Phase Separation as a Strategy Towards Controlling Dilution Effects in Macrocyclic Glaser-Hay Couplings.

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SUPPORTING INFORMATION

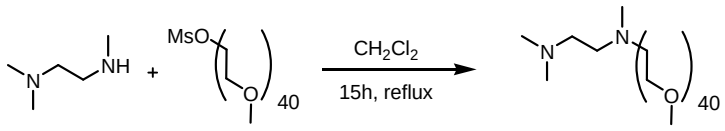
TABLE OF CONTENTS:

General:

All reactions that were carried out under anhydrous conditions were performed under an inert argon or nitrogen atmosphere in glassware that had previously been dried overnight at 120 ^{o}C or had been flame dried and cooled under a stream of argon or nitrogen.[1] All chemical products were obtained from Sigma-Aldrich Chemical Company or Strem Chemicals and were reagent quality. Allyl 4,6-O-benzylidene-D-glucopyranoside was prepared according to literature procedures.[2] Methyl-3,6-dihydroxybenzyl ester was prepared according to literature procedures.[3] Technical solvents were obtained from VWR International Co. Anhydrous solvents (CH_2Cl_2, Et_2O, THF, DMF, Toluene, and n-hexane) were dried and deoxygenated using a GlassContour system (Irvine, CA). Isolated yields reflect the mass obtained following flash column silica gel chromatography. Organic compounds were purified using the method reported by W. C. Still[4] and using silica gel obtained from Silicycle Chemical division (40-63 nm; 230-240 mesh). Analytical thin-layer chromatography (TLC) was performed on glass-backed silica gel 60 coated with a fluorescence indicator (Silicycle Chemical division, 0.25 mm, F_{254}.). Visualization of TLC plate was performed by UV (254 nm), $KMnO_4$ or *p*-anisaldehyde stains. All mixed solvent eluents are reported as v/v solutions. Concentration refers to removal of volatiles at low pressure on a rotary evaporator. All reported compounds were homogeneous by thin layer chromatography (TLC) and by ^{1}H NMR. NMR spectra were taken in deuterated $CDCl_3$ using Bruker AV-300 and AV-400 instruments unless otherwise noted. Signals due to the solvent served as the internal standard (CHCl3: δ 7.27 for ^{1}H, δ 77.0 for ^{13}C). The acquisition parameters are shown on all spectra. The ^{1}H NMR chemical shifts and coupling constants were determined assuming first-order behavior. Multiplicity is indicated by one or more of the following: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad); the list of couplings constants (*J*) corresponds to the order of the multiplicity assignment. The ^{1}H NMR assignments were made based on chemical shift and multiplicity and were confirmed, where necessary, by homonuclear decoupling, 2D COSY experiments. The ^{13}C NMR assignments were made on the basis of chemical shift and multiplicity and were confirmed, where necessary, by two dimensional correlation experiments (HSQC). High resolution mass spectroscopy (HRMS) was done by the Centre régional de spectrométrie de masse at the Département de Chimie, Université de Montréal from an Agilent LC-MSD TOF system using ESI mode of ionization unless otherwise noted.

[1] Shriver, D. F.; Drezdon, M. A. in *The Manipulation of Air-Sensitive Compounds*; Wiley-VCH: New York, 1986.
[2] Tanaka, H.; Kawai, K.; Fujiwara, K.; Murai, A. *Tetrahedron* **2002**, *5*, 10017.
[3] Zhu, J.; Beugelmans, R.; Bourdet, S.; Chastanet, J.; Roussi, G. *J. Org. Chem*. **1995**, *60*, 6389.
[4] Still, W. C.; Kahn, M.; Mitra, A.*J. Org. Chem*. **1978**, *43*, 2923.

SYNTHESIS OF $TPEG_{1900}$ 7 AND MACROCYCLIZATION PROTOCOL.



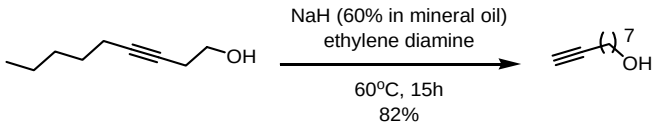
Polyethylene glycol 1900 monomethyl ether mesylate[5] (5.4 g, 2.8 mmol, 1 equiv.) was placed in a sealed tube equipped with a stirring bar. Dry dichloromethane (100 mL) and trimethylethylene diamine (2.8 mL, 28 mmol, 10 equiv.) were added and the clear solution was stirred for 15h at 60°C. The solution was then cooled to room temperature and diethylether (100 mL) was added. The mixture was placed in a laboratory refridgerator for 5h to induce precipitation. The solid was filtered and washed with diethylether (3X 100 mL). The solid was redissolved in dichloromethane and passed through a short pad of neutral alumina (15% methanol in dichloromethane). T-PEG_{1900} 7 (5.7 g, 2.8 mmol) was obtained as a white solid in quantitative yield (>98%). ^{1}H NMR (500 MHz, $CDCl_3$, 35°C) δ ppm 5.49-5.47 (m, 2H); 4.54-4.51 (m, 2H), 4.20-4.10 (m, 6H); 3.97-3.87 (m, 8H); 3.66-3.32 (m, PEG); 3.26 (s, 55H); 3.13 (bs, 150H); 2.58-2.55 (m, 16H); 2.31 (s, 10H); 2.26 (s, 6H); 2.22 (s, 8H); ^{13}C NMR (500 MHz, $CDCl_3$) δ ppm 72.4, 71.5, 70.9, 70.22, 70.16, 70.13 (PEG), 70.1, 69.8, 61.1, 58.6, 42.4; MALDI-TOF : m/z 1963.482.

General Procedure for Macrocyclization: The general procedure for the macrocylization of diynes under Glaser-Hay oxidative coupling conditions using $TPEG_{1900}$ is as follows. To a vial equipped with a stirring bar was charged with CuCl (0.065 mmol, 12 mg, 25 mol%), $Ni(NO_3)_2.6H_2O$ (0.065 mmol, 19 mg, 25 mol%) and $TPEG_{1900}$ (250 mg, 0.13 mmol, 50 mol%), methanol (5 mL) and triethylamine (0.36 mmol, 0.11 mL, 3 equiv.). The mixture was stirred at room temperature for 15 min or until the metals were solubilized. The diyne (0.26 mmol) was then added as an ether solution (5 mL) in one portion. Oxygen was bubbled in the solution for 5 min and the vial was then closed. The reaction was warmed to 60°C and monitored by TLC for consumption of the starting material (oxygen was bubbled again in the solution every 12h). When the reaction was completed by TLC, the reaction was cooled to room temperature and silica gel was added. The crude mixture was dried under reduced pressure and purified by column chromatography (100% hexanes→10% ethyl acetate in hexanes) to afford pure macrocycle.

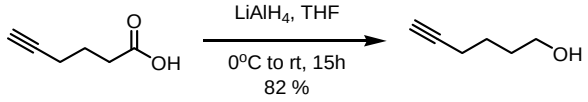
[5] Polyethylene glycol 1900 monomethyl ether mesylate was synthesised from molecular weight 1900 PEG methyl ether purchased from Alfa Aesar. See : Zhao, X.; Janda, K. D. *Tetrahedron Lett*. **1997**, *38*, 5437-5440.

SYNTHESIS OF MACROCYCLIZATION PRECURSORS.

General Procedure for Steglich Esterifications: To a stirred solution of the alcohol (1 equiv.) and the carboxylic acid (1.5 equiv.) in dry dichloromethane (0.2 M) was added N,N'-dicyclohexylcarbodiimide (DCC, 2 equiv.) and 4-dimethylaminopyridine (DMAP, 3 equiv.) at room temperature. The reaction mixture was stirred at room temperature for 15h. Upon complete conversion of the starting material, the crude reaction mixture was placed in a freezer for 5h to induce the precipitation of the urea, which was subsequently removed by filteration. The filtrate was concentrated in vacuo to provide the crude reaction mixture which was purified by column chromatography on silica-gel to afford the desired product.



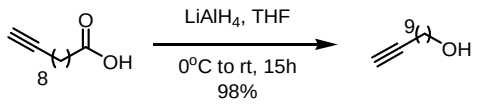
8-nonyl-1-ol: To a flask containing ethylene diamine (70 mL) at 0°C was added NaH (60% in mineral oil, 5.7 g, 142.6 mmol, 4 equiv.). The mixture was slowly warmed to room temperature and stirred for 1h. Then the reaction was warmed to 60°C and stirred for 2h. After cooling the reaction to 45°C, 3-nonyl-1-ol (5 mL, 35.7 mmol, 1 equiv.) was added in one portion and the solution was stirred at 60°C for 15h. Upon cooling to 0°C, 1M HCl (30 mL) was added and the organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate (2x), and the combined organic layers were dried over anhydrous Na_2SO_4. The suspension was filtered and the filtrate was concentrated in vacuo. Purification of the crude product by column chromatography on silica gel (20% ethyl acetate in hexanes) afforded the product as a colorless oil (4.1 g, 82%). The NMR data are in agreement with that obtained in the literature.[6]



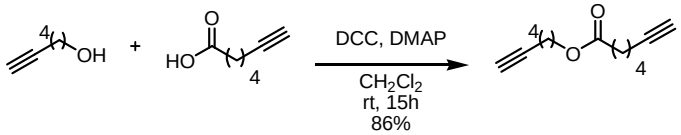
5-hexyn-1-ol: To a solution of lithium aluminum hydride (676 mg, 17.8 mmol, 2 equiv.) in anhydrous tetrahydrofuran (30 mL) at 0°C was added 5-hexynoic acid (1 mL, 8.9 mmol, 1 equiv.). The solution was warmed to room temperature and stirred for 15h. The reaction was cooled to 0°C and 2M NaOH (10 mL) was added dropwise. Water and ethyl acetate were added and the organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate (2x), and the combined organic layers were dried over anhydrous Na_2SO_4. The suspension was filtered and the filtrate was concentrated in vacuo. Purification of the crude reaction product by column chromatography on silica gel (10→20% ethyl acetate in hexanes) afforded the product as a colorless oil (713 mg, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 3.67 (t, *J* = 6.2 Hz, 2H), 2.23 (td, *J* = 6.8, 2.7 Hz, 2H), 1.96 (t, *J* = 2.6 Hz, 1H), 1.76 - 1.54 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 84.3,

[6] (a) Denmark, S. E.; Jones, T. K. *J. Org. Chem.* **1982**, *47*, 4595-4597. (b) Renauld, J. L.; Aubert, C.; Malacria, M. *Tetrahedron* **1999**, *55*, 5113-5128.

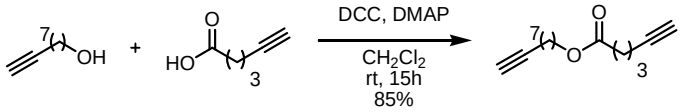
68.5, 62.3, 31.6, 24.7, 18.2 ppm; HRMS (ESI) m/z calculated for $C_6H_{11}O$ $[M+H]^+$, 99.0804; found: 99.0805.



10-undecyn-1-ol: To a solution of lithium aluminum hydride (420 mg, 11.0 mmol, 2 equiv.) in anhydrous tetrahydrofuran (28 mL) at 0°C was added 5-hexynoic acid (1 g, 5.5 mmol, 1 equiv.). The solution was warmed to room temperature and stirred for 15h. The reaction was cooled to 0°C and 2M NaOH (10 mL) was added dropwise. Water and ethyl acetate were added and the organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate (2x), and the combined organic layers were dried over anhydrous Na_2SO_4. The suspension was filtered and the filtrate was concentrated in vacuo. Purification of the crude reaction product by column chromatography on silica gel (10→20% ethyl acetate in hexanes) afforded the product as a colorless oil (924 mg, >98%). The NMR data are in agreement with that in the literature.[7]



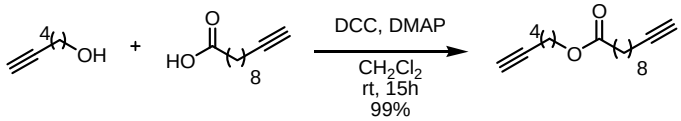
Hex-5-yn-1-yl hept-6-ynoate: Following the General Procedure, 5-hexyl-1-ol (52 mg, 0.53 mmol), 6-heptynoic acid (100 mg, 0.79 mmol), DCC (219 mg, 1.1 mmol) and DMAP (194 mg, 1.6 mmol) in anhydrous DCM (5 mL) were added to the reaction flask. Following purification by column chromatography (10% ethyl acetate in hexanes), the desired product was obtained as a colorless oil (106 mg, 86%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.09 (t, *J* = 6.4 Hz, 2H), 2.33 (t, *J* = 7.4 Hz, 2H), 2.27 - 2.15 (m, 4H), 1.95 (q, *J* = 2.6 Hz, 2H), 1.82 - 1.68 (m, 4H), 1.66 - 1.49 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 173.4, 83.9, 83.8, 68.7, 68.6, 63.6, 33.7, 27.8, 27.6, 24.9, 24.0, 18.1, 18.0 ppm; HRMS (ESI) m/z calculated for $C_{13}H_{19}O_2$ $[M+H]^+$, 206.1387; found: 207.1390.



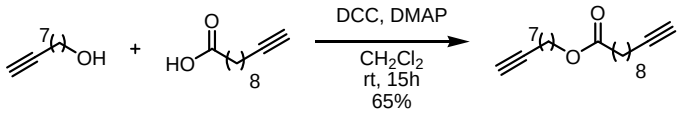
Non-8-yn-1-yl hex-5-ynoate: Following the General Procedure, 8-nonyl-1-ol (2.1 g, 14.7 mmol), 5-hexynoic acid (2.43 mL, 22.1 mmol), DCC (6.1 g, 29.4 mmol) and DMAP (5.4 g, 44.1 mmol) in anhydrous CH_2Cl_2 (74 mL) were added to the reaction flask. Following purification by column chromatography (10% ethyl acetate in hexanes), the desired product was obtained as a colorless oil (2.7 g, 85%). ^{1}H NMR (400MHz, $CDCl_3$) δ = 4.05 (t, *J* = 6.7 Hz, 2H), 2.43 (t, *J* = 7.4 Hz, 2H), 2.25 (td, *J* = 7.0, 2.6 Hz, 2H), 2.17 (td, *J* = 7.0, 2.7 Hz, 2H), 1.96 (t, *J* = 2.7 Hz, 1H), 1.93 (t, *J* = 2.7 Hz, 1H), 1.87-1.81 (m, 2H), 1.65-1.58 (m, 2H), 1.53-1.48 (m, 2H), 1.43-1.28 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ

[7] Sharma, A.; Chattopadhyay, S. *J. Org. Chem*. **1998**, *63*, 6128.

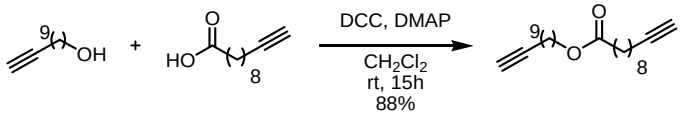
= 173.1, 84.5, 83.2, 69.0, 68.1, 64.4, 32.9, 28.6, 28.5, 28.5, 28.3, 25.7, 23.6, 18.3, 17.8 ppm; HRMS (ESI) m/z calculated for $C_{15}H_{23}O_2$ $[M+H]^+$, 235.1693; found: 235.1698.



Hex-5-yn-1-yl undec-10-ynoate: Following the General Procedure, 5-hexyl-1-ol (100 mg, 1.0 mmol), 10-undecynoic acid (278 mg, 1.5 mmol), DCC (721 mg, 2.0 mmol) and DMAP (374 mg, 3.0 mmol) in anhydrous DCM (7.7 mL) were added to the reaction flask. Following purification by column chromatography (5% ethyl acetate in hexanes), the desired product was obtained as a colorless oil (280 mg, 99%). ^{1}H NMR (400MHz, $CDCl_3$) δ = 4.07 (t, *J* = 6.5 Hz, 2H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.21 (td, *J* = 7.0, 2.7 Hz, 2H), 2.15 (td, *J* = 7.0, 2.6 Hz, 2H), 1.94 (td, *J* = 2.6, 0.6 Hz, 1H), 1.91 (td, *J* = 2.6, 0.6 Hz, 1H), 1.79 - 1.66 (m, 4H), 1.64 - 1.44 (m, 6H), 1.42 - 1.20 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 173.9, 84.7, 83.9, 68.7, 68.1, 63.7, 34.3, 29.08, 29.06, 28.9, 28.6, 28.4, 27.7, 24.9 (2C), 18.4, 18.1 ppm; HRMS (ESI) m/z calculated for $C_{17}H_{27}O_2$ $[M+H]^+$, 263.2006; found: 263.2013.

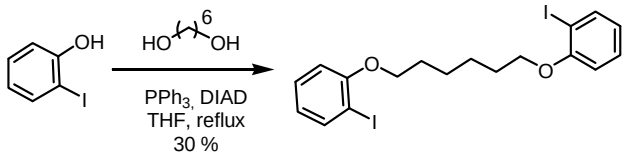


Non-8-yn-1-yl undec-10-ynoate: Following the General Procedure, 8-nonyl-1-ol (100 mg, 1.0 mmol), 10-undecynoic acid (195 mg, 1.5 mmol), DCC (294 mg, 2.0 mmol) and DMAP (260 mg, 3.0 mmol) in anhydrous DCM (5.0 mL) were added to the reaction flask. Following purification by column chromatography (5% ethyl acetate in hexanes), the desired product was obtained as a colorless oil (196 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.06 (t, *J* = 6.7 Hz, 2H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.22-2.15 (m, 4H), 1.94 (td, *J* = 2.6, 1.2 Hz, 2H), 1.65 - 1.48 (m, 8H), 1.47 - 1.23 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 173.9, 84.69, 84.59, 68.15, 68.07, 64.3, 34.4, 29.08, 29.06, 28.9, 28.7, 28.64, 28.57 (2C), 28.4, 28.3, 25.8, 25.0, 18.4, 18.3 ppm; HRMS (ESI) m/z calculated for $C_{20}H_{33}O_2$ $[M+H]^+$, 305.2475; found: 305.2462.

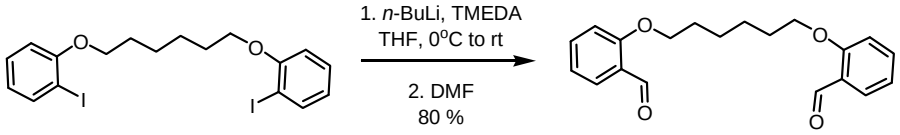


Dec-9-yn-1-yl undec-10-ynoate: Following the General Procedure, 10-undecyl-1-ol (172 mg, 1.0 mmol), 10-undecynoic acid (278 mg, 1.5 mmol), DCC (421 mg, 2.0 mmol) and DMAP (374 mg, 3.0 mmol) in anhydrous DCM (7.7 mL) were added to the reaction flask. Following purification by column chromatography (5% ethyl acetate in hexanes), the desired product was obtained as a colorless oil (297 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.03 (t, *J* = 6.7 Hz, 2H), 2.27 (t, *J* = 7.5 Hz, 2H), 2.18 - 2.13 (m, 4H), 1.91 (td, *J* = 2.6, 0.6 Hz, 2H), 1.62-145 (m, 8H), 1.41 - 1.29 (m, 16H); ^{13}C NMR (75 MHz,

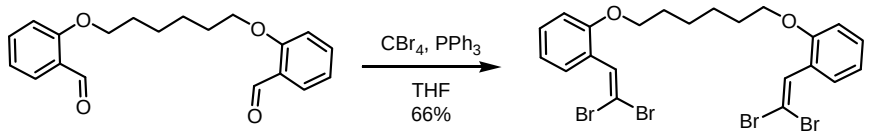
$CDCl_3$) δ = 173.8, 84.58, 84.56, 68.0, 64.3, 34.3, 29.3, 29.1, 29.02, 28.99, 28.9, 28.8, 28.61, 28.57 (2C), 28.56, 28.37, 28.35, 25.8, 24.9, 18.3 (2C) ppm; HRMS (ESI) m/z calculated for $C_{22}H_{37}O_2$ $[M+H]^+$, 333.2778; found: 333.2788.



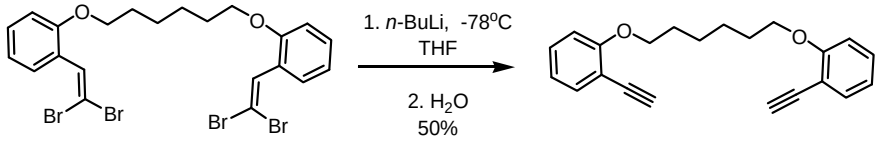
1,6-bis(2-iodophenoxy)hexane: To a stirred solution of 2-iodophenol (3.1 g, 14.1 mmol) in anhydrous THF (65 mL) was added triphenylphosphine (3.7 g, 2.2 equiv., 14.1 mmol), 1,6-hexanediol (0.76 g, 1 equiv., 6.4 mmol) and diisopropyl azodicarboxylate (2.8 mL, 2.2 equiv., 14.1 mmol) in that order under a N_2 atmosphere. The reaction mixture was heated at reflux for 15 hours. The reaction was concentrated under vacuo to provide a crude reaction mixture which was purified by column chromatography on silica-gel (100 hexanes→10% ethyl acetates in hexanes) to afford the desired product as a beige solid (1.0 g, 30%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.77 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.33 - 7.24 (m, 2H), 6.82 (dd, *J* = 8.2, 1.3, Hz, 2H), 6.71 (td, *J* = 7.6, 1.3 Hz, 2H), 4.05 (t, *J* = 6.2 Hz, 4H), 1.95 - 1.87 (m, 4H), 1.68-1.63 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 157.5, 139.3, 129.4, 122.3, 112.1, 86.7, 68.9, 29.0, 25.7 ppm; HRMS (ESI) m/z calculated for $C_{18}H_{20}I_2NaO_2$ $[M+Na]^+$, 544.9445; found: 544.9447.



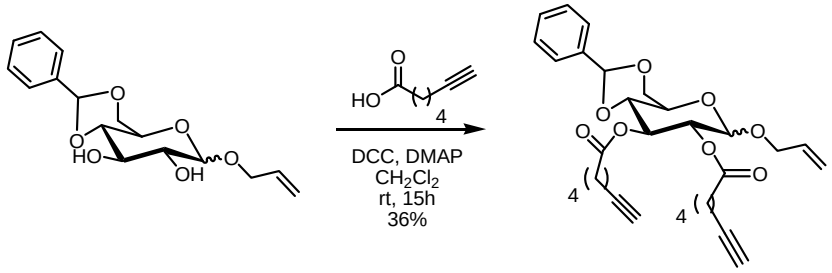
2,2'-(hexane-1,6-diylbis(oxy))dibenzaldehyde: To a solution of 1,6-bis(2-iodophenoxy)hexane (100 mg, 0.2 mmol, 1 equiv.) and tetramethylethylene diamine (22 mg, 0.2 mmol, 1 equiv.) in anhydrous tetrahydrofuran (3 mL) at 0°C under N_2 was added freshly titrated *n*-BuLi (1.4 M in Hexanes, 0.55 mL, 0.77 mmol, 4 equiv.) dropwise. The reaction mixture was then warmed to room temperature and stirred for 1h. Anhydrous dimethylformamide (0.16 mL, 0.95 mmol, 5 equiv.) was added to the mixture in one portion at room temperature and the reaction was stirred for 1h. Water and ethyl acetate are then added and the organic and aqueous layers were separated. The aqueous layer was extracted with ethyl acetate (2x), and the combined organic layers were washed (4x) with a saturated solution of $CuSO_4$, dried over anhydrous Na_2SO_4. The suspension was filtered and the filtrate was concentrated in vacuo. Purification by column chromatography on silica gel (5→15% ethyl acetate in hexanes) afforded the product as a beige solid (50 mg, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 10.52 (d, *J* = 0.6 Hz, 2H), 7.83 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.56 - 7.51 (m, 2H), 7.04 - 6.97 (m, 4H), 4.10 (t, J = 9 Hz, 4H), 1.91 (m, 4H), 1.66 - 1.55 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 189.7, 161.4, 135.9, 128.2, 124.9, 120.5, 112.4, 68.2, 29.0, 25.8 ppm; HRMS (ESI) m/z calculated for $C_{20}H_{23}O_4$ $[M+H]^+$, 327.1591; found: 327.1595.



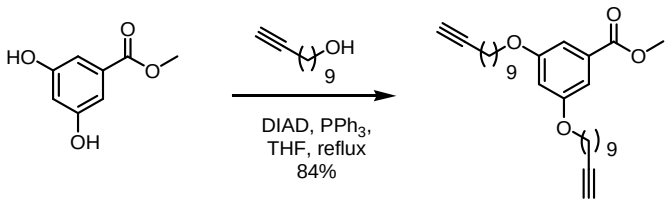
1,6-bis(2-(2,2-dibromovinyl)phenoxy)hexane: Carbon tetrabromide (234 mg, 0.7 mmol, 2 equiv.) and triphenylphosphine (413 mg, 1.6 mmol, 4.5 equiv.) were placed in a flask and dichloromethane (2.0 mL) was added at 0°C. The orange mixture was stirred 10 min at 0°C, then 2,2'-(hexane-1,6-diylbis(oxy))dibenzaldehyde (115 mg, 0.35 mmol, 1 equiv.) and 2,6-lutidine (0.1 mL, 0.7 mmol, 2 equiv.) were added as a dichloromethane solution (2.0 mL) and the reaction was stirred 2h at 0°C. After warming to room temperature, a saturated solution of NH_4Cl (5 mL) was added and the aqueous phase was extracted with dichloromethane (3x). The combined organic phases were dried with anhydrous Na_2SO_4. The suspension was filtered and the filtrate was concentrated in vacuo. Purification by column chromatography on silica gel (100% hexanes→10% ethyl acetate in hexanes) afforded the product as a yellow solid (147 mg, 66%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.70 (dd, *J* = 7.7, 1.3 Hz, 2H), 7.61 (s, 2H), 7.34 - 7.28 (m, 2H), 6.94 (t, *J* = 7.6 Hz, 2H), 6.88 (d, *J* = 7.9 Hz, 2H), 4.02 (t, J = 6 Hz, 4H), 1.92 - 1.83 (m, 4H), 1.63 - 1.56 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 156.0, 133.0, 129.9, 129.1, 124.6, 120.1, 111.7, 89.4, 68.3, 29.1, 25.9 ppm; HRMS (ESI) m/z calculated for $C_{22}H_{22}AgBr_4O_4$ $[M+Ag]^+$, 740.7399; found: 740.7431.



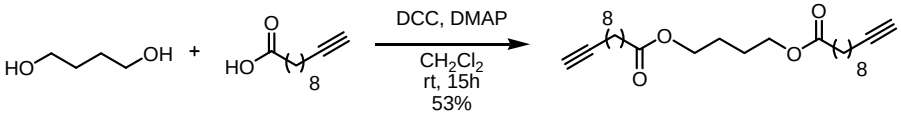
1,6-bis(2-ethynylphenoxy)hexane: To a solution of 1,6-bis(2-(2,2-dibromovinyl)phenoxy)hexane (110 mg, 0.2 mmol, 1 equiv.) in anhydrous tetrahydrofuran (3 mL) at -78°C was added a solution of freshly titrated *n*-BuLi (1.4M in Hexanes, 0.6 mL, 0.85 mmol, 5 equiv.) dropwise. The mixture was stirred 1h at -78°C then another 1h at -20°C. When complete consumption of the starting tetrabromide, the reaction is warmed to 0°C and a saturated solution of NH_4Cl (3 mL) is added dropwise. The organic and aqueous phases are separated and the aqueous phase is extracted with ethyl acetate (3x). The combined organic phases are washed with brine (1x) and dried over anhydrous Na_2SO_4. The suspension was filtered and the filtrate was concentrated in vacuo. Purification by column chromatography on silica gel (10% ethyl acetate in hexanes) afforded the product as a yellow solid (110 mg, 50%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.46 (dd, *J* = 7.5, 1.6 Hz, 2H), 7.33 - 7.27 (m, 2H), 6.93 - 6.86 (m, 4H), 4.06 (t, *J* = 6.5 Hz, 4H), 3.25 (s, 2H), 1.96 - 1.82 (m, 4H), 1.67 - 1.54 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 160.2, 134.1, 130.1, 120.3, 112.0, 111.6, 81.0, 80.1, 68.5, 28.9, 25.6 ppm; HRMS (ESI) m/z calculated for $C_{22}H_{23}O_2$ $[M+H]^+$, 319.1683; found: 319.1695.



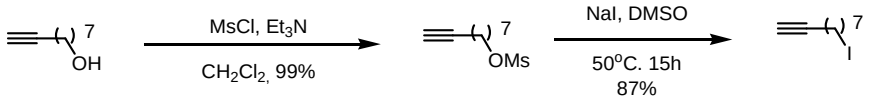
(4aR,7R,8S,8aR)-6-(allyloxy)-2-phenylhexahydropyrano[3,2-d][1,3]dioxine-7,8-diyl bis(hept-6-ynoate): Following the General Procedure, allyl 4,6-O-benzylidene-D-glucopyranoside (150 mg, 0.5 mmol, 1 equiv.), 5-hexynoic acid (0.2 mL, 1.46 mmol, 3 equiv.), DCC (412 mg, 2.0 mmol, 4 equiv.) and DMAP (366 mg, 3.0 mmol, 6 equiv.) in anhydrous DCM (5 mL) were added to the reaction flask. Following purification by column chromatography (5%→20% ethyl acetate in hexanes), the desired product was obtained as a white solid (100 mg, 36%) ^{1}H NMR (400 MHz, $CDCl_3$) (mixture of α and β anomers (0.85 :0.15), data reported for major anomer only) δ = ^{1}H NMR (300MHz, $CDCl_3$) δ = 7.46 - 7.41 (m, 2H), 7.36 - 7.32 (m, 3H), 5.94 - 5.81 (m, 1H), 5.65 (t, *J* = 9.9 Hz, 1H), 5.51 (s, 1H), 5.35 - 5.20 (m, 2H), 5.12 (d, *J* = 3.8 Hz, 1H), 4.91 (dd, *J* = 9.9, 3.8 Hz, 1H), 4.32 - 4.27 (m, 1H), 4.23 (ddt, *J* = 13.0, 5.1, 1.4 Hz, 1H), 4.04 - 3.95 (m, 2H), 3.76 (t, *J* = 10.3 Hz, 1H), 3.65 (t, J = 12 Hz, 1H), 2.39 - 2.31 (m, 4H), 2.22 (td, *J* = 7.0, 2.6 Hz, 2H), 2.12 (td, *J* = 7.0, 2.6 Hz, 2H), 1.96 (t, J = 3 Hz, 1H), 1.92 (t, *J* = 2.7 Hz, 1H), 1.78 - 1.66 (m, 4H), 1.60 - 1.45 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.7, 172.1, 136.9, 133.19, 133.16, 129.0, 128.18, 128.15, 126.1, 118.0, 101.5, 95.6, 83.8, 83.7, 79.3, 71.4, 68.8, 68.70, 68.65 (2C), 68.6, 62.5, 33.7, 33.5, 27.6, 27.5, 24.0, 23.9, 18.04, 17.96 ppm; HRMS (ESI) m/z calculated for $C_{30}H_{36}NaO_8$ $[M+Na]^+$, 547.2302; found: 547.2302.



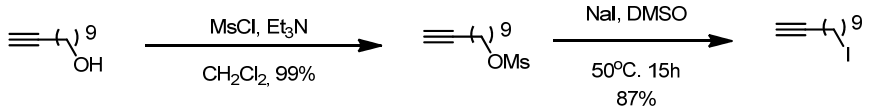
Methyl 3,5-bis(undec-10-yn-1-yloxy)benzoate: To a solution of methyl 3,6-dihydroxybenzoate (80.1 mg, 0.48 mmol) in anhydrous tetrahydrofuran (5 mL) was added triphenylphosphine (377.3 mg, 3 equiv., 1.44 mmol), 10-undedyn-1-ol (200 mg, 2.5 equiv., 1.19 mmol) and diisopropyl azodicarboxylate (0.28 mL, 3 equiv., 1.44 mmol,) in that order under a N_2 atmosphere. The reaction mixture was heated at reflux for 15 hours. The reaction was concentrated under vacuum to provide a crude reaction mixture which was purified by column chromatography on silica-gel (10% ethyl acetate in hexanes) to afford the desired product as a white solid (188 mg, 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.16 (d, *J* = 2.3 Hz, 2H), 6.64 (t, *J* = 2.3 Hz, 1H), 3.97 (t, *J* = 6.5 Hz, 4H), 3.90 (s, 3H), 2.22 - 2.16 (m, 4H), 1.95 (t, *J* = 2.7 Hz, 2H), 1.83 - 1.73 (m, 4H), 1.56 - 1.23 (m, 24H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 167.0, 160.13, 160.11, 131.8, 107.6, 106.6, 84.8, 68.3, 68.1, 52.2, 29.4, 29.3, 29.2, 29.0, 28.7, 28.5, 26.0, 18.40, 18.38 ppm; HRMS (ESI) m/z calculated for $C_{30}H_{45}O_4$ $[M+H]^+$, 469.3312; found: 469.3322.



Butan-1,4-diyl bis(undec-10-ynoate): Following the General Procedure, butane-1,4-diol (250 mg, 2.8 mmol), 10-undecynoic acid (1.51 g, 8.3 mmol), DCC (2.3 g, 11.2 mmol), DMAP (2.1 g, 16.8 mmol) and anhydrous DCM (15 mL) were added to the reaction flask. Following purification by column chromatography (20% ethyl acetate in hexanes), the desired product was obtained as a white solid (622 mg, 53%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.06 - 3.87 (m, 4H), 2.16 (t, *J* = 7.5 Hz, 4H), 2.03 (td, *J* = 7.0, 2.7 Hz, 4H), 1.82 (t, *J* = 2.6 Hz, 2H), 1.66 - 1.54 (m, 4H), 1.48 (t, *J* = 7.0 Hz, 4H), 1.44 - 1.32 (m, 4H), 1.32 - 1.10 (m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 173.2, 84.1, 68.0, 63.3, 33.8, 28.74, 28.69, 28.5, 28.3, 28.1, 25.0, 24.6, 18.0 ppm; HRMS (ESI) m/z calculated for $C_{26}H_{43}O_4$ $[M+H]^+$, 419.3156; found: 419.3154.



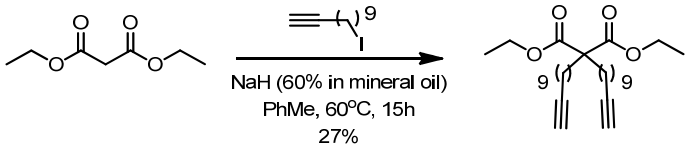
Non-8-yn-1-yl methanesulfonate: 9-nonyn-1-ol (1 g, 7.14 mmol, 1 equiv.) was dissolved in anhydrous dichloromethane (60 mL) and cooled to 0°C. Triethylamine (2 mL, 15 mmol, 2.1 equiv.) was added, followed by methanesulfonyl chloride (0.6 mL, 7.8 mmol, 1.1 equiv.). The mixture was stirred at 0°C for 1h, then warmed to room temperature and stirred for another hour. Water (50 mL) was added and the organic and aqueous phases were separated. The aqueous phase was extracted with dichloromethane (2x), dried with anhydrous Na_2SO_4, and the resulting suspension was filtered. The filtrate was concentrated in vacuo and the crude product purified by chromatography over a short pad of silica gel (10% ethyl acetate in hexanes). The product was isolated as a colorless oil (1.6 g, 7.1 mmol, 99%) and immediately used in the following reaction. **9-iodonon-1-yne:** Non-8-yn-1-yl methanesulfonate (1.6 g, 7.1 mmol, 1 equiv.) was dissolved in DMSO (15 mL) and sodium iodide was added (3.1 g, 20.5 mmol, 3 equiv.) and the mixture was stirred at 50°C for 15h. Ethyl acetate (30 mL) and water (30 mL) were added and the organic and aqueous phases were separated. The organic phase was washed with brine (5x), dried with anhydrous Na_2SO_4, the suspension was filtered and the filtrate was concentrated in vacuo to afford the pure product as a colorless oil (1.5 g, 6.2 mmol, 87%). The NMR data were in agreement with that found in the literature.[8]



Undec-10-yn-1-yl methanesulfonate: 10-undecyn-1-ol (1 g, 5.95 mmol, 1 equiv.) was dissolved in anhydrous dichloromethane (50 mL) and cooled to 0°C. Triethylamine (2

[8] Knapp, Jr. F. F.; Srivastava, P. C.; Callahan, A. P.; Cunningham, E. B.; Kabalka, G. W.; Sastry, K. A. *J. Med. Chem*. **1984**, *27*, 57.

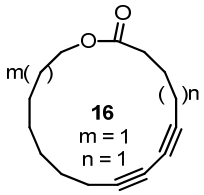
mL, 15 mmol, 2.5 equiv.) was added, followed by methanesulfonyl chloride (0.6 mL, 7.8 mmol, 1.3 equiv.). The mixture was stirred at 0°C for 1h, then warmed to room temperature and stirred for another hour. Water (50 mL) was added and the organic and aqueous phases were separated. The aqueous phase was extracted with dichloromethane (2x), dried with anhydrous Na_2SO_4, and the resulting suspension was filtered. The filtrate was concentrated in vacuo and the crude product purified by chromatography over a short pad of silica gel (10% ethyl acetate in hexanes). The product was isolated as a colorless oil (1.5 g, 99%) and immediately used in the following reaction. **10-iodoundec-1-yne:** Undec-10-yn-1-yl methanesulfonate (1.46 g, 5.95 mmol, 1 equiv.) was dissolved in DMSO (13 mL) and sodium iodide was added (3.1 g, 20.5 mmol, 3,5 equiv.) and the mixture was stirred at 50°C for 15h. Ethyl acetate (30 mL) and water (30 mL) were added and the organic and aqueous phases were separated. The organic phase was washed with brine (5x), dried with anhydrous Na_2SO_4, the suspension was filtered and the filtrate was concentrated in vacuo to afford the pure product as a colorless oil (1.36 g, 4.9 mmol, 82%). The NMR data were in agreement with that found in the literature.[9]



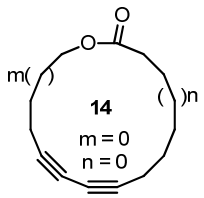
Diethyl 2,2-di(undec-10-yn-1-yl)malonate: Diethylmalonate (83.2 mg, 0.52 mmol, 1 equiv.) was dissolved in anhydrous toluene (2 mL) in a flamed dried flask equipped with a stir bar and a condenser. NaH (60% in mineral oil, 104 mg, 2.6 mmol, 5 equiv.) was added at room temperature, then 10-iodoundec-1-yne (440 mg, 1.59 mmol, 3 equiv.) was added in one portion as a toluene solution (1 mL). The mixture was warmed to 60°C and stirred for 15h. The reaction was then cooled back to room temperature, quenched with H_2O and extracted with ethyl acetate (3x). The organic phases were dried over anhydrous Na_2SO_4, and the resulting suspension was filtered. The filtrate was concentrated in vacuo and the crude product purified by chromatography (5% ethyl acetate in hexanes). The desired product was isolated as a colorless oil (65 mg, 27). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.17 (q, J = 6.0 Hz, 4H), 2.17 (td, J = 9.0, 3.0 Hz, 4H), 1.93 (t, J = 3.0, 2H), 1.87 – 1.82 (m, 4H), 1.56 - 1.46 (m, 4H), 1.43 - 1.10 (m, 30H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 172.0, 84.7, 68.0, 60.9, 57.5, 32.1, 29.8, 29.3, 29.2, 29.0, 28.7, 28.4, 23.9, 18.3, 14.1 ppm; HRMS (ESI) m/z calculated for $C_{29}H_{49}O_4$ $[M+H]^+$, 461.3625; found: 461.3633.

[9] Crisp, T. G.; Gore, J. *Tetrahedron* **1997**, *53*, 1505-1522.

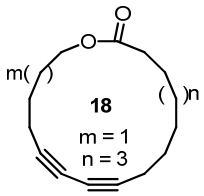
SYNTHESIS OF MACROCYCLES



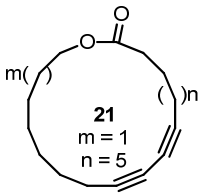
General procedure for the macrocylization of diynes under Glaser-Hay oxidative coupling conditions: Macrocycle (**3**): To a vial equipped with a stirring bar was added $CuCl_2$ (5.5 mg, 0.48 mmol, 25 mol%) and $Ni(NO_3)_2 \cdot 6H_2O$ (9.3 mg, 0.48 mmol, 25 mol%). Polyethylene glycol 400 (3.33 mL), triethylamine (0.05 mL, 0.36 mmol, 3 equiv.) and pyridine (0.05 mL, 0.6 mmol, 5 equiv.) were added and the mixture was stirred at room temperature for 15 min or until the metals were solubilized. The diyne (0.12 mmol) was added to the homogenous mixture as a methanol solution (1.67 mL) in one portion. Oxygen was bubbled in the solution for 5 min and the vial was then closed with a screw cap. The reaction was warmed to 60°C and monitored by TLC for consumption of the starting material (oxygen was bubbled again through the solution every 12h). When the starting material was completely consumed (TLC), the reaction was cooled to room temperature and the crude mixture was loaded directly on a silica column. Purification by chromatography (100% hexanes→10% ethyl acetate in hexane) afforded the product as a colorless semi-solid (31 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.09 (t, J = 8 Hz, 2H), 2.41 - 2.33 (m, 4H), 2.24 (t, *J* = 5.9 Hz, 2H), 1.93 - 1.87 (m, 2H), 1.77 – 1.70 (m, 2H), 1.55 - 1.50 (m, 4H), 1.46 - 1.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 173.4, 77.7, 75.7, 67.0, 66.6, 64.3, 33.3, 26.5, 25.2, 25.1, 24.9, 23.5, 22.1, 19.0, 18.1; HRMS (ESI) m/z calculated for $C_{15}H_{21}O_2$ $[M+H]^+$, 233.1536; found: 233.1531.



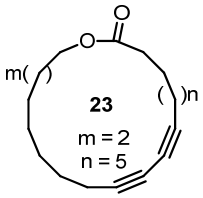
Macrocycle (8): Following the general procedure described above, macrocycle **8** was isolated. (15 mg, 62%). ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4.24 (t, *J* = 6 Hz, 2H); 2.69 (t, *J* = 6 Hz, 2H); 2.28 – 2.21 (m, 4H); 1.92 – 1.77 (m, 8H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm = 173.9, 82.8, 82.5, 67.8, 67.7, 62.9, 32.3, 27.7, 25.8, 24.9, 23.3, 19.0, 10.1; HRMS (ESI) m/z calculated for $C_{13}H_{17}O_2$ $[M+H]^+$, 205.1223; found: 205.1225.



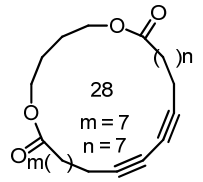
Macrocycle (9): Following the general procedure described above, macrocycle **9** was isolated. (24 mg, 74%) ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.17 (t, *J* = 6.3 Hz, 2H), 2.36 - 2.26 (m, 8H), 1.88 - 1.78 (m, 2H), 1.68 - 1.26 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm = 173.8, 78.0, 76.9, 66.6, 66.3, 63.6, 34.8, 28.7, 28.0, 27.8, 27.6, 27.0, 26.8, 25.0, 24.6, 18.9, 18.8; HRMS (ESI) m/z calculated for $C_{17}H_{25}O_2$ $[M+H]^+$, 261.1849; found: 261.1844.



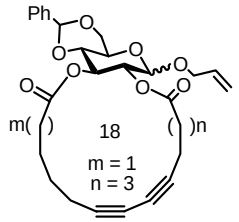
Macrocycle (10): Following the general procedure described above, macrocycle **10** was isolated. (30 mg, 0.1 mmol, 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.10 (t, *J* = 6.5 Hz, 2H), 2.36 - 2.26 (m, 6H), 1.70 - 1.61 (m, 6H), 1.50 - 1.26 (m, 14H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm = 174.0, 77.6, 77.2, 66.0, 65.8, 64.2, 34.3, 29.1, 28.5, 28.23, 28.22, 28.19, 27.93, 27.91, 27.63, 27.58, 25.7, 25.0, 19.03, 19.02; HRMS (ESI) m/z calculated for $C_{20}H_{31}O_2$ $[M+H]^+$, 303.2319; found: 303.2325.



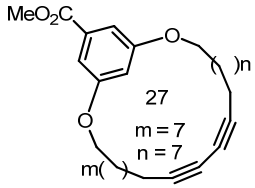
Macrocycle (11): Following the general procedure described above, macrocycle **11** was isolated. (31 mg, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 4.09 (t, *J* = 6.5 Hz, 2H), 2.35 - 2.26 (m, 6H), 1.68 - 1.62 (m, 6H), 1.53 - 1.26 (m, 16H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm = 174.0, 77.50, 77.46, 65.9, 65.7, 64.2, 34.2, 28.88, 28.86, 28.7, 28.4, 28.32, 28.28, 28.23, 28.1, 27.83, 27.81, 27.5, 25.7, 25.0, 19.07, 18.99, ; HRMS (ESI) m/z calculated for $C_{22}H_{35}O_2$ $[M+H]^+$, 331.2632; found: 331.2640.



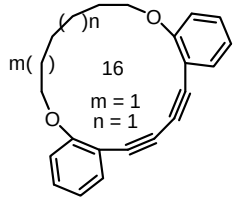
Macrocycle (12): Following the general procedure described above, macrocycle **12** was isolated. (50 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 4.16 - 4.04 (m, 4H), 2.32 (t, *J* = 7.6 Hz, 4H), 2.27 (t, *J* = 6.3 Hz, 4H), 1.72 (m, 4H), 1.69 - 1.60 (m, 4H), 1.55 - 1.39 (m, 8H), 1.38 - 1.28 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm = 173.9, 77.4, 65.6, 63.8, 34.3, 28.69, 28.68, 28.6, 28.2, 27.8, 25.4, 24.9, 19.1; HRMS (ESI) m/z calculated for $C_{26}H_{41}O_4$ $[M+H]^+$, 417.2999; found: 417.3006.



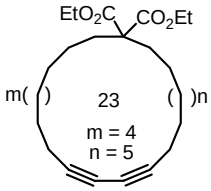
Macrocycle (13): Following the general procedure described above, macrocycle **13** was isolated. (42 mg, 0.08 mmol, 67%). ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of α and β anomers (0.75 : 0.25), data reported for major anomer only), δ = 7.49 - 7.40 (m, 2H), 7.39 - 7.31 (m, 3H), 5.86 (dddd, *J* = 17.0, 10.8, 5.8, 5.2 Hz, 1H), 5.70 (t, *J* = 10.0 Hz, 1H), 5.5 1 (s, 1H), 5.38 - 5.08 (m, 2 H), 4.83 (dd, *J* = 10.0, 3.7 Hz, 1 H), 4.30 (dd, *J* = 10.2, 4.8 Hz, 1H), 4.21 (ddt, J = 16.0, 8.0, 4.0 Hz, 1H), 4.06 - 3.94 (m, 2H), 3.77 (t, J = 12.0 Hz, 1H), 3.62 (t, J = 12.0 Hz, 1H), 2.85 - 2.69 (m, 1H), 2.65 - 2.51 (m, 1H), 2.43 - 2.26 (m, 6H), 1.98 - 1.64 (m, 5H), 1.63 - 1.43 (m, 4H); ^{13}C NMR (176 MHz, $CDCl_3$) δ ppm = 173.3, 172.4, 137.0, 133.3, 129.0, 128.2, 126.1, 117.8, 101.4, 95.6, 79.7, 78.1, 77.8, 71.9, 68.8, 68.7, 68.4, 62.6, 33.6, 33.4, 27.7, 27.5, 26.1, 26.0, 24.1, 23.6, 19.1, 18.7, 18.1, 18.0; HRMS (ESI) m/z calculated for $C_{30}H_{34}NaO_8$ $[M+Na]^+$, 545.2146; found: 545.2147.



Macrocycle (14): Following the general procedure described above, macrocycle **14** was isolated. (39 mg, 0.082 mmol, 69%). ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.17 (d, *J* = 2.2 Hz, 2H), 6.70 (t, *J* = 2.2 Hz, 1H), 4.08 - 3.99 (t, J = 6.0 Hz, 4H), 3.91 (s, 3H), 2.25 (t, *J* = 6.4 Hz, 4H), 1.84 - 1.71 (m, 4H), 1.65 - 1.14 (m, 28H); ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm = 167.0, 160.1, 131.8, 107.6, 107.4, 77.5, 68.0, 65.5, 52.2, 29.1, 28.7, 28.73, 28.66, 28.65, 28.3, 28.1, 25.8, 19.1 ppm; HRMS (ESI) m/z calculated for $C_{30}H_{43}O_4$ $[M+H]^+$, 467.3156; found: 467.3165.



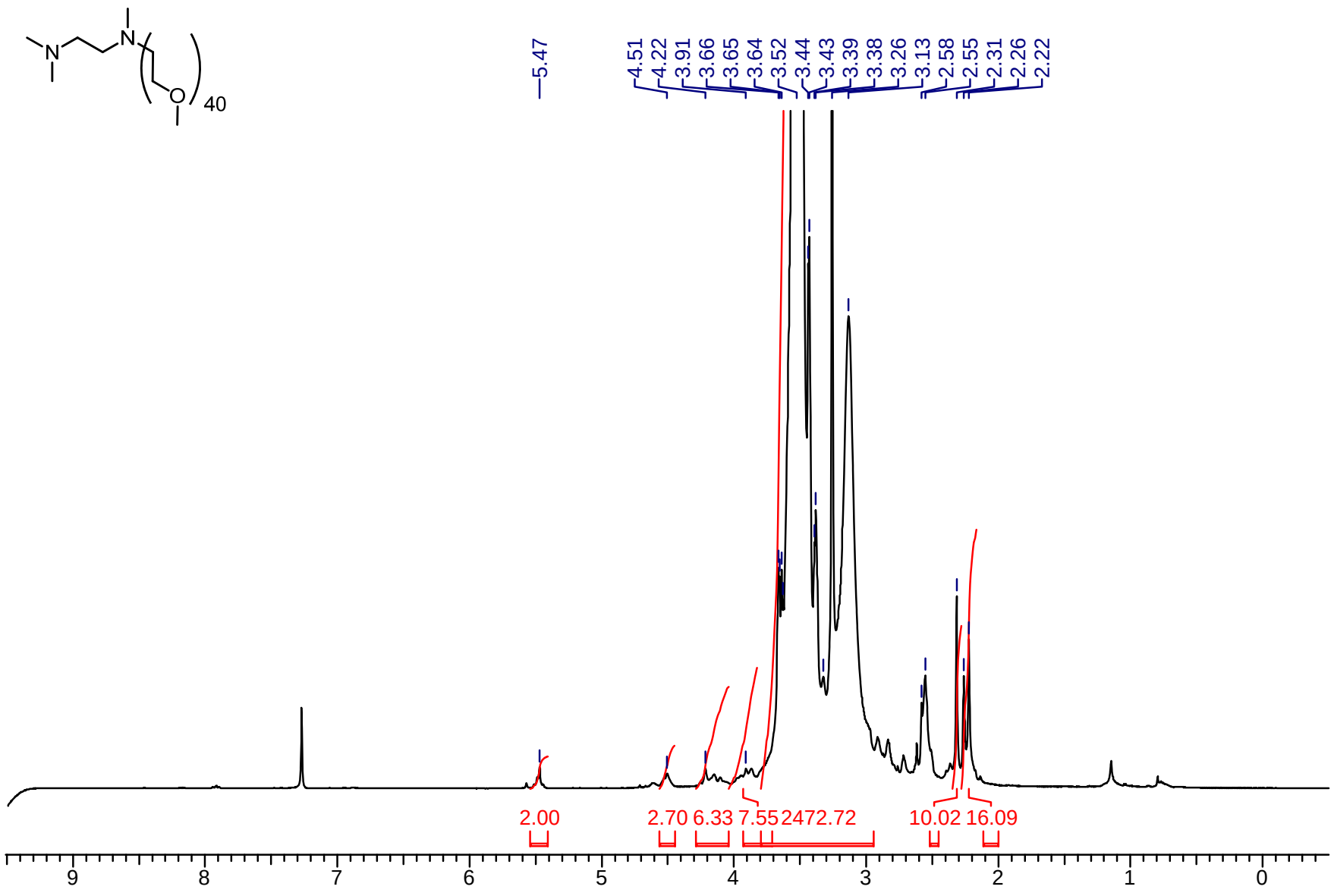
Macrocycle (16): Following the general procedure described above, macrocycle **16** was isolated. (37.3 mg, 98%). ^{1}H NMR (300 MHz ,$CDCl_3$) δ = 7.39 (dd, *J* = 7.6, 1.7 Hz, 2H), 7.33 - 7.28 (m, 2H), 6.96 - 6.86 (m, 4H), 4.09 (t, *J* = 5.3 Hz, 4H), 1.96 - 1.85 (m, 4H), 1.84 - 1.74 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm = 162.5, 132.0, 130.4, 120.8, 113.7, 112.6, 79.8, 79.2, 70.2, 30.0, 27.6 ppm; HRMS (ESI) m/z calculated for $C_{22}H_{21}O_2$ $[M+H]^+$, 317.1536; found: 317.1545.



Macrocycle (15): Following the general procedure described above, macrocycle **15** was isolated. (20 mg, 0.044 mmol, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ =4.18 (q, J = 8 Hz, 4H), 2.30 (t, J = 4 Hz, 4H), 1.91 -1.87 (m, 4H), 1.49-1.43 (m, 8H), 1.34-1.26 (m, 20H), 1.24 (t, J = 4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ ppm = 172.1, 77.2, 61.0, 57.6, 31.3, 29.9, 29.7, 29.1, 28.9, 28.3, 28.2, 27.9, 23.4, 19.2, 14.1 ppm; HRMS (ESI) m/z calculated for $C_{29}H_{47}O_4$ $[M+H]^+$, 459.3469; found: 459.3475.

Complete References From Text:

(3) Lamarre, D.; Anderson, P. C.; Bailey, M.; Beaulieu, P.; Bolger, G.; Bonneau, P.; Bös, M.; Cameron, D. R.; Cartier, M.; Cordingley, M. G.; Faucher, A.-M.; Goudreau, N.; Kawai, S. H.; Kukolj, G.; Lagacé, L.; Laplante, S. R.; Narjes, H.; Poupart, M.-A.; Rancourt, J.; Sentjens, R. E.; St-George, R.; Simoneau, B.; Steinmann, G.; Thibeault, D.; Tsantrizos, Y. S.; Weldon, S. M.; Yong, C.-L.; Llinàs-Brunet, M. *Nature* **2003**, *426*, 186-189.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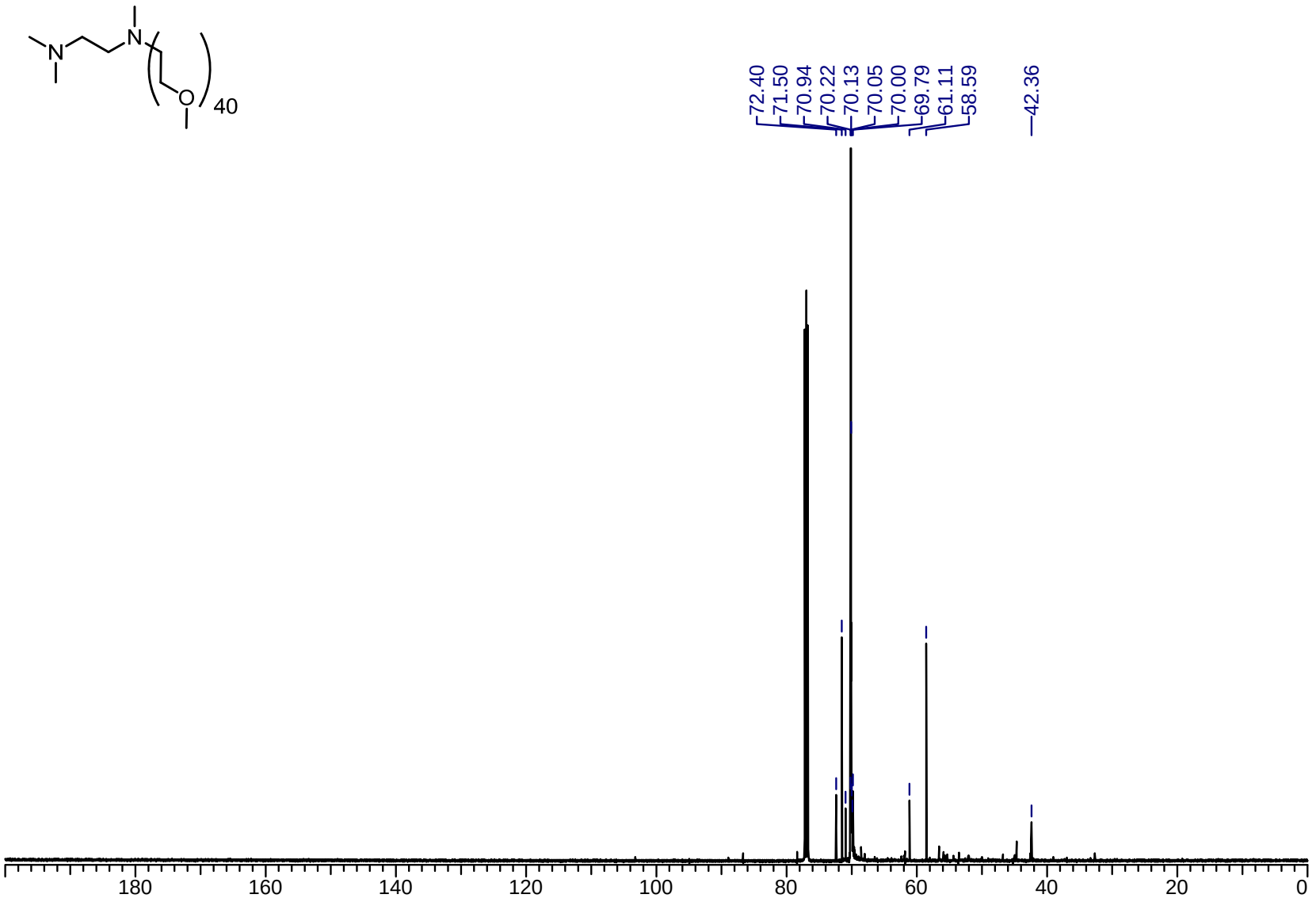
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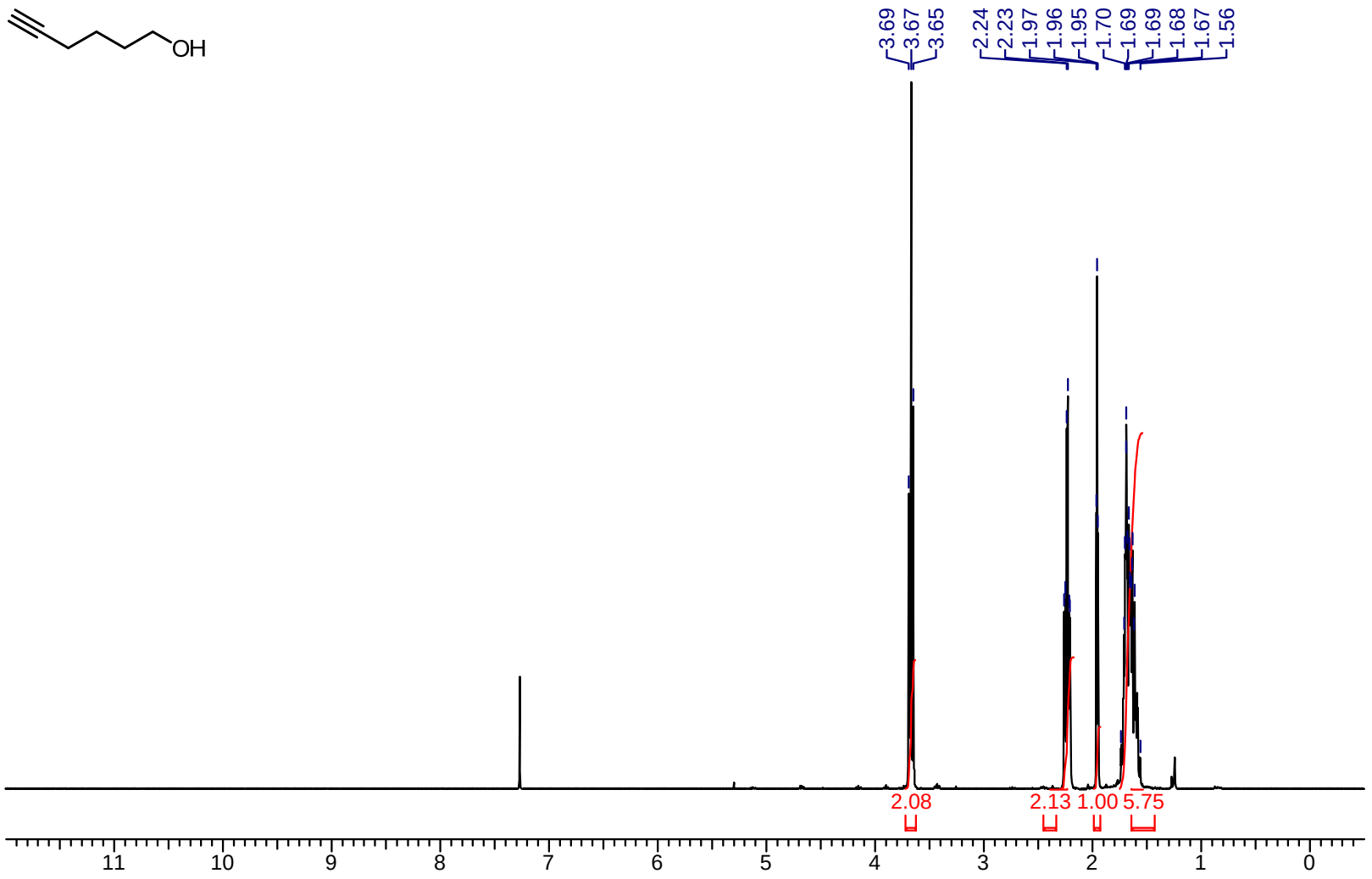
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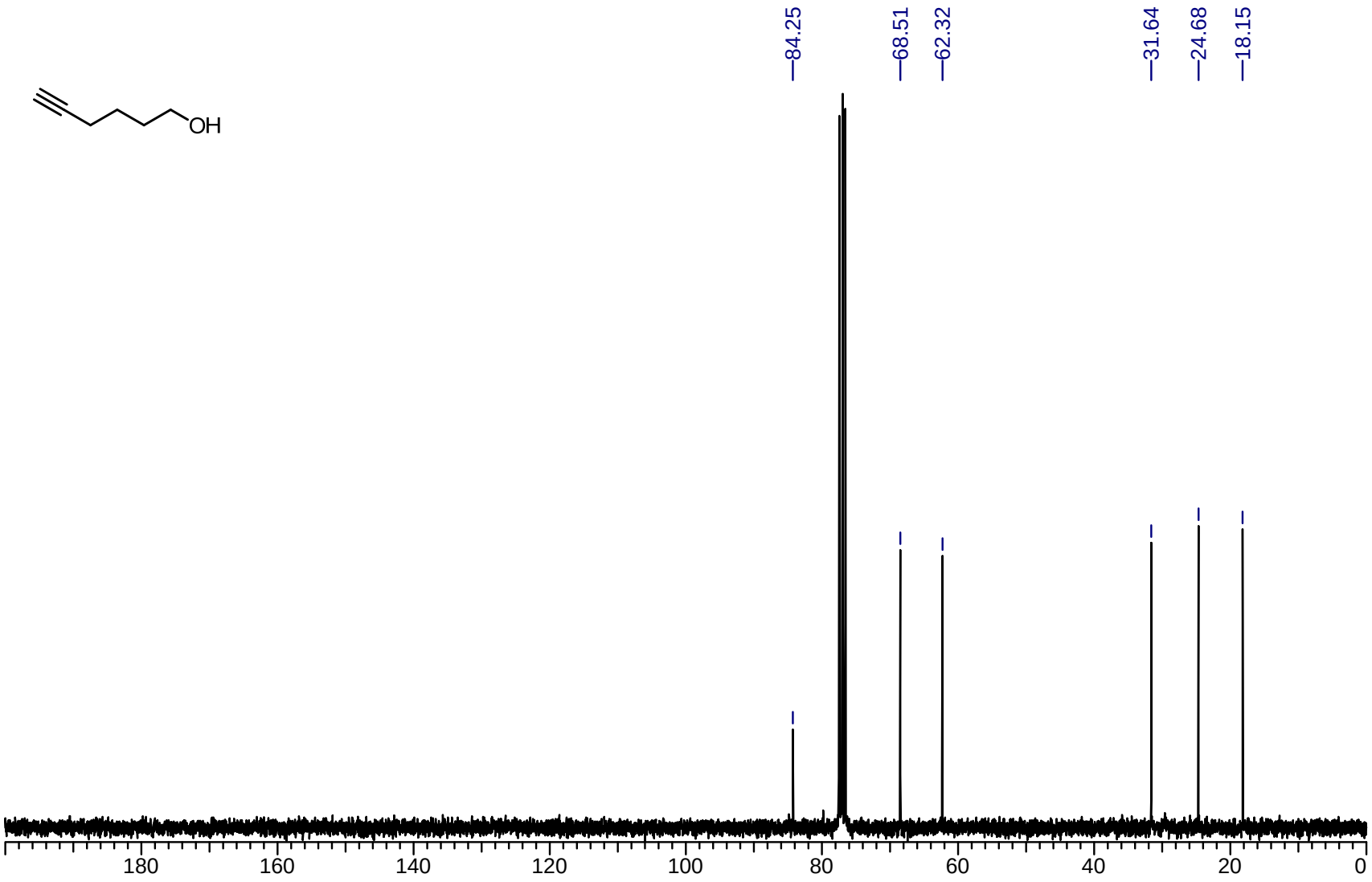
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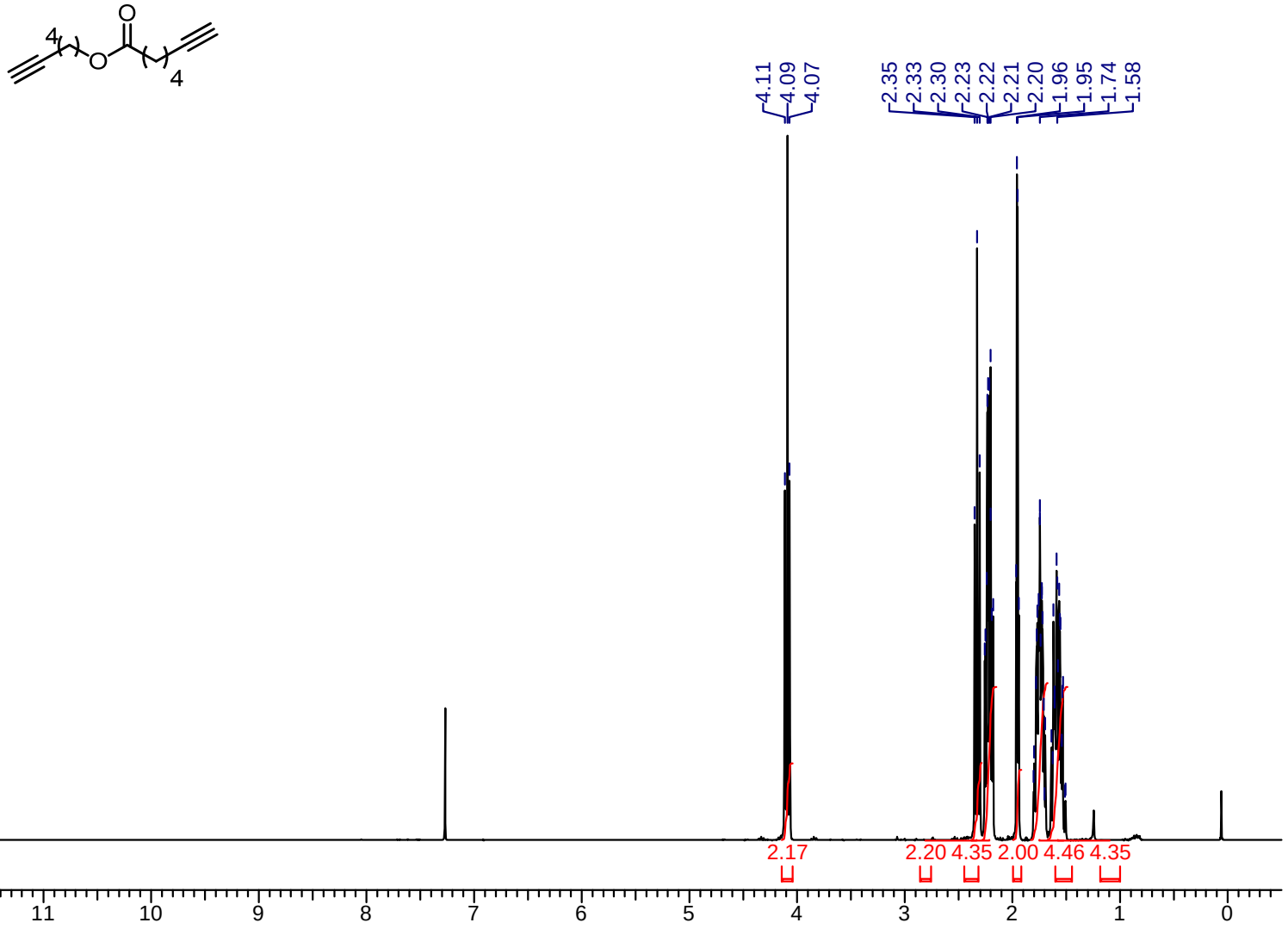
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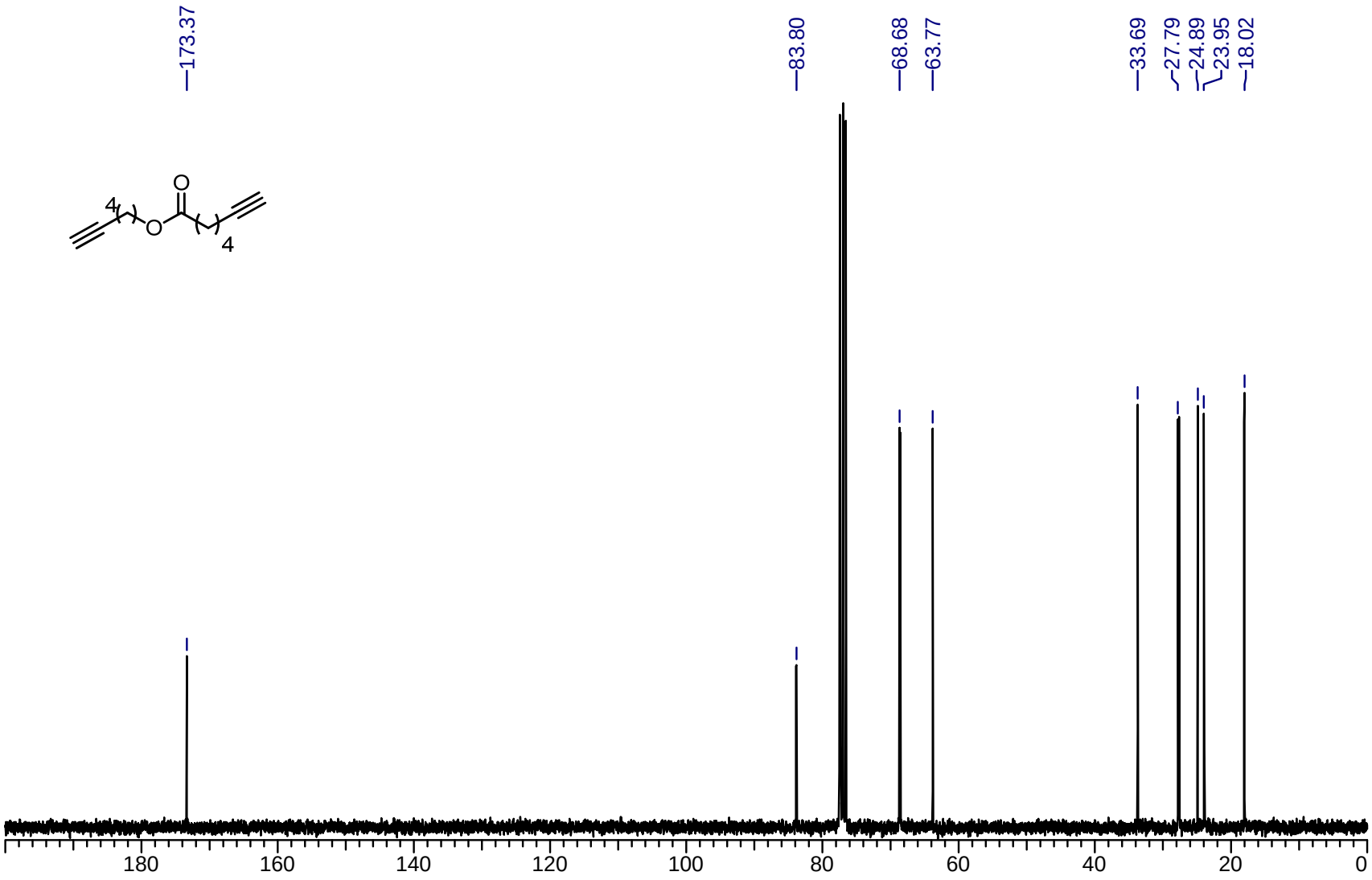
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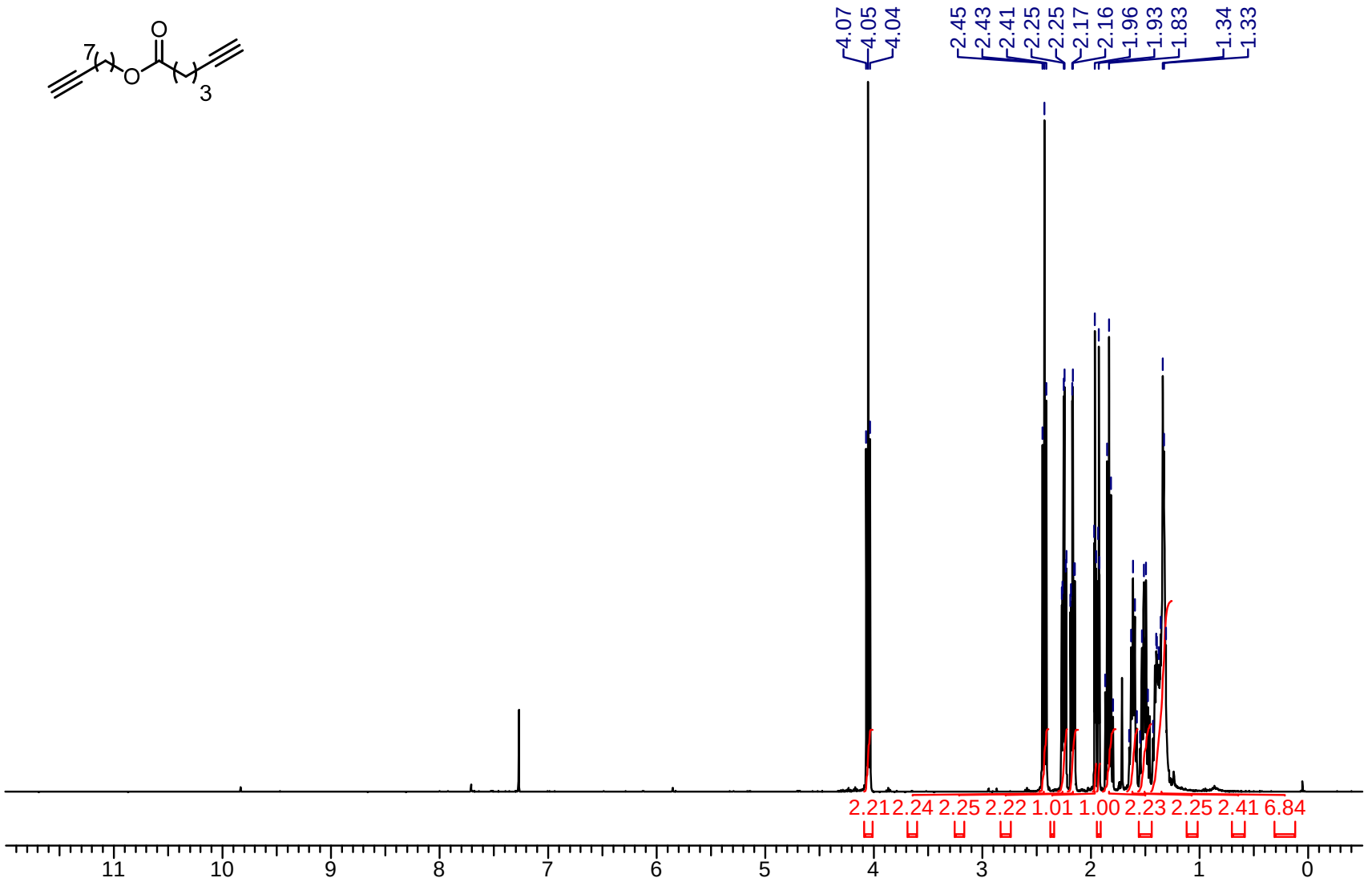
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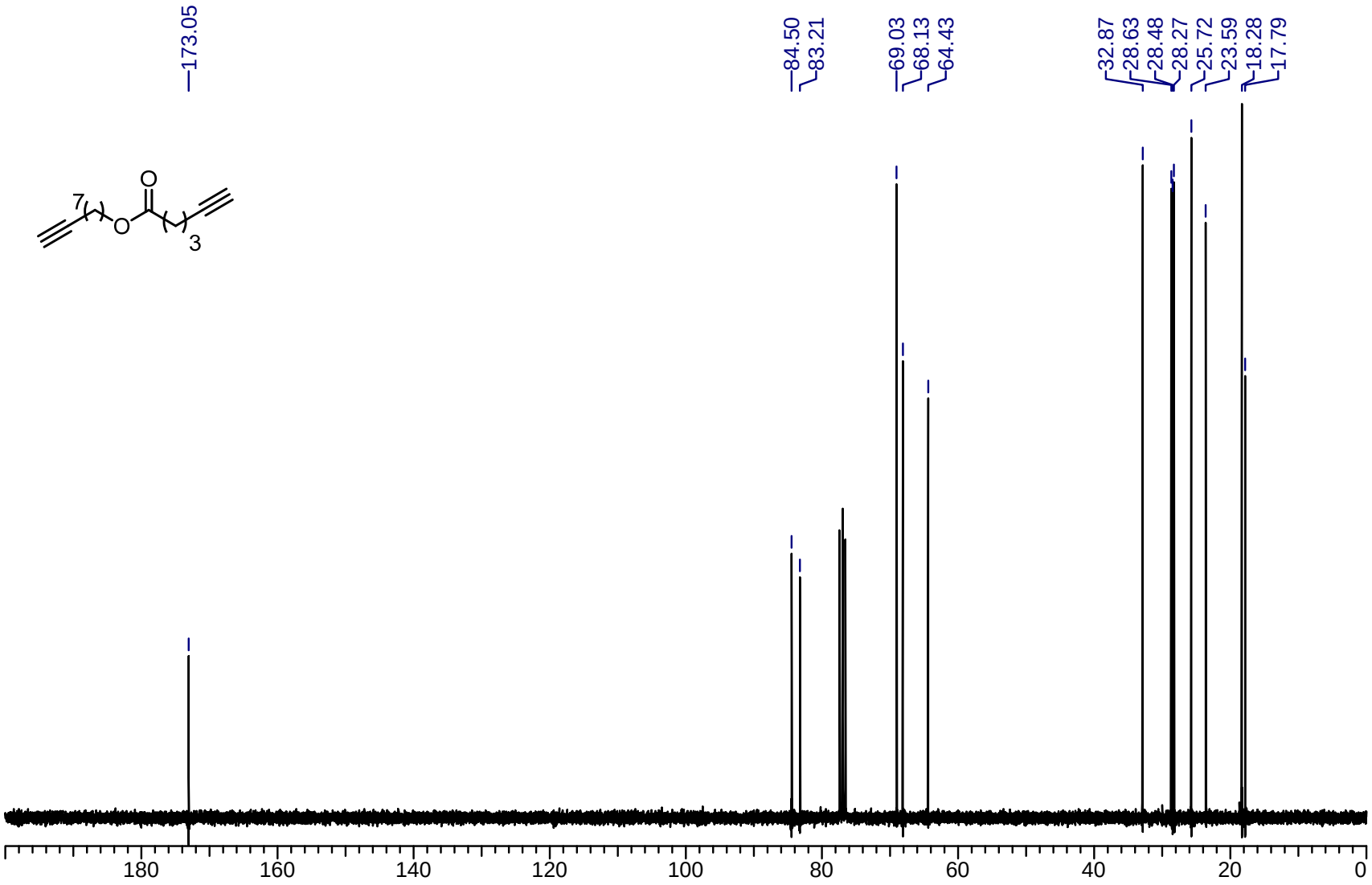
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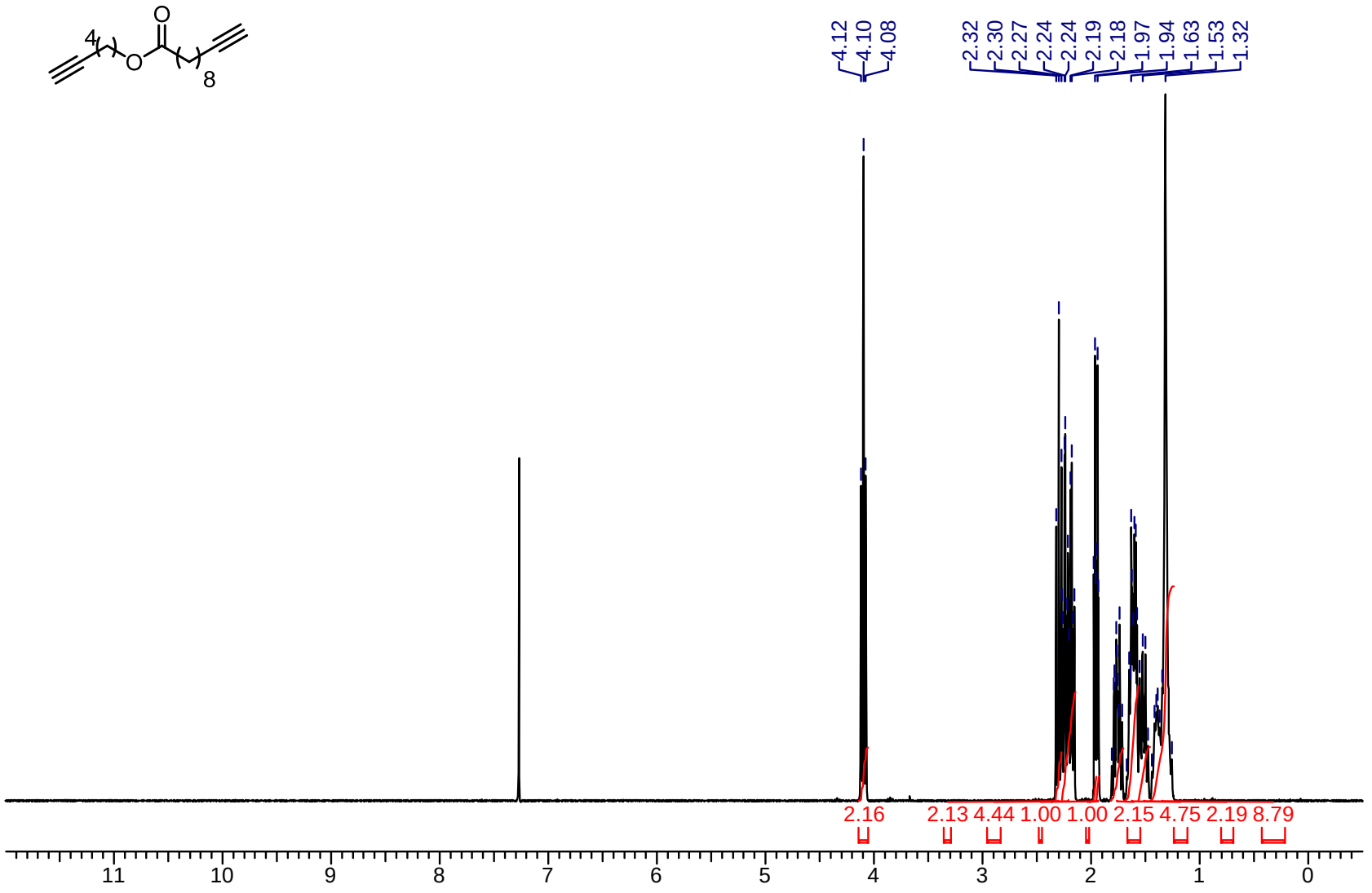
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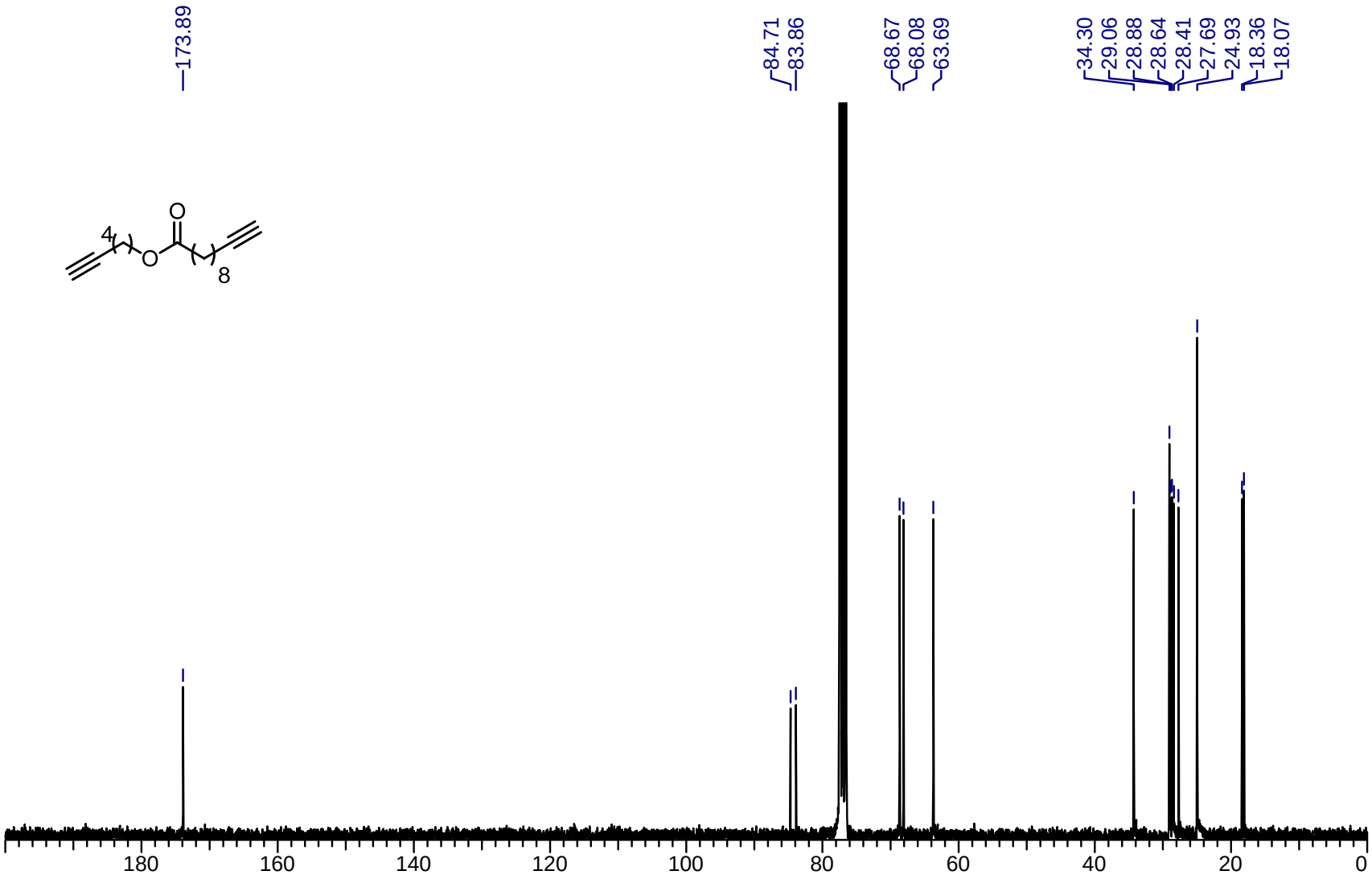
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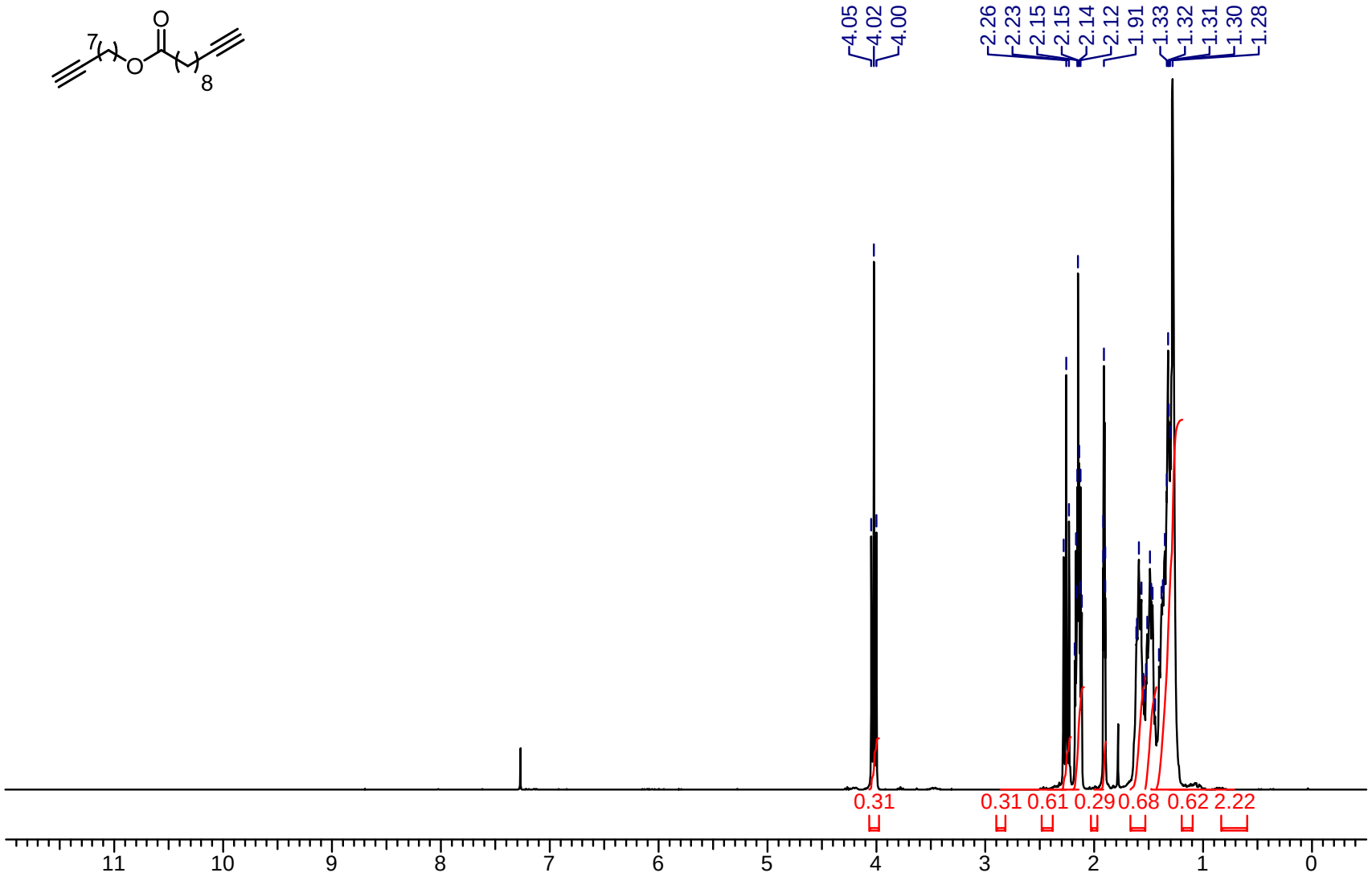
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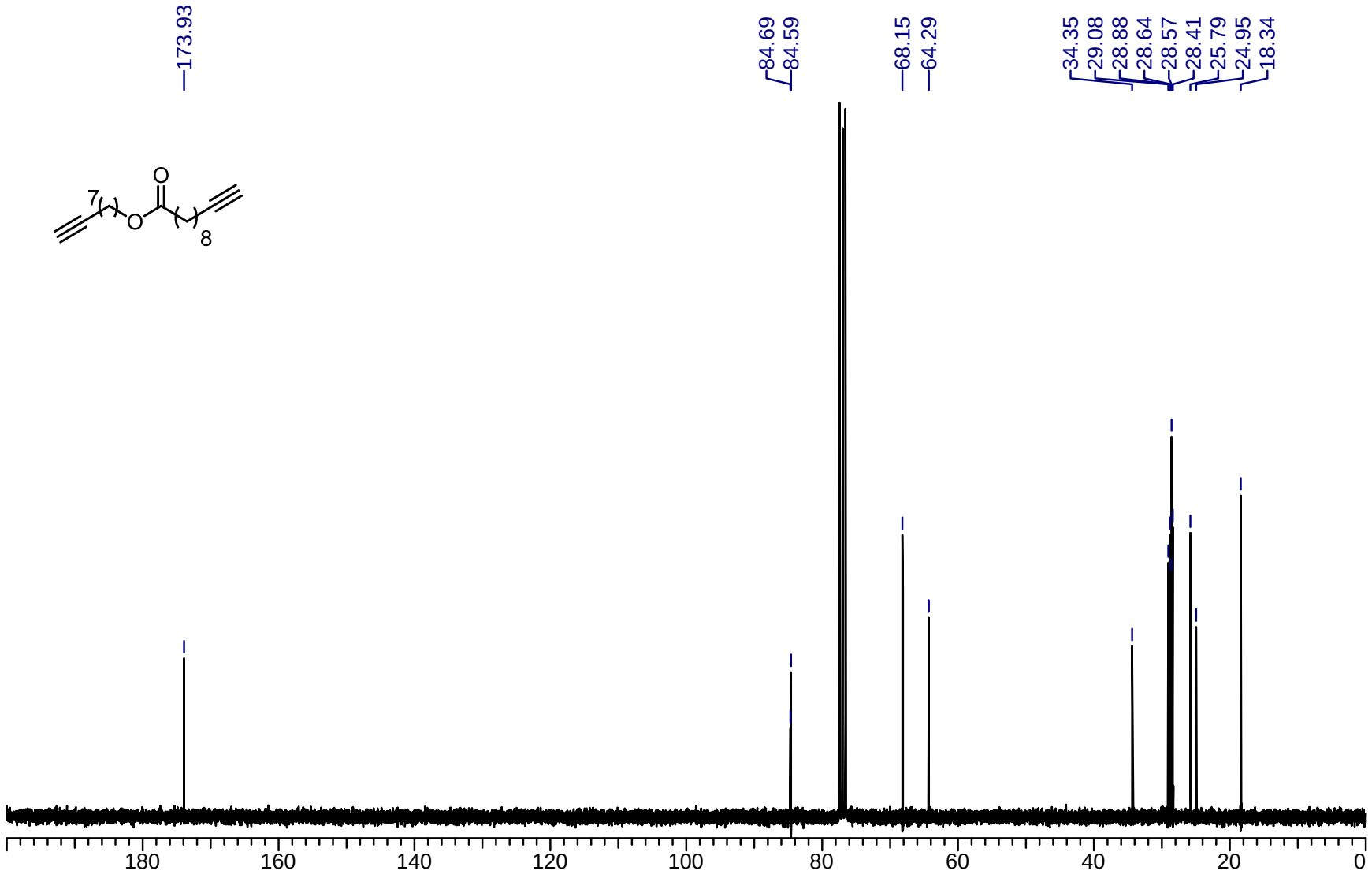
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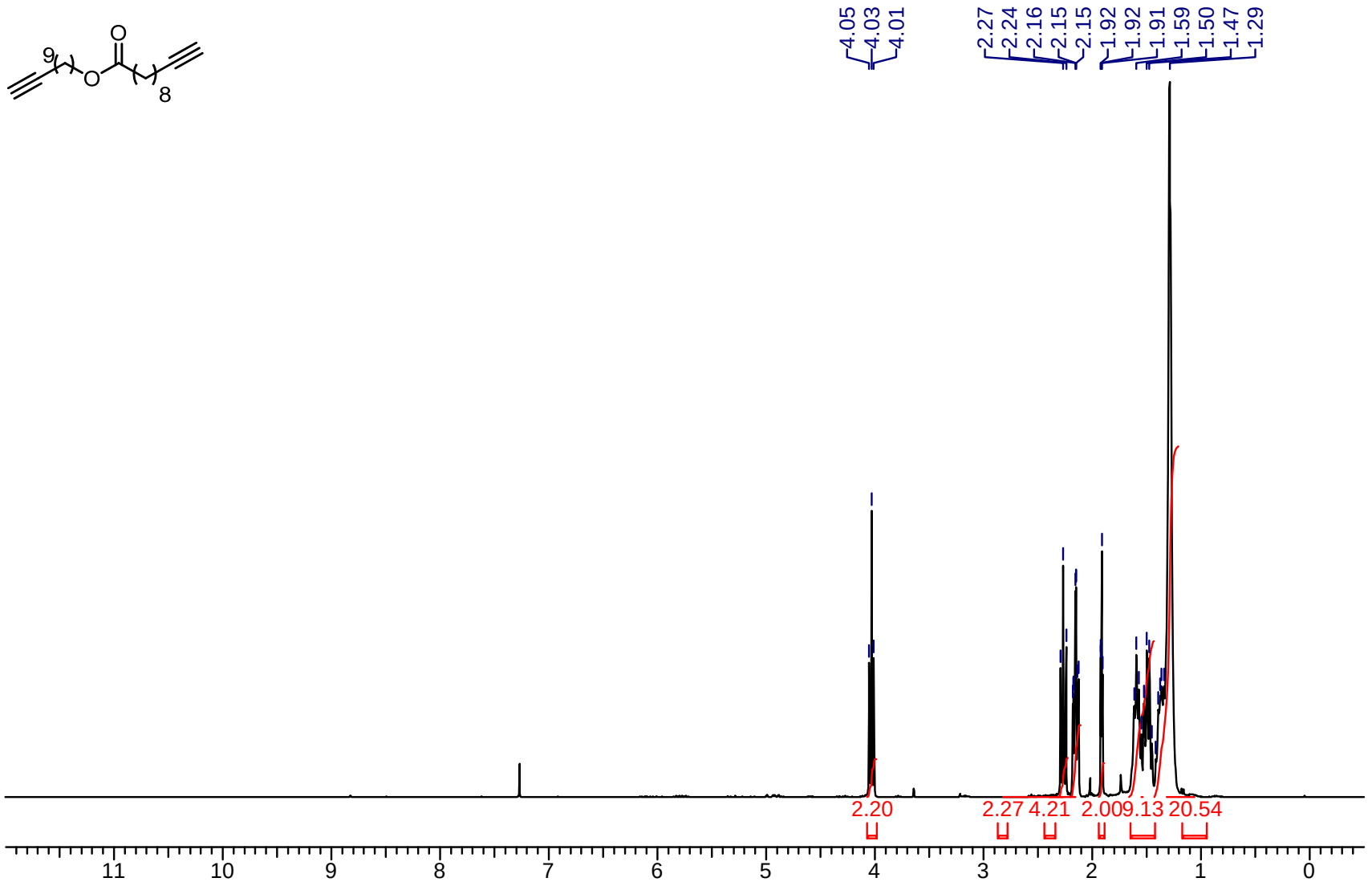
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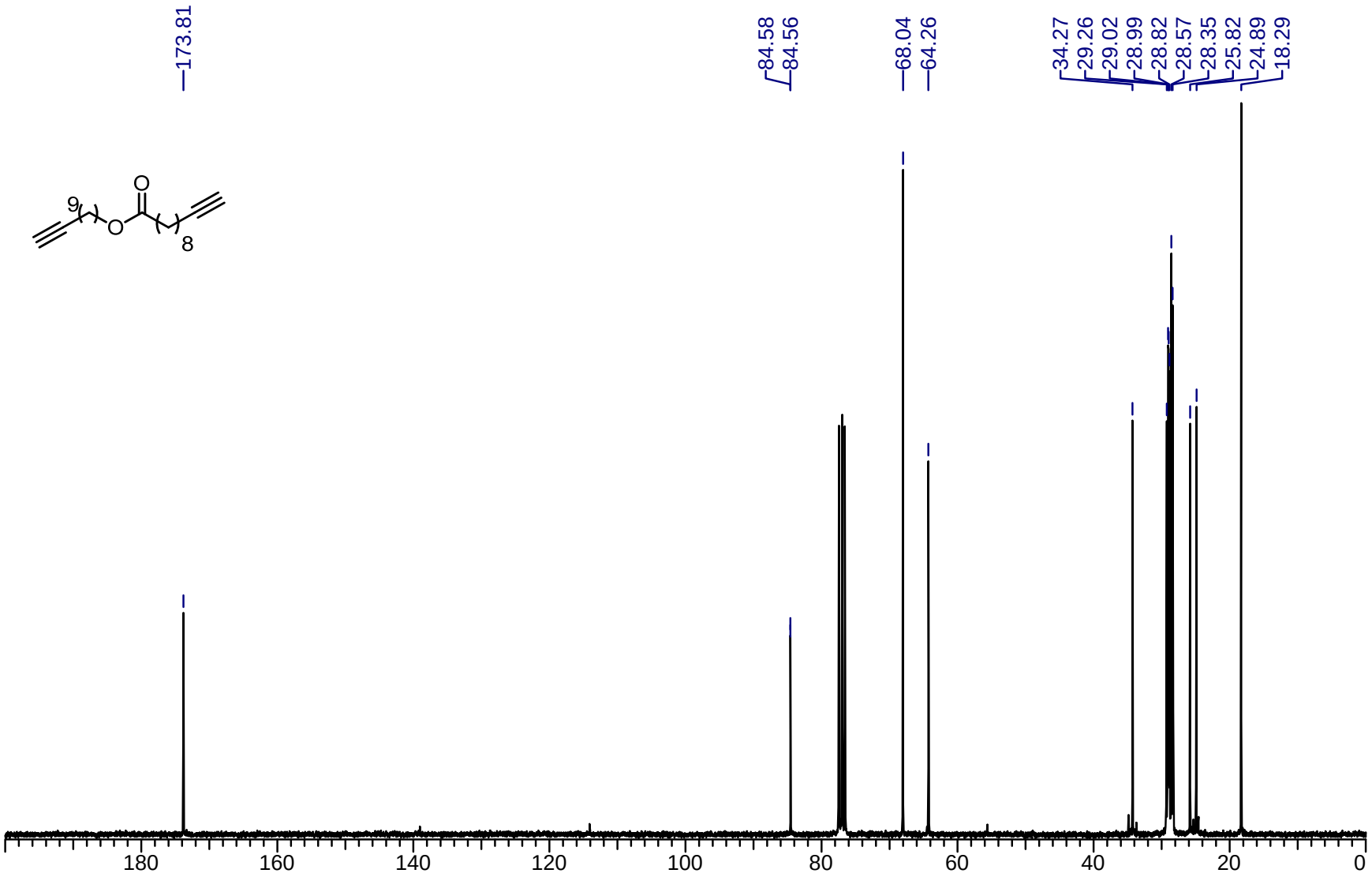
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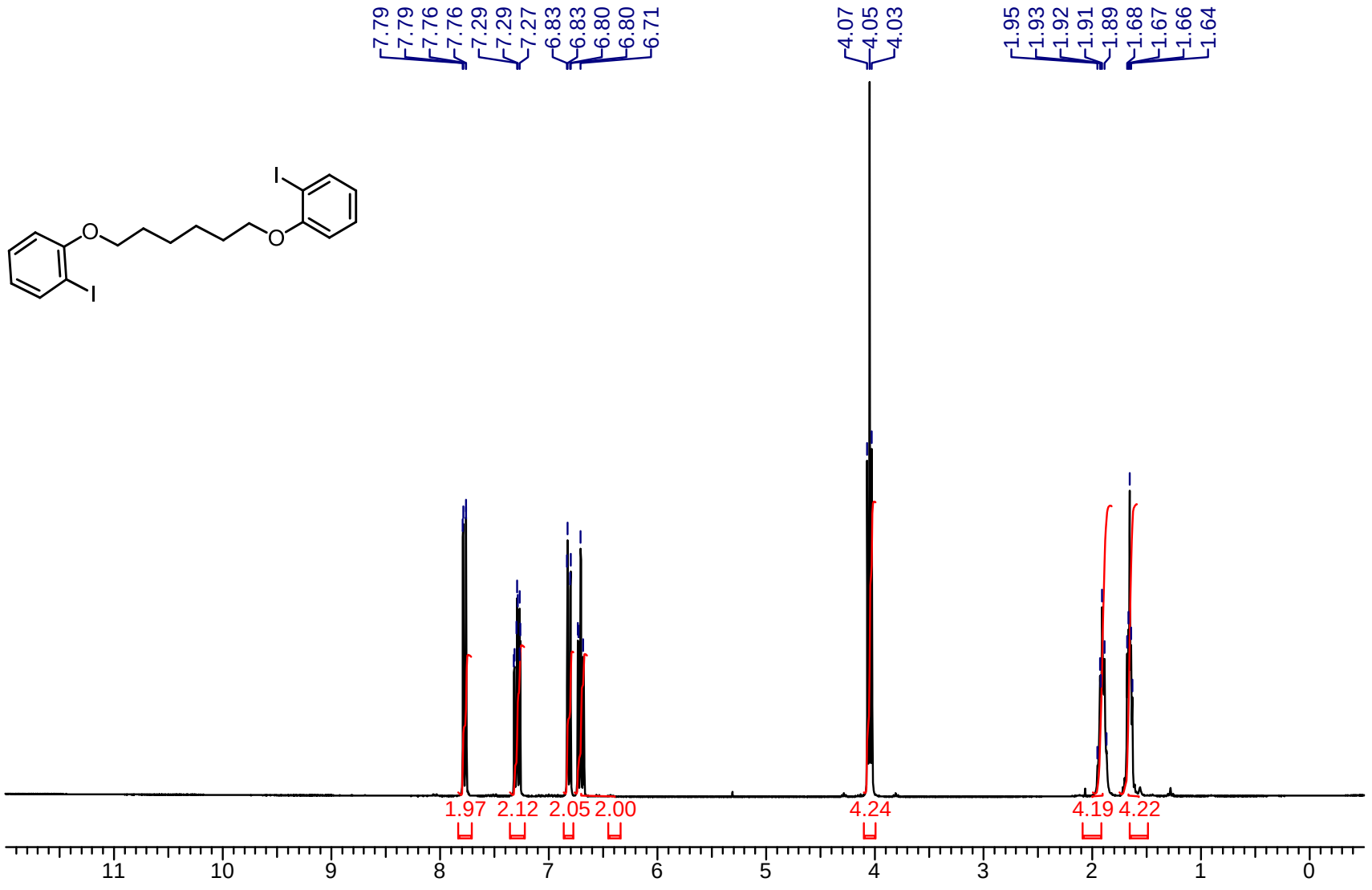
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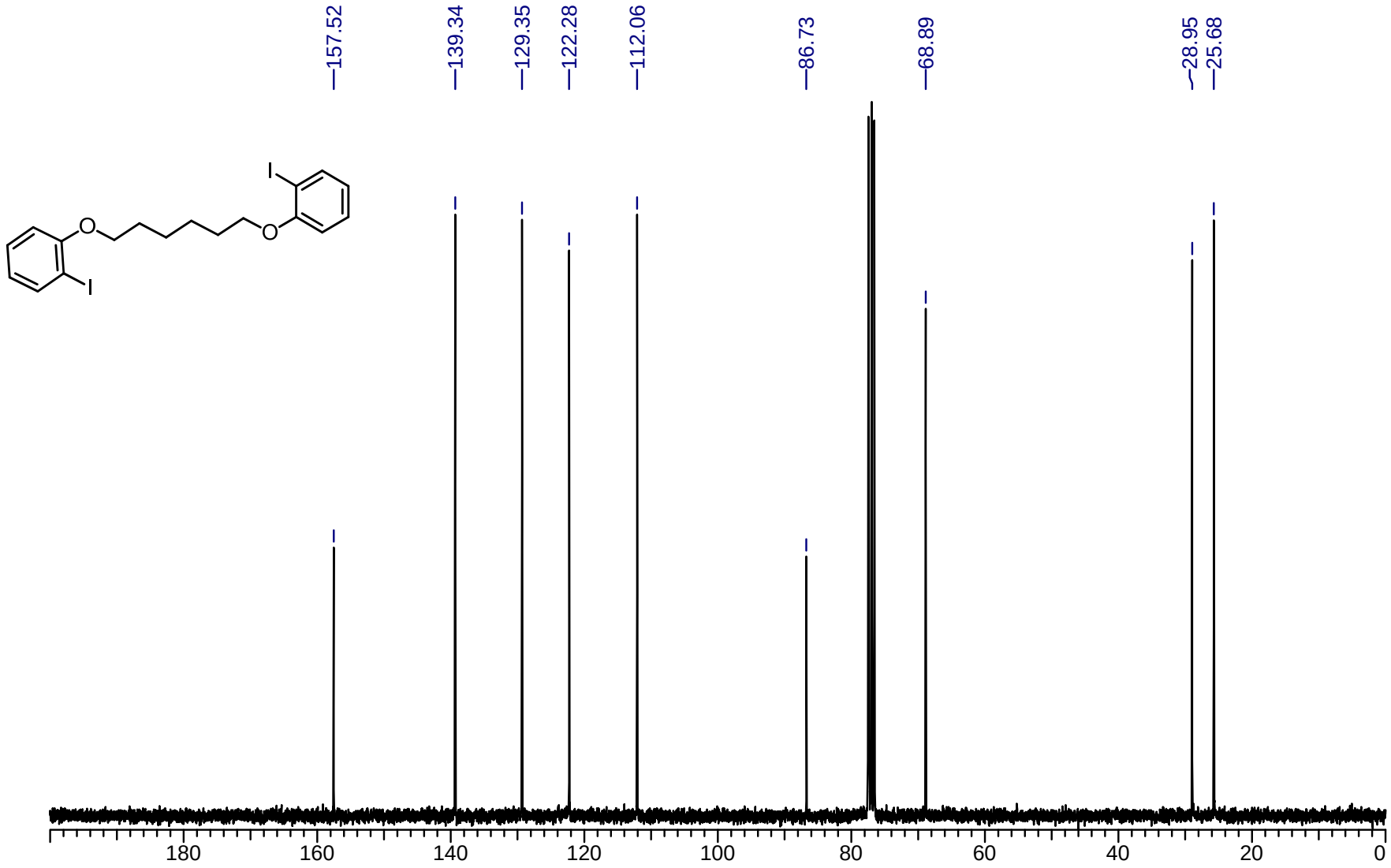
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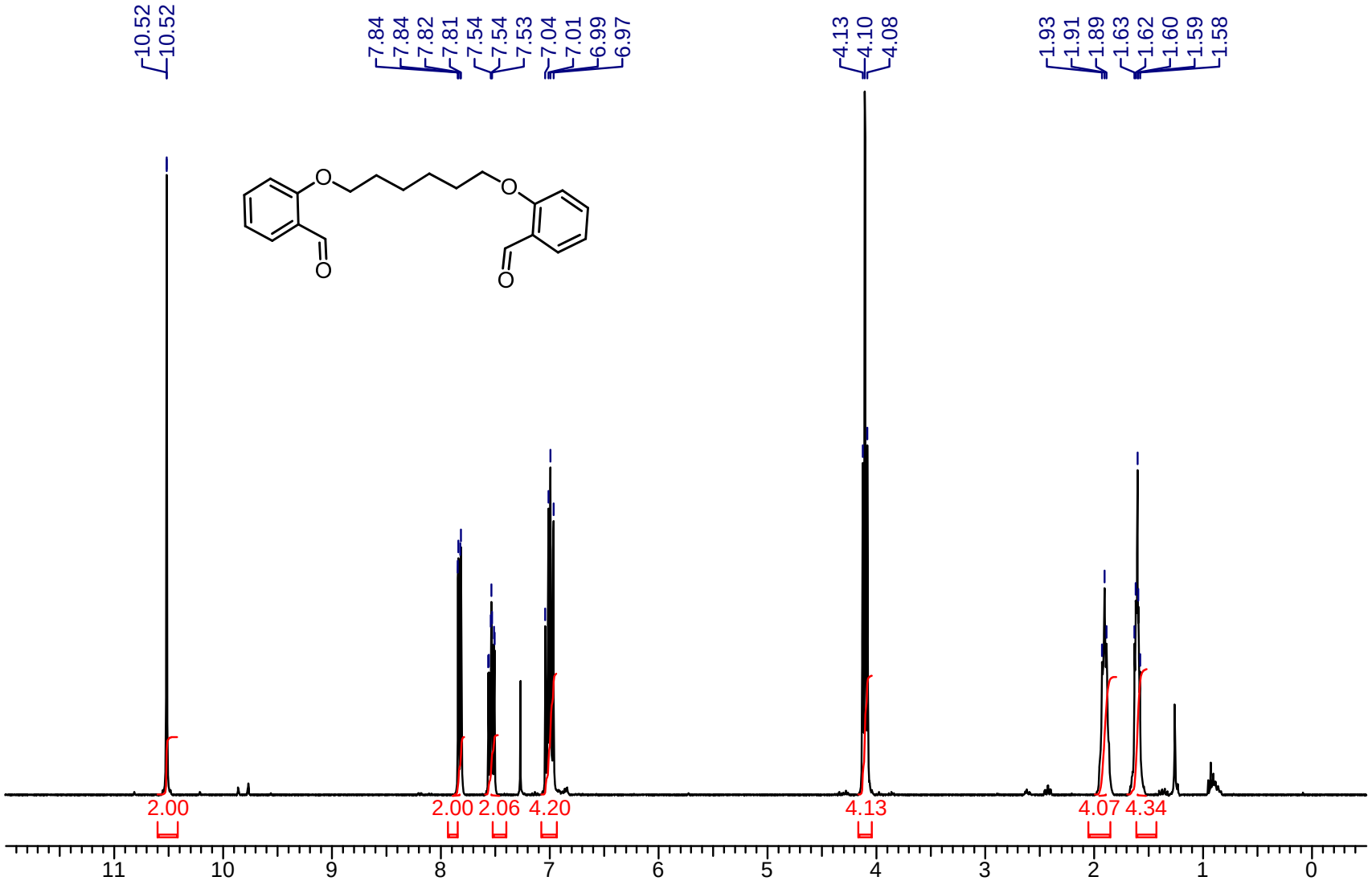
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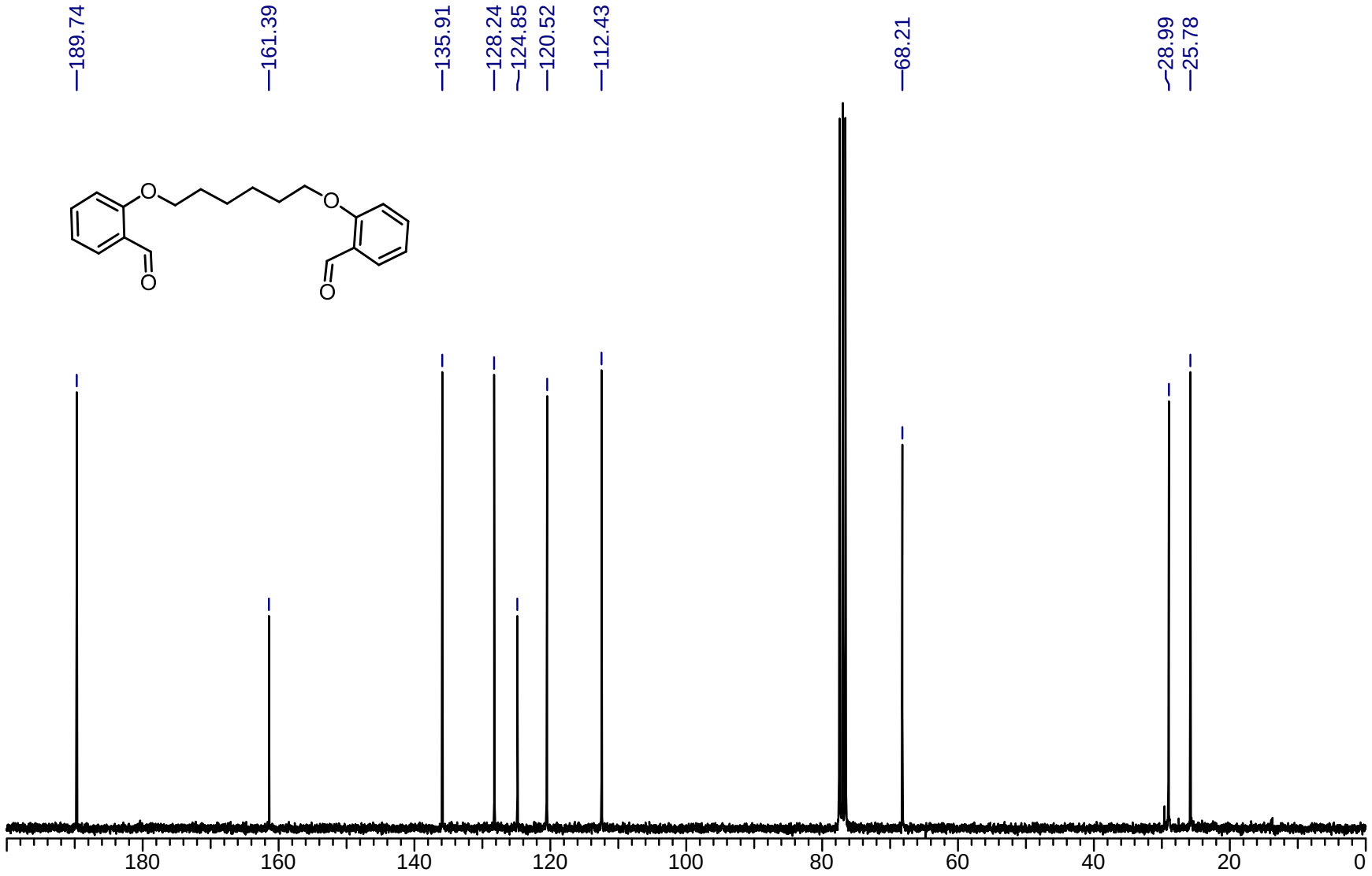
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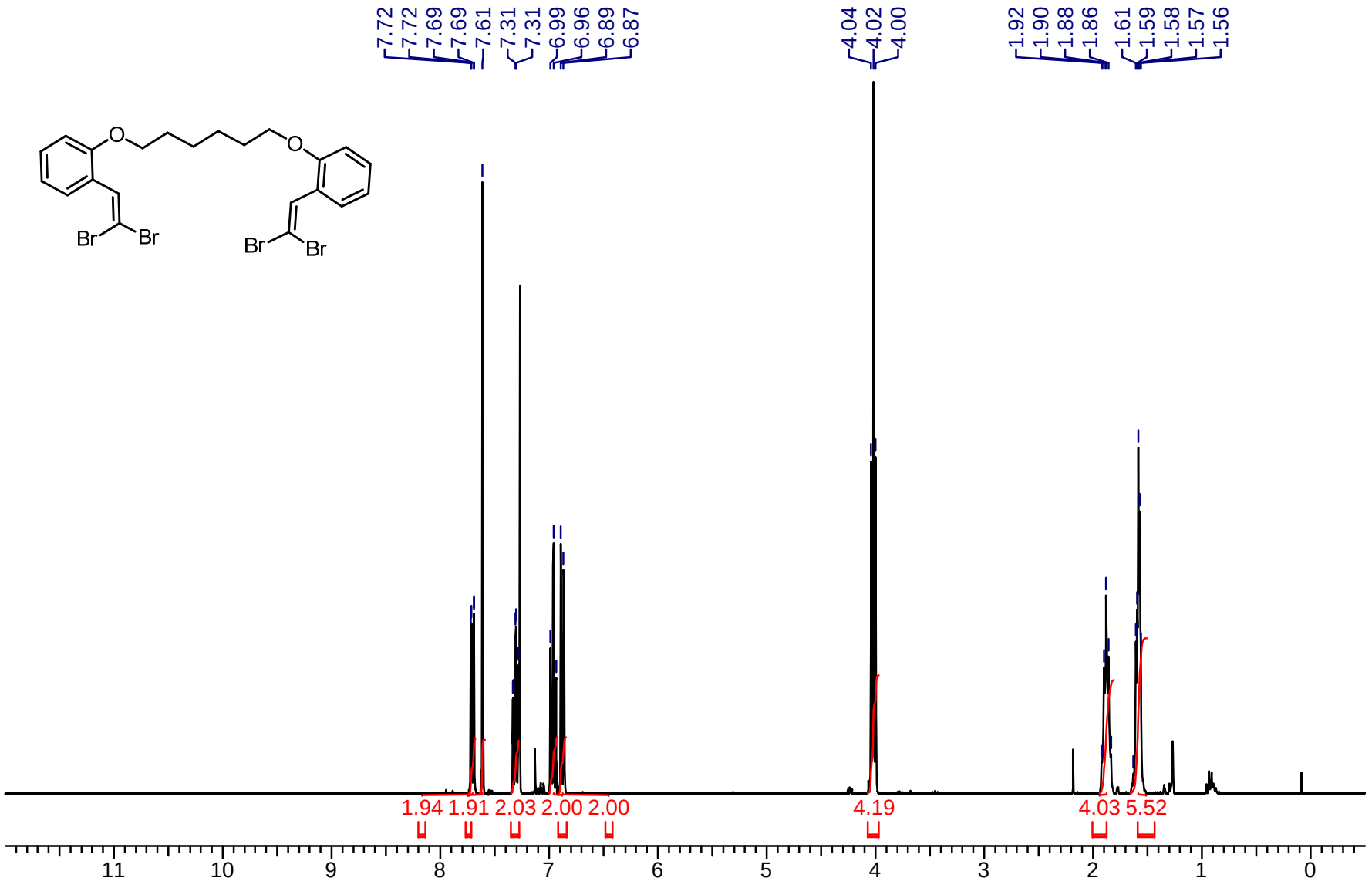
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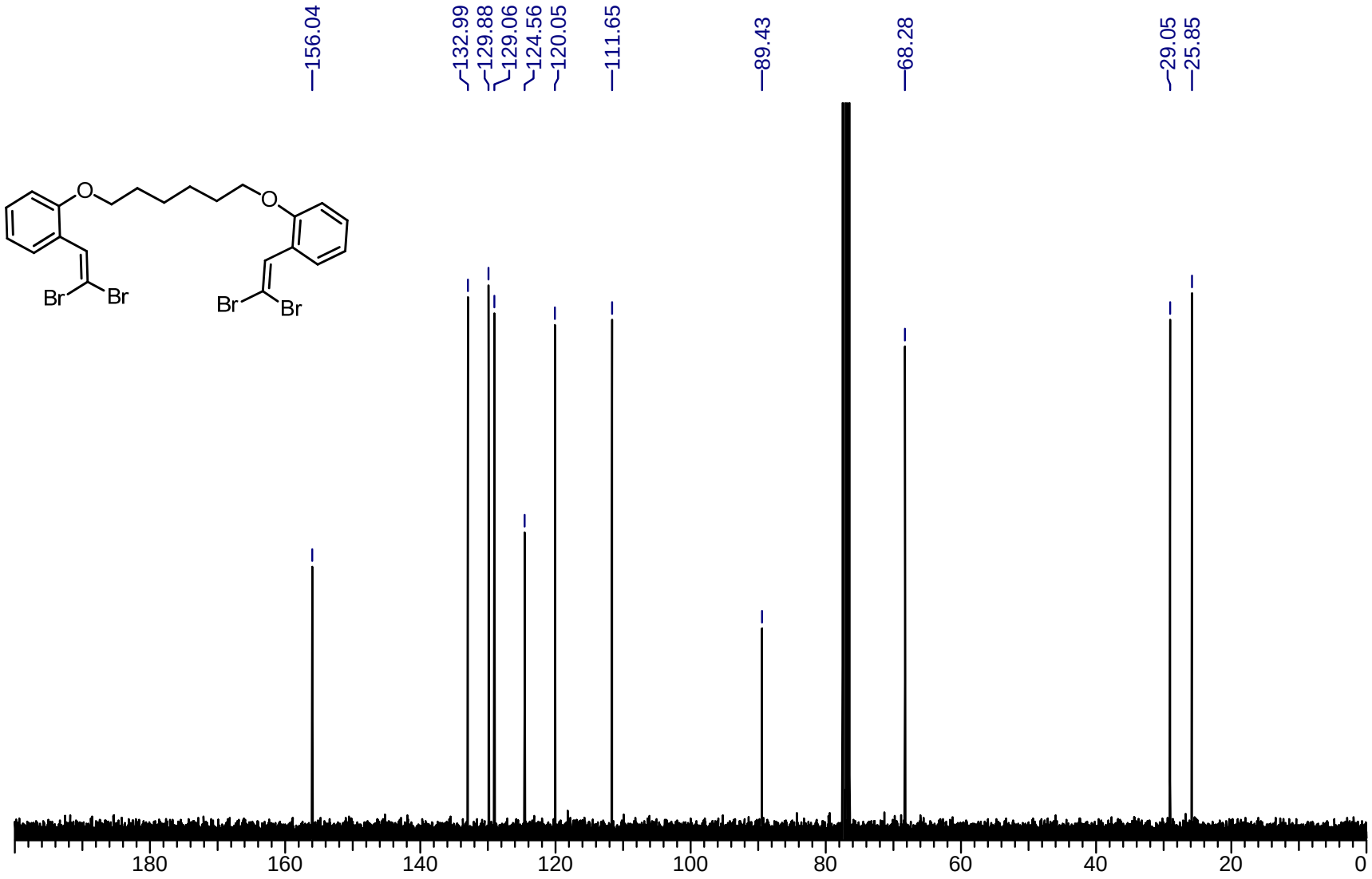
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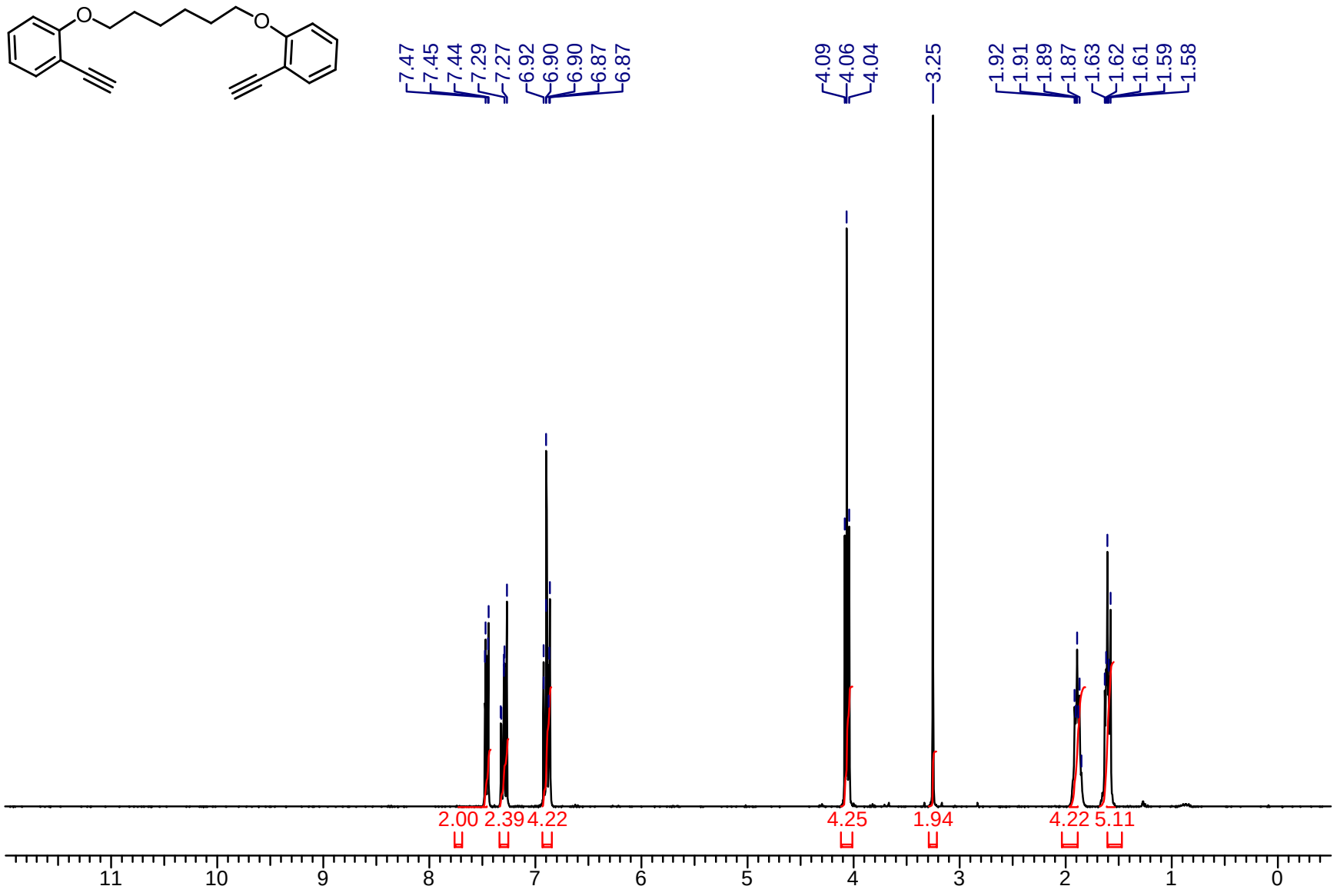
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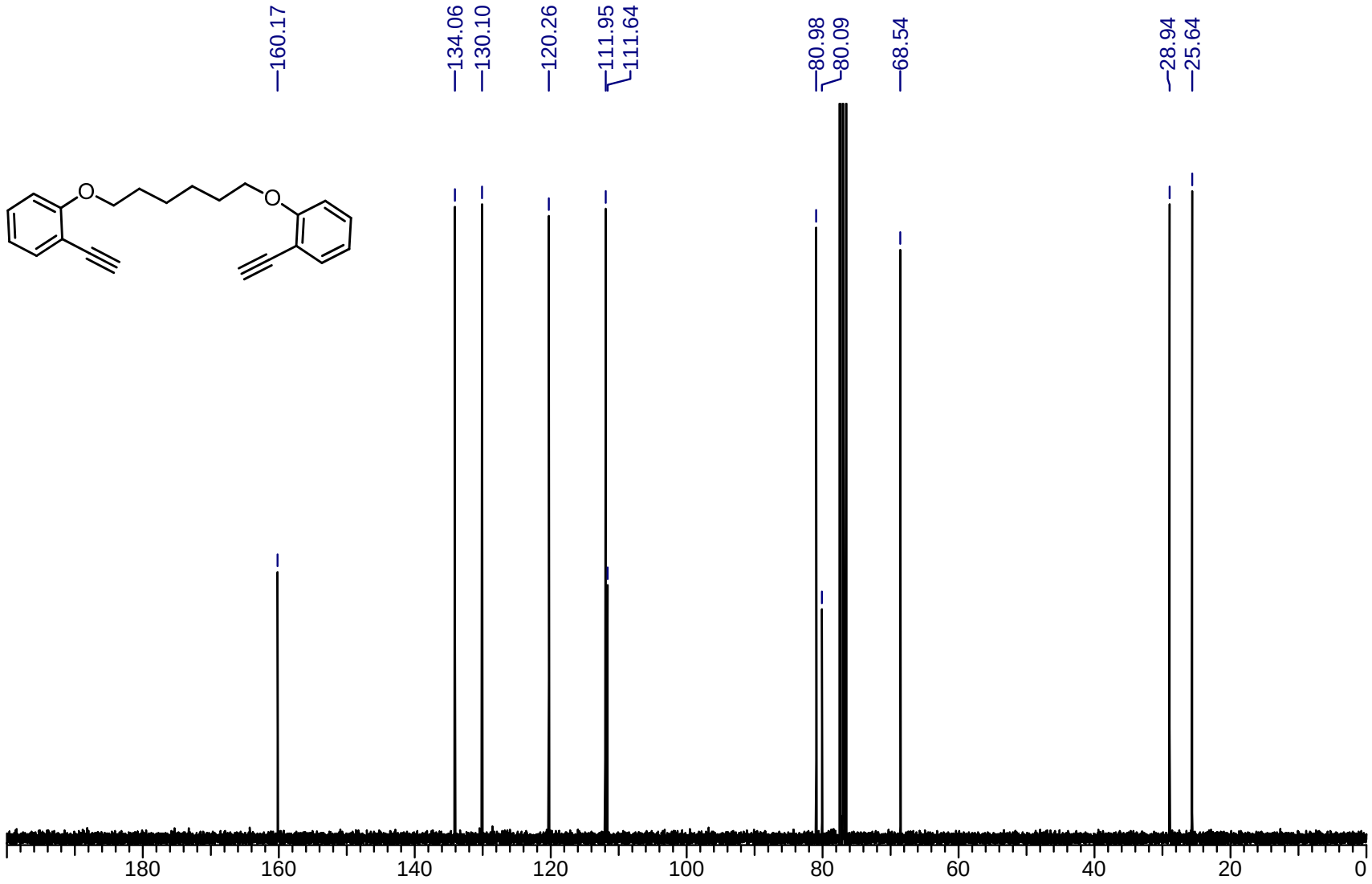
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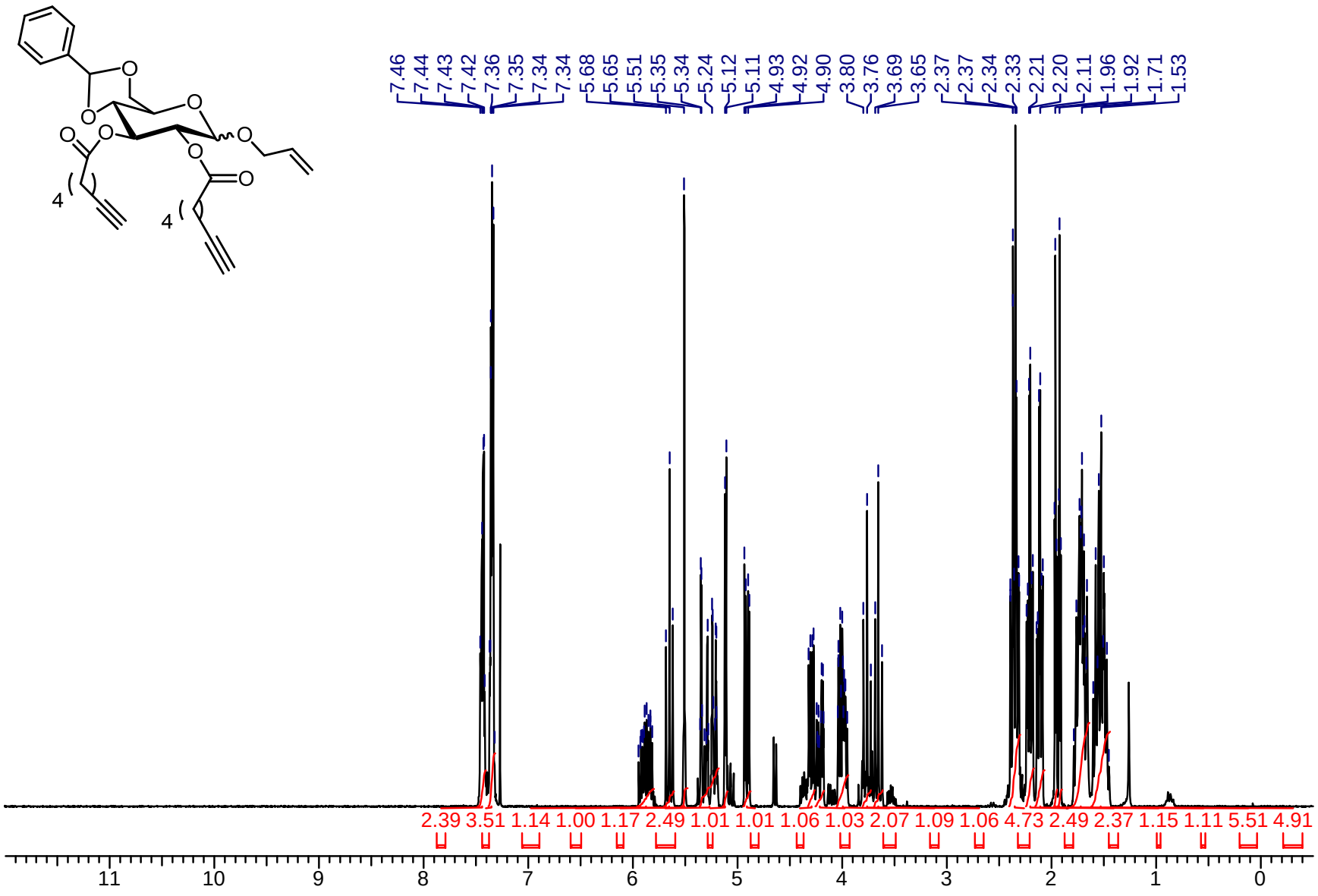
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2.39 3.51 1.14 1.00 1.17 2.49 1.01 1.01 1.06 1.03 2.07 1.09 1.06 4.73 2.49 2.37 1.15 1.11 5.51 4.91
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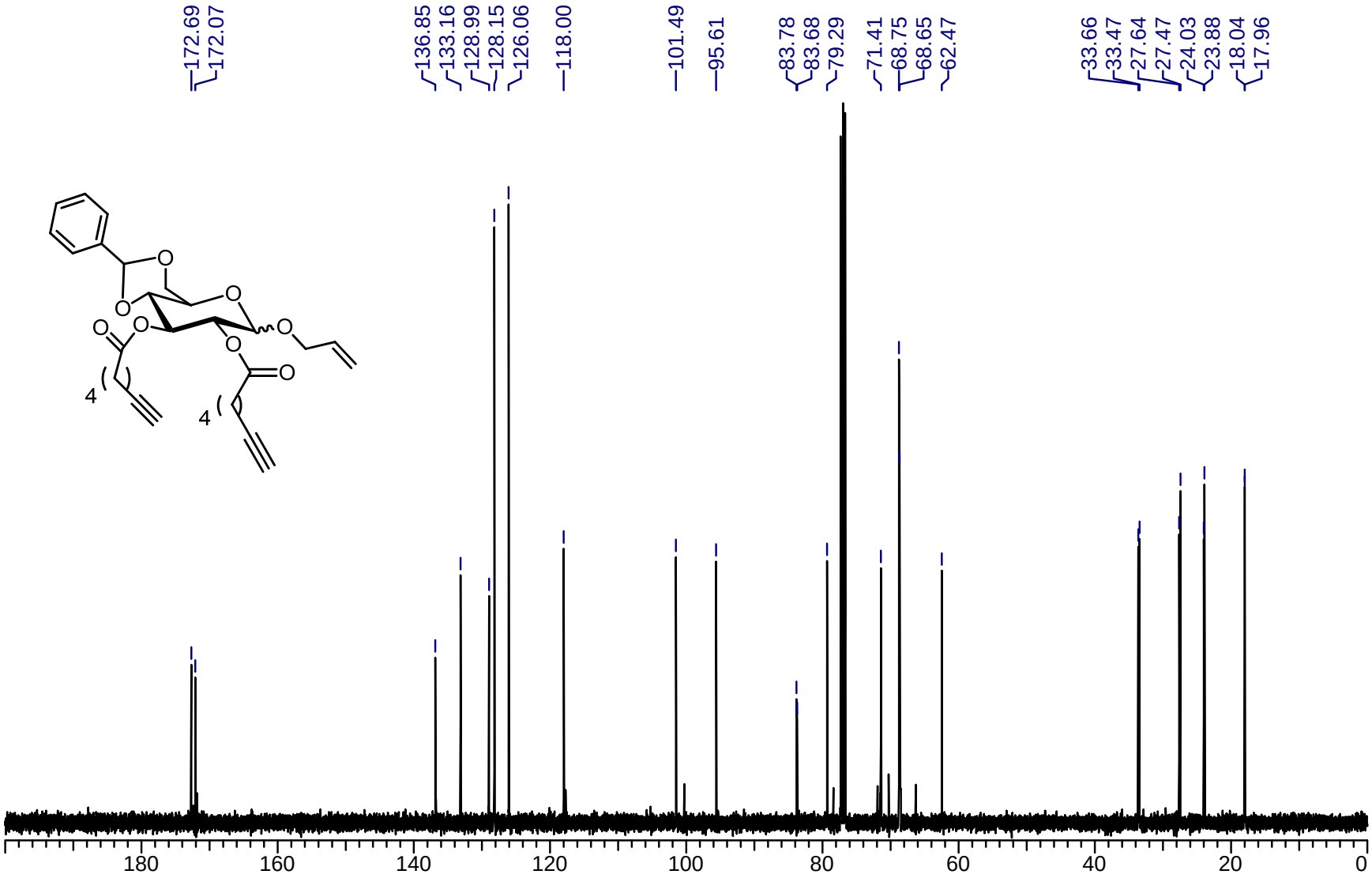
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68.75
68.65
62.47
33.66
33.47
27.64
27.47
24.03
23.88
18.04
17.96
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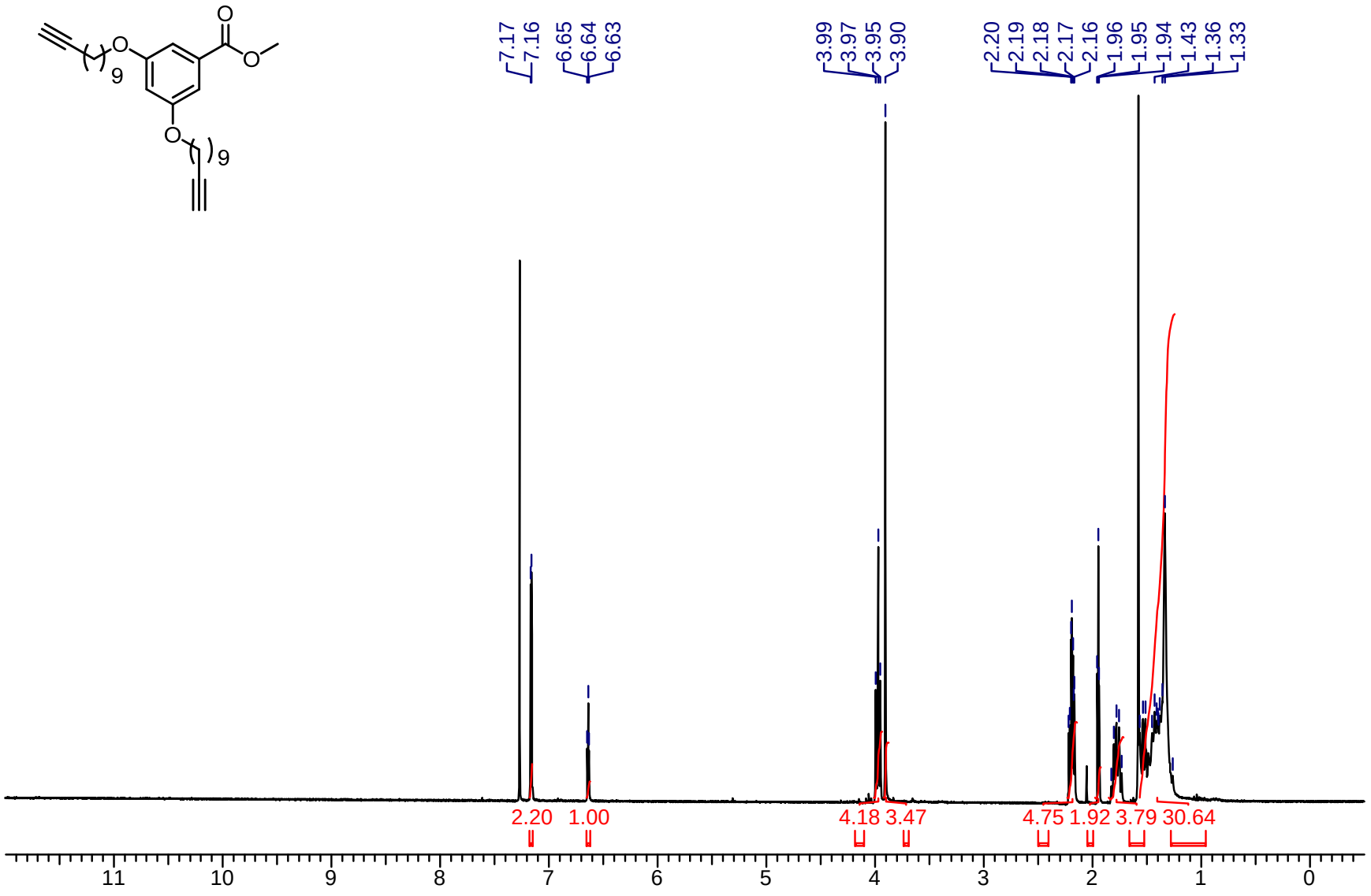
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2.17
2.16
1.96
1.95
1.94
1.43
1.36
1.33
2.20
1.00
4.18
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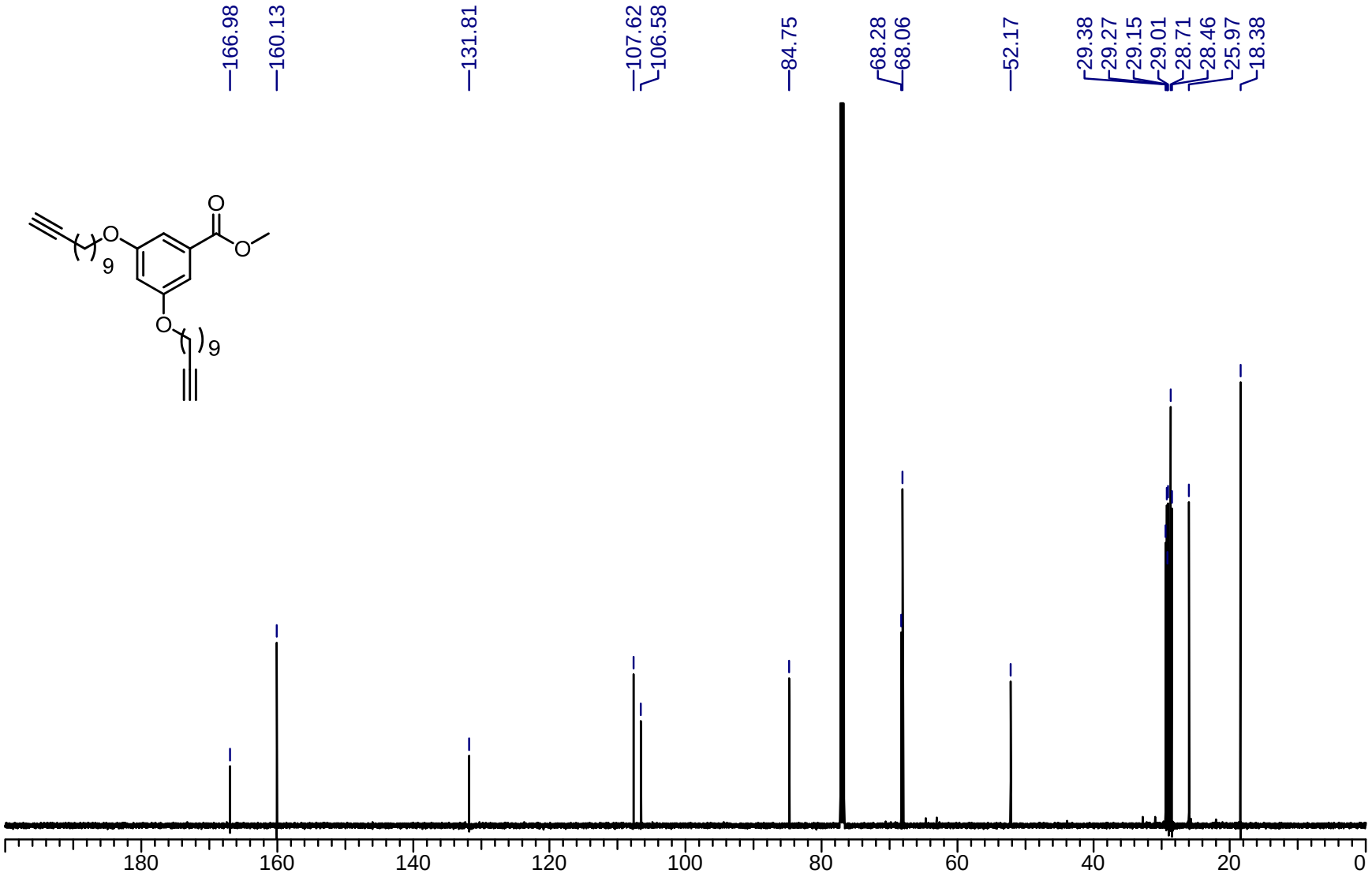
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68.06
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29.15
29.01
28.71
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18.38
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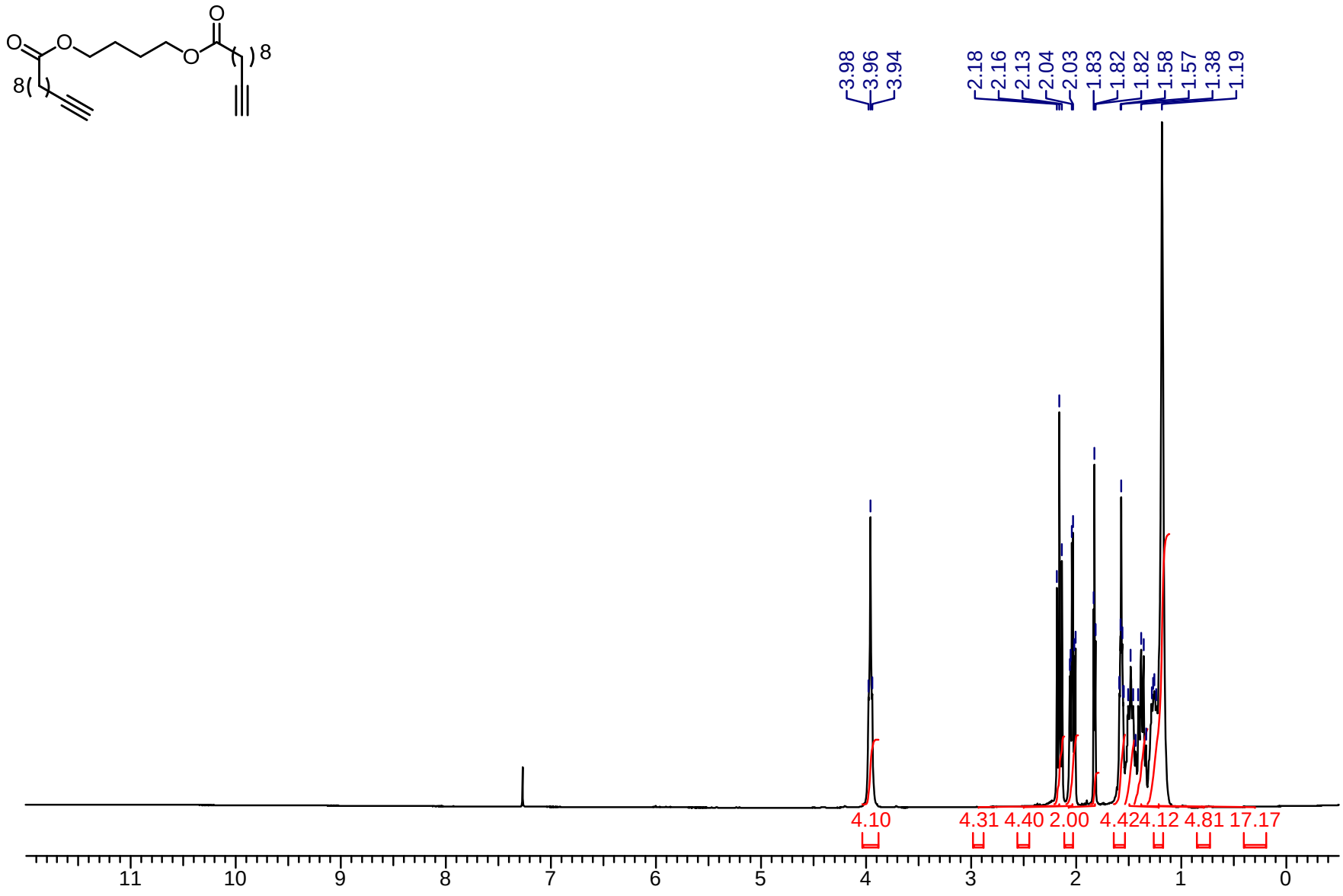
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2.03
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1.82
1.82
1.58
1.57
1.38
1.19
4.10
4.31
4.40
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4.42
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4.81
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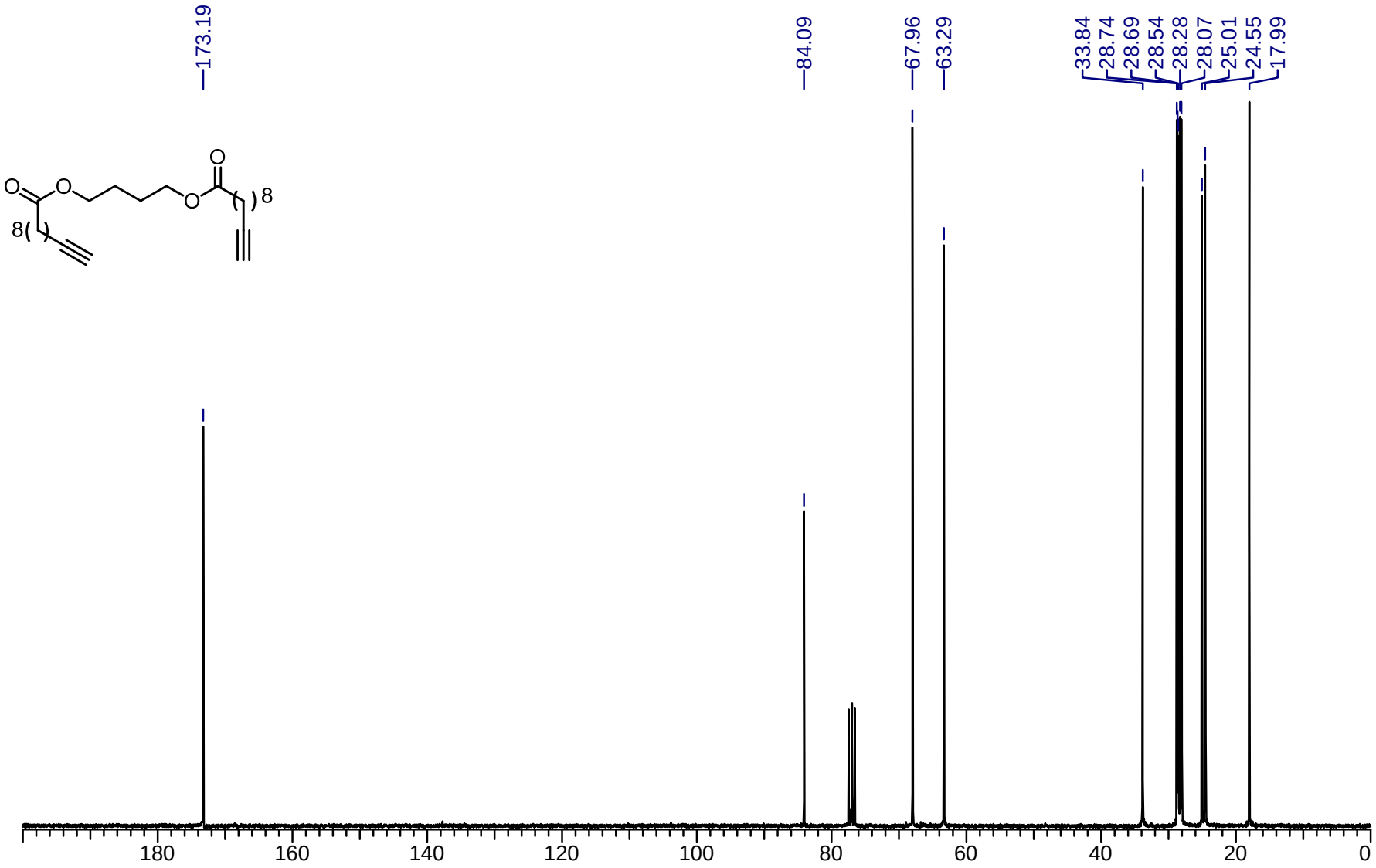
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28.69
28.54
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28.07
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O
O
O
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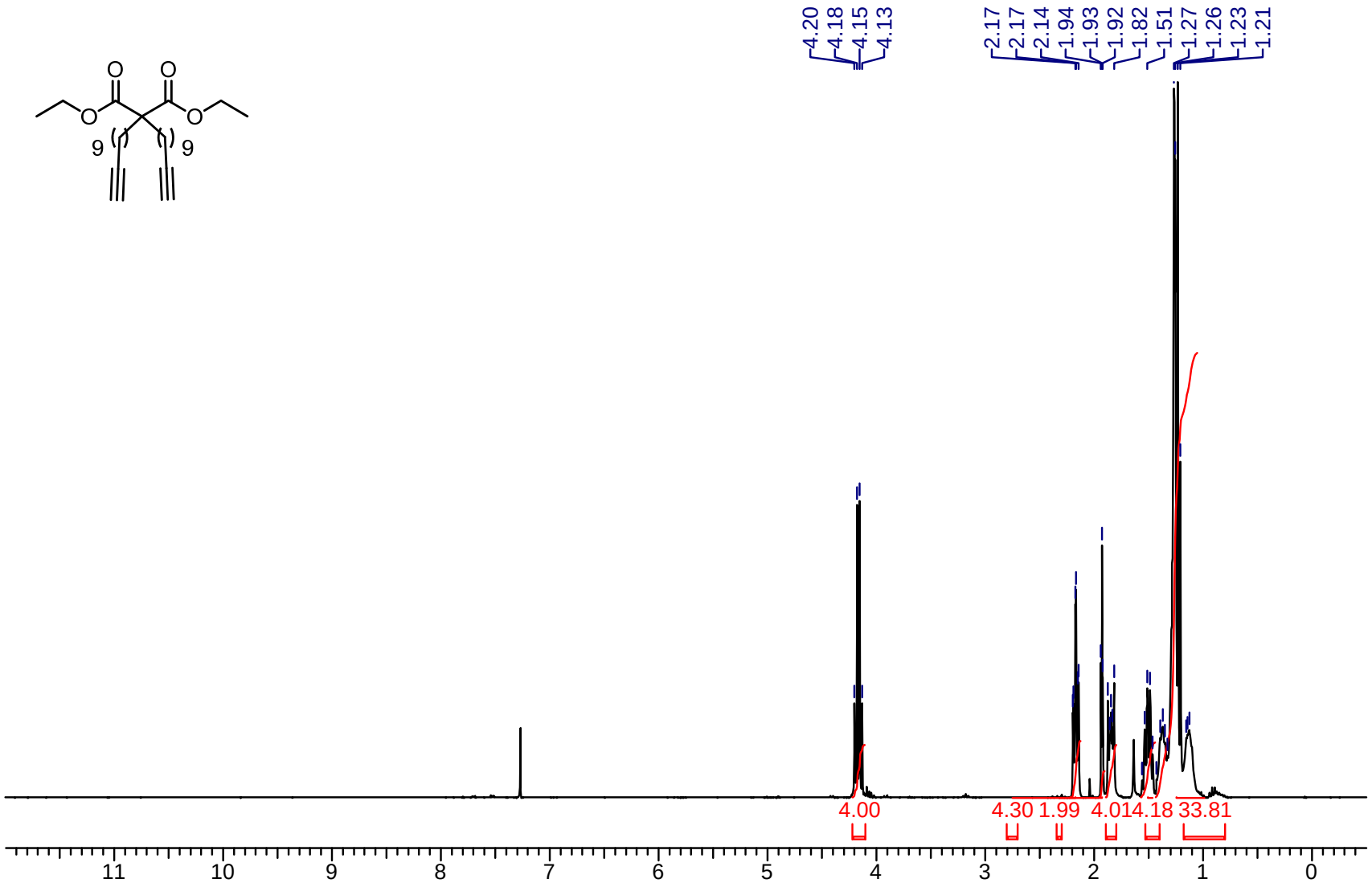
O
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9
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4.18
4.15
4.13
2.17
2.17
2.14
1.94
1.93
1.92
1.82
1.51
1.27
1.26
1.23
1.21
4.00
4.30
1.99
4.01
4.18
33.81
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7
6
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1
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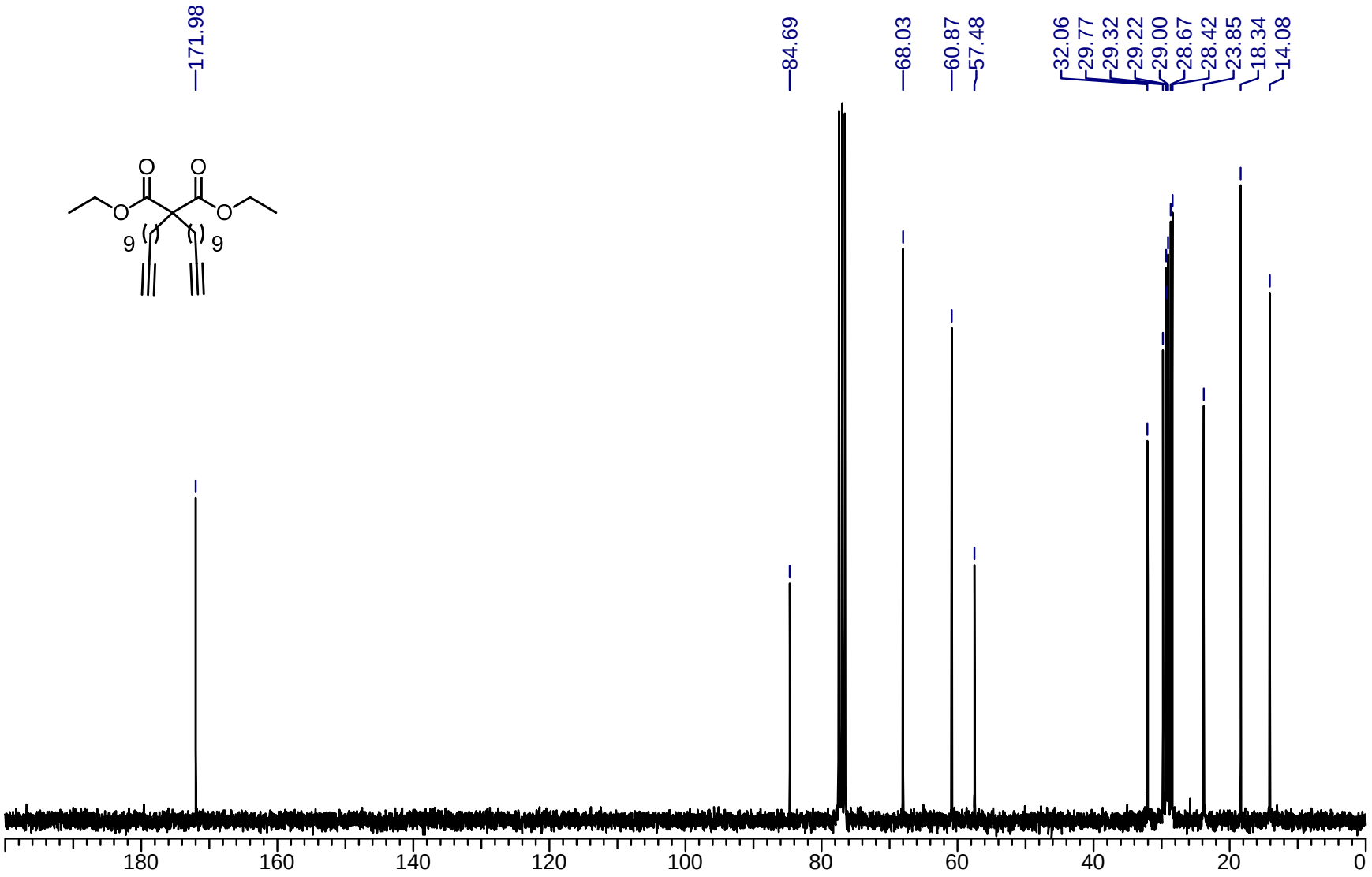
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68.03
60.87
57.48
32.06
29.77
29.32
29.22
29.00
28.67
28.42
23.85
18.34
14.08
O
O
O
O
9
9
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140
120
100
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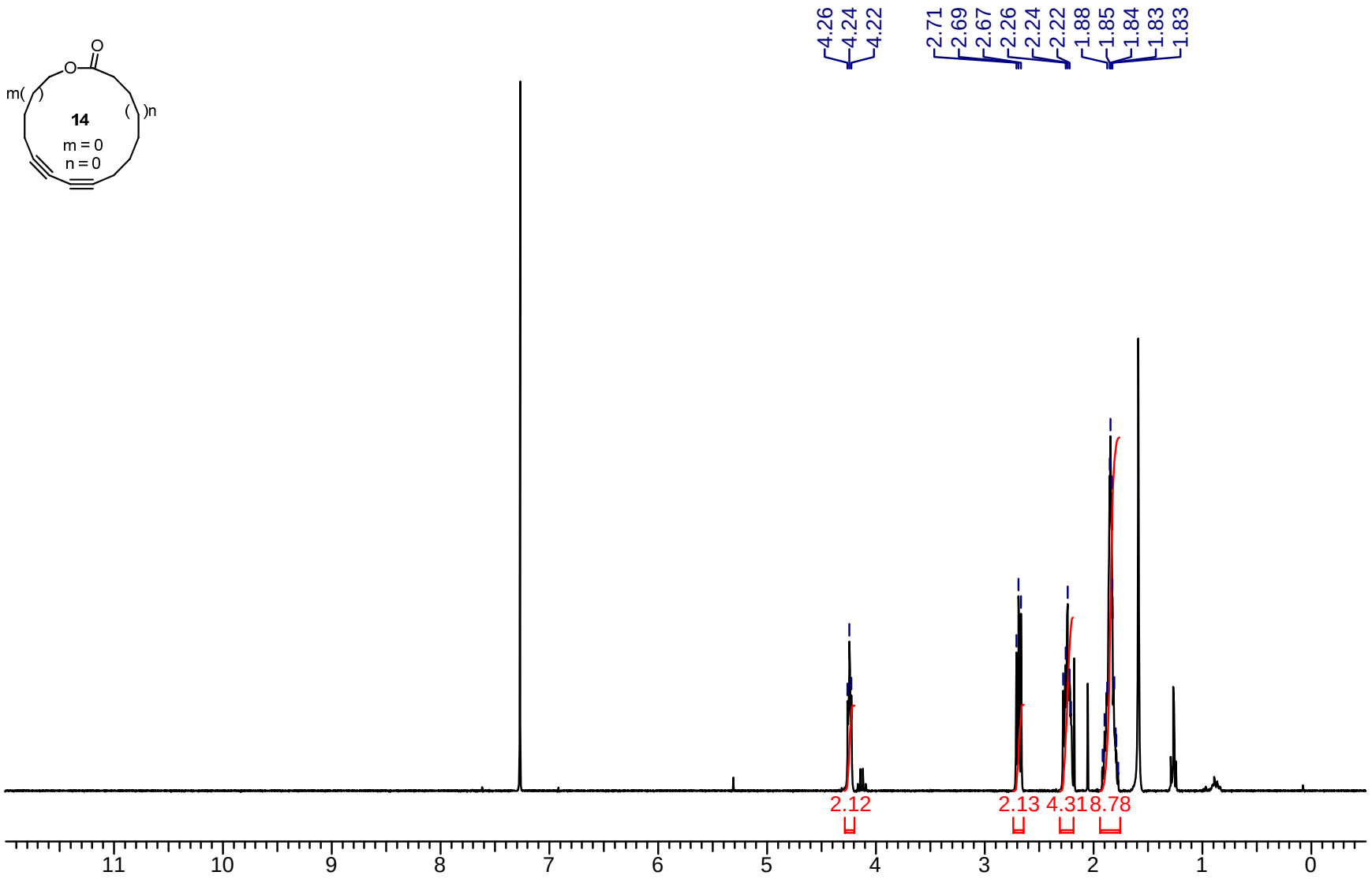
20
0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O
m( )
( )n
14
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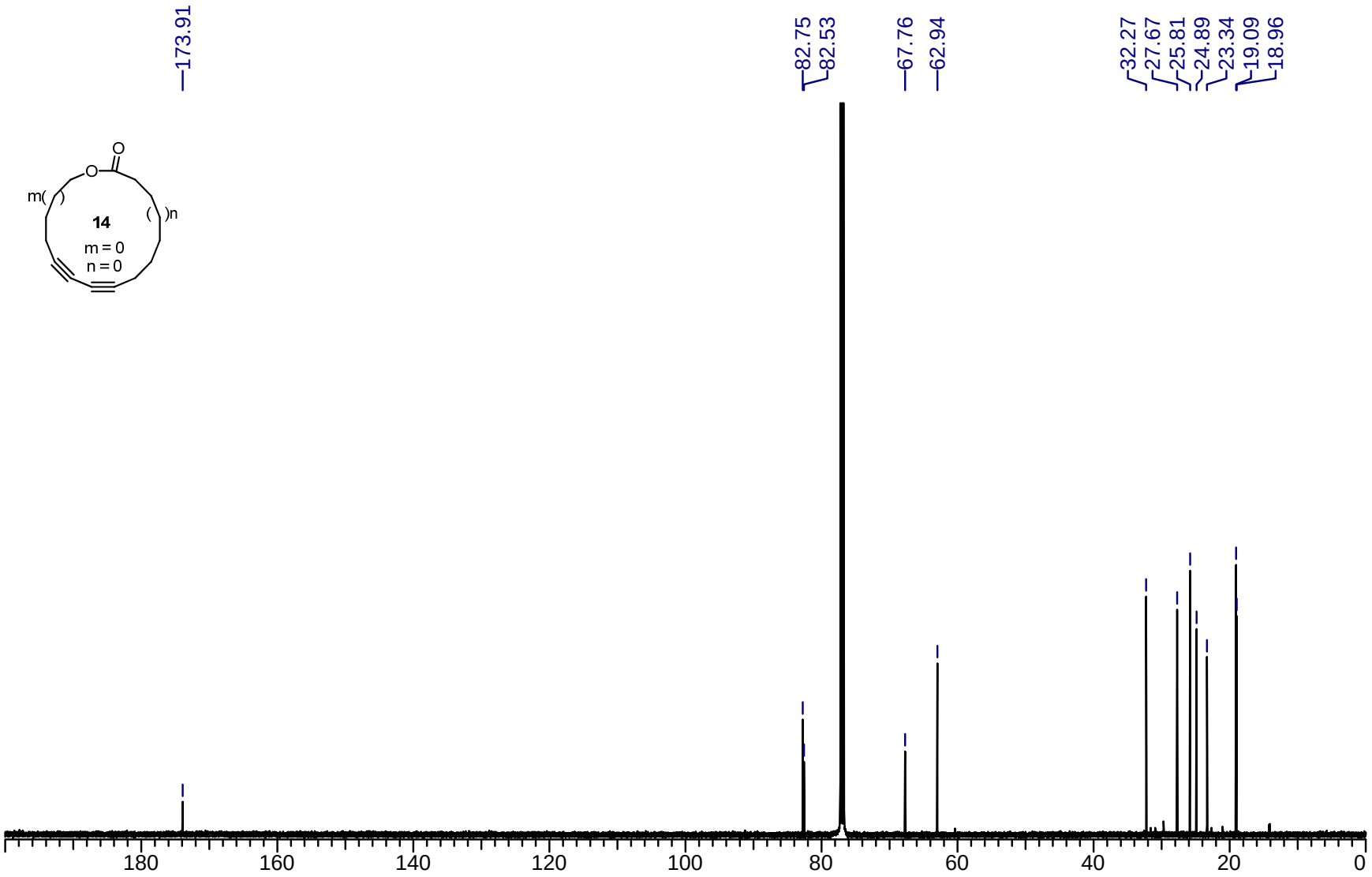
n = 0
4.26
4.24
4.22
2.71
2.69
2.67
2.26
2.24
2.22
1.88
1.85
1.84
1.83
1.83
2.12
2.13
4.31
8.78
11
10
9
8
7
6
5
4
3
2
1
0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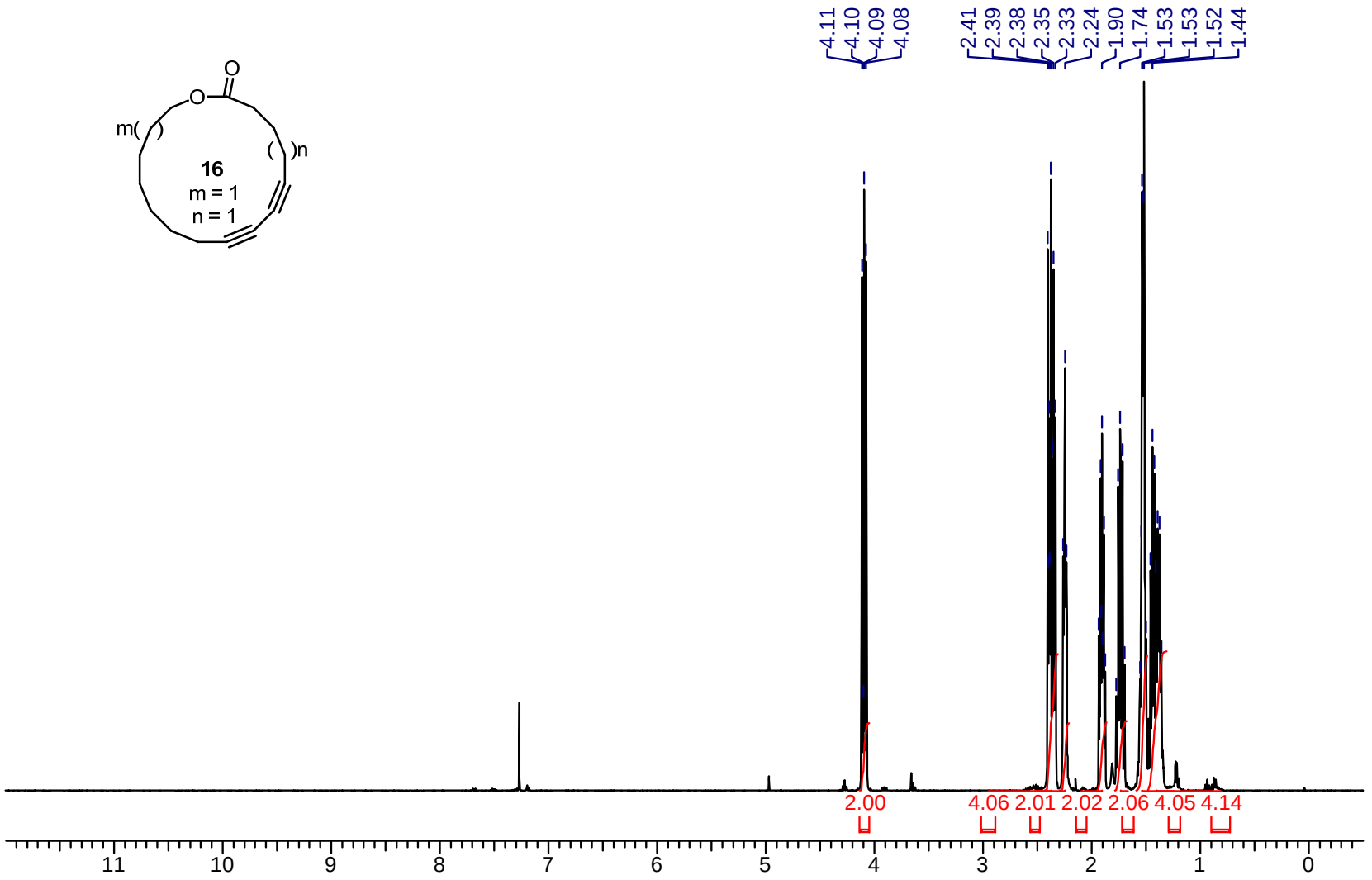
82.75
82.53
67.76
62.94
32.27
27.67
25.81
24.89
23.34
19.09
18.96
O
O
m(
)
(
)n
14
m = 0
n = 0
180
160
140
120
100
80
60
40
20
0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O
m( )
( )n
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m = 1
n = 1
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4.09
4.08
2.41
2.39
2.38
2.35
2.33
2.24
1.90
1.74
1.53
1.53
1.52
1.44
2.00
4.06
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2.02
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4.05
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1
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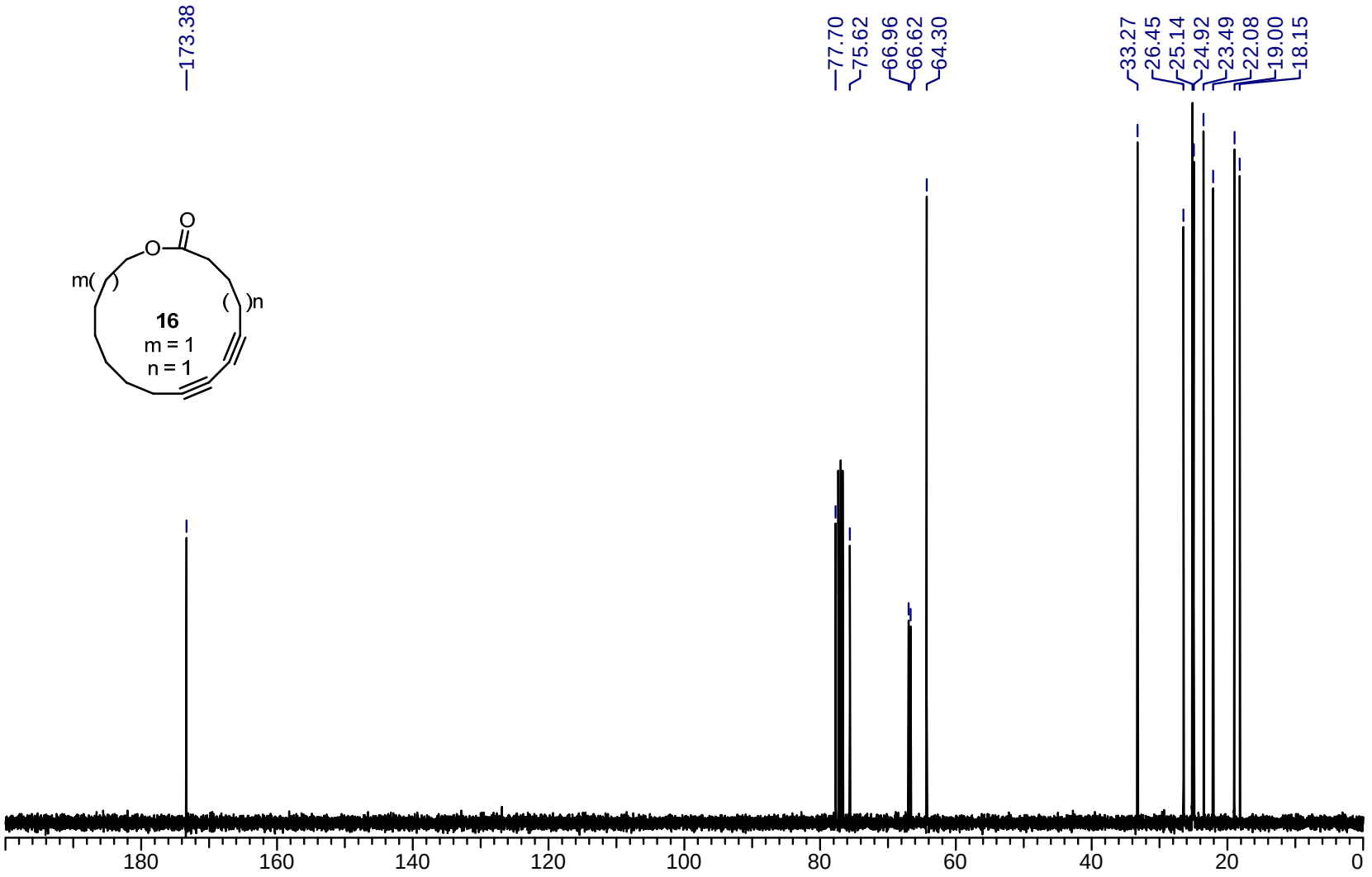
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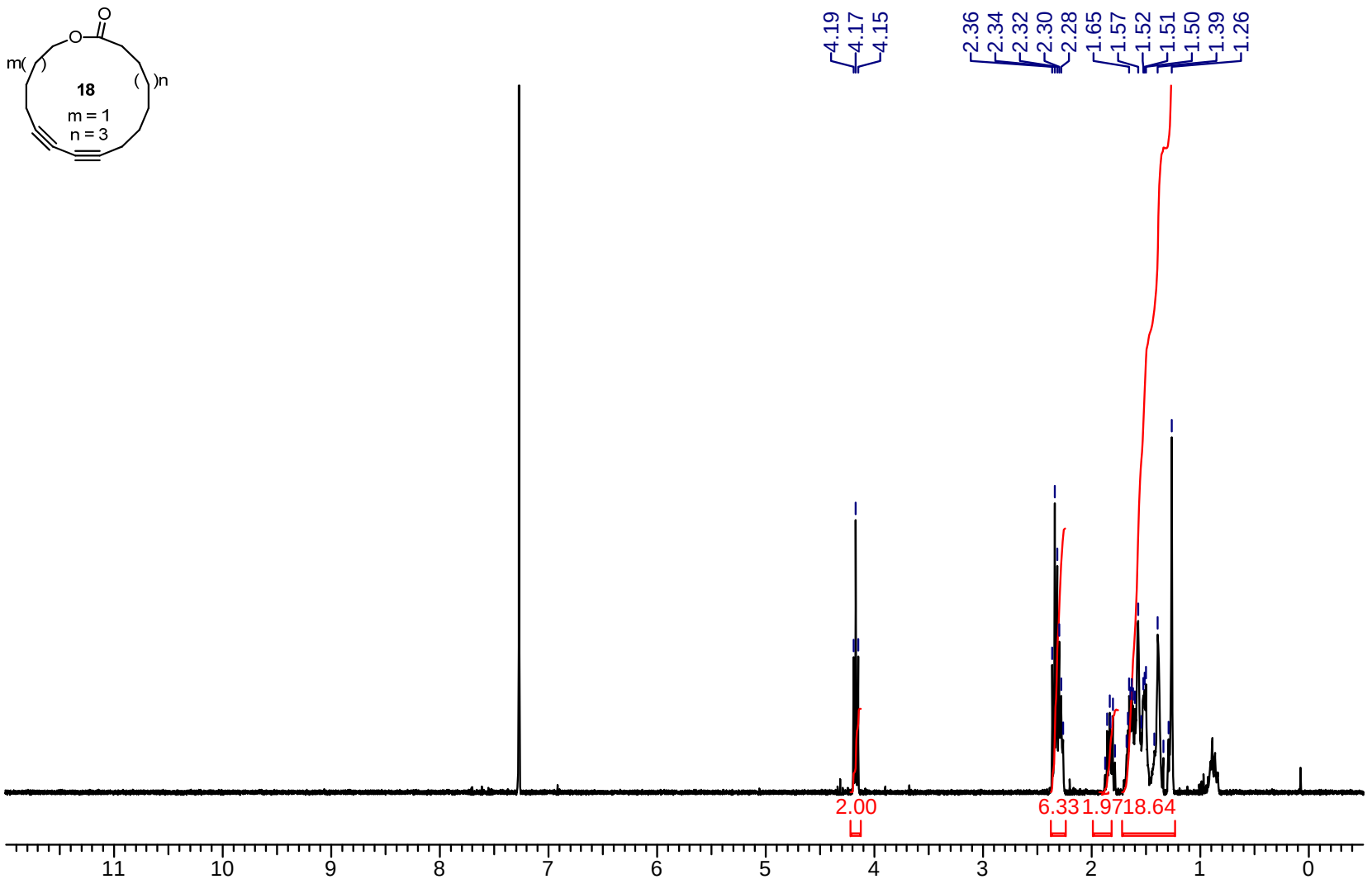
75.62
66.96
66.62
64.30
33.27
26.45
25.14
24.92
23.49
22.08
19.00
18.15
O
O
m( )
( )n
16
m = 1
n = 1
180
160
140
120
100
80
60
40
20
0


m( )
( )n
18
m = 1
n = 3
4.19
4.17
4.15
2.36
2.34
2.32
2.30
2.28
1.65
1.57
1.52
1.51
1.50
1.39
1.26
2.00
6.33
1.97
18.64
11
10
9
8
7
6
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1
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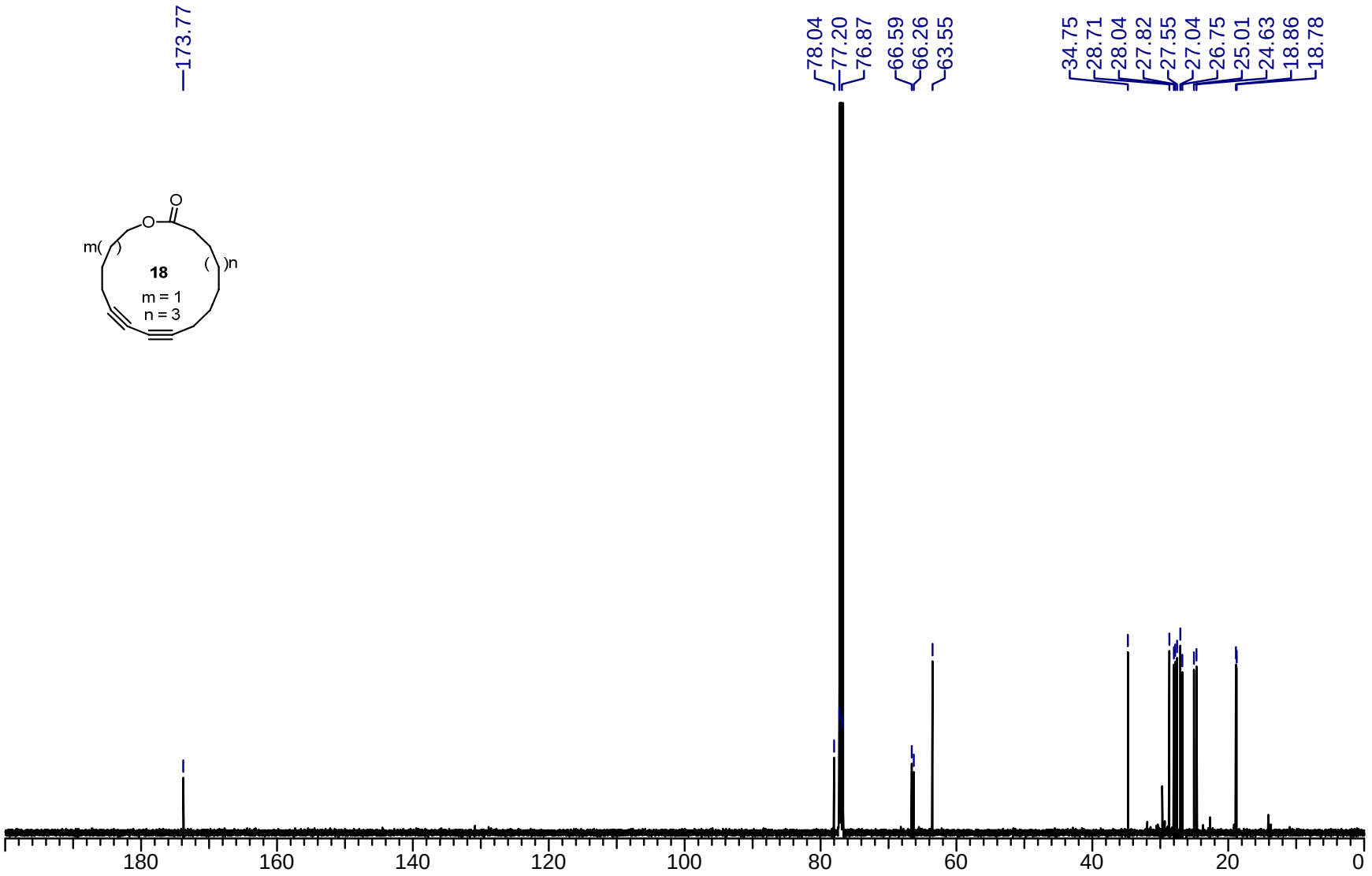
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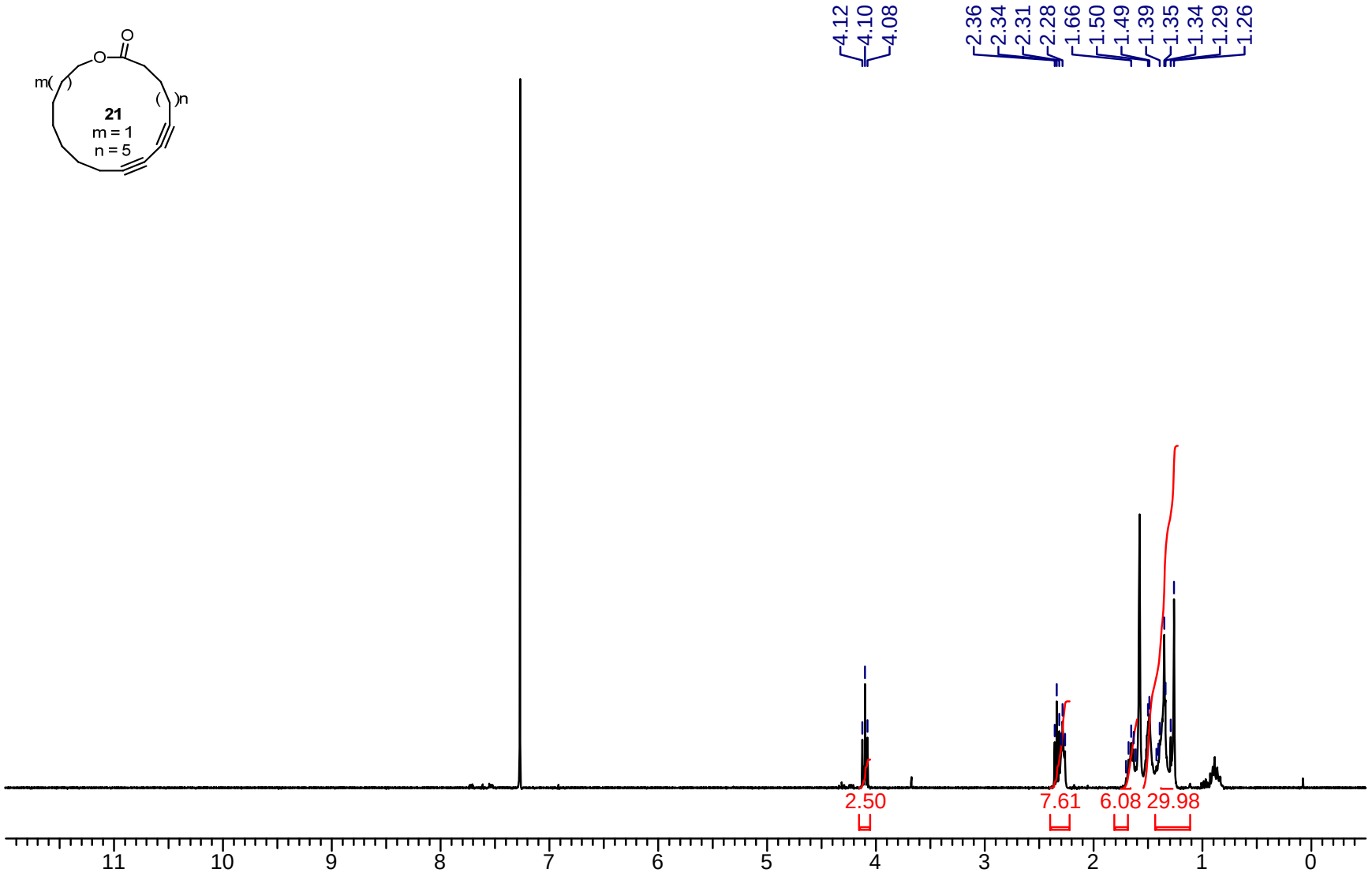
78.04
77.20
76.87
66.59
66.26
63.55
34.75
28.71
28.04
27.82
27.55
27.04
26.75
25.01
24.63
18.86
18.78
O
O
m( )
( )n
18
m = 1
n = 3
180
160
140
120
100
80
60
40
20
0


21
m = 1
n = 5
4.12
4.10
4.08
2.36
2.34
2.31
2.28
1.66
1.50
1.49
1.39
1.35
1.34
1.29
1.26
2.50
7.61
6.08
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11
10
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8
7
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5
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3
2
1
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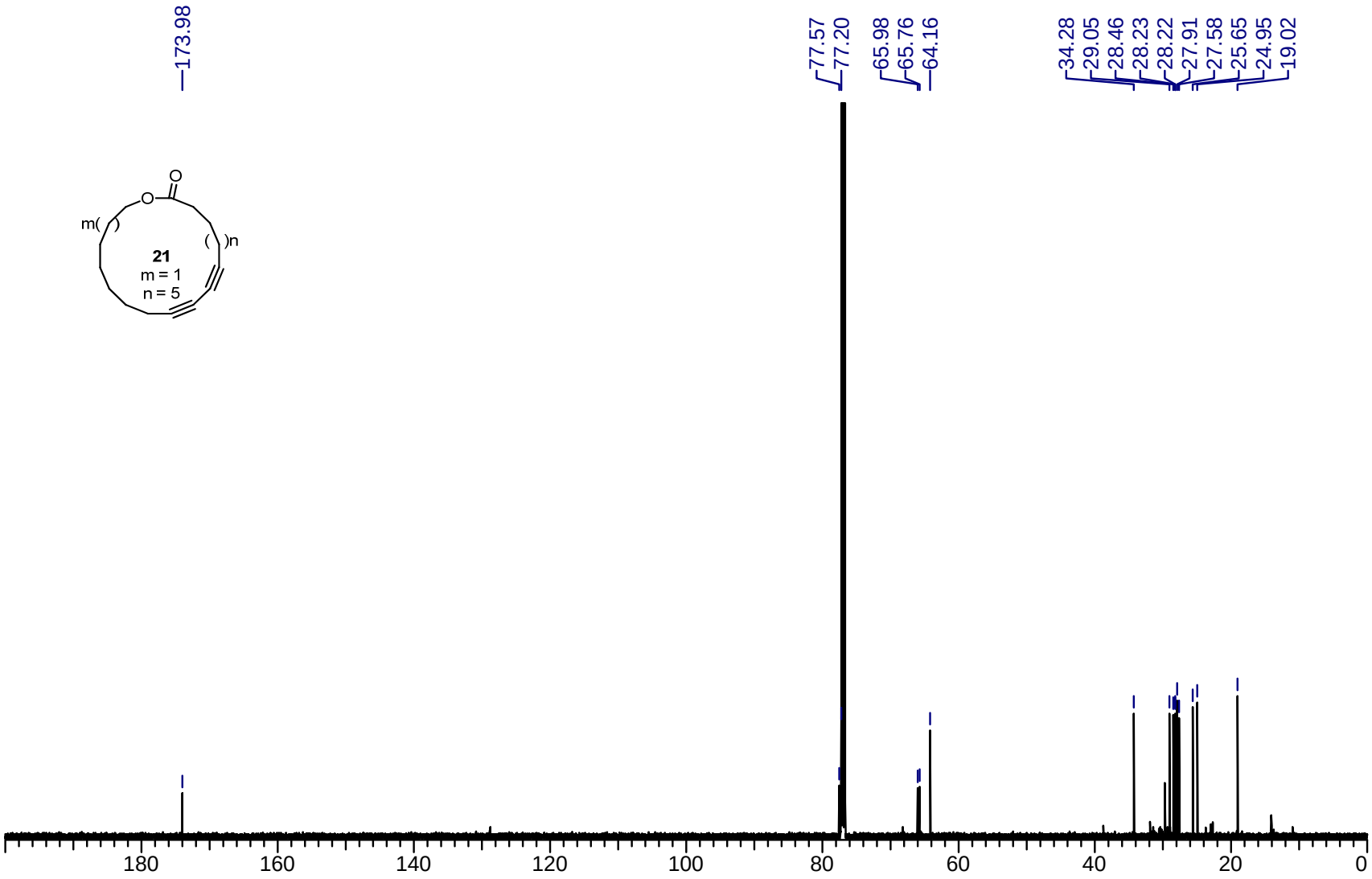
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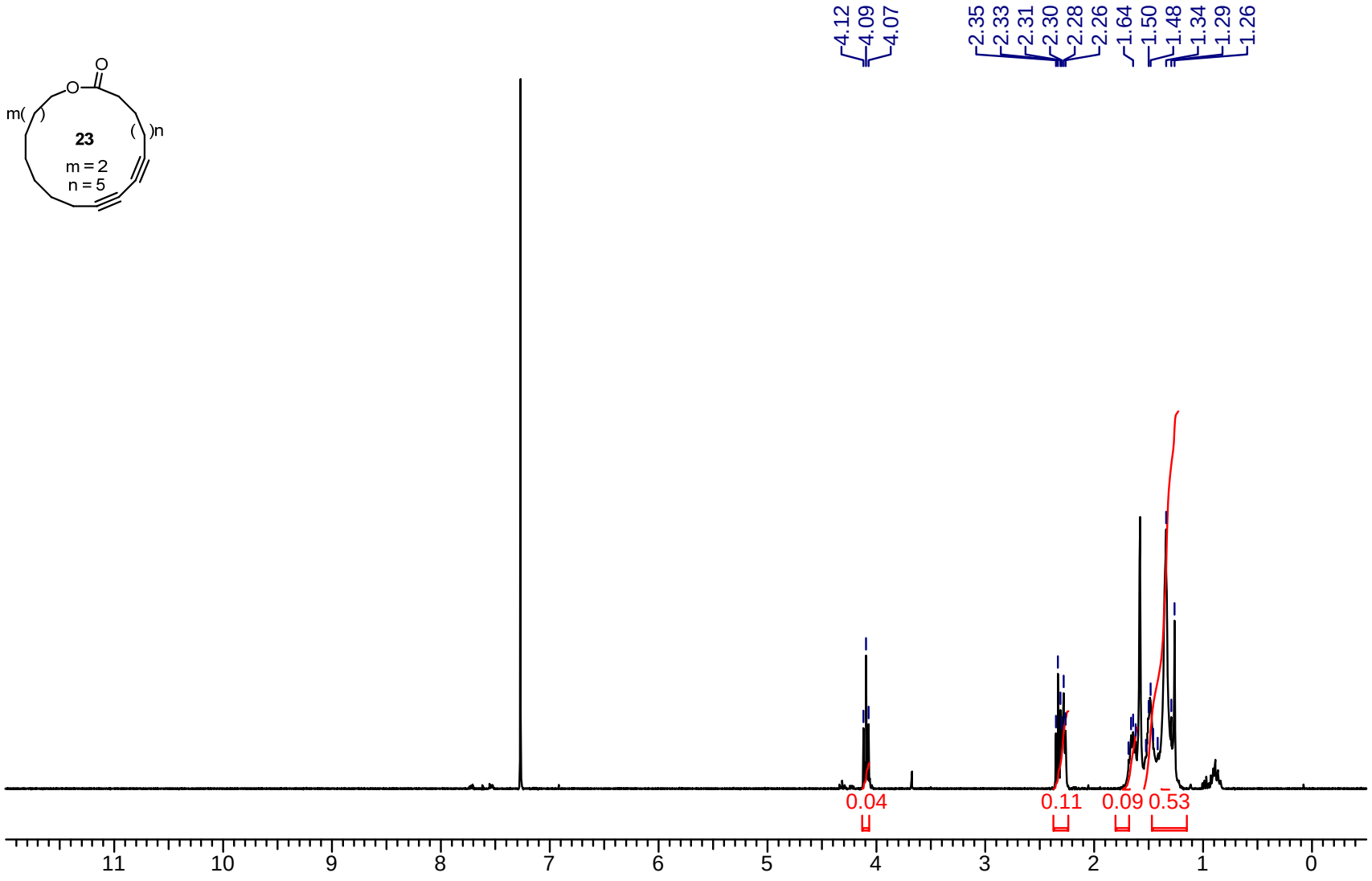
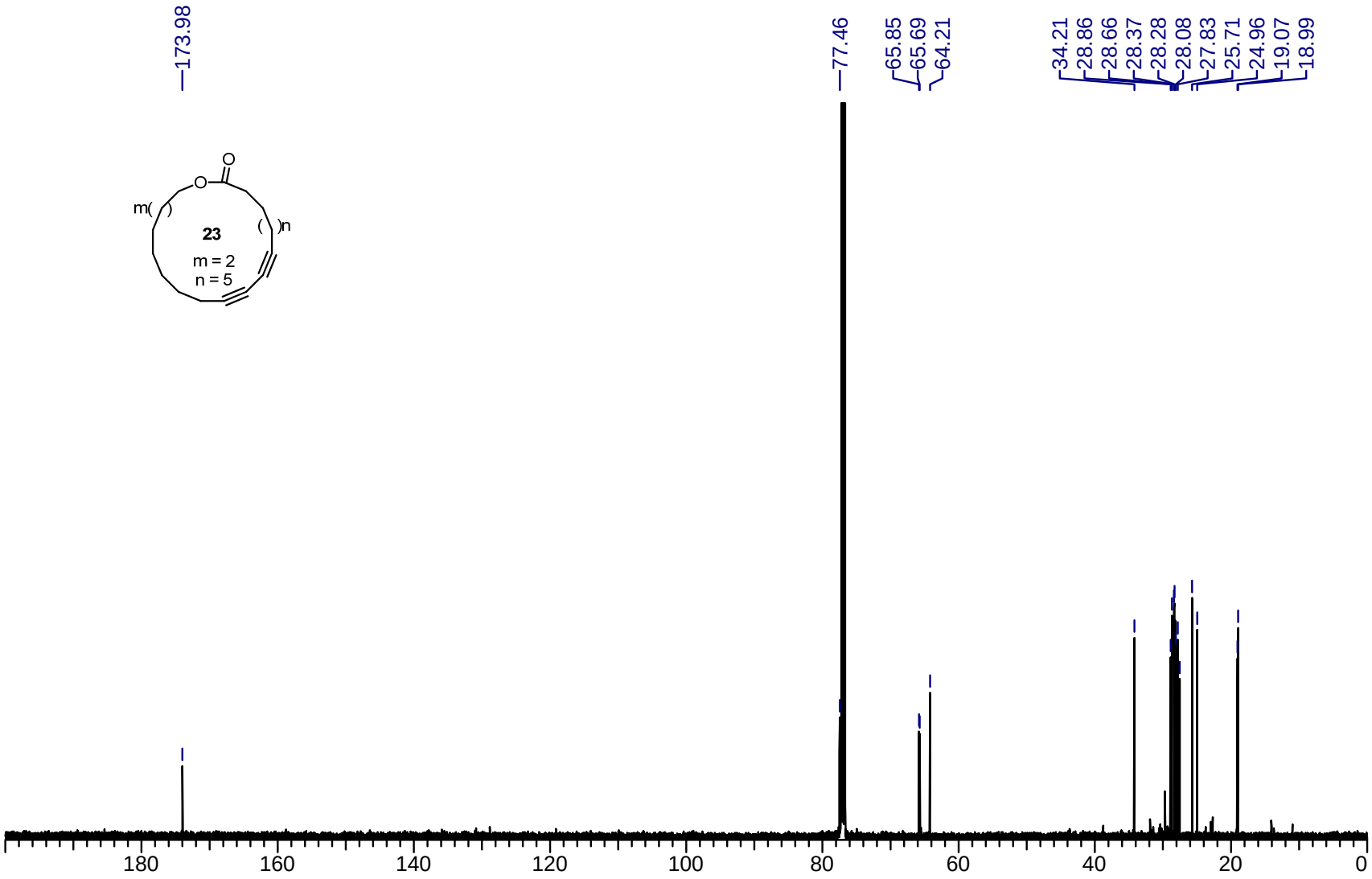
77.57
77.20
65.98
65.76
64.16
34.28
29.05
28.46
28.23
28.22
27.91
27.58
25.65
24.95
19.02
O
O
m( )
( )n
21
m = 1
n = 5
180
160
140
120
100
80
60
40
20
0


4.12
4.09
4.07
2.35
2.33
2.31
2.30
2.28
2.26
1.64
1.50
1.48
1.34
1.29
1.26
O
O
m( )
( )n
23
m = 2
n = 5
0.04
0.11
0.09
0.53
11
10
9
8
7
6
5
4
3
2
1
0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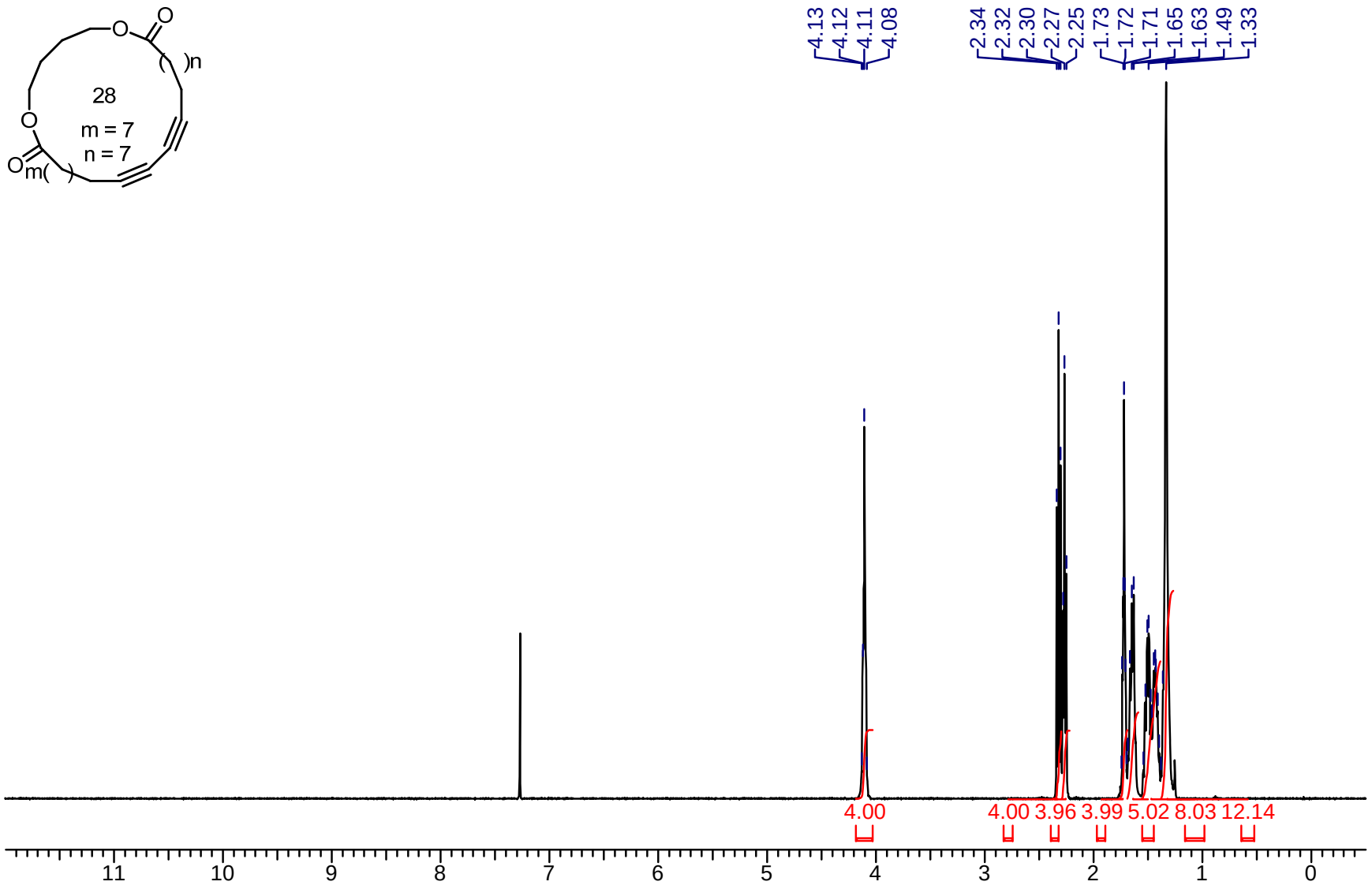
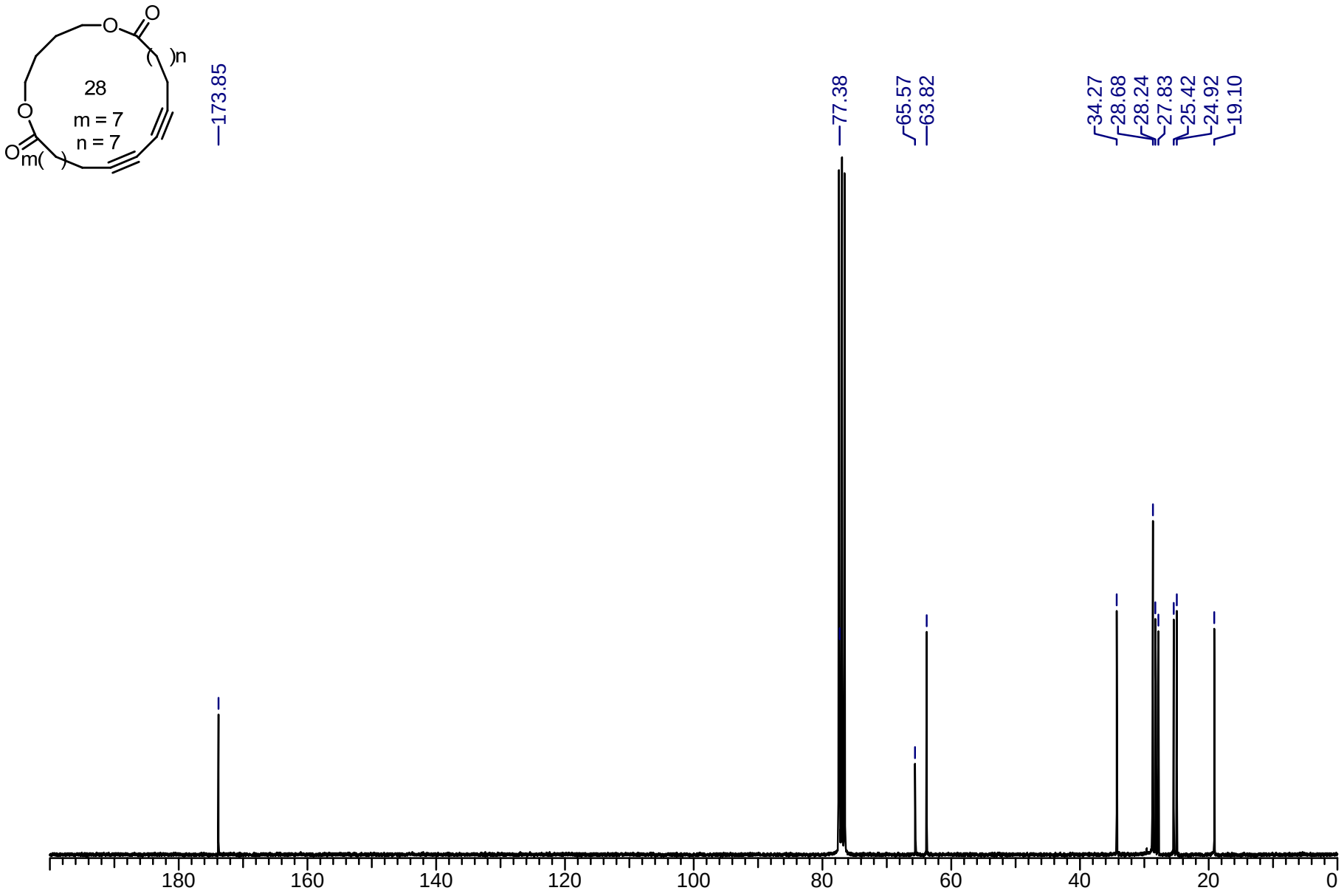
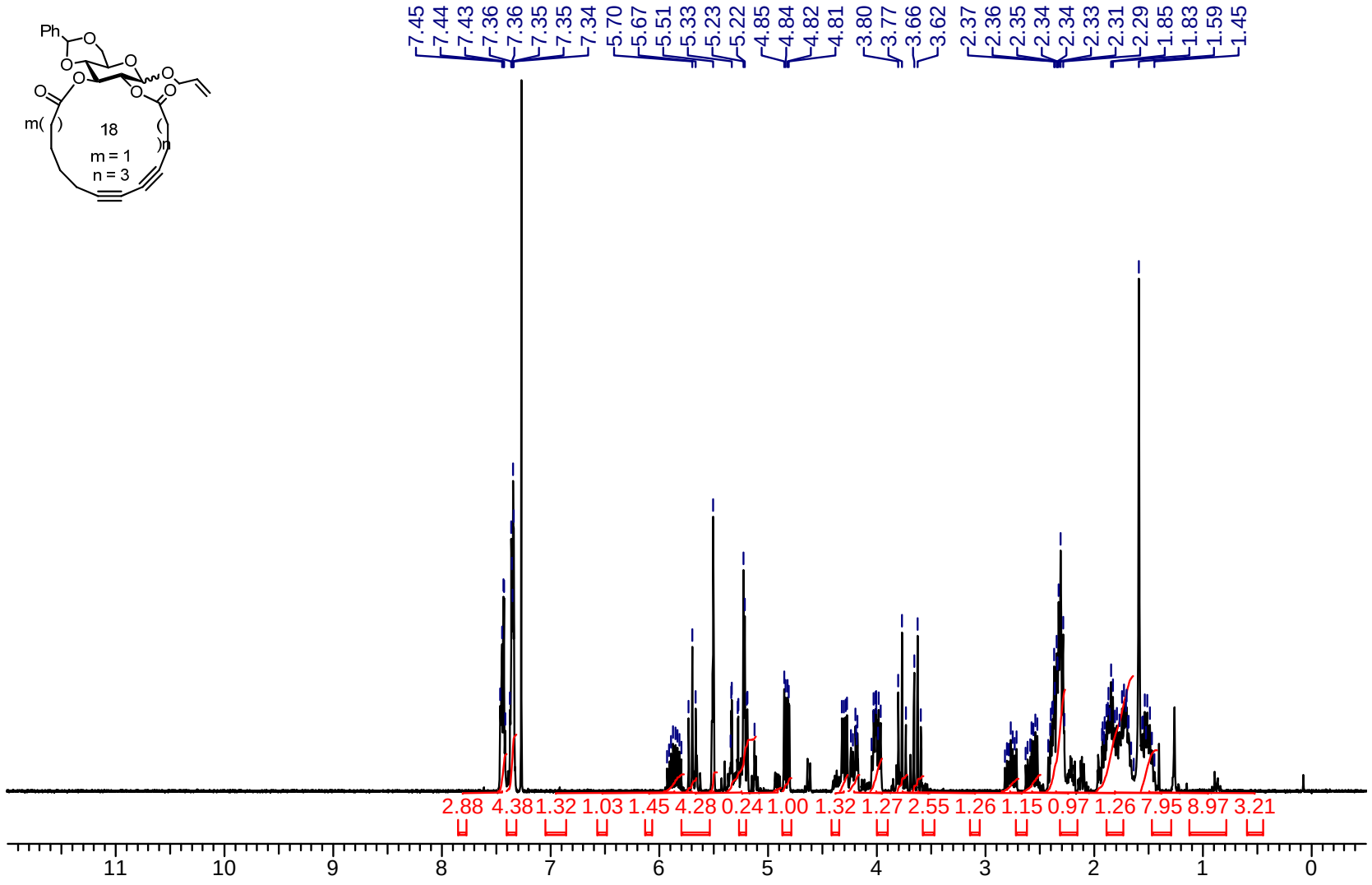
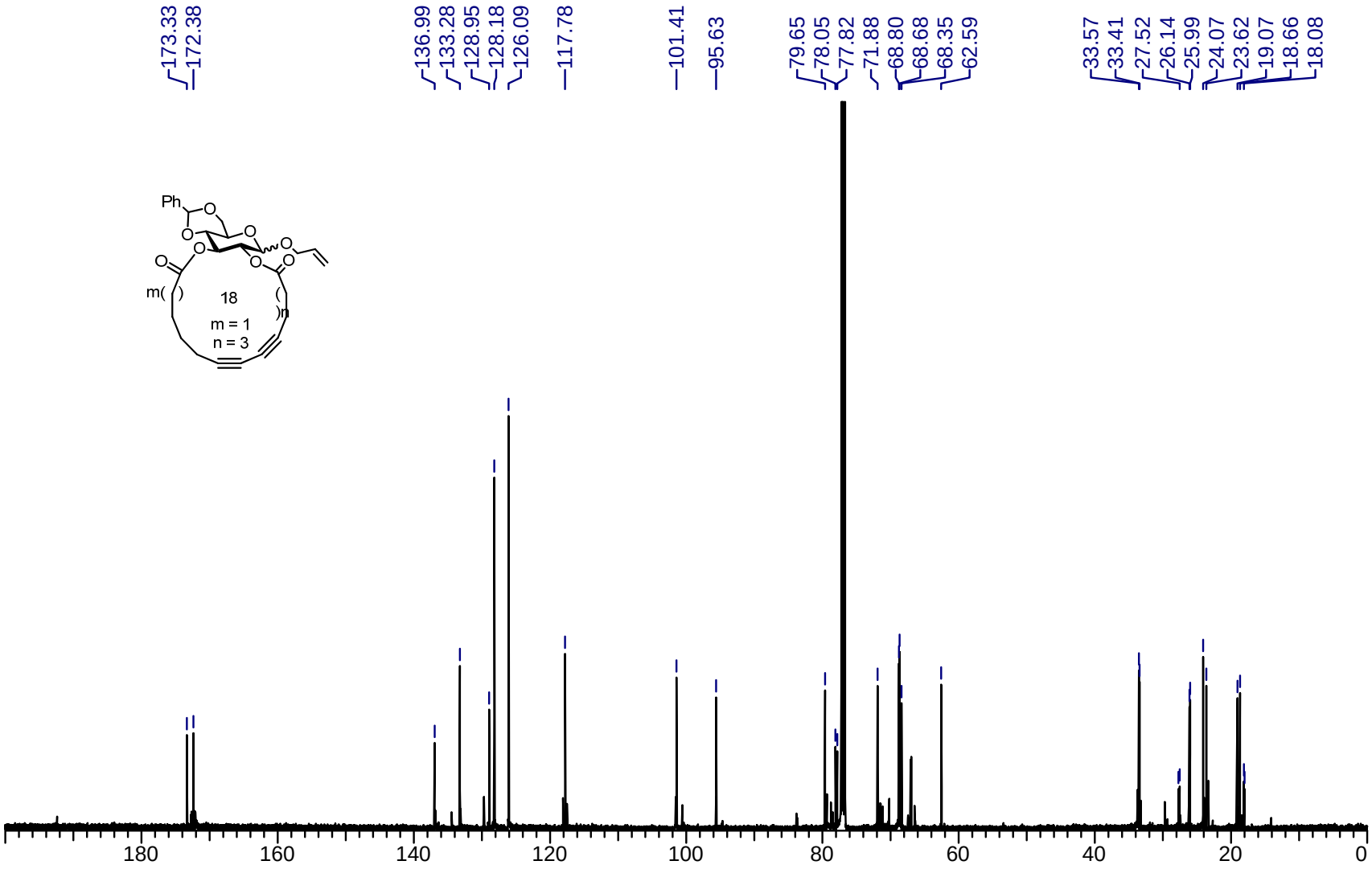
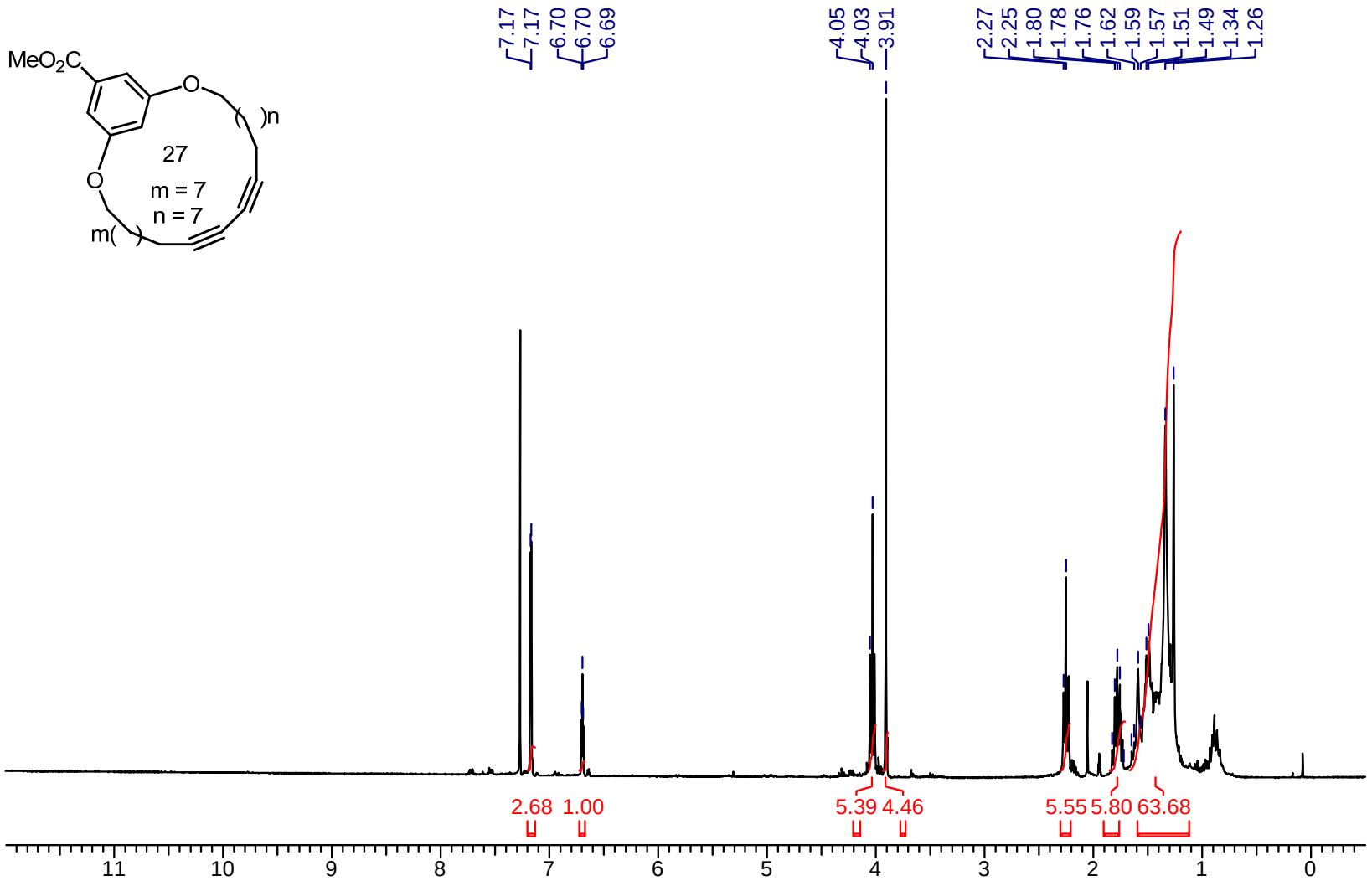
77.46
65.85
65.69
64.21
34.21
28.86
28.66
28.37
28.28
28.08
27.83
25.71
24.96
19.07
18.99
O
O
m( )
( )n
23
m = 2
n = 5
180
160
140
120
100
80
60
40
20
0


28
m = 7
n = 7
4.13
4.12
4.11
4.08
2.34
2.32
2.30
2.27
2.25
1.73
1.72
1.71
1.65
1.63
1.49
1.33
4.00
4.00 3.96 3.99 5.02 8.03 12.14
11
10
9
8
7
6
5
4
3
2
1
0


O
O
)n
28
m = 7
n = 7
O
Om( )
173.85
77.38
65.57
63.82
34.27
28.68
28.24
27.83
25.42
24.92
19.10
180
160
140
120
100
80
60
40
20
0


Ph
O
O
O
O
O
O
O
O
m( )
18
( )n
m = 1
n = 3
7.45 7.44 7.43 7.36 7.36 7.35 7.35 7.34 5.70 5.67 5.51 5.33 5.23 5.22 4.85 4.84 4.82 4.81 3.80 3.77 3.66 3.62 2.37 2.36 2.35 2.34 2.34 2.33 2.31 2.29 1.85 1.83 1.59 1.45
2.88 4.38 1.32 1.03 1.45 4.28 0.24 1.00 1.32 1.27 2.55 1.26 1.15 0.97 1.26 7.95 8.97 3.21
11 10 9 8 7 6 5 4 3 2 1 0


173.33
172.38
136.99
133.28
128.95
128.18
126.09
117.78
101.41
95.63
79.65
78.05
77.82
71.88
68.80
68.68
68.35
62.59
33.57
33.41
27.52
26.14
25.99
24.07
23.62
19.07
18.66
18.08
Ph
O
m( )
18
( )n
m = 1
n = 3
180
160
140
120
100
80
60
40
20
0


MeO2C
O
)n
27
m = 7
n = 7
O
m( )
7.17
7.17
6.70
6.70
6.69
4.05
4.03
3.91
2.27
2.25
1.80
1.78
1.76
1.62
1.59
1.57
1.51
1.49
1.34
1.26
2.68
1.00
5.39
4.46
5.55
5.80
63.68
11
10
9
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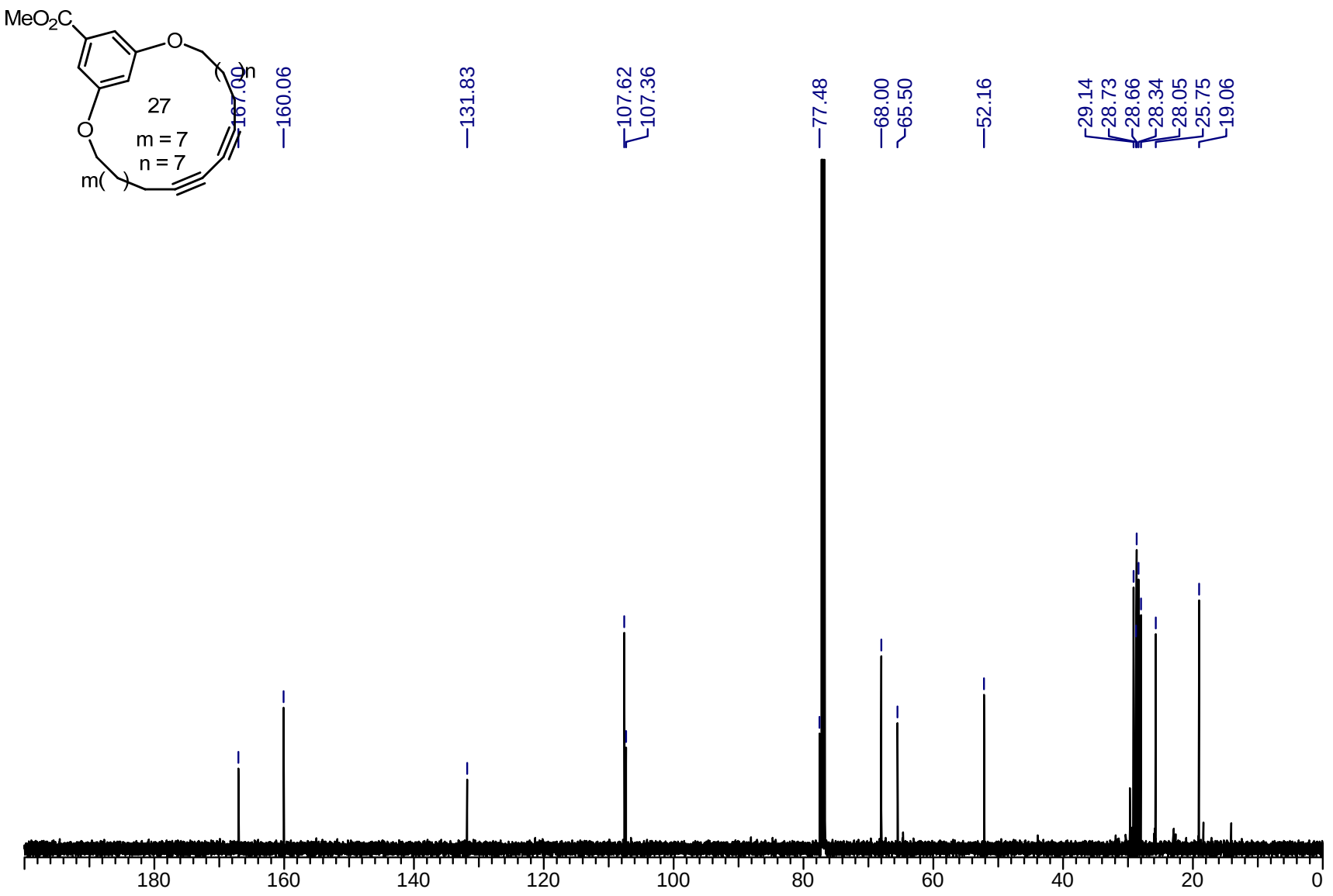
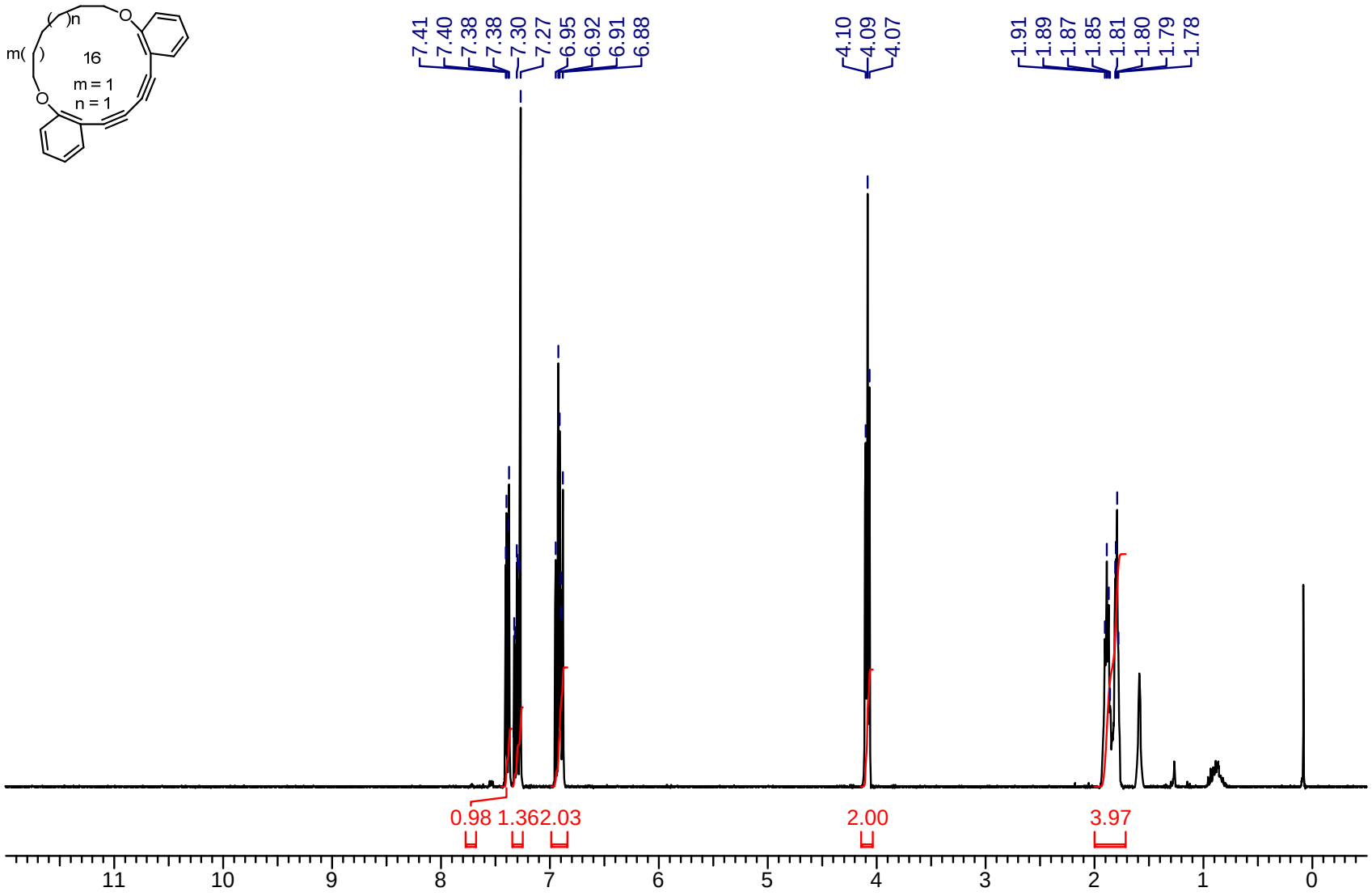
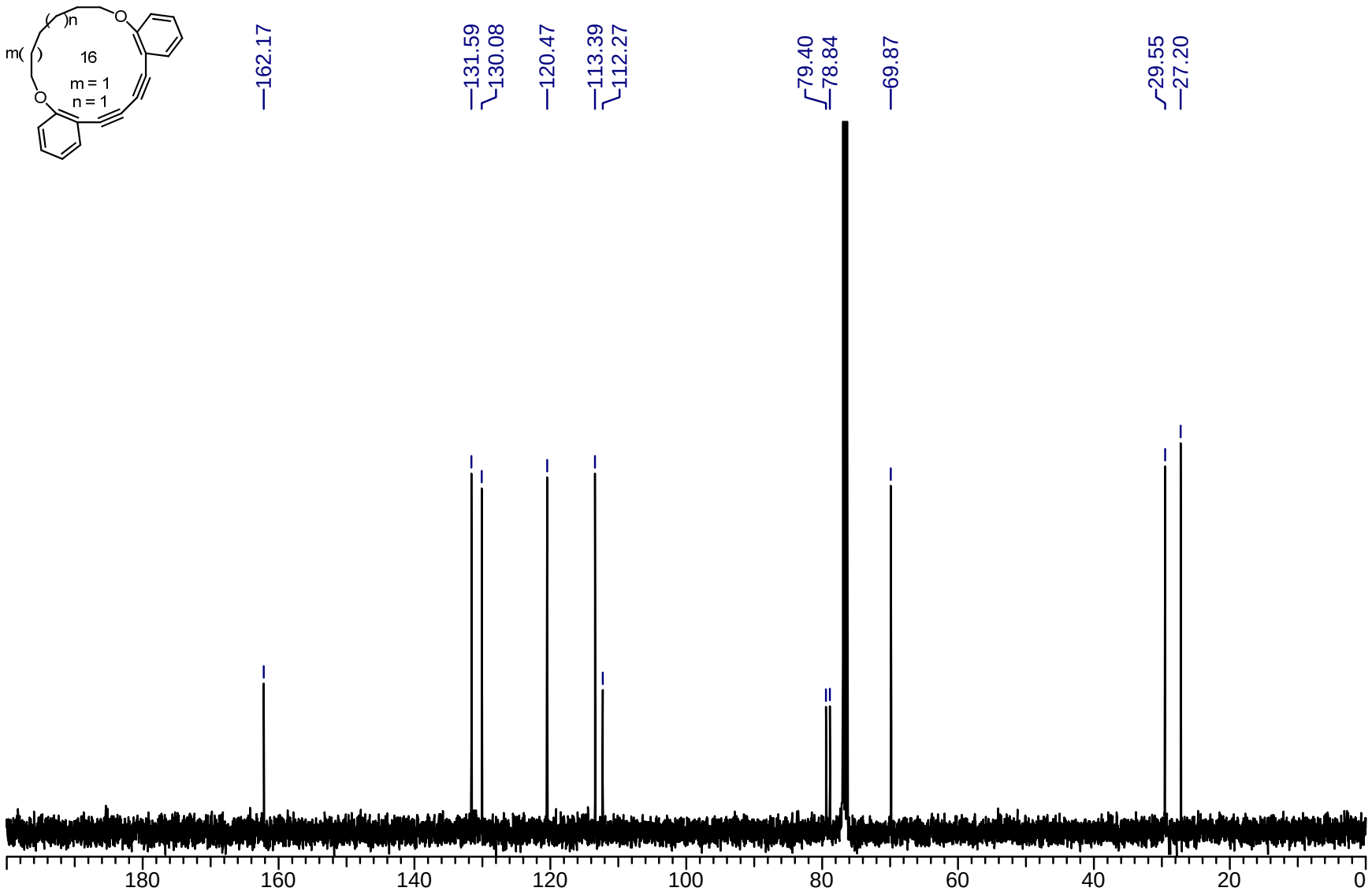
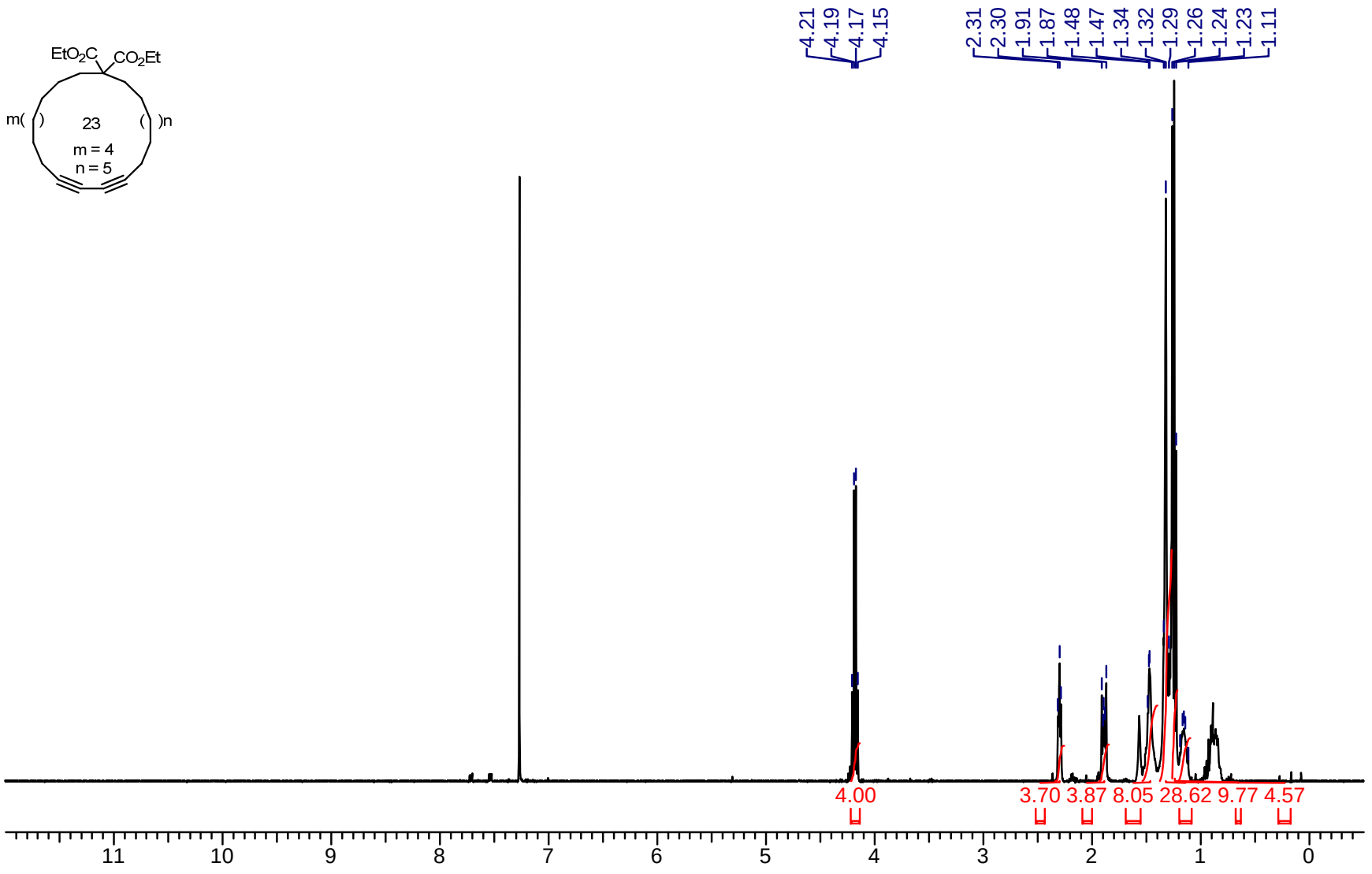
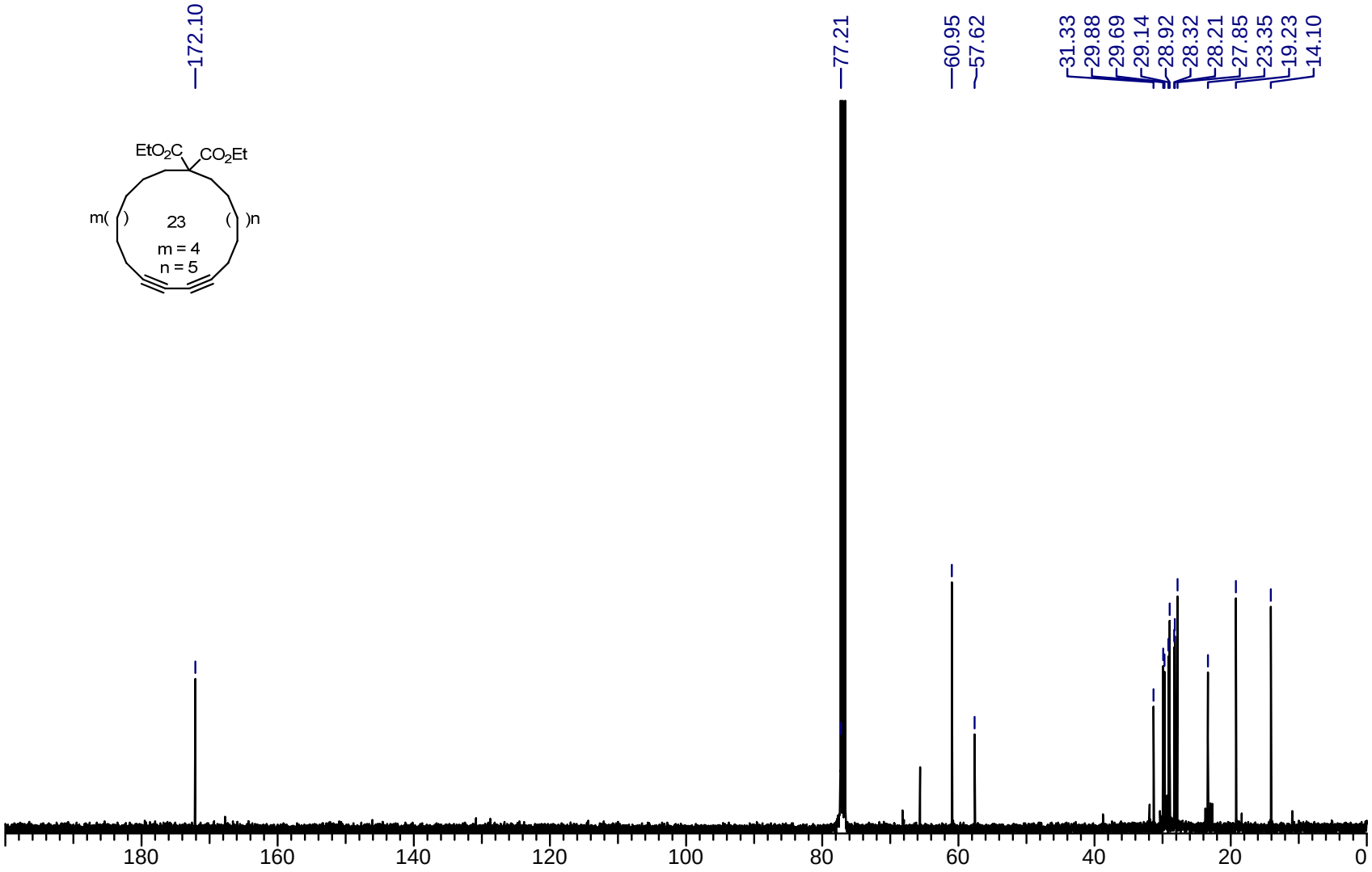
7
6
5
4
3
2
1
0


MeO2C
O
( )n
27
O
m = 7
n = 7
m( )
167.00
160.06
131.83
107.62
107.36
77.48
68.00
65.50
52.16
29.14
28.73
28.66
28.34
28.05
25.75
19.06
180
160
140
120
100
80
60
40
20
0


m( )n
16
m = 1
n = 1
O
O
7.41
7.40
7.38
7.38
7.30
7.27
6.95
6.92
6.91
6.88
4.10
4.09
4.07
1.91
1.89
1.87
1.85
1.81
1.80
1.79
1.78
0.98
1.36
2.03
2.00
3.97
11
10
9
8
7
6
5
4
3
2
1
0


m
n
16
m = 1
n = 1
162.17
131.59
130.08
120.47
113.39
112.27
79.40
78.84
69.87
29.55
27.20
180
160
140
120
100
80
60
40
20
0


EtO2C
CO2Et
m( )
23
( )n
m = 4
n = 5
4.21
4.19
4.17
4.15
2.31
2.30
1.91
1.87
1.48
1.47
1.34
1.32
1.29
1.26
1.24
1.23
1.11
4.00
3.70
3.87
8.05
28.62
9.77
4.57
11
10
9
8
7
6
5
4
3
2
1
0


172.10
77.21
60.95
57.62
31.33
29.88
29.69
29.14
28.92
28.32
28.21
27.85
23.35
19.23
14.10
EtO2C
CO2Et
m(
)
23
(
)n
m = 4
n = 5
180
160
140
120
100
80
60
40
20
0