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## Graphical Abstract

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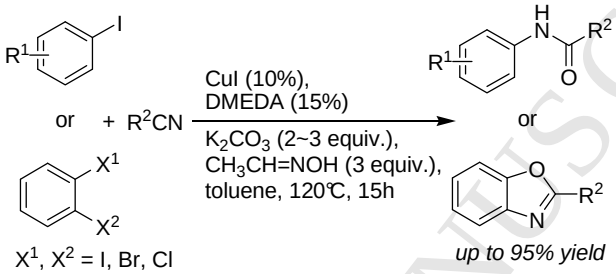
*College of Chemistry and Material Sciences, Sichuan Normal University, Chengdu 610068, Sichuan, China*



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# An improved protocol for synthesis of *N*-arylamides and benzoxazoles by the copper-catalyzed reaction of aryl halides with nitriles

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*College of Chemistry and Material Sciences, Sichuan Normal University, Chengdu 610068, Sichuan, China*
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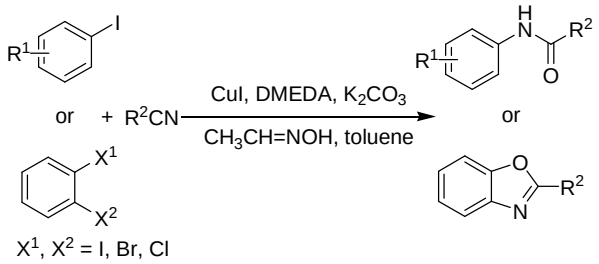
ABSTRACT

An improved protocol for the synthesis of *N*-arylamides and benzoxazoles by the copper-catalyzed reaction of aryl halides with nitriles has been developed. Use of acetaldoxime as the hydrolysis reagent instead of $H_2O$ facilitates the operation of the reaction. The significantly decreased amount of nitriles, along with use of weak base $K_2CO_3$ instead of strong base KOH, makes this transformation atom-efficient and environmentally benign. A variety of *N*-arylamides and benzoxazole derivatives can be synthesized according to this approach.



## 1. Introduction

*N*-Arylamides are present in a wide variety of biologically active molecules and organic materials.[1] Synthesis of them has aroused great interest of organic chemists.[1-3] As a common method for the synthesis of *N*-Arylamides, Goldberg reactions are usually carried out under harsh conditions.[2] In recent decades, ligands assisted copper-catalyzed Goldberg reaction has been developed greatly, which makes it possible to synthesize *N*-arylamides under mild conditions.[3] General, aryl monohalides are used as coupling partner of amides in Goldberg reaction. However, if aryl *o*-dihalides are utilized as substrates, benzoxazoles[4] can be produced through a domino C-N and C-O coupling.[5] Moreover, the reactant amides in the Goldberg reaction can be prepared easily from nitriles by hydrolysis.[6-8] Recently we developed an amination reaction of aryl halides with nitriles.[9] The use of nitriles as nitrogen nucleophiles can make the synthesis of *N*-arylamides simpler than that from amides through *in-situ* hydrolysis. A variety of *N*-arylamides or benzoxazoles can be synthesized by the approach utilizing aryl monohalides or aryl *o*-dihalides as the partners of the nitriles respectively. Despite above-mentioned advantages, however, the reaction still suffered from several limitations: (1) It is difficult to control the amount of $H_2O$ strictly; (2) Use of reactant nitriles as the solvent deviated from atom economy; (3) It is bad for functional group tolerance to use strong base KOH. Herein, we will report an improved protocol for the synthesis of *N*-arylamides and benzoxazoles by the copper-catalyzed reaction of aryl halides with nitriles (Scheme 1). The improved protocol can effectively overcome the above-mentioned shortcomings and make the synthesis of *N*-arylamides and benzoxazoles more efficient.



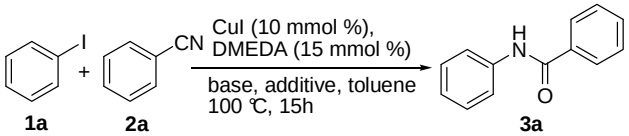

**Scheme 1**. An improved protocol.

## 2. Results and Discussion

Initially, we investigated the coupling reaction of iodobenzene **1a** with benzonitrile **2a** in toluene using KOH/$Cs_2CO_3$ as the mixed base and $H_2O$ as the hydrolysis reagent according to our previous method.[9] Under this condition, the product *N*-arylamide **3a** was obtained in a yield of 42% (entry 1, Table 1). It was very regretful that no product was available if only weak base $Cs_2CO_3$ or $K_2CO_3$ was used in the reaction (entry 2-3, Table 1). It implied that weak base $Cs_2CO_3$ or $K_2CO_3$ could not promote *in-situ* hydrolysis of nitriles in this condition. Inspired by related literature,[8] we decided to utilize acetaldoxime as the hydrolysis reagent instead of $H_2O$. The experimental results showed the reaction can undergo smoothly under the condition of weak base $Cs_2CO_3$ or $K_2CO_3$ to generate the desired product **3a** in a good yield with the aid of acetaldoxime (entries 4-5, Table 1). It was pleased, with the temperature raised to 110 °C or 120 °C, the yields were increased to 79%, 94% respectively (entries 6-7,

Table 1). Lower catalyst loading reduced the yield significantly (entry 8, Table 1).

**Table 1.** Copper-catalyzed reaction of iodobenzene **1a** with benzonitrile **2a** in different conditions.[a]




**1a** **2a** **3a**

| entry | base (2.0 equiv.) | additive (equiv.) | T (℃) | yield (%) |
|---|---|---|---|---|
| 1[b] | KOH/$Cs_2CO_3$ | $H_2O$ (8.5) | 100 | 42 |
| 2 | $Cs_2CO_3$ | $H_2O$ (8.5) | 100 | 0 |
| 3 | $K_2CO_3$ | $H_2O$ (8.5) | 100 | 0 |
| 4 | $Cs_2CO_3$ | $CH_3CH$=NOH (3.0) | 100 | 64 |
| 5 | $K_2CO_3$ | $CH_3CH$=NOH (3.0) | 100 | 63 |
| 6 | $K_2CO_3$ | $CH_3CH$=NOH (3.0) | 110 | 79 |
| 7 | $K_2CO_3$ | $CH_3CH$=NOH (3.0) | 120 | 94 |
| 8[c] | $K_2CO_3$ | $CH_3CH$=NOH (3.0) | 120 | 36 |

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), CuI (0.05 mmol), DMEDA (*N, N'*-dimethyl-1, 2-ethanediamine, 0.075 mmol), base (1.0 mmol), additive, toluene (2.0 mL), 15h, under Ar. The yields were isolated yields.

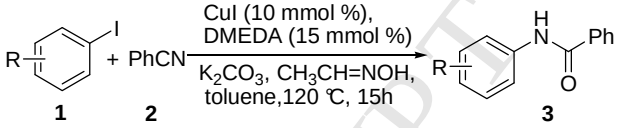
[b] KOH (0.25 mmol.), $Cs_2CO_3$ (0.75 mmol).

[c] 0.025 mmol CuI and 0.0375 mmol DMEDA were used.

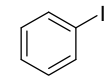
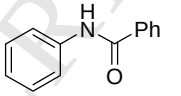
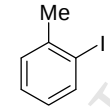
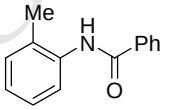
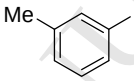
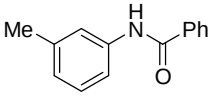
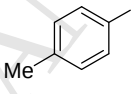
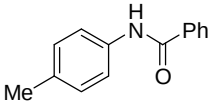
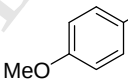
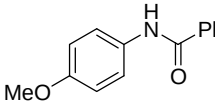
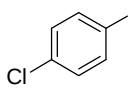
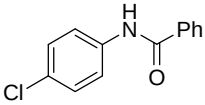
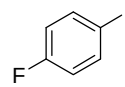
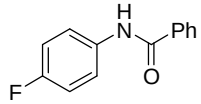
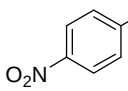
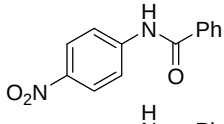
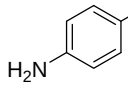
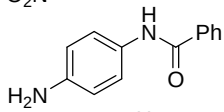
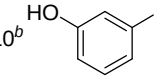
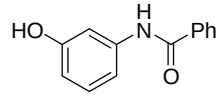
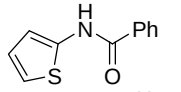
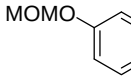
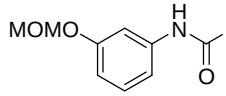
The scope of the coupling reaction of aryl halides with nitriles was expanded to a variety of substituted aryl halides **1**. Aryl halides **1** with both electron-donating groups and electron-withdrawing groups smoothly underwent the transformation generating the desired products **3** in moderate to excellent yields (25-95%, Table 2). 2-Methyliodobenzene **1b** gave the desired product in a lower yield than 3-methyliodobenzene **1c** and 4-methyliodobenzene **1d**, which indicated that the reaction wound be affected by steric effects (entries 2-4, Table 2). 4-Methoxyiodobenzene **1e** underwent this transformation to generate the desired product **3e** in a good yield of 88% (entry 5, Table 2). Substituted iodobenzene with Cl, F smoothly led to corresponding amides in excellent yields of 95%, 88% respectively, with the halogen substituent group intact (entries 6-7, Table 2). It is notable that strong electron-withdrawing group nitro almost does not affect the reaction, and the yield is 79% (entry 8, Table 2). Surprisingly, 4-aminoiodobenzene **1i** and 3-hydroxyiodobenzene **1j** could also form the corresponding products **3i** and **3j** in yields of 85%, 46% respectively, with the functional groups $NH_2$, OH compatible under the catalytic conditions which could be further transformed into other functionalities (entry 9-10, Table 2). The heterocyclic compound 2-iodothiophene **1k** sucsessfully underwent the reaction despite a low yield of 35% (entry 11, Table 2). In addition, MOM protected 3-hydroxyiodobenzene could also be transformed into the corresponding product **3l** in a good yield of 76% (entries 12, Table 2).

To investigate the scope of the nitriles in this transformation, iodobenzene **1a** was selected as the partner to react with different nitriles. The results in Table 3 show that various kinds of aryl nitriles, heteroaryl nitriles and aliphatic nitriles can undergo this transformation to generate the desired products in moderate to excellent yields (38-94%). The experimental data showed that the electronic properties of the substituents of aryl nitriles had little effect on the reation. Both electron-donating groups and electron-withdrawing groups smoothly underwent this reaction generating desired products **3** in good yields (entries 1-6, Table 3). However, it was observed that the reaction could be affected by steric effects by comparing the data from entries 2-4 in Table 3. It is notable that heteroaryl nitriles **2g**, **2h** and aliphatic nitriles **2i**, **2j** can also smoothly undergo this reaction to generate the corresponding products **3** in moderate yields (entries 7-10, Table 3).

**Table 2.** Copper-catalyzed reaction of different aryl halides **1** with benzonitrile **2a**. [a]



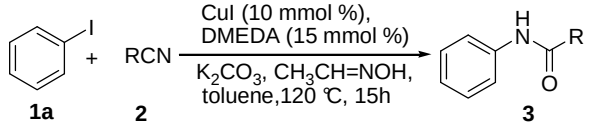

**1** **2** **3**

| entry | 1 | | 3 | | yield (%) |
|---|---|---|---|---|---|
| 1 |  | **1a** |  | **3a** | 94 |
| 2 |  | **1b** |  | **3b** | 25 |
| 3 |  | **1c** |  | **3c** | 86 |
| 4 |  | **1d** |  | **3d** | 85 |
| 5 |  | **1e** |  | **3e** | 88 |
| 6 |  | **1f** |  | **3f** | 95 |
| 7 |  | **1g** |  | **3g** | 88 |
| 8 |  | **1h** |  | **3h** | 79 |
| 9 |  | **1i** |  | **3i** | 85 |
| 10[b] |  | **1j** |  | **3j** | 46 |
| 11 |  | **1k** |  | **3k** | 35 |
| 12 |  | **1l** |  | **3l** | 76 |

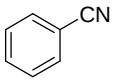
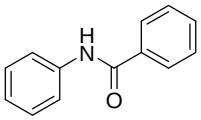
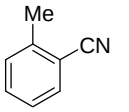
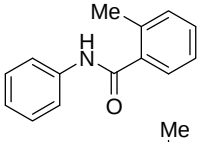
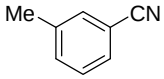
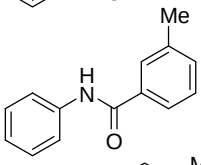
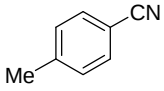
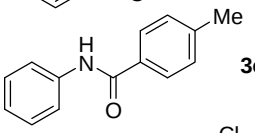
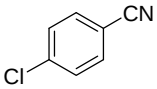
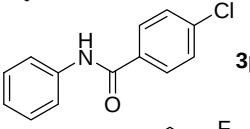
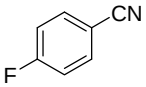
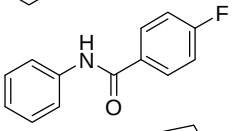
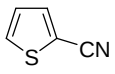
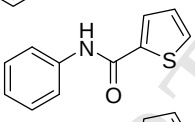
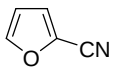
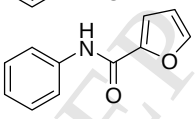
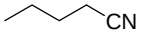
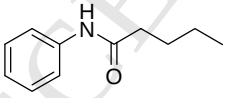
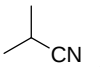
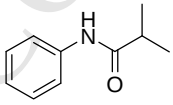
[a] Reaction conditions: **1** (0.5 mmol), **2a** (1.0 mmol), CuI (0.05 mmol), DMEDA (*N, N'*-dimethyl-1, 2-ethanediamine, 0.075 mmol), $K_2CO_3$ (1.0 mmol), $CH_3CH$=NOH (1.5 mmol), toluene (2.0 mL), 120℃, 15h, under Ar. The yields were isolated yields.

[b] 1.5 mmol $K_2CO_3$ were used.

**Table 3.** Copper-catalyzed reaction of iodobenzene **1a** with different nitriles **2**. [a]



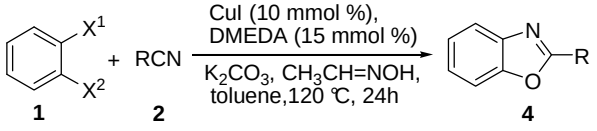

**1a** **2** **3**

| entry | 2 | 3 | yield (%) |
|---|---|---|---|
| 1 |  **2a** |  **3a** | 94 |
| 2 |  **2b** |  **3m** | 56 |
| 3 |  **2c** |  **3n** | 84 |
| 4 |  **2d** |  **3o** | 86 |
| 5 |  **2e** |  **3p** | 85 |
| 6 |  **2f** |  **3q** | 91 |
| 7 |  **2g** |  **3r** | 63 |
| 8 |  **2h** |  **3s** | 38 |
| 9 |  **2i** |  **3t** | 51 |
| 10 |  **2j** |  **3u** | 52 |

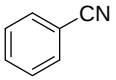
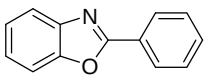
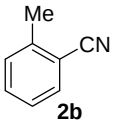
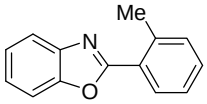
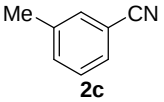
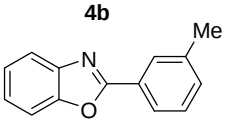
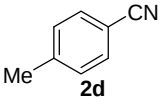
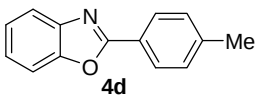
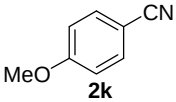
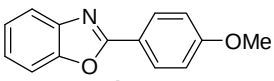
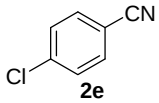
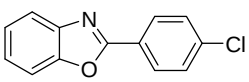
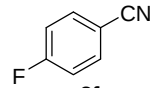
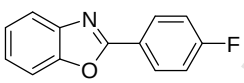
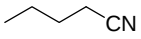
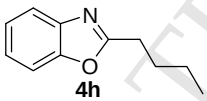
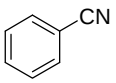
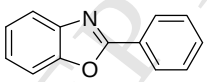
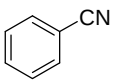
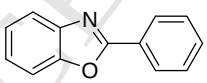
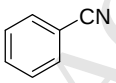
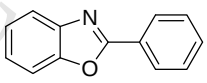
[a] Reaction conditions: **1a** (0.5 mmol), **2** (1.0 mmol), CuI (0.05 mmol), DMEDA (*N*, *N*'-dimethyl-1, 2-ethanediamine, 0.075 mmol), $K_2CO_3$ (1.0 mmol), $CH_3CH$=NOH (1.5 mmol), toluene (2.0 mL), 120℃, 15h, under Ar. The yields were isolated yields.

When *o*-dihalobenzenes were selected as reaction partners of nitriles, benzoxazole derivatives can be obtained through a domino hydrolysis, C-N and C-O coupling (Table 4). Firstly, a variety of nitriles were employed to react with 1-bromo-2-iodobenzene **1m**. The experimental data from entries 1-7 in Table 4 showed that the annulation reaction can be affected by electronic properties of the substituents of aryl nitriles. It seemed that aryl nitriles with electron-donating groups gave higher yields than ones with electron-withdrawing groups (entries 1-7, Table 4). Moreover, 2-methylbenzonitrile **2b** gave a lower yield than 3-methylbenzonitrile **2c** and 4-methylbenzonitrile **2d** indicating the annulation reaction can also be affected by steric effects (entries 2-4, Table 4). It is notable that pentanenitrile **2i** also smoothly led to desired product **4h** in a yield of 41% (entry 8, Table 4). In addition, other *o*-dihalobenzenes 1, 2-diiodobenzene **1n**, 1-chloro-2-iodobenzene **1o**, 1, 2-dibromobenzene **1p** also successfully underwent the reaction despite lower yields than 1-bromo-2-iodobenzene **1m** (entries 9-11, Table 4).

**Table 4.** Copper-catalyzed annulation reactions of *o*-dihalobenzenes **1** with nitriles **2**.[a]



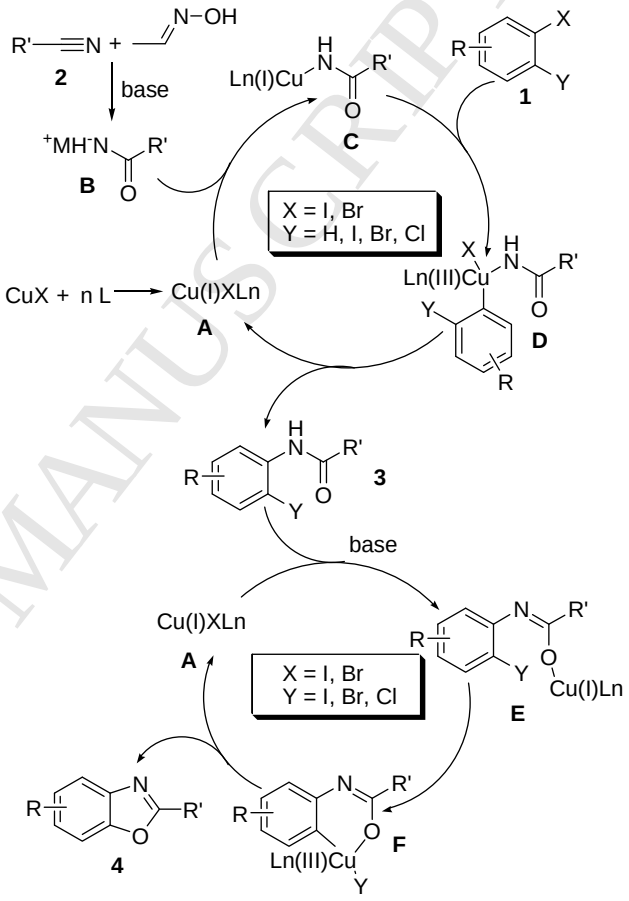

**1** **2** **4**

| entry | **1** ($X^1$, $X^2$) | **2** | **4** | yield (%) |
|---|---|---|---|---|
| 1 | I, Br |  |  | 82 |
| | **1m** | **2a** | **4a** | |
| 2 | I, Br |  |  | 55 |
| | **1m** | **2b** | **4b** | |
| 3 | I, Br |  |  | 86 |
| | **1m** | **2c** | **4c** | |
| 4 | I, Br |  |  | 87 |
| | **1m** | **2d** | **4d** | |
| 5 | I, Br |  |  | 72 |
| | **1m** | **2k** | **4e** | |
| 6 | I, Br |  |  | 34 |
| | **1m** | **2e** | **4f** | |
| 7 | I, Br |  |  | 51 |
| | **1m** | **2f** | **4g** | |
| 8 | I, Br |  |  | 41 |
| | **1m** | **2i** | **4h** | |
| 9 | I, I |  |  | 58 |
| | **1n** | **2a** | **4a** | |
| 10[b] | I, Cl |  |  | 44 |
| | **1o** | **2a** | **4a** | |
| 11 | Br, Br |  |  | 33 |
| | **1p** | **2a** | **4a** | |

[a] Reaction conditions: **1** (0.5 mmol), **2** (1.0 mmol), CuI (0.05 mmol), DMEDA (*N*, *N'*-dimethyl-1, 2-ethanediamine, 0.075 mmol), $K_2CO_3$ (1.5 mmol), $CH_3CH$=NOH (1.5 mmol), toluene (2.0 mL), 120℃, 24h, under Ar. The yields were isolated yields.

[b] 0.10 mmol CuI and 0.15 mmol DMEDA were used.

The probable catalytic mechanism for this transformation is illustrated in Scheme 2. Two catalytic cycles may be involved. Initially, the hydrolysis of nitriles **2** under basic condition using acetaldoxime as hydrolysis reagent produces the amide salts **B**, which are exposed to the copper catalyst **A** to generate the metallic intermediates **C**. Aryl halides **1** undergo an oxidative addition to intermediates **C** to form the metallic intermediates **D**, which produce the amide products **3** through the reductive elimination reaction. The amides **3** subsequently enter into the next cycle, in which metallic intermediates **E** are formed by the reactions of amides **3** with copper catalyst **A** under basic condition. Next, intermediates **E** undergo an oxidative addition reaction to get the metallic intermediates **F**. Subsequent reductive elimination reactions of intermediates **F** generate the benzoxazole products **4** and release the catalyst **A** to complete the catalytic cycle.




**Scheme 2**. A proposed mechanism.

### 3. Conclusion

In summary, we have developed an improved protocol for the synthesis of *N*-arylamides and benzoxazoles by the copper-catalyzed reaction of aryl halides with nitriles. Use of acetaldoxime as the hydrolysis reagent instead of $H_2O$ facilitates the operation of the reaction. The significantly decreased amount of nitriles, along with use of weak base $K_2CO_3$ instead of strong base KOH, makes this transformation atom-efficient and environmentally benign. A variety of *N*-arylamides and benzoxazole derivatives can be synthesized according to this approach utilizing aryl monohalides or aryl *o*-dihalides as the partners of the nitriles, respectively. Studies on other reactions of nitriles and the applications are ongoing in our laboratory.

## 4. Experimental

### 4.1 General information

All manipulations were conducted with Schlenk tube under Ar. $^1$H NMR spectra were recorded on the Varian 400 MHz WB spectrometers. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) as an internal standard in $CDCl_3$ and DMSO-d6. $^{13}$C NMR spectra were obtained by the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.00 ppm) or DMSO-d6 (δ = 39.50 ppm). Mass spectra were obtained using electrospray ionization (ESI) mass spectrometer. Toluene was freshly distilled over Na. Without otherwise note, other materials obtained from commercial suppliers were used without further purification.

### 4.2 General procedure for the synthesis of *N*-arylamides

To a suspension of CuI (9.5 mg, 0.05 mmol), $K_2CO_3$ (138.2 mg, 1.0 mmol) in toluene (2.0 mL) were added aryl monohalides **1** (0.5 mmol), nitrile **2** (1.0 mmol), DMEDA (8.0 uL, 0.075 mmol), acetaldoxime (92.0 uL, 1.5 mmol) under argon. The reaction mixture was stirred for 15 h at 120 ℃ under argon. The solution was cooled to room temperature and the solvent was removed under vacuum. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 5:1) to afford the *N*-arylamides **3**.

*N*-Phenylbenzamide (**3a**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 92.6 mg (94%) of **3a**; IR(KBr) $\nu_{max}$ 3345, 1655, 1532, 750 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$, ppm) δ 7.95 (s, 1H), 7.88-7.85 (m, 2H), 7.66-7.63 (m, 2H), 7.56-7.52 (m, 1H), 7.49-7.44 (m, 2H), 7.38-7.33 (m, 2H), 7.17-7.13 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$, ppm) δ 165.8, 137.9, 134.9, 131.8, 129.0, 128.7, 127.0, 124.5, 120.2; MS (ESI) m/z: $[M+H]^+$ 198.1.

*N*-*o*-Tolylbenzamide (**3b**): The reaction of *o*-methyliodobenzene **1b** (109.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 26.4 mg (25%) of **3b**; IR(KBr) $\nu_{max}$ 3245, 1649, 1524, 1489, 1310, 748 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$, ppm) δ 7.96 (d, *J* = 7.6Hz, 1H), 7.89 (d, *J* = 7.2 Hz, 2H), 7.70 (s, 1H), 7.57 (t, *J* = 6.8 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 2H), 7.29-7.23 (m, 2H), 7.13 (t, *J* = 7.6 Hz, 1H), 2.35 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, ppm) δ 165.7, 135.7, 134.9, 131.8, 130.5, 129.4, 128.8, 127.0, 126.8, 125.4, 123.2, 17.8; MS (ESI) m/z: $[M+H]^+$ 212.1.

*N*-*m*-Tolylbenzamide (**3c**): The reaction of *m*-methyliodobenzene **1c** (109.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 90.7 mg (86%) of **3c**; IR(KBr) $\nu_{max}$ 3266, 1648, 1538, 1308, 1259, 781, 710 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$, ppm) δ 7.86-7.84 (m, 3H), 7.56-7.45 (m, 4H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.26-7.22 (m, 1H), 6.96 (d, *J* = 7.6 Hz, 1H), 2.36 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, ppm) δ 165.8, 138.9, 137.8, 134.9, 131.7, 128.8, 128.6, 127.0, 125.3, 120.9, 117.4, 21.4; MS (ESI) m/z: $[M+H]^+$ 212.1.

*N*-*p*-Tolylbenzamide (**3d**): The reaction of *p*-methyliodobenzene **1d** (109.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 89.7 mg (85%) of **3d**; IR(KBr) $\nu_{max}$ 3311, 1647, 1597, 1511, 1317, 813, 714 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$, ppm) δ 7.89 (s, 1H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.54-7.51 (m, 3H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, ppm) δ 165.7, 135.3, 135.0, 134.2, 131.7, 129.5, 128.7, 127.0, 120.3, 20.9; MS (ESI) m/z: $[M+H]^+$ 212.1.

*N*-(4-Methoxyphenyl)benzamide (**3e**): The reaction of 4-methoxyiodobenzene **1e** (117.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 99.9 mg (88%) of **3e**; IR(KBr) $\nu_{max}$ 3333, 1647, 1602, 1515, 1458, 1414, 825, 715, 692 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$, ppm) δ 7.86 (d, *J* = 7.2 Hz, 2H), 7.80 (s, 1H), 7.56-7.53 (m, 3H), 7.50-7.46 (m, 2H), 6.93-6.90 (m, 2H), 3.82 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$, ppm) δ 165.6, 156.6, 135.0, 131.7, 130.9, 128.7, 126.9, 122.1, 114.2, 55.5; MS (ESI) m/z: $[M+Na]^+$ 250.1.

*N*-(4-Chlorophenyl)benzamide (**3f**): The reaction of 4-chloroiodobenzene **1f** (119.3 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 110.0 mg (95%) of **3f**; IR(KBr) $\nu_{max}$ 3350, 1655, 1596, 1519, 1493, 1399, 825, 718 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-*d6*, ppm) δ 10.39 (s, 1H), 7.95 (d, *J* = 7.6 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 2H), 7.63-7.52 (m, 3H), 7.42 (d, *J* = 8.8 Hz, 2H); $^{13}$C NMR (100 MHz, DMSO-*d6*, ppm) δ 165.7, 138.2, 134.7, 131.7, 128.5, 128.4, 127.7, 127.3, 121.8; MS (ESI) m/z: $[M+H]^+$ 242.1, $[M+Na]^+$ 254.1.

*N*-(4-Fluorophenyl)benzamide (**3g**): The reaction of 4-fluoroiodobenzene **1g** (111.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 94.5 mg (88%) of **3g**; IR(KBr) $\nu_{max}$ 3349,1653, 1509, 1406, 716 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-*d6*, ppm) δ 10.31 (s, 1H), 7.95 (d, *J* = 6.8 Hz, 2H), 7.83-7.77 (m, 2H), 7.62-7.52 (m, 3H), 7.23-7.17 (m, 2H); $^{13}$C NMR (100 MHz, DMSO-*d6*, ppm) δ 165.5, 159.5, 157.1, 135.5 (d, *J* = 2.2 Hz), 134.8, 131.6, 128.4, 127.6, 122.1(d, *J* = 7.9 Hz),, 115.2(d, *J* = 22.3 Hz),; MS (ESI) m/z: $[M+H]^+$ 216.1.

*N*-(4-Nitrophenyl)benzamide (**3h**): The reaction of 4-nitroiodobenzene **1h** (124.5 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 95.6 mg (79%) of **3h**; IR(KBr) $\nu_{max}$ 3335, 1656, 1506, 1345, 848, 719 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-*d6*, ppm) δ 10.83 (s, 1H), 8.30-8.26 (m, 2H), 8.10-8.06 (m, 2H), 7.99 (d, *J* = 6.8 Hz, 2H), 7.67-7.63 (m, 1H), 7.57 (t, *J* = 7.2 Hz, 2H); $^{13}$C NMR (100 MHz, DMSO-*d6*, ppm) δ 166.3, 145.5, 142.5, 134.2, 132.2, 128.5, 127.9, 124.8, 119.8; MS (ESI) m/z: $[M+H]^+$ 204.0.

*N*-(4-Aminophenyl)benzamide (**3i**): The reaction of 4-aminoiodobenzene **1i** (109.5 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 90.1 mg (85%) of **3i**; IR(KBr) $\nu_{max}$ 3339, 1641, 1514, 1426, 1322, 1261, 823, 702 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-*d6*, ppm) δ 9.89 (s,1H), 7.91 (d, *J* = 7.6 Hz, 2H), 7.57-7.48 (m, 3H), 7.37 (d, *J* = 8.4 Hz, 2H), 6.54 (d, *J* = 8.8 Hz, 2H), 4.95 (s, 2H); $^{13}$C NMR (100 MHz, DMSO-*d6*, ppm) δ 164.7, 145.3, 135.3, 131.2, 128.3, 128.1, 127.5, 122.3, 113.6; MS (ESI) m/z: $[M+Na]^+$ 235.1.

*N*-(3-Hydroxyphenyl)benzamide (**3j**): The reaction of 3-iodophenol **1j** (110.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 49.0 mg (46%) of **3j**; IR(KBr) $\nu_{max}$ 3369, 1631, 1539, 1450, 1281, 1210, 713, 683 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-*d6*, ppm) δ 10.13 (s, 1H), 9.43 (s, 1H), 7.92 (d, *J* = 7.2 Hz, 2H), 7.59-7.50 (m, 3H), 7.36 (s, 1H); 7.18-7.11 (m, 2H), 6.50 (d, *J* = 7.6 Hz, 1H), $^{13}$C NMR (100 MHz, DMSO-*d6*, ppm) δ 165.5, 157.5, 140.2, 135.2, 131.5, 129.3, 128.4, 127.7, 111.1, 110.8, 107.5; MS (ESI) m/z: $[M+Na]^+$ 236.1.

*N*-(Thiophen-2-yl)benzamide (**3k**): The reaction of 2-iodothiophene **1k** (105.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 35.3 mg (35%) of **3k**; IR(KBr) $\nu_{max}$ 3421, 1622, 1501, 1243, 746 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-*d6*, ppm) δ 11.56 (s, 1H), 8.01-7.99 (m, 2H), 7.64-7.54 (m, 3H), 7.03-7.01 (m, 1H), 6.95-6.90 (m, 2H); $^{13}$C NMR (100 MHz, DMSO-*d6*, ppm) δ 163.2, 140.0, 133.1, 131.9, 128.6, 127.6, 124.1, 117.4, 112.1; MS (ESI) m/z: $[M+H]^+$ 204.0.

*N*-(3-(Methoxymethoxy)phenyl)benzamide (**3l**): The reaction of 1-iodo-3-(methoxymethoxy)benzene **1l** (132.0 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 97.7 mg (76%) of **3l**; IR(KBr) $\nu_{max}$ 3306, 3087, 3068, 2991, 2946, 2901, 2826, 1649, 1601, 1014 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.90 (s, 1H), 7.87-7.84 (m, 2H), 7.55-7.52 (m, 1H), 7.50-7.43 (m, 3H), 7.28-7.26 (m,2H), 6.85-6.81 (m, 1H), 5.19 (s, 2H), 3.49 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 165.7, 157.8, 139.0, 134.9, 131.9, 129.9, 128.8, 127.0, 113.6, 112.5, 108.2, 94.4, 56.1; MS (ESI) m/z: $[M+Na]^+$ 280.1.

