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Graphical Abstract

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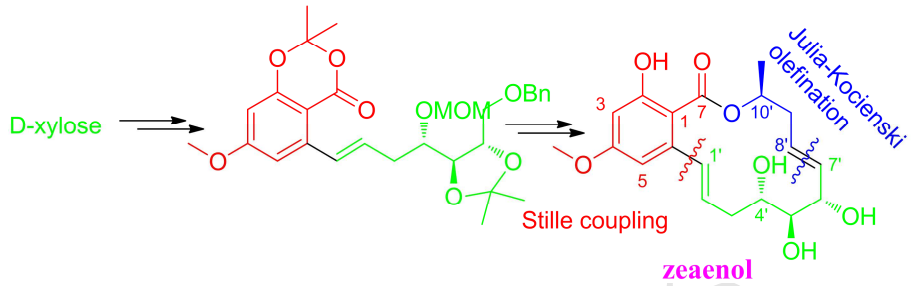

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Convergent and Stereoselective Synthesis of (-)-Zeaenol

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ABSTRACT

Stereoselective synthesis of (-)-zeaenol has been accomplished from D-xylose as a chiral pool starting material. The key steps of this convergent synthetic strategy involves a Stille coupling, a Noyori reduction, a Julia–Kocienski olefination and a macrolactonization to obtain (-)-zeaenol. We have also explored a Sonogashira coupling along with a Trost protocol for the intramolecular hydrosilylation on the homopropargylic alcohol system as an alternative synthetic approach to this molecule.

1. Introduction

β-Resorcylic acid lactones (RAL) represent new lead compounds for drug discovery, particularly as new cancer chemotherapeutic agents.[1] Recently *β*-resorcylic acid lactones, new paecilomycins A-F were isolated by *Xu et al* and co-workers from the mycelial solid culture of *Paecilomyces sp.* SC0924.[2] They exhibit various pharmacological activities such as antitumor,[3] antifungal,[4] antifouling[5] and antimalarial.[6] (5*Z*)-7-Oxozeaenol is a potent inhibitor of the NF-κB pathway and also significantly enhances the chemotherapeutic efficacy.[7] Thus the syntheses of various RALs (Fig. 1) are of great importance. (-)-Zeaenol, a 14-membered macrolide fused to a 3-methoxyphenol ring was isolated from the plant pathogenic fungus *Drechslera portulacae. Sugawara et al* determined the relative configuration of (-)-zeaenol by single crystal X-ray diffraction together with the assignments of ^{1}H and ^{13}C NMR spectra.[8] (-)-Zeaenol itself exhibits antibacterial, herbicidal activity[9], antiviral and antiprotozoan activity.[1] Due to its impressive biological activity and novel structure, several groups have disclosed total synthesis of various RALs.[10] However, out of these only three reports were resulted in the synthesis of (-)-zeaenol.[11] Very recently, *Du* and co-workers have reported the synthesis of (-)-zeaenol from L-arabinose by means of Suzuki cross-coupling and ring-closing metathesis (RCM) with an overall yield of 4.3%.[11b]

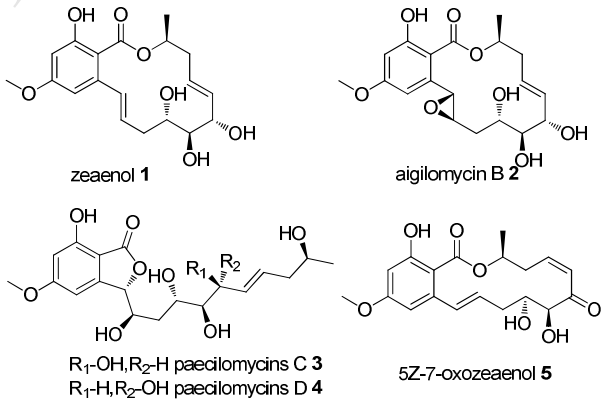
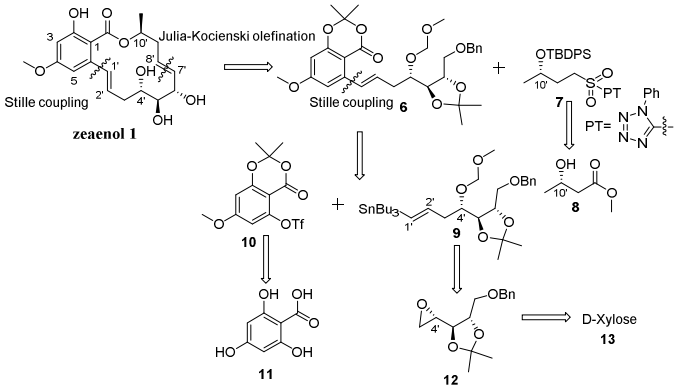


Fig. 1 Structures of (-)-zeaenol and some of the natural products having similar skeletal paecilomycins and aigilomycins.

The ability to acquire pharmaceutically active species in required quantity by economic and scalable routes is an important goal in natural product synthesis. To the best of our knowledge, Sonogashira coupling along with hydrosilylation of internal alkynes has not been studied on this type of moieties. We believe that this is one of the best alternative approaches for the construction of macrolactone core of RALs with required stereochemistry and also with good overall yield. This work lays a foundation for an eventual synthesis of β-resorcylic acid lactones to produce a library of natural products. In continuation of our research for the synthesis of new bioactive molecules, herein we wish to report enantioselective synthesis of (-)-zeaenol.

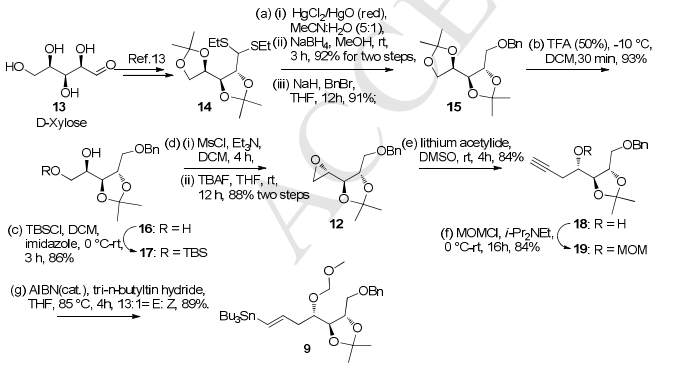
Salient features of this synthetic strategy include: The construction of three adjacent stereogenic hydroxyl groups in

macrolactone core that is achieved from commercially available D-xylose. The C10′ stereogenic centre could be easily generated by Noyori reduction of readily available methyl acetoacetate. Palladium-catalyzed Stille cross-coupling reaction was employed for the stereospecific construction of C1′- C2′ double bond. We also explored Sonogashira coupling as an alternative approach for Stille coupling in this protocol. We utilized the Trost protocol of an intramolecular hydrosilylation and a protodesilylation which required the introduction of the *trans*-alkene moiety in the sequence of the synthesis. By taking the advantage of classical Julia–Kocienski olefination, we have constructed another C7′-C8′ *trans* double bond of macrolactone core. The direct ring closure of a substituted phenolic ester derivative was achieved to form the 14-membered macrolactone.



Scheme 1 Retrosynthetic analysis of (-)-zeaenol.

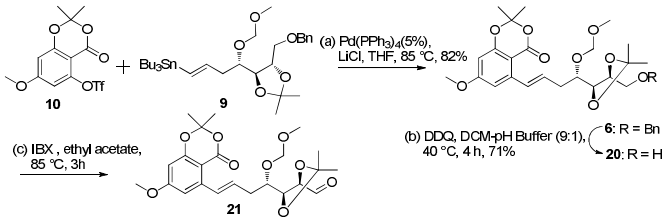
As depicted in Scheme 1, we designed our retrosynthetic strategy based on a convergent approach wherein (-)-zeaenol could be obtained from Julia–Kocienski olefination of an aldehyde derived from precursor **6** and sulfone **7**. The sulfone **7** could be achieved from *β*-hydroxy ester **8** and precursor **6** envisioned from Stille coupling of vinyl stannane **9** and Aryl triflate **10**. The vinyl stannane **9** was envisioned to come from epoxide **12** by successive implementation of the epoxide ring opening with lithium acetylide and conversion of alkyne to *trans* vinyl stannane by treating with AIBN and tributyltin hydride. Aryl triflate **10** could be obtained easily through known procedures from 2,4,6- trihydroxy benzoic acid **11**. Epoxide **12** was envisaged as being accessible from commercially available D-xylose **13**.



Scheme 2 Synthesis of Stille coupling partner **9**.

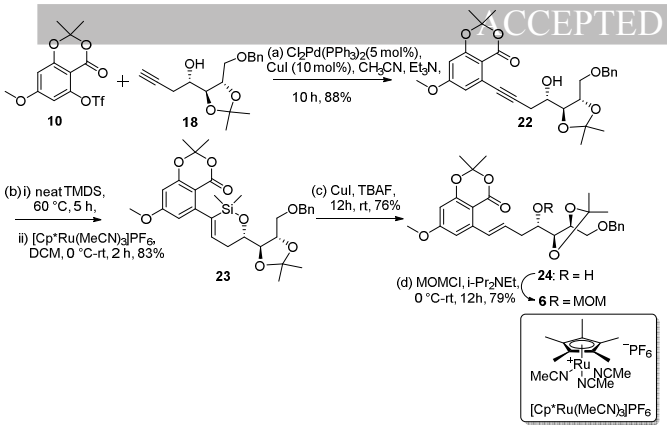
2. Results and discussion

Our initial focus relied upon the construction of *trans* vinyl stannane derivative **9** for which the synthesis was started from D-xylose. Synthesis of Stille coupling partner **9** was achieved in 10 steps from **14**. Accordingly, the ketal and thioacetal protected D-xylose **14** was synthesized from the known literature procedure with 85 % yield over two steps.[12] This material was subjected to thioacetal deprotection with HgO (red) and $HgCl_2$ in acetonitrile-water (5 : 1) that resulted in aldehyde, which was used in the next step without further purification. In order to reduce the number of synthetic steps, this aldehyde was directly treated with sulfone **7** under Julia–Kocienski olefination conditions that resulted in the decomposition of aldehyde. Therefore an alternative strategy was employed wherein the aldehyde derived from **14** was reduced with $NaBH_4$ in methanol to obtain the primary alcohol, following conversion into benzyl ether **15** by treating with NaH and BnBr. The resulting compound **15** was subjected to mono deprotection of acetonide in the presence of 60% acetic acid that resulted in diol **16** in moderate yield (64%). In order to increase yield of the diol **16** various reagents like $CuCl_2$ and triflouro acetic acid were screened by varying temperatures as well as stoichiometries. Best yields (93%) were obtained when **15** was treated with 50% triflouro acetic acid at -10 °C for 30 min under high dilution. Regioselective silylation of the primary alcohol of diol **16** using TBSCl, imidazole in CH_2Cl_2 at 0 °C afforded mono-silyl ether **17** in 86% yield. Subsequently, mesyl protection of secondary alcohol resulted in the corresponding methanesulfonate, which was directly subjected to the removal of TBS group with TBAF and consecutively TBAF-mediated epoxidation was performed to synthesize epoxide **12** in 88% yield over two steps (Scheme 2). Epoxide ring-opening of **12** was carried out using lithium acetylide and ethylenediamine complex, in DMSO afforded terminal alkyne **18** in 84% yield. The resulting secondary hydroxyl group in alkyne **18** was converted to MOM ether **19** using methoxymethyl chloride and DIPEA in THF with 84% yield. In order to execute Stille coupling, *trans* vinyl stannane precursor **9** was synthesized from terminal alkyne **19** by treating with AIBN and tri-*n*-butyltin hydride in THF. On the other side, the construction of another Stille coupling partner **10** was achieved from commercially available 2,4,6-trihydroxybenzoic acid **11** according to a literature procedure[13].



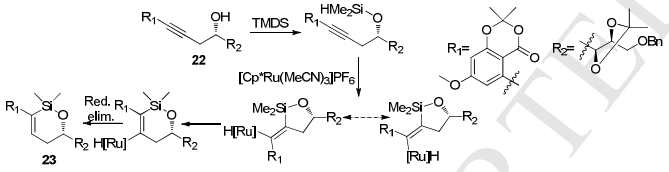
Scheme 3 Synthesis of Julia–Kocienski olefination partner aldehyde **21**.

Due to versatility and reliable nature, the Stille cross-coupling is widely employed for the formation of carbon–carbon bonds in many natural products synthesis[14]. Stille coupling between aryl triflate **10** and vinyl stannane **9** by using a catalytic amount of tetrakis(triphenylphosphine)palladium(0) and additive lithium chloride afforded coupling product **6** in 82 % yield (Scheme 3). For debenzylation, the product **6** was subjected to Lithium naphthalenide that resulted in the decomposition of the starting material. Exposure of **6** to a variety of benzyl deprotecting reagents such as Lithium naphthalenide, TMSI, $FeCl_3$ and BCl_3 failed to generate the required alcohol **20**. After screening with several reagents and reaction conditions for debenzylation, finally we optimised the reaction conditions by treating the olefin **6** with 1 equivalent of DDQ in DCM- phosphate buffer (9:1) at 40 °C for 4 h afforded the deprotected alcohol **20** in 71% yield[15]. This alcohol **20** was oxidized to aldehyde by using IBX in ethyl acetate at 85 °C reflux for 3h, which was utilised for Julia–Kocienski olefination without further purification.



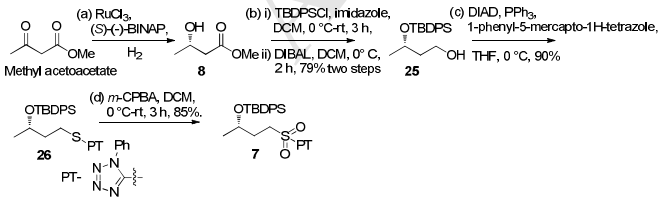
Scheme 4 Sonogashira coupling followed by intramolecular hydrosilylation and a protodesilylation.

We also employed a Sonogashira coupling[16] followed by an intramolecular hydrosilylation and a protodesilylation as an alternative approach to Stille coupling for this molecule. Accordingly, Sonogashira coupling was achieved from alkyne **18** and aryl triflate **10** by treating catalytic amounts of $Cl_2Pd(PPh_3)_2$ (5 mol%) and CuI (10 mol%) afforded **22** in 88% yield. The homopropargylic alcohol **22** was silylated in neat tetramethyldisilazane (TMDS) at 60 °C (decomposition was observed at elevated temperatures, above 80 °C) and volatile residual TMDS was removed under reduced pressure. The residue was then taken up in dichloromethane and treated with a catalytic amount of ruthenium complex $[Cp^*Ru(MeCN)_3]PF_6$ (Scheme 4) [17]. Then the homopropargylic system underwent hydrosilylation to afford cyclic siloxane product **23**. A catalytic amount of copper(I) iodide (0.1 equiv) in the presence of TBAF in THF effected clean protodesilylation of **23** to give *trans* homoallylic alcohol **24** in 76% yield[18]. The resultant homoallylic alcohol was protected as it's MOM ether using methoxymethyl chloride and DIPEA in THF with 79% yield.



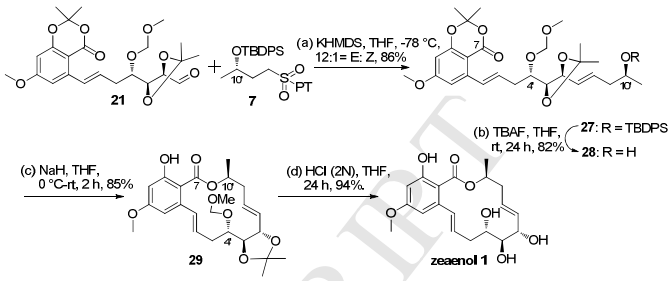
Scheme 5 A plausible mechanism for cis silylmetalation followed by isomerization.

As Trost[17] proposed, the mechanism of *trans* hydrosilylation reactions was postulated as initial *syn* silylmetalation followed by a series of rearrangements and a final reductive elimination (Scheme 5). The ruthinium complex effected an intramolecular hydrosilylation producing regioselective 6-endo-dig cyclization under very mild conditions with excellent selectivity.



Scheme 6 Synthesis of sulfone fragment **7**.

The sulfone fragment **7** was synthesized from the commercially available methyl acetoacetate over five steps. *β*-hydroxy ester **8** was achieved in quantitative yield (99% *ee*) by implementation of Noyori asymmetric hydrogenation on commercially available methyl acetoacetate using ruthenium catalyst bearing the chiral diphosphine ligand (S)-(-)-BINAP[19]. The secondary alcohol **8** was converted to TBDPS ether and was subjected to 2 equivalents of DIBAL resulted in the reduction of ester to primary alcohol **25** in 79% yield over two steps as shown in Scheme 6. Alcohol **25** was converted to the corresponding sulfide **26** under Mitsunobu conditions in 90% yield and which upon oxidation with *m*-CPBA afforded the required sulfone **7** in 85% yield.



Scheme 7 Total synthesis of (-)-zeaenol.

Finally to complete the synthesis of (-)-zeaenol, we focused on the Julia–Kocienski olefination[20] of the two fragments sulfone **7** and aldehyde **21**. Here we have optimised the reaction condition and *E: Z* ratio of the coupled olefin **27** using different bases like NaHMDS, LiHMDS and KHMDS. Accordingly, sulfone **7** was treated with 1.5 equivalents of KHMDS and aldehyde **21** was introduced at −78 °C to afford the coupled product **27** (12:1= *E: Z*) (Scheme 7) in 86% yield (based on the recovery of aldehyde). The *E: Z* ratio of the coupled olefin was confirmed based on coupling constant 15.7 Hz in ^{1}H NMR. Removal of the TBDPS group with TBAF on prolonged reaction time afforded secondary alcohol **28** in 82% yield. The product **28** was subjected to a direct macrolactonization with NaH that resulted in a tandem sequence of removal of aromatic acetonide and formation of desired 14-membered macrolactone **29** in good yield (85%). Global deprotection of the MOM and acetonide of macrolide **29** in one pot was successfully achieved using 2N HCl to generate (-)-zeaenol **1** in 94% yield. In this Stille coupling strategy, we have successfully synthesized (-)-zeaenol **1** in 17 steps from **14**. ^{1}H, ^{13}C NMR spectral data and optical rotation {$[\alpha]_D^{27}$ = -87 (c 0.5, MeOH); lit.: $[\alpha]_D^{20}$ = -92 (c 0.52, MeOH)} of synthetic product, (-)-zeaenol **1** was in complete agreement with the natural product data[8].

3. Conclusion

The significance of our synthetic sequence lies in employing natural chiral D-xylose to build three adjacent stereogenic centers on the macrocyclic skeleton. Cost-effective and readily available precursors like D-xylose and methyl acetoacetate were used as the starting material for the synthesis. The overall yield of the synthetic pathway in a Stille coupling strategy was 10.3% and in a Sonogashira coupling strategy was 10.4% starting from D-xylose, a significant enhancement over earlier synthesis which is about 4.3%. The key synthetic reactions include a Stille coupling, a Sonogashira coupling and intramolecular hydrosilylation as an alternative approach, a Julia–Kocienski olefination and a direct macrolactonization. The spectral properties and optical rotation of the synthetic compound were found to be identical with those published for the natural (-)-zeaenol. This synthetic protocol may find application in drug discovery for synthesis of variety of *β*-resorcylic acid lactones derivatives with wide range of biological activity.

4. Experimental Section

All reactions were performed under inert atmosphere. All glassware apparatus used for reactions are perfectly oven/flame dried. Anhydrous solvents were distilled prior to use: THF from Na and benzophenone; CH_2Cl_2, DMSO from CaH_2; MeOH from Mg cake. Commercial reagents were used without purification. Column chromatography was carried out by using silica gel (60–120 mesh) unless otherwise mentioned. Analytical thin layer chromatography (TLC) was run on silica gel 60 F254 pre-coated plates (250 μm thickness). Optical rotations $[\alpha]_D$ were measured on a polarimeter and given in 10^{-1} degcm^{2}g^{-1}. Infrared spectra were recorded in $CHCl_3$/KBr (as mentioned) and reported in wave number (cm^{-1}). Mass spectral data were obtained using MS (EI) ESI, HRMS mass spectrometers. High resolution mass spectra (HRMS) [ESI+] were obtained using either a TOF or a double focusing spectrometer. ^{1}H NMR spectra were recorded at 300, 400, 500 and ^{13}C NMR spectra 75, 100, 125 MHz in $CDCl_3$ solution unless otherwise mentioned, chemical shifts are in ppm downfield from tetramethylsilane and coupling constants (*J*) are reported in hertz (Hz). The following abbreviations are used to designate signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sex = sextet, m = multiplet, br = broad, ABq = AB Quartet.

(4R,4'R,5S)-5-((benzyloxy)methyl)-2,2,2',2'-tetramethyl-4,4'-bi(1,3-dioxolane) (15):

red HgO (5.4 g, 25 mmol) and $HgCl_2$ (5.43 g, 20 mmol) were added to a solution of **14** (3.36 g, 10 mmol) in MeCN/H_2O (10:2 v/v, 36 mL) stirred at ambient temperature. One hour later the mixture was filtered through Celite and washed with CH_2Cl_2 (50 mL). The filtrate and washings were washed with aq. 20% KI and sat. $NaHCO_3$ in turn and dried over anhydrous $MgSO_4$, Removal of the solvent results in colorless liquid. This aldehyde used for the next step without further purification.

To the above aldehyde in dry MeOH (40 mL) was added $NaBH_4$ (740 mg, 20 mmol) portion wise at 0 °C under a nitrogen atmosphere. After being stirred for 3 h at room temperature, saturated aq. NH_4Cl was added to the reaction mixture, MeOH concentrated under reduced pressure and residue extracted with ethyl acetate (3×50 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous Na_2SO_4, concentrated under reduced pressure and purified by column chromatography (petroleum ether–EtOAc, 2:3) to afford alcohol (2.12 g, 92 % for 2 steps) as yellowish oil. R_f = 0.4 (petroleum ether–EtOAc, 2:3); $[\alpha]_D^{27}$ = -15.7 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3467, 2988, 2935, 1457, 1377, 1253, 1217, 1159, 1055, 858, 511 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): 4.20 (dt, *J* = 7.0, 4.4 Hz, 1H), 4.06 (d, *J* = 8.2 Hz, 1H), 4.05 (dd, *J* = 8.2, 4.4 Hz, 1H), 3.98 (dd, *J* = 8.2, 4.4 Hz, 1H), 3.89-3.84 (m, 1H), 3.81 (dd, *J* = 12.1, 3.5 Hz, 1H), 3.64 (dd, *J* = 12.0, 4.2 Hz, 1H), 2.40 (br, 1H), 1.44 (s, 9H), 1.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 109.6, 109.4, 77.6, 76.8, 74.9, 65.4, 61.9, 27.0, 26.8, 26.0, 25.3; MS (ESI): *m/z* = 255 [M + Na]$^+$. HRMS: calcd. for $C_{11}H_{20}O_5Na$ [M + Na]$^+$: 255.1203: found: 255.1199.

To a stirred suspension of NaH (1.03 g, 25.86 mmol) in dry THF (20 mL) was added a solution of above alcohol (3 g, 12.93 mmol) in dry THF (10 mL) drop wise at 0 °C under a nitrogen atmosphere. After stirring at room temperature for 15 min, benzyl bromide was added and the reaction mixture stirred overnight. The reaction mixture was quenching with saturated aq. NH_4Cl at 0 °C and extracted with ether (2×50 mL). The combined organic extracts were washed with brine (30 mL), dried over anhydrous Na_2SO_4, concentrated under reduced pressure and purified by column chromatography (petroleum ether–EtOAc, 4:1) to afford pure **15** (3.79 g, 91 %). R_f = 0.6 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{27}$ = -7.5 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 2987, 2934, 2892, 1454, 1374, 1252, 1216, 1158, 1087, 1063, 864, 739, 699,511 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): 7.37-7.27 (m, 5H), 4.58 (d, *J* = 1.9 Hz, 2H), 4.16 (dt, *J* = 12.1, 6.8 Hz, 1H), 4.11 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.99 (dd, *J* = 7.9, 6.8 Hz, 1H), 3.91 (dd, *J* = 7.9,4.9 Hz, 1H), 3.81 (t, *J* = 7.9 Hz, 1H), 3.59 (d, *J* = 6.8 Hz, 2H), 1.44 (s, 3H), 1.42 (s, 3H), 1.40 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 137.8, 128.6, 128.4, 127.9, 127.8, 109.8, 109.7, 78.5, 76.5, 75.7, 73.6, 70.5, 65.7, 27.1, 27.0, 26.2, 25.5; MS (ESI): *m/z* = 345 [M + Na]$^+$. HRMS: calcd. for $C_{18}H_{26}O_5Na$ [M + Na]$^+$: 345.1673: found: 345.1666.

(R)-1-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)ethane-1,2-diol (16):

To a flask containing protected alcohol **15** (3.22 g, 10 mmol) in 100 mL DCM at -10 °C (ice-salt bath) was added 10 mL of cold TFA (50%). The reaction mixture was stirred for 30 min at -10 °C and then add sat. $NaHCO_3$ solution, stirred for 30 min at rt, The layers were separated and the aqueous layer was extracted with DCM (2x50mL), washed in turn with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure and purified by column chromatography (petroleum ether–EtOAc, 2:3) gave the diol **16** (2.63 g, 93 %) as a colorless oil. R_f = 0.3 (petroleum ether–EtOAc, 2:3); $[\alpha]_D^{27}$ = -15.3 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3423, 3064, 2987, 2932, 1454, 1375, 1250, 1215, 1166, 1088, 868, 740, 700, 605, 511 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): 7.37-7.27 (m, 5H), 4.58 (d, *J* = 1.9 Hz, 2H), 4.24 (dt, *J* = 13.2, 6.8 Hz, 1H), 3.91 (d, *J* = 8.3 Hz, 1H), 3.69-3.66 (m, 3H), 3.65 (ddd, *J* = 10.5, 7.9, 2.6 Hz, 1H), 3.58 (dd, *J* = 10.5, 5.3 Hz, 1H), 2.93-2.80 (br, 1H), 2.77-2.59 (br, 1H), 1.42 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 137.5, 128.4, 127.8, 127.7, 109.6, 79.8, 75.8, 73.6, 70.3, 70.2, 64.6, 27.0, 26.8; MS (ESI): *m/z* = 305 [M + Na]$^+$. HRMS: calcd. for $C_{18}H_{26}O_5Na$ [M + Na]$^+$: 305.1359: found: 305.1351.

(R)-1-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2-((tert-butyldimethylsilyl)oxy)ethanol (17):

To a solution of **16** (8.46 g, 30 mmol) in DCM (30 mL), imidazole (2.25 g, 33 mmol) and TBSCl (5 g, 33 mmol) were added at 0 °C. The mixture was stirred at room temperature for 3 h, after which time the reaction was quenched by adding H_2O and diluted with ethyl acetate (20 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3x100 mL). The organic layers were combined, dried over Na_2SO_4, filtered, concentrated and flash column chromatography (petroleum ether–EtOAc, 4:1) was obtained as a yellow oil **17** (10.2 g, 86%). R_f = 0.6 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{27}$ = -20.3 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3474, 2986, 2931, 2859, 1465, 1373, 1254, 1217, 1095, 1007, 839, 778, 740, 698, 669, 511 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): 7.37-7.24 (m, 5H), 4.59 (d, *J* = 1.9 Hz, 2H), 4.26 (dd, *J* = 8.3, 4.5 Hz, 1H), 3.99 (dd, *J* = 8.3, 3.0 Hz, 1H), 3.74 (qt, *J* = 10.6, 3.0 Hz, 1H), 3.68-3.54 (m, 4H), 2.19-1.97 (br, 1H), 1.42 (s, 3H), 1.42 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): 137.9, 128.3, 127.7, 127.6, 109.4, 78.0, 76.0, 73.5, 70.4, 70.3, 64.4, 27.1, 26.9, 25.8, 18.2, -3.6, -5.4; MS (ESI): *m/z* = 419 [M + Na]$^+$. HRMS: calcd. for $C_{21}H_{36}O_5SiNa$ [M + Na]$^+$: 419.2224: found: 419.2212.

(4S,5S)-4-((benzyloxy)methyl)-2,2-dimethyl-5-((S)-oxiran-2-yl)-1,3-dioxolane (12):

To a solution of **17** (3.96 g, 10 mmol) and Et_3N (2.8 mL, 20 mmol) in CH_2Cl_2 (20 mL) was added MsCl (1.17 mL, 15 mmol) at 0 °C. The mixture was stirred at room temperature for 4 h. The reaction was quenched with saturated aqueous NH_4Cl and was extracted with ethyl acetate (3x50 mL). The organic layer was

washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was dissolved in THF (5.0 mL) and then TBAF [1.0 M] solution in THF (15 mL, 15 mmol) was added to this solution at 0 °C. After the mixture was stirred for 12 h, the reaction was quenched with saturated aqueous NH_4Cl and was extracted with ethyl acetate (3x50 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc, 4:1) to give **12** (2.32 g, 88% for two steps) as a colorless oil. R_f = 0.5 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{27}$ = +6.3 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3031, 2988, 2931, 2867, 1454, 1375, 1251, 1215, 1167, m1084, 859, 740, 699, 605, 511 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 7.36-7.26 (m, 5H), 4.60 (d, *J* = 1.9 Hz, 2H), 4.17 (ddd, *J* = 12.1, 5.7, 3.7 Hz, 1H), 3.67 (dd, *J* = 7.8, 5.2 Hz, 1H), 3.63 (qd, *J* = 10.4,5.3 Hz, 2H), 3.08 (ddd, *J* = 6.6, 5.3, 2.6 Hz, 1H), 2.81 (dd, *J* = 5.0, 4.0 Hz, 1H), 2.68 (dd, *J* = 5.0, 2.6 Hz, 1H),1.44 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): 137.8, 128.3, 127.7, 127.6, 110.0, 78.1, 78.0, 73.5, 70.4, 51.7, 44.9, 26.9, 26.6; MS (ESI): *m/z* = 287 $[M + Na]^+$. HRMS: calcd. for $C_{15}H_{20}O_4Na$ $[M + Na]^+$: 287.1254: found: 287.1248.

(S)-1-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)but-3-yn-1-ol (18):

To a suspension of lithium acetylide, an ethylenediamine complex (924 mg, 10 mmol) in DMSO (5 mL) was added **12** (1.32 g, 5 mmol) in DMSO (5.0 mL) at 0 °C. The reaction mixture was stirred for 4 h at room temperature. The reaction was quenched with saturated aqueous NH_4Cl and the whole was extracted with ethyl acetate (4x100 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by silica gel column chromatography (petroleum ether–EtOAc, 7:3) to give **18** (1.22 g, 84%) as a colorless oil. R_f = 0.4 (petroleum ether–EtOAc, 1:4); $[\alpha]_D^{27}$ = -3.4 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3446, 3294, 2987, 2918, 2119, 1454, 1375, 1252, 1214, 1166, 1086, 1046, 858, 741, 699, 644, 512 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.39-7.24 (m, 5H), 4.60 (d, *J* = 1.9 Hz, 2H), 4.11 (dd, *J* = 6.0, 5.5 Hz, 1H), 3.82-3.73 (m, 2H), 3.70 (dd, *J* = 9.6, 4.9 Hz, 1H), 3.61 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.23-3.11 (br, 1H), 2.61 (td, *J* = 16.8, 2.8 Hz, 1H), 2.46 (ddd, *J* = 17.0, 6.2, 2.6 Hz, 1H), 2.05 (t, *J* = 2.6 Hz, 1H),1.39 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 137.1, 128.4, 127.8, 109.3, 80.4, 80.2, 78.2, 73.6, 70.6, 70.5, 53.6, 26.8, 23.9; MS (ESI): *m/z* = 313 $[M + Na]^+$. HRMS: calcd. for $C_{17}H_{22}O_4Na$ $[M + Na]^+$: 313.1410: found: 313.1404.

(4S,5S)-4-((benzyloxy)methyl)-5-((S)-1-(methoxymethoxy)but-3-yn-1-yl)-2,2-dimethyl-1,3-dioxolane (19):

To a solution of **18** (2.9 g, 10 mmol) in dry CH_2Cl_2 (20 mL) were added i-Pr_2NEt (3.6 mL, 20 mmol) and MOMCl (1.14 mL, 15 mmol) at 0 °C. The mixture was stirred at room temperature for 16 h. The reaction was quenched with saturated aqueous NH_4Cl and the whole was extracted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography (petroleum ether–EtOAc, 4:1) to give **19** (2.73 g, 82%) as a colorless oil. R_f = 0.5 (petroleum ether–EtOAc, 4:1); $[\alpha]_D^{27}$ = -18.9 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3289, 2987, 2932, 2119, 1454, 1374, 1250, 1214, 1100, 1035, 918, 858, 740, 699, 644, 515 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 7.37-7.27 (m, 5H), 4.76 (d, *J* = 6.9 Hz, 1H), 4.65 (d, *J* = 12.4 Hz, 1H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.56 (d, *J* = 12.4 Hz, 1H), 4.21 (dt, *J* = 7.0, 3.1 Hz, 1H), 3.96 (t, *J* = 7.0 Hz, 1H), 3.78 (dd, *J* = 11.6, 5.0 Hz, 1H), 3.71 (dd, *J* = 10.2, 3.1 Hz, 1H), 3.58 (dd, *J* = 10.4, 6.7 Hz, 1H), 3.34 (s, 3H), 2.59 (qdd, *J* = 17.2, 5.0, 2.8 Hz, 2H), 2.00 (dd, *J* = 2.8 Hz, 1H), 1.43 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 138.2, 128.5, 128.0, 127.8, 109.9, 96.2, 80.4, 78.9, 77.9, 76.2, 73.6, 71.6, 70.7, 56.1, 27.4, 27.3, 21.7; MS (ESI): *m/z* = 357 $[M + Na]^+$. HRMS: calcd. for $C_{19}H_{26}O_5Na$ $[M + Na]^+$: 357.1673: found: 357.1672.

((S,E)-4-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)but-1-en-1-yl)tributylstannane (9):

To a solution of terminal alkyne **19** (1.66 g, 5 mmol) in anhydrous benzene (30 mL) at room temperature under an argon atmosphere was added 2,2'-azobis(2-methylpropionitrile) (AIBN) (164 mg, 1 mmol) in one portion, followed by the drop wise addition of tri-n-butyltin hydride (2.7 mL, 10 mmol) and the reaction was heated to 85° C. After 4 h, the reaction was cooled to room temperature, diluted with dichloromethane (30 mL) and concentrated in vacuo. The resultant crude was purified via silica gel chromatography (petroleum ether–EtOAc, 6:1) to afford vinyl stannane **9** obtained as colorless oil. (2.78 g, 89 %, 13:1= E: Z). R_f = 0.7 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{20}$ = + 6.4 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 2956, 2925, 2854, 1729, 1599, 1548, 1457, 1376, 1271, 1253, 1122, 1098, 1073, 995, 920, 860, 738, 697, 667, 598, 547 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.36-7.30 (m, 5H), 5.99-5.96 (m, 1H), 4.69-4.65 (m, 2H), 4.65-4.61 (m, 2H), 4.55 (d, *J* = 12.4 Hz, 1H), 4.22-4.18 (m, 1H), 3.85 (dd, *J* = 7.8, 5.3 Hz, 1H), 3.81-3.77 (m, 1H), 3.68 (dd, *J* = 10.4, 3.1 Hz, 1H), 3.54 (dd, *J* = 10.4, 6.7 Hz, 1H), 3.32 (s, 3H), 2.46-2.41 (m, 2H), 1.55-1.43 (m, 6H), 1.41 (s, 3H), 1.40 (s, 3H), 1.35-1.23 (m, 6H), 0.95-0.81 (m, 15H). ^{13}C NMR (100 MHz, $CDCl_3$): 144.4, 138.1, 131.7, 128.3, 127.7, 127.6, 109.3, 96.2, 78.7, 77.9, 77.1, 73.3, 71.4, 55.8, 39.9, 29.2, 29.1, 27.3, 27.1, 13.7, 9.4; MS (ESI): *m/z* = 649 $[M + Na]^+$. HRMS: calcd. for $C_{31}H_{54}O_5SnNa$ $[M + Na]^+$: 649.2891: found: 649.2886.

5-((S,E)-4-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)but-1-en-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (6):

Tetrakis(triphenylphosphine)palladium(0) (116 mg 0.1 mmol) and lithium chloride (255 mg, 6 mmol) were added to 20 mL of dry THF. This mixture was stirred for 15 min under argon atmosphere, then a solution of Aryl Triflate **10** (712 mg, 2 mmol) and vinyl stannane **9** (1.27 g, 2.02 mmol) in 10 mL dry THF was added to the reaction mixture. The resulting reaction mixture was heated to THF reflux for 24 h. The mixture is cooled to rt and partitioned between 20 mL of water and 25 mL of diethyl ether. The aqueous layer was extracted diethyl ether (2x20 mL). The combined organic layers were washed with a saturated sodium bicarbonate solution, a brine solution, dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether–EtOAc, 7:3) to yield yellow thick liquid of the coupled product **6** (889 mg, 82%). R_f = 0.5 (petroleum ether–EtOAc, 7:3); $[\alpha]_D^{27}$ = +7.1 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 2953, 2911, 2859, 2346, 1728, 1599, 1558, 1457, 1376, 1271, 1213, 1123,1074, 1033, 961, 860, 738, 697, 633, 547, 513 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.48 (d, *J* = 15.7 Hz, 1H), 7.37-7.24 (m, 5H), 6.74 (d, *J* = 2.4 Hz, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 6.21 (dt, *J* = 15.7, 7.3 Hz, 1H), 4.72-4.65 (m, 2H), 4.64-4.54 (m, 2H), 4.25-4.18 (m, 1H), 3.90 (dd, *J* = 7.4, 5.9 Hz, 1H), 3.84 (dd, *J* = 7.4, 5.8 Hz, 1H), 3.83 (s, 3H), 3.70 (dd, *J* = 10.4, 3.1 Hz, 1H), 3.58 (dd, *J* = 10.4, 6.4 Hz, 1H), 3.32 (s, 3H), 2.65-2.54 (m, 2H), 1.69 (s, 6H), 1.43 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): 164.7, 160.0, 158.7, 143.8, 138.1, 130.9, 130.2, 128.3, 127.7, 127.5, 109.5, 108.4, 104.9, 103.7, 100.1, 96.2, 78.6, 78.3, 77.6, 73.4, 71.4, 55.8, 55.5, 35.0, 27.1, 25.7, 25.5; MS (ESI): *m/z* = 565 $[M + Na]^+$. HRMS: calcd. for $C_{30}H_{38}O_9Na$ $[M + Na]^+$: 565.2414: found: 565.2395.

5-((S,E)-4-((4S,5S)-5-(hydroxymethyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)but-1-en-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (20):

To a solution of **6** (542 mg, 1 mmol) in 9:1 DCM: pH 7.0 phosphate buffer (10mL) was added 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (227mg, 1 mmol). The reaction mixture was heated to 40 °C for 4 h. The reaction mixture was stirred until TLC analysis indicated the completion of the reaction. After completion of reaction, cool the reaction mixture to rt then add solid $NaHCO_3$ and stir for 30 min. The organic layers was filtered, washed with saturated sodium bicarbonate solution, a brine solution, dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by column chromatography (petroleum ether–EtOAc, 2:3) to yield thick liquid of the alcohol **20** (321 mg, 71%). R_f = 0.3 (petroleum ether–EtOAc, 1:1); $[\alpha]_D^{27}$ = -6 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3423, 2976, 2921, 2846, 1729, 1576, 1548, 1509, 1339, 1213, 1149, 1122, 994, 960, 859, 621, 545, 488 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.47 (d, *J* = 15.7 Hz, 1H), 6.74 (d, *J* = 2.4 Hz, 1H), 6.35 (d, *J* = 2.4 Hz, 1H), 6.20 (d, *J* = 15.4, 7.2 Hz, 1H), 4.75 (ABq, *J* = 6.7 Hz, 2H), 4.17-4.09 (m, 1H), 3.98 (dd, *J* = 7.5, 6.4 Hz, 1H), 3.87 (dd, *J* = 9.6, 5.5 Hz, 1H), 3.85 (s, 3H), 3.84 (dd, *J* = 5.7, 4.0 Hz, 1H), 3.74 (dd, *J* = 11.7, 4.7 Hz, 1H), 3.40 (s, 3H), 2.71-2.58 (m, 2H), 2.37-2.23 (br, 1H), 1.71 (s, 3H), 1.70 (s, 3H), 1.42 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): 164.8, 160.2, 158.7, 143.7, 131.2, 129.8, 109.2, 108.5, 105.0, 103.6, 100.2, 96.2, 79.3, 78.2, 77.5, 63.4, 56.0, 55.6, 35.0, 29.7, 27.1, 27.0, 25.7, 25.4; MS (ESI): *m/z* = 475 $[M + Na]^+$. HRMS: calcd. for $C_{23}H_{32}O_9Na$ $[M + Na]^+$: 475.1944: found: 475.1946.

5-((S)-4-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-hydroxybut-1-yn-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (22):

To a solution of **18** (147 mg, 0.5 mmol) in CH_3CN (4 mL) were added Et_3N (0.14 mL, 1 mmol) and $Cl_2Pd(PPh_3)_2$ (18mg, 0.025 mmol). After the mixture had been stirred for 30 min, the solution of Triflate **10** (178 mg, 0.5 mmol) and CuI (10 mg, 0.05 mmol) were added and the resulting mixture was stirred for 10 h. The reaction was quenched with saturated aqueous NH_4Cl (5 mL) and the whole was extracted with ether. The organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (petroleum ether–EtOAc, 3:2) to give **22** (217 mg, 88%) as a yellow thick liquid. R_f = 0.4 (petroleum ether–EtOAc, 4:1); $[\alpha]_D^{27}$ = -74.3 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3458, 2988, 2932, 2236, 1740, 1602, 1575, 1457, 1373, 1277, 1206, 1165, 1032, 914, 857, 741, 699, 673, 510 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.37-7.22 (m, 5H), 6.72 (d, *J* = 2.4 Hz, 1H), 6.39 (d, *J* = 2.4 Hz, 1H), 4.63 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 12.1 Hz, 1H), 4.33-4.27 (m, 2H), 3.91-3.86 (br, 1H), 3.87-3.84 (m, 2H), 3.82 (s, 3H), 3.66 (dd, *J* = 10.4, 6.4 Hz, 1H), 2.90 (dd, *J* = 17.2, 3.2 Hz, 1H), 2.72 (dd, *J* = 17.2, 6.4 Hz, 1H), 1.68 (s, 3H), 1.67 (s, 3H), 1.43 (s, 3H), 1.39 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 164.8, 159.6, 158.3, 138.1, 128.1, 127.5, 127.3, 126.7, 114.6, 109.5, 106.6, 105.6, 101.7, 93.8, 81.5, 79.9, 78.6, 73.3, 72.1, 71.3, 55.7, 27.0, 26.9, 26.4, 25.6, 25.3; MS (ESI): *m/z* = 519 $[M + Na]^+$.

5-((S)-6-((4R,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyl-5,6-dihydro-2H-1,2-oxasilin-3-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (23):

A rb flask was charged with **22** (248 mg, 0.50 mmol) under Argon atmosphere at rt. To the neat alcohol was added 1,1,3,3-tetramethyldisilazane (TMDS) (270 µL, 1.5 mmol) and the flask heated to 60 °C for 5 h. Next, the flask was cooled to rt and placed under vacuum for 45 min to remove the excess silazane. An Argon atmosphere was then re-introduced and the residue taken up in DCM (2.0 mL). The flask was cooled to 0 °C and solid $[Cp^*Ru(MeCN)_3]PF_6$ (2.5 mg, 0.005 mmol) was added to the solution. The flask was allowed to warm to rt, and after 2 h, the solution was diluted with ether (10 mL) and filtered through a short plug of florisil, washing with additional ether (3x10 mL). The volatile components were then removed under reduced pressure and the resulting residue purified on a florisil column (petroleum ether: ether, 10:1) to afford (229 mg, 83%) the desired hydrosilyl product **23** as a colorless oil. R_f = 0.6 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{27}$ = -57.5 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} =2931, 2858, 1728, 1684, 1604, 1577, 1504, 1455, 1347, 1245, 1111, 1032, 918, 839, 778, 737, 696 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.42-7.26 (m, 5H), 6.69 (dd, *J* = 9.1, 2.3 Hz, 1H), 6.47 (d, *J* = 2.3 Hz, 1H), 6.41-6.37 (m, 1H), 5.47-5.35 (m, 2H), 4.64 (dd, *J* = 12.8, 5.3 Hz, 1H), 4.19 (dd, *J* = 12.1, 6.0 Hz, 1H), 4.08 (td, *J* = 7.6, 2.7 Hz, 1H), 3.89 (s, 3H), 3.68 (td, *J* = 7.6, 2.3 Hz, 1H), 3.59-3.46 (m, 1H), 2.14-1.99 (m, 2H), 1.77 (s, 6H), 1.30 (s, 6H), 0.15 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): 165.0, 161, 158.9, 144.2, 142.4, 138.3, 131.4, 128.6, 128.0, 127.9, 127.9, 127.8, 127.7, 111.9, 110.5, 109.5, 105.7, 100.6, 80.7, 79.9, 73.6, 72.4, 71.6, 55.9, 35.4, 29.9, 27.4, 26.0, 25.9, 25.6, 0.6, 0.5; MS (ESI): *m/z* = 555 $[M + H]^+$. HRMS: calcd. for $C_{30}H_{39}O_8Si$ $[M + H]^+$: 555.2414: found: 555.2408.

5-((S,E)-4-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-hydroxybut-1-en-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (24):

The above hydrosilyl product **23** (222 mg, 0.4 mmol) was taken up in THF (3.4 mL) under Argon at rt. To the solution was added CuI (8 mg, 0.04 mmol) followed by dropwise addition of TBAF [1.0 M] solution in THF (1 mL, 1 mmol) and the resulting orange slurry was stirred for 12 h at rt. The reaction was quenched with saturated aqueous NH_4Cl and was extracted with ethyl acetate (3x10 mL). The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc, 3:2) to give **24** (151 mg, 76%) as a thick liquid. R_f = 0.3 (petroleum ether–EtOAc, 4:1); $[\alpha]_D^{20}$ = -13.1 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3447, 2989, 2929, 1734, 1606, 1575, 1457, 1311, 1281, 1208, 1159, 1034, 971, 915, 802, 700, 641 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.41 (d, *J* = 15.9 Hz, 1H), 7.36-7.23 (m, 5H), 6.72 (d, *J* = 2.7 Hz, 1H), 6.35 (d, *J* = 2.7 Hz, 1H), 6.19 (td, *J* = 15.9, 7.6 Hz, 1H), 4.60 (d, *J* = 2.3 Hz, 2H), 4.14 (td, *J* = 15.1, 7.6 Hz, 1H), 3.84 (s, 3H), 3.82-3.73 (m, 1H), 3.70-3.66 (m, 2H), 2.65 (ddd, *J* = 14.4, 6.8, 1.5 Hz, 1H), 2.40 (td, *J* = 7.6, 6.8 Hz, 1H), 1.70 (s, 6H), 1.41 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): 164.9, 160.3, 158.6, 144.0, 137.6, 131.8, 130.1, 128.4, 127.8, 127.7, 109.2, 108.6, 105.1, 103.7, 100.3, 80.9, 78.5, 73.6, 72.0, 70.9, 55.6, 37.2, 27.0, 26.9, 25.7, 25.5; MS (ESI): *m/z* = 521 $[M + Na]^+$. HRMS: calcd. for $C_{28}H_{34}O_8Na$ $[M + Na]^+$: 521.2151: found: 521.2140.

5-((S,E)-4-((4S,5S)-5-((benzyloxy)methyl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)but-1-en-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (6):

To a solution of **24** (498 mg, 1 mmol) in DCM (5.0 mL) were added i-Pr_2NEt (0.36 mL, 2 mmol) and MOMCl (0.12 mL, 1.5 mmol) at 0 °C. The mixture was stirred at room temperature for 12 h. The reaction was quenched with saturated aqueous NH_4Cl and the whole was extracted with ethyl acetate. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography (petroleum ether–EtOAc, 3:2) to give **6** (428 mg, 79%) as a yellowish thick liquid. For data see above

(S)-methyl 3-hydroxybutanoate (8):

Preparations of the *β*-hydroxy ester **8** were carried out as described by Noyori and co-workers[20] who have described the asymmetric reduction of methyl acetoacetate using a ruthenium catalyst bearing the chiral diphosphine ligand (S)-(-)-BINAP enantiomers commercially available from Aldrich Chemicals. *β*-hydroxy ester reduction was conducted on a 30 g scale in Hasteloy steel autoclave vessels using a MeOH (30 mL) solvent. The reactions were allowed to proceed at constant H_2 pressure (1500 psi) for 36 h at 25 °C. Complete conversion of the methyl acetoacetate was observed and the products were simply distilled from the crude reaction mixture. Consistent with the results of Noyori *et al*, *β*-hydroxy ester **8** was determined to be 99% enantiomerically pure. R_f = 0.2 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{20}$ = +19.6 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3424, 1735, 1440, 1379, 1296, 1175, 1087, 1007, 945, 848, 602 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 4.27-4.15 (m, 1H), 3.72 (s, 3H), 3.01-2.89 (br, 1H), 2.47 (dd, *J* = 8.3, 6.8 Hz, 2H) 1.23 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 172.8, 63.9, 51.3, 42.6, 22.3; MS (EI): *m/z* = 141 $[M + Na]^+$.

(S)-3-((tert-butyldiphenylsilyl)oxy)butan-1-ol (25):

To a solution of **8** (2.36 g, 20 mmol) in DCM (20 mL), imidazole (1.64 g, 24 mmol) and TBDPSCl (6.55 g, 24 mmol) were added at 0 °C. Then the mixture was allowed to room temperature and stirred for 3 h, after which time the reaction was quenched by adding H_2O and diluted with ethyl acetate (50 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3x100 mL). The organic layers were combined, dried over Na_2SO_4, filtered, concentrated and flash column chromatography gel (petroleum ether–EtOAc, 6:1) to obtained (S)-methyl 3-((tert-butyldiphenylsilyl)oxy)butanoate as yellow oil. R_f = 0.8 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{20}$ = +4.1 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3071, 2959, 2932, 2858, 1740, 1430, 1378, 1298, 1194, 1083, 998, 822 739, 705, 611, 509 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.72 (t, *J* = 7.1 Hz, 4H), 7.47-7.37 (m, 6H), 4.39-4.32 (m, 1H), 3.61 (s, 3H), 2.60 (dd, *J* = 14.1, 7.1 Hz, 1H), 2.43 (dd, *J* = 14.1, 6.0 Hz, 1H), 1.15 (d, *J* = 6.0 Hz, 3H), 1.07 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): 171.7, 135.7, 134.1, 133.7, 129.5, 127.4, 66.8, 51.2, 44.3, 26.8, 23.5, 19.0; MS (ESI): *m/z* = 379 $[M + Na]^+$. HRMS: calcd. for $C_{21}H_{28}O_3SiNa$ $[M + Na]^+$: 379.1699: found: 379.1697.

Diisobutylaluminium hydride (DIBAL) in hexane 2.0 M (20 mL, 40 mmol) was added dropwise under a nitrogen atmosphere at 0° C to the stirred solution of above TBDPS protected ester in dichloromethane (80 mL). Then the solution was stirred for 2 hours at room temperature. Following this, saturated ammonium chloride solution was added to the reaction mixture and dilution with diethyl ether (100 mL). The reaction solution was filtered through a Celite filter. The filtrate was dried over magnesium sulfate and the solvent was removed under reduced pressure. The residue was then separated using silica-gel column chromatography (petroleum ether–EtOAc, 1:1) to obtain alcohol **25** (3.4 g, 79 %, for two steps) as a colorless liguid. R_f = 0.4 (petroleum ether–EtOAc, 1:1); $[\alpha]_D^{20}$ = +4.3 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3381, 3070, 2961, 2931, 2857, 1468, 1427, 1378, 1109, 1027, 821, 704, 611, 507 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.79-7.65 (m,4H), 7.51-7.33 (m, 6H), 4.12 (sex, *J* = 6.0 Hz, 1H), 3.84 (ddd, *J* = 8.3, 4.5, 3.0 Hz, 1H), 3.70 (q, *J* = 5.3 Hz, 1H), 2.29-2.10 (br, 1H), 1.81 (ddd, *J* = 8.3, 5.3, 4.5 Hz, 1H), 1.65 (ddd, *J* = 10.6, 8.3, 5.3, Hz, 1H), 1.08 (d, *J* = 6.0 Hz, 3H), 1.06 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): 135.8, 135.7, 129.7, 129.6, 127.5, 68.7, 59.9, 40.6, 26.9, 23.0, 19.1; MS (ESI): *m/z* = 351 $[M + Na]^+$. HRMS: calcd. for $C_{20}H_{28}O_2SiNa$ $[M + Na]^+$: 351.1751: found: 351.1744.

(S)-5-((3-(((tert-butyldiphenylsilyl)oxy)butyl)thio)-1-phenyl-1H-tetrazole (26):

Add Diisopropyl azodicarboxylate (2.6 mL, 13 mmol) to the stirred solution of alcohol **25** (3.28 g, 10 mmol) and PPh_3 (3.15 g, 12 mmol) in THF (30 mL) at –20 °C. Then add PTSH (1-phenyl-5-mercapto-1*H*-tetrazole) (2.31 g, 13 mmol) in THF (30 mL) to the reaction mixture and stir the reaction mixture for 30 min at 0 °C, poured into water and extracted with ethyl acetate(3x30 mL). The organic layer was washed with saturated $NaHCO_3$ solution and brine, dried with anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether–EtOAc, 6:1) to obtain sulfide **26** (4.4 g, 90%) as a white solid. R_f = 0.5 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{27}$ = +3.4 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 2958, 2929, 1494, 1464, 1355, 1108, 1075, 1018, 977, 823, 764, 702, 612, 509 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.73-7.26 (m, 4H), 7.59-7.49 (m, 5H), 7.45-7.29 (m, 6H), 4.00 (sex, *J* = 6.0 Hz, 1H), 3.52-3.33 (m, 2H), 1.97 (td, *J* = 7.6, 6.3 Hz, 2H), 1.12 (d, *J* = 6.3 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): 135.8, 135.8, 129.7, 129.9, 129.6, 127.6, 129.5, 127.6, 68.0, 38.3, 29.4, 26.9, 23.1, 19.2; MS (ESI): *m/z* = 511 $[M + Na]^+$. HRMS: calcd. for $C_{27}H_{32}N_4OSSiNa$ $[M + Na]^+$: 511.1958: found: 511.1939.

(S)-5-((3-(((tert-butyldiphenylsilyl)oxy)butyl)sulfonyl)-1-phenyl-1H-tetrazole (7):

To a solution of the above sulfide **26** (976 mg, 2 mmol) in CH_2Cl_2 (10 mL) at 0 °C was added *m*-CPBA (1.03 g, 6 mmol). The reaction mixture was stirred at room temperature for 3 h and the reaction mixture was poured into $Na_2S_2O_3$ solution (10 %) and extracted with ethyl acetate (3x50 mL). The organic layer was washed with saturated $NaHCO_3$ solution and the organic layers were combined, dried over Na_2SO_4, filtered, concentrated and flash column chromatography (petroleum ether–EtOAc, 6:1) was obtained sulfone **7** (884 mg, 85%) as pale yellow thick liquid. R_f = 0.6 (petroleum ether–EtOAc, 9:1); $[\alpha]_D^{27}$ = -2.2 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 3071, 2960, 2931, 2857, 1497, 1427, 1343, 1151, 1108, 1074, 1017, 822, 763, 616, 507 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.73-7.64 (m, 5H), 7.63-7.52 (m, 4H), 7.48-7.33 (m, 6H), 4.09-4.02 (m, 1H), 3.92-3.83 (m, 1H), 3.78-3.69 (m, 1H), 2.14-1.97 (m, 2H), 1.12 (d, *J* = 6.3 Hz, 3H), 1.05 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): 153.3, 135.7, 134.4, 133.8, 133.3, 131.3, 129.8, 129.7, 129.6, 127.7, 127.5, 125.0, 67.2, 52.5, 31.0, 26.9, 22.8, 19.1; MS (ESI): *m/z* = 543 $[M + Na]^+$. HRMS: calcd. for $C_{27}H_{32}N_4O_3SSiNa$ $[M + Na]^+$: 543.1857: found: 543.1842.

5-((S,E)-4-((4S,5S)-5-((S,E)-4-((tert-butyldiphenylsilyl)oxy)pent-1-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)but-1-en-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (27):

To the stirred solution of alcohol **20** (180 mg, 0.40 mmol) in ethyl acetate (5 mL) was added IBX (370 mg, 0.6 mmol) at rt, then heat the reaction mixture at 85 °C reflux for 3 h and check TLC for the completion of reaction. After completion of reaction, quench with saturated aqueous $NaHCO_3$ (20 mL) and the mixture stirred for 30 min. The organic layer was extracted with ethyl acetate (3x20mL), dried over $MgSO_4$ and rotary evaporated to give the corresponding aldehyde **21** as a colourless oil. R*f* 0.35 (petroleum ether–EtOAc, 1:1)**.** This aldehyde used for further reaction without purification.

A solution of sulfone **7** (240 mg, 0.46 mmol) in THF (5 mL) was cooled -78 °C and KHMDS 0.5M solution in toluene (1.38 mL, 0.69 mmol) was added dropwise to the reaction mixture. After stirring for 30 minutes at -78 °C, above prepared aldehyde

21 (175 mg, 0.4 mmol) in THF (5 mL) was added to the reaction mixture at -78 °C. The resulting mixture was stirred at -78 °C for 3 h before saturated aqueous NH_4Cl (10 mL) was added. The resulting phases were separated and the aqueous layer was extracted with EtOAc (3x25 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and the solvents were evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel (petroleum ether–EtOAc, 7:3) to obtain *trans*-olefin **27** (255 mg, 86% based on recovery of aldehyde, 9:1= *E: Z*) as a colorless thick liquid. R_f = 0.3 (petroleum ether–EtOAc, 4:1); $[\alpha]_D^{27}$ = - 67 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} =2958, 2926,2856, 1729, 1605, 1574, 1460, 1378, 1275, 1206, 1158, 1111, 1069, 1034, 970, 916, 822, 704, 611, 512, 451 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.69-7.64 (m, 4H), 7.48 (d, *J* = 15.7 Hz, 1H), 7.43-7.33 (m, 6H), 6.74 (d, *J* = 2.6 Hz, 1H), 6.34 (d, *J* = 2.4 Hz, 1H), 6.20 (dt, *J* = 15.7, 7.3 Hz, 1H), 5.79 (td, *J* = 15.0, 7.3 Hz, 1H), 5.48 (dd, *J* = 15.0, 7.6 Hz, 1H), 4.72 (ABq, *J* = 6.7 Hz, 2H), 4.40 (t, *J* = 7.9 Hz, 1H), 3.94-3.84 (m, 3H), 3.88 (s, 3H), 3.36 (s, 3H), 2.60-2.44 (m, 2H), 2.33-2.17 (m, 2H), 1.70 (s, 3H), 1.69 (s, 3H), 1.41 (s, 3H), 1.40 (s, 3H), 1.06 (d, *J* = 6.3 Hz, 1H), 1.04 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): 164.7, 160.0, 158.7, 143.7, 135.8, 134.5, 134.3, 132.0, 130.8, 130.7, 130.6, 130.2, 129.5, 129.4, 128.7, 127.5, 127.4, 108.6, 108.3, 104.9, 103.6, 100.1, 82.0, 78.4, 76.6, 69.0, 55.7, 55.5, 42.3, 35.1, 27.0, 26.9, 26.8, 25.7, 25.5, 22.8, 19.4; MS (ESI): *m/z* = 767 $[M + Na]^+$. HRMS: calcd. for $C_{43}H_{56}O_9SiNa$ $[M + Na]^+$: 767.3591: found: 767.3637.

5-((S,E)-4-((4S,5S)-5-((S,E)-4-hydroxypent-1-en-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)-4-(methoxymethoxy)but-1-en-1-yl)-7-methoxy-2,2-dimethyl-4H-benzo[d][1,3]dioxin-4-one (28):

The compound **27** (224 mg, 0.3 mmol) was dissolved in THF (10 mL), and then TBAF [1.0 M] solution in THF (2.4 mL, 2.4 mmol)] was added to this solution at 0 °C. Stir the mixture at rt for 24 h. the reaction was quenched with saturated aqueous NH_4Cl and the whole was extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography on silica gel (petroleum ether–EtOAc, 2:3) to give **28** (124 mg, 82%) as a colorless oil. R_f = 0.3 (petroleum ether–EtOAc, 1:1); $[\alpha]_D^{27}$ = +56 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 2924, 2854, 1727, 1605, 1573, 1456, 1376, 1277, 1205, 1159, 1033, 970, 916, 743, 561, 512 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 7.48 (d, *J* = 15.6 Hz, 1H), 6.75 (d, *J* = 2.4 Hz, 1H), 6.35 (d, *J* = 2.4 Hz, 1H), 6.19 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.92 (d, *J* = 15.4, 7.2 Hz, 1H), 5.65 (dd, *J* = 15.4, 7.9 Hz, 1H), 4.75 (ABq, *J* = 6.7 Hz, 2H), 4.48 (t, *J* = 8.0 Hz, 1H), 3.96-3.90 (m, 1H), 3.90-3.86 (m, 2H), 3.85 (s, 3H), 3.39 (s, 3H), 2.63-2.50 (m, 2H), 2.33-2.20 (m, 2H), 2.09-2.00 (br, 1H), 1.71 (s, 3H), 1.70 (s, 3H), 1.42 (s, 6H), 1.21 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 164.7, 160.1, 158.7, 143.6, 132.2, 131.0, 130.8, 130.4, 108.6, 108.3, 104.9, 103.5, 100.2, 96.6, 81.7, 78.2, 76.2, 67.0, 55.7, 55.5, 41.9, 35.1, 27.0, 26.8, 25.6, 25.4, 22.8; MS (ESI): *m/z* = 529 $[M + Na]^+$. HRMS: calcd. for $C_{27}H_{38}O_9Na$ $[M + Na]^+$: 529.2414: found: 529.2427.

(3aS,4E,7S,14E,17S,17aS)-10-hydroxy-12-methoxy-17-(methoxymethoxy)-2,2,7-trimethyl-6,7,17,17a-tetrahydro-3aH-benzo[c][1,3]dioxolo[4,5-i][1]oxacyclotetradecin-9(16H)-one (29):

A solution of alcohol **28** (101 mg, 0.2 mmol) in anhydrous THF (5 mL) was added to a suspension of 60% NaH in mineral oil (40 mg, 1 mmol) in THF (1 mL) at 0 °C and the mixture was stirred for 2 h at rt, then quenched with saturated NH_4Cl. The organic phase was extracted with EtOAc (3x20 mL), washed with brine, dried over $MgSO_4$ and concentrated. The crude product was purified by column chromatography on silica gel (petroleum ether–EtOAc, 7:3) to afford compound **29** (76 mg, 85%) as a colorless thick liquid. R_f = 0.4 (petroleum ether–EtOAc, 4:1); $[\alpha]_D^{27}$ = -80.2 (*c* = 1.0, $CHCl_3$). IR (KBr) ν_{max} = 2924, 2854, 1711, 1649, 1548, 1458, 1377, 1315, 1253, 1210, 1116, 1035, 967, 921, 743, 631, 508, 484 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): 11.54 (s, 1H), 7.17 (dd, *J* = 15.4, 2.0 Hz, 1H), 6.46 (d, *J* = 2.6 Hz, 1H), 6.40 (d, *J* = 2.6 Hz, 1H), 5.99 (ddd, *J* = 15.4, 8.4, 7.0 Hz, 1H), 5.72 (ddd, *J* = 15.4, 10.7, 3.1 Hz, 1H), 5.54 (dd, *J* = 15.4, 8.4, 1.2 Hz, 1H), 5.45-5.38 (m, 1H), 4.48 (d, *J* = 6.7 Hz, 1H), 4.73 (d, *J* = 6.7 Hz, 1H), 4.63(t, *J* = 8.0 Hz, 1H), 4.15 (ddd, *J* = 12.4, 5.2, 1.8 Hz, 1H), 3.89 (dd, *J* = 7.8, 2.0 Hz, 1H), 3.82 (s, 3H), 3.44 (s, 3H), 2.57-2.41 (m, 2H), 2.37-2.26 (m, 2H), 1.44 (d, *J* = 6.4 Hz, 3H), 1.41 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): 170.8, 164.7, 163.9, 142.1, 133.7, 132.4, 128.9, 127.2, 108.5, 107.1, 104.3, 100.1, 97.2, 81.6, 75.5, 74.2, 70.8, 55.5, 55.3, 38.0, 36.6, 27.1, 26.6, 19.5; MS (ESI): *m/z* = 471 $[M + Na]^+$. HRMS: calcd. for $C_{24}H_{32}O_8Na$ $[M + Na]^+$: 471.1995: found: 471.2019.

(3S,5E,7S,8S,9S,11E)-7,8,9,16-tetrahydroxy-14-methoxy-3-methyl-3,4,7,8,9,10-hexahydro-1H-benzo[c][1]oxacyclotetradecin-1-one (zeaenol) (1):

HCl (2N, 10 mL) was added to a solution of macrolide **29** (68 mg, 0.15 mmol) in THF (10 mL) and the mixture was stirred for 24 h, quenched with saturated aqueous $NaHCO_3$ solution, and extracted with EtOAc. The organic layers were combined and dried with anhydrous $MgSO_4$, filtered, and concentrated under reduced vacuum. The crude product was purified by flash column chromatography (MeOH–DCM, 1:19) to yield zeaenol **1** as a white crystalline solid (51 mg, 94%). m.p. 196-199° C. R_f = 0.3 (MeOH–DCM, 1:19); $[\alpha]_D^{27}$ = -87 (*c* = 0.5, MeOH). IR (KBr) ν_{max} = 3675, 3424, 2958, 2925, 2855, 1727, 1607, 1572, 1422, 1355, 1314, 1258, 1208, 1159, 1072, 967, 830, 740, 701, 629, 556.485. cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 11.89 (s, 1H), 7.10 (d, *J* = 15.4 Hz, 1H), 6.44 (d, *J* = 2.6 Hz, 1H), 6.38 (d, *J* = 2.6 Hz, 1H), 5.97 (td, *J* = 15.4, 6.1 Hz, 1H), 5.84 (ddd, *J* = 15.3, 10.4, 3.4 Hz, 1H), 5.69 (dd, *J* = 15.4, 7.5 Hz, 1H), 5.36-5.28 (m, 1H), 4.25 (t, *J* = 7.8 Hz, 1H), 3.95 (t, *J* = 6.7 Hz, 1H), 3.81 (s, 3H), 3.88-3.72 (br, 1H), 3.59 (d, *J* = 7.9 Hz, 1H), 2.64-2.41 (br, 2H), 2.61-2.45 (m, 2H), 2.44-2.25 (m, 2H), 1.44 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$+CD_3OD-1:1): 170.9, 164.9, 163.7, 142.7, 133.4, 131.7, 129.0, 128.7, 107.3, 104.0, 100.0, 77.2, 72.4, 71.4, 55.4, 37.5, 35.8, 19.3, 12.4; MS (ESI): *m/z* = 387 $[M + Na]^+$. HRMS: calcd. for $C_{19}H_{24}O_7Na$ $[M + Na]^+$: 387.1420: found: 387.1442.

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Supporting Information

Convergent and Stereoselective Synthesis of Zeaenol

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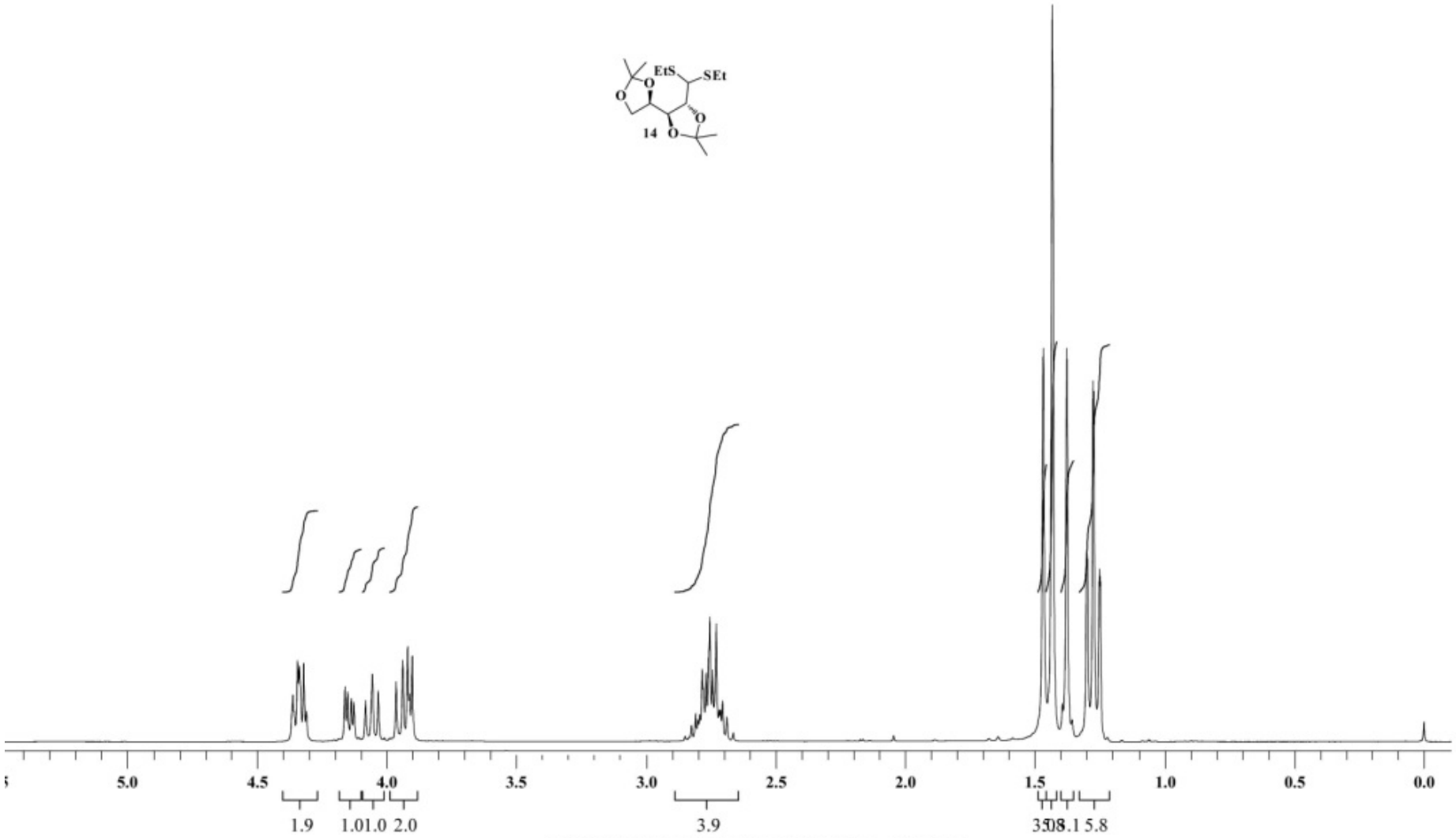
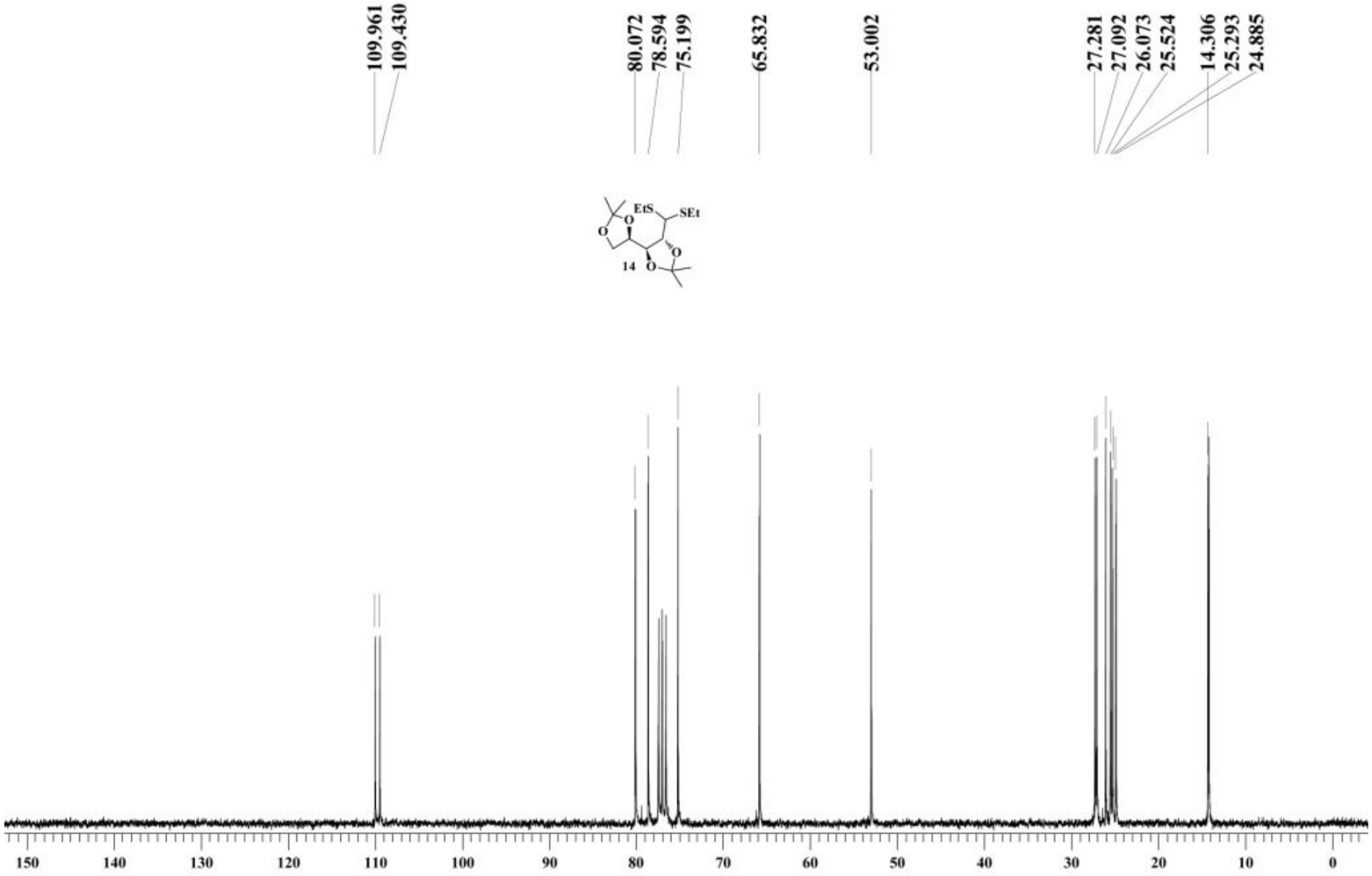
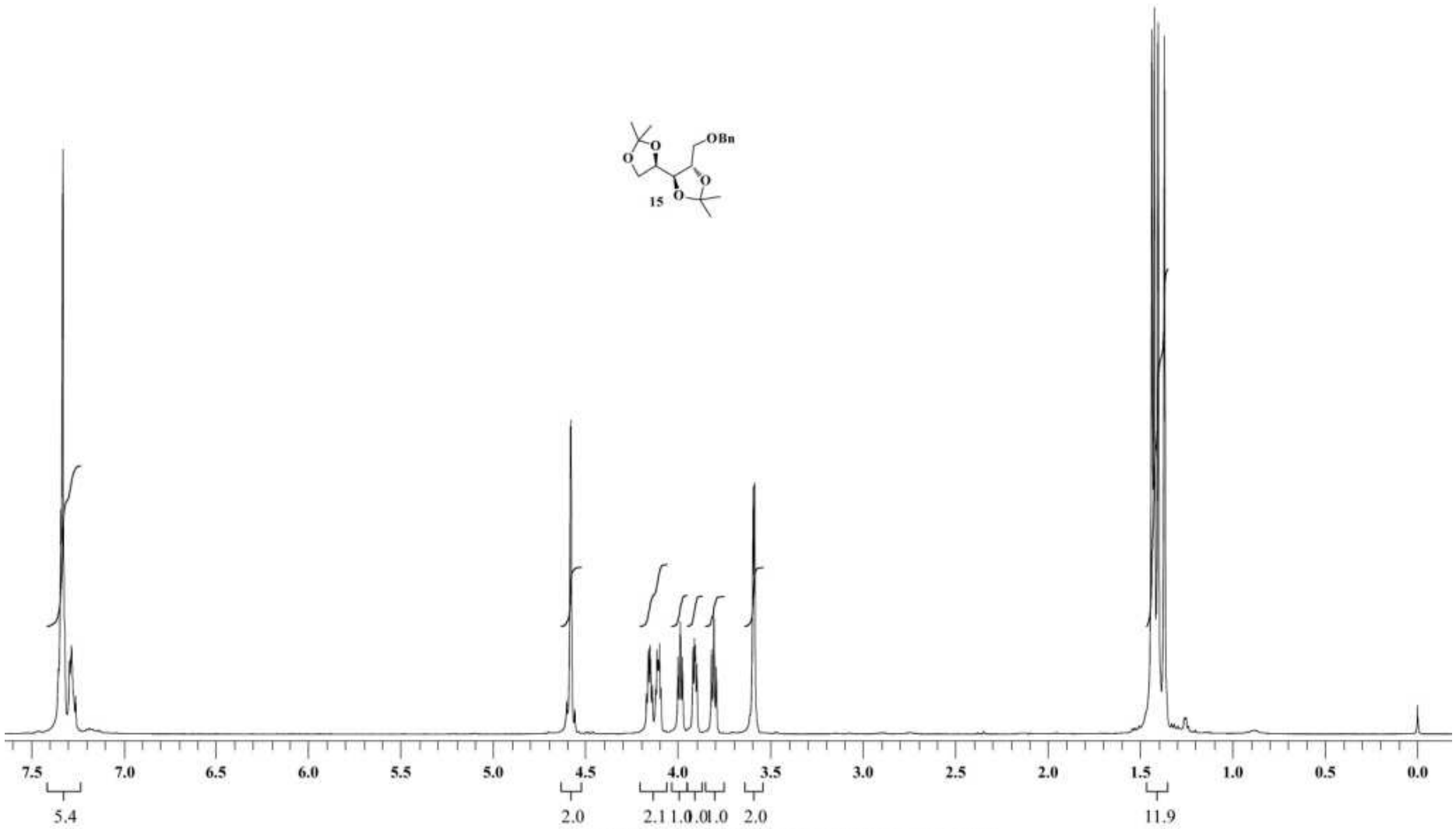
2. ^{1}H NMR and ^{13}C NMR Spectra of All New Compounds S2 – S43



1H NMR SPECTRUM (300MHz, CDCl3)



13C NMR SPECTRUM (75MHz, CDCl3)



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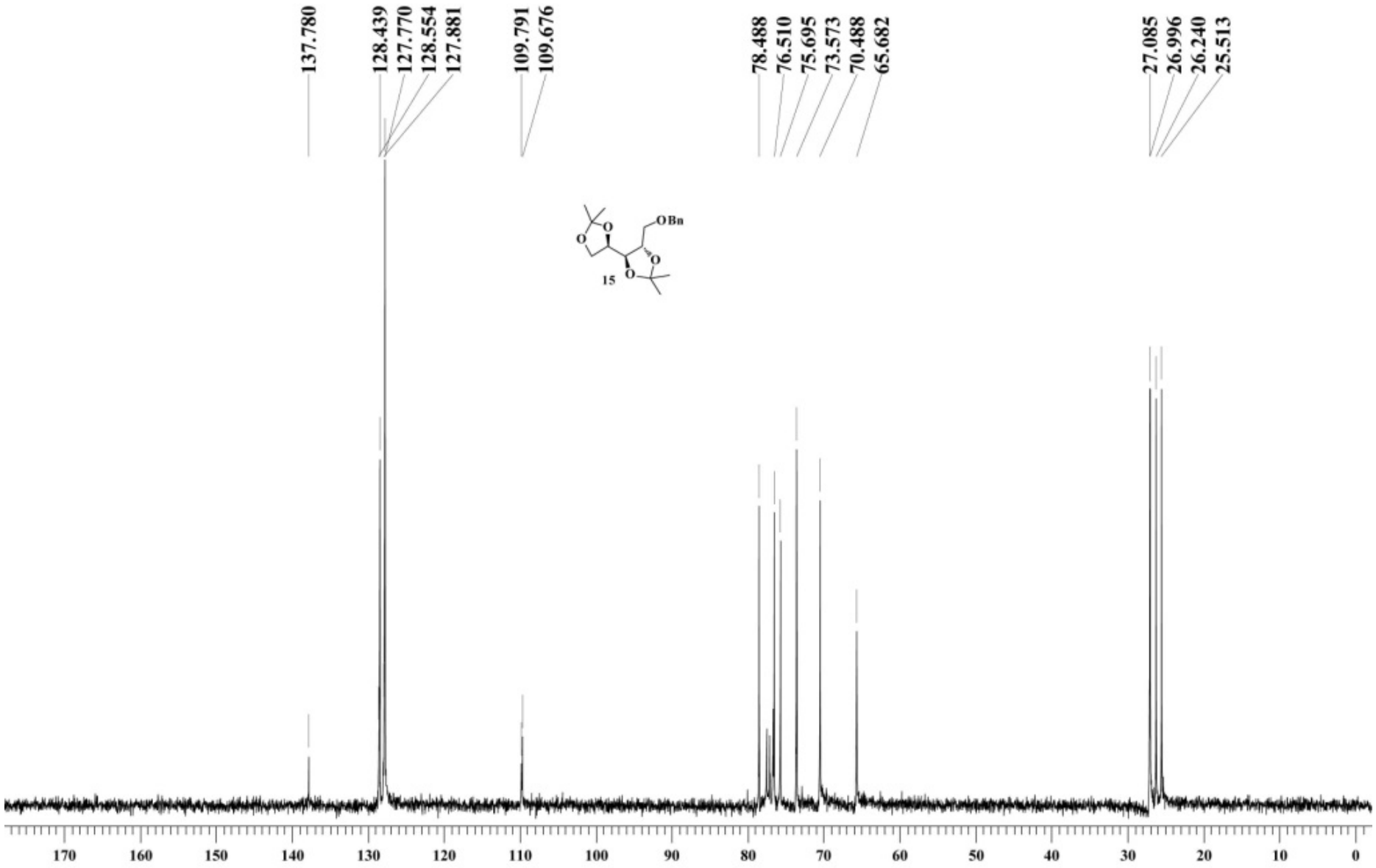

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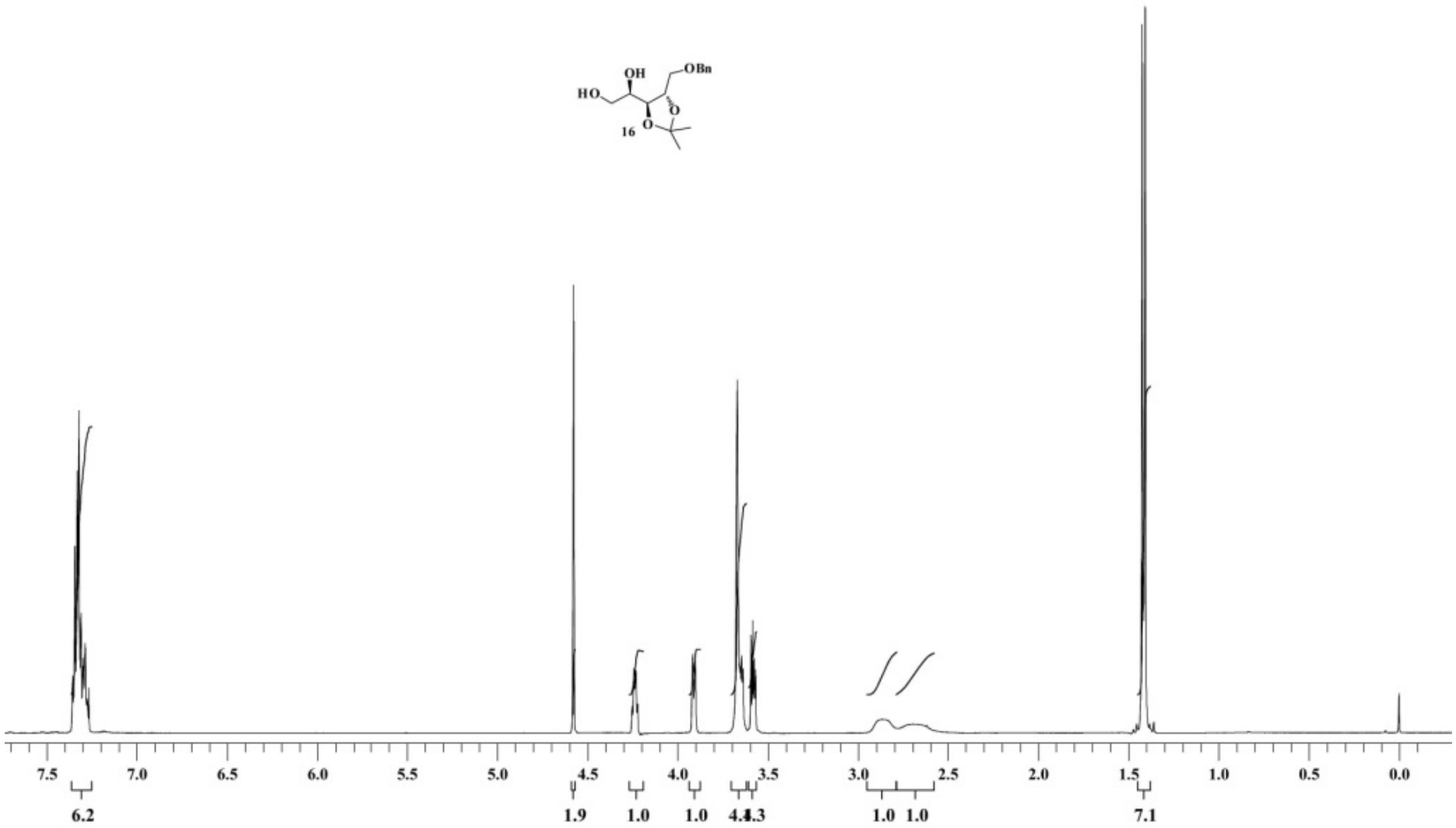

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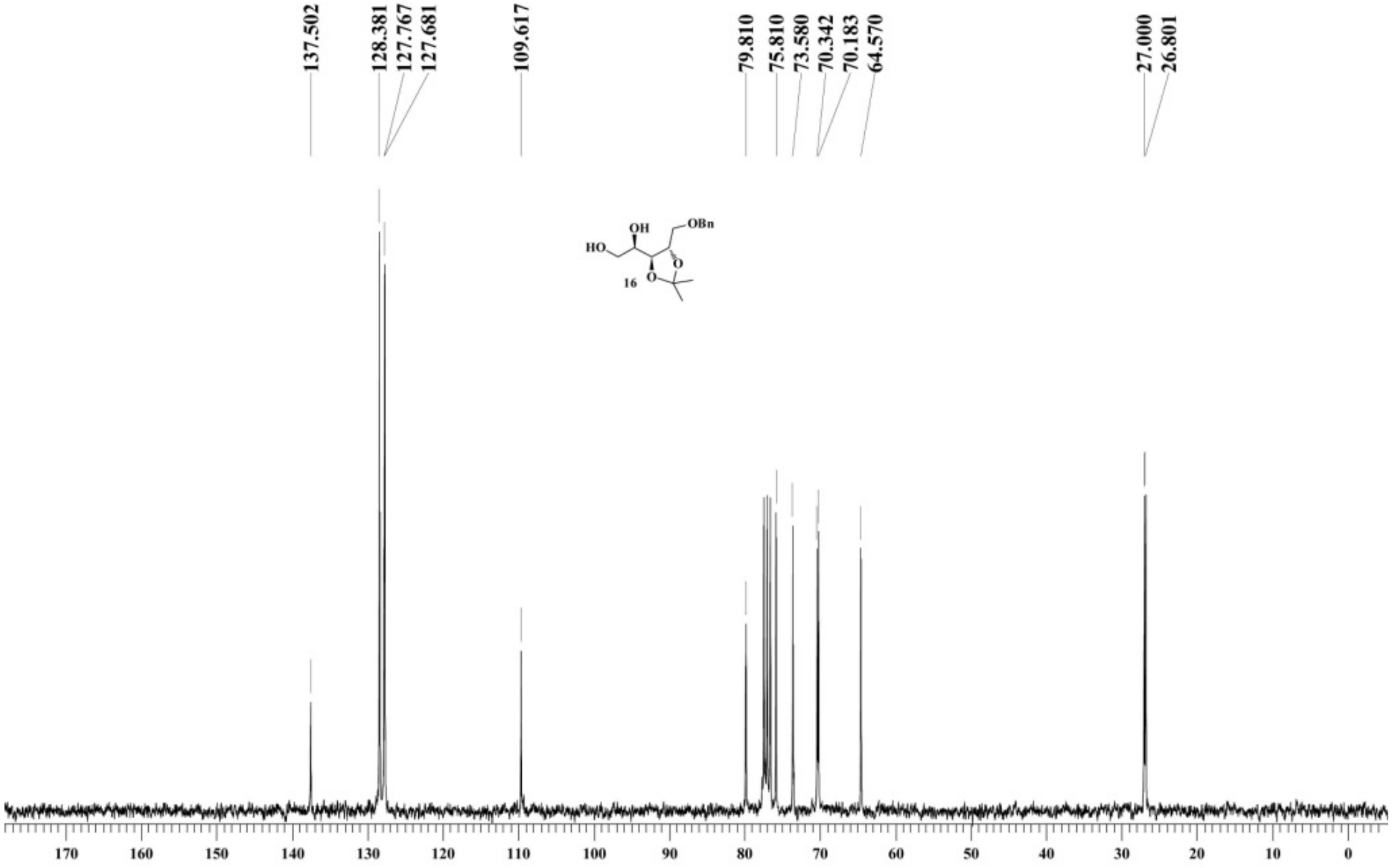

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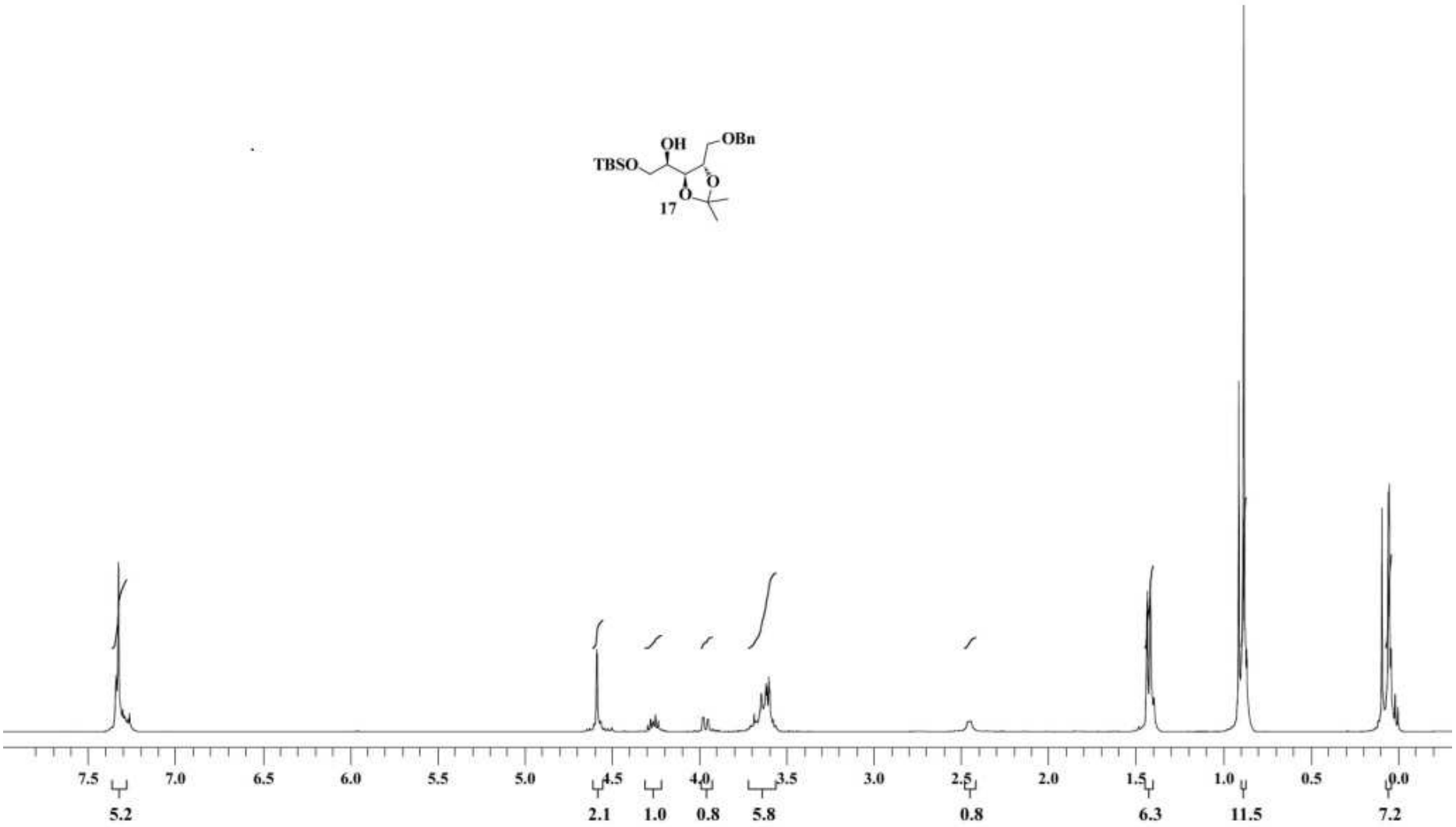

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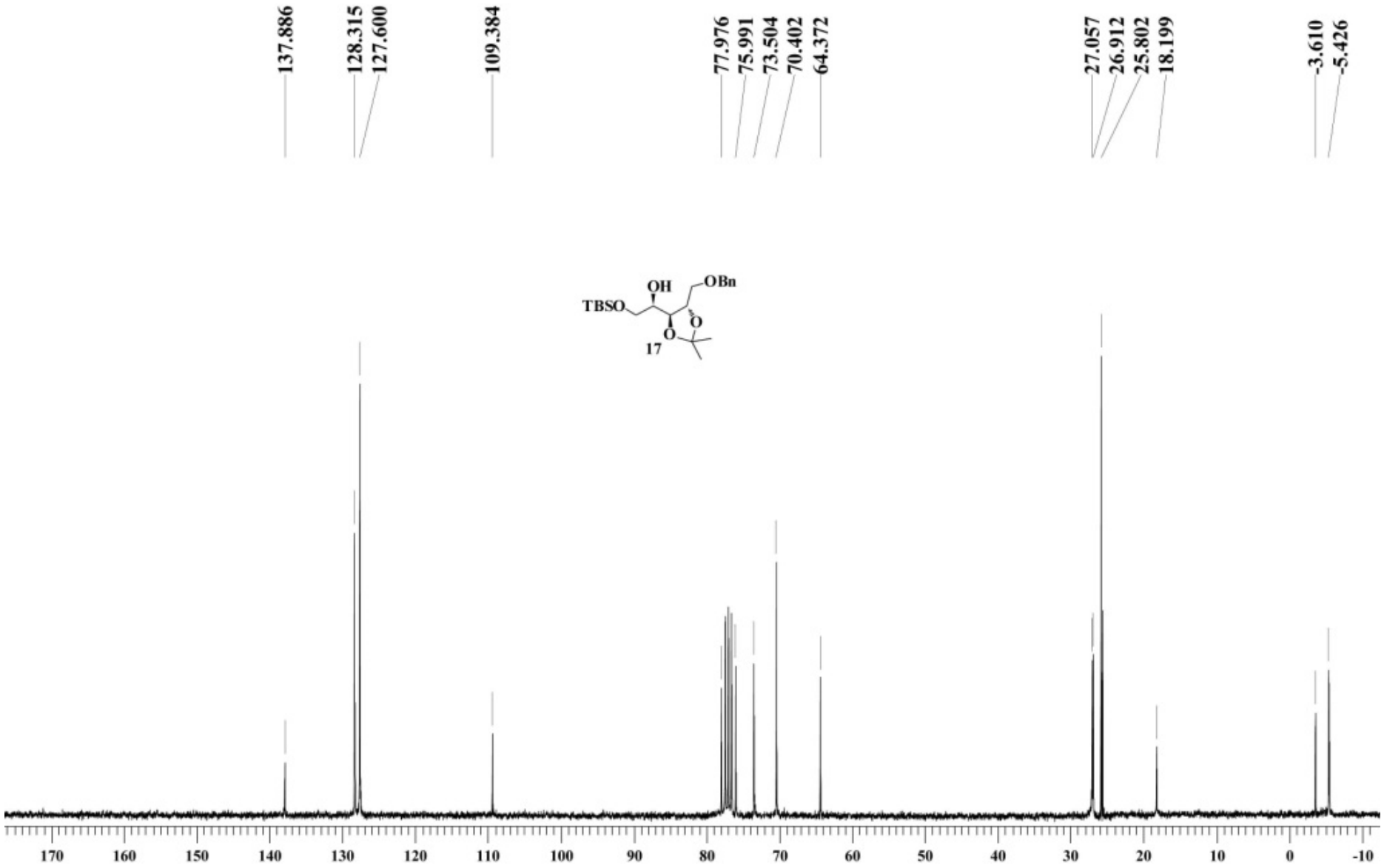

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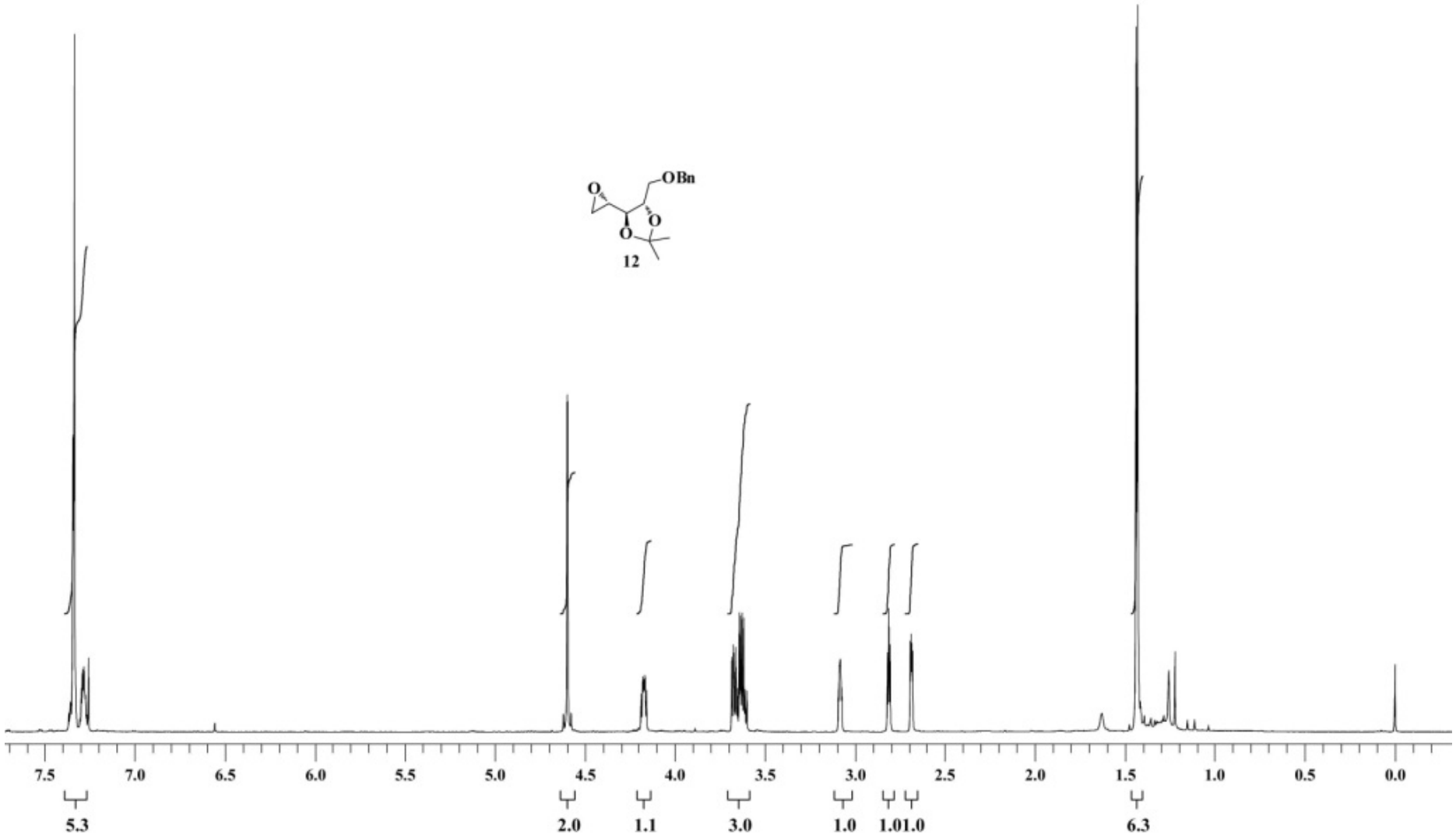

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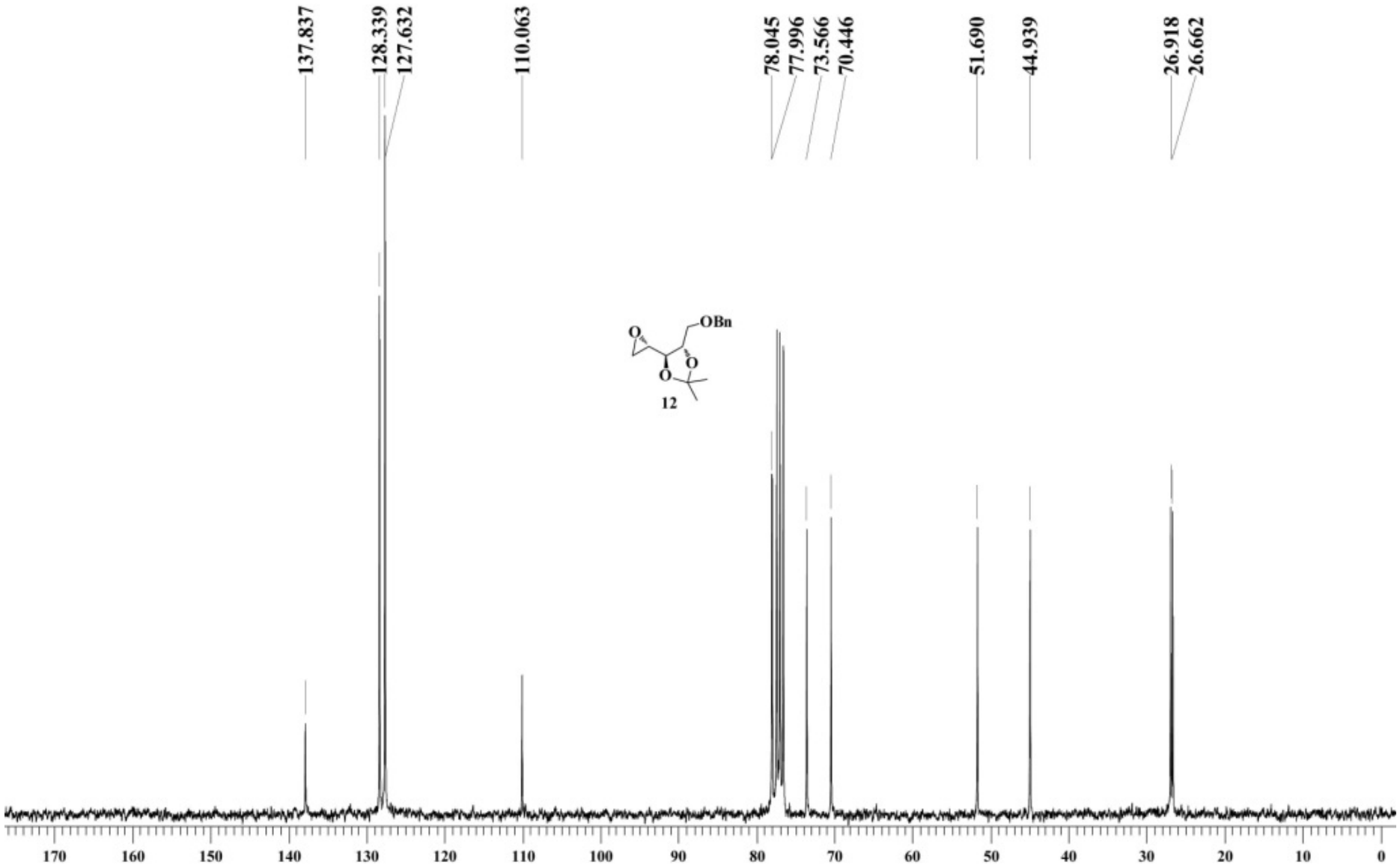

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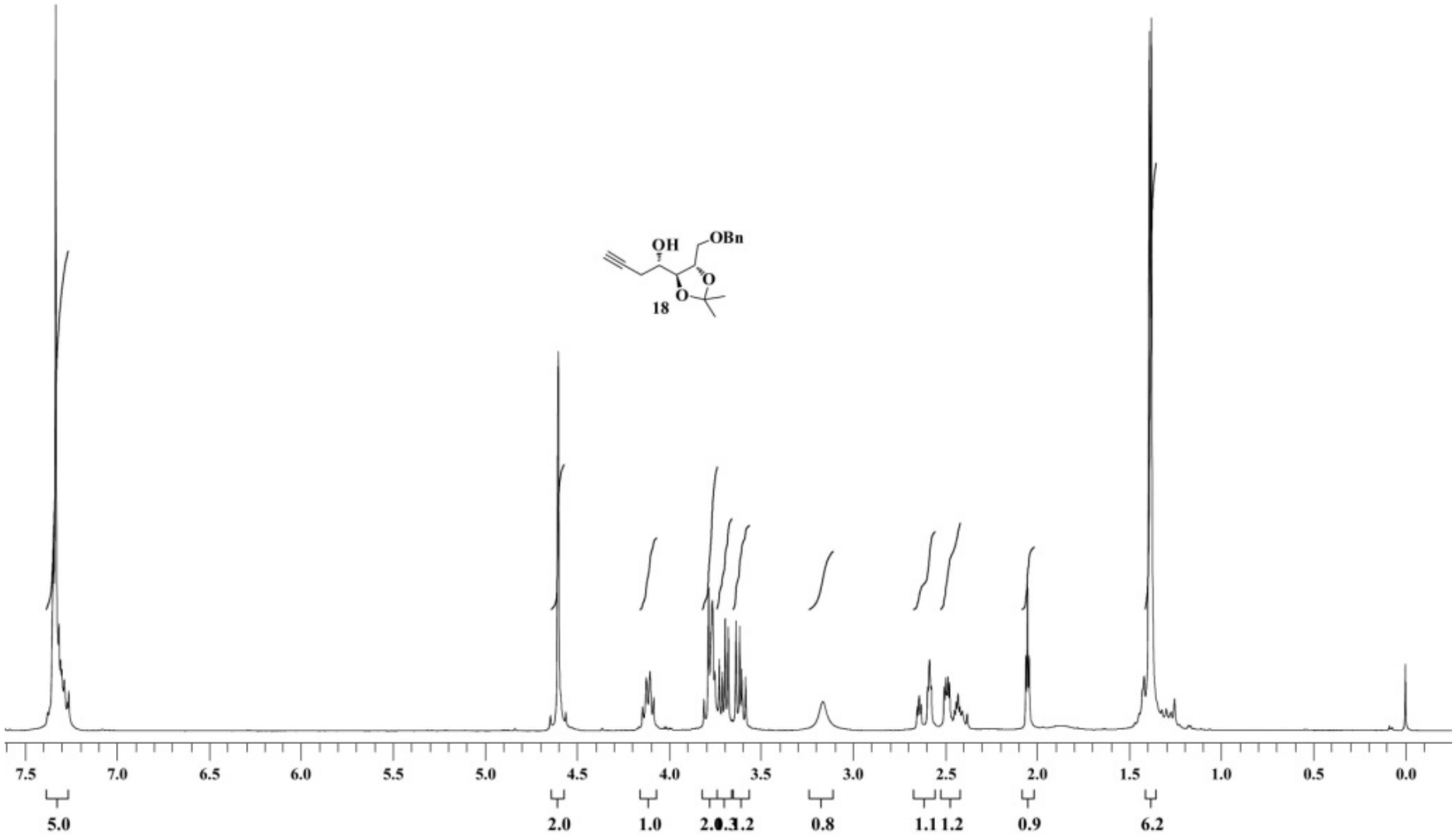

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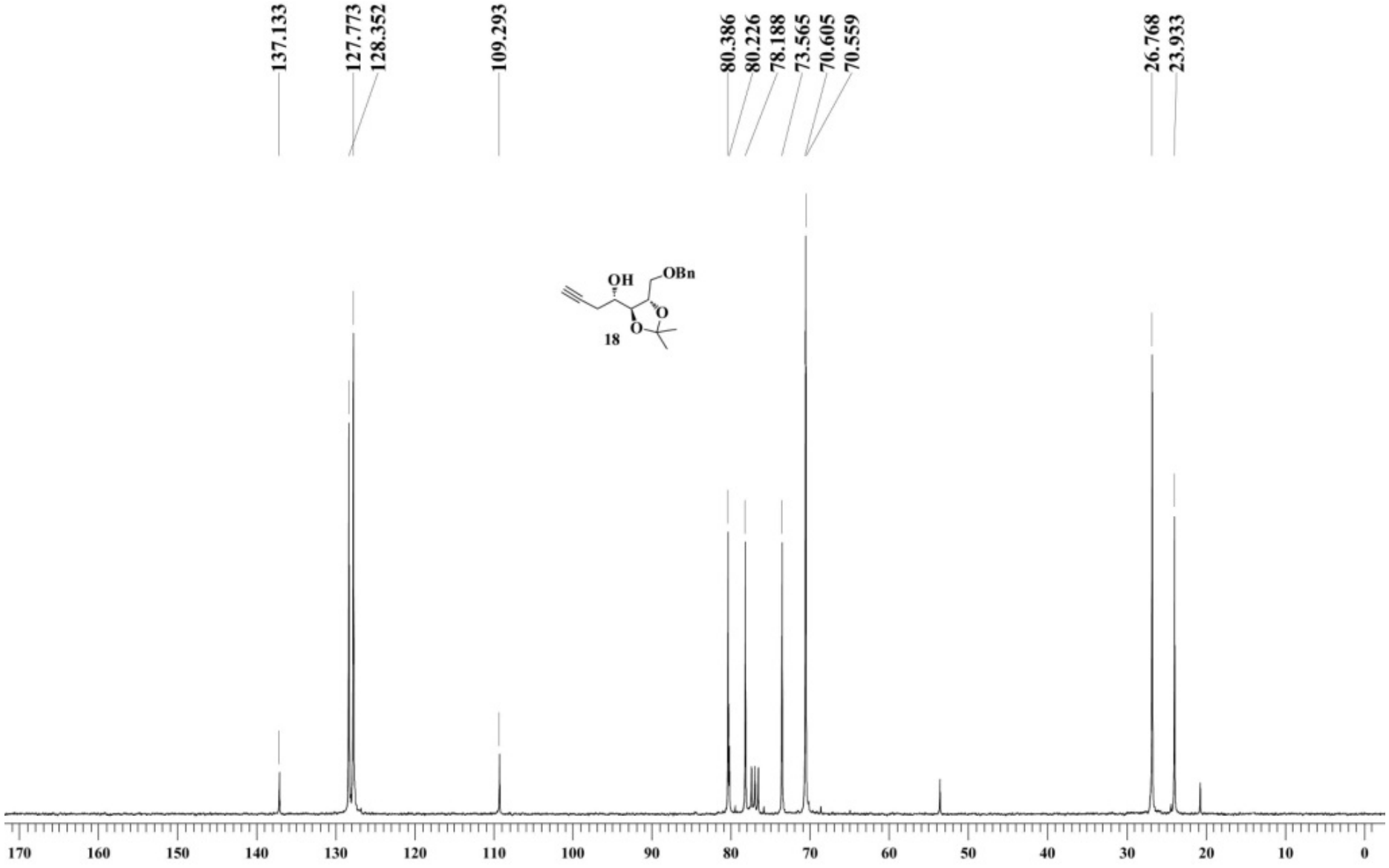

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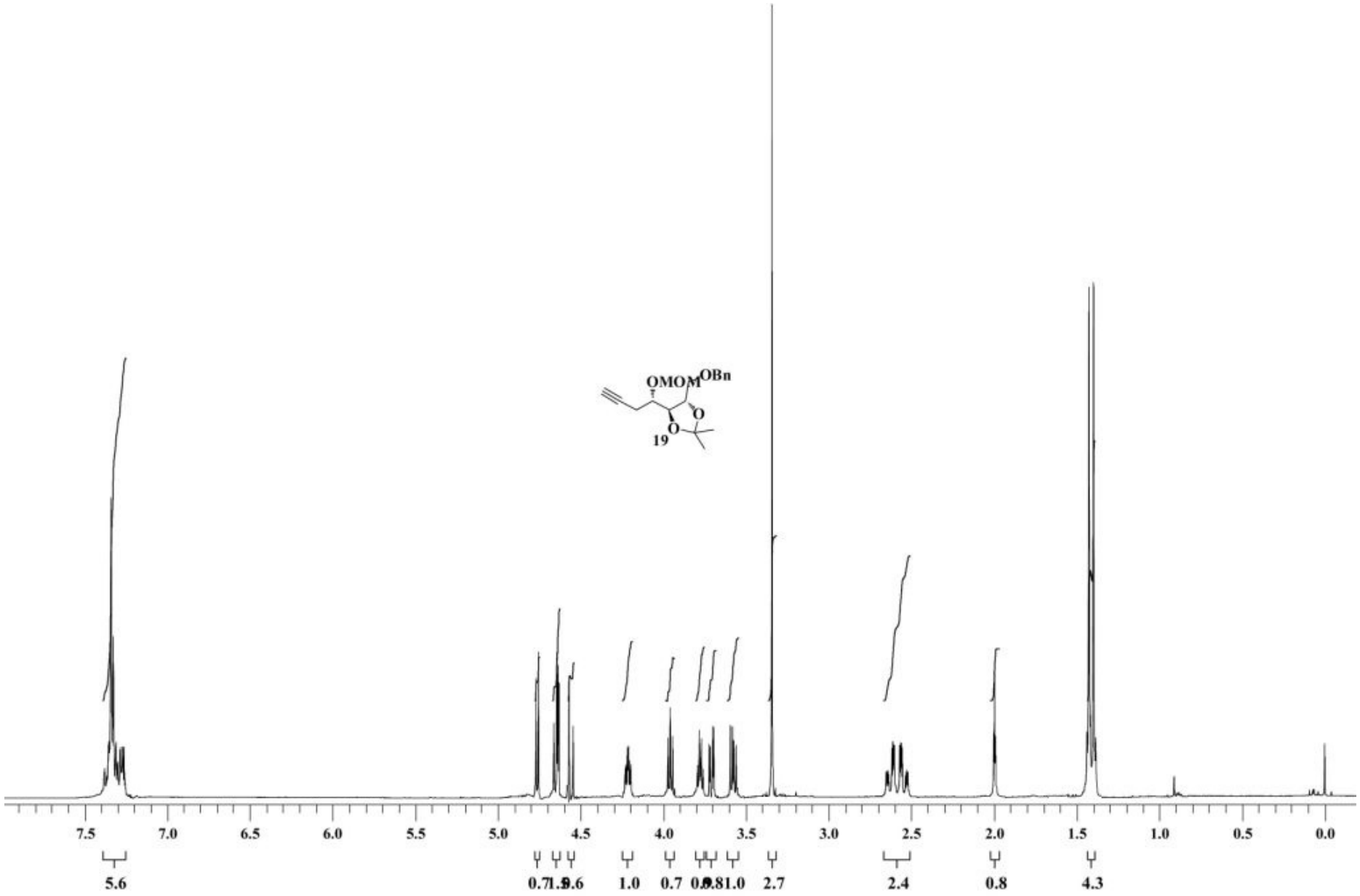

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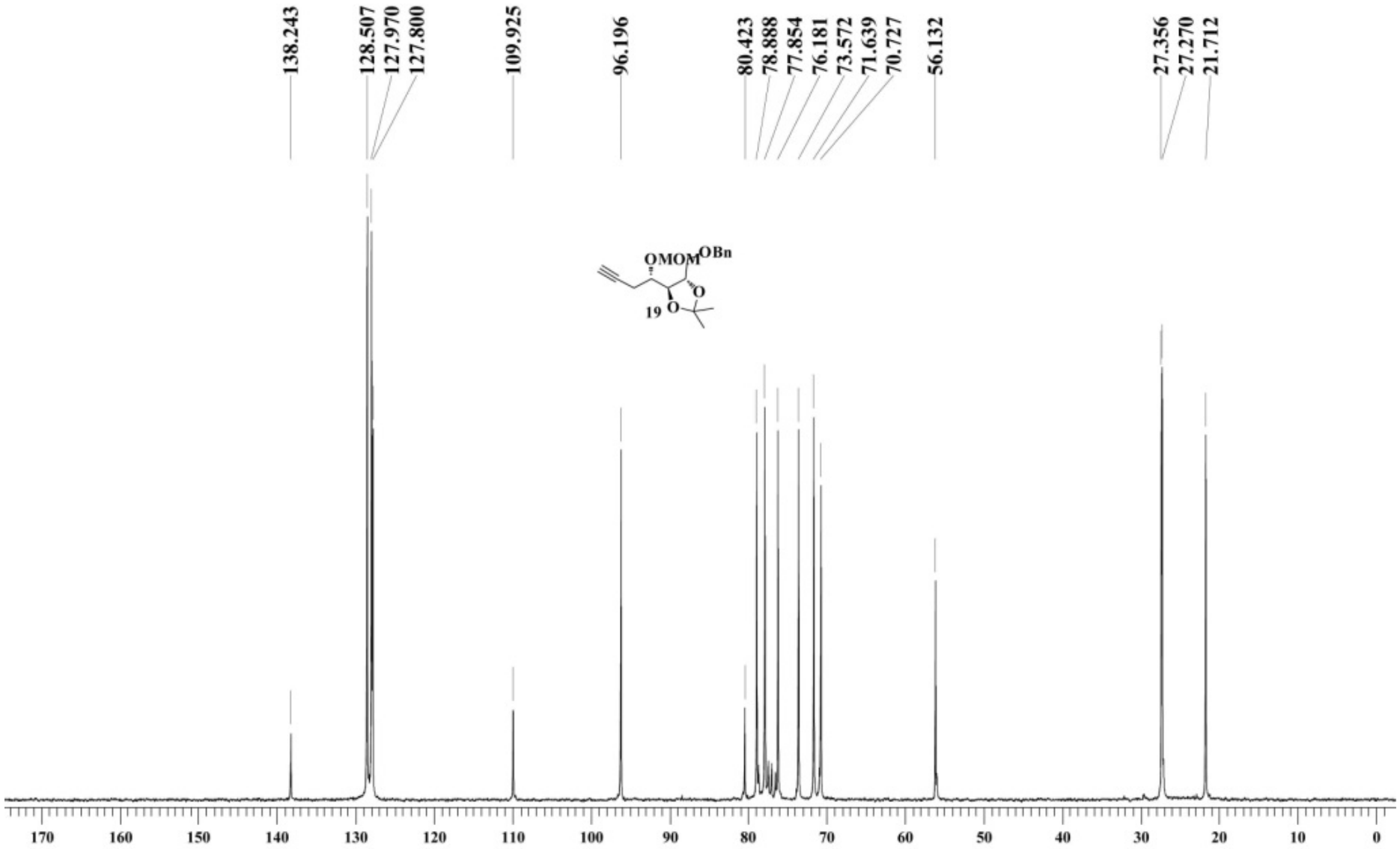

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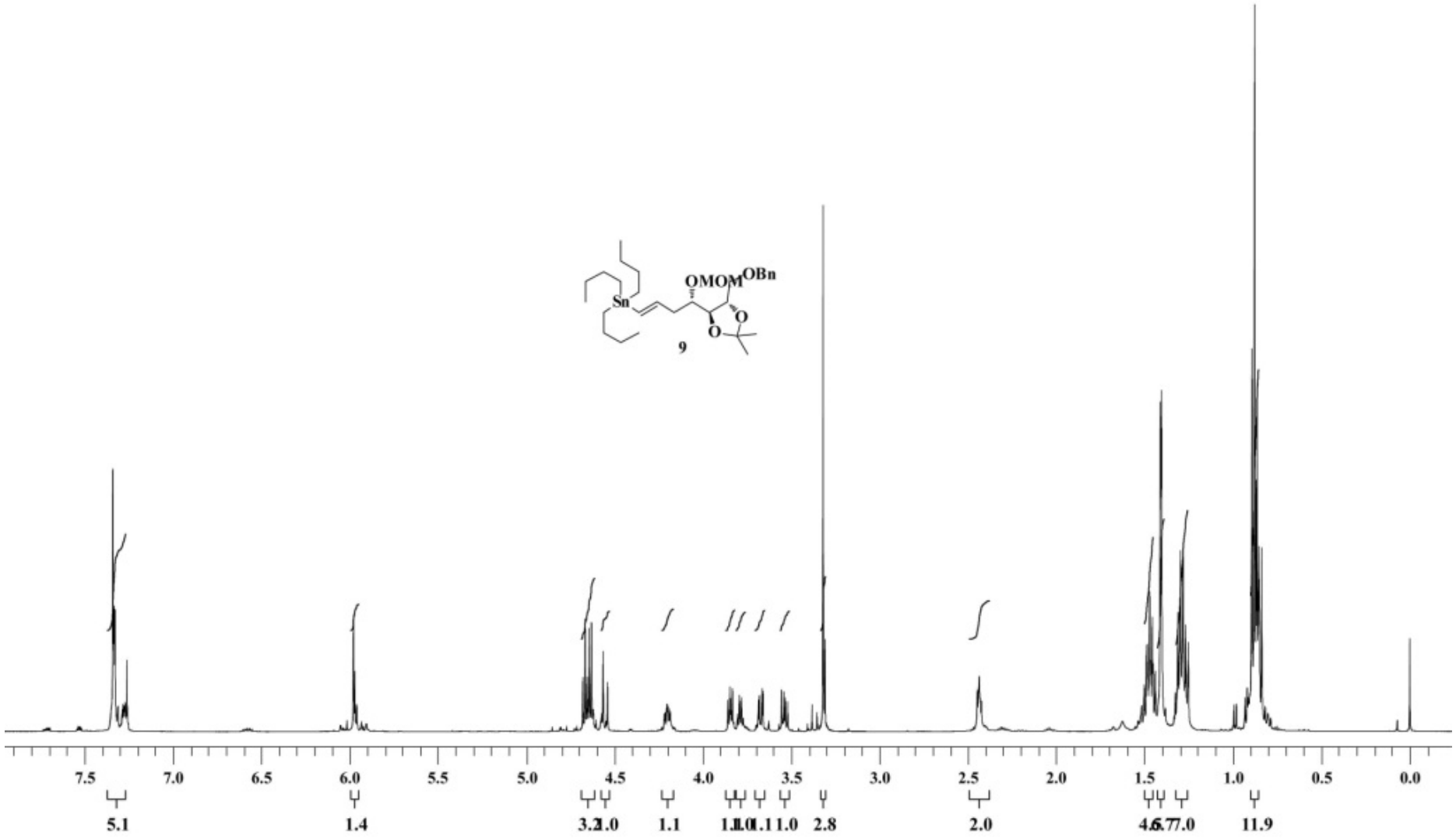

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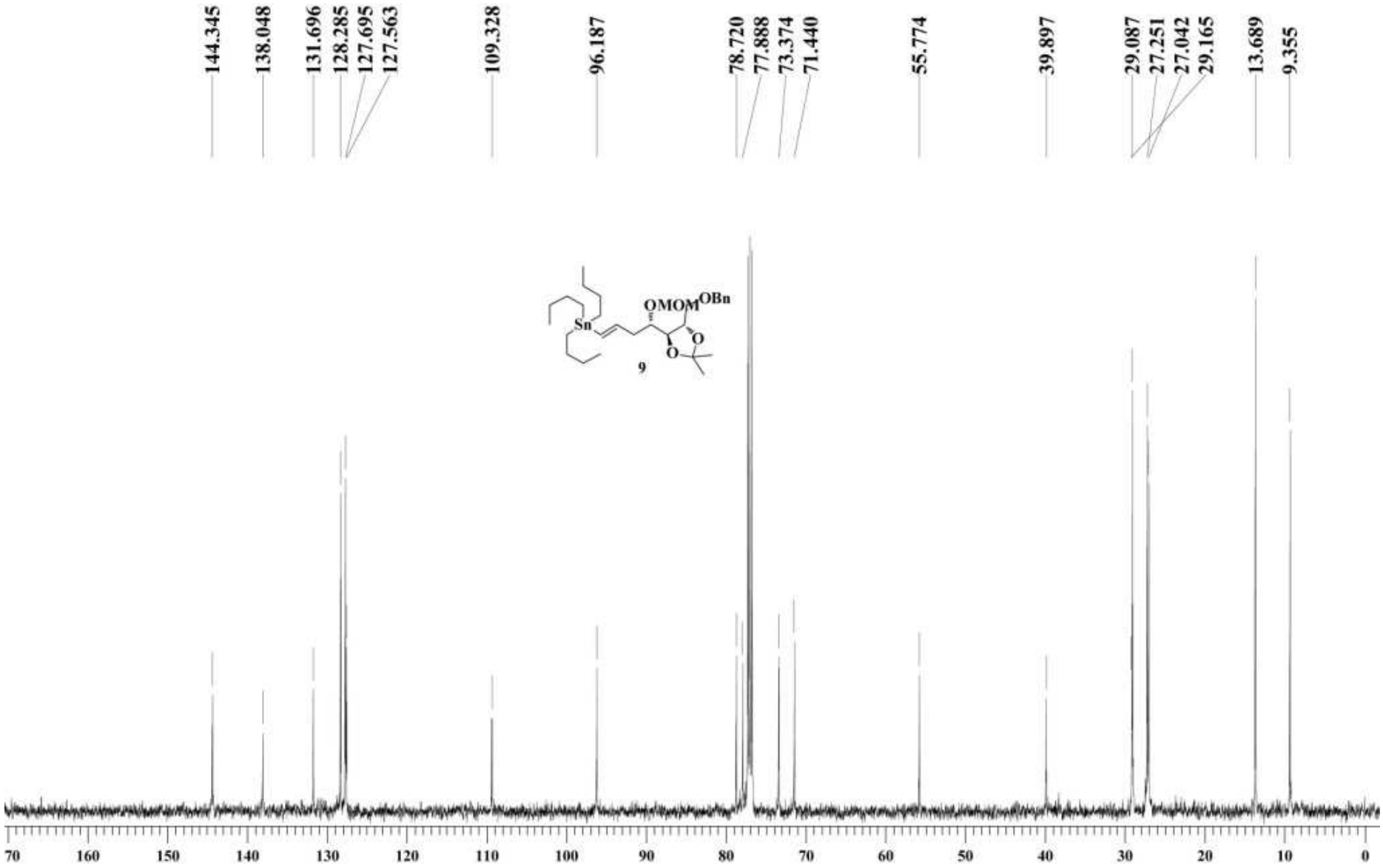

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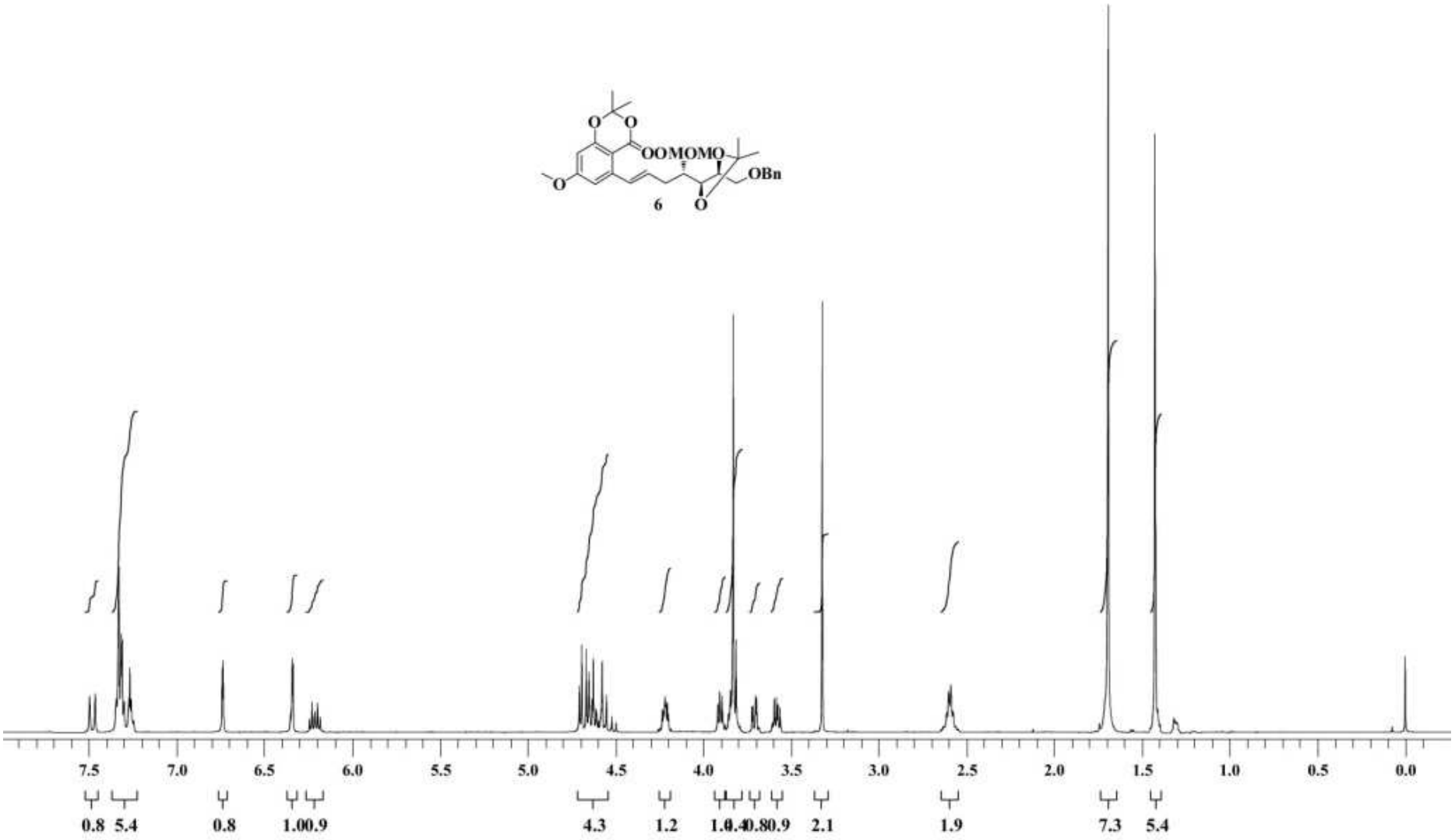

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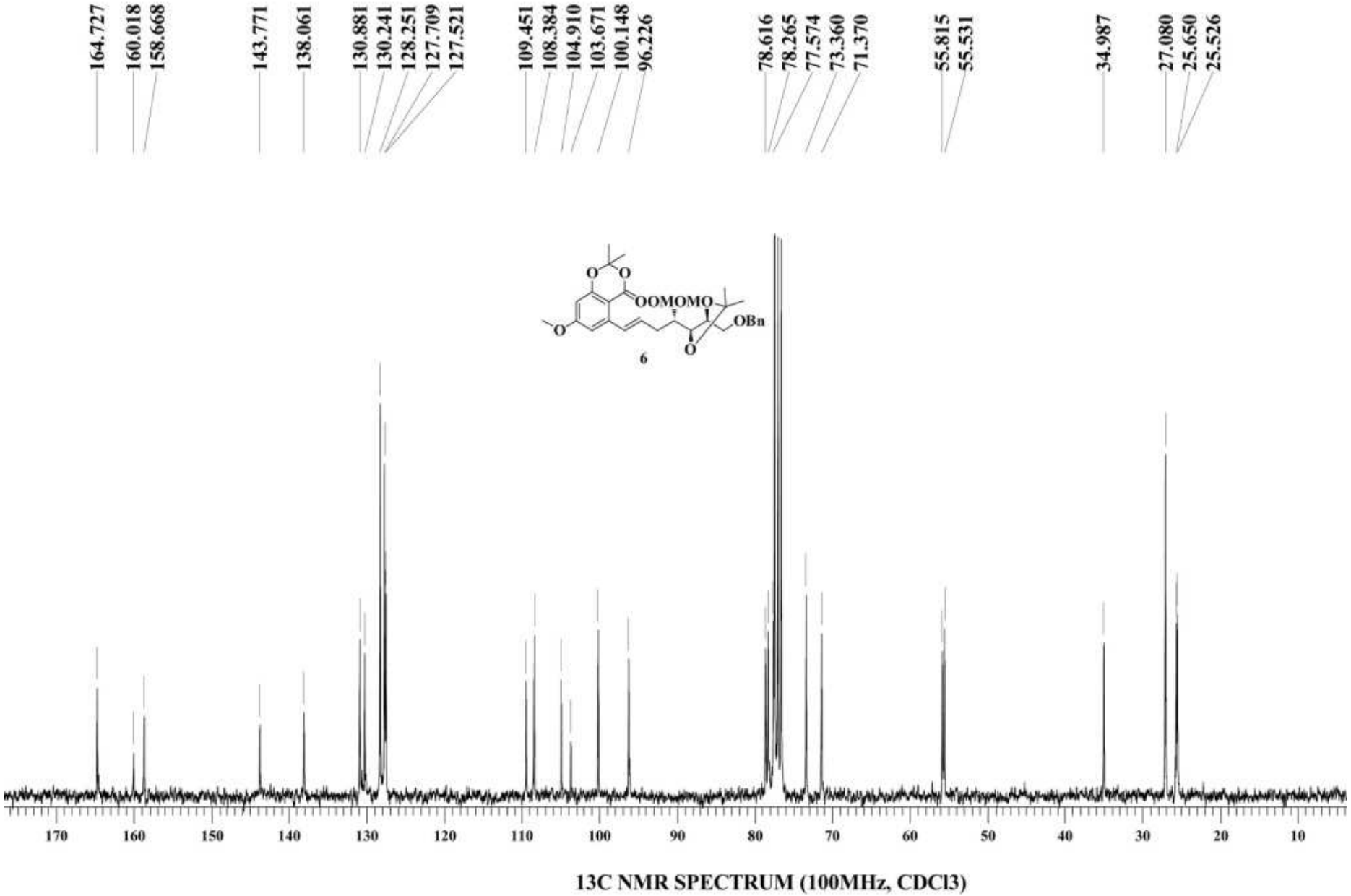

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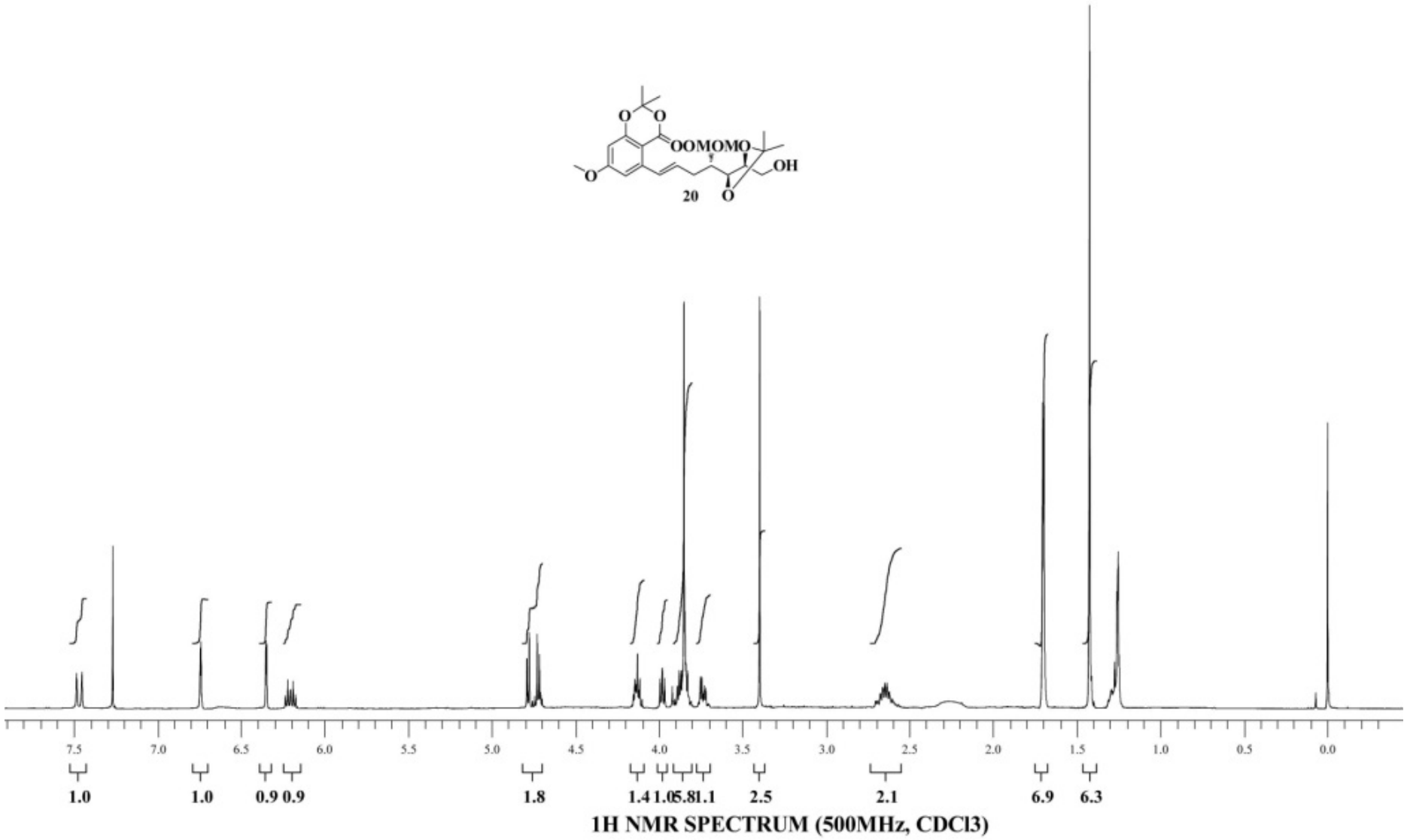

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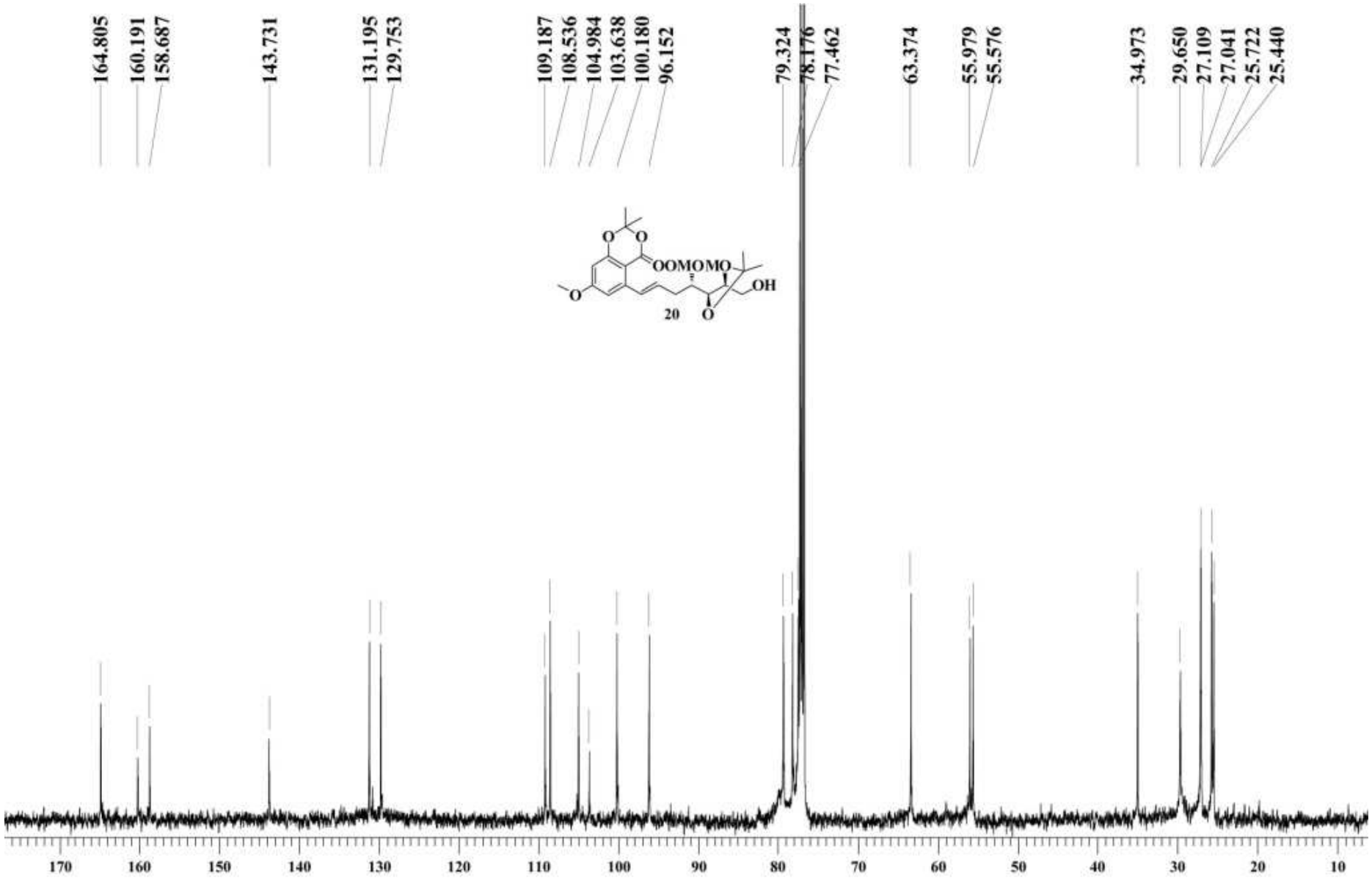

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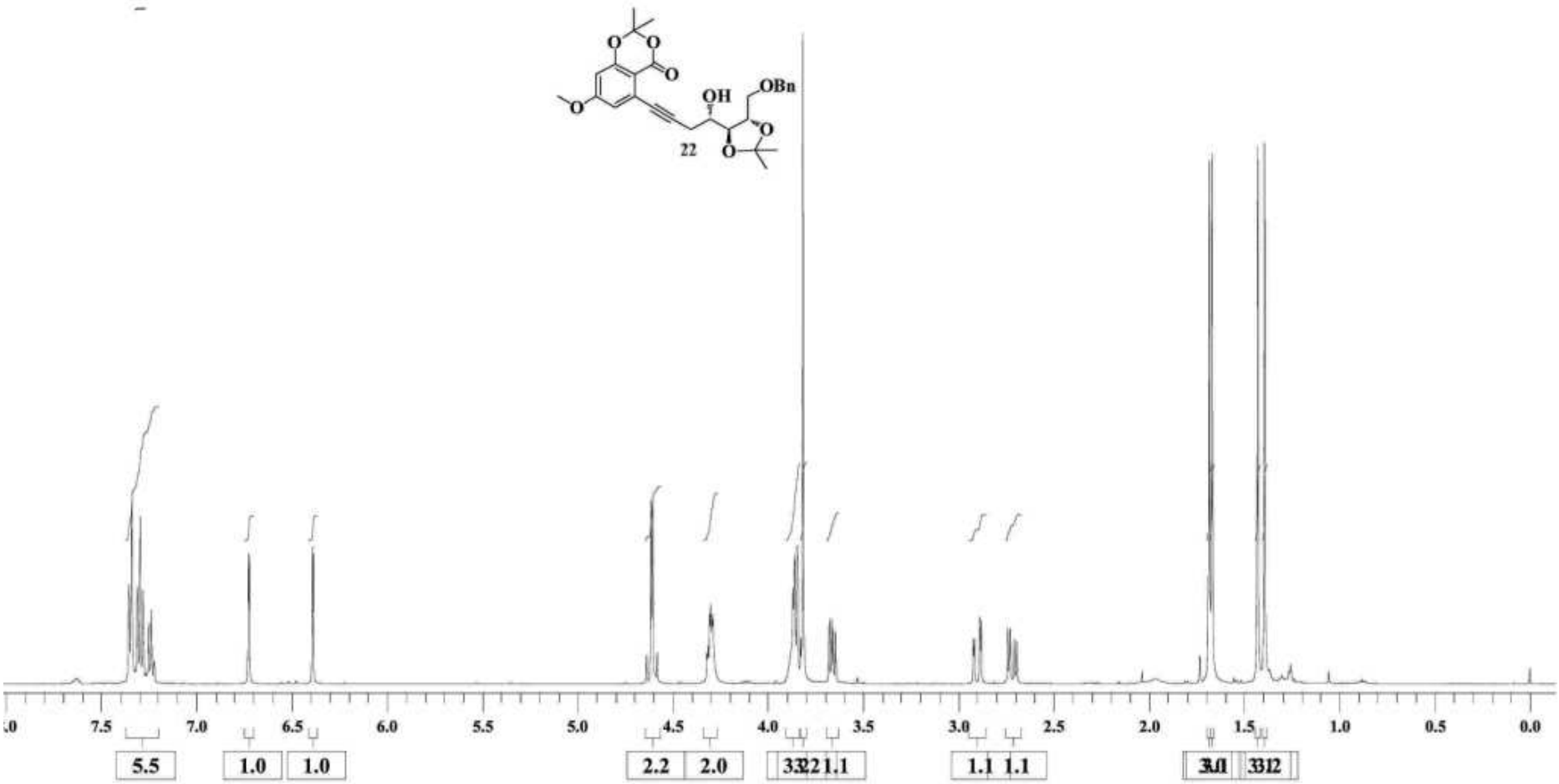

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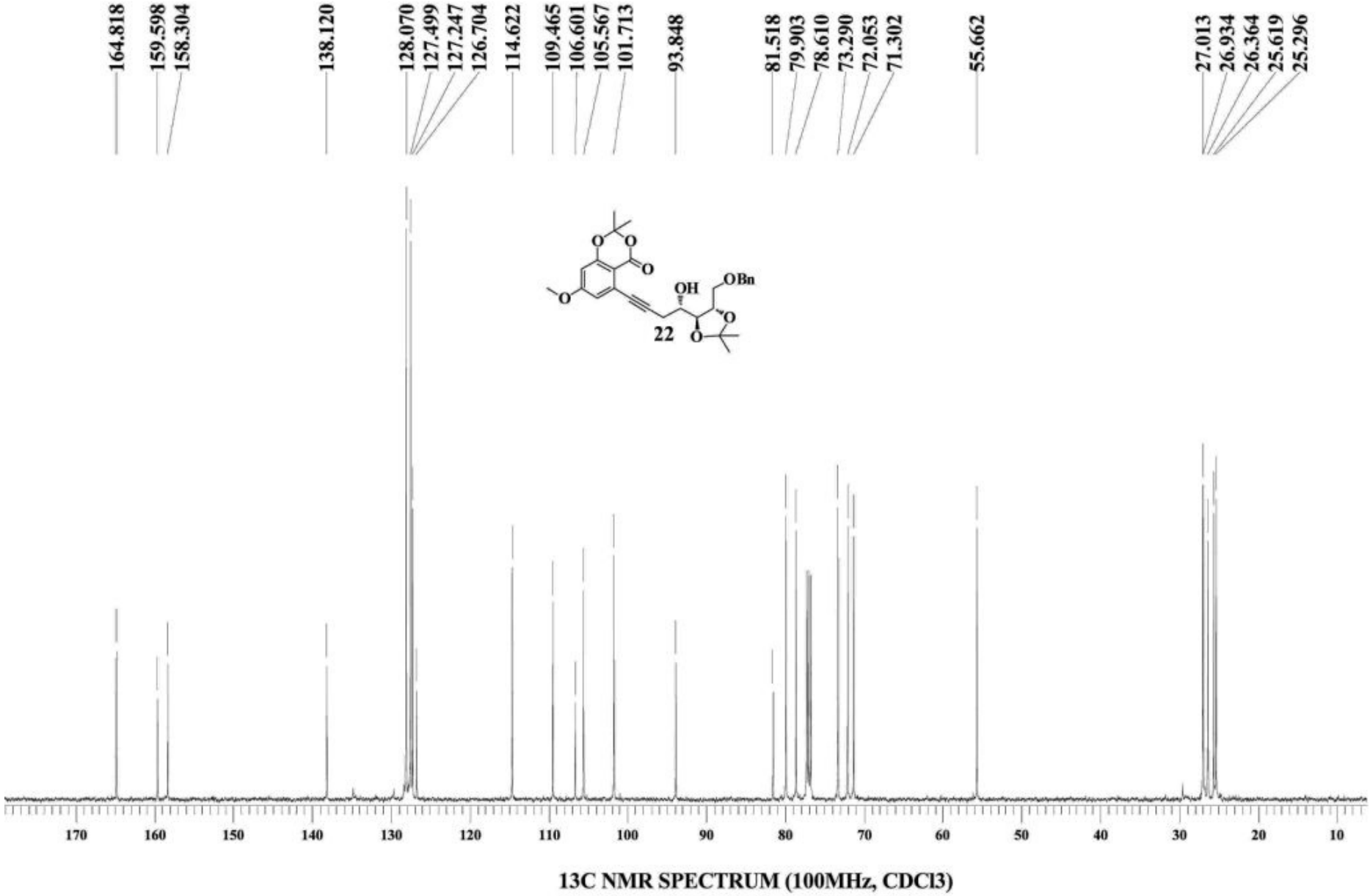

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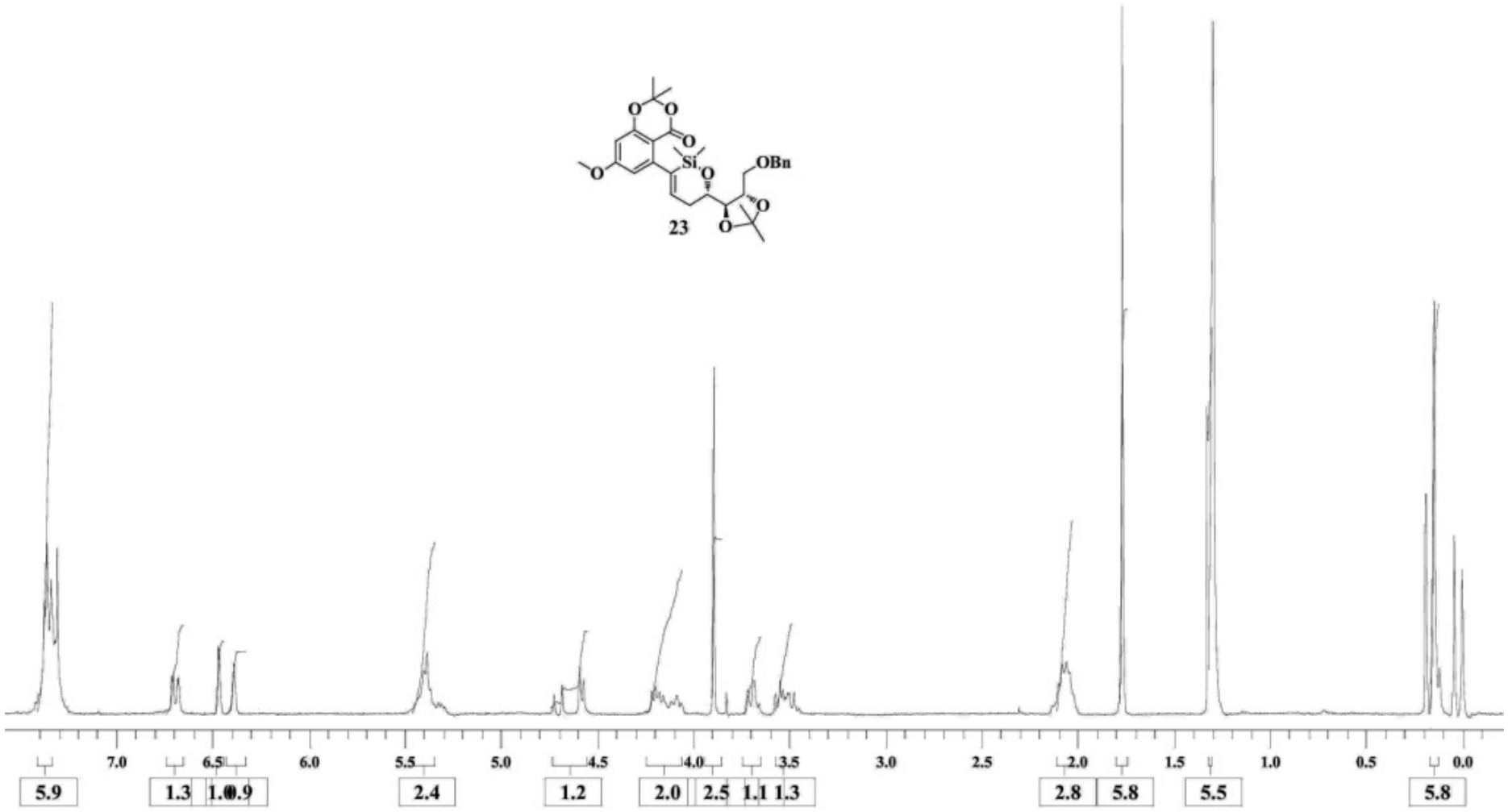

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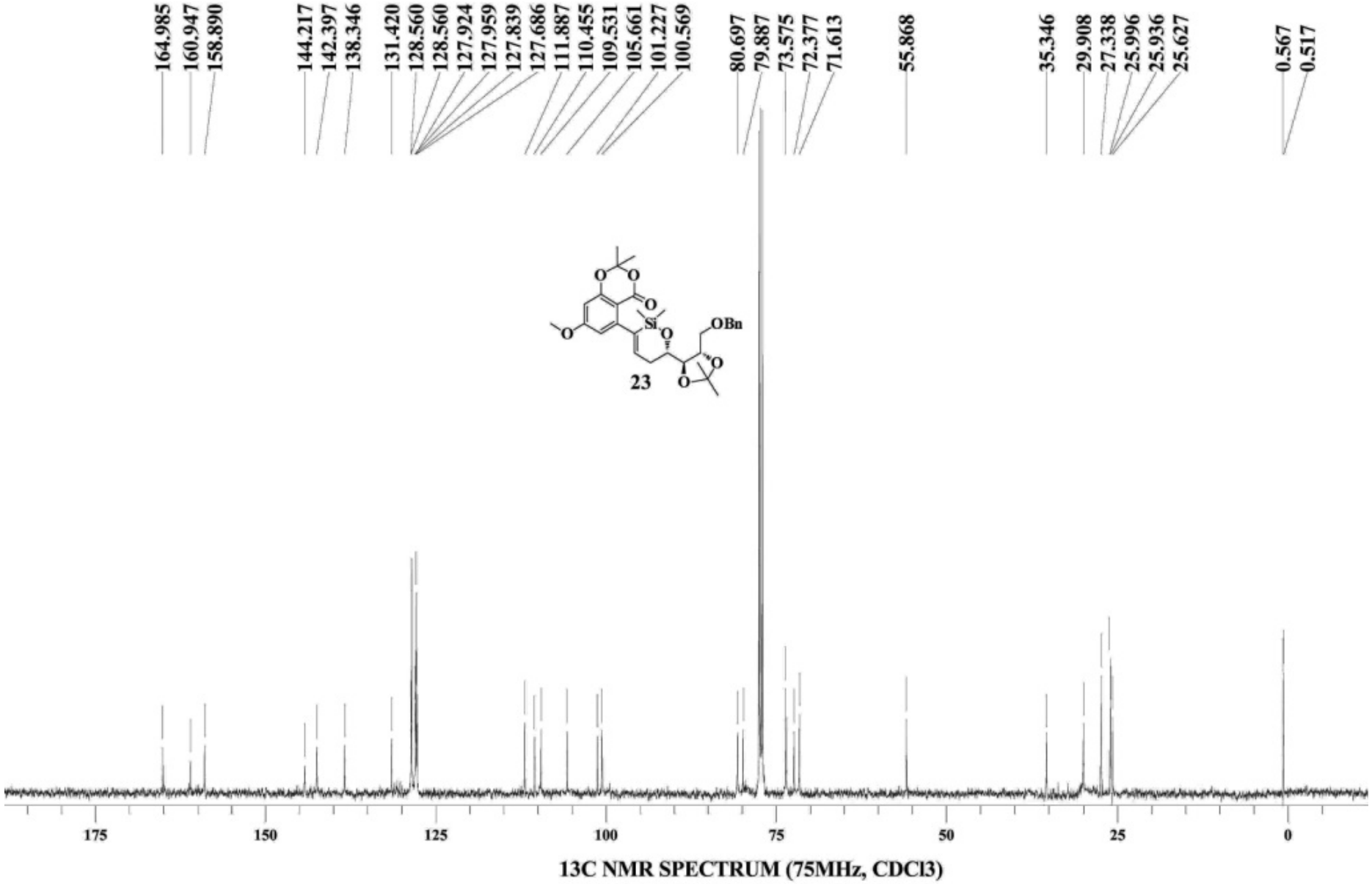

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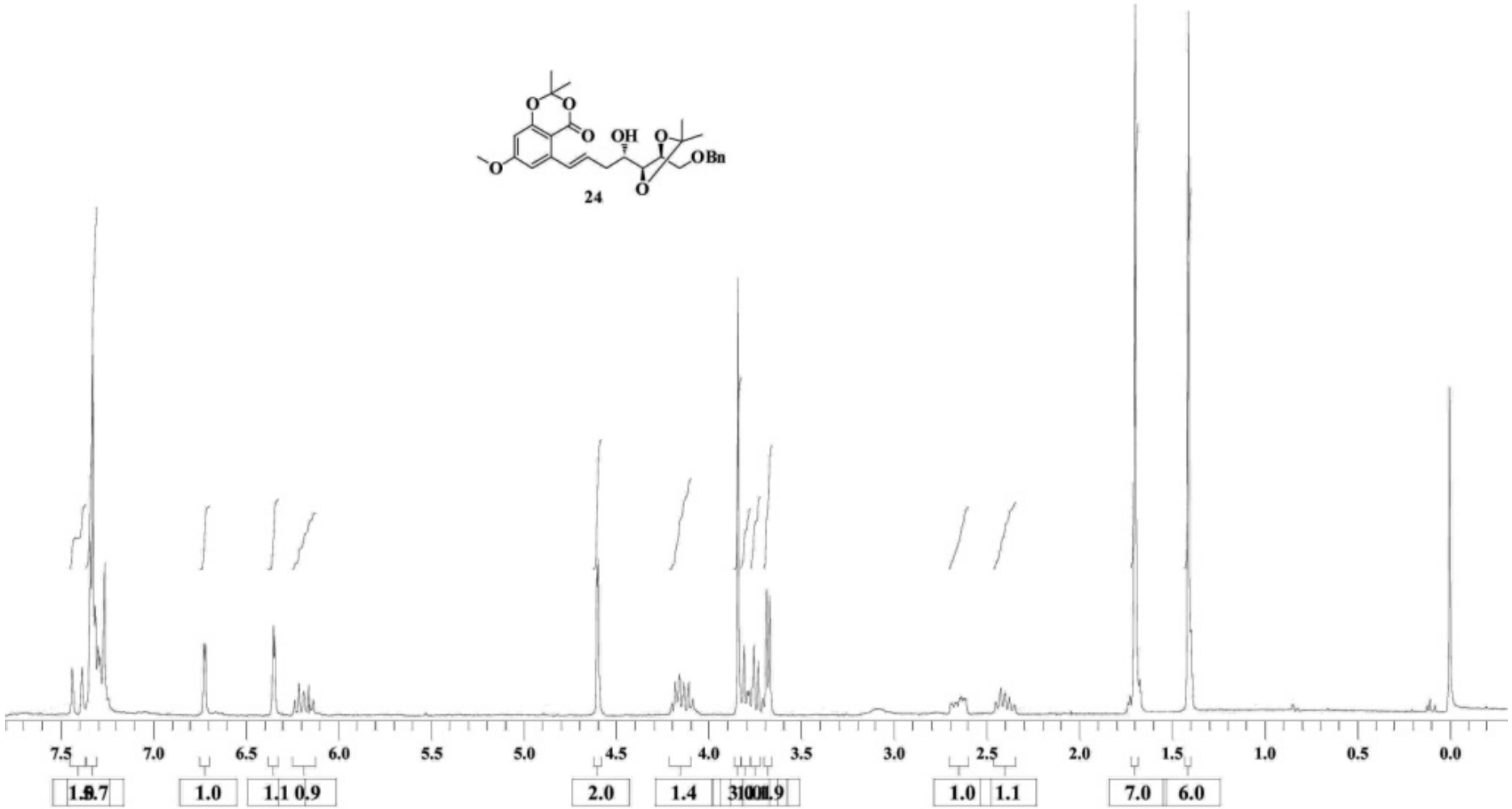

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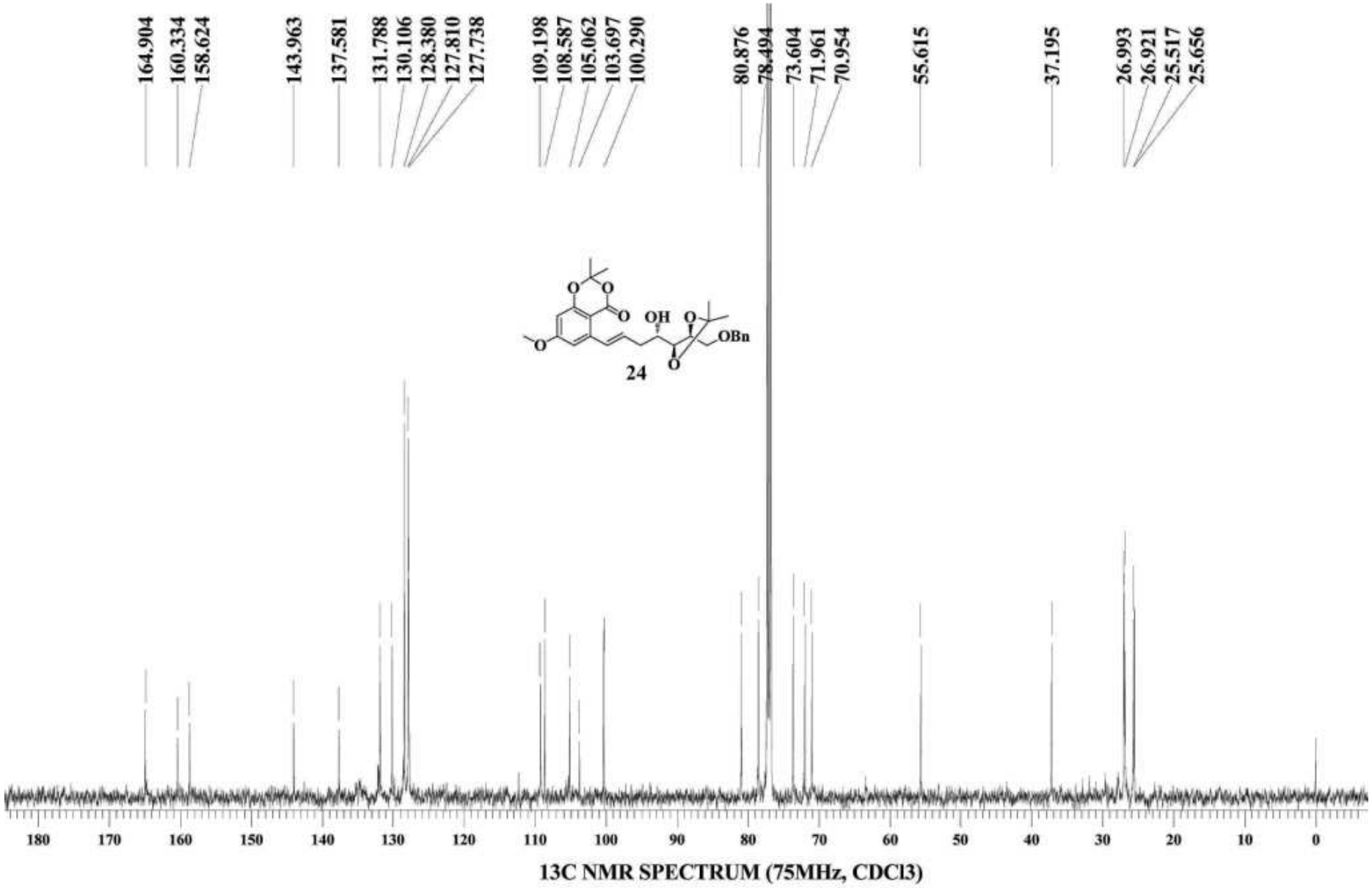
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127.810
127.738
109.198
108.587
105.062
103.697
100.290
80.876
78.494
73.604
71.961
70.954
55.615
37.195
26.993
26.921
25.517
25.656
OH
O
OBn
24
180
170
160
150
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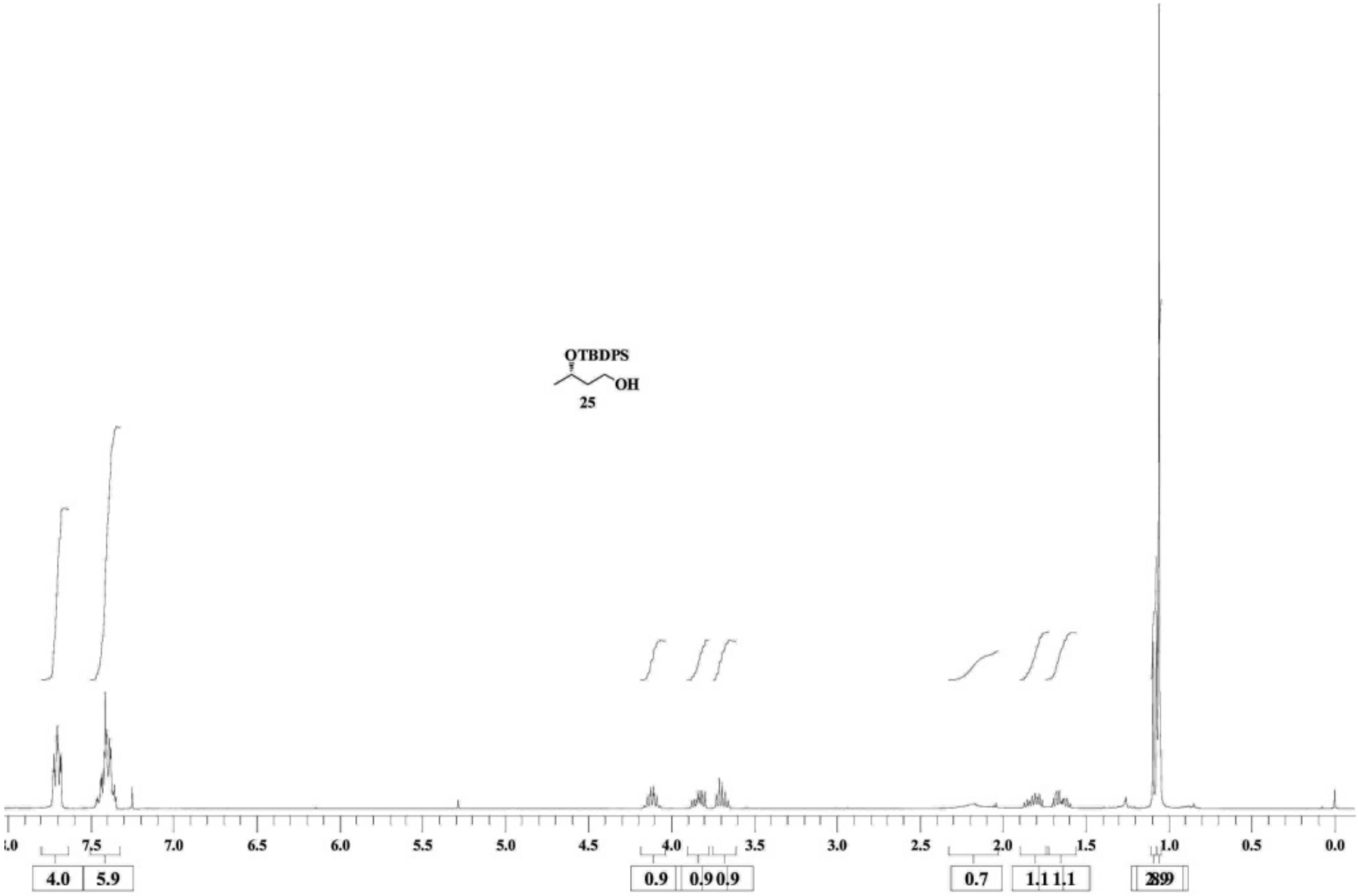

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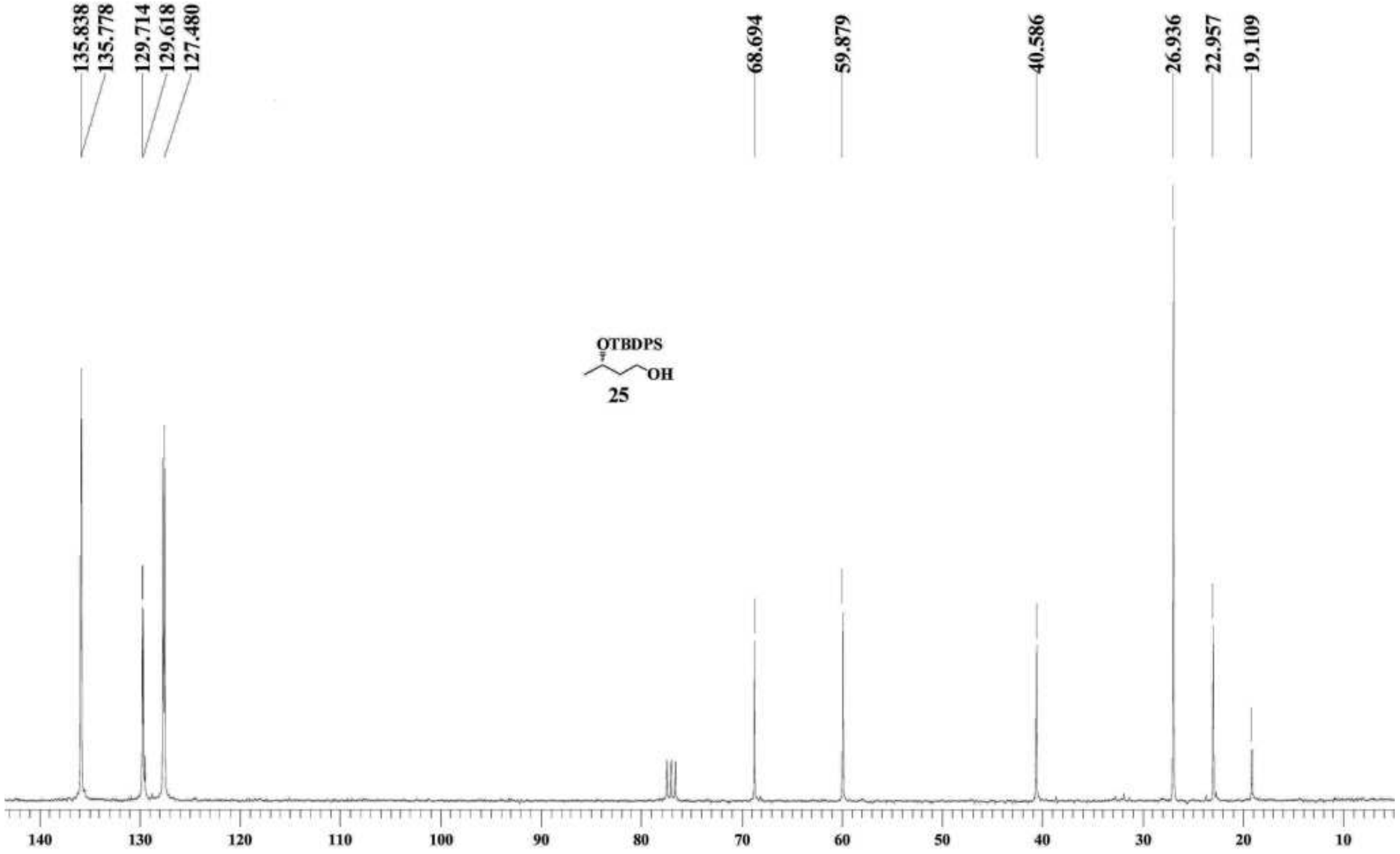

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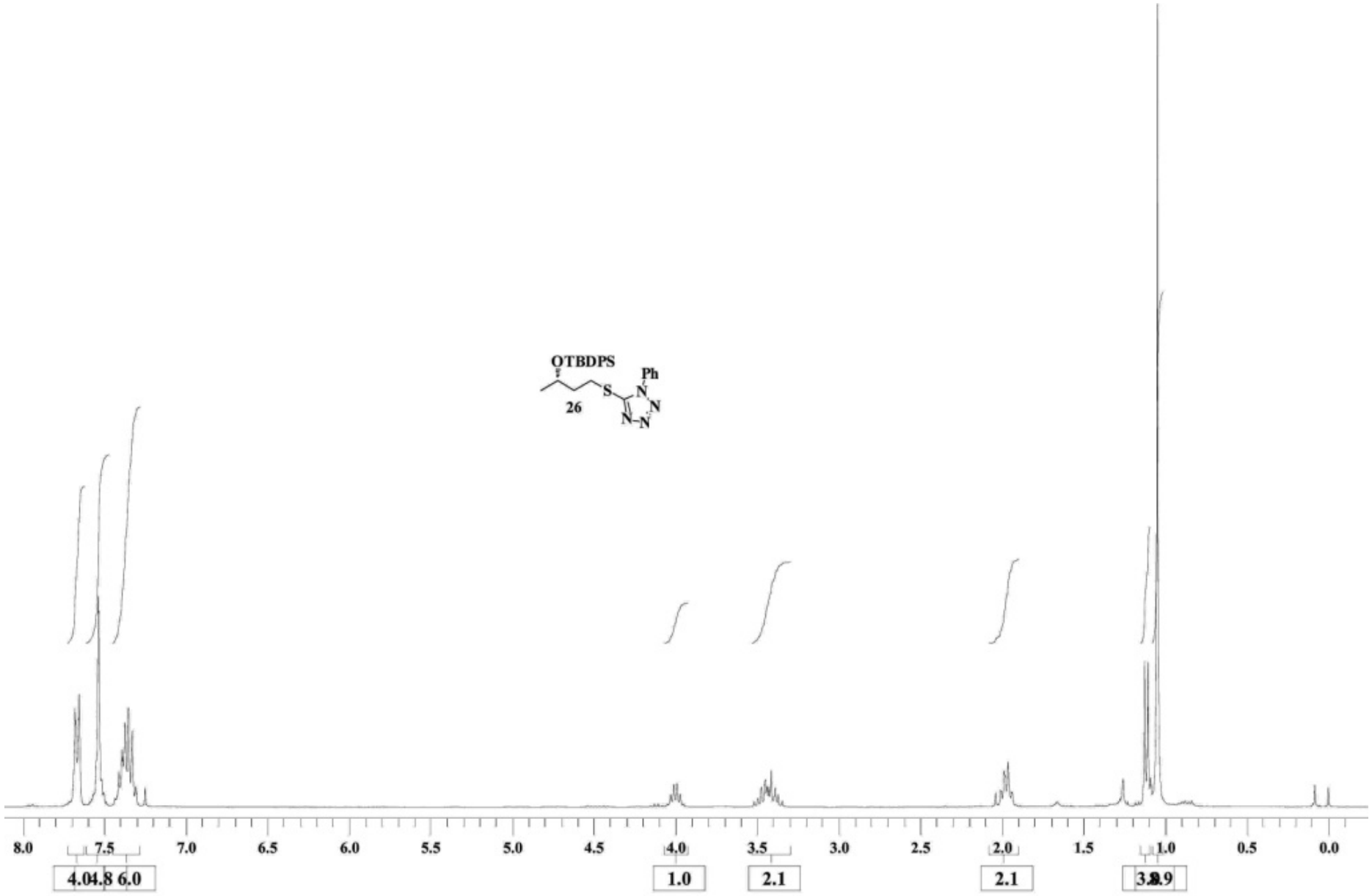

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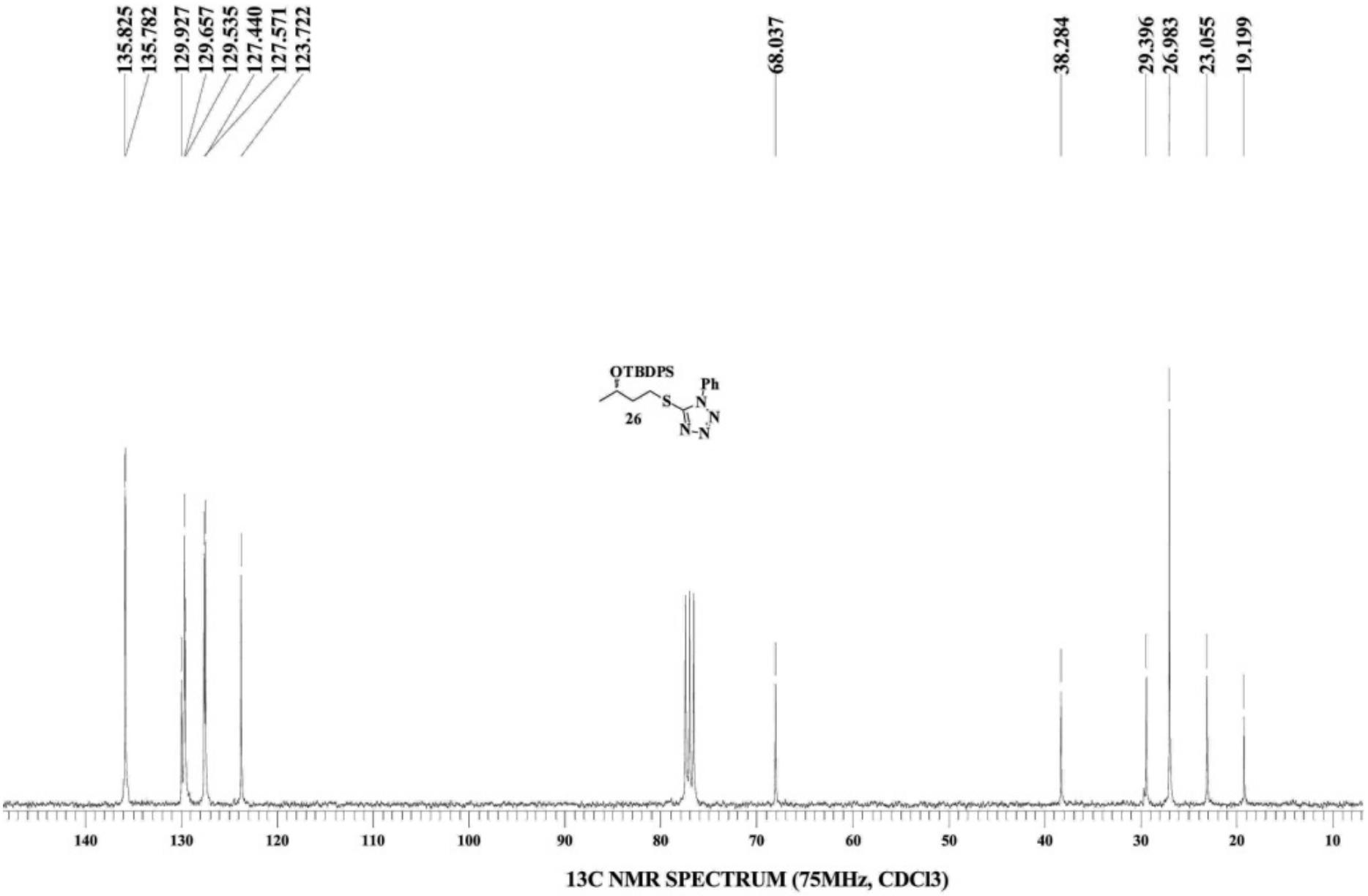

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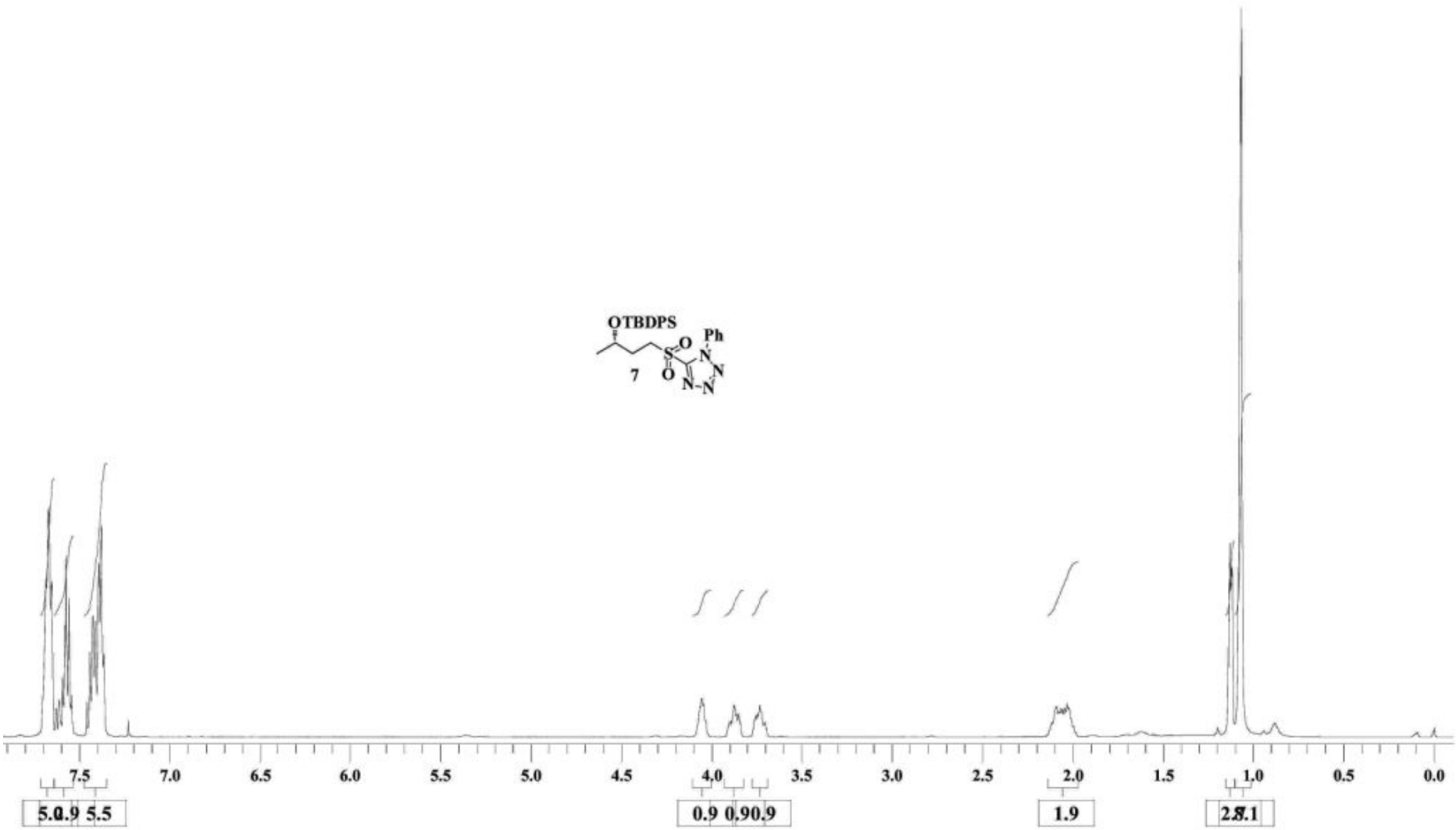

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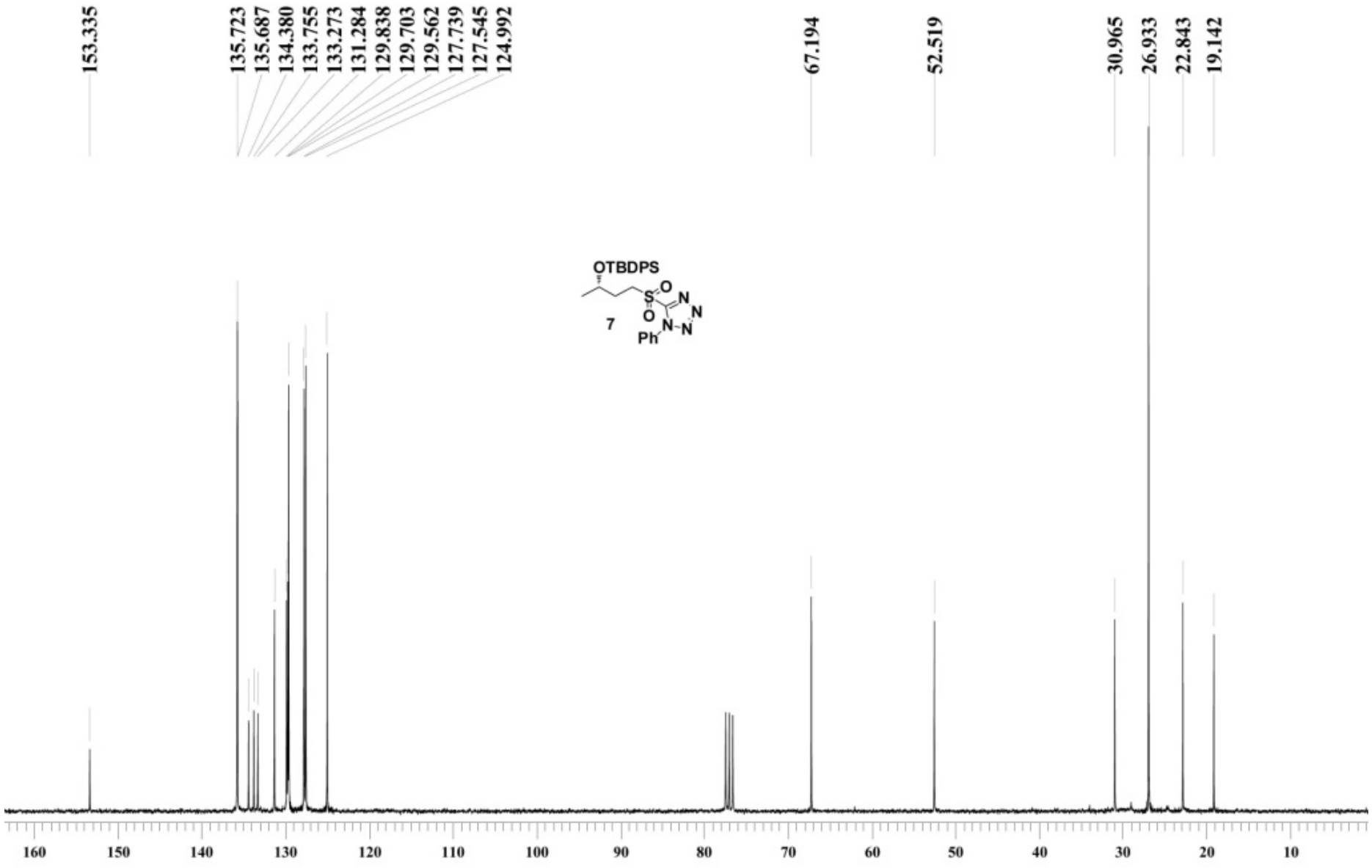

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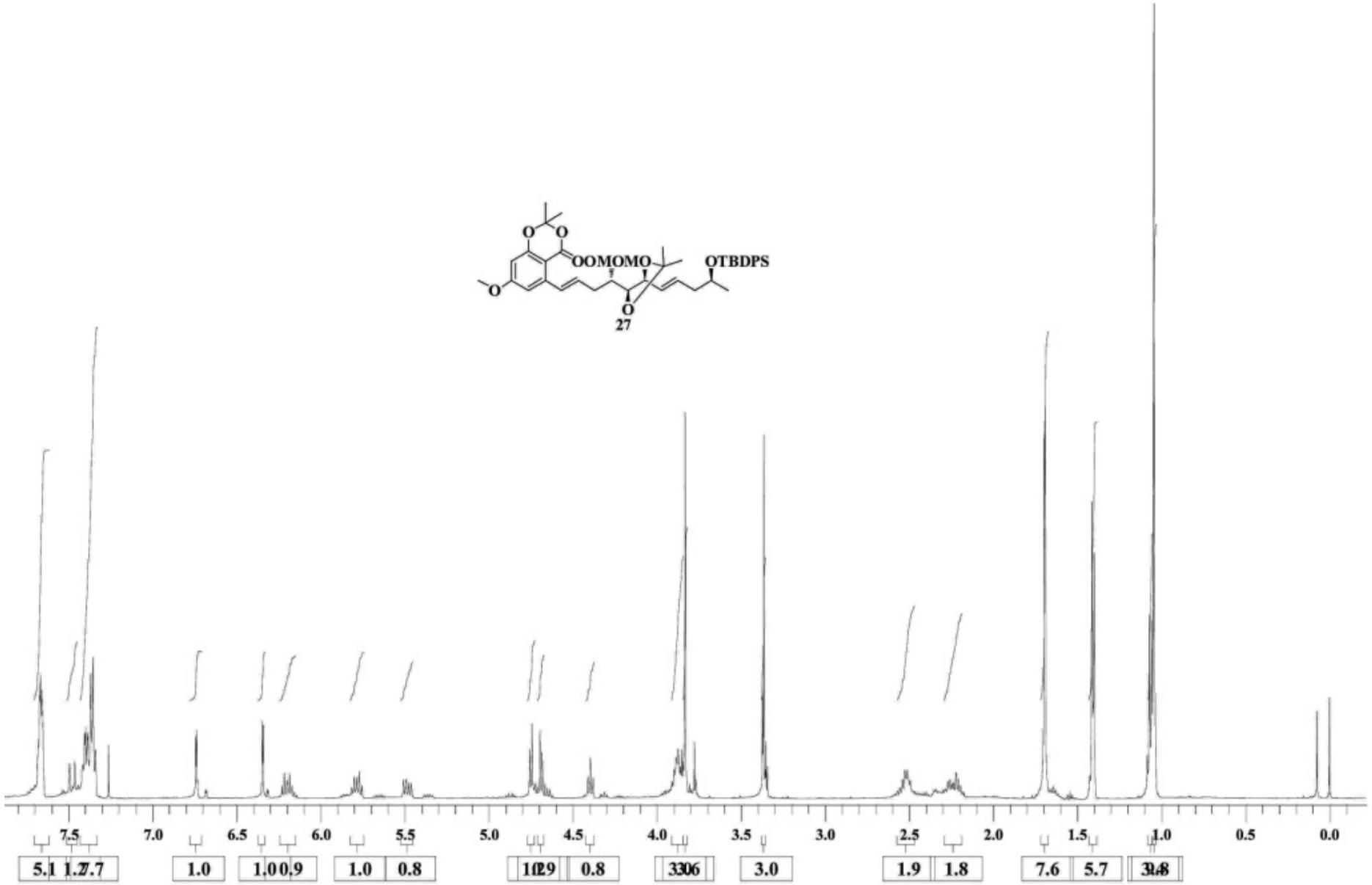

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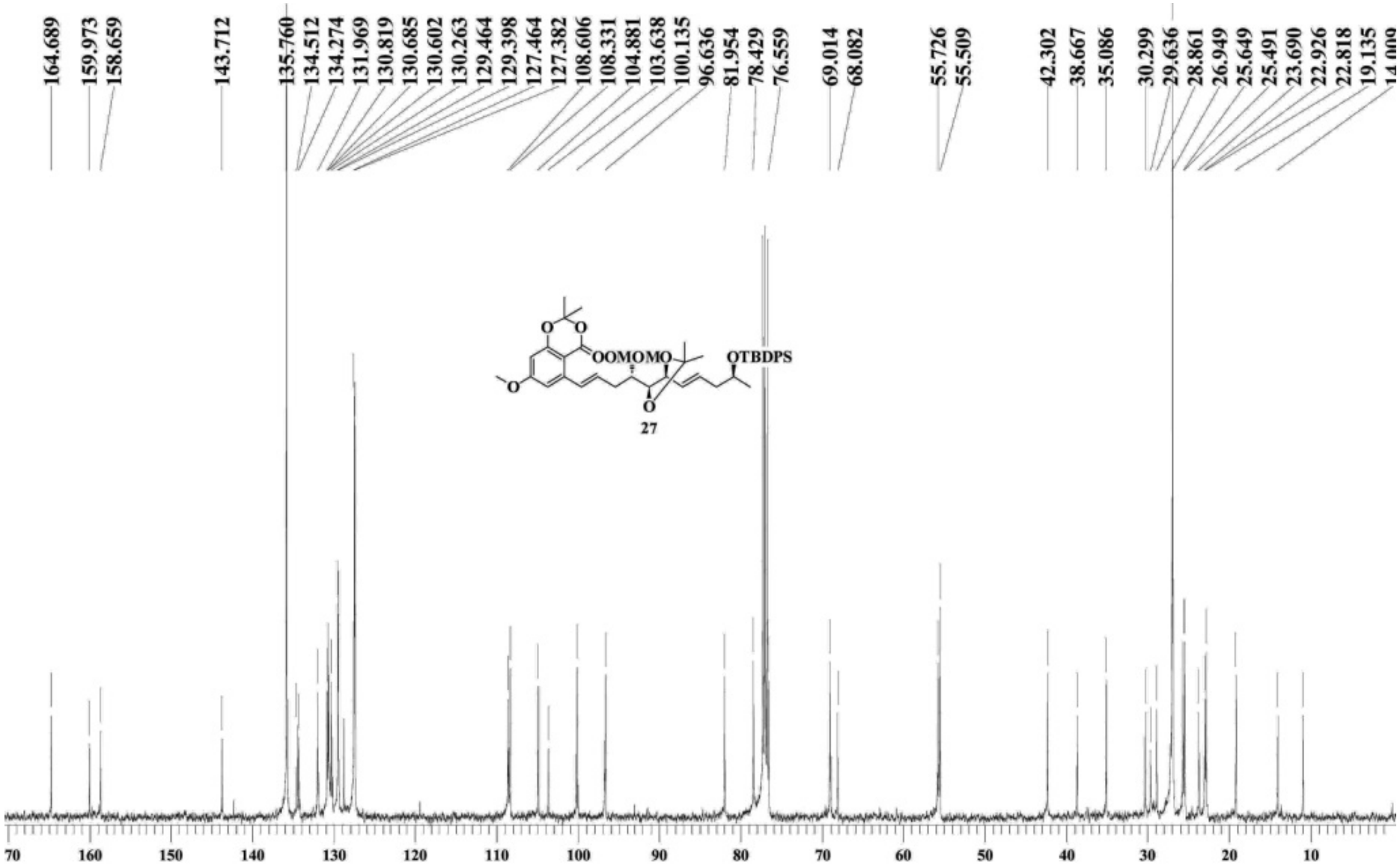

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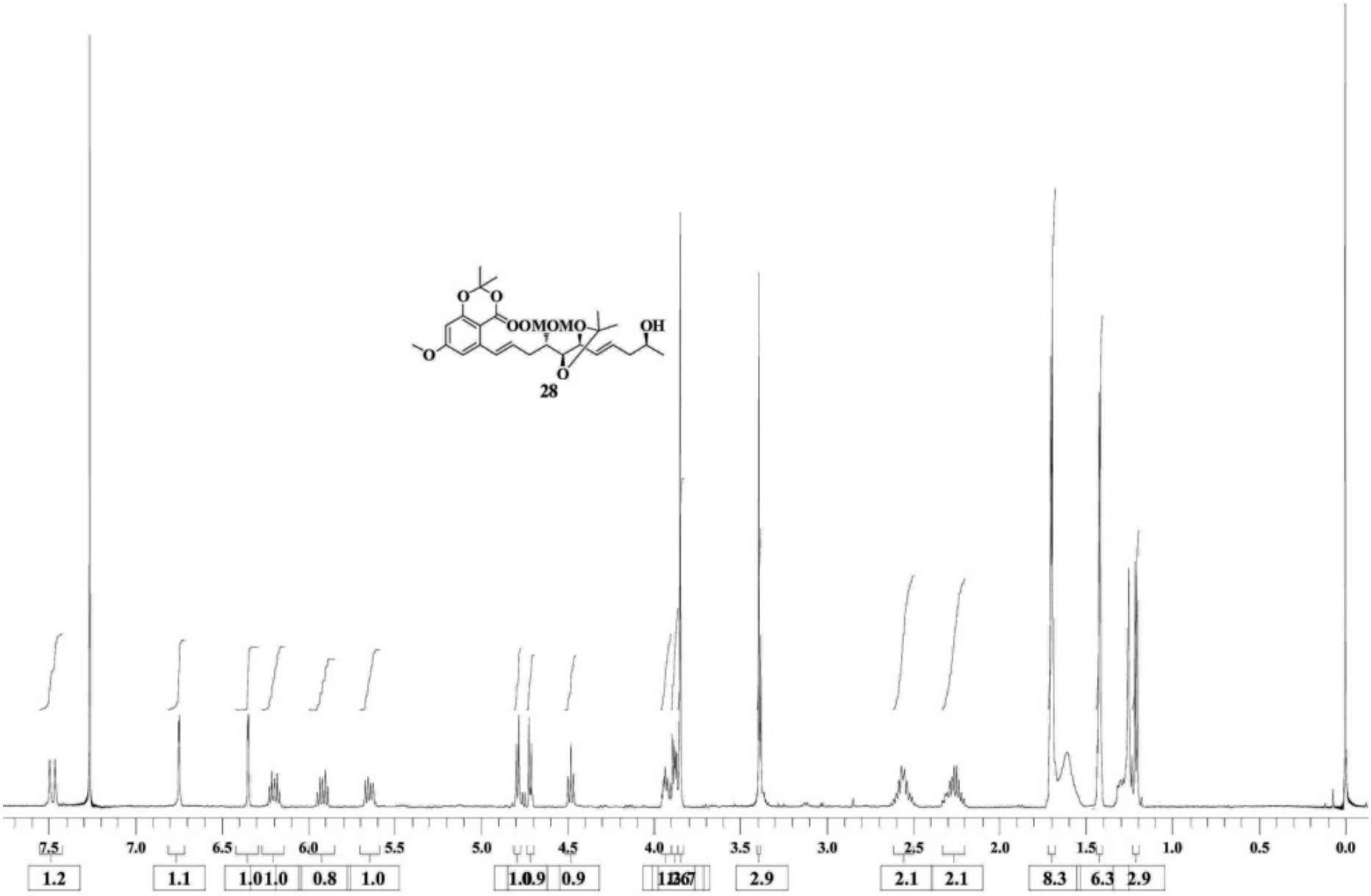

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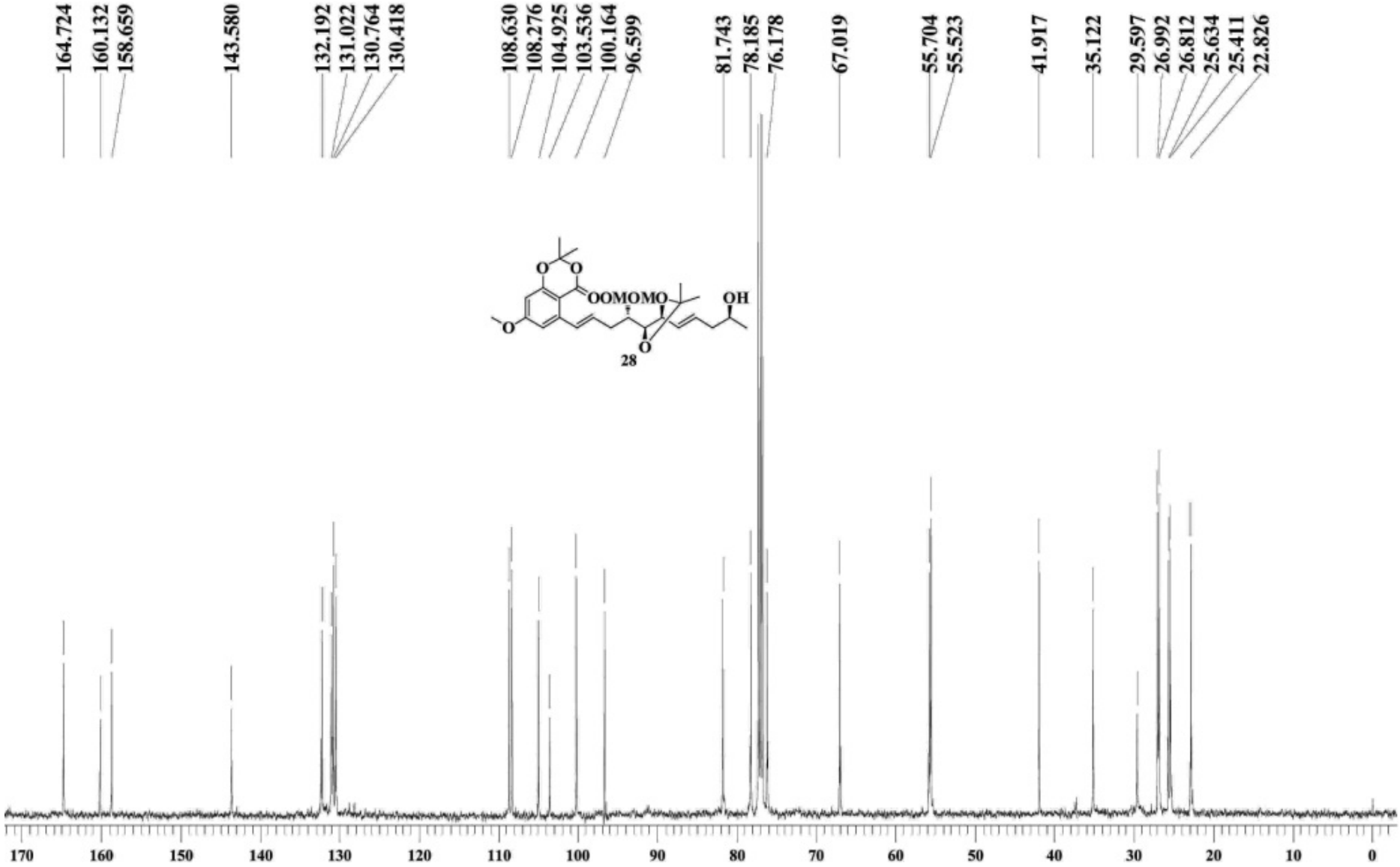
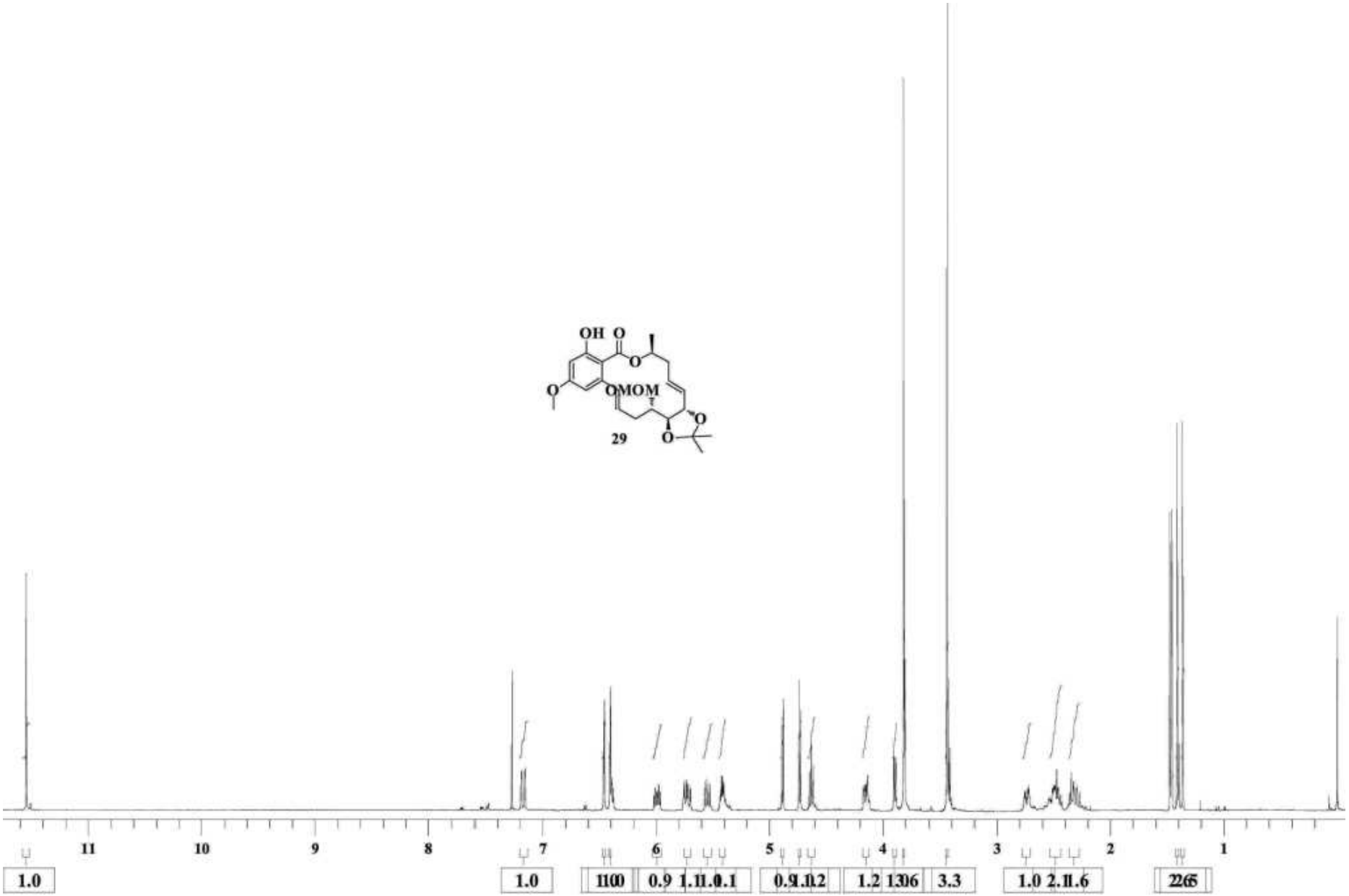
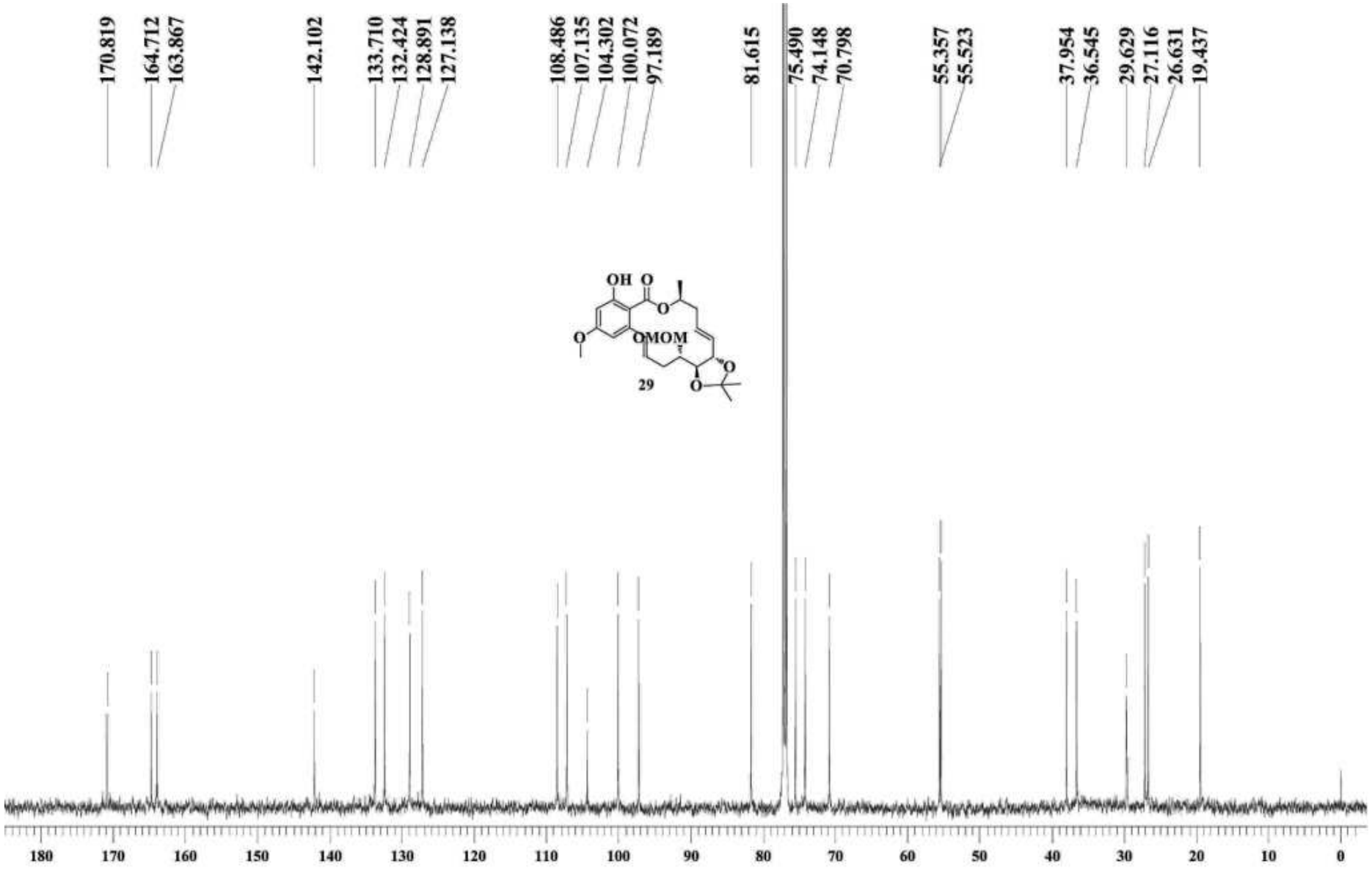


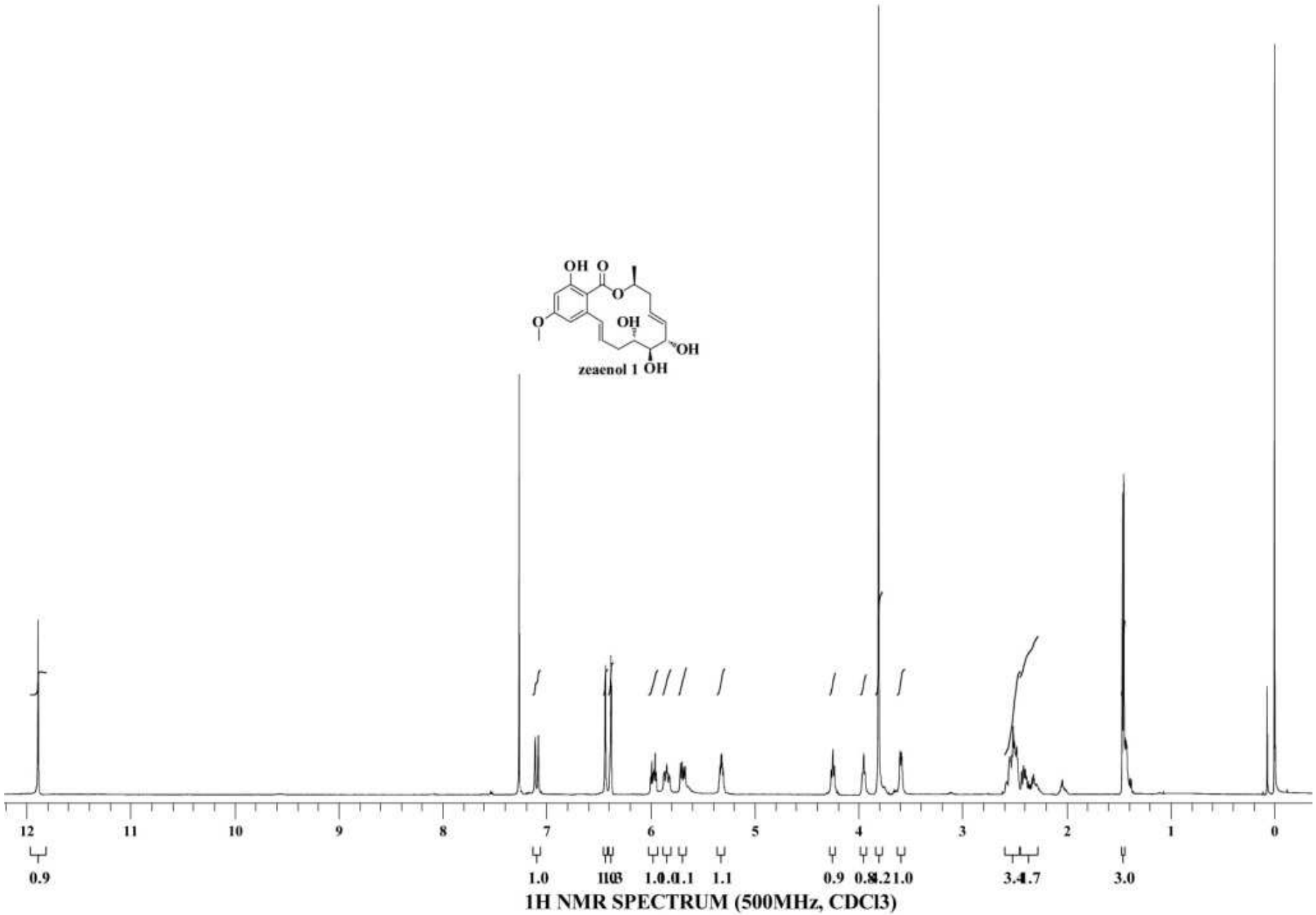
13C NMR SPECTRUM (100MHz, CDCl3)



1H NMR SPECTRUM (500MHz, CDCl3)



13C NMR SPECTRUM (100MHz, CDCl3)



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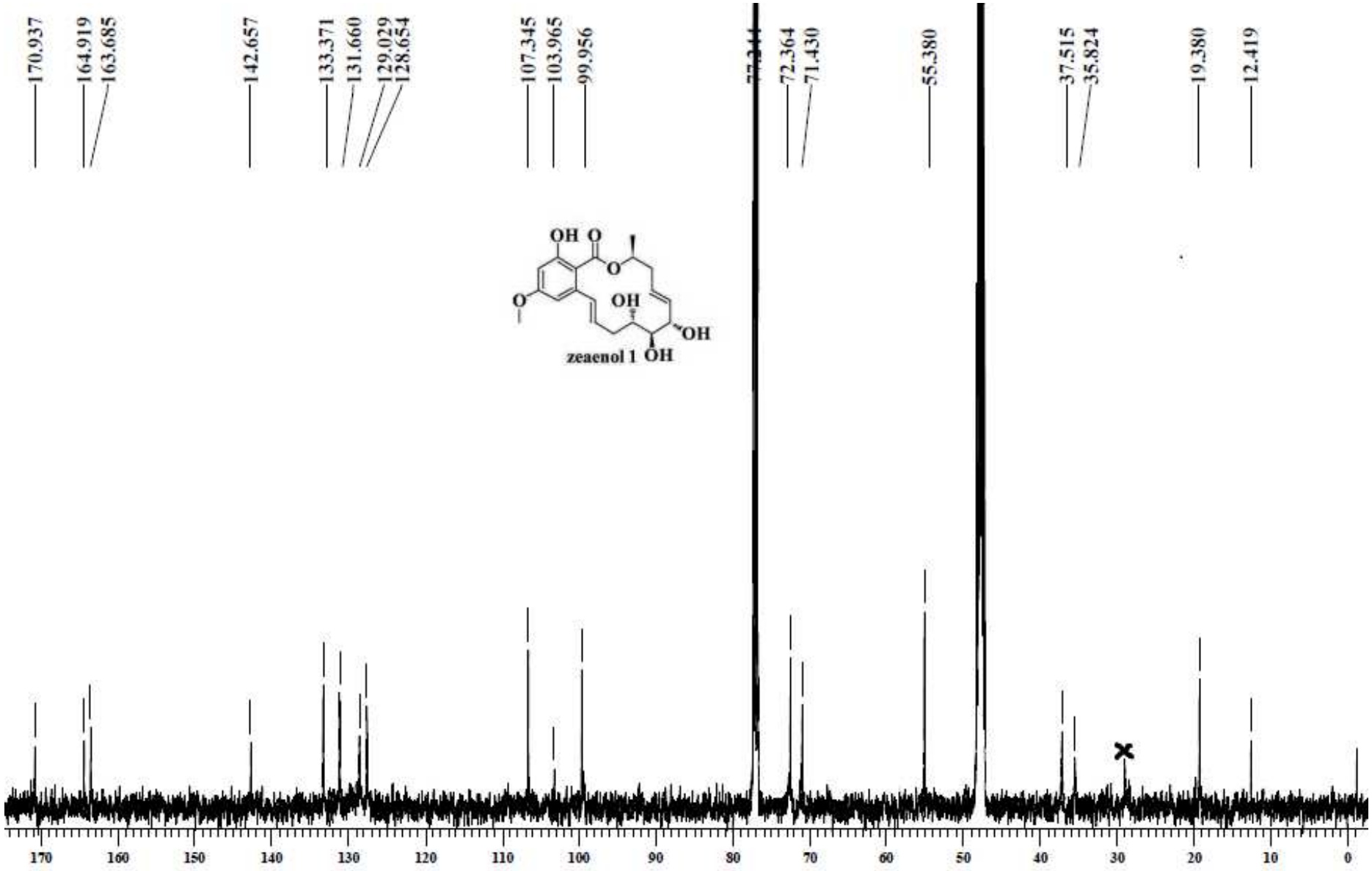

13C NMR SPECTRUM (75MHz, CDCl3+CD3OD)

Table S1: ^{1}H NMR and ^{13}C NMR data of natural zeaenol and synthesized zeaenol **1** in ($CDCl_3$+CD_3OD-1:1) solvent

Position	**Natural product zeaenol**		**Synthesized zeaenol 1**	
	δ_H (J in Hz)	δ_C	δ_H (J in Hz)	δ_C
1	--	103.8	--	103.9
2	--	165.0	--	164.9
3	6.39 (2.69)	99.9	6.38 (2.65)	100.0
4	--	163.9	--	163.7
5	6.44 (2.69)	107.5	6.44 (2.65)	107.4
6	--	142.9	--	142.7
7	--	171.0	--	170.9
1’	7.12 (15.4)	133.4	7.10 (15.4)	133.4
2’	5.82 (15.4, 10.1, 4.0)	128.9	5.84 (15.3, 10.4, 3.4)	129.0
3’a, b	2.43, 2.51 (m)	35.9	2.44-2.25 (m)	35.8
4’	3.98 (1.3, 2.0, 8.1)	12.3	3.95 (6.7)	12.4

5’	3.59 (8.1, 2.2)	77.2	3.59 (7.9)	77.2
6’	4.26 (7.4, 8.1)	72.3	4.25 (7.8)	72.4
7’	5.71 (15.4, 7.4)	131.3	5.69 (15.4, 7.5)	131.7
8’	5.98 (15.4, 6.1)	128.7	5.97 (15.4, 6.1)	128.7
9’a, b	2.53 (m)	37.5	2.61-2.45 (m)	37.5
10’	5.32 (m)	71.4	5.36-5.28 (m)	71.4
11’	1.41 (6.1)	19.3	1.44 (6.3)	19.3
Phenolic OH	11.85	--	11.89	--
Methoxy	3.82	55.3	3.81	55.5