Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION

New Families of Enantiopure Cyclohexenone *cis*-Diol, *o*-Quinol Dimer and Hydrate Metabolites from Dioxygenase-catalysed Dihydroxylation of Phenols

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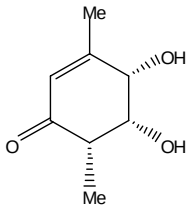
General Procedure

^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance DPX-300 and DPX-500 instruments. Chemical shifts (δ) are reported in ppm relative to $SiMe_4$ and coupling constants (J) are given in Hz. Mass spectra were run at 70 eV, on a VG Autospec Mass Spectrometer, using a heated inlet system. Accurate molecular weights were determined by the peak matching method, with perfluorokerosene as the standard. CD spectra were recorded in spectroscopic grade acetonitrile using a JASCO J-720 instrument. A PerkinElmer 341 polarimeter was used for optical rotation ($[\alpha]_D$) measurements (*ca.* 20 ºC, 10^{-1} deg cm^2 g^{-1}). Flash column chromatography and preparative layer chromatography (PLC) were performed on Merck Kieselgel type 60 (250 - 400 mesh) and $PF_{254/366}$ respectively. Merck Kieselgel type $60F_{254}$ analytical plates were employed for TLC. Phenol substrates **1b**, **1c**, **1d**, and **1f**, 3-methylcatechol **2c** and (-)-(*S*)-camphanic chloride were purchased from Aldrich and used as received.
Small scale (0.2-4.00 g) shake flask biotransformations, with the whole cells of *P. putida* UV4 (TDO), were performed using methods described earlier[1,2] for non-phenolic aromatic substrates. The biotransformation conditions were not optimised for the phenol substrates used in this study. The aq. culture medium, obtained after the biotransformation, was concentrated under reduced pressure at *ca.* 40 ºC, the concentrate repeatedly extracted (EtOAc), and the extract concentrated under reduced pressure to give the crude mixture of bioproducts. ^{1}H NMR spectra of the bioproduct mixtures were routinely recorded, before further purification. The bioproducts were separated either by flash column chromatography and/or PLC. Catechols **2d** and **2f** isolated during the study showed identical physical and spectral characteristics to those reported.[3-5] The enantiomeric excess (ee) values of metabolites **6b$_R$**, **6c$_S$**, **6d$_R$** and **6f$_S$** were indirectly estimated from NMR spectroscopic analysis of their boronate derivatives. (-)-(*S*)- and (+)-(*R*)-2-(1-Methoxyethyl)benzene boronic acids were synthesised and used according to the literature method.[6,7]

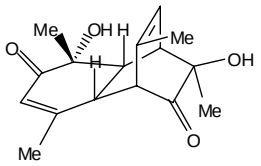
Biotransformations of phenols and other substrates using *P. putida* UV4

(i) Substrate 2,5-dimethylphenol (*p*-xylenol) 1d

The crude mixture of bioproducts (2.3 g) from substrate **1d** (1.2 g), on separation / purification by PLC (EtOAc/hexane, 3:2, two elutions), gave three compounds. These were identified as cyclohexenone *cis*-diol **6d$_R$**, *o*-quinol dimer **11d** and catechol **2d**.



(4*S*,5*R*,6*S*)-4,5-Dihydroxy-3,6-dimethylcyclohex-2-enone 6d$_R$
Enone *cis*-diol **6d$_R$** was obtained as a white crystalline solid (0.256 g, 17%), m.p. 134-36 ºC (EtOAc/hexane); R_f (0.29, EtOAc/hexane, 3:1); ee ≥ 98%; $[\alpha]_D$ + 94 (*c* 1.05, in MeOH); HRMS (EI): Found 156.0785. requires $C_8H_{12}O_3$156.0786; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.94 (1H, dq, J=3.1, 1.3 Hz, 2-H), 4.45 (1H, m, J= 3.1, 3.5, 9.3 Hz, 4-H), 4.25 (1H, m, J = 3.5, 2.4 Hz, 5-H), 2.71 (1H, d, J = 9.3 Hz, OH), 2.57 (1H, dq, J = 2.4, 7.0 Hz, 6-H), 2.26 (1H, d, J = 4.8 Hz, OH), 2.05 (3H, d, J = 1.3 Hz, Me), 1.26 (3H, d, J= 7.0 Hz, Me); ^{13}C NMR (125 MH_Z, $CDCl_3$) δ 199.1, 159.0, 127.2, 76.3, 72.2, 47.0, 20.5, 11.7; IR(KBr) ν_{max}/cm^{-1} 1646 (α,β unsaturated ketone); CD λ 209 nm ($\Delta\varepsilon$ -13.23), λ 237 nm ($\Delta\varepsilon$ +10.00).



(1*R*,2S,3*R*,7*S*,8*S*,10*R*)-3,10-Dihydroxy-3,6,10,12-tetramethyltricyclo[6.2.2.0^{2,7}]-dodeca-5,11-diene-4,9-dione 11d

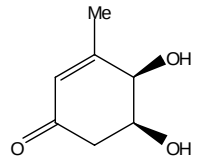
Bis-ketol **11d** was obtained as colourless plates (0.092 g, 7%), m.p. 202-04 ºC (MeOH); (lit.[8] m.p. 190-91 ºC); R_f (0.25, EtOAc/hexane, 1:1); ee ≥ 98%; $[\alpha]_D$ +62.0 (*c* 0.58, in $CHCl_3$) (lit[8] $[\alpha]_D$ +45.7); HRMS (EI): Found 276.1363. requires $C_{16}H_{20}O_4$ 276.1361; ^{1}H-NMR (500 MH_Z, $CDCl_3$) δ 6.02 (1H, br s, 5-H), 5.80 (1H, dq, *J* = 3.4, 1.6 Hz, 11-H), 4.0 (1H, br s, OH), 3.32 (1H, m, *J* = 3.4, 6.6 Hz, 7-H), 3.15 (3H, m, 1-H, 2-H and 8-H), 2.24 (1H, br s, -OH), 2.02 (3H, d, *J* = 1.2 Hz, Me), 1.60 (3H, d, *J* = 1.6, Me), 1.30 (3H, s, Me), 1.25 (3H, s, Me); ^{13}C NMR (125 MH_Z, $CDCl_3$) δ 212.8, 201.4, 156.4, 136.5, 128.3, 124.9, 73.2, 73.0, 56.9, 44.8, 44.2, 41.1, 32.0, 25.9, 22.4, 21.5. Compound **11d** showed identical physical and spectroscopic characteristics to those reported.[8]

3,6-Dimethyl-2,3-dihydroxybenzene 2d

Catechol **2d** was isolated as a white crystalline solid (0.0125 g, 9%), m.p.101-102 ºC; R_f(0.55, EtOAc/hexane, 2:3). It showed identical physical and spectroscopic characteristics to those reported.[3,4]

(ii) Substrate 3-methylphenol (*m*-cresol) 1c

An ethyl acetate solution of the crude mixture of bioproducts , obtained from substrate **1c** (0.75 g), was purified through a silica gel column. The ethyl acetate fraction collected was concentrated. The residue, on the purification by PLC (EtOAc), gave two compounds which were identified as cyclohexenone *cis*-diol **6c$_S$** and 3-methylcatechol **2c** (0.034 g, 4%).

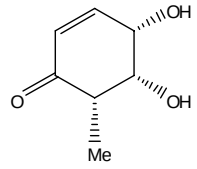


(4*R*,5*S*)-4,5-Dihydroxy-3-methylcyclohex-2-enone 6c$_S$

Colourless crystalline solid (0.146 g, 15%), m.p. 80-81 ºC (EtOAc/Et_2O); R_f (0.35, EtOAc); ee ≥ 98%; $[\alpha]_D$ −115 (*c* 1.00, in MeOH); HRMS (EI): Found 142.0632. requires $C_7H_{10}O_3$ 142.0630; ^{1}H-NMR (500 MH_Z, $CDCl_3$) δ 5.93 (1H, s, 2-H), 4.33 (1H, m, 4-H), 4.28 (1H, ddd, *J* = 6.7, 4.6, 3.6 Hz, 5-H), 3.37 (2H, m, 2 x OH), 2.74 (1H, dd, *J* = 6.7, 16.3 Hz, 6-H), 2.57 (1H, dd, *J* = 4.6, 16.3 Hz, 6′-H) 2.09 (3H, s, Me) ^{13}C NMR (125 MH_Z, $CDCl_3$) δ 195.2, 157.6, 125.2, 68.3, 67.1, 40.5, 19.2; IR(KBr) ν_{max}/cm^{-1} 1637 (α,β unsaturated ketone); CD λ 209 nm ($\Delta\varepsilon$ +5.82), λ 237 nm ($\Delta\varepsilon$ −8.73).

(iii) Substrate 2-methylphenol (*o*-cresol) 1b

The crude mixture of bioproducts obtained from substrate **1b** (2 x 1.5 g) was subjected to flash column chromatography with increasing percentage of EtOAc in hexane. The fractions collected with EtOAc/hexane (2:1) were pooled together, evaporated, and the residue purified by PLC (EtOAc/hexane, 3:1) to give cyclohexenone *cis*-diol **6b$_R$**.

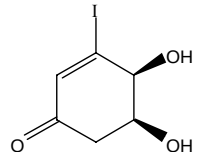


(4*S*,5*R*,6*S*)-4,5-Dihydroxy-6-methylcyclohex-2-enone 6b$_R$

Colourless crystalline solid (0.041 g, 1%), m.p. 128-30 ºC (EtOAc/hexane); R_f(0.32, EtOAc/hexane, 3:1); ee ≥ 98%; $[\alpha]_D$ +223 (*c* 0.48, in MeOH); HRMS (EI): Found 142.0624. requires $C_7H_{10}O_3$ 142.0630; ^{1}H-NMR (500 MH_Z, $CDCl_3$) δ 6.66 (1H, ddd, *J* = 10.3, 4.5, 2.5 Hz, 3-H), 6.05 (1H, dd, *J* = 10.3, 2.5 Hz, 2-H), 4.6 (1H, m, *J* = 4.5, 2.5 Hz, 4-H), 4.27 (1H, m, *J* = 4.5, 2.2 Hz, 5-H), 2.83 (1H, br s, OH), 2.58 (1H, dq, *J* = 2.2, 6.9 Hz, 6-H), 2.37 (1H, br s, OH), 1.27 (3H, d, *J* = 6.9 Hz, Me); ^{13}C NMR (75 MH_Z, $CDCl_3$) δ 202.7, 151.4, 130.2, 77.6, 71.5, 48.0, 12.3; IR(KBr) ν_{max}/cm^{-1} 1668 (α,β unsaturated ketone); CD λ 200 nm ($\Delta\varepsilon$ −18.05), λ 232 nm ($\Delta\varepsilon$ +16.10).

(iv) Substrate 3-iodophenol 1f

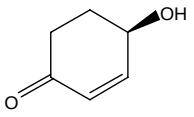
The crude mixture of bioproducts from substrate **1f** (0.8 g), on purification by PLC (EtOAc/hexane, 1:1, two elutions), gave three compounds. These were identified as cyclohexenone *cis*-diol **6f$_S$**, ketol **13** and 3-iodocatechol **2f** [5] (0.067 g, 8%).



(4*S*,5*S*)-4,5-Dihydroxy-3-iodocyclohex-2-enone 6f$_S$

Colourless crystalline solid (0.390 g, 42%), m.p. 98-100 ºC (Me_2CO); R_f (0.21, EtOAc/hexane, 1:1); ee ≥ 98%; $[\alpha]_D$ −38 (*c* 0.91, in MeOH); HRMS (EI): Found 253.9468. requires $C_6H_7IO_3$ 253.9440; ^{1}H-NMR (300 MH_Z, $CDCl_3$ + D_2O) δ 6.91 (1H, d, *J* = 1.3 Hz, 2-H), 4.52 (1H, dd, *J* = 1.3, 3.5 Hz, 4-H), 4.41 (1H, ddd, *J* = 3.5, 3.5, 5.9 Hz, 5-H), 2.82 (1H, dd, *J* = 5.9, 16.7 Hz, 6-H), 2.65 (1H, dd, *J* = 3.5, 16.7 Hz, 6′-H); ^{13}C NMR (125 MH_Z, $CDCl_3$) δ 192.4, 141.0, 130.0, 73.5, 67.8, 42.4; IR(KBr) ν_{max}/cm^{-1}1644 (α,β unsaturated ketone).

Crystal data for 6f$_S$: $C_6H_7IO_3$, *M* = 254.0, monoclinic, *a* = 6.368(5), *b* = 7.456(6), *c* = 8.308(6) Å, β =100.83(1)^0, *U* = 387.4(5) Å^3, *T* = 298(2) K, Mo-Kα radiation, λ= 0.71073 Å, space group $P2_1$ (no. 4), *Z* = 2, *F*(000) = 240, D_x = 2.178 g cm^{-3}, μ = 4.08 mm^{-1}, Bruker SMART CCD area detector diffractometer, φ/ω scans, 5.0^o < 2θ < 56^o, measured/independent reflections: 3863/1572, R_{int} = 0.021, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecule using the riding model, with isotropic vibration parameters. R_1 = 0.032 for 1545 data with $F_o > 4\sigma(F_o)$, 93 parameters, ωR_2 = 0.091 (all data), GoF = 1.10, Flack *x* = 0.01(5) establishes the absolute configuration as (4*S*,5*S*), $\Delta\rho_{min,max}$ = -0.63/0.71 e Å^{-3}. CCDC reference number 721024.

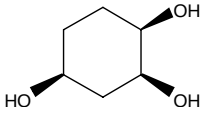


(*R*)-4-Hydroxycyclohex-2-enone 13

Light yellow oil (0.027 g, 7%); R_f (0.48, EtOAc); $[\alpha]_D$ +106.0 (*c* 1.25,in $CHCl_3$) (lit.[9,10] $[\alpha]_D$ +110); ^{1}H NMR (500 MH_Z, $CDCl_3$) δ 6.96 (1H, ddd, J = 10.3, 1.8, 3.6 Hz, 3-H), 5.97 (1H, d, J = 10.3 Hz, 2-H), 4.59 (1H, m, 4-H), 2.51-2.64 (1H, m, *H*CH), 2.32-2.41 (2H, m, H_2C),1.81-2.08 (1H, m, *H*CH). The physical and spectroscopic data of hydroxycyclohexenone **13** were identical with those reported.[9,10]

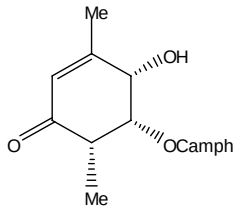
(v) Substrate (4*R*,5*S*)-4,5-dihydroxycyclohex-2-enone 6a$_S$

The crude mixture of metabolites from substrate **6a$_S$** (0.060 g) was purified by flash column chromatography with an increasing percentage of EtOAc in hexane. The fractions collected with EtOAc/hexane (1:1), on evaporation, yielded (*R*)-4-hydroxycyclohex-2-enone **13** (0.012 g, 23%), $[\alpha]_D$ +104.0 (*c* 0.5, in $CHCl_3$). The column was finally eluted with EtOAc/MeOH (9:1). The fraction was evaporated and the residual light yellow semi-solid crystallized to give cyclohexane-1,2,4-triol **14**.



(1*R*,2*S*,4*S*)-Cyclohexane-1,2,4-triol 14

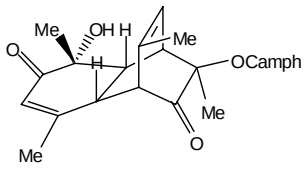
Light yellow transparent crystalline solid (0.026 g, 42%), m.p. 137-38 ºC (EtOAc/EtOH); (lit.[12] m.p. 137-38 ºC); R_f (0.24, $CHCl_3$/MeOH, 7:1); $[\alpha]_D$ +17 (*c* 0.55, in EtOH); (lit.[12] $[\alpha]_D$ +18); HRMS (EI): Found 132.0782. requires $C_6H_{12}O_3$ 132.0786; ^{1}H-NMR (500 MH_Z, CD_3OD) δ 3.79 (1H, m, 1-H), 3.66-3.60 (2H, m, 2-H and 4-H), 191-1.85 (2H, m, H_2C), 1.78-1.72 (1H, m, *H*CH), 1.64-1.60 (2H, m, H_2C), 1.49-1.42 (1H, m, *H*CH); ^{13}C NMR (125 MH_Z, CD_3OD) δ 71.9, 70.1, 69.5, 38.6, 30.1, 28.4. The physical and spectroscopic data of triol **14** were found to be identical with those reported.[11,12]



Monocamphanate ester 7d

A stirred solution of ketodiol **6d$_R$** (0.030 g, 0.19 mmol) in dry pyridine (0.4 mL) was treated with (-)-(*S*)-camphanic chloride (0.05 g, 0.23 mmol) at room temperature. After stirring the reaction mixture for 3 h at room temperature, the pyridine was distilled off under reduced pressure. The residue was extracted with EtOAc (20 mL), the extract washed with aq. 5% $NaHCO_3$ solution (15 mL) and then with water. The extract was dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The crude product, on purification by PLC (EtOAc/hexane, 1:1), separated into two compounds: the more polar ester, monocamphanate **7d** (35%) formed at the 5-hydroxyl, and the less polar diastereoisomer (65%) at the 4-hydroxy positions. Monocamphanate **7d** was obtained as white crystalline solid (0.014 g, 30%); m.p. 156-58 ºC (Et_2O); R_f (0.28, EtOAc/hexane, 1:1); $[\alpha]_D$ +39 (*c* 0.51, in $CHCl_3$); HRMS (EI): Found 336.1554. requires $C_{18}H_{24}O_6$ 336.1573; ^{1}H-NMR (500 MH_Z, $CDCl_3$) δ 5.97 (1H, br s, 2-H), 5.74 (1H, dd, J = 2.6, 2.6 Hz 5-H), 4.76 (1H, br s, 4-H), 2.75 (1H, dq, J = 2.6, 7.0 Hz, 6-H), 2.34 (1H, br s, OH), 2.31 (1H, m, camphanic H), 2.03 (1H, m, camphanic H), 2.03 (3H, d, J = 1.3 Hz, Me), 1.89 (1H, m, camphanic H), 1.67 (1H, m, camphanic H), 1.20 (3H, d, J = 7.0 Hz, Me), 1.10 (3H, s, Me), 0.97 (3H, s, Me), 0.95 (3H, s, Me);^{13}C NMR (125 MH_Z, $CDCl_3$) δ 196.9, 178.4, 168.7, 158.3, 126.9, 91.6, 78.9, 71.1, 55.3, 54.4, 44.5, 31.3, 29.7, 20.1, 17.2, 17.1, 11.7, 10.1.

Crystal data for 7d: $C_{18}H_{24}O_6$, M = 336.4, triclinic, a = 6.581(8), b = 7.123(8), c = 11.041(13)Å, α = 102.33(2), β = 96.496(2), γ = 110.325(2)^0, U = 462.6(9)Å^3, T = 298(2) K, Mo-Kα radiation, λ = 0.71073 Å, space group P1 (no. 1), Z = 1, F(000) = 180, D_x = 1.207 g cm^{-3}, μ = 0.09 mm^{-1}, Bruker SMART CCD area detector diffractometer, φ/ω scans, 3.8 < 2θ < 56.5^o, measured/independent reflections: 3590/3246, R_{int} = 0.021, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecule using the riding model, with isotropic vibration parameters. R_1 = 0.049 for 2834 data with $F_o > 4\sigma(F_o)$, 223 parameters, ωR_2 = 0.126 (all data), GoF = 1.05, $\Delta\rho_{min,max}$ = -0.16/0.18 e Å^{-3}. CCDC reference number 721025. The absolute configuration was established as (4*S*,5*R*,6*S*) relative to the known configuration (1*S*) of the attached camphanate moiety.



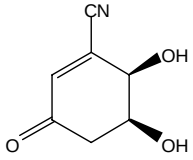
Monocamphanate ester 12d

o-Quinol dimer **11d** (0.015 g, 0.054 mmol) was reacted with (-)-(*S*)-camphanic chloride (0.015 g, .069 mmol) as described in the preceding experiment. The crude product, on purification by PLC (EtOAc/hexane, 2:3), gave monocamphanate ester **12d** as colourless crystals (0.019 g, 77%); m.p. 126-28 ºC (EtOAc/hexane); R_f (0.35, EtOAc/hexane, 2:3); $[\alpha]_D$ -2.2 (*c* 0.43, in $CHCl_3$); HRMS (EI): Found 456.2149. requires $C_{26}H_{32}O_7$ 456.2148; ^{1}H-NMR (500 MH_Z, $CDCl_3$) δ 6.03 (1H, dq, J = 2.3, 1.2 Hz, 5-H), 5.80 (1H, dq, J = 2.2, 1.6 Hz, 11-H), 4.03 (1H, s, OH), 3.86 (1H, dd, J = 2.2, 8.0 Hz, 7-H), 3.47 (1H, dd, J = 2.1, 8.0 Hz, 8-H), 3.29 (1H, dd, J = 2.1, 8.0 Hz, 1-H), 2.59 (1H, dd, J = 2.1, 8.0 Hz, 2-H), 2.47 (1H, m, camphanic H), 2.04 (1H, m,

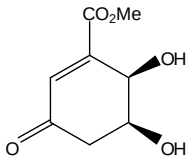
camphanic H), 2.02 (3H, d, J = 1.2 Hz, Me), 1.93 (1H, m, camphanic H), 1.69 (1H, m, camphanic H), 1.63 (3H, d, J = 1.6 Hz, Me), 1.51 (3H, s, Me), 1.27 (3H, s, Me), 1.13 (3H, s, Me), 1.06 (3H, s, Me), 1.03 (3H, s, Me).

Crystal data for 12d: $C_{26}H_{32}O_7$, M = 456.5, monoclinic, a =6.404(1), b = 13.997(3), c = 13.665(2) Å, β = 101.78(1), U = 1199.1(4) Å^3, T = 293(2) K, Mo-Kα radiation, λ =0.71073 Å, space group $P2_1$ (no.4), Z = 2, $F(000)$ = 488, D_x = 1.264 g cm^{-3}, μ = 0.09 mm^{-1}, Bruker P4 diffractometer, ω scans, 4.2° < 2θ < 55°, measured/independent reflections: 3875/3076, R_{int} = 0.019, direct methods solution, full-matrix least squares refinement on F_o^2, anisotropic displacement parameters for non-hydrogen atoms; all hydrogen atoms located in a difference Fourier synthesis but included at positions calculated from the geometry of the molecules using the riding model, with isotropic vibration parameters. R_1 = 0.044 for 2369 data with $F_o > 4\sigma(F_o)$, 306 parameters, ωR_2 = 0.102 (all data), GoF = 1.05, $\Delta\rho_{min,max}$ = -0.18/0.14 e Å^{-3}. CCDC reference number 721026. The absolute configuration was established as (1*R*,2*S*,3*R*,7*S*,8*S*,10*R*) relative to the known configuration (1*S*) of the attached camphanate moiety.

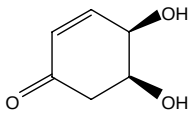
Substitution reactions of (4*S*,5*S*)-4,5-dihydroxy-3-iodocyclohex-2-enone 6f$_S$



(4*S*,5*R*)-4,5-Dihydroxy-3-cyanocyclohex-2-enone 6g$_S$
To a solution of enone *cis*-diol **6f$_S$** (0.100 g, 0.39 mmol) in anhydrous THF (10 mL) were added Bu_3SnCN (0.186 g, 0.59 mmol), $Pd(Ph_3P)_4$ (0.050 g) and Et_3N (125μL). The reaction mixture was refluxed until the starting material had been consumed (*ca*. 18 h). The cooled reaction mixture was loaded onto a column of silica gel and eluted with hexane containing an increasing percentage of EtOAc. The fractions collected with EtOAc/hexane (1:1) were evaporated and the residue purified by PLC (MeOH/$CHCl_3$, 1:19) to give cyclohexenone *cis*-diol **6g$_S$** as a light yellow oil (0.029g, 48%); R_f (0.31, MeOH/$CHCl_3$, 1:19); $[\alpha]_D$=-136 (*c* 0.85, in MeOH); HRMS (EI): Found 153.0433. requires $C_7H_7O_3N$ 153.0426; ^{1}H-NMR (500 MH_Z, CD_3OD) δ 6.44 (1H, d, J = 2.0 Hz, 2-H), 4.48 (1H, dd, J = 2.0, 3.6 Hz, 4-H), 4.18 (1H, ddd, J = 5.0, 7.0, 3.6 Hz, 5-H), 2.61 (2H, m, J = 7.0 Hz, 6-H and 6´-H); ^{13}C NMR (125 MHz, CD_3OD) δ 197.6, 139.6, 134.5, 117.9, 71.1, 69.3, 45.0.



(4*S*,5*R*)-4,5-Dihydroxy-3-carbomethoxycyclohex-2-enone 6h$_S$
To a solution of cyclohexenone *cis*-diol **6f$_S$** (0.070 g, 0.28 mmol) in MeOH (6 mL) were added $Pd(OAc)_2$ (0.013 g) and $NaOAc.3H_2O$ (0.076 g). The mixture was stirred, at room temperature under an atmosphere of carbon monoxide, until the reaction was complete (*ca.* 12 h). The reaction mixture was filtered, the filtrate concentrated, and the crude product purified by PLC (EtOAc/hexane, 3:1). Enone *cis*-diol **6h$_S$** was obtained as a colourless oil (0.034 g, 66%); R_f (0.35, EtOAc/hexane, 3:1); $[\alpha]_D$ -48 (*c* 1.34, in MeOH); HRMS (EI): Found 186.0528. requires $C_8H_{10}O_5$ 186.0522; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.68 (1H, s, 2-H), 4.73 (1H, d, J = 3.5 Hz, 4-H), 4.20 (1H, ddd, J = 8.5, 3.6, 3.6 Hz, 5-H), 3.82 (3H, s, CO_2Me), 2.79 (1H, dd, J = 8.5, 16.5 Hz, 6-H), 2.57 (1H, dd, J = 3.6, 16.5 Hz, 6´-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.8, 166.2, 143.2, 133.6, 67.1, 64.9, 52.7, 41.3.

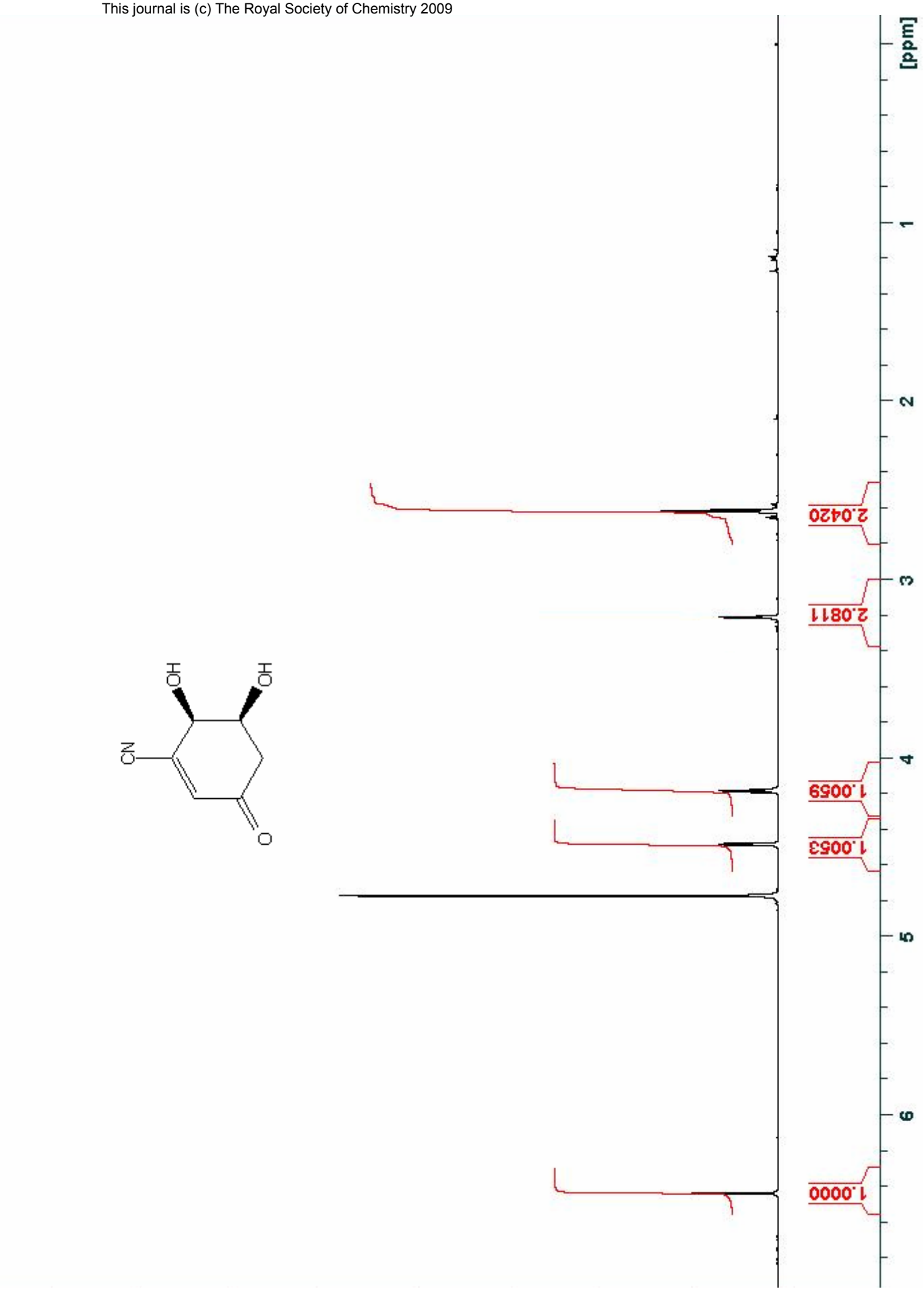


(4*R*,5*S*)-4,5-Dihydroxycyclohex-2-enone 6a$_S$
A solution of cyclohexenone *cis*-diol **6f$_S$** (0.100 g, 0.39 mmol) in MeOH (8 mL), containing Et_3N (65 μL) and 3% Pd/C (0.015 g), was stirred, overnight at room temperature, in an atmosphere of hydrogen. The catalyst was filtered off, the filtrate concentrated and the crude product purified by PLC (EtOAc/hexane, 3:1, two elutions). Enone *cis*-diol **6a$_S$** was obtained as a white crystalline solid (0.041g, 81%); m.p. 72-74 ºC; R_f (0.28, EtOAc); $[\alpha]_D$ -217 (*c* 0.92, in MeOH); HRMS (EI): Found 128.0480. requires $C_6H_8O_3$; 128.0473; ^{1}H-NMR (500 MH_Z, CD_3OD_3) δ 6.73 (1H, m, J = 10.3, 2.9 Hz, 3-H), 5.88 (1H, dd, J = 10.3, 2.1 Hz, 2-H), 4.41 (1H, dd, J = 2.9, 5.3 Hz, 4-H), 4.13 (1H, ddd, J = 5.3, 6.9, 3.7 Hz, 5-H), 2.55 (2H, m, J = 3.7, 5.3 Hz, 6-H and 6´-H); ^{13}C NMR (125 MH_Z, $CDCl_3$) δ 200.4, 152, 130.7, 71.63, 69.0, 45.2; CD λ 205 nm ($\Delta\varepsilon$ +11.80), λ 232 nm ($\Delta\varepsilon$ -14.31).
The physical and spectroscopic data of enone *cis*-diol **6a$_S$** were identical with those reported for the opposite enantiomer.[13]

References

1 D. R. Boyd, N. D. Sharma, S. A. Haughey, M. A. Kennedy, B. T. McMurray, G. N. Sheldrake, C. C. R. Allen, H. Dalton, K. Sproule, *J. Chem. Soc. Perkin Trans. 1*, 1998, 1929.
2 D. R. Boyd, N. D. Sharma, L. V. Modyanova, J. G. Carroll, J. F. Malone, C. C. R. Allen, J. T. G. Hamilton, D. T. Gibson, R. E. Parales, H. Dalton, *Can. J. Chem.,* 2002, **80**, 589.
3 A. Pezzella, L. Lista, A. Napolitano.M. d'Ischia,*Tetrahedron Lett.,* 2005, **46**, 3541.
4 M. W. Baines, D. B. Cobb, R. J. Eden, R. Fielden, J. N. Gardener, A. M. Roe, W. Tertiuk, G. L. Willey, *J. Med. Chem.,* 1965, **8**, 81.
5 K. Venkatesan, P. H. J. Kouwer, S. Yagi, P. Muller, T. M. Swager, *J. Mater. Chem.,* 2008, **18**, 400.
6 K. Burgess, A. M. Porte, *Agnew. Chem. Int. Ed. Engl.,* 1994, **33**, 1182.
7 S. M. Resnick, D. S. Torok, D. T. Gibson, *J. Org. Chem.,* 1995, **60**, 3546.

8 S. Dong, J. Zhu, J. A. Porco, *J. Am. Chem. Soc.,* 2008, **130**, 2739.
9 J. E. Audia, L. Boisvert, A. D. Patten, A. Villalobos, S. J. Danishefsky, *J. Org. Chem.,* 1989, **54**, 3738.
10 A. S. Demir, O. Sesenoglu, *Org. Lett.*, 2002, **4**, 202.
11 G. E. McCasland, M. O. Naumann, L. J. Durham, *J. Org. Chem.,* 1966, **31**, 3079.
12 C. Colas, B. Quiclet-Sire, J. Cleophax, J. M. Delaumeny, A. M. Sepulchre, S. D. Gero, *J. Am. Chem Soc.,* 1980, **102**, 857.
13 N. Ran, D. R. Knop, K. M. Draths, J. W. Frost, *J. Am. Chem Soc.,* 2001, **123**, 10927.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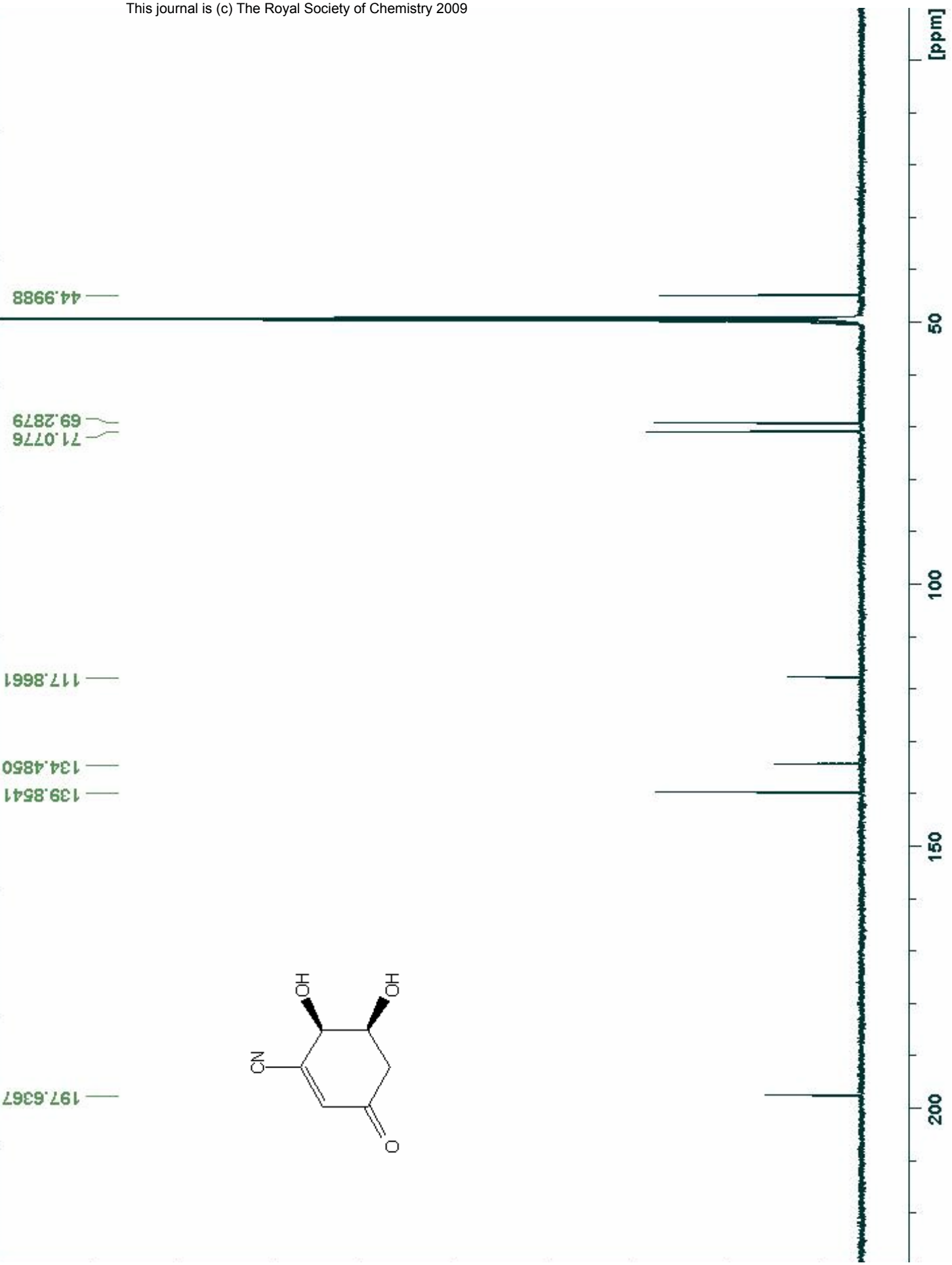
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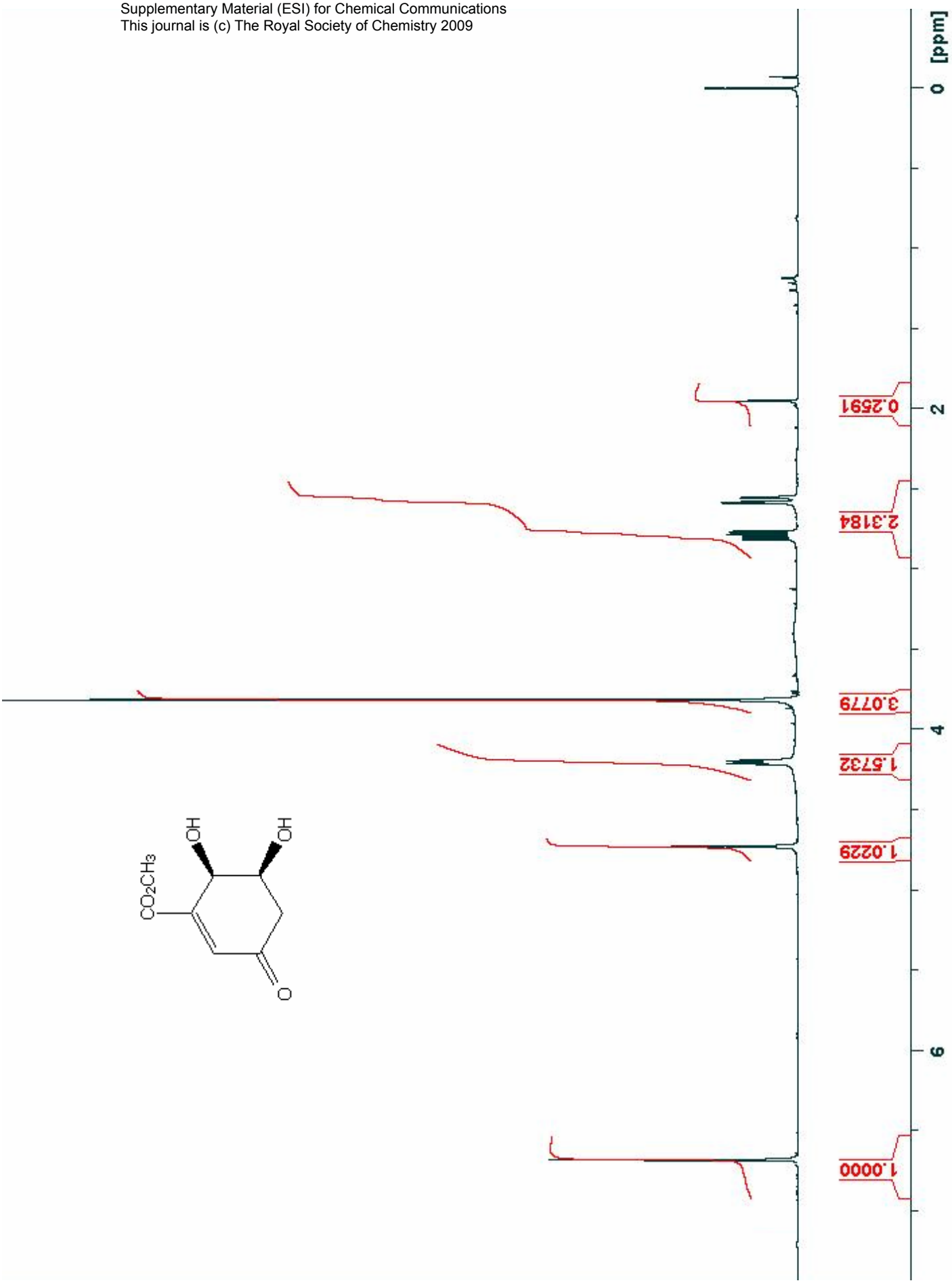
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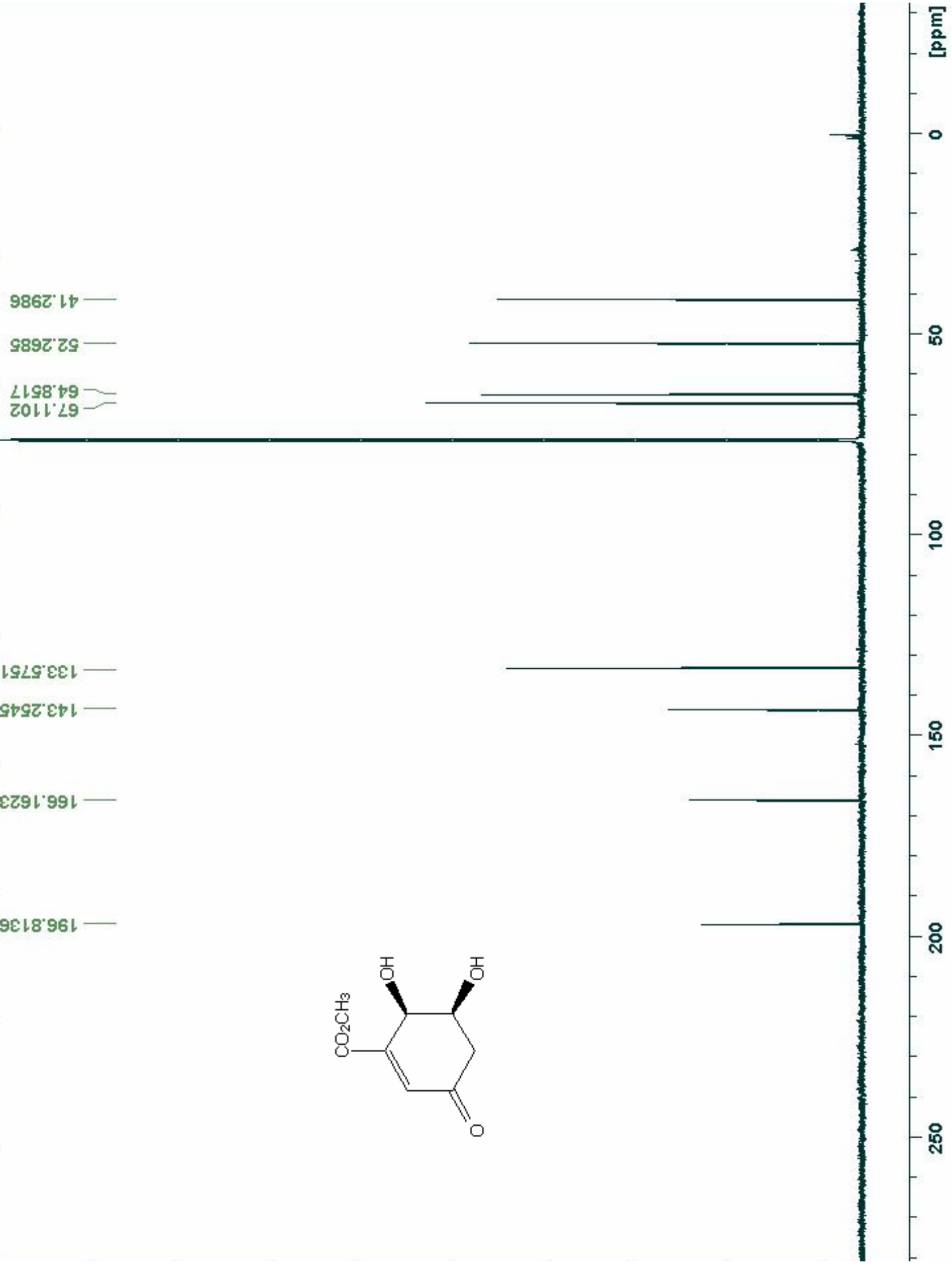
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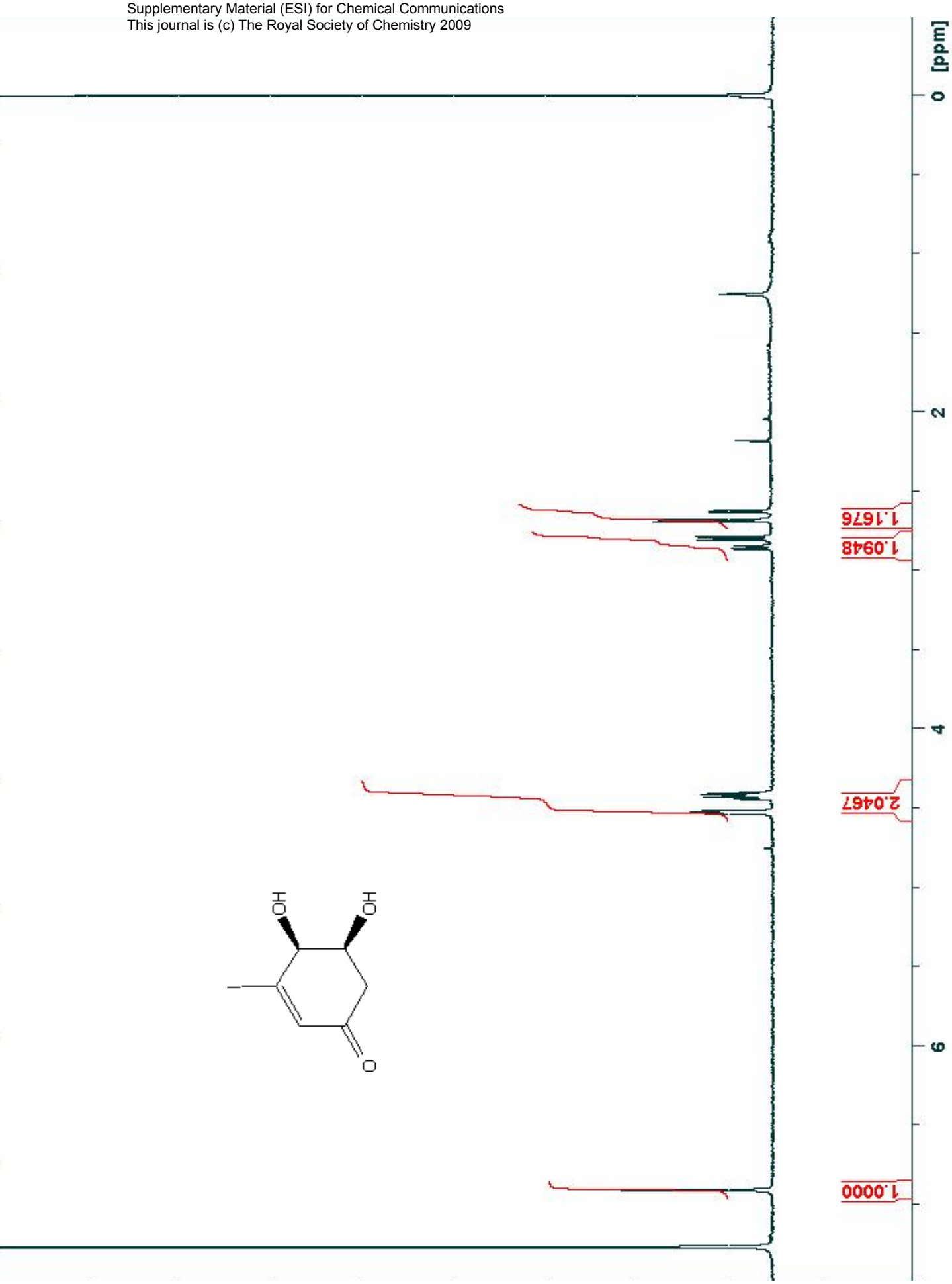
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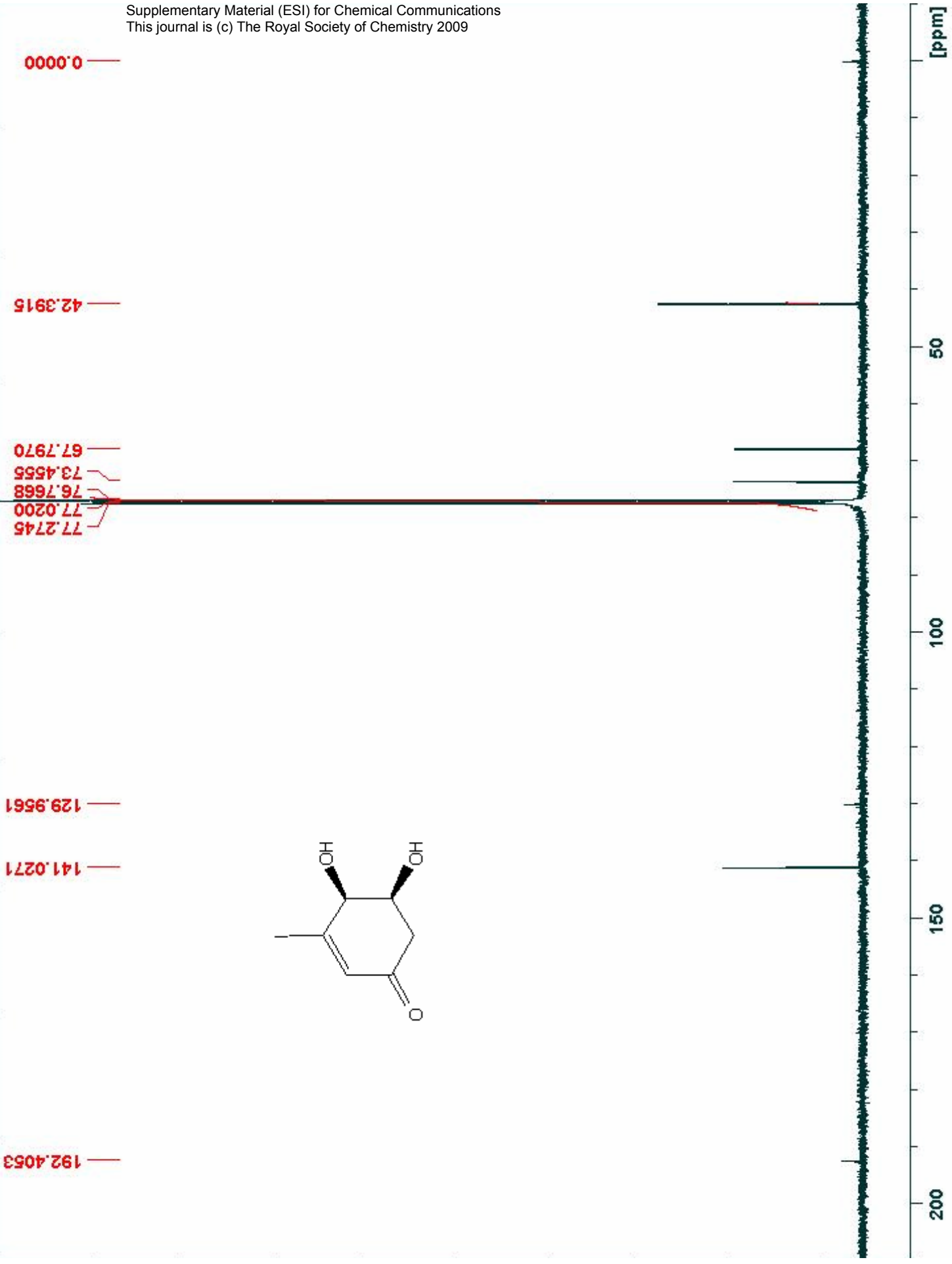
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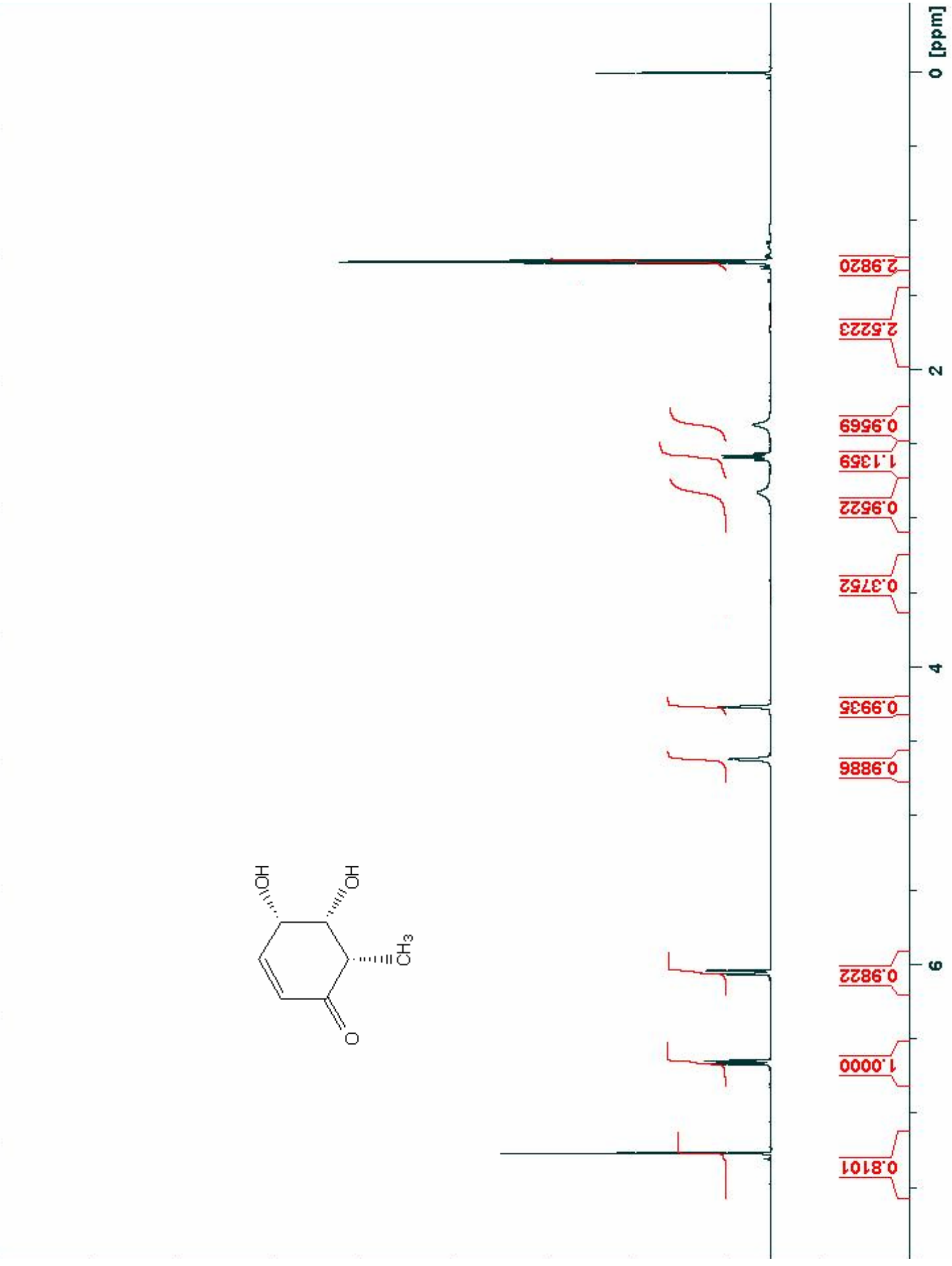
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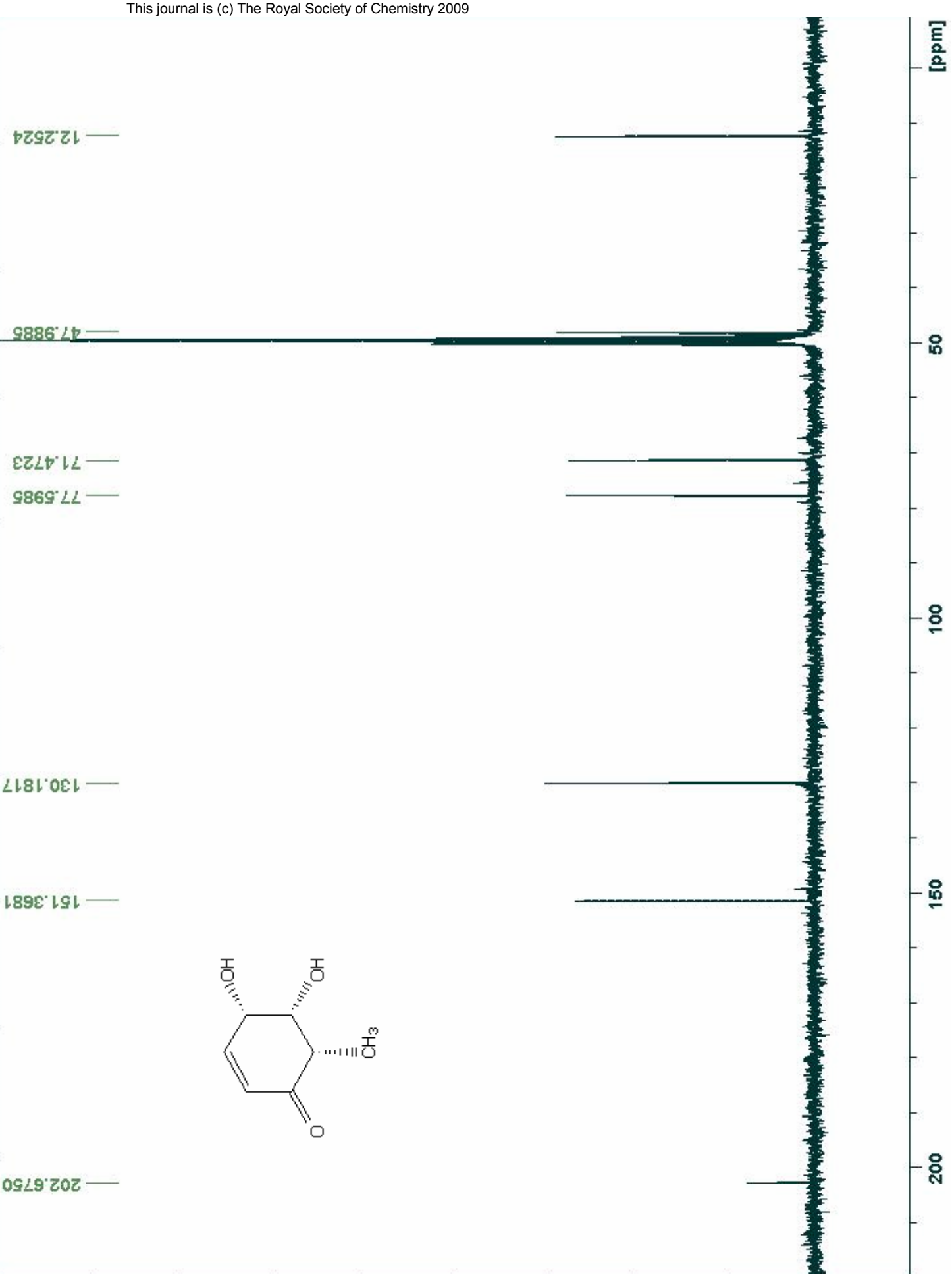
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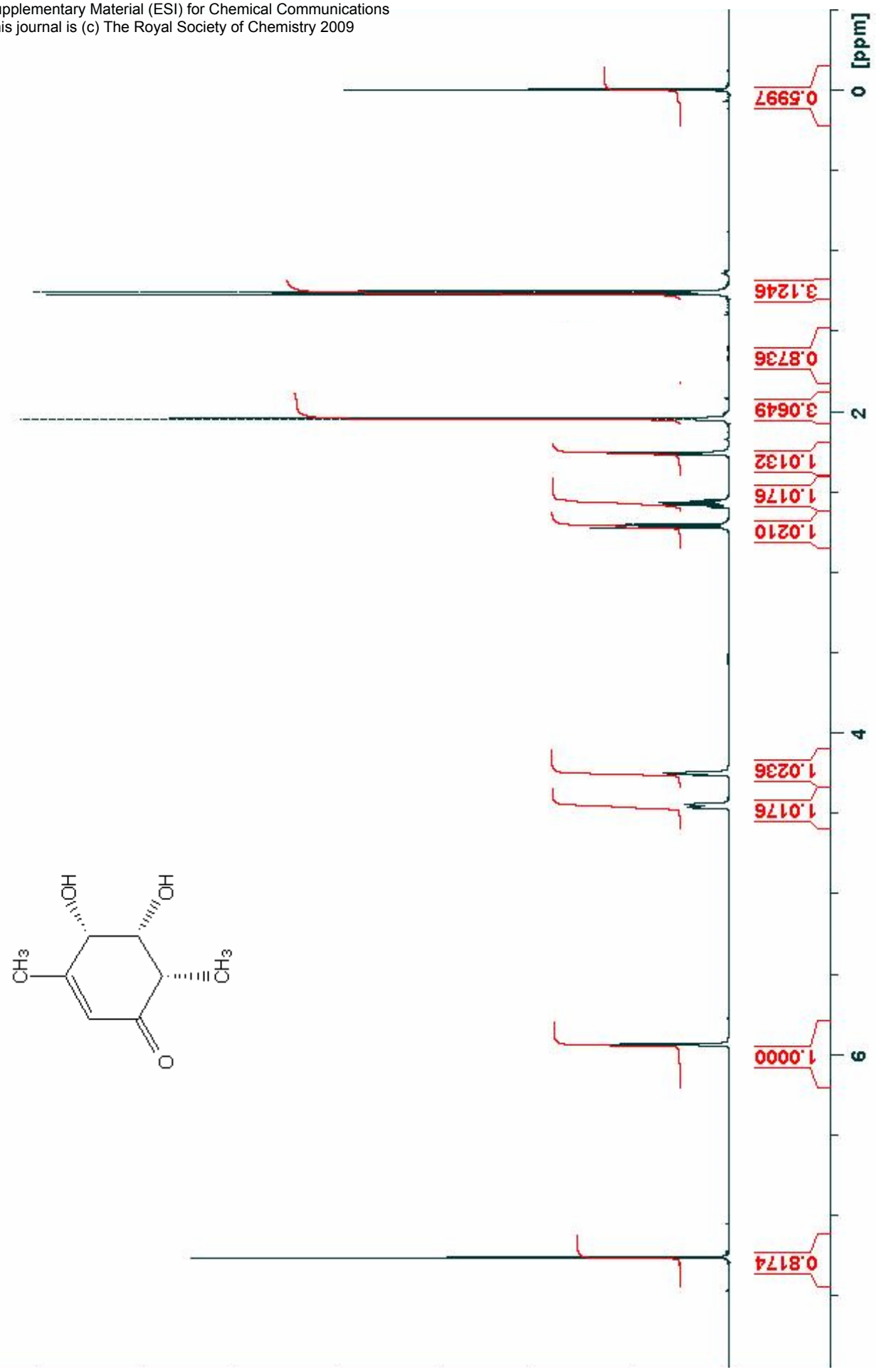
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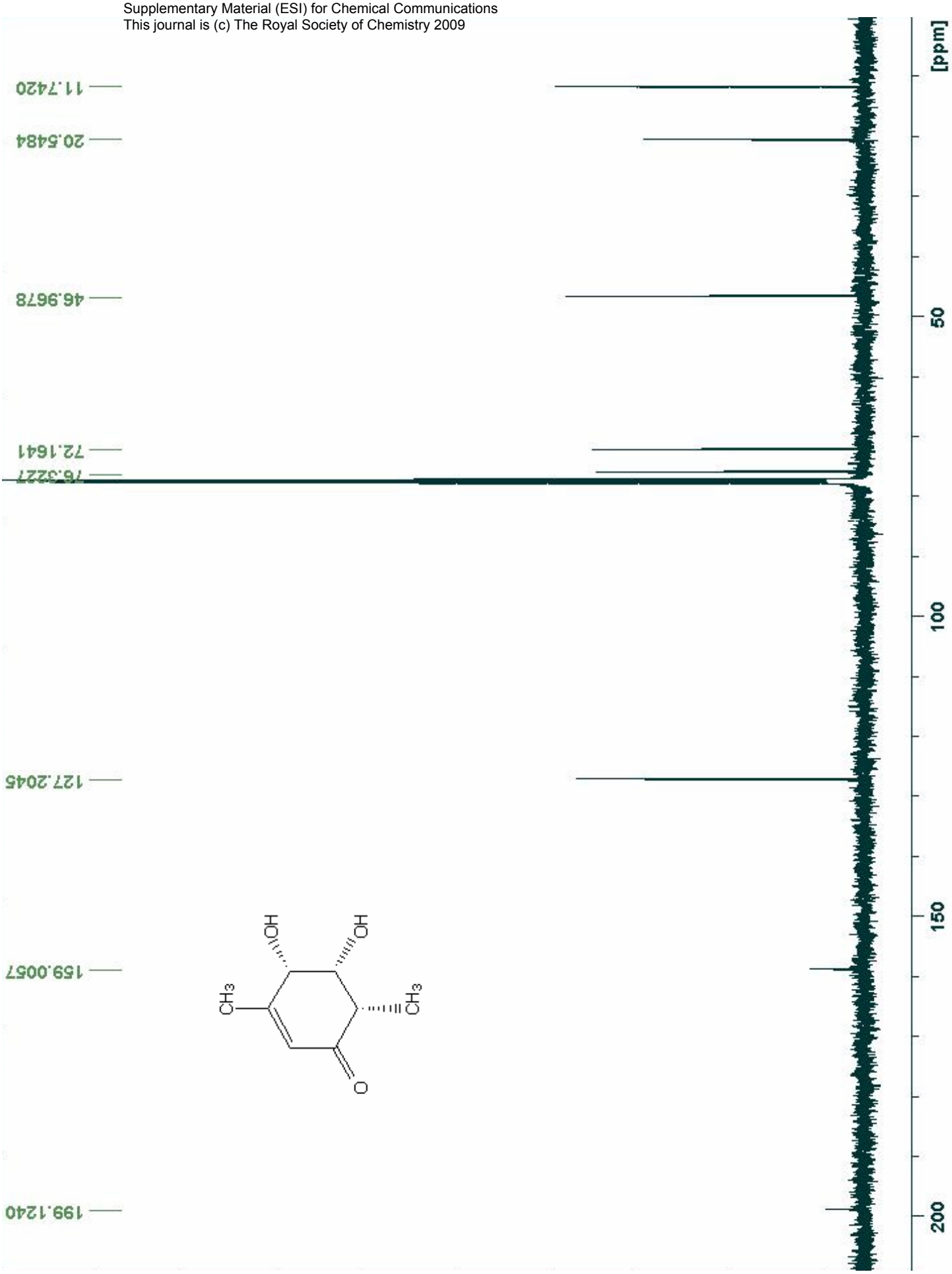
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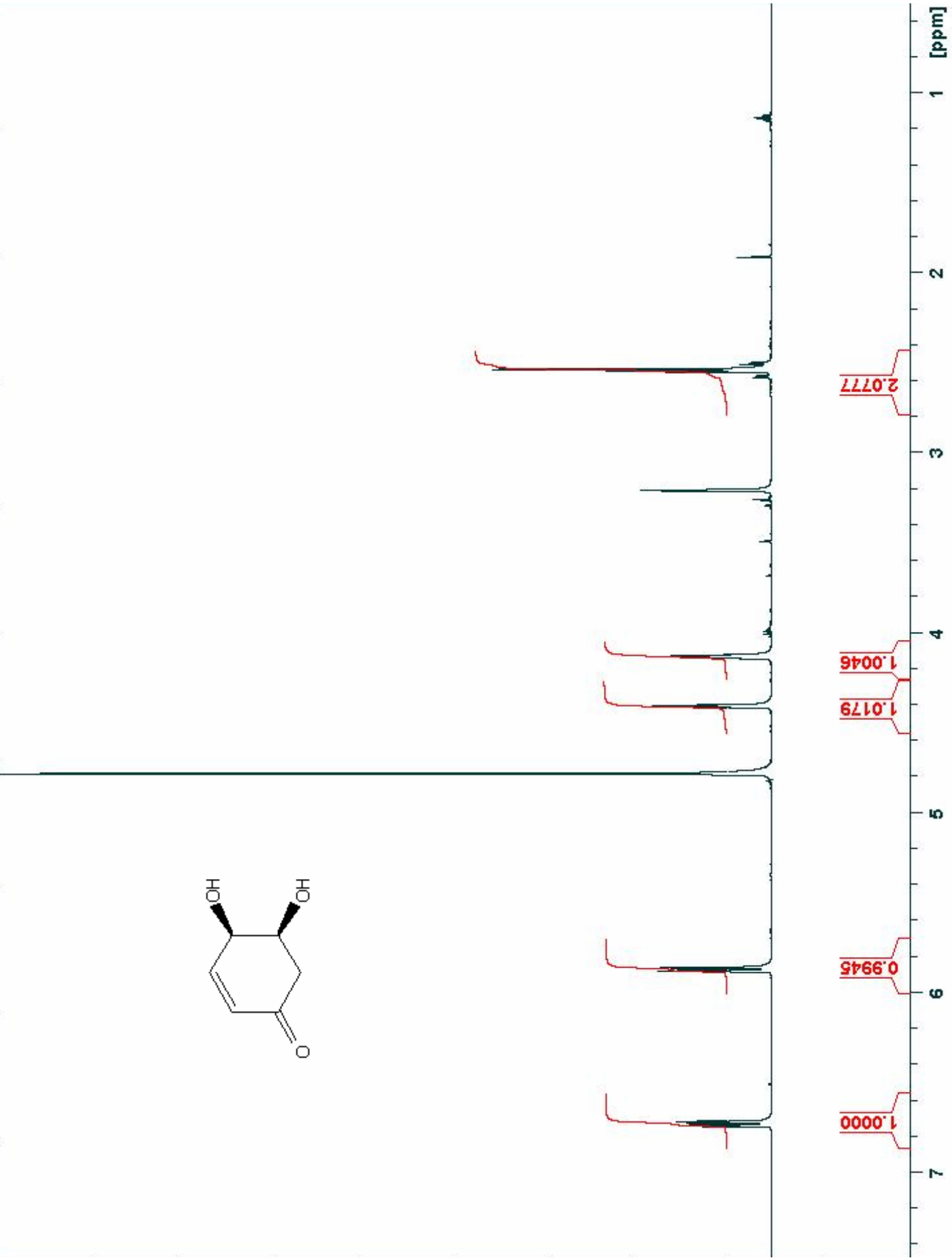
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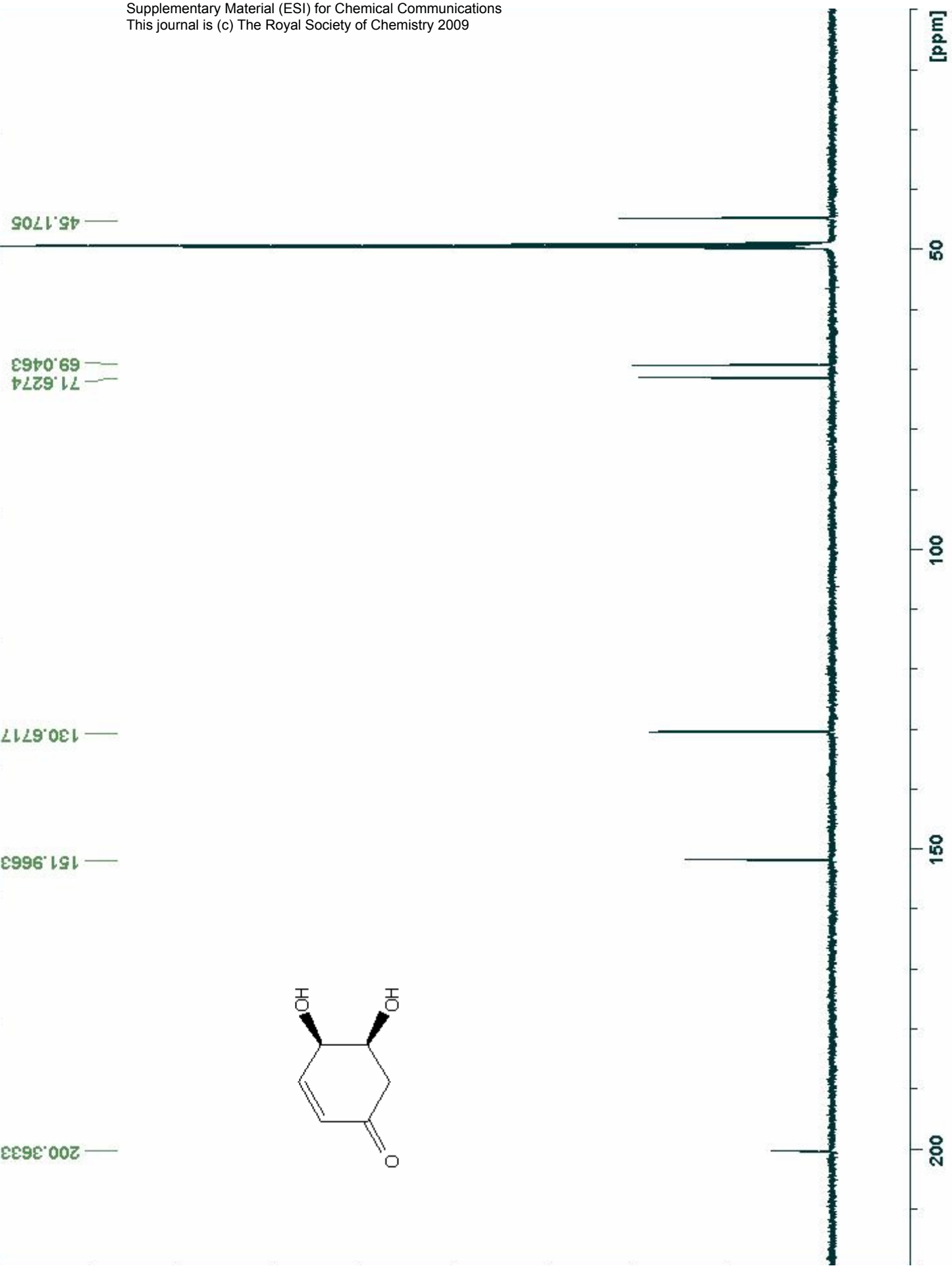
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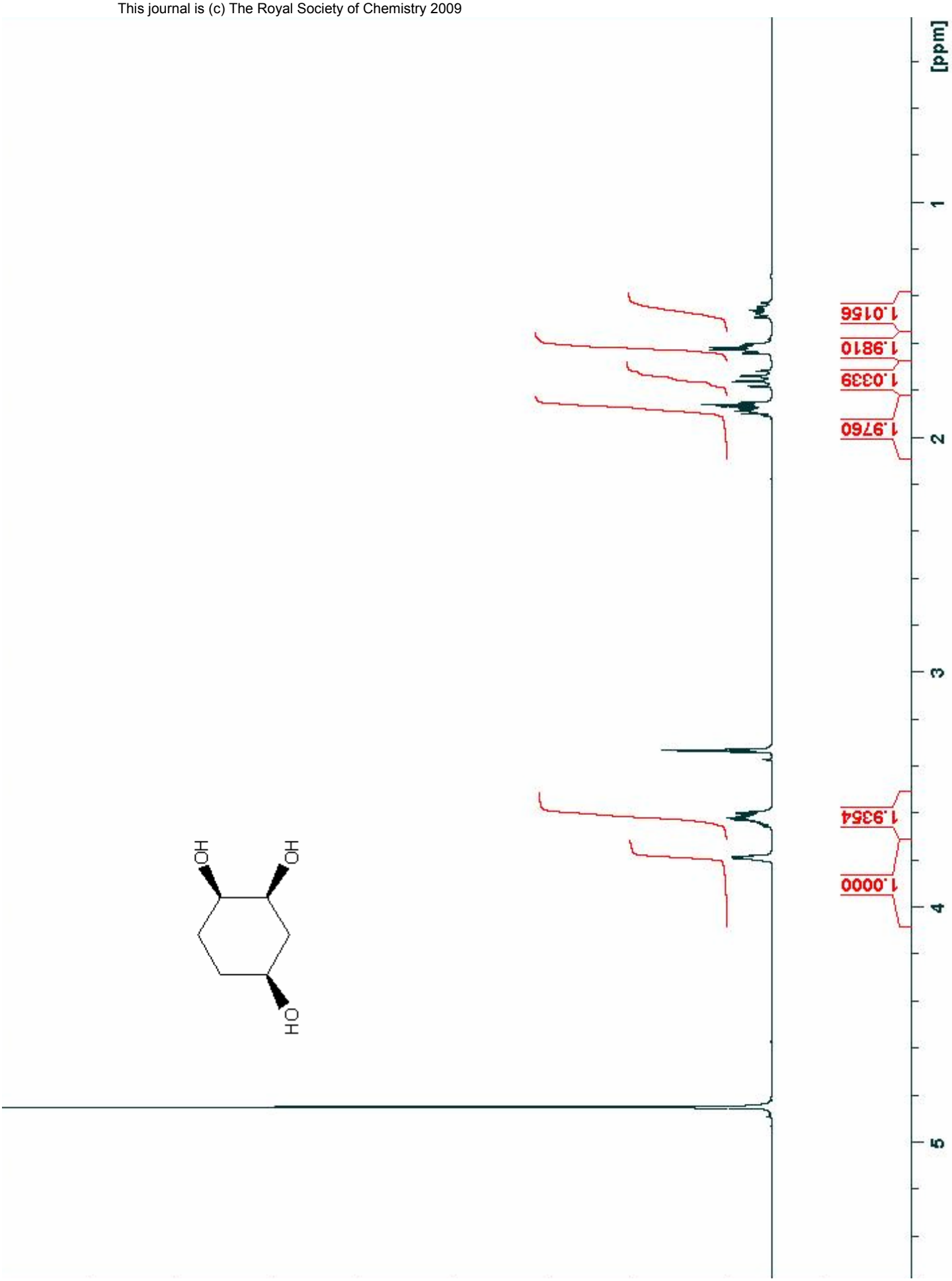
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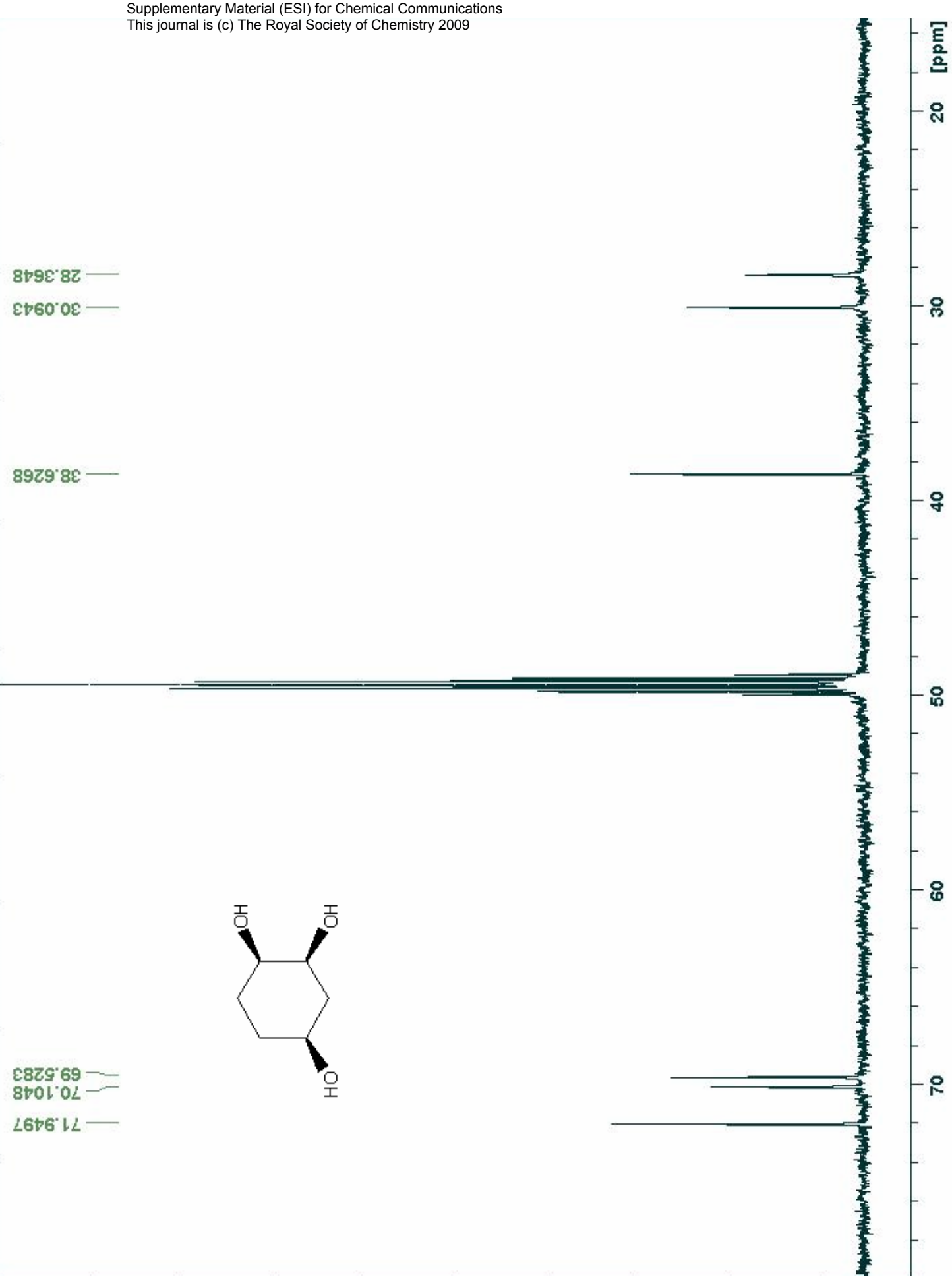
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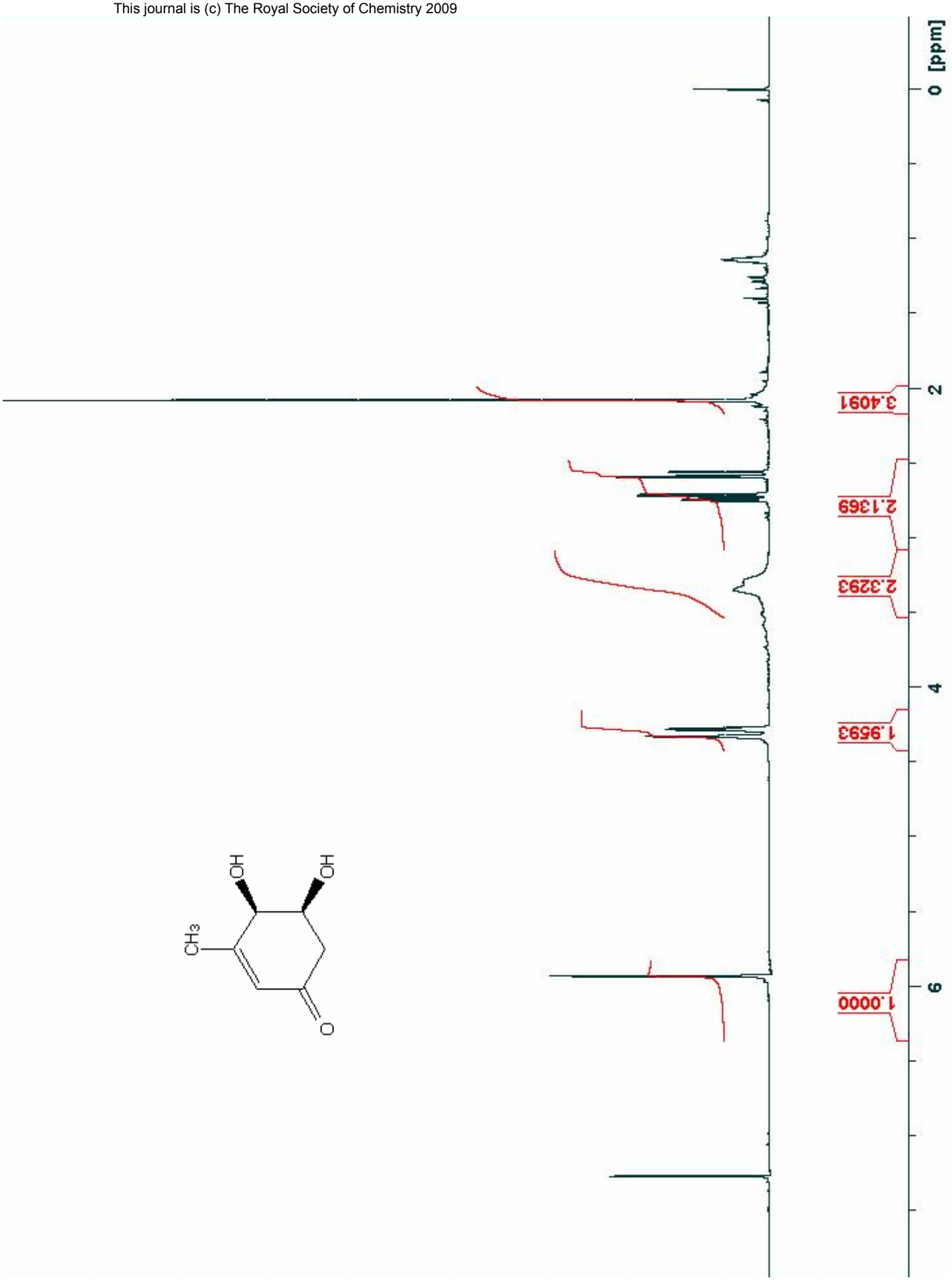
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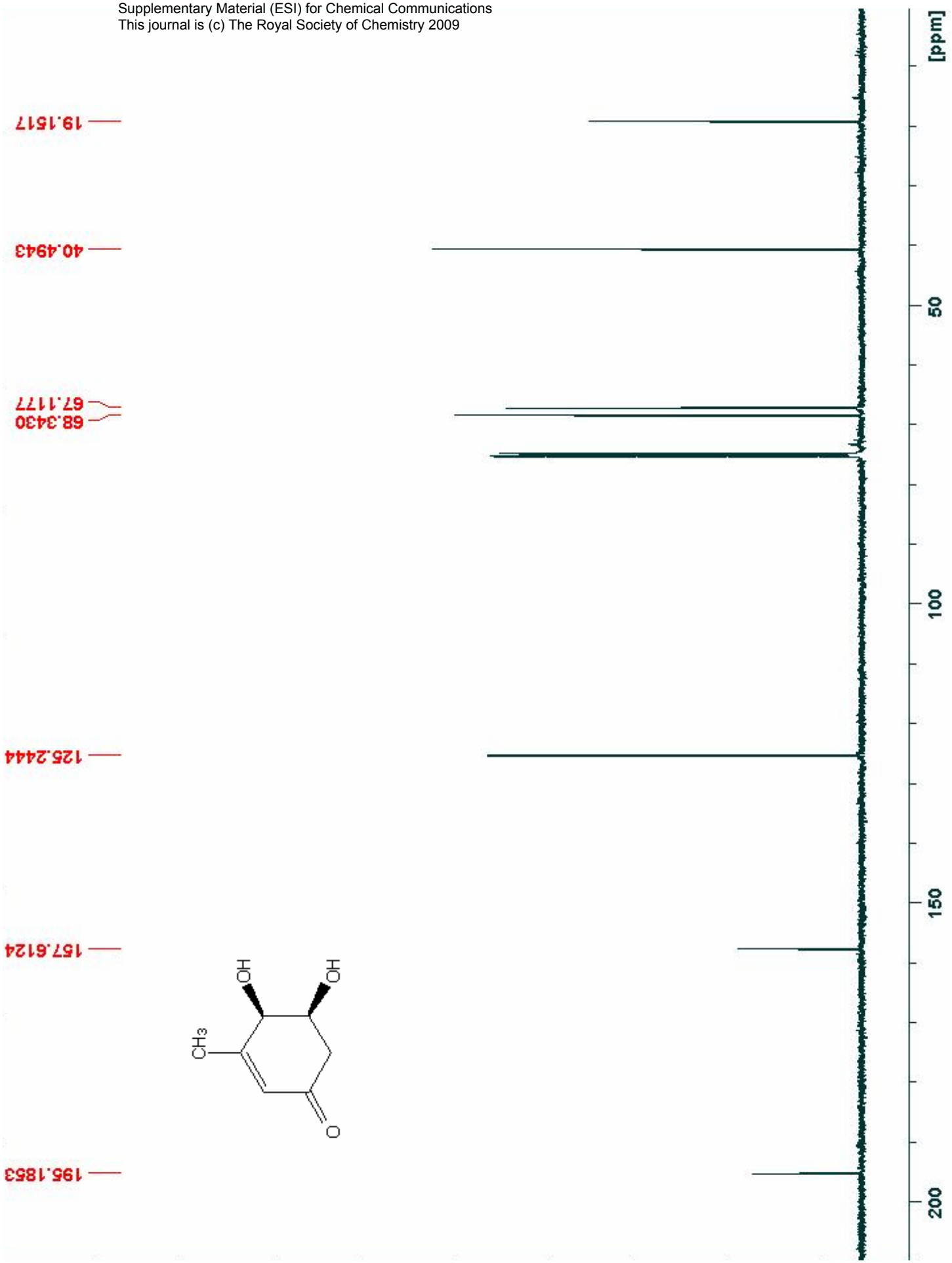
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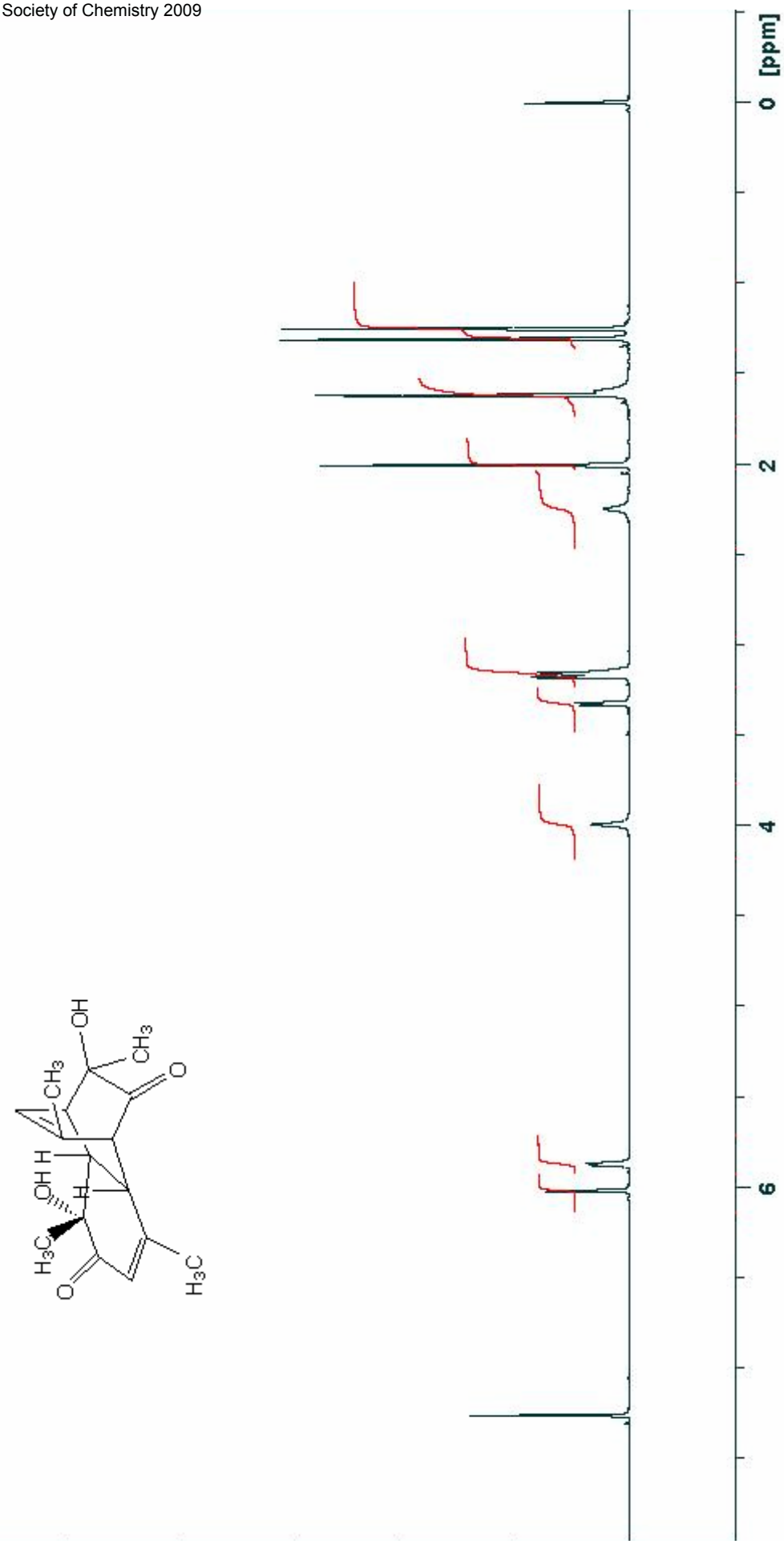
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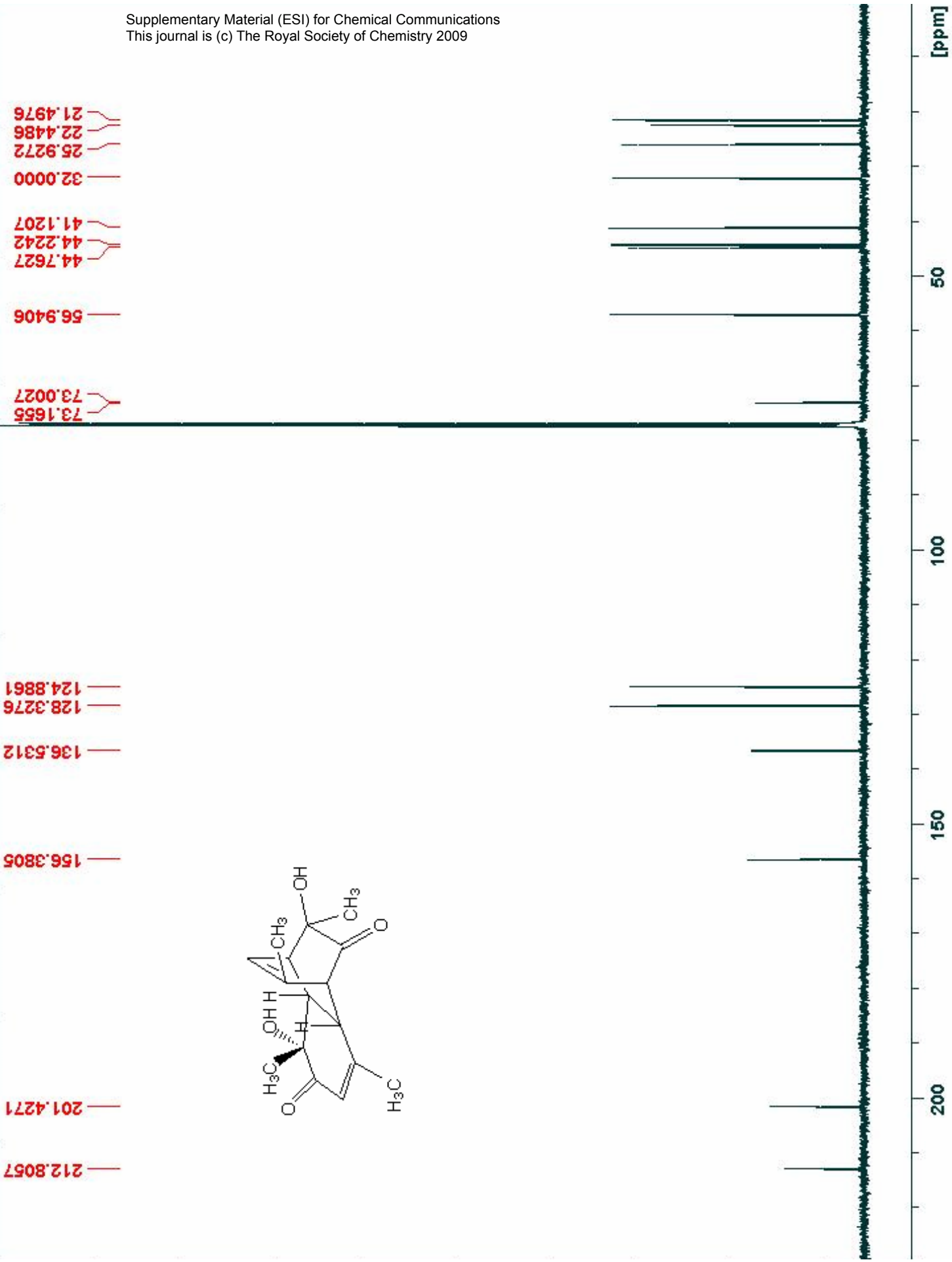
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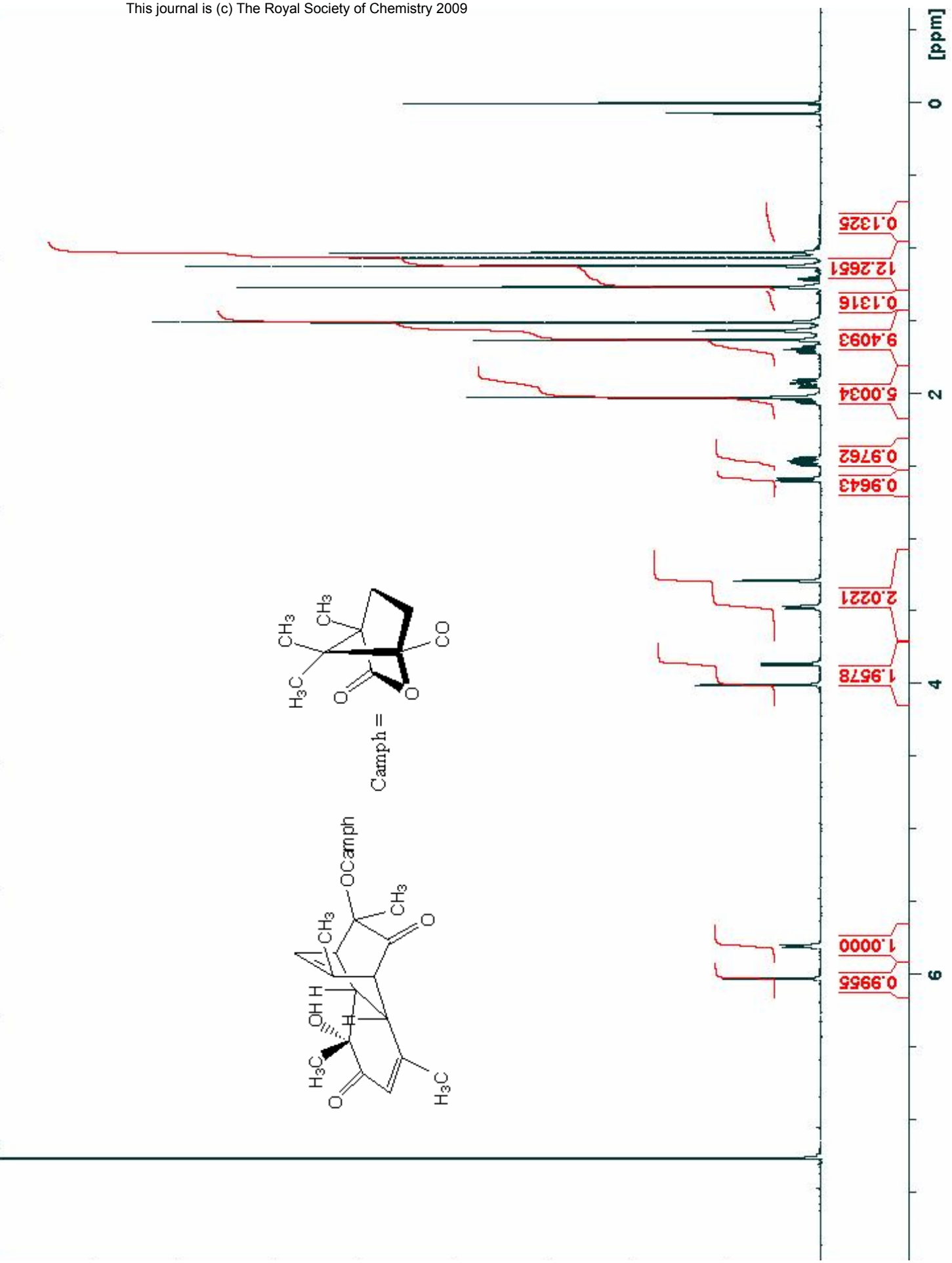
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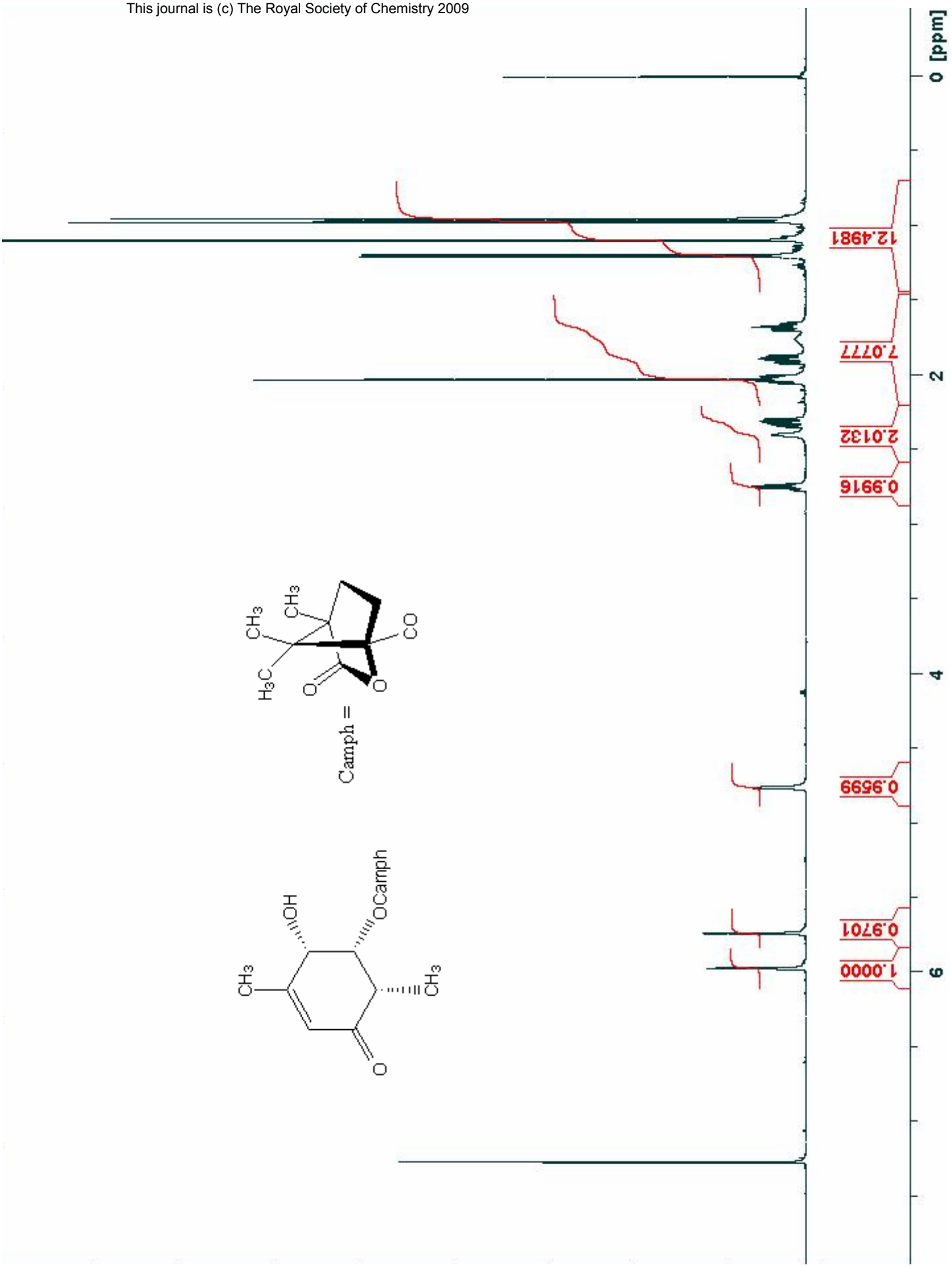
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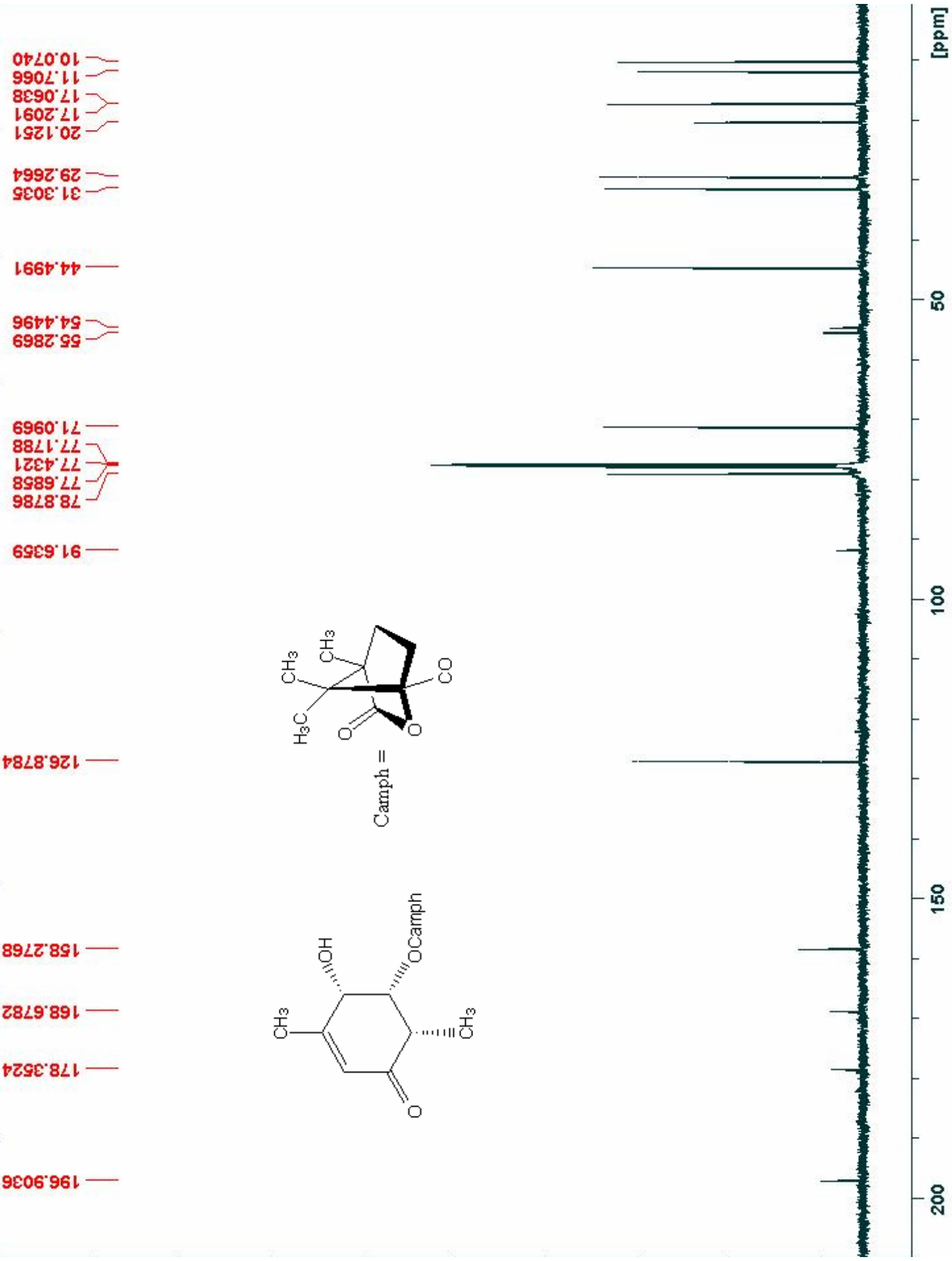
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