Metal-Free *N*-Arylation of Secondary Amides at Room Temperature

Supporting Information

Fredrik Tinnis[‡a], Elin Stridfeldt[‡a], Helena Lundberg,[a] Hans Adolfsson*[a] and Berit Olofsson*[a,b]

[a]*Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, SE-106 91 Stockholm, Sweden*
[b]*Stellenbosch Institute for Advanced Study (STIAS), Wallenberg Research Centre at Stellenbosch University, Marais Street, Stellenbosch 7600, South Africa*

1. General Experimental Procedure

All reactions were performed in oven-dried vials or round bottom flasks under nitrogen atmosphere, unless otherwise is stated. THF, acetonitrile and toluene were dried using VAC purification system and stored over activated 4Å molecular sieves. Commercial anhydrous DMF was dried over activated 4Å molecular sieves twice. Isohexane, *o*-xylene, *m*-xylene and *p*-xylene were dried over activated 4Å molecular sieves. All chemicals were purchased from commercial suppliers and used as received unless otherwise is stated. NaH (60% in mineral oil), NaOH, Cs_2CO_3 and K_3PO_4 were stored in a desiccator. *t*BuONa and *t*BuOK were stored under argon atmosphere in a desiccator. The diaryliodonium salts were synthesized according to procedures described below. For experimental details, see the reference for each method used. *m*CPBA used in the synthesis of the diaryliodonium salts was purchased from commercial supplier and then dried under vacuum at rt for 1h and subsequently the percentage of active oxidizing reagent was determined by iodometric titration.[1] TLC analysis were performed on pre-coated silica gel 60 F_{254} plates using either UV light or Seebach's "magic" stain (a mixture of phosphormolybdic acid and $Ce(SO_4)_2$) together with heat as developing agent.[2] The crude products were purified by flash column chromatography either manually using 40-60 µm, 60A silica gel as stationary phase or on an automated flash system Teledyne ISCO CombiFlash R_f 200 with RediSep R_f columns. Mixtures of EtOAc and pentane or petroleum ether were used as eluents. Melting points were measured using a STUART SMP3 and are reported uncorrected. All NMR spectra were recorded using a 400 or 500 MHz Bruker AVANCE II with a BBO probe at 263 K, 298 K, 323 K or 383 K using $CDCl_3$, MeOH-d_4 or DMSO-d_6 as solvents. Chemical shifts are given in ppm relative to the residual solvent peak (^{1}H NMR: $CDCl_3$ δ 7.26; MeOH-d_4 3.31; DMSO-d_6 2.50; ^{13}C NMR: $CDCl_3$ δ 77.16; MeOH-d_4 49.00 DMSO-d_6 39.52) with multiplicity (br=broad, s=singlet, d=doublet, t=triplet, q=quartet, quin=quintet, sex=sextet, sep=septet, m=multiplet, app=apparent), coupling constants (in Hz) and integration. Chemical shifts for ^{19}F-NMR are given in ppm relative to monofluorobenzene (-113.15 ppm) used as internal standard. Due to the restricted rotation around the C-N bond peak splitting and peak broadening was observed in ^{1}H-NMR and ^{13}C-NMR for many of the compounds. Therefore, ^{1}H-NMR and ^{13}C-NMR were conducted at different temperatures (263 K, 298 K, 323 K or 383 K) in order to either get a spectra with two distinguishable rotamers or a spectra in which the peaks for the two rotamers had coalesced. However, for all compounds, the ^{1}H-NMR at 298 K is attached as well. Due to difficulties to interpret NMR-data in some cases and due to the lack of full characterization in reported data, some compounds have been fully characterized even though they have been reported previously. High-resolution mass analyses were obtained using a Bruker microTOF ESI.

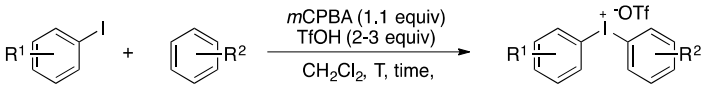
2. Synthesis of Diaryliodonium Salts

2.1. One-Pot Procedures

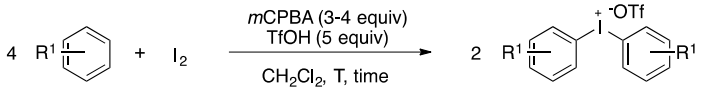
Even though many diaryliodonium salts are commercially available, the majority of the salts used in this investigation were synthesized according to one-pot procedures developed within the Olofsson group. These reactions were run without precautions

to avoid air or moisture. For experimental details, see the references for each method. Diphenyliodonium hexafluorophosphate **2d** was purchased from Alfa Aesar.

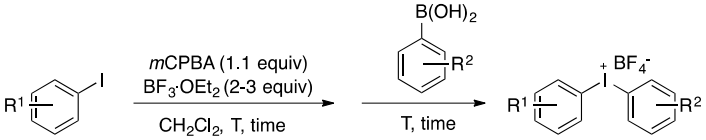
Method I)[3]



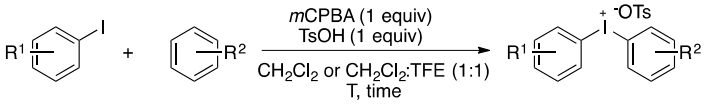
Method II)[3]



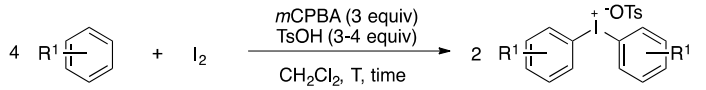
Method III)[4]



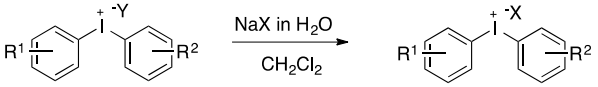
Method IV)[5]



Method V)[5]

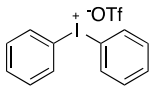
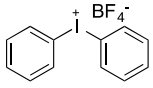
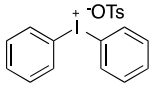
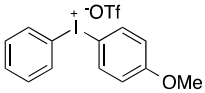
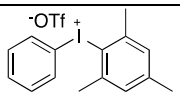
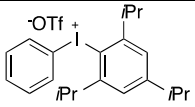
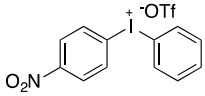
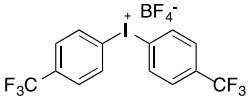
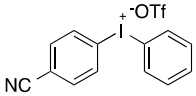
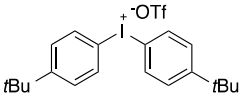
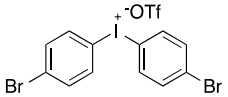
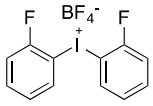


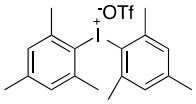
Anion exchange)[6]



NaX (85 mmol) was dissolved in H_2O (100 mL). Diaryliodonium salt (3.4 mmol) was dissolved in CH_2Cl_2 (20 mL) and washed 5 x 20 mL with the aquous solution. The organic layer was concentrated without drying. Et_2O was added and mixture was stirred at rt for 30 min. The solid was filtered, washed with Et_2O and dried under vacuum. The method was used to exchange BF_4 to OTs using NaOTs and to exchange OTs to OTf using NaOTf.

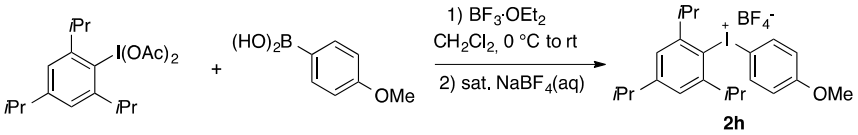
Table S1. Details for the synthesis of diaryliodonium salts **2**.[a]

2	Method	Acid (equiv)	T (°C)	time	Yield (%)[b]	Ref.
 **2a**	I	3.0	rt	30 min	95	7
 **2b**	III	2.5	rt	30 + 15 min	82	4
 **2c**	III[c]	2.5	rt	30 + 30min	24	8
 **2e**	IV[c]	1.0	rt	6 h	64	3, 9
 **2f**	I	2.0	rt	1 h	78	3b, 9
 **2g**	I	1.5	rt	16 h	59	10
 **2i**	I	2.0	80	15 h	85	7
 **2j**	III	2.5	rt	60 min + 15 min	56	4
 **2k**	I	2.0	rt	15 h	69	11
 **2l**	II	5.0	rt	20 min	78	3b
 **2m**	I	3.0	0	1 h	91	3b
 **2n**	III	2.5	rt	30 min + 15 min	85	4

 **2o**	II	4.0	rt	1 h	25	[3b]

[a] In the cases were one aryl originates from an aryl iodide that aryl is consistently drawn the left in the structure [b] Isolated yield. [c] Anion exchange was performed

2.2. Other Methods



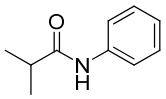
2h

Salt **2h** was synthesized according to a published procedure[10] from 1-diacetoxyiodo-2,4,6-triisopropylbenzene and 4-methoxyphenylboronic acid to give the product as a white solid in 75% yield. All spectral data is in agreement with published data.

3. Synthesis of Secondary Amides

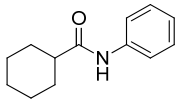
The majority of the secondary amides used in the investigation are commercially available and the following substrates were synthesized.

N-phenylisobutyramide (1c)[12]



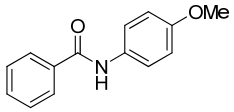
Isobutyryl chloride (10 mmol, 1.05 mL) was slowly added to a stirred solution of aniline (12 mmol, 1.1 mL) and triethylamine (12 mmol, 1.6 mL) in DCM (20 mL) at rt. The reaction was stirred for 24 hours and then extracted with 50 mL HCl (1 M) x 3 followed by 50 mL KOH (2 M) x 3. The organic phase was dried with sodium sulphate and concentrated under reduced pressure to afford compound **1c** as an off-white solid in 85% yield (1.387 g). Spectral data at 298 K is in agreement with published data.

N-phenylcyclohexanecarboxamide (1d)[12]



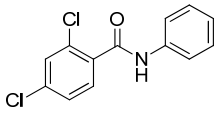
Cyclohexanecarboxylic acid (30 mmol, 3.85g) was refluxed in Thionyl chloride (25 mL) together with DMF (5 drops) for 3 h. The residual Thionyl chloride was evaporated and the crude reaction was dissolved in DCM (10 mL) and added dropwise to a stirred solution of Aniline (36 mmol, 3.3 mL) and Et_3N (36 mmol, 5.0 mL) in 50 mL DCM at rt. The reaction mixture was stirred at rt for 24 and then then extracted with 50 mL HCl (1 M) x 3 followed by 50 mL KOH (2 M) x 3. The organic phase was dried with sodium sulphate and concentrated under reduced pressure to afford compound **1d** as a white solid in 71% yield (4.33 g). Spectral data at 298 K is in agreement with published data.

_N_-(4-methoxyphenyl)benzamide (1j)[13]



Benzoyl chloride (30 mmol, 3.49 mL) was added to a stirred solution of p-Anisidine (36 mmol, 4.43 g) and Et_3N (45 mmol, 6.27 mL) in DCM (50 mL) at rt. The reaction was stirred for 6 h and then then extracted with 50 mL HCl (1 M) x 3 followed by 50 mL KOH (2 M) x 3. The organic phase was dried with sodium sulphate and concentrated under reduced pressure to afford compound **1j** as a white/pale blue solid in 82% yield (5.6 g). Spectral data at 298 K is in agreement with published data.

2,4-dichloro-_N_-phenylbenzamide (1r)

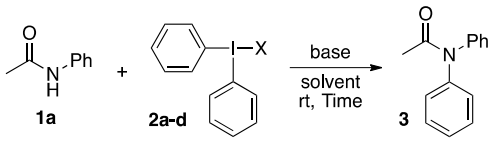


2,4-dichlorobenzoyl chloride (20 mmol, 2.8 mL) was slowly added to a stirred solution of aniline (30 mmol, 2.74 mL) and triethylamine (30 mmol, 4.2 mL) in DCM (50 mL) at rt. The reaction was stirred for 24 hours and then extracted with 50 mL HCl (1 M) x 3 followed by 50 mL KOH (2 M) x 3. The organic phase was dried with sodium sulphate and concentrated under reduced pressure to afford compound **1r** as an off-white solid in 85% yield (4.52 g). mp = 152-153 °C. ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 8.14-7.91 (bs, 1H), 7.67 (d, J = 8.26 Hz, 1H), 7.62 (d, J = 7.72 Hz, 2H), 7.44 (m, 1H), 7.42-7.30 (m, 3H), 7.18 (t, J = 7.43 Hz, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$, 298 K) δ 163.8, 137.5, 137.2, 133.7, 131.6, 131.3, 130.2, 129.2, 127.7, 125.2, 120.4. HRMS (ESI): calcd for $C_{13}H_9Cl_2NONa$ $[M + Na]^+$: 287.9953; found: 287.9941.

4. Optimization Study for the Phenylation of Acetanilide

Acetanilide **1a** (34 mg, 0.25 mmol), diaryliodonium salt **2a-d** and base were added to a dry 5 mL microwave vial, which was capped. The vial was evacuated and backfilled with nitrogen three times. The stirring was started and the anhydrous solvent (5 mL) was added. *NB: gas evolved.* The solution was stirred at the indicated temperature and time. *NB: it is important that the stirring is vigorous*.

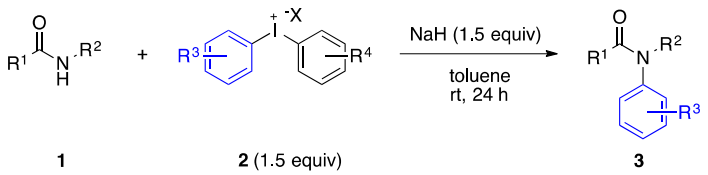
Table S2. Expanded optimisation table for the phenylation of acetanilide.



Entry	2 (equiv)	X	Base (equiv)	Solvent	Temperature (°C)	time (h)	Yield (%)[b]
1	**2a** (2.0)	OTf	NaH (2.0)	THF	rt	24	n.r.
2	**2a** (2.0)	OTf	NaH (2.0)	DMF	rt	24	11
3	**2a** (2.0)	OTf	NaH (2.0)	CH_3CN	rt	24	3
4	**2a** (2.0)	OTf	NaH (2.0)	Iso-hexane	rt	24	37
5	**2a** (2.0)	OTf	NaH (2.0)	*o*-xylene	rt	24	81
6	**2a** (2.0)	OTf	NaH (2.0)	*m*-xylene	rt	24	70
7	**2a** (2.0)	OTf	NaH (2.0)	*p*-xylene	rt	24	75
8	**2a** (2.0)	OTf	NaH (2.0)	Toluene	rt	24	76
9	**2a** (2.0)	OTf	NaOH (2.0)	Toluene	rt	24	64
10	**2a** (2.0)	OTf	*t*BuONa (2.0)	Toluene	rt	24	44
11	**2a** (2.0)	OTf	*t*BuOK (2.0)	Toluene	rt	24	32
12	**2a** (2.0)	OTf	K_3PO_4 (2.0)	Toluene	rt	24	20
13	**2a** (2.0)	OTf	Cs_2CO_3 (2.0)	Toluene	rt	24	6
14[c]	**2a** (2.0)	OTf	NaH (2.0)	Toluene	rt	24	71
15	**2a** (2.0)	OTf	NaH (1.5)	Toluene	rt	24	80
16	**2a** (1.5)	OTf	NaH (1.5)	Toluene	rt	24	76
17	**2a** (1.5)	OTf	NaH (2.0)	Toluene	rt	24	60
18	**2a** (2.0)	OTf	NaH (2.0)	Toluene	rt	24	72[d]
19	**2a** (1.5)	OTf	NaH (1.5)	Toluene	rt	24	75[d]
20[e]	**2a** (1.5)	OTf	NaH (1.5)	Toluene	rt	24	70[d]
21	**2a** (1.1)	OTf	NaH (1.1)	Toluene	rt	24	51[d]
22	**2a** (1.5)	OTf	NaH (1.5)	Toluene	rt	6	60[d]
23	**2a** (1.5)	OTf	NaH (1.5)	Toluene	60	2	75[d]
24	**2a** (1.5)	OTf	NaH (1.5)	Toluene	80	1	70[d]
25[f]	**2a** (1.5)	OTf	NaH (1.5)	Toluene	rt	24	64[d]
26	**2b** (1.5)	BF_4	NaH (1.5)	Toluene	rt	24	81[d]
27	**2c** (1.5)	OTs	NaH (1.5)	Toluene	rt	24	75[d]
28	**2d** (1.5)	PF_6	NaH (1.5)	Toluene	rt	24	59[d]

[a]Reaction conditions: Acetanilide **1a** (0.25 mmol), diaryliodonium salt **2a-d** and base were stirred in the anhydrous solvent (5 mL) at the indicated temperature for the indicated time. [b] ^{1}H-NMR yield using 1,3,5-trimethoxybenzene as internal standard. [c] With 1 equiv DPE as radical scavenger. [d] Isolated yield. [e]1 mmol scale, see section 6 for details. [f] In 2.5 mL solvent.

5. General Method for the Arylation of Secondary Amides



1 **2** (1.5 equiv) **3**

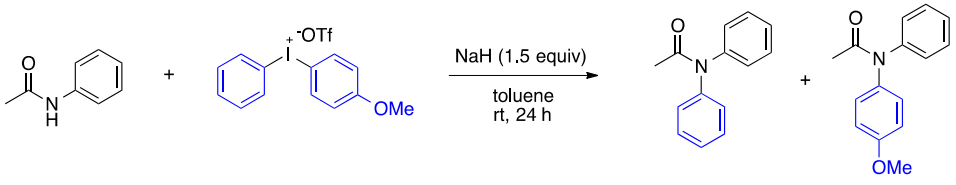
The secondary amide **1** (0.25 mmol), diaryliodonium salt **2** (0.37 mmol) and NaH (60%, 0.38 mmol) were added to a dry 5 mL microwave vial, which was capped. The vial was evacuated and backfilled with nitrogen three times. The stirring was started and anhydrous toluene (5 mL) was added. *NB: gas is evolved.* The solution was stirred at ambient temperature for 24 h. *NB: it is important that the stirring is vigorous*. The crude reaction mixture was then transferred to a round flask using ethyl acetate. The solvent was evaporated and then the crude reaction was loaded onto silica without any work-up. The crude was purified using either manual flash column chromatography or on an ISCO Combiflash using EtOAc in pentane or petroleum ether as eluent to yield product **3**.

6. Larger Scale Phenylation of Acetanilide

Acetanilide (**1a,** 1.0 mmol, 0.135 g) and **2a** (1.5 mmol, 0.645 g) were added to a dried 25 mL round-flask. The flask was equipped with a rubber septa, evacuated and backfilled with nitrogen three times. The stirring was started and dry toluene (20 mL) was added. The secondary amide and the iodonium salt were stirred for 30 min and then NaH (1.5 equiv.) was added through a funnel filled with argon. The round-bottom flask was quickly closed with the septa and fitted with a nitrogen balloon, and the stirred at rt for 24 h. The toluene was evaporated and the crude solid was dissolved in ethyl acetate and loaded onto silica. Purification was performed using ISCO Combiflash with pentane:EtOAc gradient to yield compound **3a** as a yellow solid in 70% yield (0.147 g).

7. Chemoselectivity Study of the Electrophile

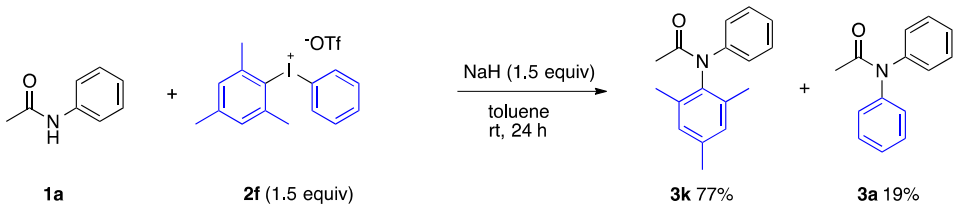
The chemoselectivity was investigated in the following reactions. The ratio between the products could not be obtained form the crude NMR due to overlapping peaks, so the chemoselectivity was determined by isolation of the two products.



1a **2e** (1.5 equiv) **3a** 45% **3i** 5%

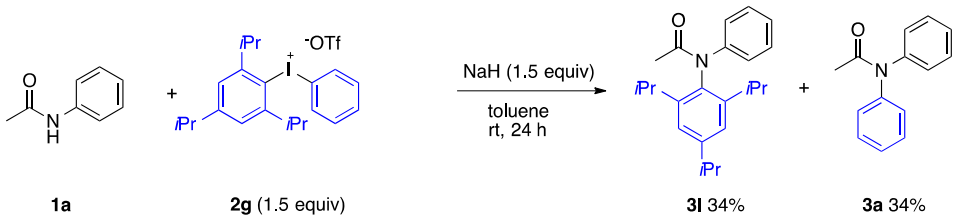
The tertiary amides **3a** and **3i** were synthesized according to the general procedure given in section 5 from acetanilide (**1a**, 34 mg, 0.25 mmol), **2e** (173 mg, 0.38 mmol) and NaH (60%, 15 mg, 0.38 mmol). The mixture was stirred at rt for 24 h. The crude was purified by flash column chromatography (silica gel, gradient 20-100% EtOAc in

pentane) to yield **3a** in 45% yield (24 mg, 0.11 mmol). Product **3i** was obtained as mixture with acetanilide and the yield was calculated to 5%.



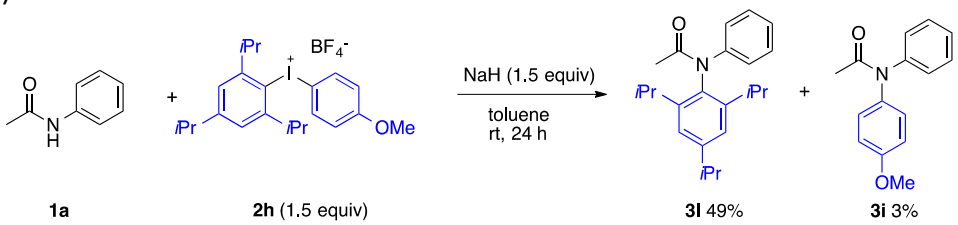
1a **2f** (1.5 equiv) **3k** 77% **3a** 19%

The tertiary amides **3k** and **3a** were synthesized according to the general procedure given in section 5 from acetanilide (**1a**, 34 mg, 0.25 mmol), **2f** (177 mg, 0.37 mmol) and NaH (60%, 15 mg, 0.38 mmol). The mixture was stirred at rt for 24 h. The crude was purified by flash column chromatography (silica gel, gradient 10-50% EtOAc in pentane) to yield **3k** in 77% (49 mg, 0.19 mmol) and **3a** in 19% yield (10 mg, 0.05 mmol).



1a **2g** (1.5 equiv) **3l** 34% **3a** 34%

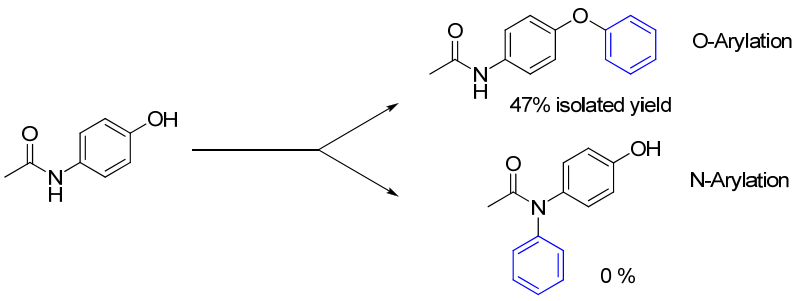
The tertiary amides **3l** and **3a** were synthesized according to general procedure given in section 5 from acetanilide (**1a**, 34 mg, 0.25 mmol), **2g** (209 mg, 0.38 mmol) and NaH (60%, 15 mg, 0.38 mmol). The mixture was stirred at rt for 24 h. The crude was purified by flash column chromatography (silica gel, gradient 5-50% EtOAc in pentane) to yield **3l** in 34% yield (29 mg, 0.09 mmol) and **3a** in 34% yield (18 mg, 0.09 mmol).



1a **2h** (1.5 equiv) **3l** 49% **3i** 3%

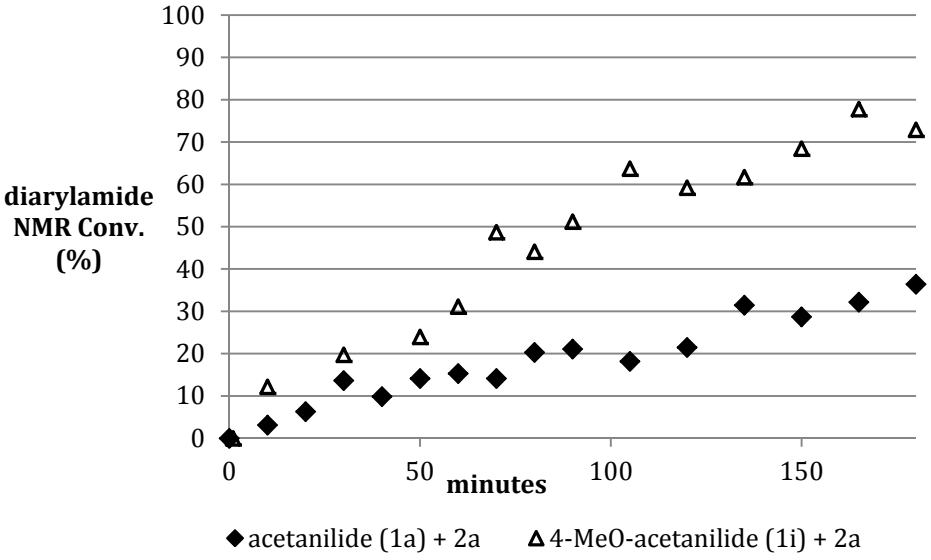
The tertiary amides **3l** and **3i** were synthesized according to general procedure given in section 5 from acetanilide (**1a**, 34 mg, 0.25 mmol), **2h** (197 mg, 0.38 mmol) and NaH (60%, 15 mg, 0.38 mmol). The mixture was stirred at rt for 24 h. The products were purified by flash column chromatography (silica gel, gradient 5-50% EtOAc in pentane) to yield **3l** in 49% yield (42 mg, 0.12 mmol). **3i** was obtained as mixture with acetanilide and the yield was calculated to 3%.

8. Chemoselectivity Study of the Nucleophile (N- Vs. O-arylation)

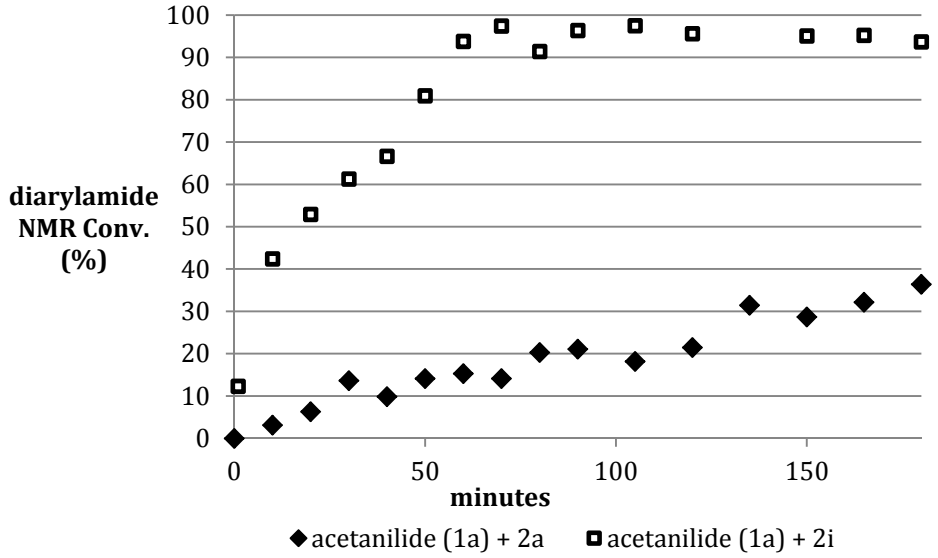


Synthesized according to the general procedure given in section 5 from *N*-(4-hydroxyphenyl)acetamide (38 mg, 0.25 mmol), NaH 60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The mixture was stirred in toluene at 60 °C for 24 h. The crude product was purified by flash chromatography (silica gel, 10-100% EtOAc in petroleum ether using ISCO CombiFlash). The *N*-arylated product was not formed in the reaction, instead a moderate yield of 47% of the *O*-arylated product (*N*-(4-phenoxyphenyl)acetamide) was obtained. The spectral data are in agreement with previous published data.[14]

9. Reaction Profiles



Reaction conditions: Anilide (0.25 mmol) and diphenyliodonium triflate **2a** (161.3 mg, 0.375 mmol) were placed in a vial equipped with a teflon-coated magnetic stirring bar. Sodium hydride (15 mg, 0.375 mmol) was added, and the vial was quickly sealed with a crimp-on cap equipped with septum. The atmosphere was exchanged for nitrogen gas and 5 mL dry toluene was added to the reaction mixture under vigorous stirring (1500 rpm) at room temperature. Samples of approximately 50 microliter were removed and injected into deuterated methanol at certain time intervals, and subjected to ^{1}H-NMR analysis.



Reaction conditions: Acetanilide **1a** (33.8 mg, 0.25 mmol) and diaryliodonium triflate (0.375 mmol) were placed in a vial equipped with a teflon-coated magnetic stirring bar. Sodium hydride (15 mg, 0.375 mmol) was added, and the vial was quickly sealed with a crimp-on cap equipped with septum. The atmosphere was exchanged for nitrogen gas and 5 mL dry toluene was added to the reaction mixture under vigorous stirring (1500 rpm) at room temperature. Samples of approximately 50 microliter were removed and injected into deuterated methanol at certain time intervals, and subjected to ^{1}H-NMR analysis. The *N*-phenyl-4-nitroacetanilide **3f** was isolated after 70 minutes in 86% yield after column chromatography.

10. Metal Analysis of the Crude Reaction Mixture

A sample for ICP-OES was prepared as follows:
The up-scaled version of the reaction was performed as described in section 6. A small sample was withdrawn after 24 h and analyzed by ^{1}H NMR to confirm product formation. The solvent was then evaporated and a small amount of purified water obtained from Purelab Ultra/Elga was added to quench residual sodium hydride. The water was evaporated and a 260 mg solid sample was sent to Medac Ltd. for ICP-OES analysis.

Results:

Element	Results	Units
Cu	1.3	ppm
Pd	<0.1	ppm

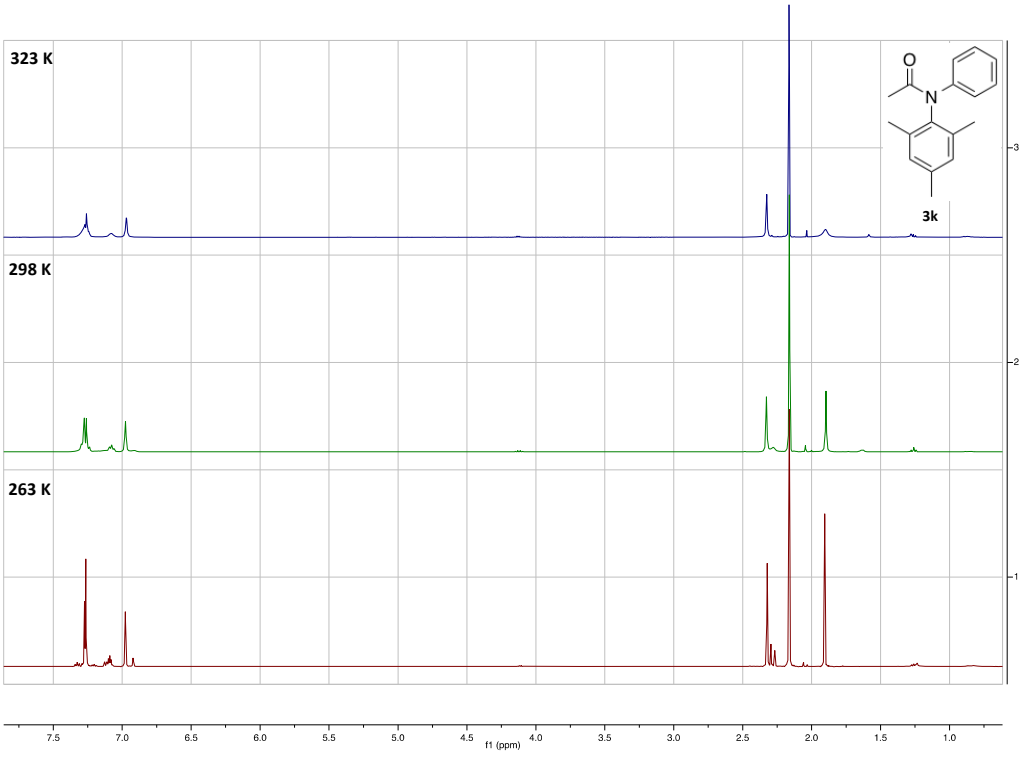
The amount of copper detected in the crude mixture corresponds to 0.0021 mol% in the reaction. Literature reports on copper-catalyzed N-arylations with diaryliodonium salts typically employ 10-20 mol% copper and elevated temperatures.[15] Previous reports on arylation of amides use stoichiometric copper in

refluxing MeOH,[16] 10 mol% in toluene at 100 °C,[17] 10 mol% in DMF at 40 °C,[18] or 5 mol% CuI at 50 °C.[19] Unsymmetric diaryliodonium salts were used in one report with the mesityl group as a dummy,[17] which is common in metal-catalyzed reactions. We observe the opposite chemoselectivity, which further supports that the reaction is not metal-catalyzed.

11. Rotamers in NMR

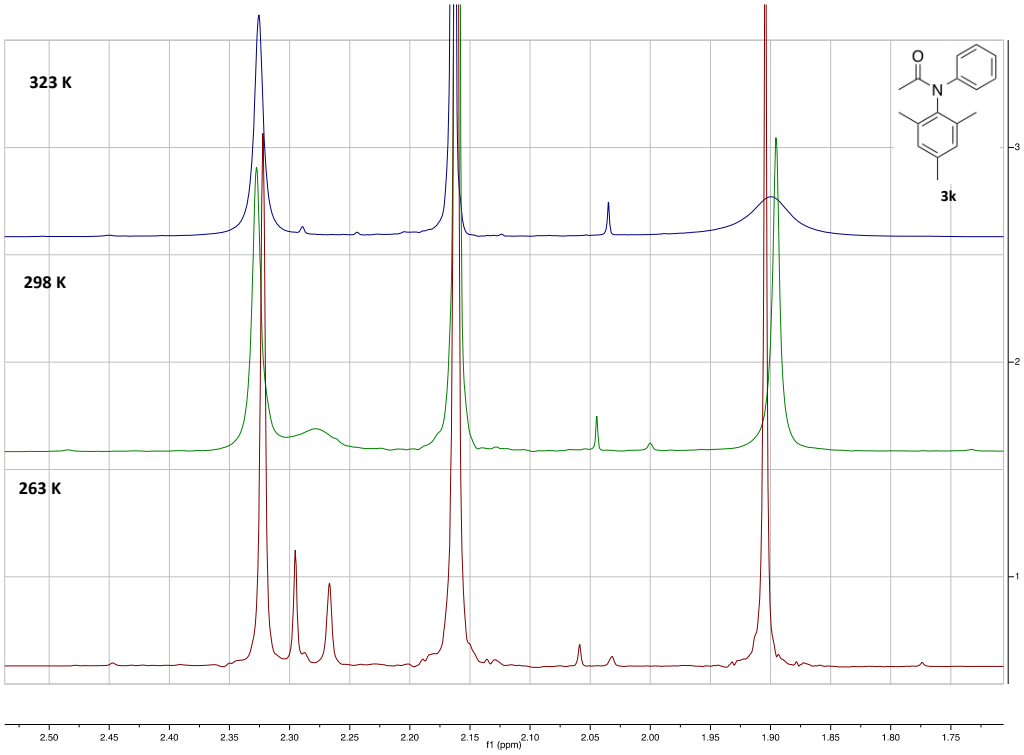
Due to the restricted rotation around the C–N bond the tertiary amides exist as rotamers. For some substrates, this caused peak splitting and peak broadening at ambient temperature. To support that this was due to rotamers, the ^{1}H-NMR and ^{13}C-NMR for compound **3k** were recorded at 263 K, 298 K and 323 K in $CDCl_3$. At 263 K the two rotamers can be distinguished in a 1:6 ratio. At 298 K the peaks for the two rotamers have started to merge and at 323 K they have coalesced.

^{1}H-NMR ($CDCl_3$, 500 MHz):

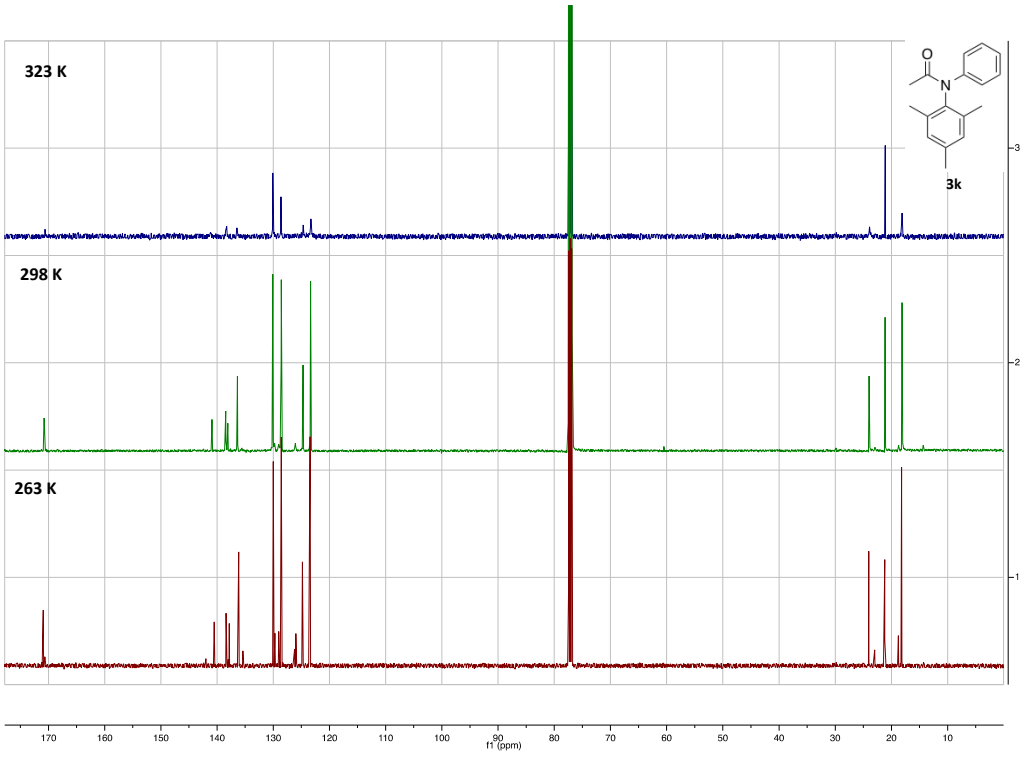


^{1}H-NMR ($CDCl_3$, 500 MHz) enlarged aromatic region:

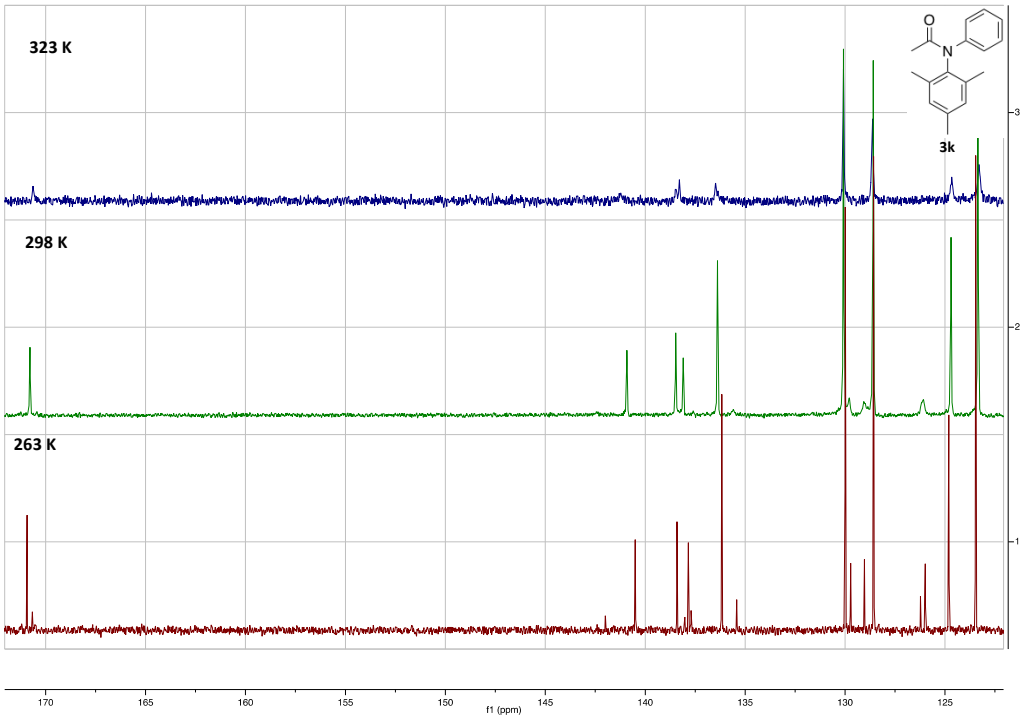
^{1}H-NMR ($CDCl_3$, 500 MHz) enlarged aliphatic region:



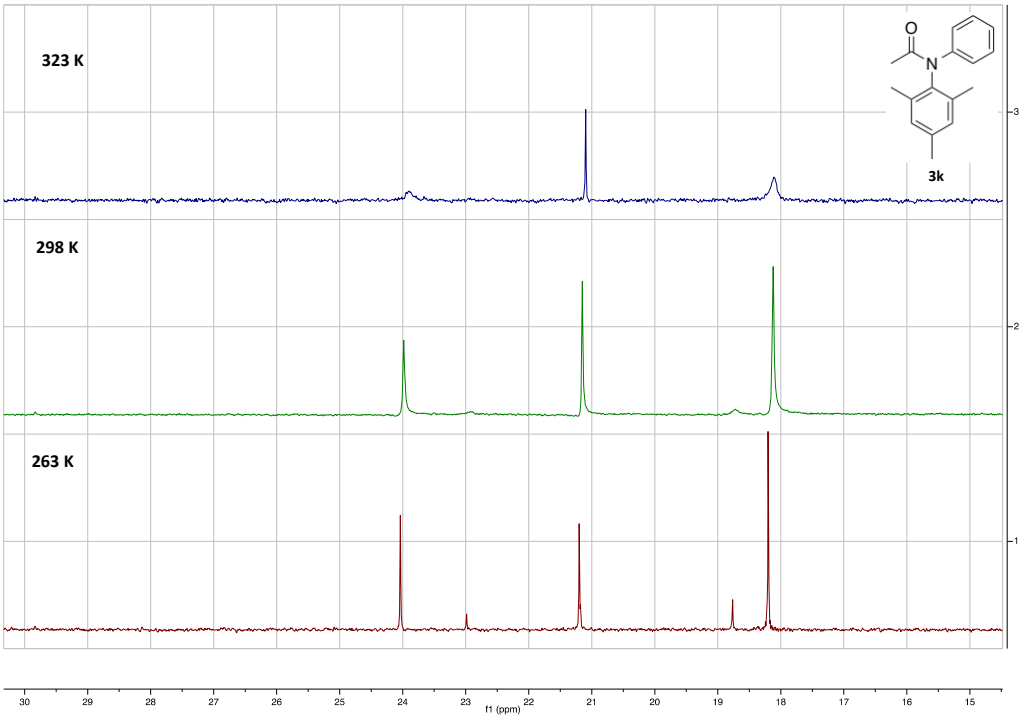
^{13}C-NMR ($CDCl_3$, 125 MHz):



^{13}C-NMR ($CDCl_3$, 125 MHz) enlarged aromatic region:

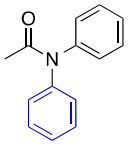


^{13}C-NMR ($CDCl_3$, 125 MHz) enlarged aliphatic region:



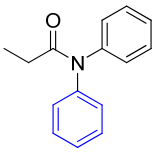
12. Analytical Data for the Arylated Amides

***N,N*-Diphenylacetamide (3a)[20]**



Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3a** as a yellow solid (41 mg, 0.19 mmol and 39 mg, 0.18 mmol) in 75% average yield over two runs. Spectral data at both 298 K and 263 K are in agreement with published data.

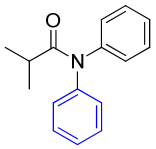
***N,N*-Diphenylpropionamide (3b)[21]**



Synthesized according to procedure given in section 5 from *N*-phenylpropionamide **1b** (37 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO

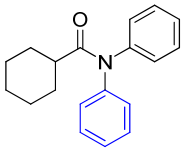
CombiFlash) to give **3b** as a pale yellow solid (41 mg, 0.18 mmol) in 72% yield. Spectral data at 298 K is in agreement with published data.

***N*,*N*-Diphenylisobutyramide (3c)[22]**



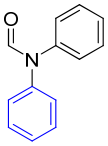
Synthesized according to procedure given in section 5 from *N*-phenylisobutyramide **1c** (41 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3c** as an off white solid (44 mg, 0.18 mmol) in 73% yield. Spectral data at 298 K is in agreement with published data.

***N*,*N*-Diphenylcyclohexanecarboxamide (3d)**



Synthesized according to procedure given in section 5 from *N*-phenylcyclohexanecarboxamide **1d** (51 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3d** as a off white solid (58 mg, 0.21 mmol) in 82% yield. mp = 120-122 °C. ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.53-7.03 (m, 10H), 2.39 (tt, *J* = 3.57, 11.49 Hz, 1H), 1.86-1.50 (qt, *J* = 3.58, 12.88 Hz, 1H), 1.10-0.94 (qt, *J* = 3.60, 12.90 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$, 298 K) δ 176.7, 143.2, 129.3, 127.1 (br), 42.4, 29.5, 25.7, 25.6. HRMS (ESI): calcd for $C_{19}H_{21}NONa$ $[M + Na]^+$: 302.1515; found: 302.1497.

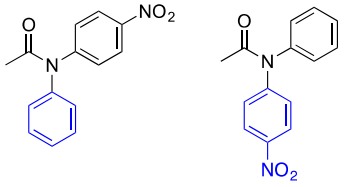
***N*,*N*-Diphenylformamide (3e)[23]**



N-phenylformamide **1e** (30 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol) were stirred in dry toluene (5 mL) for 3 h at 60 °C. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3e** as a pale brown solid (30 mg, 0.15 mmol) in 61% yield. Spectral data at 298 K is in agreement with published data.

Additional information: A large amount of starting material was recovered by performing the reaction according to the general procedure dictated in section 5. The reactivity of the substrate was increased when performing the reaction at 60 °C; however, at this temperature two unidentified by-products were formed which limited the isolated yield of the desired product to the moderate 61%.

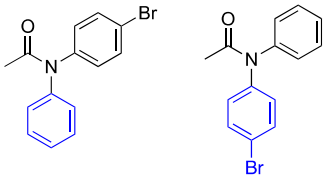
***N*-Phenyl-4-nitroacetanilide (3f)[24]**



A: *N*-(4-nitrophenyl)acetamide **1f** (45 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol) were stirred in dry toluene (5 mL) for 5 h at 60 °C. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3f** as a pale yellow solid (50 mg, 0.19 mmol) in 77% yield.

B: Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2i** (178 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 20% EtOAc in pentane) to give **3f** as a pale yellow solid in 99% yield (64 mg, 0.25 mmol). mp = 84-87 °C (lit. 99.5-100 °C)[24] ^{1}H-NMR is in agreement with published data, but ^{13}C-NMR has not been reported. ^{13}C-NMR (100 MHz, $CDCl_3$, 298 K) δ 170.7, 148.3, 144.7, 142.1, 130.4, 128.8, 128.8, 125.7, 124.4, 24.6. HRMS (ESI): calcd for $C_{14}H_{12}N_2O_3Na$ $[M + Na]^+$: 279.0740; found: 279.0742.

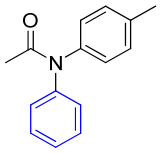
***N*-(4-Bromophenyl)-N-phenylacetamide (3g)[20a, 25]**



A: Synthesized according to procedure given in section 5 from *N*-(4-bromophenyl)acetamide **1g** (54 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3g** as of white solid (63 mg, 0.22 mmol) in 87% yield.

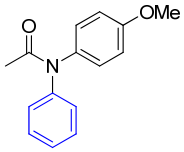
B: Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2m** (220 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 20-50% EtOAc in pentane) to give **3g** as a colorless oil, that slowly crystalized upon scratching to a white solid, in 40% yield (29 mg, 0.10 mmol). mp = 74-76 °C (lit. 77 °C)[25] .^{1}H-NMR and ^{13}C-NMR at 298 K is in agreement with published data. For clarity, ^{1}H-NMR and ^{13}C-NMR at 263 K are also attached, in which a 1:2 ratio of rotamers could be seen. HRMS (ESI): calcd for $C_{14}H_{12}BrNONa$ $[M + Na]^+$: 311.9994; found: 311.9983.

***N*-Phenyl-*N*-(*p*-tolyl)acetamide (3h)[20a]**



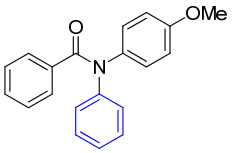
Synthesized according to procedure given in section 5 from *N*-p-tolylacetamide **1h** (37 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3h** as a pale yellow solid (45 mg, 0.20 mmol) in 80% yield. Spectral data at 298 K is in agreement with published data.

***N*-Phenyl-4-methoxyacetanilide (3i)[26]**



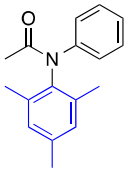
Synthesized according to procedure given in section 5 from *N*-(4-methoxyphenyl)acetamide **1i** (41 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3i** as a pale yellow oil (51 mg, 0.21 mmol) in 85% yield. Spectral data at 298 K is in agreement with published data.

***N*-(4-Methoxyphenyl)-*N*-phenylbenzamide (3j)[26]**



Synthesized according to procedure given in section 5 from *N*-(4-methoxyphenyl)benzamide **1j** (57 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2a** (161 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3j** as a pale yellow solid (55 mg, 0.18 mmol) in 73% yield. Spectral data at 298 K is in agreement with published data.

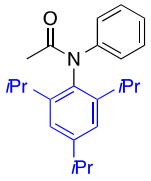
***N*-Phenyl-2,4,6-trimethylacetanilide (3k)[27]**



Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2o** (193 mg, 0.38 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 20% EtOAc in pentane) to give **3k** as a white solid (63 mg, 0.25 mmol) in 99% yield. mp = 106-108 °C (lit. 106-108 °C)[27]. ^{1}H-NMR at 298 K is in agreement with published data. No ^{13}C-NMR has been reported and therefore a full

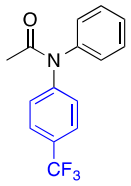
characterization was performed. The product was characterized as a mixture of rotamers in a 1:6 ratio at 263 K. ^{1}H-NMR (500 MHz, $CDCl_3$, 263 K) *major rotamer:* δ 7.30-7.24 (m, 4H), 7.14-7.05 (m, 1H), 6.98 (s, 2H), 2.32 (s, 3H), 2.16 (s, 6H), 1.90 (s, 3H). *minor rotamer:* δ 7.33 (t, *J* = 7.8 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.14-7.05 (m, 2H), 6.92 (s, 2H), 2.30 (s, 3H), 2.27 (s, 3H), 2.16 (s, 6H). ^{13}C-NMR (125 MHz, $CDCl_3$, 263 K) *major rotamer:* δ 170.9, 140.5, 138.4, 137.8, 136.2, 130.0, 128.6, 124.8, 123.5, 24.0, 21.2, 18.2. *minor rotamer:* δ 170.7, 142.0, 138.0, 137.7, 135.4, 129.7, 129.0, 126.2, 126.0, 23.0, 21.2, 18.8. HRMS (ESI): calcd for $C_{17}H_{19}NONa$ $[M + Na]^+$: 276.1359; found: 276.1356.

_N_-Phenyl-_N_-(2,4,6-triisopropylphenyl)acetamide (3l)



Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2h** (197 mg, 0.38 mmol) in *o*-xylene (5mL). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 5-50% EtOAc in pentane) to give **3l** as a colorless oil in 55% yield (47 mg, 0.14 mmol). The product was characterized as a mixture of rotamers in a 1:5 ratio at 263 K. ^{1}H-NMR (500 MHz, $CDCl_3$, 263 K) *major rotamer:* δ 7.36-7.29 (m, 2H), 7.29-7.22 (m, 2H), 7.07 (s, 2H), 7.09-7.03 (m, 1H). 3.09-2.98 (m, 2H), 2.98-2.83 (m, 1H), 1.94 (s, 3H), 1.28 (d, *J* = 6.9 Hz, 6H), 1.21 (d, *J* = 6.9 Hz, 6H), 0.93 (d, *J* = 6.3 Hz, 6H). *minor rotamer*: δ 7.36-7.29 (m, 2H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 7.5 z, 2H), 7.02 (s, 2H), 3.09-2.98 (m, 2H), 2.98-2.93 (m, 1H), 2.35 (s, 3H), 1.24 (d, *J* = 6.9 Hz, 6H), 1.21 (d, *J* = 6.9 Hz, 6H), 0.97 (d, *J* = 6.8 Hz, 6H). ^{13}C-NMR (125 MHz, $CDCl_3$, 263 K) *major rotamer:* δ 171.7, 149.8, 146.0, 142.2, 134.9, 128.4, 124.4, 123.2, 123.0, 34.2, 28.2, 24.9, 24.7, 24.2, 24.1. *minor rotamer*: δ 171.4, 148.6, 145.3, 143.3, 135.0, 129.0, 125.8, 125.7, 122.5, 34.1, 28.9, 24.3, 24.1, 23.3. HRMS (ESI): calcd for $C_{23}H_{31}NONa$ $[M + Na]^+$: 360.2298; found: 360.2290.

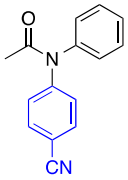
_N_-Phenyl-4-trifluoromethylacetanilide (3m)



Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2j** (189 mg, 0.38 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 20% EtOAc in pentane) to give **3m** as a white solid in >99% yield (70 mg, 0.25 mmol). mp = 72-74 °C. ^{1}H-NMR (500 MHz, $CDCl_3$, 323 K) δ 7.58 (d, *J* = 8.5 Hz, 2H), 7.47-7.41 (m, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.35 (t, *J* = 7.3 Hz, 1H), 7.29-7.22 (m, 2H), 2.07 (s, 3H). ^{13}C-NMR (125 MHz, $CDCl_3$, 323 K) δ 170.4, 146.2, 142.9, 130.0, 128.5, 128.1, 126.7, 126.3, 126.3, 124.1 (q, $J_{C\text{-}F}$ = 271.9 Hz), 24.1. ^{19}F-

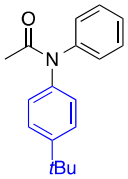
NMR (376 MHz, $CDCl_3$, 298 K) δ -62.52. HRMS (ESI): calcd for $C_{15}H_{12}F_3NONa$ $[M + Na]^+$: 302.0763; found: 302.0760.

_N_-Phenyl-4-cyanoacetanilide (3n)[24, 28]



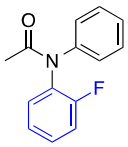
Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2k** (171 mg, 0.38 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 30-50% EtOAc in pentane) to give **3n** as a white solid in 98% yield (58 mg, 0.25 mmol). mp = 95-97 °C (lit. 96-97 °C)[24] ^{1}H-NMR at 298 K is in agreement with published data. ^{13}C-NMR has two more peaks compared to reported data.[28] ^{13}C-NMR (100 MHz, $CDCl_3$, 298 K) δ 170.6, 146.7, 142.2, 132.9, 130.3, 128.7, 128.6, 126.2, 118.6, 109.1, 24.5. HRMS (ESI): calcd for $C_{15}H_{12}N_2ONa$ $[M + Na]^+$: 259.0842; found: 259.0845.

_N_-(4-_tert_-Butylphenyl)-_N_-phenylacetamide (3o)[29]



Synthesized according to procedure given in section 5from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2l** (203 mg, 0.37 mmol). The reaction mixture was stirred at 60 °C for 24 h. The crude product was purified by flash chromatography (silica gel, 20-50% EtOAc in pentane) to give **3o** as a white solid in 64% yield (43 mg, 0.16 mmol). mp = 106-108 °C (lit. 108 °C)[29]. ^{1}H-NMR and ^{13}C-NMR at 298 K is agreement with published data. For clarity, ^{1}H-NMR at ^{13}C-NMR at 263 K are also attached, in which a 1:1 ratio of rotamers could be seen. The reported data lacks HRMS or elemental analysis. HRMS (ESI): calcd for $C_{18}H_{21}NONa$ $[M + Na]^+$: 290.1515; found: 290.1509.

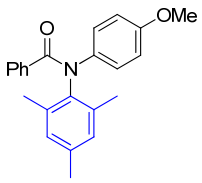
_N_-Phenyl-2-fluoroacetanilide (3p)[24]



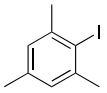
Synthesized according to procedure given in section 5 from acetanilide (34 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2n** (151 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 30% EtOAc in pentane) to give **3p** as a white solid in >99% yield (58 mg, 0.25 mmol). mp = 121-123 °C. (lit. 121-121.5 °C)[24]. ^{1}H-NMR in $CDCl_3$ at 298 K is in agreement with published data, but ^{13}C-NMR was not reported.

Therefore, the compound was fully characterized. ^{1}H-NMR (500 MHz, DMSO-d_6, 383 K) δ 7.49-7.43 (m, 1H), 7.43-7.32 (m, 5H), 7.32-7.20 (m, 3H), 1.97 (s, 3H). ^{13}C-NMR (125 MHz, DMSO-d_6, 383 K) δ 168.5, 157.2 (d, J_{C-F} = 248.4 Hz), 142.1, 130.2 (d, J_{C-F} = 12.9 Hz), 129.9, 129.0 (d, J_{C-F} = 7.6 Hz), 128.5, 126.4, 126.3 (*should be a doublet due to C-F coupling, but overlaps with other peak*), 124.5 (d, J_{C-F} = 3.7 Hz), 115.8 (d, J_{C-F} = 20.3 Hz), 21.6. ^{19}F-NMR (376 MHz, $CDCl_3$, 298 K) δ -119.49, -120.99. HRMS (ESI): calcd for $C_{14}H_{12}FNONa$ [M + Na]$^+$: 252.0795; found: 252.0784.

_N_-Mesityl-_N_-(4-methoxyphenyl)benzamide (3q)

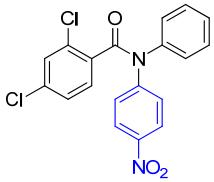


Synthesized according to procedure given in section 5 from *N*-(4-methoxyphenyl)benzamide **1j** (57 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2o** (193 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3q** as a white solid (72 mg, 0.21 mmol) in 84% yield. mp = 128-120 °C. The product was characterized as a mixture of rotamers in almost 1:1 ratio at 298 K. ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 7.57-7.36 (m, 2H), 7.36-7.09 (m, 4H), 6.95 (s, 1H), 6.90-6.70 (m, 3H), 6.69-6.55 (m, 1H), 3.79 and 3.70 (two s, total 3H), 2.36-2.06 (m, 9H). ^{13}C-NMR (100 MHz, $CDCl_3$, 298 K) δ. 170.4, 169.6, 156.9, 156.8, 138.7, 138.4, 137.8, 137.6, 136.8, 136.1, 135.8, 135.5, 134.9, 130.3, 130.2, 129.9, 129.3, 128.3, 128.1, 127.6, 126.9, 125.9, 113.93, 113.87, 55.5, 55.4, 21.1, 21.0, 18.8, 18.6. HRMS (ESI): calcd for $C_{23}H_{23}NO_2Na$ [M + Na]$^+$: 368.1621; found: 368.1612.



2-Iodo-1,3,5-trimethylbenzene was recovered from the synthesis of **3q** in 81 % isolated yield (50 mg, 0.20 mmol)

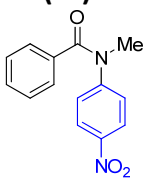
2,4-Dichloro-_N_-(4-nitrophenyl)-_N_-phenylbenzamide (3r)



Synthesized according to procedure given in section 5 from 2,4-dichloro-*N*-phenylbenzamide **1k** (67 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2i** (178 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3r** as a pale yellow solid (92 mg, 0.24 mmol) in 95% yield. mp = 134-136 °C. ^{1}H-NMR (400 MHz, $CDCl_3$, 298 K) δ 8.31-8.06 (m, 2H), 7.63-7.36 (bs, 2H), 7.36-7.23 (m, 5H), 7.23-7.08 (m, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$, 298 K) δ 167.3, 147.9, 145.3, 141.0, 136.2, 134.5, 131.6, 130.1, 129.8, 129.7, 128.4, 128.3

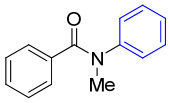
(br), 127.2, 126.5 (br), 124.5. HRMS (ESI): calcd for $C_{19}H_{12}Cl_2N_2O_3Na$ $[M + Na]^+$: 409.0117; found: 409.0109.

_N_-Methyl-_N_-(4-nitrophenyl)benzamide (3s)[28]



Synthesized according to procedure given in section 5 from *N*-methylbenzamide **1l** (35 mg, 0.25 mmol), NaH (60%, 15 mg, 0.38 mmol) and **2i** (178 mg, 0.37 mmol). The reaction mixture was stirred at rt for 24 h. The crude product was purified by flash chromatography (silica gel, 0-100% EtOAc in petroleum ether using ISCO CombiFlash) to give **3s** as a pale yellow solid (33 mg, 0.14 mmol) in 52% yield. Spectral data at 298 K is in agreement with published data.

_N_-methyl-_N_-phenylbenzamide



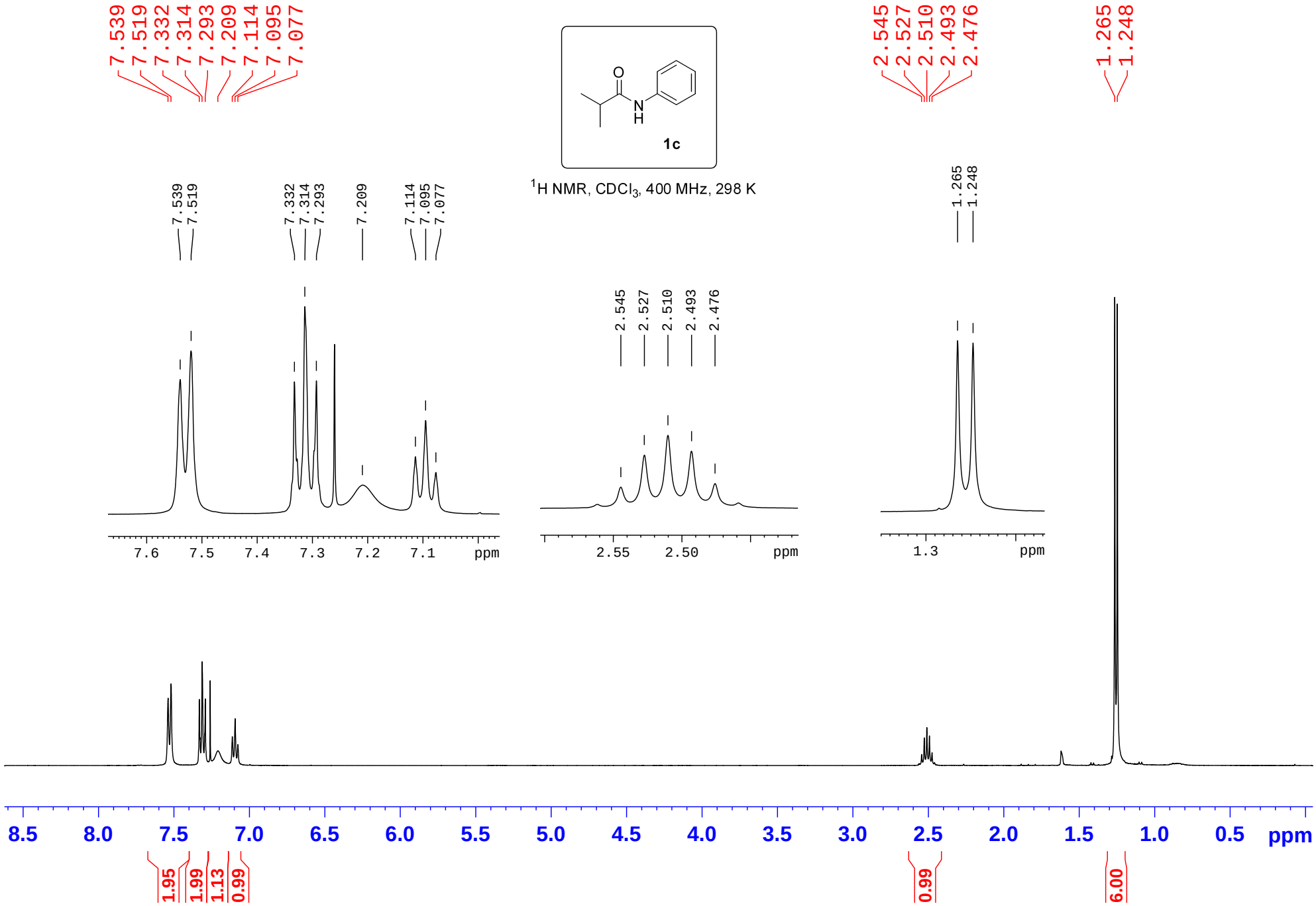
The substrate with aliphatic *N*-substituent (*N*-Methylbenzamide) reacted poorly when performing the reaction under the general reaction conditions given in section **5**. Increasing the reaction temperature to 60 °C unfortunately only gave the desired product in less than 30 % according to crude ^{1}H NMR. Unreacted starting material was recovered and the *N*-methyl-*N*-phenylbenzamide was difficult to isolate due to the formation of multiple byproducts.

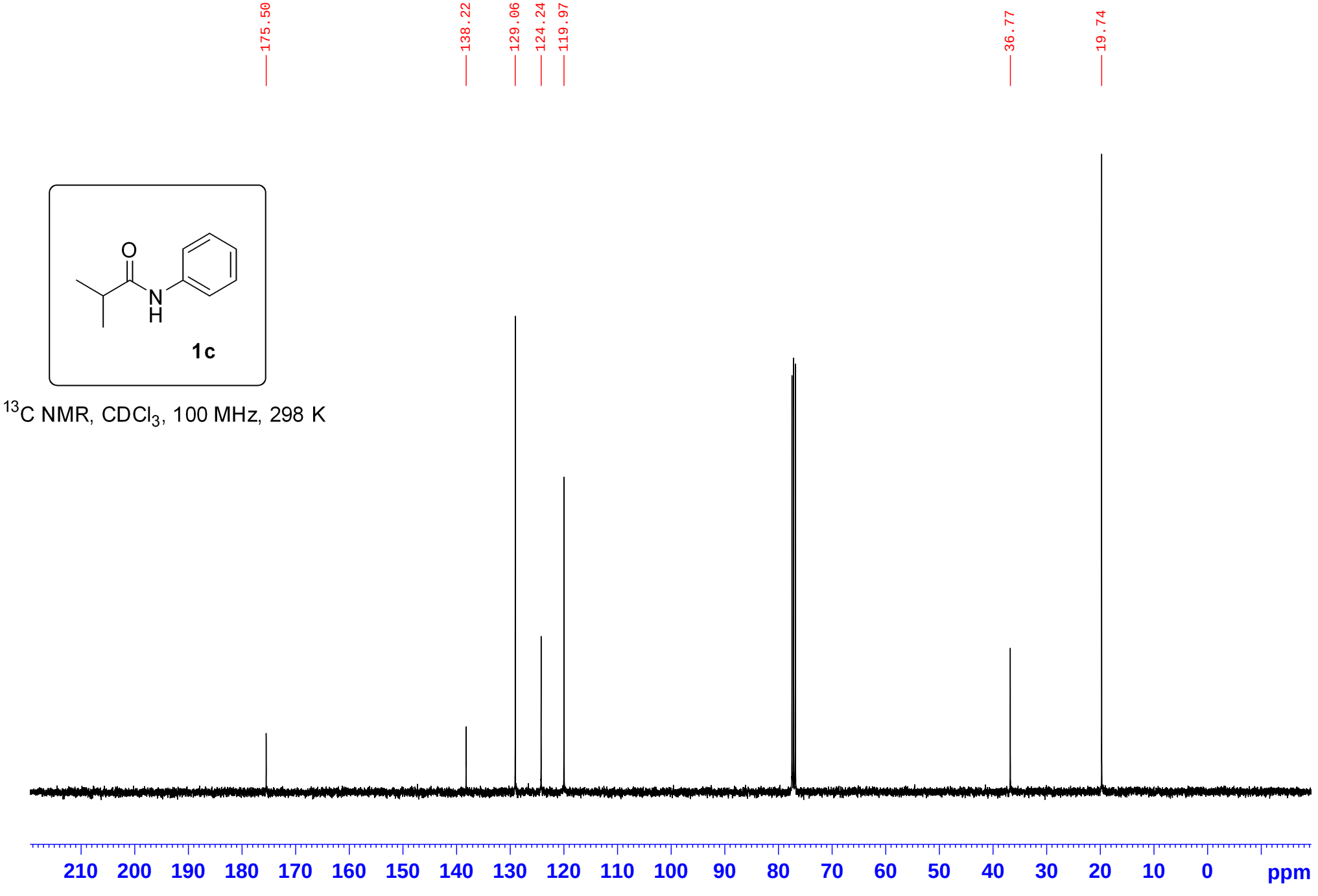
13. References

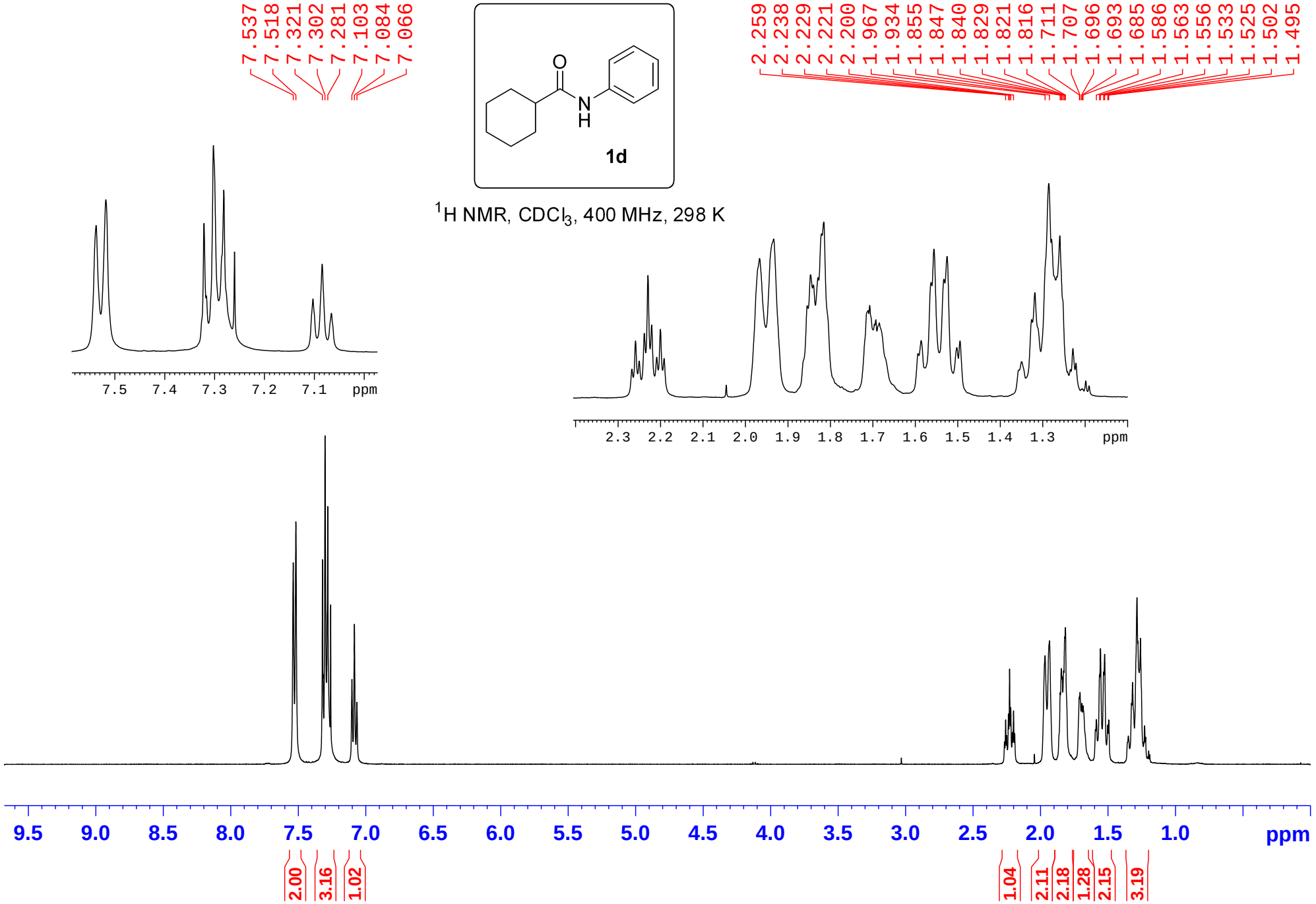
(1) A. I. Vogel, B. S. F., A. J. Hannaford, V. Rogers, P. W. G. Smith, A. R. Tatchell,, *Vogel's Textbook of Practical Organic Chemistry*. 1978.
(2) Seebach, D.; Imwinkelried, R.; Stucky, G., *Helv. Chim. Acta* **1987,** *70*, 448-464.
(3) (a) Bielawski, M.; Olofsson, B., *Chem. Commun.* **2007**, 2521-2523; (b) Bielawski, M.; Zhu, M.; Olofsson, B., *Adv. Synth. Catal.* **2007,** *349*, 2610-2618.
(4) Bielawski, M.; Aili, D.; Olofsson, B., *J. Org. Chem.* **2008,** *73*, 4602-4607.
(5) Zhu, M.; Jalalian, N.; Olofsson, B., *Synlett* **2008**, 592-596.
(6) Jalalian, N.; Petersen, T. B.; Olofsson, B., *Chem. Eur. J.* **2012,** *18*, 14140-14149.
(7) Hossain, M. D.; Kitamura, T., *Tetrahedron* **2006,** *62*, 6955-6960.
(8) Hossain, M. D.; Kitamura, T., *Bull. Chem. Soc. Jpn.* **2007,** *80*, 2213-2219.
(9) Kitamura, T.; Matsuyuki, J.-i.; Nagata, K.; Furuki, R.; Taniguchi, H., *Synthesis* **1992**, 945-946.
(10) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J., *J. Am. Chem. Soc.* **2008,** *130*, 8172-8174.
(11) Ghosh, R.; Lindstedt, E.; Jalalian, N.; Olofsson, B., *ChemistryOpen* **2014,** *3*, 54-57.
(12) Wang, W.; Cong, Y.; Zhang, L.; Huang, Y.; Wang, X.; Zhang, T., *Tetrahedron Lett.* **2014,** *55*, 124-127.
(13) Kaicharla, T.; Thangaraj, M.; Biju, A. T., *Org. Lett.* **2014,** *16*, 1728-1731.
(14) Jalalian, N.; Ishikawa, E. E.; Silva, L. F.; Olofsson, B., *Org. Lett.* **2011,** *13*, 1552-1555.
(15) (a) Li, P.; Cheng, G.; Zhang, H.; Xu, X.; Gao, J.; Cui, X., *J. Org. Chem.* **2014,** *79*, 8156-8162; (b) Wang, Y.; Chen, C.; Peng, J.; Li, M., *Angew. Chem. Int. Ed.* **2013,** *52*, 5323-5327.
(16) Chen, W.-Y.; Gilman, N. W., *J. Heterocycl. Chem.* **1983,** *20*, 663-666.
(17) Mao, S.; Guo, F.; Li, J.; Geng, X.; Yu, J.; Han, J.; Wang, L., *Synlett* **2013,** *24*, 1959-1962.
(18) Zhou, T.; Li, T.-C.; Chen, Z.-C., *Helv. Chim. Acta* **2005,** *88*, 290-296.
(19) Kang, S.-K.; Lee, S.-H.; Lee, D., *Synlett* **2000**, 1022-1024.
(20) (a) He, C.; Chen, C.; Cheng, J.; Liu, C.; Liu, W.; Li, Q.; Lei, A., *Angew. Chem. Int. Ed.* **2008,** *47*, 6414-6417; (b) Güell, I.; Ribas, X., *Eur. J. Org. Chem.* **2014**, 3188-3195; (c) Heyde, C.; Zug, I.; Hartmann, H., *Eur. J. Org. Chem.* **2000**, 3273-3278.
(21) Pintori, D. G.; Greaney, M. F., *Org. Lett.* **2010,** *12*, 168-171.
(22) Buswell, M.; Fleming, I.; Ghosh, U.; Mack, S.; Russell, M.; Clark, B. P., *Org. Biomol. Chem.* **2004,** *2*, 3006-3017.
(23) Ansari, M. I.; Hussain, M. K.; Yadav, N.; Gupta, P. K.; Hajela, K., *Tetrahedron Lett.* **2012,** *53*, 2063-2065.
(24) Dharmasena, P. M.; Oliveira-Campos, A.-M. F.; Raposo, M. M. M.; Shannon, P. V. R., *J. Chem. Res. miniprint* **1994,** *8*, 1601-1611.
(25) Welzel, P., *Chemische Berichte* **1970,** *103*, 1318-1333.
(26) Racine, E.; Monnier, F.; Vors, J.-P.; Taillefer, M., *Org. Lett.* **2011,** *13*, 2818-2821.