2-Methyl-*N*-phenylbenzamide (**3m**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with 2-methylbenzonitrile **2b** (117.1 mg, 1.0 mmol) afforded 59.1 mg (56%) of **3m**; IR(KBr) $\nu_{max}$ 3286, 1652, 1597, 1533, 1439, 1321, 1260, 889, 757 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.61 (d, *J* = 7.6 Hz, 2H), 7.57 (s, 1H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 3H), 7.26-7.22 (m,2H), 7.14 (t, *J* = 7.2 Hz, 1H), 2.49 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 168.1, 138.0, 136.3, 136.3, 131.1, 130.2, 129.0, 126.6, 125.8, 124.4, 119.9, 19.7; MS (ESI) m/z: $[M+H]^+$ 212.1.

3-Methyl-*N*-phenylbenzamide (**3n**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with 3-methylbenzonitrile **2c** (117.1 mg, 1.0 mmol) afforded 89.0 mg (84%) of **3n**; IR(KBr) $\nu_{max}$ 3266, 1650, 1597, 1541, 1490, 1442, 1328, 856, 754 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.84 (s, 1H), 7.69 (s, 1H), 7.64 (d, *J* = 7.2 Hz, 3H), 7.39-7.36 (m, 4H), 7.15 (t, *J* = 7.2 Hz, 1H), 2.43 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 166.0, 138.6, 138.0, 134.9, 132.5, 129.0, 128.6, 127.8, 124.5, 123.9, 120.2, 21.3; MS (ESI) m/z: $[M+H]^+$ 212.1.

4-Methyl-*N*-phenylbenzamide (**3o**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with 4-methylbenzonitrile **2d** (117.1 mg, 1.0 mmol) afforded 90.8 mg (86%) of **3o**; IR(KBr) $\nu_{max}$ 3352, 1650, 1524, 754 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.82 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.65-7.63 (m, 2H), 7.39-7.35 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.17-7.13 (m, 1H), 2.43 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 165.7, 142.4, 138.0, 132.1, 129.4, 129.1, 127.0, 124.4, 120.1, 21.5; MS (ESI) m/z: $[M+Na]^+$ 234.1.

4-Chloro-*N*-phenylbenzamide (**3p**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with 4-chlorobenzonitrile **2e** (92.0 mg, 1.0 mmol) afforded 98.6 mg (85%) of **3p**; IR(KBr) $\nu_{max}$ 3353, 1653, 1599, 1487, 1439, 847, 755; $^1H$ NMR (400MHz, DMSO-*d6*, ppm) δ 10.32 (s, 1H), 7.99 (d, *J*=8.8Hz, 2H), 7.77 (d, *J*=8Hz, 2H), 7.62 (d, *J*=8.4Hz, 2H), 7.36 (t, *J*=7.6Hz, 2H), 7.11(t, *J*=7.6Hz, 1H); $^{13}C$ NMR (100 MHz, DMSO-*d6*, ppm) δ 164.4, 139.0, 136.4, 133.6, 129.6, 128.6, 128.5, 123.8, 120.4; MS (ESI) m/z: $[M+H]^+$ 232.1.

4-Fluoro-*N*-phenylbenzamide (**3q**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with 4-fluorobenzonitrile **2f** (121.0 mg, 1.0 mmol) afforded 97.9 mg (91%) of **3q**; IR(KBr) $\nu_{max}$ 3353, 1655, 1506, 752 $cm^{-1}$; $^1H$ NMR (400 MHz, DMSO-d6, ppm) δ 10.28 (s, 1H), 8.08-8.03 (m, 2H), 7.80-7.77 (m, 2H), 7.41-7.34 (m, 4H), 7.13-7.10 (m, 1H); $^{13}C$ NMR (100 MHz, DMSO-d6, ppm) δ 165.3, 164.4, 162.8，139.1, 131.4 (d, *J* = 3.2 Hz), 130.4 (d, *J* = 8.3 Hz), 128.6, 123.7, 120.4, 115.3 (d, *J* = 21.8 Hz); MS (ESI) m/z: $[M+H]^+$ 216.1.

*N*-Phenylthiophene-2-carboxamide (**3r**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with thiophene-2-carbonitrile **2g** (109.2 mg, 1.0 mmol) afforded 63.9 mg (63%) of **3r**; IR(KBr) $\nu_{max}$ 3303, 1631, 1595, 1535, 1445, 1323, 755 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.75 (s, 1H), 7.64-7.61 (m, 3H), 7.55 (d, *J* = 5.2 Hz, 1H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.17-7.12 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 159.9, 139.2, 137.5, 130.8, 129.1, 128.4, 127.8, 124.6, 120.2; MS (ESI) m/z: $[M+H]^+$ 204.1.

*N*-phenylfuran-2-carboxamide (**3s**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with furan-2-carbonitrile **2h** (93.0 mg, 1.0 mmol) afforded 35.5 mg (38%) of **3s**; IR:(KBr) $\nu_{max}$ 3435, 3282, 3141, 1655, 1599, 1479, 1324, 758 $cm^{-1}$; $^1H$NMR (400 MHz, $CDCl_3$, ppm) δ 8.11 (s, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.52 (s, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.27-7.25 (m, 1H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.58-6.57 (m, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 156.0, 147.7, 144.2, 137.3, 129.1, 124.5, 119.9, 115.3, 112.6; MS (ESI) m/z: $[M+H]^+$ 188.2.

*N*-phenylpentanamide (**3t**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with pentanenitrile **2i** (83.0 mg, 1.0 mmol) afforded 45.1 mg (51%) of **3t**; IR(KBr) $\nu_{max}$ 3246, 2931, 1657, 1547, 760 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.48 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.27-7.23 (m, 2H), 7.08-7.04 (m, 1H), 2.32 (t, *J* = 7.6 Hz, 2H), 1.69-1.62 (m, 2H), 1.38-1.29 (m, 2H), 0.88 (t, *J* = 7.2 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 172.3, 138.1, 128.6, 123.9, 120.1, 37.1, 27.7, 22.2, 13.7; MS (ESI) m/z: $[M+Na]^+$ 200.1.

*N*-phenylisobutyramide (**3u**): The reaction of iodobenzene **1a** (102.0 mg, 0.5 mmol) with isobutyronitrile **2j** (69.0 mg, 1.0 mmol) afforded 42.4 mg (52%) of **3u**; IR(KBr) $\nu_{max}$ 3301, 3263, 1662, 1549, 1442, 759 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.54 (d, *J* = 7.6 Hz, 2H), 7.48 (s, 1H), 7.32-7.26 (m, 2H), 7.11-7.07 (m, 1H), 2.55-2.49 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 175.4, 138.0, 128.9, 124.1, 119.8, 36.6, 19.6; MS (ESI) m/z: $[M+Na]^+$ 186.0.

### 4.3 General procedure for the synthesis of benzoxazoles

To a suspension of CuI (9.5 mg, 0.05 mmol), $K_2CO_3$ (207.3 mg, 1.5 mmol) in toluene (2.0 mL) were added aryl *o*-dihalides **1** (0.5 mmol), nitrile **2** (1.0 mmol), DMEDA (8.0 uL, 0.075 mmol), acetaldoxime (92.0 uL, 1.5 mmol) under argon. The reaction mixture was stirred for 15 h at 120 ℃ under argon. The solution was cooled to room temperature and the solvent was removed under vacuum. The crude product was purified by column chromatography on silica gel (eluent: petroleum ether / ethyl acetate = 30:1) to afford the benzoxazoles **4**.

2-Phenylbenzoxazole (**4a**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with benzonitrile **2a** (103.0 mg, 1.0 mmol) afforded 80.0 mg (82%) of **4a**; IR(KBr) $\nu_{max}$ 3060, 1551, 1446, 744 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.28-8.26 (m, 2H), 7.80-7.78 (m, 1H), 7.61-7.53 (m, 4H), 7.37-7.35 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.0, 150.7, 141.9, 131.6, 128.9, 127.6, 127.0, 125.1, 124.6, 120.0, 110.6; MS (ESI) m/z: $[M+H]^+$ 196.1.

2-*o*-Tolylbenzoxazole (**4b**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with 2-methylbenzonitrile **2b** (117.2 mg, 1.0 mmol) afforded 57.9 mg (55%) of **4b**; IR(KBr) $\nu_{max}$ 3060, 1551, 1446, 744 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.19-8.17 (m, 1H), 7.82-7.80 (m, 1H), 7.61-7.58 (m, 1H), 7.42-7.26 (m, 5H), 2.82 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.4, 150.2, 142.1, 138.8, 131.8, 130.9, 129.9, 126.2, 126.0, 125.0, 124.4, 120.1, 110.5, 22.2; MS (ESI) m/z: $[M+H]^+$ 210.1.

2-*m*-Tolylbenzoxazole (**4c**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with 3-methylbenzonitrile **2c** (117.1 mg, 1.0 mmol) afforded 89.9mg (86%) of **4c**; IR(KBr) $\nu_{max}$ 3433, 1551, 1446, 744 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.11 (s, 1H), 8.05 (d, *J* = 7.6 Hz, 1H), 7.79-7.77 (m, 1H), 7.60-7.58 (m, 1H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.38-7.35 (m, 3H), 2.46 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$,

ppm) δ 163.2, 150.7, 142.0, 138.7, 132.4, 128.8, 128.1, 126.9, 125.0, 124.7, 124.5, 119.9, 110.5, 21.4; MS (ESI) m/z: $[M+H]^+$ 210.1.

2-*p*-Tolylbenzoxazole (**4d**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with 4-methylbenzonitrile **2d** (117.1 mg, 1.0 mmol) afforded 90.9 mg (87%) of **4d**; IR(KBr) $\nu_{max}$ 3054, 2919, 1502, 746 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.15 (d, *J* = 8.4 Hz, 2H), 7.78-7.75 (m, 1H), 7.59-7.56 (m, 1H), 7.36-7.32 (m, 4H), 2.45 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.3, 150.6, 142.1, 142.1, 129.6, 127.6, 124.9, 124.5, 124.3, 119.8, 110.5, 21.6; MS (ESI) m/z: $[M+H]^+$ 210.1.

2-(4-Methoxyphenyl)benzoxazole (**4e**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with 4-methoxybenzonitrile **2k** (133.1 mg, 1.0 mmol) afforded 80.6mg (72%) of **4e**; IR(KBr) $\nu_{max}$ 3435, 1619, 1501, 1453, 831, 741, 729 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.20 (d, *J* = 9.2 Hz, 2H), 7.76-7.73 (m, 1H), 7.58-7.55(m,1H), 7.35-7.32 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 3.90 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 163.2, 162.3, 150.6, 142.2, 129.4, 124.6, 124.4, 119.6, 119.6, 114.3, 110.4, 55.4; MS (ESI) m/z: $[M+H]^+$ 226.2.

2-(4-Chlorophenyl)benzoxazole (**4f**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with 4-chlorobenzonitrile **2e** (92.0 mg, 1.0 mmol) afforded 42.8mg (34%) of **4f**; IR(KBr) $\nu_{max}$ 3060, 1551, 1446, 744 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.20 (d, *J* = 8.0 Hz, 2H), 7.79-7.77 (m, 1H), 7.61-7.58 (m, 1H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.40-7.36 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 162.0, 150.7, 141.9, 137.7, 129.3, 129.3, 128.8, 125.4, 124.7, 120.0, 110.6; MS (ESI) m/z: $[M+H]^+$ 230.1.

2-(4-Fluorophenyl)benzoxazole (**4g**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with 4-fluorobenzonitrile **2f** (121.0 mg, 1.0 mmol) afforded 54.3 mg (51%) of **4g**; IR(KBr) $\nu_{max}$ 1617, 688 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 8.24-8.22 (m, 2H), 7.72-7.70 (m, 1H), 7.69-7.52 (m, 3H), 7.33-7.26 (m, 1H), 7.14-7.09 (m, 1H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 164.8 (d, *J* = 250.7 Hz), 162.2, 150.7, 142.0, 129.8 (d, *J* = 9.9 Hz), 125.1, 124.7, 123.4 (d, *J* = 3.0 Hz), 119.9, 116.2 (d, *J* = 22.2 Hz), 110.6; MS (ESI) m/z: $[M+H]^+$ 214.2.

2-butylbenzoxazole (**4h**): The reaction of 1,2-diiodobenzene **1m** (141.5 mg, 0.5 mmol) with pentanenitrile **2i** (83.0 mg, 1.0 mmol) afforded 35.9 mg (41%) of **4h**; IR(KBr) $\nu_{max}$ 3059, 2960, 2933, 2873, 1615, 1572, 746 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$, ppm) δ 7.69-7.66 (m, 1H), 7.49-7.46 (m, 1H), 7.32-7.27 (m, 2H), 2.94 (t, *J* = 7.6 Hz, 2H), 1.97-1.84 (m, 2H), 1.51-1.41 (m, 2H), 0.97 (t, *J* = 7.6 Hz, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$, ppm) δ 167.3, 150.7, 141.2, 124.3, 124.0, 119.4, 110.2, 28.8, 28.3, 22.2, 13.7; MS (ESI) m/z: $[M+H]^+$ 176.1.

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# An improved protocol for synthesis of *N*-arylamides and benzoxazoles by the copper-catalyzed reaction of aryl halides with nitriles

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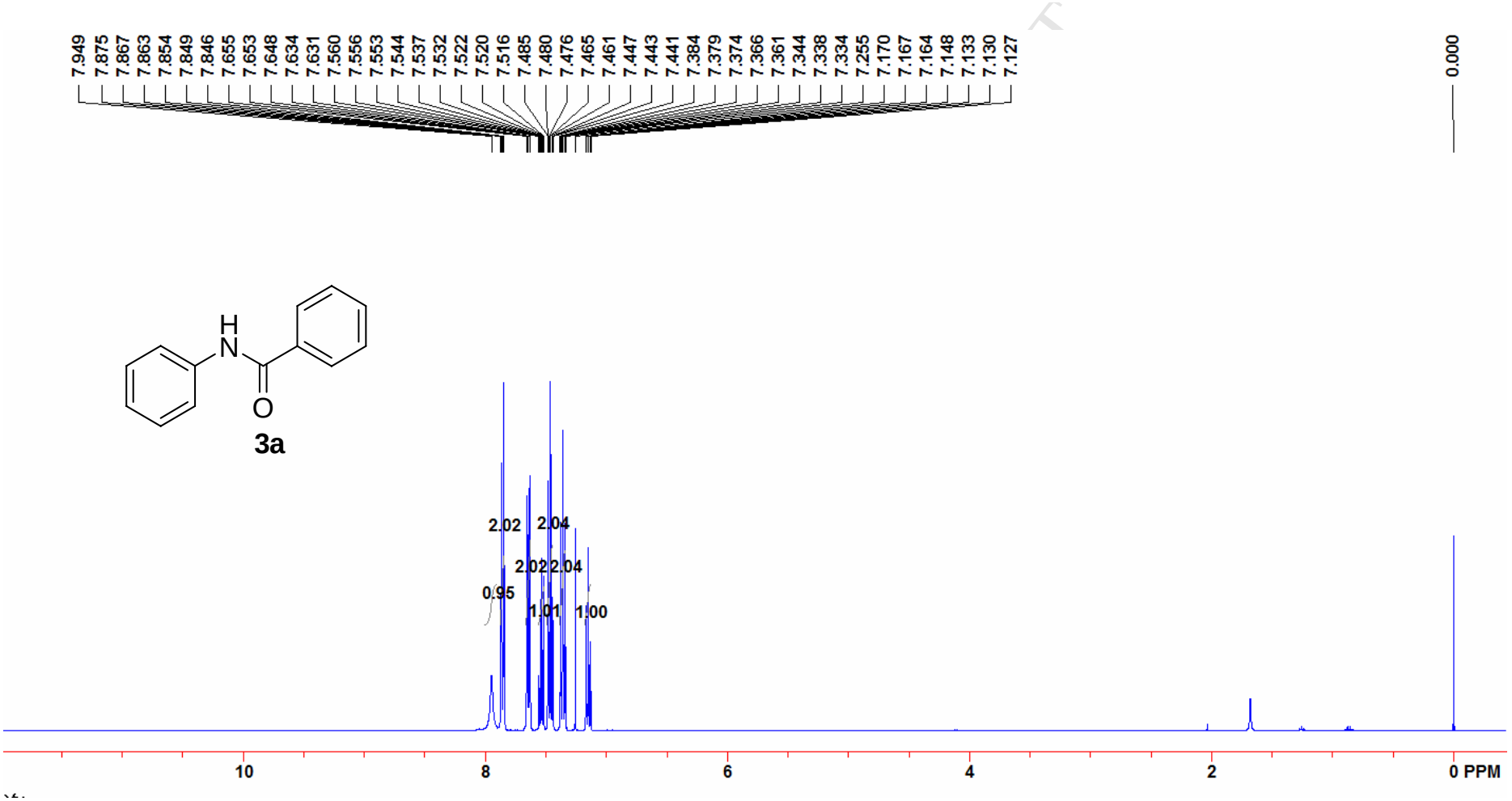
E-mail: xiangsk@hotmail.com；wangbiqin1964@126.com
Fax: +86-028-84766730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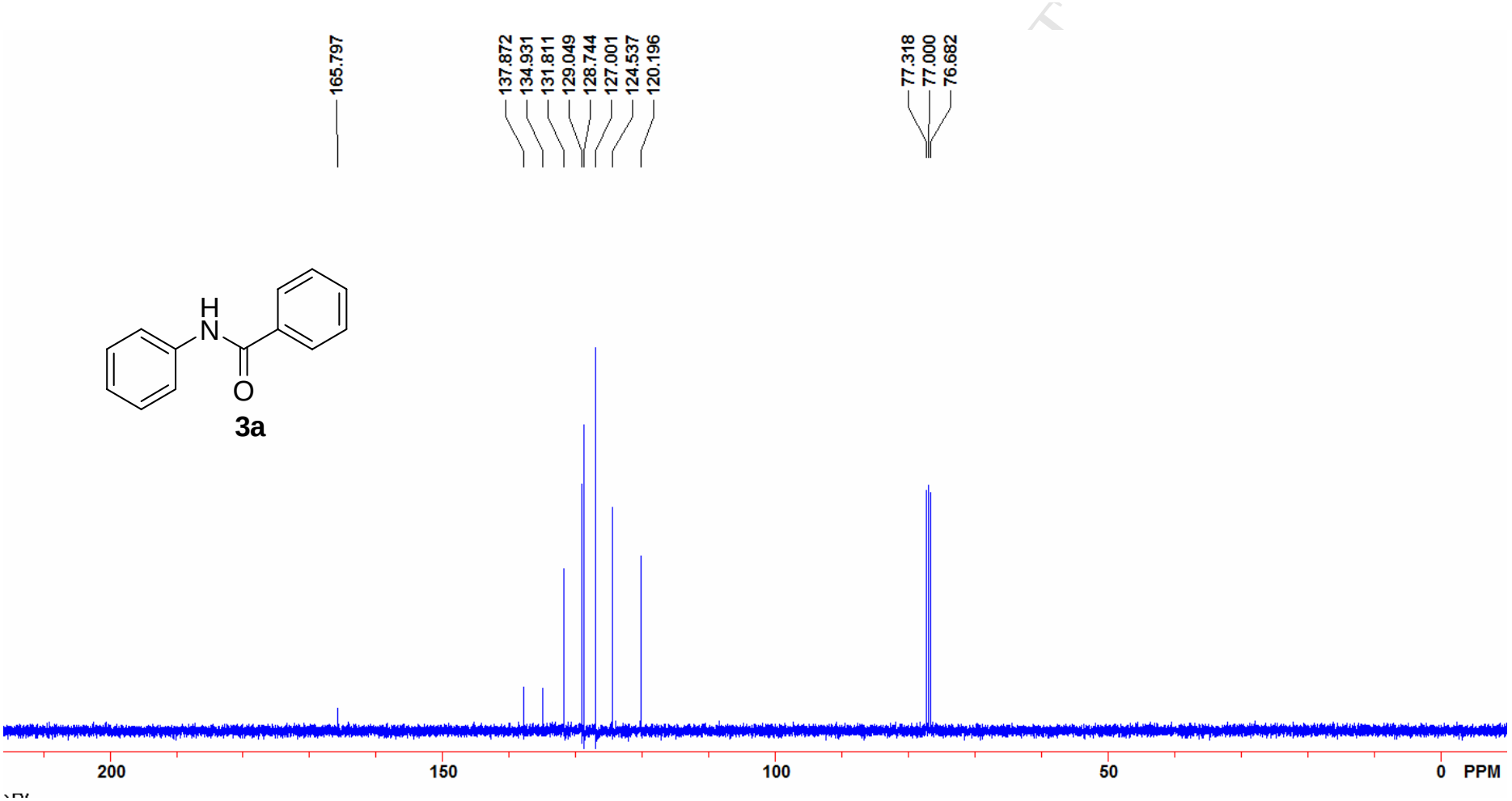
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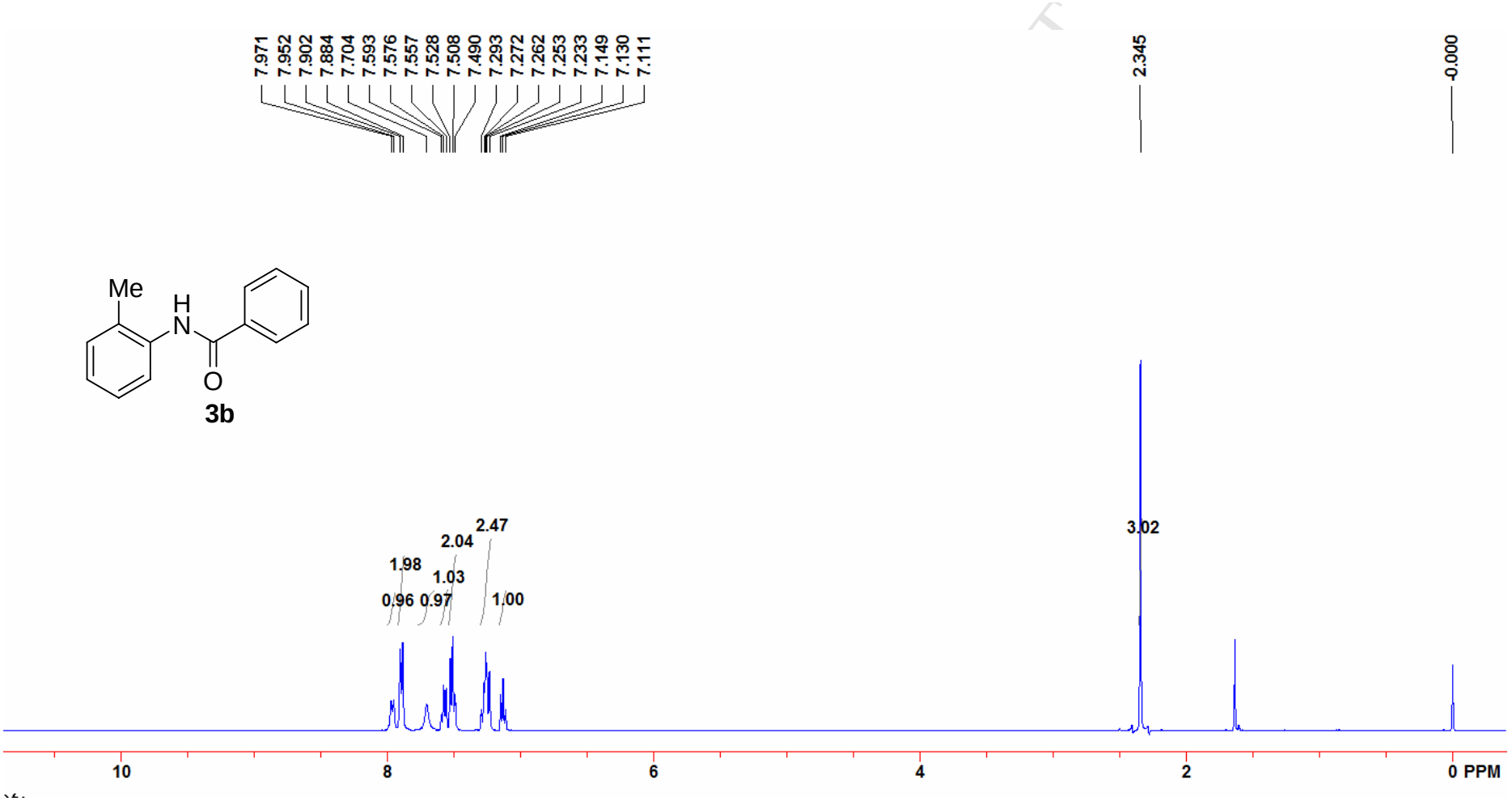
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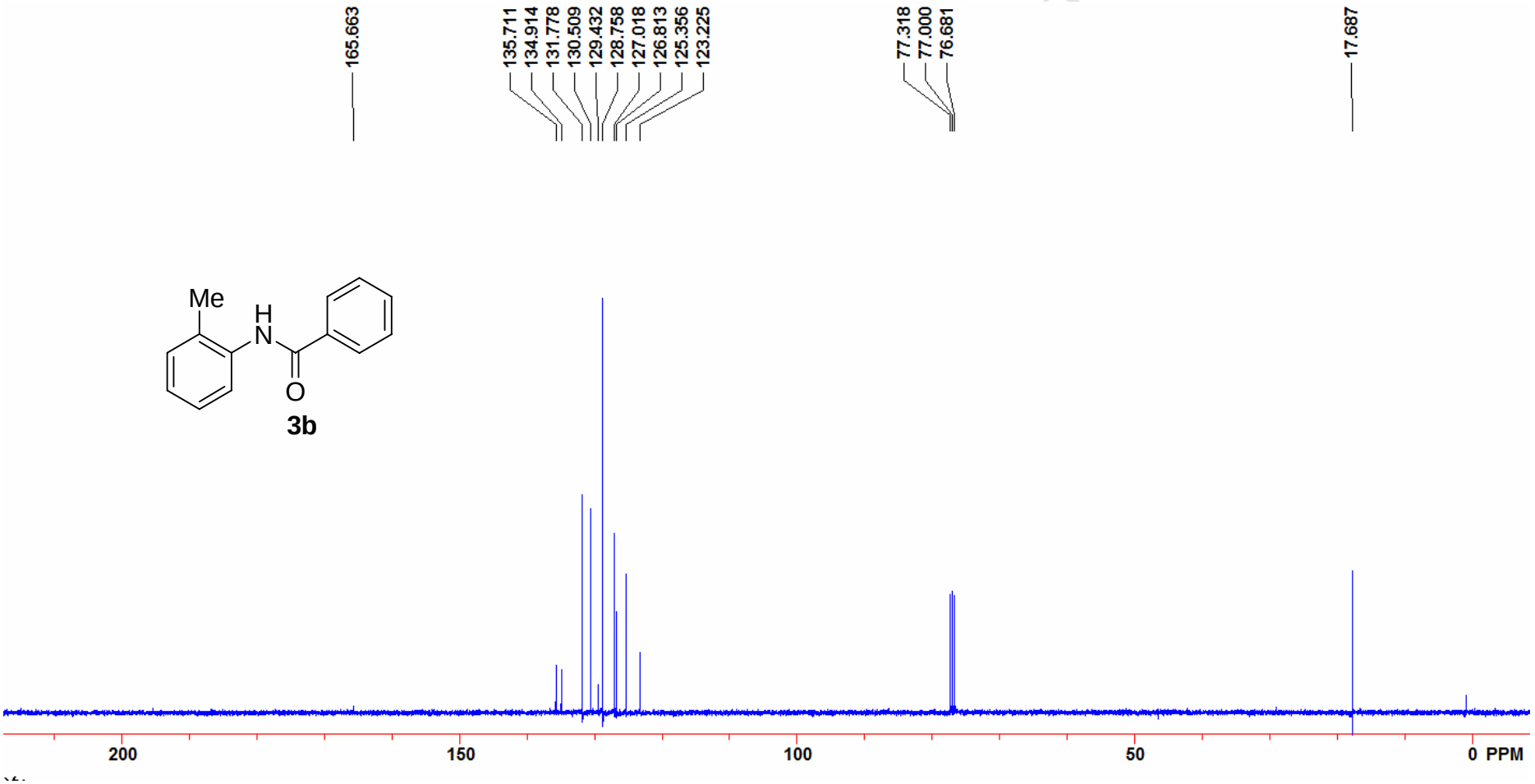

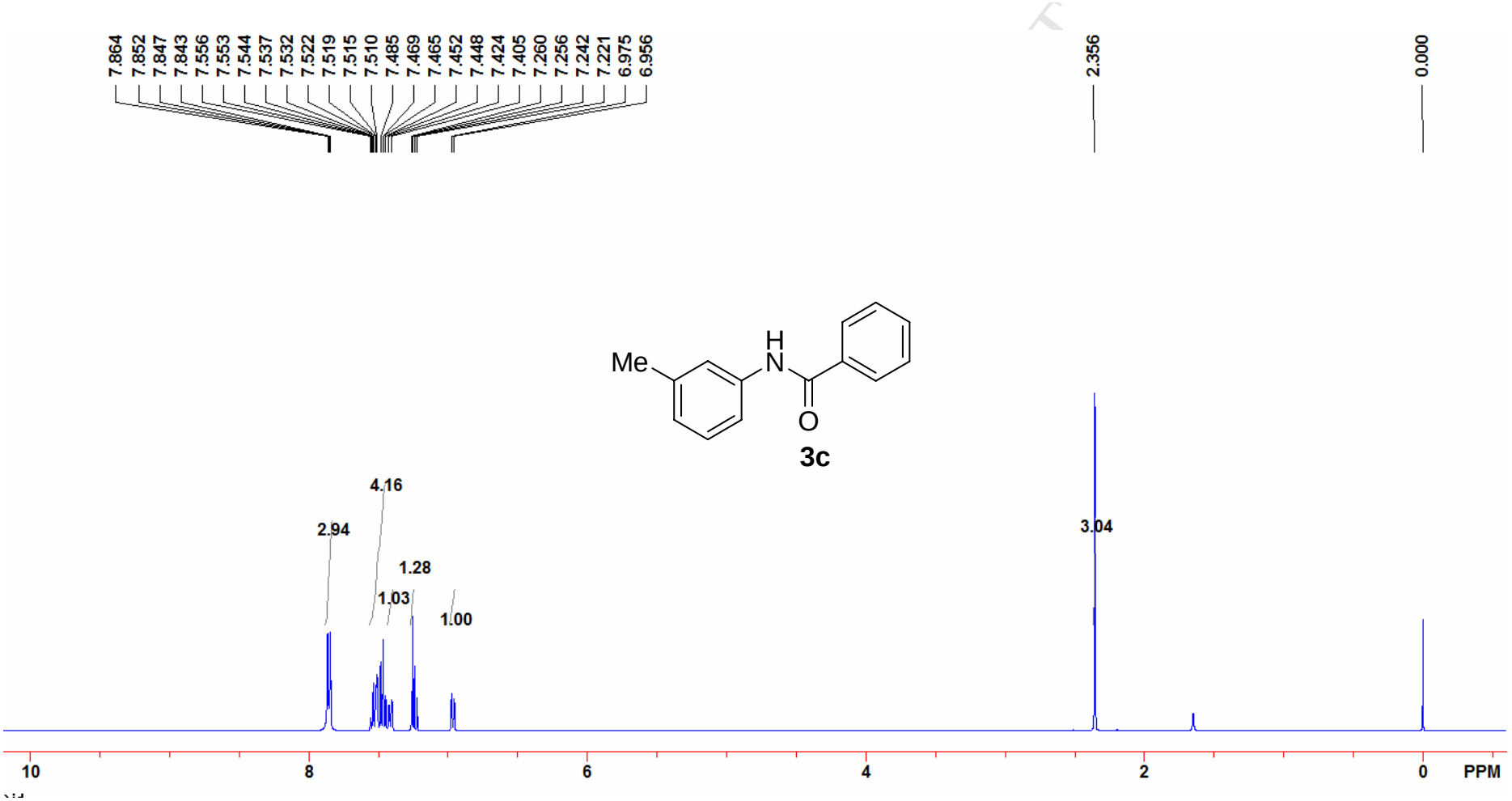
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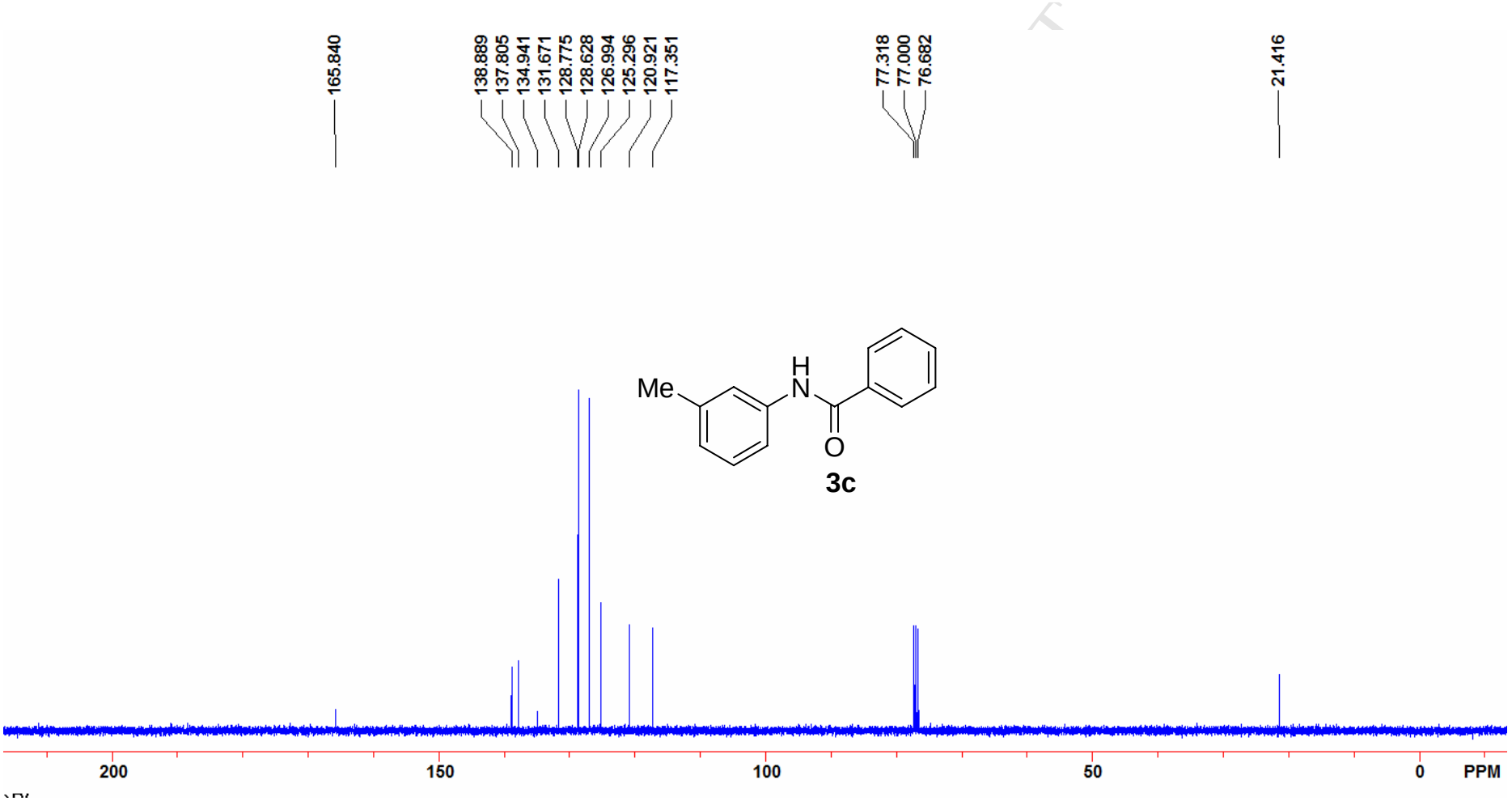

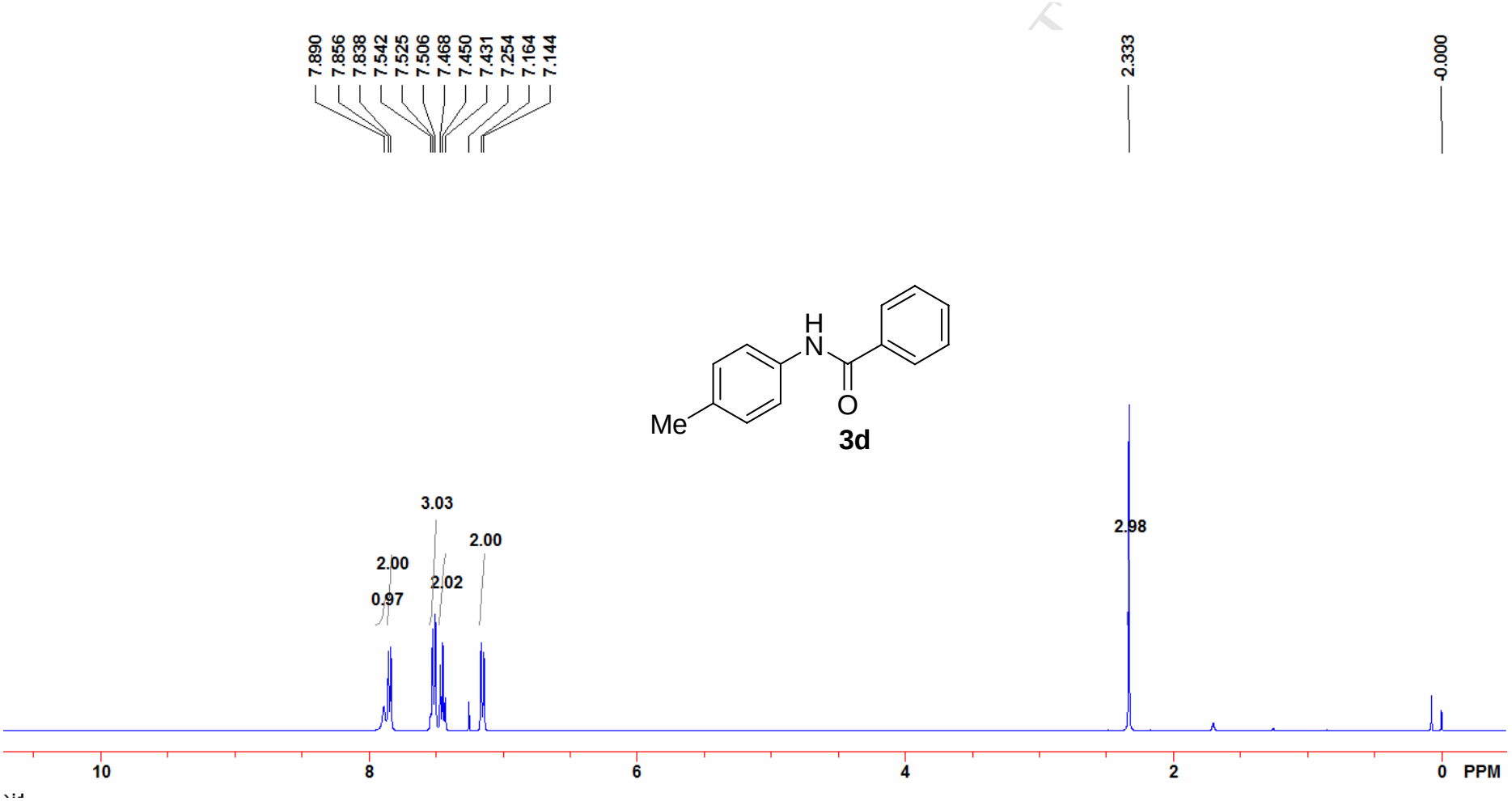
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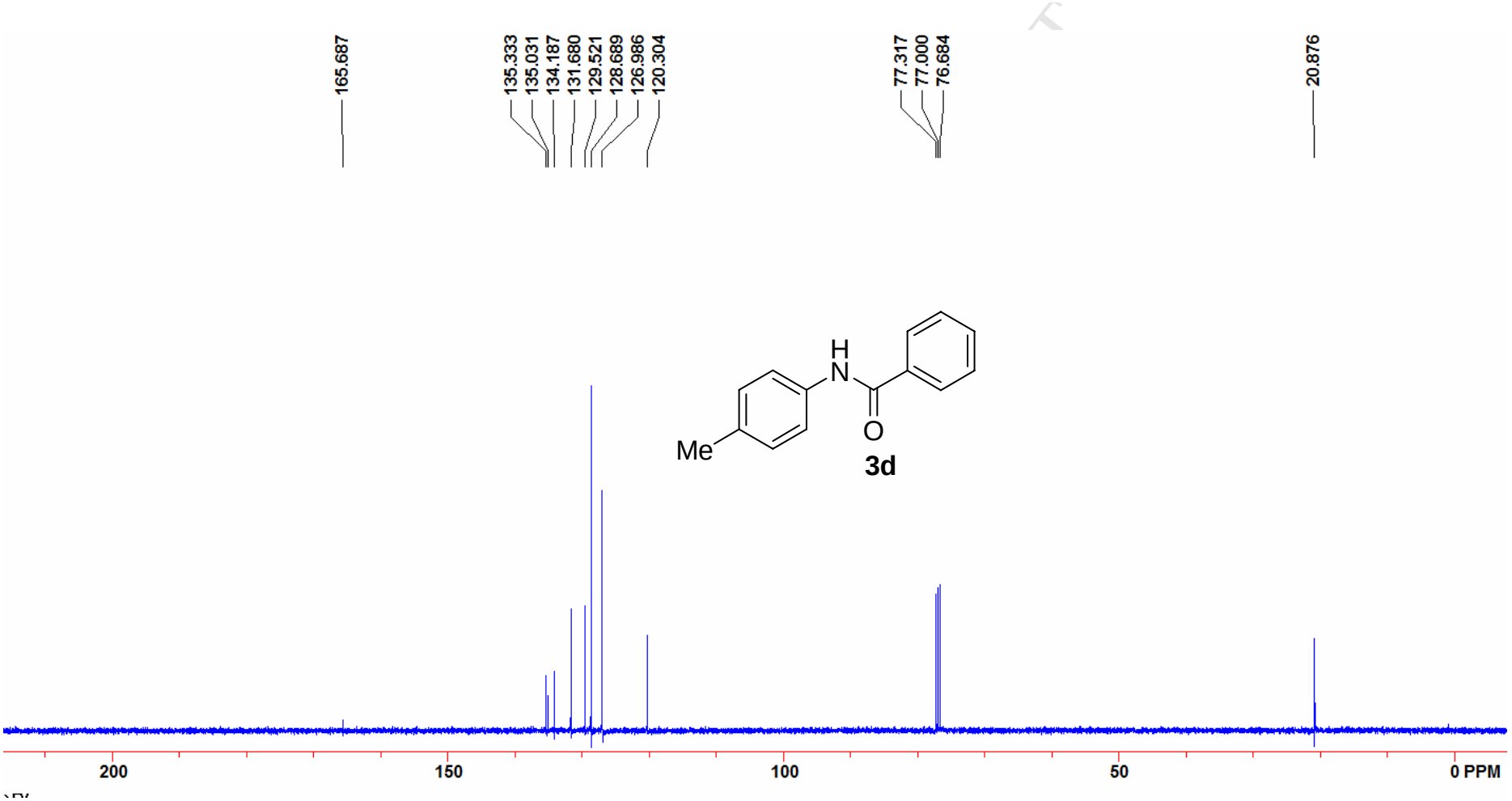
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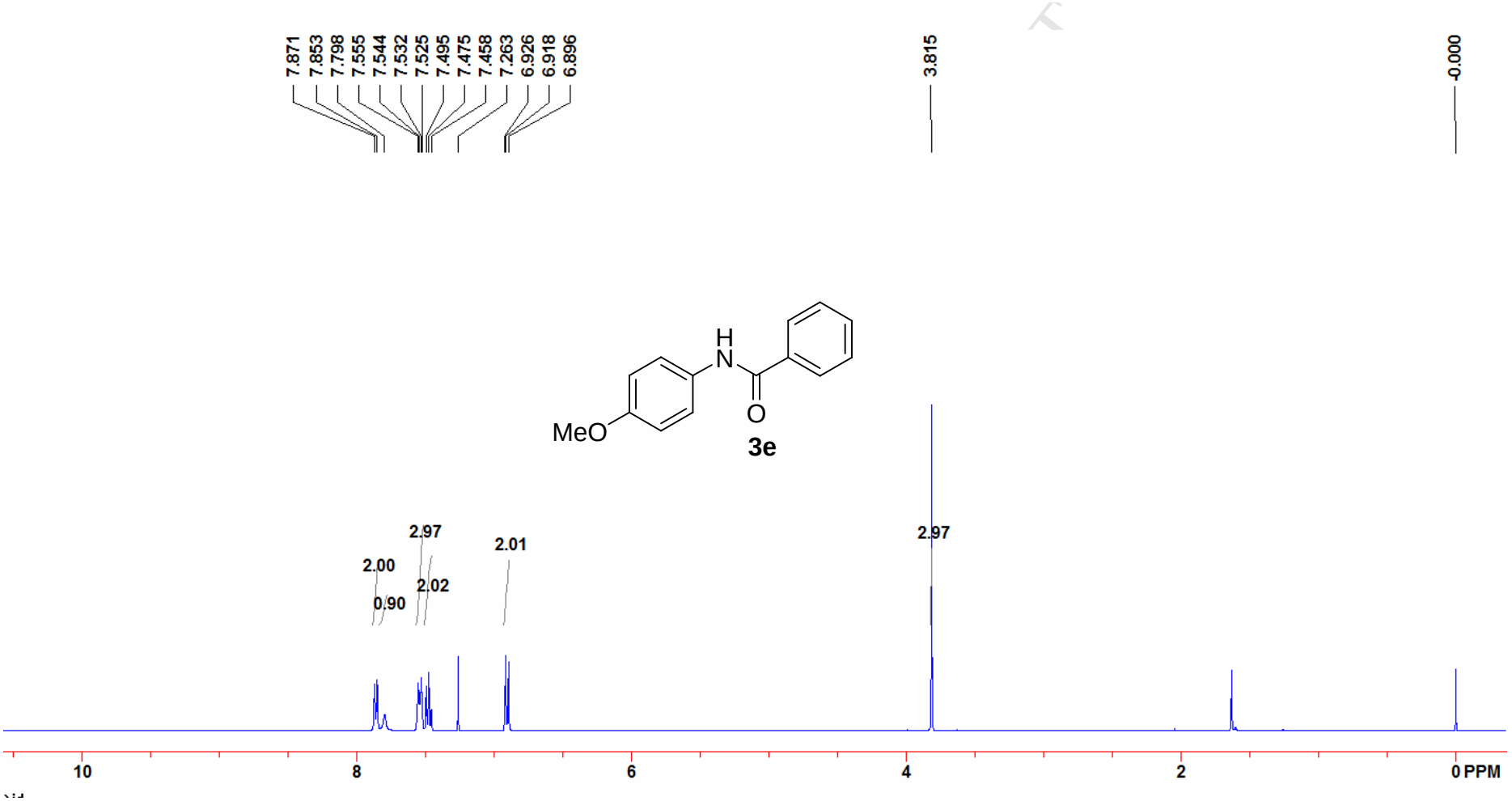
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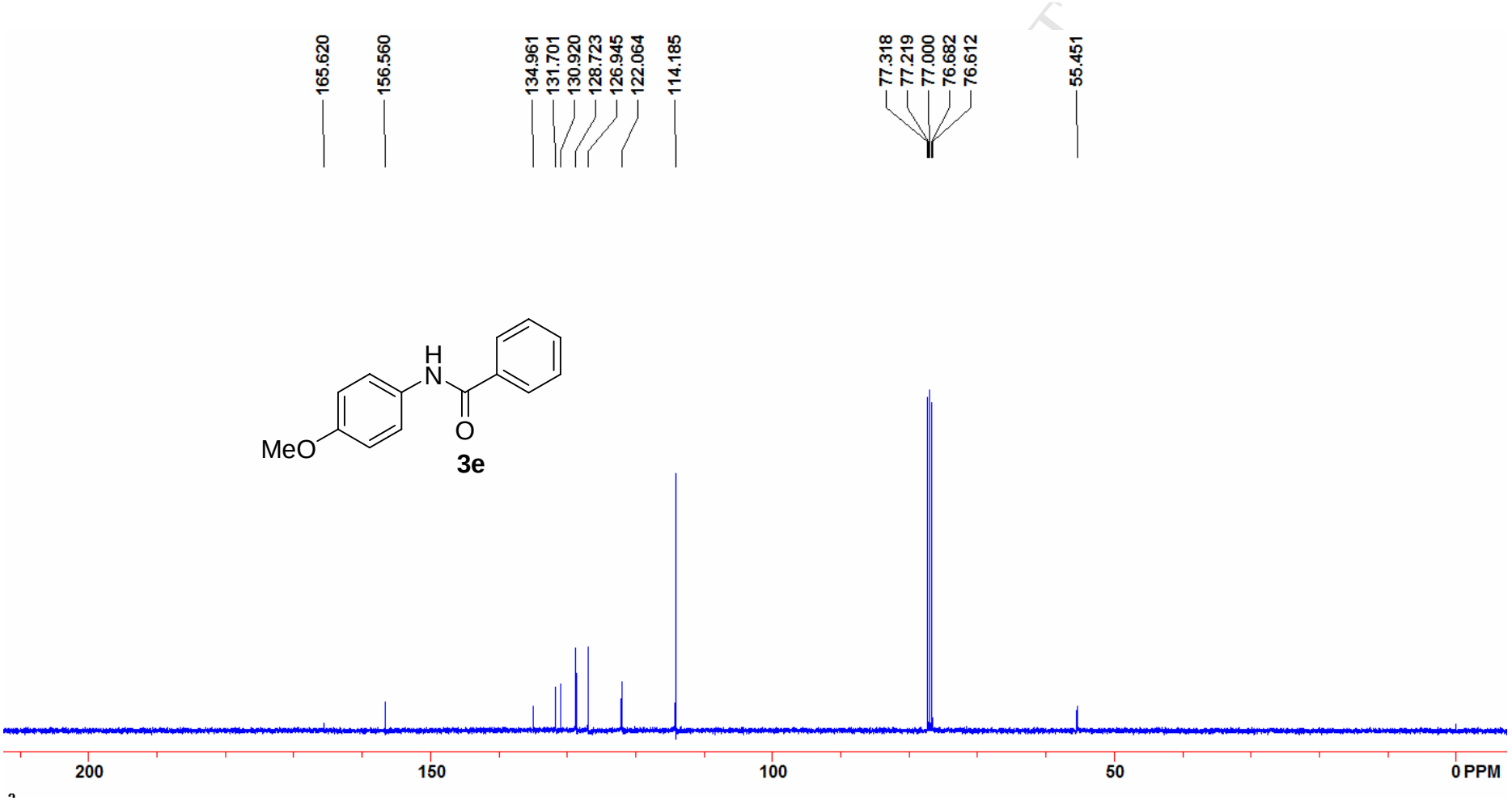
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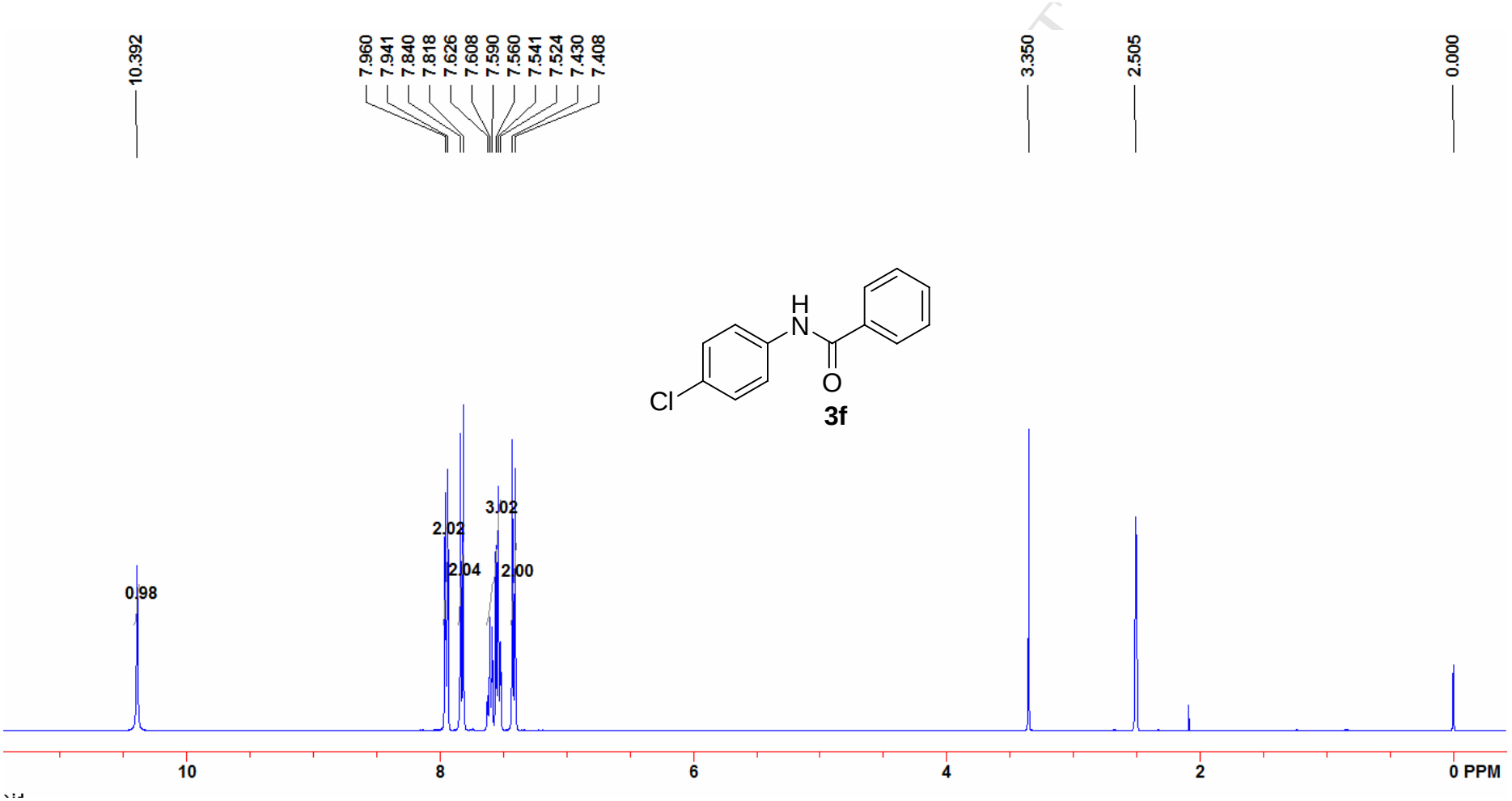
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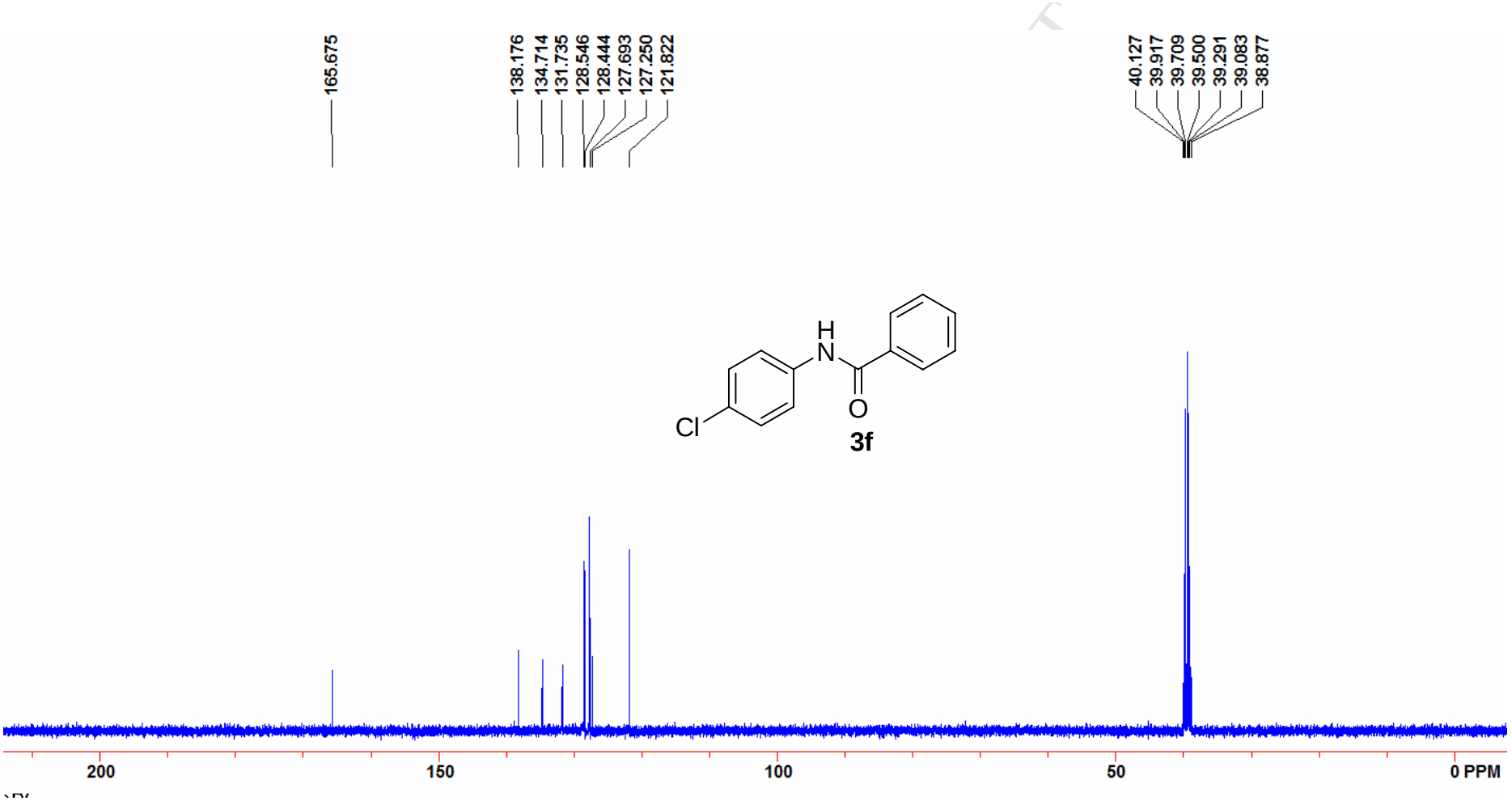

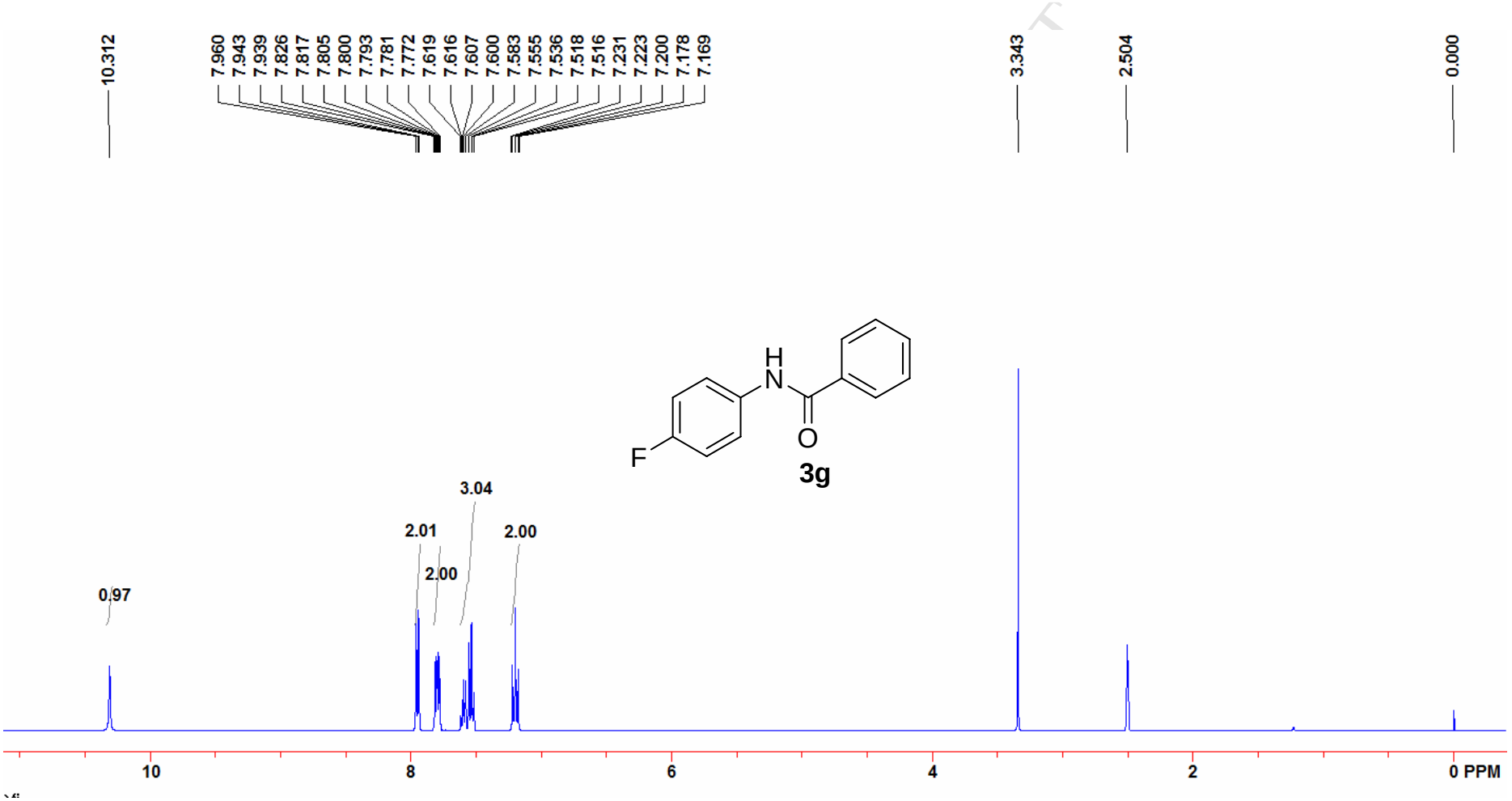
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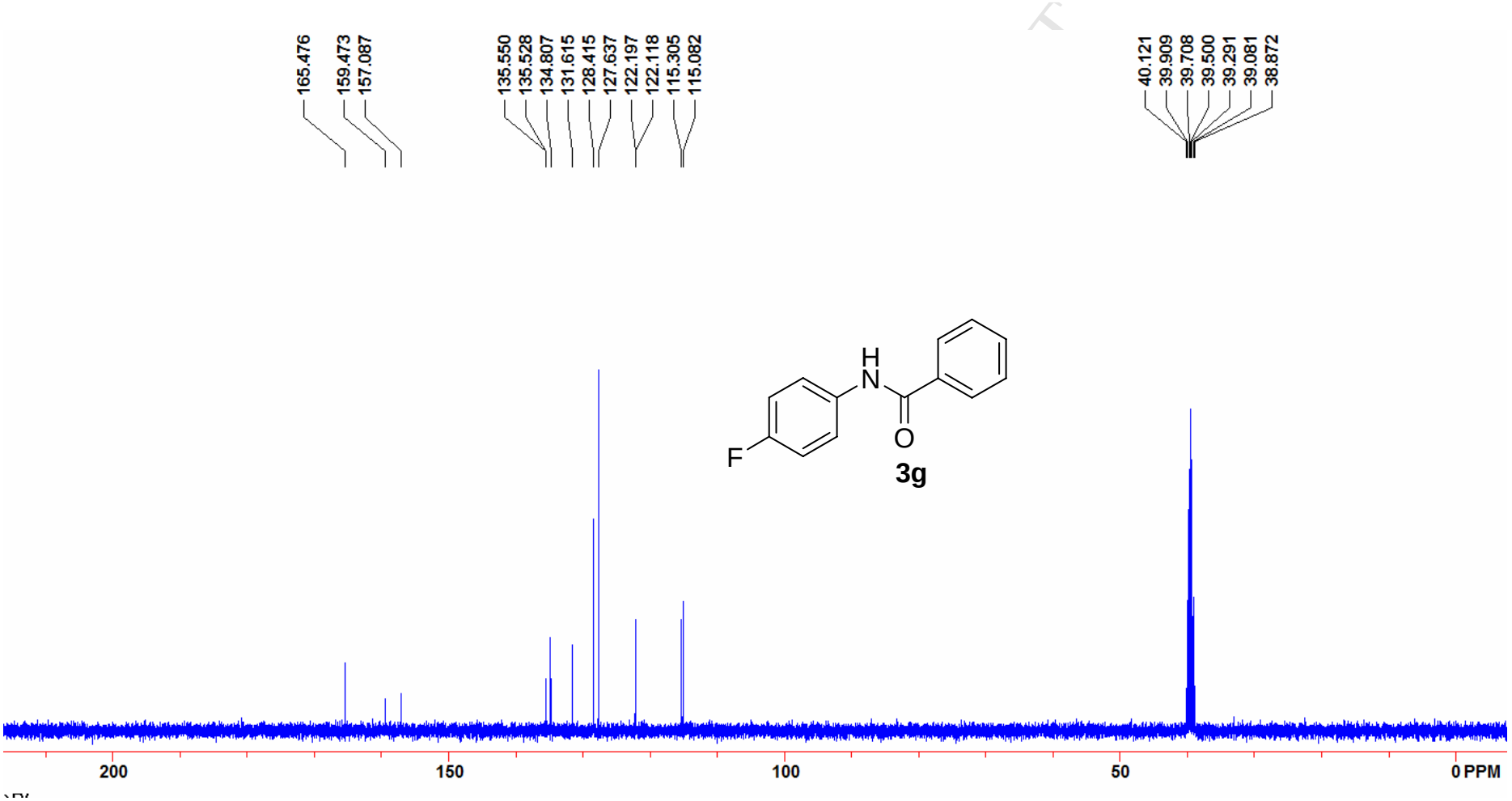
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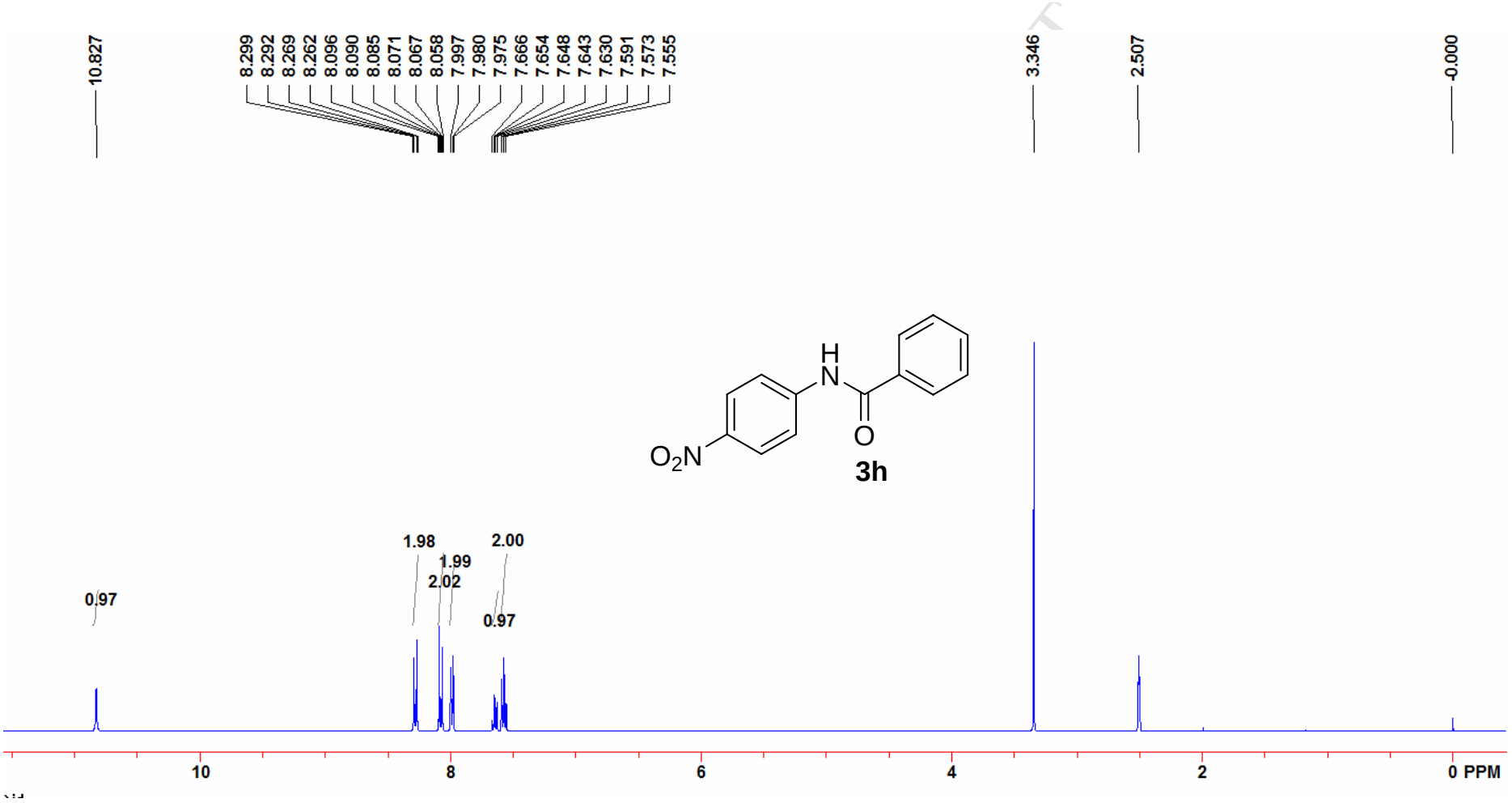
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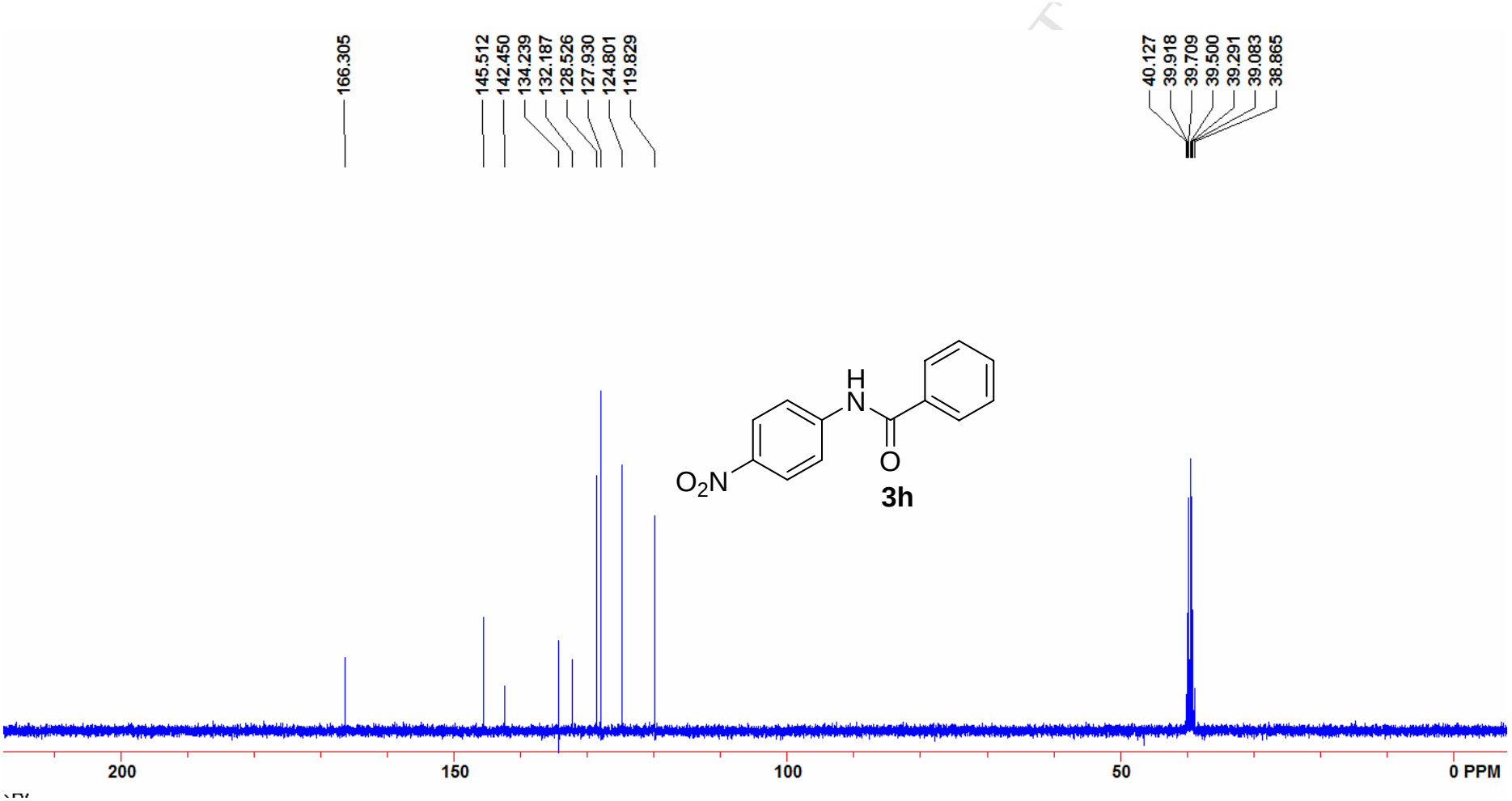
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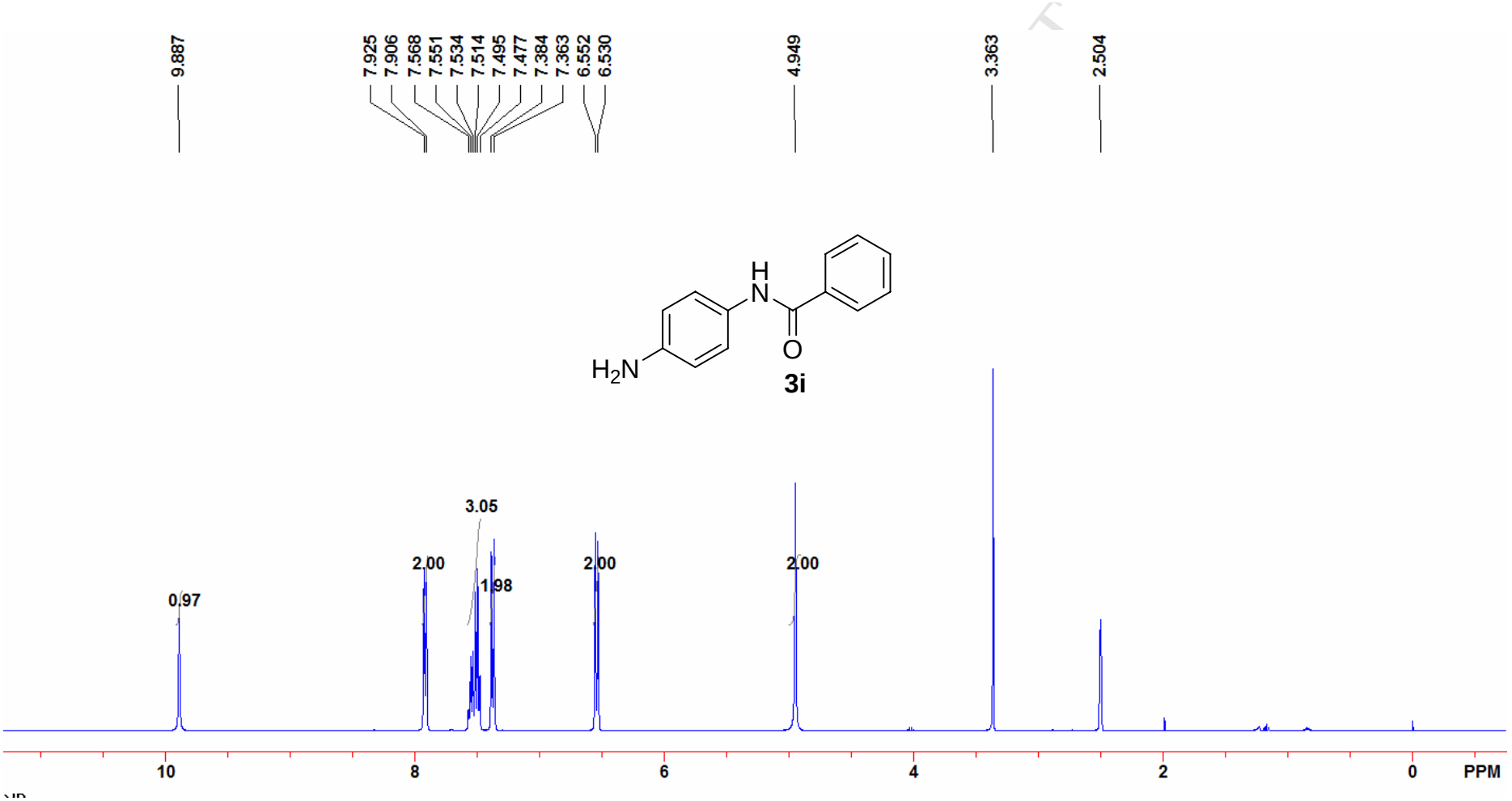
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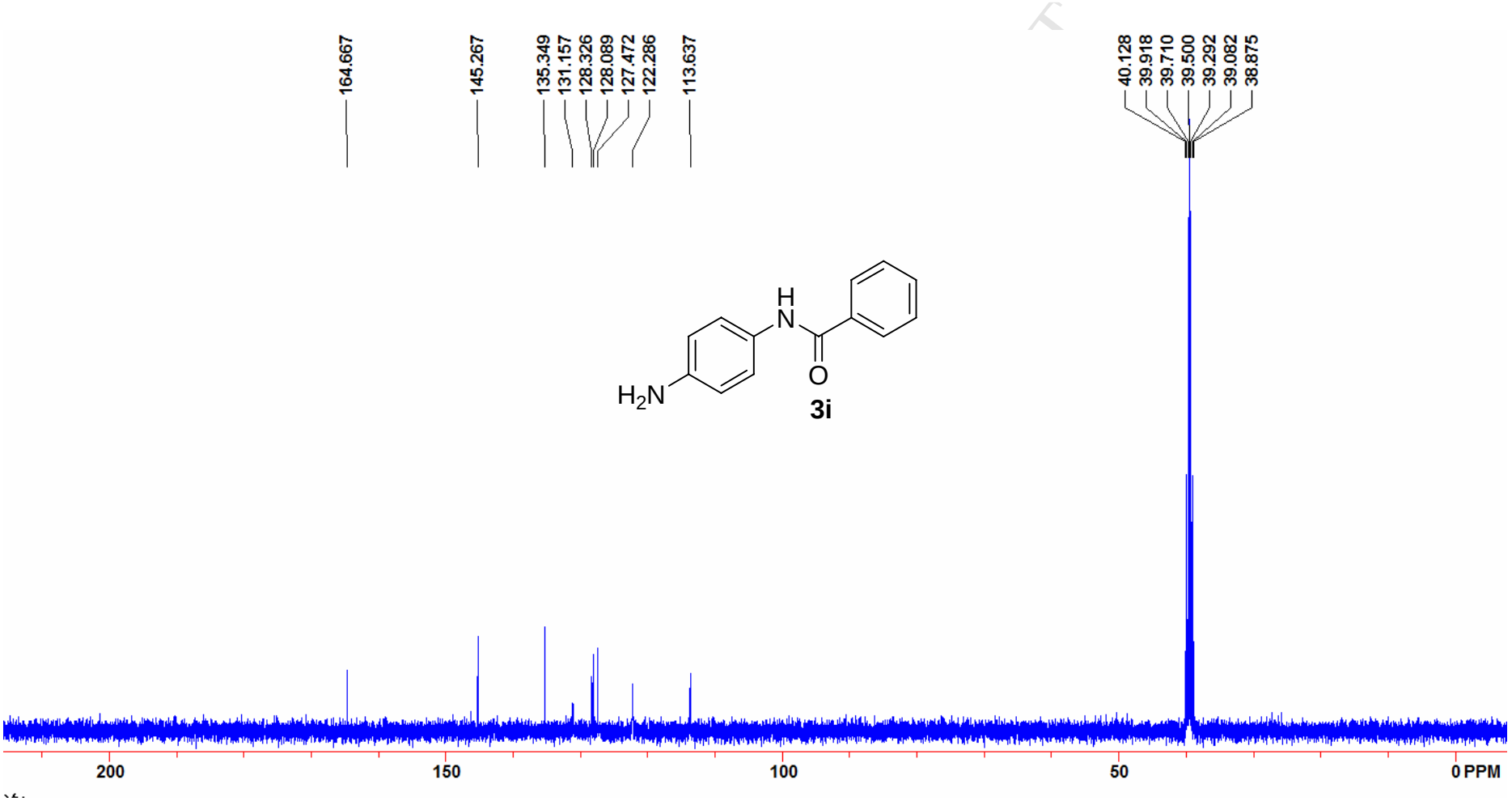

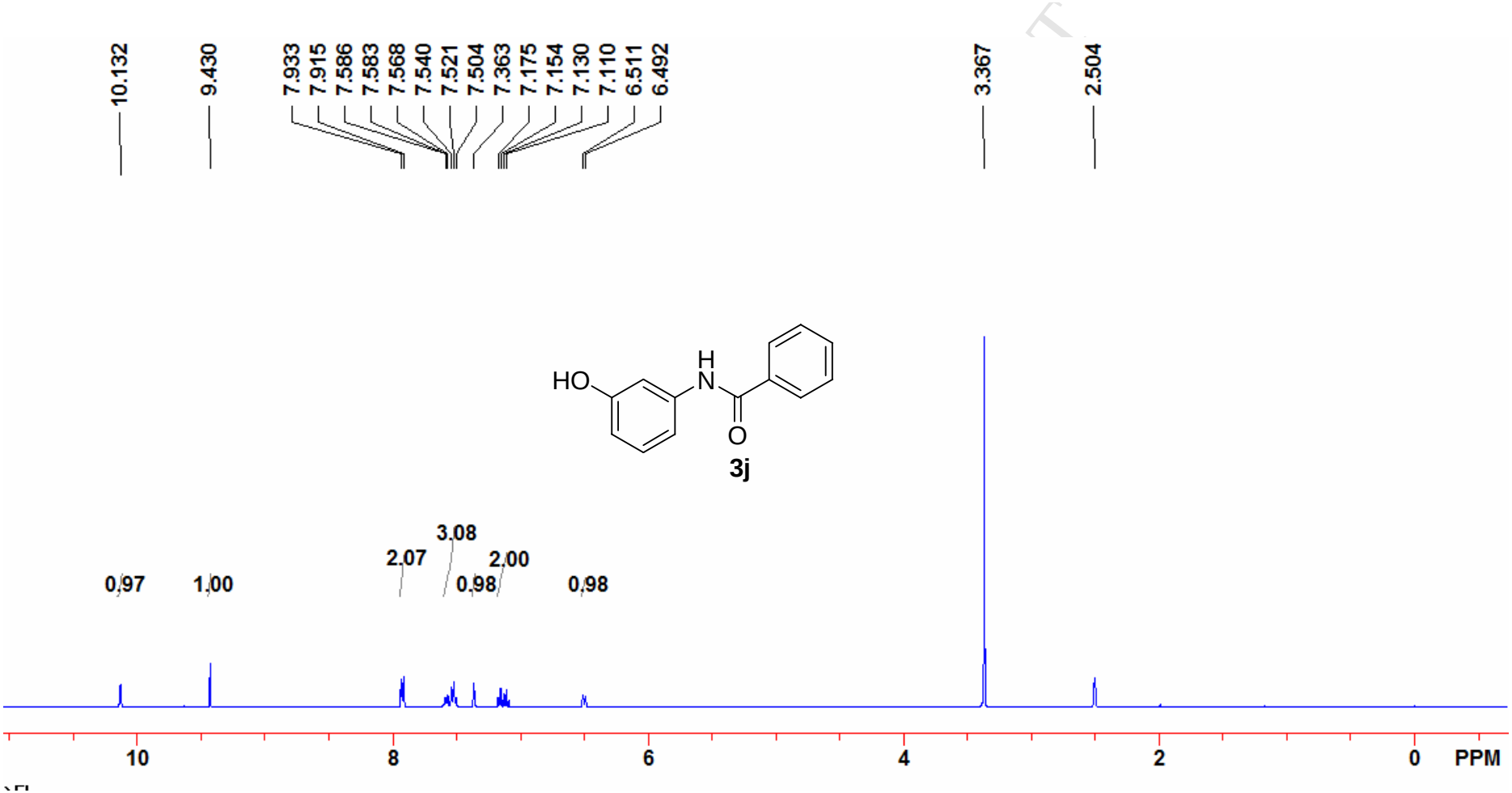
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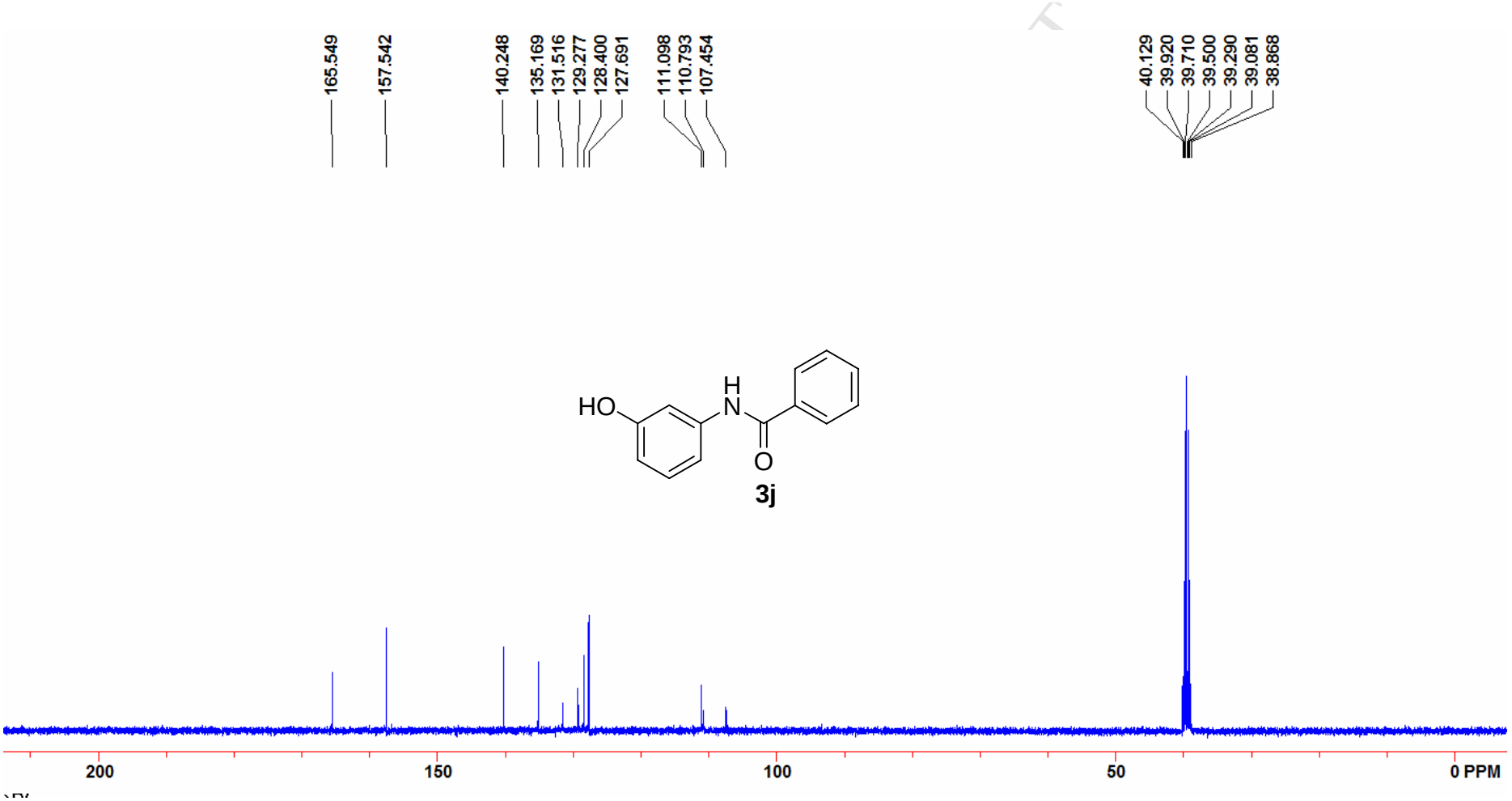
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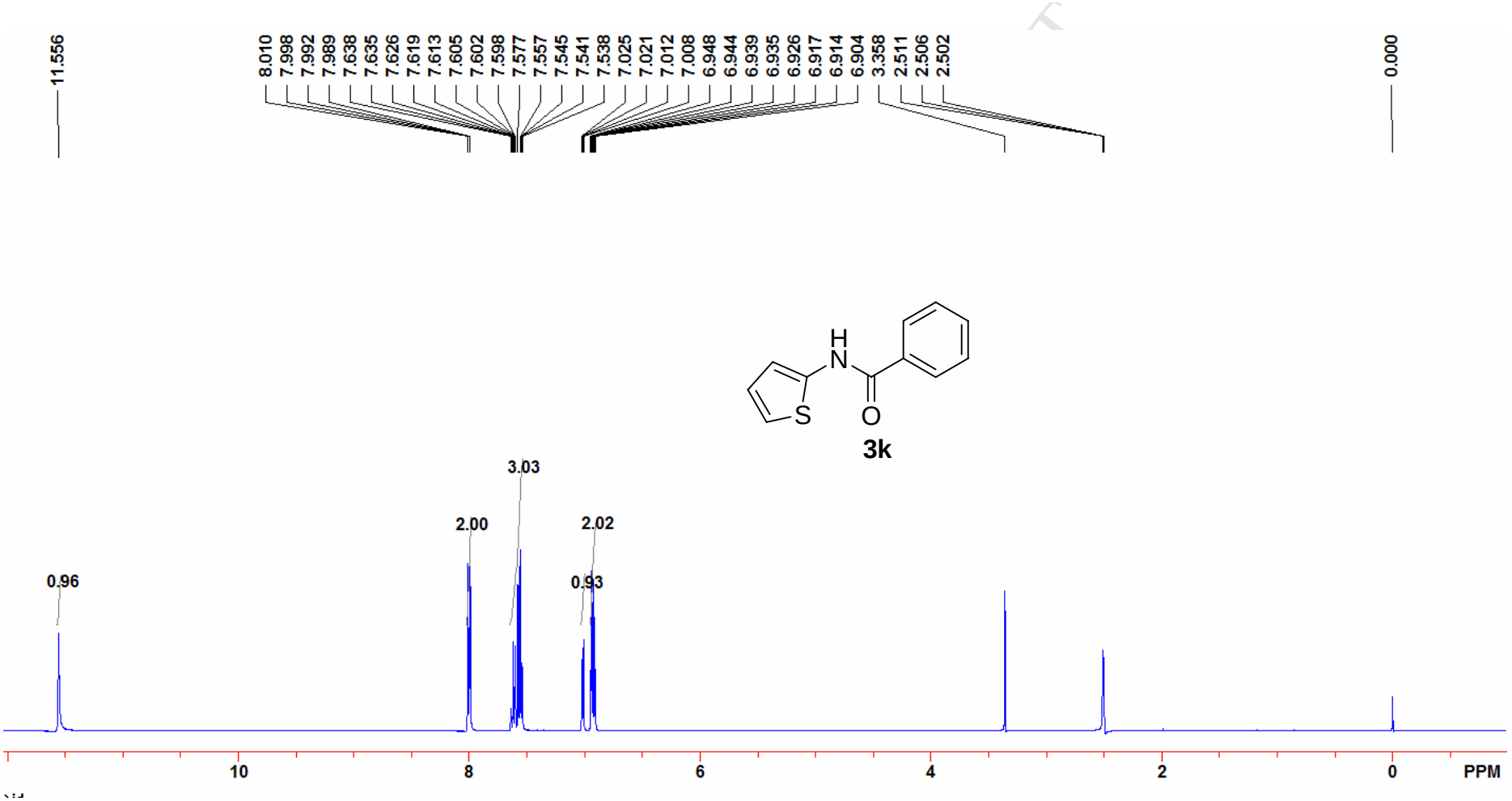
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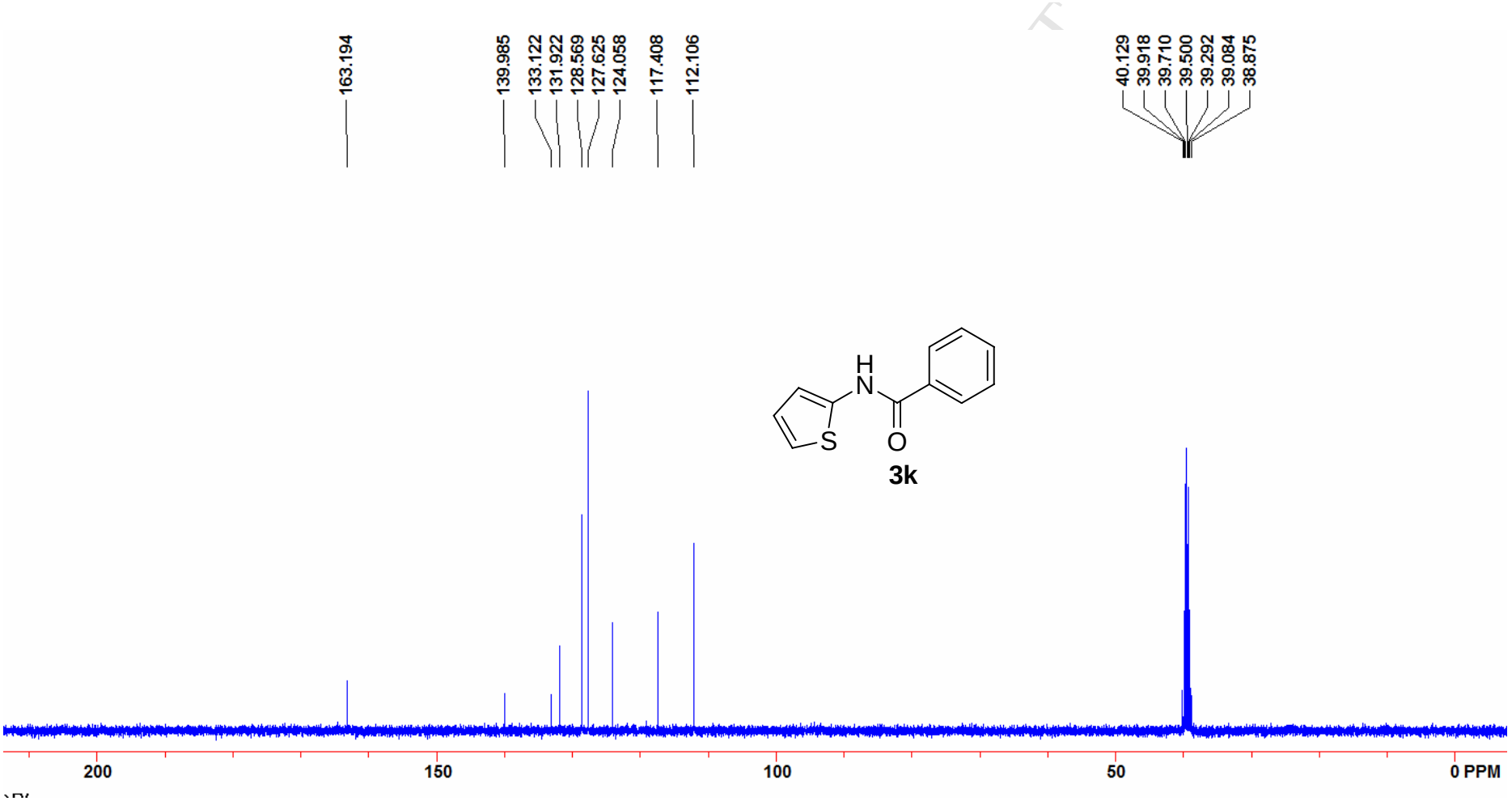

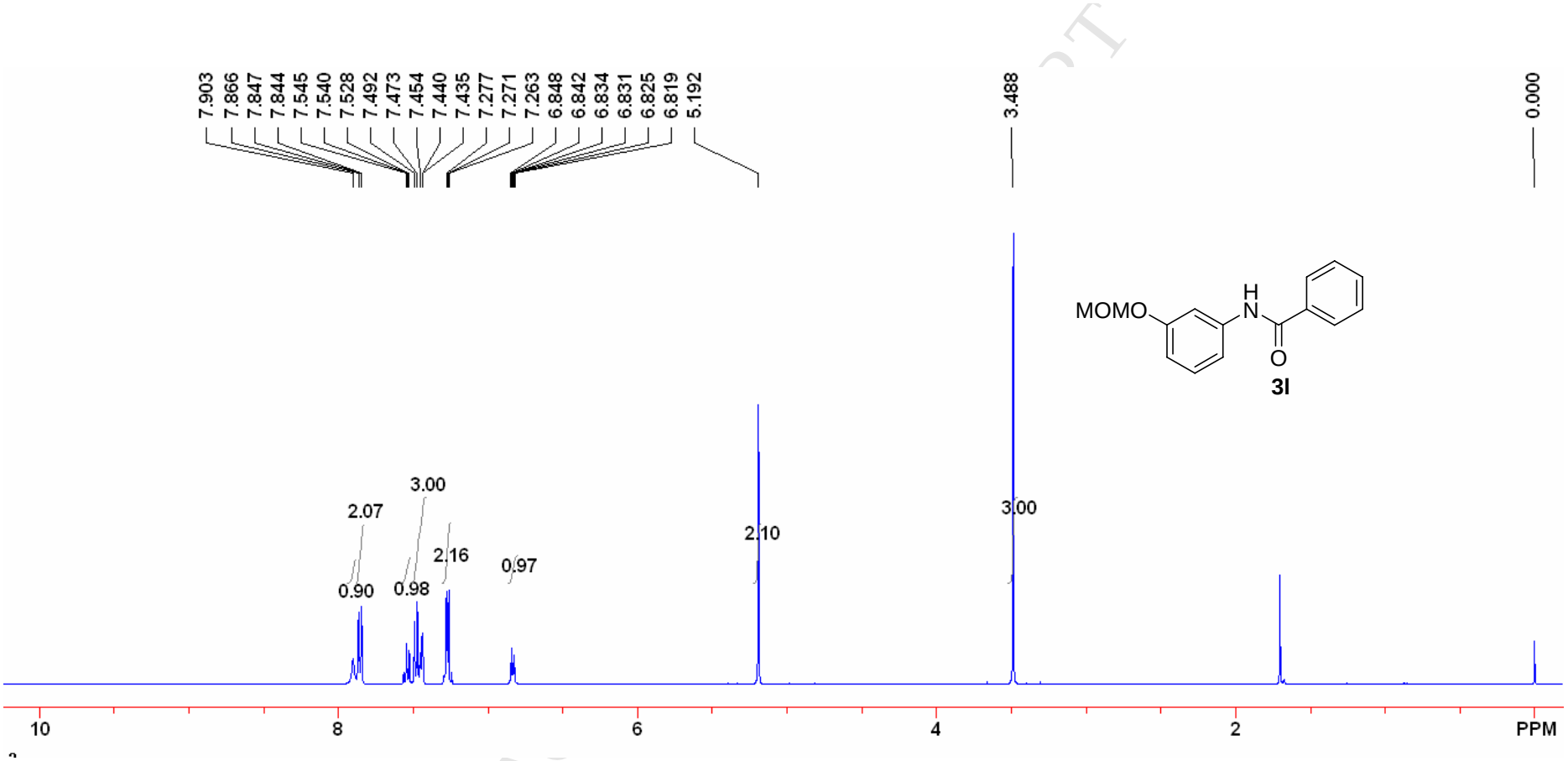
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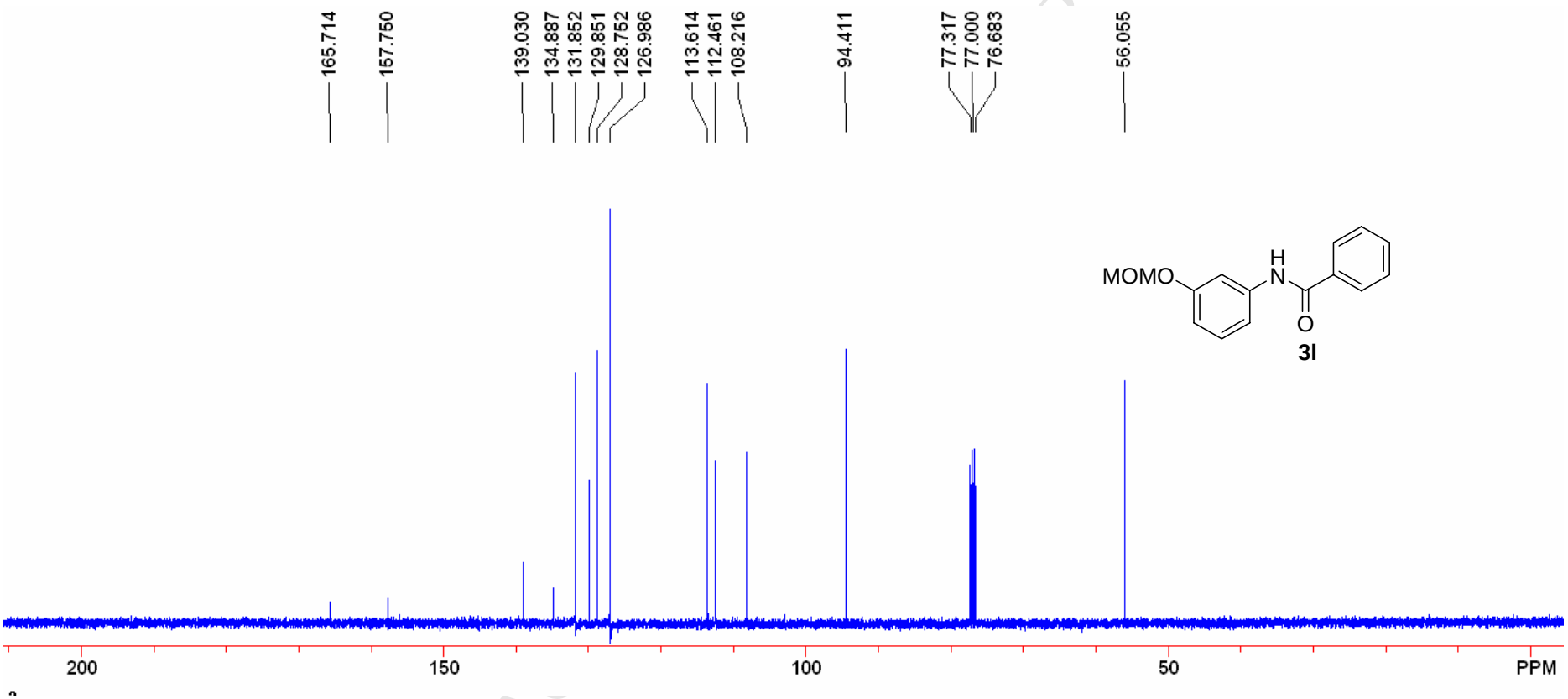
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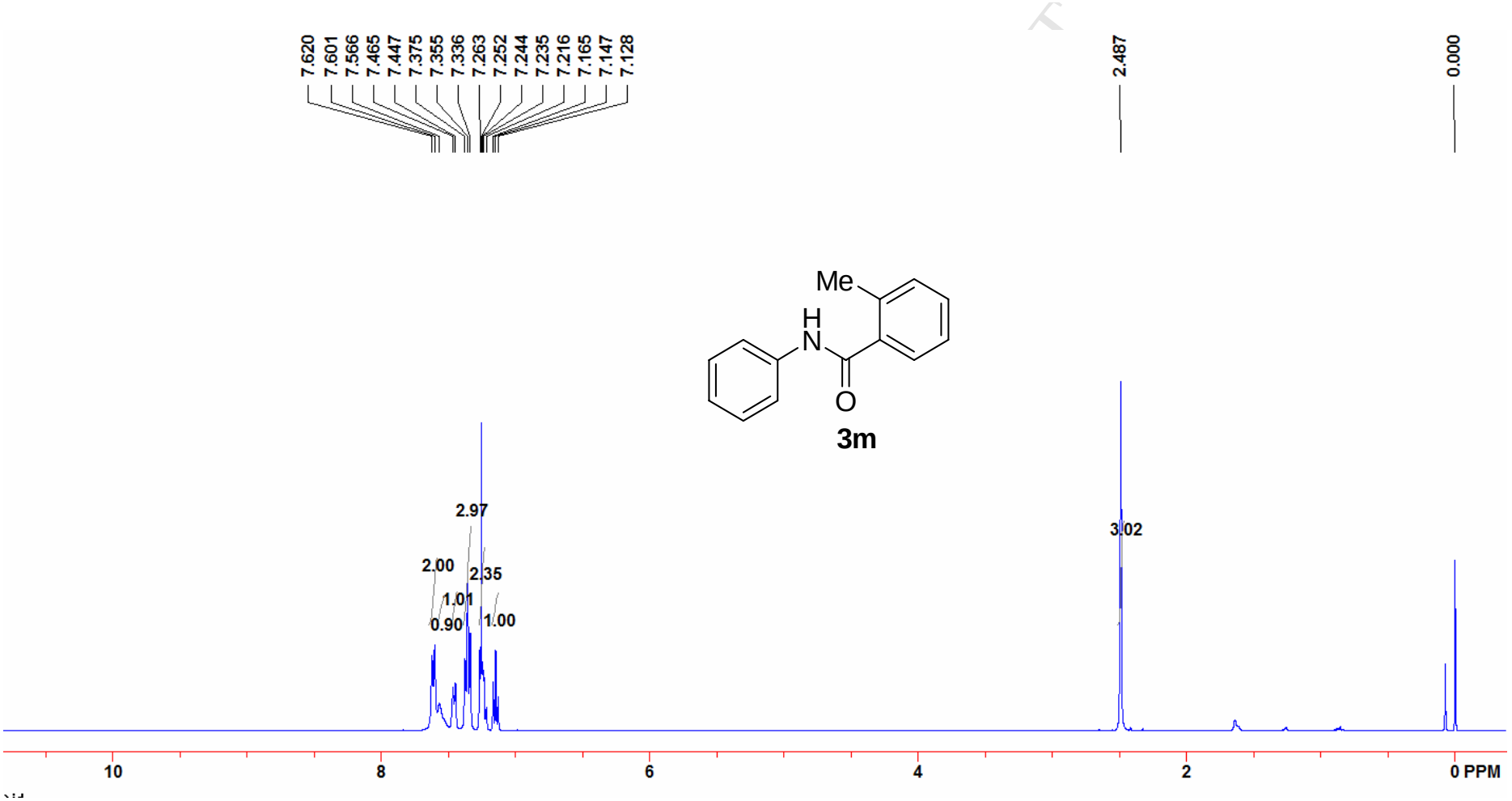

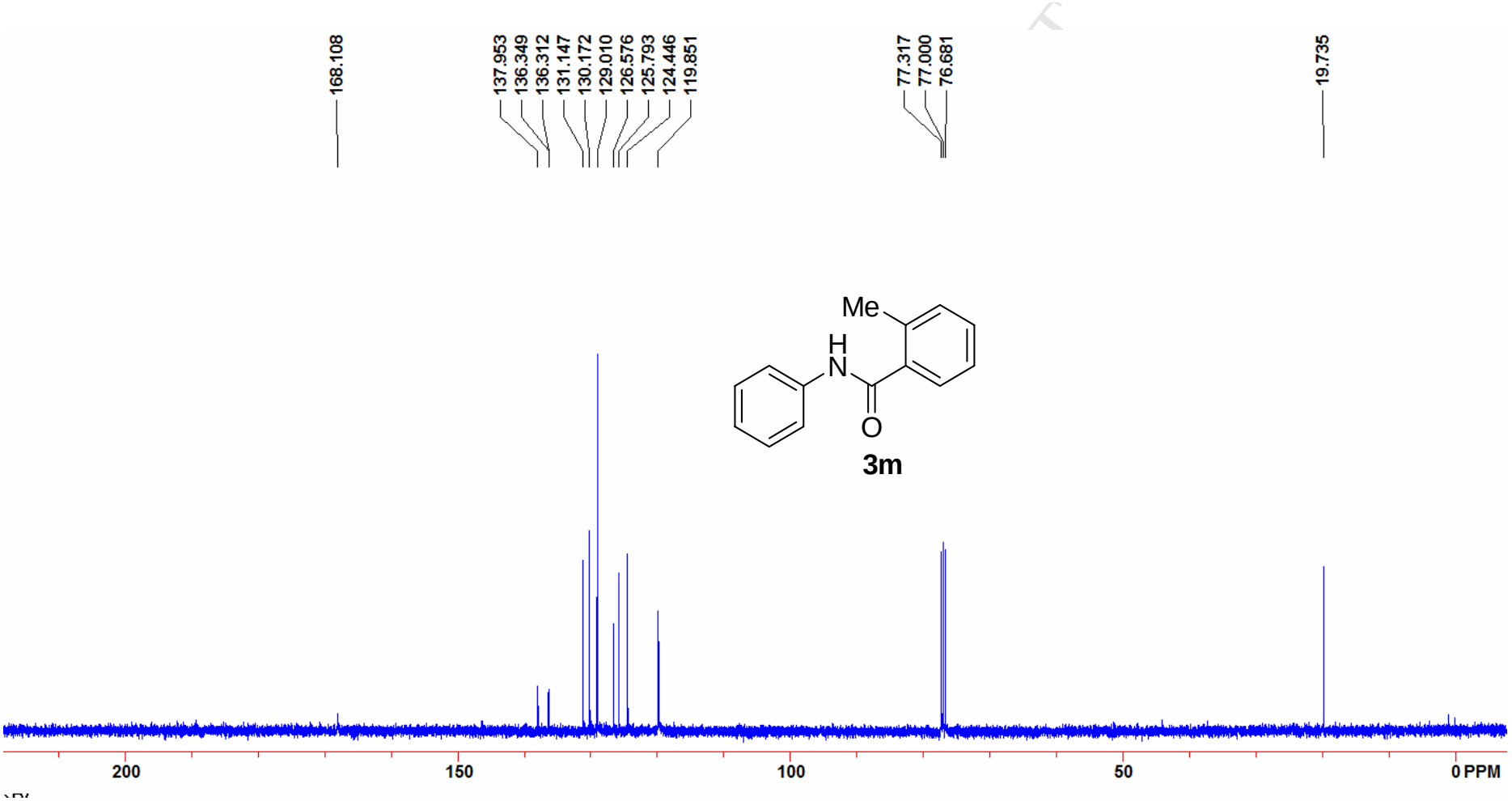

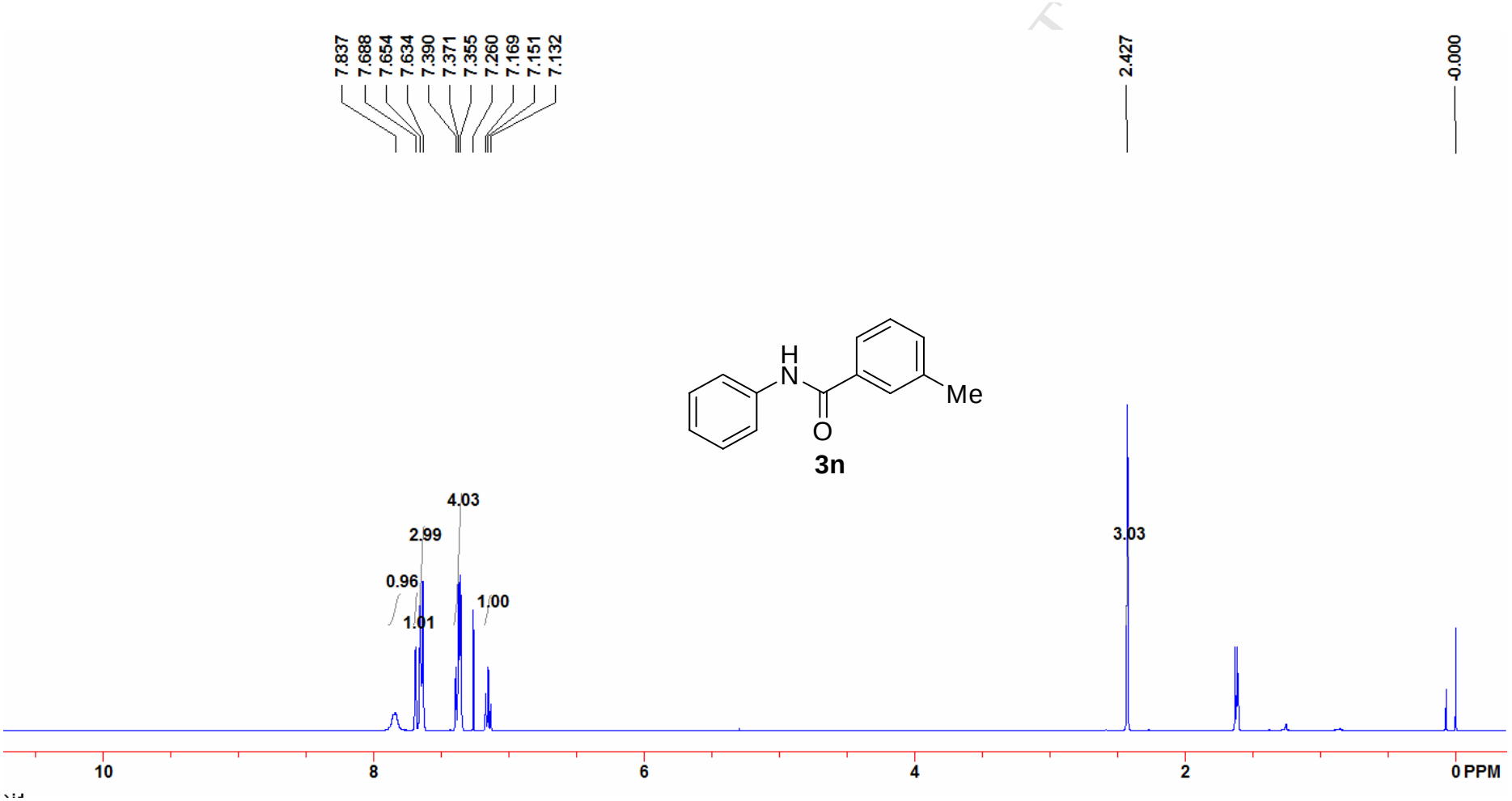
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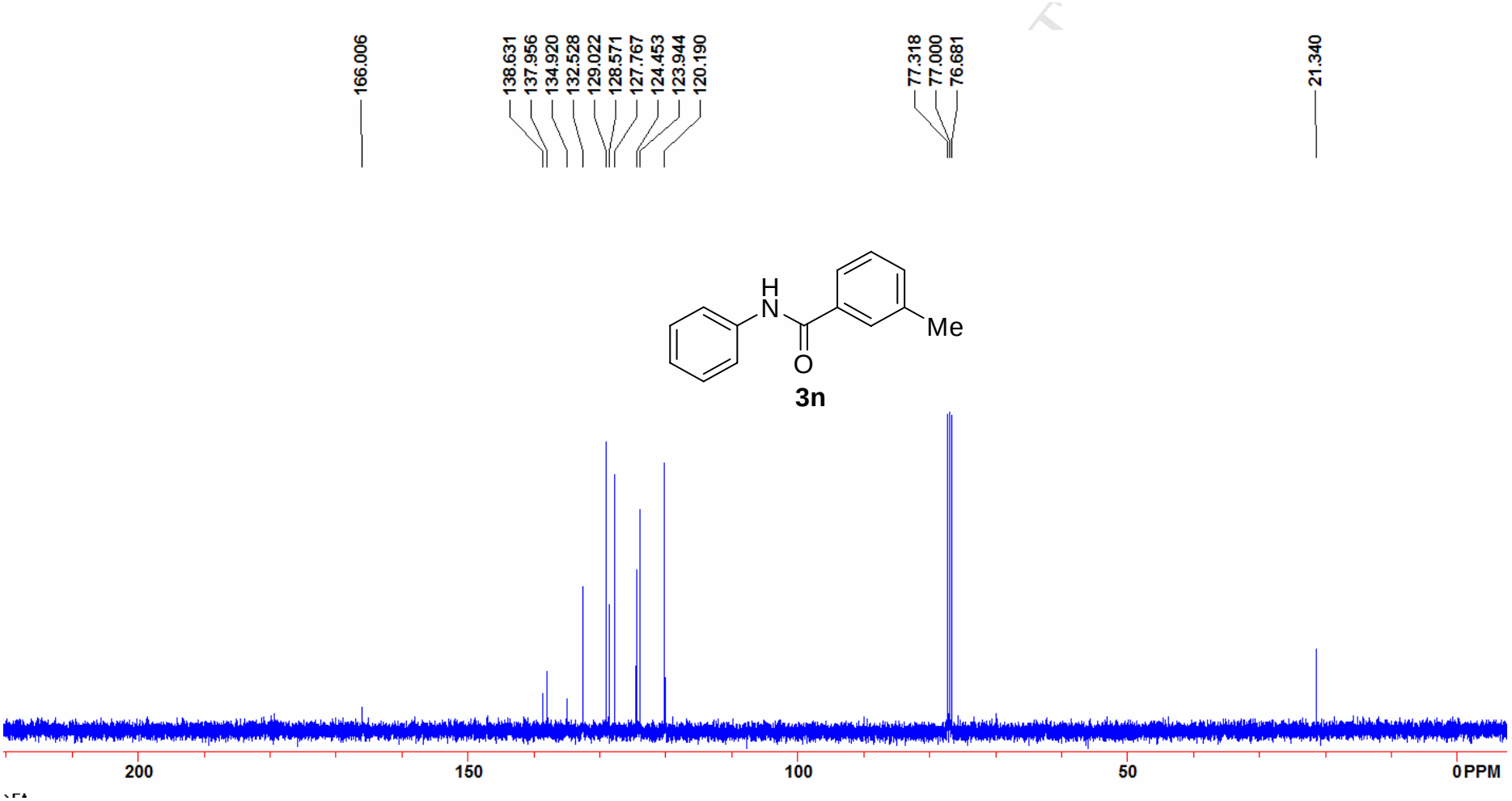
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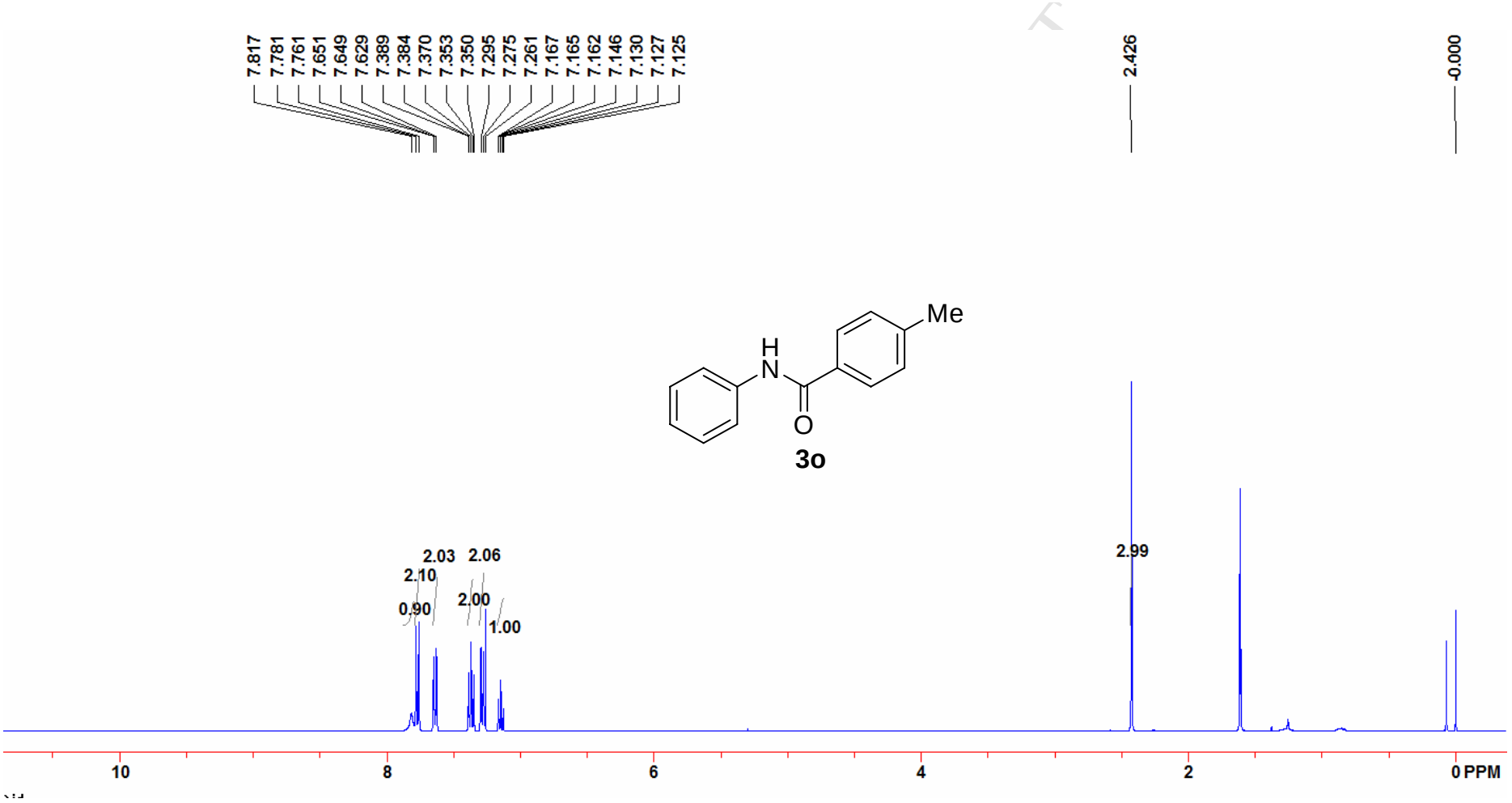

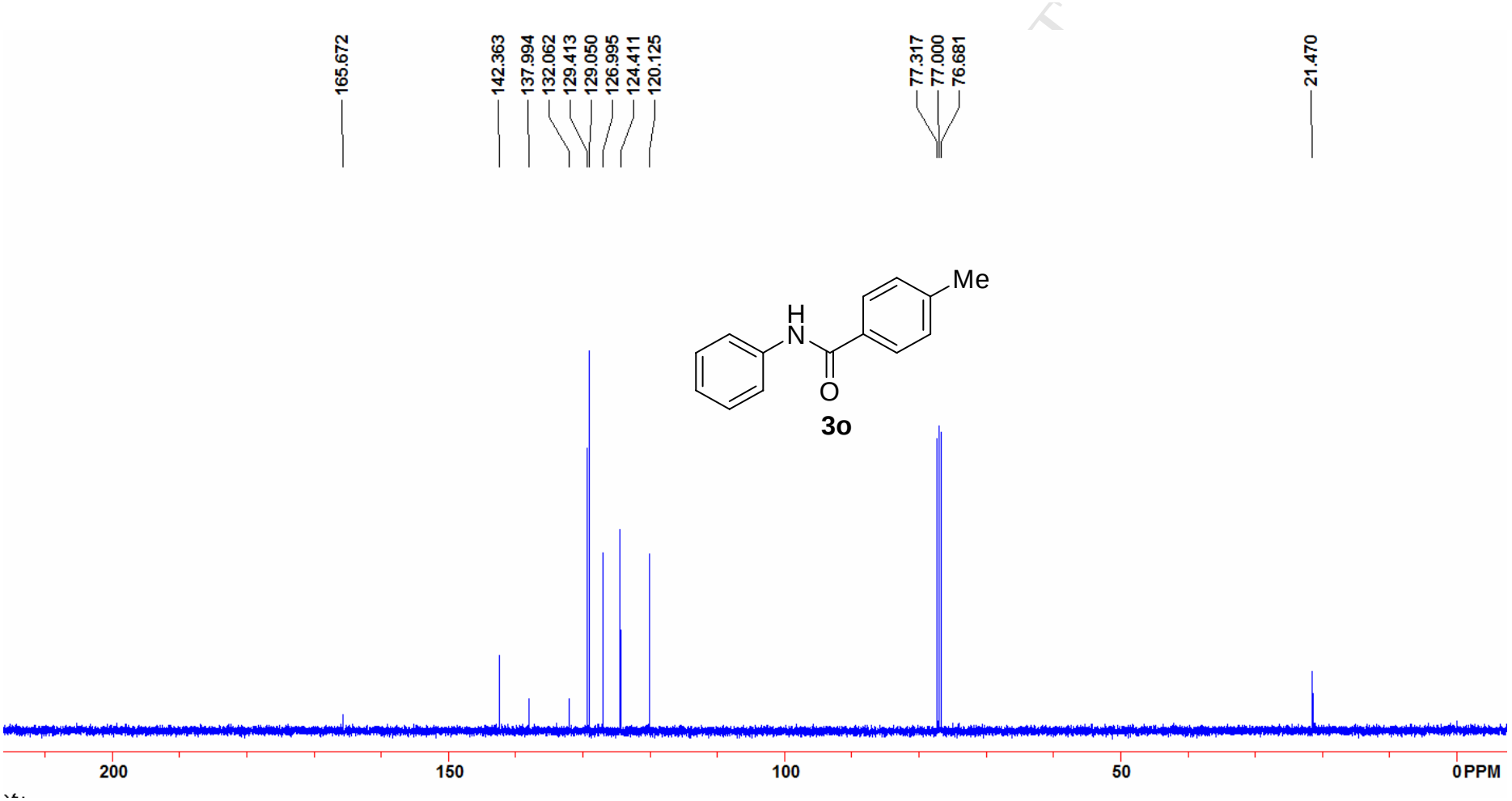

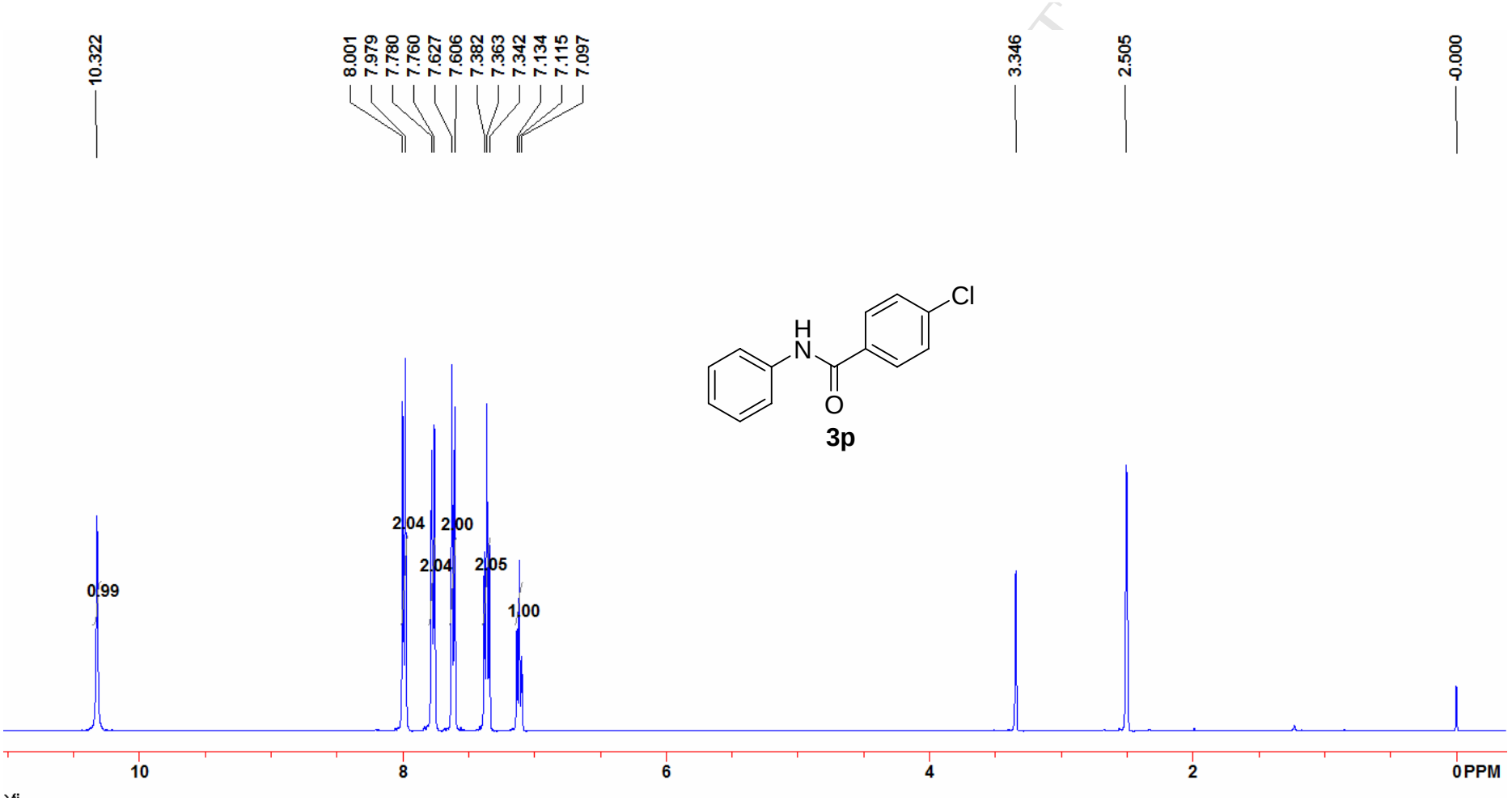

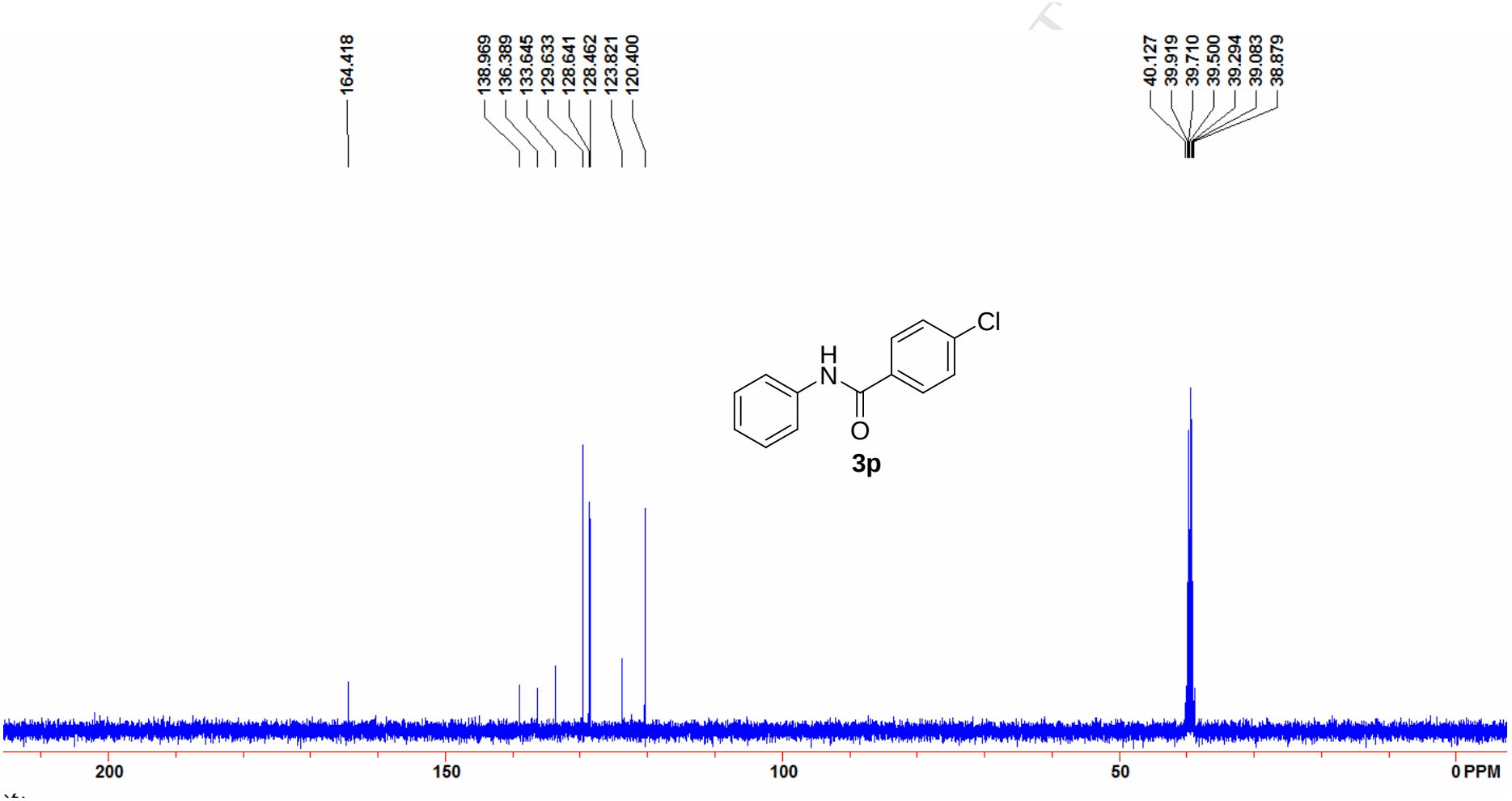

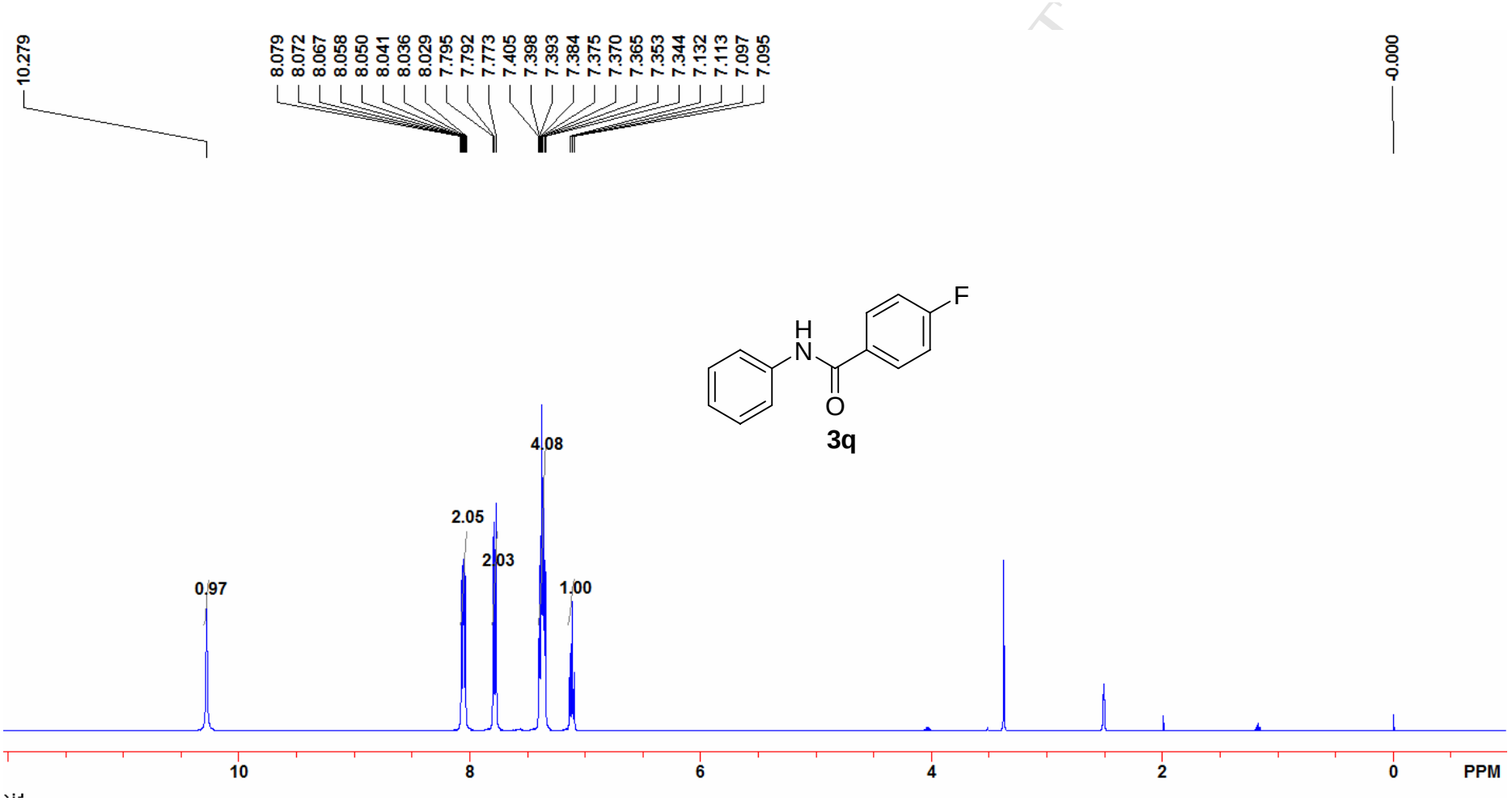
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7.095
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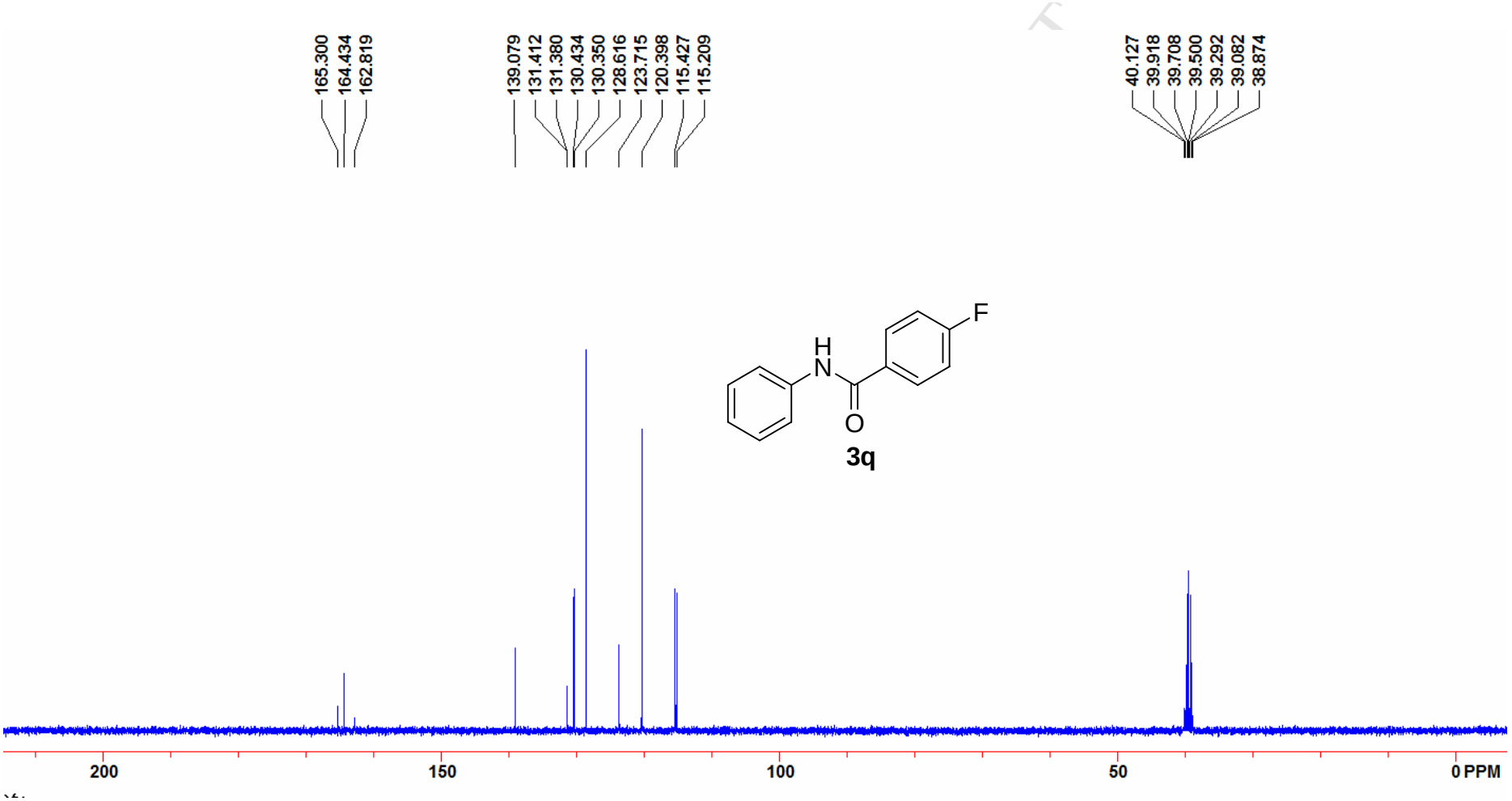

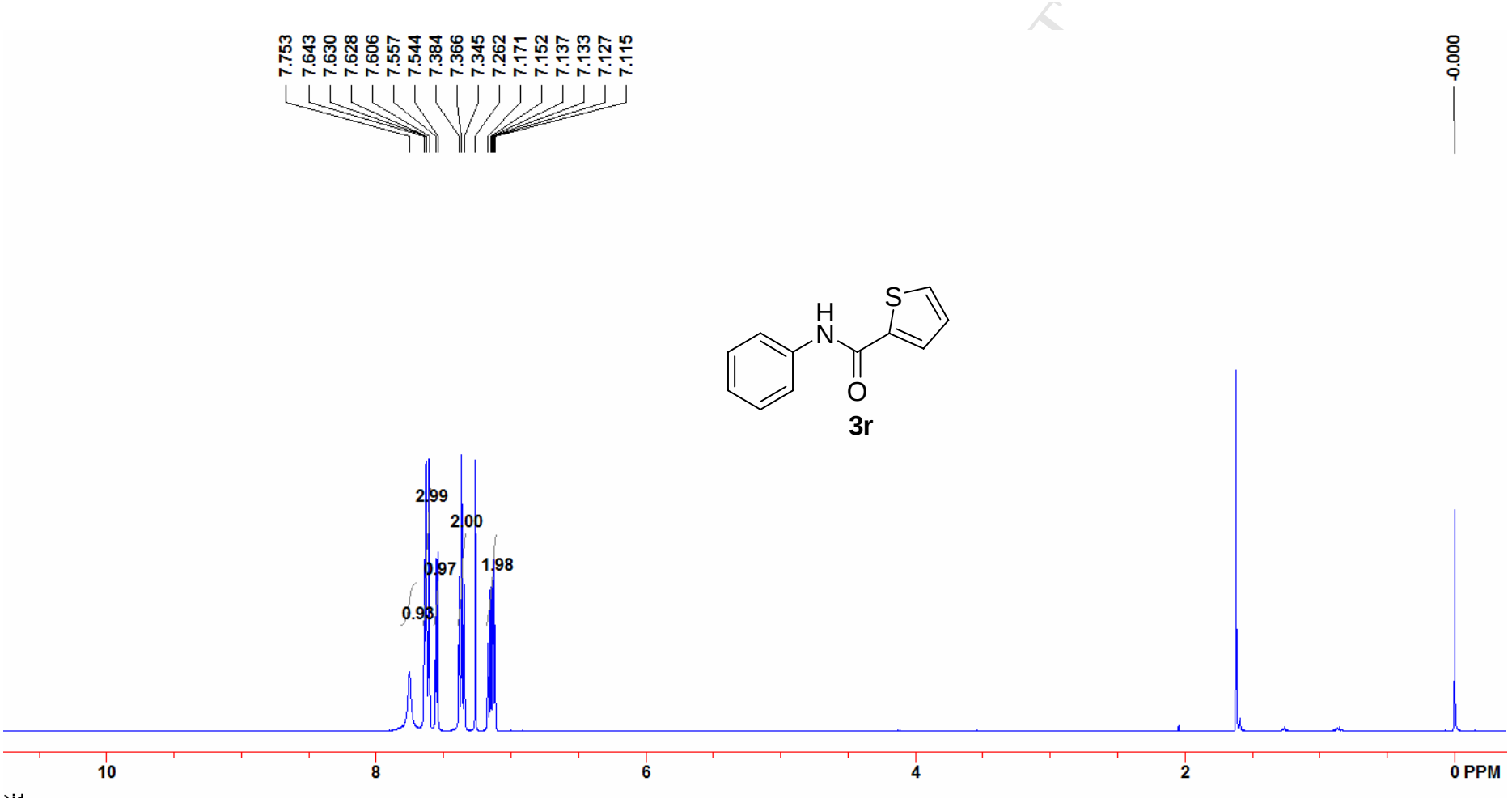
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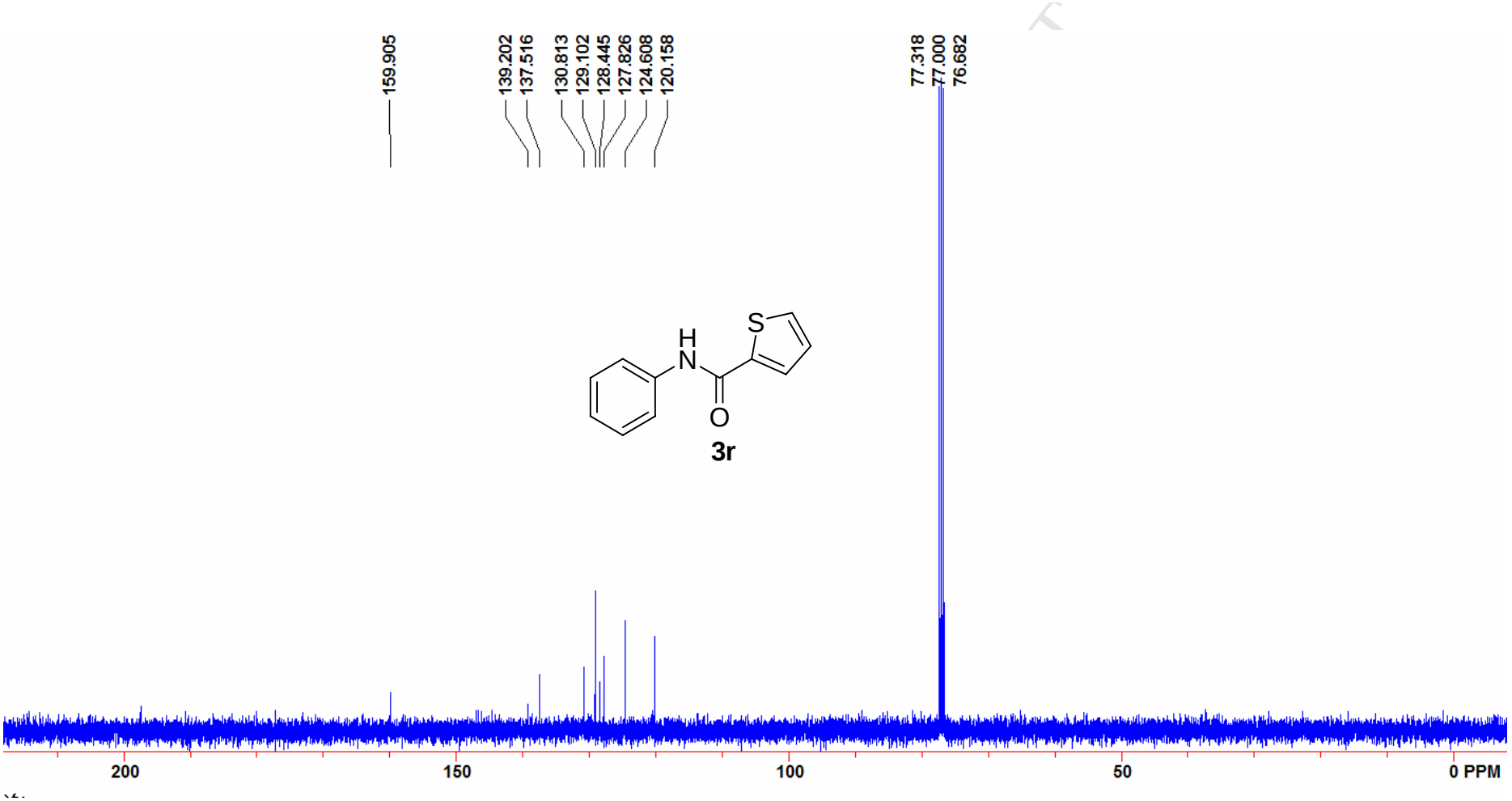

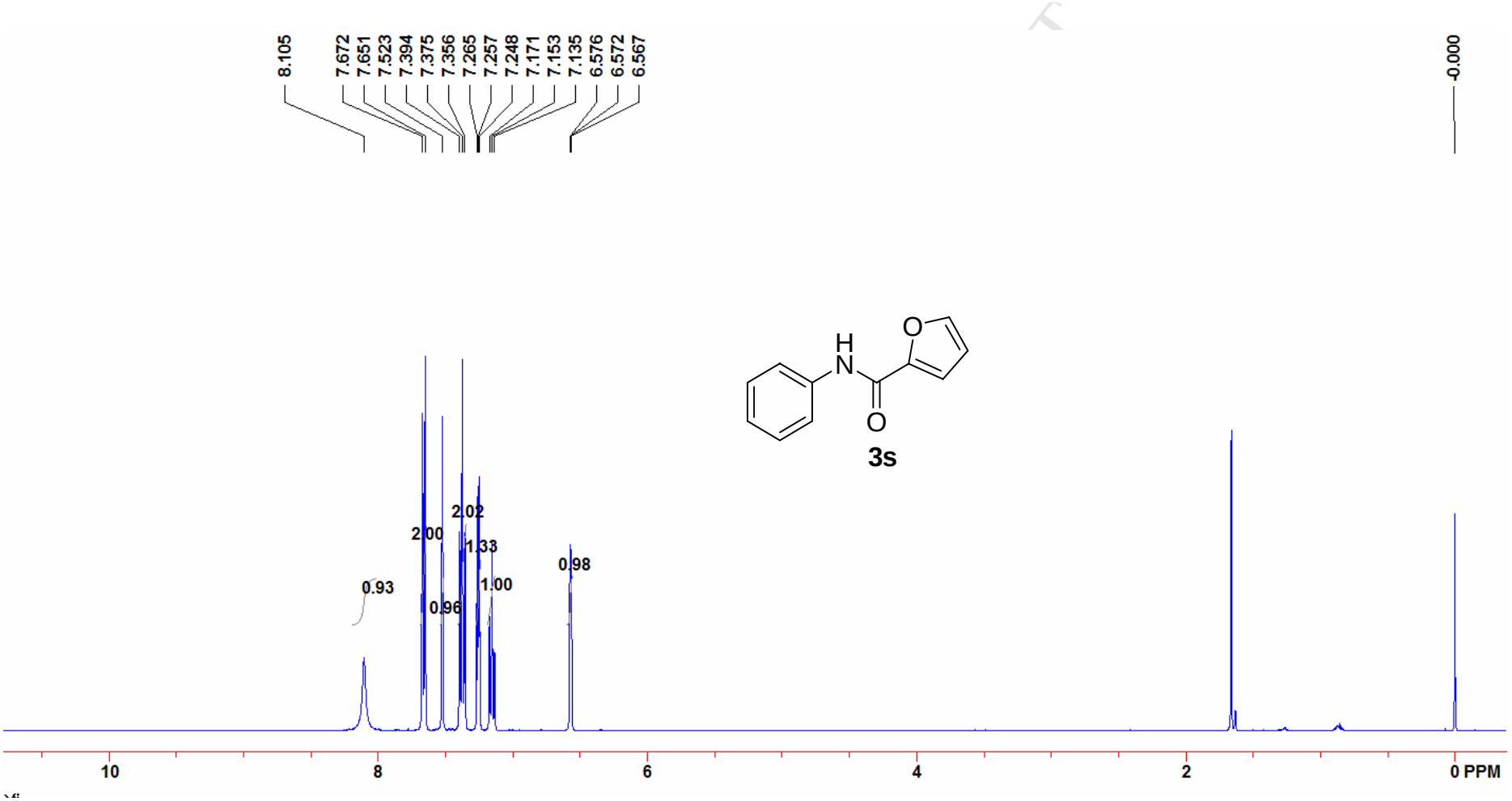

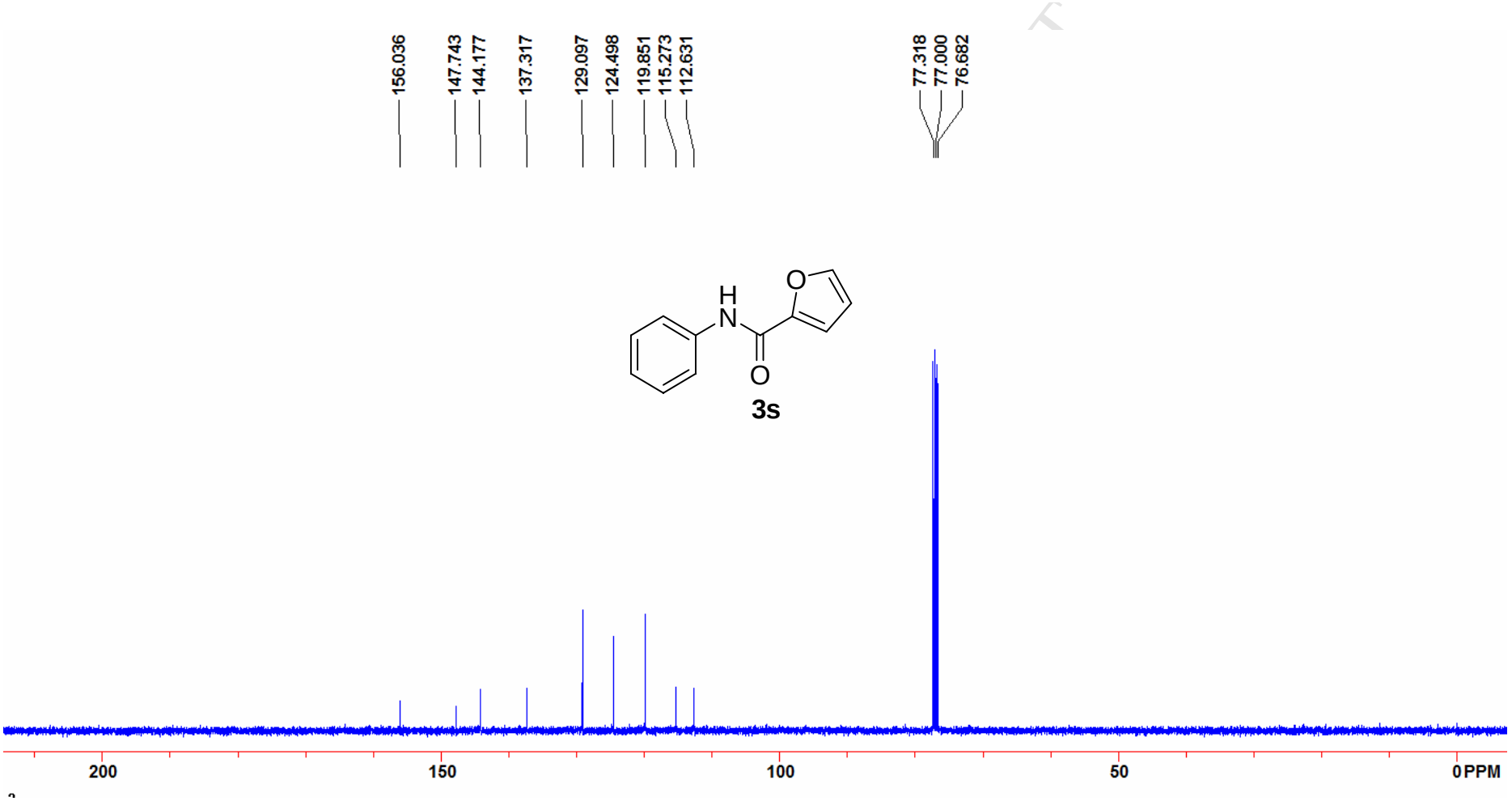
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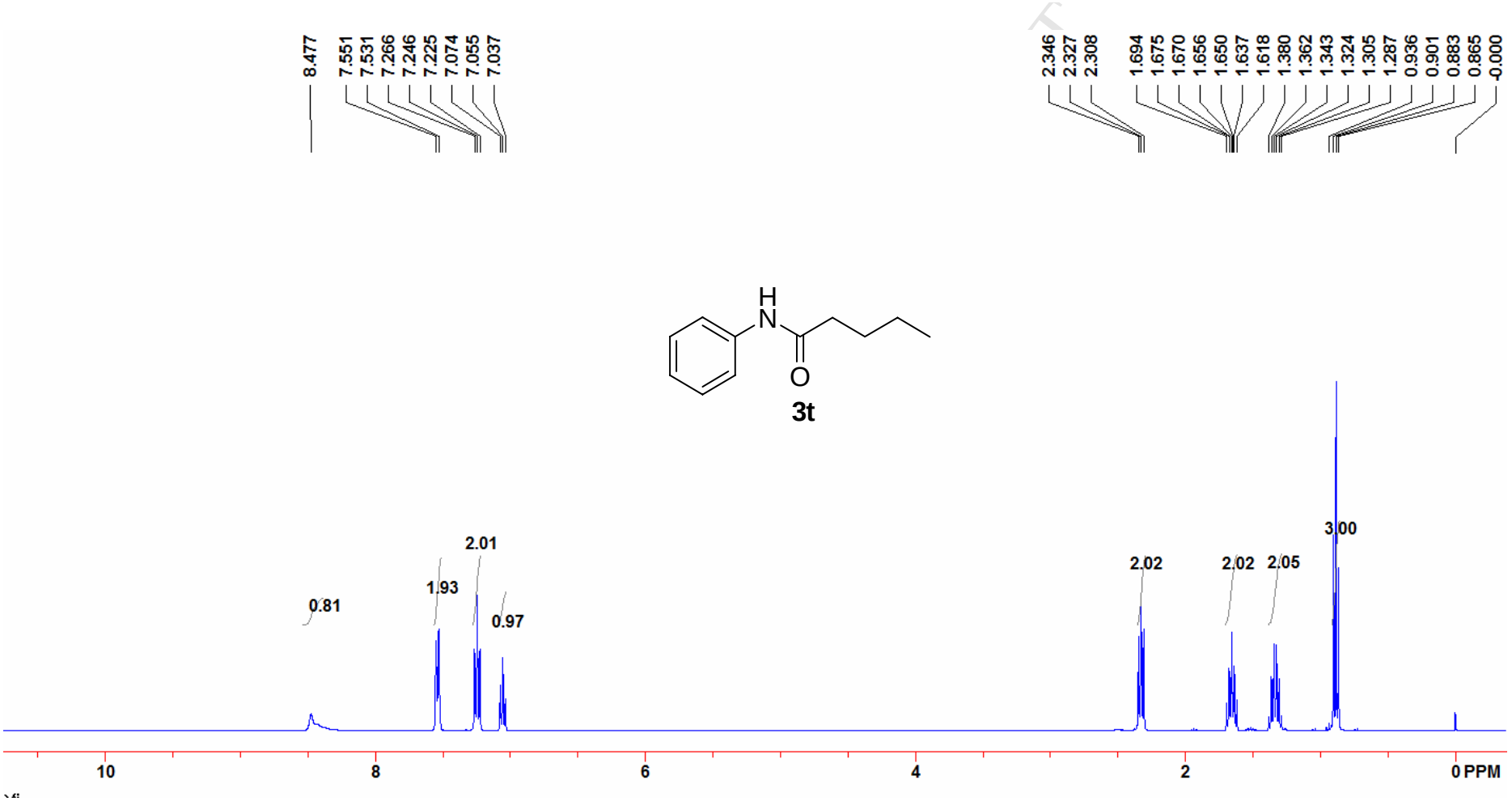
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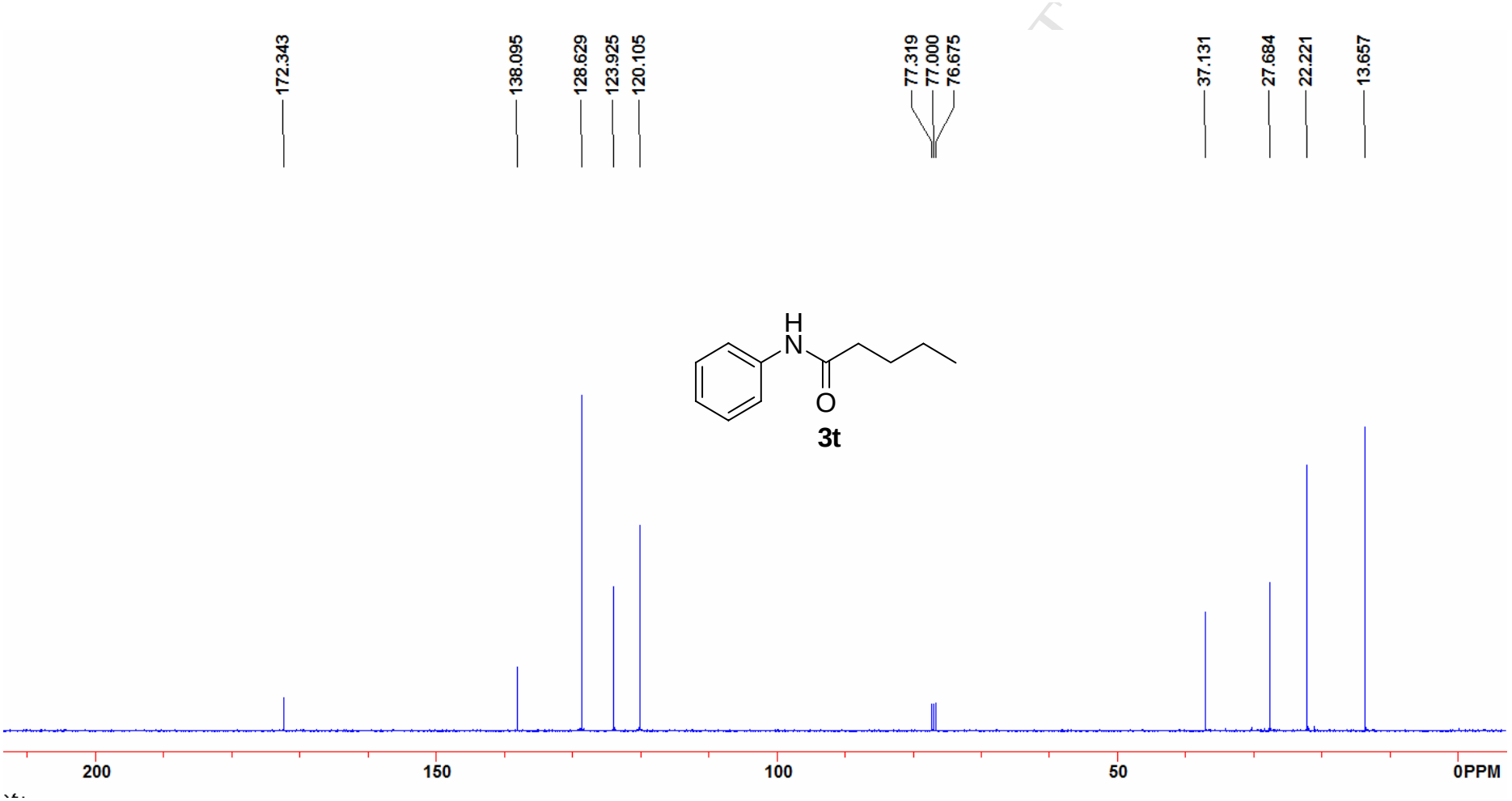

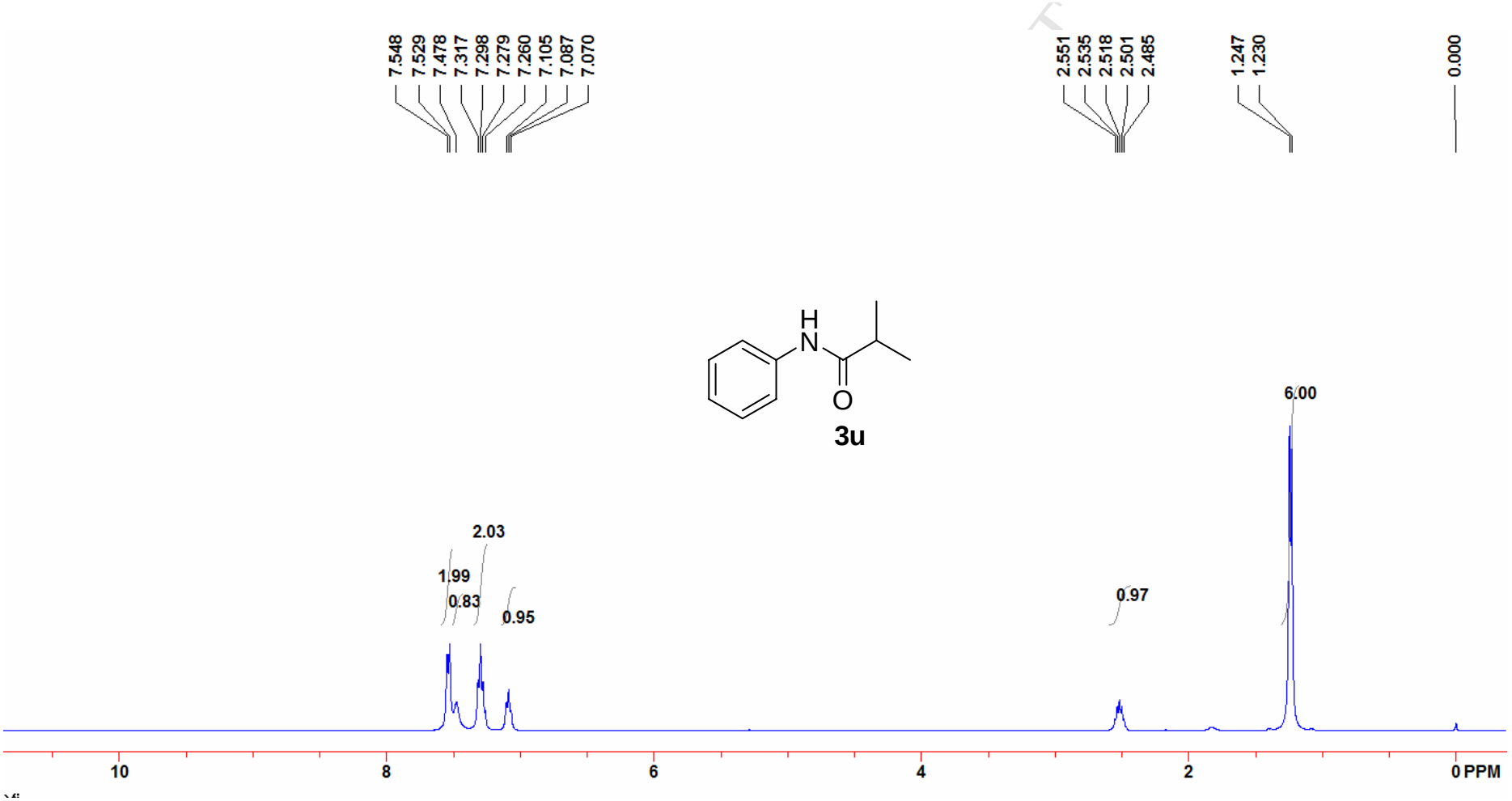

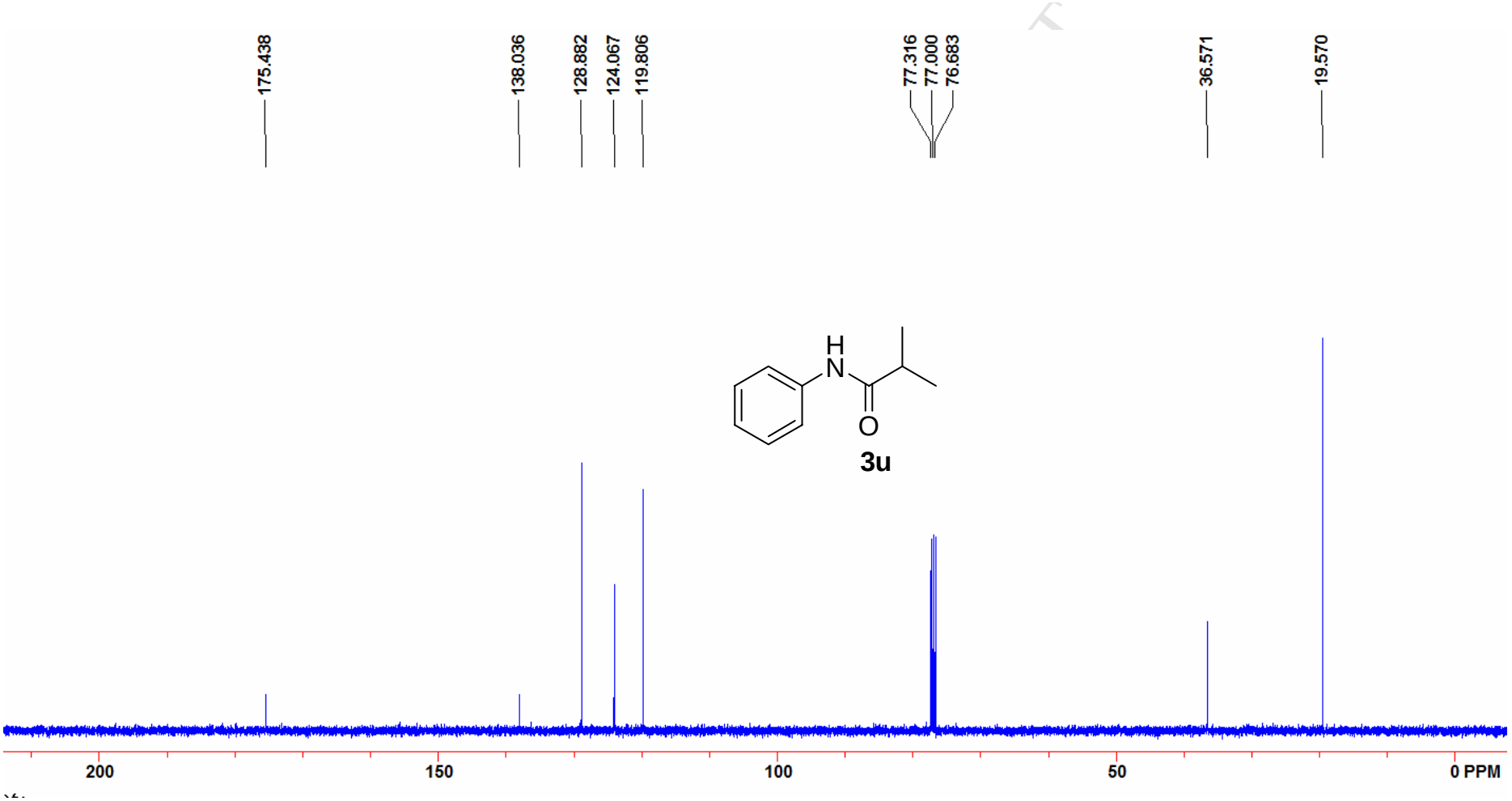

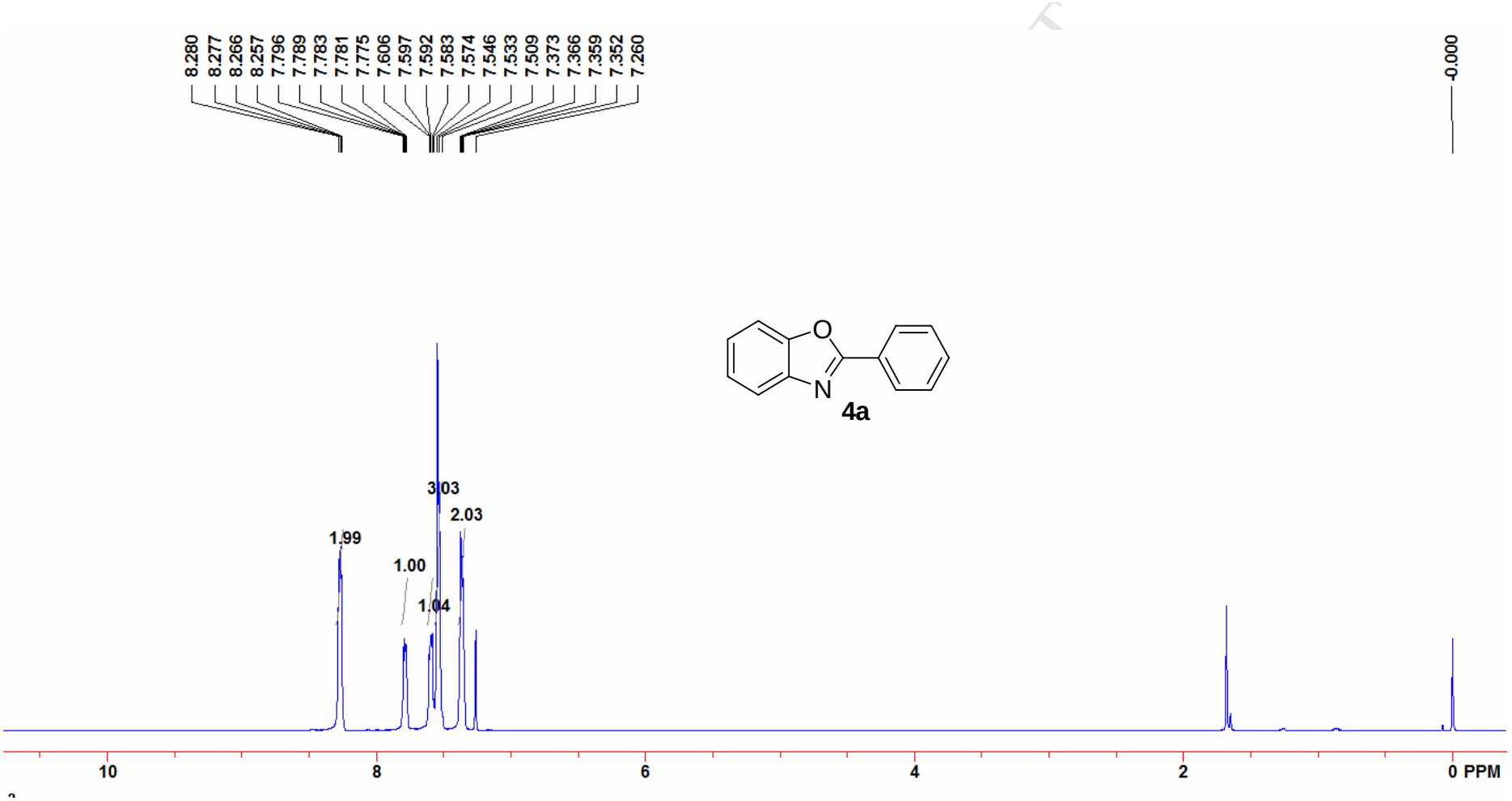
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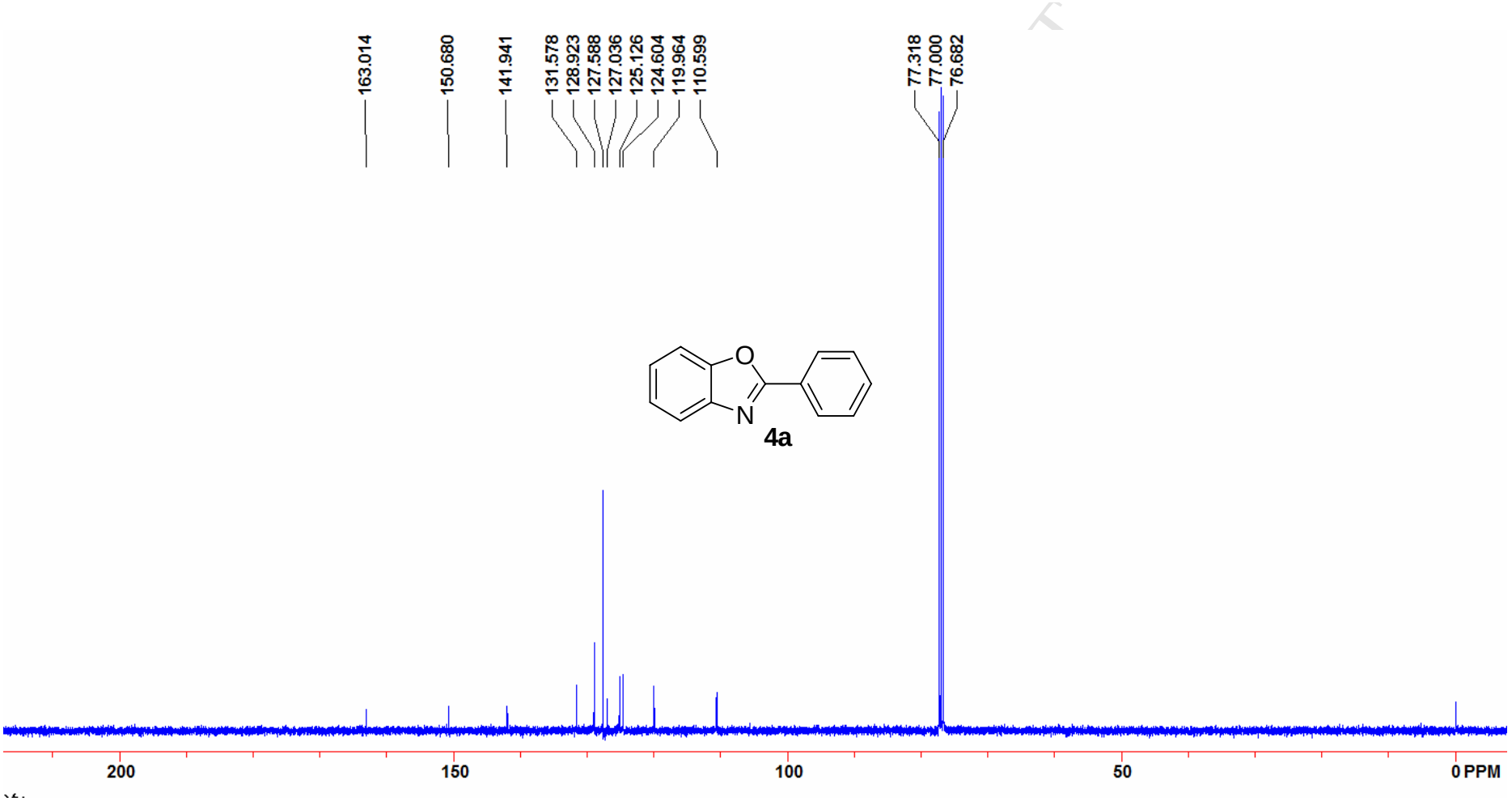

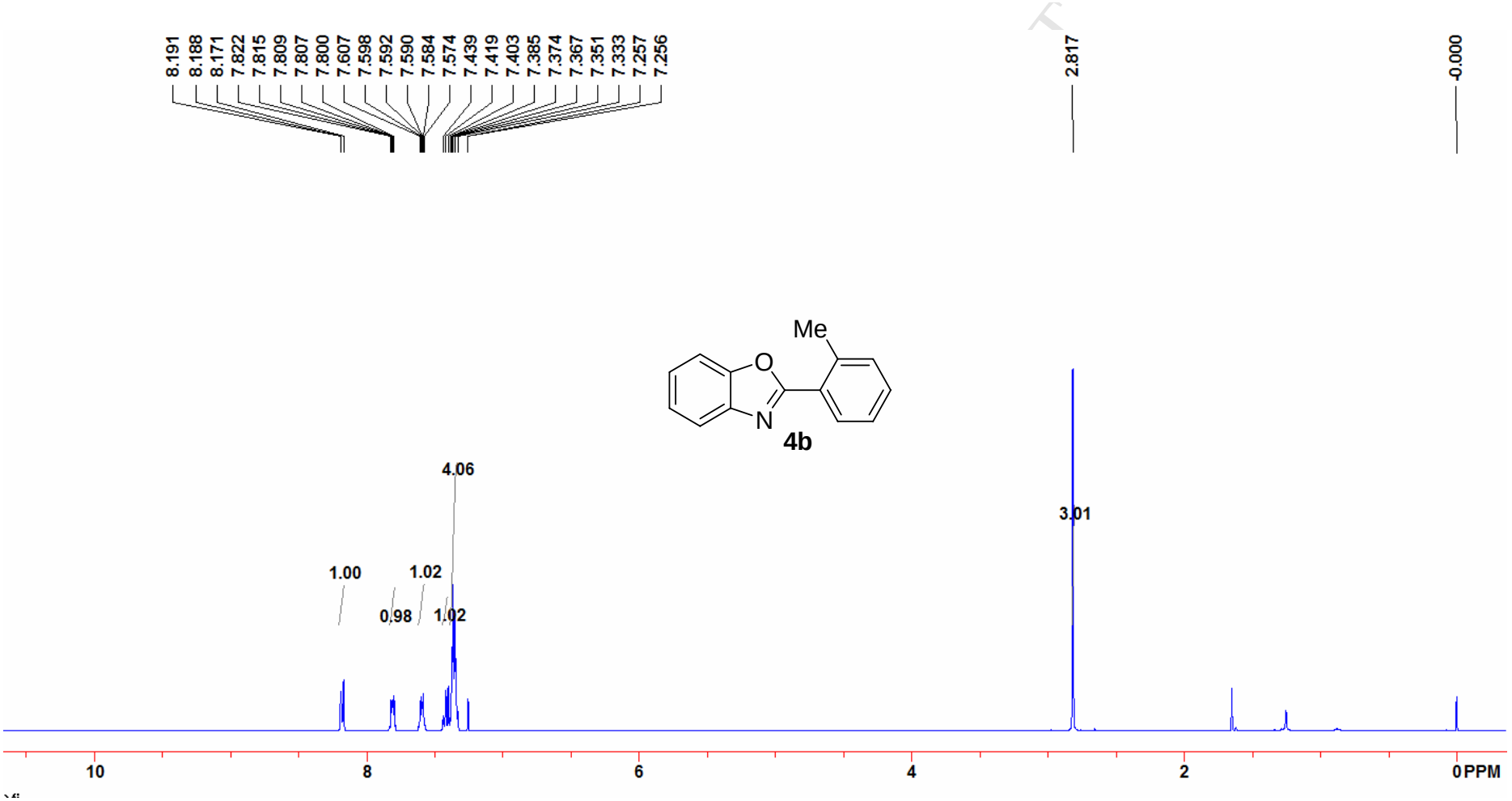
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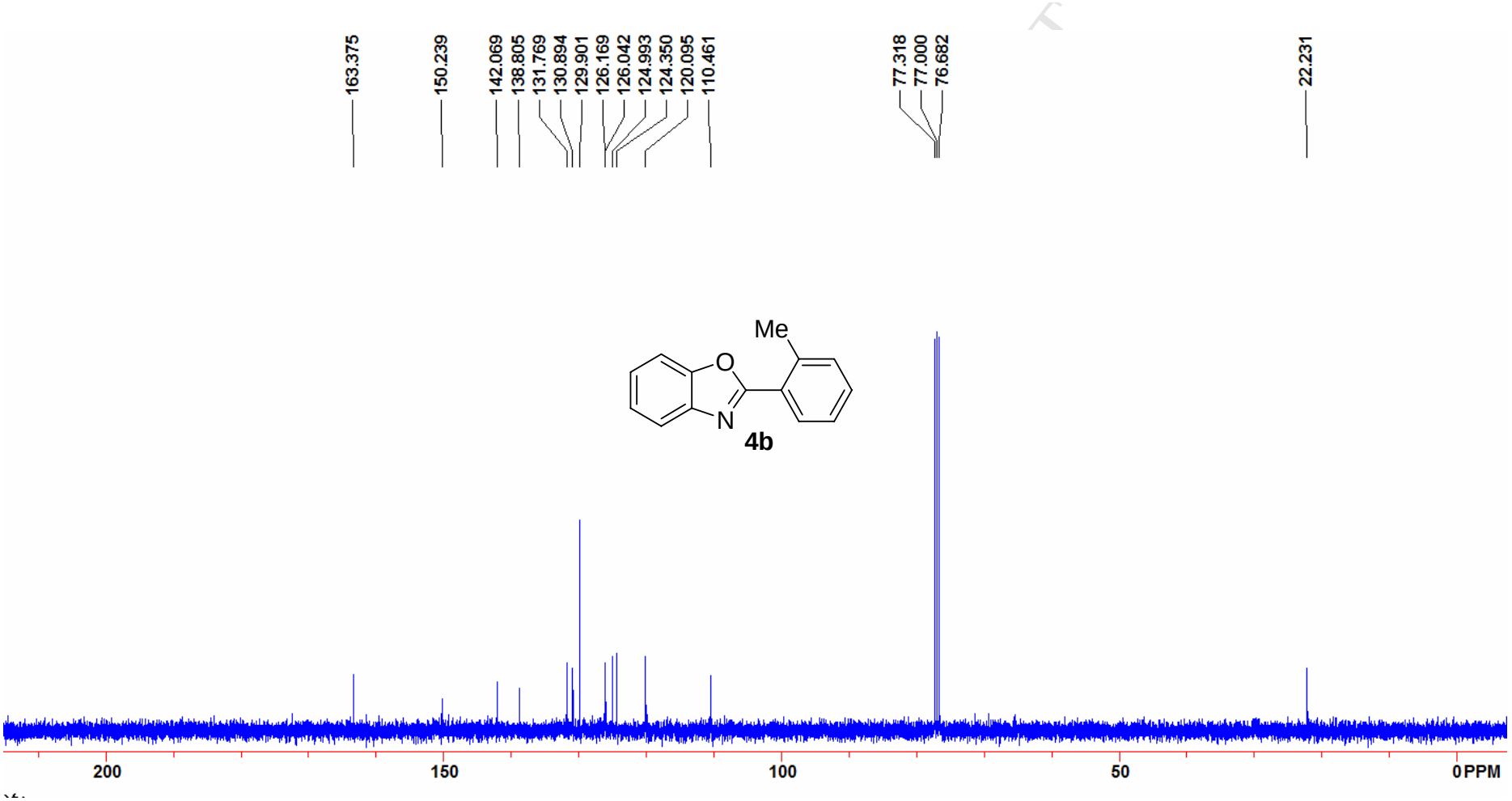

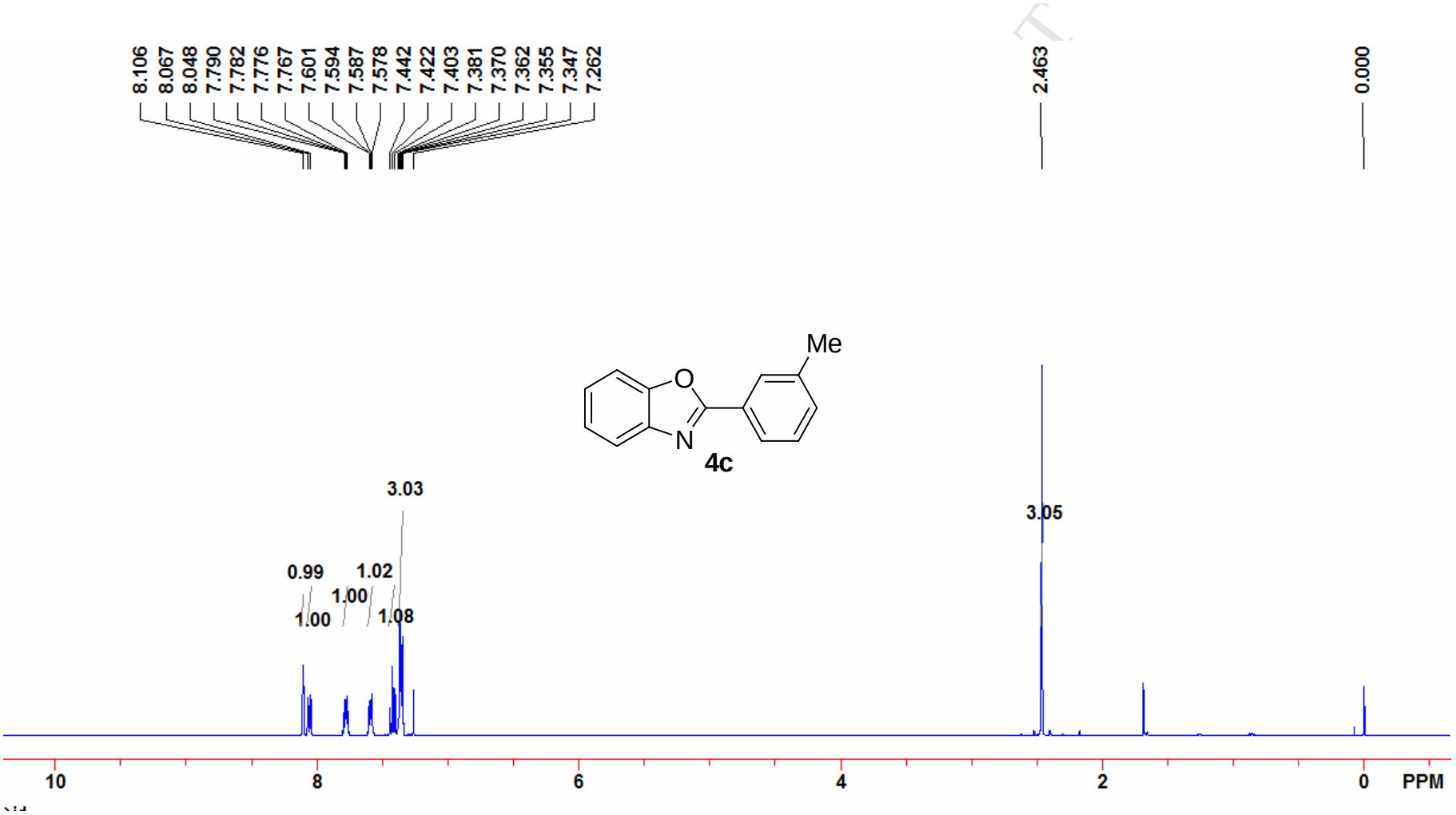
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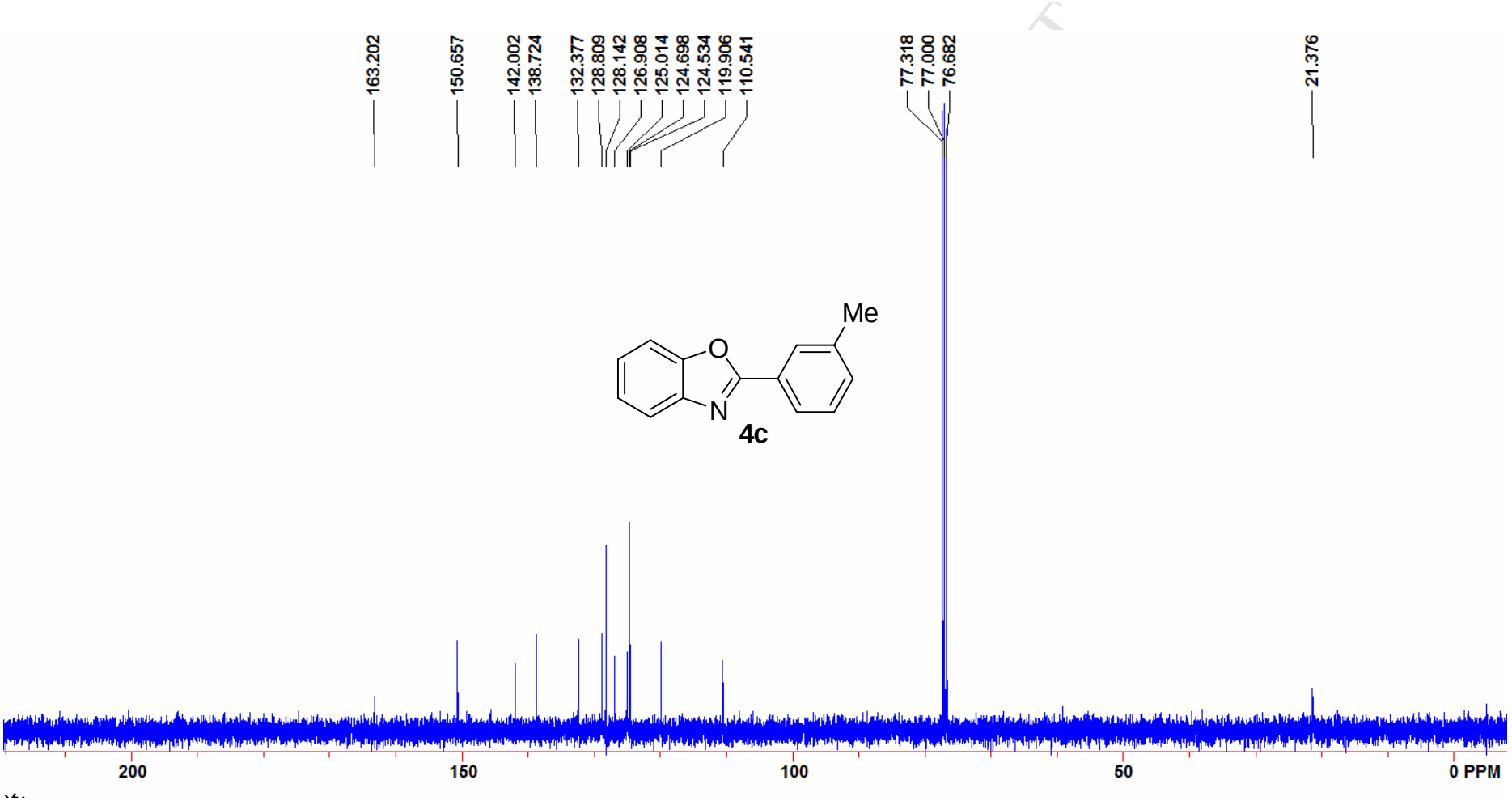
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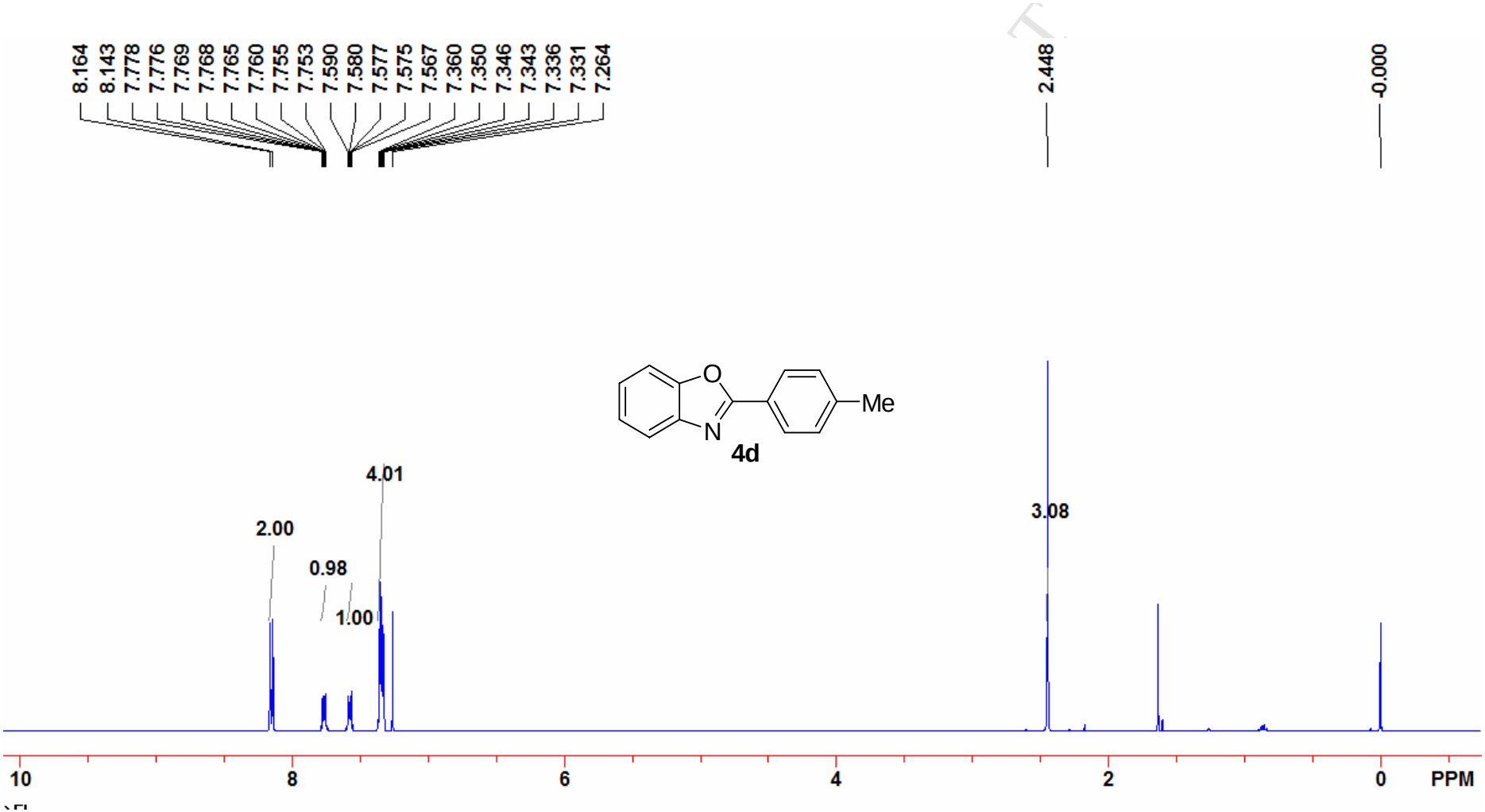
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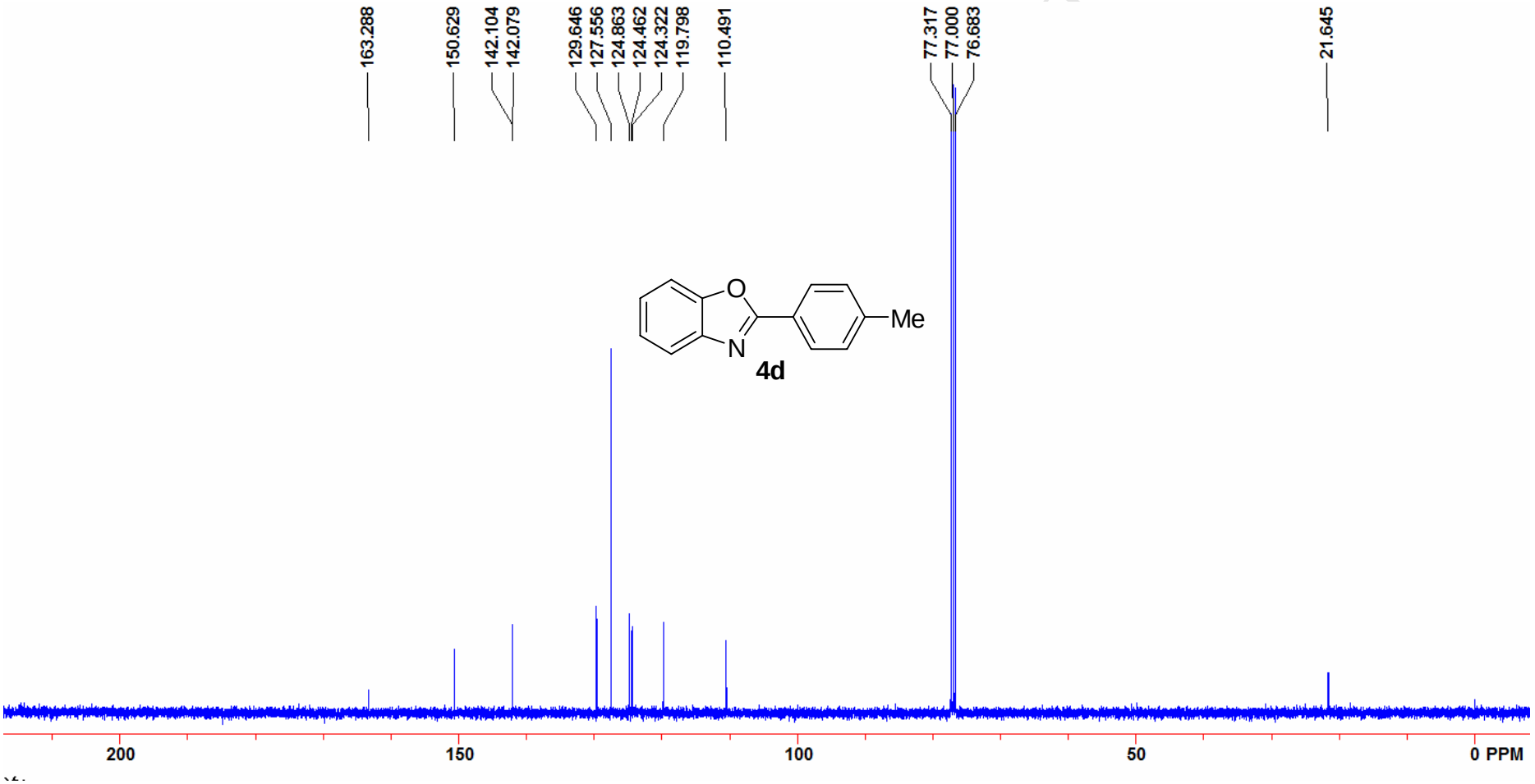

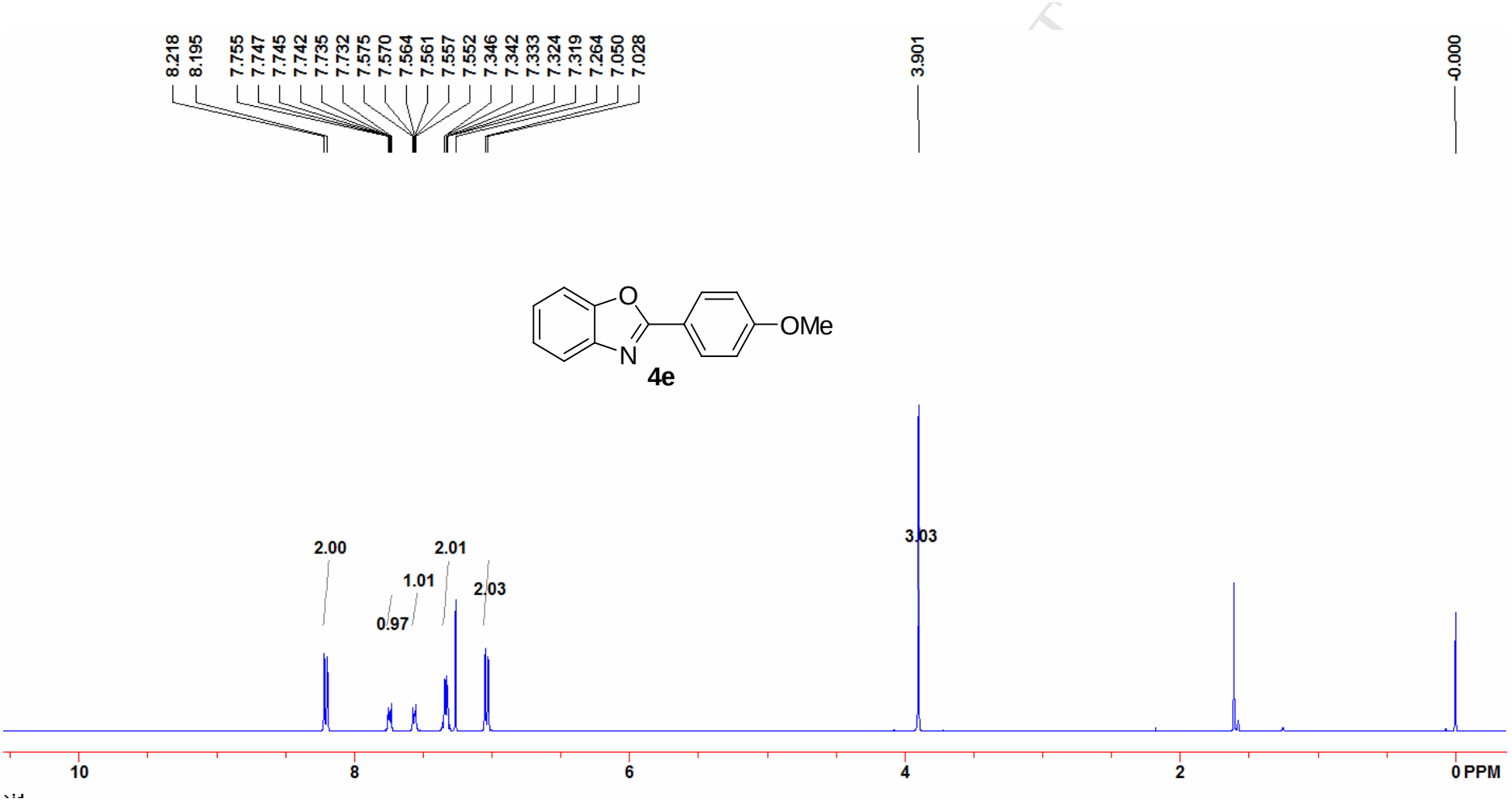
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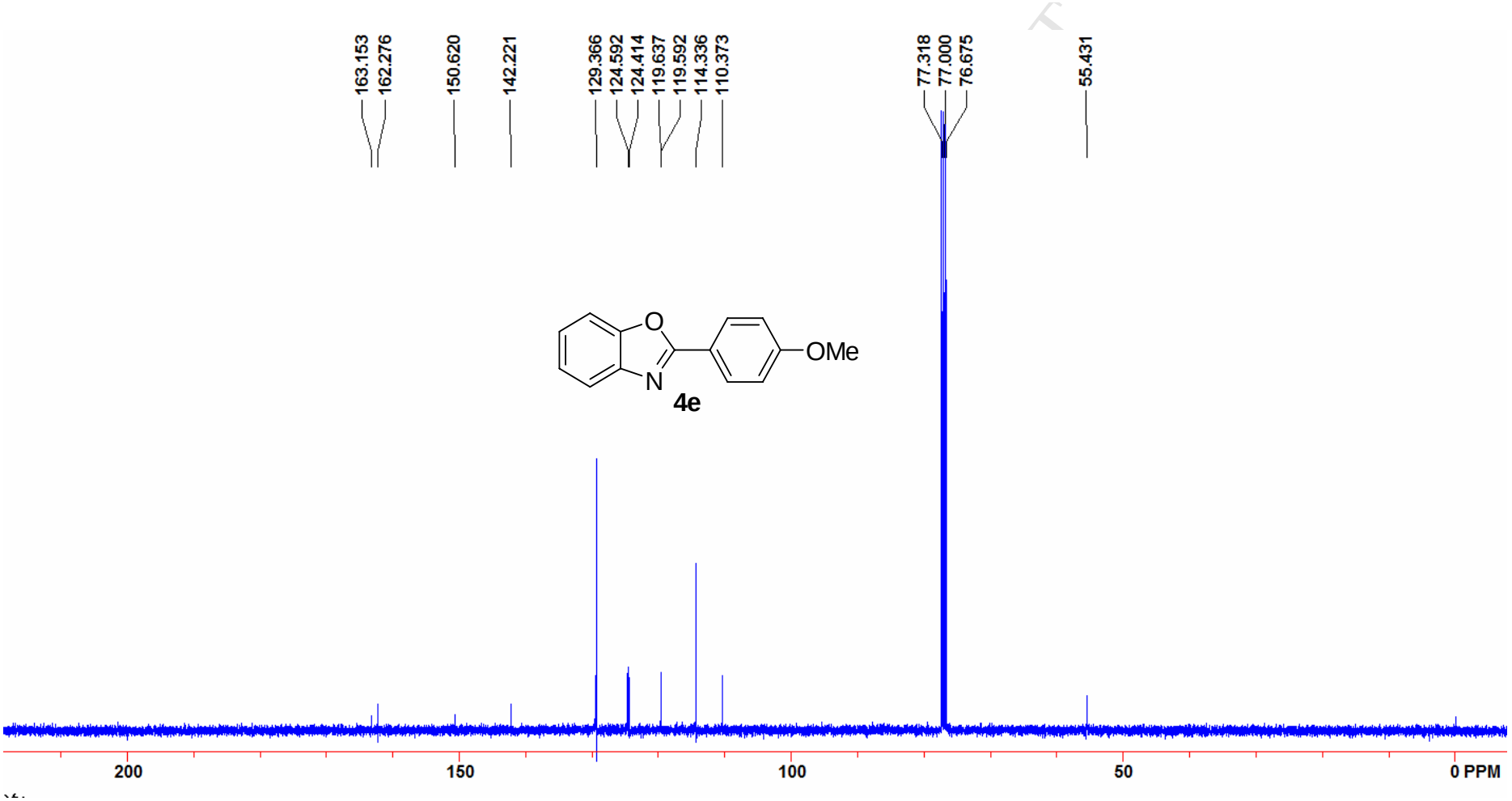

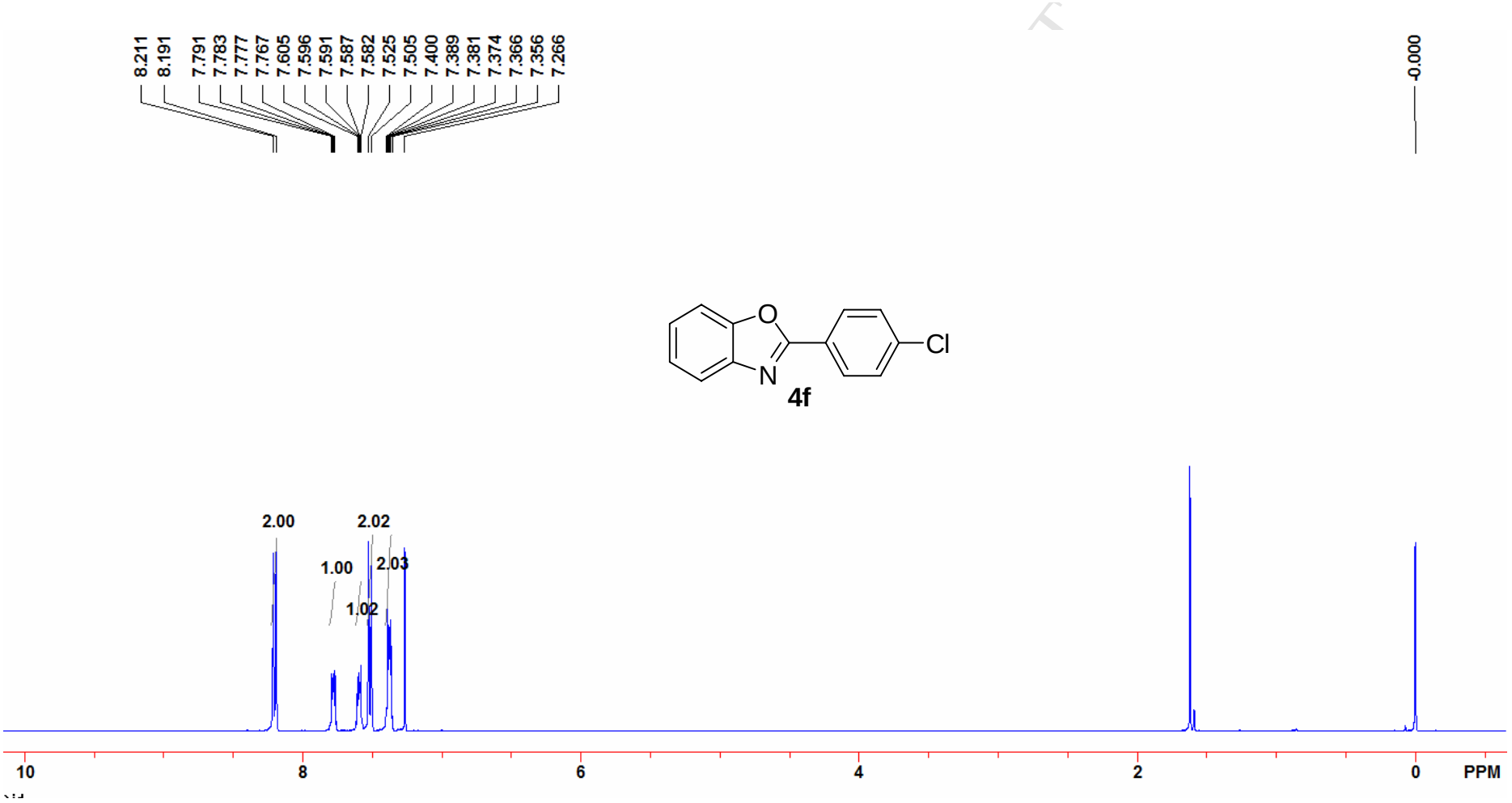
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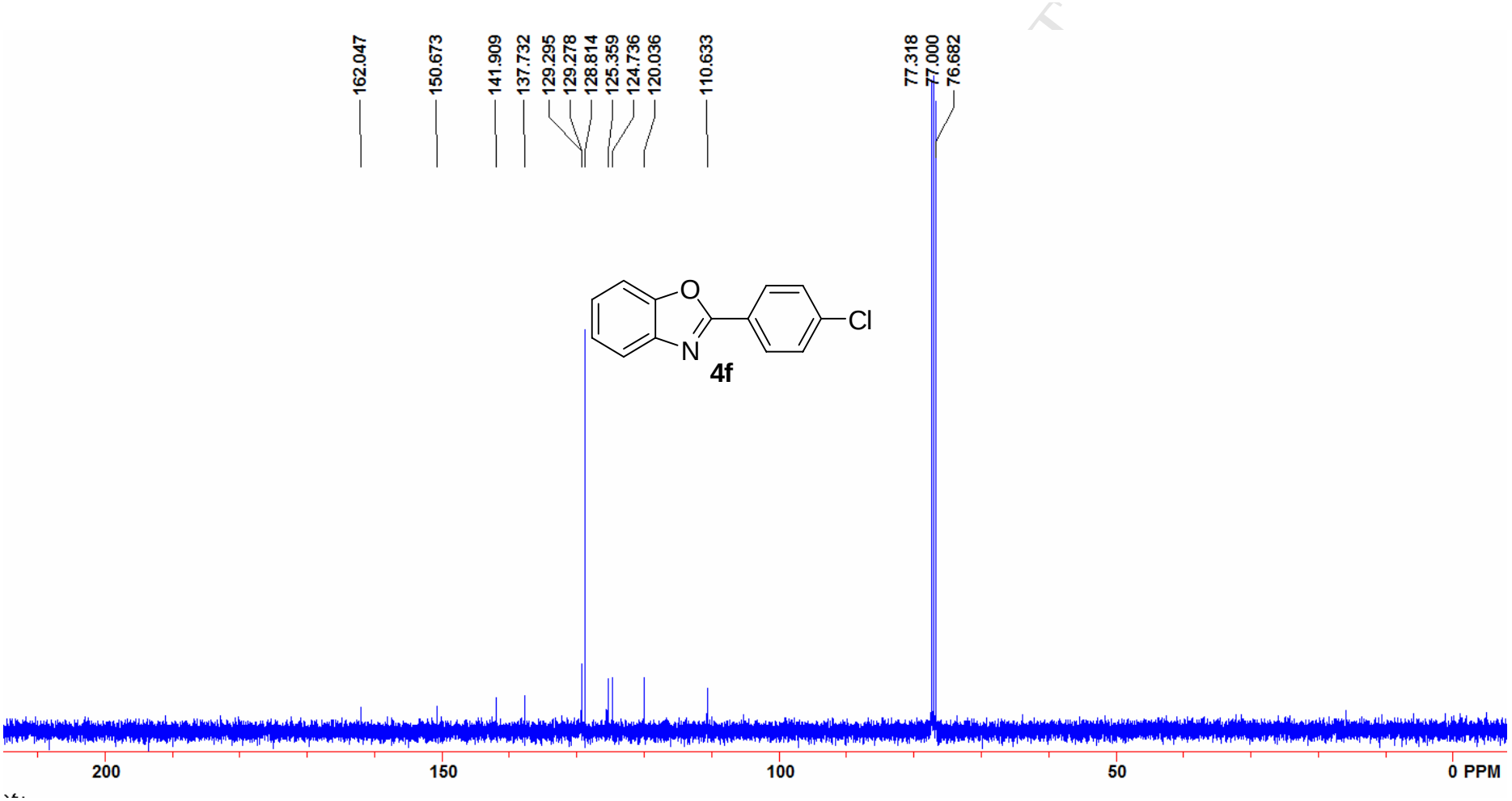

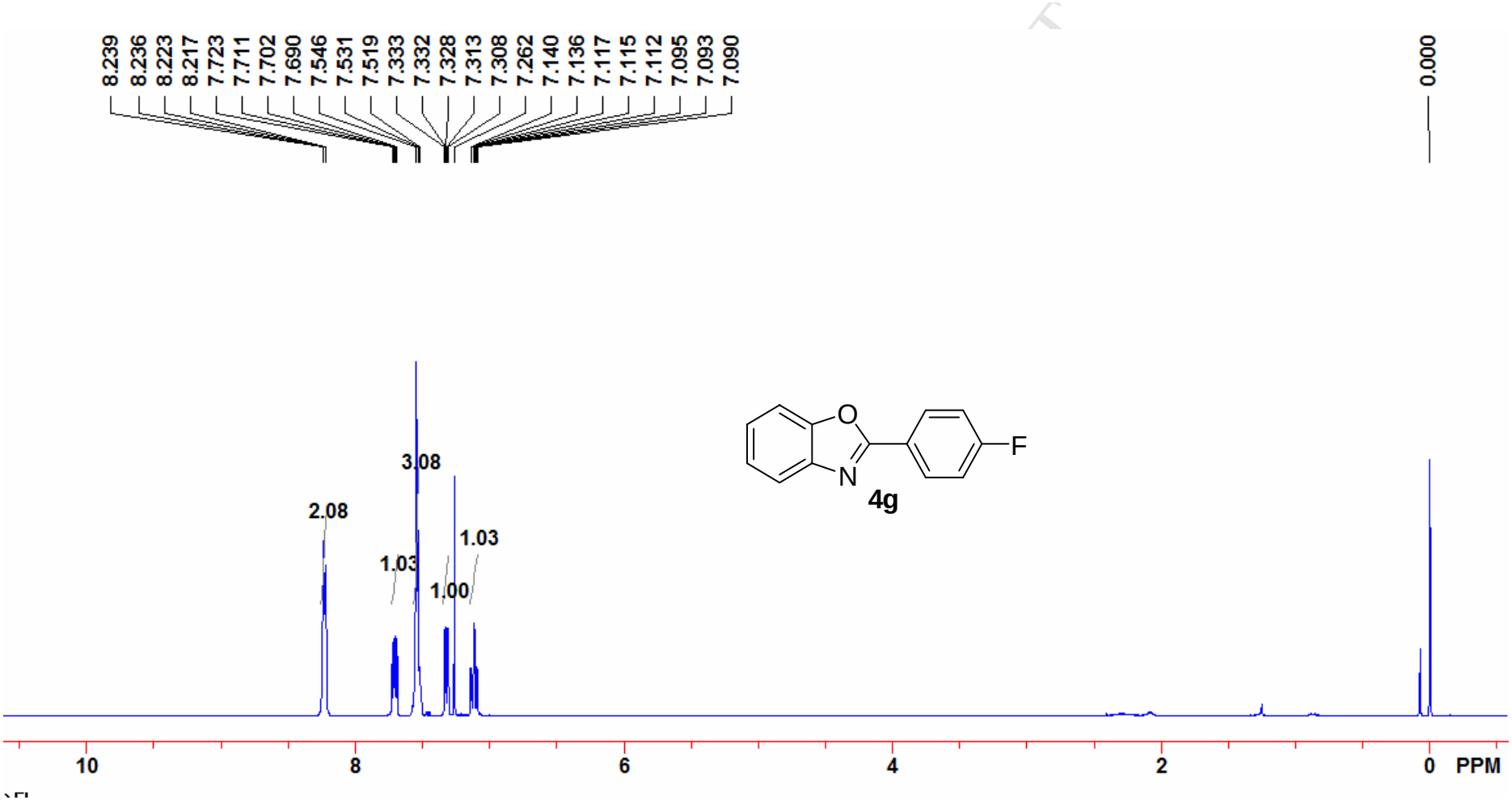
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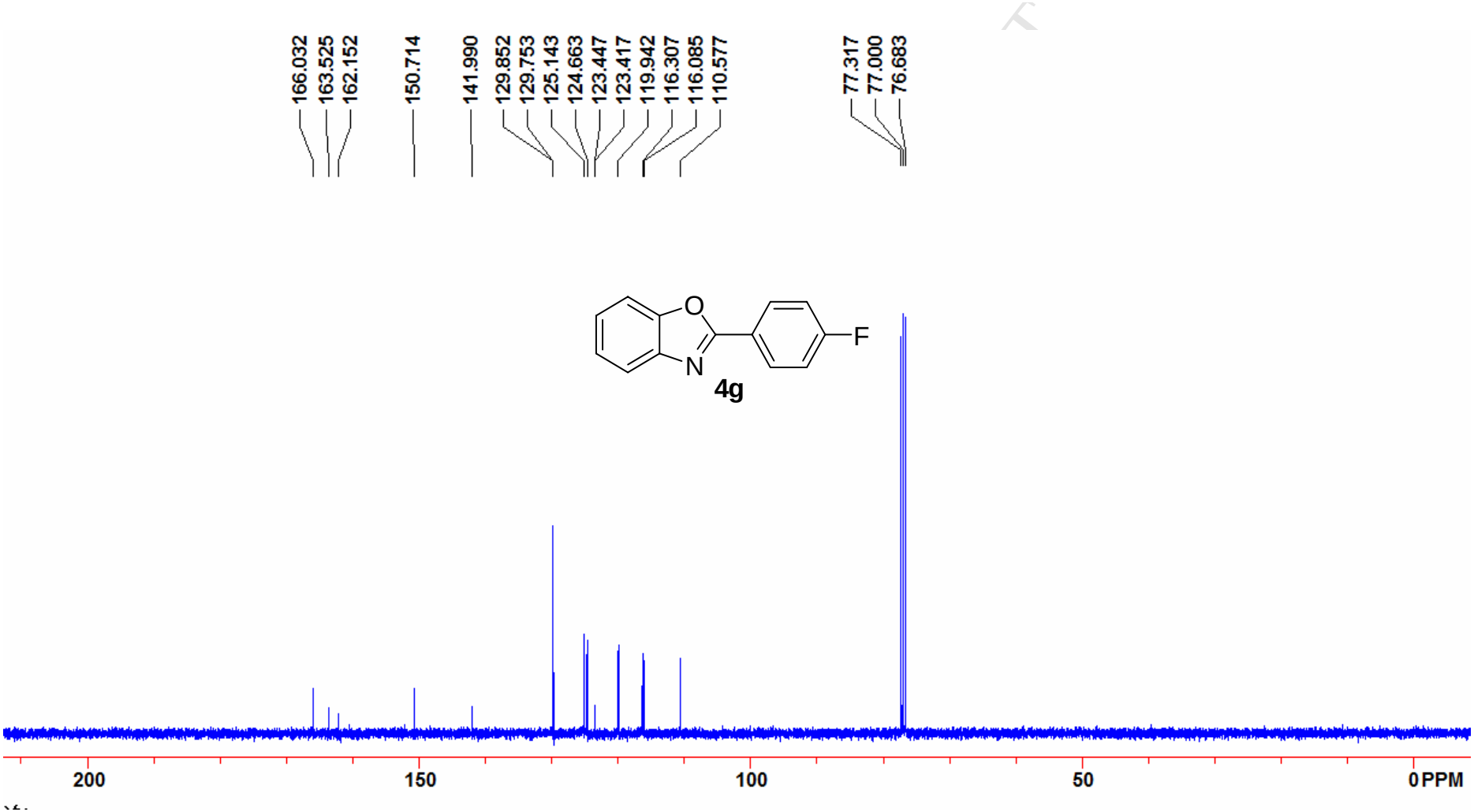
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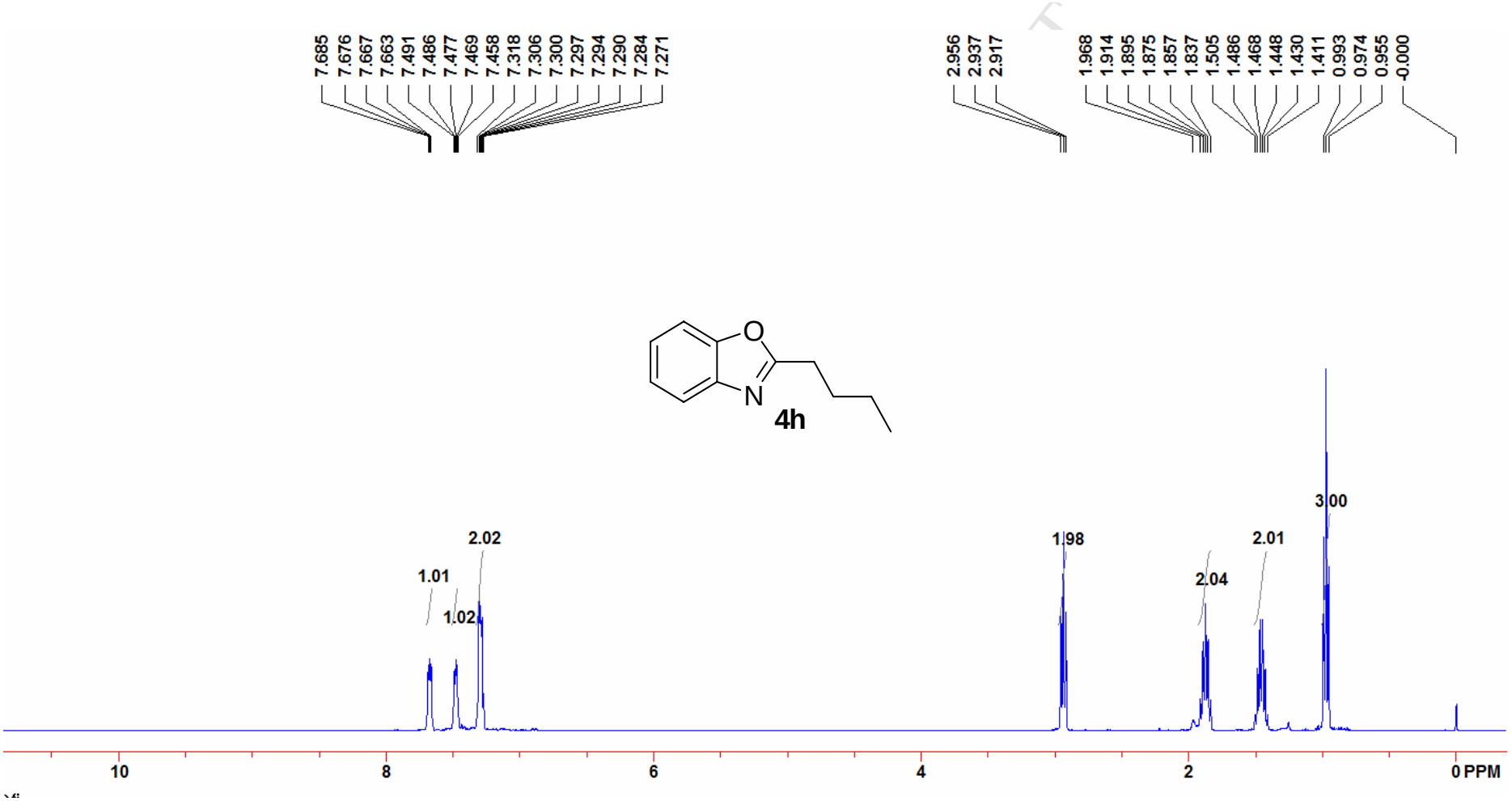
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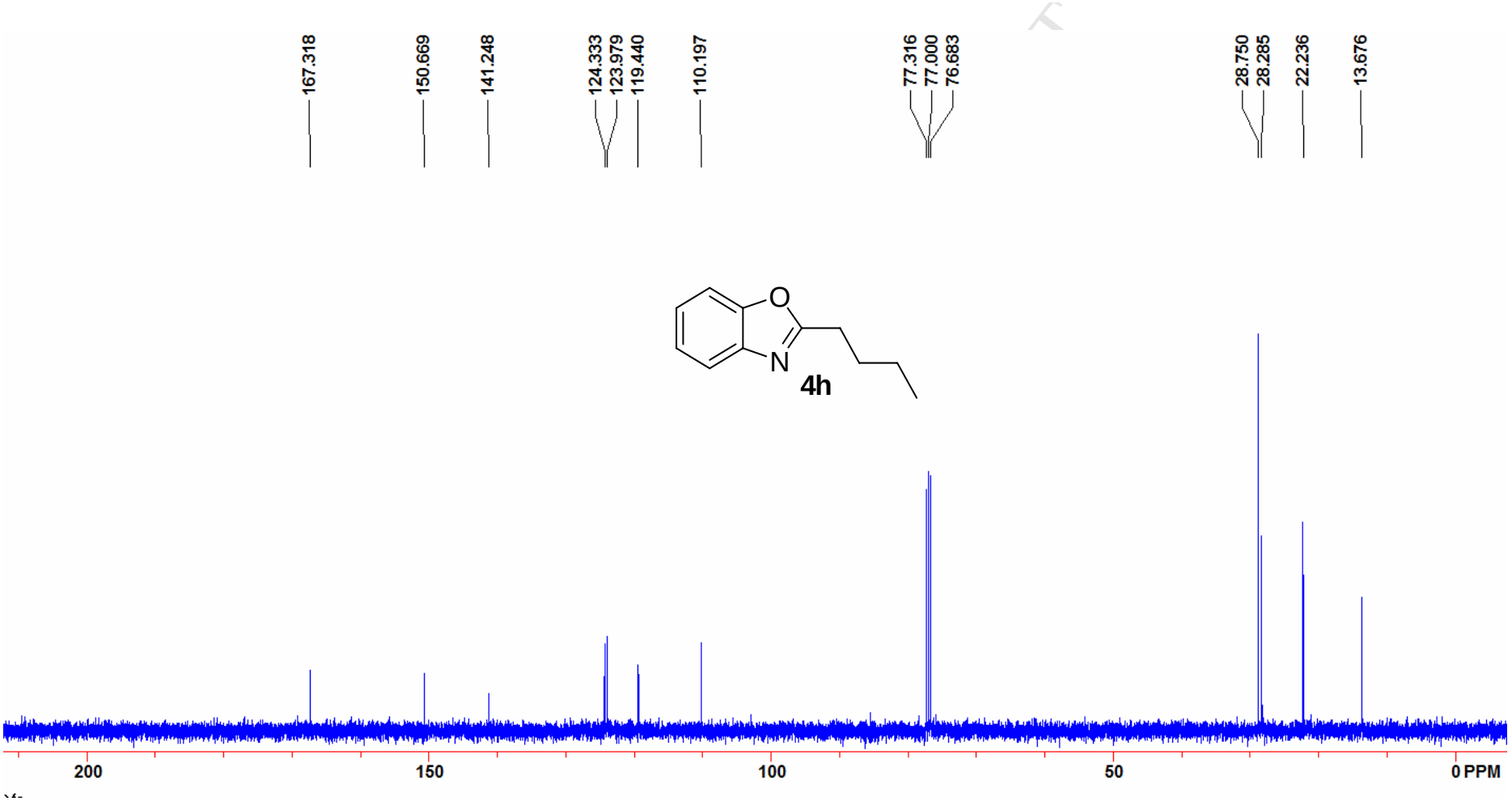
2
0 PPM


167.318
150.669
141.248
124.333
123.979
119.440
110.197
77.316
77.000
76.683
28.750
28.285
22.236
13.676
O
N
4h
200
150
100
50
0 PPM