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σ–Ferrier Rearrangement of Carbohydrate Derived Vinylcyclopropanes: A Facile Approach to Oxepane Analogs

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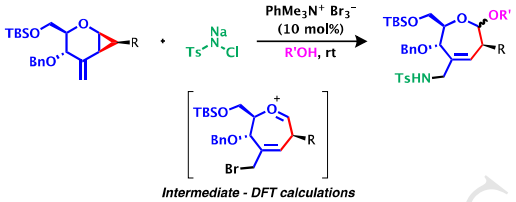

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σ–Ferrier Rearrangement of Carbohydrate Derived Vinylcyclopropanes: A Facile Approach to Oxepane Analogs

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ABSTRACT

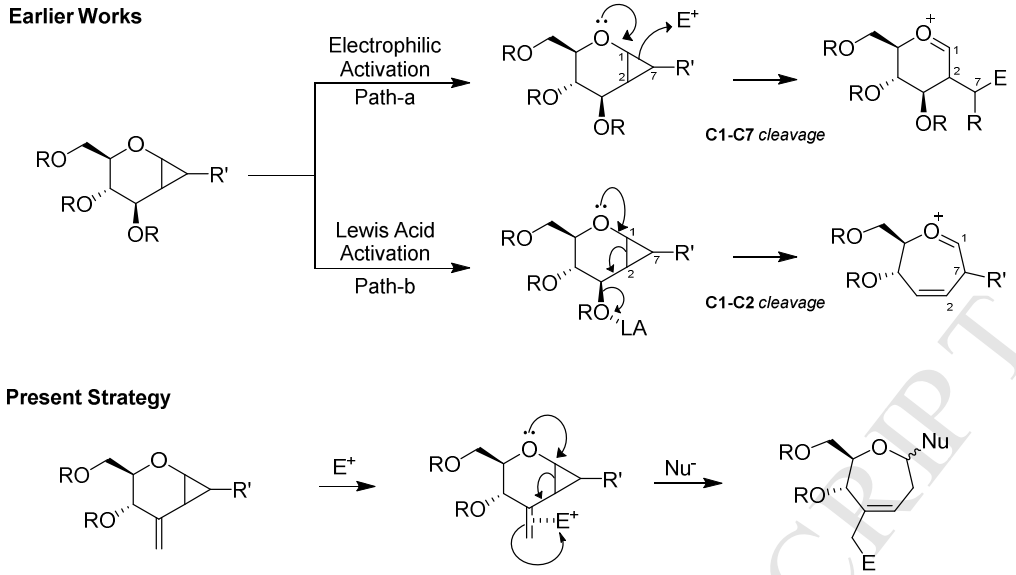
This article presents our work on the σ–Ferrier ring-expansion of carbohydrate derived vinylcyclopropanes (VCPs) under electrophilic conditions mediated by chloramine-T and a phase-transfer catalyst. The present work serves as the first example on the studies of the reactivity of carbohydrate VCPs towards the synthesis of densely functionalized oxepane analogues. The work elaborates on a reasonable mechanism for the product formation and our observations on the diastereoselectivity based on control experiments and gas-phase calculations.

1. Introduction

Seven membered oxacycles have gained tremendous significance due to their increasing prominence in numerous naturally occurring biologically active compounds.[1-6] The increasing number of polyether natural products from marine sources containing a seven membered oxacyclic core has encouraged the development of new synthetic routes to achieve highly functionalized oxepanes.[7-17] Seven-membered ring systems such as polyhydroxylated azepanes and septanosides have received considerable attention as potential non-natural surrogates for pyranoses in a number of biochemical processes.[18-21] Glycosylation of septanosides and the kinetics of hydrolysis of such linkage have been carried out extensively to gain insight on the stability and reactivity of these polysaccharides compared to their pyranose counter-parts under physiological conditions.[22-24] Various routes like intramolecular epoxide ring-opening reaction,[10, 12, 25-26] nitrone-alkene cycloaddition reaction,[27-28] skeletal rearrangements,[29-31] cyclization reaction[32-34] and ring-expansion chemistry,[14, 35-44] starting from both racemic and chiral synthons have been developed. Pioneering efforts of Hoberg towards the synthesis of optically active oxepane derivatives by the ring expansion of carbohydrate derived cyclopropanes promoted by Lewis acids in the presence of an external nucleophile are noteworthy.[42-43, 45] The reaction has been proposed to proceed through a planar oxonium intermediate following a Ferrier type rearrangement of C–C σ–bond. Recently, Sridhar *et al.* extended this methodology to the synthesis of septano-oligosaccharides from cyclopropanones with glycans as nucleophiles.[36] Earlier, Sugita *et al.* employed silyl enol ethers as nucleophiles for ring expansion reactions of cyclopropanones.[14, 35] The chemistry involving ring expansion of carbohydrate derived dihalocyclopropanes, mediated by bases was demonstrated by Nagarajan *et al.*[37] and Harvey *et al.*[44] Jayaraman and coworkers[38-41] further extended the methodology towards a practical accessibility to septanosides and respective polysaccharides.

To the best of our knowledge, ring opening of carbohydrate derived cyclopropanes mediated by electrophiles always led to a ring-opening reaction through C1-C7 bond cleavage. Ring-expansion by the cleavage of C1-C2 σ-bond has not been observed so far (path-a, Scheme 1). Conversely, Lewis acid catalysts are shown to be the best to effect ring-expansions (path-b, Scheme 1).[46-47] In the present study, we planned to install an exocyclic methylene group, utilizing the electron-rich character of the π-bond (in comparison to the cyclopropane σ-bonds), to demonstrate an electrophile mediated ring-expansion by the rupture of C1-C2 σ-bond, which is not a typical reactivity pattern observed in the chemistry of carbohydrate-derived cyclopropanes (Scheme 1).

For several years, our group has been actively involved in exploring the reactivity of vinylcyclopropanes as masked donor–acceptor systems, and synthetic methodologies on carbohydrate systems in parallel. Our earlier reports on the electrophile mediated ring–opening reaction of vinylcyclopropanes [48, 49] led us to believe that the reaction of carbohydrate derived vinylcyclopropane **6** in the presence of electrophiles would possibly effect a σ-Ferrier type ring



Scheme 1. General strategy of reactivity of carbohydrate derived VCPs.

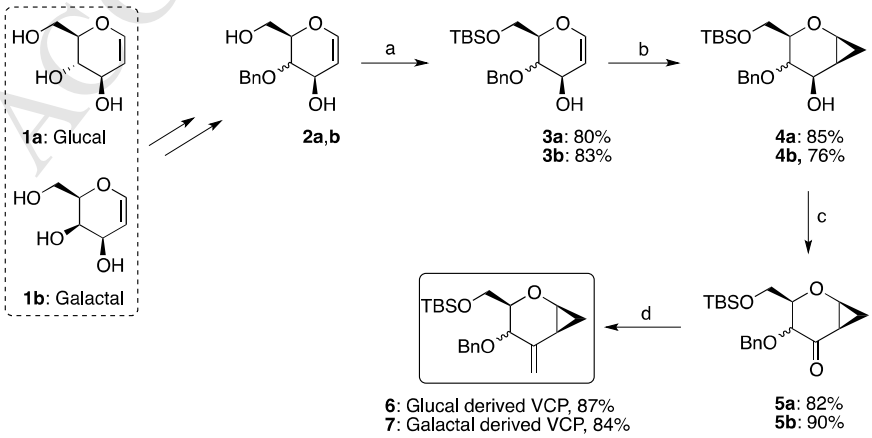
expansion through a tight-carbocation intermediate to densely functionalized oxepanes. We convincingly showed that the overlap between the π–orbital of vinyl group and the cyclopropane C–C σ*–orbital facilitates the ring–opening to a great extent.[48-50] In the present case, a minimum overlap is expected between the π–bond and the C–C σ–bond due to their orthogonality and restricted conformational freedom. The reactivity of VCP **6** could be interesting due to the orthogonal orientation of the π–bond and the cyclopropane C–C σ–bond of interest.

2. Results and Discussion

To study these aspects we planned the synthesis of the carbohydrate derived vinylcyclopropane **6**, starting from *D*-glucal. Glucal **1a** was first converted to C–4 *O*–benzylated glucal **2a** using known procedure from the literature,[51] followed by regioselective protection of the C–6 hydroxyl group as its TBS ether **3a** using a standard protocol. The C–3 hydroxyl group was used as a handle to carry out Simmons–Smith cyclopropanation at the β–face with high stereoselectivity to get **4a** exclusively. The C–3 hydroxyl in **4a** was later oxidized to the corresponding 1,2–cyclopropylketone **5a** using the Dess–Martin reagent, which was then subjected to Wittig reaction to furnish the desired *gluco*–VCP **6** in good yield (Scheme 2).

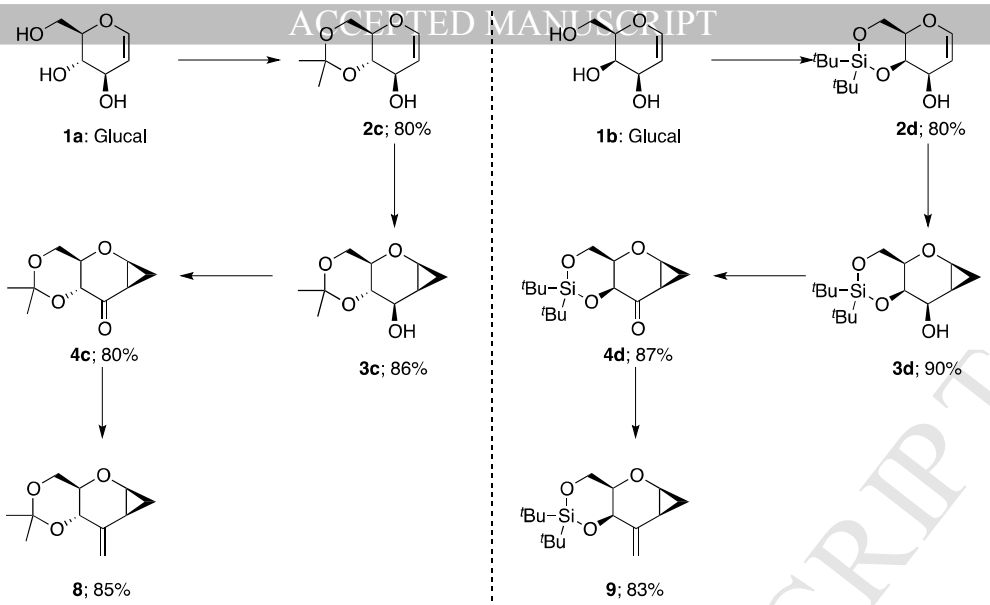
The galacto-VCP **7** was also prepared following a similar reaction sequence used for **6**. To introduce rigidity and to study the effect of steric bulk on the reaction, we planned to protect the C-4 and C-6 hydroxyl groups of both D-glucal and D-galactal with cyclic protecting groups so as to have the C-3 hydroxyl group for guided cyclopropanation under Simmon–Smith conditions. Accordingly the glucal **1a** was converted to acetonide protected derivative **2c**[52] and the galactal **1b** was protected as the silyl derivative **2d**.[53,54] The protected glycals **2c** and **2d** were converted to the corresponding VCPs **8** and **9** following a similar reaction sequence used for the synthesis of **6** and **7** (Scheme 3).

VCP **6** was subjected to a ring–expansion reaction using chloramine–T trihydrate **10** and phenyltrimethylammonium tribromide (PTAB, **11**) as catalyst in MeOH (rt, 4 h). After 4 h, VCP **6** successfully underwent ring–opening to furnish a highly functionalized oxepane **12a** in excellent yield as a mixture of anomers (3:2) (Scheme 4). The configuration at the anomeric position was established with help of 2D-NMR (NOESY spectrum shown in Scheme 4) and by comparing the reported resonance frequency of the anomeric carbon.[38-41]



Reagents and Conditions: (a) TBSCl (1.05 equiv), Imidazole (2 equiv), DMF, 0 °C to rt, 3 h; (b) Et_2Zn (1.5 equiv), CH_2I_2 (2 equiv), DCM, 0 °C, 4 h; (c) DMP (1.1 equiv), DCM, 0 °C, 2 h; (d) $[Ph_3PCH_3]^+I^-$, *n*-BuLi, THF, 0 °C, 5 h

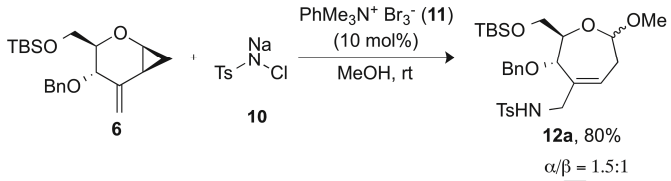
Scheme 2. Synthesis of gluco- and galacto-VCPs **6** and **7**.



Reagents and Conditions: (a) 2,2-DMP (5 equiv), *p*-TsOH (pH ~ 3), DMF, rt, 4 h; (b) Et_2Zn (1.5 equiv), CH_2I_2 (2 equiv), DCM, 0 °C, 4 h; (c) DMP (1.1 equiv), DCM, 0 °C, 2 h; (d) $[Ph_3PCH_3]^+I^-$, *n*-BuLi, THF, 0 °C, 5 h; (e) $^tBu_2Si(OTf)_2$ (1.2 equiv), pyridine, DCM, 0 °C, 6 h.

Scheme 3. Synthesis of gluco- and galacto-VCPs **8** and **9**.

From the literature, it is known that the β–anomer resonates (^{13}C) generally at a higher frequency compared to the α-anomer.[38-41] Unlike in the case of furanosides and pyranosides, the resonance frequencies of the anomeric carbon of α– and β–anomer are indistinct. For **12a**, the carbon-13 of the α–anomer resonates at 100.2 ppm and β–anomer at 100.6 ppm. Quantum chemical predictions of the chemical shift of anomeric carbon using GIAO method (at M06-2x/6-31+G* level) suggested that the β–anomer resonates at higher frequency when compared with α-anomer (α-anomer: 104.0 ppm, β-anomer: 106.0 ppm).



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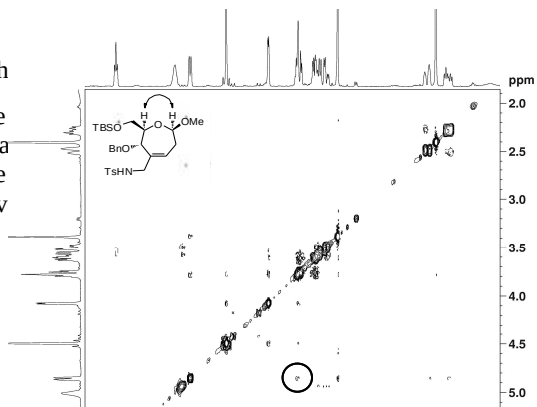


reaction of *galacto*–VCP **7** under standard reaction conditions in the presence of different alcohol nucleophiles was promising which led to successful ring–opening to the corresponding oxepane derivatives **13a-c**. We envisaged that the introduction of cyclic bifunctional protecting groups (like acetonide and di–*t*–butylsilyl protection) will impart more rigidity to the skeleton and steric crowding, which in-turn will help in improving the selectivity at the anomeric center. However, in both the VCPs (**8** and **9**), no appreciable improvement in the selectivity was observed in the product (**14a-c** and **15a-c, Table 1**). This observation suggested the intermediacy of a planar oxonium intermediate as proposed by Hoberg.[45]

Our present observation does not corroborate with our earlier results with vinylcyclopropanes in support of the existence of an intimate carbocation. Hence, we undertook an exercise to explore the possible intermediate through which the ring expansion can occur. Geometry optimization of the bromenium intermediate at M06-2x/6-31+G* level showed the existence of a tight carbocation as observed by us earlier but purely as a transient intermediate (**A**), which spontaneously undergoes complete ring-opening to the more

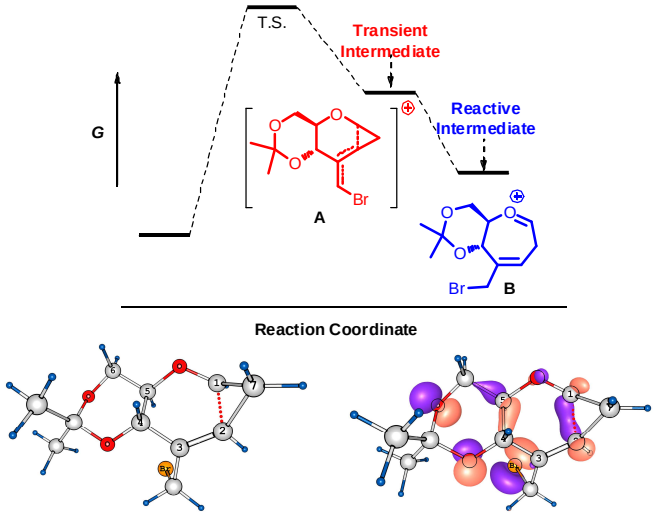
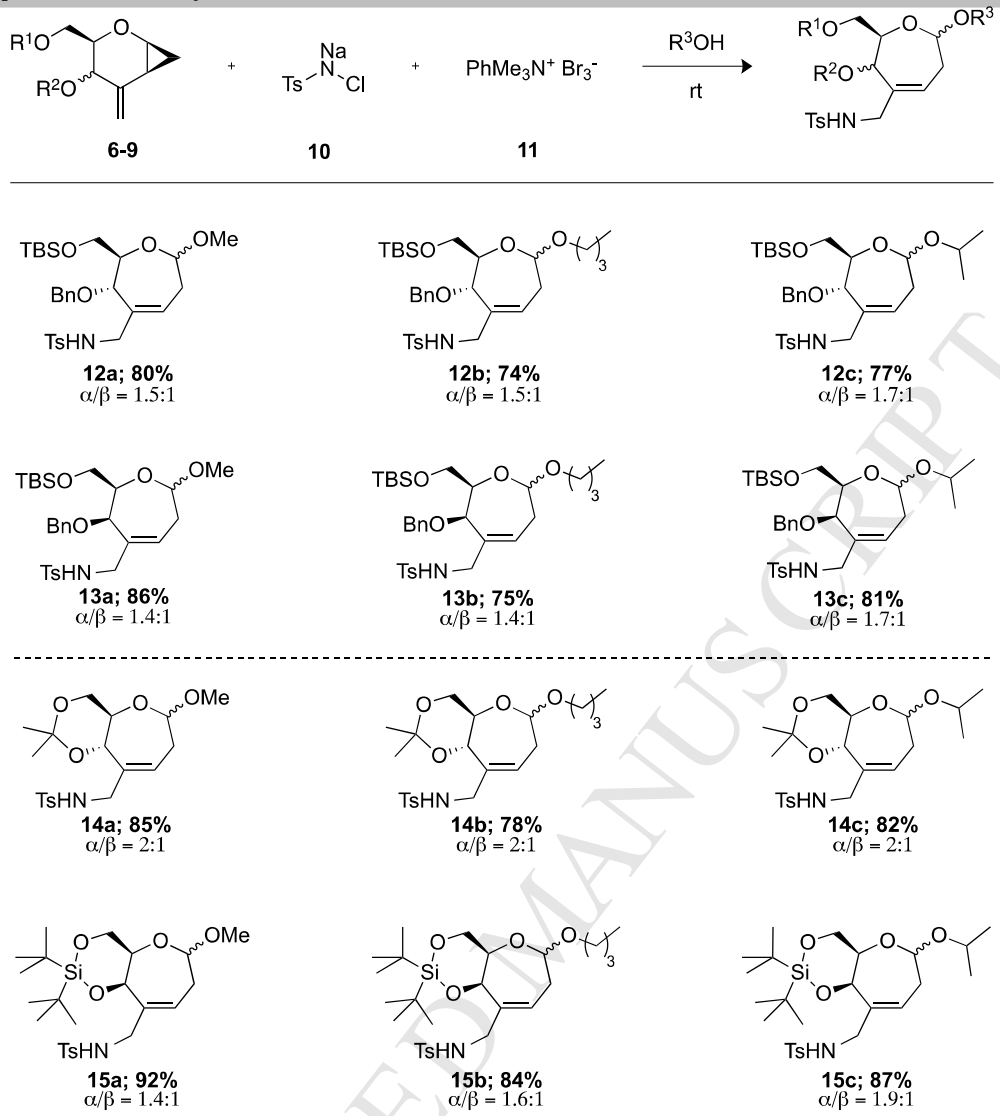
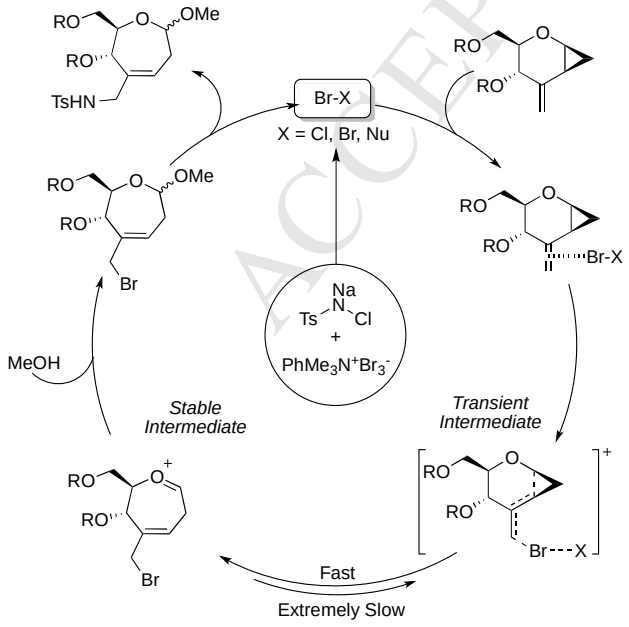


Figure 1. Energy profile for the ring-expansion reaction *(Color only in Web version)*

Table 1. Ring-expansion of carbohydrate derived VCPs



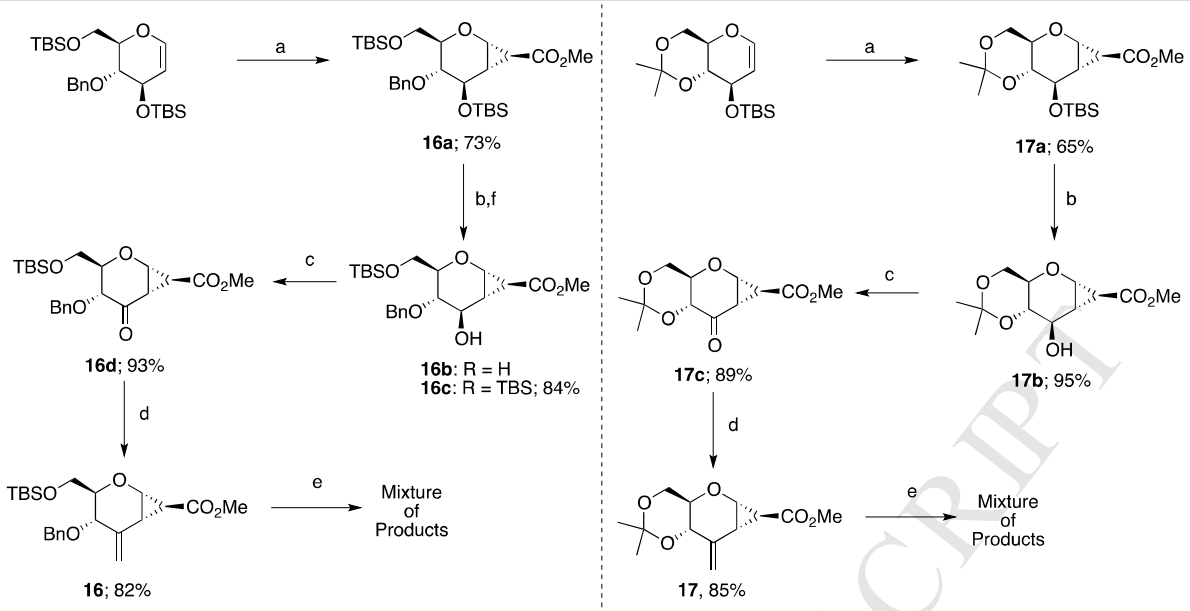


Scheme 5. Plausible mechanism for ring expansion of VCPs

stable (~4 kcal) planar oxonium ion **B** (Figure 1). Since, the conversion of the transient intermediate **A** to the oxonium ion **B** is a barrierless transition, trapping of **A** via an S_N2 pathway occurs to a negligible extent compared to the ring-expansion process. Hence, the reaction proceeds typically through a planar oxonium ion intermediate, resulting in poor diastereoselectivity.

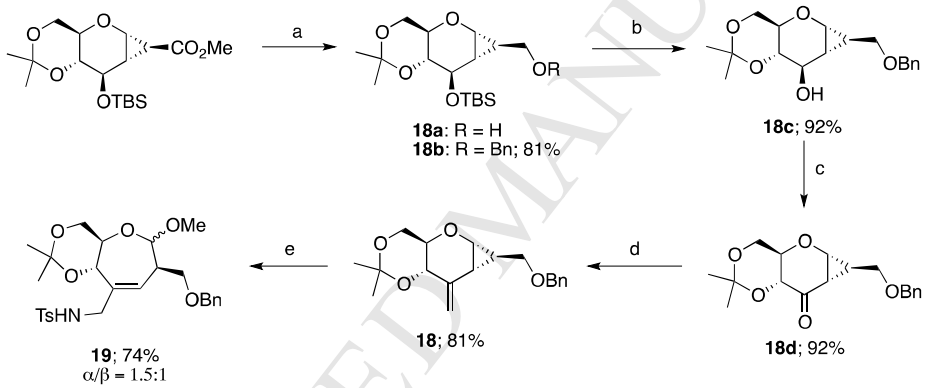
Based on our earlier studies on the reactivity of VCPs with halogen electrophiles and DFT calculations a plausible catalytic cycle for ring expansion of carbohydrate derived VCPs has been proposed (Scheme 5). In the first step, the reaction of chloramine-T with PTAB (catalyst, 10 mol%) enables the formation of interhalogen compounds *in situ* in catalytic amounts. These interhalogen compounds undergo addition across the VCP's double bond inducing the ring expansion through a transient tight carbocation intermediate. This transient intermediate spontaneously undergoes complete ring opening to give a planar oxonium intermediate. Subsequent attack of alcohol (MeOH) nucleophiles and displacement of bromo group by NTs^- results in the formation of the desired oxepane analogoues.

Further, we were interested in functionalizing the methylene carbon of the cyclopropane ring anticipating that the reaction will lead to a densely functionalized oxepane. Hence, we synthesized the corresponding carboxylate derived cyclopropane **16a** using $Rh_2(OAc)_4$ catalyzed cyclopropanation of the fully protected glucal with methyl diazoacetate. The resulting cyclopropane



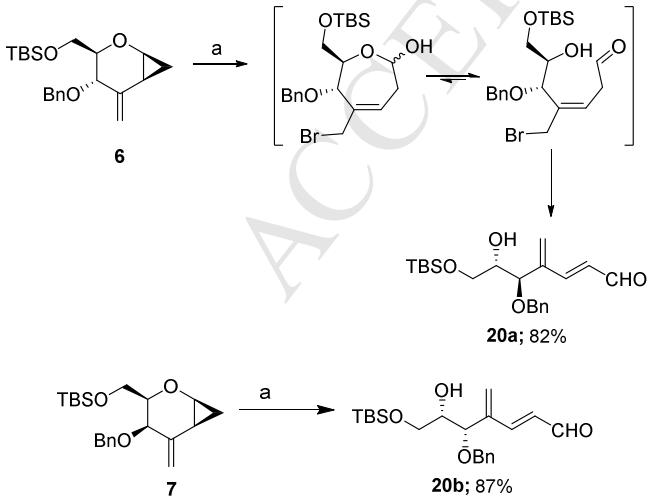
Reagents and conditions: (a) N_2CHCO_2Me (2 equiv), $Rh_2(OAc)_4$ (10 mol%), DCM, rt, 4 h; (b) TBAF (1.2 equiv/TBS group), THF, 2 h; (c) DMP (1.1 equiv), DCM, 0 °C, 2 h; (d) $[Ph_3PCH_3]^+I^-$ (2 equiv), *n*-BuLi (1.5 equiv), THF, 0 °C, 5 h; (e) Chloramine-T, PTAB (10 mol%), MeOH, rt, 6 h.

Scheme 6. Reactivity of vinyl cyclopropane carboxylates **16** and **17**.



Reagents and conditions: (a) (i) $LiAlH_4$ (1 equiv), THF, 0 °C; (ii) BnBr (1.05 equiv), NaH (1.5 equiv), DMF, 0 °C; (b) TBAF (1.2 equiv/TBS group), THF, 2 h; (c) DMP (1.1 equiv), DCM, 0 °C, 2 h; (d) $[Ph_3PCH_3]^+I^-$ (2 equiv), *n*-BuLi (1.5 equiv), THF, 0 °C, 5 h; (e) chloramine-T, PTAB (10 mol%), MeOH, rt, 6 h; (f) TBS-Cl (1.1 equiv), imidazole (2 equiv), DMF, 0 °C-rt, 3 h; (g).

Scheme 7. Ring expansion of **18** to a densely functionalized oxepane **19**



Reagents and Conditions: (a) **10** (1.1 equiv), **11** (0.1 equiv), Moist MeCN (0.5 mL H_2O/ 5mL MeCN).

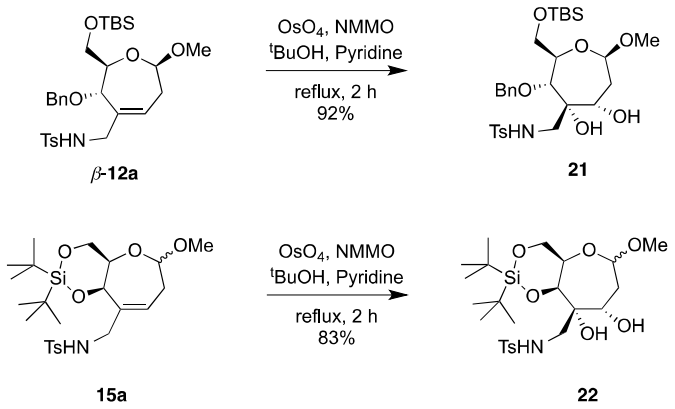
Scheme 8. Reactivity of VCP **6** and **7** in the presence of water

ester **16a** was converted to the desired VCP **16** using a standard protocol. Reaction of **16** under ring–expansion conditions (chloramine-T, PTAB) led to a complex mixture of products (Scheme 6). This result was further confirmed by subjecting VCP ester **17** to similar reaction conditions, which led to a mixture of products as well. We speculate that the possible side reactions could be due to the activation of the ester carbonyl under the influence of an electrophile due to the inherent donor-acceptor nature of the carbohydrate derived VCP esters. The ring–opening of such cyclopropane carboxylate systems under the influence of an electrophile have been explored extensively by our group.[55, 56]

To confirm our speculation, we decided to convert the cyclopropane carboxylate **17a** to the reduced derivative **18a**. The desired VCP **18** was obtained by the deprotection of the silyl group followed by oxidation and the Wittig reaction sequence. Reaction of **18** under standard reaction conditions (chloramine-T, PTAB) in methanol led to the ring- expanded oxepane **19** in good yield but with poor selectivity. (Scheme 7)

Interestingly, with water as the nucleophile, the *gluco*-VCP **6** under similar conditions using moist acetonitrile, led to the ring-opened product followed by elimination of bromide to yield an

open chain polyhydroxylated diene **20a** in excellent yield (Scheme 8). Similar reactivity was observed in the case of galacto-VCP **7** which resulted in the formation of epimeric diene **20b**. These polyhydroxylated dienes are potential synthons for the synthesis of zaragozic acids and amphidinolides.



Scheme 9. Synthesis of 2-deoxyseptanoside derivatives **21**, **22**.

The oxepane ***β*-12a** (separated by flash column chromatography) and **15a** were further dihydroxylated in a diastereoselective fashion using OsO_4/NMMO in *t*-butanol under reflux to the corresponding 2-deoxyseptanoside derivatives **21** (92%) and **22** (83%) respectively (Scheme 9).

3. Conclusion

In summary, we have developed a novel route to access densely functionalized oxepanes and 2-deoxyseptanosides through a σ-Ferrier type ring-expansion of carbohydrate derived VCPs. Attempts were made to improve the diastereoselectivity at the anomeric position. Since the reaction proceeds through a planar oxonium intermediate, controlling the diastereoselectivity at the anomeric position is challenging. Our efforts are being continued to access the transient, tight-carbocation intermediate.

4. Experimental section

4.1 General Information

All solvents for routine isolation of products and chromatography were laboratory grade and redistilled. Acetonitrile and DCM used for the reaction were dried under reflux over CaH_2 and stored over 3 Å molecular sieves. Flash chromatography was performed using silica gel (230−400 mesh) with indicated solvents. All reactions were monitored by thin-layer chromatography on 0.25 mm silica plates (F-254) visualizing with UV light and developed using phosphomolybdate or vanillin solution. ^{1}H, ^{13}C-NMR spectra were recorded on a 400 MHz NMR spectrometer. Chemical shifts in ppm, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in Hertz (Hz), and number of protons. HRMS were measured with electrospray ionization (ESI) and quadrupolar mass analyzer. Gaussian 09 program was used for energy minimization.

4.2 Experimental Procedure and Spectral Details

*1,5-Anhydro-2-deoxy-4-O-benzyl-6-O-TBS-D-arabino-hex-1-enitol (**3a**):* To a stirred solution of glycal **2a** (11.8 g, 50 mmol, 1 equiv) in DMF (150 mL) at -15 °C was added imidazole (6.8 g, 100 mmol, 2.0 equiv) and TBS-Cl (7.8 g, 52 mmol, 1.05 equiv) in parts under nitrogen atmosphere. After the addition, the reaction mixture was allowed to warm to room temperature .The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X200 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the *title compound* in its pure form. Gummy; R_f = 0.58 (hexanes/EtOAc, 8 : 2); Yield: 14 g, 80%; $[\alpha]^{25}_D$= +27.6 ($CHCl_3$, c = 1.7) (lit. $[\alpha]^{25}_D$= +27.2 ($CHCl_3$, c = 1.0):[57] IR (neat): 3422, 2954, 2930, 2884, 2858, 1651, 1253, 1538, 1109, 837, 778 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37-7.30 (5H, m, Ph), 6.36 (1H, d, *J* = 6.0 Hz, O-C<u>H</u>=CH), 4.79 (2H, dd, *J* = 12.4 Hz, O-C<u>H</u>$_2$-Ph), 4.71 (1H, dd, *J* = 2.8 Hz, 6.0 Hz, O-CH=C<u>H</u>), 4.29-4.28 (1H, m, C<u>H</u>-O), 3.95 (2H, d, *J* = 2.0 Hz, C<u>H</u>$_2$-OTBS), 3.87-3.85 (1H, m, C<u>H</u>-O), 3.68 (1H, dd, *J* = 6.4 Hz, 7.2 Hz, C<u>H</u>-O), 2.33 (1H, s, -O<u>H</u>), 0.92 (9H, s, Si(<u>t</u>Bu)), 0.09 (6H, s, Si(<u>Me</u>)$_2$); ^{13}C-NMR (100 MHz, $CDCl_3$): 144.5, 138.4, 128.5, 127.9, 102.1, 77.5, 77.0, 73.6, 67.9, 62.4, 25.8, 18.3, -5.2, -5.5; HRMS m/z: calcd for $C_{19}H_{30}O_4Si$ $[M+Na]^+$: 373.1811; found: 373.1811.

*1,5-Anhydro-2-deoxy-4-O-benzyl-6-O-TBS-β-1,2-C-methylene-D-arabino-hexitol (**4a**):* To a stirred solution of diethyl zinc (1M solution in toluene, 15 mL,15.0 mmol, 1.5 equiv) in DCM (15 mL) at -15 °C was added a solution of CH_2I_2 (4.6 g, 17 mmol, 1.7 equiv) in DCM (30 mL) drop wise under nitrogen atmosphere. The solution was stirred for 20 min to form iodozinc methyl iodide as a yellowish white precipitate. To the reaction mixture a solution of glycal **3a** (3.5 g, 10 mmol, 1 equiv) in DCM (3X2 mL) was added at -15 °C. After the addition, the reaction mixture was allowed to warm to room temperature .The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was poured into ice-cold sat. NH_4Cl solution and then washed with water and extracted with CH_2Cl_2 (2X50 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided **4a** in its pure form. Gummy, R_f = 0.51 (hexanes /EtOAc, 8 : 2); Yield: 3.1 g, 85%; $[\alpha]^{25}_D$= +21.2 ($CHCl_3$, c = 1.3) IR (neat): 3442, 2952, 2928, 2856, 1107, 1076, 1054, 949, 836, 774 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.25 (5H, m, Ph), 4.72 (2H, s, O-C<u>H</u>$_2$-Ph), 4.26-4.25 (1H, m, C<u>H</u>-O), 3.81 (1H, d, *J* = 11.6 Hz, C<u>H</u>-O), 3.73 (1H, d, *J* = 11.6 Hz, C<u>H</u>-O), 3.71-3.67 (1H, m, C<u>H</u>-O), 3.29-3.27 (2H, m, C<u>H</u>$_2$-O), 2.18 (1H, s, -O<u>H</u>), 1.40-1.32 (1H, m, CH-C<u>H</u>-CH$_2$), 0.90 (9H, s, Si(<u>t</u>Bu)), 0.70-0.64 (2H, m, CH-C<u>H</u>$_2$-CH), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): 138.6, 128.5, 127.8, 127.8, 79.3, 78.8, 74.0, 70.7, 62.4, 53.3, 25.9, 18.3, 17.9, 11.1, -5.1, -5.4; HRMS m/z: calcd for $C_{20}H_{32}O_4Si$ $[M+Na]^+$: 387.1968; found: 387.1975.

*1,5-Anhydro-2-deoxy-1,2-C-methylene-4-O-benzyl-6-O-TBS-α-D-erythro-hex-3-ulose (**5a**):* To a stirred solution of cyclopropane alcohol **4a** (1.82 g, 5 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added Dess–Martin periodinane (DMP) (2.3 g, 5.5 mmol, 1.1 equiv). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction was quenched by adding 10% aqueous solution of $Na_2S_2O_3$ (20 mL)/ sat. solution of $NaHCO_3$ (*aq*) (20 mL) with vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3X50 mL). The combined organic layer was washed with sat. solution of $NaHCO_3$ (*aq*) and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding cyclopropyl ketone **5a** in its pure form. Gummy, R_f = 0.51 (hexanes/EtOAc, 8 : 2); Yield: 1.48 g, 82%; $[\alpha]^{25}_D$= +35.5 ($CHCl_3$, c = 1.0); IR (neat): 2954, 2929, 2883, 2857, 1708, 1137, 1097, 836, 777 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.40-7.26 (5H, m, Ph), 4.96 (1H, d, *J* = 10.8 Hz, O-C<u>H</u>$_2$Ph), 4.53 (1H, d, *J* = 10.8 Hz, O-C<u>H</u>$_2$Ph), 4.14 (1H, dd, *J* = 4.4 Hz, 8.8 Hz, C<u>H</u>-O), 3.93 (1H, d, *J* = 10.0 Hz, C<u>H</u>-O), 3.85 (2H, d, *J* = 10.0 Hz, C<u>H</u>$_2$-

OTBS), 3.78 (1 H, dd, *J* = 3.6 Hz, 1.6 Hz, CH-O), 1.92-1.87 (1H, m, O=C-CH-CH_2), 1.30-1.26 (2H, m, CH-CH_2-CH), 0.91 (9H, s, Si(^{t}Bu)), 0.08 (3H, s, Si-Me), 0.08 (3H, s, Si-Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 205.5, 137.7, 128.3, 128.1, 127.8, 82.7, 77.5, 74.3, 62.1, 57.7, 25.9, 25.8, 19.9, 18.3, -5.1, -5.5; HRMS m/z: calcd for $C_{20}H_{30}O_4Si$ $[M+Na]^+$: 385.1811; found: 385.1814.

*1,5-Anhydro-2,3-di-deoxy-1,2-C-methylene-4-O-benzyl-6-O-TBS-α-D-erythro-hexityl-exo-3-methylene (**6**)* To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **5a** (0.18 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding VCP in its pure form. Gummy, R_f = 0.50 (hexanes/EtOAc, 8 : 2); Yield: 0.159 mg, 87%; $[\alpha]^{25}_D$= +30.6 ($CHCl_3$, c = 0.5); ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37-7.28 (5H, m, Ph), 5.24 (1H, s, C=CH), 5.17 (1H, s, C=CH), 4.64 (1H, d, *J* =11.2 Hz, O-CHPh), 4.62 (1H, d, *J* = 11.2 Hz, O-CHPh), 3.85 (1H, d, *J* = 8.8 Hz, CH-O), 3.76-3.71 (3H, m, CH_2-OTBS, CH-O), 3.48-3.44 (1H, m, CH-O), 1.79-1.73 (1H, m, CH-CH-CH2), 0.90 (9H, s, Si^{t}Bu), 0.88-0.83 (1H, m, CH-CH_2-CH), 0.73-0.69 (1H, m, CH-CH_2-CH), 0.08 (3H, s, SiMe), 0.07 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 144.0, 138.3, 128.3, 127.9, 127.6, 110.2, 80.7, 76.4, 62.8, 53.1, 25.9, 19.0, 18.3, 16.1, -5.0, -5.3; HRMS m/z: calcd for $C_{21}H_{32}O_3Si$ $[M+Na]^+$: 383.2018; found: 383.2003.

*(2R,3S)-3-(Benzyloxy)-2-(TBS-oxymethyl)-7-(α/β)-methoxy-4-(N-p-toluenesulfonamido methyl)-2,3,6,7-tetrahydrooxepine (**12a**)* To a stirred solution of VCP **6** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **12a** in its pure form. R_f = 0.33 (hexanes/EtOAc, 7 : 3); Yield: 0.090 g, 80%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.68 (2H, d, *J* = 8.0 Hz, Ph), 7.36-7.26 (7H, m, Ph), 5.60 (1H, dd, *J* = 4.8 Hz, 4.8 Hz, C=CH), 4.96 (1H, dd, *J* = 5.6 Hz, 6.4 Hz, -NHTs), 4.85 (1H, dd, *J* = 5.Hz, 7.6 Hz, O-CH-OMe), 4.50 (2H, dd, *J* = 11.6 Hz, 13.6 Hz, O-CHPh), 4.08 (1H, d, *J* = 2.8 Hz, CH-O), 3.81-3.75 (2H, m, -CHOTBS), 3.64-3.56 (3H, m, CH-O, CH_2-N), 3.39 (3H, s, -OMe), 2.50 (1H, d, *J* = 17.2 Hz, CH-CH-CH), 2.41 (3H, s, Ph-Me), 2.33-2.25 (1H, m, CH-CH-CH), 0.90 (9H, s, Si^{t}Bu), 0.09 (3H, s, SiMe), 0.08 (3H, s, Si-Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.2, 137.7, 137.2, 134.3, 129.6, 128.5, 127.9, 127.1, 127.1, 100.6, 79.7, 78.6, 72.3, 63.6, 55.6, 50.4, 36.4, 29.6, 25.8, 21.4, 18.3, -5.3, -5.5; HRMS m/z: calcd for $C_{29}H_{43}NO_6SSi$ $[M+Na]^+$: 584.2478; found: 584.2479.

*(2R,3S)-3-(Benzyloxy)-2-(TBS-oxymethyl)-7-(α/β)-butoxy-4-(N-p-toluenesulfonamidomethyl)-2,3,6,7-tetrahydrooxepine (**12b**)* To a stirred solution of VCP **6** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **12b** in its pure form. R_f = 0.56 (hexanes/EtOAc, 7 : 3); Yield: 0.089 g, 74%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.69 (1.2H, d, *J* = 7.2 Hz, Ph), 7.67 (2H, d, *J* = 7.2 Hz, Ph), 7.35-7.26 (13H, m, Ph), 5.66 (1H, dd, *J* = 4.0 Hz, 8.8 Hz, C=CH), 5.60 (1H, dd, *J* = 3.6 Hz, 3.6 Hz, C=CH), 4.94-4.90 (2H, m, -NH), 4.64 (1H, dd, *J* = 3.6 Hz, 8.8 Hz, O-CH-O), 4.49 (3.6 H, dd, *J* = 11.2 Hz, 15.2 Hz, O-CHPh), 4.07 (1H d, *J* = 3.2 Hz, CH-O), 3.81-3.73 (4.8H, m, CH-OTBS, CH-O), 3.63-3.43 (4H, m, CH-N), 3.40-3.32 (1.6 H, m, CH-O), 2.63-2.57 (0.6H, m, CH-CH-CH), 2.50-2.45 (1H, m, CH-CH-CH), 2.41 (4.8H, s, Me), 2.33-2.25 (1.6H, m, CH-CH-CH), 1.57-1.50 (3.2H, m, CH), 1.39-1.30 (3.2H, m, CH_3), 0.93 (5.4H, s, Si^{t}Bu), 0.89 (9H, s, Si^{t}Bu), 0.1 (1.8H, s, SiMe), 0.09 (1.8H, s, SiMe), 0.08 (3H, s, SiMe), 0.07 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.2, 143.1, 138.1, 137.8, 136.9, 136.5, 138.1, 137.8, 136.9, 136.5, 134.2, 129.6, 128.5, 128.4, 127.8, 127.5, 127.1, 127.1, 124.9, 99.4, 98.8, 79.7, 78.8, 72.3, 71.2, 69.8, 68.0, 67.5, 64.4, 63.6, 50.5, 48.4, 36.7, 31.6, 26.0, 25.8, 21.4, 19.3, 19.2, 18.5, 18.3, 13.8, -5.3, -5.5; HRMS m/z: calcd for $C_{32}H_{49}NO_6SSi$ $[M+Na]^+$: 626.2948; found: 626.2946.

*(2R,3S)-3-(Benzyloxy)-2-(TBS-oxymethyl)-7-(α/β)-isopropoxy-4-(N-p-toluenesulfonamidomethyl)-2,3,6,7-tetrahydrooxepine (**12c**)* To a stirred solution of VCP **6** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **12c** in its pure form.R_f = 0.52 (hexanes/EtOAc, 7 : 3); Yield: 0.093 g, 77%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.70 (2H, d, *J* = 8.0 Hz, Ph), 7.35-7.28 (7H, m, Ph), 5.67 (1H, dd, *J* = 4.4 Hz, 9.2 Hz, C=CH), 5.07 (1H, dd, *J* = 5.6 Hz, 6.4 Hz, -NHTs), 4.75 (1H, dd, *J* = 2.4 Hz, 9.2 Hz, O-CH-O), 4.50 (2H dd, *J* = 10.8 Hz, 21.2 Hz,O-CHPh), 4.19-4.12 (1H, m, CH-O), 4.08-4.01 (1H, m, CH-O), 3.87-3.75 (2H, m, CH-OTBS), 3.65 (2H, m, CH-N), 3.45 (1H, dd, *J* = 4.8 Hz, 13.6 Hz, Me_2CH-O), 2.62-2.56 (1H, m, CH-CH-CH), 2.41 (s, 3H, Me), 2.26-2.19 (1H, m, CH-CH-CH), 1.18 (3H, d, *J* = 6.4 Hz, Me_2CH), 1.10 (3H, d, *J* = 6.4 Hz, Me_2CH), 0.93 (9H, s, Si^{t}Bu), 0.10 (3H, s, SiMe), 0.09 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.3, 138.0, 136.9, 136.5, 129.6, 128.4, 128.0, 127.8, 127.1, 125.0, 96.0, 71.3, 69.7, 67.7, 64.4, 48.6, 31.4, 26.0, 23.4, 21.4, 21.0, 18.5, -5.3, -5.4; HRMS m/z: calcd for $C_{31}H_{47}NO_6SSi$ $[M+Na]^+$: 612.2791; found: 612.2799.

*1,5-Anhydro-2-deoxy-4-O-benzyl-6-O-TBS-D-lyxo-hex-1-enitol (**3b**):* To a stirred solution of glycal **2b** (11.8 g, 50 mmol, 1 equiv) in DMF (150 mL) at -15 °C was added imidazole (6.8 g, 100 mmol, 2.0 equiv) and TBS-Cl (7.8 g, 52 mmol, 1.05 equiv) in parts under nitrogen atmosphere. After the addition, the reaction mixture was allowed to warm to room temperature .The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X300 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash

chromatography of the crude product provided the title compound in its pure form. R_f = 0.57 (hexanes/ EtOAc, 8 : 2); Yield: 14.5 g, 83%; $[\alpha]^{25}_D$= -10.44 ($CHCl_3$, c = 1.7); IR (neat): 3422, 2955, 2930, 2885, 2858, 1647, 1252, 1233, 1110, 839, 778 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36-7.25 (5H, m, Ph), 6.31 (1H, d, *J* = 6.4 Hz, O-C<u>H</u>=), 4.76 (2H, s, O-CH_2Ph), 4.71 (1H, dd, *J* = 2.8 Hz, 6.0 Hz, C=C<u>H</u>), 4.33-4.30 (1H, m, C<u>H</u>-O), 4.00-3.89 (3H, m, C<u>H</u>-O, C<u>H$_2$</u>-OTBS), 3.80 (1H, dd, *J* = 6.4 Hz, 10.4 Hz, C<u>H</u>-O), 2.68 (1H, d, *J* = 10.0 Hz, O<u>H</u>), 0.91 (9H, s, Si<u>^{t}Bu</u>), 0.08 (6H, s, Si<u>Me$_2$</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 144.2, 137.9, 128.5, 127.9, 102.9, 76.4, 74.1, 72.7, 62.6, 61.0, 25.8, 18.2, -5.4; HRMS m/z: calcd for $C_{19}H_{30}O_4Si$ [M+Na] $^+$: 373.1811; found: 373.1812.

*1,5-Anhydro-2-deoxy-4-O-benzyl-6-O-TBS-β-1,2-C-methylene-D-lyxo-hexitol (**4b**)* To a stirred solution of diethyl zinc (1M solution in toluene, 7.5 mL, 7.5 mmol, 1.5 equiv) in DCM (15 mL) at -15 °C was added a solution of CH_2I_2 (2.3 g, 8.5 mmol, 1.7 equiv) in DCM (20 mL) drop wise under nitrogen atmosphere. The solution was stirred for 20 min to form iodozinc methyl iodide as a yellowish white precipitate. To the reaction mixture a solution of glycal **2b** (1.75 g, 5 mmol, 1 equiv) in DCM (3X2 mL) was added at -15 °C. After the addition, the reaction mixture was allowed to warm to room temperature .The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was poured into ice-cold sat. NH_4Cl solution and then washed with water and extracted with CH_2Cl_2 (2X100 mL) The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided **4b** in its pure form. R_f = 0.53 (hexanes/EtOAc, 8 : 2); Yield: 1.4 g, 76%; $[\alpha]^{25}_D$= -39.31 ($CHCl_3$, c = 1.0); IR (neat): 3454, 2954, 2929, 2857, 2884, 1254, 1108, 838, 777 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.26 (5H, m, Ph), 4.70 (1H, d, *J* = 11.6 Hz, O-C<u>H$_2$</u>Ph), 4.64 (1H, d, *J* = 11.6 Hz, O-C<u>H$_2$</u>Ph), 4.20-4.14 (1H, m, C<u>H</u>-O), 3.87 (1H, d, *J* = 5.2 Hz, C<u>H</u>-O), 3.77-3.70 (2H, m, CH_2-OTBS), 3.58 (1H, dd, *J* = 8.8 Hz, 8.8Hz, C<u>H</u>-O), 3.38 (1H, dd, *J* = 5.6 Hz, 8.4 Hz, C<u>H</u>-O), 2.37 (1H, d, *J* = 10.8 Hz, O<u>H</u>), 1.27-1.21 (1H, m, C<u>H</u>-CH_2), 1.11-1.08 (1H, m, CH-C<u>H$_2$</u>-CH), 0.90 (9H, s, Si<u>^{t}Bu</u>), 0.62-0.57 (1H, m, CH-C<u>H$_2$</u>-CH), 0.06 (3H, s, Si<u>Me</u>), 0.05 (3H, s, Si<u>Me</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 138.4, 128.4, 127.6, 127.4, 77.3, 76.0, 75.6, 65.4, 61.1, 54.0, 25.8, 18.1, 17.2, 11.2, -5.4, -5.5; HRMS m/z: calcd for $C_{20}H_{32}O_4Si$ [M+Na] $^+$: 387.1968; found: 387.1969.

*1,5-Anhydro-2-deoxy-1,2-C-methylene-4-O-benzyl-6-O-TBS-β-D-threo-hex-3-ulose (**5b**):* To a stirred solution of cyclopropane alcohol **4b** (1.4 g, 3.85 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added Dess–Martin periodinane (DMP) (1.8 g, 4.23 mmol, 1.1 equiv). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction was quenched by adding 10% aqueous solution of $Na_2S_2O_3$ (20 mL)/ sat. solution of $NaHCO_3$ (*aq*) (10 mL) with vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3X50 mL). The combined organic layer was washed with sat. solution of $NaHCO_3$ (*aq*) and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding cyclopropyl ketone in its pure form. R_f = 0.55 (hexanes/EtOAc, 8 : 2); Yield: 1.26 g, 90%; $[\alpha]^{25}_D$= -137.07 ($CHCl_3$, c = 3.0); IR (neat): 2954, 2930, 2858, 2884, 1699, 1252, 1113, 838 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34-7.25 (5H, m, Ph), 4.62 (1H, d, *J* = 11.6 Hz, O-C<u>H$_2$</u>Ph), 4.43 (1H, d, *J* = 11.6 Hz, O-C<u>H$_2$</u>Ph), 4.14 (1H, dd, *J* = 5.2 Hz, 8.8 Hz, C<u>H</u>-O), 3.88 (1H, dd, *J* = 6.8 Hz, 6.8 Hz, C<u>H</u>-O), 3.72 (s, 2H), 3.70 (1H, s, C<u>H</u>-O), 1.89-1.85 (1H, m, C<u>H</u>-CH_2), 1.79-1.74 (1H, m, CH-C<u>H$_2$</u>-CH), 1.26-1.21 (1H, m, CH-C<u>H$_2$</u>-CH), 0.85 (9H, s, Si<u>^{t}Bu</u>), 0.03 (3H, s, Si<u>Me</u>), 0.02 (3H, s, Si<u>Me</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 202.4, 137.0, 128.3, 127.9, 127.8, 81.8, 79.4, 71.8, 60.5, 58.1, 25.8, 24.2, 19.0, 18.1, -5.5, -5.6; HRMS m/z: calcd for $C_{20}H_{30}O_4Si$ [M+Na] $^+$: 385.1811; found: 385.1814.

*1,5-Anhydro-2,3-di-deoxy-1,2-C-methylene-4-O-benzyl-6-O-TBS-β-D-threo-hexityl-3-exo-methylene (**7**)* To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **5b** (0.18 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided **7** in its pure form. R_f = 0.57 (hexanes/EtOAc, 8 : 2); Yield: 0.152 g, 84%; $[\alpha]^{25}_D$= -71.21 ($CHCl_3$, c = 3.0); IR (neat): 2955, 2930, 2884, 2858, 1640, 1463, 1093, 1061, 836, 777 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.33-7.23 (5H, m, Ph), 5.29 (1H, s, C=C<u>H$_2$</u>), 5.01 (1H, s, C=C<u>H$_2$</u>), 4.63 (1H, d, *J* = 12.0 Hz,O-CH_2Ph), 4.30 (1H, d, *J* = 12.0 Hz,O-CH_2Ph), 3.84-3.81 (2H, m, C<u>H$_2$</u>-OTBS), 3.76-3.66 (2H, m, C<u>H</u>-O), 3.54 (1H, dd, *J* = 6.0 Hz, 7.2 Hz, C<u>H</u>-O), 1.66-1.60 (1H, m, C<u>H</u>-CH_2), 1.21-1.17 (1H, m, CH-C<u>H$_2$</u>-CH), 0.89-0.82 (1H, m, CH-C<u>H$_2$</u>-CH), 0.87 (9H, s, Si<u>^{t}Bu</u>), 0.04 (6H, s, Si<u>Me</u>) ; ^{13}C-NMR (100 MHz, $CDCl_3$): 139.7, 138.3, 128.2, 127.7, 127.3, 115.1, 79.0, 76.2, 68.9, 61.8, 53.7, 25.9, 18.2, 17.5, 16.2, -5.4, -5.5; HRMS m/z: calcd for $C_{21}H_{32}O_3Si$ [M+Na] $^+$: 383. 1820; found: 383.1835.

*(2R,3R)-3-(Benzyloxy)-2-(TBS-oxymethyl)-7-(α/β)-methoxy-4-(N-p-toluenesulfonamidomethyl)-2,3,6,7-tetrahydrooxepine (**13a**)* To a stirred solution of VCP **7** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **13a** in its pure form. R_f = 0.52 (hexanes/EtOAc, 8 : 2); Yield: 0.096 g, 86%;^{1}H-NMR (400 MHz, $CDCl_3$): 7.69 (2H, d, *J* = 8.0 Hz, Ph), 7.65 (2H, d, *J* = 8.0 Hz, Ph), 7.34-7.24 (15.4H, m, Ph), 5.73 (1H, dd, *J* = 3.2 Hz, 9.2 Hz, C=C<u>H</u>), 5.63 (1.1H, dd, *J* = 6.4 Hz, C=C<u>H</u>), 4.82 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, N<u>H</u>), 4.74 (1H, dd, *J* = 4.0 Hz, 6.4 Hz, O-C<u>H</u>-O), 4.62-4.57 (4.2H, m, O-C<u>H$_2$</u>Ph), 4.44 (d, *J* = 12.0 Hz, 1H, C<u>H</u>-O), 4.13-4.08 (2.1H, m, C<u>H</u>-O), 3.97-3.93 (2.1H, m, C<u>H$_2$</u>-OTBS), 3.79 (1H, m, C<u>H$_2$</u>-OTBS), 3.69-3.65 (1H, m, C<u>H</u>-O), 3.55-3.34 (5H, m, C<u>H$_2$</u>-N), 3.40 (3H, s, O<u>Me</u>), 3.34 (3H, s, O<u>Me</u>), 2.73-2.67 (1H, m, CH-C<u>H$_2$</u>-CH), 2.63-2.55 (1H, m, CH-C<u>H$_2$</u>-CH), 2.41 (3H, s, <u>Me</u>), 2.40 (3H, s, <u>Me</u>), 2.35-2.26 (2.2H, m, CH-C<u>H$_2$</u>-CH), 0.91 (9H, s, Si<u>^{t}Bu</u>), 0.90 (10H, s, Si<u>^{t}Bu</u>), 0.08 (3H, s, Si<u>Me</u>), 0.07 (3H, s, Si<u>Me</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.4, 143.2, 138.5, 138.3, 137.2, 137.0, 136.8, 129.6, 128.5, 128.4, 128.2, 128.0, 127.7, 127.6, 127.4, 127.1, 127.0, 126.0, 104.2, 100.4, 79.4, 76.4, 75.1, 72.3, 71.5, 70.7, 62.9, 62.5, 55.5, 55.1, 50.2, 48.9, 35.4, 32.3, 25.9, 25.8, 21.4, 18.2, 18.2, -5.4,-5.5; HRMS m/z: calcd for $C_{29}H_{43}NO_6SSi$ [M+Na] $^+$: 584.2478; found: 584.2482.

*(2R,3R)-3-(Benzyloxy)-2-(TBS-oxymethyl)-7-(α/β)-butoxy-4-(N-p-toluenesulfonamidomethyl)-2,3,6,7-tetrahydrooxepine (**13b**)* To

a stirred solution of VCP **7** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **13b** in its pure form. R_f = 0.52 (hexanes/EtOAc, 8 : 2); Yield: 0.091 g, 75%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.68 (1.5H, d, *J* = 8.0 Hz, 1.5 Hz, Ph), 7.64 (2H, d, *J* = 8.0 Hz, Ph), 7.33-7.25 (13.5H, m, Ph), 5.75 (0.7H, dd, *J* = 2.0 Hz, 8.4 Hz, C=CH), 5.62 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, C=CH), 4.84 (1H, dd, *J* = 4.0 Hz, 6.8 Hz, NH), 4.64-4.57 (3.6H, m, O-CH-O, O-CH_2Ph), 4.45 (0.8H, d, *J* = 7.6 Hz, CH-O), 4.38 (1H, dd, *J* = 7.6 Hz, 6.4 Hz, CH-O), 4.33 (1H, d, *J* = 8.8 Hz, CH-O), 3.98 (1H, dd, *J* = 7.6 Hz, 7.6 Hz, CH-O), 3.96 (0.8H, s, CH-O), 3.87-3.63 (5.7H, m, CH_2-OTBS), 3.53 (1H, dd, *J* = 7.2 Hz, 14.0 Hz, CH-O), 3.44-3.30 (5H, m, CH_2-N), 2.73 (0.7H, dd, *J* = 8.8 Hz, CH-CH_2-CH), 2.52 (1H, ddd, *J* = 4.0 Hz, 6.8 Hz, 16Hz, CH-CH_2-CH), 2.42 (2H, s, Me), 2.41 (3H, s, Me), 2.38-2.27 (2H, m, CH-CH_2-CH), 1.58-1.49 (3.7H, m, CH-CH_2-CH_2), 1.37-1.32 (3.6H, m, CH_2-CH_2-CH_3), 0.93-0.89 (22H, m, Si^{t}Bu, CH_2-Me), 0.08 (6H, s, SiMe), 0.07 (4H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.4, 143.2, 138.6, 138.3, 137.1, 137.0, 136.5, 129.6, 129.5, 128.4, 128.2, 128.1, 127.8, 127.7, 127.7, 127.4, 127.1, 127.1, 126.0, 103.2, 99.2, 79.5, 76.5, 75.2, 72.6, 71.3, 70.7, 67.9, 67.3, 63.0, 62.3, 50.3, 48.9, 35.7, 32.5, 31.6, 31.5, 25.9, 21.5, 19.4, 19.2, 18.2, 13.9, -5.4, -5.5; HRMS m/z: calcd for $C_{32}H_{49}NO_6SSi$ $[M+Na]^+$: 626.2948; found: 626.2944.