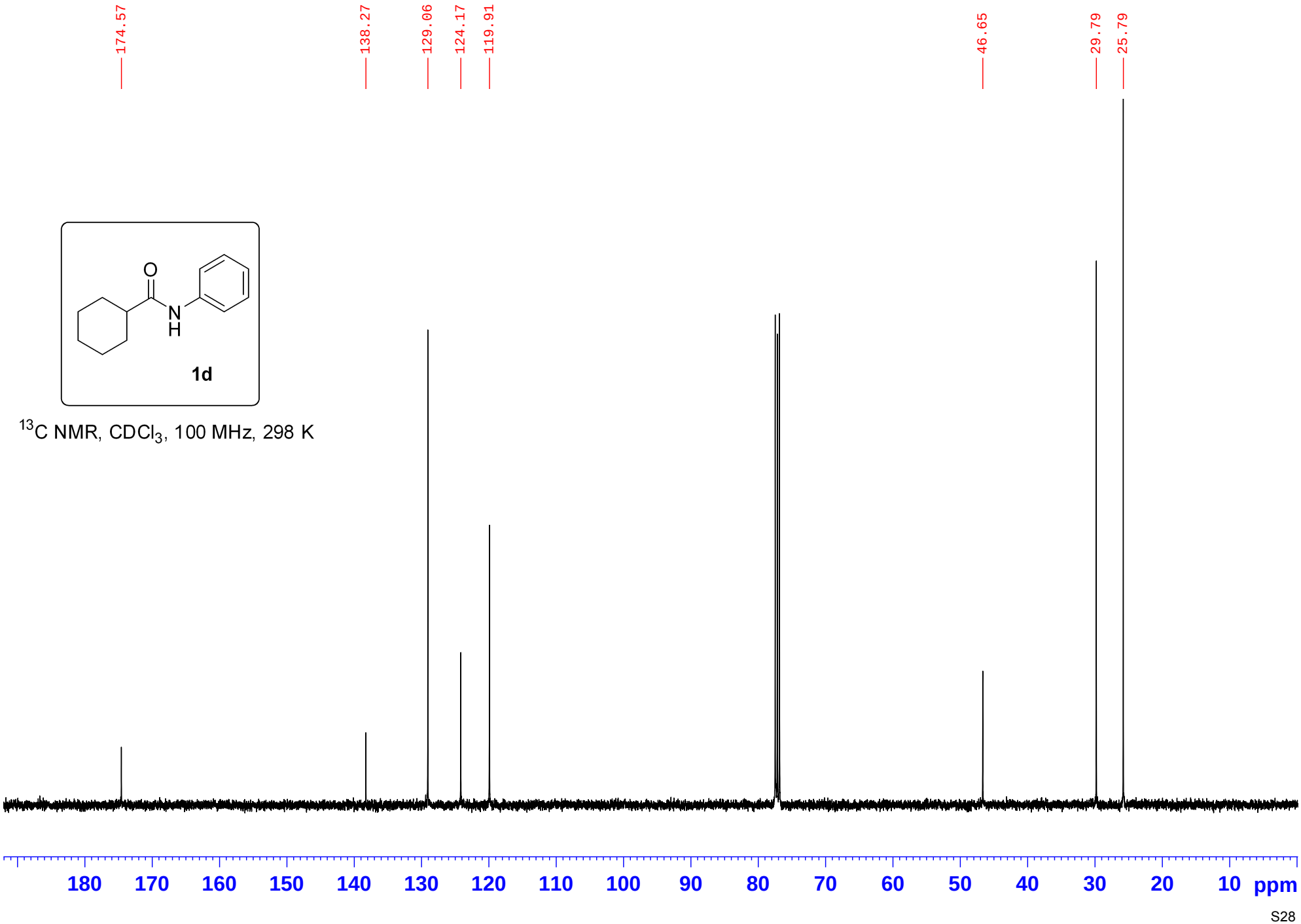
(27) Freeman, H. S.; Butler, J. R.; Freedman, L. D., *J. Org. Chem.* **1978,** *43*, 4975-4978.
(28) Yin, J.; Buchwald, S. L., *Org. Lett.* **2000,** *2*, 1101-1104.
(29) Hicks, J. D.; Hyde, A. M.; Cuezva, A. M.; Buchwald, S. L., *J. Am. Chem. Soc.* **2009,** *131*, 16720-16734.

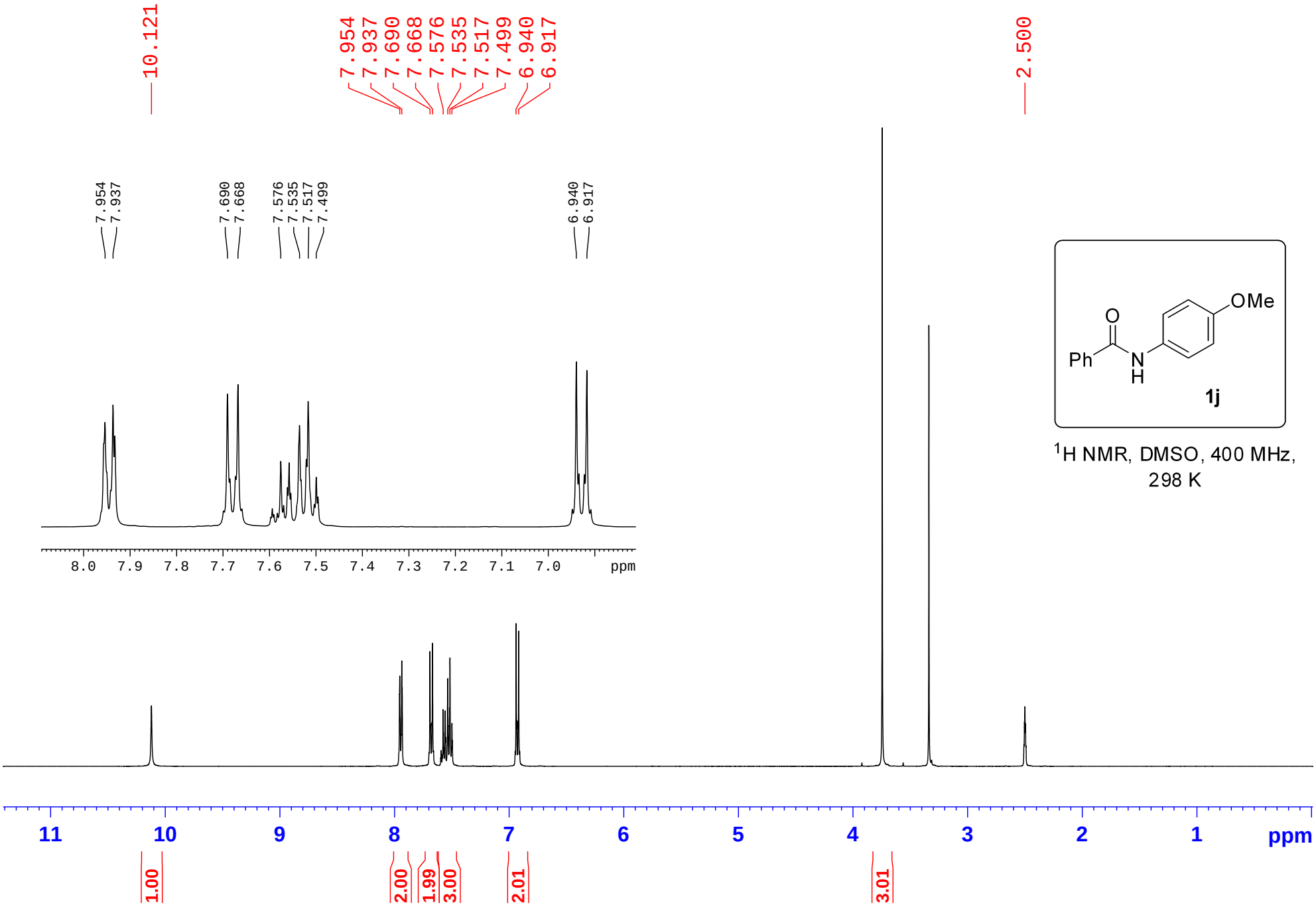
14. Copies of ^{1}H-NMR and ^{13}C-NMR

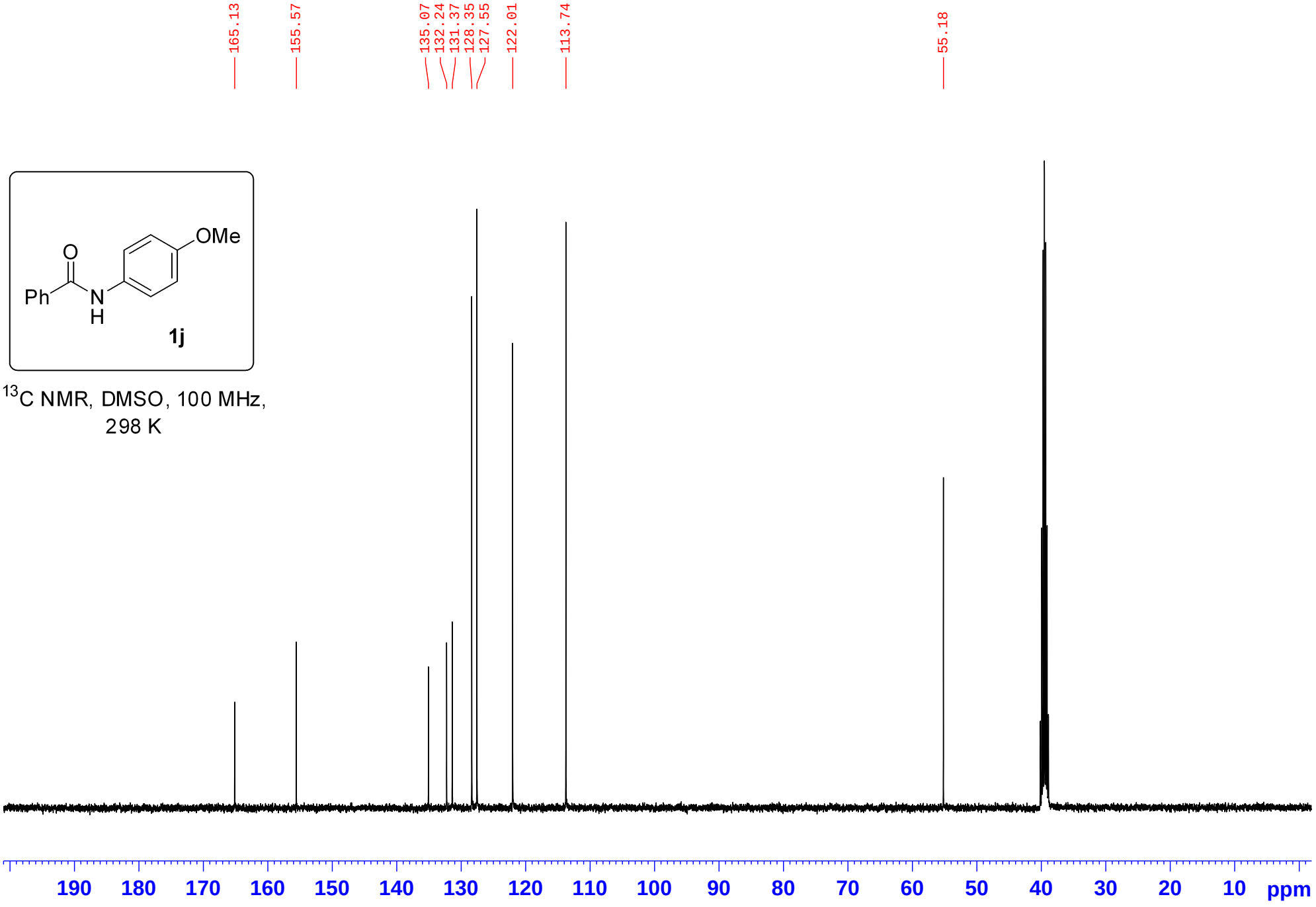

7.539
7.519
7.332
7.314
7.293
7.209
7.114
7.095
7.077
2.545
2.527
2.510
2.493
2.476
1.265
1.248
1c
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
1.95
1.99
1.13
0.99
0.99
6.00


175.50
138.22
129.06
124.24
119.97
36.77
19.74
O
N
H
1c
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

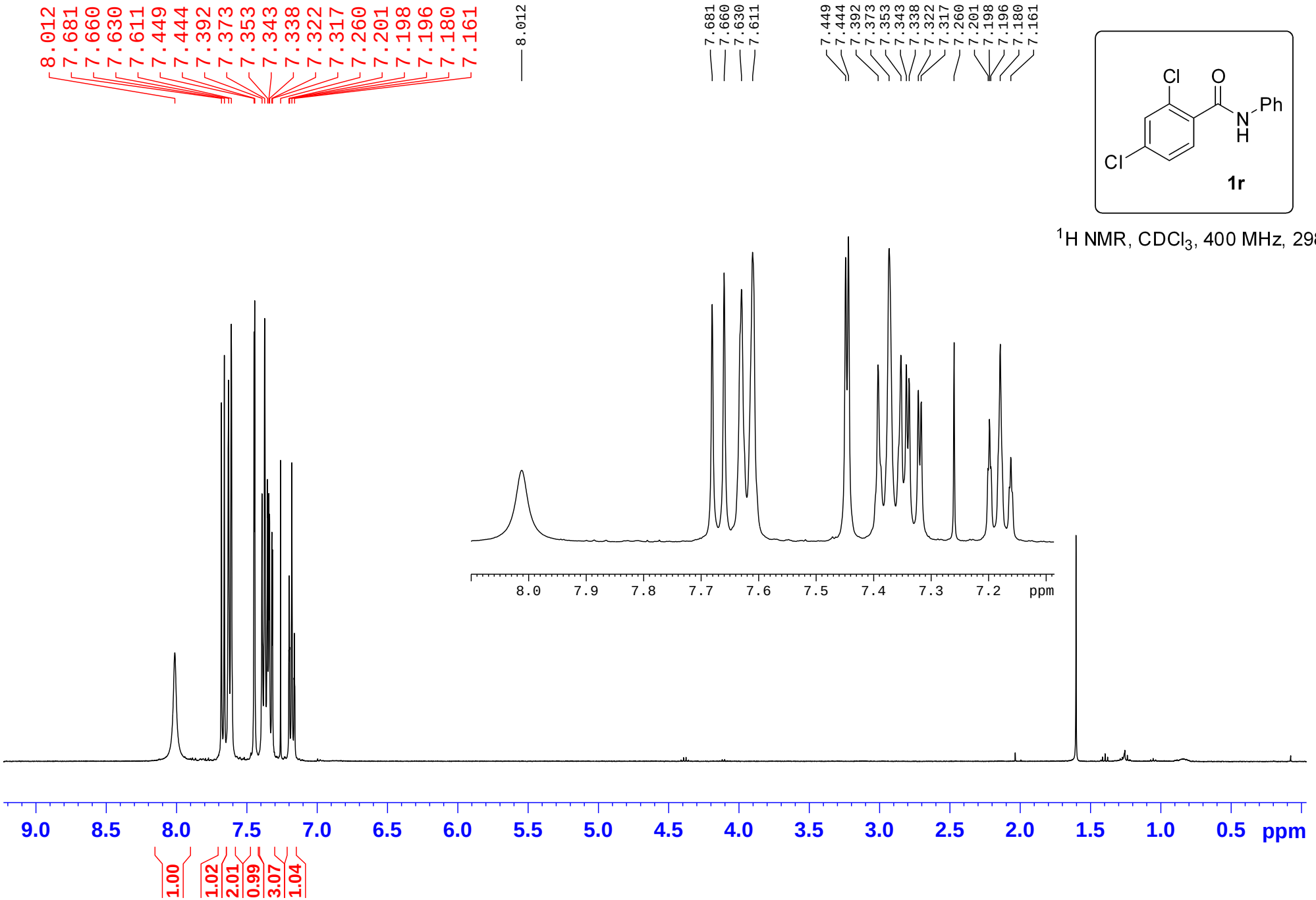

7.537
7.518
7.321
7.302
7.281
7.103
7.084
7.066
2.259
2.238
2.229
2.221
2.200
1.967
1.934
1.855
1.847
1.840
1.829
1.821
1.816
1.711
1.707
1.696
1.693
1.685
1.586
1.563
1.556
1.533
1.525
1.502
1.495
O
N
H
1d
1H NMR, CDCl3, 400 MHz, 298 K
7.5 7.4 7.3 7.2 7.1 ppm
2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 ppm
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 ppm
2.00
3.16
1.02
1.04
2.11
2.18
1.28
2.15
3.19

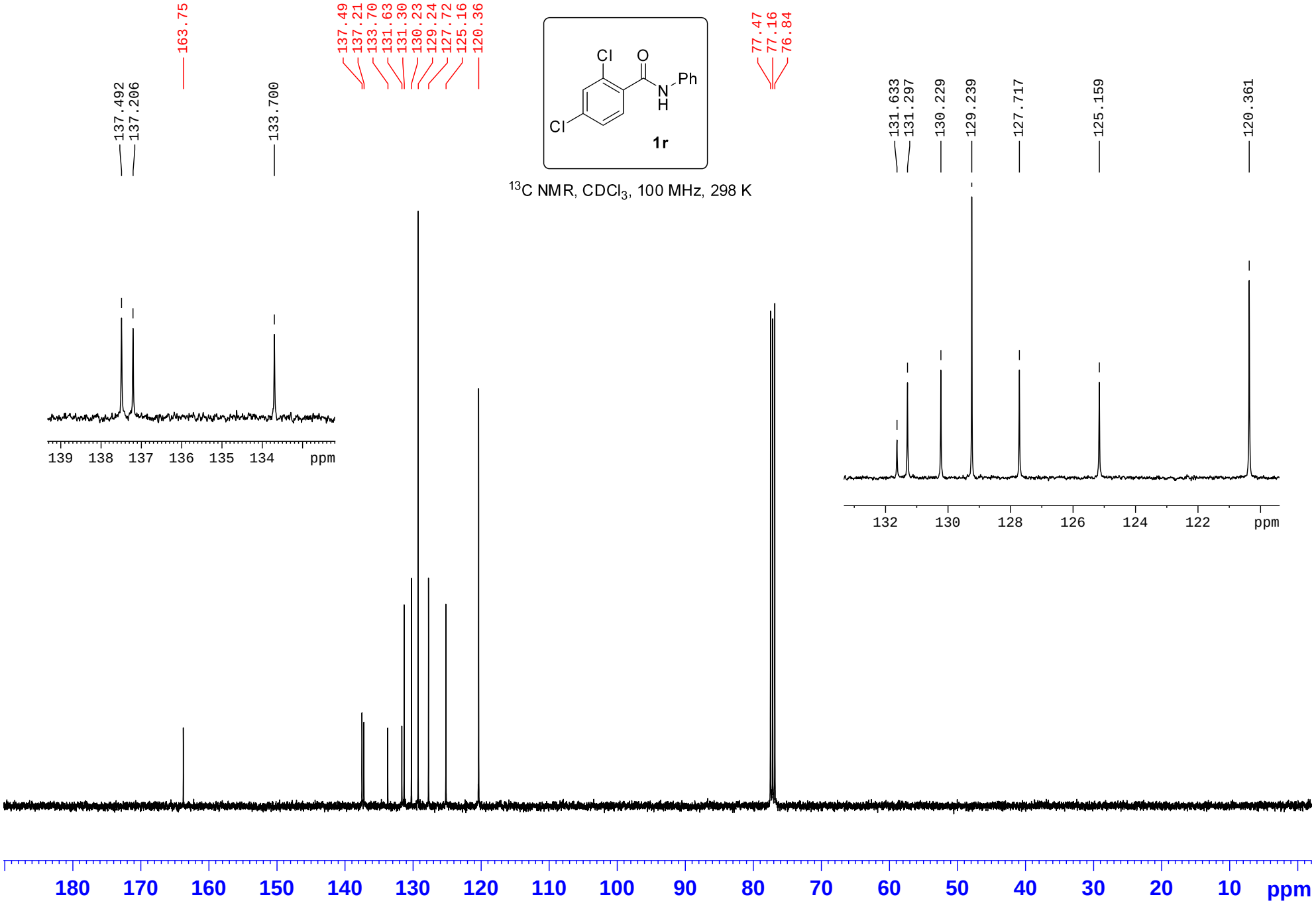

174.57
138.27
129.06
124.17
119.91
46.65
29.79
25.79
O
N
H
1d
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

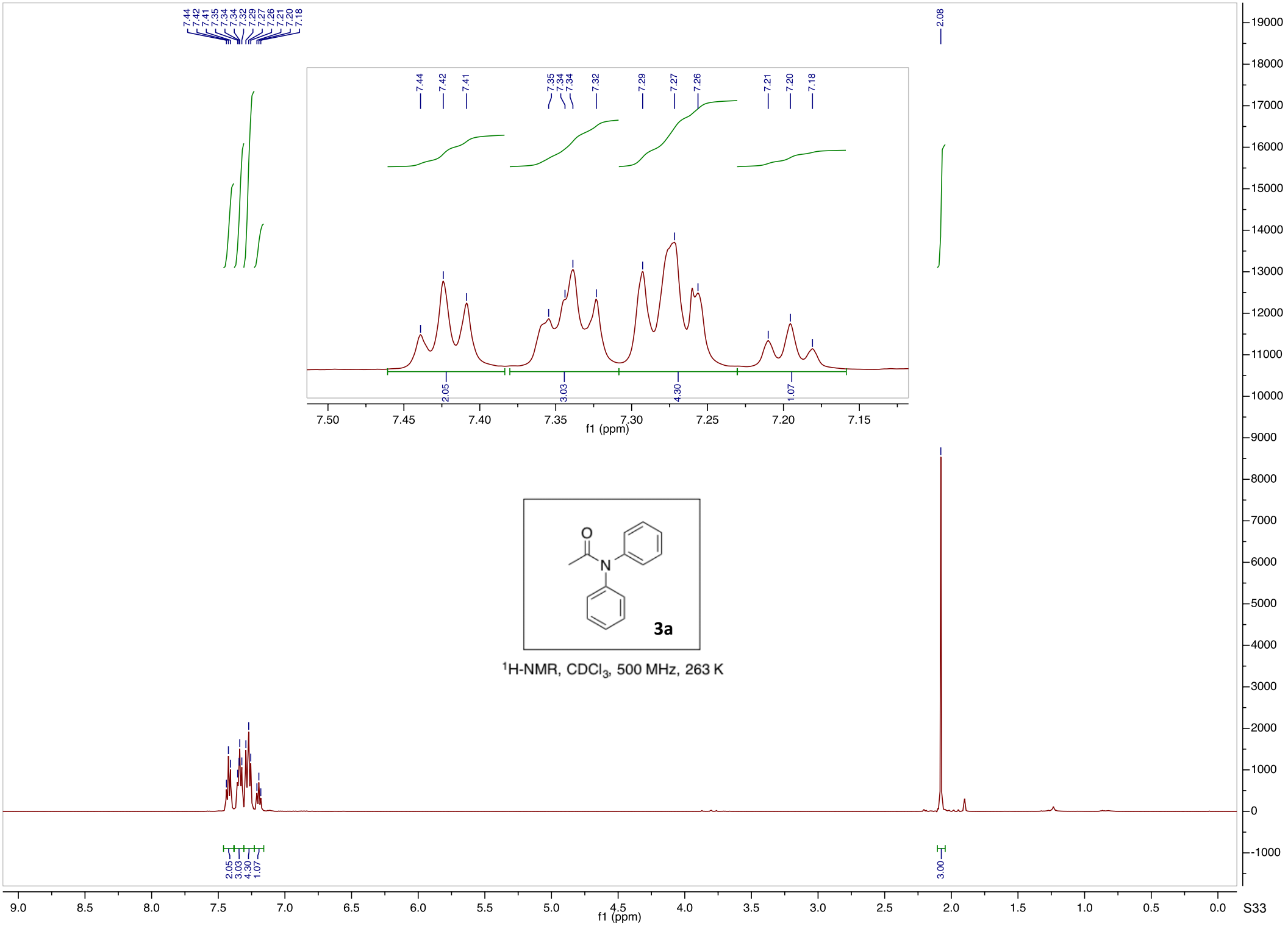

10.121
7.954
7.937
7.690
7.668
7.576
7.535
7.517
7.499
6.940
6.917
2.500
OMe
O
Ph
N
H
1j
1H NMR, DMSO, 400 MHz,
298 K
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 ppm
11 10 9 8 7 6 5 4 3 2 1 ppm
1.00
2.00
1.99
3.00
2.01
3.01



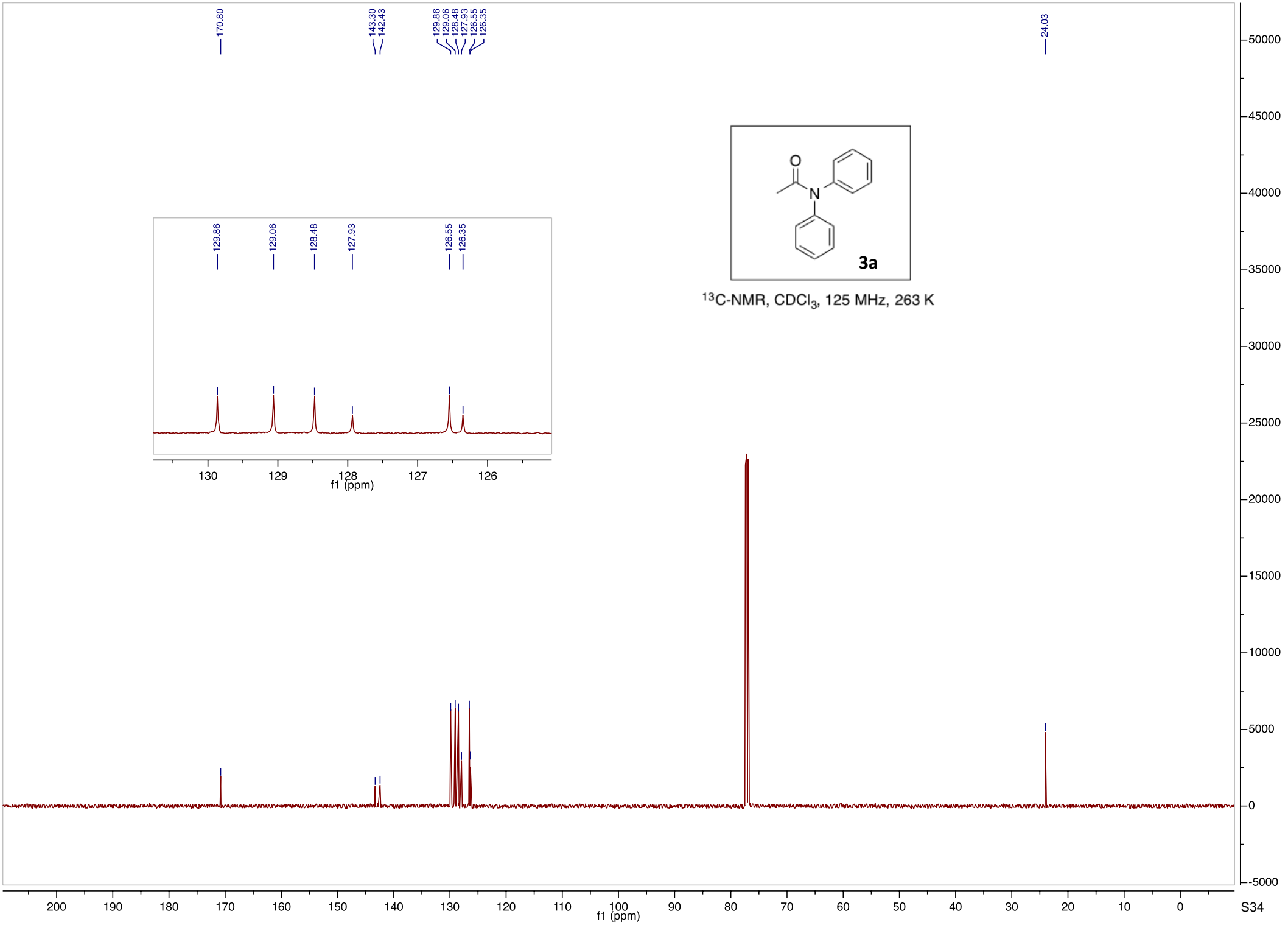
^{13}C NMR, DMSO, 100 MHz, 298 K

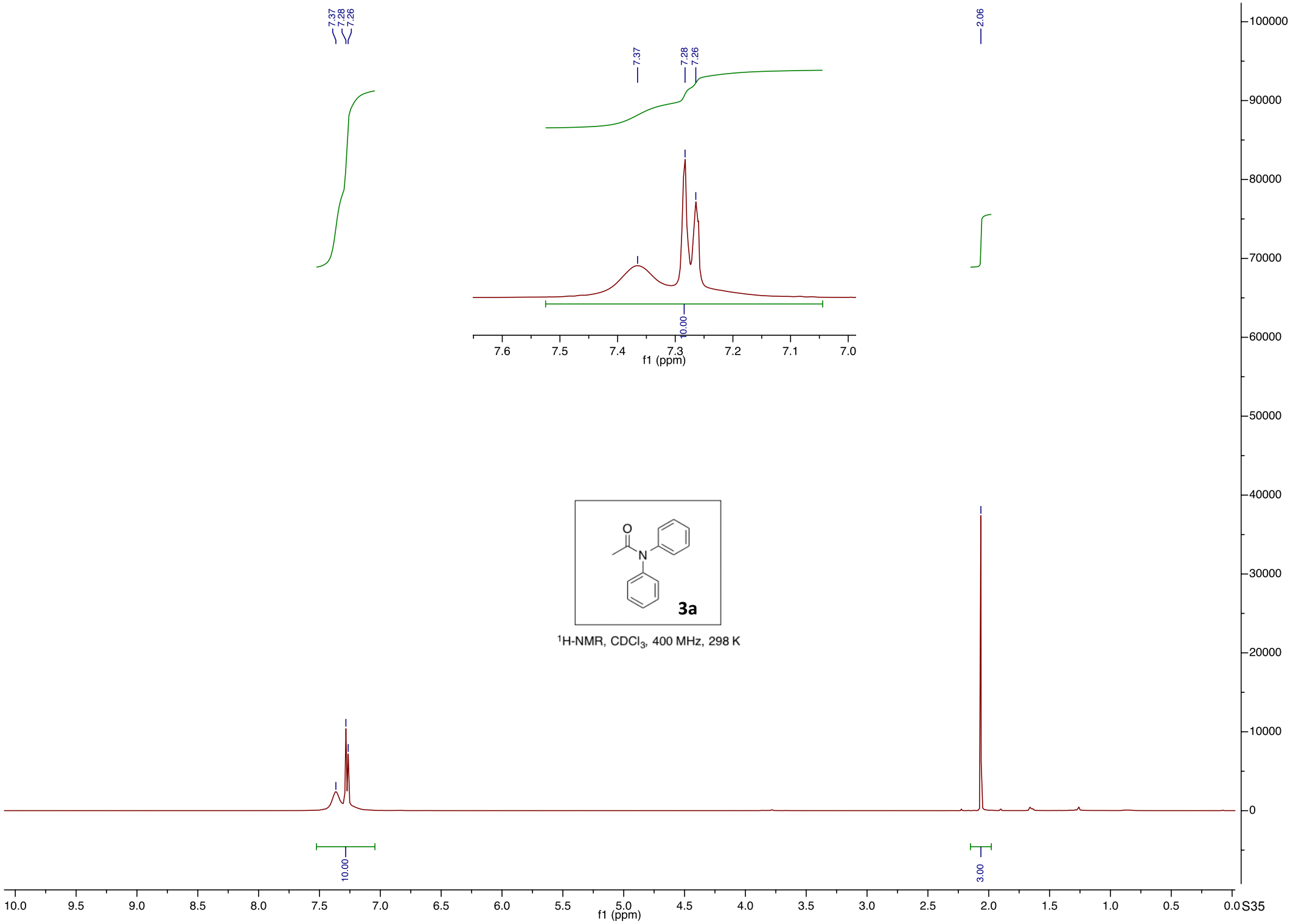

8.012
7.681
7.660
7.630
7.611
7.449
7.444
7.392
7.373
7.353
7.343
7.338
7.322
7.317
7.260
7.201
7.198
7.196
7.180
7.161
Cl
O
Ph
N
H
Cl
1r
1H NMR, CDCl3, 400 MHz, 298 K
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.02
2.01
0.99
3.07
1.04

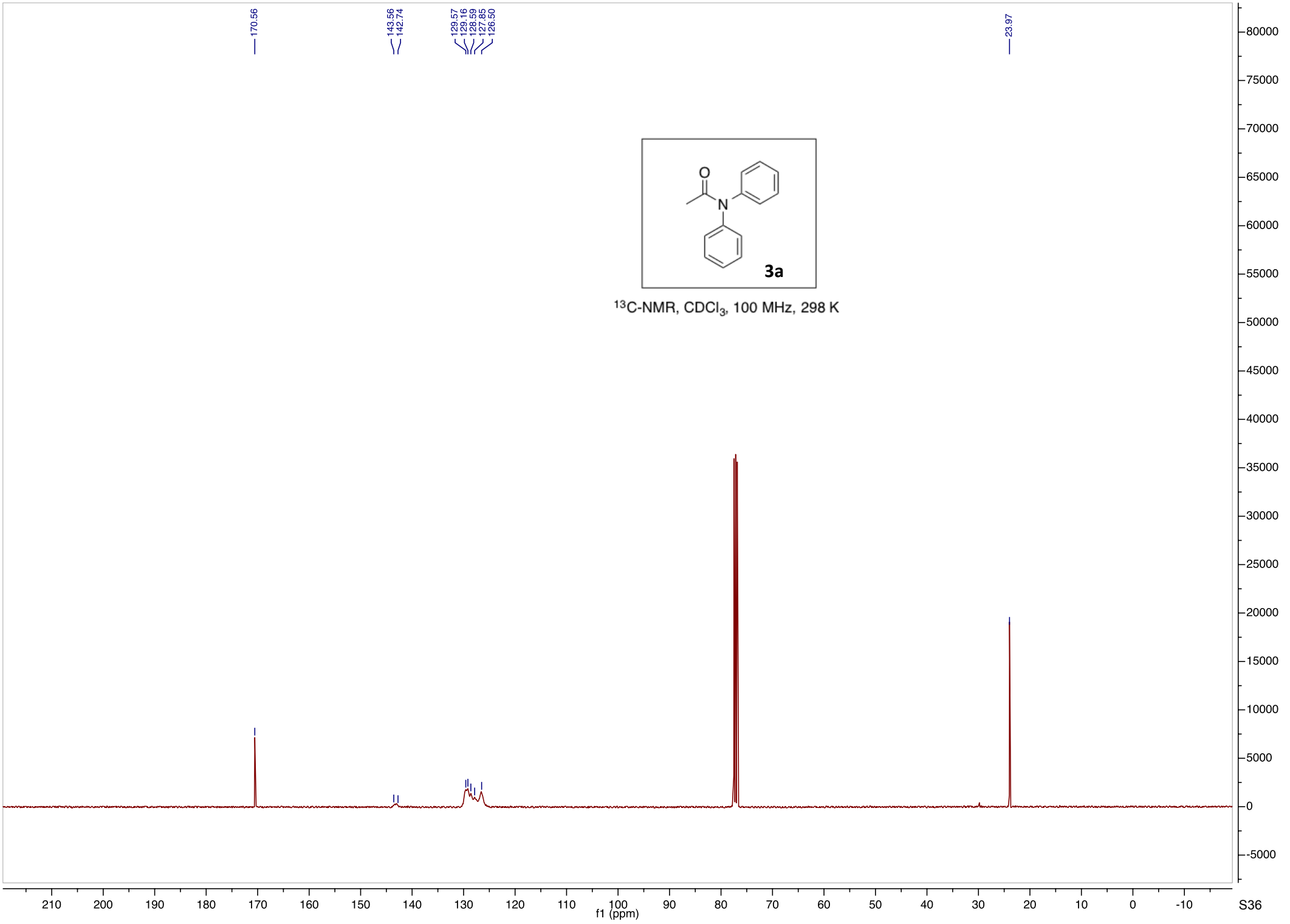

163.75
137.49
137.21
133.70
131.63
131.30
130.23
129.24
127.72
125.16
120.36
77.47
77.16
76.84
137.492
137.206
133.700
131.633
131.297
130.229
129.239
127.717
125.159
120.361
Cl
O
Ph
N
H
Cl
1r
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K
139 138 137 136 135 134 ppm
132 130 128 126 124 122 ppm
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

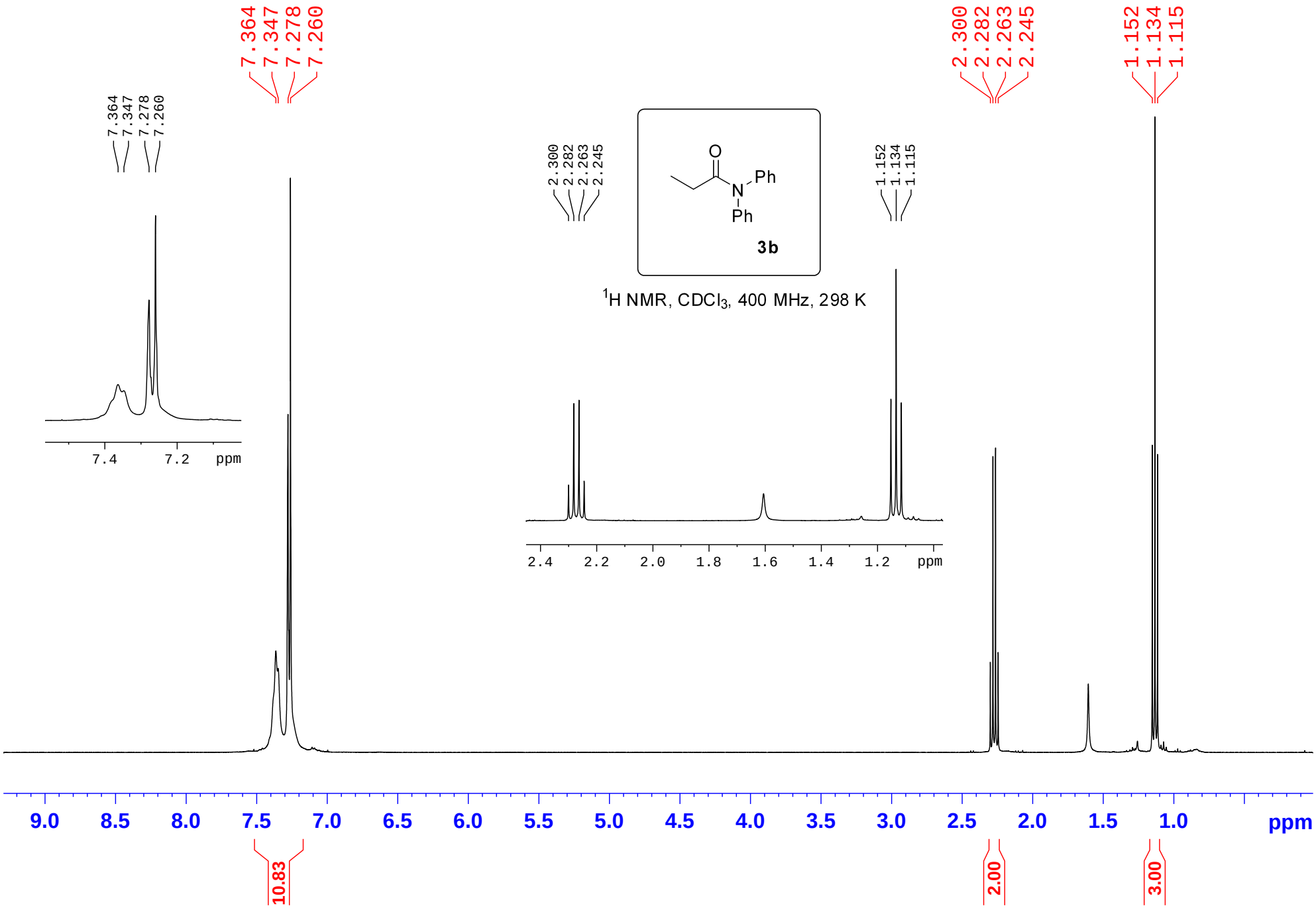


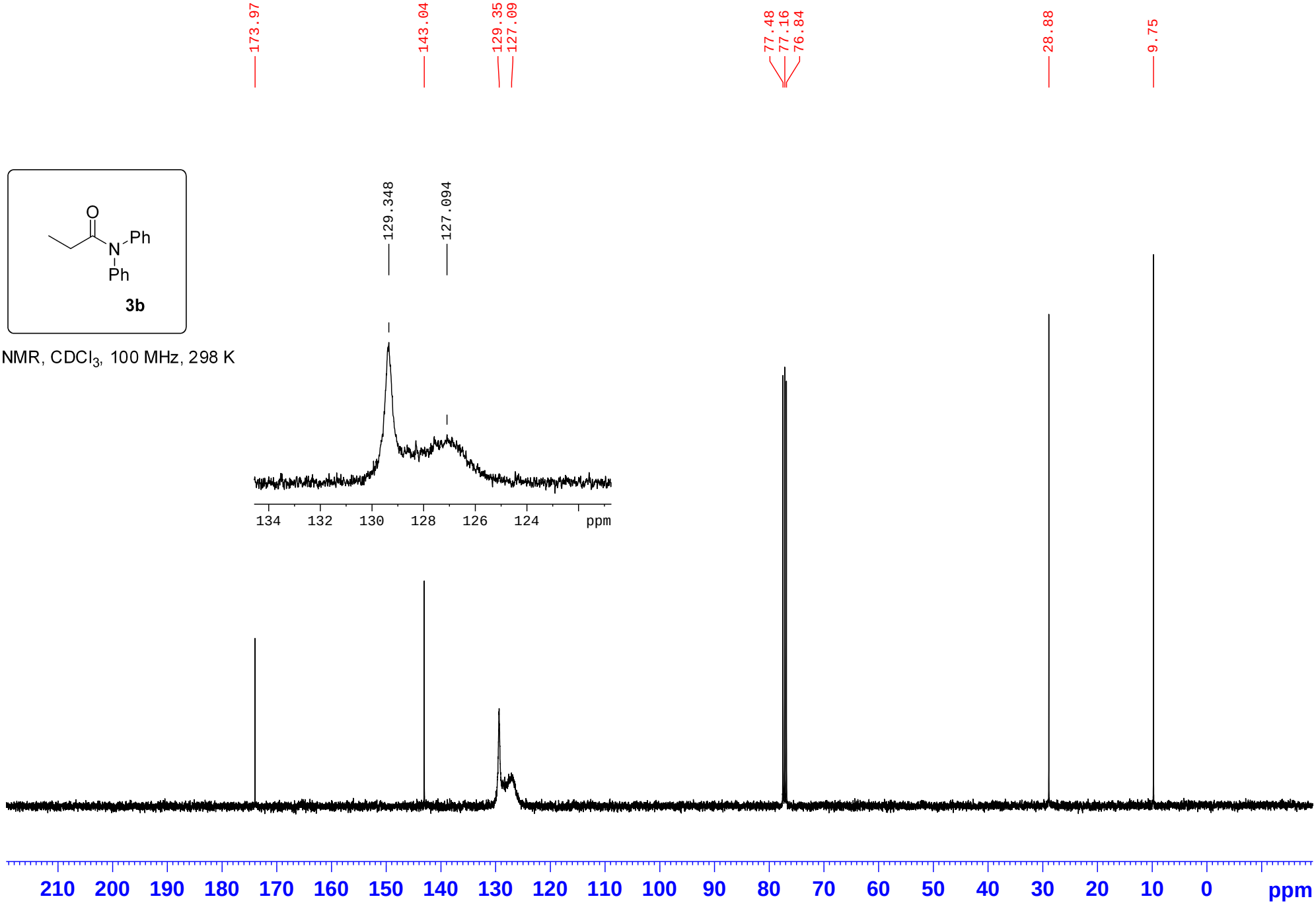
^{1}H-NMR, $CDCl_3$, 500 MHz, 263 K


170.80
143.30
142.43
129.86
129.06
128.48
127.93
126.55
126.35
24.03
O
N
3a
^{13}C-NMR, $CDCl_3$, 125 MHz, 263 K
f1 (ppm)
f1 (ppm)

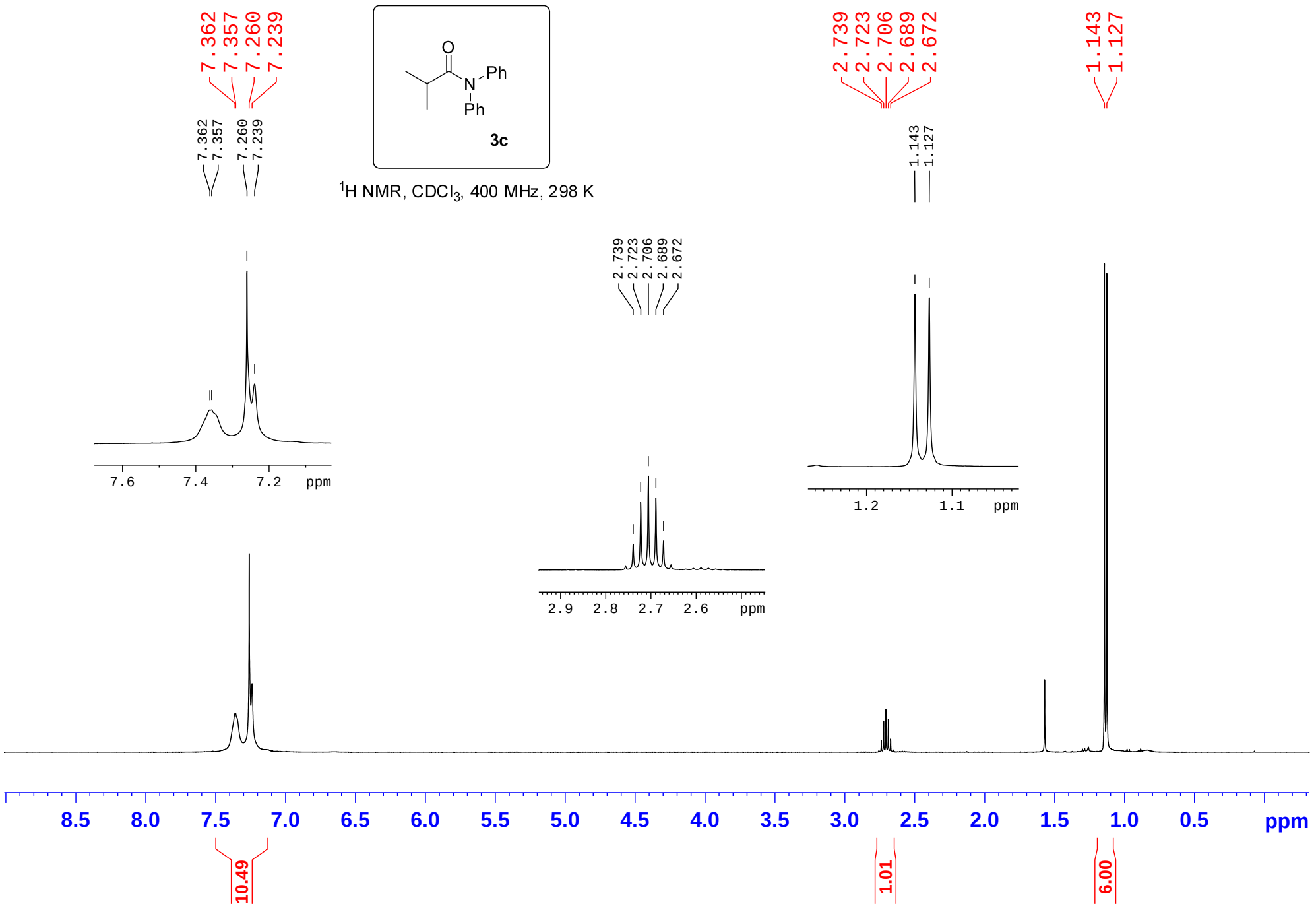

7.37
7.28
7.26
2.06
10.00
3.00
f1 (ppm)
3a
^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K

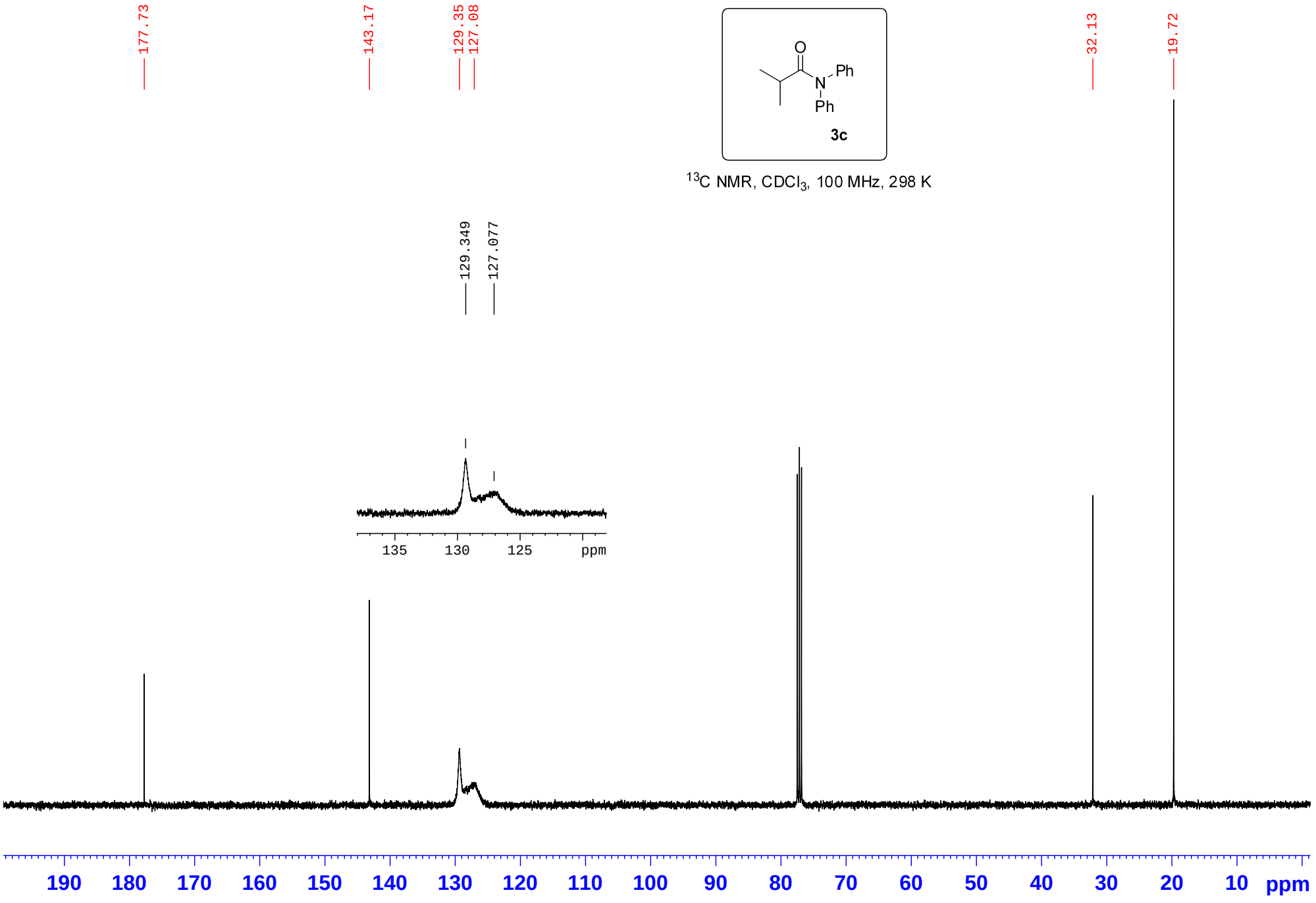

170.56
143.56
142.74
129.57
129.16
128.59
127.85
126.50
23.97
O
N
3a
^{13}C-NMR, $CDCl_3$, 100 MHz, 298 K
80000
75000
70000
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

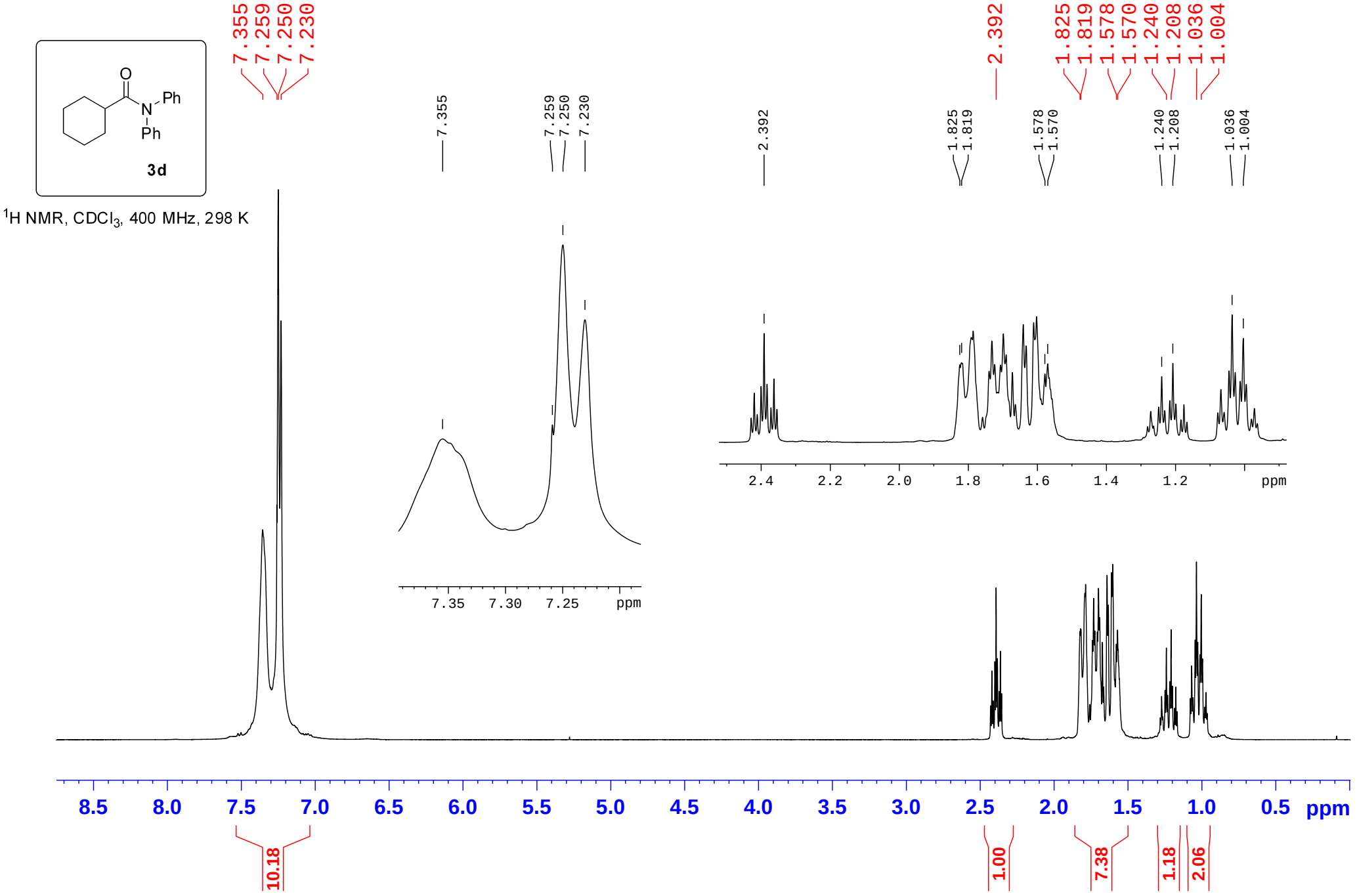

7.364
7.347
7.278
7.260
2.300
2.282
2.263
2.245
1.152
1.134
1.115
O
N
Ph
Ph
3b
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K
7.4
7.2
ppm
2.4
2.2
2.0
1.8
1.6
1.4
1.2
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
10.83
2.00
3.00

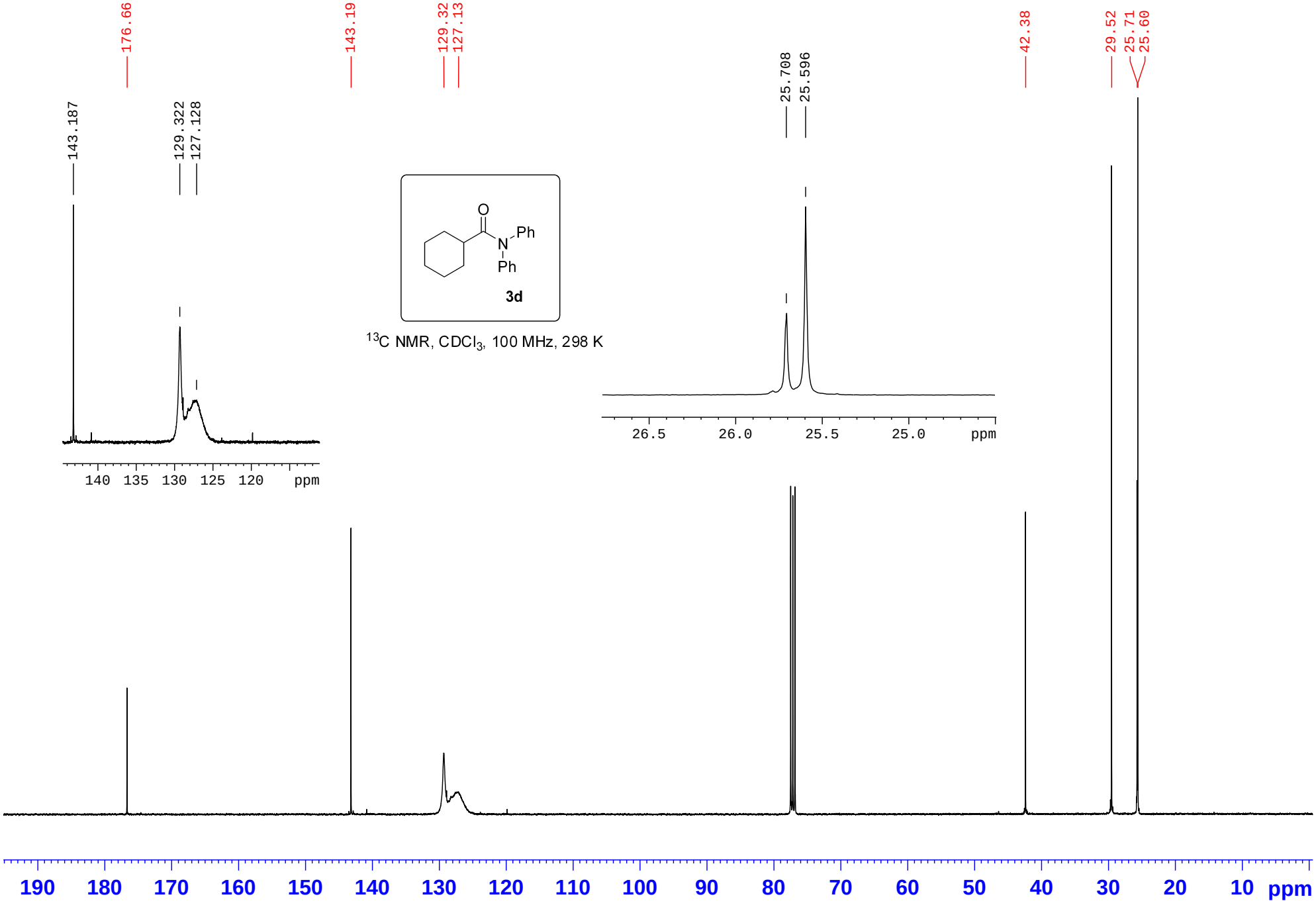


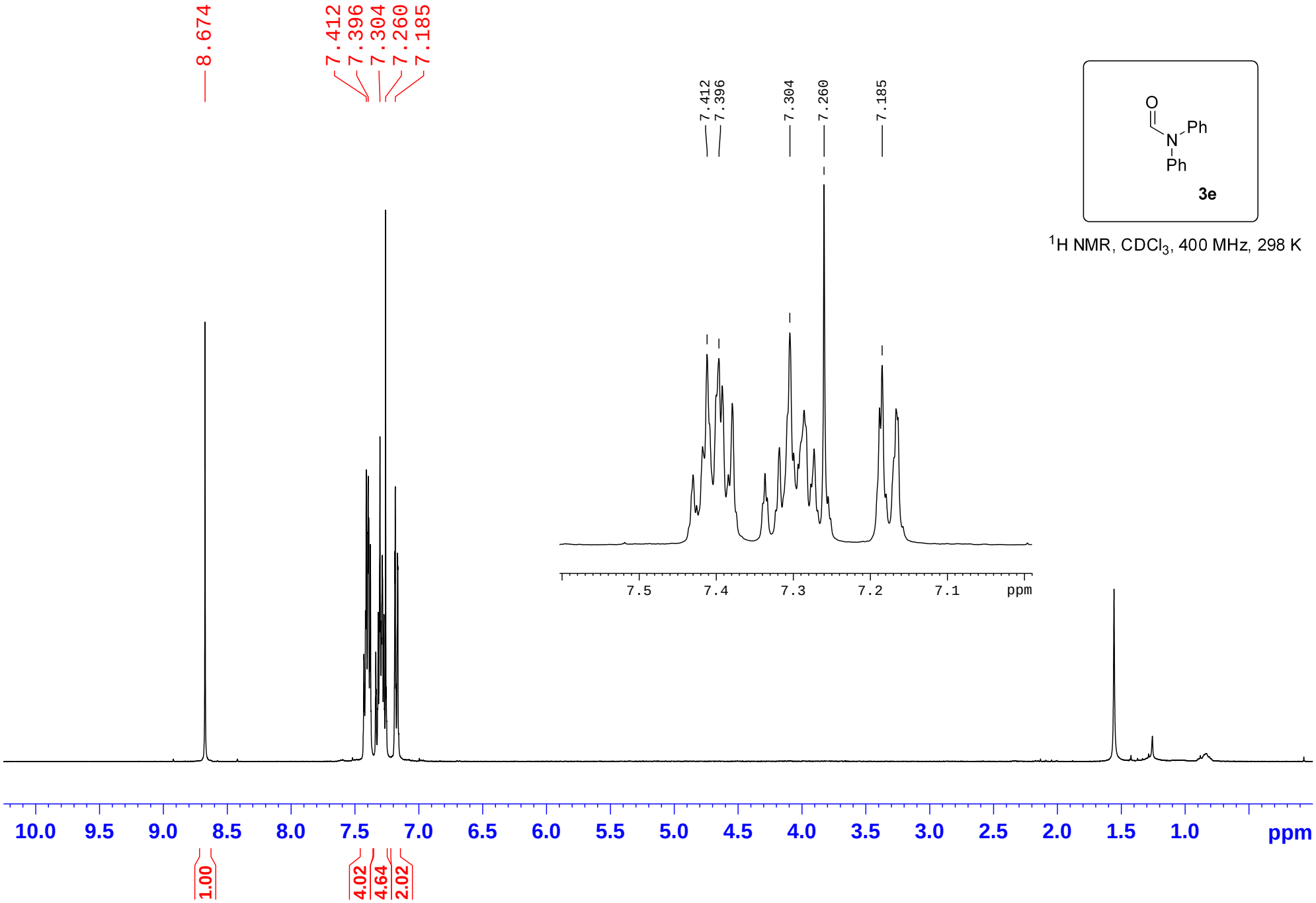
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K

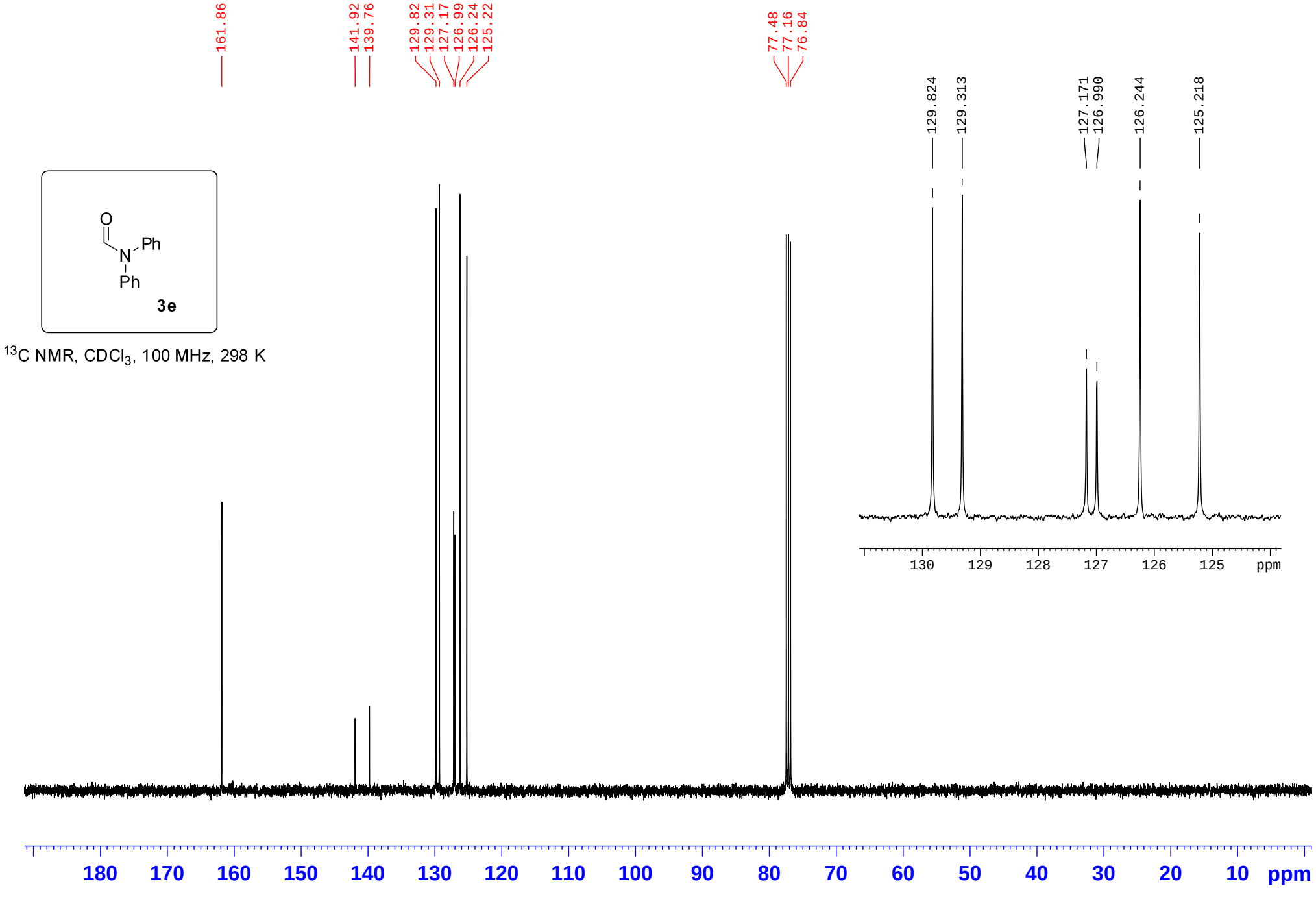

7.362
7.357
7.260
7.239
O
N
Ph
Ph
3c
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K
2.739
2.723
2.706
2.689
2.672
1.143
1.127
7.6
7.4
7.2
ppm
2.9
2.8
2.7
2.6
ppm
1.2
1.1
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
10.49
1.01
6.00

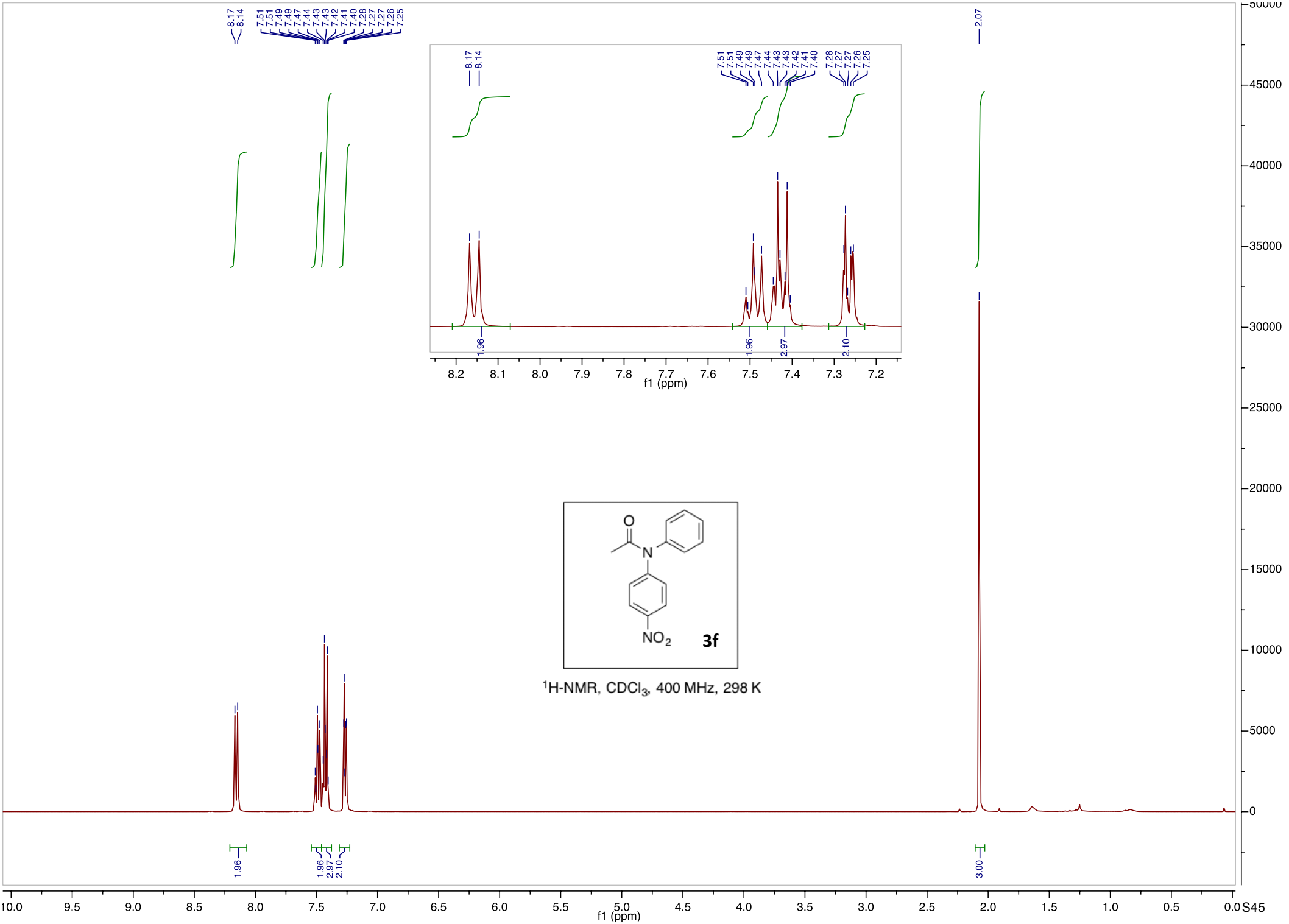

177.73
143.17
129.35
127.08
32.13
19.72
O
N
Ph
Ph
3c
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K
129.349
127.077
135
130
125
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

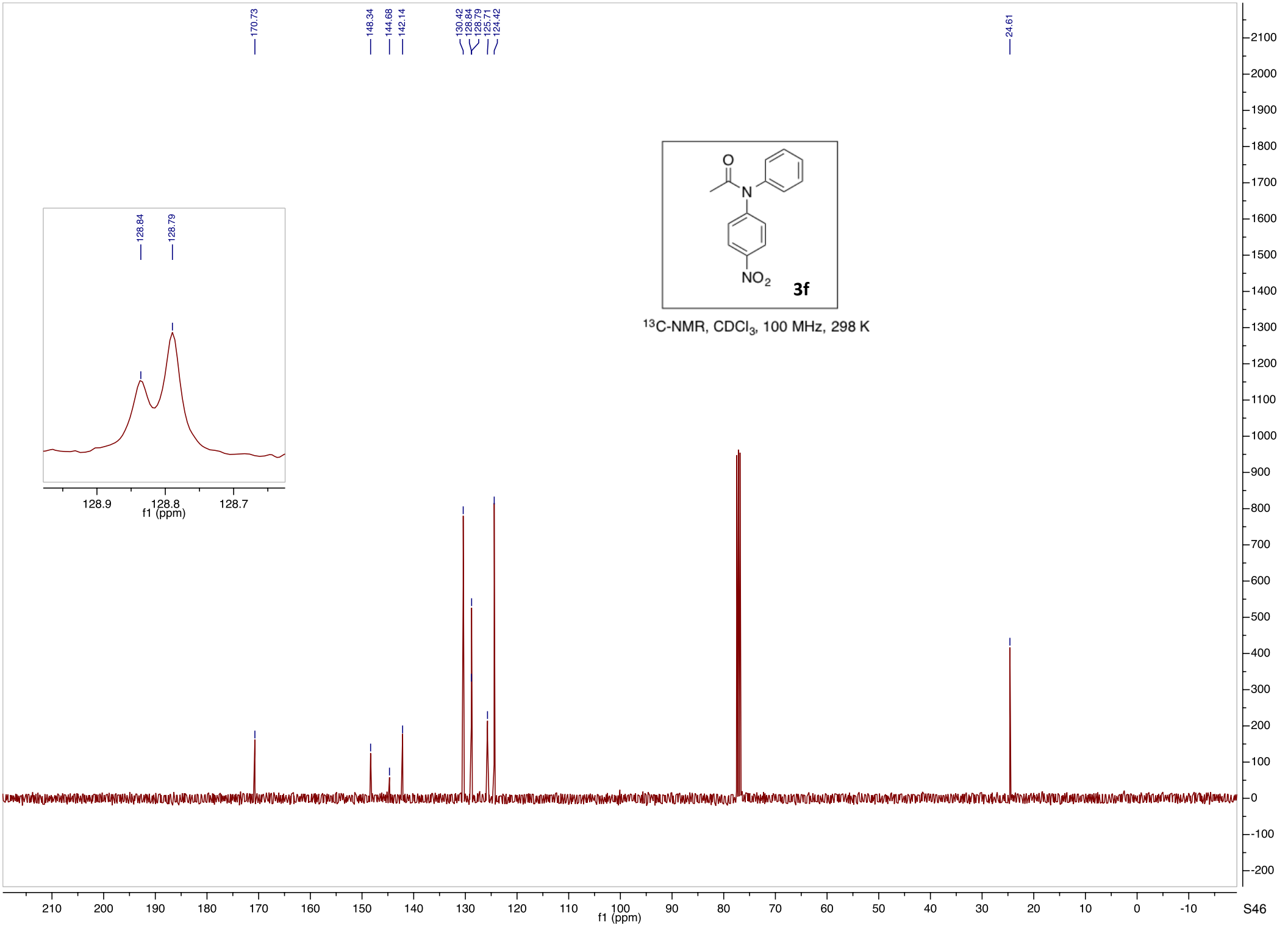

7.355
7.259
7.250
7.230
2.392
1.825
1.819
1.578
1.570
1.240
1.208
1.036
1.004
O
N
Ph
Ph
3d
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K
7.35
7.30
7.25
ppm
2.4
2.2
2.0
1.8
1.6
1.4
1.2
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
10.18
1.00
7.38
1.18
2.06

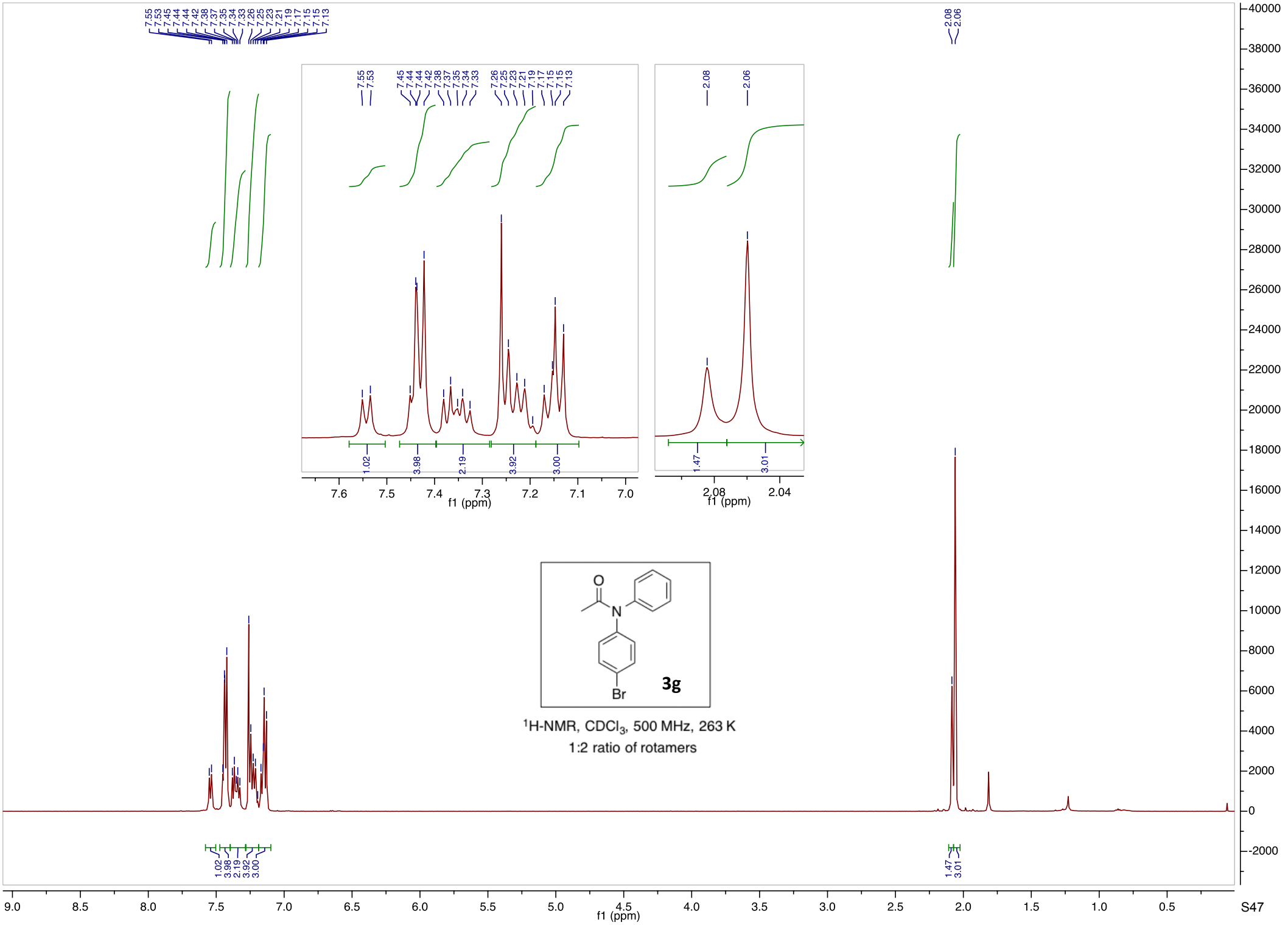

176.66
143.19
129.32
127.13
42.38
29.52
25.71
25.60
143.187
129.322
127.128
25.708
25.596
O
N
Ph
Ph
3d
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K
140 135 130 125 120 ppm
26.5 26.0 25.5 25.0 ppm
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

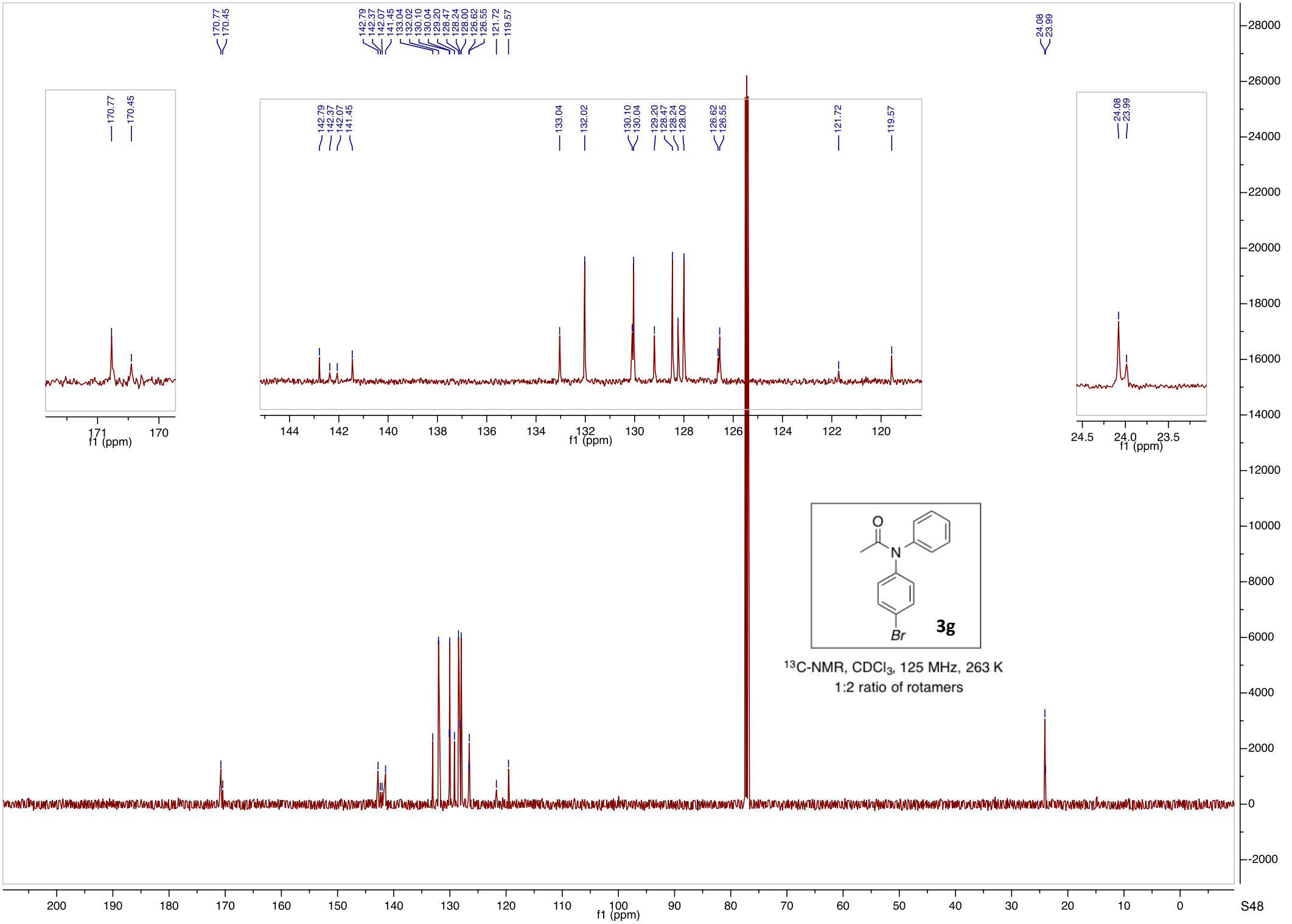

8.674
7.412
7.396
7.304
7.260
7.185
7.412
7.396
7.304
7.260
7.185
7.5
7.4
7.3
7.2
7.1
ppm
O
Ph
N
Ph
3e
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
4.02
4.64
2.02

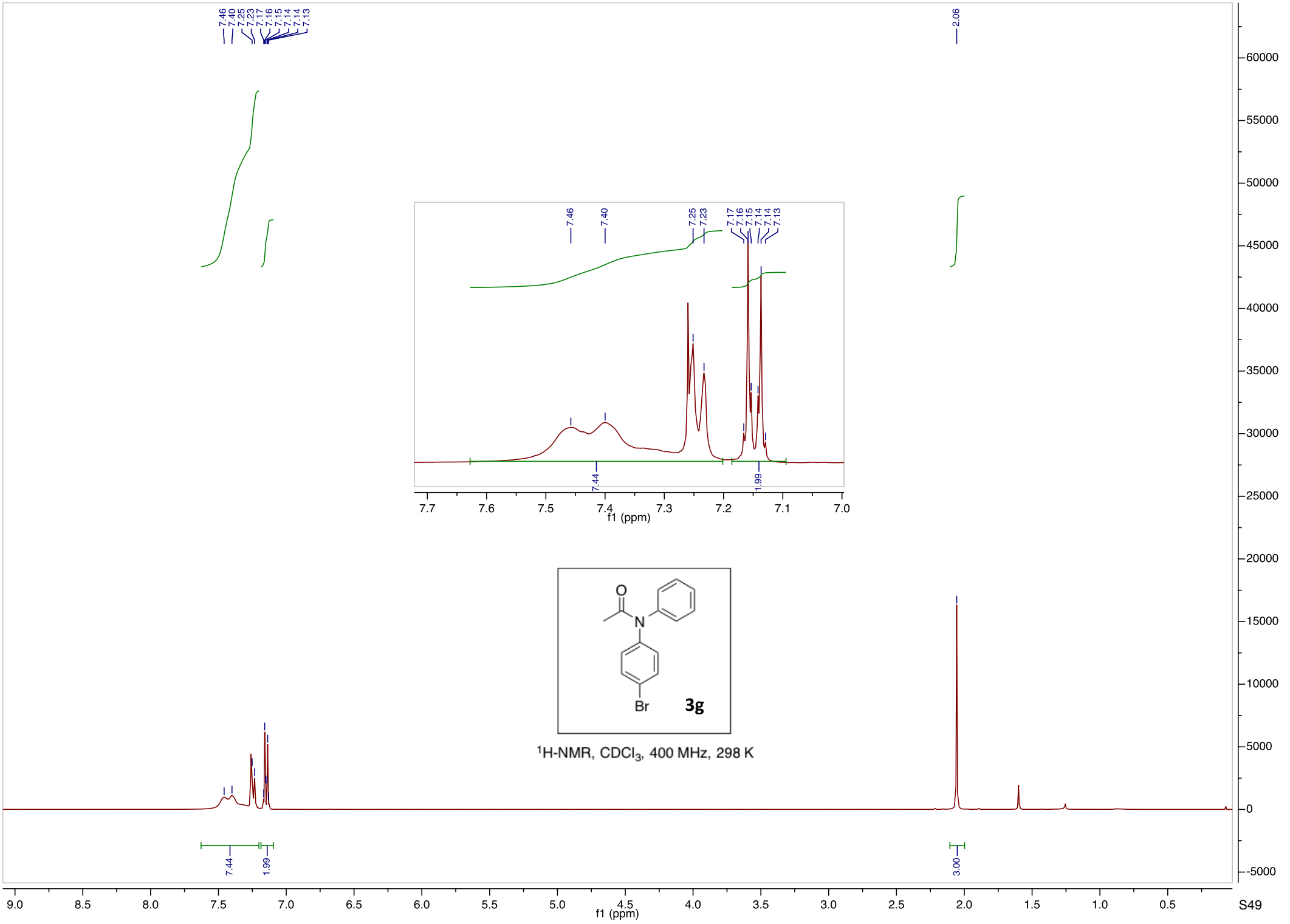

161.86
141.92
139.76
129.82
129.31
127.17
126.99
126.24
125.22
77.48
77.16
76.84
O
N
Ph
Ph
3e
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K
129.824
129.313
127.171
126.990
126.244
125.218
130
129
128
127
126
125
ppm
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.17
8.14
7.51
7.51
7.49
7.49
7.47
7.44
7.43
7.43
7.42
7.41
7.40
7.28
7.27
7.27
7.26
7.25
2.07
1.96
1.96
2.97
2.10
3.00
f1 (ppm)
O
N
NO2
3f
1H-NMR, CDCl3, 400 MHz, 298 K

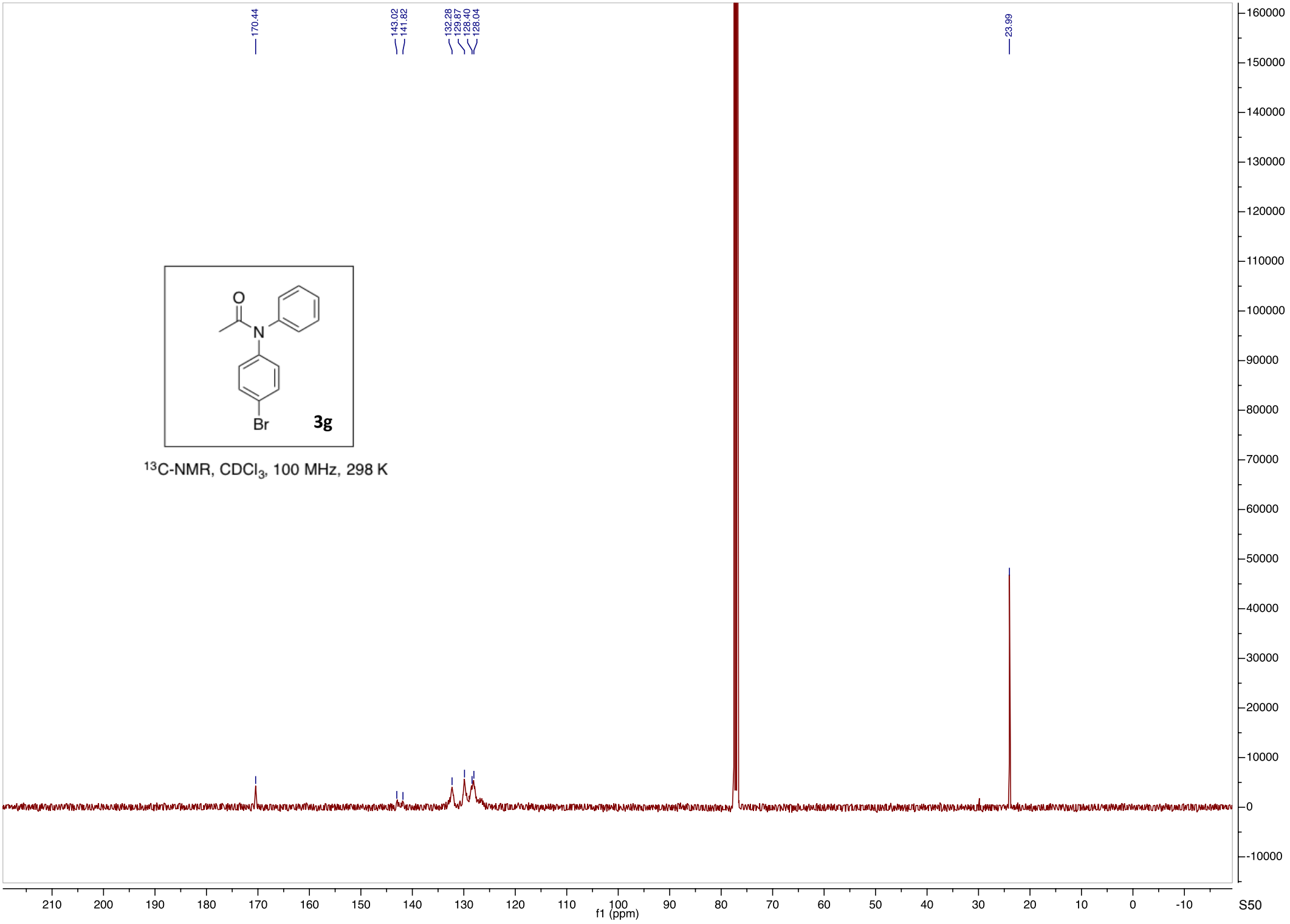

170.73
148.34
144.68
142.14
130.42
128.84
128.79
125.71
124.42
24.61
128.84
128.79
128.9
128.8
128.7
f1 (ppm)
O
N
NO2
3f
13C-NMR, CDCl3, 100 MHz, 298 K
f1 (ppm)

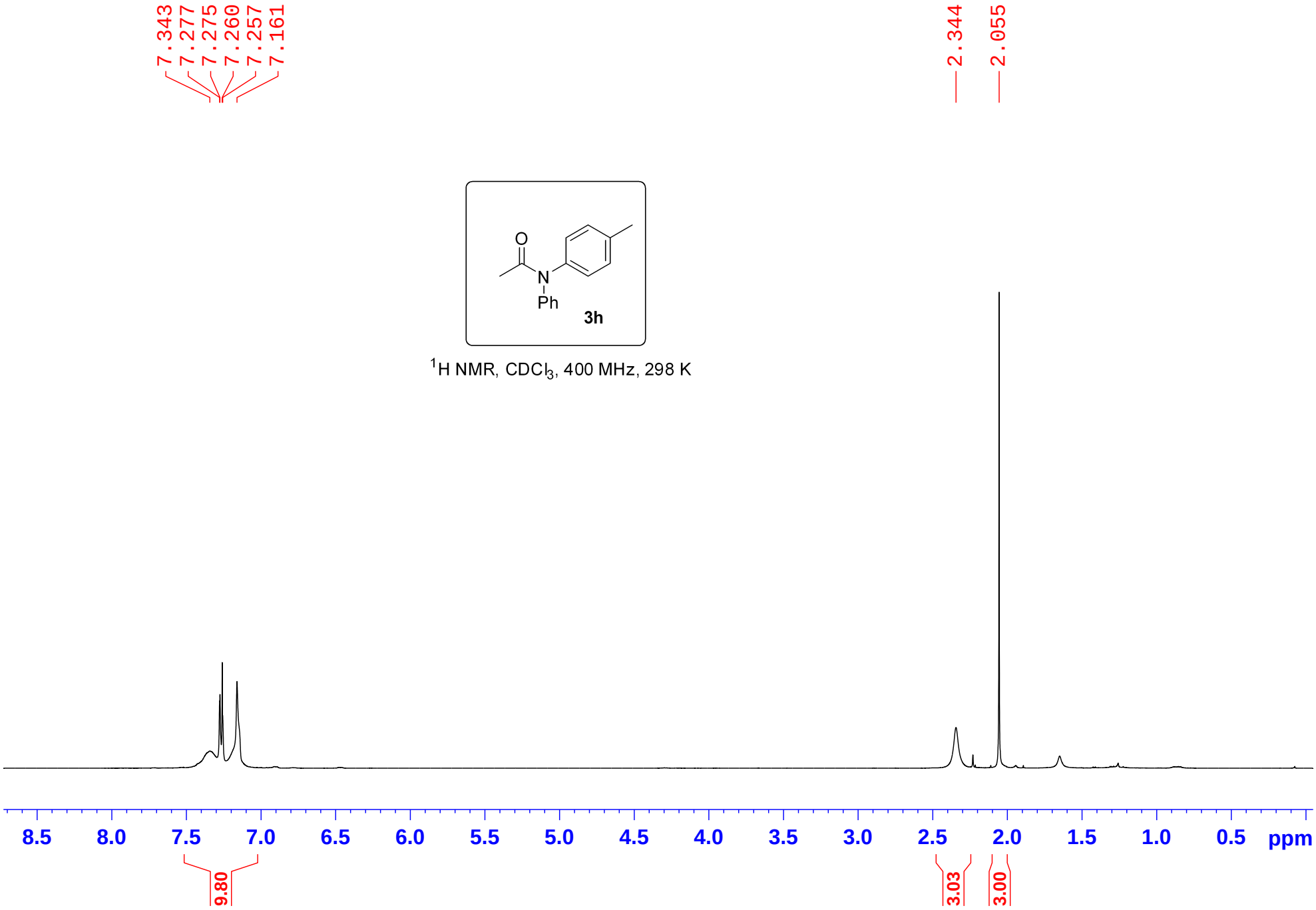

7.55
7.53
7.45
7.44
7.44
7.42
7.38
7.37
7.35
7.34
7.33
7.26
7.25
7.23
7.21
7.19
7.17
7.15
7.15
7.13
2.08
2.06
1.02
3.98
2.19
3.92
3.00
1.47
3.01
f1 (ppm)
O
N
Br
3g
1H-NMR, CDCl3, 500 MHz, 263 K
1:2 ratio of rotamers


170.77
170.45
142.79
142.37
142.07
141.45
133.04
132.02
130.10
130.04
129.20
128.47
128.24
128.00
126.62
126.55
121.72
119.57
24.08
23.99
f1 (ppm)
O
N
Br
3g
13C-NMR, CDCl3, 125 MHz, 263 K
1:2 ratio of rotamers

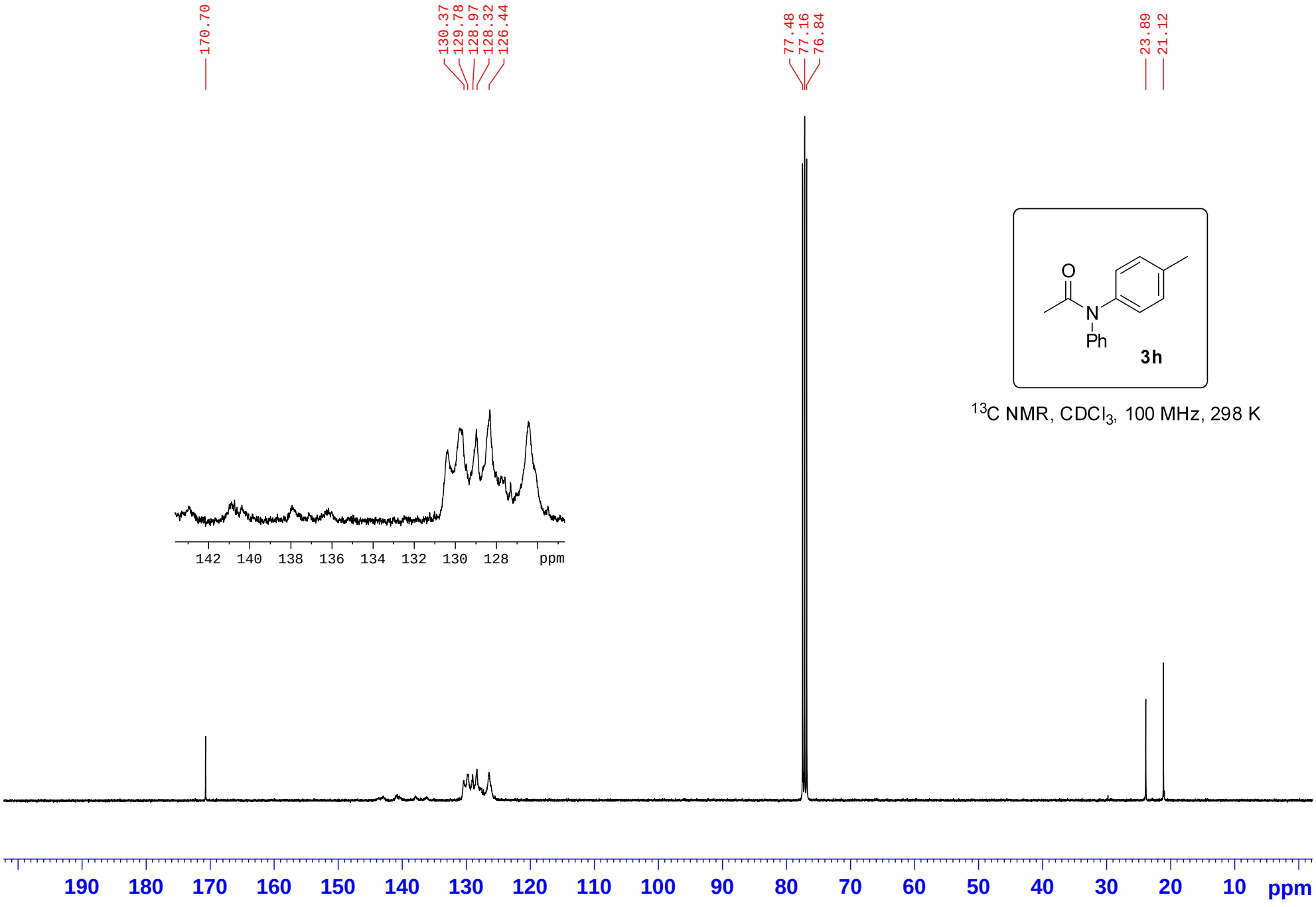


^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K

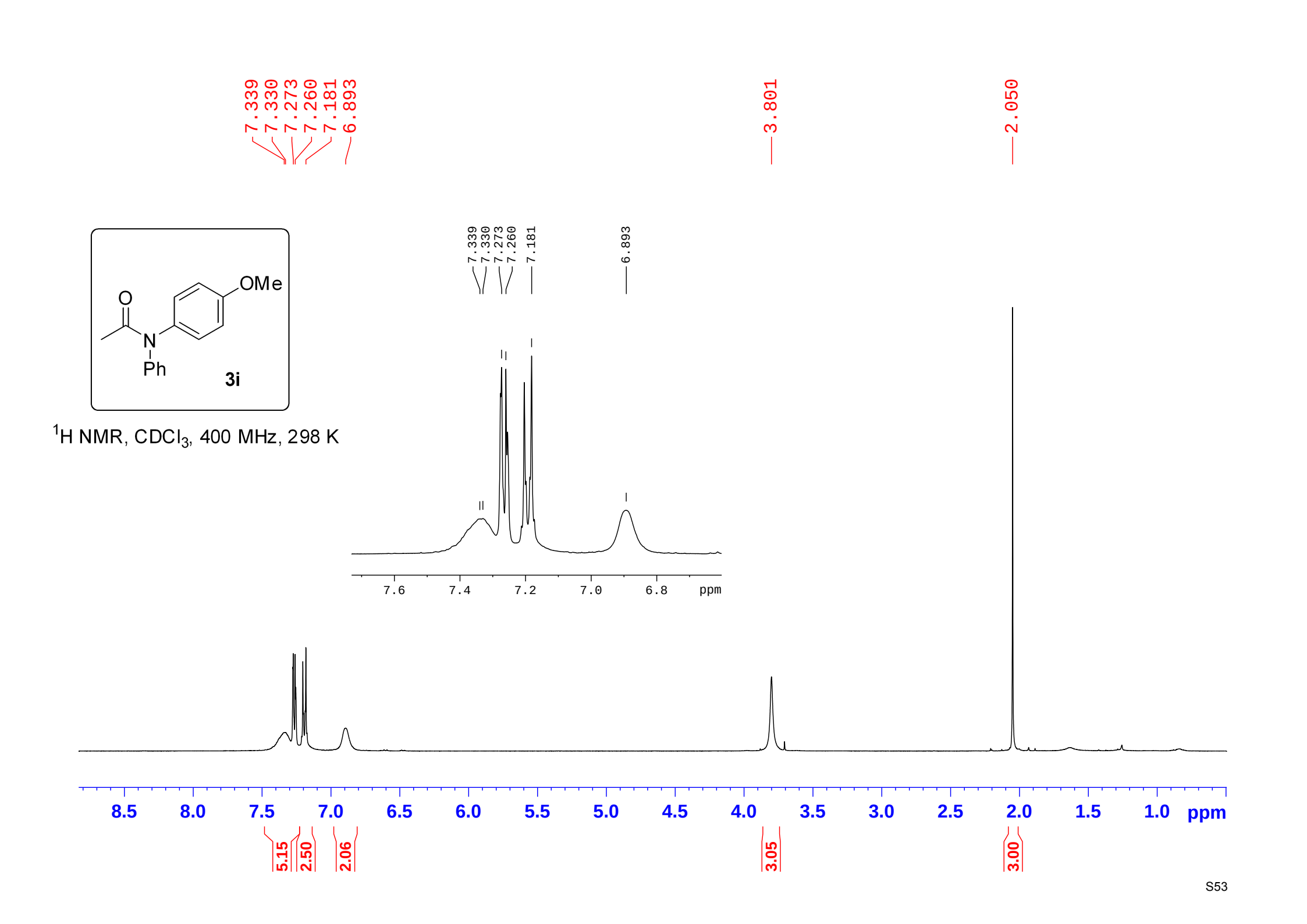

170.44
143.02
141.82
132.28
129.87
128.40
128.04
23.99
O
N
Br
3g
^{13}C-NMR, $CDCl_3$, 100 MHz, 298 K
160000
150000
140000
130000
120000
110000
100000
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
-10000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

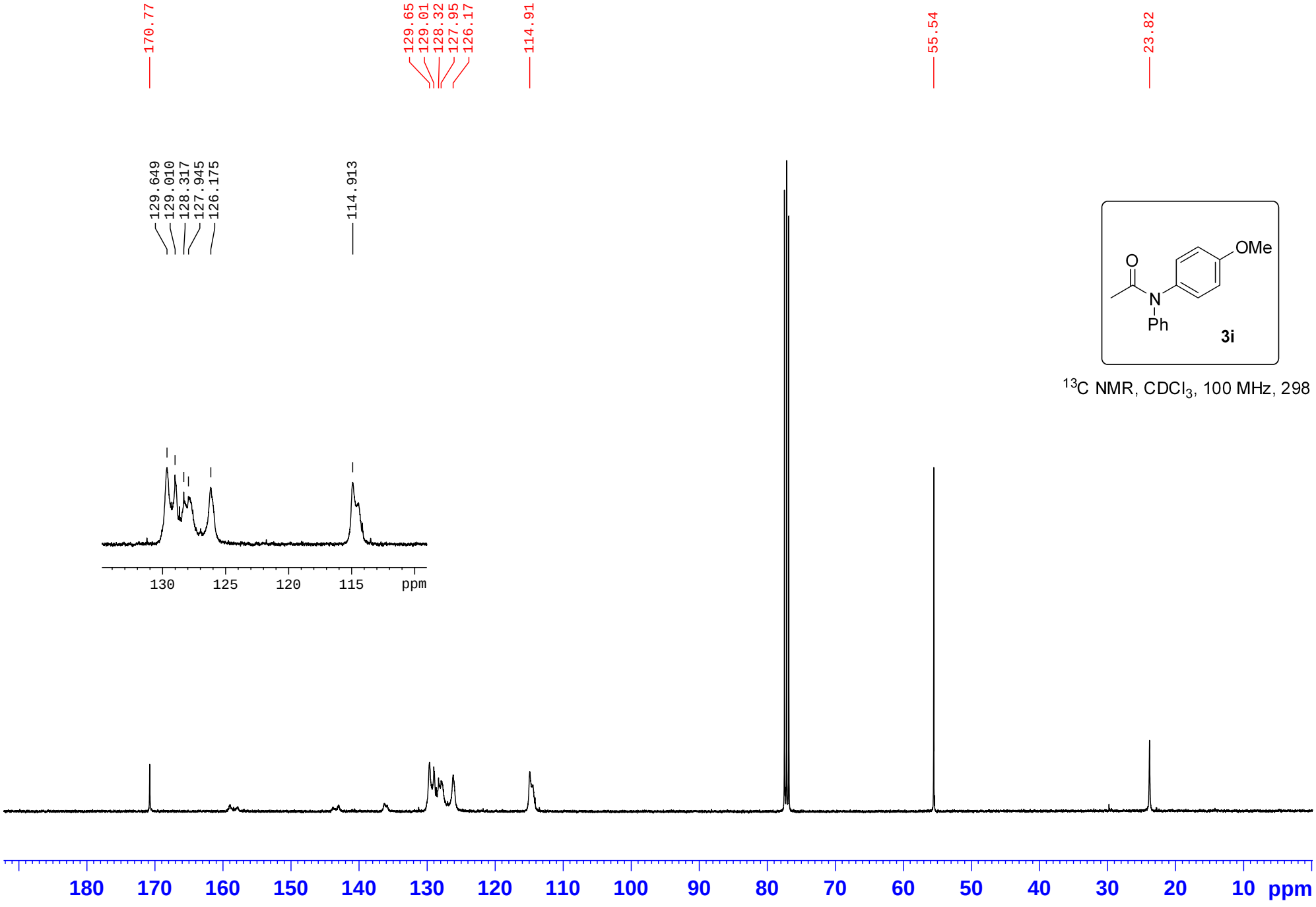


^{1}H NMR, $CDCl_3$, 400 MHz, 298 K

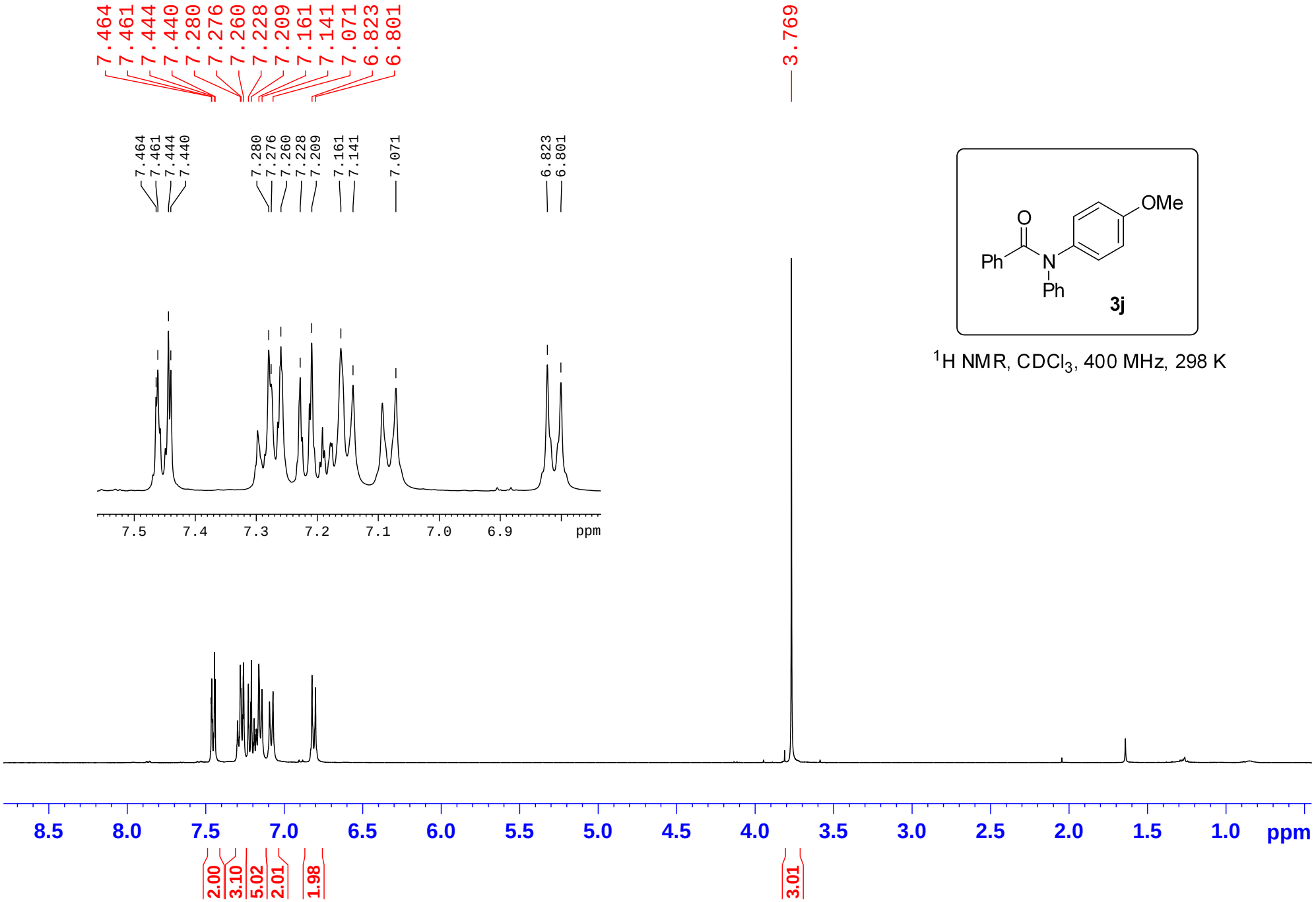


^{13}C NMR, $CDCl_3$, 100 MHz, 298 K

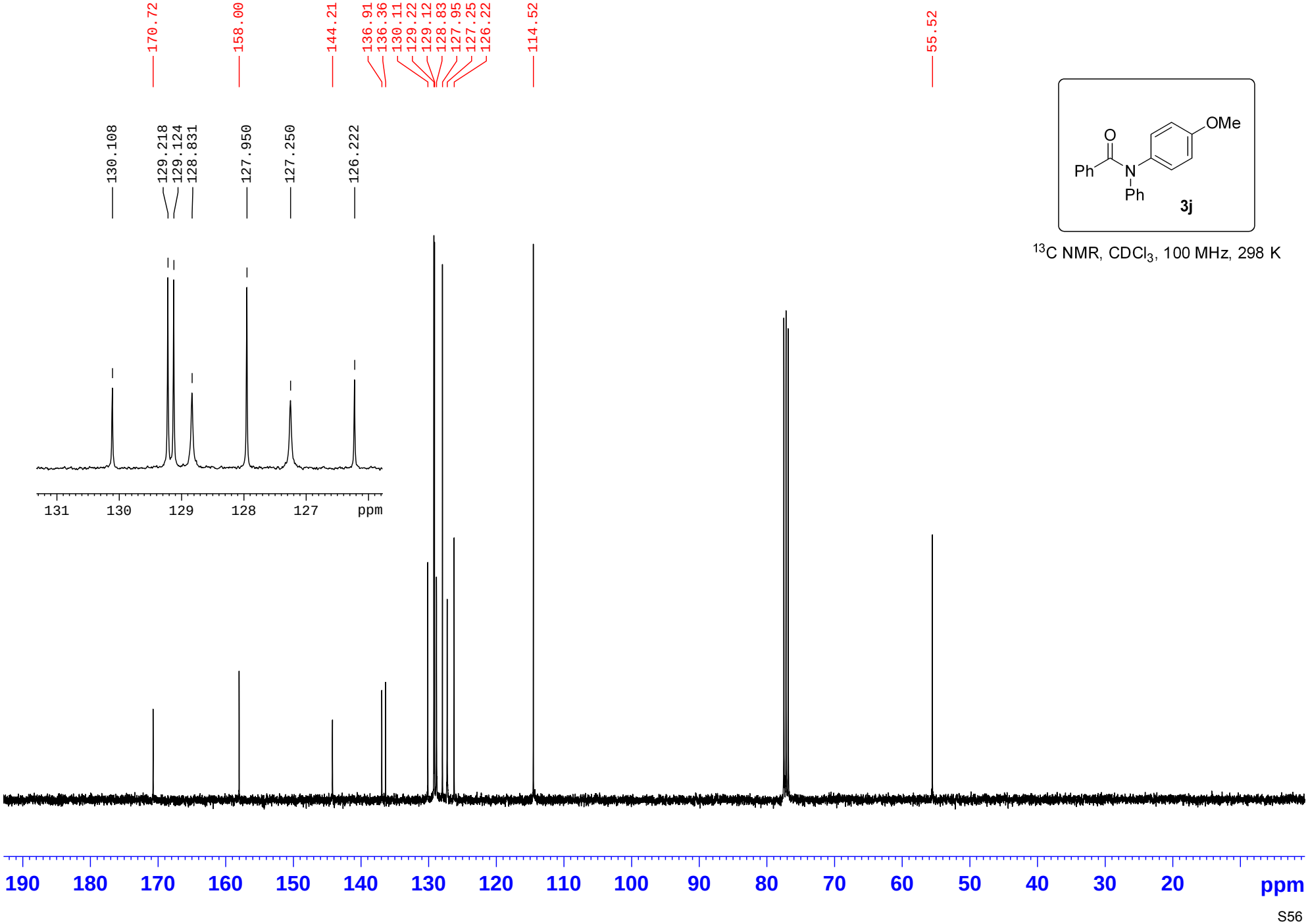

7.339
7.330
7.273
7.260
7.181
6.893
3.801
2.050
OMe
O
N
Ph
3i
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K
7.6
7.4
7.2
7.0
6.8
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
5.15
2.50
2.06
3.05
3.00



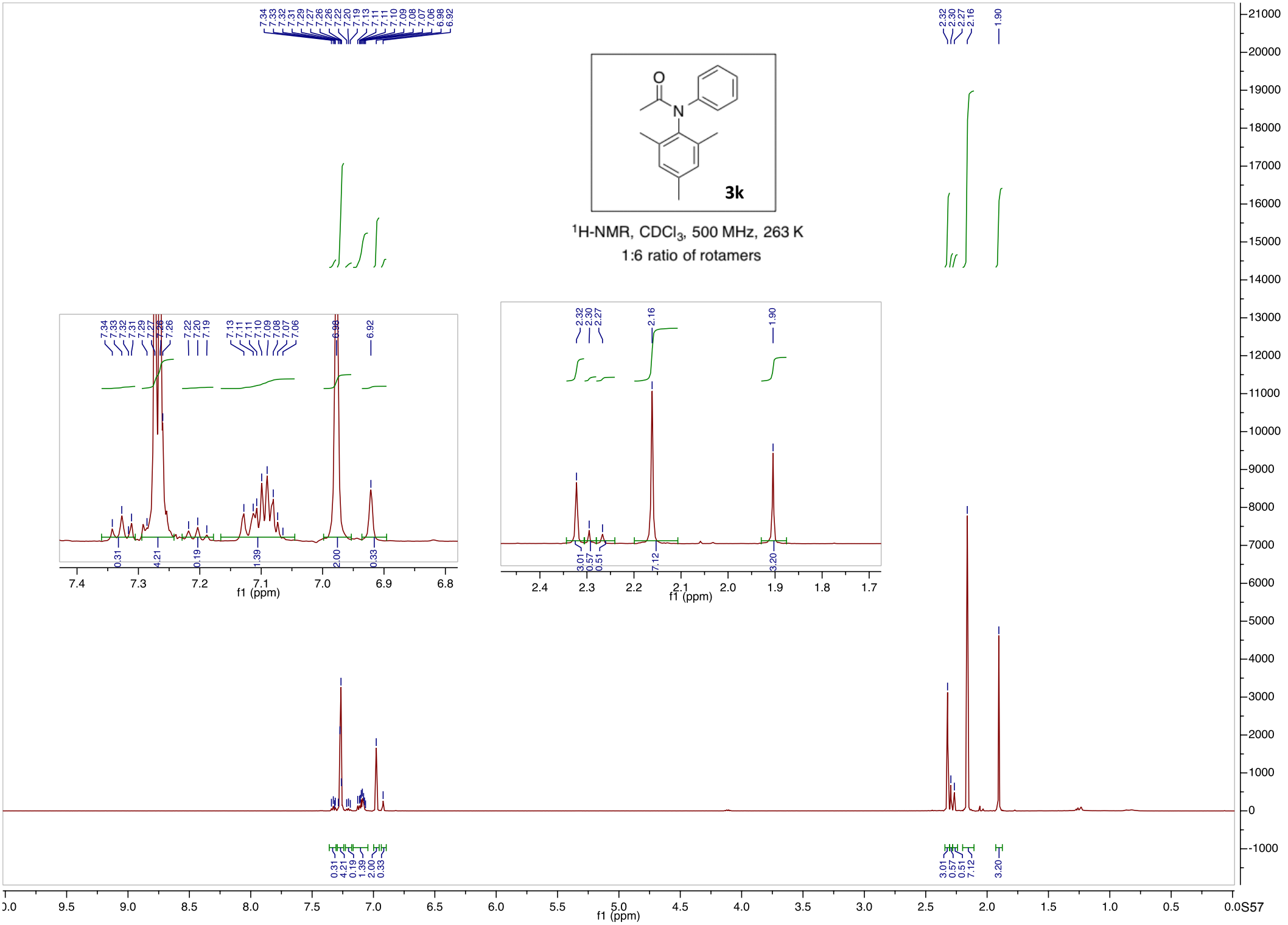
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K

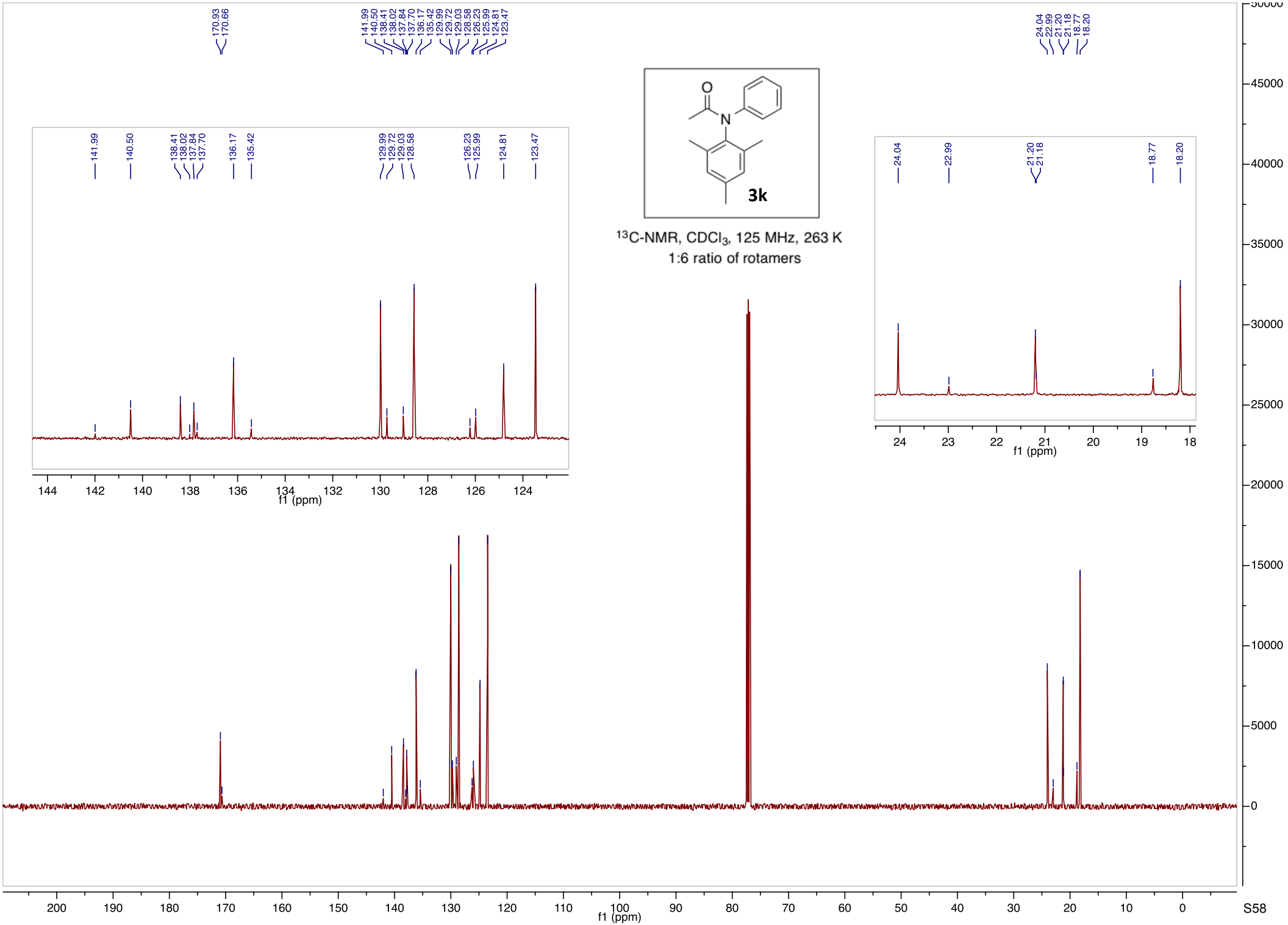


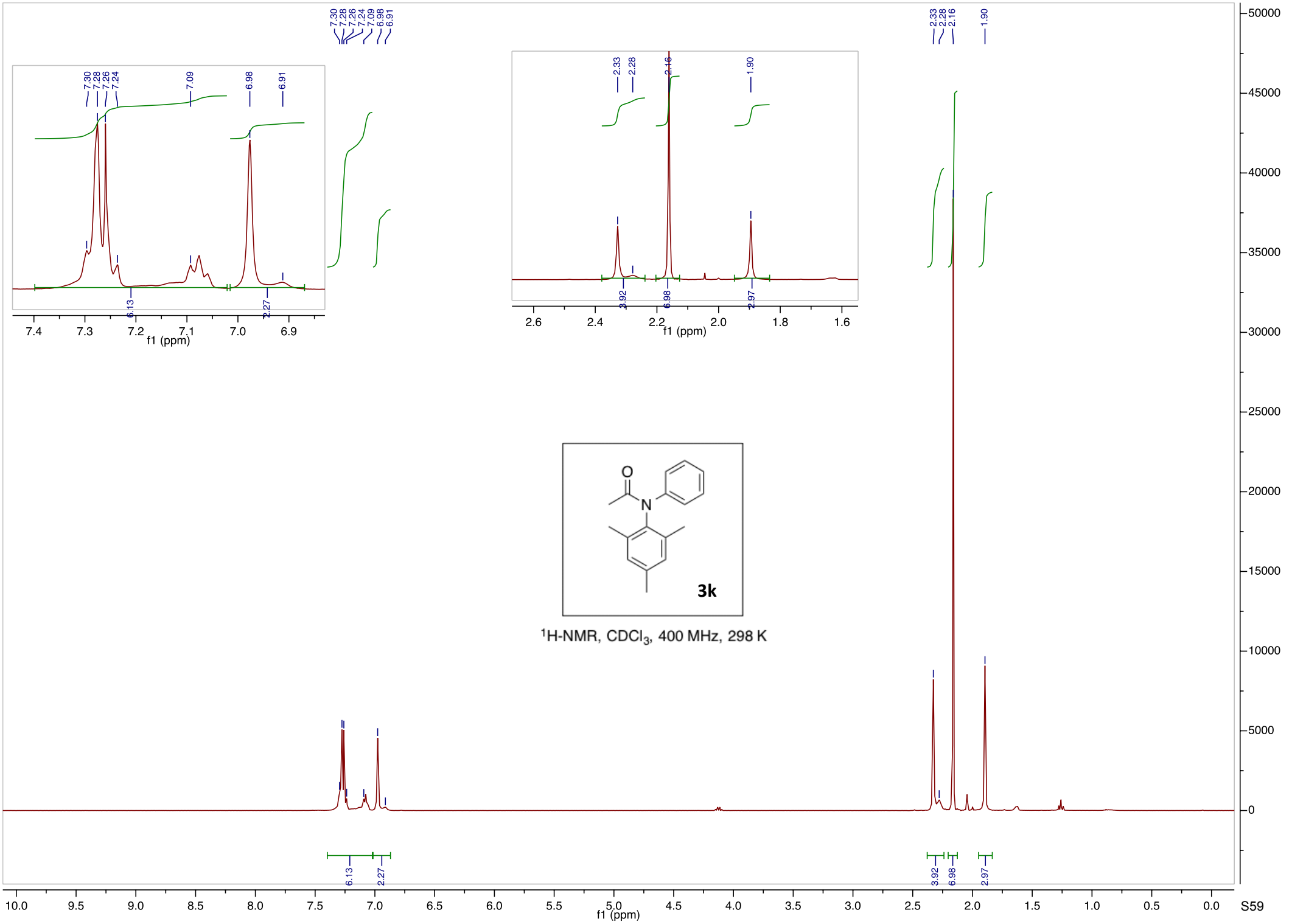
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K

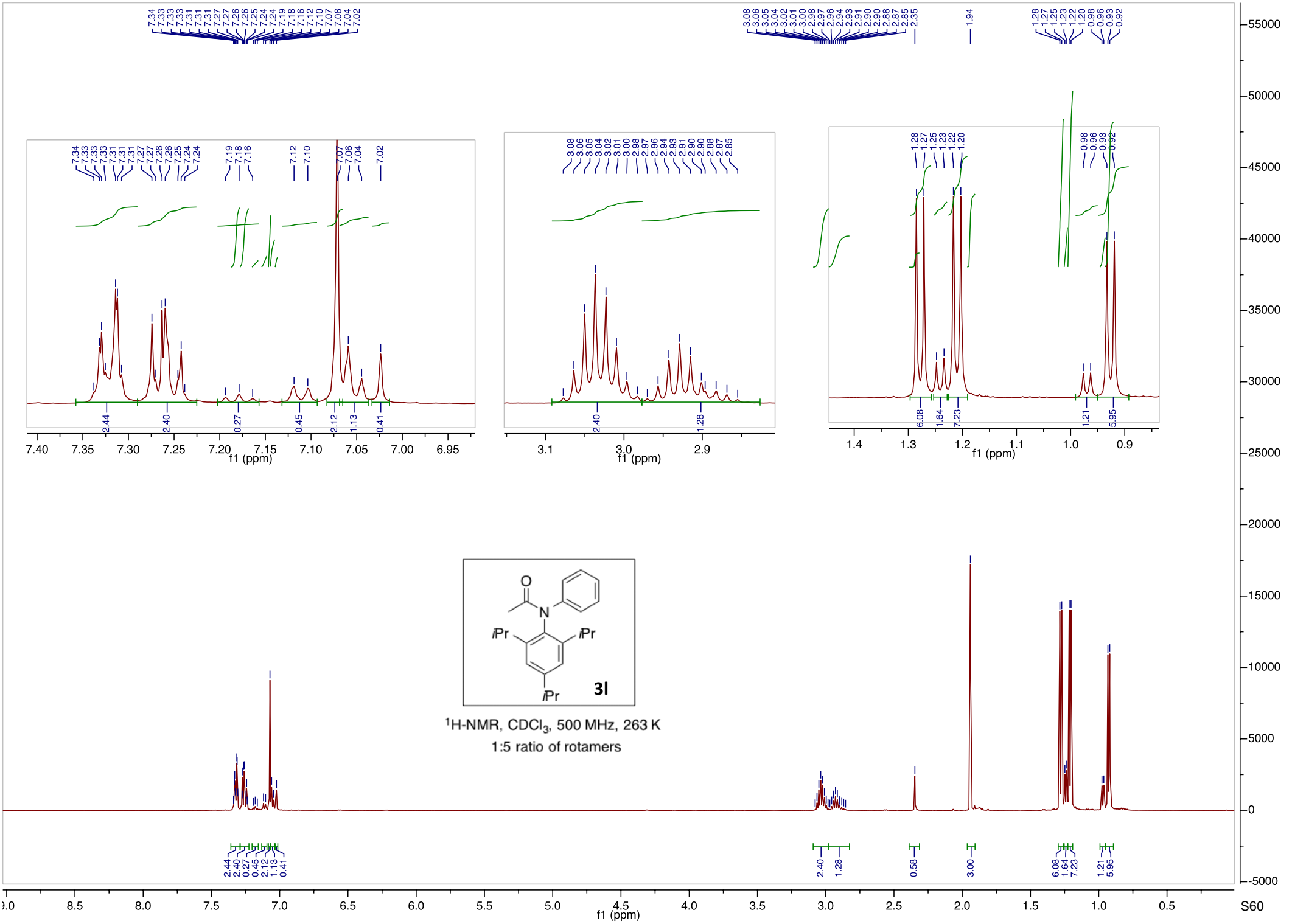


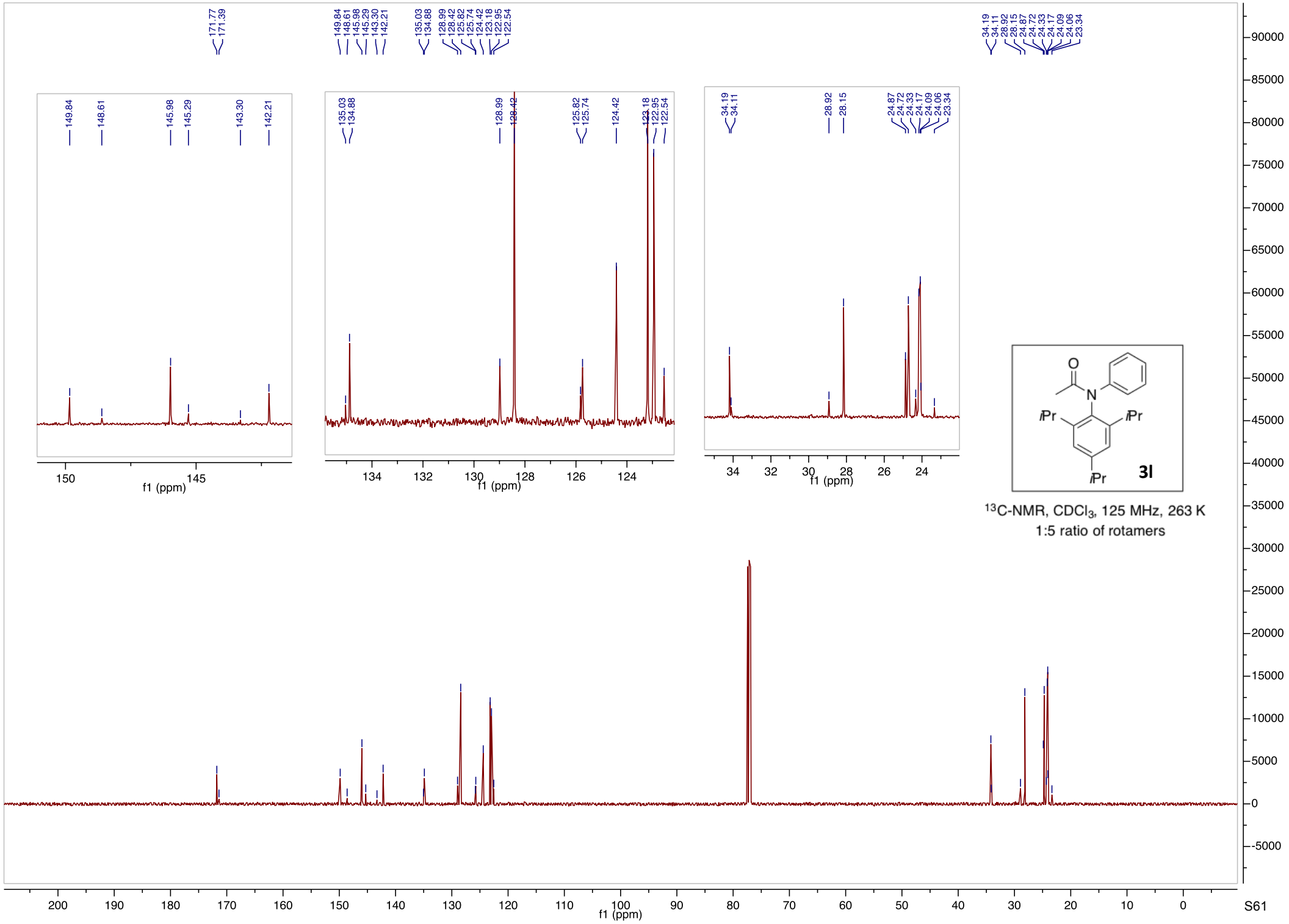
^{13}C NMR, $CDCl_3$, 100 MHz, 298 K

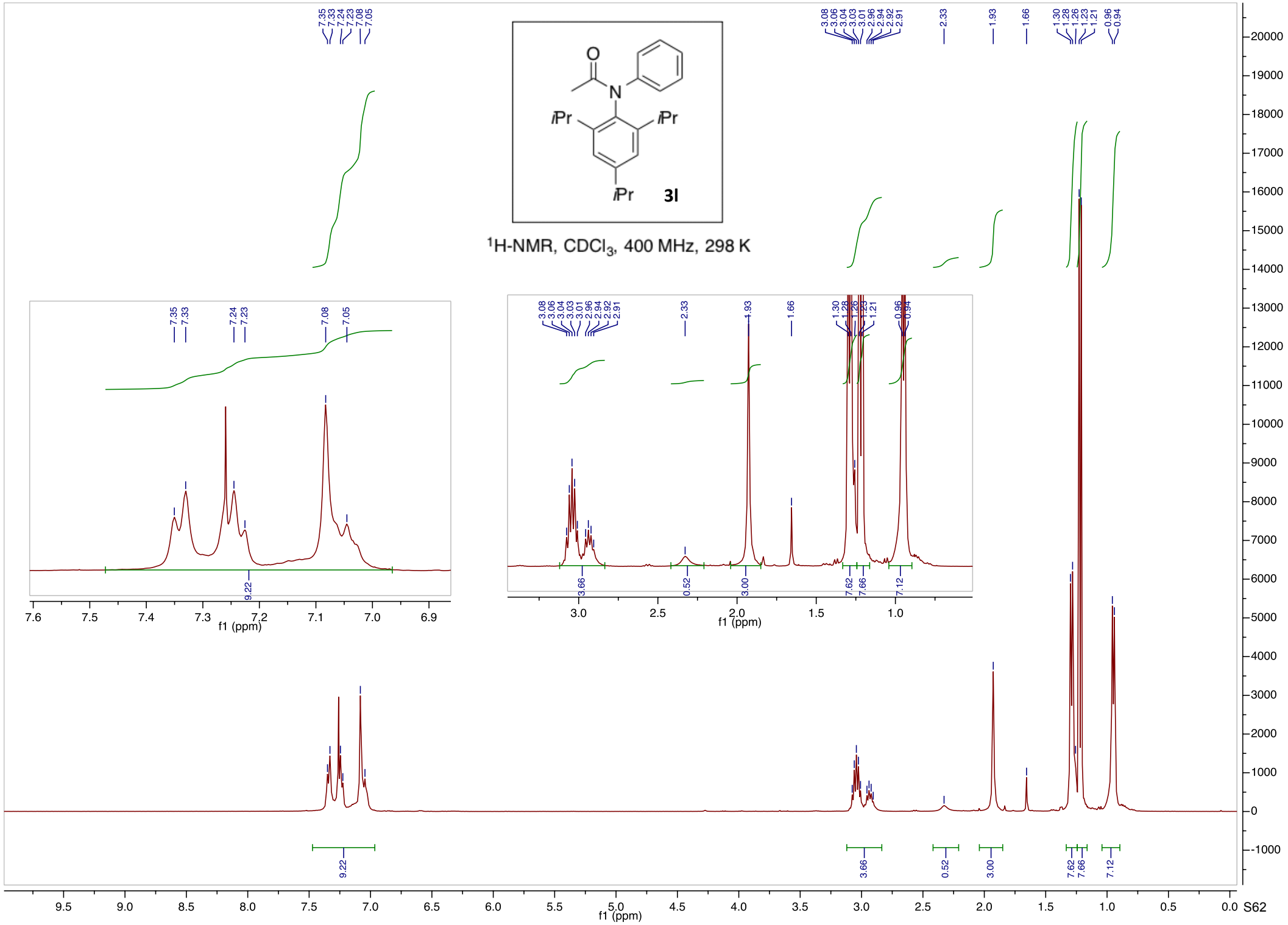

3k
^{1}H-NMR, $CDCl_3$, 500 MHz, 263 K
1:6 ratio of rotamers
f1 (ppm)

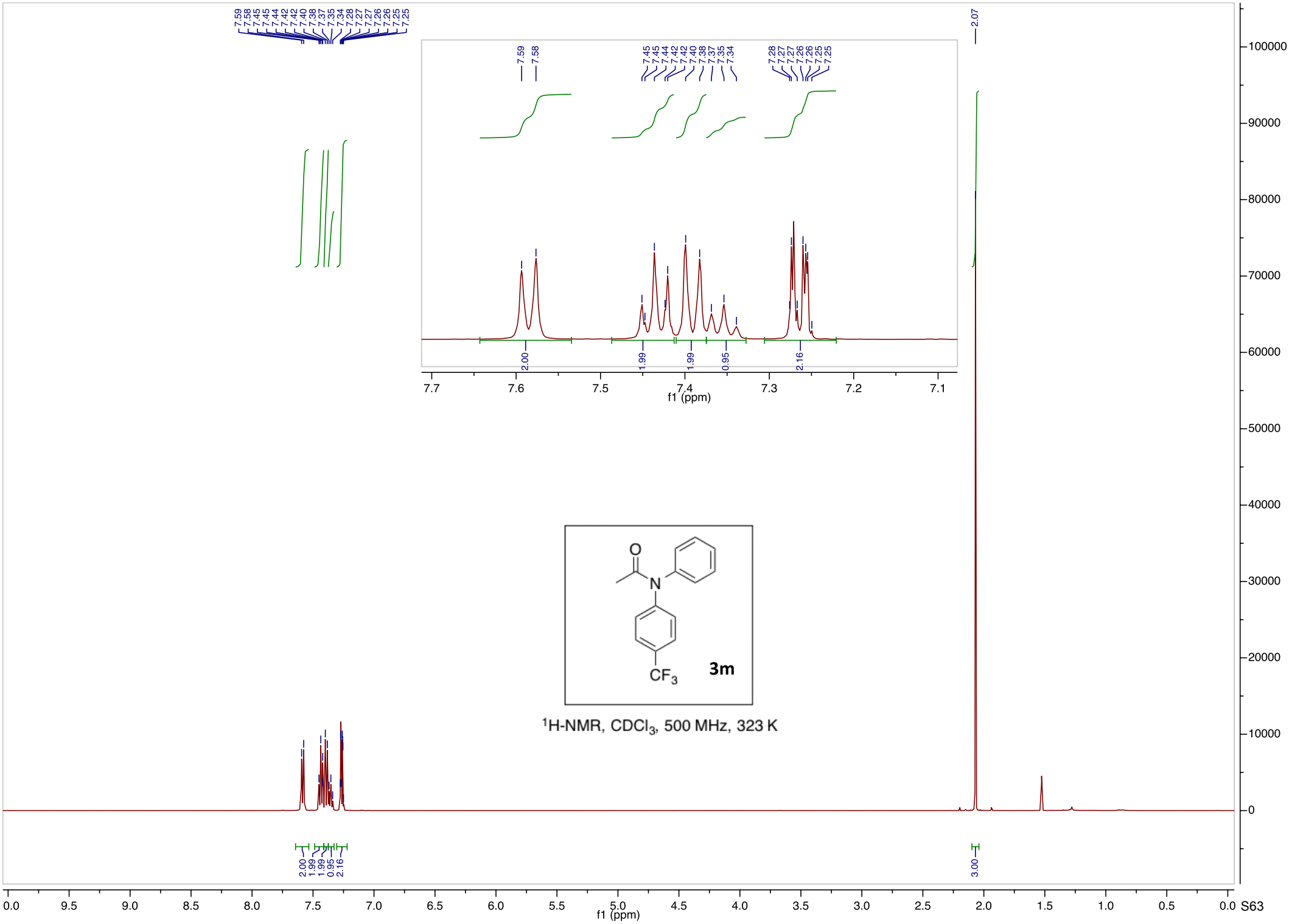

170.93
170.66
141.99
140.50
138.41
138.02
137.84
137.70
136.17
135.42
129.99
129.72
129.03
128.58
126.23
125.99
124.81
123.47
24.04
22.99
21.20
21.18
18.77
18.20
O
N
3k
^{13}C-NMR, $CDCl_3$, 125 MHz, 263 K
1:6 ratio of rotamers
f1 (ppm)

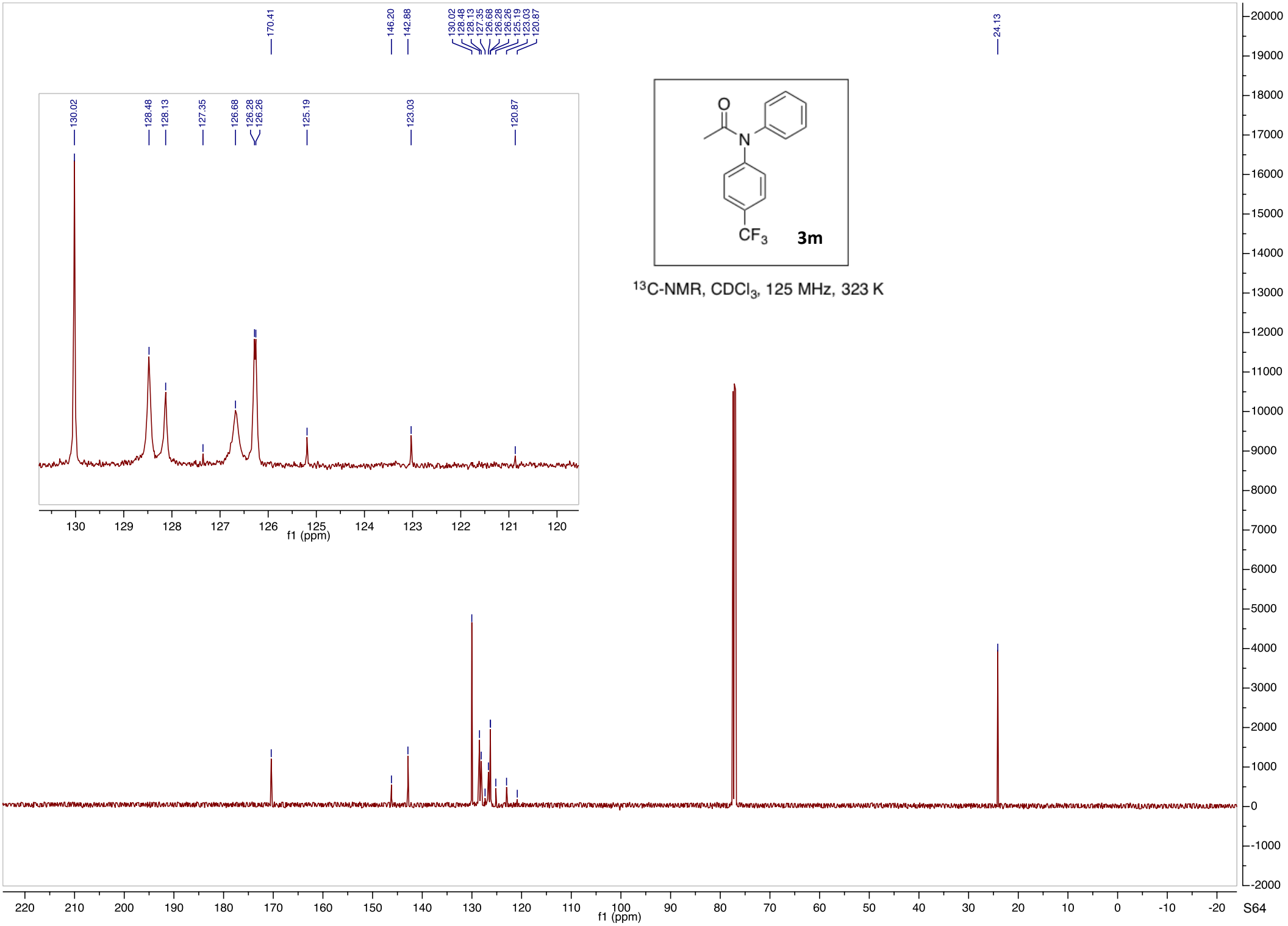

7.30
7.28
7.26
7.24
7.09
6.98
6.91
6.13
2.27
2.33
2.28
2.16
1.90
3.92
6.98
2.97
f1 (ppm)
3k
^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K

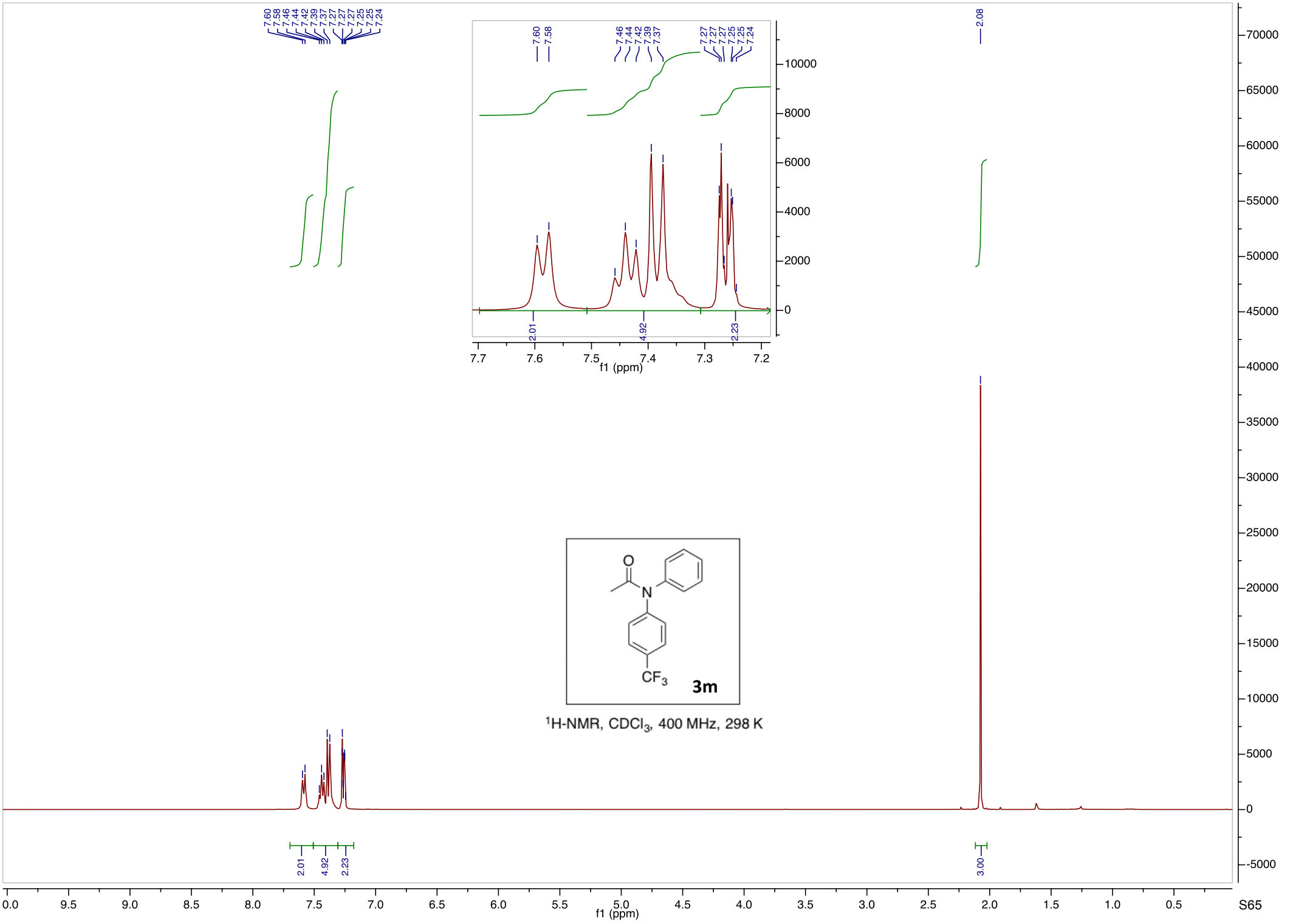

7.34 7.33 7.33 7.33 7.31 7.31 7.31 7.27 7.27 7.26 7.26 7.25 7.24 7.24 7.19 7.18 7.16 7.12 7.10 7.07 7.06 7.04 7.02
3.08 3.06 3.05 3.04 3.02 3.01 3.00 2.98 2.97 2.96 2.94 2.93 2.91 2.90 2.90 2.88 2.87 2.85 2.35
1.94
1.28 1.27 1.25 1.23 1.22 1.20 0.98 0.96 0.96 0.93 0.92
2.44 2.40 0.27 0.45 2.12 1.13 0.41
2.40 1.28
6.08 1.64 7.23 1.21 5.95
f1 (ppm)
O
N
iPr
iPr
iPr
3l
1H-NMR, CDCl3, 500 MHz, 263 K
1:5 ratio of rotamers
S60


171.77
171.39
149.84
148.61
145.98
145.29
143.30
142.21
135.03
134.88
128.99
128.42
125.82
125.74
124.42
123.18
122.95
122.54
34.19
34.11
28.92
28.15
24.87
24.72
24.33
24.17
24.09
24.06
23.34
f1 (ppm)
O
N
iPr
iPr
iPr
3l
13C-NMR, CDCl3, 125 MHz, 263 K
1:5 ratio of rotamers
S61

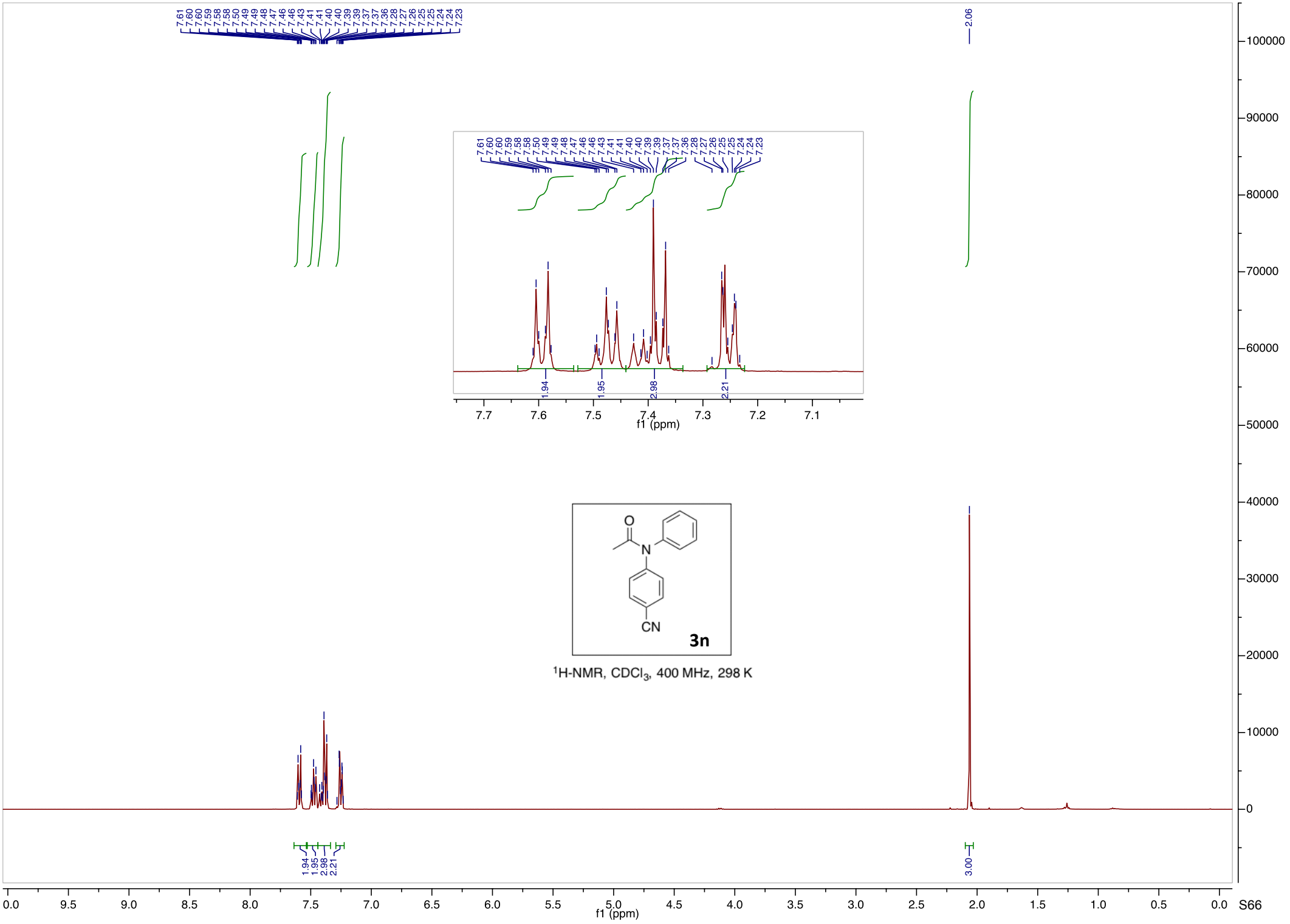

O
N
iPr
iPr
iPr
3l
1H-NMR, CDCl3, 400 MHz, 298 K
f1 (ppm)
S62


7.59
7.58
7.45
7.45
7.44
7.42
7.42
7.40
7.38
7.37
7.35
7.34
7.28
7.27
7.27
7.26
7.26
7.25
7.25
2.07
2.00
1.99
1.99
0.95
2.16
f1 (ppm)
O
N
CF3
3m
1H-NMR, CDCl3, 500 MHz, 323 K
3.00
f1 (ppm)

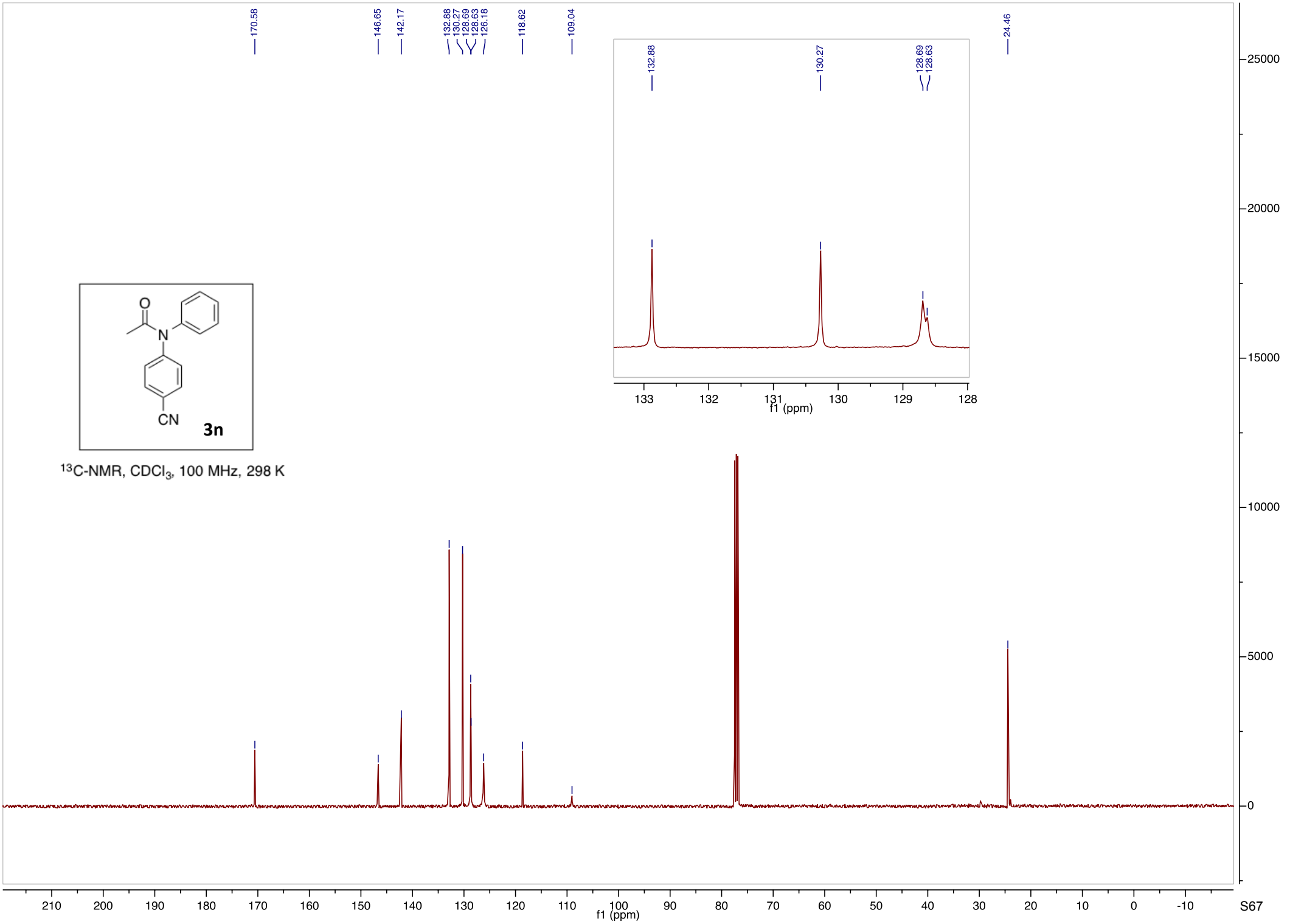

170.41
146.20
142.88
130.02
128.48
128.13
127.35
126.68
126.28
126.26
125.19
123.03
120.87
24.13
O
N
CF3
3m
13C-NMR, CDCl3, 125 MHz, 323 K
f1 (ppm)
S64

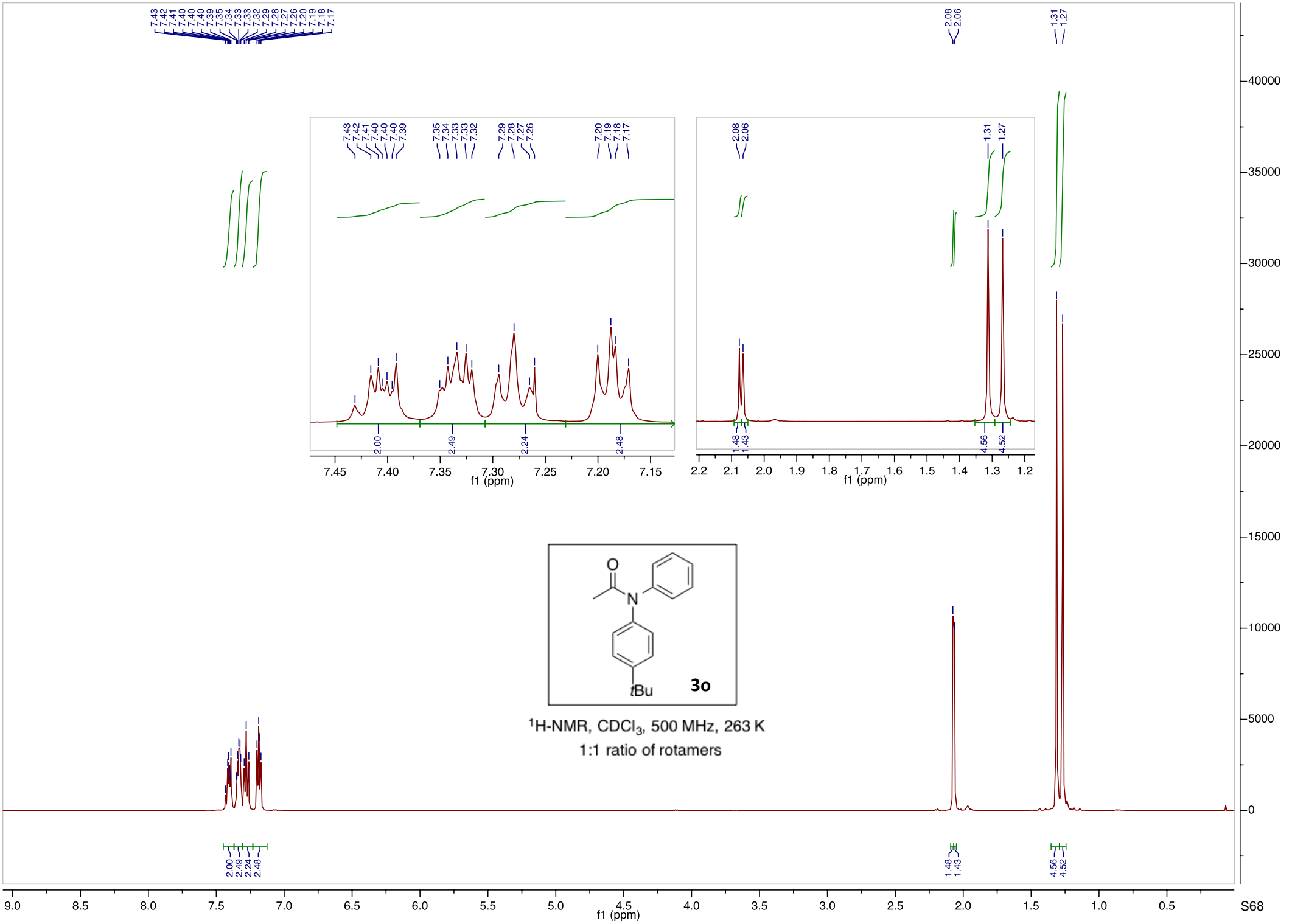


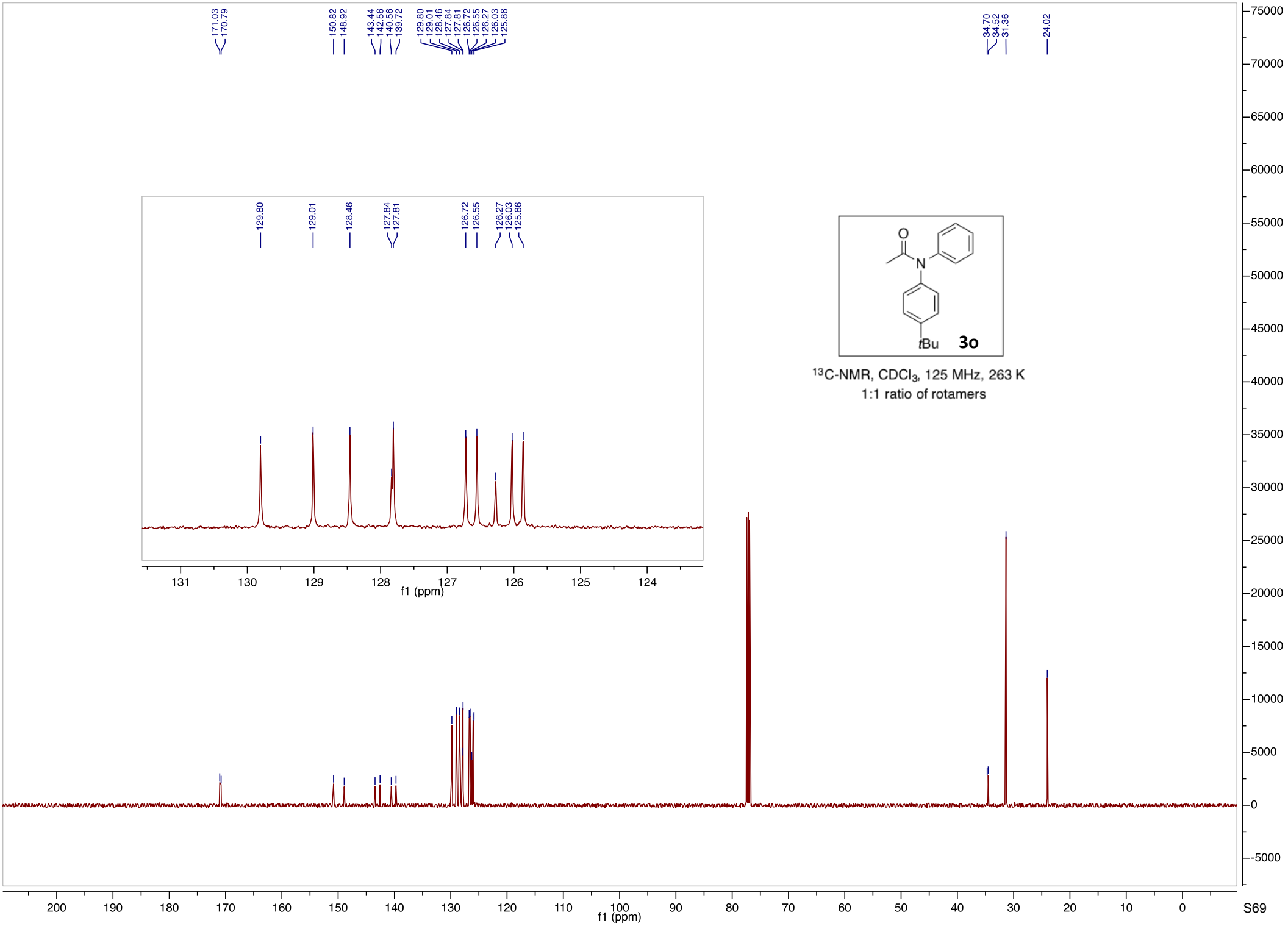
^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K

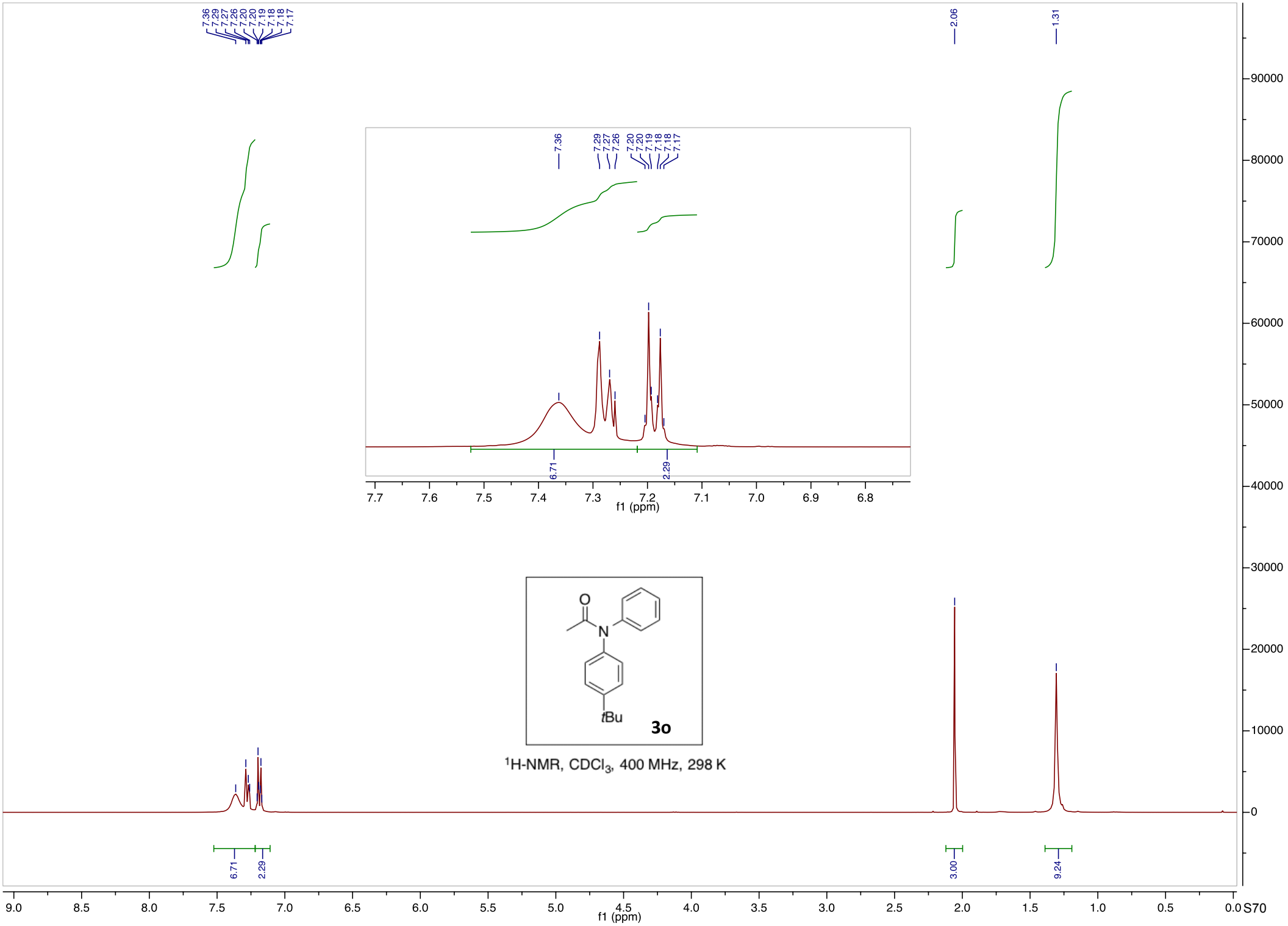


^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K

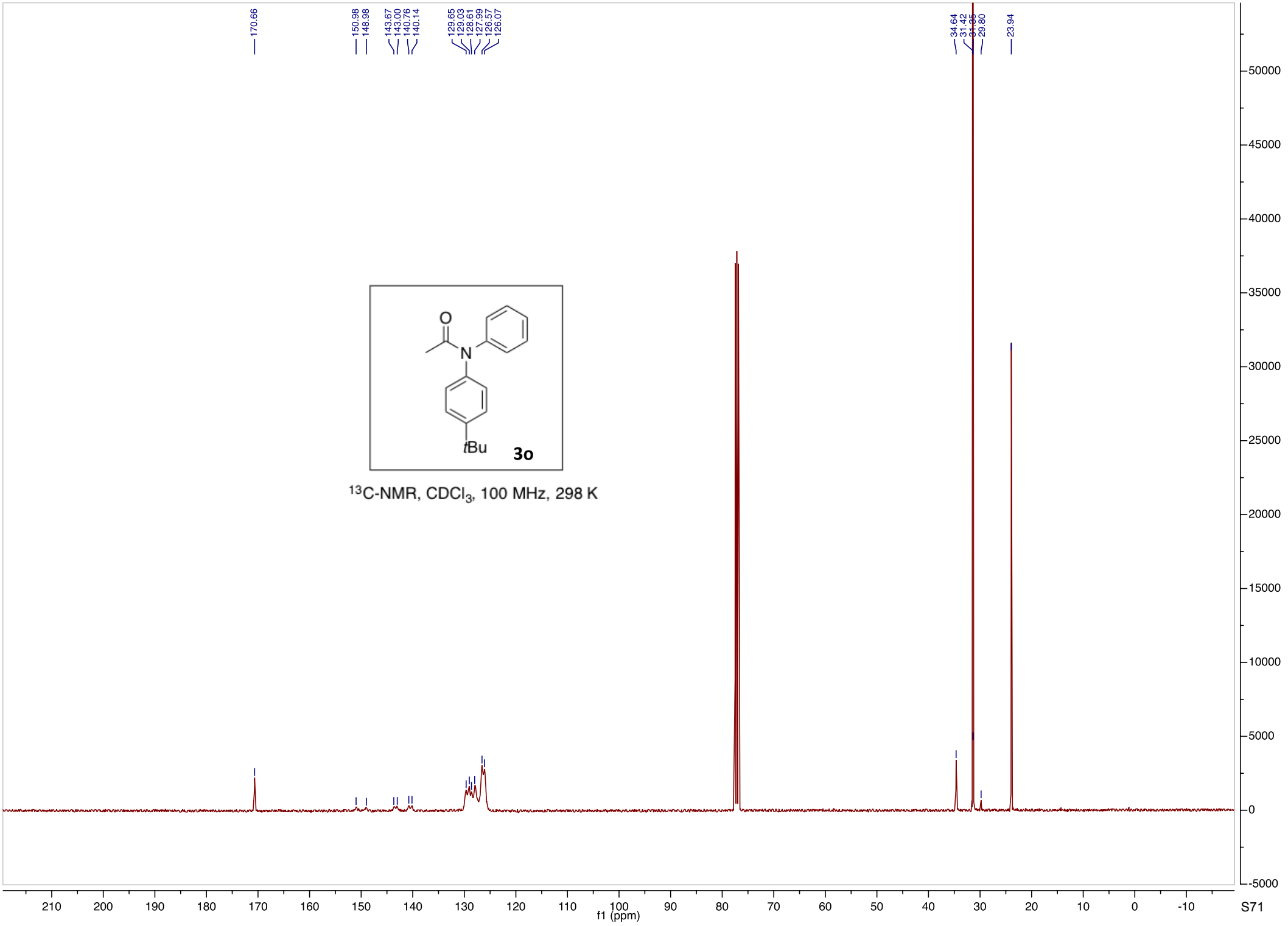

170.58
146.65
142.17
132.88
130.27
128.69
128.63
126.18
118.62
109.04
24.46
O
N
CN
3n
^{13}C-NMR, $CDCl_3$, 100 MHz, 298 K
f1 (ppm)
S67

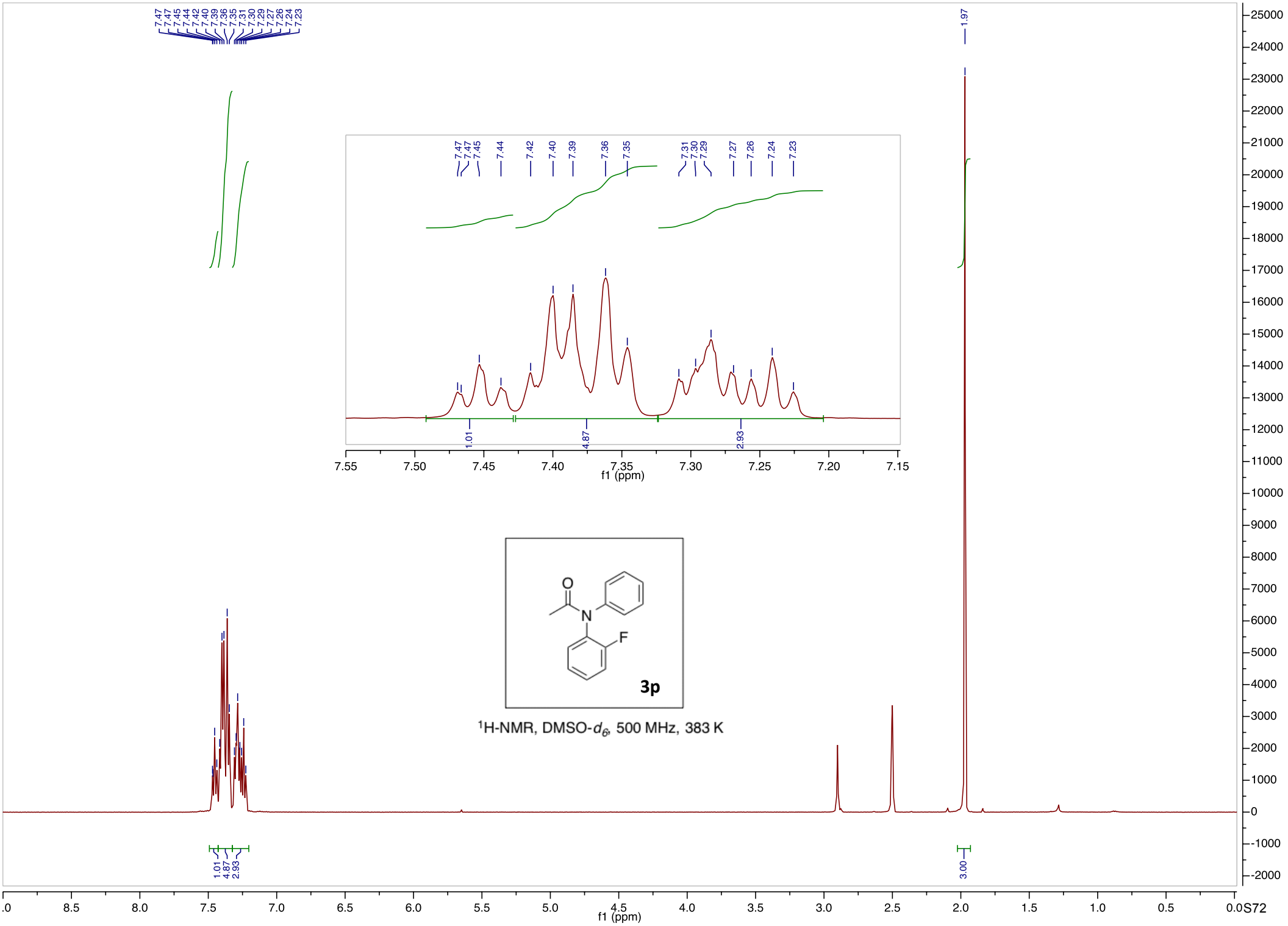

7.43 7.42 7.41 7.40 7.40 7.40 7.39 7.35 7.34 7.33 7.33 7.32 7.29 7.28 7.27 7.26 7.20 7.19 7.18 7.17
2.08 2.06
1.31 1.27
2.00 2.49 2.24 2.48
1.48 1.43
4.56 4.52
f1 (ppm)
O
N
tBu
3o
1H-NMR, CDCl3, 500 MHz, 263 K
1:1 ratio of rotamers


171.03
170.79
150.82
148.92
143.44
142.56
140.56
139.72
129.80
129.01
128.46
127.84
127.81
126.72
126.55
126.27
126.03
125.86
34.70
34.52
31.36
24.02
O
N
tBu
3o
^{13}C-NMR, $CDCl_3$, 125 MHz, 263 K
1:1 ratio of rotamers
f1 (ppm)
f1 (ppm)

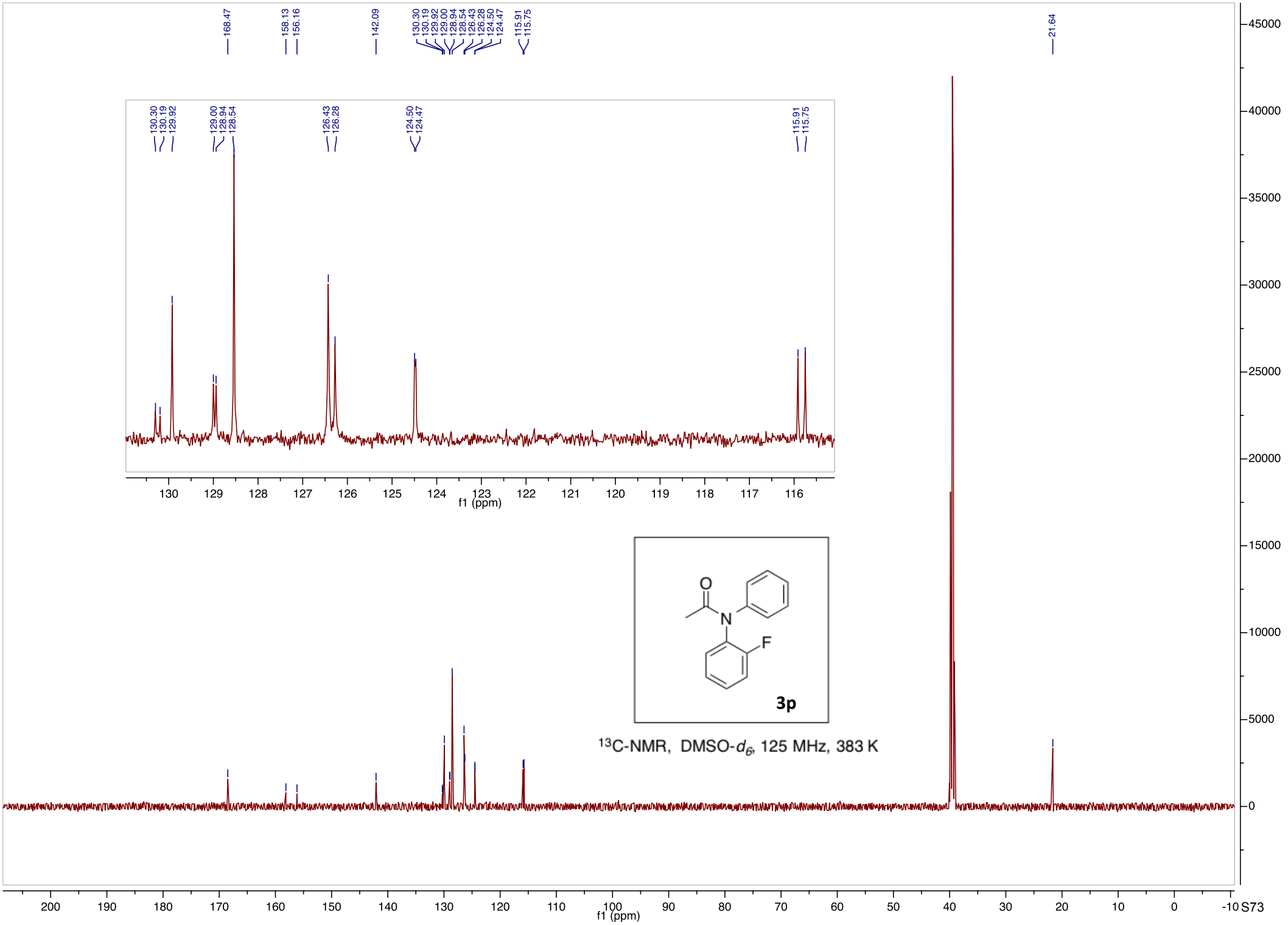


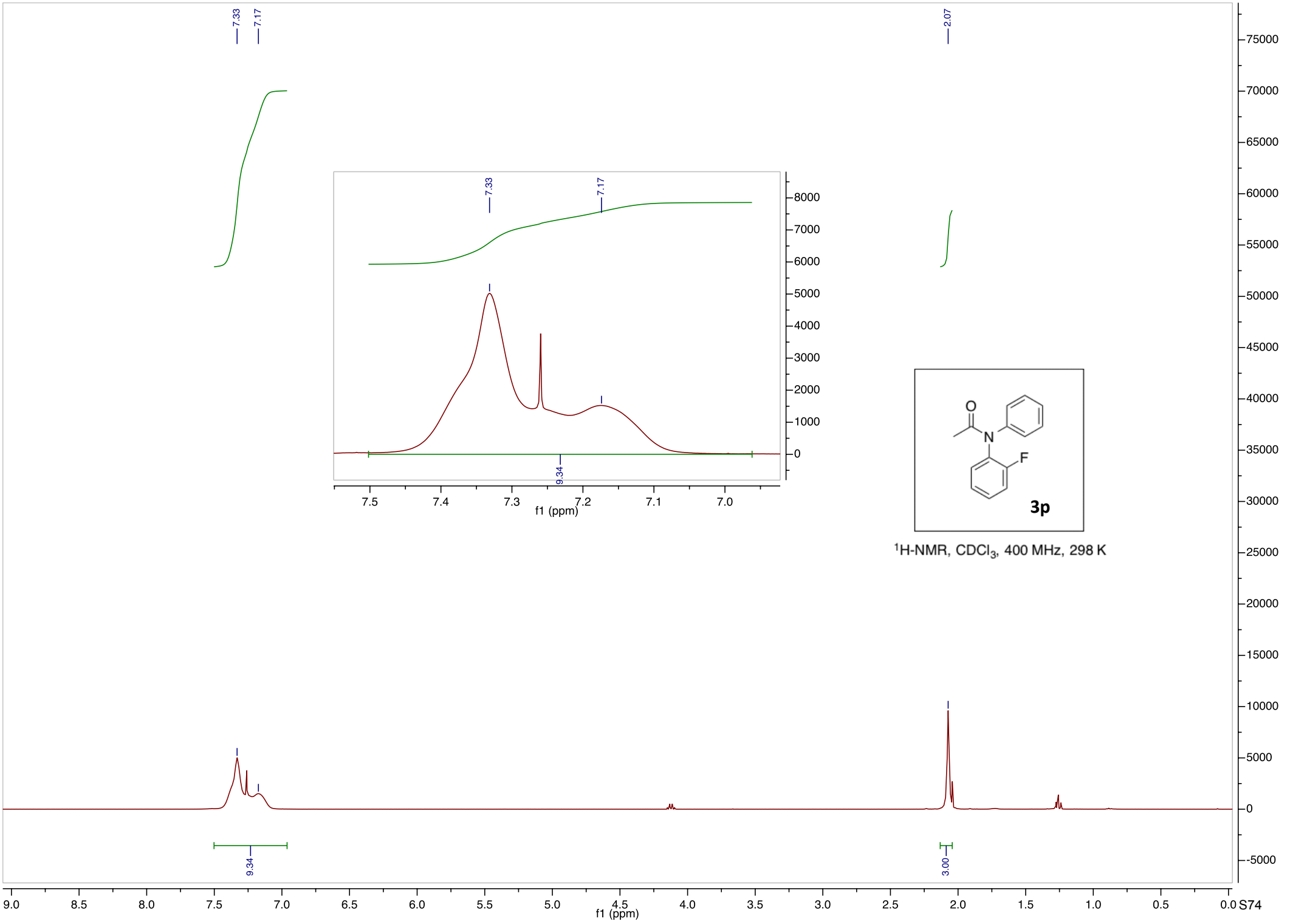
^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K


170.66
150.98
148.98
143.67
143.00
140.76
140.14
129.65
129.03
128.61
127.99
126.57
126.07
34.64
31.42
31.35
29.80
23.94
O
N
tBu
3o
^{13}C-NMR, $CDCl_3$, 100 MHz, 298 K
f1 (ppm)

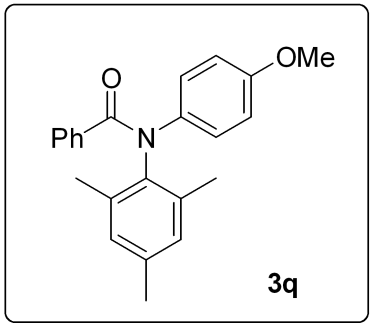


^{1}H-NMR, DMSO-d_6, 500 MHz, 383 K

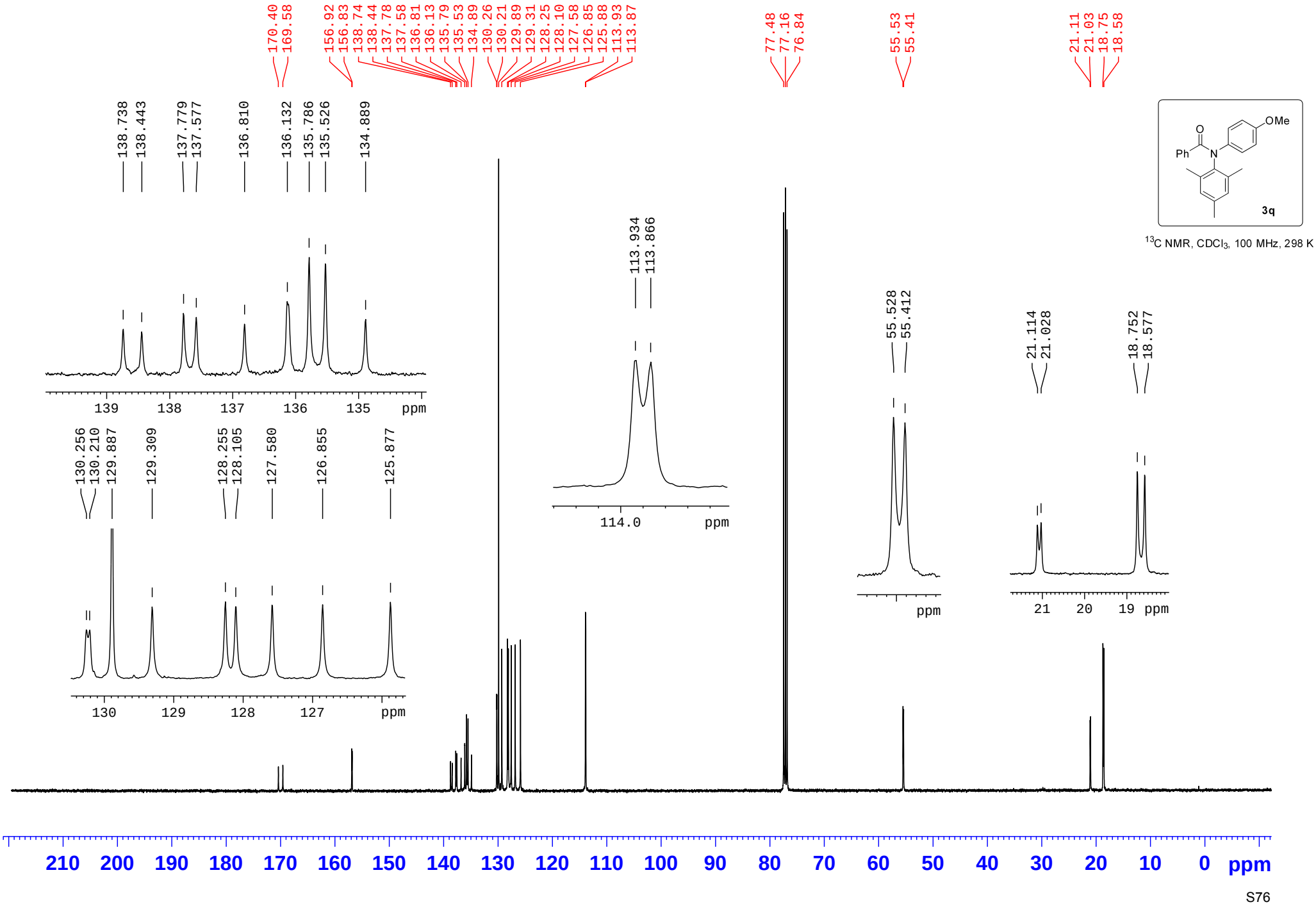

168.47
158.13
156.16
142.09
130.30
130.19
129.92
129.00
128.94
128.54
126.43
126.28
124.50
124.47
115.91
115.75
21.64
f1 (ppm)
3p
^{13}C-NMR, DMSO-d_6, 125 MHz, 383 K

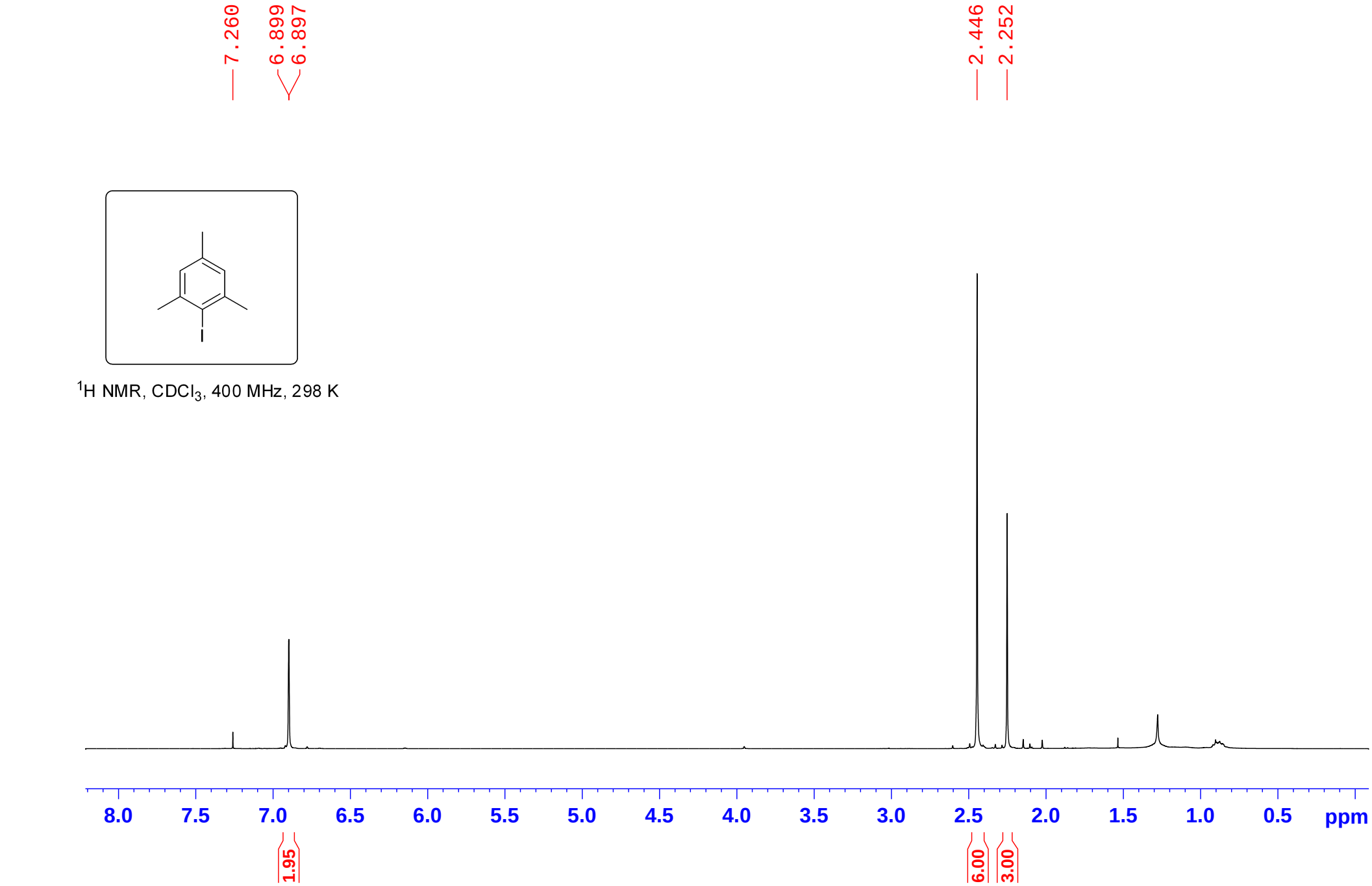


^{1}H-NMR, $CDCl_3$, 400 MHz, 298 K

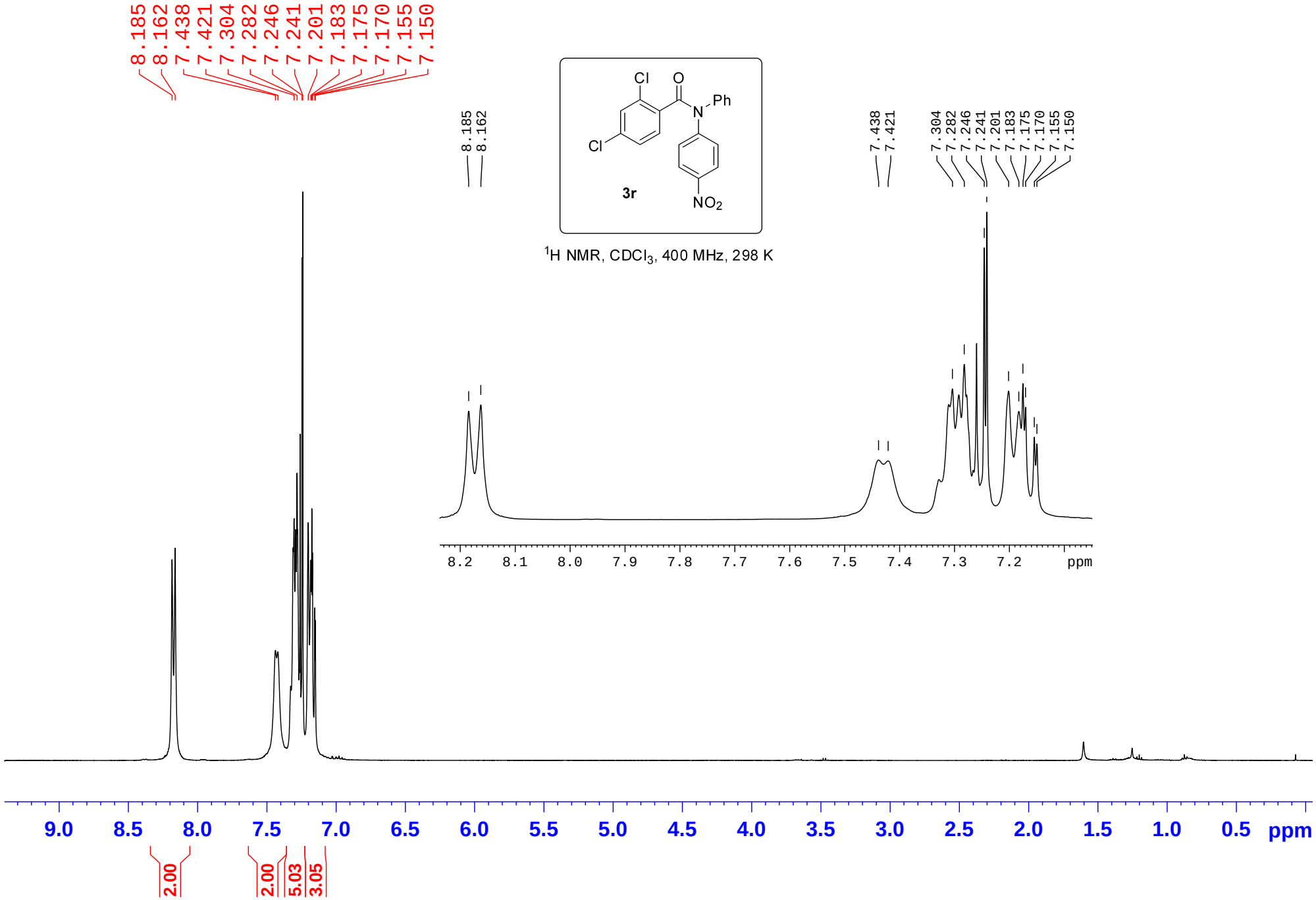


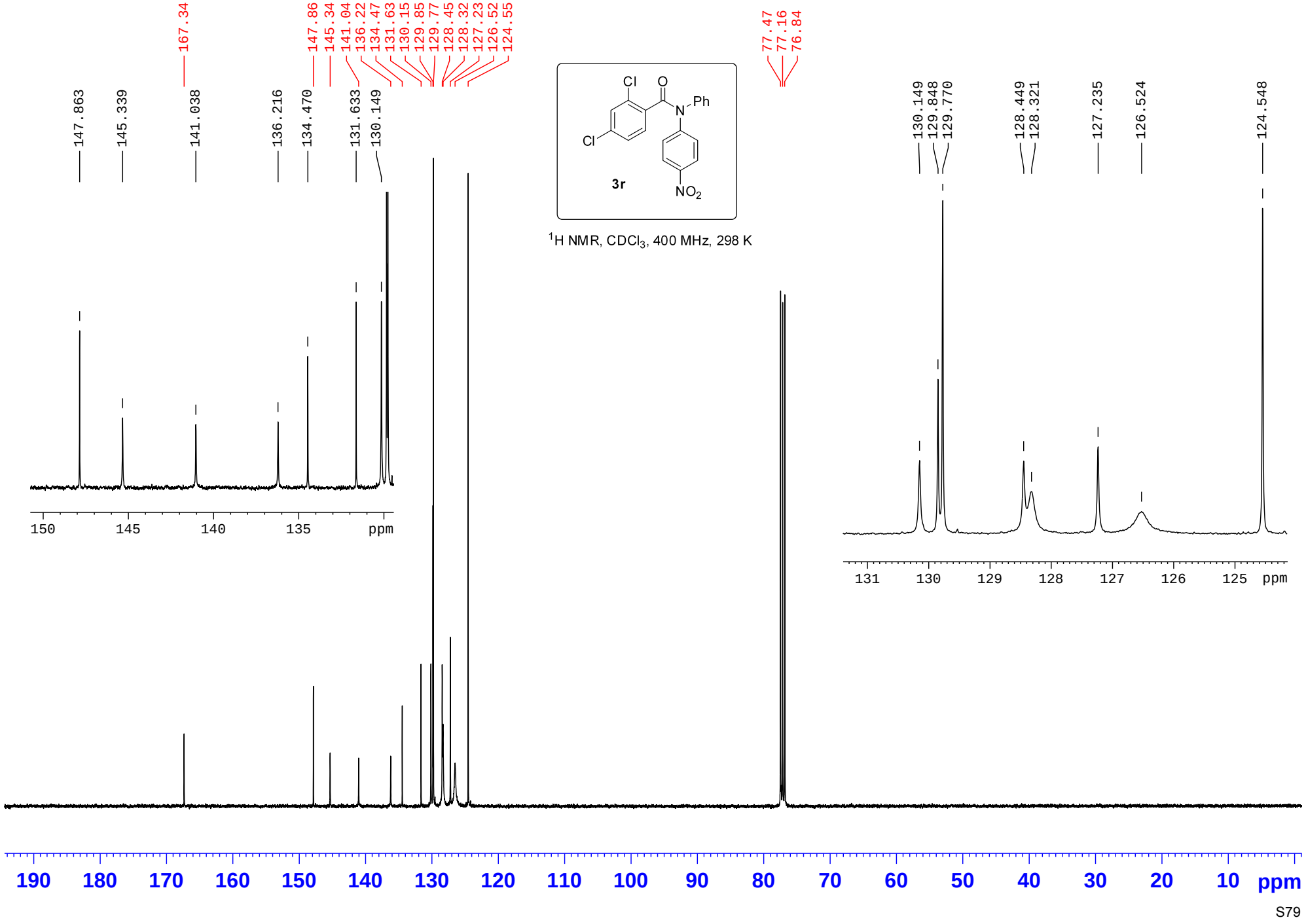
^{1}H NMR, $CDCl_3$, 400 MHz, 298 K

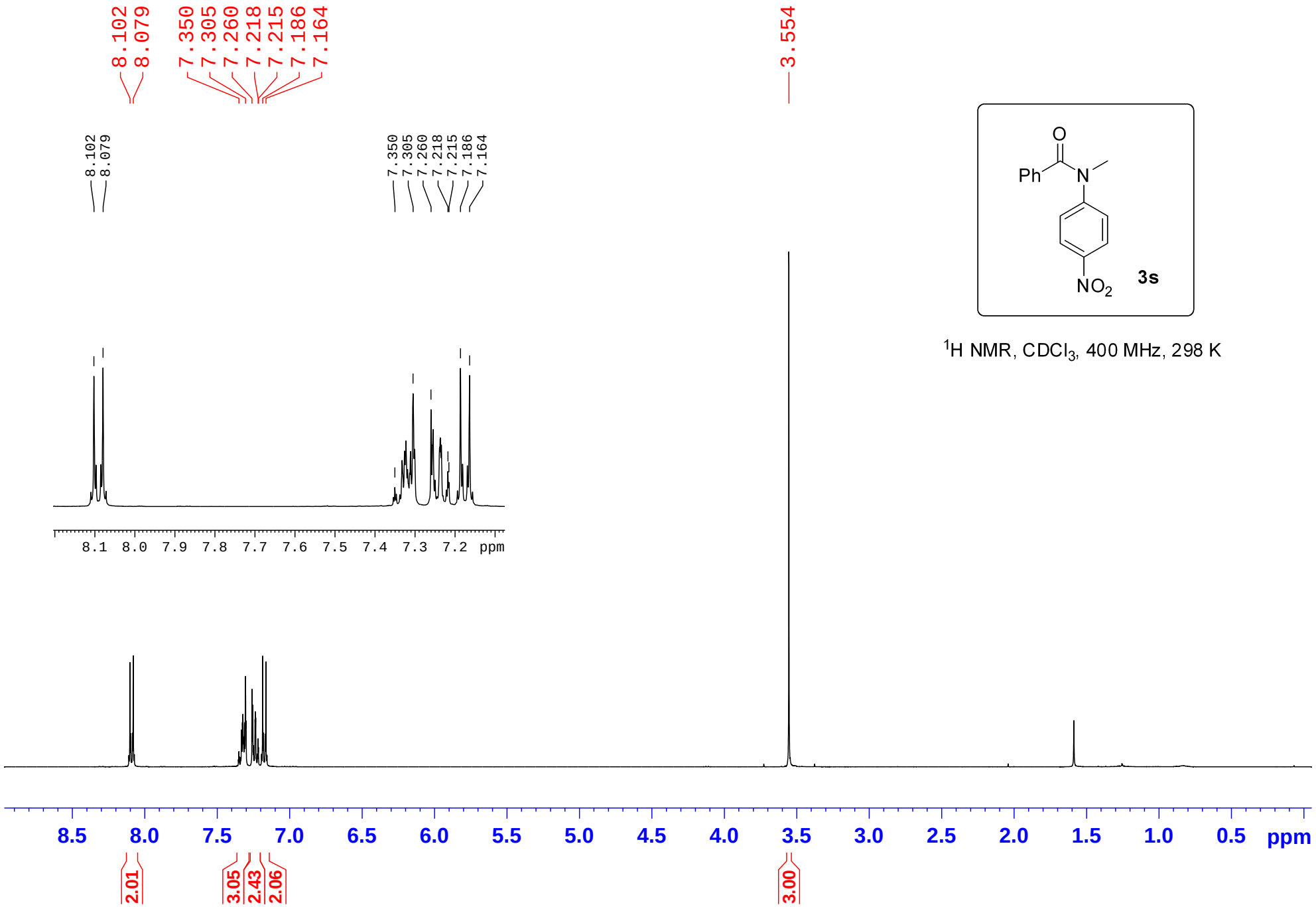

170.40
169.58
156.92
156.83
138.74
138.44
137.78
137.58
136.81
136.13
135.79
135.53
134.89
130.26
130.21
129.89
129.31
128.25
128.10
127.58
126.85
125.88
113.93
113.87
77.48
77.16
76.84
55.53
55.41
21.11
21.03
18.75
18.58
138.738
138.443
137.779
137.577
136.810
136.132
135.786
135.526
134.889
139
138
137
136
135
ppm
130.256
130.210
129.887
129.309
128.255
128.105
127.580
126.855
125.877
130
129
128
127
ppm
113.934
113.866
114.0
ppm
55.528
55.412
ppm
21.114
21.028
18.752
18.577
21
20
19
ppm
OMe
Ph
N
O
3q
^{13}C NMR, CDCl$_3$, 100 MHz, 298 K
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

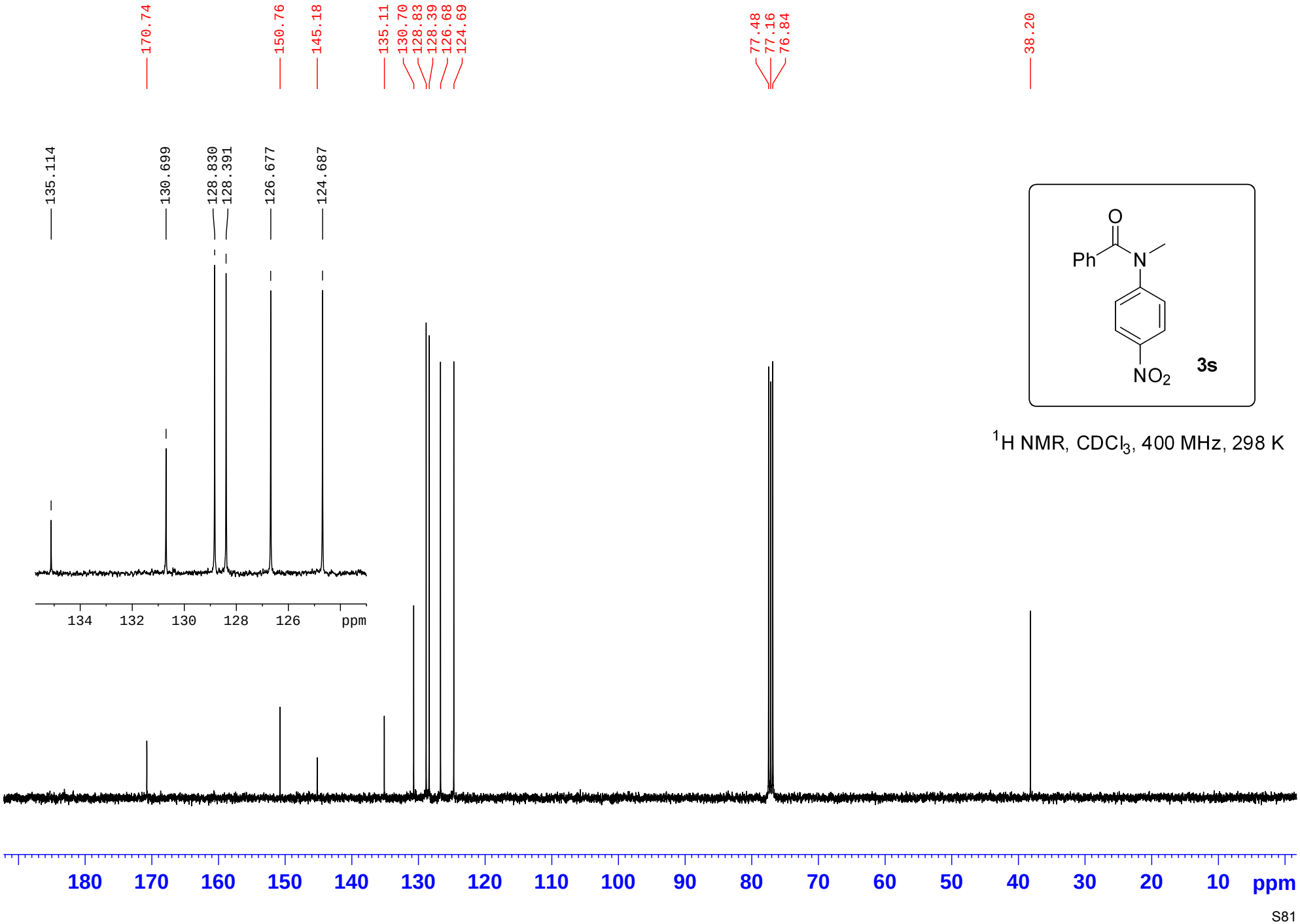


^{1}H NMR, $CDCl_3$, 400 MHz, 298 K


8.185
8.162
7.438
7.421
7.304
7.282
7.246
7.241
7.201
7.183
7.175
7.170
7.155
7.150
Cl
O
N
Ph
Cl
3r
NO2
1H NMR, CDCl3, 400 MHz, 298 K
8.2
8.1
8.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
ppm
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
ppm
2.00
2.00
5.03
3.05


167.34
147.86
145.34
141.04
136.22
134.47
131.63
130.15
129.85
129.77
128.45
128.32
127.23
126.52
124.55
77.47
77.16
76.84
147.863
145.339
141.038
136.216
134.470
131.633
130.149
130.149
129.848
129.770
128.449
128.321
127.235
126.524
124.548
Cl
O
N
Ph
Cl
NO2
3r
1H NMR, CDCl3, 400 MHz, 298 K
150
145
140
135
ppm
131
130
129
128
127
126
125
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


8.102
8.079
7.350
7.305
7.260
7.218
7.215
7.186
7.164
3.554
8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 ppm
Ph
N
O
NO2
3s
1H NMR, CDCl3, 400 MHz, 298 K
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 ppm
2.01
3.05
2.43
2.06
3.00


170.74
150.76
145.18
135.11
130.70
128.83
128.39
126.68
124.69
77.48
77.16
76.84
38.20
135.114
130.699
128.830
128.391
126.677
124.687
134
132
130
128
126
ppm
O
Ph
N
NO2
3s
1H NMR, CDCl3, 400 MHz, 298 K
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm