Supporting Information

Synthesis of *meta*-Substituted Anilines via Three-Component Reaction of Acetone, Amines, and 1,3-Diketones

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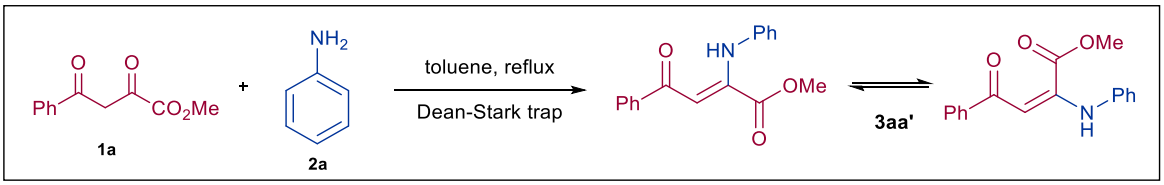
1. Synthesis of methyl 4-oxo-4-phenyl-2-(phenylamino)but-2-enoate (3′aa)



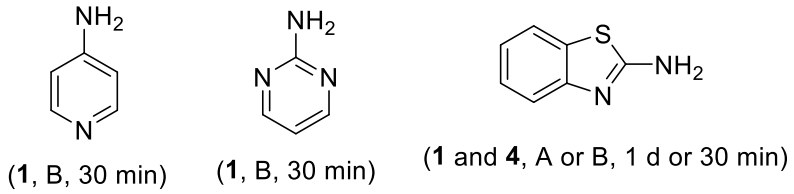
Compound **3aa′** is prepared according to the published method[1].

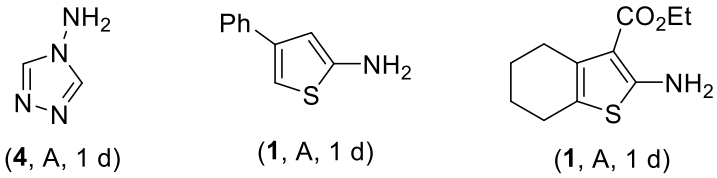
^{1}H NMR (400 MHz, DMSO-d_6, ratio 4.3:1, reported as major (*Z*)/minor (*E*) peak) δ [11.92 (s) & 9.76 (s), Σ1H], [7.99 (d, *J* = 7.1 Hz) & 7.79 (d, *J* = 7.0 Hz), Σ2H], [7.60 (t, *J* = 7.3 Hz) & 7.57–7.48 (m), Σ1H], [7.53 (t, *J* = 7.3 Hz) & 7.48–7.43 (m), Σ2H], [7.41–7.32 (m) & 7.45–7.41 (m), Σ2H], [7.08 (d, *J* = 7.4 Hz) & 7.28 (d, *J* = 7.3 Hz), Σ2H], [7.17 (td, *J* = 7.3, 1.1 Hz) & 7.23–7.17 (m), Σ1H], [6.48 (s) & 6.43 (s), Σ1H], [3.74 (s) & 3.84 (s), Σ3H].

^{13}C NMR (101 MHz, DMSO-d_6) δ (major) 189.9, 164.1, 149.1, 139.0, 138.0, 132.3, 129.2 (2C), 128.6 (2C), 127.2 (2C), 124.8, 120.9 (2C), 95.9, 52.9; (minor) 186.4, 165.9, 150.3, 138.7, 131.6, 129.4 (2C), 128.4 (2C), 127.1 (2C), 124.8, 121.9 (2C), 92.4, 52.4.

2. List of tested heterocycles

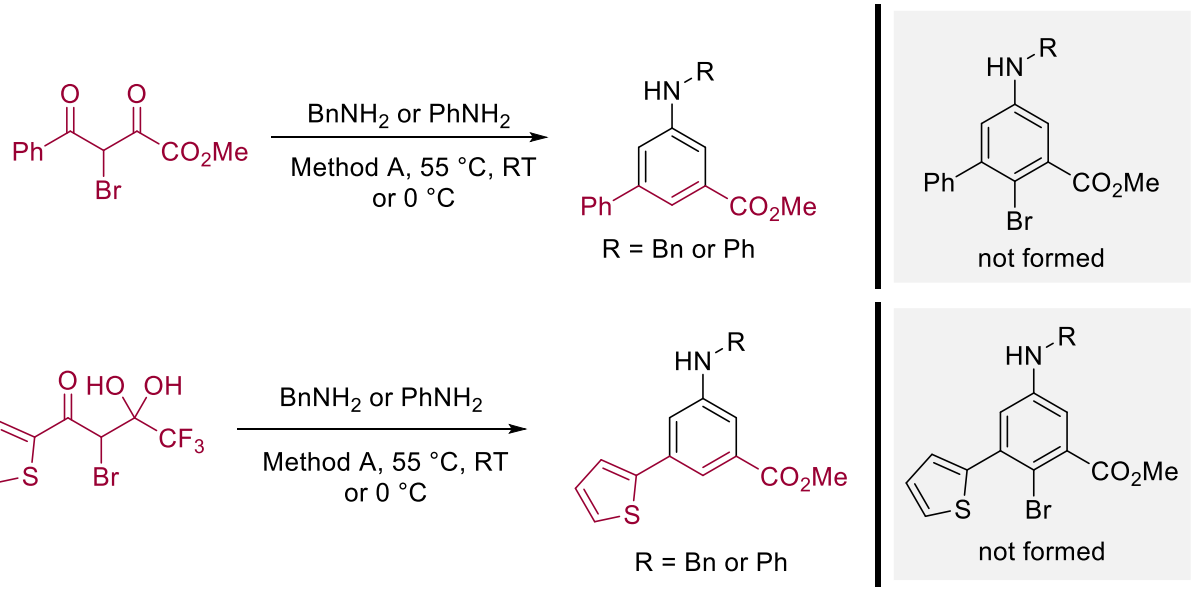
Heterocycles, which failed in reaction, are shown below, in parenthesis are: tested β-diketone type, method, time. In each case, only trace amounts of products could be detected by LC-MS.



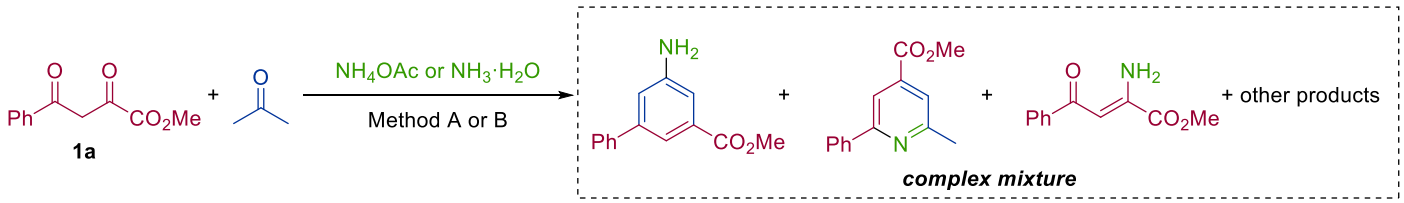


3. Reaction with brominated 1 and 4[2]

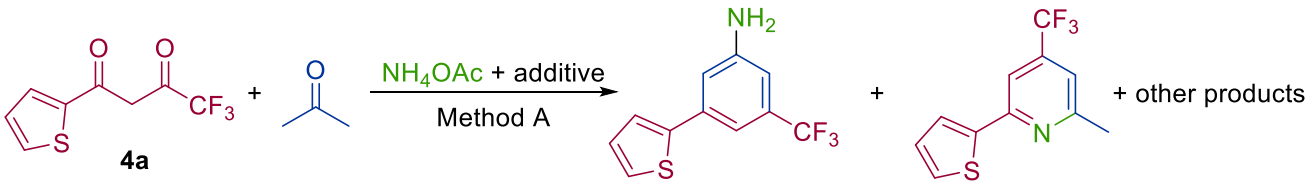
Different attempts are illustrated below. In each case, rapid development of red color has been seen (within minutes), as a result of debromination of starting material.



4. Reaction of diketones 1 and 4 with NH_3 sources



Tested condition for reaction of **4a** and NH_4OAc (ratio of products was determined by LC-MS):



Additive:				
	none	1	:	3
	EtOH	1	:	5
	DMSO	1	:	1
	DMF	1	:	1

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5. Single crystal X-ray data

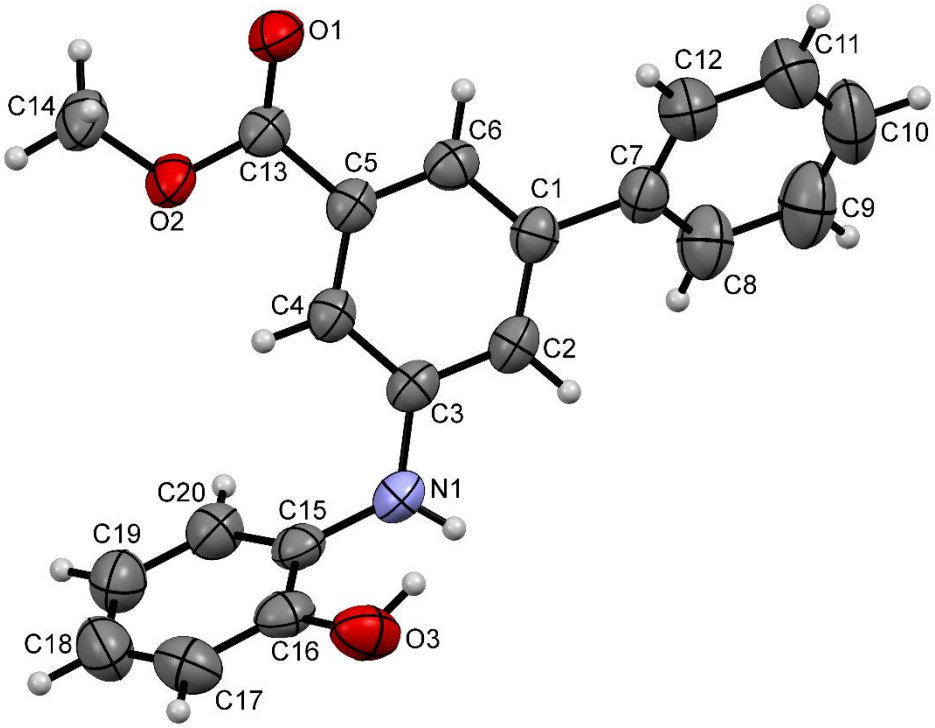


Fig. 1. *Molecular structure of compound* ***3ab*** *showing 50% probability amplitude displacement ellipsoids (CCDC 1905222).*

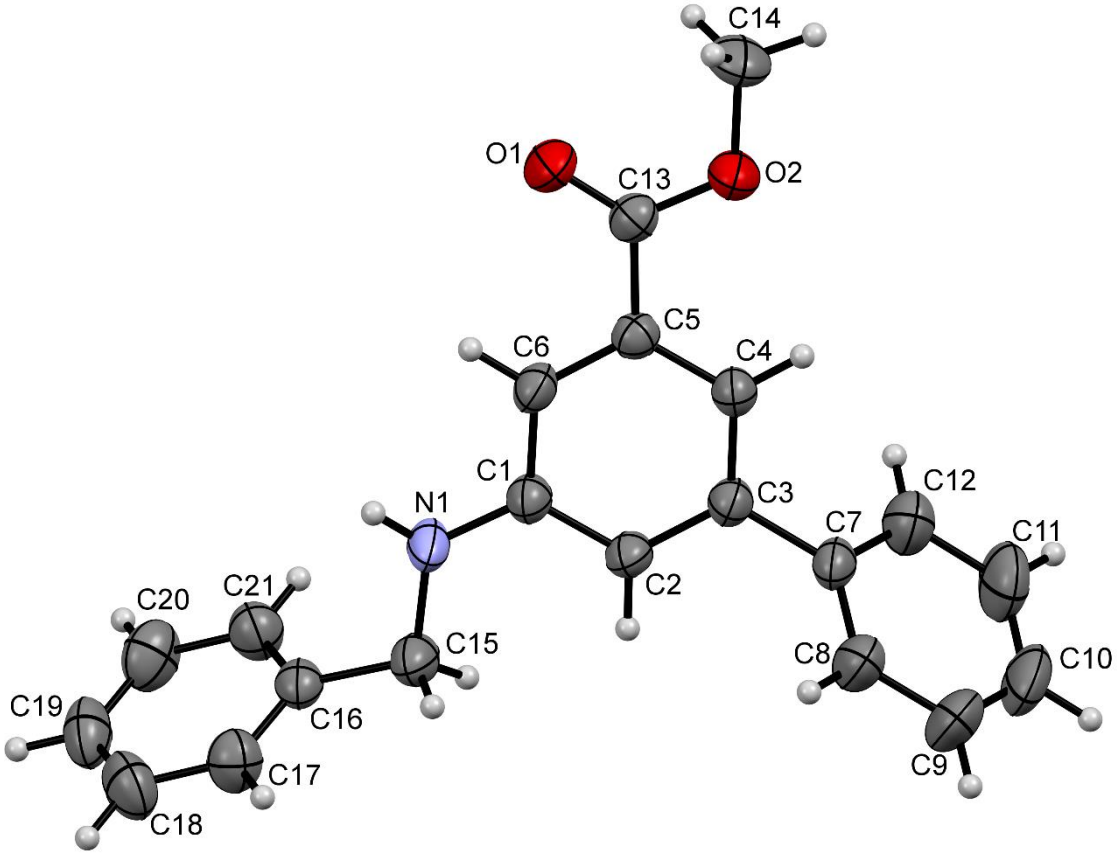


Fig. 2. *Molecular structure of compound* ***3ae*** *showing 50% probability amplitude displacement ellipsoids (CCDC 1905220).*

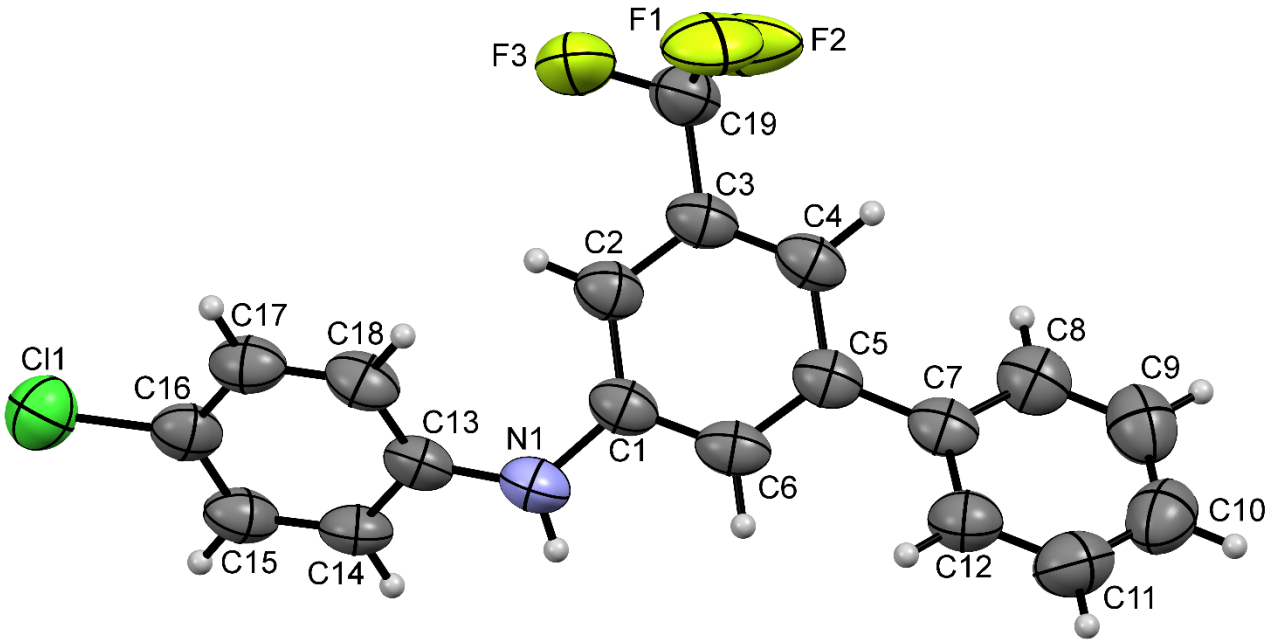


Fig. 3. *Molecular structure of compound* ***5bc*** *showing 50% probability amplitude displacement ellipsoids (CCDC 1905223).*

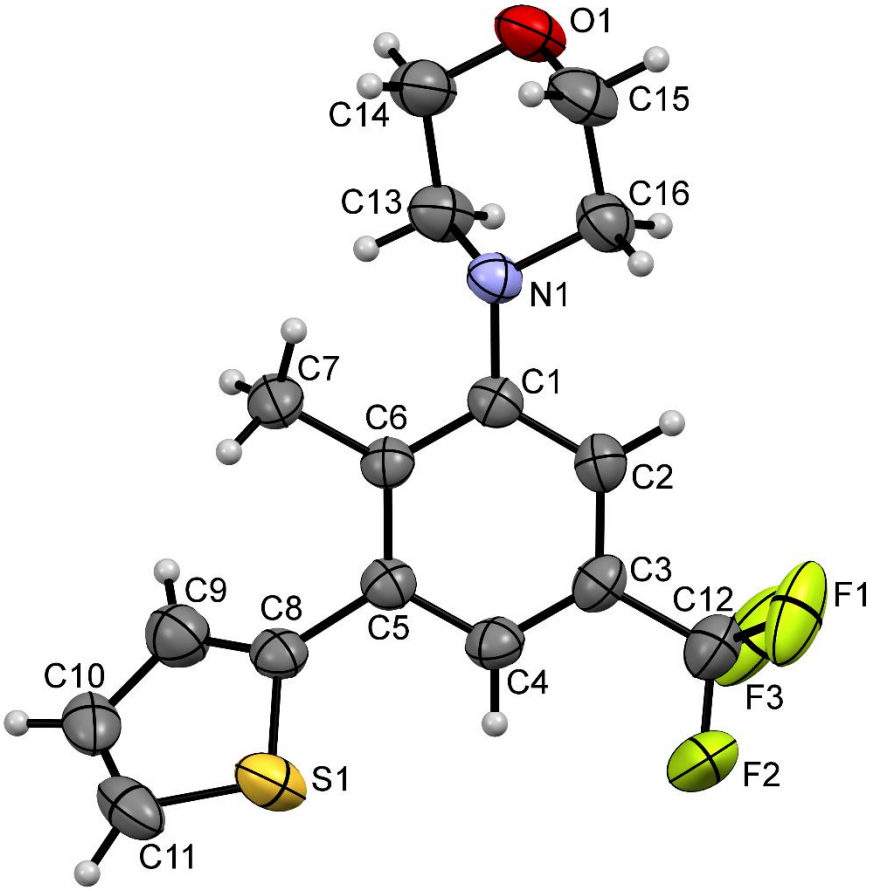


Fig. 4. *Molecular structure of compound* ***8ka*** *showing 50% probability amplitude displacement ellipsoids (CCDC 1960904).*

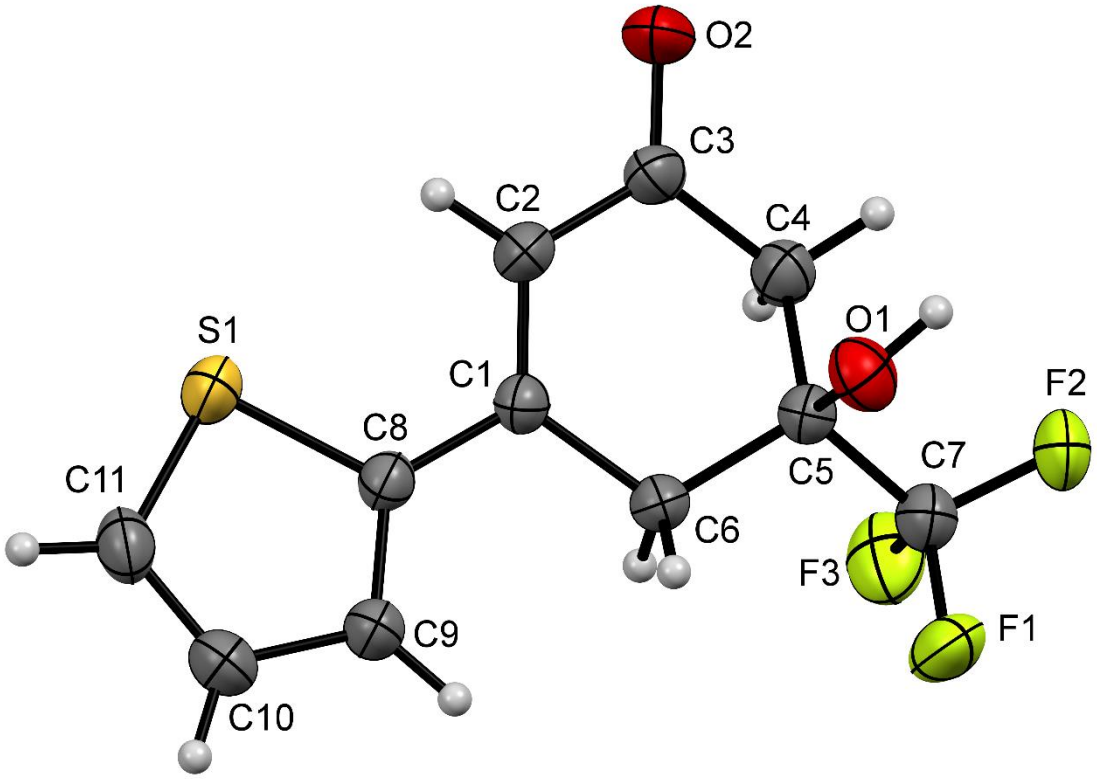


Fig. 5. *Molecular structure of compound* ***9b*** *showing 50% probability amplitude displacement ellipsoids (CCDC 1905221).*

Crystal structure determination

The unit cell parameters and the X-ray diffraction intensities were measured on a Xcalibur Ruby diffractometer. The empirical absorption correction was introduced by multi-scan method using SCALE3 ABSPACK algorithm[3]. Using OLEX2[4] or WinGX[5] (for **3ae**), the structures were solved with the olex2.solve program[6] (for **5bc**) or with the SHELXS program[7] and refined by the full-matrix least-squares method in the anisotropic approximation for all non-hydrogen atoms using the SHELXL[8] program. Hydrogen atoms bound to carbon were located from the Fourier synthesis of the electron density and refined using a riding model. The hydrogen atoms of NH and OH groups were refined freely with isotropic displacement parameters.

Crystal Data of ***3ab***. $C_{20}H_{17}NO_3$, M = 319.35, triclinic, a = 7.6883(17) Å, b = 9.4591(15) Å, c = 11.7328(19) Å, α = 82.664(14) °, β = 79.063(17) °, γ = 76.170(16) °, V = 810.4(3) Å^3, T = 295(2), space group P–1, Z = 2, μ(Mo Kα) = 0.088 mm^{-1}. The final refinement parameters: R_1 = 0.0592, wR_2 = 0.1545 [for observed 2429 reflections with $I > 2\sigma(I)$]; R_1 = 0.0855, wR_2 = 0.1868 (for all independent 3760 reflections, R_{int} = 0.0357), S = 1.050.

Crystal Data of ***3ae***. $C_{21}H_{19}NO_2$, M = 317.37, triclinic, a = 6.3877(14) Å, b = 9.9122(19) Å, c = 14.758(3) Å, α = 79.468(16)°, β = 78.355(18) °, γ = 72.386(18) °, V = 864.8(3) Å^3, T = 295(2), space group P–1, Z = 2, μ(Mo Kα) = 0.078 mm^{-1}. The final refinement parameters: R_1 = 0.0570, wR_2 = 0.1359 [for observed

2418 reflections with $I > 2\sigma(I)$]; R_1 = 0.0975, wR_2 = 0.1607 (for all independent 3957 reflections, R_{int} = 0.0361), S = 0.988.

Crystal Data of ***5bc***. $C_{19}H_{13}ClF_3N$, M = 347.75, orthorhombic, a = 19.452(7) Å, b = 16.461(7) Å, c = 10.122(3) Å, V = 3241(2) Å^3, T = 295(2), space group $Pccn$, Z = 8, μ(Mo Kα) = 0.266 mm^{-1}. The final refinement parameters: R_1 = 0.0562, wR_2 = 0.1083 [for observed 2212 reflections with $I > 2\sigma(I)$]; R_1 = 0.1124, wR_2 = 0.1354 (for all independent 3920 reflections, R_{int} = 0.0444), S = 1.038.

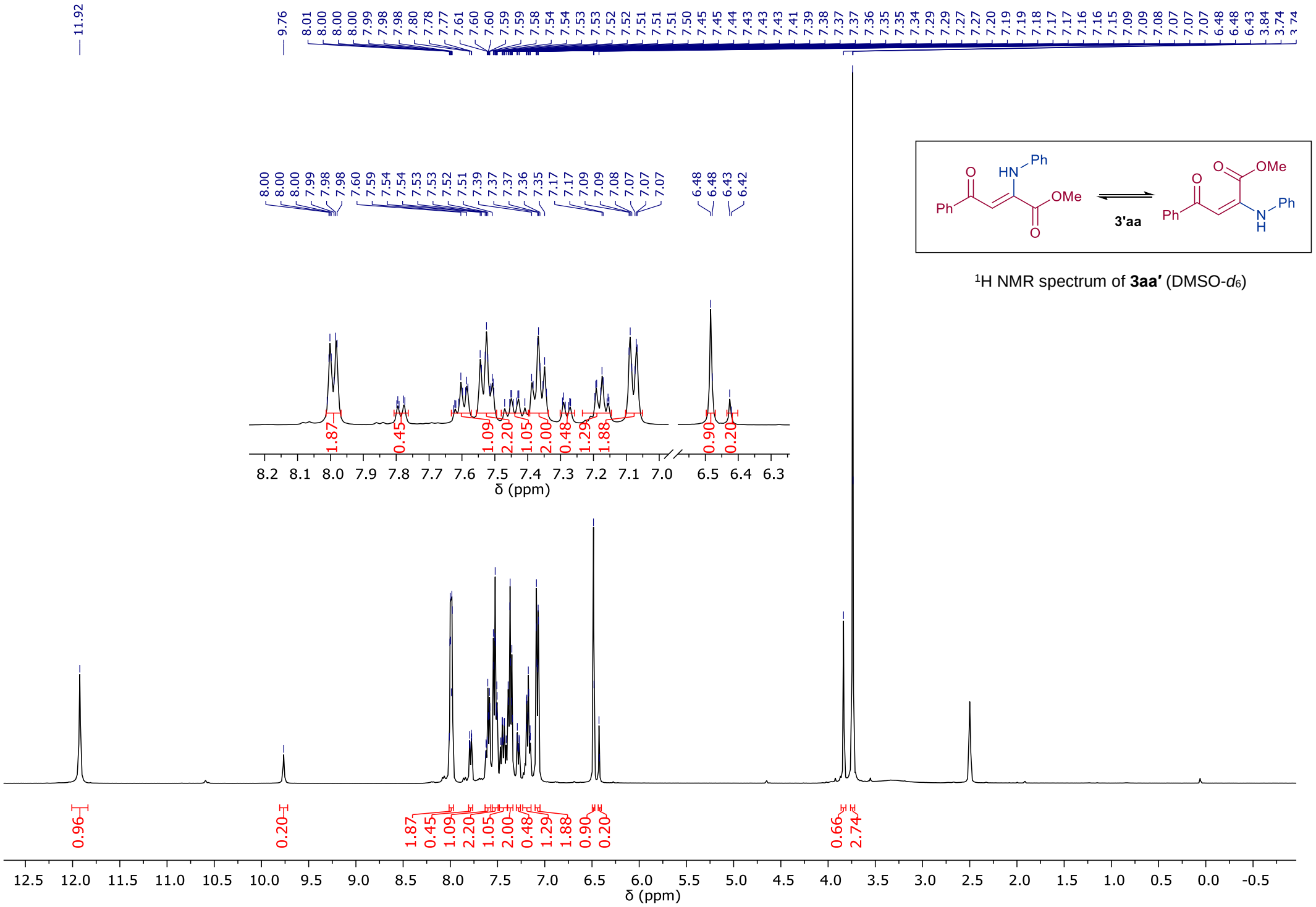
Crystal Data of ***8ka***. $C_{16}H_{16}F_3NOS$, M = 327.26, monoclinic, a = 13.153(4) Å, b = 15.177(5) Å, c = 7.937(2) Å, β = 106.57(3) °, V = 1518.6(8) Å^3, T = 295(2), space group $P2_1/c$, Z = 4, μ(Mo Kα) = 0.246 mm^{-1}. The final refinement parameters: R_1 = 0.0479, wR_2 = 0.1065 [for observed 2418 reflections with $I > 2\sigma(I)$]; R_1 = 0.0756, wR_2 = 0.1271 (for all independent 3526 reflections, R_{int} = 0.0335), S = 1.033.

Crystal Data of ***9b***. $C_{11}H_9F_3O_2S$, M = 262.24, monoclinic, a = 8.470(2) Å, b = 13.267(3) Å, c = 9.675(2) Å, β = 91.53(2) °, V = 1086.8(4) Å^3, T = 295(2), space group $P2_1/n$, Z = 4, μ(Mo Kα) = 0.325 mm^{-1}. The final refinement parameters: R_1 = 0.0435, wR_2 = 0.1132 [for observed 2093 reflections with $I > 2\sigma(I)$]; R_1 = 0.0561, wR_2 = 0.1221 (for all independent 2635 reflections, R_{int} = 0.0233), S = 1.066.

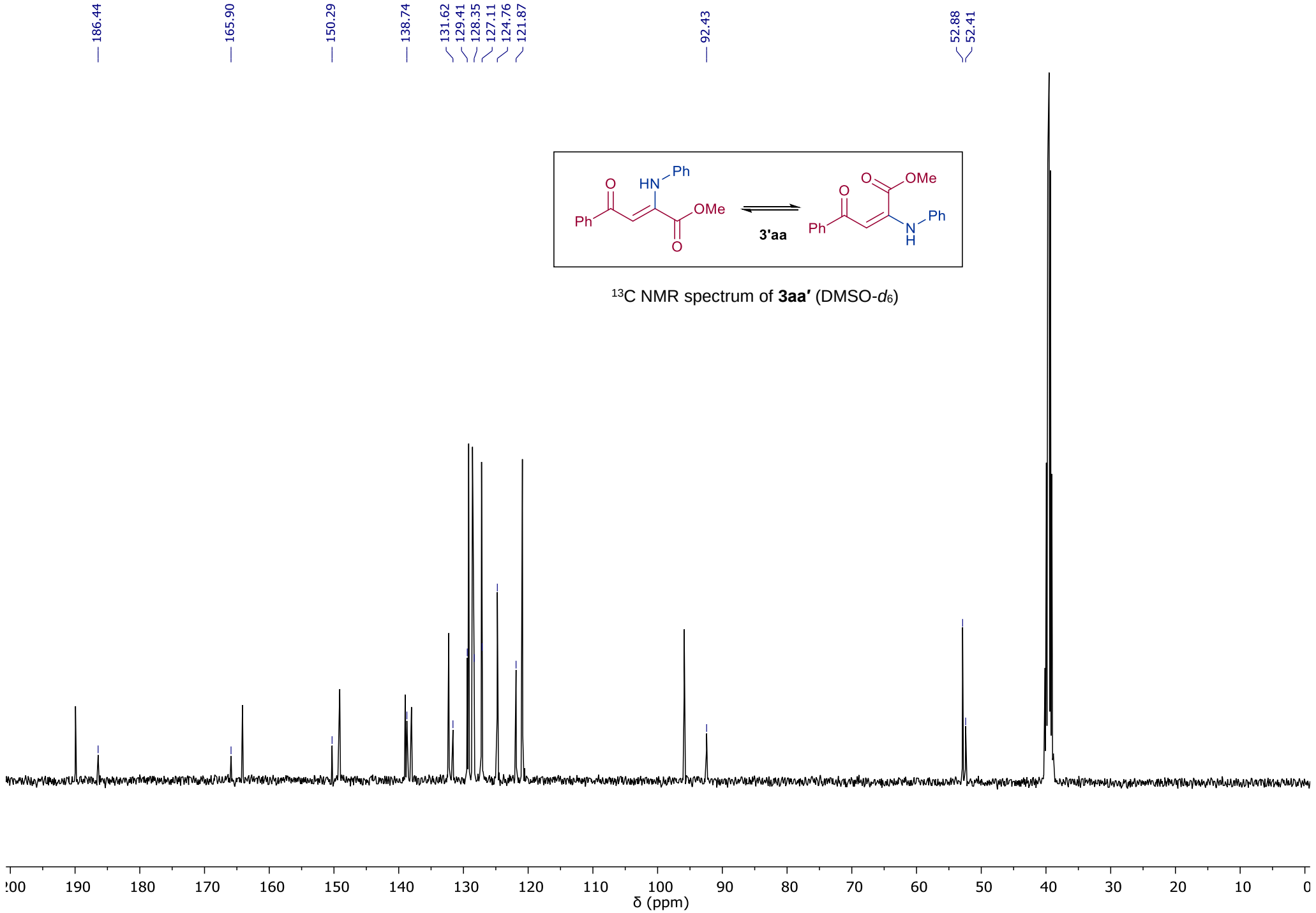
6. References

(1) Yu. S. Andreichikov, A. N. Maslivets, L. I. Smirnova, O. P. Krasnykh, A. P. Kozlov and L. A. Perevozchikov,*Zh. Org. Khim.*, **1987**, *23*, 1534-1543.
(2) Pravst, I.; Zupan, M.; Stavber, S. Solvent-free bromination of 1,3-diketones and β-keto esters with NBS. *Green Chem.* **2006**, *8*, 1001-1005.
(3) CrysAlisPro, Agilent Technologies, Version 1.171.37.33 (release 27-03-2014 CrysAlis171 .NET).
(4) Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K., Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339.
(5) Farrugia, L. J. *J. Appl. Cryst.* **2012**, *45*, 849.
(6) Bourhis, L.J., Dolomanov, O.V., Gildea, R.J, Howard, J.A.K., Puschmann, H. *ActaCryst*. **2015**, *A71*, 59.
(7) Sheldrick, G.M., *Acta Cryst*. **2008**, *A64*, 112.
(8) Sheldrick, G.M. *ActaCryst*. **2015**, *C71*, 3.

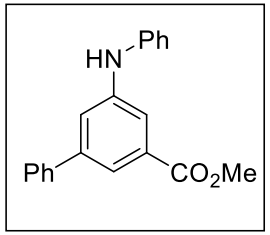
7. NMR spectra



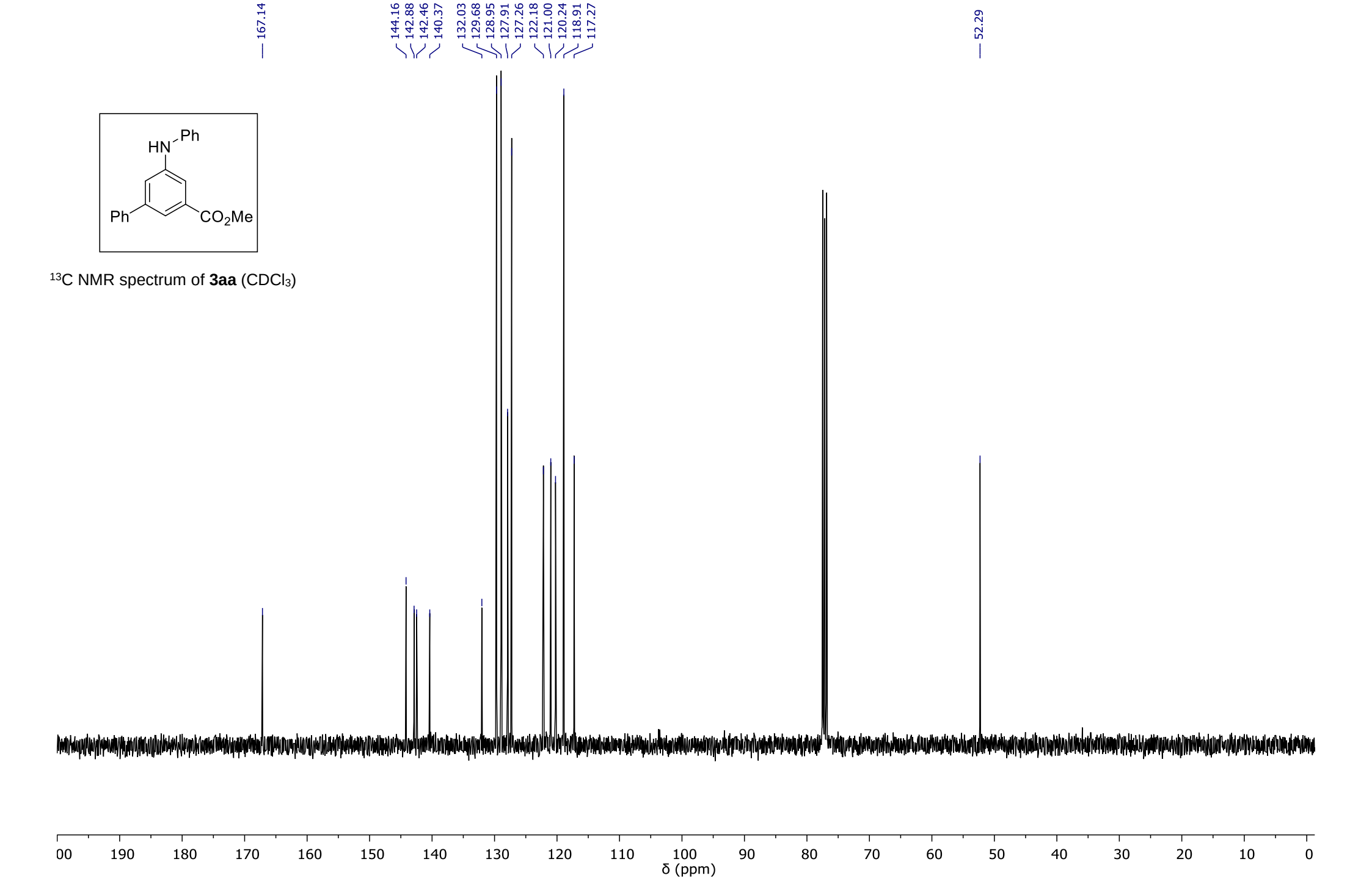
^{1}H NMR spectrum of **3aa′** (DMSO-d_6)



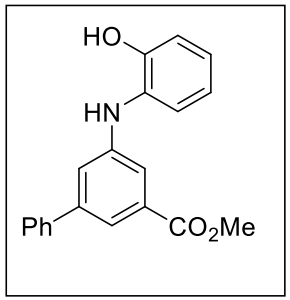
^{13}C NMR spectrum of **3aa′** (DMSO-d_6)



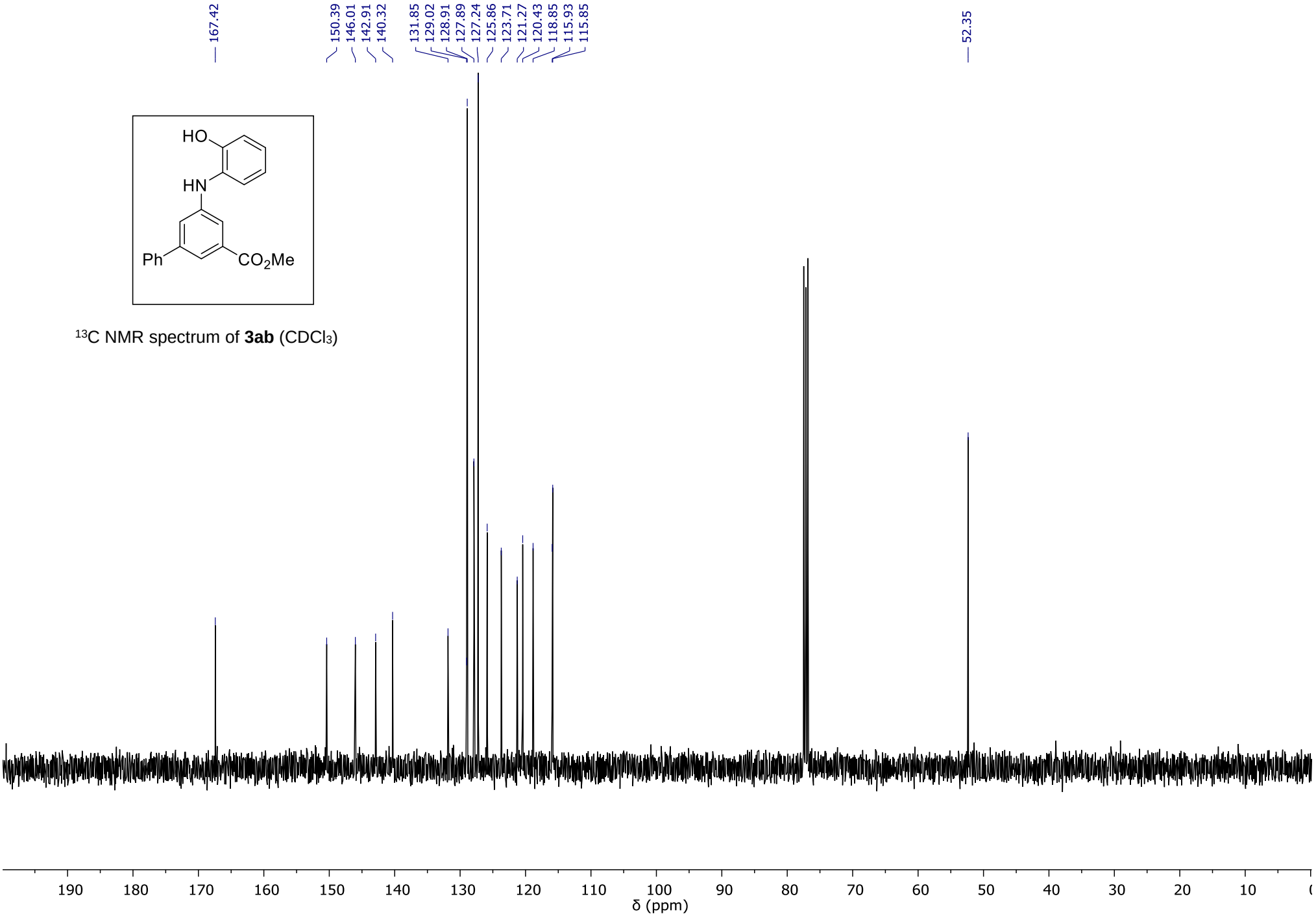
^{1}H NMR spectrum of **3aa** ($CDCl_3$)



^{13}C NMR spectrum of **3aa** ($CDCl_3$)



^{1}H NMR spectrum of **3ab** ($CDCl_3$)



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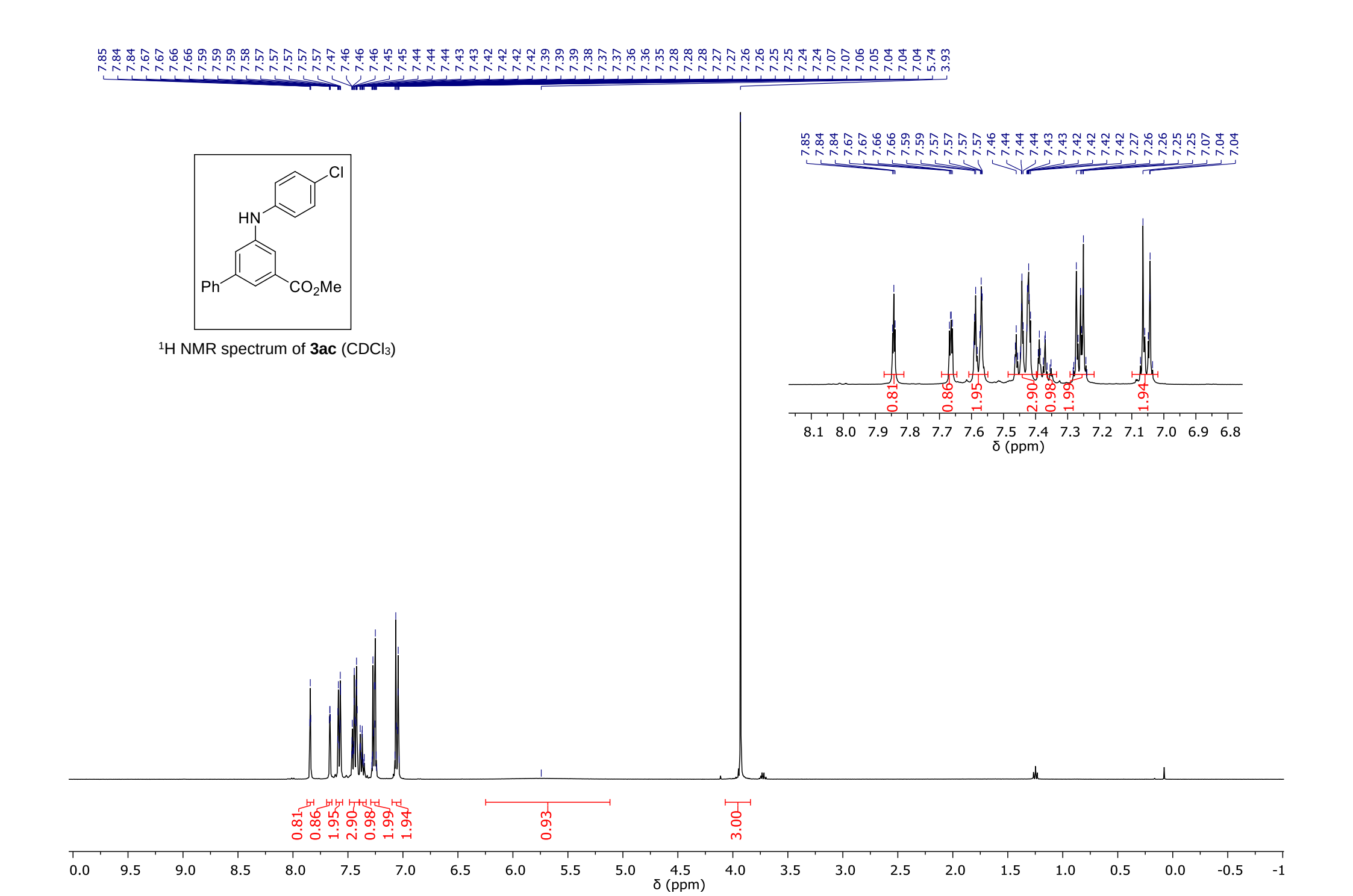

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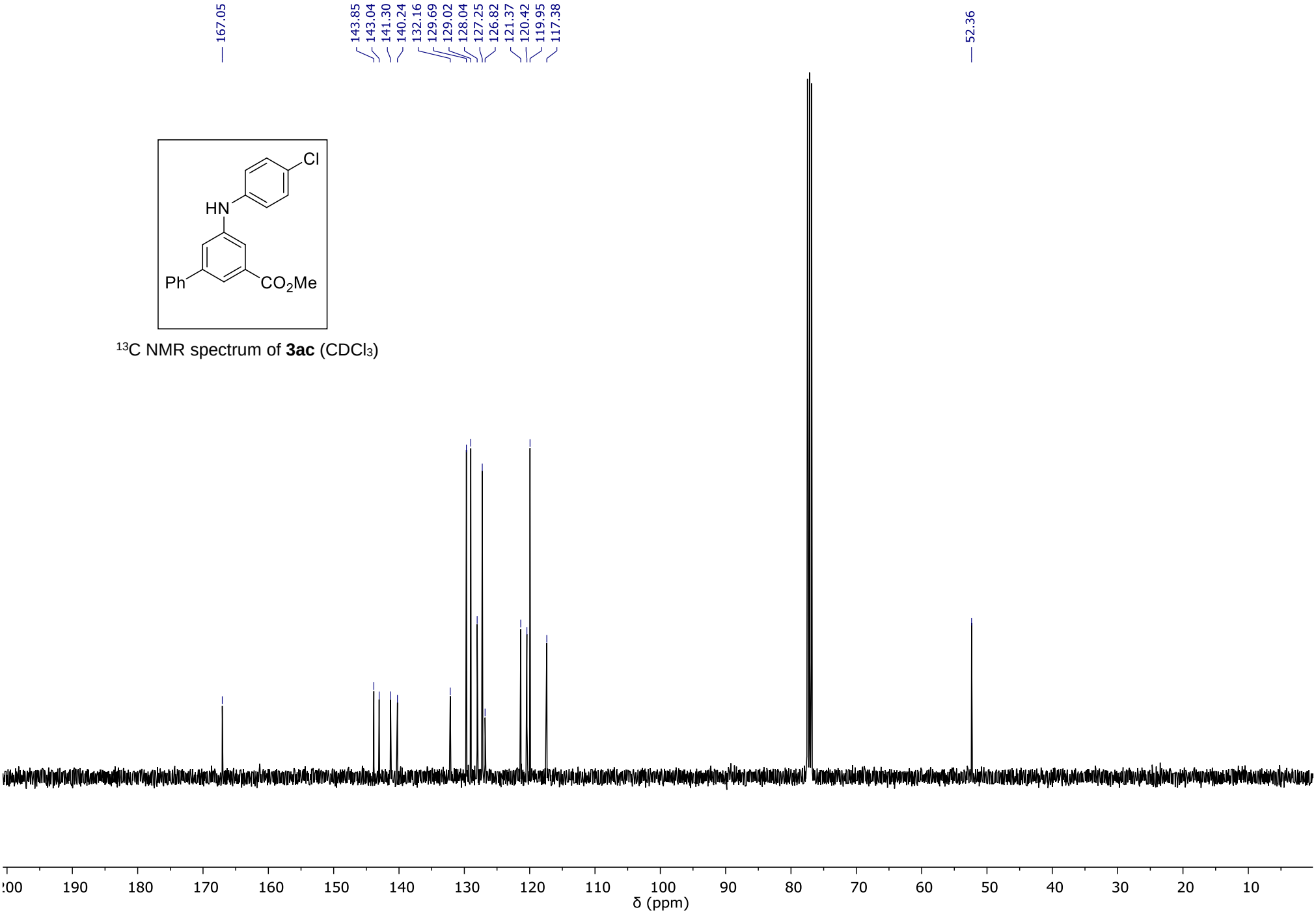

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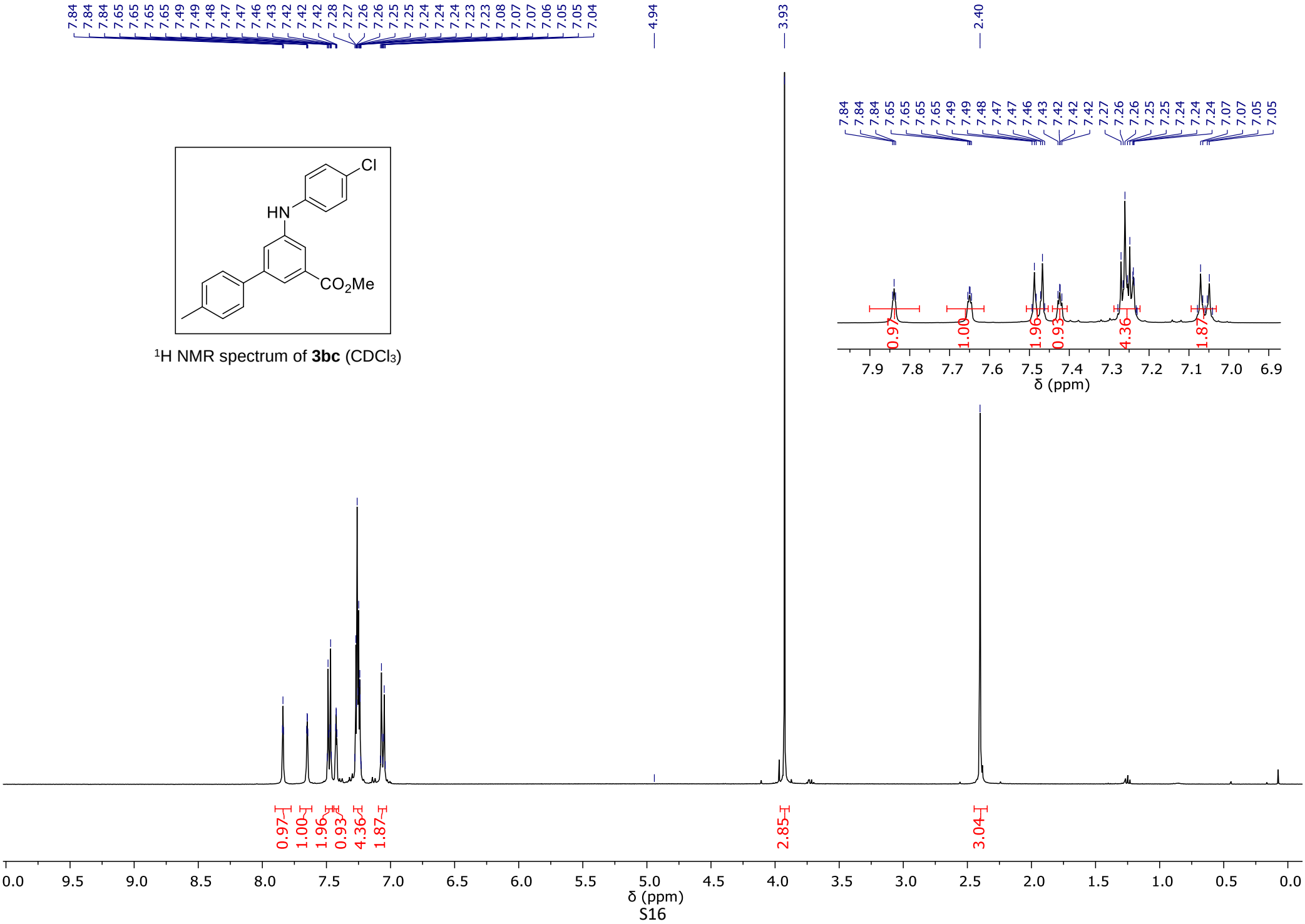

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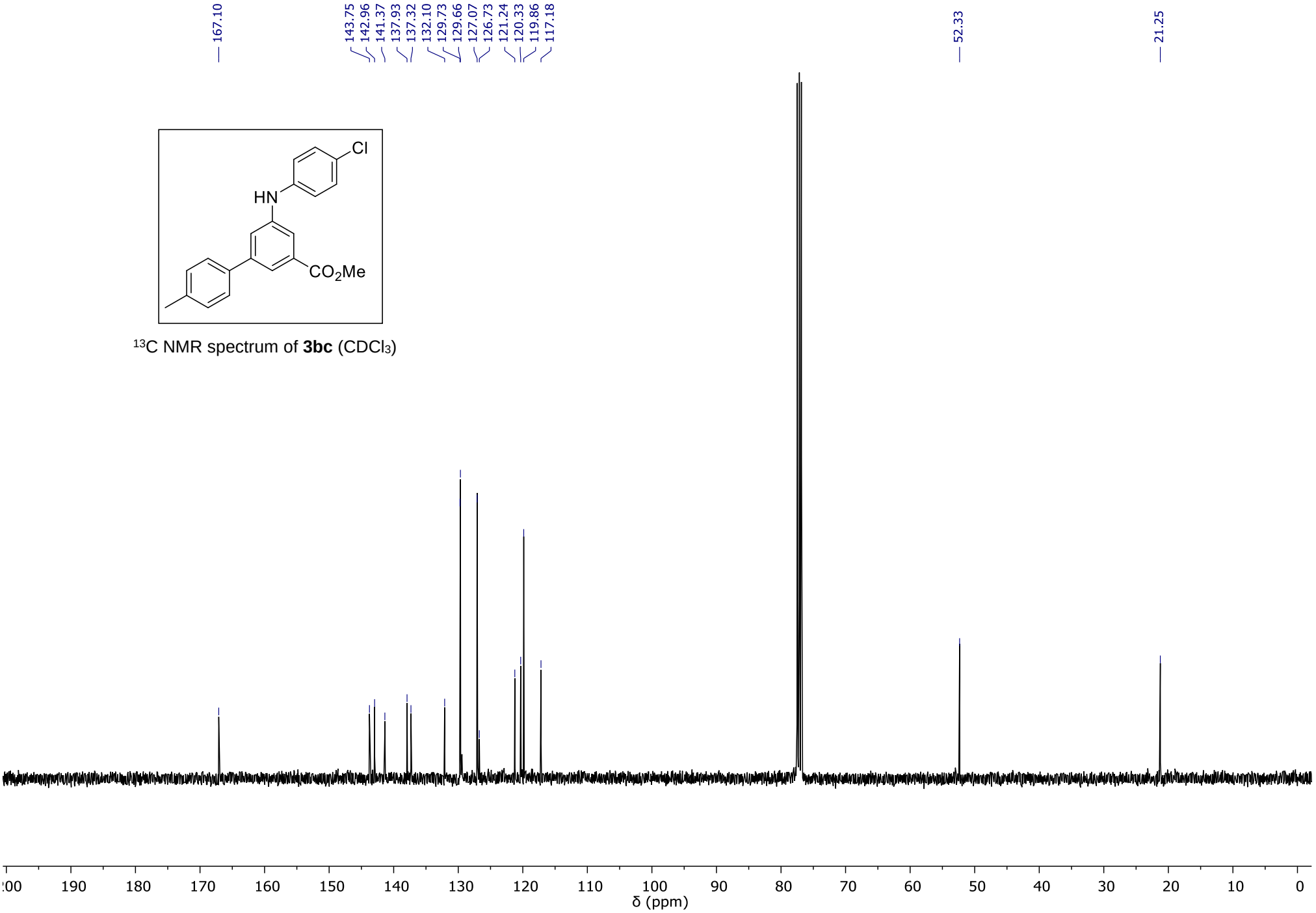

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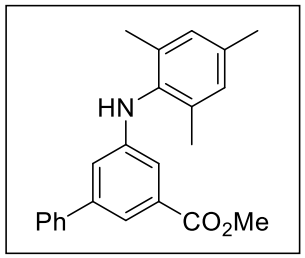

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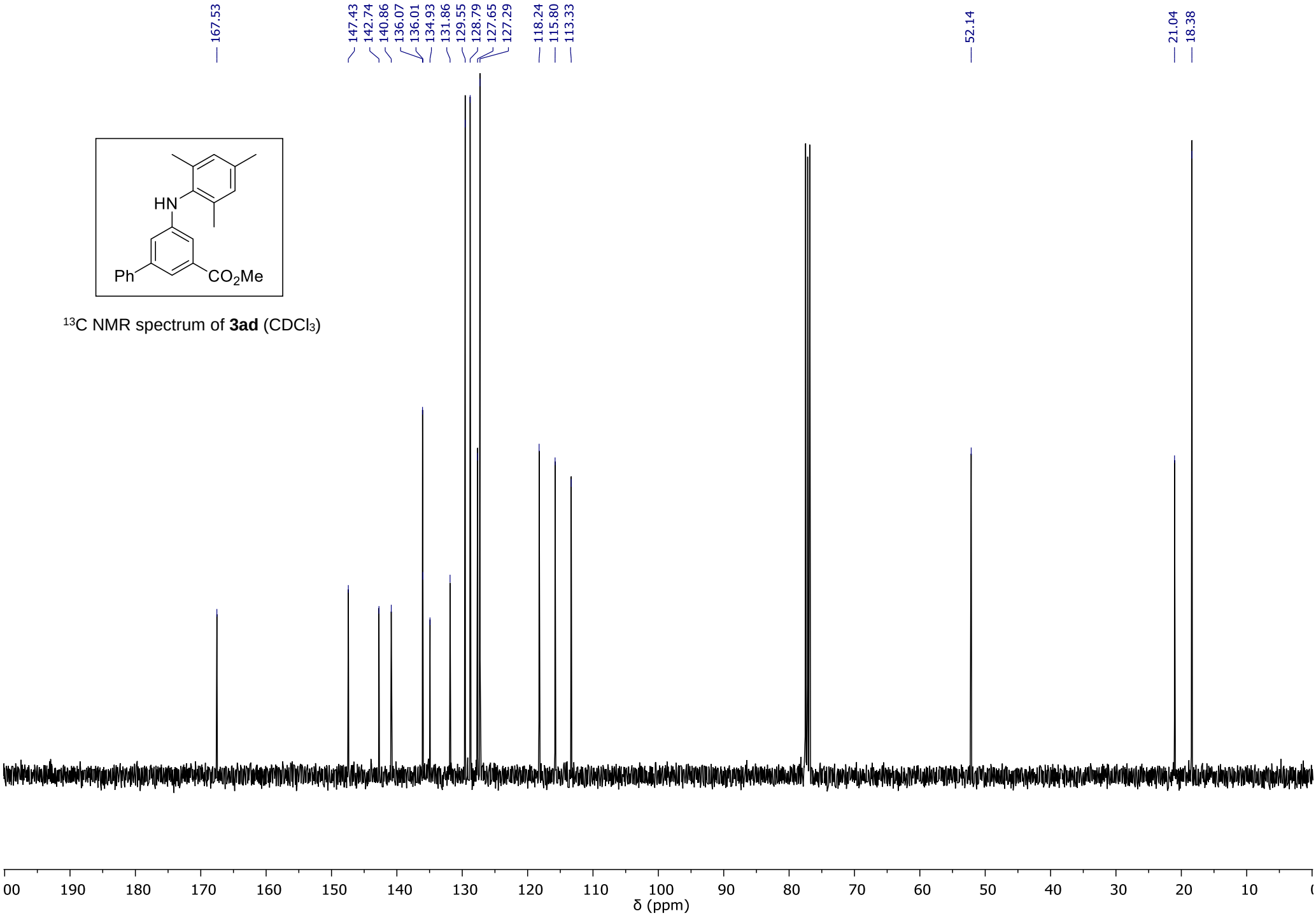

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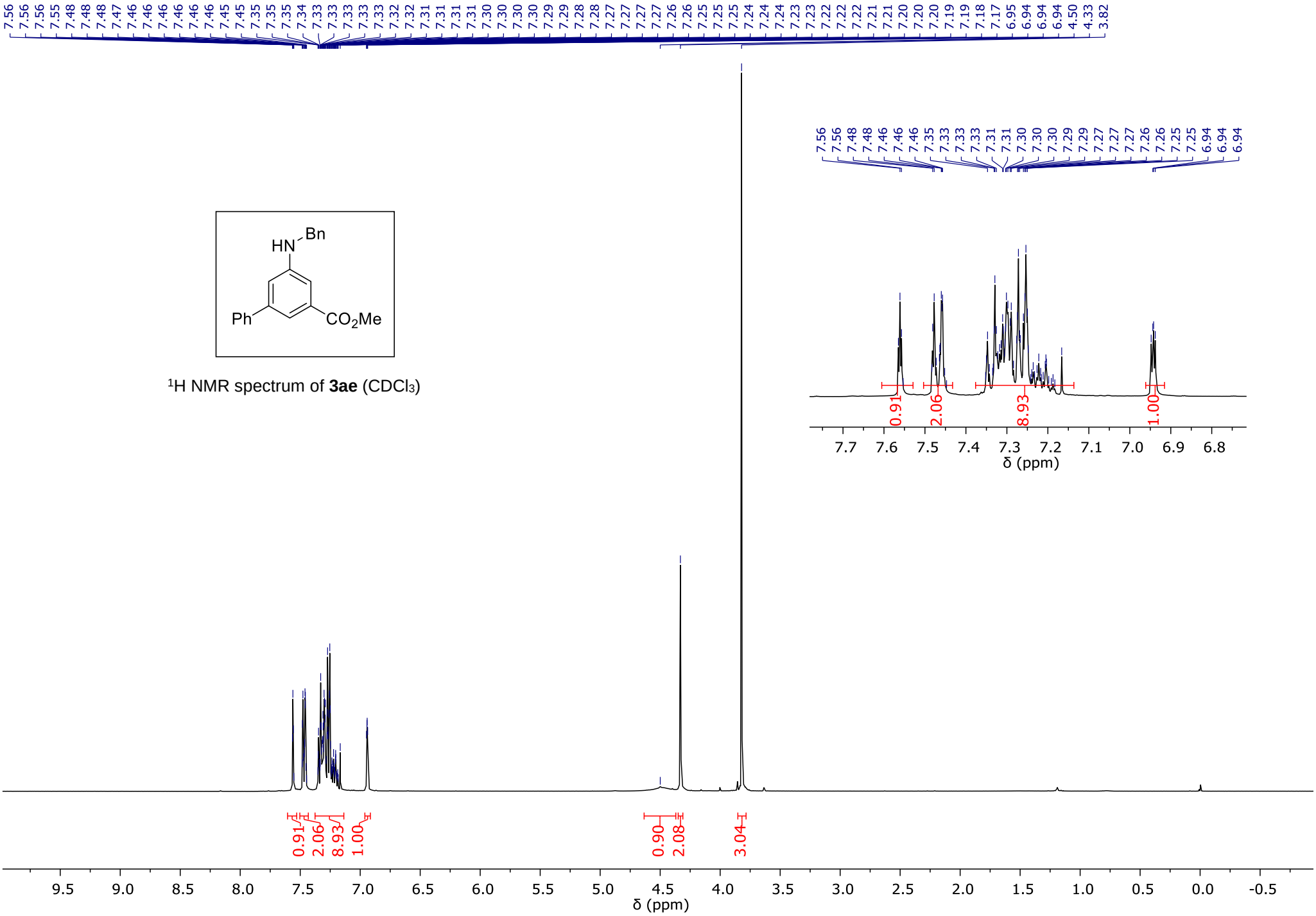

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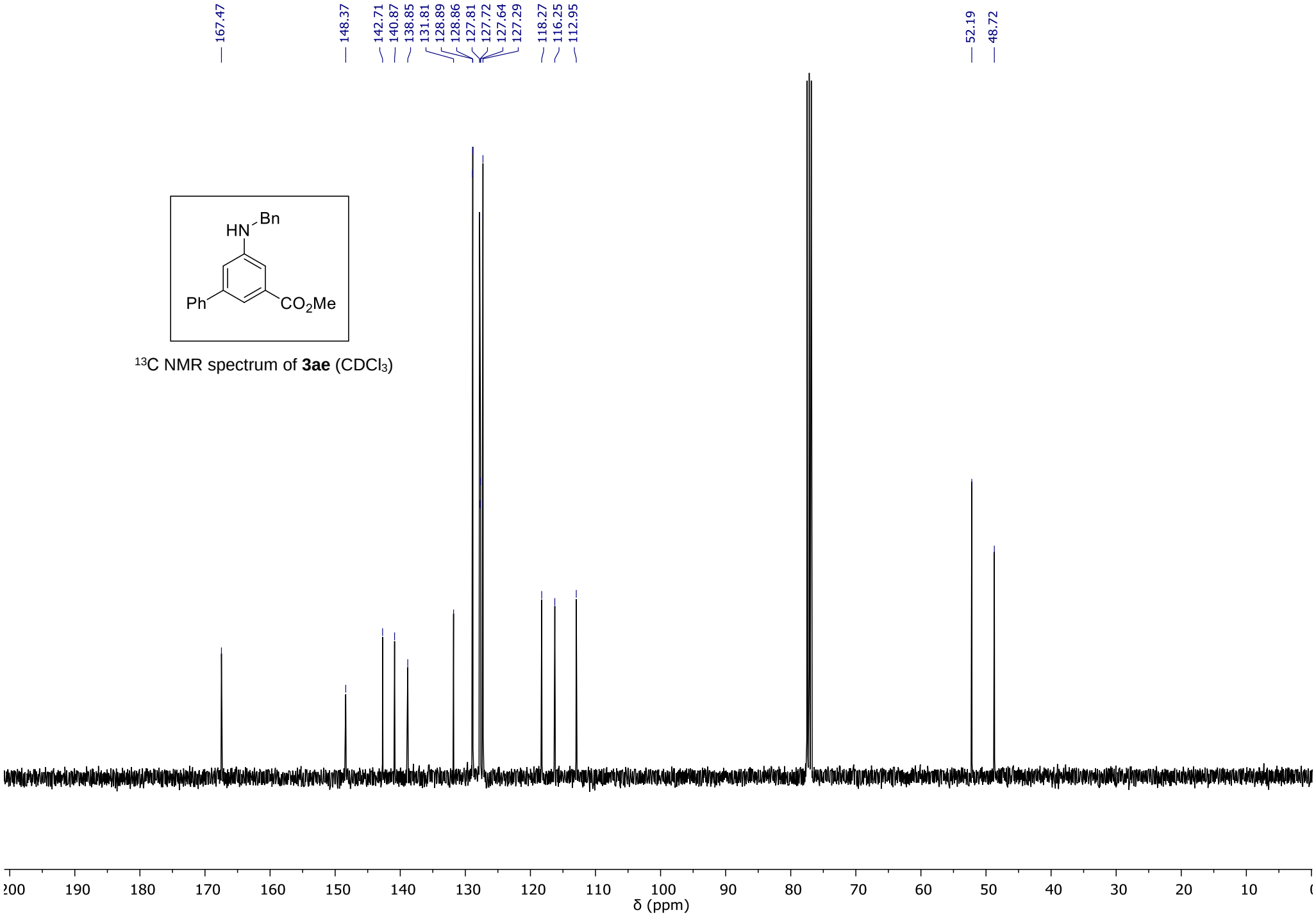

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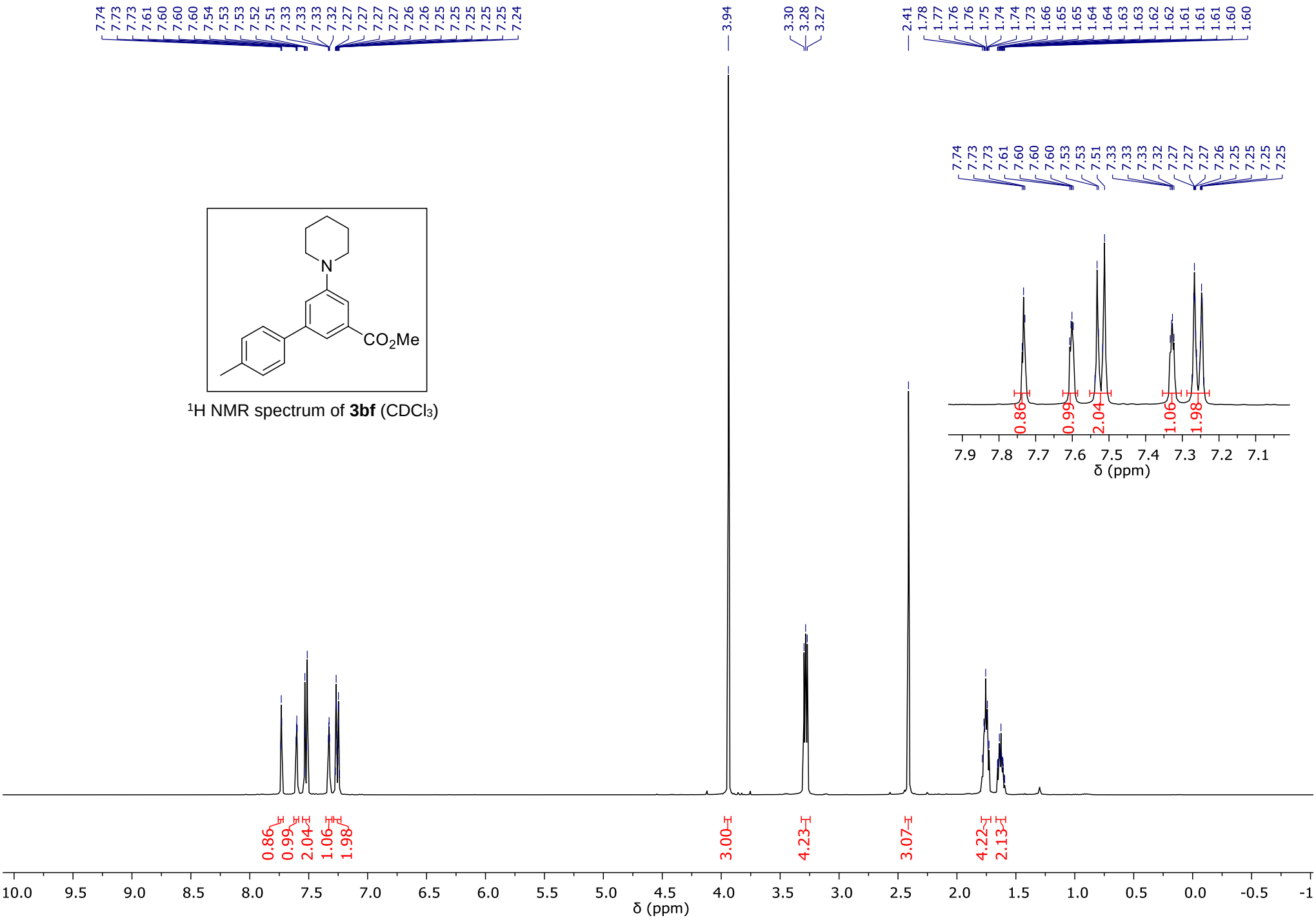

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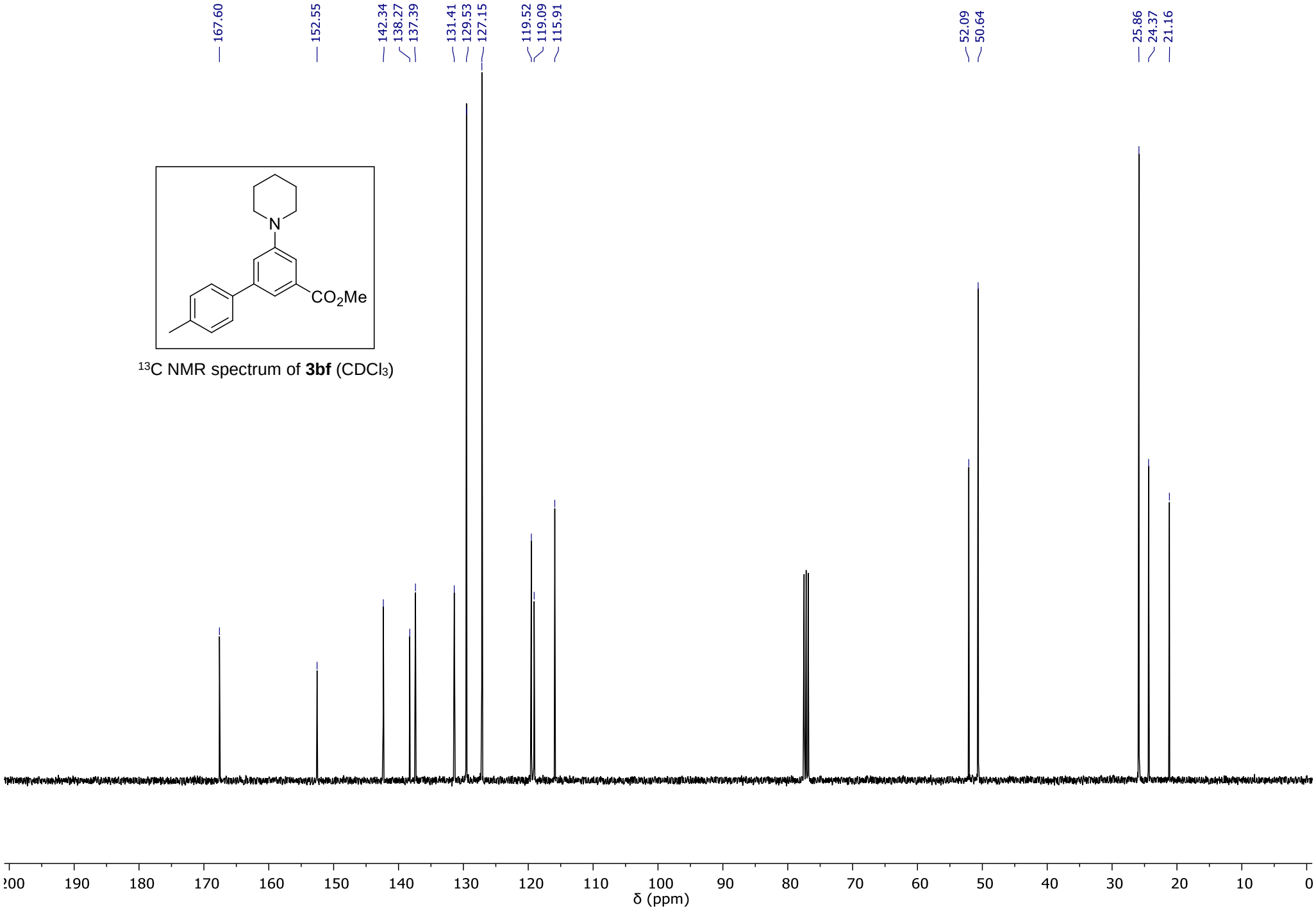

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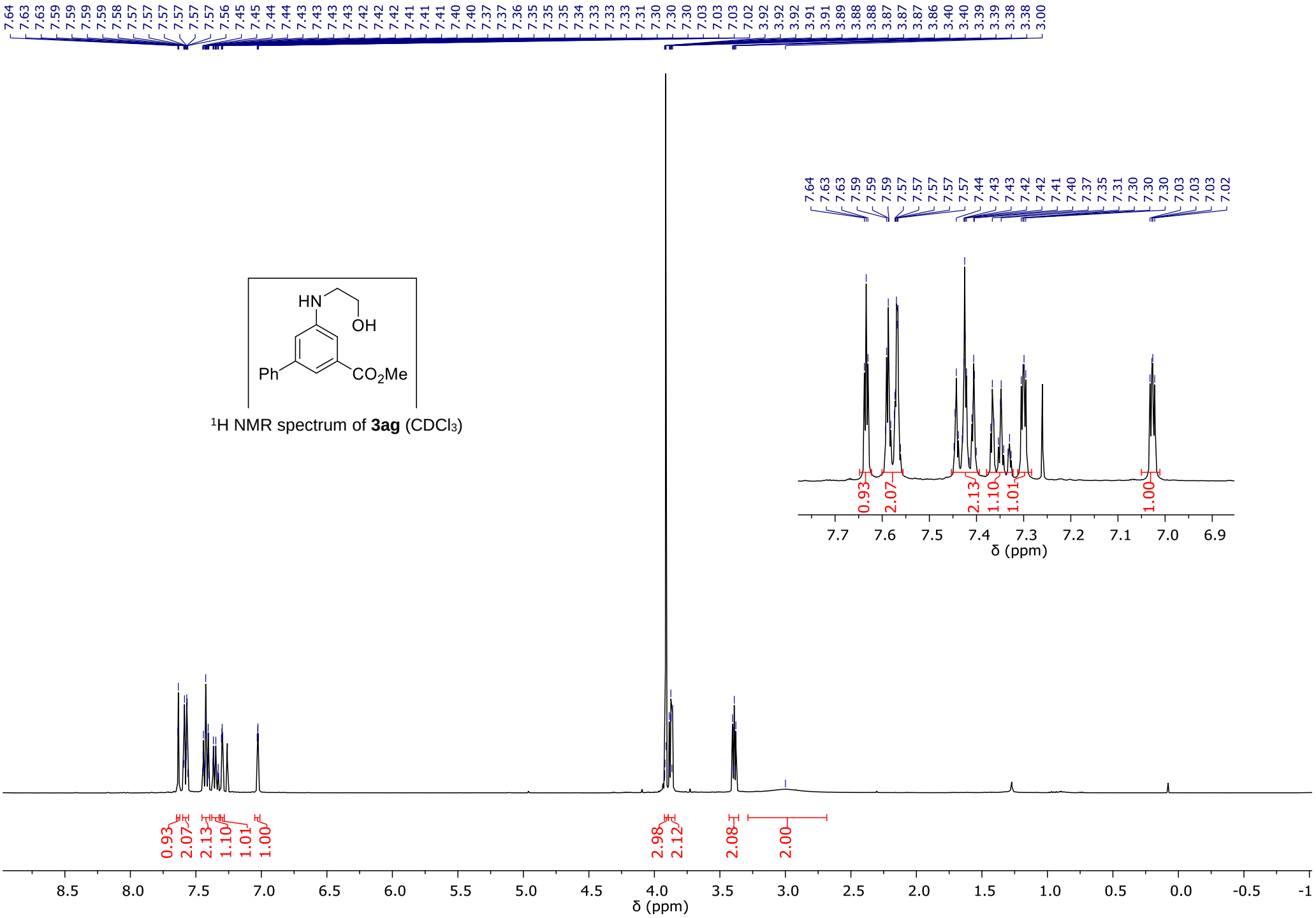

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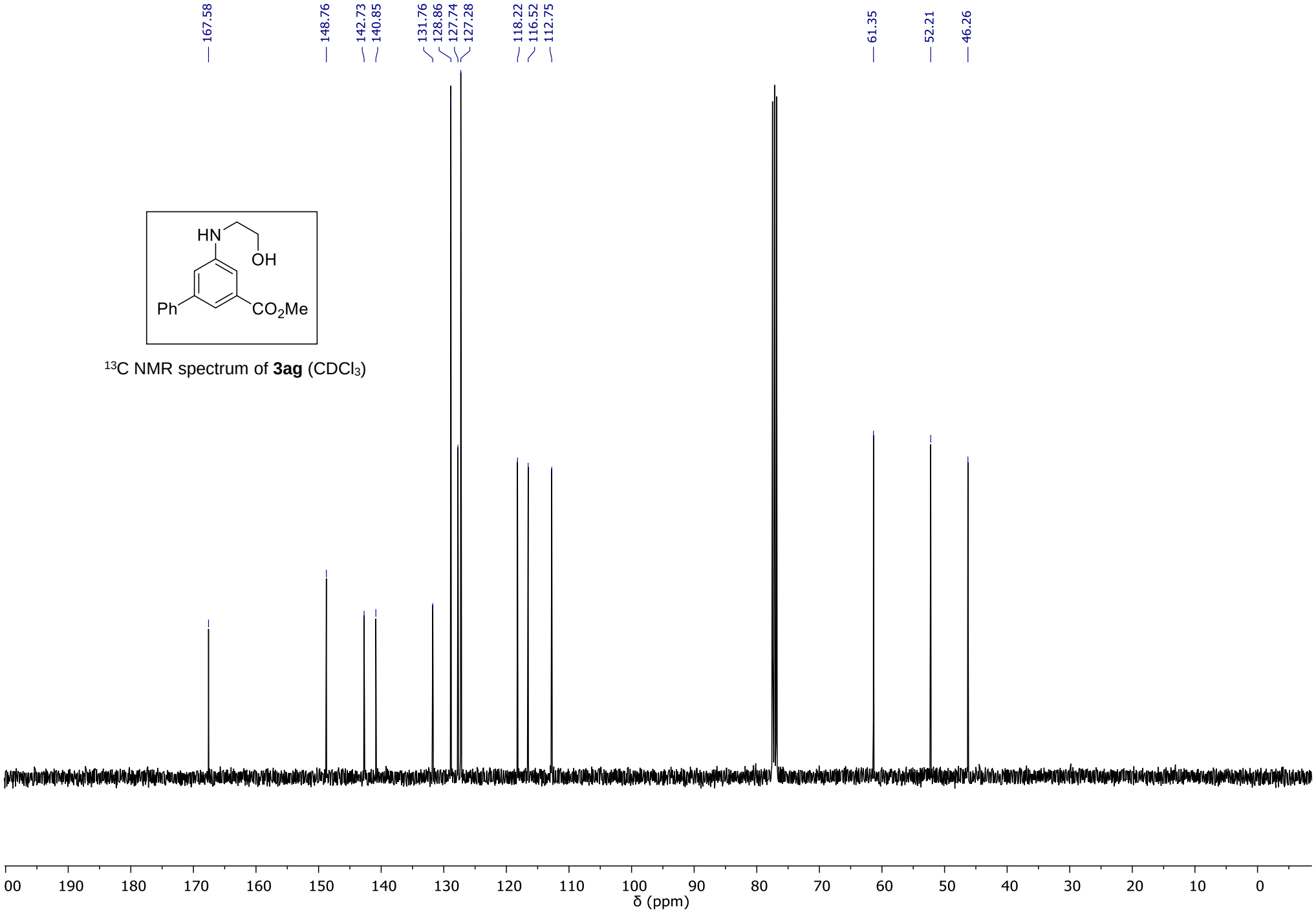

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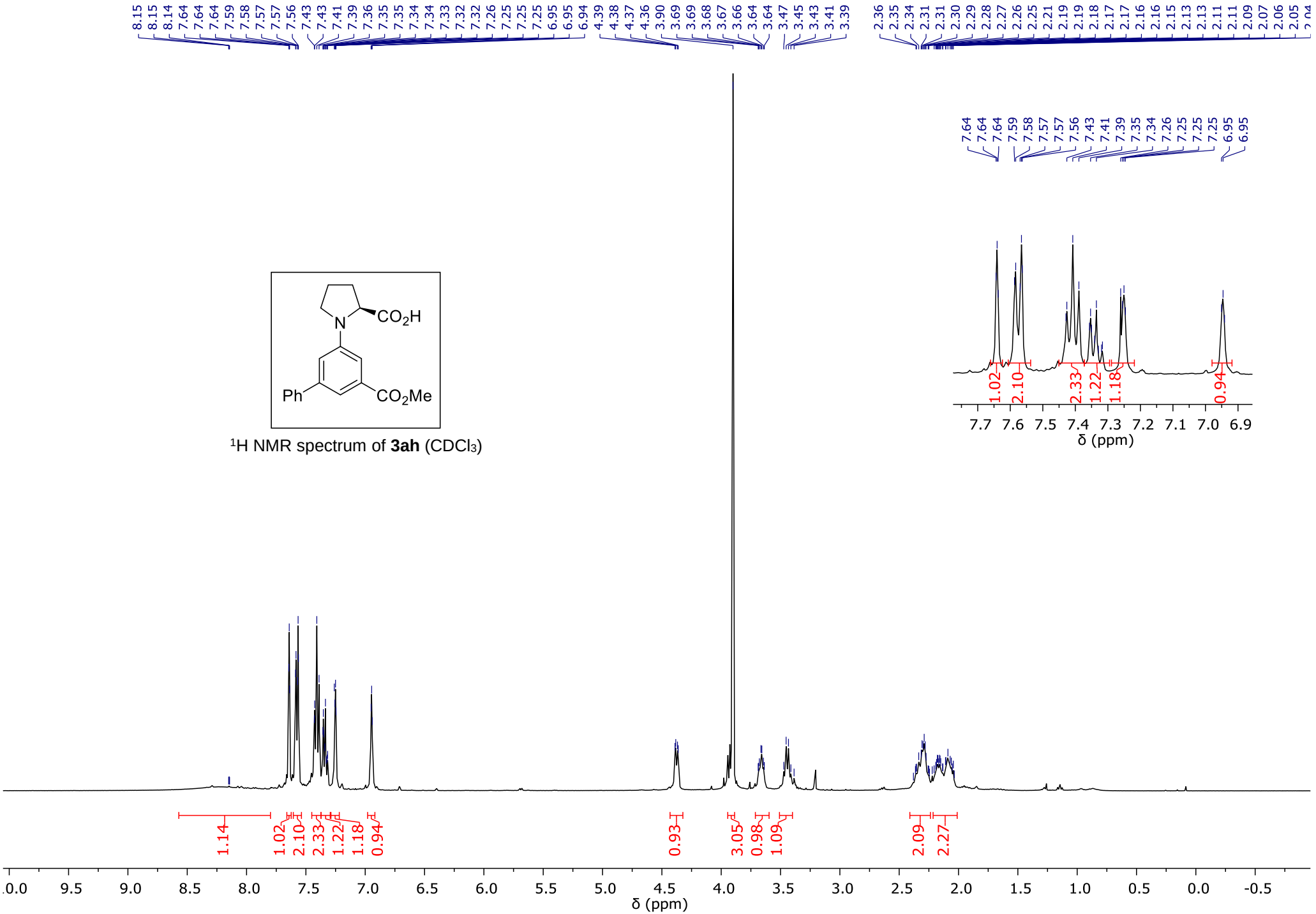

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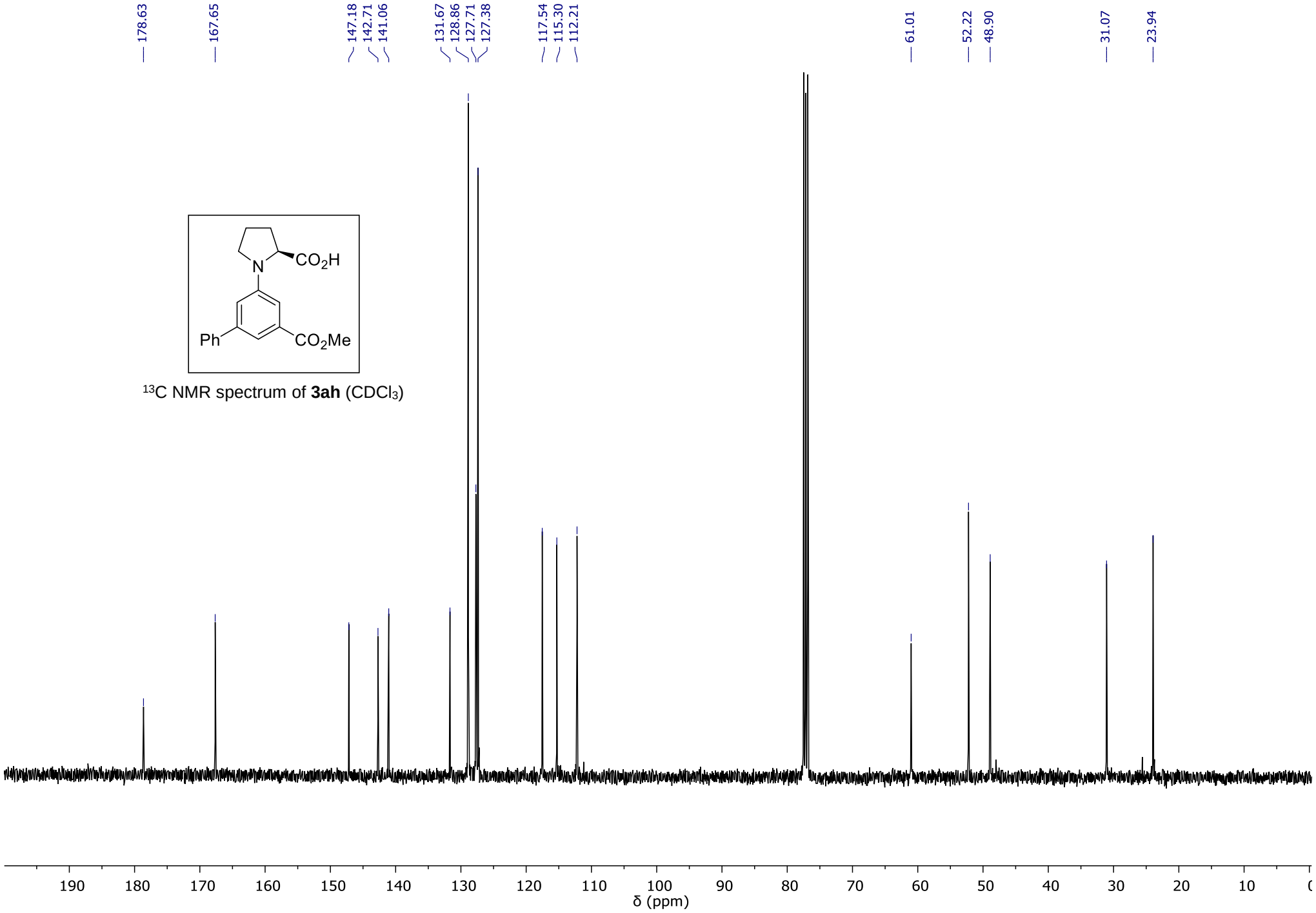

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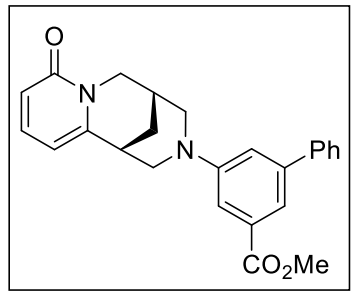

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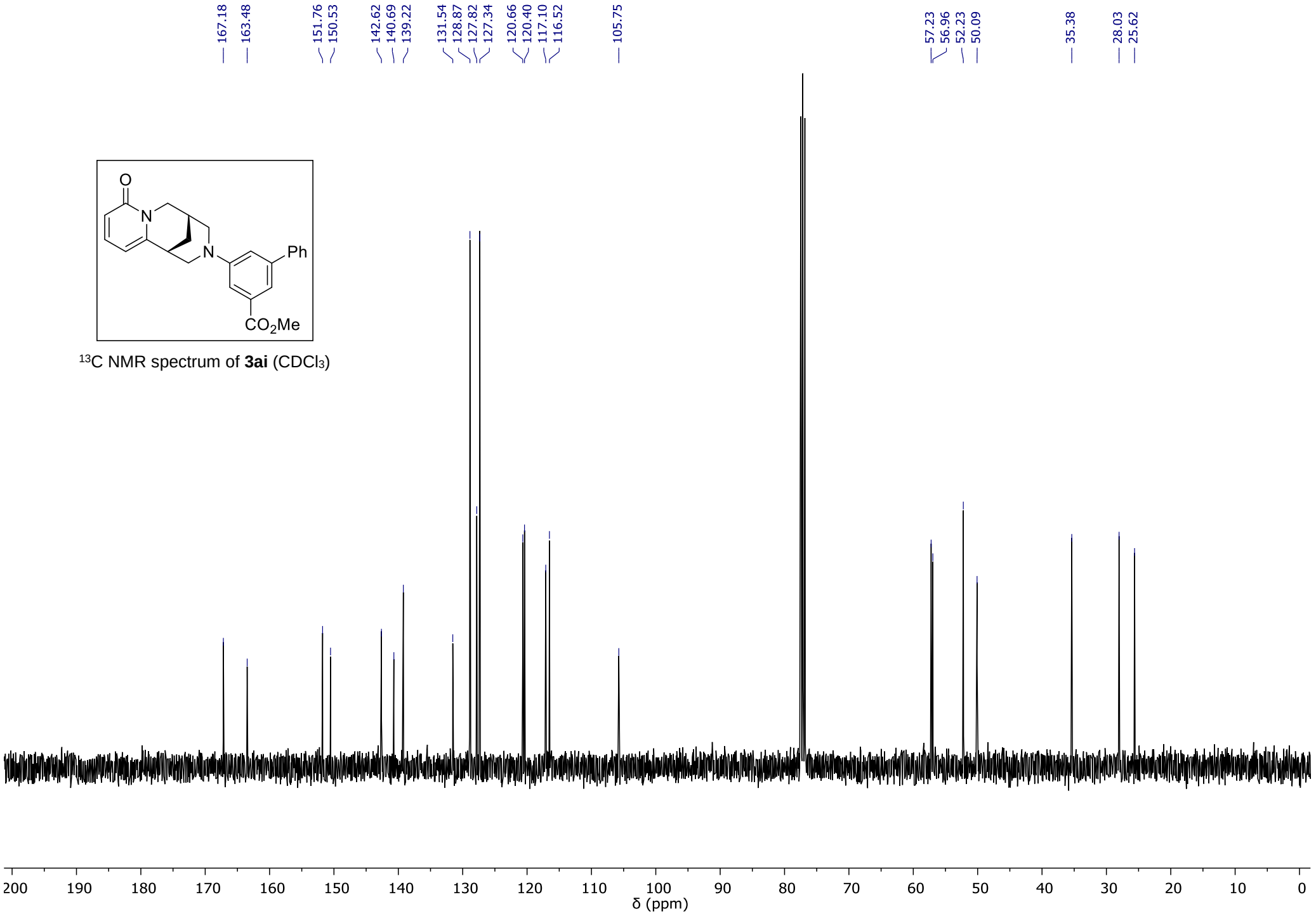

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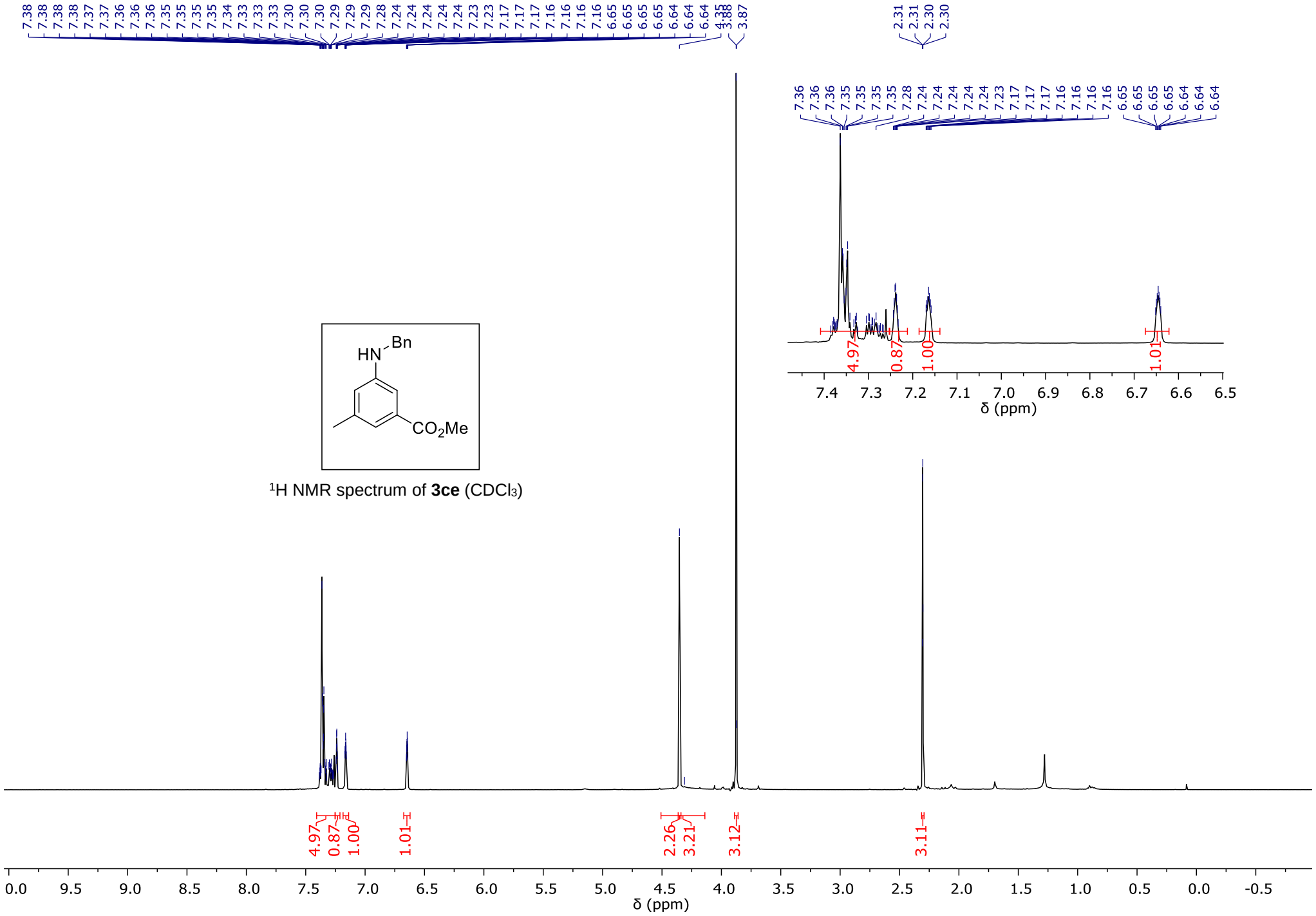

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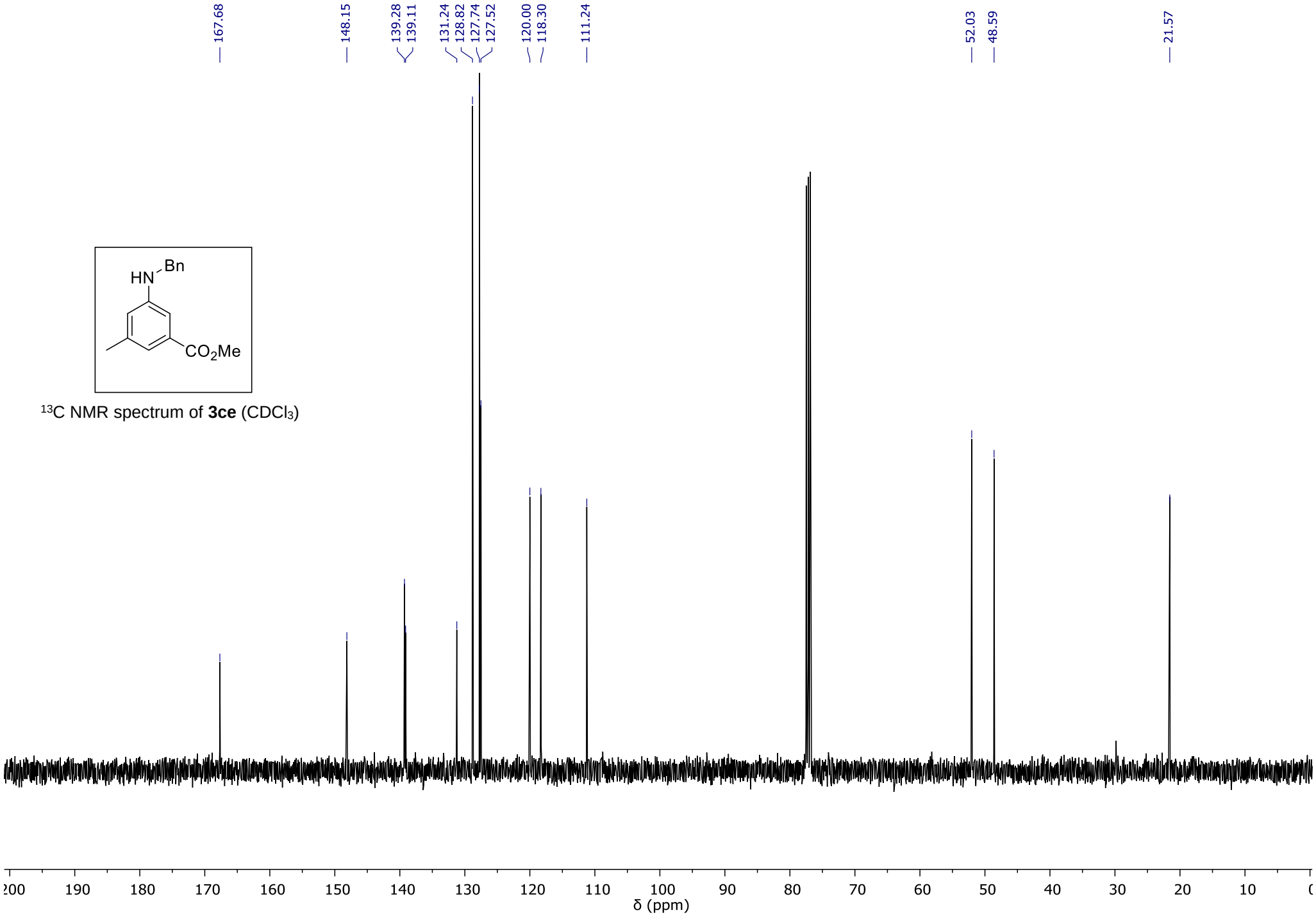
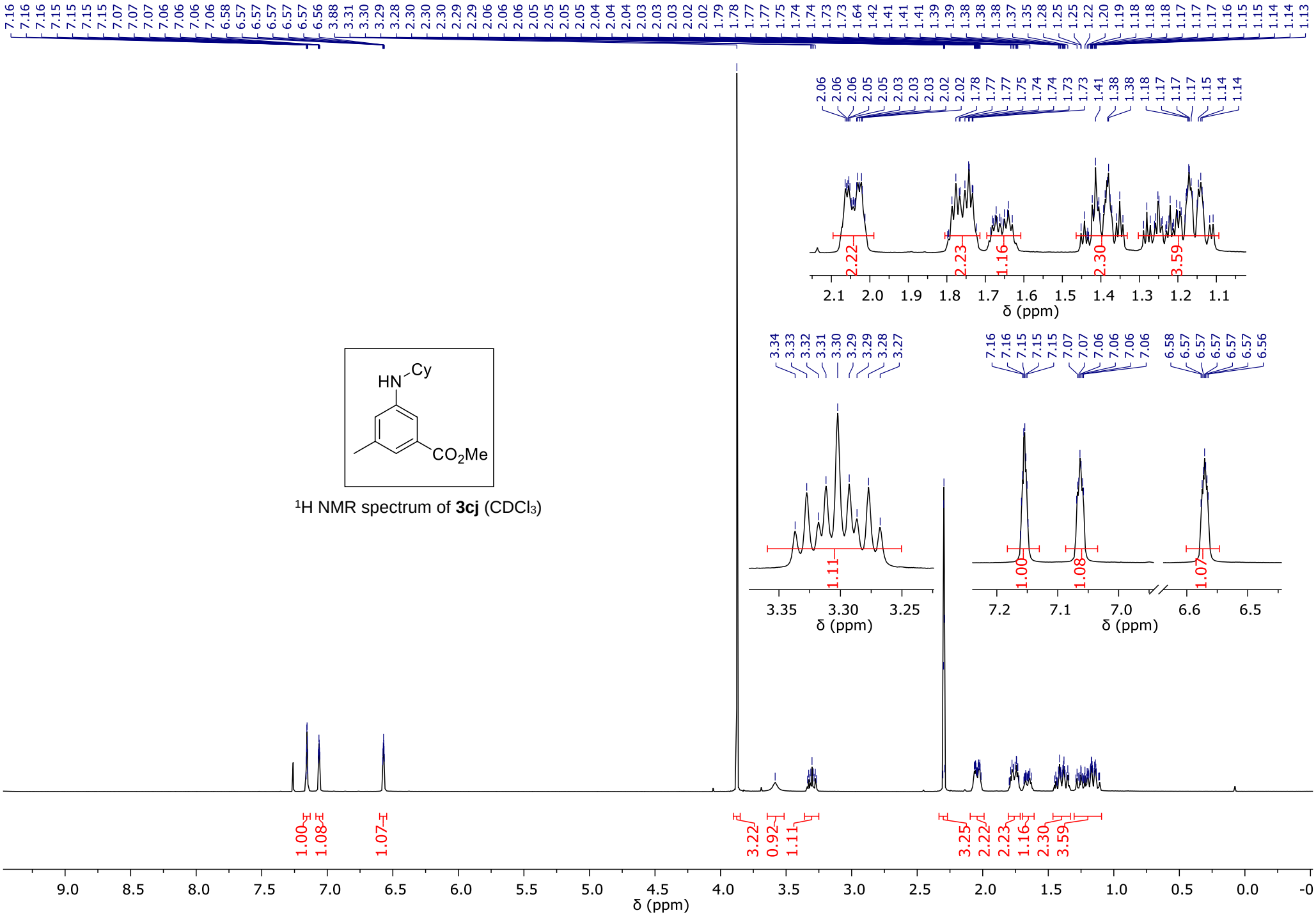


^{13}C NMR spectrum of **3ce** ($CDCl_3$)



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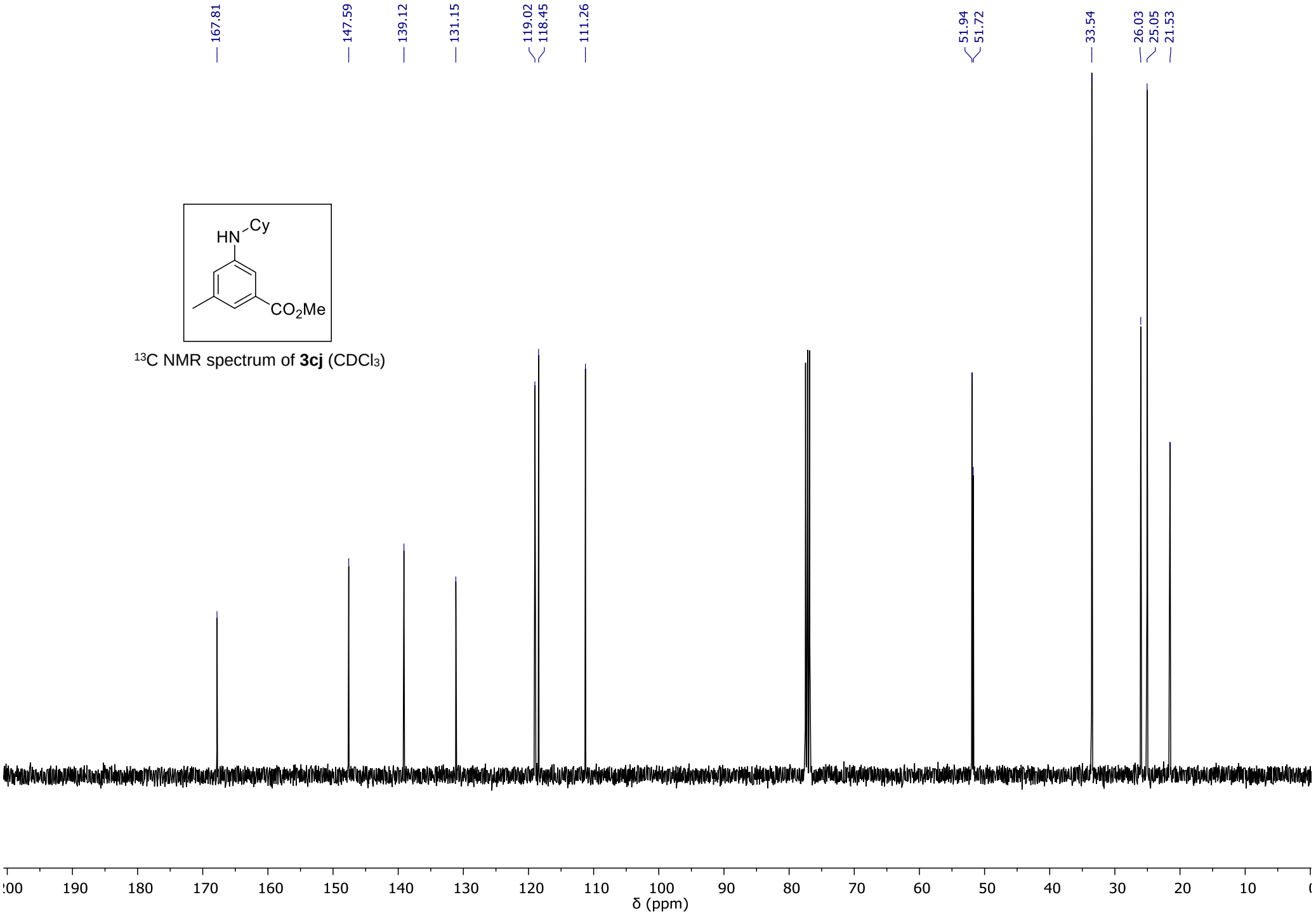
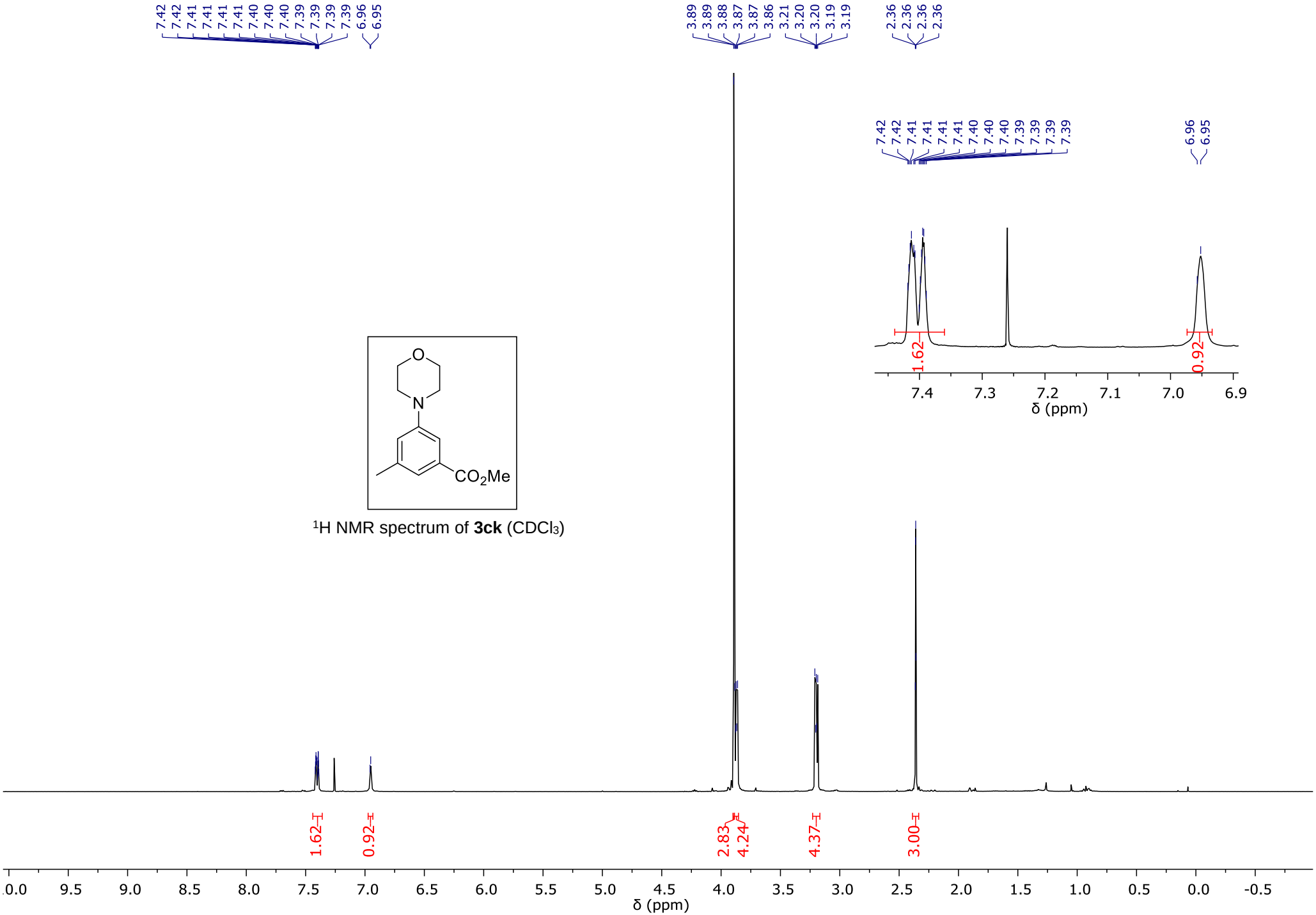
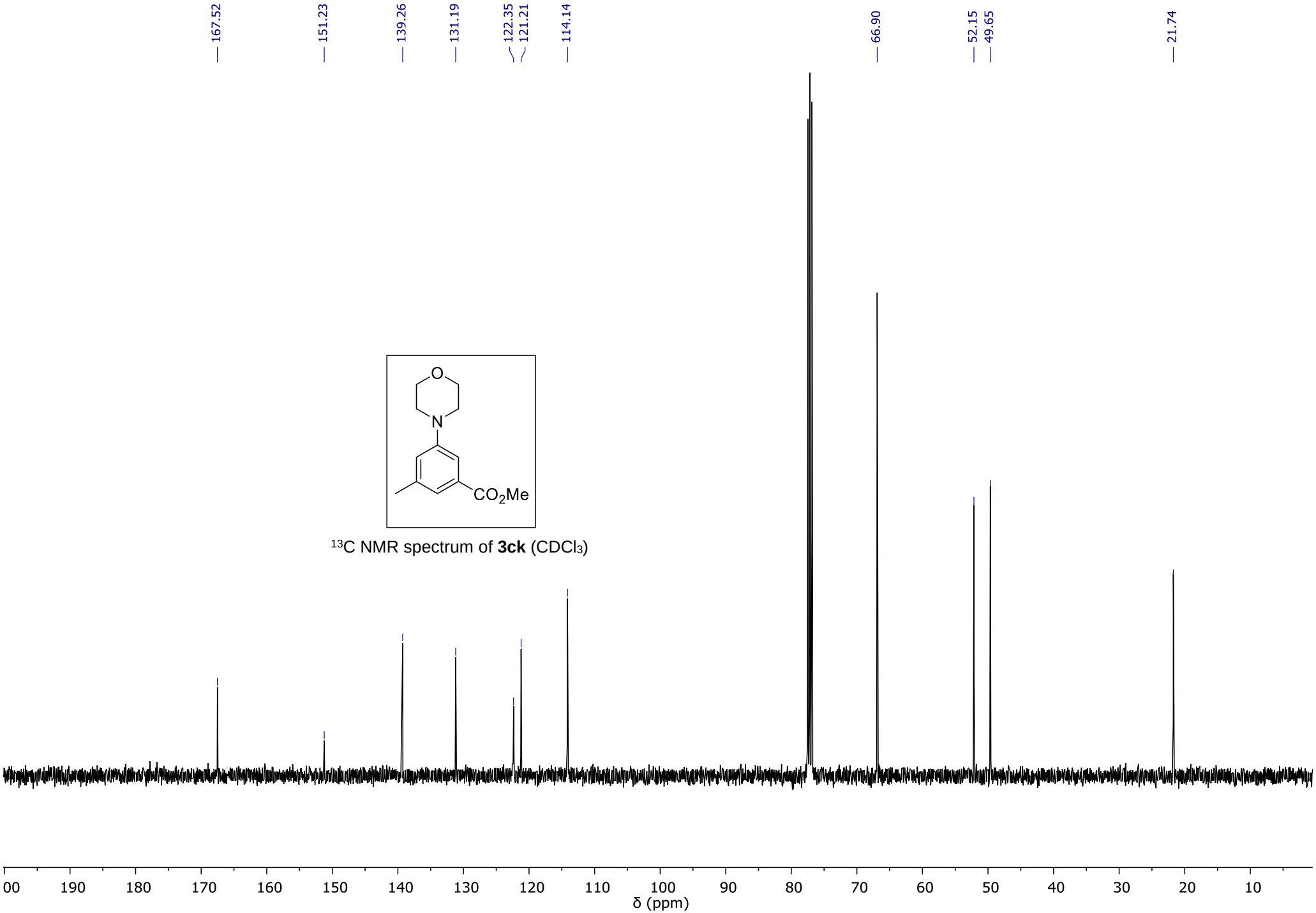


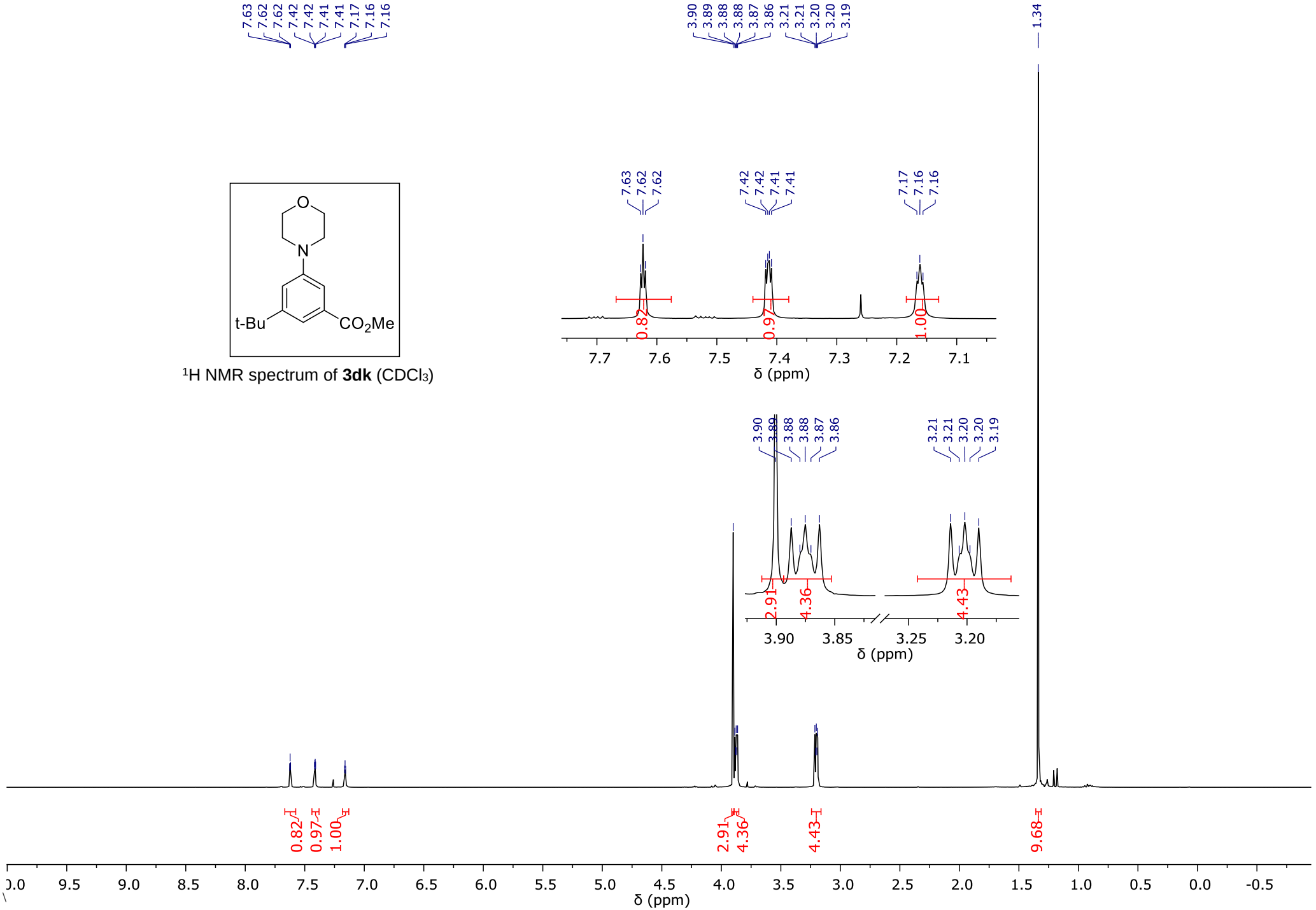
^{13}C NMR spectrum of **3cj** ($CDCl_3$)



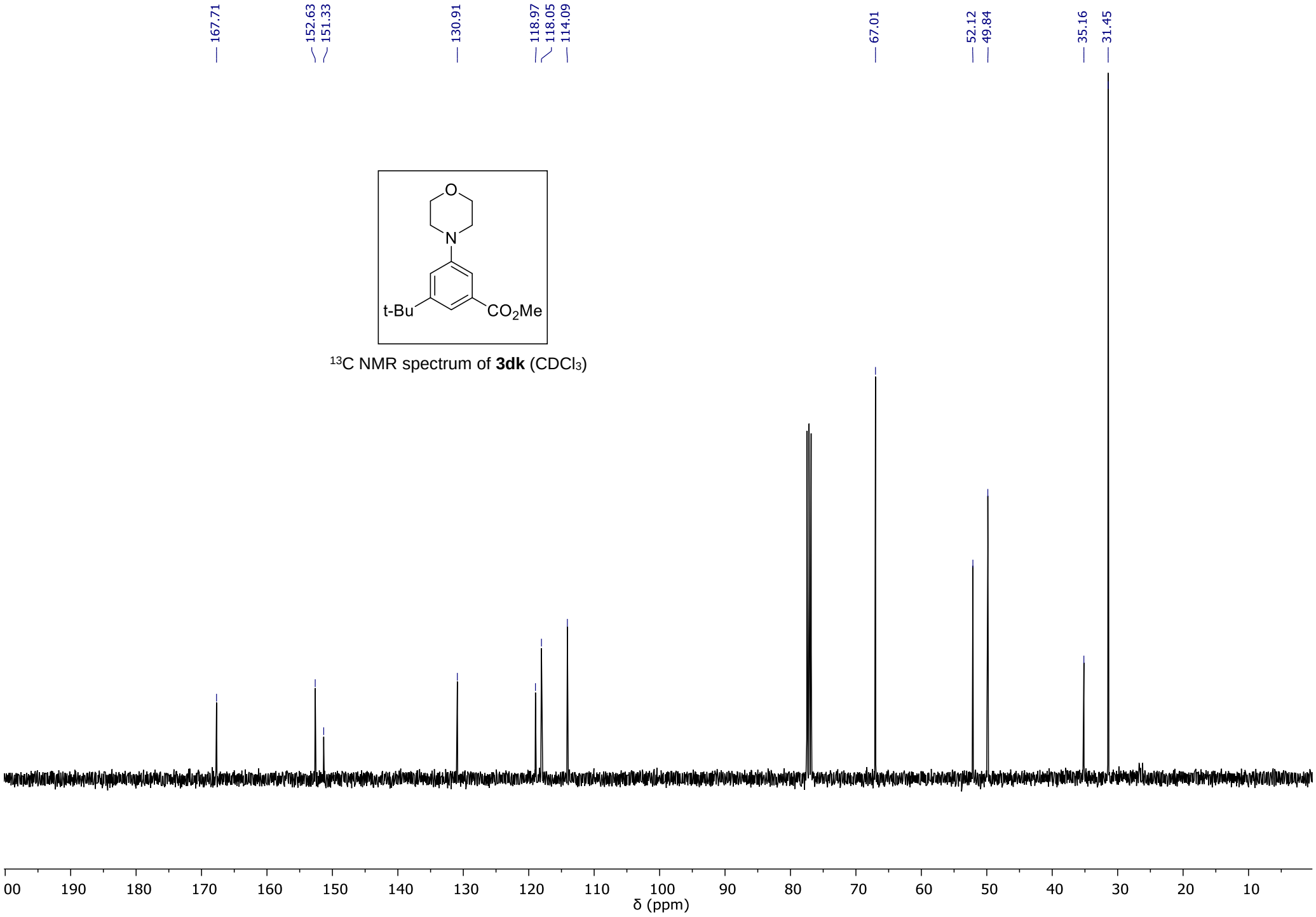
^{1}H NMR spectrum of **3ck** ($CDCl_3$)



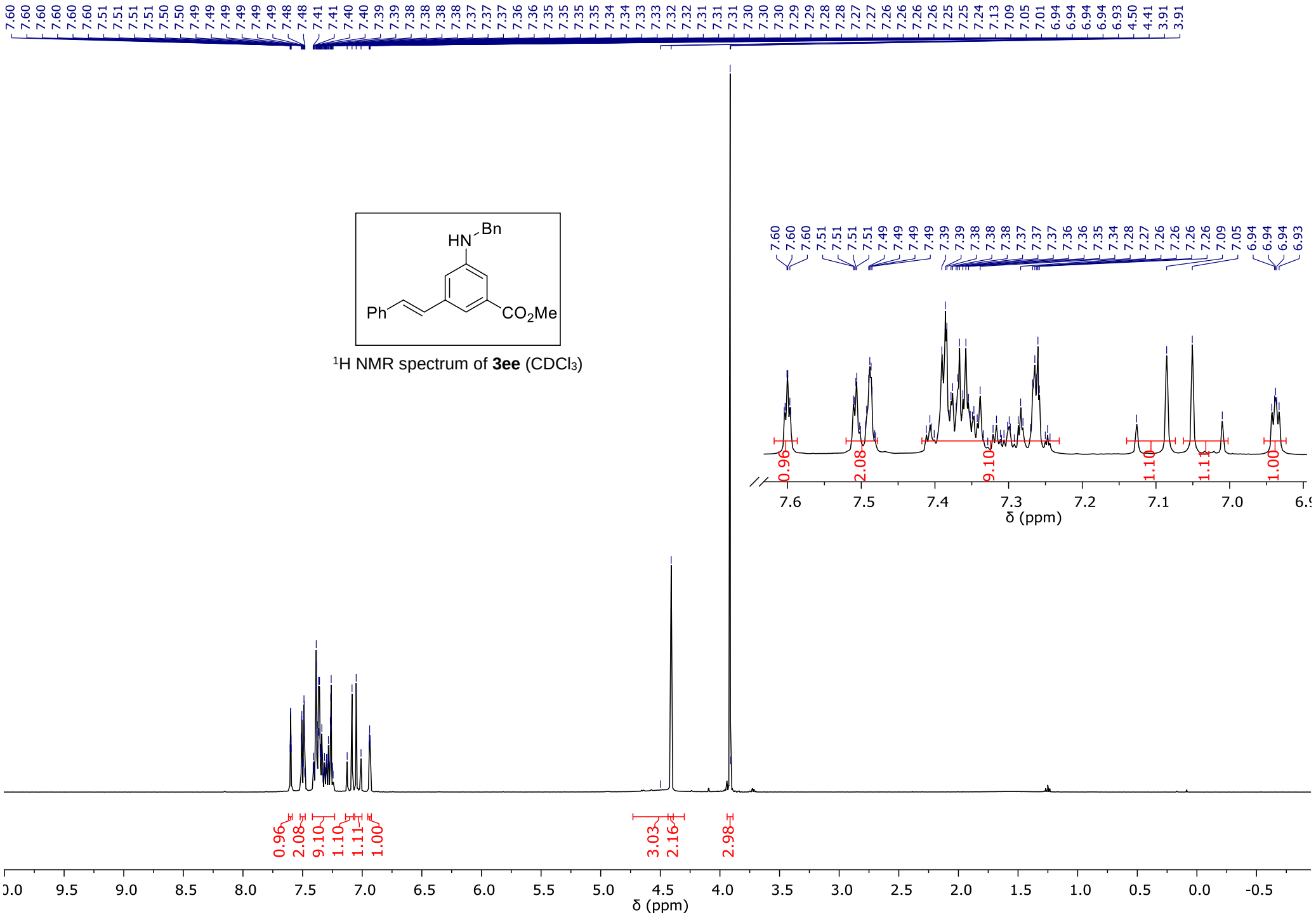
^{13}C NMR spectrum of **3ck** ($CDCl_3$)



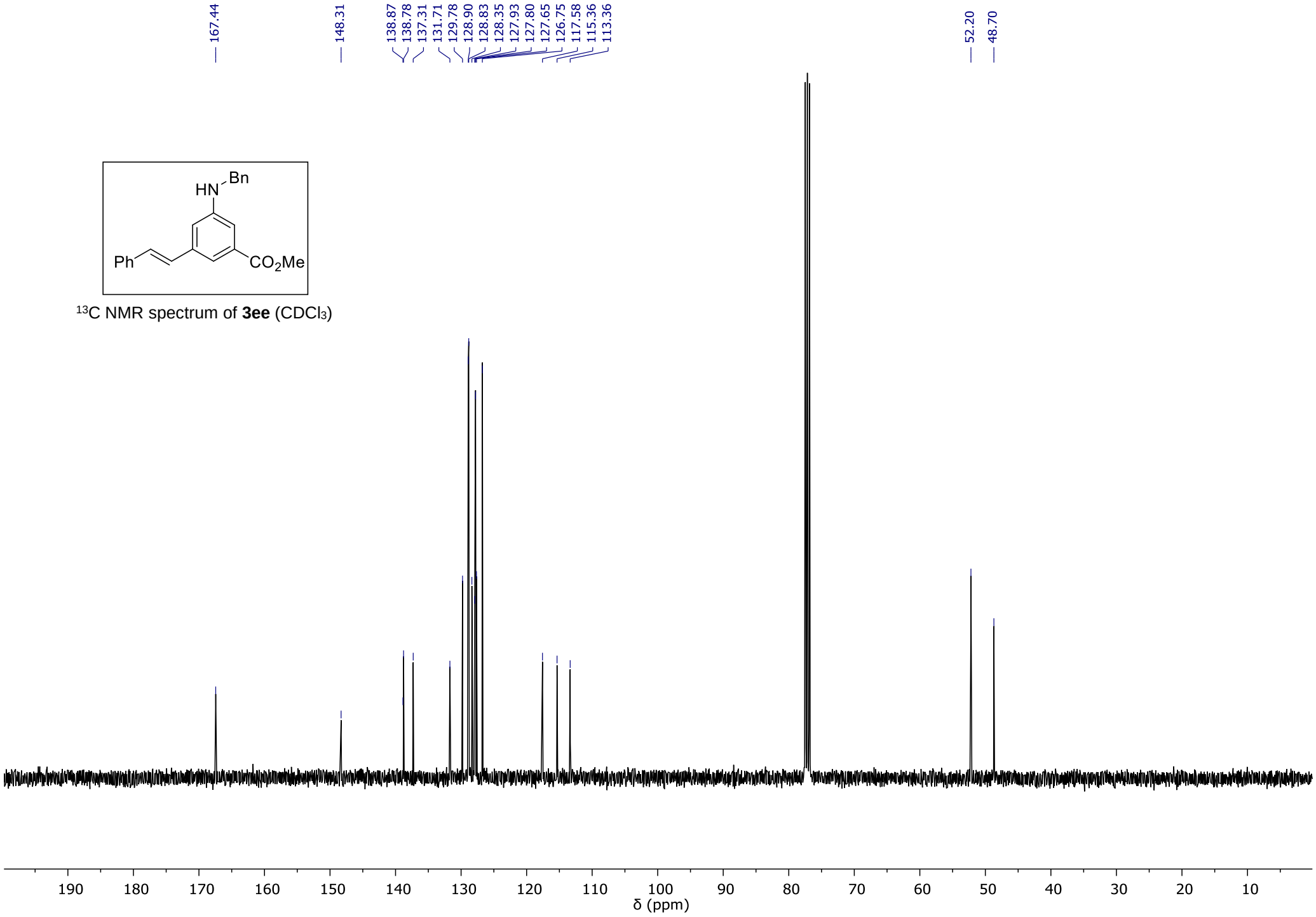
^{1}H NMR spectrum of **3dk** ($CDCl_3$)



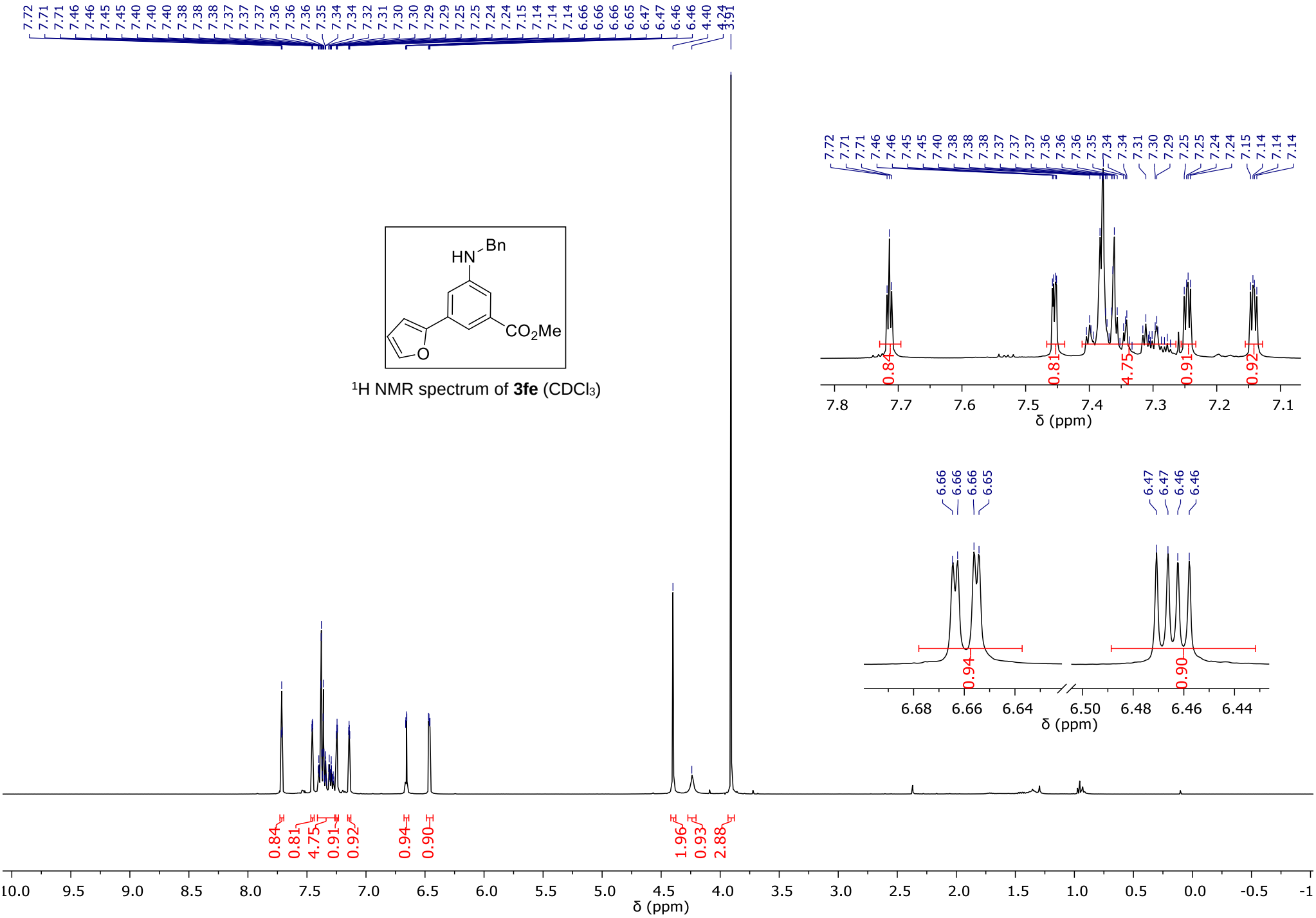
^{13}C NMR spectrum of **3dk** ($CDCl_3$)



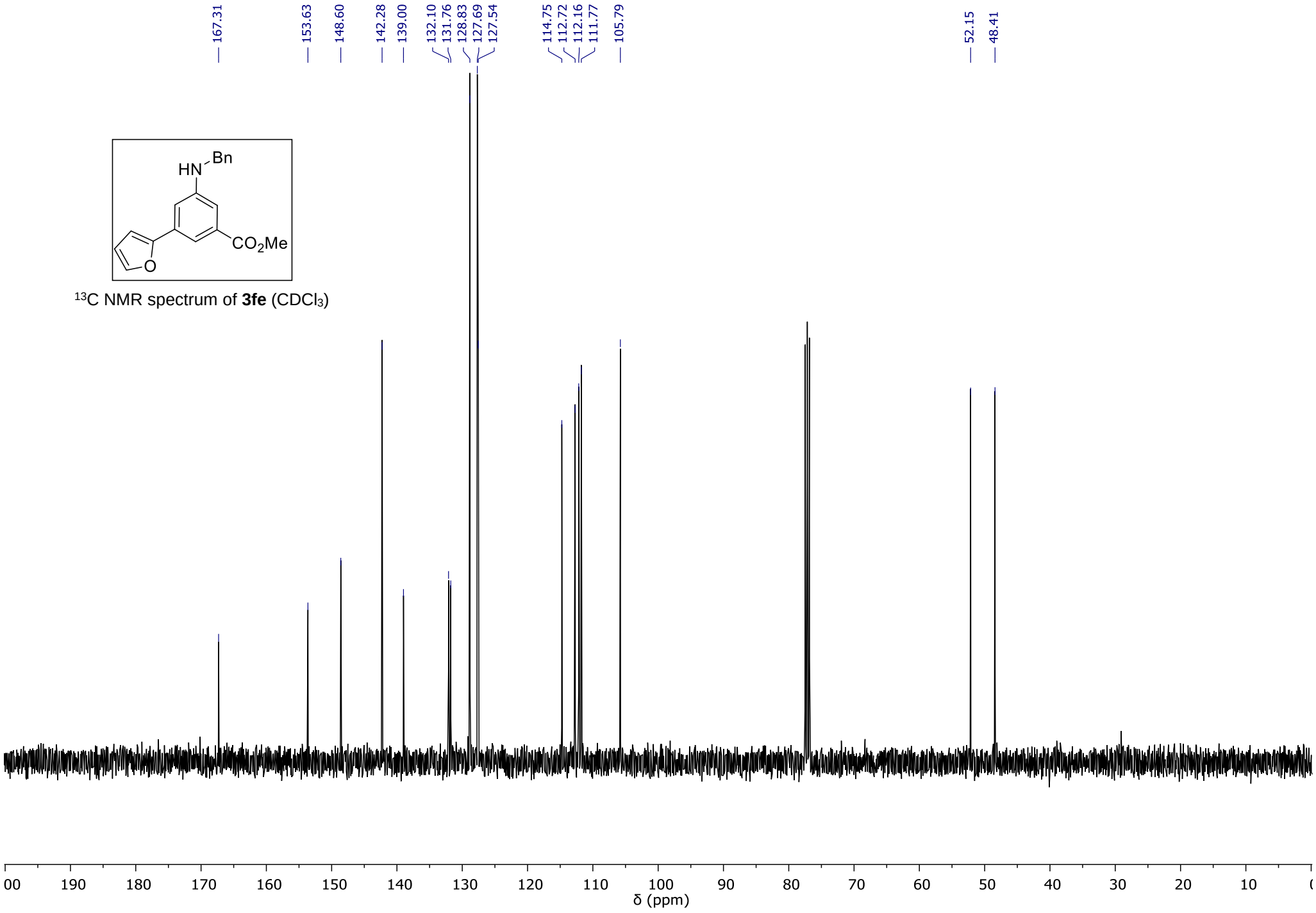
^{1}H NMR spectrum of **3ee** ($CDCl_3$)



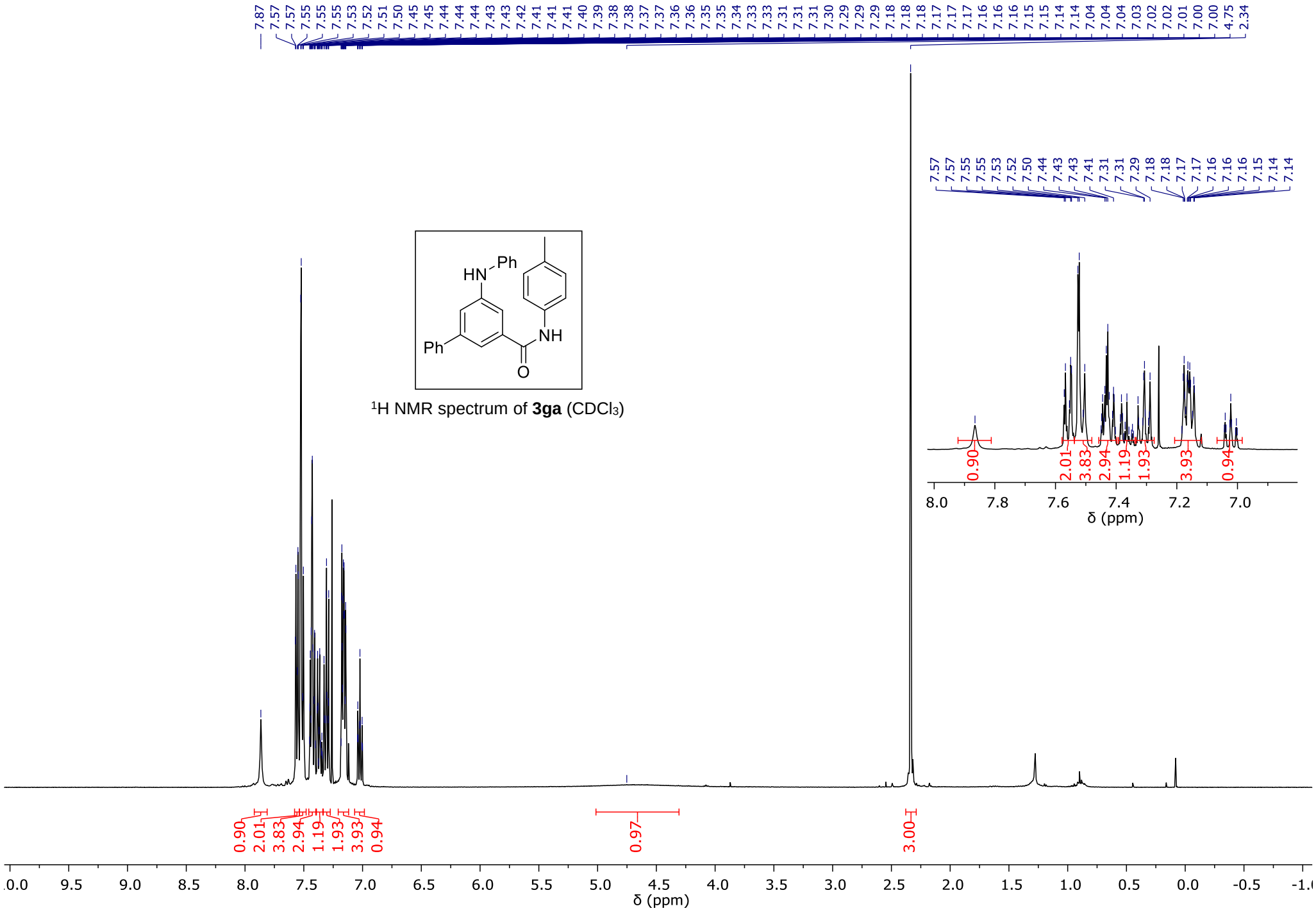
^{13}C NMR spectrum of **3ee** ($CDCl_3$)



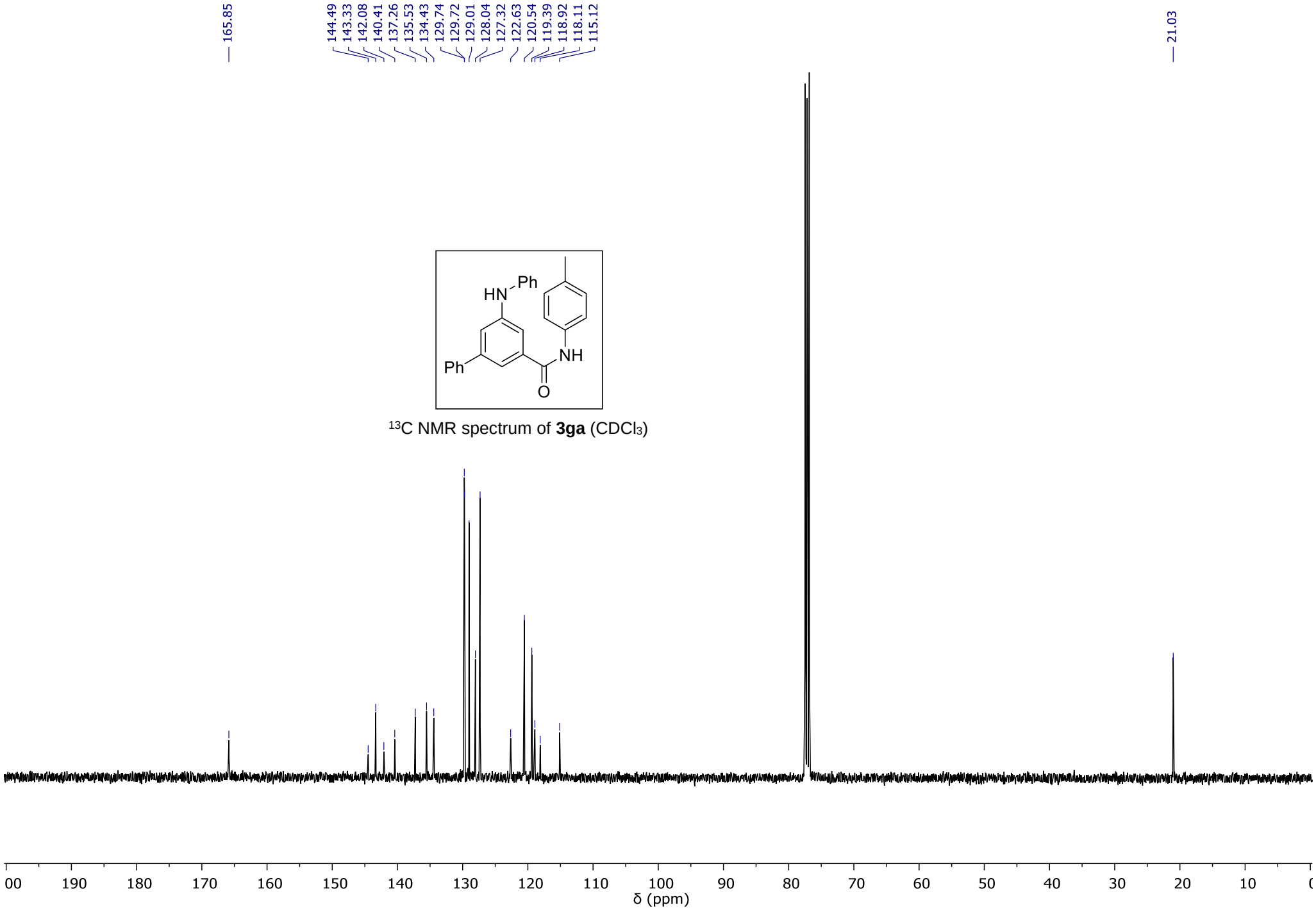
^{1}H NMR spectrum of **3fe** ($CDCl_3$)



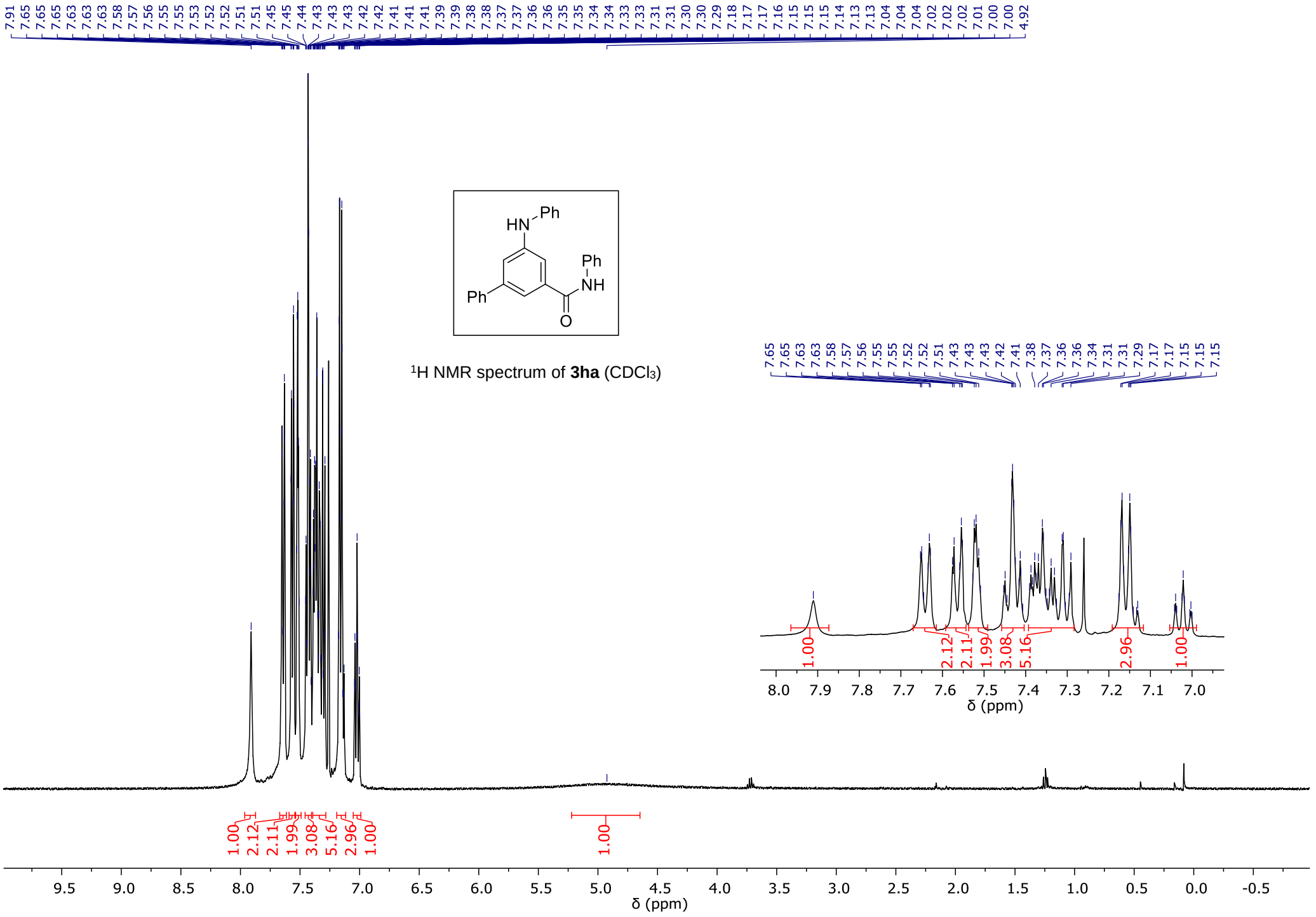
^{13}C NMR spectrum of **3fe** ($CDCl_3$)



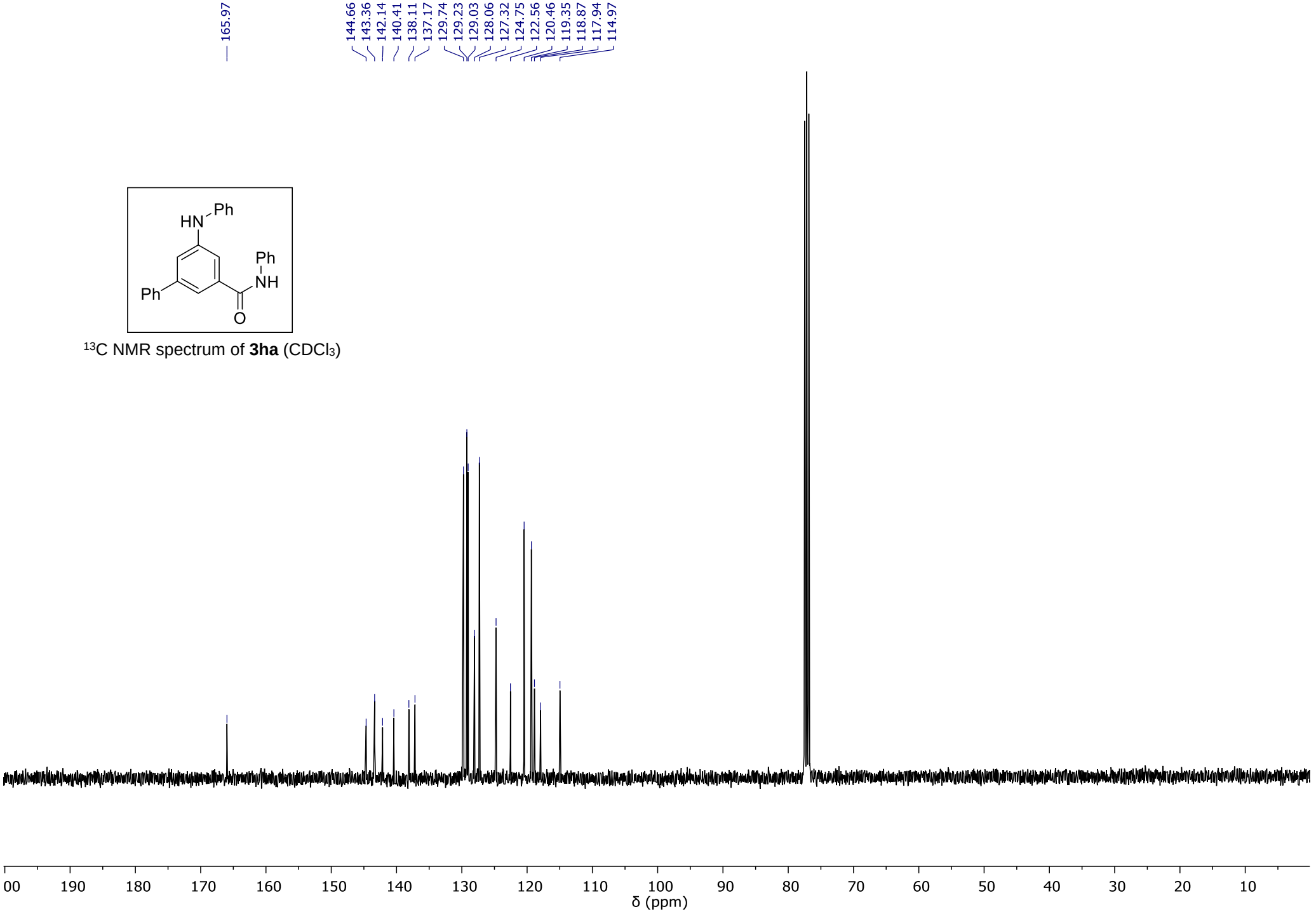
^{1}H NMR spectrum of **3ga** ($CDCl_3$)



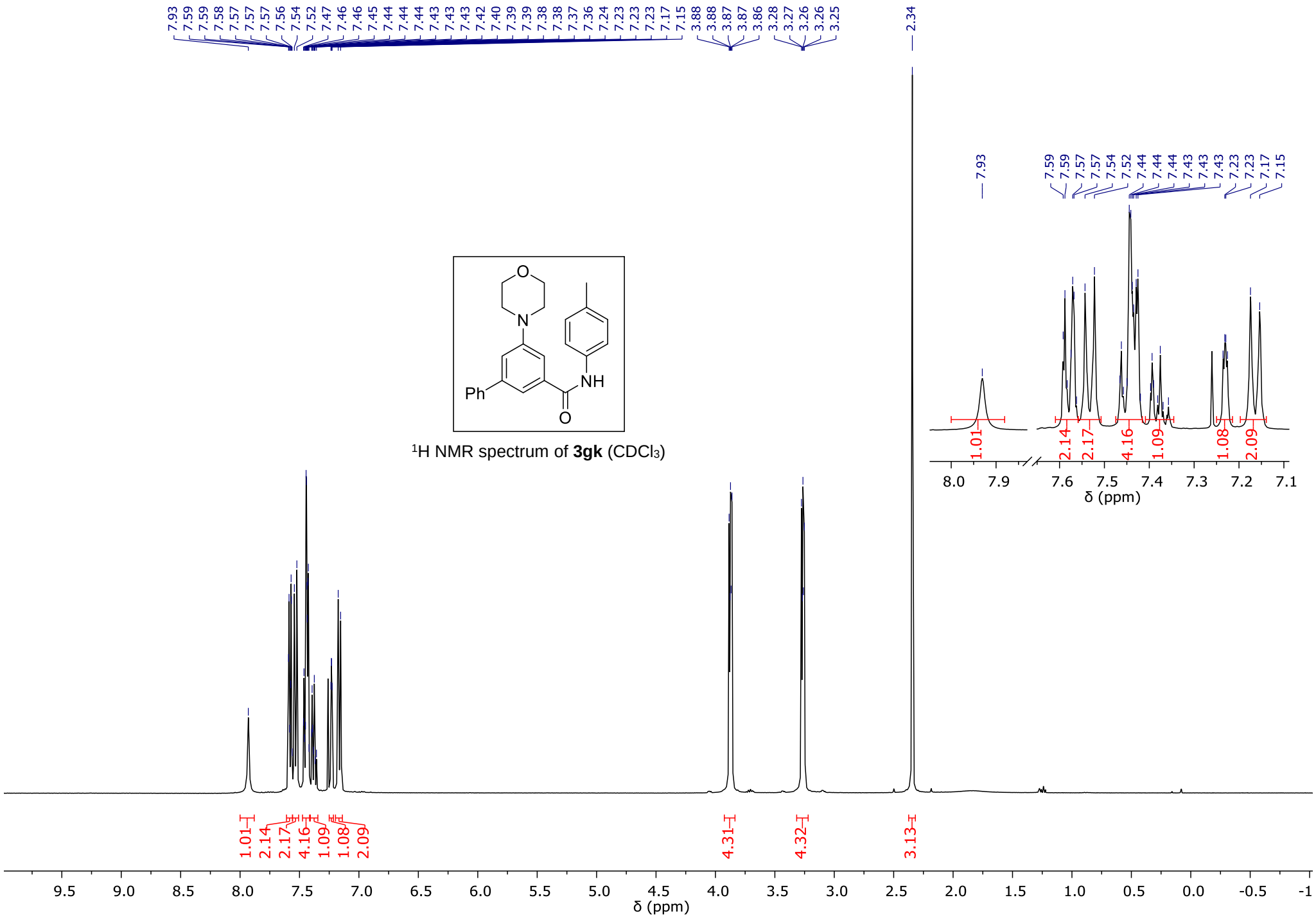
^{13}C NMR spectrum of **3ga** ($CDCl_3$)



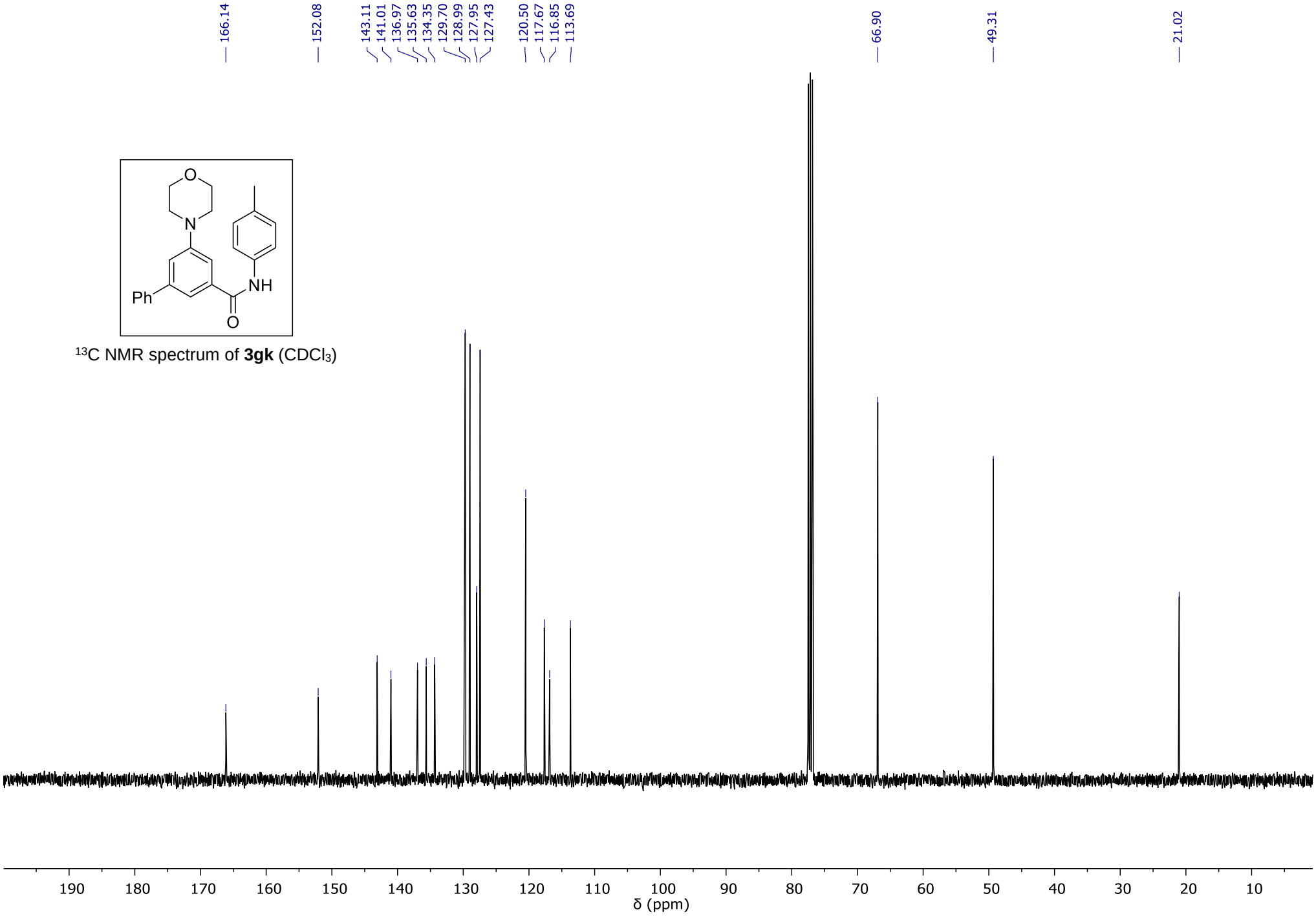
^{1}H NMR spectrum of **3ha** ($CDCl_3$)



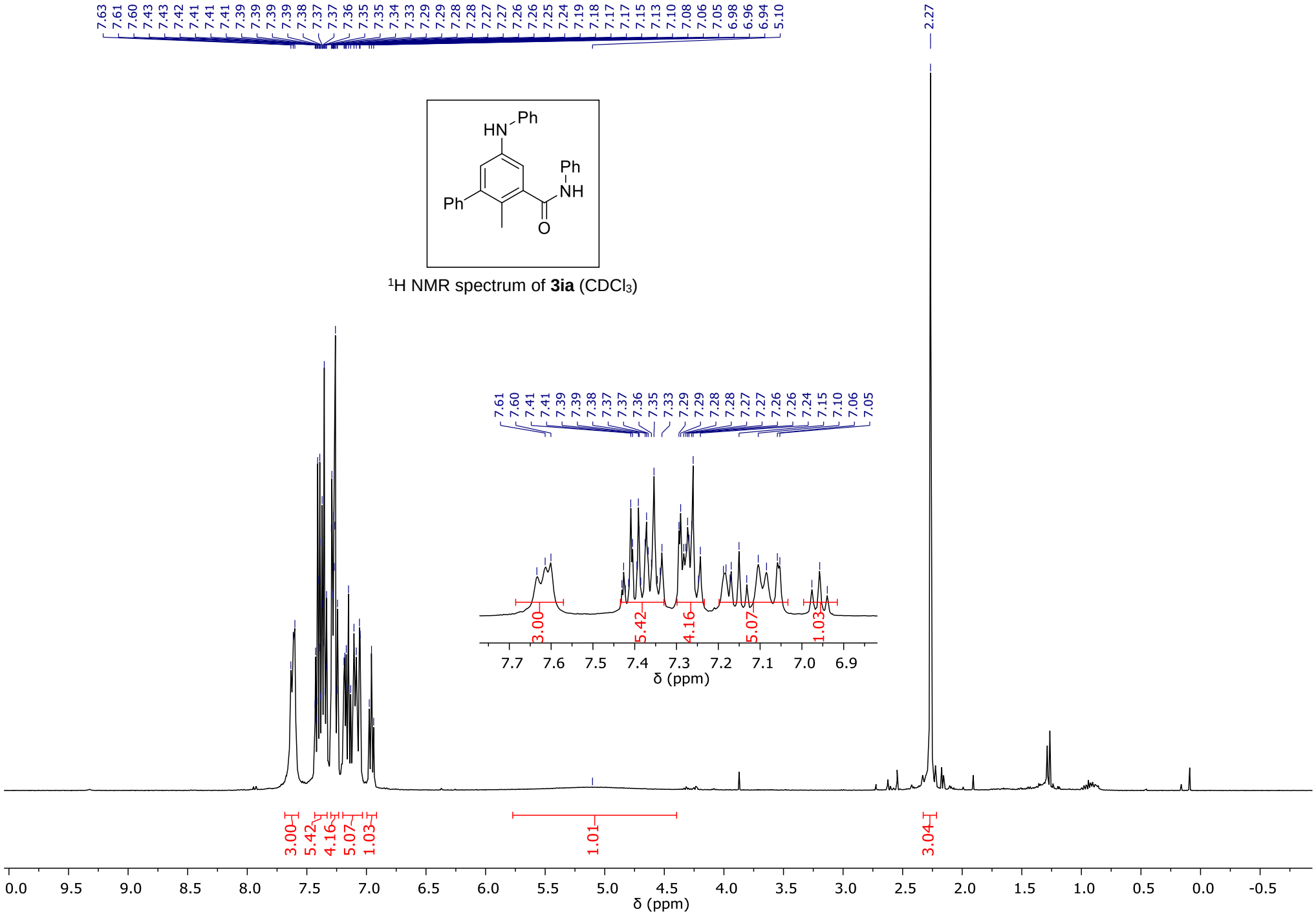
^{13}C NMR spectrum of **3ha** ($CDCl_3$)



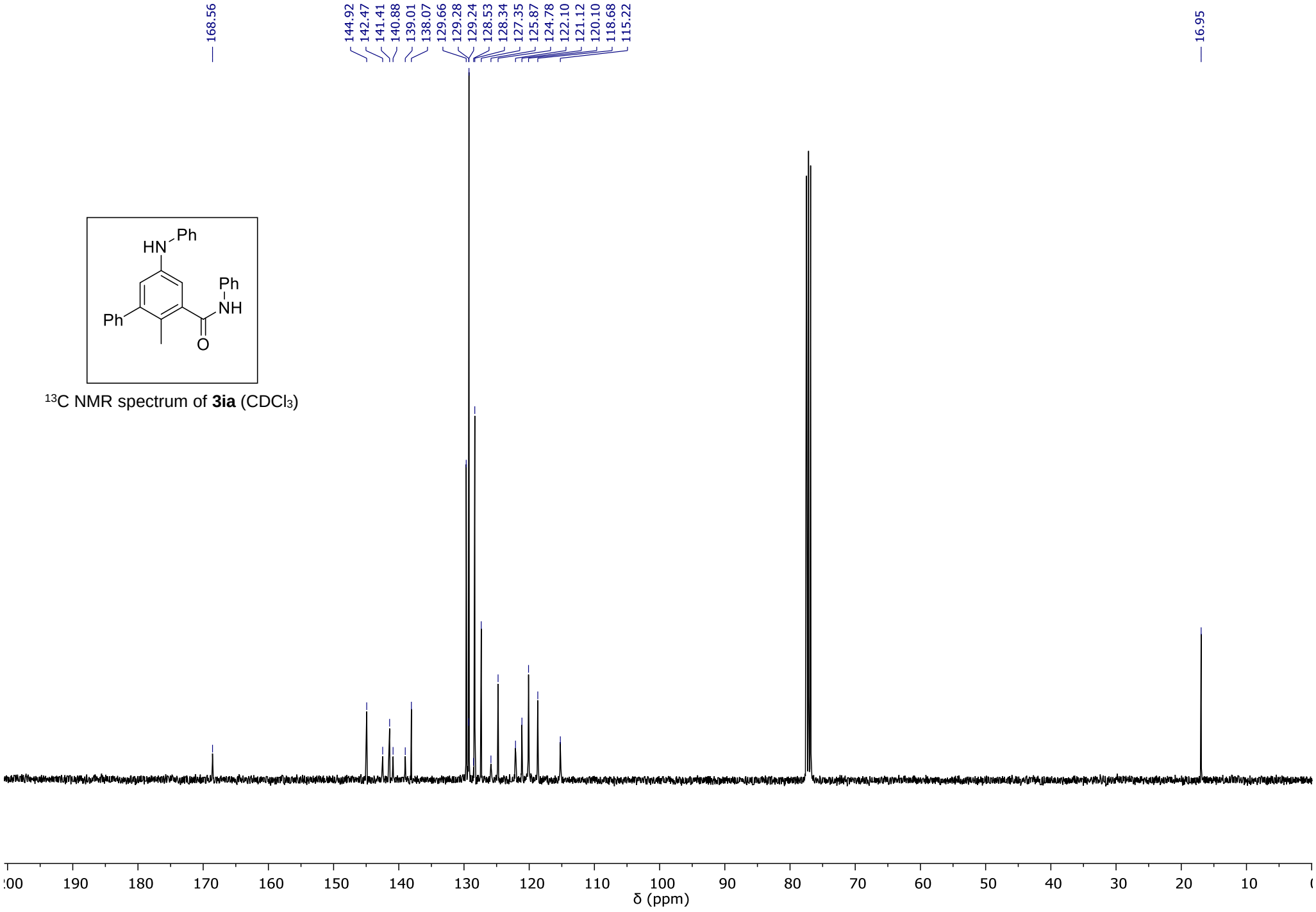
^{1}H NMR spectrum of **3gk** ($CDCl_3$)



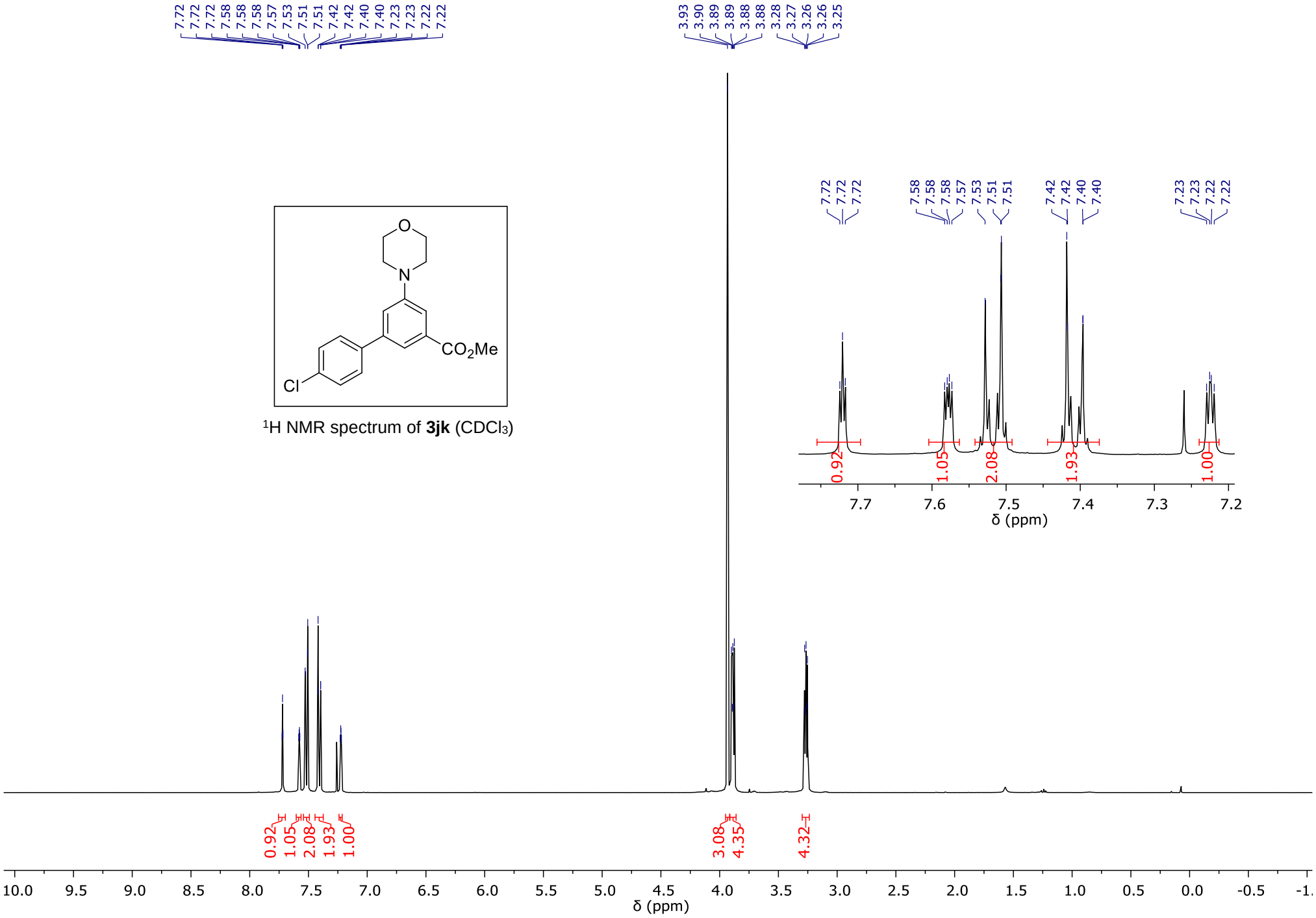
^{13}C NMR spectrum of **3gk** ($CDCl_3$)



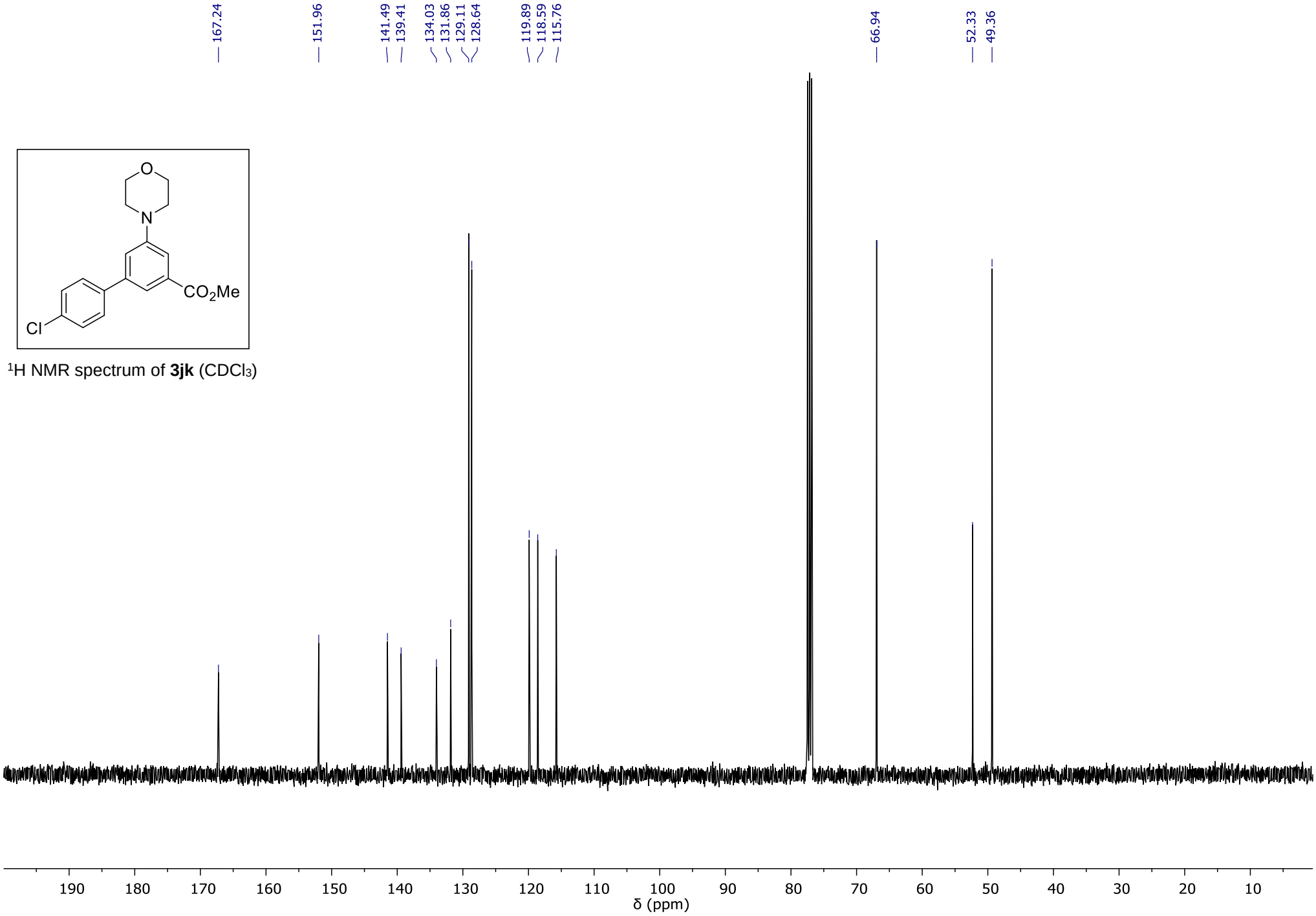
^{1}H NMR spectrum of **3ia** ($CDCl_3$)



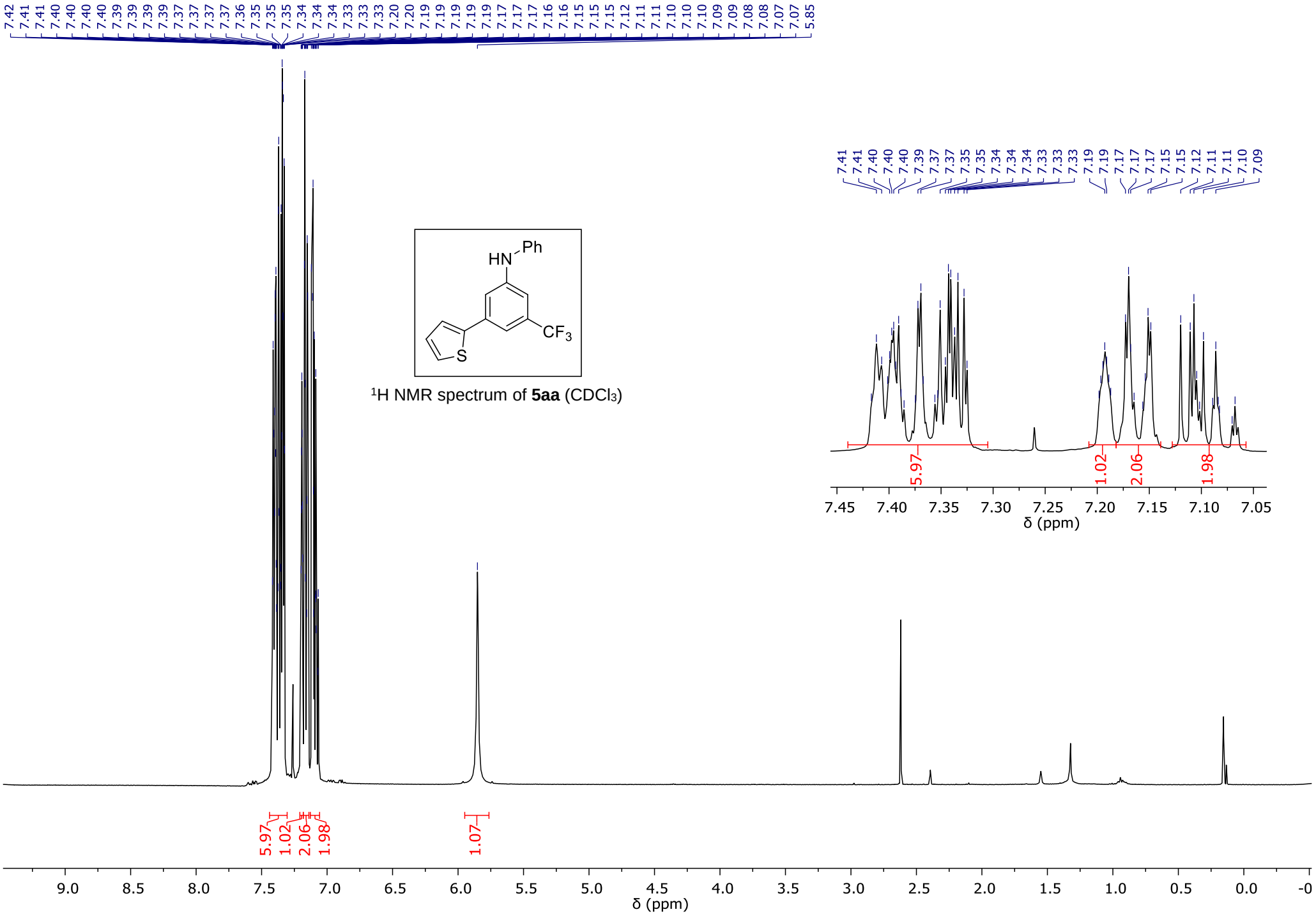
^{13}C NMR spectrum of **3ia** ($CDCl_3$)



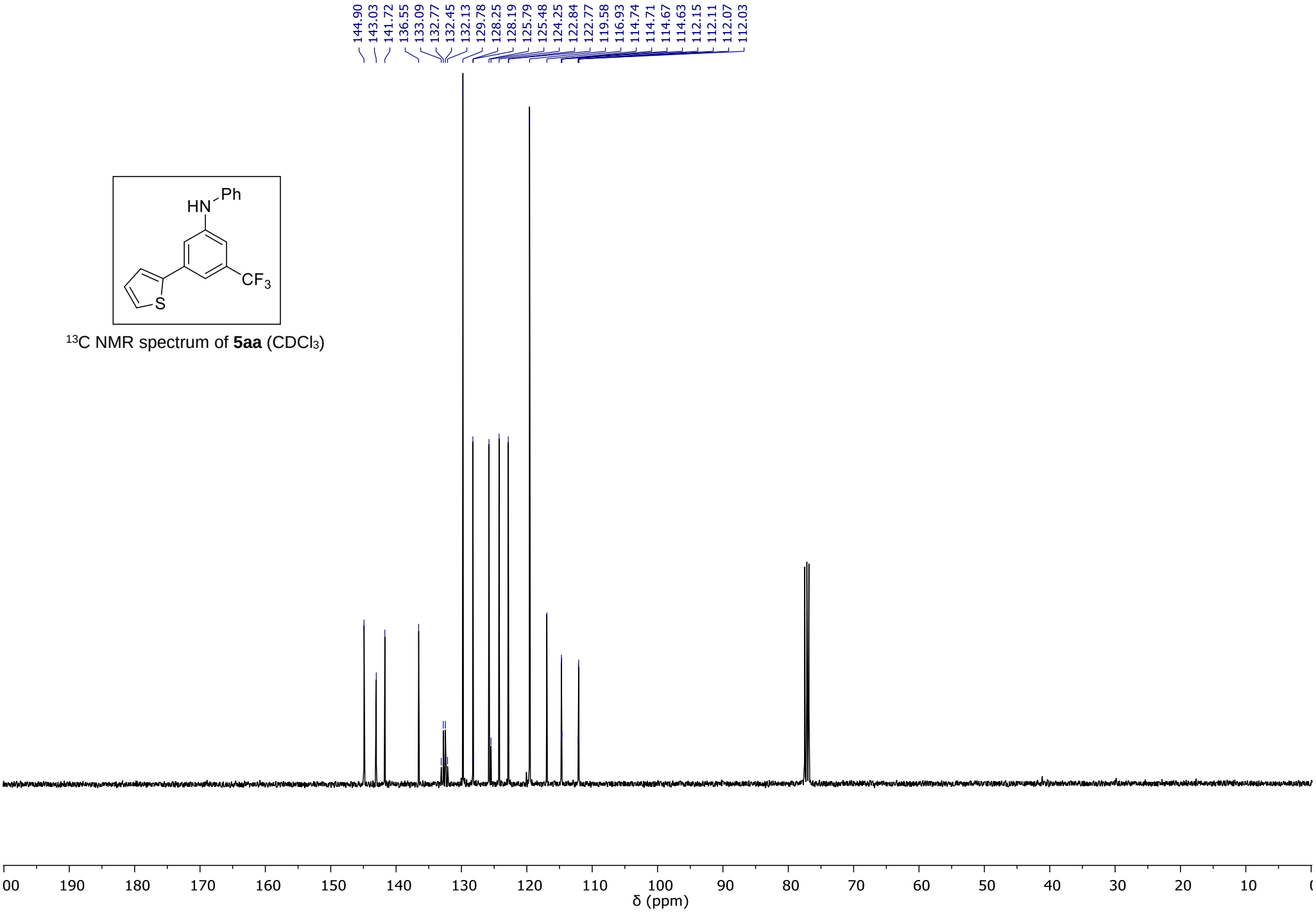
^{1}H NMR spectrum of **3jk** ($CDCl_3$)



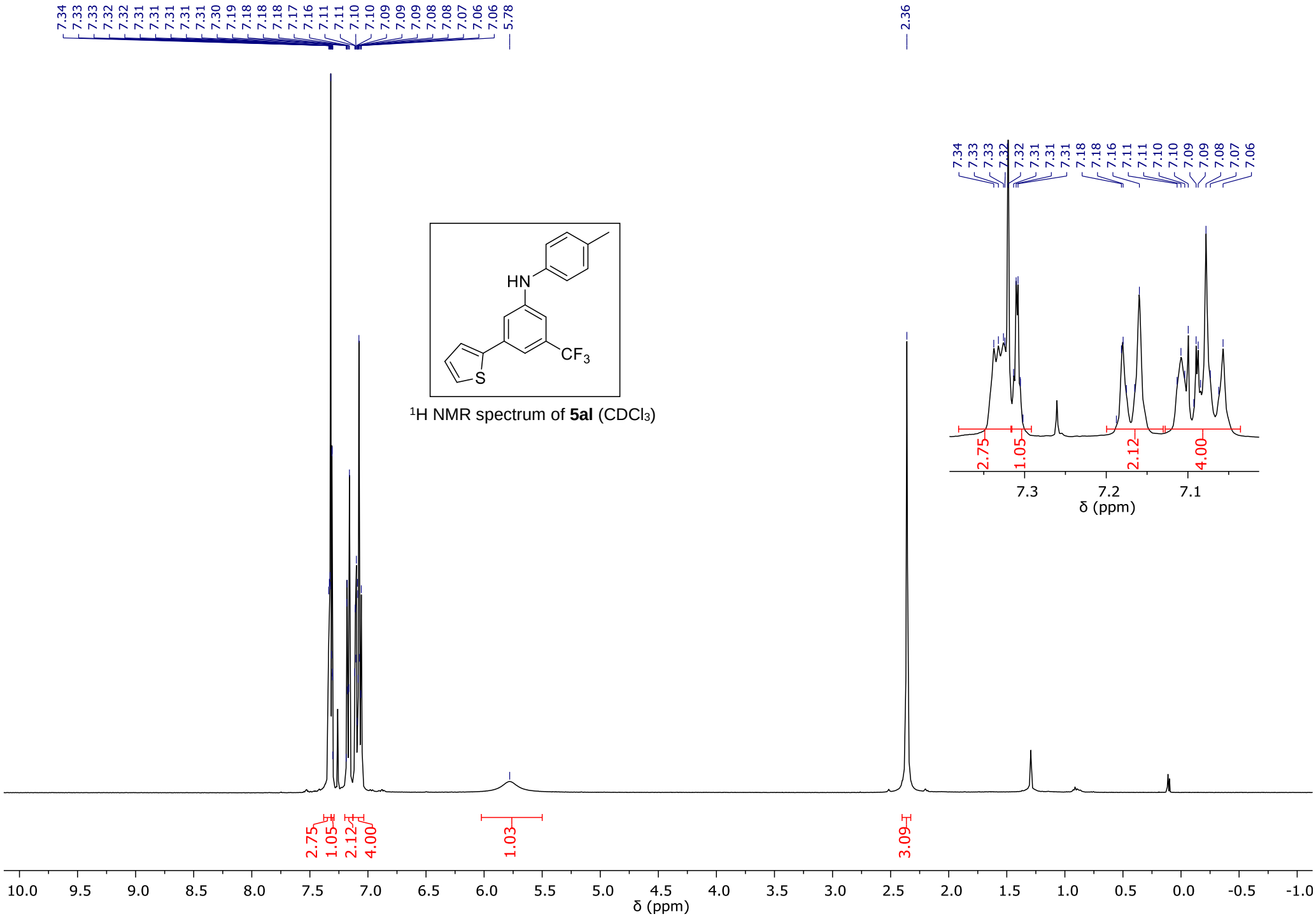
^{1}H NMR spectrum of **3jk** ($CDCl_3$)



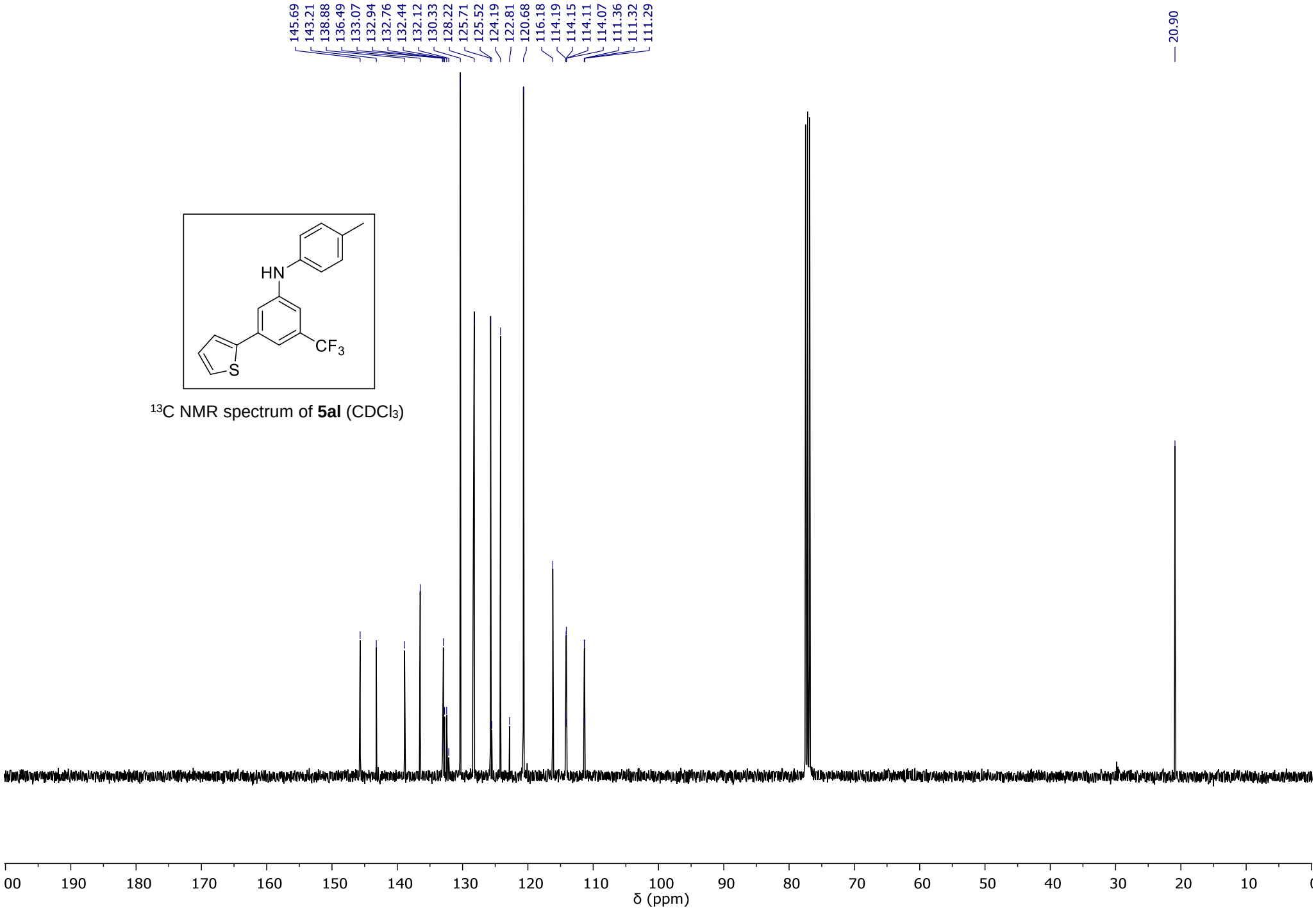
^{1}H NMR spectrum of **5aa** ($CDCl_3$)



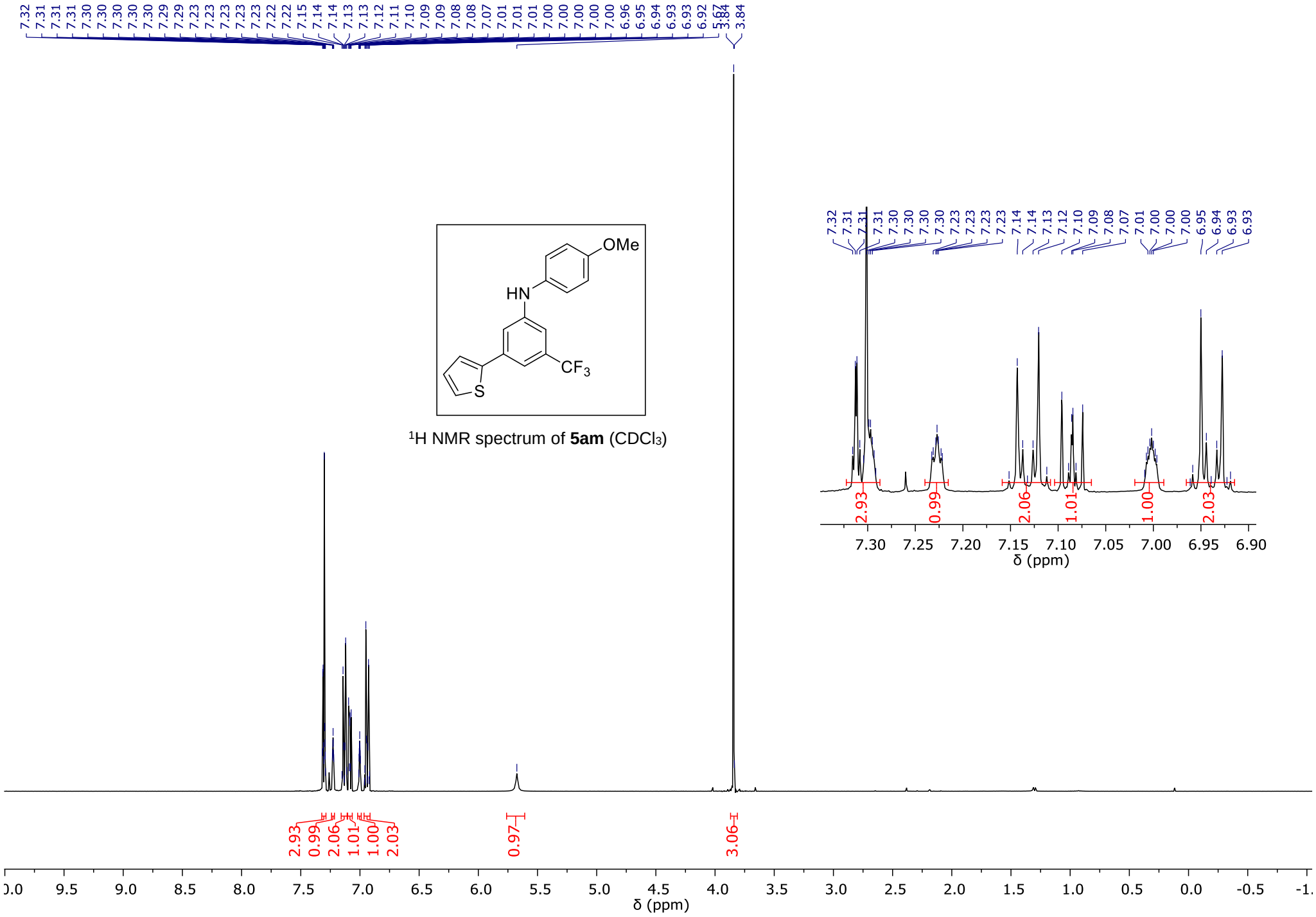
^{13}C NMR spectrum of **5aa** ($CDCl_3$)



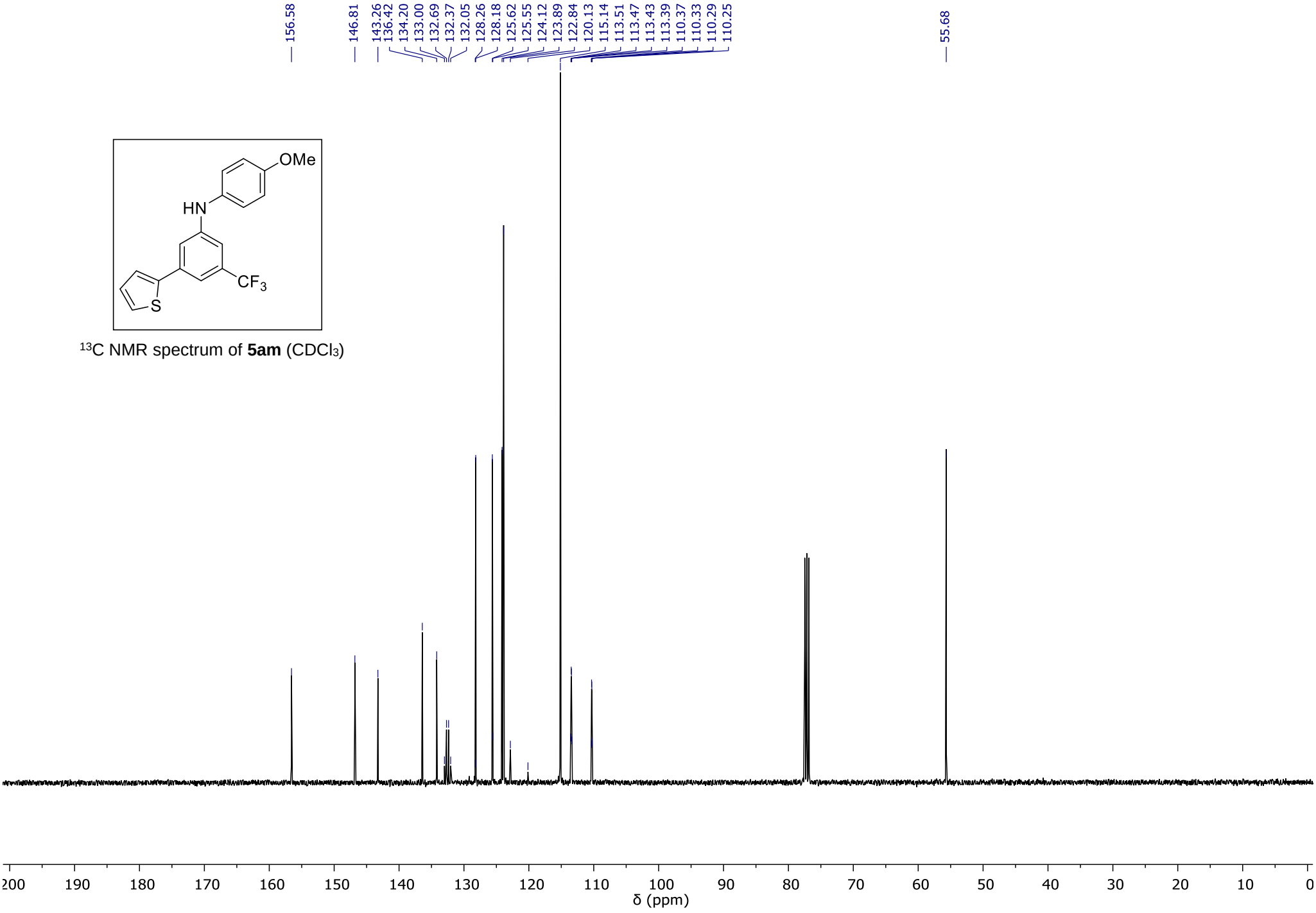
^{1}H NMR spectrum of **5al** ($CDCl_3$)



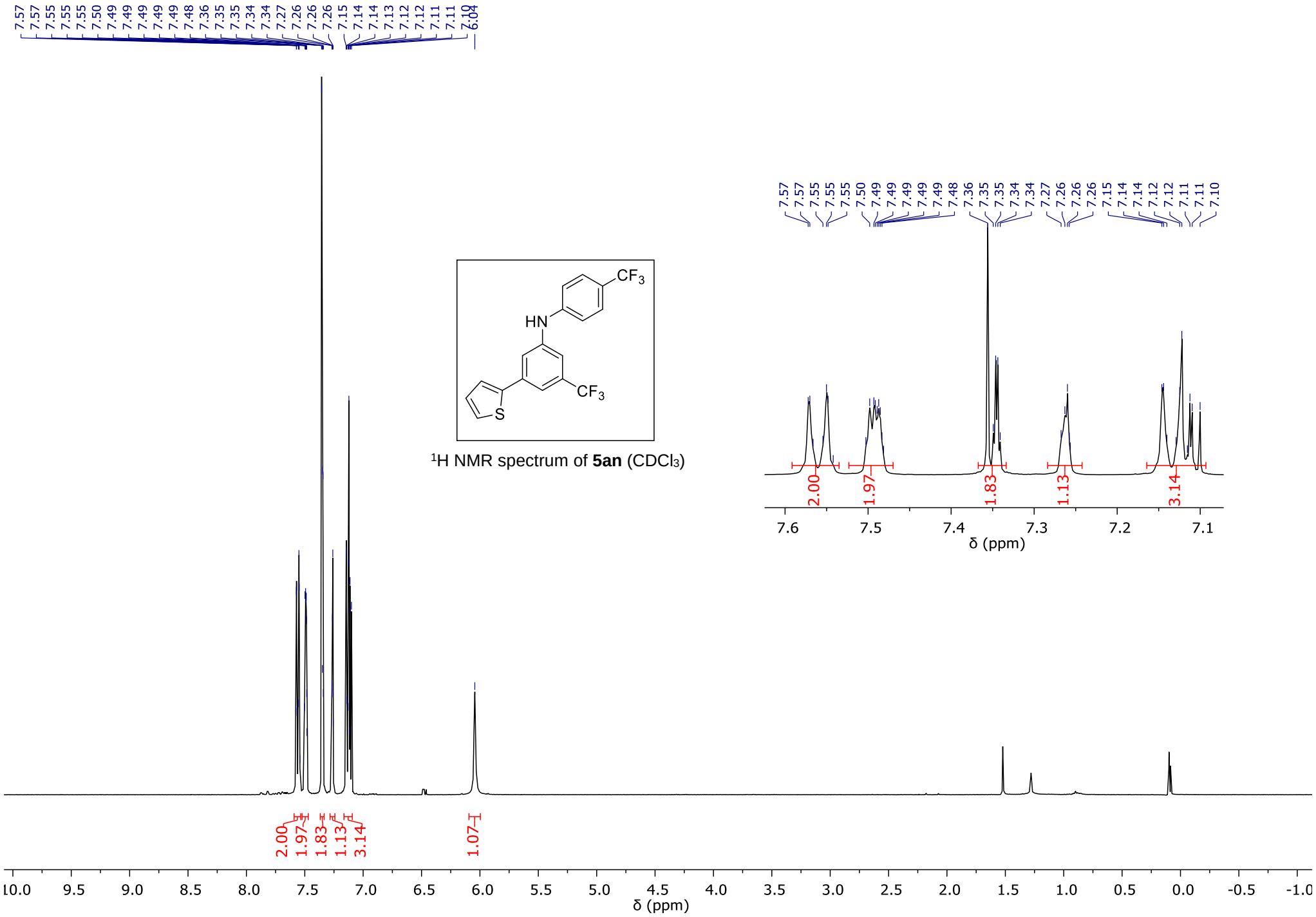
^{13}C NMR spectrum of **5al** ($CDCl_3$)



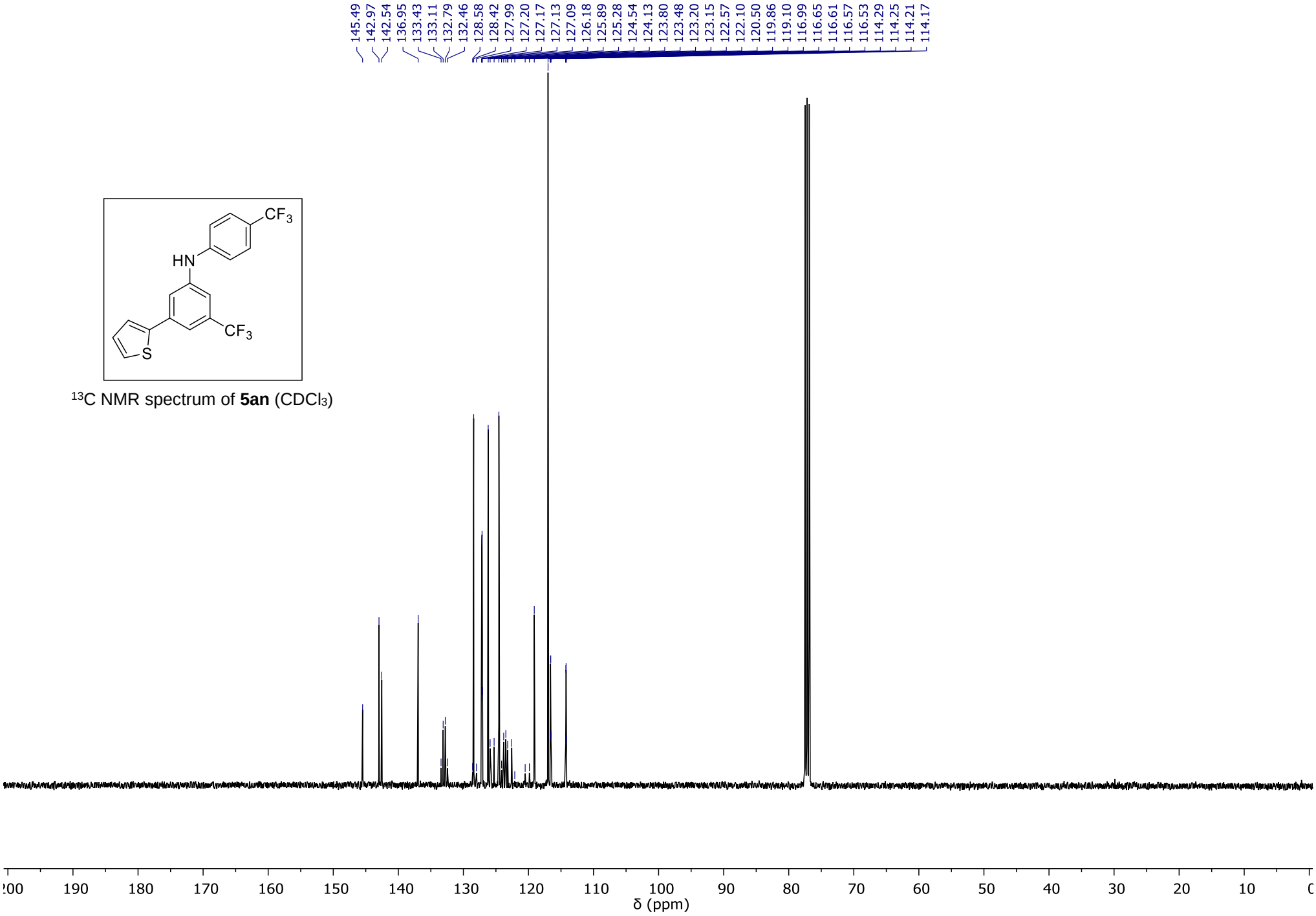
^{1}H NMR spectrum of **5am** ($CDCl_3$)



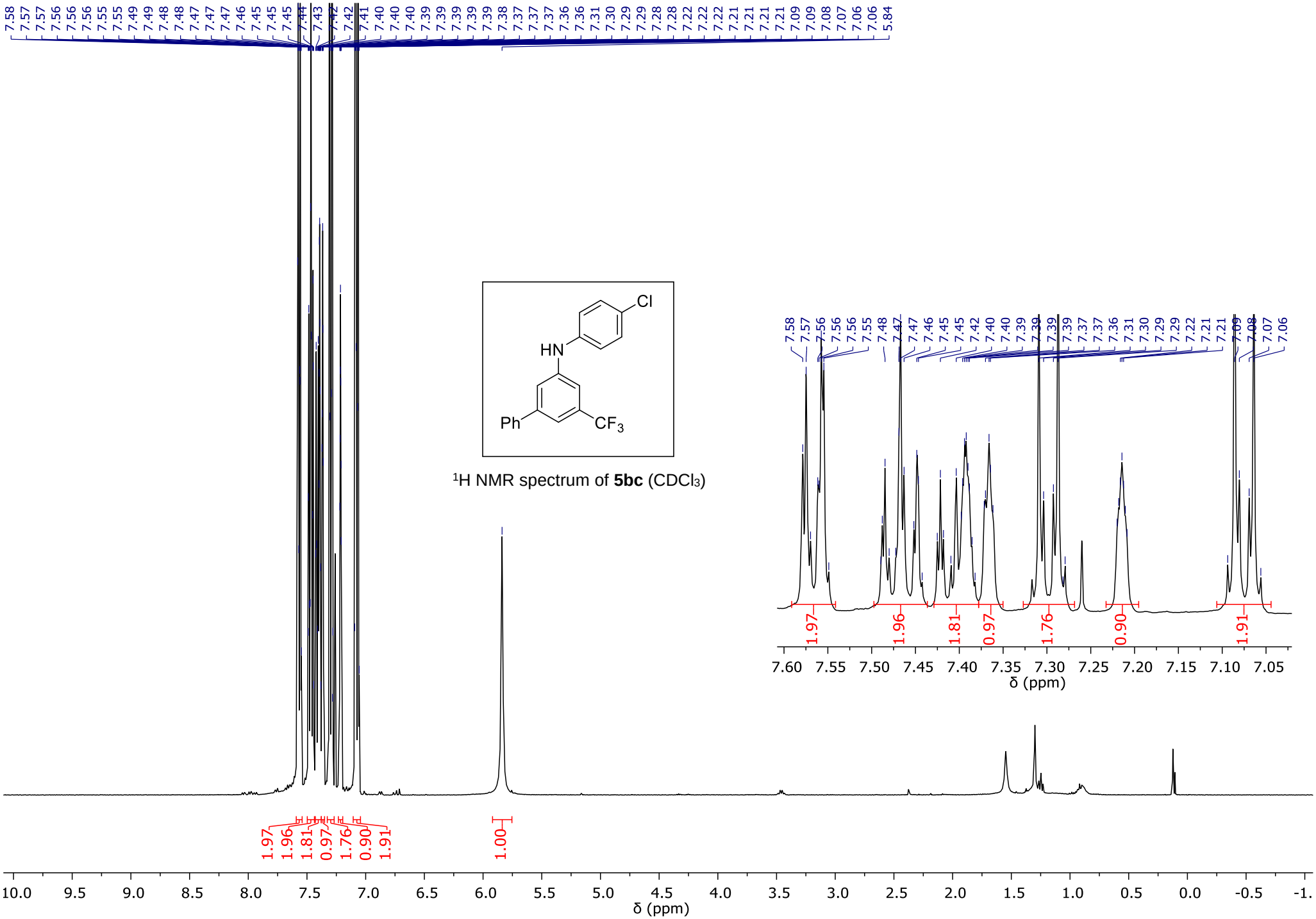
^{13}C NMR spectrum of **5am** ($CDCl_3$)



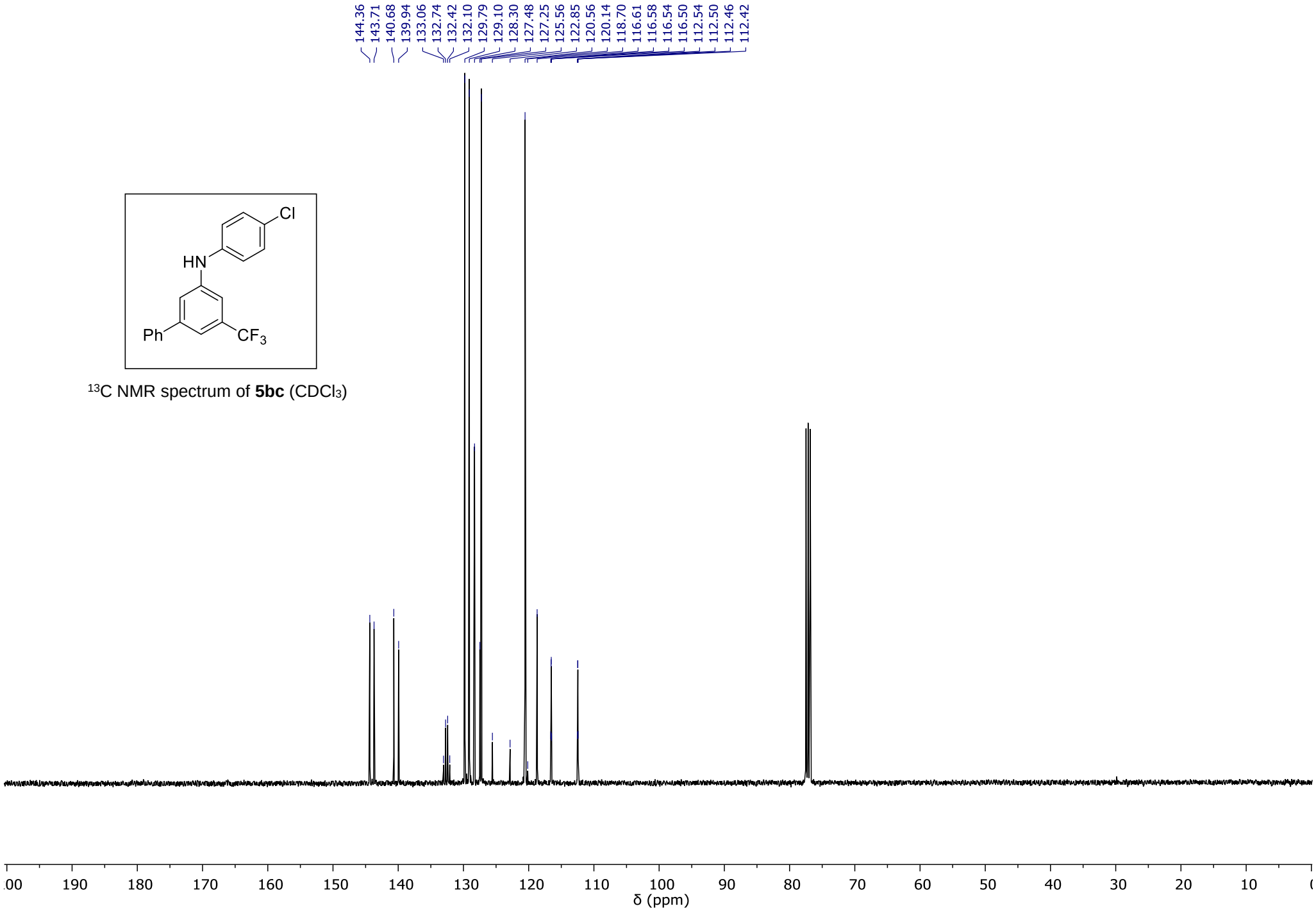
^{1}H NMR spectrum of **5an** ($CDCl_3$)



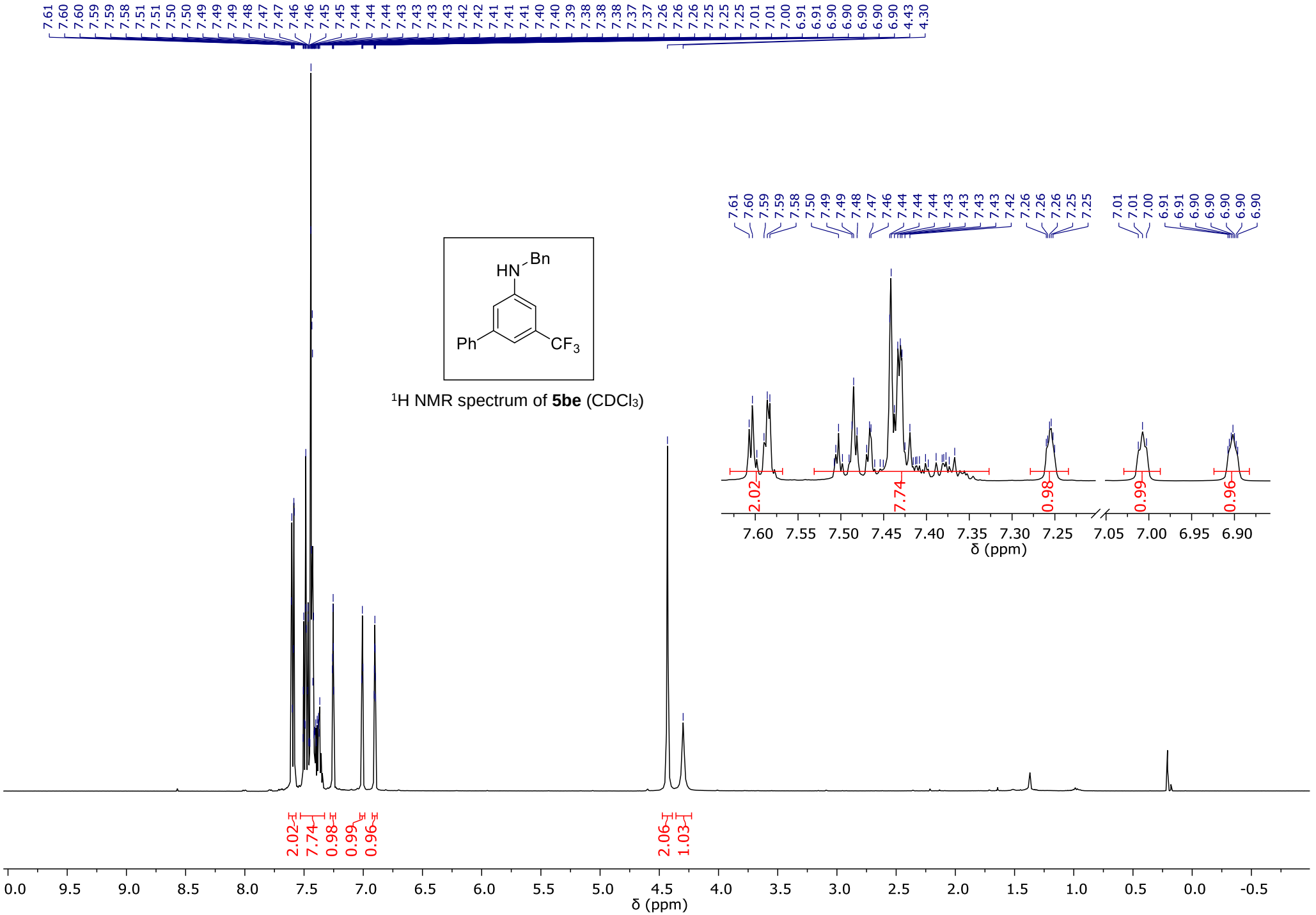
^{13}C NMR spectrum of **5an** ($CDCl_3$)



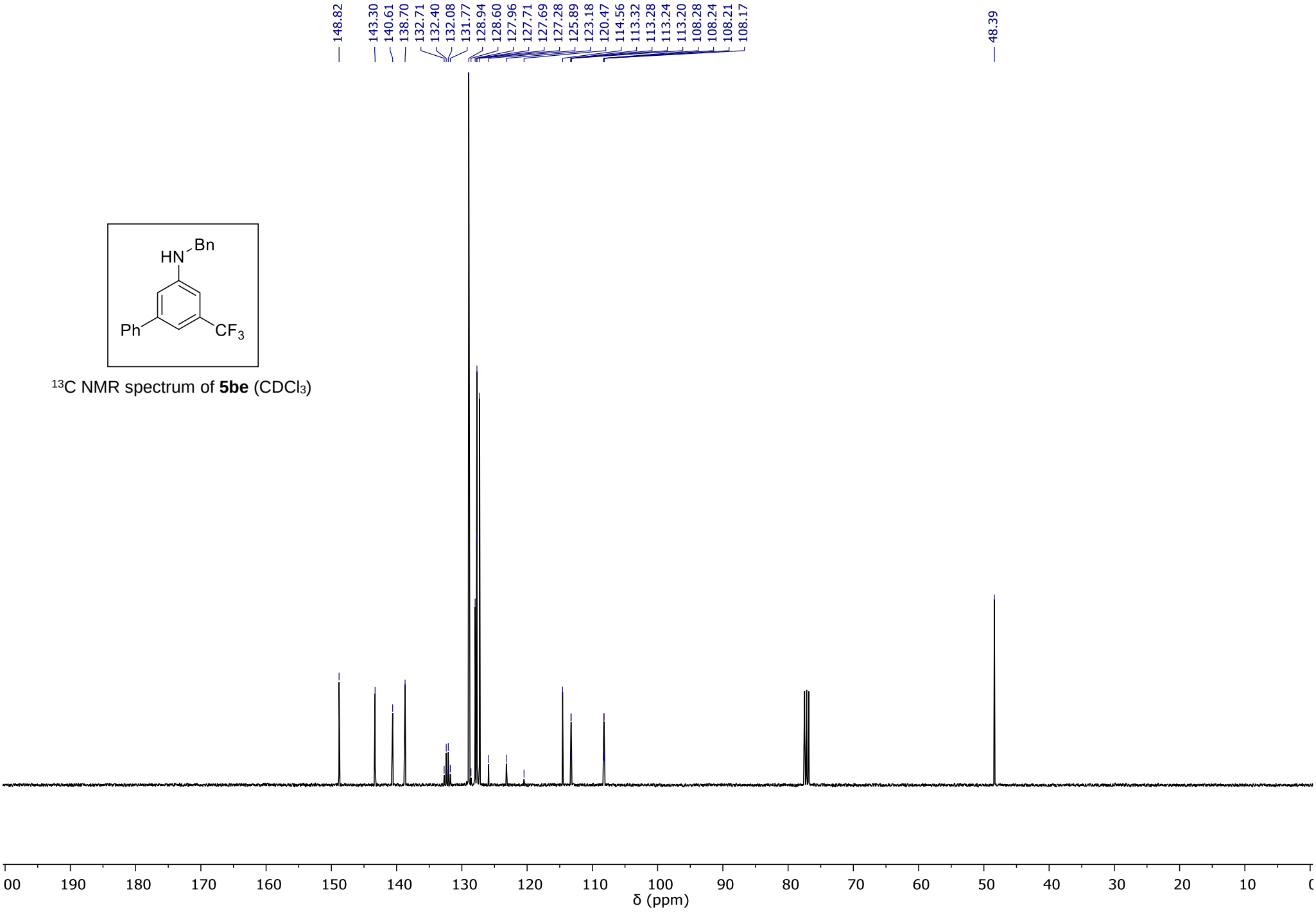
^{1}H NMR spectrum of **5bc** ($CDCl_3$)



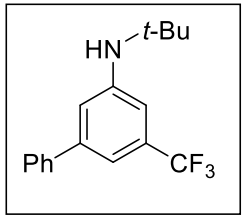
^{13}C NMR spectrum of **5bc** ($CDCl_3$)



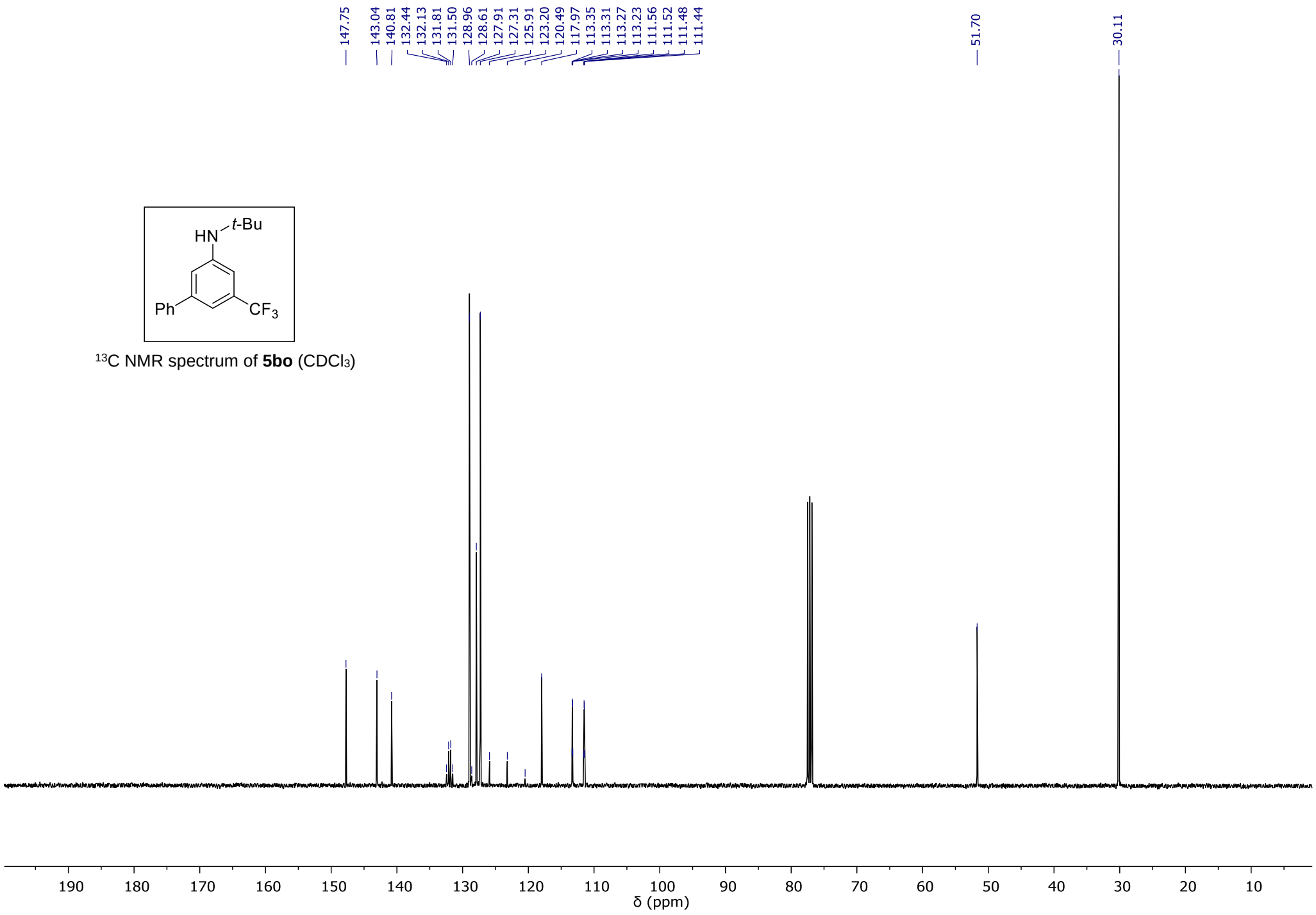
^{1}H NMR spectrum of **5be** ($CDCl_3$)



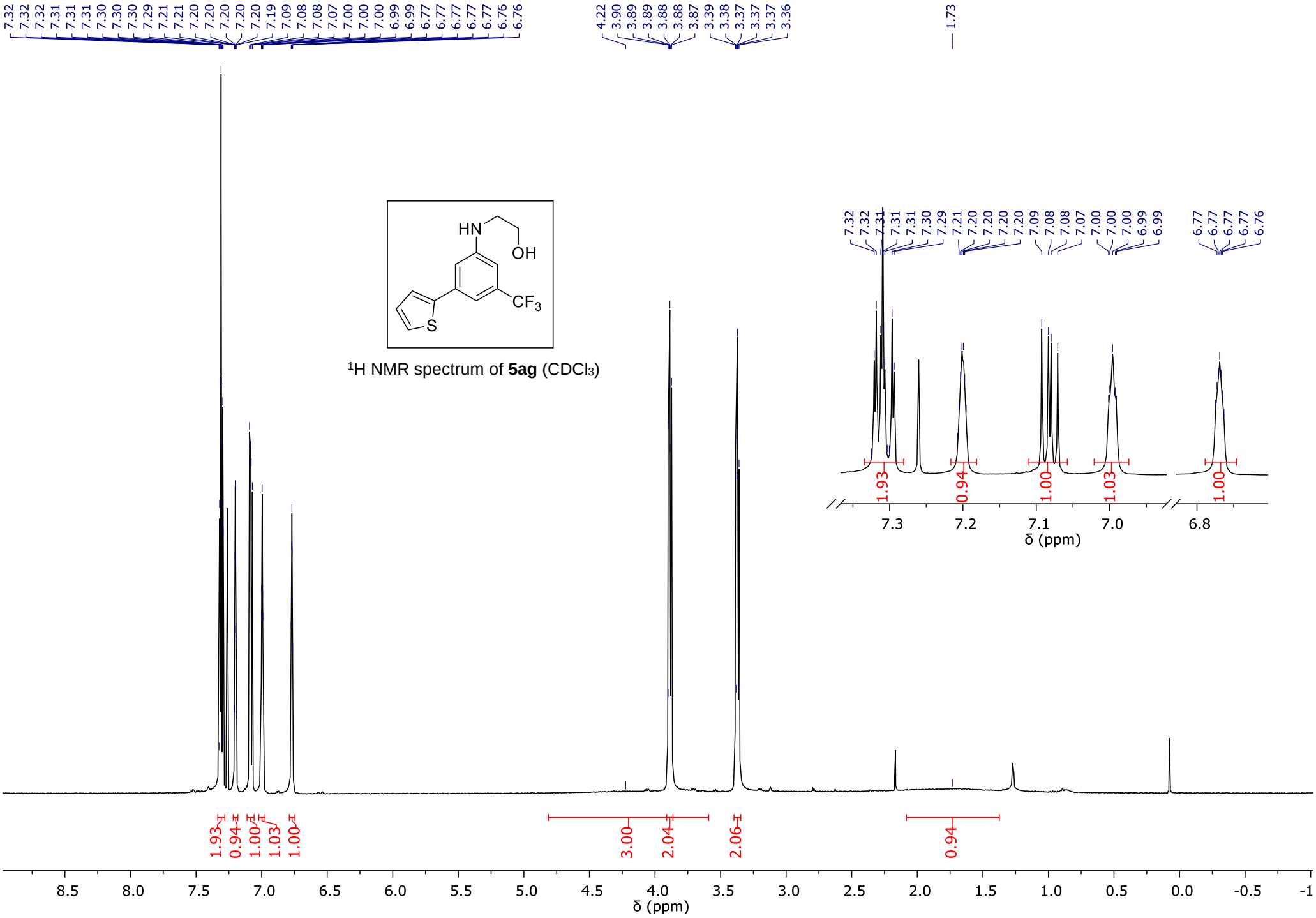
^{13}C NMR spectrum of **5be** ($CDCl_3$)



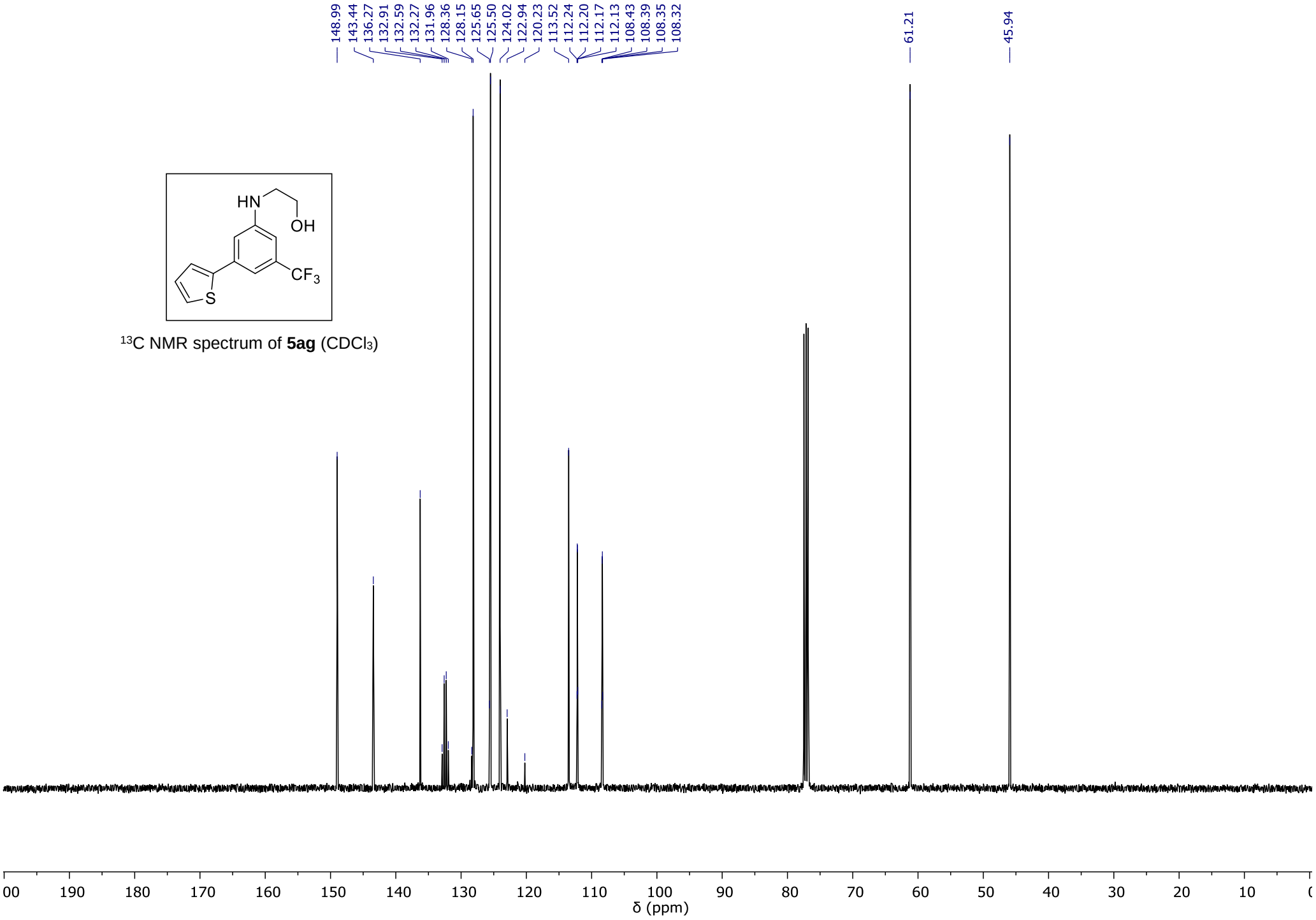
^{1}H NMR spectrum of **5bo** ($CDCl_3$)



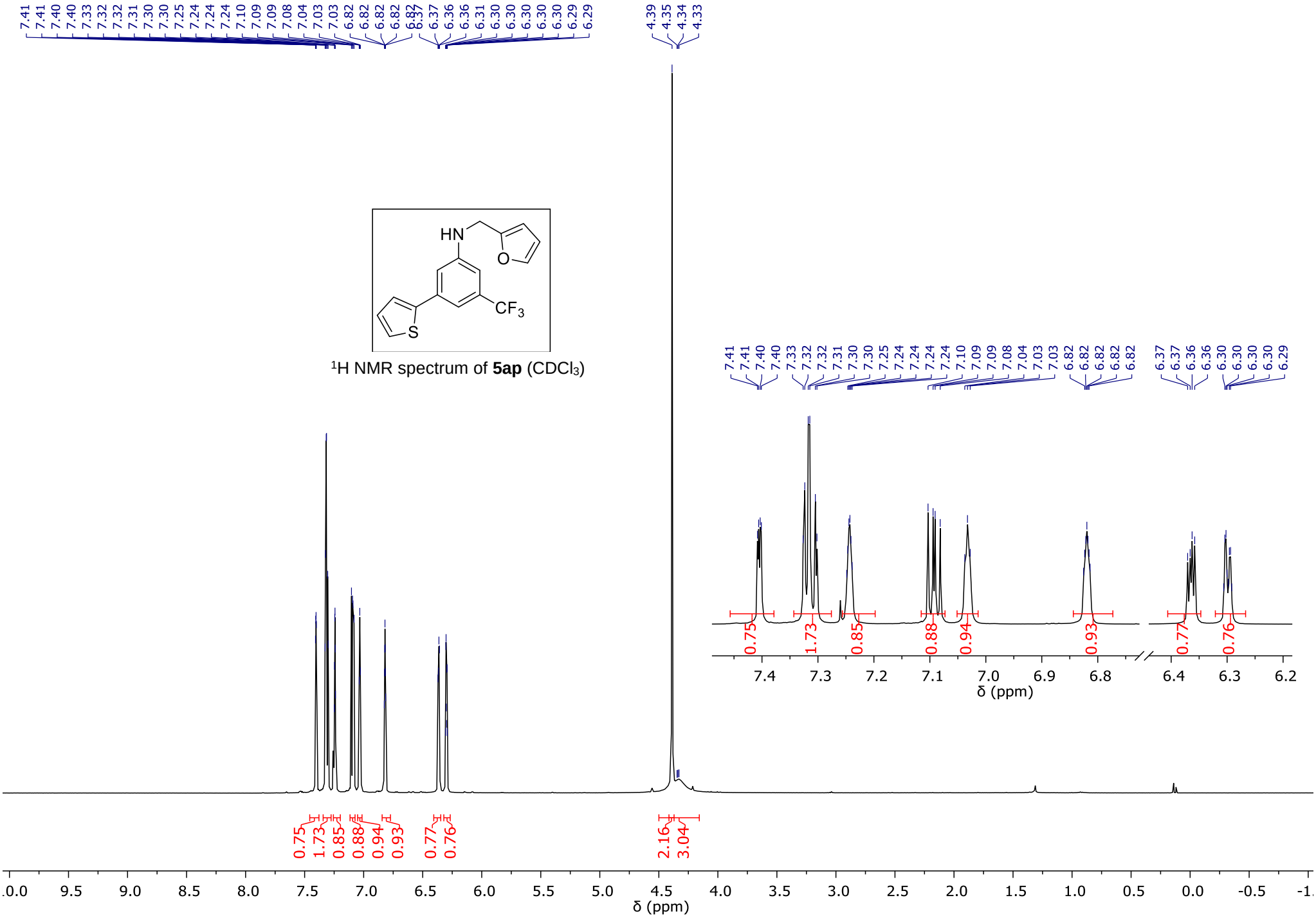
^{13}C NMR spectrum of **5bo** ($CDCl_3$)



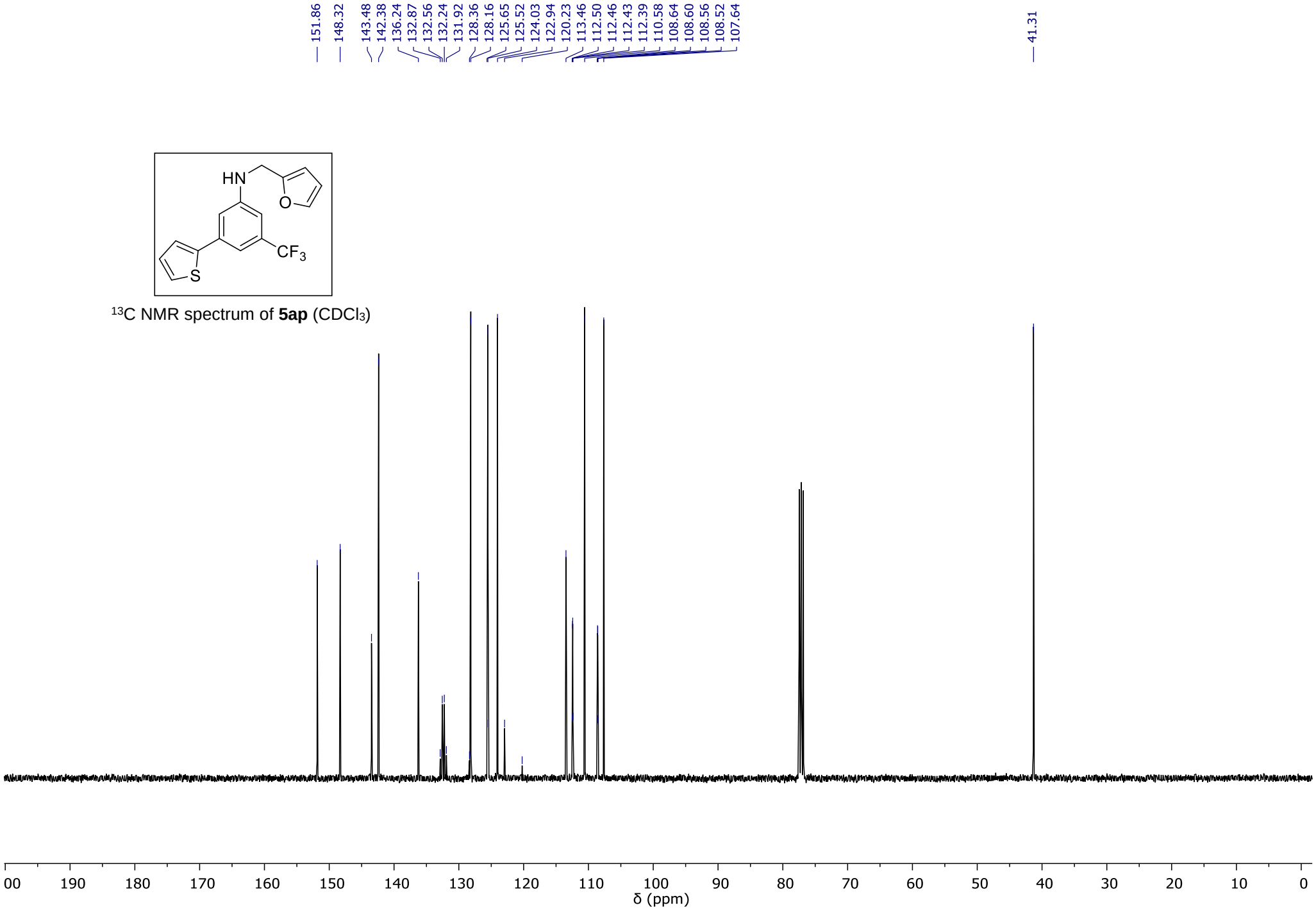
^{1}H NMR spectrum of **5ag** ($CDCl_3$)



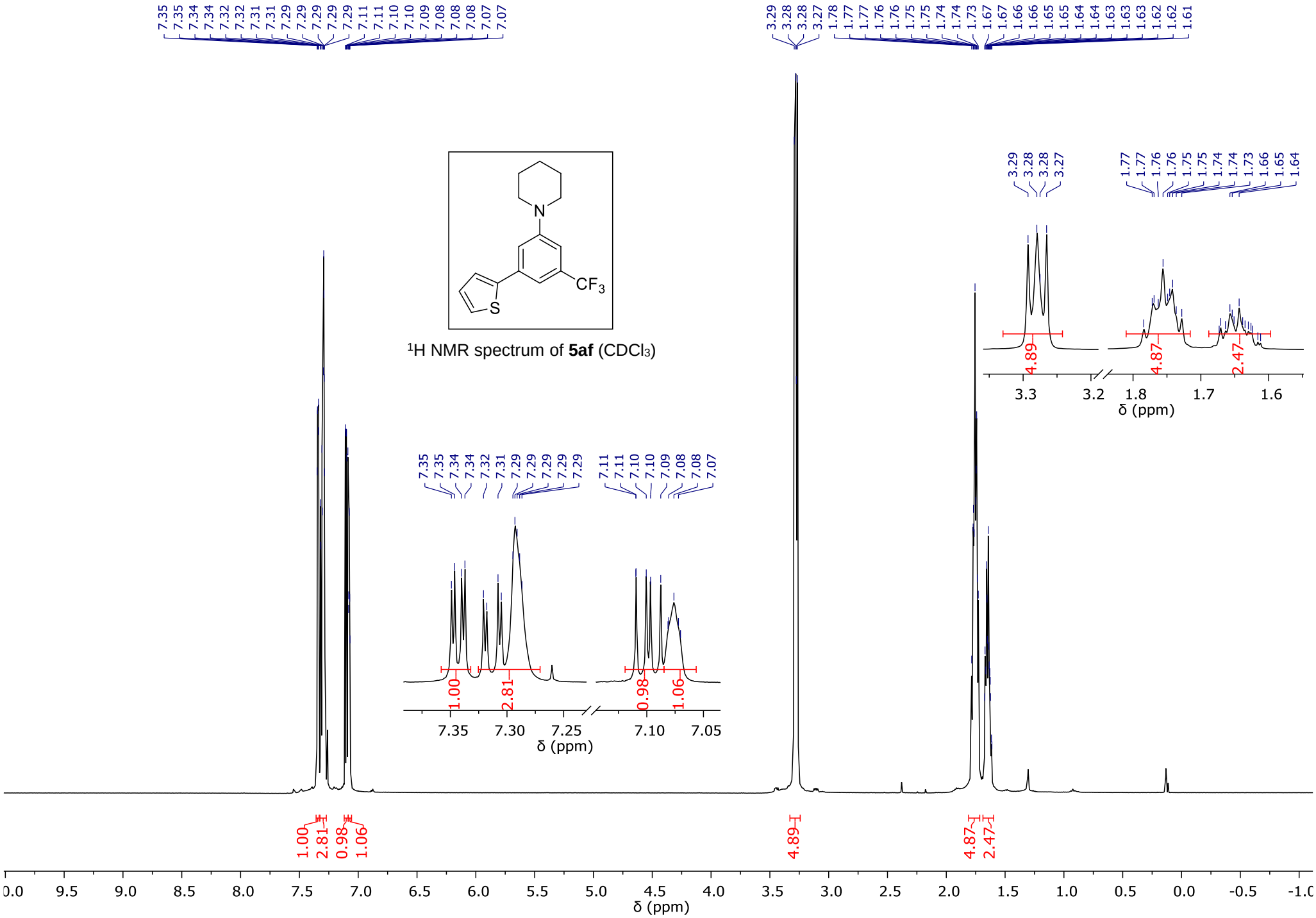
^{13}C NMR spectrum of **5ag** ($CDCl_3$)

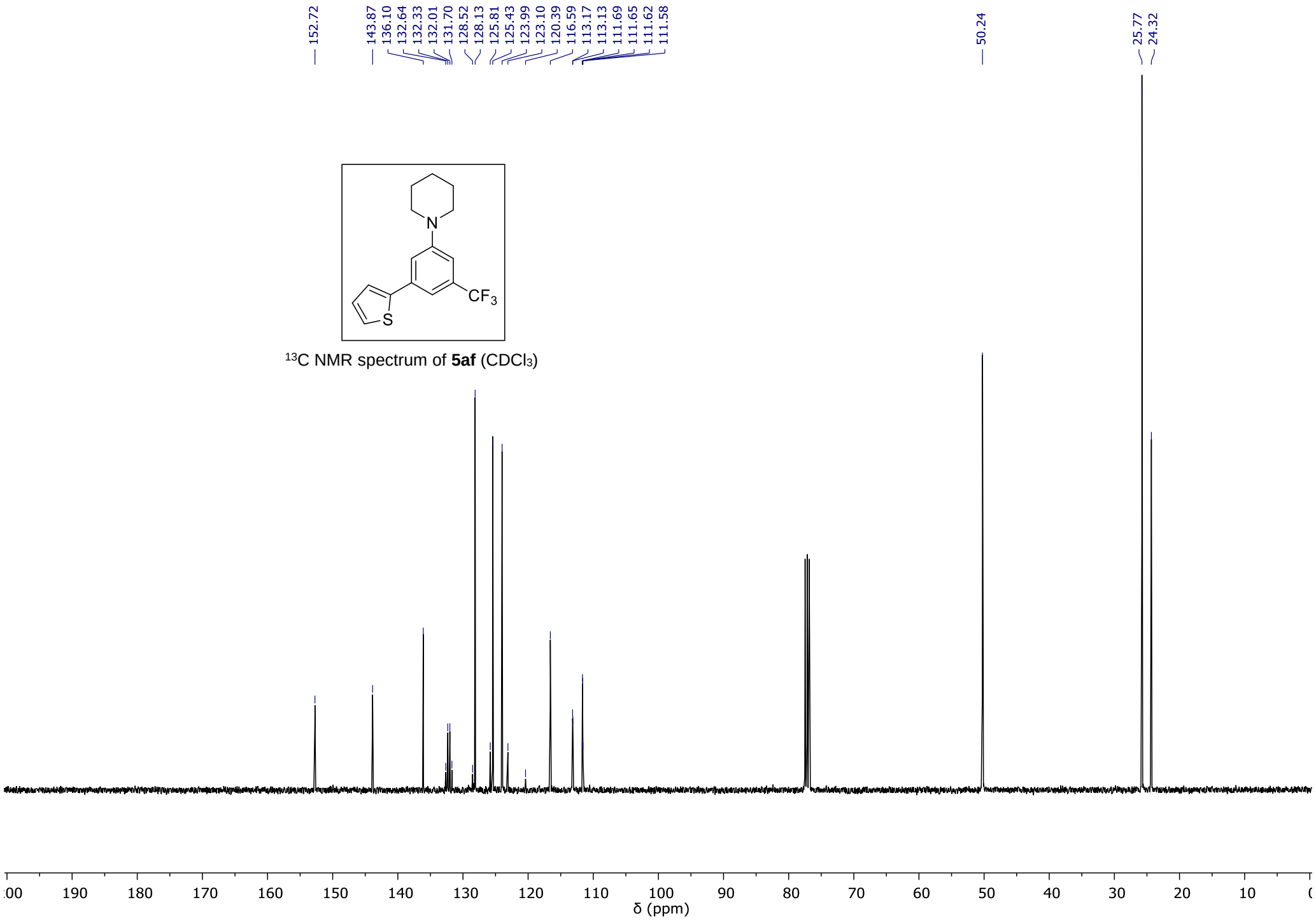


^{1}H NMR spectrum of **5ap** ($CDCl_3$)

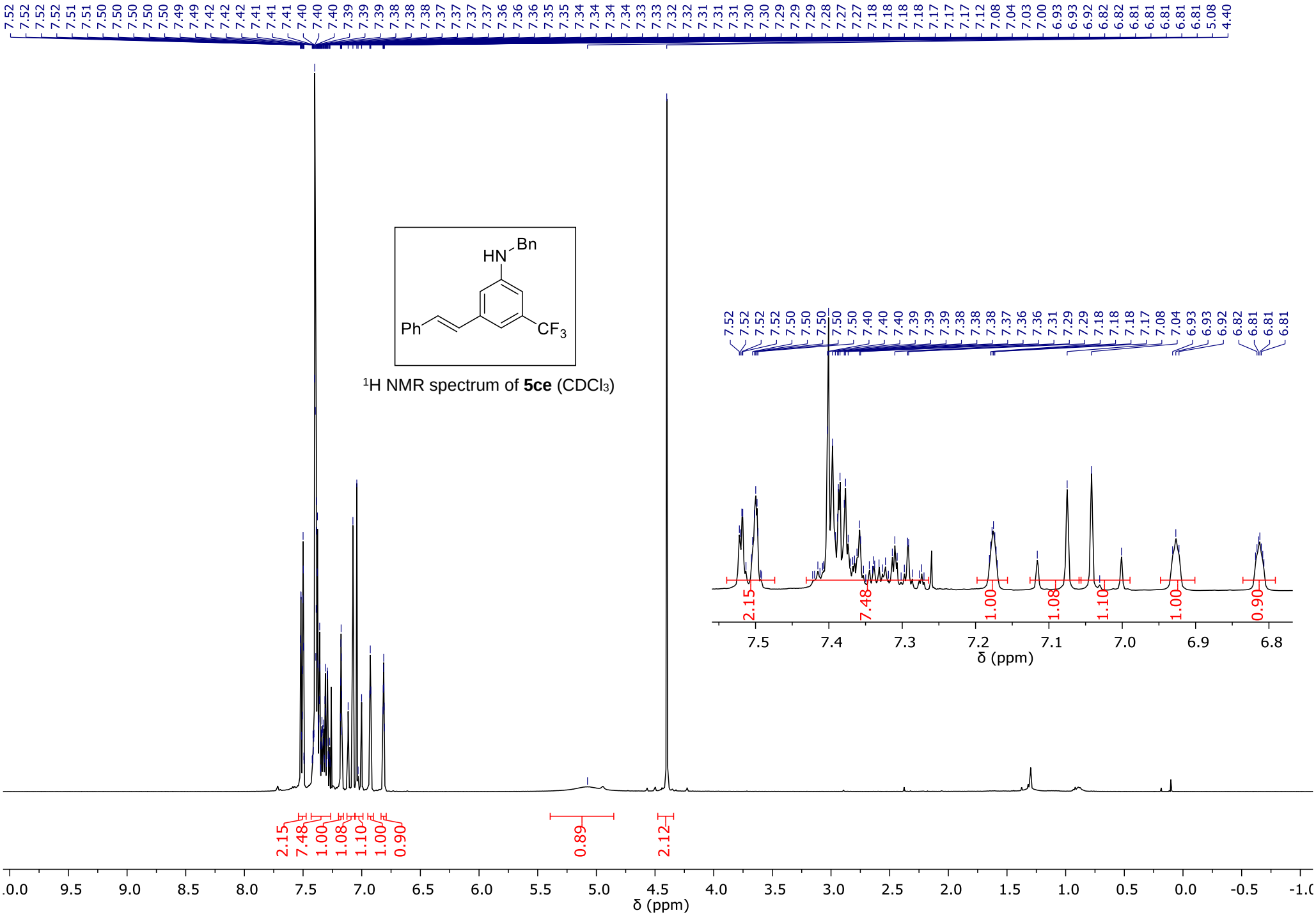


^{13}C NMR spectrum of **5ap** ($CDCl_3$)

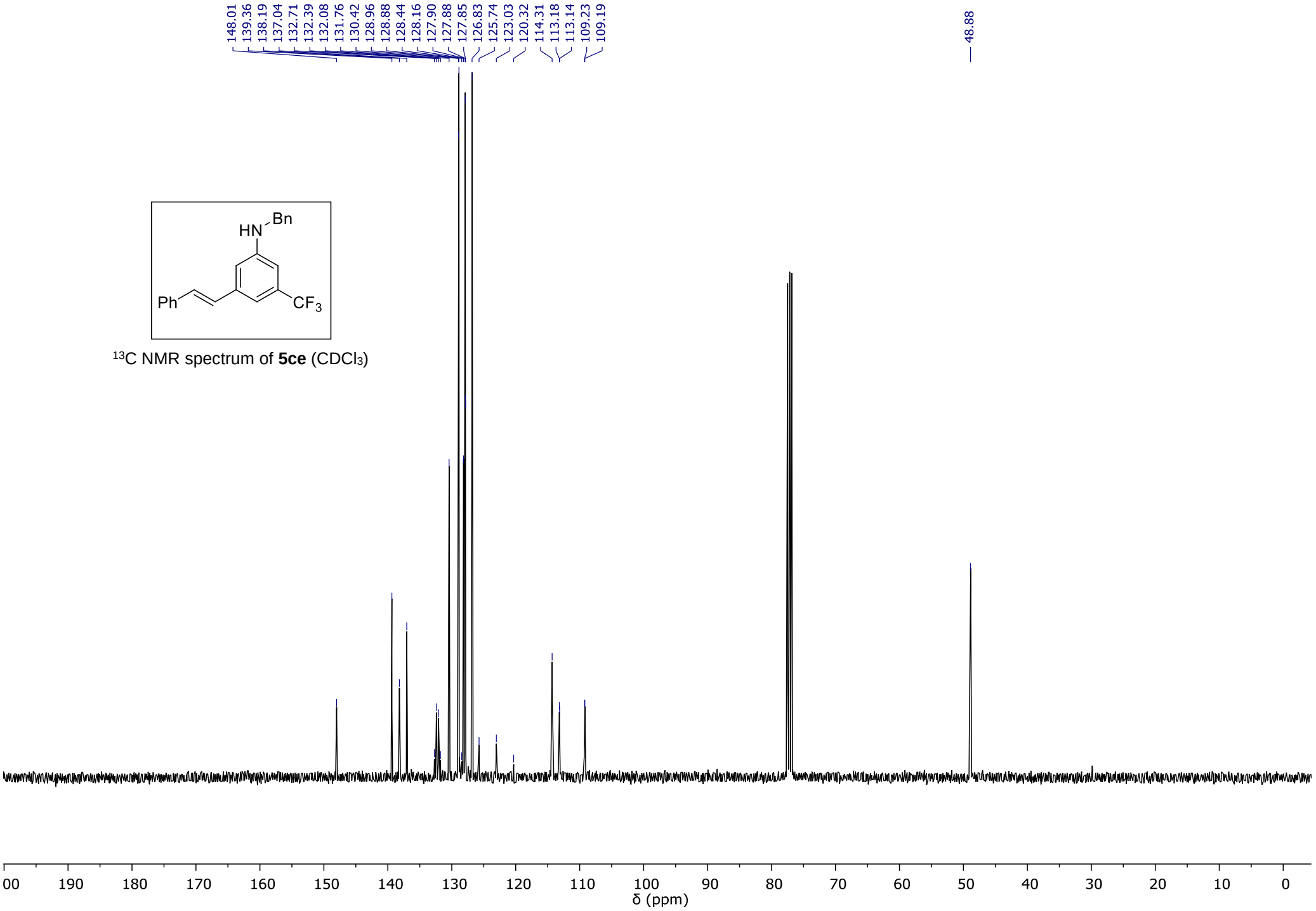

7.35 7.35 7.34 7.34 7.32 7.32 7.31 7.31 7.29 7.29 7.29 7.29 7.11 7.11 7.10 7.10 7.09 7.08 7.08 7.08 7.07 7.07
3.29 3.28 3.28 3.27 1.78 1.77 1.77 1.76 1.76 1.75 1.75 1.74 1.74 1.73 1.67 1.67 1.66 1.66 1.65 1.65 1.64 1.64 1.63 1.63 1.62 1.62 1.61
N
CF3
S
1H NMR spectrum of 5af (CDCl3)
1.00 2.81 0.98 1.06
4.89
4.87 2.47
δ (ppm)



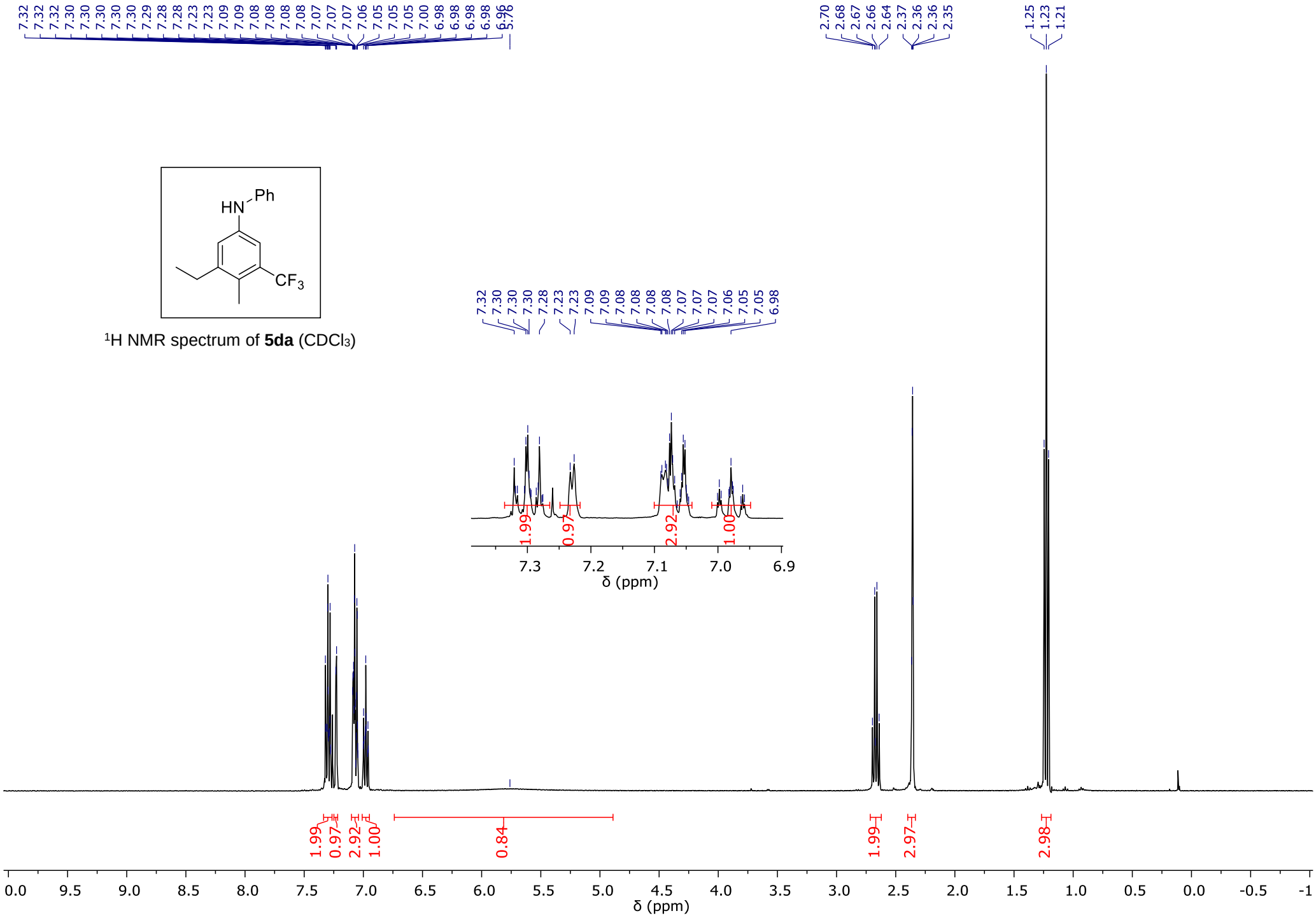
^{13}C NMR spectrum of **5af** ($CDCl_3$)



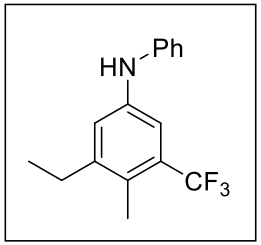
^{1}H NMR spectrum of **5ce** ($CDCl_3$)



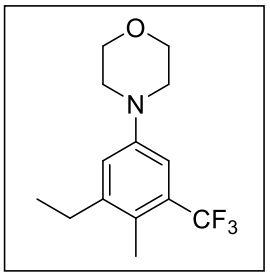
^{13}C NMR spectrum of **5ce** ($CDCl_3$)



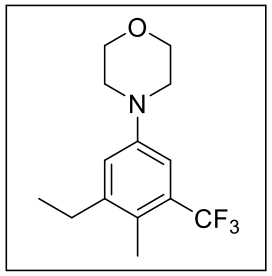
^{1}H NMR spectrum of **5da** ($CDCl_3$)



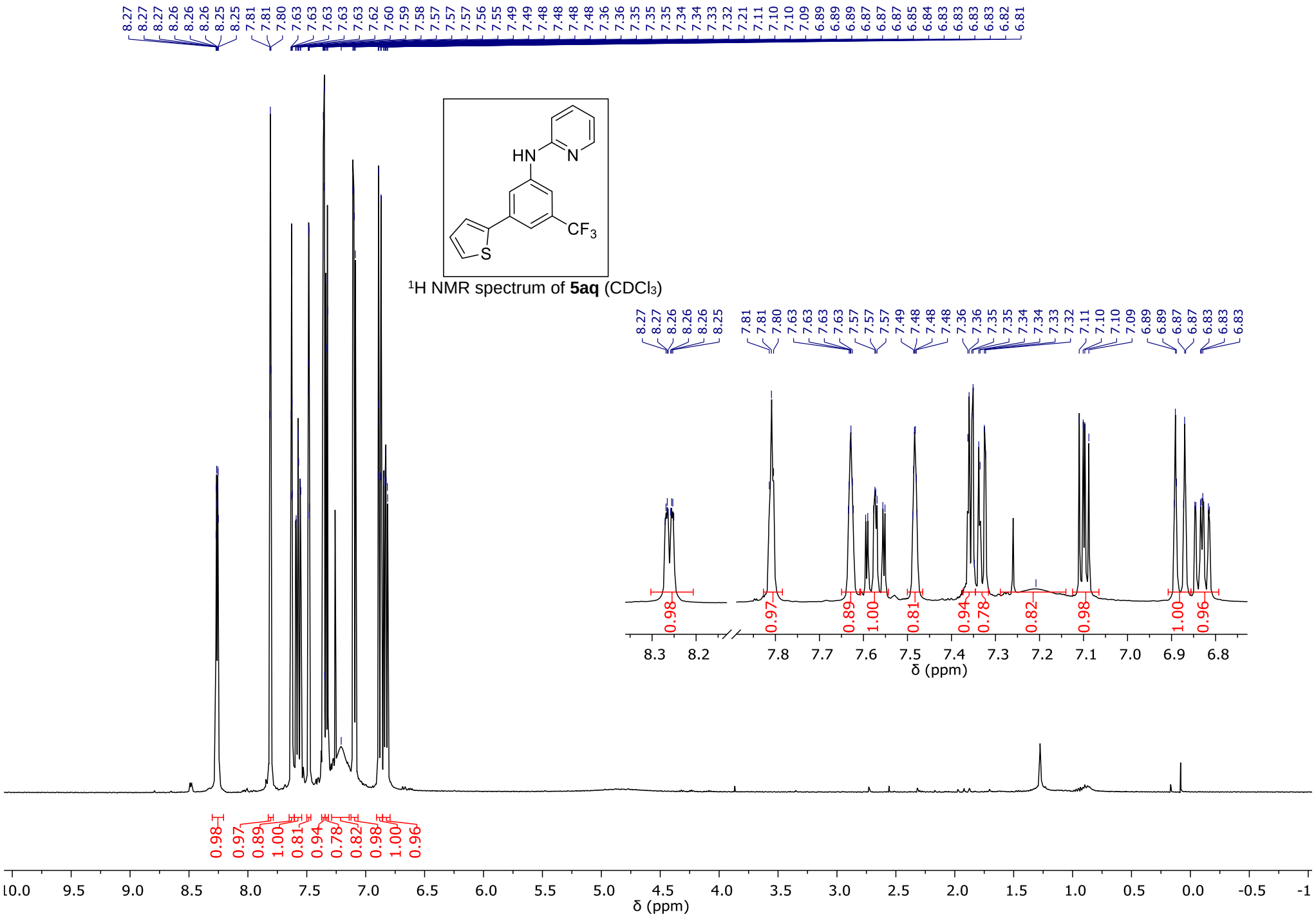
^{13}C NMR spectrum of **5da** ($CDCl_3$)



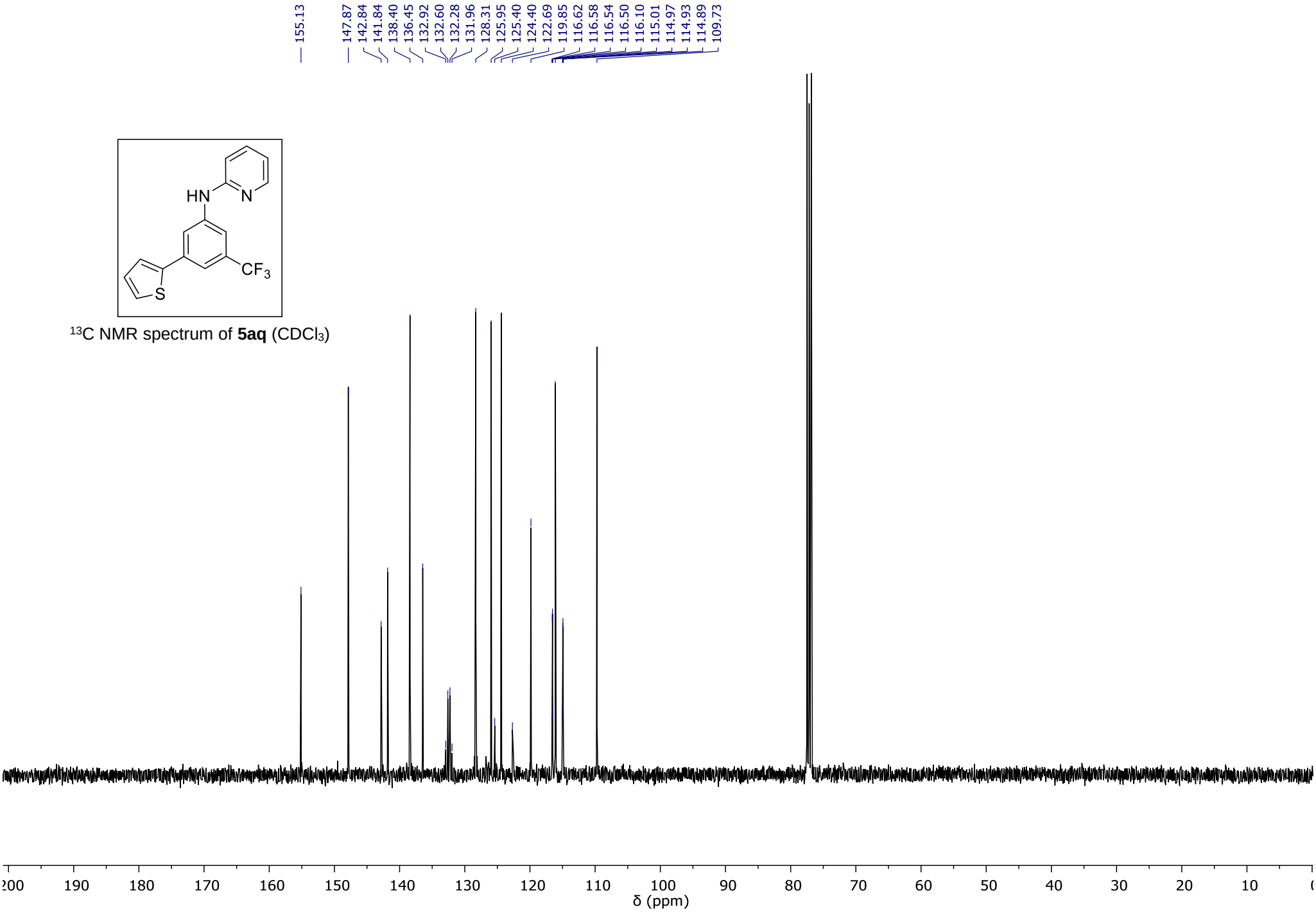
^{1}H NMR spectrum of **5dk** ($CDCl_3$)



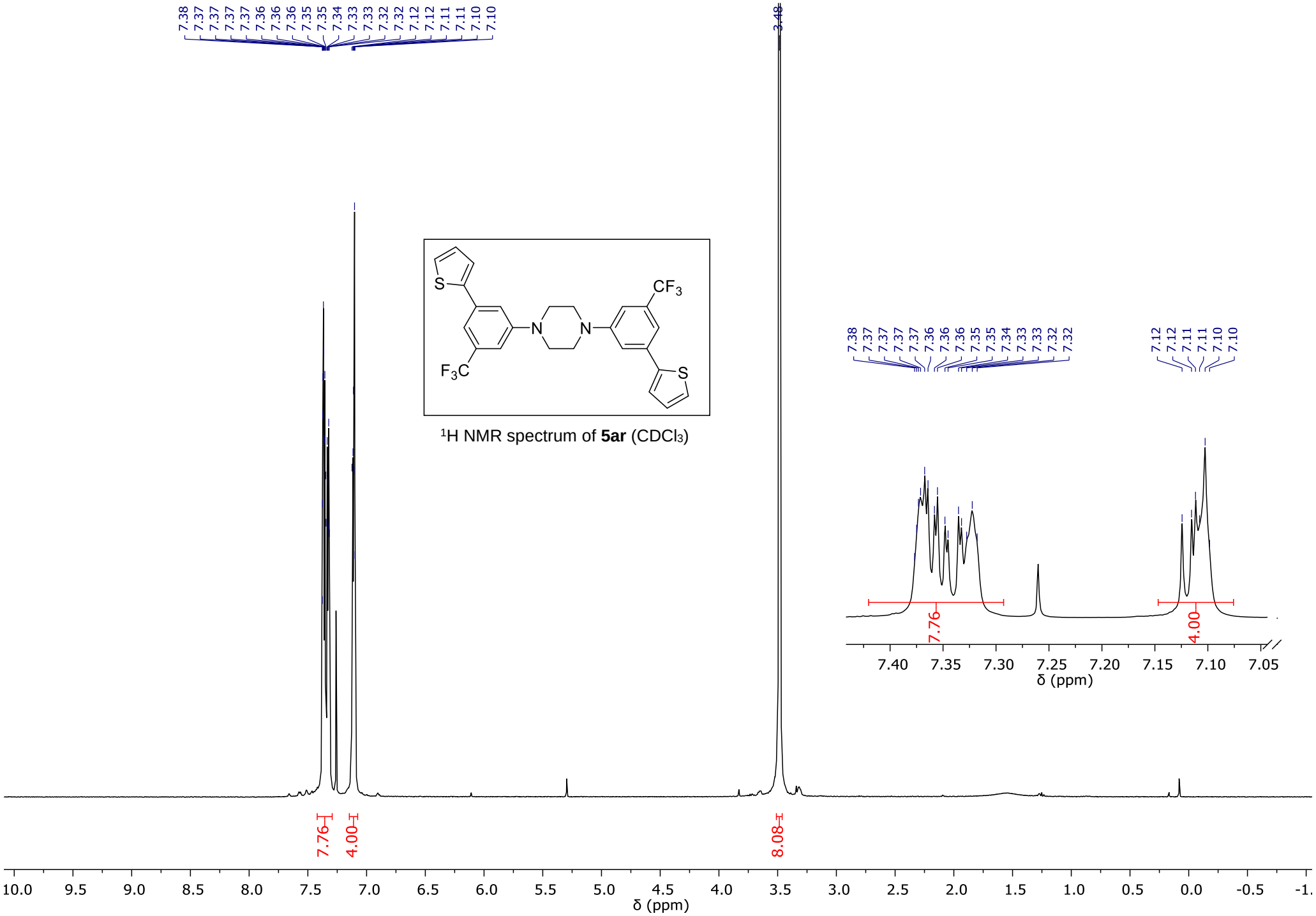
^{13}C NMR spectrum of **5dk** ($CDCl_3$)



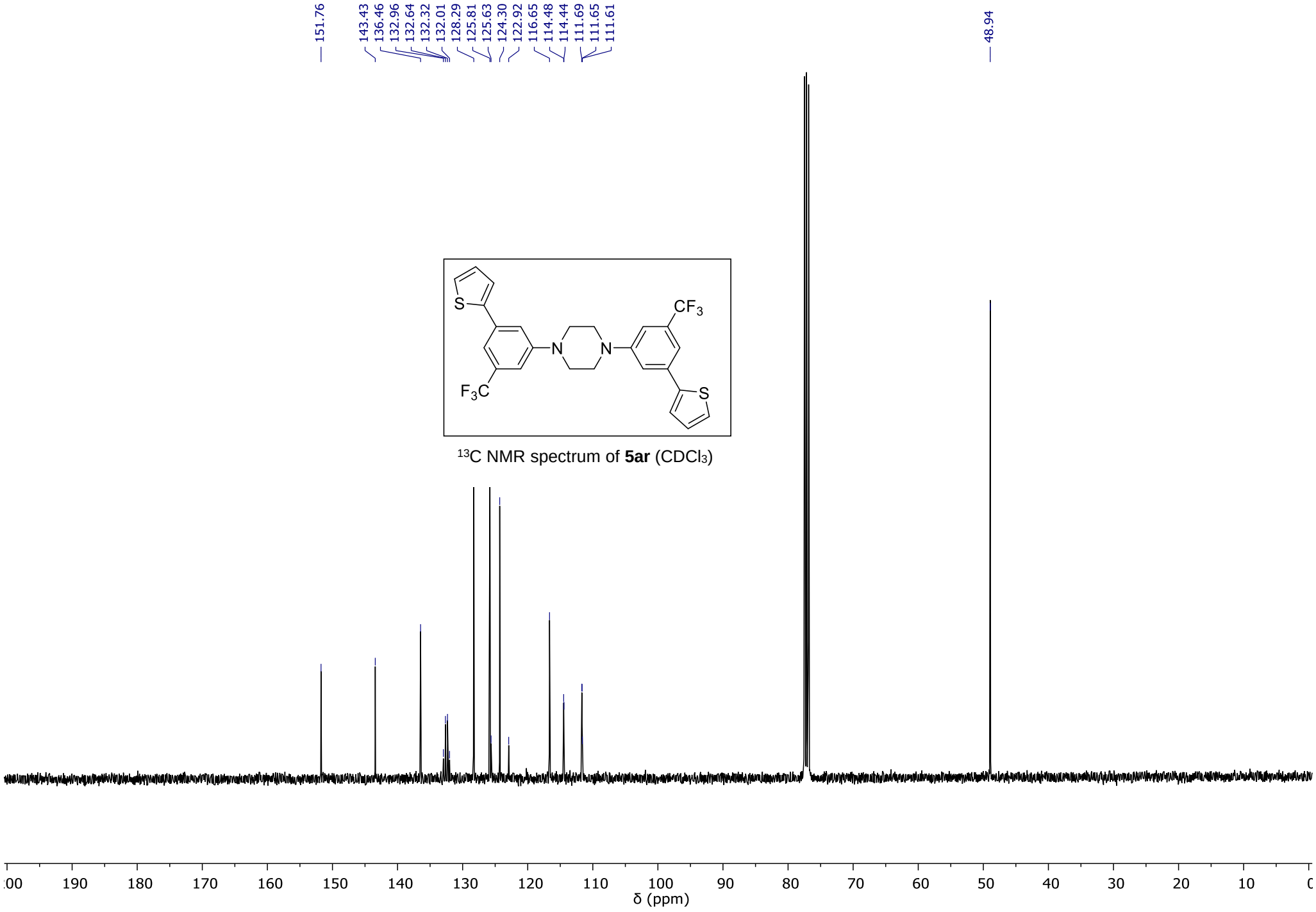
^{1}H NMR spectrum of **5aq** ($CDCl_3$)



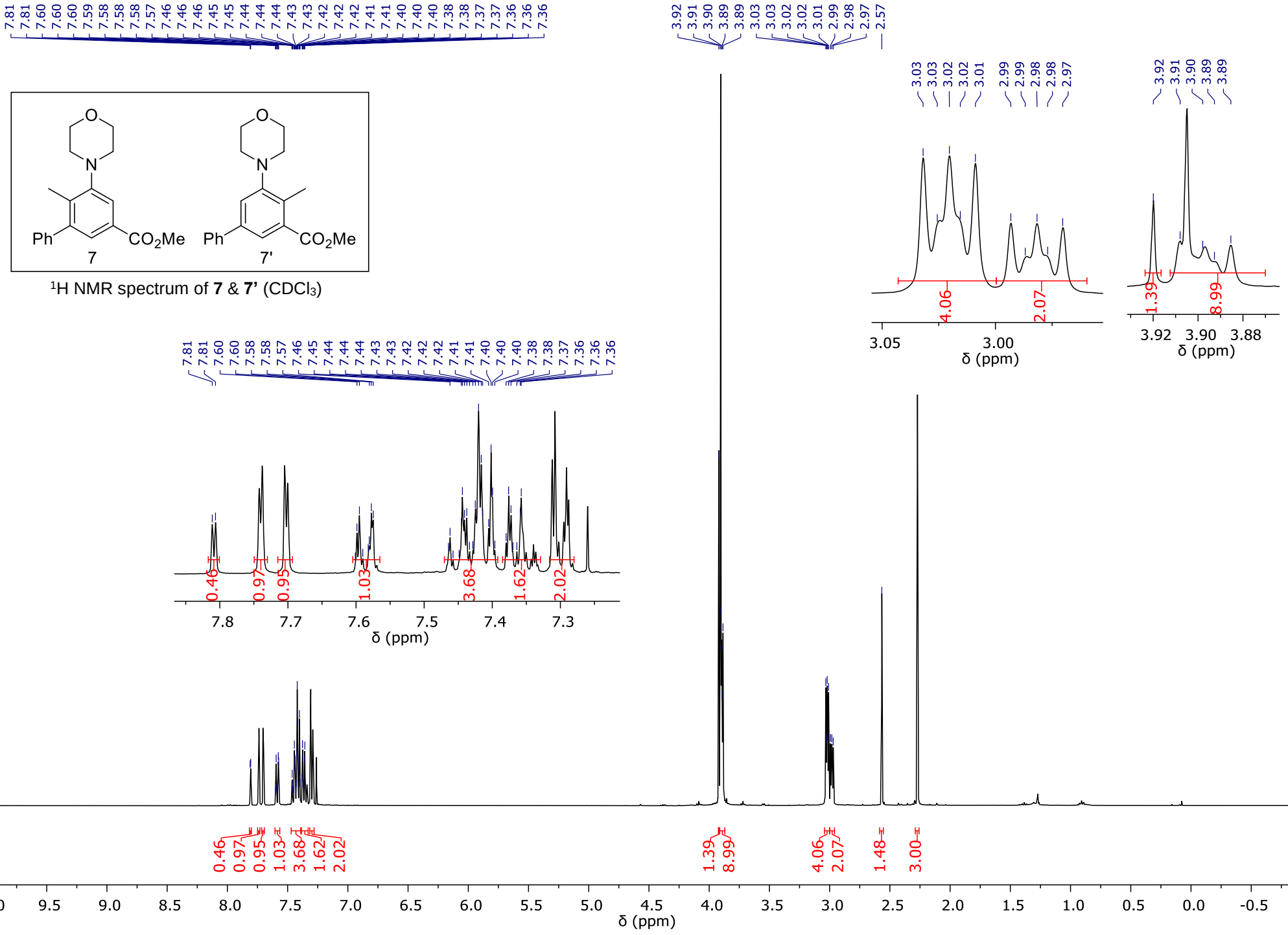
^{13}C NMR spectrum of **5aq** ($CDCl_3$)



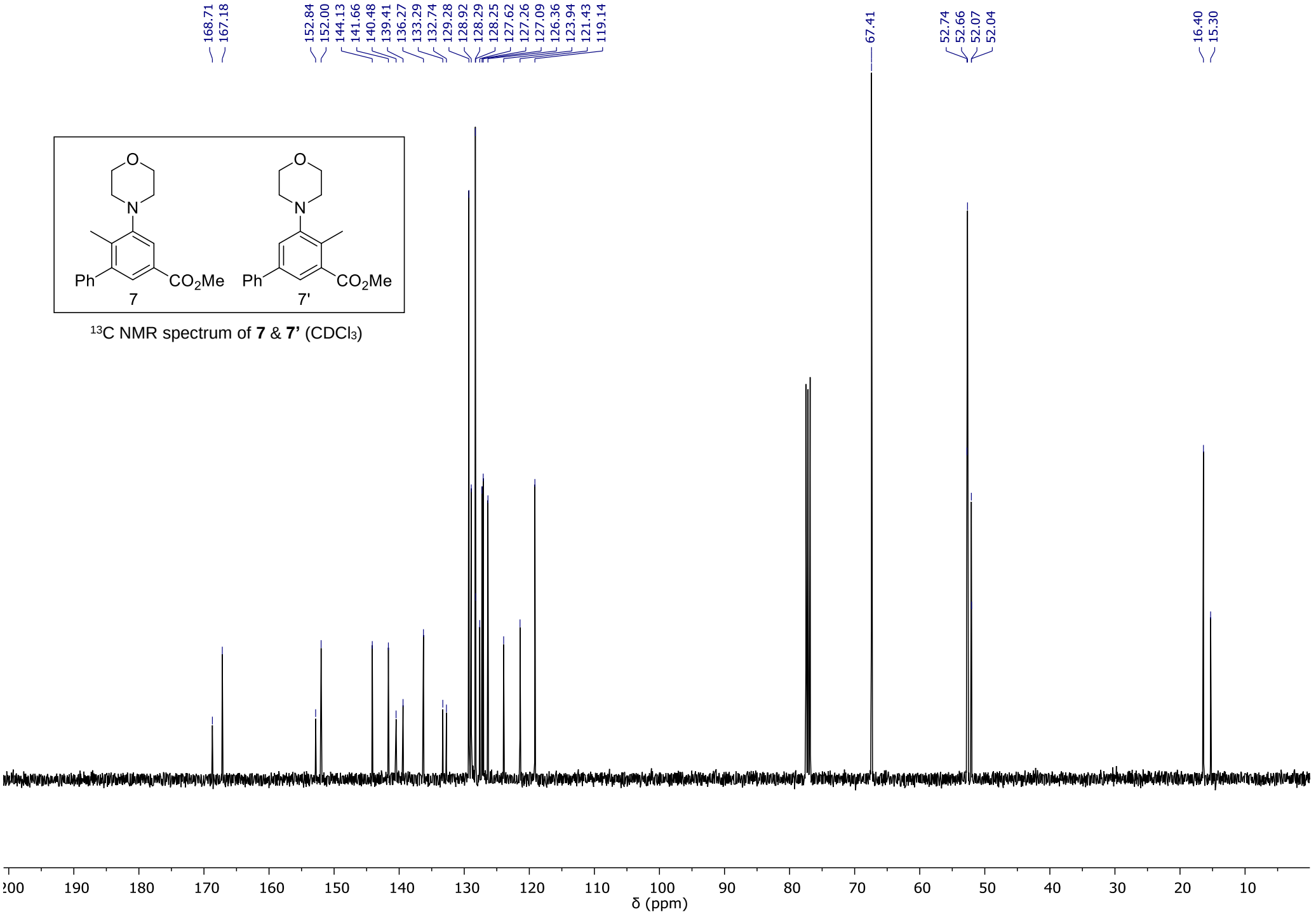
^{1}H NMR spectrum of **5ar** ($CDCl_3$)



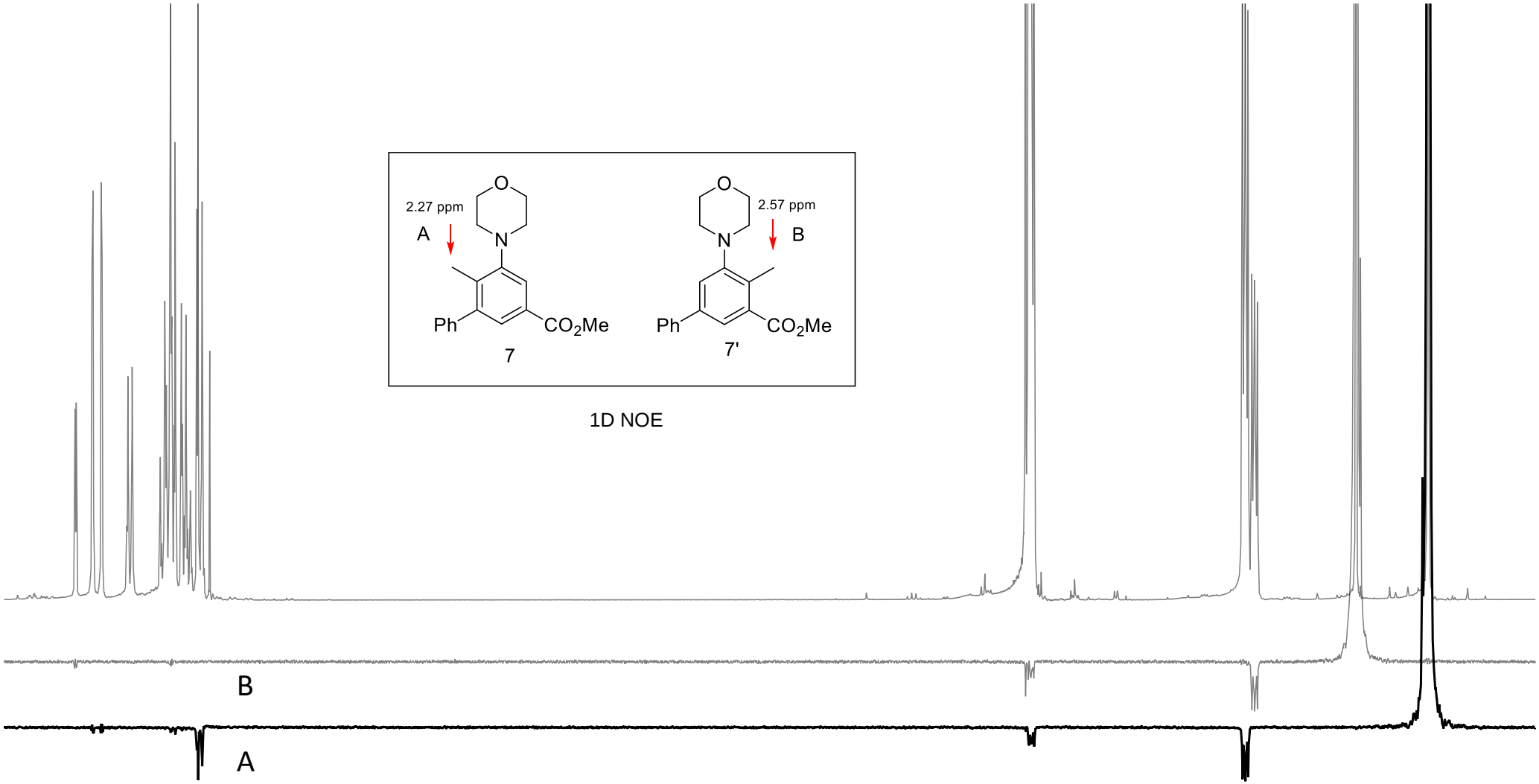
^{13}C NMR spectrum of **5ar** ($CDCl_3$)

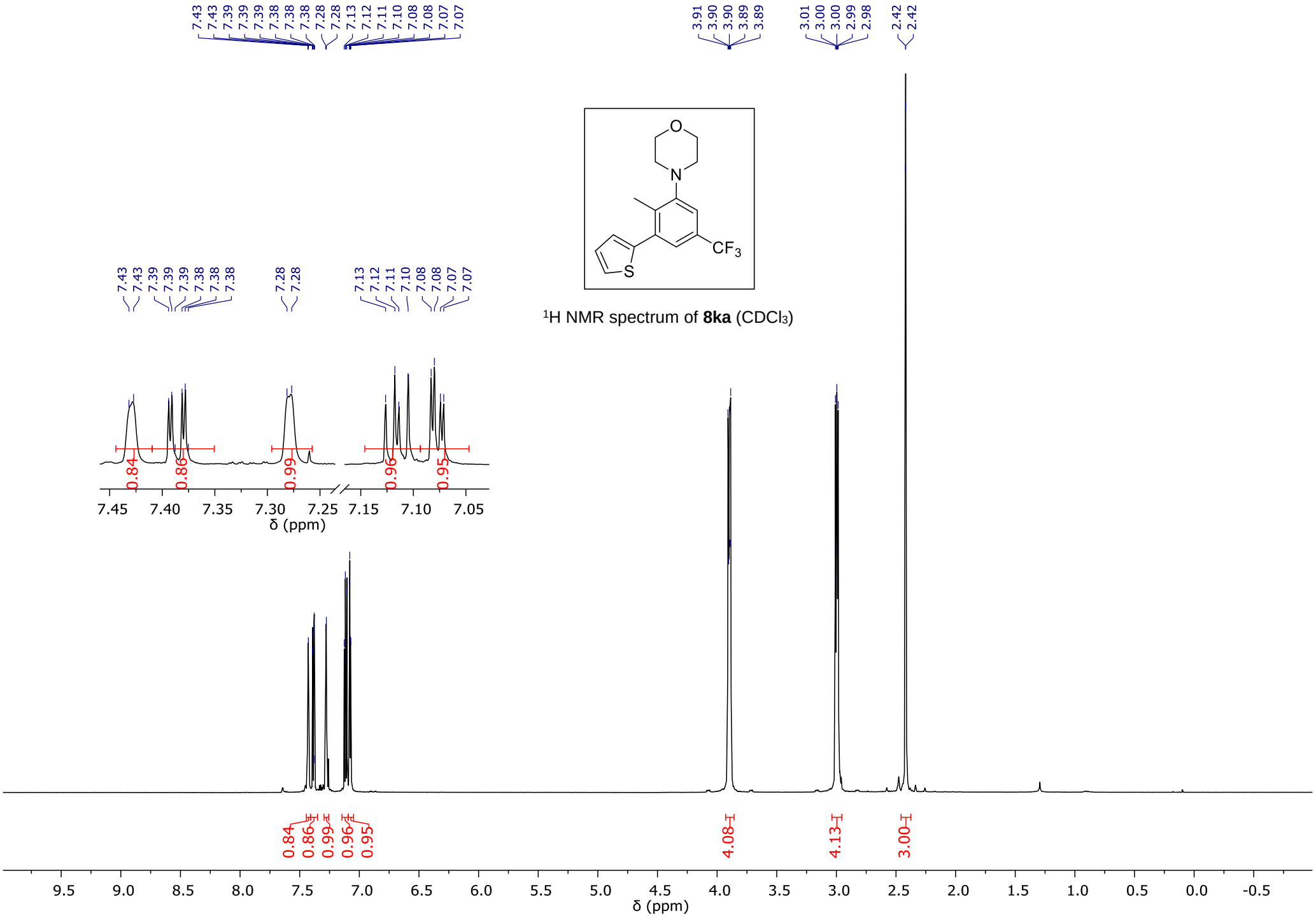


^{1}H NMR spectrum of **7** & **7'** ($CDCl_3$)

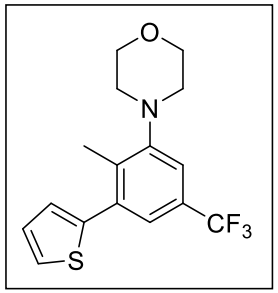


^{13}C NMR spectrum of **7** & **7'** ($CDCl_3$)

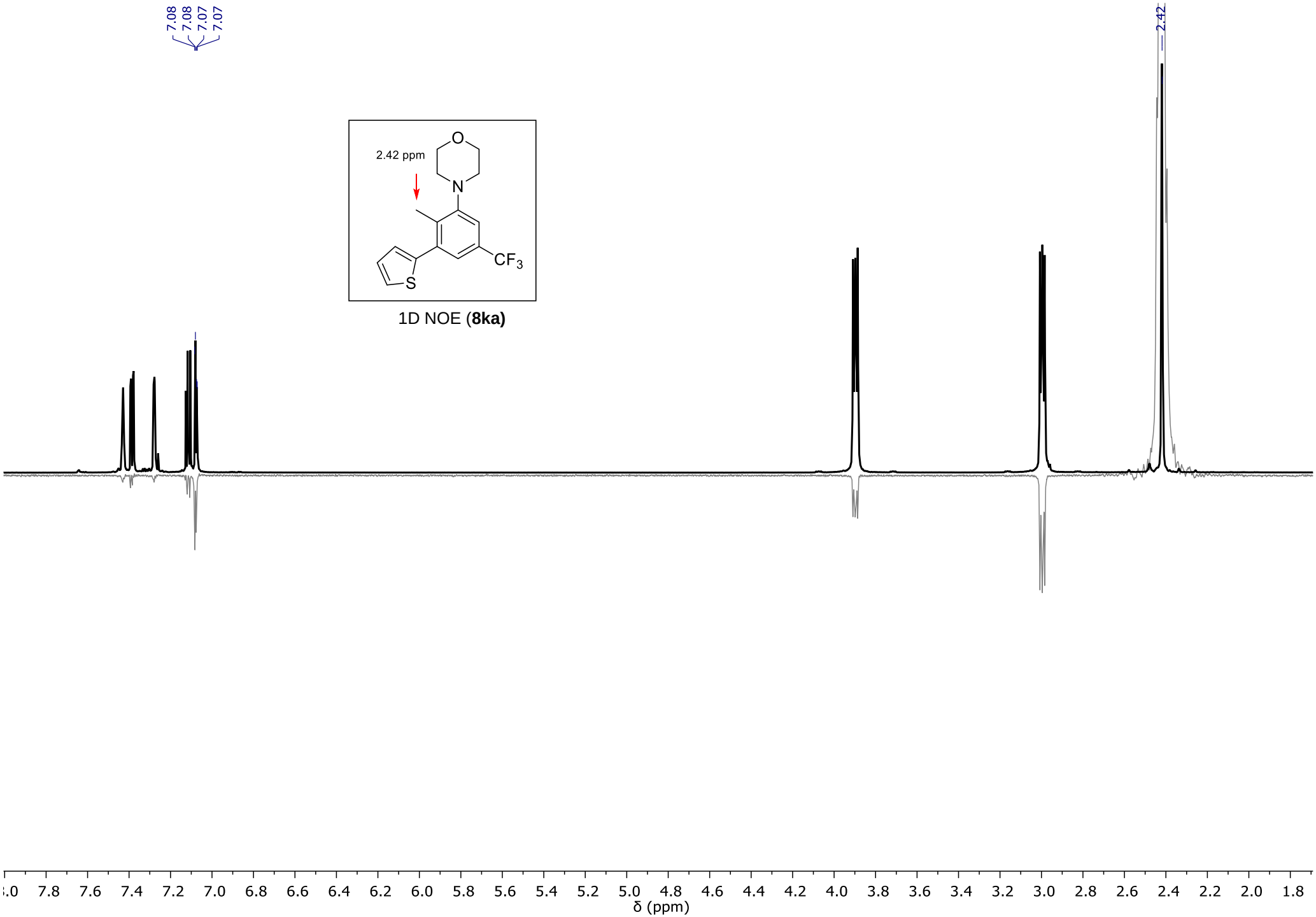

2.27 ppm
A
O
N
Ph
CO2Me
7
2.57 ppm
B
O
N
Ph
CO2Me
7'
1D NOE
B
A
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
δ (ppm)



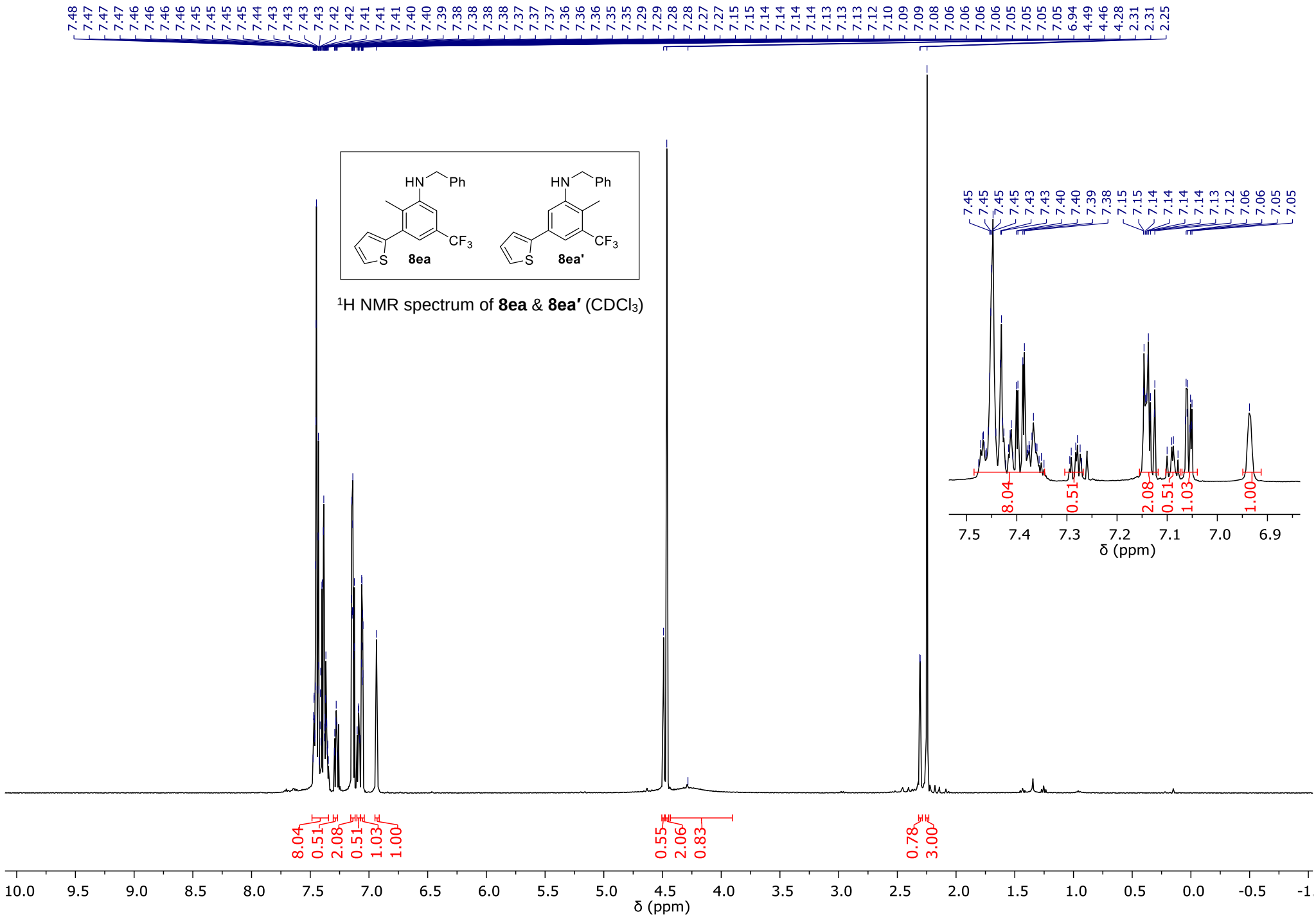
^{1}H NMR spectrum of **8ka** ($CDCl_3$)



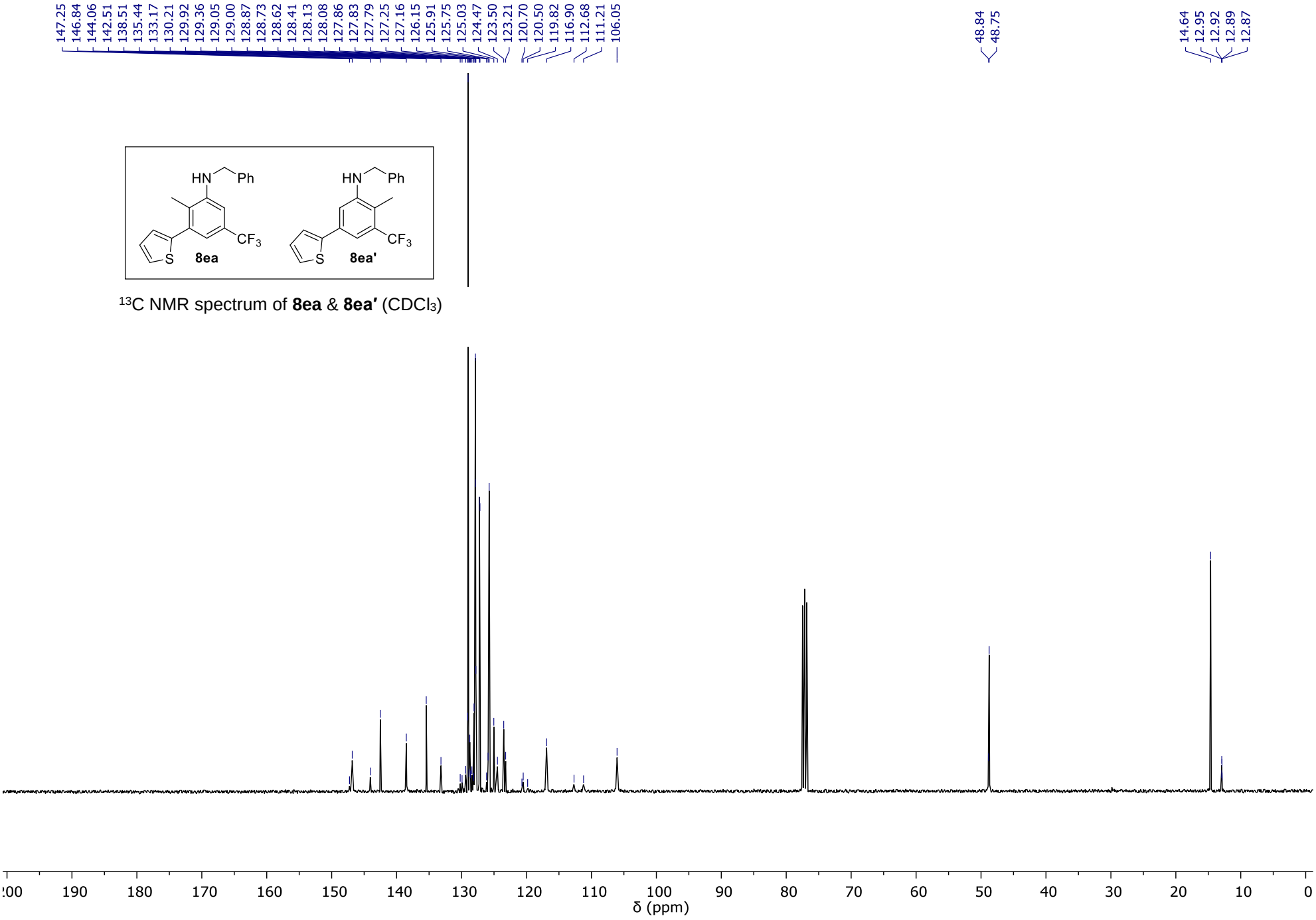
^{13}C NMR spectrum of **8ka** ($CDCl_3$)


7.08
7.08
7.07
7.07
2.42
2.42 ppm
O
N
S
CF3
7.8
7.6
7.4
7.2
7.0
6.8
6.6
6.4
6.2
6.0
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
δ (ppm)

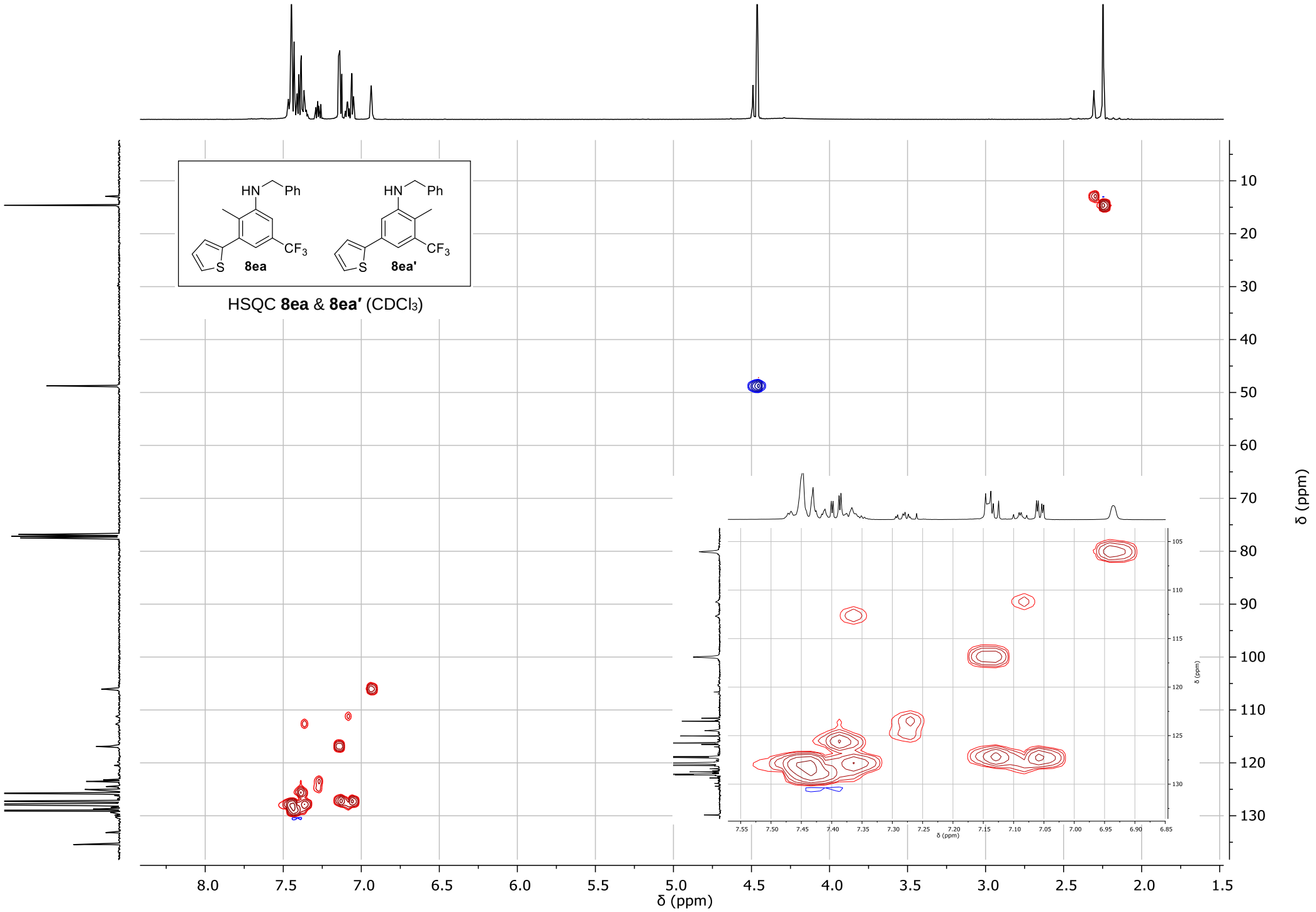
1D NOE (**8ka)**

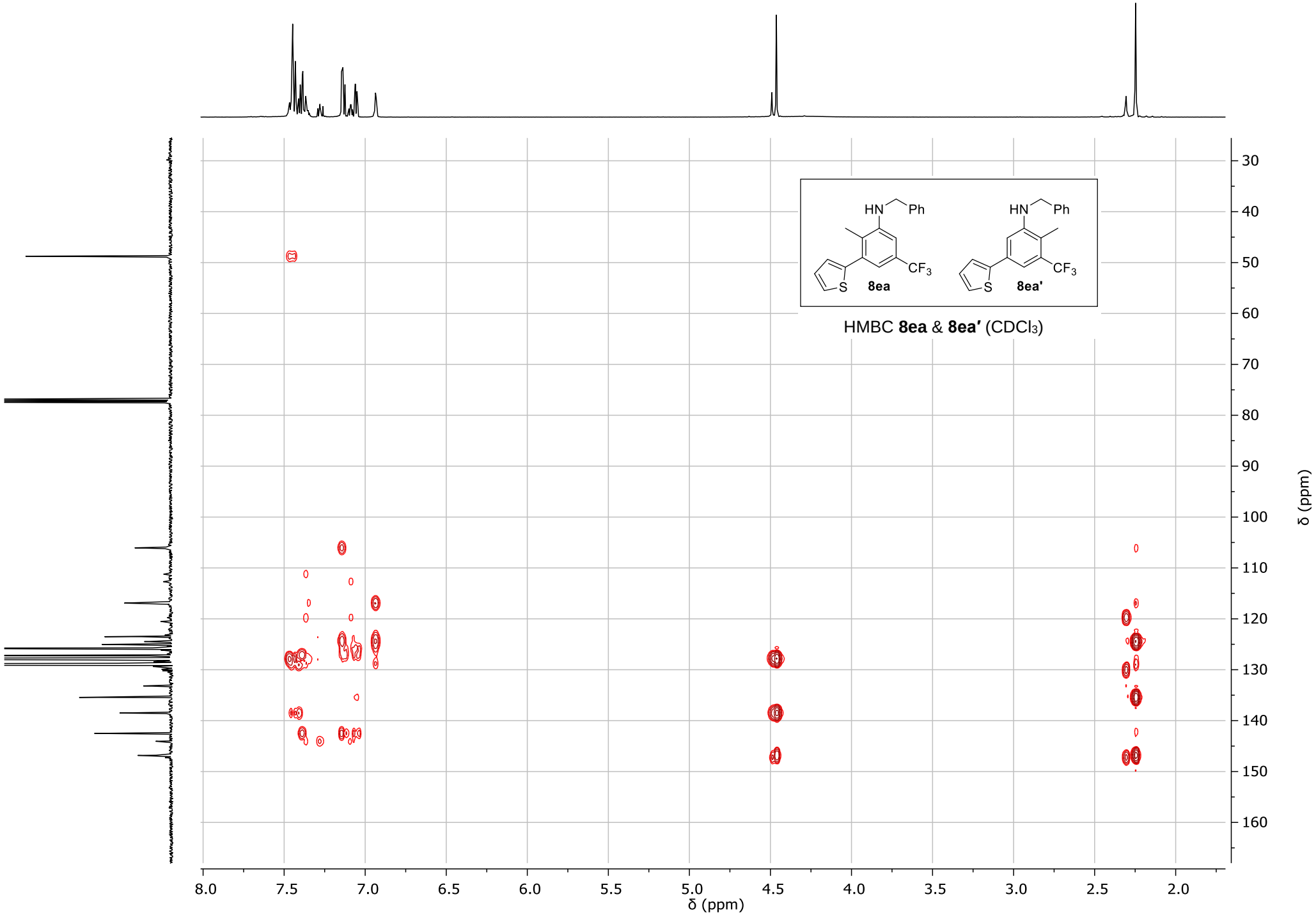


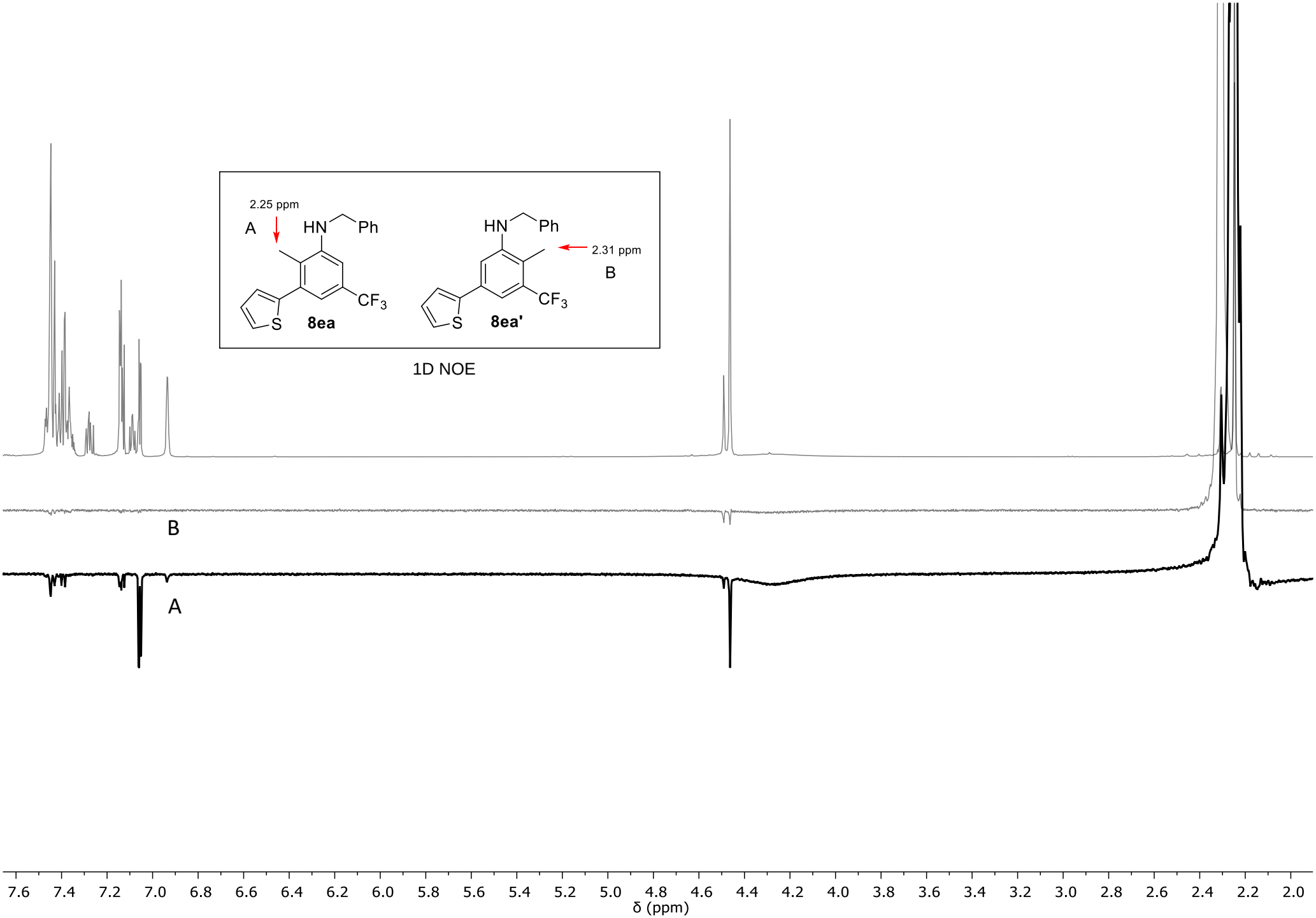
^{1}H NMR spectrum of **8ea** & **8ea'** ($CDCl_3$)

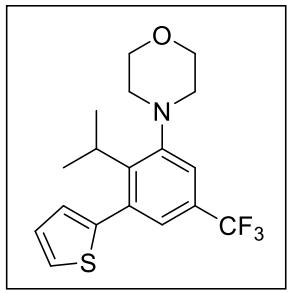


^{13}C NMR spectrum of **8ea** & **8ea′** ($CDCl_3$)

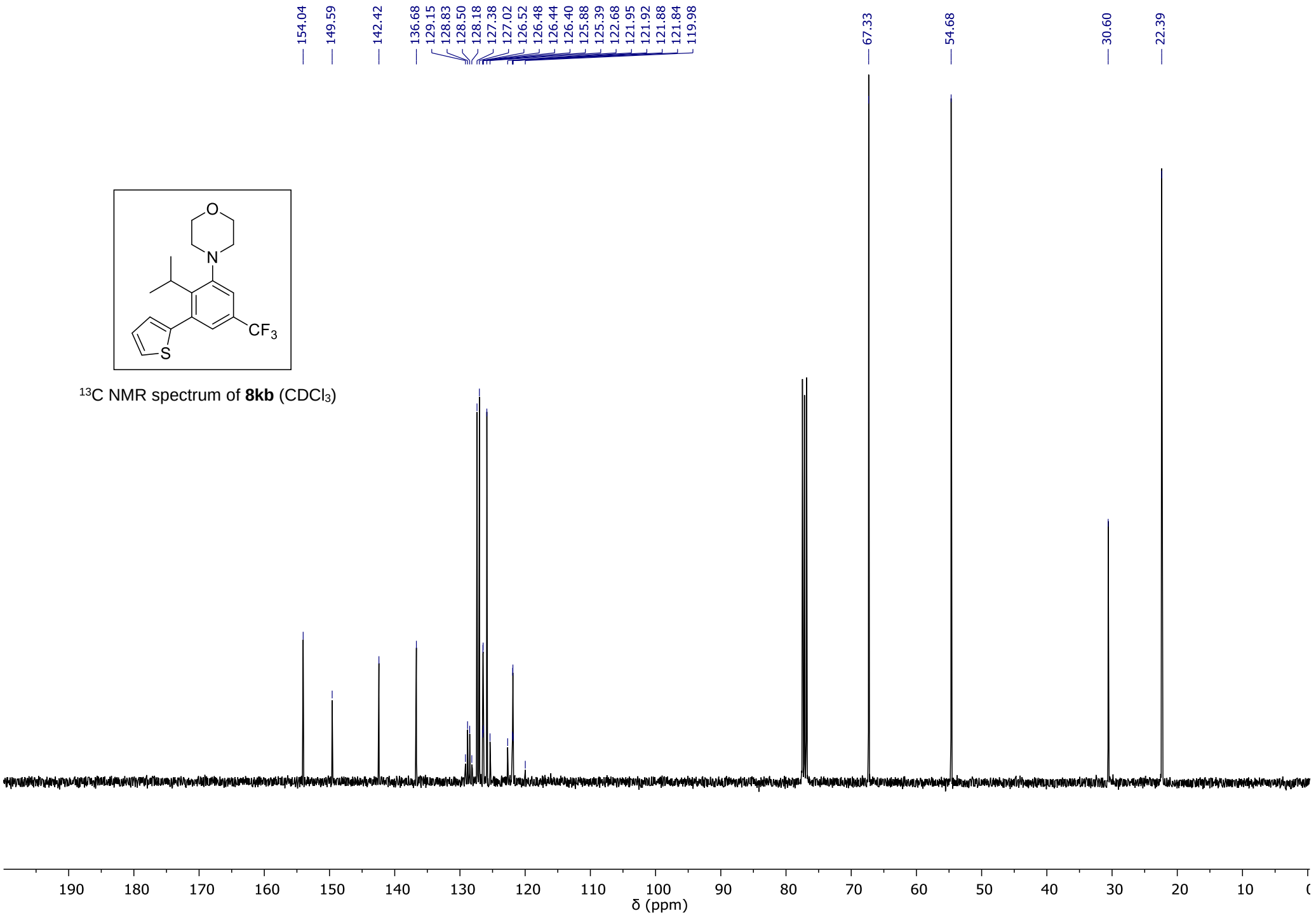

HN
Ph
CF3
S
8ea
8ea'
HSQC 8ea & 8ea' (CDCl3)
δ (ppm)


HN
Ph
CF3
S
8ea
HN
Ph
CF3
S
8ea'
HMBC 8ea & 8ea' (CDCl3)
δ (ppm)
δ (ppm)

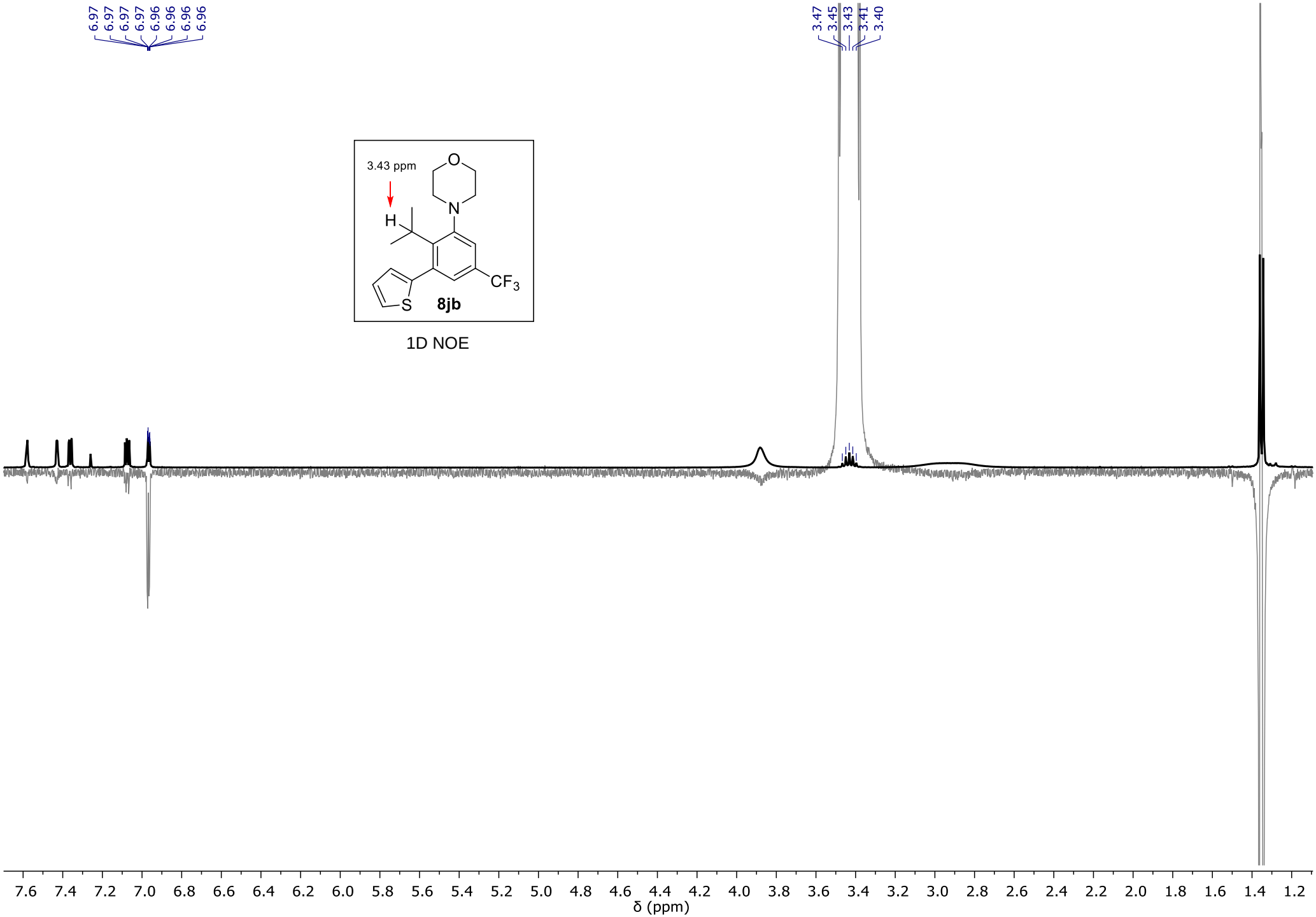

2.25 ppm
A
HN
Ph
CF3
S
8ea
HN
Ph
2.31 ppm
B
CF3
S
8ea'
1D NOE
B
A
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
δ (ppm)

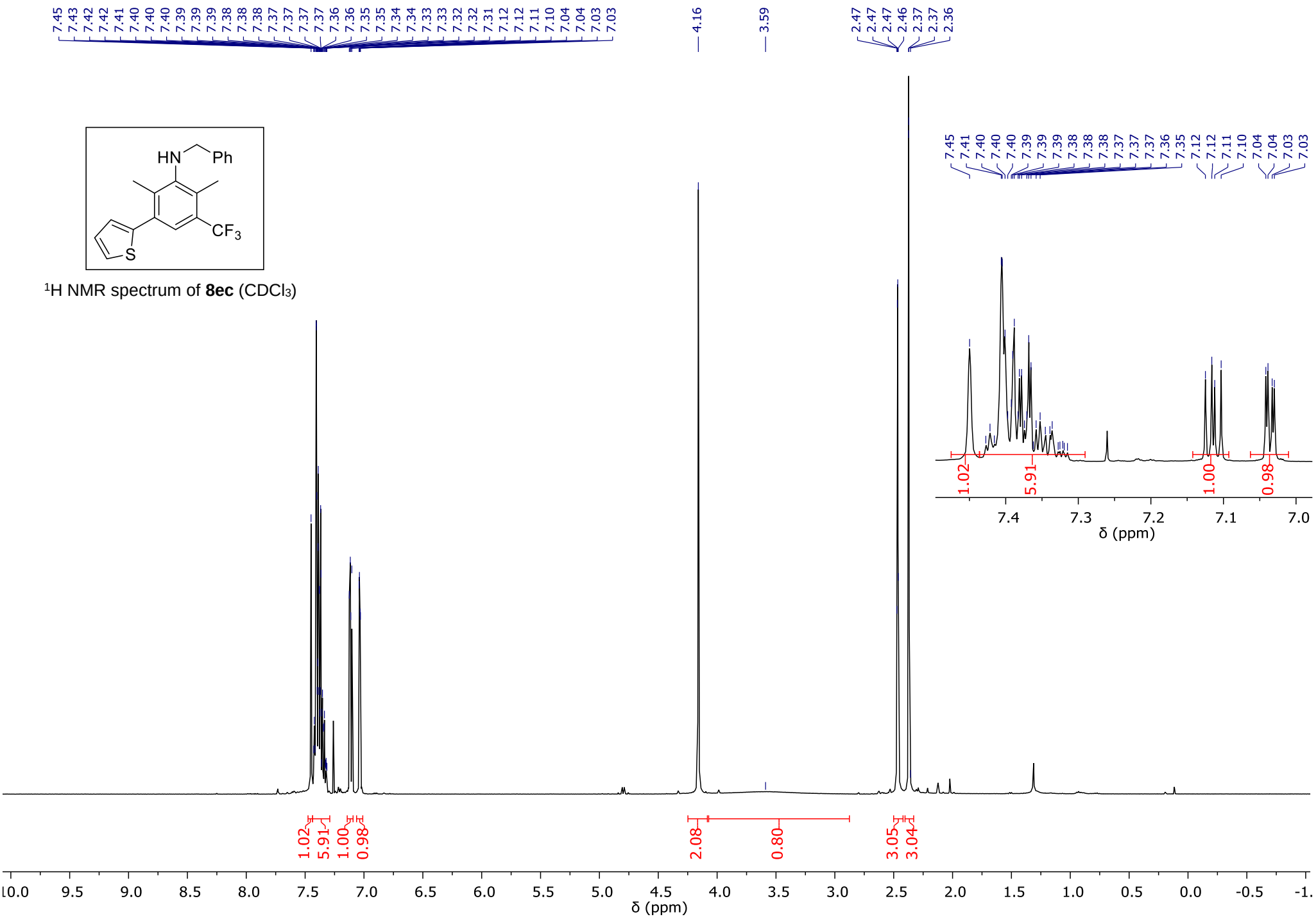


^{1}H NMR spectrum of **8kb** ($CDCl_3$)

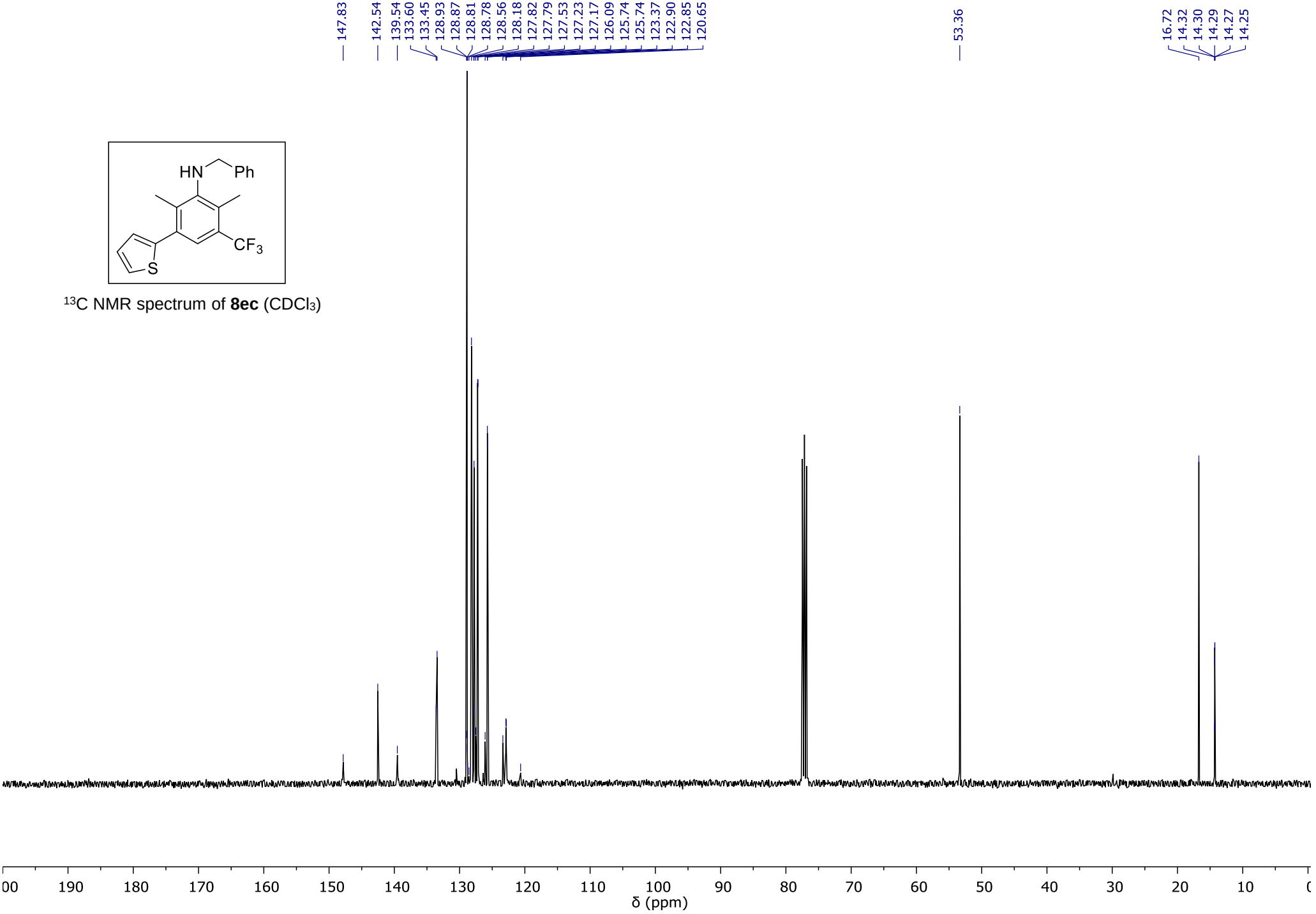


^{13}C NMR spectrum of **8kb** ($CDCl_3$)

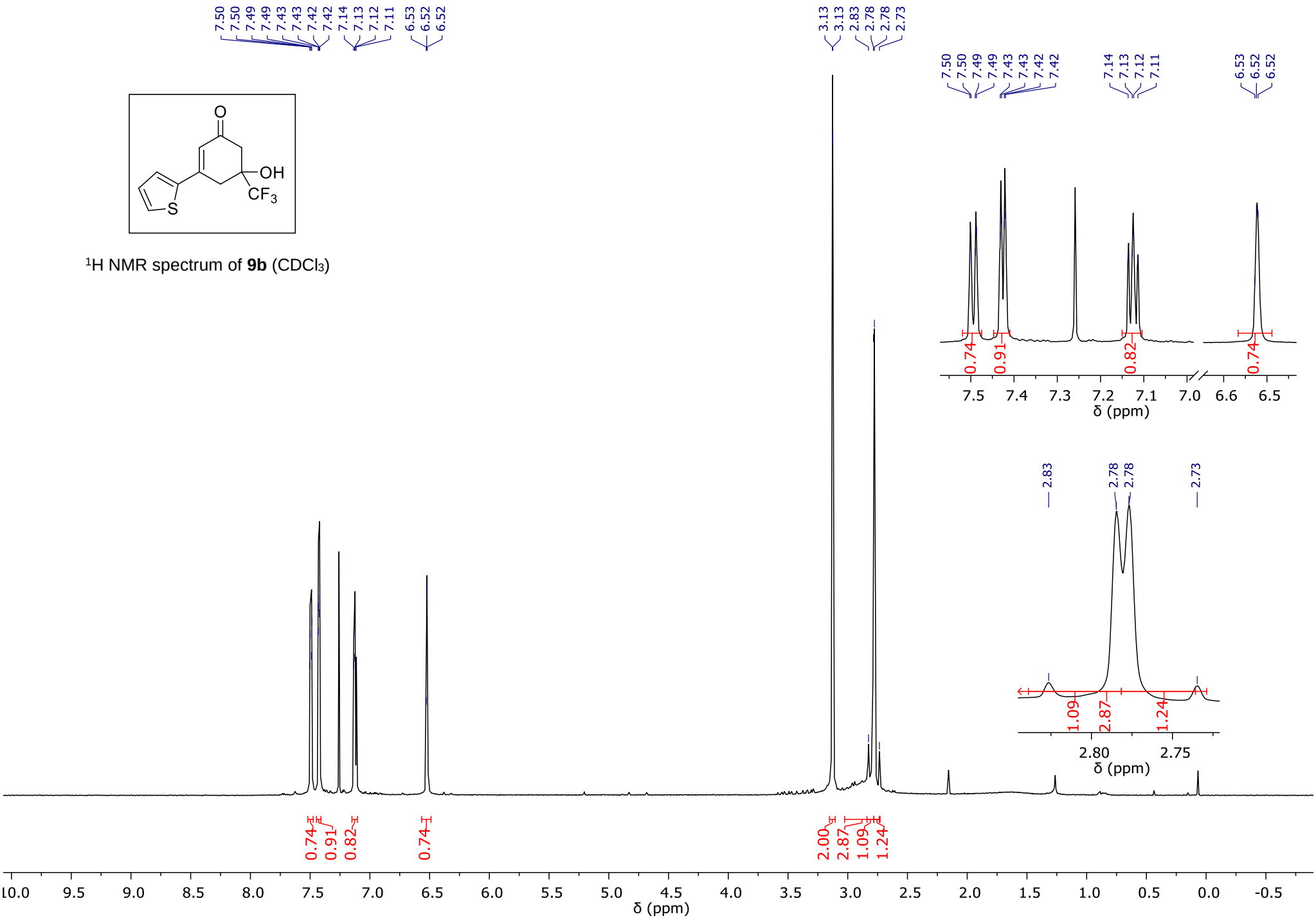

6.97
6.97
6.97
6.97
6.96
6.96
6.96
6.96
3.47
3.45
3.43
3.41
3.40
3.43 ppm
O
N
H
CF3
S
8jb
1D NOE
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2
δ (ppm)



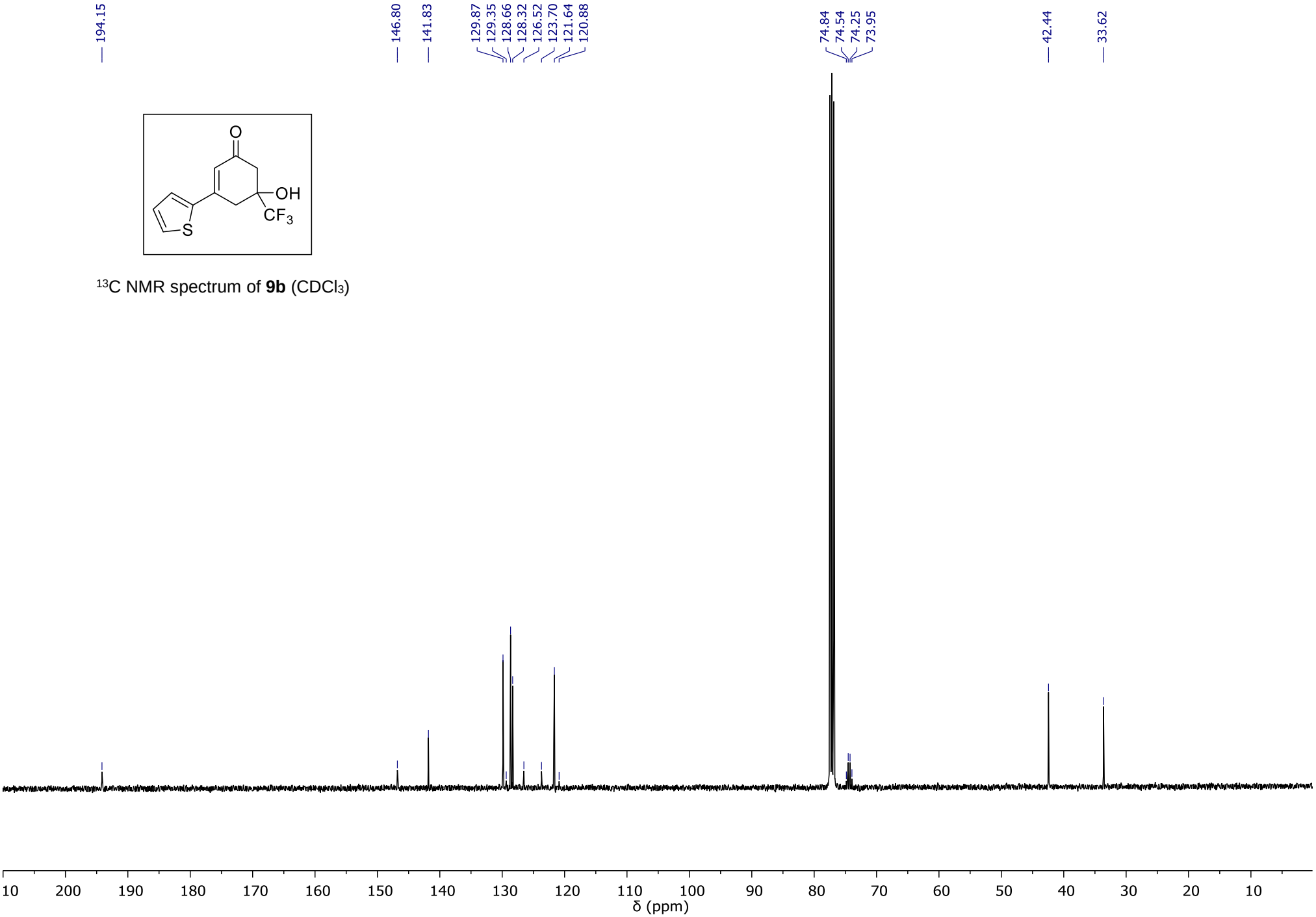
^{1}H NMR spectrum of **8ec** ($CDCl_3$)



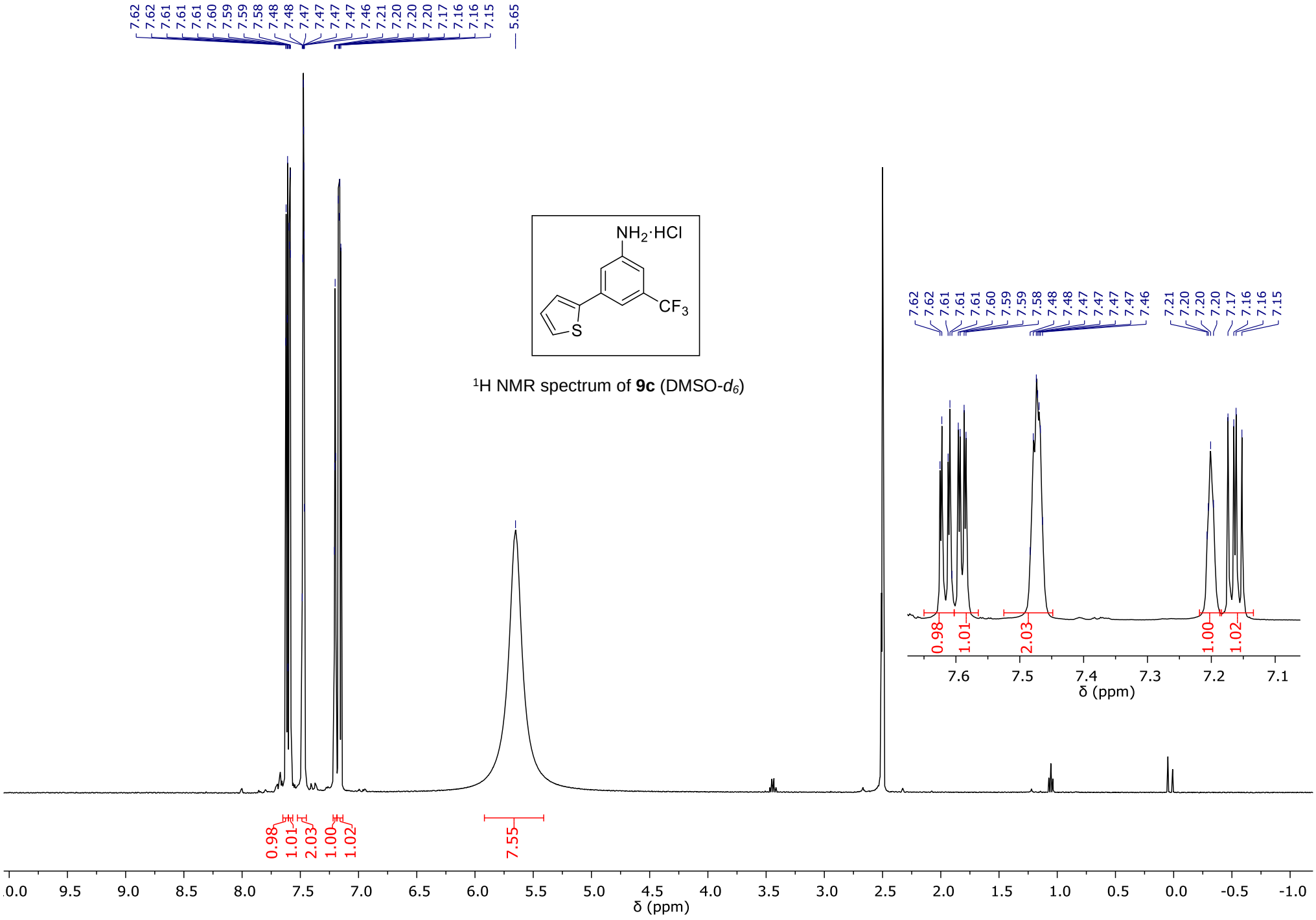
^{13}C NMR spectrum of **8ec** ($CDCl_3$)



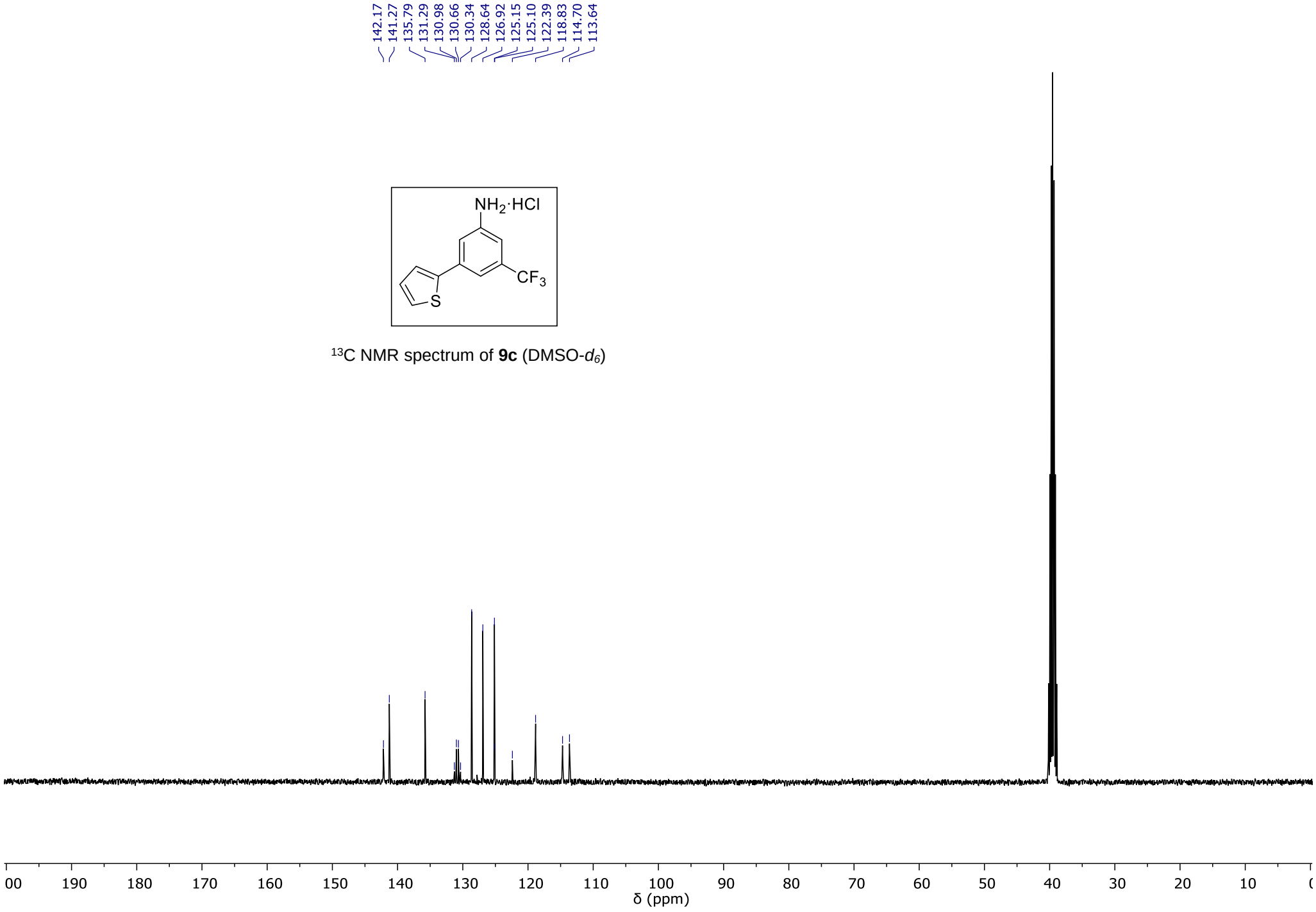
^{1}H NMR spectrum of **9b** ($CDCl_3$)



^{13}C NMR spectrum of **9b** ($CDCl_3$)



^{1}H NMR spectrum of **9c** (DMSO-d_6)



^{13}C NMR spectrum of **9c** (DMSO-d_6)