Electronic Supplementary Information

Pd-catalyzed cascade Heck-Saegusa reactions: direct synthesis of enals from aryl iodides and allyl alcohol

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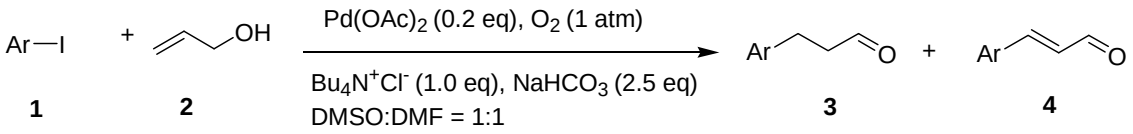
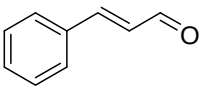
General Information: Commercial reagents were used as received, unless otherwise stated. Qingdao Haiyang Chemical HG/T2354-92 silica gel was used for chromatography, and Huanghai silica gel plates with fluorescence F_{254} were used for thin-layer chromatography (TLC) analysis. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AMX-400, and tetramethylsilane (TMS) was used as a reference. Data for ^{1}H are reported as follows: chemical shift (ppm), and multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Data for ^{13}C NMR are reported as ppm. Mass Spectra were recorded on a MAT-95 spectrometer. Melting points were tested on a melting point apparatus (SGW X-4) and are uncorrected.

General procedures for $Pd(OAc)_2$ catalyzed cascade Heck-Saegusa reactions (Table 2).



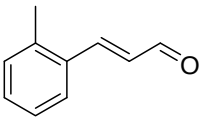
1 **2** **3** **4**

Standard reaction condition: **1** (0.49 mmol), allyl alcohol (0.74 mmol), $Pd(OAc)_2$ (0.098 mmol), tertrabutylammonium chloride (0.49 mmol), sodium bicarbonate (1.2 mmol), DMSO (0.5 mL) and DMF (0.5 mL) was stirred for 3-30 h at 60 ºC in an atmosphere of oxygen. The crude product was purified by column chromatography on silica gel to give the desired product **4**.



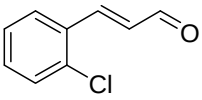
Cinnamaldehyde (4a) (Table 2, entry 1)

The title compound was prepared according to the general procedure described above, and the yield was 79%. yellow oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (dd, J = 8.0 and 16.0 Hz, 1H), 7.43-7.45 (m, 4H), 7.56-7.58 (m, 2H), 9.71 (d, J = 8.0 Hz, 1H,); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 128.5, 128.6, 129.1, 131.3, 134.0, 152.7, 193.6; HRMS (EI) m/z calcd for C_9H_8O (M^+) 132.0575, found 132.0573.



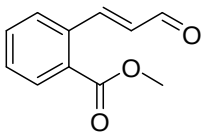
2-Methyl-cinnamaldehyde (4b) (Table 2, entry 2)

The title compound was prepared according to the general procedure described above, and the yield was 81%. oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.49 (s, 3H), 6.71 (dd, J = 8.0 and 16.0 Hz, 1H), 7.24-7.28 (m, 2H), 7.36 (m, 1H), 7.61 (d, J =7.2, 1H), 7.80 (d, J = 16.0 Hz, 1H), 9.75 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.7, 126.6, 126.8, 129.6, 131.0, 131.1, 132.8, 137.9, 150.3, 193.9; HRMS (EI) m/z calcd for $C_{10}H_{10}O$ (M^+) 146.0732, found 146.0733.



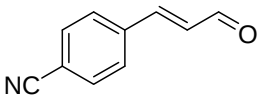
2-Chloro-cinnamaldehyde (4c) (Table 2, entry 3)

The title compound was prepared according to the general procedure described above, and the yield was 81%. Mp 49-51 ºC (lit. mp 51-53 ºC);[1] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.73 (dd, J = 7.6 and 16.0 Hz, 1H), 7.30-7.38 (m, 2H), 7.47 (d, J = 7.6 Hz, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.95 (d, J = 16.0 Hz, 1H), 9.77 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 127.3, 127.9, 130.3, 130.5, 132.0, 132.1, 135.2, 147.9, 193.5; HRMS (EI) m/z calcd for C_9H_7ClO (M^+) 166.0185, found 166.0180.



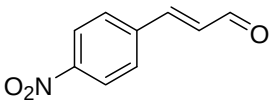
2-Acetyl-cinnamaldehyde (4d) (Table 2, entry 4)

The title compound was prepared according to the general procedure described above, and the yield was 80%. oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.95 (s, 3H), 6.64 (dd, J = 7.6 and 15.6 Hz, 1H), 7.52 (m, 1H), 7.61 (m, 1H), 7.67 (d, J = 8.0 Hz, 1H), 8.04 (d, J = 7.6 Hz, 1H), 8.46 (d, J = 15.6 Hz, 1H), 9.78 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 52.5, 126.5, 128.0, 129.5, 130.3, 131.1, 132.6, 135.9, 151.5, 167.0, 194.1; HRMS (EI) m/z calcd for $C_{11}H_{10}O_3$ (M^+) 190.0630, found 190.0614.



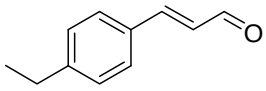
4-Cyano-cinnamaldehyde (4e) (Table l, entry 5)

The title compound was prepared according to the general procedure described above, and the yield was 68%. Mp 128-130 ºC (lit. mp 128-129 ºC);[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.79 (dd, J =7.6 and 16.0 Hz, 1H), 7.51 (d, J = 16.0 Hz, 1H), 7.68 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.0 Hz, 2H), 9.76 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 114.2, 118.1, 128.8, 131.2, 132.8, 138.2, 149.5, 192.9; HRMS (EI) m/z calcd for $C_{10}H_7NO$ (M^+) 157.0528, found 157.0522.



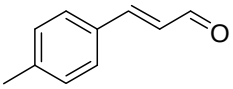
4-Nitro-cinnamaldehyde (4f) (Table 2, entry 6)

The title compound was prepared according to the general procedure described above, and the yield was 60%. Mp 138-139 ºC (lit. mp 139-140 ºC);[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.84 (dd, J = 7.2 and 16.0 Hz, 1H), 7.55 (d, J = 16.0 Hz, 1H), 7.75 (d, J = 8.8 Hz, 2H), 8.31 (d, J = 8.8 Hz, 2H), 9.79 (d, J = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 124.3, 129.0, 131.7, 139.9, 148.8, 149.0, 192.8; HRMS (EI) m/z calcd for $C_9H_7NO_3$ (M^+) 177.0426, found 177.0427.



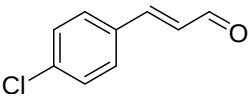
4-Ethyl-cinnamaldehyde (4g) (Table 2, entry 7)

The title compound was prepared according to the general procedure described above, and the yield was 72%. Mp 126-128ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.28 (t, J = 7.6 Hz, 3H), 2.73 (q, J = 7.6 Hz, 2H), 6.73 (dd, J = 7.6 and 16.0 Hz, 1H), 7.28 (d, J = 8.0 Hz, 2H), 7.45-7.51 (m, 3H), 9.70 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 15.2, 28.9, 30.9, 127.8, 128.7, 131.5, 148.2, 153.0, 193.8; HRMS (EI) m/z calcd for C_9H_8O (M^+) 160.0888, found 160.0891.



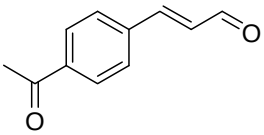
4-Methyl-cinnamaldehyde (4h) (Table 2, entry 8)

The title compound was prepared according to the general procedure described above, and the yield was 81%. Mp 45-47 ºC (lit. mp 42-43 ºC);[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.38 (s, 3H), 6.70 (dd, J = 7.6 and 16.0 Hz, 1H), 7.23 (d, J = 7.6 Hz, 2H), 7.41-7.46 (m, 3H), 9.68 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 127.7, 128.5, 129.8, 131.3, 141.9, 152.9, 193.7; HRMS (EI) m/z calcd for $C_{11}H_{12}O$ (M^+) 146.0732, found 146.0735.



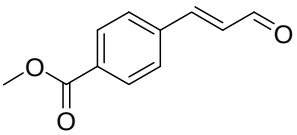
4-Chloro-cinnamaldehyde (4i) (Table 2, entry 9)

The title compound was prepared according to the general procedure described above, and the yield was 62%. Mp 59-60 ºC (lit. mp 59-60 ºC);[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.72 (dd, J = 7.6 and 16.0 Hz, 1H), 7.40-7.45 (m, 3H), 7.50 (d, J = 8.4 Hz, 2H), 9.71 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 129.0, 129.4, 129.6, 132.5, 137.3, 151.0, 193.3; HRMS (EI) m/z calcd for C_9H_7ClO (M^+) 166.0185, found 166.0189.



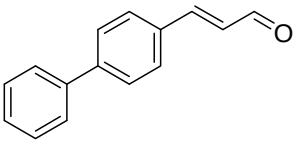
4-Acetyl-cinnamaldehyde (4j) (Table 2, entry 10)

The title compound was prepared according to the general procedure described above, and the yield was 67%. Mp 49-51 ºC (lit. mp 49-50 ºC);[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.64 (s, 3H), 6.82 (dd, J = 7.6 and 16.0 Hz, 1H), 7.55 (d, J = 16.0 Hz, 1H), 7.68 (d, J = 8.4 Hz, 2H), 8.03 (d, J = 8.4 Hz, 2H), 9.76 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 26.7, 128.5, 128.9, 130.4, 138.2, 138.7, 150.7, 193.3, 197.2; HRMS (EI) m/z calcd for C_9H_8O (M^+) 174.0681, found 174.0683.



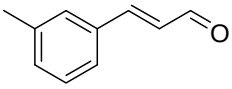
4-Methoxycarbonyl-cinnamaldehyde (4k) (Table 2, entry 11)

The title compound was prepared according to the general procedure described above, and the yield was 80%. Mp 100-102 ºC (lit. mp 102-104);[3] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.95 (s, 3H), 6.82 (dd, J = 7.6 and 16.0 Hz, 1H), 7.53 (d, J = 16.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 2H), 8.11 (d, J = 8.0 Hz, 2H), 9.77 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 52.4, 128.3, 130.2, 130.3, 132.2, 138.1, 150.9, 166.3, 193.4; HRMS (EI) m/z calcd for $C_{11}H_{10}O_3$ (M^+) 190.0630, found 190.0629.



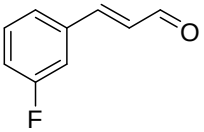
4-Phenyl-cinnamaldehyde (4l) (Table 2, entry 12)

The title compound was prepared according to the general procedure described above, and the yield was 80%. Mp 121-123 ºC (lit. mp 121-122 ºC);[2] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.80 (dd, J = 7.6 and 16.0 Hz, 1H), 7.43 (m, 1H), 7.47-7.54 (m, 3H), 7.63-7.69 (m, 6H), 9.75 (d, J = 7.6 Hz, 1H,); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 127.1, 127.7, 128.1, 128.4, 129.0, 129.1, 133.0, 139.9, 144.0, 152.3, 193.6; HRMS (EI) m/z calcd for $C_{15}H_{12}O$ (M^+) 208.0888, found 208.0890.



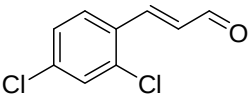
3-Methyl-cinnamaldehyde (4m) (Table p, entry 13)

The title compound was prepared according to the general procedure described above, and the yield was 78%. oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.40 (s, 3H), 6.74 (dd, J = 7.6 and 16 Hz, 1H), 7.27 (d, J = 8.0 Hz, 1H), 7.30-7.38 (m, 3H), 7.47 (d, J = 16.0 Hz, 1H), 9.70 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.3, 125.7, 128.4, 129.0, 129.1, 132.1, 134.0, 138.8, 153.1, 193.8; HRMS (EI) m/z calcd for $C_{10}H_{10}O$ (M^+) 146.0732, found 146.0728.



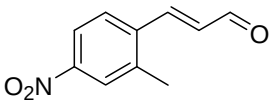
3-Fluoro-cinnamaldehyde (4n) (Table l, entry 14)

The title compound was prepared according to the general procedure described above, and the yield was 59%. oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.74 (dd, J =7.6 and 16.0 Hz, 1H), 7.17 (m, 1H), 7.28 (m, 1H), 7.36 (d, J = 7.6 Hz, 1H), 7.39-7.47 (m, 2H), 9.73 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 114.8 (d, J = 21.9 Hz), 118.2 (d, J = 21.3 Hz), 124.4 (d, J = 2.8 Hz), 129.6, 130.7 (d, J = 8.2 Hz), 136.2 (d, J = 7.6 Hz), 151.0 (d, J = 2.5 Hz), 164.2 (d, J = 246.0 Hz), 193.3; HRMS (EI) m/z calcd for C_9H_7FO (M^+) 150.0481, found 150.0479.



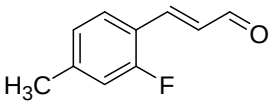
3-(2,4-Dichloro)-cinnamaldehyde (4o) (Table 2, entry 15)

The title compound was prepared according to the general procedure described above, and the yield was 77%. M p 102-104 ºC (lit. mp 105-107 ºC);[3] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.69 (dd, J = 7.6 and 16.0 Hz, 1H), 7.32 (dd, J = 2.0 and 8.4 Hz, 1H), 7.47 (d, J = 2.0 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 16.0 Hz, 1H), 9.76 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 127.8, 128.6, 130.2, 130.7, 130.8, 135.7, 137.4, 146.5, 193.2; HRMS (EI) m/z calcd for $C_9H_6Cl_2O$ (M^+) 199.9796, found 199.9803.



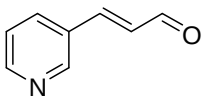
2-Methyl-4-nitro-cinnamaldehyde (4p) (Table 2, entry 16)

The title compound was prepared according to the general procedure described above, and the yield was 58%. M p 108-104 ºC (lit. mp 106-108 ºC);[4] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.59 (s, 3H), 6.77 (dd, J = 7.6 and 16.0 Hz, 1H), 7.71-7.78 (m, 2H), 8.10-8.13 (m, 2H), 9.81 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.9, 121.6, 125.7, 127.7, 132.6, 139.1, 139.2, 146.8, 148.6, 193.0; HRMS (EI) m/z calcd for $C_{10}H_9NO_3$ (M^+) 191.0582, found 191.0583.



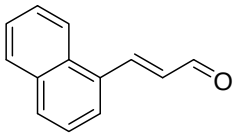
2-Fluoro-4-Methyl-cinnamaldehyde (4q) (Table 2, entry 17)

The title compound was prepared according to the general procedure described above, and the yield was 67%. Mp 53-55 ºC; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.30 (d, J = 1.6 Hz, 3H), 6.67 (dd, J = 7.6 and 16.0 Hz, 1H), 7.18-7.24 (m, 3H), 7.41 (d, J = 16 Hz, 1H), 9.68 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.7 (d, J = 3.4 Hz), 114.4 (d, J = 22.8 Hz), 124.3 (d, J = 3.2 Hz), 128.7, 128.7 (d, J = 17.4 Hz), 132.1 (d, J = 5.3 Hz), 133.7 (d, J = 7.6 Hz), 151.4 (d, J = 2.5 Hz), 162.7 (d, J = 244.7 Hz), 193.4; HRMS (EI) m/z calcd for $C_{10}H_9FO$ $(M)^+$ 164.0637, found 164.0638.



(*E*)-3-(pyridin-3-yl)acrylaldehyde (4r) (Table 2, entry 18)

The title compound was prepared according to the general procedure described above, and the yield was 57%. Mp 50-52 ºC (lit. mp 51-53 ºC);[5] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.81 (dd, J = 7.6 and 16.0 Hz, 1H), 7.40 (dd, J = 4.0 and 8.0 Hz, 1H), 7.51 (d, J = 16.0 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 8.66 (dd, J = 1.6 and 4.8 Hz, 1H), 8.79 (d, J = 1.6 Hz, 1H,), 9.75 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 123.9, 129.8, 130.2, 134.4, 148.5, 150.1, 151.9, 193.0; HRMS (EI) m/z calcd for C_8H_7NO $(M)^+$ 133.0528, found 133.0515.

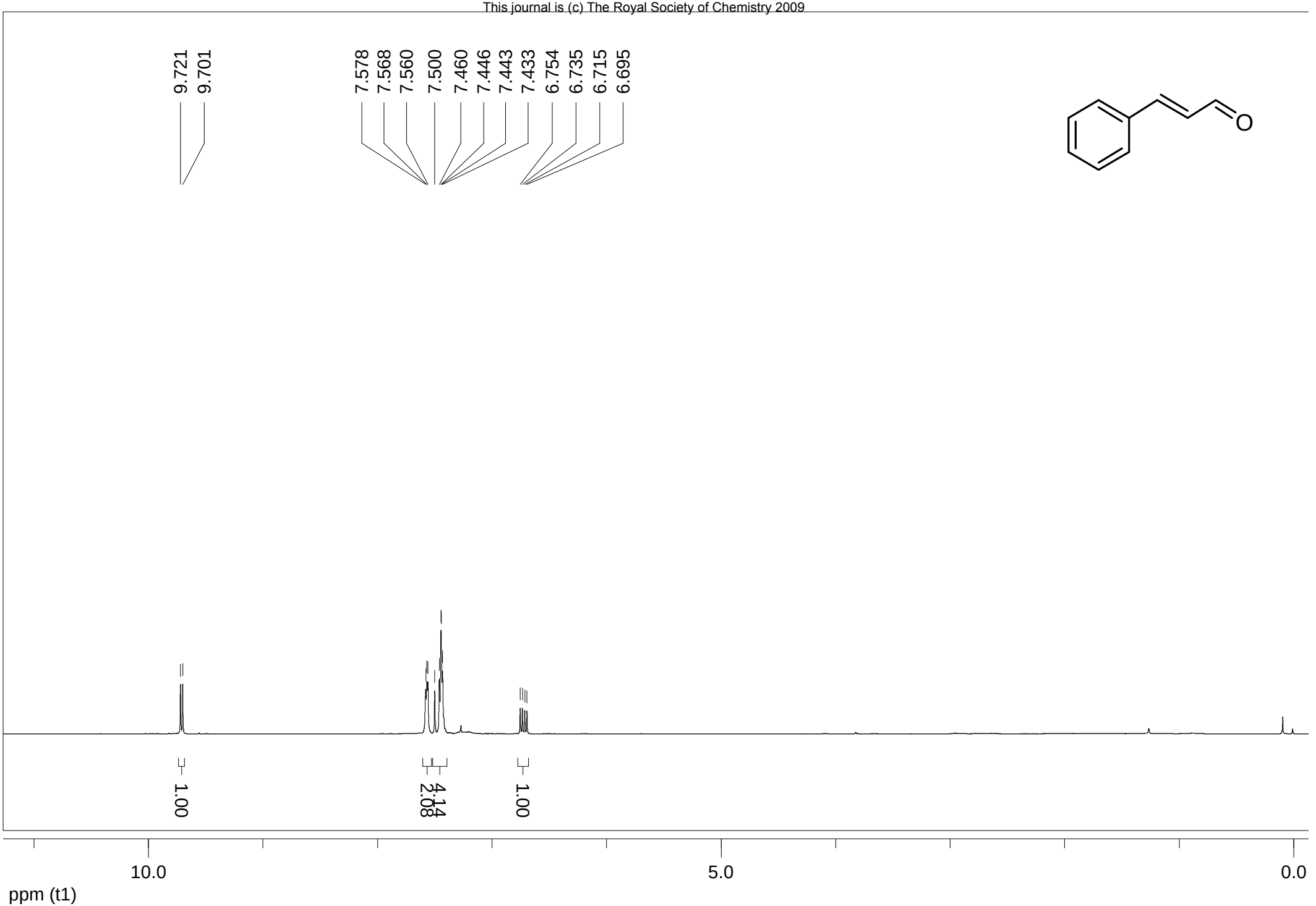


(*E*)-3-(naphthalen-1-yl)acrylaldehyde (4s) (Table 2, entry 19)

The title compound was prepared according to the general procedure described above, and the yield was 82%. Mp 122-124 ºC (lit. mp 123-124 ºC);[4] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.89 (dd, J = 7.6 and 16.0 Hz, 1H), 7.52-7.66 (m, 3H), 7.85 (d, J = 7.2 Hz, 1H), 7.94 (d, J = 8.4, 1H), 7.98 (d, J = 8.4, 1H), 8.22 (d, J = 8.4, 1H), 8.37 (d, J = 16.0, 1H), 9.89 (d, J = 7.6, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 122.8, 125.5, 125.7, 126.4, 127.3, 129.0, 130.9, 130.9, 131.2, 131.6, 133.8, 149.3, 193.7; HRMS (EI) m/z calcd for C_9H_8O $(M)^+$ 182.0732, found 182.0729.

References

1. G. Cignarella, E. Occelli and E. Testa, *J. Med. Chem.*, 1965, **8**, 326.
2. G. Battistuzzi, S. Cacchi and G. Fabrizi, *Org. Lett.*, 2003, **5**, 777.
3. J. Zhu, J. Liu, R. -Q. Ma, H. -X. Xie, J. Li, H. –L. Jiang and W. Wang, *Adv. Synth. Catal.*, 2009, **351**, 1229.
4. J. Liu, J. Zhu, H. -L. Jiang, W. Wang and J. Li, *Chem. Asian J.*, In press.
5. A. I. Meyers, A. Nabeya, H. W. Adickes, I. R. Politzer, G. R. Malone, A. C. Kovelesky, R. L. Nolen and R. C. Portnoy, *J. Org. Chem.*, 1973, **38**, 36.



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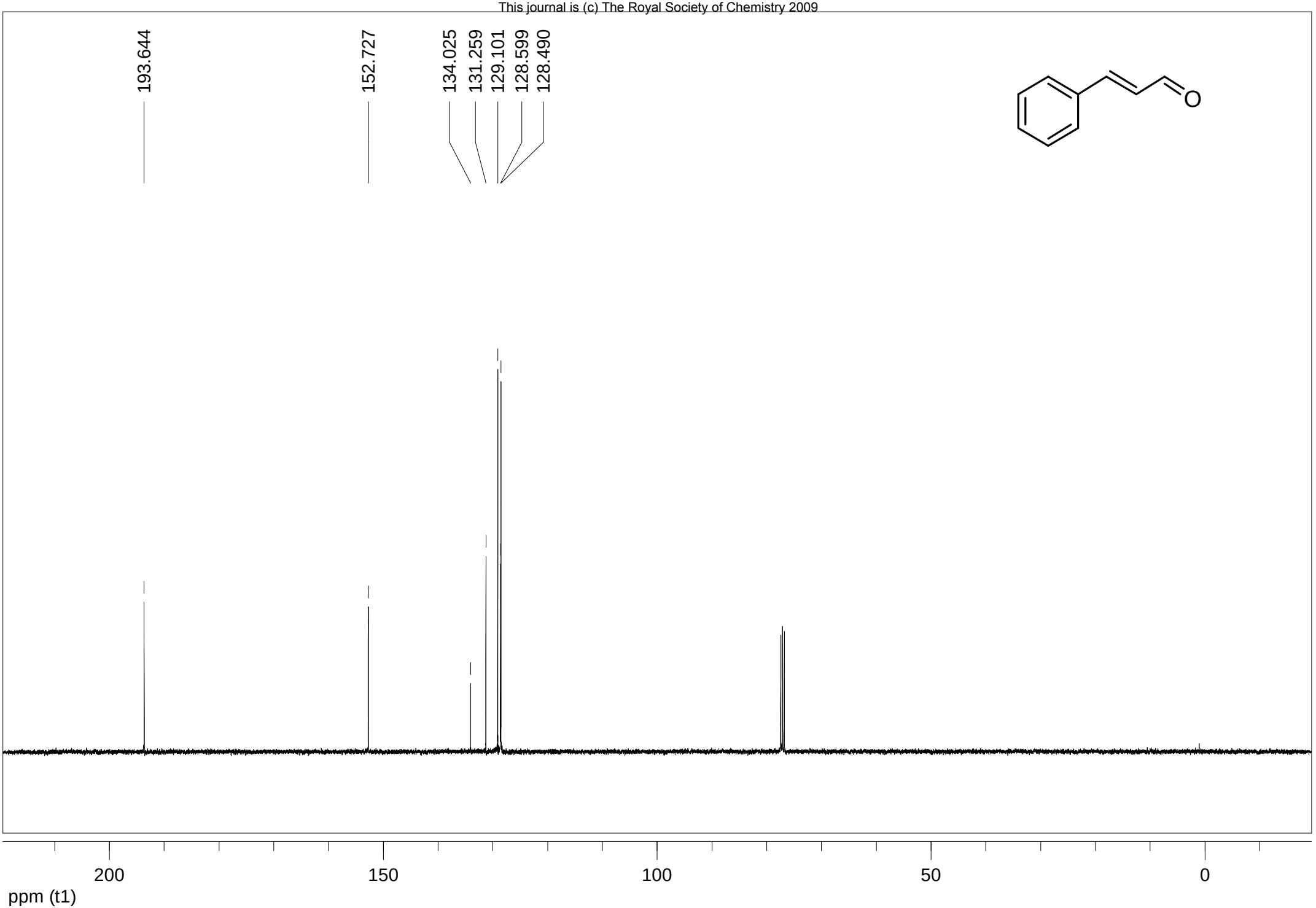

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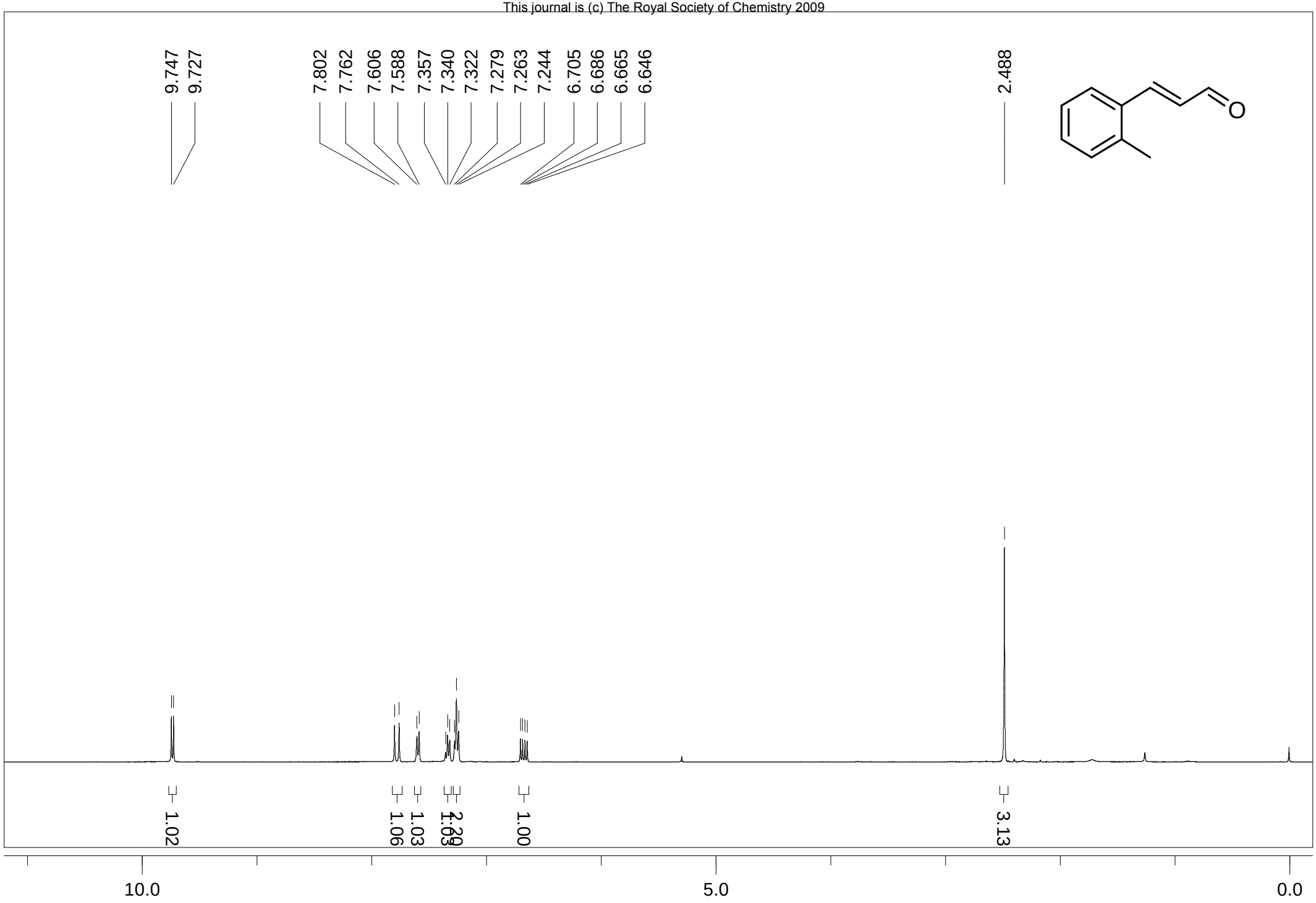

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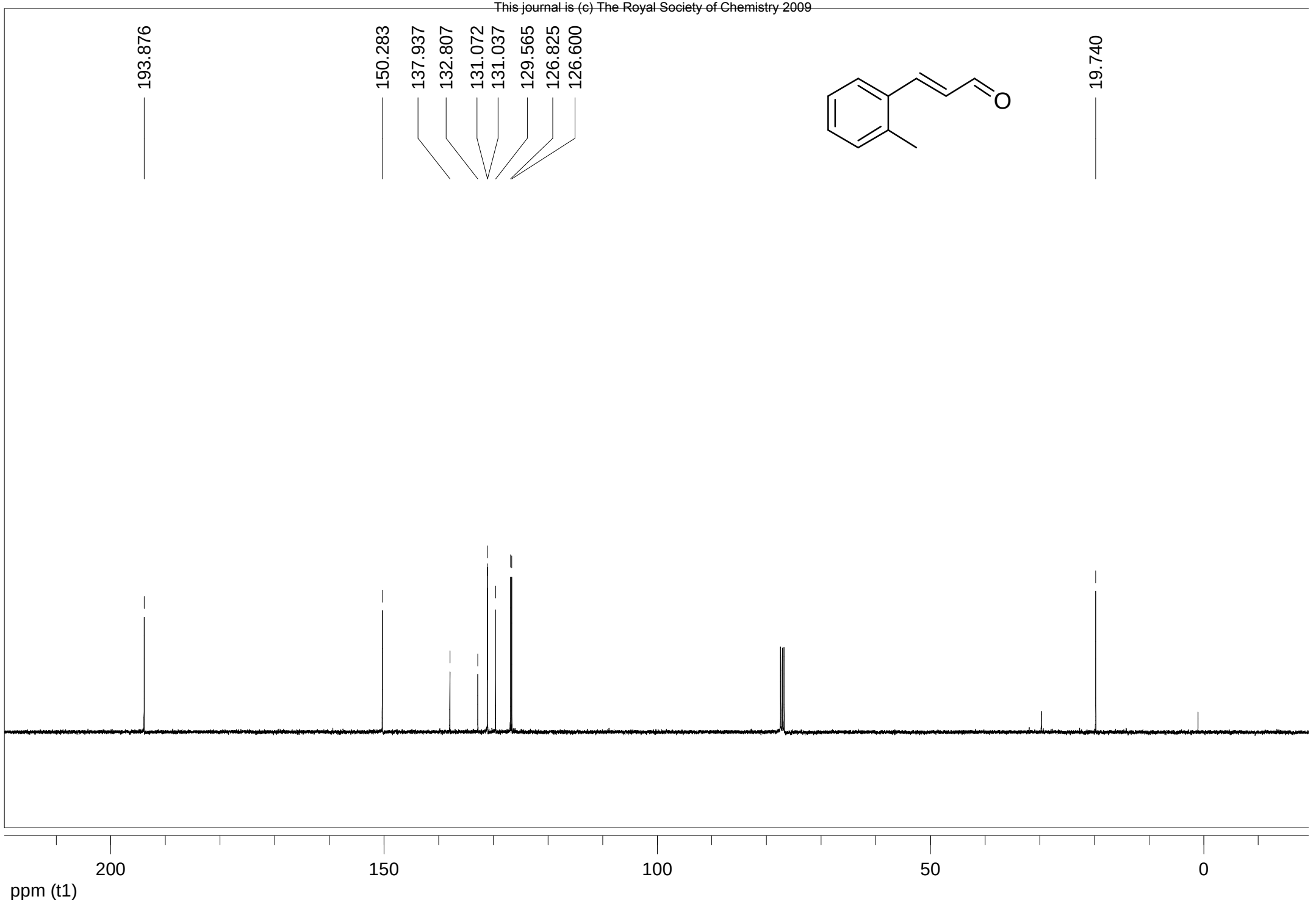

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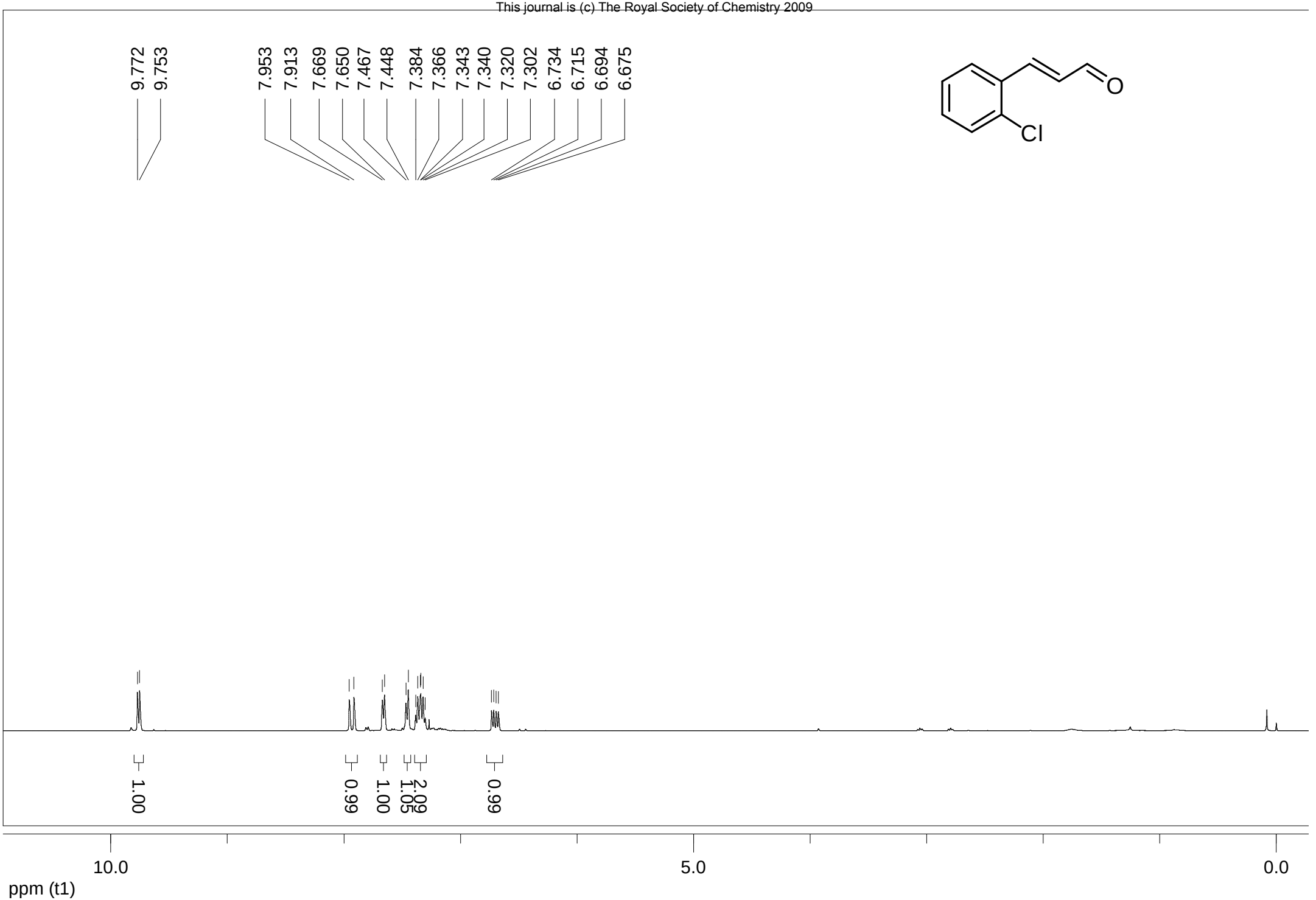

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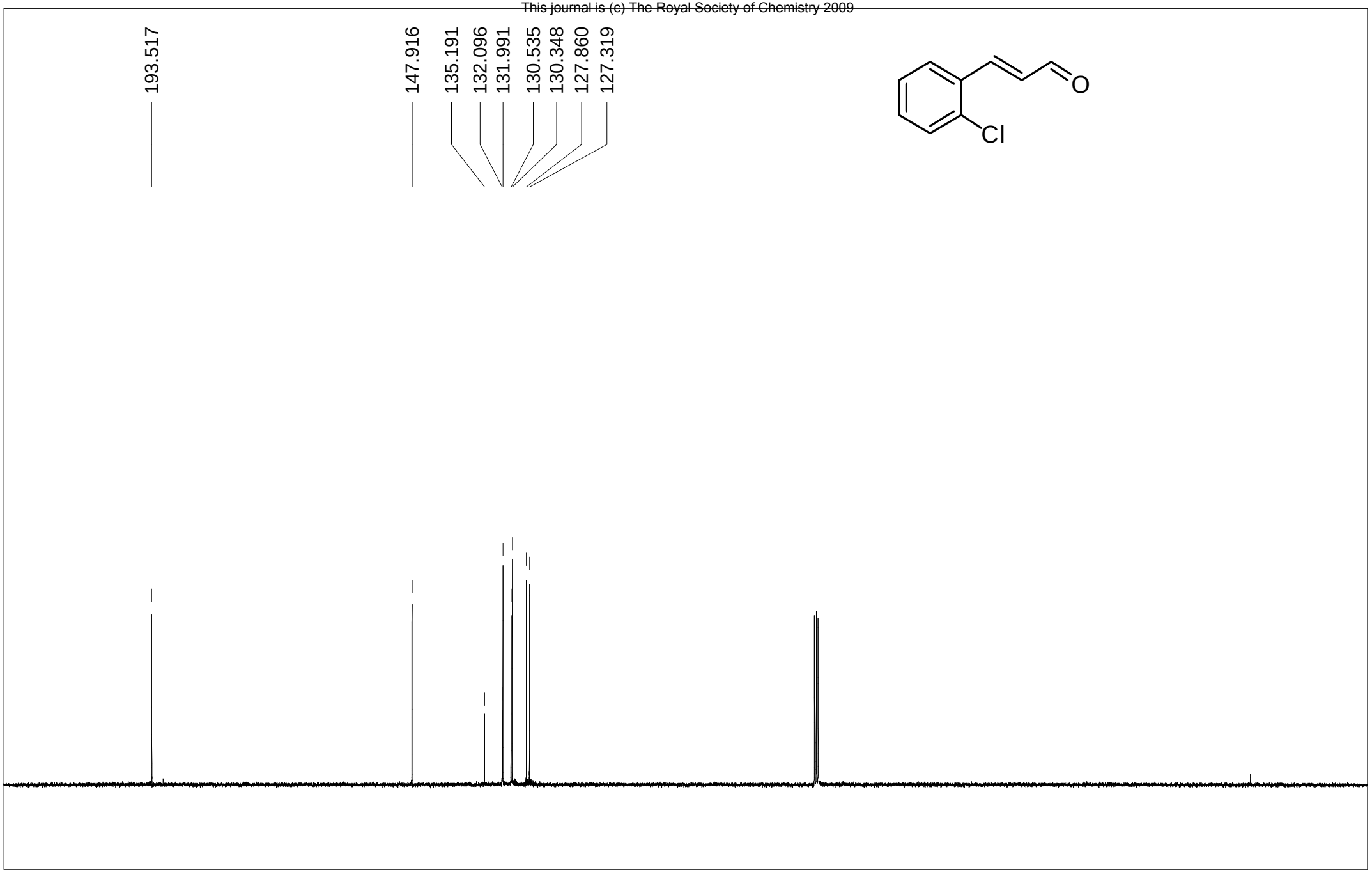

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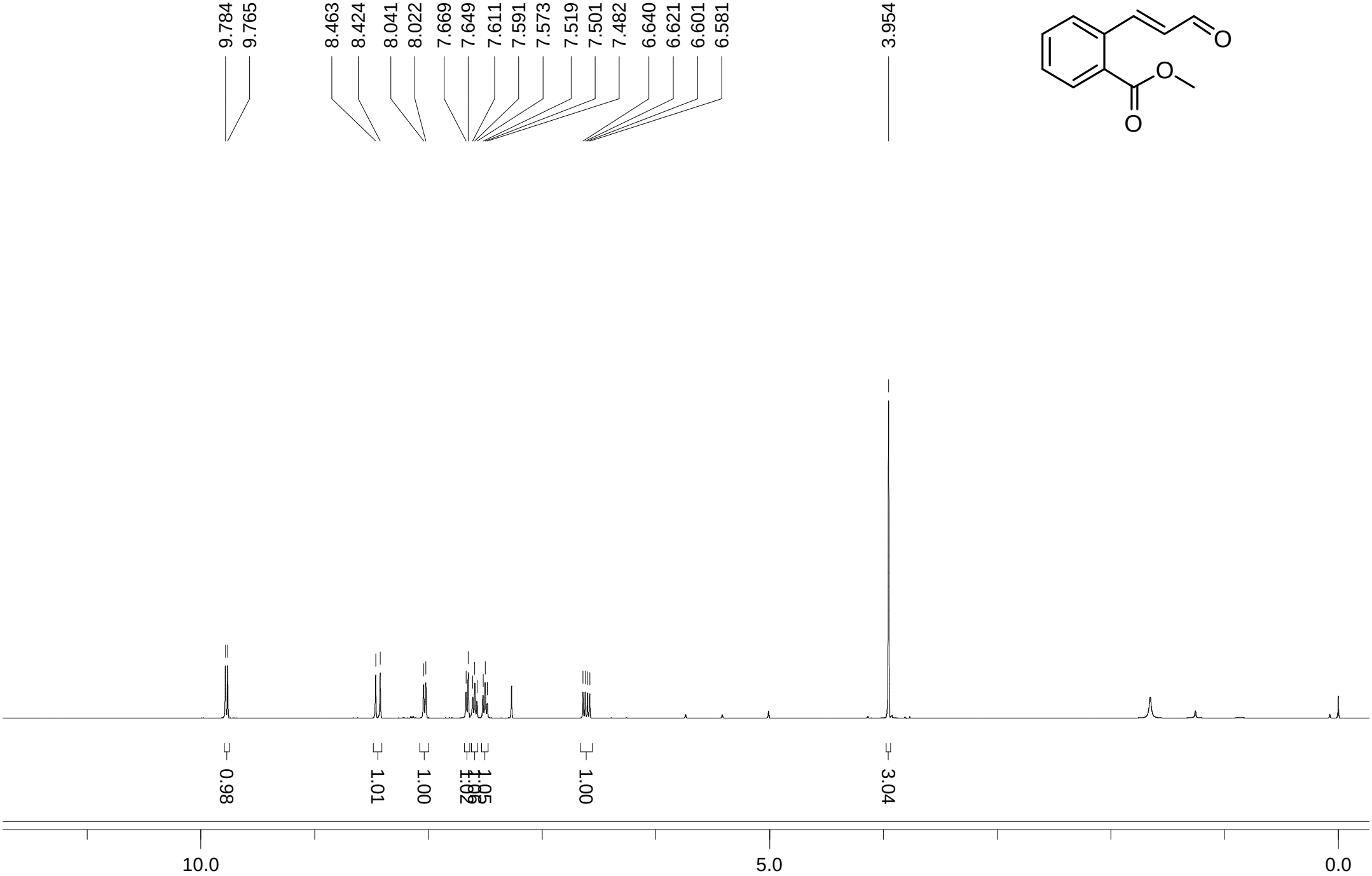

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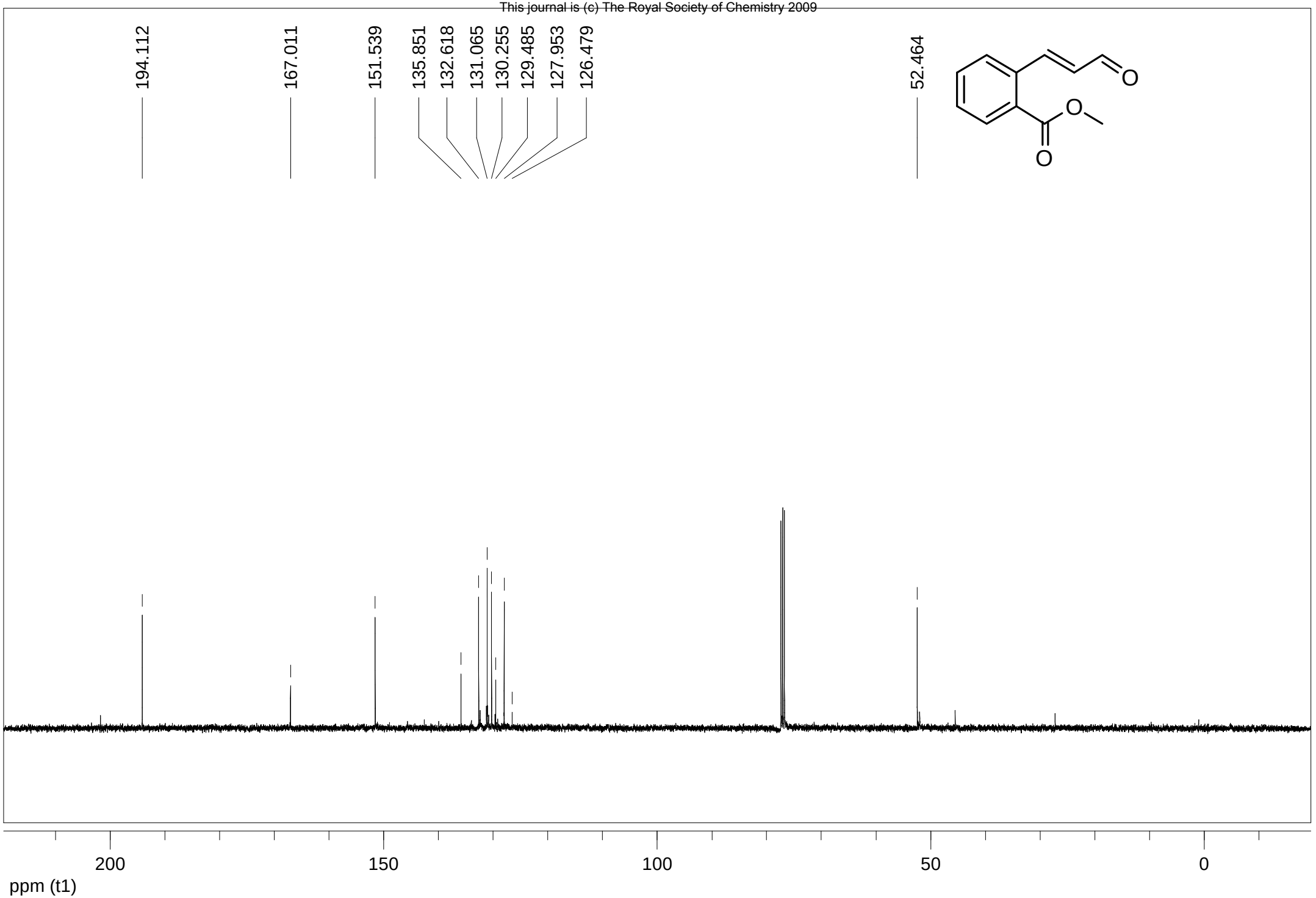

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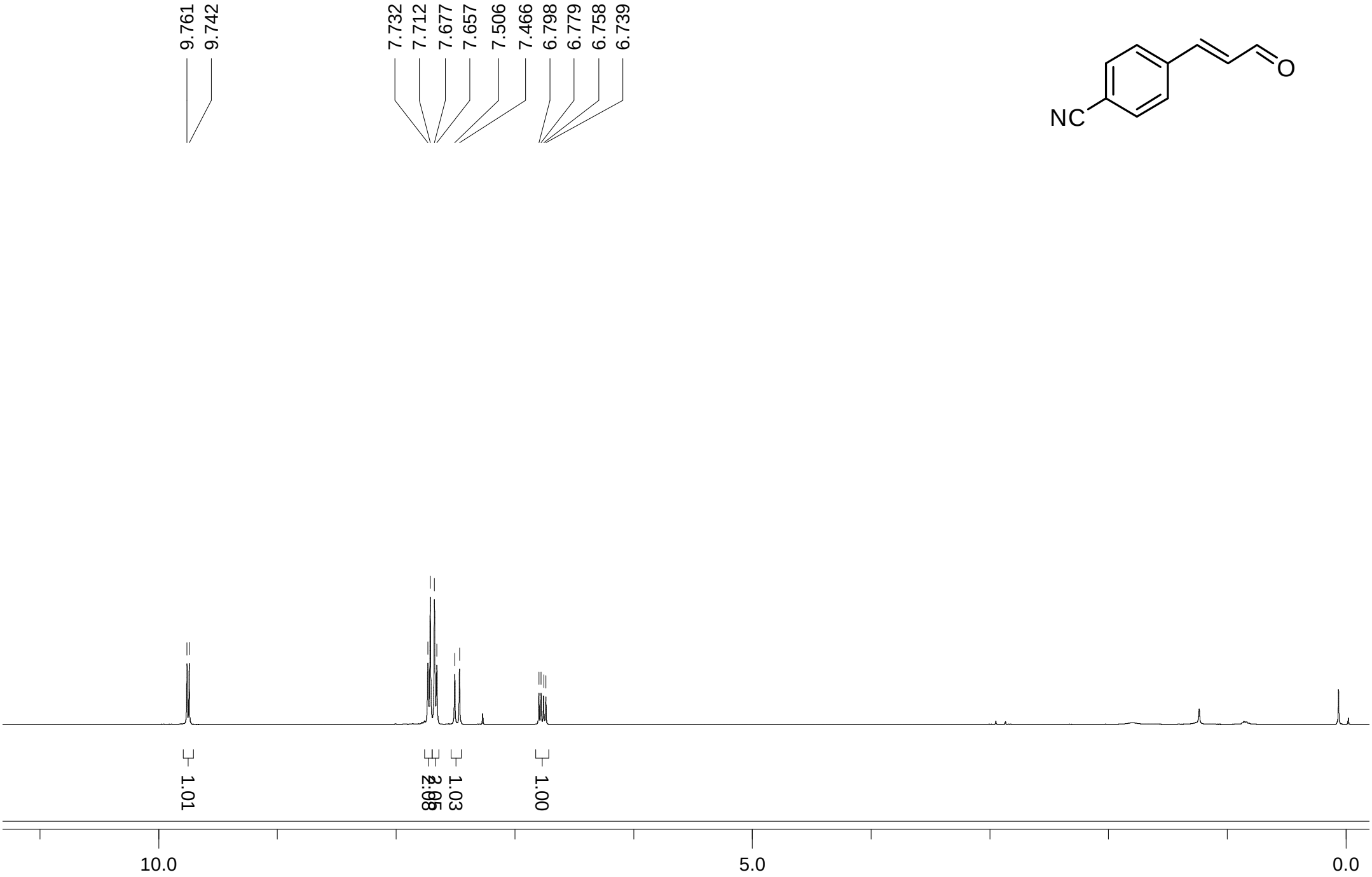

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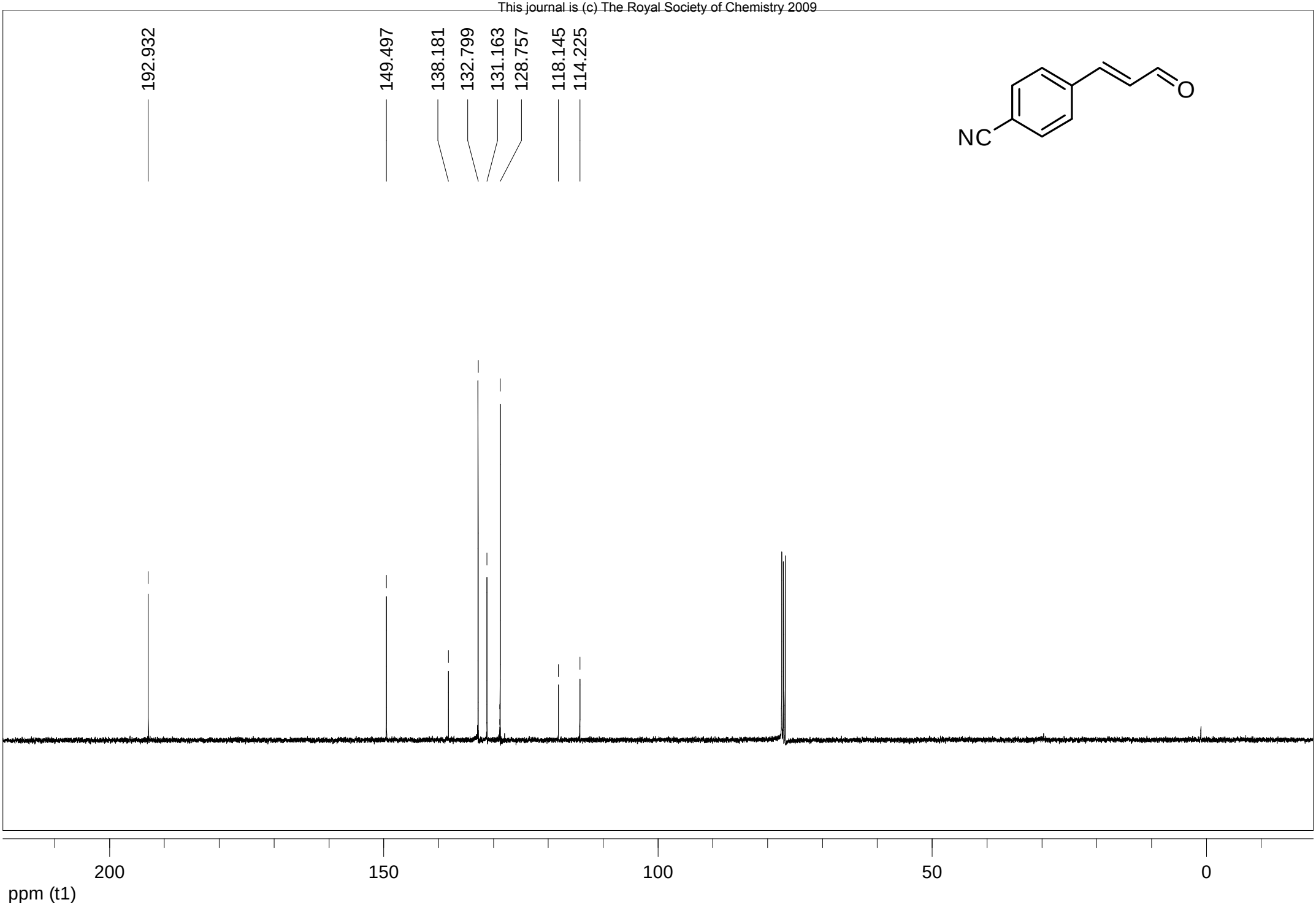

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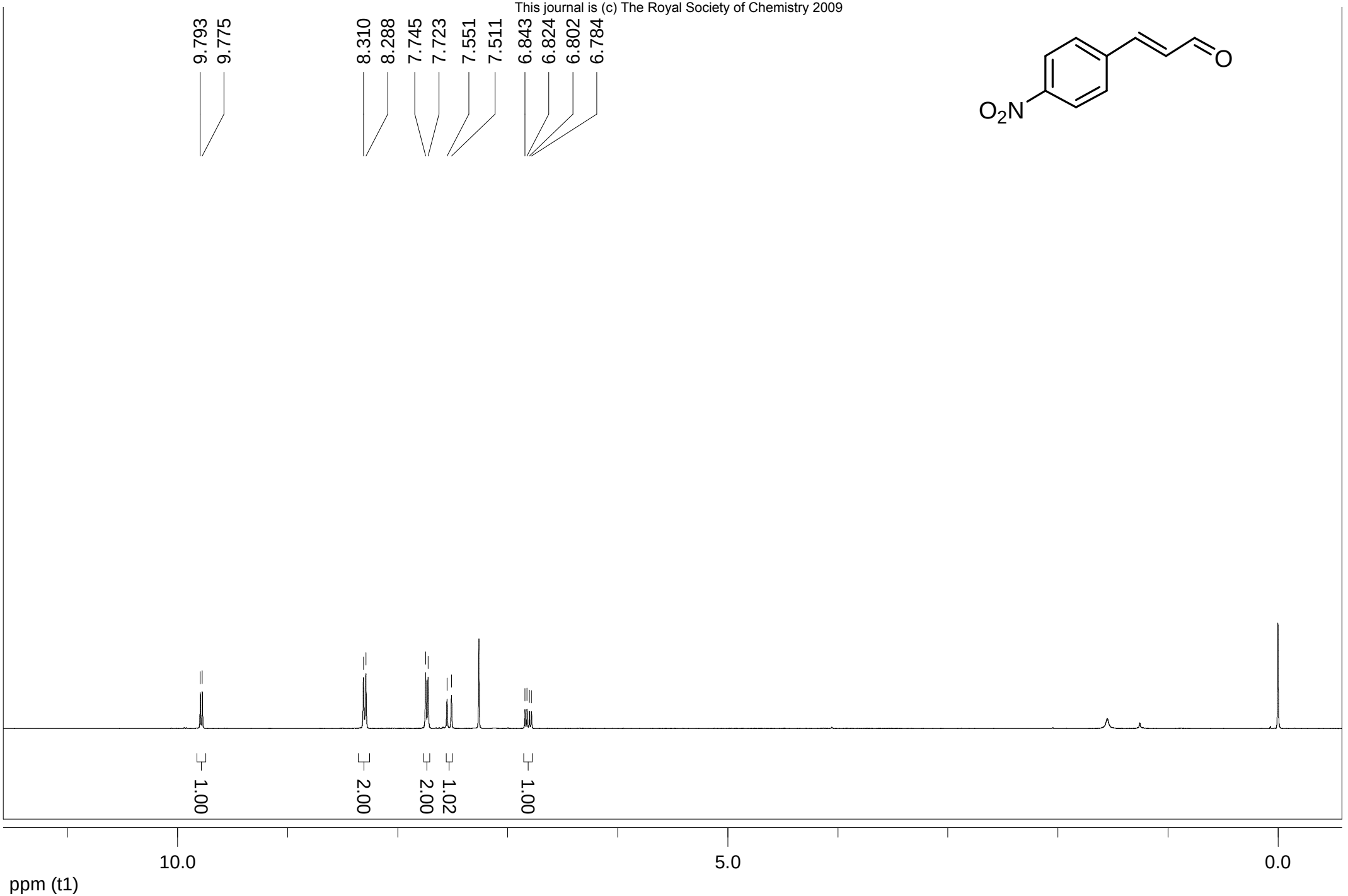

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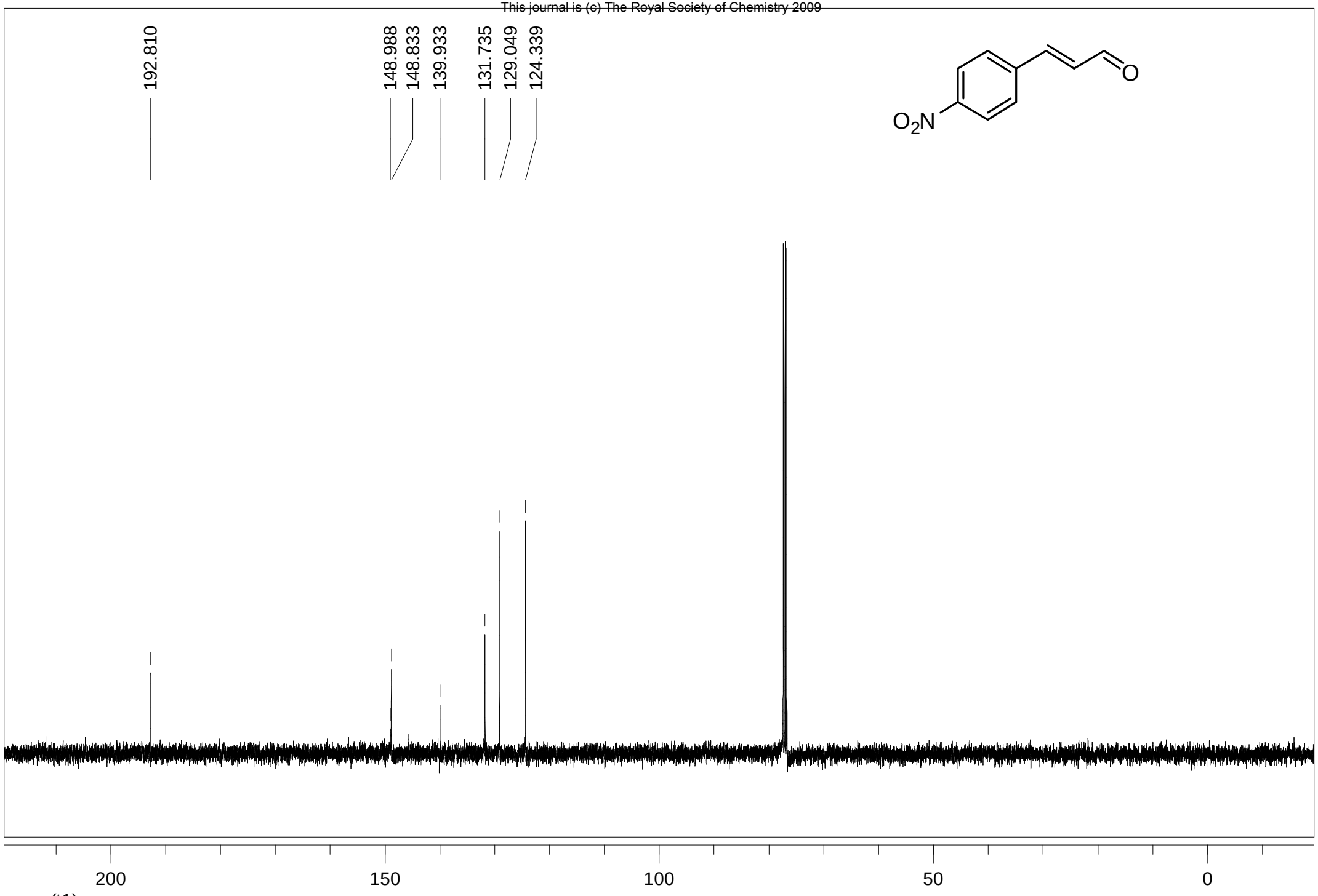

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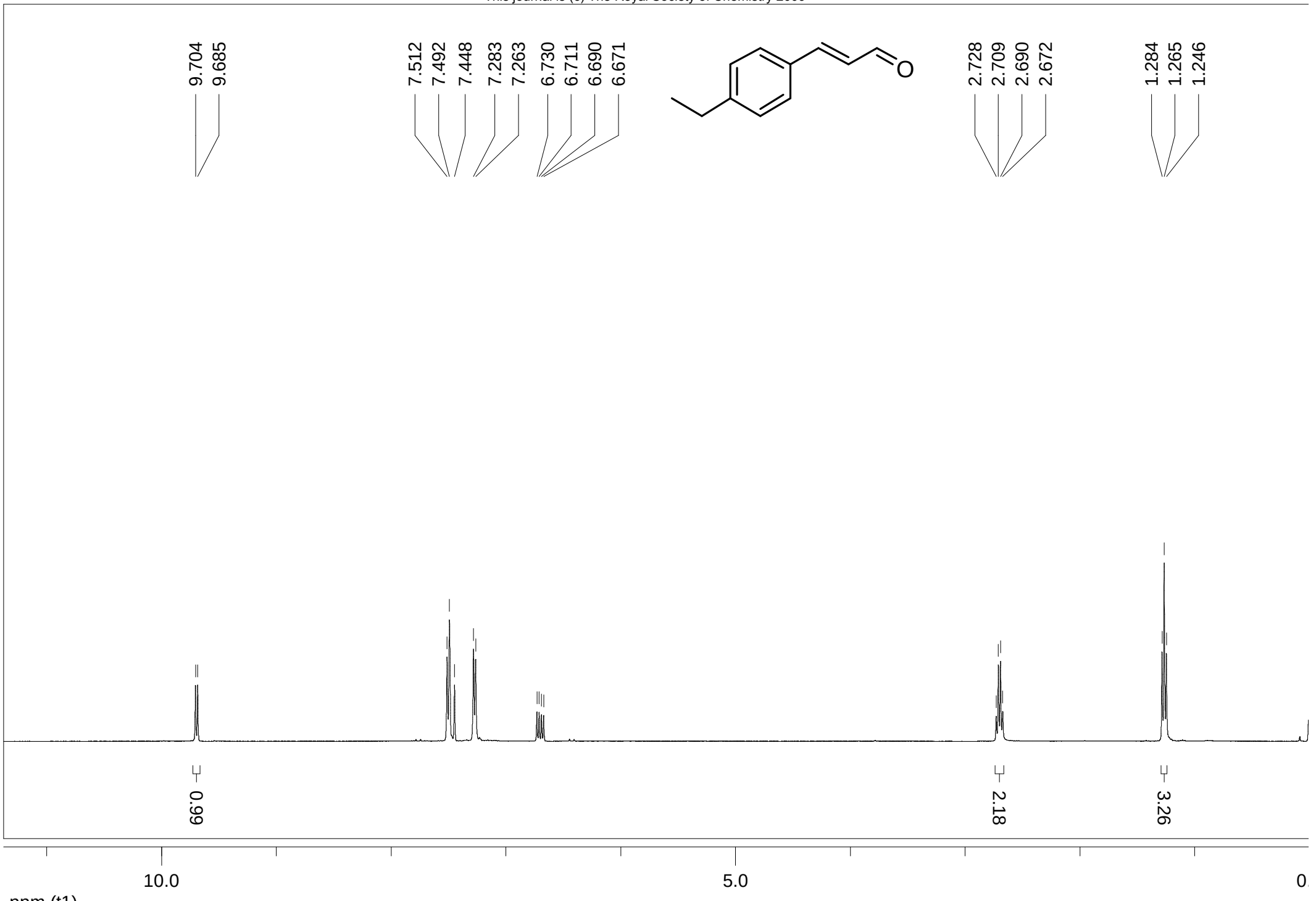

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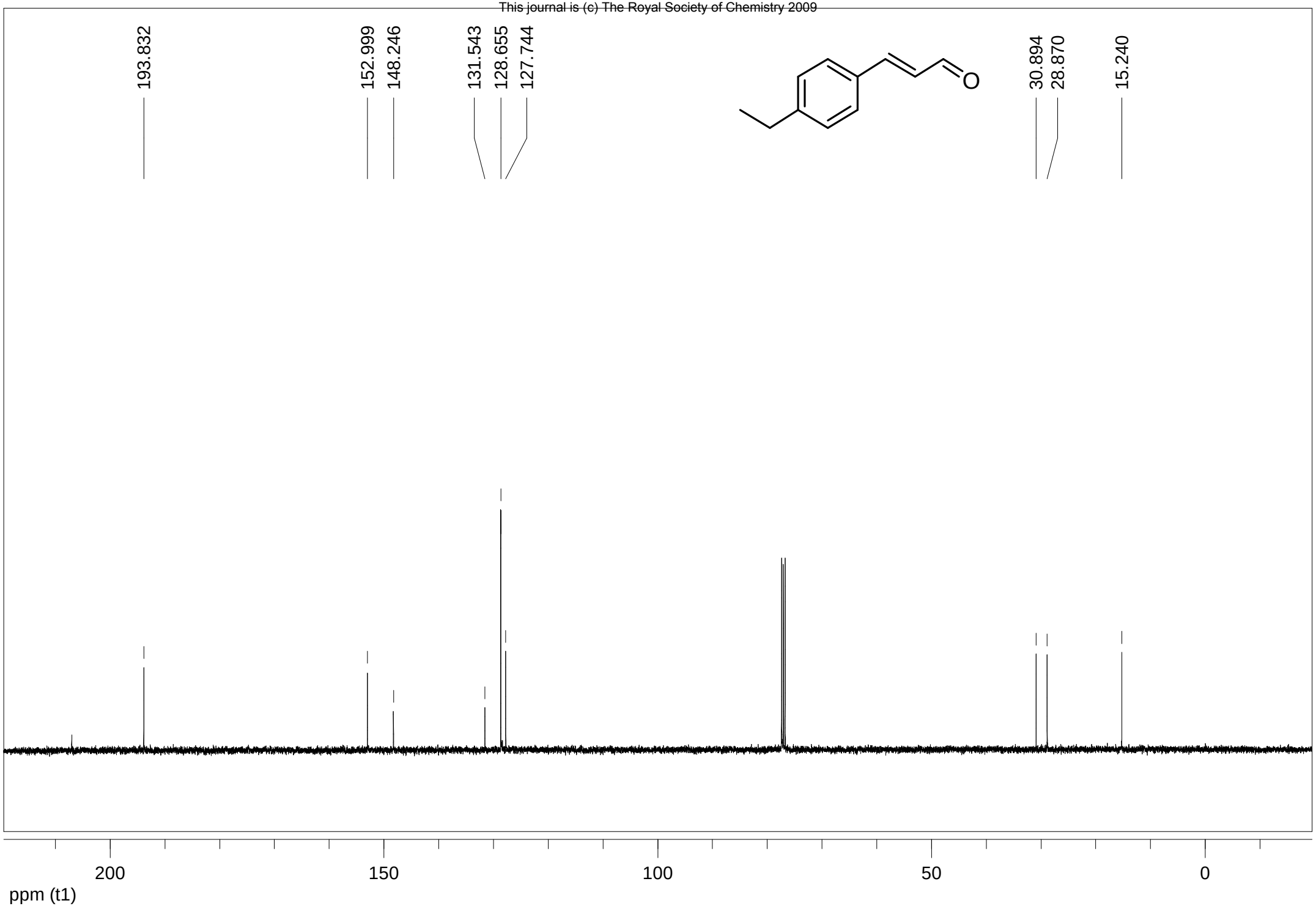

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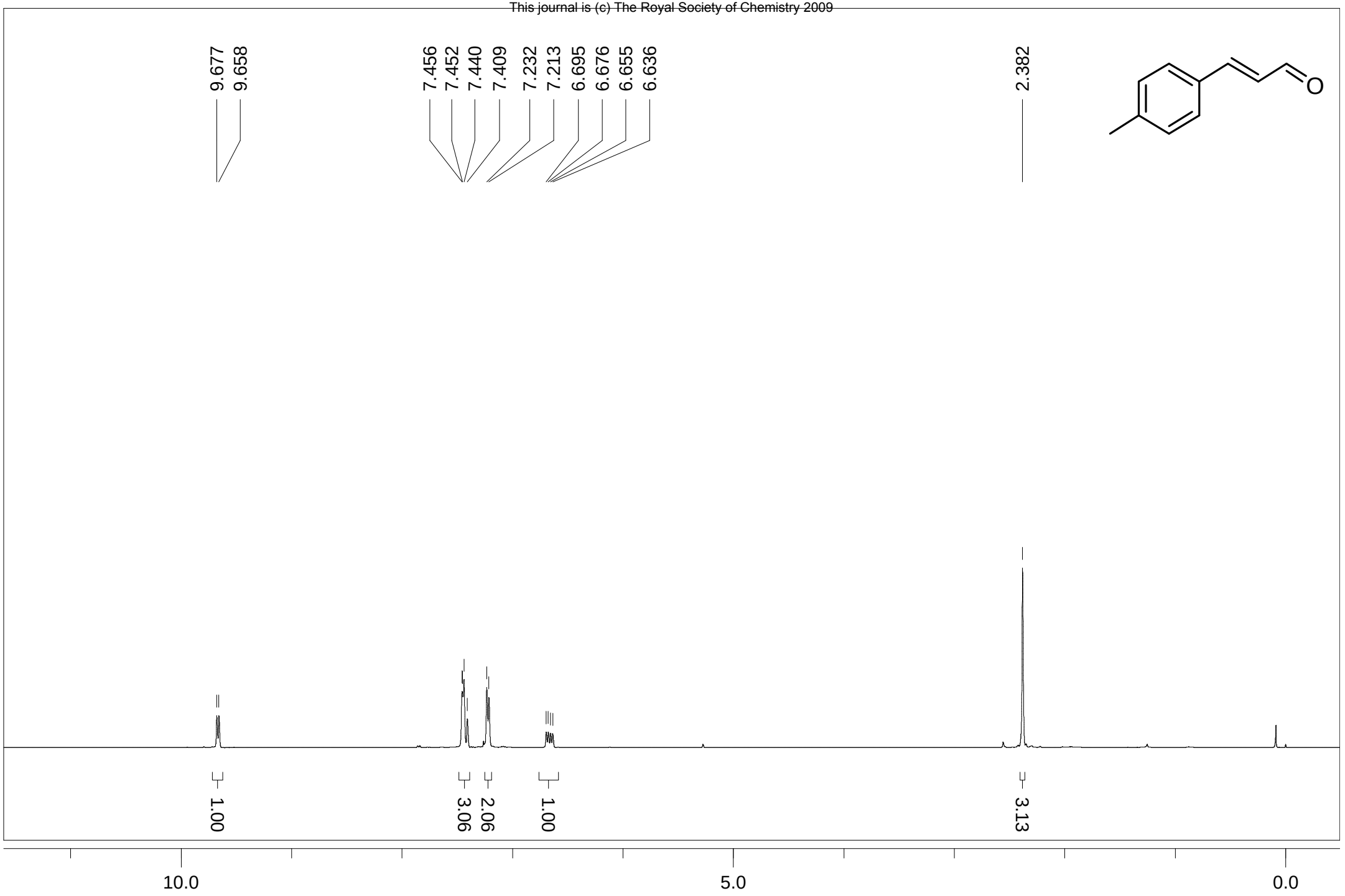

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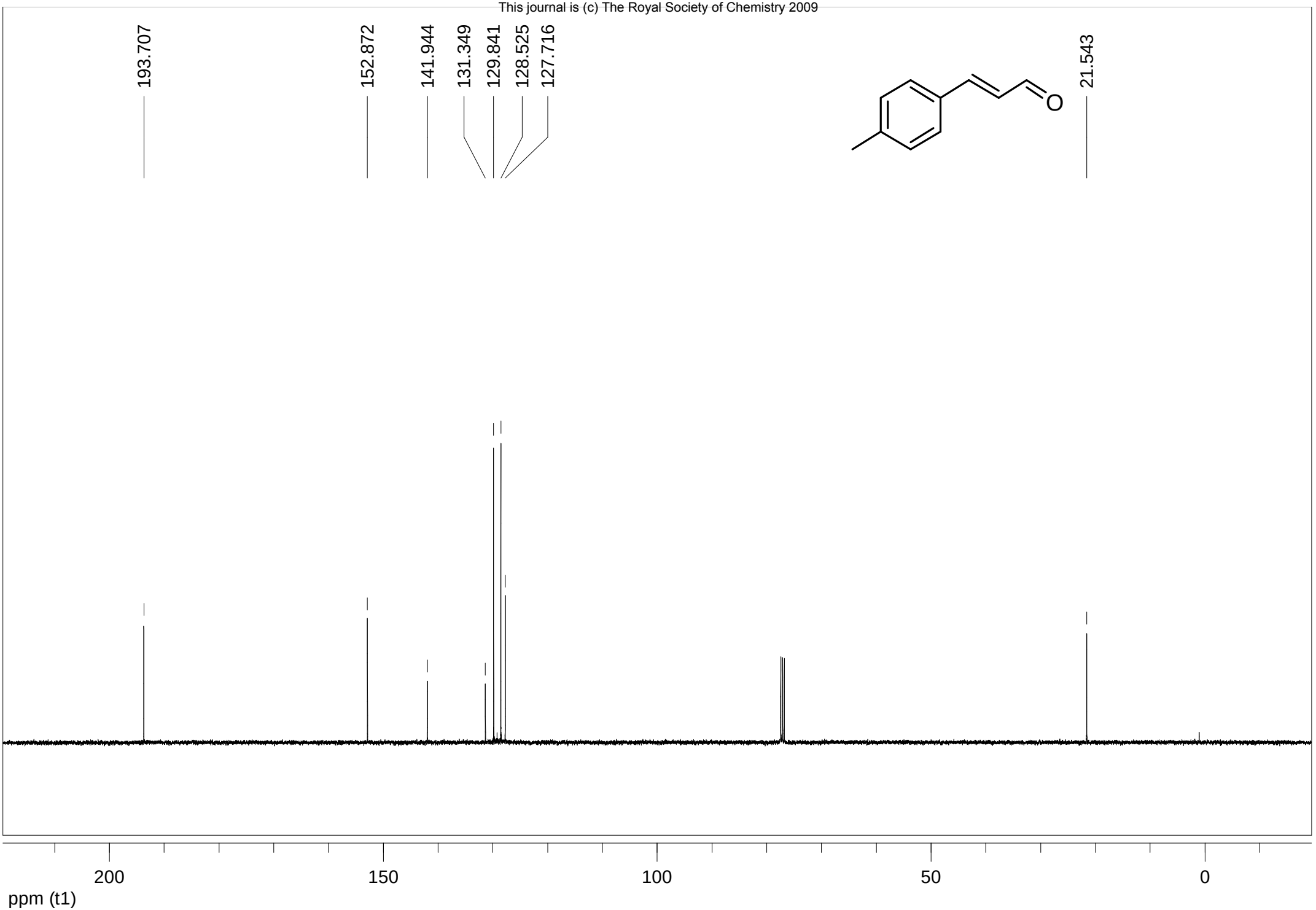

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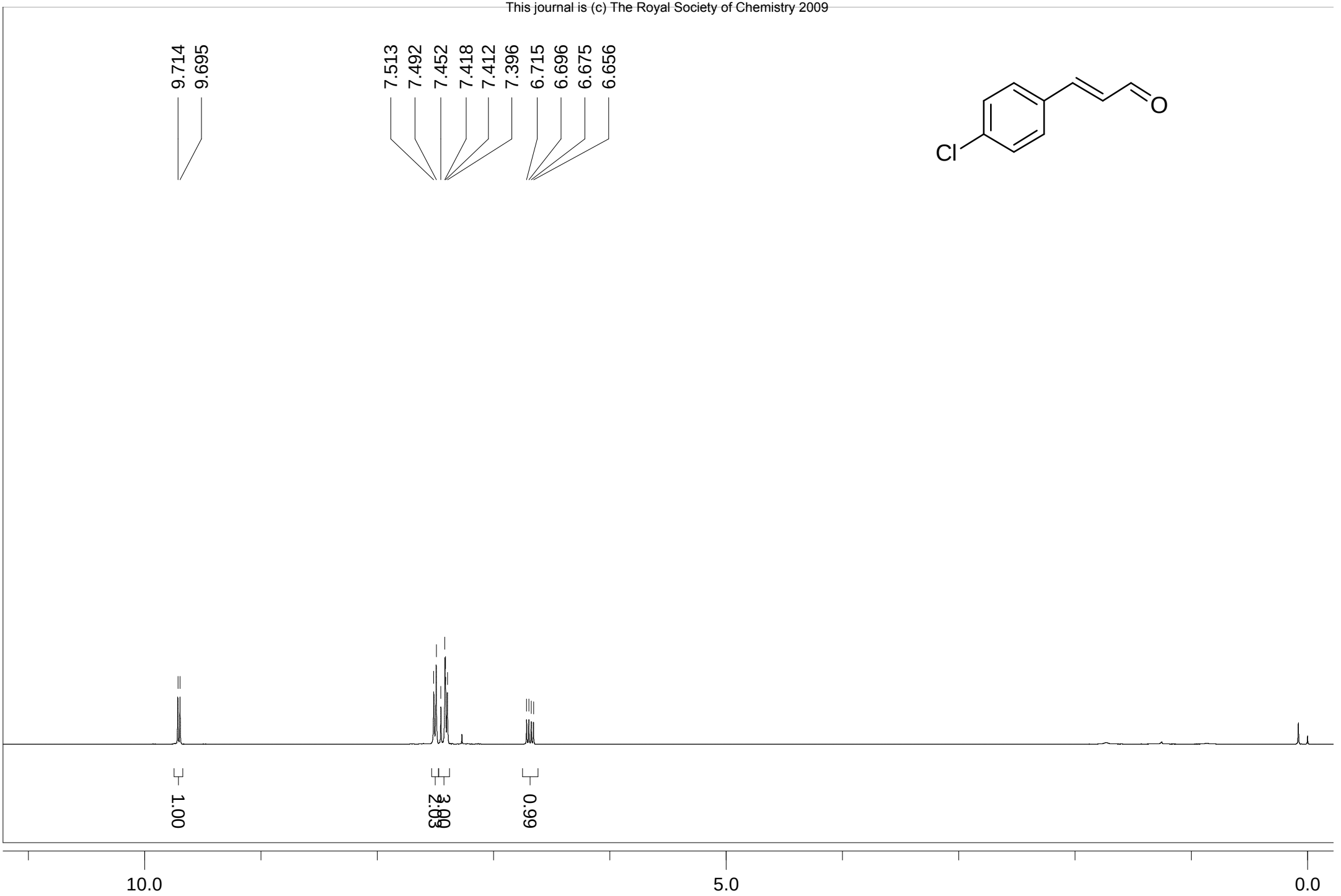

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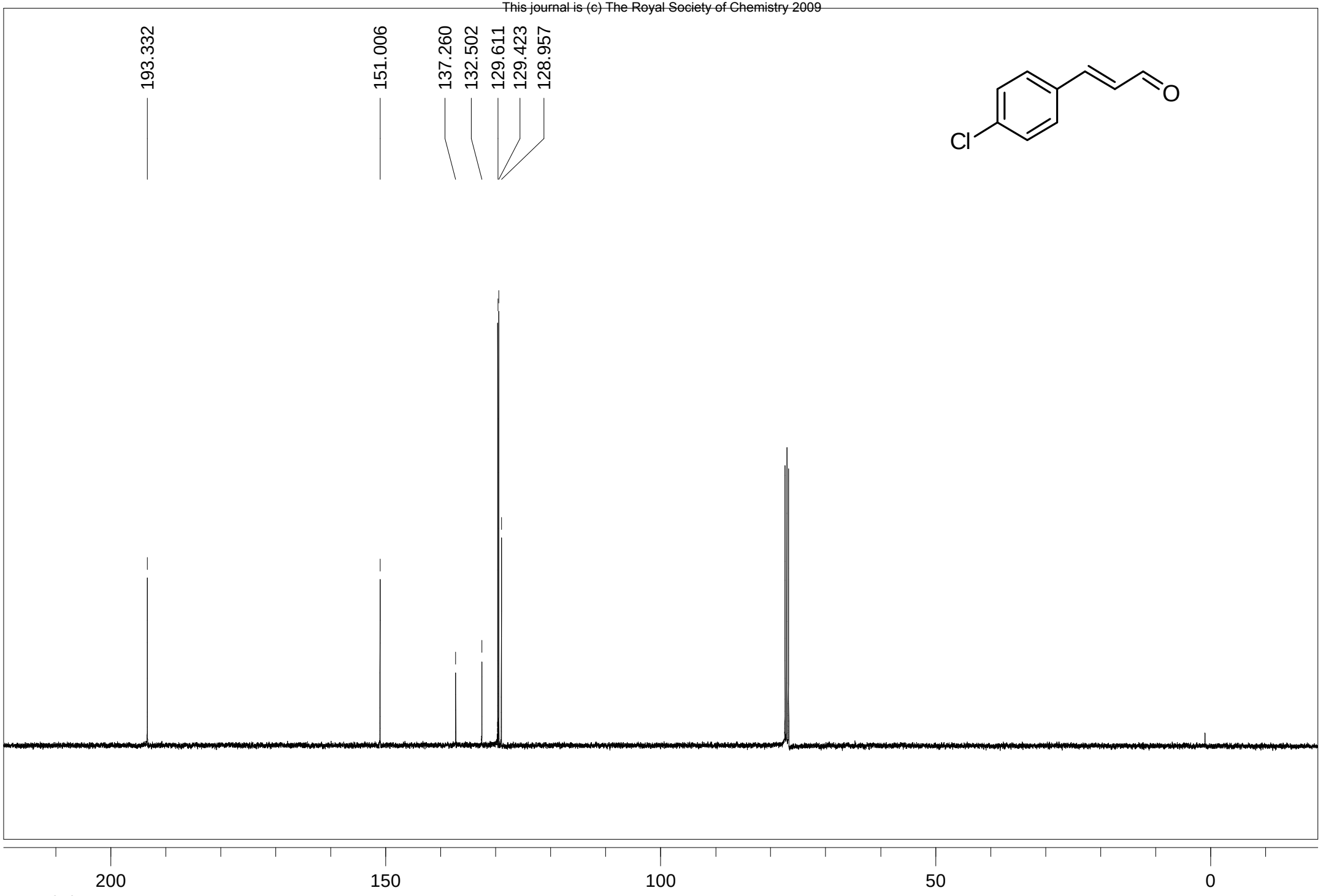

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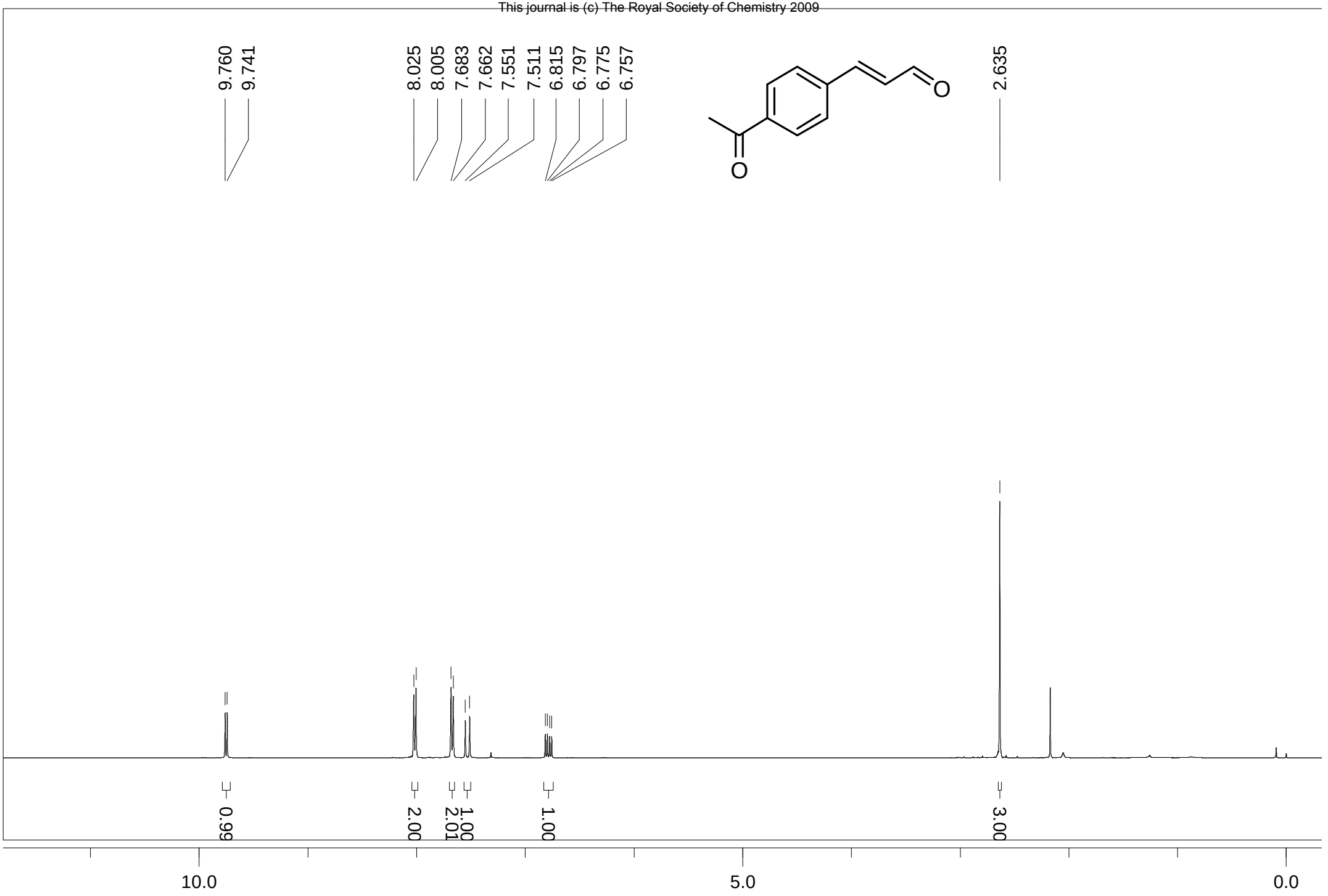

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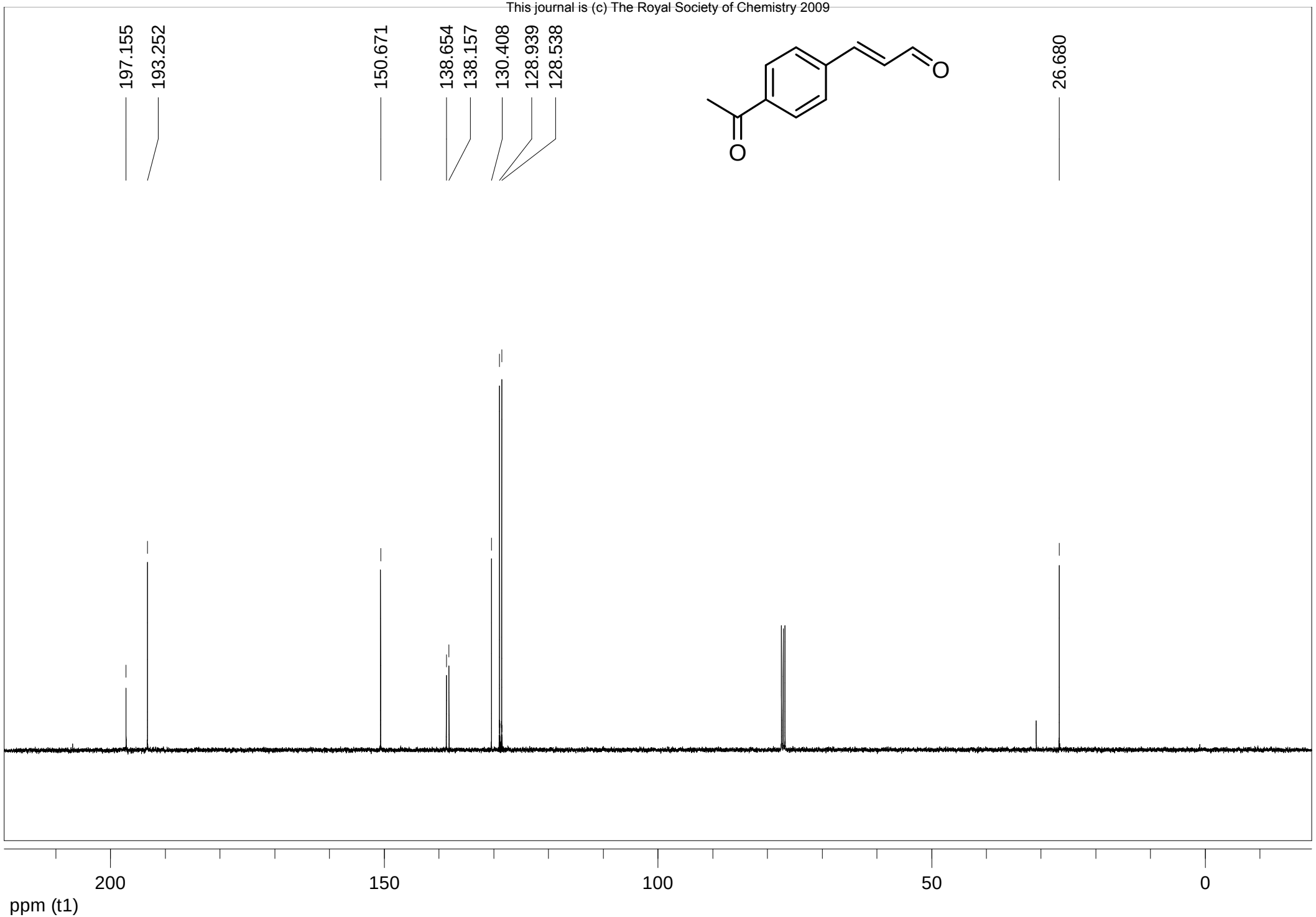

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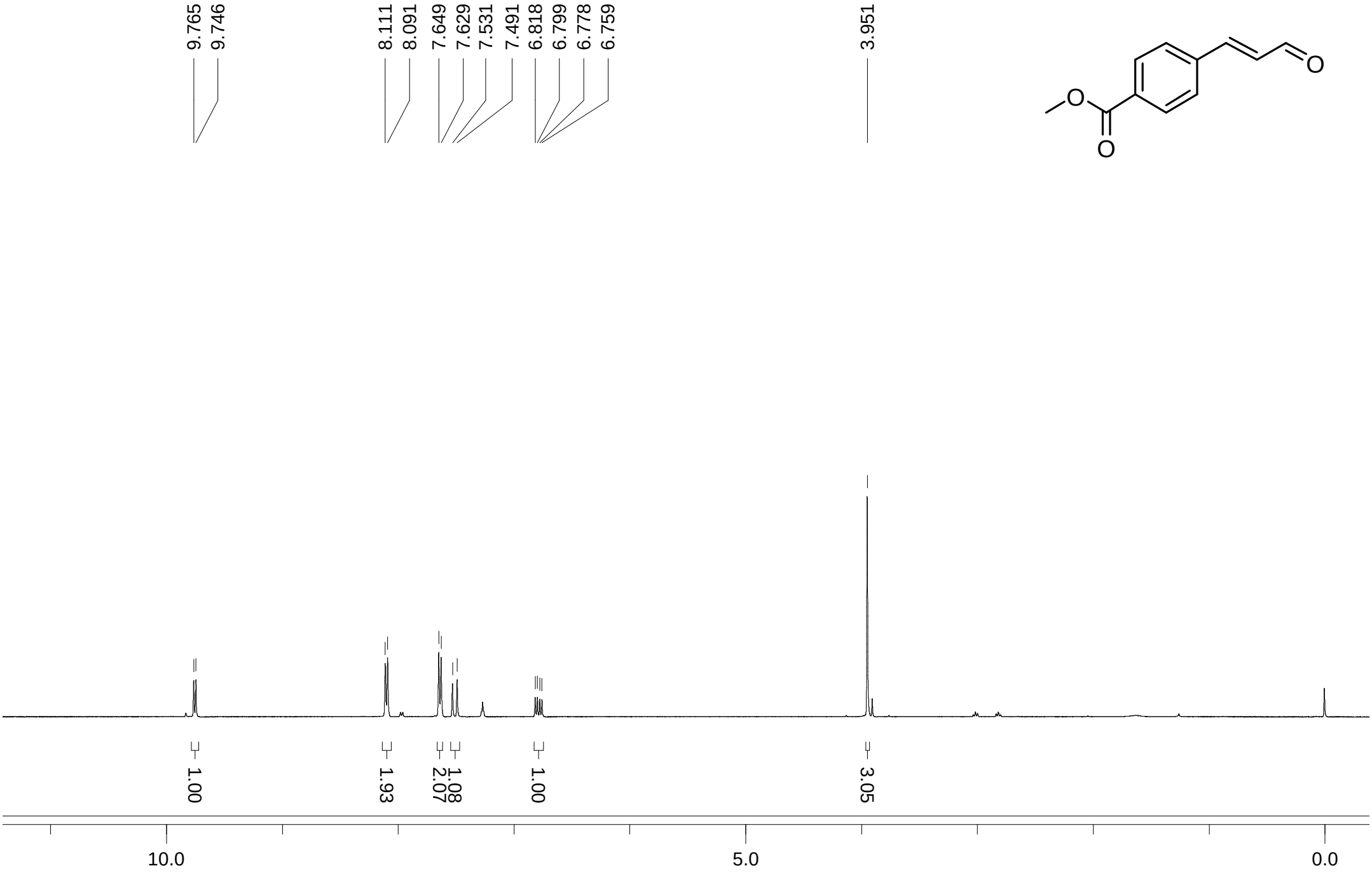

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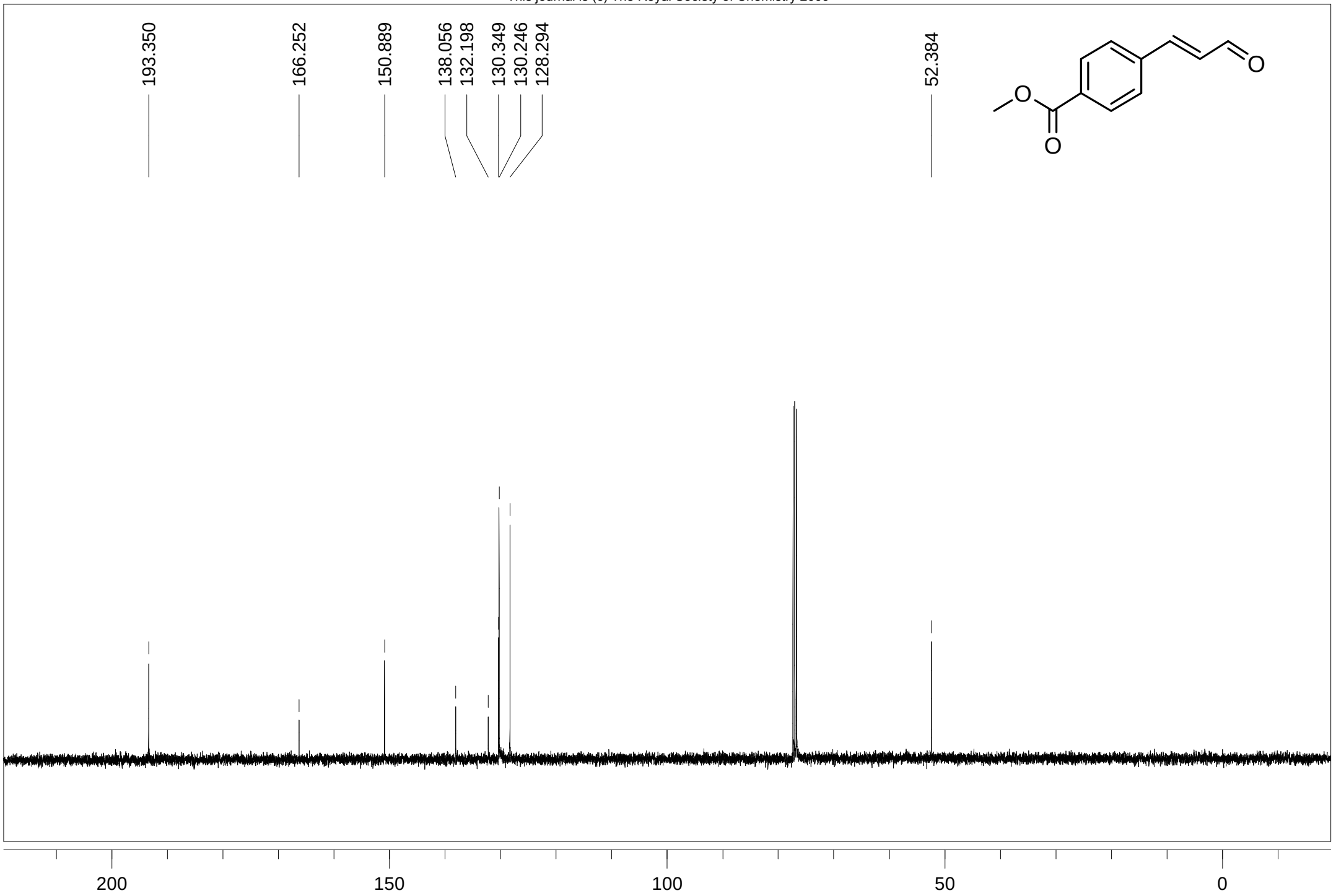

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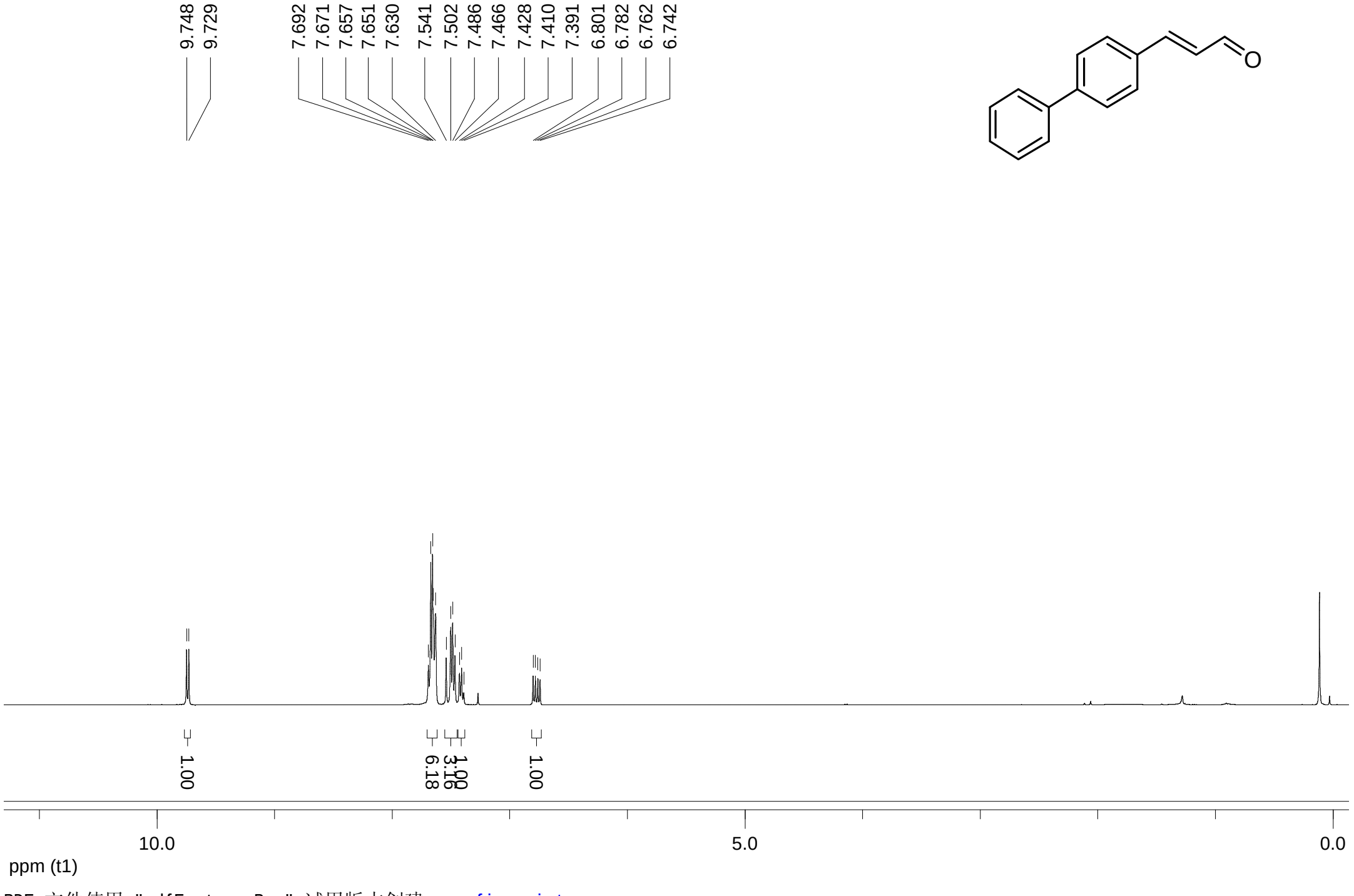

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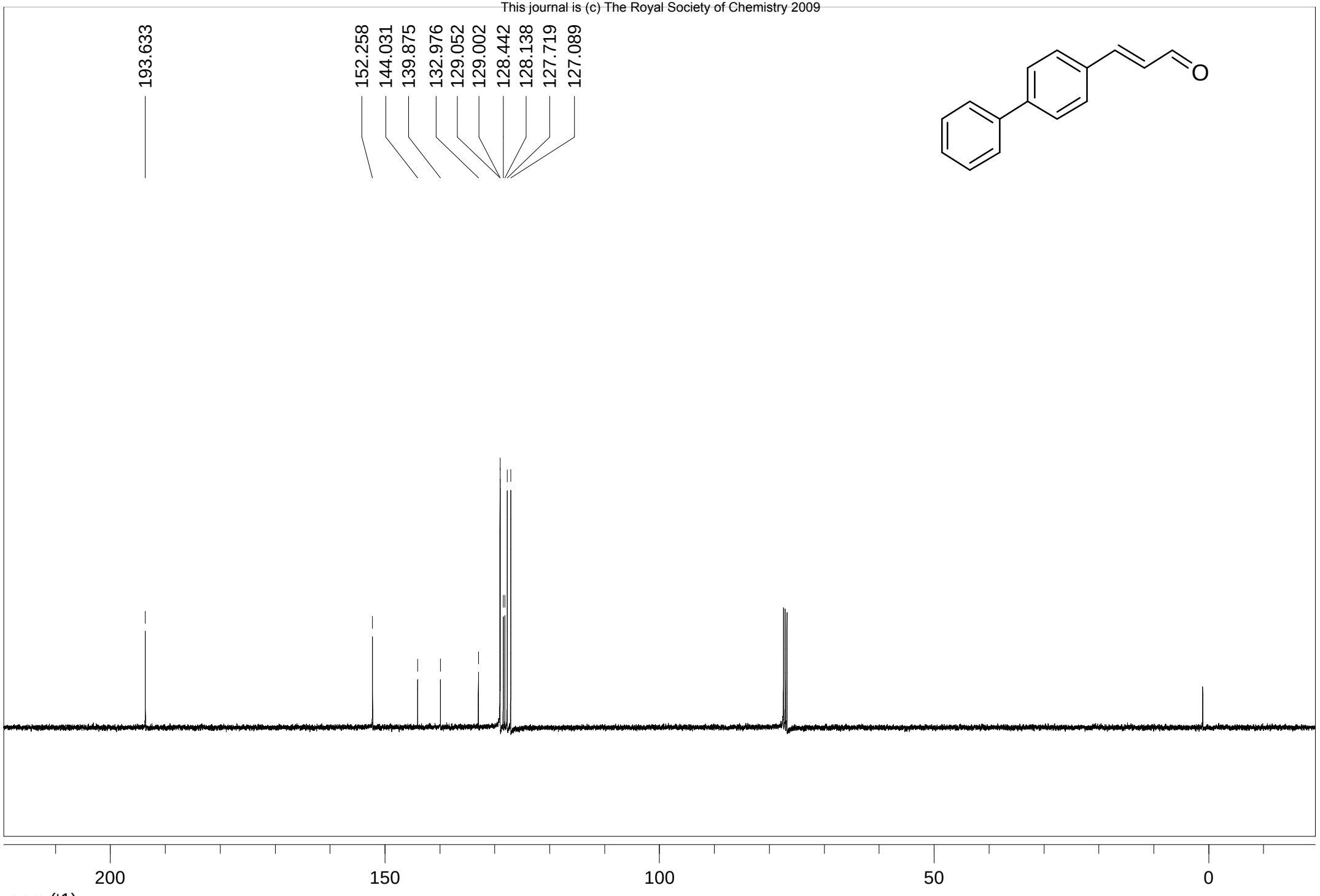

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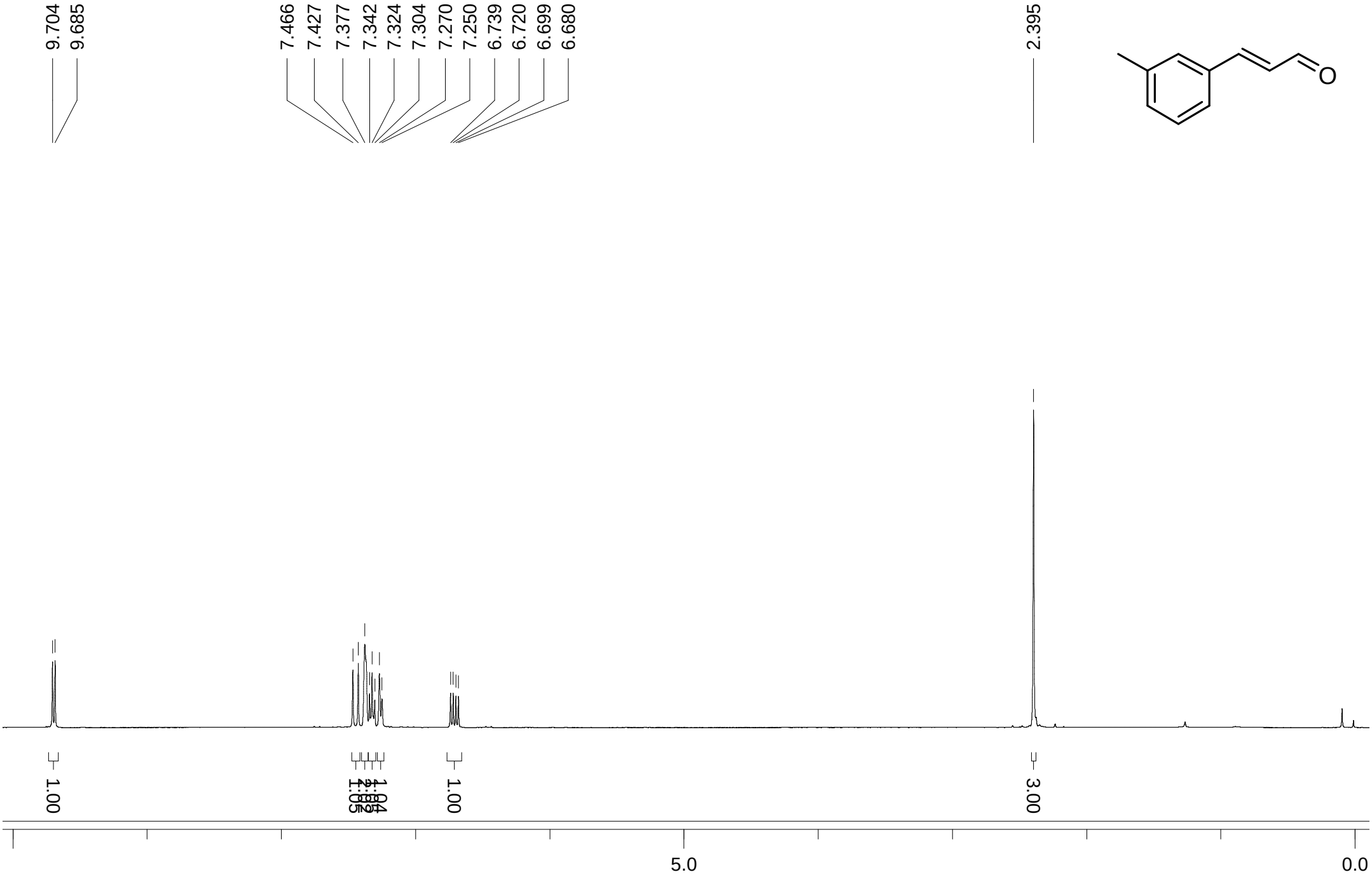

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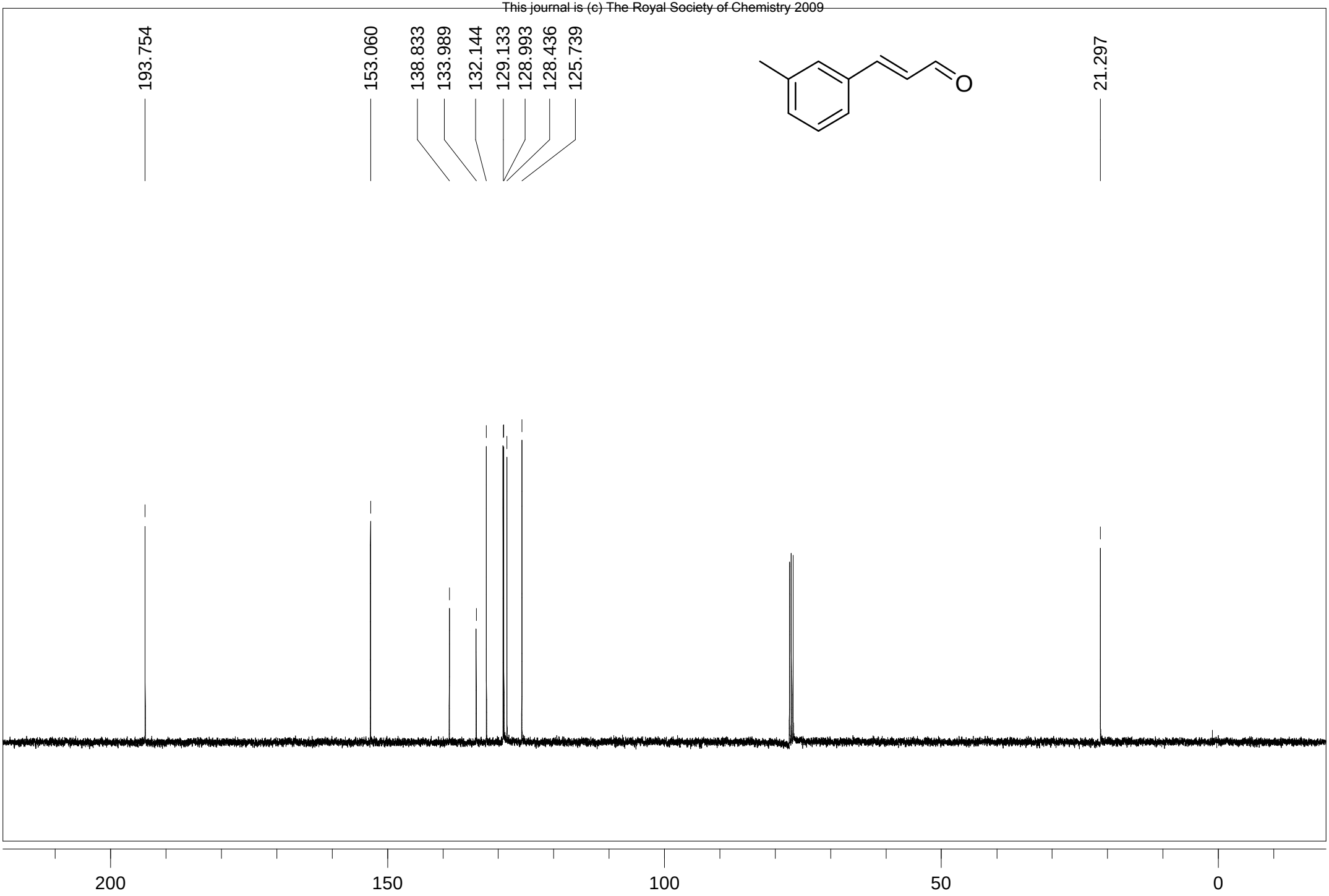

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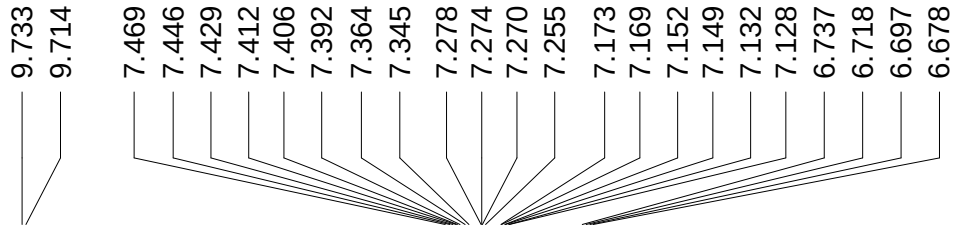

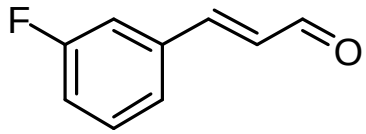

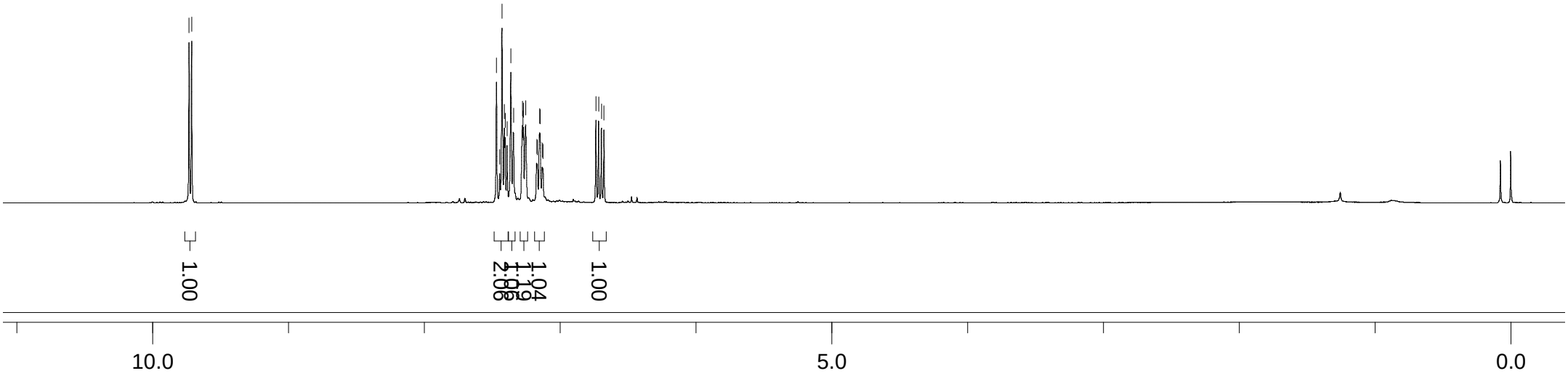

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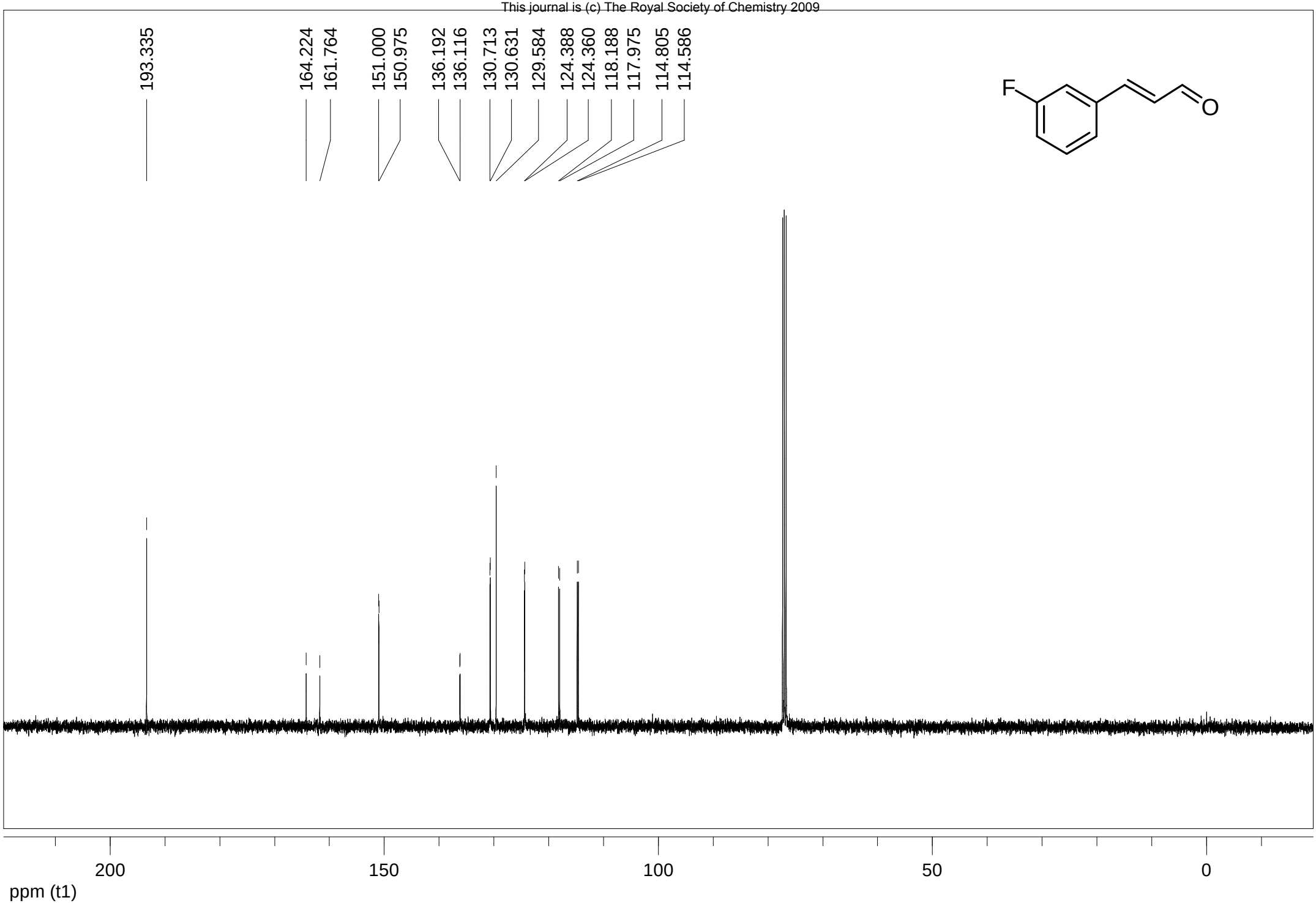

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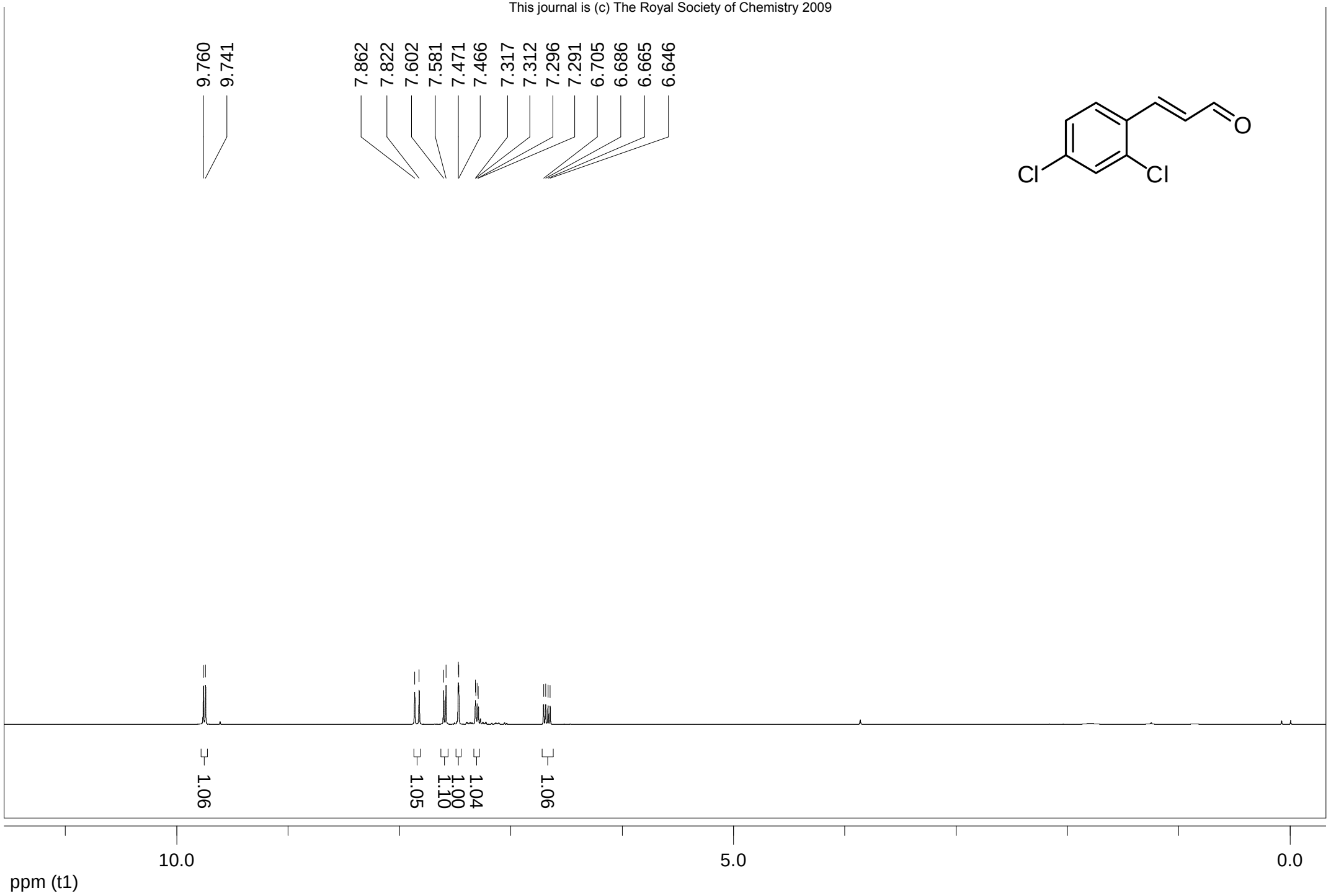

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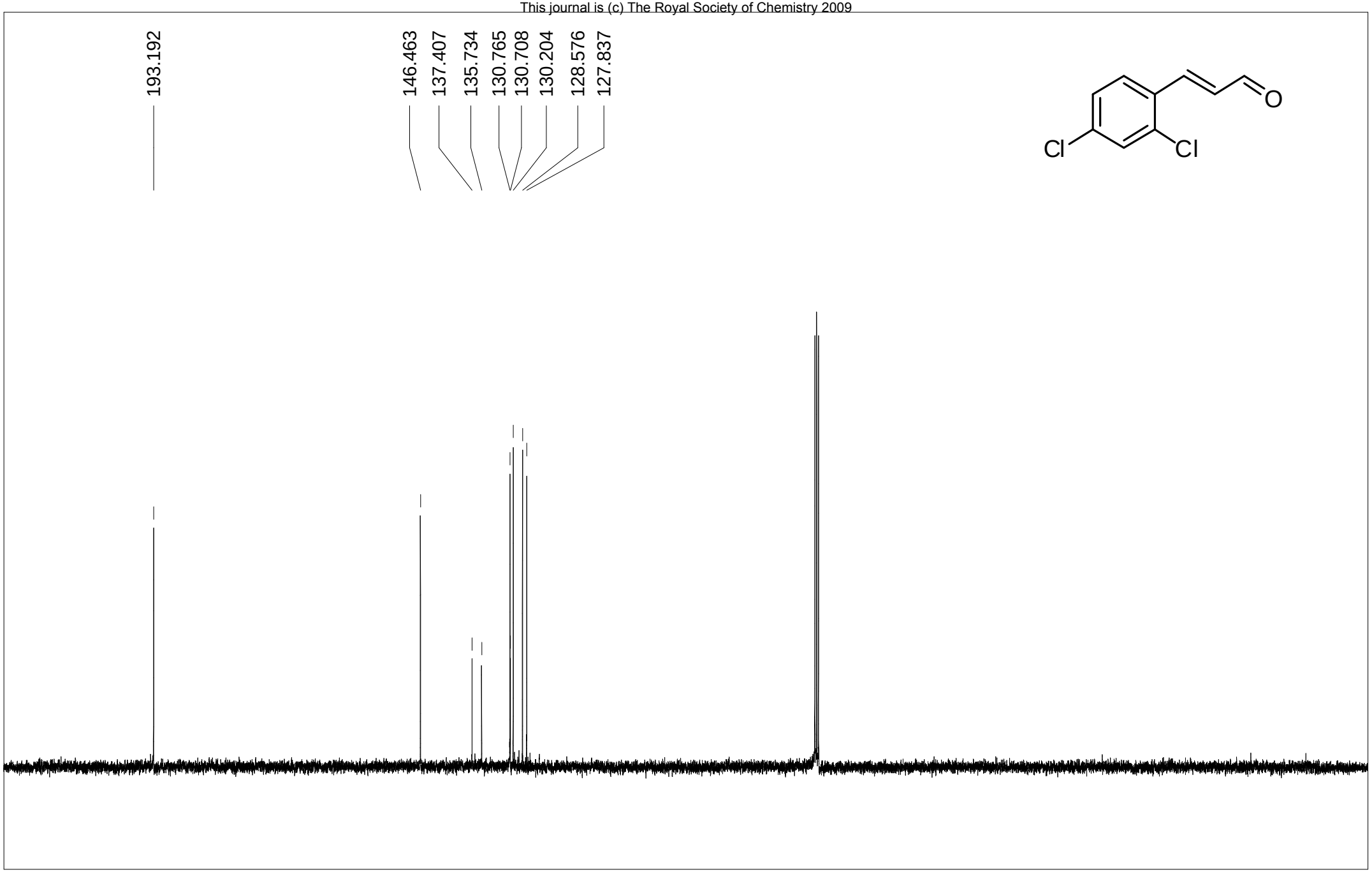

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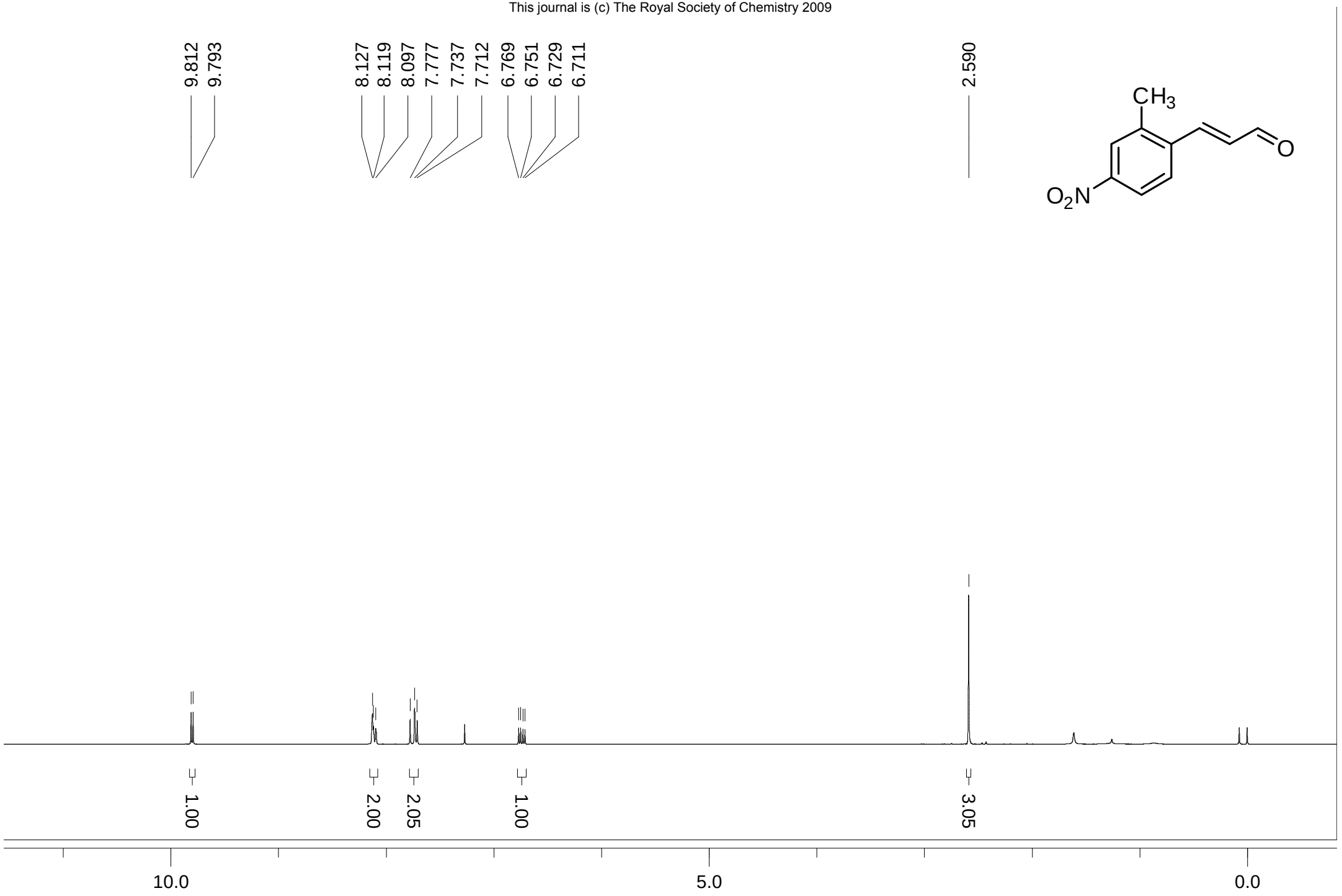

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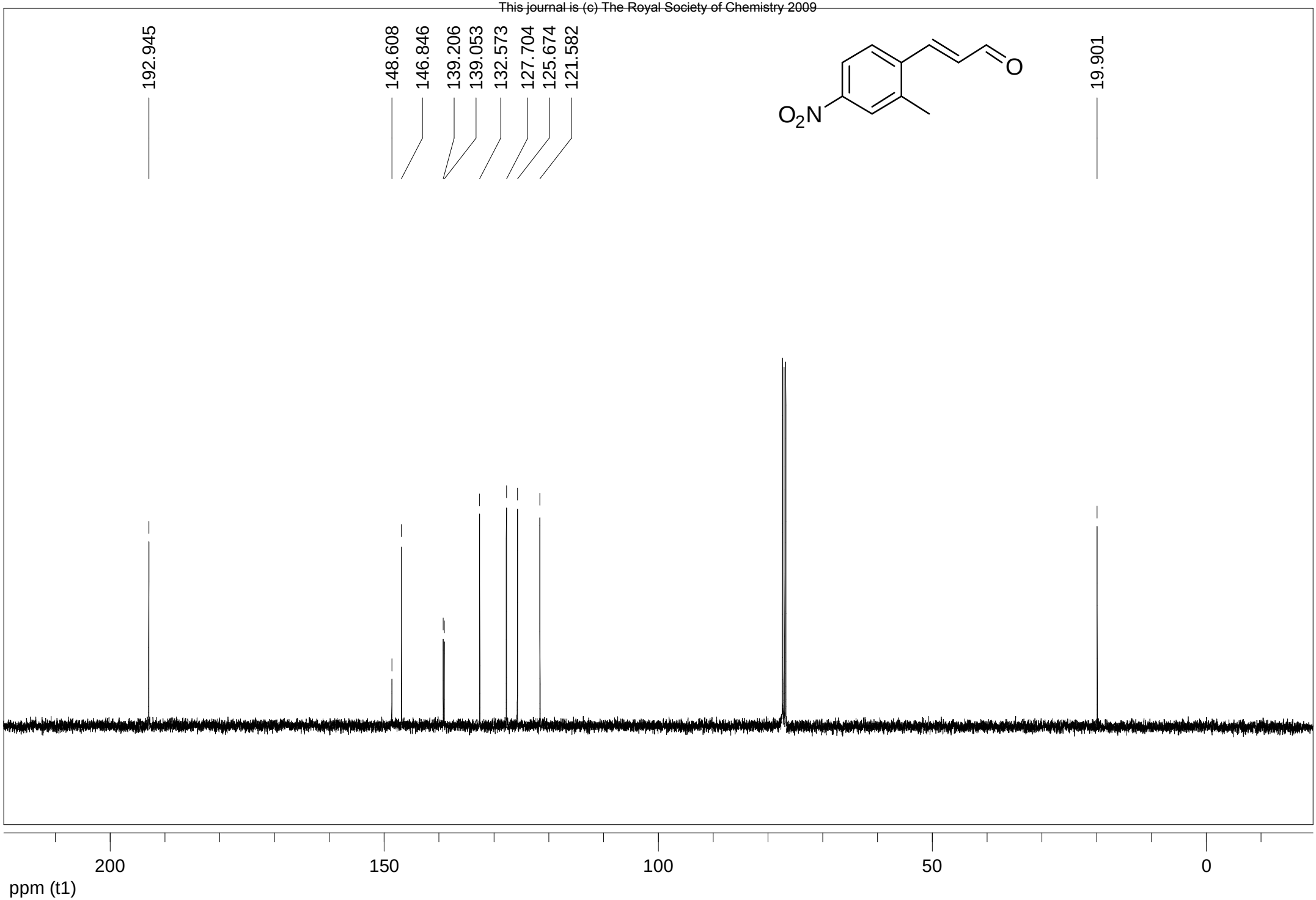

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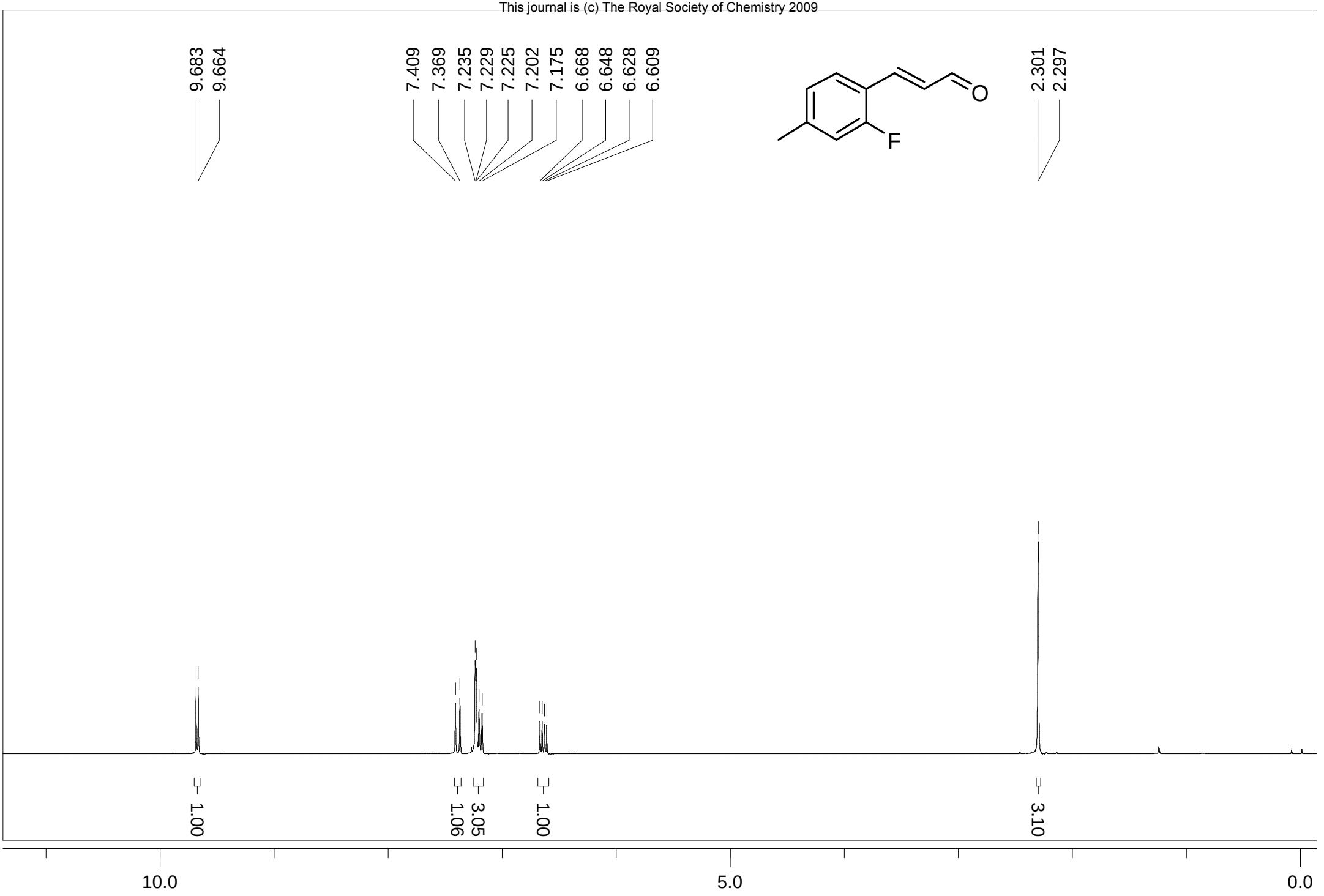

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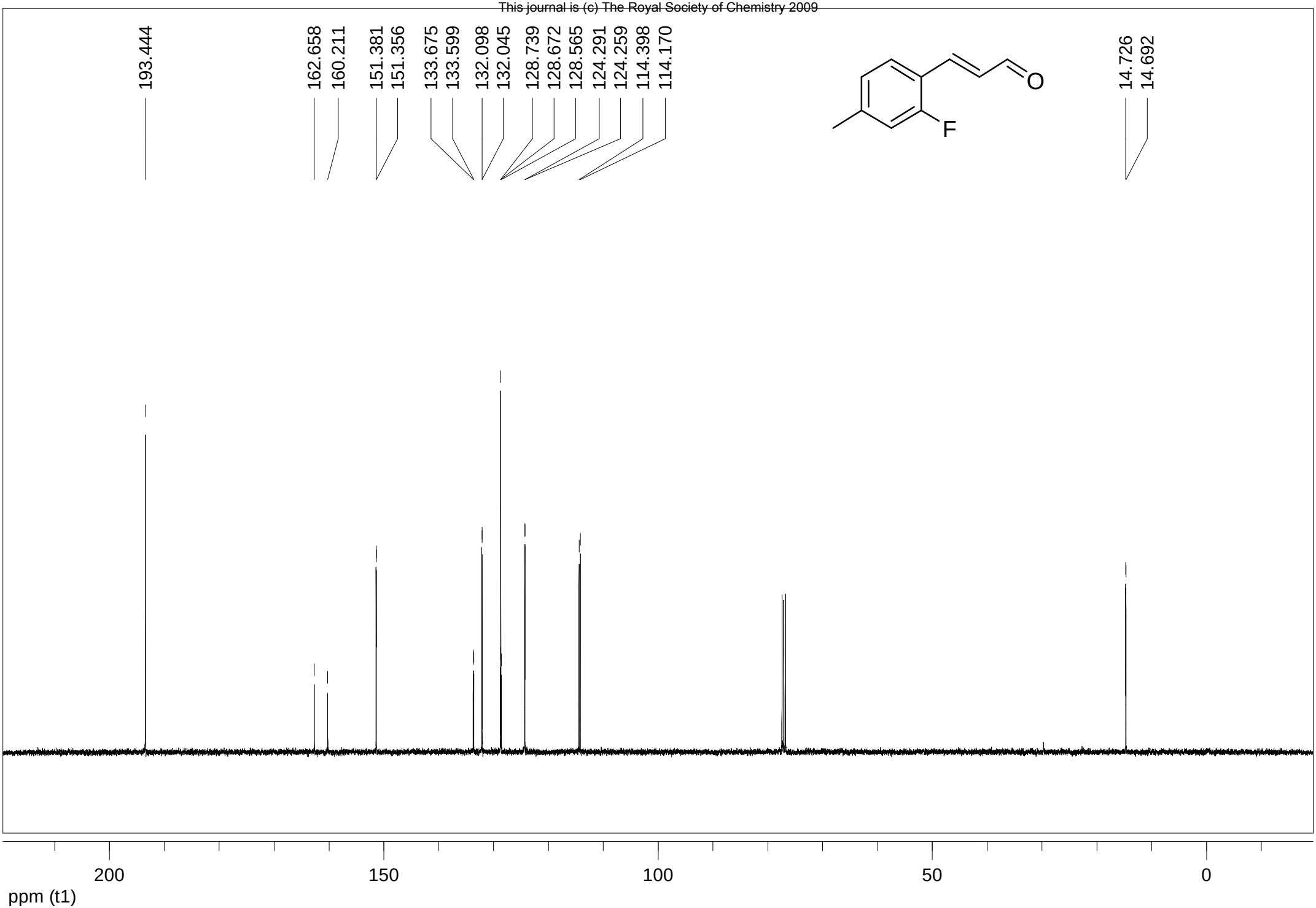

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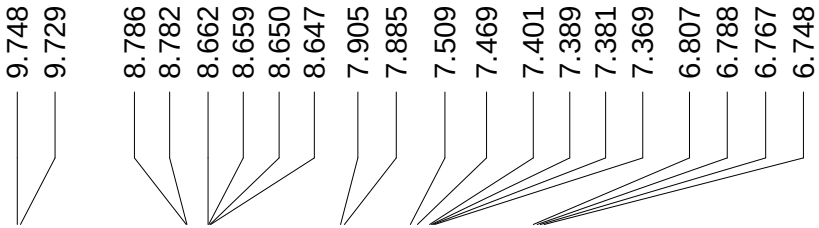

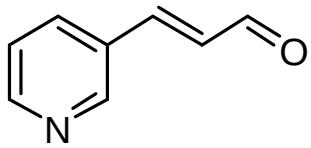

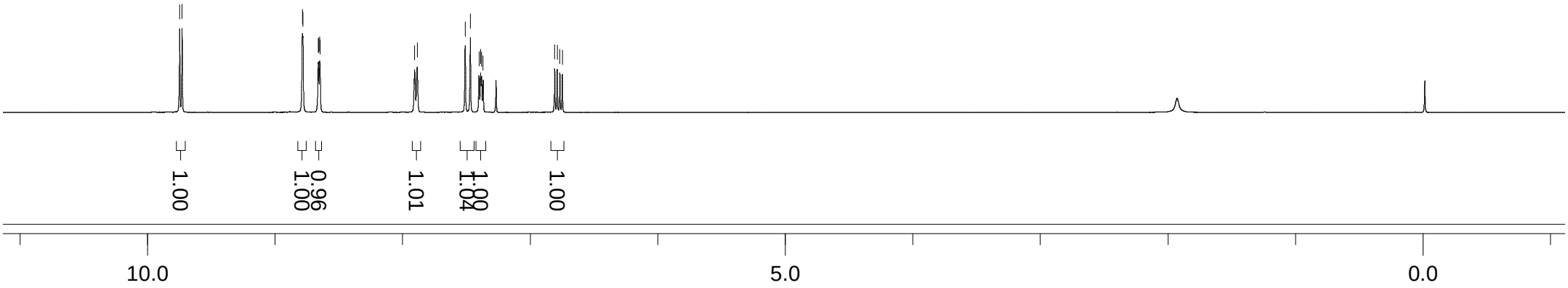

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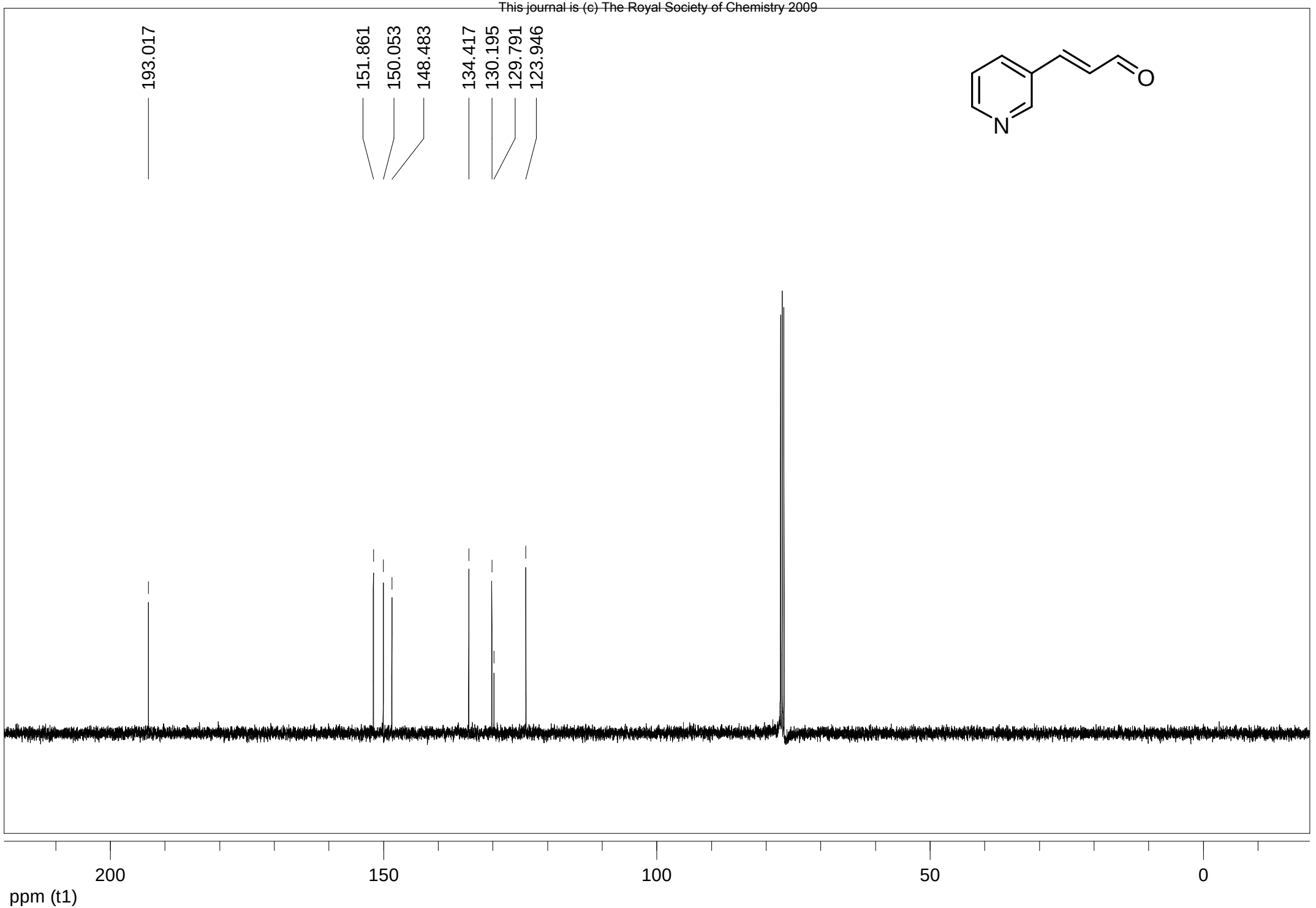

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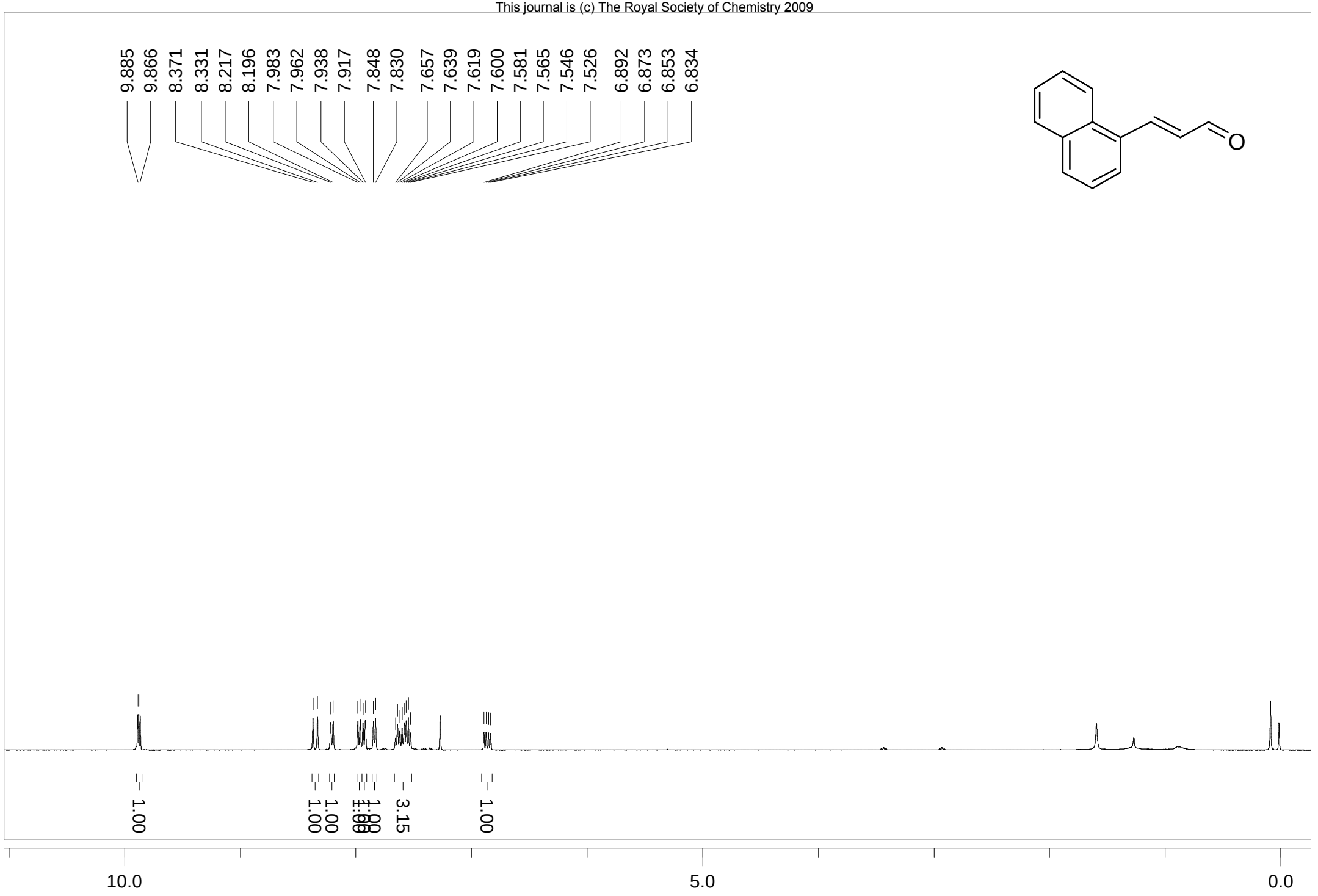

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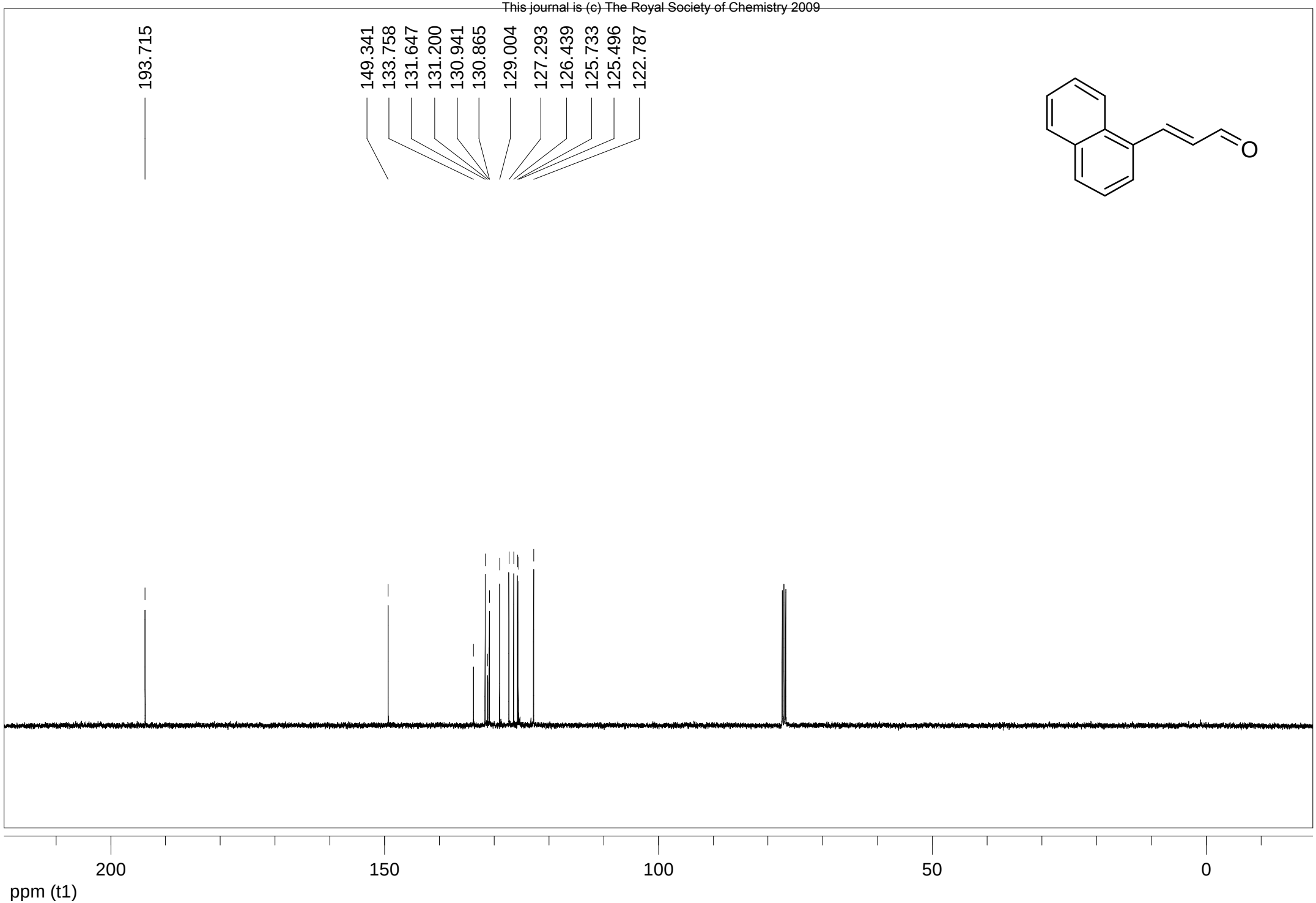

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