Supporting Information

Combining Cross-metathesis and Activity-based Protein Profiling: New β-Lactone Motifs for Targeting Serine Hydrolases

Kaddy Camara[1], Siddhesh S. Kamat[2], Celina C. Lasota[1], Benjamin F. Cravatt[2]*, and Amy R. Howell[1]*

1. Department of Chemistry, University of Connecticut, Storrs, Connecticut 06269-3060, United States

2. Department of Chemical Physiology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92307, United States

Email: amy.howell@uconn.edu

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EXPERIMENTAL

General Experimental

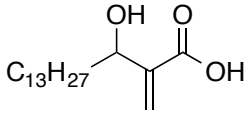
Tetrahydrofuran (THF) was dried using a solvent dispensing system (SDS) with a column of neutral alumina. Pyridine, toluene, dimethylformamide (DMF), methylene chloride (CH_2Cl_2), deuterated chloroform ($CDCl_3$), methanol (MeOH), deuterated methanol (CD_3OD) and ethanol (EtOH) were dried over 4 Å molecular sieves.

All reagents were purchased from Acros, Aldrich or Alfa Aesar and used without further purification. All reactions were conducted under an atmosphere of N_2 in glassware that had been dried overnight in an oven at 120 ^{o}C. Where appropriate, control of the reaction temperature was achieved with a solid CO_2/acetone bath, an ice bath or a heated oil bath.

NMR Spectra were obtained on a Bruker Avance DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C), Bruker Avance (500 MHz ^{1}H, 125 MHz ^{13}C), or Bruker Avance (300 MHz ^{1}H, 75 MHz ^{13}C) spectrometer. ^{1}H and ^{13}C chemical shifts are reported in parts per million (ppm) and calibrated to the residual $CHCl_3$ peak at 7.26 or the $CDCl_3$ signal at 77.23 ppm, respectively.

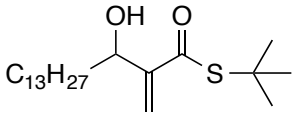
IR spectra were recorded on a Brucker FT-IR spectrometer. GC/MS spectra were obtained on a gas chromatograph equipped with a HP-1 methyl siloxane column and detected on a low-resolution 5970 series mass selective detector. High-resolution mass spectra were obtained on a AccuTOF instrument equipped with

a DART ionization source. Melting points were observed in open Pyrex capillary tubes and are uncorrected. Flash chromatography was performed on Silica Gel, 40 micron, 32-63 flash silica. Thin layer chromatography was performed on silica gel. Compounds were visualized by UV, 5% phosphomolybdic acid in ethanol, 0.5% potassium permanganate in water or a solution of ethanol/H_2SO_4/AcOH/*p*-anisaldehyde (135:5:1.5:3.7).



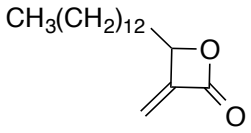
3-Hydroxy-2-methylenehexadecanoic acid (**7**)**.** Tetradecanal (4.93 g, 23.2 mmol) and methyl acrylate (4.20 mL, 46.8 mmol) were combined in an empty flask. 3- Hydroxyquinuclidine (0.74 g, 5.81 mmol) was added, followed by MeOH (0.70 mL) The resulting mixture was allowed to stir for 3 d. MeOH and excess methyl acrylate were removed under reduced pressure. The resulting residue was diluted with a H_2O/sat. NH_4Cl solution (5:1, 120 mL), and the resulting mixture was extracted with CH_2Cl_2 (3 X 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated. Methyl 3-hydroxy-2-methylenehexadecanoate was obtained as a white solid (5.82 g, 84%) and used without further purification. Methyl 3-hydroxy-2-methylenehexadecanoate (5.82 g, 19.5 mmol) was dissolved in EtOH/H_2O (2:1, 45 mL). Lithium hydroxide monohydrate (0.45 g, 19.5 mmol) was added; the resulting solution was allowed to stir overnight. The reaction was quenched with 1 M HCl (200 mL), and the solution was extracted with CH_2Cl_2 (3 X 100 mL). The combined organic layers were washed with H_2O

(100 mL) and dried ($MgSO_4$); CH_2Cl_2 was removed under reduced pressure.[1] Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 85:15) gave 3-hydroxy-2-methylenehexadecanoic acid (5.38 g, 95%) as a white solid: mp: 72.4–73.5 ˚C; IR (KBr) 3853, 2918, 2850, 2594, 2360, 1697, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.38 (s, 1H), 5.91 (s, 1H), 4.43 (dd, *J* = 6.5, 6.5 Hz, 1H), 1.68–1.66 (m, 2H), 1.43–1.41 (m, 1H), 1.30–1.26 (m, 22H), 0.90 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 142.1, 127.6, 71.8, 36.4, 32.1, 29.9, 29.9, 29.9, 29.8, 29.8, 29.6, 29.6, 26.0, 22.9, 14.3; MS (EI) *m/z* 266 $(M - OH)^+$, 221, 192, 116, 101 (100), 83, 71, 57; HRMS (FAB) calcd for $C_{17}H_{32}NaO_3$ $[M + Na]^+$ *m/z* 307.2244, found 307.2258.



***S*-*tert*-Butyl 3-hydroxy-2-methylenehexadecanethioate** (**8**)**.** DABCO (0.040 g, 0.37 mmol) was added to a mixture of thio-tert-butyl acrylate[2] (1.14 g, 7.87 mmol) and tetradecanal (0.84 g, 3.7 mmol). The reaction mixture was allowed to stir for a week. It was diluted with CH_2Cl_2 (100 mL) and washed with 1 M aqueous HCl (50 mL), followed by sat. $NaHCO_3$ (50 mL). The organic layer was dried (Na_2SO_4) and concentrated. Purification by flash chromatography on silica gel (petroleum ether/EtOAc 95:5) gave **8** (1.03 g, 84%) as slightly yellow oil: IR (neat) 2921, 2852, 1655, 1456, 1363, 967, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.05 (s, 1H), 5.71 (d, *J* = 1.0 Hz, 1H), 4.38 (dd, *J* = 6.7, 6.7 Hz, 1H), 2.40 (br. s, 1H), 1.65–1.56 (m, 2H), 1.49 (s, 9H), 1.45–1.41 (m, 1H), 1.33–1.25 (m, 21H), 0.88 (t,

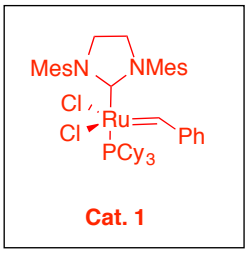
J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.8, 151.4, 121.7, 72.3, 48.4, 36.4, 32.1, 30.0, 29.9, 29.8, 29.7, 29.6, 29.6, 25.9, 22.9, 14.3; HRMS (ESI) calcd for $C_{21}H_{41}O_2S$ $[M + H]^+$ *m/z* 357.2822, found 357.2822.



3-Methylene-4-tridecyloxetan-2-one (**9**)**. Pathway A:**[1] 3-Hydroxy-2-methyl-enehexadecanoic acid (5.38 g, 18.9 mmol) was dissolved in dry CH_2Cl_2 (70 mL). Oven-dried Na_2CO_3 (20.1 g, 18.9 mmol) was added, and the resulting suspension was stirred for 30 min. *o*-Nosyl chloride (8.50 g, 37.7 mmol) was added, and the resulting mixture was stirred for 3 d. The reaction was diluted with CH_2Cl_2 (200 mL), and then 1 M HCl (200 mL) was added and separated. The aqueous layer was then extracted with CH_2Cl_2 (3 X 75 mL); the combined organic layers were dried (Na_2SO_4) and concentrated. Purification of the residue via flash chromatography on silica gel (petroleum ether/EtOAc 95:5) gave **9** (2.19 g, 43%) as a white solid: **Pathway B:**[3] $Hg(O_2CCF_3)_2$ (0.72 g, 1.68 mmol), was added to a solution of *S*-*tert*-butyl 3-hydroxy-2-methylenehexadecanethio-ate (**8**) (0.30 g, 0.84 mmol) in dry CH_3CN (50 mL). The reaction mixture was stirred in a preheated oil bath for 10 min at 50 ˚C. ^{1}H NMR was used to monitor the reaction. The reaction mixture was filtered, and the filtrate concentrated. Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 95:5) gave **9** (0.15 g, 67%) as a white solid: mp: 34–35.5 ˚C; IR (neat) 2916, 2849, 1810, 1468, 1085, 962, 818 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)

δ 5.90 (dd, *J* = 2.0, 2.0 Hz, 1H), 5.41 (dd, *J* = 1.7 1.7 Hz, 1H), 4.98–4.94 (m, 1H), 1.92–1.79 (m, 2H), 1.54–1.40 (m, 2H), 1.37–1.26 (m, 20H), 0.88 (t, *J* = 6.7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 146.7, 115.0, 79.9, 33.5, 32.1, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 24.8, 22.9, 14.3; MS (EI) *m/z* 266 (M^+), 108, 95, 83 (100), 67, 55; HRMS (ESI) calcd for $C_{17}H_{31}O_2$ $[M + H]^+$ *m/z* 267.2319, found 267.2335.

Catalyst used in olefin cross metathesis



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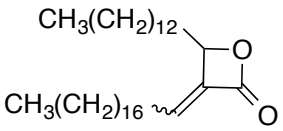
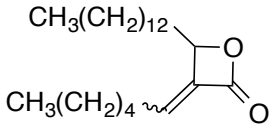


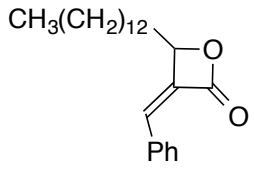
(*E/Z*)-3-Octadecylidene-4-tridecyloxetan-2-one (*Z/E*-**4a**)**.** Catalyst **1** (40 mg, 0.047 mmol) was added to a solution of 3-methylene-4-tridecyloxetan-2-one (**9**) (0.25 g, 0.94 mmol) and 1-nonadecene (0.38 g, 1.4 mmol) in dry CH_2Cl_2 (46 mL). The mixture was stirred overnight at 40 ˚C.[4] The next day ^{1}H NMR showed complete consumption of **9**. The reaction was allowed to cool to rt followed by removal of CH_2Cl_2 under reduced pressure to yield a brownish residue. Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 98:2) gave *Z/E*-**4a**, (*Z/E*, 2.2/1), (0.56 g, 75%) as a white solid. The isomers were separated by careful chromatography using the same solvent

system. *E*-**4a:** mp 49–50 ˚C; IR (neat) 2917, 2849, 1791, 1466, 1127 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.33 (dt, *J* = 7.9, 1.4 Hz, 1H), 4.99 (m, 1H), 2.10 (dt, *J* = 7.4, 7.4 Hz, 2H), 2.00–1.88 (m, 1H), 1.82–1.72 (m, 1H), 1.52–1.43 (m, 4H), 1.37–1.26 (m, 48H), 0.88 (t, *J* = 6.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 137.8, 134.2, 79.4, 33.5, 32.1, 29.9, 29.9, 29.9, 29.9, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.1, 28.6, 24.9, 22.9, 14.3; MS (EI) *m/z* 194,117, 91 (100), 77, 65, 51; HRMS (ESI) calcd for $C_{34}H_{65}O_2$ $[M + H]^+$ *m/z* 505.4957, found 505.5003. *Z*-**4a:** mp 61.5–62.5 ˚C; IR (neat) 2914, 2848, 1795, 1471, 1117, 1070 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84 (t, *J* = 7.5 Hz, 1H), 4.85 (t, *J* = 6.3 Hz, 1H), 2.48 (dt, *J* = 7.4, 7.4 Hz, 2H), 1.86–1.73 (m, 2H), 1.47–1.39 (m, 4H), 1.35–1.26 (m, 48H), 0.88 (t, *J* = 6.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 137.7, 136.5, 78.9, 34.0, 32.1, 29.9, 29.9, 29.8, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 29.5, 29.3, 29.1, 29.1, 24.8, 22.9, 14.3; MS (EI) *m/z* 460 $(M - CO_2)^+$, 355, 341, 293, 281, 236, 207 (100), 194, 110, 95, 81, 67, 55; HRMS (ESI) calcd for $C_{34}H_{65}O_2$ $[M + H]^+$ *m/z* 505.4957, found 505.4957.

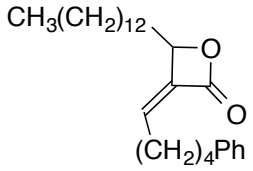


***(E/Z)*-3-Hexylidene-4-tridecyloxetan-2-one** (*Z/E*-**4b**)**.** Catalyst **1** (0.02 g, 0.04 mmol) was added to a solution of 3-methylene-4-tridecyloxetan-2-one (**9**) (0.20 g, 0.75 mmol) and 1-heptene (0.15 g, 1.5 mmol) in dry CH_2Cl_2 (29 mL). The mixture was stirred overnight at 40 ˚C.[4] The next day ^1H NMR showed complete consumption of 3-methylene-4-tridecyloxetan-2-one. The reaction was cooled to

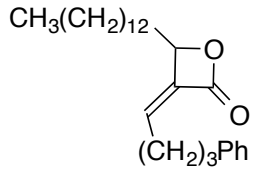
rt followed removal of the CH_2Cl_2 under reduced pressure to yield a brownish residue. Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 98:2) gave *Z/E*-**4b** (*Z/E*, 3.3/1), (0.24 g, 97%) as a colorless oil. The isomers were separated by careful chromatography using the same solvent system. *E*-**4b:** IR (neat) 2922, 2852, 1813, 1464, 1117 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.33 (t, *J* = 7.6 Hz, 1H), 4.99 (m, 1H), 2.11 (dt, *J* = 7.1, 7.1 Hz, 2H), 1.96–1.88 (m, 1H), 1.81–1.72 (m, 1H), 1.50–1.43 (m, 4H), 1.31–1.26 (m, 24), 0.90 (m, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 137.8, 134.1, 79.4, 33.5, 32.1, 31.6, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6 29.5, 29.0, 28.3, 24.9, 22.9, 22.6, 14.3, 14.1; MS (EI) *m/z* 336 (M^+), 178 (100); HRMS (ESI) calcd for $C_{22}H_{41}O_2$ $[M + H]^+$ *m/z* 337.3101, found 337.3124. *Z*-**4b:** IR (neat) 2914, 2848, 1793, 1721, 1470, 1116, 1070, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.84 (dt, *J* = 7.9, 1.0 Hz, 1H), 4.84 (dd, *J* = 6.2, 6.2 Hz, 1H), 2.55–2.41 (m, 2H), 1.84–1.73 (m, 2H), 1.50–1.39 (m, 4H), 1.33–1.26 (m, 24H), 0.89 (m, 3H), 0.88 (t, *J* = 7.0 Hz 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 137.7, 136.4, 78.8, 33.9, 32.1, 31.4, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 29.0, 28.7, 24.8, 22.9, 22.6, 14.3, 14.1; MS (EI) *m/z* 336 (M^+), 275, 111, 81, 67, 55 (100); HRMS (ESI) calcd for $C_{22}H_{41}O_2$ $[M + H]^+$ *m/z* 337.3101, found 337.3123.



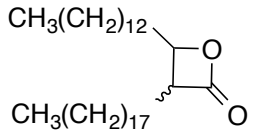
***(Z)*-3-Benzylidene-4-tridecyloxetan-2-one** (*Z*-**4c**)**.** Catalyst **1** (0.01 g, 0.01 mmol) was added to a solution of 3-methylene-4-tridecyloxetan-2-one (**9**) (0.060 g, 0.21 mmol) and styrene (0.050 g, 0.43 mmol) in dry CH_2Cl_2 (8 mL) The mixture was stirred overnight at 40 ˚C.[4] The next day TLC showed incomplete consumption of **9**; so 1 equiv more of styrene was added, and the reaction was allowed to stir for 6 h at 40 ^{o}C. After the reaction mixture was allowed to cool to rt, the CH_2Cl_2 was removed under reduced pressure to yield a brown residue. Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 98:2) gave *Z*-**4c** (0.030 g, 40%) as a white solid: mp 61–62 ˚C; IR (neat) 2914, 2848, 1780, 1687, 1468, 1212, 1156, 1128, 1068 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 6.8 Hz, 2H), 7.43–7.41 (m, 3H), 6.53 (s, 1H), 4.96 (dd, *J* = 5.6, 5.6 Hz, 1H), 1.97–1.83 (m, 2H), 1.59–1.45 (m, 2H), 1.40–1.26 (m, 20H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 136.0, 133.4, 133.2, 130.8, 130.4, 129.1, 78.0, 34.0, 32.1, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 24.8, 22.9, 14.3; MS (EI) *m/z* 342 (M^+), 159, 130 (100); HRMS (ESI) calcd for $C_{23}H_{35}O_2$ $[M + H]^+$ *m/z* 343.2632, found 343.2655.



***(Z)*-3-(5-Phenylpentylidene)-4-tridecyloxetan-2-one** (*Z*-**4d**)**.** Catalyst **1** (0.03 g, 0.04 mmol) was added to a solution of 3-methylene-4-tridecyloxetan-2-one (**9**) (0.20 g, 0.75 mmol) and 6-phenyl-1-hexene (0.24 g, 1.50 mmol) in dry CH_2Cl_2 (29 mL). The mixture was stirred overnight at 40 ˚C.[4] The next day TLC showed incomplete consumption of **9**; so 1 equiv more of 6-phenyl-1-hexene was added, and the reaction was allowed to stir for 6 h at 40 ˚C. After the reaction was allowed to cool to rt, the CH_2Cl_2 was removed under reduced pressure to yield a brown residue. Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 97:3) gave *Z*-**4d** (0.20 g, 68%) as a wax: mp 34–35 ˚C; IR (neat) 2914, 2848, 1793, 1723, 1468, 1182.70, 1120, 1071 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.22–7.19 (m, 2H), 7.13–7.09 (m, 3H), 5.75 (t, *J* = 7.8 Hz, 1H), 4.77 (dd, *J* = 6.0, 6.0 Hz, 1H), 2.56 (t, *J* = 7.2 Hz, 2H), 2.51– 2.38 (m, 2H), 1.77–1.69 (m, 2H), 1.60 (quin, *J* = 7.6 Hz, 2H), 1.47–1.33 (m, 4H), 1.28–1.19 (m, 20H), 0.81 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 142.4, 138.0, 136.0, 128.6, 128.5, 126.0, 78.9, 35.7, 33.9, 32.1, 30.9, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 28.9, 28.5, 24.8, 22.9, 14.3; MS (EI) *m/z* 354 $(M - CO_2)^+$, 104, 91(100); HRMS (ESI) calcd for $C_{27}H_{43}O_2$ $[M + H]^+$ *m/z* 399.3263, found 399.3258.

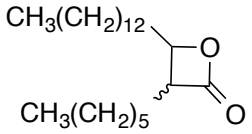


***(Z)*-3-(4-Phenylbutylidene)-4-tridecyloxetan-2-one** (*Z*-**4e**)**.** Catalyst **1** (0.02 g, 0.04 mmol) was added to a solution of 3-methylene-4-tridecyloxetan-2-one (**9**) (0.20 g, 0.75 mmol) and 5-phenyl-1-pentene (0.44 g, 3.00 mmol) in dry CH_2Cl_2 (29 mL). The mixture was stirred overnight at 40 ˚C.[4] The next day TLC showed incomplete consumption of **9**; so 1 equiv more of 5-phenyl-1-pentene was added and the reaction was allowed to stir for 6 h at 40 ˚C. After the reaction was allowed to cool to rt, the CH_2Cl_2 was removed under reduced pressure to yield a brown residue. Purification of the residue by flash chromatography on silica gel (petroleum ether/EtOAc 97:3) gave *Z*-**4e** (0.15 g, 51%) as a colorless oil: IR (neat) 2921, 2852, 1805, 1454, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.31–7.27 (m, 2H), 7.21–7.18 (m, 3H), 5.84 (t, *J* = 7.6 Hz, 1H), 4.86 (dd, *J* = 6.0, 6.0 Hz, 1H), 2.67 (t, *J* = 7.2 Hz, 2H), 2.56 (dt, *J* = 7.8, 7.8 Hz, 2H), 1.84–1.77 (m, 4H), 1.50–1.43 (m, 2H), 1.36–1.27 (m, 20H), 0.89 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 141.8, 138.1, 135.8, 128.6, 126.2, 78.9, 35.6, 33.9, 32.1, 30.8, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 28.8, 24.8, 22.9, 14.3; MS (EI) *m/z* 384 (M^+), 104 (100), 91; HRMS (ESI) calcd for $C_{26}H_{41}O_2$ $[M + H]^+$ *m/z* 385.3101, found 385.3114.



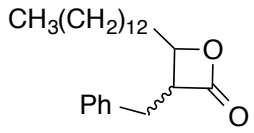
***(cis/trans)*-3-Octadecyl-4-tridecyloxetan-2-one** (*trans*/*cis*-**5a**)**.** 3-Octylidene-4-tridecyloxetan-2-one (0.10 g, 0.20 mmol) (*Z/E*-**4a**), was dissolved in a mixture of THF:MeOH (1.6:0.32 mL). This solution was cooled to −10 ˚C, followed by the addition of $CoCl_2(PPh)_3$ (0.02 g, 0.04 mmol) and then portion-wise addition of $NaBH_4$ (39.0 mg, 1.2 mmol) within 10 min.[5] The mixture was vigorously stirred for 2 h between −7 and −5 ˚C. The reaction mixture was filtered through a pad of celite, and the celite was then washed with $CHCl_3$ (10 mL). The filtrate was washed with 2M HCl (10 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (petroleum ether/ EtOAc, 98:2) gave a mixture of (*trans*/*cis*-**5a**) (*trans/cis* 2/1), (0.06 g, 61%) as a white solid. The isomers were separated by careful chromatography using the same solvent system. *cis*-**5a:** mp 63−64 ˚C; IR (neat) 2916, 2849, 1790, 1464, 1146, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.52 (ddd, *J* = 9.9, 6.3, 4.1 Hz, 1H), 3.59 (ddd, *J* = 8.1, 6.9, 6.9 Hz, 1H), 1.82−1.72 (m, 2H), 1.69−1.55 (m, 2H), 1.52−1.48 (m, 2H), 1.39−1.26 (m, 52H), 0.88 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 76.0, 52.9, 32.1, 30.4, 29.9, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.6, 29.5, 27.8, 25.8, 24.2, 22.9,14.3; MS (EI) *m/z* 463 $(M - CO_2)^+$, 281, 207, 111, 97(100), 83, 57; HRMS (ESI) calcd for $C_{34}H_{67}O_2$ $[M + H]^+$ *m/z* 507.5136, found 507.5158. *trans*-**5a; nocardiolactone**: mp 64−65 ˚C (Lit.[6] 66−68 ^oC); IR (neat) 2915, 2847, 1796, 1468, 1154, cm^{-1}; ^1H NMR (400 MHz,

$CDCl_3$) δ 4.21 (ddd, *J* = 6.8, 6.8, 3.9 Hz, 1H), 3.17 (ddd, *J* = 10.3, 6.5, 4.0 Hz, 1H), 1.89–1.79 (m, 2H), 1.76–1.66 (m, 2H), 1.45–1.25 (m, 54H), 0.88 (t, *J* = 7.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 78.4, 56.4, 34.7, 32.1, 29.9, 29.9, 29.8, 29.7, 29.7, 29.6, 29.6, 29.5, 29.5, 28.1, 27.2, 25.2, 22.9, 14.3; MS (EI) *m/z* 462 $(M - CO_2)^+$, 281, 207, 111, 97 (100), 83, 57; HRMS (ESI) calcd for $C_{34}H_{67}O_2$ $[M + H]^+$ *m/z* 507.5136, found 507.5157.



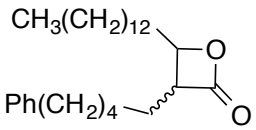
***(cis/trans)*-3-Hexyl-4-tridecyloxetan-2-one** (*trans/cis*-**5b**)**.** *(E/Z)*-3-Hexylidene-4-tridecyloxetan-2-one (*Z/E*-**4b**) (0.03 g, 0.09 mmol), was dissolved in a mixture of THF:MeOH (0.70 mL: 0.14 mL). This solution was cooled to –10 ˚C, followed by the addition of $CoCl_2(PPh)_3$ (0.01 g, 0.01 mmol) and then portion-wise addition of $NaBH_4$ (9.9 mg, 27.0 mmol) within 10 min.[5] The mixture was vigorously stirred for 2 h between –7 to –5 ˚C. The reaction mixture was filtered through a pad of celite, and the celite was then washed with $CHCl_3$ (5 mL). The filtrate was washed with 2M HCl (5 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (petroleum ether/ EtOAc 98:2) gave mixture of *trans/cis*-**5b** (*trans/cis*, 1.3/1), (14 mg, 44%). The isomers were separated by careful column chromatography using the same solvent system. *cis*-**5b** (colorless oil): IR (neat) 2921, 2852, 1820, 1464, 1121 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.57–4.49 (m, 1H), 3.61–3.56 (m, 1H), 1.78–1.51 (m, 6H), 1.39–1.26 (m, 28H), 0.91–0.87 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6,

76.0, 52.9, 32.1, 31.7, 30.4, 29.9, 29.9, 29.7, 29.6, 29.6, 29.5, 29.3, 27.8, 25.8, 24.2, 22.9, 22.8, 14.3, 14.2; MS (EI) *m/z* 294 $(M - CO_2)^+$, 207, 125, 111, 97 (100), 83, 69, 55; HRMS (ESI) calcd for $C_{22}H_{43}O_2$ $[M + H]^+$ *m/z* 339.3258, found 339.3295. *trans*-**5b** (waxy solid): mp 29–30 ˚C; IR (neat) 2918, 2850, 1794, 1466, 1142, 1076 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.24–4.17 (m, 1H), 3.18–3.13 (m, 1H), 1.85–1.79 (m, 2H), 1.73–1.69 (m, 2H), 1.43–1.26 (m, 30H), 0.89–0.86 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 78.4, 56.4, 34.7, 32.1, 31.7, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 29.2, 28.1, 27.2, 25.2, 22.9, 22.7, 14.3, 14.2; MS (EI) *m/z* 294 $(M - CO_2)^+$, 281, 207, 125, 111, 97, 83 (100), 69, 55; HRMS (ESI) calcd for $C_{22}H_{43}O_2$ $[M + H]^+$ *m/z* 339.3258, found 339.3296.



***(cis/trans)*-3-Benzyl-4-tridecyloxetan-2-one** (*trans/cis*-**5c**)**.** *(Z)*-3-Benzylidene-4-tridecyloxetan-2-one (*Z*-**4c**) (0.05 g, 0.15 mmol) was dissolved in a mixture of THF:MeOH (1.1 mL:0.05 mL). This solution was cooled to –10 ˚C, followed by the addition of $CoCl_2(PPh)_3$ (0.02 g, 0.03 mmol) and then portion-wise addition of $NaBH_4$ (16.0 mg, 0.44 mmol) within 10 min.[5] The mixture was vigorously stirred for 2 h between –7 to –5 ˚C. The reaction mixture was filtered through a pad of celite, and the celite was then washed with $CHCl_3$ (5 mL). The filtrate was washed with 2M HCl (5 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (petroleum ether/EtOAc 99:1) gave *trans/cis*-**5c** (*trans/cis,* 2/1), (0.02 g, 39%) as a wax. The isomers were separated by careful

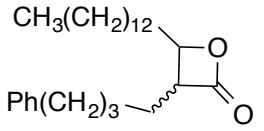
column chromatography using the same solvent system. *cis*-**5c** (white solid): mp 43–44 ˚C; IR (neat) 2917, 2849, 1797, 1466, 1136, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 7.24–7.21 (m, 3H), 4.60 (ddd, *J* = 10.0, 6.4, 3.6 Hz, 1H), 4.01 (ddd, *J* = 9.0, 6.9, 6.9 Hz, 1H), 3.19 (dd, *J* = 15.1, 7.1 Hz, 1H), 2.98 (dd, *J* = 15.1, 9.0 Hz, 1H), 1.86–1.76 (m, 1H), 1.71–1.63 (m, 1H), 1.57–1.46 (m, 1H), 1.37–1.26 (m, 21H), 0.88 (t, *J* = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 137.9, 129.0, 128.6, 127.0, 76.3, 53.5, 32.1, 30.6, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 25.8, 22.9, 14.3; MS (EI) *m/z* 300 $(M - CO_2)^+$, 117, 104 (100), 91; HRMS (ESI) calcd for $C_{23}H_{37}O_2$ $[M + H]^+$ *m/z* 345.2788, found 345.2817. *trans*-**5c** (white solid): mp 40–41 ˚C; IR (neat) 2916, 2849, 1800, 1134, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.30 (m, 2H), 7.27–7.25 (m, 2H), 7.20 (d, *J* = 7.0 Hz, 1H), 4.27 (ddd, *J* = 6.7, 6.7, 4.1 Hz, 1H), 3.45 (ddd, *J* = 9.5, 5.6, 4.2 Hz, 1H), 3.18 (dd, *J* = 14.3, 5.7 Hz, 1H), 3.00 (dd, *J* = 14.3, 9.4 Hz, 1H), 1.83–1.74 (m, 1H), 1.62–1.57 (m, 1H), 1.35–1.18 (m, 22H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 137.4, 129.1, 128.9, 127.3, 77.8, 57.6, 34.4, 34.0, 32.1, 29.9, 29.9, 29.8, 29.6, 29.6, 29.6, 29.3, 24.8, 22.9, 14.3; MS (EI) *m/z* 300 $(M - CO_2)^+$, 117, 104 (100), 91; HRMS (ESI) calcd for $C_{23}H_{37}O_2$ $[M + H]^+$ *m/z* 345.2788, found 345.2814.



***(cis/trans)*-3-(5-Phenylpentyl)-4-tridecyloxetan-2-one** (*trans/cis*-**5d**)**.** *(Z)*-3-(5-Phenylpentyli-dene)-4-tridecyloxetan-2-one (*Z*-**4d**) (0.10 g, 0.25 mmol) was

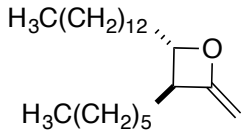
dissolved in a mixture of THF:MeOH (2.0:0.4 mL). This solution was cooled to −10 ˚C, followed by the addition of $CoCl_2(PPh)_3$ (0.03 g, 0.04 mmol) and then portion-wise addition of $NaBH_4$ (28.0 mg, 0.75 mmol), within 10 min.[5] The mixture was vigorously stirred for 4 h between −7 to −5 ˚C. The reaction mixture was filtered through a pad of celite, and the celite was washed with $CHCl_3$ (15 mL). The filtrate was washed with 2M HCl (10 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (petroleum ether/EtOAc 99:1) gave a mixture of *trans/cis*-**5d** (*trans*/cis, 2/1), (0.03 g, 32%) as a colorless oil. The isomers were separated by careful column chromatography using the same solvent system. *cis*-**5d:** IR (neat) 2916, 2846, 1805, 1464, 1135, 1064 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29−7.26 (m, 2H), 7.20−7.16 (m, 3H), 4.55−4.49 (m, 1H), 3.57 (ddd, *J* = 8.9, 6.8, 6.8 Hz, 1H), 2.61 (t, *J* = 7.4 Hz, 2H), 1.82−1.70 (m, 2H), 1.68−1.52 (m, 4H), 1.45−1.26 (m, 26H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 142.7, 128.6, 128.5, 125.9, 75.9, 52.8, 36.0, 32.1, 31.3, 30.4, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 29.2, 27.7, 25.8, 24.1, 22.9, 14.3; MS (GC) *m/z* 356 $(M - CO_2)^+$, 117, 104 (100), 91; HRMS (ESI) calcd for $C_{27}H_{45}O_2$ $[M + H]^+$ *m/z* 401.3414, found 401.3441. *trans*-**5d:** IR (neat) 2921, 2852, 1819, 1454, 1114 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32−7.28 (m, 2H), 7.20 (m, 3H), 4.23−4.19 (m, 1H), 3.19−3.14 (m, 1H), 2.64 (t, *J* = 7.1 Hz, 2H), 1.87−1.80 (m, 2H), 1.74−1.63 (m, 4H), 1.50−1.29 (m, 26H), 0.91 (br. t, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 142.6, 128.6, 128.5, 125.9, 78.3, 56.3, 36.0, 34.6, 32.1, 31.3, 29.9, 29.9, 29.8, 29.7, 29.6,

29.6, 29.5, 29.1, 28.0, 27.1, 25.2, 22.9, 14.3; MS (EI) *m/z* 356 $(M - CO_2)^+$, 117, 104 (100), 91; HRMS (ESI) calcd for $C_{27}H_{45}O_2$ $[M + H]^+$ *m/z* 401.3414, found 401.3447.



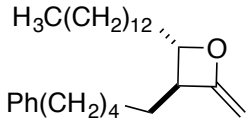
***(cis/trans)*-3-(4-Phenylbutyl)-4-tridecyloxetan-2-one** (*trans/cis*-**5e**)**.** *(Z)*-3-(4-Phenylbutylidene)-4-tridecyloxetan-2-one (*Z*-**4e**) (0.05 g, 0.13 mmol)) was dissolved in a mixture of THF:MeOH (1:0.2 mL). This solution was cooled to −10 ˚C, followed by the addition of $CoCl_2(PPh)_3$ (15.0 mg, 0.02 mmol) and then portion-wise addition of $NaBH_4$ (14 mg, 0.39 mmol) within 10 min.[5] The mixture was vigorously stirred for 1.5 h between −7 to −5 ˚C. The reaction mixture was filtered through a pad of celite, and the celite was washed with $CHCl_3$ (10 mL). The filtrate was washed with 2M HCl (5 mL), dried ($MgSO_4$) and concentrated. Purification by flash chromatography on silica gel (petroleum ether/EtOAc 98:2) gave *trans/cis*-**5e** (*trans*/cis, 1.4/1), (24 mg, 46%) as a colorless oil. The isomers were separated by careful column chromatography using the same solvent system. *cis*-**5e**: IR (neat) 2919, 2850, 1818, 1462, 1052 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 7.20–7.16 (m, 3H), 4.51 (ddd, *J* = 10.0, 6.2, 4.0 Hz, 1H), 3.58 (ddd, *J* = 8.6, 6.7, 7.7 Hz, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 1.85–1.77 (m, 1H), 1.75–1.62 (m, 6H), 1.51–1.26 (m, 21H), 0.88 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 142.3, 128.6, 126.0, 75.9, 52.8, 35.8, 32.1, 31.3, 30.4, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 27.4, 25.7, 24.0, 22.9, 14.3; MS

(EI) *m/z* 342 $(M - CO_2)^+$, 117, 104 (100), 91; HRMS (ESI) calcd for $C_{26}H_{43}O_2$ $[M + H]^+$ *m/z* 387.3258, found 387.3261. *trans*-**5e**: IR (neat) 2917, 2851, 1804, 1470, 1140 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.20–7.15 (m, 3H), 4.19 (ddd, *J* = 6.5, 6.5, 3.9 Hz, 1H), 3.15 (m, 1H), 2.63 (t, *J* = 7.5 Hz, 2H), 1.90–1.81 (m, 2H), 1.79–1.62 (m, 4H), 1.51–1.26 (m, 24H), 0.88 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 142.3, 128.6, 126.1, 78.3, 56.3, 35.8, 34.6, 32.1, 31.3, 29.9, 29.9, 29.8, 29.7, 29.6, 29.6, 29.5, 28.0, 26.8, 25.2, 22.9, 14.3; MS (EI) *m/z* 342 $(M - CO_2)^+$, 117, 104 (100), 91; HRMS (ESI) calcd for $C_{26}H_{43}O_2$ $[M + H]^+$ *m/z* 387.3258, found 387.3259.



(*trans*)-3-Hexyl-2-methylene-4-tridecyloxetane (*trans*-**11b**)**.** *(trans)*-3-Hexyl-4-tridecyloxetan-2-one (*trans*-**5b**) (12 mg, 34 mmol) and Petasis solution (0.2 mL, 0.72 M) were stirred in a pre-heated oil bath at 80 ˚C for 6 h.[7] TLC showed remaining starting material so 0.2 mL more of the Petasis solution was added, and stirring was continued for 2 h. Petroleum ether (10 mL) was added to quench the reaction, and the mixture was allowed to stir overnight. The mixture was then filtered through a pad of celite until the filtrate was colorless, and the filtrate was concentrated to 1 mL solution. Purification by flash column chromatography on silica gel (petroleum ether/ EtOAc/ Et_3N, 96:3:1) gave *trans*-**11b** (4.5 mg, 38%) as a slightly yellow oil: IR (neat) 2924, 2854, 1689, 784 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.39 (m, 1H), 4.06 (br s, 1H), 3.72 (br s, 1H), 2.96–2.91 (m, 1H), 1.85–1.78 (m, 1H), 1.71–1.62 (m, 3H), 1.29–1.26 (m, 30H),

0.89–0.86 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 86.3, 78.5, 47.5, 36.0, 32.3, 32.2, 31.9, 29.9 29.9, 29.7, 29.7, 29.6, 29.4, 27.0, 24.7, 22.9, 22.8, 14.3, 14.3; HRMS (ESI) calcd for $C_{23}H_{45}O$ $[M + H]^+$ *m/z* 337.3465, found 337.3469**.**



(*trans*)-2-Methylene-3-(5-phenylpentyl)-4-tridecyloxetane *trans*-**11d.** (*trans*)-3-(5-Phenylpentyl)-4-tridecyloxetan-2-one (*trans*-**11d**), (11 mg, 27 mmol) and Petasis solution (0.080 mL, 0.50 M) were stirred in a pre-heated oil bath at 80 ˚C for 5 h.[7] Petroleum ether (10 mL) was added to quench the reaction, and the mixture was allowed to stir overnight. The mixture was then filtered through a pad of celite, and the filtrate was concentrated to 1 mL solution. Purification by flash column chromatography on silica gel (petroleum ether/EtOAc/Et_3N 96:3:1) gave *trans*-**11d** (3.2 mg, 40%) as a colorless oil: IR (neat) 2922, 2852, 1687, 1454 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.26 (m, 2H), 7.19–7.16 (m, 3H), 4.38 (m, 1H), 4.06 (m, 1H), 3.71 (m, 1H), 2.94–2.90 (m, 1H), 2.64 (t, *J* = 7.5 Hz, 2H), 1.84–1.76 (m, 1H), 1.70–1.62 (m, 5H), 1.36–1.26 (m, 26H), 0.91 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.8, 142.8, 128.6, 128.5, 125.9, 86.2, 78.5, 47.5, 36.1, 36.0, 32.2, 32.1, 31.5, 29.9, 29.9, 29.8, 29.7, 29.6, 29.4, 27.0, 24.7, 22.9, 14.3; MS (EI) *m/z* 398 (M^+), 104 (100), 91; HRMS (ESI) calcd for $C_{28}H_{47}O$ $[M + H]^+$ *m/z* 399.3621, found 399.3594.

Competitive Gel-based ABPP analysis. Competitive gel-based ABPP were performed as described previously with slight modifications.[8] Briefly the tissue (mouse brain) and cell (COLO205 cancer cell line) membrane proteomes were adjusted to a final concentration 1 mg/mL in a reaction volume of 100 µL and treated with the β-lactone compounds at a final concentration of 25 µM for 30 minutes at 37 ˚C with constant shaking. Thereafter 2 µM FP-rhodamine was added to label the proteins to assess their activities in gel for 30 minutes at 37 ˚C with constant shaking. The reactions were quenched by adding 40 µL of 4X SDS-PAGE loading buffer for reducing gels, followed by boiling for 2 minutes. All samples were visualized in-gel using an FMBio II Multiview flatbed fluorescence scanner (Hitachi). The fluorescence from rhodamine is presented in gray scale.

ABPP-SILAC sample preparation and analysis. All ABPP-SILAC experiments were performed using the human COLO205 colon cancer cell line. Light and heavy amino acid-labeled COLO205 cancer cell lines were generated using standard SILAC culturing protocols, using SILAC RPMI media. 2 mg/mL light proteome (0.5 mL) and 2 mg/mL heavy proteome (0.5 mL) were treated separately with 25 µM KC6-10-3 and DMSO respectively for 30 minutes at 37 ˚C, and subsequently labeled with FP-biotin (5 µM final concentration) for 45 minutes at 37 ˚C with constant shaking. After FP-biotin labeling, the proteomes were combined, denatured and precipitated using 4:1 MeOH: $CHCl_3$, re-suspended in 0.5 mL of 6M urea in PBS, reduced using tris(2-carboxyethyl)-phosphine (TCEP) (10 mM final concentration) for 30 minutes at 37 ˚C, and then

alkylated using iodoacetamide (40 mM final concentration) for 30 minutes at 25 ˚C in the dark. The biotinylated proteins were enriched with PBS washed avidin-agarose beads (100 µL) (Sigma-Aldrich) by shaking at 25 ˚C for 1.5 hours in PBS with 2% SDS to final volume of 5.5 mL. After enrichment, the beads were separated from the unlabeled/un-enriched proteome by centrifugation at 2800 x g for 10 minutes and washed sequentially, first with 10 mL PBS with 0.2% SDS (x 3 times), then with 10 mL PBS (x 3 times) and finally with 10 mL DI H_2O (x 3 times). On bead digestion was performed using sequence-grade trypsin (2 µg) (Promega Catalog # V5111) in 2M urea in PBS with 2 mM $CaCl_2$ for 12 – 14 hours at 37 ^{o}C. Peptides obtained from this procedure were acidified using 5% (vol/vol) formic acid, and stored at -80 ˚C prior to analysis. Extensive probe-probe, probe-no probe experiments were done prior to testing compounds in the SILAC cell lines, to ensure complete labeling of heavy proteomes, and enrichment of SH targets by FP-biotin probe (data not shown). Peptide samples were analyzed using the multidimensional protein identification technology (MudPIT) that employs liquid chromatography with tandem mass spectrometry.[9,10] Briefly, peptides are eluted in a 5-step MudPIT experiment utilizing 0%, 25%, 50%, 80% and 100% salt bumps of ammonium acetate (aqueous), and the data was collected in data-dependent acquisition mode as described previously.[11] The MS2 spectra were extracted from the raw file using the RAW Xtractor software (version 1.9.9.2, available at http://fields.scripps.edu/downloads.php). The MS2 spectra were searched using the ProLuCID algorithm (available from

http://fields.scripps.edu/downloads.php) against the latest non-redundant protein IDs for human or mouse proteins listed in Uniprot database.[12] ProLuCID has provisions for identification of static modification like alkylation of cysteine residues (+57.02146), methionine oxidation (+15.9949), and mass shifts from heavy amino acids in SILAC experiments (+10.0083 for arginine, and +8.0142 for lysine), enzyme specificity (half-tryptic specificity) and a precursor ion mass tolerance (50 ppm was used in this study). Lastly the MS2 spectra searches were subjected to filters using the DTASelect (version 2.0) for minimum number of peptides per protein, statistics with delta mass (-- mass), statistics with modifications (-- modstat), and statistics with tryptic status (--trypstat). The light/heavy peptide ratios for ABPP-SILAC experiments were computed using the in-house software CIMAGE.[13] Reported ratios in this study represent the median of the unique quantified peptides per protein. Proteins with less than 2 quantified peptides were excluded from this study. The ABPP-SILAC experiments were conducted using an Agilent 1200-series quaternary pump, and a Thermo Scientific Finnigan series LTQ-Orbitrap ion trap mass spectrometer.

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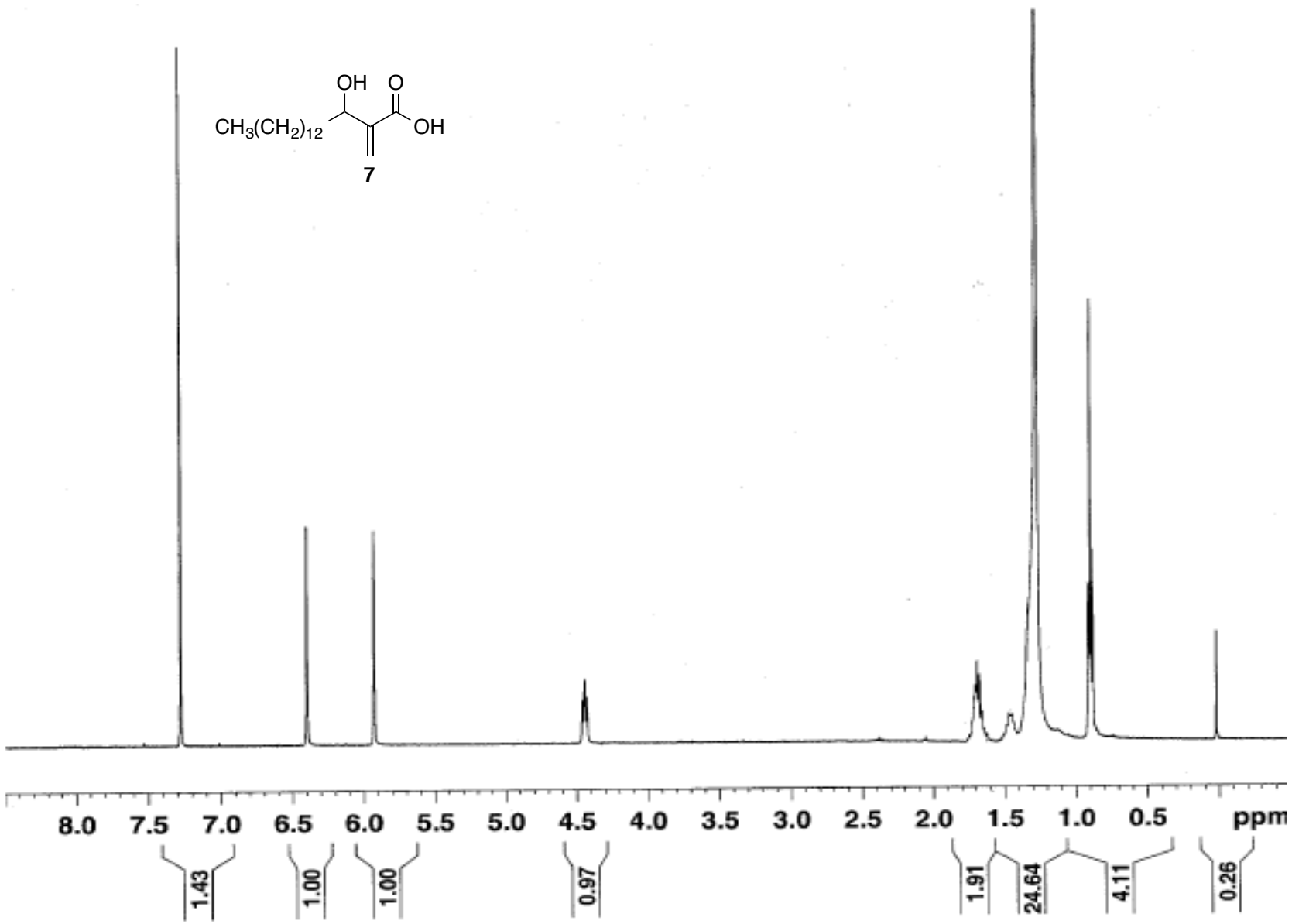
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4.0
3.5
3.0
2.5
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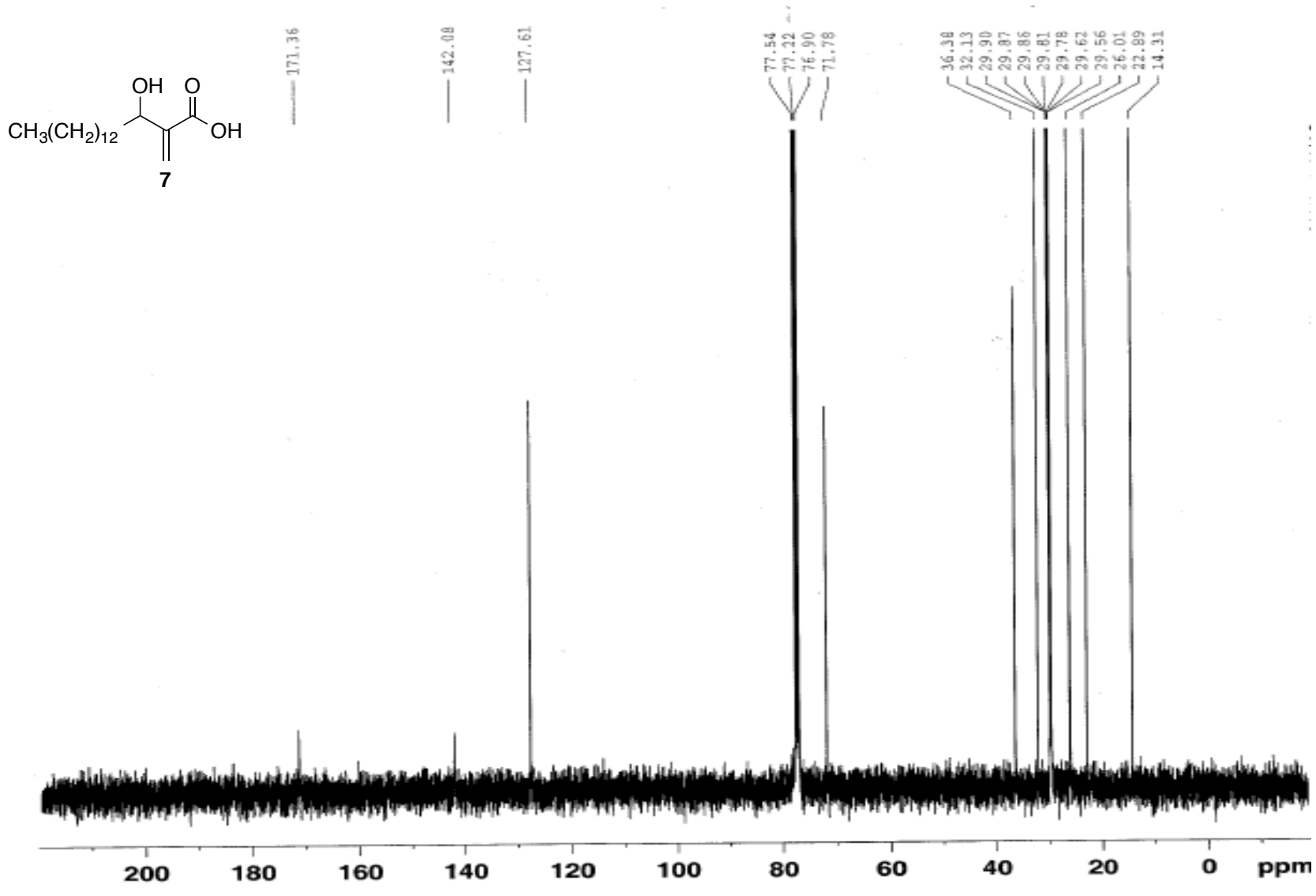
0.26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32.13
29.90
29.87
29.86
29.81
29.78
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120
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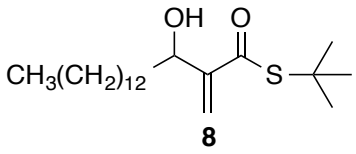
0
ppm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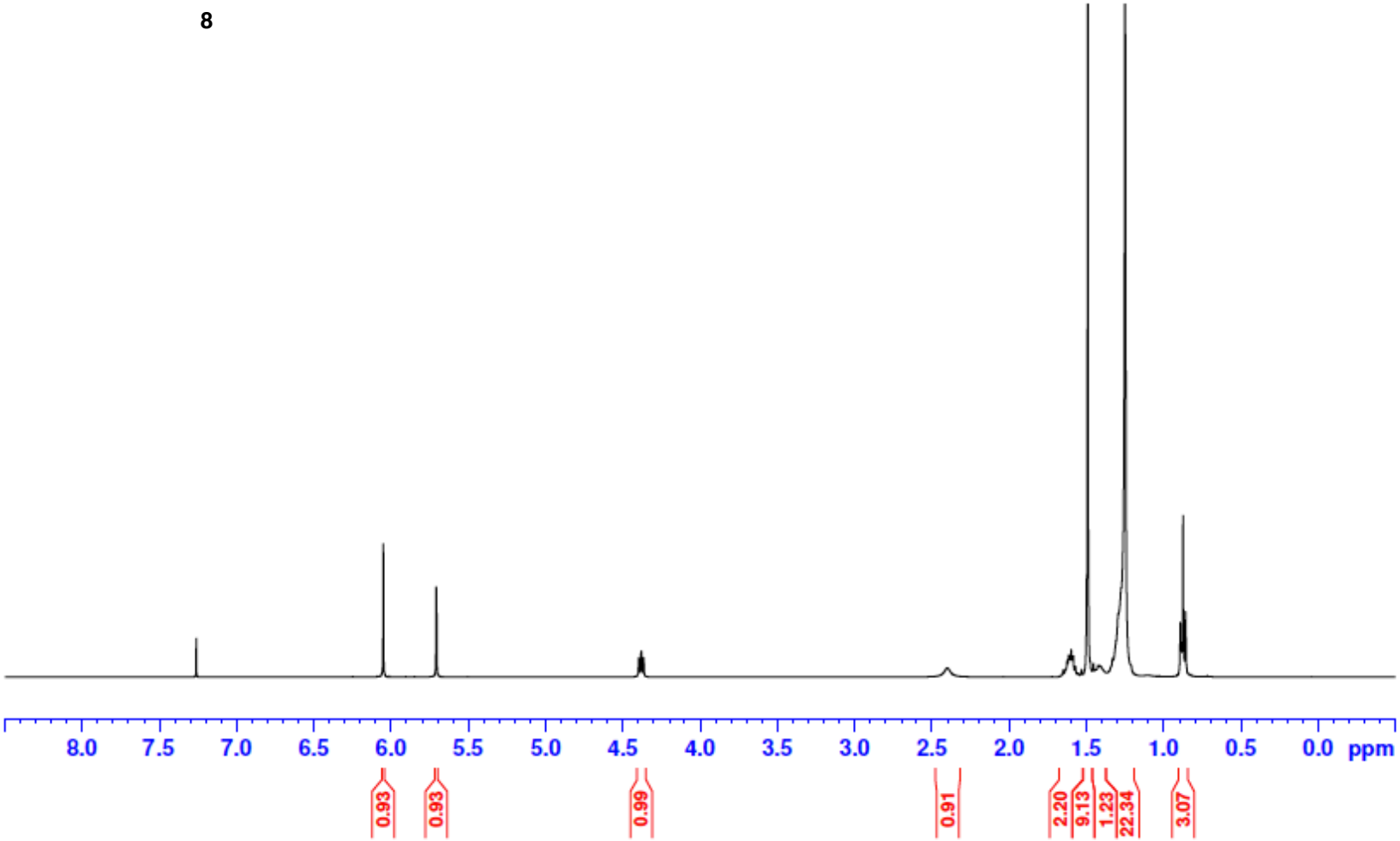
8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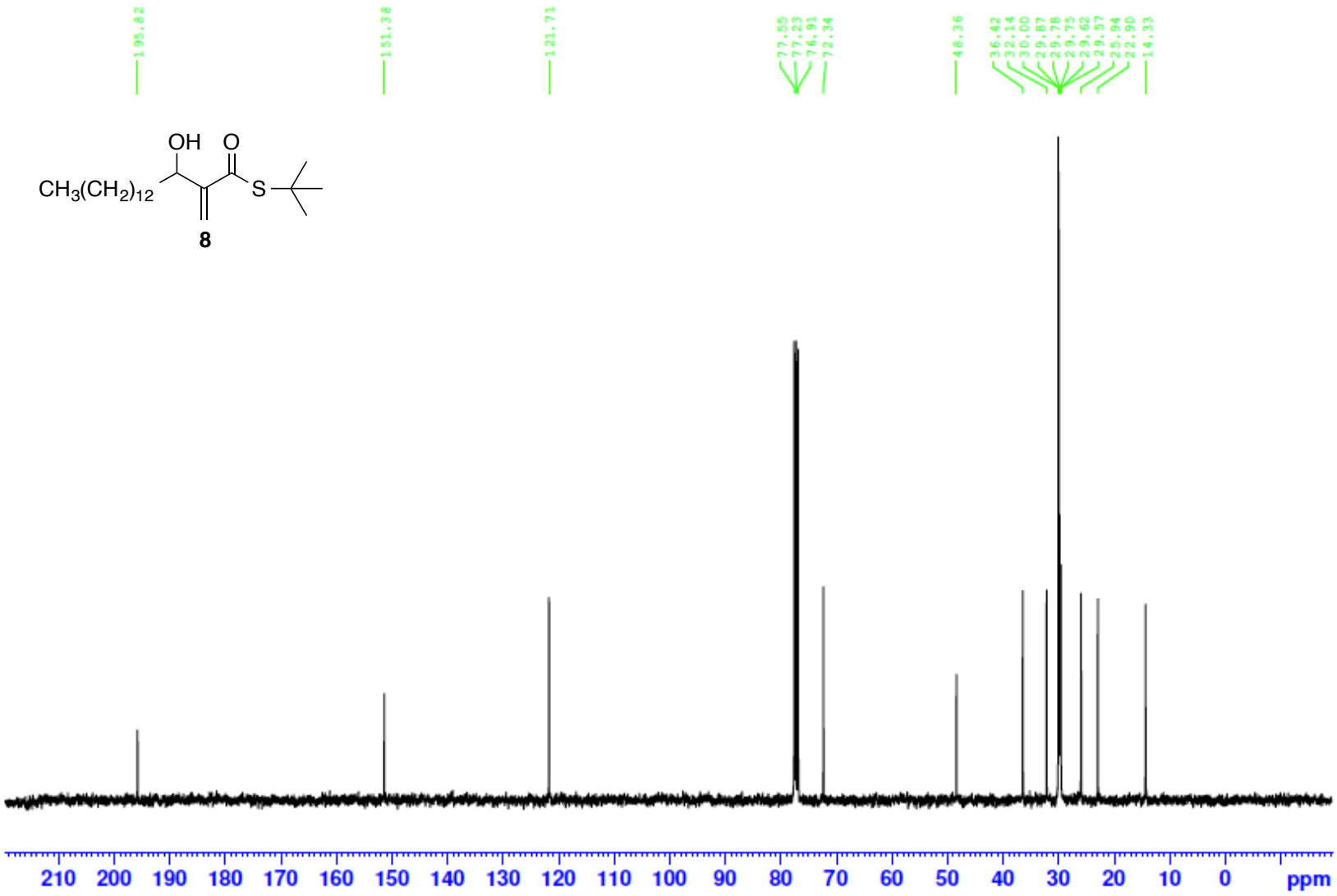
3.07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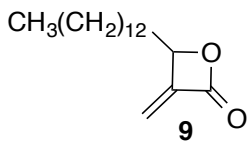
30.00
29.87
29.78
29.75
29.62
29.57
25.94
22.90
14.33
OH
O
S
CH3(CH2)12
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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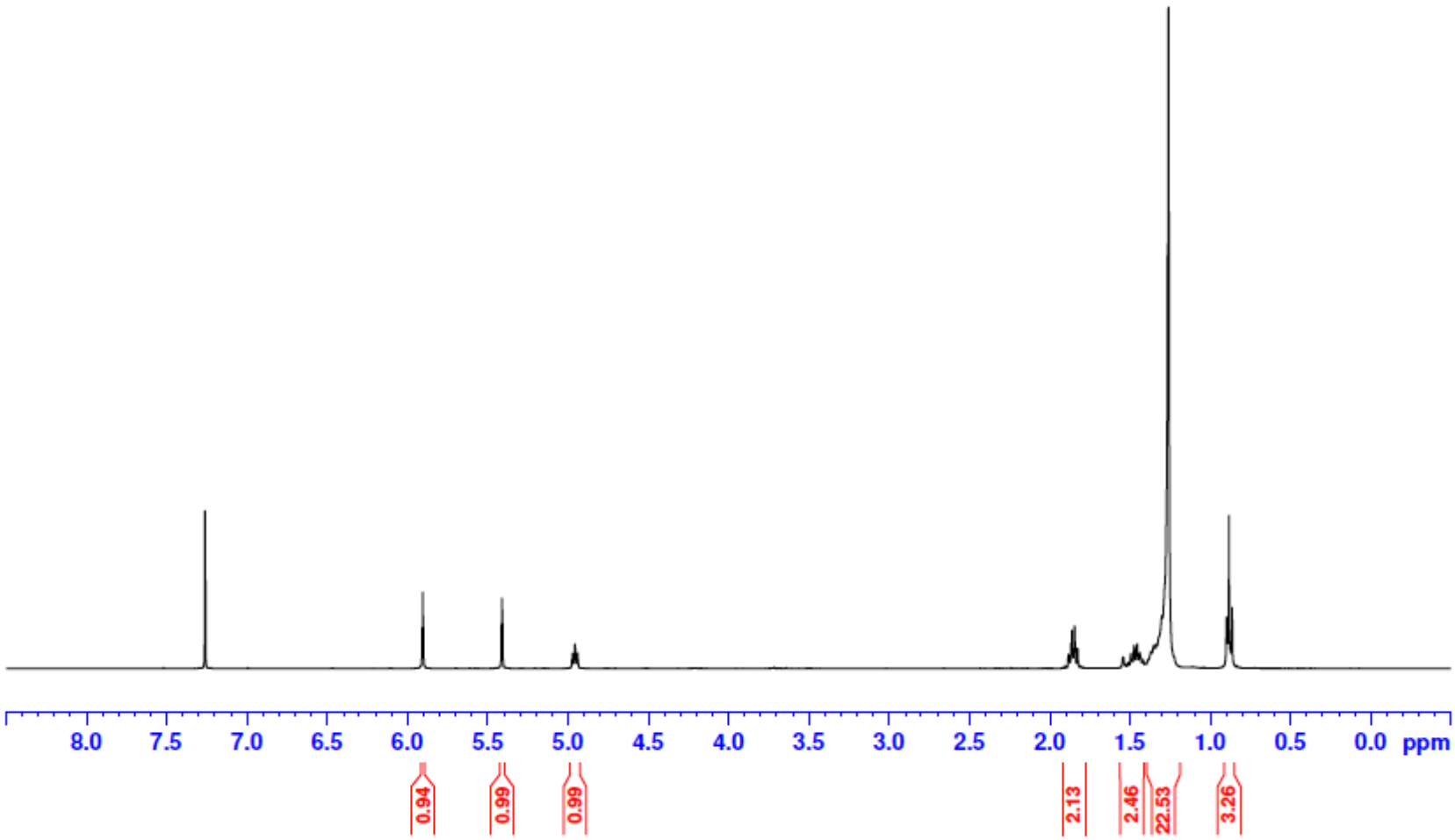
O
O

9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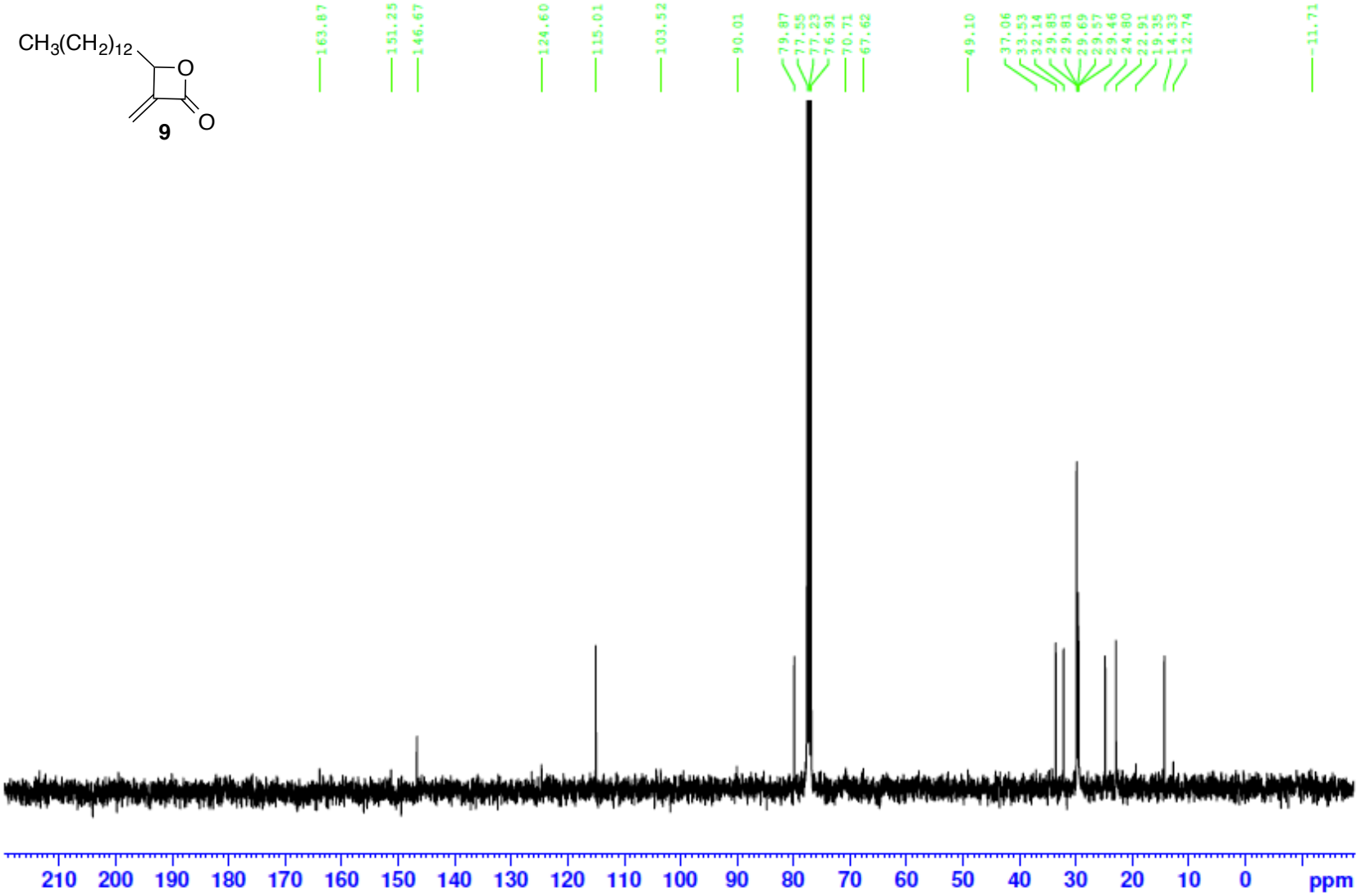
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O
9
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103.52
90.01
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77.55
77.23
76.91
70.71
67.62
49.10
37.06
33.53
32.14
29.85
29.81
29.69
29.57
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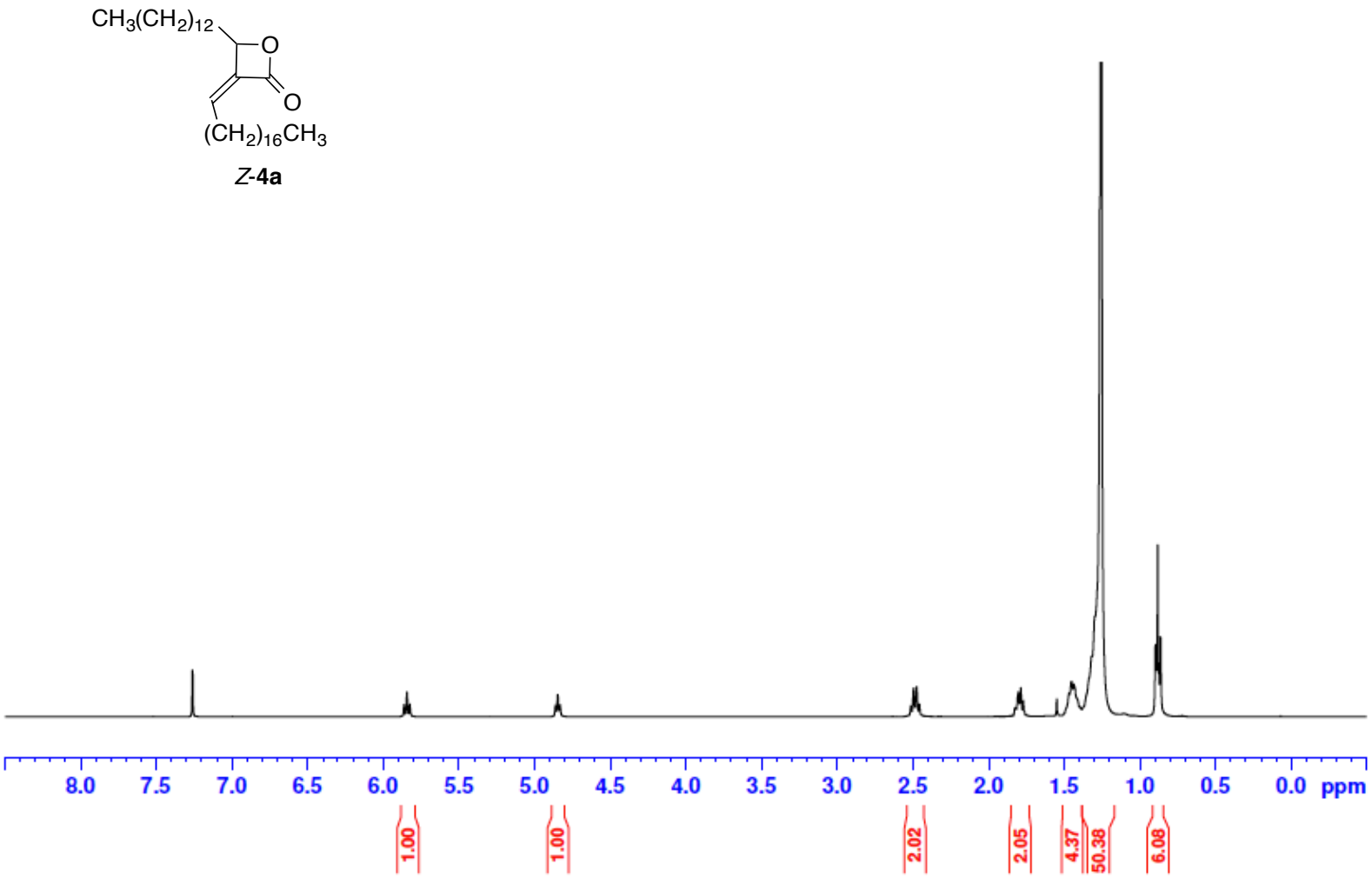
22.91
19.35
14.33
12.74
11.71
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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O
(CH2)16CH3
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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ppm
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4.37
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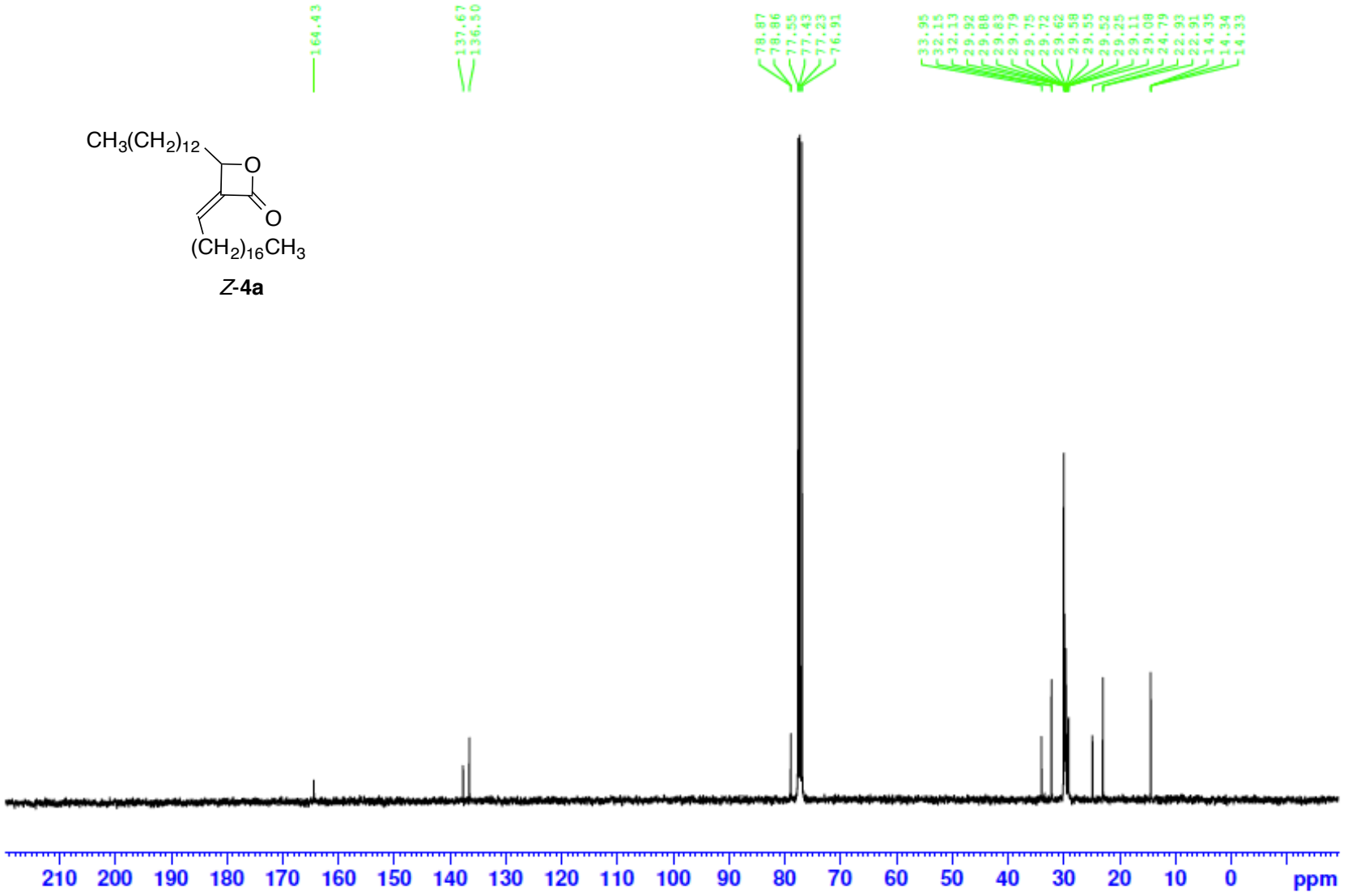
6.08

***Z*-4a**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29.88
29.83
29.79
29.75
29.72
29.62
29.58
29.55
29.52
29.25
29.11
29.08
24.79
22.93
22.91
14.35
14.34
14.33
CH3(CH2)12
O
O
(CH2)16CH3
Z-4a
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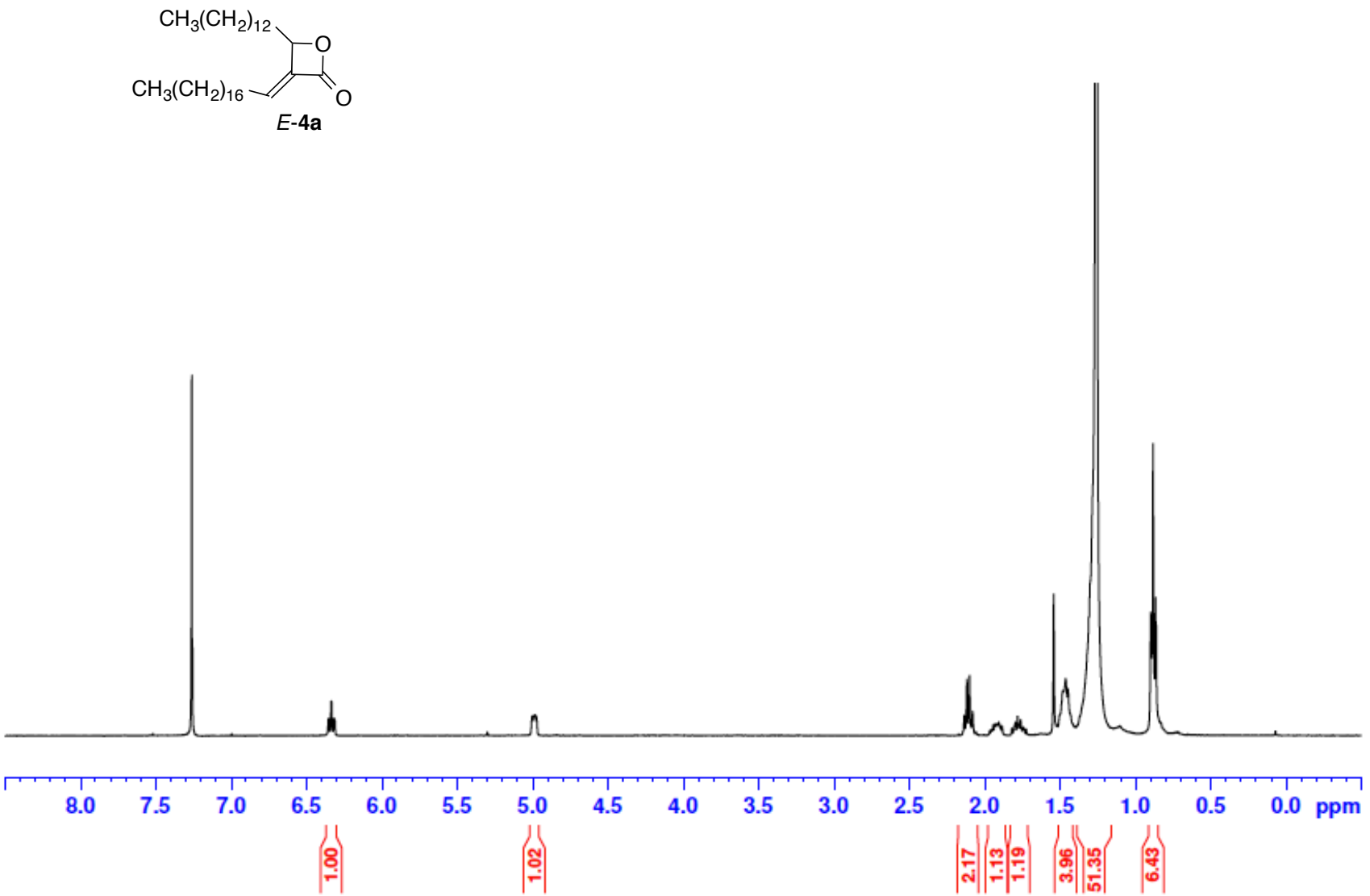
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O
CH3(CH2)16
O
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
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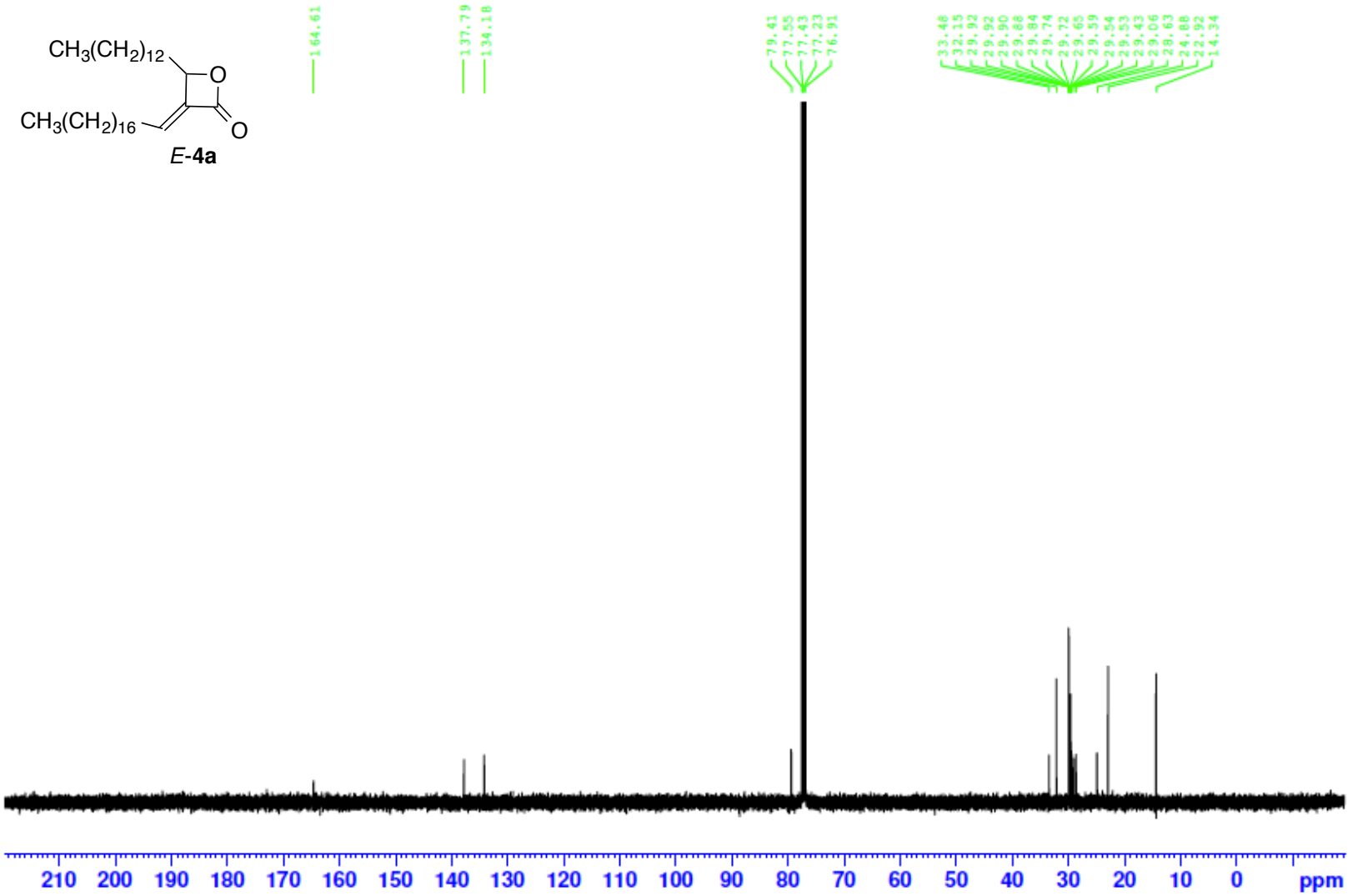
51.35
6.43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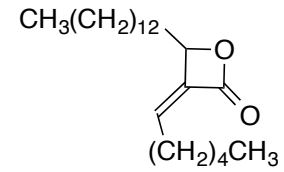
76.91
33.46
32.15
29.92
29.92
29.90
29.88
29.84
29.74
29.72
29.65
29.59
29.54
29.53
29.43
29.06
28.63
24.88
22.92
14.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm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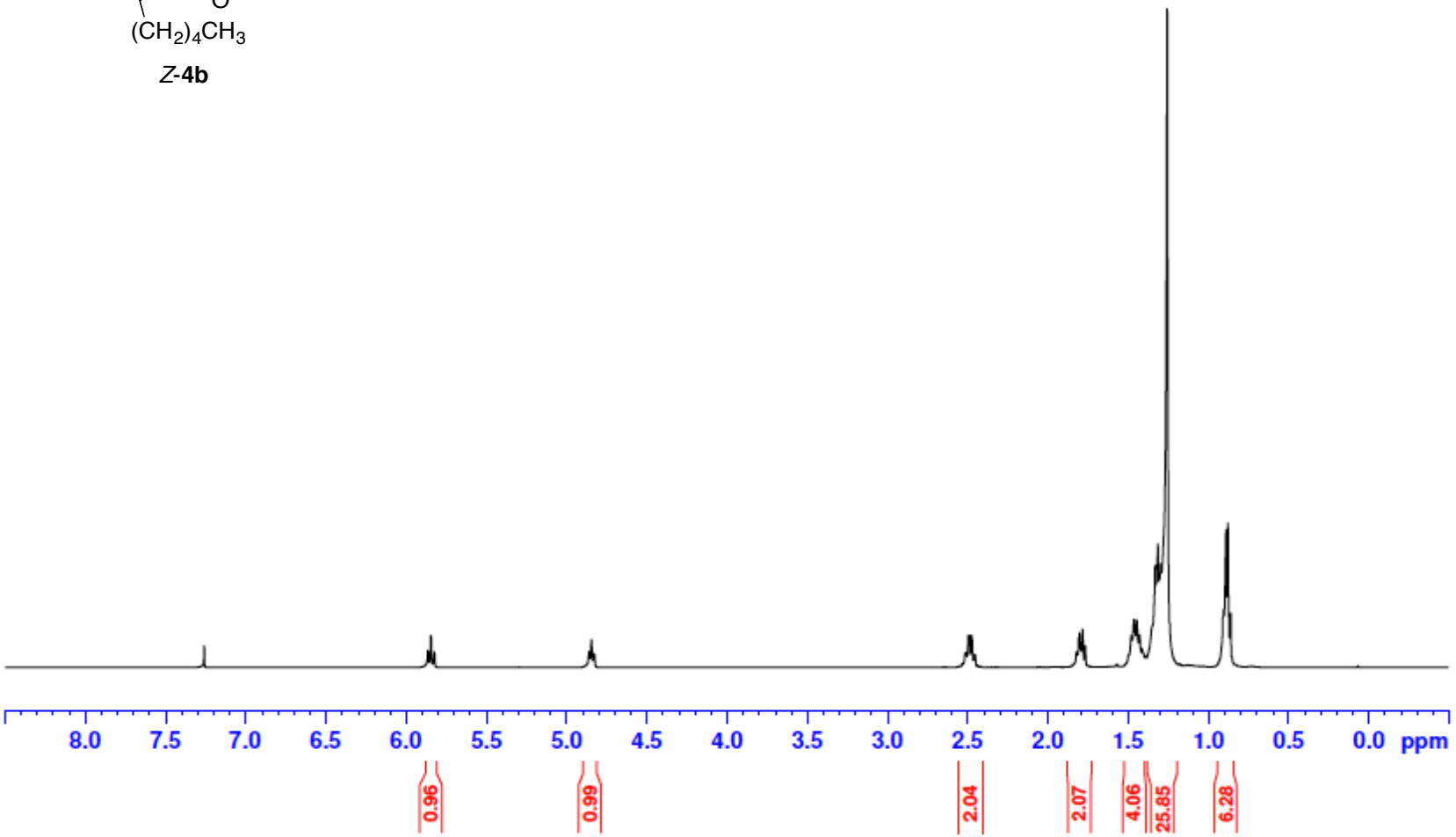
O
O
(CH2)4CH3

Z-**4b**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5.0
4.5
4.0
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3.0
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2.0
1.5
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0.5
0.0
ppm
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2.04
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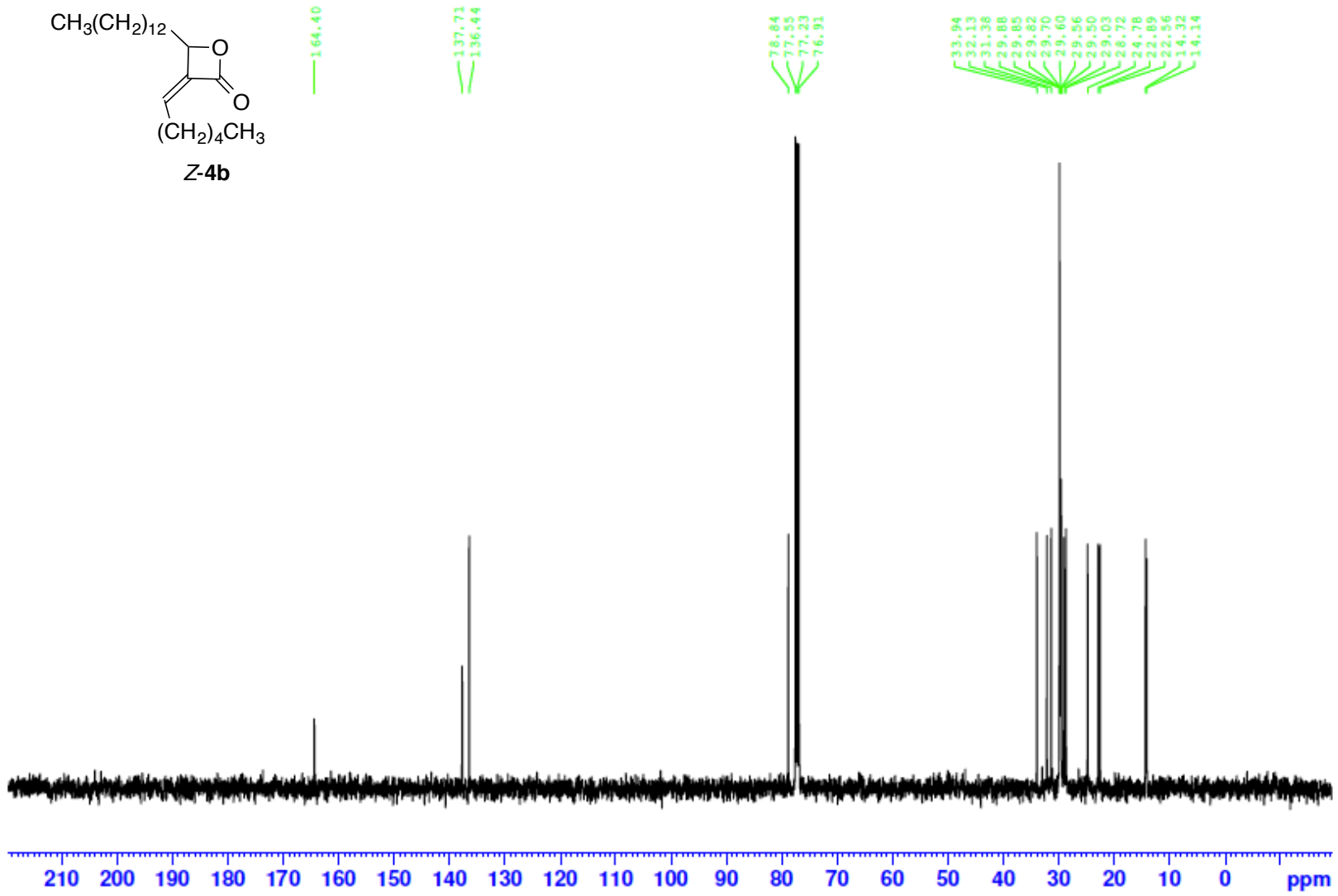
4.06
25.85
6.28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O
(CH2)4CH3
Z-4b
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76.91
33.94
32.13
31.38
29.88
29.85
29.82
29.70
29.60
29.56
29.50
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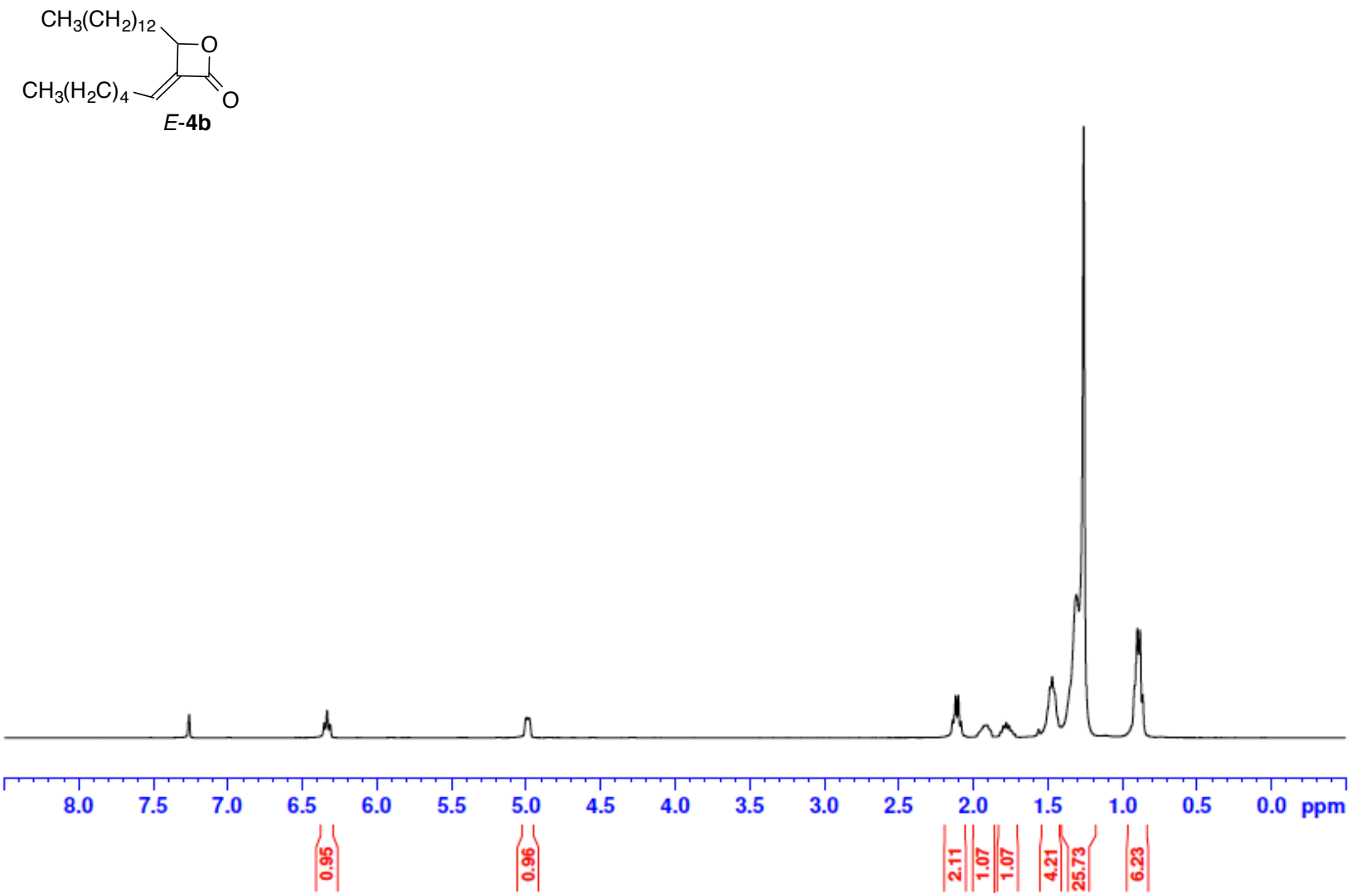
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CH3(H2C)4
O
E-4b
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
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ppm
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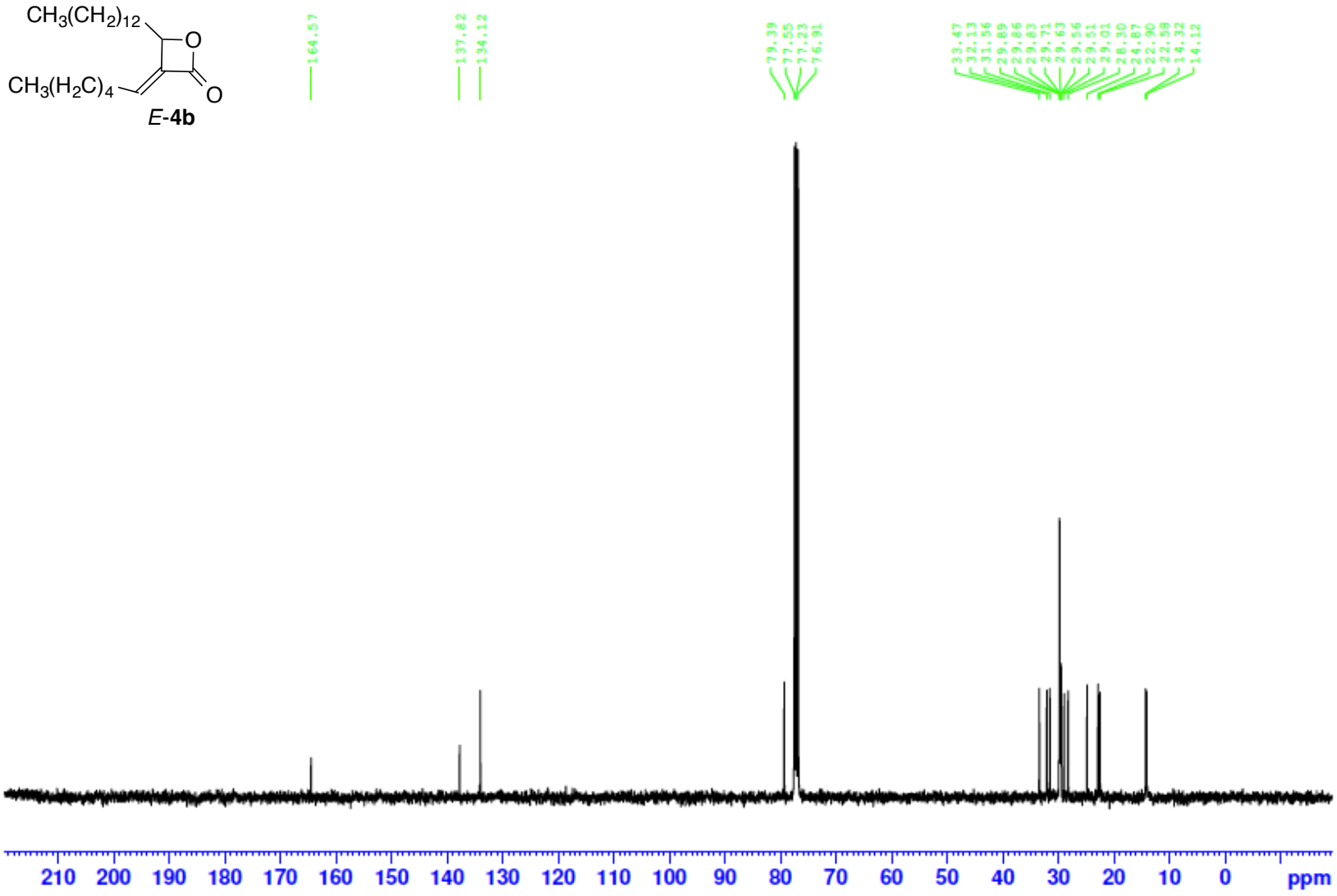
1.07
4.21
25.73
6.23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CH3(H2C)4
O
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29.83
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29.63
29.56
29.51
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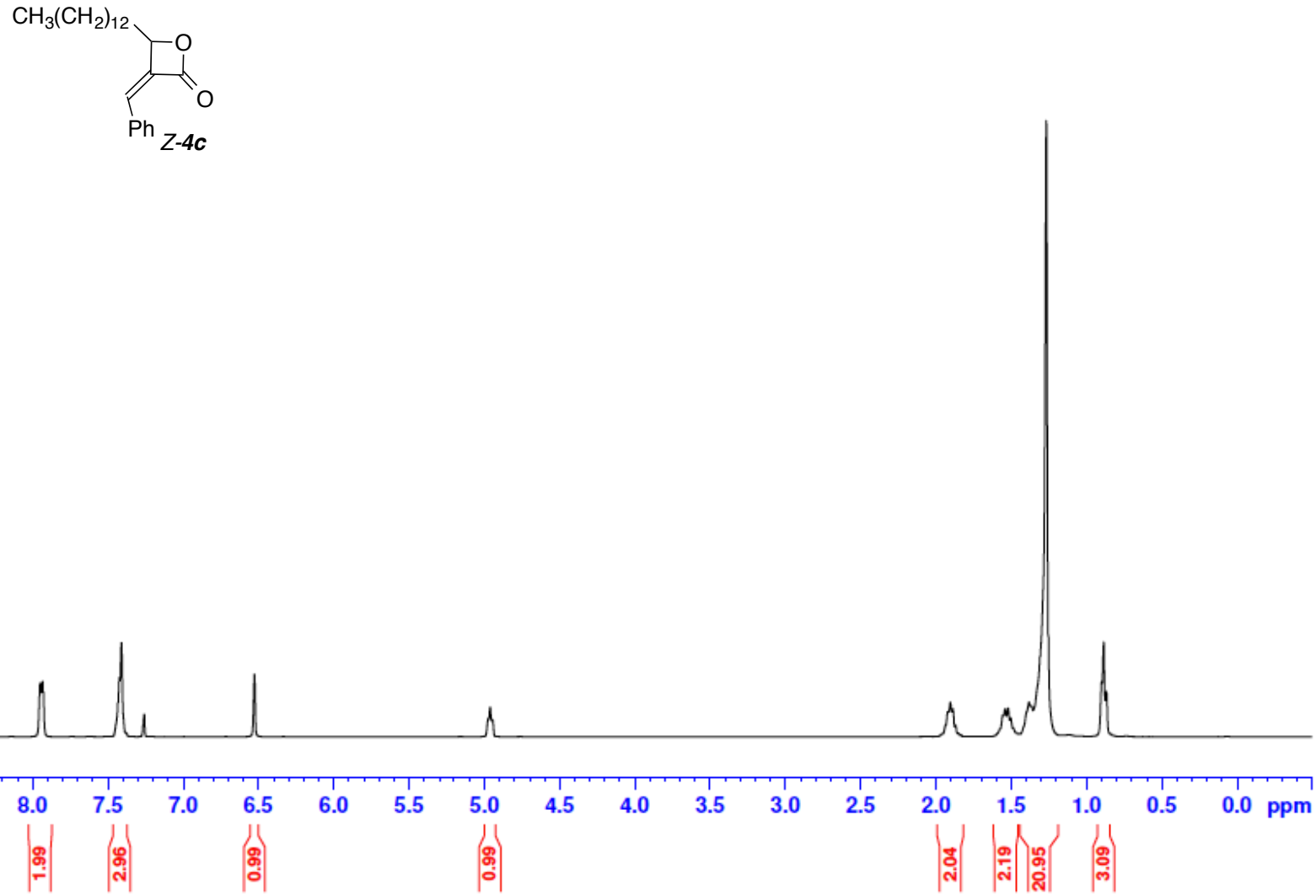
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O
Ph
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4.5
4.0
3.5
3.0
2.5
2.0
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ppm
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0.99
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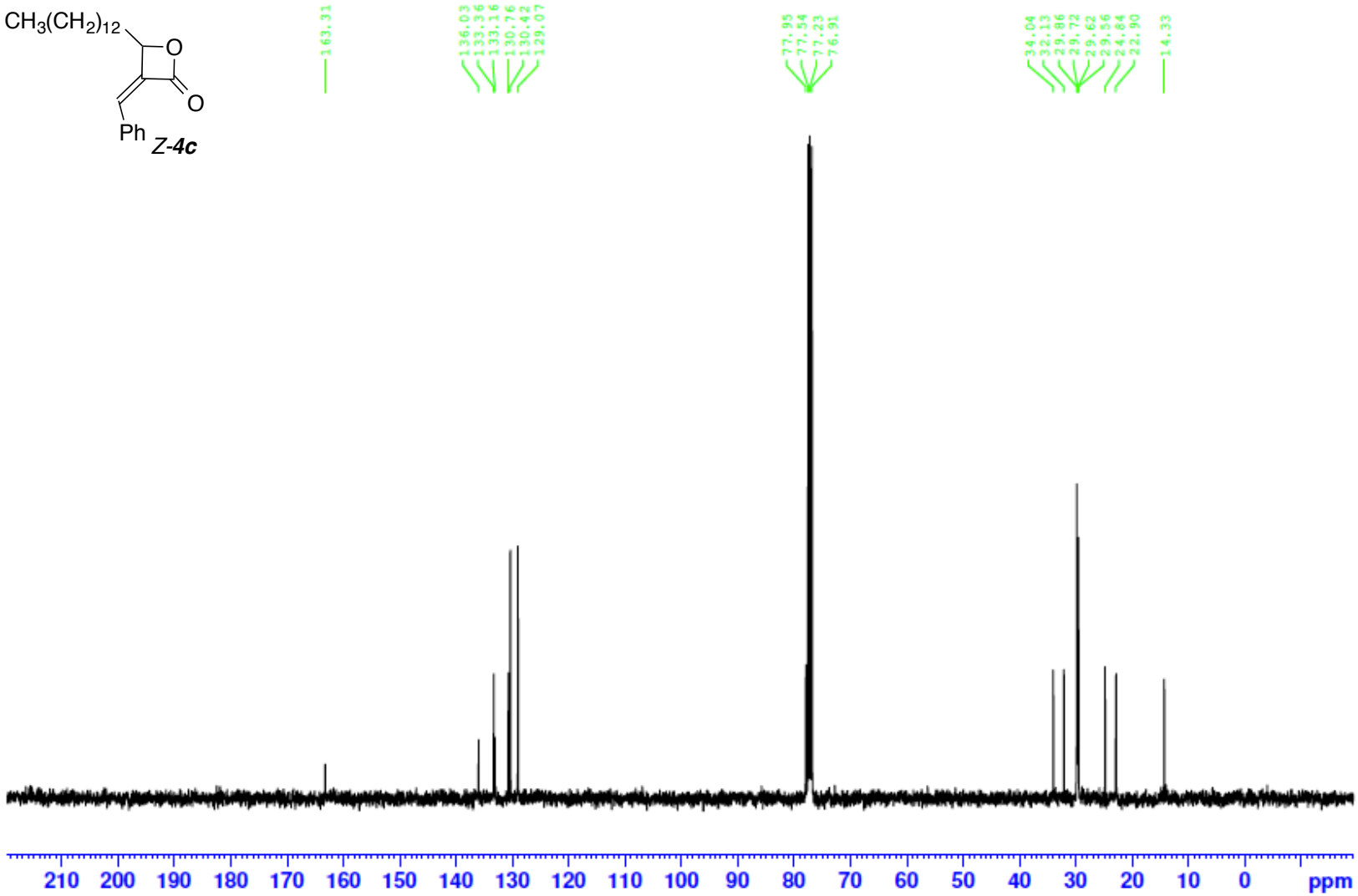
2.19
20.95
3.09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O
Ph
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77.95
77.54
77.23
76.91
34.04
32.13
29.86
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29.56
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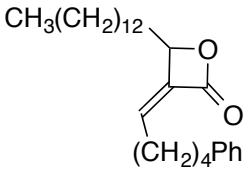
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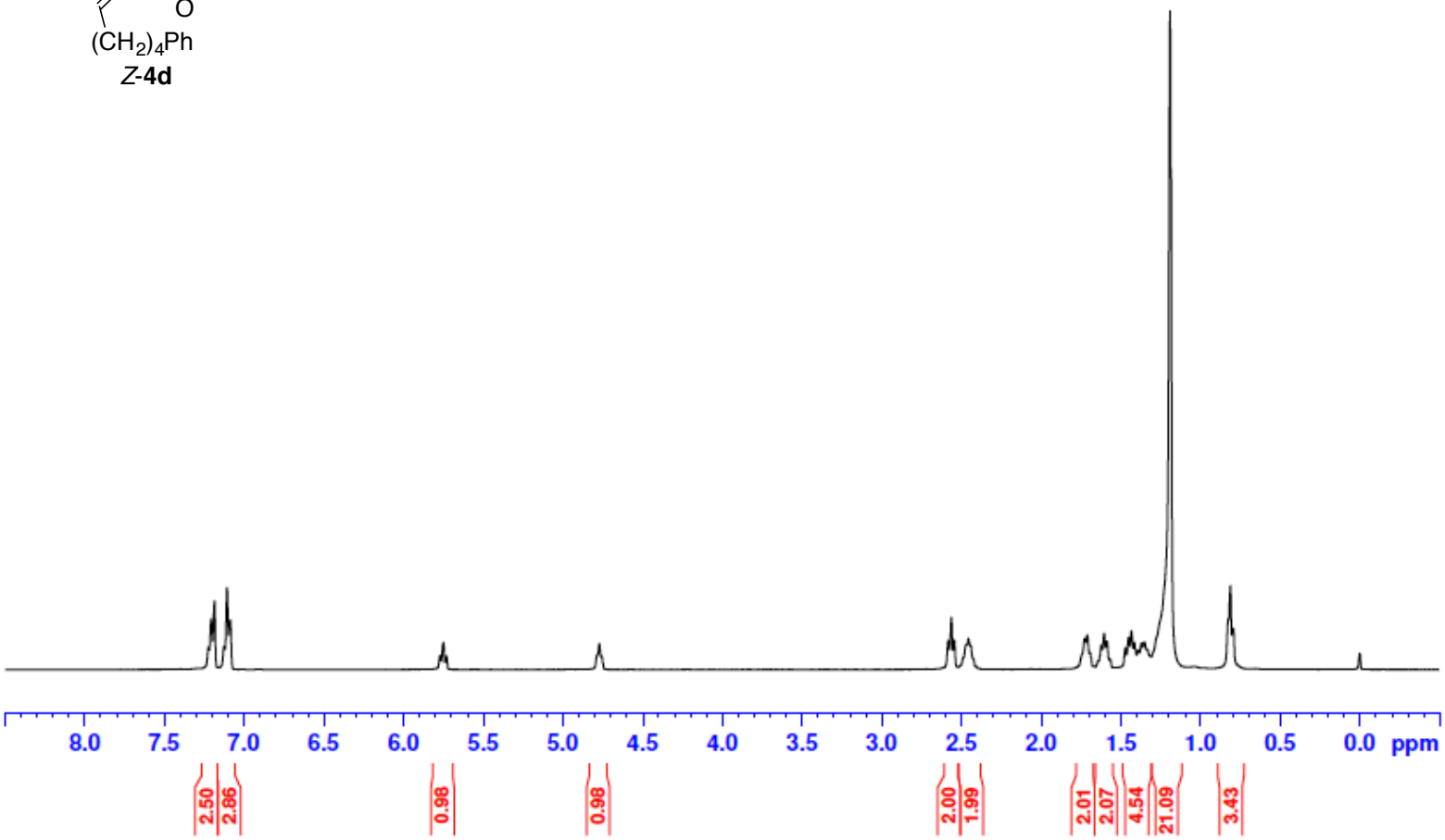
O
(CH2)4Ph

Z-**4d**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1.5
1.0
0.5
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ppm
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0.98
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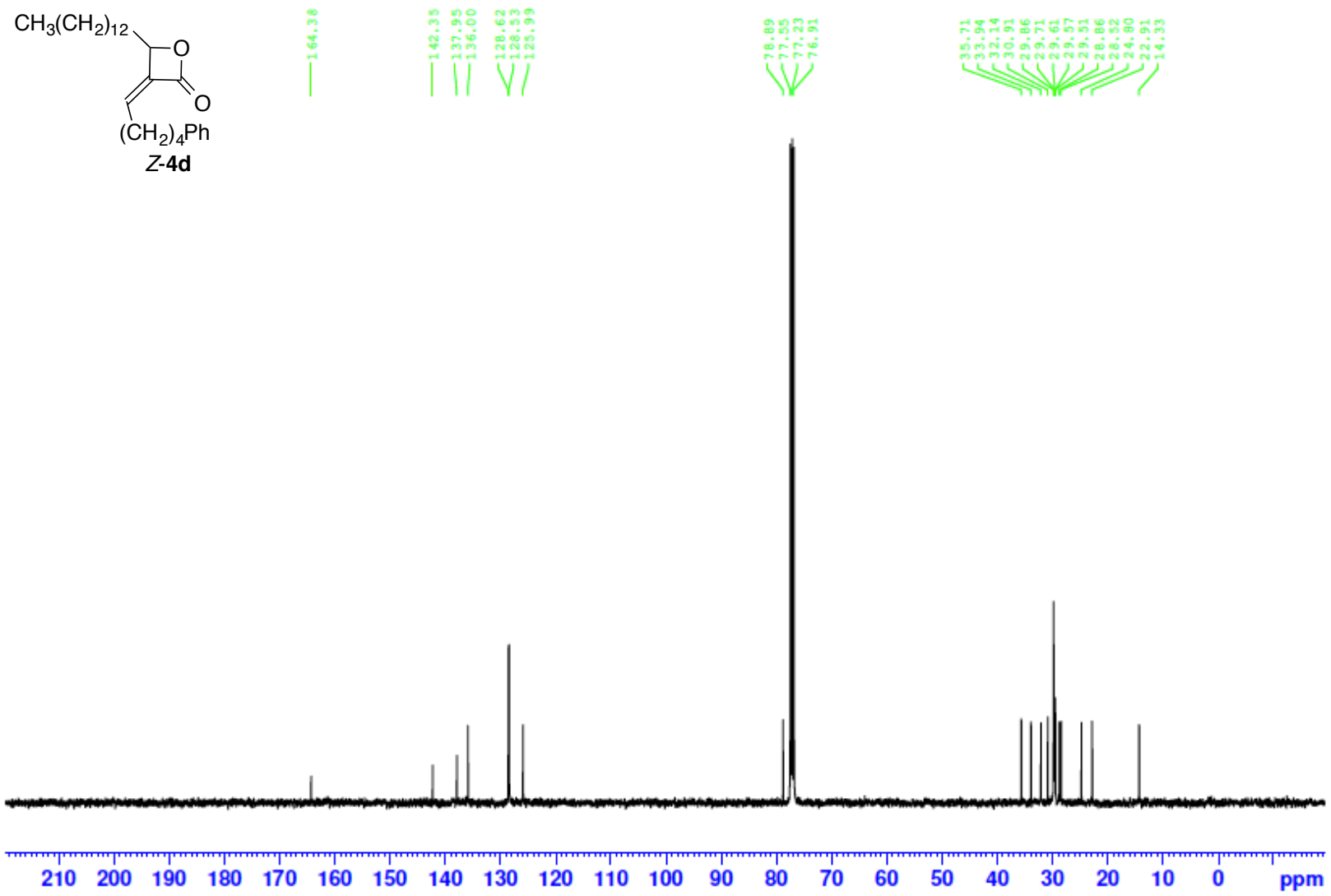
21.09
3.43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O
O
(CH2)4Ph
Z-4d
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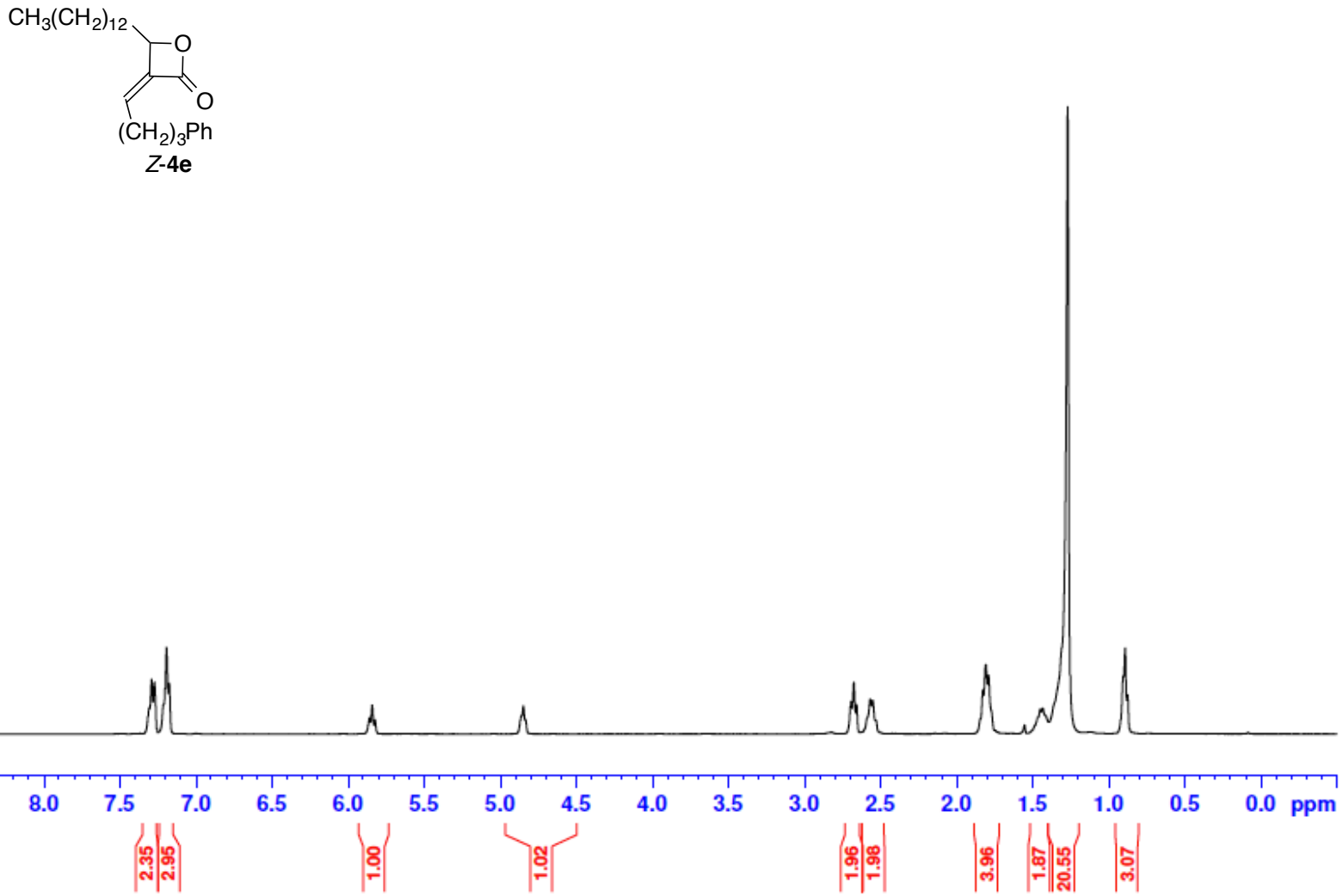
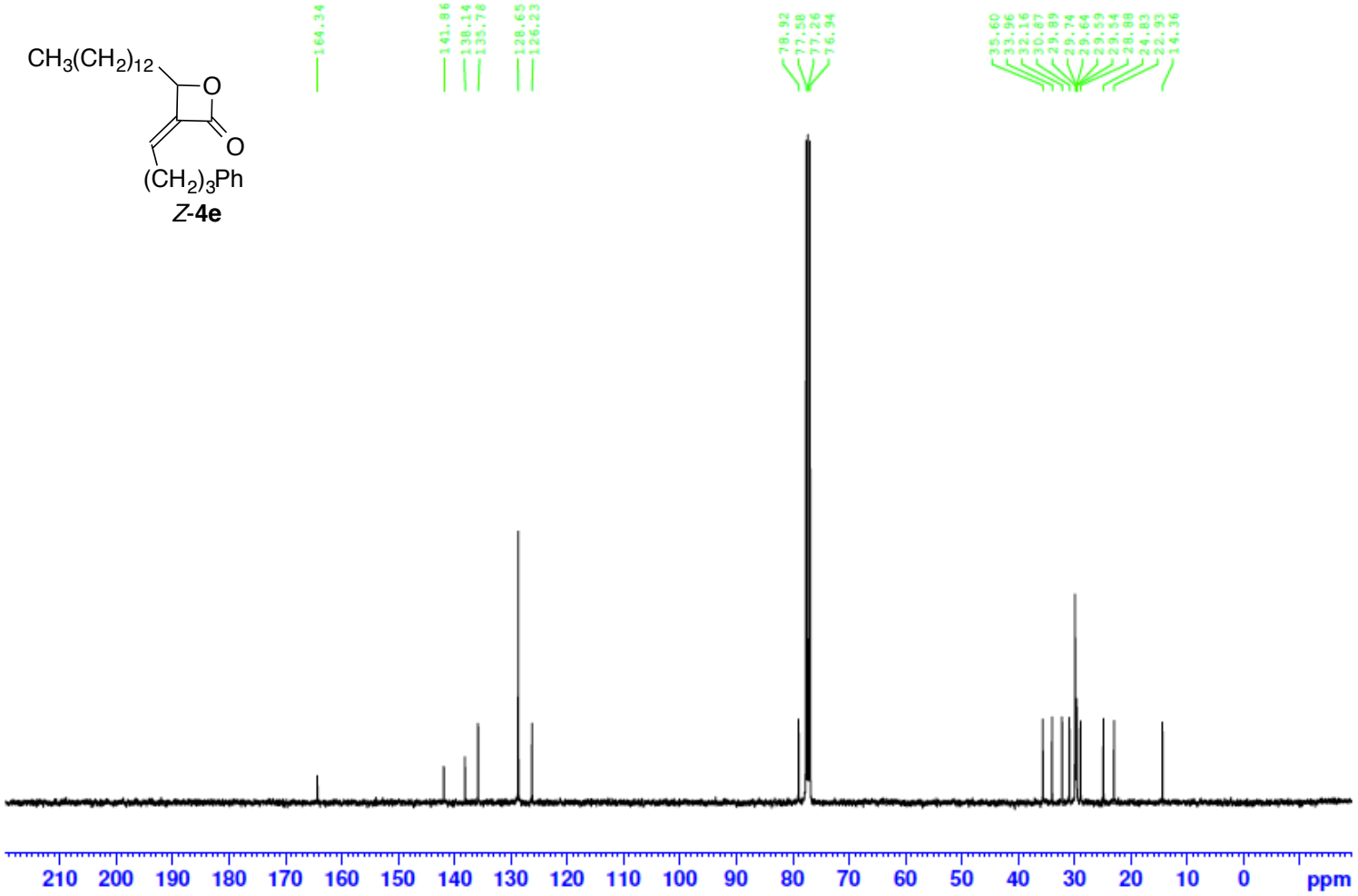
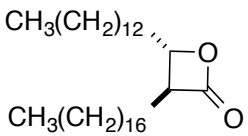
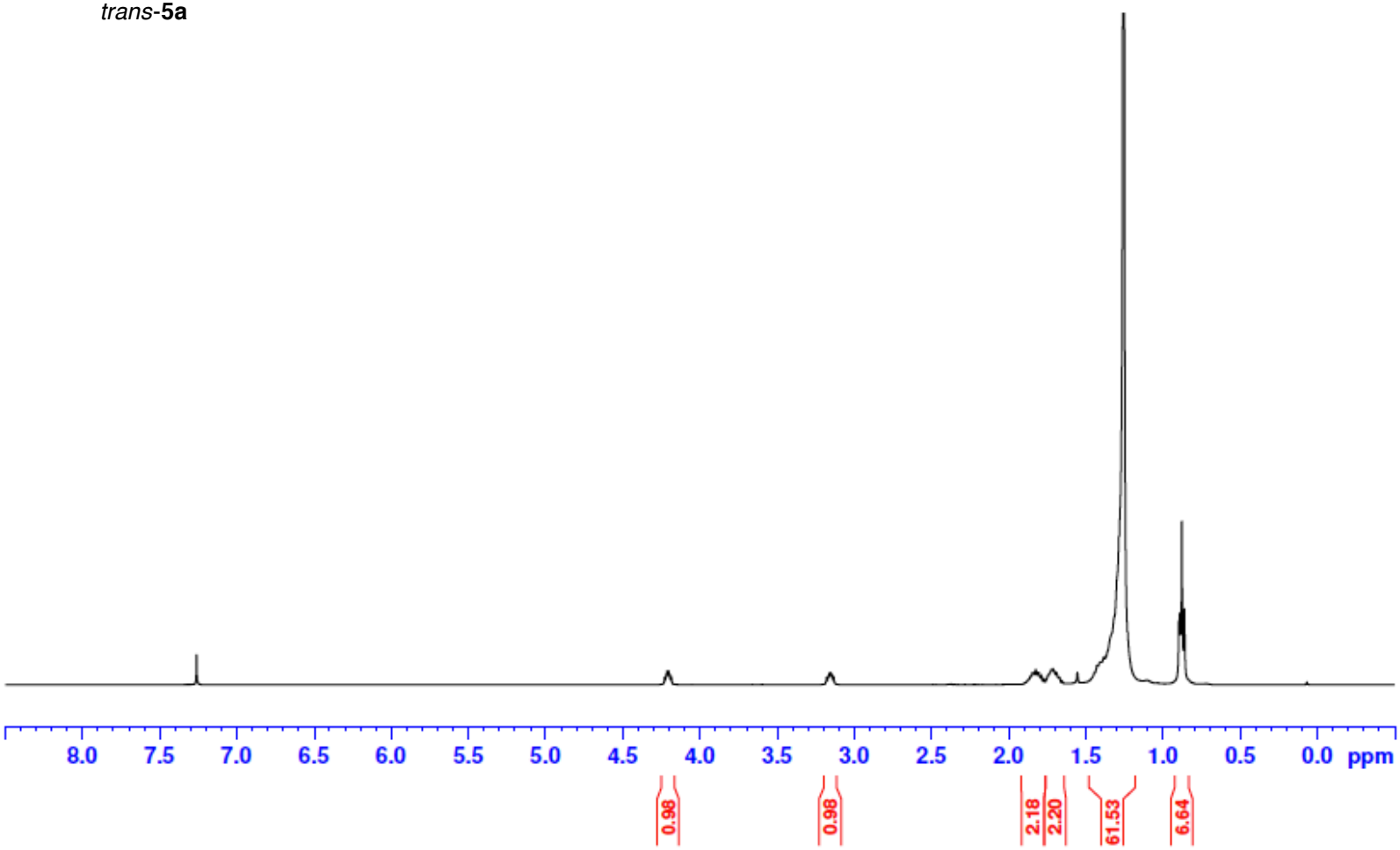
128.53
125.99
78.89
77.55
77.23
76.91
35.71
33.94
32.14
30.91
29.86
29.71
29.61
29.57
29.51
28.86
28.52
24.80
22.91
14.33
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

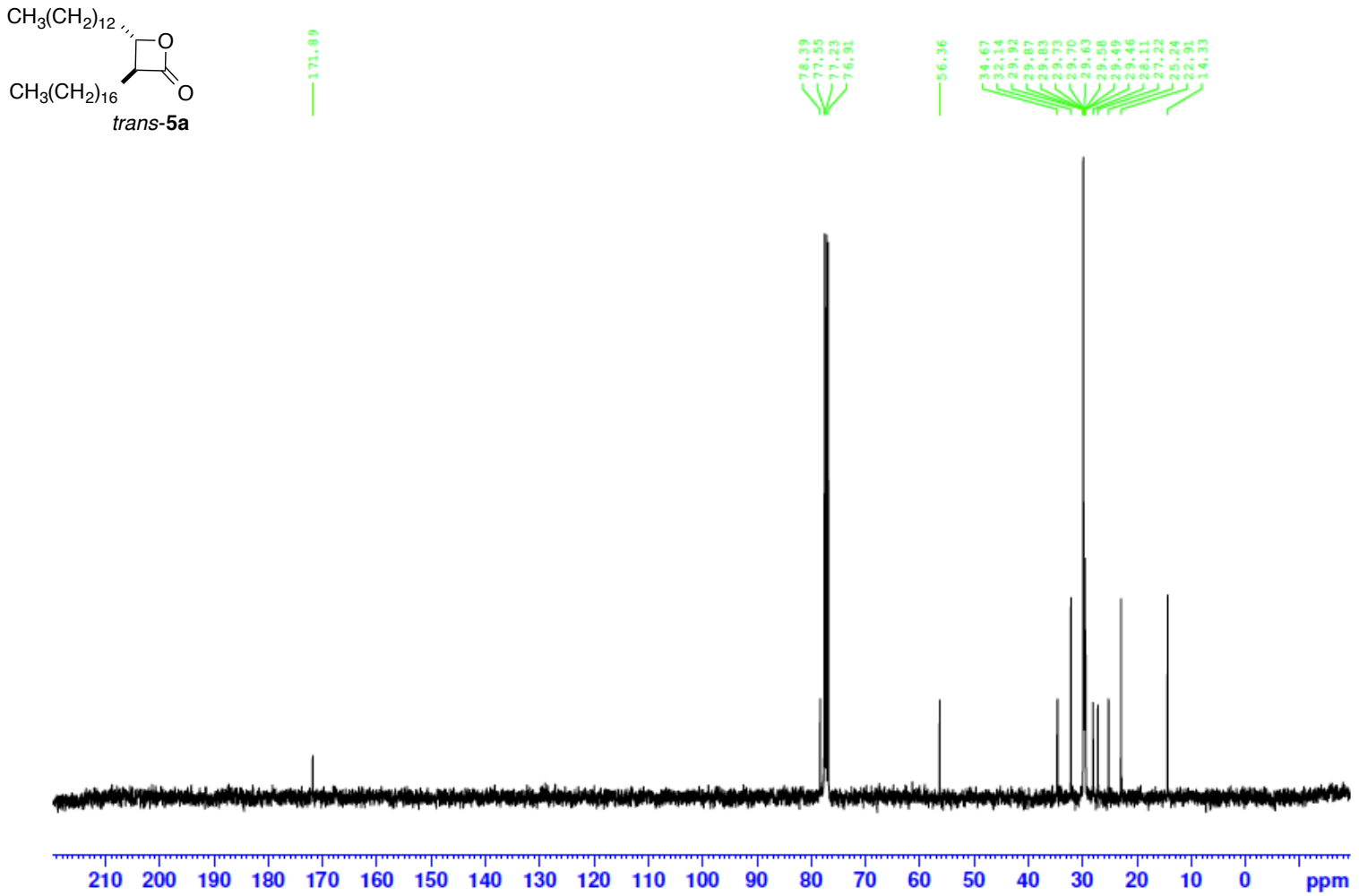

CH3(CH2)12
O
O
(CH2)3Ph
Z-4e
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.35
2.95
1.00
1.02
1.96
1.98
3.96
1.87
20.55
3.07

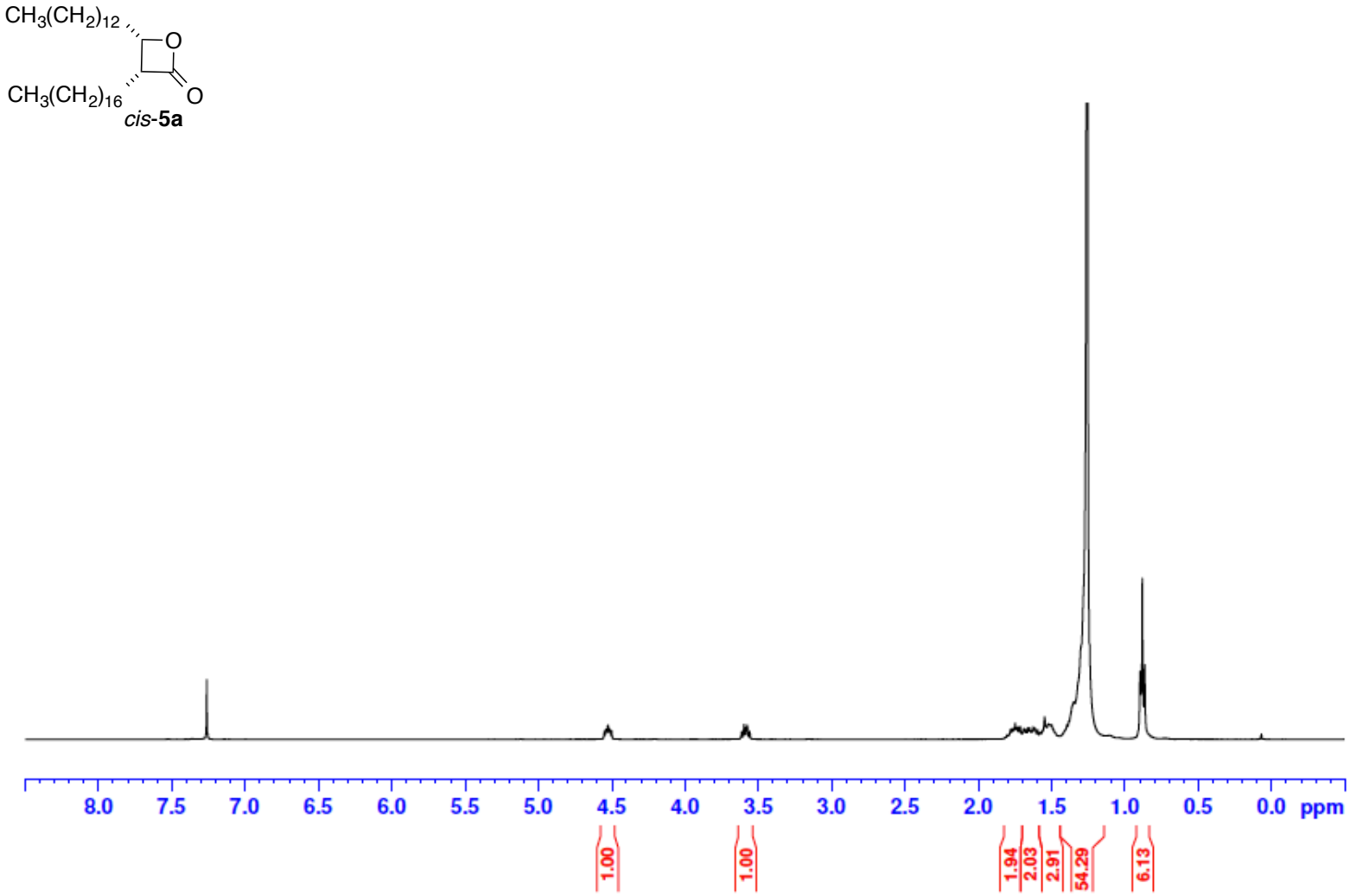

CH3(CH2)12
O
O
(CH2)3Ph
Z-4e
164.34
141.86
138.14
135.78
128.65
126.23
78.92
77.58
77.26
76.94
35.60
33.96
32.16
30.87
29.89
29.74
29.64
29.59
29.54
28.88
24.83
22.93
14.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

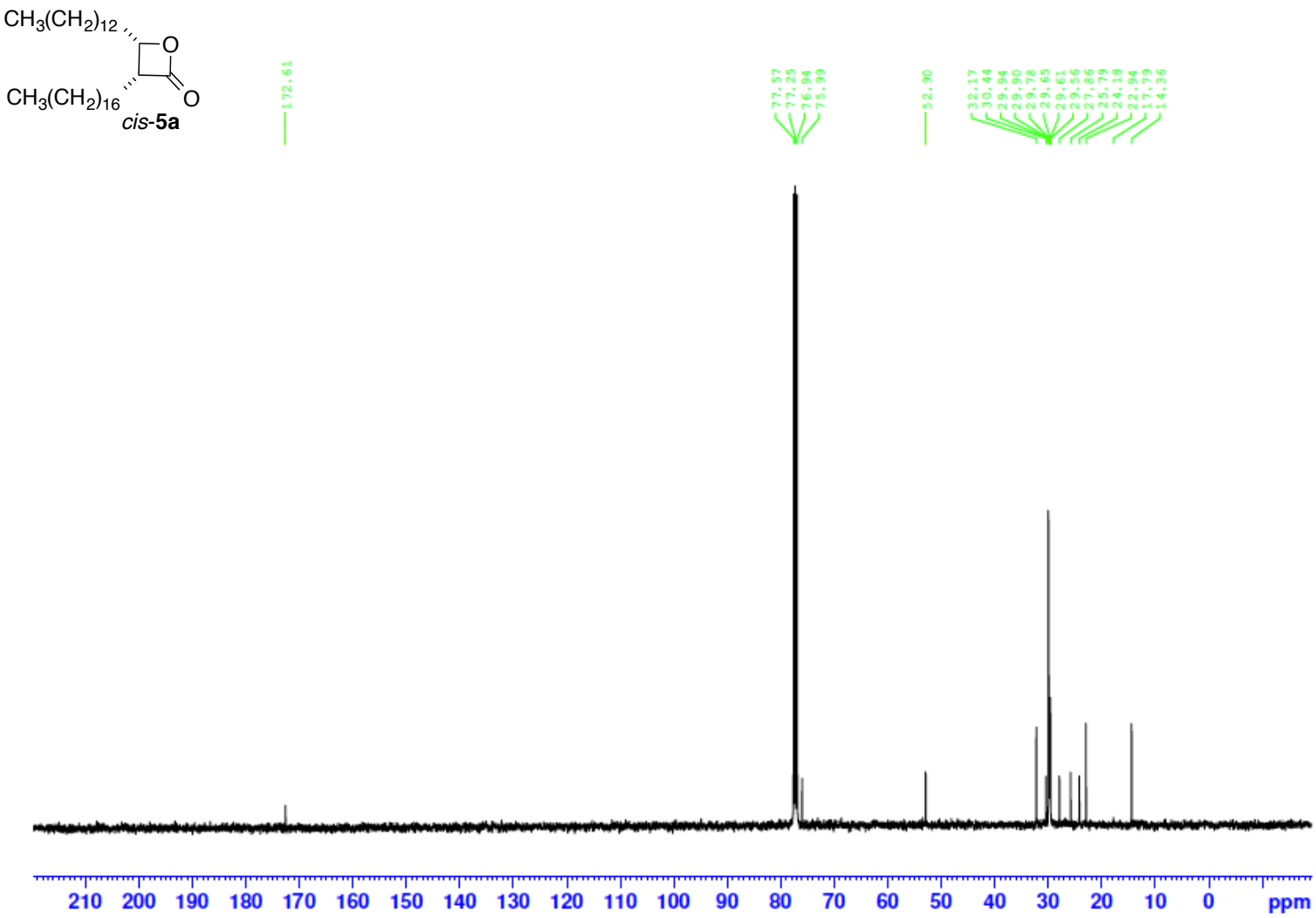

CH3(CH2)12
O
CH3(CH2)16
O

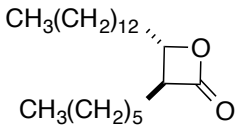
trans-**5a**


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.98
0.98
2.18
2.20
61.53
6.64

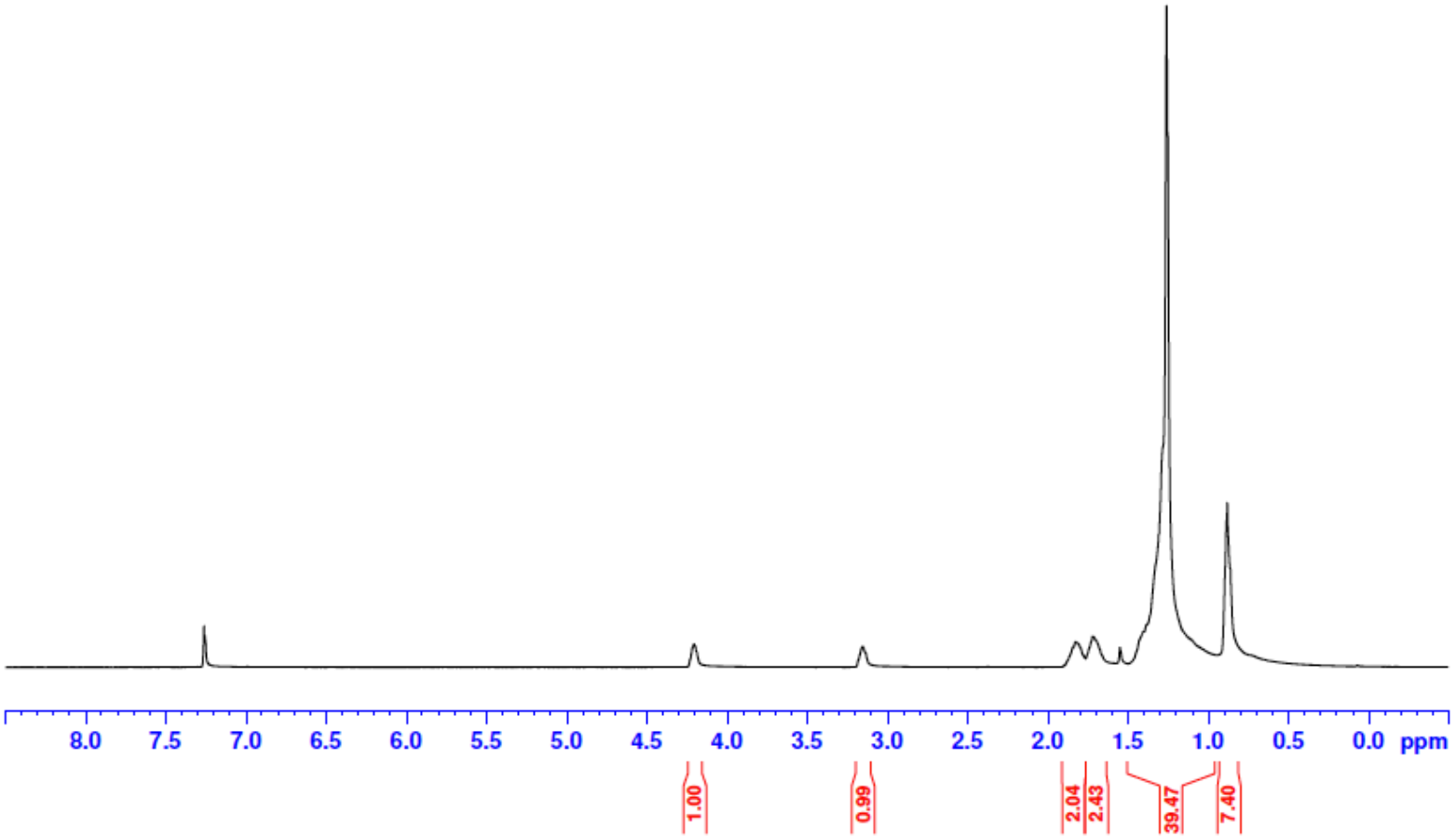

CH3(CH2)12
O
CH3(CH2)16
O
trans-5a
171.89
78.39
77.55
77.23
76.91
56.36
34.67
32.14
29.92
29.87
29.83
29.73
29.70
29.63
29.58
29.49
29.46
28.11
27.22
25.24
22.91
14.33
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

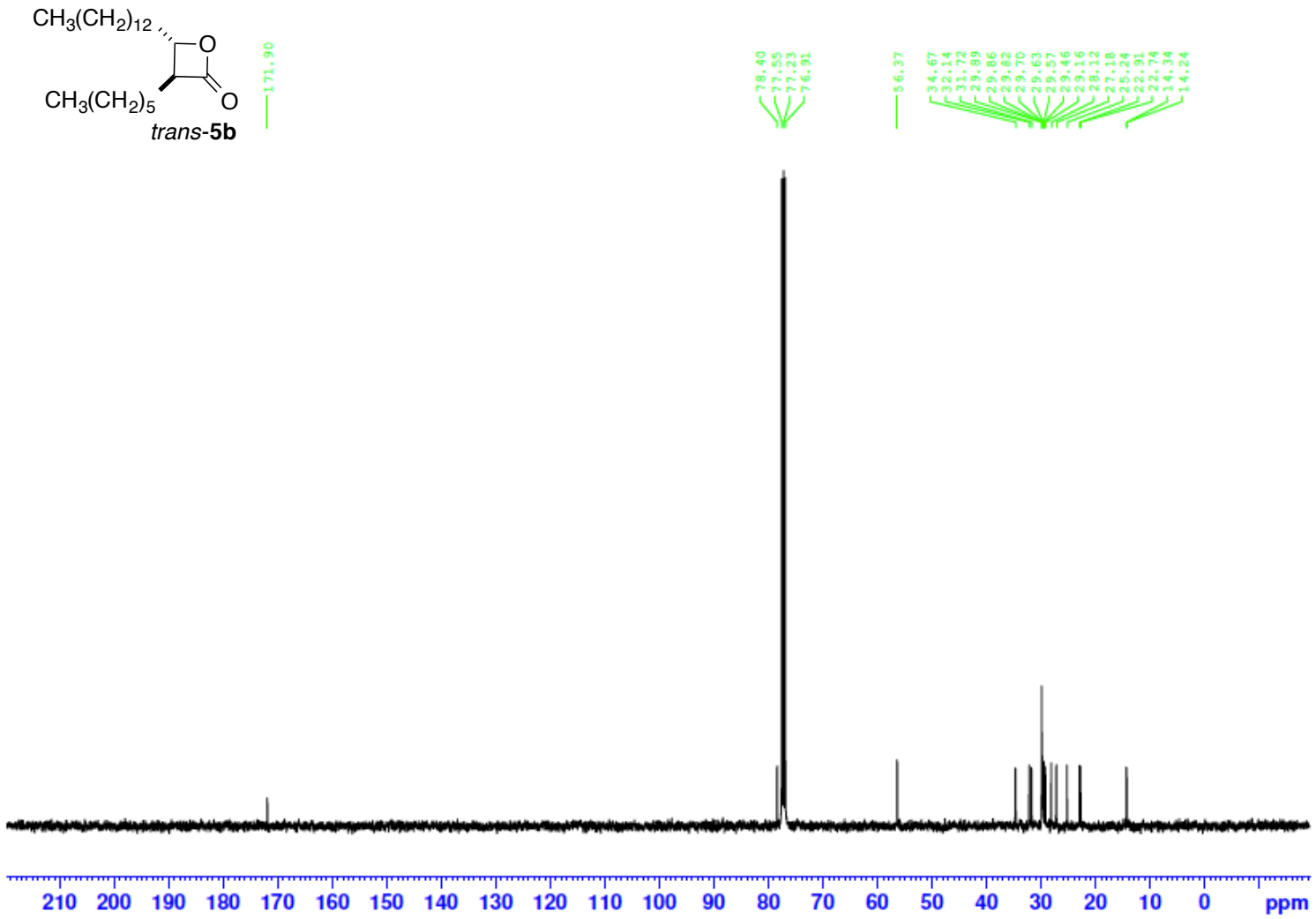

CH3(CH2)12
O
CH3(CH2)16
O
cis-5a
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.00
1.94
2.03
2.91
54.29
6.13

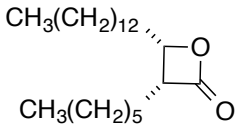

CH3(CH2)12
CH3(CH2)16
O
O
cis-5a
172.61
77.57
77.25
76.94
75.99
52.90
32.17
30.44
29.94
29.90
29.78
29.65
29.61
29.56
27.86
25.79
24.18
22.94
17.79
14.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


CH3(CH2)12
O
CH3(CH2)5
O

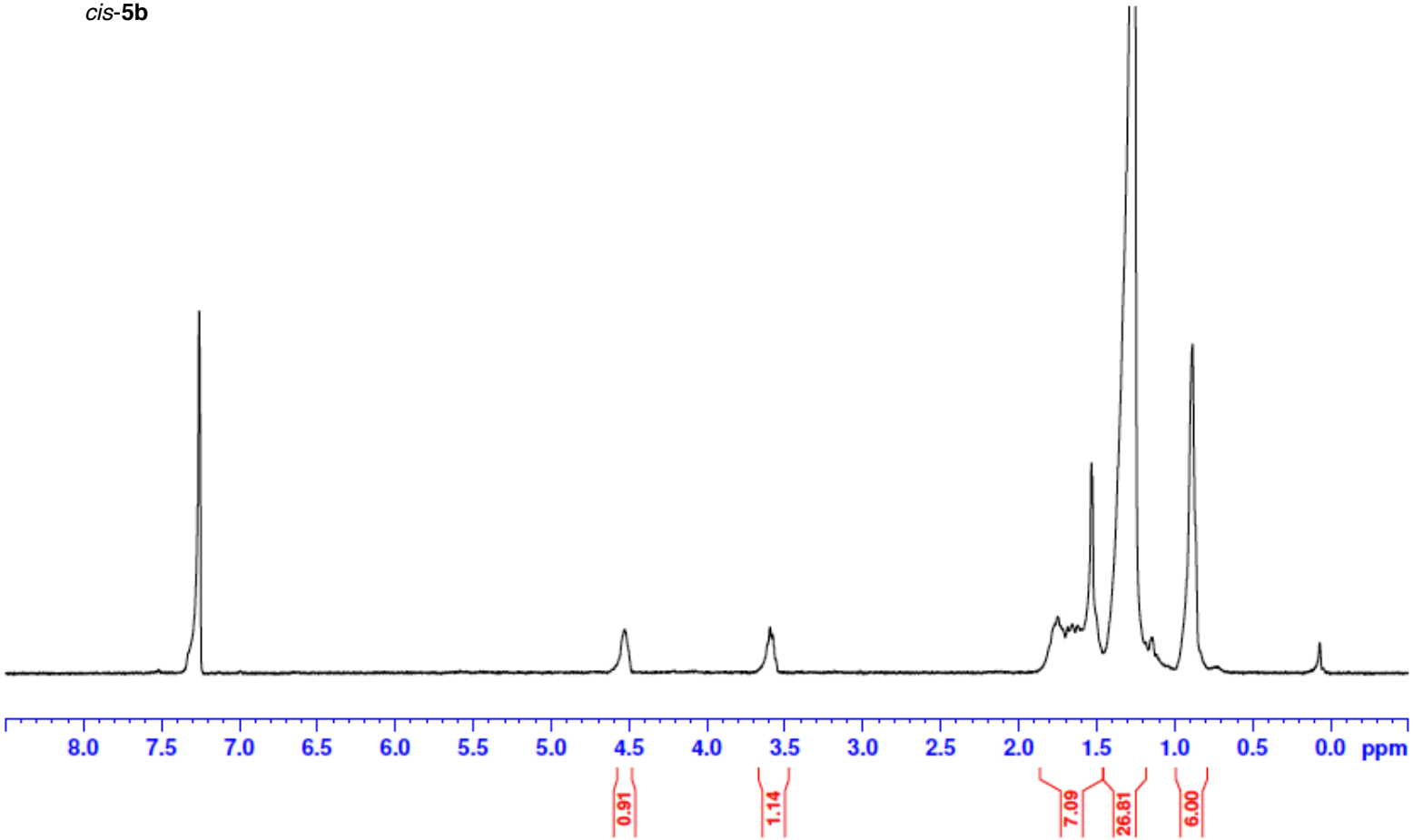
trans-**5b**

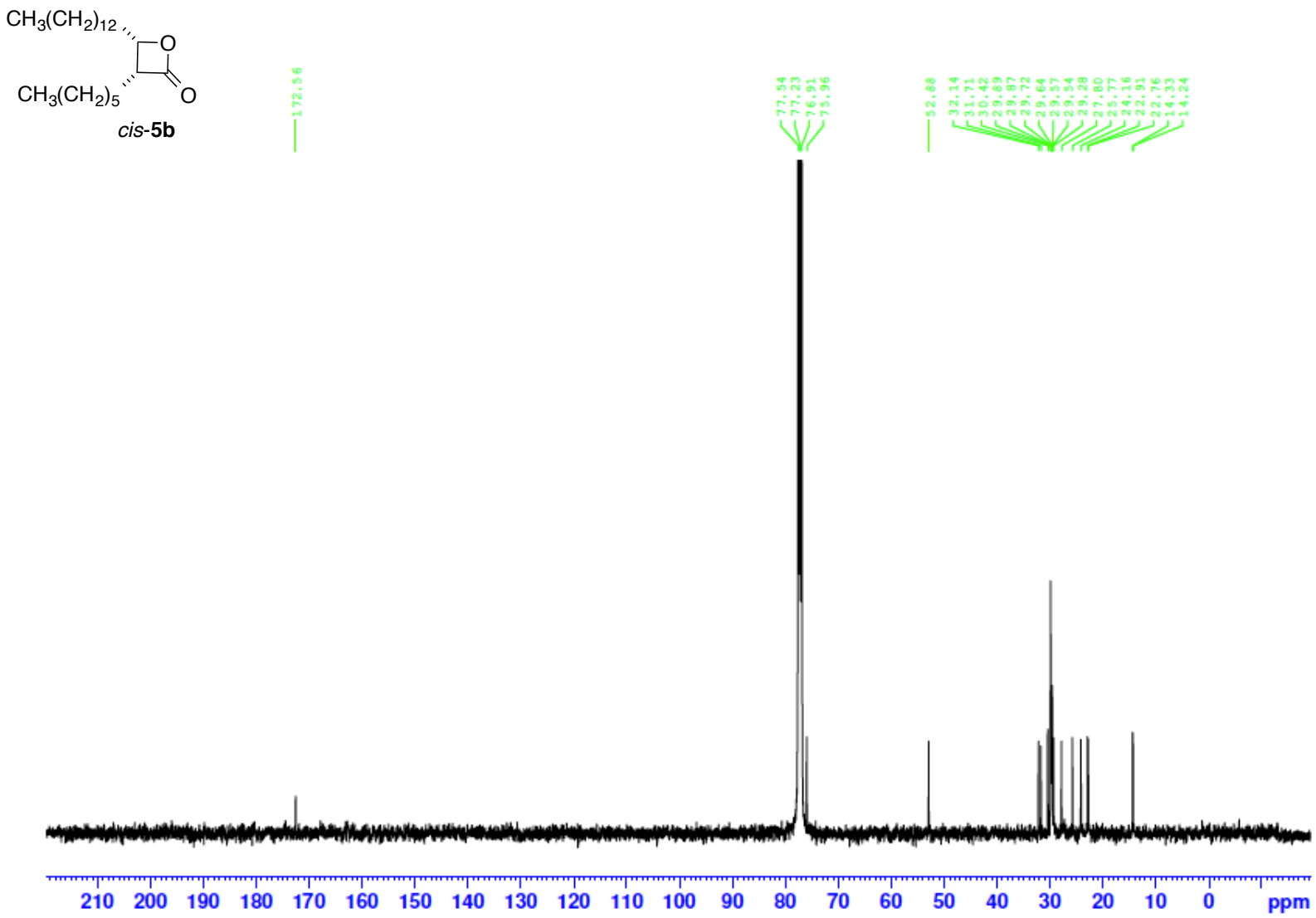

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.99
2.04
2.43
39.47
7.40

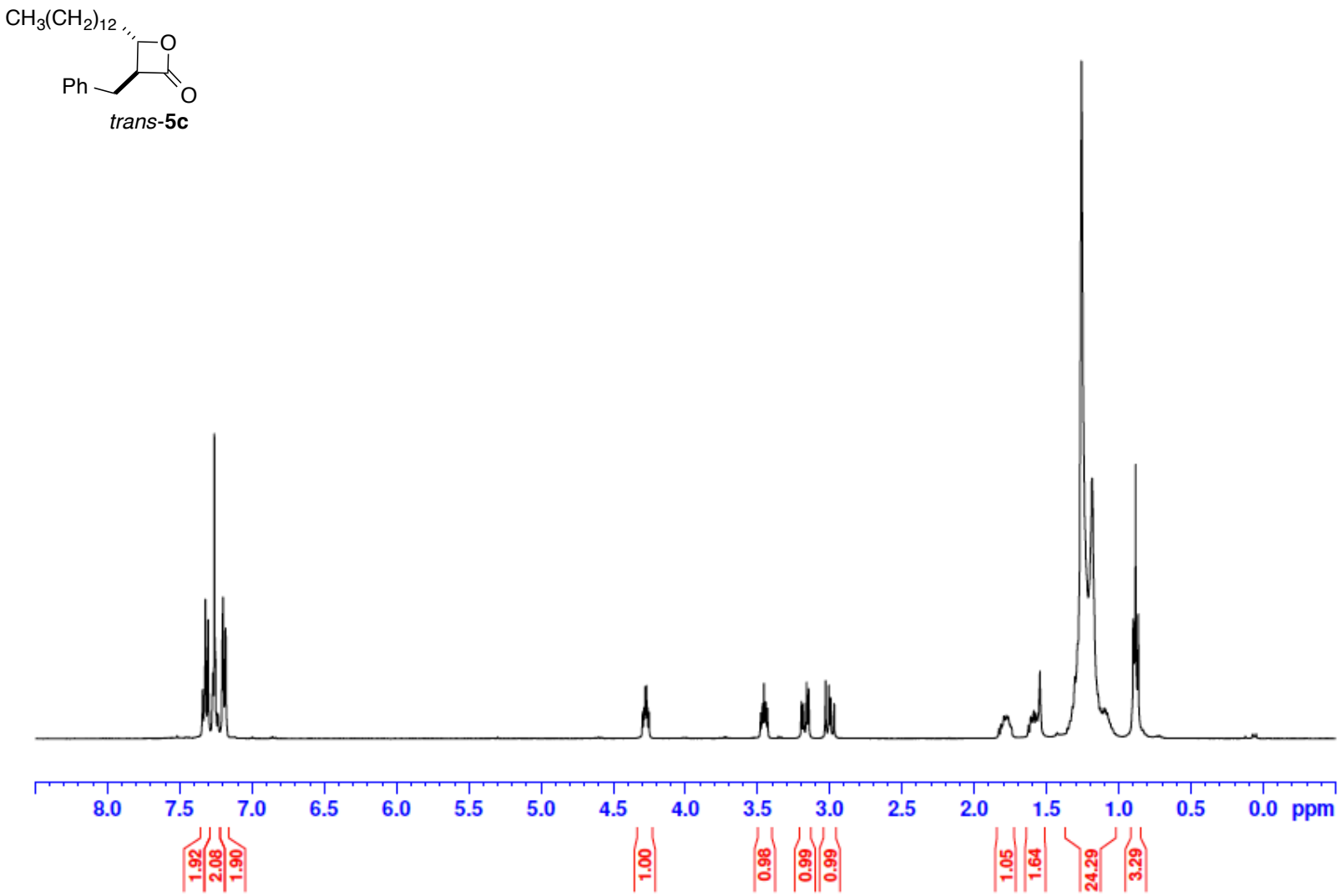

CH3(CH2)12
O
CH3(CH2)5
O
trans-5b
171.90
78.40
77.55
77.23
76.91
56.37
34.67
32.14
31.72
29.89
29.86
29.82
29.70
29.63
29.57
29.46
29.16
28.12
27.18
25.24
22.91
22.74
14.34
14.24
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

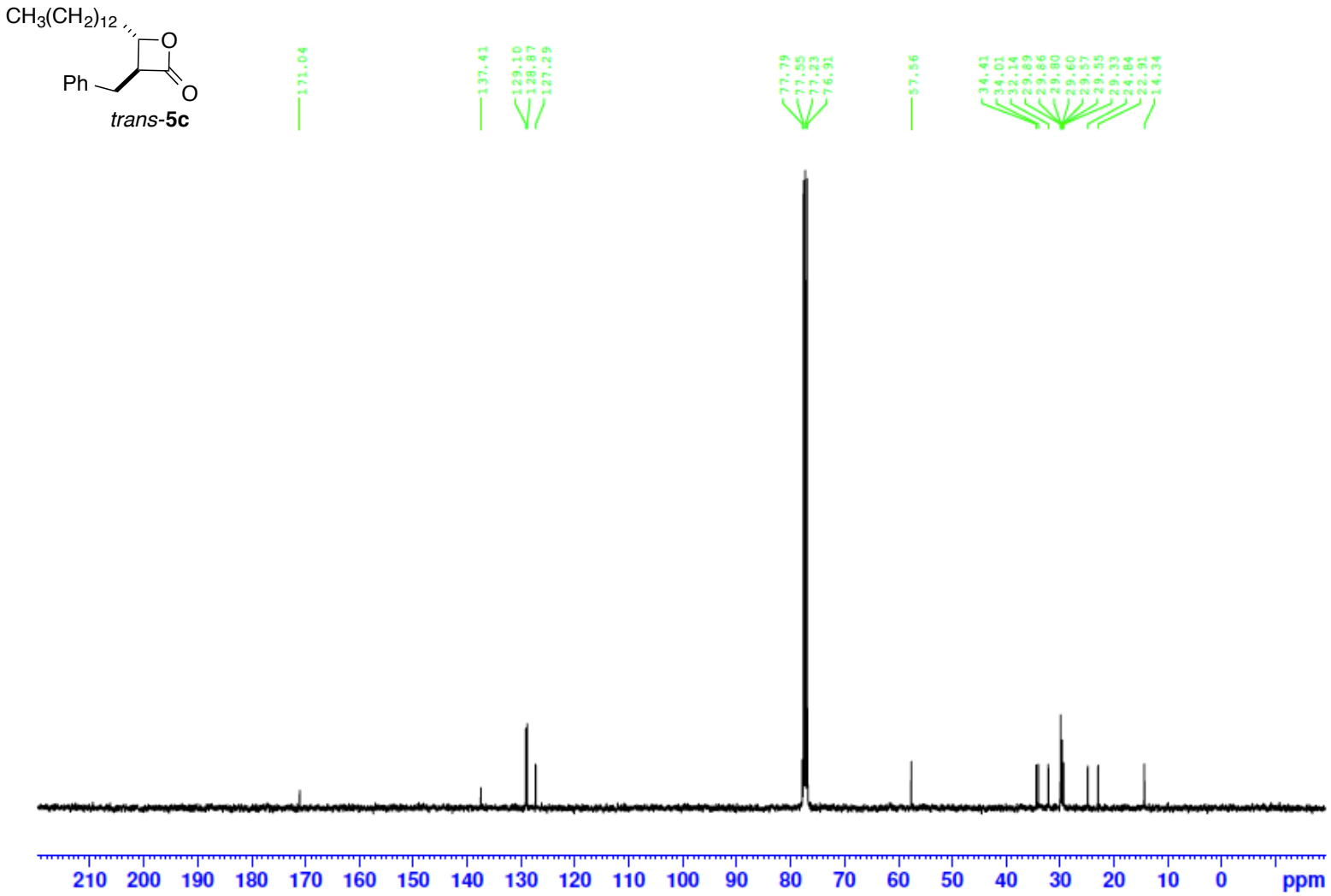

CH3(CH2)12
O
CH3(CH2)5
O

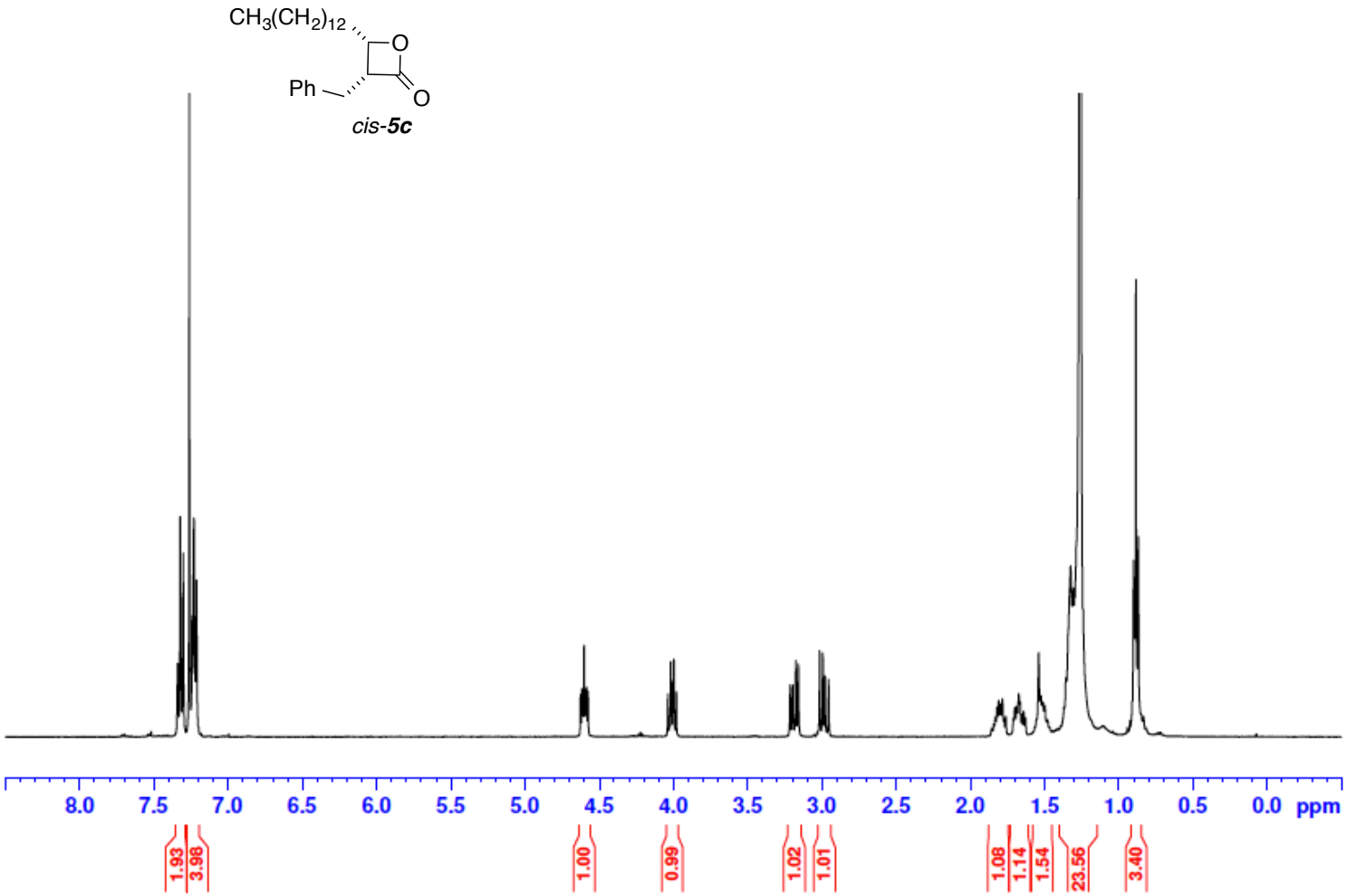
cis-**5b**

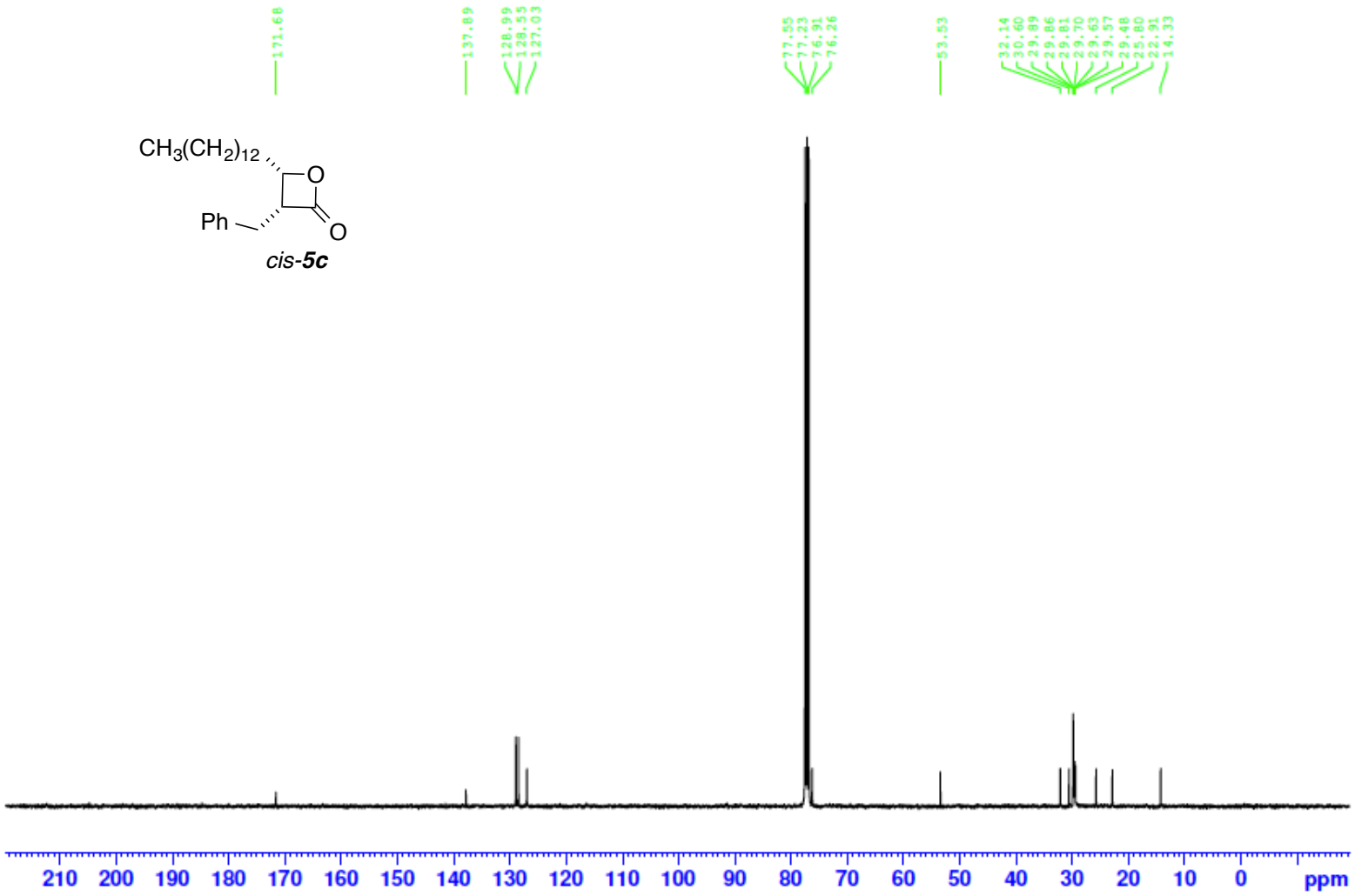

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
0.91
1.14
7.09
26.81
6.00

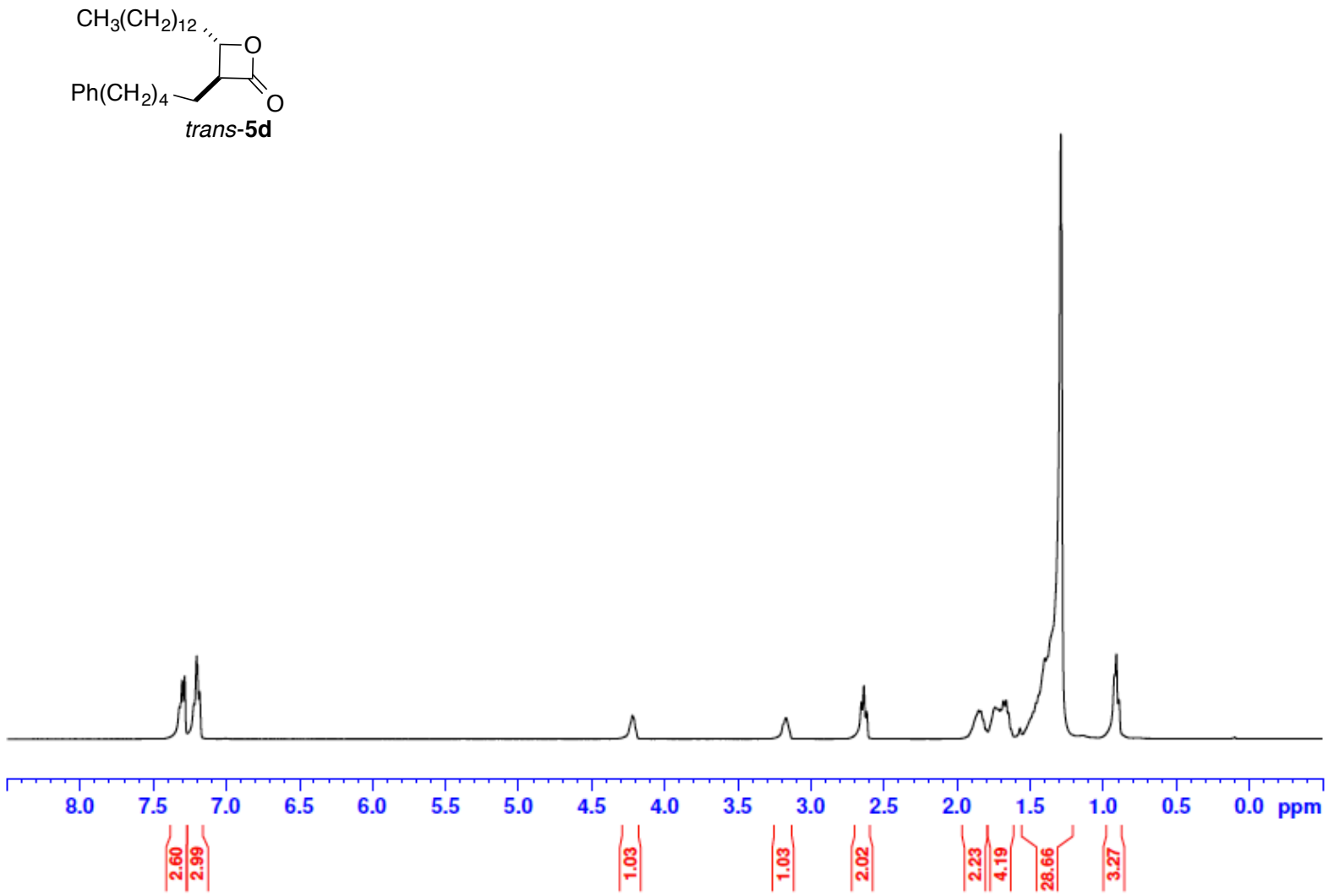

CH3(CH2)12
O
CH3(CH2)5
O
cis-5b
172.56
77.54
77.23
76.91
75.96
52.88
32.14
31.71
30.42
29.89
29.87
29.72
29.64
29.57
29.54
29.28
27.80
25.77
24.16
22.91
22.76
14.33
14.24
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

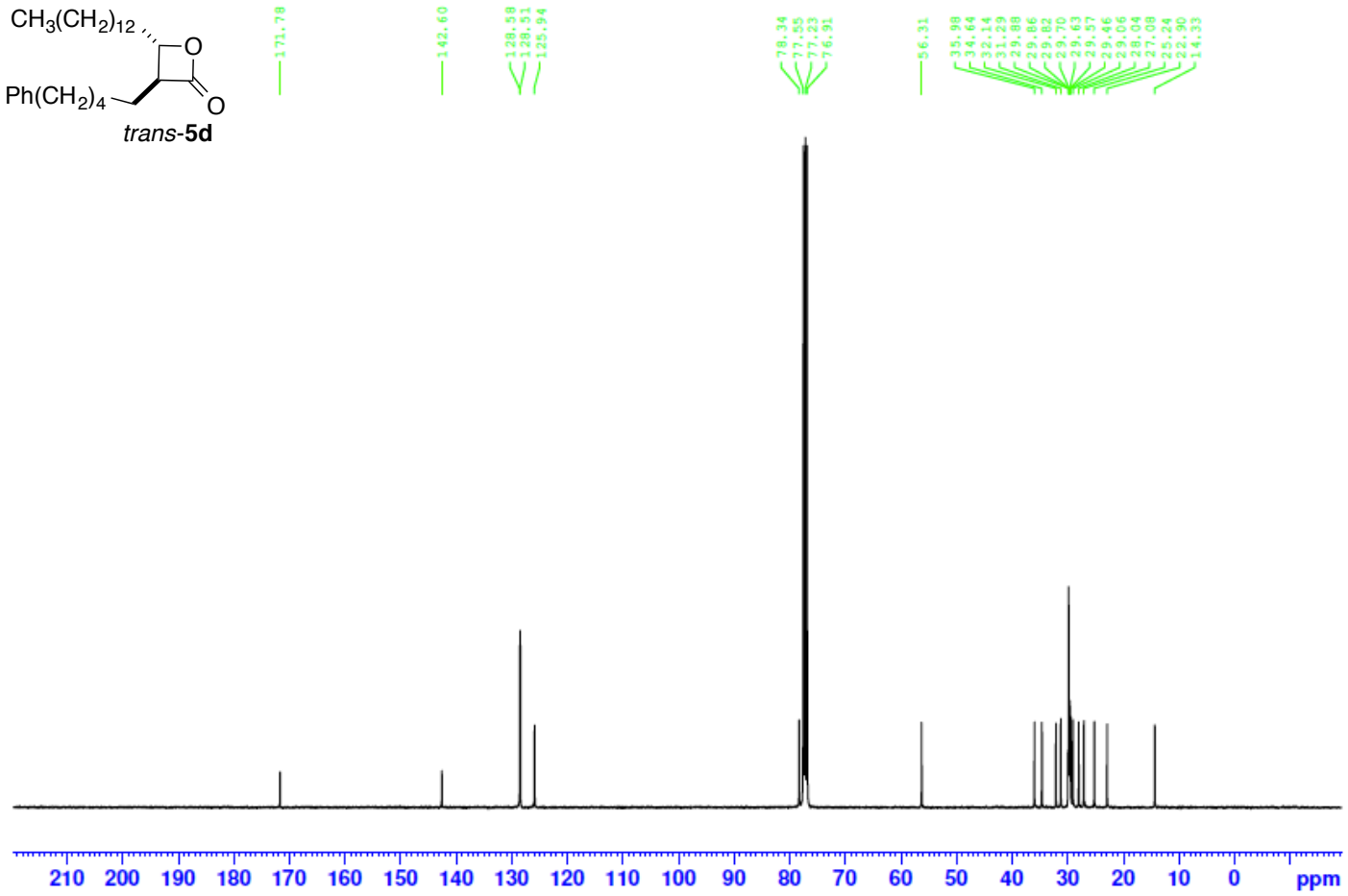

CH3(CH2)12
O
Ph
O
trans-5c
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.92
2.08
1.90
1.00
0.98
0.99
0.99
1.05
1.64
24.29
3.29

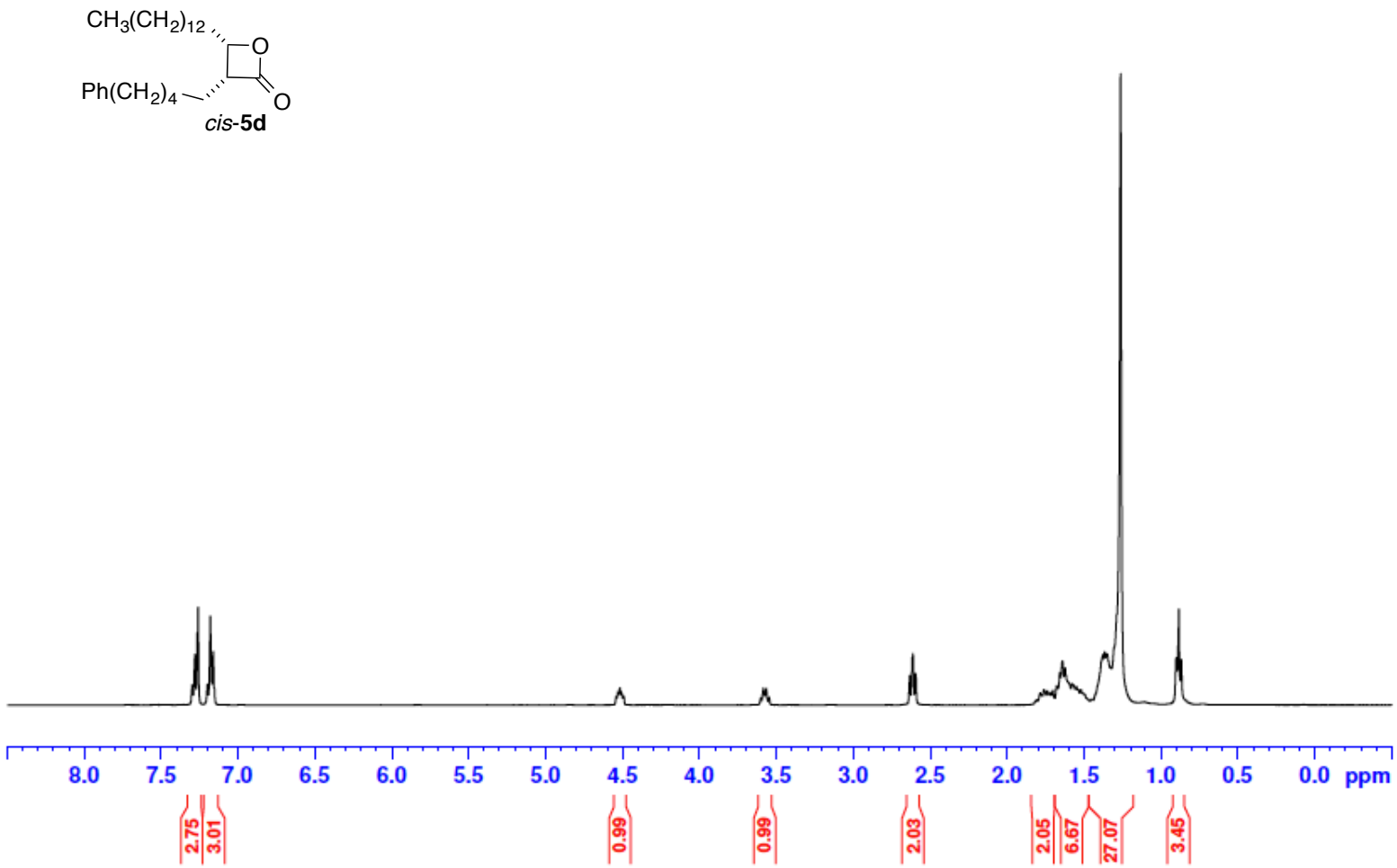

CH3(CH2)12
O
Ph
O
trans-5c
171.04
137.41
129.10
128.87
127.29
77.79
77.55
77.23
76.91
57.56
34.41
34.01
32.14
29.89
29.86
29.80
29.60
29.57
29.55
29.33
24.84
22.91
14.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

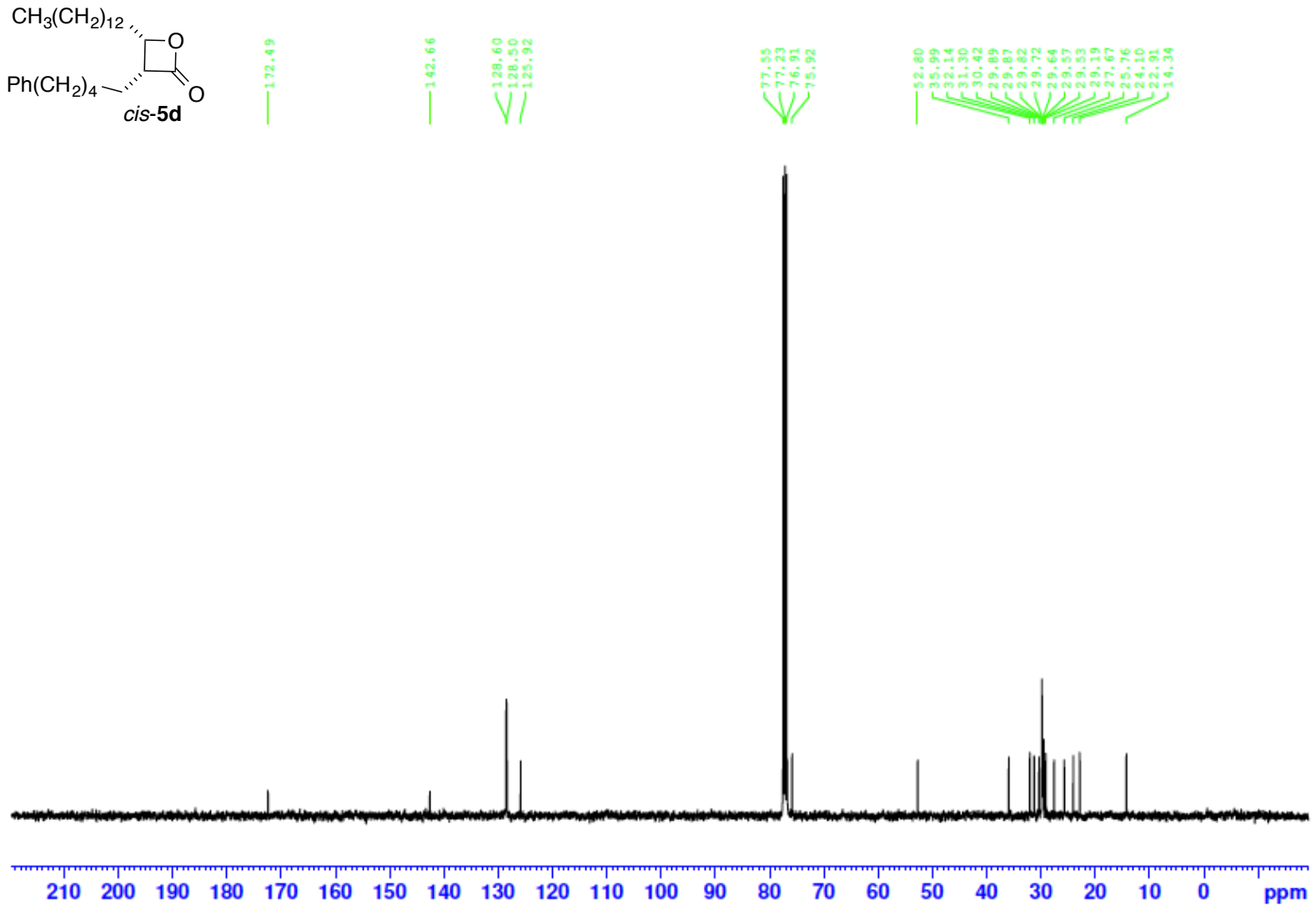

CH3(CH2)12
O
Ph
O
cis-5c
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.93
3.96
1.00
0.99
1.02
1.01
1.08
1.14
1.54
23.56
3.40

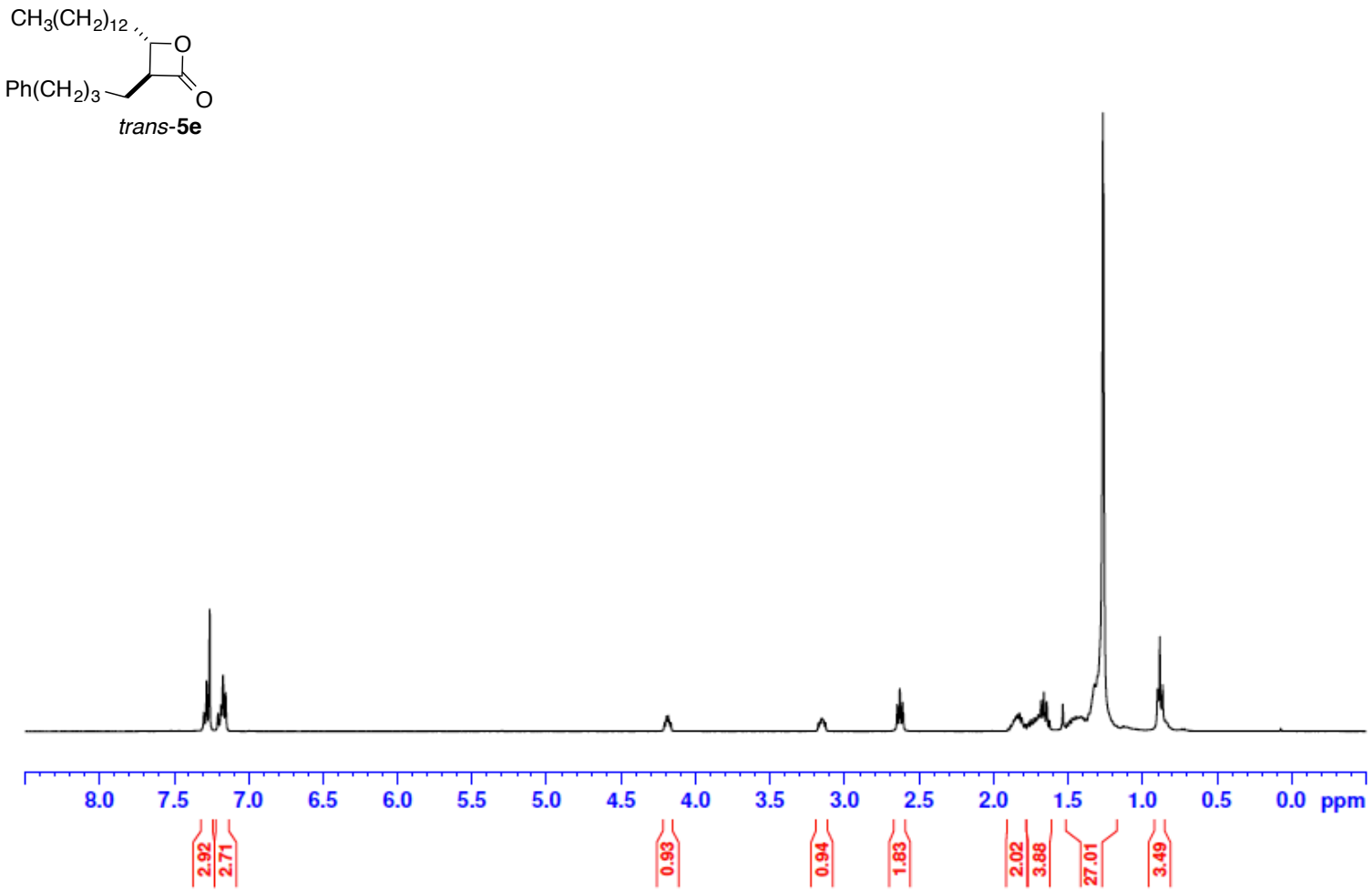

171.68
137.89
128.99
128.55
127.03
77.55
77.23
76.91
76.26
53.53
32.14
30.60
29.89
29.86
29.81
29.70
29.63
29.57
29.48
25.80
22.91
14.33
CH3(CH2)12
O
Ph
O
cis-5c
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

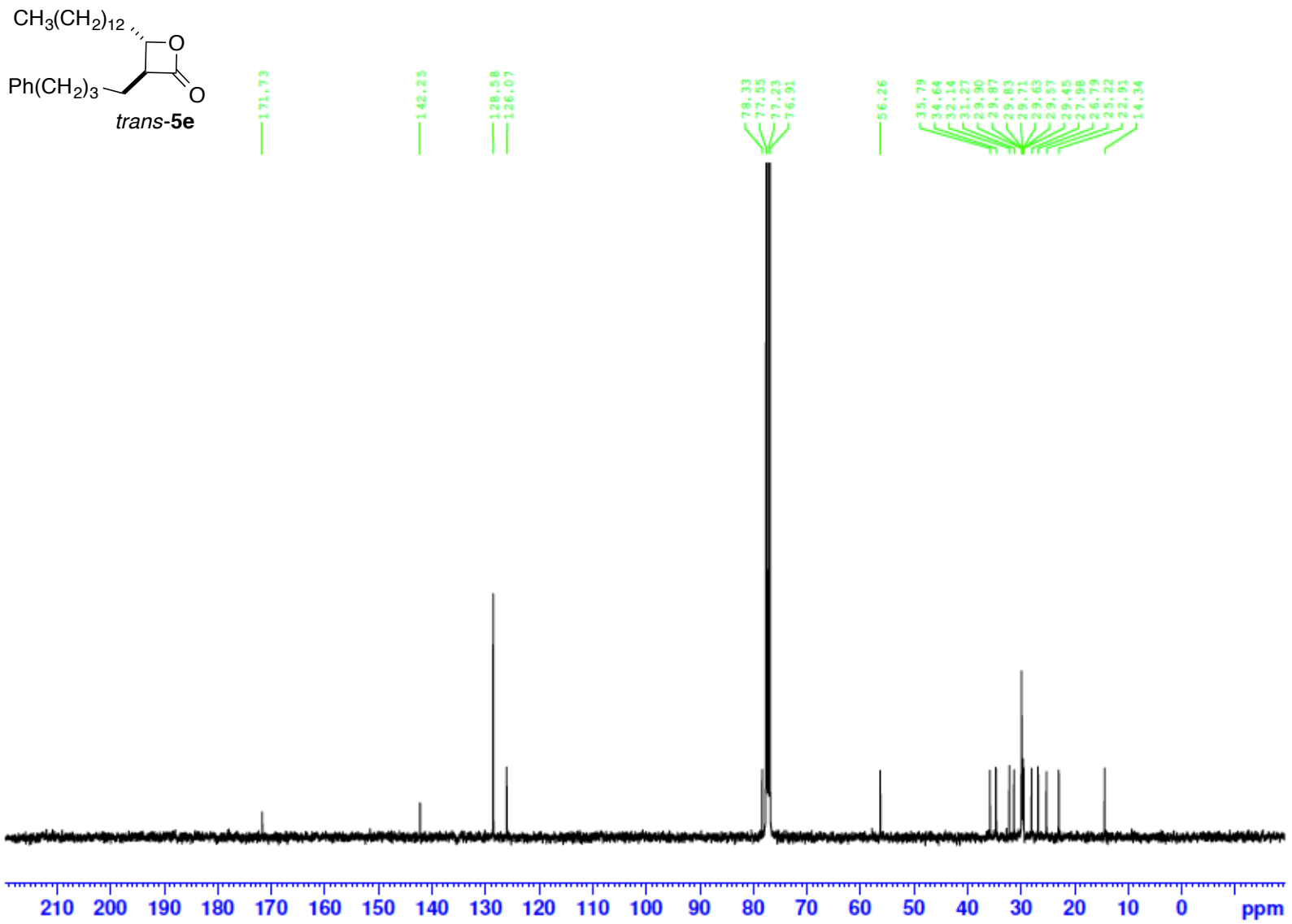

CH3(CH2)12
O
Ph(CH2)4
O
trans-5d
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.60
2.99
1.03
1.03
2.02
2.23
4.19
28.66
3.27

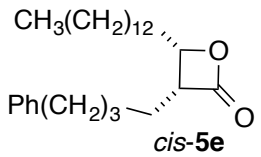

CH3(CH2)12
Ph(CH2)4
O
O
trans-5d
171.78
142.60
128.58
128.51
125.94
78.34
77.55
77.23
76.91
56.31
35.98
34.64
32.14
31.29
29.88
29.86
29.82
29.70
29.63
29.57
29.46
29.06
28.04
27.08
25.24
22.90
14.33
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


CH3(CH2)12
O
Ph(CH2)4
O
cis-5d
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.75
3.01
0.99
0.99
2.03
2.05
6.67
27.07
3.45

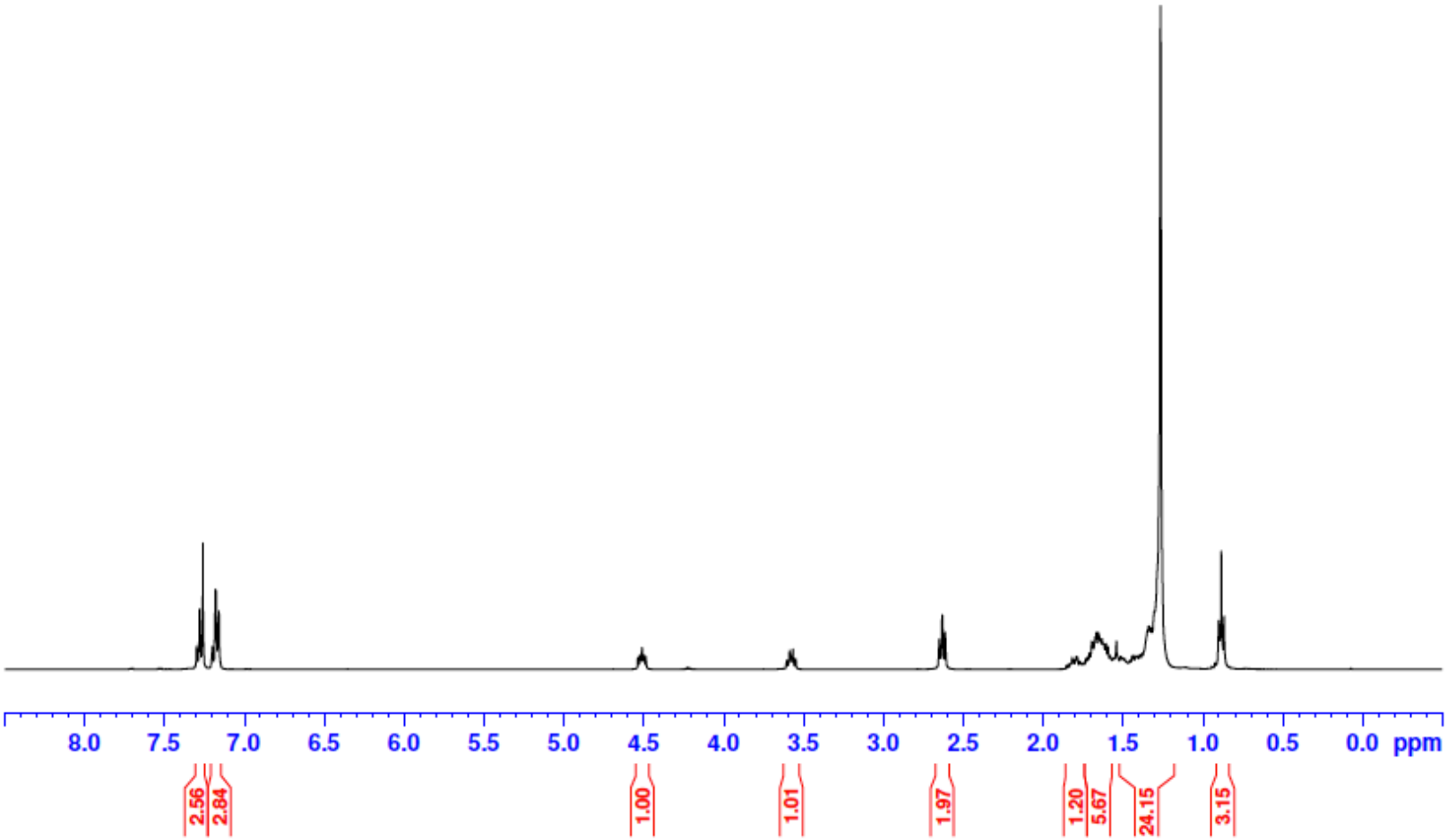

CH3(CH2)12
Ph(CH2)4
O
O
cis-5d
172.49
142.66
129.60
128.50
125.92
77.55
77.23
76.91
75.92
52.80
35.99
32.14
31.30
30.42
29.89
29.87
29.82
29.72
29.64
29.57
29.53
29.19
27.67
25.76
24.10
22.91
14.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

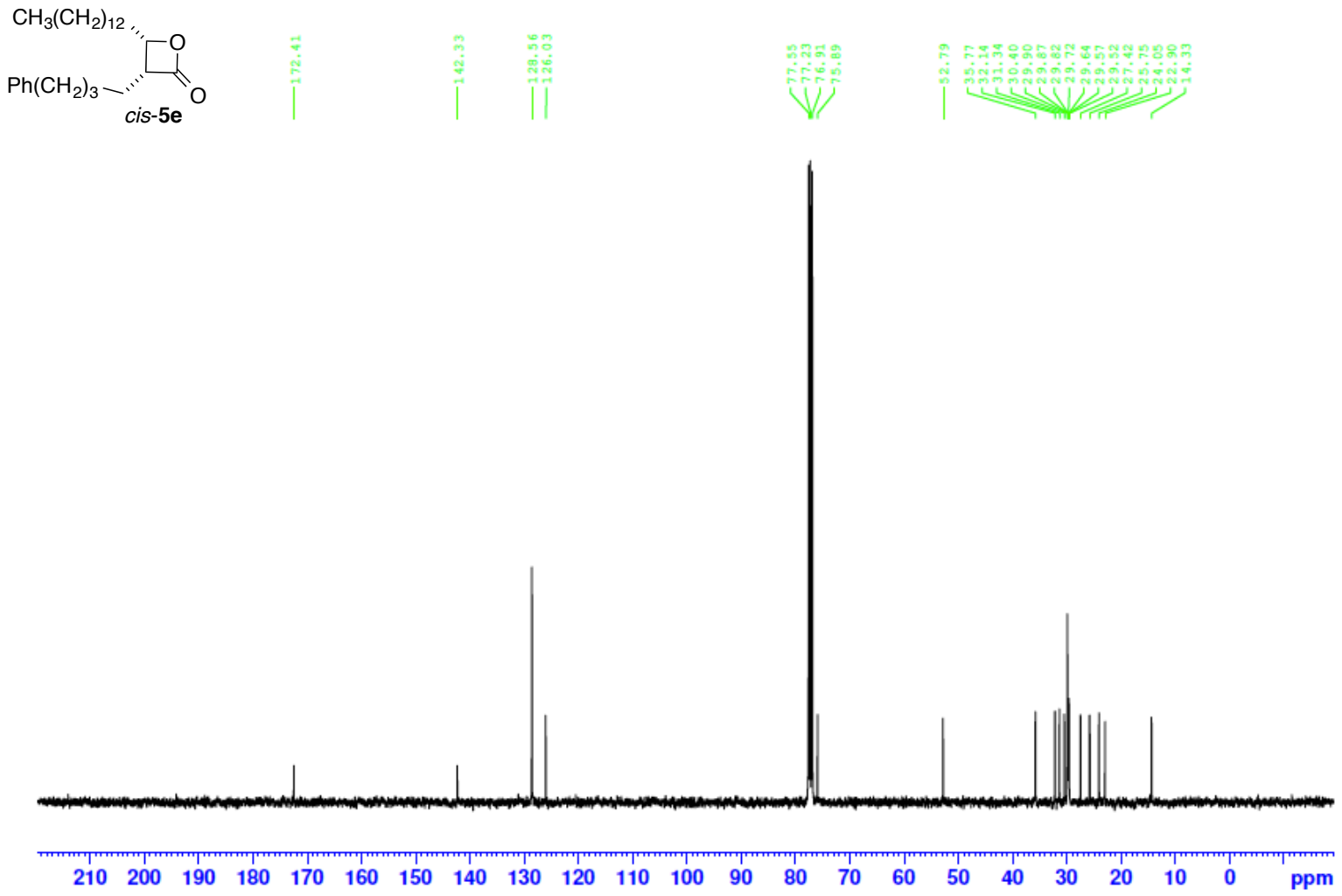

CH3(CH2)12
O
Ph(CH2)3
O
trans-5e
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.92
2.71
0.93
0.94
1.83
2.02
3.88
27.01
3.49

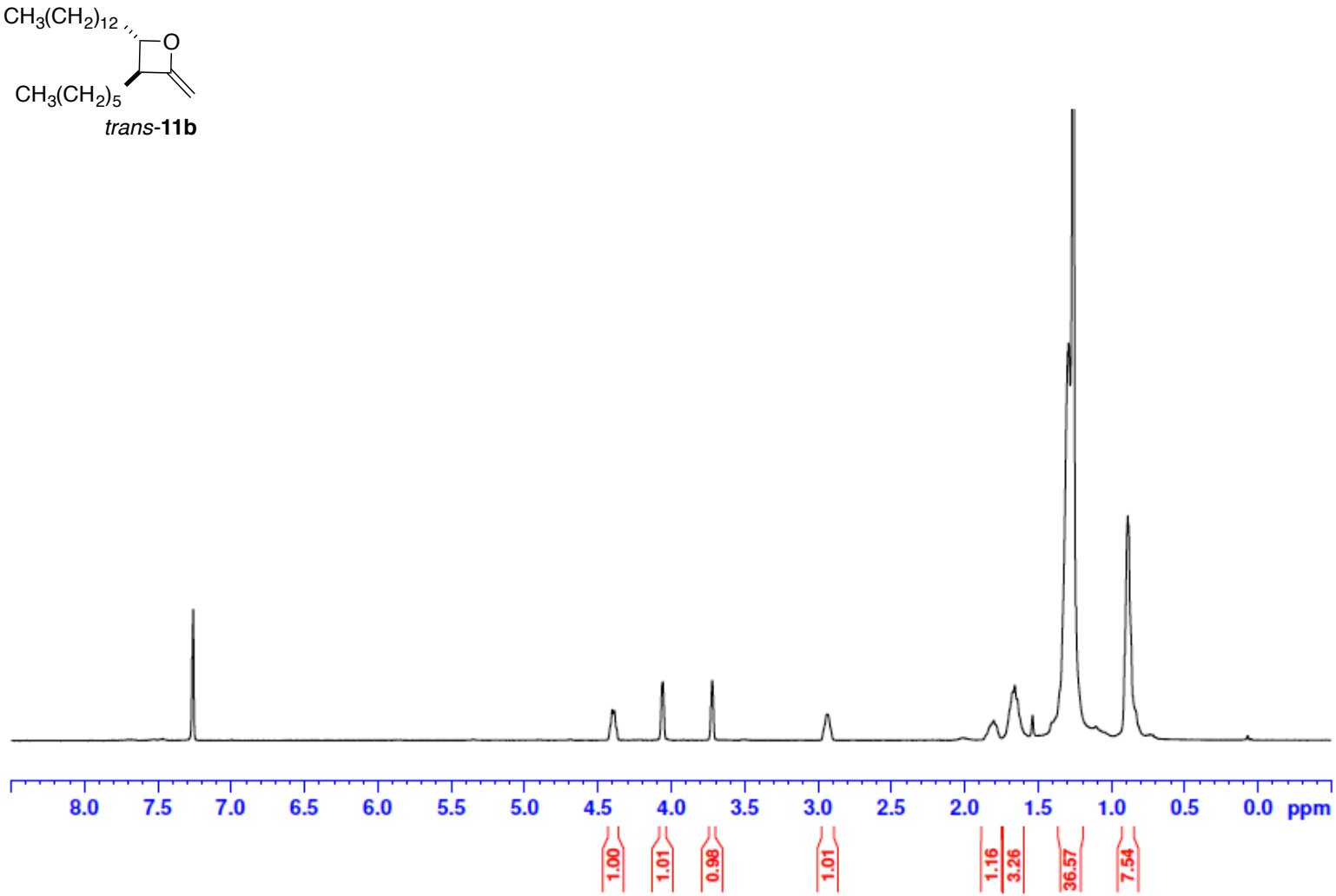

CH3(CH2)12
Ph(CH2)3
O
O
trans-5e
171.73
142.25
128.58
126.07
78.33
77.55
77.23
76.91
56.26
35.79
34.64
32.14
31.27
29.90
29.87
29.83
29.71
29.63
29.57
29.45
27.98
26.79
25.22
22.91
14.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

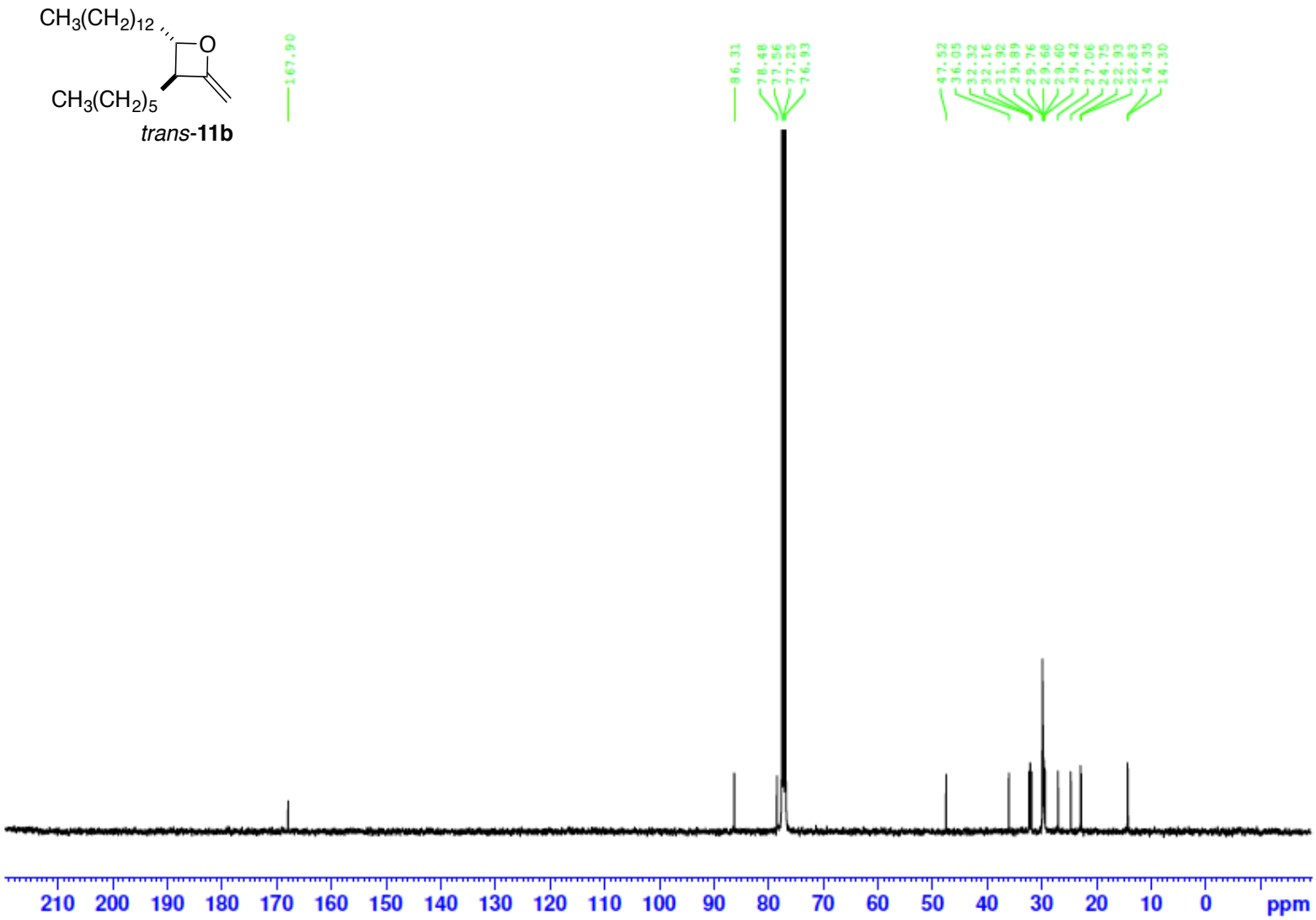

CH3(CH2)12
O
Ph(CH2)3
O

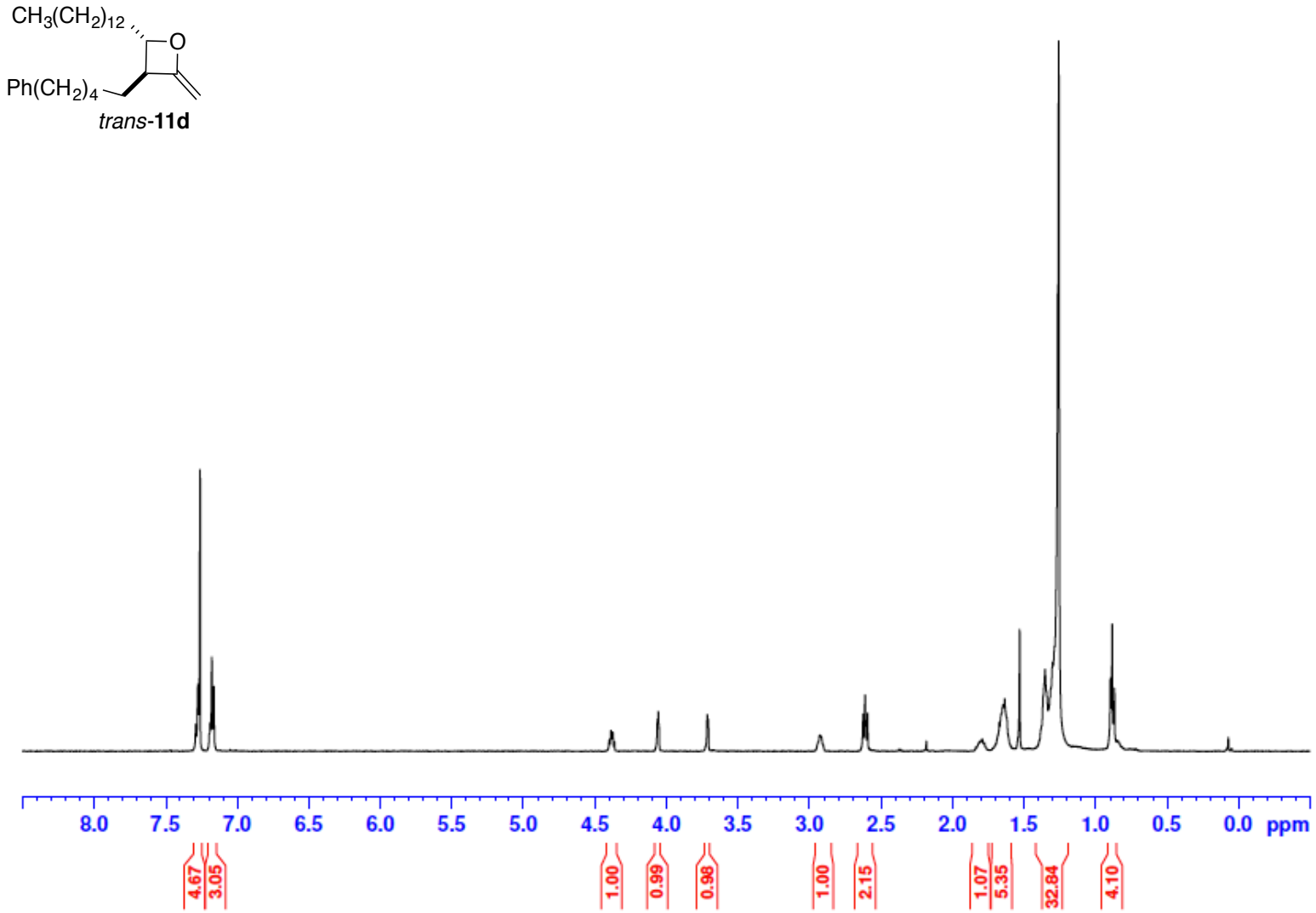
cis-**5e**

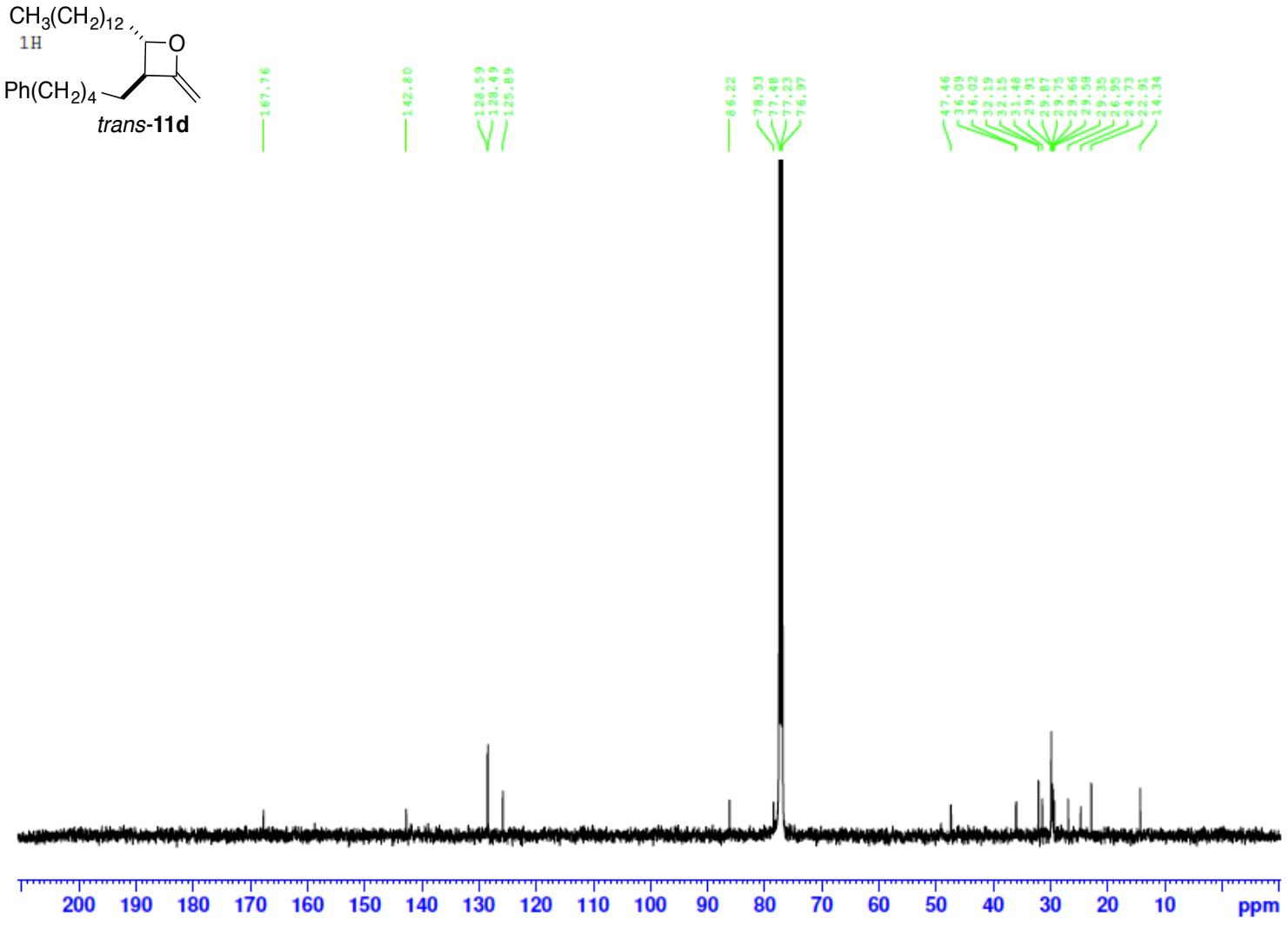

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.56
2.84
1.00
1.01
1.97
1.20
5.67
24.15
3.15


CH3(CH2)12
Ph(CH2)3
O
O
cis-5e
172.41
142.33
128.56
126.03
77.55
77.23
76.91
75.89
52.79
35.77
32.14
31.34
30.40
29.90
29.87
29.82
29.72
29.64
29.57
29.52
27.42
25.75
24.05
22.90
14.33
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


CH3(CH2)12
O
CH3(CH2)5
trans-11b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.01
0.98
1.01
1.16
3.26
36.57
7.54


CH3(CH2)12
O
CH3(CH2)5
trans-11b
167.90
86.31
78.48
77.56
77.25
76.93
47.52
36.05
32.32
32.16
31.92
29.89
29.76
29.68
29.60
29.42
27.06
24.75
22.93
22.83
14.35
14.30
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


CH3(CH2)12
O
Ph(CH2)4
trans-11d
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
4.67
3.05
1.00
0.99
0.98
1.00
2.15
1.07
5.35
32.84
4.10


CH3(CH2)12
1H
O
Ph(CH2)4
trans-11d
167.76
142.80
128.59
128.49
125.89
86.22
78.53
77.48
77.23
76.97
47.46
36.09
36.02
32.19
32.15
31.48
29.91
29.87
29.75
29.66
29.58
29.35
26.95
24.73
22.91
14.34
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm