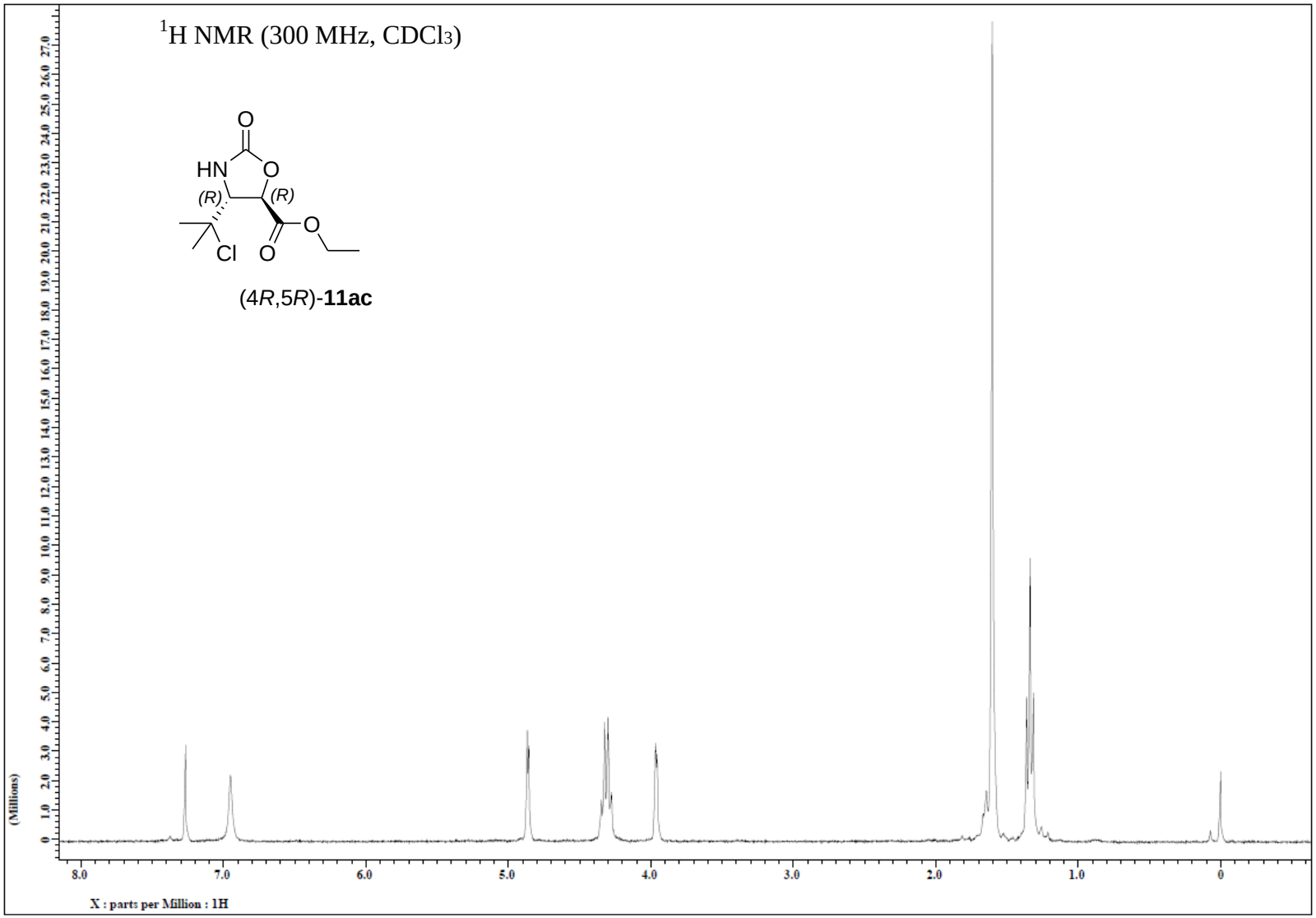


(4*R*,5*R*)-**11aa**

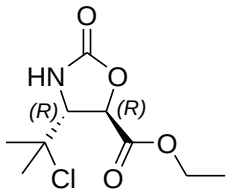

13C NMR (75 MHz, CDCl3)
O
HN
O
(R)
(R)
O
Cl
O
(4R,5R)-11aa
(Millions)
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
2.0
2.1
2.2
2.3
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
X : parts per Million : 13C


^{1}H NMR (300 MHz, CDCl$_3$)
HN
O
O
(R)
(R)
O
Cl
O
Me
(4R,5R)-11ab
(Millions)
50.0
40.0
30.0
20.0
10.0
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H


13C NMR (75 MHz, CDCl3)
O
HN
O
(R)
(R)
O
Cl
O
Me
(4R,5R)-11ab
(Millions)
4.0
3.0
2.0
1.0
0
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
X : parts per Million : 13C


^{1}H NMR (300 MHz, CDCl$_3$)
O
HN
O
(R)
(R)
O
Cl
O
(4R,5R)-11ac
(Millions)
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
15.0
16.0
17.0
18.0
19.0
20.0
21.0
22.0
23.0
24.0
25.0
26.0
27.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H

^{13}C NMR (75 MHz, $CDCl_3$)



(4*R*,5*R*)-**11ac**