

Supporting Information

for

**Aerobic radical multifunctionalization of alkenes using
tert-butyl nitrite and water**

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**Experimental details, characterization data of all products, and copies
of NMR spectra.**

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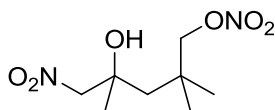
Experimental details

General methods: All glassware was oven dried. All reagents purchased commercially were used without further purification. All solvents were used after dried by distillation from appropriate dehydrating reagents such as calcium hydride, sodium/benzophenone, or molecular sieves. Deuterated chloroform was passed through an alumina column before the use. ^1H and ^{13}C NMR spectra were recorded on JEOL JNM ECA600 (600 MHz and 150 MHz, respectively) spectrometer. Chemical shifts (δ) are quoted relative to tetramethylsilane (^1H NMR) and the residual signals of chloroform (^{13}C NMR). Silica gel column chromatography was carried out on silica gel 60N (Kanto Kagaku Co., Ltd., spherical, neutral, 63–210 μm). Mass spectra were recorded on JEOL JMS-700 spectrometers (fast atom bombardment, FAB).

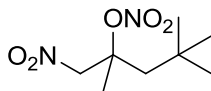
Starting materials: Compounds **1**, **5**, **6**, **7**, **8**, **11** and **14** were commercially available. Compounds **9** [1], **10** [2], **12** [3] and **13** [4] were prepared according to literature procedures.

General procedure for multifunctionalization reactions using *tert*-butyl nitrite, water and oxygen:

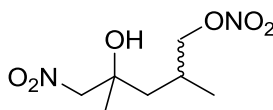
To a stirred solution of alkene (1.00 mmol) in pentane (5.0 mL) and were added water (540 mg, 30.0 mmol) and *tert*-butyl nitrite (310 mg, 3.00 mmol), and the mixture was stirred at room temperature under O_2 atmosphere (1 atm, balloon). The mixture was diluted with water and extracted with Et_2O . The organic layer was washed with brine and dried with MgSO_4 . After the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography (hexane/ EtOAc) to give the product. Since several products were unstable, these needed to be analyzed as soon as possible after purification.



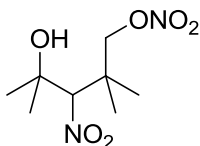
4-Hydroxy-2,2,4-trimethyl-5-nitropentyl nitrate (3) Elute: hexane/ EtOAc , 5:1 (second elute). 13–37% yield. colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 4.51 (d, J = 12.0 Hz, 1H), 4.43 (d, J = 10.2 Hz, 1H), 4.39 (d, J = 10.2 Hz, 1H), 4.38 (d, J = 12.0 Hz, 1H), 3.11 (s, 1H), 1.63 (s, 2H), 1.41 (s, 3H), 1.16 (s, 3H) 1.14 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 85.6, 80.4, 72.3, 46.2, 34.7, 26.8, 26.3; HRFABMS calcd for $\text{C}_8\text{H}_{17}\text{N}_2\text{O}_6$ [$\text{M} + \text{H}$] $^+$ 237.1087, found: 237.1007.



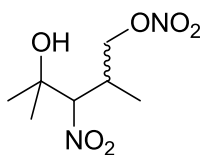
2,4,4-trimethyl-1-nitropent-2-yl nitrate (4) [5] : Elute: hexane/EtOAc, 5:1 (first elute). 28-54% yield. colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 5.00 (d, $J = 12.0$ Hz, 1H), 4.78 (d, $J = 12.0$ Hz, 1H), 2.13 (d, $J = 15.0$ Hz, 1H), 1.74 (d, $J = 15.0$ Hz, 1H), 1.70 (s, 3H), 1.08 (s, 9H); ^{13}C NMR (150 MHz, CDCl_3) δ 88.8, 80.4, 47.0, 31.3, 31.0, 22.0.



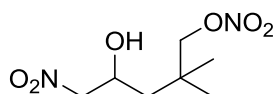
4-Hydroxy-2,4-dimethyl-5-nitropentyl nitrate (15) 12 h. Elute: hexane/EtOAc, 6:1 $\rightarrow$ 3:1. 86.6 mg, 40% yield (as an inseparable mixture of two diastereomers, ca. 90:10 dr); colorless oil. ^1H NMR (600 MHz, CDCl_3 , for major isomer) δ 4.50 (d, $J = 12.0$ Hz, 1H), 4.43 (d, $J = 12.0$ Hz, 1H), 4.45–4.40 (m, 1H), 4.29 (dd, $J = 10.8, 6.6$ Hz, 1H), 2.99 (s, 1H), 2.27–2.16 (m, 1H), 1.75–1.66 (m, 1H), 1.50–1.43 (m, 1H), 1.37 (s, 3H), 1.12 (d, $J = 6.9$ Hz, 3H); ^1H NMR (600 MHz, CDCl_3 , for partial peaks of minor isomer) δ 4.58 (dd, $J = 10.8, 5.4$ Hz, 1H), 3.04 (s, 1H), 1.35 (s, 3H), 1.10 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 84.8 (minor), 84.4, 77.7, 77.5 (minor), 71.6, 71.5 (minor), 42.2, 42.1 (minor), 27.4, 27.3 (minor), 24.9, 24.1 (minor), 19.0 (minor), 18.6; HRFABMS calcd for $\text{C}_7\text{H}_{15}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 223.0930, found: 223.0923.



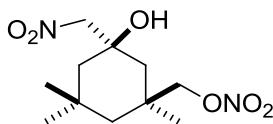
4-Hydroxy-2,2,4-trimethyl-3-nitropentyl nitrate (16) 12 h. Elute: hexane/EtOAc, 5:1. 66.2 mg, 29% yield. colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 4.73 (d, $J = 10.8$ Hz, 1H), 4.51 (s, 1H), 4.47 (d, $J = 10.8$ Hz, 1H), 2.70 (s, 1H), 1.47 (s, 3H), 1.39 (s, 3H), 1.292–1.288 (m, 6H); ^{13}C NMR (150 MHz, CDCl_3) δ 100.0, 77.4, 72.6, 38.5, 30.1, 28.6, 24.9, 23.4; HRFABMS calcd for $\text{C}_8\text{H}_{17}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 237.1087, found: 237.1088.



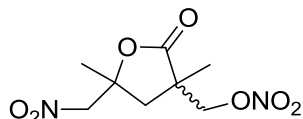
4-Hydroxy-2,4-dimethyl-3-nitropentyl nitrate (17) 12 h. Elute: hexane/EtOAc, 6:1 → 4:1. 82.1 mg, 38% yield (>95:5 dr. Although a trace amount of a minor isomer was detected by ^1H NMR analysis of a crude product, it could not be isolated due to the small amount); colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 4.51–4.49 (m, 3H), 2.77–2.71 (m, 1H), 2.70 (s, 1H), 1.41 (s, 3H), 1.34 (s, 3H), 1.15 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 94.5, 74.0, 71.5, 31.6, 27.00, 26.98, 13.5; HRFABMS calcd for $\text{C}_7\text{H}_{15}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 223.0930, found: 223.0922.



4-Hydroxy-2,2-dimethyl-5-nitro-pentyl nitrate (18) 12 h. Elute: hexane/EtOAc, 5:1 → 3:1. 35.2 mg, 16% yield; colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 4.48–5.51 (m, 1H), 4.39–4.38 (m, 3H), 4.30 (d, $J = 10.2$ Hz, 1H), 2.74 (br, 1H), 1.66 (dd, $J = 14.8$, 10.3 Hz, 1H), 1.35 (dd, $J = 14.8$, 2.1 Hz, 1H), 1.12 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 81.1, 80.1, 65.8, 41.4, 33.7, 25.8, 24.2; HRFABMS calcd for $\text{C}_7\text{H}_{14}\text{N}_2\text{O}_6$ $[\text{M}]^+$ 222.0851, found: 222.0871.

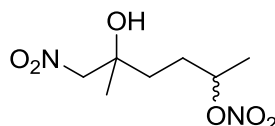


[(1R*,3S*)-3-Hydroxy-1,5,5-trimethyl-3-nitromethylcyclohexyl]methyl nitrate (19) 12 h. Elute: hexane/EtOAc, 10:1 → 5:1. 76.2 mg, 28% yield (as a single isomer); colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 4.77 (d, $J = 9.6$ Hz, 1H), 4.71 (d, $J = 9.6$ Hz, 1H), 4.37 (d, $J = 12.0$ Hz, 1H), 4.33 (d, $J = 12.0$ Hz, 1H), 3.07 (s, 1H), 1.87 (dt, $J = 14.6$, 2.1 Hz, 1H), 1.76 (dt, $J = 10.7$, 2.1 Hz, 1H), 1.64 (dt, $J = 9.3$, 2.4 Hz, 1H), 1.24 (d, $J = 13.8$ Hz, 1H), 1.21 (s, 3H), 1.10 (t, $J = 13.1$ Hz, 2H), 1.03 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 86.3, 78.3, 72.6, 46.8, 45.2, 41.5, 35.9, 34.3, 30.6, 29.9, 28.2; HRFABMS calcd for $\text{C}_{11}\text{H}_{21}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 277.1400, found: 277.1400.

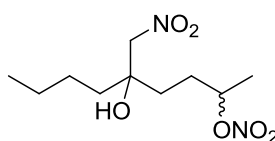


[3,5-Dimethyl-5-(nitromethyl)-2-oxotetrahydrofuran-3-yl]methyl nitrate (20) 12 h. Elute: hexane/EtOAc, 8:1 → 1:1. 75.0 mg, 31% yield (as an inseparable mixture of two diastereomers, ca. 50:50 dr); colorless oil. ^1H NMR (600 MHz, CDCl_3 , for a mixture of

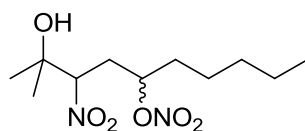
two isomers) δ 4.70–4.56 (m, 3H + 3H), 4.44 (d, J = 10.0 Hz, 1H), 4.38 (d, J = 10.0 Hz, 1H), 2.76 (d, J = 14.4 Hz, 1H), 2.53 (d, J = 14.4 Hz, 1H), 2.36 (d, J = 14.4 Hz, 1H), 2.13 (d, J = 14.1 Hz, 1H), 1.65 (s, 3H), 1.64 (s, 3H), 1.48 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3 , for a mixture of two isomers) δ 176.4, 176.2, 81.61, 81.53, 79.3, 79.2, 75.8, 75.4, 44.1, 43.8, 40.8, 39.9, 26.6, 26.4, 23.2, 22.3; HRFABMS calcd for $\text{C}_8\text{H}_{13}\text{N}_2\text{O}_7$ $[\text{M} + \text{H}]^+$ 249.0723, found: 249.0723.



5-Hydroxy-5-methyl-6-nitrohex-2-yl nitrate (21) 12 h. Elute: hexane/EtOAc, 6:1 $\rightarrow$ 2:1. 62.9 mg, 31% yield (as an inseparable mixture of two diastereomers, ca. 50:50 dr); colorless oil. ^1H NMR (600 MHz, CDCl_3 , for a mixture of two isomers) δ 5.12–5.07 (m, 1H + 1H), 4.47–4.41 (m, 2H + 2H), 2.97 (s, 1H + 1H), 1.86–1.58 (m, 4H + 4H), 1.40–1.38 (m, 3H+3H), 1.328, (s, 3H), 1.320 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3 , for a mixture of two isomers) δ 84.2, 84.0, 80.9, 80.7, 71.1, 34.7, 34.6, 27.91, 27.85, 24.4, 24.1, 18.5, 18.3; HRFABMS calcd for $\text{C}_7\text{H}_{15}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 223.0930, found: 223.0922.



5-Hydroxy-5-nitromethylnon-2-yl nitrate (22) 12 h. Elute: hexane/EtOAc, 5:1 $\rightarrow$ 4:1. 86.8 mg, 33% yield (as an inseparable mixture of two diastereomers, ca. 50:50 dr); colorless oil. ^1H NMR (600 MHz, CDCl_3 , for a mixture of two isomers) δ 5.09–5.06 (m, 1H + 1H), 4.49–4.42 (m, 2H + 2H), 2.884 (s, 1H), 2.876 (s, 1H), 1.79–1.53 (m, 6H + 6H), 1.39–1.28 (m, 7H + 7H), 0.94–0.91 (m, 3H + 3H); ^{13}C NMR (150 MHz, CDCl_3 , for a mixture of two isomers) δ 82.5, 82.4, 80.9, 80.8, 73.2, 36.8, 36.5, 32.06, 32.02, 27.7, 27.6, 25.6, 25.5, 22.8, 18.5, 18.3, 13.8; HRFABMS calcd for $\text{C}_{10}\text{H}_{21}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 265.1400, found: 265.1404.

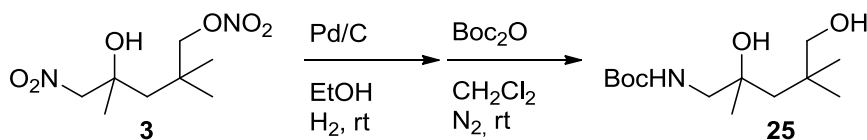


2-Hydroxy-2-methyl-3-nitrodec-5-yl nitrate (23) 12 h. Elute: hexane/EtOAc, 8:1 $\rightarrow$ 6:1. 49.2 mg+52.6 mg, 37% yield (as a separable mixture of two diastereomers, ca. 50:50 dr). First elute (**23**): 49.2 mg, 18%; colorless oil. ^1H NMR (600 MHz, CDCl_3) δ 4.90–4.87 (m, 1H), 4.62–4.59 (m, 1H), 2.59 (ddd, J = 15.8, 11.7, 2.7 Hz, 1H), 2.36 (s,

1H), 2.12 (ddd, $J = 16.2, 10.7, 2.7$ Hz, 1H), 1.76–1.73 (m, 1H), 1.66–1.63 (m, 1H), 1.37–1.26 (m, 12H), 0.89 (t, $J = 7.2$ Hz, 3H) ^{13}C NMR (150 MHz, CDCl_3) δ 92.3, 80.5, 71.1, 33.1, 31.38, 31.32, 27.2, 26.0, 24.2, 22.3, 13.9; HRFABMS calcd for $\text{C}_{11}\text{H}_{23}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 279.1556, found: 279.1554.

Second elute (**23'**): 52.6 mg, 19%; colorless oil. A small amount of inseparable impurities is detected by ^1H and ^{13}C NMR, but the influence on the yield is small because the diastomeric ratio calculated from the isolated yields is consistent with that estimated by ^1H NMR analysis of the crude product. ^1H NMR (600 MHz, CDCl_3) δ 5.08–5.06 (m, 1H), 4.50 (dd, $J = 10.2, 1.8$ Hz, 1H), 2.57 (ddd, $J = 16.2, 9.6, 6.0$ Hz, 1H), 2.35 (s, 1H), 2.28 (ddd, $J = 16.2, 6.0, 2.4$ Hz, 1H), 1.70–1.64 (m, 2H), 1.40–1.26 (m, 6H), 1.32 (s, 3H), 1.30 (s, 3H), 0.89 (t, $J = 6.6$ Hz, 3H) ^{13}C NMR (150 MHz, CDCl_3) δ 92.6, 81.6, 71.3, 31.9, 31.5, 31.3, 26.6, 26.0, 24.5, 22.3, 13.8; HRFABMS calcd for $\text{C}_{11}\text{H}_{23}\text{N}_2\text{O}_6$ $[\text{M} + \text{H}]^+$ 279.1556, found: 279.1550.

***tert*-Butyl 2,5-dihydroxy-2,4,4-trimethylpentyl carbamate (**25**):**

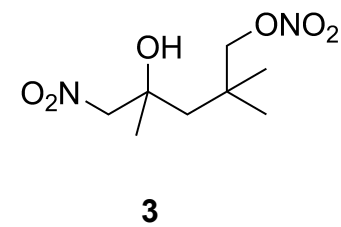
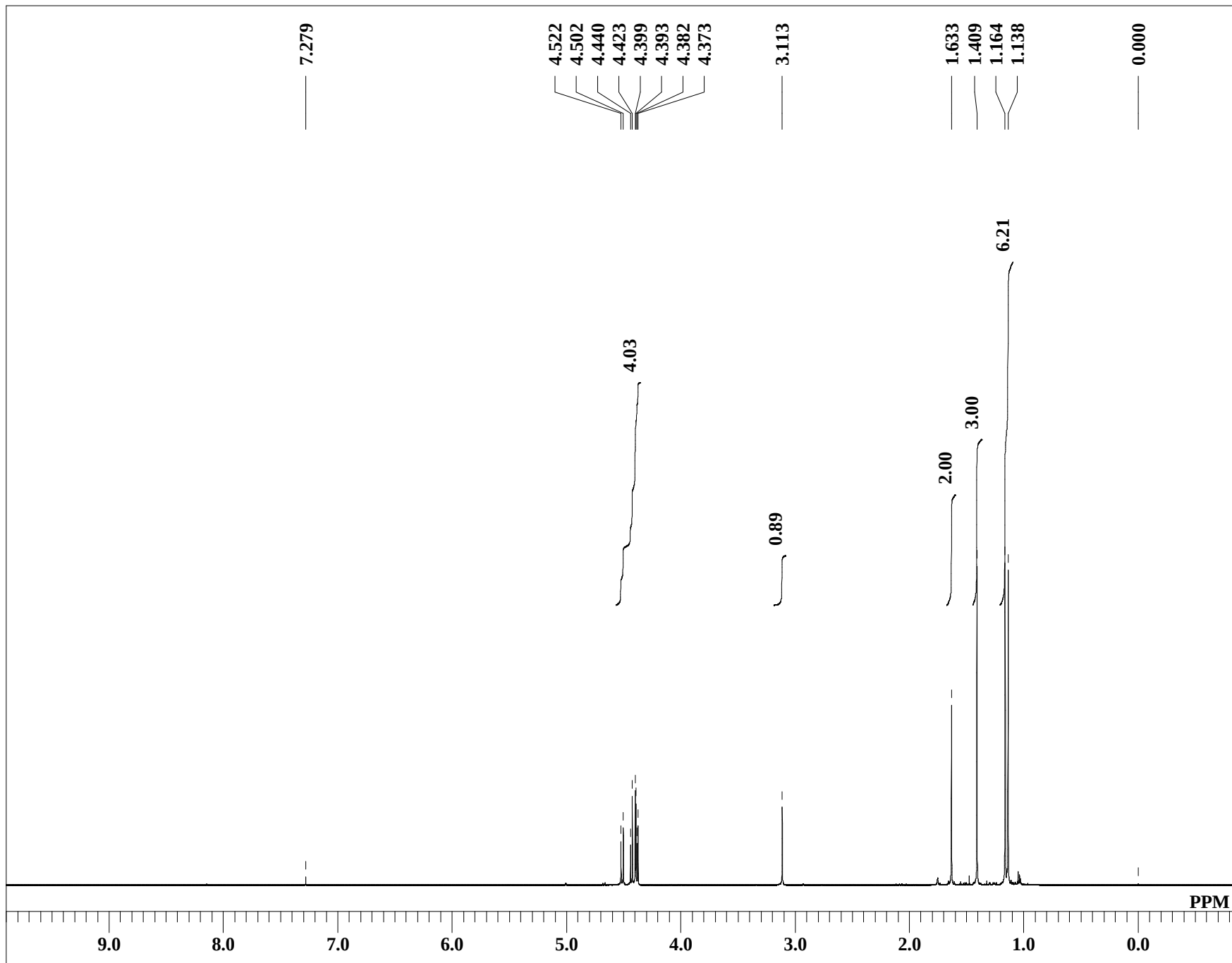


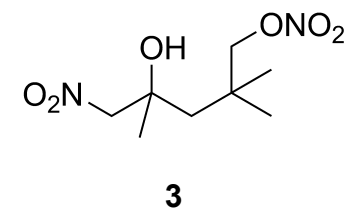
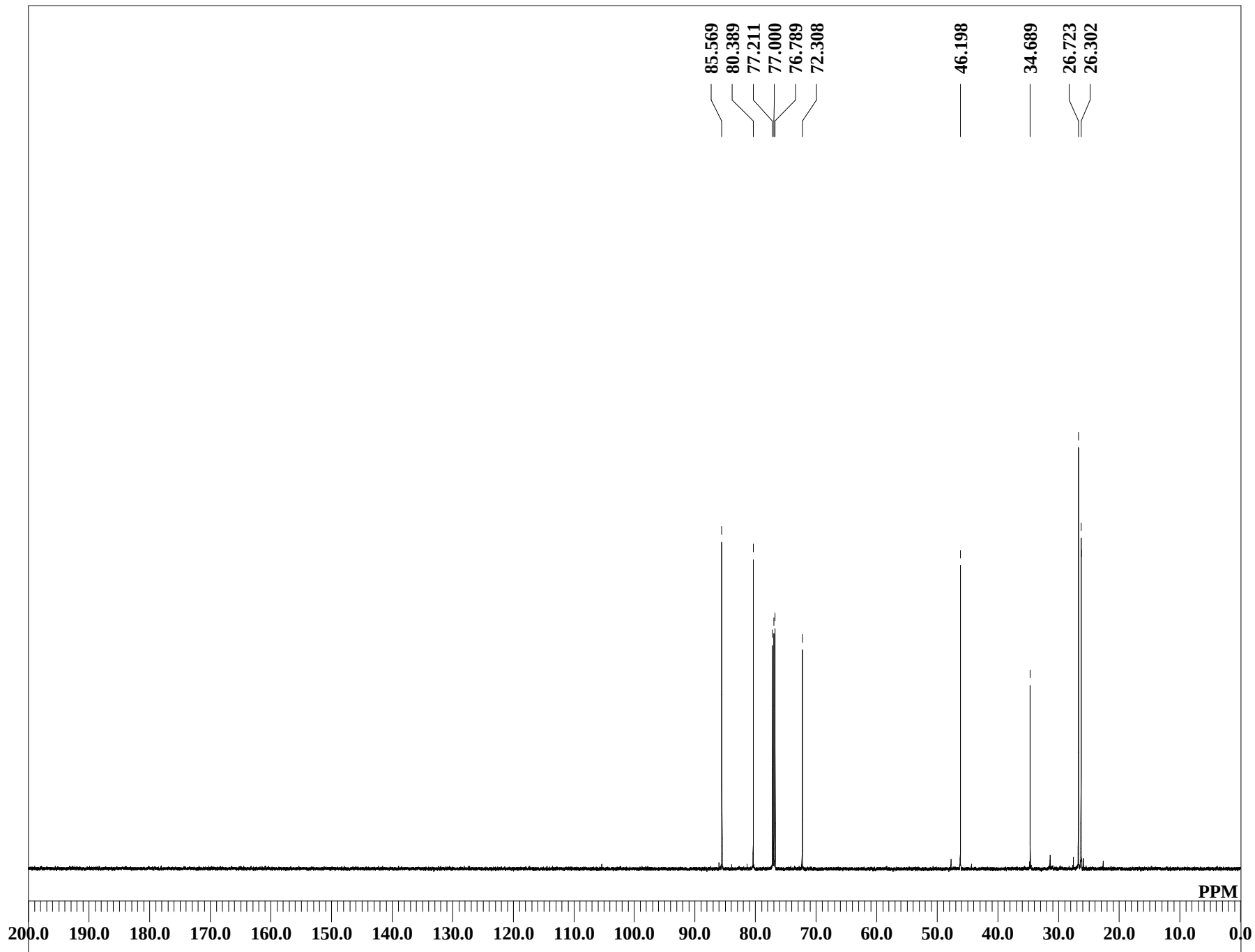
To a solution of **3** (59.0 mg, 0.250 mmol) in EtOH (10.0 mL) was added Pd/C (10%, 20.0 mg) at room temperature, and the mixture was vigorously stirred for 12 h under a hydrogen atmosphere (1 atm, balloon). The reaction mixture was filtered through CeliteTM and concentrated under reduced pressure. After the residue was dissolved in CH_2Cl_2 (2.5 mL), Boc_2O (57.2 mg, 0.263 mmol) was added, and the mixture was stirred for 20 h at room temperature. The mixture was diluted with water and extracted with CH_2Cl_2 . The organic layer was dried with MgSO_4 . After the solvent was removed under reduced pressure, the residue was purified by silica gel chromatography (hexane/EtOAc, 2:1) to give the **25** (52.3 mg, 81%) as a colorless oil.

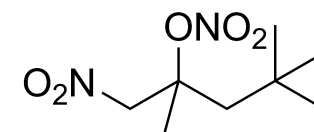
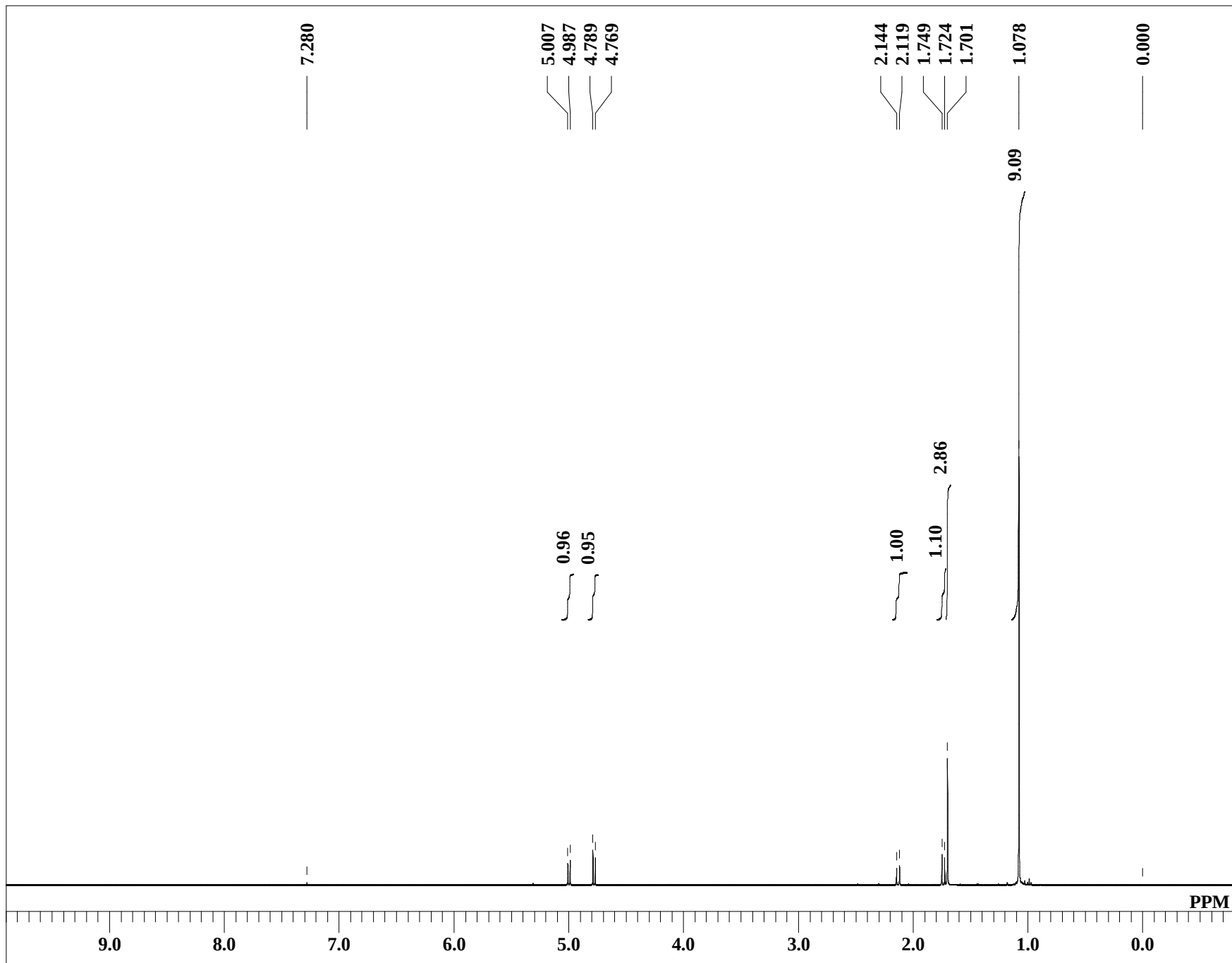
^1H NMR (600 MHz, CDCl_3) δ 5.11 (br-s, 1H), 4.65 (br, 1H), 4.32 (br, 1H), 3.48 (d, $J = 11.0$ Hz, 1H), 3.38 (d, $J = 11.0$ Hz, 1H), 3.19 (dd, $J = 14.1, 5.8$ Hz, 1H), 3.05 (dd, $J = 13.0, 6.9$ Hz, 1H), 1.62 (d, $J = 15.1$ Hz, 1H), 1.45 (s, 9H), 1.38 (d, $J = 15.1$ Hz, 1H), 1.26 (s, 3H), 1.04 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (150 MHz, CDCl_3) δ 157.5, 79.8, 73.7, 71.0, 52.4, 49.3, 36.3, 29.0, 28.3, 26.4, 25.7; HRFABMS calcd for $\text{C}_{13}\text{H}_{28}\text{NO}_4$ $[\text{M} + \text{H}]^+$ 262.2018, found: 262.2011.

References

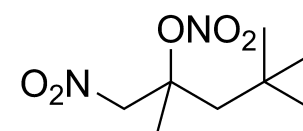
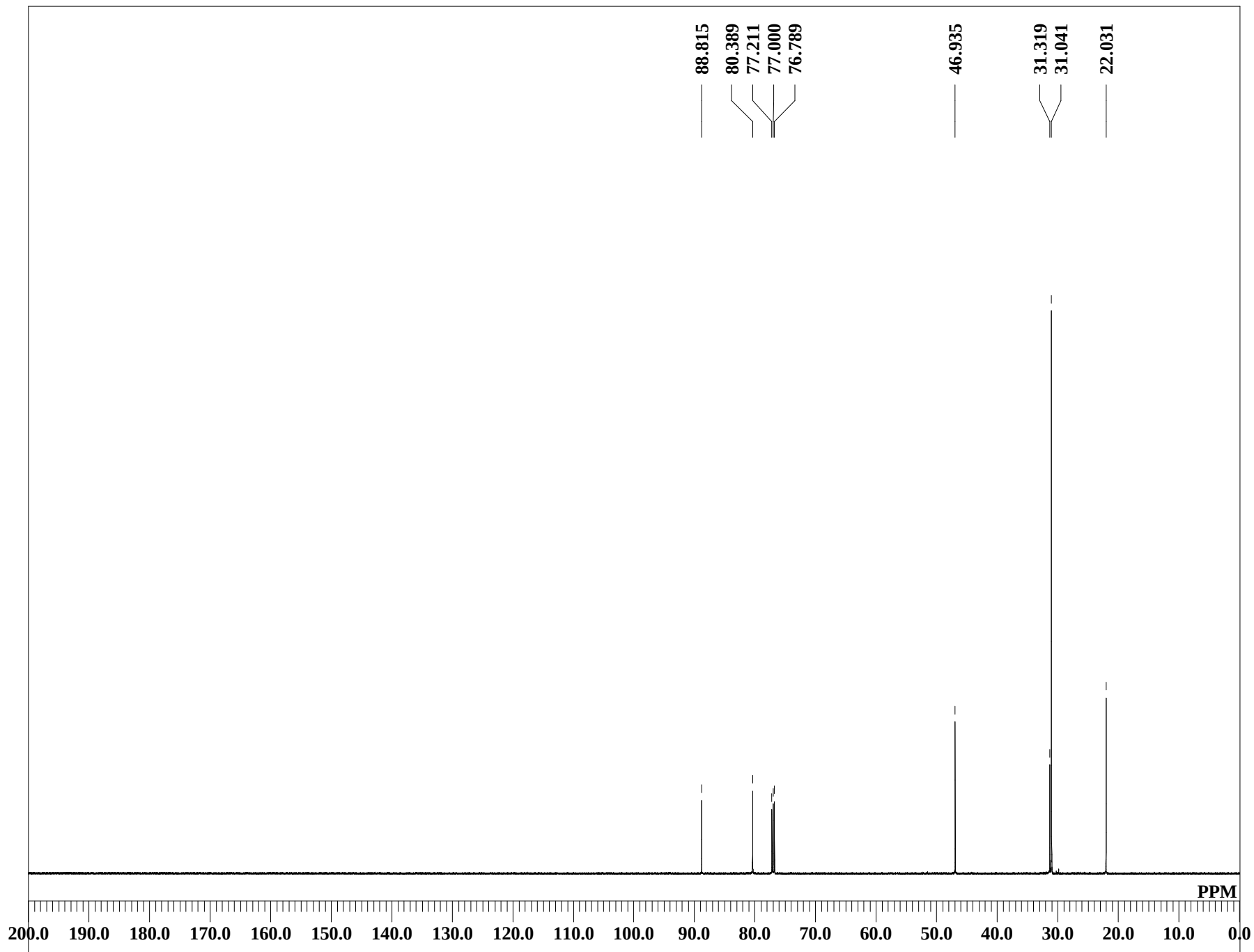
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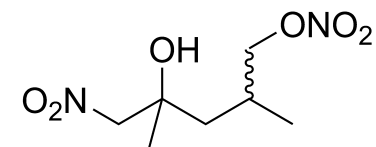
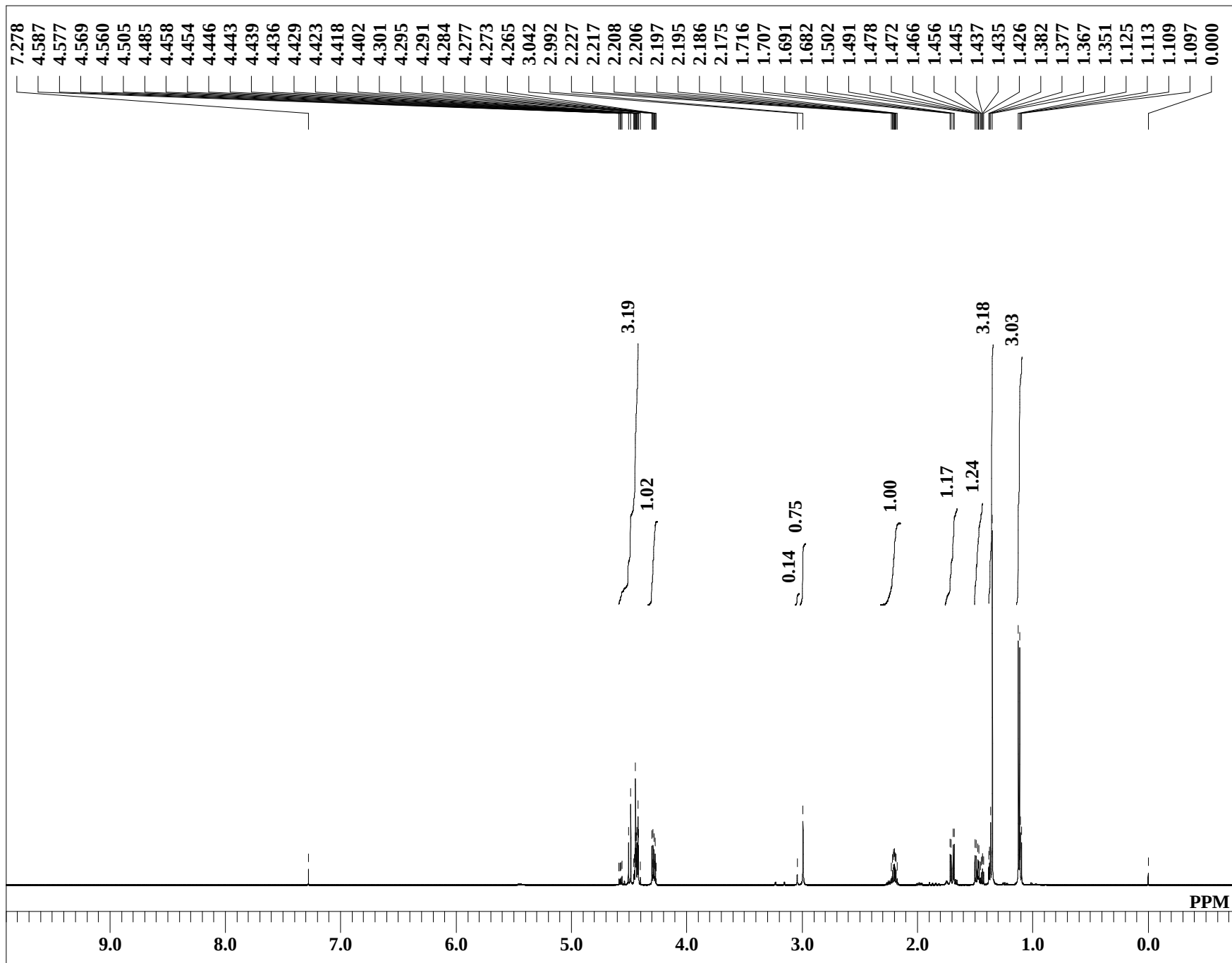




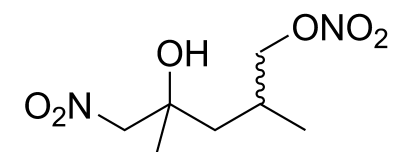
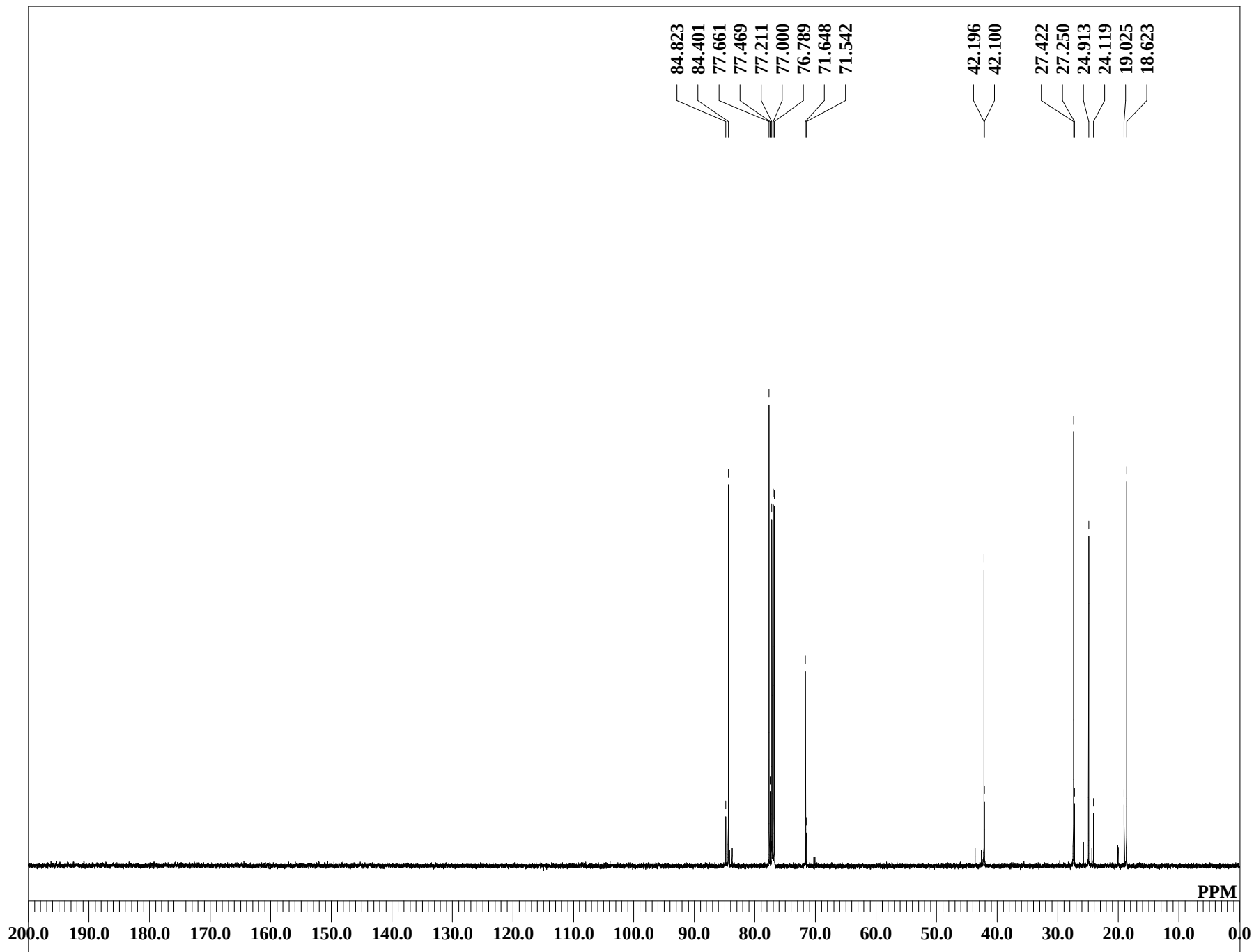
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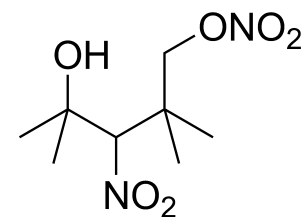
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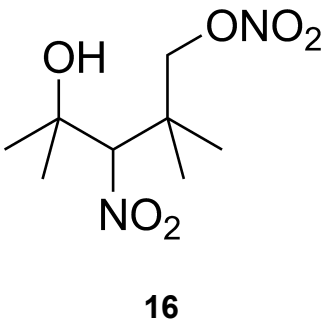


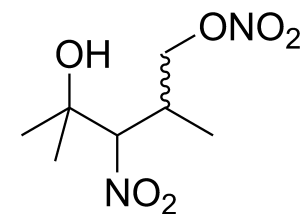
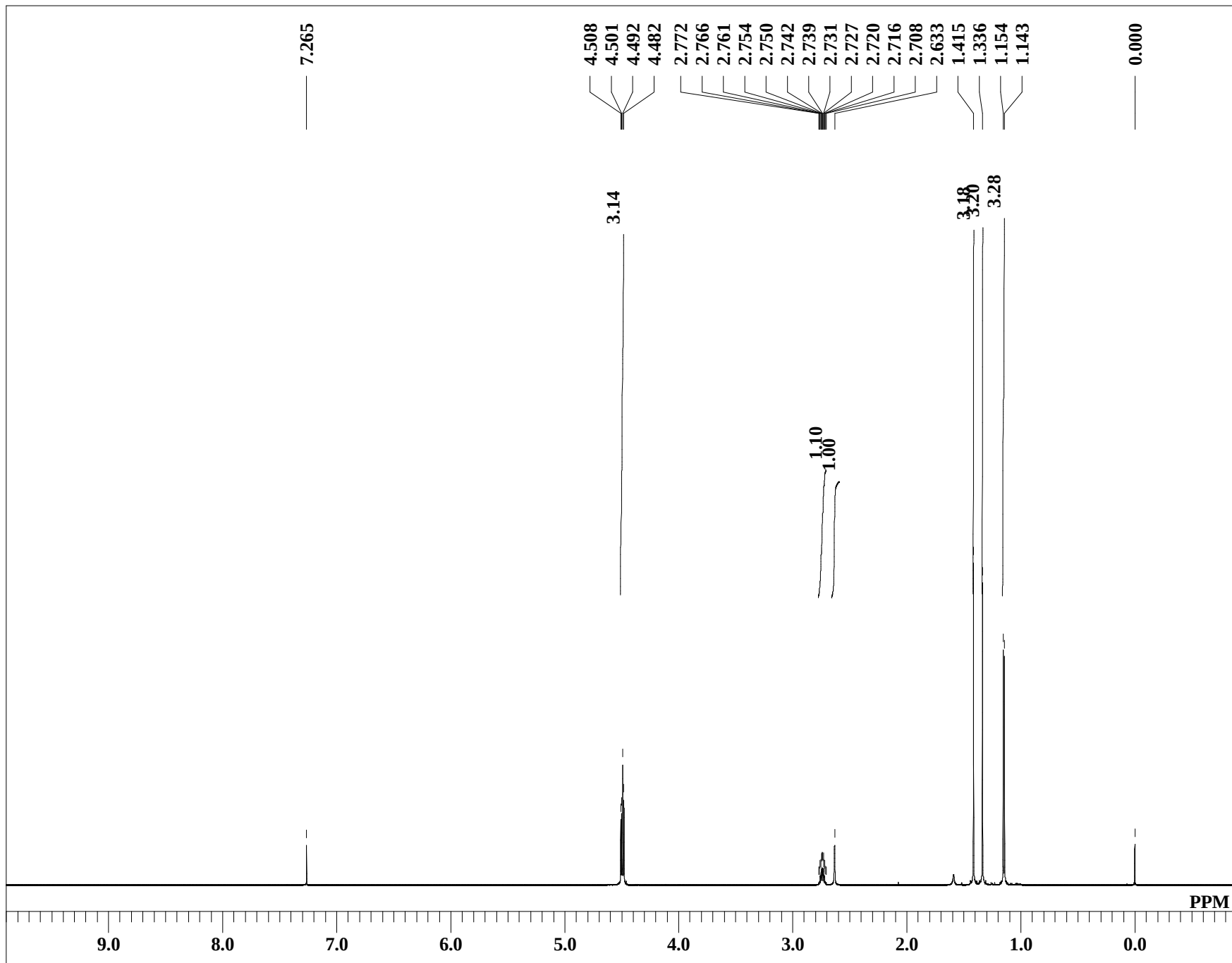
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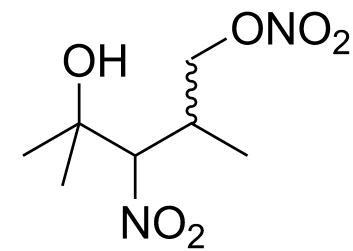
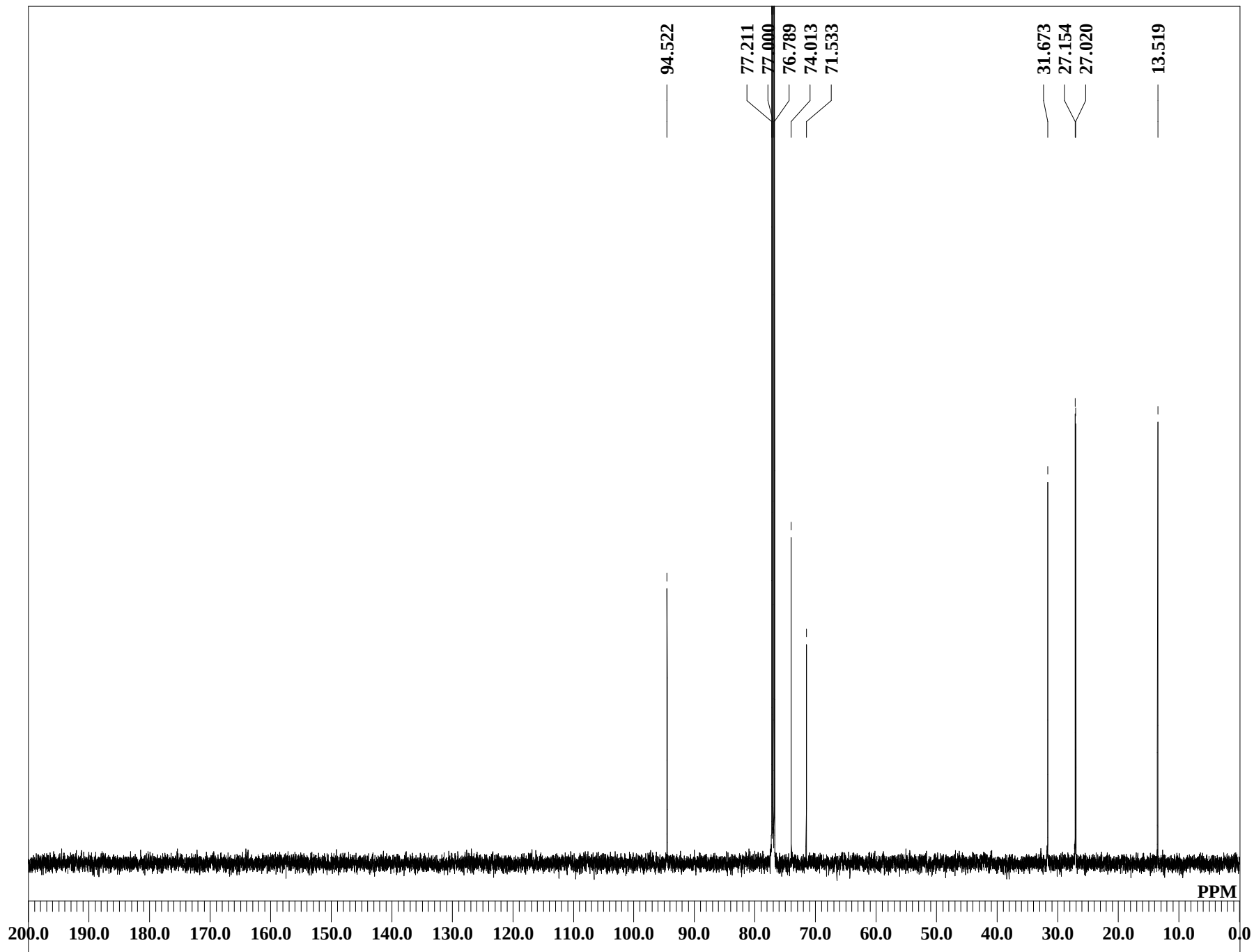
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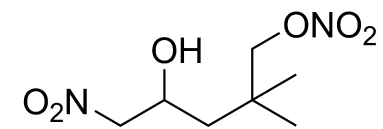
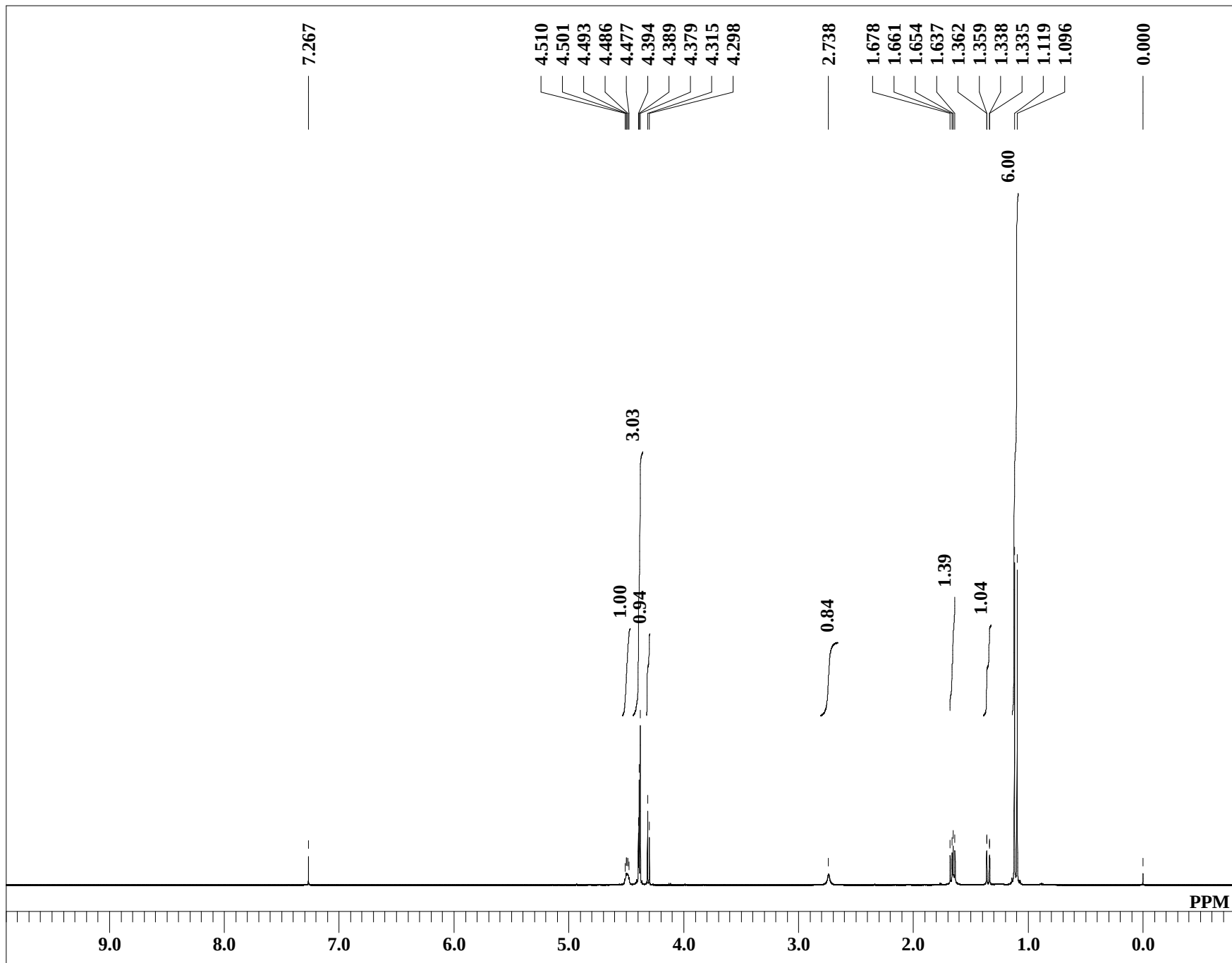




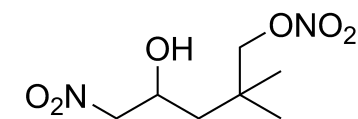
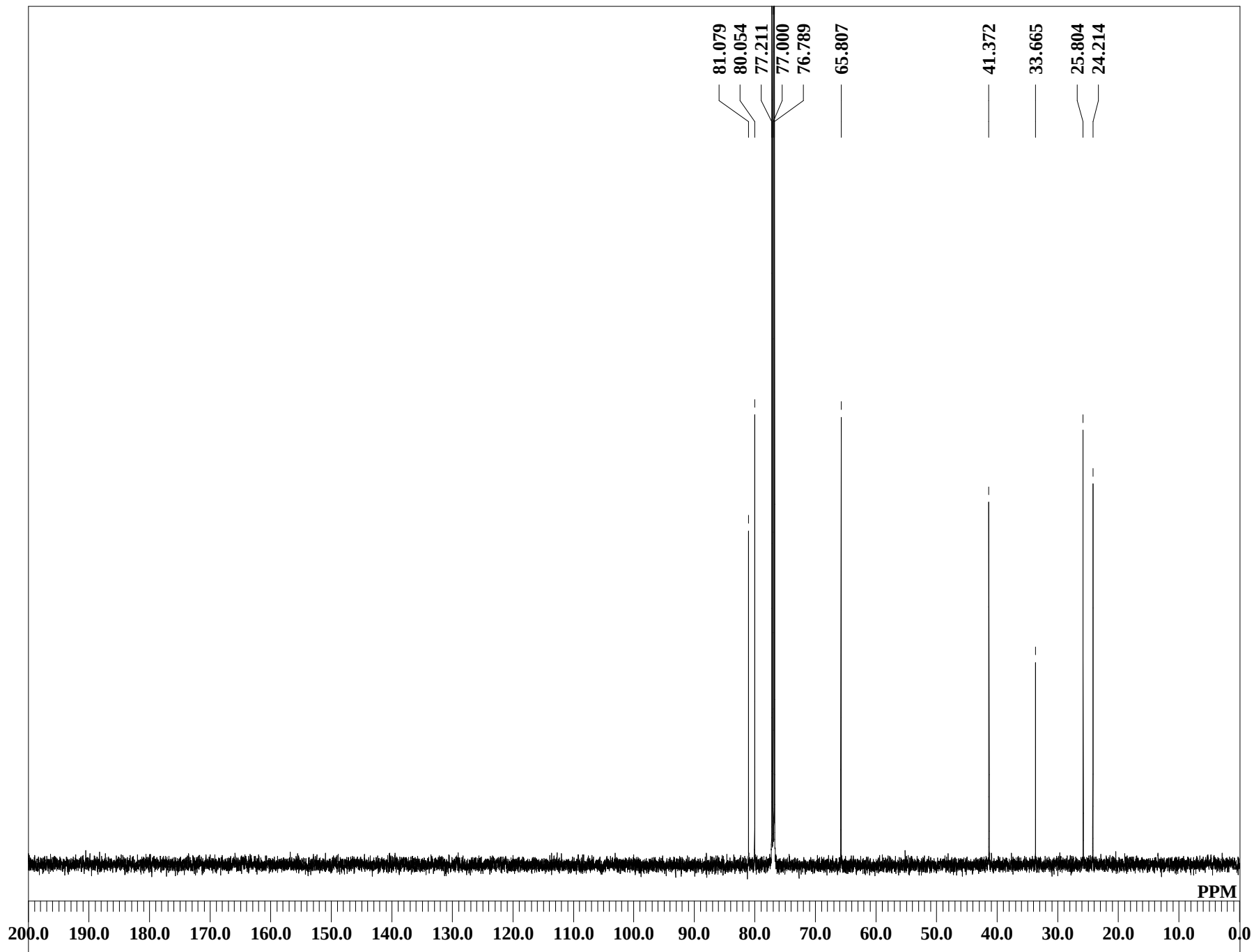
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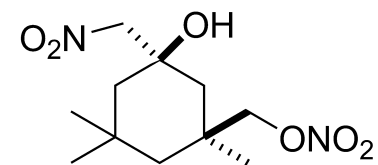
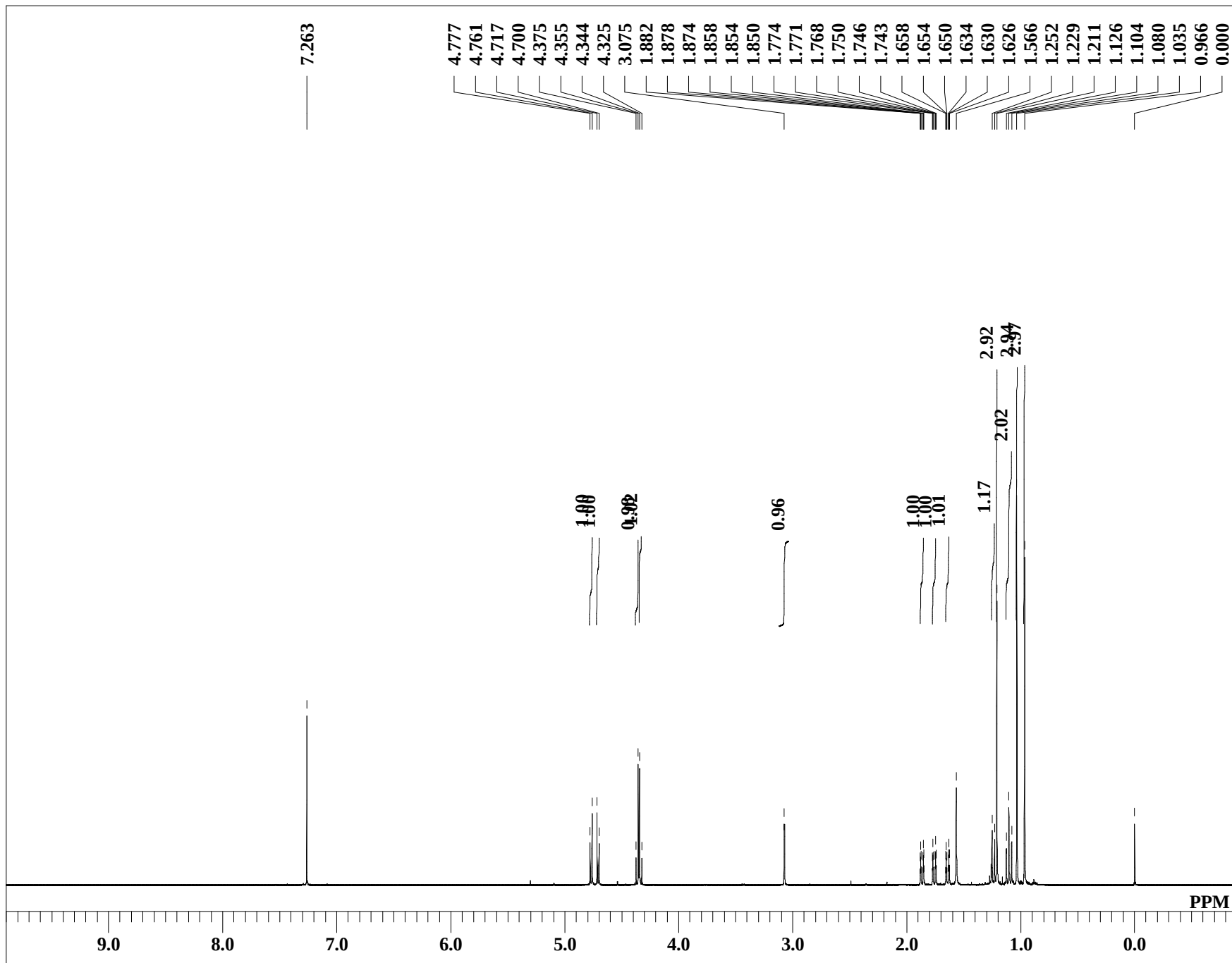
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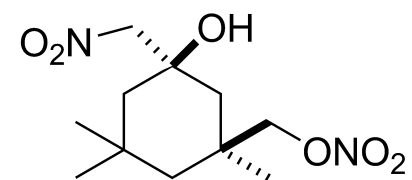
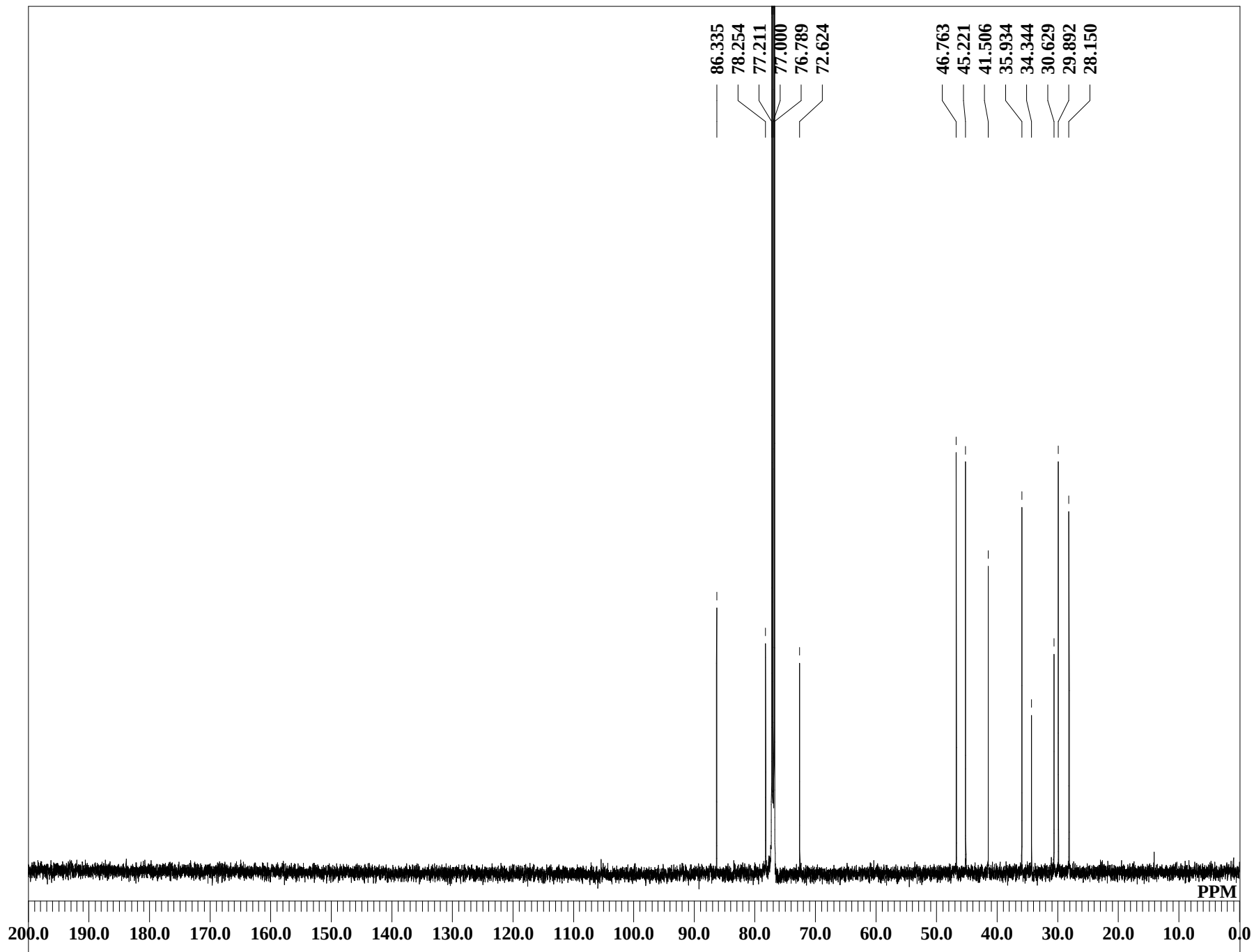
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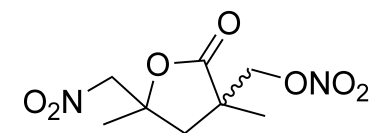
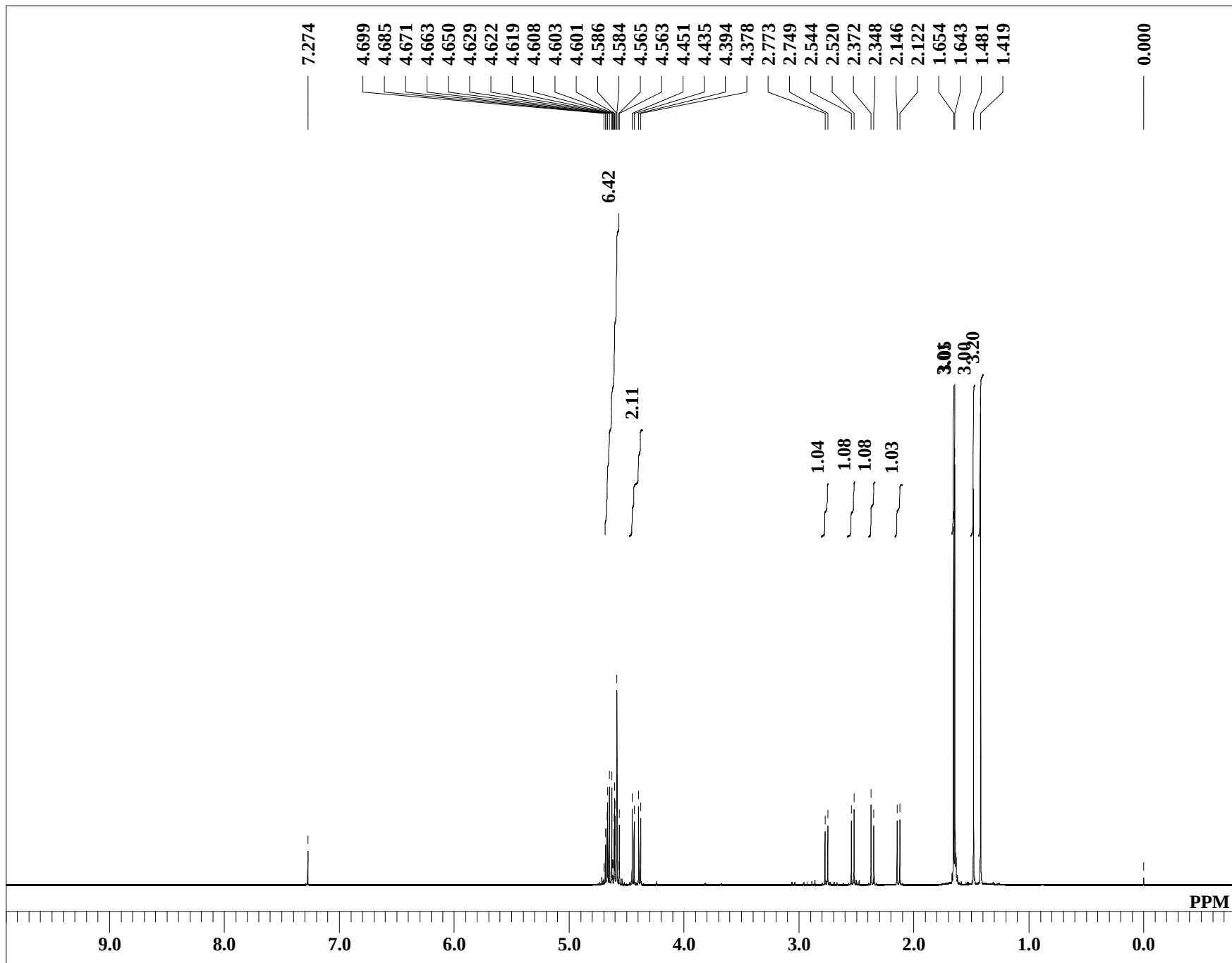
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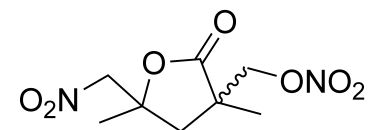
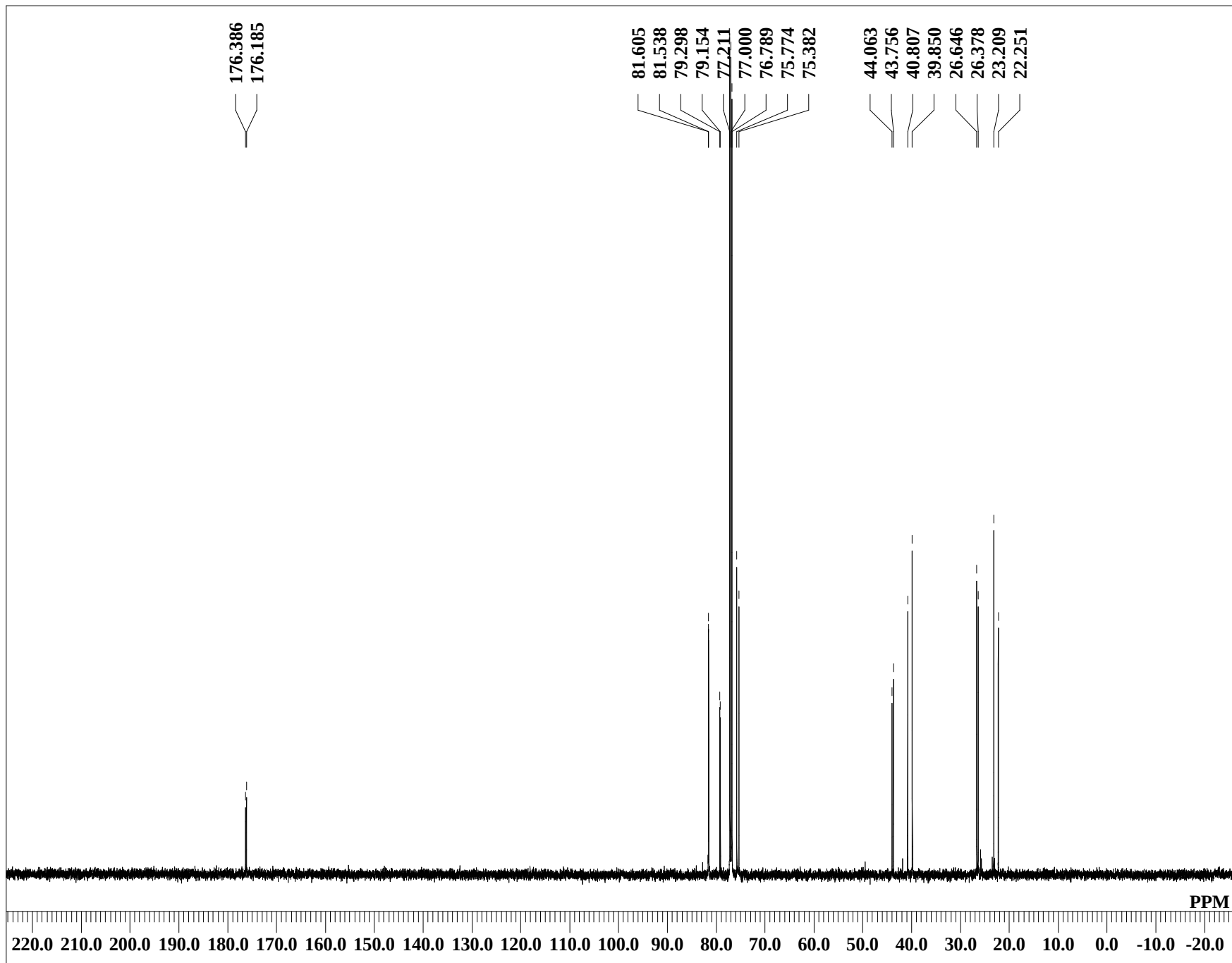
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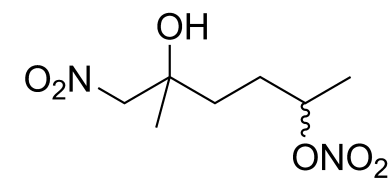
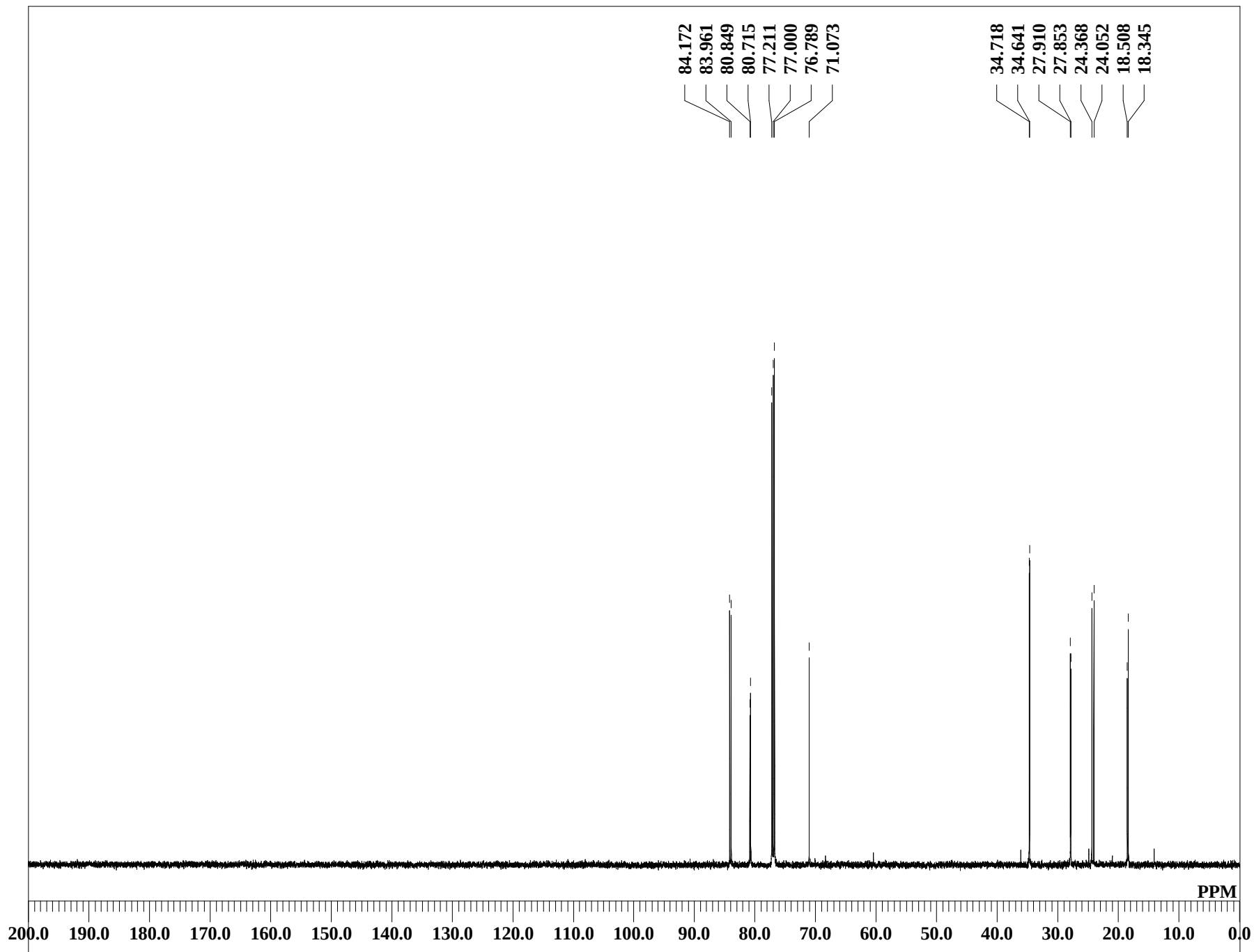
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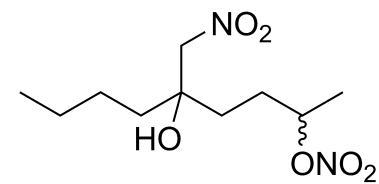
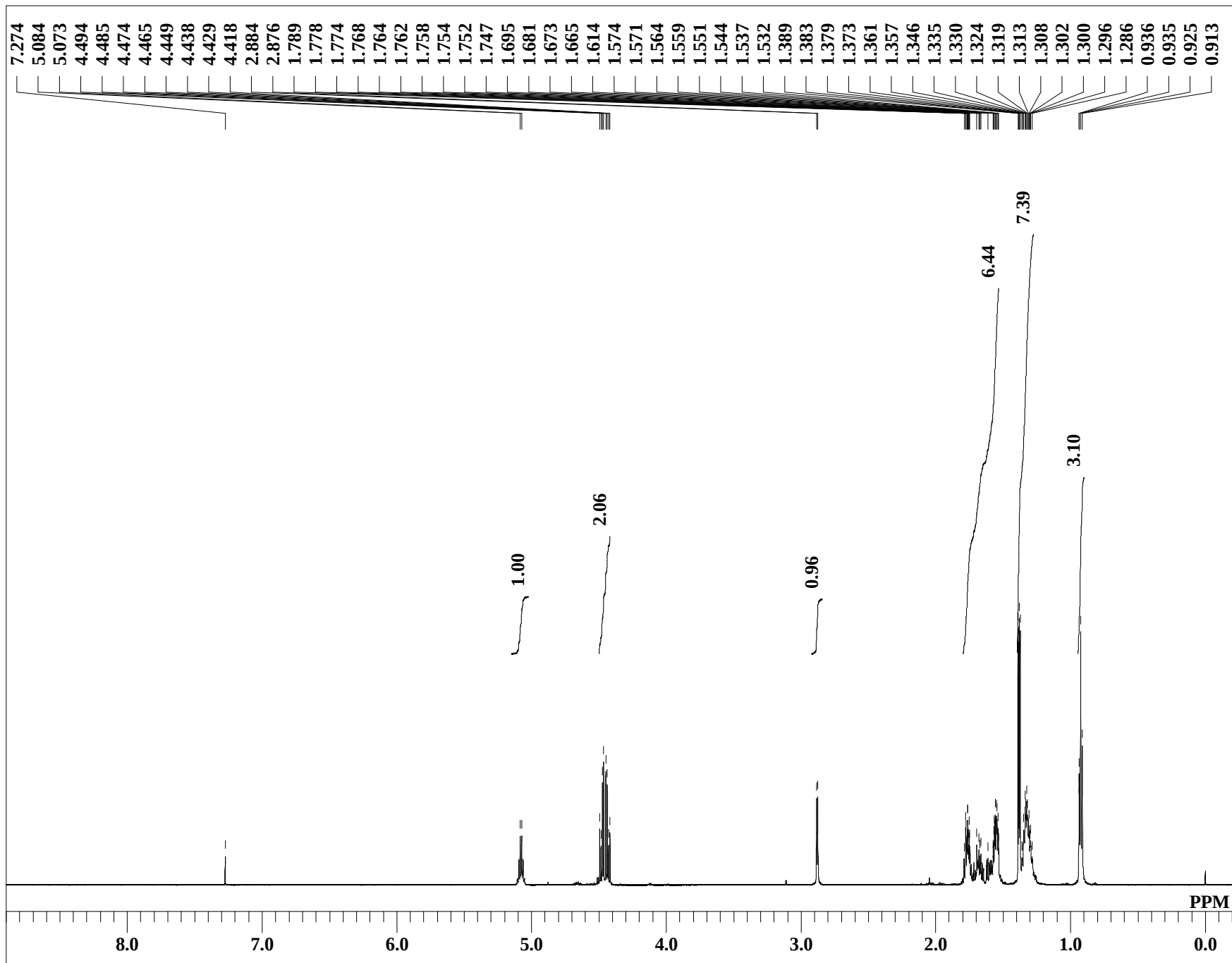
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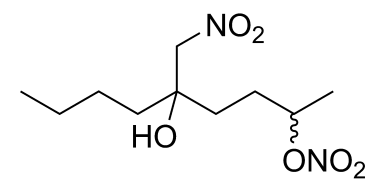
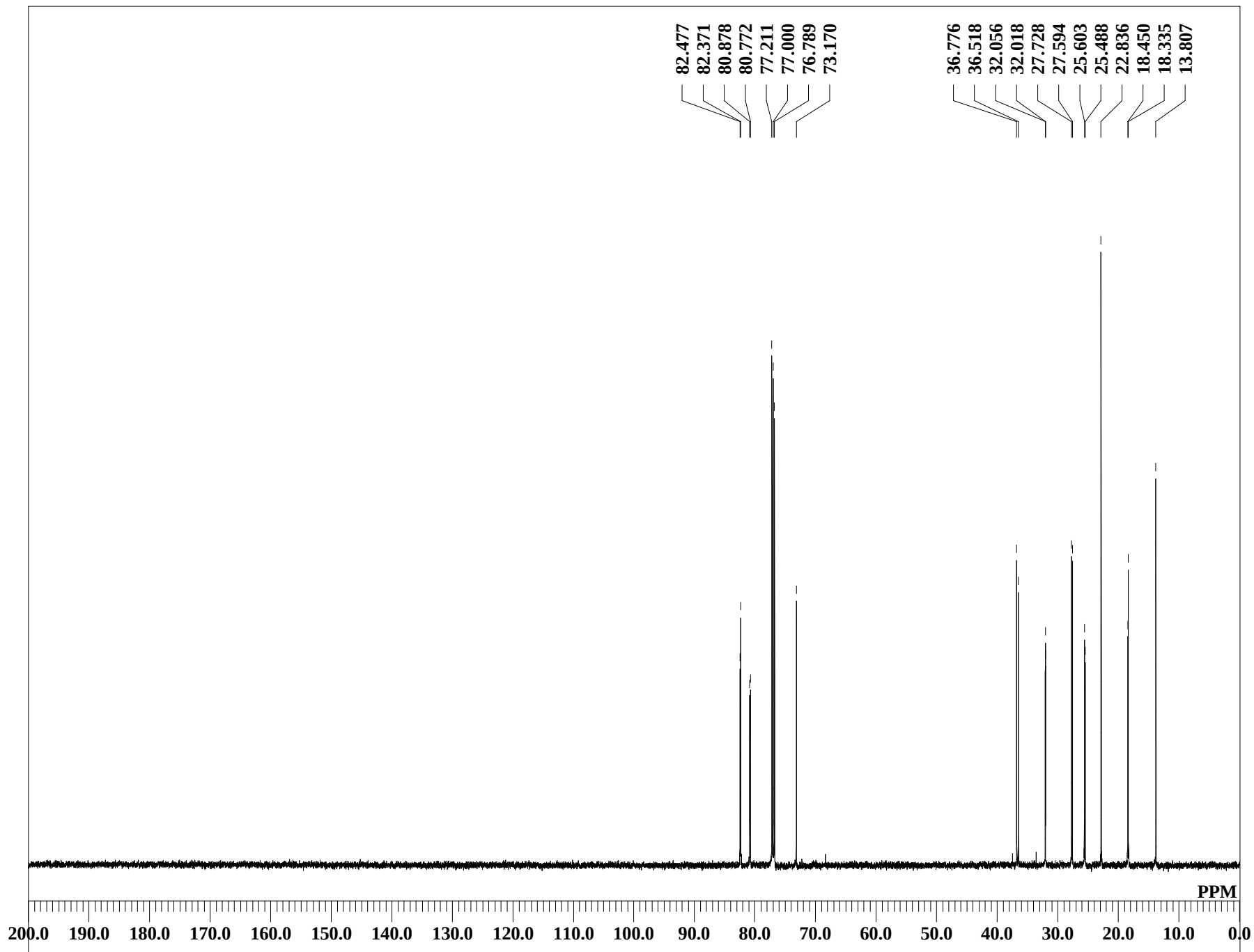
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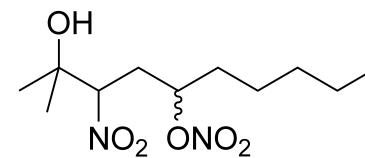
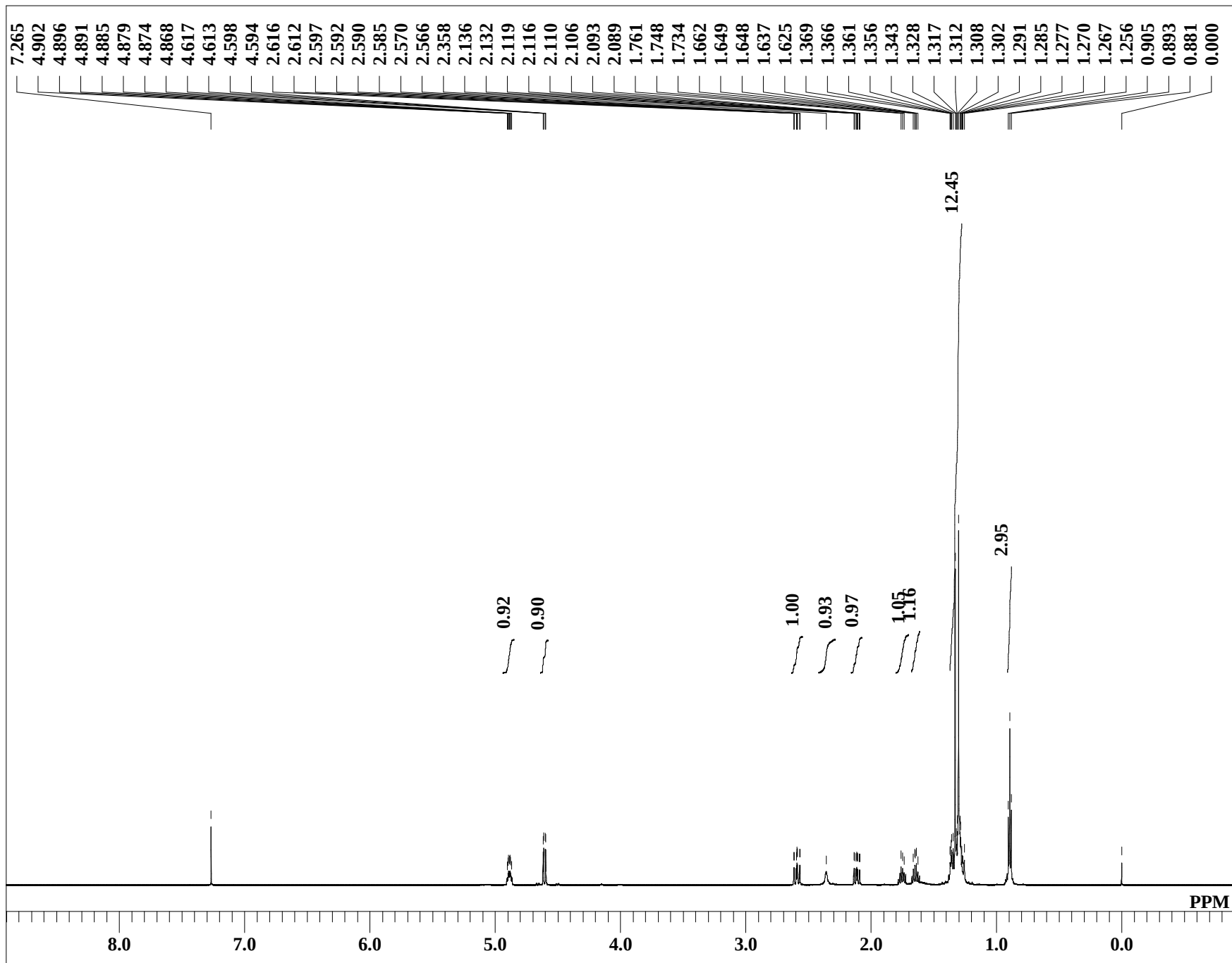
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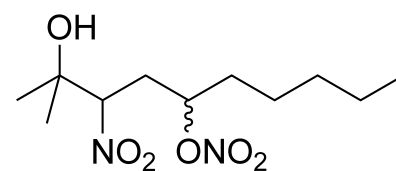
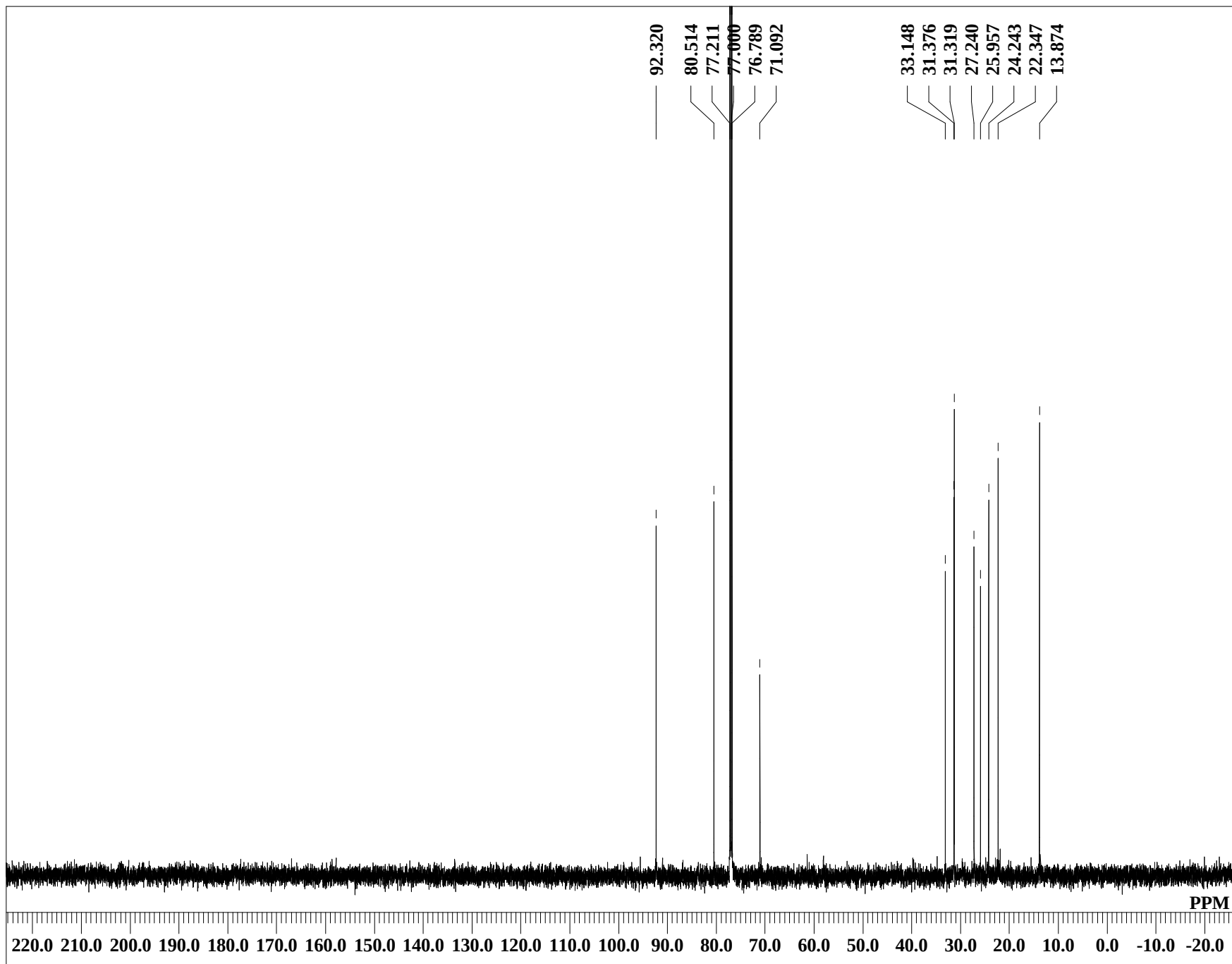
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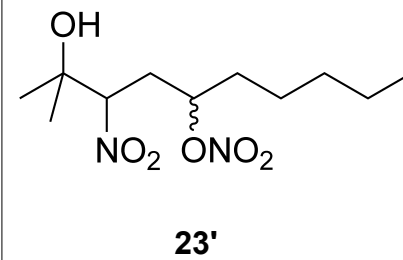
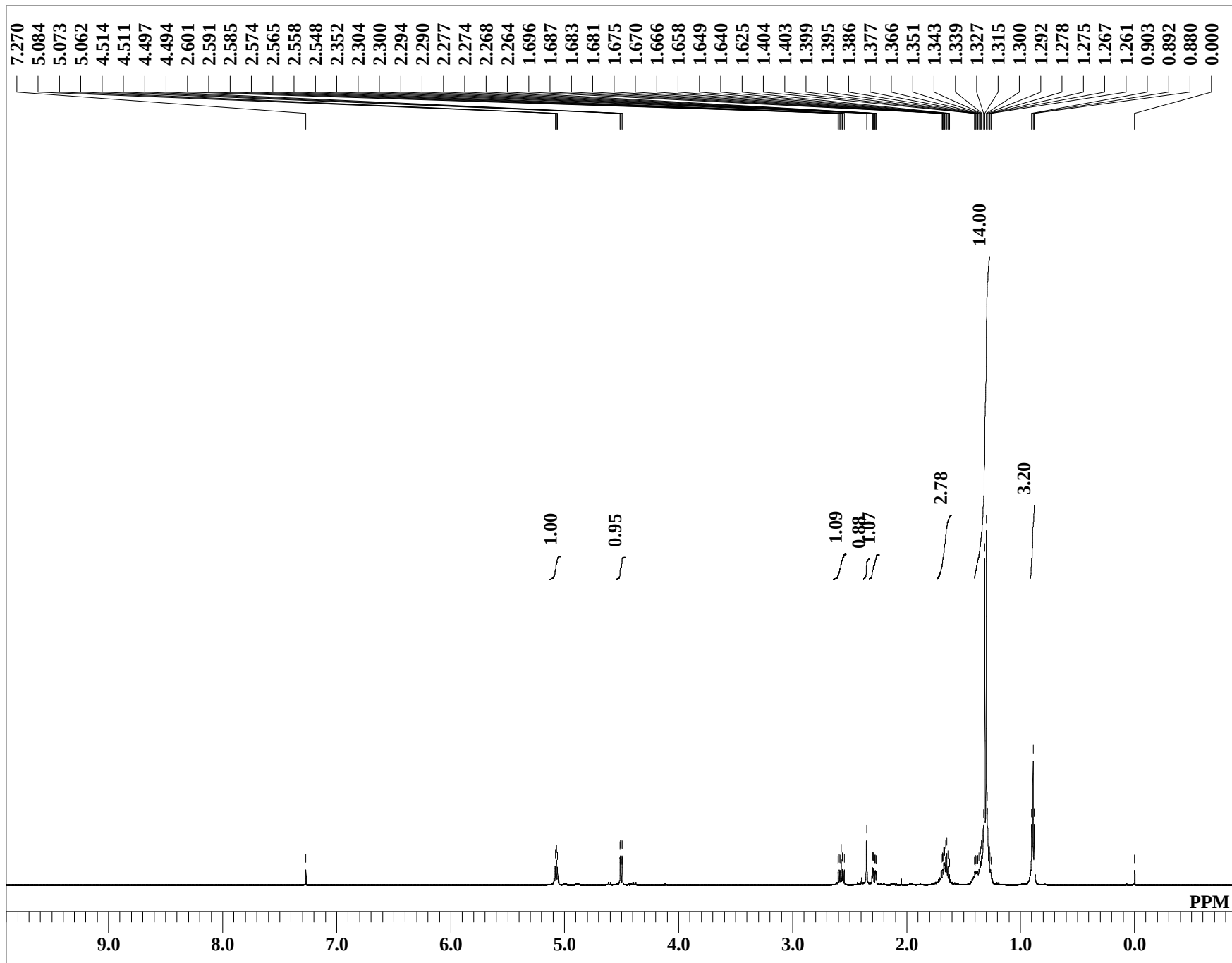
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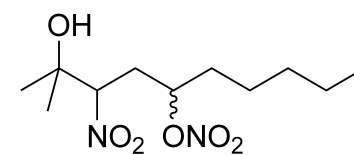
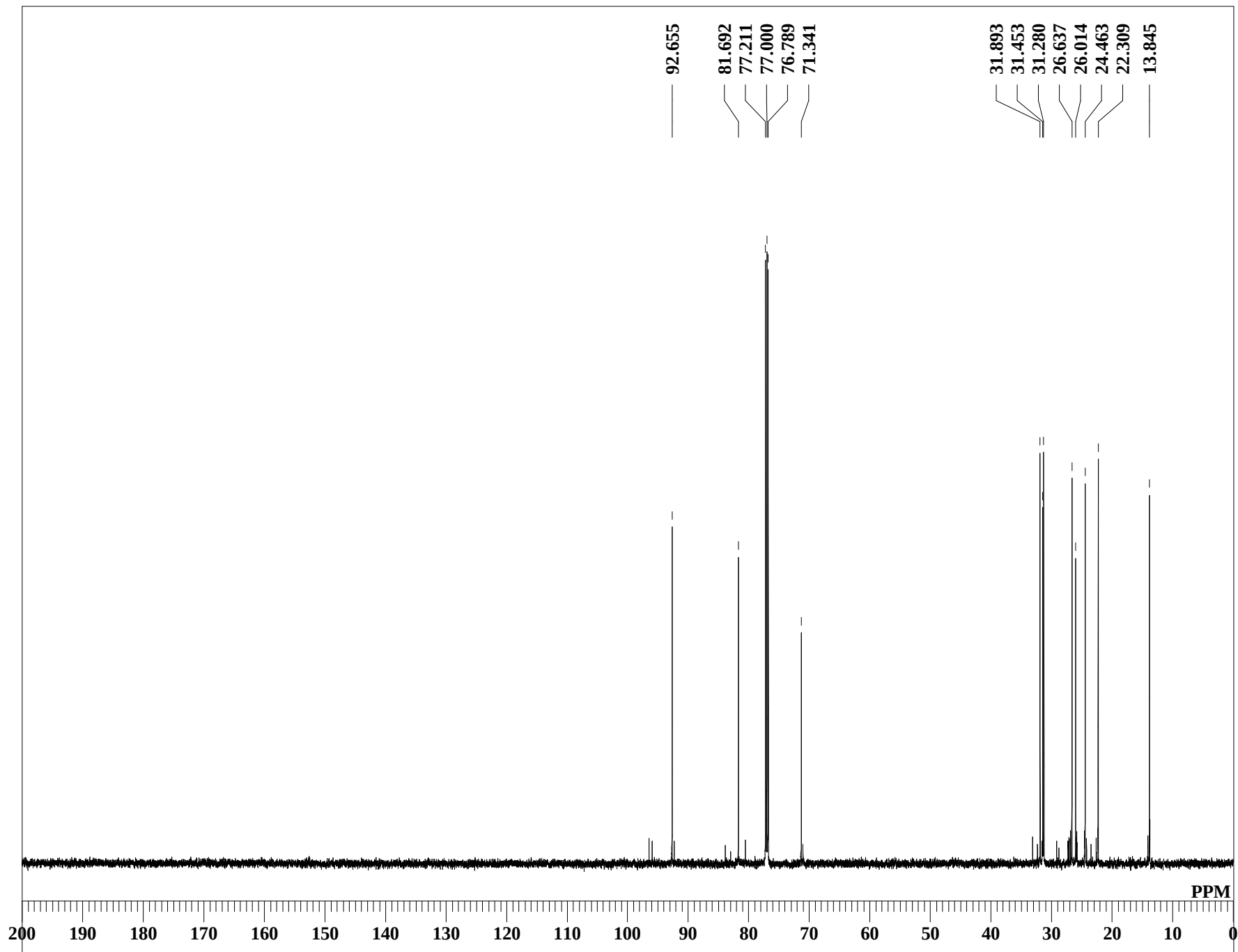


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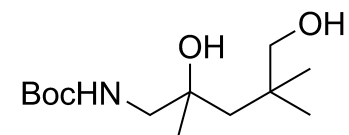
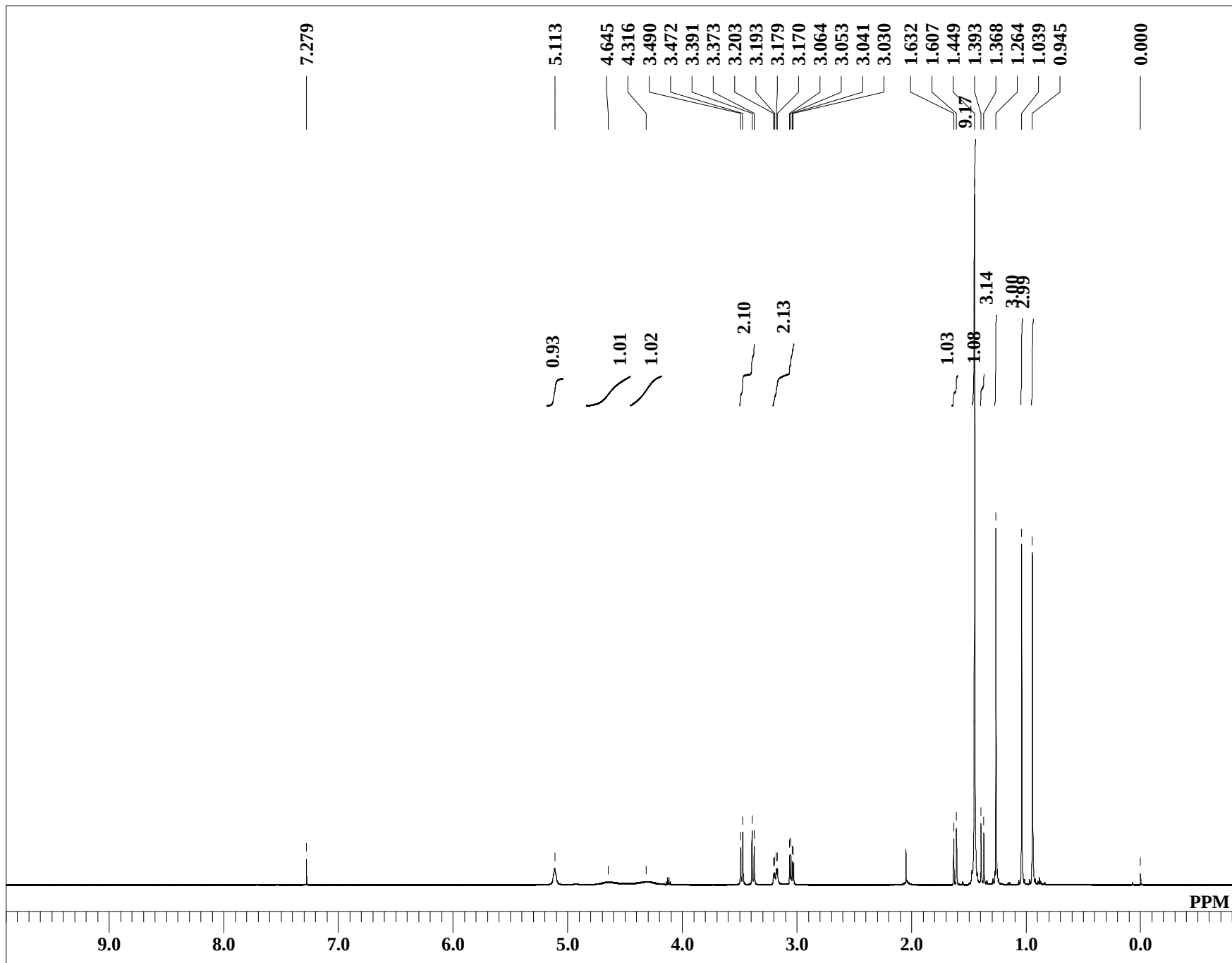


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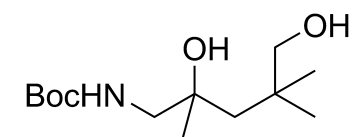
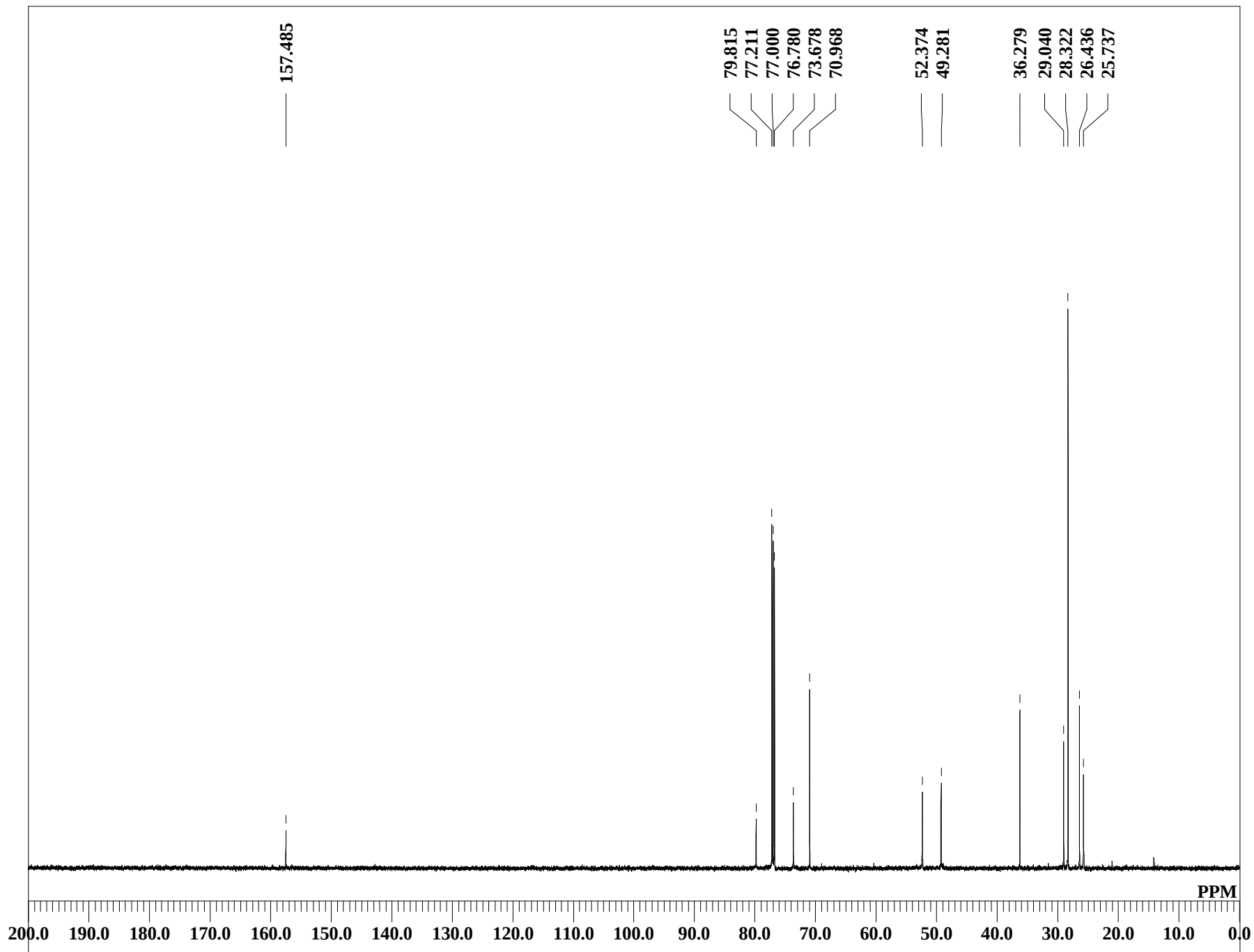




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