*(2R,3R)-3-(Benzyloxy)-2-(TBS-oxymethyl)-7-(α/β)-isopropoxy-4-(N-p-toluenesulfonamidomethyl)-2,3,6,7-tetrahydrooxepine (**13c**)* To a stirred solution of VCP **7** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **13c** in its pure form. R_f = 0.55 (hexanes/EtOAc, 8 : 2); Yield: 0.096 g, 81%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.68 (2H,d, *J* = 8.0 Hz, 1 Hz, Ph), 7.64 (2H d, *J* = 8.0 Hz, Ph), 7.35-7.25 (12H, m, Ph), 5.75 (0.6H, d, *J* = 8.0 Hz, C=CH), 5.63-5.58 (1H, m, C=CH), 4.97-4.94 (1H, m, NH), 4.68-4.57 (3H, m, NH, O-CH_2Ph), 4.47-4.42 (0.7H, m, O-CH_2Ph), 4.36-4.31 (1H, m, O-CH_2Ph), 4.14-4.10 (1H, m, CH-O), 4.03-3.91 (3H, m, CH-O, CH_2-OTBS), 3.82-3.62 (3H, m, CH_2-N), 3.56-3.51 (1H, m, CH_2-N), 3.45-3.40 (2H, m, O-CHMe_2), 2.49-2.22 (2H, m, CH-CH_2-CH), 2.41 (5H, s, Me), 1.20-1.07 (10H, m, Me_2), 0.93 (9H, s, Si^{t}Bu), 0.91 (6H, s, Si^{t}Bu), 0.09 (6H, s, SiMe), 0.07 (3.7H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.2, 138.6, 138.3, 137.1, 136.4, 129.6, 129.5, 128.4, 128.2, 128.1, 127.7, 127.4, 127.1, 125.9, 100.7, 96.7, 79.7, 75.3, 72.7, 71.2, 70.7, 68.5, 67.9, 63.2, 62.2, 50.3, 48.9, 36.2, 32.9, 25.9, 23.4, 21.4, 21.1, 18.2, -5.5; HRMS m/z: calcd for $C_{31}H_{47}NO_6SSi$ $[M+Na]^+$: 612.2791; found: 612.2790.

*1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-β-1,2-C-methylene-D-arabino-hexitol (**3c**)* To a stirred solution of diethyl zinc (1M solution in toluene, 15 mL, 15.0 mmol, 1.5 equiv) in DCM (30 mL) at -15 °C was added a solution of CH_2I_2 (4.6 g, 17 mmol, 1.7 equiv) in DCM (50 mL) drop wise under nitrogen atmosphere. The solution was stirred for 20 min to form iodozinc methyl iodide as a yellowish white precipitate. To the reaction mixture a solution of glycal **2c** (1.86 g, 10 mmol, 1 equiv) in DCM (3X2 mL) was added at -15 °C. After the addition, the reaction mixture was allowed to warm to room temperature .The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was poured into ice-cold sat. NH_4Cl solution and then washed with water and extracted with CH_2Cl_2 (2X150 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided **3c** in its pure form. R_f = 0.53 (hexanes/EtOAc, 8 : 2); Yield: 1.72 g 86%; ^{1}H-NMR (400 MHz, $CDCl_3$): 4.19 (1H, dd, *J* = 7.6 Hz, CH-O), 3.86 (1H, dd, *J* = 5.6 Hz, 10.8 Hz, CH-O), 3.80-3.76 (1H, m, CH-O), 3.53 (1H, dd, *J* = 10.4 Hz, 21.2 Hz, CH-O), 3.35 (1H, dd, *J* = 11.6 Hz, 18.0 Hz, CH-O), 3.26 (1H, td, *J* = 5.6 Hz, 10.0 Hz, CH-O), 2.48 (1H, m, CH-CH_2-CH), 1.47 (3H, s, Me), 1.46-1.40 (3H, s, Me), 0.85-0.76 (2H, m, CH-CH_2-CH); ^{13}C-NMR (100 MHz, $CDCl_3$): 99.3, 74.6, 69.3, 68.6, 61.7, 54.6, 29.0, 19.0, 17.7, 11.7; HRMS m/z: calcd for $C_{10}H_{16}O_4$ $[M+Na]^+$: 223.0946; found: 223.0946.

*1,5-Anhydro-2-deoxy-4,6-O-isopropylidene-1,2-C-methylene-β-D-erythro-hex-3-ulose (**4c**)* To a stirred solution of cyclopropane alcohol **4b** (1.72 g, 8.6 mmol, 1 equiv) in CH_2Cl_2 (45 mL) at 0 °C was added Dess–Martin periodinane (DMP) (4.0 g, 9.5 mmol, 1.1 equiv). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction was quenched by adding 10% aqueous solution of $Na_2S_2O_3$ (20 mL)/ sat. solution of $NaHCO_3$ (*aq*) (20 mL) with vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3X100 mL). The combined organic layer was washed with sat. solution of $NaHCO_3$ (*aq*) and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding cyclopropyl ketone in its pure form. R_f = 0.56 (hexanes/EtOAc, 8 : 2); Yield: 1.36 g, 80%; $[\alpha]^{25}_D$= -97.91 ($CHCl_3$, c = 3.0); ^{1}H-NMR (400 MHz, $CDCl_3$): 4.21 (1H, dd, *J* = 5.2 Hz, 9.2 Hz, CH-O), 4.11 (d, 1H, *J* = 10.0 Hz, CH-O), 3.95 (1H, dd, *J* = 5.2 Hz, 10.4 Hz, CH-O), 3.84 (1H, td, *J* = 5.2 Hz, 10.0 Hz, CH-O), 3.75-3.70 (1H, m, CH-O), 1.97-1.91 (1H, m, CH-CH_2), 1.49 (3H, s, Me), 1.48 (3H, s, Me), 1.44-1.36 (2H, m, CH-CH_2-CH); ^{13}C-NMR (100 MHz, $CDCl_3$): 200.2, 100.0, 74.3, 73.5, 61.8, 59.0, 28.6, 25.4, 20.5, 18.5; HRMS m/z: calcd for $C_{10}H_{14}O_4$ $[M+Na]^+$: 221.0790; found: 221.0791.

*1,5-Anhydro-2,3-deoxy-4,6-O-isopropylidene-1,2-C-methylene-β-D-erythro-hexityl-exo-3-methylene (**8**)* To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **4c** (0.1 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding VCP **8** in its pure form. R_f = 0.59 (hexanes/EtOAc, 8 : 2); Yield: 0.082 g, 84%; $[\alpha]^{25}_D$= -97.91 ($CHCl_3$, c = 3.0); ^{1}H-NMR (400 MHz, $CDCl_3$): 5.11 (2H, d, *J* = 8.4 Hz, C=CH_2), 3.93 (1H, d, *J* = 10.0 Hz, CH-O), 3.87 (1H, dd, *J* = 9.2 Hz, 10.8 Hz, CH-O), 3.81 (1H, td, *J* = 2.8 Hz, 6.4 Hz, CH-O), 3.59 (1H, dd, *J* = 10.4 Hz, CH-O), 3.34 (1H, td, *J* = 5.6 Hz, 10.0 Hz, CH-O), 1.84-1.78 (1H, m, CH-CH_2), 1.49 (s, 3H),

1.43 (s, 3H), 0.96-0.91 (m, 1H), 0.84-0.80 (m, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): 141.6, 106.8, 99.2, 71.8, 70.2, 62.4, 54.2, 29.0, 19.7, 18.9, 16.3; HRMS m/z: calcd for $C_{11}H_{16}O_3$ $[M+Na]^+$: 219.0997; found: 219.1001.

*(4aR,9aS)-6-(α/β)-Methoxy-2,2-dimethyl-9-(N-p-toluenesulfamidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3]dioxino[5,4-b]oxepine (**14a**)* To a stirred solution of VCP **8** (0.039 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **14a** in its pure form. R_f = 0.54 (hexanes/EtOAc, 8 : 2); Yield: 0.066 g, 85%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.21 (2H, d, *J* = 8.0 Hz, Ph), 7.30 (2H, d, *J* = 8.0 Hz, Ph), 5.55-5.54 (1H, m, C=C<u>H</u>), 4.97 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, N<u>H</u>), 4.25 (1H, d, *J* = 8.8 Hz, O-C<u>H</u>-O), 4.10 (1H, d, *J* = 7.2 Hz, C<u>H</u>$_2$-O), 3.82 (1H, dd, *J* = 5.6 Hz, 11.6 Hz, C<u>H</u>-O), 3.73 (1H, dd, *J* = 8.0 Hz, 14.0 Hz, C<u>H</u>-O), 3.67-3.58 (2H, m, C<u>H</u>$_2$-N), 3.35 (3H, s, OMe), 3.20 (1H, td, *J* 6.4 Hz, 9.2 Hz, C<u>H</u>-O), 2.43 (3H, s, Me), 2.32-2.20 (2H, m, CH_2), 1.41 (3H, s, Me), 1.38 (3H, s, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.1, 138.5, 138.0, 129.4, 127.2, 123.9, 102.8, 98.5, 73.6, 70.8, 62.3, 55.6, 47.9, 35.1, 28.4, 21.4, 18.7; HRMS m/z: calcd for $C_{19}H_{27}NO_6S$ $[M+Na]^+$: 420.1457; found: 420.1457.

*(4aR,9aS)-6-(α/β)-Butoxy-2,2-dimethyl-9-(N-p-toluenesulfamidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3]dioxino[5,4-b]oxepine (**14b**)* To a stirred solution of VCP **8** (0.039 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded **14b** in its pure form. R_f = 0.50 (hexanes/EtOAc, 8 : 2); Yield: 0.068 g, 78%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.71 (2.6H, d, *J* = 8.0 Hz, Ph), 7.30 (2.6H, d, *J* = 8.0 Hz, Ph), 5.56-5.53 (1.3H, m, C=CH), 4.94 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, N<u>H</u>), 4.25 (1H, d, *J* = 8.8 Hz, O-C<u>H</u>-O), 4.21 (1H, d, *J* = 8.8 Hz, C<u>H</u>-O), 4.16 (1H, dd, *J* = 4.8 Hz, 4.8 Hz, C<u>H</u>-O), 3.82-3.77 (1.3H, m, C<u>H</u>-O), 3.75-3.68 (2.6H, m, C<u>H</u>$_2$-OTBS), 3.67-3.58 (2.6H, m, C<u>H</u>$_2$-N), 3.33-3.27 (1.3H, m, C<u>H</u>-O), 3.15 (1H, td, *J* = 6.0 Hz, 9.2 Hz, C<u>H</u>-O), 2.43 (4H, s, Me), 2.26 (2.2H, dd, *J* = 6.0 Hz, 6.0 Hz, CH-C<u>H</u>$_2$-CH$_2$), 1.55 (2H, m, CH$_2$-C<u>H</u>$_2$), 1.42-1.32 (11H, m, Me$_2$), 0.91 (4H, t, *J* = 7.2 Hz, CH$_2$-C<u>H</u>$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.1, 138.5, 138.0, 129.4, 127.2, 124.2, 123.9, 101.9, 98.7, 98.4, 74.0, 73.7, 70.7, 68.3, 67.6, 63.1, 62.4, 48.0, 47.5, 35.5, 33.0, 31.5, 28.5, 21.4, 19.2, 18.9, 18.7, 13.7; HRMS m/z: calcd for $C_{22}H_{33}NO_6S$ $[M+Na]^+$: 462.1926; found: 462.1926.

*(4aR,9aS)-6-(α/β)-Isopropoxy-2,2-dimethyl-9-(N-p-toluenesulfamidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3]dioxino[5,4-b]oxepine (**14c**)* To a stirred solution of VCP **8** (0.039 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.062 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded **14c** in its pure form.R_f = 0.51 (hexanes/EtOAc, 8 : 2); Yield: 0.070 g 82%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.71 (2H, d, *J* = 8.0 Hz, Ph), 7.30 (2H, d, *J* = 8.0 Hz, Ph), 5.55-5.53 (1H, m, C=C<u>H</u>), 4.97 (1H, dd, *J* = 6.8 Hz, 6.8 Hz, N<u>H</u>), 4.28-4.23 (2H, m, C<u>H</u>$_2$-OTBS), 3.87-3.58 (4H, m, C<u>H</u>$_2$-N, C<u>H</u>-O), 3.14 (1H, td, *J* = 6.0 Hz, 9.2 Hz, C<u>H</u>-O), 2.42 (3H, s, Me), 2.26-2.21 (2H, m, CH-C<u>H</u>$_2$-CH), 1.40 (3H, s, Me), 1.38 (3H, s, Me), 1.17 (3H, d, *J* = 6.4 Hz, <u>Me</u>CH), 1.10 (3H, d, *J* = 6.4 Hz, <u>Me</u>CH); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.0, 138.5, 138.0, 129.4, 127.2, 124.3, 99.8, 98.4, 73.7, 70.8, 69.6, 62.4, 48.0, 36.0, 28.5, 23.4, 21.4, 18.7; HRMS m/z: calcd for $C_{21}H_{31}NO_6S$ $[M+Na]^+$: 448.1770; found: 448.1770.

*1,5-Anhydro-2,3-deoxy-4,6-O-di-tert-butylsilyl-1,2-C-methylene-β-D-threo-hexityl-exo-3-methylene (**9**)* To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **4d** (0.15 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided **9** in its pure form. R_f = 0.52 (hexanes/EtOAc, 8 : 2); Yield: 0.122 g, 83%; $[\alpha]^{25}_D$= -29.11° ($CHCl_3$, c = 1.8); ^{1}H-NMR (400 MHz, $CDCl_3$): 5.22 (1H, s, C=C<u>H</u>$_2$), 5.15 (1H, s, C=C<u>H</u>$_2$), 4.56 (1H, s, C<u>H</u>-O), 4.23-4.15 (2H, m, C<u>H</u>$_2$OSi), 3.85 (1H, td, *J* = 2.8 Hz, 6.0 Hz, C<u>H</u>-O), 3.42 (1H, s, C<u>H</u>-O), 1.57 (1H, dt, *J* = 6.4 Hz, 10.4 Hz, C<u>H</u>-CH$_2$), 1.32 (1H, td, *J* = 3.2 Hz, 6.4 Hz, CH-C<u>H</u>$_2$-CH), 1.06 (9H, s, Si<u>^{t}Bu</u>), 1.04 (9H, s, Si<u>^{t}Bu</u>), 0.95-0.88 (1H, m, CH-C<u>H</u>$_2$-CH); ^{13}C-NMR (100 MHz, $CDCl_3$): 142.7, 114.8, 75.1, 74.4, 67.6, 53.9, 27.7, 27.5, 23.3, 20.5, 16.1, 15.6; HRMS m/z: calcd for $C_{16}H_{28}O_3Si$ $[M+Na]^+$: 319.1705; found: 319.1705.

*(4aR,9aR)-2,2-Di-tert-butyl-6-methoxy-9-(N-p-toluenesulfonamidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3,2]dioxasilino[5,4-b]oxepine (**15a**)* To a stirred solution of VCP **9** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.060 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **15a** in its pure form. R_f = 0.54 (hexanes/EtOAc, 8 : 2); Yield: 0.089g 92%; IR (neat): 3278, 2934, 2860, 1462, 1329, 1161, 1064, 898, 781 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.75-7.72 (2.5H, m, Ph), 7.32-7.30 (2.5H, m, Ph), 5.53 (1H, dd, *J* = 2.8 Hz, 8.4 Hz, C=C<u>H</u>), 5.52-5.48 (0.3H, m, N<u>H</u>), 5.03 (0.3H, dd, *J* = 4.0 Hz, 6.8 Hz, O-C<u>H</u>-O), 4.96-4.93 (1H, m, O-C<u>H</u>-O), 4.68 (0.3H, dd, *J* = 4.8 Hz, .4 Hz, C<u>H</u>-O), 4.64 (0.3H, s, C<u>H</u>-O), 4.56 (1H, s, C<u>H</u>-O), 4.30 (1H, d, *J* = 8.4 Hz, C<u>H</u>$_2$-OTBS), 4.28 (0.3H d, *J* = 8.4 Hz, CH-O), 4.24-4.10 (3H, m, OC<u>H</u>$_2$), 3.75 (0.3H, dd, *J* = 8.0 Hz, 9.2 Hz, C<u>H</u>-O), 3.66 (1H, dd, *J* = 7.2 Hz, 13.2 Hz, C<u>H</u>-O), 3.50 (1H, dd, *J* = 4.0 Hz, 13.6 Hz,CH2-N), 3.39 (3H, s, OMe), 3.35 (0.9H,

s, OMe), 2.55 (1H, dd, *J* = 8.8 Hz, 16.4 Hz, CH-C<u>H</u>$_2$-CH), 2.43 (3H, s, Me), 2.30 (1.3H, dd, *J*= 8.0 Hz, 16.0 Hz, CH-C<u>H</u>$_2$-CH), 1.04-1.01 (23H, m, Si^t<u>Bu</u>$_2$); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.4, 136.8, 136.7, 129.6, 129.5, 127.2, 126.5, 104.7, 101.3, 75.0, 74.7, 68.9, 69.5, 67.4, 60.3, 55.3, 55.0, 50.9, 35.5, 30.9, 27.4, 27.1, 23.3, 21.4, 20.9, 14.1; HRMS m/z: calcd for $C_{24}H_{39}NO_6SSi$ $[M+Na]^+$: 520.2165; found: 520.2164.

*(4aR,9aR)-2,2-Di-tert-butyl-6-butoxy-9-(N-p-toluenesulfonamidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3,2]dioxasilino[5,4-b]oxepine (**15b**)* To a stirred solution of VCP **9** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.060 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **15b** in its pure form. R_f = 0.52 (hexanes/EtOAc, 8 : 2); Yield: 0.088 g, 84%; IR (neat): 3289, 2934, 2860, 1473, 1337, 1161, 1038, 904 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.75-7.72 (3.3H, m, Ph), 7.14-7.28 (3.3H, m, Ph), 5.53 (1H, dd, *J* = 2.4 Hz, 8.0 Hz, C=C<u>H</u>), 5.49 (0.7H, dd, *J* = 4.0 Hz, 8.8 Hz, C=C<u>H</u>), 5.04 (0.7H, dd, *J* = 4.0 Hz, 6.4 Hz, N<u>H</u>), 4.98-4.90 (1H, m, N<u>H</u>), 4.77 (0.7H, dd, *J* = 4.4 Hz, 8.4 Hz, O-C<u>H</u>-O), 4.64 (0.7H, s, C<u>H</u>-O), 4.55 (1H, s, C<u>H</u>-O), 4.37 (1H, d, *J* = 8.4 Hz, C<u>H</u>-O), 4.26-4.15 (2.8H, m, C<u>H</u>$_2$-OTBS), 4.07-4.04 (0.7H, m, C<u>H</u>-O), 3.93 (0.7H, s, C<u>H</u>-O), 3.81-3.62 (3.5H, m, C<u>H</u>$_2$-N), 3.53-3.49 (1.6H, m, CH-O), 3.40-3.33 (2.6H, m, C<u>H</u>$_2$), 2.60-2.55 (1.6H, m, CH-C<u>H</u>$_2$-CH), 2.43 (3H, s, Me), 2.42 (2.5H, s, Me), 2.31-2.22 (1.7H, m, CH-C<u>H</u>$_2$-CH), 1.57-1.48 (3.5H, m, C<u>H</u>$_2$-CH$_2$), 1.41-1.29 (4.3H, m, CH2-C<u>H</u>$_2$), 1.04-1.01 (30H, s, Si^t<u>Bu</u>$_2$), 0.91 (5H, t, *J* = 7.2 Hz, CH$_2$-C<u>H</u>$_3$); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.4, 143.2, 137.2, 136.9, 136.8, 129.6, 129.5, 127.2, 126.8, 123.5, 103.4, 99.9, 76.8, 75.0, 74.7, 69.0, 68.5, 67.5, 60.3, 51.0, 48.7, 35.7, 31.6, 31.6, 31.1, 27.5, 27.4, 27.2, 23.3, 23.2, 21.5, 21.0, 20.6, 19.3, 14.1, 13.8, 13.7; HRMS m/z: calcd for $C_{27}H_{45}NO_6SSi$ $[M+Na]^+$: 562.2634; found: 562.2678.

*(4aR,9aR)-2,2-Di-tert-butyl-6-isopropoxy-9-(N-p-toluenesulfon amidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3,2]dioxasilino[5,4-b]oxepine (**15c**)* To a stirred solution of VCP **9** (0.072 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.060 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **15c** in its pure form. R_f = 0.56 (hexanes/EtOAc, 8 : 2); Yield: 0.091 g, 87%; IR (neat): 3283, 2969, 2860, 1474, 1332, 1161, 1035, 902, 825, 780, 651 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.75-7.72 (3H, m, Ph), 7.32-7.28 (3H, m, Ph), 5.53 (1H, dd, *J* = 4.4 Hz, 9.2 Hz, C=CH), 5.49 (0.5H, dd, *J* = 4.4 Hz, 9.2 Hz, C=CH), 5.05-4.82(2H, m, N<u>H</u>), 4.64 (0.5H, s, O-C<u>H</u>-O), 4.53 (1H, s, O-C<u>H</u>-O), 4.47 (1H, d, *J* = 8.4 Hz, C<u>H</u>-O), 4.25-4.04 (3H, m, C<u>H</u>$_2$O), 3.97-3.87 (2H, m, C<u>H</u>-O), 3.73 (0.5H, dd, *J* = 8.0Hz, 13.2 Hz, C<u>H</u>-O), 3.64 (1H, dd, *J* = 6.8 Hz, 13.2 Hz, C<u>H</u>$_2$-N), 3.55-3.51 (1H, m, C<u>H</u>$_2$-N), 3.51-3.44 (0.5H, s, C<u>H</u>-O), 3.36 (1H, s, C<u>H</u>-O), 2.58 (1H, dd, *J* = 9.6 Hz, 20 Hz, CH-C<u>H</u>$_2$-CH), 2.43 (3H, s, Me), 2.42 (2H, s, Me), 2.24 (1H, dd, *J* = 8.4 Hz, 16.8 Hz, CH-C<u>H</u>$_2$-CH), 2.20-2.16 (0.5H, m, C<u>H</u>), 1.20 (3H, d, *J* = 6.0 Hz, <u>Me</u>CH), 1.16 (1.5H, d, *J* = 6.0 Hz, <u>Me</u>CH), 1.10 (4.5H, d, *J* = 6.0 Hz, <u>Me</u>CH), 1.05 (9H, s, Si^t<u>Bu</u>$_2$), 1.04 (9H, s, Si^t<u>Bu</u>$_2$), 1.02 (4.5H, s, Si^t<u>Bu</u>$_2$), 1.00 (4.5H, s, Si^t<u>Bu</u>$_2$); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.4, 137.2, 136.9, 136.8, 136.5, 129.6, 129.5, 127.2, 127.2, 127.1, 123.5, 101.6, 97.9, 75.0, 74.7, 69.2, 69.1, 68.5, 68.5, 67.2, 51.1, 48.7, 36.2, 31.4, 29.6, 27.5, 27.4, 27.2, 23.6, 23.4, 23.3, 23.2, 21.6, 21.5, 21.0, 20.6; HRMS m/z: calcd for $C_{26}H_{43}NO_6SSi$ $[M+Na]^+$: 548.2478; found: 548.2480.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-3,6-O-di-TBS-4-O-benzyl-α- D-arabino-hexitol (**16a**):* To a stirred solution of glucal (3.0 g, 6.4 mmol, 1 equiv) in DCM (100 mL) at room temperature was added $Rh_2(OAc)_4$ (0.141 g, 0.32 mmol, 0.05 equiv) and allowed to stir under nitrogen atmosphere. A solution of methyldiazoacetate (0.96 g, 9.6 mmol, 1.5 equiv) in DCM (70 mL) was added drop wise using a dropping funnel under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 6 h. The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. Flash chromatography of the crude product provided the cyclopropyl ester **16a** in its pure form. R_f = 0.53 (hexanes/EtOAc, 8 : 2); Yield: 1.98 g, 73%; $[\alpha]^{25}_D$= +31.95 ($CHCl_3$, c = 1.7) IR (neat): 2954, 2930, 2858, 1729, 1257, 1122, 1096, 837, 777 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.28 (5H, m, Ph), 4.64 (2H, dd, *J* = 11.6 Hz, 23.2 Hz, PhC<u>H</u>$_2$O), 3.95 (1H, dd, *J* = 2.0 Hz, 5.6 Hz, C<u>H</u>-O), 3.90-3.85 (2H, m, C<u>H</u>-O), 3.68-3.60 (2H, m, C<u>H</u>$_2$O), 3.66 (3H, s, OMe), 3.40 (1H, dd, *J* = 5.6 Hz, 5.6 Hz, C<u>H</u>-O), 2.03 (1H, dd, *J* = 1.6 Hz, 6.0 Hz, C<u>H</u>), 1.68-1.65 (1H, m, C<u>H</u>), 0.90 (18H, s, Si<u>t</u>Bu), 0.06 (12H, s, Si<u>Me</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 172.2, 138.1, 128.3, 127.7, 127.6, 73.0, 69.3, 62.8, 57.1, 51.7, 28.1, 25.9, 25.3, 18.3, 17.8, -5.3, -5.4; HRMS m/z: calcd for $C_{28}H_{48}O_6Si_2$ $[M+Na]^+$: 559.2887; found: 559.2889.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-4-O-benzyl-α- D-arabino-hexitol (**16b**):* To a stirred solution of protected sugar **16a** (1.98 g, 3.5 mmol, 1 equiv) in THF (25 mL) was added a 1 M solution of TBAF (5.2 mL, 5.2 mmol, 1.5 equiv) in THF at 0 °C. The reaction was monitored by TLC. After complete conversion of the starting material, the reaction mixture was washed with water (50 mL) and extracted with DCM (2 X 80 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the desired deprotected product in its pure form. R_f = 0.54 (hexanes/EtOAc, 8 : 2); Yield: 1.37 g, 93%; $[\alpha]^{25}_D$= +28.15 ($CHCl_3$, c = 3.2) IR (neat): 3247, 3029, 2953, 1725, 1599, 1443, 1297, 1089, 748 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34-7.21 (5H, m, Ph), 4.65 (2H, dd, *J* = 11.6 Hz, 16.0 Hz, PhC<u>H</u>$_2$O), 4.03 (1H, d, *J* = 5.2 Hz, C<u>H</u>-O), 3.97 (1H, dd, *J* = 1.6 Hz, 7.2 Hz, C<u>H</u>-O), 3.80-3.72 (2H, m, C<u>H</u>$_2$OH), 3.64 (3H, s, OMe), 3.54 (1H, dd, *J* = 5.2 Hz, 9.6 Hz, CH-O), 3.39 (1H, dd, *J* = 5.6 Hz, CH-O), 2.12 (1H, dd, *J* = 1.6 Hz, 6.4 Hz, C<u>H</u>), 1.75 (1H, dd, *J* = 6.4 Hz, 6.4 Hz, O<u>H</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 172.5, 137.8, 128.5, 127.9, 127.8, 77.4, 73.9, 73.0, 67.4, 62.2, 57.9, 51.9, 26.5, 23.7; HR-MS m/z: calcd for $C_{16}H_{20}O_6$ $[M+Na]^+$: 331.1158; found: 331.1155.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-4-O-benzyl-6-O-TBS-α- D-arabino-hexitol (**16c**):* To a stirred solution of **16b** (0.9 g, 2.9 mmol, 1 equiv) in DMF (10 mL) at -15 °C was added imidazole (1 mmol, 5.8 equiv) and TBS-Cl (3.0 mmol, 1.05 equiv) in parts under nitrogen atmosphere. After the addition, the reaction mixture was allowed to warm to room temperature .The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed

with water and extracted with CH_2Cl_2 (3X20 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding mono-*O*-TBS protected compound in its pure form. R_f = 0.51 (hexanes/EtOAc, 8 : 2); Yield: 1.1 g, 91%; $[\alpha]^{25}_D$= -32.08 ($CHCl_3$, c = 0.6) IR (neat): 3451, 2954, 2930, 2858, 1726, 1120, 1095, 837 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.37-7.27 (5H, m, Ph), 4.65 (2H, d, *J* = 12.4 Hz, 12.4 Hz, PhC$\underline{H}_2$O), 3.98 (1H, d, *J* = 4.8 Hz, C$\underline{H}$-O), 3.94 (1H, d, *J* = 7.2 Hz, CH-O), 3.87-3.78 (3H, m, C$\underline{H}_2$O), 3.64 (3H, s, OMe), 3.59 (1H, d, *J* = 3.6 Hz, 7.6 Hz, C$\underline{H}$-O), 3.50 (1H, dd, *J* = 5.2 Hz, 5.2 Hz, C$\underline{H}$-O), 2.09 (1H, dd, *J* = 1.2 Hz, 5.6 Hz, C$\underline{H}$), 1.78 (1H, dd, *J* = 6.8 Hz, 6.8 Hz, OH), 0.92 (9H, s, Si^{t}Bu), 0.12 (3H, s, Si$\underline{Me}$), 0.10 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 172.2, 137.9, 128.5, 127.8, 127.7, 78.1, 74.9, 72.7, 66.6, 63.9, 57.9, 51.7, 26.9, 25.7, 24.9, 18.2, -5.3, -5.6; HRMS m/z: calcd for $C_{22}H_{34}O_6Si$ $[M+Na]^+$: 445.2022; found: 445.2021.

1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-4-O-benzyl-6-O-TBS-α-D-erythro-hex-1-en-3-ulose ***(16d)*** To a stirred solution of cyclopropane alcohol **16c** (1.1 g, 2.6 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added Dess–Martin periodinane (DMP) (1.2 g, 2.86 mmol, 1.1 equiv). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction was quenched by adding 10% aqueous solution of $Na_2S_2O_3$ (8 mL)/ sat. solution of $NaHCO_3$ (*aq*) (8 mL) with vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3X50 mL). The combined organic layer was washed with sat. solution of $NaHCO_3$ (*aq*) and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding cyclopropyl ketone **16d** in its pure form. R_f = 0.50 (hexanes/EtOAc, 8 : 2); Yield: 1.02 g, 93%; $[\alpha]^{25}_D$= +56.11 ($CHCl_3$, c = 1.4) IR (neat): 2955, 2931, 2860, 1725, 1120, 837 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.29 (5H, m, Ph), 4.78 (1H, d, *J* = 13.2 Hz, PhC$\underline{H}_2$O), 4.51 (1H, d, *J* = 13.2 Hz, PhC$\underline{H}_2$O), 4.29 (1H, dd, *J* = 2.4 Hz, 6.4 Hz, C$\underline{H}$-O), 3.96 (1H, dd, *J* = 4.0 Hz, 8.0 Hz, C$\underline{H}$-O), 3.78-3.75 (3H, m, C$\underline{H}_2$O), 3.69 (3H, s, OMe), 2.99 (1H, dd, *J* = 2.4 Hz, 5.2 Hz, C$\underline{H}$-CO), 2.38 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, C$\underline{H}$), 0.87 (9H, s, Si^{t}Bu), 0.05 (3H, s, SiMe), 0.04 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 198.0, 169.9, 136.8, 128.4, 128.2, 128.0, 78.6, 78.0, 72.7, 63.2, 61.2, 52.3, 31.8, 28.4, 25.7, 18.2, -5.6, -5.7; HRMS m/z: calcd for $C_{22}H_{32}O_6Si$ $[M+Na]^+$: 443.1866; found: 443.1861.

1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-4-O-benzyl-6-O-TBS-α-D-erythro-hexityl-exo-3-methylene ***(16)*** To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **16c** (0.21 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding VCP in its pure form. R_f = 0.55 (hexanes/EtOAc, 8 : 2); Yield: 0.17 g, 82%; $[\alpha]^{25}_D$= +32.71 ($CHCl_3$, c = 1.2) IR (neat): 2953, 2928, 2857, 1725, 1444, 1117, 837, 777 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36-7.26 (5H, m, Ph), 5.47 (1H, s, CH_2), 5.13 (1H, s, CH_2), 4.65 (1H, d, *J* = 12.0 Hz, PhC$\underline{H}_2$-O), 4.38 (1H, d, *J* = 12.0 Hz, PhC$\underline{H}_2$-O), 3.95-3.92 (2H, m, C$\underline{H}_2$OTBS), 3.85 (1H, s, C$\underline{H}$), 3.70-3.66 (1H, m, C$\underline{H}$-O), 3.67 (3H, s, OMe), 3.48 (1H dd, *J* = 10.0 Hz, 10.0 Hz, C$\underline{H}$-O), 2.55-2.53 (1H, m, C$\underline{H}$-CO_2Me), 2.37 (1H, dd, *J* = 6.4 Hz, 6.4 Hz, C$\underline{H}$-CO), 0.82 (9H, s, Si^{t}Bu), 0.01 (3H, s, SiMe), 0.00 (3H, s, SiMe) ; ^{13}C-NMR (100 MHz, $CDCl_3$): 172.0, 137.7, 133.4, 128.4, 127.8, 127.5, 119.4, 75.9, 69.3, 61.5, 57.7, 51.8, 29.4, 27.9, 25.7, 18.0, -5.5, -5.6; HRMS m/z: calcd for $C_{23}H_{34}O_5Si$ $[M+Na]^+$: 441.2073; found: 441.2073.

1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-3-O-TBS-4,6-O-isopropylidene-α-D-arabino-hexitol ***(17a)*** To a stirred solution of glucal (1.50 g, 5 mmol, 1 equiv) in DCM (10 mL) at room temperature was added $Rh_2(OAc)_4$ (0.11 g, 0.25 mmol, 0.05 equiv) and allowed to stir under nitrogen atmosphere. A solution of methyldiazoacetate (0.75 g, 7.5 mmol, 1.5 equiv) in DCM (10 mL) was added drop wise using a dropping funnel under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 6 h. The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. Flash chromatography of the crude product provided the cyclopropyl ester **17a** in its pure form. R_f = 0.57 (hexanes/EtOAc, 8 : 2); Yield: 1.19 g, 65%; $[\alpha]^{25}_D$= +43.1 ($CHCl_3$, c = 0.8) IR (neat): 2994, 2954, 2932, 2892, 2858, 1731, 1294, 1265, 1117, 1102, 838, 779 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.95 (1H, dd, *J* = 2.8 Hz, 7.6 Hz, C$\underline{H}$-O), 3.83-3.78 (2H, m, C$\underline{H}_2$O), 3.69 (3H, s, OMe), 3.63 (1H, dd, *J* = 10.4 Hz, 10.4 Hz, C$\underline{H}$-O), 3.53 (1H, dd, *J* = 8.4Hz, 10.0 Hz, C$\underline{H}$-O), 3.09 (1H, td, *J* = 5.6 Hz, 10.0 Hz, C$\underline{H}$-O), 2.03 (1H, dd, *J* = 2.4 Hz, 6.0 Hz, C$\underline{H}$$CO_2$Me), 1.64 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, CH), 1.46 (3H, s, Me), 1.36 (3H, s, Me), 0.90 (9H, s, Si$^t\underline{Bu}$), 0.1 (3H, s, SiMe), 0.08 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 172.2, 99.4, 73.4, 69.7, 64.0, 62.2, 59.9, 51.9, 28.9, 26.8, 25.8, 20.6, 18.8, 18.2, -4.6, -5.0; HRMS m/z: calcd for $C_{18}H_{32}O_6Si$ $[M+Na]^+$: 395.1866; found: 395.1865.

1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-4,6-O-isopropylidene-α-D-arabino-hexitol ***(17b)****:* To a stirred solution of protected sugar (1.19 g, 3.1 mmol, 1 equiv) in THF (15 mL) was added a 1 M solution of TBAF (4.6 mL, 4.6 mmol, 1.5 equiv) in THF at 0 °C. The reaction was monitored by TLC. After complete conversion of the starting material, the reaction mixture was washed with water (20 mL) and extracted with DCM (2 X 50 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the desired deprotected product in its pure form. R_f = 0.53 (hexanes/EtOAc, 8 : 2); Yield: 0.761 g, 95%; $[\alpha]^{25}_D$= +66.5 ($CHCl_3$, c = 0.8) IR (neat): 3468, 2998, 2895, 1716, 1446, 1199, 1088, 1048, 868, 828 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.98 (1H, dd, *J* = 2.4 Hz, 7.6 Hz, CH-O), 3.89-3.87 (1H, m, C$\underline{H}_2$O), 3.83 (1H, dd, *J* = 5.6 Hz, 10.8 Hz, C$\underline{H}_2$O), 3.68 (3H, s, OMe), 3.66 (1H, dd, *J* = 10.8 Hz, 10.8 Hz, C$\underline{H}$-O), 3.57 (1H, dd, *J* = 8.4 Hz, 10.0 Hz, C$\underline{H}$-O), 3.12 (1H, td, *J* = 5.6 Hz, 10.0 Hz, CH), 2.94-2.92 (1H, m, OH), 2.04 (1H, dd, *J* = 2.8 Hz, 5.6 Hz, C$\underline{H}$-CO_2Me), 1.71 (1H, dd, *J* = 6.8 Hz, 6.8 Hz, C$\underline{H}$), 1.50 (3H, s, Me), 1.39 (3H, s, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 172.1, 99.8, 73.6, 68.9, 63.7, 62.0, 59.3, 51.9, 28.8, 25.1, 21.2, 18.9; HRMS m/z: calcd for $C_{12}H_{18}O_6$ $[M+Na]^+$: 281.1001; found: 281.1000.

1,5-Anhydro-2-deoxy-1,2-C-(exo-carbmethoxymethylene)-4,6-O-isopropylidene-α-D-erythro-hex-3-ulose ***(17c)*** To a stirred solution of cyclopropane alcohol **17b** (0.516 g, 2.0 mmol, 1 equiv) in CH_2Cl_2 (5 mL) at 0 °C was added Dess–Martin periodinane (DMP) (0.932 g, 2.2 mmol, 1.1 equiv). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction was quenched by adding 10% aqueous solution of $Na_2S_2O_3$ (8 mL)/ sat. solution of $NaHCO_3$ (*aq*) (8 mL) with vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3X10 mL). The combined organic layer was washed with sat. solution of $NaHCO_3$ (*aq*) and

brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding cyclopropyl ketone **17c** in its pure form. R_f = 0.59 (hexanes/EtOAc, 8 : 2); Yield: 0.456 g, 89%; $[\alpha]^{25}_D$= +74.94 ($CHCl_3$, c = 0.8) IR (neat): 3012, 2930, 1733, 1719, 1523, 1181, 868, 820 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 4.27 (1H, dd, *J* = 2.8 Hz, 6.4 Hz, C<u>H</u>$_2$-O), 4.23 (1H, d, *J* = 14.8 Hz, C<u>H</u>-O), 3.91 (dd, *J* = 5.2 Hz, 10.8 Hz, 1H), 3.79 (dd, *J* = 11.6 Hz, 1H), 3.71 (s, 3H), 3.63 (1H, td, *J* = 5.6 Hz, 10.4 Hz, C<u>H</u>-O), 2.80 (1H, dd, *J* = 2.8 Hz, 5.2 Hz, C<u>H</u>-CO_2Me), 2.35 (1H, dd, *J* = 5.6 Hz, 5.6 Hz, C<u>H</u>), 1.50 (3H, s, Me), 1.47 (3H, s, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 169.9, 100.8, 74.5, 63.5, 62.2, 58.9, 52.5, 28.6, 28.5, 20.2, 18.4; HRMS m/z: calcd for $C_{12}H_{16}O_6$ $[M+Na]^+$: 279.0845; found: 279.0846.

*1,5-Anhydro-2,3-deoxy-1,2-C-(exo-carbmethoxymethylene)-4,6-O-isopropylidene-α-D-erythro-hexityl-exo-3-methylene (**17**)* To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **17c** (0.128 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding VCP **17** in its pure form. R_f = 0.56 (hexanes/EtOAc, 8 : 2); Yield: 0.108 g, 85%; $[\alpha]^{25}_D$= +13.95 ($CHCl_3$, c = 0.8) IR (neat): 2993, 2936, 2832, 1729, 1290, 1265, 1116, 1102, 866, 776 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 5.41 (1H, s, C<u>H</u>$_2$), 5.27 (1H, s, C<u>H</u>$_2$), 4.11 (1H, d, *J* = 10.4 Hz, CH_2O), 4.02 (1H, dd, *J* = 2.4 Hz, 7.2 Hz, C<u>H</u>$_2$O), 3.83 (1H, dd, *J* = 5.6 Hz, 11.2 Hz, C<u>H</u>-O), 3.73-3.66 (1H, m, C<u>H</u>-O), 3.69 (3H, s, OMe), 3.22 (1H, td, *J* = 5.2 Hz, 10.0 Hz, CH-O), 2.35 (1H, dd, *J* = 6.0 Hz, 6.4 Hz, C<u>H</u>-CO_2Me), 2.26-2.24 (1H, m, C<u>H</u>), 1.50 (3H, s, Me), 1.43 (3H, s, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 172.1, 137.5, 112.9, 99.8, 68.9, 65.6, 62.6, 59.3, 51.9, 29.6, 29.0, 23.5, 18.9; HRMS m/z: calcd for $C_{13}H_{18}O_5$ $[M+Na]^+$: 277.1052; found: 277.1065.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-hydroxymethylmethylene)-3-O-TBS-4,6-O-isopropylidene-α-D-arabino-hexitol (**18a**):* To a stirred suspension of $LiAlH_4$ (0.2 g, 5 mmol, 1 equiv) in THF (30 mL) at 0 °C was added dropwise a solution of the cyclopropane ester **17a** (1.86 g, 5 mmol, 1 equiv) in THF (10 mL). After the reaction mixture was warmed to room temperature while stirring for 3 h, it was quenched by the addition of EtOAc at 0 °C, followed by the treatment of sat. citric acid solution. The mixture was extracted with EtOAc (2 X 50 mL) and the organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography provided the alcohol **18a** in its pure form. R_f = 0.52 (hexanes/EtOAc, 8 : 2); Yield: 1.445 g, 84%; $[\alpha]^{25}_D$= +25.23 ($CHCl_3$, c = 1.8) IR (neat): 3420, 2953, 2930, 2890, 2859, 1265, 1105, 1036, 838, 779 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 3.71 (2H, dd, *J* = 5.2 Hz, 5.2 Hz, C<u>H</u>$_2$-O), 3.54 (1H, dd, *J* = 10.4 Hz, 10.4 Hz, C<u>H</u>-O), 3.43-3.39 (2H, m, C<u>H</u>$_2$O), 3.29 (1H, dd, *J* = 7.2 Hz, 11.2 Hz, C<u>H</u>-O), 3.03 (1H, td, *J* = 5.6 Hz, 10.0 Hz, C<u>H</u>-O), 2.08 (1H, s, O<u>H</u>), 1.37 (3H, s, Me), 1.28 (3H, s, Me), 1.20-1.10 (1H, m, C<u>H</u>-CH-CH), 0.84 (9H, s, Si<u>t</u>-<u>Bu</u>), 0.77 (1H, dd, *J* = 6.4 Hz, 6.4 Hz, CH-C<u>H</u>-CH), 0.03 (3H, s, SiMe), 0.02 (3H, s, Si<u>Me</u>); ^{13}C-NMR (100 MHz, $CDCl_3$): 99.3, 73.8, 63.9, 63.4, 62.4, 56.8, 28.9, 25.7, 21.4, 20.9, 18.8, 18.2, -4.6, -4.9; HRMS m/z: calcd for $C_{17}H_{32}O_5Si$ $[M+Na]^+$: 367.1917; found: 367.1915.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-benzoxymethyloxymethylene)-3-O-TBS-4,6-O-isopropylidene-α-D-arabino-hexitol (**18b**):* To a stirred suspension of NaH (60%) (0.32 g, 8 mmol, 2 equiv) in DMF (30 mL) at 0 °C was added dropwise a solution of the cyclopropane methanol **18a** (1.4 g, 4 mmol, 1 equiv) in DMF (10 mL). After the reaction mixture was warmed to room temperature while stirring for 3 h, it was quenched by the addition of EtOAc at 0 °C, followed by the treatment of sat. citric acid solution. The mixture was extracted with EtOAc (2 X 50 mL) and the organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography provided the benzyl ether **18b** in its pure form. R_f = 0.57 (hexanes/EtOAc, 8 : 2); Yield: 1.67 g, 96%; $[\alpha]^{25}_D$= +23.46 ($CHCl_3$, c = 1.0) IR (neat): 2930, 2888, 2857, 1265, 1101, 859, 838 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36-7.25 (5H, m, Ph), 4.49 (2H, dd, *J* = 18.0 Hz, 18.4 Hz, OC<u>H</u>$_2$Ph), 3.82-3.77 (2H, m, C<u>H</u>$_2$-OTBS), 3.61 (1H, dd, *J* = 9.8 Hz, 9.8 Hz, C<u>H</u>-O), 3.48-3.46 (2H, m, C<u>H</u>$_2$-O), 3.34 (1H, dd, *J* = 6.8 Hz, 10.4 Hz, C<u>H</u>-O), 3.26 (1H, dd, *J* = 6.8 Hz, 10.4 Hz, C<u>H</u>-O), 3.10 (1H, td, *J* = 5.6 Hz, 10.0 Hz, C<u>H</u>-O), 1.44 (3H, s, Me), 1.35 (3H, s, Me), 0.91 (9H, s, Si<u>t</u>-<u>Bu</u>), 0.91-0.89 (1H, m, C<u>H</u>-CH-CH), 0.11 (3H, s, CH-C<u>H</u>-CH), 0.09 (6H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 138.2, 128.3, 127.5, 127.5, 99.2, 73.9, 72.3, 70.7, 70.6, 63.6, 62.5, 57.0, 28.9, 21.8, 18.9, 18.3, 18.2, -4.6, -4.9; HRMS m/z: calcd for $C_{24}H_{38}O_5Si$ $[M+Na]^+$: 457.2386; found: 457.2387.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-benzoxymethyloxymethylene)-4,6-O-isopropylidene-α-D-arabino-hexitol (**18c**):* To a stirred solution of protected sugar **18b** (1.67g, 3.84 mmol, 1 equiv) in THF (25 mL) was added a 1 M solution of TBAF (5.8 mL, 5.8 mmol, 1.5 equiv) in THF at 0 °C. The reaction was monitored by TLC. After complete conversion of the starting material, the reaction mixture was washed with water (20 mL) and extracted with DCM (2 X 70 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the desired deprotected product **18c** in its pure form. R_f = 0.53 (hexanes/EtOAc, 8 : 2); Yield: 1.13 g, 92%; $[\alpha]^{25}_D$= +34.39 ($CHCl_3$, c = 2.0) IR (neat): 3430, 2993, 2942, 2885, 1374, 1269, 1093, 1079, 870, 742, 521 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.35-7.26 (5H, m, Ph), 4.49 (2H, dd, *J* = 13.2 Hz, 13.2 Hz, OC<u>H</u>$_2$Ph), 3.80 (2H dd, *J* = 7.2 Hz, 12. 4 Hz, C<u>H</u>$_2$O), 3.65-3.59 (1H, m, C<u>H</u>-O), 3.52-3.46 (2H, m, C<u>H</u>$_2$-OBn), 3.30 (2H, d, *J* = 6.8 Hz, C<u>H</u>-O), 3.11 (1H, td, *J* = 5.6 Hz, 10.0 Hz, C<u>H</u>-O), 1.48 (3H, s, Me), 1.38 (3H, s, Me), 1.20-1.15 (1H, m, C<u>H</u>-CH-CH), 0.91 (1H, dd, *J* = 6.8 Hz, 6.8 Hz, CH-C<u>H</u>-CH); ^{13}C-NMR (100 MHz, $CDCl_3$): 138.0, 128.4, 127.6, 99.6, 74.1, 72.5, 70.4, 69.9, 63.3, 62.3, 56.6, 29.0, 20.2, 19.0, 18.7; HRMS m/z: calcd for $C_{18}H_{24}O_5$ $[M+Na]^+$: 343.1521; found: 343.1522.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-benzoxymethyloxymethylene)-4,6-O-isopropylidene-α- D-erythro-hex-3-ulose (**18d**)* To a stirred solution of cyclopropane alcohol **18c** (0.8 g, 2.5 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at 0 °C was added Dess–Martin periodinane (DMP) (1.17 g, 2.75 mmol, 1.1 equiv). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction was quenched by adding 10% aqueous solution of $Na_2S_2O_3$ (15 mL)/ sat. solution of $NaHCO_3$ (*aq*) (15 mL) with vigorous stirring. The aqueous layer was extracted with CH_2Cl_2 (3X20 mL). The combined organic layer was washed with sat. solution of $NaHCO_3$ (*aq*) and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding cyclopropyl ketone **18d** in its pure form. R_f = 0.56 (hexanes/EtOAc, 8 : 2); Yield: 92%; $[\alpha]^{25}_D$= -1.76 ($CHCl_3$, c = 2.0) IR (neat): 2994, 2924, 2868, 1725, 1258, 1199, 1128, 1089, 869, 743, 699 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.36-7.27 (5H, m, Ph), 4.49 (2H, s, PhC<u>H</u>$_2$O), 4.10 (1H, d, *J* = 10.4

Hz, CH-O), 3.97 (1H, dd, *J* = 3.6 Hz, 5.6 Hz, CH-O), 3.88 (1H, dd, *J* = 5.2 Hz, 10.8 Hz, CH-O), 3.75 (1H, dd, *J* = 9.6 Hz, 9.6 Hz, CH-O), 3.68-3.57 (2H, m, CH_2-O), 3.35 (1H, dd, *J* = 5.6 Hz, 10.4 Hz, CH-O), 2.37-2.32 (1H, m, CH-CO), 1.76 (1H, dd, *J* = 5.6 Hz, 5.6 Hz, CH-CH-CH), 1.48 (3H, s, Me), 1.47 (3H, s, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 197.8, 137.6, 128.4, 127.8, 127.6, 100.7, 74.7, 72.7, 68.0, 62.7, 62.5, 57.3, 28.7, 25.4, 19.3, 18.4; HRMS m/z: calcd for $C_{18}H_{22}O_5$ $[M+Na]^+$: 341.1365; found: 341.1363.

*1,5-Anhydro-2-deoxy-1,2-C-(exo-benzoxymethyloxymethylene)-4,6-O-isopropylidene-α- D-erythro-hexityl-exo-3-methylene (**18**)* To a stirred suspension of phosphonium iodide (0.404 g, 1 mmol, 2 equiv) in THF (6 mL) at -15 °C was added *n*-BuLi (1.6 M in hexanes, 0.57 mL, 0.90 mmol, 1.8 equiv) under nitrogen atmosphere. After the addition, the reaction mixture was allowed to stir for 20 min. The supernatant was cannulated into a solution of **18d** (0.159 g, 0.5 mmol, 1 equiv) in THF (3 mL). The progress of the reaction was monitored by TLC. After complete consumption of the starting material, the reaction mixture was concentrated *in vacuo*. The residue was then washed with water and extracted with CH_2Cl_2 (2X15 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product provided the corresponding VCP **18** in its pure form. R_f = 0.52 (hexanes/EtOAc, 8 : 2); Yield: 0.128 g, 81%; $[\alpha]^{25}_D$= +39.74 ($CHCl_3$, c = 1.0) IR (neat): 2994, 2927, 2856, 1375, 1198, 1126, 1086, 866, 736, 698 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.34-7.25 (5H, m, Ph), 5.31 (1H, s, C=CH_2), 5.16 (1H, s, C=CH_2), 4.52 (2H, dd, *J* = 12.4 Hz, 16.8 Hz, CH_2O), 4.08 (1H, d, *J* = 9.6 Hz, CH-O), 3.82 (1H, dd, *J* = 5.6 Hz, 11.2 Hz, CH-O), 3.67 (1H dd, *J* = 10.8 Hz, 10.8 Hz, CH-O), 3.57 (1H, dd, *J* = 3.2 Hz, 7.2 Hz, CH-O), 3.39 (2H, d, *J* = 6.8 Hz, CH-O), 3.26 (1H, dt, *J* = 5.6 Hz, 10.0 Hz, CH-O), 2.32-2.36 (1H, m, CH-C=), 1.74-1.72 (1H, m, CH-CH-CH), 1.50 (3H, s, Me), 1.43 (3H, s, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): 140.0, 138.5, 128.5, 127.5, 110.7, 99.8, 72.5, 70.4, 69.8, 65.1, 32.9, 56.8, 29.9, 28.2, 21.0, 19.1, 18.8; HRMS m/z: calcd for $C_{19}H_{24}O_4$ $[M+Na]^+$: 339.1572; found: 339.1574.

*(4aR,7R,9aS)-7-(Benzyloxymethyl)-6-methoxy-2,2-dimethyl-9-(N-p-toluenesulfonamidomethyl)-4a,6,7,9a-tetrahydro-4H-[1,3]dioxino [5,4-b]oxepine (**19**)* To a stirred solution of VCP **18** (0.063 g, 0.2 mmol, 1 equiv) in the chosen alcohol (1 mL) as nucleophile at rt was added solid chloramine-T (0.060 g, 0.22 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.008 g, 0.02 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete conversion of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 10 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane **19** in its pure form. R_f = 0.51 (hexanes/EtOAc, 8 : 2); Yield: 0.077 g, 74%; IR (neat): 3293, 2922, 2855, 1329, 1161, 1113, 1093, 1075, 814, 664 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.71-7.68 (4H, m, Ph), 7.36-7.23 (14H, m, Ph), 5.44 (1H, d, *J* = 3.6 Hz, C=CH), 5.29 (1H, s, C=CH), 4.91 (1H dd, *J* = 3.6 Hz, 7.6 Hz, O-CH-O), 4.84 (1H, dd, *J* = 3.6 Hz, 7.6 Hz, O-CH-O), 4.59 (1H, d, *J* = 6.0 Hz, CH-O), 4.53-4.46 (5H, m, PhCH_2O), 4.33 (1H, dd, *J* = 8.8 Hz, CH-O), 4.19 (1H d, *J*= 9.6 Hz, CH-O), 3.96-3.87 (1H, m, CH-O), 3.84-3.52 (7H, m, CH_2O, CH_2-O), 3.51-3.37 (6H, m, CH_2-N), 3.31 (3H, s, OMe), 3.28 (3H, s, OMe), 2.74-2.72 (1H, m, CH-CH_2OBn), 2.67-2.65 (m, CH-CH_2OBn), 2.41 (3H, s, Me), 2.39 (3H, s, Me), 1.42 (3H, s, MeC), 1.37 (6H, s, MeC); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.1, 143.0, 137.9, 137.7, 137.3, 135.9, 134.9, 129.5, 128.4, 127.7, 127.2, 127.1, 127.0, 103.0, 102.0, 99.0, 98.7, 73.7, 73.1, 72.7, 71.3, 69.7, 69.6, 63.4, 63.3, 62.7, 55.6, 55.3, 48.1, 43.4, 42.4, 29.6, 28.9, 28.1, 21.4, 19.0, 18.7; HRMS m/z: calcd for $C_{27}H_{35}NO_7S$ $[M+Na]^+$: 540.2032; found: 540.2034.

*(5S,6R)-5-(benzyloxy)-7-(TBS-oxy)-6-hydroxy-4-methylene hept-2-E-enal (**20a**)* To a stirred solution of VCP **6** (0.5 mmol, 1 equiv) in moist MeCN (0.5 mL H_2O/ 5mL MeCN) (3 mL) as nucleophile at rt was added solid chloramine-T (0.155 g, 0.55 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.019 g, 0.05 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete consumption of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 20 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane in its pure form. R_f = 0.56 (hexanes/EtOAc, 8 : 2); Yield: 0.154 g, 82%; ^{1}H-NMR (400 MHz, $CDCl_3$): 9.57 (1H, d, *J* = 7.6 Hz, CHO), 7.29-7.26 (5H, m, Ph), 7.22 (1H, d, *J* = 16.0 Hz, CH-CHO), 6.53 (1H, dd, *J* = 8.0 Hz, 16.0 Hz, CH=CHCHO), 5.84 (1H, s, C=CH_2), 5.70 (1H, s, C=CH_2), 4.53 (1H d, *J* = 11.6 Hz, PhCH_2O), 4.29 (1H, d, *J* = 11.6 Hz, PhCH_2O), 4.09 (1H, d, *J* = 7.6 Hz, CH-O), 3.80-3.71 (2H, m, CH_2-O), 3.36-3.33 (1H, m, CH-O), 2.47 (1H, d, *J* = 4.4 Hz, OH), 0.89 (9H, s, Si^{t}Bu), 0.07 (3H, s, SiMe), 0.06 (3H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 194.2, 151.5, 142.3, 137.4, 130.0, 128.4, 127.8, 126.5, 79.8, 72.3, 70.7, 63.5, 25.8, 18.2, -5.5; HRMS m/z: calcd for $C_{21}H_{32}O_4Si$ $[M+Na]^+$: 399.1968; found: 399.1965.

*(5R,6R)-5-(benzyloxy)-7-(TBS-oxy)-6-hydroxy-4-methylene hept-2-E-enal (**20b**)* To a stirred solution of VCP **7** (0.5 mmol, 1 equiv) in moist MeCN (0.5 mL H_2O/ 5mL MeCN) (3 mL) as nucleophile at rt was added solid chloramine-T (0.155 g, 0.55 mmol, 1.1 equiv) and phenyltrimethylammonium tribromide (PTAB, 0.019 g, 0.05 mmol, 0.1 equiv). The reaction was monitored by TLC. After complete consumption of the starting material and the intermediate bromide, the reaction mixture was concentrated *in vacuo*, and then washed with water (10 mL) extracted with DCM (2 X 20 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the oxepane in its pure form. R_f = 0.53 (hexanes/EtOAc, 8 : 2); Yield: 0.162 g, 87%; ^{1}H-NMR (400 MHz, $CDCl_3$): 9.57 (1H, d, *J* = 7.6 Hz, , CHO), 7.37-7.29 (5H, m, Ph), 7.18 (1H, d, *J* = 16.0 Hz, CH-CHO), 6.42 (1H, dd, *J* = 7.6 Hz, 16.0 Hz, CH=CHCHO), 5.81 (1H, s, C=CH_2), 5.76 (1H, s, C=CH_2), 4.60 (1H, d, *J* = 11.6 Hz, CH-O), 4.37-4.33 (2H, m, PhCH_2-O), 3.71-3.56 (3H, m, CH_2-O, CH-O), 2.52 (1H, d, *J* = 5.6 Hz, OH), 0.88 (9H, s, Si^{t}Bu), 0.04 (6H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 193.8, 151.3, 141.7, 137.3, 129.6, 128.5, 128.0, 126.0, 77.9, 73.2, 71.3, 63.2, 25.8, 18.2, -5.5; HRMS m/z: calcd for $C_{21}H_{32}O_4Si$ $[M+Na]^+$: 399.1968; found: 399.1967.

*Methyl-1,6-anhydro-2-deoxy-5-O-benzyl-6-O-TBS-4-(N-p-toluene sulfonamidomethyl)-(β)- D-talo-septanoside (**21**):* To a stirred solution of unsaturated oxepane derivative *β* -**12a** (0.056 g, 0.1 mmol, 1 equiv) in t-butyl alcohol (1.5 mL) was added solid NMMO (0.018 g, 0.15 mmol, 1.5 equiv) and a crystal OsO_4 weighing 0.3 mg was added at rt. The reaction was refluxed at the boiling point of t-butyl alcohol and monitored by TLC. After complete conversion of the starting material, the reaction mixture was washed with water (20 mL) and extracted with EtOAc (2 X 20 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the desired deprotected product **21** in its pure form. R_f = 0.57 (hexanes/ EtOAc, 8 : 2); Yield: 0.053 g, 89%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.71 (2H, d, *J* = 8.0 Hz, Ph), 7.34-7.26

(7H, m, Ph), 4.86 (1H, dd, *J* = 4.0 Hz, 10.4 Hz, NH), 4.75 (dd, *J* = 2.4 Hz, 9.6 Hz, 1H, O-CH-OMe), 4.60 (2H, s, PhCH$_2$O), 4.31 (1H, s, CH-O), 4.08-4.05 (2H, m, CH$_2$OTBS), 3.59-3.56 (2H, m, CH-O), 3.49 (1H, dd, *J* = 4.8 Hz, 10.4 Hz, CH-O), 3.36 (3H, s, OMe), 3.35 (1H, dd, *J* = 10.4 Hz, 18.8 Hz, CH-O), 2.89-2.85 (2H, m, CH$_2$N), 2.41 (3H, s, Me), 2.31-2.24 (1H, m, CH-CH$_2$-CH), 2.08-2.02 (1H, m, CH-CH$_2$-CH), 0.92 (9H, s, Si^{t}Bu), 0.09 (6H, s, SiMe); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.5, 137.8, 136.4, 129.7, 128.4, 128.2, 127.9, 127.0, 99.1, 77.5, 75.9, 74.5, 73.6, 68.8, 65.8, 55.4, 47.1, 36.6, 25.9, 21.4, 18.3, -5.4, -5.5; HRMS m/z: calcd for $C_{29}H_{45}NO_8SSi[M+Na]^+$: 618.2533; found: 618.2535.

*Methyl-1,6-anhydro-2-deoxy-5,6-O-(di-tert-butylsilyl)-4-(N-p-toluenesulfonamidomethyl)-(α/β)- D-manno-septanoside (**22**):* To a stirred solution of unsaturated oxepane derivative **15a** (0.050 g, 0.1 mmol, 1 equiv) in t-butyl alcohol (1.5 mL) was added solid NMMO (0.018 g, 0.15 mmol, 1.5 equiv) and a crystal OsO_4 weighing 0.3 mg was added at rt. The reaction was refluxed at the boiling point of t-butyl alcohol and monitored by TLC. After complete conversion of the starting material, the reaction mixture was washed with water (20 mL) and extracted with EtOAc (2 X 20 mL). The organic layer was dried over anhyd. Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the crude product afforded the desired deprotected product in its pure form. R_f = 0.55 (hexanes/EtOAc, 8 : 2); Yield: 0.046 g, 86%; ^{1}H-NMR (400 MHz, $CDCl_3$): 7.73 (2H, d, *J* = 8.0 Hz, Ph), 7.31 (2H, d, *J* = 8.0 Hz, Ph), 5.40 (1H, dd, *J* = 6.0 Hz, 6.0 Hz, NH), 4.64 (1H, dd, *J* = 4.4 Hz, 4.4 Hz, O-CH-O), 4.45-4.42 (1H, m, CH-O), 4.19-4.10 (3H, m, CH$_2$-OSi), 3.70 (1H, s, CH-O), 3.40 (3H, s, OMe), 3.37-3.18 (2H, m, CH-O), 2.64 (1H, s, OH), 2.43 (3H, s, Me), 2.38-2.33 (1H, m, CH-CH$_2$-CH), 2.04-1.98 (1H, m, CH-CH$_2$-CH), 1.02 (9H, s, Si^{t}Bu), 1.00 (9H, s, Si^{t}Bu); ^{13}C-NMR (100 MHz, $CDCl_3$): 143.7, 136.1, 129.8, 127.00, 101.9, 79.5, 76.4, 70.8, 68.6, 67.5, 55.8, 49.5, 38.3, 27.5, 27.3, 23.1, 21.5, 20.7; HRMS m/z: calcd for $C_{24}H_{41}NO_8SSi$ $[M+Na]^+$: 554.2220; found: 554.2221.

5. Acknowledgments

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6. References and notes

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σ–Ferrier Rearrangement of Carbohydrate Derived Vinylcyclopropanes: A Facile Approach to Oxepane Analogs.

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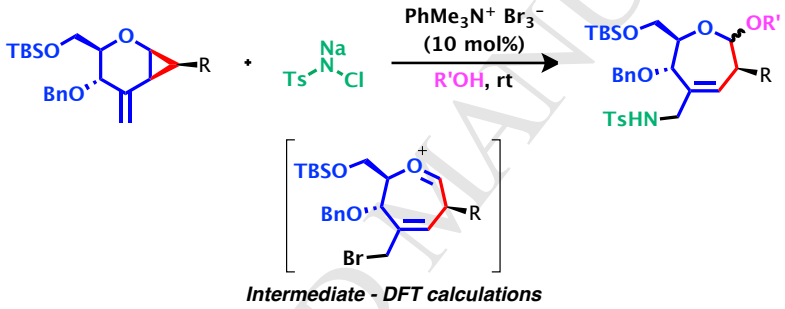

Supporting Information

Experimental section

General Information: All solvents for routine isolation of products and chromatography were reagent grade and redistilled. Acetonitrile and DCM used for the reaction were dried under reflux over CaH_2 and stored over 3 Å molecular sieves. Flash chromatography was performed using silica gel (230−400 mesh) with indicated solvents. All reactions were monitored by thin-layer chromatography on 0.25 mm silica plates (F-254) visualizing with UV light and developed using phosphomolybdate or vanillin solution. ^{1}H, ^{13}C NMR spectra were recorded on a 400 MHz NMR spectrometer. Chemical shifts, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant in hertz (Hz), and number of protons. HRMS were measured with electrospray ionization (ESI) and quadrupolar mass analyzer. Gaussian 09 program was used for energy minimization.

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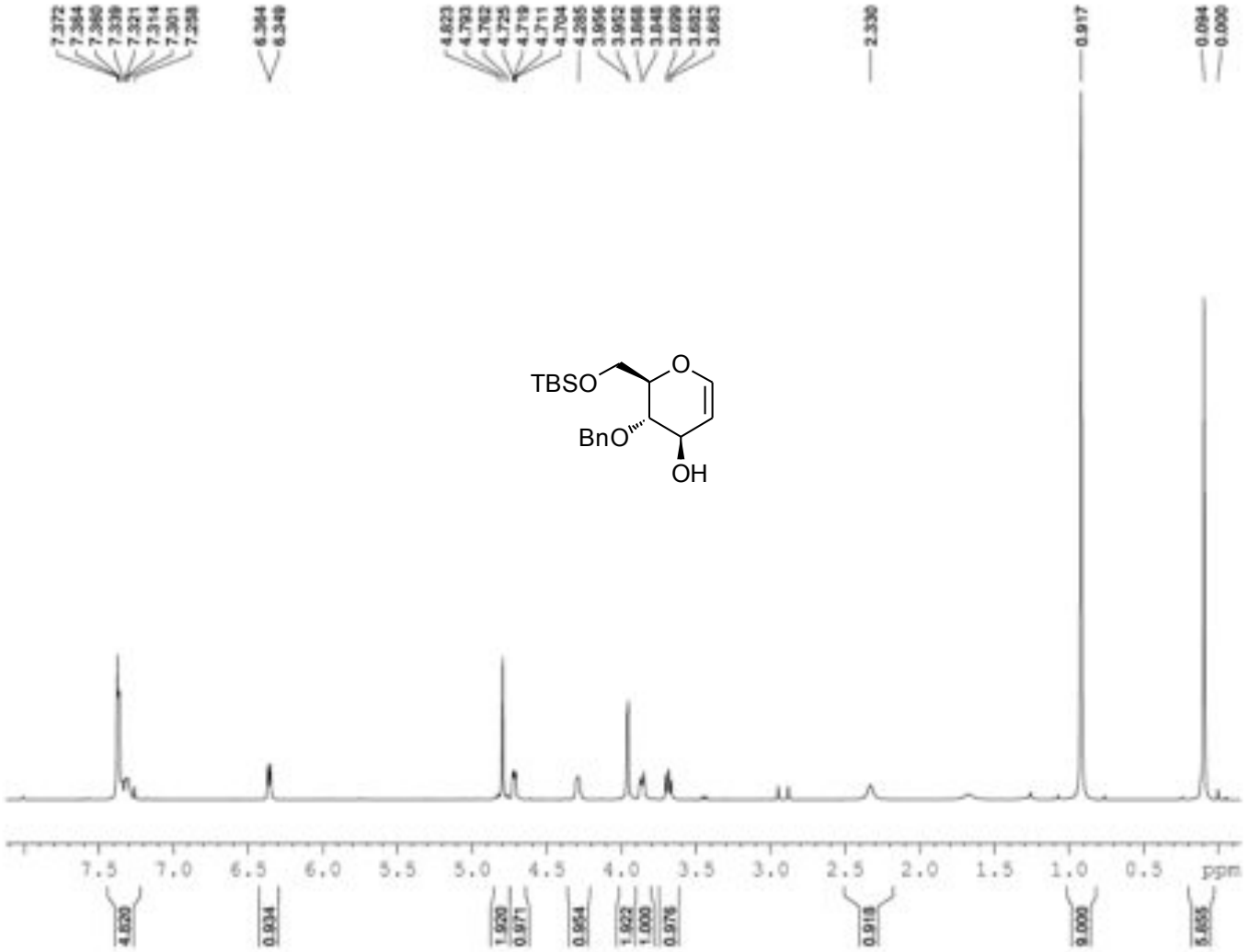

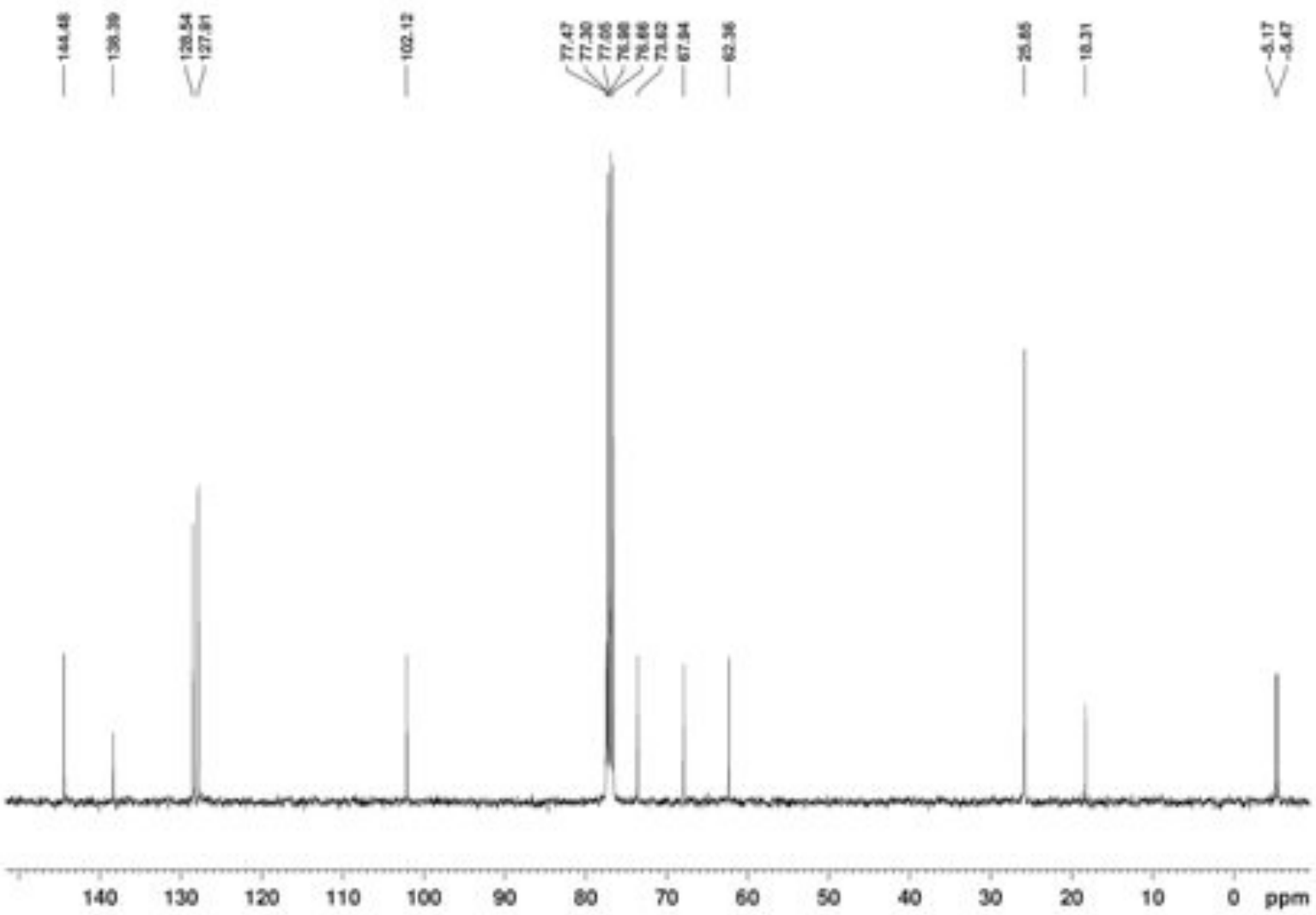
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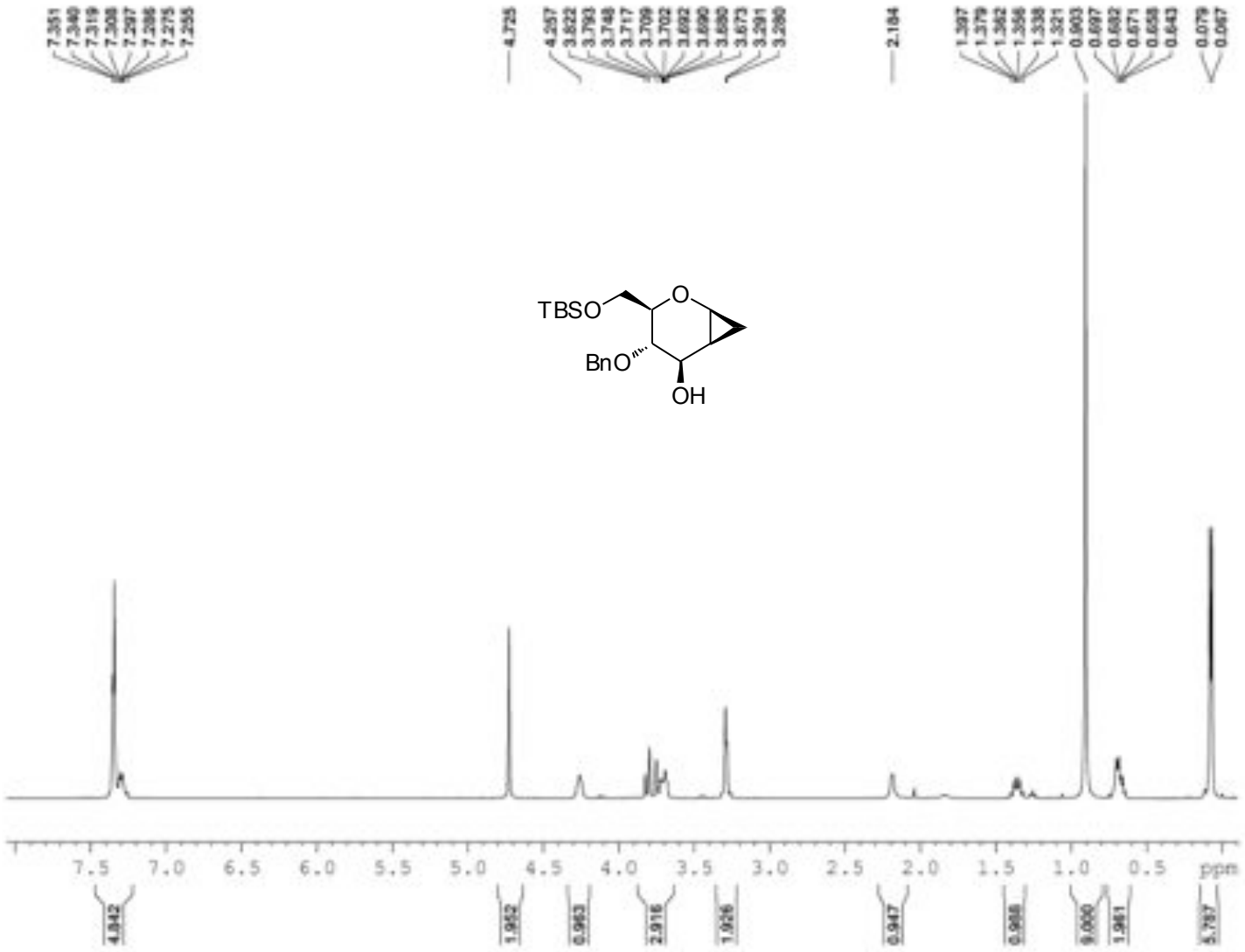
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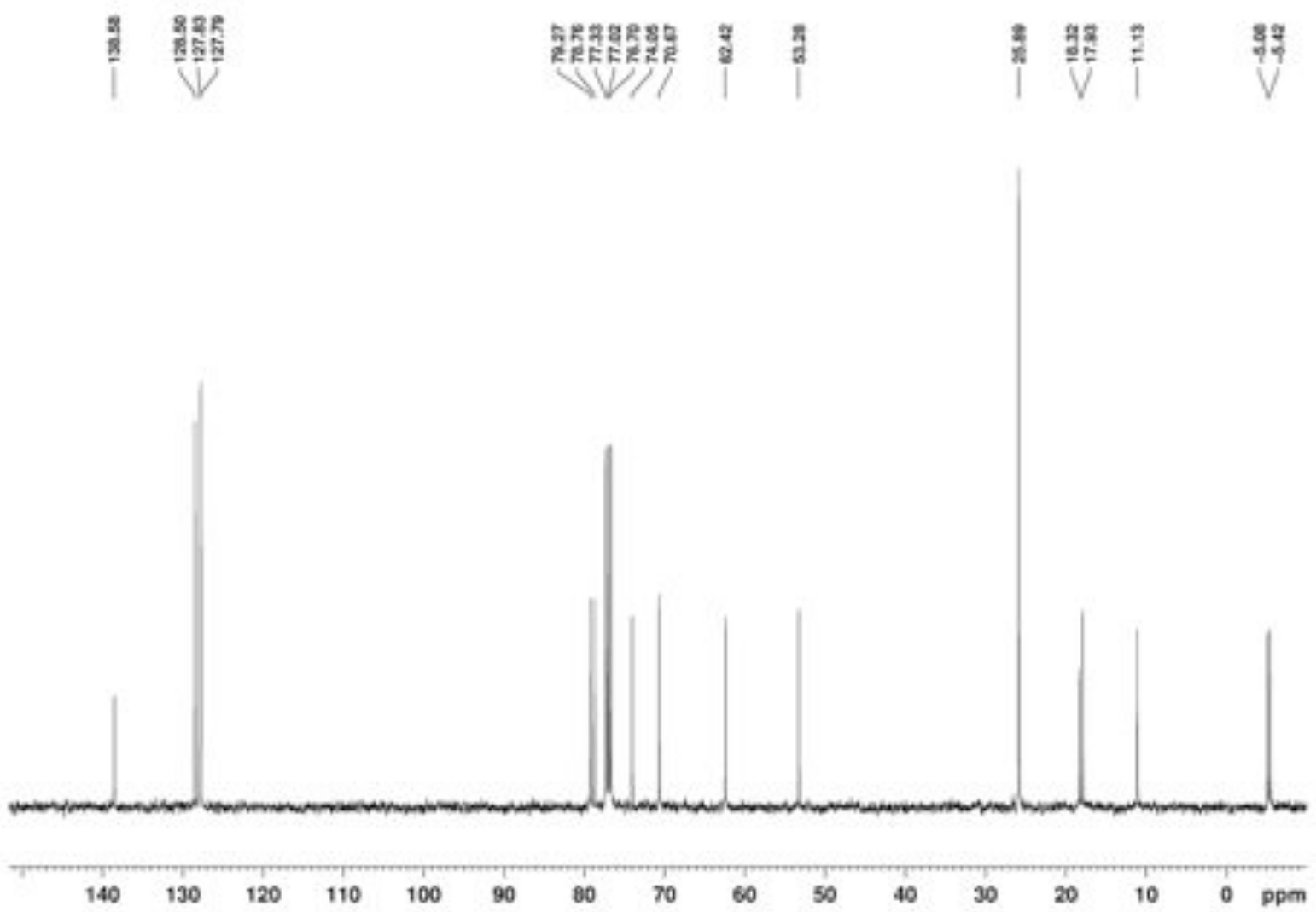
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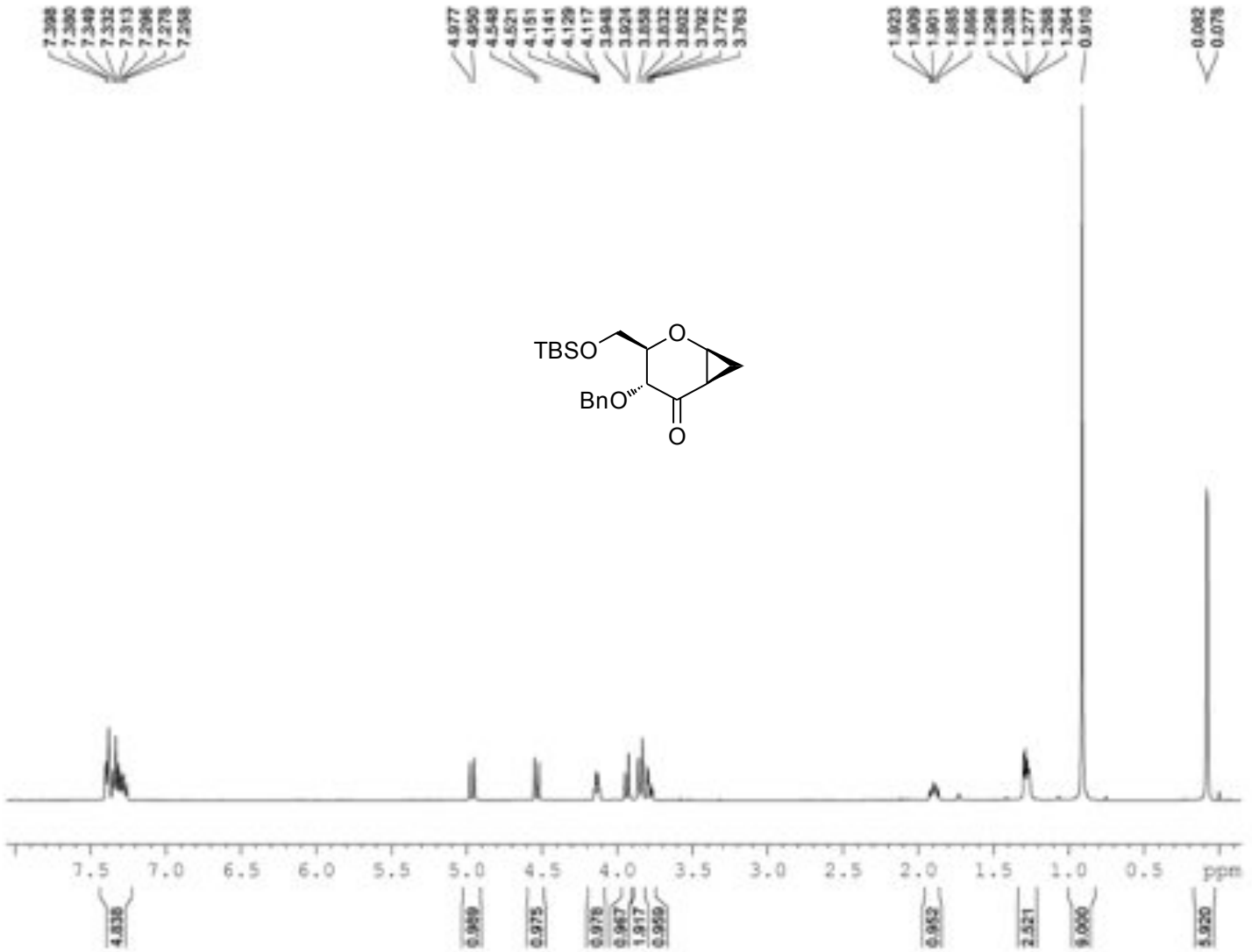
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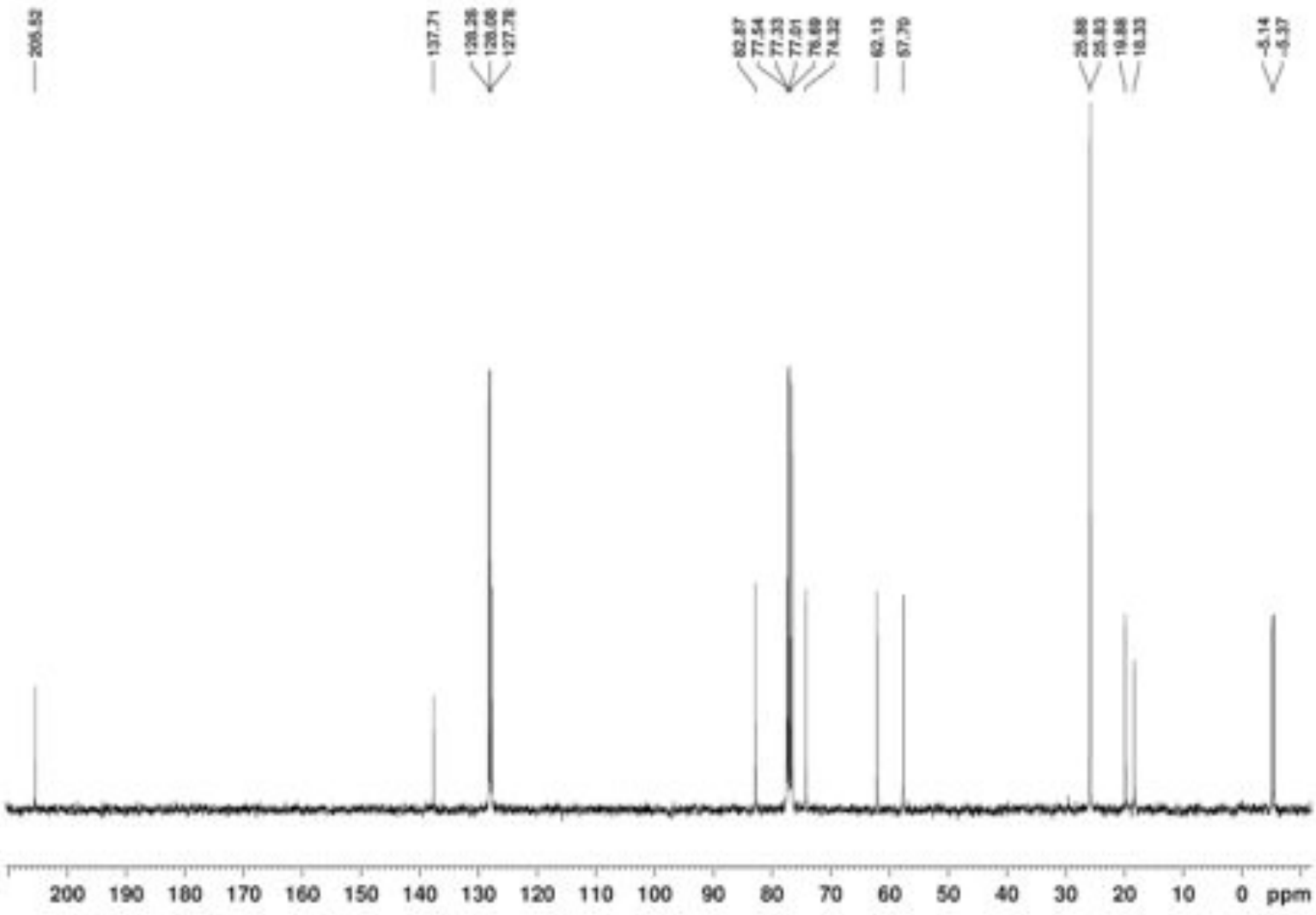
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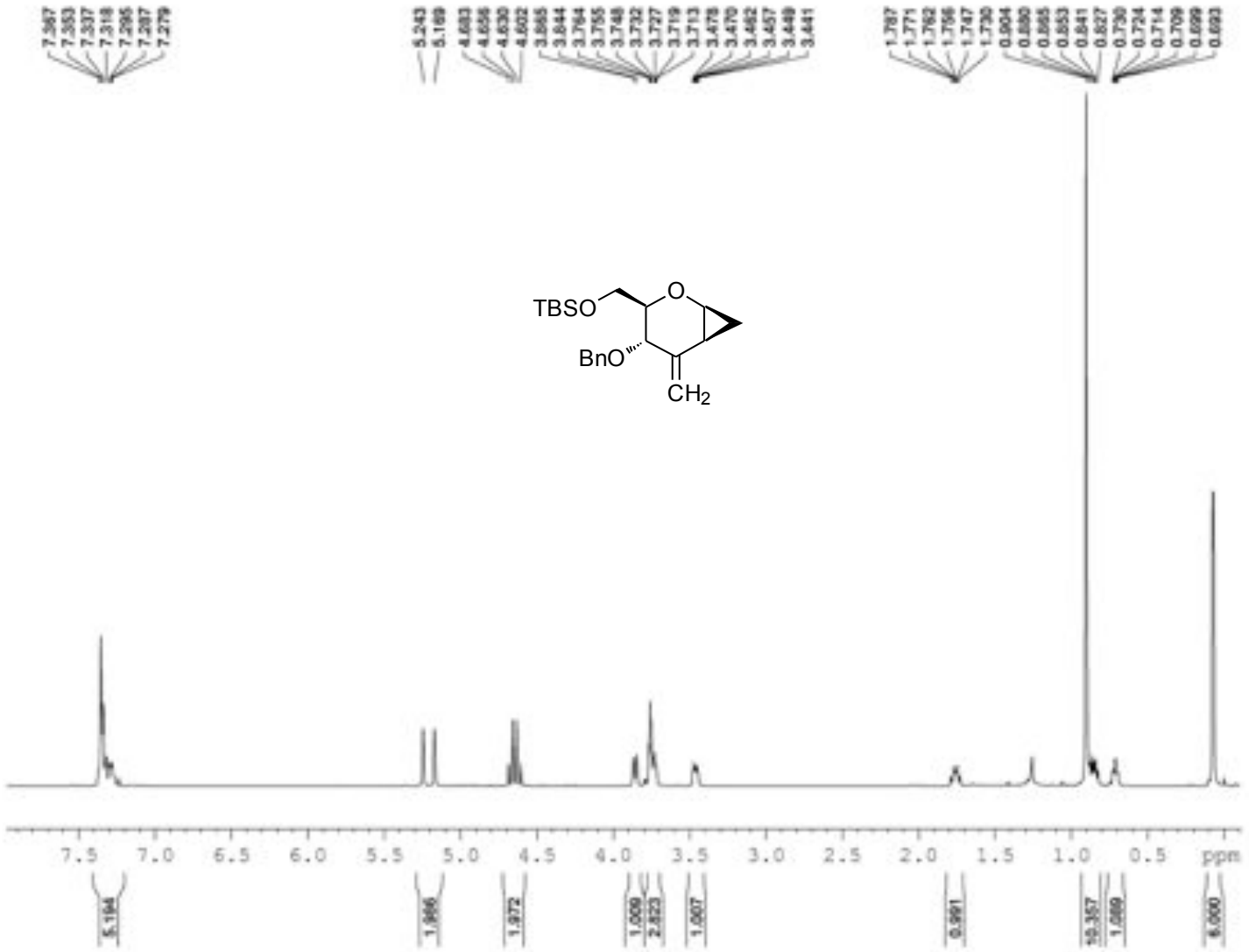
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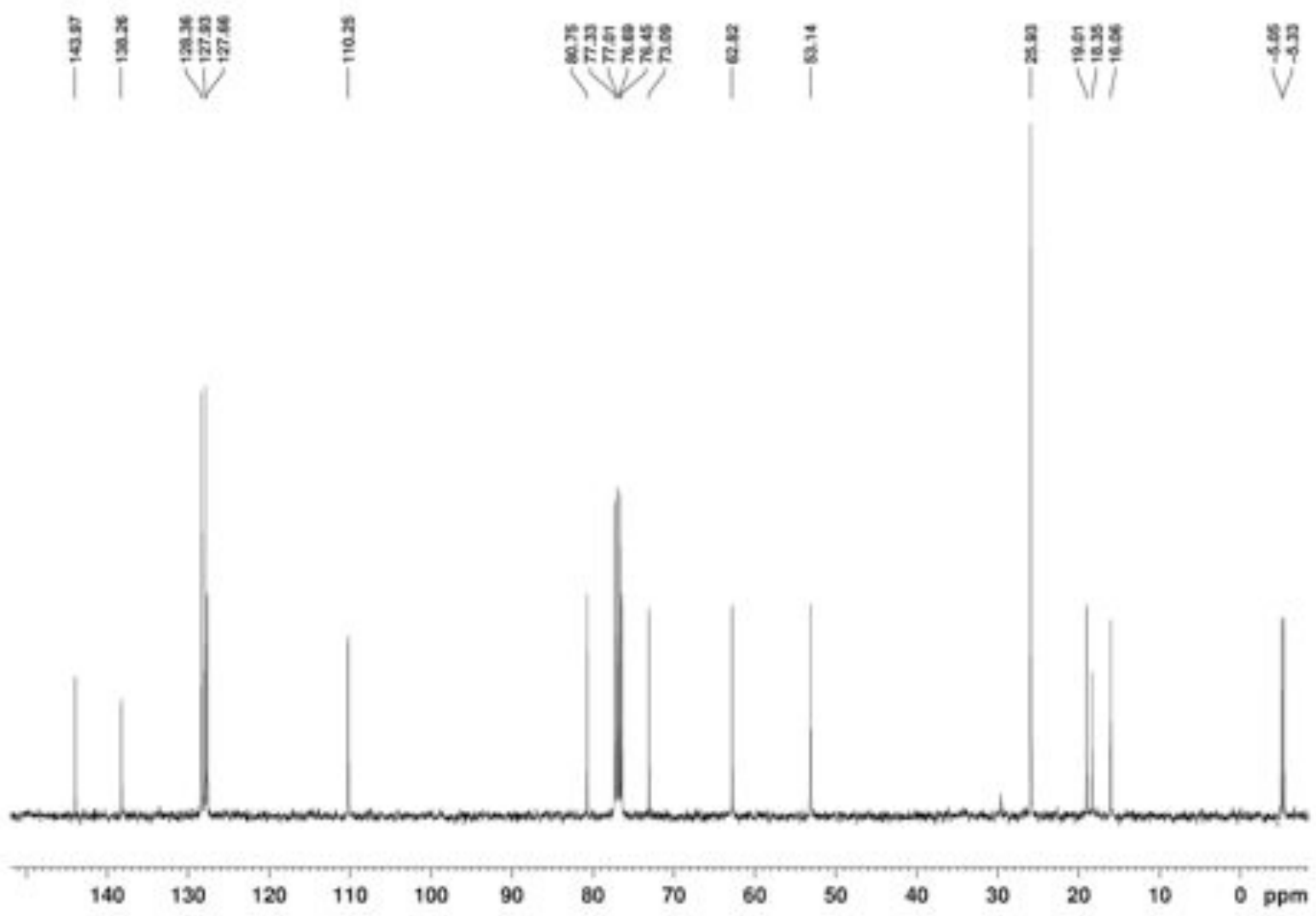
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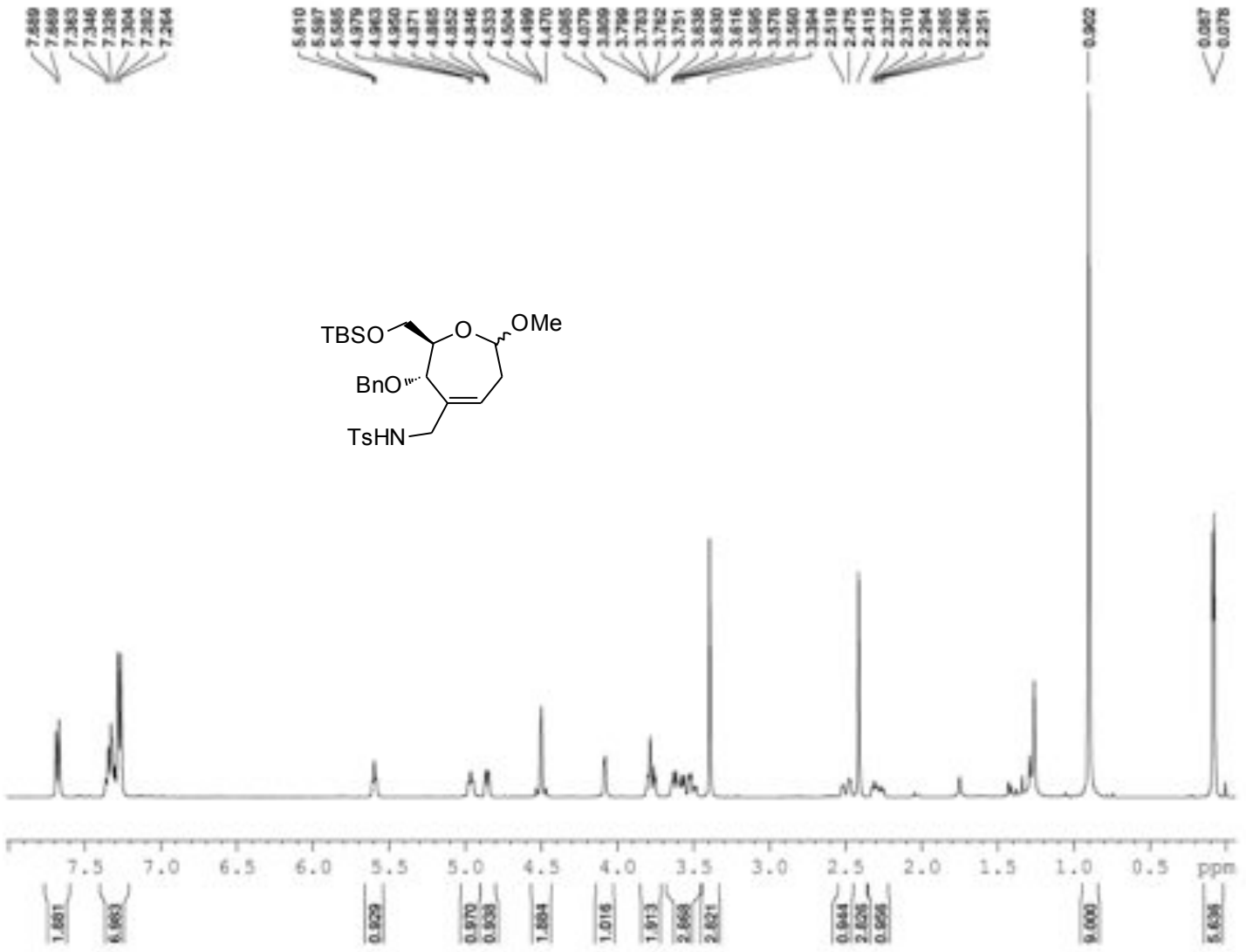
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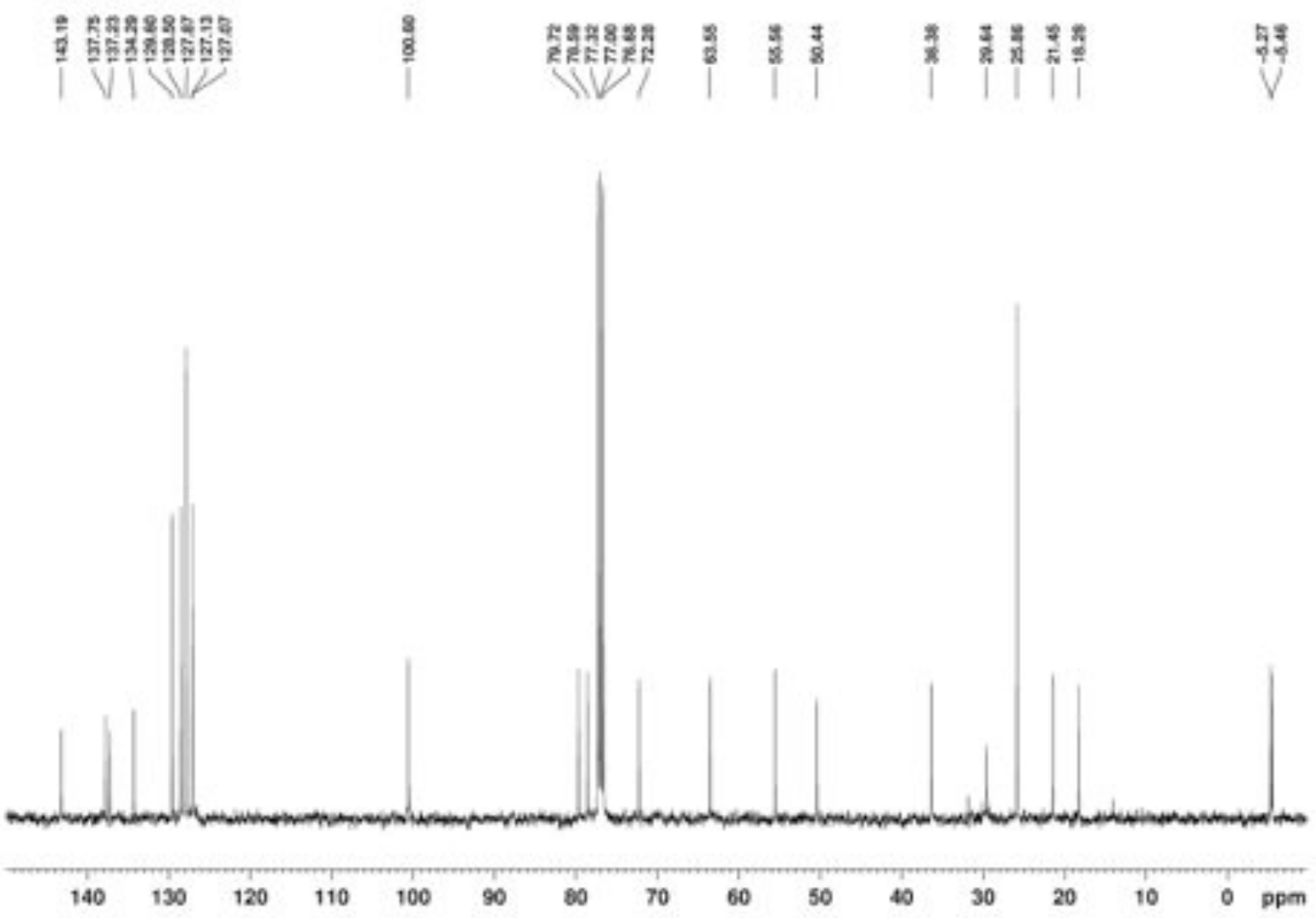
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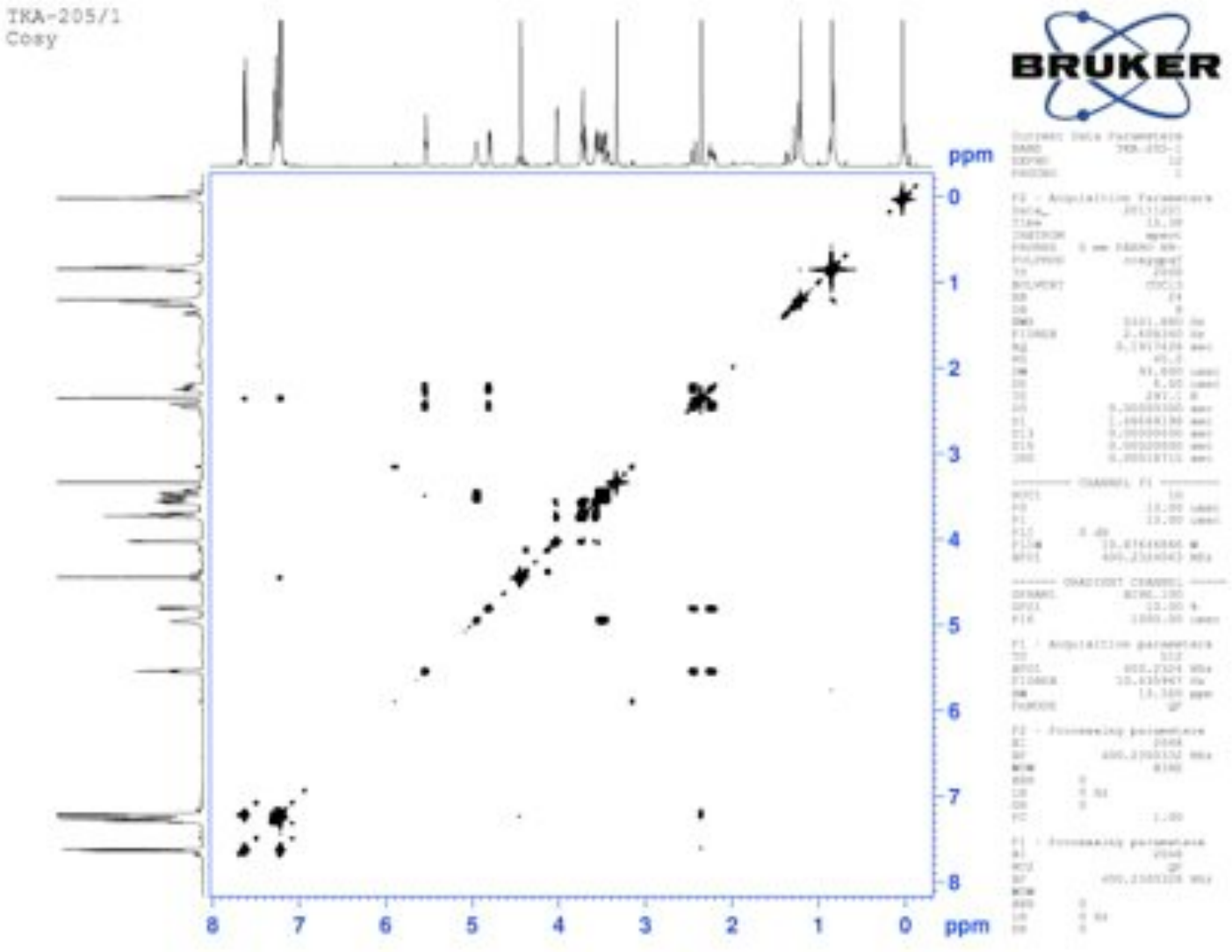
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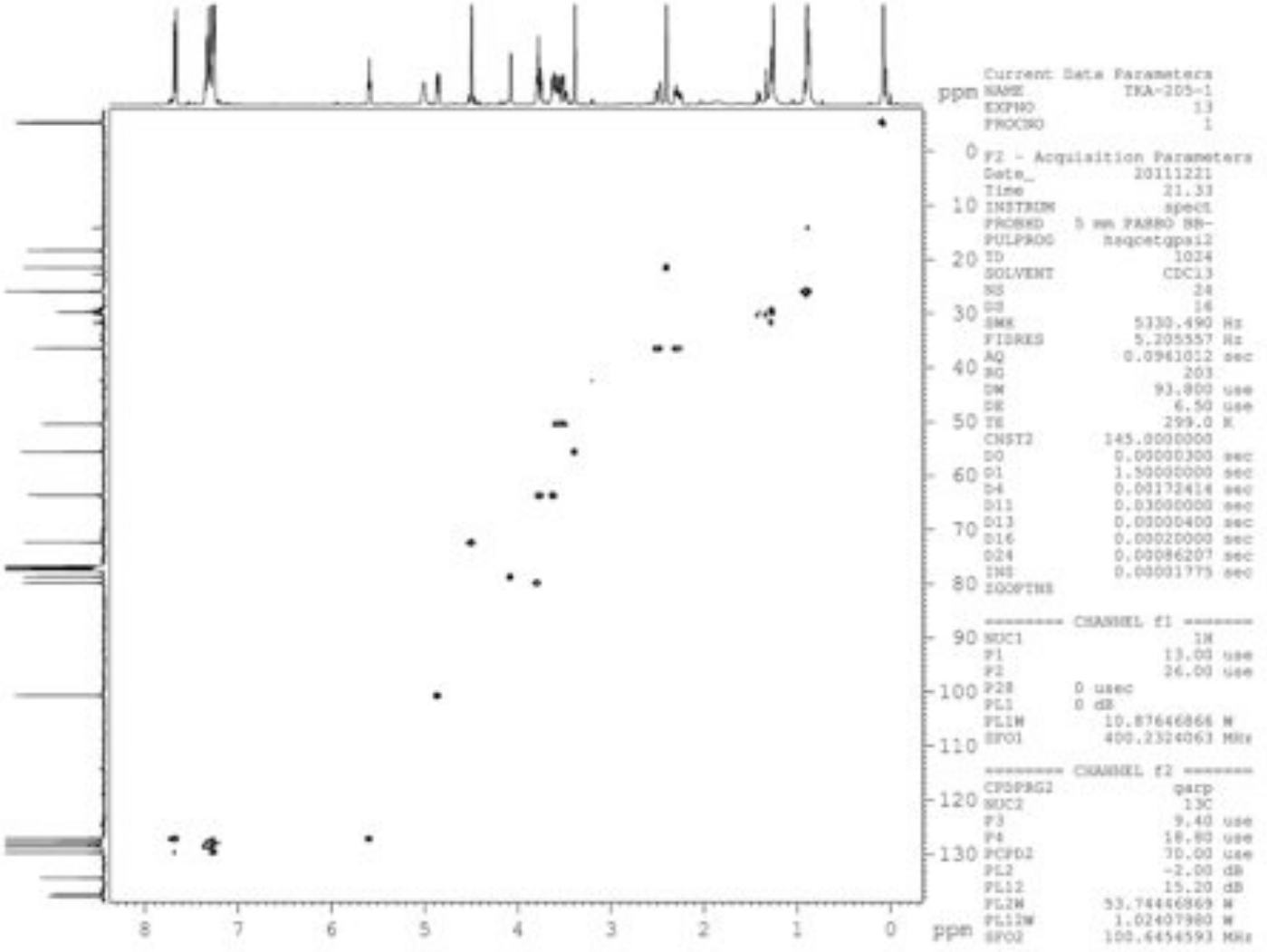
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F2 - Acquisition Parameters
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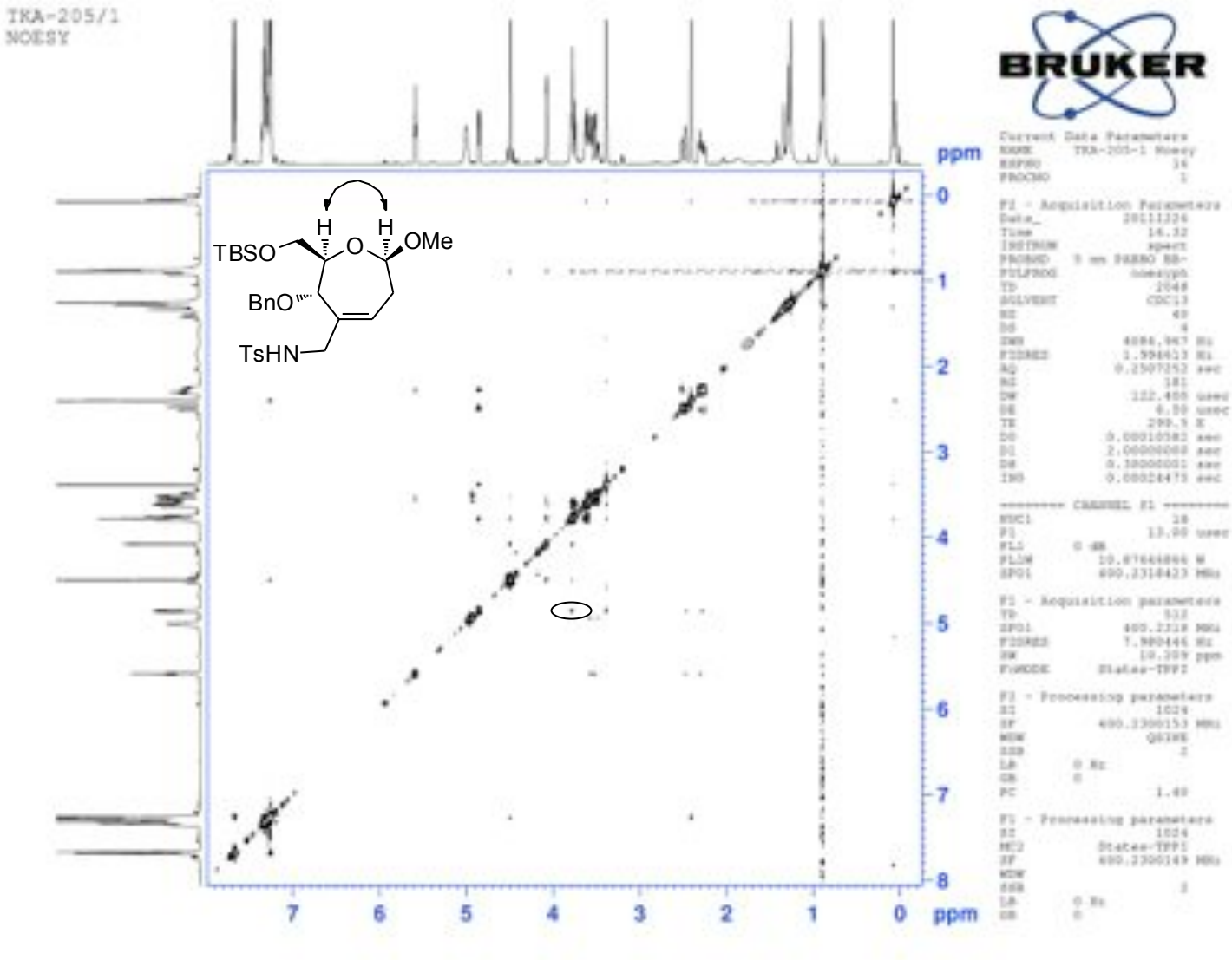
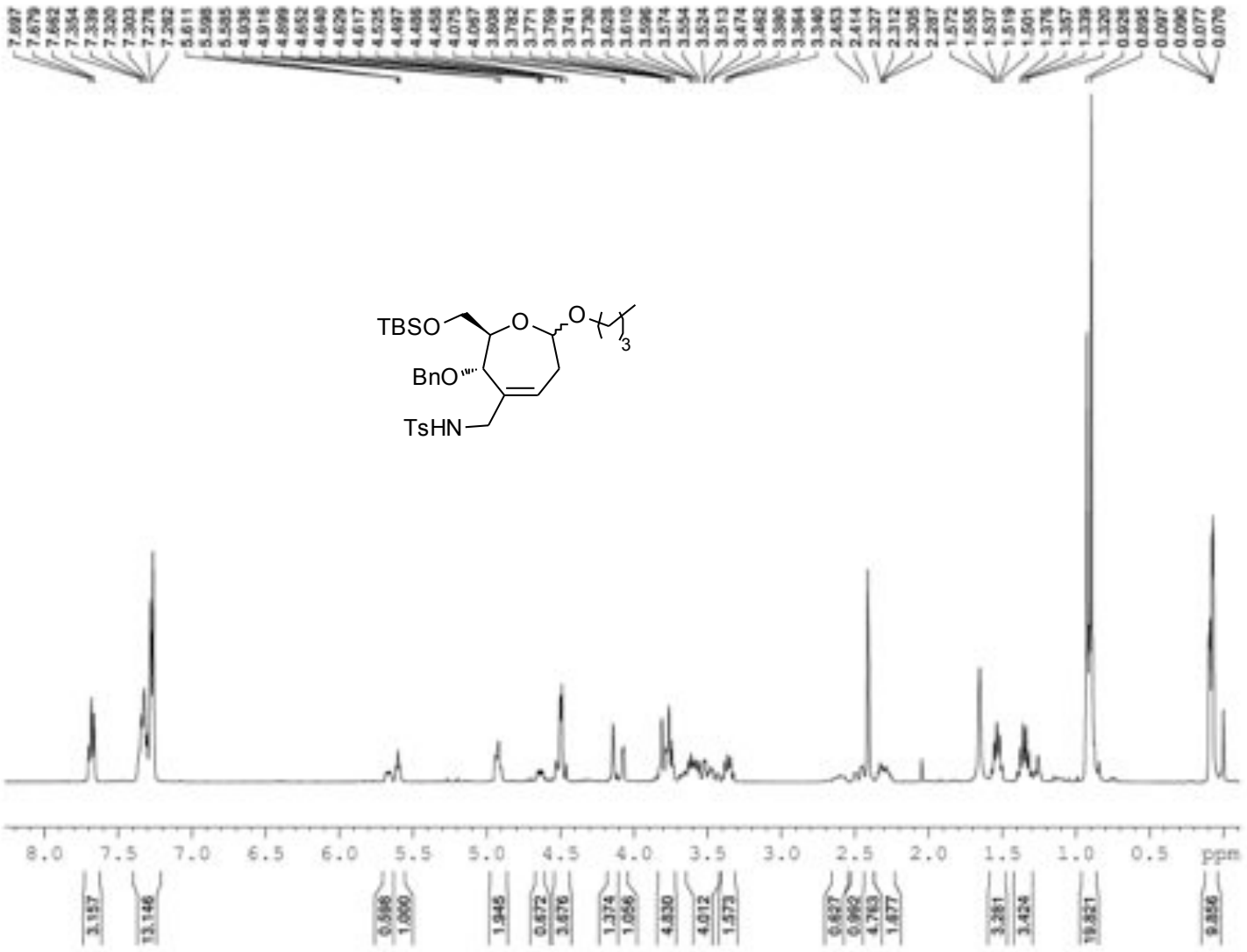
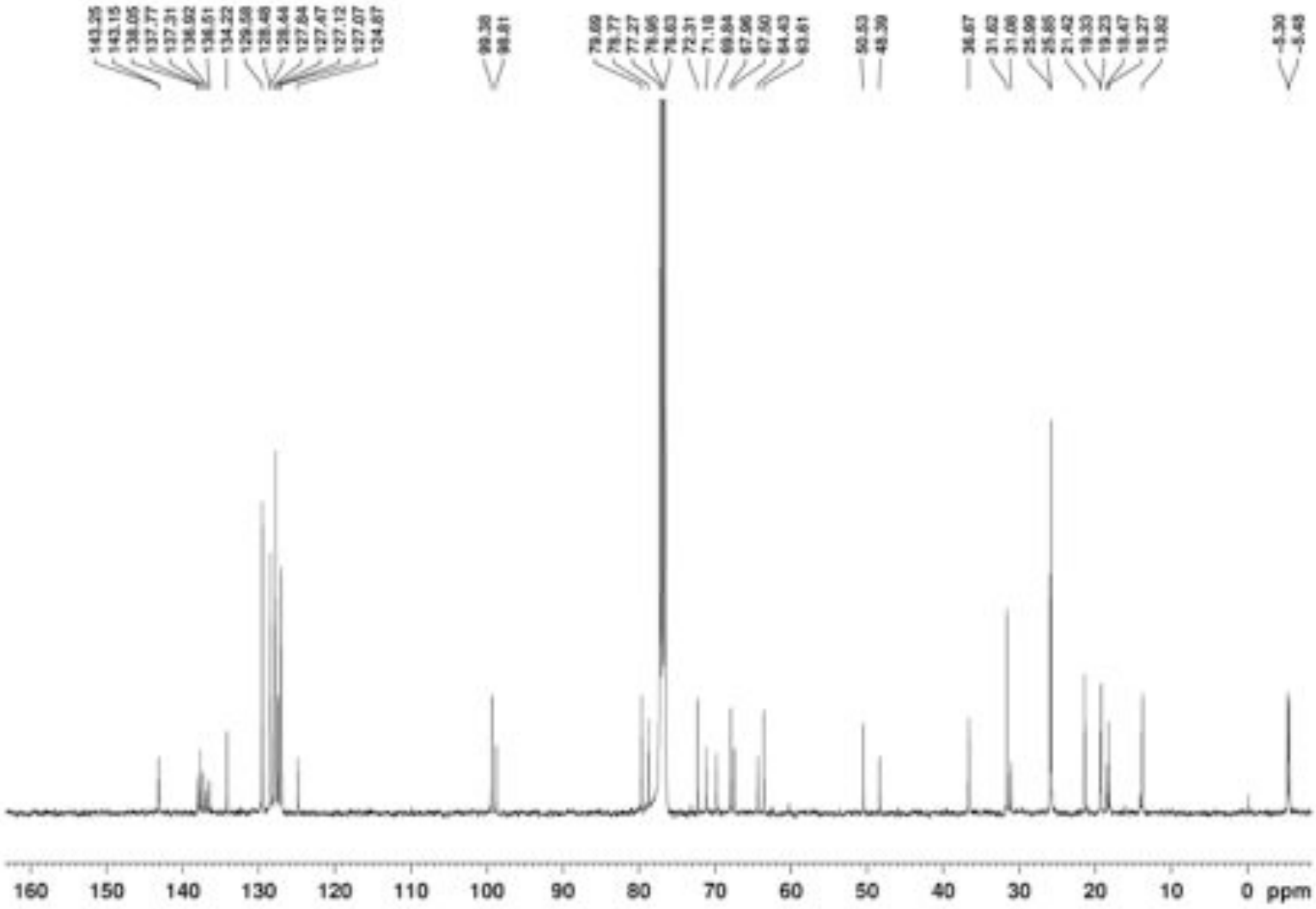
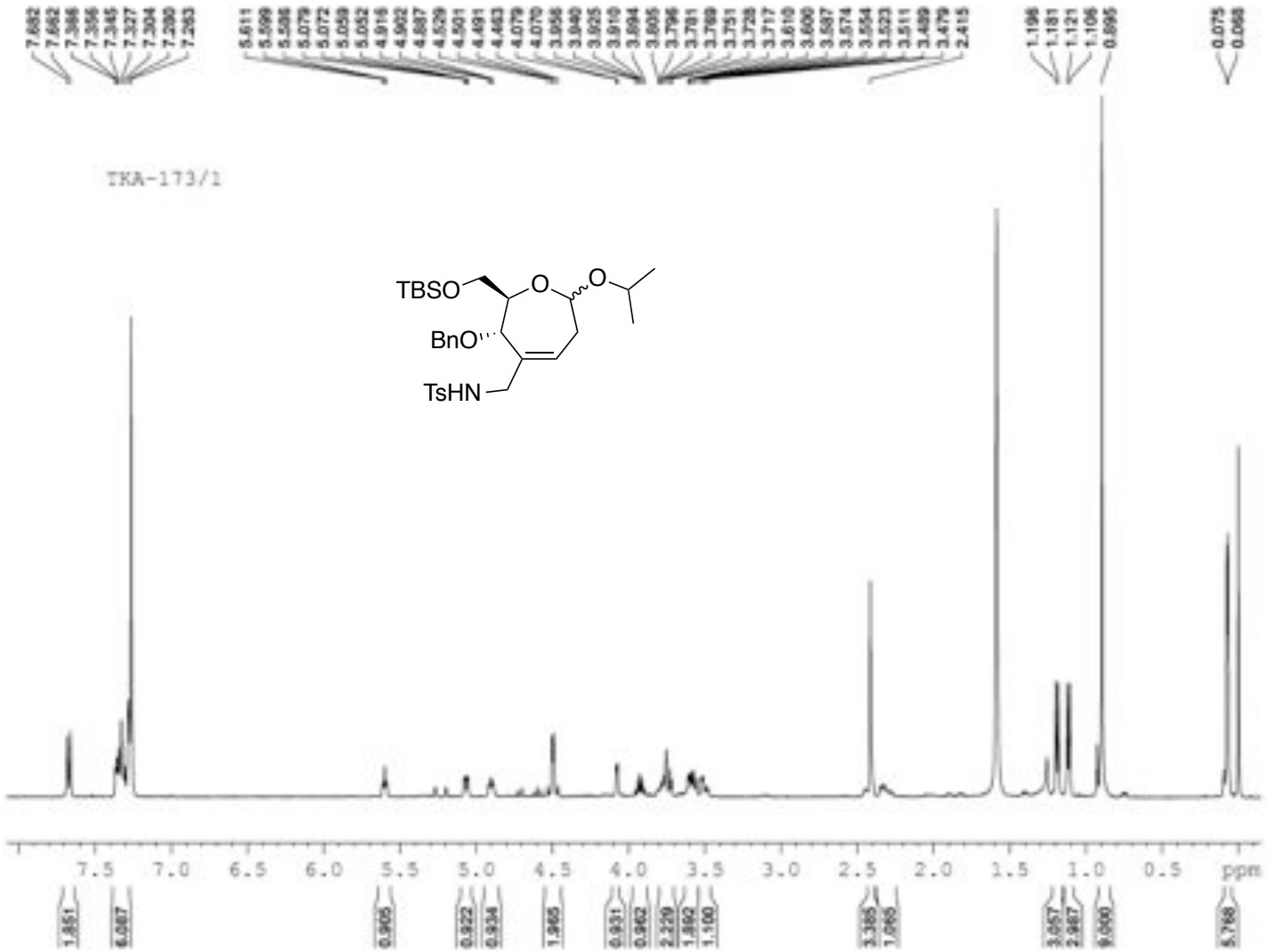
Time 21.33
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zeqcetgpsi2
TD 1024
SOLVENT CDCl3
NS 24
DS 16
SWH 5330.490 Hz
FIDRES 5.205557 Hz
AQ 0.0961012 sec
RG 203
DW 93.800 use
DE 6.50 use
TE 299.0 K
CNST2 145.0000000
D0 0.00000300 sec
D1 1.50000000 sec
D4 0.00172414 sec
D11 0.03000000 sec
D13 0.00000400 sec
D16 0.00020000 sec
D24 0.00086207 sec
IN8 0.00031775 sec
2GOPTNS
======== CHANNEL f1 ========
NUC1 1H
P1 13.00 use
P2 26.00 use
P28 0 usec
PL1 0 dB
PL1W 10.87646866 W
SFO1 400.2324063 MHz
======== CHANNEL f2 ========
CPDPRG2 garp
NUC2 13C
P3 9.40 use
P4 18.80 use
PCPD2 70.00 use
PL2 -2.00 dB
PL12 15.20 dB
PL2W 53.74446869 W
PL12W 1.02407980 W
SFO2 100.6454593 MHz


TKA-205/1
NOESY
TBSO
H
O
H
OMe
BnO
TsHN
ppm
0
1
2
3
4
5
6
7
8
7
6
5
4
3
2
1
0
ppm
BRUKER


TBSO
O
O
3
BnO
TsHN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


143.25
143.15
138.05
137.77
137.31
136.92
136.51
134.22
129.58
128.49
128.44
127.84
127.47
127.12
127.07
124.67
99.38
98.81
79.69
79.77
77.27
76.95
76.63
72.31
71.18
69.84
67.96
67.50
64.43
63.61
50.53
49.39
36.67
31.62
31.06
25.99
25.85
21.42
19.33
19.23
18.47
18.27
13.92
-5.30
-5.48
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


TKA-173/1
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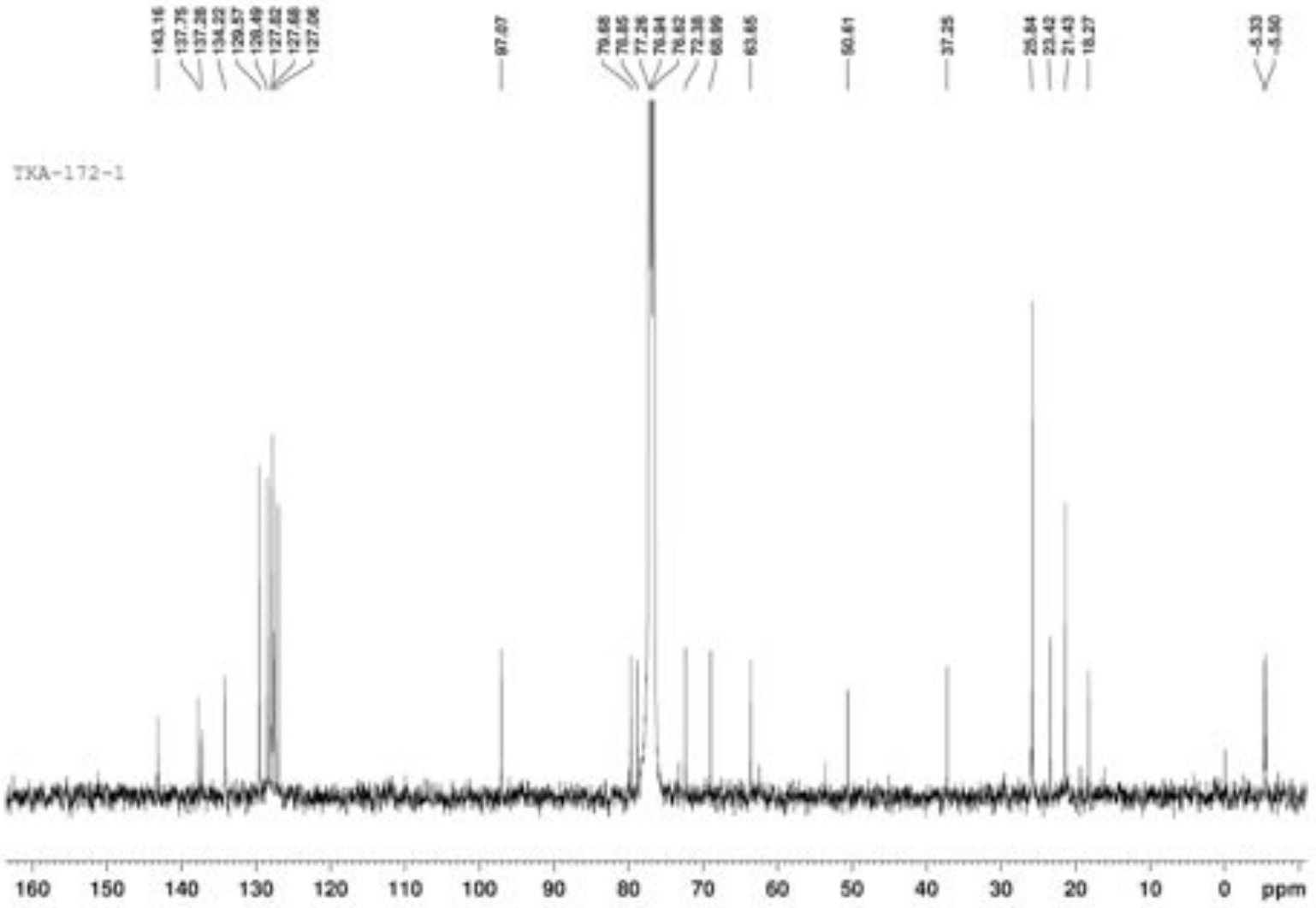
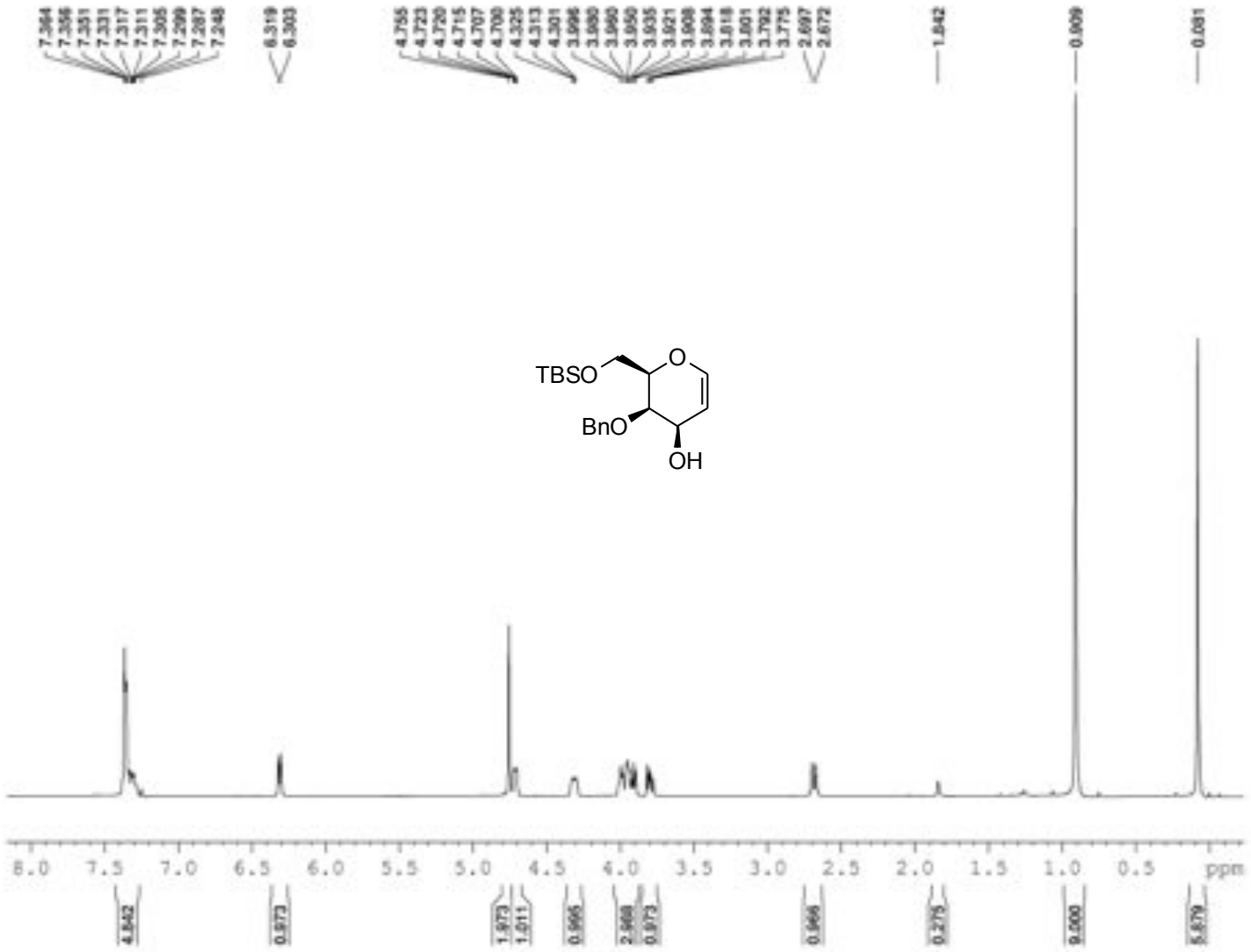
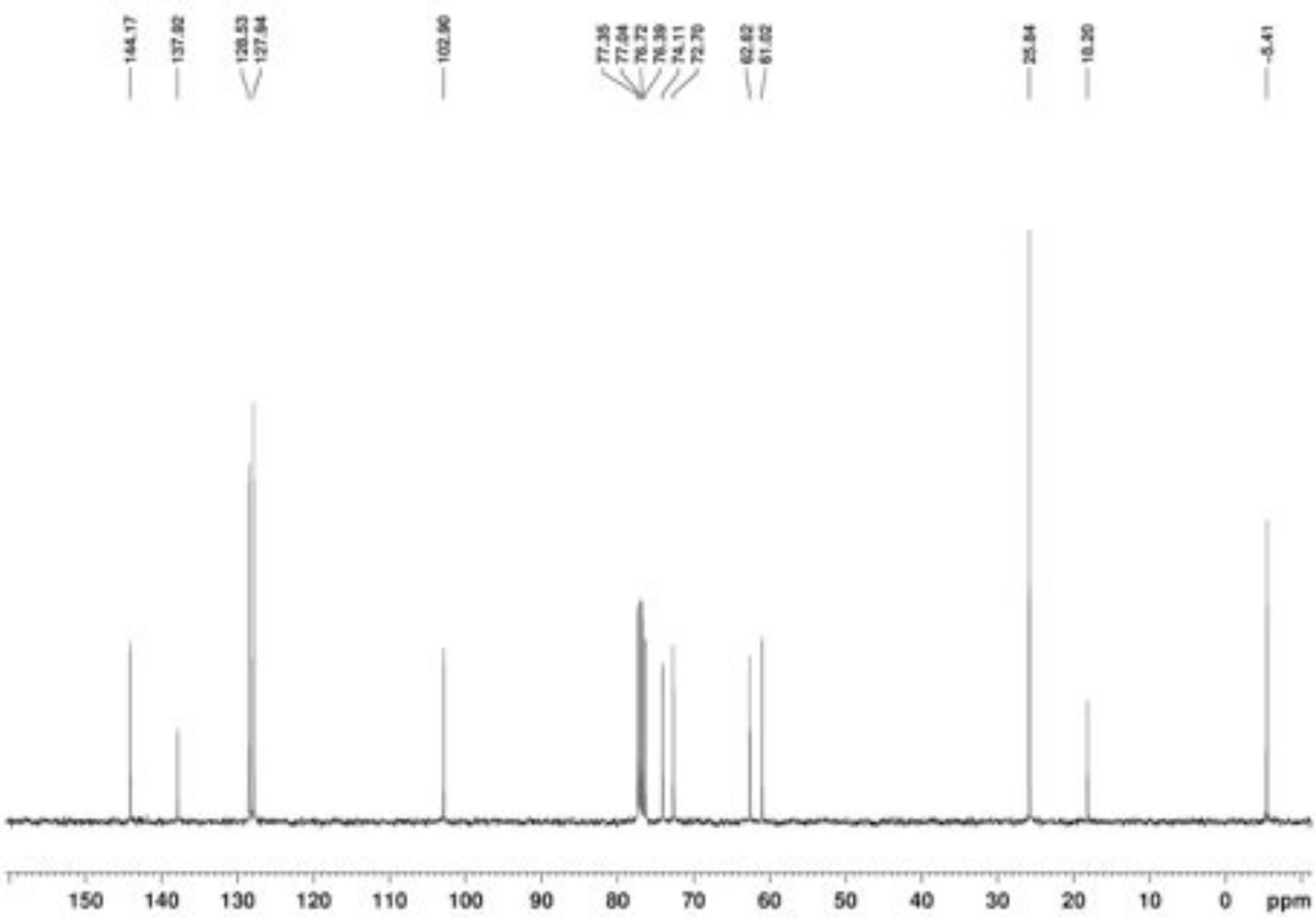
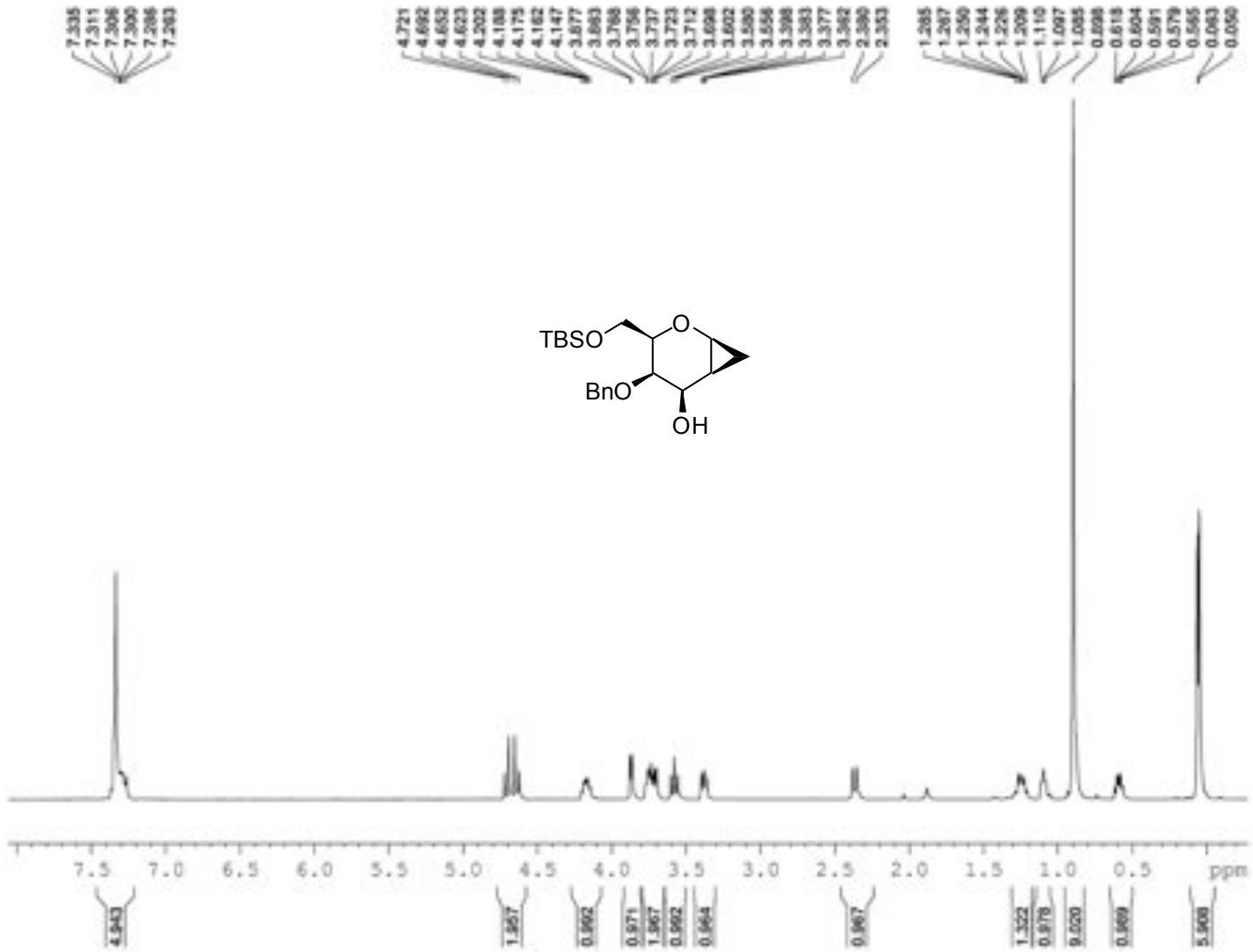
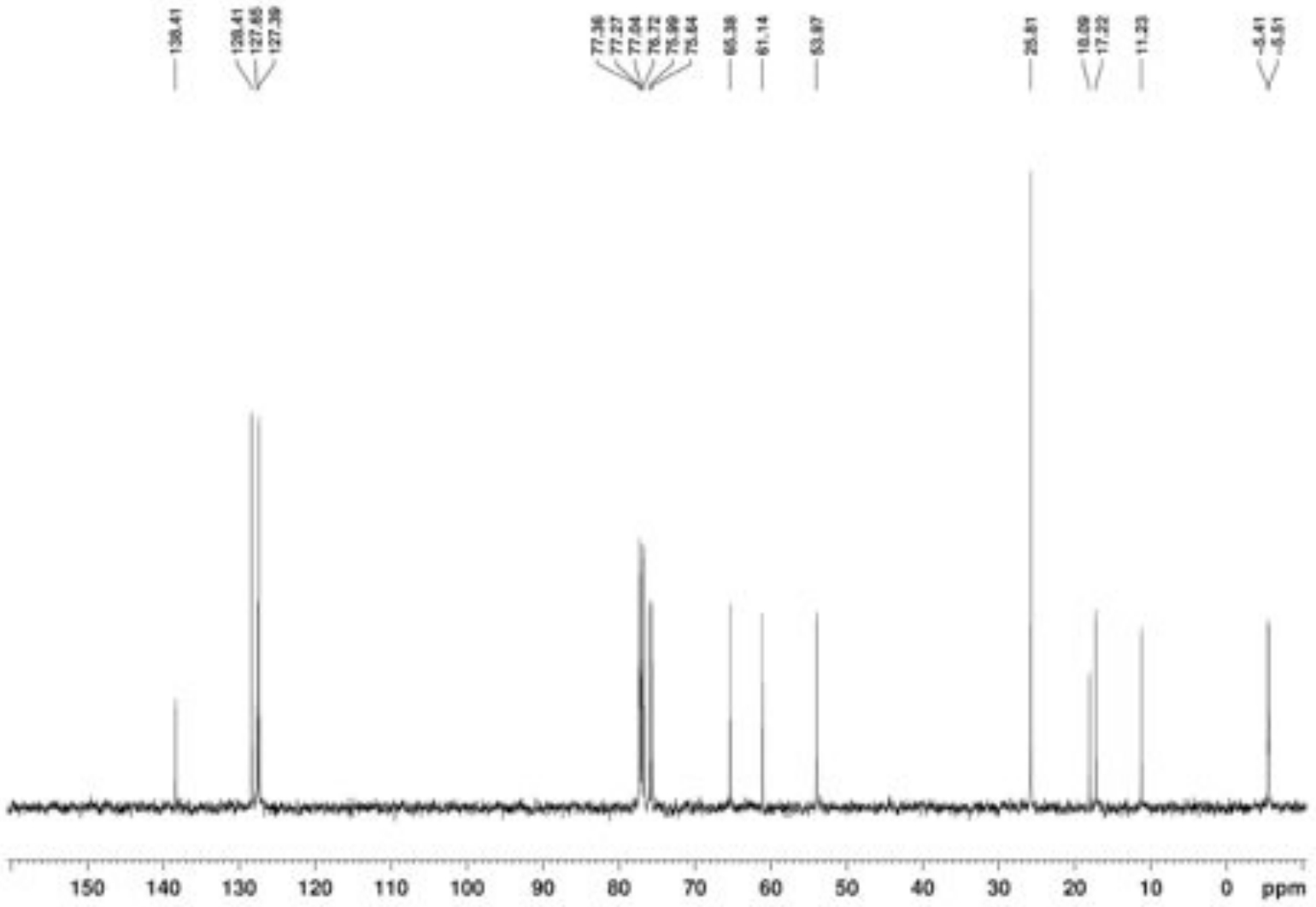
O
O
BnO
TsHN
ppm


143.16
137.75
137.28
134.22
129.57
128.49
127.82
127.68
127.06
97.07
79.88
79.85
77.26
76.84
76.62
72.38
69.99
63.65
50.61
37.25
25.84
23.42
21.43
18.27
-5.33
-5.50
TKA-172-1
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.364
7.358
7.351
7.331
7.317
7.311
7.305
7.299
7.287
7.248
6.319
6.303
4.755
4.723
4.720
4.715
4.707
4.700
4.325
4.313
4.301
3.996
3.980
3.960
3.950
3.935
3.921
3.908
3.894
3.818
3.801
3.792
3.775
2.697
2.672
1.842
0.009
0.081
TBSO
O
BnO
OH
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.842
0.973
1.873
1.011
0.995
2.968
0.973
0.966
0.275
9.000
5.879


144.17
137.92
128.53
127.84
102.90
77.35
77.04
76.72
76.39
74.11
72.70
62.82
61.02
25.84
18.20
-5.41
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.335
7.311
7.306
7.300
7.286
7.263
4.721
4.692
4.653
4.623
4.202
4.188
4.175
4.162
4.147
3.877
3.863
3.768
3.756
3.737
3.723
3.712
3.698
3.602
3.580
3.558
3.398
3.383
3.377
3.362
2.380
2.353
1.285
1.267
1.250
1.244
1.226
1.209
1.110
1.097
1.085
0.618
0.604
0.591
0.579
0.565
0.063
0.050
TBSO
O
BnO
OH
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.943
1.957
0.992
0.971
1.967
0.992
0.964
0.967
1.322
0.976
9.020
0.969
5.908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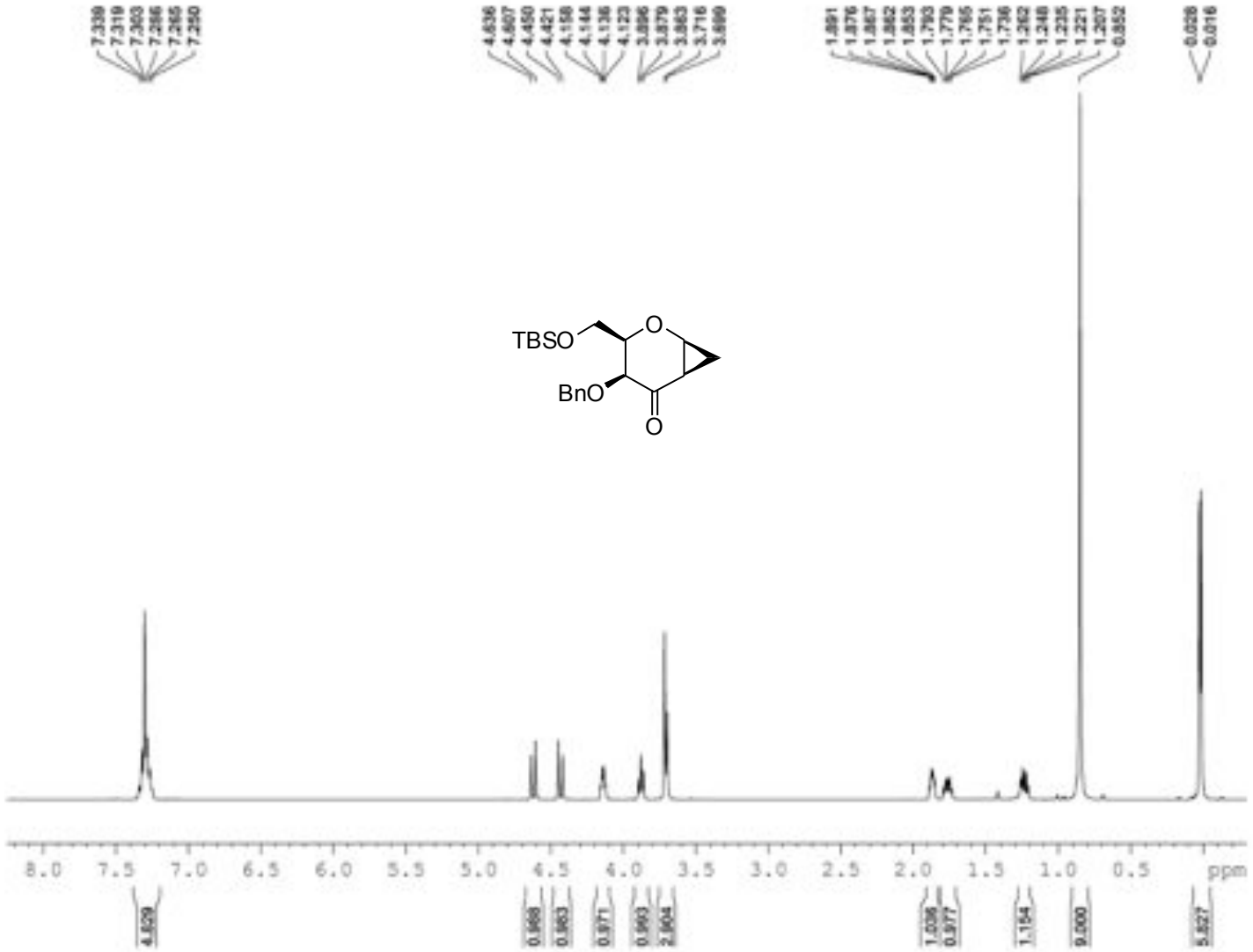
128.41
127.85
127.39
77.36
77.27
77.04
76.72
75.89
75.64
65.38
61.14
53.87
25.81
18.09
17.22
11.23
-5.41
-5.51
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.319
7.303
7.286
7.265
7.250
4.636
4.607
4.450
4.421
4.158
4.144
4.136
4.123
3.886
3.879
3.863
3.716
3.699
1.891
1.876
1.867
1.862
1.853
1.793
1.779
1.765
1.751
1.736
1.262
1.248
1.235
1.221
1.207
0.852
0.026
0.016
TBSO
O
BnO
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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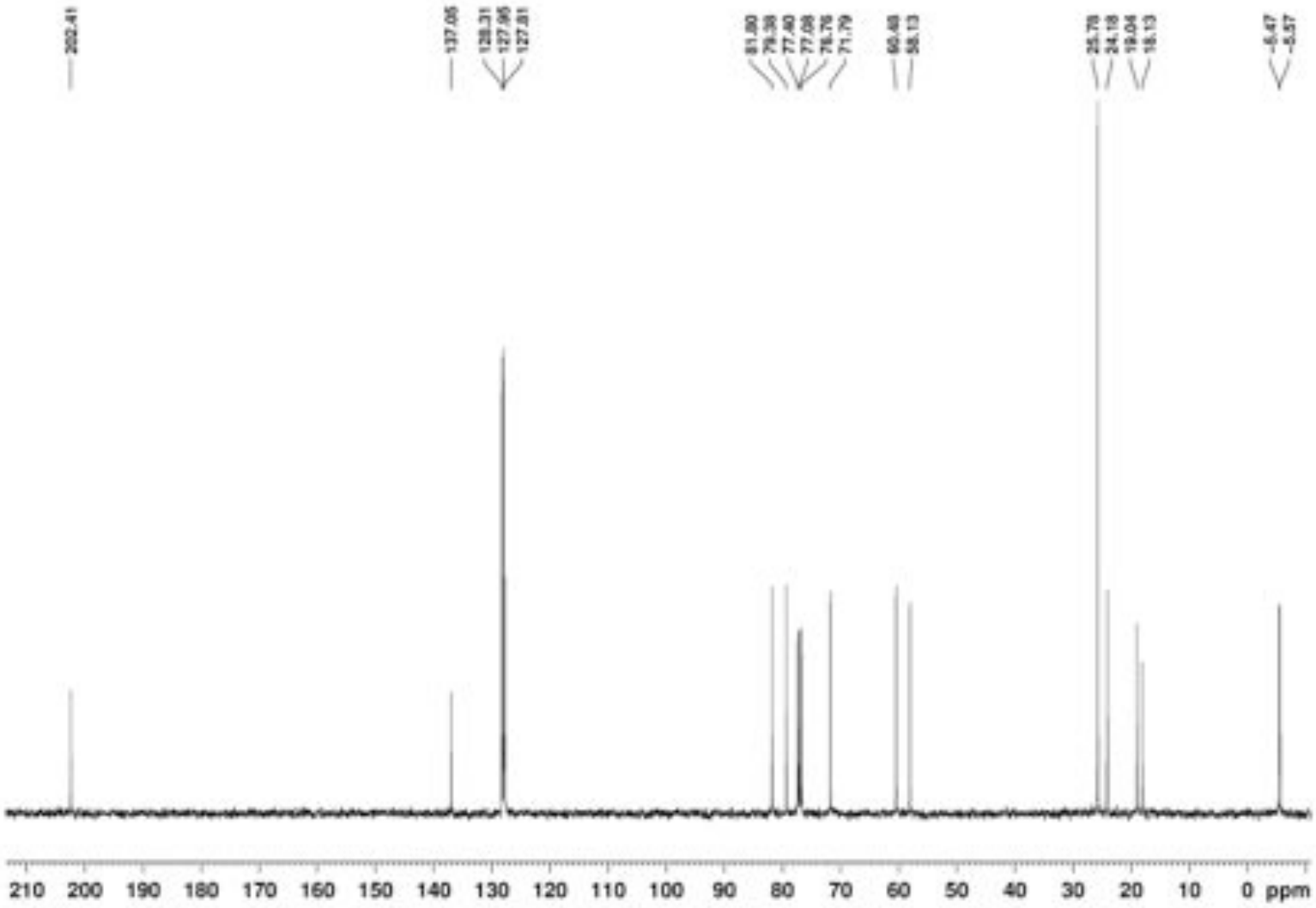
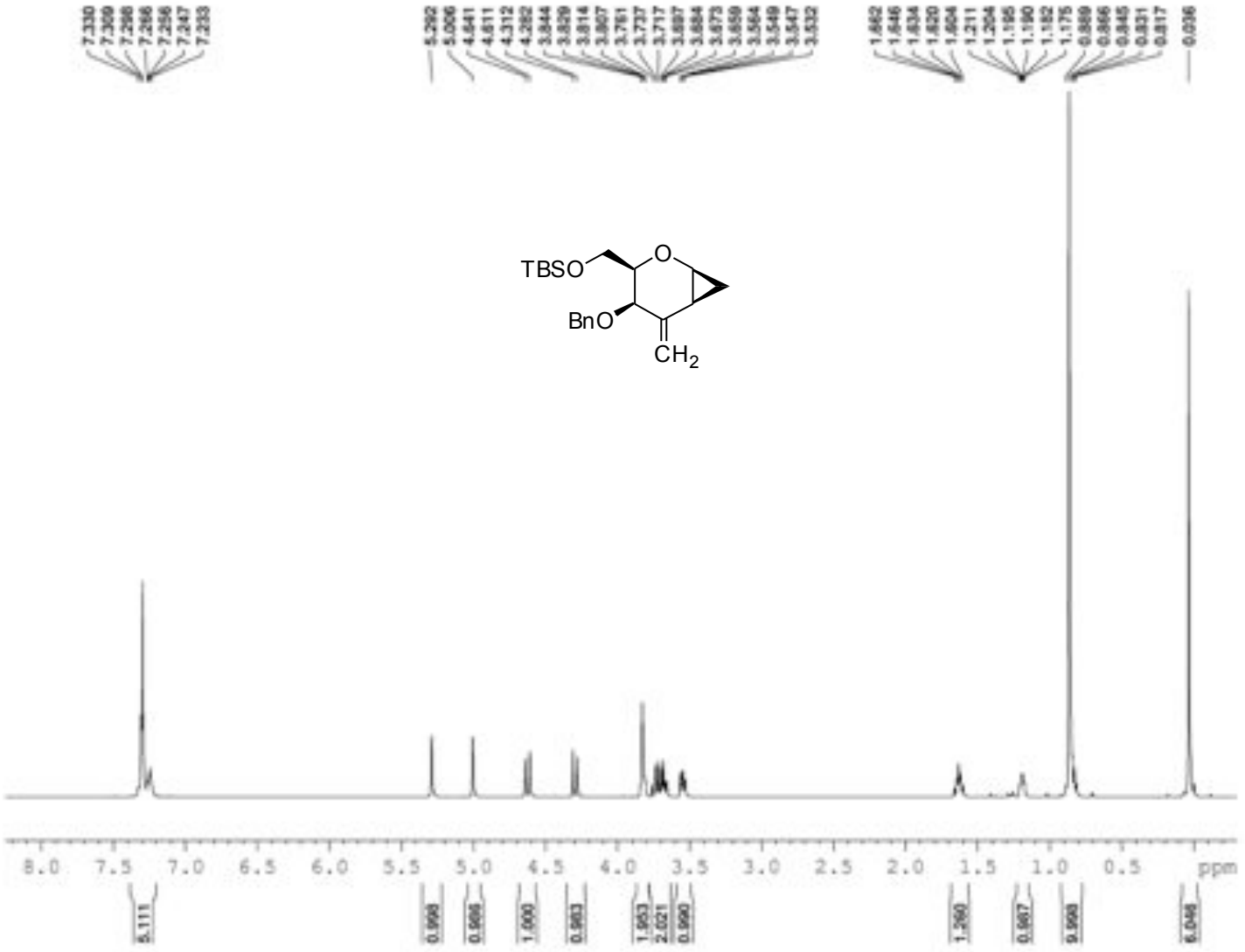
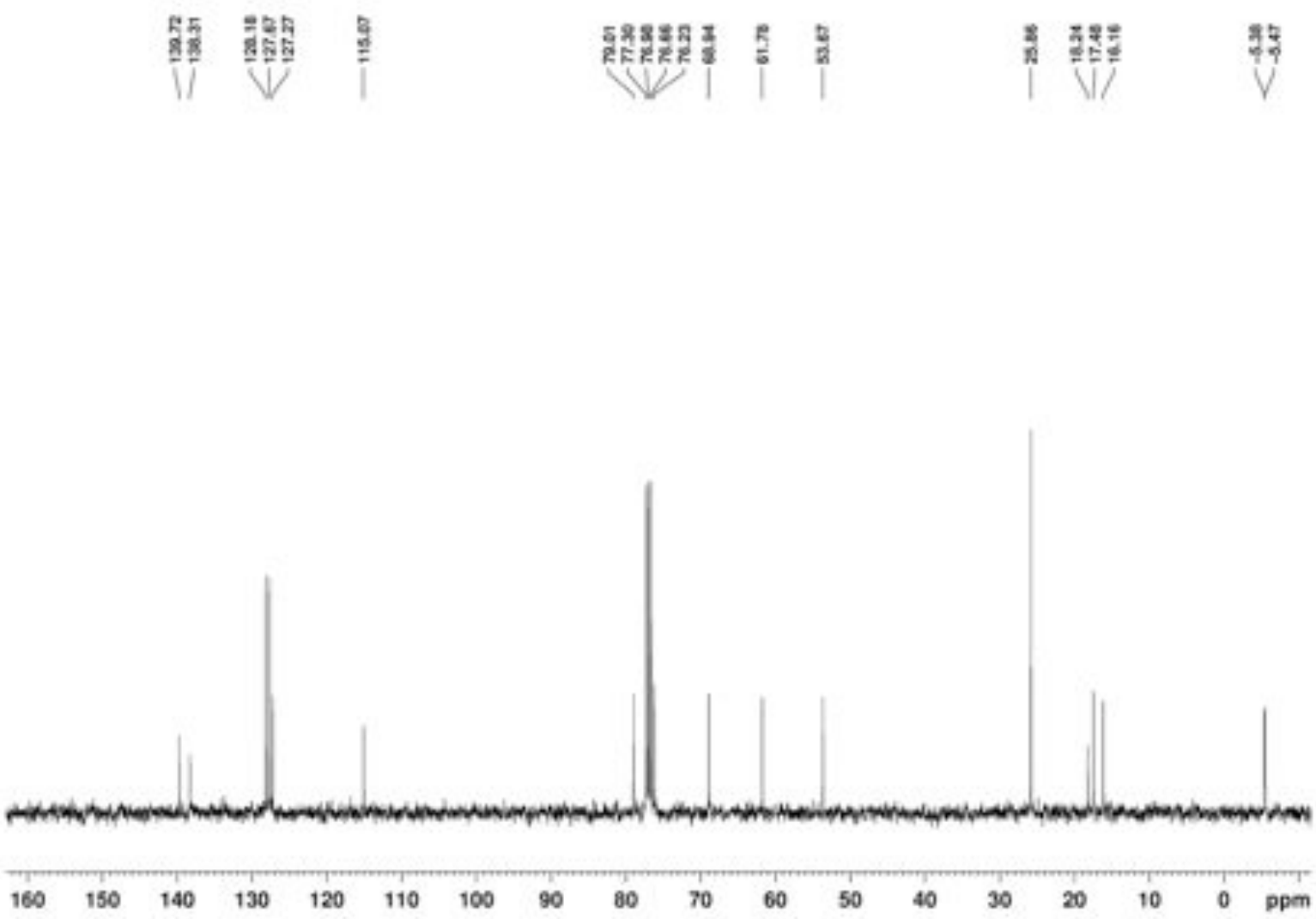
0.963
0.971
0.993
2.904
1.036
0.977
1.154
9.000
5.527


202.41
137.05
128.31
127.95
127.81
81.80
79.38
77.40
77.08
76.76
71.79
60.48
58.13
25.78
24.18
18.04
16.13
-5.47
-5.57
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


7.330
7.309
7.298
7.286
7.256
7.247
7.233
5.292
5.006
4.641
4.611
4.312
4.282
3.844
3.829
3.814
3.807
3.761
3.737
3.717
3.697
3.684
3.673
3.659
3.564
3.549
3.547
3.532
1.862
1.846
1.834
1.820
1.804
1.211
1.204
1.195
1.190
1.182
1.175
0.889
0.866
0.845
0.831
0.817
0.036
TBSO
O
BnO
CH2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.111
0.998
0.986
1.000
0.983
1.953
2.021
0.990
1.560
0.987
9.998
6.046


139.72
138.31
128.18
127.67
127.27
115.07
79.01
77.30
76.98
76.66
76.23
68.84
61.78
53.67
25.86
18.24
17.48
16.16
-5.38
-5.47
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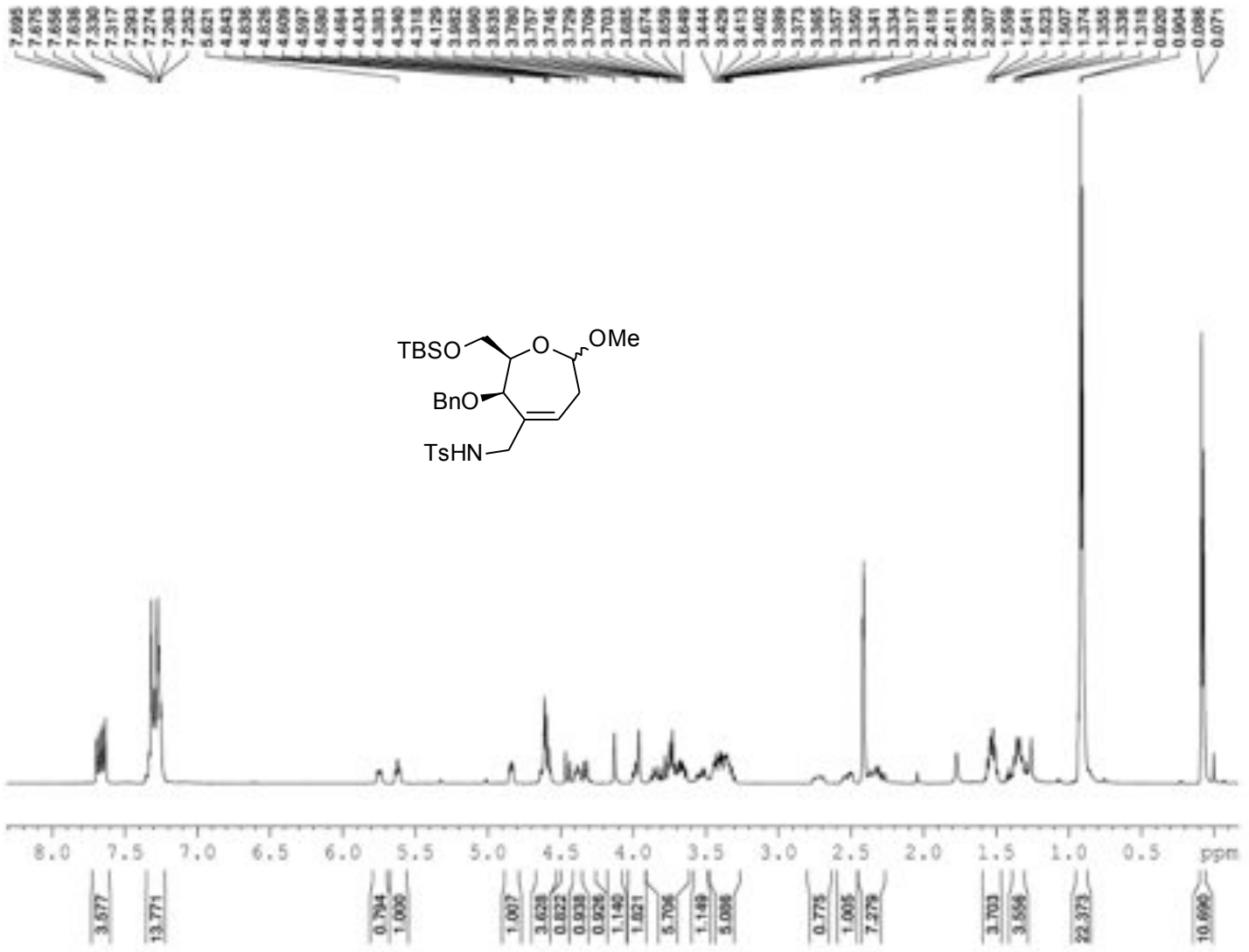
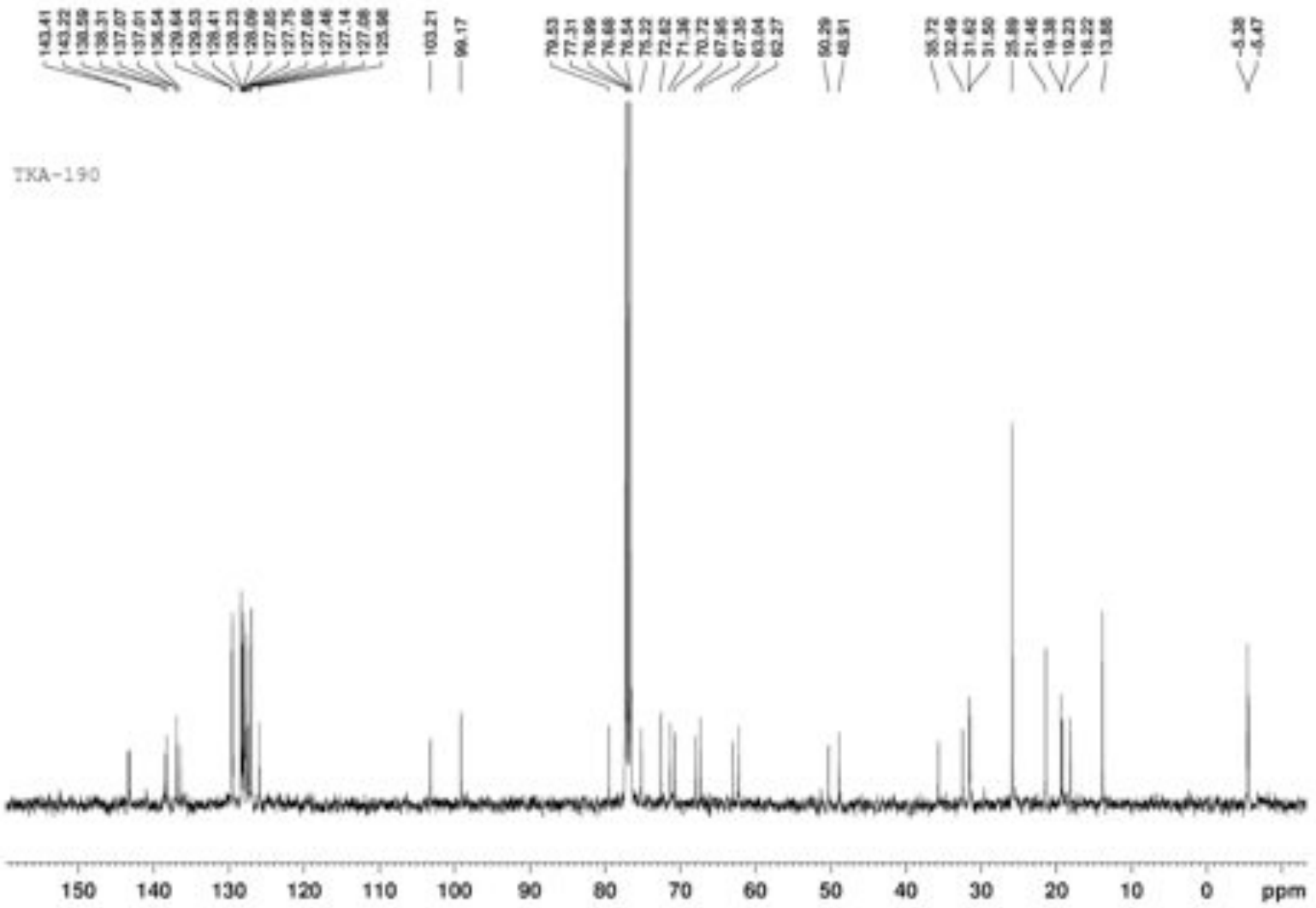
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


TBSO
O
OMe
BnO
TsHN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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129.64
129.53
128.41
128.23
128.09
127.85
127.75
127.69
127.46
127.14
127.08
125.98
103.21
99.17
79.53
77.31
76.99
76.68
76.54
75.22
72.82
71.36
70.72
67.86
67.35
63.04
62.27
50.29
48.91
35.72
32.49
31.62
31.50
25.89
21.46
19.38
19.23
18.22
13.88
-5.38
-5.47
TKA-190
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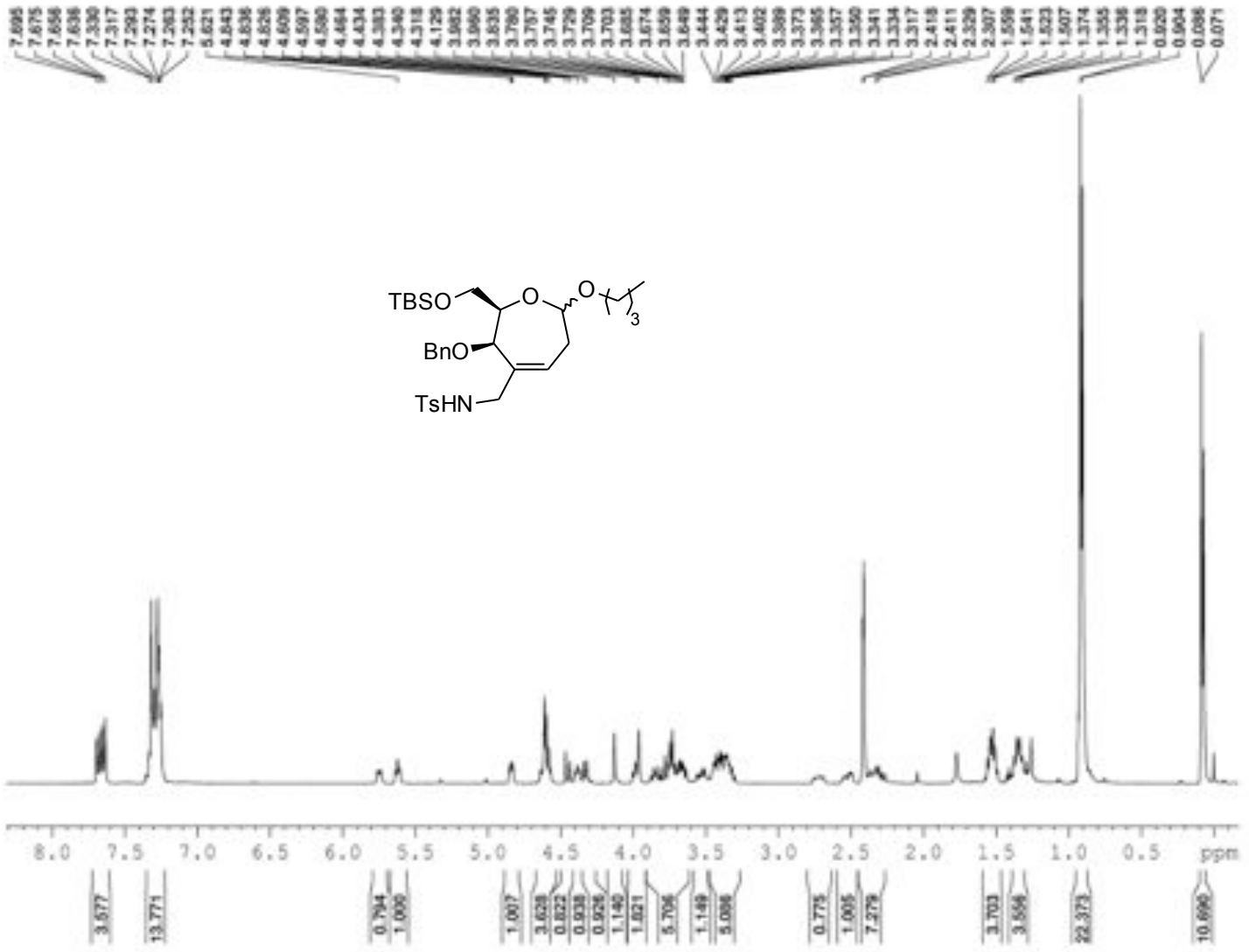
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


TBSO
O
O
3
BnO
TsHN
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7.5
7.0
6.5
6.0
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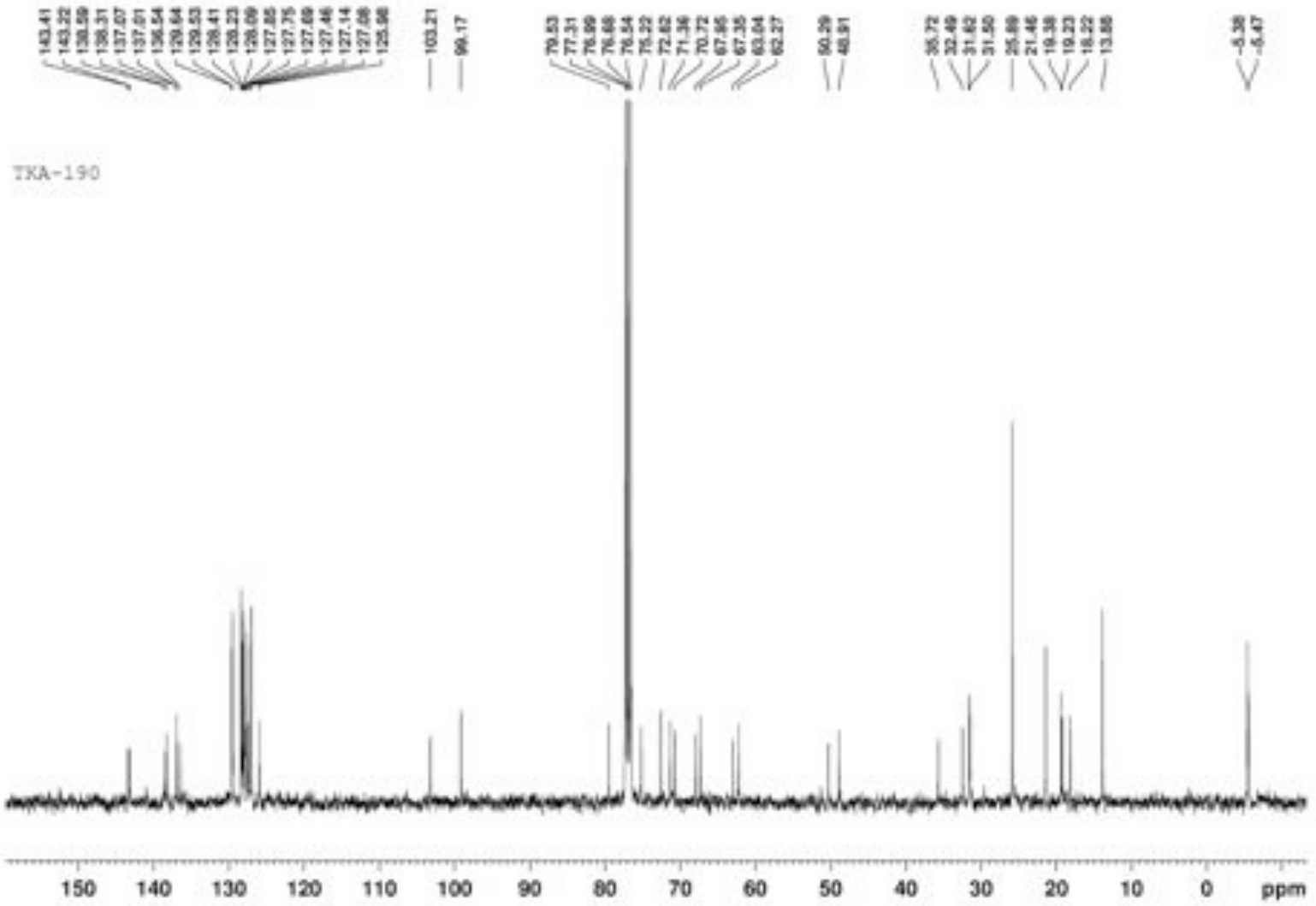
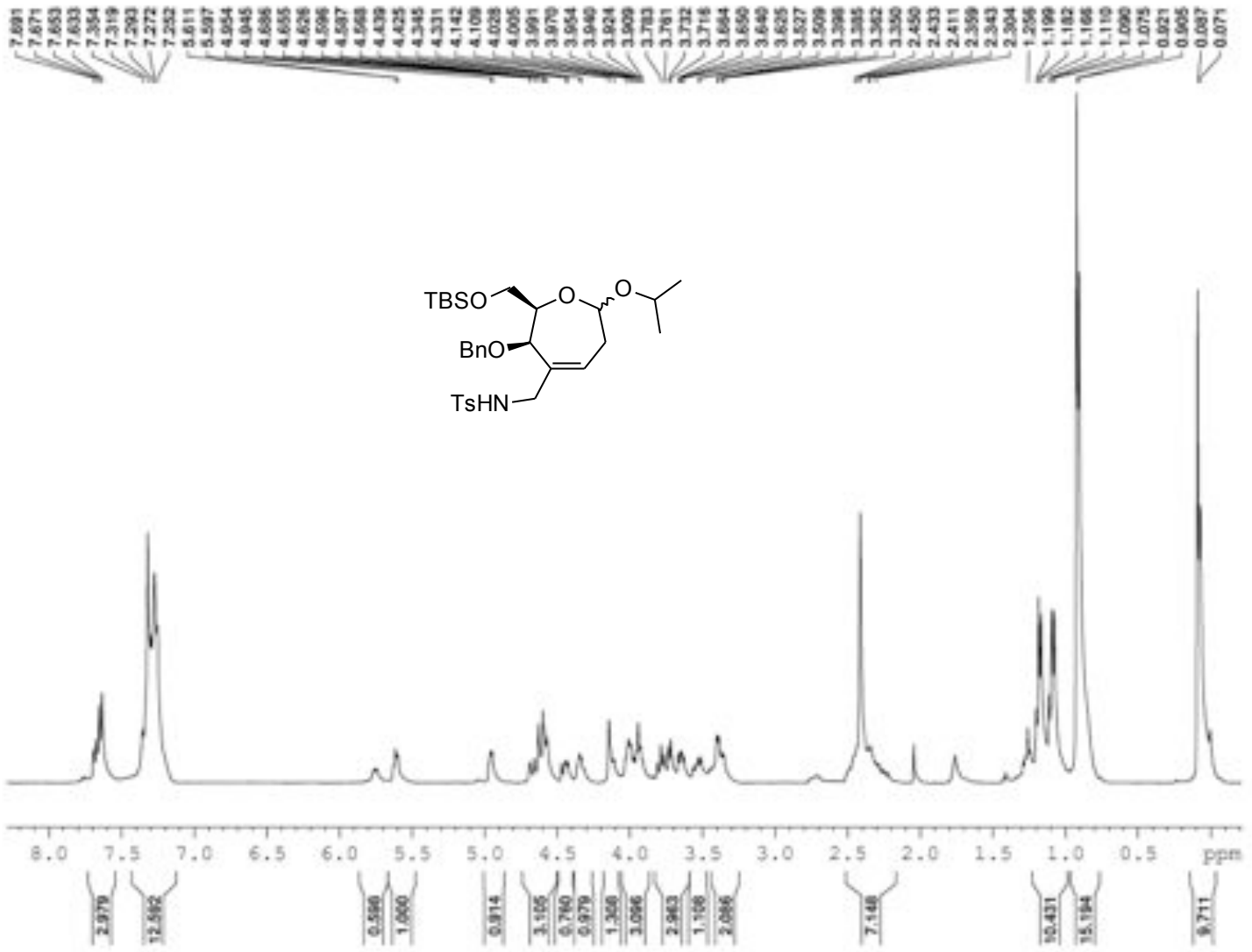
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


143.41
143.22
138.59
138.31
137.07
137.01
136.54
129.64
129.53
128.41
128.23
128.09
127.85
127.75
127.69
127.46
127.14
127.08
125.98
103.21
99.17
79.53
77.31
76.99
76.68
76.54
75.22
72.82
71.36
70.72
67.86
67.35
63.04
62.27
50.29
48.91
35.72
32.49
31.62
31.50
25.89
21.46
19.38
19.23
18.22
13.88
-5.38
-5.47
TKA-190
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


TBSO
O
O
BnO
TsHN
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7.5
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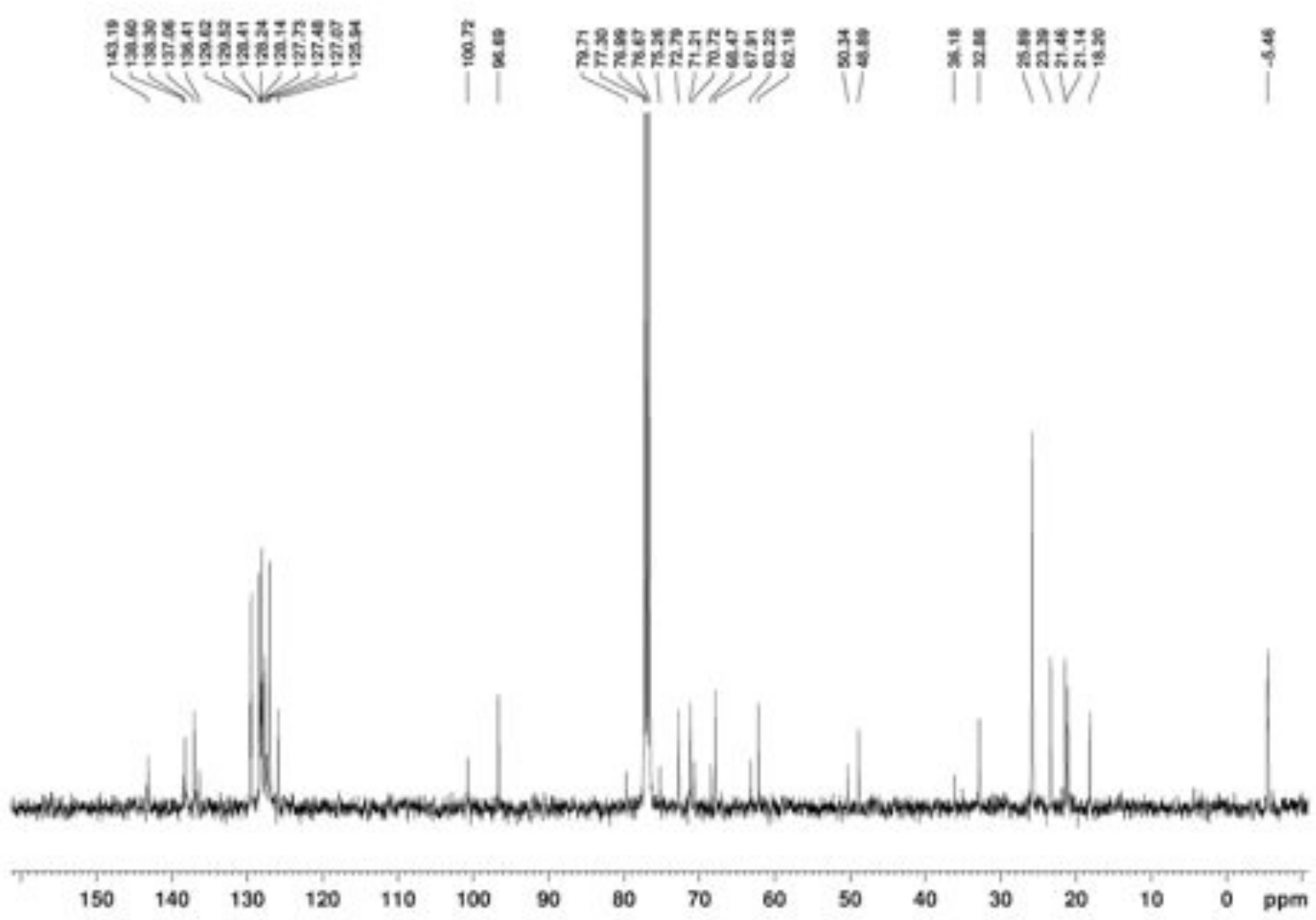
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


143.19
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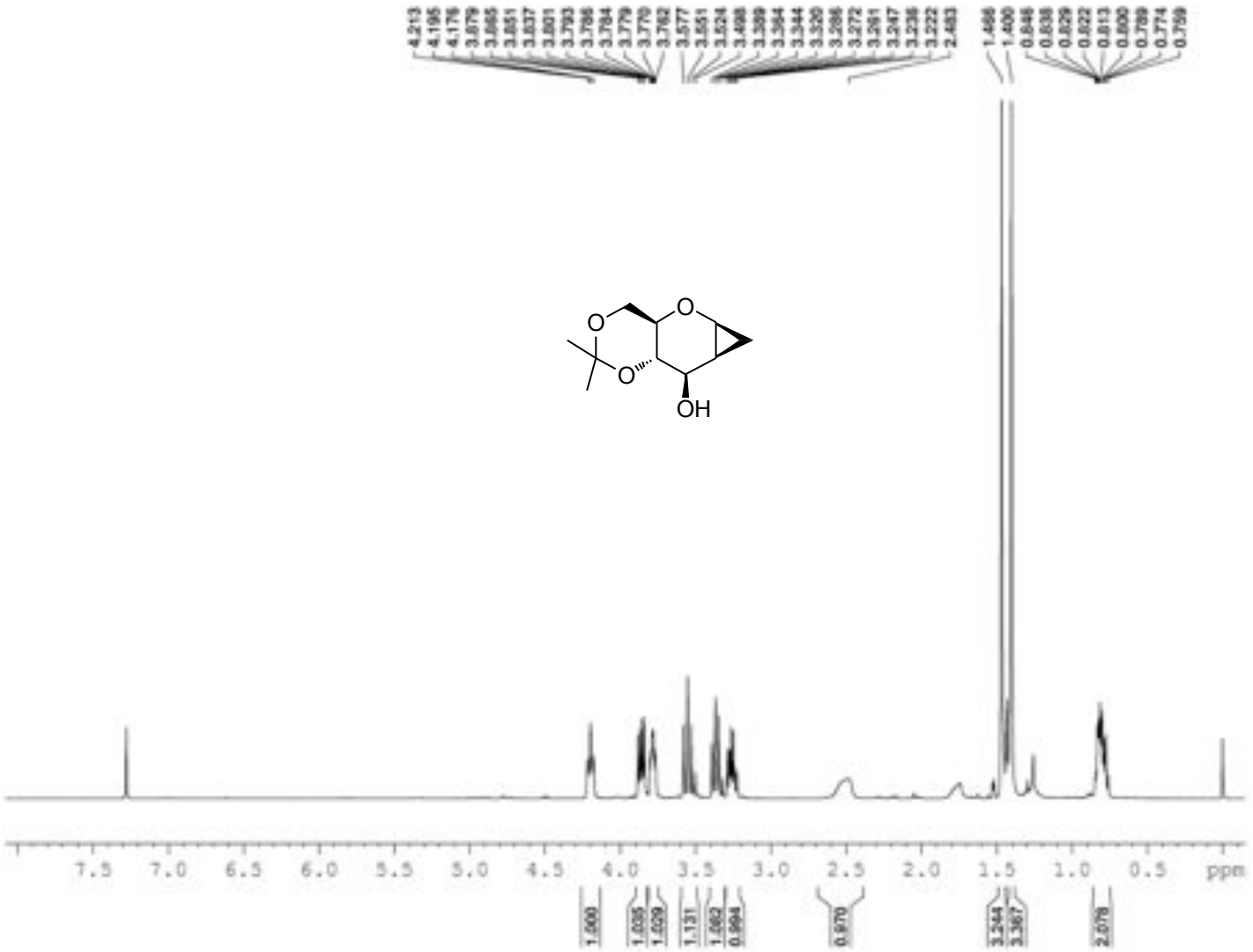
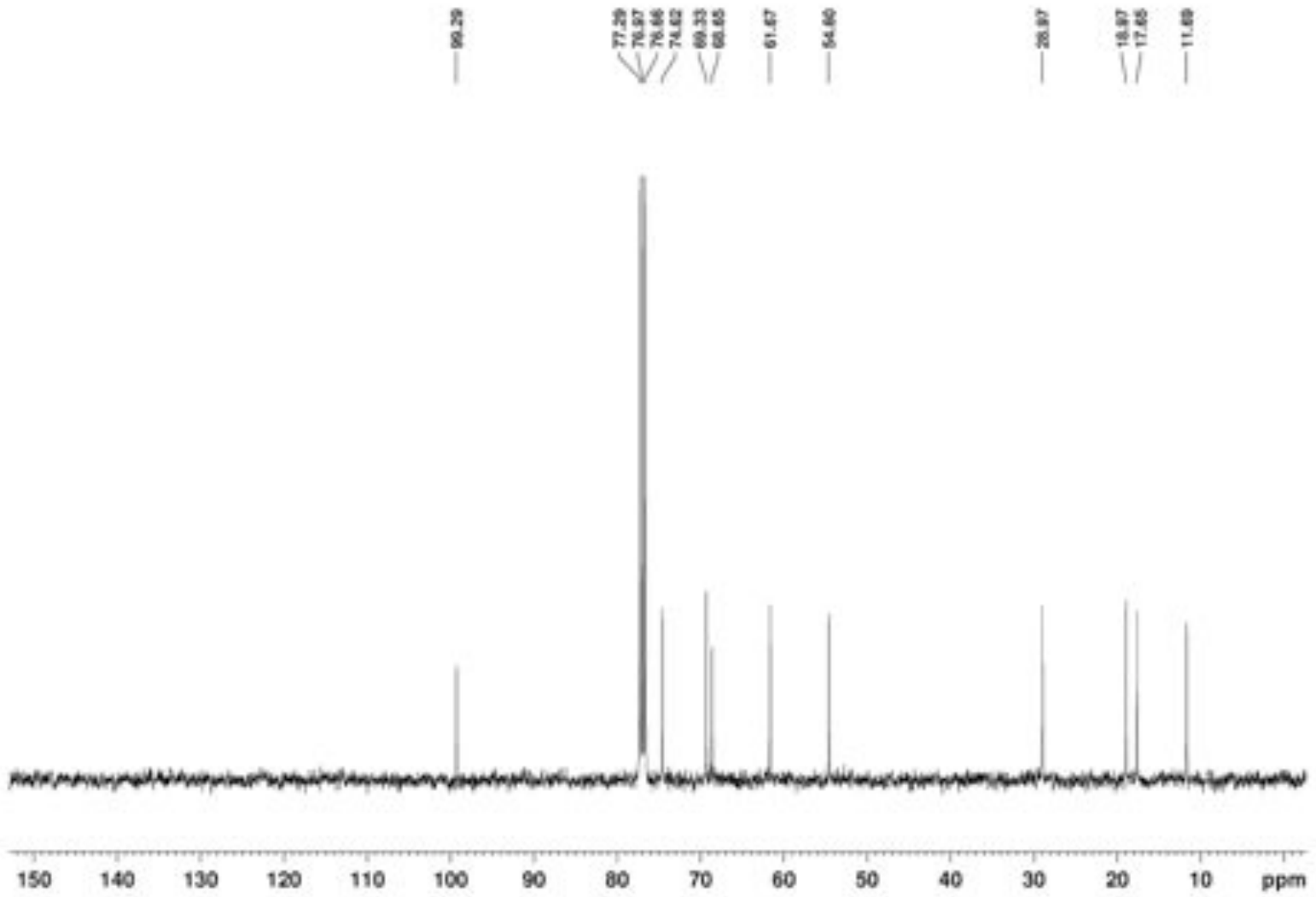
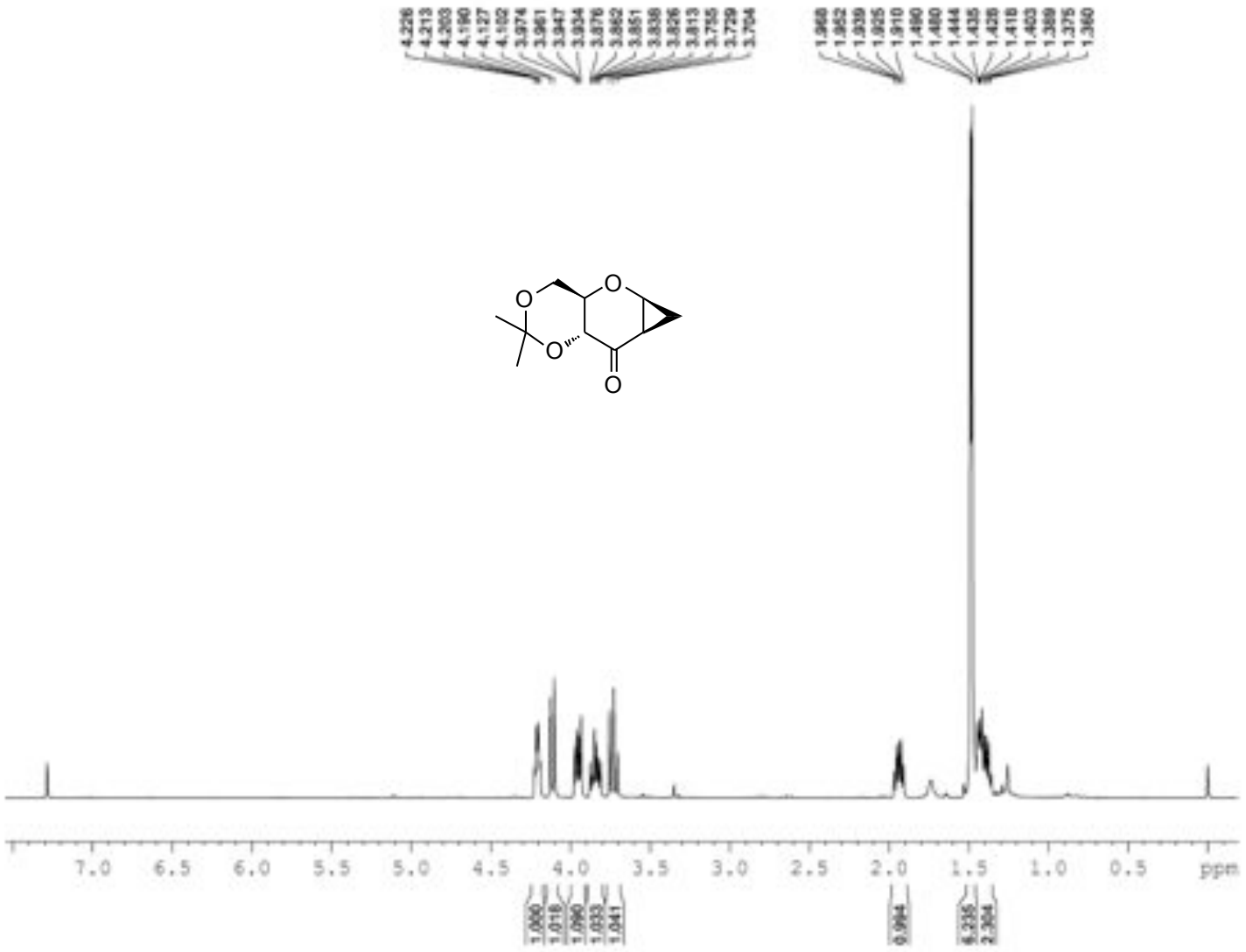
138.30
137.66
136.41
129.62
129.52
128.41
128.24
128.14
127.73
127.48
127.07
125.84
100.72
96.69
79.71
77.30
76.99
76.67
75.26
72.79
71.21
70.72
68.47
67.91
63.22
62.18
50.34
48.89
36.18
32.88
25.89
23.39
21.46
21.14
18.20
-5.46
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


4.213
4.195
4.176
3.879
3.865
3.851
3.837
3.801
3.793
3.786
3.784
3.779
3.770
3.762
3.577
3.551
3.524
3.488
3.399
3.364
3.344
3.320
3.286
3.272
3.261
3.247
3.238
3.222
2.483
1.466
1.400
0.846
0.838
0.829
0.822
0.813
0.800
0.789
0.774
0.759
O
O
O
OH
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.000
1.035
1.009
1.131
1.062
0.994
0.970
3.244
3.367
2.078


99.29
77.29
76.87
76.66
74.62
69.33
68.65
61.67
54.80
29.97
18.97
17.65
11.69
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


4.226
4.213
4.203
4.190
4.127
4.102
3.974
3.961
3.947
3.934
3.876
3.862
3.851
3.838
3.826
3.813
3.755
3.729
3.704
1.968
1.952
1.939
1.925
1.910
1.490
1.480
1.444
1.435
1.428
1.416
1.403
1.389
1.375
1.360
O
O
O
O
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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1.018
1.090
1.033
1.041
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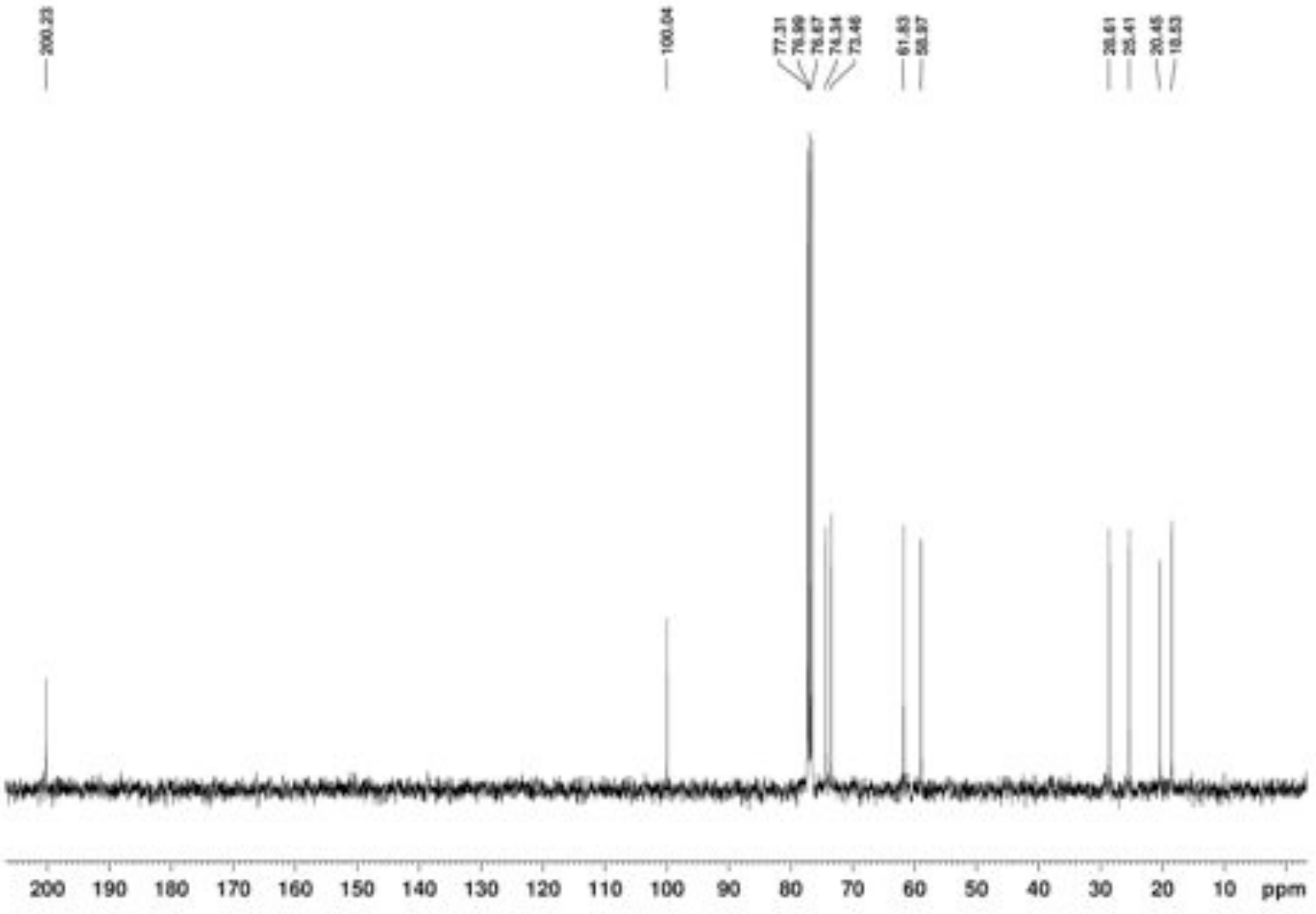
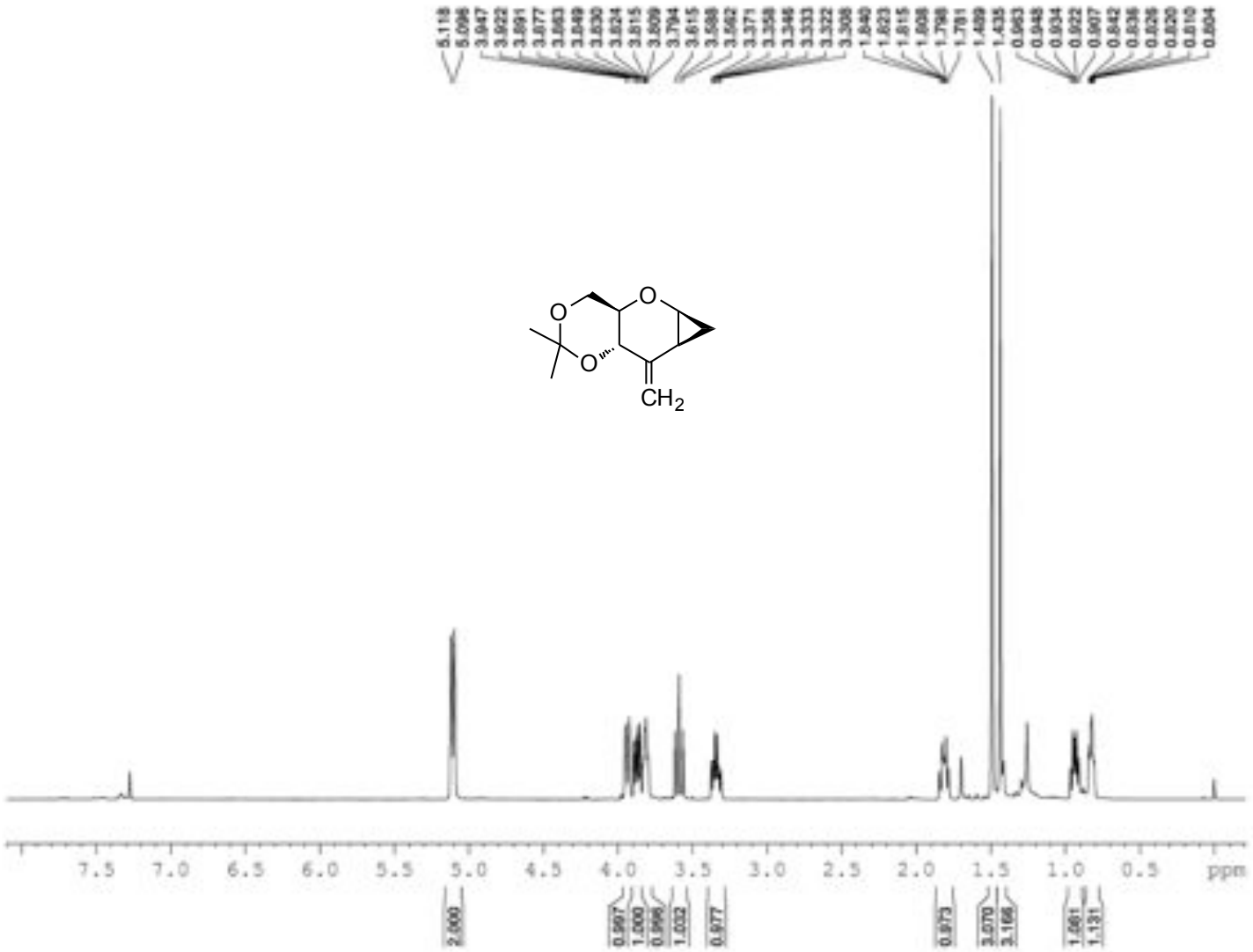
6.235
2.304


200.23
100.04
77.31
76.99
76.67
74.34
73.46
61.83
58.87
28.61
25.41
20.45
18.53
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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3.830
3.824
3.815
3.809
3.794
3.615
3.588
3.562
3.371
3.358
3.346
3.333
3.322
3.308
1.840
1.823
1.815
1.808
1.798
1.781
1.489
1.435
0.963
0.948
0.934
0.922
0.907
0.842
0.836
0.826
0.820
0.810
0.804
O
O
O
CH2
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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1.000
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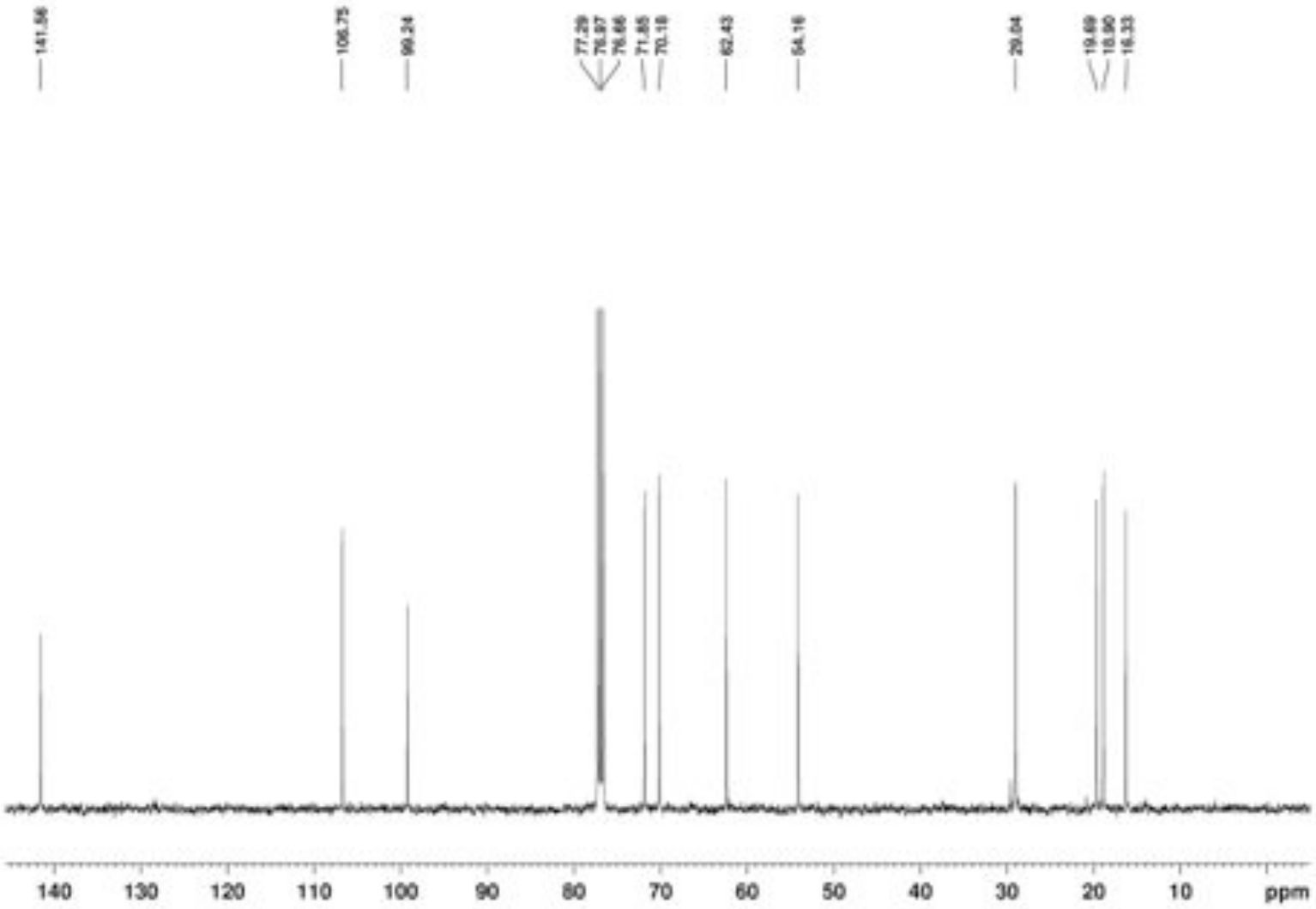
1.661
1.131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106.75
99.24
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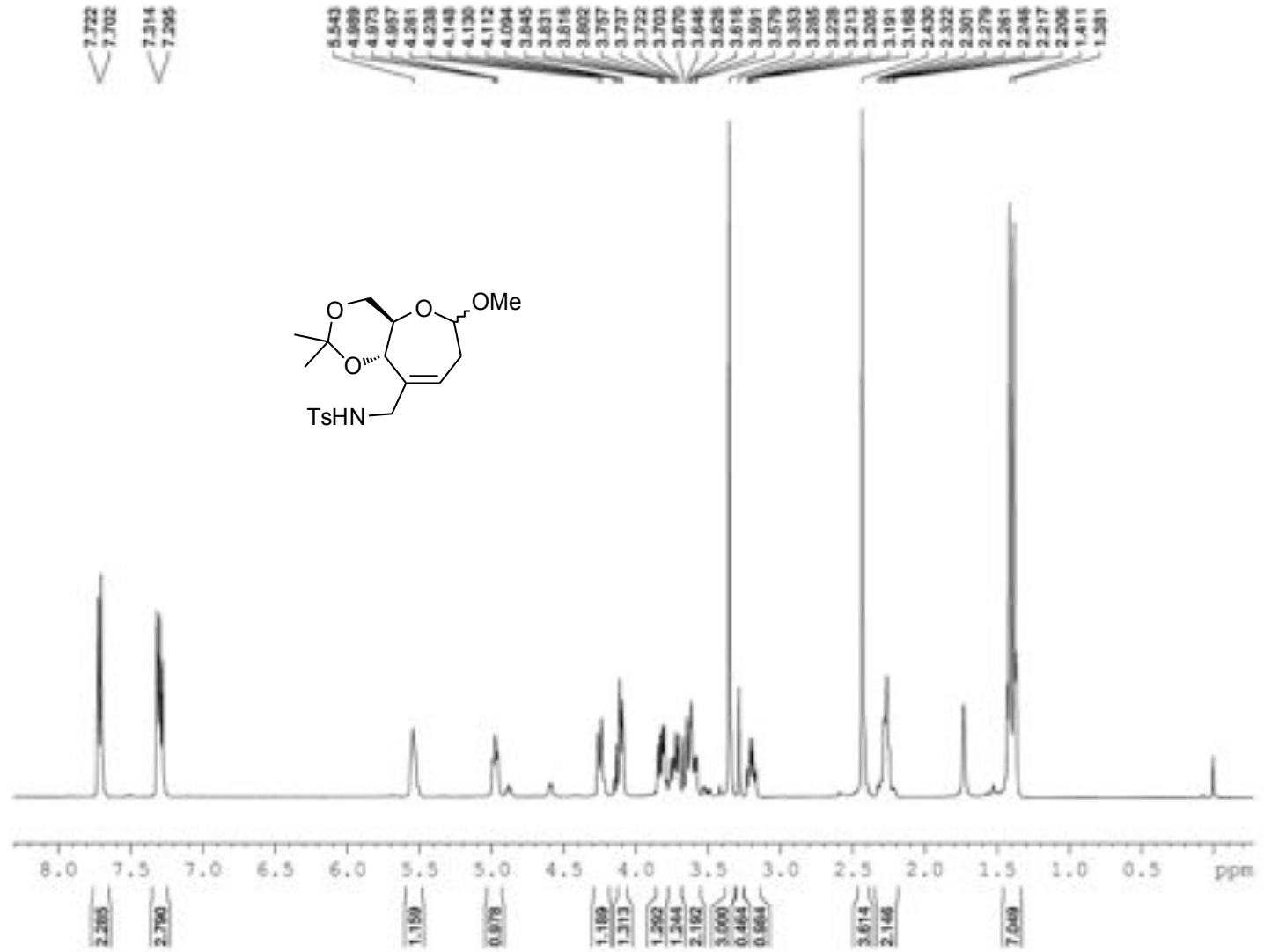
76.66
71.85
70.18
62.43
54.16
29.04
19.69
18.90
16.33
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.702
7.314
7.295
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4.973
4.957
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4.148
4.130
4.112
4.094
3.845
3.831
3.816
3.802
3.767
3.737
3.722
3.703
3.670
3.646
3.628
3.616
3.591
3.579
3.353
3.285
3.228
3.213
3.205
3.191
3.168
2.430
2.322
2.301
2.279
2.261
2.248
2.217
2.206
1.411
1.381
O
O
OMe
O
TsHN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.285
2.790
1.159
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1.292
1.244
2.192
3.000
0.464
0.984
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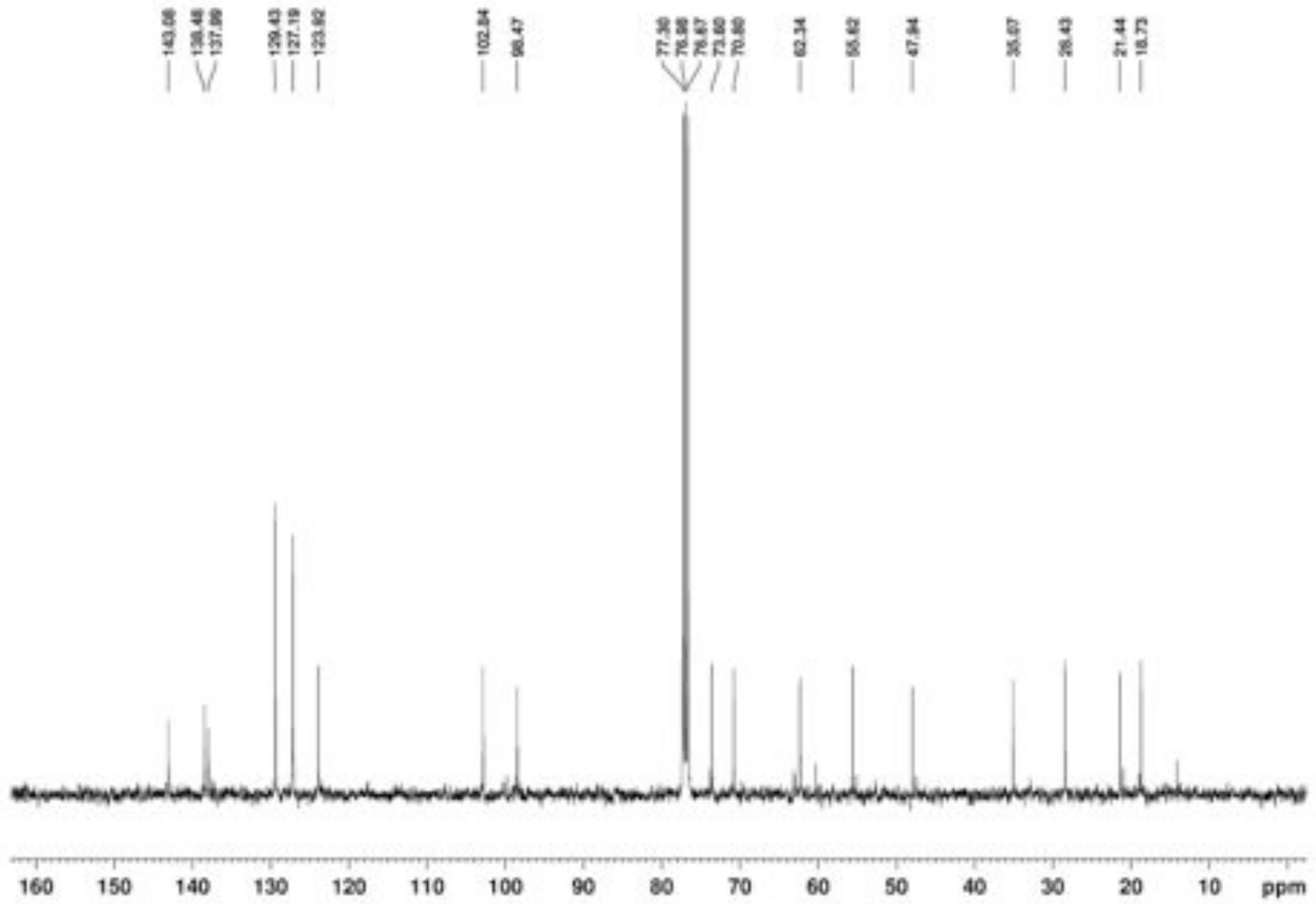
2.146
7.049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123.92
102.84
98.47
77.36
76.98
76.67
73.60
70.86
62.34
55.62
47.84
35.07
28.43
21.44
18.73
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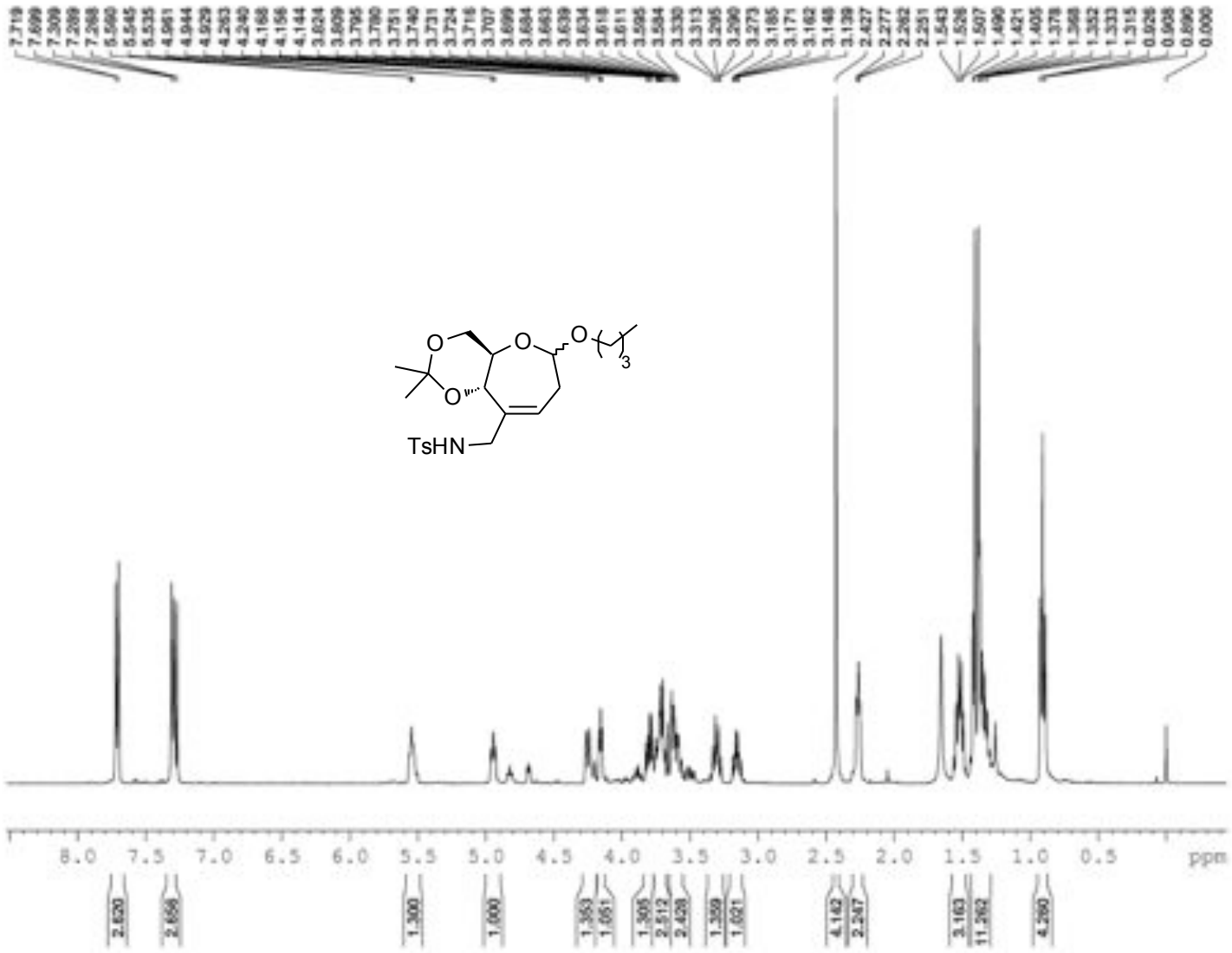
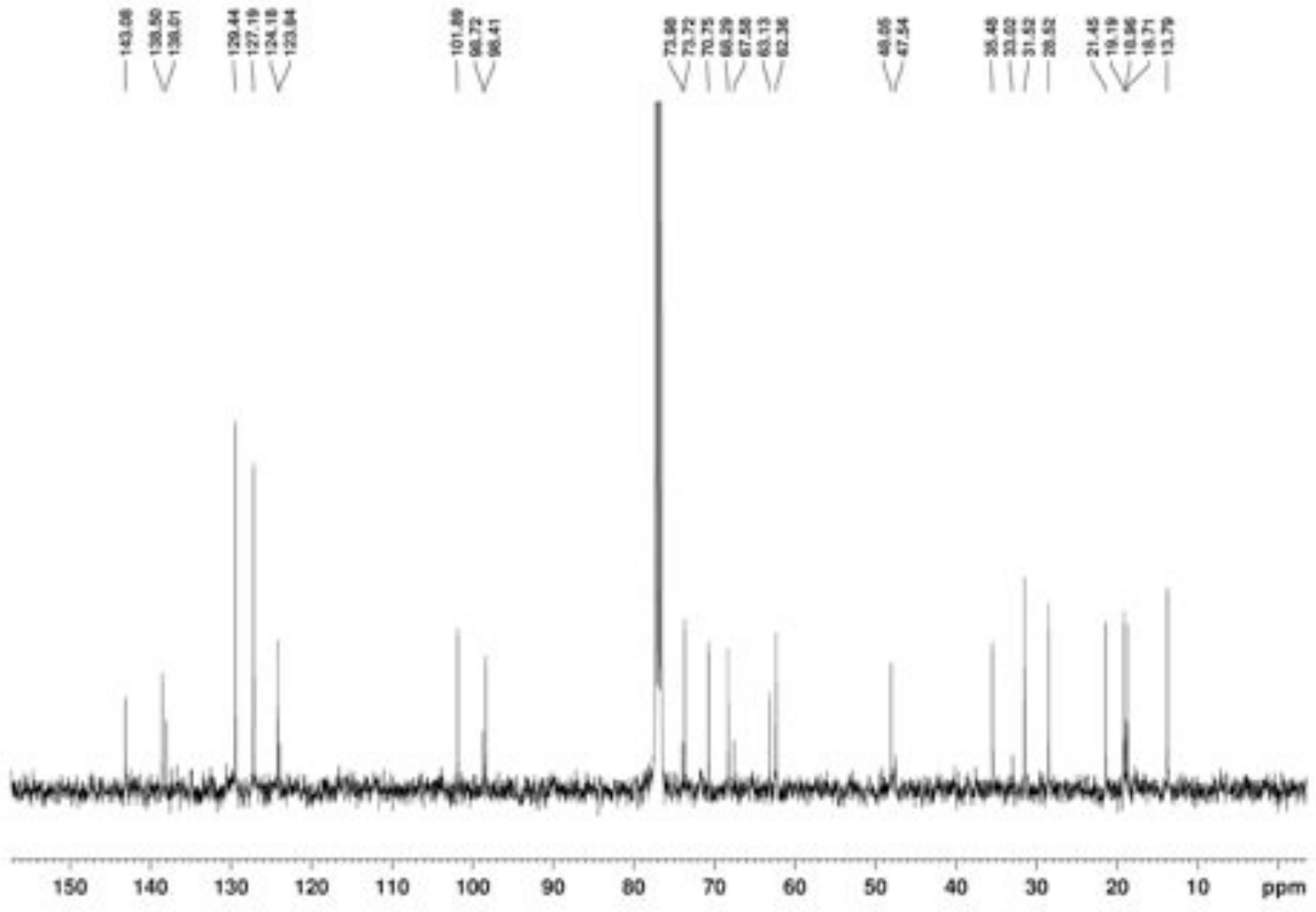
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


TsHN
ppm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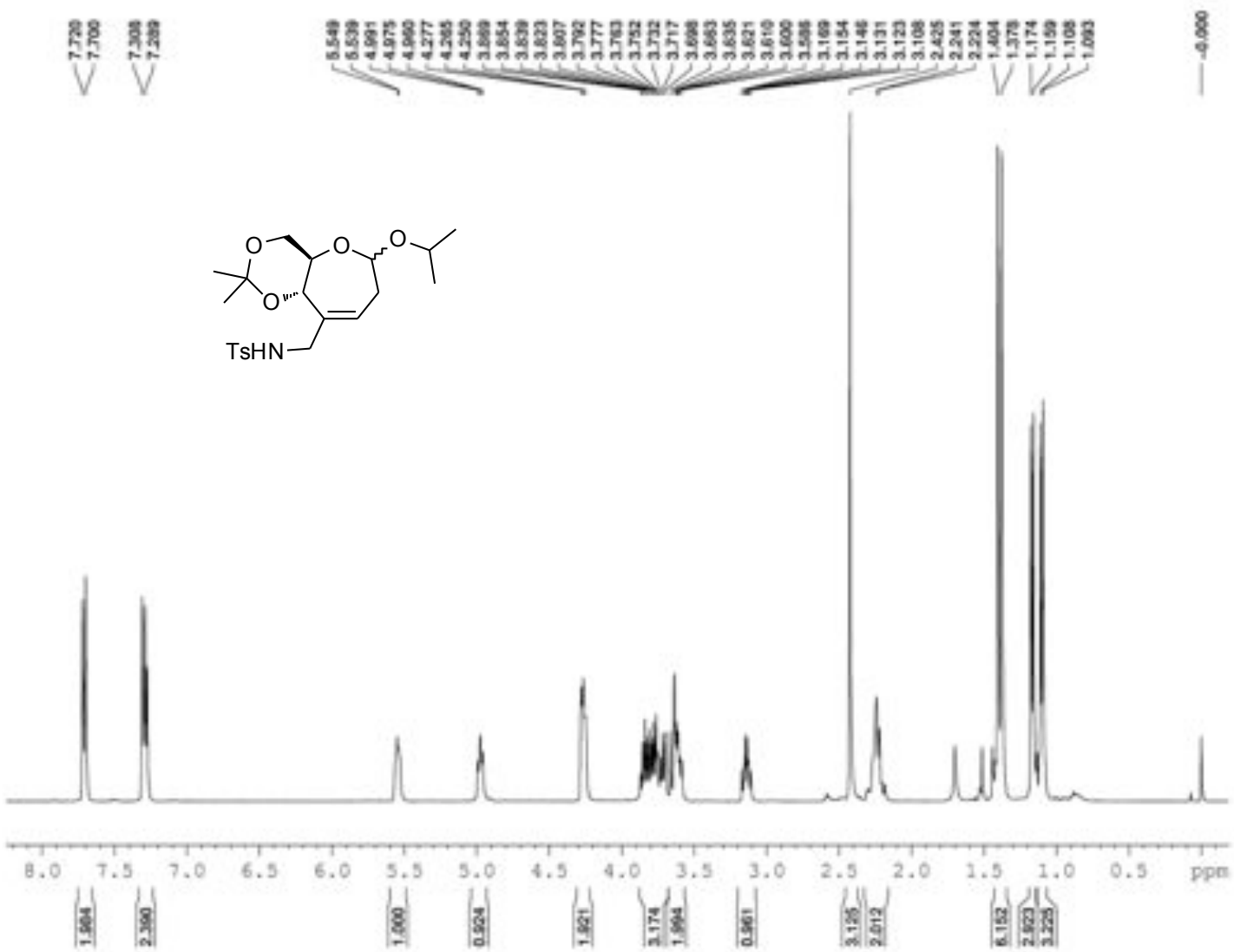
124.18
123.84
101.89
98.72
98.41
73.98
73.72
70.75
68.29
67.58
63.13
62.36
49.65
47.54
35.48
33.02
31.52
28.52
21.45
19.19
18.96
18.71
13.79
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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7.700
7.308
7.289
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5.539
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4.975
4.960
4.277
4.265
4.250
3.869
3.854
3.839
3.823
3.807
3.792
3.777
3.763
3.752
3.732
3.717
3.698
3.663
3.635
3.621
3.610
3.600
3.588
3.169
3.154
3.146
3.131
3.123
3.108
2.425
2.241
2.224
1.404
1.378
1.174
1.159
1.108
1.093
-0.000
TsHN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.984
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3.174
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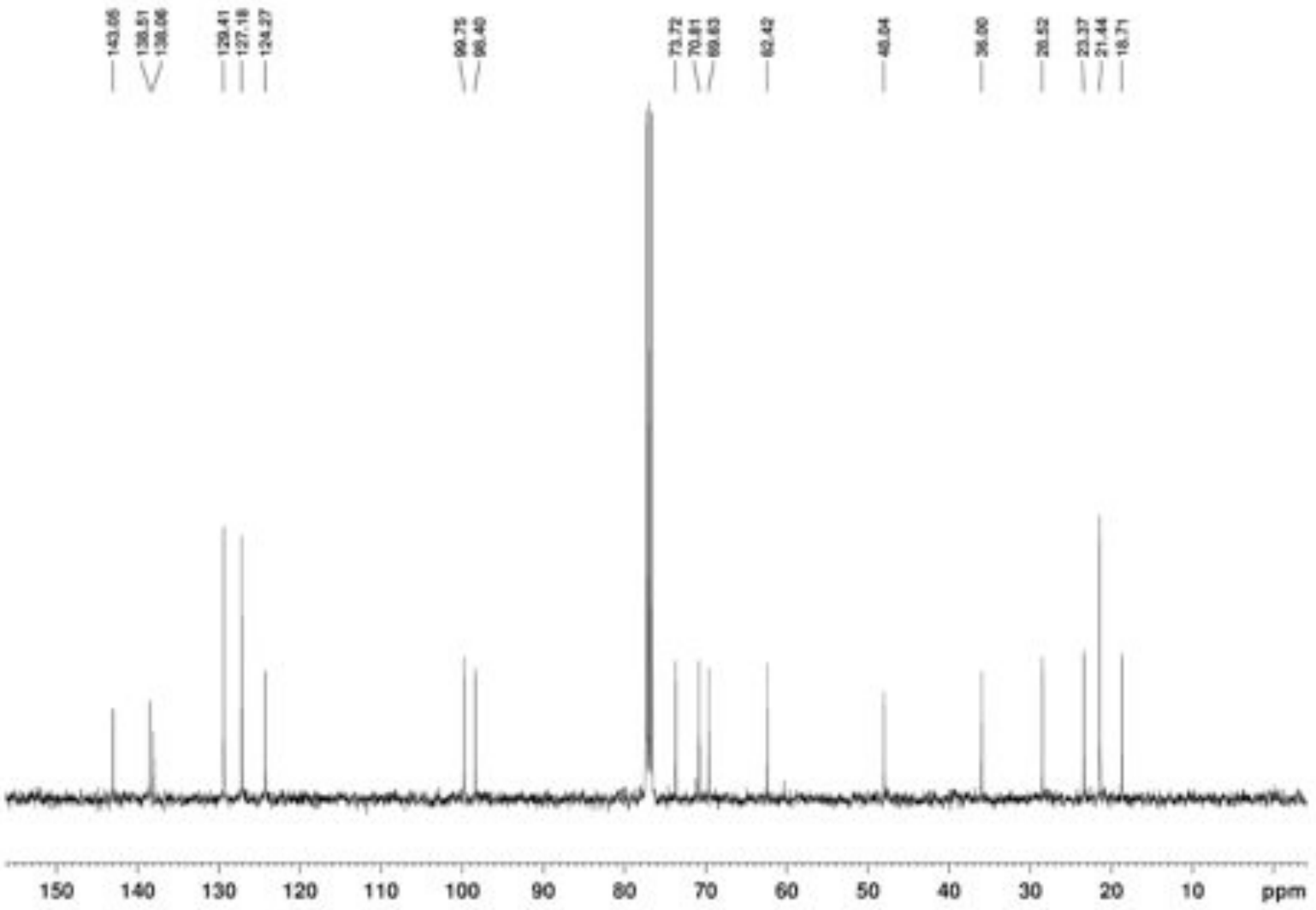
6.152
2.923
3.225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138.06
129.41
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124.27
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98.40
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70.81
69.63
62.42
49.04
36.00
28.52
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140
130
120
110
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80
70
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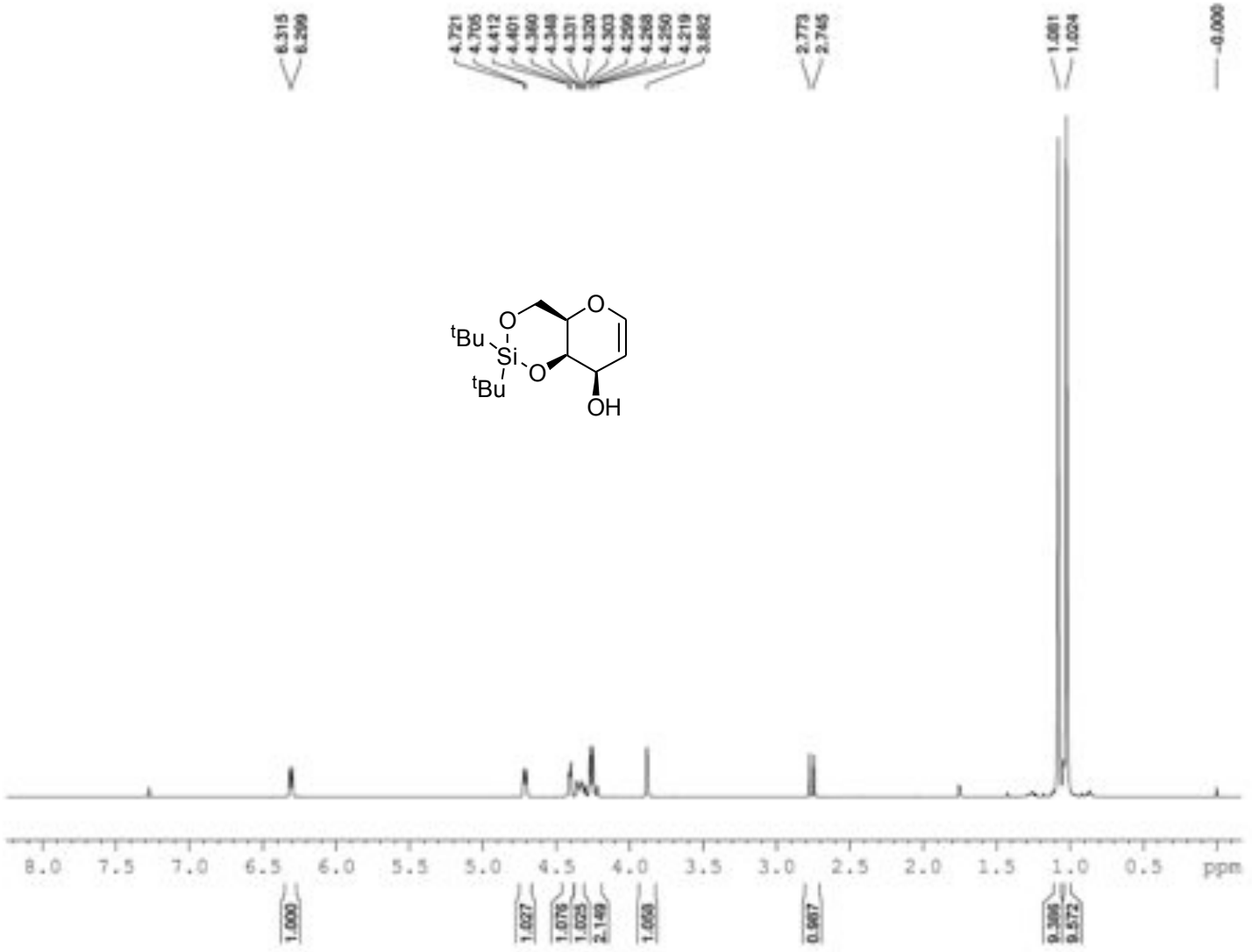
50
40
30
20
10
ppm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6.299
4.721
4.705
4.412
4.401
4.360
4.348
4.331
4.320
4.303
4.259
4.248
4.250
4.219
3.882
2.773
2.745
1.061
1.024
-0.000
tBu
Si
O
tBu
O
O
OH
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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1.025
2.149
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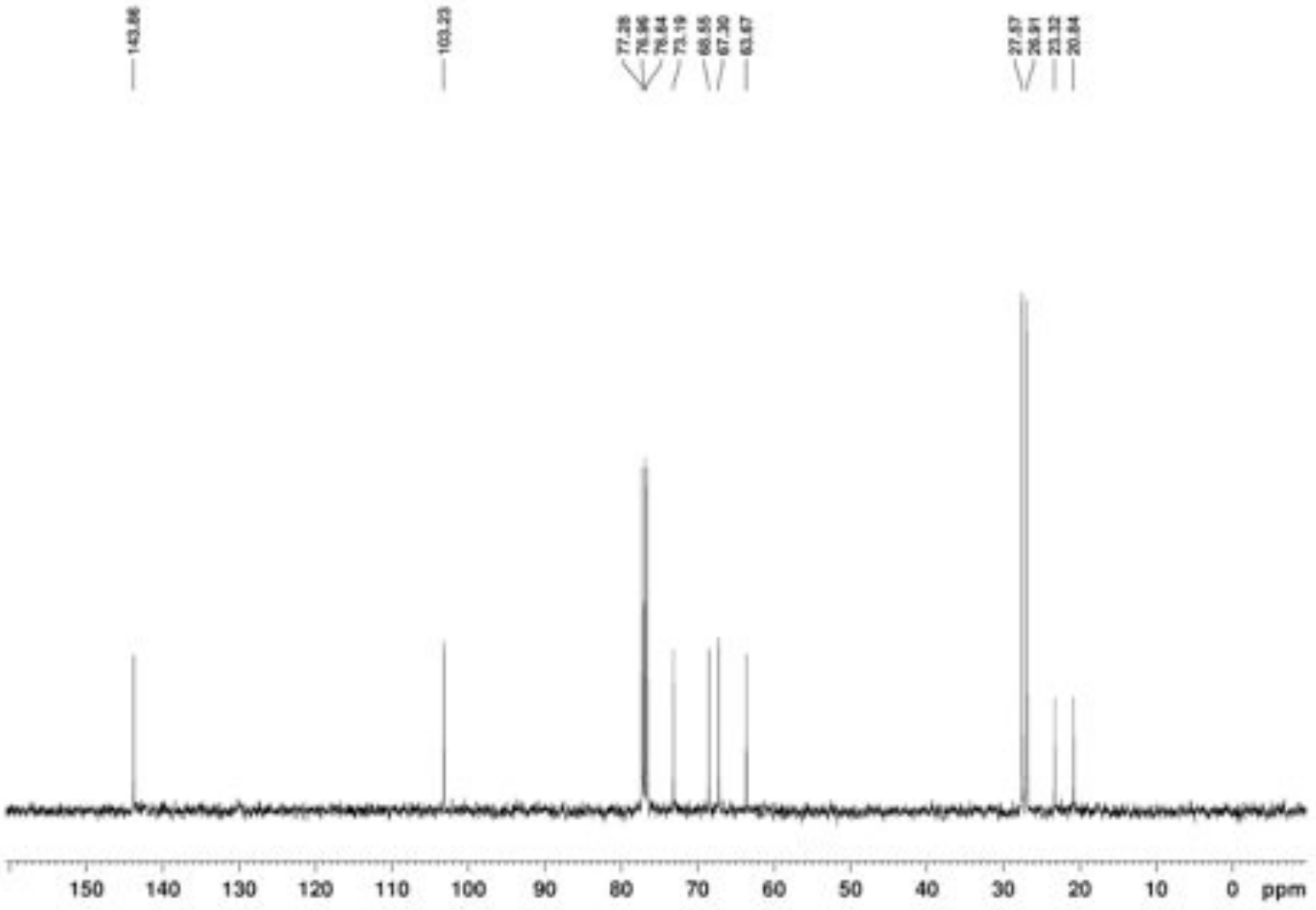
9.386
9.572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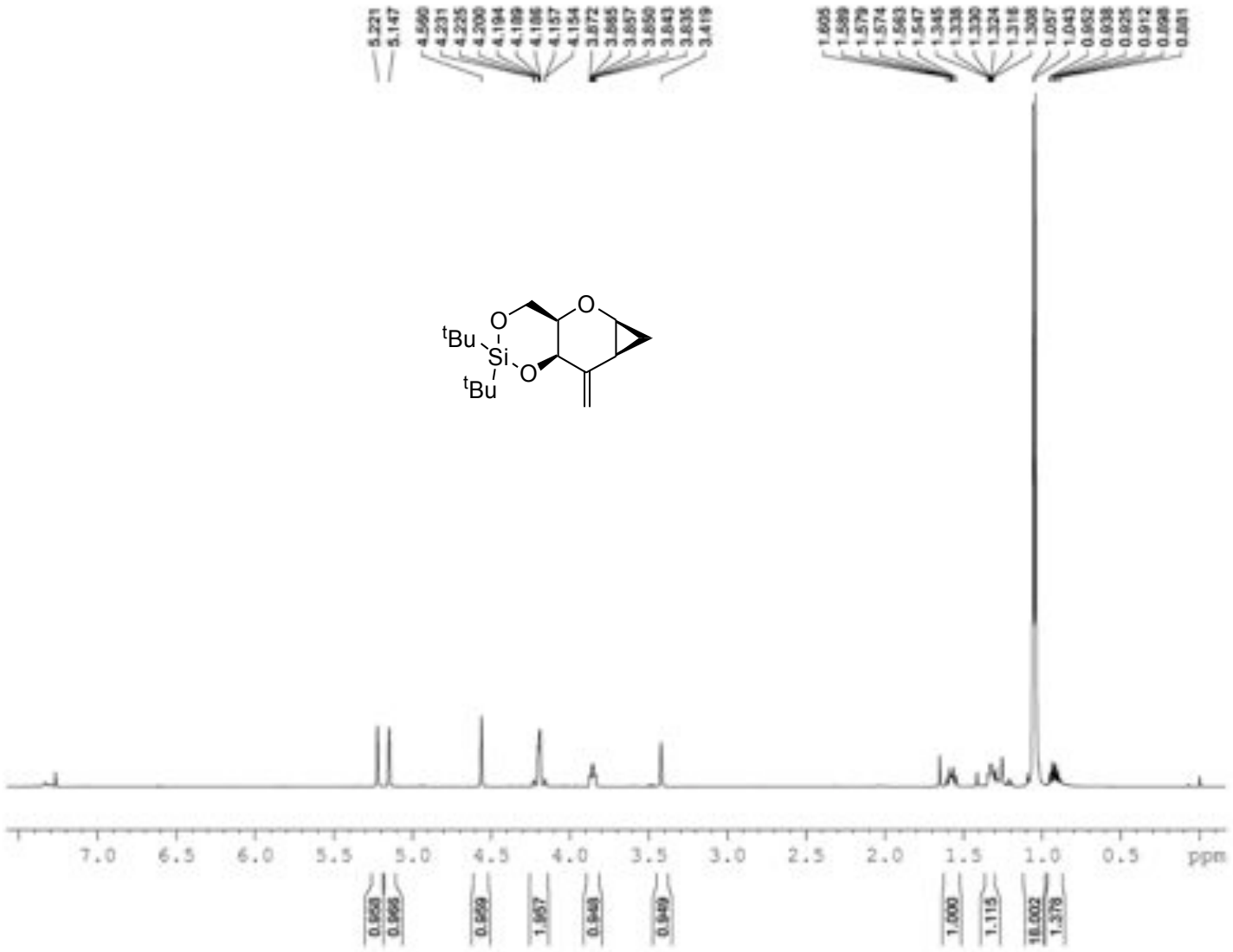
103.23
77.28
76.96
76.64
73.19
68.55
67.30
63.67
27.57
26.91
23.32
20.84
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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4.231
4.225
4.200
4.194
4.189
4.186
4.157
4.154
3.872
3.865
3.857
3.850
3.843
3.835
3.419
1.605
1.589
1.579
1.574
1.563
1.547
1.345
1.338
1.330
1.324
1.316
1.308
1.057
1.043
0.952
0.938
0.925
0.912
0.898
0.881
O
O
tBu
Si
O
tBu
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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0.966
0.959
1.957
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0.949
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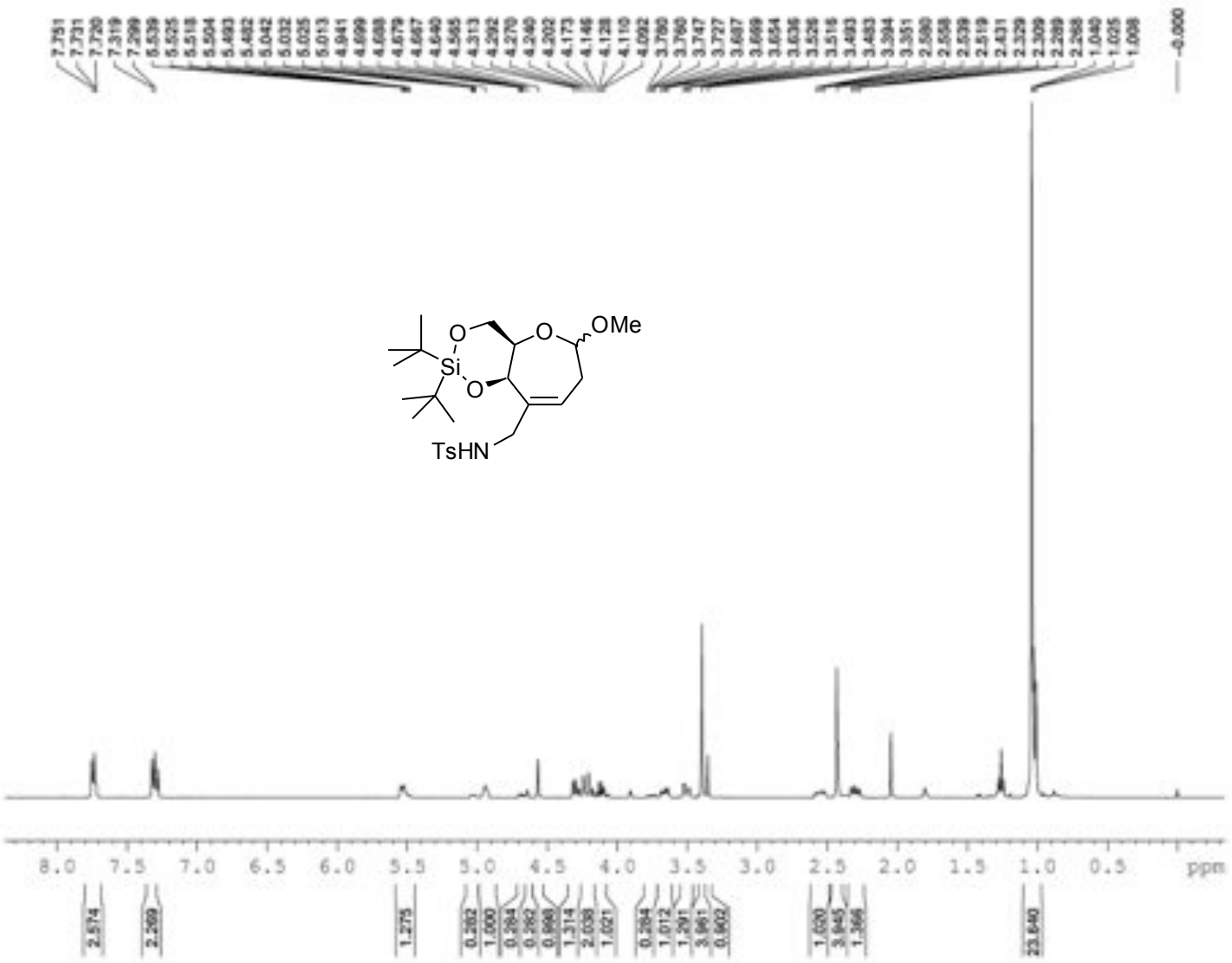
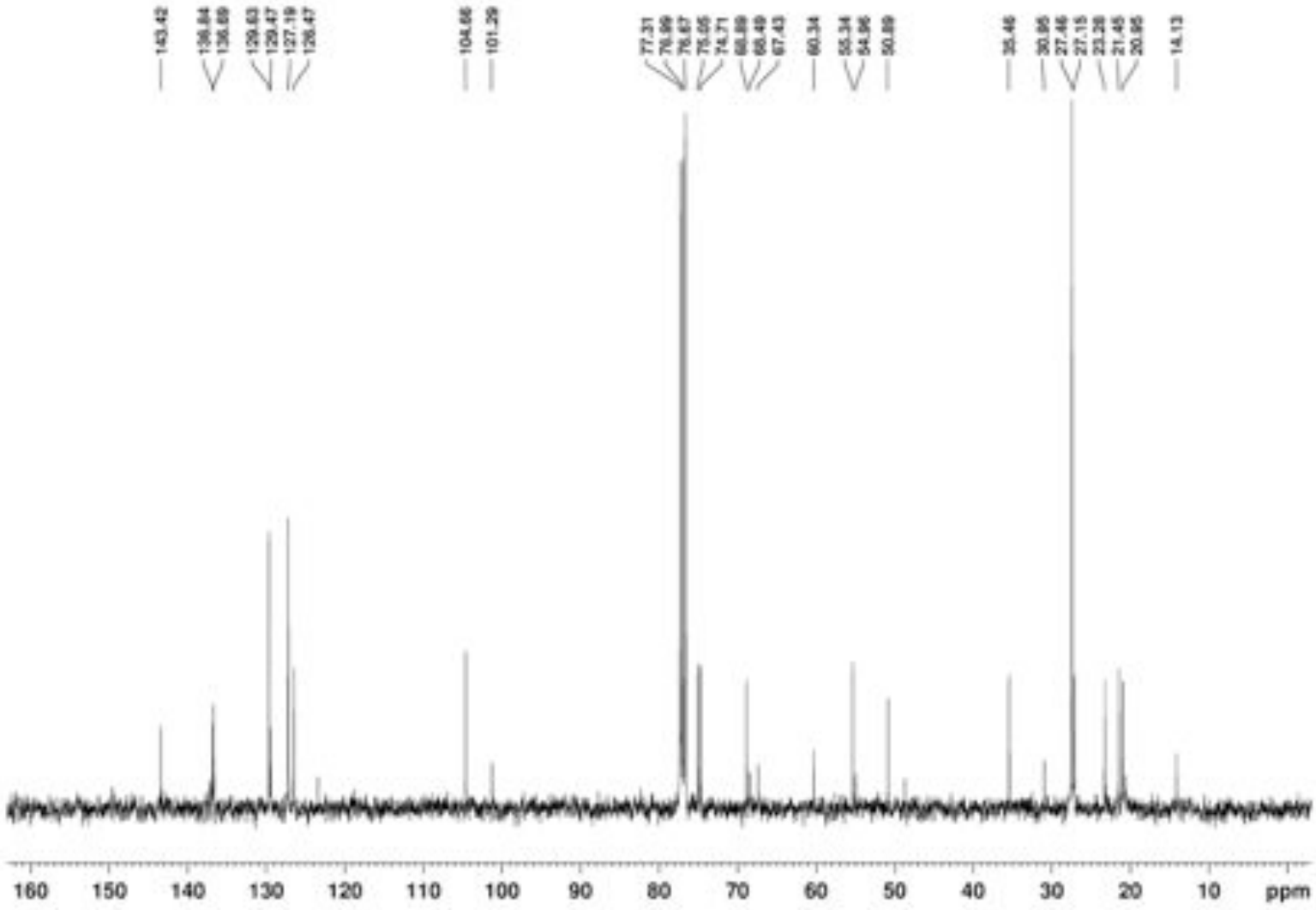
18.002
1.376


OMe
O
O
Si
O
TsHN
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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127.19
126.47
104.66
101.29
77.31
76.99
76.67
75.05
74.71
68.89
68.49
67.43
60.34
55.34
54.96
50.89
35.46
30.95
27.46
27.15
23.28
21.45
20.95
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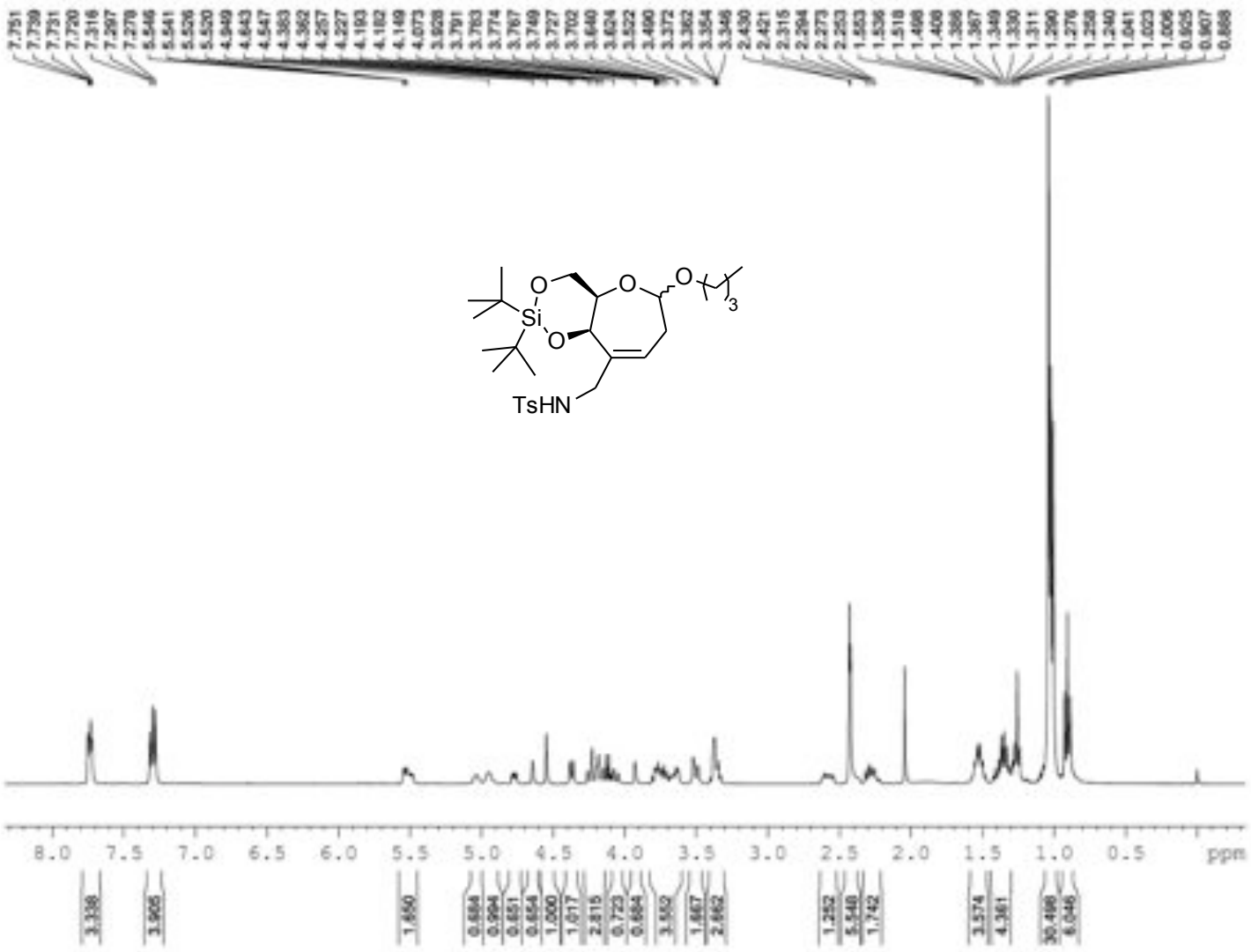
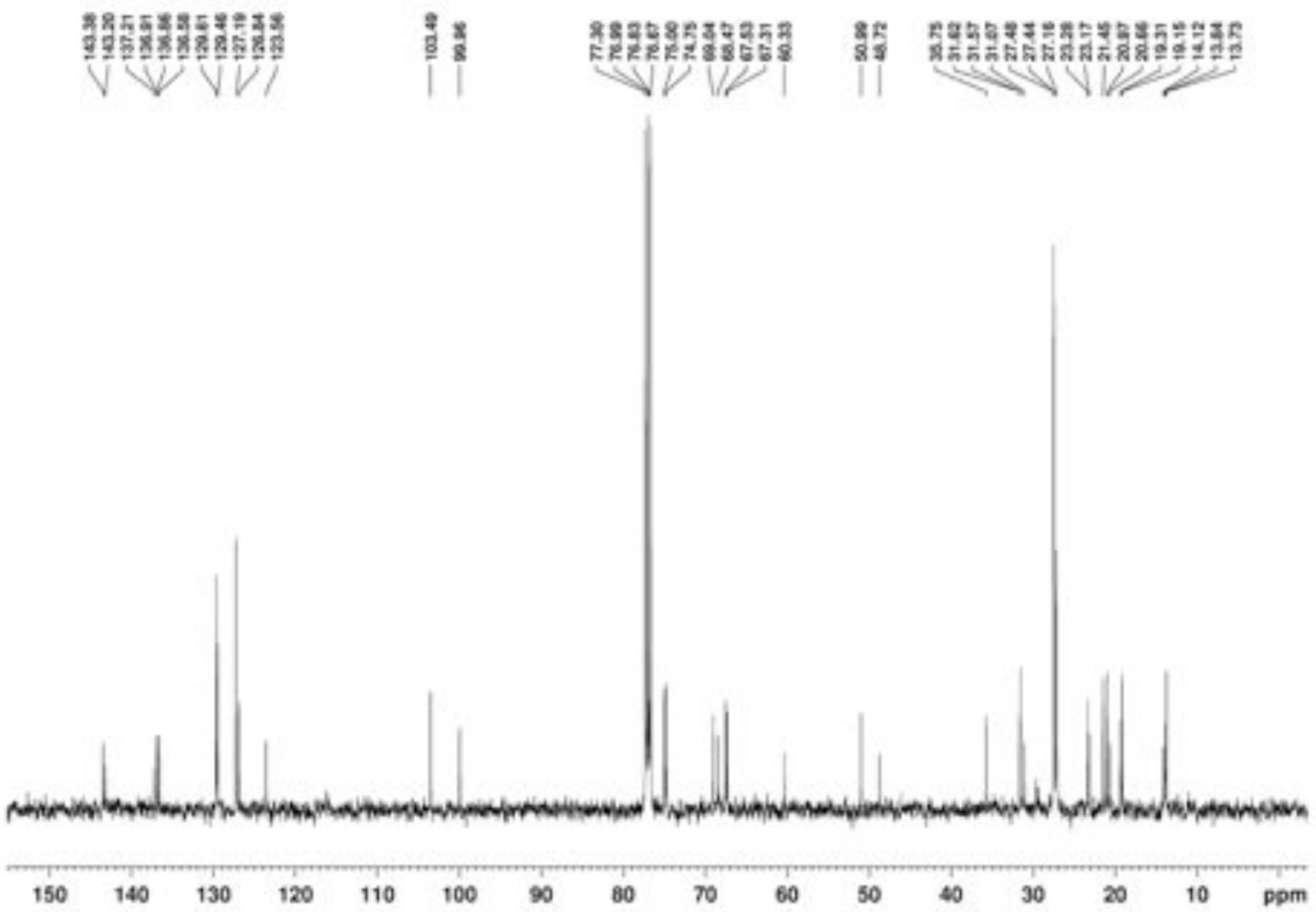
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


TsHN
Si
O
ppm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136.58
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129.46
127.19
126.84
123.56
103.49
99.96
77.30
76.99
76.83
76.67
75.00
74.75
69.64
68.47
67.53
67.31
60.33
50.99
48.72
35.75
31.62
31.57
31.07
27.48
27.44
27.16
23.28
23.17
21.45
20.97
20.66
19.31
19.15
14.12
13.84
13.73
150
140
130
120
110
100
90
80
70
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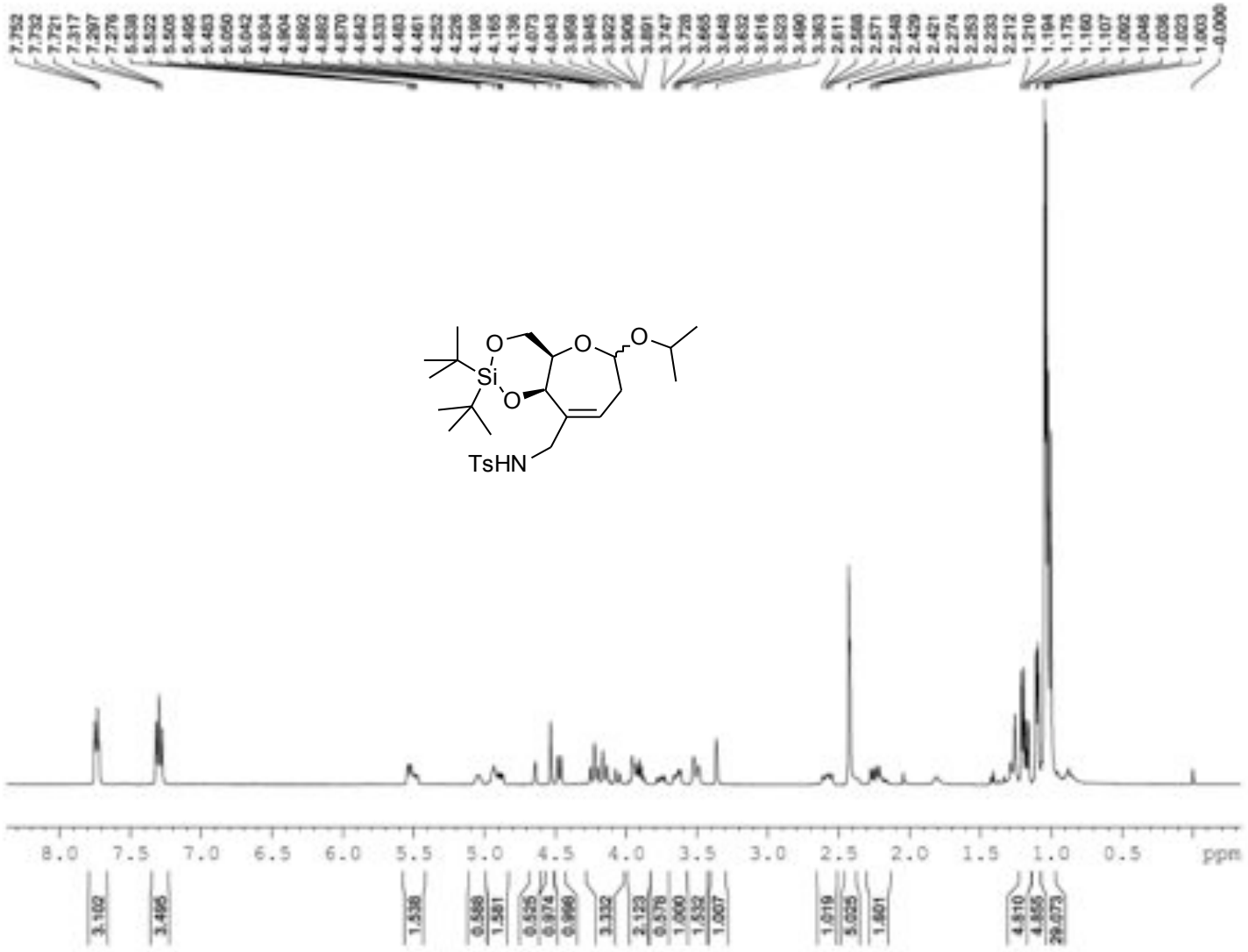
30
20
10
ppm


TsHN
Si
O
O
O
O
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7.0
6.5
6.0
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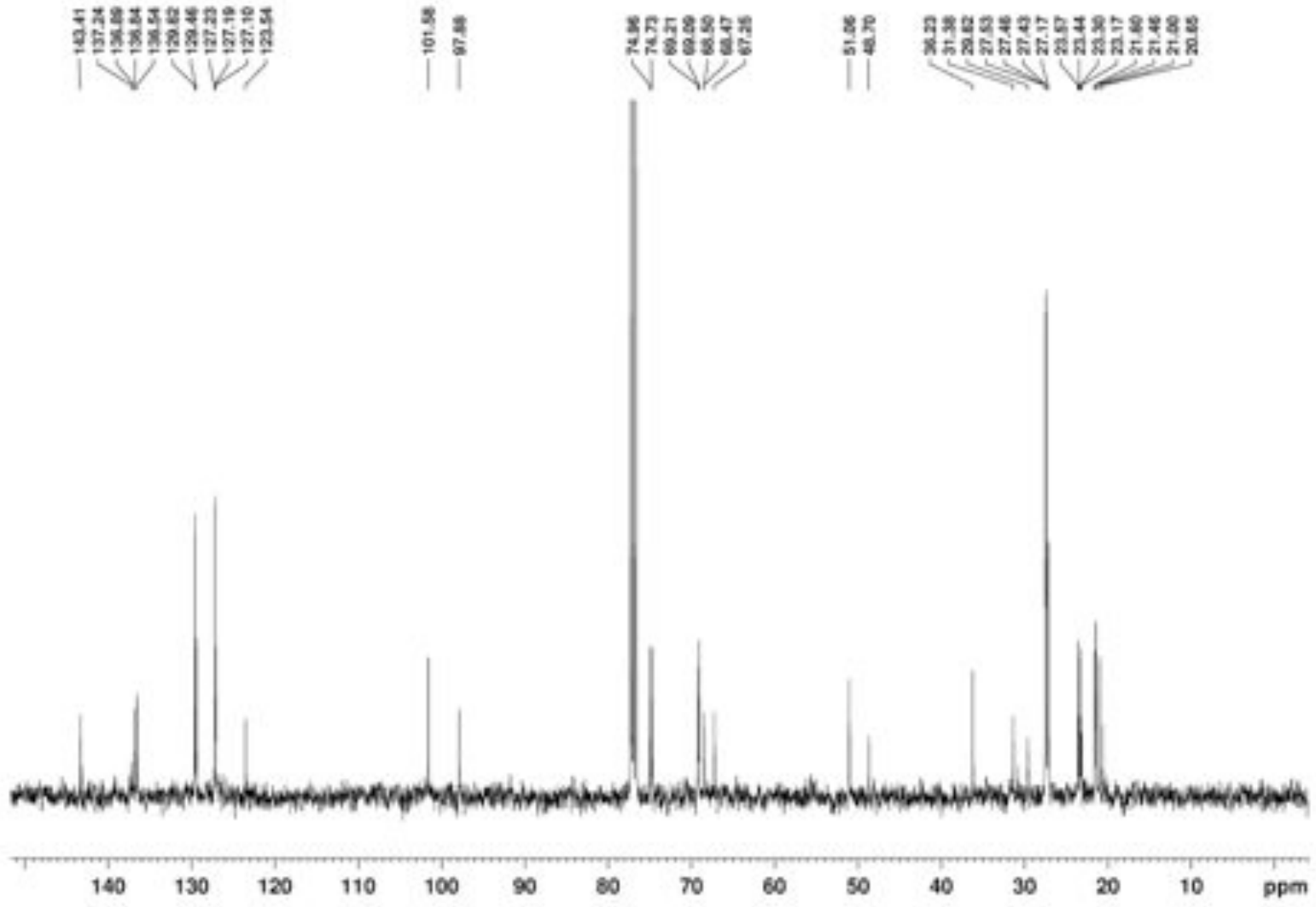
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm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129.62
129.46
127.23
127.19
127.10
123.54
101.58
97.88
74.96
74.73
69.21
69.09
68.50
68.47
67.25
51.06
48.70
36.23
31.38
29.82
27.53
27.46
27.43
27.17
23.57
23.44
23.30
23.17
21.60
21.46
21.00
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140
130
120
110
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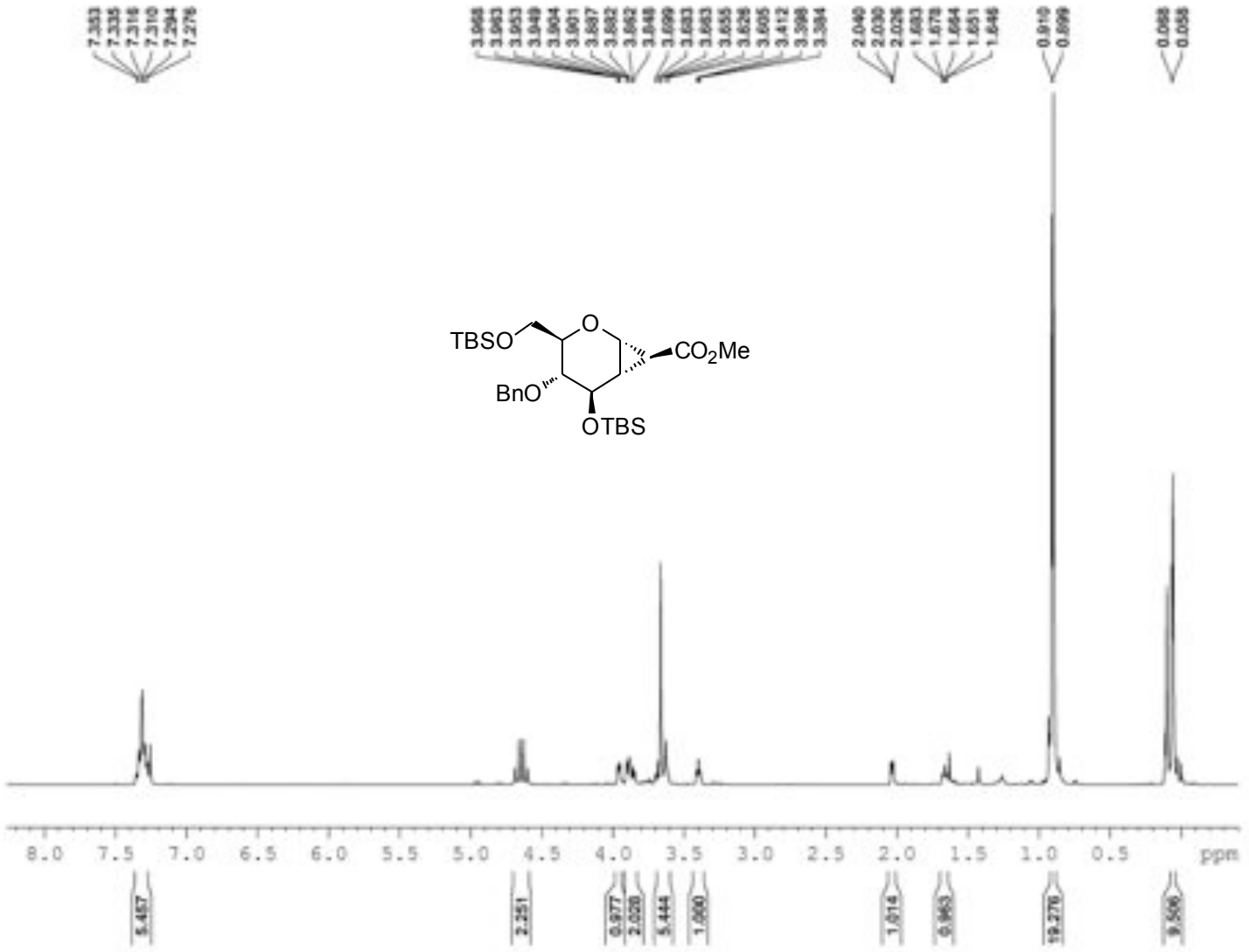
90
80
70
60
50
40
30
20
10
ppm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3.949
3.904
3.901
3.887
3.882
3.862
3.848
3.699
3.683
3.663
3.655
3.626
3.605
3.412
3.398
3.384
2.040
2.030
2.026
1.683
1.678
1.664
1.651
1.646
0.910
0.899
0.068
0.058
TBSO
O
CO2Me
BnO
OTBS
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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1.000
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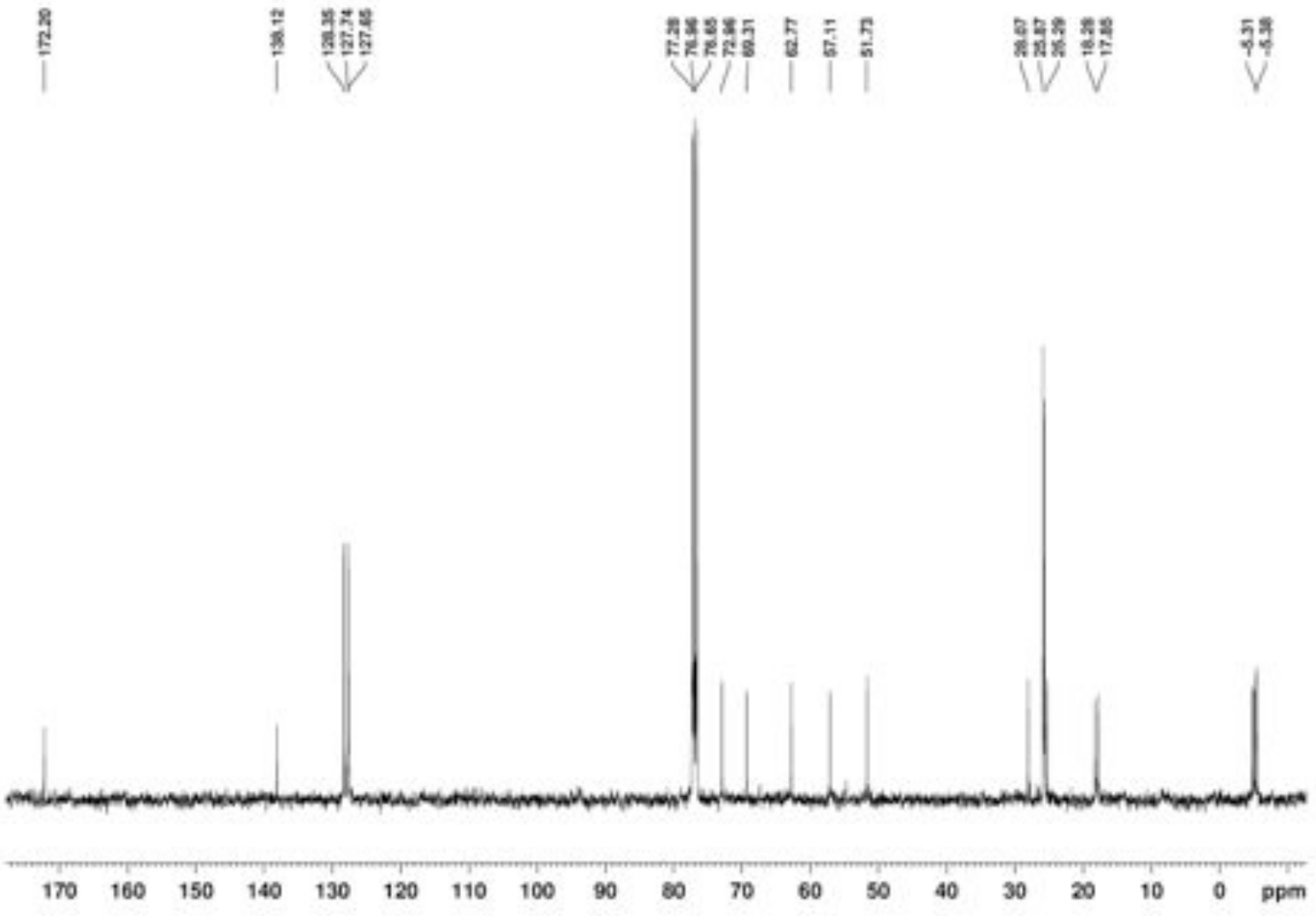
19.276
9.506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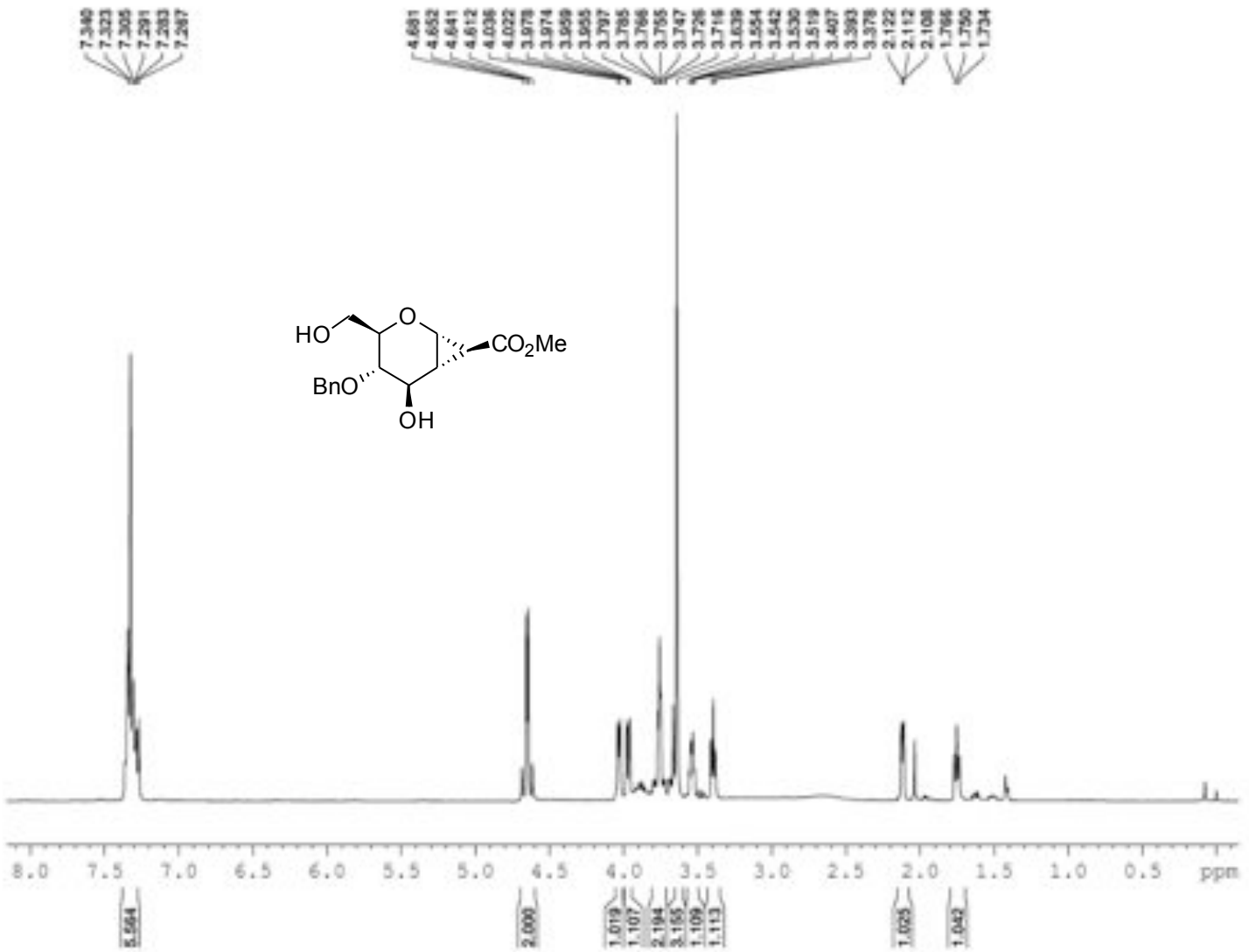
127.74
127.65
77.28
76.86
76.65
72.96
69.31
62.77
57.11
51.73
28.67
25.87
25.29
18.28
17.85
-5.31
-5.38
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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4.652
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4.022
3.978
3.974
3.959
3.955
3.797
3.785
3.766
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3.726
3.716
3.639
3.554
3.542
3.530
3.519
3.407
3.393
3.378
2.122
2.112
2.108
1.766
1.750
1.734
HO
O
CO2Me
BnO
OH
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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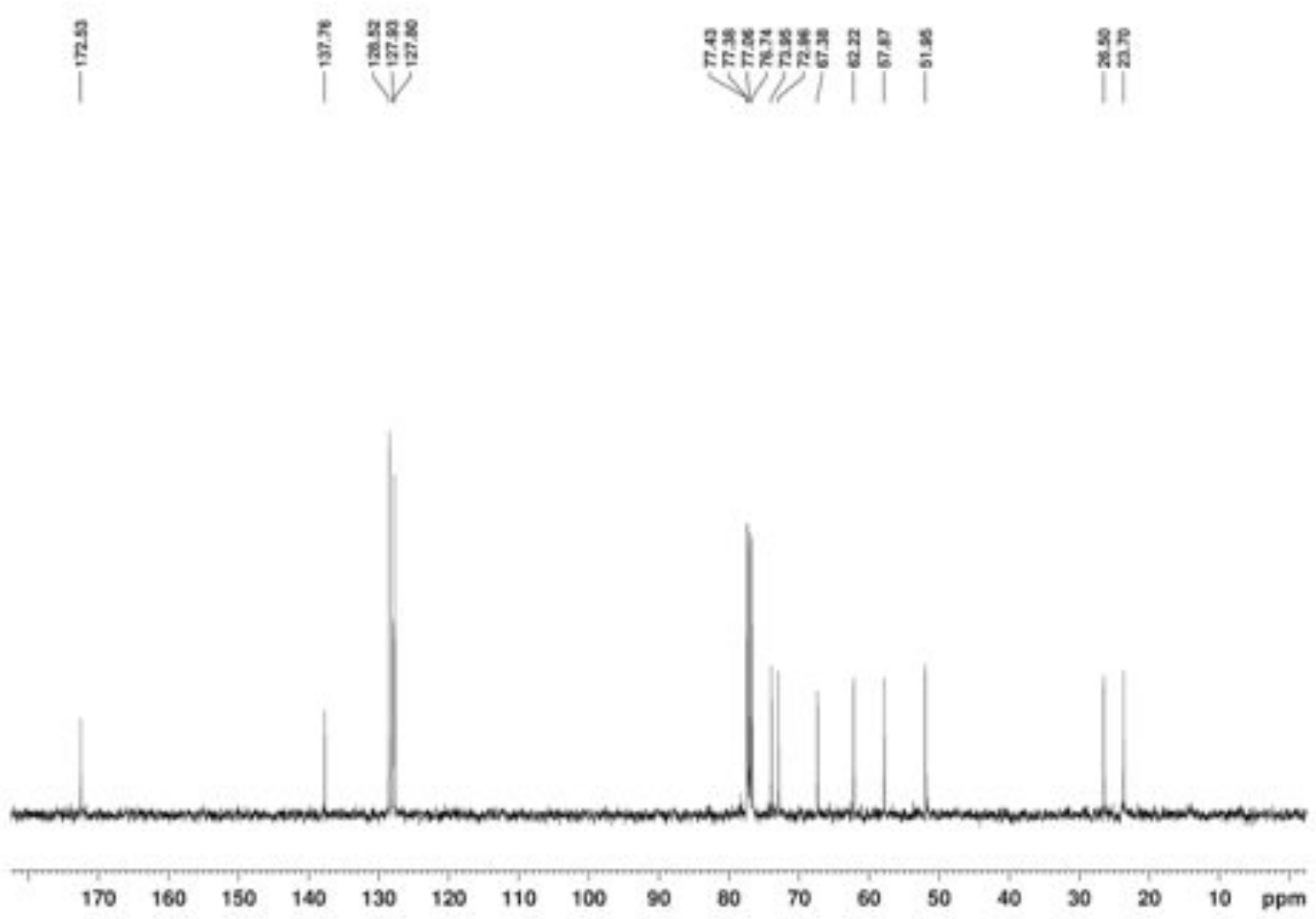
1.042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77.06
76.74
73.95
72.86
67.38
62.22
57.87
51.95
26.50
23.70
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150
140
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120
110
100
90
80
70
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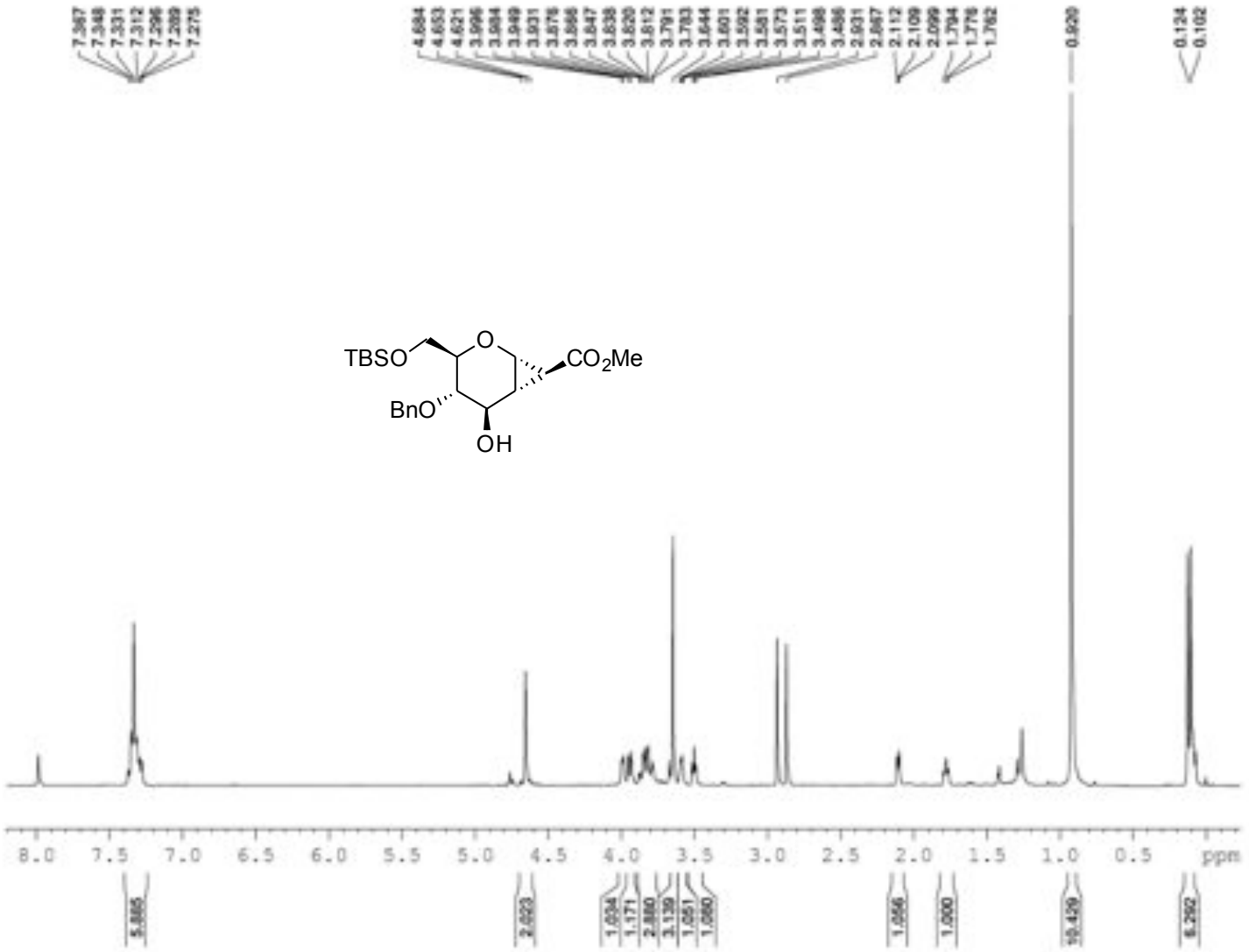
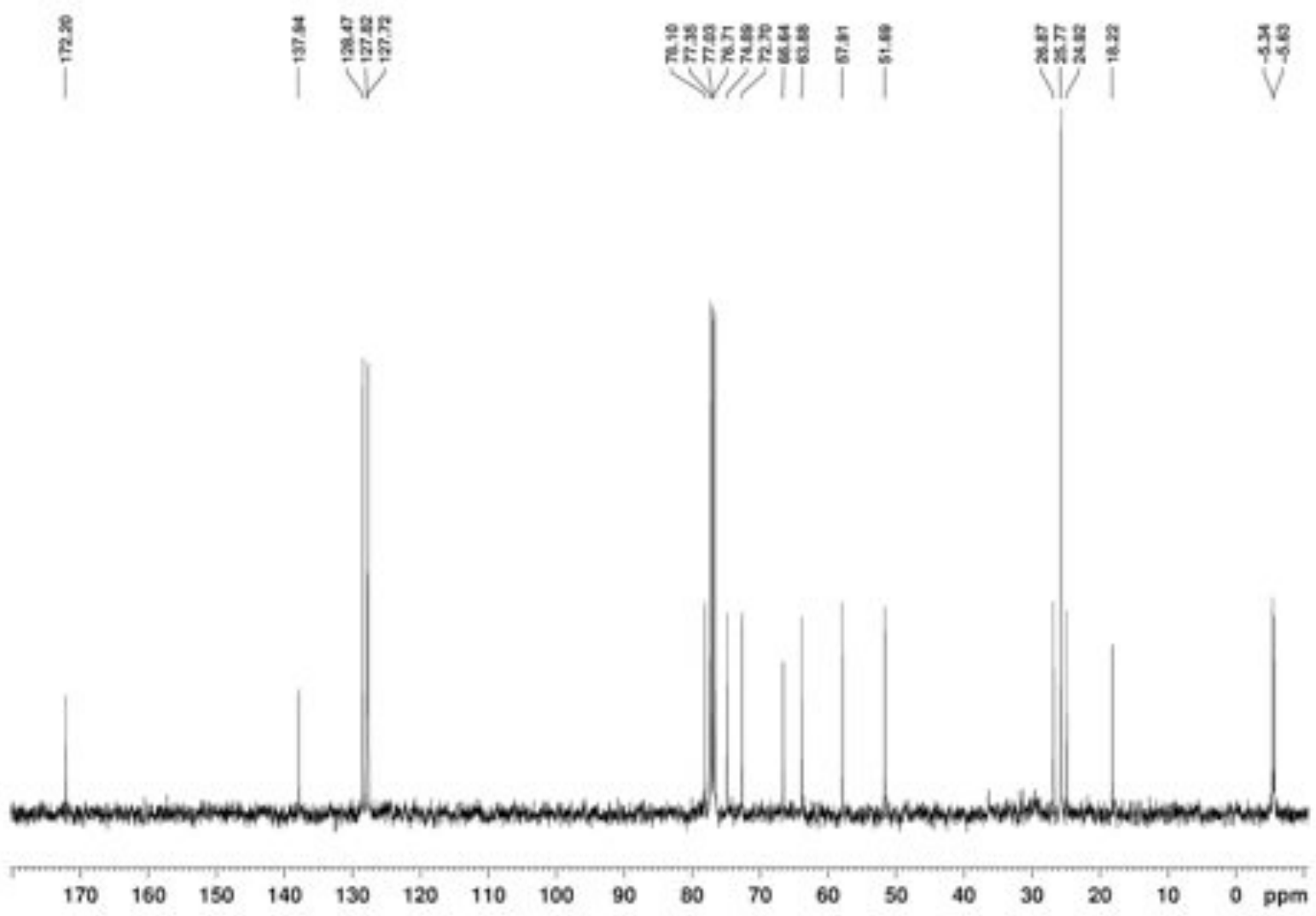
50
40
30
20
10
ppm


TBSO
O
CO2Me
BnO
OH
ppm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127.72
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77.03
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74.89
72.70
66.64
63.88
57.81
51.89
26.87
25.77
24.82
18.22
-5.34
-5.63
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140
130
120
110
100
90
80
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60
50
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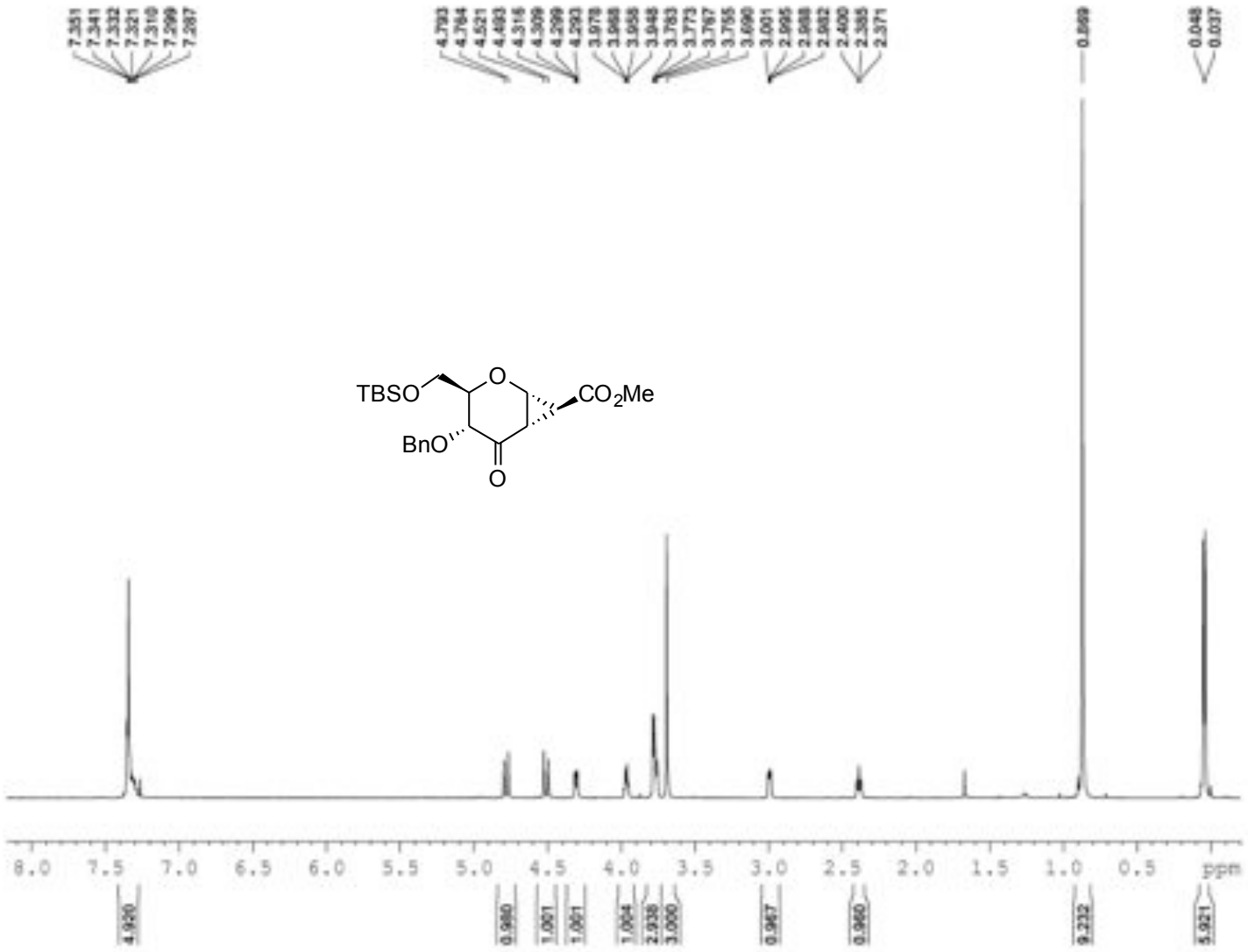
30
20
10
0
ppm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4.493
4.316
4.309
4.299
4.293
3.978
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3.948
3.783
3.773
3.767
3.755
3.690
3.031
2.995
2.988
2.982
2.400
2.385
2.371
0.869
0.048
0.037
TBSO
O
CO2Me
BnO
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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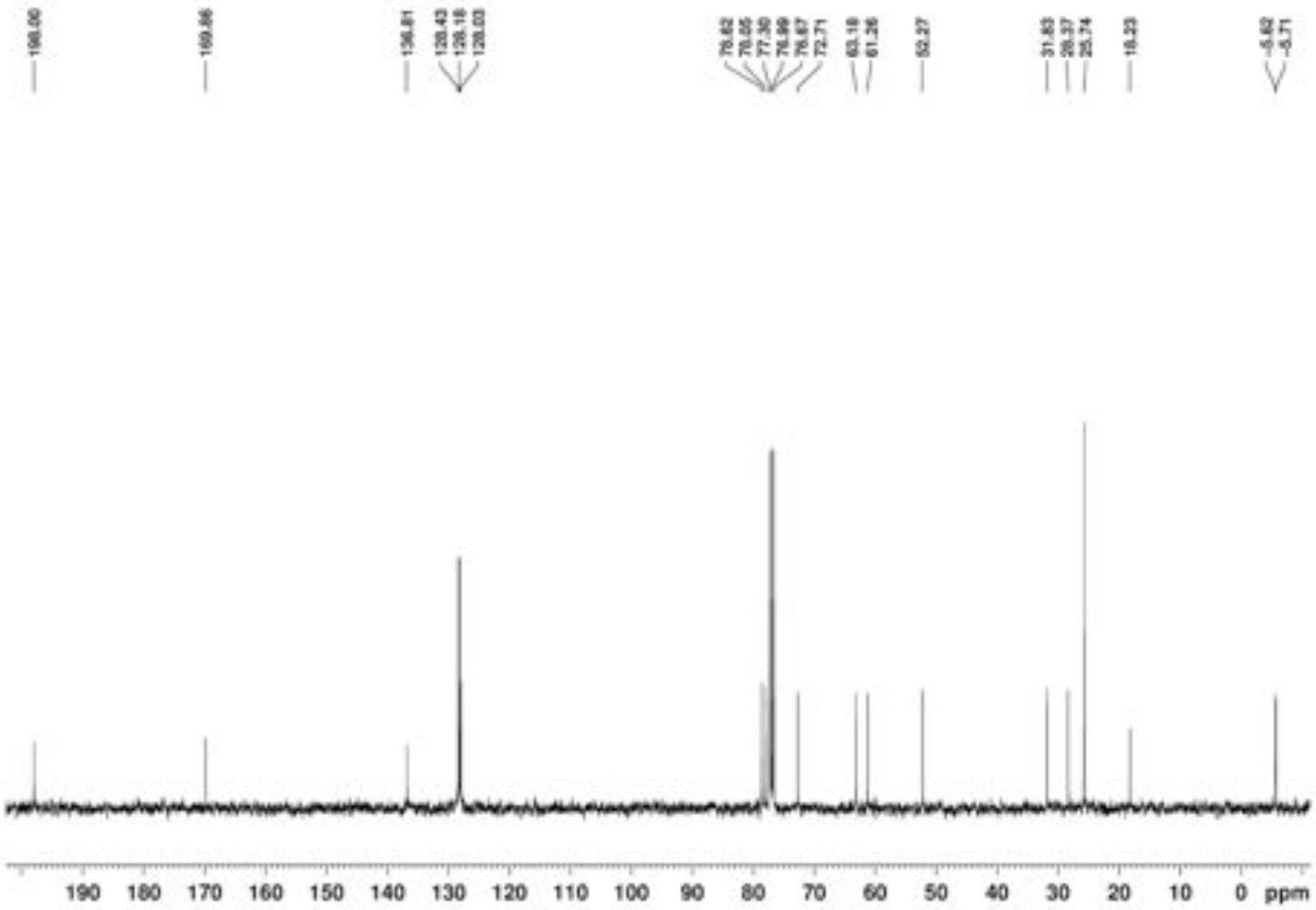
1.061
1.004
2.038
3.000
0.967
0.960
9.232
5.921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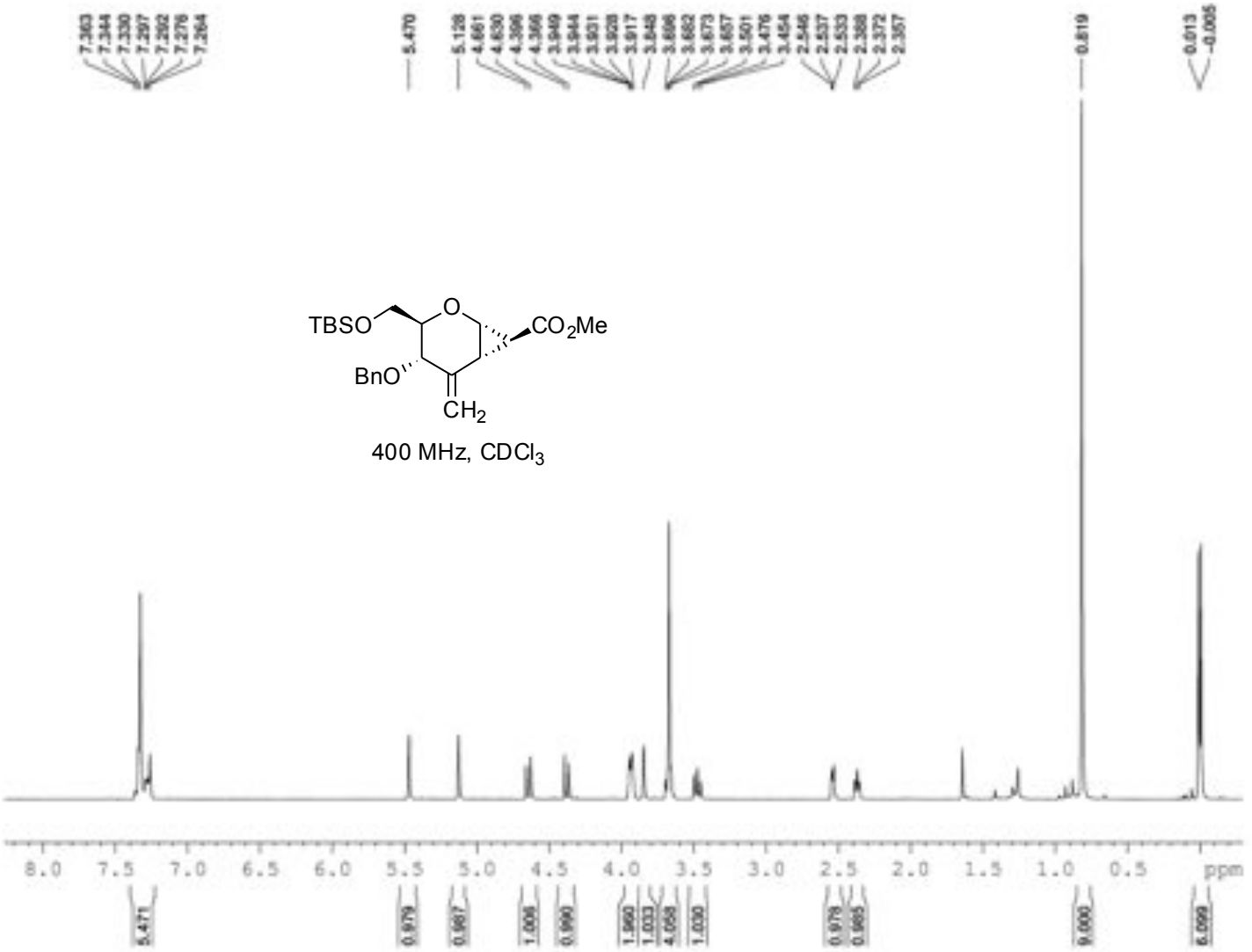
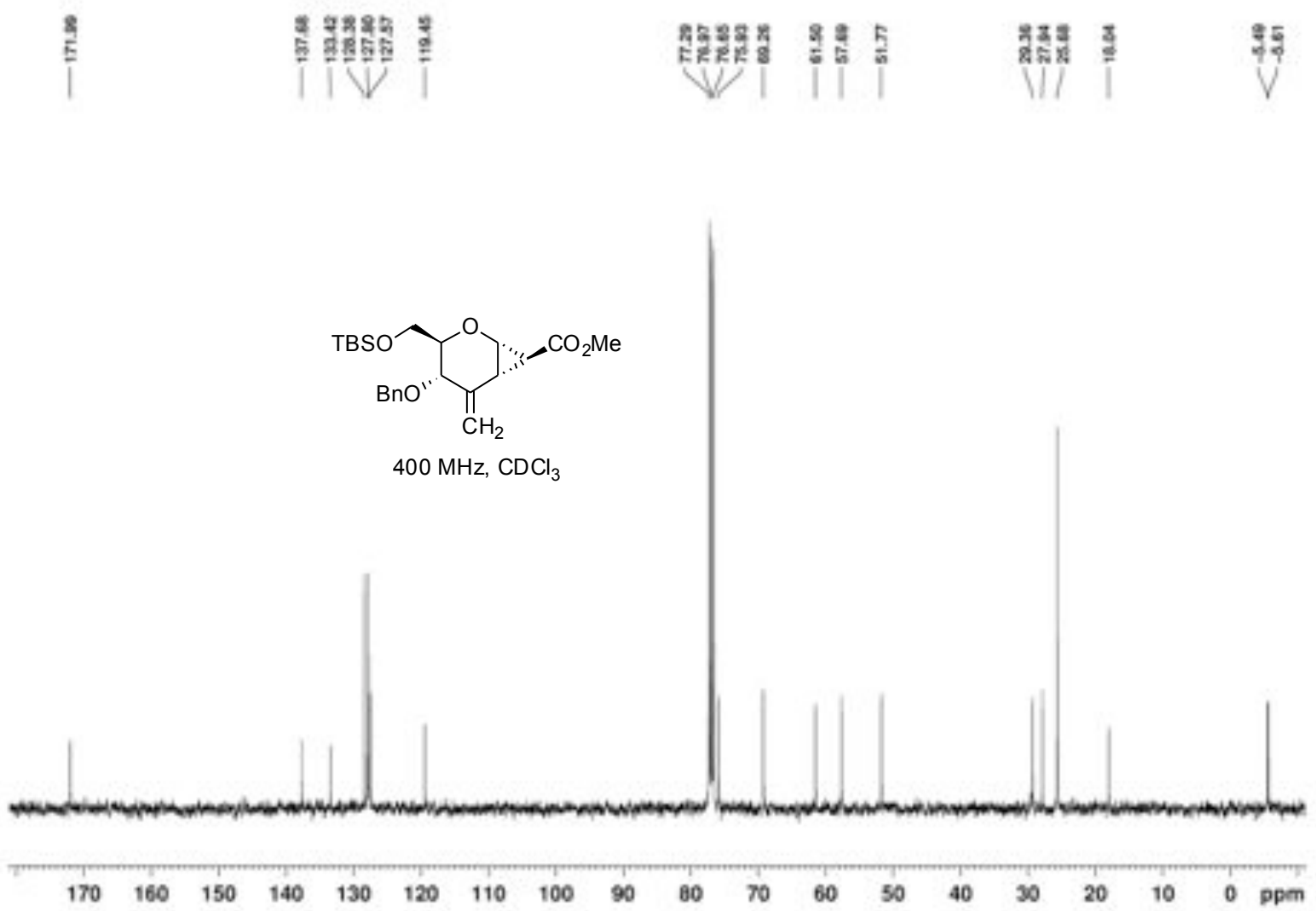
169.86
136.81
128.43
128.18
128.03
70.82
70.65
77.30
76.99
76.67
72.71
63.18
61.26
52.27
31.83
28.37
25.74
18.23
-5.82
-5.71
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



400 MHz, $CDCl_3$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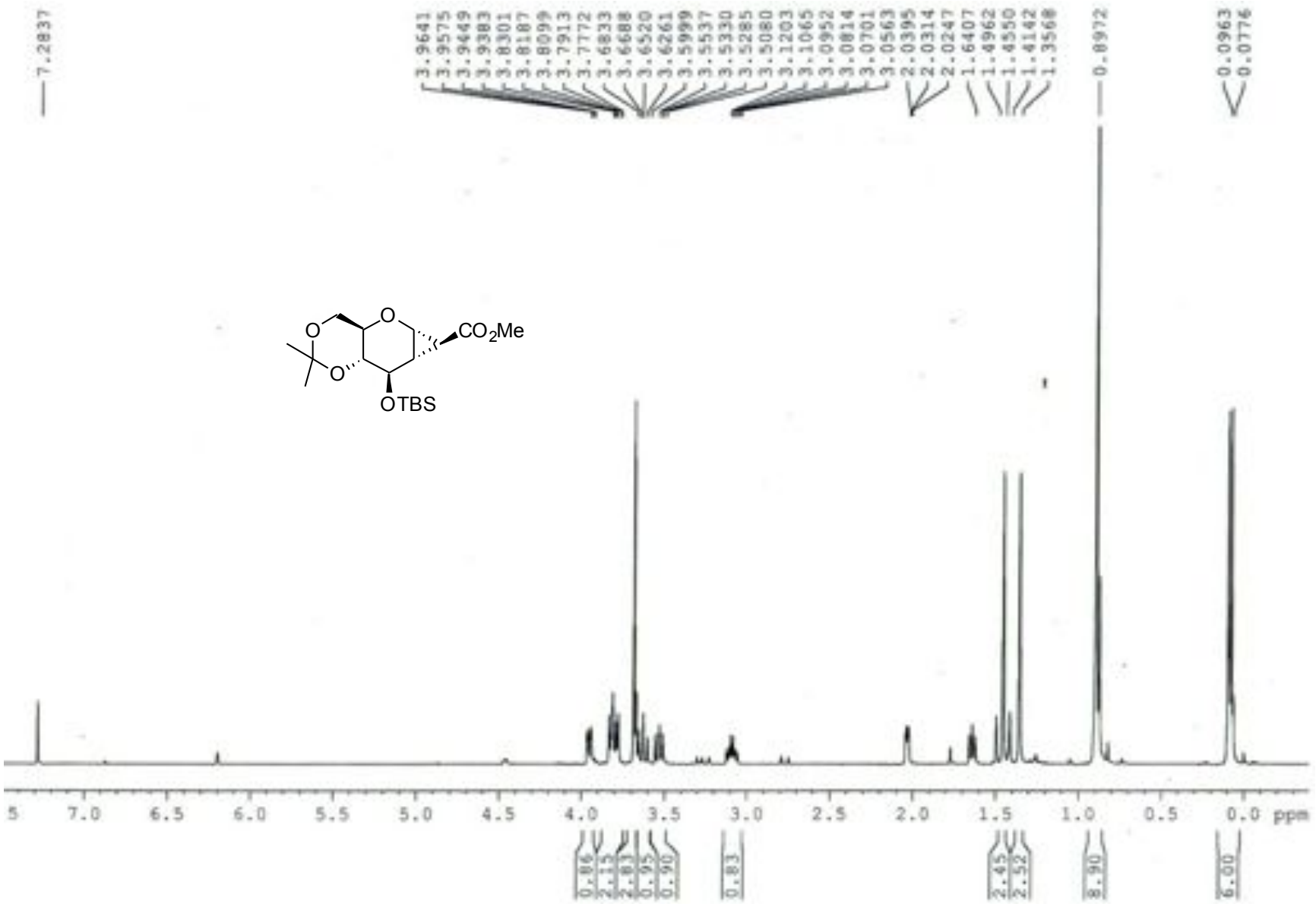
133.42
128.38
127.80
127.57
119.45
77.29
76.97
76.65
75.93
69.26
61.50
57.69
51.77
29.36
27.94
25.68
18.04
-5.49
-5.61
TBSO
O
CO2Me
BnO
CH2
400 MHz, CDCl3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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3.9575
3.9449
3.9383
3.8301
3.8187
3.8099
3.7913
3.7772
3.6833
3.6688
3.6520
3.6261
3.5999
3.5537
3.5330
3.5285
3.5080
3.1203
3.1065
3.0952
3.0814
3.0701
3.0563
2.0395
2.0314
2.0247
1.6407
1.4962
1.4550
1.4142
1.3568
0.8972
0.0963
0.0776
CO2Me
OTBS
ppm
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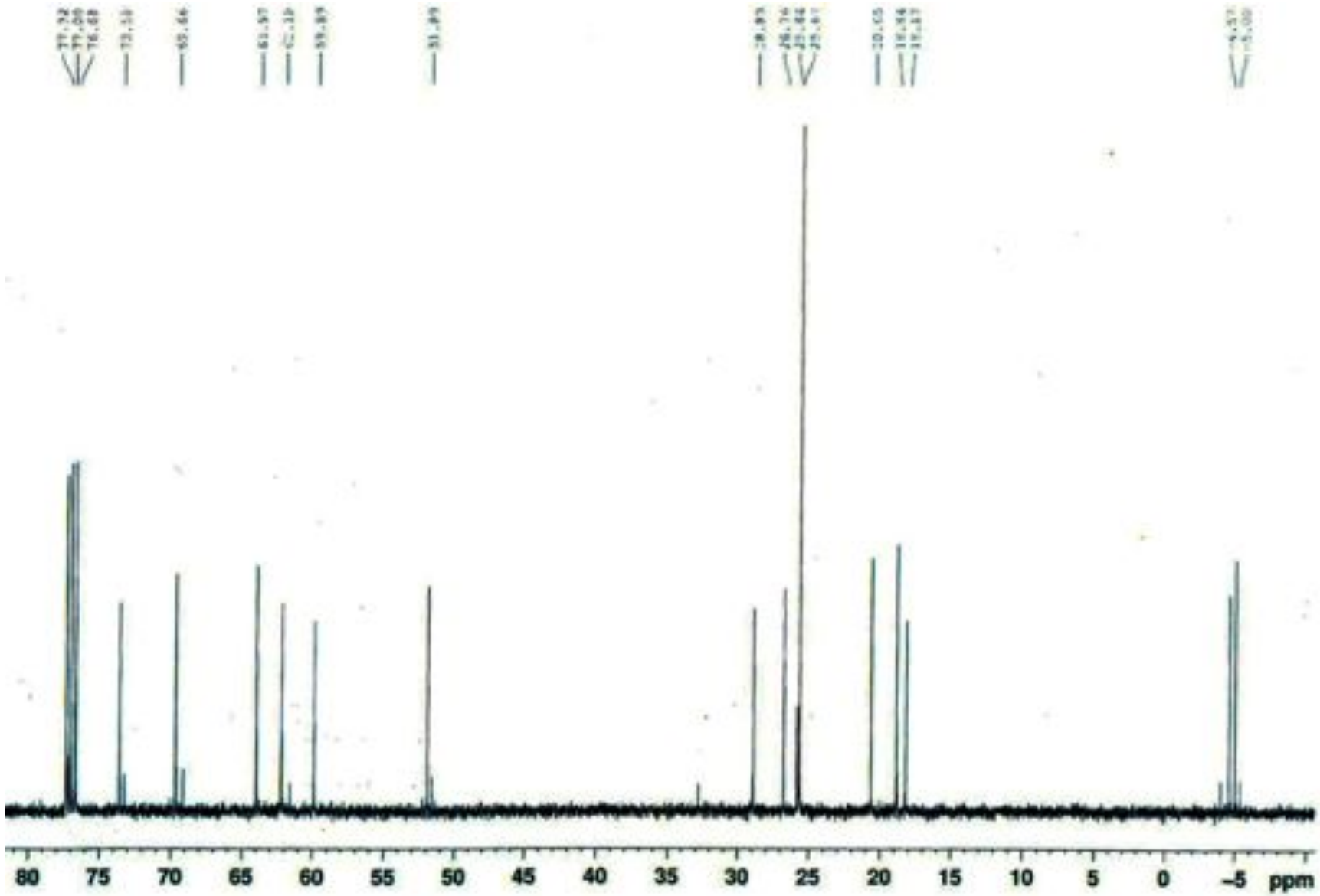
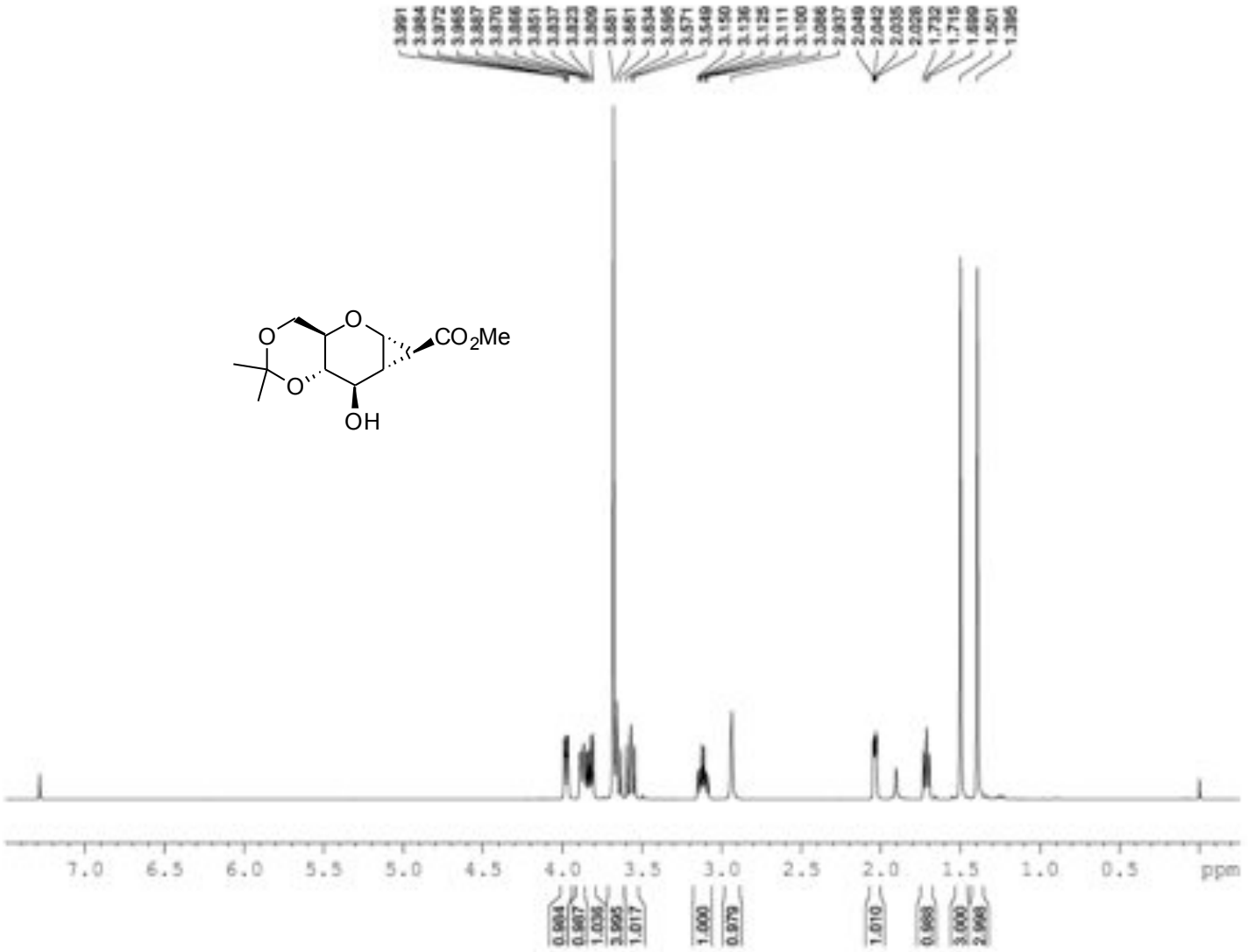
2.15
2.83
0.95
0.90
0.83
2.45
2.52
8.90
6.00


77.32
77.00
76.68
73.10
65.66
61.57
60.19
59.85
51.89
28.85
26.74
25.84
25.61
20.05
18.54
18.17
-4.57
-5.00
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
ppm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3.984
3.972
3.965
3.887
3.870
3.866
3.851
3.837
3.823
3.809
3.681
3.661
3.634
3.595
3.571
3.549
3.150
3.136
3.125
3.111
3.100
3.086
2.937
2.049
2.042
2.035
2.028
1.732
1.715
1.699
1.501
1.395
O
O
O
CO2Me
OH
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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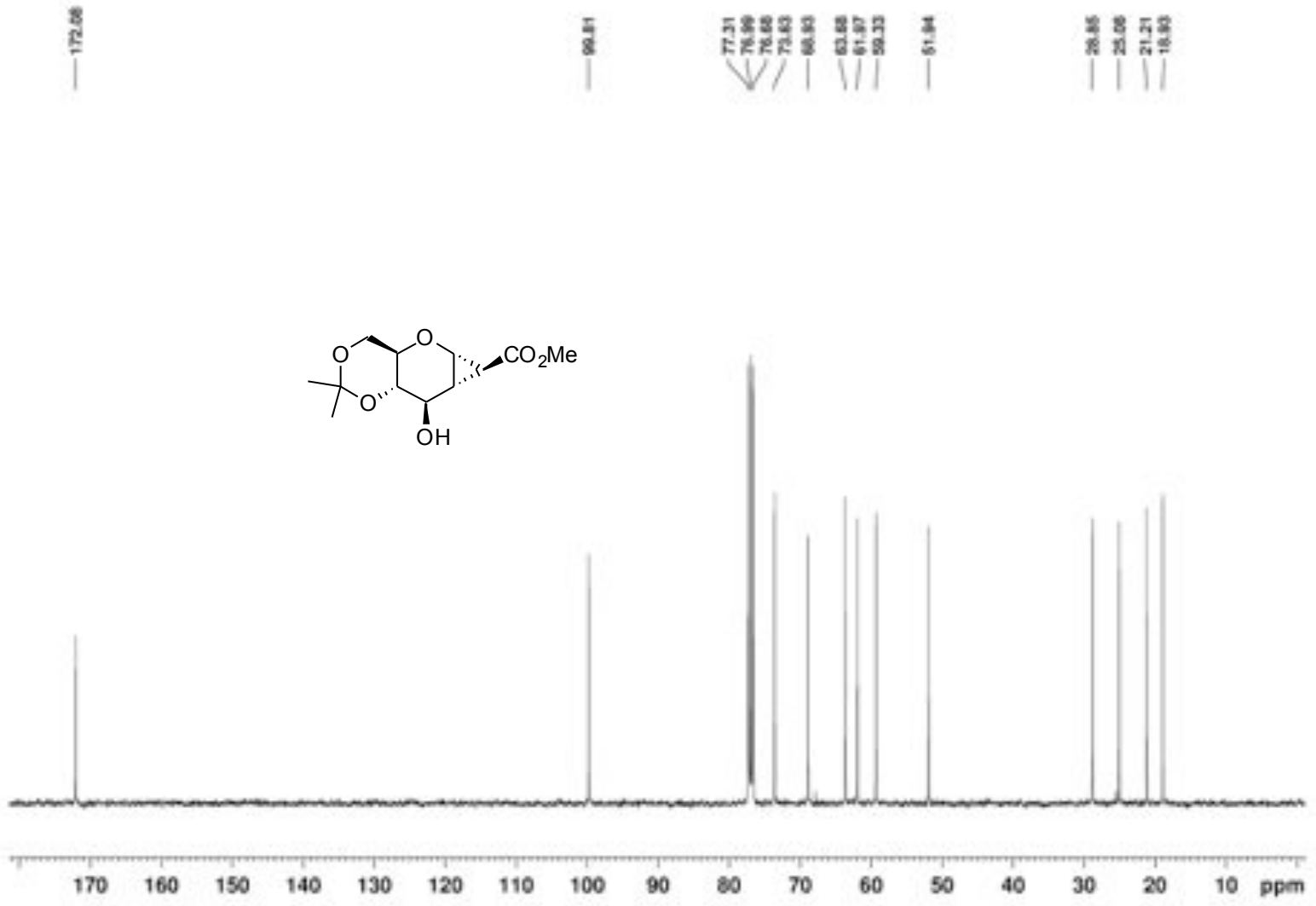
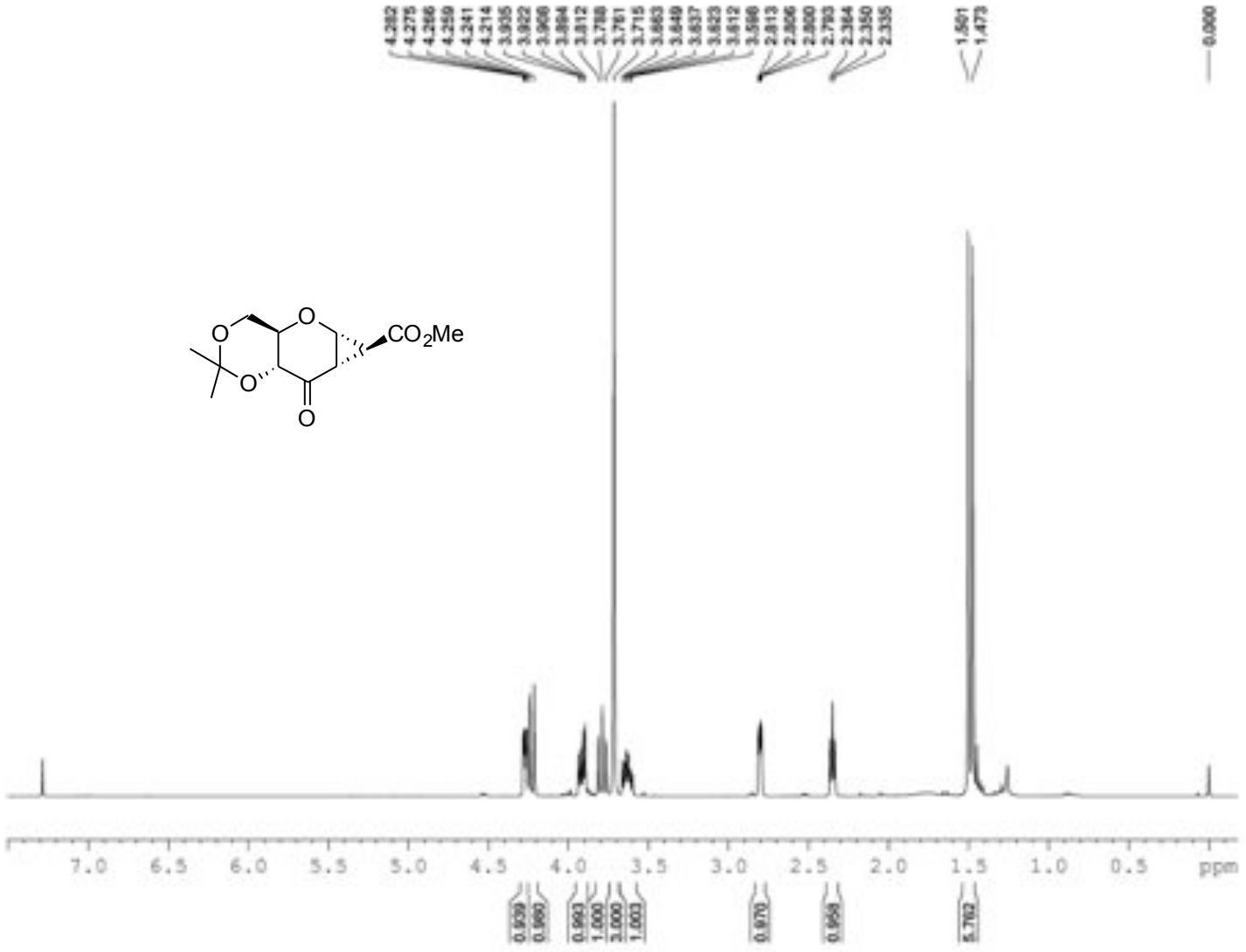
0.987
1.036
2.995
1.017
1.000
0.979
1.010
0.998
3.000
2.998


172.08
99.81
77.31
76.99
76.68
73.63
68.93
63.68
61.97
59.33
51.84
28.85
25.06
21.21
18.93
O
O
O
CO2Me
OH
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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4.275
4.266
4.259
4.241
4.214
3.935
3.922
3.908
3.894
3.812
3.788
3.761
3.715
3.663
3.649
3.637
3.623
3.612
3.586
2.813
2.806
2.800
2.793
2.364
2.350
2.335
1.501
1.473
0.000
O
O
O
O
CO2Me
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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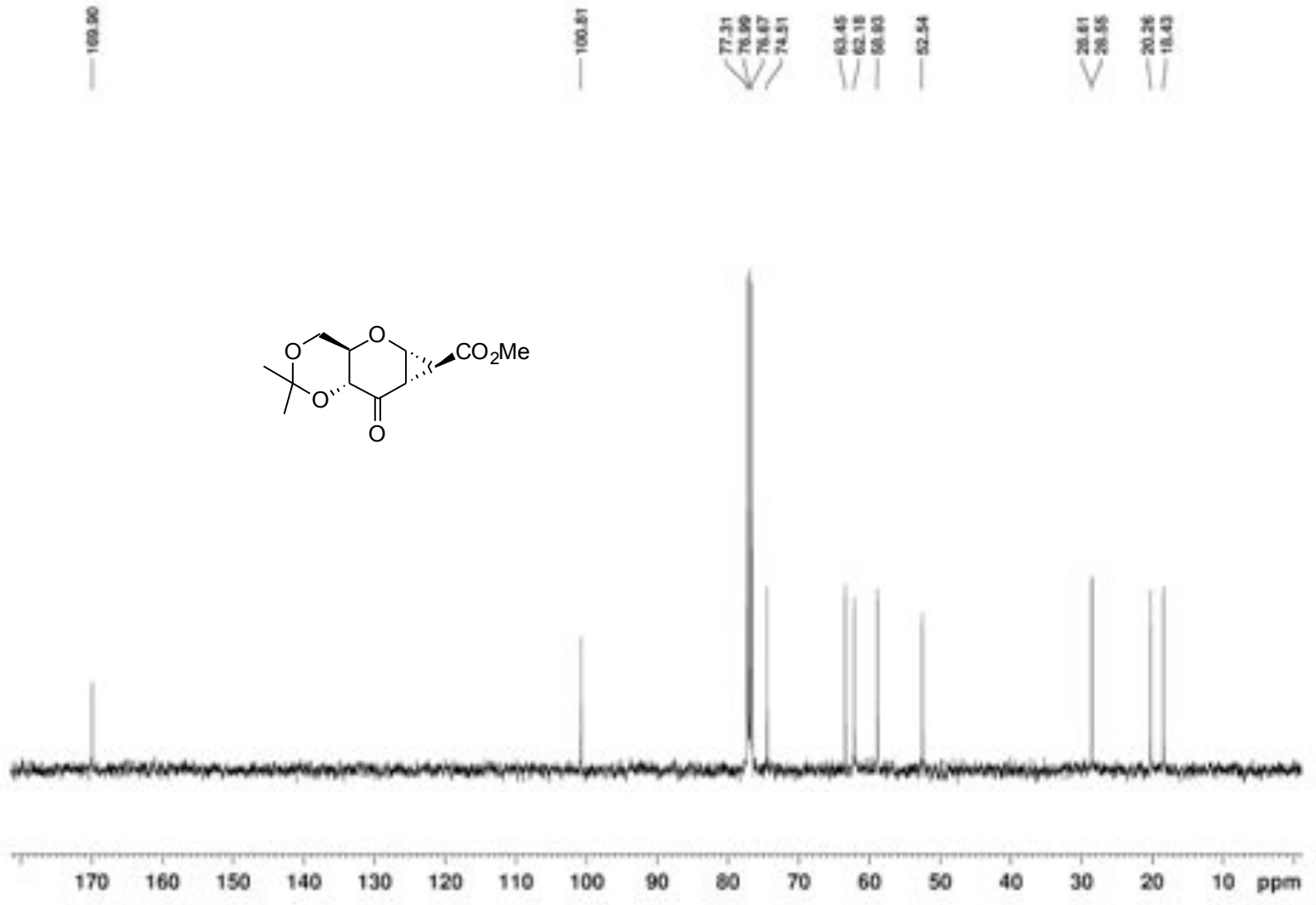
0.880
0.993
1.000
3.000
1.003
0.970
0.958
5.762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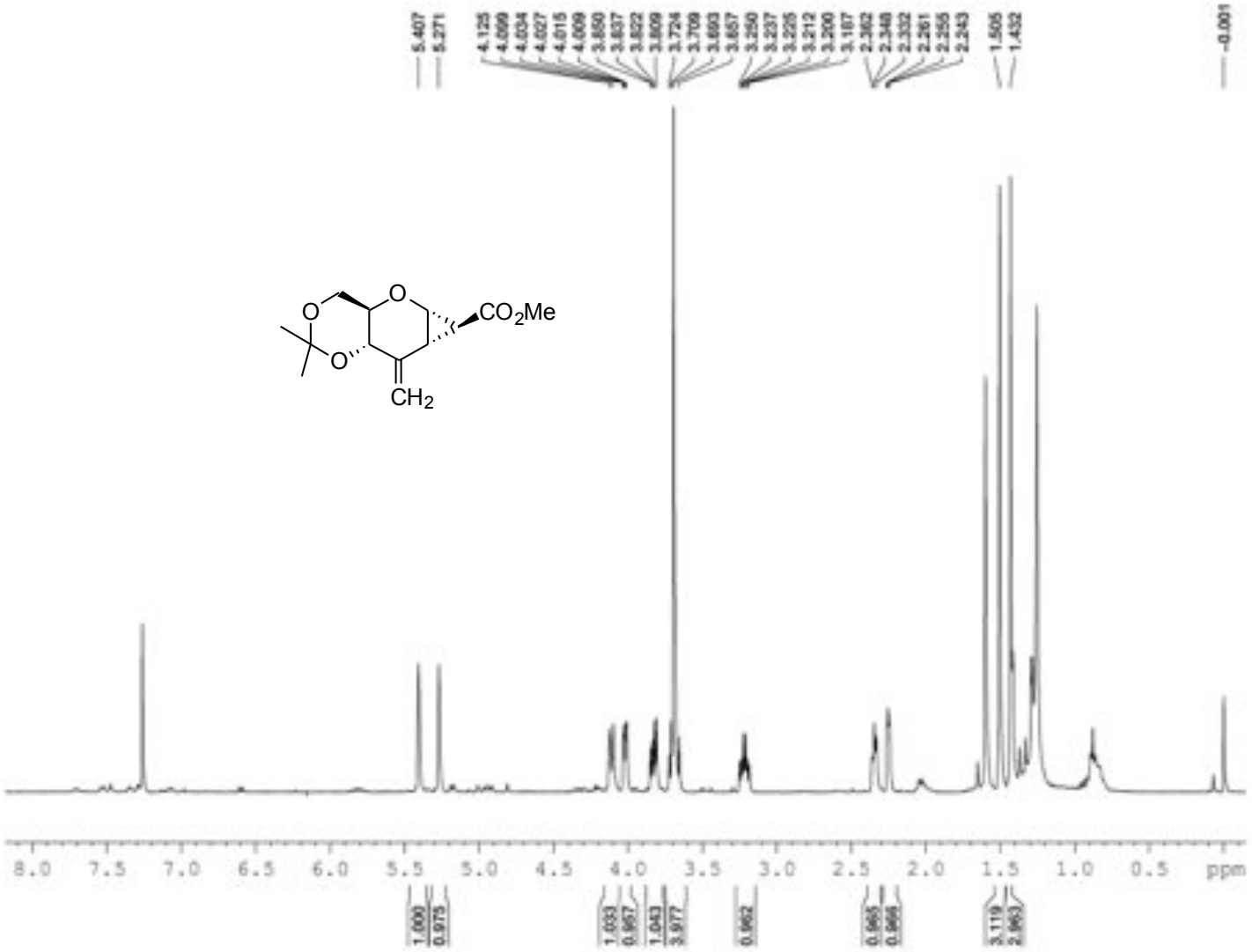
100.81
77.31
76.99
76.67
74.51
63.45
62.18
58.93
52.54
28.61
28.55
20.26
18.43
O
O
O
O
CO2Me
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm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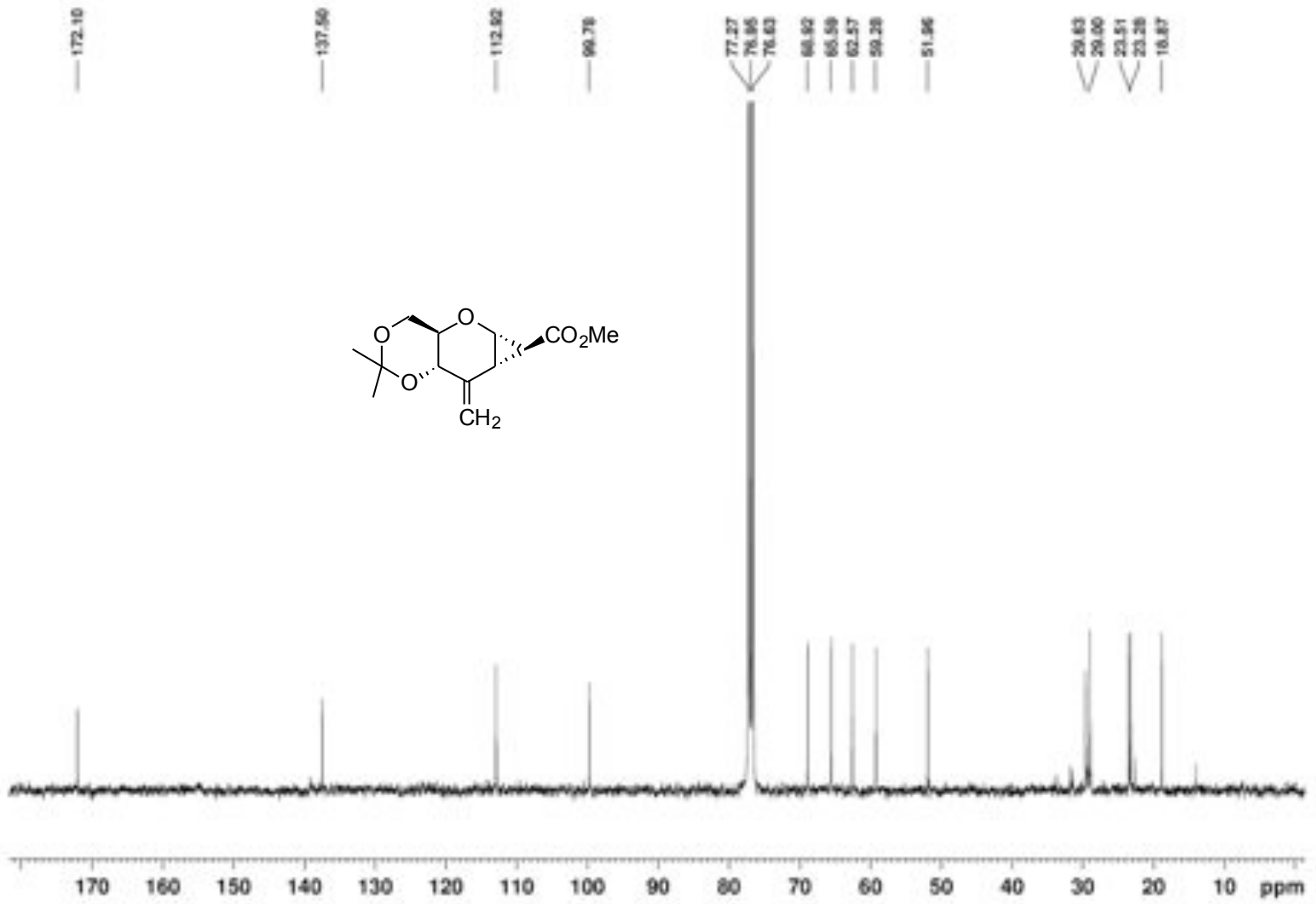
5.271
4.125
4.099
4.034
4.027
4.015
4.009
3.850
3.837
3.822
3.809
3.724
3.709
3.693
3.657
3.250
3.237
3.225
3.212
3.200
3.187
2.362
2.348
2.332
2.261
2.255
2.243
1.505
1.452
-0.001
O
O
O
CO2Me
CH2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.000
0.975
1.033
0.967
1.043
3.977
0.962
0.965
0.966
3.119
2.963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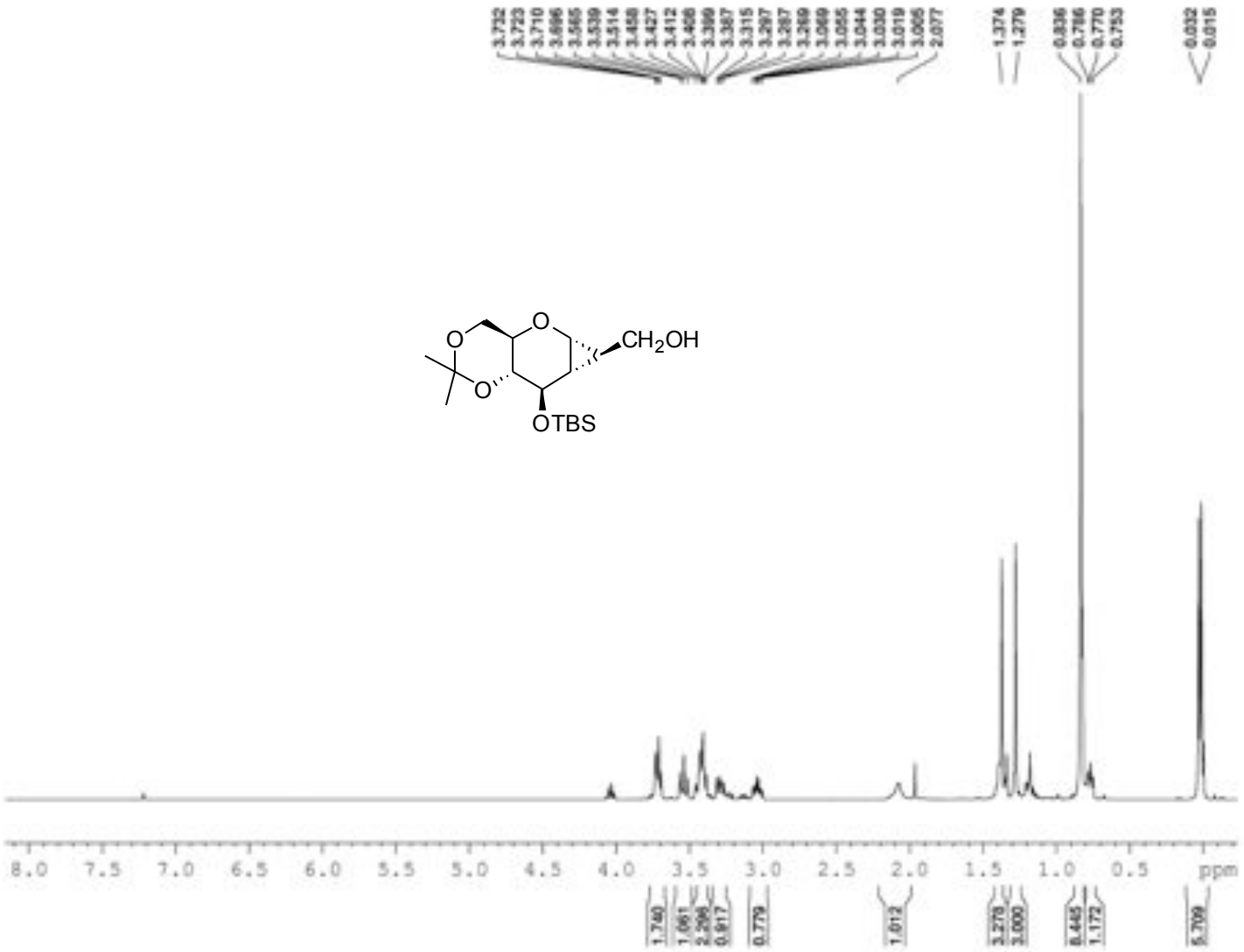
77.27
76.95
76.63
68.92
65.59
62.57
59.28
51.96
29.83
29.00
23.51
23.28
18.87
O
O
O
CO2Me
CH2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


3.732
3.723
3.710
3.696
3.565
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3.514
3.458
3.427
3.412
3.408
3.399
3.387
3.315
3.297
3.287
3.269
3.069
3.055
3.044
3.030
3.019
3.005
2.077
1.374
1.279
0.836
0.786
0.770
0.753
0.032
0.015
O
O
O
CH2OH
OTBS
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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2.298
0.917
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3.278
3.000
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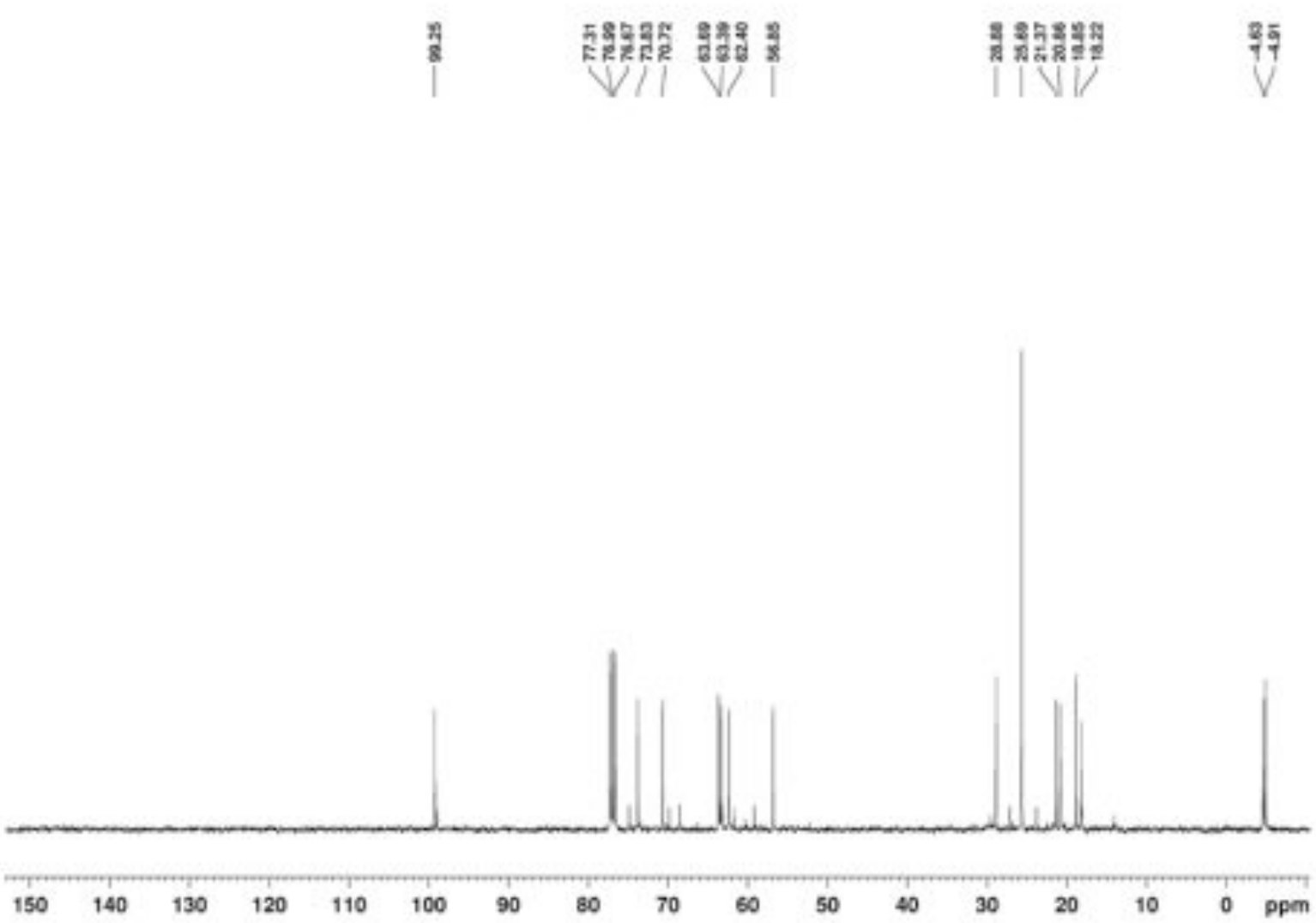
1.172
5.709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76.67
73.83
70.72
63.69
63.39
62.40
56.85
28.88
25.69
21.37
20.86
18.85
18.22
-4.63
-4.91
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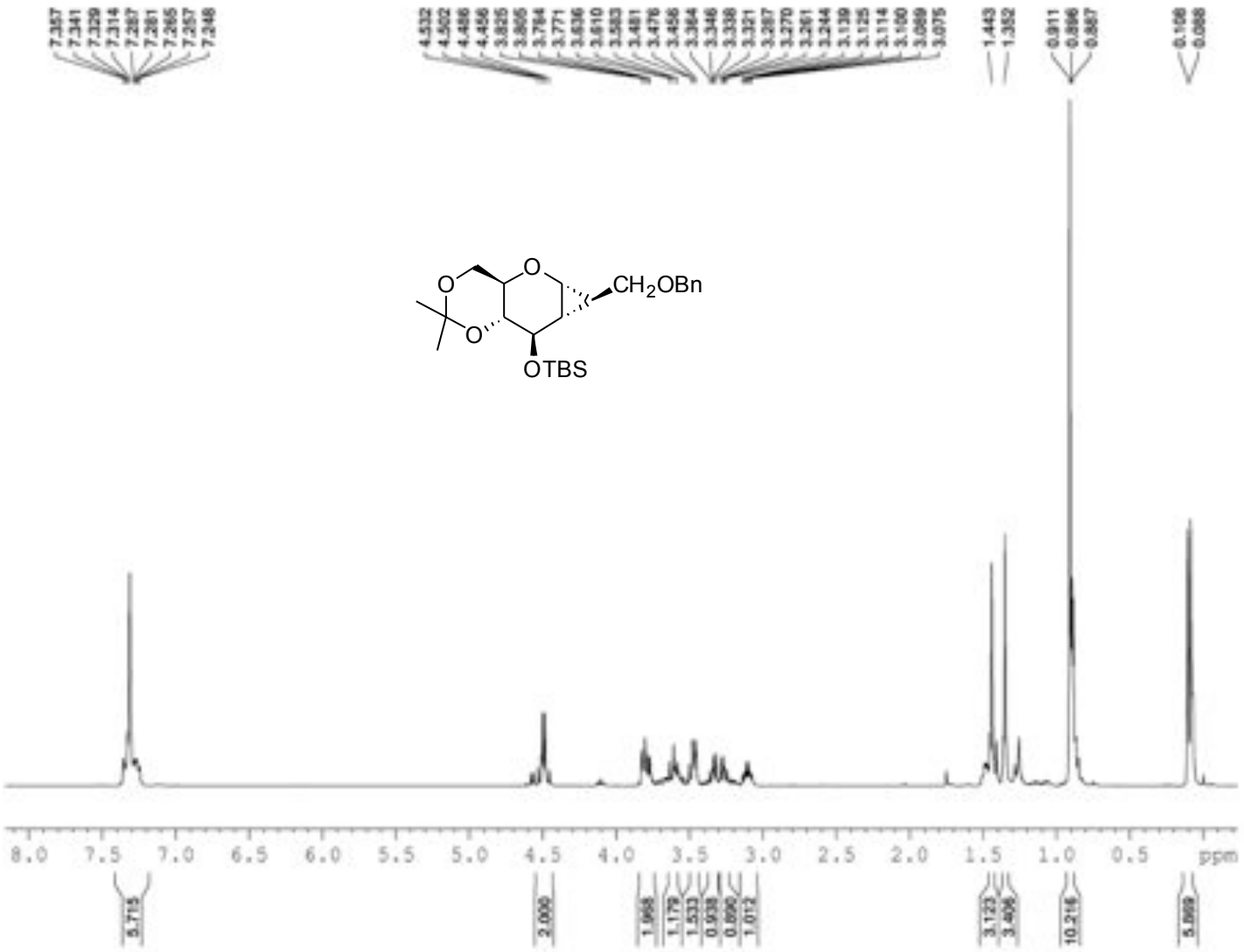
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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7.329
7.314
7.287
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7.257
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4.532
4.502
4.486
4.456
3.825
3.805
3.784
3.771
3.636
3.610
3.583
3.481
3.476
3.456
3.364
3.346
3.338
3.321
3.287
3.270
3.261
3.244
3.139
3.125
3.114
3.100
3.089
3.075
1.443
1.352
0.911
0.896
0.867
0.108
0.088
O
O
O
CH2OBn
OTBS
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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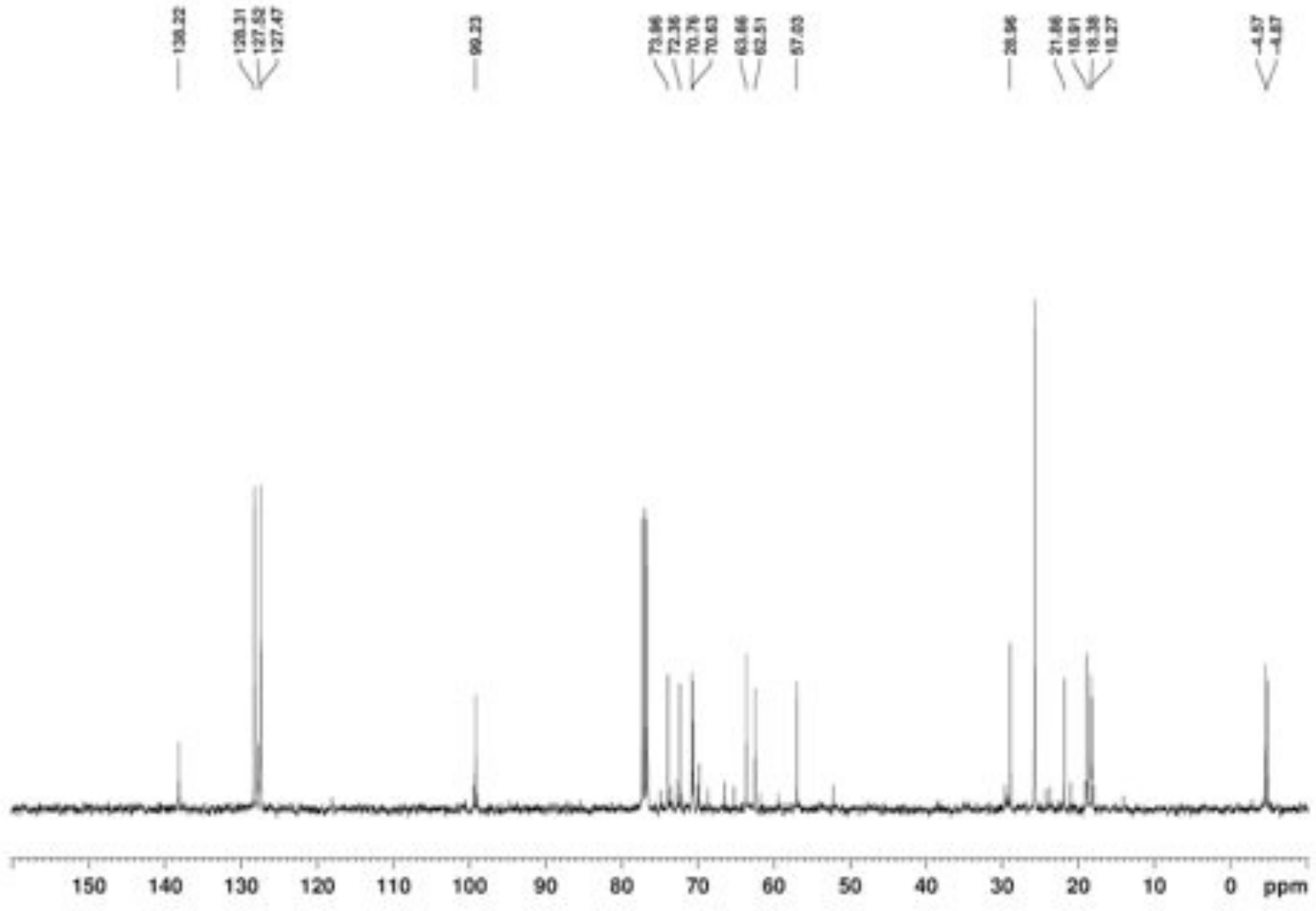
10.216
5.869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127.47
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72.36
70.76
70.63
63.66
62.51
57.03
28.96
21.86
18.91
18.38
18.27
-4.57
-4.87
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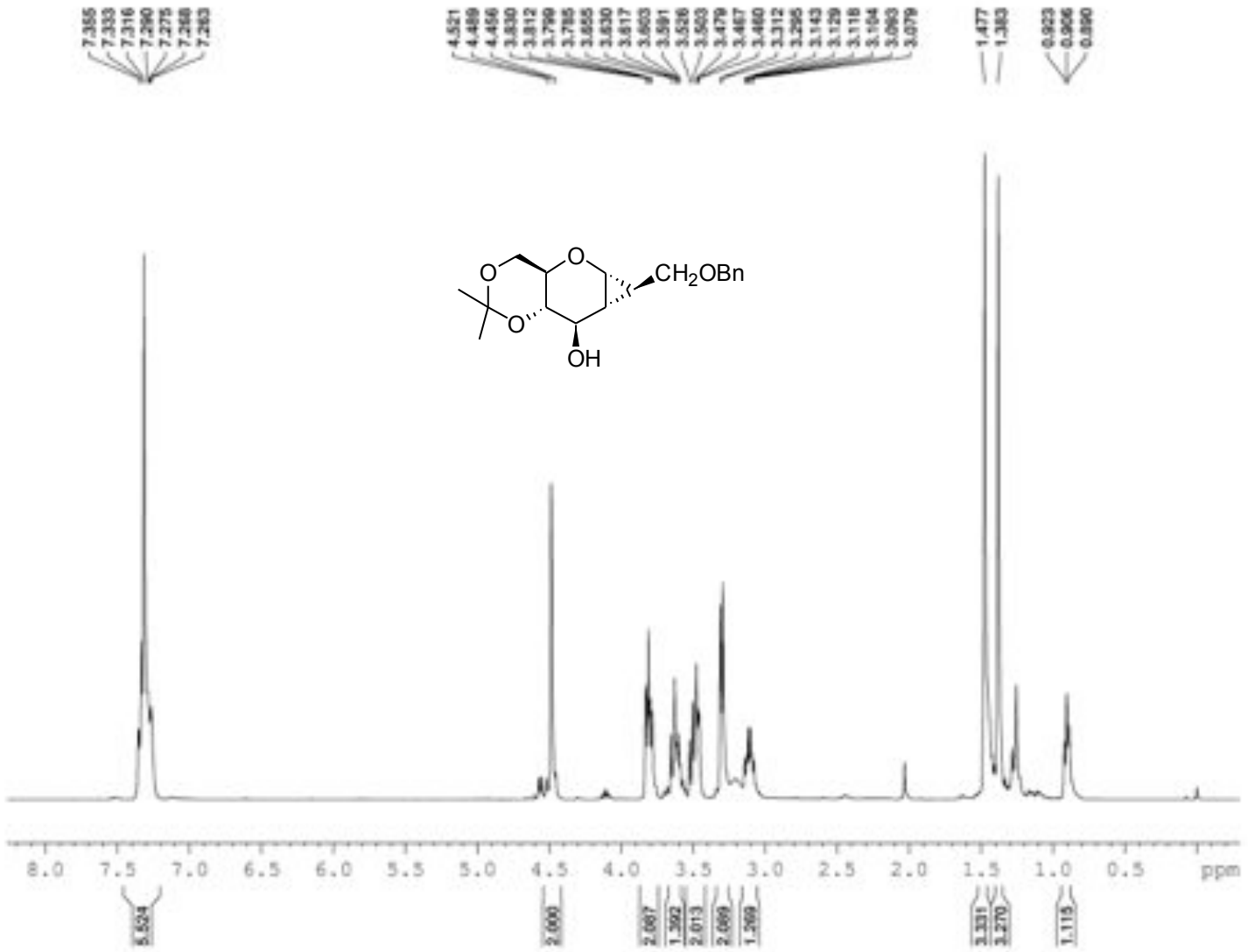
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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4.456
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3.812
3.799
3.785
3.655
3.630
3.617
3.603
3.591
3.526
3.503
3.479
3.467
3.460
3.312
3.295
3.143
3.129
3.118
3.104
3.093
3.079
1.477
1.383
0.923
0.906
0.890
O
O
O
CH2OBn
OH
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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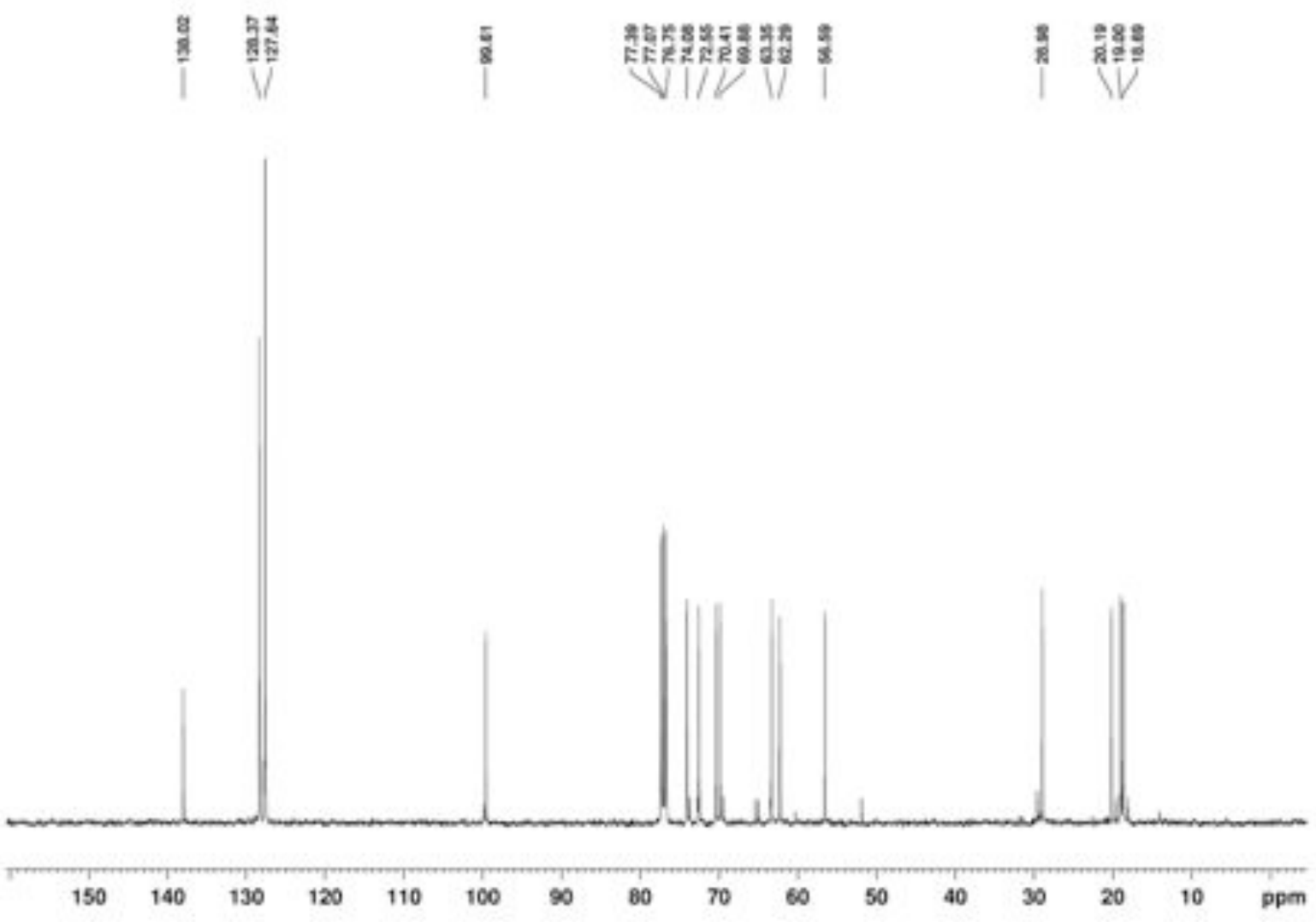
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76.75
74.08
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70.41
69.88
63.35
62.29
54.59
28.98
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150
140
130
120
110
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70
60
50
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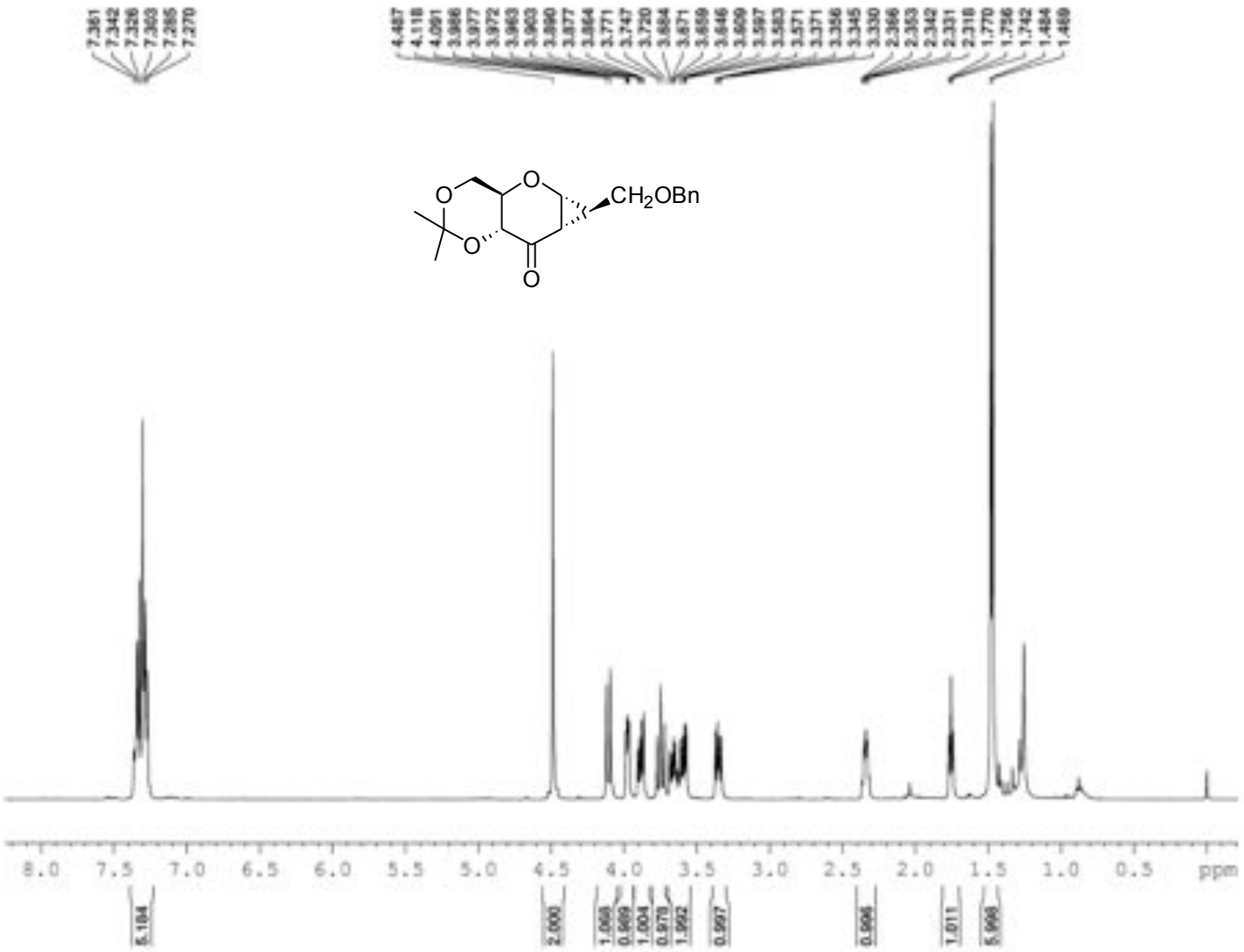
30
20
10
ppm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7.303
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7.270
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4.118
4.091
3.986
3.977
3.972
3.963
3.903
3.890
3.877
3.864
3.771
3.747
3.720
3.684
3.671
3.659
3.646
3.609
3.597
3.583
3.571
3.371
3.356
3.345
3.330
2.366
2.353
2.342
2.331
2.318
1.770
1.756
1.742
1.484
1.469
O
O
O
O
CH2OBn
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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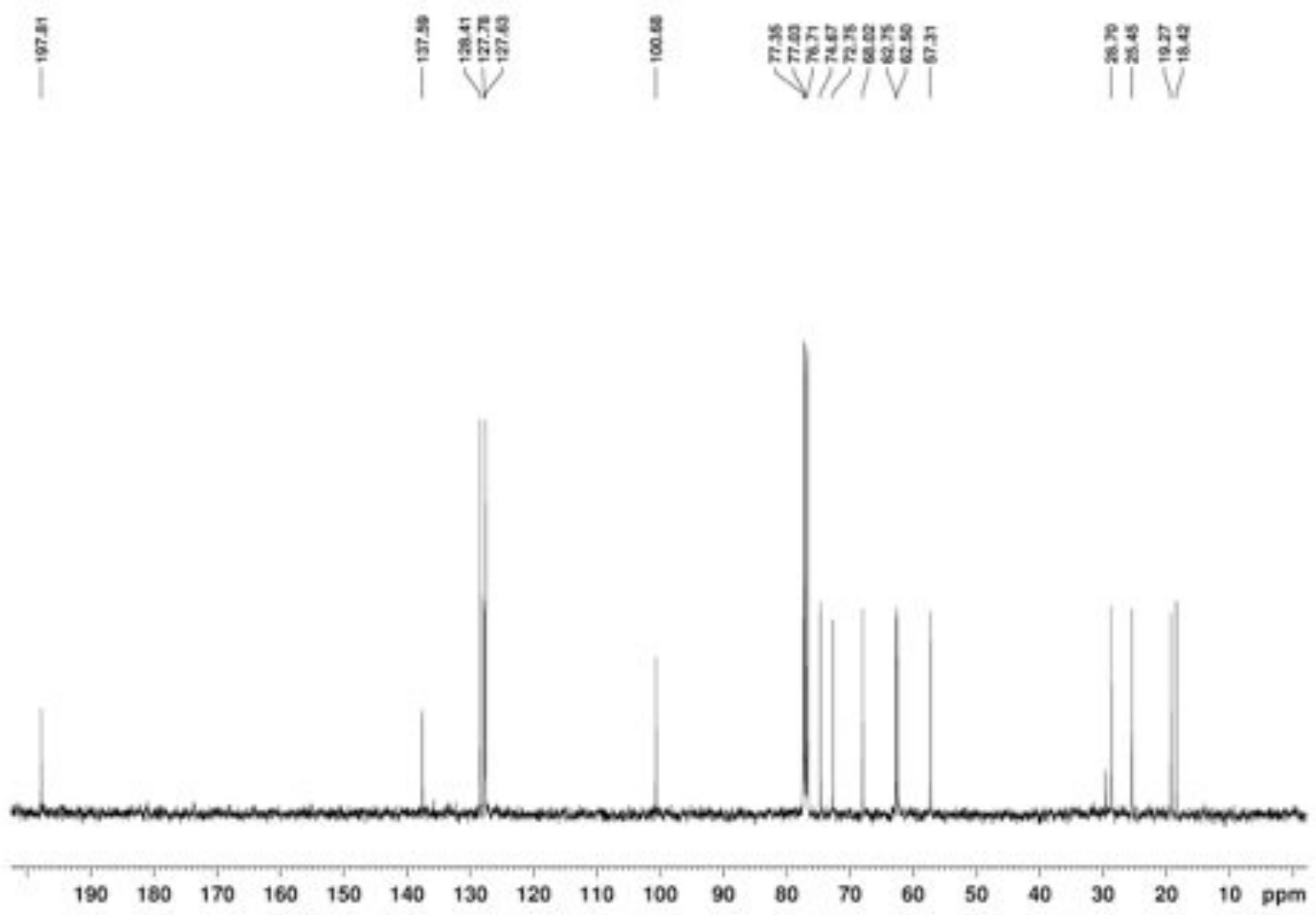
5.998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74.67
72.75
68.02
62.75
62.50
57.31
29.70
25.45
19.27
18.42
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150
140
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90
80
70
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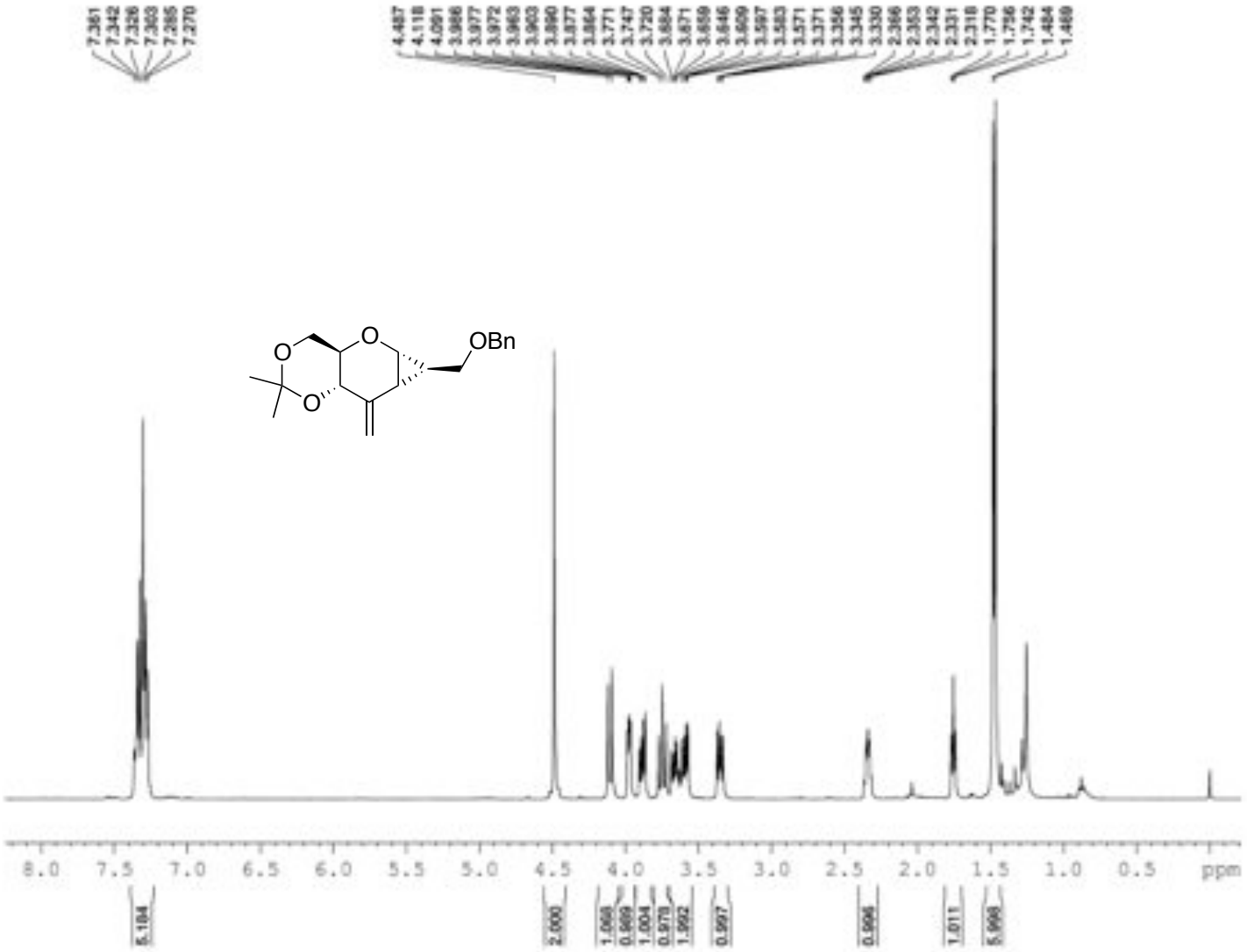
50
40
30
20
10
ppm


7.361
7.342
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7.303
7.285
7.270
4.487
4.118
4.091
3.986
3.977
3.972
3.963
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3.890
3.877
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3.747
3.720
3.684
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3.583
3.571
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2.331
2.318
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1.756
1.742
1.484
1.469
O
O
O
OBn
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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1.992
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0.996
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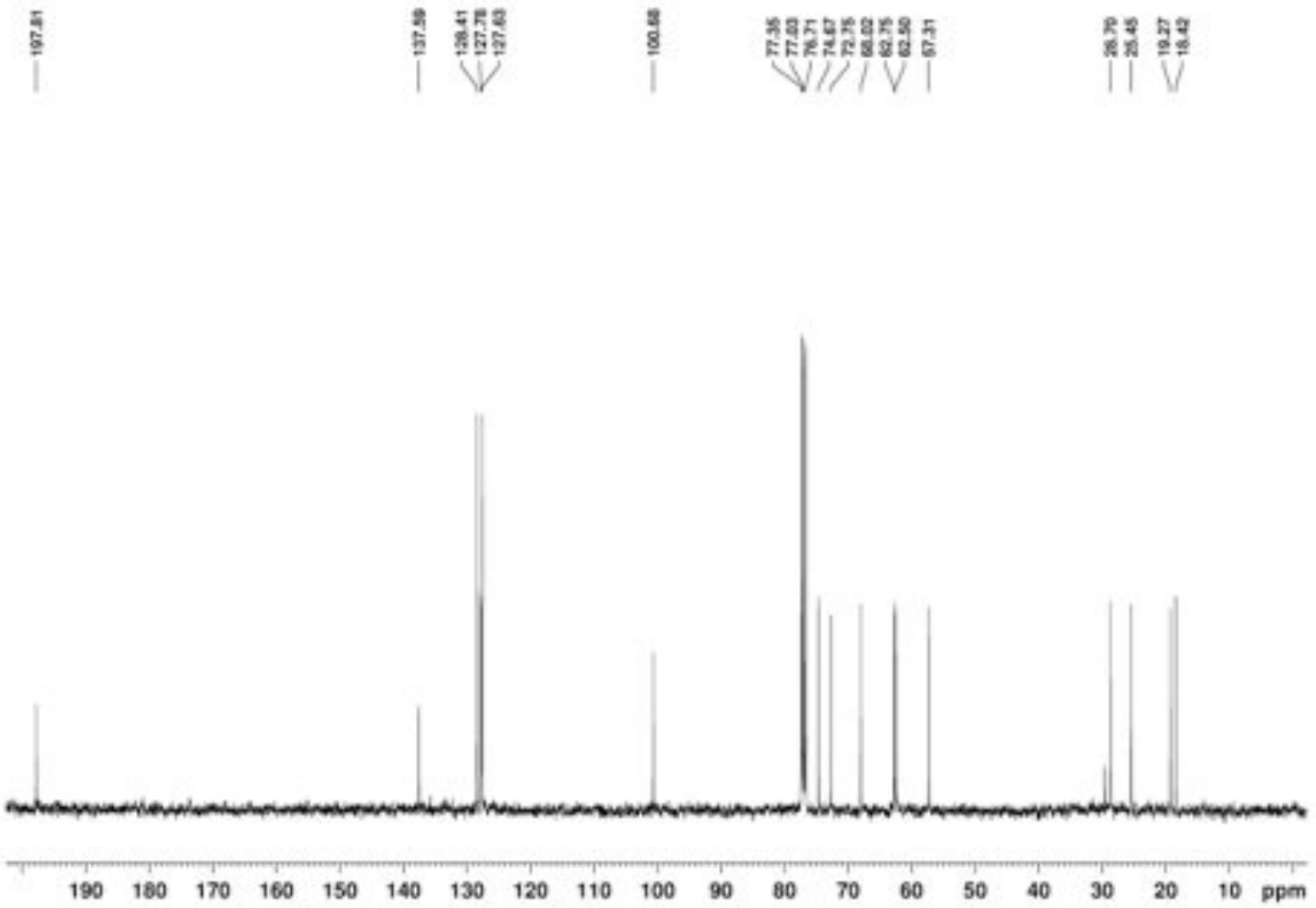
5.998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128.41
127.78
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74.67
72.75
68.02
62.75
62.50
57.31
29.79
25.45
19.27
18.42
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70
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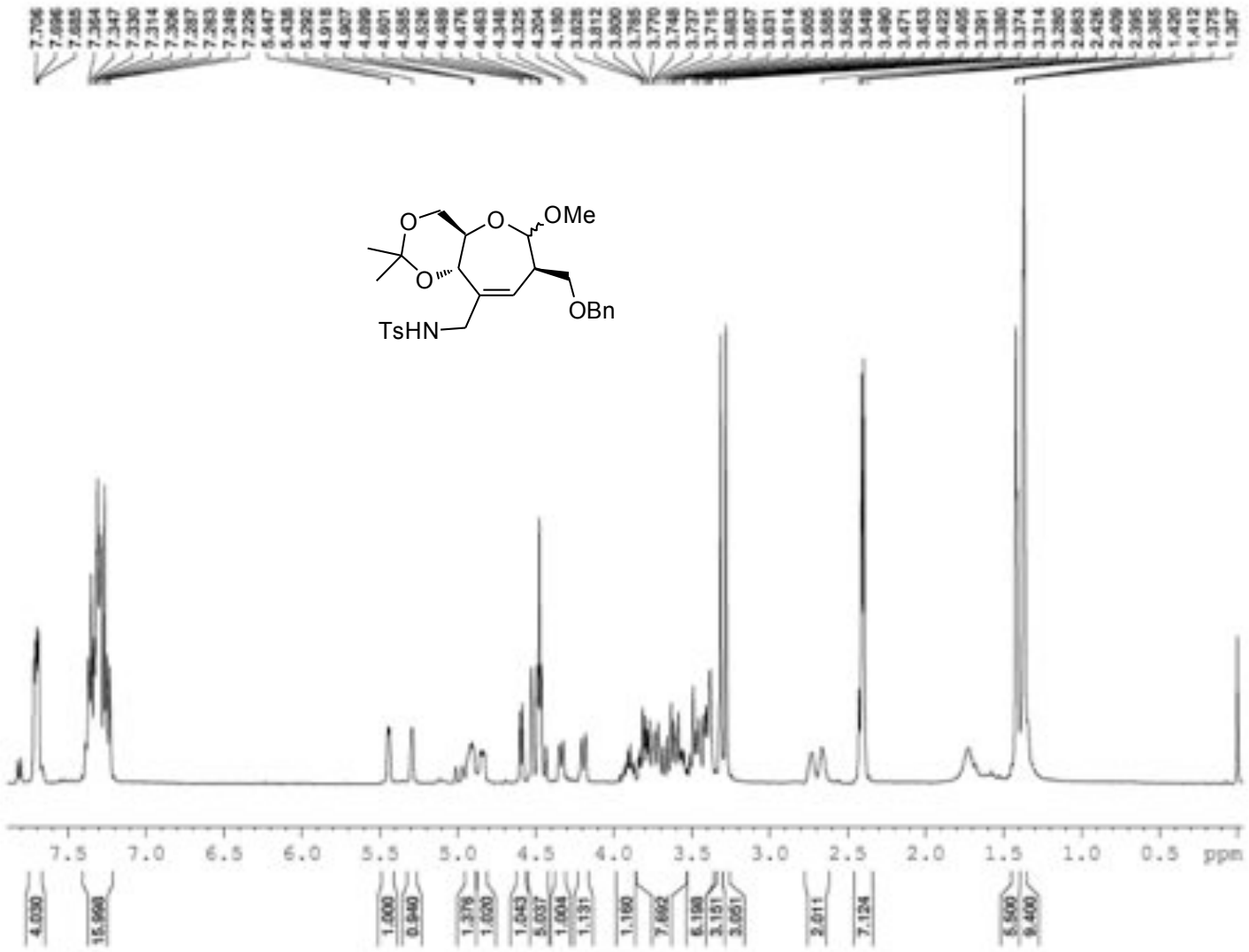
10
ppm


OMe
OBn
TsHN
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7.0
6.5
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4.0
3.5
3.0
2.5
2.0
1.5
1.0
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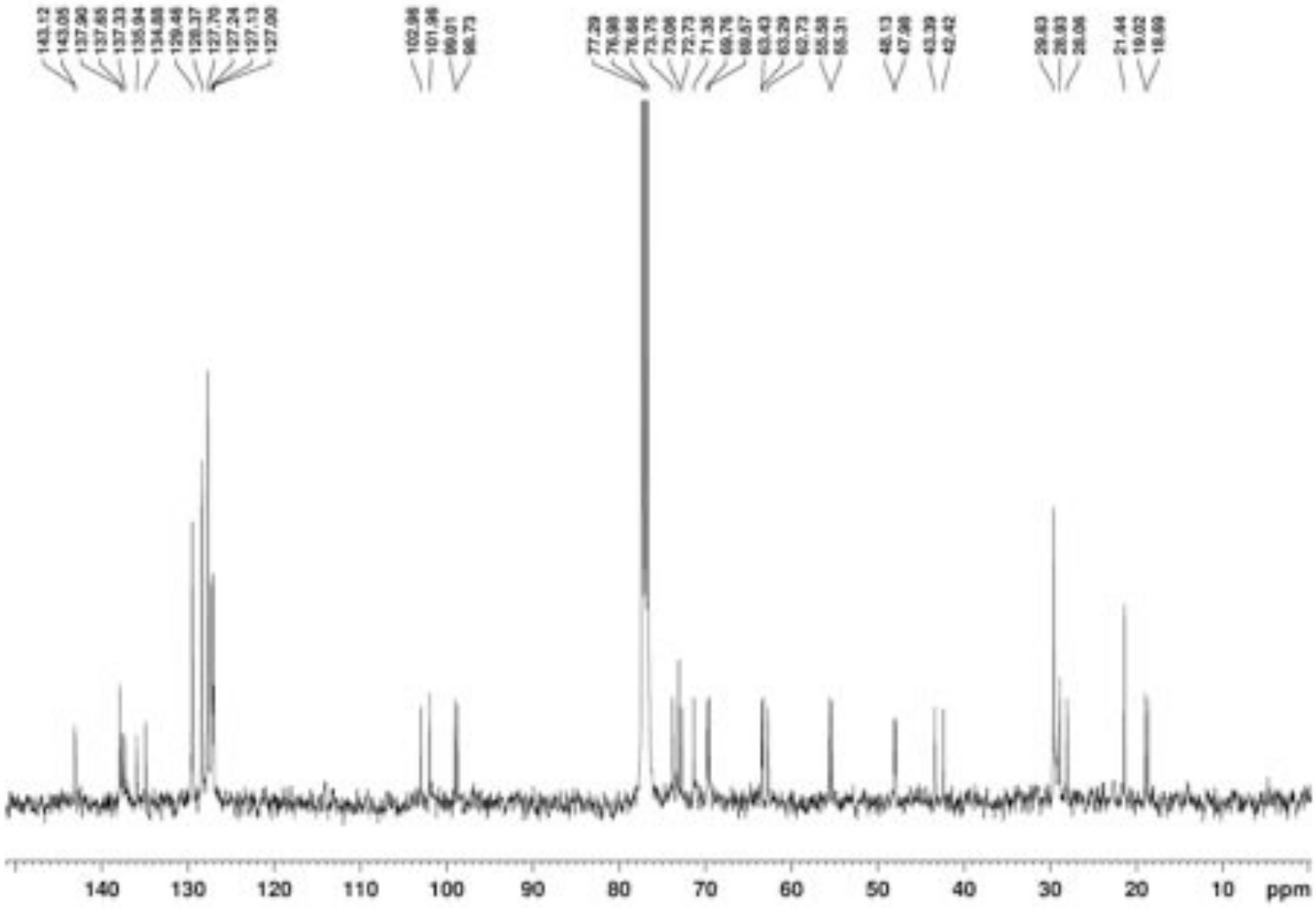
ppm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127.70
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127.13
127.00
102.96
101.96
99.01
98.73
77.29
76.98
76.66
73.75
73.06
72.73
71.35
69.76
69.57
63.43
63.29
62.73
55.58
55.31
48.13
47.98
43.39
42.42
29.83
28.93
28.06
21.44
19.02
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130
120
110
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70
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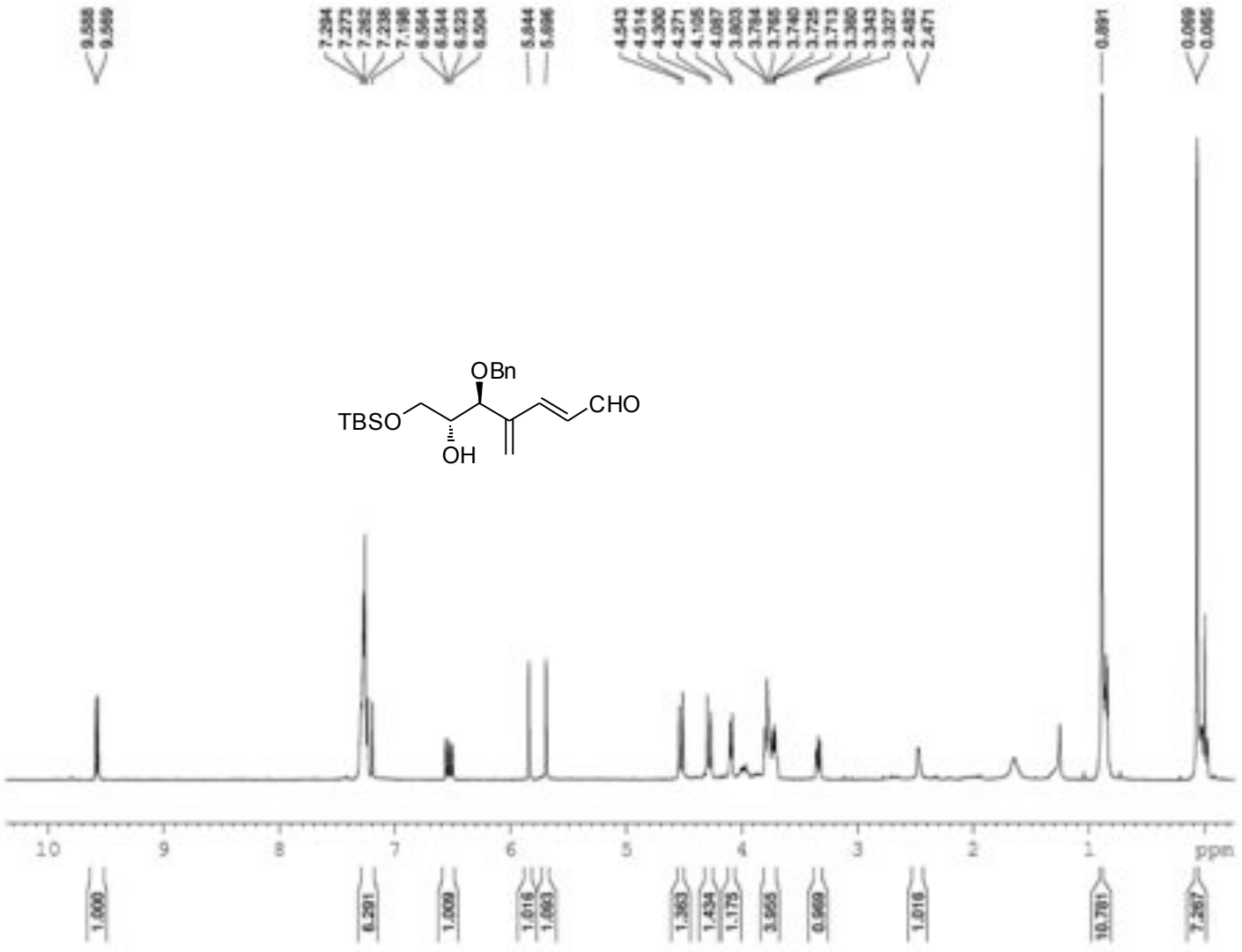
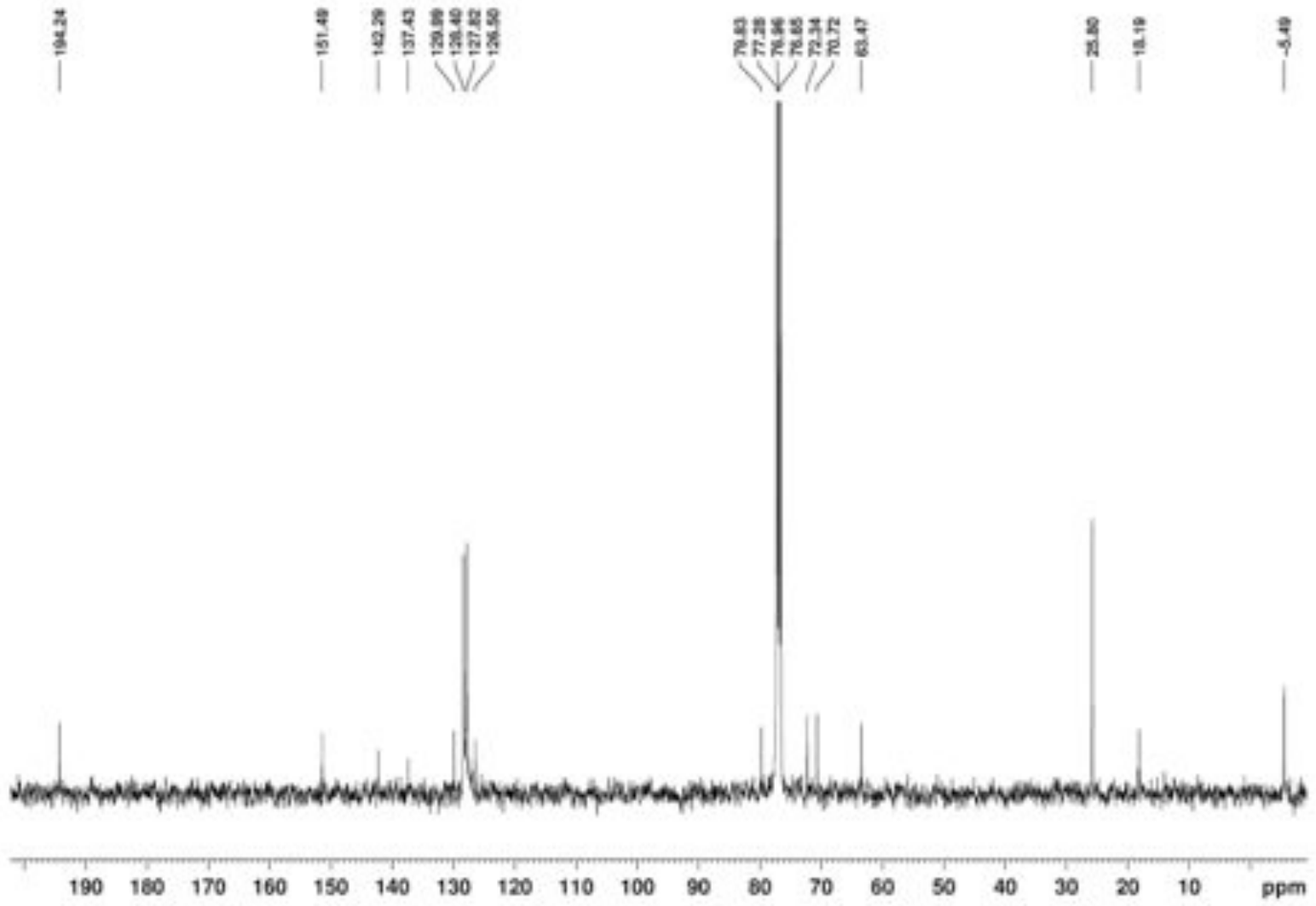
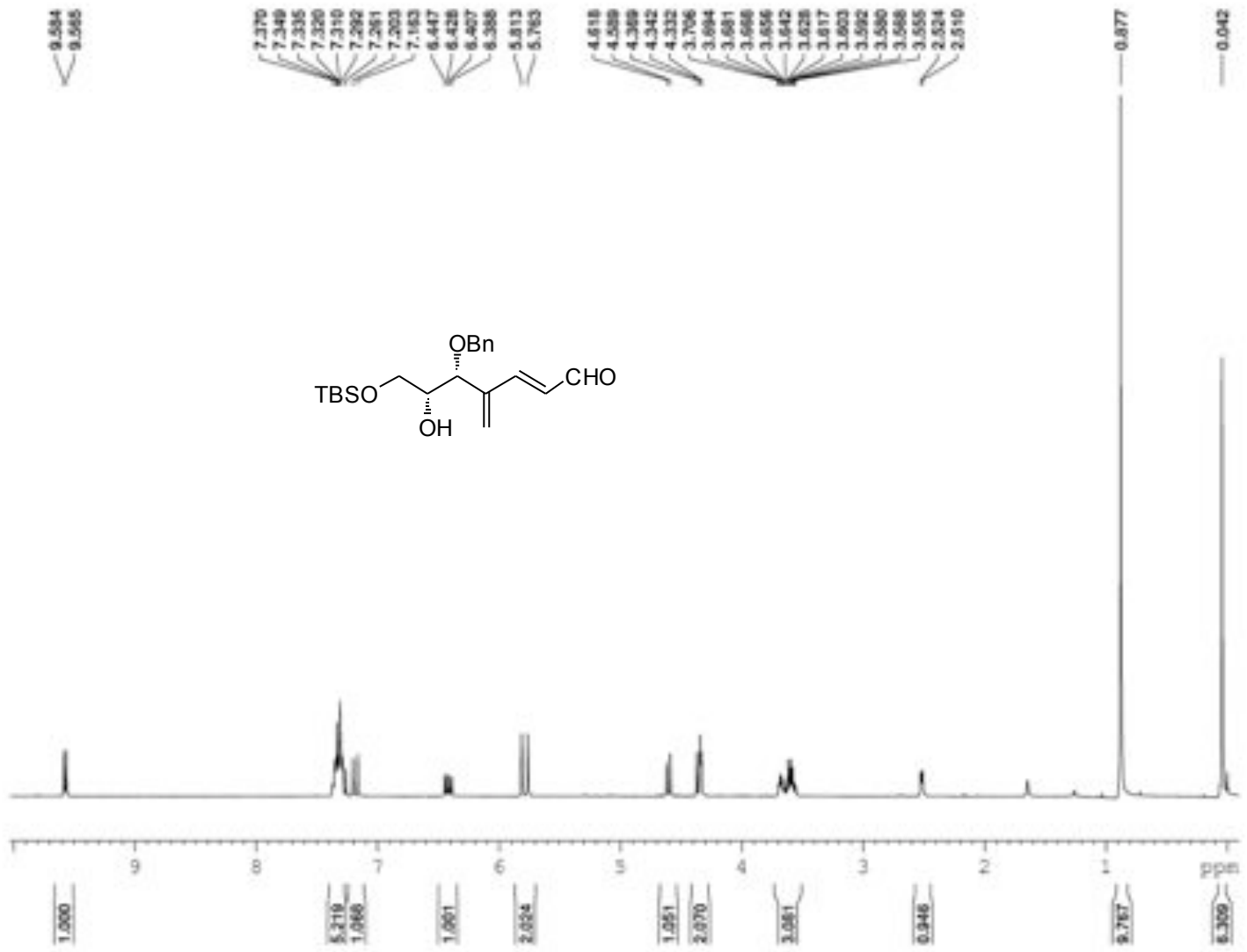
40
30
20
10
ppm


9.588
9.569
7.294
7.273
7.262
7.239
7.198
6.564
6.544
6.523
6.504
5.844
5.696
4.543
4.514
4.300
4.271
4.105
4.087
3.803
3.784
3.765
3.740
3.725
3.713
3.360
3.343
3.327
2.482
2.471
0.891
0.069
0.065
OBn
TBSO
CHO
OH
10
9
8
7
6
5
4
3
2
1
ppm
1.000
6.291
1.009
1.016
1.093
1.383
1.434
1.175
3.955
0.969
1.016
10.781
7.267


194.24
151.49
142.29
137.43
129.89
128.40
127.82
126.50
76.83
77.28
76.96
76.65
72.34
70.72
63.47
25.80
18.19
-5.49
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm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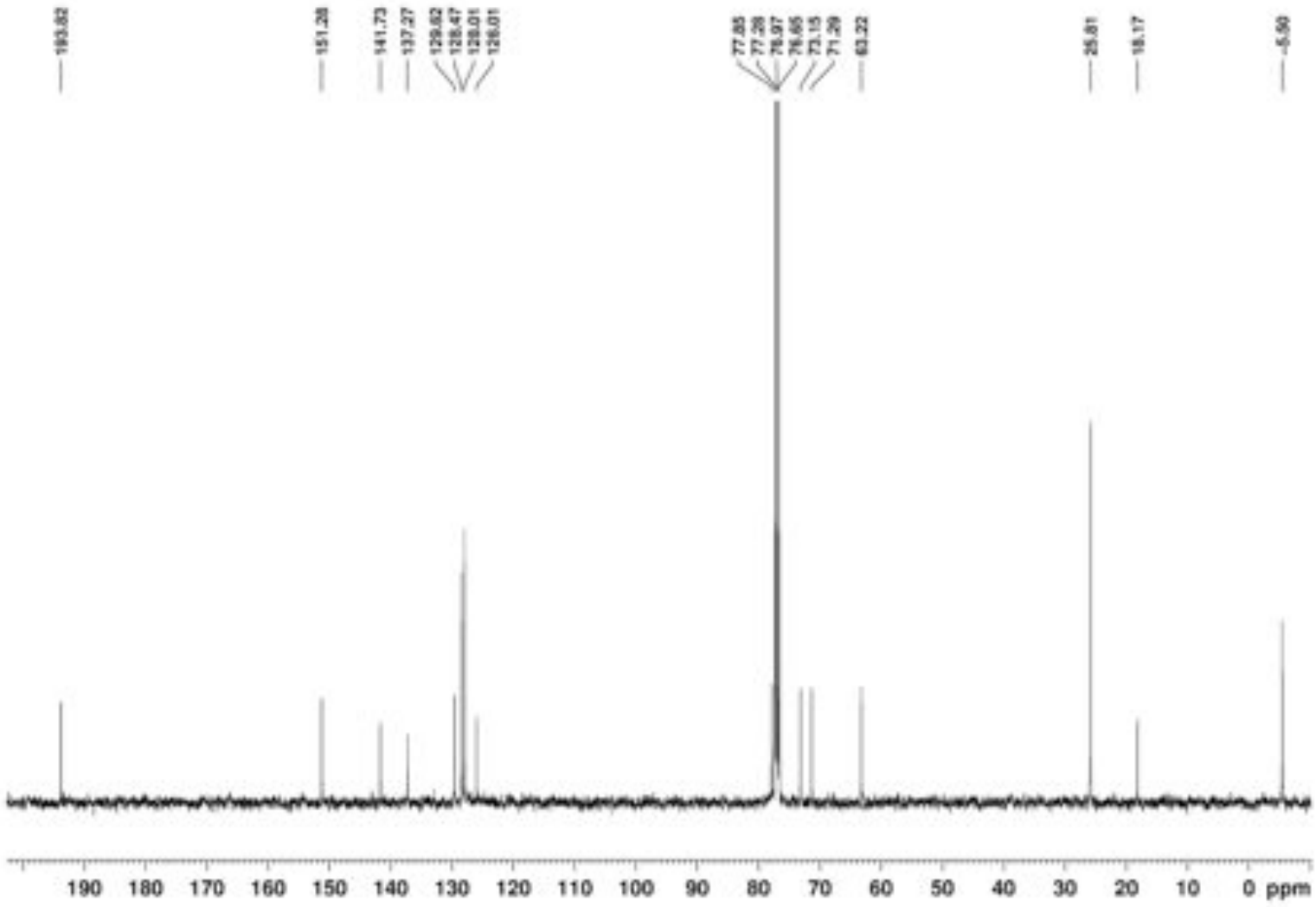
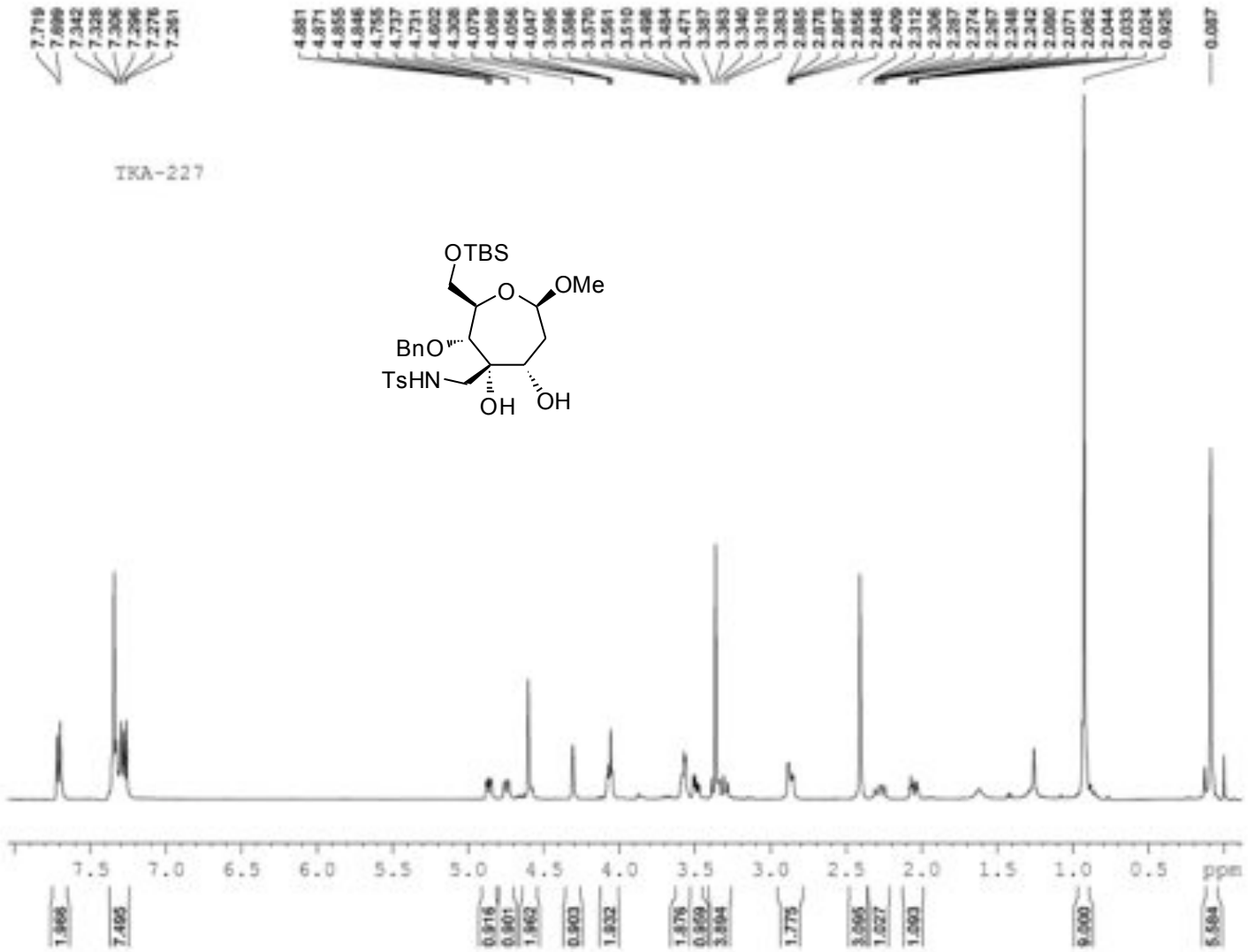
9.565
7.370
7.349
7.335
7.320
7.310
7.292
7.281
7.203
7.163
6.447
6.428
6.407
6.388
5.813
5.763
4.618
4.589
4.369
4.342
4.332
3.706
3.694
3.681
3.668
3.656
3.642
3.628
3.617
3.603
3.592
3.580
3.568
3.555
2.524
2.510
0.877
0.042
OBn
TBSO
CHO
OH
9
8
7
6
5
4
3
2
1
ppm
1.000
5.319
1.066
1.061
2.024
1.051
2.070
3.061
0.946
9.767
6.309


193.62
151.28
141.73
137.27
129.62
128.47
128.01
126.01
77.85
77.28
76.97
76.65
73.15
71.29
63.22
25.81
18.17
-5.50
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


IKA-227
OTBS
O
OMe
BnO
TsHN
OH
OH
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6.5
6.0
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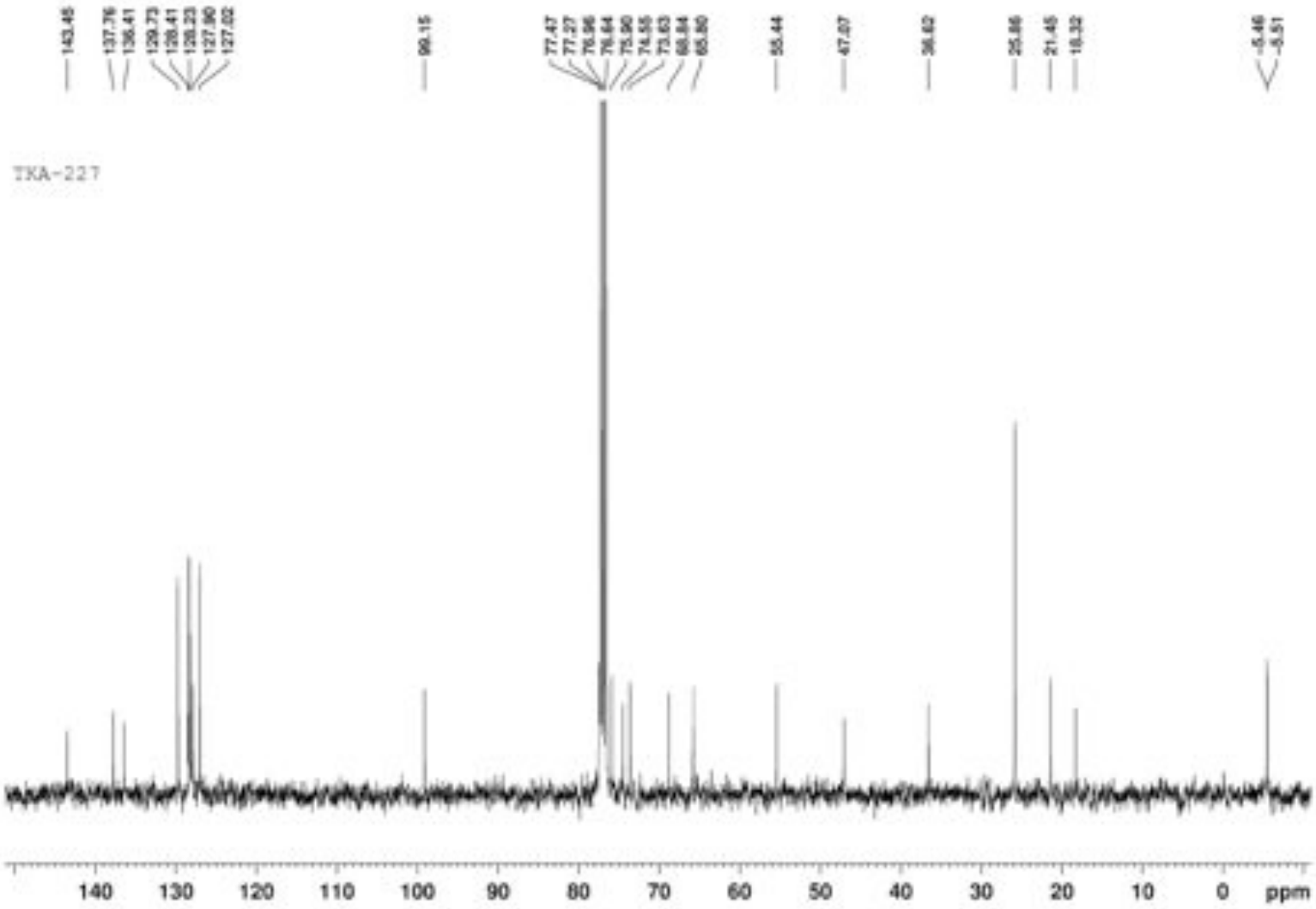
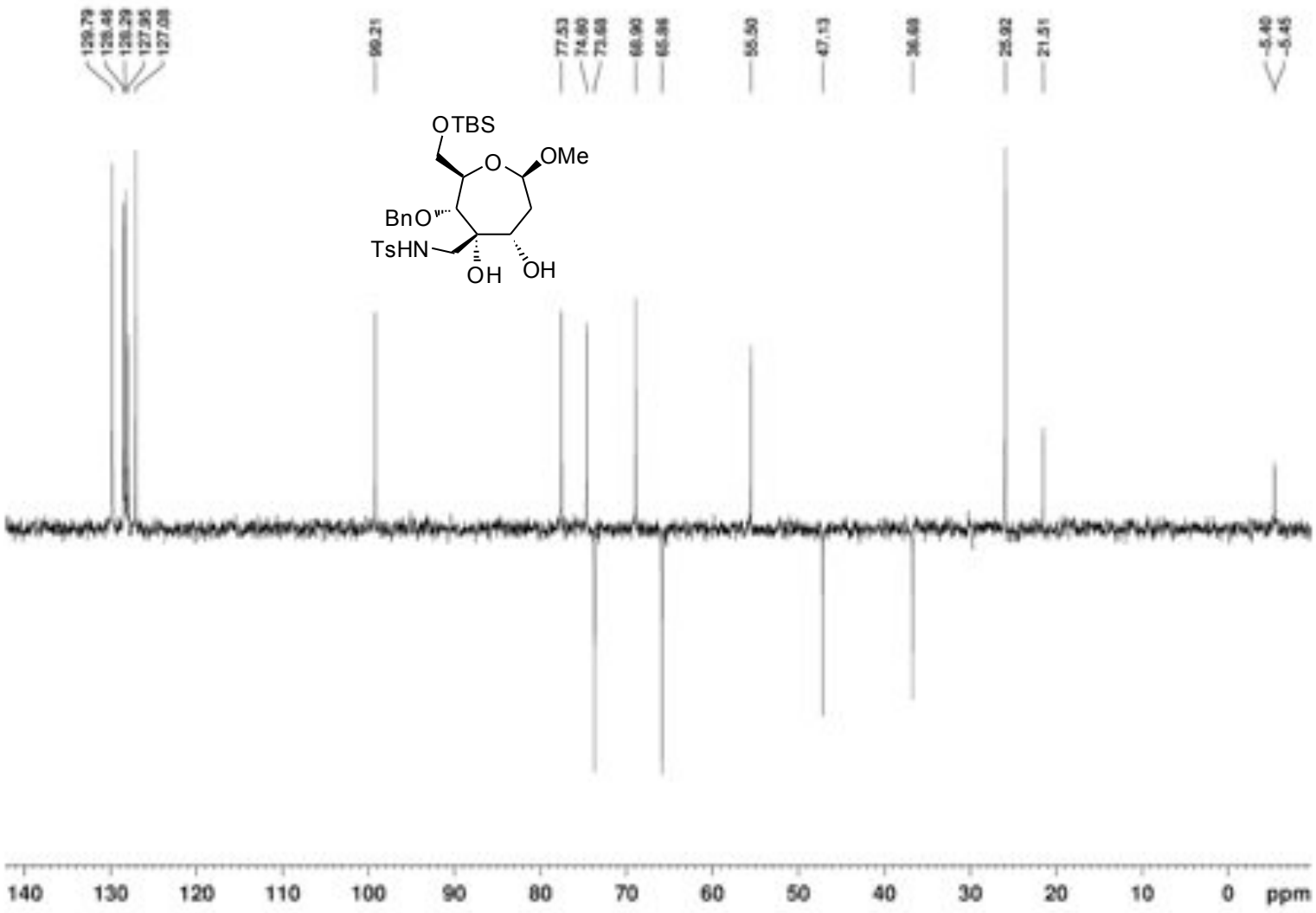
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


143.48
137.76
136.41
129.73
128.41
128.23
127.90
127.02
99.15
77.47
77.27
76.96
76.64
75.90
74.55
73.63
69.84
65.90
55.44
47.07
36.62
25.86
21.45
18.32
-5.46
-5.51
TKA-227
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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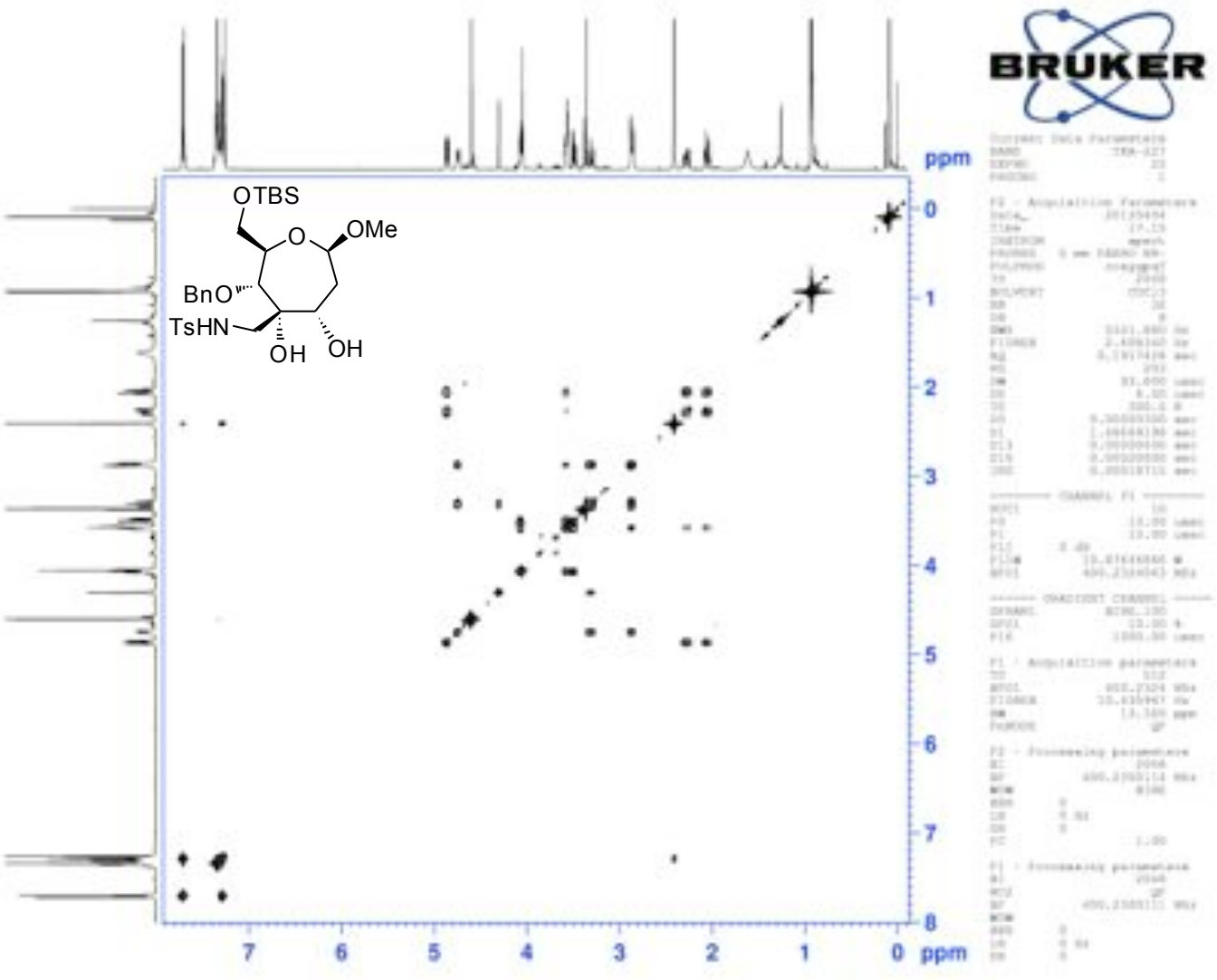
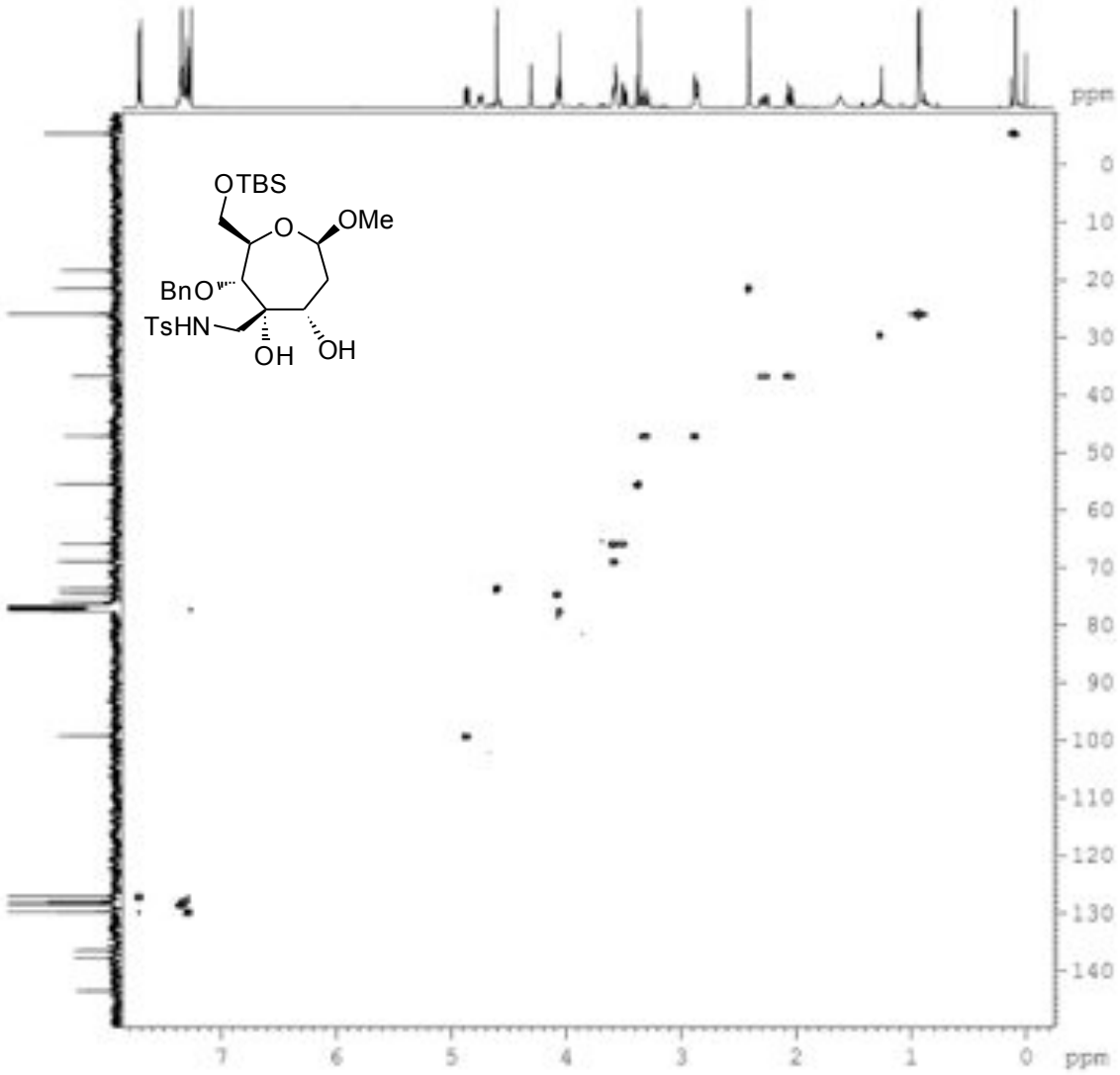
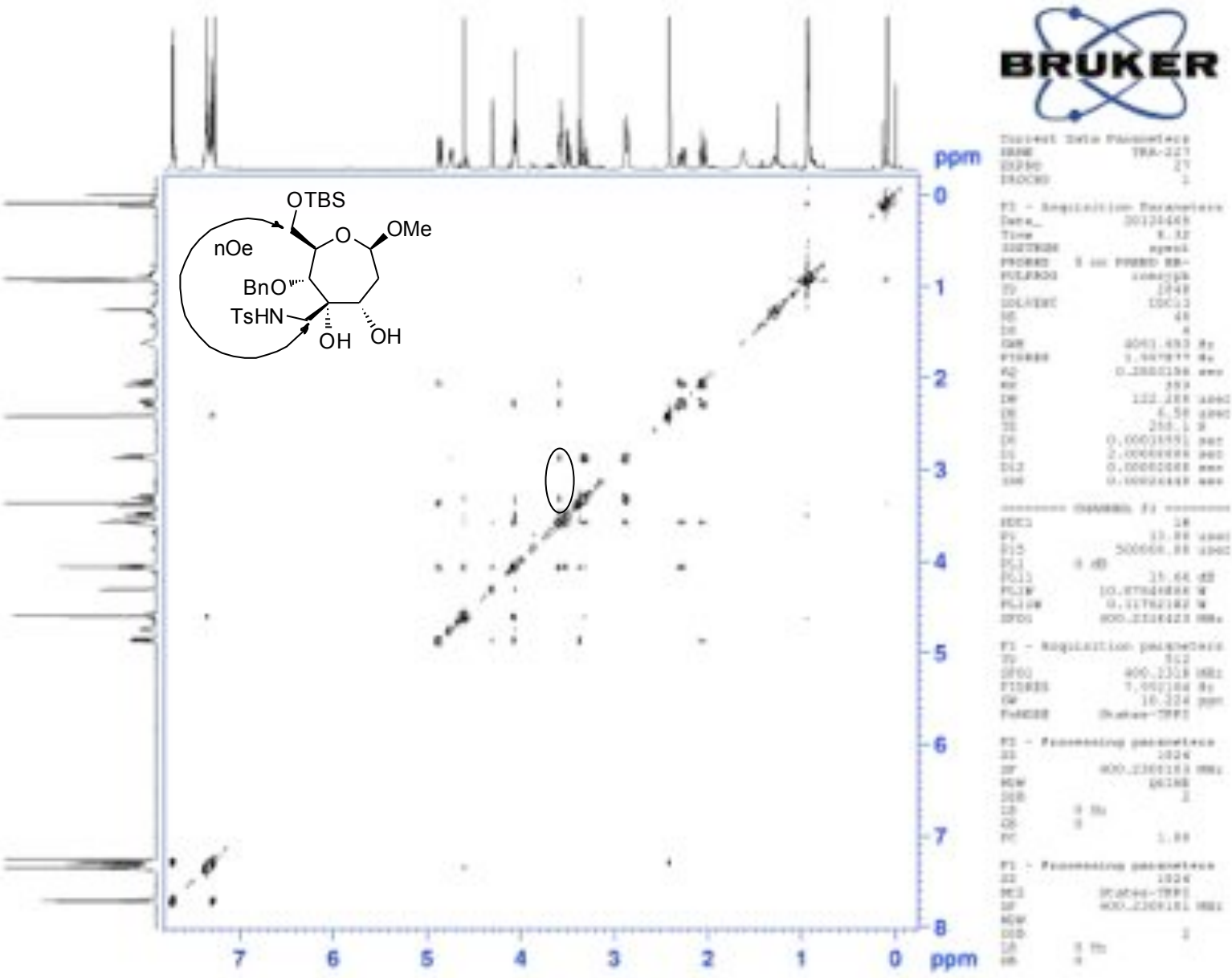
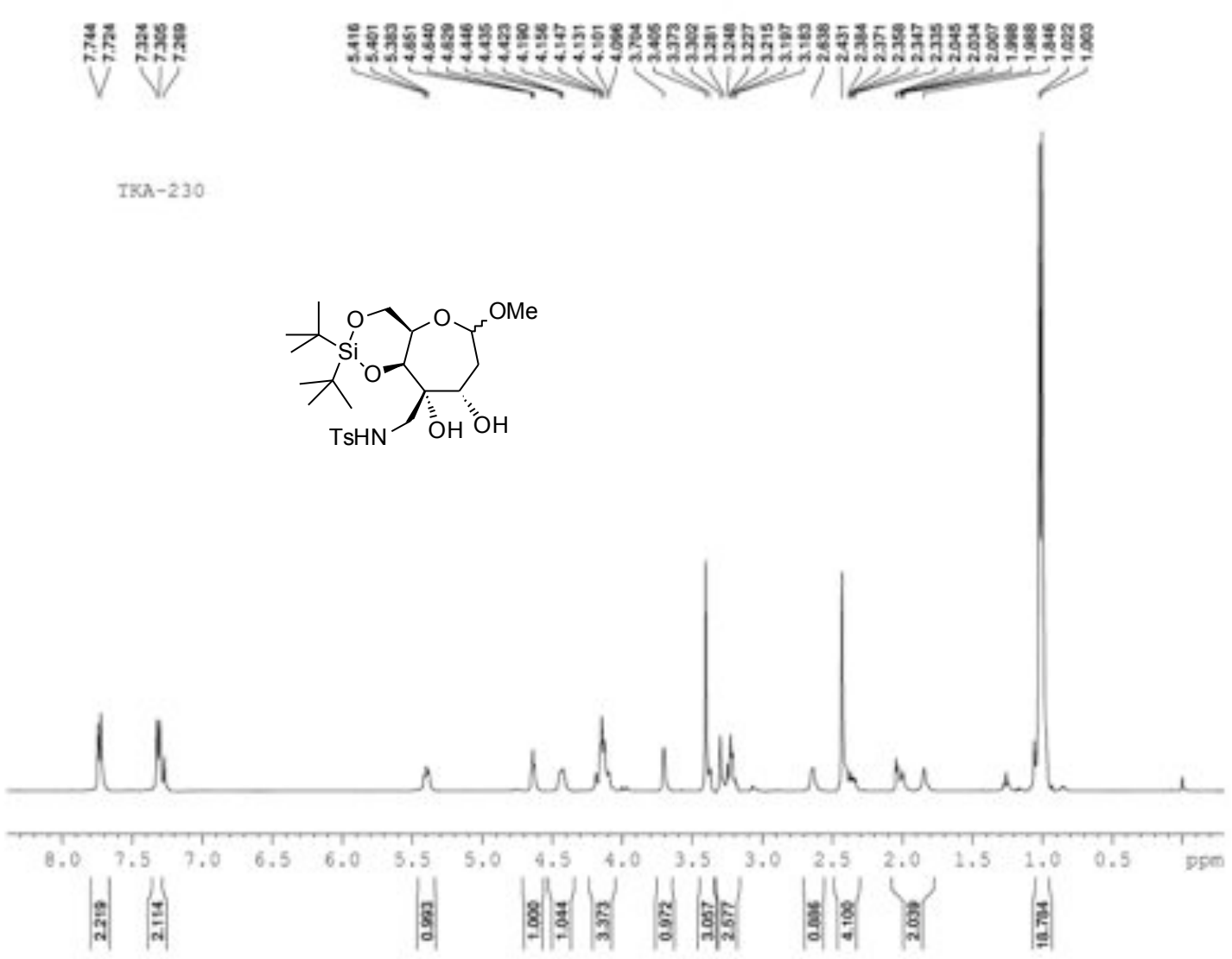
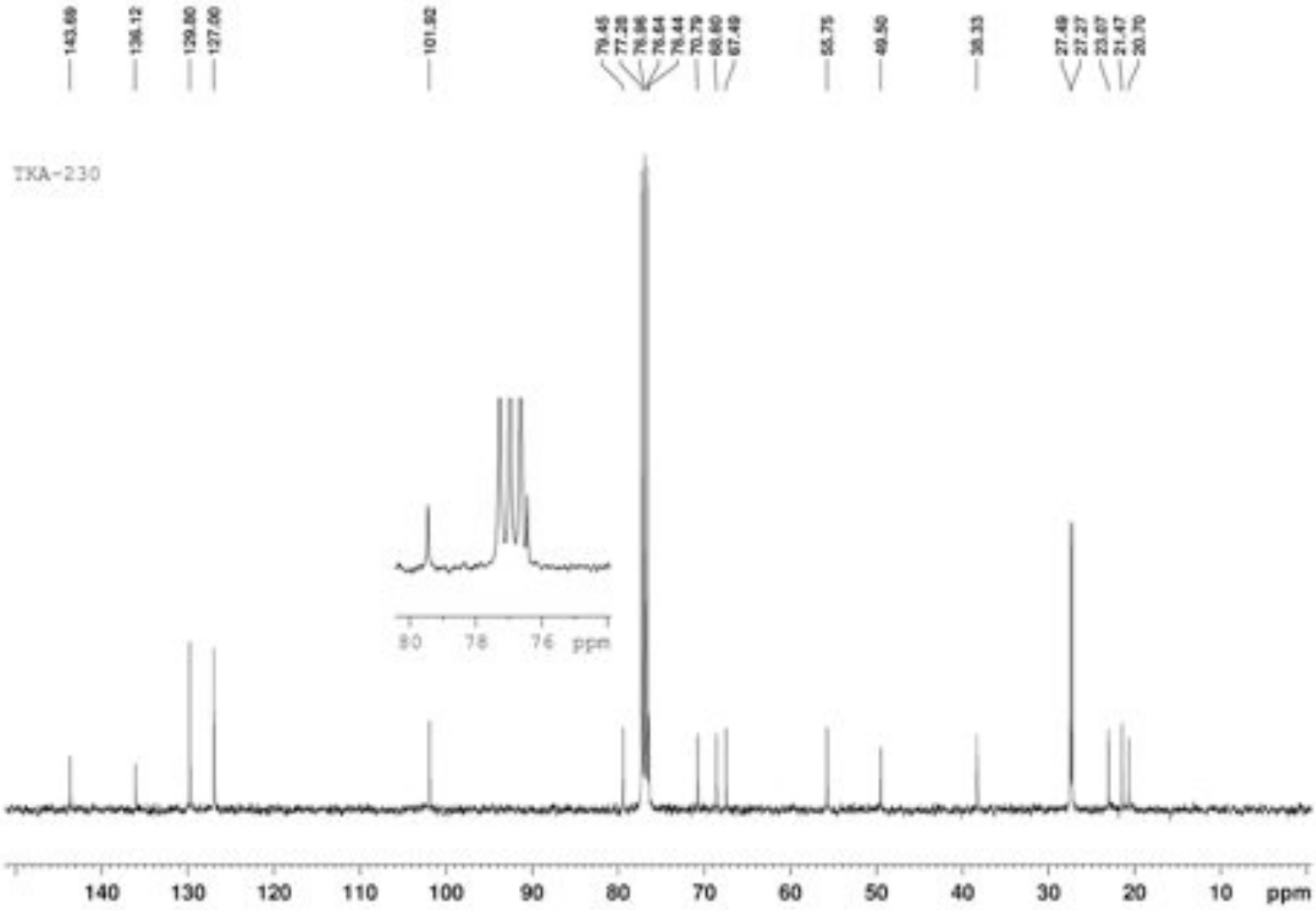
128.44
128.29
127.95
127.08
99.21
77.53
74.60
73.68
68.90
65.88
55.50
47.13
36.69
25.92
21.51
-5.40
-5.45
OTBS
O
OMe
BnO
TsHN
OH
OH
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OTBS
O
OMe
BnO
TsHN
OH
OH
ppm
0
1
2
3
4
5
6
7
8
7
6
5
4
3
2
1
0
ppm
BRUKER


OTBS
O
OMe
BnO
TsHN
OH
OH
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
7
6
5
4
3
2
1
0
ppm


OTBS
O
OMe
nOe
BnO
TsHN
OH
OH
ppm
0
1
2
3
4
5
6
7
8
7
6
5
4
3
2
1
0
ppm
BRUKER


IKA-230
OMe
O
O
Si
O
OH
OH
TsHN
ppm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136.12
129.80
127.60
101.92
79.45
77.28
76.86
76.64
76.44
70.79
68.60
67.49
55.75
49.50
38.33
27.49
27.27
23.67
21.47
20.70
TKA-230
80
78
76 ppm
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm